Electronic Supplementary Material (ESI) for Chemical Science.

Site-selective ^{18}F fluorination of unactivated C-H bonds mediated by a manganese porphyrin

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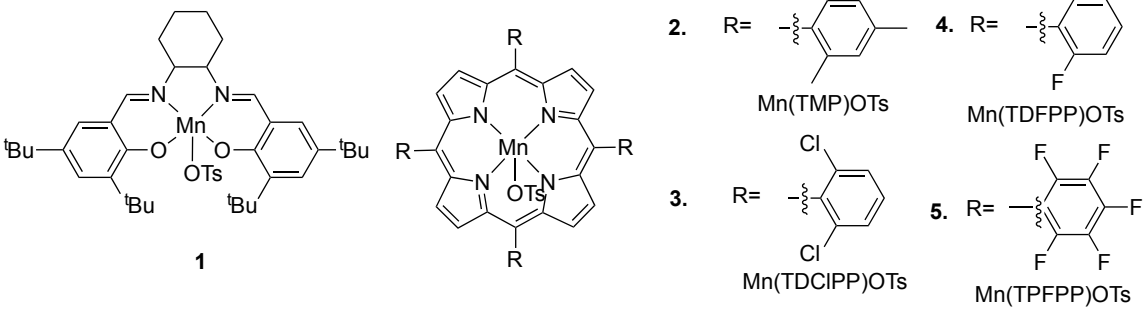
SUPPORTING INFORMATION

1. General information

Manganese tetrakis(pentafluorophenyl)porphyrin chloride (Mn(TPFPP)Cl) was prepared by refluxing the free base with manganese acetate, followed by HCl treatment. Mn(TPFPP)OTs was prepared by treating Mn(TPFPP)Cl with stoichiometric amounts of silver tosylate in refluxing toluene. Iodosylbenzene (PhIO) was prepared by hydrolysis of iodobenzene diacetate with sodium hydroxide solution. Other purchased materials were of the highest purity available from Aldrich and used without further purification. ^{1}H NMR spectra were obtained on a Bruker NB 300 spectrometer or a Bruker Avance-III (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at δ 7.26, acetone-d_6 at 2.04, or methylene chloride-d_2 at 5.32). Data reported as: chemical shift (δ), multiplicity (s= singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz); integrated intensity. ^{13}C NMR spectra were recorded on a Bruker 500 (125 MHz) spectrometer and are reported in ppm using solvents as an internal standard ($CDCl_3$ at 77.15 ppm, acetone-d_6 at 29.92 ppm, or methylene chloride-d_2 at 54.0). ^{19}F NMR spectra (282 MHz) were obtained on a Bruker NB 300 spectrometer and were referenced relative to relative to $CFCl_3$. GC/MS analyses were performed on an Agilent 7890A gas chromatograph equipped with an Agilent 5975 mass selective detector. High-resolution mass spectra were obtained from the Princeton University mass spectrometer facility by electrospray ionization (ESI). High-performance liquid chromatography (HPLC) was performed on an Agilent 1100 series instrument with a binary pump and a diode array detector.

Structures of the catalysts used in this study (Table 1)

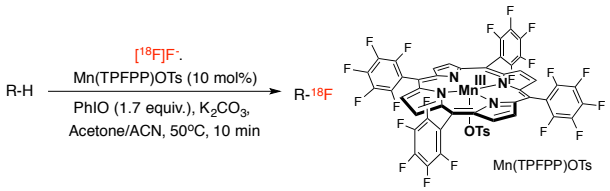


2. Radiochemistry

General methods

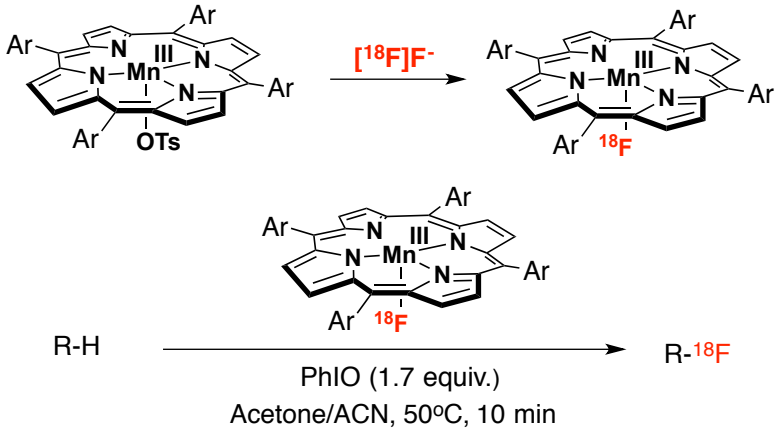
No-carrier-added [^{18}F]fluoride was produced from water 97% enriched in ^{18}O (ISOFLEX, USA) by the nuclear reaction ^{18}O(p,n)^{18}F using a Siemens Eclipse HP cyclotron and a silver-bodied target at Massachusetts General Hospital Athinoula A. Martinos Center for Biomedical Imaging. The produced [^{18}F]fluoride in water was transferred from the cyclotron target by helium push.

Radiosynthesis of ^{18}F labeled molecules



A 4 mL vial with a screw cap was charged with Mn(TPFPP)OTs (16 mg, 0.022 mmol), substrate (0.25 mmol) and a stir bar (2 × 5 mm), followed with 0.4 mL acetonitrile. A portion of aqueous [^{18}F]fluoride solution (40 – 50 µL, 4 – 5 mCi) obtained from the cyclotron was loaded on to an Chromafix PS-HCO_3 IEX cartridge, which had been previously washed with 5 mg/mL K_2CO_3 in Milli-Q water followed by 5 mL of Milli-Q water. Then, the cartridge loaded with [^{18}F]fluoride was washed with 2 mL Milli-Q water and [^{18}F]fluoride was released from the cartridge using 0.8 mL 5.0 mg/mL K_2CO_3 in Milli-Q water. A portion of the resulting [^{18}F]fluoride solution (25 µL, 125 – 150 µCi) was diluted with 3.0 mL acetone. 0.2 mL of this [^{18}F]fluoride acetone solution was added to the vial containing the catalyst and the substrate. The resulting solution was stirred for 1 min at room temperature. Then 80 mg (0.25 mmol) iodosylbenzene (PhIO) was added to the solution, and the vial was capped and stirred at 50 ^{o}C for 10 min. After 10 min, an aliquot of the reaction mixture was taken and spotted on a silica gel TLC plate. The plate was developed in an appropriate eluent and scanned with a Bioscan AR-2000 Radio TLC Imaging Scanner.

Dry-down free procedure for radiosynthesis of ^{18}F labeled molecules



A 4 mL vial with a screw cap was charged with substrate (0.33 mmol) and a stir bar (2 × 5 mm) 80 mg PhIO, followed with 0.4 mL acetonitrile. A portion of aqueous [^{18}F]fluoride solution (40 – 50 µL, 4 – 5 mCi) obtained from the cyclotron was loaded on to a Chromafix PS-HCO_3 IEX cartridge, which had been previously washed with 5 mg/mL K_2CO_3 in Milli-Q water followed by 3 mL of Milli-Q water. Then, the cartridge loaded with [^{18}F]fluoride was washed with 3 mL Milli-Q water and the residual water was removed by air purge. [^{18}F]fluoride was then slowly eluted using 0.5 mL of an acetone

solution of Mn(TPFPP)OTs (16 mg) (> 90% radioactivity being eluted). The obtained solution was added to the vial containing the substrate. The vial was capped and stirred at 50 °C for 10 min. After 10 min, an aliquot of the reaction mixture was taken and spotted on a silica gel TLC plate. The plate was developed in an appropriate eluent and scanned with a Bioscan AR-2000 Radio TLC Imaging Scanner.

Scale-up synthesis of [18F]F-ACPC

The synthesis was performed with a Gilson automated liquid handler. The QMA resin containing the [18F]fluoride was obtained from Siemens Molecular Imaging, Inc., North Wales, PA. A 1 mL Wheaton conical glass vial was charged with 10 mg precursor, 10 mg PhIO, and 0.1 mL of acetonitrile. Vortex the vial until a suspension was formed and then placed the vial in a microwave cavity. A stock solution of Mn(TPFPP)OTs was prepared by dissolving 10 mg Mn(TPFPP)OTs in 1 mL acetonitrile. Passing 0.6 mL of the Mn(TPFPP)OTs solution through the QMA resin to elute the 18F. The elution efficiency was around 80%. Adding 0.3 mL of the eluted catalyst solution to the 1 mL conical vial containing the precursor and oxidant. Heat the vial with microwave reactor (50 °C, 50 W, 10 min). After the reaction, 0.5 mL water was added to the reaction mixture and then subjected to prep-HPLC separation.

Determination of specific activity of [^{18}F]Butylbenzoate 2

The produced [^{18}F]fluoride in water (256 mCi) was transferred from the cyclotron target by helium push (@ 9:30 am). A portion of aqueous [^{18}F]fluoride solution (3.7 mCi) was loaded on to a Chromafix PS-HCO_3 IEX cartridge and [^{18}F]Mn(TPFPP)F acetone solution was obtained followed by the dry-down free procedure described above (3.4 mCi, 92% trapping efficiency, @10:30 pm). 30 mg of butyl benzoate was added to the [^{18}F]Mn(TPFPP)F acetone solution and then stirred at 50 °C for 1 min. Then, 50 mg PhIO was added to the reaction solution and the vial was capped and stirred for 10 min at 50 °C. The resulting mixture was passed through a syringe filter and was then subjected to prep-HPLC (2.7 mCi injected, @10:55 pm) The collected radioactive peak gave 550 μCi of [^{18}F]**2** (14.9 % non-decay corrected RCY, @11:15 pm).

The calibration curve was made according to the following procedure: solutions of different concentrations of fluorinated butyl benzoate were injected at constant volume on the HPLC. By multiplying the concentration times the volume we get nmol. The samples were analyzed by analytical HPLC and the peak area was recorded and used to construct a calibration curve. (**Figure S2-1**) A 50 μL sample of the collected fraction of [^{18}F]butylbenzoate was used for purity analysis by HPLC (18 μCi, @11:25 pm) A UV absorbance of 544 of [^{18}F]butylbenzoate was determined, corresponding to 2.9 nmol of **25**. The specific activity was thus calculated to be 1.24 Ci/μmol @EOB.

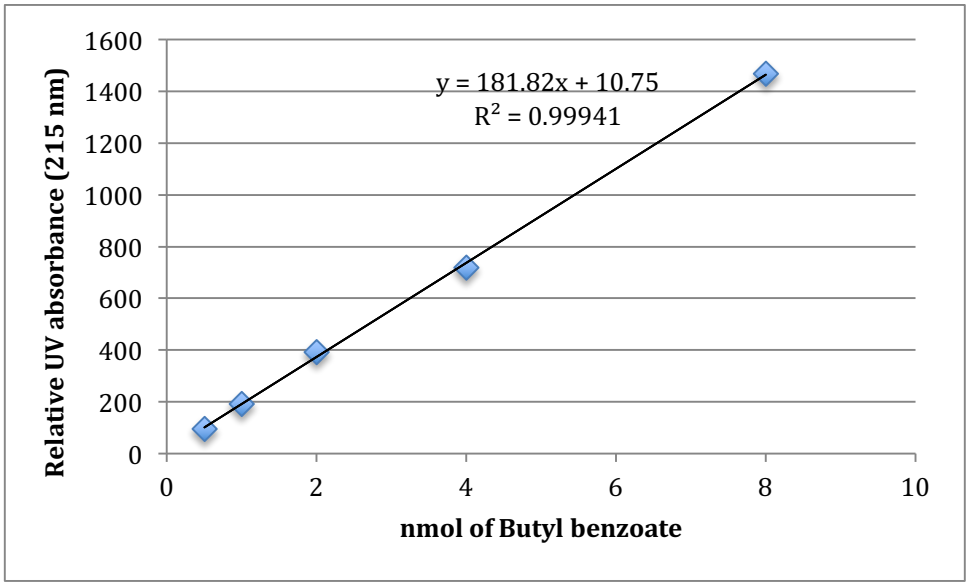
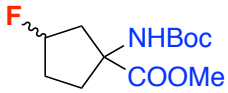
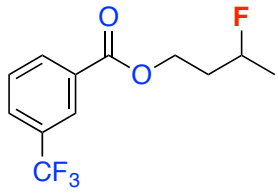


Figure S2-1. Standard curve of UV absorbance *vs* amount of fluorinated butyl benzoate

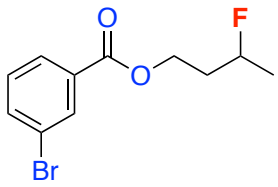
3. Preparation and characterization of the new ^{19}F authentic samples



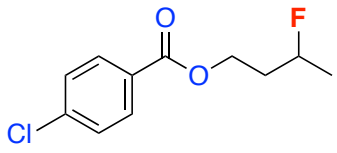
Compound 1. Synthesized according to published Mn-fluorination procedure. White solid ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.13 (d, J = 53.8 Hz, 1H), 5.00 (d, J = 56.5 Hz, 1H), 3.74 (s, 3H), 2.80 - 1.83 (m, 6H), 1.43 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.24, 155.18, 95.50, 80.08, 65.26, 52.70, 44.62, 35.58, 32.81, 28.41; ^{19}F NMR (282 MHz, $CDCl_3$) δ 167.9 (major), 170.9 (minor) HRMS (ESI) m/z cal'd $C_{12}H_{20}FNNaO_4$ $[M+Na]^+$: 284.1274, found 284.1290.



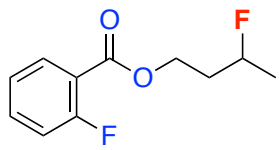
Compound 3. Synthesized according published procedure. colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (tt, J = 1.6, 0.7 Hz, 1H), 8.26 - 8.19 (m, 1H), 7.85 - 7.79 (m, 1H), 7.59 (tt, J = 7.7, 0.8 Hz, 1H), 4.98 - 4.78 (m, 1H), 4.58 - 4.44 (m, 2H), 2.19 - 1.93 (m, 2H), 1.42 (dd, J = 23.9, 6.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.38, 132.94, 131.11, 129.68, 129.20, 126.70, 124.92, 122.77, 87.87 (d, J = 160 Hz), 61.88, 36.18, 21.35. ^{19}F NMR (282 MHz, $CDCl_3$) δ 175.75; MS (EI) m/z cal'd $C_{12}H_{12}F_4O_2$ $[M]^+$264.1, found 264.1



Compound 4. Synthesized according published procedure. Colorless oil. Contaminated with 10% non-fluorinated precursor. ^{1}H NMR (501 MHz, $CDCl_3$) δ 8.17 (m, 1H), 7.97 (ddd, J = 7.8, 1.6, 1.1 Hz, 1H), 7.68 (m, 1H), 7.32 (td, J = 7.9, 3.1 Hz, 1H), 4.87 (dm, J = 49.7 Hz, 1H), 4.53 – 4.39 (m, 2H), 2.18 – 1.92 (m, 2H), 1.42 (dd, J = 23.9, 6.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.14, 135.96, 132.56, 132.08, 129.92, 128.17, 122.48, 87.77 (d, J = 165 Hz) 61.59, 36.01, 21.14; ^{19}F NMR (282 MHz, $CDCl_3$) δ -176.31; MS (EI) m/z cal'd $C_{11}H_{12}BrFO_2$ $[M]^+$ 274.0, found 274.0;

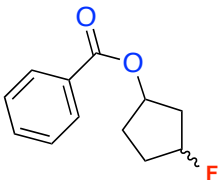


Compound 5. Synthesized according published procedure. Colorless oil; ^{1}H NMR (501 MHz, $CDCl_3$) δ 7.97 (d, J = 8.3 Hz, 2H) 7.41 (d, J = 8.5 Hz, 2H), 4.87 (d, J = 48.6 Hz, 1H), 4.46 (m, 2H), 2.23 – 1.85 (m, 2H), 1.41 (dd, J = 23.9, 6.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.85, 139.70, 131.18, 128.99, 128.82, 88.05 (d, J = 166 Hz), 61.63, 36.25, 21.37; ^{19}F NMR (282 MHz, $CDCl_3$) δ -175.63; MS (EI) m/z cal'd $C_{11}H_{12}ClFO_2$ $[M]^+$ 230.1, found 230.1;

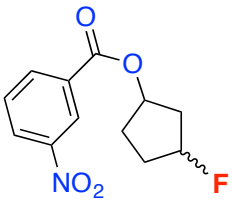


Compound 6. Synthesized according published procedure. Colorless oil; ^{1}H NMR (501 MHz, $CDCl_3$) δ 7.93 (td, J = 7.5, 1.8 Hz, 1H), 7.52 (dddd, J = 8.4, 7.4, 4.8, 1.9 Hz, 1H),

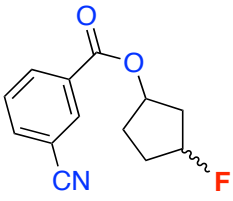
7.16 (m, 2H), 4.89 (dm, J = 49.6 Hz, 1H), 4.46 (m, 2H), 2.20 – 1.89 (m, 2H), 1.41 (dd, J = 23.9, 6.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.67 (d, J = 174 Hz), 160.92, 134.55, 132.13, 123.99, 118.67, 117.01, 87.80 (d, J = 165 Hz), 61.45, 35.97, 21.11; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.32, -175.89; MS (EI) m/z cal'd $C_{11}H_{12}F_2O_2$ $[M]^+$ 214.1, found 214.1;



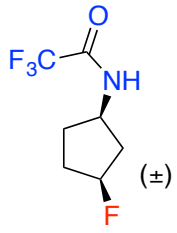
Compound 7. Synthesized according published procedure. Colorless oil; ^{1}H NMR (501 MHz, CD_3CN) δ 8.12 – 7.93 (m, 2H), 7.69 – 7.57 (m, 1H), 7.57 – 7.44 (m, 2H), 5.39 (m, 1H), 5.22 (dddt, J = 54.9, 6.2, 3.2, 1.7 Hz, 1H), 2.32 – 1.83 (m, 6H); ^{13}C NMR (126 MHz, CD_3CN) δ 167.07, 134.05, 131.67, 130.25, 129.58, 96.29 (d, J = 172 Hz), 76.79, 40.76, 32.76, 31.42; ^{19}F NMR (282 MHz, CD_3CN) δ -169.83; MS (EI) m/z cal'd $C_{12}H_{13}FO_2$ $[M]^+$ 208.1, found 208.1;



Compound 8. Synthesized according published procedure. Colorless oil; ^{1}H NMR (501 MHz, Chloroform-*d*) δ 8.79 (s, 1H), 8.41 (d, J = 8.1 Hz, 1H), 8.34 (d, J = 7.7 Hz, 1H), 7.65 (t, J = 8.0 Hz, 1H), 5.61 (m, 1H), 5.31 (d, J = 52.1, 1H), 2.76 – 1.64 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.06, 148.25, 135.28, 132.09, 129.65, 127.44, 124.44, 95.37, (d, J =168 Hz), 40.86, 32.78, 31.82, 30.40; ^{19}F NMR (282 MHz, $CDCl_3$) δ -171.47; MS (EI) m/z cal'd $C_{12}H_{12}FNO_4$ $[M]^+$ 253.1, found 253.1;

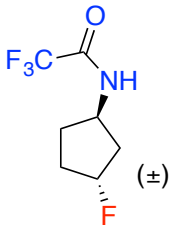


Compound 9. Synthesized according published procedure. Colorless oil; ^{1}H NMR (501 MHz, Chloroform-*d*) δ 8.27 (s, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.58 (t, J = 7.8 Hz, 1H), 5.59 (tdd, J = 6.4, 3.7, 2.4 Hz, 1H), 5.23 (dt, J = 54.0, 4.8 Hz, 1H), 2.51 (dddt, J = 26.6, 15.9, 6.8, 1.8 Hz, 1H), 2.33 - 1.92 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.37, 136.21, 133.85, 133.41, 131.84, 129.68, 118.12, 113.17, 95.18 (d, J = 172 Hz), 77.08, 41.11, 31.55, 30.63; ^{19}F NMR (282 MHz, $CDCl_3$) δ -171.44; MS (EI) m/z cal'd $C_{13}H_{12}FNO_2$ $[M+Na]^+$ 233.1, found 233.1;

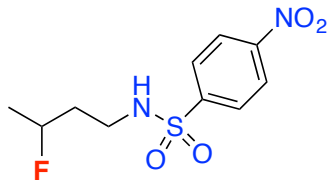


Compound 10a. Synthesized according published procedure. White solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.61 (br, 1H), 5.52 (dm, J = 53.1 Hz, 1H), 4.54 (m, 1H), 2.29-1.71 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.22, 115.77 (q, J = 287.8 Hz), 96.61 (d, J = 169.1 Hz), 49.91, 40.22, 32.08, 31.03; ^{19} F NMR (282 MHz, $CDCl_3$) δ -76.01, -168.03; MS(EI) m/z cal'd $C_7H_9F_4NO$

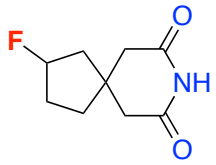
$[M]^+$ 199.1, found 199.1;



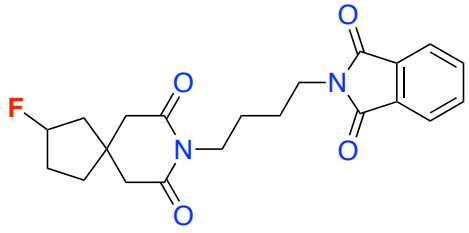
Compound 10b. Synthesized according published procedure. White solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.24 (br, 1H), 5.21 (dm, *J* = 53.7 Hz, 1H), 4.49, (m, 1H), 2.58 – 1.50 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.86, (q, *J* = 283.9 Hz), 94.45 (d, *J* = 173.3 Hz); 50.58, 40.35, 31.68, 30.14; ^{19} F NMR (282 MHz, $CDCl_3$) δ -76.01, -170.11; MS(EI) m/z cal'd $C_7H_9F_4NO$ $[M]^+$ 199.1, found 199.1;



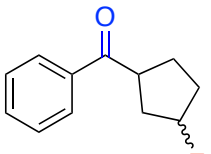
Compound 11. Synthesized by treating the corresponding alcohol with DAST. Yellow solid ^{1}H NMR (501 MHz, $CDCl_3$) δ 8.45 – 8.31 (m, 2H), 8.11 – 7.99 (m, 2H), 4.91 - 4.81 (br, 1H), 4.73 (dm, *J* = 47.6 Hz, 1H), 3.32 – 3.03 (m, 2H), 1.91 – 1.71 (m, 2H), 1.33 (dd, *J* = 24.3, 6.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.10, 145.81, 128.31, 124. 46, 89.69 (d, *J* = 164 Hz), 40.28, 36.48, 20.93; ^{19}F NMR (282 MHz, $CDCl_3$) -174.99; HRMS (ESI) m/z cal'd $C_{10}H_{14}FN_2O_4S$ $[M+H]^+$ 277.0658, found 277.0654;



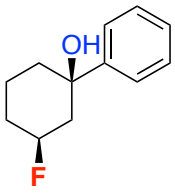
Compound 12. Synthesized according published procedure. White solid. ^{1}H NMR (501 MHz, $CDCl_3$) δ 7.83 (br, 1H), 5.21 (dt, *J* = 53.0, 4.2 Hz, 1H), 2.74 (m, 2H), 2.57 (m, 2H), 2.24 – 1.63 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171. 44, 171.34, 95.86 (d, *J* = 173 Hz), 45.38, 45.21, 44.46, 39.95, 35.45, 32.65; ^{19}F NMR (282 MHz, $CDCl_3$) δ -167.79; HRMS (ESI) m/z cal'd $C_9H_{13}FNO_2$ $[M+H]^+$ 186.0930, found 186.0936;



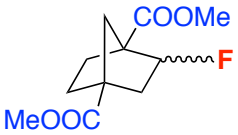
Compound 13. Synthesized by treating compound 12 with corresponding alkyl bromide. White solid. ^{1}H NMR (501 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.70 (dd, *J* = 5.5, 3.1 Hz, 2H), 5.15 (dtt, *J* = 53.3, 4.8, 1.6 Hz, 1H), 3.79 (t, *J* = 7.0 Hz, 2H), 3.68 (t, *J* = 6.9 Hz, 2H), 2.82 – 2.48 (m, 4H), 2.20 – 1.45 (m, 10H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.63, 171.59, 168.36, 133.91, 132.10, 123.21, 95.89 (d, *J* = 173 Hz), 45.44, 45.24, 45.07, 39.00, 38.74, 37.57, 35.23, 32.61, 26.07, 25.32; ^{19}F NMR (282 MHz, $CDCl_3$) -167.88; HRMS (ESI) m/z cal'd $C_{21}H_{24}FN_2O_4$ $[M+H]^+$ 387.1720, found 387.1722;



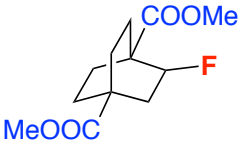
Compound 14. Synthesized according published procedure. Colorless oil; ^{1}H NMR (501 MHz, $CDCl_3$) δ 8.02 – 7.96 (m, 2H), 7.61 – 7.54 (m, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 5.29 (d, *J* = 52.6 Hz, 1H), 4.04 (qd, *J* = 8.6, 5.6 Hz, 1H), 2.31 – 2.14 (m, 3H), 2.12 – 1.98 (m, 1H), 1.99 – 1.78 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.52, 136.36, 133.14, 128.68, 128.53, 96.92 (d, *J* = 171 Hz), 44.02, 36.76, 32.93, 27.79; ^{19}F NMR (282 MHz, $CDCl_3$) -170.59; MS (EI) m/z cal'd $C_{12}H_{13}FO$ $[M]^+$ 192.1, found 192.1;



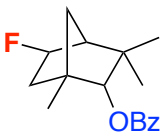
Compound 15. Synthesized according published procedure. White solid; ^{1}H NMR (501 MHz, $CDCl_3$) δ 7.61 – 7.50 (m, 2H), 7.44 – 7.34 (m, 2H), 7.32 – 7.24 (m, 1H), 5.11 (dp, *J* =47.8, 3.3 Hz, 1H), 3.08 (br, 1H), 2.38 – 1.87 (m, 6H), 1.81 – 1.49 (m, 2H) *Axial fluoride configuration is evidenced by the splitting of F-C-**H** (doublet of pentet)*; ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.59, 128.26, 126.87, 124.61, 91.54 (d, *J* = 164 Hz), 72.82, 42.47, 38.15, 29.92, 16.34; ^{19}F NMR (282 MHz, $CDCl_3$) -178.64; HRMS (ESI) m/z cal'd $C_{12}H_{16}FO$ $[M+H]^+$ 195.1185, found 195.1199;



Compound 16. Synthesized according published procedure. White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.96 – 4.76 (m, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 2.27 – 1.85 (m, 6H), 1.56 – 1.48 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.91, 172.19, 95.14 (d, *J* = 189 Hz), 57.37, 52.00, 50.26, 42.14, 39.93, 32.09, 31.60, 27.65. ^{19}F NMR (282 MHz, $CDCl_3$) δ 164.02 (major), 157.77 (mionr). MS (EI) m/z cal'd $C_{11}H_{15}FO_4$ $[M]^+$230.1, found 230.1

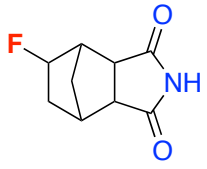


Compound 17. Synthesized according published procedure. Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.16 (ddt, *J* = 53, 8.8, 1.6 Hz, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 2.34 – 1.61 (m, 10H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.48, 175.20, 90.66 (d, *J* = 155 Hz), 52.15, 51.99, 27.75, 27.33, 26.72, 26.07, 26.02, 20.31, 20.27; ^{19}F NMR (282 MHz, $CDCl_3$) δ 173.17; MS (EI) m/z cal'd $C_{12}H_{17}FO_4$ $[M]^+$ 243.1, found 243.1

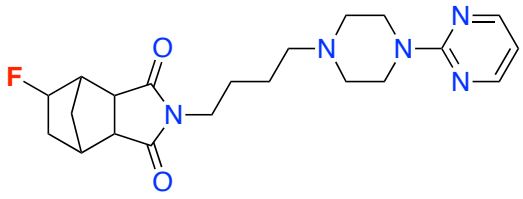


Compound 18. Synthesized according published procedure. Colorless oil; ^{1}H NMR (501 MHz, $CDCl_3$) δ 8.14 – 7.90 (m, 2H), 7.68 – 7.52 (m, 1H), 7.48 (m, 2H), 5.04 (dd, *J* = 55.2, 4.9 Hz, 1H), 4.61 (d, *J* = 1.7 Hz, 1H), 2.46 (dddd, *J* = 22.7, 14.6, 6.2, 2.4 Hz, 1H), 2.09 (dt, *J* = 8.1, 1.5 Hz, 1H), 1.77 – 1.31 (m, 3H), 1.26 (s, 3H), 1.17 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.99, 133.15, 130.02, 129.49, 128.48, 94.18 (d, *J* = 177 Hz), 85.05, 53.59, 47.66, 39.06, 37.56, 37.08, 29.45, 19.39, 18.47; ^{19}F NMR (282 MHz, $CDCl_3$) -167.61; MS (EI) m/z cal'd $C_{17}H_{21}FO_2$ $[M]^+$

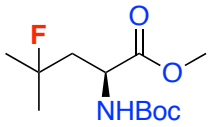
276.1, found 276.1;



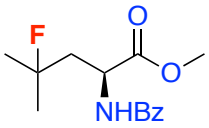
Compound 19. Synthesized according published procedure. White solid; ^{1}H NMR (501 MHz, CD_3CN) δ 4.76 (ddq, *J* = 54.8, 6.3, 1.3 Hz, 1H), 2.72 (d, *J* = 8.4 Hz, 1H), 2.61 (d, *J* = 4.6 Hz, 1H), 2.53 (s, 2H), 1.89 – 1.53 (m, 4H), 1.36 – 1.23 (m, 1H); ^{1}H NMR (501 MHz, $CDCl_3$) δ 178.04, 177.55, 93.36 (d, *J* = 186 Hz), 49.22, 45.20, 44.43, 38.61, 38.15, 29.91; ^{19}F NMR (282 MHz, CD_3CN) -165.96; HRMS (ESI) m/z cal'd $C_9H_{11}FNO_2$ $[M+H]^+$ 184.0774, found 184.0779;



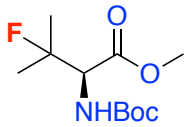
Compound 20. Synthesized by treating compound 19 with corresponding alkyl bromide. White solid; ^{1}H NMR (501 MHz, $CDCl_3$) δ 8.30 (d, *J* = 4.8 Hz, 2H), 6.47 (t, *J* = 4.7 Hz, 1H), 4.71 (d, *J* = 53.7 Hz, 1H), 3.82 (t, *J* = 5.1 Hz, 4H), 3.51 (t, *J* = 7.0 Hz, 2H), 2.92 (d, *J* = 8.0 Hz, 1H), 2.78 (s, 1H), 2.49 (m, 6H), 2.38 (t, *J* = 7.2 Hz, 2H), 1.92 – 1.35 (m, 6H), 1.25 (t, *J* = 7.2 Hz, 1H) , 1.11 (d, *J* = 11.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.77, 177.32, 161.64, 157.71, 109.81, 93.53 (d, *J* = 186 Hz), 58.05, 53.11, 47.78, 45.27, 43.65, 42.95, 38.85, 38.66, 38.19, 29.72, 25.83, 24.22; ^{19}F NMR (282 MHz, $CDCl_3$) δ -165.14; HRMS (ESI) m/z cal'd $C_{21}H_{29}FN_5O_2$ $[M+H]^+$ 402.2305, found 402.2312;



Compound 21a. Synthesized according published procedure. White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.16 (br, 1H), 4.43 (t, *J* = 6.9 Hz, 1H), 3.77 (s, 3H), 2.25 - 1.92 (m, 3H), 1.57 (d, *J* = 9.2 Hz, 1H), 1.41 (s, 5H), 0.96 (ddt, *J* = 31.5, 16.3, 7.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.38, 155.49, 95.26 (d, *J*=179.5 Hz), 80.28, 52.67, 51.06, 42.84, 28.55, 27.43, 26.78; ^{19}F NMR (282 MHz, $CDCl_3$) δ -136.62; HRMS (ESI) m/z cal'd $C_{12}H_{22}FNNaO_4$ $[M+Na]^+$ 286.1431, found 286.1420.

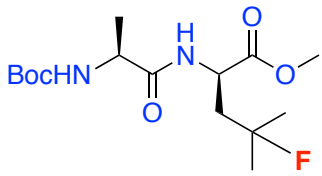


Compound 21b. Synthesized according published procedure. White solid. ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.04 - 7.86 (m, 2H), 7.64 - 7.39 (m, 3H), 4.92 - 4.82 (m, 1H), 3.71 (s, 3H), 2.43 - 2.17 (m, 2H), 1.45 (dd, *J* = 21.3, 7.3 Hz, 6H), (N-H signal not observed). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.41, 165.95, 134.26, 131.42, 128.29, 127.20, 94.42 (d, *J*=173 Hz), 51.53, 49.52, 41.67, 26.33, 25.96; ^{19}F NMR (282 MHz, $CDCl_3$) 136.77; HRMS (ESI) m/z cal'd $C_{14}H_{18}FNNaO_3$ $[M+Na]^+$ 290.1168, found 290.1163

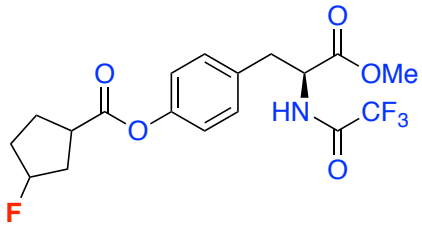


Compound 22. Synthesized according published procedure. White solid. Synthesized according published procedure ^{1}H NMR (501 MHz, $CDCl_3$) δ 5.35 (br, 1H), 4.39 (dd, *J* = 20.4, 9.6 Hz, 1H), 3.78 (s, 3H), 1.45 (s, 9H), 1.50 – 1.37 (dd, *J* = 21.3, 10.3 Hz 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ170.19, 155.40, 95.26, 80.30, 60.21, 52.37, 28.27, 24.60 (d, *J* = 23.8 Hz), 24.34 (d, *J* =

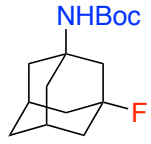
24.1 Hz); ^{19}F NMR (282 MHz, CD_3CN) δ -148.90; HRMS (ESI) m/z cal'd $C_{11}H_{21}FNO_4$ $[M+H]^+$ 250.2904, found 250.2917



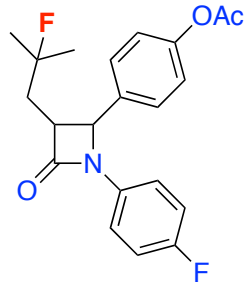
Compound 23. Synthesized according published procedure. White solid, contaminated with ~5% DCU; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (s, 1H), 4.98 (s, 1H), 4.63 (ddd, *J* = 8.4, 7.1, 5.0 Hz, 1H), 4.14 (dq, *J* = 18.2, 7.1 Hz, 1H), 3.72 (s, 3H), 2.25 – 1.52 (m, 2H), 1.44 (s, 9H) 1.42 (s, 3H), 1.38 - 1.33(m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.51, 172.37, 155.33, 95.82, 94.48, 52.52, 49.64, 41.97, 41.79, 28.20, 27.36, 26.03, 17.97; ^{19}F NMR (282 MHz, $CDCl_3$) δ 136.3 HRMS (ESI) m/z cal'd $C_{15}H_{27}FN_2NaO_5$ $[M+Na]^+$: 357.1802, found 357.1810.



Compound 24. Synthesized according published procedure. White solid. ^{1}H NMR (501 MHz, $CDCl_3$) δ 7.14 – 6.99 (m, 4H), 6.88 – 6.75 (m, 1H), 5.25 (dt, *J* = 52.9, 3.4, 1H), 4.86 (dt, *J* = 7.6, 5.6 Hz, 1H), 3.78 (s, 3H), 3.44 – 3.23 (m, 1H), 3.23 – 3.12 (m, 2H), 2.49 – 1.85 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.28, 170.24, 156.57, 150.16, 132.18, 130.19, 121.84, 115.53 (q, *J* = 287.7), 96.20 (d, *J* = 172 Hz), 53.52, 52.95, 41.71, 37.44, 36.63, 32.85, 27.46; ^{19}F NMR (282 MHz, $CDCl_3$) δ -75.91 ($-CF_3$), -171.04 (-F); HRMS (ESI) m/z cal'd $C_{18}H_{20}F_4NO_5$ $[M+H]^+$ 406.1278, found 406.1271;

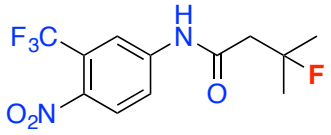


Compound 26. Synthesized according published procedure. White solid; ^{1}H NMR (501 MHz, $CDCl_3$) δ 4.46 (br, 1H), 2.33 (s, 2H), 2.10 (d, *J* = 5.9 Hz, 2H), 1.91 – 1.73 (m, 8H), 1.54 (d, *J* = 3.7 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ154.02, 92.54 (d, *J* = 185 Hz), 79.08, 53.67, 46.78, 41.66, 40.45, 34.72, 30.95, 28.45; ^{19}F NMR (282 MHz, $CDCl_3$) δ -132.67 HRMS (ESI) m/z cal'd $C_{15}H_{24}FNNaO_2$ $[M+Na]^+$ 292.1689, found 292.1678;



Compound 27. Synthesized according published procedure. Yellow oil; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.50 – 7.29 (m, 2H), 7.31 – 7.16 (m, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 7.00 – 6.85 (m, 2H), 4.83 (t, *J* = 1.8 Hz, 1H), 3.27 (ddd, *J* = 10.6, 5.5, 2.2 Hz, 1H), 2.29 (s, 1H), 2.26 –

2.12 (m, 2H), 1.44 (d, J = 21.3 Hz, 3H), 1.27 (d, J = 21.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.27, 166.87, 159.04 (d, J = 243.5 Hz), 150.68, 134.86, 133.73, 127.23, 122.24, 118.46, 115.90, 95.13 (d, J = 166.3 Hz), 61.46, 40.08, 34.70, 28.54, 25.44, 21.18



Compound 28. Synthesized according published procedure. Yellow solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 (d, J = 8.4 Hz, 0H), 8.01 (dd, J = 7.7, 1.7 Hz, 0H), 2.80 (d, J = 23.1 Hz, 0H), 1.55 (d, J = 22.0 Hz, 1H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.18 , 141.95 , 127.13 , 125.90 – 124.58 (m), 122.14 , 120.64 , 118.27, 95.15 (d, J = 165.4 Hz), 49.72, 26.81; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -60.52 , -135.37 (dqd, J = 44.3, 22.3, 8.2 Hz) ; HRMS (ESI) m/z cal'd $C_{12}H_{13}F_4N_2O_3$ $[M+H]^+$ 309.0862, found 309.0869;

4. Radio-HPLC characterization of the ^{18}F labeled products

All ^{18}F-labeled molecules were characterized by comparing the radio-HPLC trace of the crude reaction mixture to the HPLC UV trace of the authentic reference sample with methods detailed below.

HPLC column: Agilent Eclipse XDB-C18, 5 µm, 4.6 x 150 mm
Gradient: H_2O (0.1% TFA, A) and ACN (0.1% TFA, B), 5% B – 95% B, 20 min, 1.0 ml/min

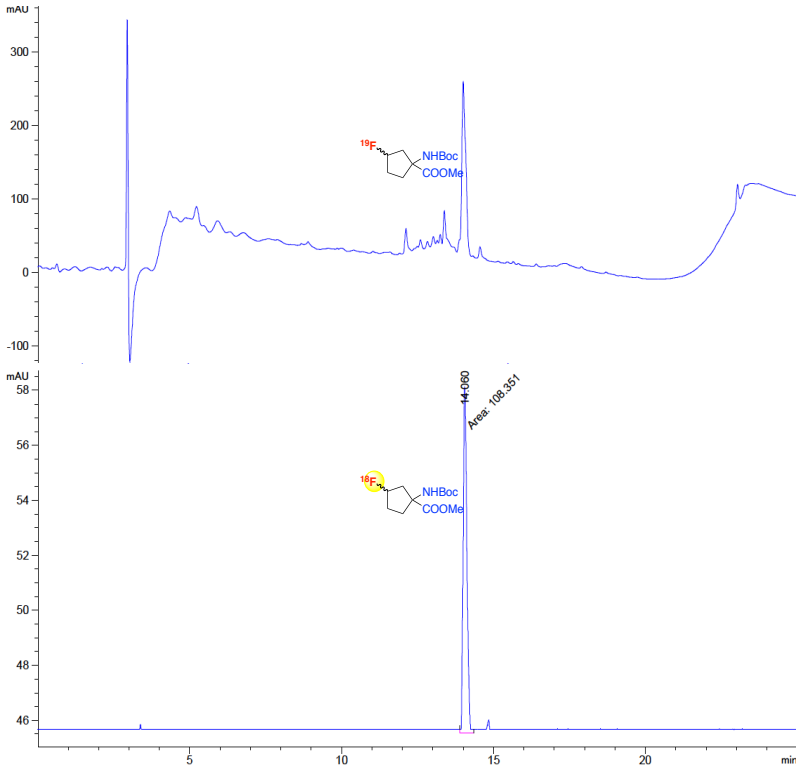


Figure S4a. UV and radio-HPLC traces of protected-FACPC

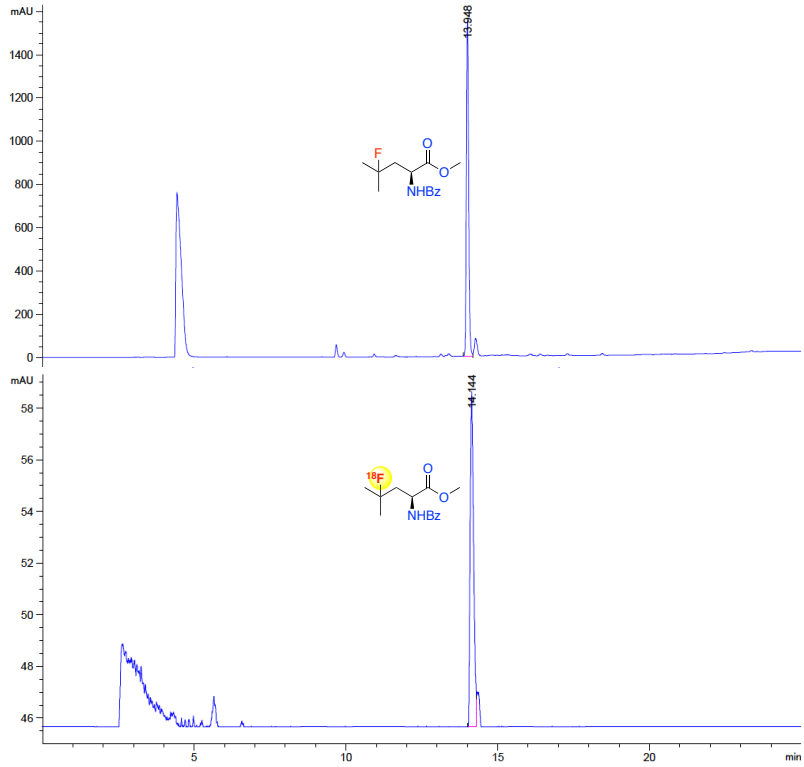


Figure S4b. UV and radio-HPLC traces of F-Leucine derivative

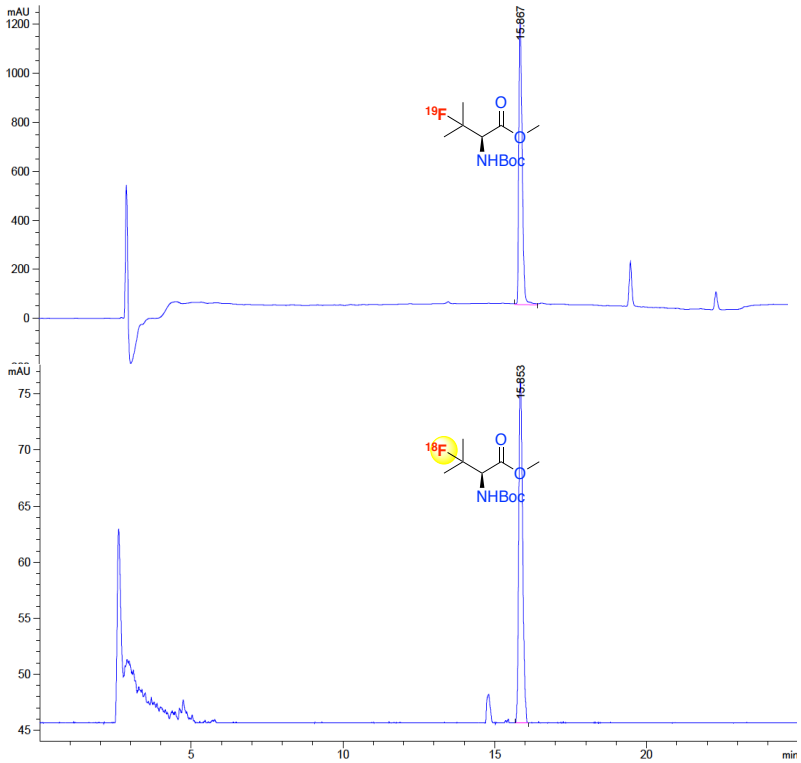


Figure S4c. UV and radio-HPLC traces of F-Valine derivative

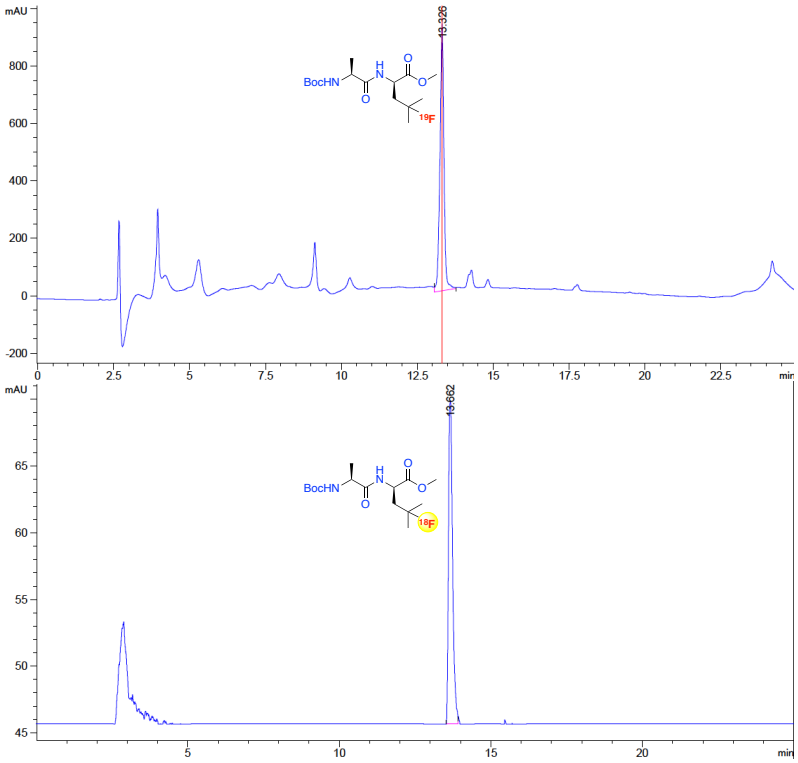


Figure S4d. UV and radio-HPLC traces of F-NBoc-Ala-Leu-OMe.

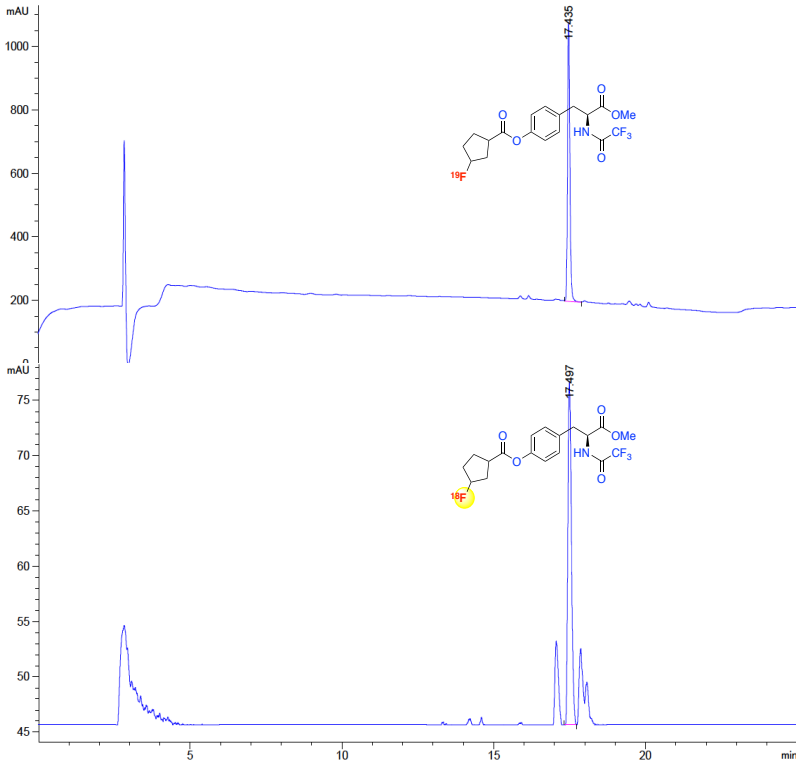


Figure S4e**.** UV and radio-HPLC traces F-tyrosine derivative.

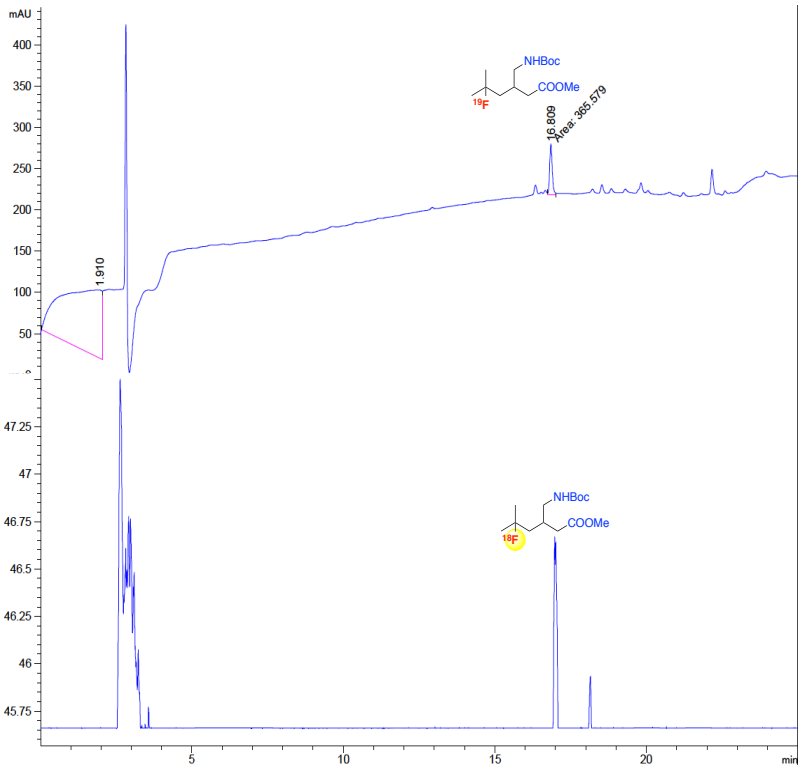


Figure S4f**.** UV and radio-HPLC traces F-pregabalin.

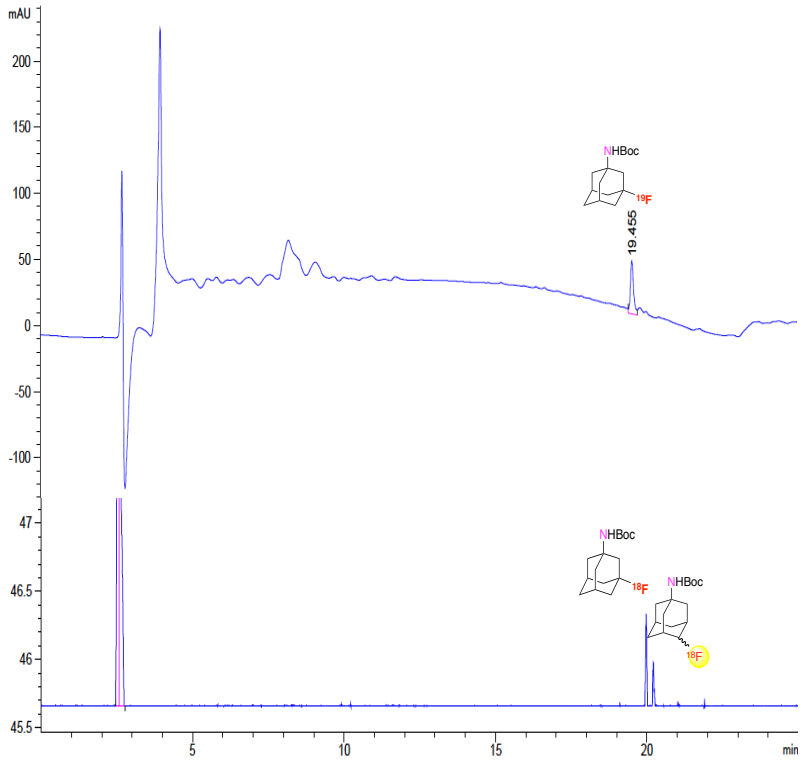


Figure S4g UV and radio-HPLC traces of F-N-Boc-amatadine.

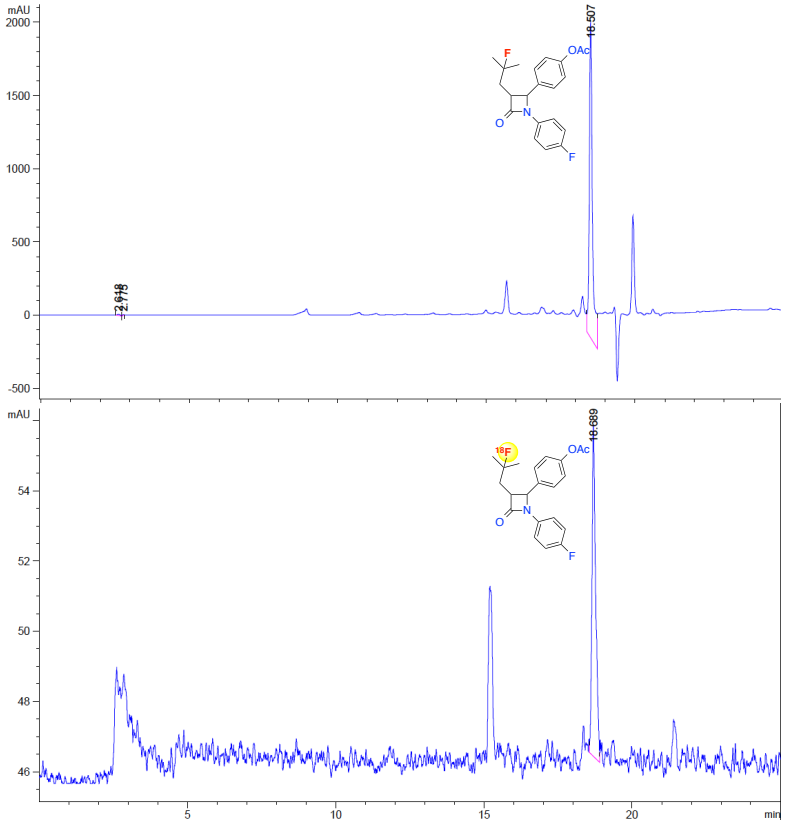


Figure S4h UV and radio-HPLC traces of ezetimibe analog.

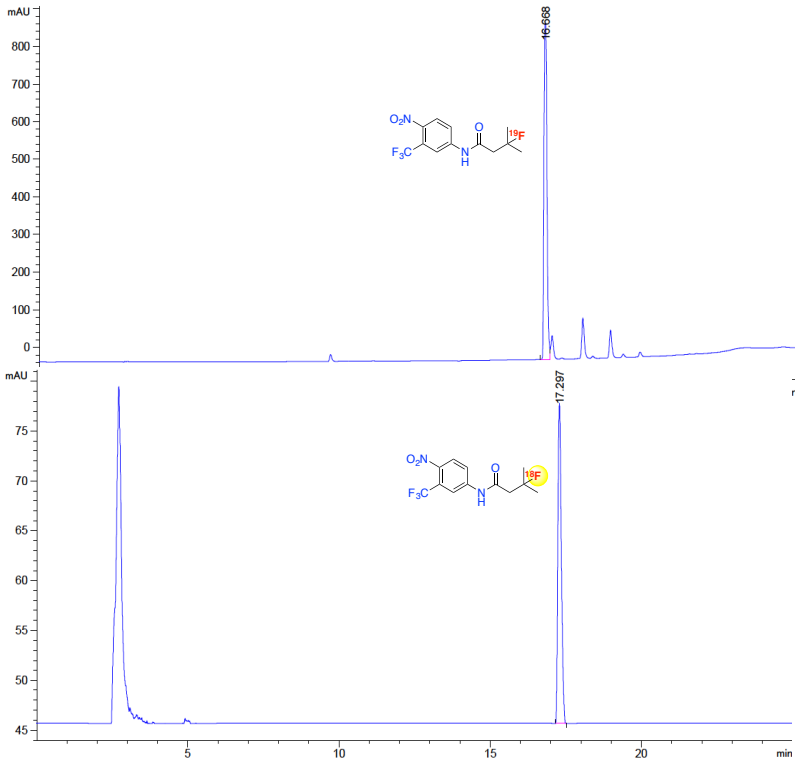


Figure S4h UV and radio-HPLC traces of F-flutamide analog.

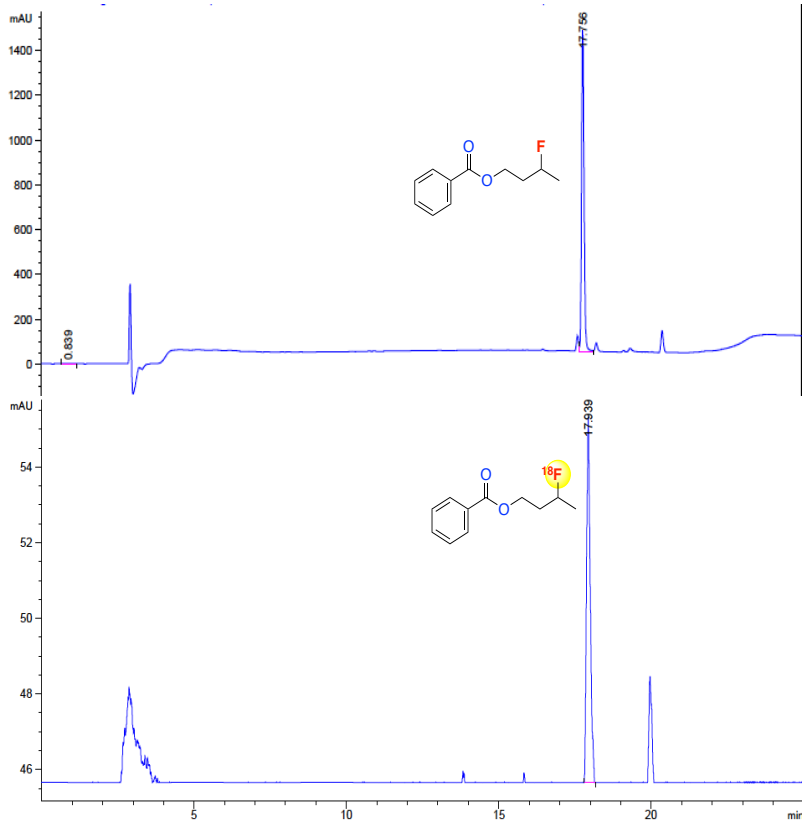


Figure S4i UV and radio-HPLC traces of compound 2

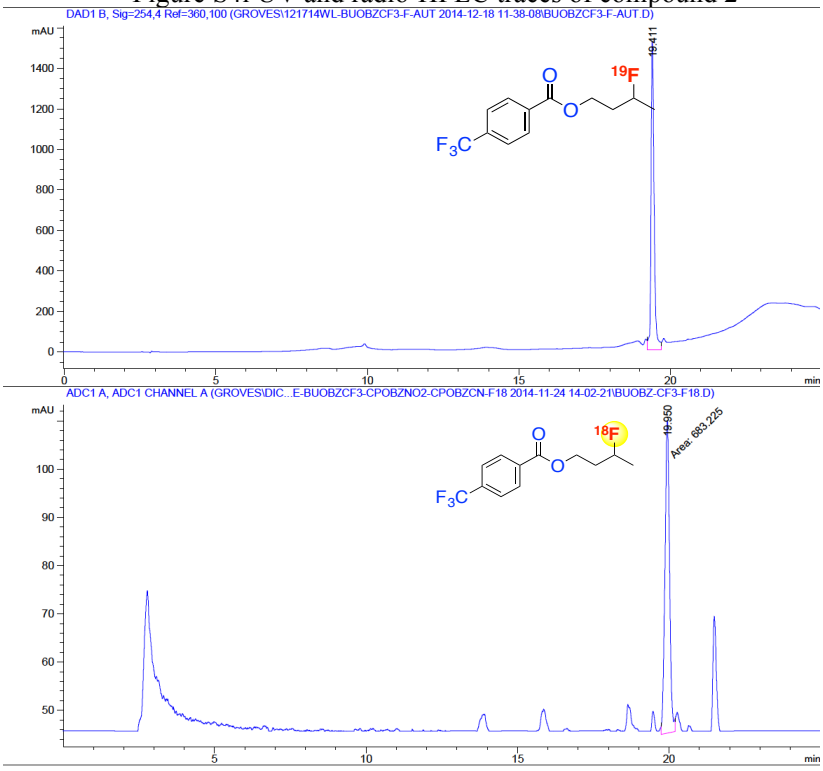


Figure S4j. UV and radio-HPLC traces of compound 3

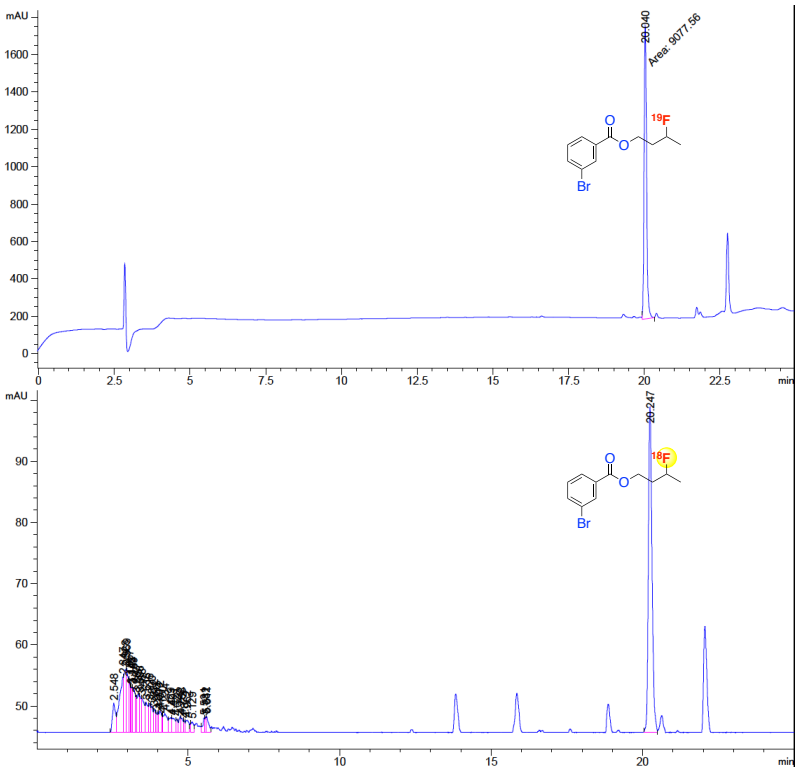


Figure S4k. UV and radio-HPLC traces of compound 4

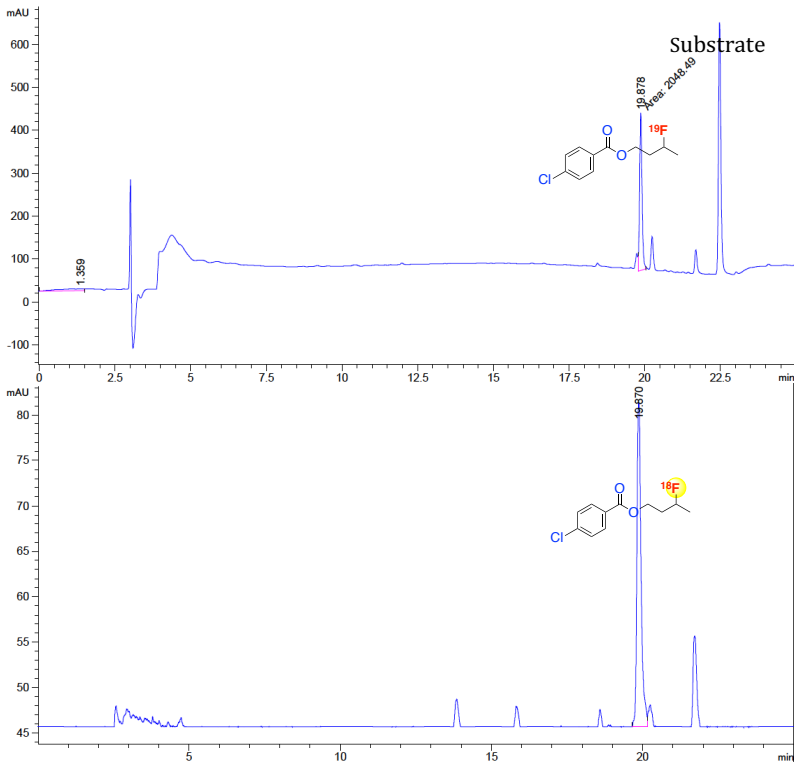


Figure S4l. UV and radio-HPLC traces of compound 5

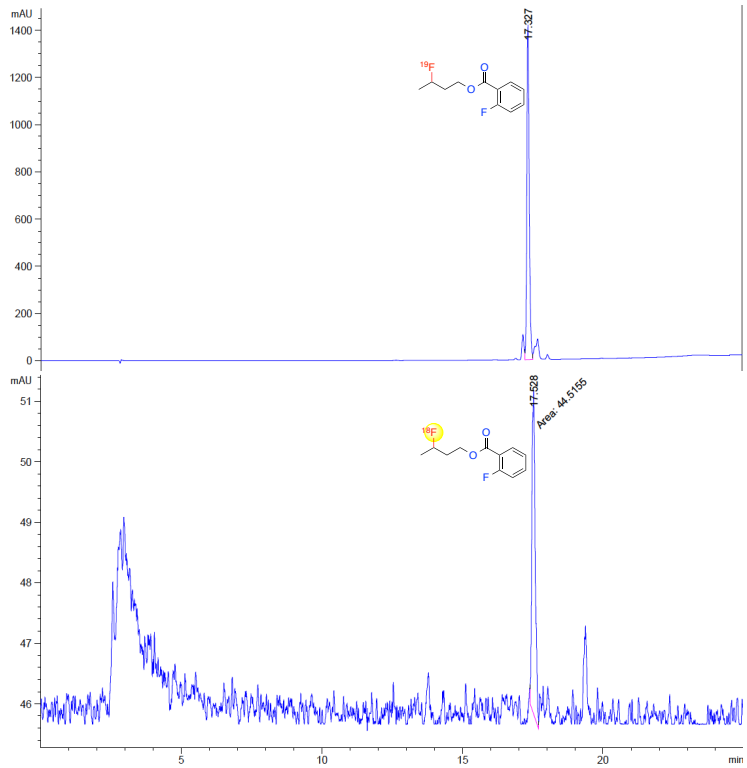


Figure S4m. UV and radio-HPLC traces of compound 6

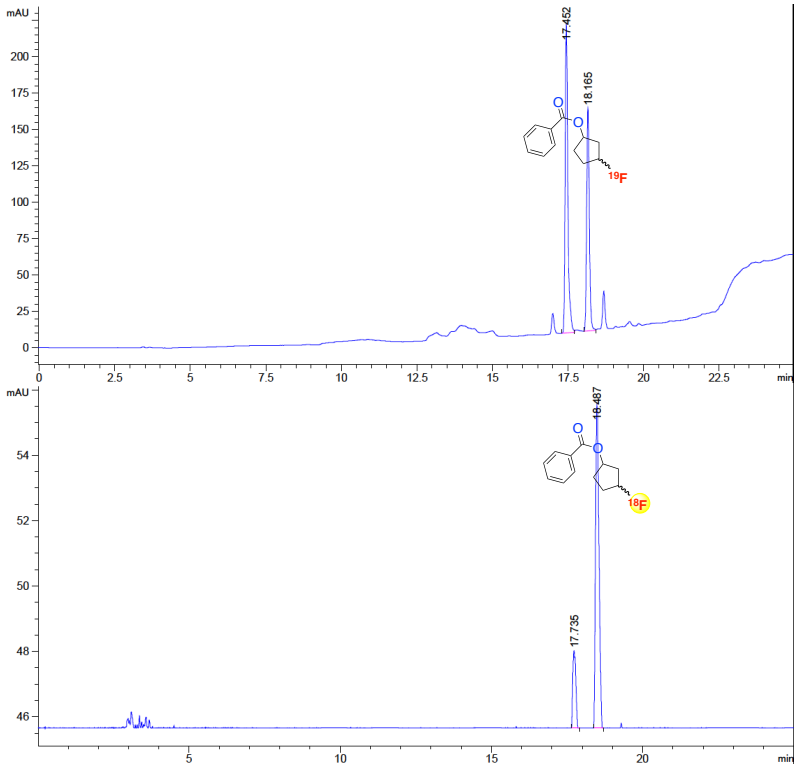


Figure S4m. UV and radio-HPLC traces of compound 7

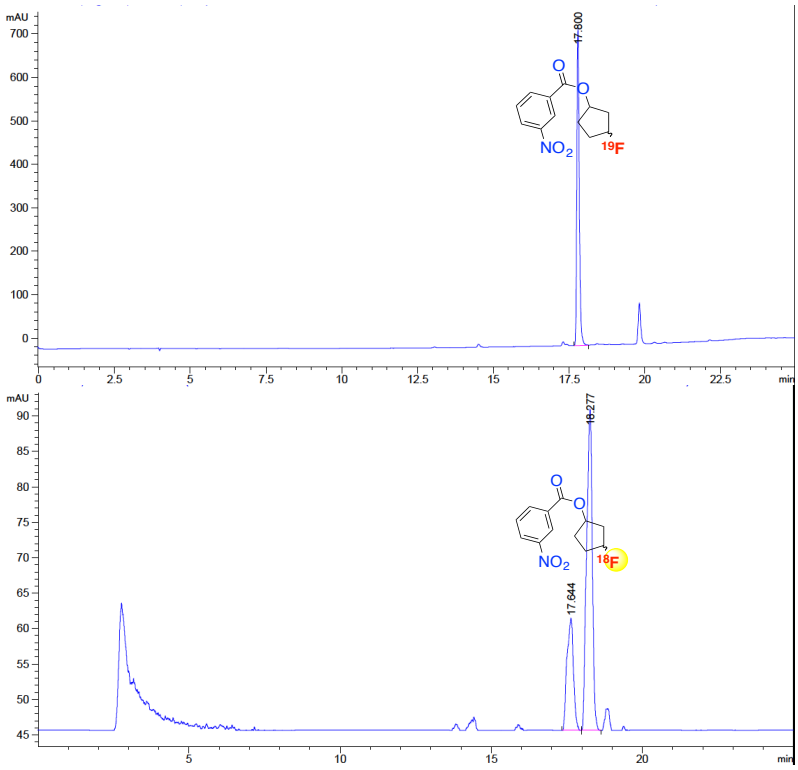


Figure S4n. UV and radio-HPLC traces of compound 8

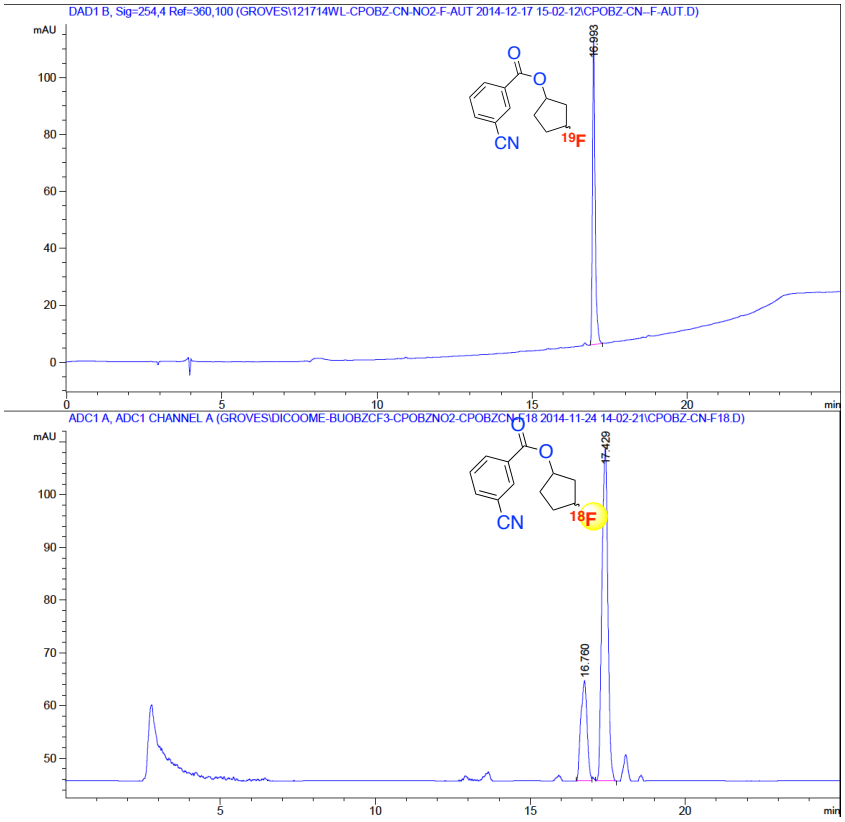


Figure S4o. UV and radio-HPLC traces of compound 9

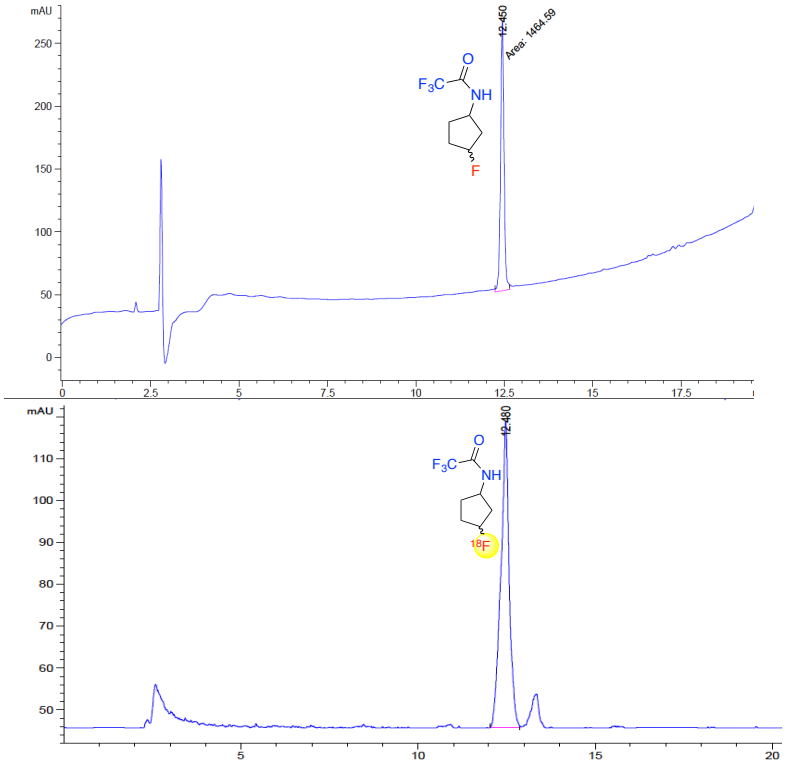


Figure S4p. UV and radio-HPLC traces of compound 10

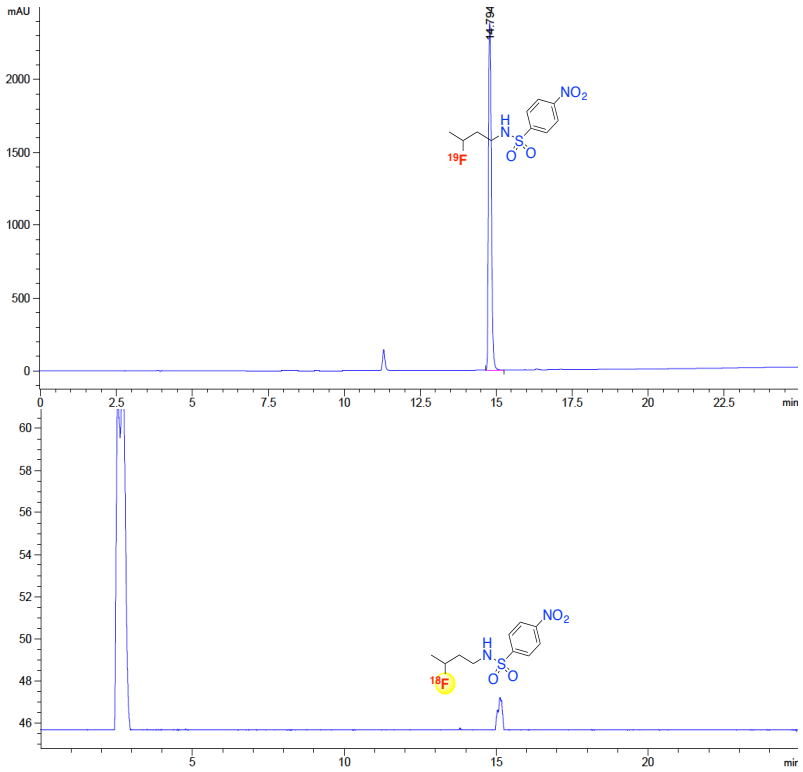


Figure S4q. UV and radio-HPLC traces of compound 11

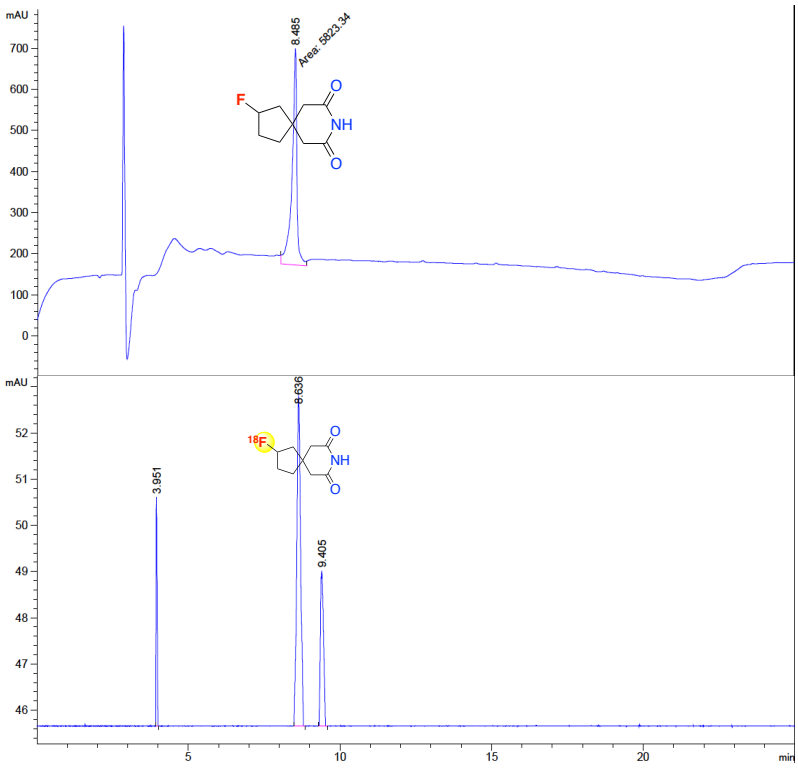


Figure S4r. UV and radio-HPLC traces of compound 12

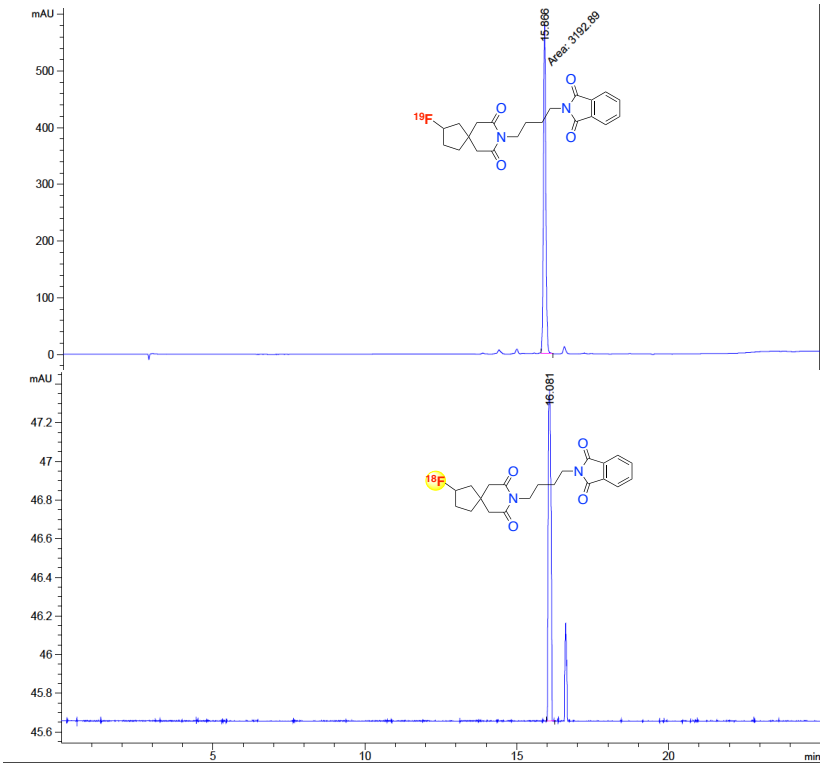


Figure S4s. UV and radio-HPLC traces of compound 13

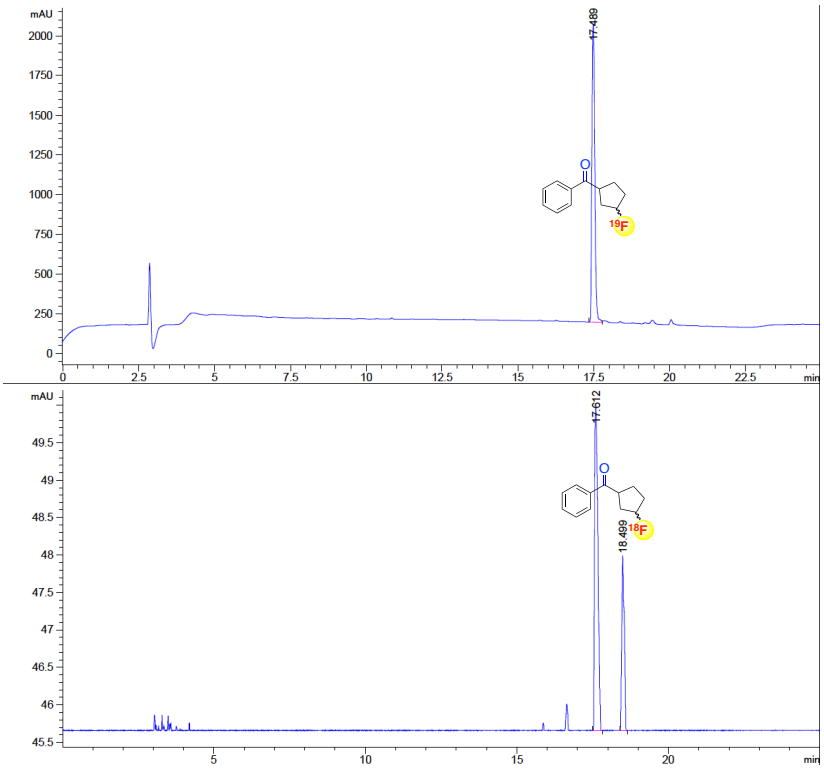


Figure S4t. UV and radio-HPLC traces of compound 14

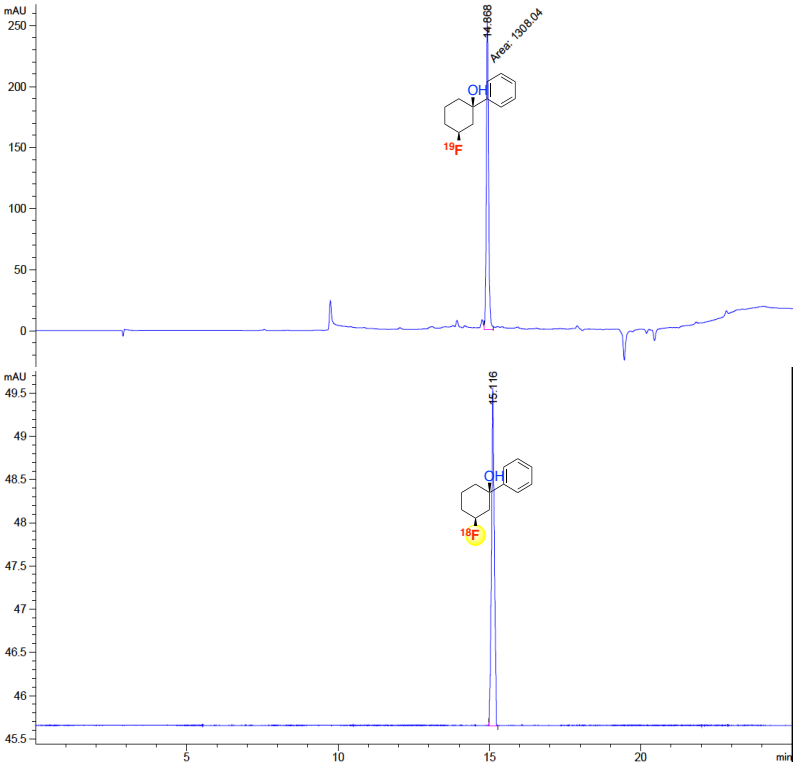


Figure S4u. UV and radio-HPLC traces of compound 15

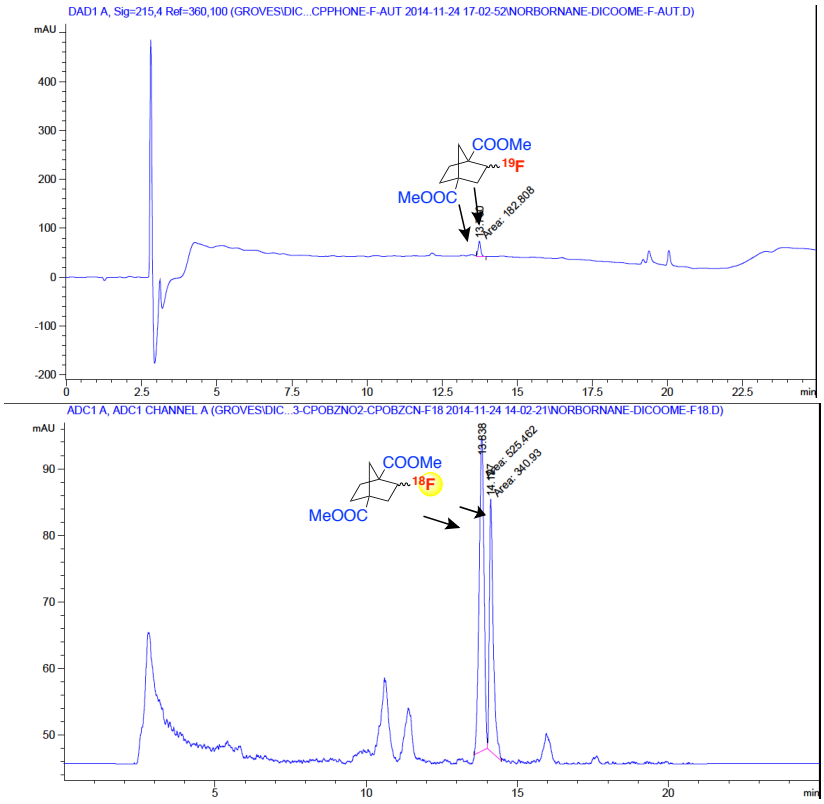


Figure S4v. UV and radio-HPLC traces of compound 16

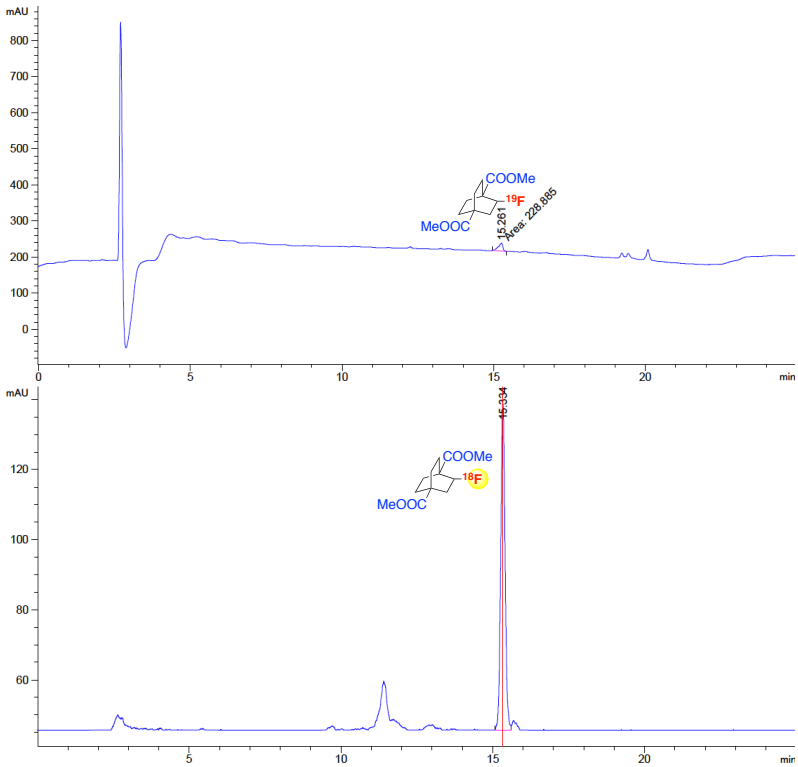


Figure S4w. UV and radio-HPLC traces of compound 17

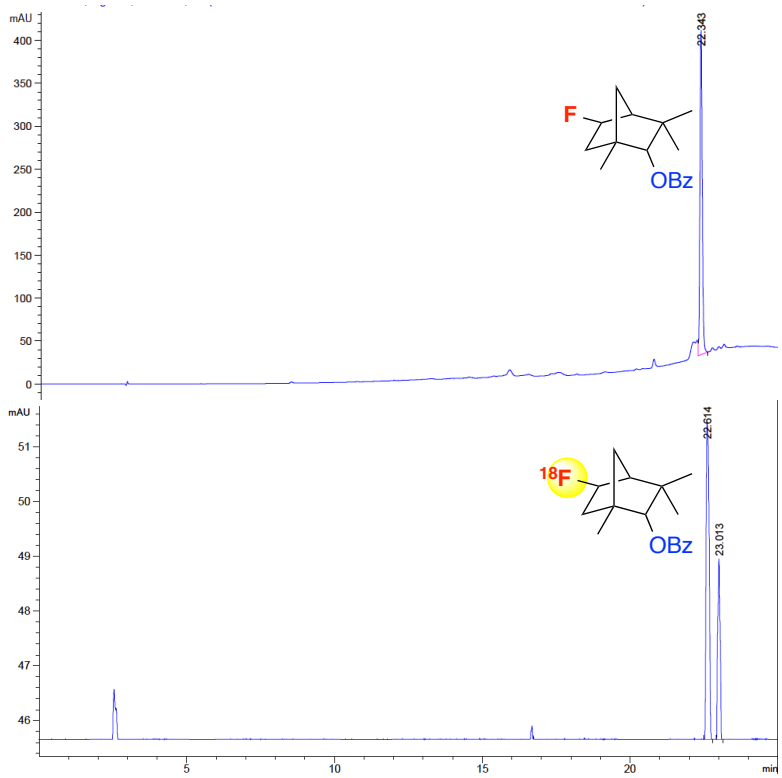


Figure S4w. UV and radio-HPLC traces of compound 18

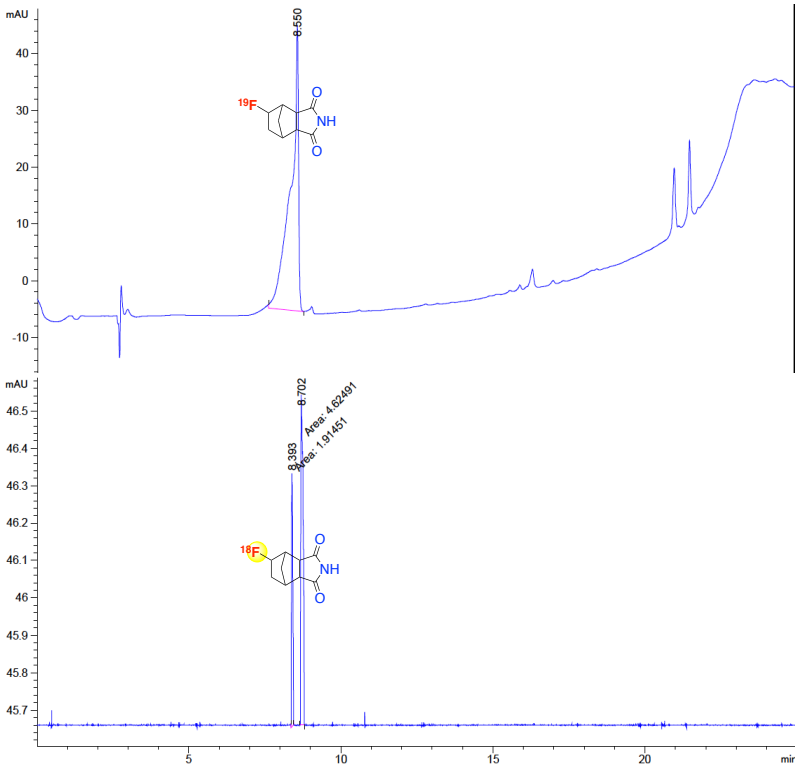


Figure S4w. UV and radio-HPLC traces of compound 19

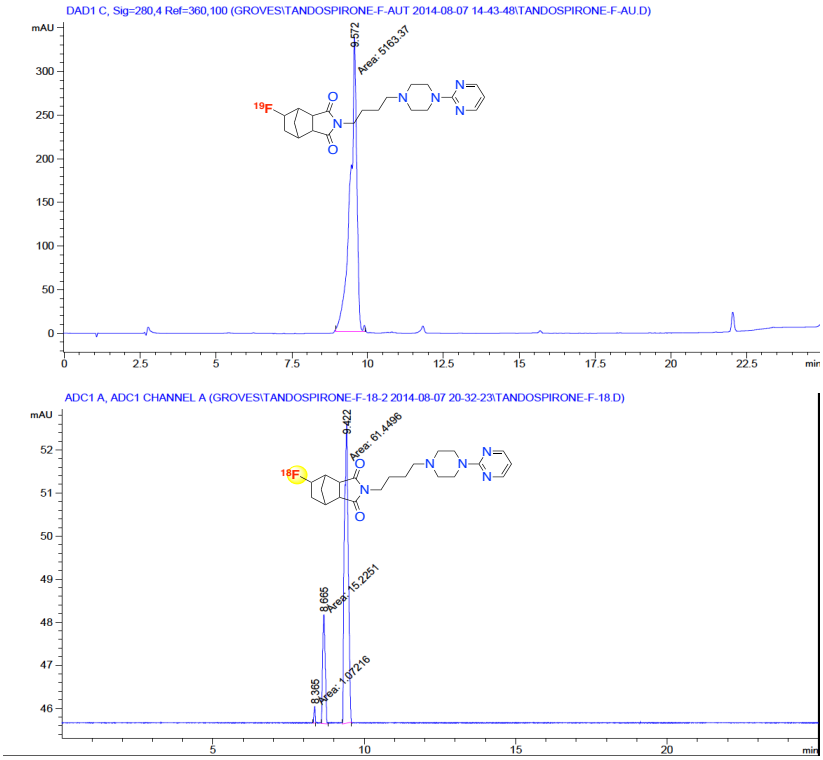
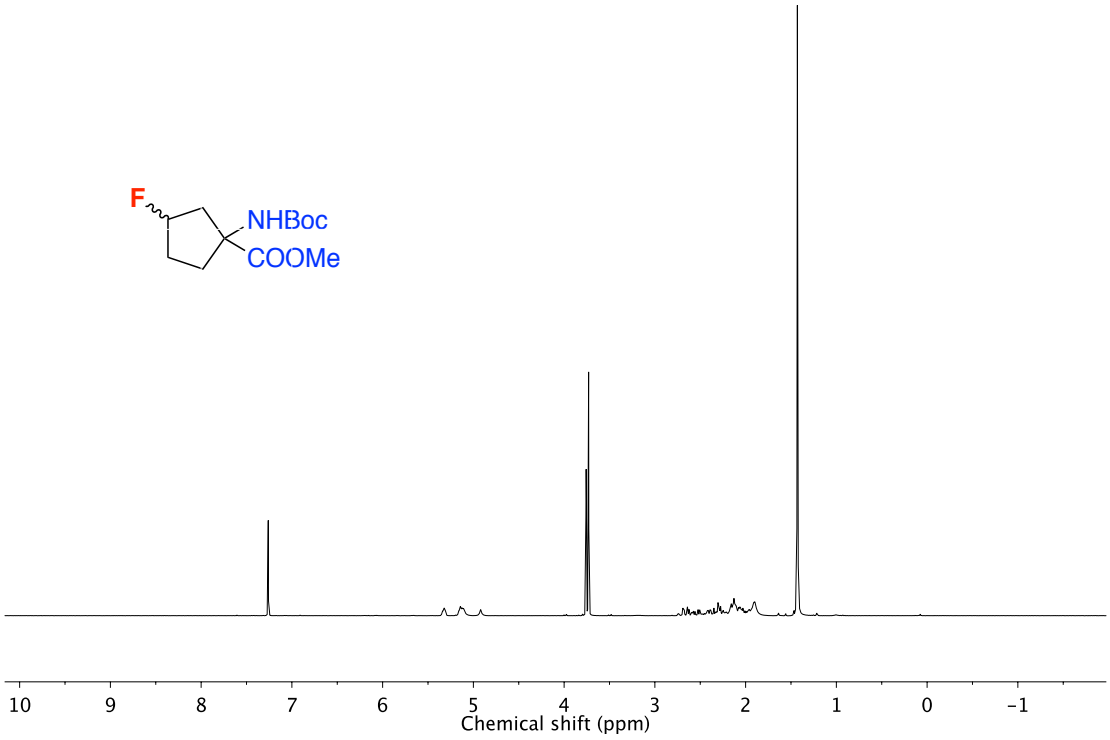
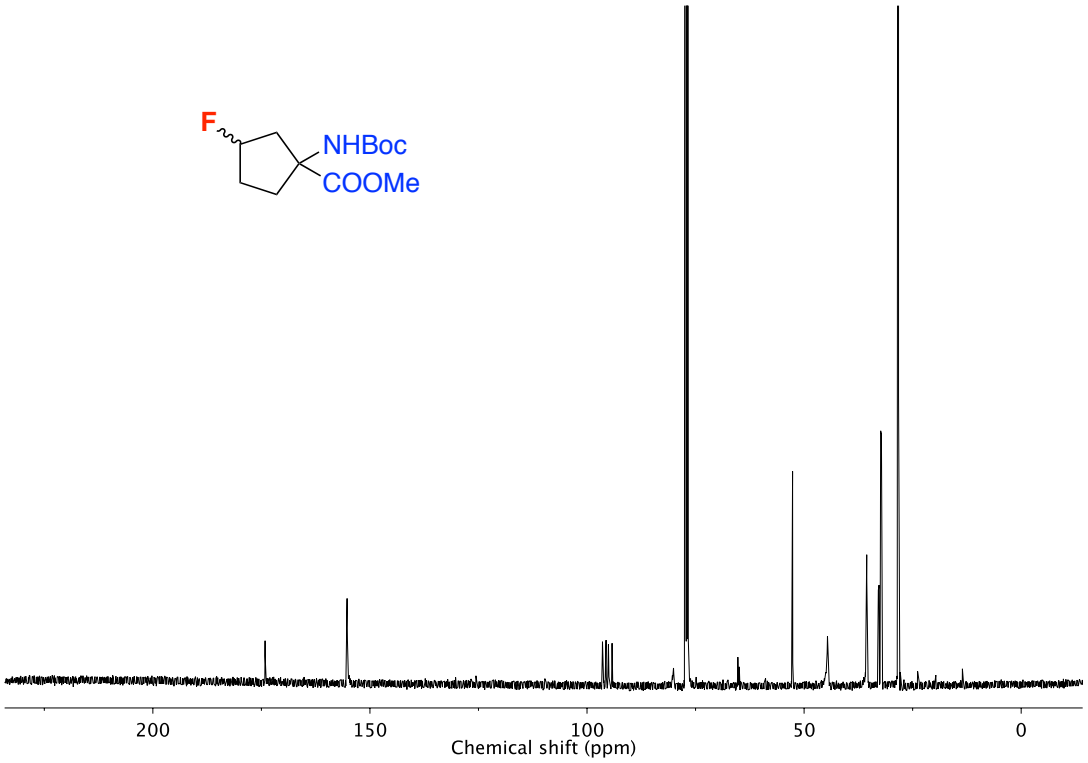
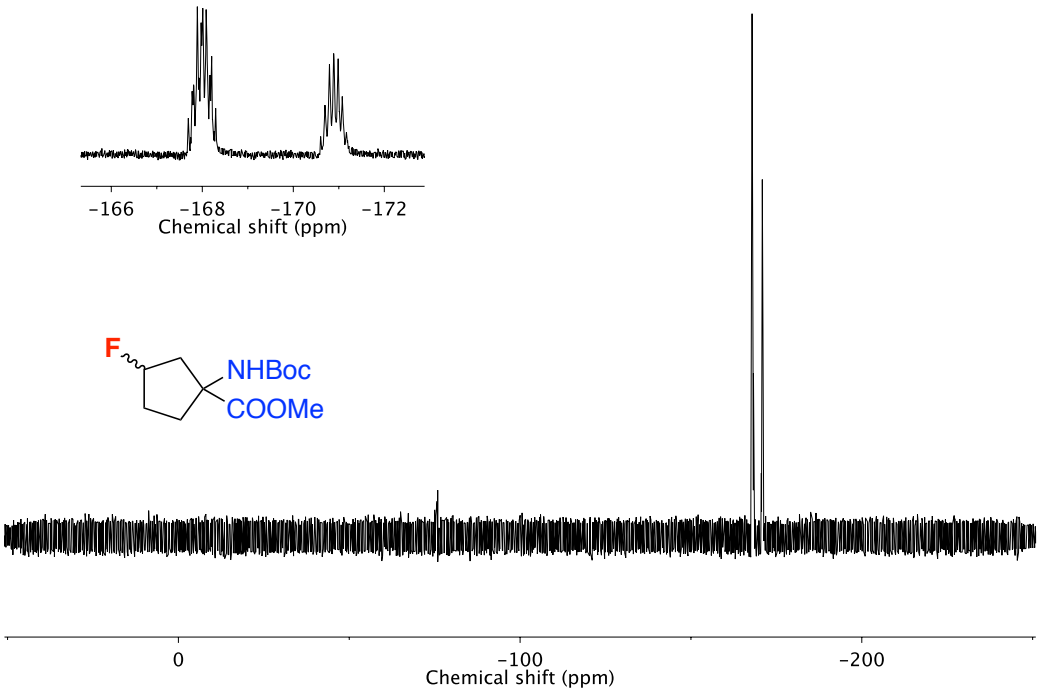
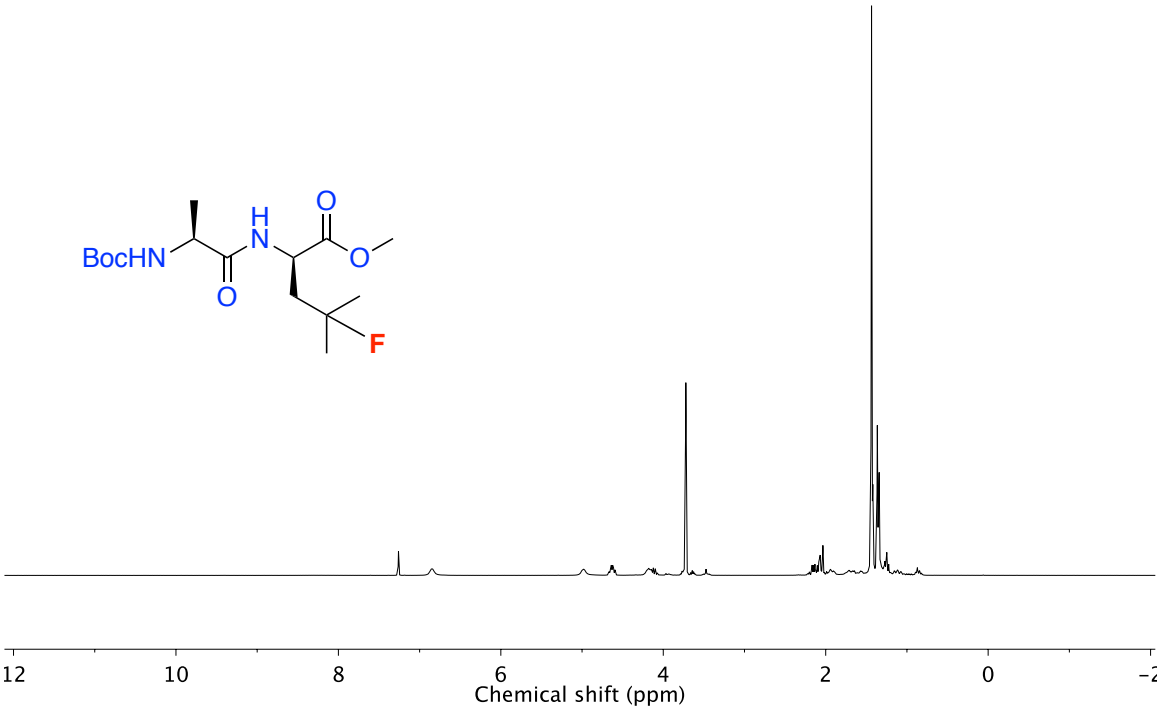


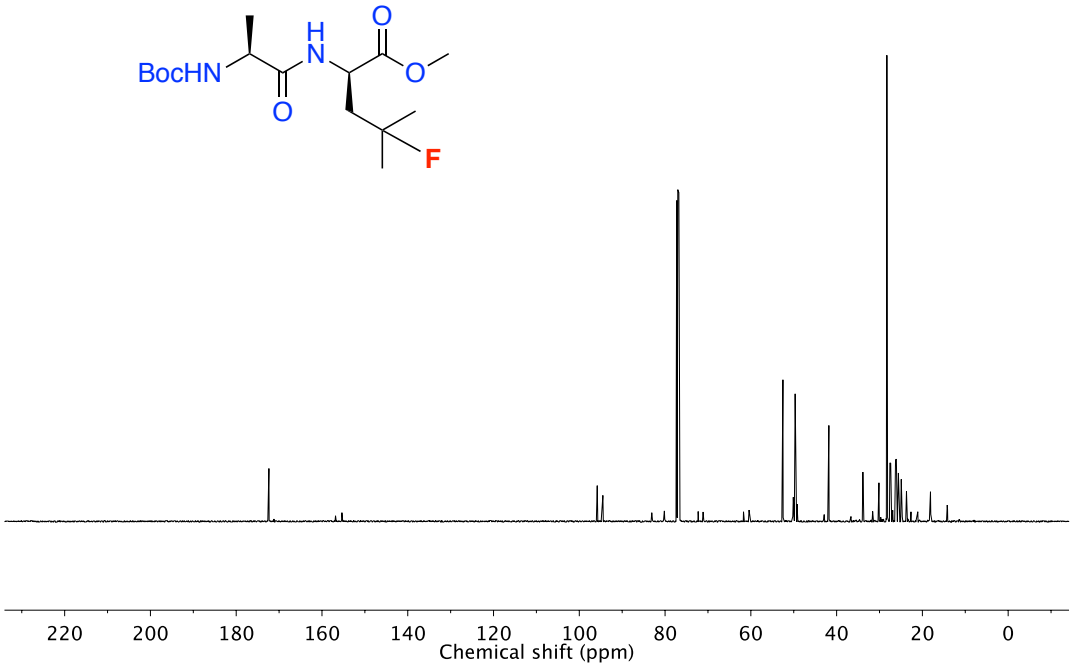
Figure S4x. UV and radio-HPLC traces of compound 20

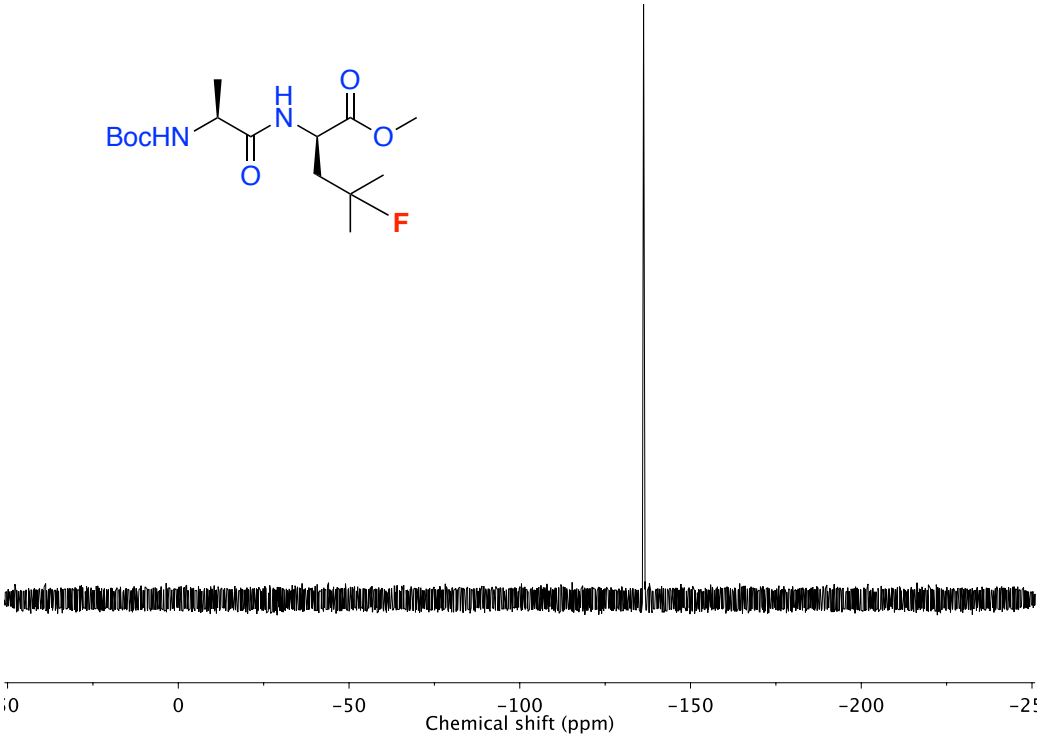


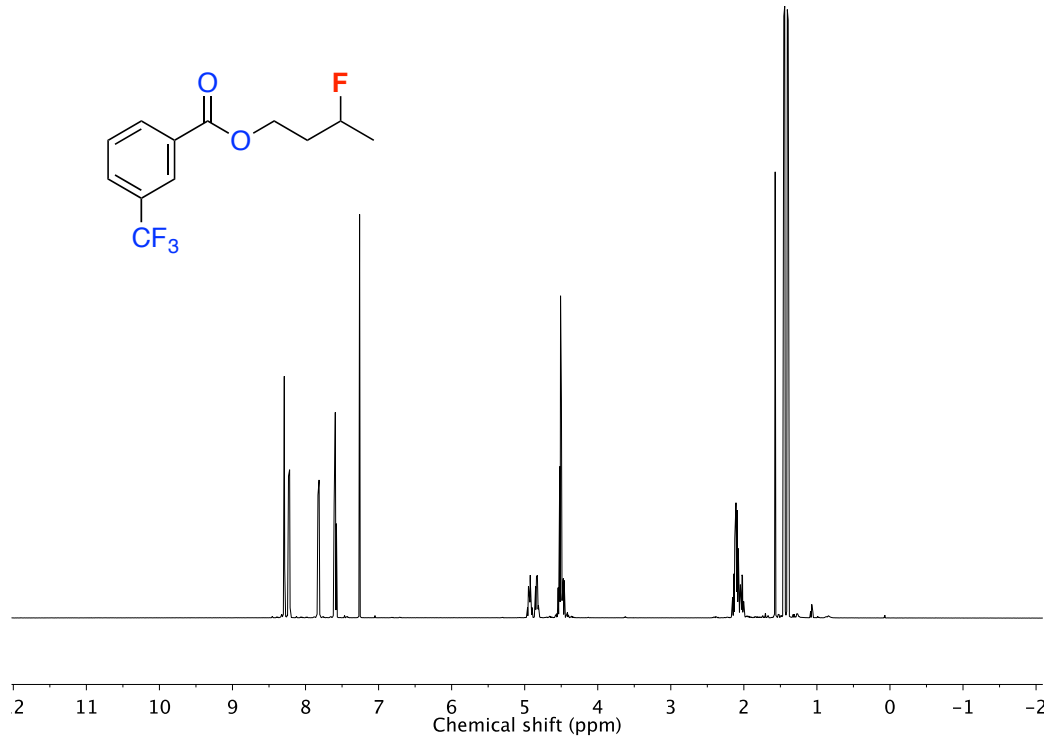

F
NHBoc
COOMe
200
150
100
50
0
Chemical shift (ppm)

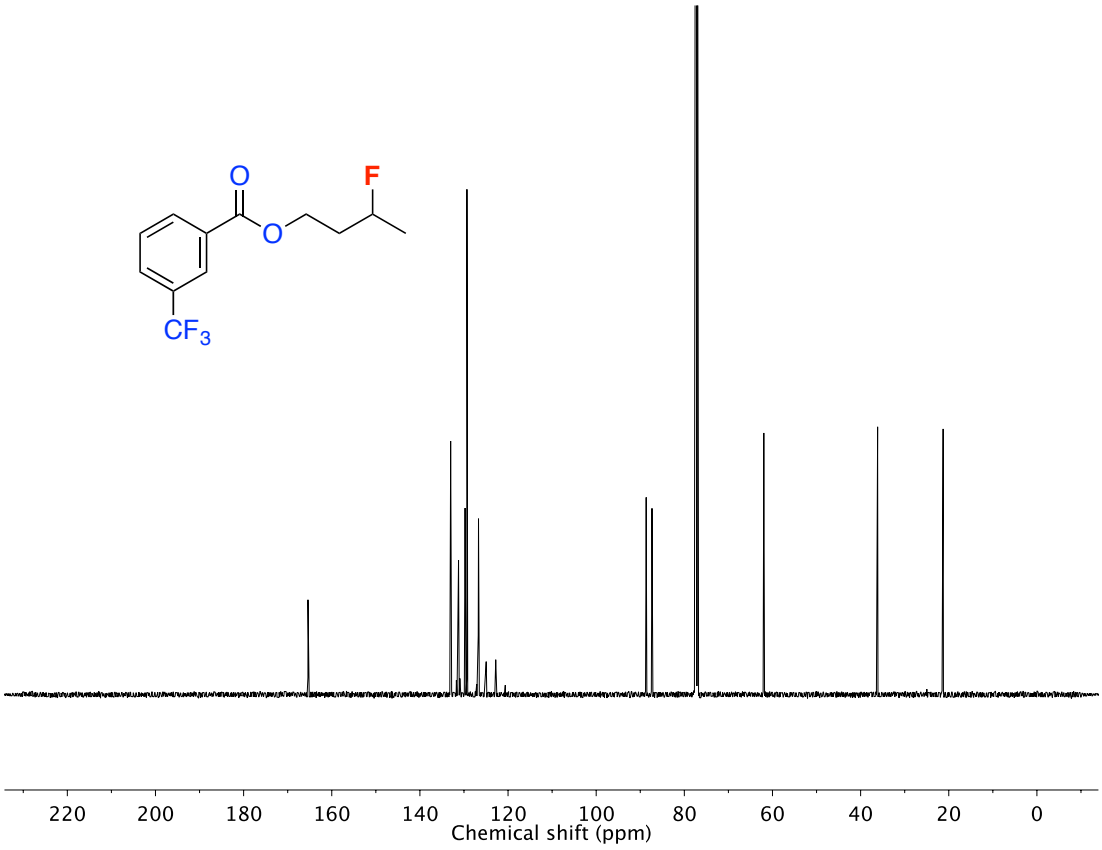

-166
-168
-170
-172
Chemical shift (ppm)
F
NHBoc
COOMe
0
-100
-200
Chemical shift (ppm)

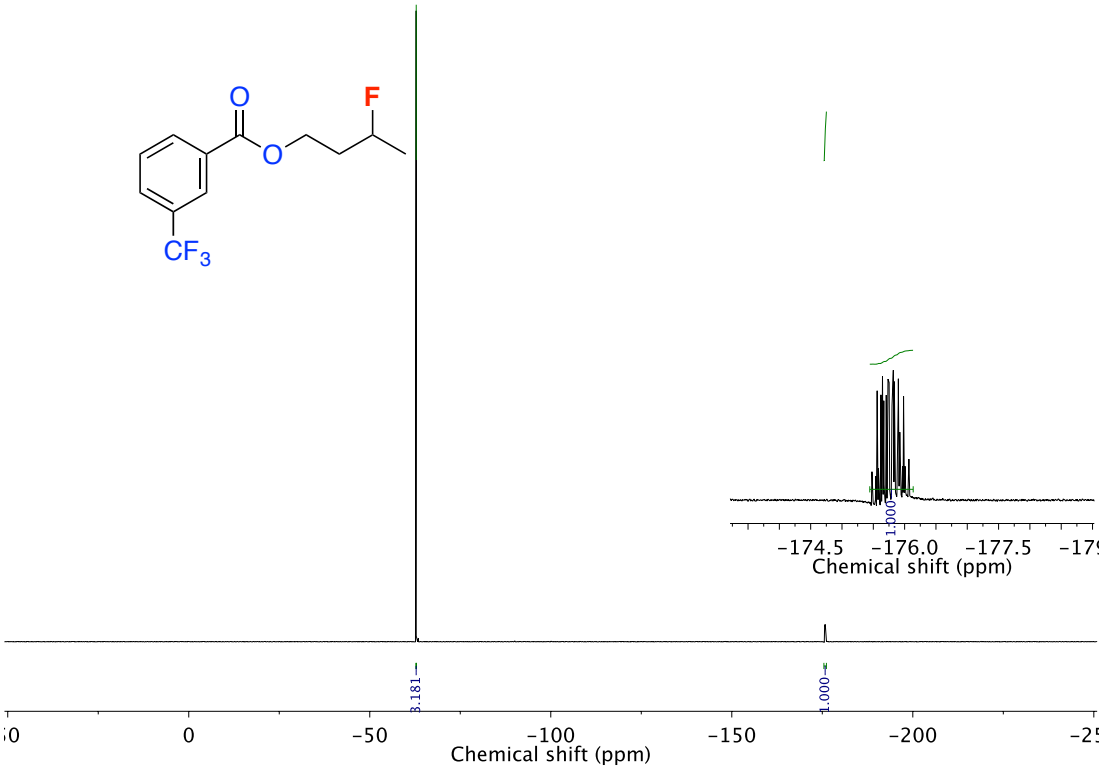

BocHN
H
N
O
O
O
F
12
10
8
6
4
2
0
Chemical shift (ppm)

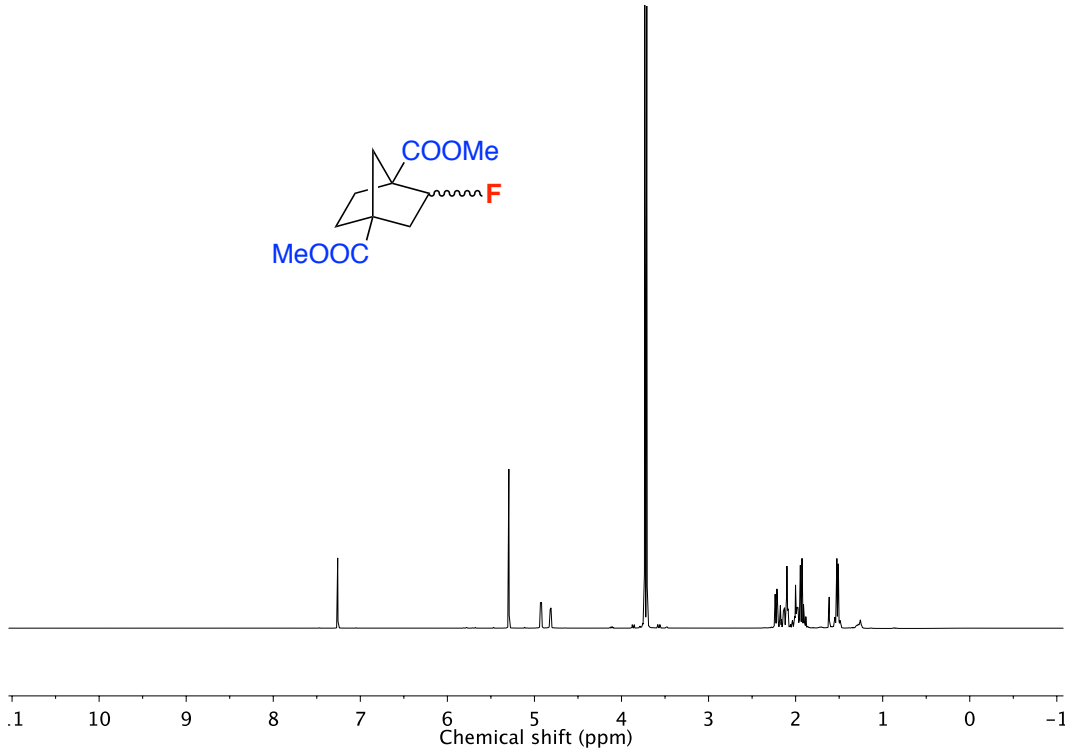

BocHN
H
N
O
O
O
F
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

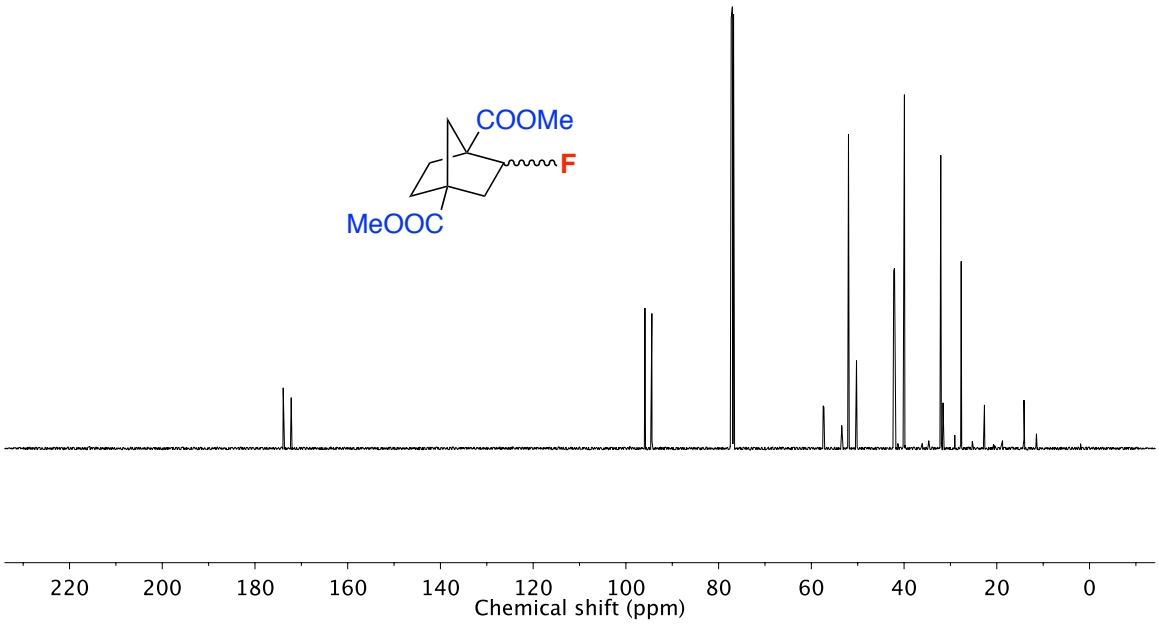

BocHN
H
N
O
O
O
F
0
-50
-100
-150
-200
Chemical shift (ppm)

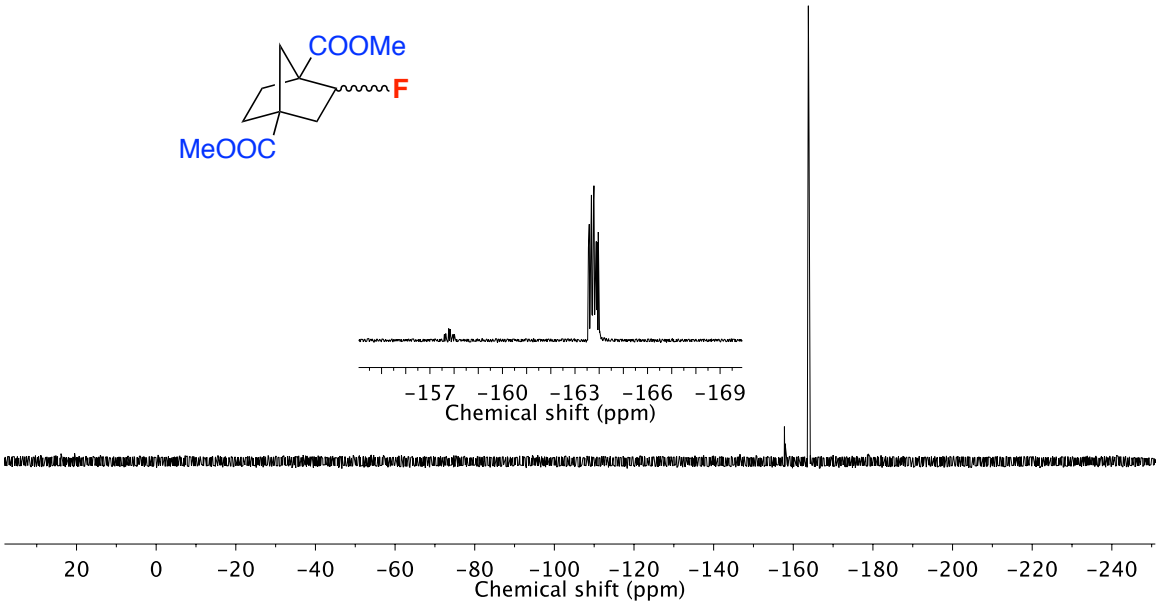

O
F
O
CF3
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

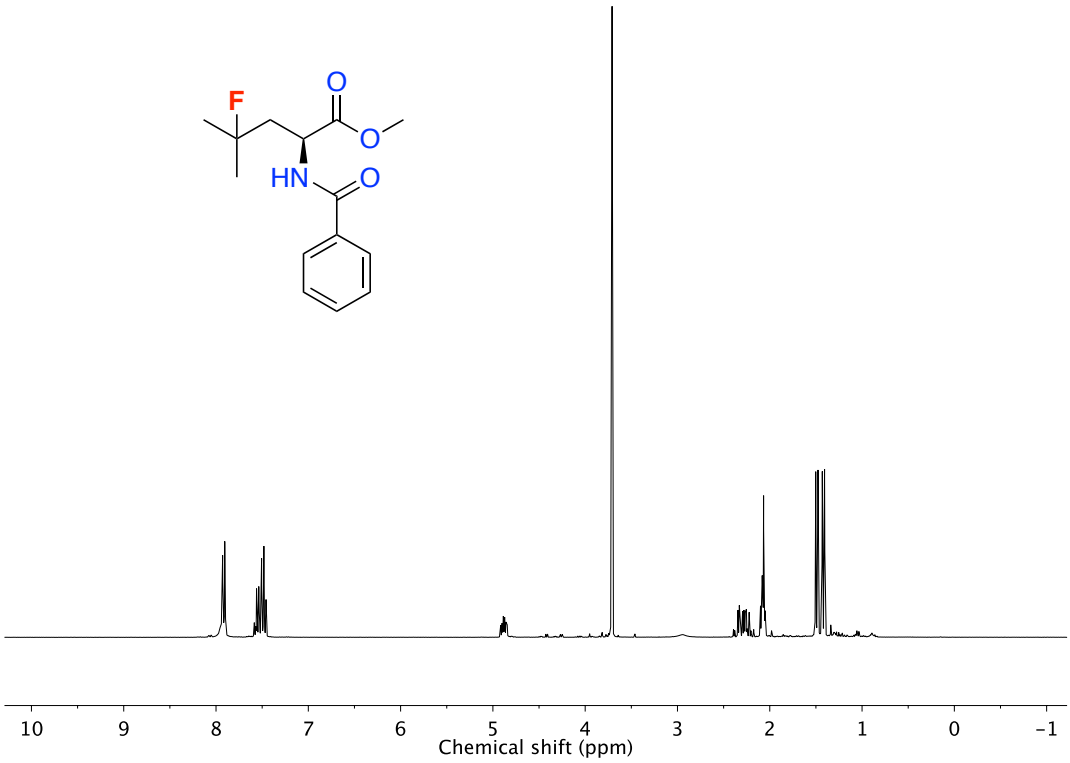

O
F
O
CF3
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

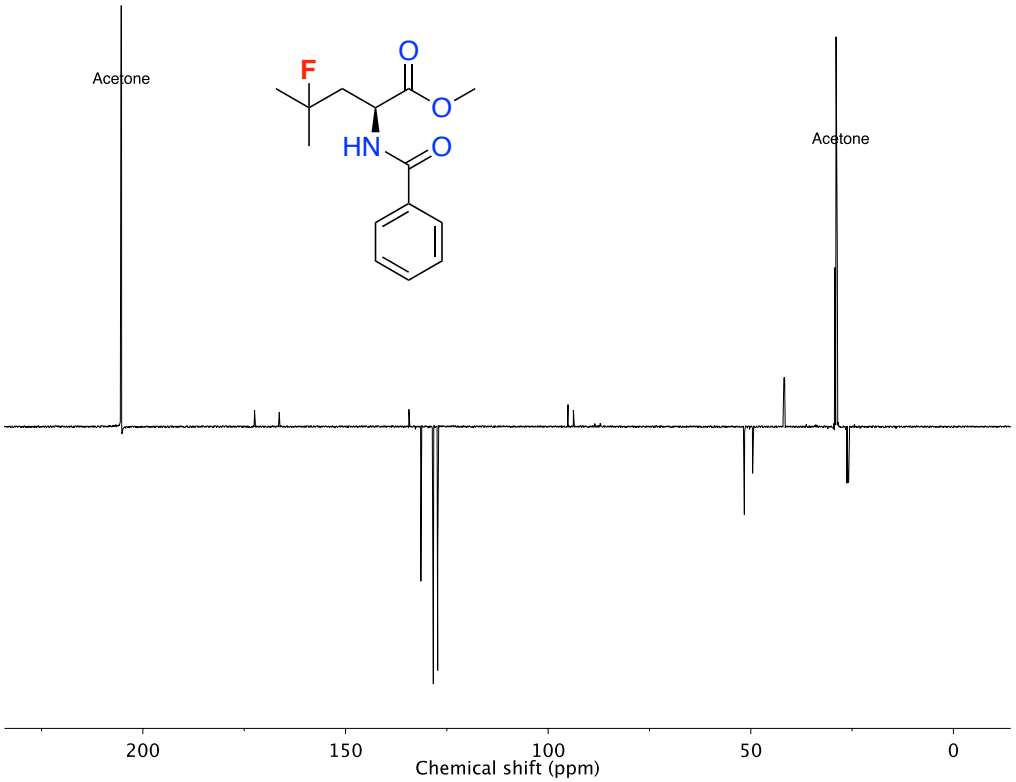

O
F
O
CF3
1.000
-174.5
-176.0
-177.5
Chemical shift (ppm)
3.181
1.000
0
-50
-100
-150
-200
Chemical shift (ppm)

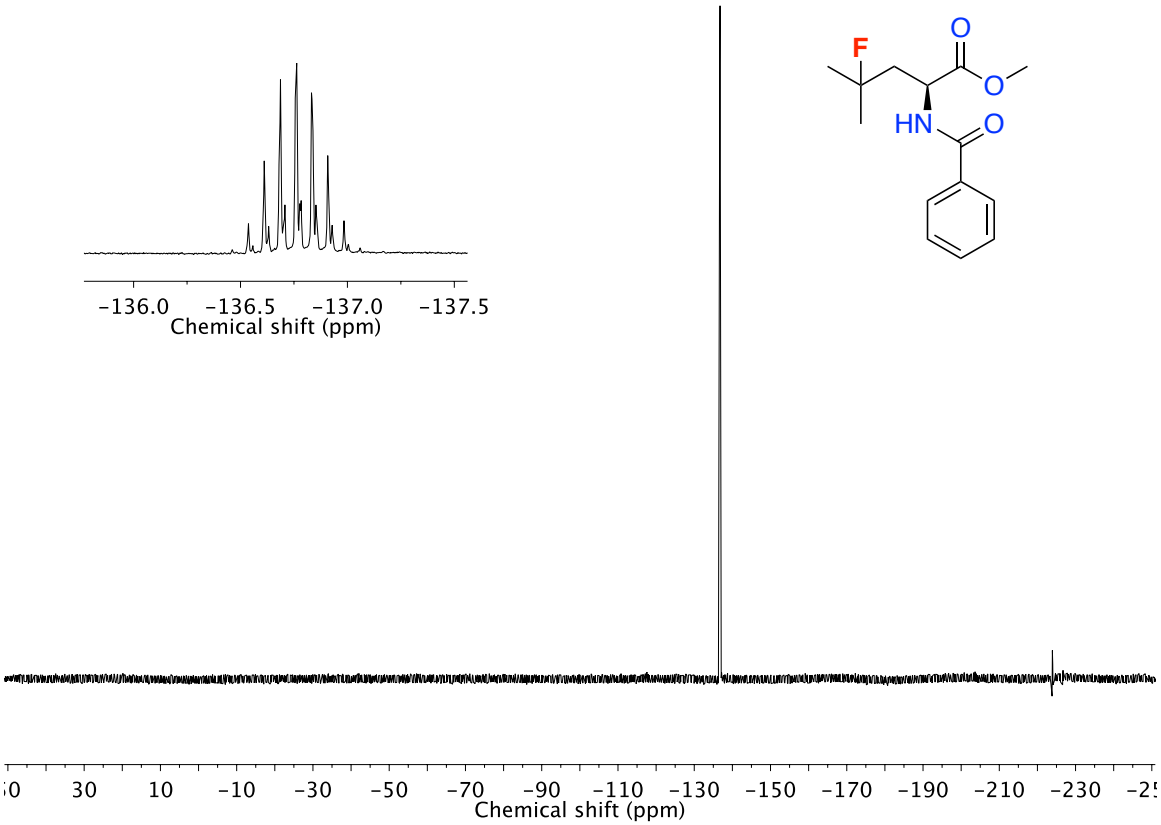

COOMe
F
MeOOC
.1
10
9
8
7
6
5
4
3
2
1
0
−1
Chemical shift (ppm)

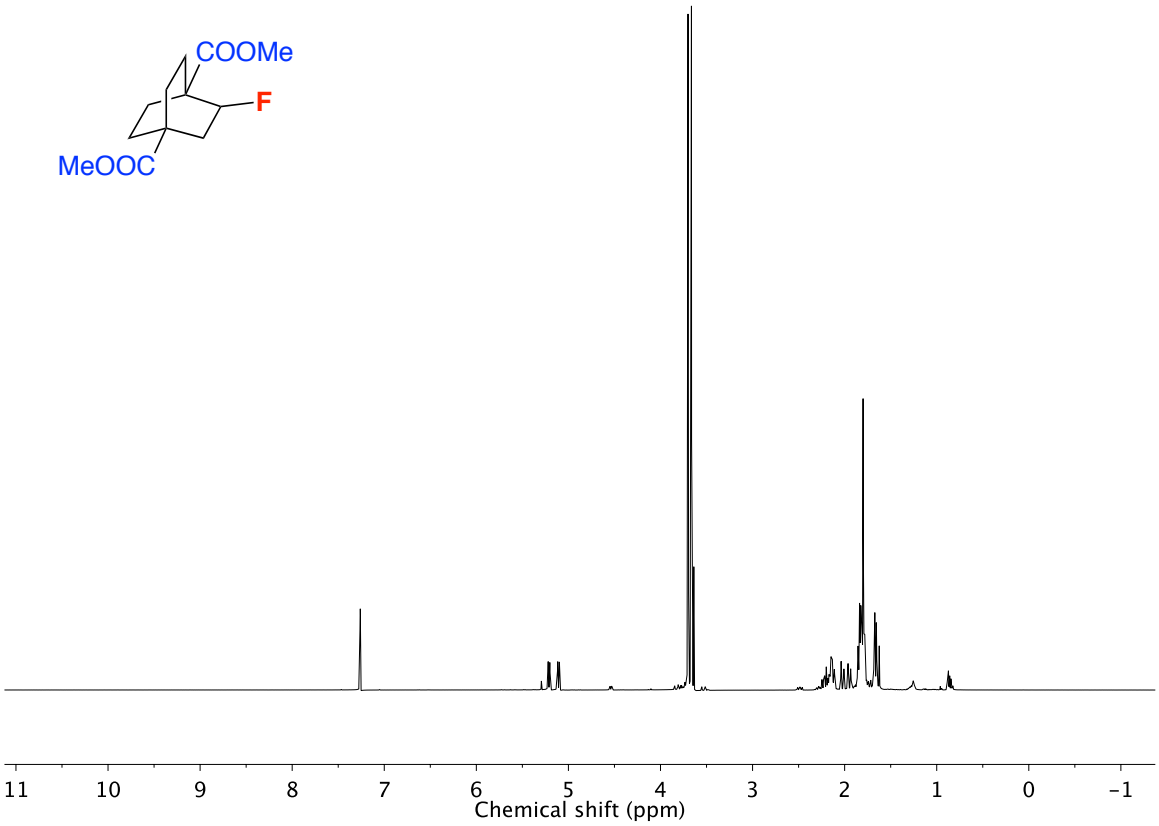

COOMe
F
MeOOC
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

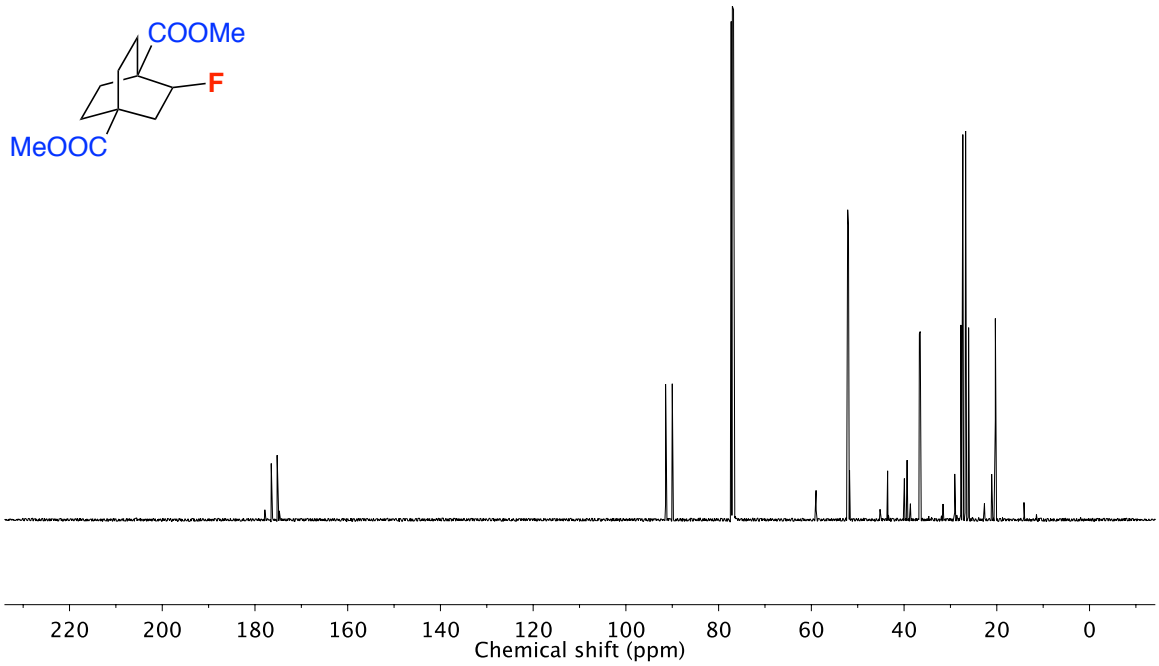

COOMe
F
MeOOC
-157 -160 -163 -166 -169
Chemical shift (ppm)
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
Chemical shift (ppm)

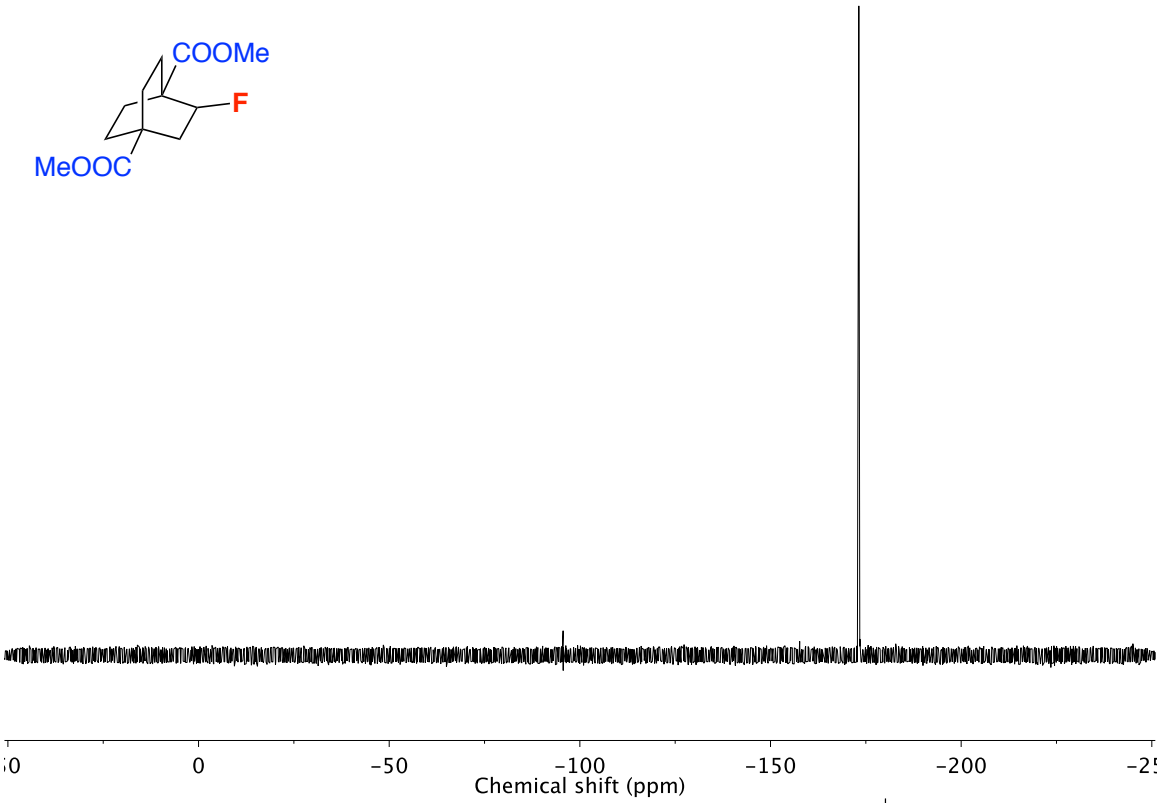

F
O
O
HN
O
10 9 8 7 6 5 4 3 2 1 0 -1
Chemical shift (ppm)

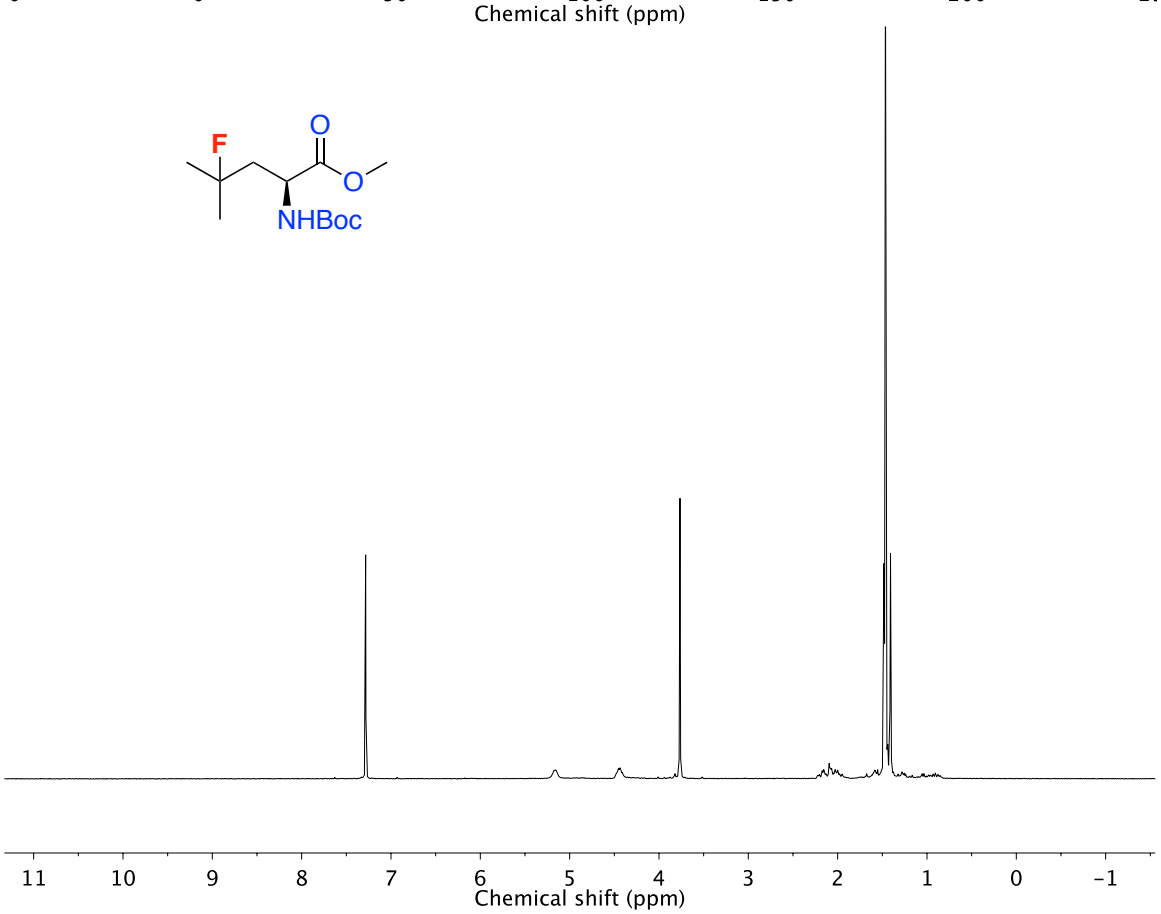

Acetone
F
O
O
HN
O
Acetone
200
150
100
50
0
Chemical shift (ppm)

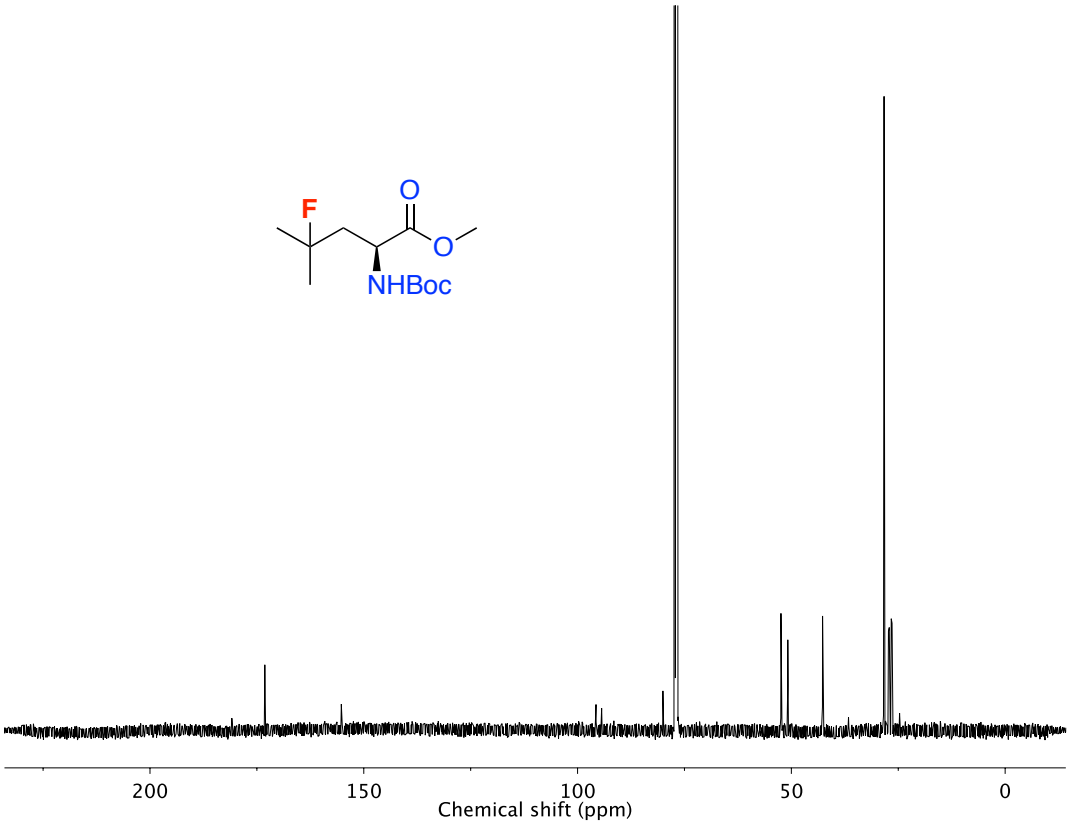

F
O
O
HN
O
−136.0
−136.5
−137.0
−137.5
Chemical shift (ppm)
30
10
−10
−30
−50
−70
−90
−110
−130
−150
−170
−190
−210
−230
Chemical shift (ppm)

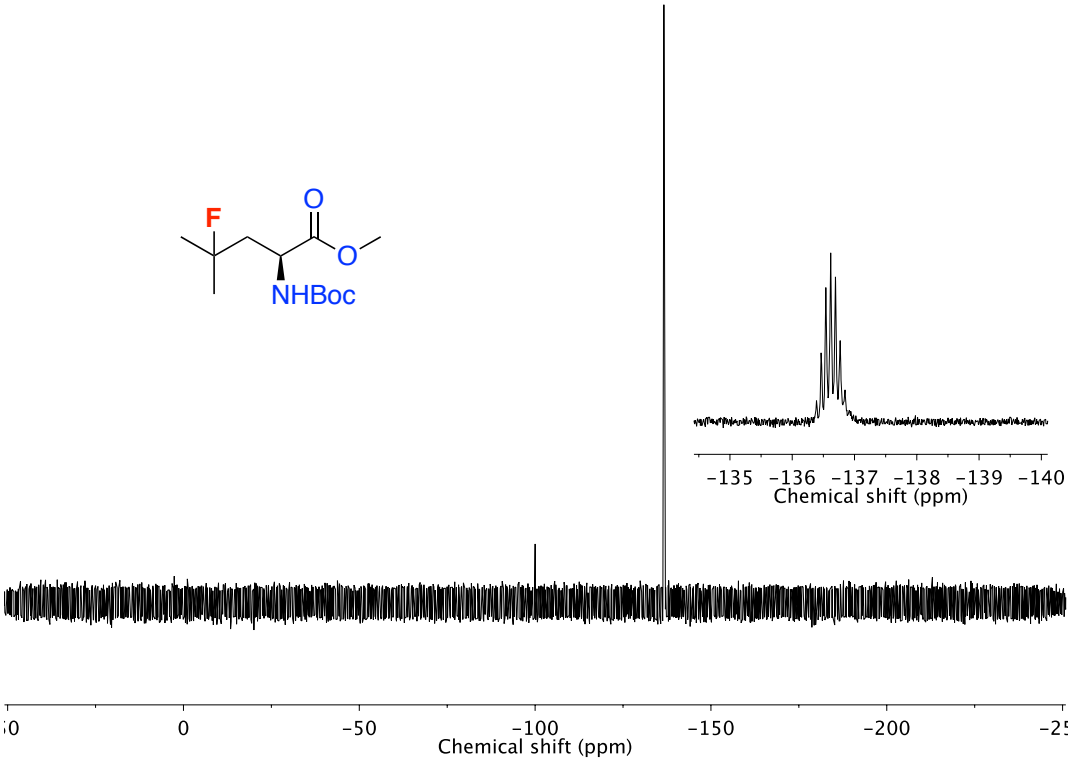

COOMe
F
MeOOC
11
10
9
8
7
6
5
4
3
2
1
0
−1
Chemical shift (ppm)

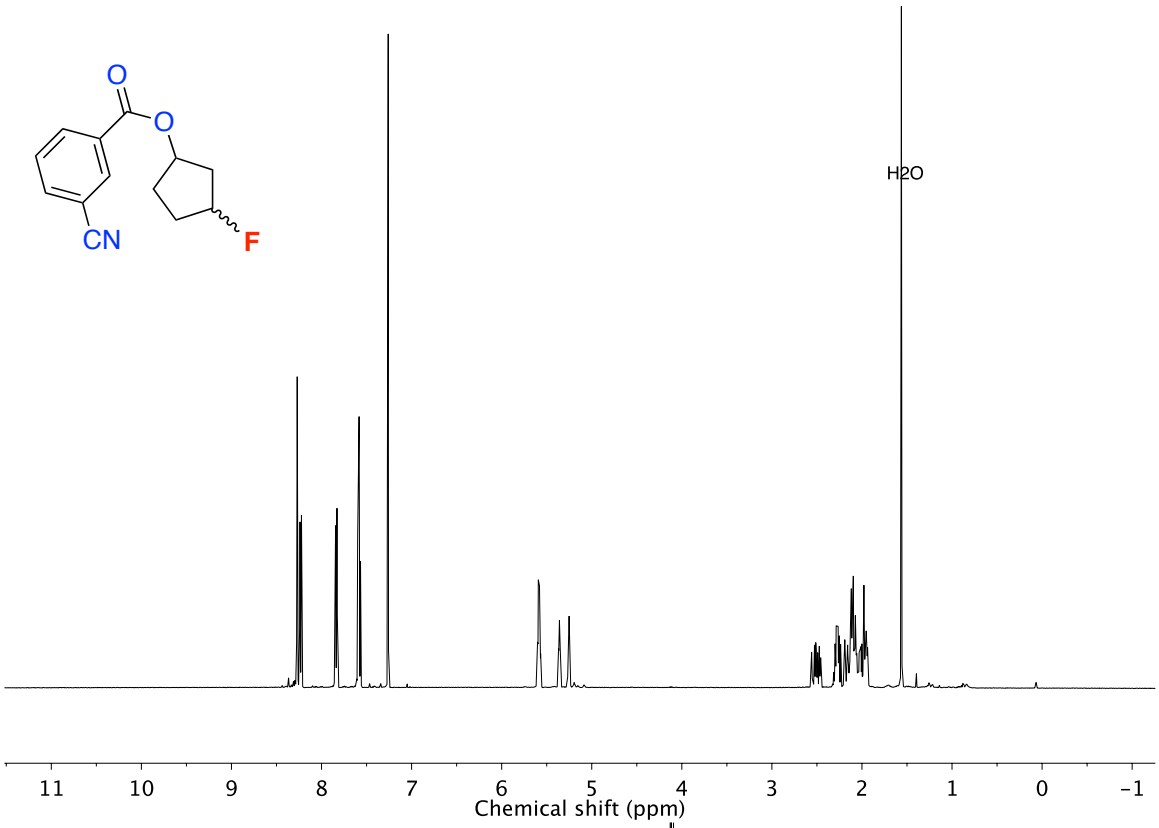

COOMe
F
MeOOC
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

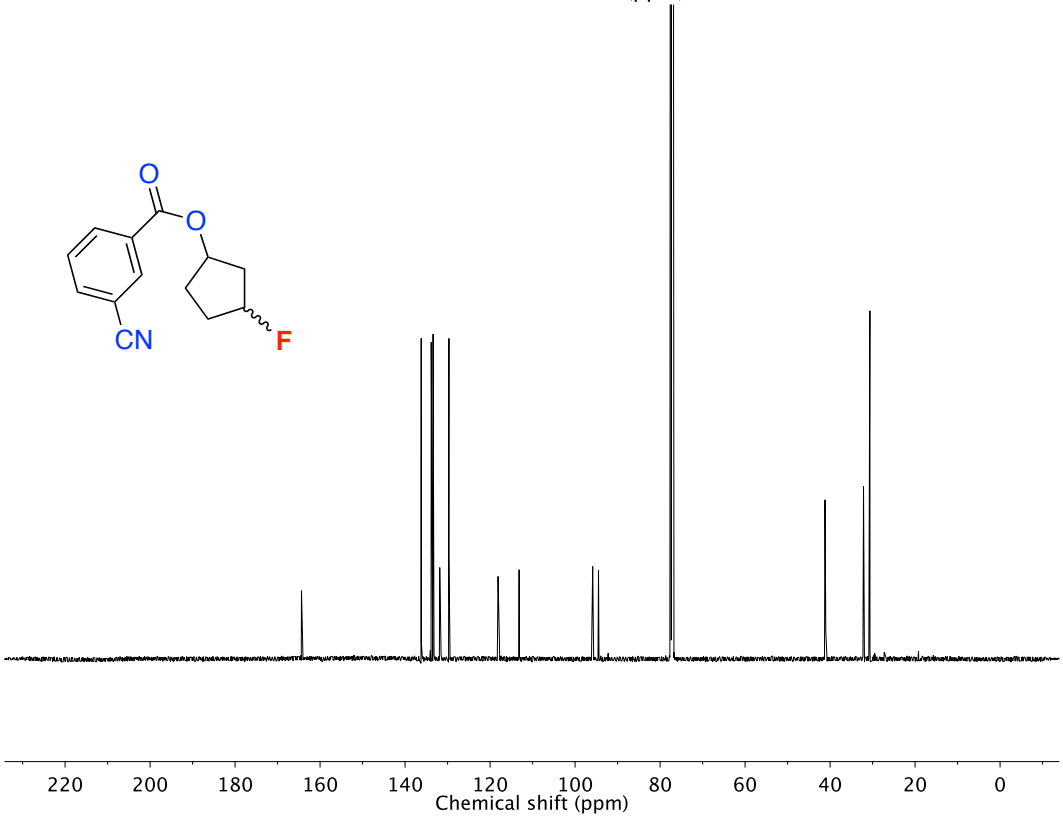

COOMe
F
MeOOC
0
-50
-100
-150
-200
Chemical shift (ppm)

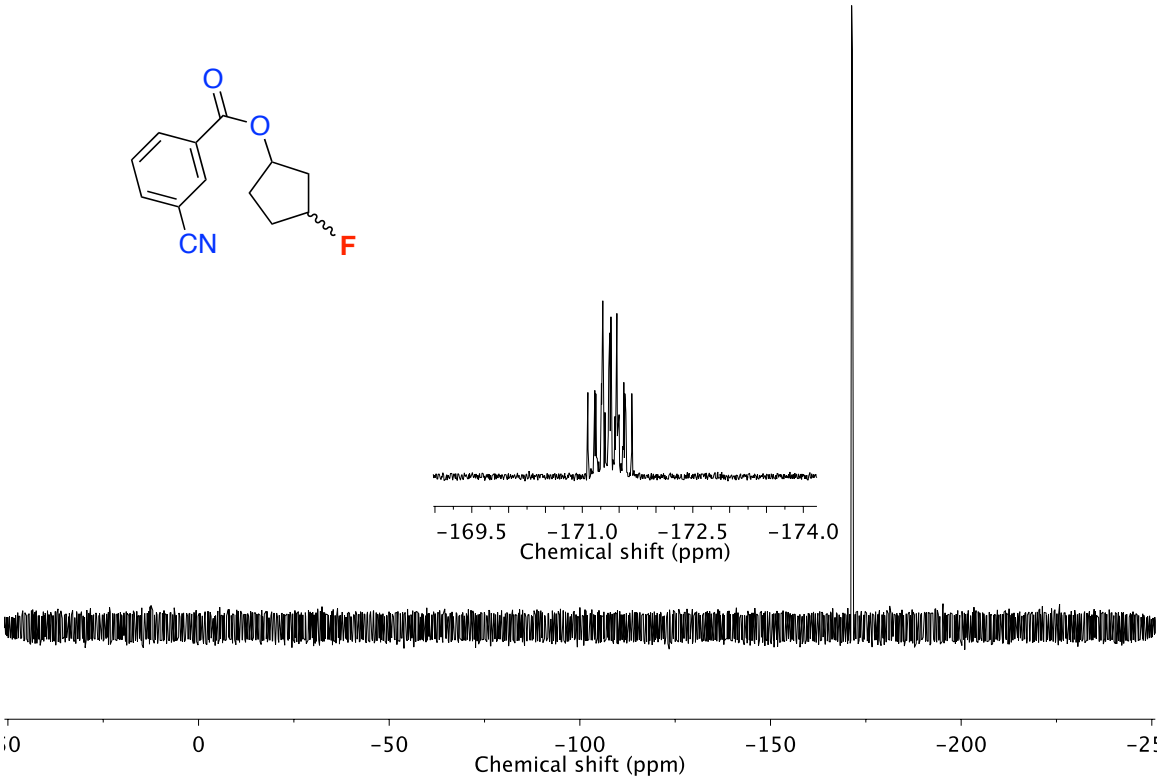

F
O
O
NHBoc
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

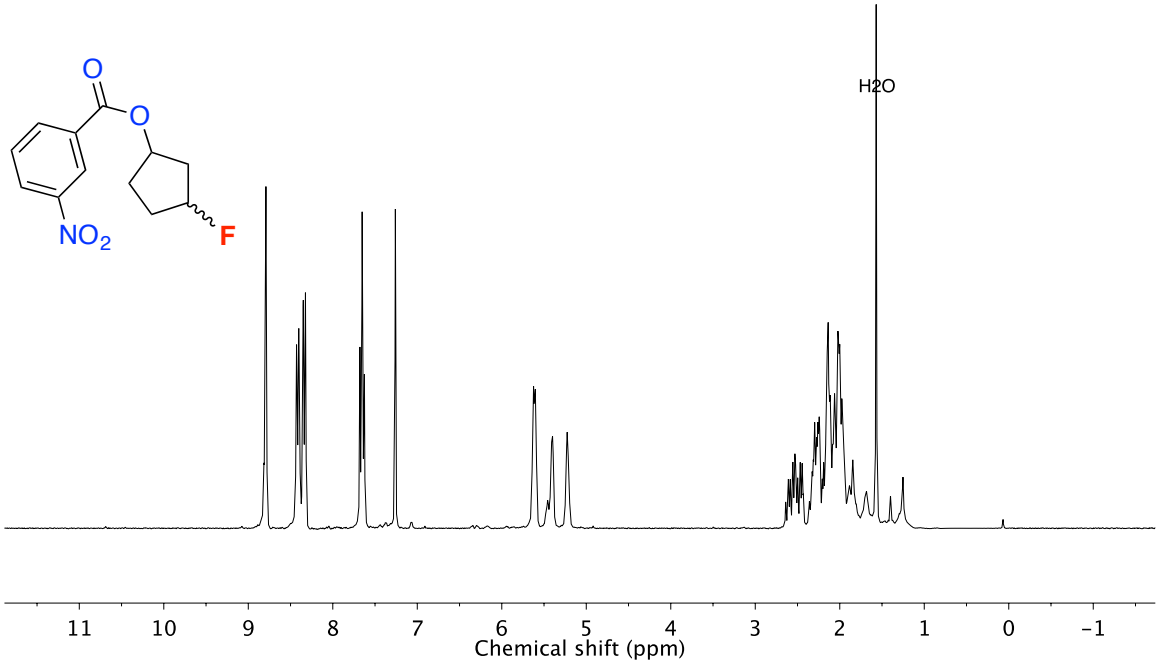

F
O
O
NHBoc
200
150
100
50
0
Chemical shift (ppm)

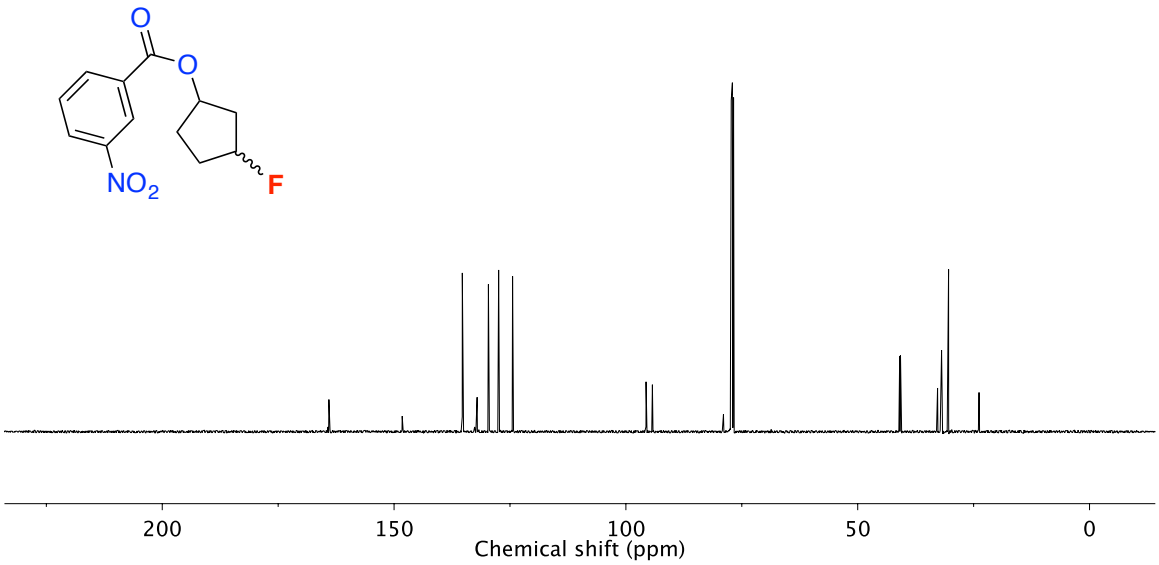

F
O
O
NHBoc
-135 -136 -137 -138 -139 -140
Chemical shift (ppm)
0
-50
-100
-150
-200
Chemical shift (ppm)

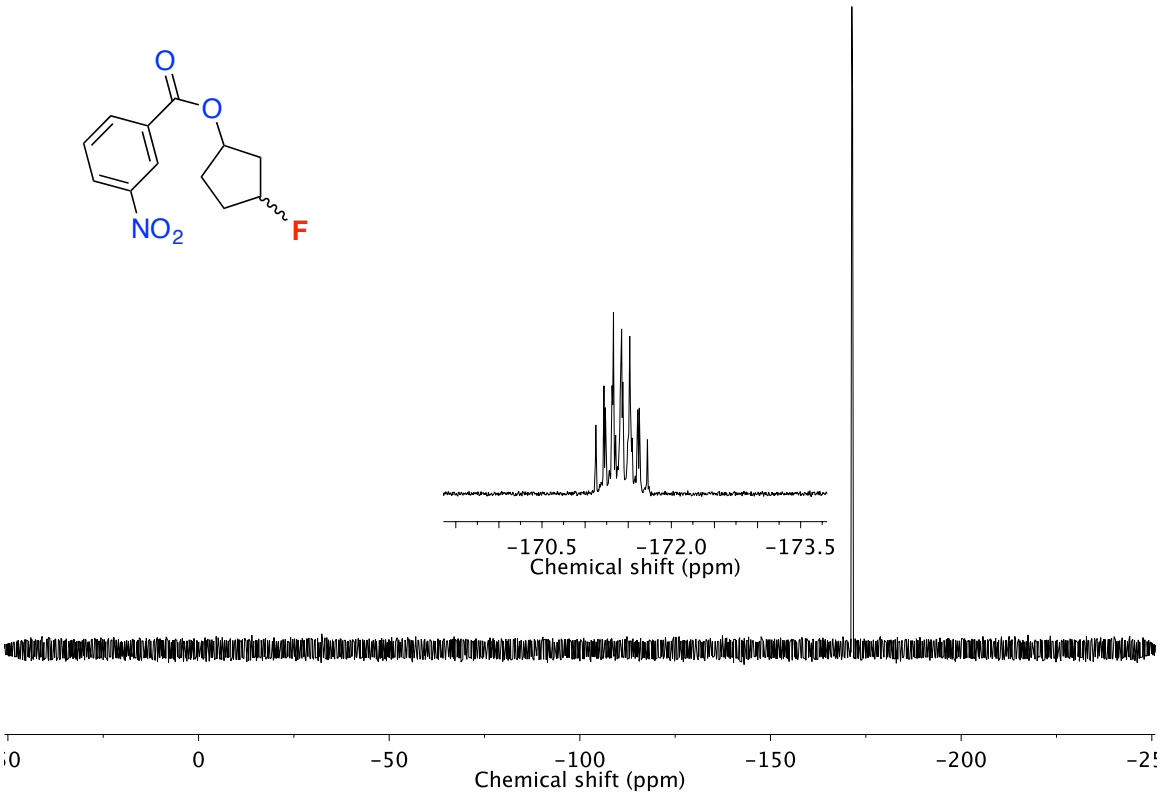

O
O
CN
F
H2O
11
10
9
8
7
6
5
4
3
2
1
0
−1
Chemical shift (ppm)

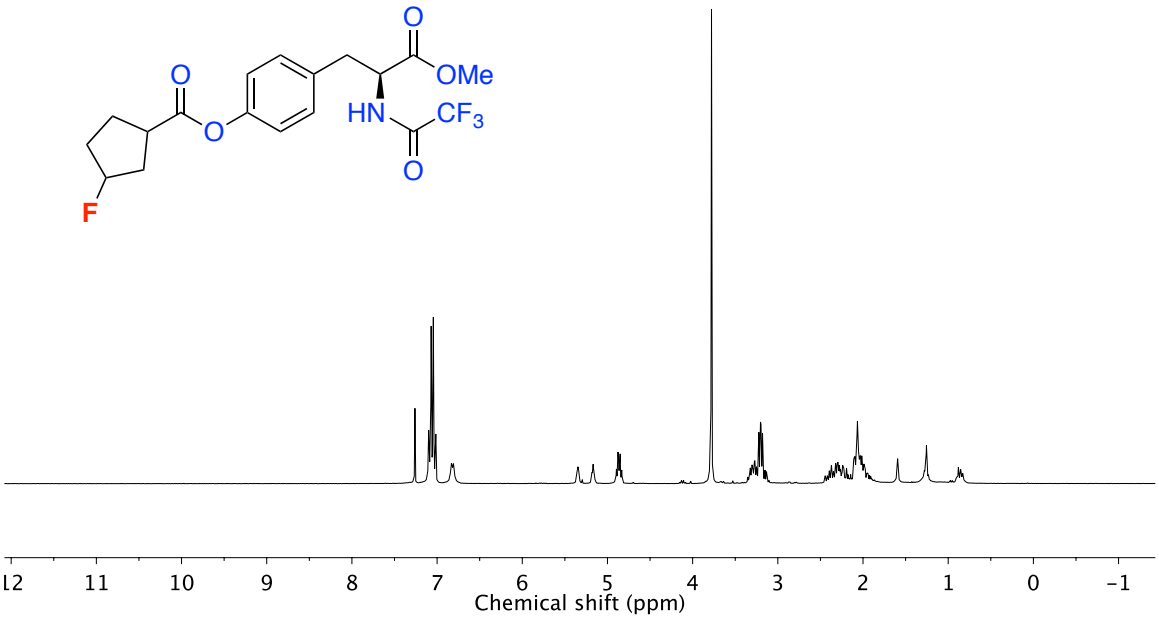

O
O
CN
F
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

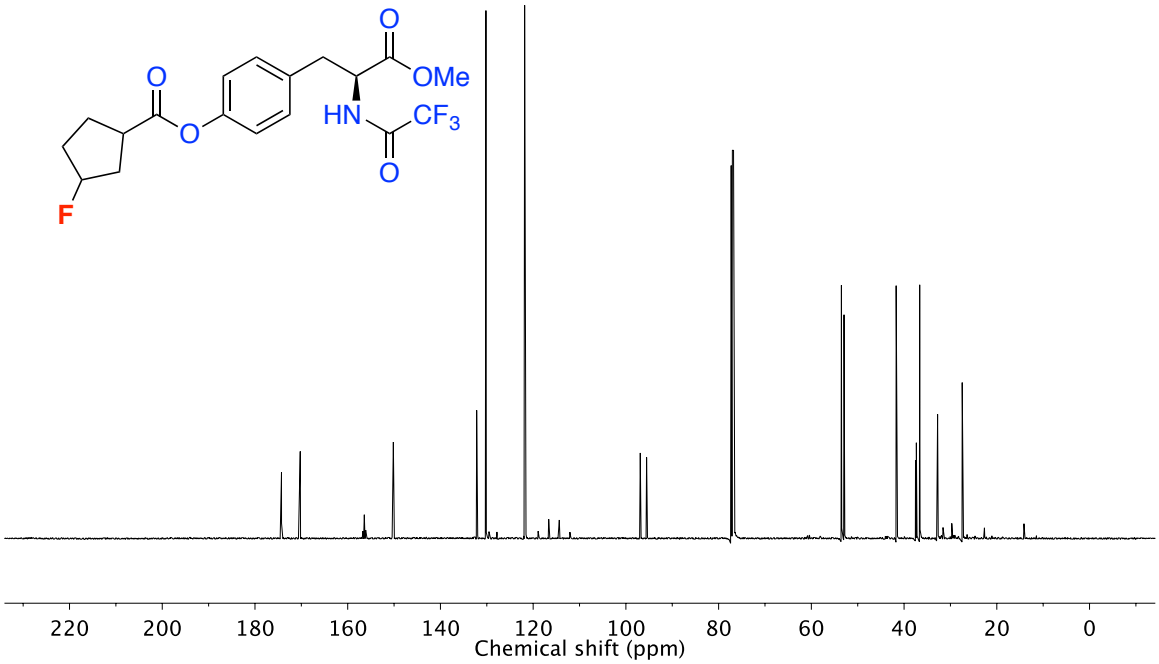

O
O
CN
F
-169.5
-171.0
-172.5
-174.0
Chemical shift (ppm)
0
-50
-100
-150
-200
Chemical shift (ppm)

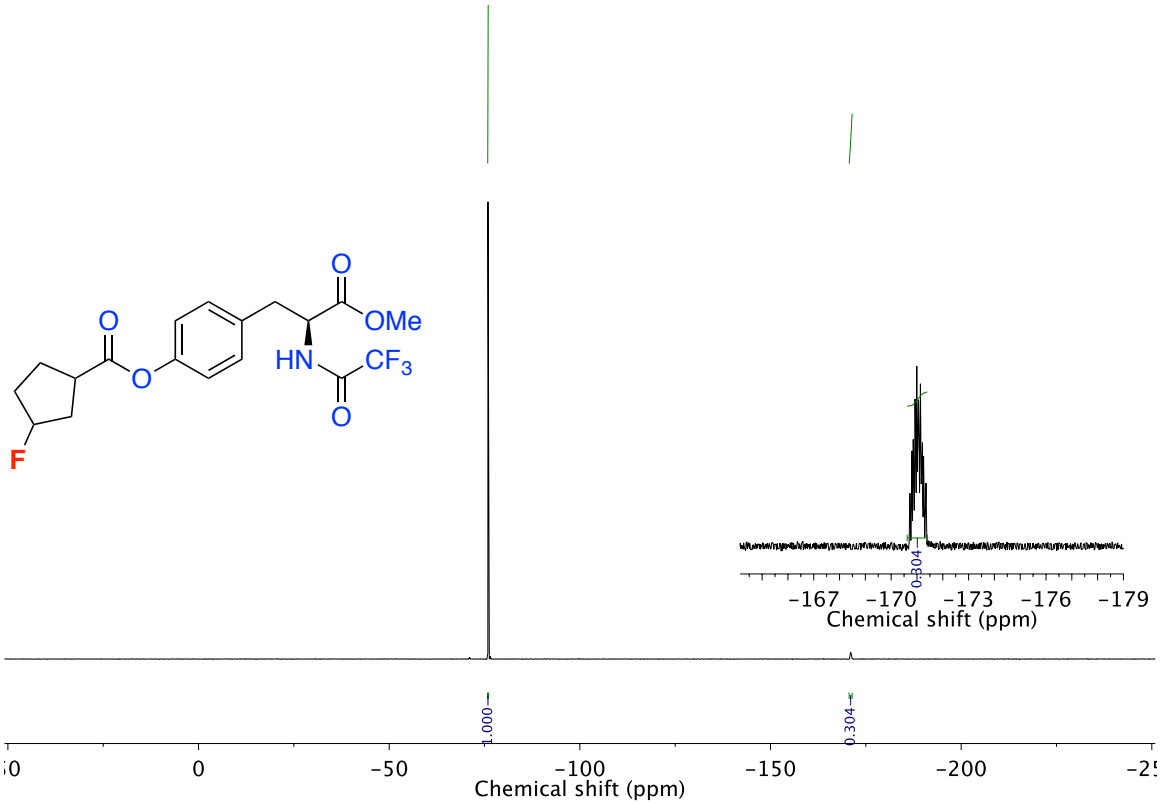

O
O
NO2
F
H2O
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

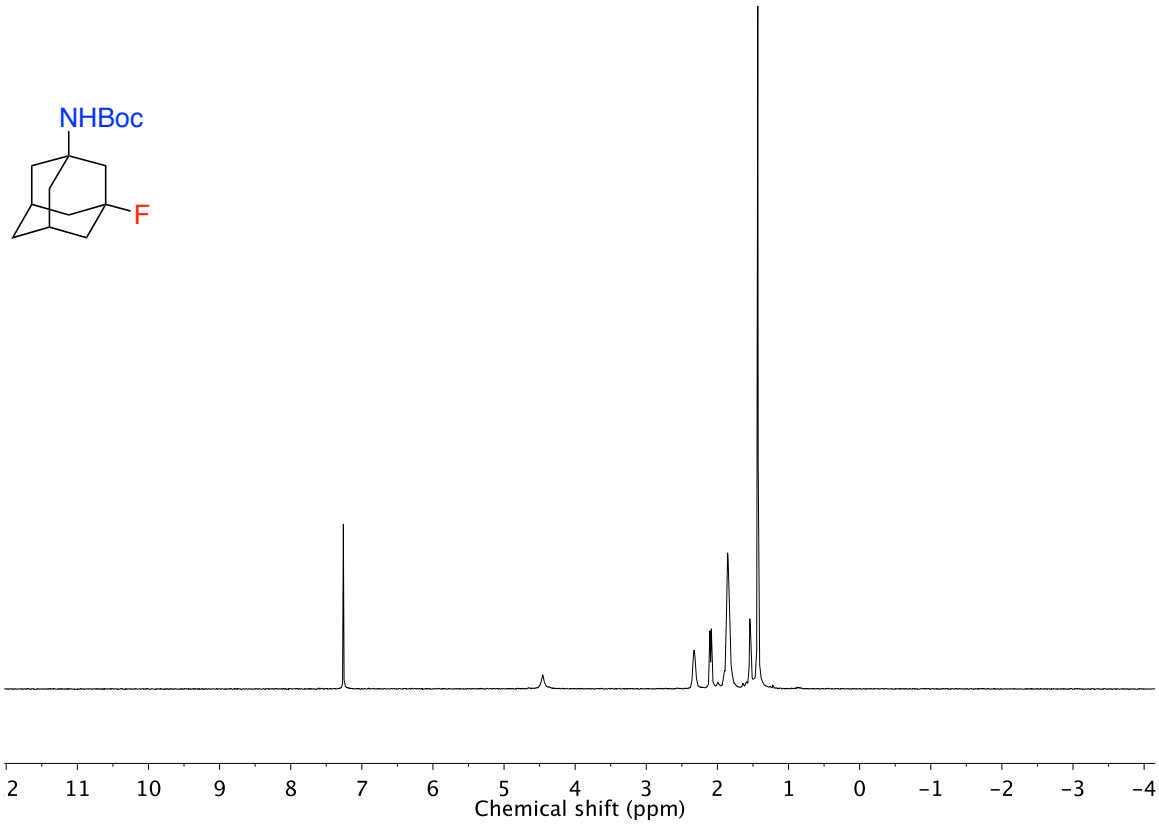

O
O
NO2
F
200
150
100
50
0
Chemical shift (ppm)

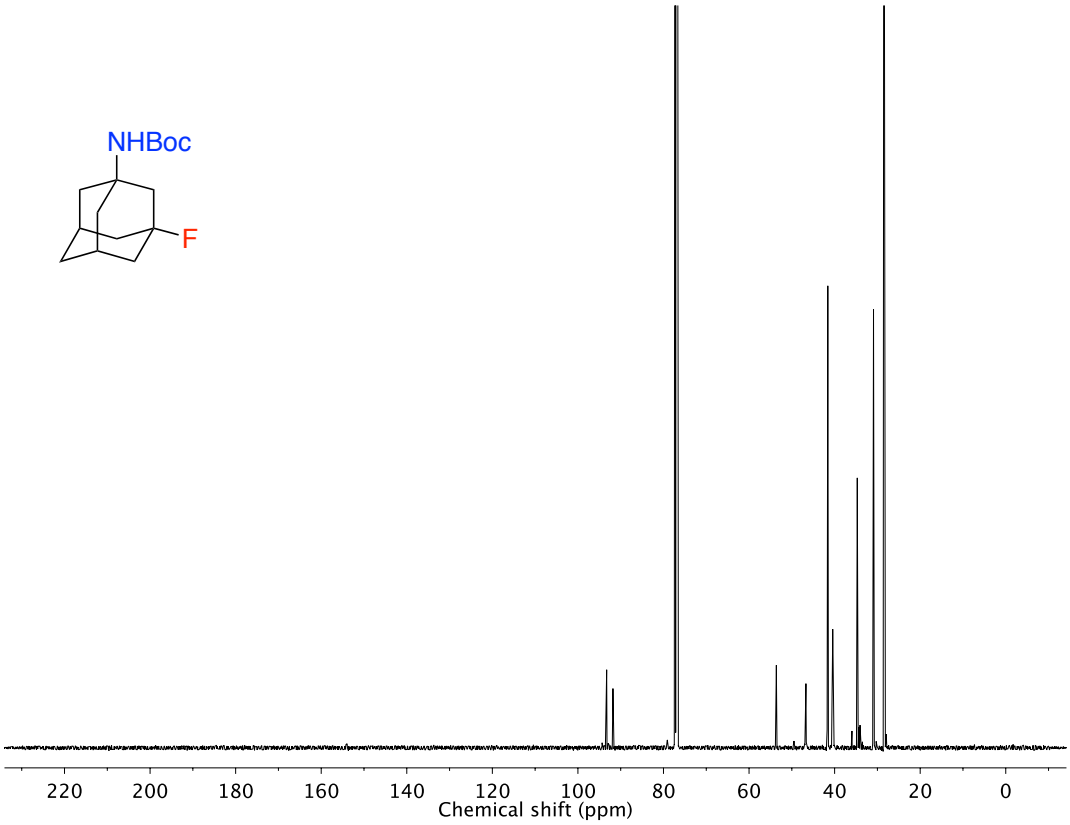

O
O
NO2
F
-170.5
-172.0
-173.5
Chemical shift (ppm)
0
-50
-100
-150
-200
Chemical shift (ppm)

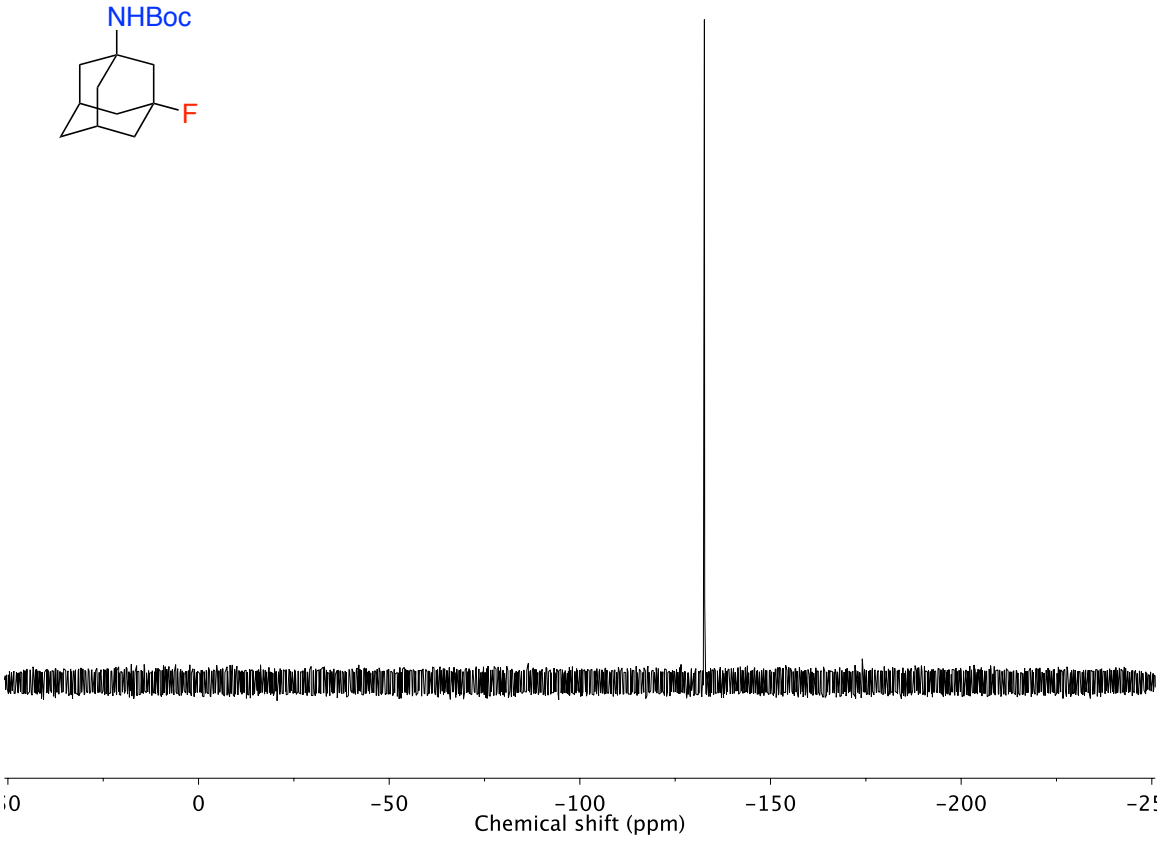

O
OMe
HN
CF3
O
O
O
F
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
Chemical shift (ppm)

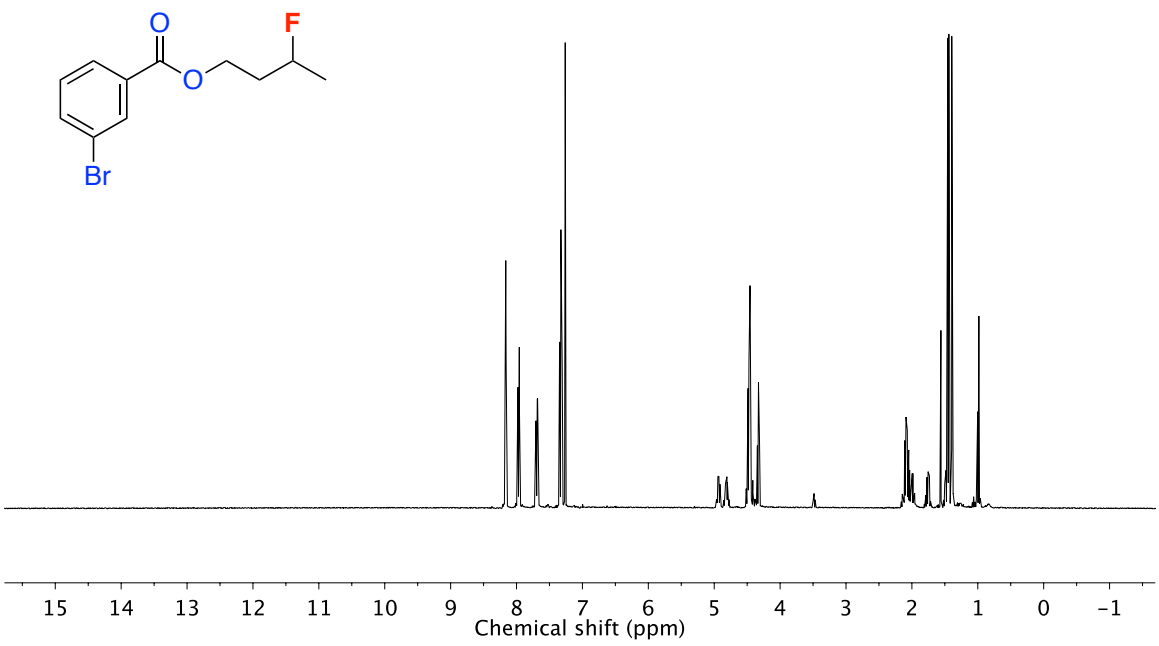

O
OMe
HN
CF3
O
O
O
F
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

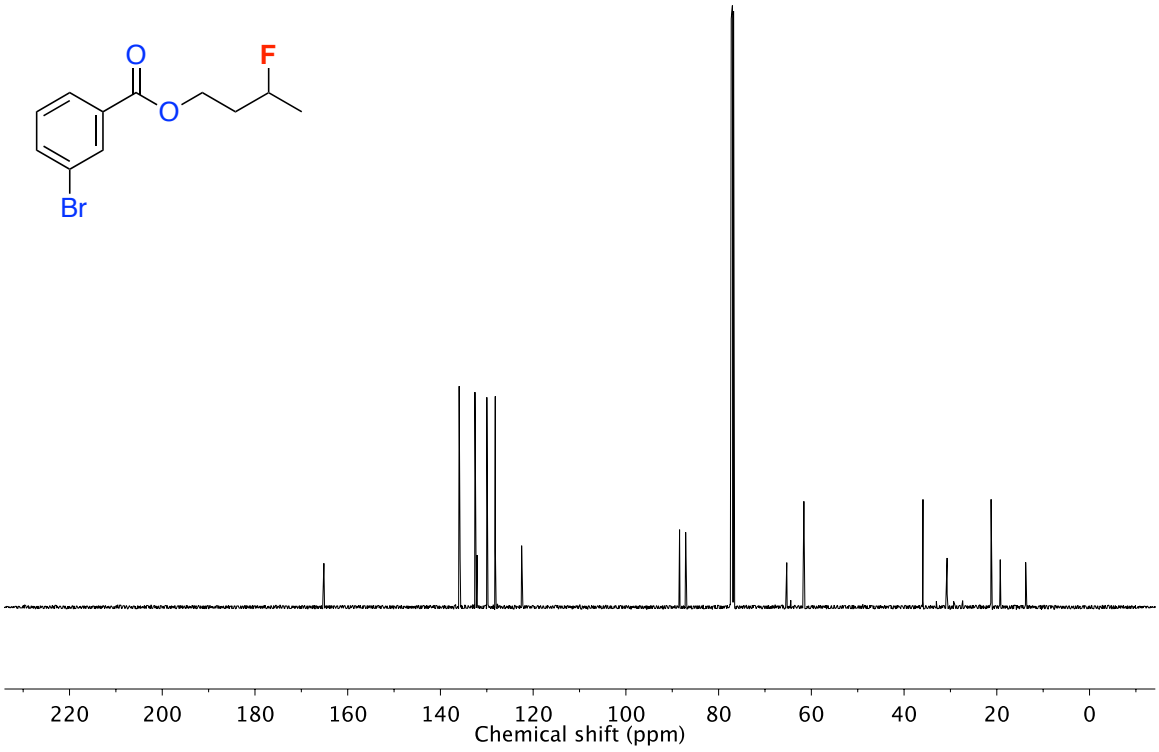

O
O
O
OMe
HN
CF3
O
F
1.000
0.304
-167
-170
-173
-176
-179
Chemical shift (ppm)
0
-50
-100
-150
-200
Chemical shift (ppm)

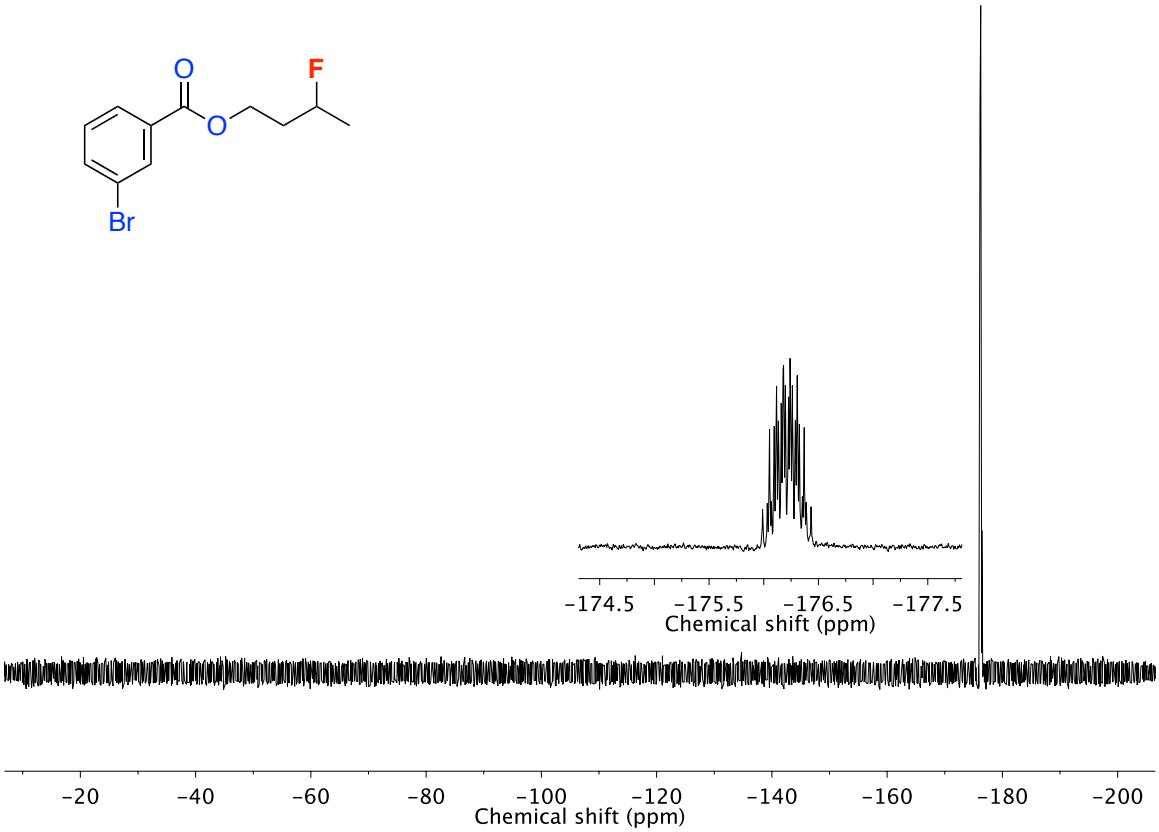

NHBoc
F
2
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
Chemical shift (ppm)

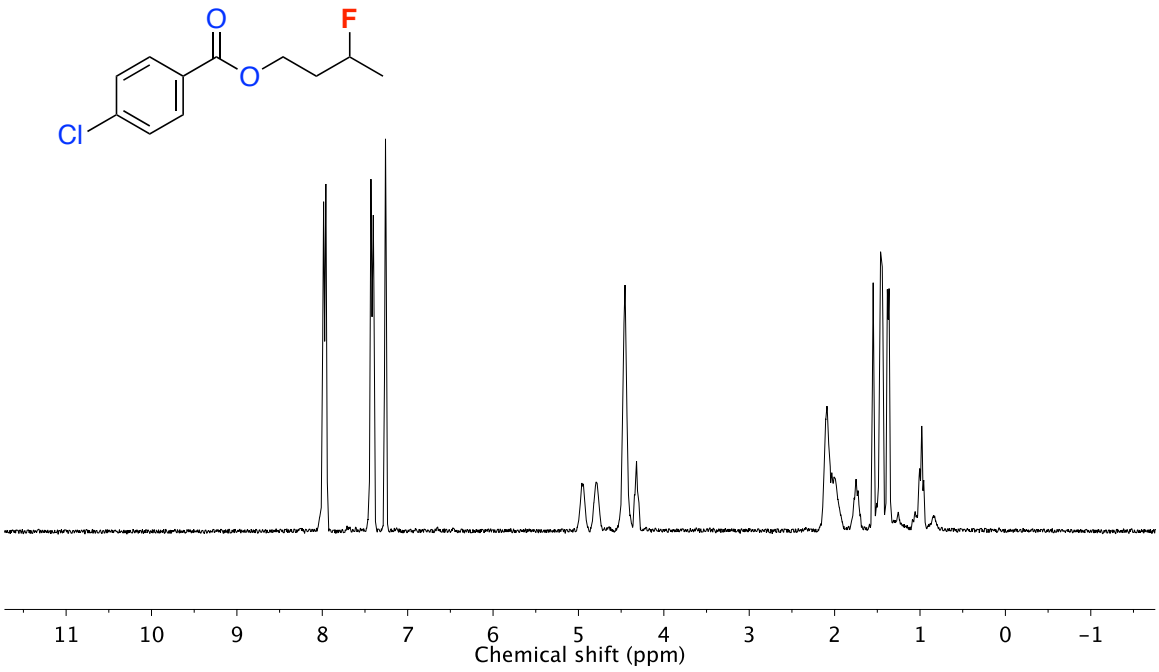

NHBoc
F
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

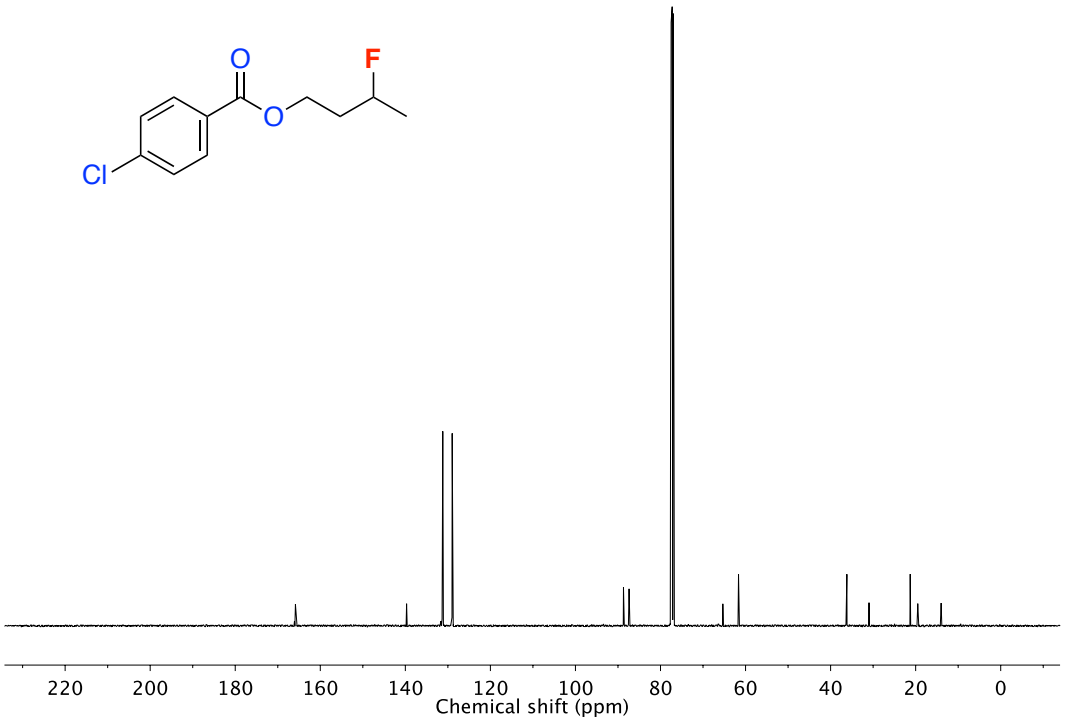

NHBoc
F
0
-50
-100
-150
-200
Chemical shift (ppm)

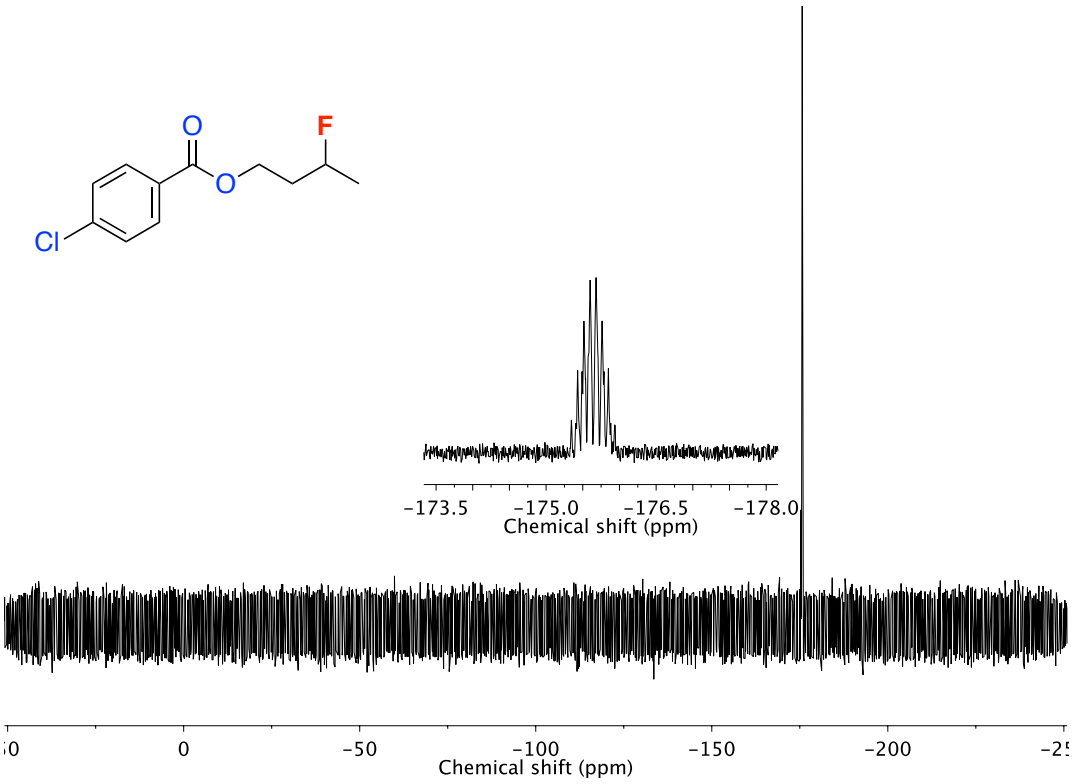

O
F
O
Br
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
Chemical shift (ppm)

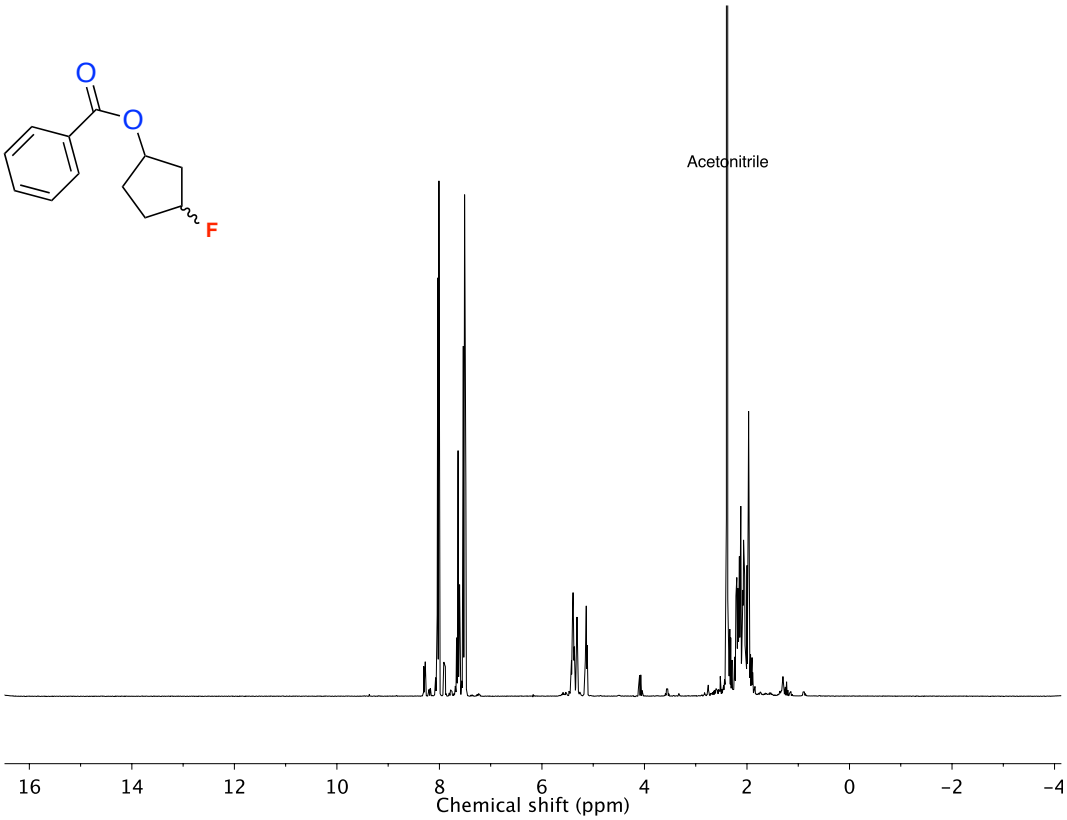

O
F
O
Br
220 200 180 160 140 120 100 80 60 40 20 0
Chemical shift (ppm)

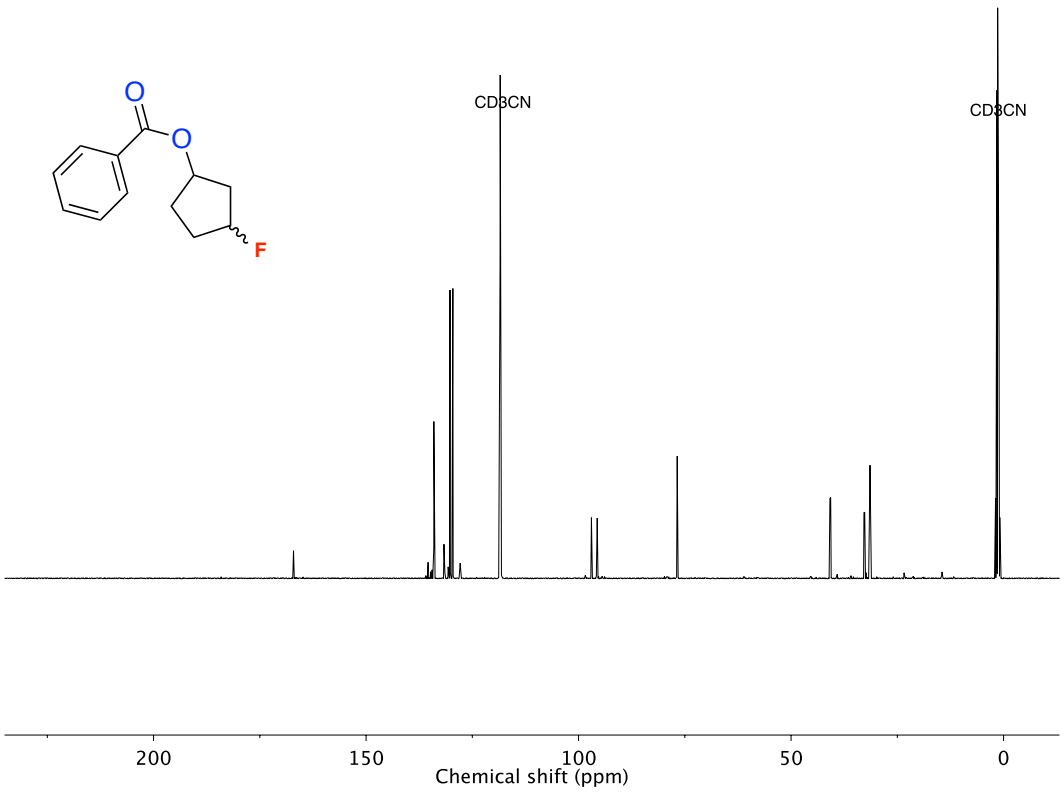

O
F
O
Br
-174.5
-175.5
-176.5
-177.5
Chemical shift (ppm)
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
Chemical shift (ppm)

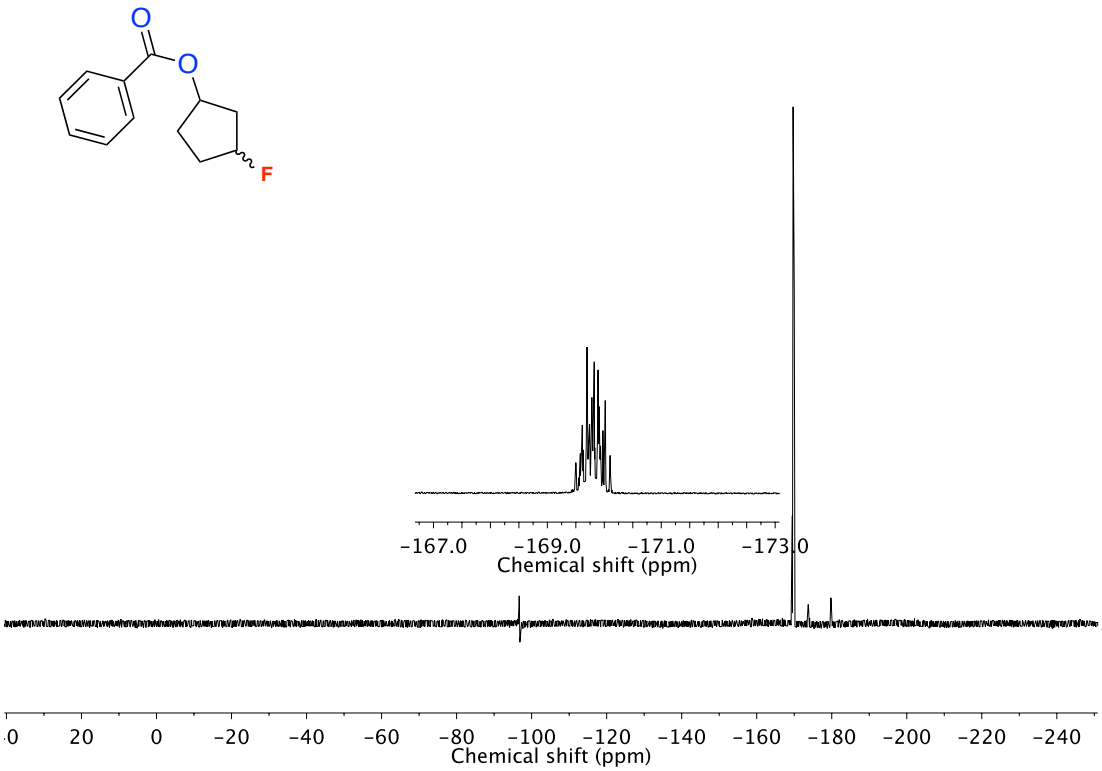

O
F
O
Cl
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

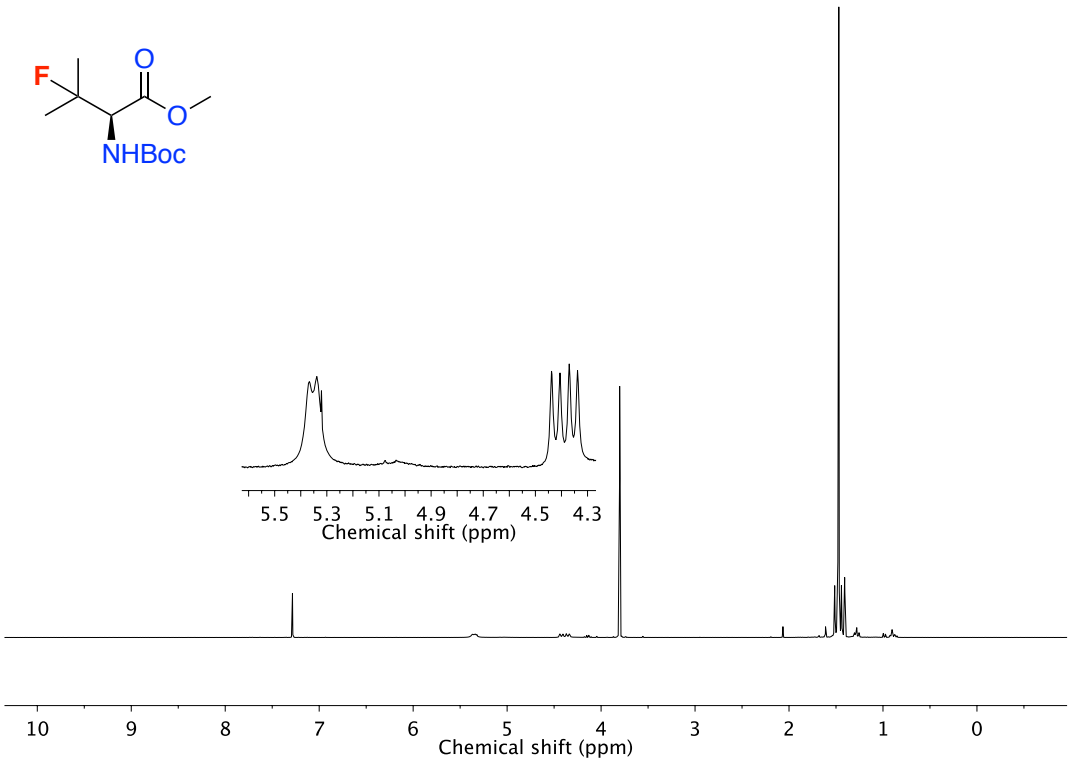

O
F
O
Cl
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

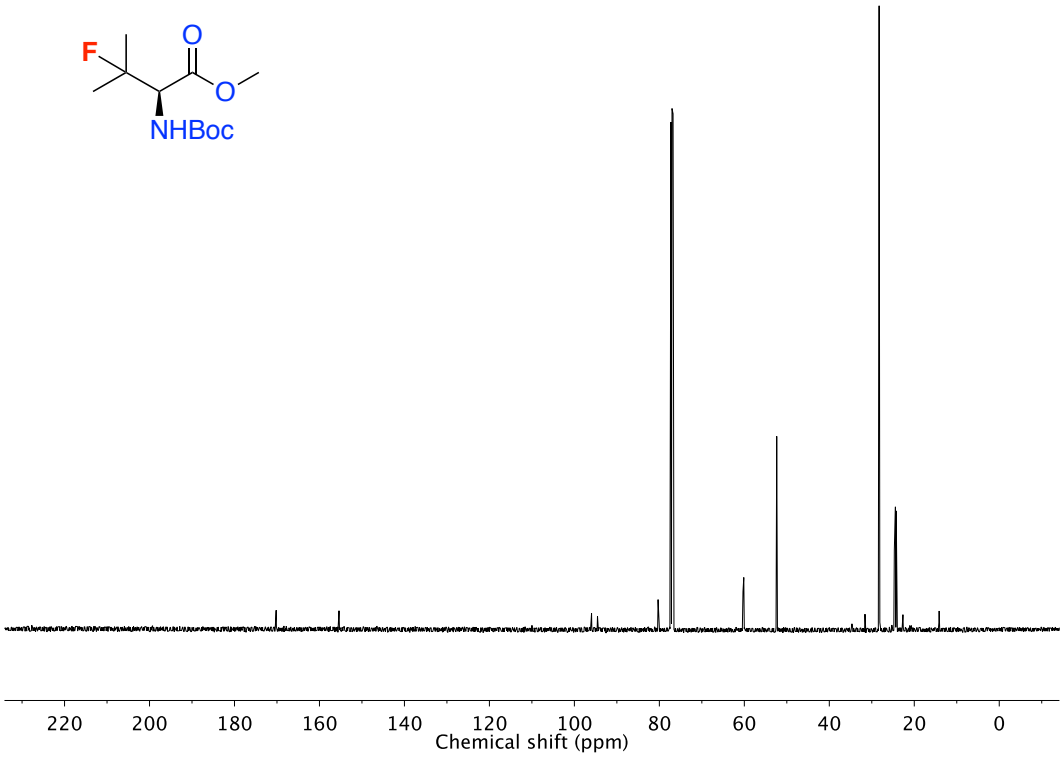

O
F
O
Cl
−173.5
−175.0
−176.5
−178.0
Chemical shift (ppm)
0
−50
−100
−150
−200
Chemical shift (ppm)

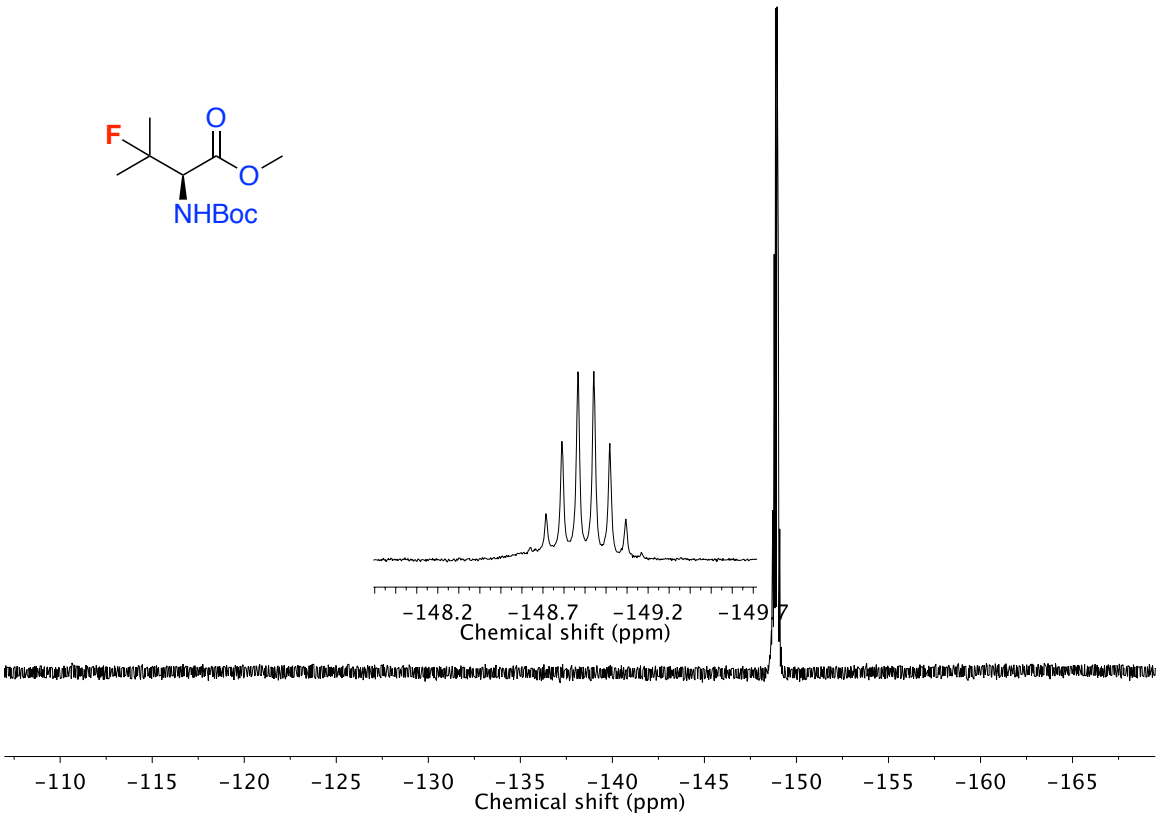

O
O
F
Acetonitrile
16
14
12
10
8
6
4
2
0
−2
−4
Chemical shift (ppm)

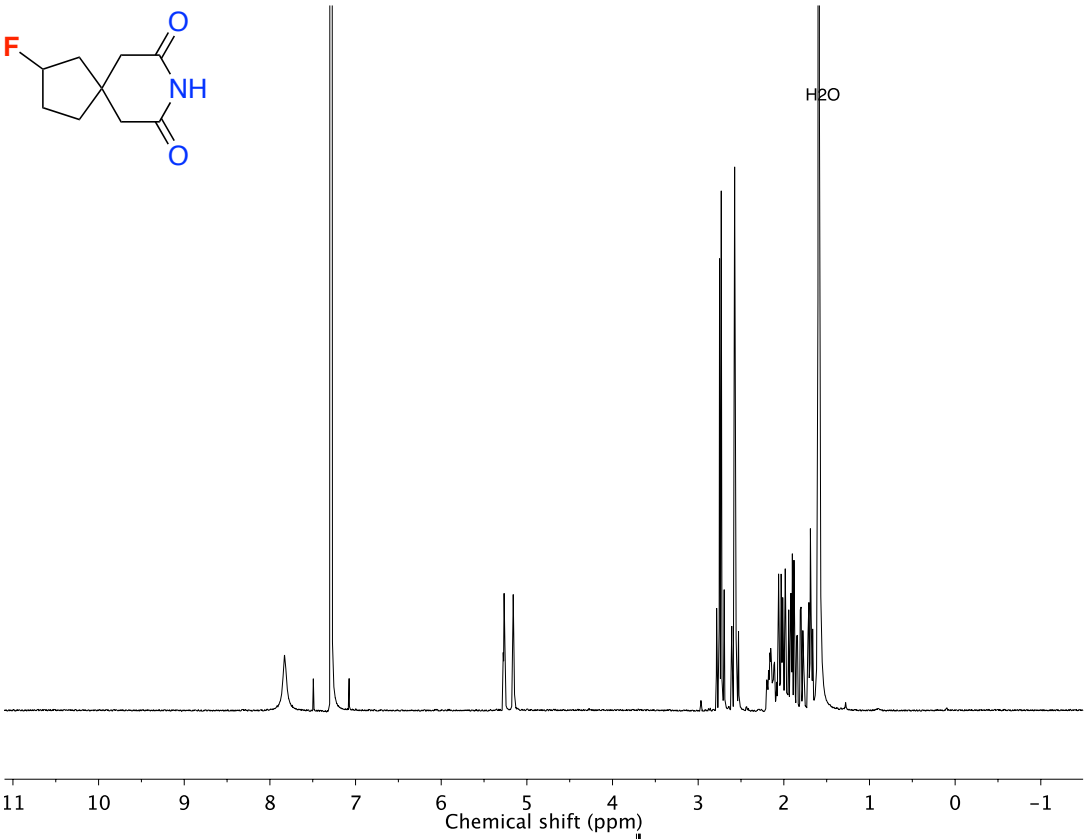

O
O
F
CD3CN
CD3CN
200
150
100
50
0
Chemical shift (ppm)

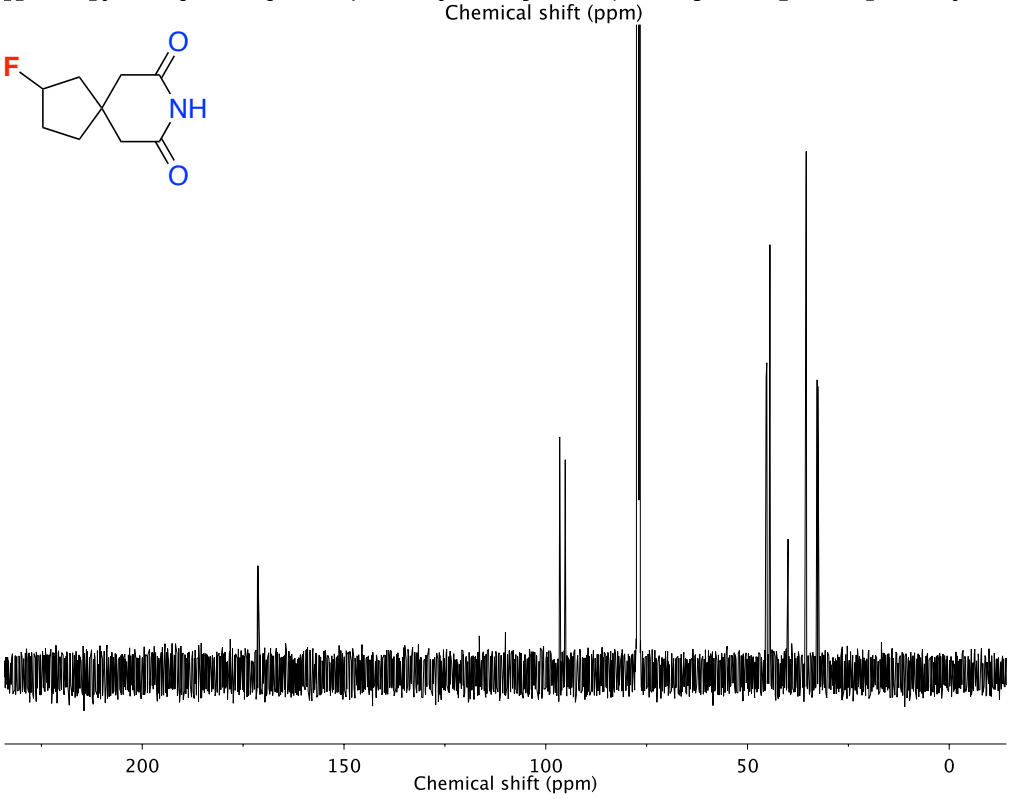

O
O
F
−167.0
−169.0
−171.0
−173.0
Chemical shift (ppm)
0
20
0
−20
−40
−60
−80
−100
−120
−140
−160
−180
−200
−220
−240
Chemical shift (ppm)

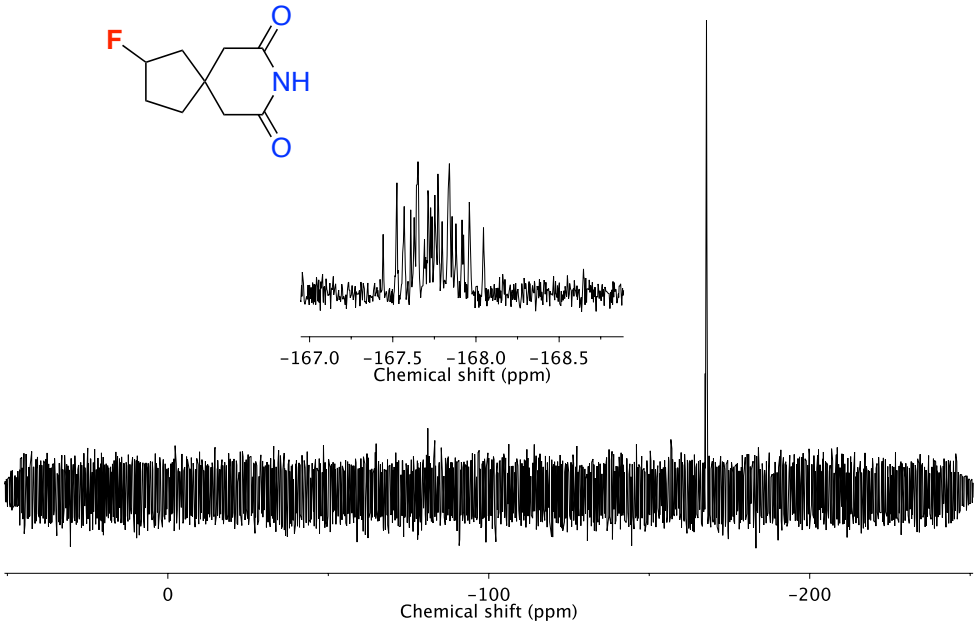

F
O
O
NHBoc
5.5
5.3
5.1
4.9
4.7
4.5
4.3
Chemical shift (ppm)
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

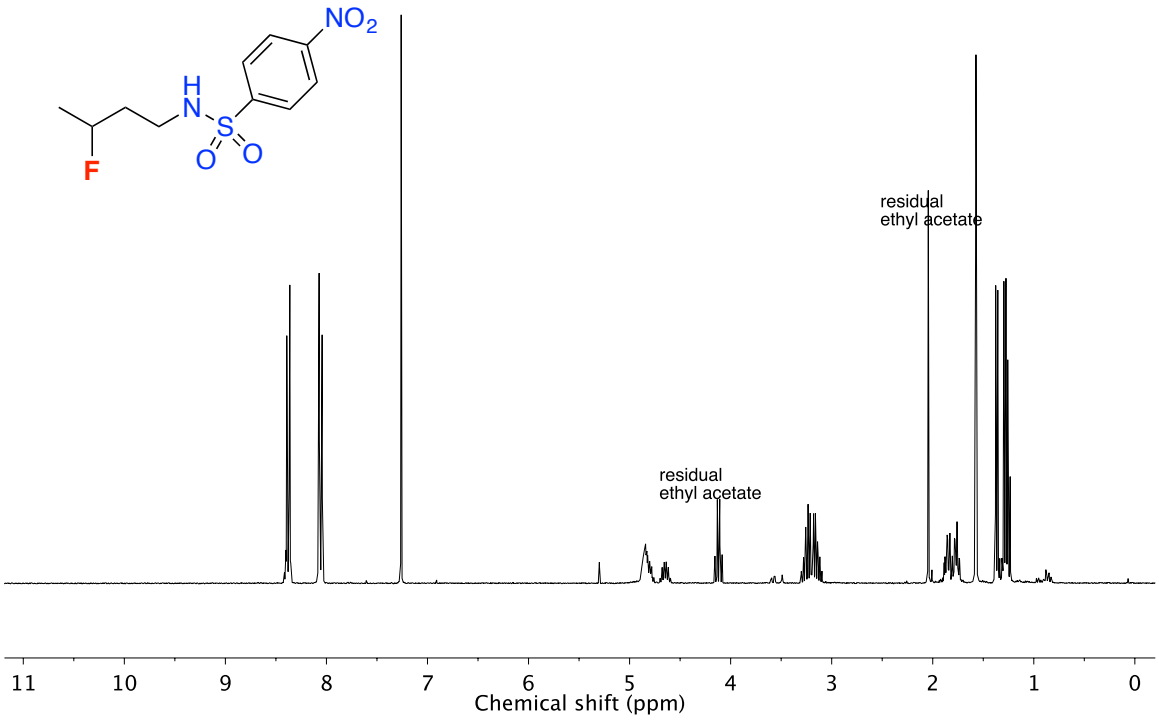

F
O
O
NHBoc
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

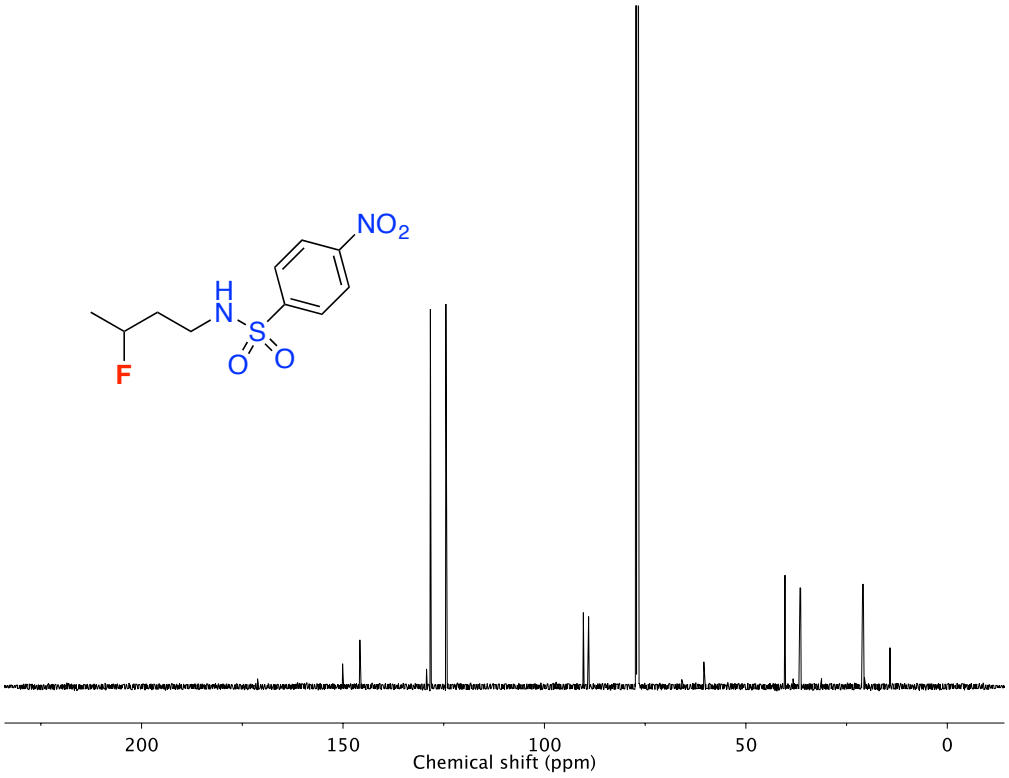

F
O
O
NHBoc
-148.2
-148.7
-149.2
-149.7
Chemical shift (ppm)
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
Chemical shift (ppm)

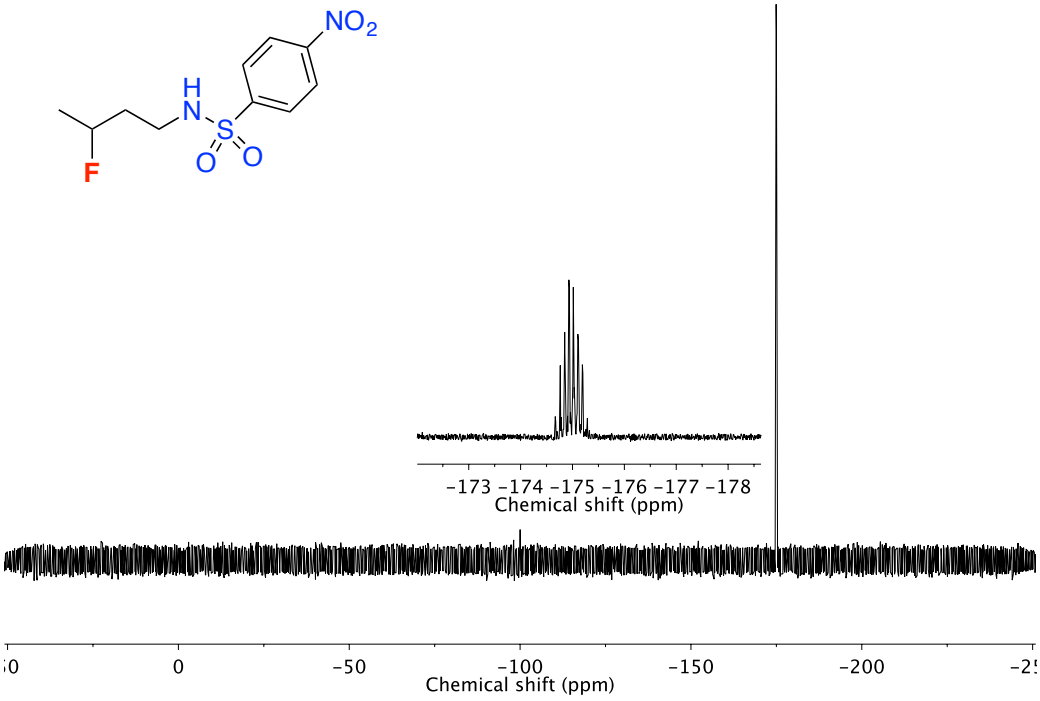

F
O
NH
O
H2O
11
10
9
8
7
6
5
4
3
2
1
0
−1
Chemical shift (ppm)

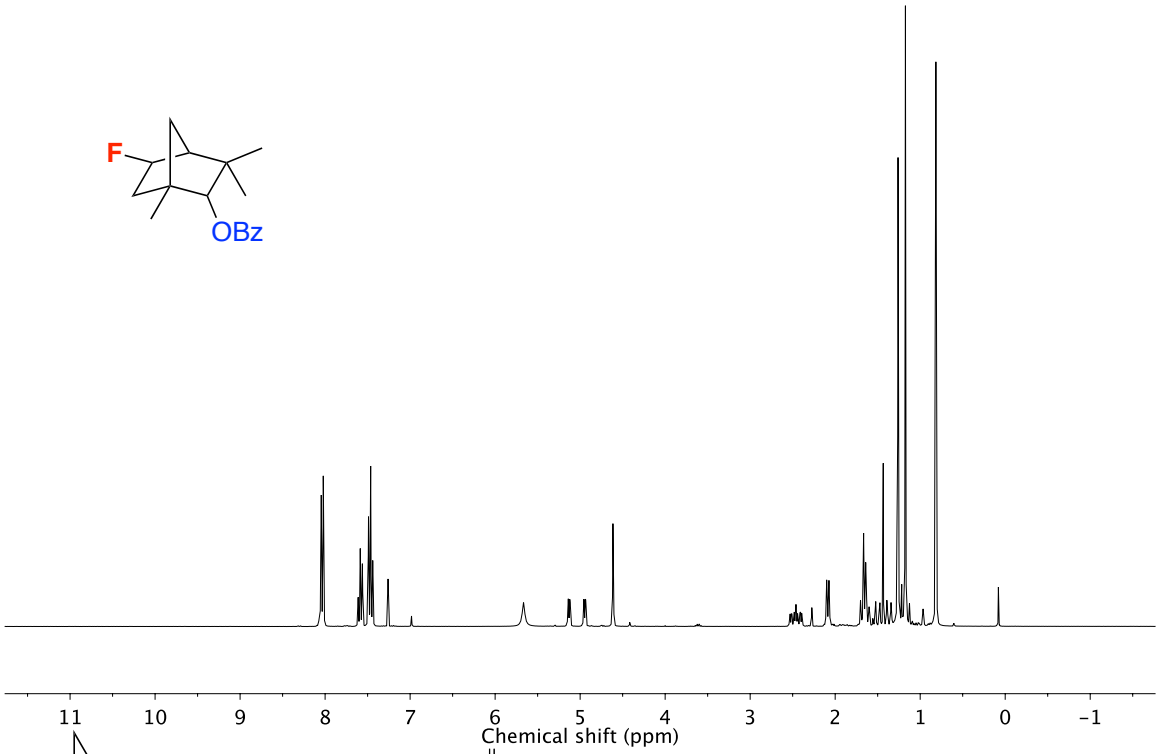

F
O
NH
O
200
150
100
50
0
Chemical shift (ppm)

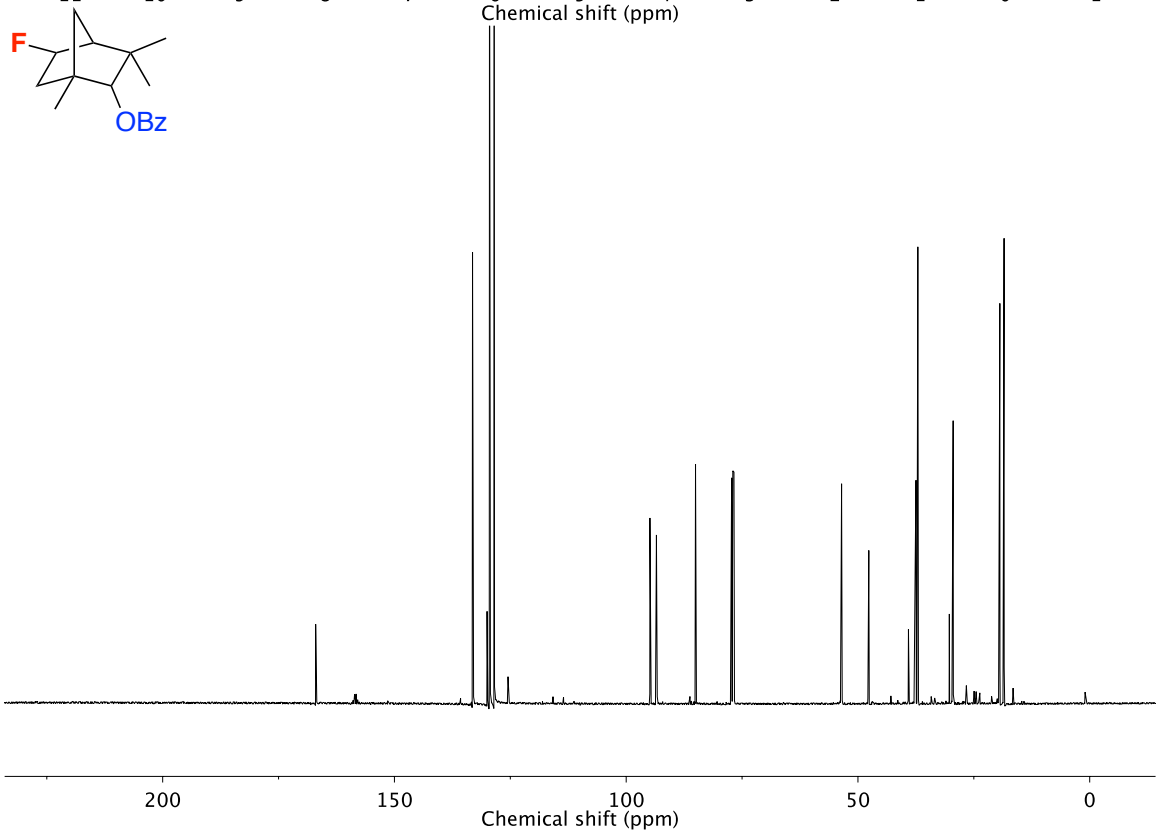

F
O
NH
O
−167.0
−167.5
−168.0
−168.5
Chemical shift (ppm)
0
−100
−200
Chemical shift (ppm)

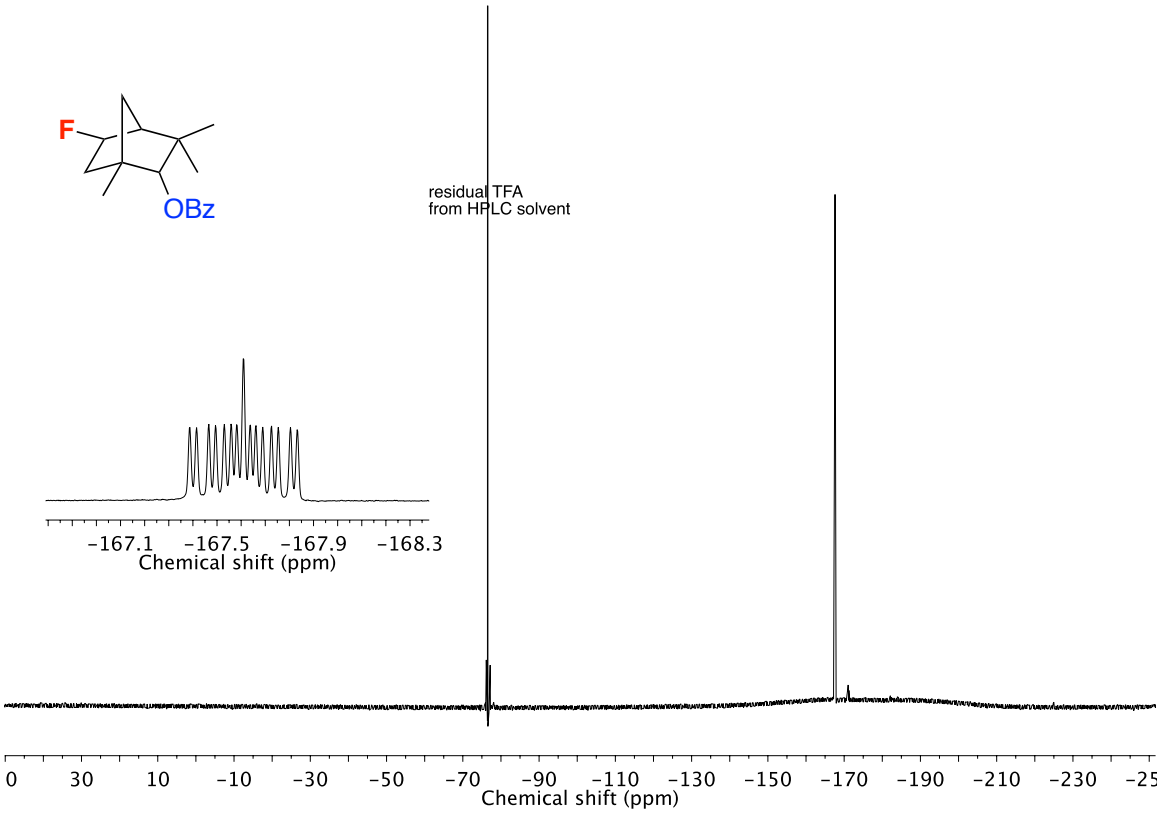

NO2
H
N
S
O
O
F
residual
ethyl acetate
residual
ethyl acetate
11
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

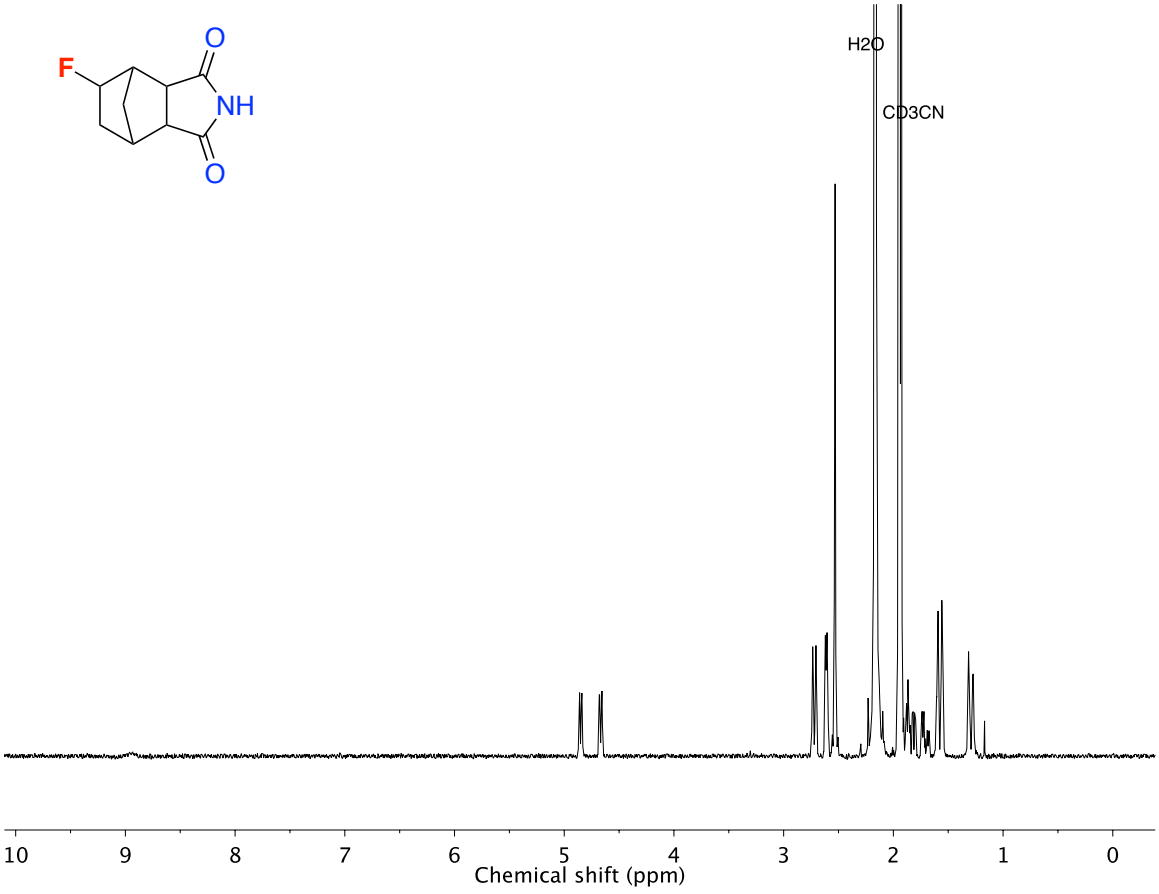

NO2
H
N
S
O
O
F
200
150
100
50
0
Chemical shift (ppm)

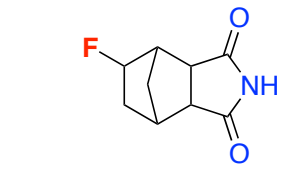

NO2
H
N
S
O
O
F
−173 −174 −175 −176 −177 −178
Chemical shift (ppm)
0
−50
−100
−150
−200
Chemical shift (ppm)


F
OBz
11
10
9
8
7
6
5
4
3
2
1
0
−1
Chemical shift (ppm)

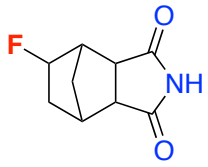

F
OBz
200
150
100
50
0
Chemical shift (ppm)


F
OBz
residual TFA
from HPLC solvent
-167.1
-167.5
-167.9
-168.3
Chemical shift (ppm)
0
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
Chemical shift (ppm)

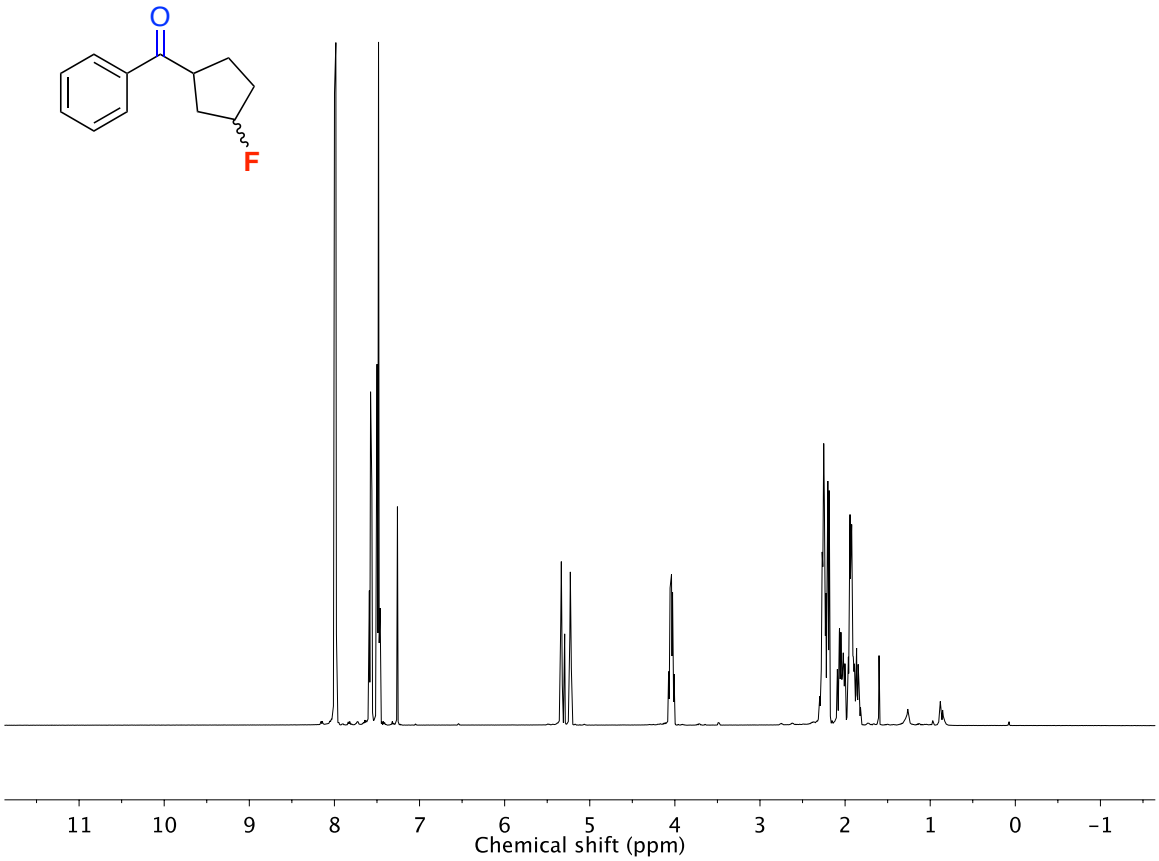

F
O
NH
O
H2O
CD3CN
10
9
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

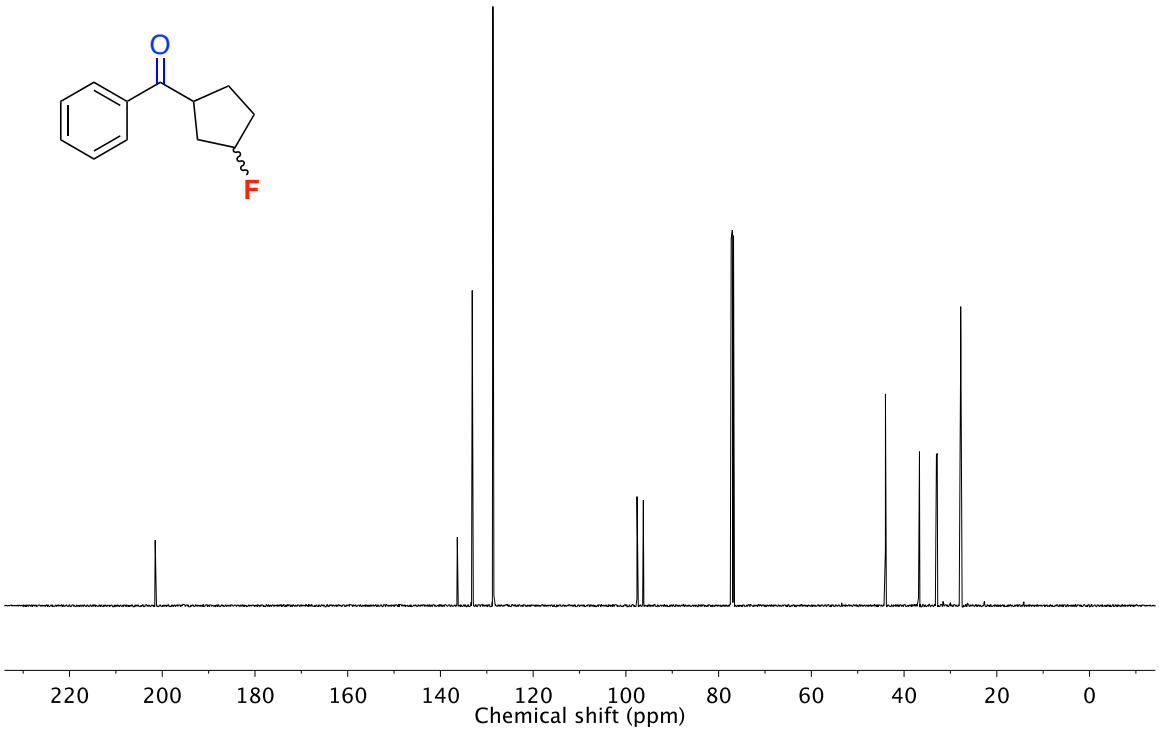

F
O
NH
O

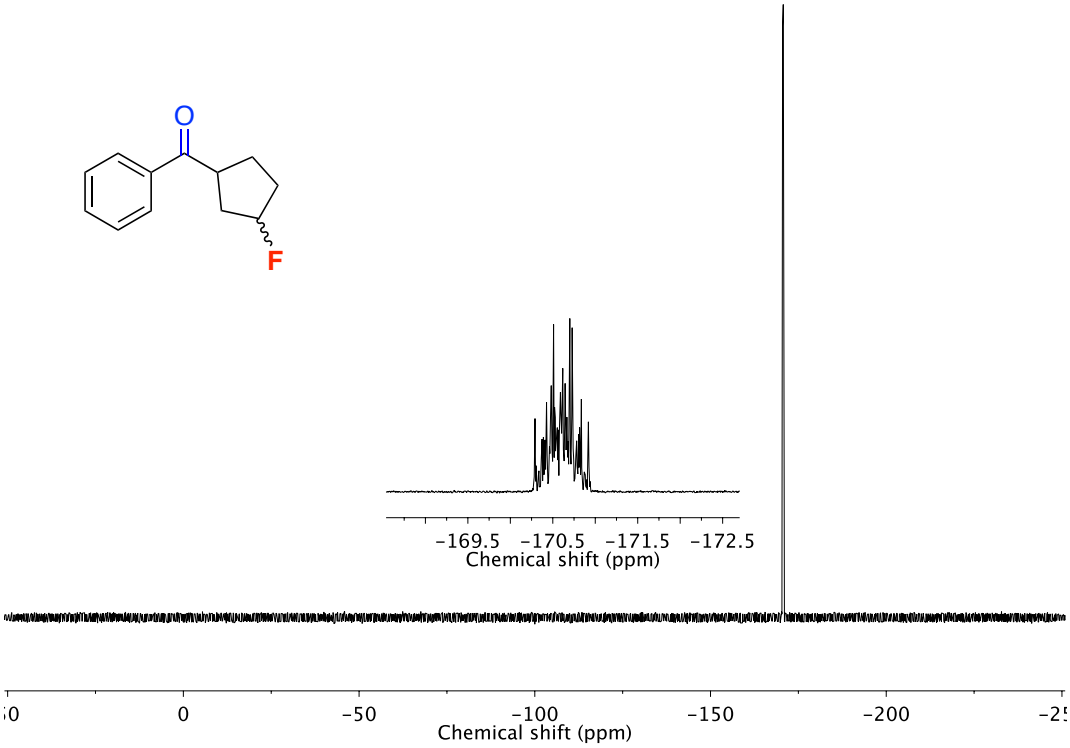
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

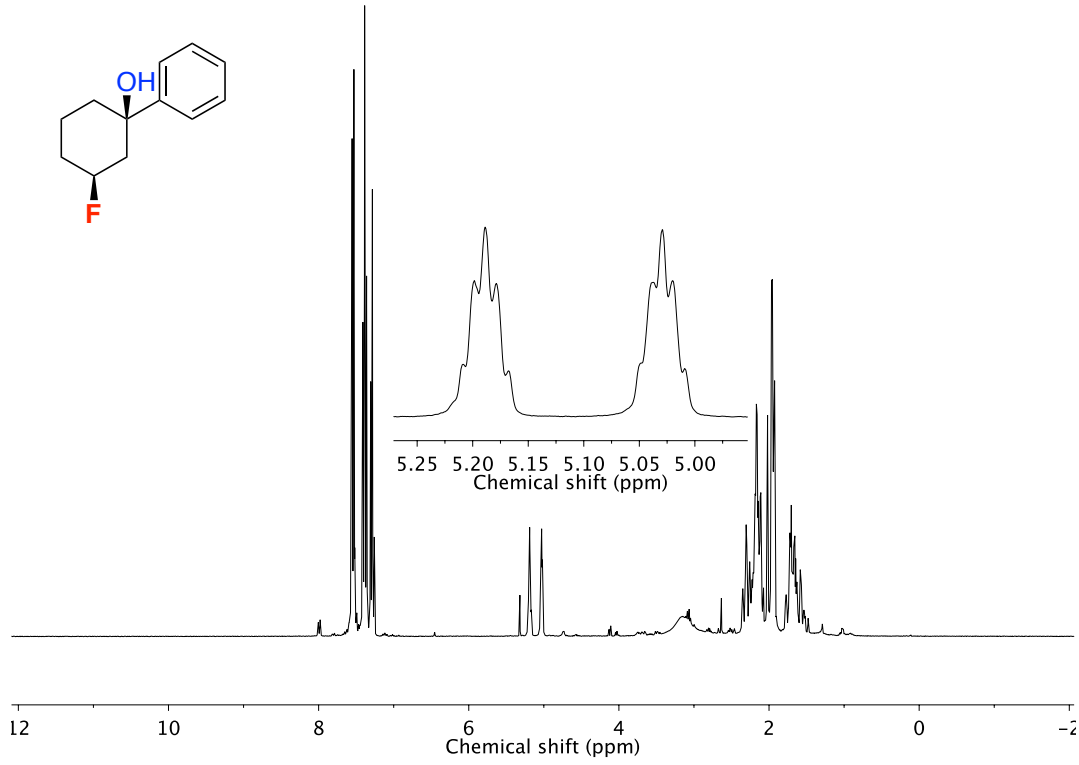

F
O
NH
O

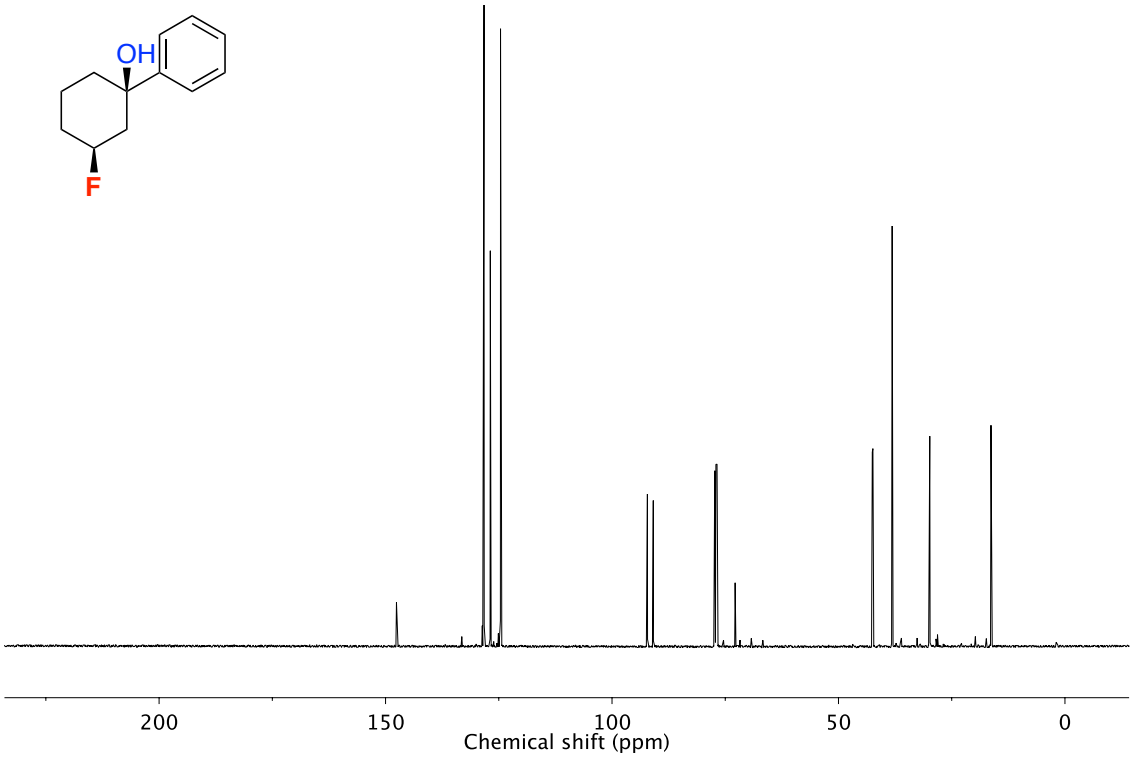
-165.2
-165.6
-166.0
-166.4
Chemical shift (ppm)
0
-50
-100
-150
-200
Chemical shift (ppm)

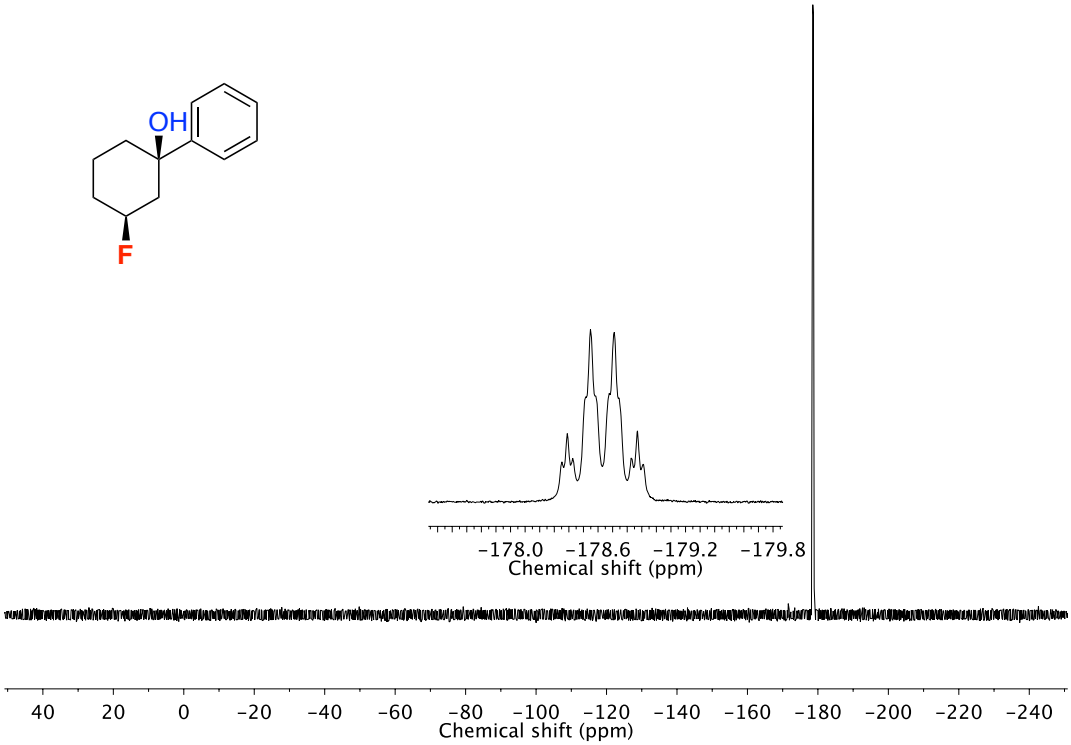

O
F
11
10
9
8
7
6
5
4
3
2
1
0
−1
Chemical shift (ppm)

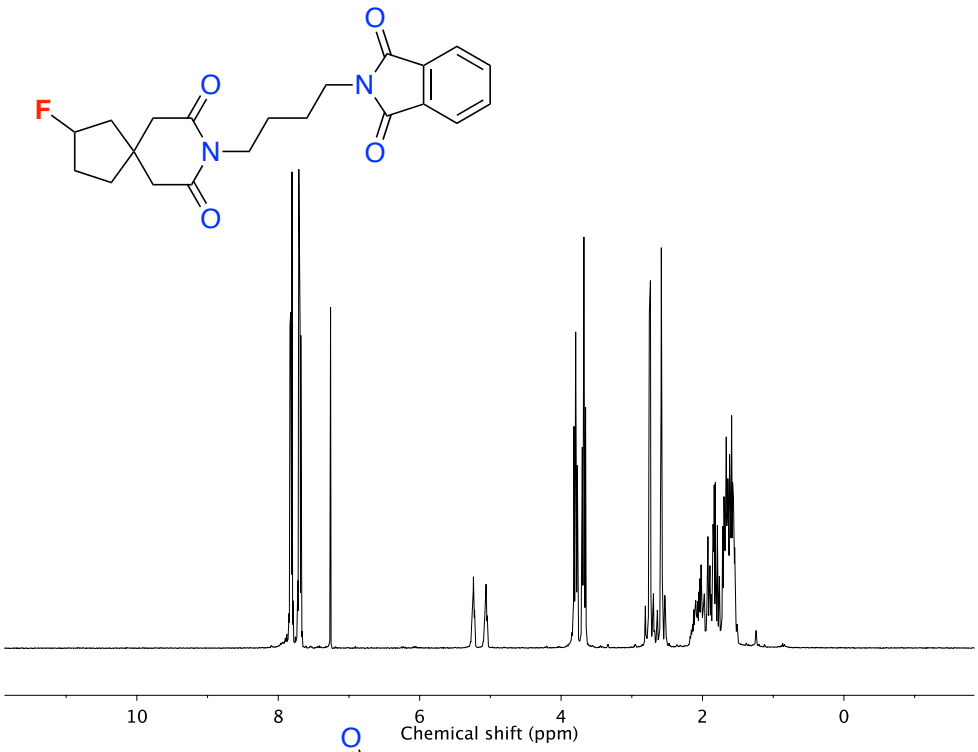

O
F
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

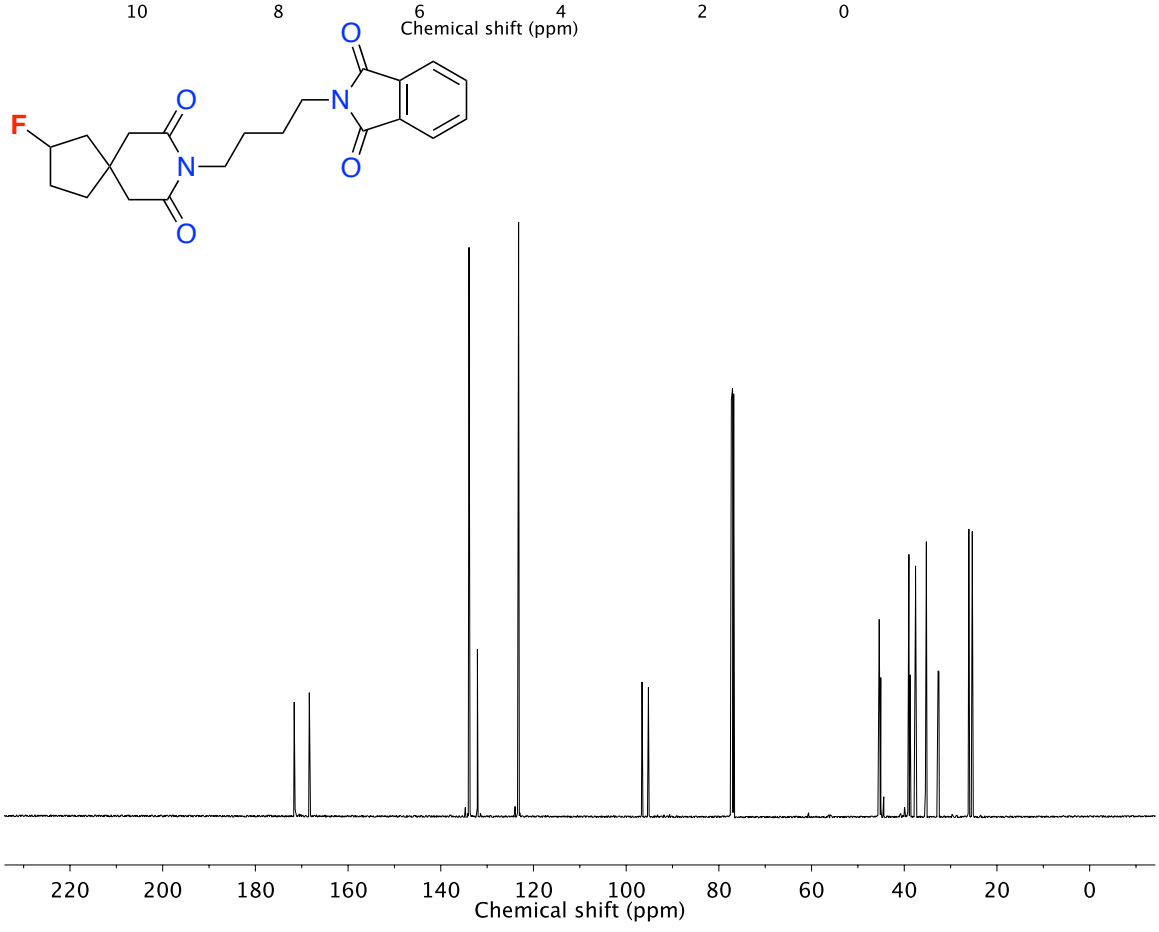

O
F
-169.5 -170.5 -171.5 -172.5
Chemical shift (ppm)
0 -50 -100 -150 -200
Chemical shift (ppm)

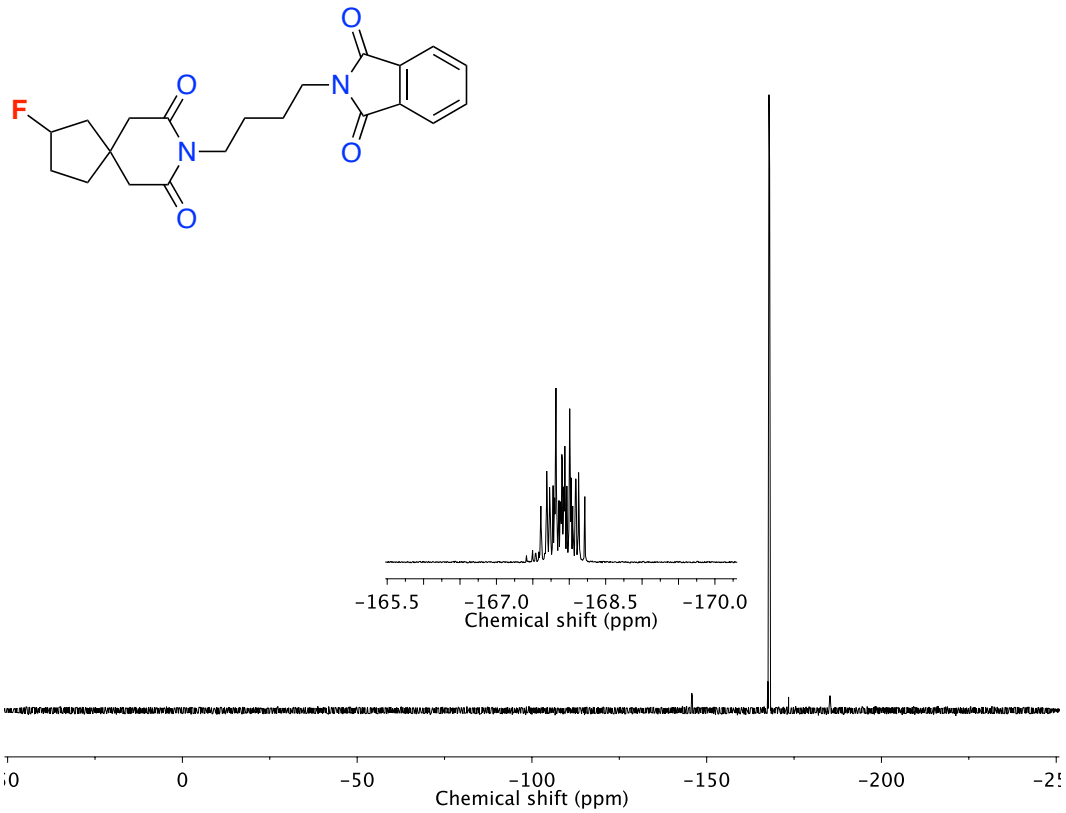

OH
F
5.25 5.20 5.15 5.10 5.05 5.00
Chemical shift (ppm)
12 10 8 6 4 2 0
Chemical shift (ppm)

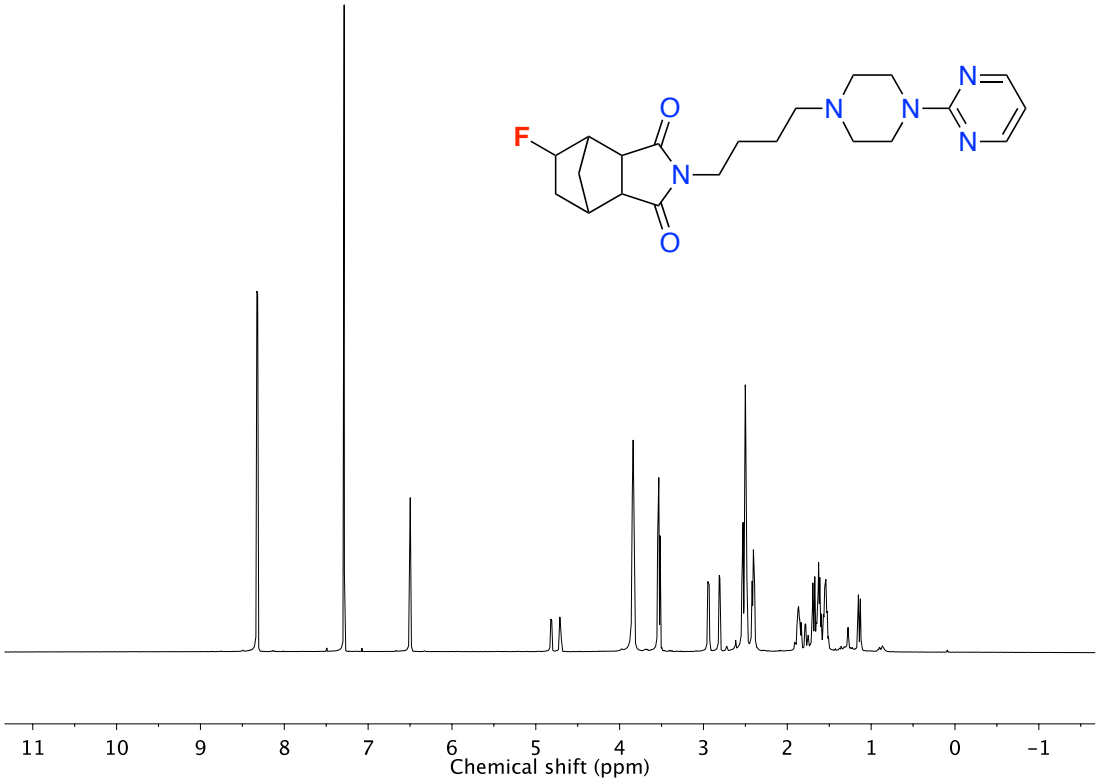

OH
F
200
150
100
50
0
Chemical shift (ppm)

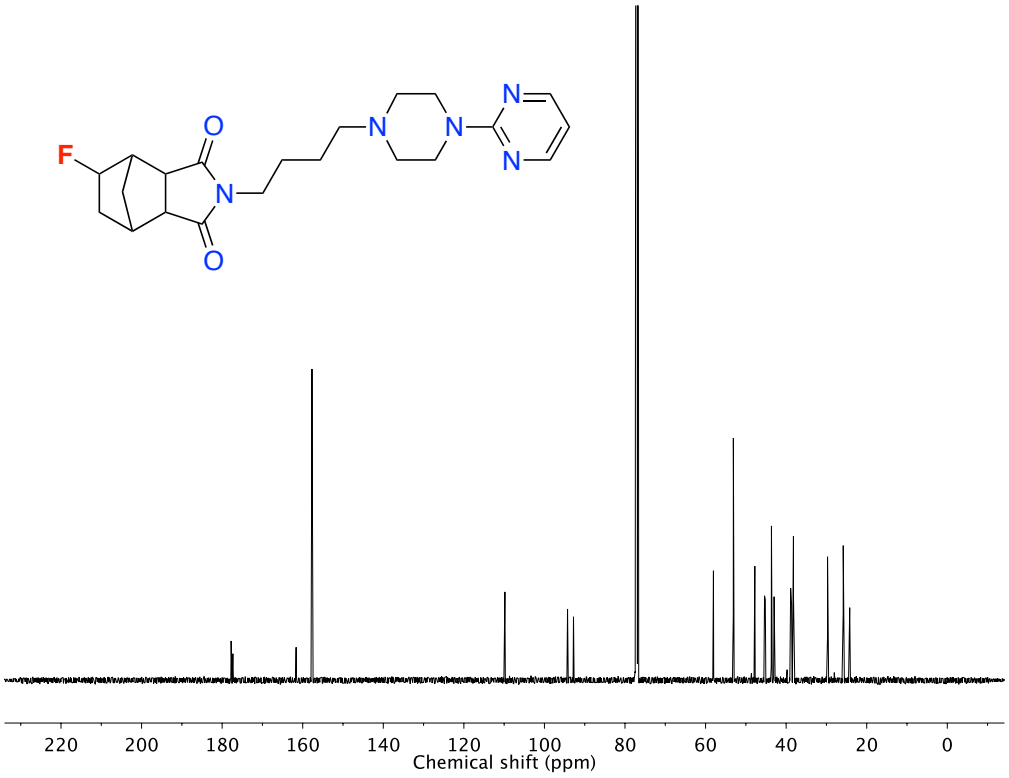

OH
F
-178.0
-178.6
-179.2
-179.8
Chemical shift (ppm)
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
Chemical shift (ppm)

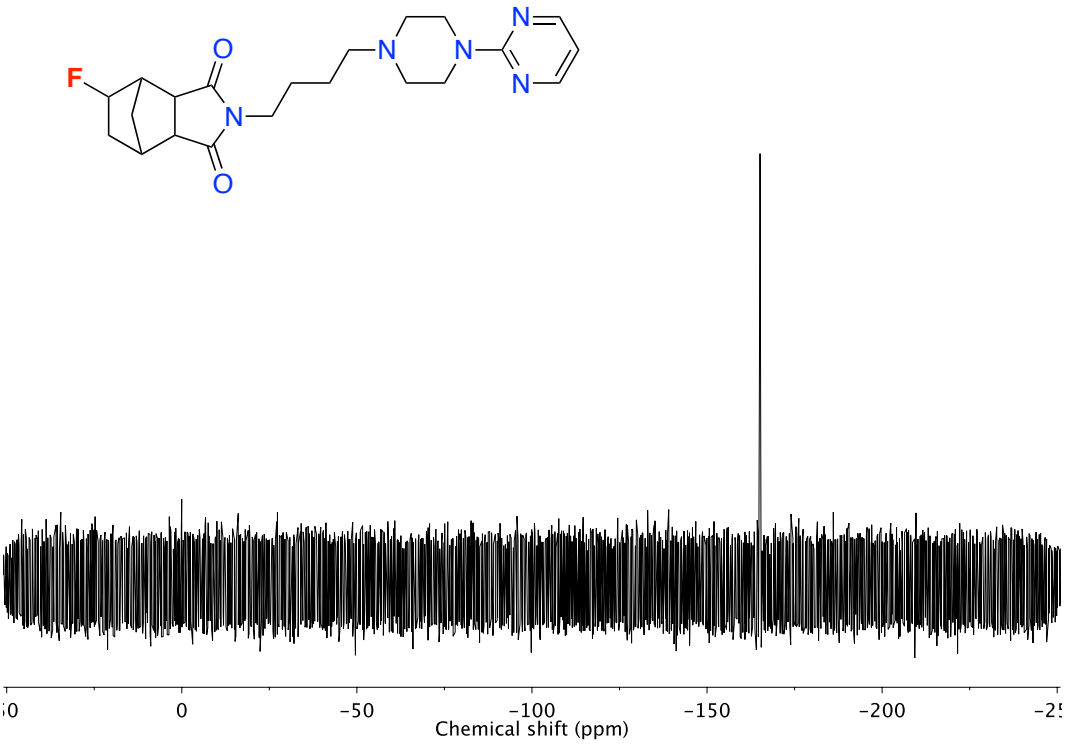

F
O
N
O
O
N
O
O
10
8
6
4
2
0
Chemical shift (ppm)

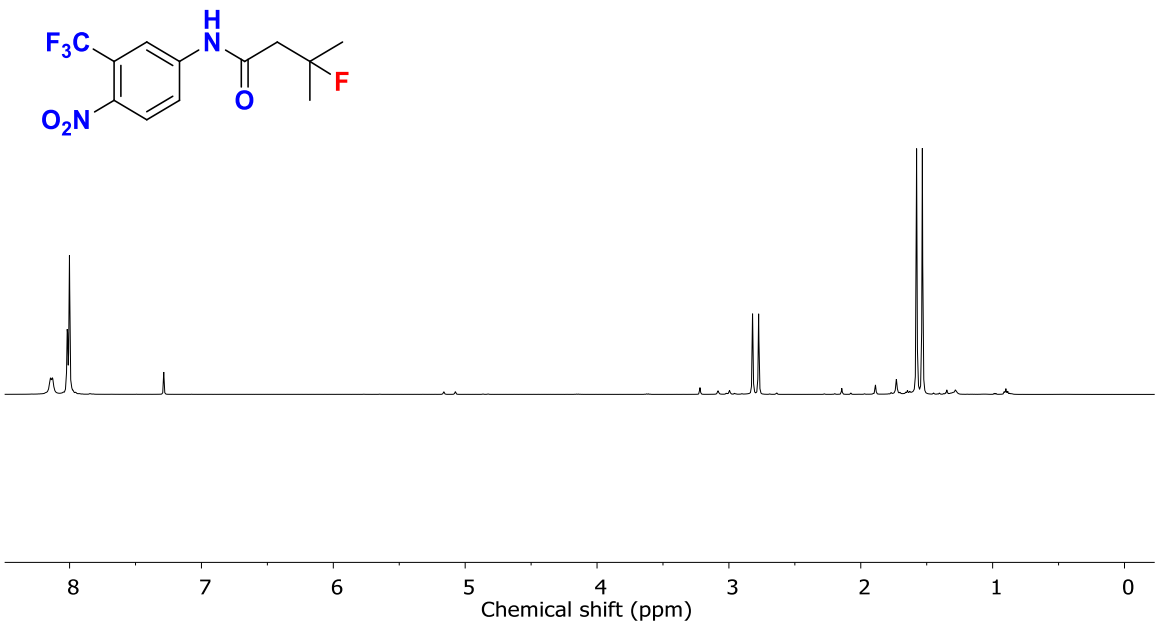

F
O
N
O
O
N
O
O
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

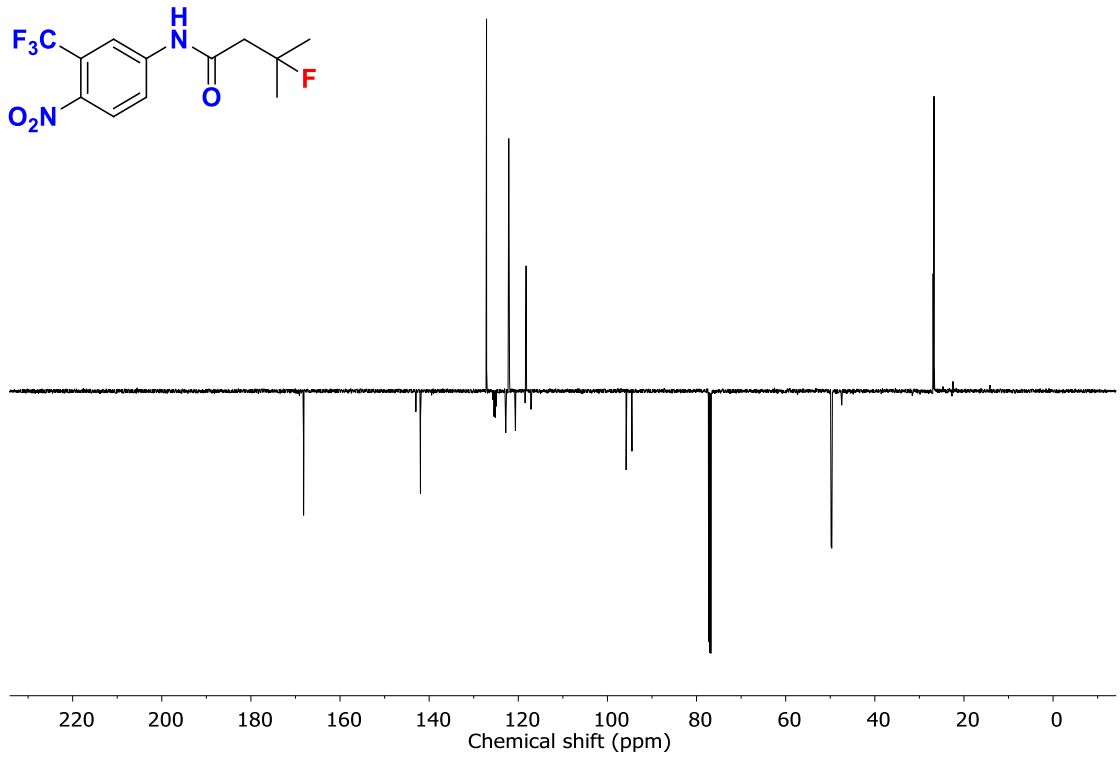

F
O
N
O
O
N
O
-165.5
-167.0
-168.5
-170.0
Chemical shift (ppm)
0
-50
-100
-150
-200
Chemical shift (ppm)

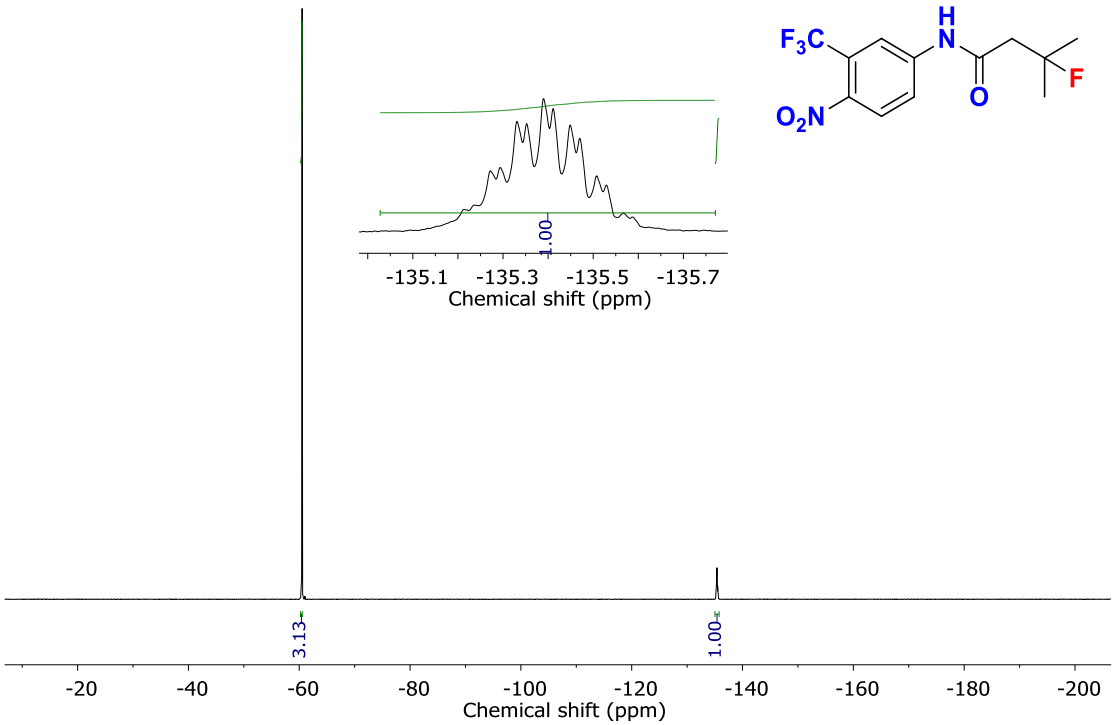

F
O
N
O
N
N
N
N
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

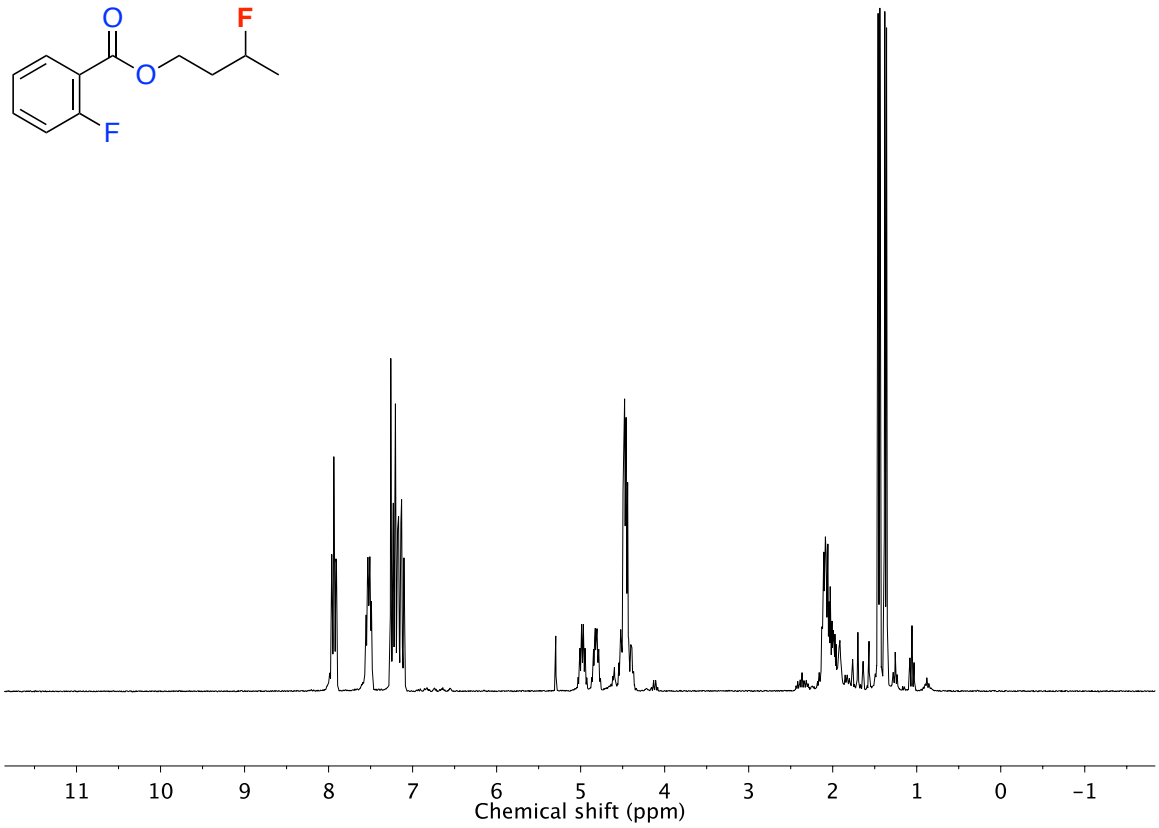

F
O
N
O
N
N
N
N
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

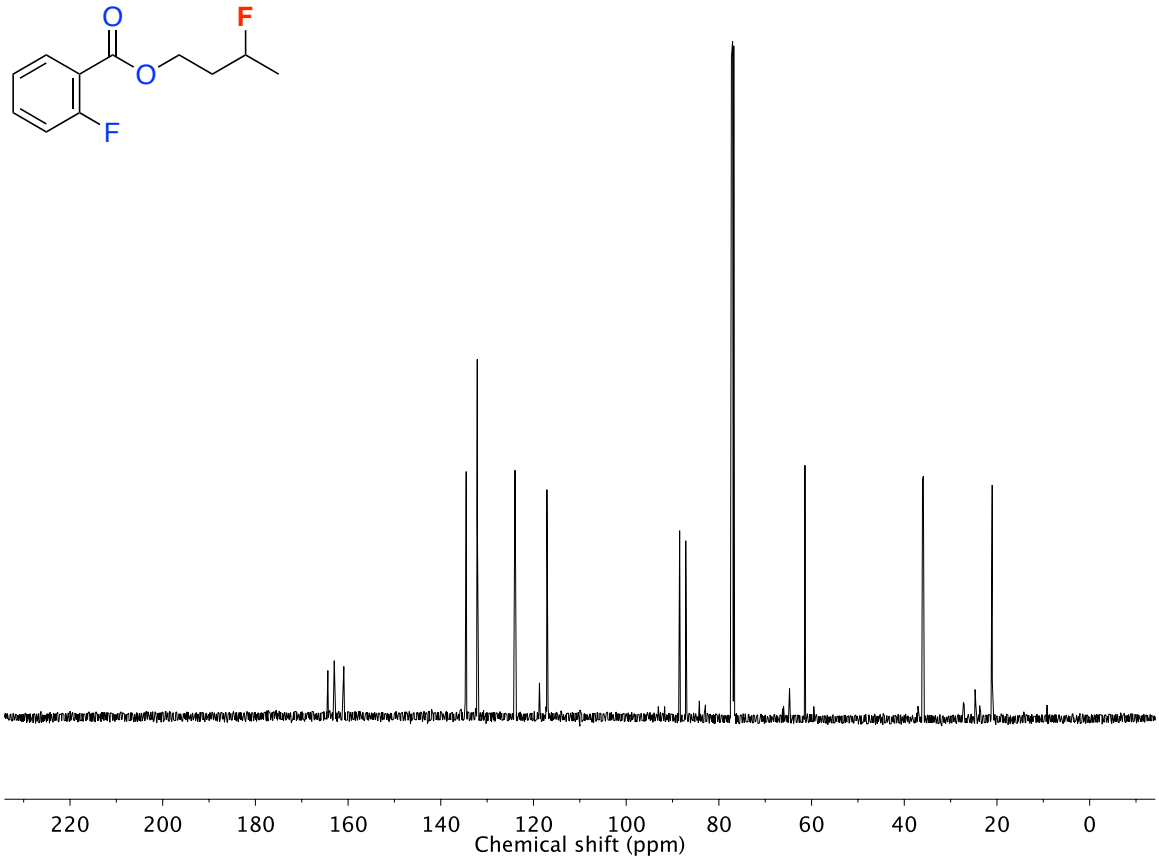

F
O
N
O
N
N
N
N
0
−50
−100
−150
−200
Chemical shift (ppm)

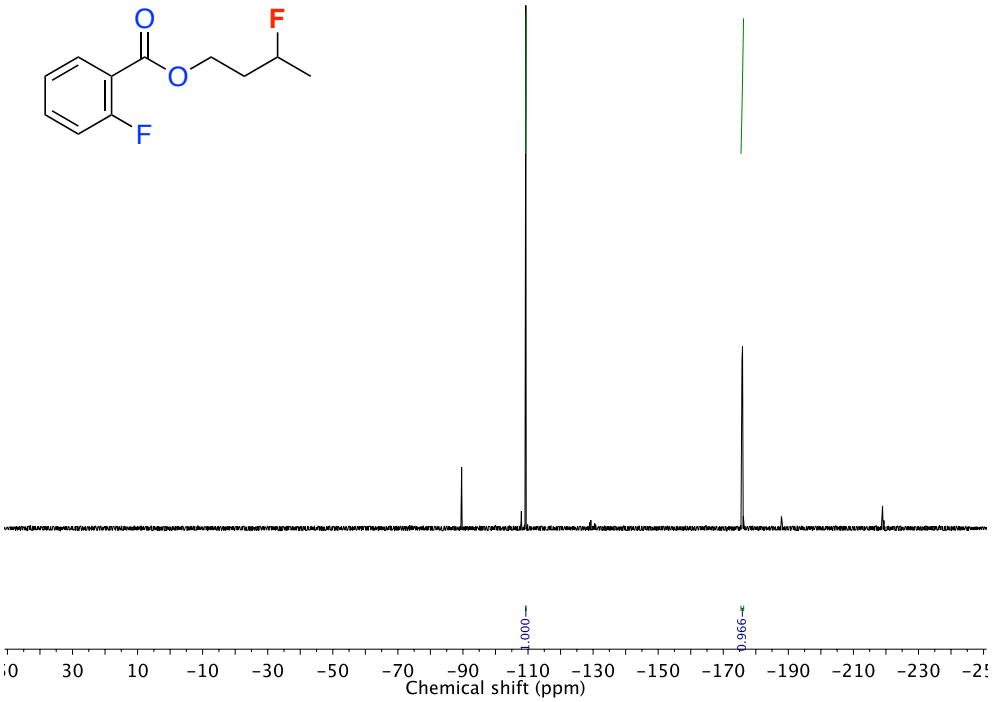

F3C
H
N
O
F
O2N
8
7
6
5
4
3
2
1
0
Chemical shift (ppm)

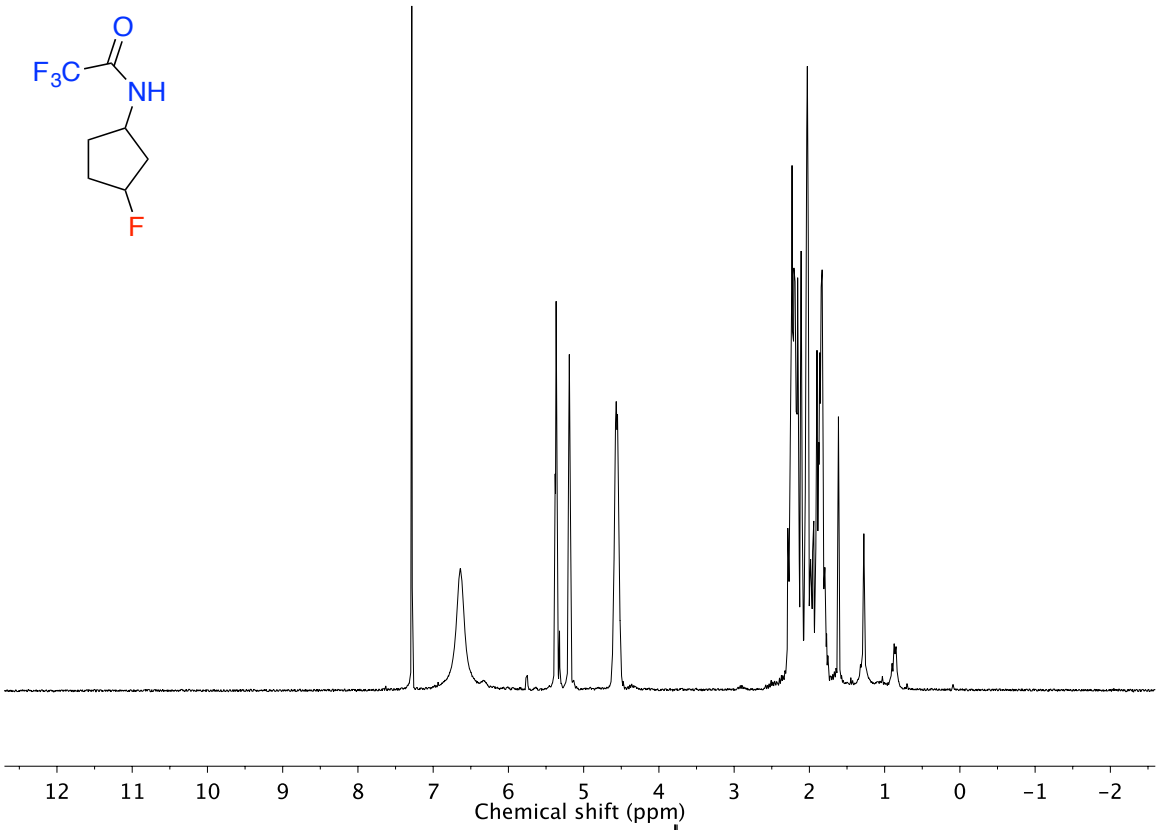

F3C
H
N
O
F
O2N
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

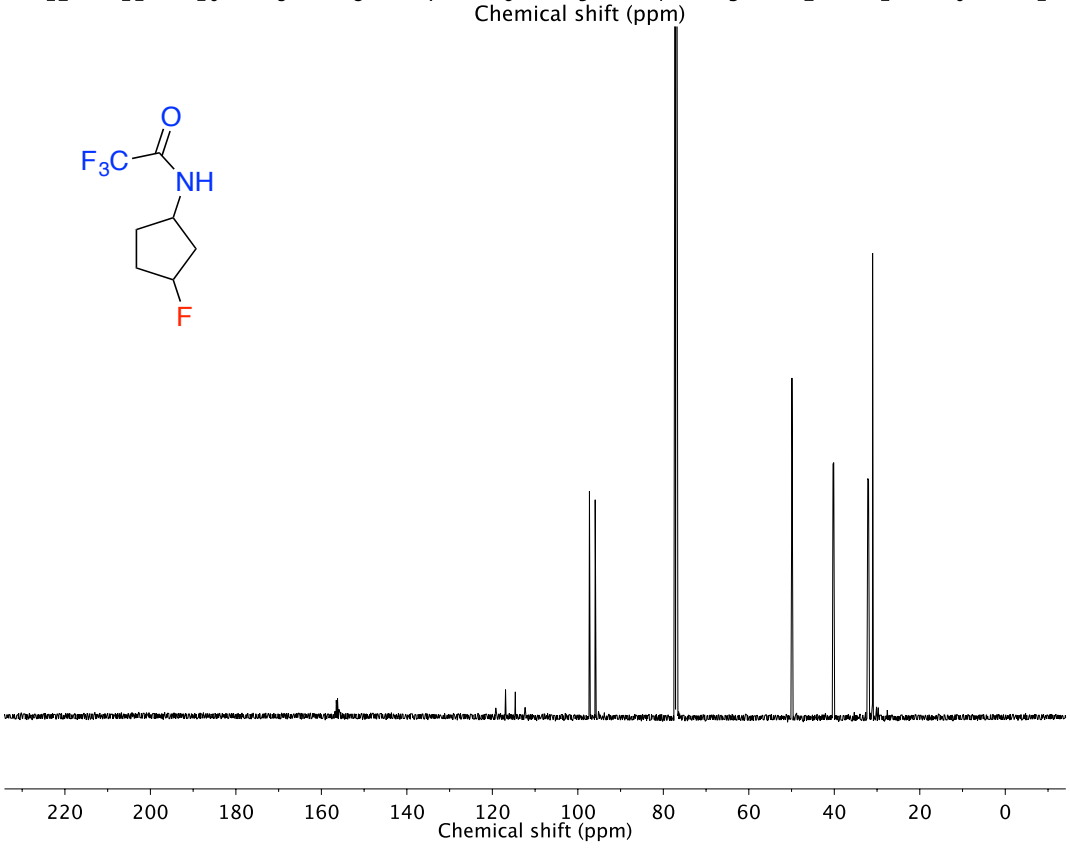

F3C
H
N
O2N
O
F
1.00
-135.1
-135.3
-135.5
-135.7
Chemical shift (ppm)
3.13
1.00
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
Chemical shift (ppm)

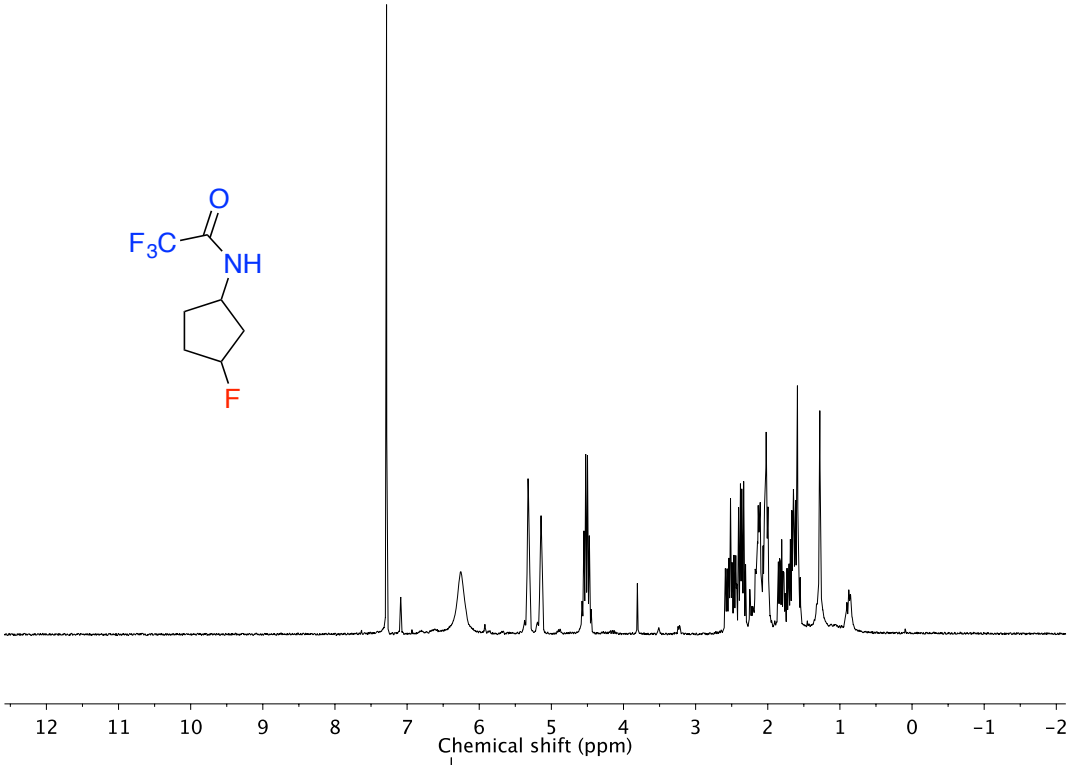

O
F
O
F
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

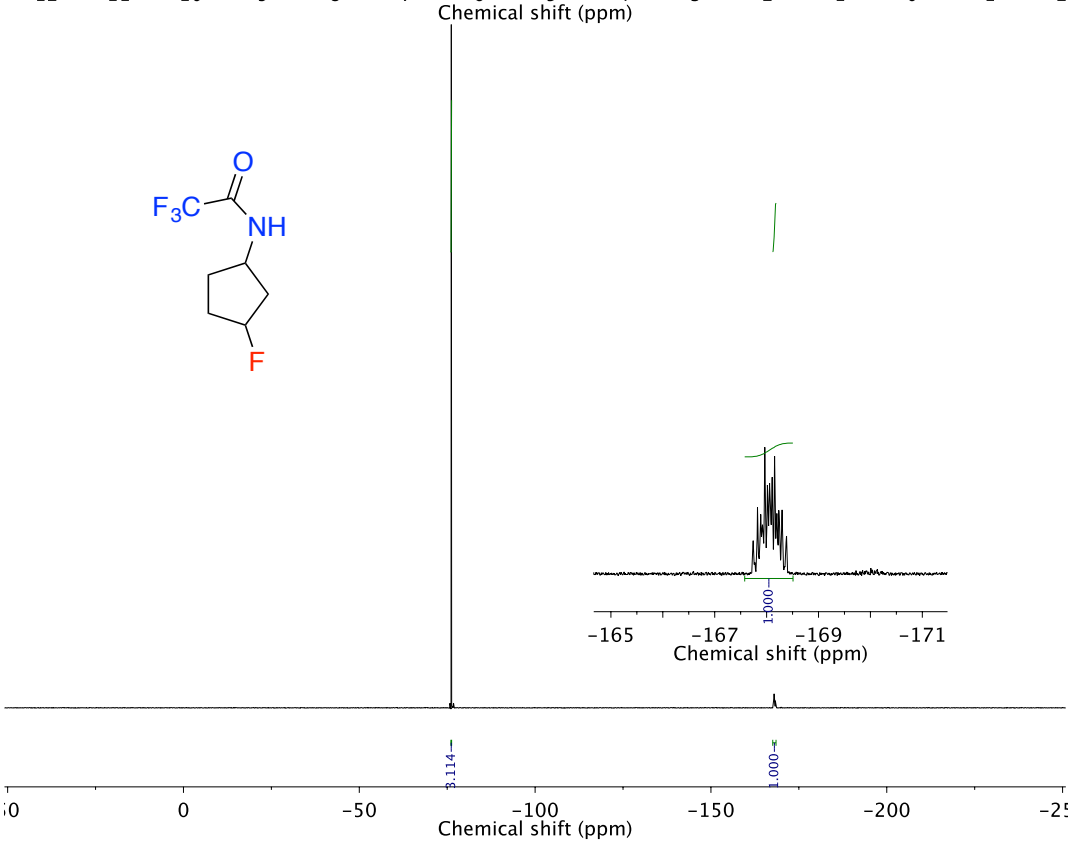

O
F
O
F
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)

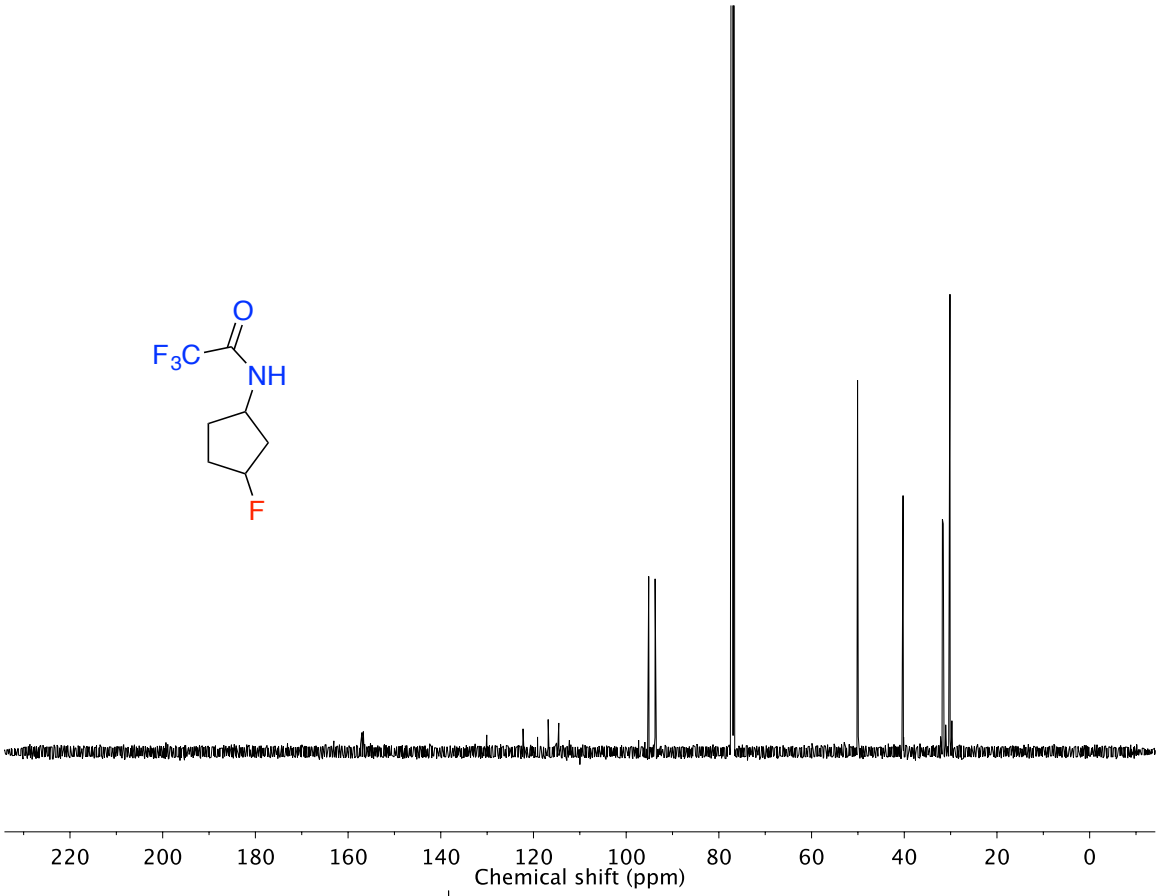

O
F
O
F
1.000
0.966
30
10
−10
−30
−50
−70
−90
−110
−130
−150
−170
−190
−210
−230
Chemical shift (ppm)

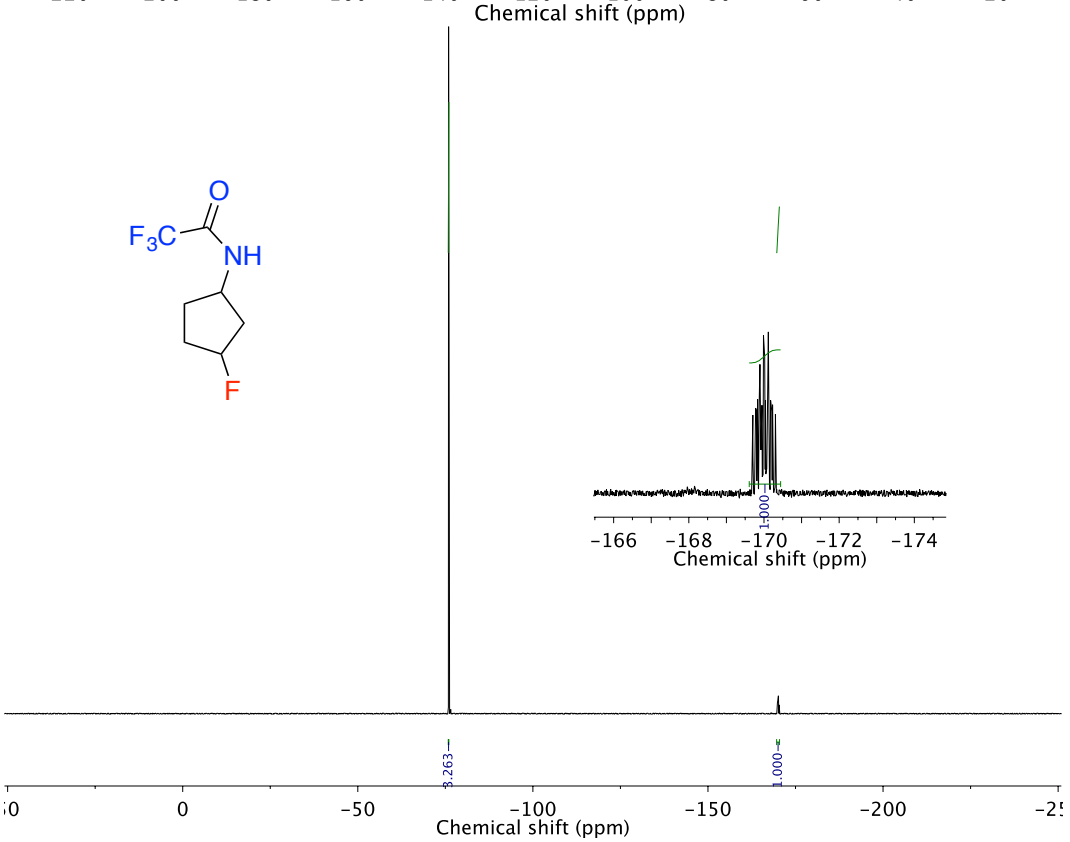

O
F3C
NH
F
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
Chemical shift (ppm)


O
F3C
NH
F
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


O
F3C
NH
F
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
Chemical shift (ppm)


O
F3C
NH
F
1.000
−165
−167
−169
−171
Chemical shift (ppm)
3.114
1.000
0
−50
−100
−150
−200
Chemical shift (ppm)


O
F3C
NH
F
220
200
180
160
140
120
100
80
60
40
20
0
Chemical shift (ppm)


O
F3C
NH
F
1.000
−166
−168
−170
−172
−174
Chemical shift (ppm)
3.263
1.000
0
−50
−100
−150
−200
Chemical shift (ppm)