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MATERIALS AND METHODS

All manipulations were performed using flame-dried glassware and standard Schlenk techniques under an atmosphere of nitrogen, unless otherwise stated.

Solvents

Dry toluene, tetrahydrofuran, acetonitrile, dichloromethane methanol, chlorobenzene and benzene were purchased from Sigma-Aldrich. Chloroform-d_1 was purchased from Cambridge Isotope Laboratories.

Chromatography

Thin layer chromatography (TLC) was performed using EMD TLC plates pre-coated with 250 μm thickness silica gel 60 F_{254} plates and visualized by fluorescence quenching under UV light and $KMnO_4$ stain. Flash chromatography was performed using silica gel (230-400 mesh) purchased from Silicycle Inc.

Spectroscopy and Instruments

NMR spectra were recorded on a Varian Unity/Inova 500 spectrometer operating at 500 MHz, 470 MHz and 125 MHz for ^{1}H, ^{19}F and ^{13}C acquisitions. Chemical shifts are reported in ppm with the solvent resonance as the internal standard. For ^{1}H NMR: $CDCl_3$, δ 7.26; For ^{13}C NMR: $CDCl_3$, δ 77.16. ^{19}F chemical shifts were externally referenced with 1-fluoro-3-nitrobenzene ($\delta = -112.0$). Data is reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, m = multiplet, br = broad; coupling constants in Hz; integration.

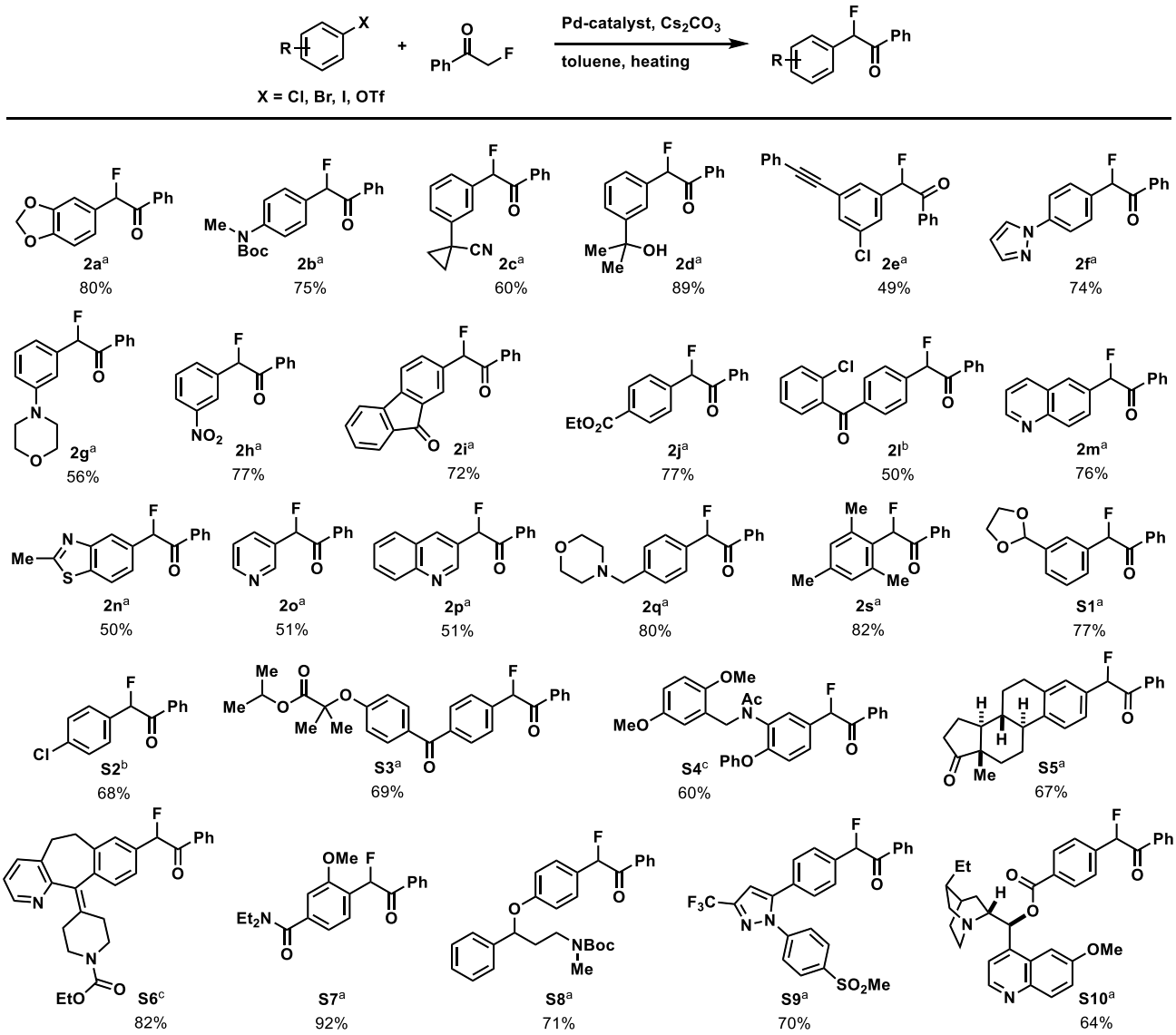
Starting materials

All substrates were used as received from commercial suppliers, unless otherwise stated. XPhos-Pd-G2, $Pd(dba)_2$, Ad_2^nBuP-Pd-G2, Ad_2^nBuP were purchased from Sigma-Aldrich. 2-Fluoroacetophenone was purchased from Combi-Blocks. 2,2-difluoroacetophenone was purchased from Alfa Aesar. 2-Phenyl-2-fluoro-acetophenone[1], *N*-Boc-*N*-methyl-difluoromethylaniline[2], (6-difluoromethyl)quinoline[2], and CHF_2-analepticon[3] were prepared according to a literature procedure

EXPERIMENTAL DATA

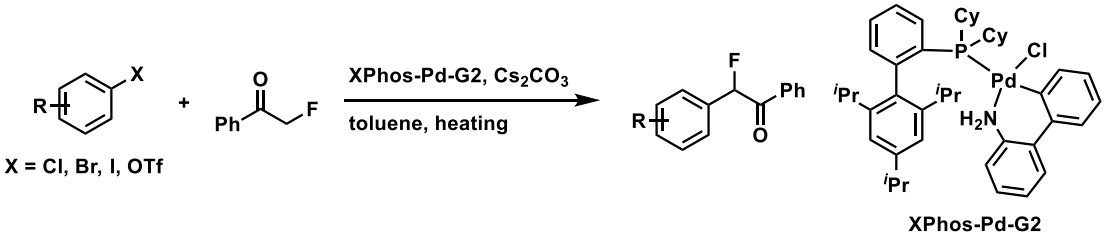
Syntheses of Labeling Precursors

Table S1. Pd-catalyzed fluoroacetophenonation of arenes



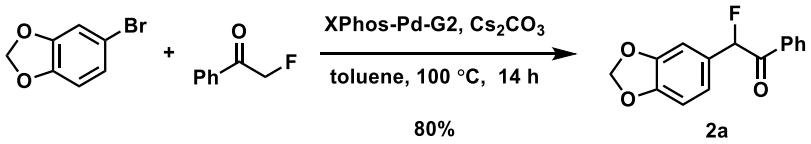
General conditions: (a) arene (1 mmol, 1 equiv.), XPhos-Pd-G2 (3 mol%), fluoroacetophenone (1.2 equiv.), Cs_2CO_3 (1.5 equiv.), toluene (0.2 M), 100 °C. (b) 80 °C. (c) $Ad_2{}^nBuP$-Pd-G2 (3 mol%).

General procedure of Pd-catalyzed fluoroacetophenonation



Arene (1.00 mmol, 1.00 equiv), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 13 to 20 hours, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography afforded the title compound.

(Methylenedioxy)phenyl-fluoroacetophenone (2a)



XPhos-Pd-G2 (47.3 mg, 60.0 μmol, 3.00 mol%) and Cs_2CO_3 (978 mg, 3.00 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (10 mL), 1-Bromo-3,4-(methylenedioxy)benzene (241 μL, 2.00 mmol, 1.00 equiv.) and 2-fluoroacetophenone (291 μL, 2.40 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 14 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 8 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 15:1 to 8:1 v/v) afforded 410 mg of the title compound as an off-white solid (80% yield).

R_f = 0.45 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

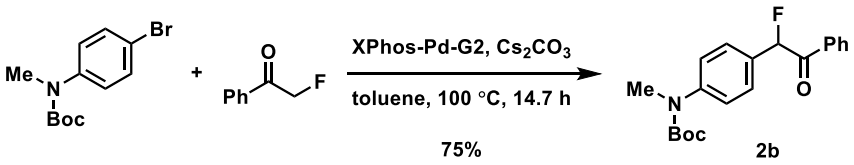
1H NMR (500 MHz, $CDCl_3$, 24 ºC, δ): 7.92 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 2H), 6.97 (dt, *J* = 8.0, 2.1 Hz, 1H), 6.93 (s, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.44 (d, *J* = 48.6 Hz, 1H), 5.95 (d, *J* = 1.4 Hz, 1H), 5.94 (d, *J* = 1.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.1 (d, *J* = 21.1 Hz), 149.0 (d, *J* = 3.0 Hz), 148.4, 134.1, 133.9, 129.0 (d, *J* = 2.3 Hz), 128.8, 127.9 (d, *J* = 20.3 Hz), 122.4 (d, *J* = 6.1 Hz), 108.9 (d, *J* = 1.4 Hz), 108.0 (d, *J* = 4.6 Hz), 101.6, 93.4 (d, *J* = 185.9 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 24 ºC, δ): −174.5 (d, *J* = 48.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{15}H_{11}FNaO_3$ $[M+Na]^+$: 281.0584; found: 281.0572.

(4-*N*-Boc-methylamino)phenyl-fluoroacetophenone (2b)



4-Bromo-*N*-Boc-methylaniline (286 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 14.7 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 3:1 v/v) afforded 257 mg of the title compound as an orange liquid (75% yield).

R_f = 0.15 (hexanes/EtOAc = 8:1 v/v).

NMR Spectroscopy:

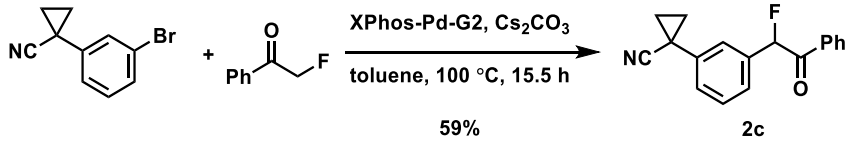
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.94 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.40–7.37 (m, 3H), 7.35–7.33 (m, 1H), 6.50 (d, *J* = 48.5 Hz), 1.74 (dd, *J* = 7.0 Hz, 4.5 Hz, 2H), 1.40 (dd, *J* = 7.0 Hz, 4.5 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.2 (d, *J* = 21.1 Hz), 154.6, 145.1 (d, *J* = 2.8 Hz), 134.1, 133.9, 130.8 (d, *J* = 20.2 Hz), 129.2 (d, *J* = 2.5 Hz), 128.8, 127.9 (d, *J* = 5.3 Hz), 125.7, 93.5 (d, *J* = 185.7 Hz), 80.9, 37.1, 28.4.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –180.2 (d, *J* = 48.0 Hz).

HRMS-FIA(m/z) calc'd for $C_{20}H_{22}FKNO_3$ $[M+K]^+$: 382.1215; found: 382.1226.

(3-Cyanocyclopropyl)phenyl-fluoroacetophenone (2c)



1-(3-Bromophenyl)cyclopropanecarbonitrile (222 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2-

fluoroacetophenone (145 µL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 15.5 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 3:1 v/v) afforded 166 mg of the title compound as an orange solid (59% yield).

R_f = 0.40 (hexanes/EtOAc = 2:1 v/v).

NMR Spectroscopy:

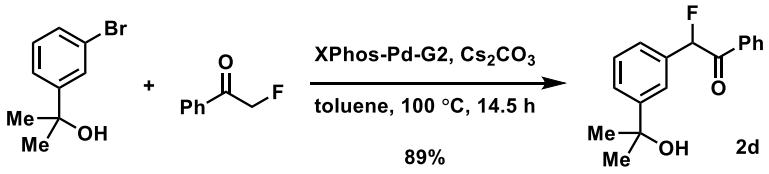
^{1}H NMR (500 MHz, $CDCl_3$, 22 ºC, δ): 7.94 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.40–7.37 (m, 3H), 7.35–7.33 (m, 1H), 6.50 (d, *J* = 48.5 Hz), 1.74 (dd, *J* = 7.0 Hz, 4.5 Hz, 2H), 1.40 (dd, *J* = 7.0 Hz, 4.5 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.1 (d, *J* = 21.5 Hz), 137.3, 135.3 (d, *J* = 20.5 Hz), 134.1, 134.0, 129.8, 129.2 (d, *J* = 3.3 Hz), 128.9, 127.3 (d, *J* = 2.1 Hz), 126.5 (d, *J* = 5.4 Hz), 124.3 (d, *J* = 5.4 Hz), 122.2, 93.6 (d, *J* = 187.4 Hz), 18.6, 18.5, 13.9.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –180.2 (d, *J* = 48.0 Hz).

HRMS-FIA(m/z) calc'd for $C_{18}H_{14}FNNaO$ $[M+Na]^+$: 302.0952; found: 302.0941.

(3-Hydroxypropanyl)phenyl-fluoroacetophenone (2d)



XPhos-Pd-G2 (23.6 mg, 30.0 µmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). A solution of 2-(3-bromophenyl)propan-2-ol (215 mg, 1.00 mmol, 1.00 equiv.) in toluene (5 mL) and 2-fluoroacetophenone (145 µL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 14.5 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 5:1 v/v to 4/1 v/v) afforded 243 mg of the title compound as a yellow solid (89% yield).

R_f = 0.17 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.96 (d, *J* = 7.0 Hz, 2H), 7.65 (s, 1H), 7.56 (t, *J* = 8.0 Hz, 1H),

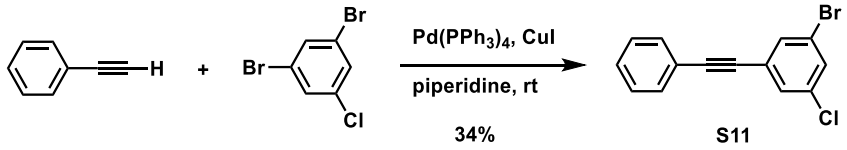
7.53–7.50 (m, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.39–7.37 (m, 2H), 6.53 (d, *J* = 48.5 Hz, 1H), 1.78 (s, 1H), 1.573 (s, 3H), 1.567 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.5 (d, *J* = 21.3 Hz), 150.4, 134.2 (d, *J* = 10.1 Hz) 134.2, 133.9, 129.2, 129.1 (d, *J* = 13.8 Hz) 128.8, 126.0 (d, *J* = 3.3 Hz), 125.8 (d, *J* = 5.3 Hz), 123.7 (d, *J* = 5.4 Hz), 93.7 (d, *J* = 29.9 Hz), 72.5, 31.8, 31.8.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): −178.4 (d, *J* = 48.0 Hz).

HRMS-FIA(m/z) calc'd for $C_{17}H_{17}FNaO_2$ $[M+Na]^+$: 295.1105; found: 295.1107.

1-Bromo-3-chloro-5-(phenylethynyl)benzene (S11)



1,3-Dibromo-5-chlorobenzene (3.63 g, 13.4 mmol, 2.03 equiv.), $Pd(PPh_3)_4$ (194 mg, 168 µmol, 2.54 mol%) and CuI (61.5 mg, 324 µmol, 4.91 mol%) were added to a flame-dried Schlenk flask. Piperidine (40 mL) and phenylacetylene (725 µL, 6.60 mmol, 1.00 equiv.) were added. The solution was degassed by letting bubbling nitrogen inside for 20 min. The resulting mixture was stirred at room temperature for 24.5 h. The reaction mixture was poured into NH_4Cl aqueous solution (100 mL) and extracted with DCM (3 × 50 mL). The combined organic layers were washed with NH_4Cl aqueous solution (3 × 150 mL) and then dried with $MgSO_4$. After the solvent was removed in vacuo, purification by flash silica gel column chromatography (hexanes) afforded 650 mg of the title compound as a white solid (34% yield).

R_f = 0.68 (hexanes).

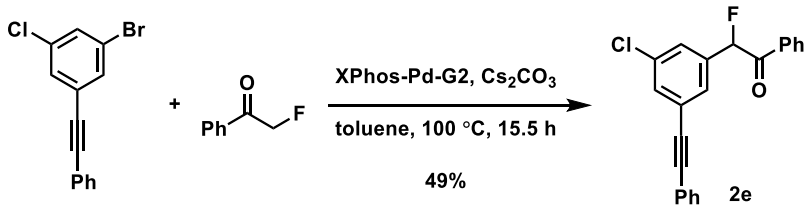
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.57 (t, *J* = 1.5 Hz, 1H), 7.54–7.50 (m, 2H), 7.48 (t, *J* = 1.9 Hz, 1H), 7.45 (t, *J* = 1.6 Hz, 1H), 7.40–7.34 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 135.1, 132.7, 131.9, 131.4, 130.3, 129.1, 128.6, 126.6, 122.6, 122.4, 92.0, 86.7.

HRMS-FIA(m/z) calc'd for $C_{14}H_9BrCl$ $[M+H]^+$: 290.9571; found: 290.9566.

(3-Chloro-5-phenylacetylenyl)phenyl-fluoroacetophenone (2e)



Aryl bromide **S11** (320 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 15.5 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 8:1 v/v) afforded 171 mg of the title compound as an orange oil (49% yield).

R_f = 0.45 (hexanes/EtOAc = 8:1 v/v).

NMR Spectroscopy:

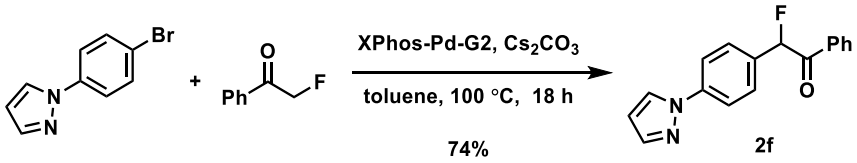
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.96 (d, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.54 (s, 1H), 7.53–7.51 (m, 3H), 7.49–7.45 (m, 3H), 7.38–7.35 (m, 3H), 6.43 (d, *J* = 48.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 193.7 (d, *J* = 22.6 Hz), 136.4 (d, *J* = 20.4 Hz), 135.1, 134.3, 133.7, 132.4, 131.8, 129.3 (d, *J* = 3.3 Hz), 129.0, 129.0, 128.5, 128.1 (d, *J* = 6.4 Hz), 126.7 (d, *J* = 6.4 Hz), 125.9, 122.4, 93.0 (d, *J* = 188.4 Hz), 91.7, 87.3.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –181.8 (d, *J* = 48.0 Hz).

HRMS-FIA(m/z) calc'd for $C_{22}H_{14}ClFNaO$ $[M+Na]^+$: 371.0609; found: 371.0594.

(4-Pyrazolyl)phenyl-fluoroacetophenone (2f)



1-(4-Bromophenyl)-1*H*-pyrazole (223 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 18 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 6:1 v/v) afforded 208 mg of the title compound as a yellow solid (74% yield).

R_f = 0.63 (hexanes/EtOAc = 2:1 v/v).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.99–7.91 (m, 3H), 7.75 (t, *J* = 8.1 Hz, 3H), 7.62–7.53 (m, 3H),

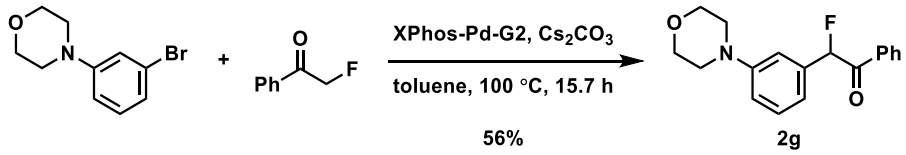
7.45 (t, *J* = 7.7 Hz, 2H), 6.57 (d, *J* = 48.5 Hz, 1H), 6.48 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.2 (d, *J* = 21.6 Hz), 141.7, 141.1, 134.1, 132.3 (d, *J* = 20.0 Hz), 129.20 (d, *J* = 2.8 Hz), 128.9, 128.8 (d, *J* = 5.3 Hz), 126.9, 119.7, 108.2, 93.5 (d, *J* = 185.9 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 24 ºC, δ): –178.5 (d, *J* = 47.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{17}H_{14}FN_2O$ $[M+H]^+$: 281.1085; found: 281.1091.

(3-Morpholino)phenyl-fluoroacetophenone (2g)



XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). A solution of 4-(3-bromophenyl)morpholine (242 mg, 1.00 mmol, 1.00 equiv.) in toluene (5 mL) and 2-fluoroacetophenone (145 µL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 15.7 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 4:1 v/v) afforded 166 mg of the title compound as an orange solid (56% yield).

R_f = 0.22 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

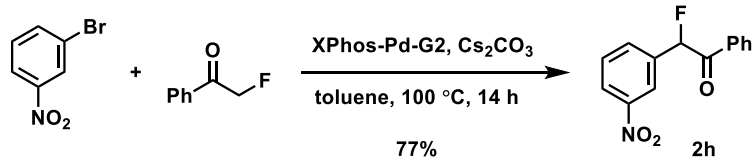
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.94 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 1H), 6.99 (s, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.46 (d, *J* = 48.5 Hz, 1H), 3.83 (t, *J* = 5.0 Hz, 4H), 3.15 (t, *J* = 5.0 Hz, 4H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.4 (d, *J* = 21.5 Hz), 151.9, 135.3 (d, *J* = 20.5 Hz), 134.2, 133.8, 130.0, 129.2 (d, *J* = 2.1 Hz), 128.8, 118.8 (d, *J* = 5.3 Hz), 116.6 (d, *J* = 3.2 Hz), 114.0 (d, *J* = 6.4 Hz), 94.1 (d, *J* = 185.2 Hz), 66.9, 49.0.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –178.9 (d, *J* = 50.4 Hz).

HRMS-FIA(m/z) calc'd for $C_{18}H_{18}FNNaO_2$ $[M+Na]^+$: 322.1214; found: 322.1199.

(3-Nitro)phenyl-fluoroacetophenone (2h)



1-Bromo-3-nitrobenzene (404 mg, 2.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (47.3 mg, 60.0 μmol, 3.00 mol%) and Cs_2CO_3 (978 mg, 3.00 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (10 mL) and 2-fluoroacetophenone (291 μL, 2.40 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 14 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 8 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 6:1 v/v) afforded 400 mg of the title compound as an orange solid (77% yield).

R_f = 0.28 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

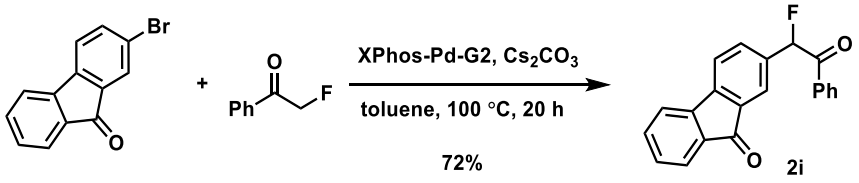
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.39 (s, 1H), 8.25 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.98 (d, *J* = 7.9 Hz, 2H), 7.82 (d, J = 7.6 Hz, 1H), 7.67–7.56 (m, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 6.57 (d, *J* = 48.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 193.5 (d, *J* = 21.4 Hz), 148.5, 136.4 (d, *J* = 20.9 Hz), 134.4, 133.7, 132.8 (d, *J* = 5.9 Hz), 130.2, 129.3 (d, *J* = 3.6 Hz), 129.0, 124.4, 122.0 (d, *J* = 7.2 Hz), 92.7 (d, *J* = 188.5 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –178.9 (d, *J* = 50.4 Hz).

HRMS-FIA(m/z) calc'd for $C_{14}H_{10}FNaNO_3$ $[M+Na]^+$: 282.0537; found: 282.0540

Fluoren-9-onyl-fluoroacetophenone (2i)



2-Bromo-9-fluorenone (518 mg, 2.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (47.3 mg, 60.0 μmol, 3.00 mol%) and Cs_2CO_3 (977 mg, 3.00 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (10 mL) and 2-fluoroacetophenone (291 μL, 2.40 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 20 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 8 mL). The filtrate was

evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 8:1 v/v) afforded 456 mg of the title compound as a yellow solid (72% yield).

R_f = 0.21 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

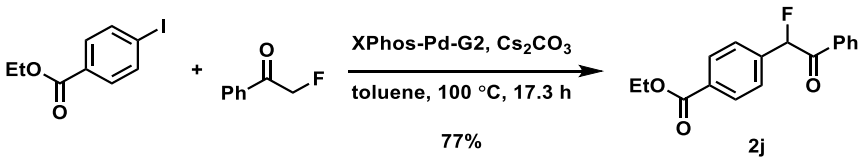
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.96 (d, *J* = 7.5 Hz, 2H), 7.79 (s, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.58–7.40 (m, 6H), 7.32 (t, *J* = 7.1 Hz, 1H), 6.52 (d, *J* = 48.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 193.8 (d, *J* = 21.5 Hz), 192.9, 145.6 (d, *J* = 2.1 Hz), 143.6, 135.4 (d, *J* = 20.1 Hz), 135.0, 134.9, 134.3, 134.1, 133.8, 133.6 (d, *J* = 6.6 Hz), 129.7, 129.1 (d, *J* = 2.1 Hz), 128.9, 124.6, 123.2 (d, *J* = 5.4 Hz), 121.0, 120.8, 93.3 (d, *J* = 187.2 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –180.0 (d, *J* = 48.0 Hz).

HRMS-FIA(m/z) calc'd for $C_{22}H_{14}FO_2$ $[M+H]^+$: 317.0972; found: 317.0975.

(4-Ethyl-carboxyl)phenyl-fluoroacetophenone (2j)



XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), ethyl 4-iodobenzoate (276 mg, 1.00 mmol, 1.00 equiv.) and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 17.3 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 5:1 v/v) afforded 221 mg of the title compound as a white solid (77% yield).

R_f = 0.40 (hexanes/EtOAc = 2:1 v/v).

NMR Spectroscopy:

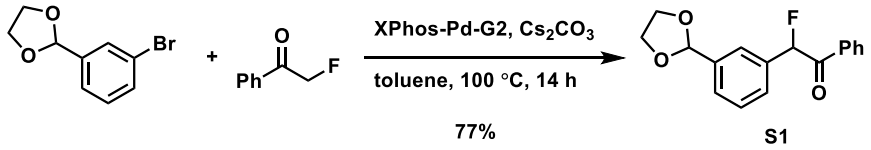
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.06 (d, *J* = 8.6 Hz, 2H), 7.93 (d, *J* = 7.2 Hz, 2H), 7.63–7.50 (m, 3H), 7.42 (t, *J* = 7.5 Hz, 2H), 6.53 (d, *J* = 48.4 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.0 (d, *J* = 21.1 Hz), 166.0, 138.9 (d, *J* = 19.6 Hz), 134.1, 133.9, 131.6 (d, *J* = 2.1 Hz), 130.3, 129.3 (d, *J* = 3.1 Hz), 128.9, 126.9 (d, *J* = 6.1 Hz), 93.8 (d, *J* = 187.6 Hz), 61.3, 14.4.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –182.6 (d, *J* = 48.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{17}H_{16}FO_3$ $[M+H]^+$: 287.1078; found: 287.1087.

(3-Dioxolanyl)phenyl-fluoroacetophenone (S1)



XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), 2-(3-bromophenyl)-1,3-dioxolane (152 mL, 1.00 mmol, 1.00 equiv.) and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 14 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 6:1 v/v) afforded 220 mg of the title compound as a yellow liquid (77% yield).

R_f = 0.25 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

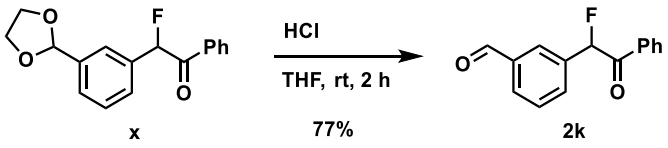
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.93 (d, *J* = 8.0 Hz, 2H), 7.63 (s, 1H), 7.58–7.46 (m, 3H), 7.46–7.38 (m, 3H), 6.52 (d, *J* = 48.5 Hz, 1H), 5.80 (s, 1H), 4.20–3.92 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 194.2 (d, *J* = 21.5 Hz), 139.2, 134.5 (d, *J* = 20.2 Hz), 134.0, 133.9, 129.3, 129.2 (d, *J* = 2.9 Hz), 128.8, 128.1 (d, *J* = 5.5 Hz), 127.9 (d, *J* = 2.5 Hz), 125.6 (d, *J* = 5.8 Hz), 103.2 (d, *J* = 4.6 Hz), 93.9 (d, *J* = 187.3 Hz), 65.4.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –179.3 (d, *J* = 48.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{17}H_{16}FO_3$ $[M+H]^+$: 287.1078; found: 287.1091.

(3-Formyl)phenyl-fluoroacetophenone (2k)



(3-Dioxolanyl)phenyl-fluoroacetophenone, x, (100 mg, 0.350 mmol) was dissolved in THF (5 mL). HCl aqueous solution (2 N, 1.2 mL) was added. The reaction mixture was stirred at room temperature for 2 h. EtOAc (30 mL) was added. The mixture was washed with NaOH aqueous solution (1 N, 5 mL) and brine (5 mL). The organic layer was dried over Na_2SO_4, filtered and evaporated. Purification by flash silica gel column chromatography (hexanes/EtOAc = 4:1 v/v) afforded 65.0 mg of the title compound as a white solid

(77% yield).

R_f = 0.61 (hexanes/EtOAc = 2:1 v/v).

NMR Spectroscopy:

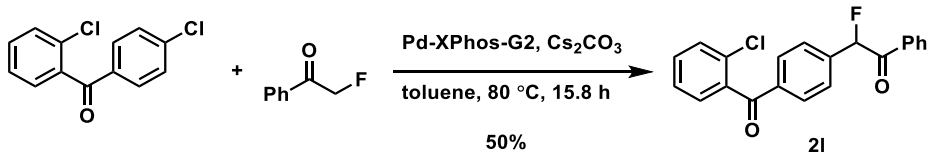
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 10.01 (d, *J* = 0.8 Hz, 1H), 8.02 (s, 1H), 7.96 (d, *J* = 7.7 Hz, 2H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.63–7.52 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 6.58 (d, *J* = 48.2 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): δ 194.0 (d, *J* = 21.4 Hz), 191.6 (d, *J* = 7.0 Hz), 137.1, 135.7 (d, *J* = 20.6 Hz), 134.3, 133.9, 132.8 (d, *J* = 5.6 Hz), 130.8 (d, *J* = 2.1 Hz), 130.0, 129.3 (d, *J* = 3.4 Hz), 129.0, 128.24 (d, *J* = 6.3 Hz), 93.4 (dd, *J* = 187.3, 2.7 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –181.3 (d, *J* = 48.4 Hz).

HRMS-FIA(m/z) calc'd for $C_{15}H_{12}FO_2$ $[M+H]^+$: 243.0816; found: 243.0807.

(2-Chlorophenyl-methanonyl)phenyl-fluoroacetophenone (2l)



2-Chlorophenyl-4-chlorophenyl-methanone (243 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 80 °C. After 15.8 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 5:1 v/v) afforded 176 mg of the title compound as an orange oil (50% yield).

R_f = 0.33 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

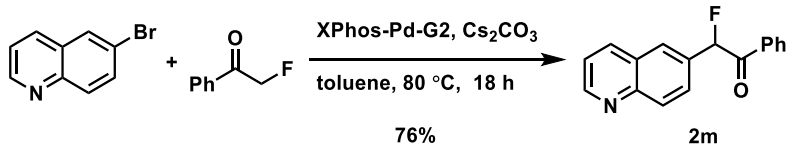
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.97 (d, *J* = 8.1 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 2H), 7.64–7.56 (m, 3H), 7.50–7.42 (m, 4H), 7.40–7.34 (m, 2H), 6.56 (d, J = 48.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.6, 193.9 (d, *J* = 21.4 Hz), 139.7 (d, *J* = 19.8 Hz), 138.2, 137.3 (d, *J* = 2.0 Hz), 134.2, 133.9, 131.5, 131.5, 130.7, 130.3, 129.3 (d, *J* = 3.5 Hz), 129.3, 128.9, 127.0 (d, *J* = 6.3 Hz), 126.9, 93.8 (d, *J* = 188.2 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –183.3 (d, *J* = 47.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{21}H_{15}ClFO_2$ $[M+H]^+$: 353.0739; found: 353.0730.

Quinoline-6-fluoroacetophenone (2m)



XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). A solution of 6-bromoquinoline (135 μL, 1.00 mmol, 1.00 equiv.) in toluene (5 mL) and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 80 °C. After 13.7 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 3:1 v/v) afforded 201 mg of the title compound as a white solid (76% yield).

R*f* = 0.10 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

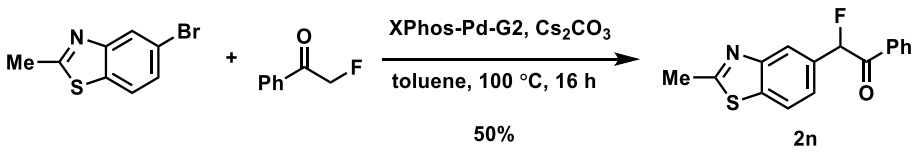
^{1}H NMR (500 MHz, $CDCl_3$, 24 ºC, δ): 8.94 (d, *J* = 4.2 Hz, 1H), 8.16 (t, *J* = 9.4 Hz, 2H), 8.01–7.94 (m, 3H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.46–7.39 (m, 3H), 6.69 (d, *J* = 48.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.2 (d, *J* = 21.4 Hz), 151.6, 148.5 (d, *J* = 2.0 Hz), 136.5, 134.1, 134.1, 132.7 (d, *J* = 19.9 Hz), 130.8, 129.3 (d, *J* = 3.1 Hz), 128.9, 128.2, 127.8 (d, *J* = 4.9 Hz), 127.0 (d, *J* = 6.9 Hz), 121.9, 93.9 (d, *J* = 187.1 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 24 ºC, δ): −179.8 (d, *J* = 47.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{17}H_{13}FNO$ $[M+H]^+$: 266.0976; found: 266.0966.

(2-Methylbenzo[*d*]thiazol-5-yl)-fluoroacetophenone (2n)



5-Bromo-2-methylbenzothiazole (228 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2-fluoroacetophenone (145 μL, 1.28 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 16 h, the oil bath was removed, and the Schlenk tube was allowed to cool to

room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 3:1 v/v) afforded 142 mg of the title compound as a yellow-white solid (50% yield).

R_f = 0.35 (hexanes/EtOAc = 2:1 v/v).

NMR Spectroscopy:

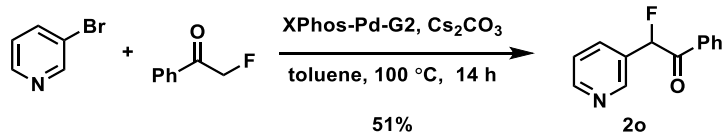
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 8.10 (s, 1H), 7.98 (d, *J* = 7.0 Hz, 2H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 2H), 6.66 (d, *J* = 49.0 Hz, 1H), 2.84 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 193.0 (d, 21.5 Hz), 168.5, 153.7, 137.1, 134.0, 133.9, 132.4 (d, *J* = 20.4 Hz), 129.2 (d, *J* = 2.3 Hz), 128.8, 123.5 (d, *J* = 5.4 Hz), 122.3, 121.7 (d, *J* = 5.3 Hz), 93.8 (d, *J* = 187.4 Hz), 20.3.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –177.7 (d, *J* = 49.4 Hz).

HRMS-FIA(m/z) calc'd for $C_{16}H_{13}FNOS$ $[M+H]^+$: 286.0696; found: 286.0687.

Pyridine-3-fluoroacetophenone (2o)



XPhos-Pd-G2 (47.3 mg, 60.0 μmol, 3.00 mol%) and Cs_2CO_3 (978 mg, 3.00 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (10 mL), 3-bromo-pyridine (193 μL, 2.00 mmol, 1.00 equiv.) and 2-fluoroacetophenone (291 μL, 2.40 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 14 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 8 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 4:1 v/v to 3:2 v/v) afforded 220 mg of the title compound as a yellow liquid (51% yield).

R_f = 0.25 (hexanes/EtOAc = 2:1 v/v).

NMR Spectroscopy:

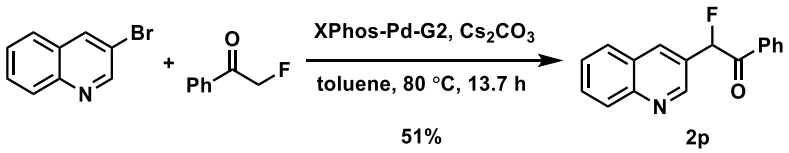
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 8.77 (s, 1H), 8.63 (d, *J* = 4.8 Hz, 1H), 7.95 (s, 1H), 7.79 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 15.7 Hz, 1H), 7.34 (dd, *J* = 8.0, 4.8 Hz, 1H), 6.57 (d, *J* = 48.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 193.6 (d, *J* = 21.5 Hz), 150.8, 148.7, 135.0 (d, *J* = 5.0 Hz), 134.5, 133.8, 130.5 (d, *J* = 20.7 Hz), 129.2 (d, *J* = 3.2 Hz), 129.0, 124.0, 91.8 (dd, *J* = 187.2, 2.3 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –182.1 (d, *J* = 48.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{13}H_{11}FNO$ $[M+H]^+$: 216.0819; found: 216.0824.

Quinoline-3-fluoroacetophenone (2p)



XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 2.80 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.40 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). A solution of 3-bromoquinoline (157 μL, 1.07 mmol, 1.00 equiv.) in toluene (5 mL) and 2-fluoroacetophenone (223 mg, 1.28 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 80 °C. After 13.7 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 4:1 v/v) afforded 136 mg of the title compound as a yellow-white solid (51% yield).

R_f = 0.17 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

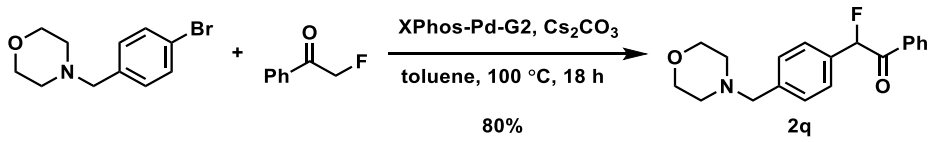
^{1}H NMR (500 MHz, $CDCl_3$, 22 ºC, δ): 9.05 (s, 1H), 8.26 (s, 1H), 8.11 (d, *J* = 9.0 Hz, 1H), 7.98 (d, *J* = 7.5 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.75 (t, *J* = 8.5 Hz, 1H), 7.59–7.55 (m, 2H), 7.44 (t, *J* = 7.5 Hz, 2H), 6.76 (d, *J* = 48.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 193.6 (d, *J* = 21.4 Hz), 149.0 (d, *J* = 4.3 Hz), 148.5, 135.1 (d, *J* = 6.4 Hz), 134.3, 133.8, 130.8, 129.5, 129.2, 129.0, 128.3, 127.6, 127.5, 127.3 (d, *J* = 20.5 Hz), 92.1 (d, *J* = 187.4 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): −180.4 (d, *J* = 48.5 Hz).

HRMS-FIA(m/z) calc'd for $C_{17}H_{13}FNO$ $[M+H]^+$: 266.0976; found: 266.0988.

(Morpholinomethyl)phenyl-fluoroacetophenone (2q)



XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). A solution of 4-(4-bromobenzyl)morpholine (256 mg, 1.00 mmol, 1.00 equiv.) in toluene (5 mL) and 2-

fluoroacetophenone (145 µL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 18 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 2:1 v/v with 1% Et_3N) afforded 250 mg of the title compound as a colorless liquid (80% yield).

R_f = 0.40 (hexanes/EtOAc = 1:1 v/v with 1% Et_3N).

NMR Spectroscopy:

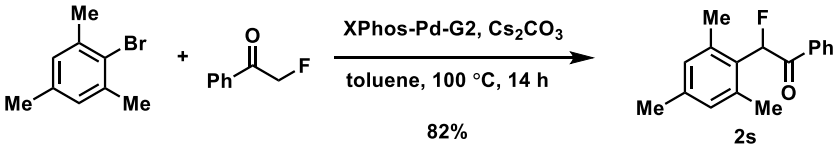
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.94 (d, *J* = 7.5 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.45–7.41 (m, 4H), 7.36 (d, *J* = 7.9 Hz, 2H), 6.50 (d, *J* = 48.6 Hz, 1H), 3.68 (t, *J* = 4.6 Hz, 4H), 3.47 (s, 2H), 2.41 (t, *J* = 4.5 Hz, 4H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.3 (d, *J* = 21.4 Hz), 139.8, 134.2, 133.9, 133.2 (d, *J* = 20.4 Hz), 129.9, 129.2 (d, *J* = 3.0 Hz), 128.8, 127.5 (d, *J* = 6.0 Hz), 93.9 (d, *J* = 181.7 Hz), 67.1, 63.0, 53.7.

^{19}F NMR (470 MHz, $CDCl_3$, 24 ºC, δ): –178.0 (d, *J* = 48.0 Hz).

HRMS-FIA(m/z) calc'd for $C_{19}H_{21}FNO_2$ $[M+H]^+$: 314.1551; found: 314.1549.

Mesitylenyl-fluoroacetophenone (2s)



XPhos-Pd-G2 (23.6 mg, 30.0 µmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), 2-Bromomesitylene (153 mL, 1.00 mmol, 1.00 equiv.) and 2-fluoroacetophenone (145 µL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 14 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 20:1 v/v) afforded 209 mg of the title compound as a white solid (82% yield).

R_f = 0.56 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.85 (dd, *J* = 8.2, 1.0 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 6.89 (s, 2H), 6.69 (d, *J* = 45.9 Hz, 1H), 2.35 (d, *J* = 2.1 Hz, 6H), 2.28 (d, *J* = 2.6 Hz, 3H).

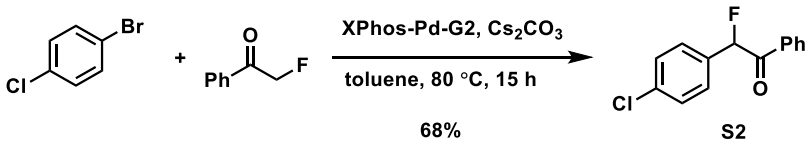
^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 196.6 (d, *J* = 21.4 Hz), 139.7 (d, *J* = 3.5 Hz), 137.9 (d, *J* = 3.3 Hz),

135.0, 133.5, 130.3 (d, *J* = 2.4 Hz), 129.5 (d, *J* = 17.6 Hz), 128.67, 128.65 (d, *J* = 3.1 Hz), 91.9 (d, *J* = 183.6 Hz), 21.1, 20.4.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –180.9 (d, *J* = 45.6 Hz).

HRMS-FIA(m/z) calc'd for $C_{17}H_{17}FNaO$ $[M+Na]^+$: 279.1156; found: 279.1149.

(3-Chloro)phenyl-fluoroacetophenone (S2)



4-Chloro-bromobenzene (191 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 80 °C. After 15 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 15:1 v/v) afforded 170 mg of the title compound as an off-white solid (68% yield).

R_f = 0.48 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

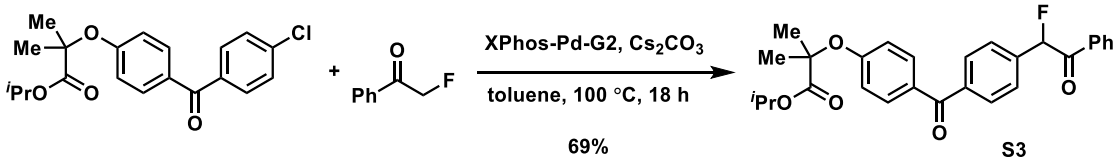
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.92 (d, *J* = 6.9 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46–7.40 (m, 4H), 7.37 (dd, *J* = 8.8, 1.0 Hz, 2H), 6.48 (d, *J* = 48.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 195.1 (d, *J* = 21.6 Hz), 136.9 (d, *J* = 3.2 Hz), 135.1, 134.9, 133.9 (d, *J* = 20.3 Hz), 130.5, 130.2 (d, *J* = 3.0 Hz), 129.9, 129.7 (d, *J* = 5.6 Hz), 94.3 (d, *J* = 186.4 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –179.6 (d, *J* = 48.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{14}H_{10}ClFNaO$ $[M+Na]^+$: 271.0296; found: 271.0307.

(1-Fluoro-2-oxo-2-phenylethyl)-fenofibrate (S3)



Fenofibrate (361 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was

evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2-fluoroacetophenone (145 µL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 18 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 8:1 v/v) afforded 320 mg of the title compound as an orange liquid (69% yield).

R_f = 0.23 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

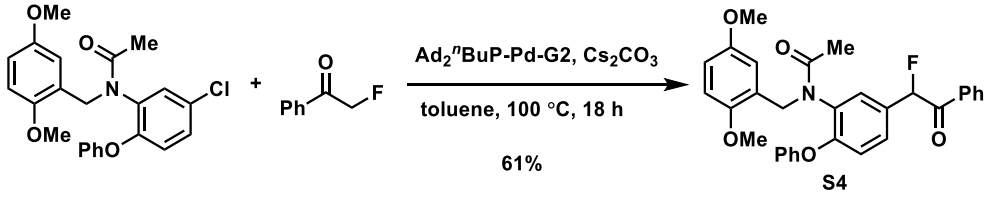
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.97 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 9.0 Hz, 2H), 7.61–7.56 (m, 3H), 7.45 (t, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 7.0 Hz, 2H), 6.56 (d, *J* = 48.5 Hz, 1H), 5.07 (sep, *J* = 6.3 Hz, 1H), 1.65 (s, 6H), 1.19 (d, *J* = 6.0 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 194.8, 194.1 (d, *J* = 22.6 Hz), 173.2, 159.9, 139.2 (d, *J* = 2.3 Hz), 137.9 (d, *J* = 19.3 Hz), 134.2, 134.0, 132.2, 130.4, 130.2, 129.3 (d, *J* = 3.2 Hz), 128.9, 126.9 (d, *J* = 6.6 Hz), 117.3, 93.8 (d, *J* = 187.4 Hz), 79.5, 69.5, 25.5, 21.6.

^{19}F NMR (470 MHz, $CDCl_3$, 24 ºC, δ): –181.9 (d, *J* = 48.5 Hz).

HRMS-FIA(m/z) calc'd for $C_{28}H_{28}FO_5$ $[M+H]^+$: 463.1915; found: 463.1910.

(1-Fluoro-2-oxo-2-phenylethyl)-DAA1106 (S4)



N-(5-Chloro-2-phenoxyphenyl)-*N*-(2,5-dimethoxybenzyl)acetamide[4] (412 mg, 1.00 mmol, 1.00 equiv.), $Ad_2{}^nBuP$-Pd-G2 (20.1 mg, 30.0 µmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), and 2-fluoroacetophenone (145 µL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 18 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 2:1 v/v) afforded 315 mg of the title compound as a yellow liquid (61% yield).

R_f = 0.20 (hexanes/EtOAc = 2:1 v/v).

NMR Spectroscopy:

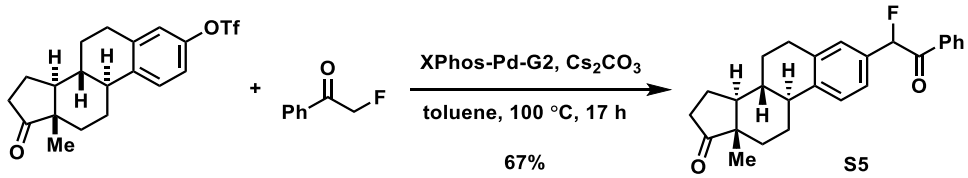
^{1}H NMR (500 MHz, $CDCl_3$, 55 ºC, compound exists as a 1:1 mixture of rotamers δ): 7.86 (d, *J* = 7.8 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.30–7.22 (m, 1H), 7.20–7.10 (m, 2H), 6.98–6.86 (m, 3H), 6.81 (d, *J* = 8.5 Hz, 1H), 6.72–6.61 (m, 1H), 6.56 (dd, *J* = 22.7, 9.0 Hz, 1H), 6.32 (d, *J* = 48.6 Hz, 1H), 5.24–5.03 (m, 1H), 4.79–4.63 (m, 1H), 3.65 (s, 3H), 3.44 (d, *J* = 11.3 Hz, 3H), 1.88 (d, *J* = 11.3 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, compound exists as a 1:1 mixture of rotamers, δ): 193.9 (d, J = 22.7 Hz), 193.7 (d, J = 22.7 Hz), 170.7, 170.7, 155.3, 155.3, 155.2 (d, J = 2.6 Hz), 155.1 (d, J = 2.2 Hz), 153.5 (d, J = 4.0 Hz), 151.9 (d, J = 7.2 Hz), 134.0, 134.0, 133.2 (d, J = 5.5 Hz), 130.1, 129.1 (d, J = 2.8 Hz), 129.1 (d, J = 2.6 Hz), 128.9, 128.9, 128.4 (d, J = 4.9 Hz), 128.3 (d, J = 5.1 Hz), 126.2, 126.1, 124.8, 119.9, 118.04, 117.99, 116.7, 116.7, 113.9, 111.5, 111.4, 92.9 (d, J = 186.4 Hz), 92.8 (d, J = 186.4 Hz), 55.79, 55.75, 55.7, 46.0, 45.8, 22.4.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, compound exists as a 1:1 mixture of rotamers, δ): –176.6 (d, *J* = 48.9 Hz), –176.7 (d, *J* = 47.5 Hz).

HRMS-FIA(m/z) calc'd for $C_{31}H_{29}FNO_5$ $[M+H]^+$: 514.2024; found: 514.2043.

(1-Fluoro-2-oxo-2-phenylethyl)-estrone (S5)



Estrone-triflate (402 mg, 1.00 mmol, 1.00 equiv.)[5], XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. Afte 17 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 6:1 v/v) afforded 262 mg of the title compound as a yellow-white solid (67% yield).

R*f* = 0.31 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 7.95 (d, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 6.5 Hz, 1H), 7.2, 7.20 (s, 1H), 6.47 (d, *J* = 48.5 Hz, 1H), 2.91–2.87 (m, 2H), 2.52–2.46 (m, 1H), 2.41–2.36 (m, 1H), 2.24–2.30 (m, 1H), 2.17–2.09 (m, 1H), 2.07–1.98 (m, 2H), 1.97–1.93 (m, 1H), 1.65–1.37 (m, 6H), 0.88 (d, *J* = 2.0 Hz, 3H).

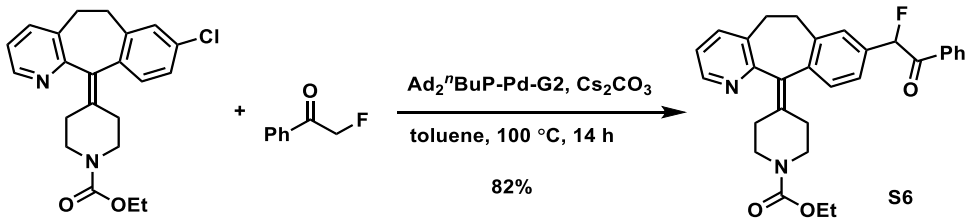
^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 220.7, 194.3 (d, *J* = 21.5 Hz), 141.6, 137.6, 134.1, 133.8, 131.6 (d,

J = 20.4 Hz), 129.1, 128.7, 128.0 (d, *J* = 5.4 Hz), 126.2, 125.0 (d, *J* = 5.3 Hz), 93.7 (d, *J* = 185.2 Hz), 50.5, 47.9, 44.4, 37.9, 35.9, 31.6, 29.3, 26.3, 25.6, 21.6, 13.9.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –177.2 (d, *J* = 49.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{26}H_{27}FNaO_2$ $[M+Na]^+$: 413.1887; found: 413.1895.

(1-Fluoro-2-oxo-2-phenylethyl)-claritin (S6)



Claritin (383 mg, 1.00 mmol, 1.00 equiv.), PAd_2^nBu-Pd-G2 (20.1 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 14 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 1:2 v/v) afforded 398 mg of the title compound as a yellow solid (82% yield).

R_f = 0.25 (hexanes/EtOAc = 1:2 v/v).

NMR Spectroscopy:

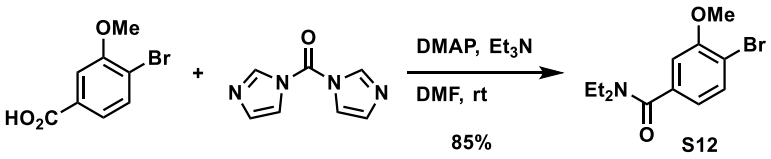
^{1}H NMR (500 MHz, $CDCl_3$, 24 ºC, δ): 8.38 (d, *J* = 4.9 Hz, 1H), 7.99–7.91 (m, 2H), 7.60–7.50 (m, 1H), 7.46–7.39 (m, 3H), 7.33–7.27 (m, 2H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.13–7.04 (m, 1H), 6.46 (d, *J* = 48.6 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.79 (brs, 2H), 3.48–3.27 (m, 2H), 3.20–3.04 (m, 2H), 2.90–2.74 (m, 2H), 2.55–2.41 (m, 1H), 2.38–2.24 (m, 3H), 1.24 (t, *J* = 7.1 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, compound exists as a 1:1 mixture of rotamers, δ): 194.2 (d, *J* = 21.7 Hz), 194.2 (d, *J* = 21.8 Hz), 157.2, 155.6, 146.8, 140.8, 138.8, 137.7 (d, *J* = 4.2 Hz), 137.6 (d, *J* = 3.2 Hz), 134.8, 134.7, 134.2, 134.2, 134.0, 133.7, 133.5, 133.3, 130.21, 130.19, 129.34 (d, *J* = 2.7 Hz), 129.31 (d, *J* = 2.7 Hz), 128.9, 128.1 (d, *J* = 5.0 Hz), 125.5 (d, *J* = 5.5 Hz), 125.4, 122.4, 93.7 (d, *J* = 185.6 Hz), 93.6 (d, *J* = 185.5 Hz), 61.5, 45.0, 44.9, 32.0, 31.7, 30.9, 30.7, 14.8.

^{19}F NMR (470 MHz, $CDCl_3$, 24 ºC, δ): –178.2 (d, *J* = 48.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{30}H_{29}FNaN_2O_3$ $[M+Na]^+$: 507.2054; found: 507.2070.

4-Bromo-*N*,*N*-diethyl-3-methoxybenzamide (S12)



To a solution of 4-bromo-3-methoxybenzoic acid (1.00 g, 4.33 mmol, 1.00 equiv.) in DMF (20 mL) were added CDI (1.05 g, 6.50 nnol, 1.50 equiv.), DMAP (793 mg, 6.50 mmol, 1.50 equiv.) and Et_3N (0.899 mL, 8.66 mmol, 2 equiv.). The reaction mixture was stirred at room temperature overnight. Water (40 mL) was added and extracted with EtOAc (3 × 30 mL). The combined organic layer was washed with water (30 mL) and brine (30 mL). The solution was dried with $MgSO_4$. After the solvent was removed in vacuo, purification by flash silica gel column chromatography (hexanes/EtOAc = 2:1 v/v) afforded 1.05 g of the title compound as a white solid (85% yield).

R_f = 0.19 (hexanes/EtOAc = 12:1 v/v).

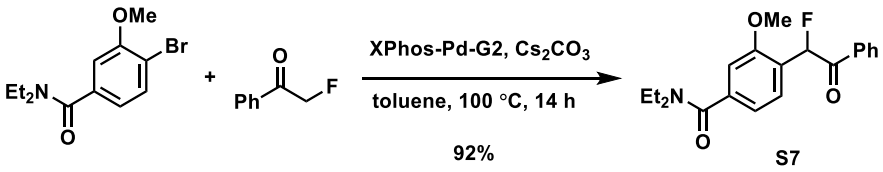
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, −15 ºC, compound exists as a 1:1 mixture of rotamers, δ): 7.55 (d, *J* = 7.9 Hz, 1H), 6.92 (s, 1H), 6.83 (d, *J* = 7.9 Hz, 1H), 3.92 (s, 3H), 3.53 (q, *J* = 7.1 Hz, 2H), 3.24 (q, *J* = 7.1 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, −15 ºC, compound exists as a 1:1 mixture of rotamers, δ): 170.2, 155.8, 137.5, 133.2, 119.20, 119.17, 112.4, 110.0, 109.9, 56.4, 56.3, 43.3, 39.3, 14.43, 14.39, 13.0, 12.9.

HRMS-FIA(m/z) calc'd for $C_{12}H_{16}BrNaNO_2$ $[M+Na]^+$: 308.0257; found: 308.0271.

(1-Fluoro-2-oxo-2-phenylethyl)-analepticon (S7)



4-Bromo-*N,N*-diethyl-3-methoxybenzamide (286 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 14 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 3:2 v/v) afforded 315 mg of the title compound as a colorless liquid (92% yield).

R_f = 0.37 (hexanes/EtOAc = 1:1 v/v).

NMR Spectroscopy:

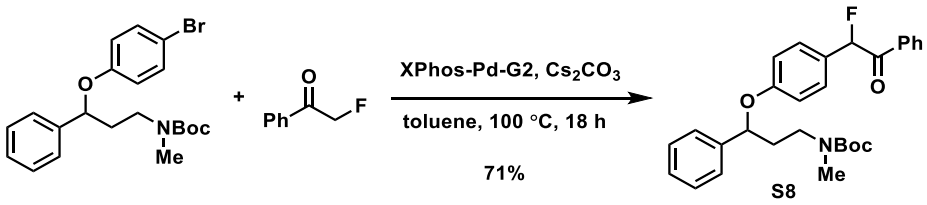
^{1}H NMR (500 MHz, $CDCl_3$, –15 ºC, compound exists as a 1:1 mixture of rotamers, δ): 7.90 (d, *J* = 7.8 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.10 (d, *J* = 47.3 Hz, 1H), 6.97 (s, 1H), 6.91 (d, *J* = 7.8 Hz, 1H), 3.96 (s, 3H), 3.51 (q, *J* = 7.2 Hz, 2H), 3.22 (q, *J* = 7.1 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, –15 ºC, compound exists as a 1:1 mixture of rotamers, δ): 194.0 (d, *J* = 20.5 Hz), 170.3, 156.7 (d, *J* = 3.4 Hz), 140.2 (d, *J* = 4.4 Hz), 134.1, 133.4, 129.4, 128.8, 128.5, 123.1 (d, *J* = 19.6 Hz), 118.5, 109.5, 86.7 (d, *J* = 180.6 Hz), 56.0, 55.9, 43.3, 39.2, 14.4, 14.3, 12.90, 12.87.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –181.9 (d, *J* = 47.5 Hz).

HRMS-FIA(m/z) calc'd for $C_{20}H_{23}FNO_3$ $[M+H]^+$: 344.1656; found: 344.1663.

(1-Fluoro-2-oxo-2-phenylethyl)-*N*-Boc-fluoxetine (S8)



t-Butyl (3-(4-bromophenoxy)-3-phenylpropyl)(methyl)carbamate[6] (420 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 18 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 5:1 v/v) afforded 341 mg of the title compound as a yellow liquid (71% yield).

R_f = 0.28 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 55 ºC, δ): 7.91 (d, *J* = 7.7 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.36–7.30 (m, 6H), 7.29–7.22 (m, 1H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.40 (d, *J* = 48.9 Hz, 1H), 5.13 (dd, *J* = 8.7, 4.2 Hz, 1H), 3.48–3.30 (m, 2H), 2.84 (s, 3H), 2.26–2.13 (m, 1H), 2.13–2.02 (m, 1H), 1.38 (s, 9H).

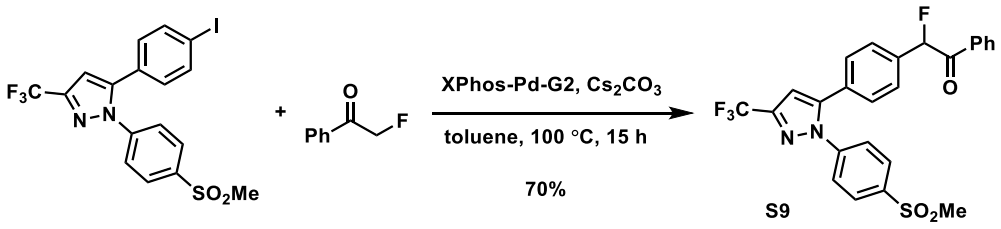
^{13}C NMR (125 MHz, $CDCl_3$, 55 ºC, compound exists as a 1:1 mixture of diastereoisomers, δ): 194.4 (d, *J* = 22.0 Hz), 194.4 (d, *J* = 22.0 Hz), 159.4, 155.8, 141.4, 134.6, 133.6, 129.27 (d, *J* = 4.9 Hz), 129.25 (d, *J*

= 4.9 Hz), 129.2, 129.1, 128.9, 128.7, 127.9, 126.8 (d, *J* = 20.7 Hz), 125.9, 116.6, 93.6 (d, *J* = 185.3 Hz), 79.5, 78.3, 45.9, 37.1, 34.6, 28.5.

^{19}F NMR (470 MHz, $CDCl_3$, 25 ºC, δ): –174.4 (brs).

HRMS-FIA(m/z) calc'd for $C_{29}H_{32}FNaNO_4$ $[M+Na]^+$: 500.2208; found: 500.2229.

(1-Fluoro-2-oxo-2-phenylethyl)-SC-58125 (S9)



Aryl iodide[7] (492 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), and 2-fluoroacetophenone (145 µL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 15 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 3:1 v/v) afforded 350 mg of the title compound as a yellow solid (70% yield).

R_f = 0.23 (hexanes/EtOAc = 2:1 v/v).

NMR Spectroscopy:

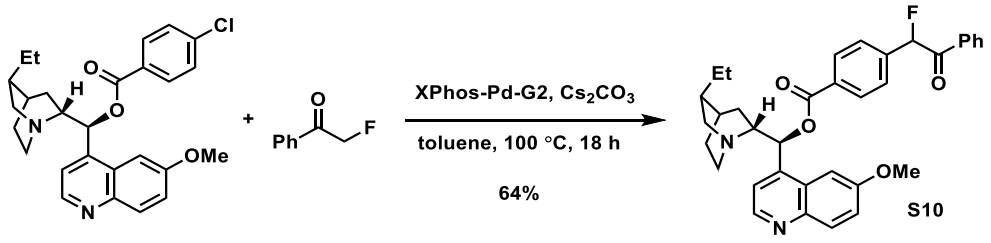
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.96 (d, *J* = 7.4 Hz, 2H), 7.94–7.88 (m, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.56–7.43 (m, 6H), 7.28 (d, *J* = 7.8 Hz, 2H), 6.78 (s, 1H), 6.51 (d, *J* = 48.3 Hz, 1H), 3.07 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 194.0 (d, *J* = 22.1 Hz), 144.6 (d, *J* = 38.7 Hz), 144.3, 143.2, 140.3, 136.0 (d, *J* = 20.3 Hz), 134.3, 134.0, 129.8 (d, *J* = 2.3 Hz), 129.5, 129.3 (d, *J* = 3.7 Hz), 129.0, 128.8, 127.8 (d, *J* = 6.1 Hz), 125.8, 121.0 (q, *J* = 269.2 Hz), 107.2, 93.5 (d, *J* = 187.5 Hz), 44.6.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –65.9, –182.0 (d, *J* = 48.4 Hz).

HRMS-FIA(m/z) calc'd for $C_{25}H_{19}F_4N_2O_3S$ $[M+H]^+$: 503.1047; found: 503.1045.

Hydroquinidine 4-(1-fluoro-2-oxo-2-phenylethyl)-benzoate (S10)



Hydroquinidine 4-chlorobenzoate (465 mg, 1.00 mmol, 1.00 equiv.), XPhos-Pd-G2 (23.6 mg, 30.0 μmol, 3.00 mol%) and Cs_2CO_3 (489 mg, 1.50 mmol, 1.50 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), and 2-fluoroacetophenone (145 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 18 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc/DCM/Et_3N = 4:1:1:1 v/v/v/v to 2:1:1:1 v/v/v/v) afforded 362 mg of the title compound as an off-white solid (64% yield).

R_f = 0.26 (hexanes/EtOAc/DCM/Et_3N = 3:1:1:1 v/v/v/v).

NMR Spectroscopy:

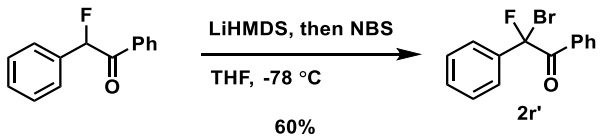
^{1}H NMR (500 MHz, $CDCl_3$, 55 ºC, δ): 8.70 (d, *J* = 4.6 Hz, 1H), 8.12 (d, *J* = 8.1 Hz, 2H), 8.01 (d, J = 9.2 Hz, 1H), 7.94 (d, *J* = 7.8 Hz, 2H), 7.66–7.51 (m, 5H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.40–7.34 (m, 2H), 6.91 (brs, 1H), 6.50 (d, *J* = 48.5 Hz, 1H), 3.99 (s, 3H), 3.44 (q, *J* = 8.6 Hz, 1H), 3.14–2.57 (m, 4H), 2.11–1.85 (m, 1H), 1.79 (s, 1H), 1.72–1.43 (m, 5H), 0.89 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, compound exists as a 1:1 mixture of diastereoisomers, δ): 193.9 (d, *J* = 21.3 Hz), 193.9 (d, *J* = 21.4 Hz), 164.9, 158.2, 147.4, 144.8, 143.5, 139.6 (d, *J* = 20.3 Hz), 134.2, 133.8, 131.9, 130.7, 130.4, 129.3 (d, *J* = 1.4 Hz), 129.2 (d, *J* = 1.4 Hz), 128.9, 127.1 (d, *J* = 6.3 Hz), 127.0 (d, *J* = 6.3 Hz), 122.1, 118.6, 101.4, 93.6 (d, *J* = 187.9 Hz), 93.6 (d, *J* = 187.8 Hz), 74.2, 59.4, 55.9, 50.8, 49.9, 37.2, 26.9, 26.1, 25.5, 23.7, 11.9.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, compound exists as a 1:1 mixture of diastereoisomers, δ): –183.2 (d, *J* = 47.9 Hz), –183.4 (d, *J* = 47.5 Hz)

HRMS-FIA(m/z) calc'd for $C_{35}H_{36}FN_2O_4$ $[M+H]^+$: 567.2654; found: 567.2677.

Phenyl-bromo-fluoroacetophenone (2r')



Phenyl-fluoroacetophenone[1] (428 mg, 2.00 mmol, 1.00 equiv.) was dissolved in dry THF (16 mL), and then the solution was cooled to −78 °C. LiHMDS (1.0 M in THF, 2.10 mL, 2.10 mmol, 1.05 equiv.) was added dropwise. The reaction mixture was stirred at for 50 min. NBS (392 mg, 1.10 mmol, 1.10 equiv.) was added in one portion. After 3 h, a saturated aqueous solution of NH_4Cl (15 mL) was added and the mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous $NaSO_4$ and concentrated in vacuo to give a crude residue. Purification by flash silica gel column chromatography (hexanes/EtOAc = 40:1 v/v) afforded 354 mg of the title compound as a colorless liquid (60% yield).

R_f = 0.52 (hexanes/EtOAc = 10:1 v/v).

NMR Spectroscopy:

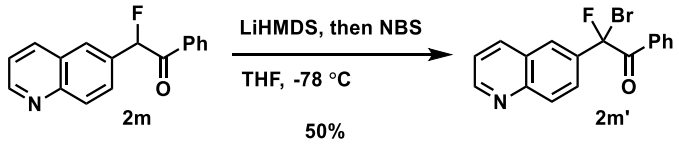
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, δ): 8.04 (d, *J* = 7.6 Hz, 2H), 7.75–7.67 (m, 2H), 7.60 (td, *J* = 7.5, 1.1 Hz, 1H), 7.51–7.41 (m, 5H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 89.3 (d, *J* = 28.5 Hz), 137.4 (d, *J* = 21.4 Hz), 133.9, 132.2 (d, *J* = 3.1 Hz), 130.8 (d, *J* = 4.9 Hz), 130.4, 128.7, 128.5, 126.2 (d, *J* = 7.7 Hz), 104.8 (d, *J* = 267.1 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –112.3.

HRMS-FIA(m/z) calc'd for $C_{14}H_{10}BrFNaO$ $[M+Na]^+$: 314.9791; found: 314.9784.

Quinoline-6-bromo-fluoroacetophenone (2m')



Quinoline-6-fluoroacetophenone (265 mg, 1.00 mmol, 1.00 equiv.) was dissolved in dry THF (10 mL), and then the solution was cooled to −78 °C. LiHMDS (1.0 M in THF, 1.20 mL, 1.20 mmol, 1.20 equiv.) was added dropwise. The reaction mixture was stirred at for 45 min. NBS (214 mg, 1.20 mmol, 1.20 equiv.) was added in one portion. After 45 min, a saturated solution of NH_4Cl (6 mL) and a saturated solution of $Na_2S_2O_3$ (6 mL) were added and the mixture was extracted with EtOAc (3 × 12 mL). The combined organic layers were dried over anhydrous $NaSO_4$, and then concentrated in vacuo to give a crude residue. Purification by flash silica gel column chromatography (hexanes/EtOAc = 6:1 v/v) afforded 173 mg of the title compound as an off-white solid (50% yield).

R_f = 0.30 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.98 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.20 (t, *J* = 8.5 Hz, 2H), 8.14 (d, *J* = 2.2 Hz, 1H), 8.07 (d, *J* = 8.3 Hz, 2H), 7.99 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.53–7.38 (m, 3H).

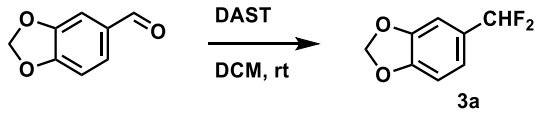
^{13}C NMR (125 MHz, $CDCl_3$, 25 ºC, δ): 189.1 (d, *J* = 28.5 Hz), 152.0, 148.5, 137.1, 135.6 (d, *J* = 21.3 Hz), 134.2, 132.1 (d, *J* = 3.6 Hz), 130.8 (d, *J* = 5.4 Hz), 130.1, 128.7, 127.5 (d, *J* = 6.0 Hz), 127.5, 125.5 (d, *J* = 9.5 Hz), 122.2, 104.0 (d, *J* = 268.4 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –114.5.

HRMS-FIA(m/z) calc'd for $C_{17}H_{12}BrFNO$ $[M+H]^+$: 344.0081; found: 344.0080.

Syntheses of Difluoromethyl-arenes

Difluoromethyl-benzodioxole (3a)



Piperonal (150 mg, 1.00 mmol, 1.00 equiv.) was dissolved in dry DCM (10 mL). DAST (396 µL, 3.00 mmol, 3.00 equiv.) was added to the solution at 0 °C. The reaction mixture was stirred at room temperature for 35 h. Cold water (8 mL) was added. The mixture was extracted with DCM (3 × 4 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 and concentrated in vacuo to give a crude residue. Purification by flash silica gel column chromatography (hexanes/EtOAc = 10/1 v/v) afforded 110 mg of the title compound as a colorless liquid (64% yield).

R_f = 0.52 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

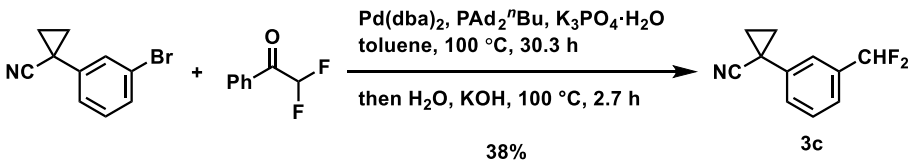
^{1}H NMR (500 MHz, $CDCl_3$, 24 °C, δ): 7.01–6.94 (m, 2H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.54 (t, *J* = 56.6 Hz, 1H), 6.01 (s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 149.7, 148.2, 128.4 (t, *J* = 22.8 Hz), 120.3 (t, *J* = 7.1 Hz), 114.8 (t, *J* = 236.8 Hz), 108.4, 105.9 (t, *J* = 5.5 Hz), 101.7.

^{19}F NMR (470 MHz, $CDCl_3$, 24 °C, δ): −110.9 (d, *J* = 55.9 Hz).

HRMS-FIA(m/z) calc'd for $C_8H_7F_2O_2$ $[M+H]^+$: 173.0409; found: 173.0406.

3-Cyanocyclopropyl-difluoromethylbenzene (3c)



Based on a reported procedure[2]: 1-(3-Bromophenyl)cyclopropanecarbonitrile (222 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 µmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 µmol, 4.00 mol%) and

$K_3PO_4 \cdot H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 30.3 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture. After 2.7 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 15:1 v/v to 10/1 v/v) afforded 114 mg of the title compound as an orange liquid (38% yield).

R_f = 0.29 (hexanes/EtOAc = 5:1 v/v).

NMR Spectroscopy:

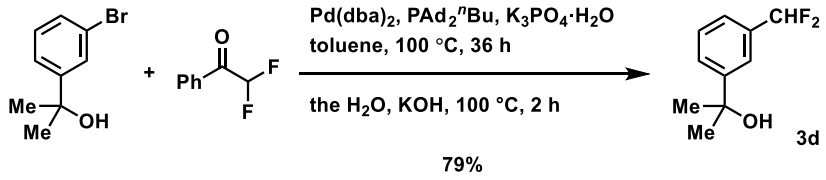
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.49–7.42 (m, 4H), 6.65 (t, *J* = 56.5 Hz, 1H), 1.79 (dd, *J* = 8.0 Hz, 5.5 Hz, 2H), 1.46 (dd, *J* = 8.0 Hz, 5.5 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 137.1, 135.3 (t, *J* = 22.6 Hz), 129.6, 128.3, 125.0 (t, 5.4 Hz), 122.9 (t, *J* = 6.4 Hz), 122.2, 114.3 (t, *J* = 240.1 Hz), 18.5, 13.9.

^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, δ): −114.0 (d, *J* = 55.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{11}H_9F_2NaN$ $[M+Na]^+$: 216.0595; found: 216.0595.

3-*Iso*propanolyl-difluoromethylbenzene (3d)



Based on a reported procedure[2]: $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4 \cdot H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), 2-(3-bromophenyl)propan-2-ol (215 mg, 1.00 mmol, 1.00 equiv.) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 36 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture. After 2 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 7:1 v/v) afforded 147 mg of the title compound as a yellow liquid (79% yield).

R_f = 0.40 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

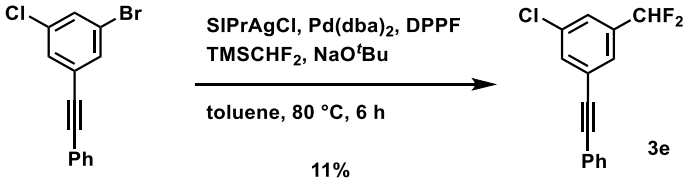
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.65 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.45–7.38 (m, 2H), 6.65 (t, *J* = 56.5 Hz, 1H), 1.82 (s, 1H), 1.60 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 150.0, 134.4 (t, *J* = 22.6 Hz), 128.8, 127.0, 124.0 (t, *J* = 5.4 Hz), 121.8 (t, *J* = 6.4 Hz), 115.0 (t, *J* = 239.0 Hz), 72.6, 31.9.

^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, δ): -113.1 (d, *J* = 56.5 Hz).

HRMS-FIA(m/z) calc'd for $C_{10}H_{12}F_2NaO$ $[M+Na]^+$: 209.0748; found: 209.0755.

3-Chloro-(5-phenylethynyl)-difluoromethylbenzene (3e)



Based on a reported procedure[3]: In a N_2-filled glove box, aryl bromide **S11** (117 mg, 0.400 mmol, 1.00 equiv), $Pd(dba)_2$ (16.1 mg, 28.0 μmol, 7.00 mol%), DPPF (31.0 mg, 56.0 μmol, 14.0 mol%), (SIPr)AgCl (42.7 mg, 80.0 μmol, 20 mol%), and NaO^tBu (96.1 mg, 1.0 mmol, 2 equiv) were combined in a 20 mL vial. To this vial was added 5.0 mL of anhydrous toluene, followed by trimethyl(difluoromethyl)silane (148.8 mg, 1.2 mmol, 2.4 equiv). The vial was sealed and moved out from the glove box. The mixture was stirred at 80 °C for 6 hours. The dark solution was diluted with H_2O (12 mL). The mixture was filtered through a short plug of Celite, and washed with DCM (3 ×15 mL). The organic layer was combined, dried over Na_2SO_4, and concentrated under vacuum. Purification by flash silica gel column chromatography (hexanes) afforded 12.0 mg of the title compound as a colorless liquid (11% yield).

R_f = 0.23 (hexanes).

NMR Spectroscopy:

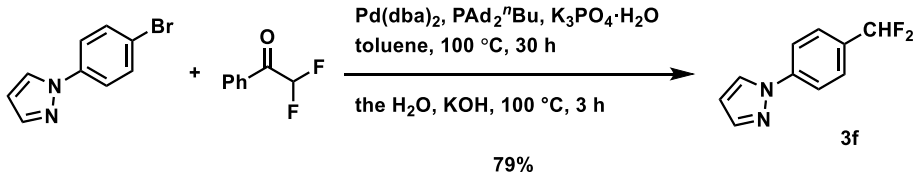
^{1}H NMR (500 MHz, $CDCl_3$, 23 °C, δ): 7.62 (s, 1H), 7.57–7.50 (m, 3H), 7.46 (s, 1H), 7.41–7.32 (m, 3H), 6.61 (t, *J* = 56.1 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 °C, δ): 136.3 (t, *J* = 23.0 Hz), 135.0, 133.6, 131.9, 129.1, 128.6, 127.1 (t, J = 6.3 Hz), 125.9, 125.6 (t, *J* = 6.1 Hz), 122.4, 113.4 (t, *J* = 239.4 Hz), 91.8, 87.1.

^{19}F NMR (470 MHz, $CDCl_3$, 23 °C, δ): -115.1 (d, *J* = 55.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{15}H_{10}ClF_2$ $[M+H]^+$: 263.0434; found: 263.0430.

4-Pyrazolyl-difluoromethylbenzene (3f)



Based on a reported procedure[2]: $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4 \cdot H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), 1-(4-Bromophenyl)-1*H*-pyrazole (223 mg, 1.00 mmol, 1.00 equiv.) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 30 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture. After 3 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 12:1 v/v) afforded 145 mg of the title compound as a white solid (75% yield).

R_f = 0.48 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

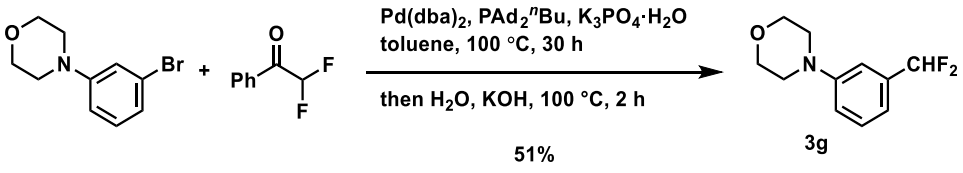
^{1}H NMR (500 MHz, $CDCl_3$, 23 °C, δ): 7.97 (d, *J* = 2.5 Hz, 1H), 7.86–7.69 (m, 3H), 7.60 (d, *J* = 8.2 Hz, 2H), 6.69 (t, *J* = 56.4 Hz, 1H), 6.51 (t, *J* = 2.2 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 °C, δ): 141.9, 141.8, 132.3 (t, *J* = 22.7 Hz), 127.0 (t, *J* = 6.1 Hz), 126.9, 119.1, 114.4 (td, *J* = 238.7, 3.2 Hz), 108.3.

^{19}F NMR (470 MHz, $CDCl_3$, 21 °C, δ): -113.4 (d, *J* = 55.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{10}H_9F_2N_2$ $[M+H]^+$: 195.0729; found: 195.0732.

3-Morpholino-difluoromethylbenzene (3g)



Based on a reported procedure[2]: $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4 \cdot H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), 4-(3-bromophenyl)morpholine (242 mg, 1.00 mmol, 1.00 equiv.) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at

100 °C. After 30 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 µL) were added to the mixture. After 2 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 10:1 v/v to 8/1 v/v) afforded 109 mg of the title compound as an yellow liquid (51% yield).

R_f = 0.45 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

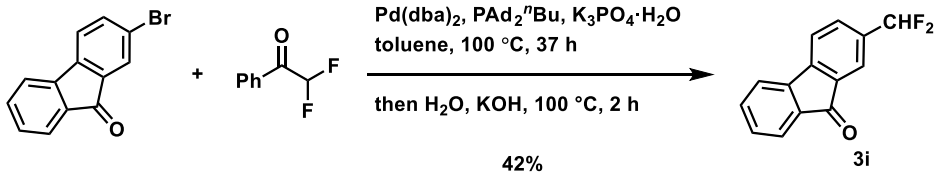
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.35 (t, *J* = 7.5 Hz, 1H), 7.03 (s, 1H), 7.02–6.98 (m, 2H), 6.60 (t, *J* = 57.0 Hz, 1H), 3.87 (t, *J* = 5.0 Hz, 4H), 3.20 (t, J = 5.0 Hz, 4H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 151.6, 135.4 (t, *J* = 21.4 Hz), 129.7, 117.8, 117.0 (t, *J* = 6.6 Hz), 115.0 (t, *J* = 240.2 Hz), 112.3 (t, *J* = 6.4 Hz), 66.9, 49.1.

^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, δ): −113.5 (d, *J* = 55.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{11}H_{14}F_2NO_2$ $[M+H]^+$: 214.1038; found: 214.1047.

2-Difluoromethylfluoren-9-one (3i)



Based on a reported procedure[2]: 2-Bromofluoren-9-one (259 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 µmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 µmol, 4.00 mol%) and $K_3PO_4{\cdot}H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 µL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 37 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 µL) were added to the mixture. After 2 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 40:1 v/v) afforded 104 mg of the title compound as a yellow solid (42% yield).

R_f = 0.20 (hexanes/EtOAc = 40:1 v/v).

NMR Spectroscopy:

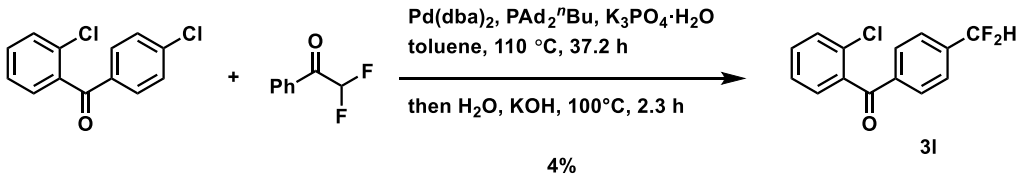
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.78 (s, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 6.65 (t, *J* = 56.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 190.3, 144.2, 141.1, 133.0 (t, *J* = 22.6 Hz), 132.7, 132.2, 132.0, 129.6 (t, *J* = 6.6 Hz), 127.5, 122.3, 119.3 (t, *J* = 5.4 Hz), 118.6, 118.2, 111.7 (t, *J* = 240.0 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, δ): −114.1 (d, *J* = 56.5 Hz).

HRMS-FIA(m/z) calc'd for $C_{14}H_8F_2NaO$ $[M+Na]^+$: 253.0435; found: 253.0433.

2-Chlorophenyl-(4-difluoromethyl)phenyl-methanone (3l)



Based on a reported procedure[2]: 2-Chlorophenyl-4-chlorophenyl-methanone (243 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4·H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 110 °C. After 37.2 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture and the temperature of the oil bath was decreased to 100°C. After 2.3 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/DCM = 3:1 v/v) afforded 11.0 mg of the title compound as a colorless liquid (4% yield).

R_f = 0.50 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

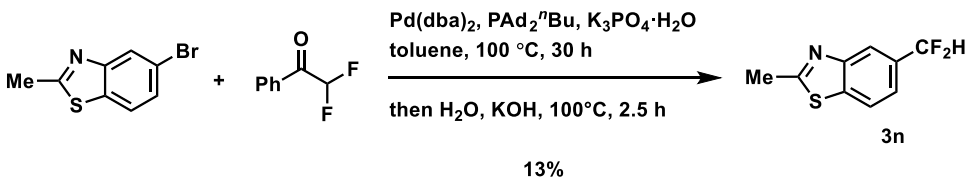
^{1}H NMR (500 MHz, $CDCl_3$, 24 °C, δ): 7.89 (d, *J* = 7.9 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.51–7.43 (m, 2H), 7.43–7.36 (m, 2H), 6.70 (t, *J* = 56.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 194.7, 139.1 (t, *J* = 22.4 Hz), 138.6, 138.2, 131.7, 131.5, 130.4, 130.4, 129.4, 127.0, 126.1 (t, *J* = 6.1 Hz), 114.0 (t, *J* = 240.1 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 24 °C, δ): −115.5 (d, *J* = 55.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{14}H_9ClF_2NaO$ $[M+Na]^+$: 289.0202; found: 289.0207.

5-Difluoromethyl-2-methylbenzo[*d*]thiazole (3n)



Based on a reported procedure[2]: 5-Bromo-2-methylbenzothiazole (228 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4•H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 30 h 10 min, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture. After 2.5 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (cyclohexane/EtOAc = 6:1 v/v) afforded 25 mg of the title compound as an off-white solid (13% yield).

R_f = 0.22 (cyclohexane/EtOAc = 5:1 v/v).

NMR Spectroscopy:

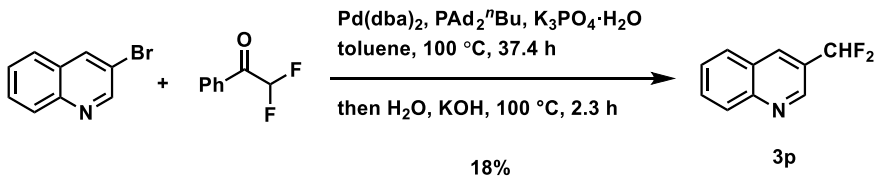
^{1}H NMR (500 MHz, $CDCl_3$, 23 °C, δ): 8.07 (s, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.51 (d, *J* = 8.3 Hz, 1H), 6.78 (t, *J* = 56.4 Hz, 1H), 2.86 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 °C, δ): 168.8, 153.3, 138.2, 132.7 (t, *J* = 22.6 Hz), 122.1, 121.7 (t, *J* = 5.6 Hz), 120.0 (t, *J* = 6.8 Hz), 114.8 (t, *J* = 239.3 Hz), 20.4.

^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, δ): –112.3 (d, *J* = 56.4 Hz).

HRMS-FIA(m/z) calc'd for $C_9H_8F_2NS$ $[M+H]^+$: 200.0340; found: 200.0349.

3-Difluoromethylquinoline (3p)



Based on a reported procedure[2]: $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4·H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL), 3-bromoquinoline (208 mg, 1.00 mmol, 1.00 equiv.) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 37.4 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture. After 2.3 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 6:1 v/v) afforded 31.9 mg of the title compound as a yellow liquid (18% yield).

R_f = 0.35 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

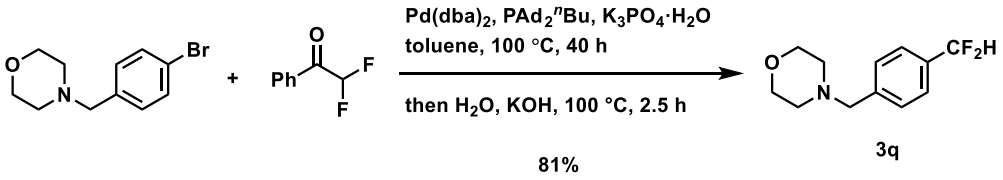
^{1}H NMR (500 MHz, $CDCl_3$, 23 °C, δ): 9.05 (s, 1H), 8.32 (s, 1H), 8.18 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.83 (t, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.3 Hz, 1H), 6.90 (t, *J* = 55.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 °C, δ): 149.1, 147.2, 134.2 (t, *J* = 6.7 Hz), 131.3, 129.6, 128.5, 127.8, 127.3 (t, *J* = 25.0 Hz), 127.0, 113.8 (t, *J* = 240.1 Hz).

^{19}F NMR (470 MHz, $CDCl_3$, 23 °C, δ): -114.6 (d, J = 55.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{10}H_8F_2N$ $[M+H]^+$: 180.0620; found: 180.0628.

4-Morpholinomethyl-difluoromethylbenzene (3q)



Based on a reported procedure[2]: 4-(4-Bromobenzyl)morpholine (256 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4 \cdot H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 40 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture. After 2.5 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 3:1 v/v, 1% Et_3N) afforded 185 mg of the title compound as a yellow liquid (81% yield).

R_f = 0.33 (hexanes/EtOAc = 2:1 v/v, 1% Et_3N).

NMR Spectroscopy:

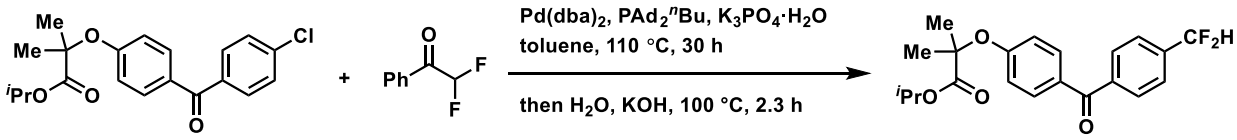
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.46 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 6.63 (t, *J* = 57.0 Hz, 1H), 3.71 (t, *J* = 4.5 Hz, 4H), 3.53 (s, 2H), 2.44 (t, *J* = 4.5 Hz, 4H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 141.0, 133.4 (t, *J* = 21.5 Hz), 129.4, 125.6 (t, *J* = 5.3 Hz), 114.8 (t, *J* = 239.1 Hz), 67.1, 63.1, 53.7.

^{19}F NMR (470 MHz, $CDCl_3$, 24 °C, δ): −113.1 (d, *J* = 57.3 Hz).

HRMS-FIA(m/z) calc'd for $C_{12}H_{16}F_2NO$ $[M+H]^+$: 228.1192; found: 228.1204.

Difluoromethyl-fenofibrate



Based on a reported procedure[2]: Fenofibrate (361 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4{\cdot}H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 110 °C. After 30 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture and the temperature of the oil bath was decreased to 100°C. After 2.3 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 15:1 v/v) afforded 104 mg of the title compound as an off-white solid (28% yield).

R_f = 0.40 (hexanes/EtOAc = 6:1 v/v).

NMR Spectroscopy:

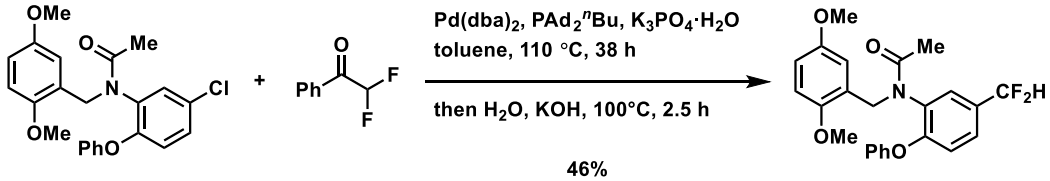
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.81 (d, *J* = 7.8 Hz, 2H), 7.76 (d, *J* = 7.8 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.72 (t, *J* = 56.5 Hz, 1H), 5.09 (sep, *J* = 6.5 Hz, 1H), 1.66 (s, 6H), 1.20 (d, *J* = 6.5 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 194.7, 173.2, 160.0, 140.5, 137.5 (t, *J* = 22.6 Hz), 132.2, 130.2, 130.0, 125.6 (t, *J* = 5.4 Hz), 117.4, 114.2 (t, *J* = 240.0 Hz), 79.6, 69.5, 25.5, 21.6.

^{19}F NMR (470 MHz, $CDCl_3$, 24 °C, δ): −114.8 (d, *J* = 56.0 Hz).

HRMS-FIA(m/z) calc'd for $C_{21}H_{22}F_2NaO_4$ $[M+Na]^+$: 399.1378; found: 399.1380.

Difluoromethyl-DAA1106



Based on a reported procedure[2]: Aryl chloride (412 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4{\cdot}H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 μL, 1.20 mmol, 1.20 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 110 °C. After 38 h, KOH (500 mg,

8.91 mmol, 8.91 equiv.) and H_2O (250 µL) were added to the mixture and the temperature of the oil bath was decreased to 100°C. After 2.5 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 4:1 v/v) afforded 198 mg of the title compound as a yellow liquid (46% yield).

R_f = 0.30 (hexanes/EtOAc = 3:1 v/v).

NMR Spectroscopy:

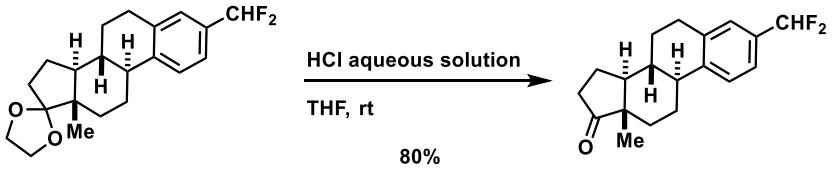
^{1}H NMR (500 MHz, $CDCl_3$, 55 °C, δ): 7.35 (t, *J* = 7.9 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 1H), 7.19 (d, *J* = 7.9 Hz, 2H), 6.99 (d, *J* = 3.1 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 1H), 6.73 (dd, *J* = 8.9, 3.1 Hz, 1H), 6.65 (d, *J* = 8.8 Hz, 1H), 6.50 (t, *J* = 56.5 Hz, 1H), 5.13 (d, *J* = 14.2 Hz, 1H), 4.77 (d, *J* = 14.4 Hz, 1H), 3.67 (s, 3H), 3.50 (s, 3H), 1.96 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 °C, δ): 170.9, 156.0, 155.2, 153.6, 151.9, 133.1, 130.2, 129.0 (t, *J* = 23.3 Hz), 128.2, 126.4 (t, *J* = 5.9 Hz), 126.2, 124.9, 120.0, 117.6, 116.8, 114.0 (d, *J* = 238.5 Hz), 113.9, 111.3, 55.8, 55.7, 46.1, 22.4.

^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, compound exists as a 1:1 mixture of rotamers, δ): –112.3 (d, *J* = 55.9 Hz), –112.4 (d, *J* = 55.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{24}H_{24}F_2NO_4$ $[M+H]^+$: 428.1668; found: 428.1682.

Difluoromethyl-estrone



To a solution of difluorormethyl-estrone-ketal[3] (60.0 mg, 0.172 mmol) in THF (2.5 mL) was added HCl aqueous solution (2 M, 1 mL). The resulting mixture was stirred at room temperature. After 2.5 h, the reaction mixture was poured into saturated $NaHCO_3$ aqueous solution (6 mL) and extracted with DCM (3 × 5 mL). The combined organic layer was dried with $MgSO_4$. After the solvent was removed in vacuo, purification by flash silica gel column chromatography (hexanes/EtOAc = 12:1 v/v) afforded 42.0 mg of the title compound as a white solid (80% yield).

R_f = 0.27 (hexanes/EtOAc = 10:1 v/v).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 °C, δ): 7.38 (d, *J* = 8.1 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1 H), 7.24 (s, 1H), 6.59 (t, *J* = 56.6 Hz, 1H), 3.01–2.89 (m, 2H), 2.52 (dd, *J* = 19.0, 8.5 Hz, 1H), 2.47–2.40 (m, 1H), 2.39–2.28 (m, 1H), 2.21–2.01 (m, 3H), 2.01–1.94 (m, 1H), 1.70–1.44 (m, 6H), 0.92 (s, 3H).

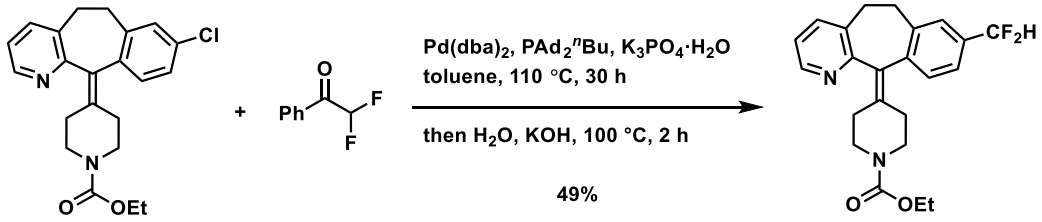
^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 220.7, 142.7, 137.2, 132.0 (t, *J* = 22.4 Hz), 126.2 (t, *J* = 5.9 Hz),

125.9, 123.0, 115.0 (t, *J* = 238.2 Hz), 50.6, 48.0, 44.6, 38.0, 35.9, 31.7, 29.4, 26.4, 25.8, 21.7, 13.9.

^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, δ): –112.9 (dd, *J* = 56.9 Hz, 8.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{19}H_{22}F_2NaO$ $[M+Na]^+$: 327.1531; found: 327.1521.

Difluoromethyl-Claritin



Based on a reported procedure[2]: Claritin (383 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4{\cdot}H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 110 °C. After 30 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture and the temperature of the oil bath was decreased to 100°C. After 2 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/dioxane/dichloromethane = 6:1:1 v/v/v) afforded 195 mg of the title compound as an orange solid (49% yield).

R_f = 0.33 (hexanes/EtOAc = 1:2 v/v).

NMR Spectroscopy:

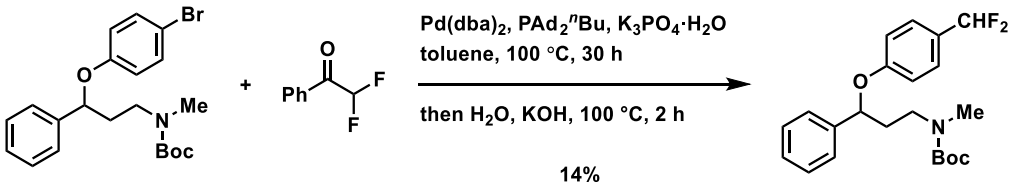
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 8.40 (d, *J* = 4.5 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.34–7.26 (m, 3H), 7.11–7.08 (m, 1H), 6.70 (t, *J* = 56.5 Hz, 1H), 4.12 (q, *J* = 7.0 Hz, 2H), 3.81 (brs, 2H), 3.50–3.43 (m, 1H), 3.41–3.35 (m, 1H), 3.18–3.12 (m, 2H), 2.91–2.84 (m, 2H), 2.53–2.47 (m, 1H), 2.40–2.30 (m, 3H), 1.25 (t, *J* = 7.0 H, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, δ): 156.9, 155.6, 146.9, 142.1, 138.5, 137.8, 137.7, 134.7, 133.5 (t, *J* = 21.4 Hz), 133.5, 129.7, 126.2 (t, *J* = 5.3 Hz), 123.5 (t, *J* = 5.4 Hz), 122.4, 114.8 (t, *J* = 239.0 Hz), 61.4, 44.9, 44.9, 32.0, 31.7, 30.9, 30.6, 14.8.

^{19}F NMR (470 MHz, $CDCl_3$, 24 °C, δ): −113.2 (d, *J* = 56.0 Hz).

HRMS-FIA(m/z) calc'd for $C_{23}H_{25}F_2N_2O_2$ $[M+H]^+$: 399.1879; found: 399.1887.

Difluoromethyl-*N*-Boc-Fluoxetine



Based on a reported procedure[2]: Aryl bromide (420 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4{\cdot}H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 30 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 μL) were added to the mixture. After 2 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 4:1 to 3:1 v/v) afforded 54.3 mg of the title compound as a yellow liquid (14% yield).

R_f = 0.30 (hexanes/EtOAc = 4:1 v/v).

NMR Spectroscopy:

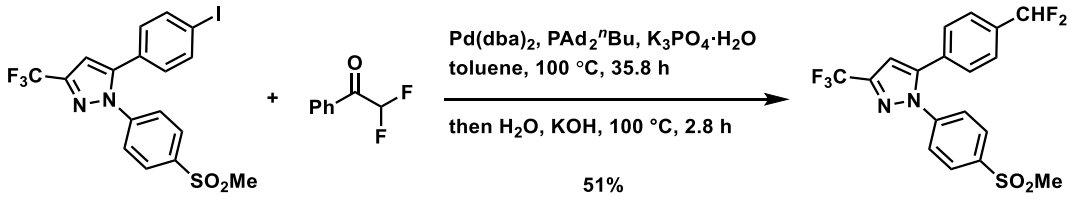
^{1}H NMR (500 MHz, $CDCl_3$, 50 °C, δ): 7.29–7.23 (m, 5H), 7.21–7.17 (m, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.45 (t, *J* = 56.8 Hz, 1H), 5.10 (dd, *J* = 8.6, 4.2 Hz, 1H), 3.50–3.20 (m, 2H), 2.78 (s, 3H), 2.19–2.07 (m, 1H), 2.07–1.98 (m, 1H), 1.34 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$, 50 °C, δ): 160.1, 155.9, 141.3, 129.0, 128.0, 127.1 (t, *J* = 6.0 Hz), 125.9, 116.1, 115.0 (t, *J* = 237.1 Hz), 80.0, 78.3, 46.0, 37.2, 34.7, 28.6.

^{19}F NMR (470 MHz, $CDCl_3$, 21 °C, δ): −111.5 (d, *J* = 57.3 Hz).

HRMS-FIA(m/z) calc'd for $C_{22}H_{27}F_2NaNO_3$ $[M+Na]^+$: 414.1851; found: 414.1859.

Difluoromethyl-SC-58125



Based on a reported procedure[2]: Aryl iodide (492 mg, 1.00 mmol, 1.00 equiv.), $Pd(dba)_2$ (17.3 mg, 30.0 μmol, 3.00 mol%), $PAd_2{}^nBu$ (14.3 mg, 40.0 μmol, 4.00 mol%) and $K_3PO_4{\cdot}H_2O$ (921 mg, 4.00 mmol, 4.00 equiv.) were added to a flame-dried Schlenk tube. The Schlenk tube was evacuated and back-filled with nitrogen (3 ×). Toluene (5 mL) and 2,2-difluoroacetophenone (264 μL, 2.00 mmol, 2.00 equiv.) were added to the

mixture. The Schlenk tube was immersed into a pre-heated oil bath at 100 °C. After 35.8 h, KOH (500 mg, 8.91 mmol, 8.91 equiv.) and H_2O (250 µL) were added to the mixture. After 2.8 h, the oil bath was removed, and the Schlenk tube was allowed to cool to room temperature. The reaction mixture was filtered through Celite and eluted with EtOAc (3 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc = 7:2 v/v) afforded 214 mg of the title compound as a white-orange solid (51% yield).

R_f = 0.37 (hexanes/EtOAc = 2:1 v/v).

NMR Spectroscopy:

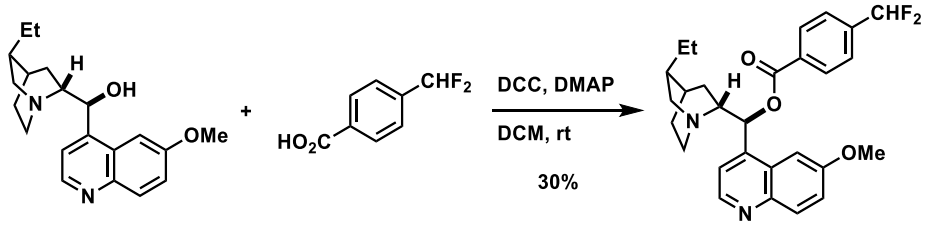
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, δ): 7.96 (d, *J* = 8.5 Hz, 2H), 7.58–7.49 (m, 4H), 7.34 (d, *J* = 7.9 Hz, 2H), 6.83 (s, 1H), 6.67 (t, *J* = 56.2 Hz, 1H), 3.25–2.86 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 °C, δ): 144.6 (q, *J* = 38.7 Hz), 144.2, 143.2, 140.4, 135.7 (t, *J* = 22.6 Hz), 131.0, 129.3, 128.8, 126.6 (t, *J* = 6.0 Hz), 125.9, 121.0 (q, *J* = 269.2 Hz), 114.0 (t, *J* = 239.5 Hz), 107.4, 44.6.

^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, δ): –65.5, –114.8 (d, *J* = 56.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{18}H_{13}F_5NaN_2O_2S$ $[M+Na]^+$: 439.0510; found: 439.0498.

Hydroquinidine 4-difluoromethylbenzoate



Hydroquinidine (326 mg, 1.00 mmol, 1.00 equiv.), 2-(difluoromethyl)benzoic acid (189 mg, 1.10 mmol, 1.10 equive.) were dissolved in dry DCM (5 mL). DCC (227 mg, 1.10 mmol, 1.10 mol) and DMAP (12.2 mg, 0.10 mmol, 0.01 equiv.) were added. The reaction mixture was stirred at room temperature for 16 h. Then the suspension was filtered through Celite and eluted with DCM (2 × 4 mL). The filtrate was evaporated under reduced pressure. Purification by flash silica gel column chromatography (hexanes/EtOAc/DCM/Et_3N = 4:1:1:1 v/v/v/v) afforde 144 mg of the title compound as a white solid (30% yield).

R_f = 0.60 (hexanes/EtOAc/DCM/Et_3N = 2:1:1:1 v/v/v/v).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 25°C, δ): 8.73 (d, *J* = 4.6 Hz, 1H), 8.20 (d, *J* = 8.1 Hz, 2H), 8.03 (d, *J* = 9.2 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.59 (brs, 1H), 7.47–7.36 (m, 2H), 7.01 (s, 1H), 6.72 (t, *J* = 56.0 Hz, 1H), 4.04 (s, 3H), 3.47 (q, *J* = 8.8 Hz, 1H), 3.19–2.71 (m, 4H), 2.15–1.95 (m, 1H), 1.85 (s, 1H), 1.74–1.49 (m, 6H), 0.93 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 25°C, δ): 164.56, 158.4, 147.4, 144.9, 143.2, 139.2 (t, *J* = 22.5 Hz), 132.00, 131.95, 130.2, 127.0, 126.1 (t, *J* = 6.0 Hz), 122.4, 118.4, 113.9 (t, *J* = 240.4 Hz), 101.4, 74.0, 59.5, 56.2, 50.7, 50.0, 37.0, 26.6, 26.1, 25.45, 23.0, 11.9.

^{19}F NMR (470 MHz, $CDCl_3$, 25°C, δ): –115.4 (d, *J* = 55.9 Hz).

HRMS-FIA(m/z) calc'd for $C_{28}H_{31}F_2N_2O_2$ $[M+H]^+$: 481.2297; found: 481.2317.

Syntheses of ^{18}F-Difluoromethylarenes

General Methods for Radioisotope Preparation

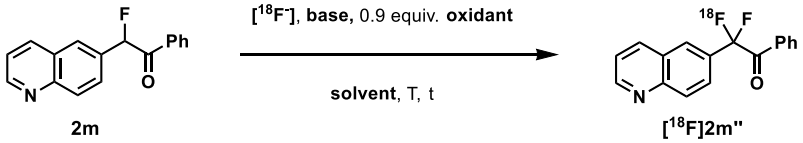
A GE PETtrace 16.5 MeV cyclotron was used for [^{18}F]fluoride production by the ^{18}O(p,n)^{18}F nuclear reaction to irradiate ^{18}O-enriched water. [^{18}F]fluoride was delivered to a lead-shielded hot cell in ^{18}O-enriched water by nitrogen gas pressure. [^{18}F]Fluoride was prepared for radiofluorination by the following method: a solution of TEAB (2 mg) in acetonitrile and water (1 mL, v/v 7:3) was added to an aliquot of target water (≤ 1 mL) containing the appropriate amount of [^{18}F]fluoride (2−4 mCi) in a V-shaped vial sealed with a Teflon-lined septum. The vial was heated to 110 °C while nitrogen gas was passed through a P_2O_5-Drierite™ column followed by a vented needle. When no liquid was visible in the vial, it was removed from heat, anhydrous acetonitrile (1 mL) was added, and the heating was resumed until dryness. This step was repeated an additional two times. The vial was then cooled to room temperature under nitrogen flow (10 mL/min). The contents were redissolved in the anhydrous acetonitrile (80 µL, solution A).

General Methods for Analysis of Radiofluorination Reactions

RadioTLC: EMD TLC Silica gel 60 plates (10 x 2 cm) were spotted with an aliquot (1−5 µL) of crude reaction mixture approximately 1 cm from the bottom of the plate (baseline). TLC plates were developed in a chamber containing ethyl acetate until within 1 cm of the top of the plate (front). Analysis was performed using a Bioscan AR-2000 radio-TLC imaging scanner and WinScan software.

RadioHPLC: A Phenomenex Luna C18, 250 x 4.6 mm, 5 µm HPLC column was used with a Waters 1515 Isocratic HPLC Pump equipped with a Waters 2487 Dual λ Absorbance Detector, a Bioscan Flow-Count equipped with a NaI crystal, and Breeze software.

Table S2. Optimization of ^{18}F-Labeling Conditions



2m
0.01 mmol

[^{18}F]2m''

base	oxidant	T	t	solvent	RCC (TLC)
TEAB (3.5 mg)	**NBS (1.6 mg)**	**80 °C**	**10 min**	**MeCN** (0.22 mL)	**10%**
TEAB (3.5 mg)	**NBS (1.6 mg)**	**80 °C**	**10 min**	**MeCN/PhH** (20 μL/0.2 mL)	**36%**
TEAB (3.5 mg)	**NBS (1.6 mg)**	**80 °C**	**10 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**42%**
TEAB (3.5 mg)	**NBS (1.6 mg)**	**80 °C**	**10 min**	**MeCN/THF** (20 μL/0.2 mL)	**4%**
TEAB (3.5 mg)	**NBS (1.6 mg)**	**80 °C**	**10 min**	**MeCN/Bu_2O** (20 μL/0.2 mL)	**37%**
TEAB (3.5 mg)	**NBS (1.6 mg)**	**100 °C**	**10 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**68%**
TEAB (3.5 mg)	**NBS (1.6 mg)**	**120 °C**	**10 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**55%**
K_2CO_3/18-C-6 (2 mg/10 mg)	**NBS (1.6 mg)**	**100 °C**	**10 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**53%**
TEAB (5.5 mg)	**NBS (1.6 mg)**	**100 °C**	**10 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**66%**
TEAB (1.5 mg)	**NBS (1.6 mg)**	**100 °C**	**10 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**53%**
TEAB (3.5 mg)	**NIS (2.0 mg)**	**100 °C**	**10 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**26%**
TEAB (3.5 mg)	**NCS (1.2 mg)**	**100 °C**	**10 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**13%**
TEAB (3.5 mg)	**NBP (2.0 mg)**	**100 °C**	**10 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**73%**
TEAB (3.5 mg)	**NBP (2.0 mg)**	**100 °C**	**5 min**	**MeCN/PhCl** (20 μL/0.2 mL)	**72%**

A 1-dram (4 mL) glass vial loaded with base, precursor 2m (2.7 mg, 10 μmol) and oxidant (9 μmol) were added solvent (0.2 mL) and the solution A (20 μL). The radioactivity of the mixture was measured. Then the reaction vessel was heated at given temperature. After the reaction time was over, the reaction vessel was cooled down to room temperature. MeCN (2 mL) was added to the reaction mixture. An aliquot from combined solution was removed and analyzed by radio TLC for radiochemical conversion and radio HPLC for product identity.

Radio HPLC chromatogram:
Column: Luna 5u C18 100 Å 250 × 4.6 mm
Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)
Flow rate: 1 mL/min

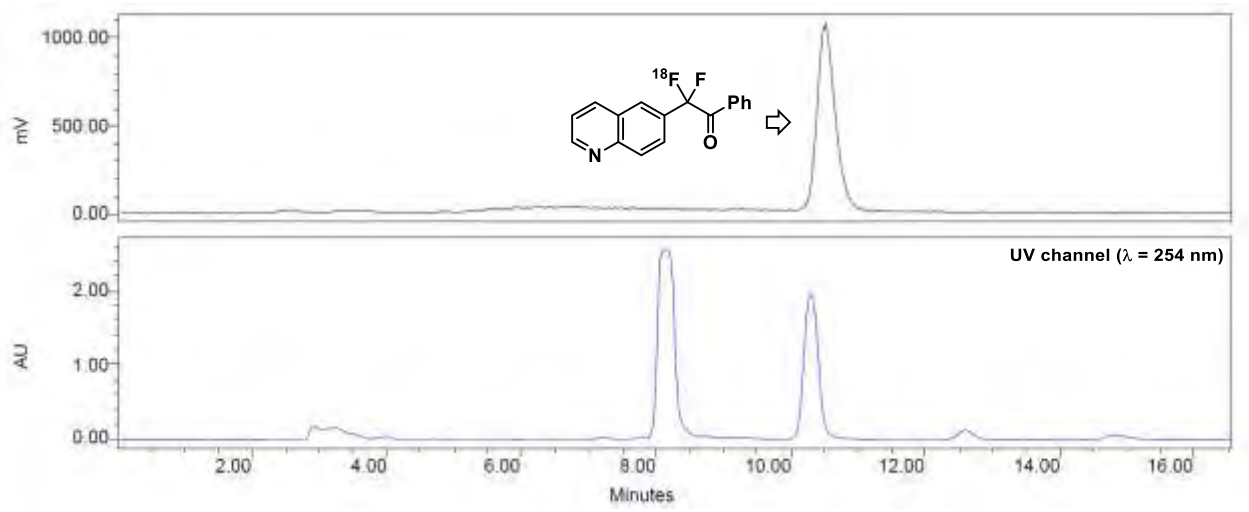


Figure S1. Co-injection radio-HPLC chromatogram of **[^{18}F]2m''**

General Procedure for Syntheses of ^{18}F-Difluoromethylarenes

To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2** (10 μmol) and N-bromophthalimide (2 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 x 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio-TLC and radio-HPLC (column: Luna 5u C18 100 Å 250 × 4.6 mm. UV wavelength: 230, 254, or 290 nm for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, whichever lower number form radio-TLC or radio-HPLC results. Each radiochemical labeling was conducted three times (n = 3).

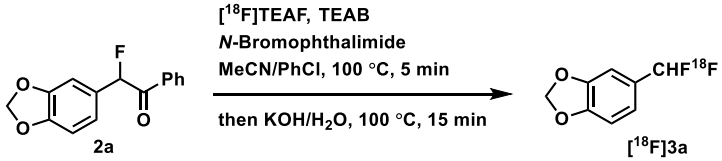
Method of the RCY determination by SPE

All the radiolabeled compounds were purified by flash chromatography (a short silica cartridge purchased from Waters, Inc Catalog # WAT023537), which removed precipitates and unreacted ^{18}F-fluoride. The overall radioactivity of filtrate was measured and an aliquot was removed and analyzed by radio-TLC and radio-HPLC. The radiochemical purity was determined by the ratio of peak area between [^{18}F]difluoromethylarene and all radioactive peaks. The radiochemical yield of [^{18}F]difluoromethylarene was calculated by the following equation.

$$\mathrm{RCY} = \frac{[\text{radiochemical purity}]\ \mathrm{X}\ [\text{all collected activity by silica cartridge method}]}{[\text{starting radioactivity as 18F fluoride}]}$$

.

[^{18}F]Difluoromethyl-benzodioxole ([^{18}F]3a)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2a** (2.9 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	625 μCi	213 μCi	98%	95%	32%
2	831 μCi	227 μCi	98%	98%	27%
3	740 μCi	202 μCi	98%	100%	27%

RCY = 29 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 50% CH_3CN, 50% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

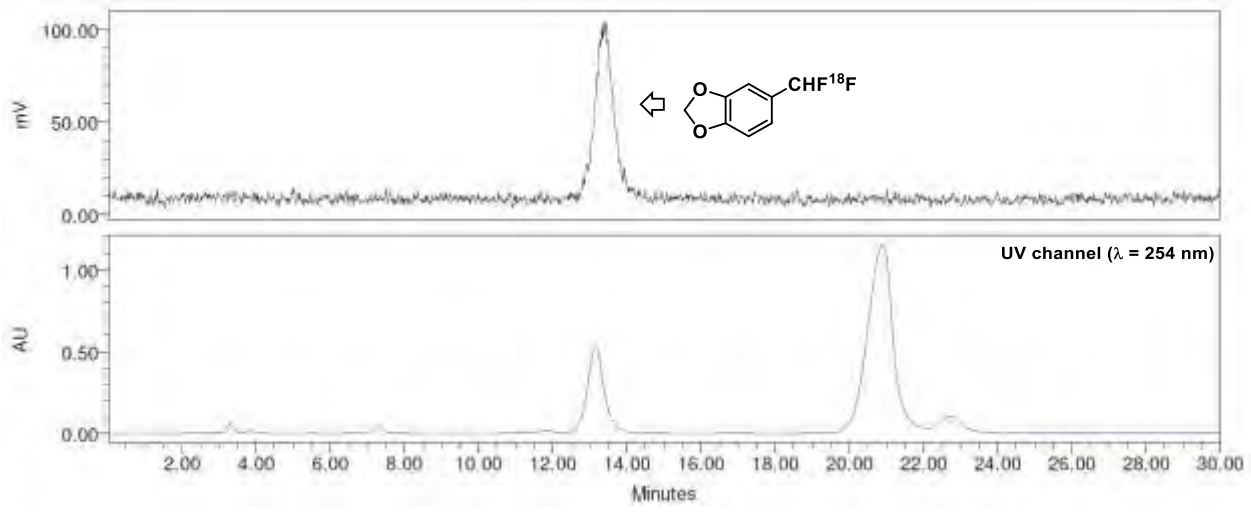
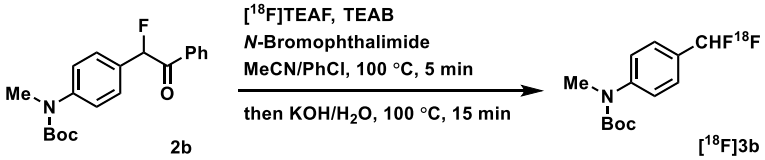


Figure S2. Co-injection radio HPLC chromatogram of **[^{18}F]3a**

[^{18}F]*N*-Boc-*N*-methyl-difluoromethylaniline ([^{18}F]3b)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2b** (3.4 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	546 μCi	222 μCi	100%	72%	29%
2	392 μCi	146 μCi	100%	75%	28%
3	432 μCi	176 μCi	100%	76%	31%

RCY = 29 ± 1% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

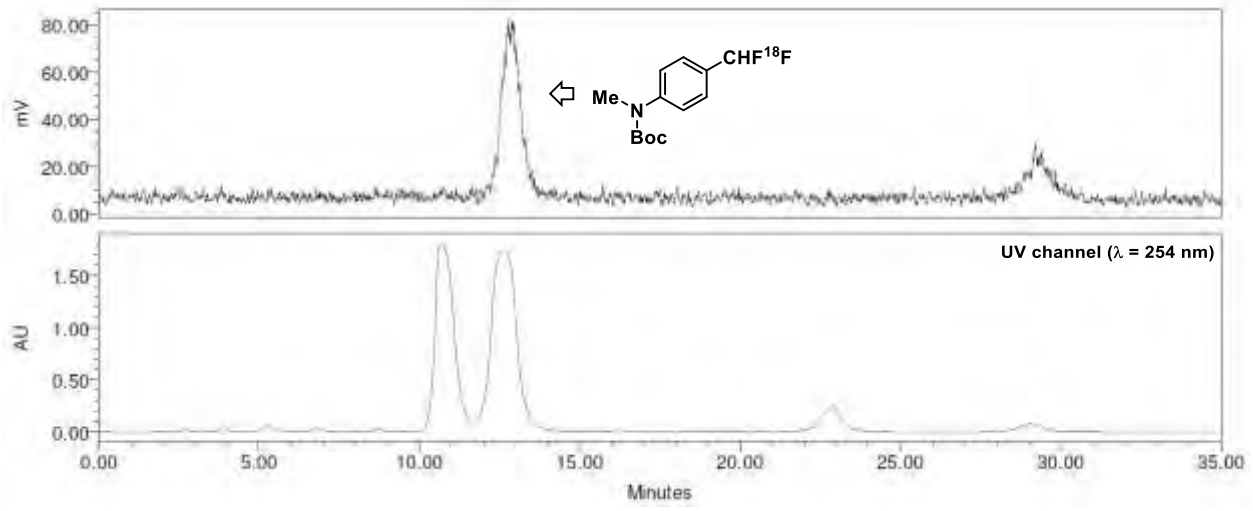
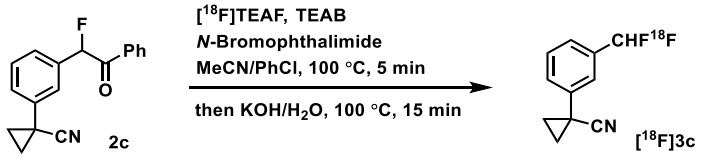


Figure S3. Co-injection radio HPLC chromatogram of **[^{18}F]3b**

[^{18}F]3-Cyanocyclopropyl-difluoromethylbenzene ([^{18}F]3c)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2c** (2.8 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	629 μCi	384 μCi	95%	96%	58%
2	700 μCi	407 μCi	95%	94%	55%
3	560 μCi	293 μCi	95%	96%	50%

RCY = 54 ± 3% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

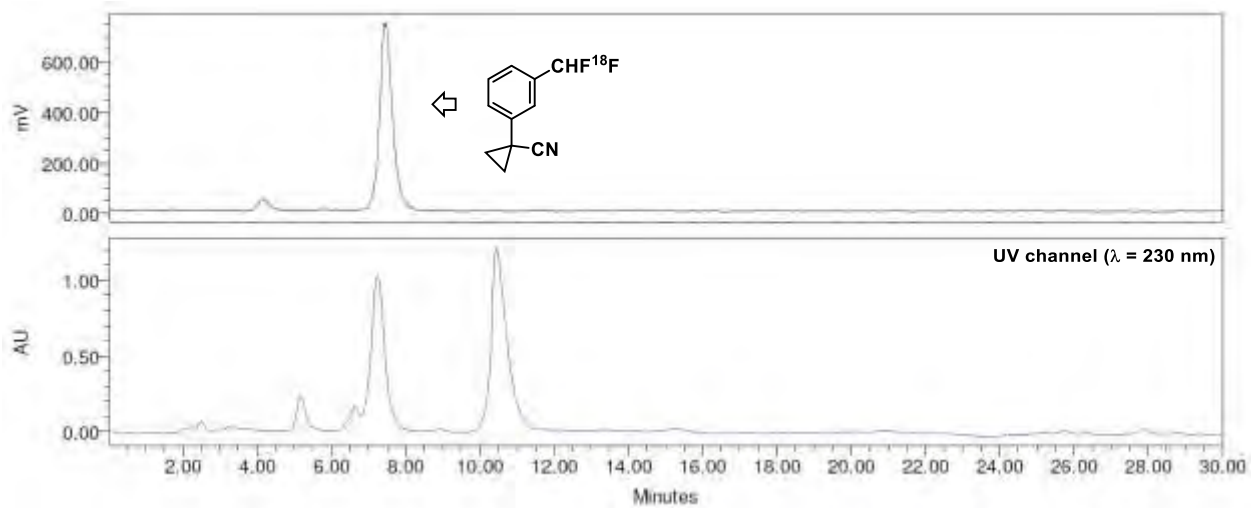
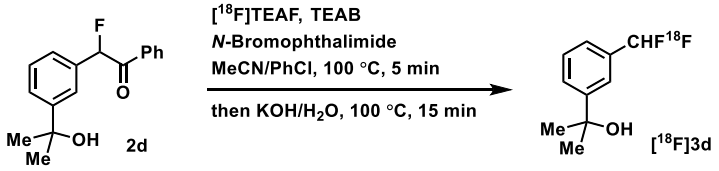


Figure S4. Co-injection radio HPLC chromatogram of **[^{18}F]3c**

[^{18}F]3-*Iso*propanolyl-difluoromethylbenzene ([^{18}F]3d)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2d** (2.7 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	797 μCi	323 μCi	99%	98%	40%
2	615 μCi	210 μCi	99%	96%	33%
3	543 μCi	195 μCi	97%	98%	35%

RCY = 36 ± 3% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 50% CH_3CN, 50% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

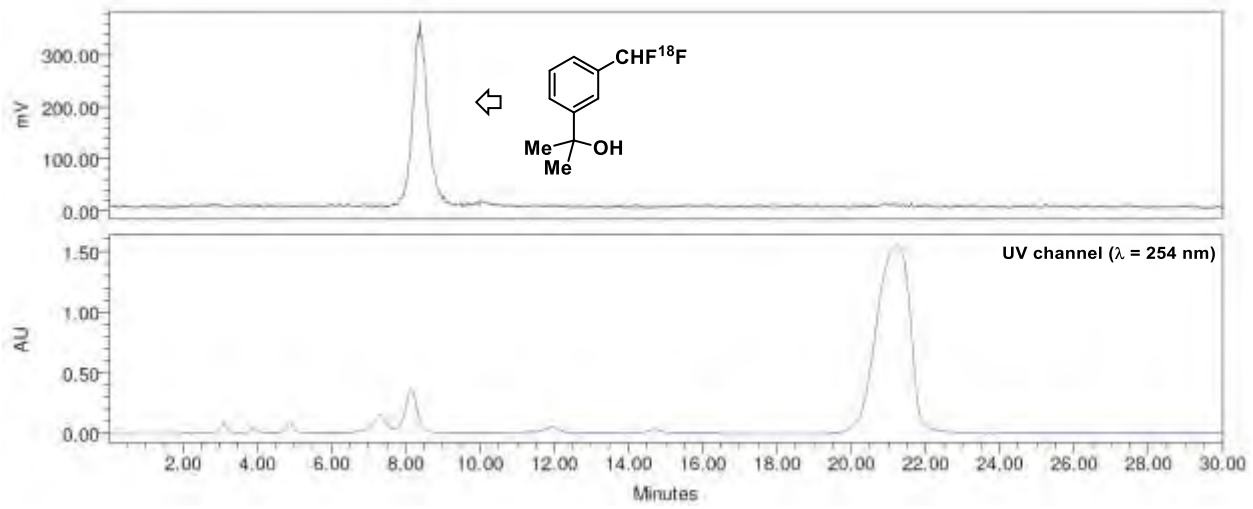
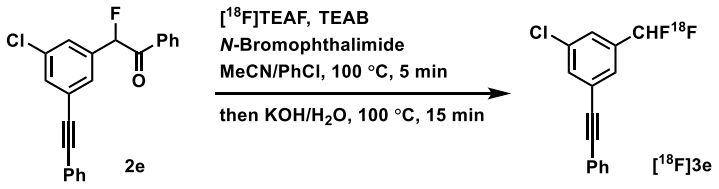


Figure S5. Co-injection radio HPLC chromatogram of **[^{18}F]3d**

[^{18}F]3-Chloro-5-(phenylethynyl)-difluoromethylbenzene ([^{18}F]3e)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2e** (3.5 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	510 μCi	326 μCi	100%	100%	64%
2	470 μCi	272 μCi	100%	100%	58%
3	460 μCi	275 μCi	100%	100%	60%

RCY = 61 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 80% CH_3CN, 20% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

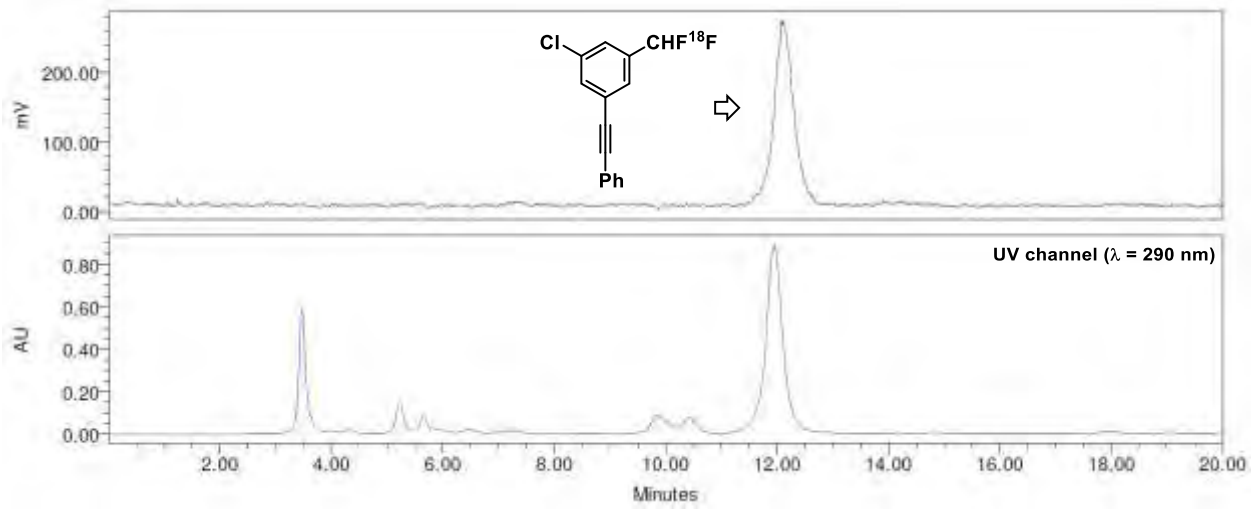
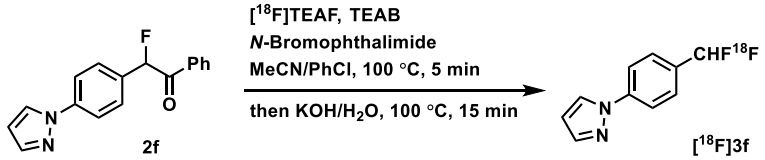


Figure S6. Co-injection radio HPLC chromatogram of **[^{18}F]3e**

[^{18}F]4-Pyrazolyl-difluoromethylbenzene ([^{18}F]3f)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2f** (2.8 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	574 μCi	298 μCi	100%	100%	52%
2	501 μCi	251 μCi	100%	100%	50%
3	710 μCi	350 μCi	100%	99%	49%

RCY = 50 ± 1% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

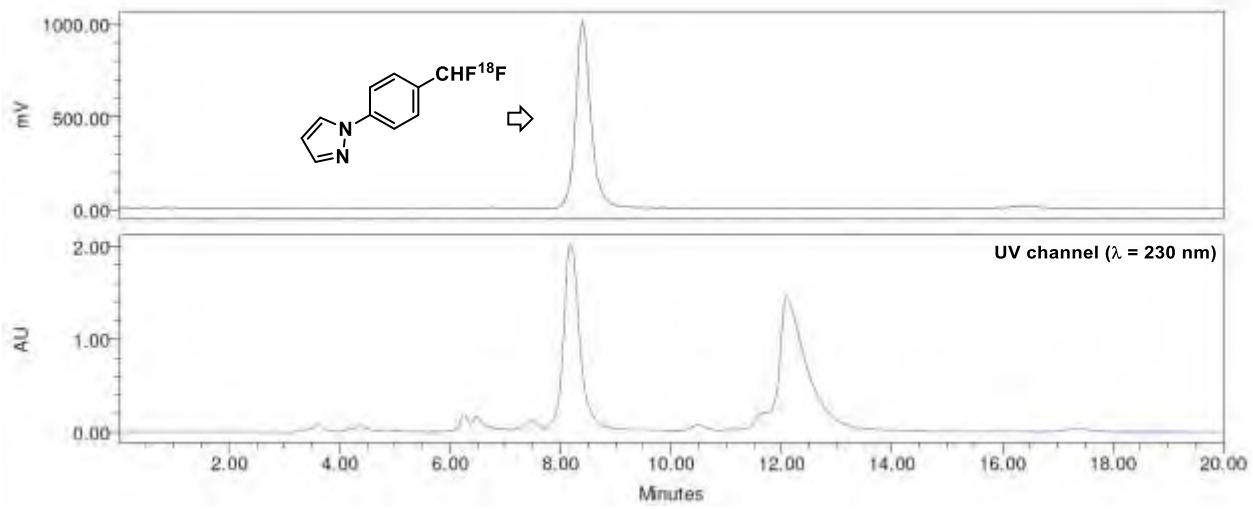
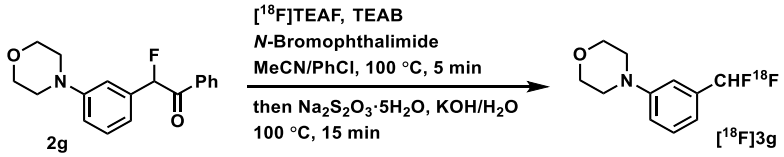


Figure S7. Co-injection radio HPLC chromatogram of **[^{18}F]3f**

[^{18}F]3-Morpholino-difluoromethylbenzene ([^{18}F]3g)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **1d** (3.0 mg, 10 μmol) and *N*-bromophthalimide (4.2 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, $Na_2S_2O_3·5H_2O$ (5 mg) and aqueous KOH solution (45 w%, 40 μL) were added. The mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	383 μCi	100 μCi	78%	60%	16%
2	394 μCi	105 μCi	75%	50%	13%
3	520 μCi	155 μCi	75%	60%	18%

RCY = 16 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 50% CH_3CN, 50% 0.1 M $NH_4·HCO_2$ (aq)

Flow rate: 1 mL/min

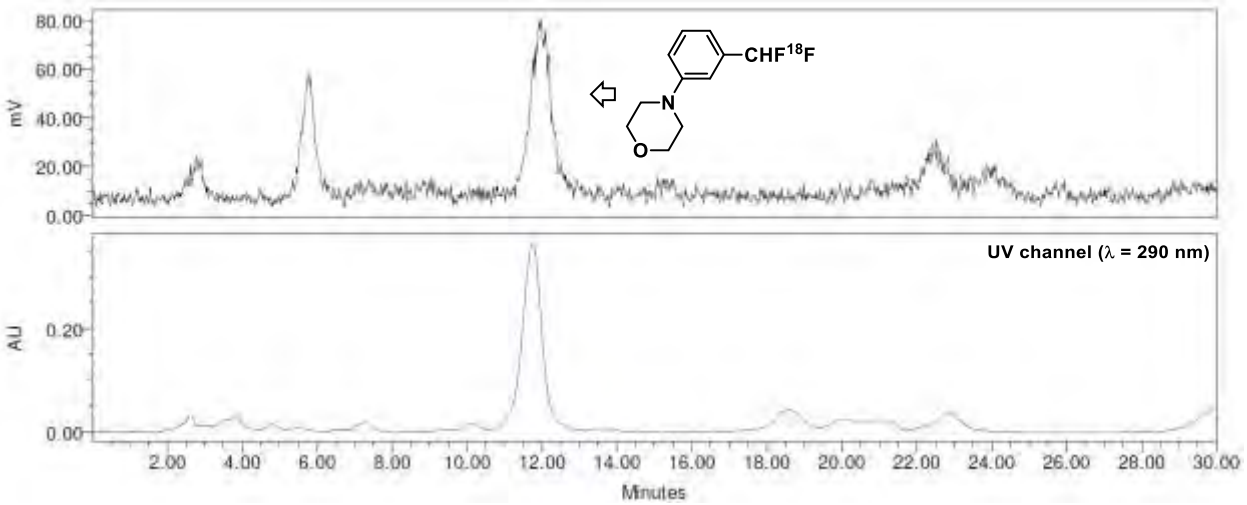
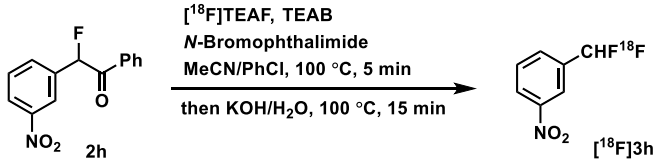


Figure S8. Co-injection radio HPLC chromatogram of **[^{18}F]3g**

[^{18}F]3-Nitro-difluoromethylbenzene ([^{18}F]3h)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2h** (2.6 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	356 μCi	156 μCi	99%	99%	43%
2	541 μCi	268 μCi	99%	99%	49%
3	474 μCi	230 μCi	99%	99%	48%

RCY = 47 ± 3% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

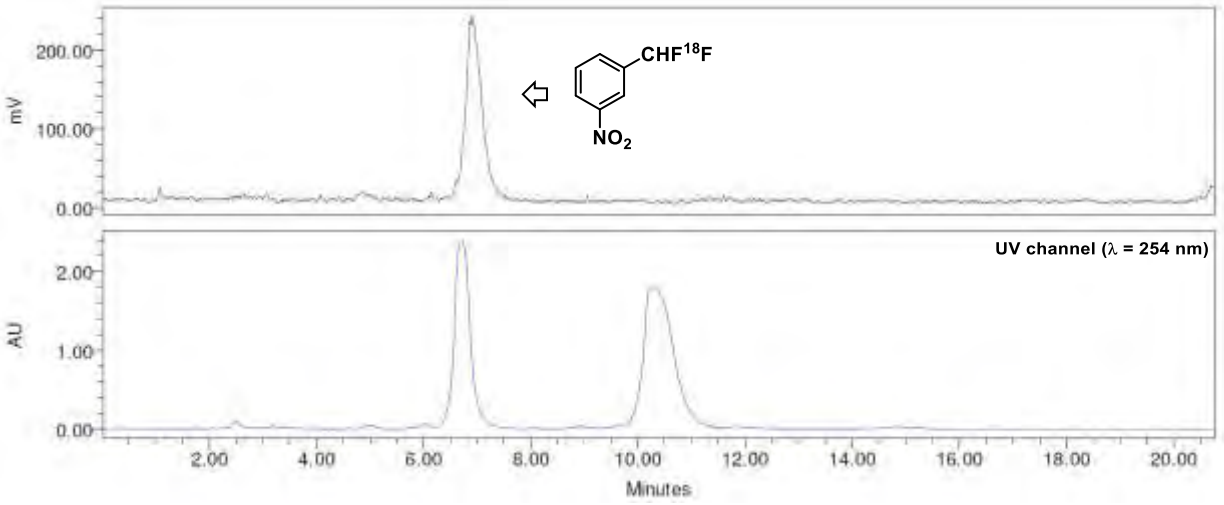
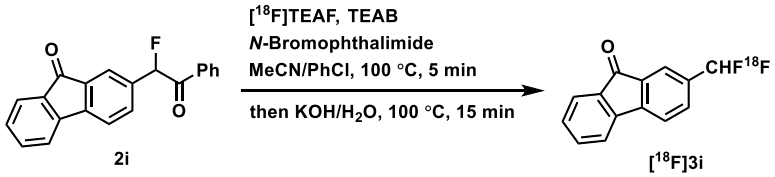


Figure S9. Co-injection radio HPLC chromatogram of **[^{18}F]3h**

[^{18}F]2-Difluoromethylfluoren-9-one ([^{18}F]3i)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2i** (3.2 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	160 μCi	66 μCi	99%	97%	40%
2	112 μCi	48 μCi	100%	100%	43%
3	375 μCi	150 μCi	100%	100%	40%

RCY = 41 ± 1% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 70% CH_3CN, 30% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

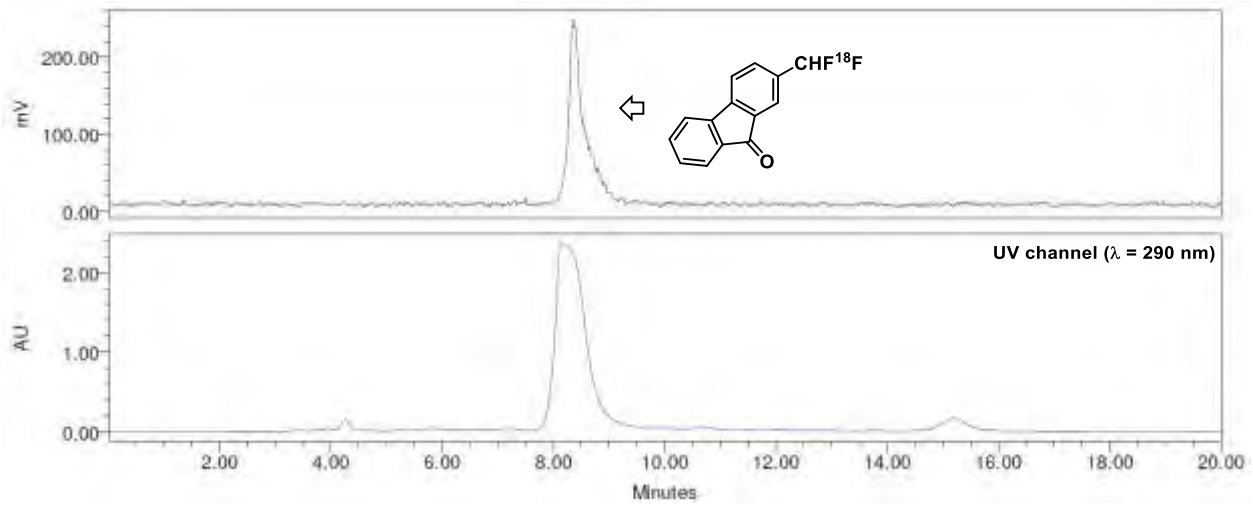
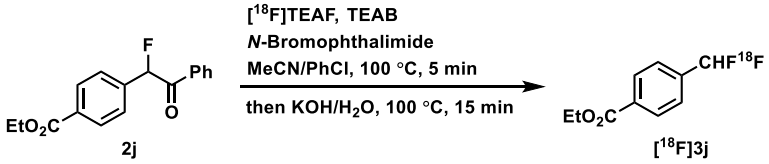


Figure S10. Co-injection radio HPLC chromatogram of **[^{18}F]3i**

[^{18}F]Ethyl 4-difluoromethyl-benzoate ([^{18}F]3j)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2j** (2.9 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 60 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	492 μCi	175 μCi	93%	80%	28%
2	757 μCi	205 μCi	98%	89%	24%
3	767 μCi	233 μCi	99%	81%	25%

RCY = 26 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

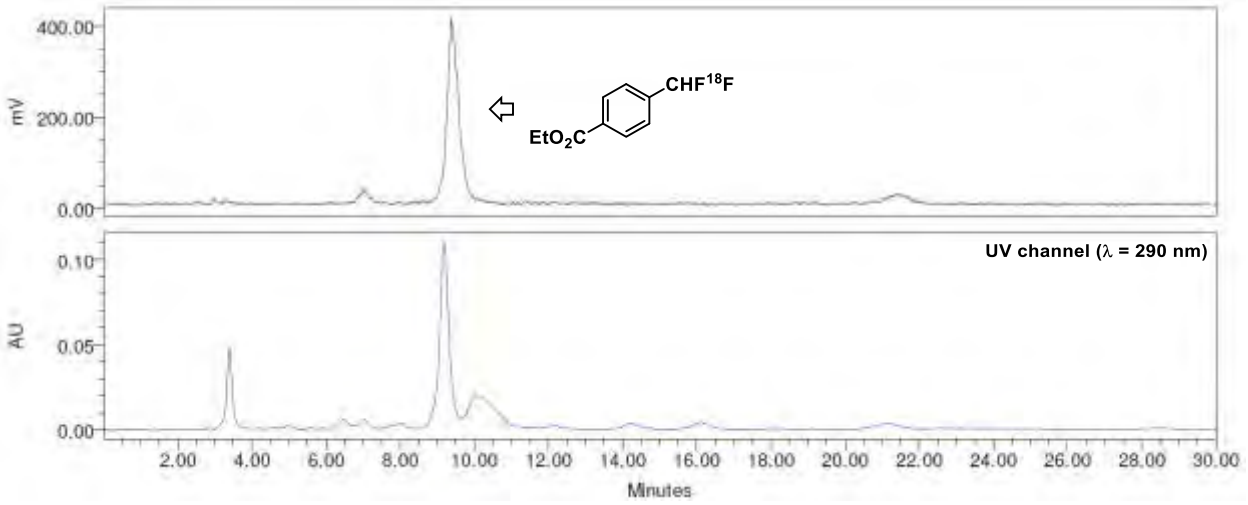
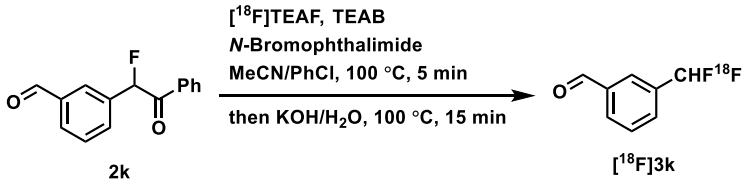


Figure S11. Co-injection radio HPLC chromatogram of **[^{18}F]3j**

[^{18}F]3-Difluoromethyl-benzoaldehyde ([^{18}F]3k)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2k** (3.5 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 60 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	501 μCi	115 μCi	85%	65%	15%
2	875 μCi	216 μCi	80%	40%	10%
3	784 μCi	175 μCi	85%	62%	14%

RCY = 13 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 50% CH_3CN, 50% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

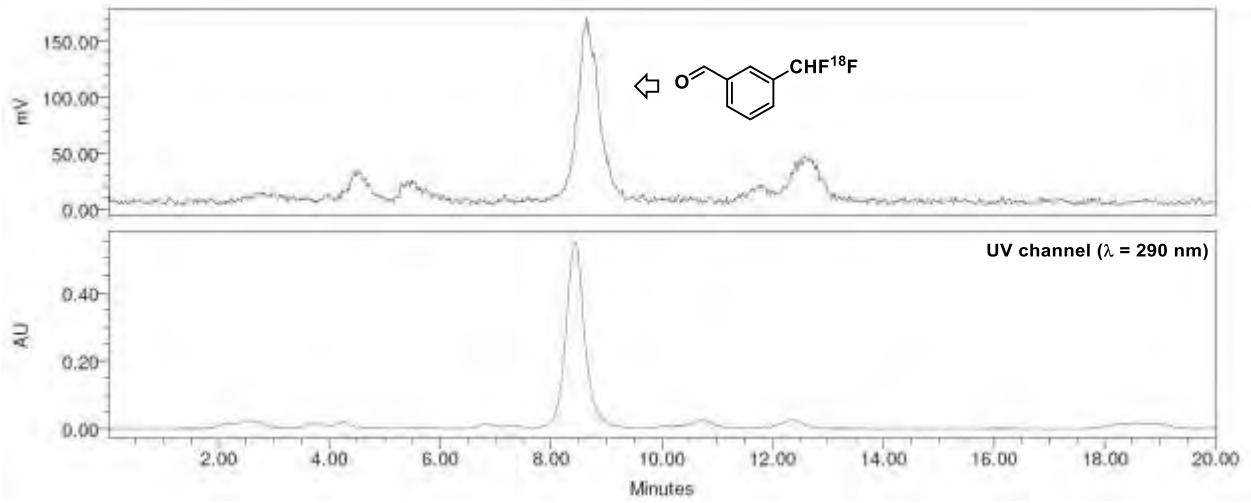
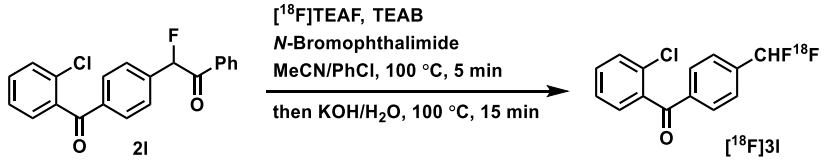


Figure S12. Co-injection radio HPLC chromatogram of **[^{18}F]3k**

[^{18}F]2-Chlorophenyl-(4-difluoromethyl)phenyl-methanone ([^{18}F]3l)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2l** (3.5 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	410 μCi	218 μCi	90%	100%	48%
2	449 μCi	210 μCi	92%	100%	43%
3	401 μCi	210 μCi	88%	100%	46%

RCY = 46 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 70% CH_3CN, 30% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

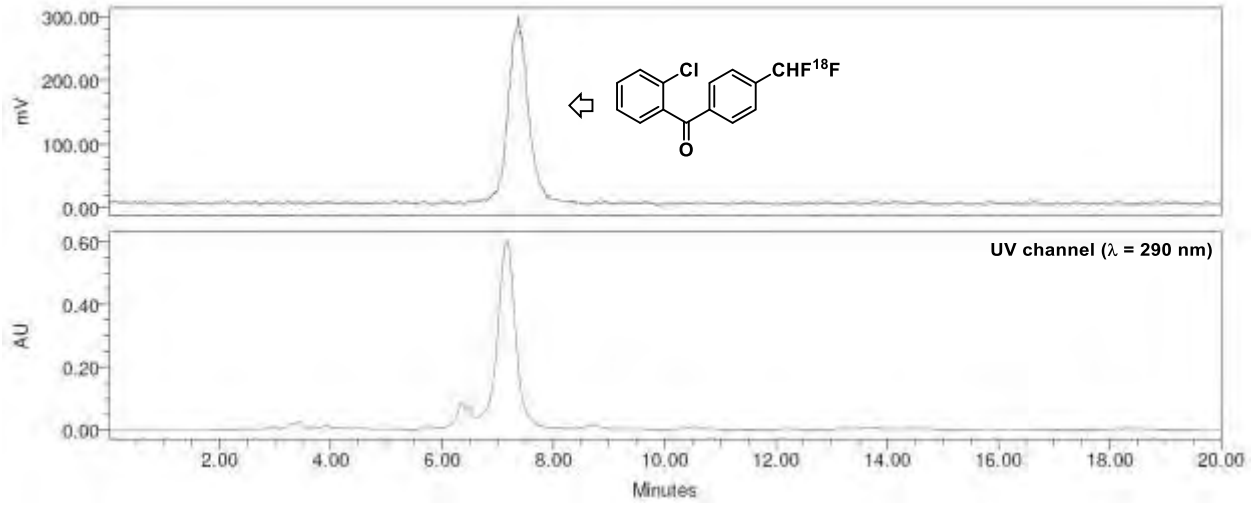
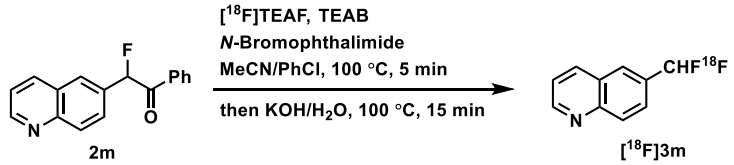


Figure S13. Co-injection radio HPLC chromatogram of **[^{18}F]3l**

[^{18}F]6-Difluoromethylquinoline ([^{18}F]3m)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2m** (2.7 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	PhCl	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	anhydrous	203 μCi	95 μCi	95%	100%	45%
2	anhydrous	343 μCi	175 μCi	100%	100%	51%
3	anhydrous	293 μCi	152 μCi	99%	100%	51%

RCY = 49 ± 3% (*n* = 3)

entry	PhCl	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	water saturated	478 μCi	234 μCi	100%	100%	49%
2	water saturated	551 μCi	266 μCi	95%	91%	44%
3	water saturated	490 μCi	235 μCi	99%	100%	47%

RCY = 47 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

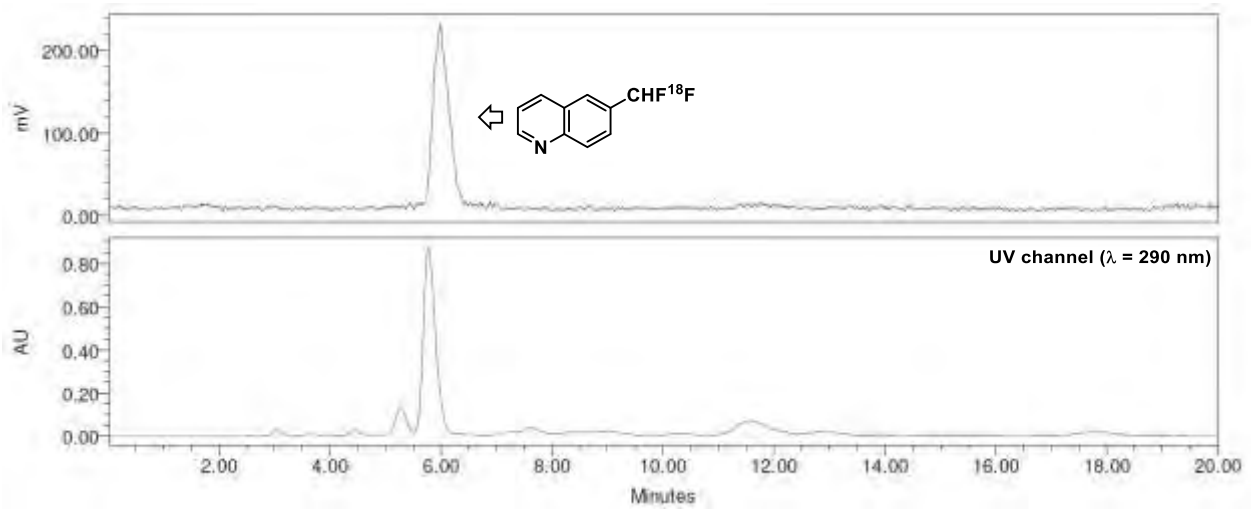
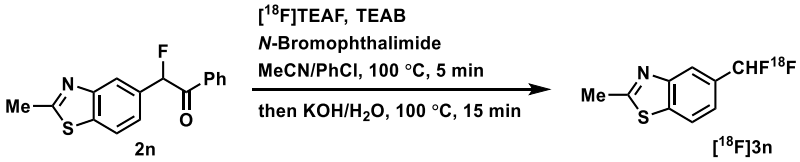


Figure S14. Co-injection radio HPLC chromatogram of **[^{18}F]3m**

[^{18}F]5-Difluoromethyl-2-methylbenzo[*d*]thiazole ([^{18}F]3n)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2n** (2.9 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	491 μCi	195 μCi	94%	95%	37%
2	444 μCi	173 μCi	96%	97%	37%
3	421 μCi	160 μCi	95%	95%	36%

RCY = 37 ± 1% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

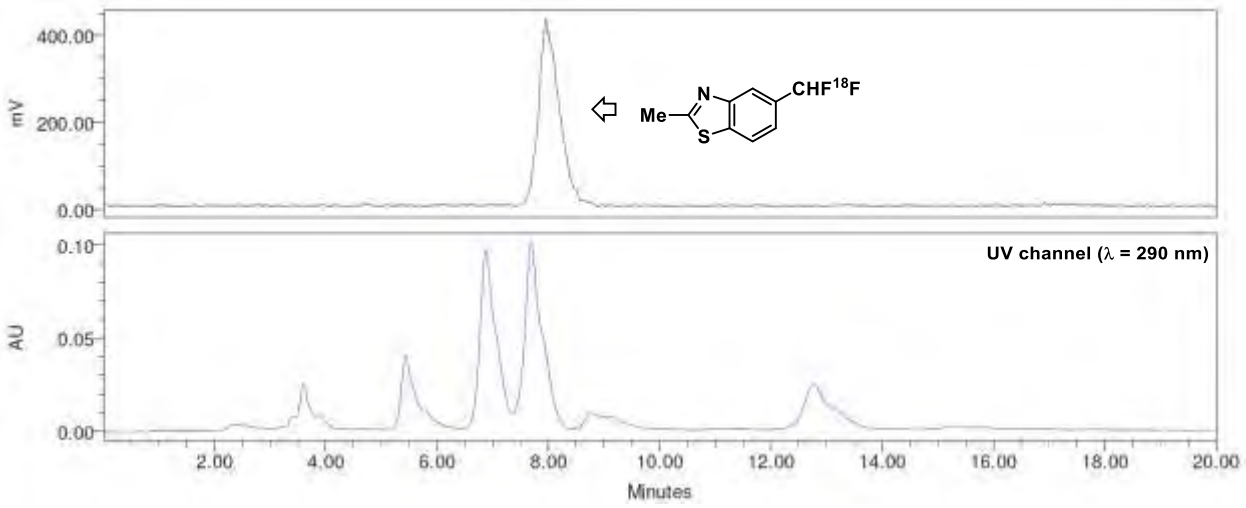
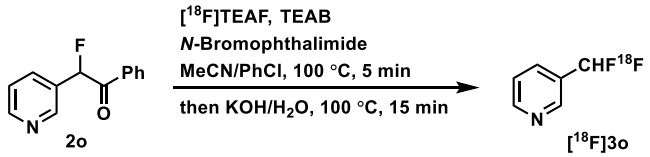


Figure S15. Co-injection radio HPLC chromatogram of **[^{18}F]3n**

[^{18}F]3-Difluoromethylpyridine ([^{18}F]3o)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2o** (2.2 mg, 10 μmol) and *N*-bromophthalimide (2 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridgeand eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	465 μCi	212 μCi	99%	100%	45%
2	524 μCi	200 μCi	99%	100%	38%
3	640 μCi	244 μCi	99%	100%	38%

RCY = 40 ± 3% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 30% CH_3CN, 70% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

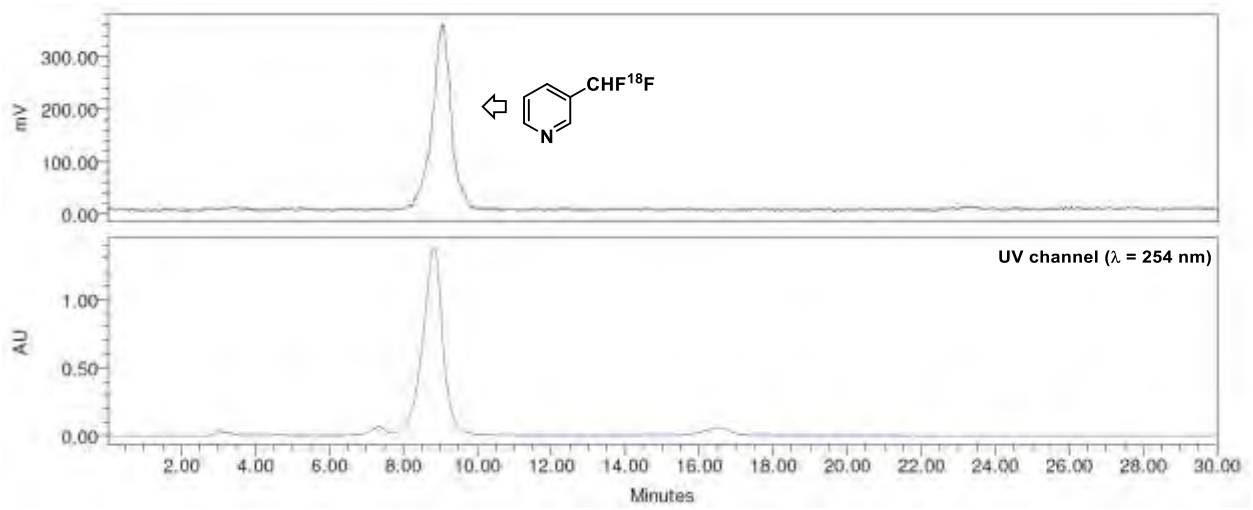
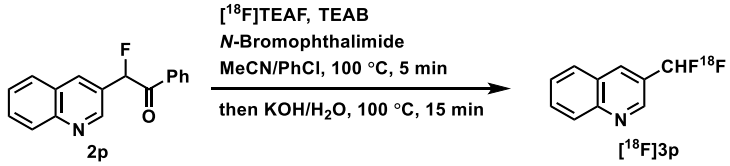


Figure S16. Co-injection radio HPLC chromatogram of **[^{18}F]3o**

The radioactivity balance of ^{18}F-labeling was measured. No significant volatile byproducts were detected.

entry	Initial radio-activity (t=0 min)	**[^{18}F]3o**	Radioactivity remained in vial, cartridge and syringe	Total measured radioactivity	Activity decay-corrected to t=0 min
1	140 μCi	58 μCi	60 μCi	118 μCi	138 μCi
2	744 μCi	268 μCi	362μCi	630 μCi	738 μCi
3	671 μCi	249 μCi	318 μCi	567 μCi	664 μCi

[^{18}F]3-Difluoromethylquinoline ([^{18}F]3p)



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **2p** (2.7 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	209 μCi	109 μCi	99%	100%	52%
2	214 μCi	100 μCi	99%	100%	46%
3	215 μCi	95 μCi	100%	100%	44%

RCY = 47 ± 3% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 50% CH_3CN, 50% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

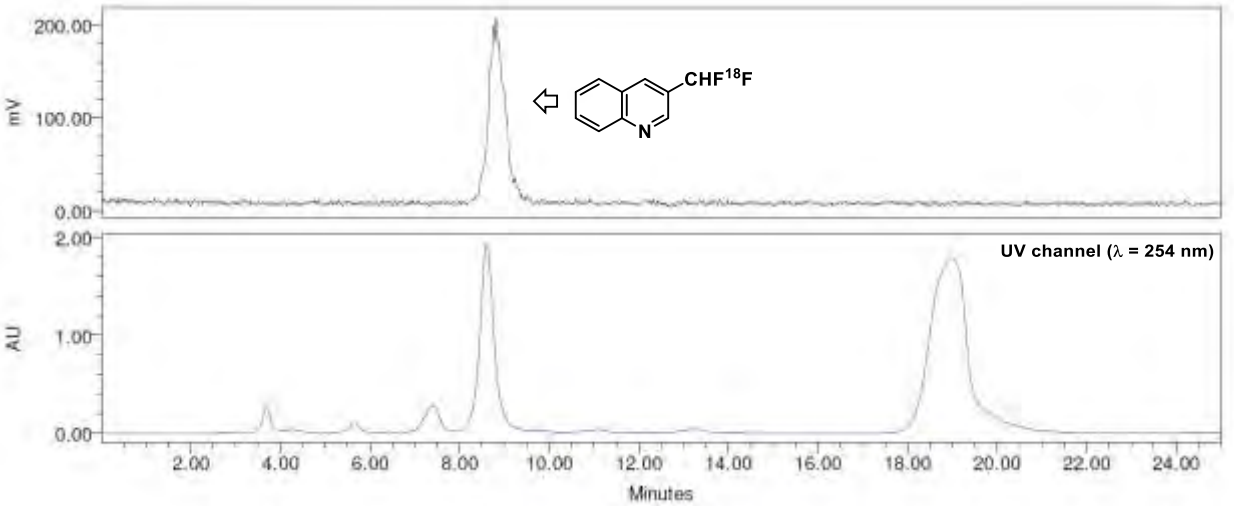
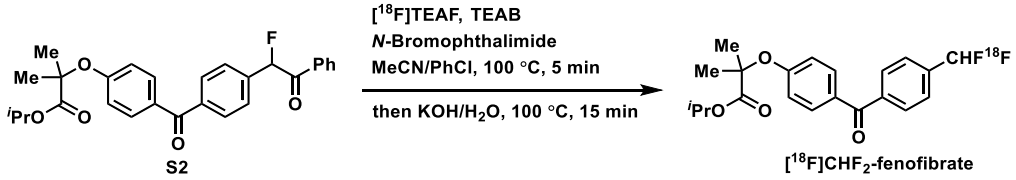


Figure S17. Co-injection radio HPLC chromatogram of **[^{18}F]3p**

[^{18}F]Difluoromethyl-fenofibrate



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **S2** (4.6 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	554 μCi	285 μCi	100%	100%	51%
2	489 μCi	216 μCi	100%	100%	44%
3	602 μCi	270 μCi	100%	100%	45%

RCY = 47 ± 3% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 70% CH_3CN, 30% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

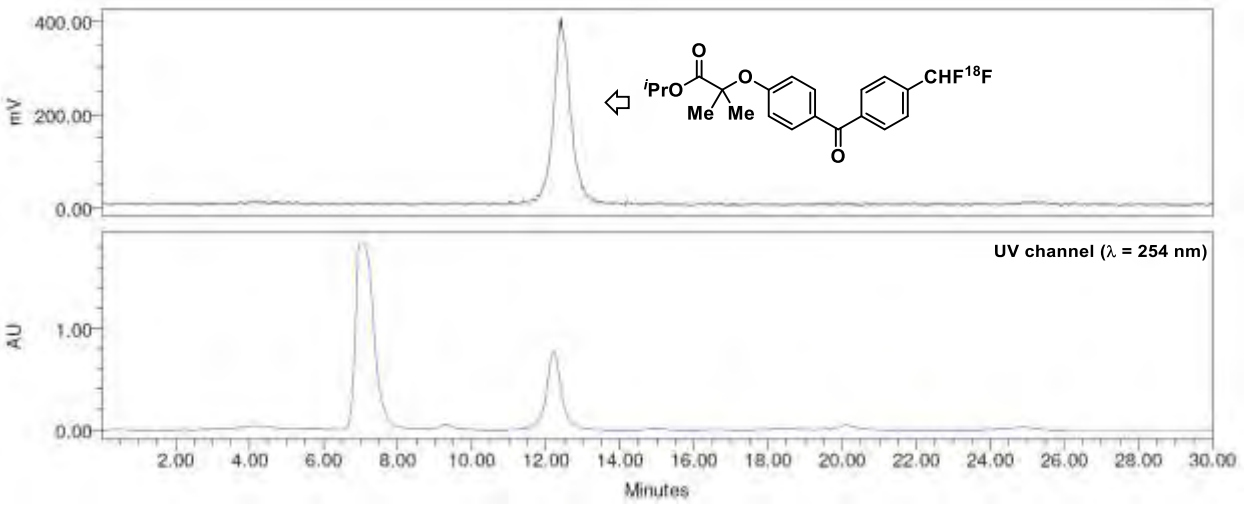
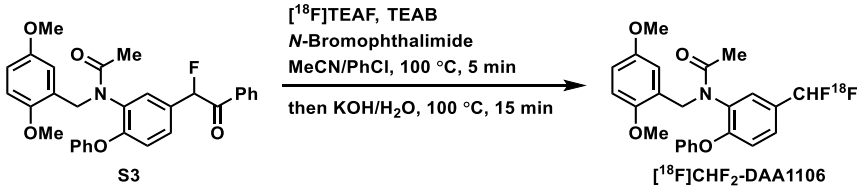


Figure S18. Co-injection radio HPLC chromatogram of **[^{18}F]CHF_2-fenofibrate**

[^{18}F]Difluoromethyl-DAA1106



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **S3** (5.1 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	542 µCi	171 µCi	100%	96%	30%
2	498 µCi	215 µCi	97%	98%	42%
3	442 µCi	158 µCi	99%	100%	35%

RCY = 36 ± 5% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

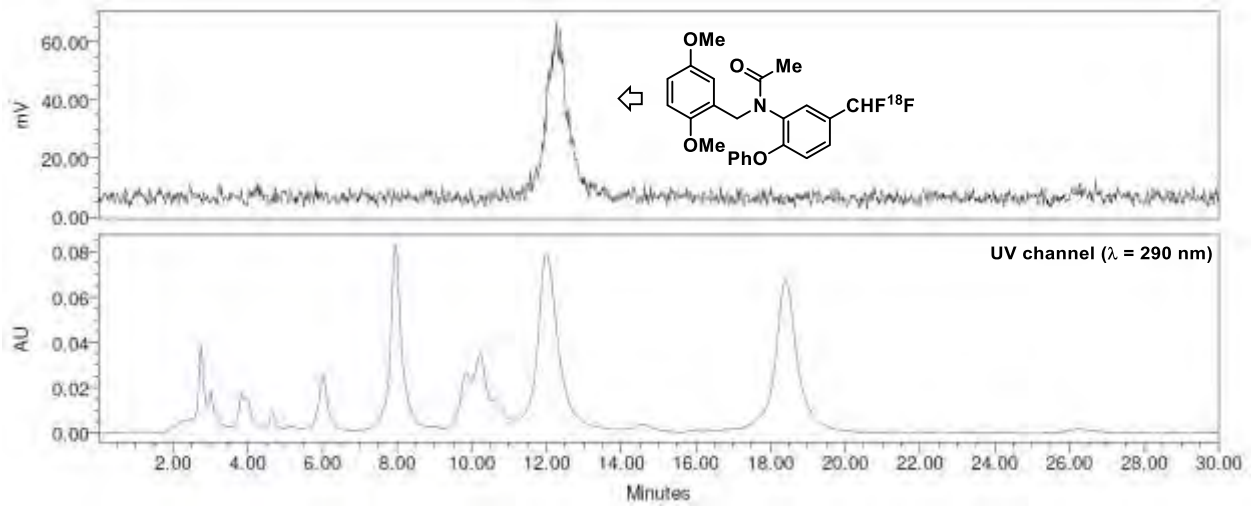
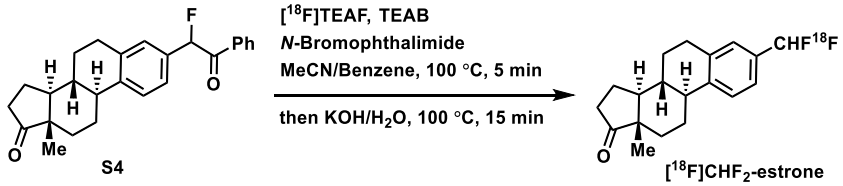


Figure S19. Co-injection radio HPLC chromatogram of **[^{18}F]CHF_2-DAA1106**

[^{18}F]Difluoromethyl-estrone



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **S4** (3.9 mg, 10 µmol) and *N*-bromophthalimide (2 mg) was added benzene (0.2 mL). Then solution A (20 µL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 60 µL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridgeand eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	616 μCi	122 μCi	94%	60%	12%
2	643 μCi	130 μCi	94%	53%	11%
3	670 μCi	122 μCi	90%	55%	10%

RCY = 11 ± 1% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 80% CH_3CN, 20% 0.1 M $NH_4 \cdot HCO_2$ (aq)

Flow rate: 1 mL/min

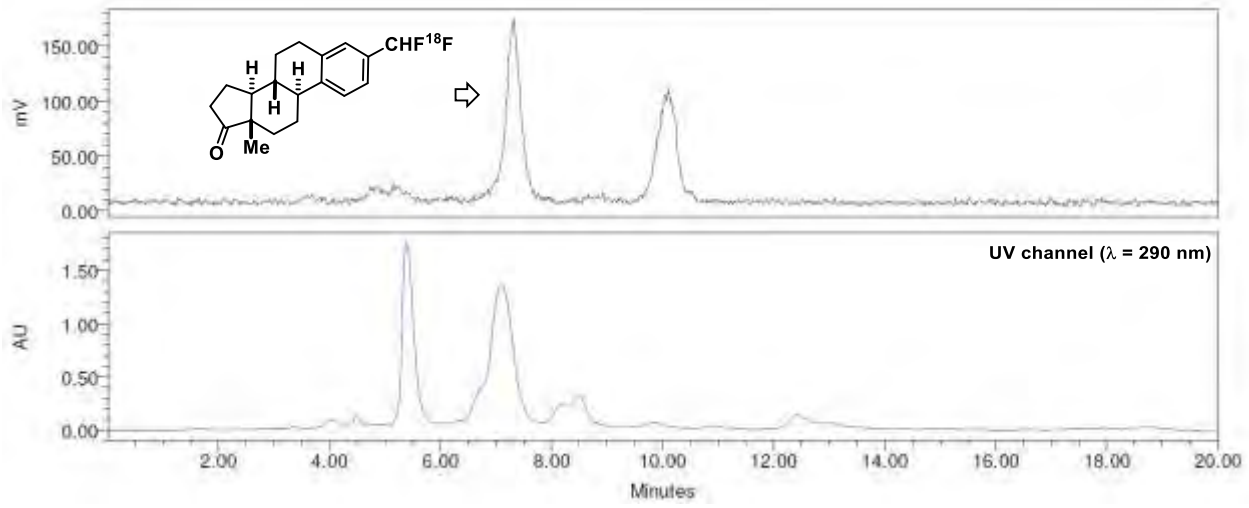
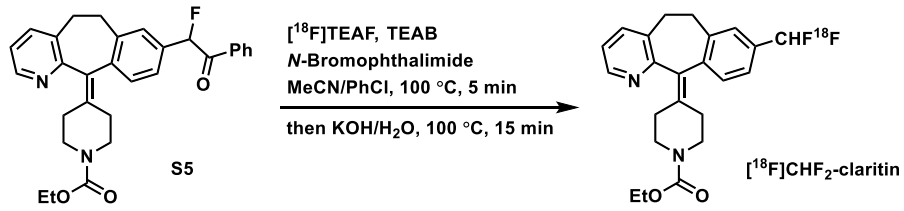


Figure S20. Co-injection radio HPLC chromatogram of **[^{18}F]CHF_2-estrone**

[^{18}F]Difluoromethyl-claritin



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **S5** (4.8 mg, 10 μmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 60 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	515 µCi	190 µCi	94%	55%	20%
2	729 µCi	243 µCi	98%	72%	24%
3	647 µCi	173 µCi	98%	75%	20%

RCY = 21 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4 \cdot HCO_2$ (aq)

Flow rate: 1 mL/min

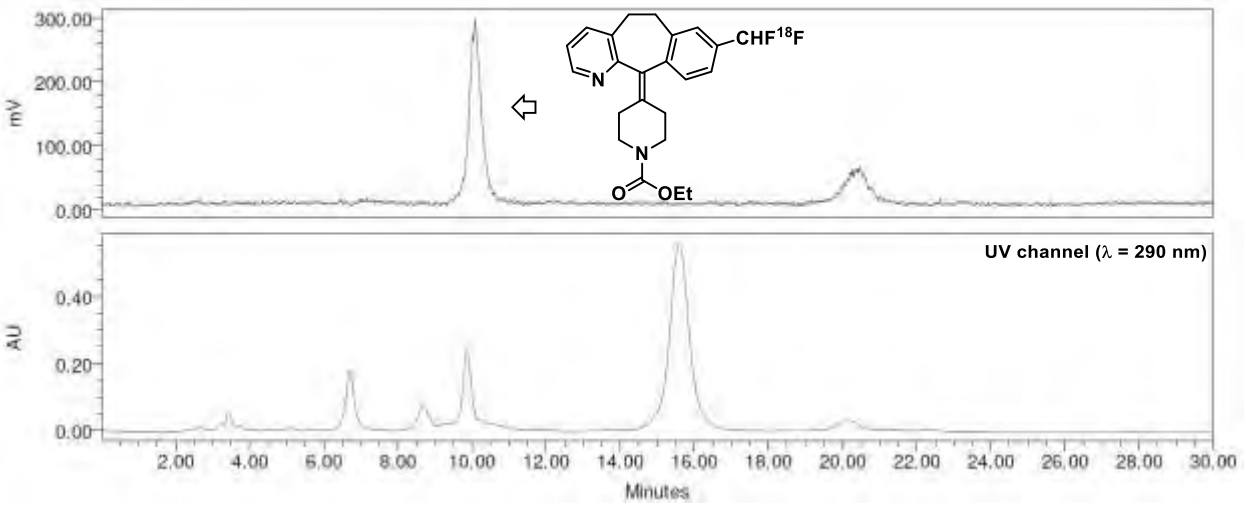
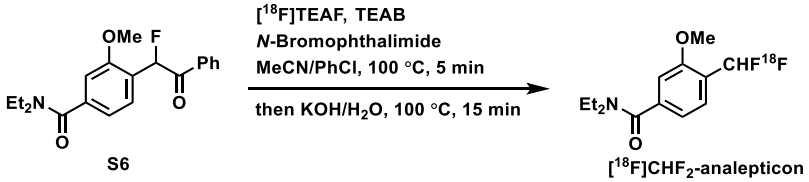


Figure S21. Co-injection radio HPLC chromatogram of **[^{18}F]CHF_2-claritin**

[^{18}F]Difluoromethyl-analepticon



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **S6** (3.4 mg, 10 µmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 µL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 µL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	880 µCi	115 µCi	99%	90%	12%
2	885 µCi	90.5 µCi	98%	87%	9%
3	768 µCi	98.4 µCi	99%	86%	11%

RCY = 11 ± 1% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

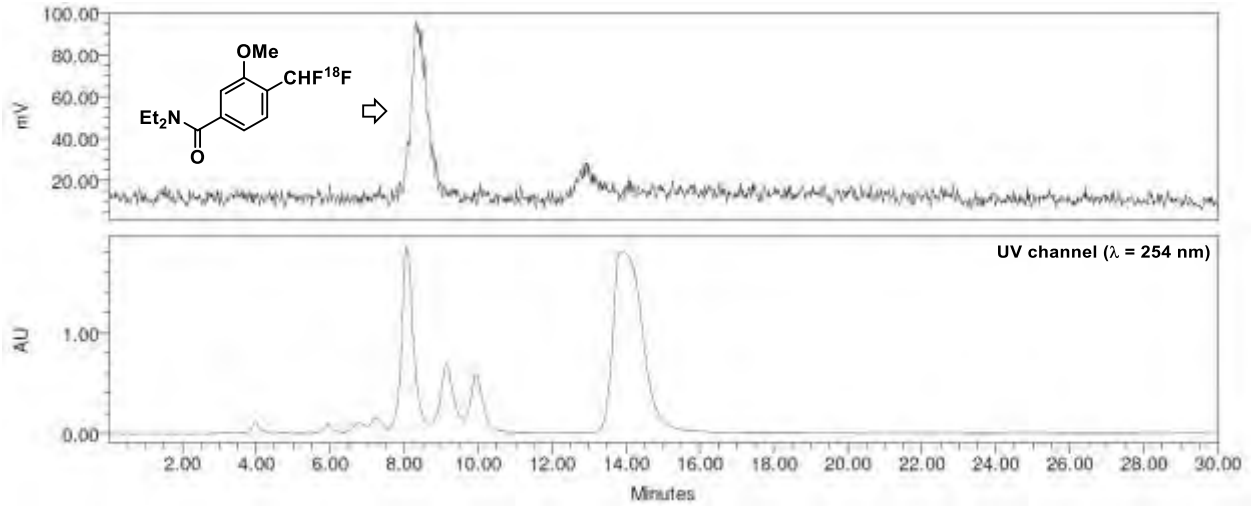
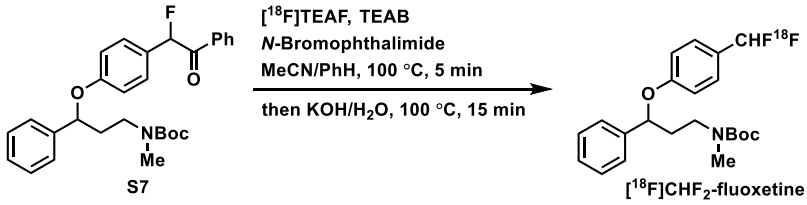


Figure S22. Co-injection radio HPLC chromatogram of **[^{18}F]CHF_2-analepticon**

[^{18}F]Difluoromethyl-fluoxetine



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **S7** (4.6 mg, 10 µmol) and *N*-bromophthalimide (2.0 mg) was added benzene (0.2 mL). Then solution A (20 µL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 60 µL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical purity and product identity. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	482 µCi	145 µCi	96%	65%	20%
2	410 µCi	120 µCi	98%	60%	18%
3	739 µCi	175 µCi	96%	58%	14%

RCY = 17 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 80% CH_3CN, 20% 0.1 M $NH_4 \cdot HCO_2$ (aq)

Flow rate: 1 mL/min

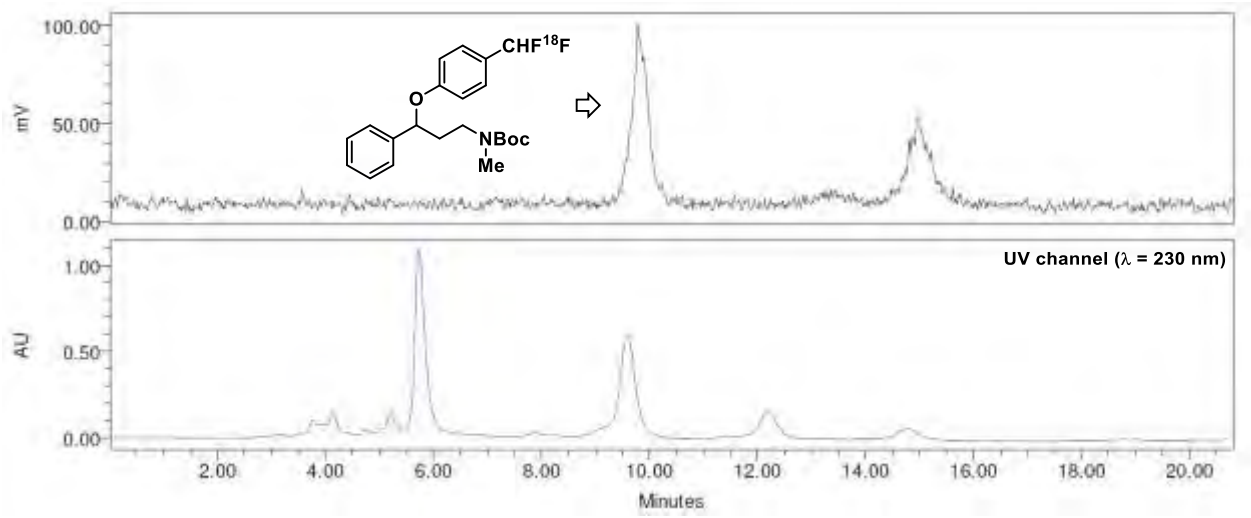
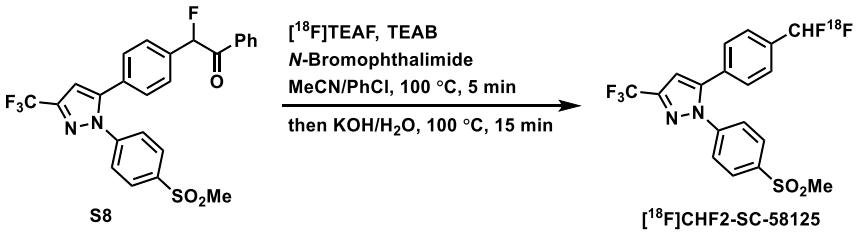


Figure S23. Co-injection radio HPLC chromatogram of **[^{18}F]CHF$_2$-fluoxetine**

[^{18}F]Difluoromethyl-SC-58125



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **S8** (5.0 mg, 10 µmol) and *N*-bromophthalimide (2.0 mg) was added chlorobenzene (0.2 mL). Then solution A (20 µL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 µL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical yield, purity and product identity respectively. The

radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	770 μCi	379 μCi	99%	100%	49%
2	732 μCi	346 μCi	99%	100%	47%
3	700 μCi	315 μCi	99%	100%	45%

RCY = 47 ± 2% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 70% CH_3CN, 30% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

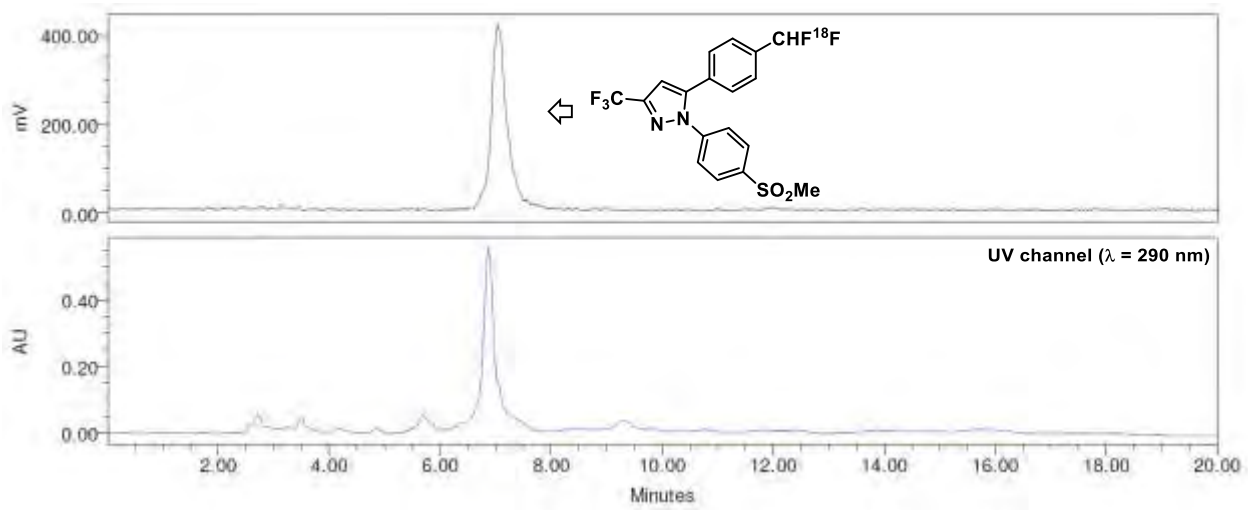
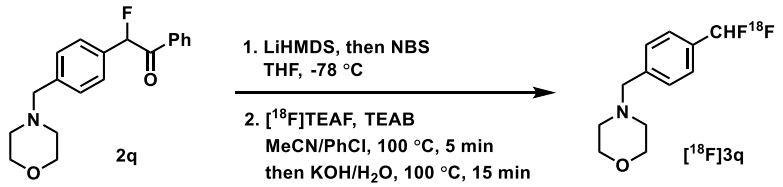


Figure S24. Co-injection radio HPLC chromatogram of **[^{18}F]CHF_2-SC-58125**

[^{18}F]4-Morpholinomethyl-difluoromethylbenzene ([^{18}F]3q)



Compound **2q** (mg, 10 μmol, 1.0 equiv.) was dissolved in dry THF (0.25 mL). LiHMDS (1.0 M in THF, 12 μL, 12 μmol, 1.2 equiv.) was added at −78 °C, and then the reaction mixture was stirred for 45 min. A solution of NBS (1.8 mg, 10 μmol, 1.0 equiv.) in THF (0.1 mL) was added. The reaction mixture was stirred at −78 °C for 45 min, and evaporated under vacuum at room temperature. Toluene (0.4 mL) was added and the mixture was filtered through glass microfibre into a 1-dram (4 mL) glass vial and eluted with toluene (2 × 0.4 mL). The filtrate was evaporated under reduced pressure. TEAB (3.0 mg) and chlorobenzene (0.2 mL) were added into the vial. Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added,

and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical yield, purity and product identity respectively. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	765 μCi	205 μCi	90%	75%	20%
2	802 μCi	202 μCi	93%	72%	18%
3	642 μCi	163 μCi	91%	71%	18%

RCY = 19 ± 1% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

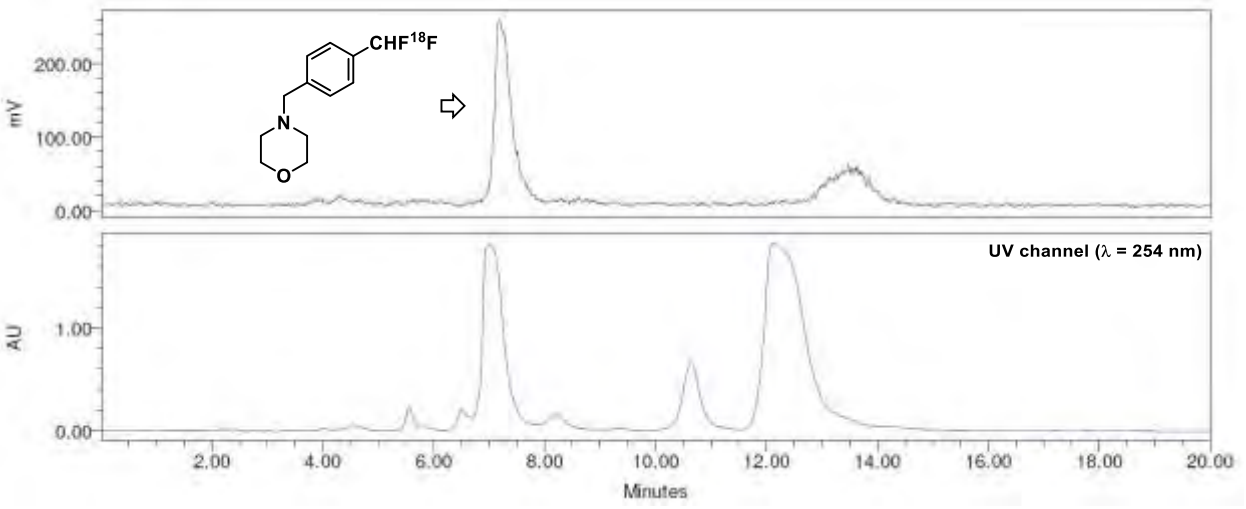
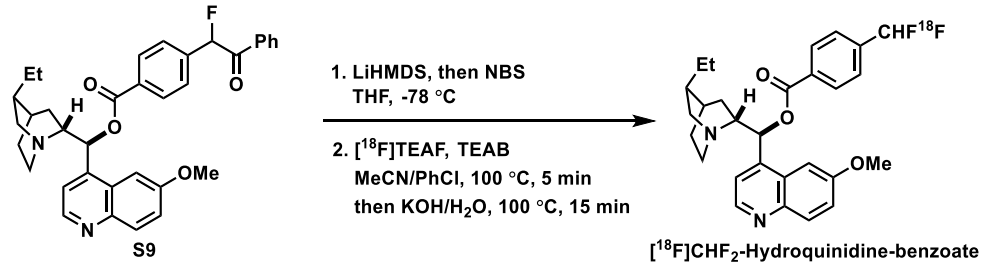


Figure S25. Co-injection radio HPLC chromatogram of **[^{18}F]3q**

[^{18}F]Hydroquinidine 4-difluoromethylbenzoate



Compound **S9** (5.7 mg, 10 μmol, 1.0 equiv.) was dissolved in dry THF (0.25 mL). LiHMDS (1.0 M in THF, 12

μL, 12 μmol, 1.2 equiv.) was added at −78 °C, and then the reaction mixture was stirred for 45 min. A solution of NBS (1.8 mg, 10 μmol, 1.0 equiv.) in THF (0.1 mL) was added. The reaction mixture was stirred at −78 °C for 45 min, and evaporated under vacuum at room temperature. Toluene (0.4 mL) was added and the mixture was filtered through glass microfibre into a 1-dram (4 mL) glass vial and eluted with toluene (2 × 0.4 mL). The filtrate was evaporated under reduced pressure. TEAB (3.0 mg) and chlorobenzene (0.2 mL) were added into the vial. Then solution A (20 μL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 μL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled down to room temperature and added MeCN (0.4 mL). The mixture was filtered through light silica cartridge and eluted with MeCN (2 × 0.8 mL). The radioactivity of the combined filtrate was measured to calculate the radiochemical yield. An aliquot from combined filtrate was removed and analyzed by radio TLC and HPLC for radiochemical yield, purity and product identity respectively. The radiochemical yield was corrected by the radiochemical purity, the lower one of radio TLC or HPLC.

entry	Initial radio-activity	Collected radio-activity	Radio-TLC purity	Radio-HPLC purity	RCY
1	636 μCi	214 μCi	90%	95%	30%
2	571 μCi	147 μCi	88%	90%	23%
3	544 μCi	166 μCi	85%	91%	26%

RCY = 26 ± 3% (*n* = 3)

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

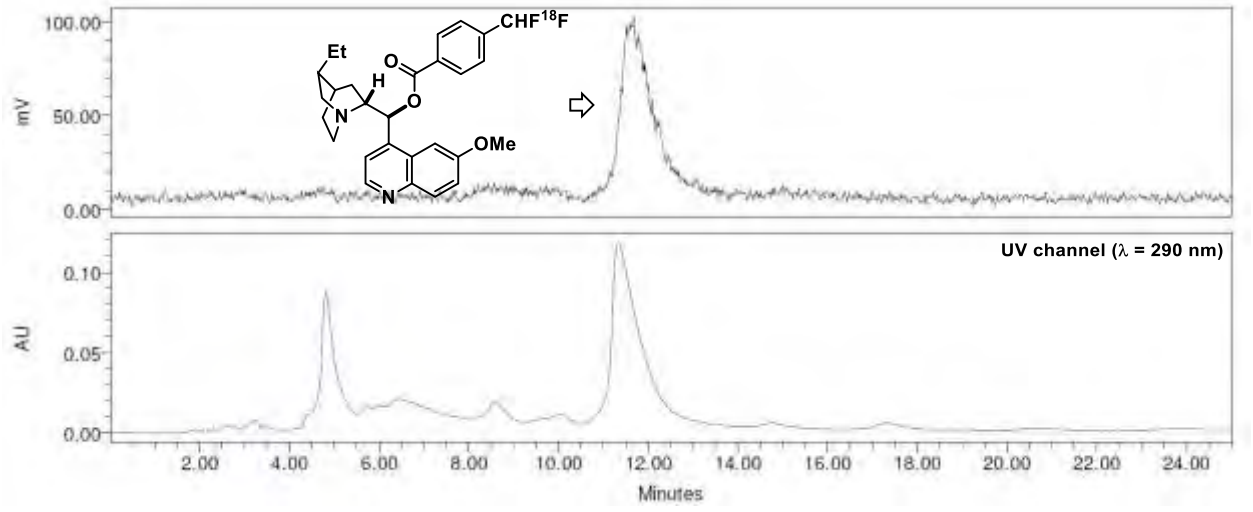


Figure S26. Co-injection radio HPLC chromatogram of **[^{18}F]CHF_2-hydroquinidine-benzoate**

HPLC Separation

[^{18}F]Fluoride was prepared for radiofluorination by the following method: ^{18}F-fluoride aqueous solution was

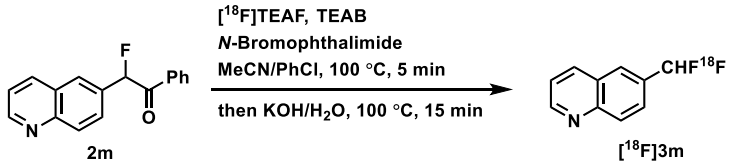
loaded onto a Sep-Pak® QMA cartridge. The cartridge was eluted with a solution of tetraethylammonium bicarbonate (TEAB, 2 mg) in acetonitrile and water (1 mL, v/v 7:3). The [^{18}F]TEAF/TEAB solution was collected in a V−shaped vial and sealed with a teflon-lined septum. The vial was heated to 110 °C while nitrogen gas was passed through a P_2O_5-Drierite™ column followed by a vented needle. When no liquid was visible in the vial, it was removed from heat, anhydrous acetonitrile (1 mL) was added, and the heating was resumed until dryness. This step was repeated an additional two times. The vial was then cooled down to room temperature under nitrogen flow (10 mL/min). The contents were redissolved in the anhydrous acetonitrile (20 µL, solution B).

To a 1-dram (4 mL) glass vial containing TEAB (1.5 mg), precursor **2** (10 µmol) and *N*-bromophthalimide (2 mg) was added chlorobenzene (0.2 mL). Then solution B (20 µL) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 µL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled to room temperature. The reaction mixture was loaded on a light silica cartridge. Hexane (0.5 mL) was added into the reaction vessel, and the formed mixture was used to wash the silica cartridge. The silica cartridge was dried by nitrogen gas for 10 seconds, and then eluted with MeCN (2 x 1 mL). 0.1 M $NH_4 \cdot HCO_2$ aqueous solution (1 mL) was added into the combined MeCN filtrate, and the formed solution was subjected to purification by semi-preparative HPLC. The fraction corresponding to radiolabeled product was collected and was measured to calculate the radiochemical yield.

Table S3

Compound	Decay-corrected RCY (SPE)	Decay-corrected RCY (HPLC)
[^{18}F]Difluoromethyl-SC-58125	55%	51%
[^{18}F]6-Difluoromethylquinoline	57%	57%
[^{18}F]Difluoromethyl-fenofibrate	55%	54%

[^{18}F]6-Difluoromethylquinoline ([^{18}F]3m)



To a 1-dram (4 mL) glass vial containing TEAB (1.5 mg), precursor **2m** (10 µmol, 2.7 mg) and *N*-bromophthalimide (2 mg) was added chlorobenzene (0.2 mL). Then solution B (20 µL, 2.08 mCi) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 µL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled to room temperature. The reaction mixture was loaded on a light silica cartridge. Hexane (0.5 mL) was added into the reaction vessel, and the formed mixture was used to wash the silica cartridge. The silica cartridge was dried by nitrogen gas for 10 seconds, and then eluted with MeCN

(2 x 1 mL). 0.1 M $NH_4 \cdot HCO_2$ aqueous solution (1 mL) was added into the combined MeCN filtrate, and the formed solution was subjected to purification by semi-preparative HPLC. The fraction corresponding to radiolabeled product was collected and was measured to contain 0.892 mCi.

Initial radio-activity	**[^{18}F]3m**	RCY (HPLC)	Time in total	Decay-corrected RCY (HPLC)
2.08 mCi	0.89 mCi	43%	45 min	57%

Radio HPLC chromatogram:

Column: XBridge Shield RP 18 3.5 µm 100 × 4.6 mm

Mobile phase: 25% CH_3CN, 75% 0.1 M $NH_4 \cdot HCO_2$ (aq)

Flow rate: 1 mL/min

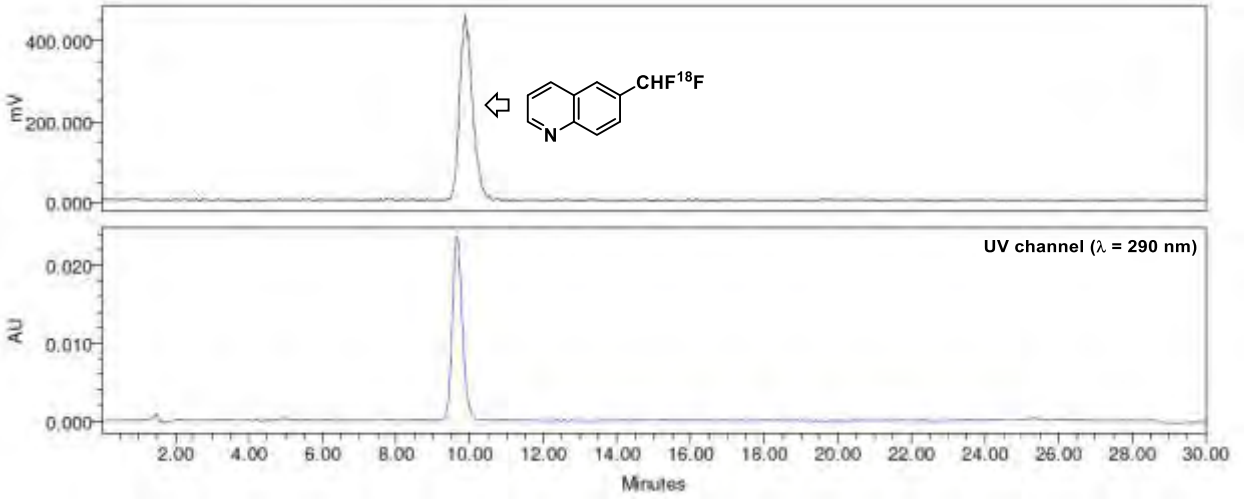


Figure S27. HPLC chromatogram (XBridge) of **[^{18}F]6-difluoromethylquinoline**

Radio HPLC chromatogram:

Column: Synergi 4u Hydro-RP 80A 4 µm 150 × 4.6 mm

Mobile phase: 40% CH_3CN, 60% 0.1 M $NH_4 \cdot HCO_2$ (aq)

Flow rate: 1 mL/min

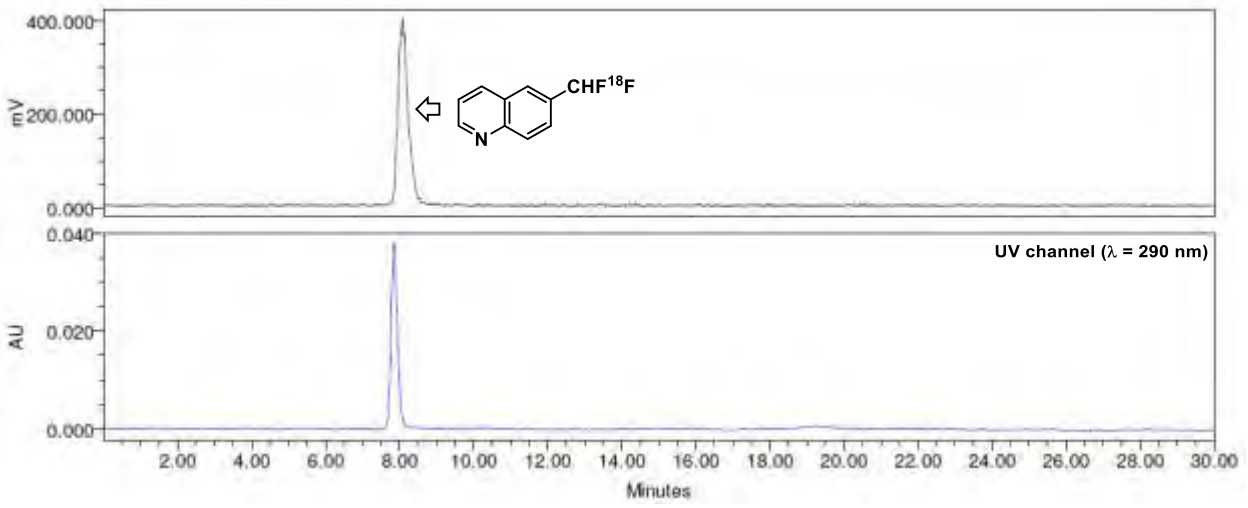


Figure S28. HPLC chromatogram (Synergi) of **[^{18}F]6-difluoromethylquinoline**

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 50% CH_3CN, 50% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

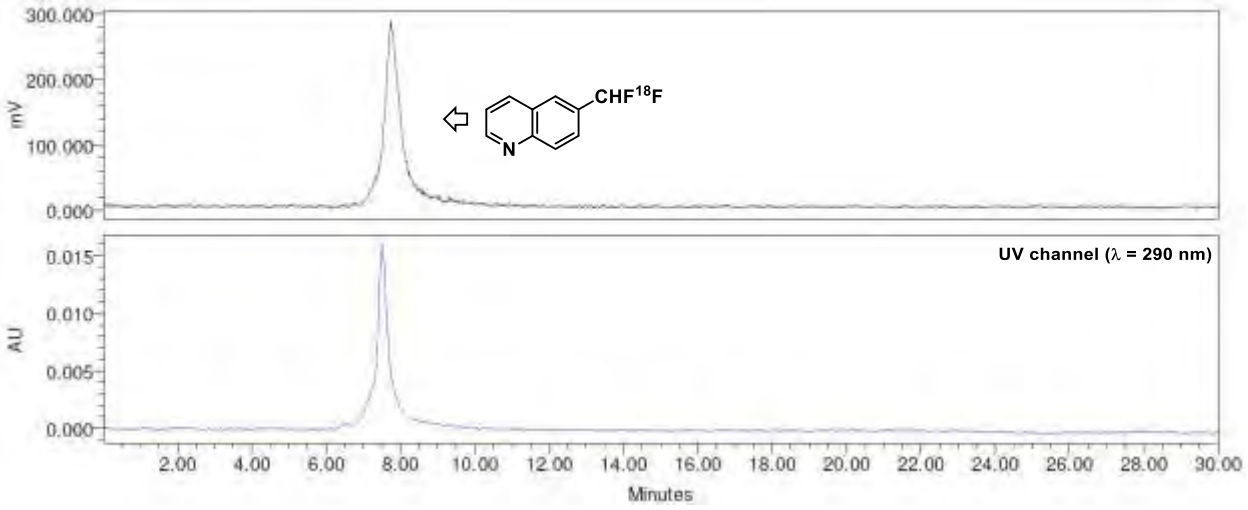
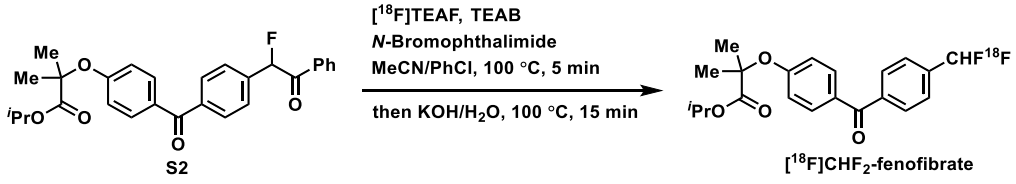


Figure S29. HPLC chromatogram (Luna) of **[^{18}F]6-difluoromethylquinoline**

[^{18}F]Difluoromethyl-fenofibrate



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **S2** (10 μmol, 4.6 mg) and *N*-bromophthalimide (2 mg) was added chlorobenzene (0.2 mL). Then solution A (20 μL, 3.37 mCi) was added

and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 µL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled to room temperature. The reaction mixture was loaded on a light silica cartridge. Hexane (0.5 mL) was added into the reaction vessel, and the formed mixture was used to wash the silica cartridge. The silica cartridge was dried by nitrogen gas for 10 seconds, and then eluted with MeCN (2 x 1 mL). 0.1 M $NH_4 \cdot HCO_2$ aqueous solution (1 mL) was added into the combined MeCN filtrate, and the formed solution was subjected to purification by semi-preparative HPLC. The fraction corresponding to radiolabeled product was collected and was measured to contain 1.32 mCi.

Initial radio-activity	**[^{18}F]Difluoromethyl-fenofibrate**	RCY (HPLC)	Time in total	Decay-corrected RCY (HPLC)
3.37 mCi	1.32 mCi	39%	50 min	54%

Radio HPLC chromatogram:

Column: XBridge Shield RP 18 3.5 µm 100 × 4.6 mm

Mobile phase: 45% CH_3CN, 55% 0.1 M $NH_4 \cdot HCO_2$ (aq)

Flow rate: 1 mL/min

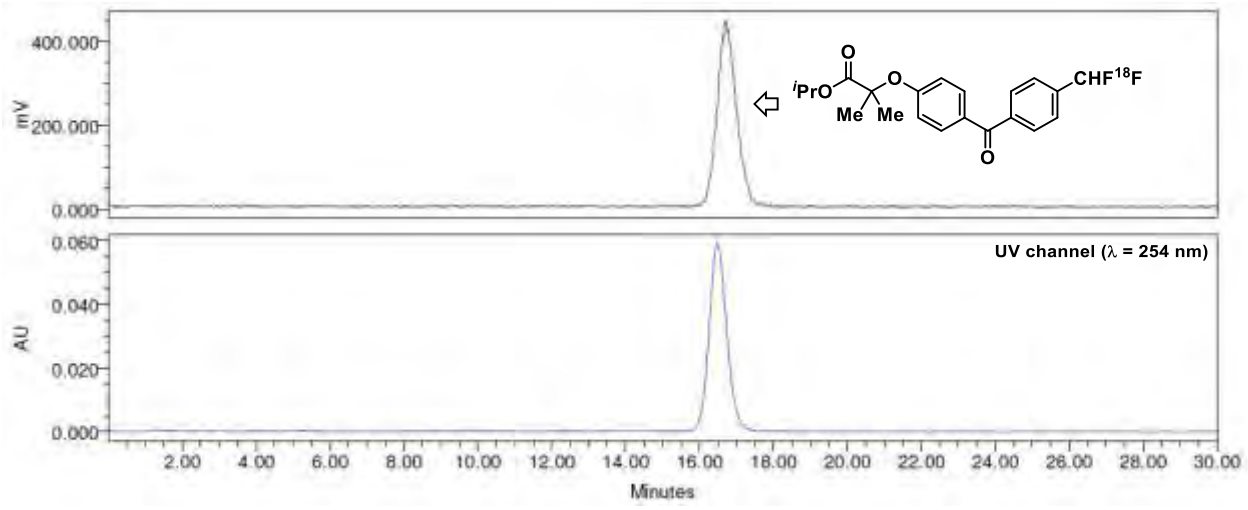


Figure S30. HPLC chromatogram (XBridge) of **[^{18}F]difluoromethyl-fenofibrate**

Radio HPLC chromatogram:

Column: Synergi 4u Hydro-RP 80A 4 µm 150 × 4.6 mm

Mobile phase: 65% CH_3CN, 35% 0.1 M $NH_4 \cdot HCO_2$ (aq)

Flow rate: 1 mL/min

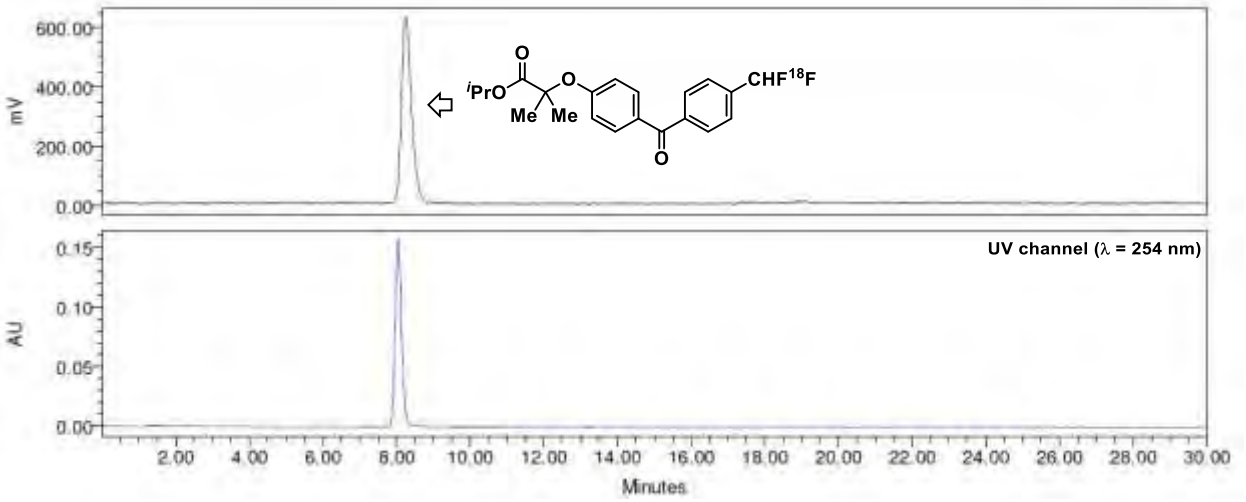


Figure S31. HPLC chromatogram (Synergi) of **[^{18}F]difluoromethyl-fenofibrate**

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 70% CH_3CN, 30% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

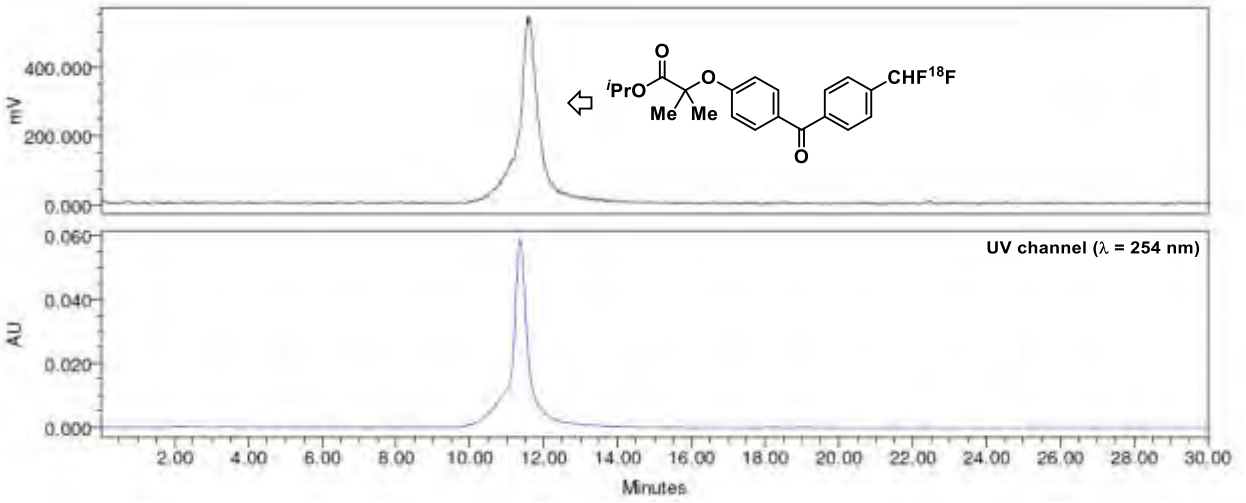
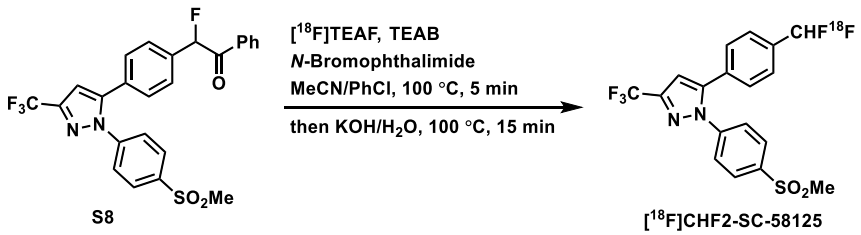


Figure S32. HPLC chromatogram (Luna) of **[^{18}F]difluoromethyl-fenofibrate**

[^{18}F]Difluoromethyl-SC-58125



To a 1-dram (4 mL) glass vial containing TEAB (3.0 mg), precursor **S8** (10 µmol, 5 mg) and *N*-

bromophthalimide (2 mg) was added chlorobenzene (0.2 mL). Then solution A (20 µL, 3.77 mCi) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After that, aqueous KOH solution (45 w%, 40 µL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled to room temperature. The reaction mixture was loaded on a light silica cartridge. Hexane (0.5 mL) was added into the reaction vessel, and the formed mixture was used to wash the silica cartridge. The silica cartridge was dried by nitrogen gas for 10 seconds, and then eluted with MeCN (2 x 1 mL). 0.1 M $NH_4 \cdot HCO_2$ aqueous solution (1 mL) was added into the combined MeCN filtrate, and the formed solution was subjected to purification by semi-preparative HPLC. The fraction corresponding to radiolabeled product was collected and was measured to contain 1.39 mCi.

Initial radio-activity	**[^{18}F]Difluoromethyl-SC-58125**	RCY (HPLC)	Time in total	Decay-corrected RCY (HPLC)
3.77 mCi	1.39 mCi	37%	50 min	51%

Radio HPLC chromatogram:
Column: XBridge Shield RP 18 3.5 µm 100 × 4.6 mm
Mobile phase: 50% CH_3CN, 50% 0.1 M $NH_4 \cdot HCO_2$ (aq)
Flow rate: 1 mL/min

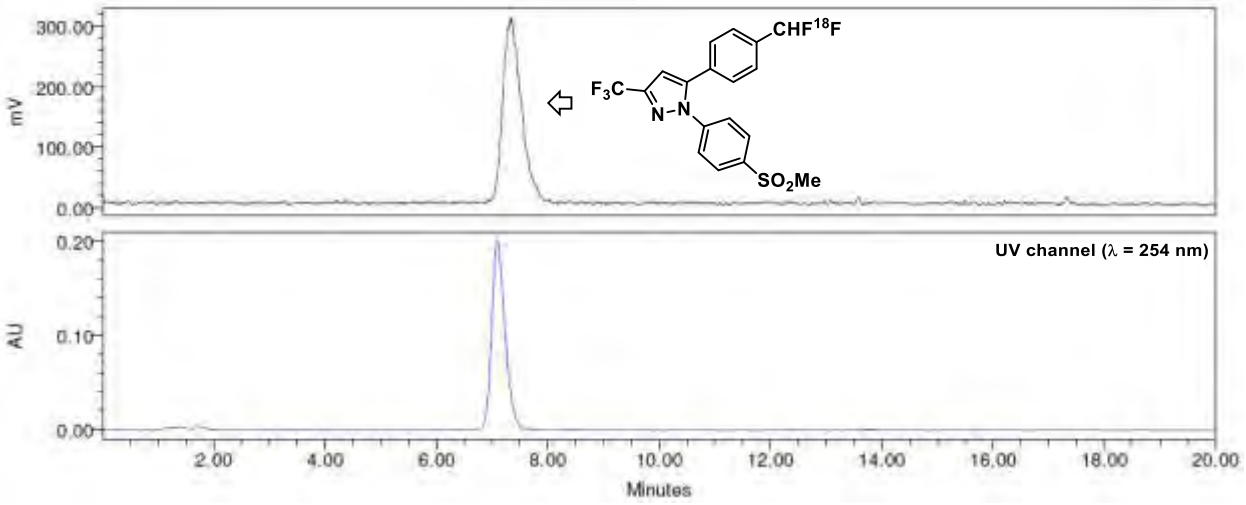


Figure S33. HPLC chromatogram (XBridge) of **[^{18}F]difluoromethyl-SC-58125**

Radio HPLC chromatogram:
Column: Synergi 4u Hydro-RP 80A 4 µm 150 × 4.6 mm
Mobile phase: 50% CH_3CN, 50% 0.1 M $NH_4 \cdot HCO_2$ (aq)
Flow rate: 1 mL/min

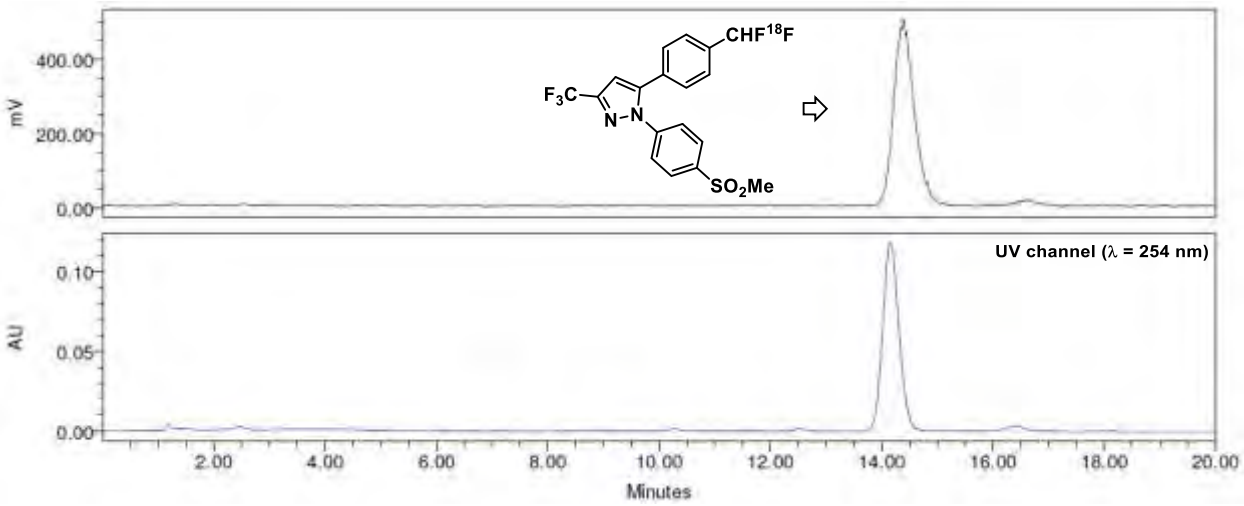


Figure S34. HPLC chromatogram (Synergi) of **[^{18}F]difluoromethyl-SC-58125**

Radio HPLC chromatogram:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M $NH_4{\cdot}HCO_2$ (aq)

Flow rate: 1 mL/min

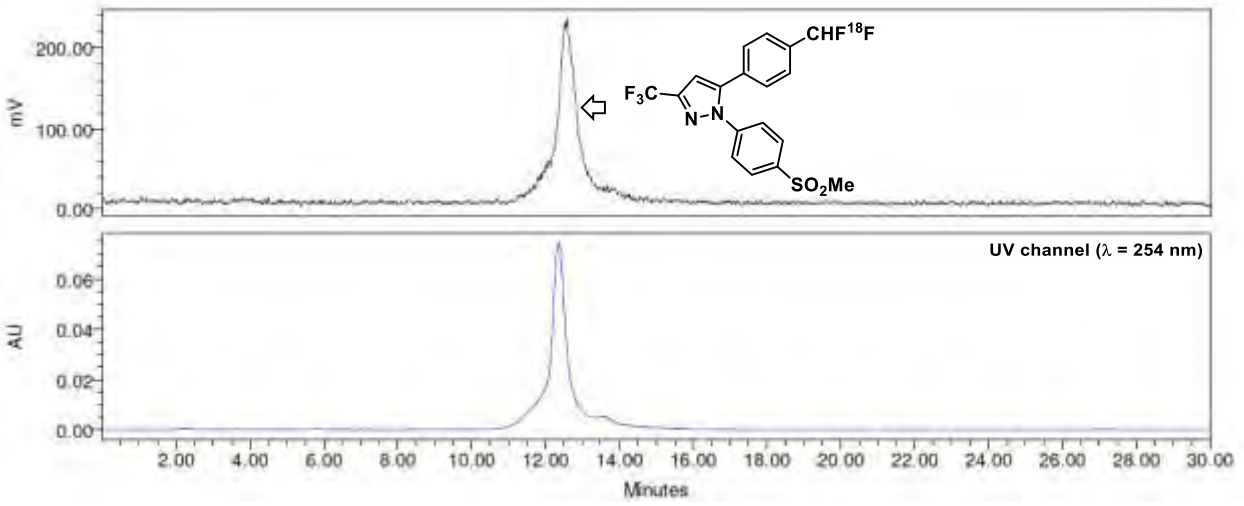
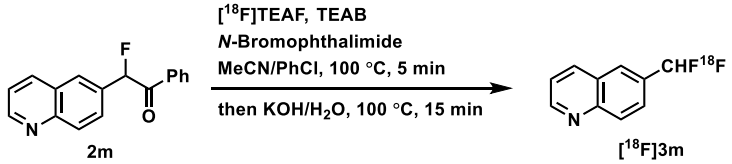


Figure S35. Luna HPLC chromatogram of **[^{18}F]difluoromethyl-SC-58125**

Specific Activity of [^{18}F]3m (General Method)



To a 1-dram (4 mL) glass vial containing TEAB (1.5 mg), precursor **2m** (10 μmol, 2.7 mg) and *N*-bromophthalimide (2 mg) was added chlorobenzene (0.2 mL). Then solution B (20 μL, 2.08 mCi) was added and radioactivity of the mixture was measured. The reaction vessel was heated at 100 °C for 5 min. After

that, aqueous KOH solution (45 w%, 40 µL) was added, and the mixture was heated at 100 °C for 15 min. The reaction vessel was cooled to room temperature. The reaction mixture was loaded on a light silica cartridge. Hexane (0.5 mL) was added into the reaction vessel, and the formed mixture was used to wash the silica cartridge. The silica cartridge was dried by nitrogen gas for 10 seconds, and then eluted with MeCN (2 x 1 mL). 0.1 M $NH_4 \cdot HCO_2$ aqueous solution (1 mL) was added into the combined MeCN filtrate, and the formed solution was subjected to purification by semi-preparative HPLC. The fraction corresponding to radiolabeled product was collected and was measured to contain 0.892 mCi. An aliquot (20 µL) was injected to analytical radio-HPLC and specific activity (0.49 mCi/µmol) was calculated based on mass calibration curve.

Analytical HPLC conditions:
Column: Luna 5u C18 100 Å 250 × 4.6 mm
Mobile phase: 50% CH_3CN, 50% 0.1 M $NH_4 \cdot HCO_2$ (aq)
Flow rate: 1 mL/min

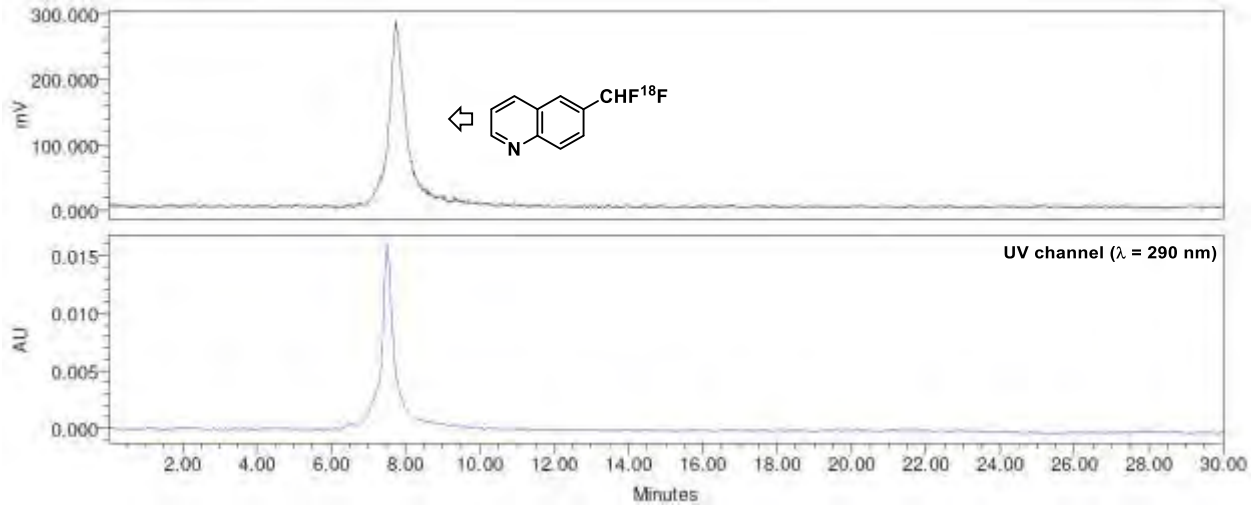


Figure S36. HPLC chromatogram of **[^{18}F]6-difluoromethylquinoline**

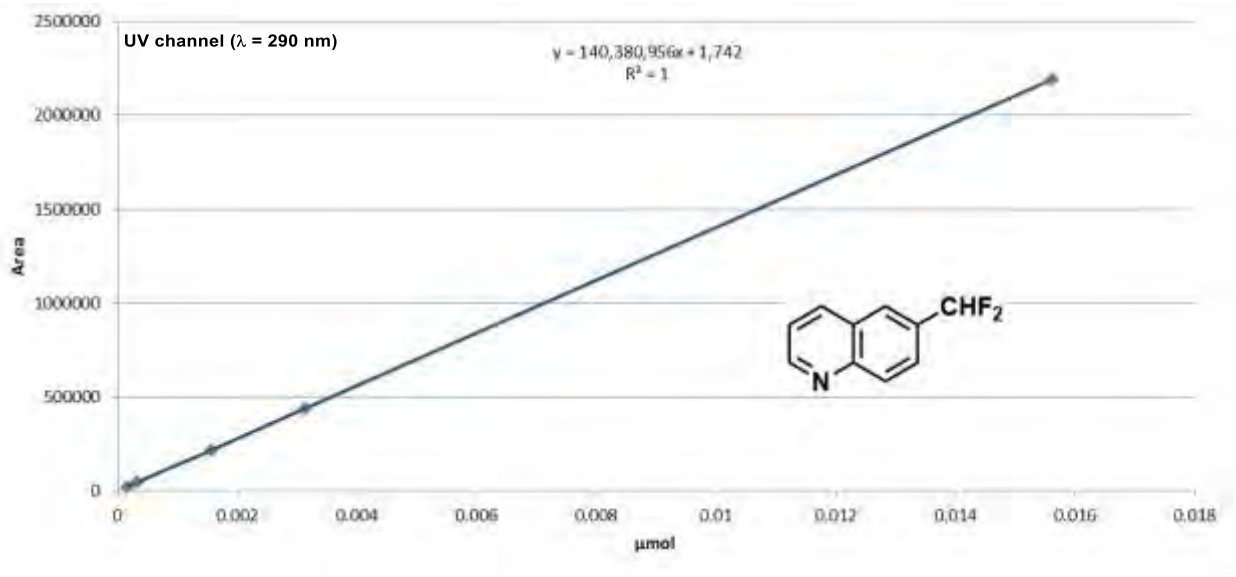
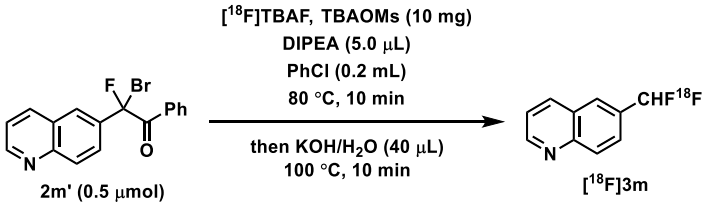


Figure S37. Calibration curve of **6-difluoromethylquinoline** (**3m**)

Improvement of Specific Activity

[^{18}F]Fluoride was prepared for radiofluorination by the following method: Sep-Pak® QMA cartridge was washed with an aqueous KOMs solution (0.2 M, 1 mL) and water (10 mL). ^{18}F-fluoride aqueous solution was loaded onto the cartridge. The cartridge was washed with dry MeOH (1 mL), and then eluted with a solution of tetrabutylammonium methanesulfonate (TBAOMs, 10 mg) in methanol (0.6 mL). The [^{18}F]TBAF/TBAOMs methanol solution was collected in a V−shaped vial and sealed with a teflon-lined septum. The vial was heated to 100 °C while nitrogen gas was passed through a P_2O_5-Drierite™ column followed by a vented needle. When no liquid was visible in the vial, it was removed from heat. The vial was then cooled down to room temperature under nitrogen flow (10 mL/min). The contents were dissolved in the anhydrous chlorobenzene (0.2 mL, solution c).



To a 1-dram (4 mL) glass vial containing precursor **2m'** (0.17 mg, 0.5 µmol) was added the solution c (0.2 mL) and DIPEA (5.0 µL). The radioactivity of the mixture was measured. The reaction vessel was heated at 80 °C for 10 min. After that, aqueous KOH solution (45 w%, 40 µL) was added, and the mixture was heated at 100 °C for 10 min. The reaction vessel was cooled to room temperature. The reaction mixture was loaded on a light silica cartridge. Hexane (0.5 mL) was added into the reaction vessel, and the formed mixture was used to wash the silica cartridge. The silica cartridge was dried by nitrogen gas for 10 seconds, and then eluted with MeCN (2 x 1 mL). 0.1 M $NH_4 \cdot HCO_2$ aqueous solution (1 mL) was added into the combined MeCN filtrate, and the formed solution was subjected to purification by semi-preparative HPLC. An aliquot (20 µL or

40 µL) was injected to analytical radio-HPLC and specific activity was calculated based on mass calibration curve.

entry	Initial radio-activity	**[^{18}F]3m**	RCY (HPLC)	SA
1	12 mCi	1.9 mCi	16%	38 mCi/µmol
2	18 mCi	1.3 mCi	7%	64 mCi/µmol
3	39 mCi	3.1 mCi	8%	81 mCi/µmol

Analytical HPLC conditions:

Column: Luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 45% CH_3CN, 55% 0.1 M $NH_4 \cdot HCO_2$(aq)

Flow rate: 1.0 mL/min

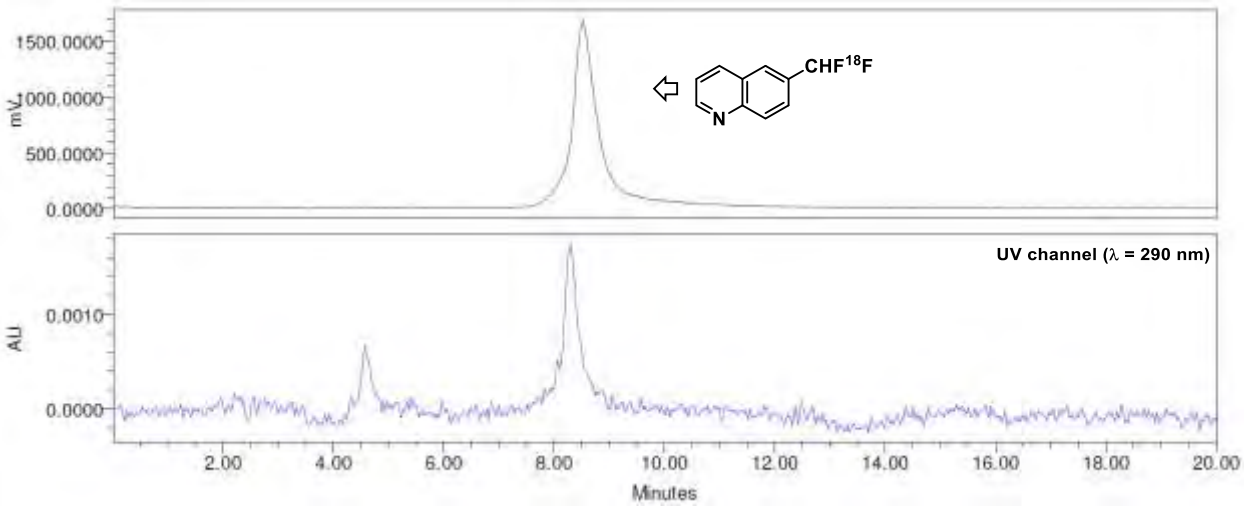


Figure S38. HPLC chromatogram of **[^{18}F]6-difluoromethylquinoline** (entry 3)

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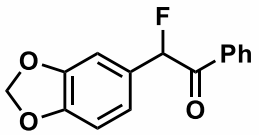
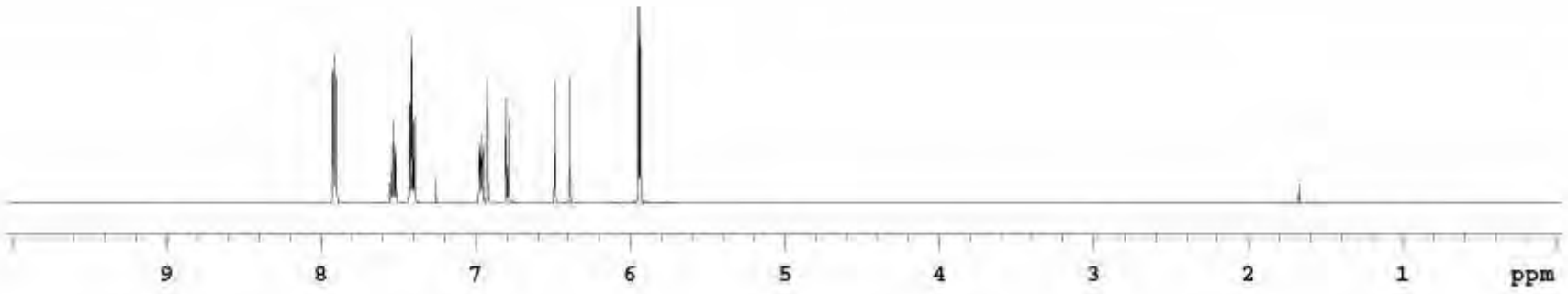
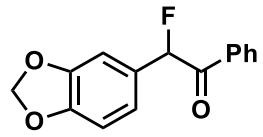
^{1}H NMR of (Methylenedioxy)phenyl-fluoroacetophenone (2a)



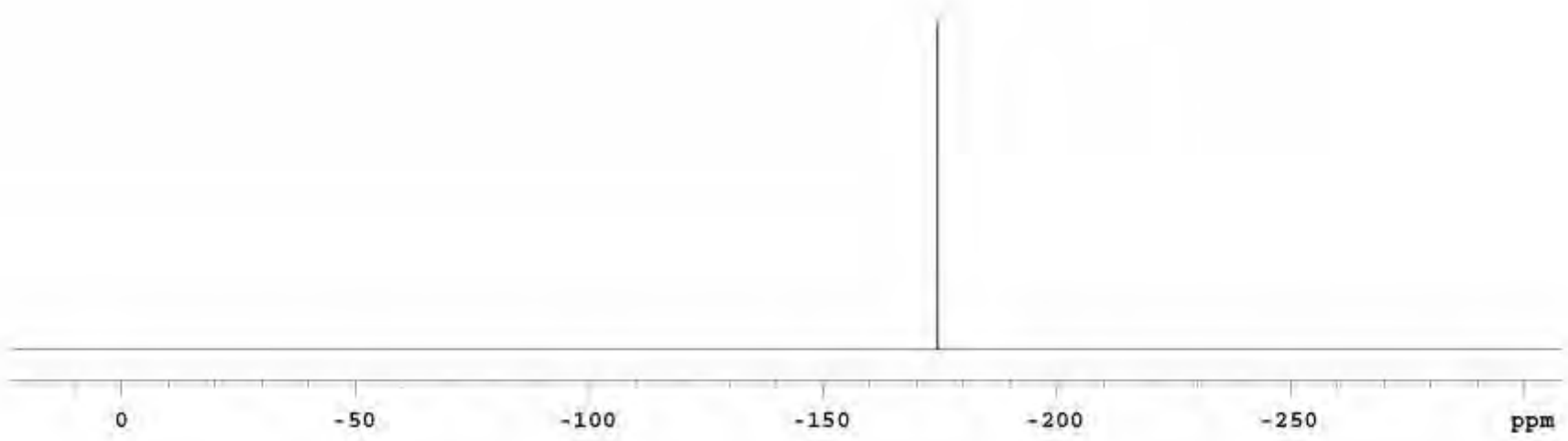
$CDCl_3$, 24 ºC



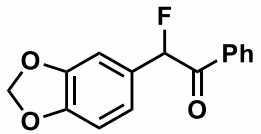
^{19}F NMR of (Methylenedioxy)phenyl-fluoroacetophenone (2a)



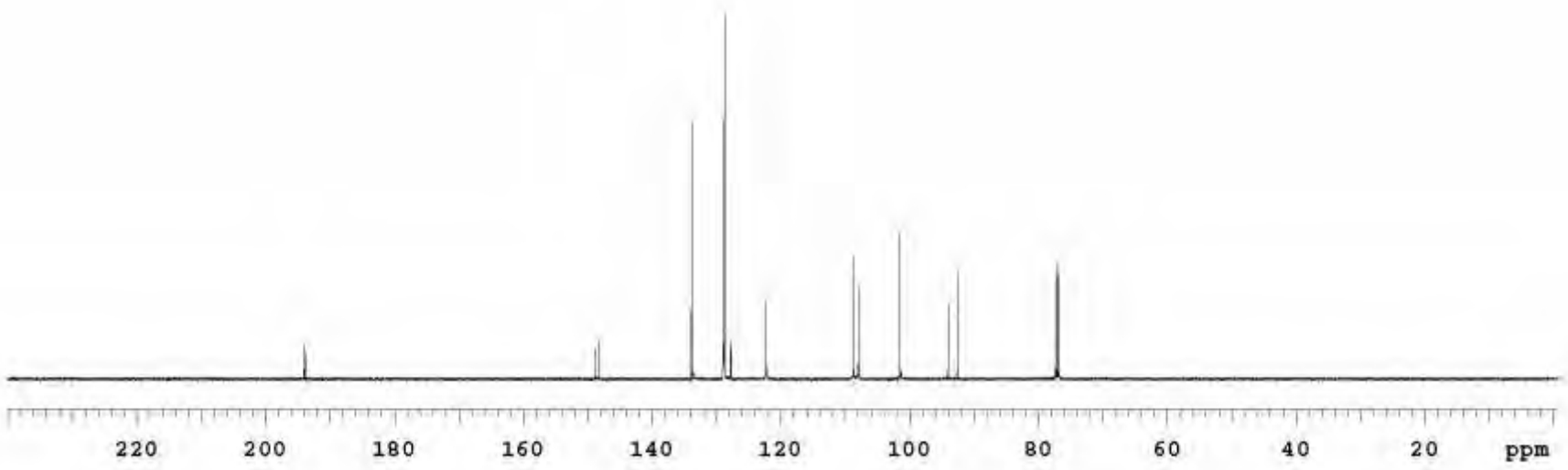
$CDCl_3$, 24 ºC



^{13}C NMR of (Methylenedioxy)phenyl-fluoroacetophenone (2a)

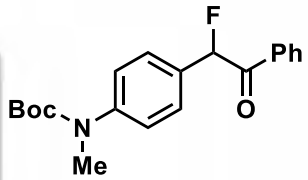


$CDCl_3$, 25 ºC

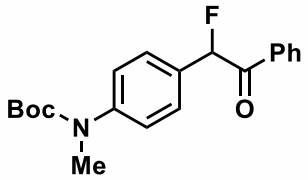


^{1}H NMR of (4-*N*-Boc-methylamino)phenyl-fluoroacetophenone (2b)

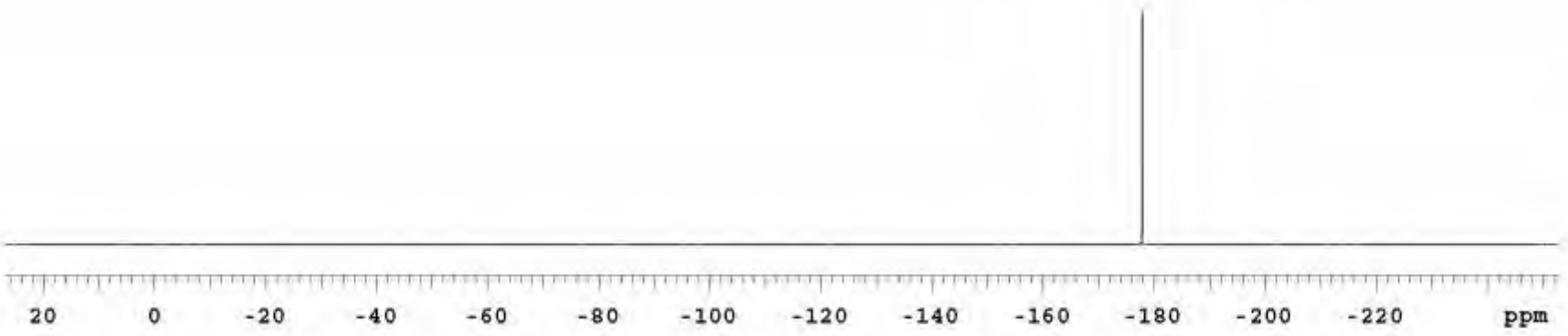
$CDCl_3$, 25 ºC



^{19}F NMR of (4-*N*-Boc-methylamino)phenyl-fluoroacetophenone (2b)

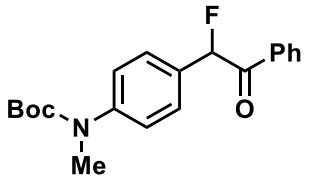


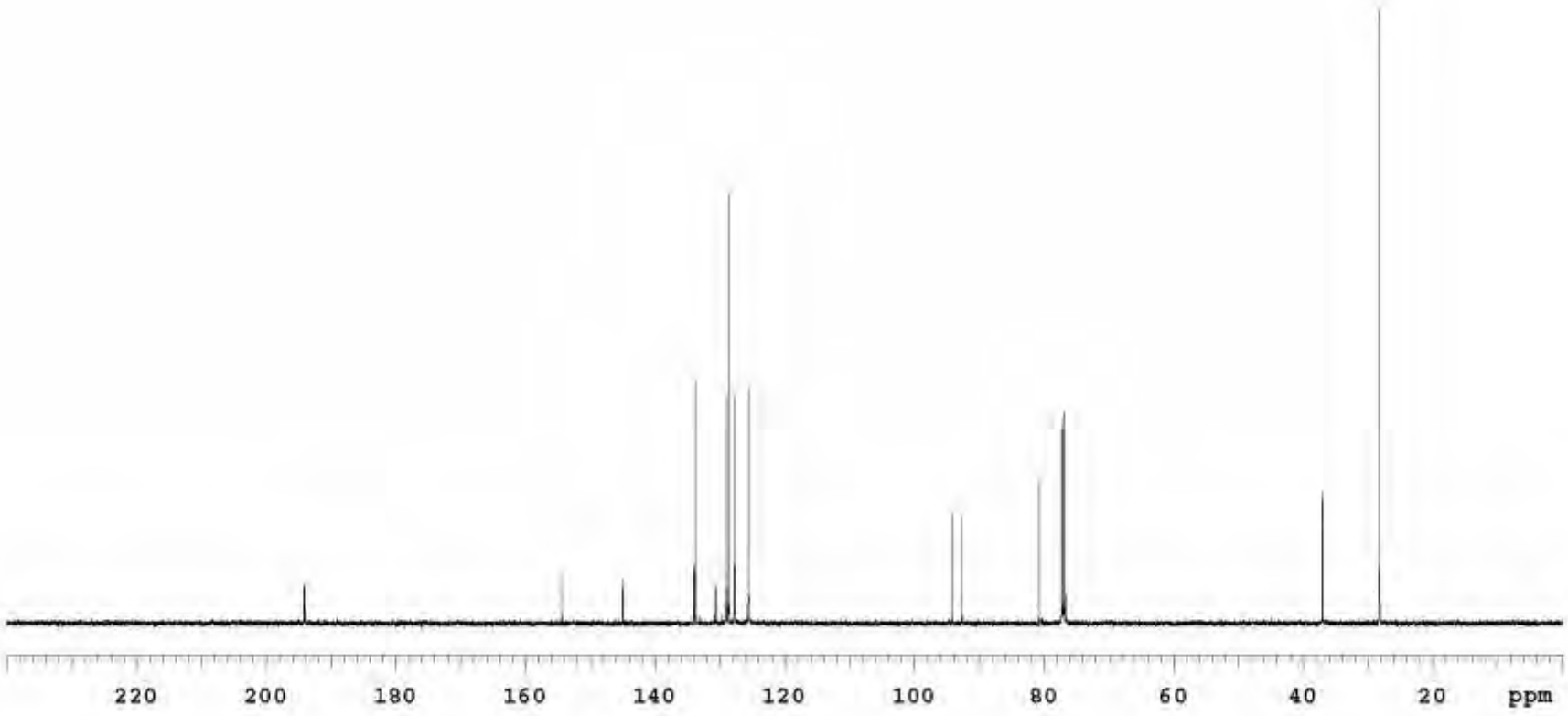
$CDCl_3$, 25 ºC



^{13}C NMR of (4-*N*-Boc-methylamino)phenyl-fluoroacetophenone (2b)

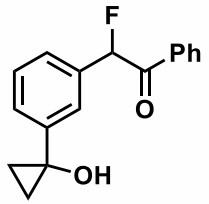
$CDCl_3$, 25 ºC

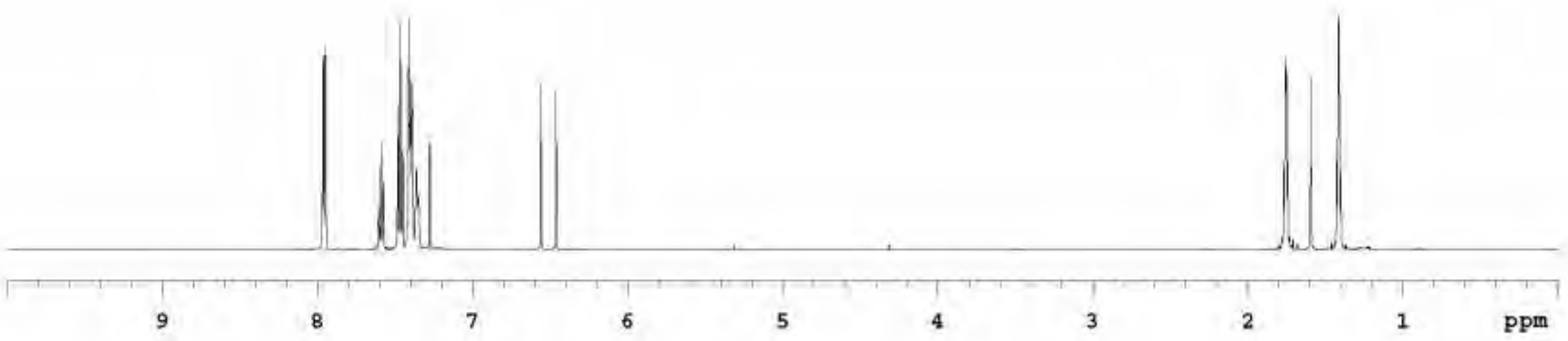




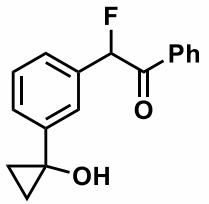
^{1}H NMR of (3-Hydroxypropanyl)phenyl-fluoroacetophenone (2c)

$CDCl_3$, 22 ºC

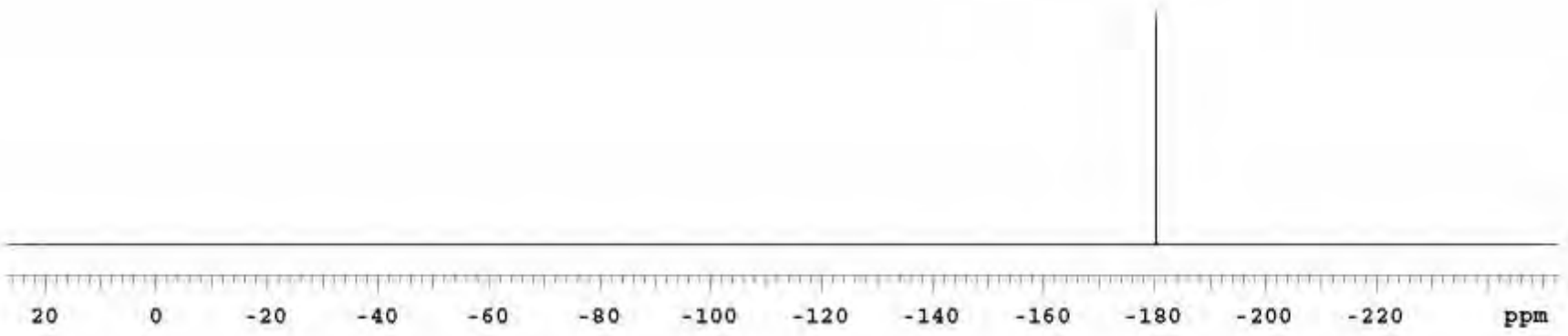




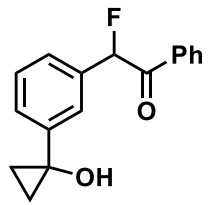
^{19}F NMR of (3-Hydroxypropanyl)phenyl-fluoroacetophenone (2c)



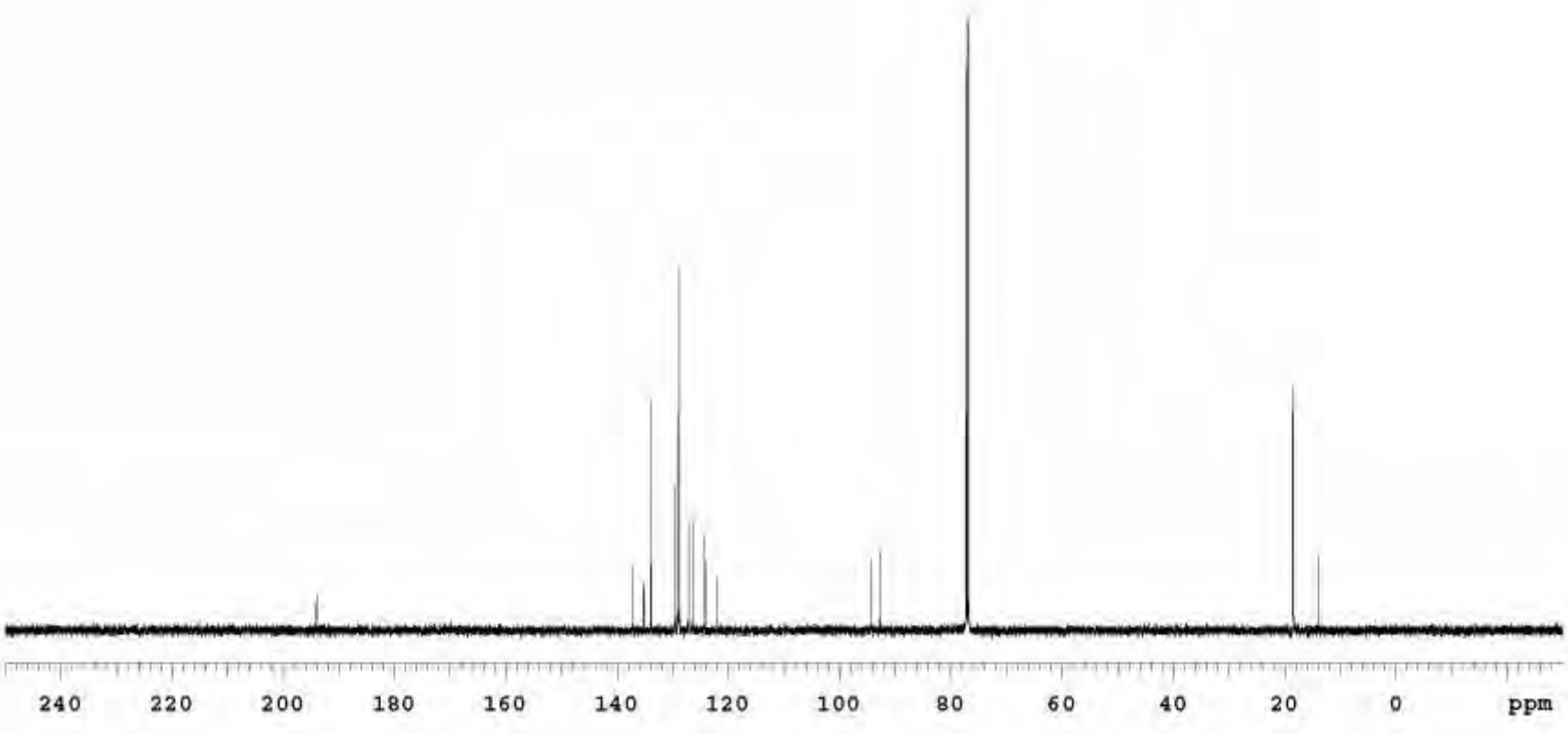
$CDCl_3$, 23 ºC



^{13}C NMR of (3-Hydroxypropanyl)phenyl-fluoroacetophenone (2c)

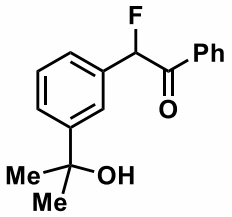


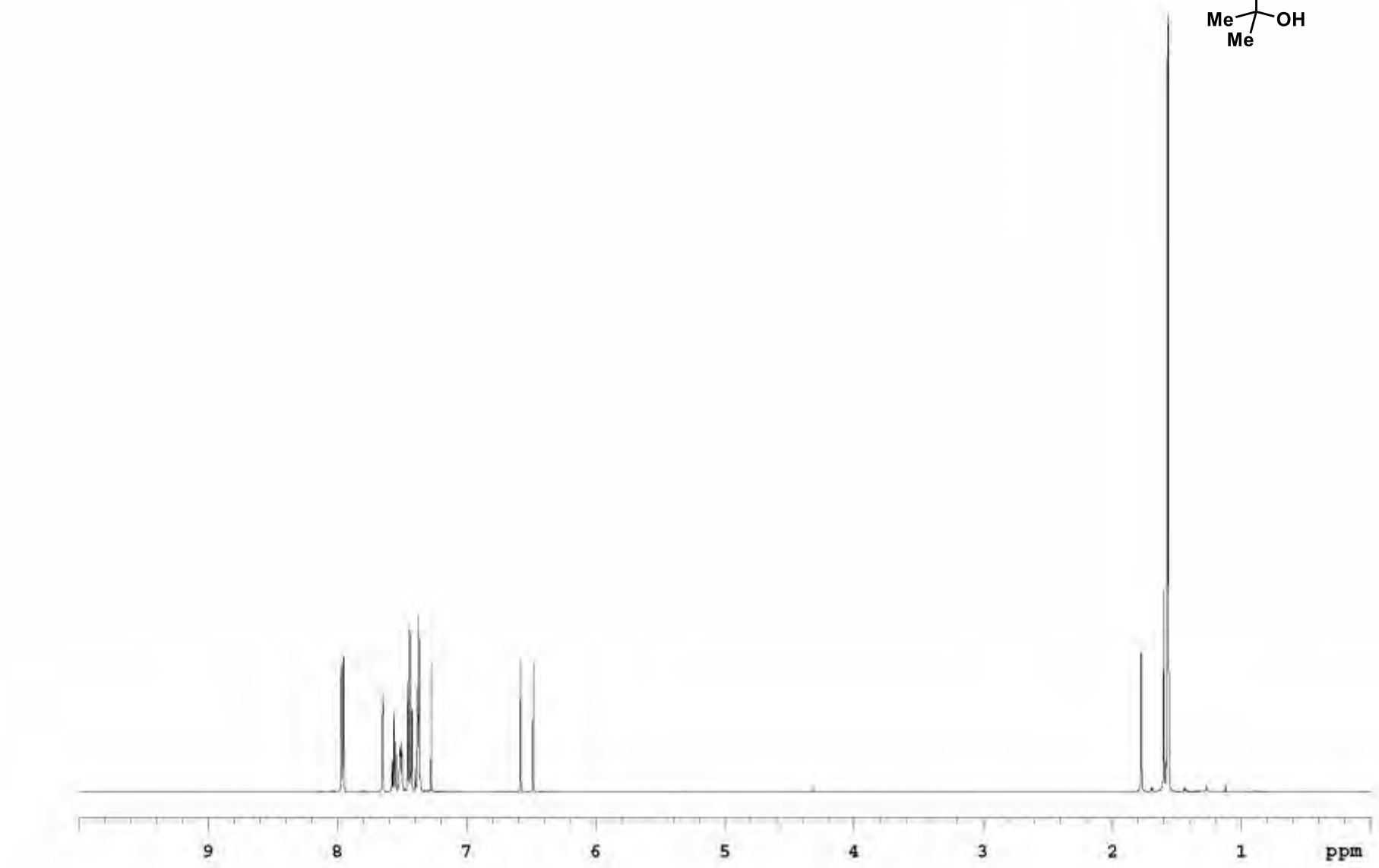
$CDCl_3$, 25 ºC



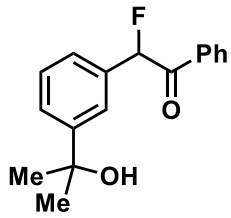
^{1}H NMR of (3-Hydroxypropanyl)phenyl-fluoroacetophenone (2d)

$CDCl_3$, 25 ºC

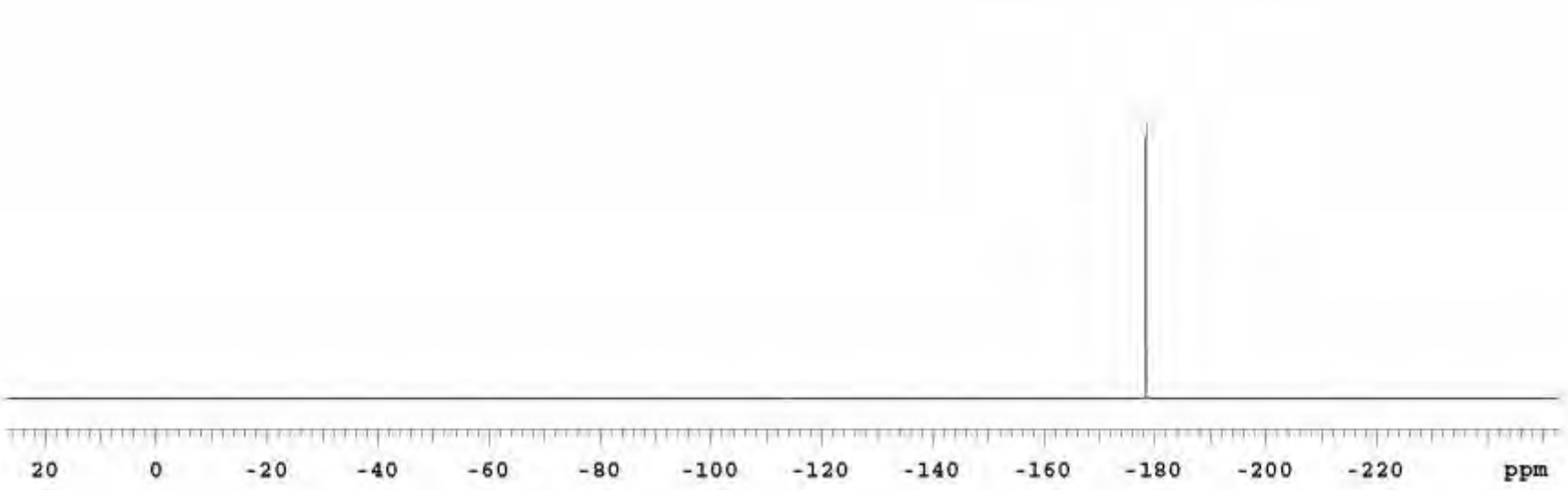




^{19}F NMR of (3-Hydroxypropanyl)phenyl-fluoroacetophenone (2d)

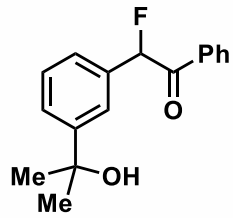


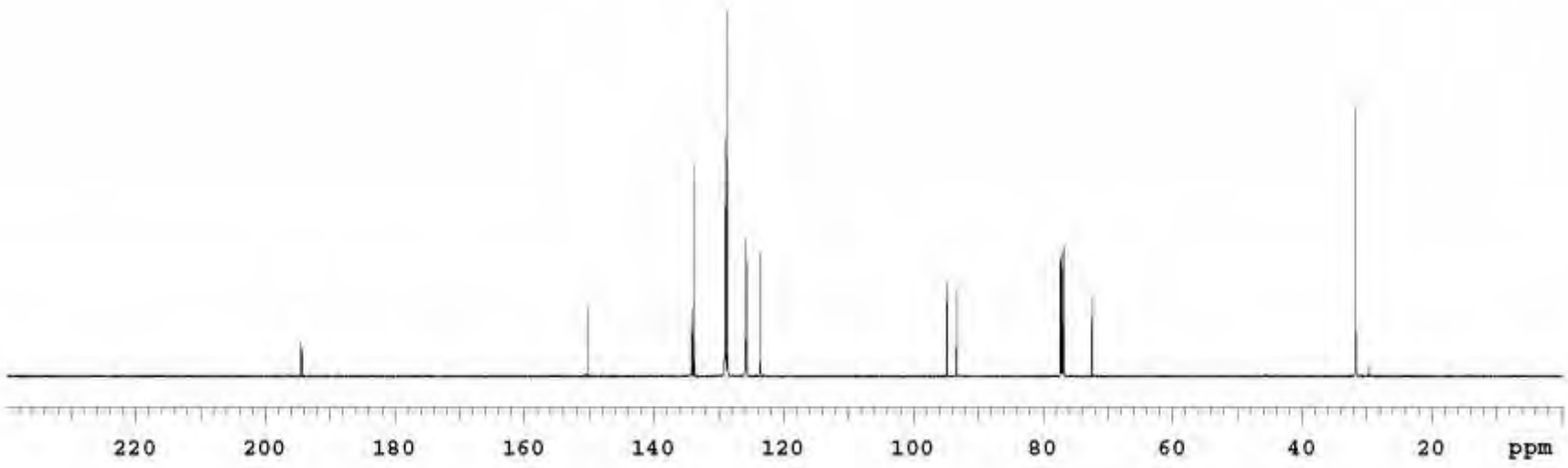
$CDCl_3$, 25 ºC



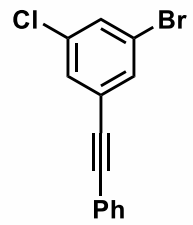
^{13}C NMR of (3-Hydroxypropanyl)phenyl-fluoroacetophenone (2d)

$CDCl_3$, 25 ºC

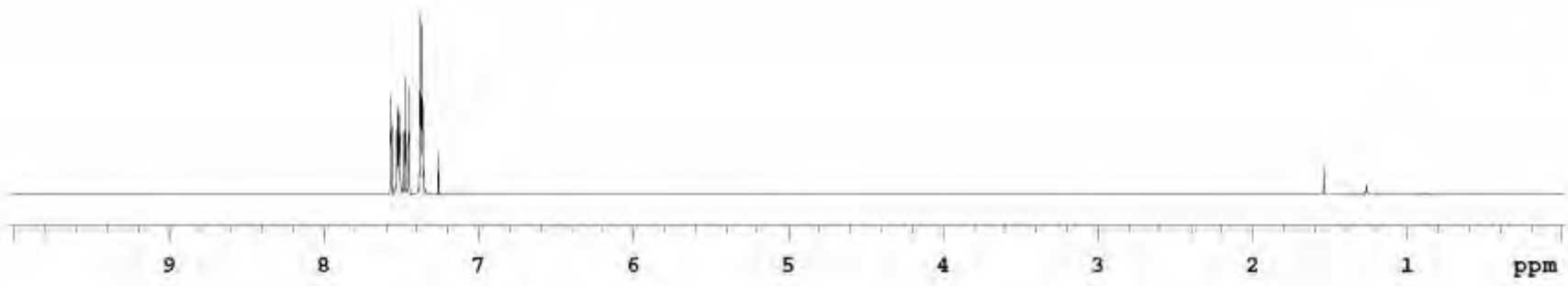




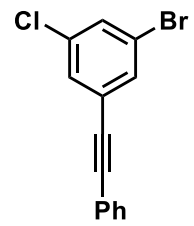
^{1}H NMR of 1-Bromo-3-chloro-5-(phenylethynyl)benzene (S11)



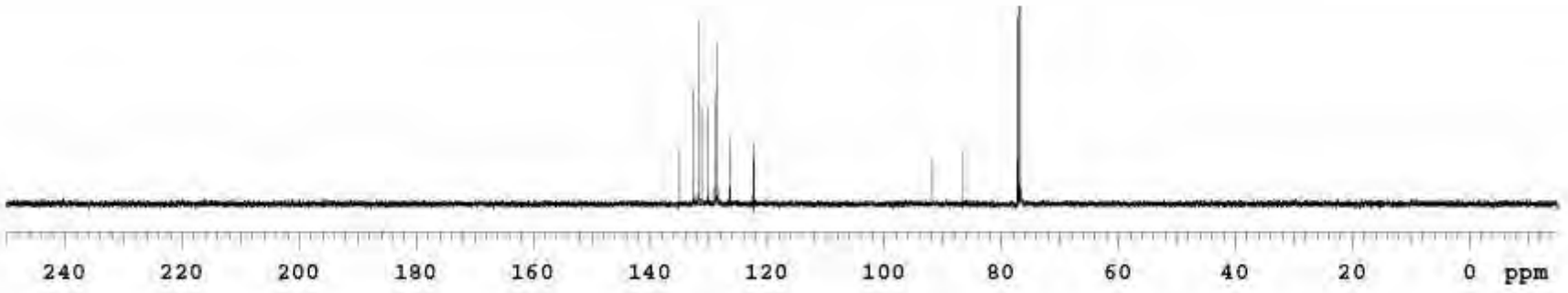
$CDCl_3$, 25ºC



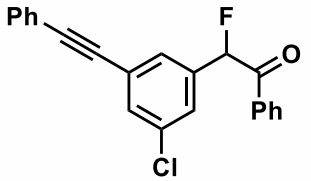
^{13}C NMR of 1-Bromo-3-chloro-5-(phenylethynyl)benzene (S11)



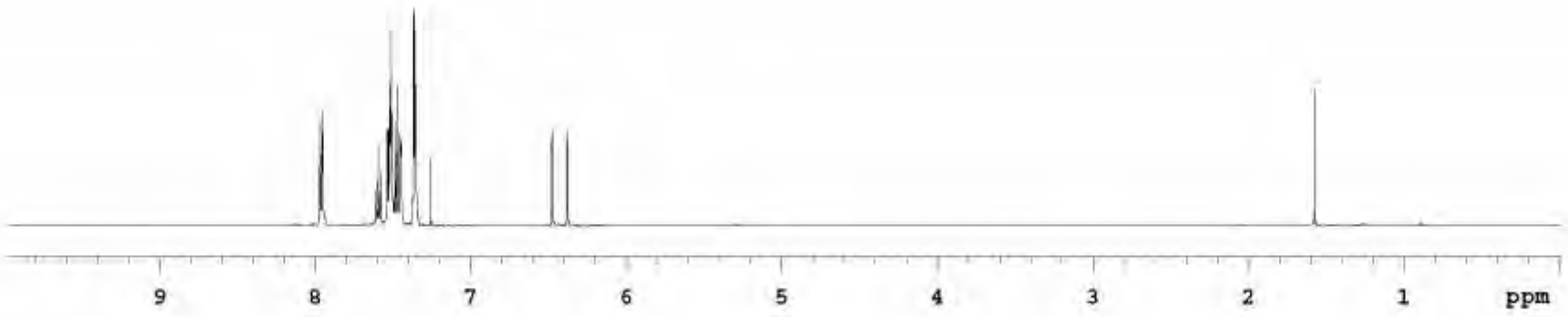
$CDCl_3$, 25 ºC



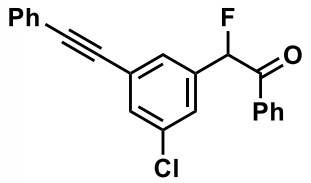
^{1}H NMR of (3-Phenylacetylenyl-5-chlorophenyl)-fluoroacetophenone (2e)



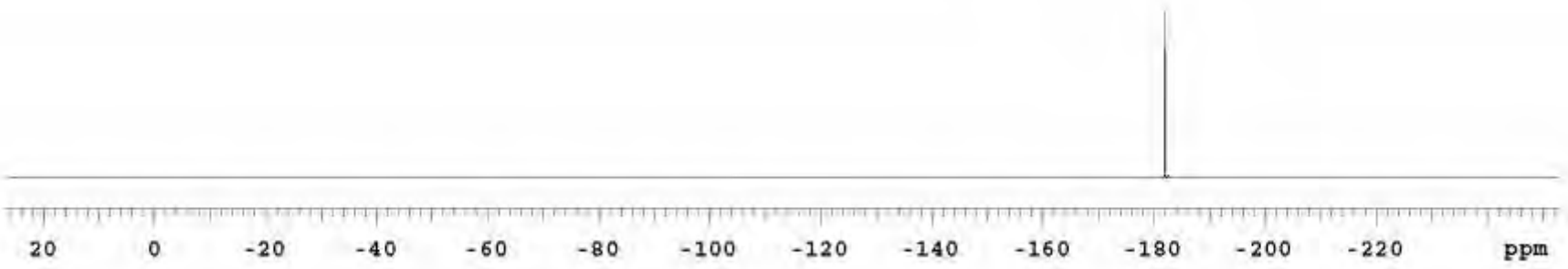
$CDCl_3$, 25ºC



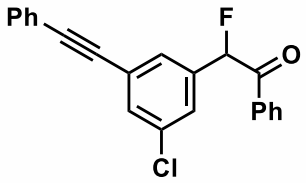
^{19}F NMR of (3-Phenylacetylenyl-5-chlorophenyl)-fluoroacetophenone (2e)



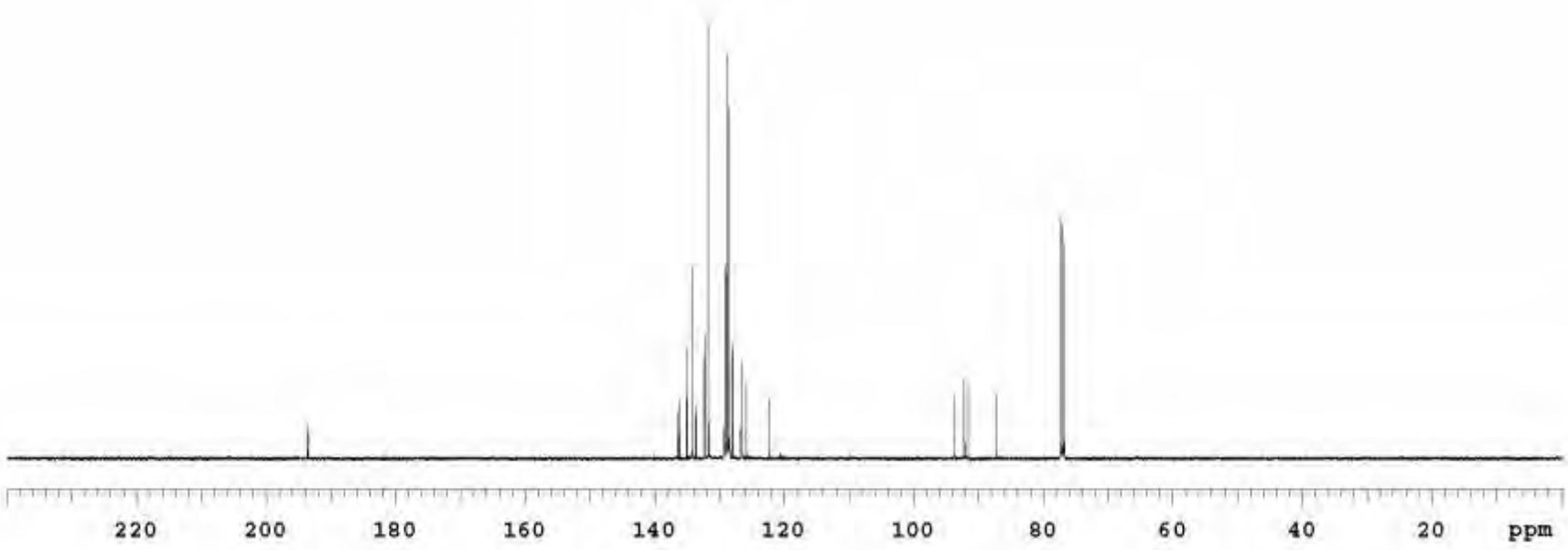
$CDCl_3$, 25 ºC



^{13}C NMR of (3-Phenylacetylenyl-5-chlorophenyl)-fluoroacetophenone (2e)

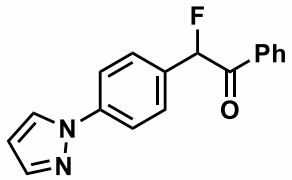


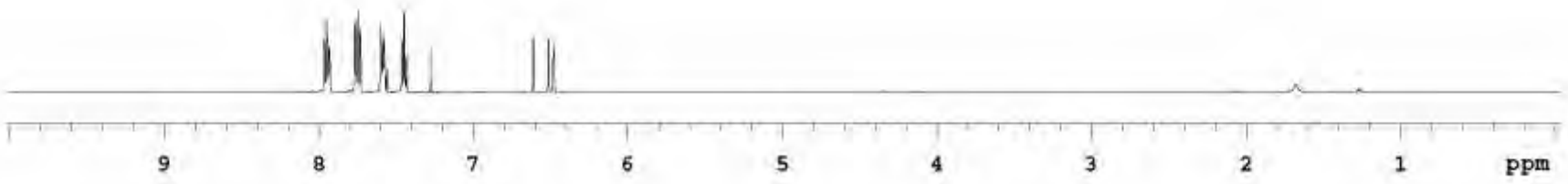
$CDCl_3$, 25 ºC



^{1}H NMR of (4-Pyrazolyl)phenyl-fluoroacetophenone (2f)

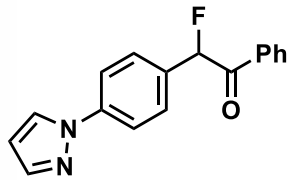
$CDCl_3$, 25 ºC

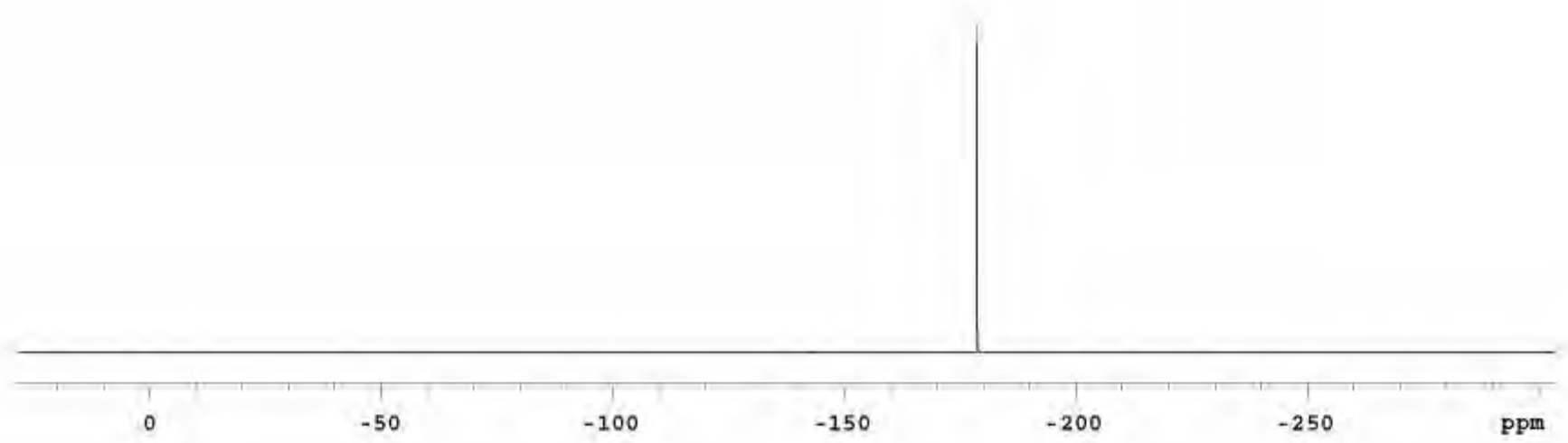




^{19}F NMR of (4-Pyrazolyl)phenyl-fluoroacetophenone (2f)

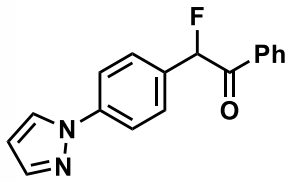
$CDCl_3$, 24 ºC

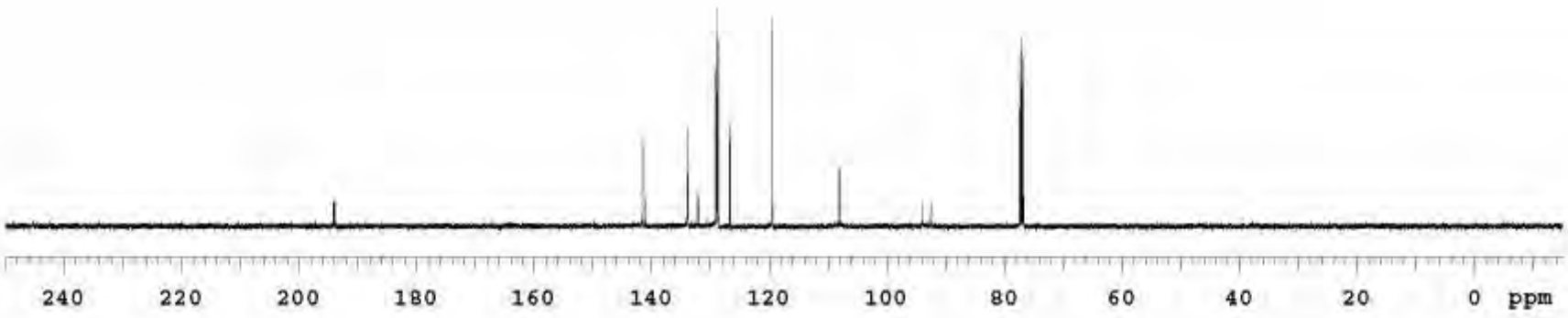




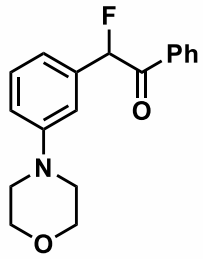
^{13}C NMR of (4-Pyrazolyl)phenyl-fluoroacetophenone (2f)

$CDCl_3$, 25 ºC

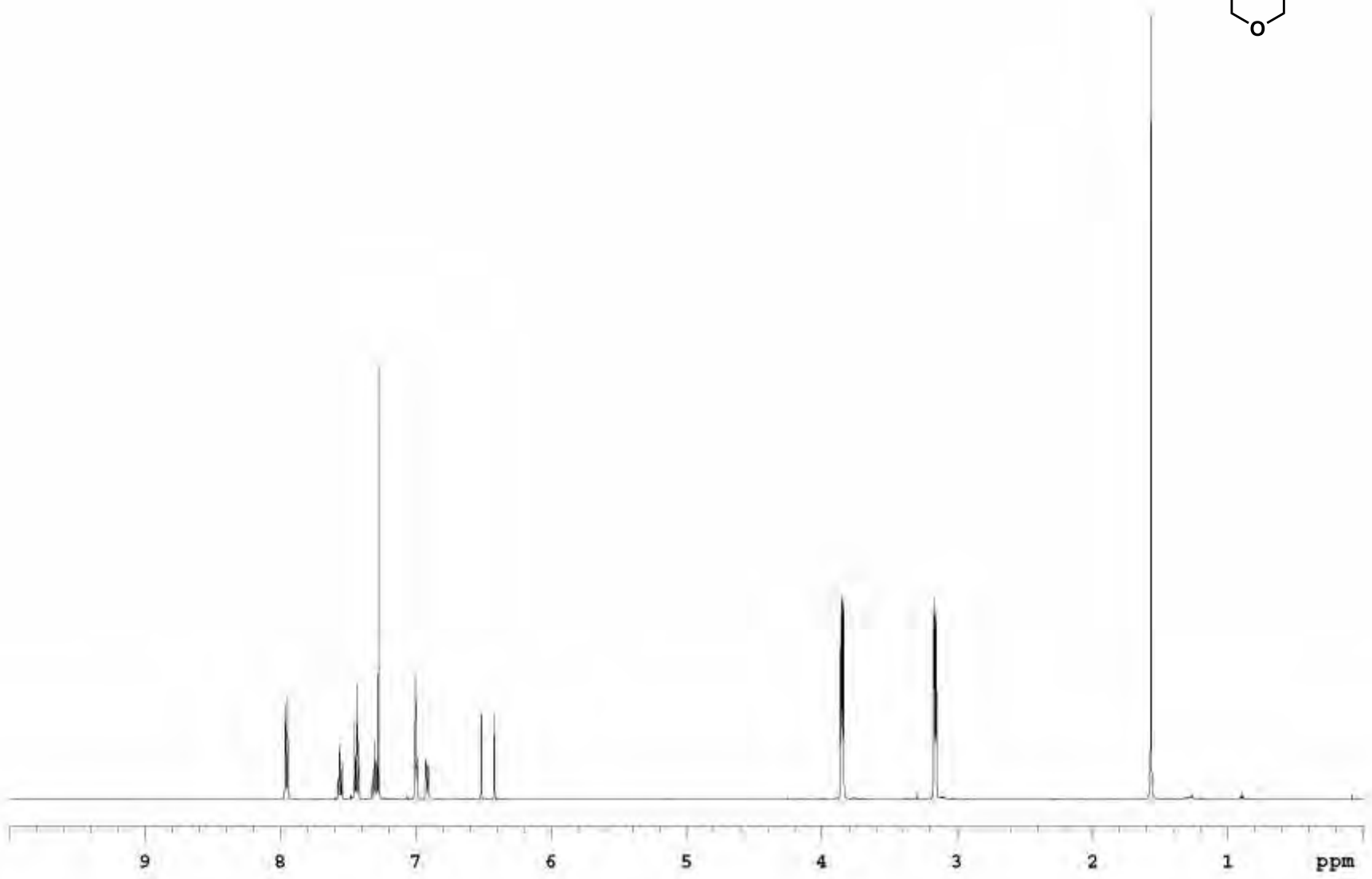




^{1}H NMR of (3-Morpholino)phenyl-fluoroacetophenone (2g)

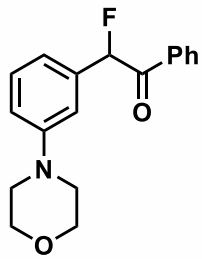


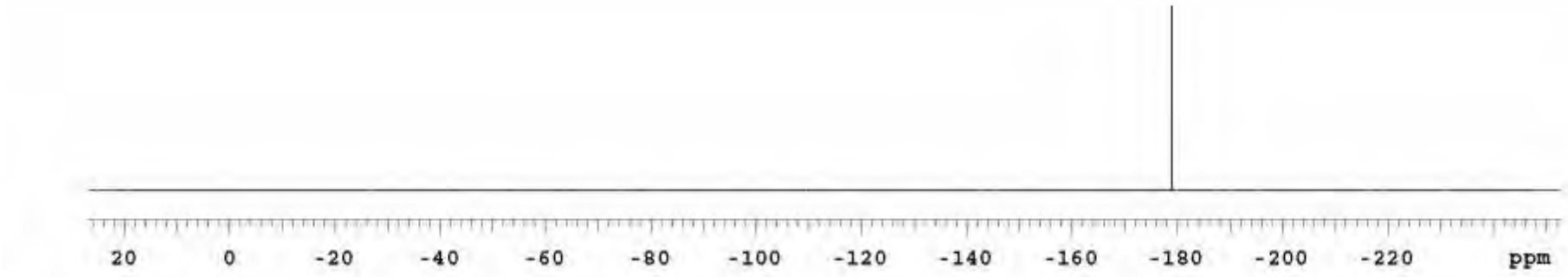
$CDCl_3$, 25 ºC



^{19}F NMR of (3-Morpholino)phenyl-fluoroacetophenone (2g)

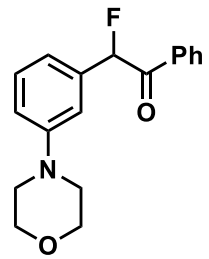
$CDCl_3$, 23 ºC

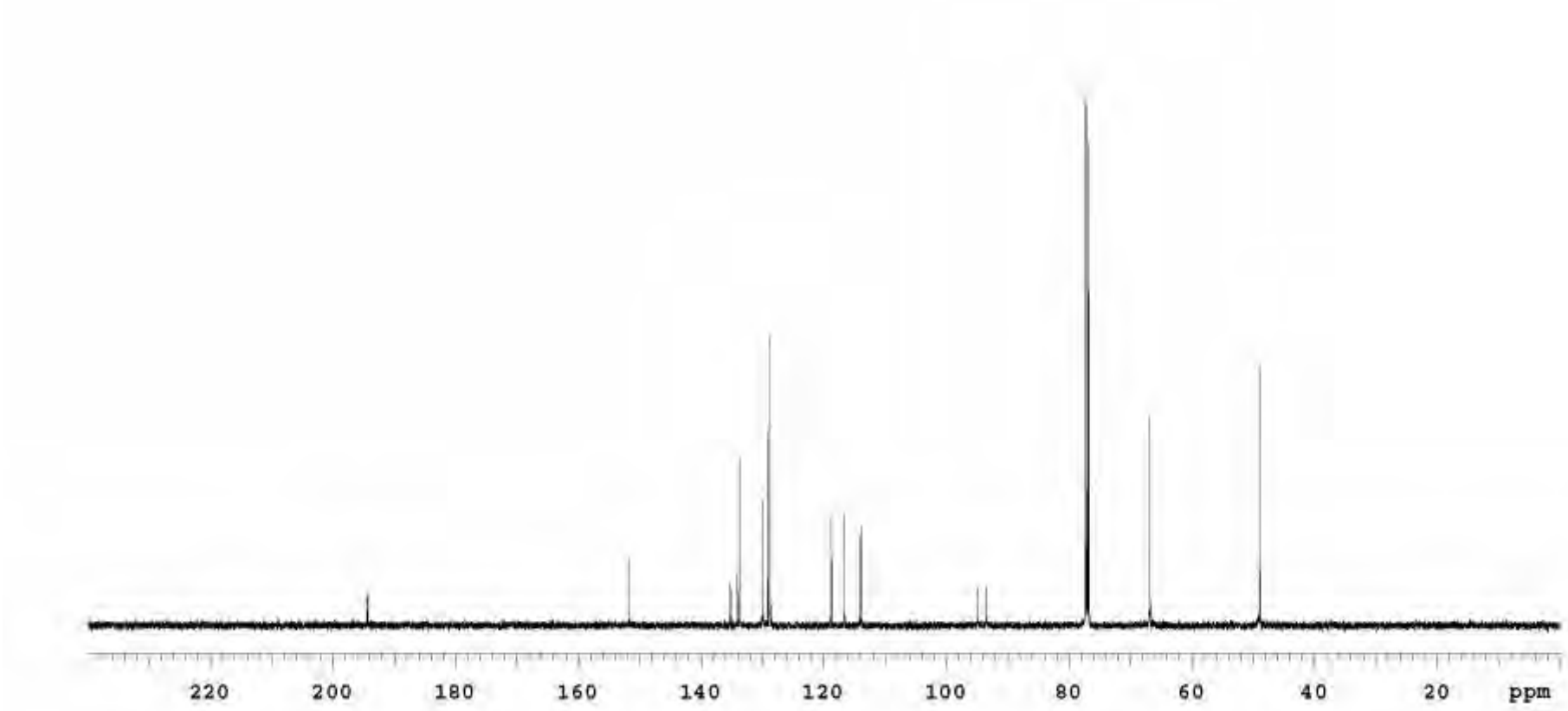




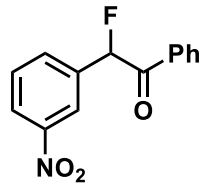
^{13}C NMR of (3-Morpholino)phenyl-fluoroacetophenone (2g)

$CDCl_3$, 25 ºC

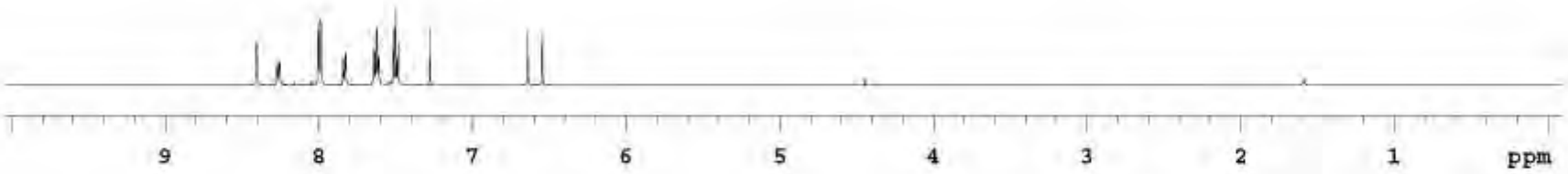




^{1}H NMR of (3-Nitro)phenyl-fluoroacetophenone (2h)

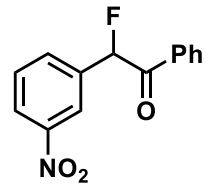


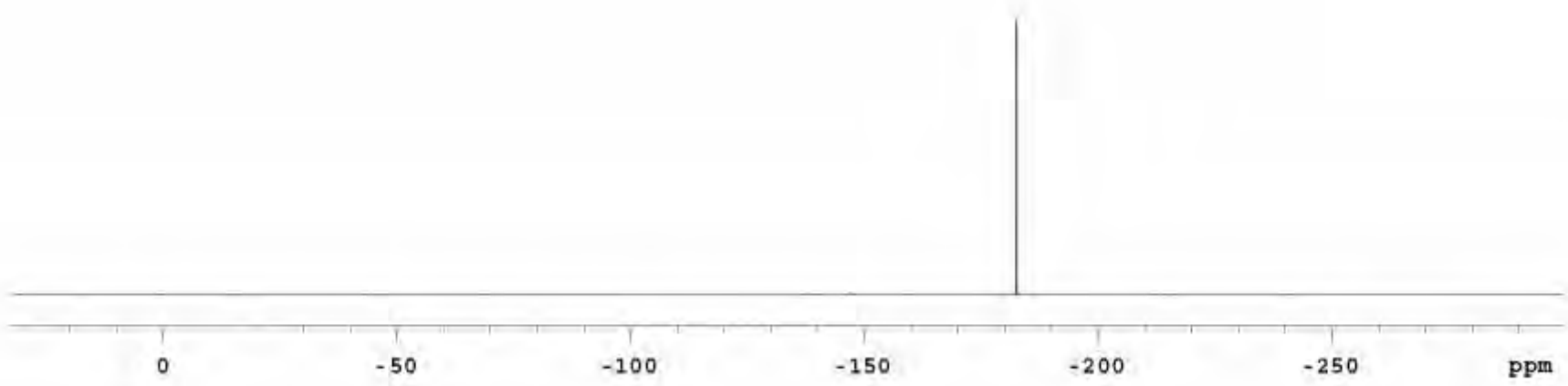
$CDCl_3$, 23 ºC



^{19}F NMR of (3-Nitro)phenyl-fluoroacetophenone (2h)

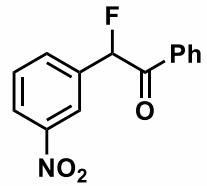
$CDCl_3$, 23 ºC

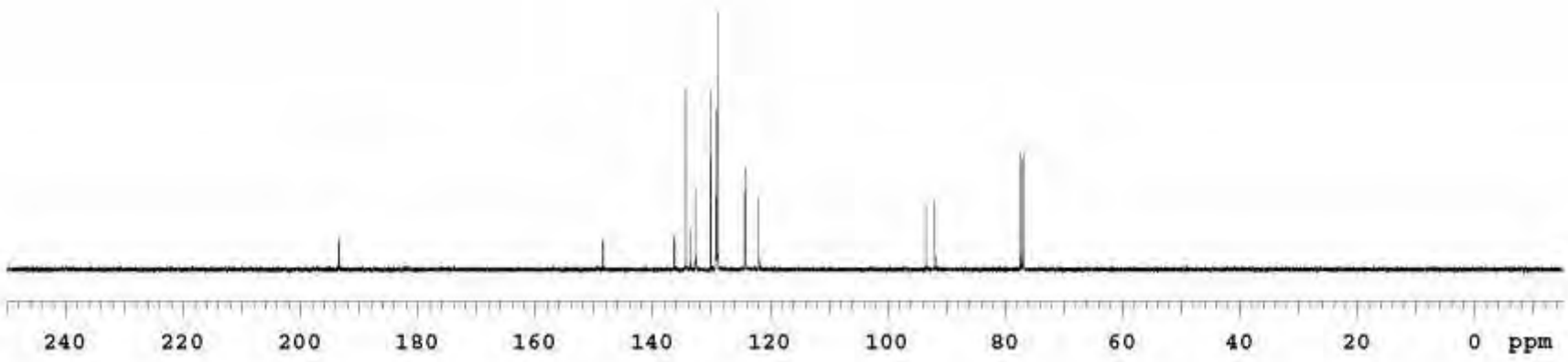




^{13}C NMR of (3-Nitro)phenyl-fluoroacetophenone (2h)

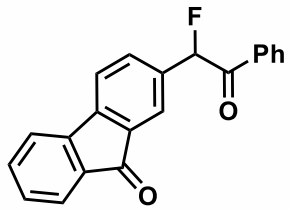
$CDCl_3$, 25 ºC

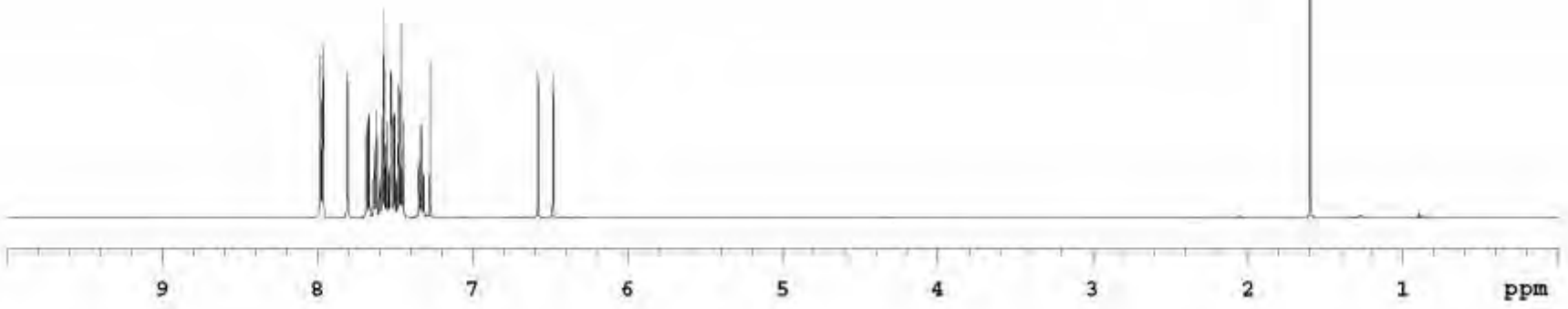




^{1}H NMR of Fluoren-9-onyl-fluoroacetophenone (2i)

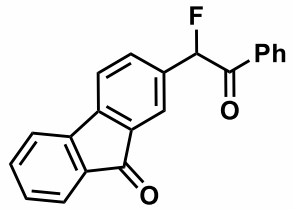
$CDCl_3$, 25 ºC

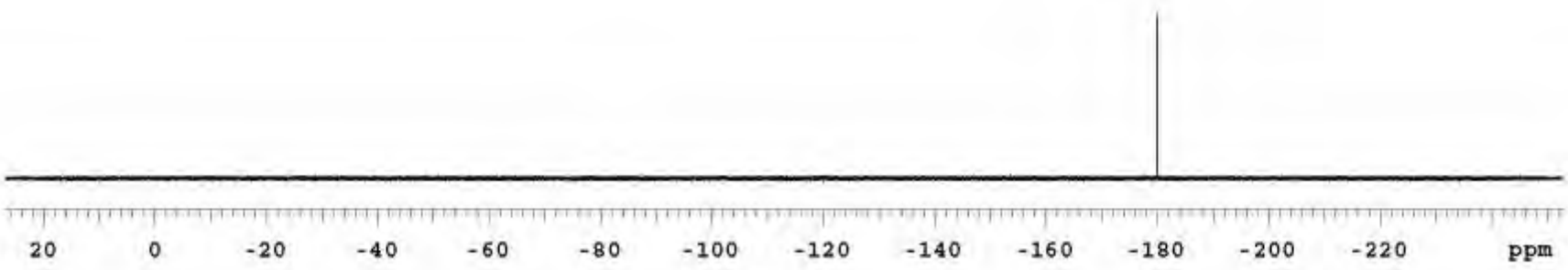




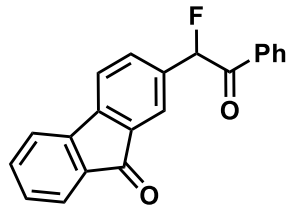
^{19}F NMR of Fluoren-9-onyl-fluoroacetophenone (2i)

$CDCl_3$, 25 ºC

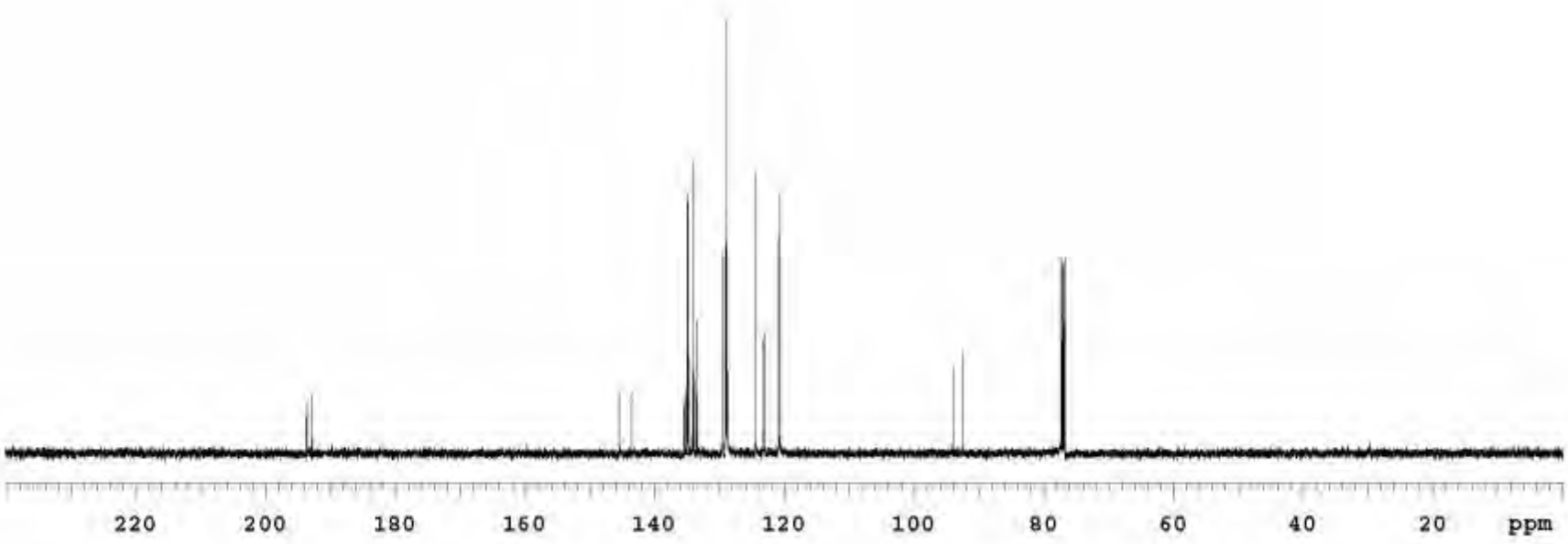




^{13}C NMR of Fluoren-9-onyl-fluoroacetophenone (2i)

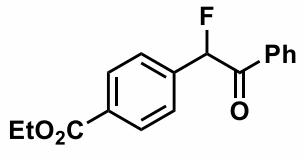


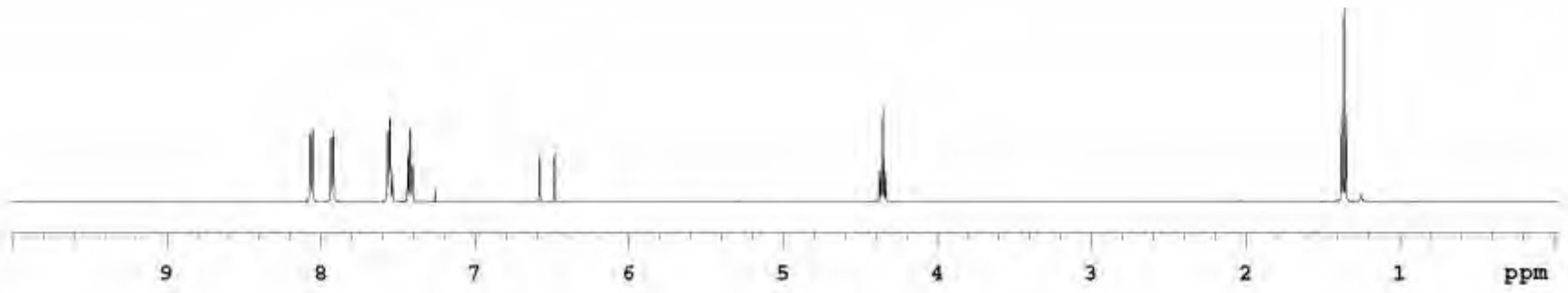
$CDCl_3$, 25 ºC



^{1}H NMR of (4-Ethyl-carboxyl)phenyl-fluoroacetophenone (2j)

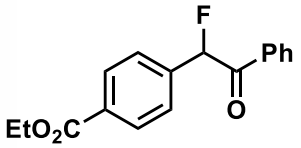
$CDCl_3$, 23 ºC

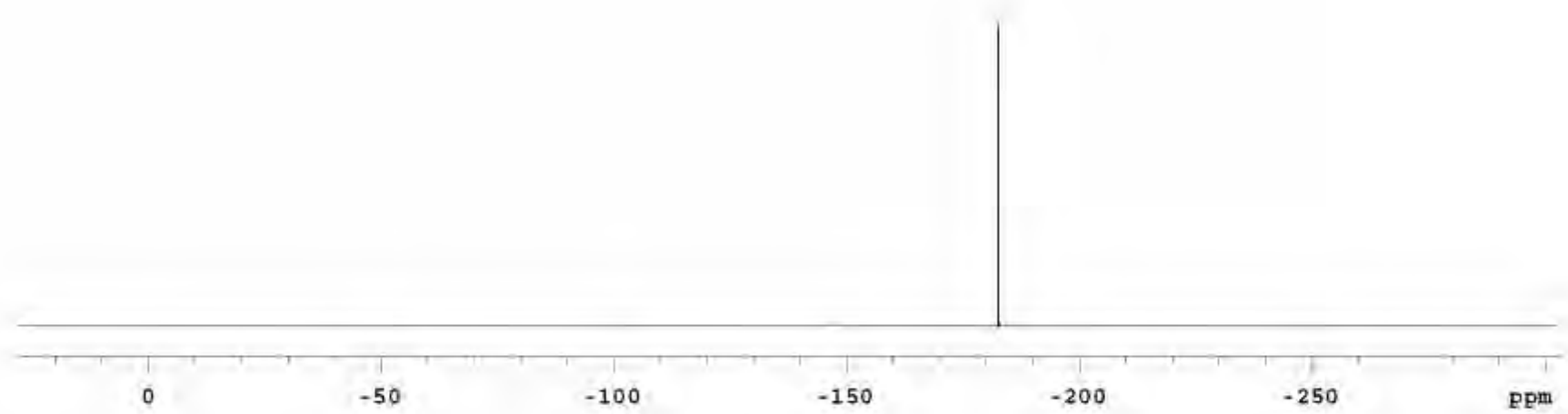




^{19}F NMR of (4-Ethyl-carboxyl)phenyl-fluoroacetophenone (2j)

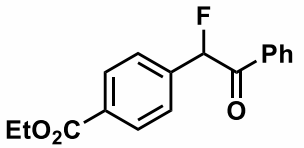
$CDCl_3$, 23 ºC

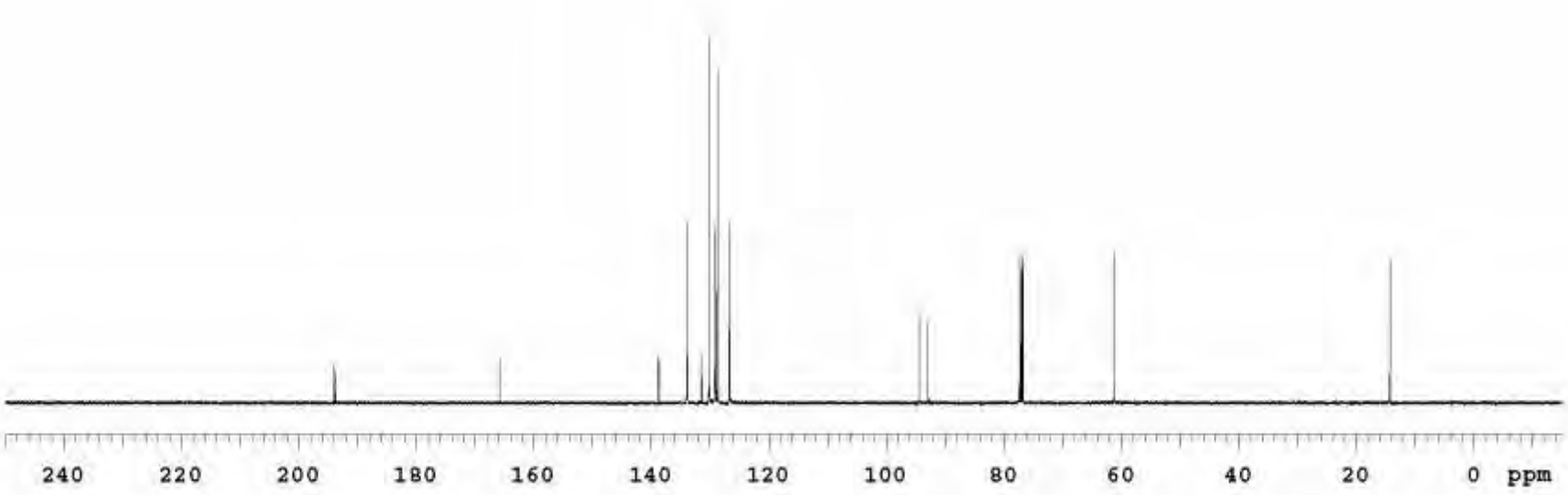




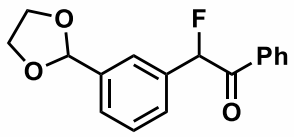
^{13}C NMR of (4-Ethyl-carboxyl)phenyl-fluoroacetophenone (2j)

$CDCl_3$, 25 ºC

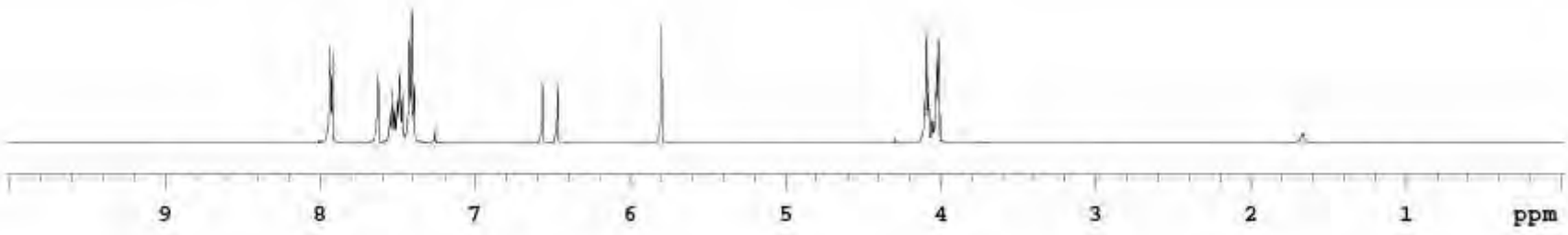




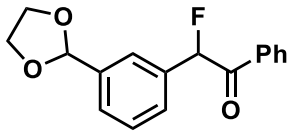
^{1}H NMR of (3-Dioxolanyl)phenyl-fluoroacetophenone (S1)



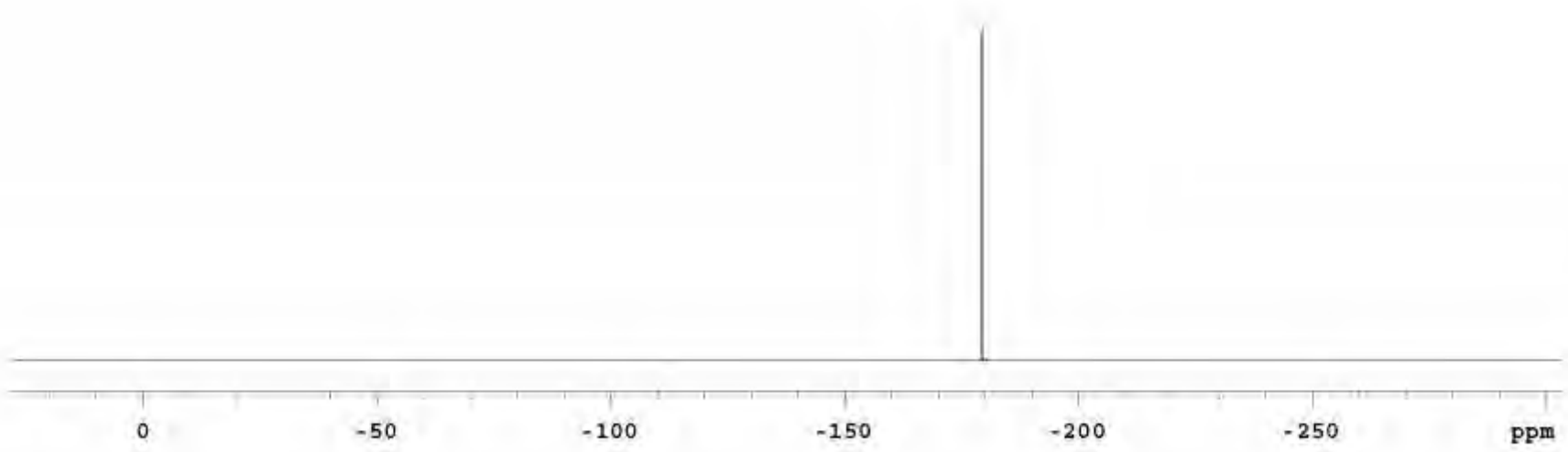
$CDCl_3$, 25 ºC



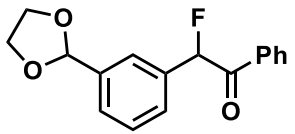
^{19}F NMR of (3-Dioxolanyl)phenyl-fluoroacetophenone (S1)



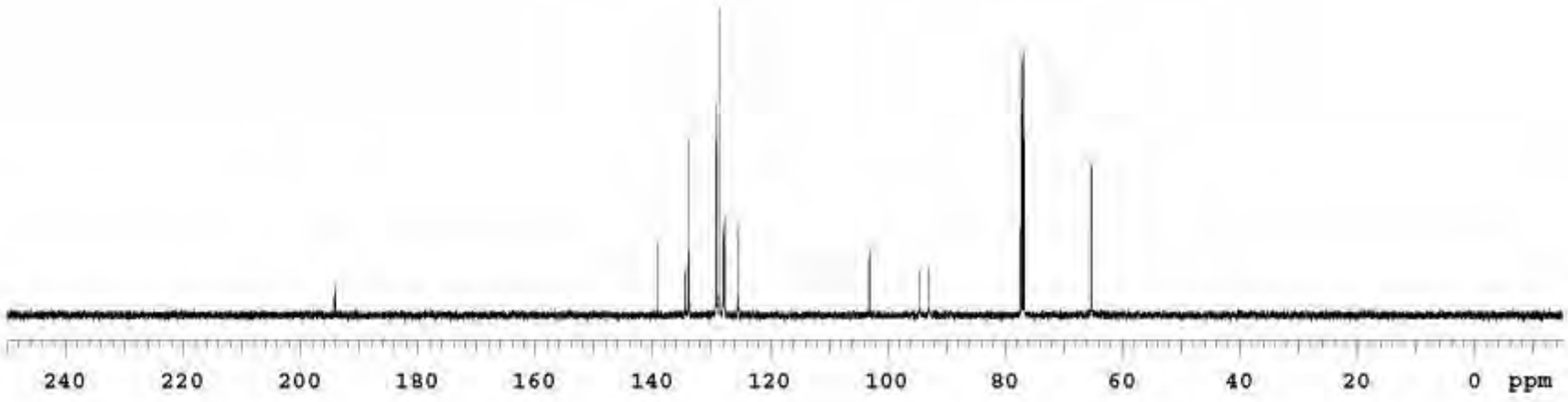
$CDCl_3$, 25 ºC



^{13}C NMR of (3-Dioxolanyl)phenyl-fluoroacetophenone (S1)

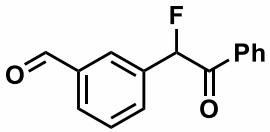


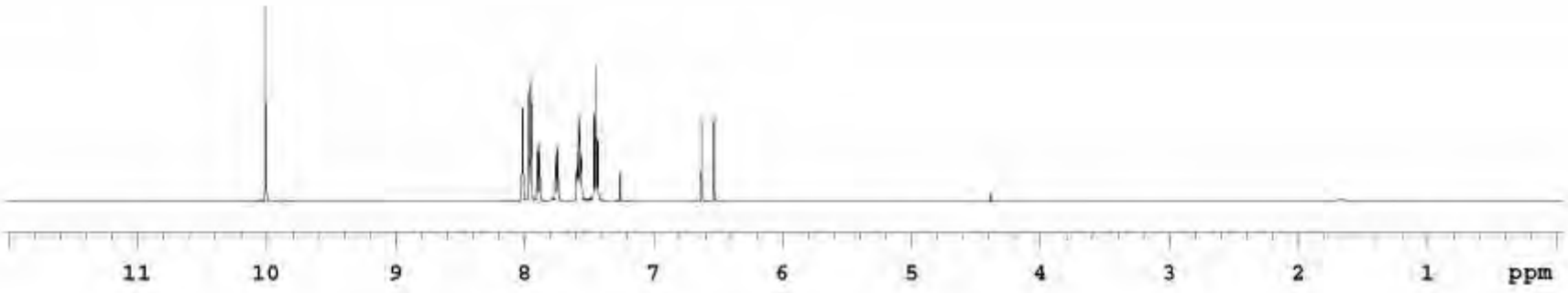
$CDCl_3$, 23 ºC



^{1}H NMR of (3-Formyl)phenyl-fluoroacetophenone (2k)

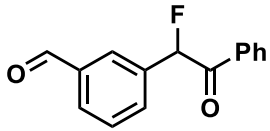
$CDCl_3$, 25 ºC

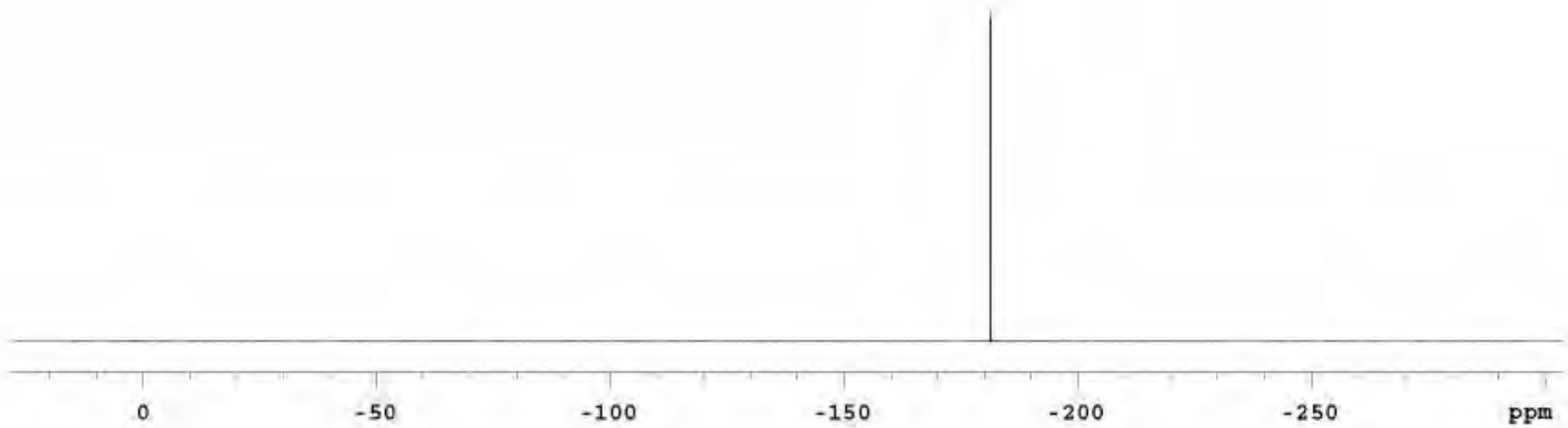




^{19}F NMR of (3-Formyl)phenyl-fluoroacetophenone (2k)

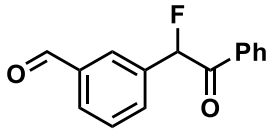
$CDCl_3$, 25 ºC

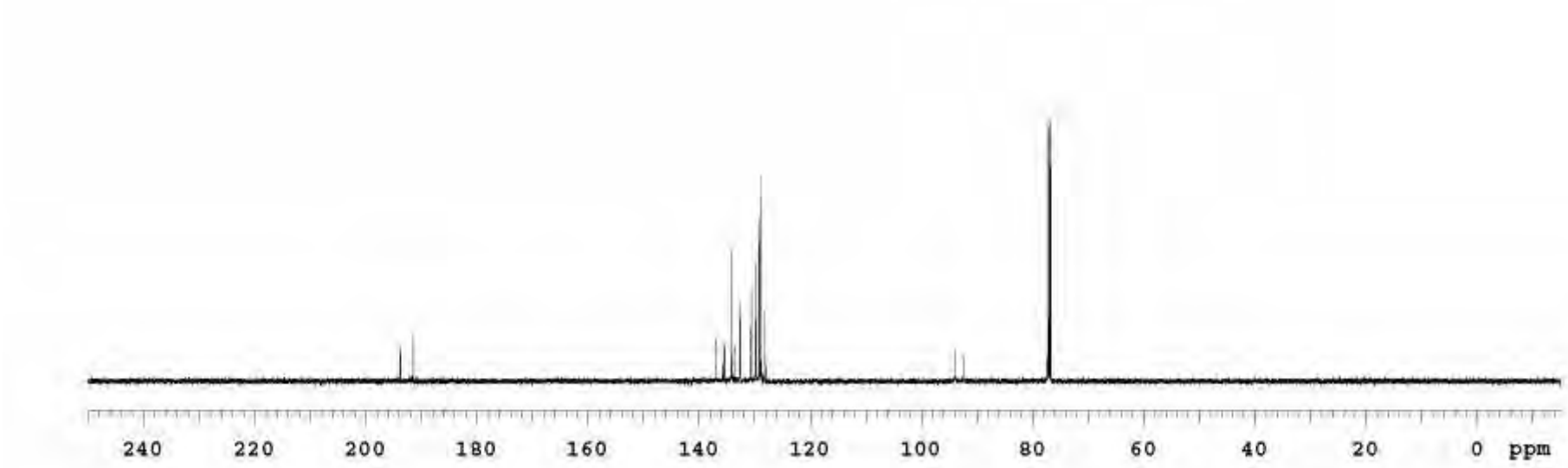




^{13}C NMR of (3-Formyl)phenyl-fluoroacetophenone (2k)

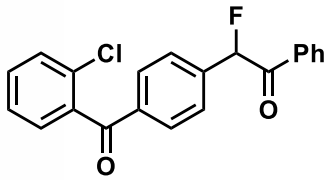
$CDCl_3$, 23 ºC

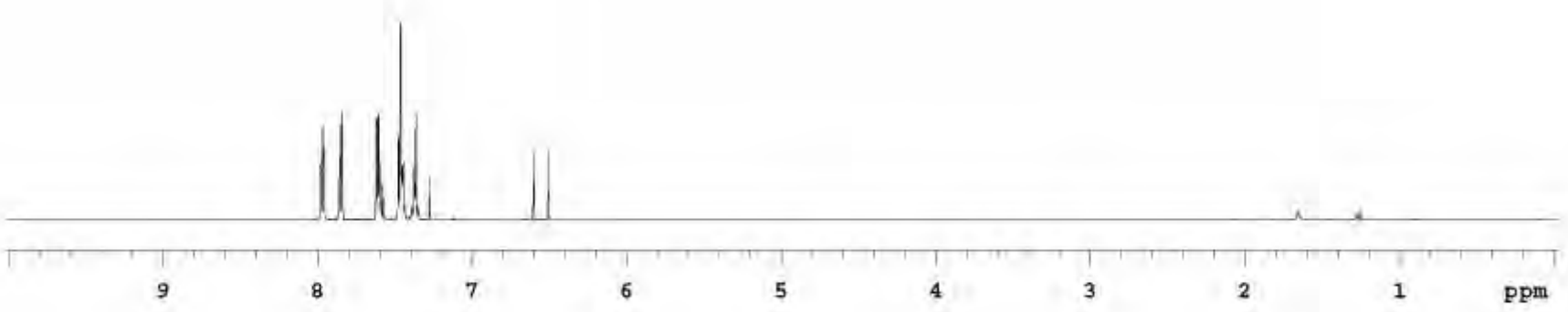




^{1}H NMR of (2-Chlorophenylmethanonyl)phenyl-fluoroacetophenone (2l)

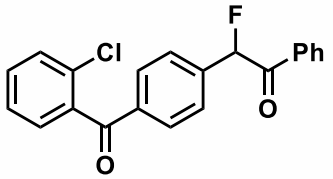
$CDCl_3$, 25 ºC

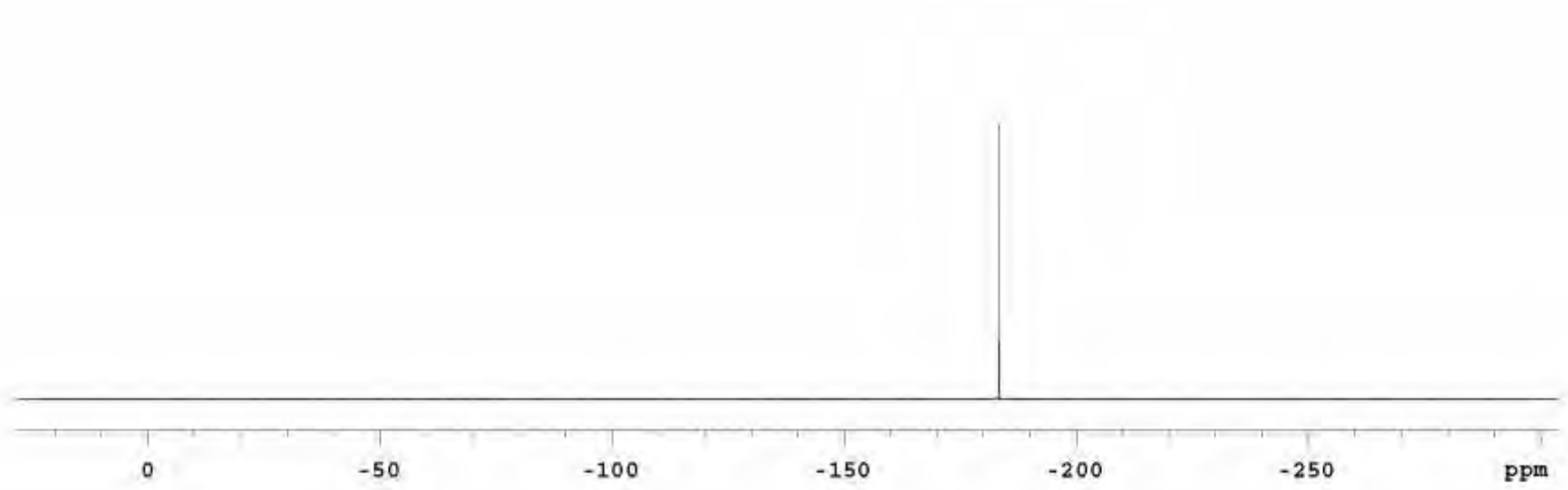




^{19}F NMR of (2-Chlorophenylmethanonyl)phenyl-fluoroacetophenone (2l)

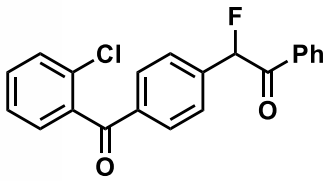
$CDCl_3$, 23 ºC

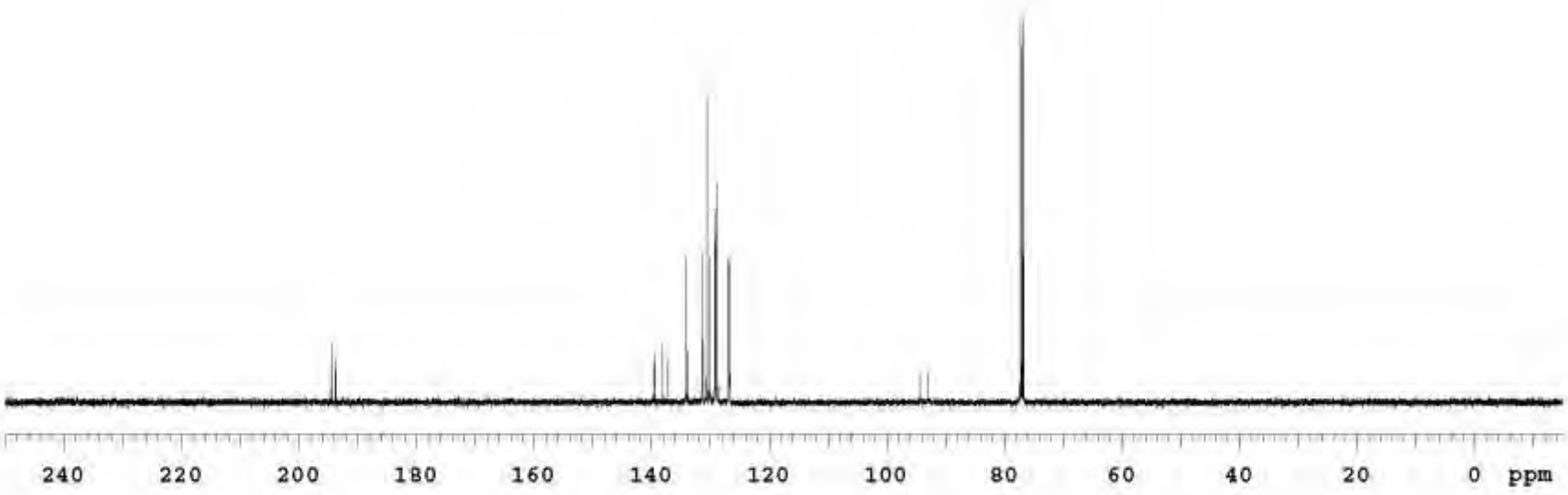




^{13}C NMR of (2-Chlorophenylmethanonyl)phenyl-fluoroacetophenone (2l)

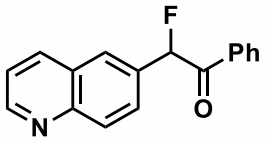
$CDCl_3$, 25 ºC

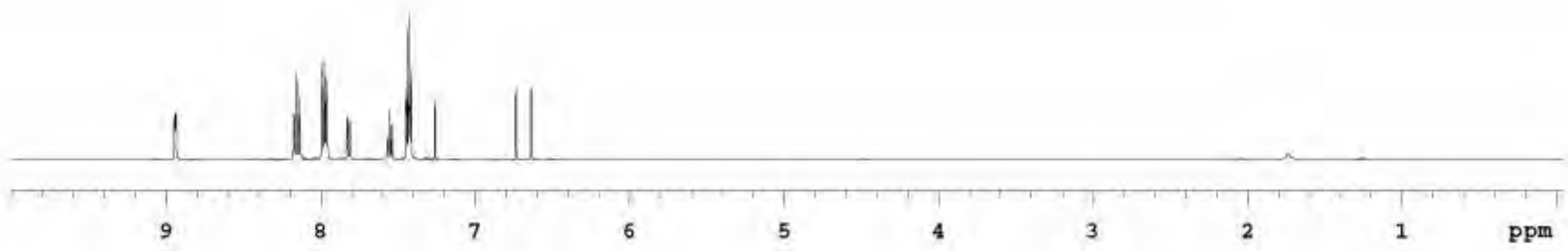




^{1}H NMR of Quinoline-6-fluoroacetophenone (2m)

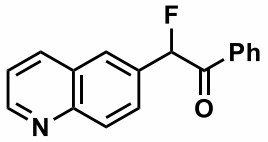
$CDCl_3$, 24 ºC

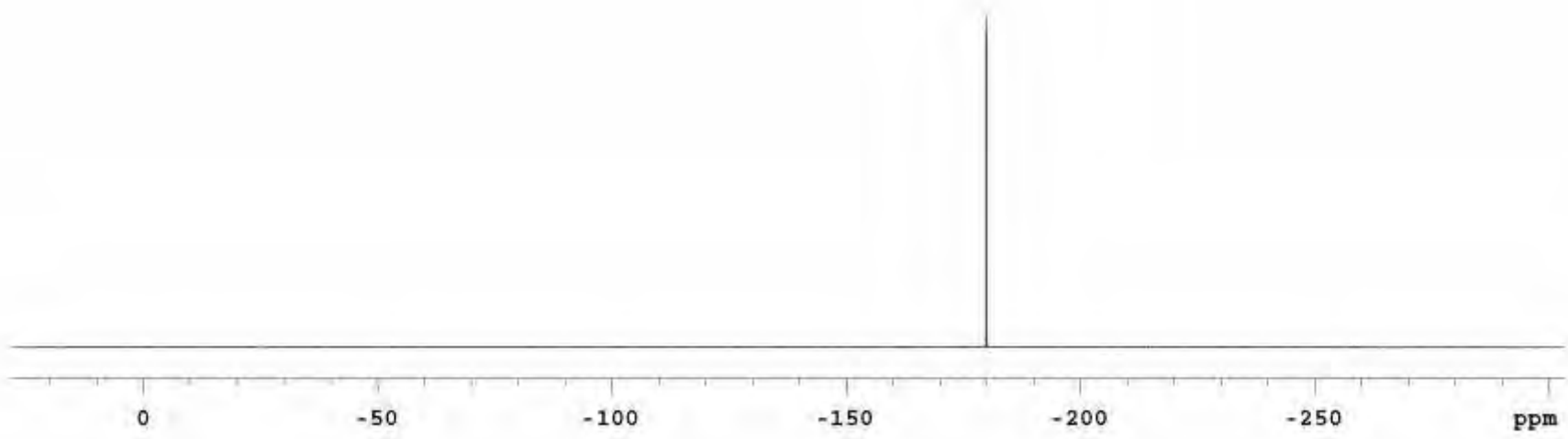




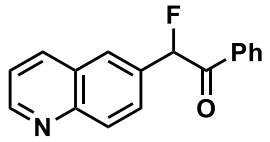
^{19}F NMR of Quinoline-6-fluoroacetophenone (2m)

$CDCl_3$, 24 ºC

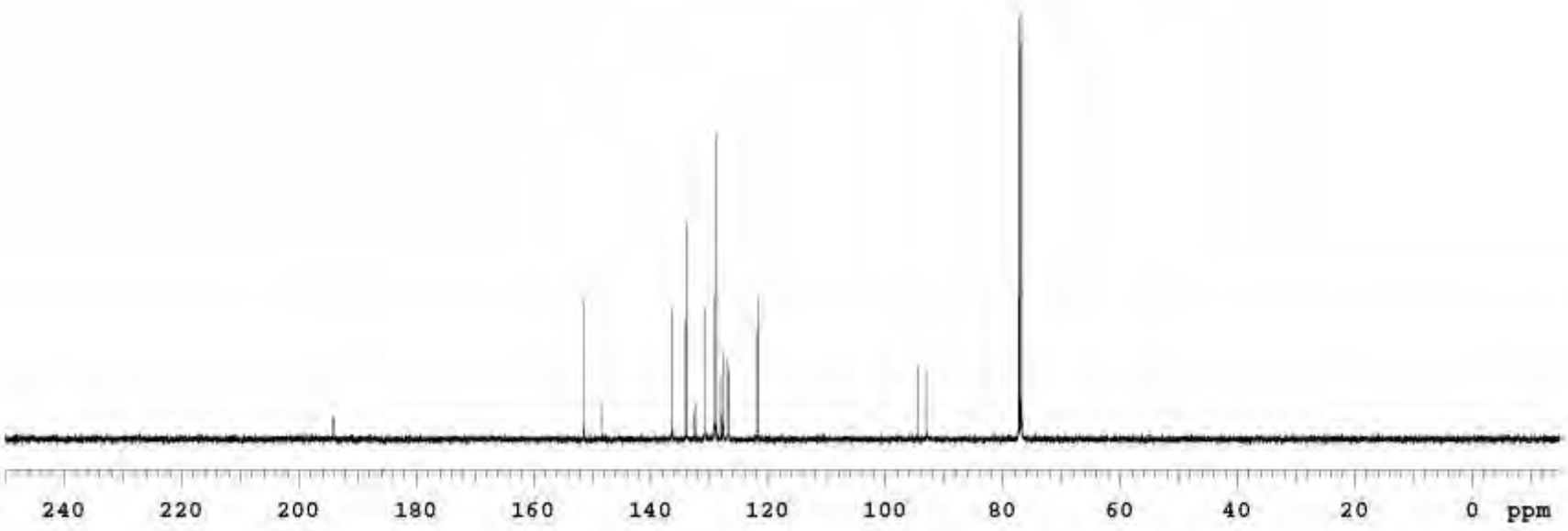




^{13}C NMR of Quinoline-6-fluoroacetophenone (2m)

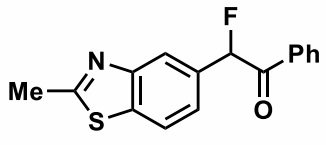


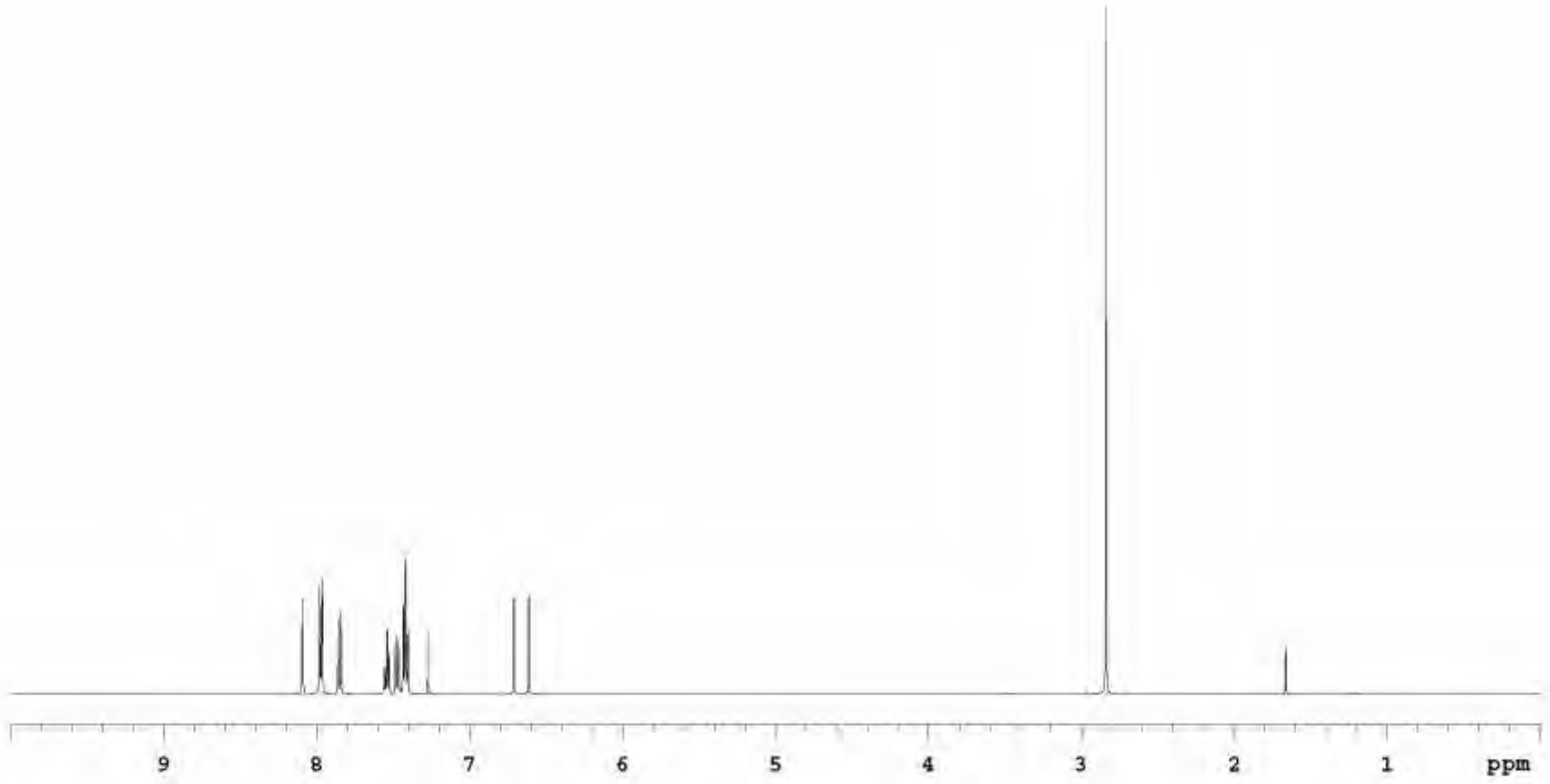
$CDCl_3$, 25 ºC



^{1}H NMR of (2-Methylbenzo[*d*]thiazol-5-yl)-fluoroacetophenone (2n)

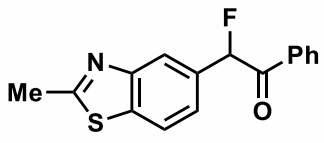
$CDCl_3$, 25 ºC

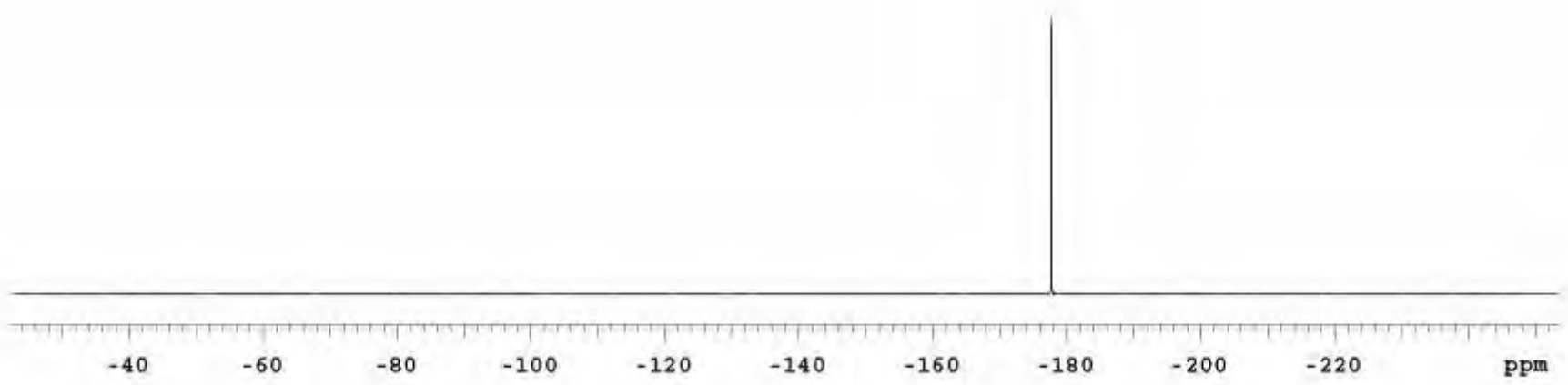




^{19}F NMR of (2-Methylbenzo[*d*]thiazol-5-yl)-fluoroacetophenone (2n)

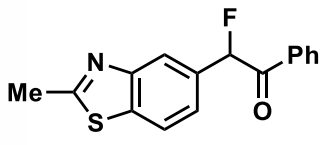
$CDCl_3$, 25 ºC

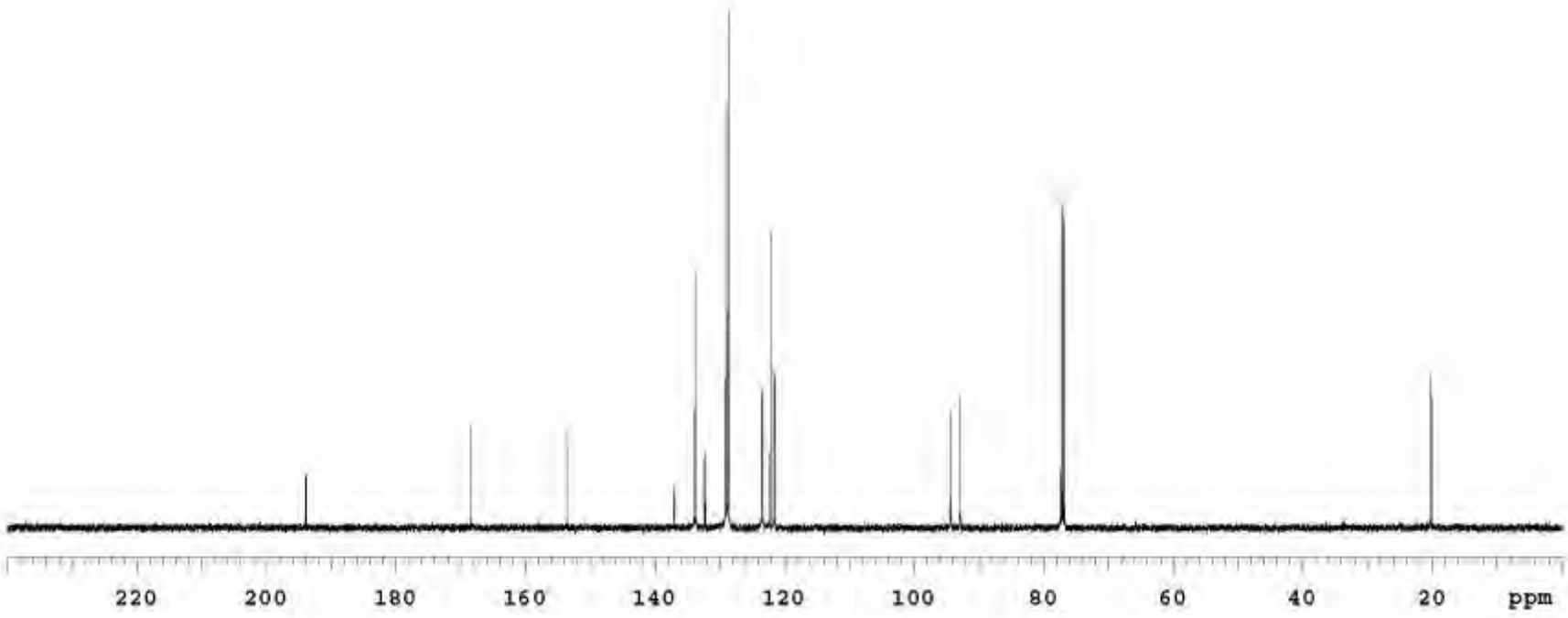




^{13}C NMR of (2-Methylbenzo[*d*]thiazol-5-yl)-fluoroacetophenone (2n)

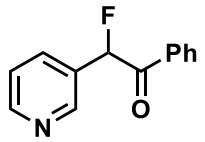
$CDCl_3$, 25 ºC

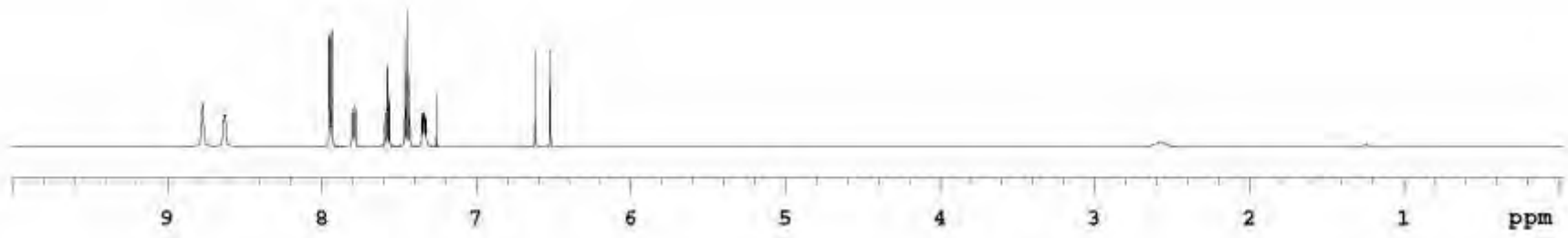




^{1}H NMR of Pyridine-3-fluoroacetophenone (2o)

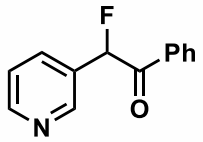
$CDCl_3$, 25 ºC

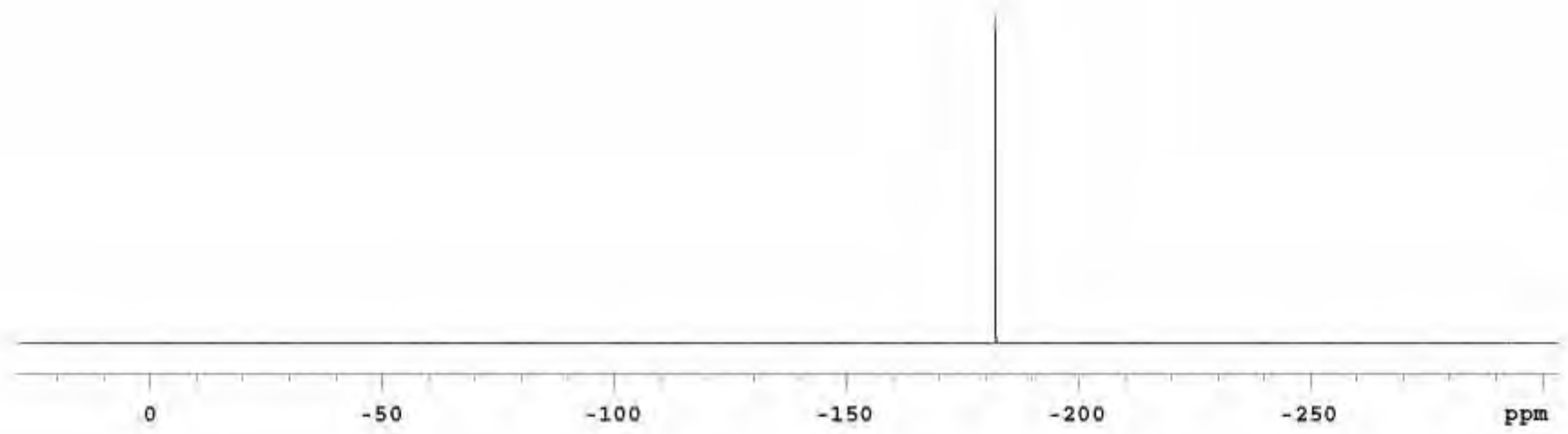




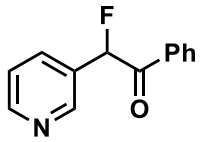
^{19}F NMR of Pyridine-3-fluoroacetophenone (2o)

$CDCl_3$, 25 ºC

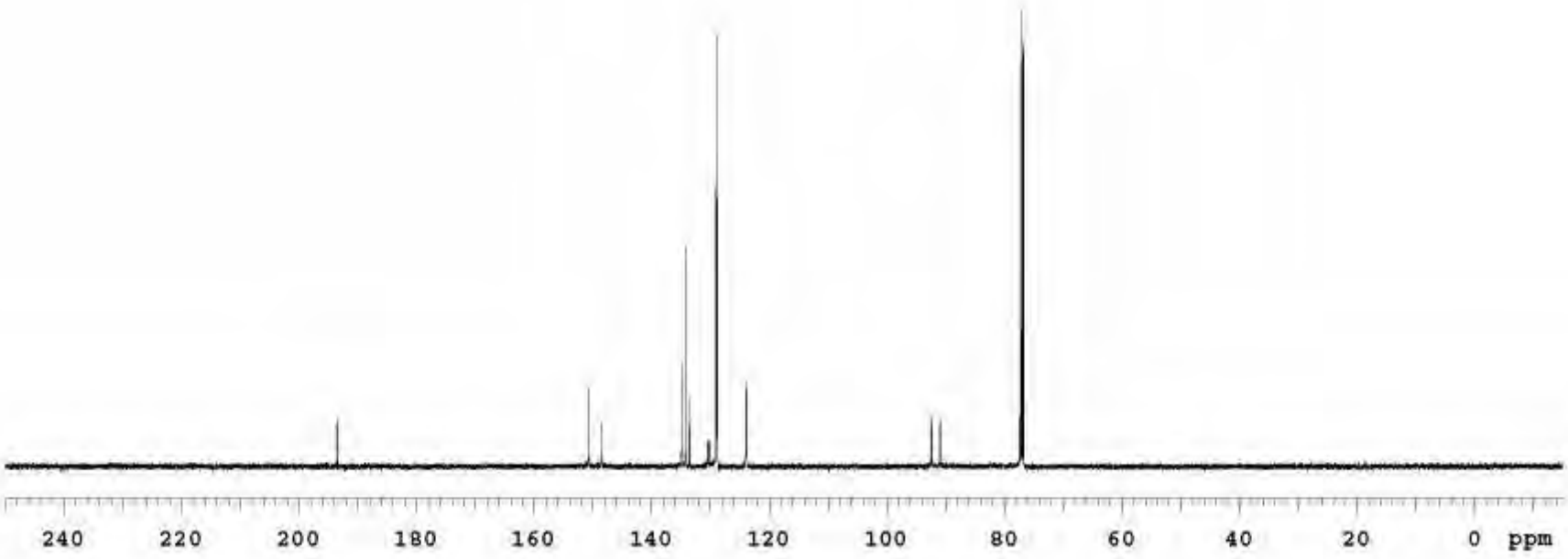




^{13}C NMR of Pyridine-3-fluoroacetophenone (2o)

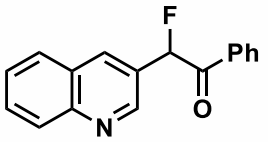


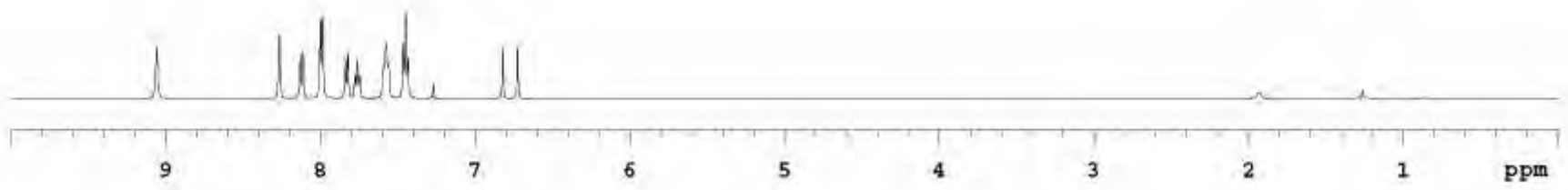
$CDCl_3$, 23 ºC



^{1}H NMR of Quinoline-3-fluoroacetophenone (2p)

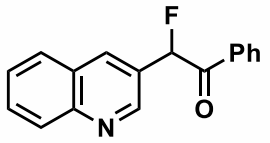
$CDCl_3$, 22 ºC

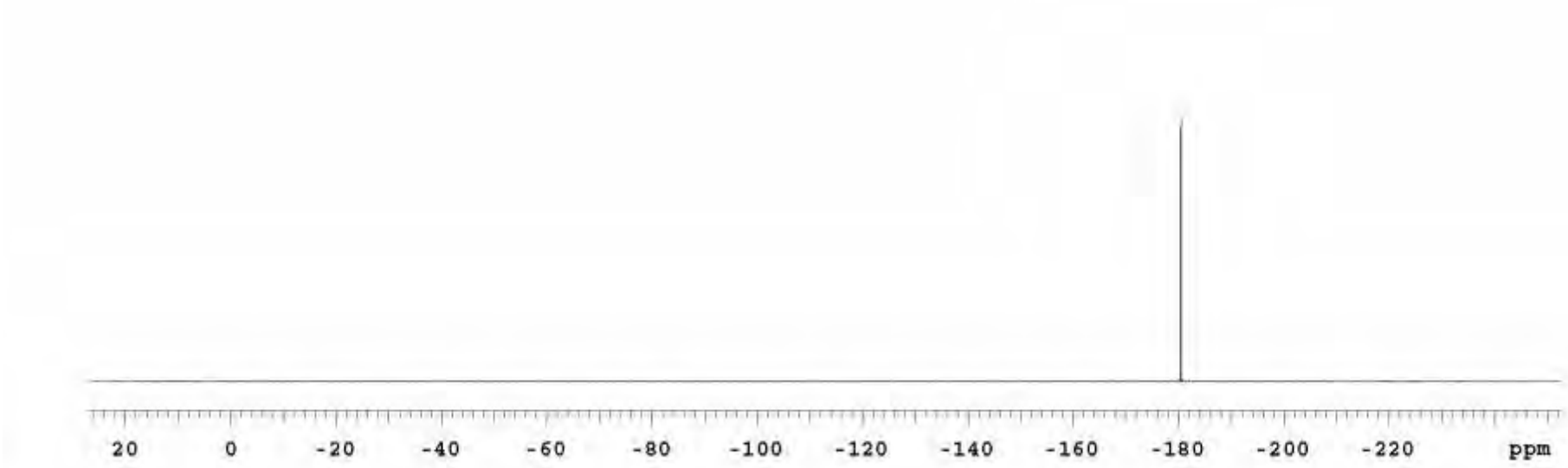




^{19}F NMR of Quinoline-3-fluoroacetophenone (2p)

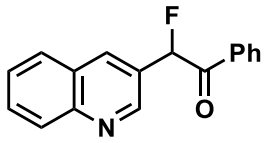
$CDCl_3$, 25 ºC

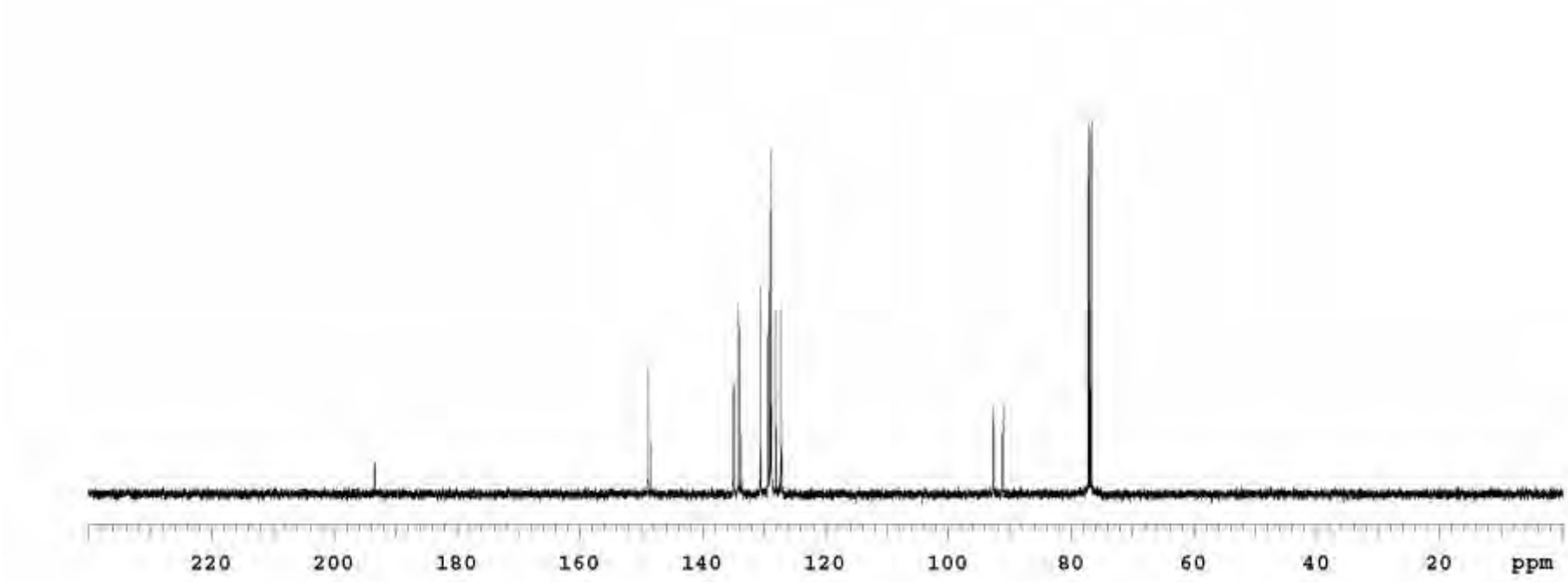




^{13}C NMR of Quinoline-3-fluoroacetophenone (2p)

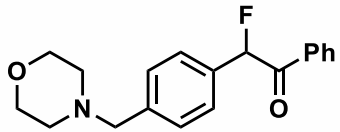
$CDCl_3$, 25 ºC

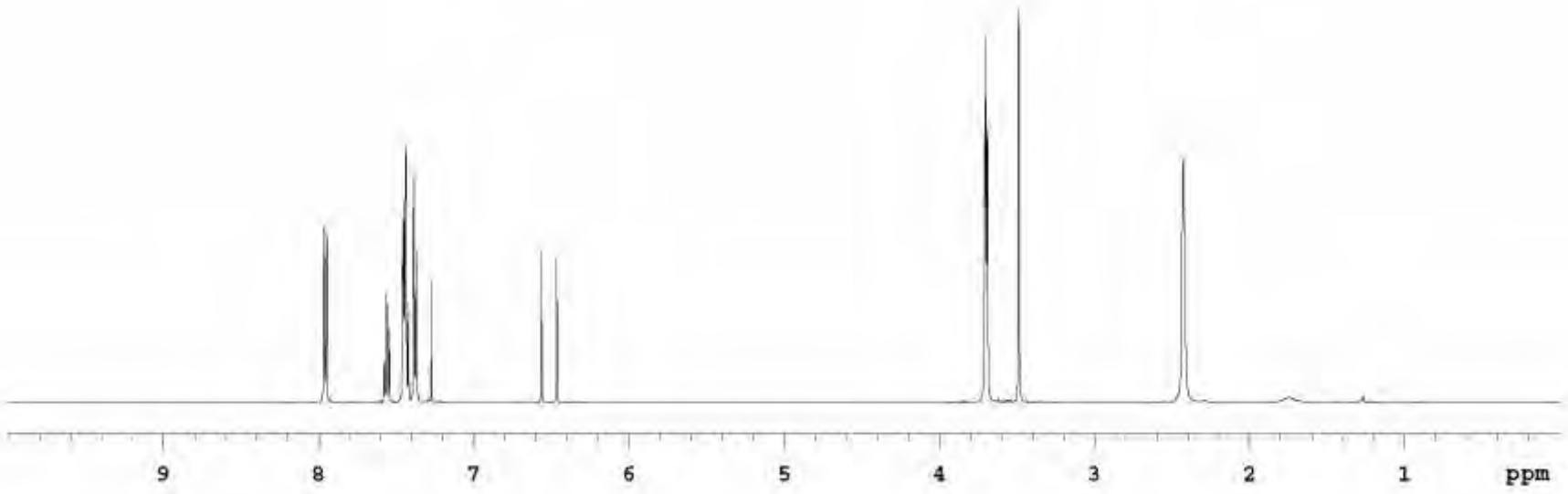




^{1}H NMR of (3-Morpholinomethyl)phenyl-fluoroacetophenone (2q)

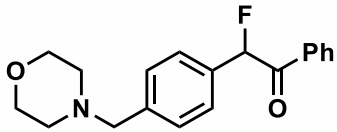
$CDCl_3$, 25 ºC

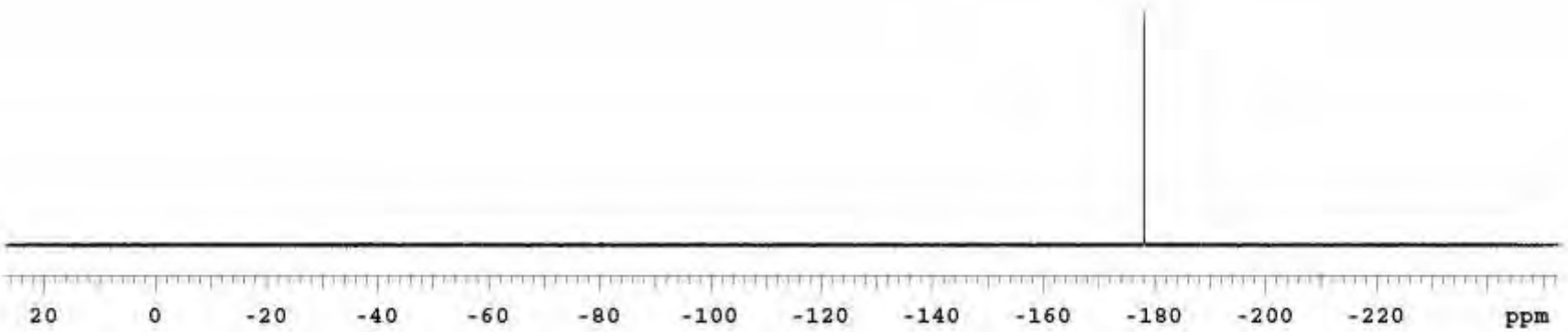




^{19}F NMR of (3-Morpholinomethyl)phenyl-fluoroacetophenone (2q)

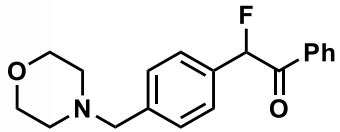
$CDCl_3$, 24 ºC

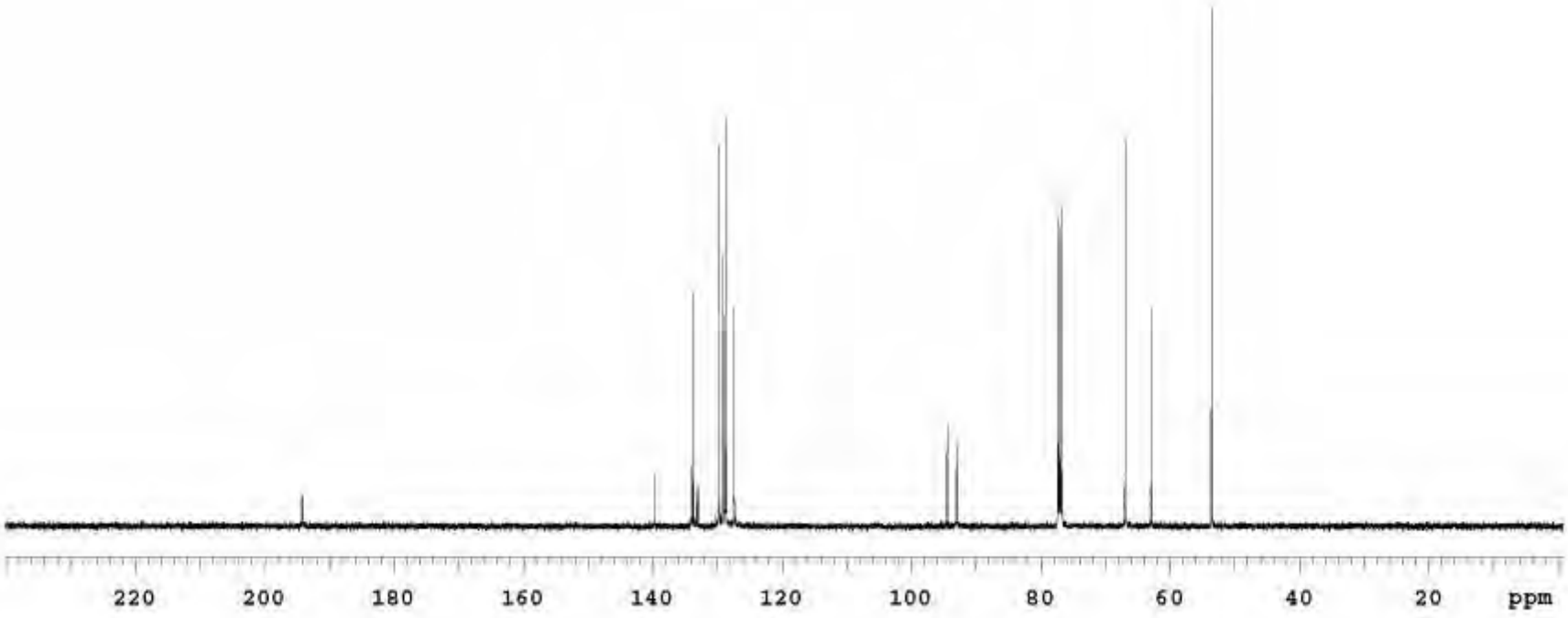




^{13}C NMR of (3-Morpholinomethyl)phenyl-fluoroacetophenone (2q)

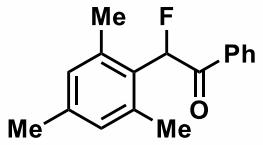
$CDCl_3$, 25 ºC

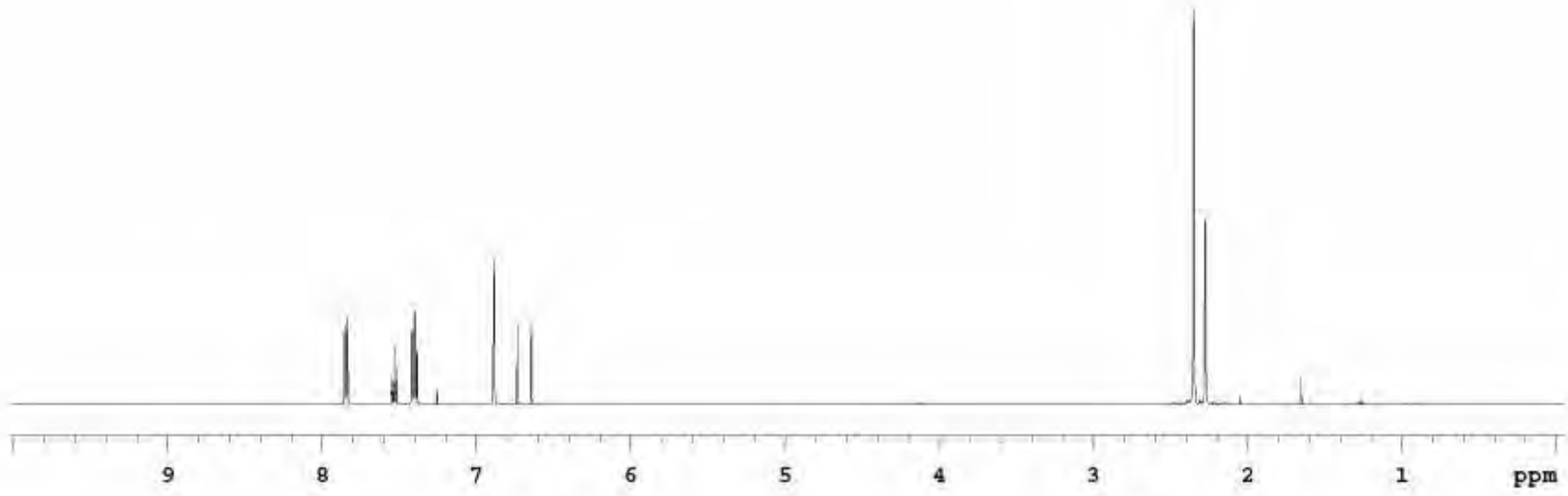




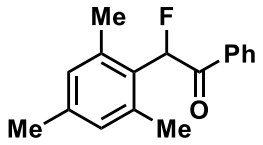
^{1}H NMR of Mesitylenyl-fluoroacetophenone (2s)

$CDCl_3$, 25 ºC

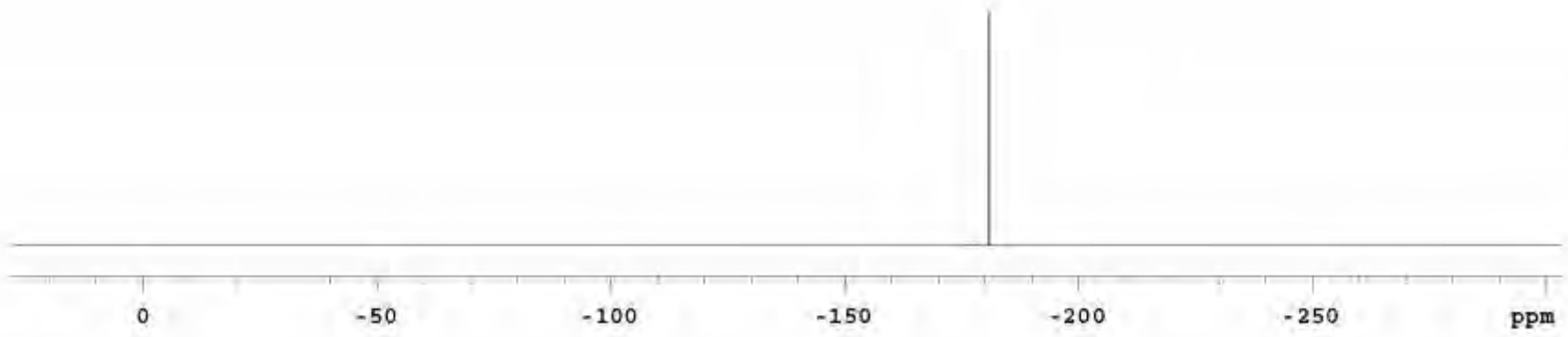




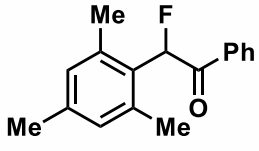
^{19}F NMR of Mesitylenyl-fluoroacetophenone (2s)



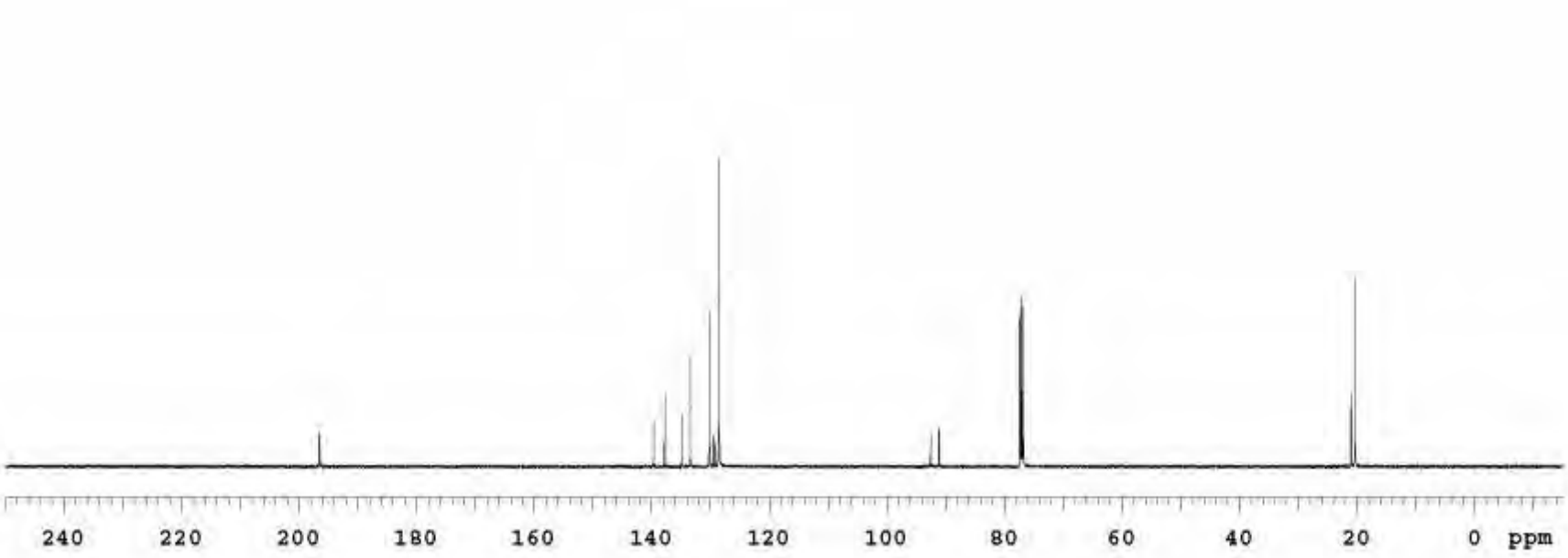
$CDCl_3$, 25 ºC



^{13}C NMR of Mesitylenyl-fluoroacetophenone (2s)

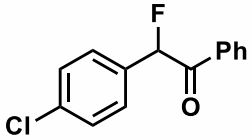


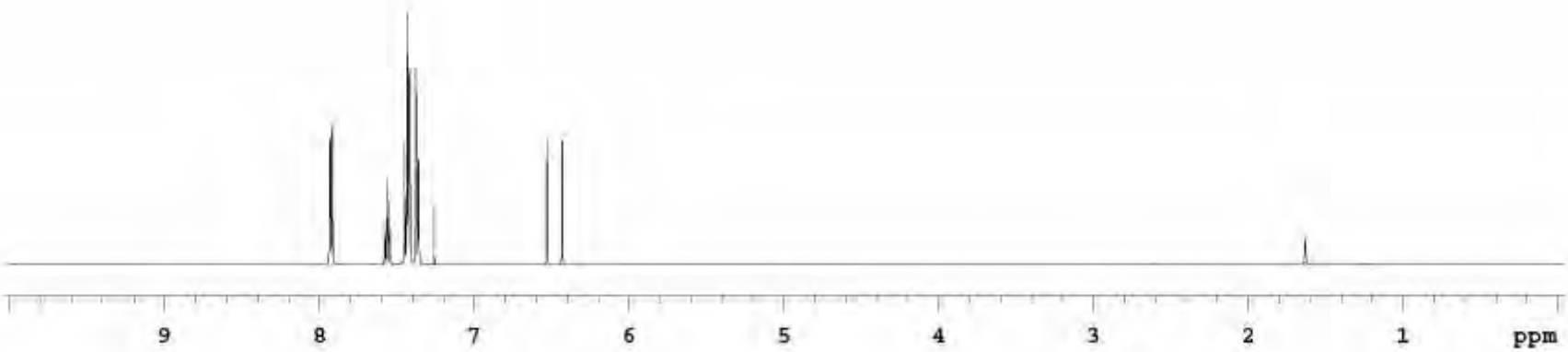
$CDCl_3$, 23 ºC



^{1}H NMR of (3-Chloro)phenyl-fluoroacetophenone (S2)

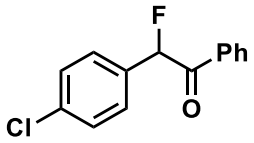
$CDCl_3$, 23 ºC

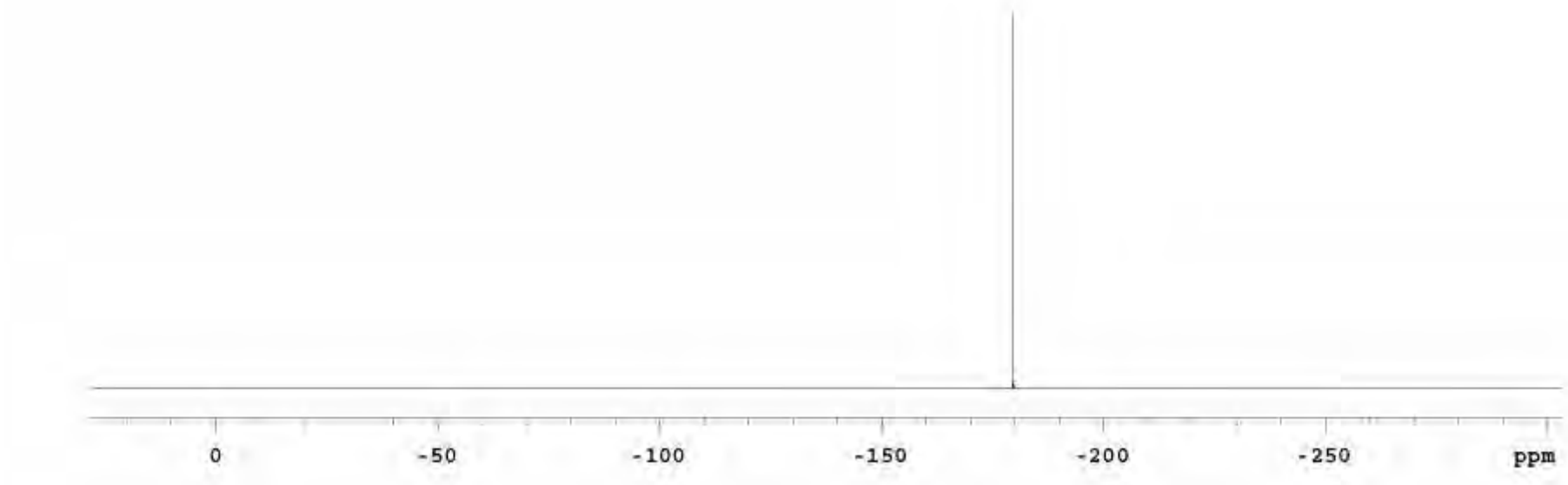




^{19}F NMR of (3-Chloro)phenyl-fluoroacetophenone (S2)

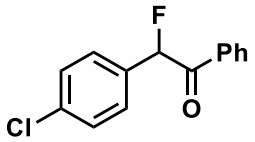
$CDCl_3$, 23 ºC

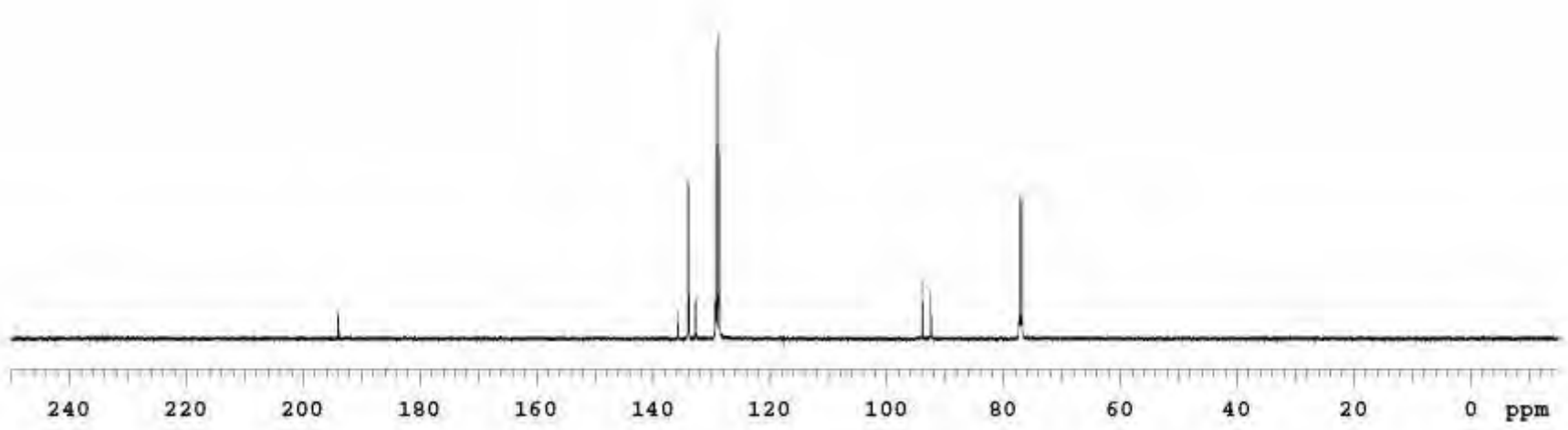




^{13}C NMR of (3-Chloro)phenyl-fluoroacetophenone (S2)

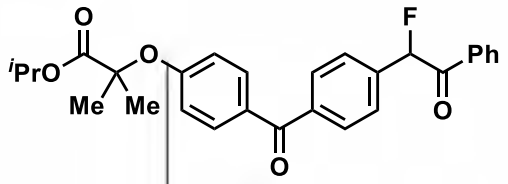
$CDCl_3$, 25 ºC

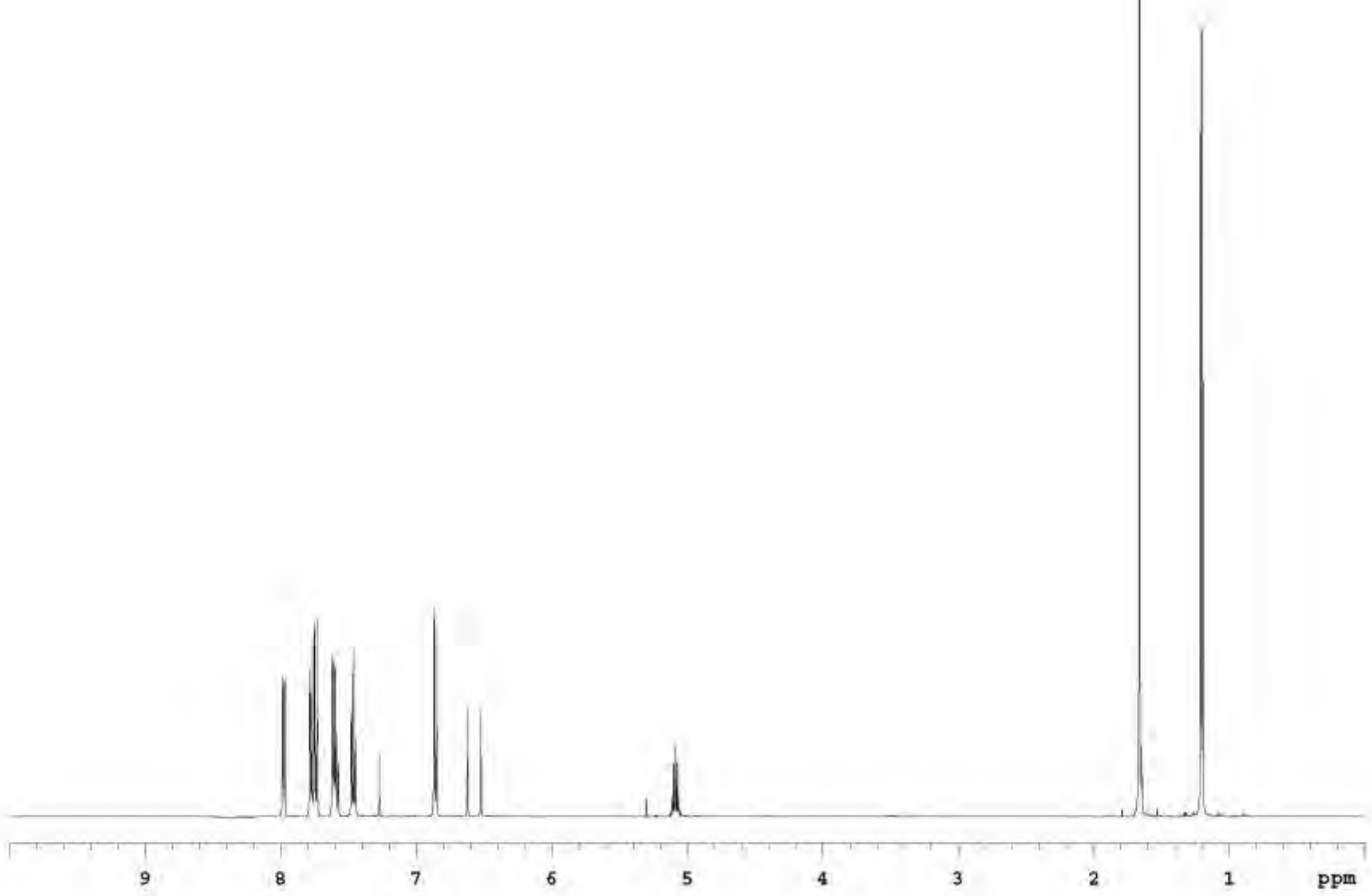




^{1}H NMR of (1-Fluoro-2-oxo-2-phenylethyl)-fenofibrate (S2)

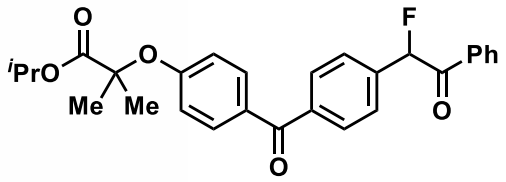
$CDCl_3$, 25 ºC

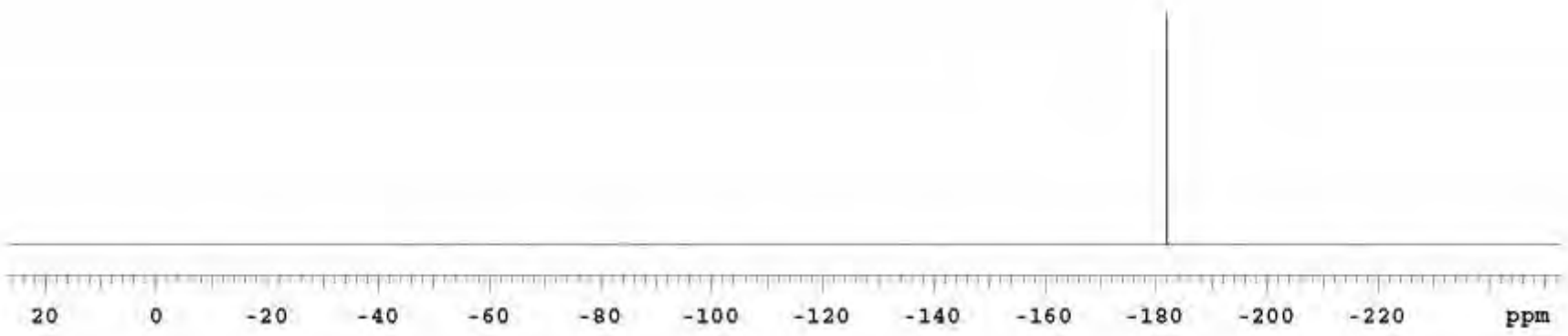




^{19}F NMR of (1-Fluoro-2-oxo-2-phenylethyl)-fenofibrate (S2)

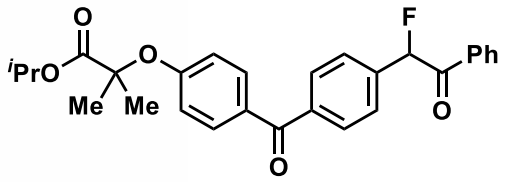
$CDCl_3$, 24 ºC

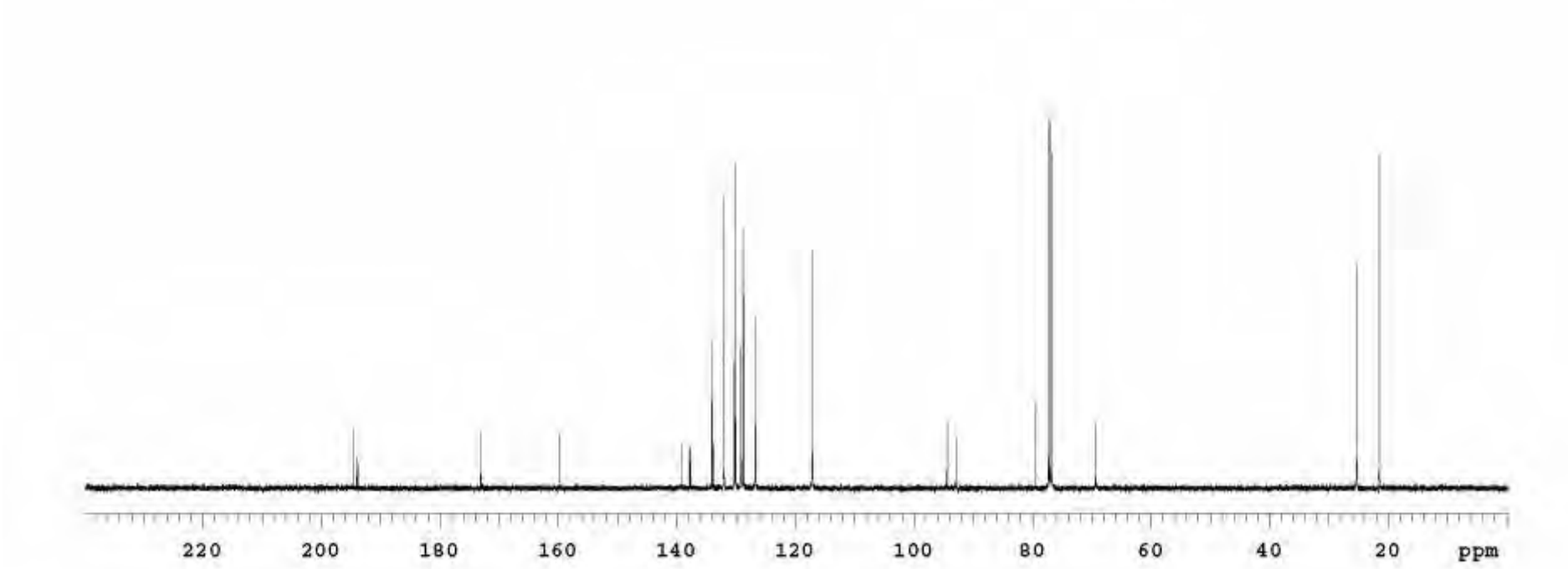




^{13}C NMR of (1-Fluoro-2-oxo-2-phenylethyl)-fenofibrate (S2)

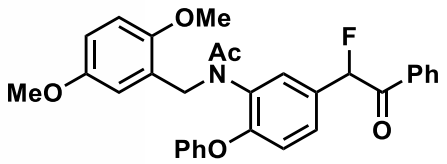
$CDCl_3$, 25 ºC

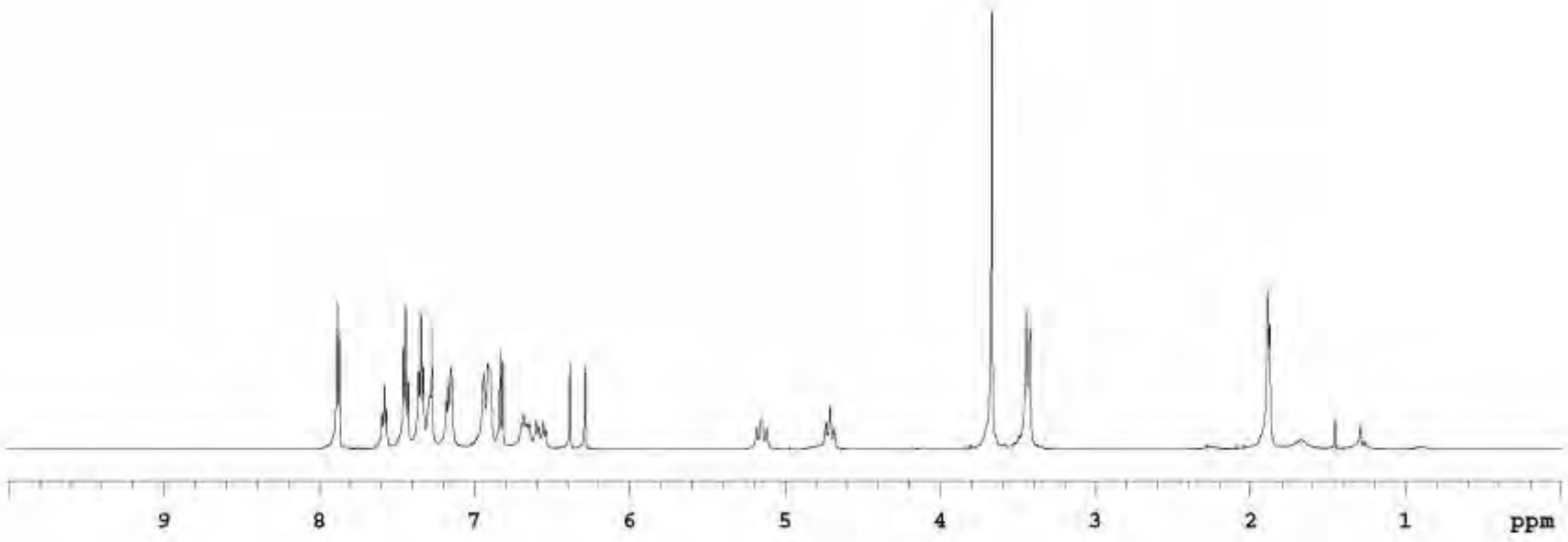




^{1}H NMR of (1-Fluoro-2-oxo-2-phenylethyl)-DAA1106 (S3)

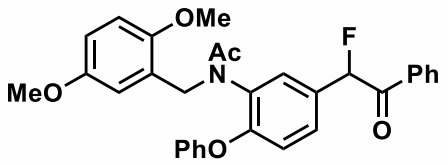
$CDCl_3$, 55 ºC

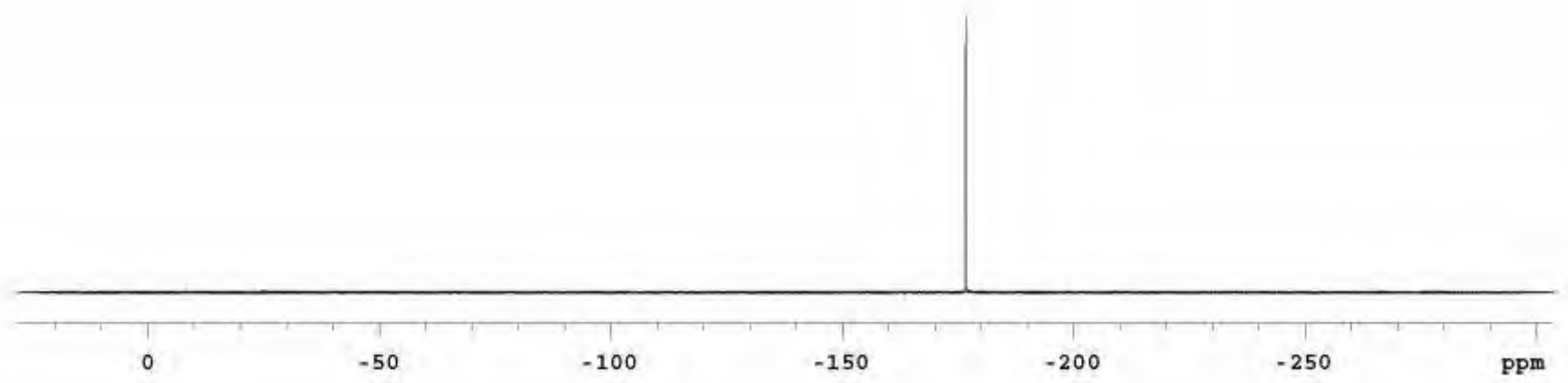




^{19}F NMR of (1-Fluoro-2-oxo-2-phenylethyl)-DAA1106 (S3)

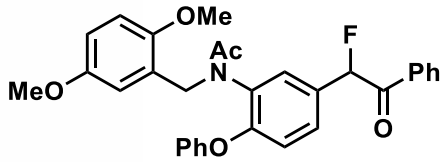
$CDCl_3$, 25 ºC

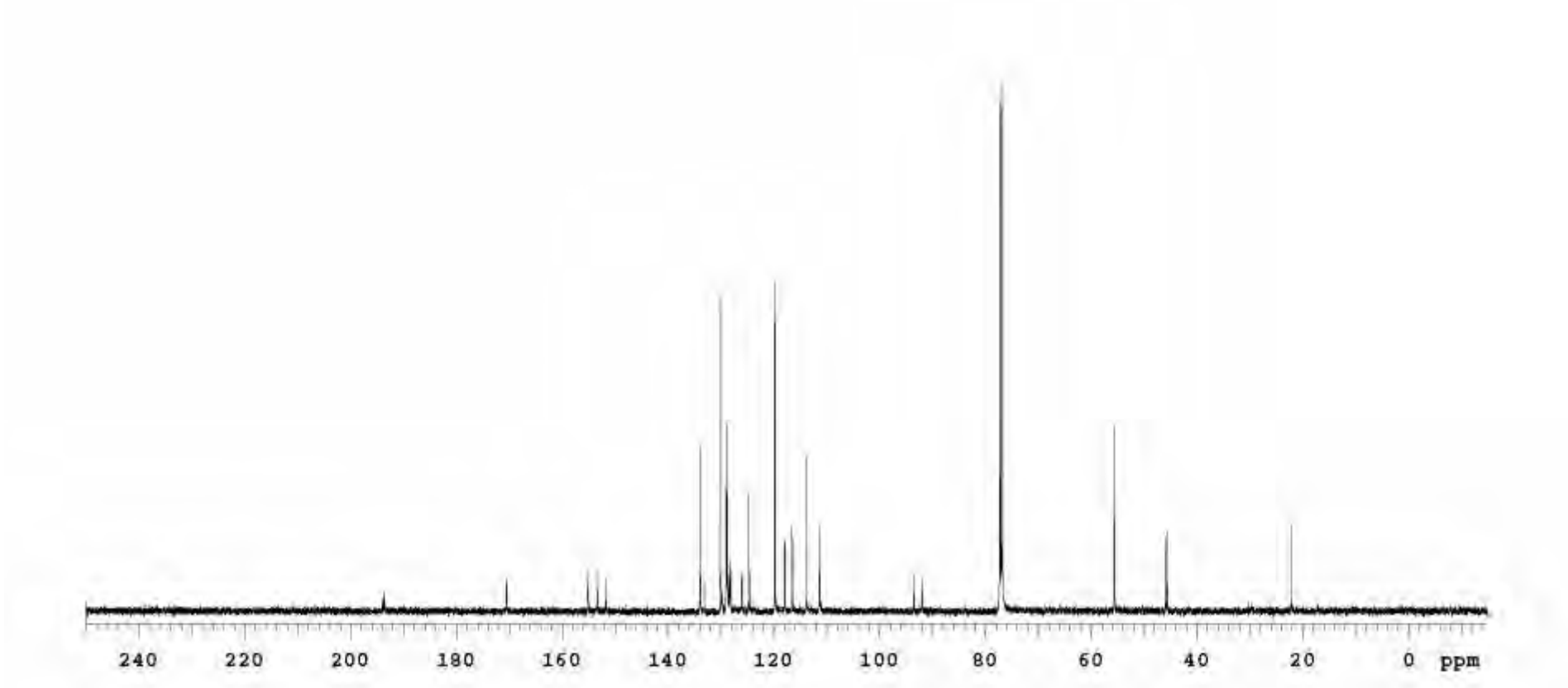




^{13}C NMR of (1-Fluoro-2-oxo-2-phenylethyl)-DAA1106 (S3)

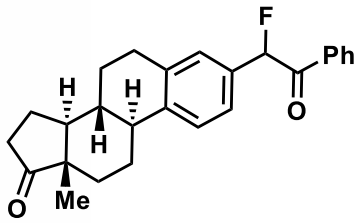
$CDCl_3$, 25 ºC

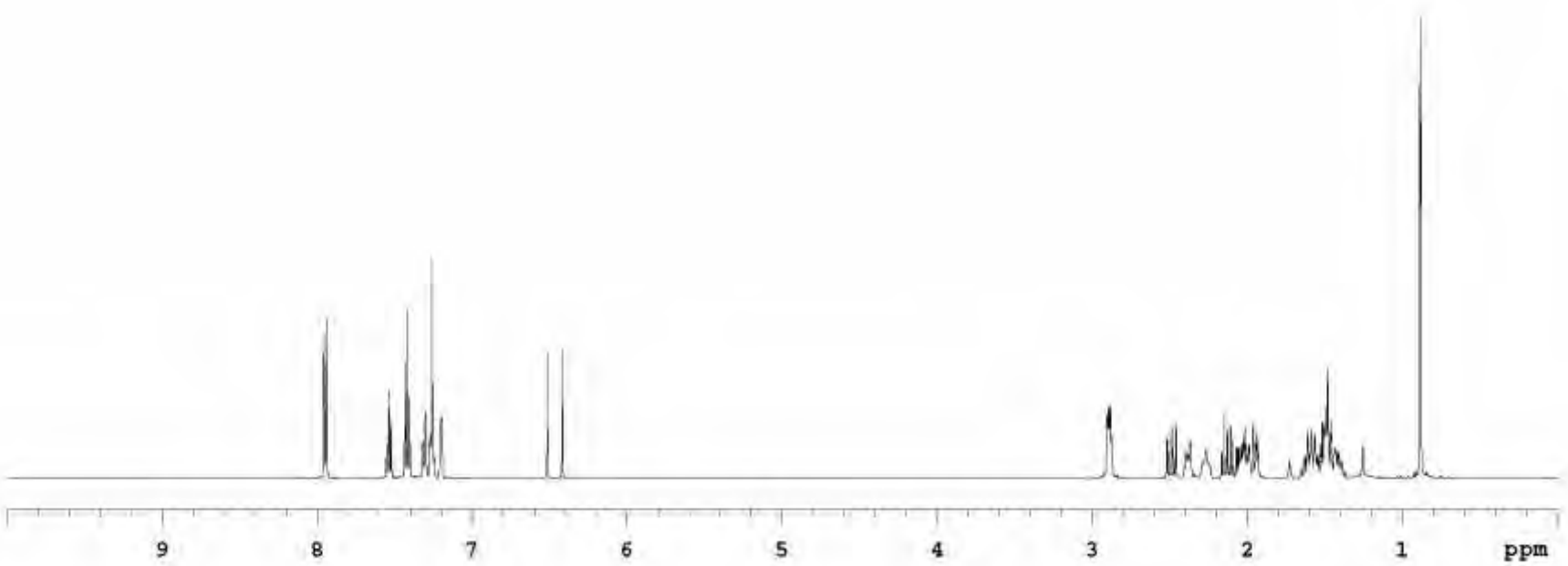




^{1}H NMR of (1-Fluoro-2-oxo-2-phenylethyl)-estrone (S4)

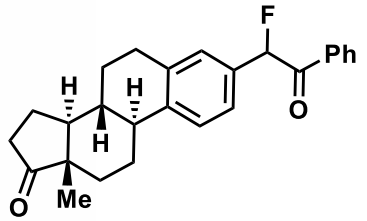
$CDCl_3$, 25 ºC

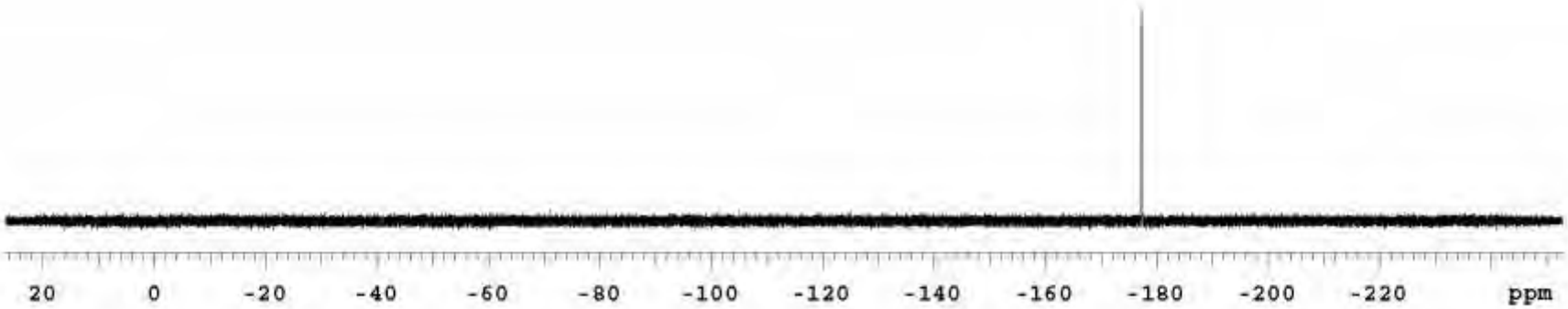




^{19}F NMR of (1-Fluoro-2-oxo-2-phenylethyl)-estrone (S4)

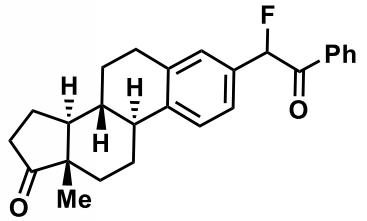
$CDCl_3$, 25 ºC

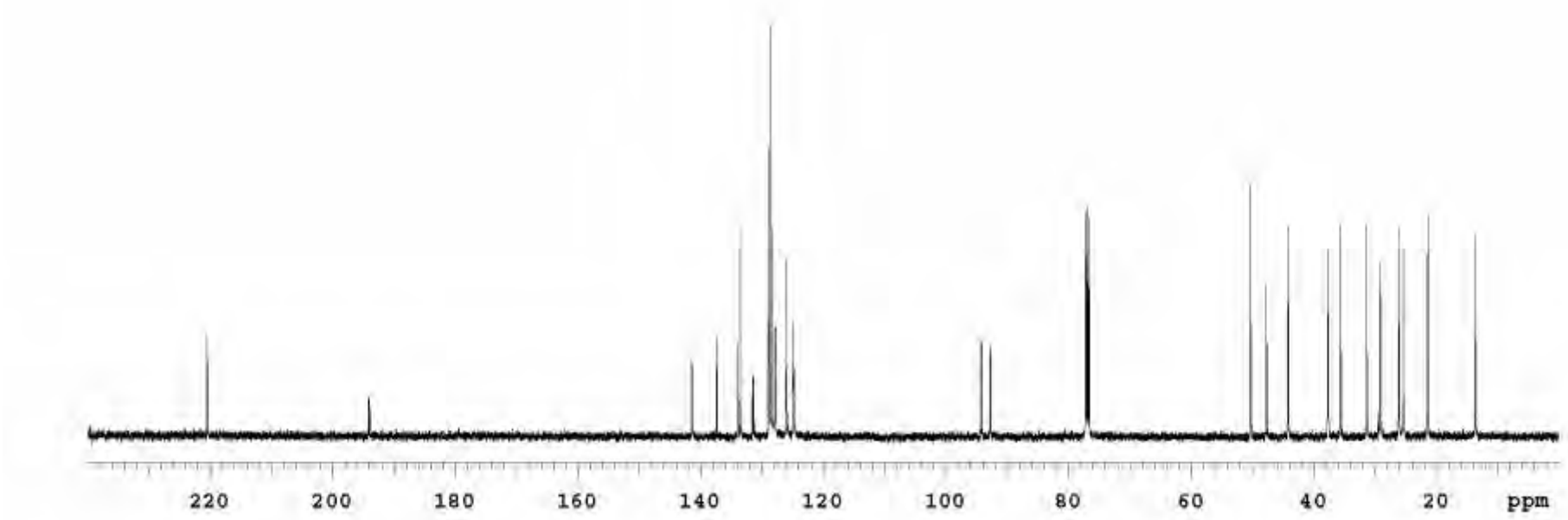




^{13}C NMR of (1-Fluoro-2-oxo-2-phenylethyl)-estrone (S4)

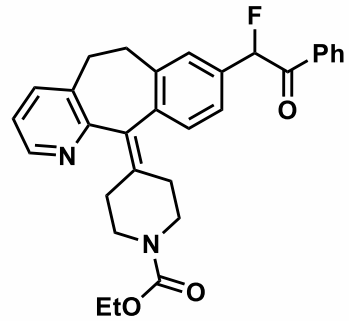
$CDCl_3$, 25 ºC

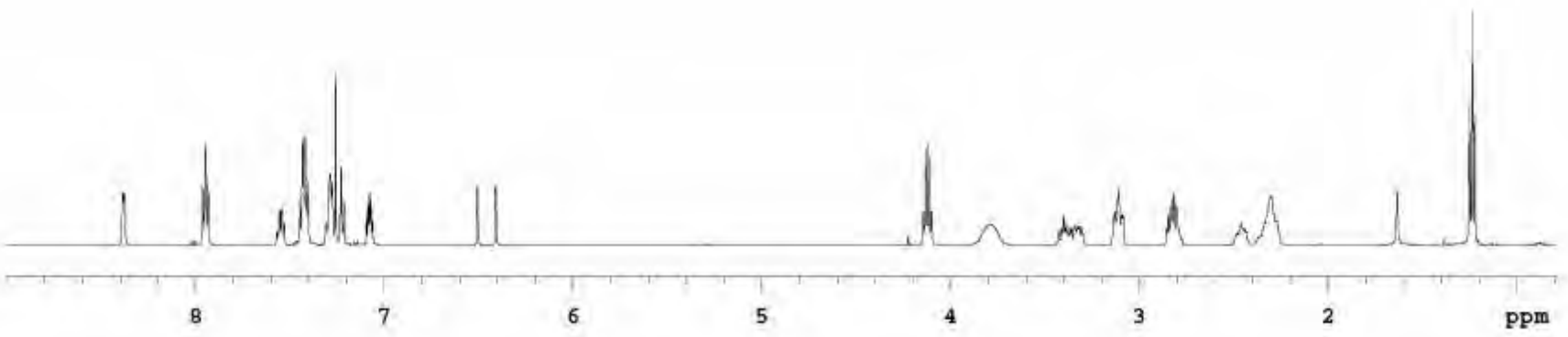




^{1}H NMR of (1-Fluoro-2-oxo-2-phenylethyl)-claritin (S5)

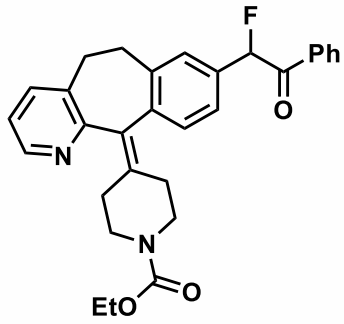
$CDCl_3$, 24 ºC

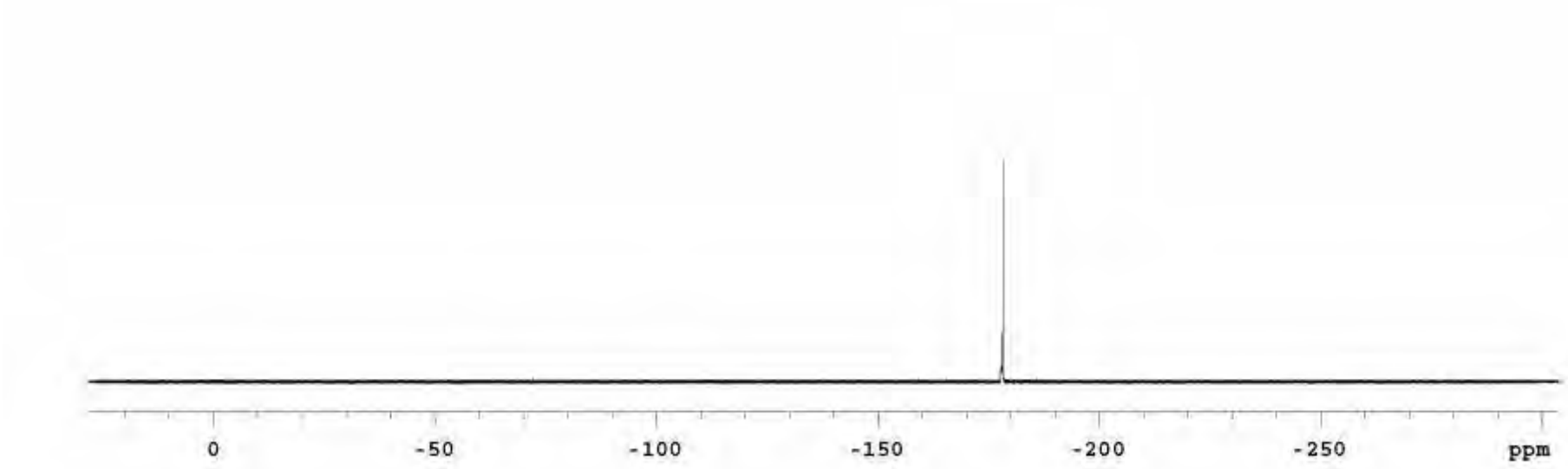




^{19}F NMR of (1-Fluoro-2-oxo-2-phenylethyl)-claritin (S5)

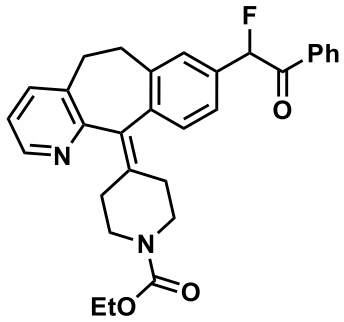
$CDCl_3$, 24 ºC

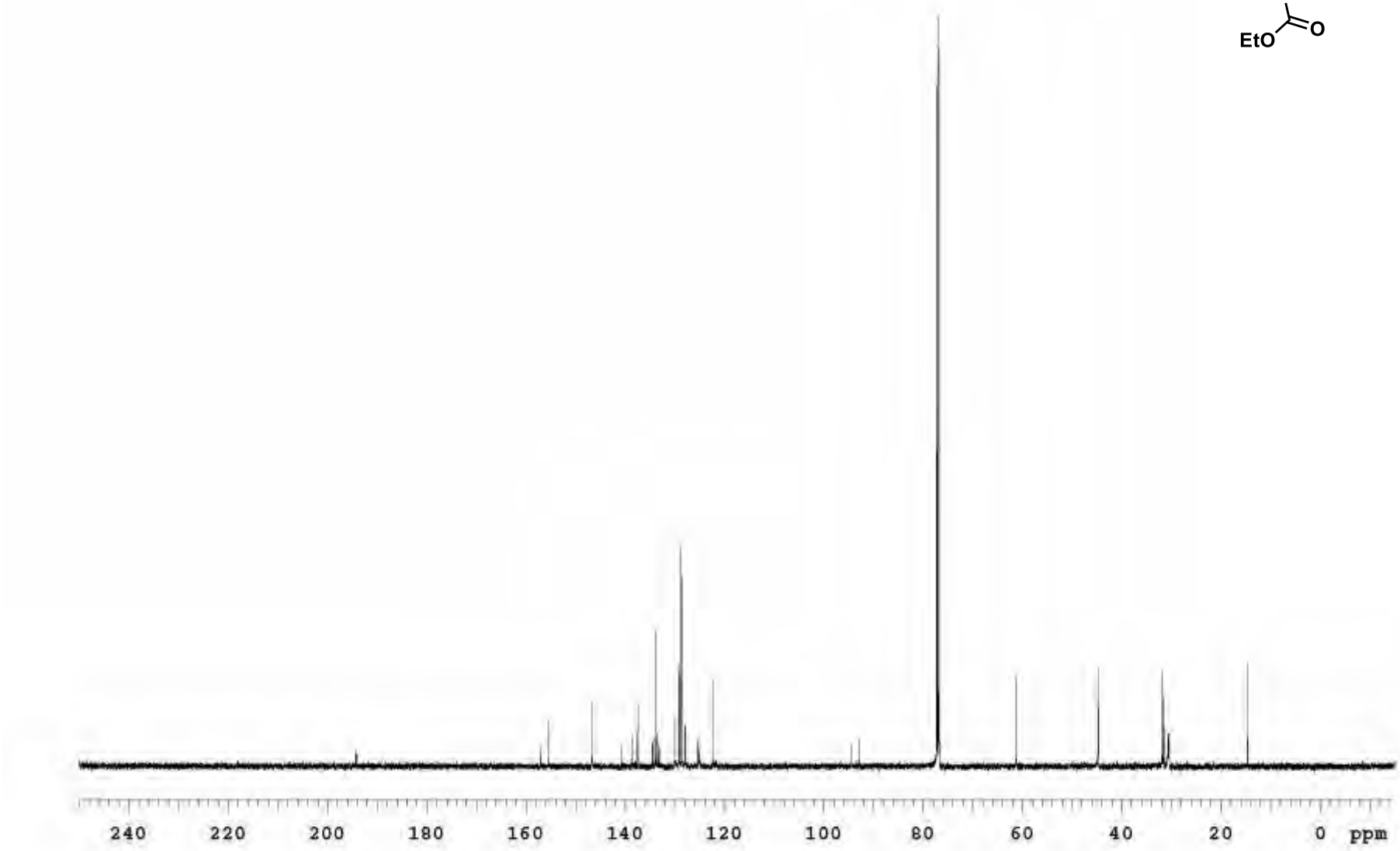




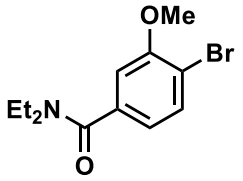
^{13}C NMR of (1-Fluoro-2-oxo-2-phenylethyl)-claritin (S5)

$CDCl_3$, 25 ºC

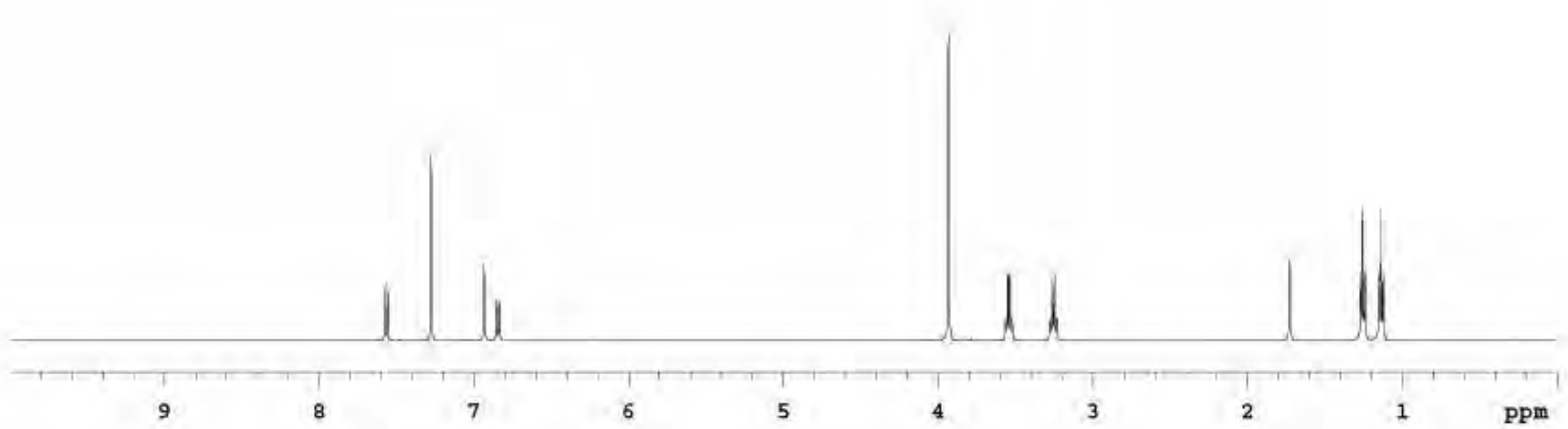




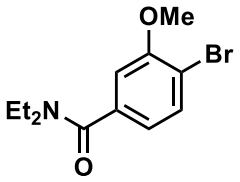
^{1}H NMR of 4-Bromo-*N*,*N*-diethyl-3-methoxybenzamide (S12)



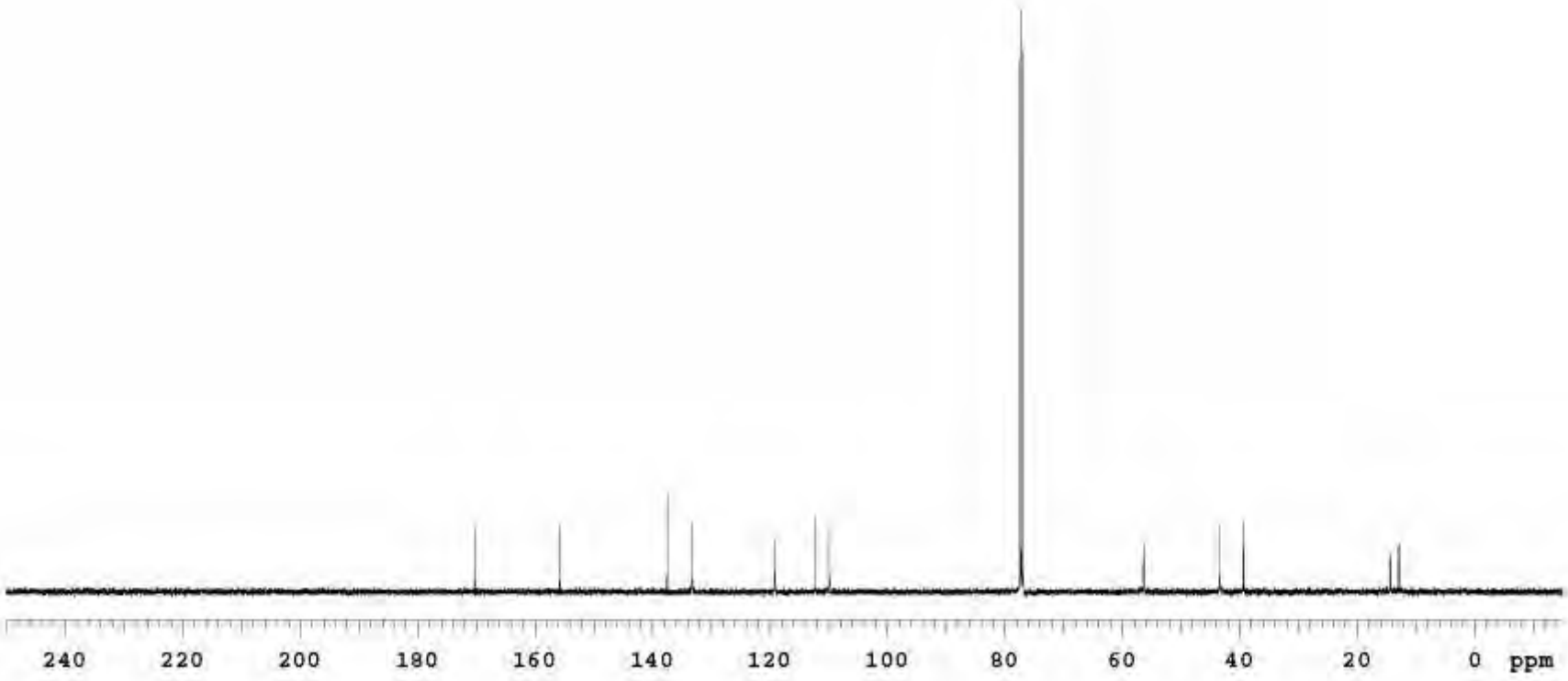
$CDCl_3$, −15ºC



^{13}C NMR of 4-Bromo-*N*,*N*-diethyl-3-methoxybenzamide (S12)

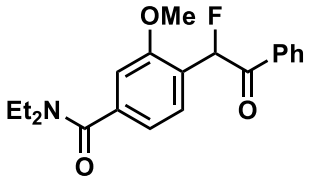


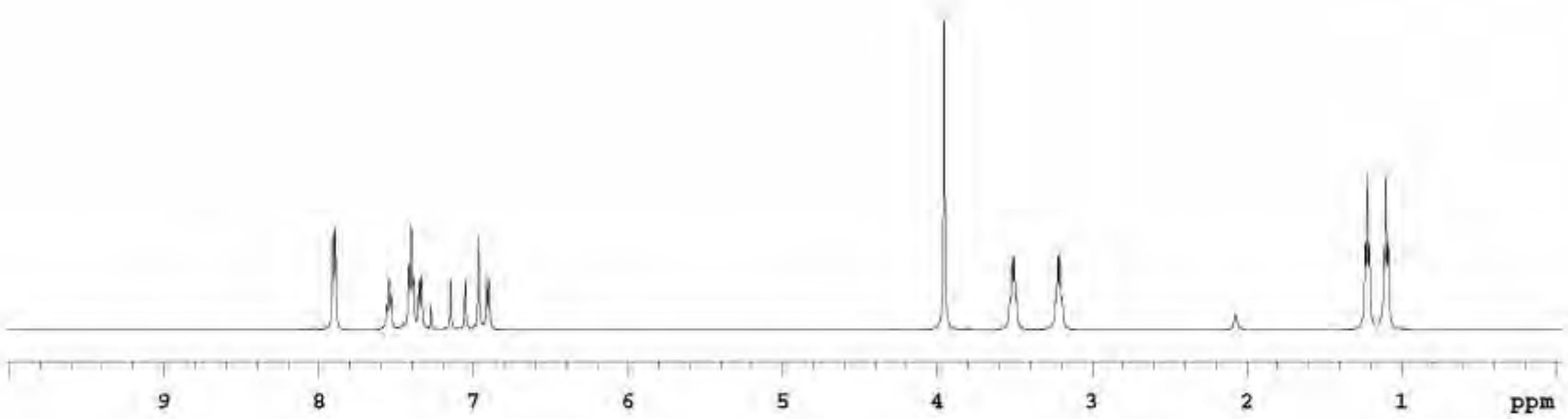
$CDCl_3$, −15 ºC



^{1}H NMR of (1-Fluoro-2-oxo-2-phenylethyl)-analepticon (S6)

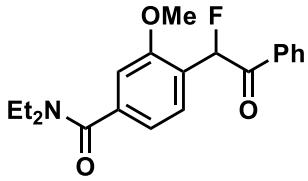
$CDCl_3$, −15 ºC

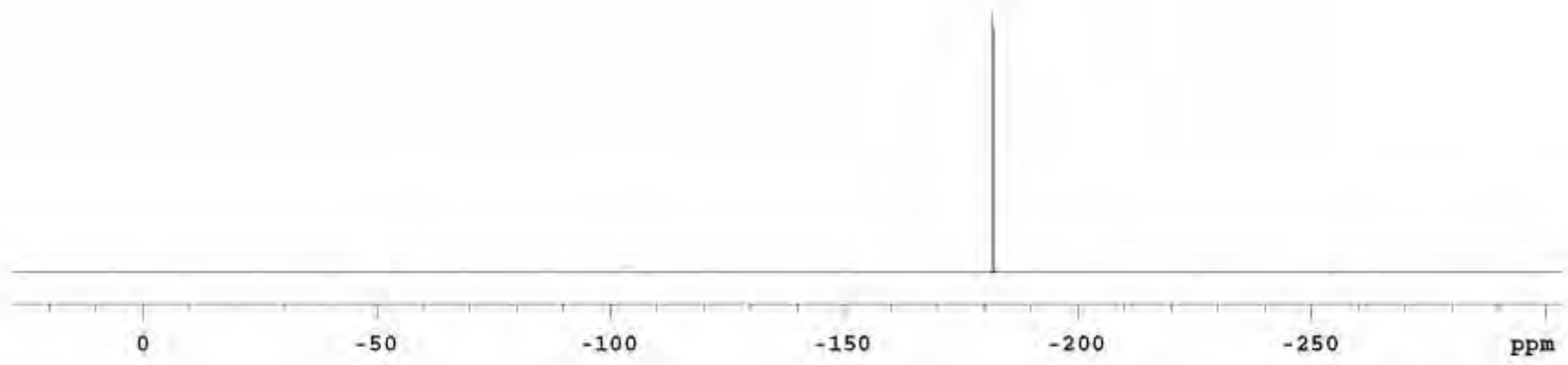




^{19}F NMR of (1-Fluoro-2-oxo-2-phenylethyl)-analepticon (S6)

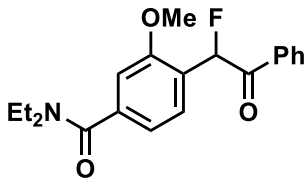
$CDCl_3$, 25 ºC

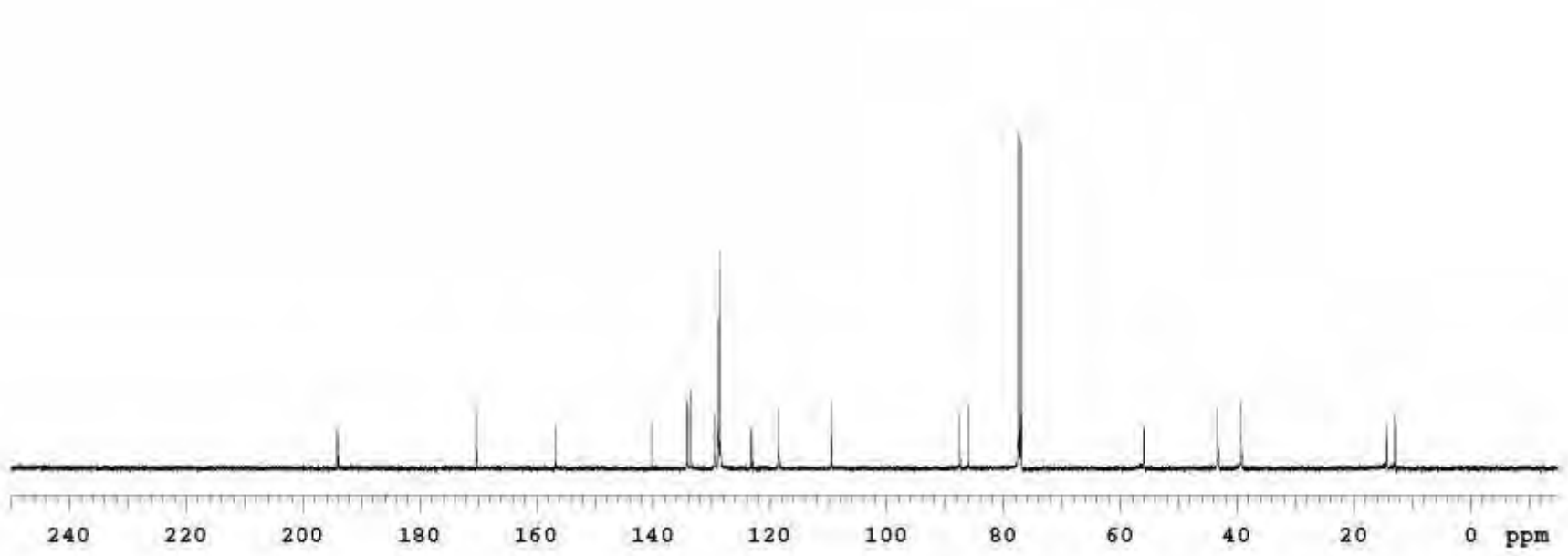




^{13}C NMR of (1-Fluoro-2-oxo-2-phenylethyl)-analepticon (S6)

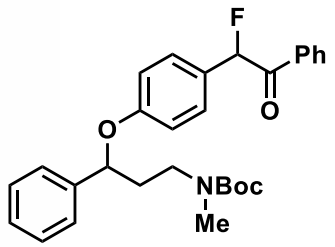
$CDCl_3$, −15 ºC

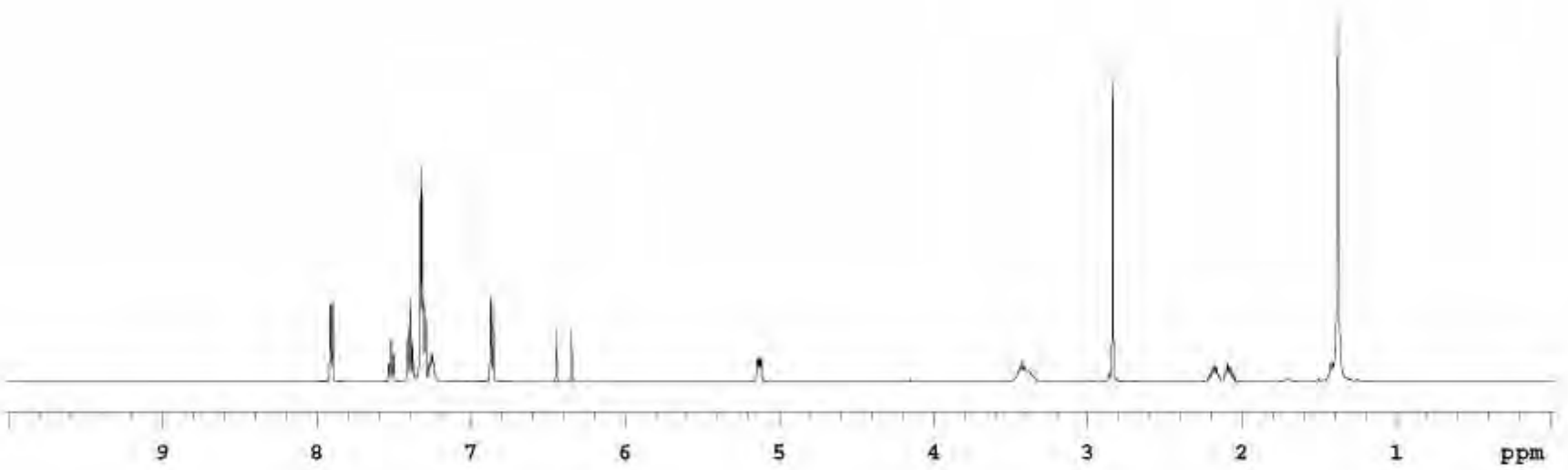




^{1}H NMR of (1-Fluoro-2-oxo-2-phenylethyl)-*N*-Boc-fluoxetine (S7)

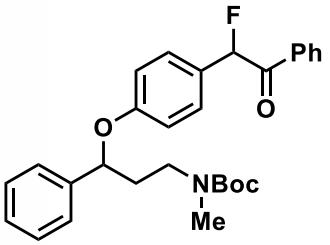
$CDCl_3$, 55 ºC

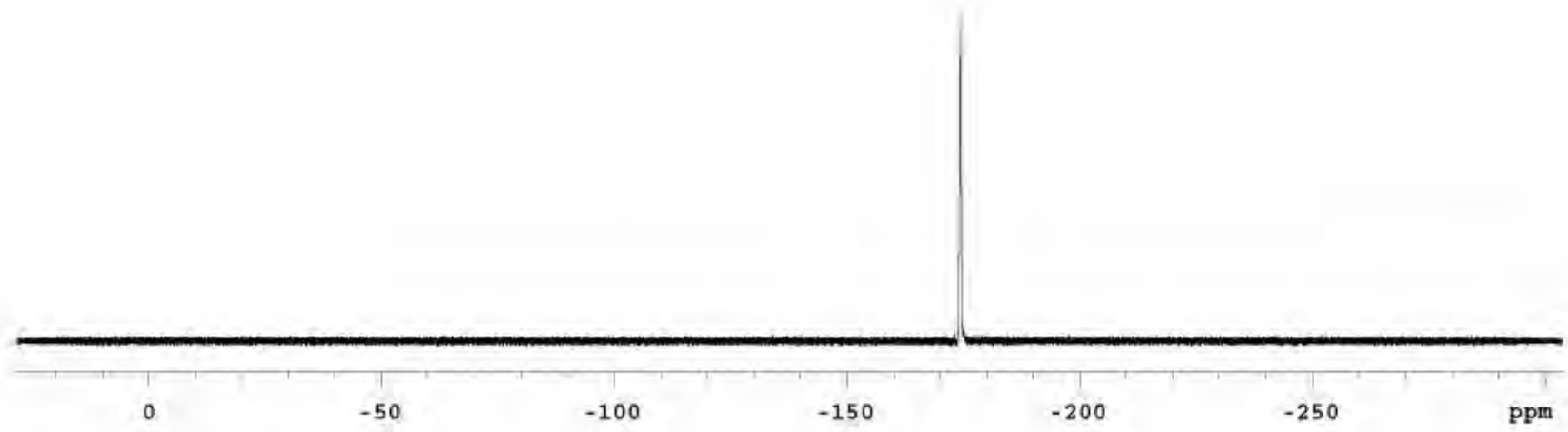




^{19}F NMR of (1-Fluoro-2-oxo-2-phenylethyl)-*N*-Boc-fluoxetine (S7)

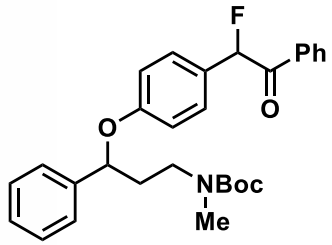
$CDCl_3$, 25 ºC

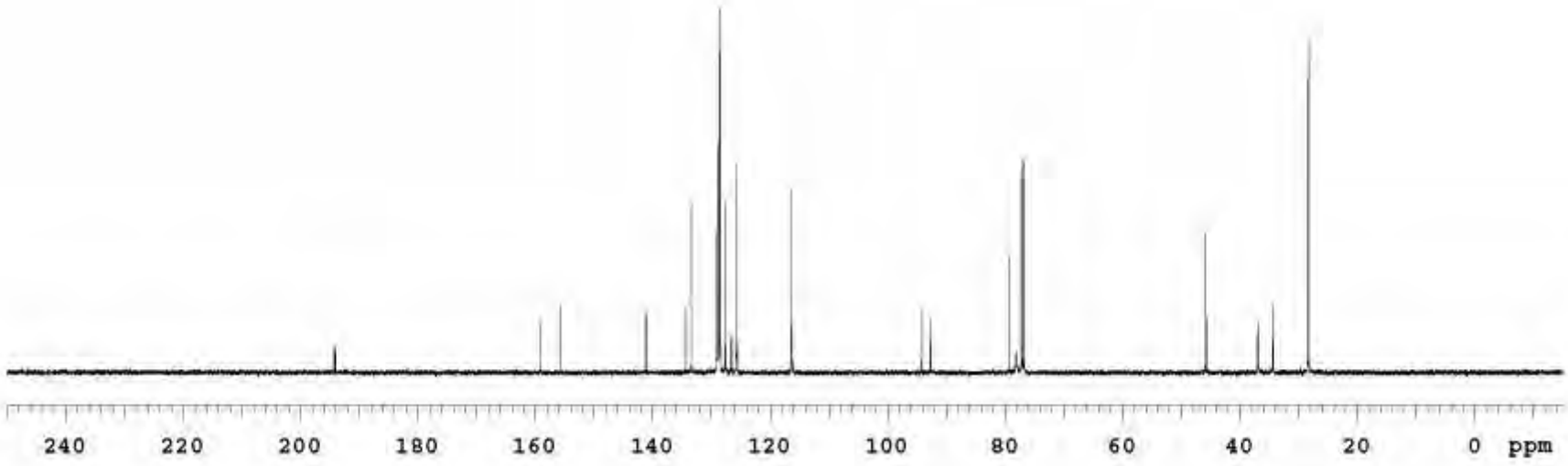




^{13}C NMR of (1-Fluoro-2-oxo-2-phenylethyl)-*N*-Boc-fluoxetine (S7)

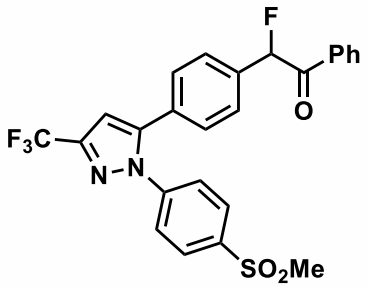
$CDCl_3$, 55 ºC

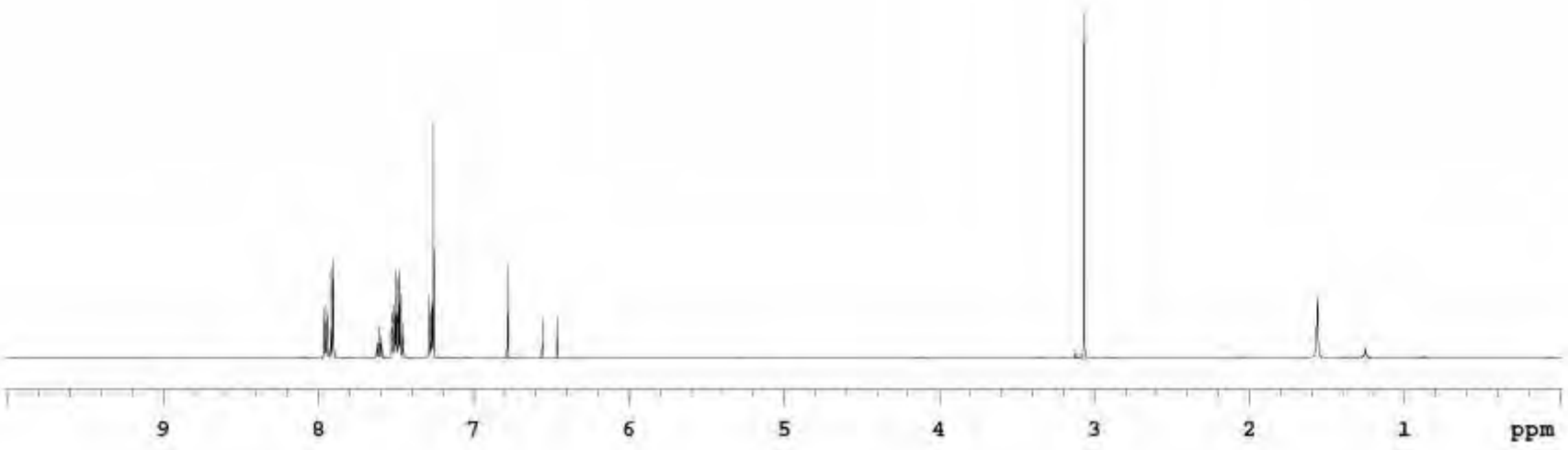




^{1}H NMR of (1-Fluoro-2-oxo-2-phenylethyl)-SC-58125 (S8)

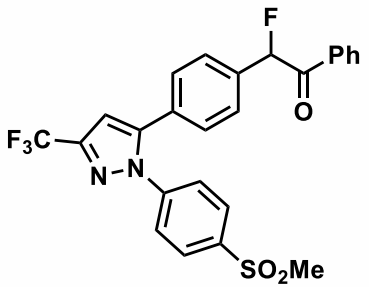
$CDCl_3$, 23 ºC

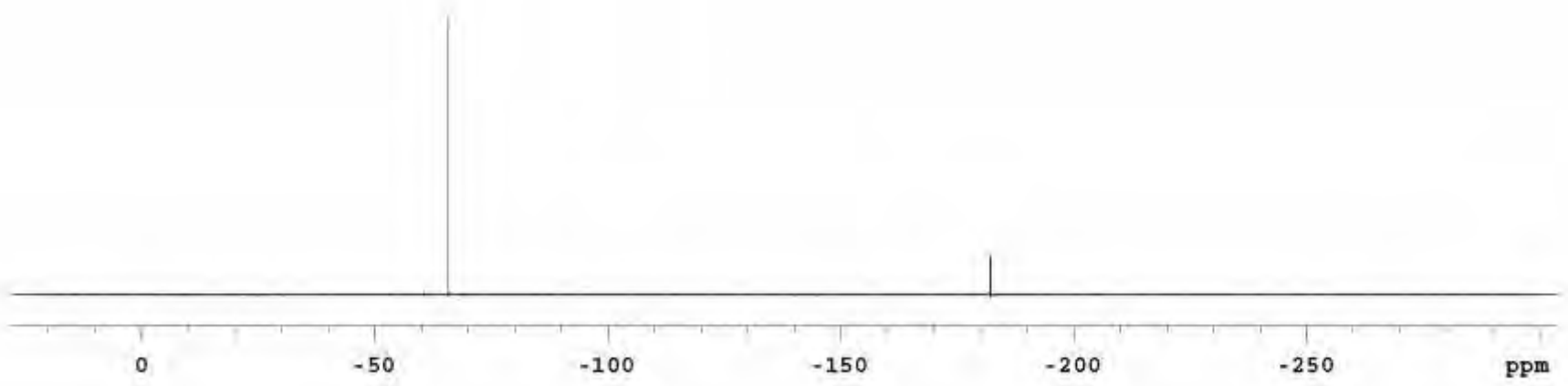




^{19}F NMR of (1-Fluoro-2-oxo-2-phenylethyl)-**SC-58125** (S8)

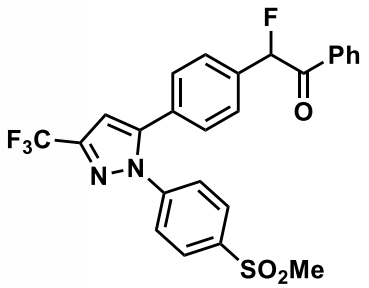
$CDCl_3$, 23 ºC

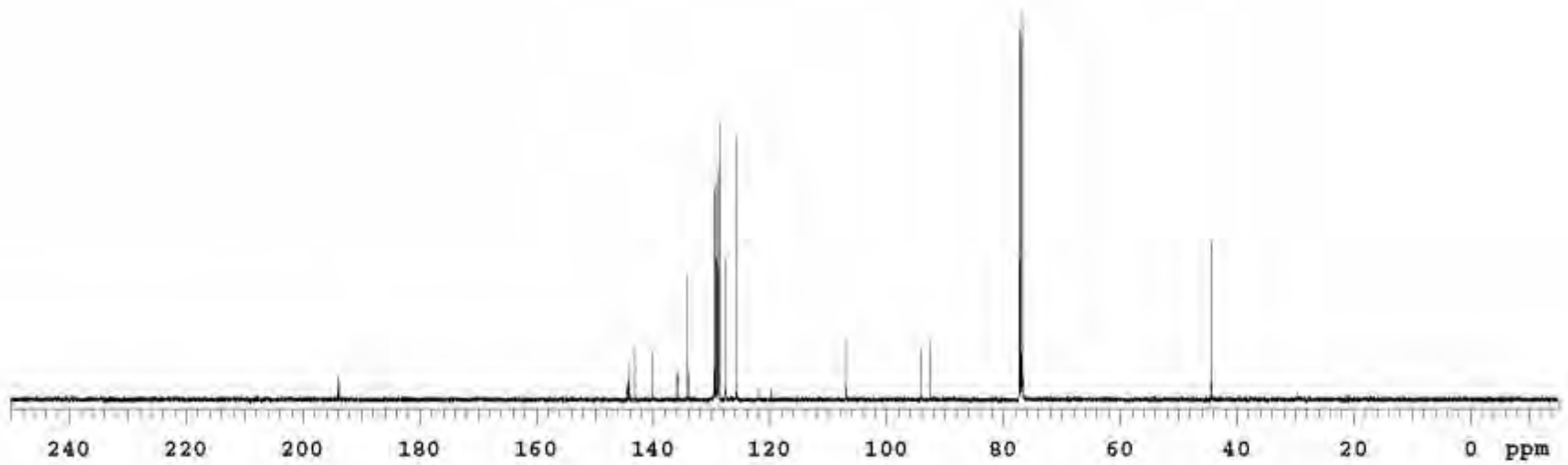




^{13}C NMR of (1-Fluoro-2-oxo-2-phenylethyl)-SC-58125 (S8)

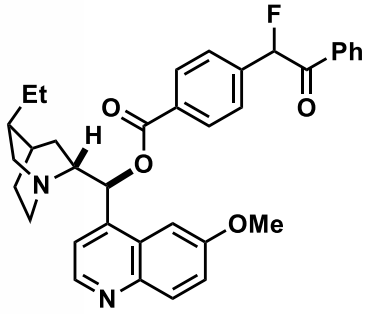
$CDCl_3$, 23 ºC





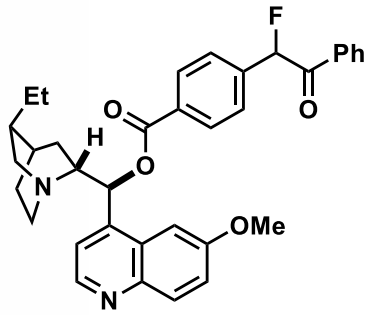
^{1}H NMR of Hydroquinidine 4-(1-Fluoro-2-oxo-2-phenylethyl)-benzoate (S9)

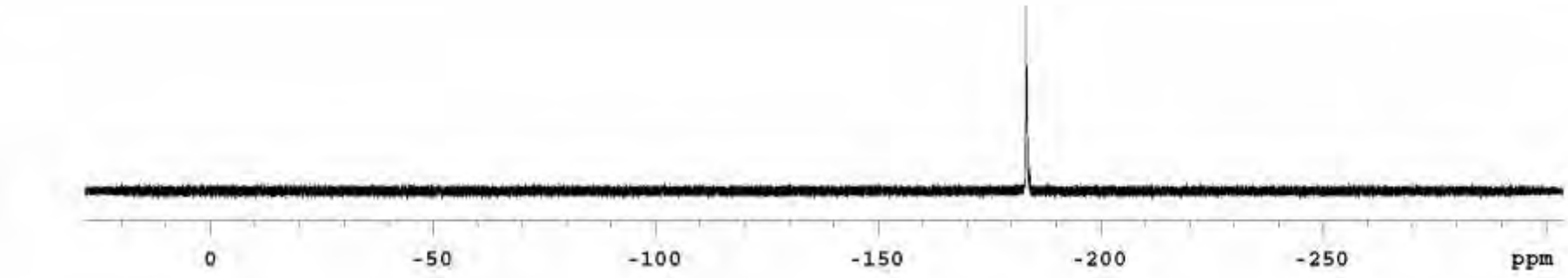
$CDCl_3$, 55 ºC



^{19}F NMR of Hydroquinidine 4-(1-Fluoro-2-oxo-2-phenylethyl)-benzoate (S9)

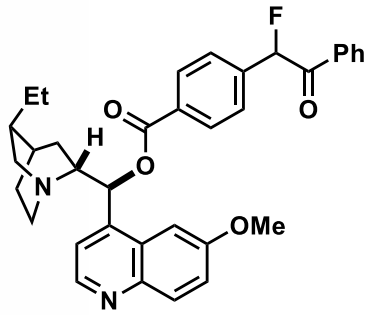
$CDCl_3$, 23 ºC

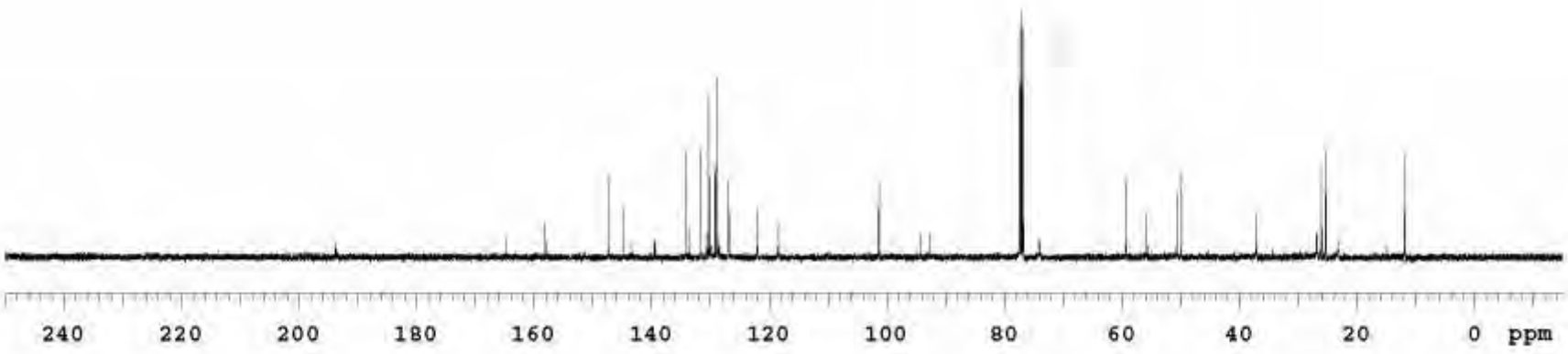




^{13}C NMR of Hydroquinidine 4-(1-Fluoro-2-oxo-2-phenylethyl)-benzoate (S9)

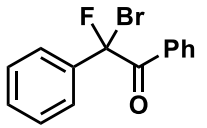
$CDCl_3$, 25 ºC

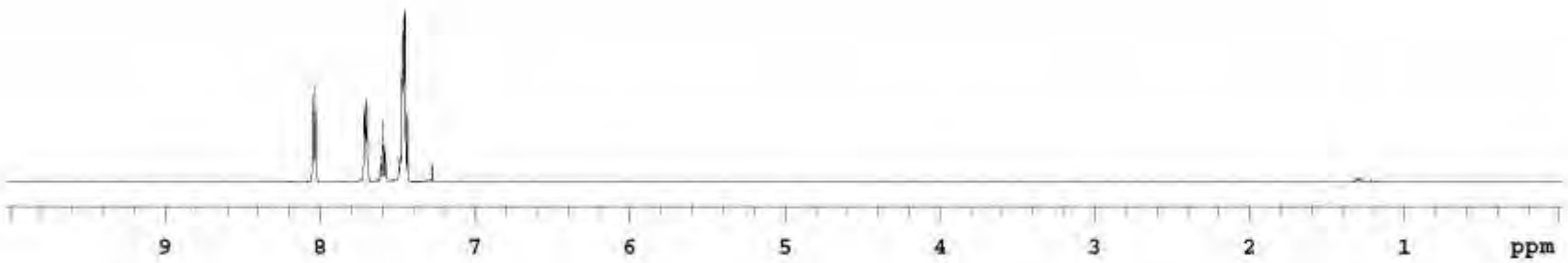




^{1}H NMR of Phenyl-bromo-fluoroacetophenone (2r')

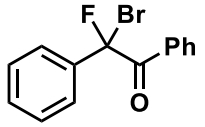
$CDCl_3$, 25 ºC

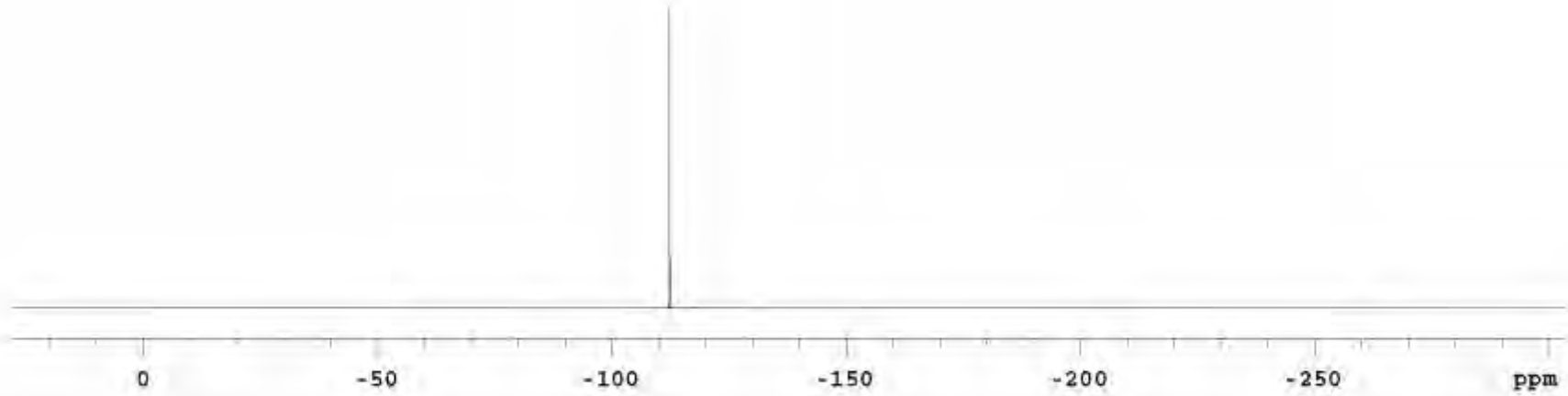




^{19}F NMR of Phenyl-bromo-fluoroacetophenone (2r')

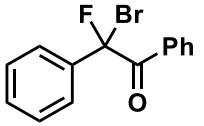
$CDCl_3$, 23 ºC

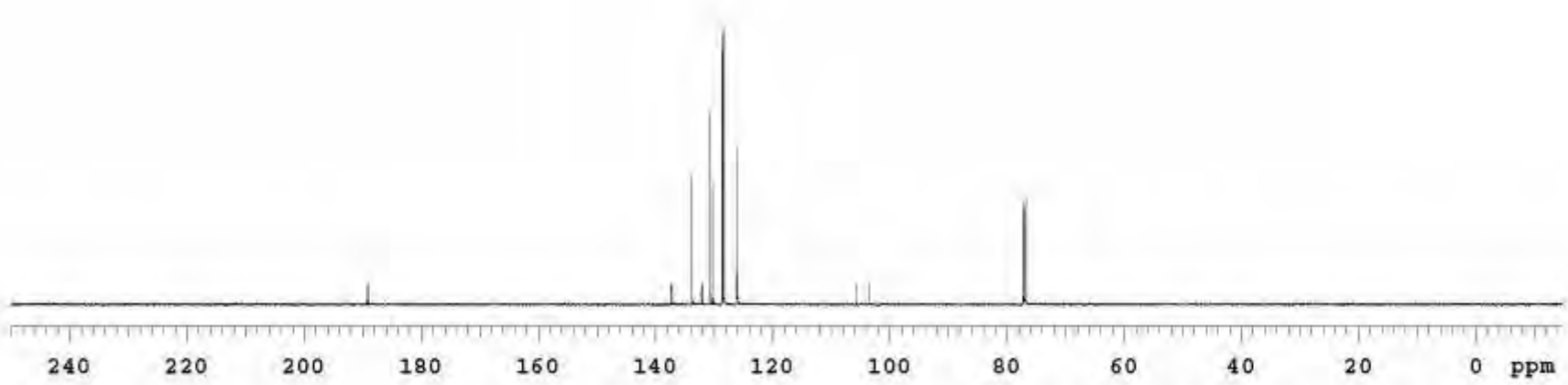




^{13}C NMR of Phenyl-bromo-fluoroacetophenone (2r')

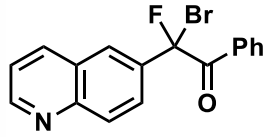
$CDCl_3$, 25 ºC

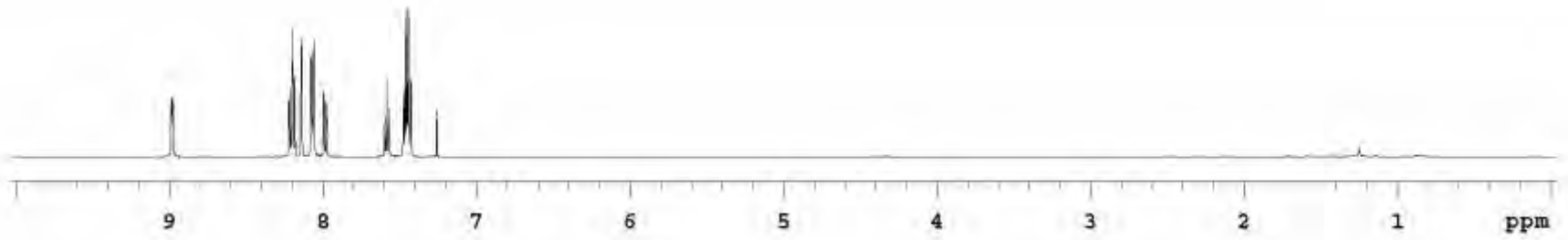




^{1}H NMR of Quinoline-6-bromo-fluoroacetophenone (2m')

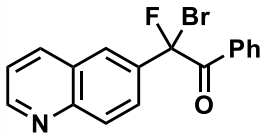
$CDCl_3$, 23 ºC

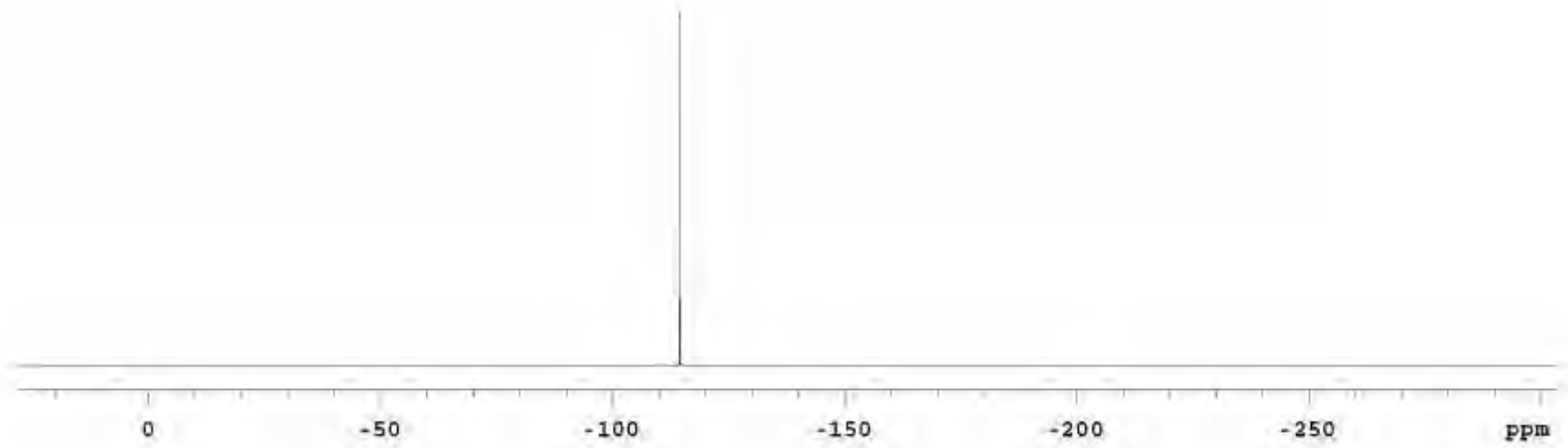




^{19}F NMR of Quinoline-6-bromo-fluoroacetophenone (2m')

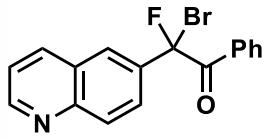
$CDCl_3$, 23 ºC

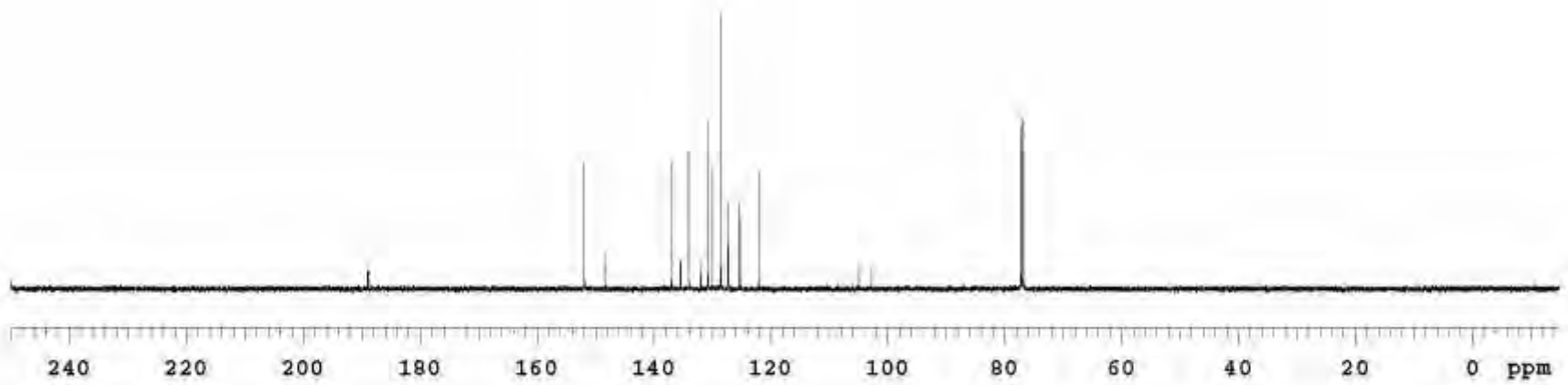




^{13}C NMR of Quinoline-6-bromo-fluoroacetophenone (2m')

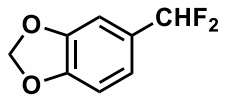
$CDCl_3$, 25 ºC

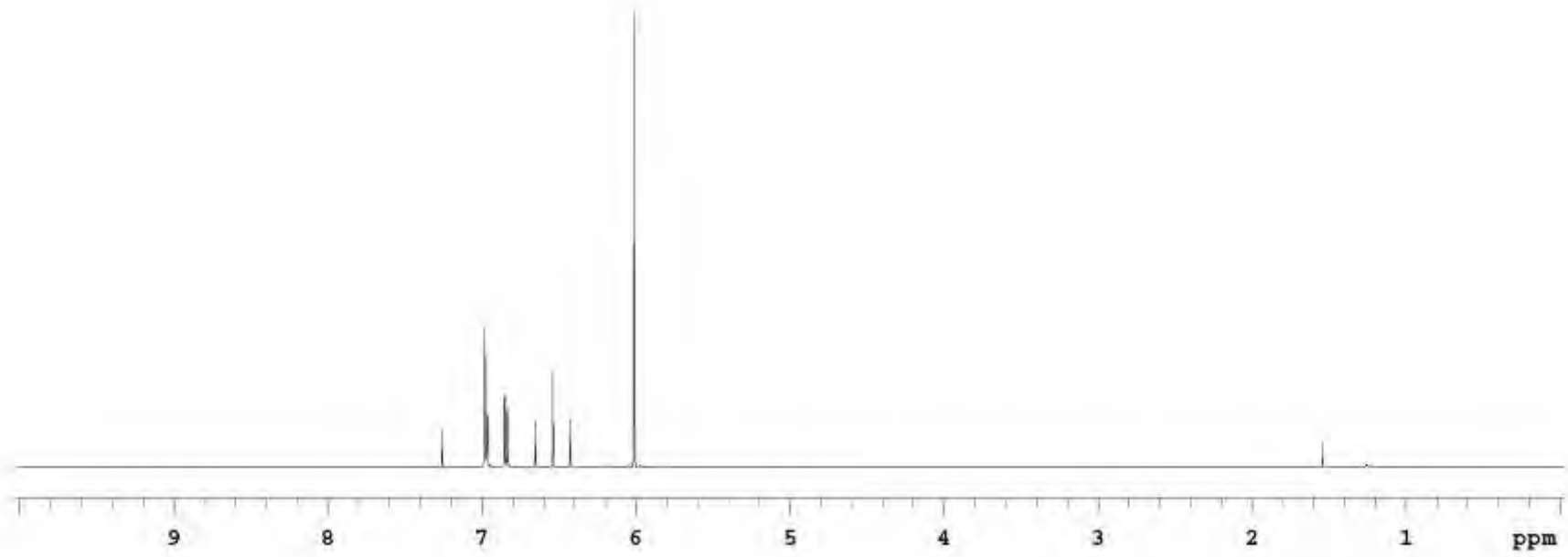




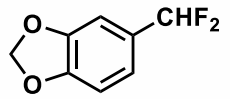
^{1}H NMR of Difluoromethyl-benzodioxole (3a)

$CDCl_3$, 24 ºC

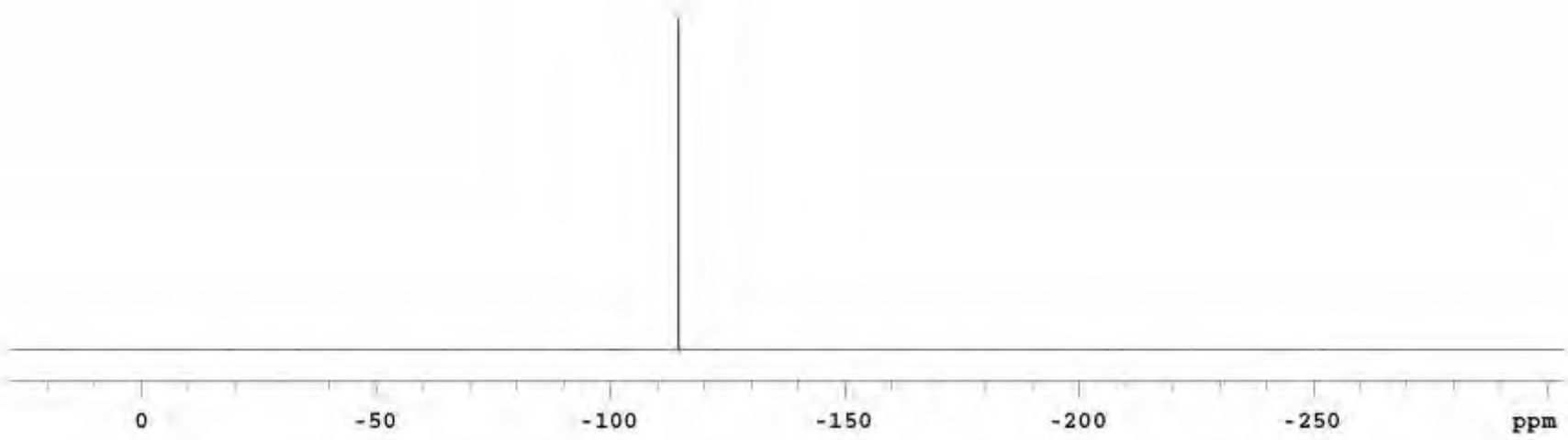




^{19}F NMR of Difluoromethyl-benzodioxole (3a)

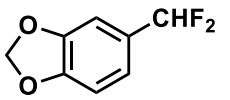


$CDCl_3$, 24 ºC

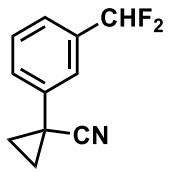


^{13}C NMR of Difluoromethyl-benzodioxole (3a)

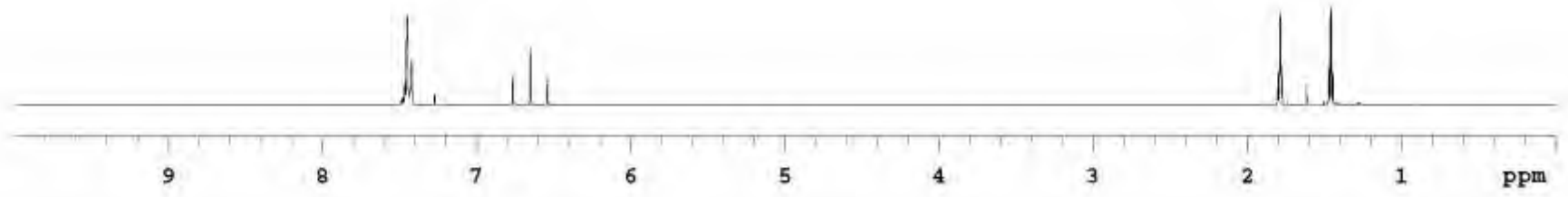
$CDCl_3$, 25 ºC



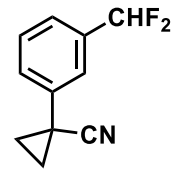
^{1}H NMR of 3-Cyanocyclopropyl-difluoromethylbenzene (3c)



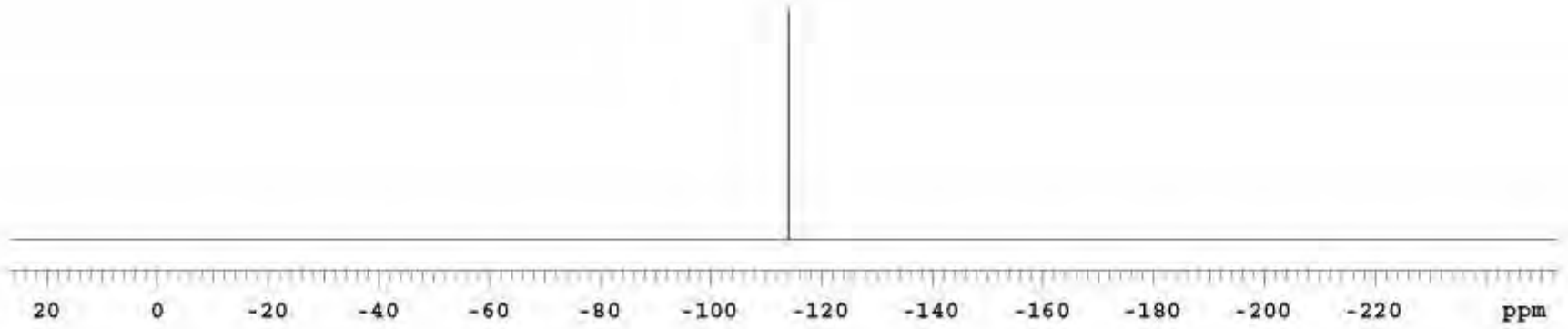
$CDCl_3$, 25 ºC



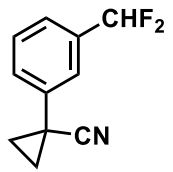
^{19}F NMR of 3-Cyanocyclopropyl-difluoromethylbenzene (3c)



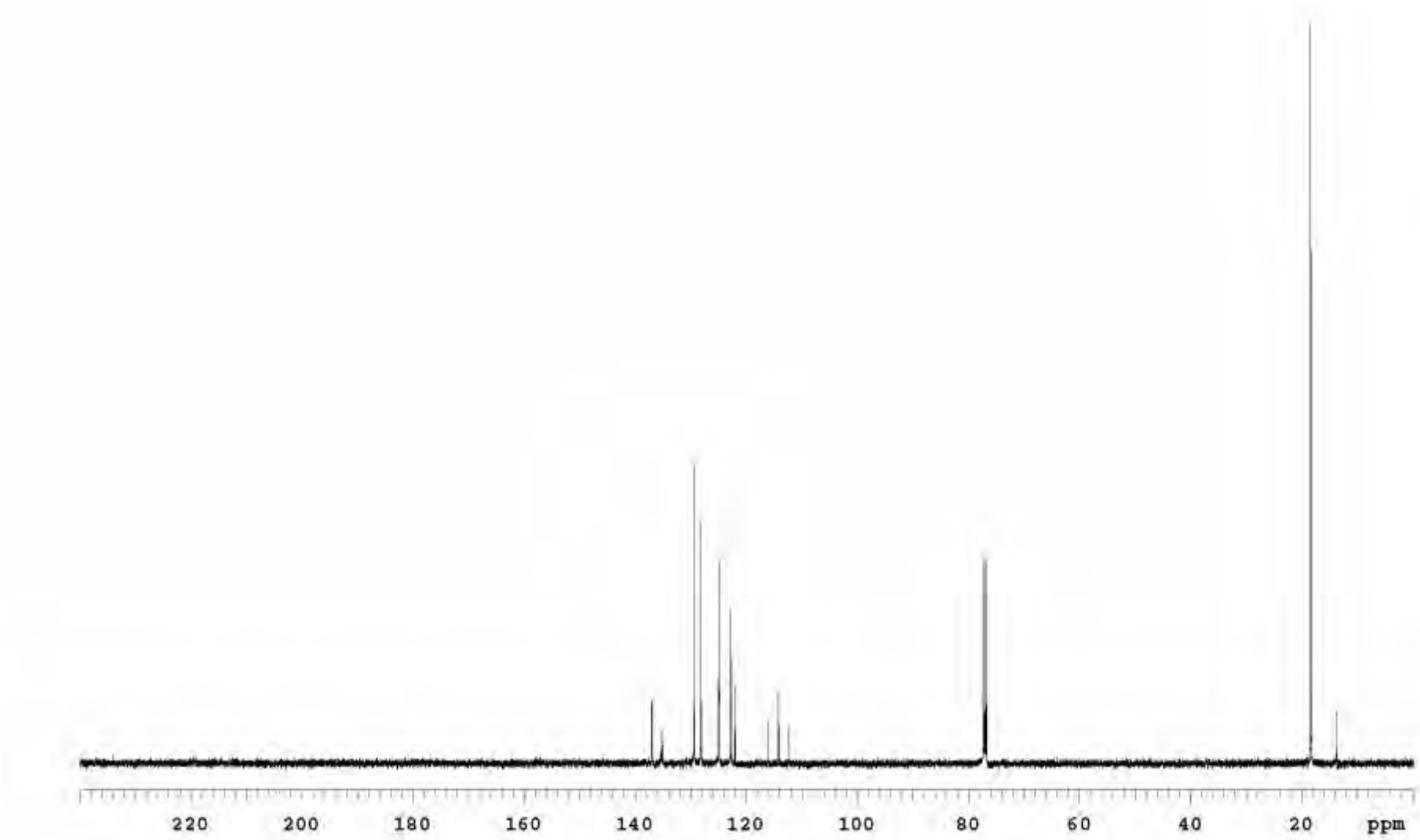
$CDCl_3$, 25 ºC



^{13}C NMR of 3-Cyanocyclopropyl-difluoromethylbenzene (3c)

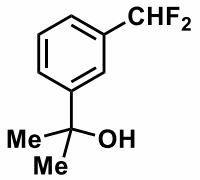


$CDCl_3$, 25 ºC

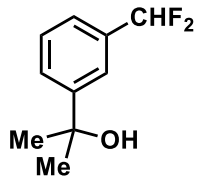


^{1}H NMR of 3-*iso*propanolyl-difluoromethylbenzene (3d)

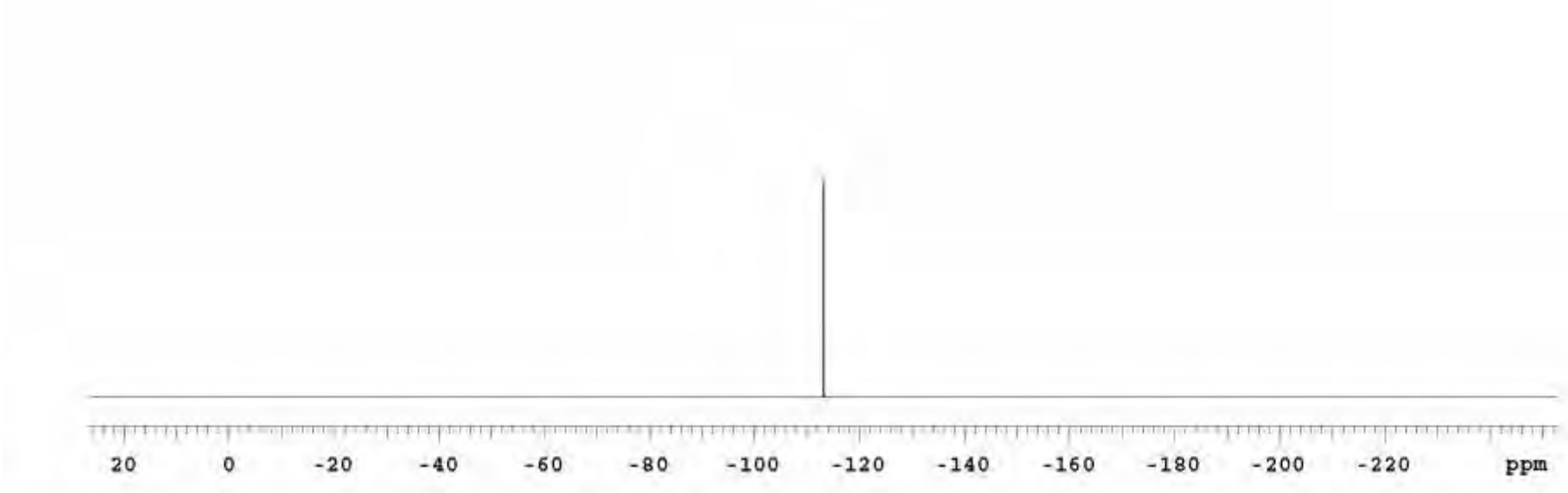
$CDCl_3$, 25 ºC



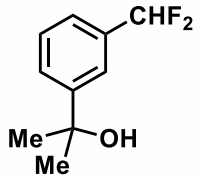
^{19}F NMR of 3-*iso*propanolyl-difluoromethylbenzene (3d)



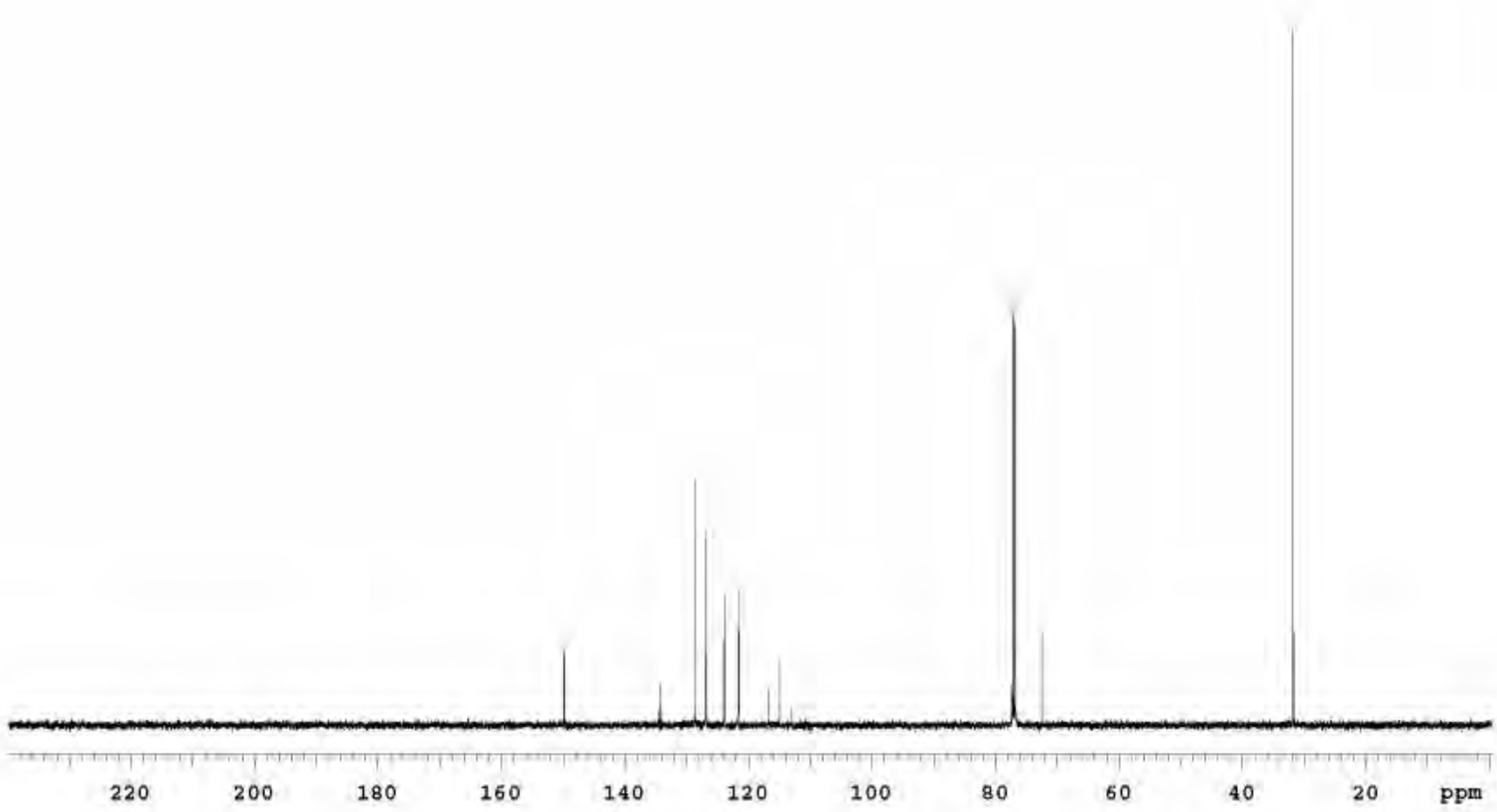
$CDCl_3$, 25 ºC



^{13}C NMR of 3-*iso*propanolyl-difluoromethylbenzene (3d)

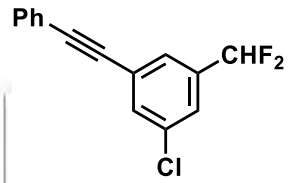


$CDCl_3$, 25 ºC

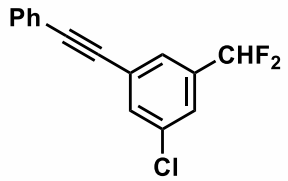


^{1}H NMR of 3-Chloro-5-(phenylethynyl)-difluoromethylbenzene (3e)

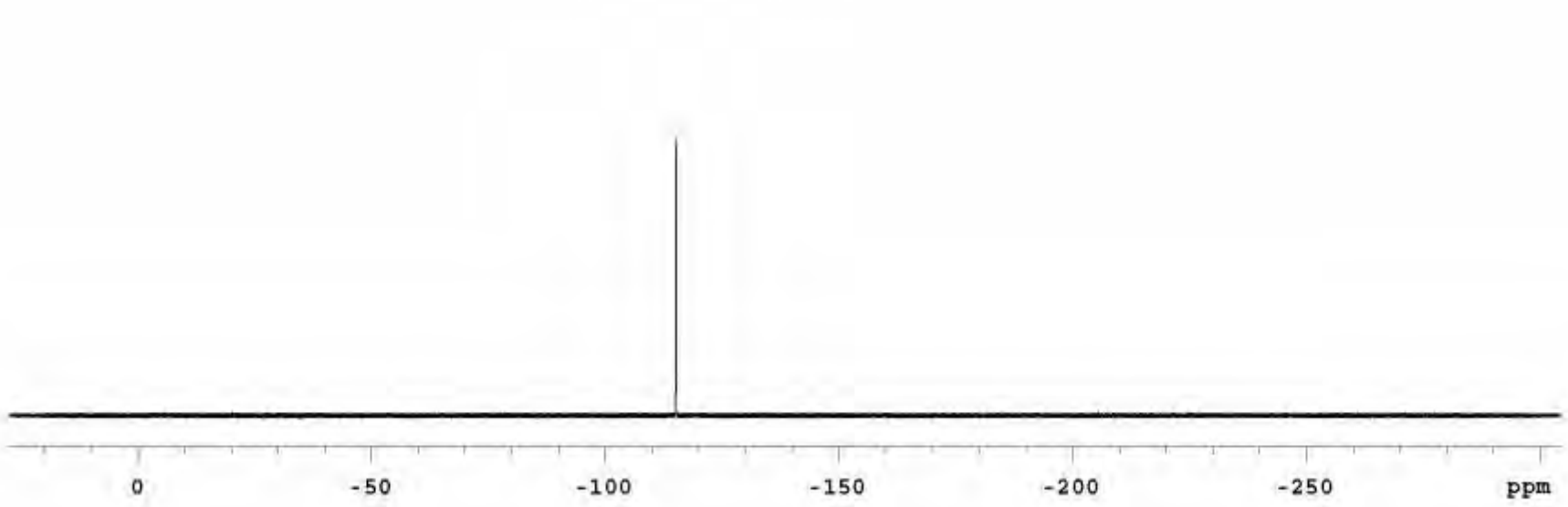
$CDCl_3$, 23 ºC



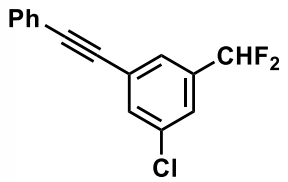
^{19}F NMR of 3-Chloro-5-(phenylethynyl)-difluoromethylbenzene (3e)



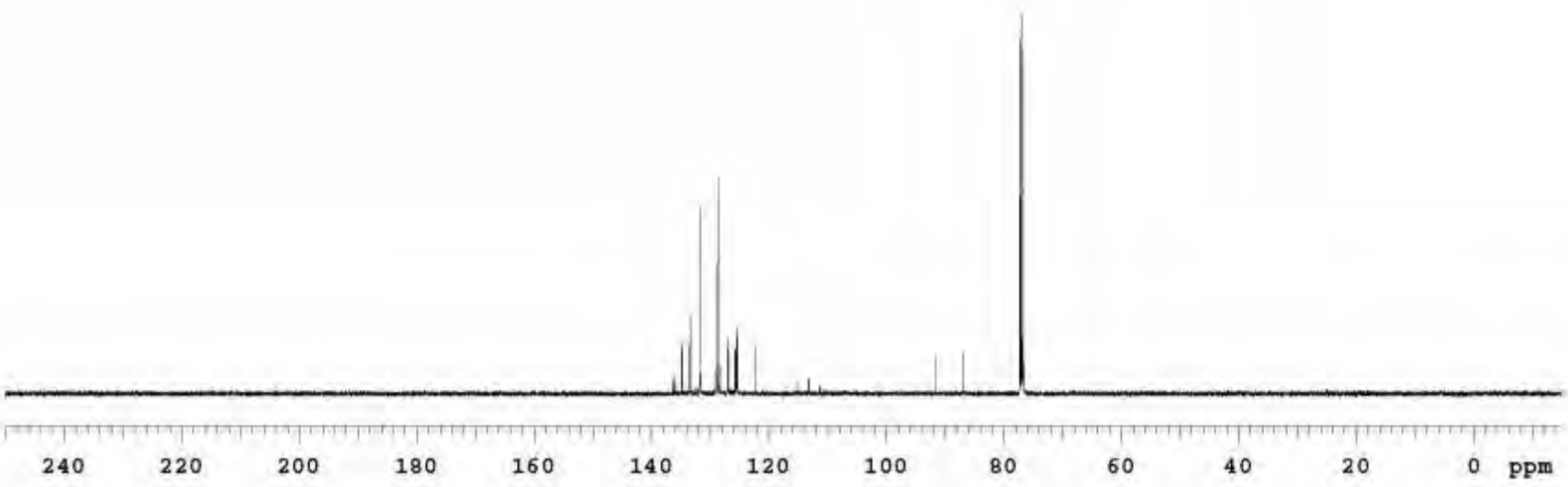
$CDCl_3$, 23 ºC



^{13}C NMR of 3-Chloro-5-(phenylethynyl)-difluoromethylbenzene (3e)

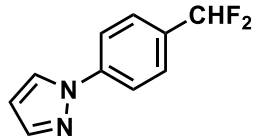


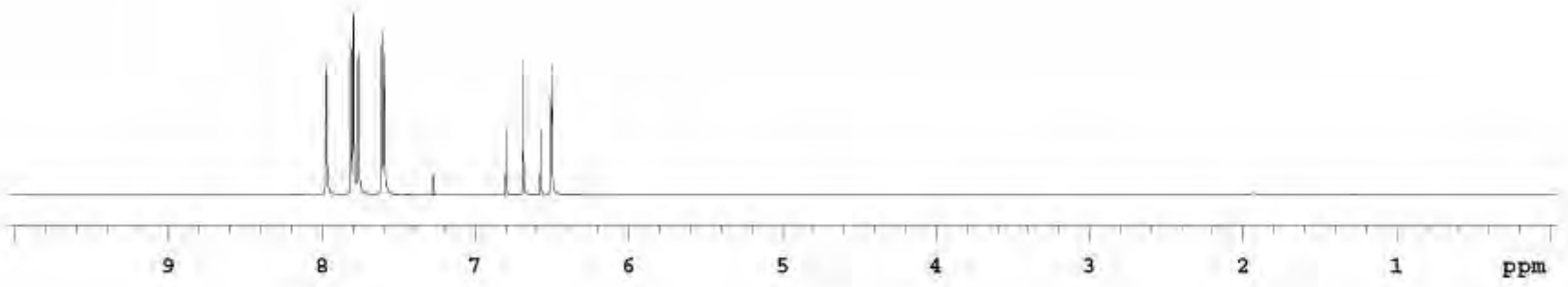
$CDCl_3$, 23 ºC



^{1}H NMR of 4-Pyrazolyl-difluoromethylbenzene (3f)

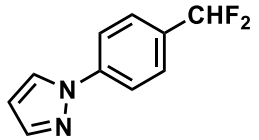
$CDCl_3$, 23 ºC

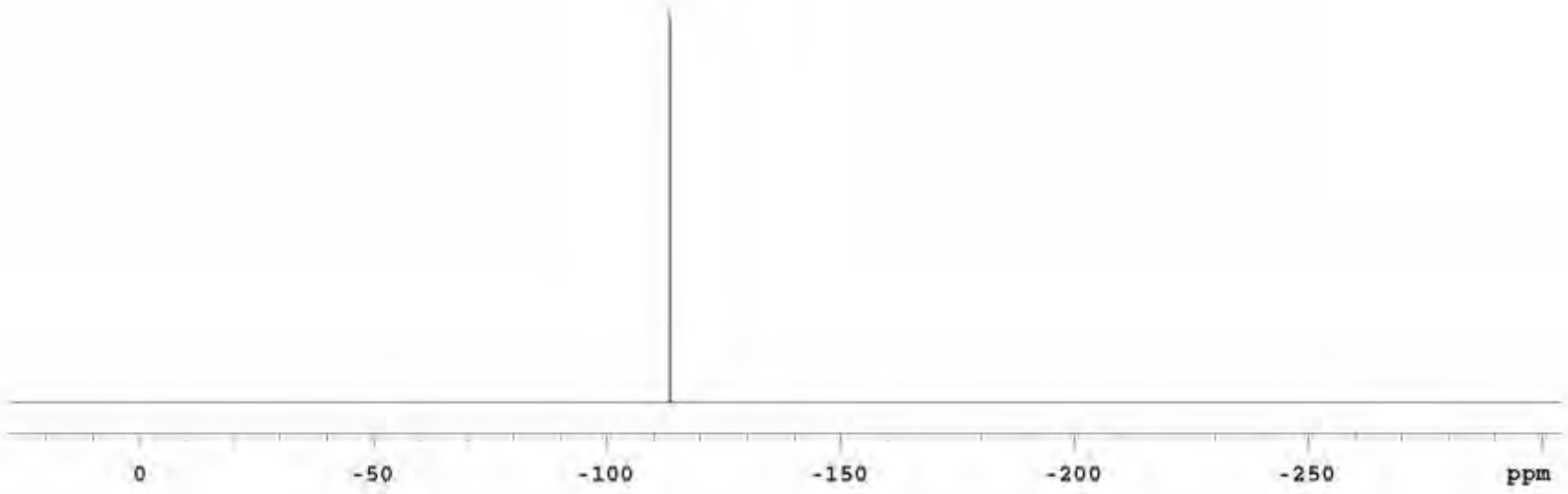




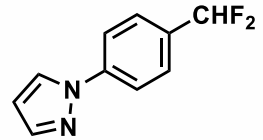
^{19}F NMR of 4-Pyrazolyl-difluoromethylbenzene (3f)

$CDCl_3$, 21 ºC

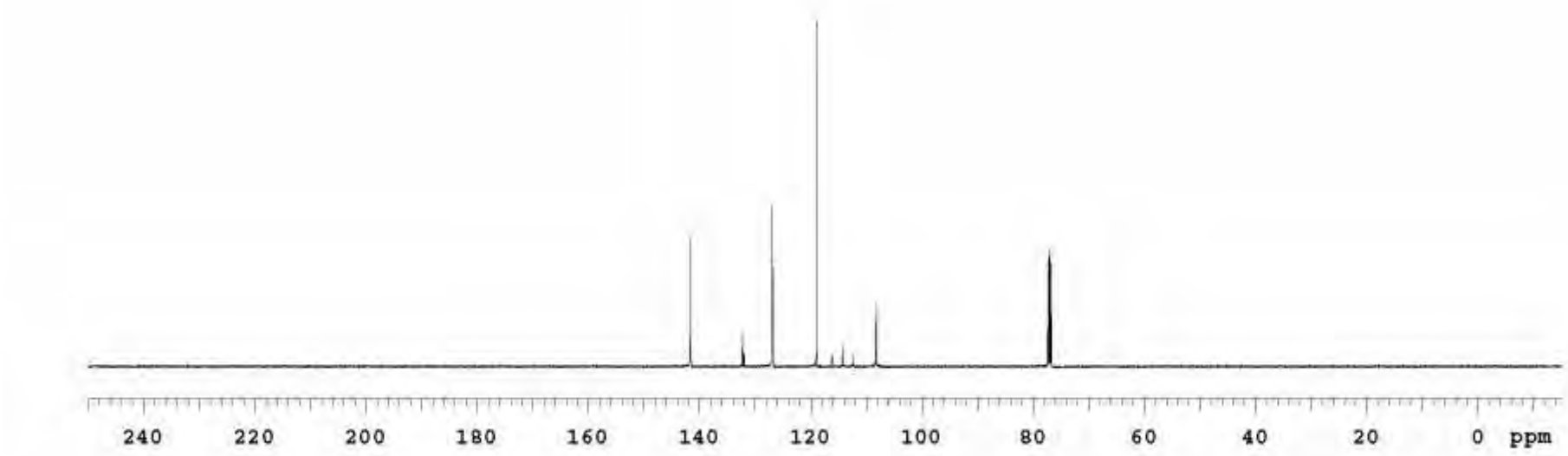




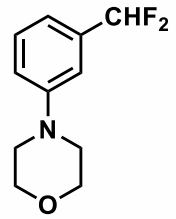
^{13}C NMR of 4-Pyrazolyl-difluoromethylbenzene (3f)



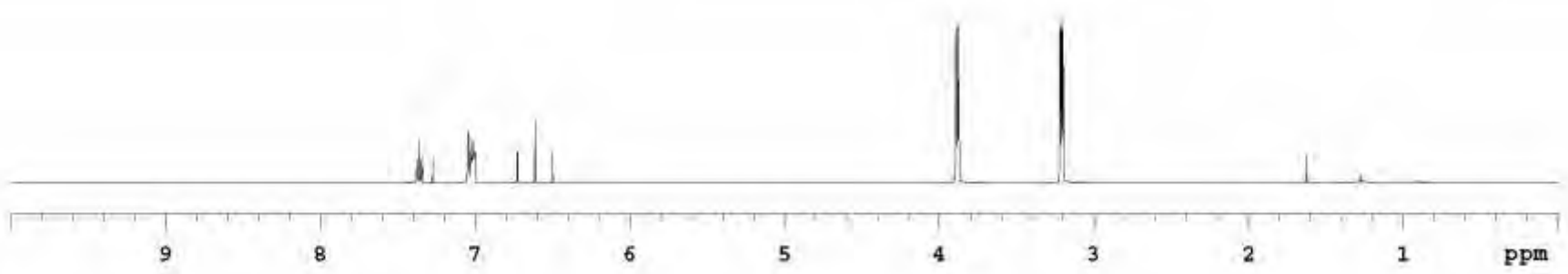
$CDCl_3$, 23 ºC



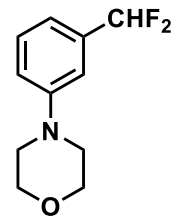
^{1}H NMR of 3-Morpholino-difluoromethylbenzene (3g)



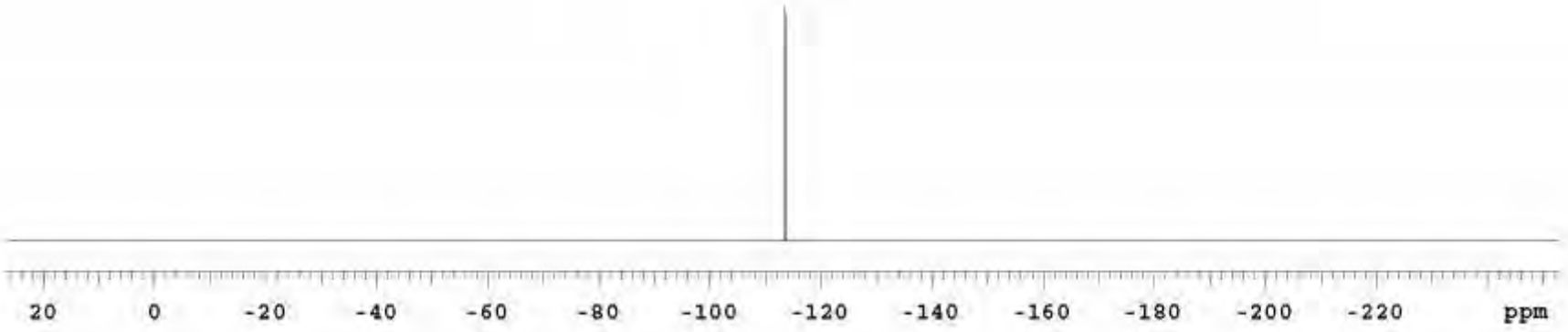
$CDCl_3$, 25 ºC



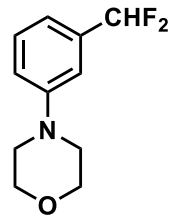
^{19}F NMR of 3-Morpholino-difluoromethylbenzene (3g)



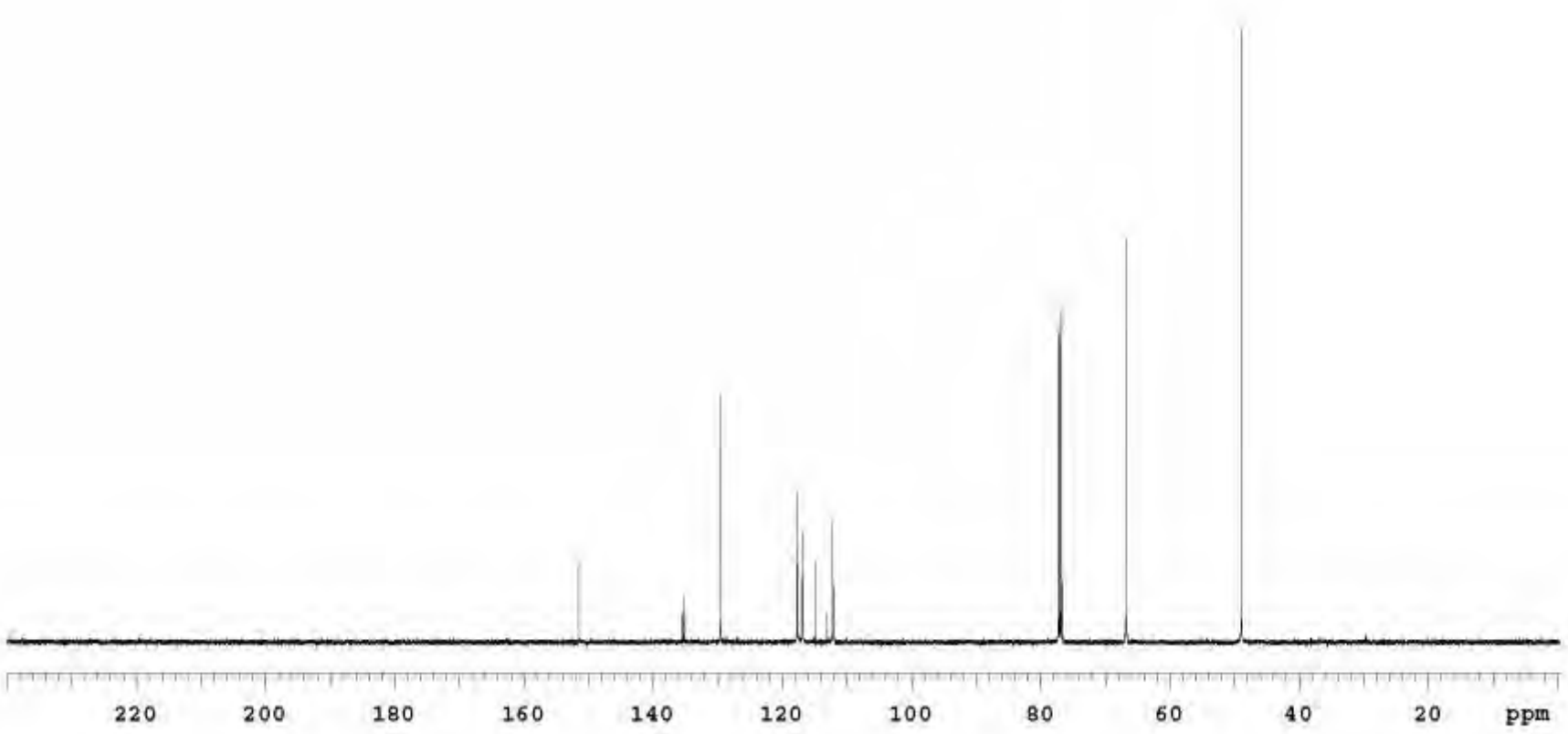
$CDCl_3$, 25 ºC



^{13}C NMR of 3-Morpholino-difluoromethylbenzene (3g)

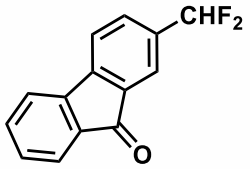


$CDCl_3$, 25 ºC



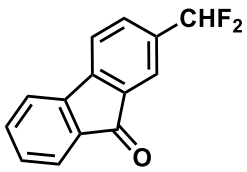
^{1}H NMR of 2-Difluoromethylfluoren-9-one (3i)

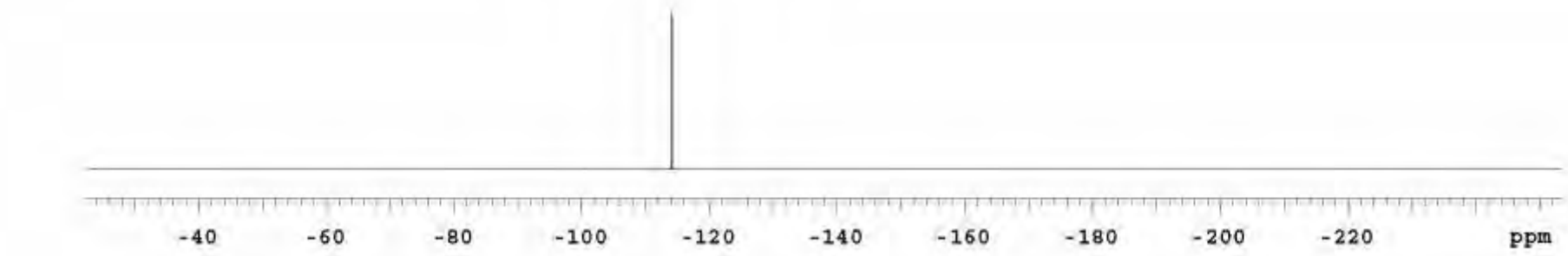
$CDCl_3$, 25 ºC



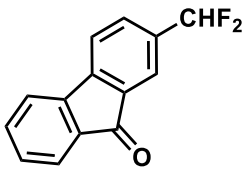
^{19}F NMR of 2-Difluoromethylfluoren-9-one (3i)

$CDCl_3$, 25 ºC

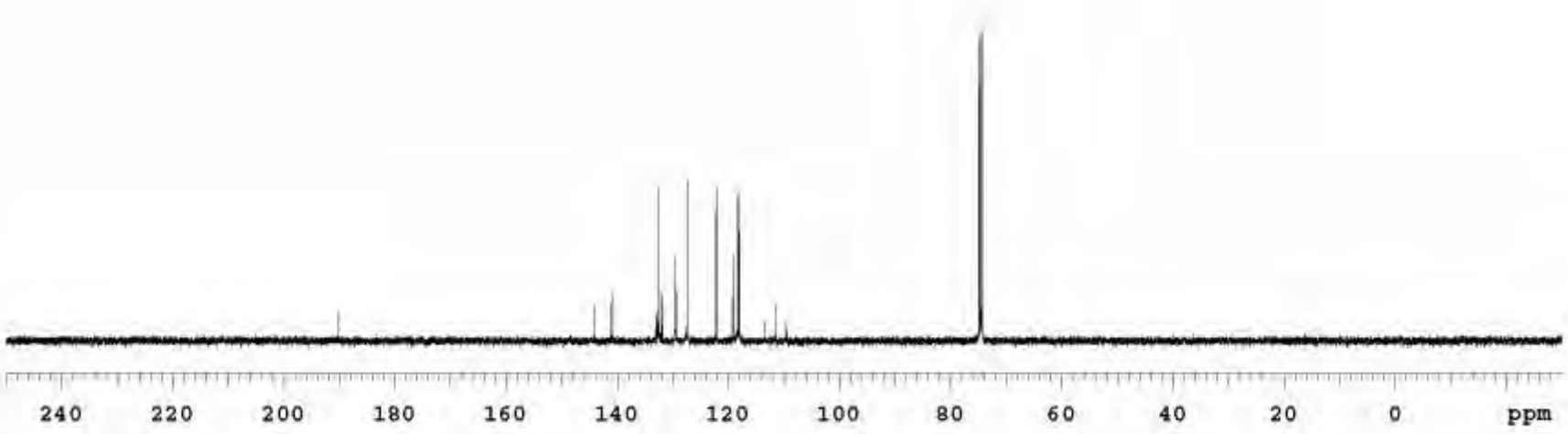




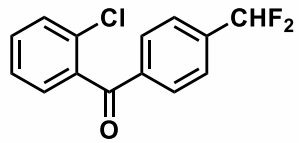
^{13}C NMR of 2-Difluoromethylfluoren-9-one (3i)



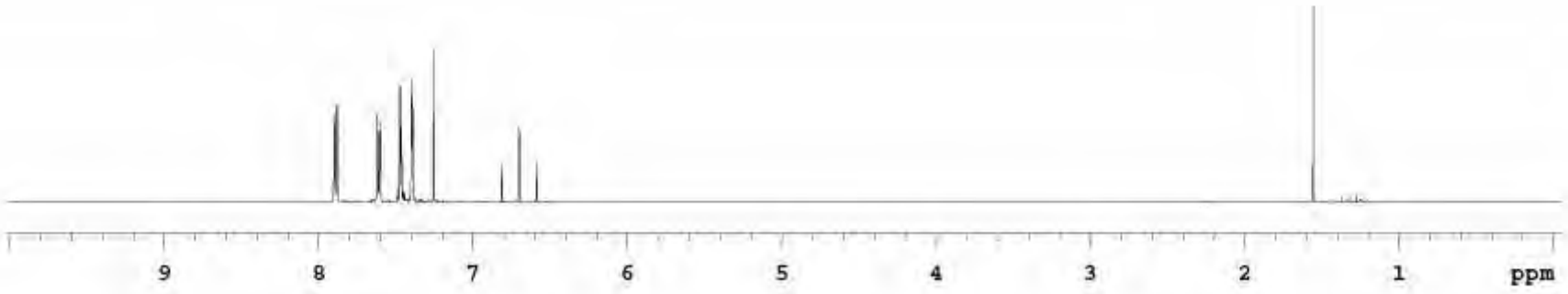
$CDCl_3$, 25 ºC



^{1}H NMR of 2-Chlorophenyl-(4-difluoromethyl)phenyl-methanone (3l)

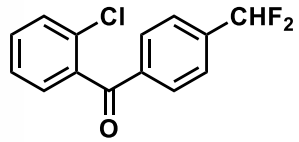


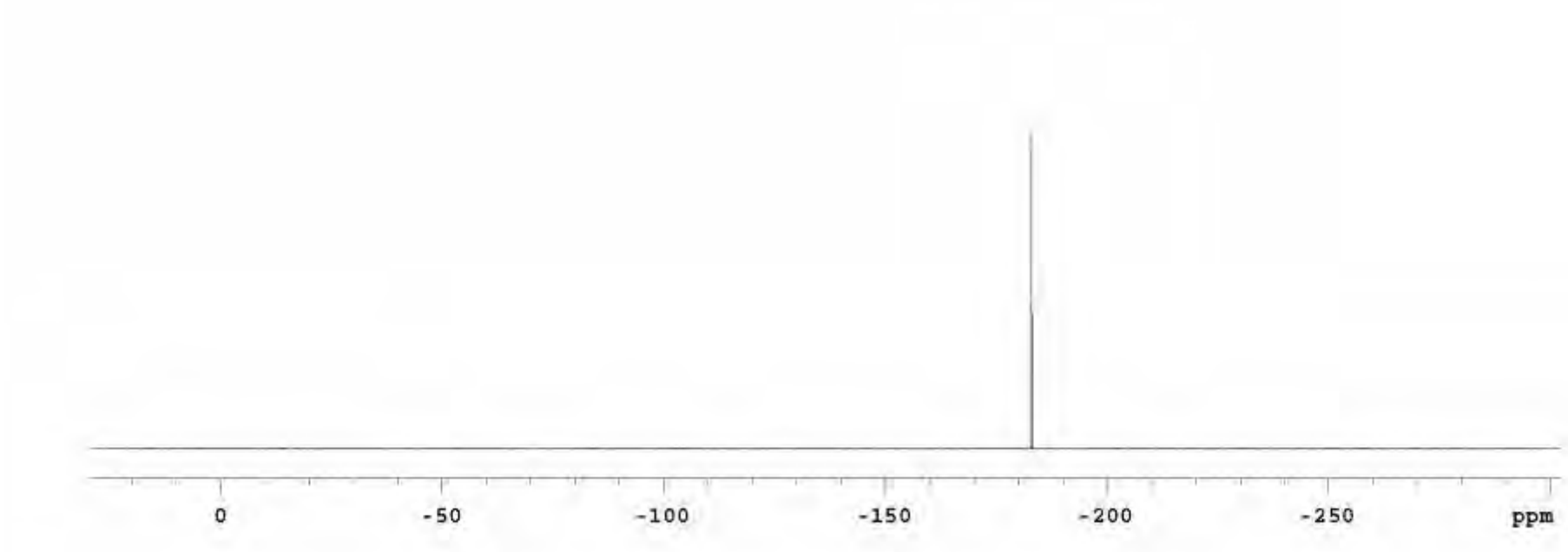
$CDCl_3$, 24 ºC



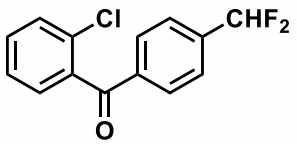
^{19}F NMR of 2-Chlorophenyl-(4-difluoromethyl)phenyl-methanone (3l)

$CDCl_3$, 24 ºC

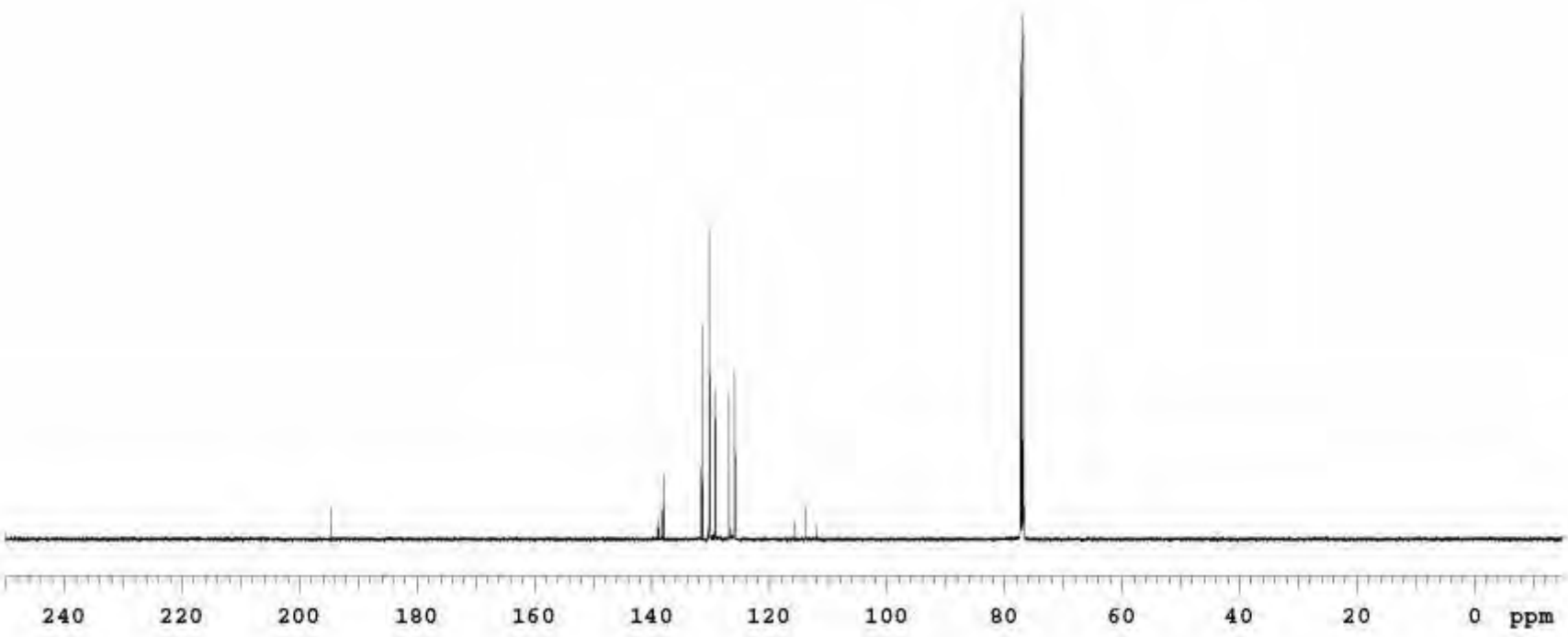




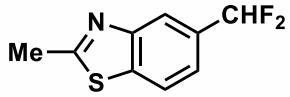
^{13}C NMR of 2-Chlorophenyl-(4-difluoromethyl)phenyl-methanone (3l)



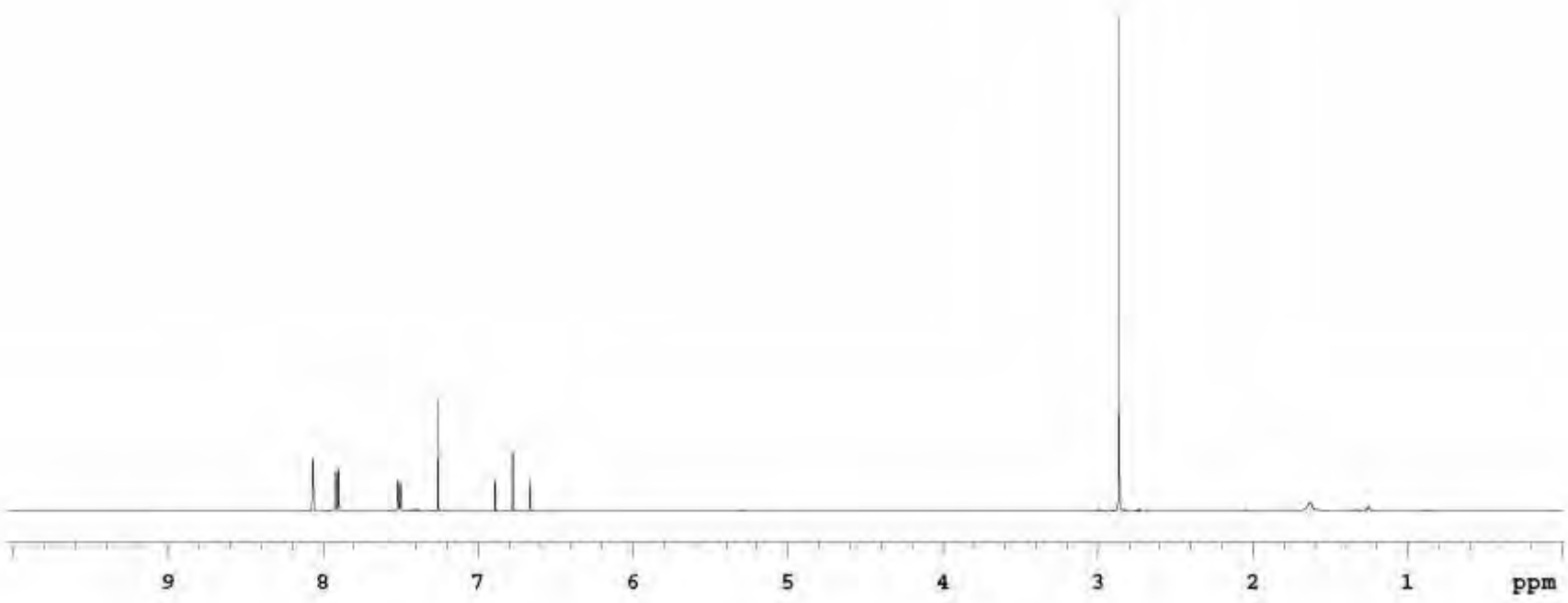
$CDCl_3$, 25 ºC



^{1}H NMR of 5-Difluoromethyl-2-methylbenzo[*d*]thiazole (3n)

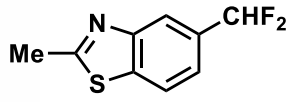


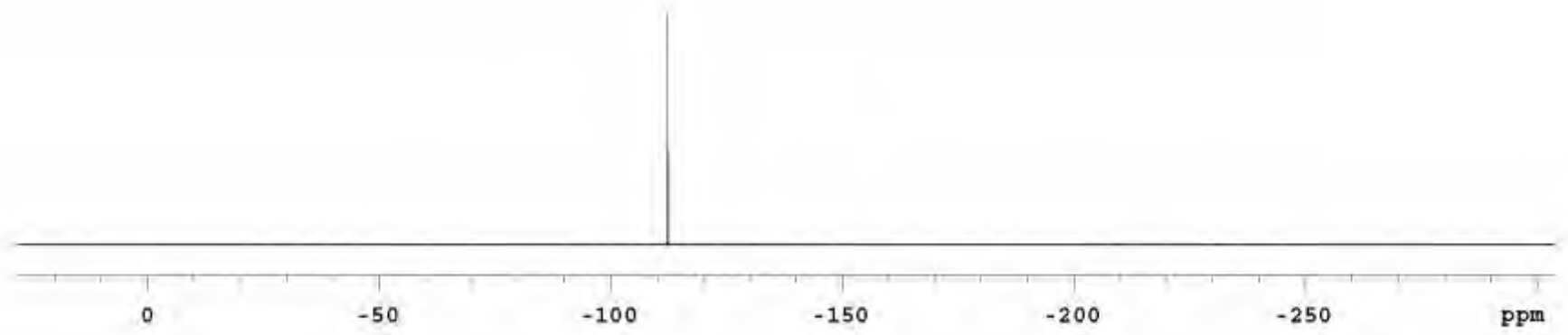
$CDCl_3$, 23 ºC



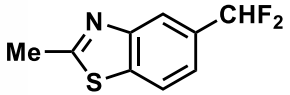
^{19}F NMR of 5-Difluoromethyl-2-methylbenzo[*d*]thiazole (3n)

$CDCl_3$, 25 ºC

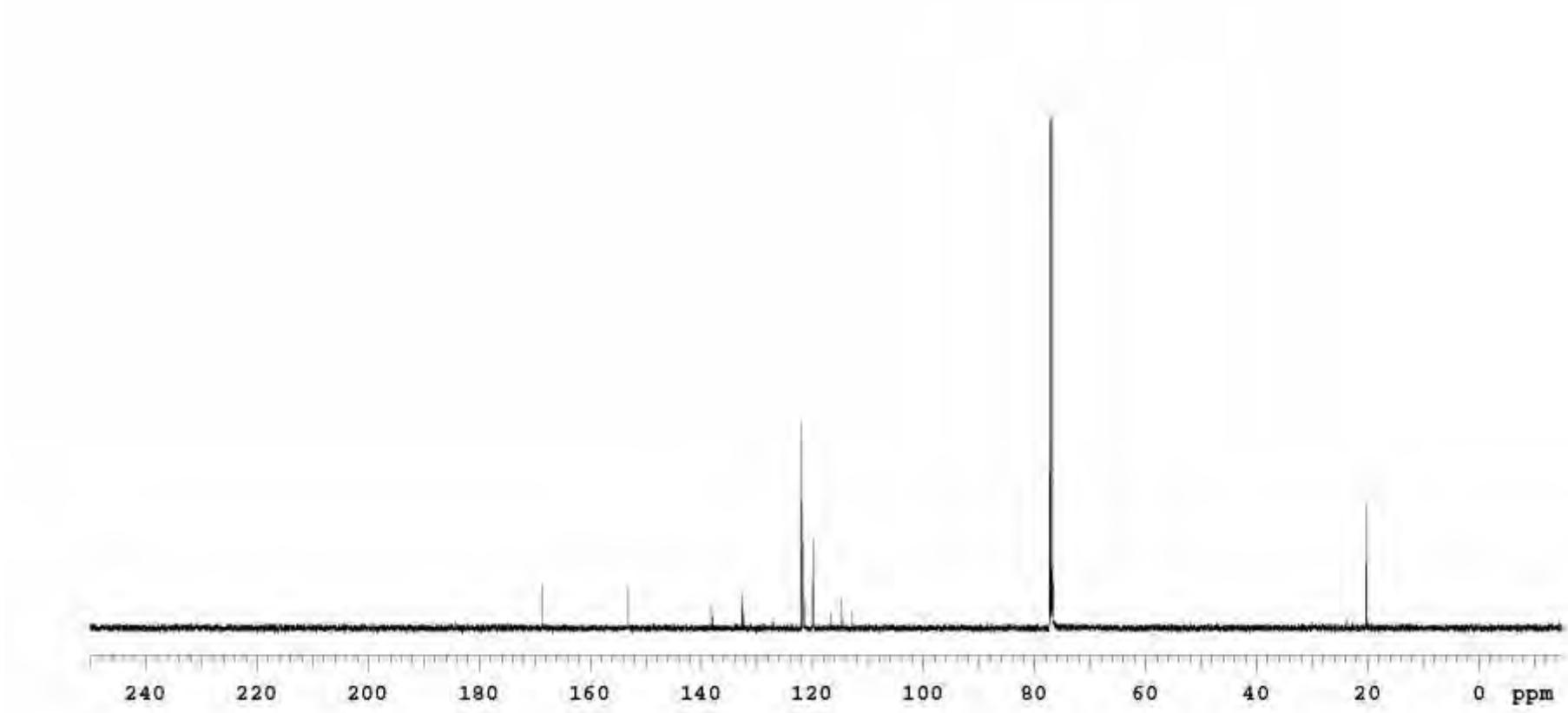




^{13}C NMR of 5-Difluoromethyl-2-methylbenzo[*d*]thiazole (3n)

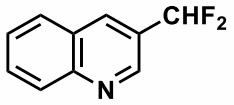


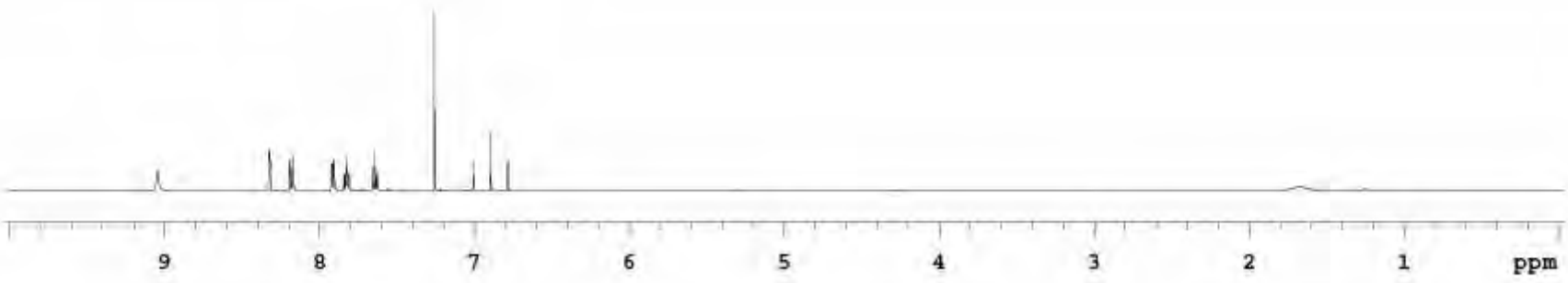
$CDCl_3$, 23 ºC



^{1}H NMR of 3-Difluoromethylquinoline (3p)

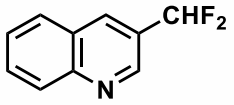
$CDCl_3$, 23 ºC

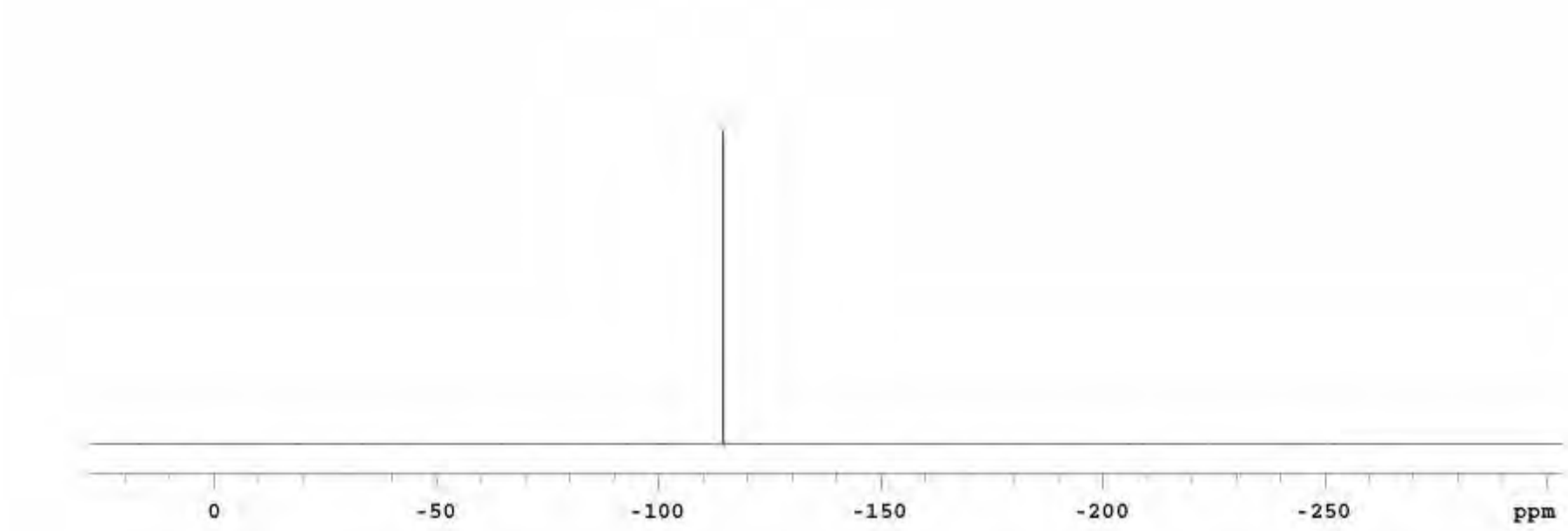




^{19}F NMR of 3-Difluoromethylquinoline (3p)

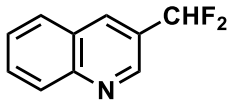
$CDCl_3$, 23 ºC





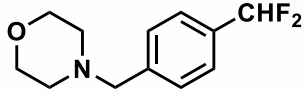
^{13}C NMR of 3-Difluoromethylquinoline (3p)

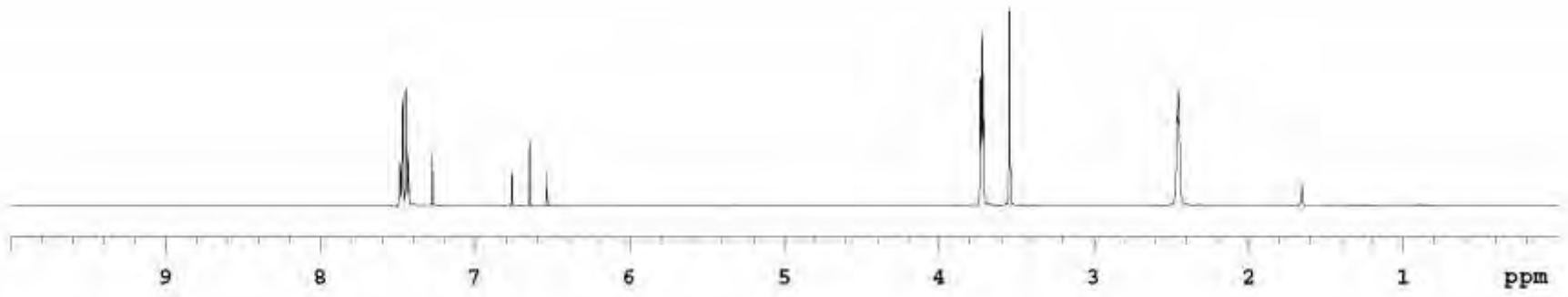
$CDCl_3$, 23 ºC



^{1}H NMR of 4-Morpholinomethyl-difluoromethylbenzene (3q)

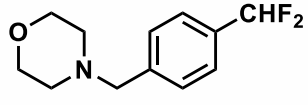
$CDCl_3$, 25 ºC

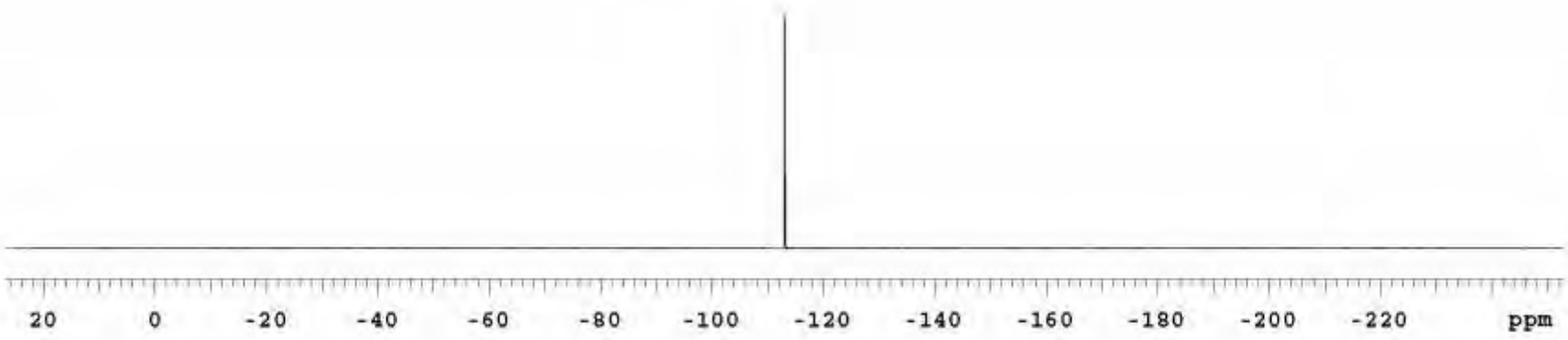




^{19}F NMR of 4-Morpholinomethyl-difluoromethylbenzene (3q)

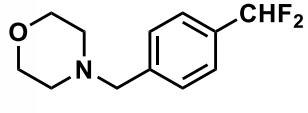
$CDCl_3$, 24 ºC

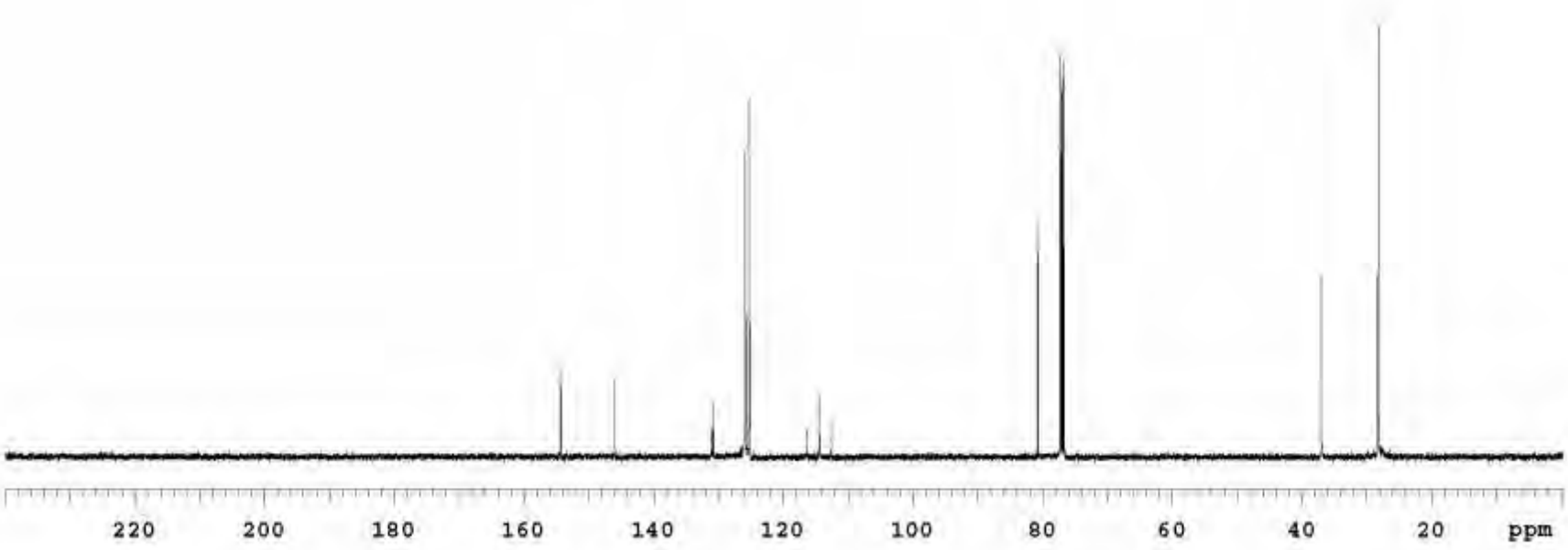




^{13}C NMR of 4-Morpholinomethyl-difluoromethylbenzene (3q)

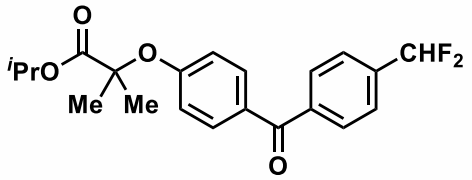
$CDCl_3$, 25 ºC

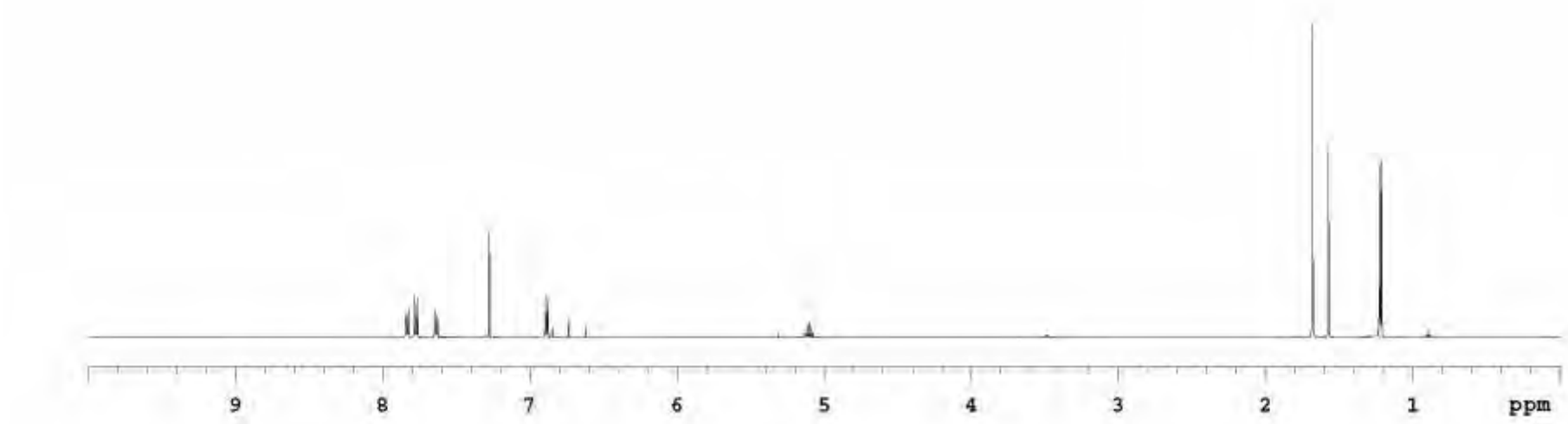




^{1}H NMR of Difluoromethyl-fenofibrate

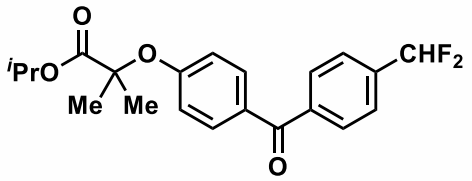
$CDCl_3$, 25 ºC

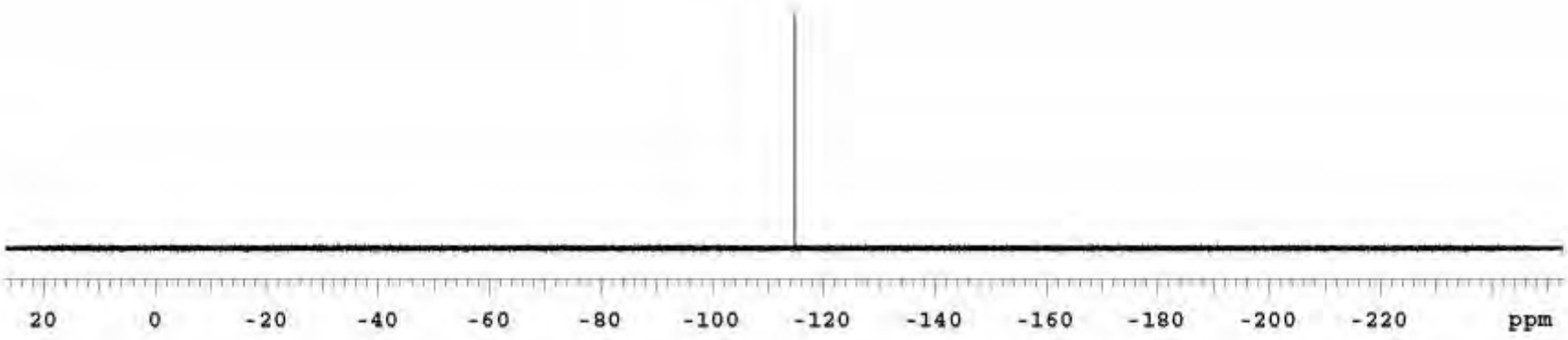




^{19}F NMR of Difluoromethyl-fenofibrate

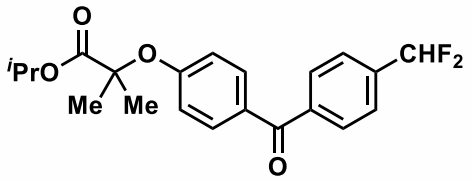
$CDCl_3$, 24 ºC

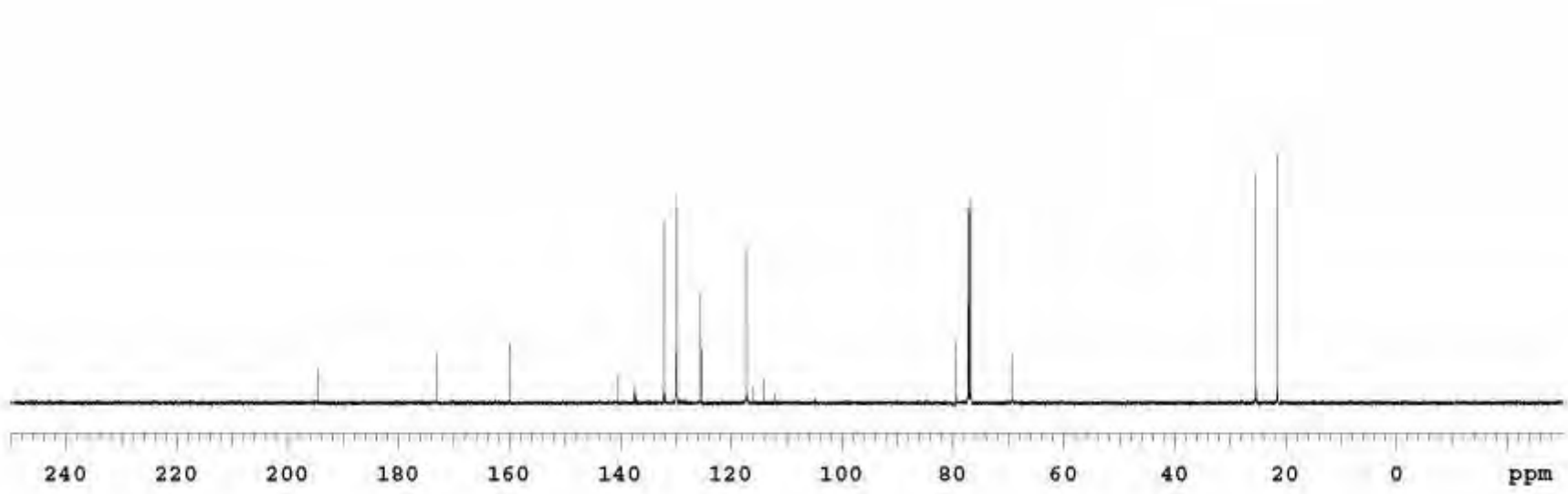




^{13}C NMR of Difluoromethyl-fenofibrate

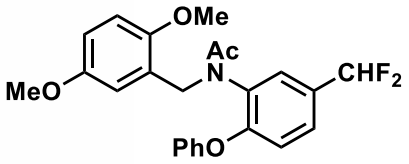
$CDCl_3$, 25 ºC

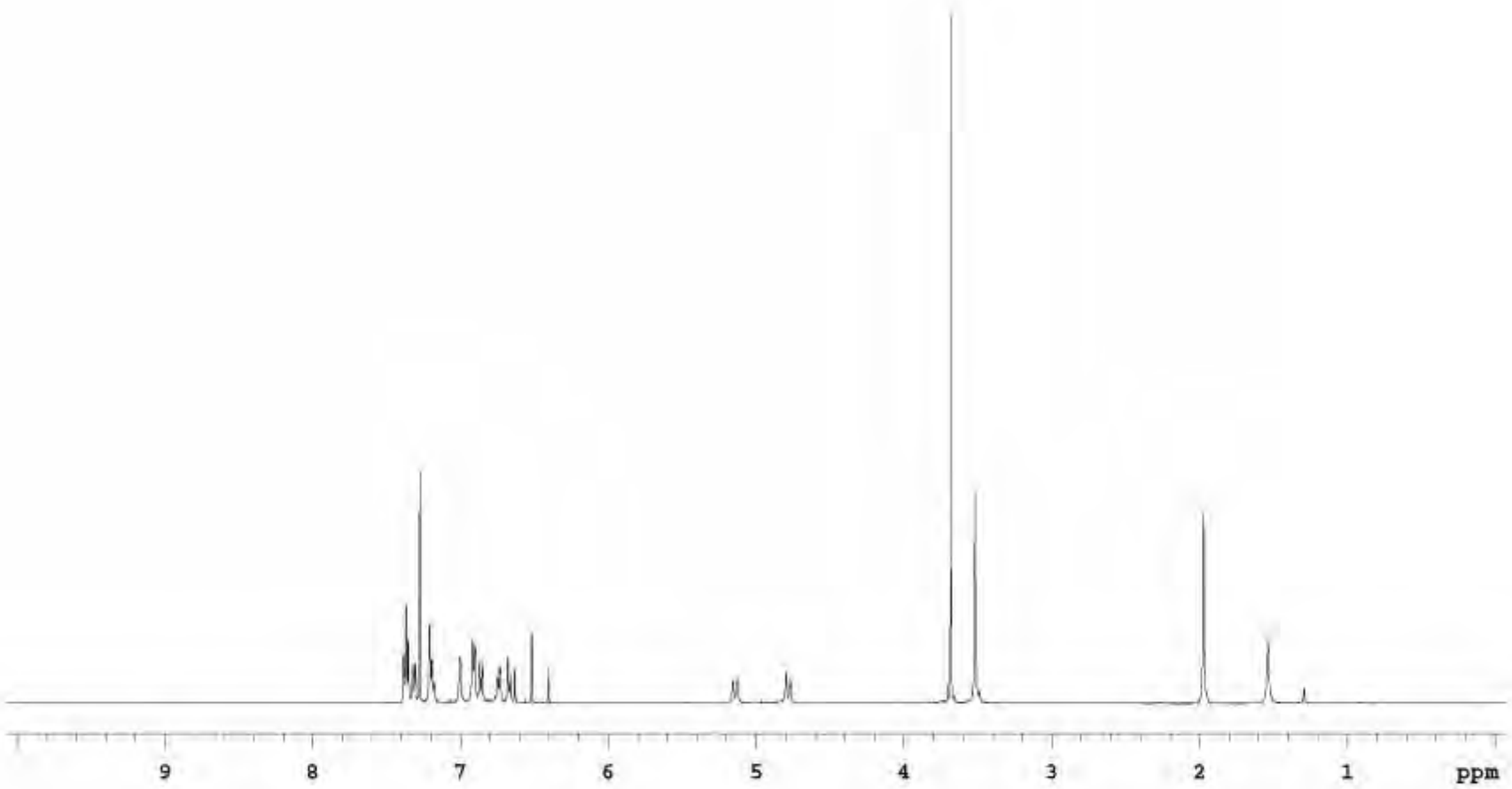




^{1}H NMR of Difluoromethyl-DAA1106

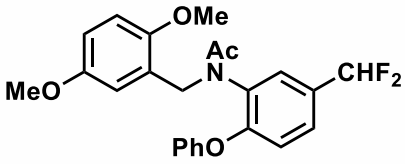
$CDCl_3$, 55 ºC

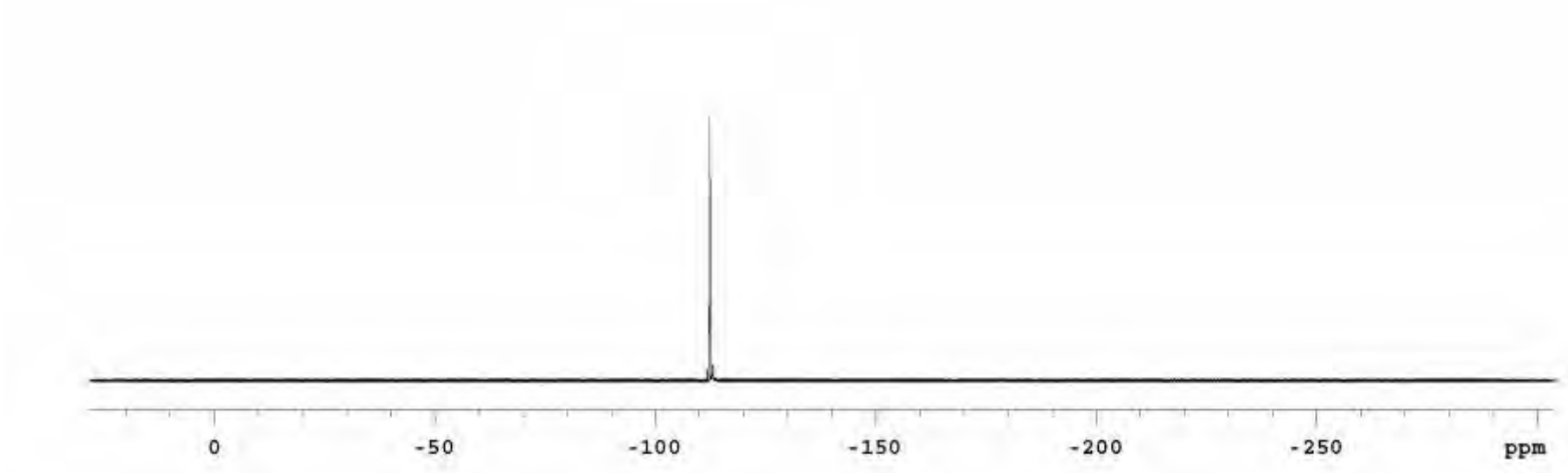




^{19}F NMR of Difluoromethyl-DAA1106

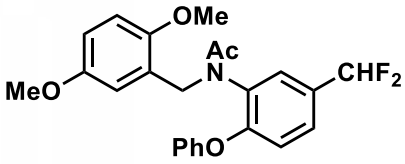
$CDCl_3$, 25 ºC





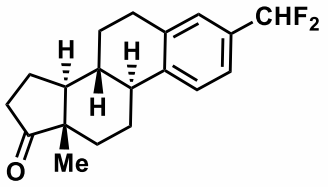
^{13}C NMR of Difluoromethyl-DAA1106

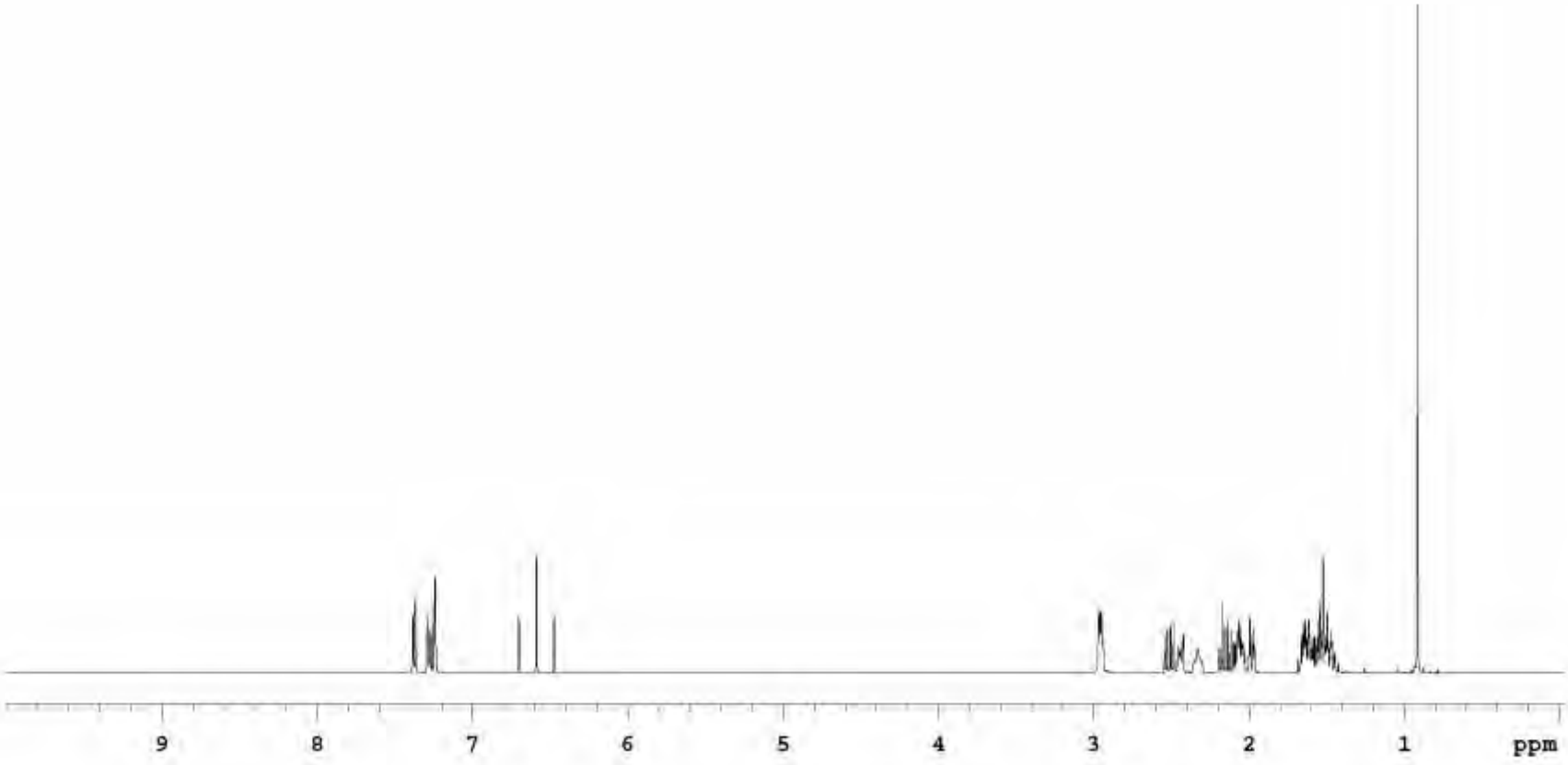
$CDCl_3$, 23 ºC



^{1}H NMR of Difluoromethyl-estrone

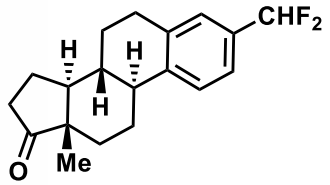
$CDCl_3$, 23 ºC

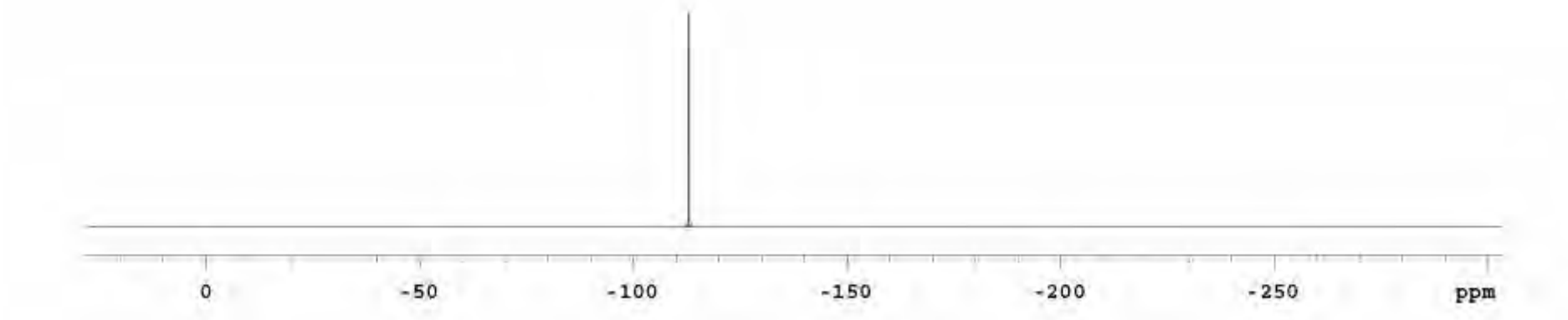




^{19}F NMR of Difluoromethyl-estrone

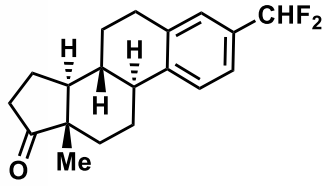
$CDCl_3$, 25 ºC

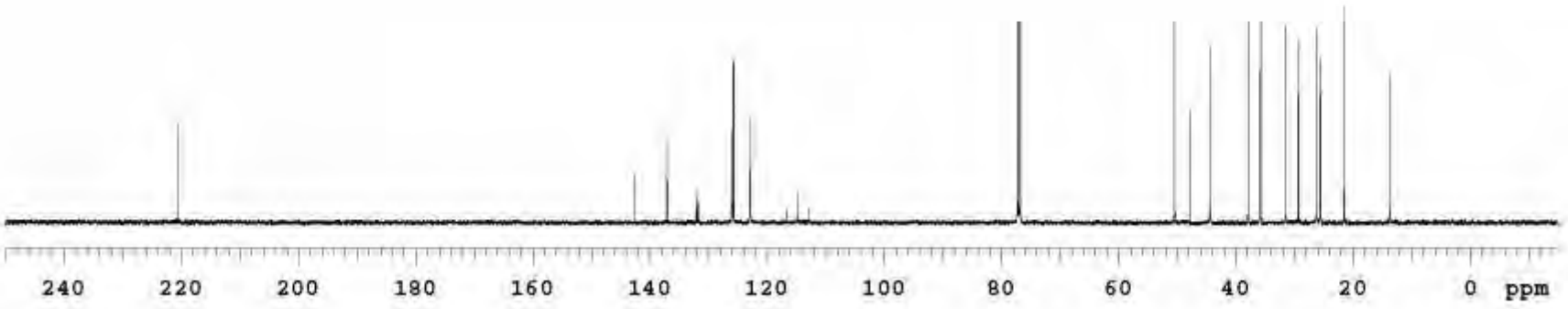




^{13}C NMR of Difluoromethyl-estrone

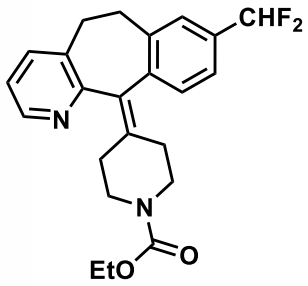
$CDCl_3$, 25 ºC

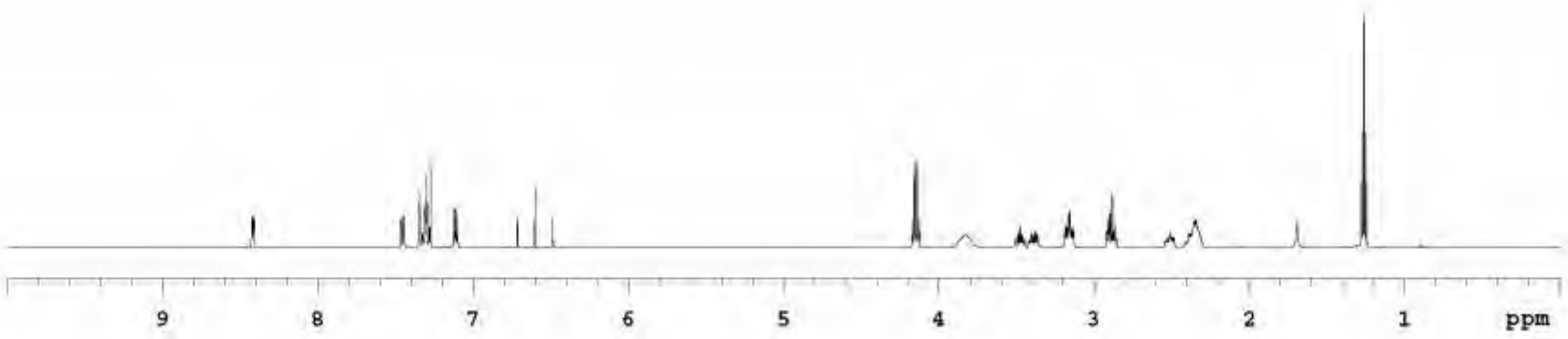




^{1}H NMR of Difluoromethyl-claritin

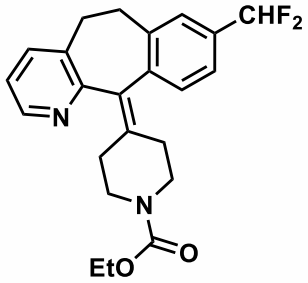
$CDCl_3$, 25 ºC

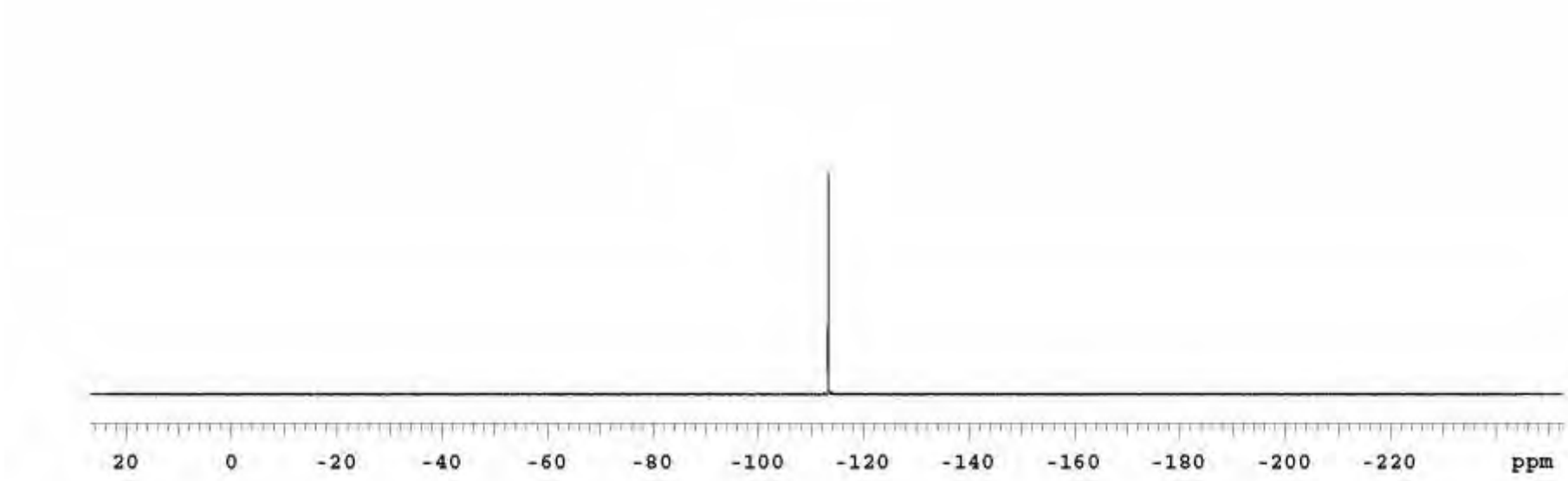




^{19}F NMR of Difluoromethyl-claritin

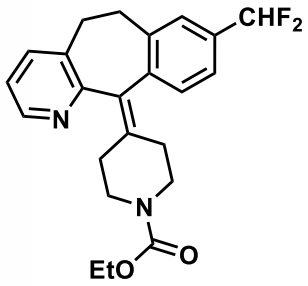
$CDCl_3$, 24 ºC

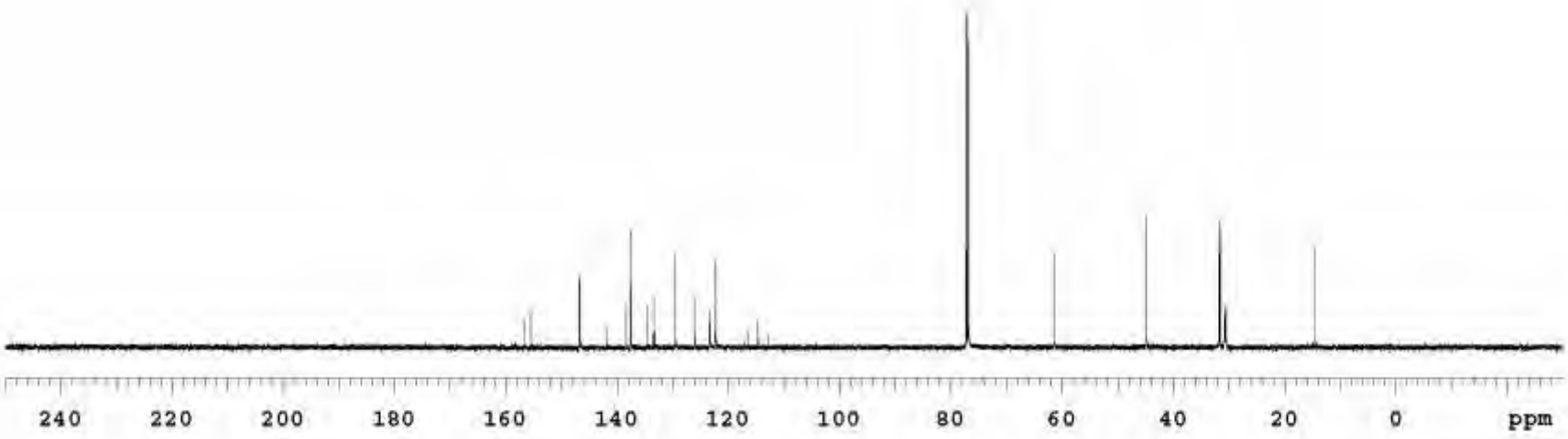




^{13}C NMR of Difluoromethyl-claritin

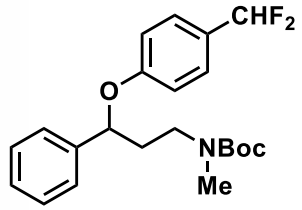
$CDCl_3$, 25 ºC

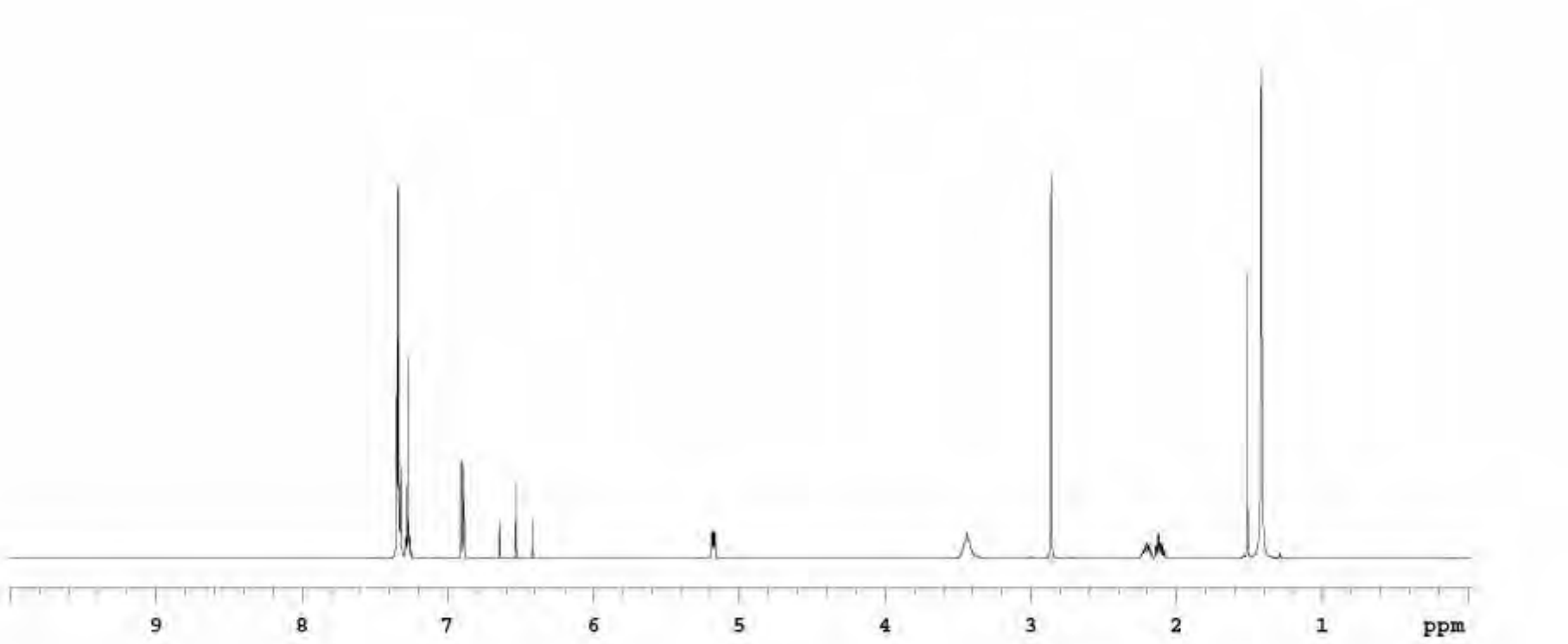




^{1}H NMR of Difluoromethyl-*N*-Boc-fluoxetine

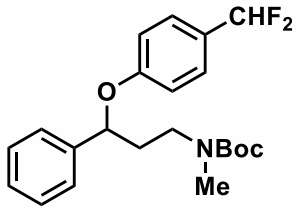
$CDCl_3$, 50 ºC

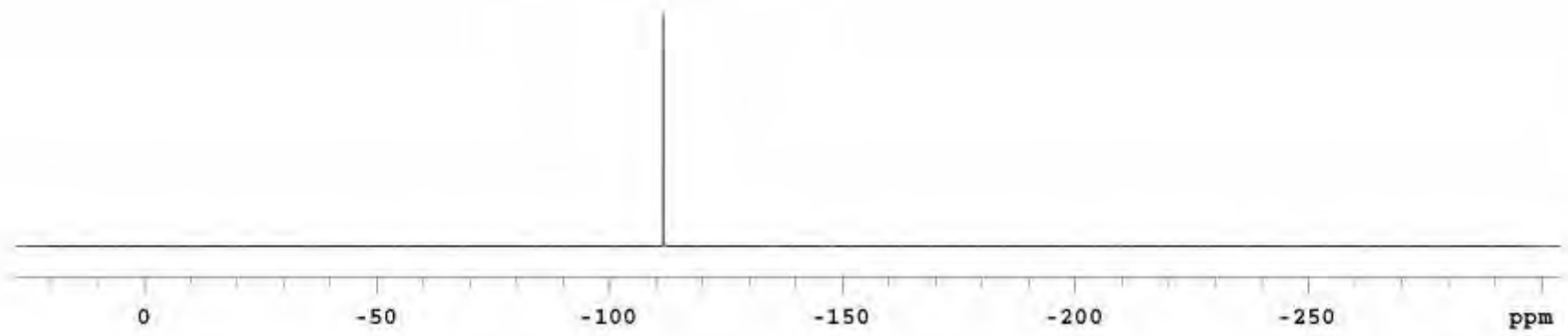




^{19}F NMR of Difluoromethyl-*N*-Boc-fluoxetine

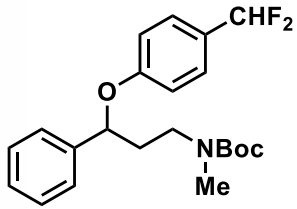
$CDCl_3$, 21 ºC

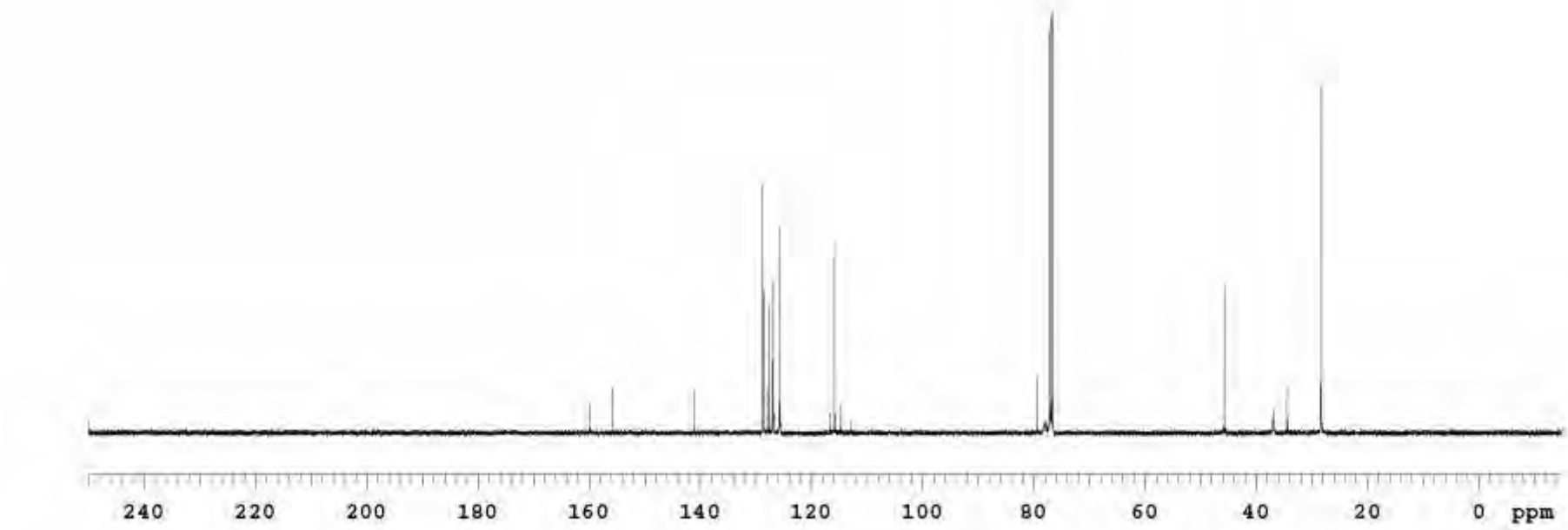




^{13}C NMR of Difluoromethyl-*N*-Boc-fluoxetine

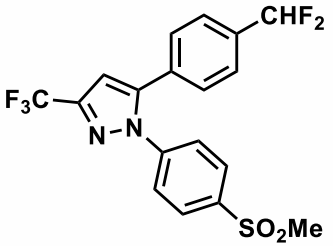
$CDCl_3$, 50 ºC

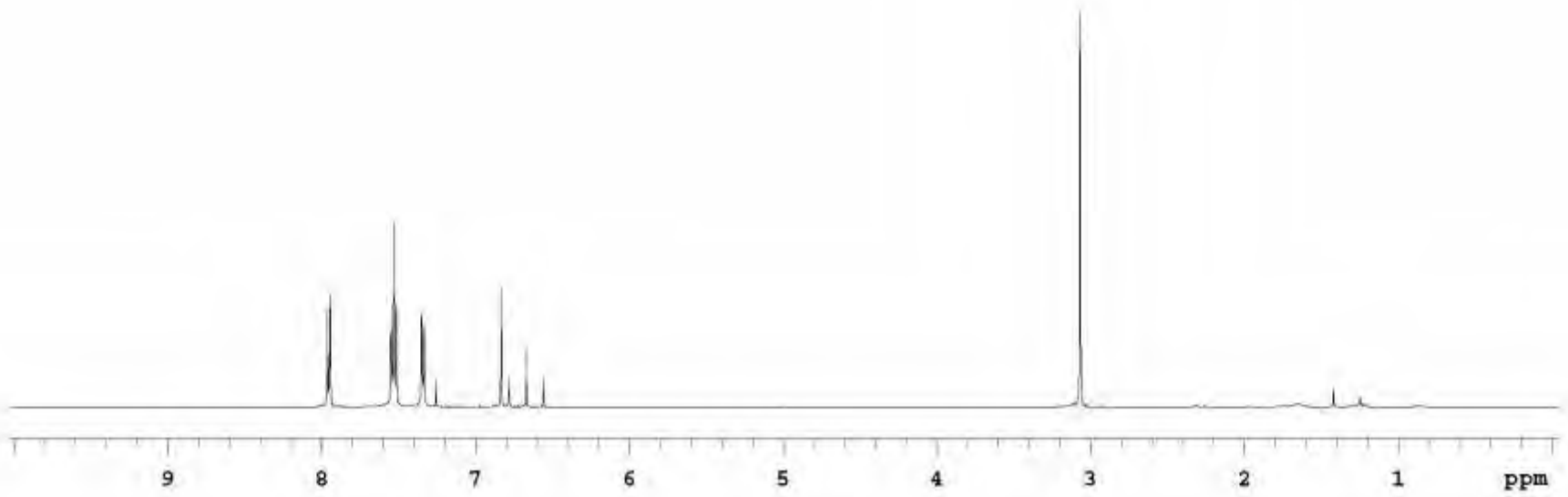




^{1}H NMR of Difluoromethyl-SC-58125

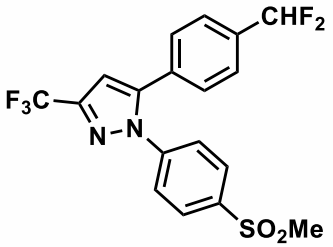
$CDCl_3$, 25 ºC

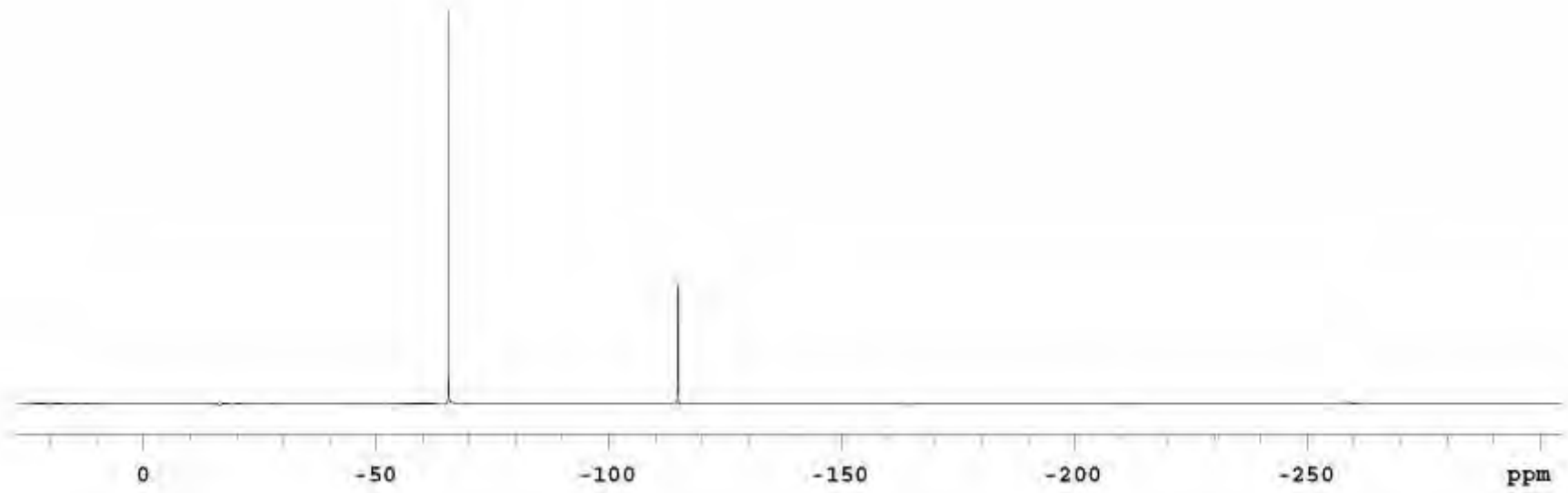




^{19}F NMR of Difluoromethyl-SC-58125

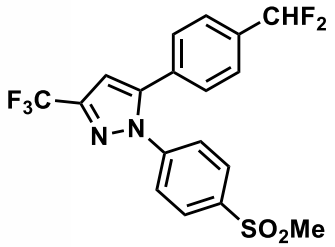
$CDCl_3$, 25 ºC

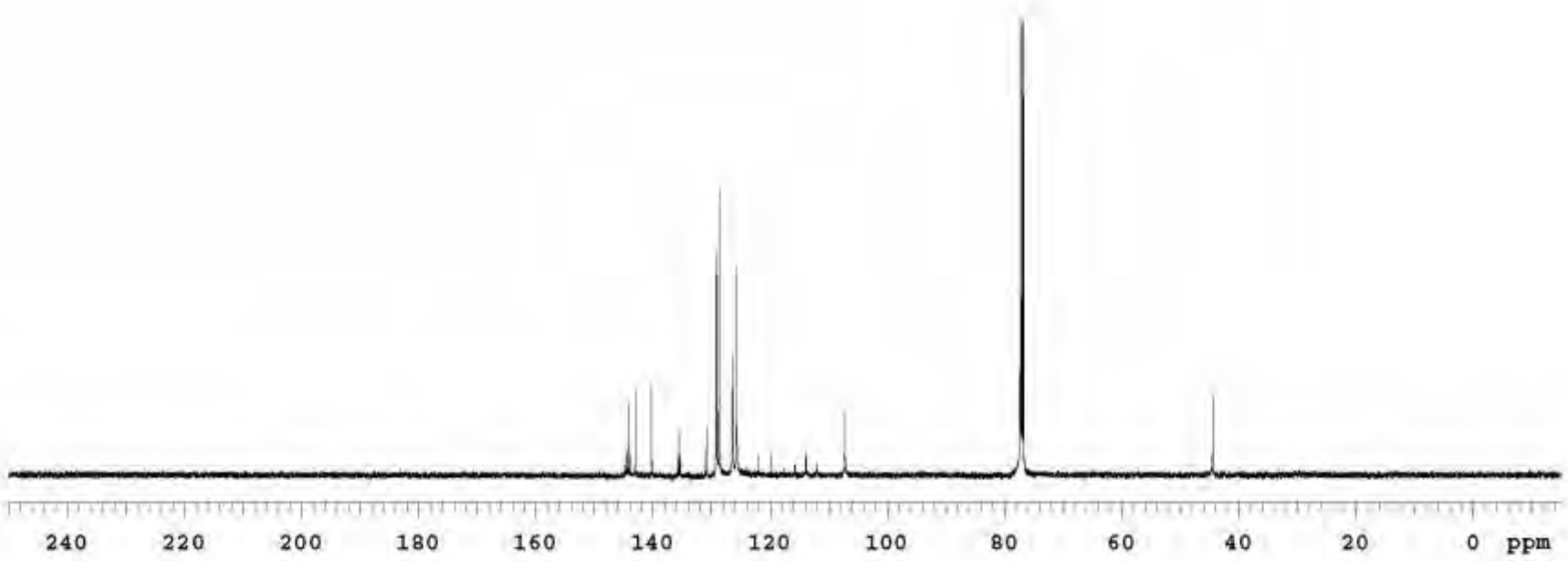




^{13}C NMR of Difluoromethyl-SC-58125

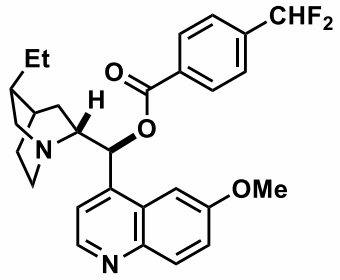
$CDCl_3$, 23 ºC

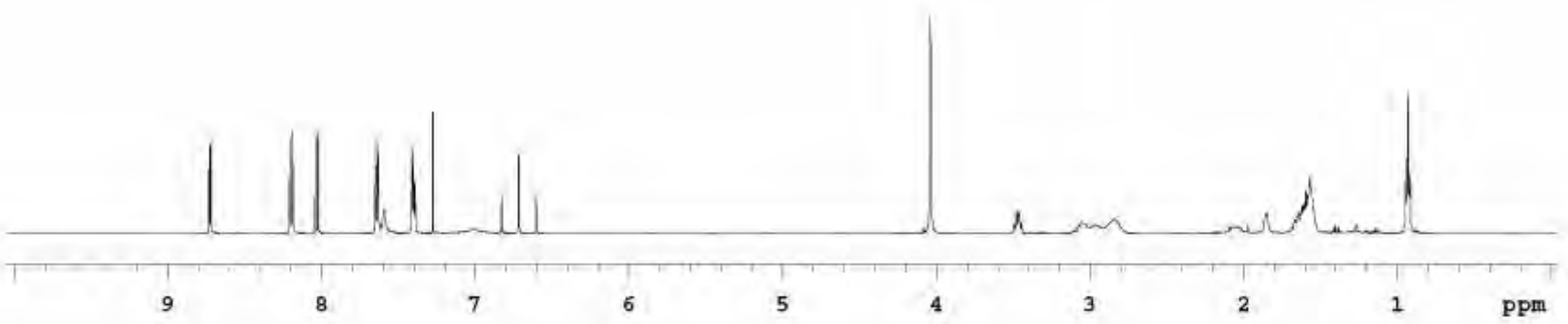




^{1}H NMR of Hydroquinidine 4-difluoromethylbenzoate

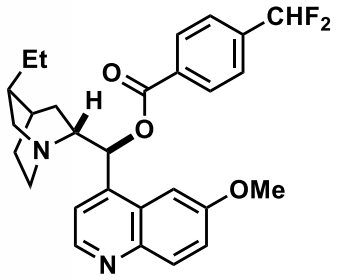
$CDCl_3$, 25 ºC

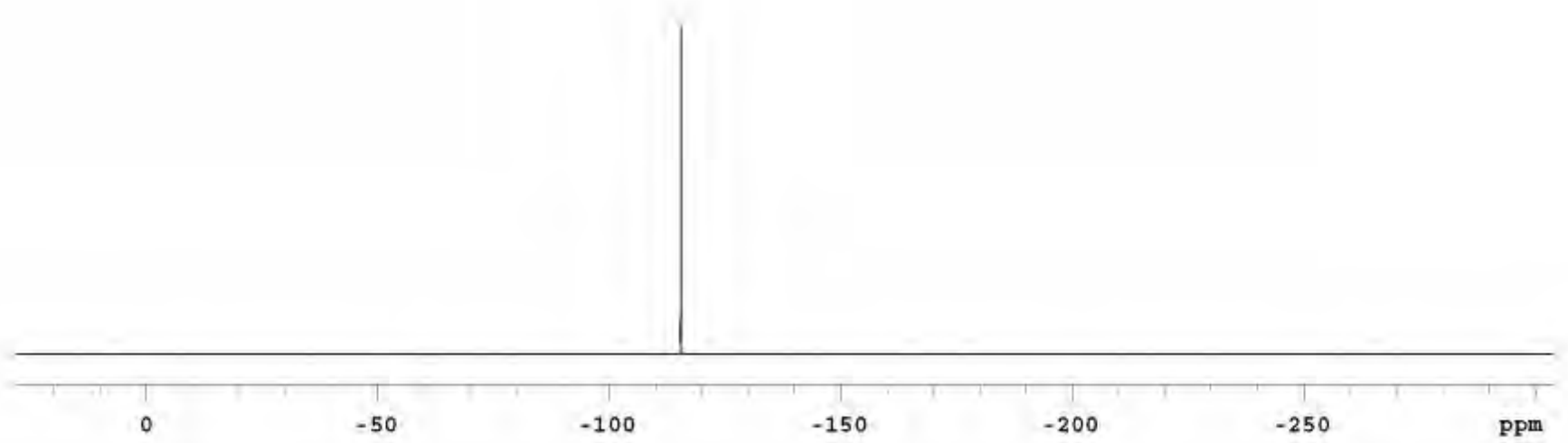




^{19}F NMR of Hydroquinidine 4-difluoromethylbenzoate

$CDCl_3$, 25 ºC





^{13}C NMR of Hydroquinidine 4-difluoromethylbenzoate

$CDCl_3$, 25 ºC