Supporting Information

Fully Automated Radiosynthesis of [^{11}C]Guanidines for Cardiac PET Imaging

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Table of Contents

1. General Procedures and Materials and Methods

All the chemicals were purchased from commercially available suppliers and used without purification. Automated flash chromatography was performed with Biotage Isolera Prime system. NMR spectra were recorded with a Varian 400 MHz MR NMR (400.53 MHz for ^{1}H; 376.87 MHz for ^{19}F; 100 MHz for ^{13}C) in $CDCl_3$ or MeOH-d_4 at room temperature with tetramethylsilane (TMS) as an internal standard. Mass spectra were measured on an Agilent 6230 TOF HPLC-MS, Agilent Q-TOF HPLC-MS, or a Micromass VG 70-250-S Magnetic sector mass spectrometer employing the electrospray ionization (ESI) method.

2. General Chemistry

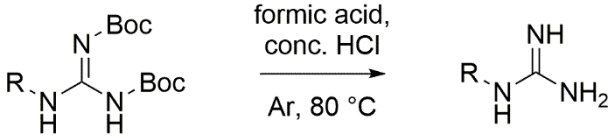
2.1 General Procedure for Guanidine Substrates

General Procedure for Pseudourea Addition

1 **3-Boc**

Amine **1** (1 equiv) was dissolved in a solution of anhydrous DMF (0.3 M) and triethylamine (5 equiv) and cooled to 0 °C. 1,3-bis(*tert*-butoxycarbonyl)-2-methyl-2-thipseudourea (1.3 equiv) was then added portionwise and the resulting mixture was allowed to warm to room temperature and stirred overnight. The mixture was then diluted with ethyl acetate, washed with saturated NH_4Cl, extracted with ethyl acetate (2x), washed with brine, dried over Na_2SO_4, and purified by flash silica gel chromatography.

General Procedure for Boc Deprotection



3-Boc **3**

Deprotection Method A:

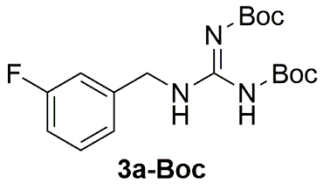
The *tert*-butyloxycarbonyl protected guanidine **3-Boc** (0.1 M) was dissolved in a solution of formic acid (10 equiv) and concentrated HCl (1 equiv). The resulting mixture was then stirred overnight under argon at 80 °C. The mixture was then concentrated under vacuum. The residue was then dissolved in methanol and concentrated under vacuum again. This resulting residue was finally purified by flash silica gel chromatography.

Deprotection Method B:

The *tert*-butyloxycarbonyl protected guanidine **3-Boc** (0.25 M) was dissolved in dioxane (5 equiv) and cooled to 0 °C. Then, 4N HCl in dioxane (1 equiv) was slowly added and stirred overnight.

The solid precipitate was filtered off and washed with Et_2O and dried under vacuum. The resulting residue was finally purified by flash silica gel chromatography.

2.1.1 MFBG Standard

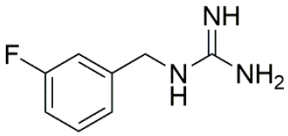


3a-Boc

*N′,N″-Bis(tert-butoxycarbonyl)-N-(3-fluorobenzyl)guanidine (**3a-Boc**)*.
The general pseudourea procedure was followed using 3-fluorobenzylamine (0.2000 g; 1.60 mmol). The crude product was purified by flash silica gel chromatography (7:1 Hex:EtOAc) to produce a white solid (0.3849 g; 66%).

^{1}H NMR (400 MHz; $CDCl_3$)/δ (ppm): 7.16 (td, *J* = 8.0, 5.9 Hz, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.91 (dt, *J* = 9.6, 2.1 Hz, 1H), 6.84 (td, *J* = 8.5, 2.6 Hz, 1H), 4.51 (d, *J* = 5.4 Hz, 2H), 1.39 (s, 9H), 1.36 (s, 9H); **^{13}C NMR** (100 MHz; $CDCl_3$)/δ (ppm): 163.42, 162.82 (d, *J* = 245 Hz), 156.10, 153.04, 139.92 (d, *J* = 7 Hz), 130.10 (d, *J* = 8 Hz), 123.09 (d, *J* = 2 Hz), 114.50 (d, *J* = 15 Hz), 114.29 (d, *J* = 14 Hz), 83.05, 79.14, 44.09, 28.14, 27.87; **^{19}F NMR** (376 MHz; $CDCl_3$)/δ (ppm): -112.60. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{18}H_{27}FN_3O_4$: 368.1986; found 368.1983.

Note: Peaks corresponding to the NH protons of the guanidine group were not observed.



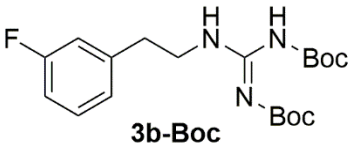
3a

*1-(3-fluorobenzyl)guanidine (**3a**)*.
Deprotection Method A was followed using **3a-Boc** (0.3849 g; 1.05 mmol). The crude product was purified by flash silica gel chromatography (20% MeOH in DCM) to produce a white solid (0.1781 g; 82%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 7.40 (td, *J* = 8.0, 5.9 Hz, 1H), 7.17 (m, 1H), 7.10 (dt, *J* = 9.8, 2.1 Hz, 1H), 7.04 (td, *J* = 8.6, 2.6 Hz, 1H), 4.45 (s, 2H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 163.00 (d, *J* = 244 Hz), 157.38, 139.24 (d, *J* = 7 Hz), 130.35, 122.76 (d, *J* = 3 Hz), 114.24 (d, *J* = 21 Hz), 113.71 (dd, *J* = 23, 5 Hz), 43.92; **^{19}F NMR** (376 MHz; MeOH-d_4)/δ (ppm): -114.65. **HRMS (ESI)** $[M+H]^+$ Calculated for $C_8H_{11}FN_3$: 168.0932; found 168.0930.

Note: Peaks corresponding to the NH protons of the guanidine group were not observed.

2.1.2 MFPG Standard

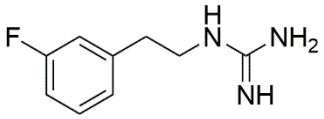


3b-Boc

*N′,N″-Bis(tert-butoxycarbonyl)-N-(3-fluorophenethyl)guanidine (**3b-Boc**)*.
The general pseudourea procedure was followed using 3-fluorophenethylamine (0.2000 g; 1.44 mmol). The crude product was purified by flash silica gel chromatography (7:1 Hex:EtOAc) to produce a white solid (0.4032 g; 73%).

^{1}H NMR (400 MHz; $CDCl_3$)/δ (ppm): 7.14 (dd, *J* = 14.1, 7.5 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.82 (m, 2H), 3.56 (q, *J* = 6.6 Hz, 2H), 2.76 (t, *J* = 7.2 Hz, 2H), 1.41 (s, 9H), 1.37 (s, 9H); **^{13}C NMR** (100 MHz; $CDCl_3$)/δ (ppm): 163.46, 162.79 (d, *J* = 245 Hz), 156.03, 153.01, 140.99 (d, *J* = 7 Hz), 129.87, 124.33 (d, *J* = 3 Hz), 115.60 (d, *J* = 21 Hz), 113.33 (d, *J* = 21 Hz), 82.88, 79.00, 41.74, 34.92 (d, *J* = 2 Hz), 28.17 (d, *J* = 6 Hz), 27.86 (d, *J* = 6 Hz); **^{19}F NMR** (376 MHz; $CDCl_3$)/δ (ppm): -113.32. **HRMS (ESI)** $[M+H]^+$ Calculated for $C_{19}H_{29}FN_3O_4$: 382.2142; found 382.2147.

Note: Peaks corresponding to the NH protons of the guanidine group were not observed.



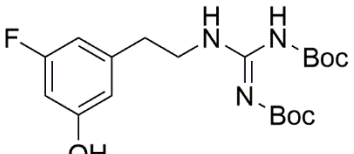
3b

*1-(3-fluorophenethyl)guanidine (**3b**)*.
Deprotection Method A was followed using **3b-Boc** (0.4802 g; 1.26 mmol). The crude product was purified by flash silica gel chromatography (20% MeOH in DCM) to produce a yellow syrup (0.2638 g; 96%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 7.29 (td, *J* = 8.0, 6.1 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 7.05 (dt, *J* = 10.1, 2.1 Hz, 1H), 6.93 (td, *J* = 8.6, 2.6 Hz, 1H), 3.47 (m, 2H), 2.89 (t, *J* = 7.1 Hz, 2H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 162.88 (d, *J* = 243 Hz), 157.21, 140.83 (d, *J* = 7 Hz), 130.03 (d, *J* = 8 Hz), 124.58 (d, *J* = 2 Hz), 115.34 (d, *J* = 22 Hz), 113.08 (d, *J* = 21 Hz), 42.18, 34.30; **^{19}F NMR** (376 MHz; MeOH-d_4)/δ (ppm): -115.02. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_9H_{13}FN_3$: 182.1088; found 182.1084.

Note: Peaks corresponding to the NH protons of the guanidine group were not observed.

2.1.3 5F-MHPG Standard

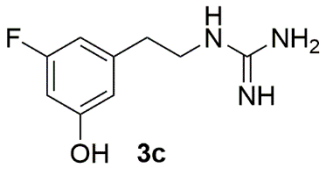


3c-Boc

*N',N''-Bis(tert-butoxycarbonyl)-N-(3-fluoro-5-hydroxyphenethyl)guanidine (**3c-Boc**)*.
The general pseudourea procedure was followed using 3-fluoro-5-hydroxyphenethylamine (0.0500 g; 0.32 mmol). The crude product was purified by flash silica gel chromatography (3:1 Hex:EtOAc) to produce a white solid (0.0779 g; 61%).

^{1}H NMR (400 MHz; $CDCl_3$)/δ (ppm): 6.48 (dt, *J* = 10.4, 2.2 Hz, 1H), 6.44 (t, *J* = 1.8 Hz, 1H), 6.33 (dt, *J* = 9.5, 1.8 Hz, 1H), 3.51 (dd, *J* = 15.7, 5.7 Hz, 2H), 2.72 (m, 2H), 1.49 (s, 9H), 1.45 (s, 9H); **^{13}C NMR** (100 MHz; $CDCl_3$)/δ (ppm): 163.29 (d, *J* = 243 Hz), 162.93, 158.07 (d, *J* = 12 Hz), 156.31, 153.15, 140.83 (d, *J* = 10 Hz), 111.73 (d, *J* = 3 Hz), 106.72 (d, *J* = 18 Hz), 101.33 (d, *J* = 25 Hz), 83.51, 80.00, 41.81, 35.12, 28.14, 28.01; **^{19}F NMR** (376 MHz; $CDCl_3$)/δ (ppm): -113.23. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{19}H_{29}FN_3O_5$: 398.2086; found 398.2096.

Note: Peaks corresponding to the NH protons of the guanidine group and the OH group were not observed.



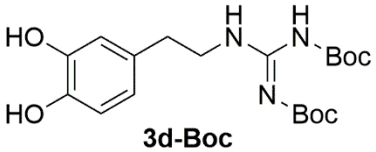
3c

*1-(3-fluoro-5-hydroxyphenethyl)guanidine (**3c**)*.
Deprotection Method A was followed using **3c-Boc** (0.0779 g; 0.20 mmol). The crude product was purified by flash silica gel chromatography (30% MeOH in DCM) to produce a clear syrup (0.0168 g; 43%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 6.48 (m, 2H), 6.37 (d, *J* = 10.7 Hz, 1H), 3.42 (t, *J* = 7.1 Hz, 2H), 2.79 (t, 7.0 Hz, 2H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 163.7 (d, *J* = 242 Hz), 159.03, 157.14, 141.11, 111.42, 105.80, 100.66, 41.90, 34.35; **^{19}F NMR** (376 MHz; MeOH-d_4)/δ (ppm): -114.85. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_9H_{13}FN_3O$: 198.1037; found 198.1046.

Note: Peaks corresponding to the NH protons of the guanidine group and the OH group were not observed.

2.1.4 DOPG Standard

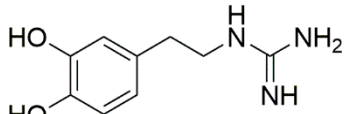


3d-Boc

*N',N''-Bis(tert-butoxycarbonyl)-N-3,4-dihydroxyphenethylguanidine (**3d-Boc**)*.
The general pseudourea procedure was followed using 4-(2-aminoethyl)benzene-1,2-diol (0.2000 g; 1.31 mmol). The crude product was purified by flash silica gel chromatography (1:1 Hex:EtOAc) to produce a white solid (0.3900 g; 75%).

^{1}H NMR (400 MHz; $CDCl_3$)/δ (ppm): 6.74 (d, *J* = 8.0 Hz, 1H), 6.64 (d, *J* = 2.0 Hz, 1H), 6.50 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.50 (q, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 1.47 (s, 9H), 1.43 (s, 9H); **^{13}C NMR** (100 MHz; $CDCl_3$)/δ (ppm): 162.98, 156.26, 153.05, 144.30, 142.95, 130.23, 120.48, 115.56 (d, *J* = 3 Hz), 115.36, 83.35, 79.88, 42.61, 34.52, 28.14, 28.00. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{19}H_{30}N_3O_6$: 396.2135; found 396.2138.

Note: Peaks corresponding to the NH protons of the guanidine group and the OH groups were not observed.



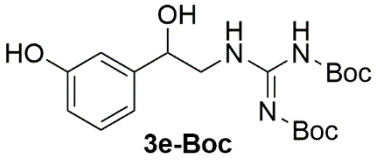
3d

*1-(3,4-dihydroxyphenethyl)guanidine (**3d**)*.
Deprotection Method A was followed using **3d-Boc** (0.3900; 0.99 mmol). Crude product was purified by flash chromatography (20% MeOH in DCM) to give a white solid (0.1445 g; 63%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 6.72 (m, 2H), 6.57 (dd, *J* = 8.0, 2.1 Hz, 1H), 3.38 (t, *J* = 7.1 Hz, 2H), 2.72 (t, *J* = 7.1 Hz, 2H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 157.11, 144.93, 143.64, 129.41, 119.83, 115.58, 115.18, 42.64, 33.93. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_9H_{14}N_3O_2$: 196.1086; found 196.1087.

Note: Peaks corresponding to the NH protons of the guanidine group and the OH groups were not observed.

2.1.5 GMO Standard

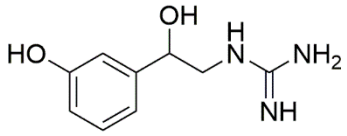


3e-Boc

*N',N''-Bis(tert-butoxycarbonyl)-N-(2-hydroxy-2-(3-hydroxyphenyl)ethyl)guanidine (**3e-Boc**)*.
The general pseudourea procedure was followed using 3-(2-amino-1-hydroxyethyl)phenol (0.2000 g; 1.31 mmol). The crude product was purified by flash silica gel chromatography (2:1 Hex:EtOAc) to produce a white solid (0.4837 g; 84%).

^{1}H NMR (400 MHz; $CDCl_3$)/δ (ppm): 7.10 (t, *J* = 7.8 Hz, 1H), 6.81 (m, 2H), 6.73 (ddd, *J* = 8.1, 2.5, 1.0 Hz, 1H), 4.74 (dd, *J* = 8.2, 2.7 Hz, 1H), 3.62 (ddd, *J* = 14.2, 6.3, 2.8 Hz, 1H), 3.51 (ddd, *J* = 14.2, 8.2, 4.6 Hz, 1H), 1.46 (s, 9H), 1.44 (s, 9H); **^{13}C NMR** (100 MHz; $CDCl_3$)/δ (ppm): 162.75 (d, *J* = 4 Hz), 162.49, 157.01 (d, *J* = 35 Hz), 152.82, 143.30, 129.38, 117.19, 114.91, 113.07, 83.53, 79.80, 73.81 (d, *J* = 7 Hz), 49.10, 28.14, 27.98. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{19}H_{29}N_3O_6$: 396.2135; found 396.2140.

Note: Peaks corresponding to the NH protons of the guanidine group and the OH groups were not observed.



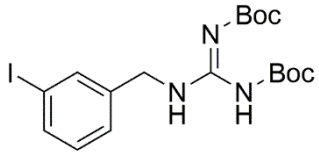
3e

*1-(2-hydroxy-2-(3-hydroxyphenyl)ethyl)guanidine (**3e**)*.
Deprotection Method A was followed using **3e-Boc** (0.4837 g; 1.22 mmol). The crude product was purified by flash silica gel chromatography (20% MeOH in DCM) to produce a white solid (0.0344 g; 12%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 7.17 (t, J = 8.1 Hz, 1H), 6.87 (m, 2H), 6.71 (m, 1H), 4.76 (dd, J = 7.6, 3.7 Hz, 1H), 3.42 (dd, J = 13.9, 3.8 Hz, 1H), 3.32 (m, 1H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 157.96, 157.30, 143.23, 129.15, 116.76, 114.35, 112.54, 71.91 (d, J = 11 Hz), 48.61. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_9H_{14}N_3O_2$: 196.1086; found 196.1082.

Note: Peaks corresponding to the NH protons of the guanidine group and the OH groups were not observed.

2.1.6 MIBG Standard

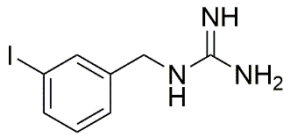


3f-Boc

*N',N''-Bis(tert-butoxycarbonyl)-N-(3-iodobenzyl)guanidine (**3f-Boc**)*.
The general pseudourea procedure was followed using 3-iodobenzylamine (0.2000 g; 0.86 mmol). The crude product was purified by flash silica gel chromatography (3:1 Hex:EtOAc) to produce a clear syrup-like solid (0.4385 g).

^{1}H NMR (400 MHz; $CDCl_3$)/δ (ppm): 7.58 (t, J = 1.7 Hz, 1H), 7.50 (dt, J = 7.9, 1.3 Hz, 1H), 7.18 (d, J = 7.7 Hz, 1H), 6.96 (t, J = 7.8 Hz, 1H), 4.48 (d, J = 5.4 Hz, 2H), 1.42 (s, 9H), 1.39 (s, 9H); **^{13}C NMR** (100 MHz; $CDCl_3$)/δ (ppm): 163.41, 156.04, 153.04, 139.74, 136.77 (d, J = 6 Hz), 136.58 (d, J = 3 Hz), 130.34, 126.98, 94.56, 83.13, 79.23, 43.94, 28.27, 28.02. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{18}H_{27}IN_3O_4$: 476.1046; found 476.1039.

Note: Peaks corresponding to the NH protons of the guanidine group were not observed.



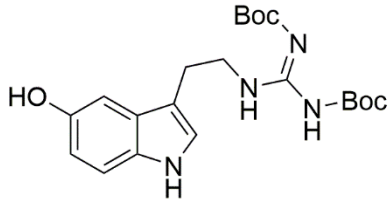
3f

*1-(3-iodobenzyl)guanidine (**3f**)*.
Deprotection Method A was followed using **3f-Boc** (0.4385 g; 0.92 mmol). The crude product was purified by flash silica gel chromatography (20% MeOH in DCM) to produce a white solid (0.2675 g; 93%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 7.73 (t, J = 1.8 Hz, 1H), 7.64 (dt, J = 7.9, 1.4 Hz, 1H), 7.36 (ddd, J = 7.7, 1.8, 1.0 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 4.42 (s, 2H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 157.28 (t, J = 5 Hz), 138.88, 136.73 (d, J = 6 Hz), 135.97 (d, J = 6 Hz), 130.42 (d, J = 3 Hz), 126.42 (d, J = 4 Hz), 94.20, 43.79. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_8H_{11}IN_3$: 275.9998; found 275.9994.

Note: Peaks corresponding to the NH protons of the guanidine group were not observed.

2.1.7 HTG Standard

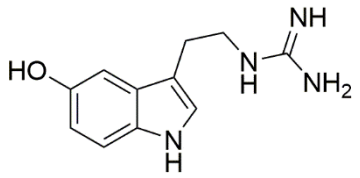


3g-Boc

*N′,N″-Bis(tert-butoxycarbonyl)-N-(2-(5-hydroxy-1H-indol-3-yl)ethyl)guanidine (**3g-Boc**)*.
The general pseudourea procedure was followed using serotonin (0.2000 g; 1.13 mmol). The crude product was purified by flash silica gel chromatography (2% MeOH in DCM) to produce a clear gel (0.3147 g; 67%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 7.15 (dd, J = 8.6, 0.6 Hz, 1H), 7.05 (s, 1H), 6.92 (dd, J = 2.3, 0.6 Hz, 1H), 6.66 (dd, J = 8.7, 2.4 Hz, 1H), 3.63 (t, J = 6.9 Hz, 2H), 2.93 (t, J = 6.9 Hz, 2H), 1.47 (s, 18H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 163.15, 156.08, 152.58, 149.80, 131.71, 127.85, 123.18 (d, J = 3 Hz), 111.32, 111.09, 110.34, 102.09, 82.91, 78.93, 41.04, 27.23, 26.81, 24.44. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{21}H_{31}N_4O_5$: 419.2294; found 419.2289.

Note: Peaks corresponding to the NH protons of the guanidine group and indole ring as well as the OH group were not observed.



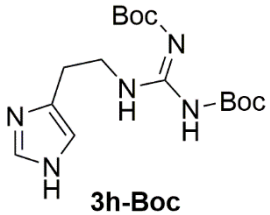
3g

*1-(2-(5-hydroxy-1H-indol-3-yl)ethyl)guanidine (**3g**)*.
Deprotection Method B was followed using **3g-Boc** (0.1886 g; 0.45 mmol). The crude product was purified by flash silica gel chromatography (30% MeOH in DCM) to produce an opaque solid (0.0302 g; 26%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 7.18 (dd, J = 8.7, 0.6 Hz, 1H), 7.08 (s, 1H), 6.92 (dd, J = 2.3, 0.6 Hz, 1H), 6.68 (dd, J = 8.7, 2.3 Hz, 1H), 3.47 (t, J = 6.9 Hz, 2H), 2.95 (t, J = 6.9 Hz, 2H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 157.18, 149.88 (d, J = 3 Hz), 131.72, 127.75, 123.40 (d, J = 63 Hz), 111.43 (d, J = 63 Hz), 109.66, 102.05, 41.60, 24.38. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{11}H_{15}N_4O$: 219.1246; found 219.1237.

Note: Peaks corresponding to the NH protons of the guanidine group and indole ring as well as the OH group were not observed.

2.1.8 IEG Standard

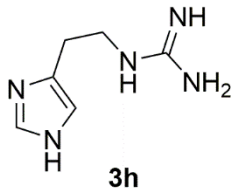


3h-Boc

*N',N''-Bis(tert-butoxycarbonyl)-N-(2-(1H-imidazol-4-yl)ethyl)guanidine (**3h-Boc**)*.
The general pseudourea procedure was followed using histamine (0.2000 g; 1.80 mmol). The crude product was purified by flash silica gel chromatography (10% MeOH in DCM) to produce an off-white crystal (0.2979 g; 47%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 7.60 (d, J = 1.2 Hz, 1H), 6.87 (d, J = 1.2 Hz, 1H), 3.60 (t, J = 7.0 Hz, 2H), 2.84 (t, J = 7.1 Hz, 2H), 1.48 (s, 9H), 1.46 (s, 9H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 163.08 (d, J = 2 Hz), 156.00, 152.66, 134.99 (d, J = 6 Hz), 134.03, 117.15, 82.94, 78.72, 40.27, 27.59, 27.22, 26.30. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{16}H_{28}N_5O_4$: 354.2141; found 354.2133.

Note: Peaks corresponding to the NH protons of the guanidine group and imidazole ring were not observed.



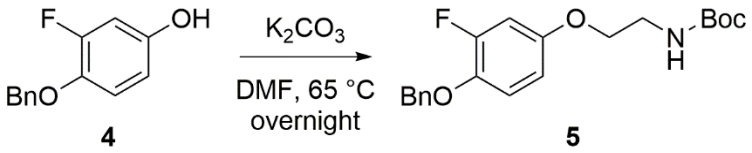
3h

*1-(2-(1H-imidazol-4-yl)ethyl)guanidine (**3h**).*
Deprotection Method B was followed using **3h-Boc** (0.2979 g; 0.84 mmol). The crude product was purified by flash silica gel chromatography (20% MeOH in DCM) to produce a white solid (0.1483 g; 93%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 8.62 (s, 1H), 7.38 (s, 1H), 3.57 (t, J = 7.0 Hz, 2H), 3.02 (t, J = 7.0 Hz, 2H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 157.26 (d, J = 5 Hz), 134.02, 131.13, 116.82, 40.15, 24.45. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_6H_{12}N_5$: 154.1087; found 154.1081.

Note: Peaks corresponding to the NH protons of the guanidine group and imidazole ring were not observed.

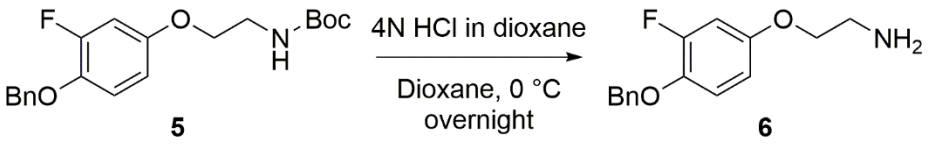
2.2 Synthesis of 3F-PHPOG Standard and Precursor



4 **5**

*Tert-butyl (2-(4-(benzyloxy)-3-fluorophenoxy)ethyl)carbamate (**5**).*
4-(benzyloxy)-3-fluorophenol **4** (0.2000 g; 0.92 mmol; 1 equiv), 2-(boc-amino)ethyl bromide (0.2465 g; 1.10 mmol; 1.2 equiv), and potassium carbonate (1.3351 g; 9.66 mmol; 10.5 equiv) were dissolved in DMF (3.1 mL) and stirred at 65 ℃ overnight. The reaction mixture was quenched with water and the solid was filtered off. The product was then extracted with ethyl acetate (3x), washed with water (2x), washed with brine (1x), dried over sodium sulfate, and purified by flash silica gel chromatography (4:1 Hex:EtOAc). The product was a clear syrup-like solid (0.2784 g; 84% yield).

^{1}H NMR (400 MHz; $CDCl_3$)/δ (ppm): 7.36 (m, 5H), 6.88 (t, J = 9.2 Hz, 1H), 6.67 (dd, J = 12.5, 2.9 Hz, 1H), 6.52 (ddd, J = 9.0, 3.0, 1.5 Hz, 1H), 5.04 (s, 2H), 3.90 (t, J = 5.2 Hz, 2H), 3.47 (t, J = 2.7 Hz, 2H), 1.45 (s, 9H); **^{13}C NMR** (100 MHz; $CDCl_3$)/δ (ppm): 155.96, 153.44 (d, J = 245 Hz), 153.43 (d, J = 9 Hz), 140.80 (d, J = 11 Hz), 136.83, 128.55 (d, J = 35 Hz), 128.06 (d, J = 35 Hz), 127.58 (d, J = 33 Hz), 117.41, 109.26 (d, J = 18 Hz), 104.01 (dd, J = 21, 8 Hz), 79.42, 72.41, 67.68, 40.00, 28.40 (d, J = 17 Hz); **^{19}F NMR** (376 MHz; $CDCl_3$)/δ (ppm): -130.33. **HRMS (ESI)** $[M + Na]^+$ Calculated for $C_{20}H_{24}FNO_4Na$: 384.1587; found 384.1585.

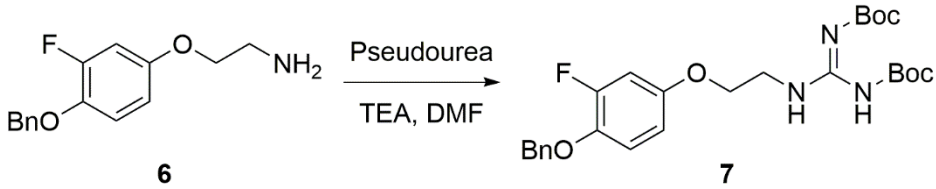


5 **6**

*2-(4-(benzyloxy)-3-fluorophenoxy)ethan-1-amine (**6**).*
Tert-butyl (2-(4-(benzyloxy)-3-fluorophenoxy)ethyl)carbamate **5** (0.2784 g; 0.77 mmol) was dissolved in dioxane (0.55 mL) and cooled to 0 °C. Then, 4N HCl in dioxane (2.57 mL) was slowly added and stirred overnight. The solid precipitate was filtered off and washed with Et_2O and dried under vacuum. The crude solid was then purified by flash silica gel chromatography (20% MeOH in DCM). The product was a beige solid (0.1297 g, 57% yield).

^{1}H NMR (400 MHz; $CDCl_3$)/δ (ppm): 7.38 (m, 5H), 7.04 (t, J = 9.3 Hz, 1H), 6.83 (dd, J = 12.7, 2.9 Hz, 1H), 6.70 (ddd, J = 9.0, 3.0, 1.6 Hz, 1H), 5.05 (s, 2H), 4.11 (t, J = 5.1 Hz, 2H), 3.25 (t, J = 5.0 Hz, 2H); **^{13}C NMR** (100 MHz; $CDCl_3$)/δ (ppm): 153.26 (d, J = 244 Hz), 152.94 (d, J = 10 Hz), 141.06 (d, J = 11 Hz), 136.97, 128.28, 127.73 (d, J = 35 Hz), 127.20, 117.14 (d, J = 26 Hz), 109.30 (d, J = 4 Hz), 103.73 (dd, J = 24, 10 Hz), 71.83, 65.52, 39.14; **^{19}F NMR** (376 MHz; $CDCl_3$)/δ (ppm): -132.66. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{15}H_{17}FNO_2$: 262.1238; found 262.1229.

Note: Peaks corresponding to the NH protons of the amine were not observed.



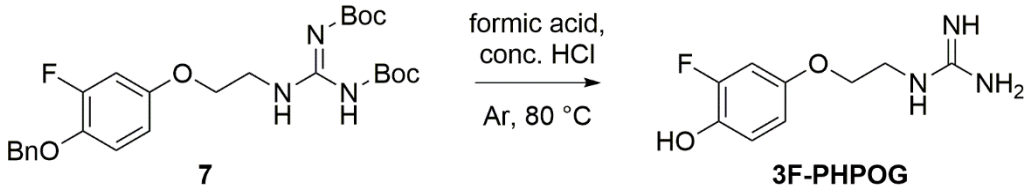
6 **7**

*N',N''-Bis(tert-butoxycarbonyl)-N-(2-(4-(benzyloxy)-3-fluorophenoxy)ethyl)guanidine (**7**).*
2-(4-(benzyloxy)-3-fluorophenoxy)ethan-1-amine **6** (0.1297 g; 0.44 mmol; 1 equiv) was dissolved in a solution of anhydrous DMF (1.47 mL) and triethylamine (0.31 mL; 2.2 mmol; 5 equiv) and cooled to 0 °C. 1,3-bis(*tert*-butoxycarbonyl)-2-methyl-2-thipseudourea (0.1655 g; 0.57 mmol; 1.3 equiv) was then added portionwise and the resulting mixture was allowed to warm to room temperature and stirred overnight. The mixture was then diluted with ethyl acetate, washed with saturated NH_4Cl, extracted with ethyl acetate (2x), washed with brine, dried over Na_2SO_4, and purified by flash silica gel chromatography (7:1 Hex:EtOAc). The product was a clear syrup-like solid (0.1679 g; 76%).

^{1}H NMR (400 MHz; $CDCl_3$)/δ (ppm): 7.36 (m, 5H), 6.88 (t, J = 9.2 Hz, 1H), 6.73 (dd, J = 12.5, 2.9 Hz, 1H), 6.57 (ddd, J = 9.0, 3.0, 1.5 Hz, 1H), 5.04 (s, 2H), 3.99 (t, J = 5.2 Hz, 2H), 3.79 (q, J = 5.31 Hz, 2H), 1.50 (s, 9H), 1.48 (s, 9H); **^{13}C NMR** (100 MHz; $CDCl_3$)/δ (ppm): 163.45, 156.34, 153.46 (d, J = 246 Hz), 153.24 (d, J = 10 Hz), 153.03, 140.94 (d, J = 11 Hz), 136.80, 128.52 (d, J = 40 Hz), 128.03 (d, J = 41 Hz), 127.53 (d, J = 38 Hz), 117.45, 109.46, 104.45, 83.17, 79.32, 72.49, 66.96, 40.02, 28.28 (d, J = 19 Hz), 28.03 (d, J = 19 Hz); **^{19}F NMR** (376 MHz; $CDCl_3$)/δ (ppm): -130.36. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_{26}H_{35}FN_3O_6$: 504.2504; found 504.2501.

Note: Peaks corresponding to the NH protons of the guanidine group were not observed.

2.1.1 3F-PHPOG Standard (3i)



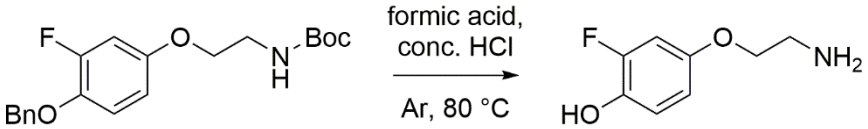
7 **3F-PHPOG**

*1-(2-(4-(hydroxy)-3-fluorophenoxy)ethyl)guanidine (**3F-PHPOG**).*
N',N''-Bis(tert-butoxycarbonyl)-N-(2-(4-(benzyloxy)-3-fluorophenoxy)ethyl)guanidine **7** (0.1679 g; 0.33 mmol) was dissolved in a solution of formic acid (3.0 mL; 10 equiv) and concentrated HCl (0.3 mL; 1 equiv). The resulting mixture was then stirred overnight under argon at 80 °C. The yellow mixture was then concentrated under vacuum. The residue was then dissolved in methanol and concentrated under vacuum again. This resulting residue was finally purified by flash silica gel chromatography (20% MeOH in DCM). The product was a white solid (0.0604 g; 86%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 6.84 (dd, J = 9.9, 8.8 Hz, 1H), 6.73 (dd, J = 12.5, 2.9 Hz, 1H), 6.61 (ddd, J = 8.9, 2.9, 1.4 Hz, 1H), 4.03 (t, J = 5.0 Hz, 2H), 3.57 (t, J = 5.0 Hz, 2H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 157.63, 151.60 (d, J = 9 Hz), 151.43 (d, J = 240 Hz), 138.99, 117.64 (d, J = 6 Hz), 109.87, 103.33, 66.81, 40.85; **^{19}F NMR** (376 MHz; MeOH-d_4)/δ (ppm): -136.43. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_9H_{13}FN_3O_2$: 214.0986; found 214.0985.

Note: Peaks corresponding to the NH protons of the guanidine group and the OH group were not observed.

2.1.2 3F-PHPOG Precursor (1i)



5 **1i**

*4-(2-aminoethoxy)-2-fluorophenol (**1i**).*
Tert-butyl (2-(4-(benzyloxy)-3-fluorophenoxy)ethyl)carbamate **5** (0.2950 g; 0.82 mmol) was dissolved in a solution of formic acid (7.45 mL; 10 equiv) and concentrated HCl (.75 mL; 1 equiv). The resulting mixture was then stirred overnight under argon at 80 °C. The mixture was then concentrated under vacuum. The residue was then dissolved in methanol and concentrated under vacuum again. This resulting residue was finally purified by flash silica gel chromatography (20% MeOH in DCM). The product was a white solid (0.1053 g; 75%).

^{1}H NMR (400 MHz; MeOH-d_4)/δ (ppm): 6.87 (t, J = 9.4 Hz, 1H), 6.79 (dd, J = 12.5, 2.9 Hz, 1H), 6.66 (ddd, J = 8.1, 2.5, 1.0 Hz, 1H), 4.15 (t, J = 4.9 Hz, 2H), 3.33 (t, J = 5.0 Hz, 2H); **^{13}C NMR** (100 MHz; MeOH-d_4)/δ (ppm): 151.42 (d, J = 239 Hz), 151.27 (d, J = 9 Hz), 139.15, 117.60, 110.04, 103.36, 64.67, 39.00; **^{19}F NMR** (376 MHz; MeOH-d_4)/δ (ppm): -136.27. **HRMS (ESI)** $[M + H]^+$ Calculated for $C_8H_{11}FNO_2$: 172.0768; found 172.0764.

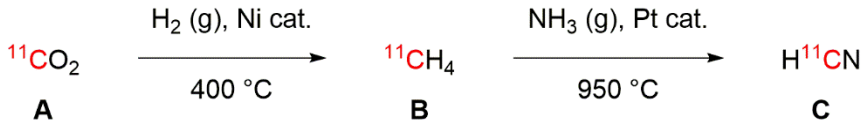
Note: Peaks corresponding to the NH protons of the amine and the OH group were not observed.

3. Radiochemistry

3.1 Materials and Methods

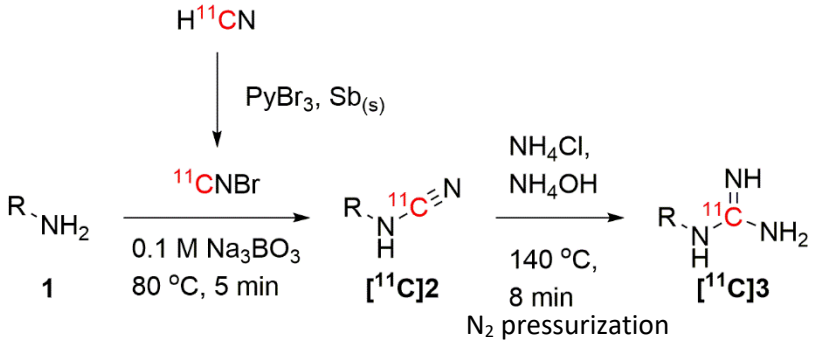
All the chemicals were purchased from commercially available suppliers and used without purification: Ammonium Acetate, Ammonium Chloride, Ammonium Hydroxide, Sodium Acetate, Phosphoric Acid, and Acetic Acid (glacial) was obtained from Fisher Scientific; and HPLC columns were acquired from Phenomenex. High-performance liquid chromatography (HPLC) was performed using a Shimadzu LC-2010A HT system equipped with a Bioscan B-FC-1000 radiation detector.

3.2 Synthesis of Hydrogen [^{11}C]Cyanide



Hydrogen [^{11}C]cyanide (~ 900 mCi) was produced following reported procedure[1]. Briefly, [^{11}C]carbon dioxide **A** (~3 Ci) was produced by General Electric (GE) Medical Systems PETtrace cyclotron. The GE Carbon-11 target was loaded with [^{14}N]N_2 and 0.5% [^{16}O]O_2 gas and bombarded with a proton beam to generate [^{11}C]carbon dioxide **A** by the $^{14}N(p,\alpha)^{11}C$ nuclear reaction. [^{11}C]Carbon dioxide **A** was then transferred to a GE Process Cabinet to be converted into [^{11}C]HCN **C**. First, [^{11}C]carbon dioxide **A** was trapped on molecular sieves (4A, 80/100 mesh) and then passed through a nickel catalyst column (Shimalite-Ni reduced, 80/100 mesh) with H_2 (g) at 400 °C to afford [^{11}C]methane **B**. After passage through a drying tower containing P_2O_5 and an ascarite trap, the [^{11}C]methane **B** formed was mixed with ammonia gas and passed through a quartz furnace containing a platinum catalyst (Platinum gauze, 100 mesh) held at 950 °C to yield hydrogen [^{11}C]cyanide **C**.

3.3 Radiochemical Synthesis of [^{11}C]Guanidines



Production of [^{11}C]guanidines was carried out using a TracerLab FX_M automated radiochemistry synthesis module with modification. (**Figure S1**). To maintain the reaction pressure during heating, the lines from V1 and V2 to the reactor were shortened to their minimum length. The line from V3 and V4 was removed from reactor and replaced with a plugger. A column containing $PyBr_3$/Sb was inserted between HCN deliver line and the needle of reactor. In a typical run

hydrogen [^{11}C]cyanide (~900 mCi) produced from the GE PETtrace cyclotron and process panel[1] was passed through a quartz tube containing pyridinium bromide perbromide and antimony powder to yield [^{11}C]CNBr (~500 mCi), and bubbled into the reactor containing 24 µmol of amine precursor **1** dissolved in 250 µL 0.1 M sodium borate (pH 8.0). This process was held for 6 minutes and 30 seconds. The reaction vessel was then heated to 80 °C and held for 5 minutes to produce [^{11}C]cyanamide intermediate **[^{11}C]2**. The solution was then cooled to 70 °C. After the solution reached 70 °C, 250 µL of 35% NH_4Cl in 28% NH_4OH was added to the reactor and the valve was kept open for 1 minute to add nitrogen carrier gas to increase pressure in the reactor after the vent valve closed. The reaction was then heated to 140 °C and held for 8 minutes to produce crude [^{11}C]guanidine product **[^{11}C]3**. After heating, the solution was cooled to 40 °C. The cooled solution was then diluted with 500 µL HPLC solvent (10% EtOH in 60 mM NH_4OAc) plus 200 µL acetic acid. The mixture was loaded onto a semi-preparative HPLC loop (Phenomenex Synergi HydroRP 80A, 10µ, 250 x 10.00 mm) and eluted with 10% EtOH in 60 mM ammonium acetate at a flow rate of 5.0 mL/min. The radioactive product peak was collected and QC analyses were performed.

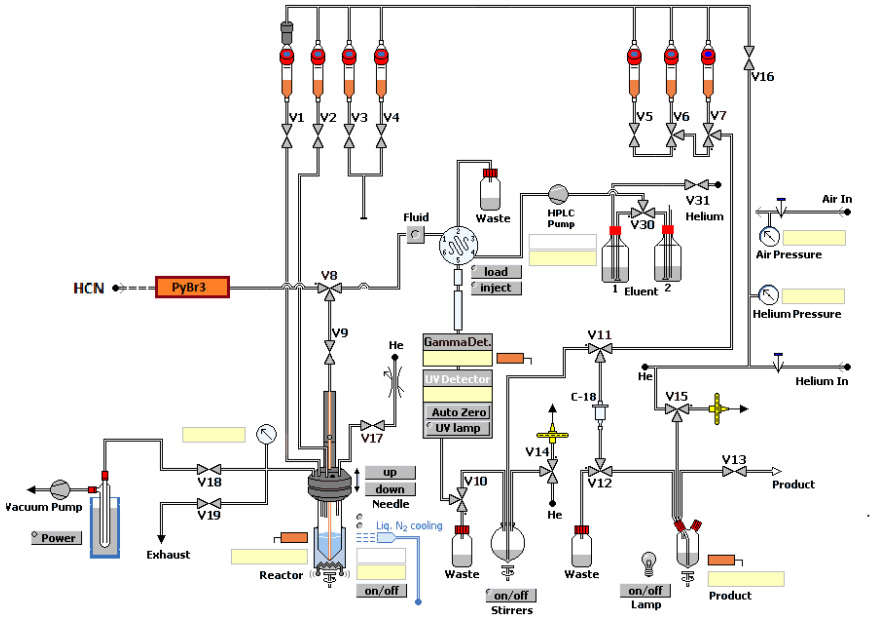


Figure S1: GE TracerLab FX_M with modification

Automation allowed for improved control over the pressure in the conversion of [^{11}C]cyanamides to [^{11}C]guanidines but, on occasion, the high pressure and temperature resulted in the reaction solution partially escaping into the lower pressure lines between the reactor and external valves, resulting in lower conversion. To address this we modified the module by eliminating extra lines and shortening the lines connected to the reactor to limit dead space in the system.

3.4 General QC HPLC Conditions

Two general sets of HPLC conditions were used: a gradient method (Conditions A) and an isocratic method (Conditions B).

<u>HPLC Conditions A:</u>

Condition: 0-50% gradient of EtOH in 10 mM NaOAc
Temperature: 40 °C
Flow rate: 2 mL/min
Column: Phenomenex Synergi HydroRP 80A 150 x 4.6 mm. 4µ.

0-5 min	0% EtOH	isocratic
5-20 min	0% to 50% EtOH	linear increase
20-30 min	0% EtOH	isocratic

HPLC Conditions B:

Condition: 10% EtOH in 60 mM NH_4OAc
Temperature: 40 °C
Flow rate: 1.2 mL/min
Column: Phenomenex Synergi HydroRP 80A 250 x 4.6 mm. 10µ.

3.5 Determination of Radiochemical Yield

Radiochemical yield was determined by HPLC analysis of the crude product.

$$\% \text{ RCY} = [\text{Area of } [^{11}\text{C}]\text{guanidine product peak} / \text{Total area of all } ^{11}\text{C-labeled species peaks}] \times 100$$

Activity yield was determined by measurement of isolated product.

$$\% \text{ AY} = [\text{mCi of } [^{11}\text{C}]\text{guanidine product} / \text{mCi } [^{11}\text{C}]\text{BrCN}] \times 100$$

4. Pre-clinical PET Imaging

4.1 General Considerations

Rabbit imaging studies were performed at the University of Michigan, in accordance with the standards set by the Institutional Animal Care and Use Committee (IACUC) and all applicable federal, state, local, and institutional laws or guidelines governing animal research.

4.2 Rabbit Imaging Protocol

PET imaging studies (Figure S2) were performed using a Concorde Microsystems P4 PET scanner (Siemens, Knoxville, TN, USA). The animals (New Zealand white rabbit, 3.8 – 4.0 kg) were masked with gas anesthesia isoflurane (Patterson Veterinary Supply Inc., Devens, MA, USA). Anesthesia was maintained throughout the duration of the PET scan. 2.8 ± 0.4 mCi of [^{11}C]3F-PHPOG was administered in a bolus dose over one minute (n=2). Emission data were collected beginning with the injection and continued for 60.0 min (12x10s, 2x30s, 2x60s, 2x150s, 2x300s, 4x600s frames). Data were corrected for attenuation and scatter and reconstructed using the three dimensional–maximum a priori method (3D MAP algorithm). The dynamic sequence of PET images was summed and regions-of-interest (ROIs) were drawn manually on multiple planes to generate time-activity curves (Figure S3).

4.3 Rabbit PET Images and Time-Radioactivity Curves

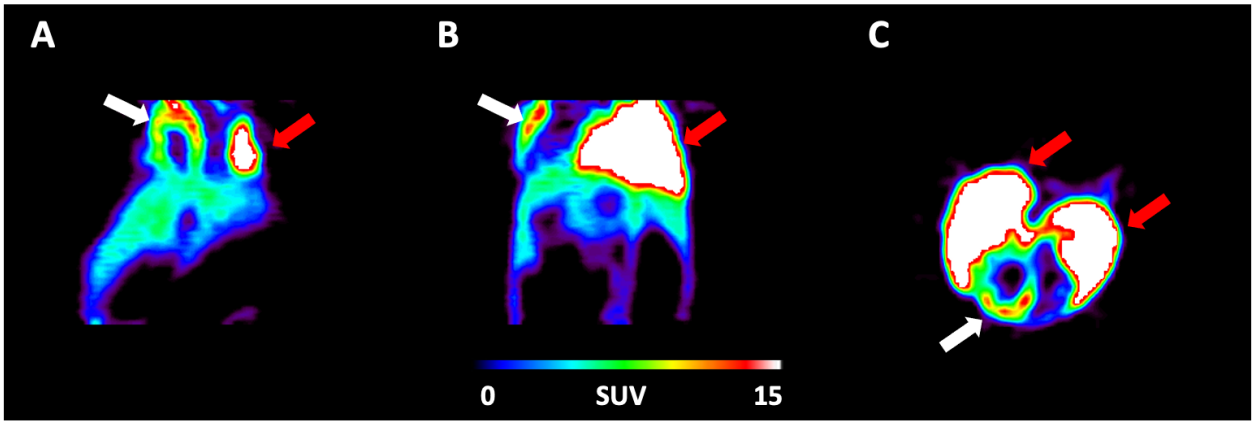


Figure S2. Representative coronal (**A**), sagittal (**B**) and transverse (**C**) PET images of rabbit heart (0 – 60 min post-injection of 2.8 ± 0.4 mCi [^{11}C]3F-PHPOG) showing heart (white arrows) and lung (red arrows) regions

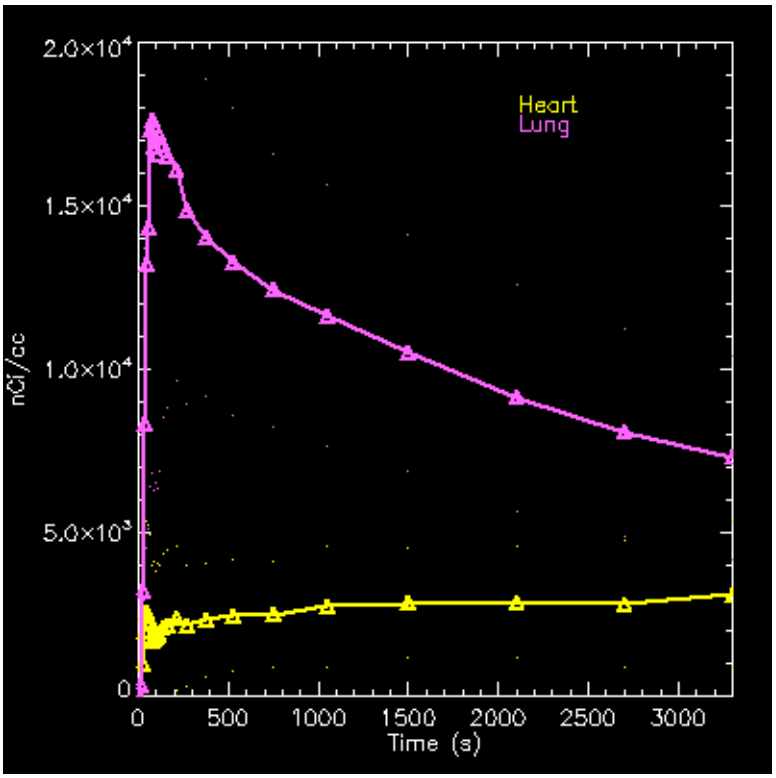


Figure S3. Heart and Lung Time-Radioactivity Curves for [^{11}C]3F-PHPOG

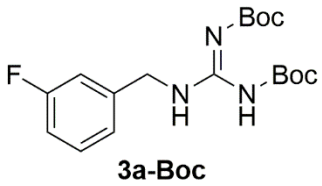
5. References

[1] Shao, X.; Rodnick, M. E.; Brooks, A. F.; Scott, P. J. H. Synthesis and Applications of [^{11}C]Hydrogen Cyanide. In *Radiochemical Syntheses, Volume 2: Further Radiopharmaceuticals for Positron Emission Tomography and New Strategies for Their Production*; Scott, P. J. H., Eds.; John Wiley & Sons, Incorporated: New Jersey, 2015; pp 233-240.

6. Spectra Data

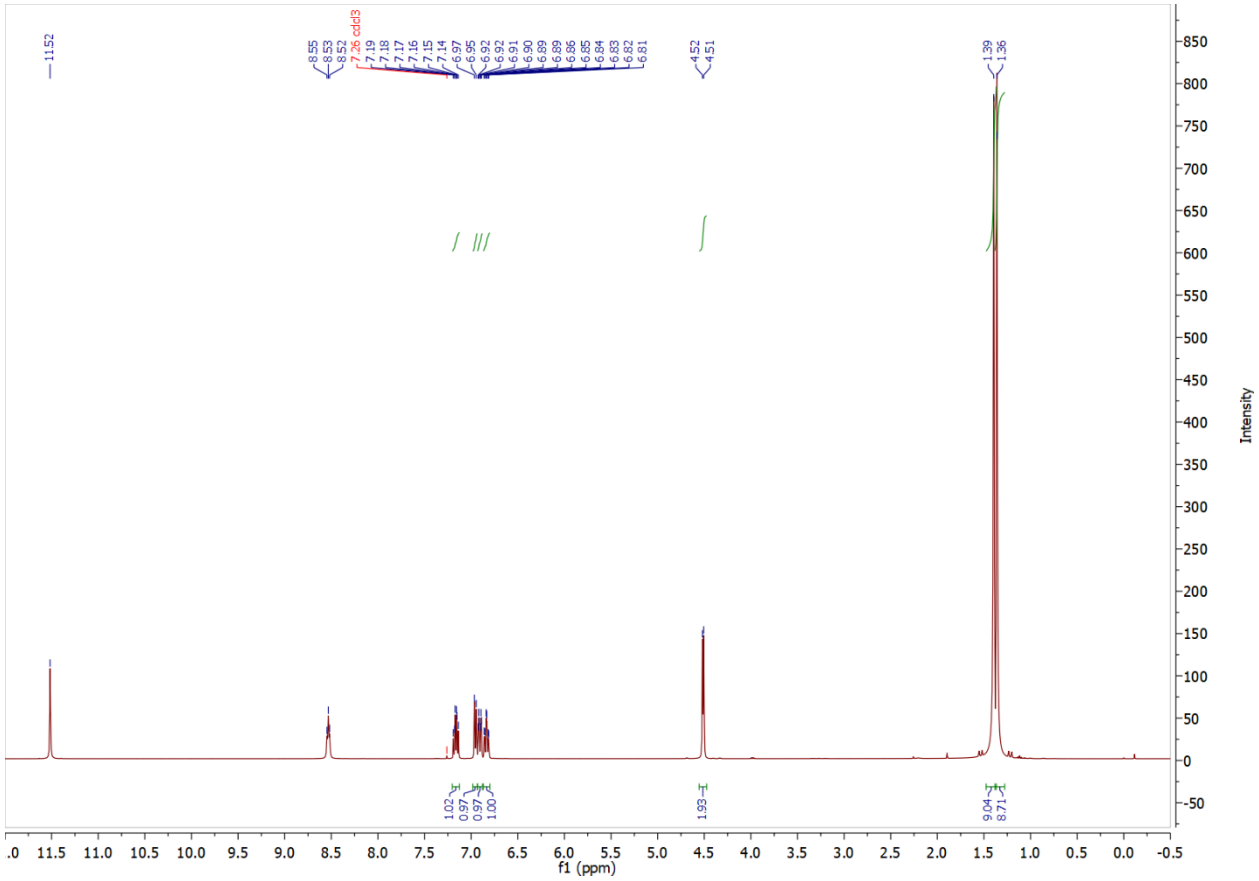
6.1 NMR Spectra

6.1.1 MFBG

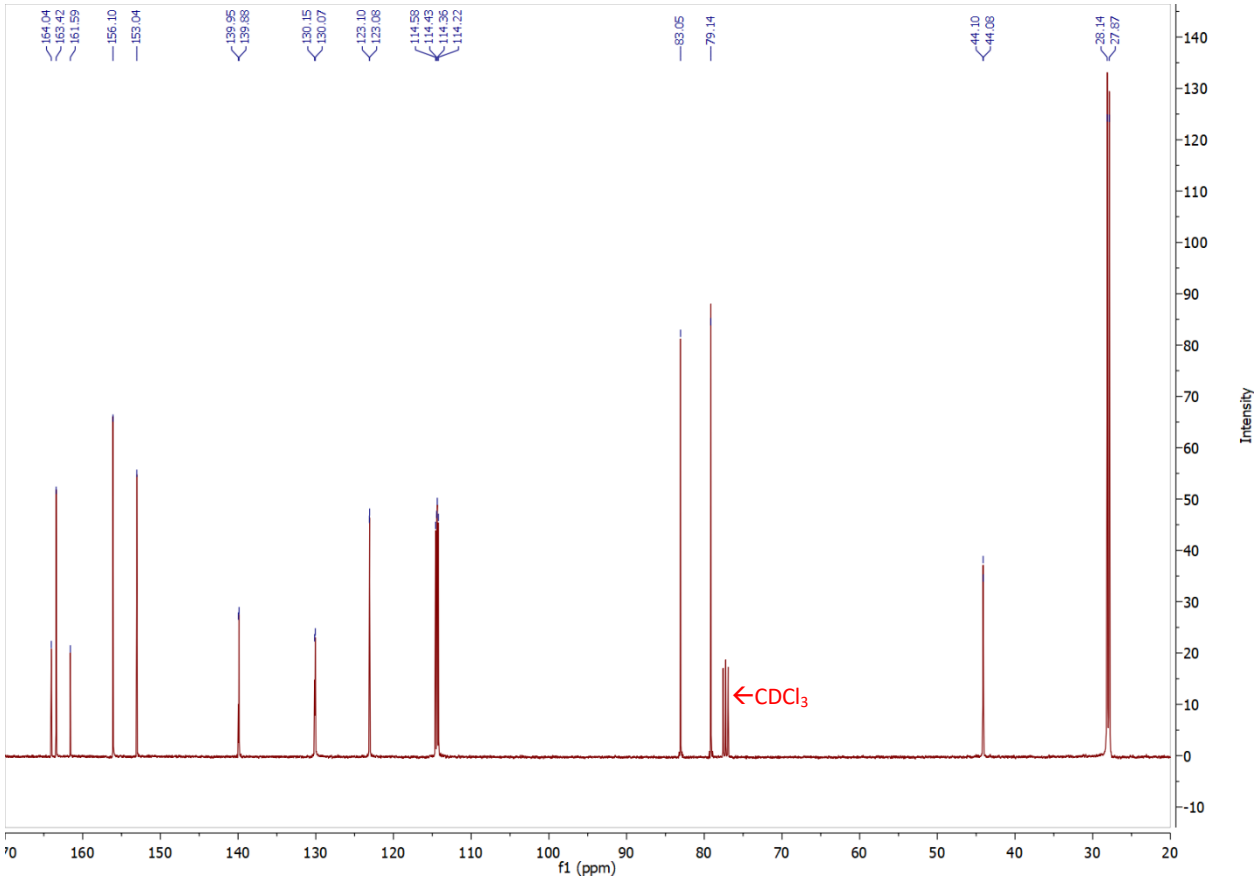


3a-Boc

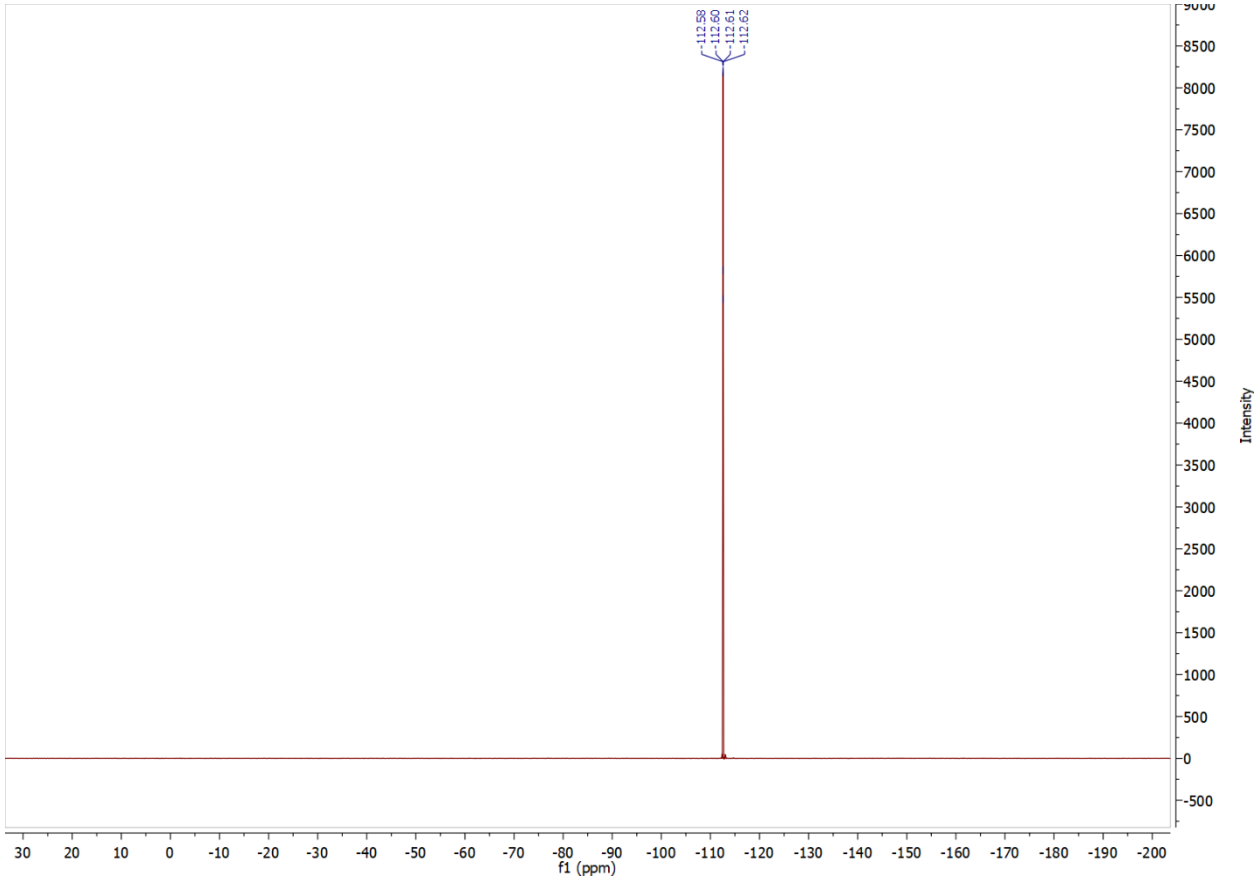
^{1}H NMR for **3a-Boc**

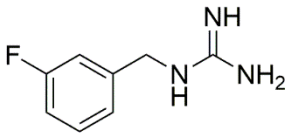


^{13}C NMR for **3a-Boc**



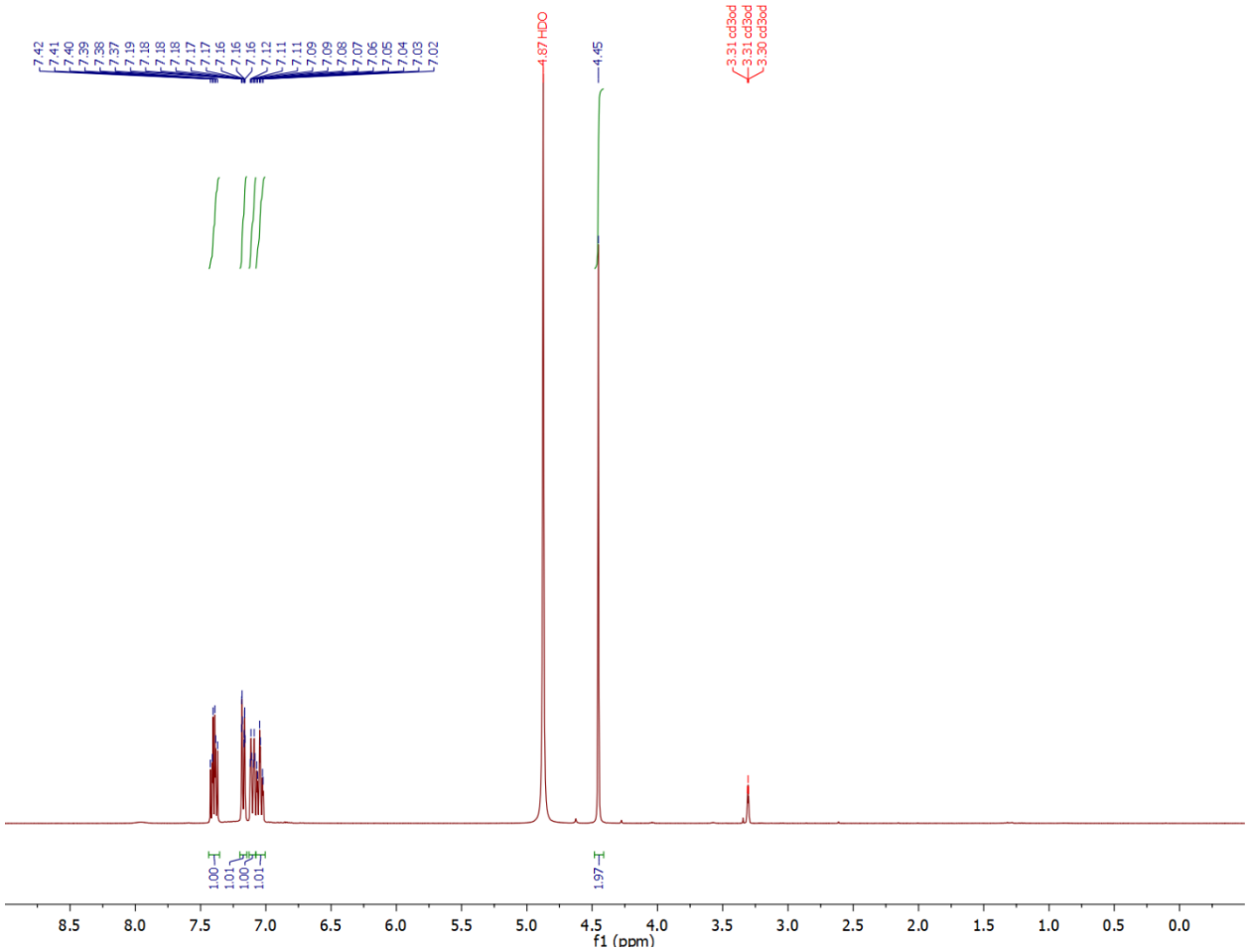
^{19}F NMR for **3a-Boc**



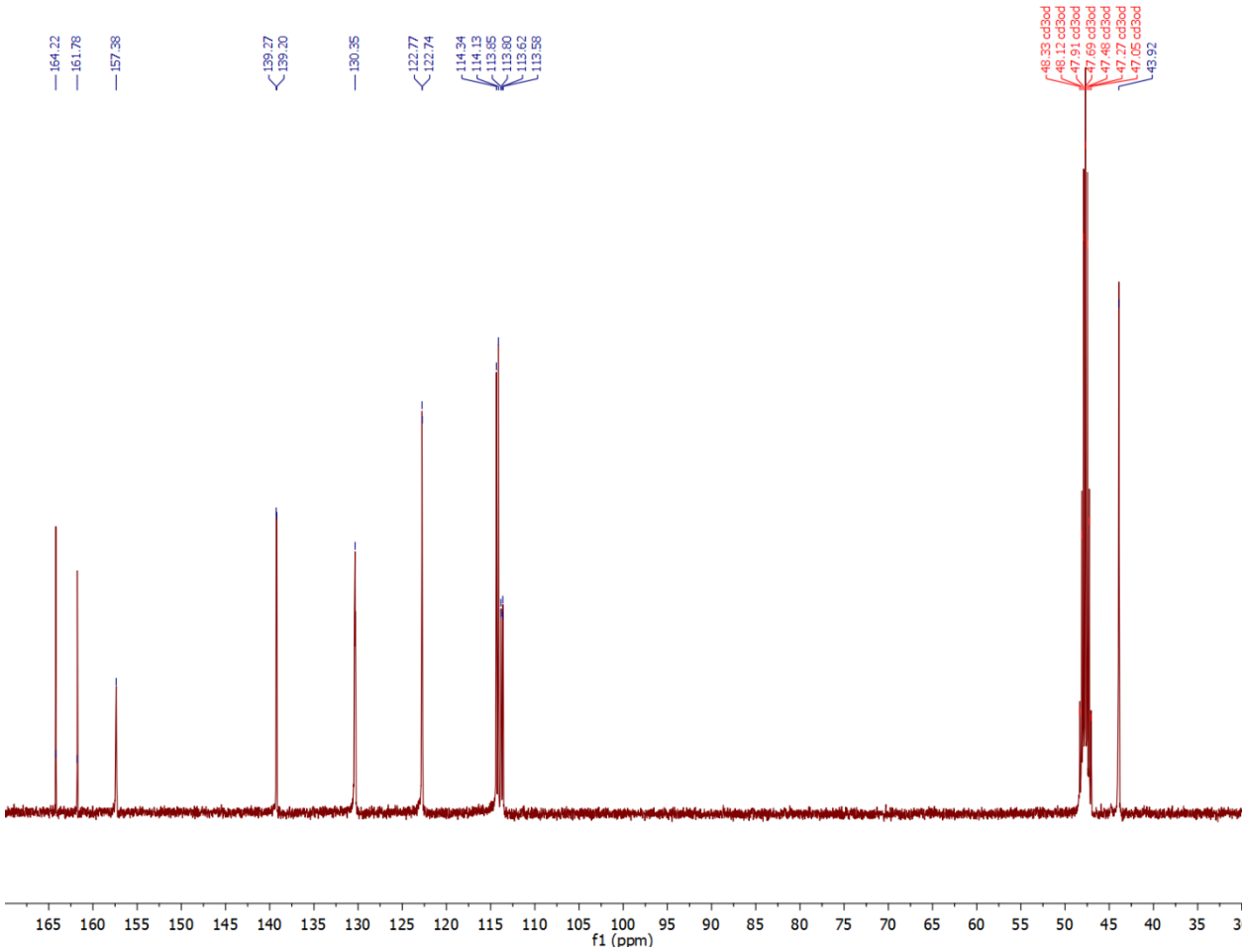


3a

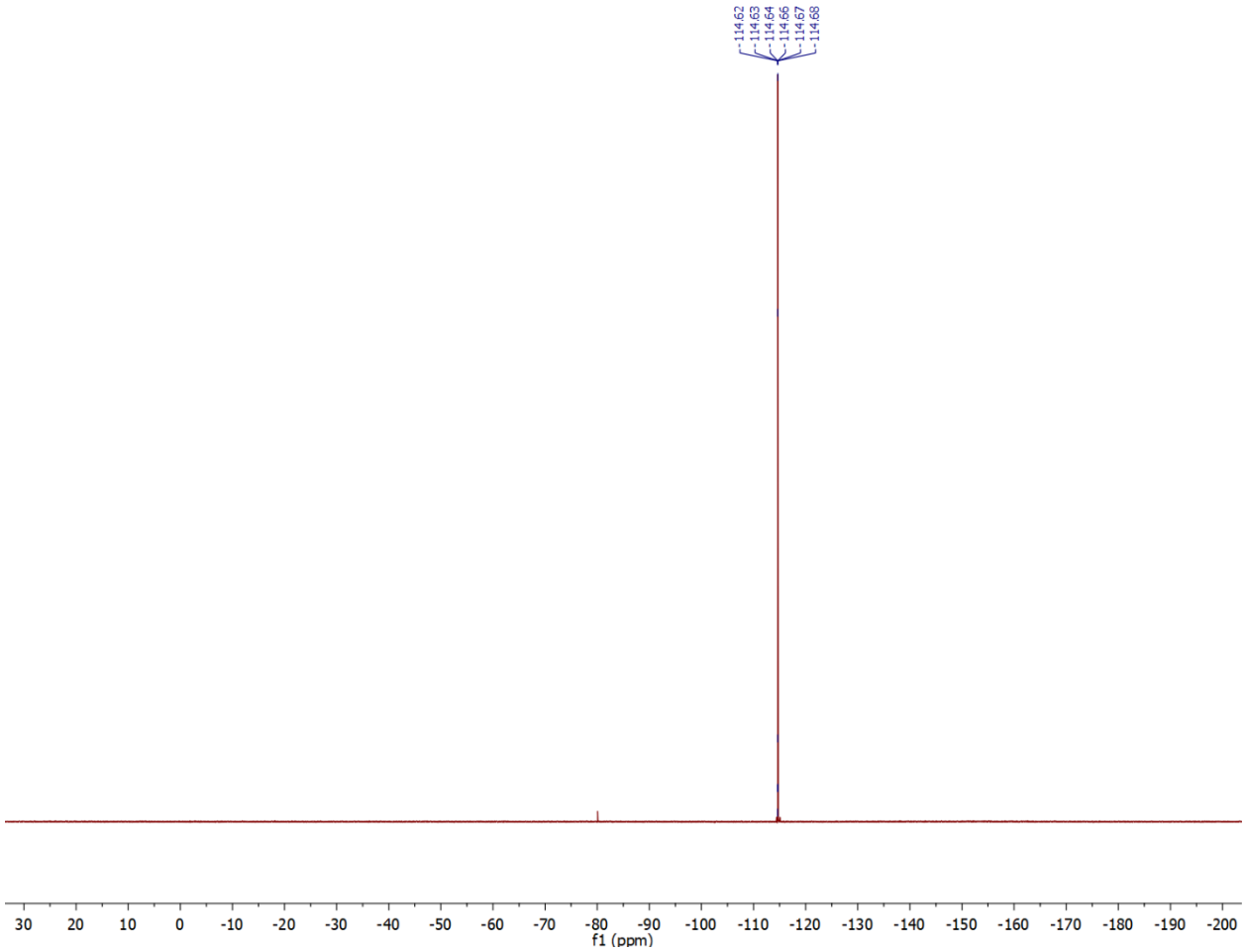
^{1}H NMR for **3a**



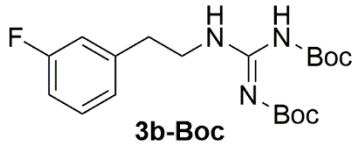
^{13}C NMR for **3a**



^{19}F NMR for **3a**

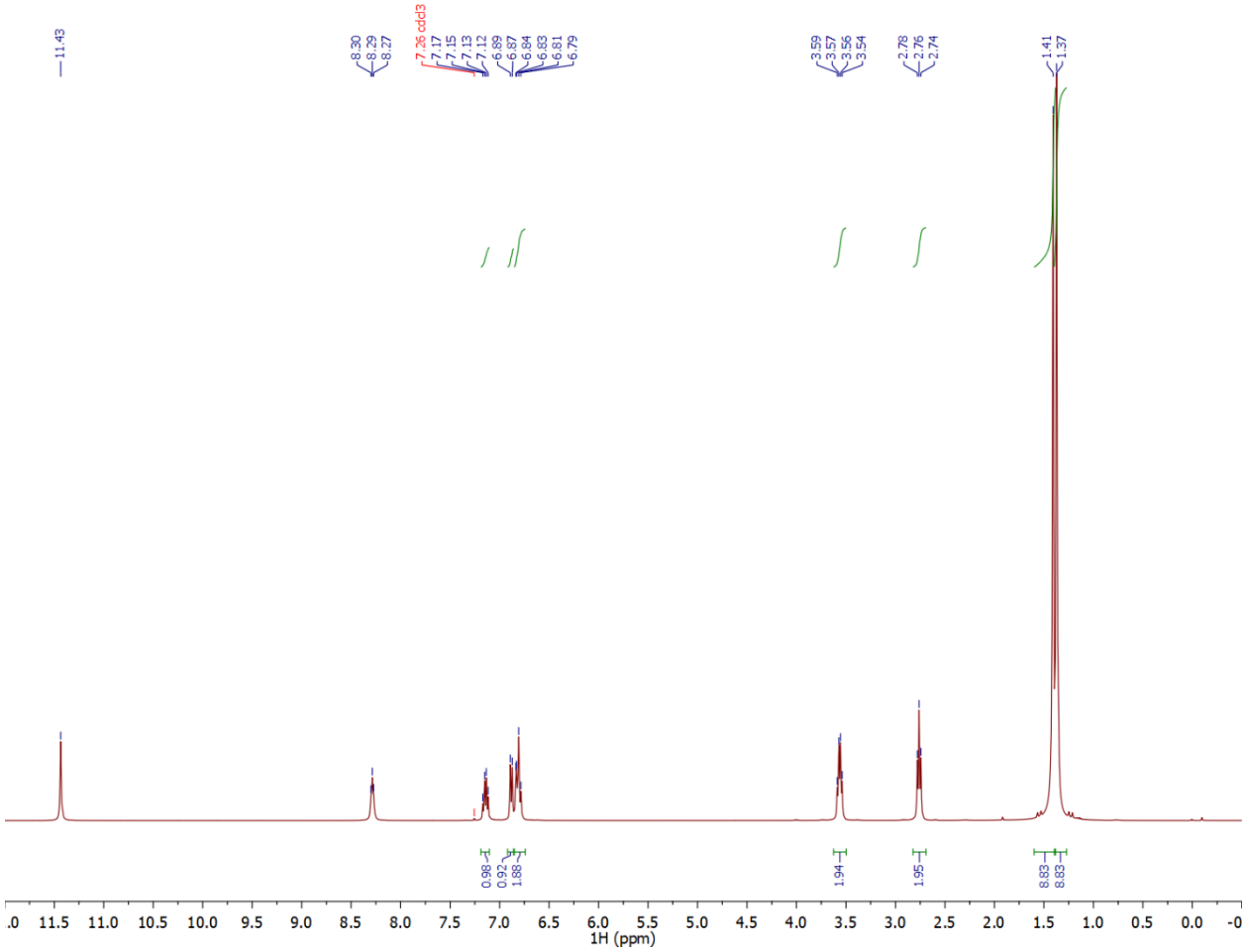


6.1.2 MFPG

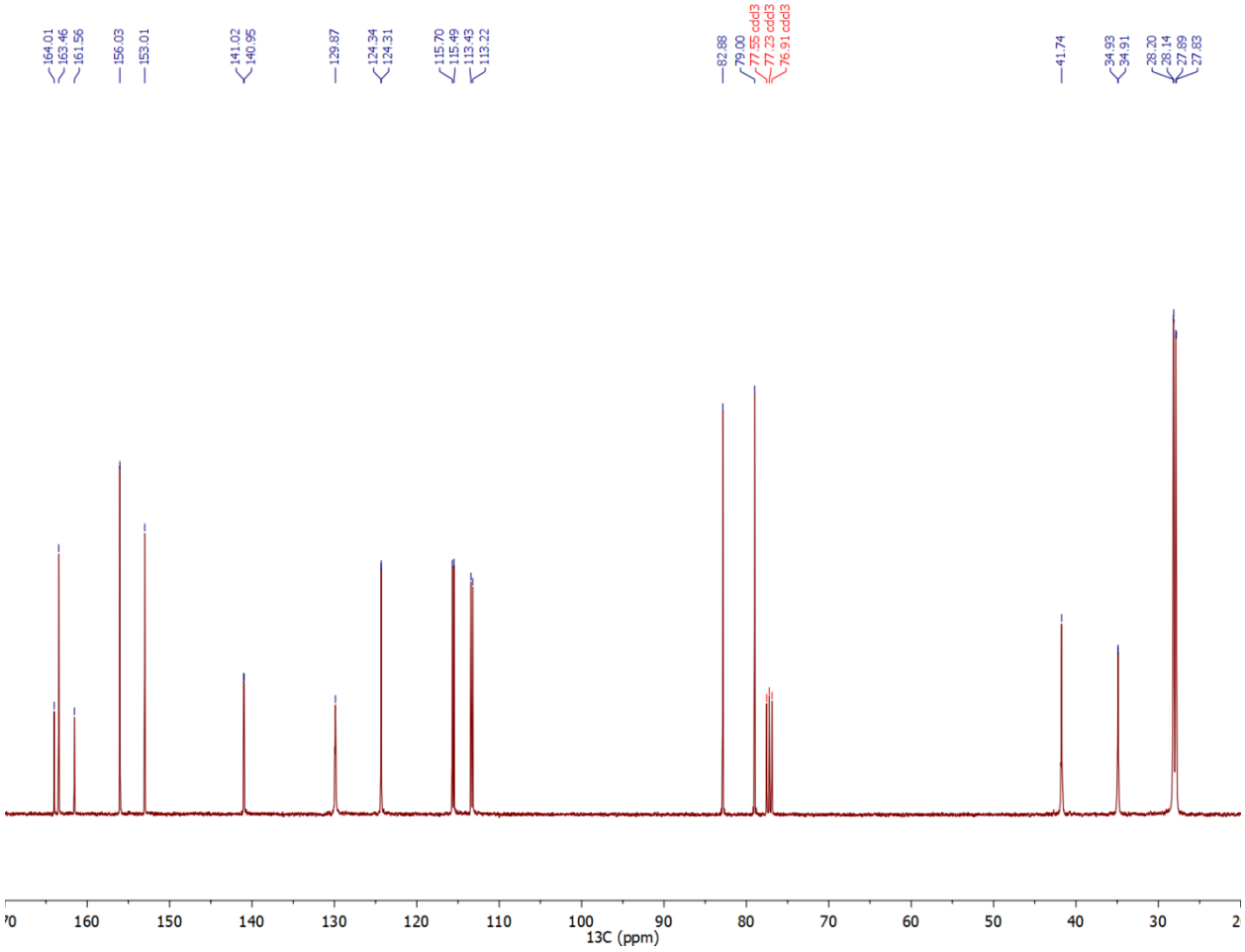


3b-Boc

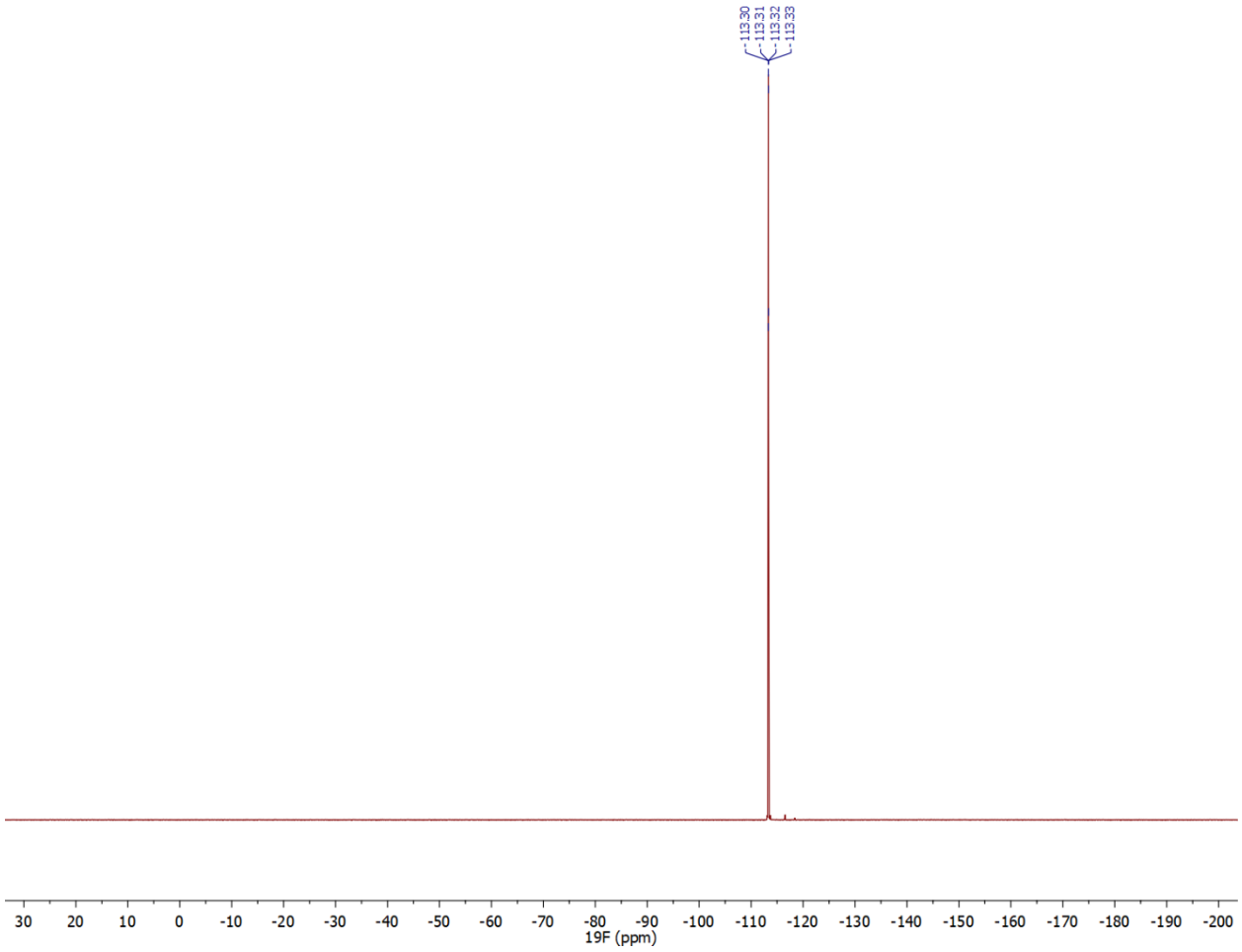
^{1}H NMR for **3b-Boc**

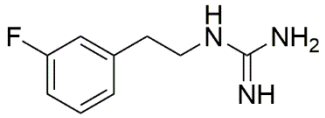


^{13}C NMR for **3b-Boc**



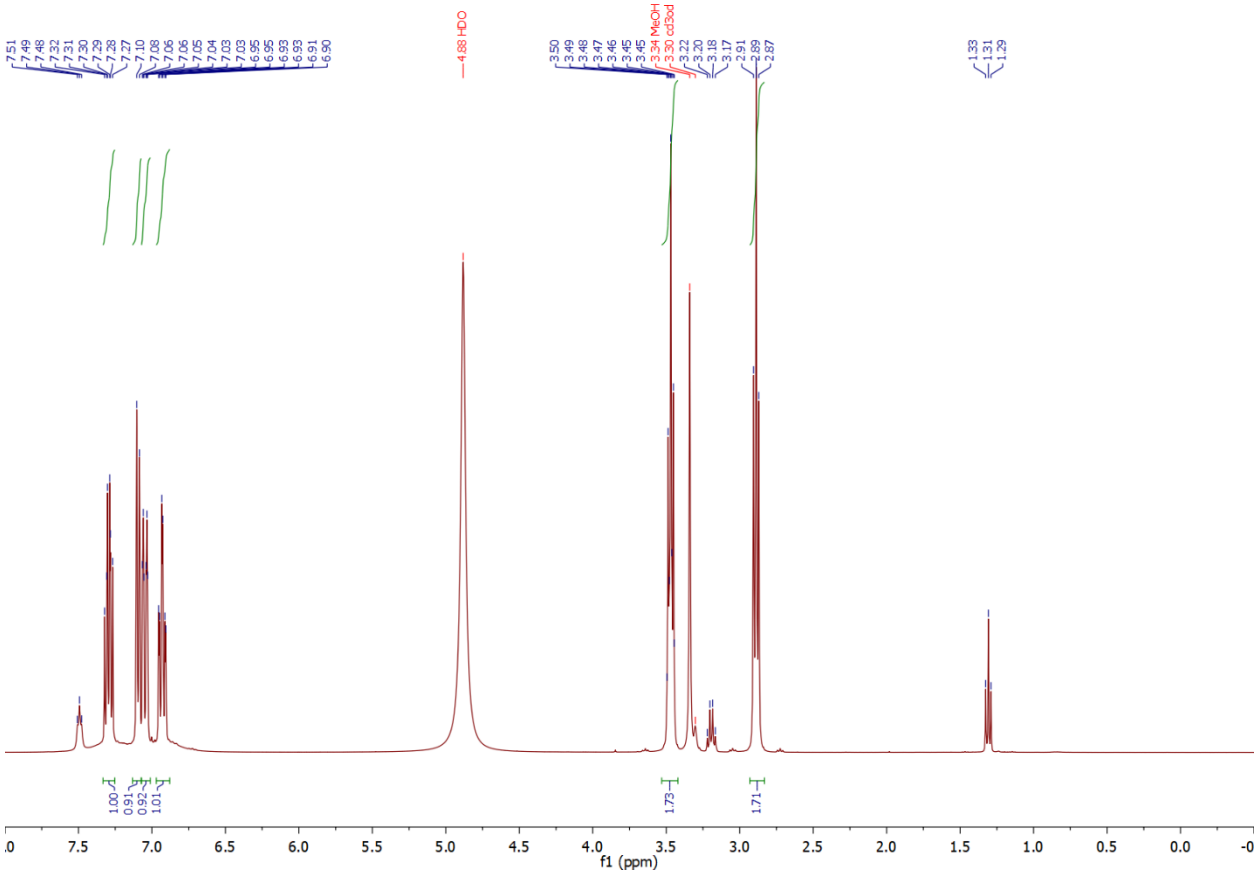
^{19}F NMR for **3b-Boc**



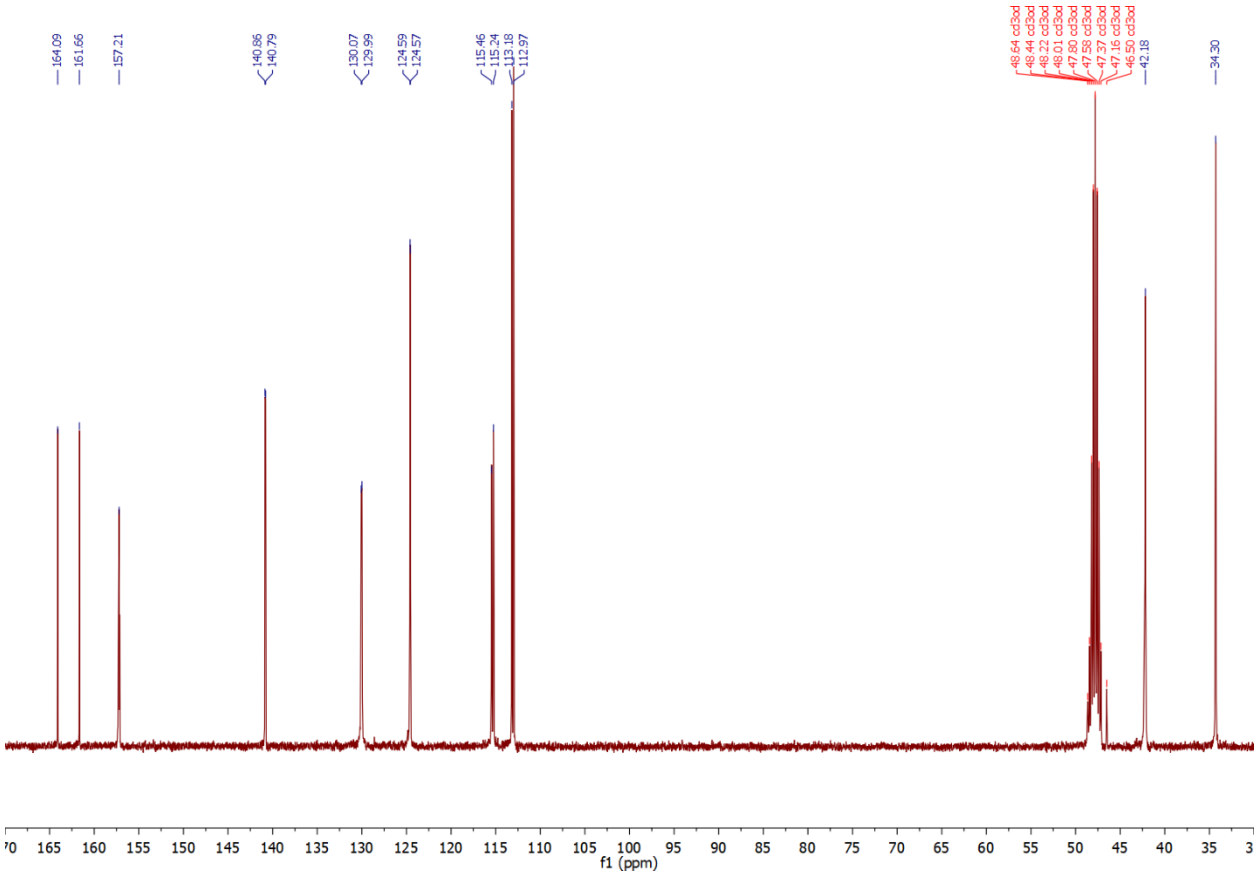


3b

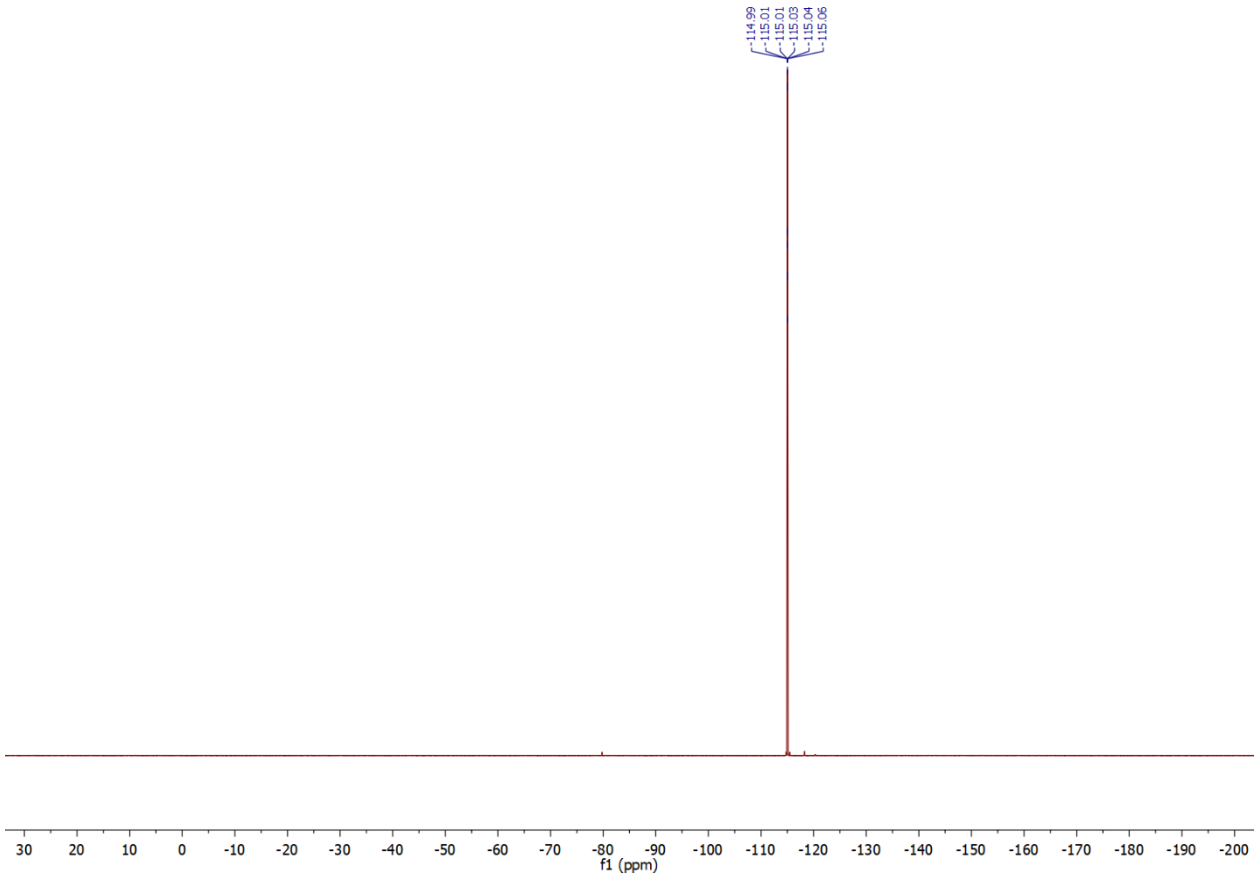
^{1}H NMR for **3b**



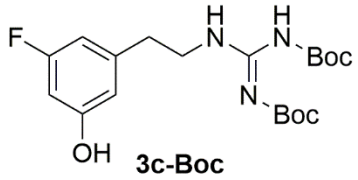
^{13}C NMR for **3b**



^{19}F NMR for **3b**

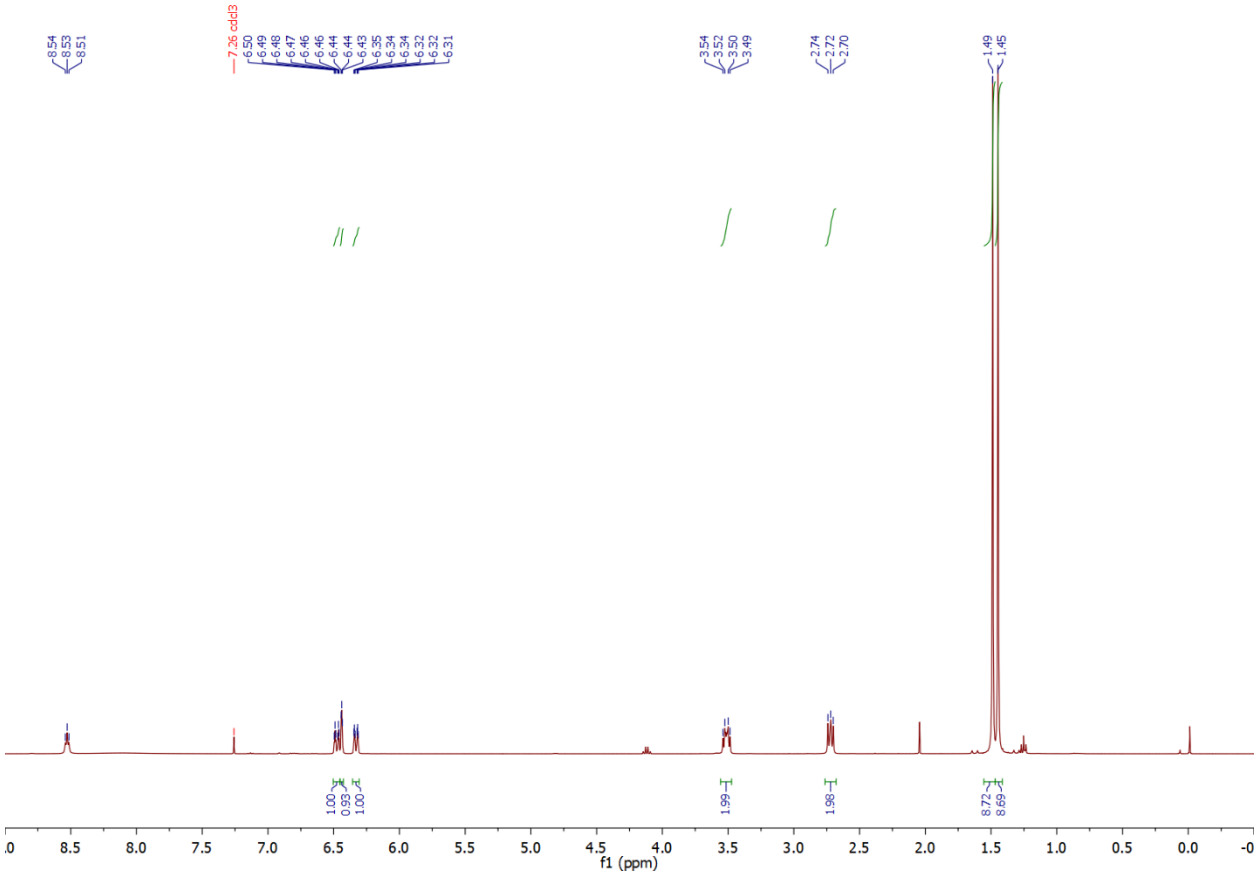


6.1.3 5F-MHPG

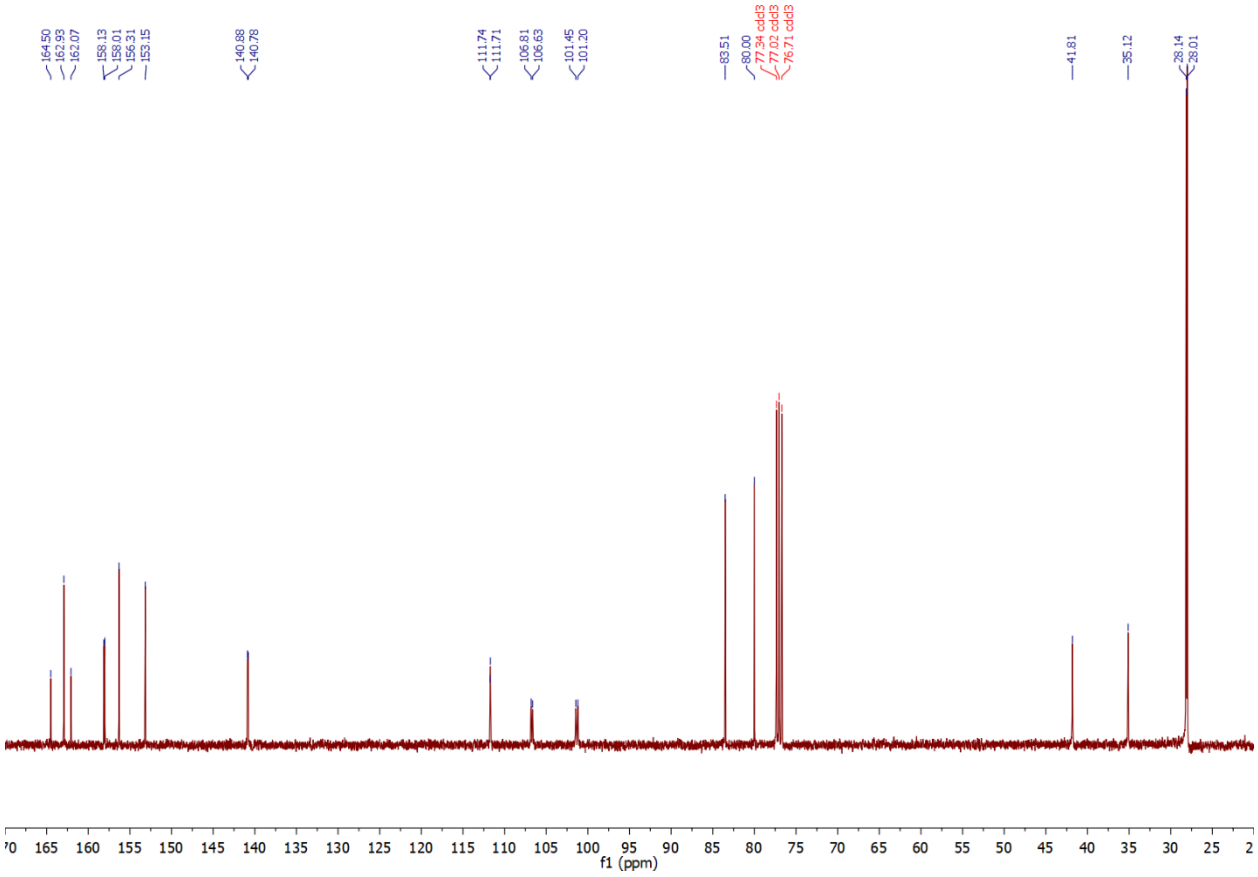


3c-Boc

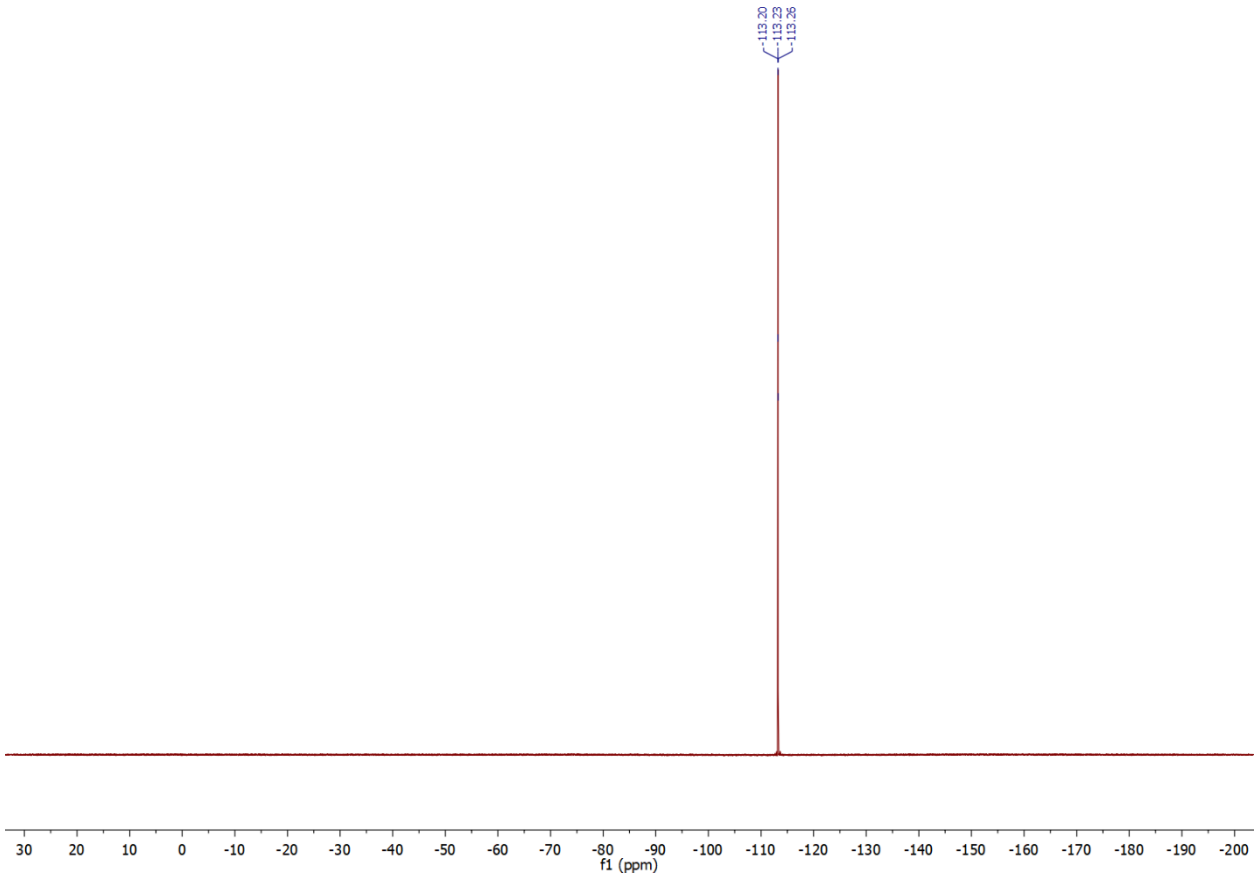
^{1}H NMR for **3c-Boc**

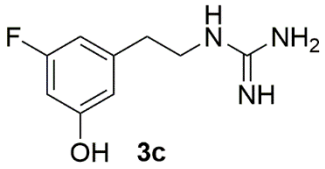


^{13}C NMR for **3b-Boc**



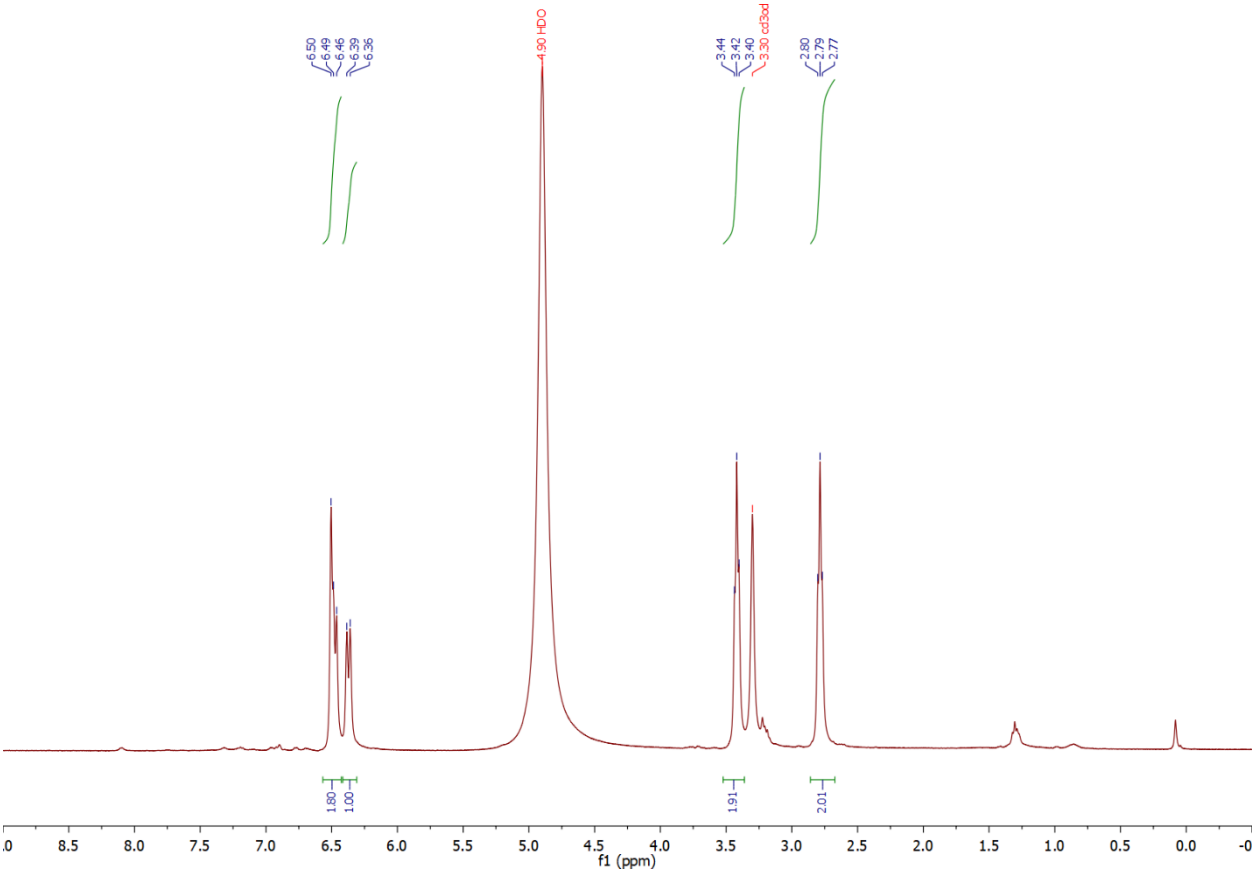
^{19}F NMR for **3b-Boc**



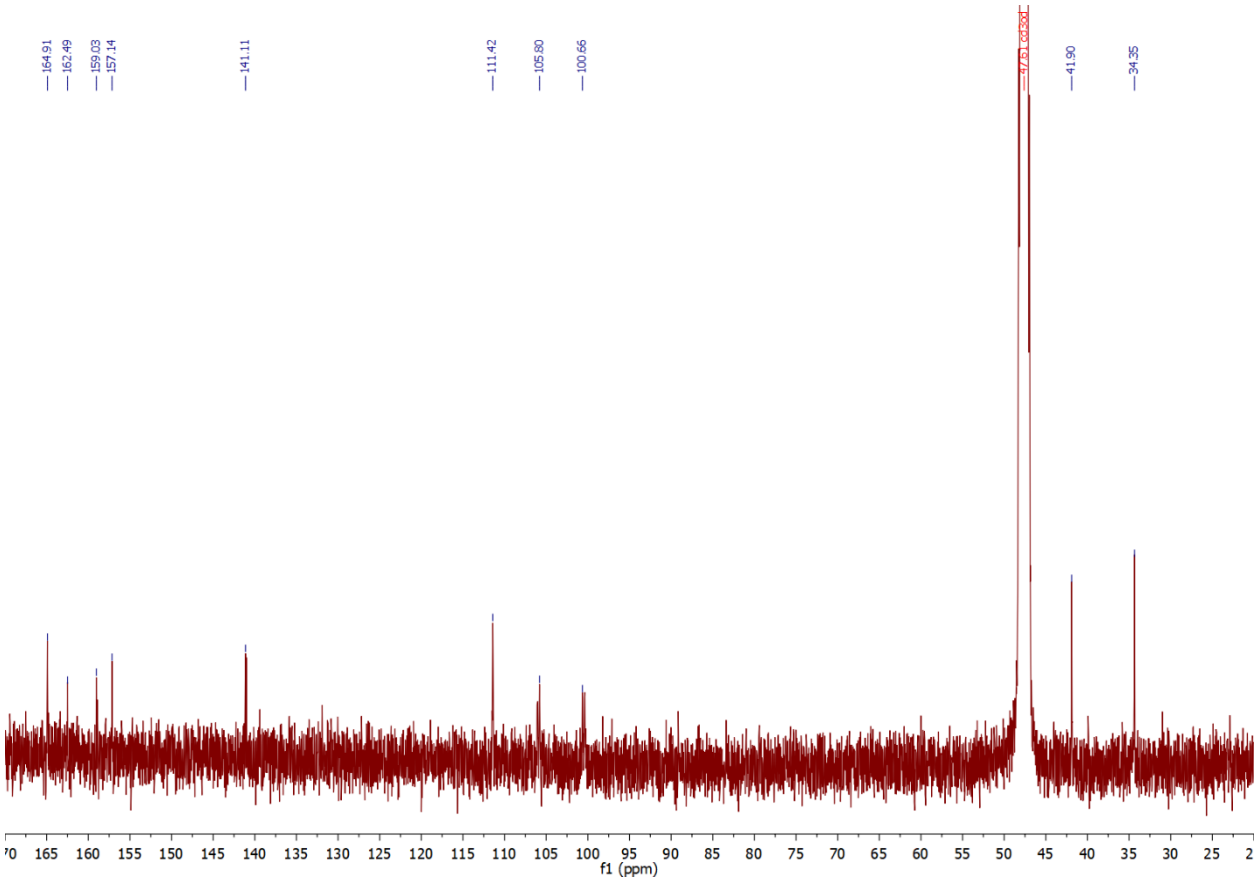


3c

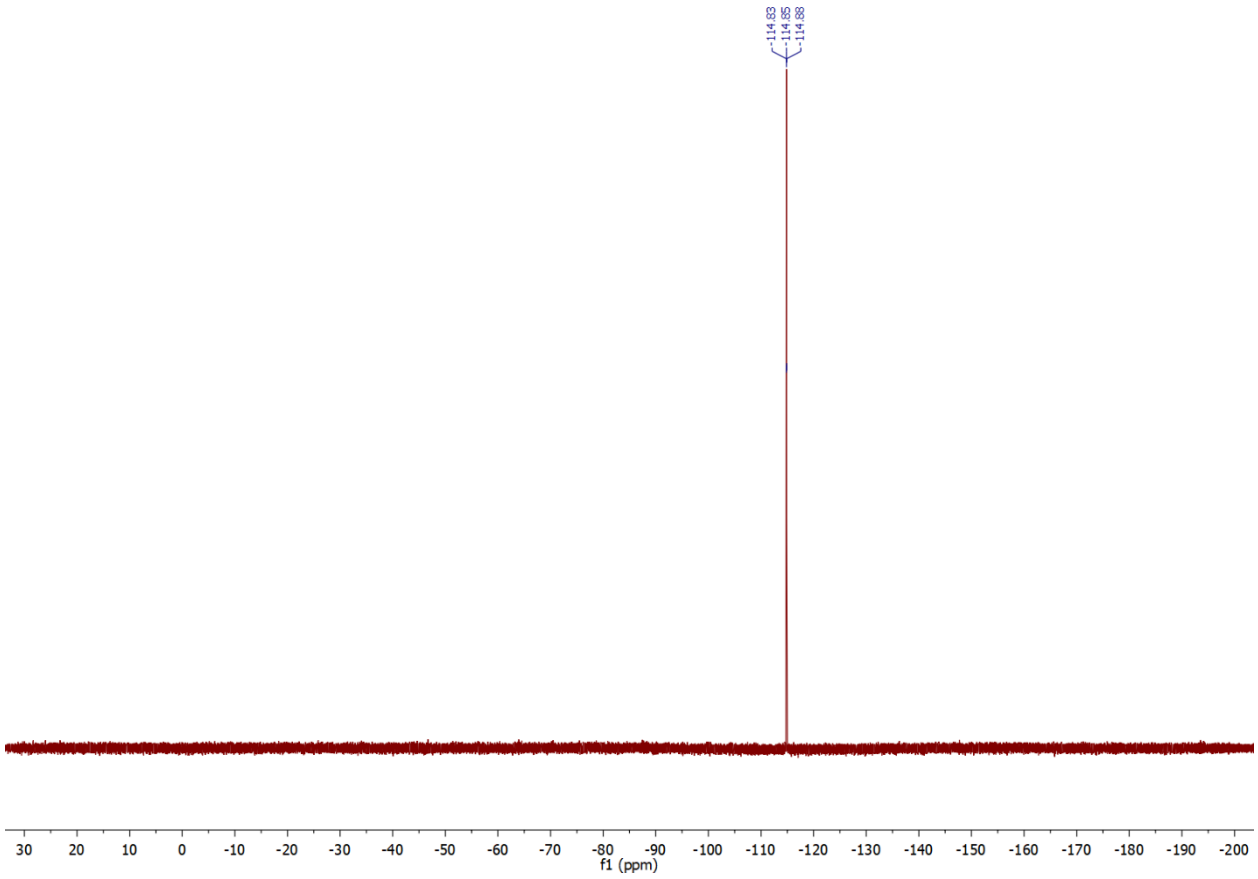
^{1}H NMR for **3c**



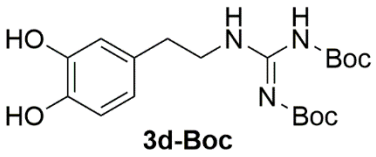
^{13}C NMR for **3c**



^{19}F NMR for **3c**

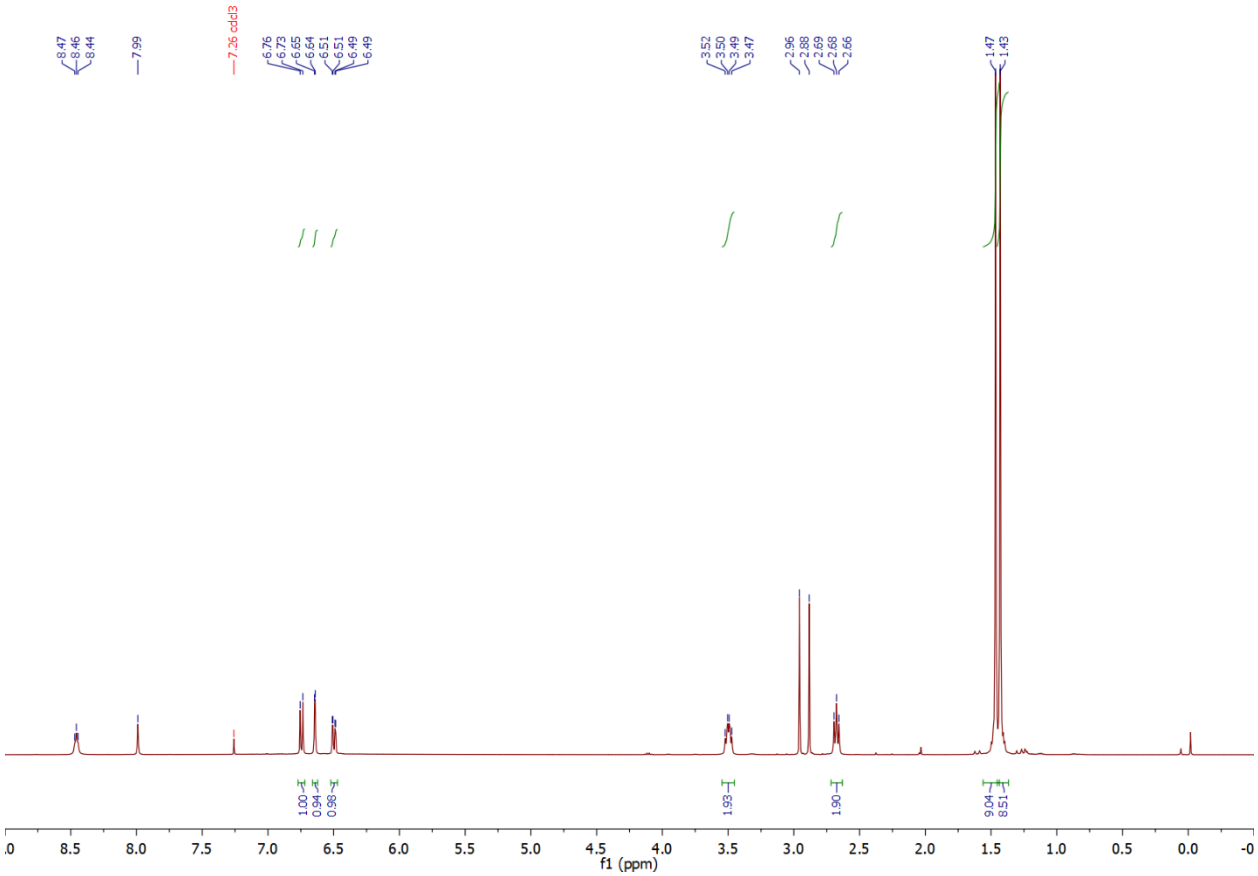


6.1.4 DOPG

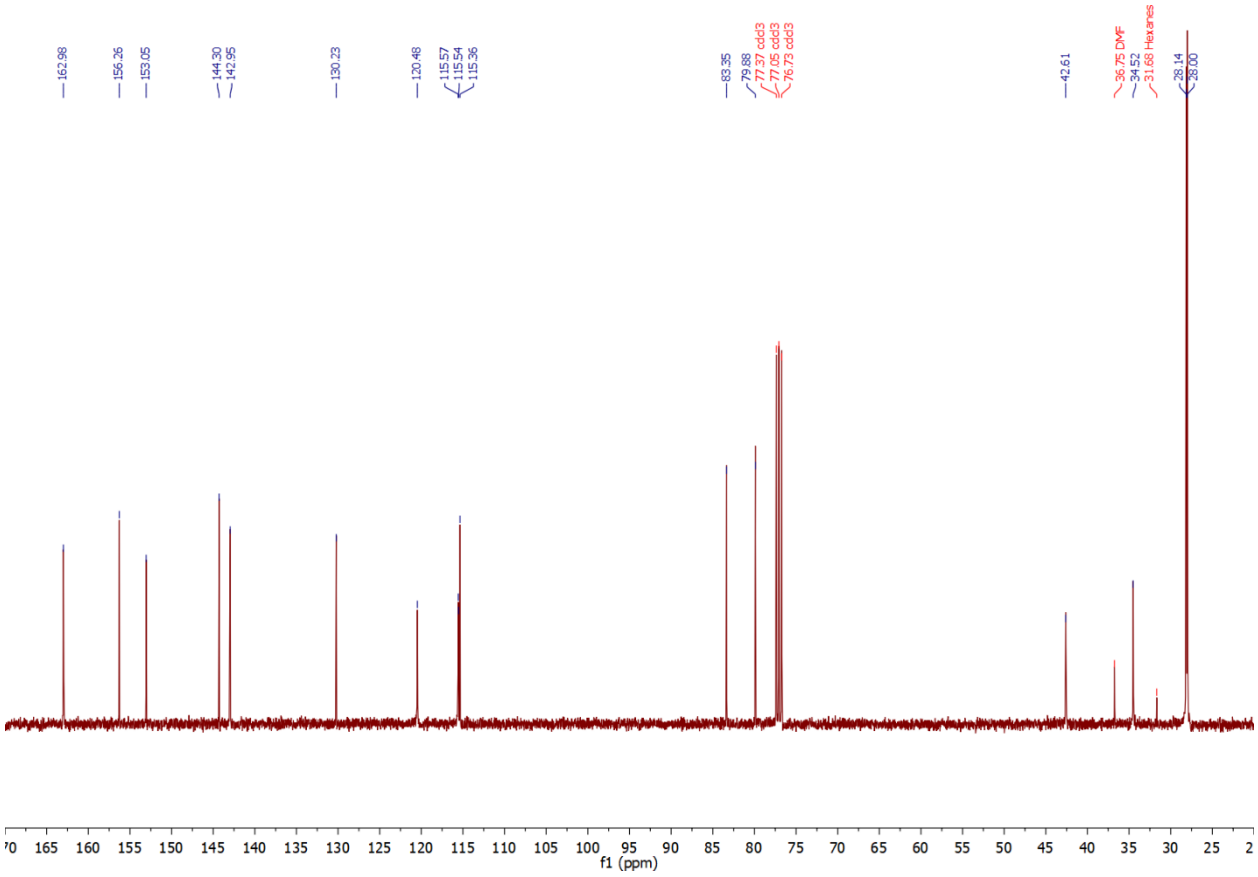


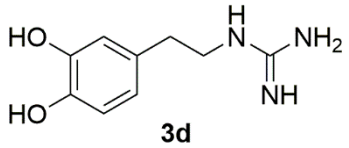
3d-Boc

^{1}H NMR for **3d-Boc**



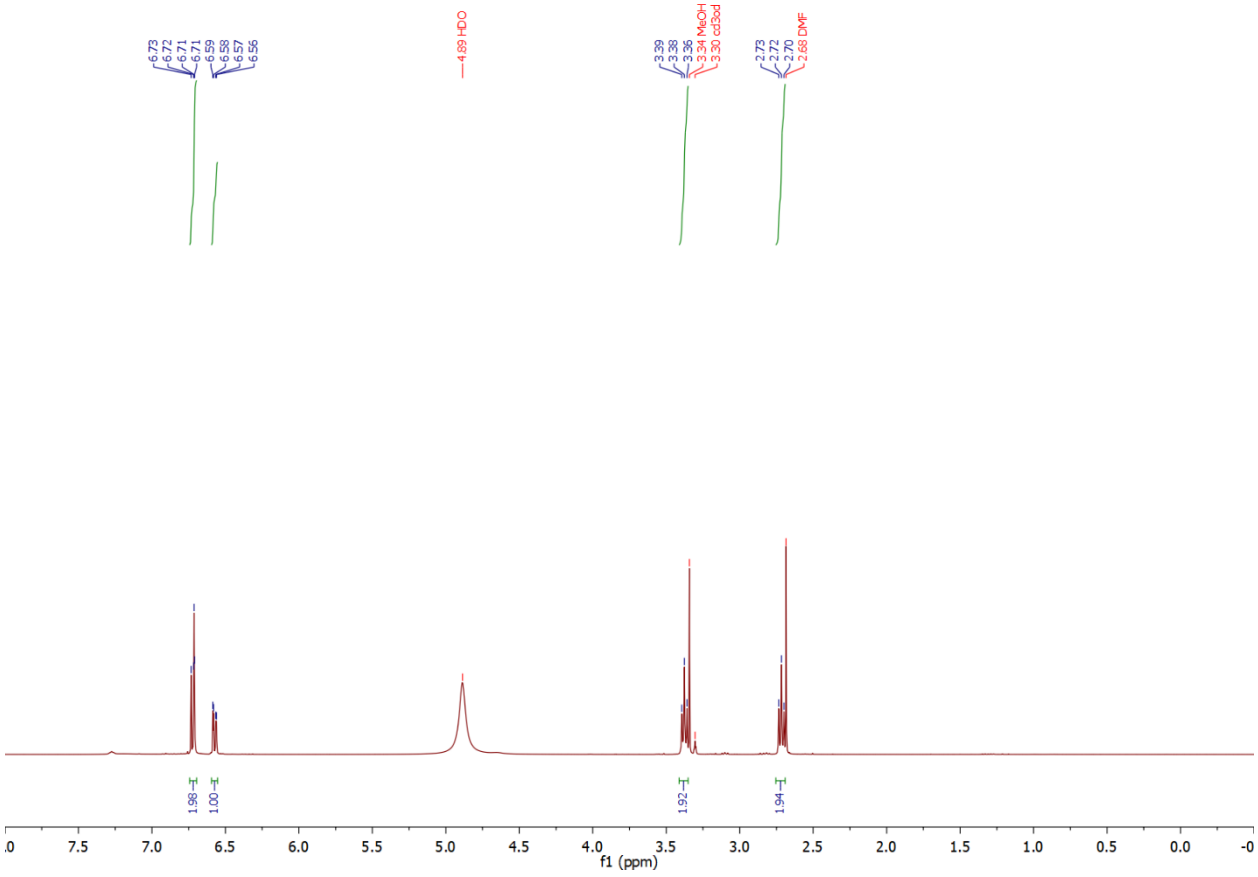
^{13}C NMR for **3d-Boc**



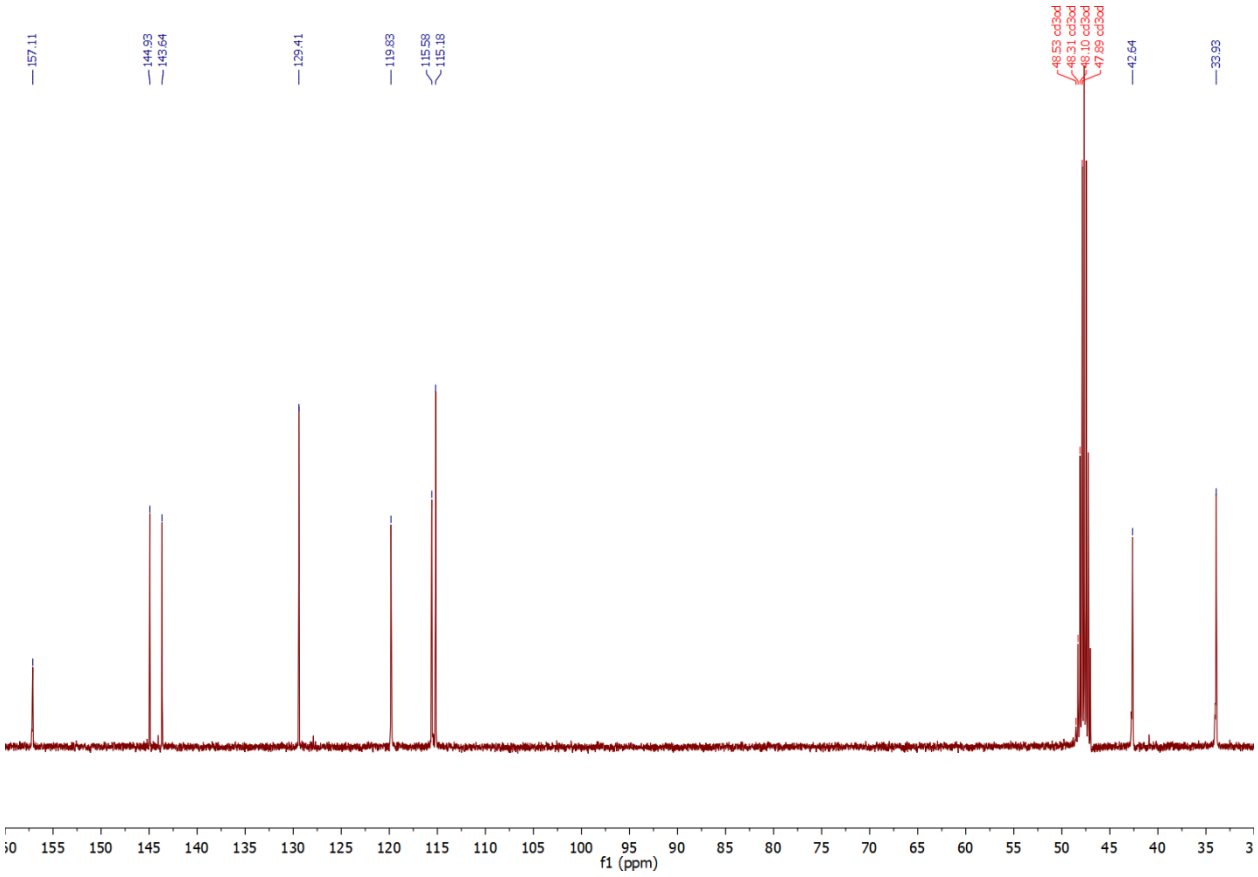


3d

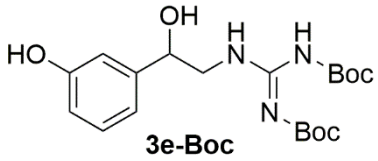
^{1}H NMR for **3d**



^{13}C NMR for **3d**

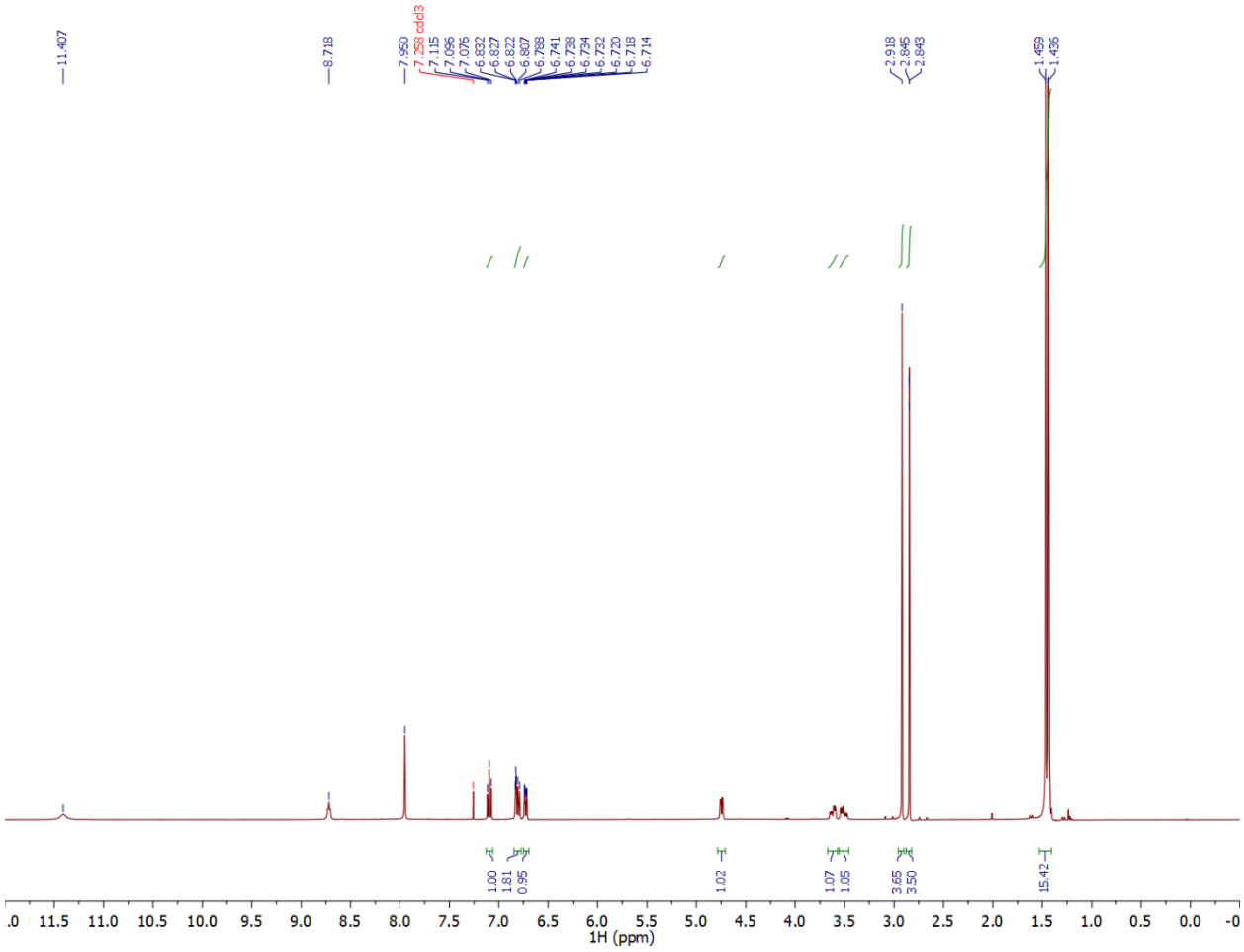


6.1.5 GMO

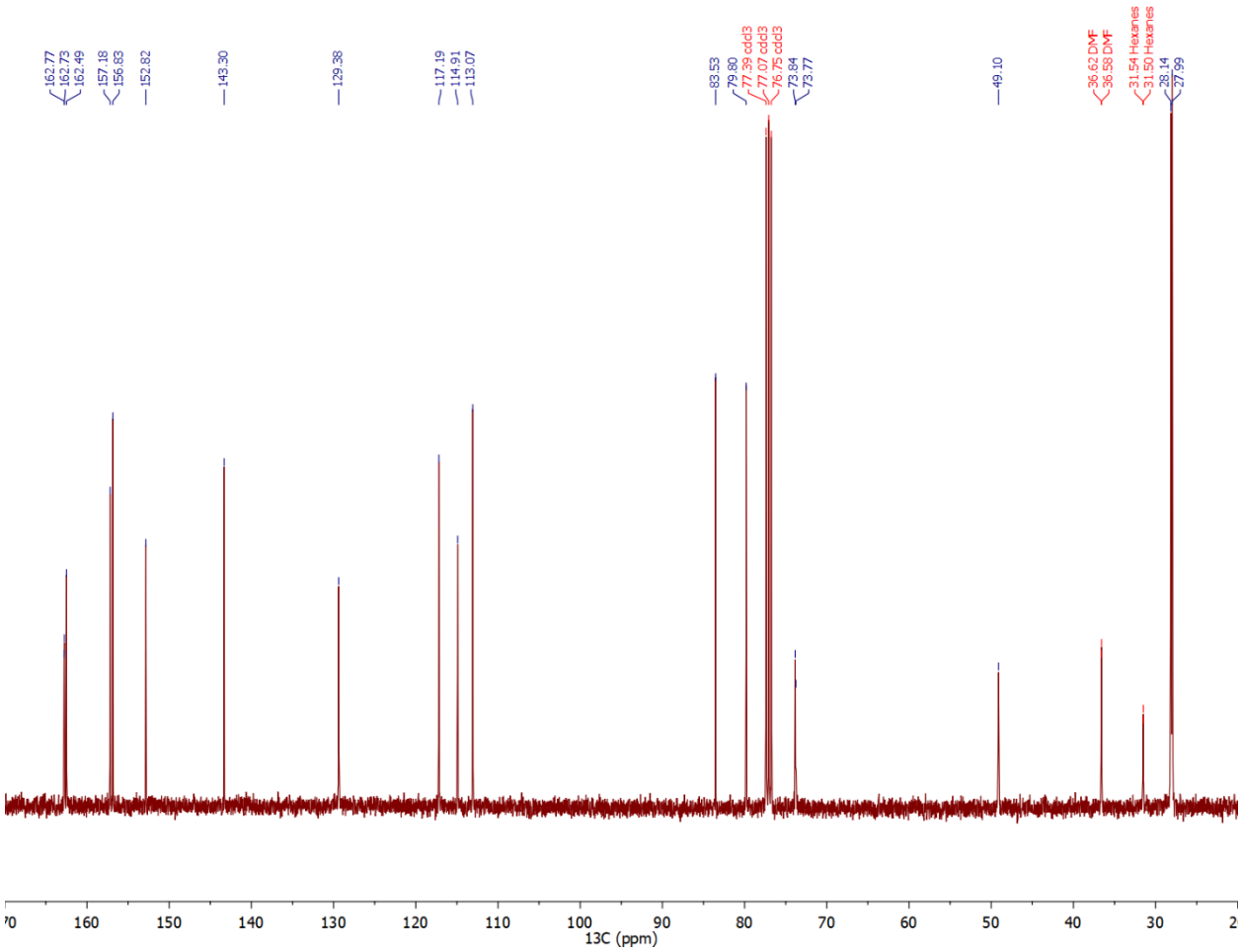


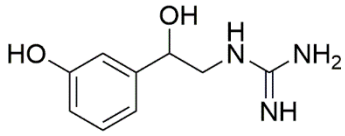
3e-Boc

^{1}H NMR for **3e-Boc**



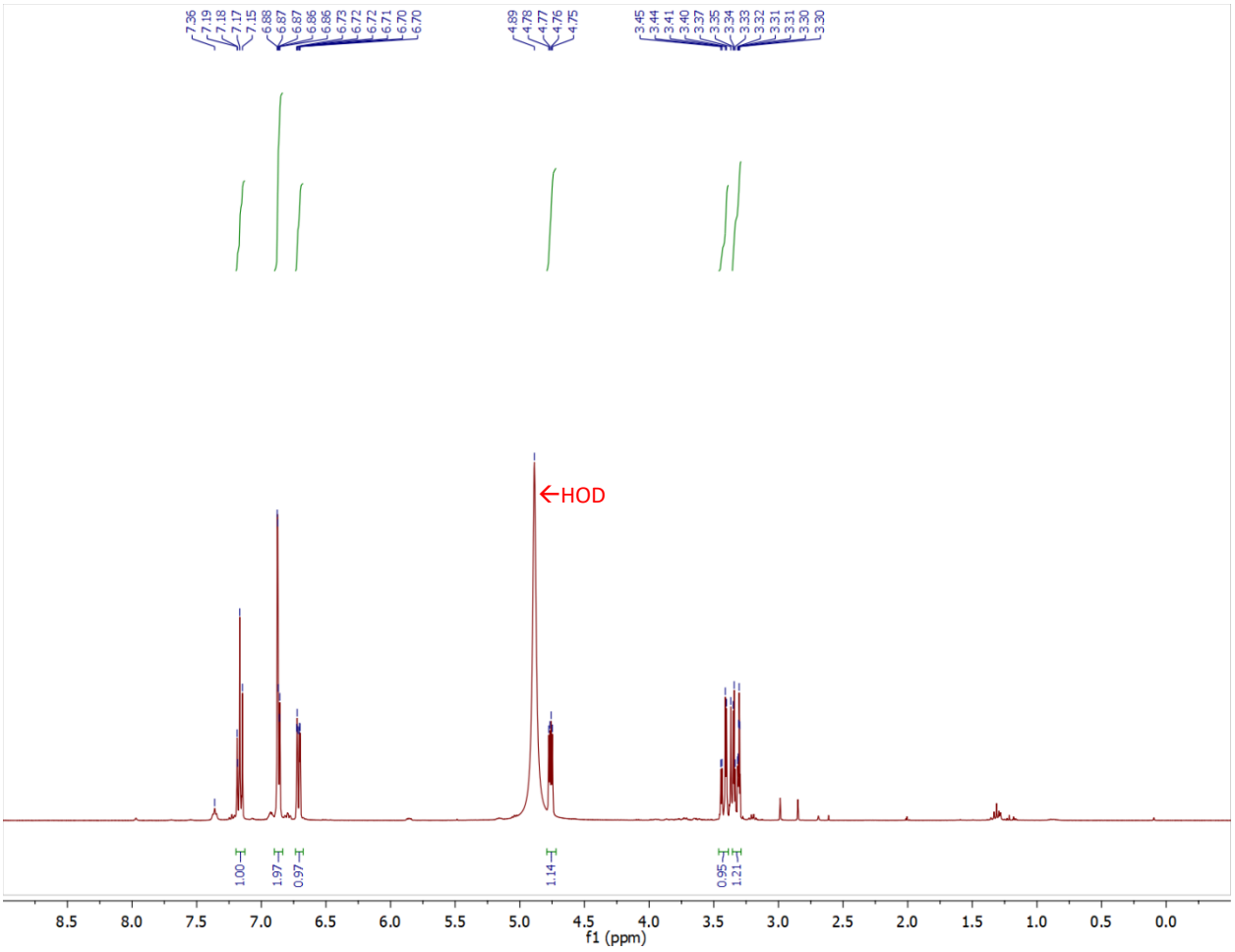
^{13}C NMR for **3e-Boc**



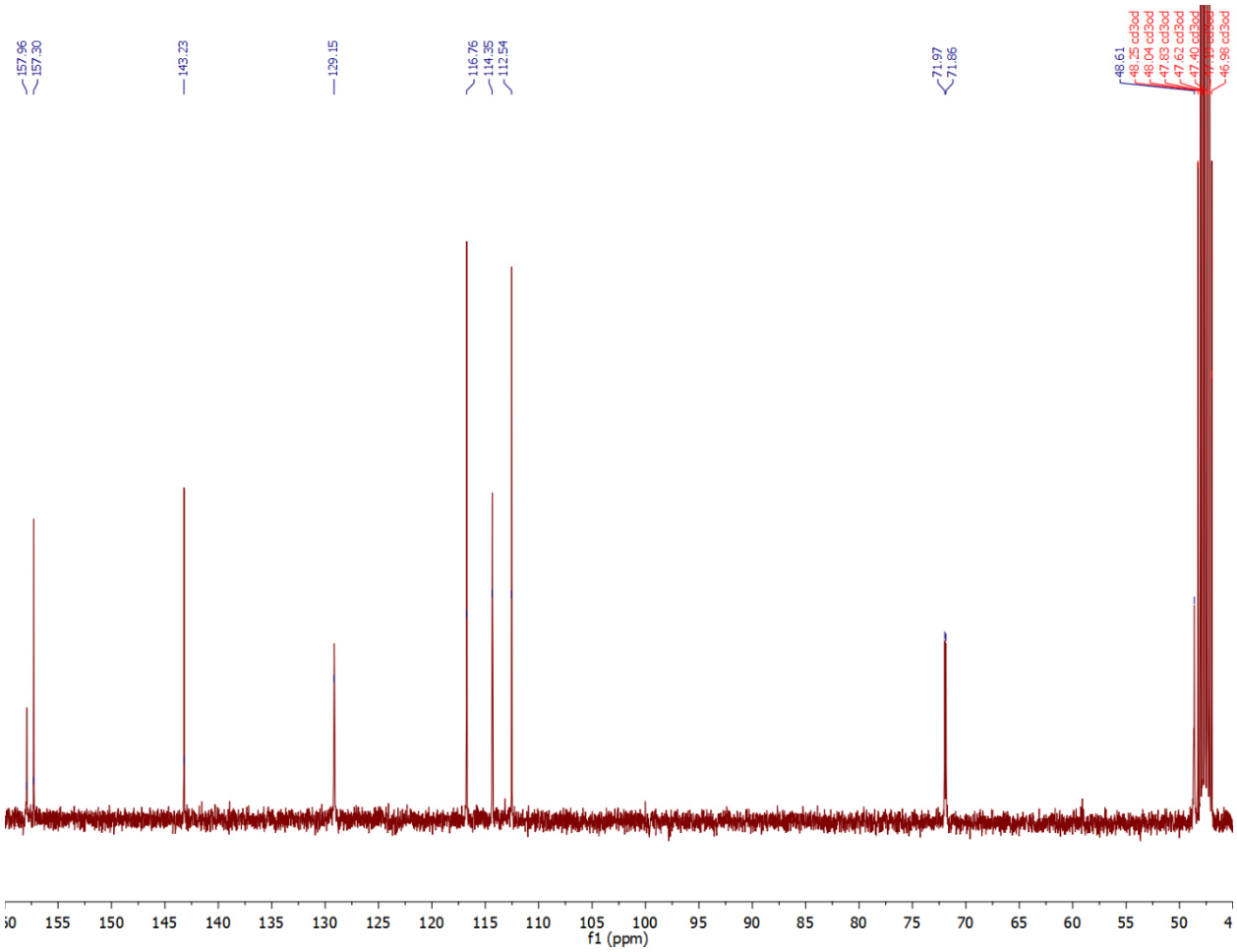


3e

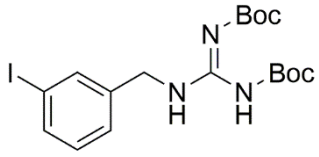
^{1}H NMR for **3e**



^{13}C NMR for **3e**

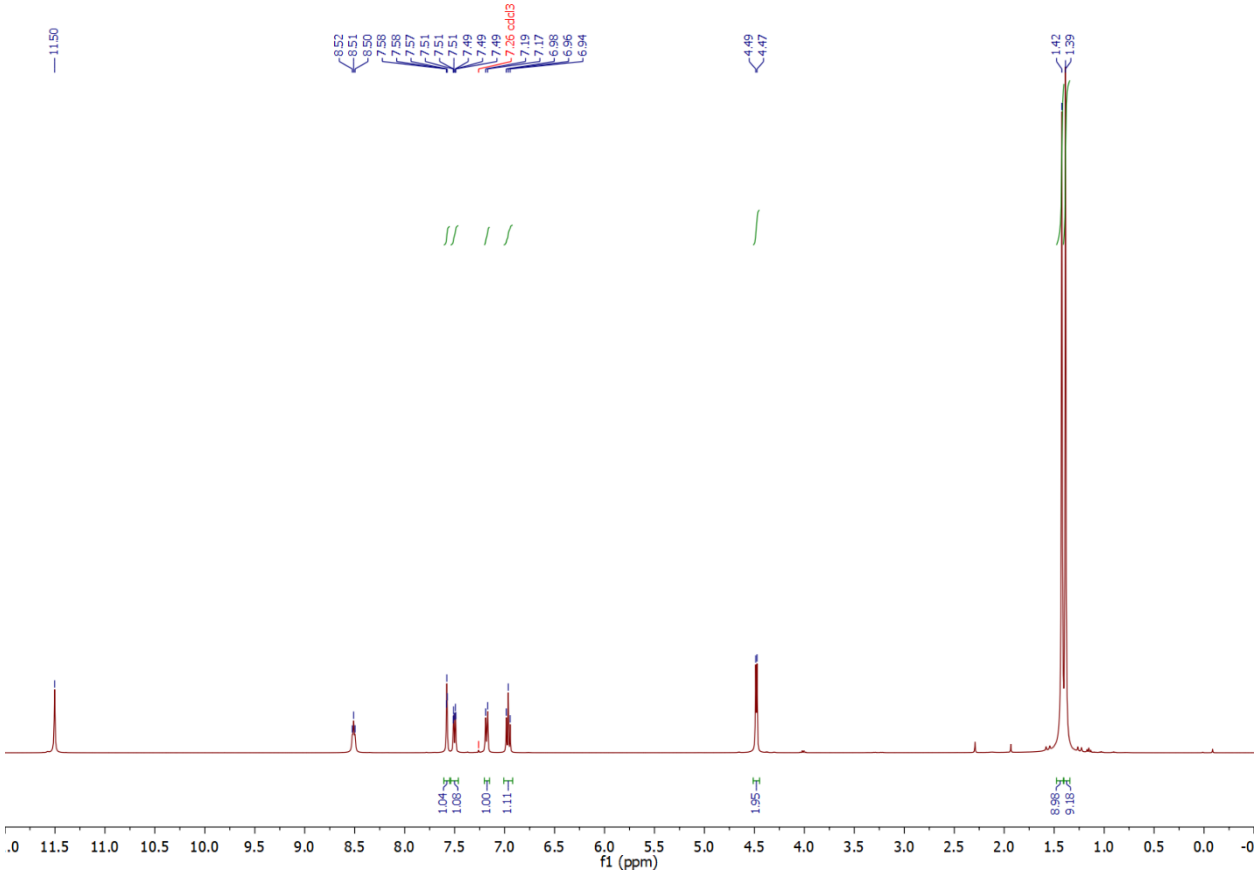


6.1.6 MIBG

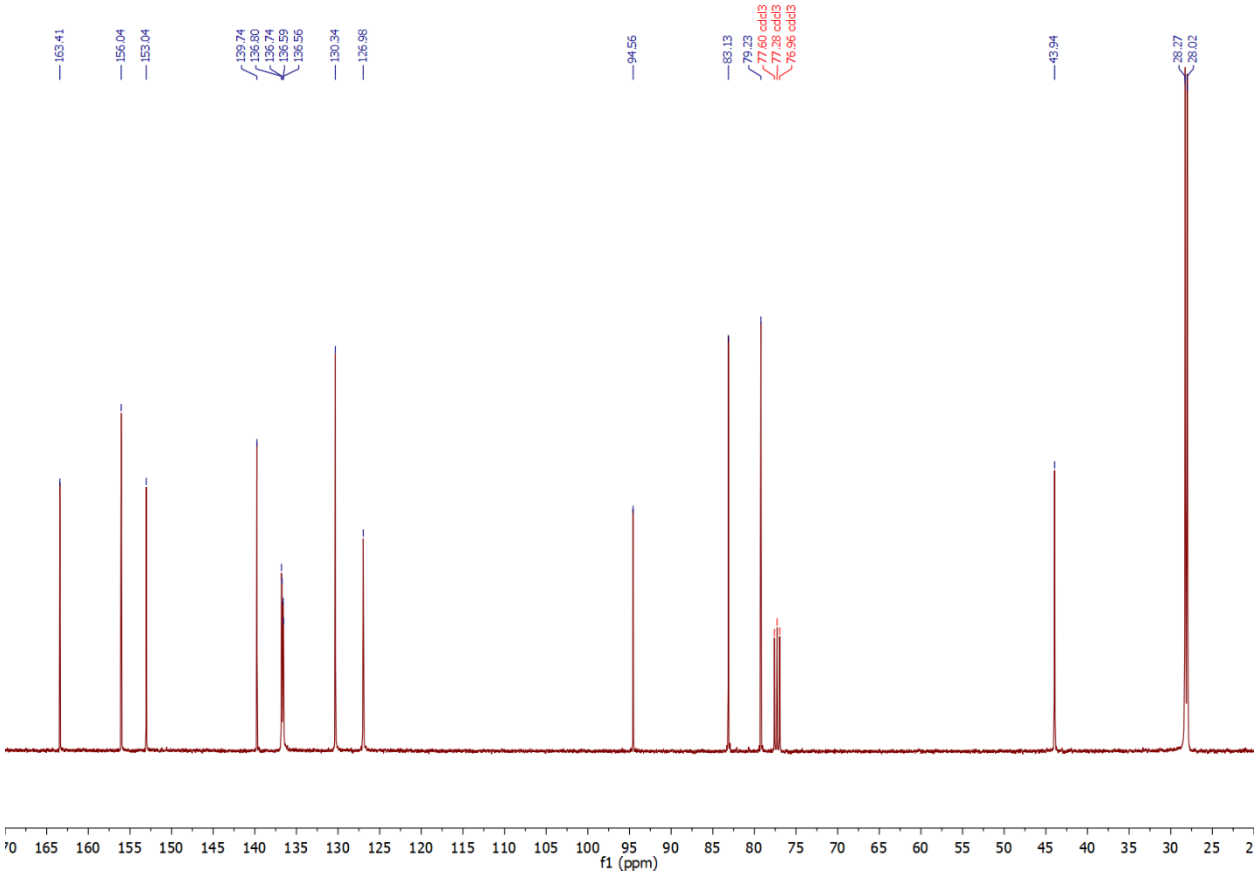


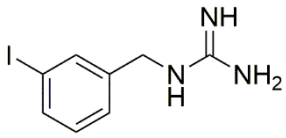
3f-Boc

^{1}H NMR for **3f-Boc**



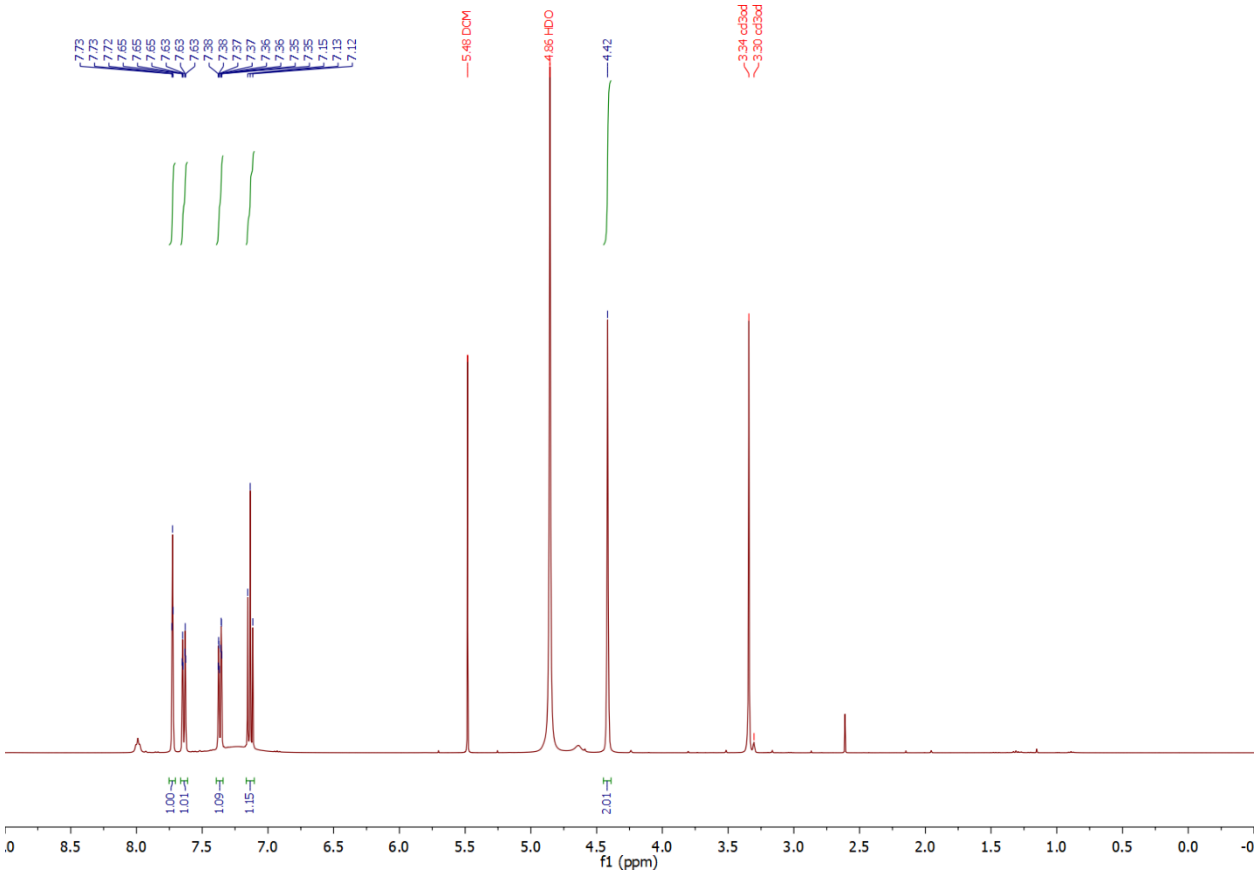
^{13}C NMR for **3f-Boc**



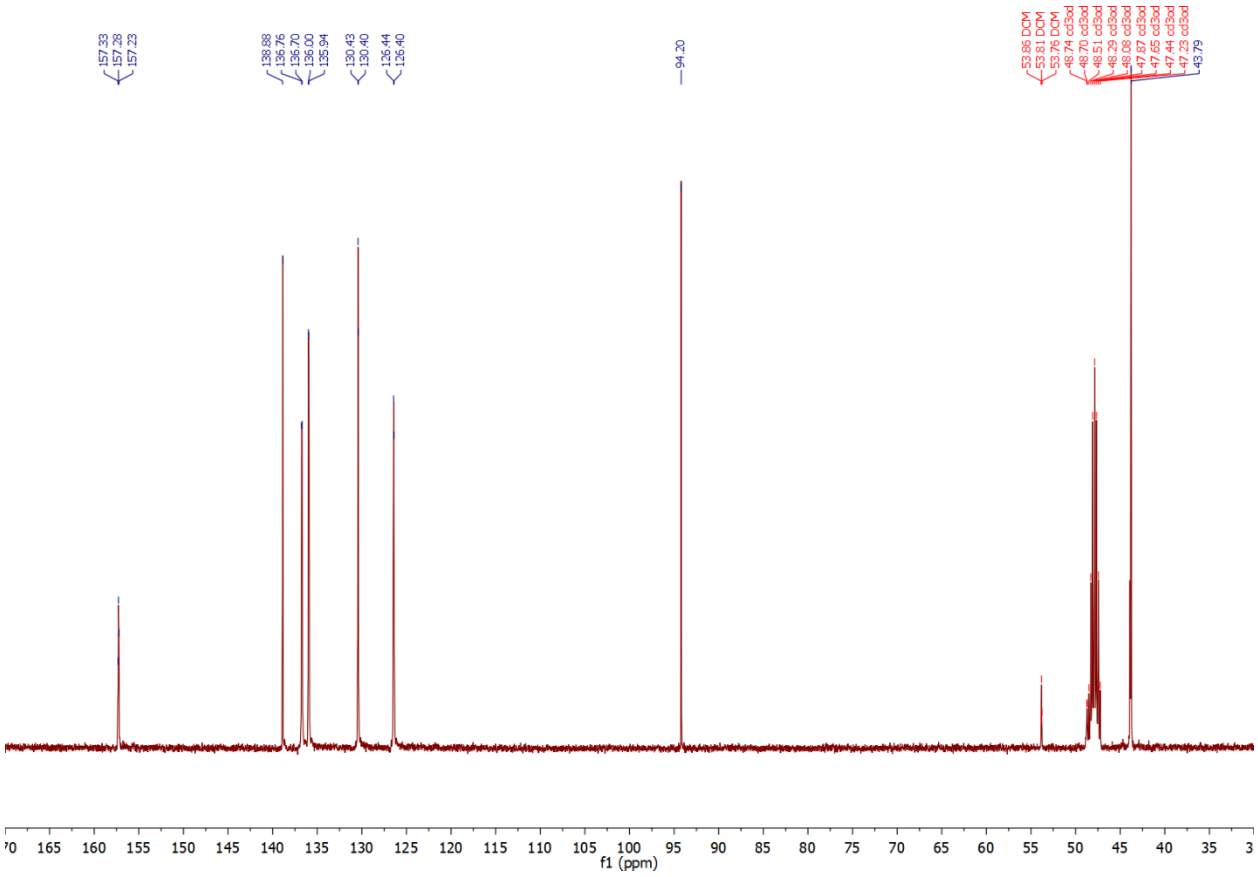


3f

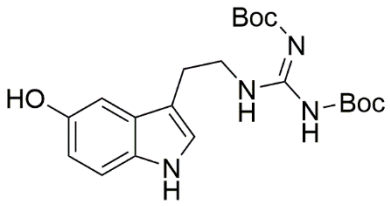
^{1}H NMR for **3f**



^{13}C NMR for **3f**

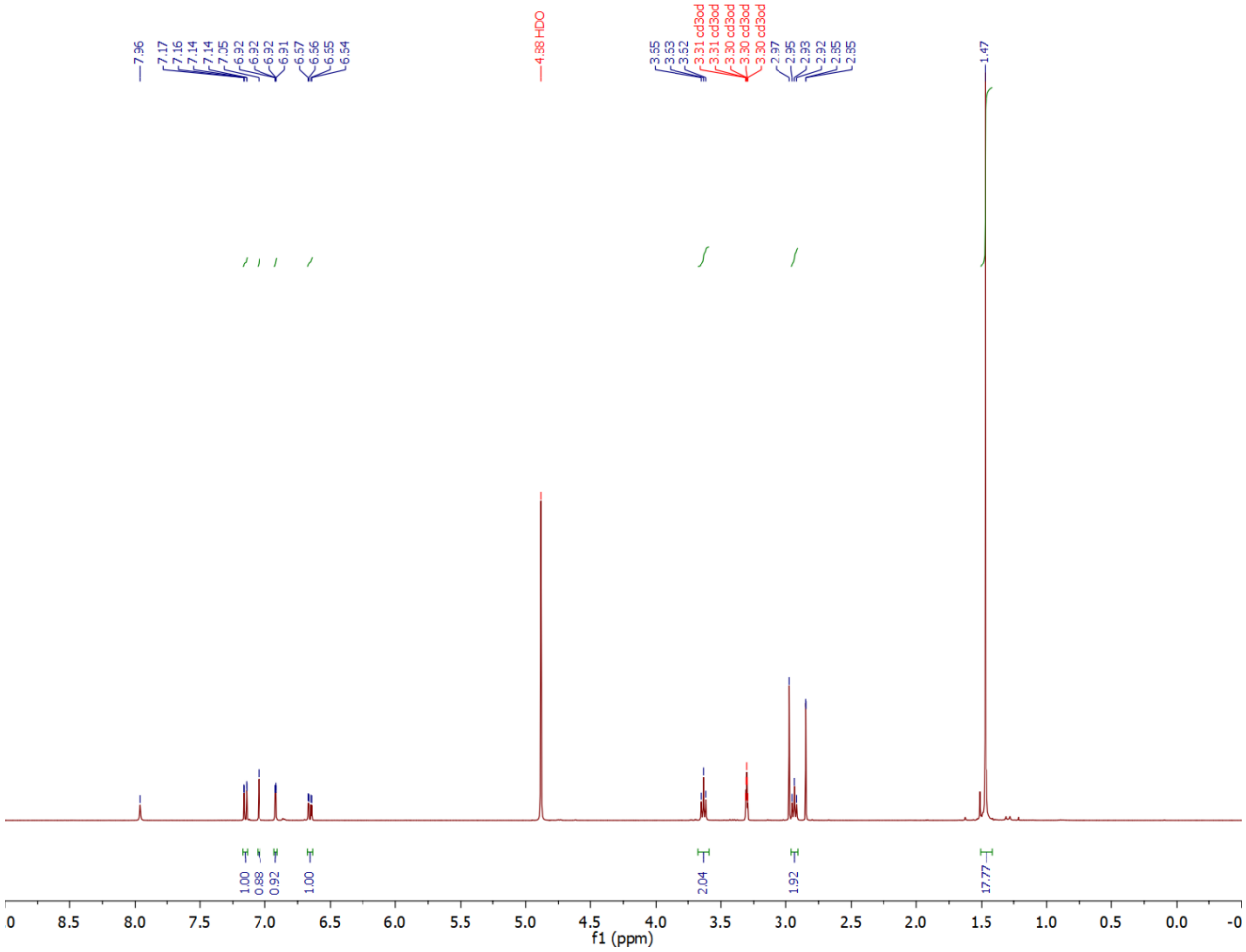


6.1.7 HTG

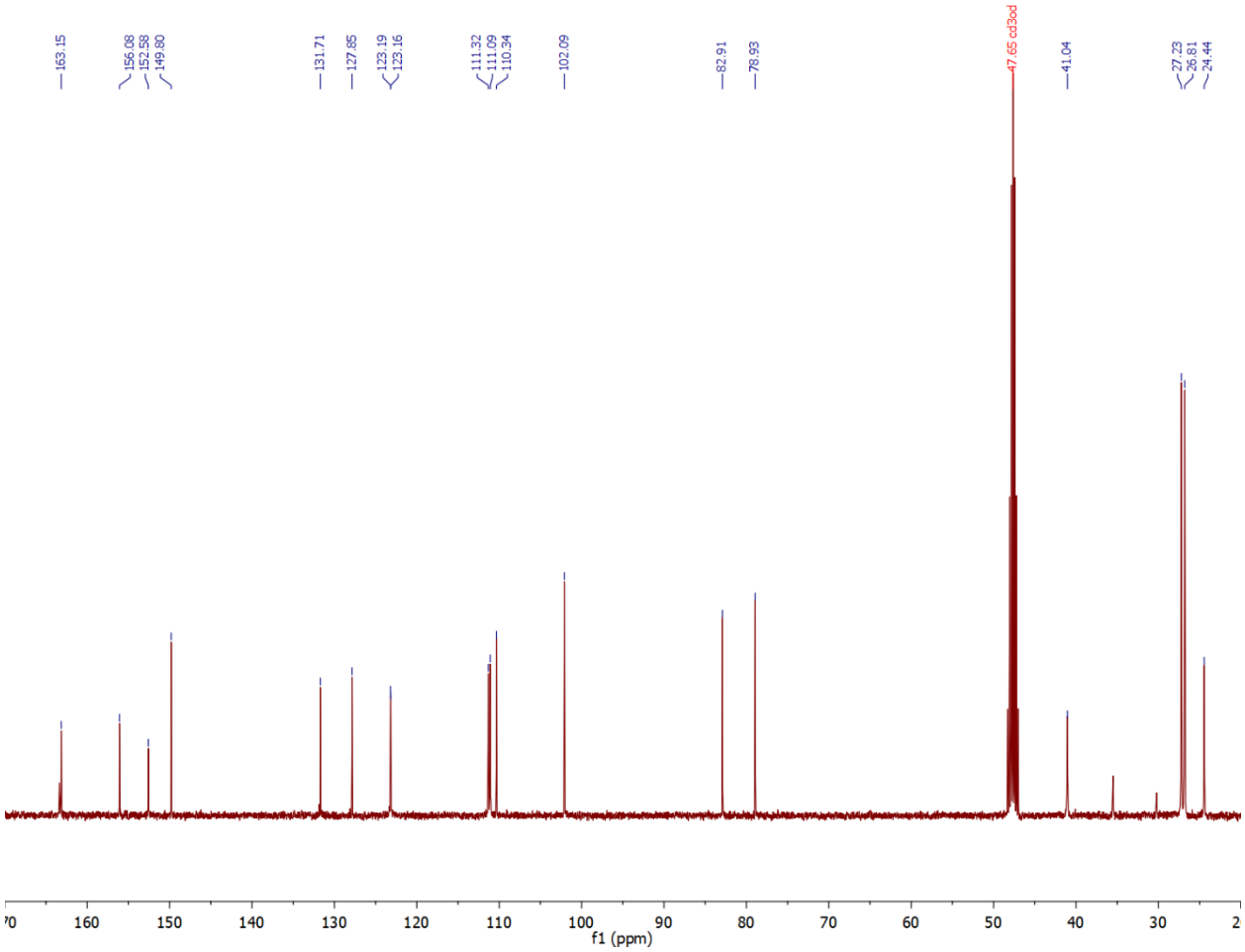


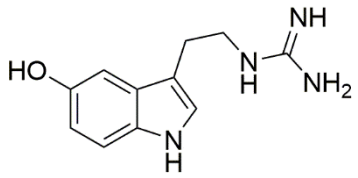
3g-Boc

^{1}H NMR for **3g-Boc**



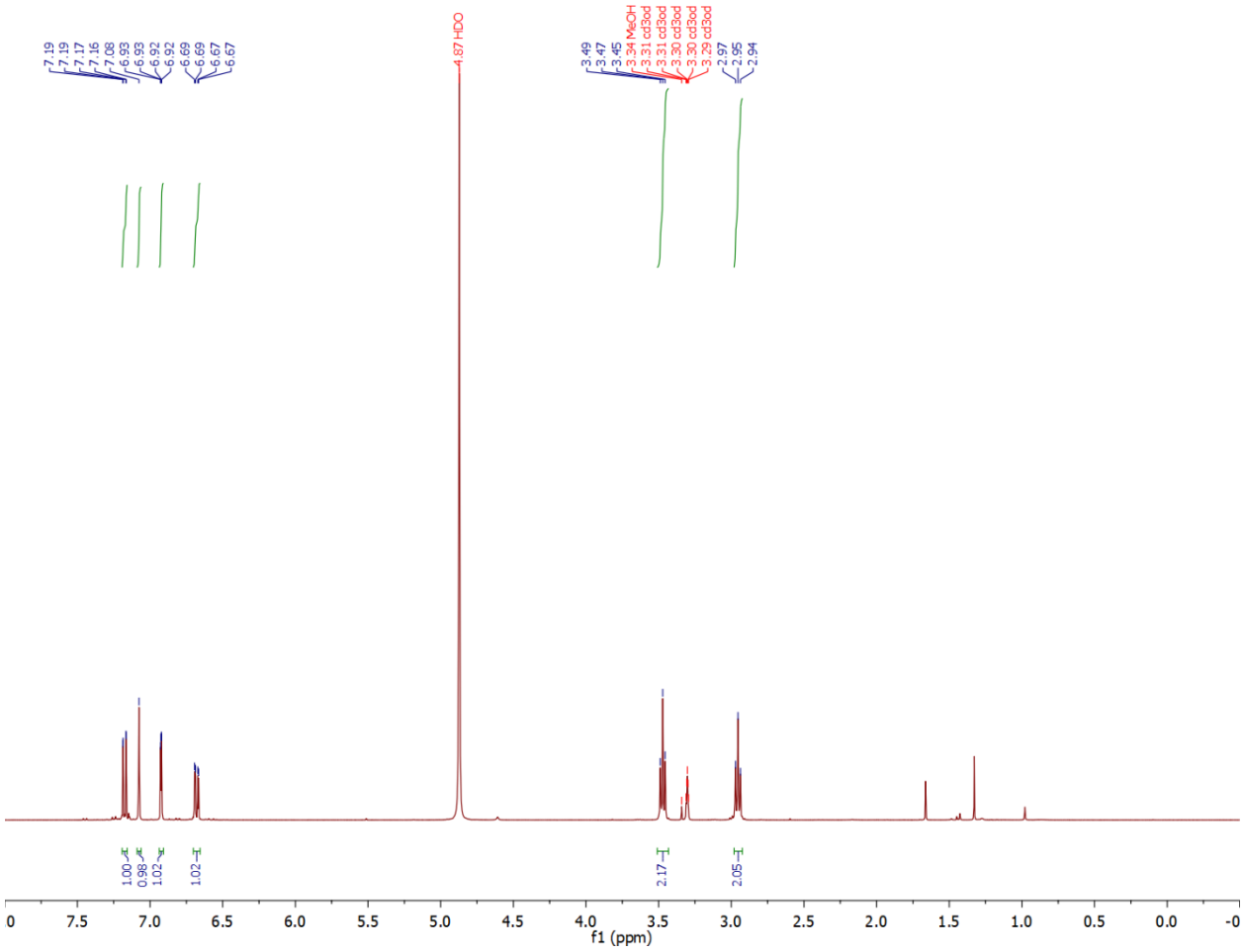
^{13}C NMR for **3g-Boc**



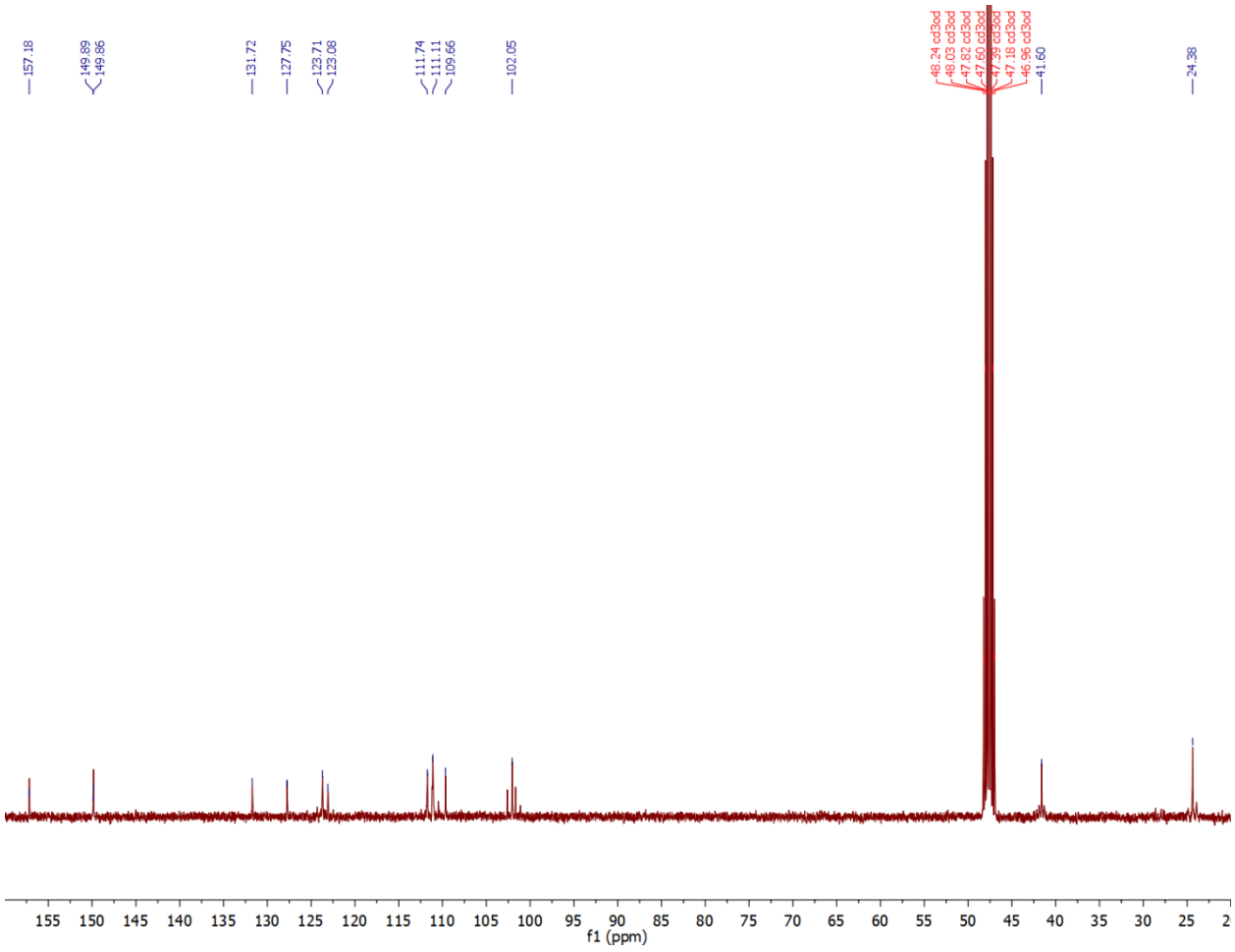


3g

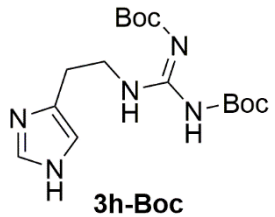
^{1}H NMR for **3g**



^{13}C NMR for **3g**

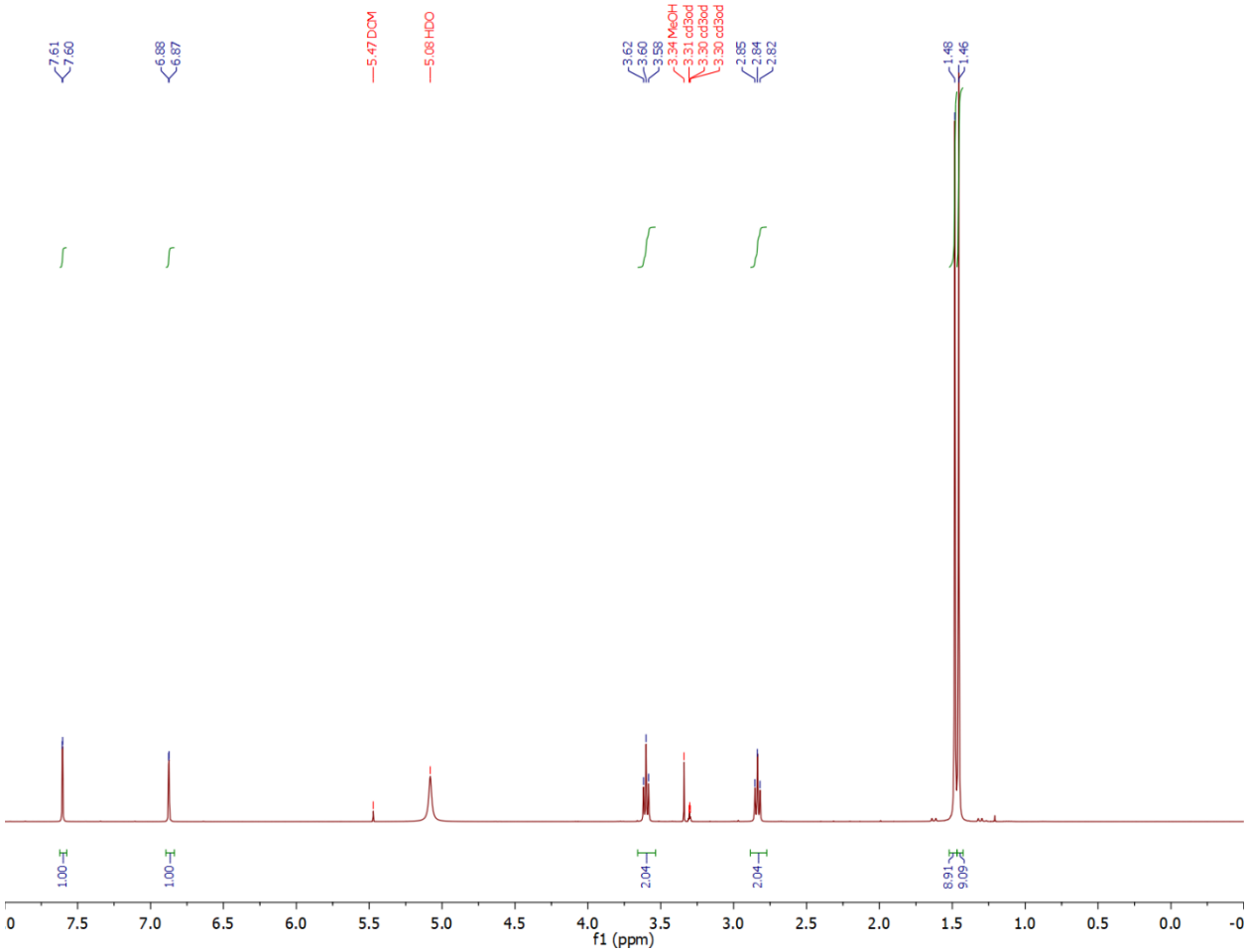


6.1.8 IEG

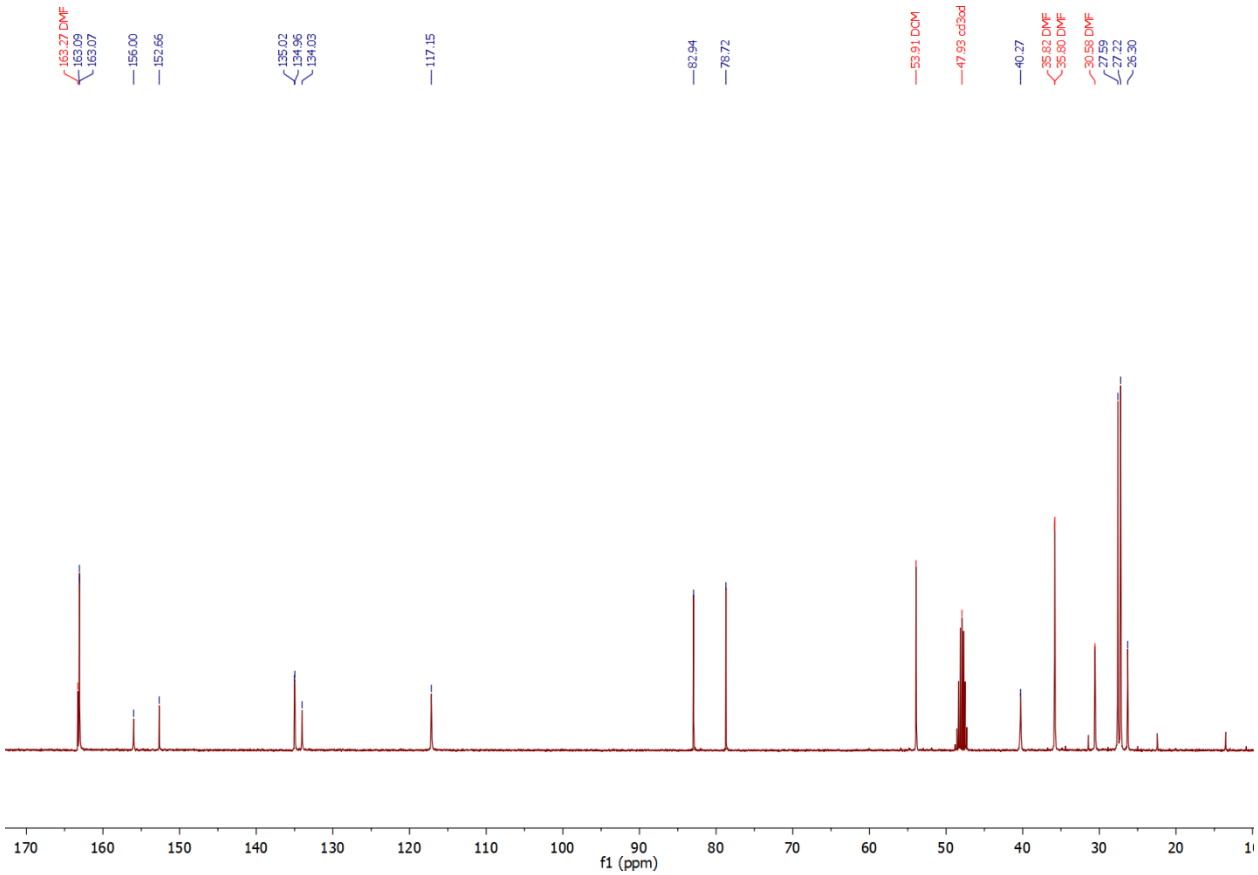


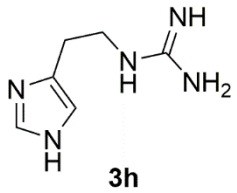
3h-Boc

^{1}H NMR for **3h-Boc**



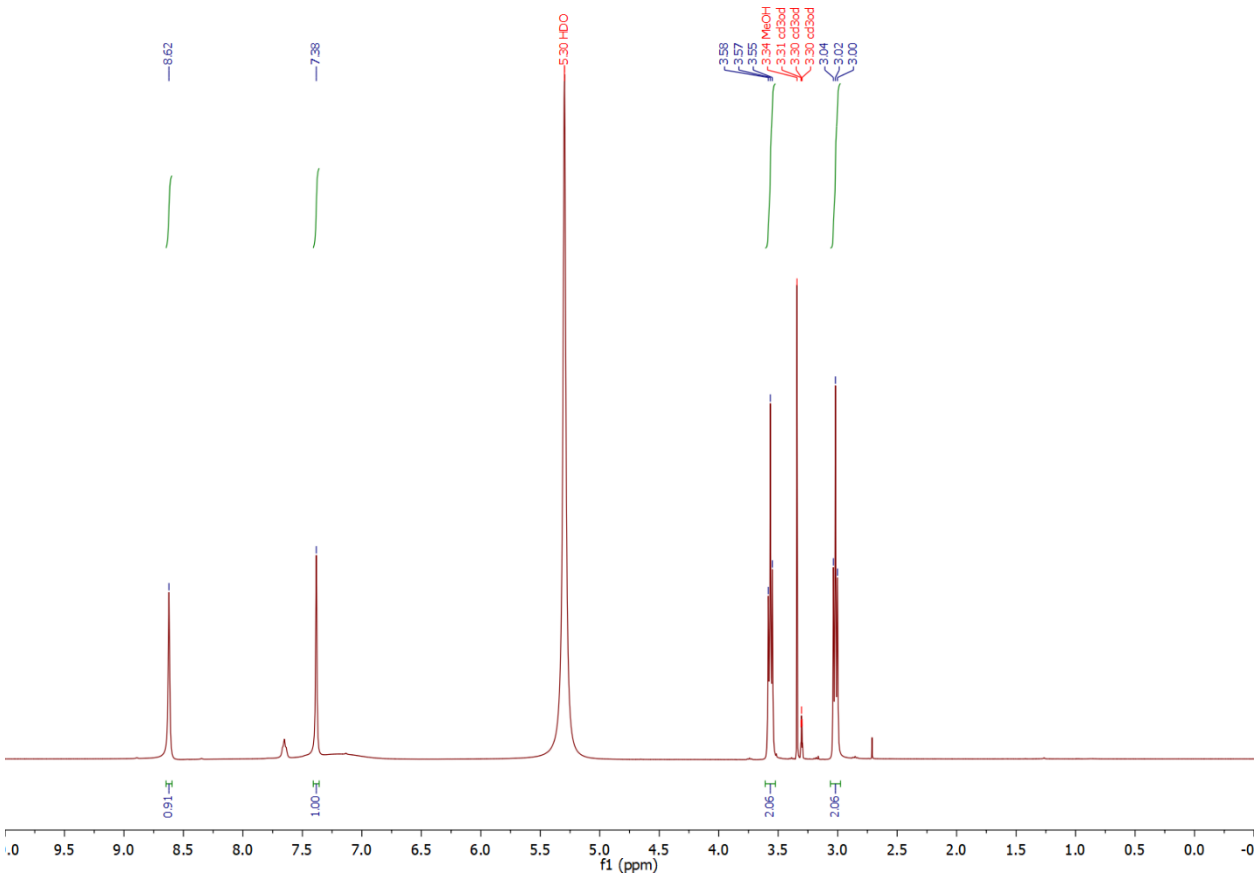
^{13}C NMR for **3h-Boc**



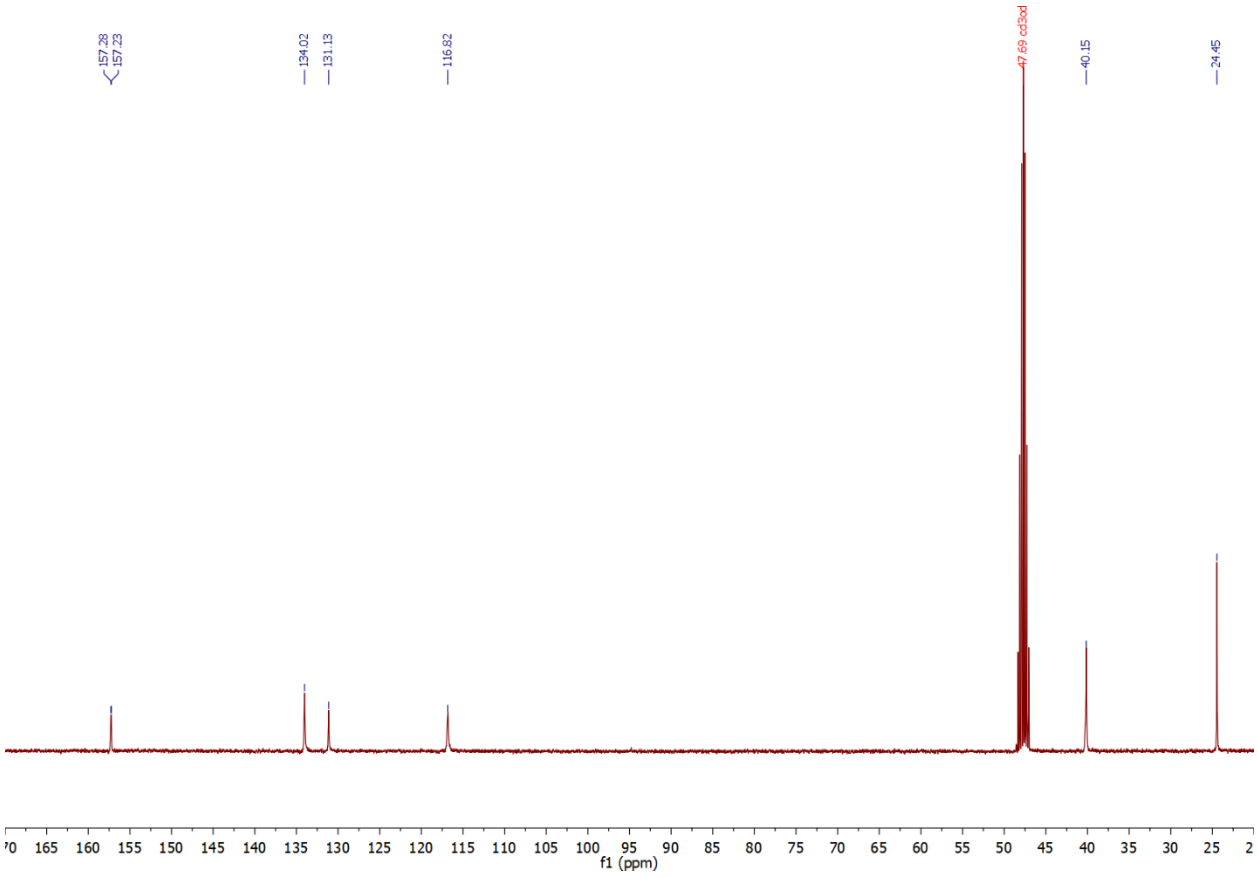


3h

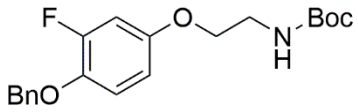
^{1}H NMR for **3h**



^{13}C NMR for **3h**

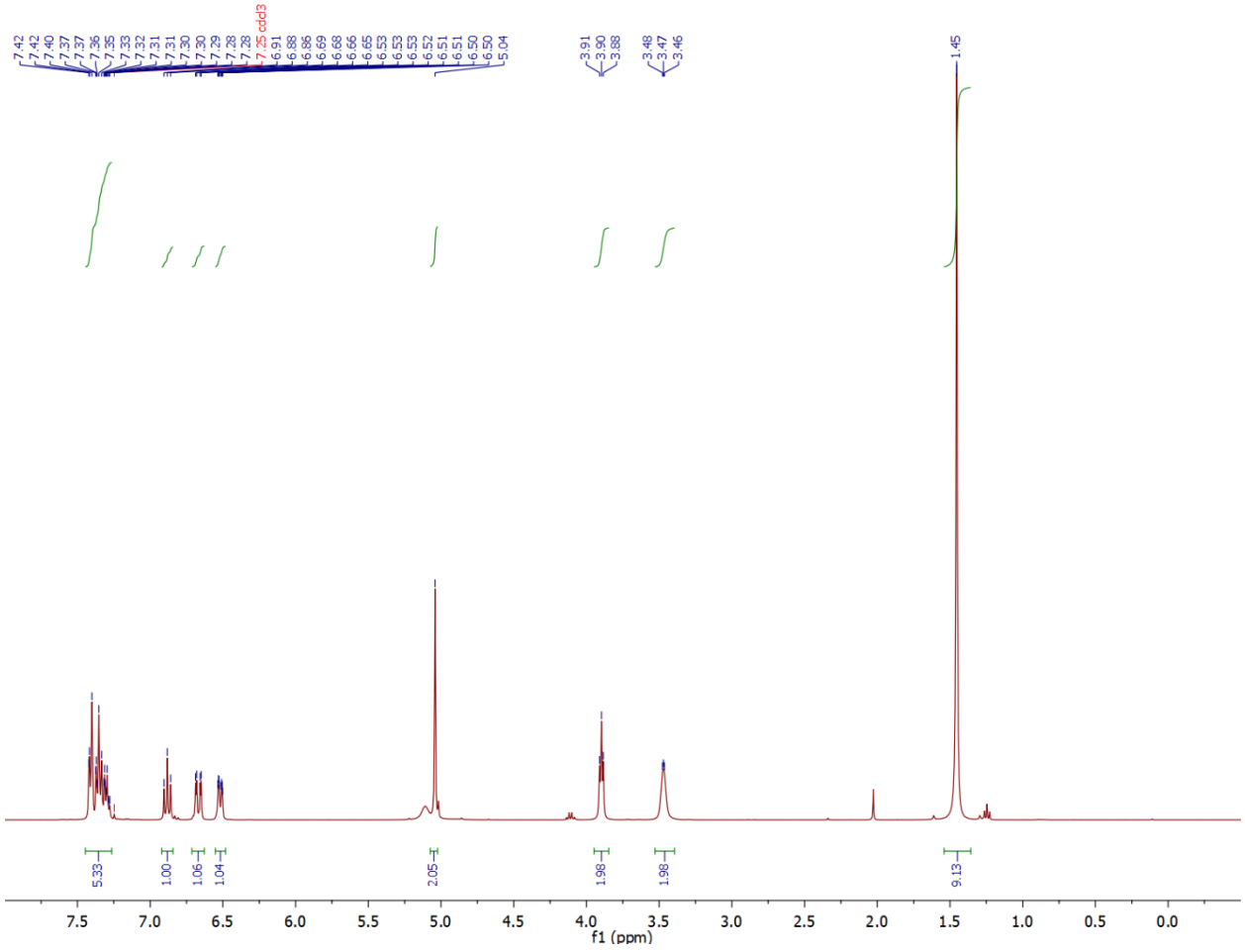


6.1.9 3F-PHPOG

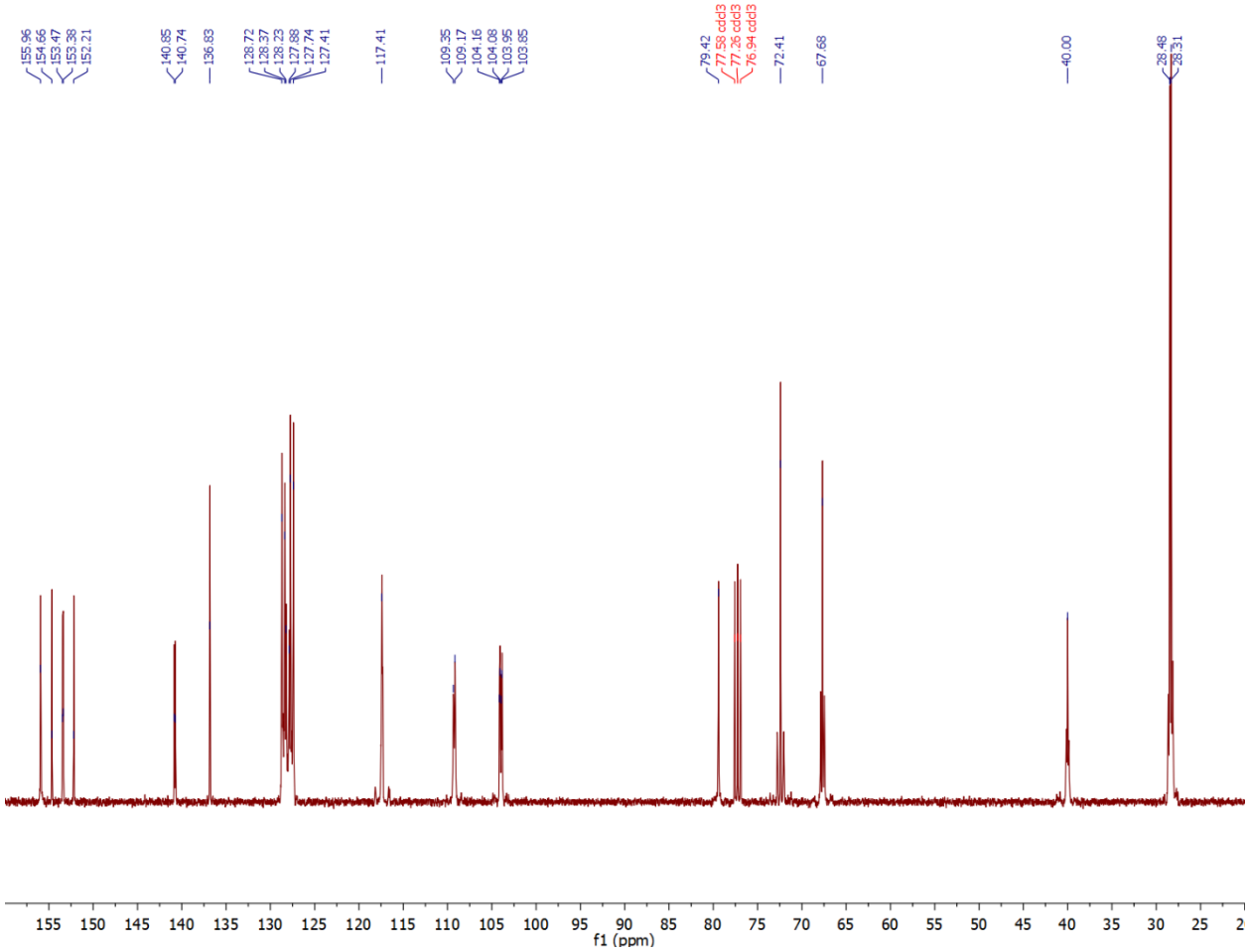


5

^{1}H NMR for **5**



^{11}C NMR for **5**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154.66
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140.85
140.74
136.83
128.72
128.37
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127.88
127.74
127.41
117.41
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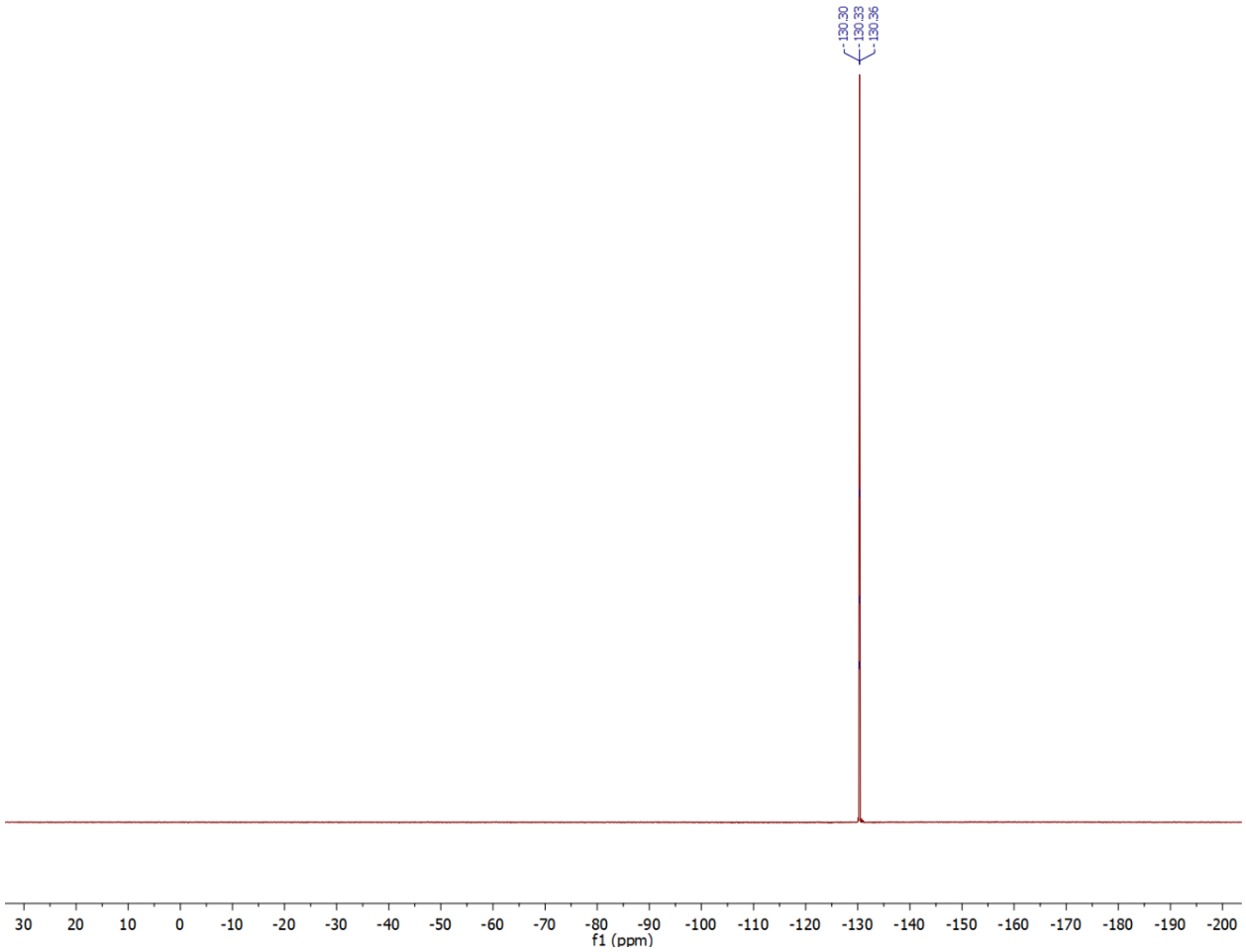
109.17
104.16
104.08
103.95
103.85
79.42
77.58 cdd3
77.26 cdd3
76.94 cdd3
72.41
67.68
40.00
28.48
28.31
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 2
f1 (ppm)

^{19}F NMR for **5**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-130.33
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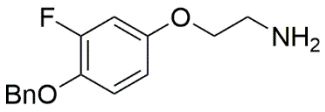
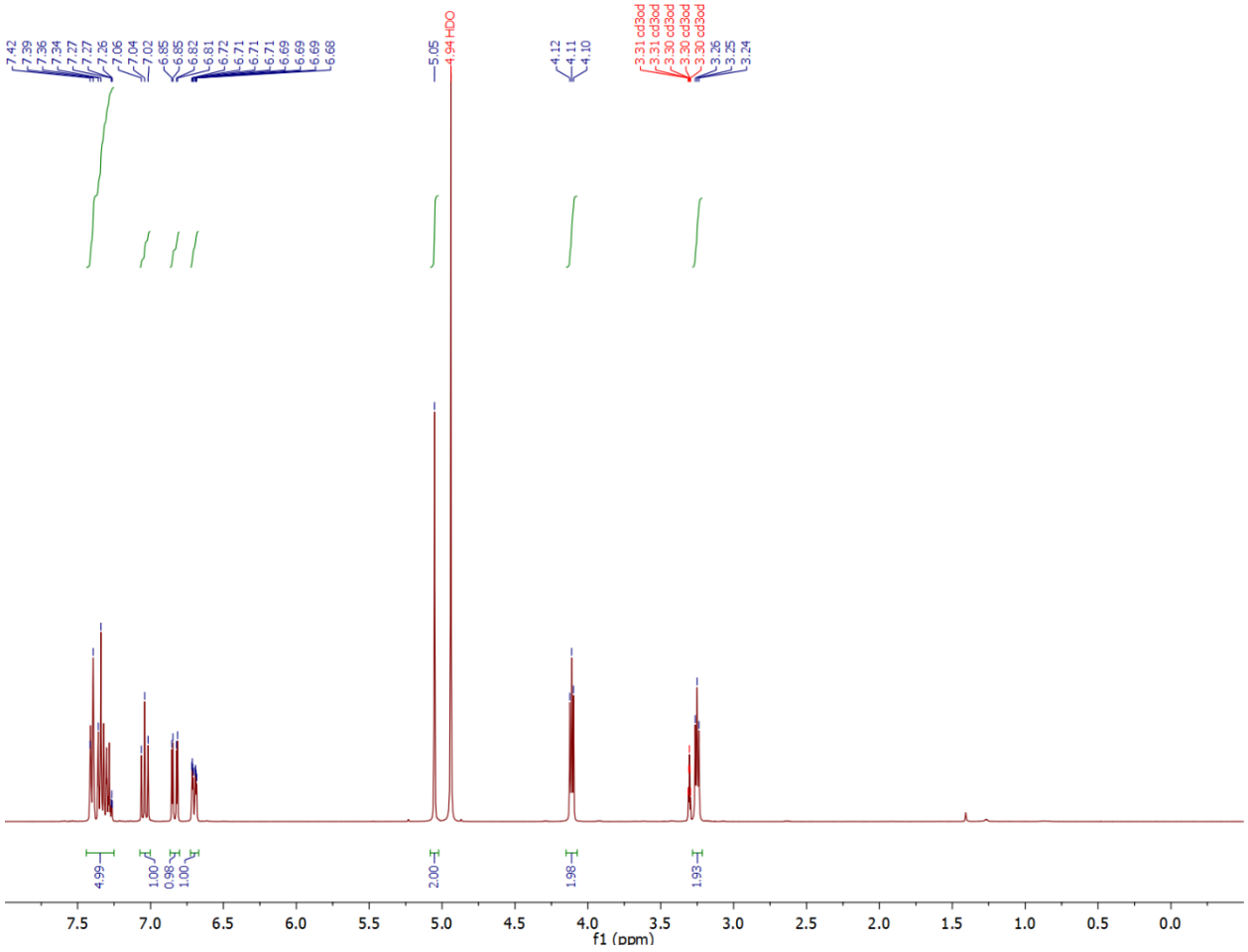
f1 (ppm)

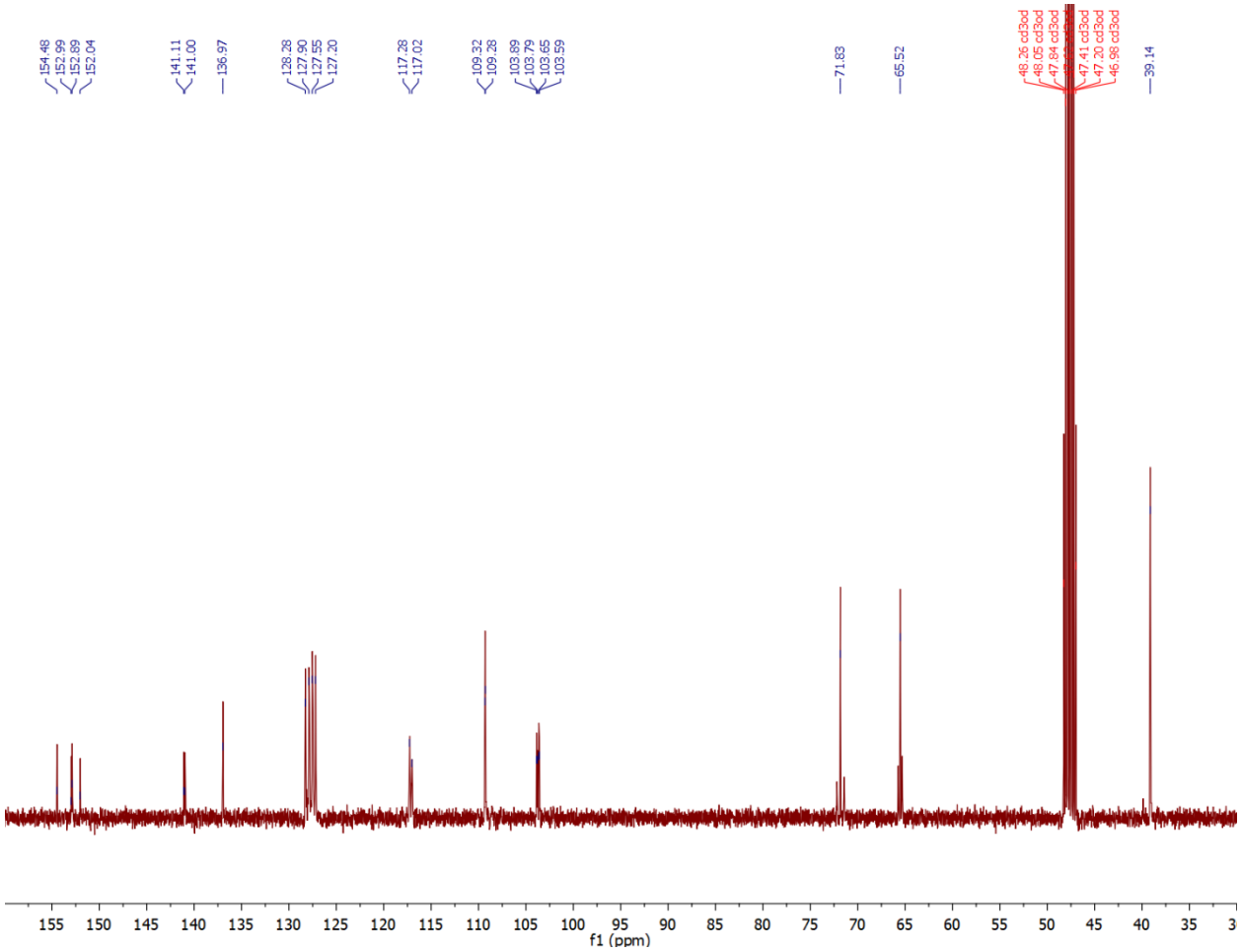

F
O
NH2
BnO

6

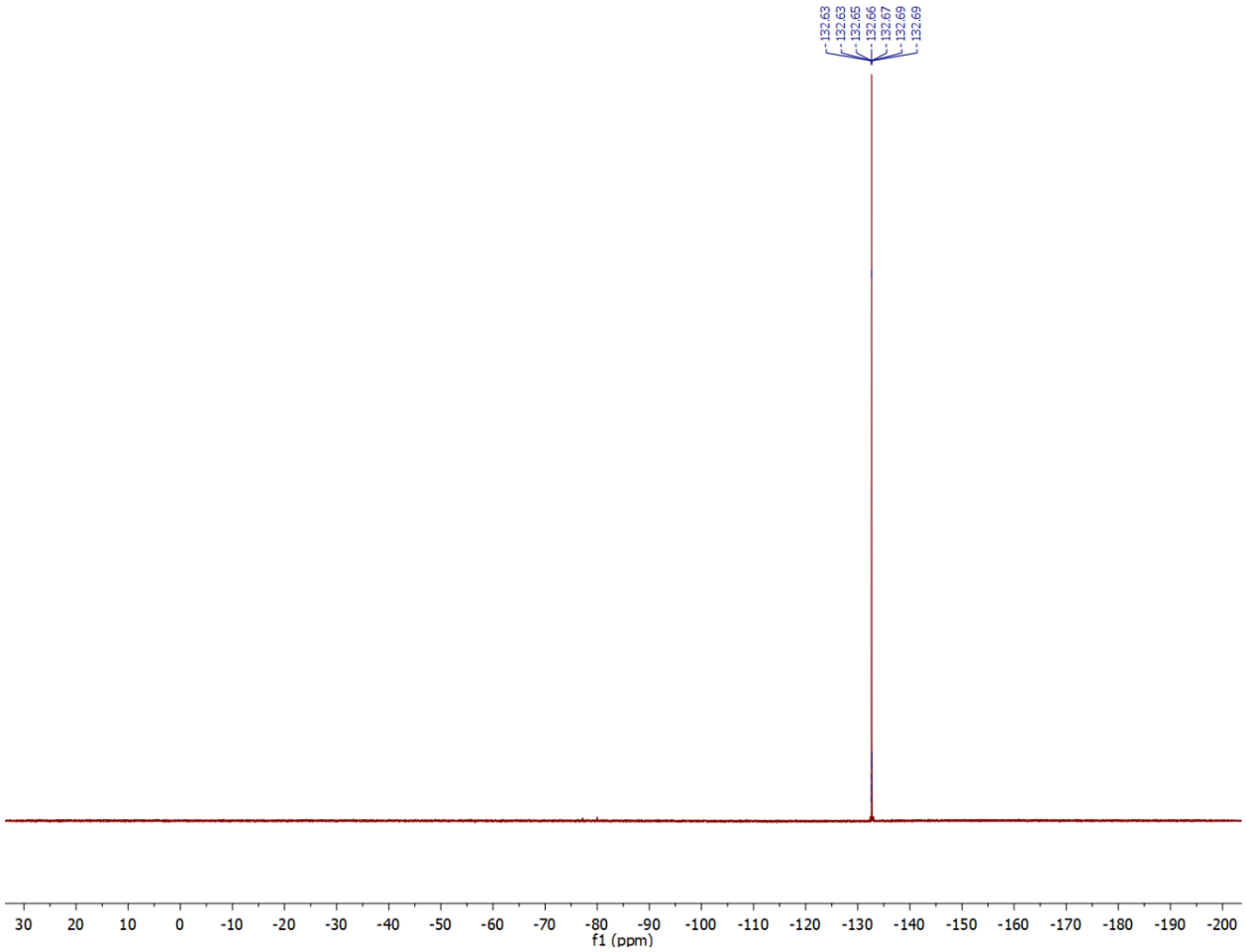
^{1}H NMR for **6**

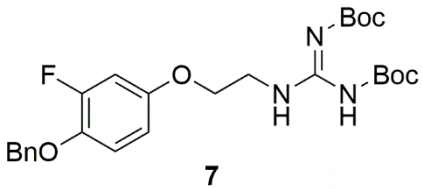

7.42
7.39
7.36
7.34
7.27
7.27
7.27
7.26
7.06
7.04
7.02
6.85
6.85
6.82
6.81
6.72
6.71
6.71
6.71
6.69
6.69
6.69
6.68
5.05
4.94 HDO
4.12
4.11
4.10
3.31 cd3od
3.31 cd3od
3.30 cd3od
3.30 cd3od
3.30 cd3od
3.30 cd3od
3.26
3.25
3.24
4.99
1.00
0.98
1.00
2.00
1.98
1.93
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

^{13}C NMR for **6**


154.48
152.99
152.89
152.04
141.11
141.00
136.97
128.28
127.90
127.55
127.20
117.28
117.02
109.32
109.28
103.89
103.79
103.65
103.59
71.83
65.52
48.26 cd3od
48.05 cd3od
47.84 cd3od
47.41 cd3od
47.20 cd3od
46.98 cd3od
39.14
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 3
f1 (ppm)

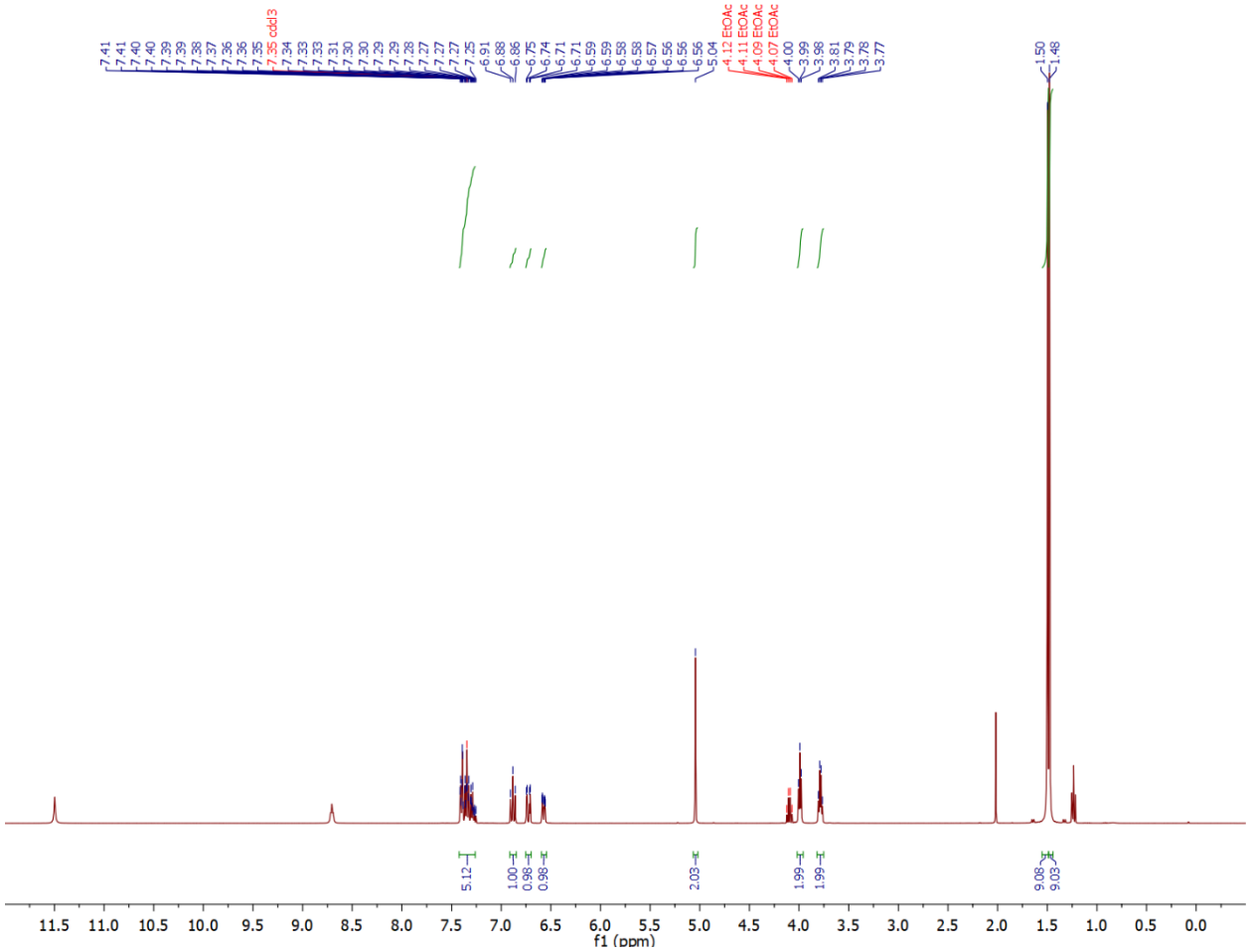
^{19}F NMR for **6**


132.63
132.63
132.65
132.66
132.67
132.69
132.69
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

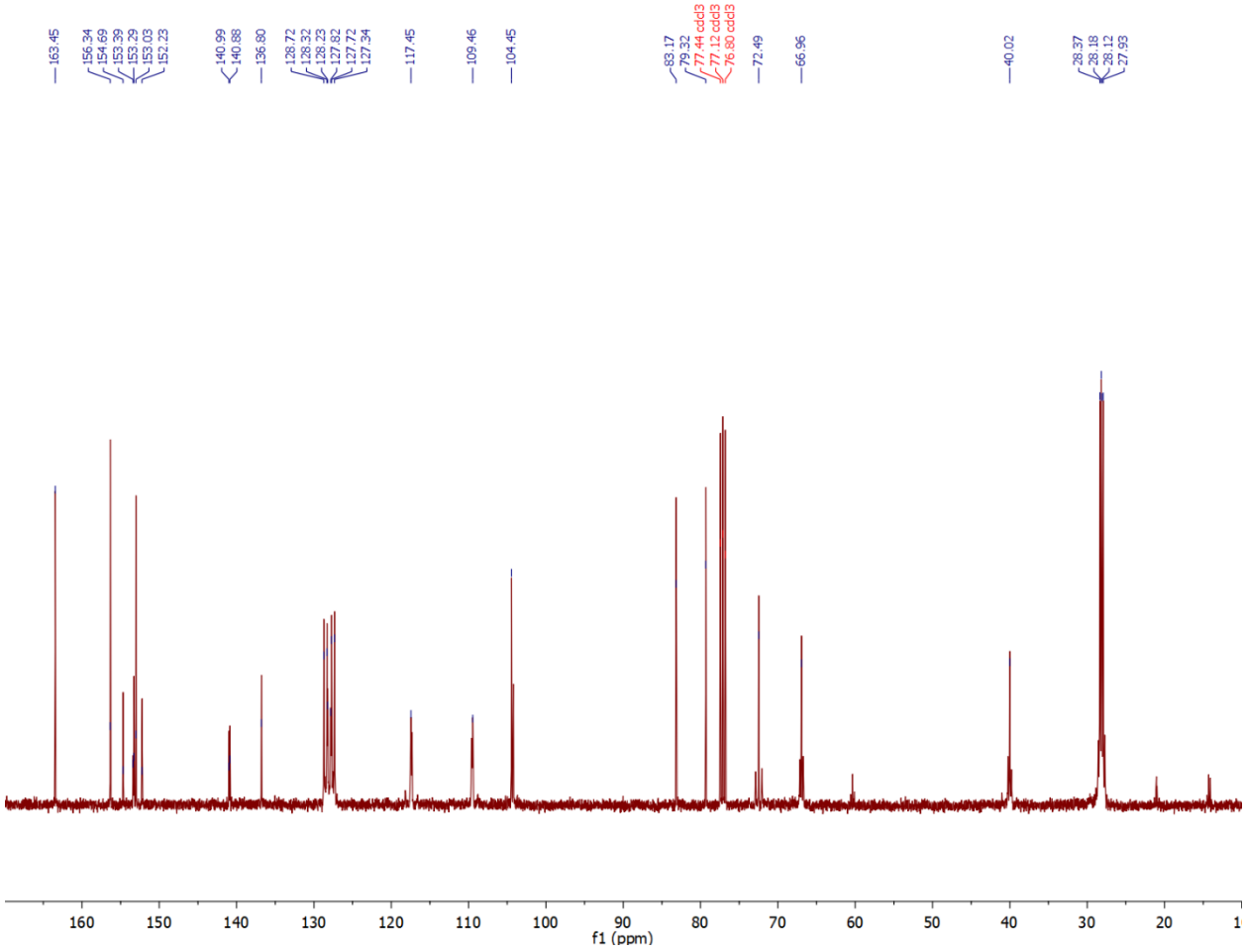

Boc
N
F
O
N
Boc
H
N
H
BnO

7

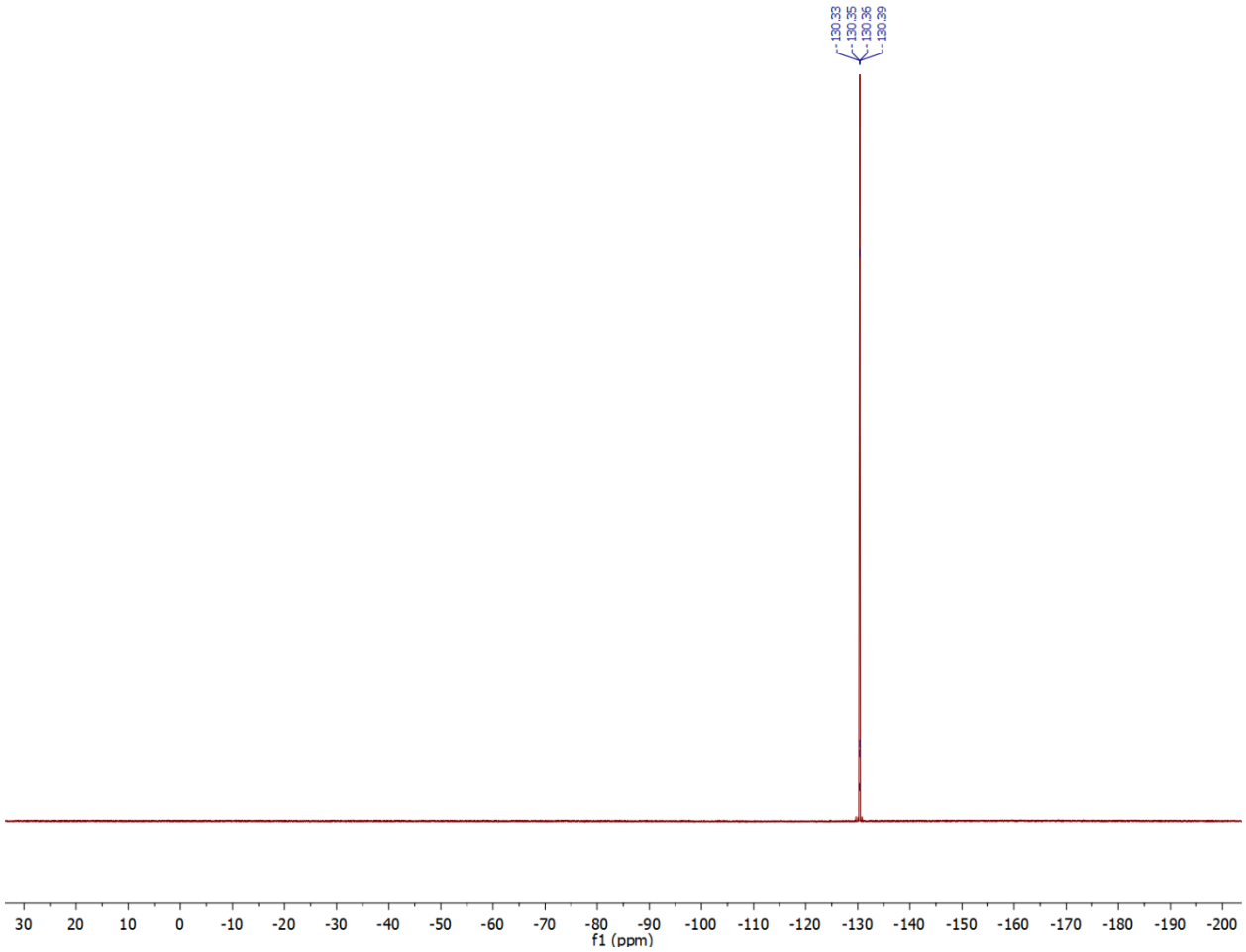
^{1}H NMR for **7**

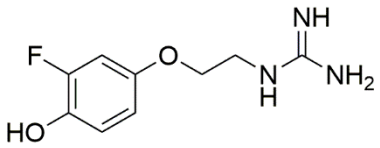

7.41
7.41
7.40
7.40
7.39
7.39
7.38
7.37
7.36
7.36
7.35
7.35 cdcl3
7.34
7.33
7.33
7.31
7.30
7.30
7.29
7.29
7.28
7.27
7.27
7.27
7.25
6.91
6.88
6.86
6.75
6.74
6.71
6.59
6.59
6.59
6.58
6.58
6.57
6.56
6.56
6.56
5.04
4.12 EtOAc
4.11 EtOAc
4.09 EtOAc
4.07 EtOAc
4.00
3.99
3.98
3.81
3.79
3.78
3.77
1.50
1.48
5.12
1.00
0.98
0.98
2.03
1.99
1.99
9.08
9.03
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{13}C NMR for **7**


163.45
156.34
154.69
153.39
153.29
153.03
152.23
140.99
140.88
136.80
128.72
128.32
128.23
127.82
127.72
127.34
117.45
109.46
104.45
83.17
79.32
77.44 cdd3
77.12 cdd3
76.80 cdd3
72.49
66.96
40.02
28.37
28.18
28.12
27.93
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

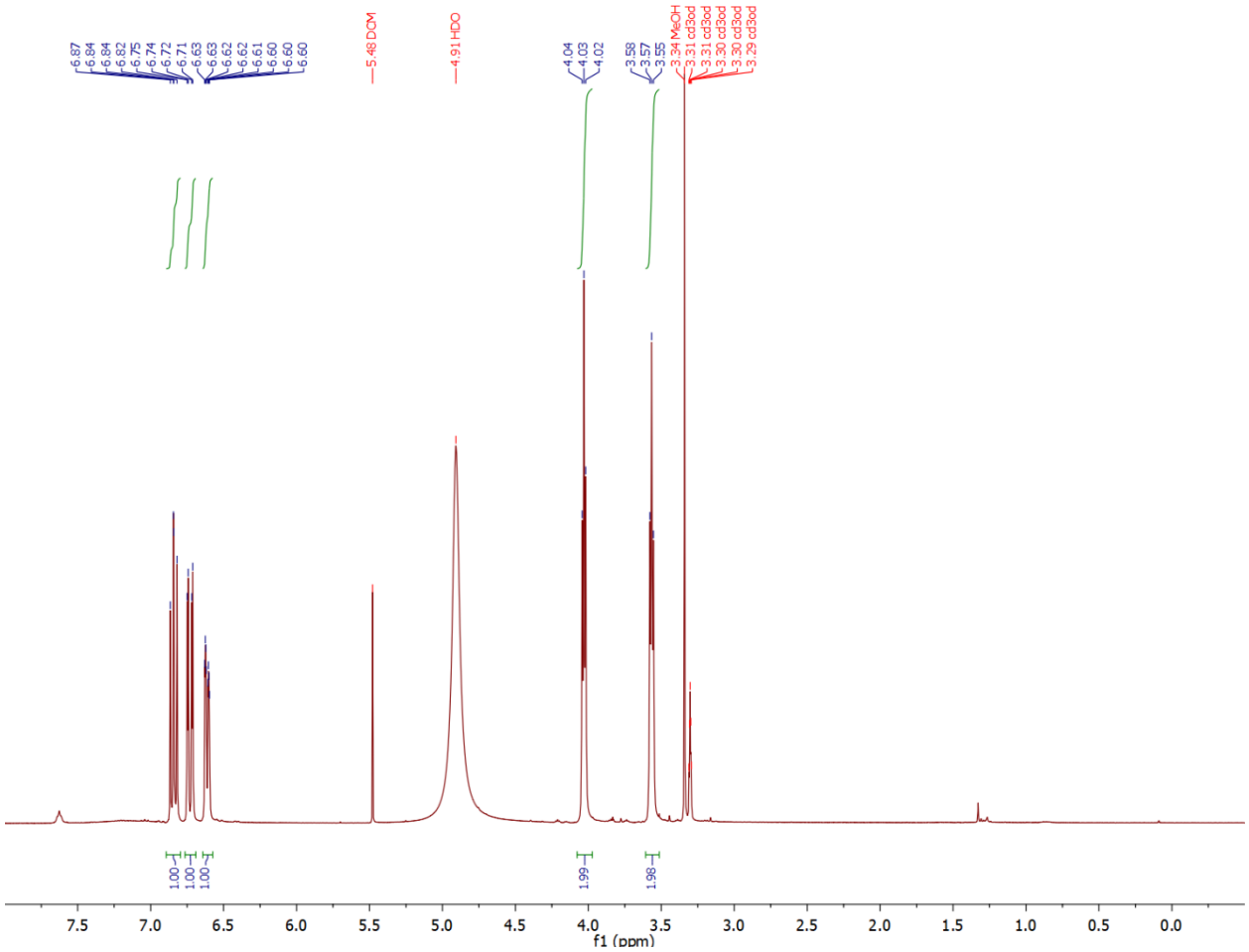
^{19}F NMR for **7**


-130.33
-130.35
-130.36
-130.39
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

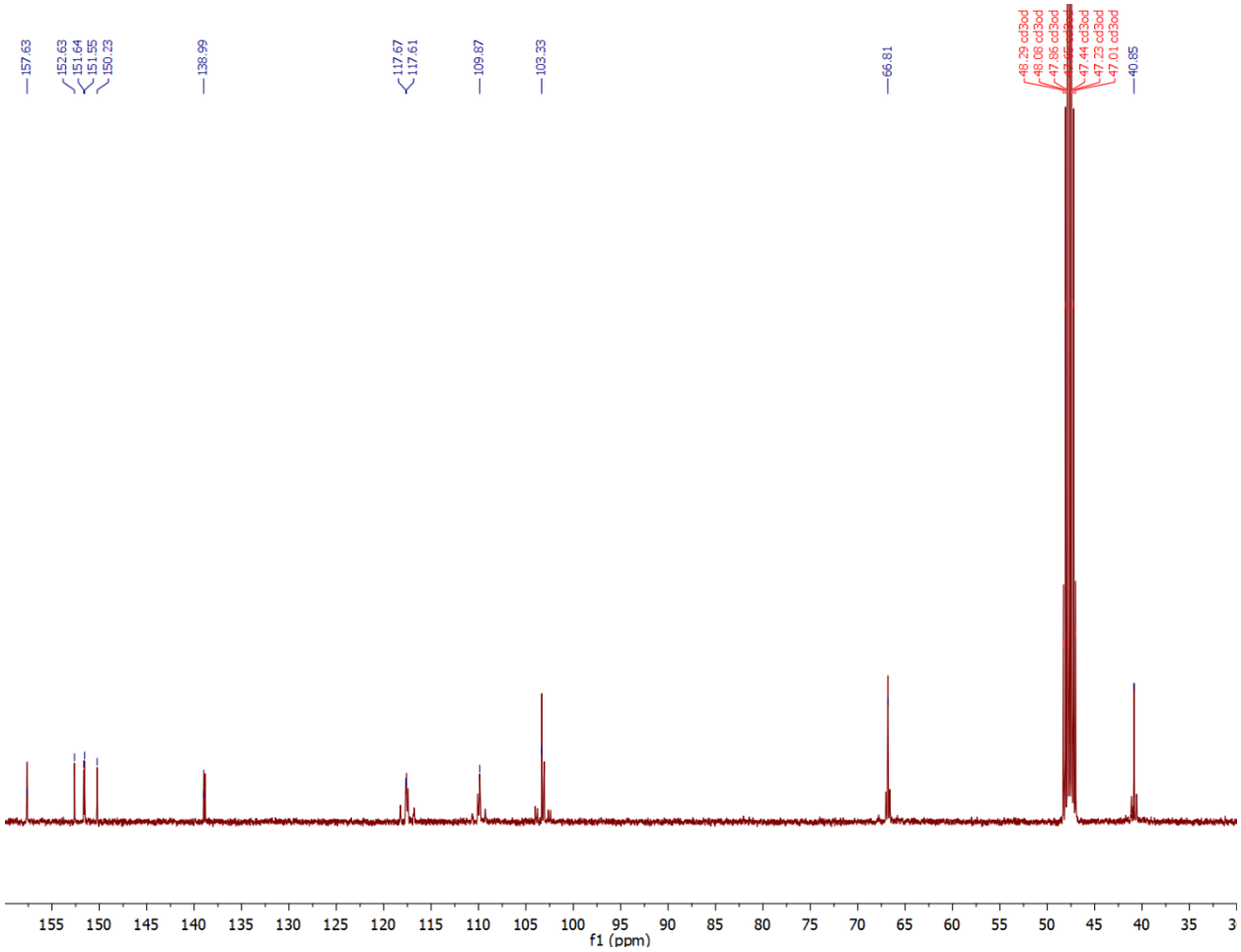


3F-PHPOG

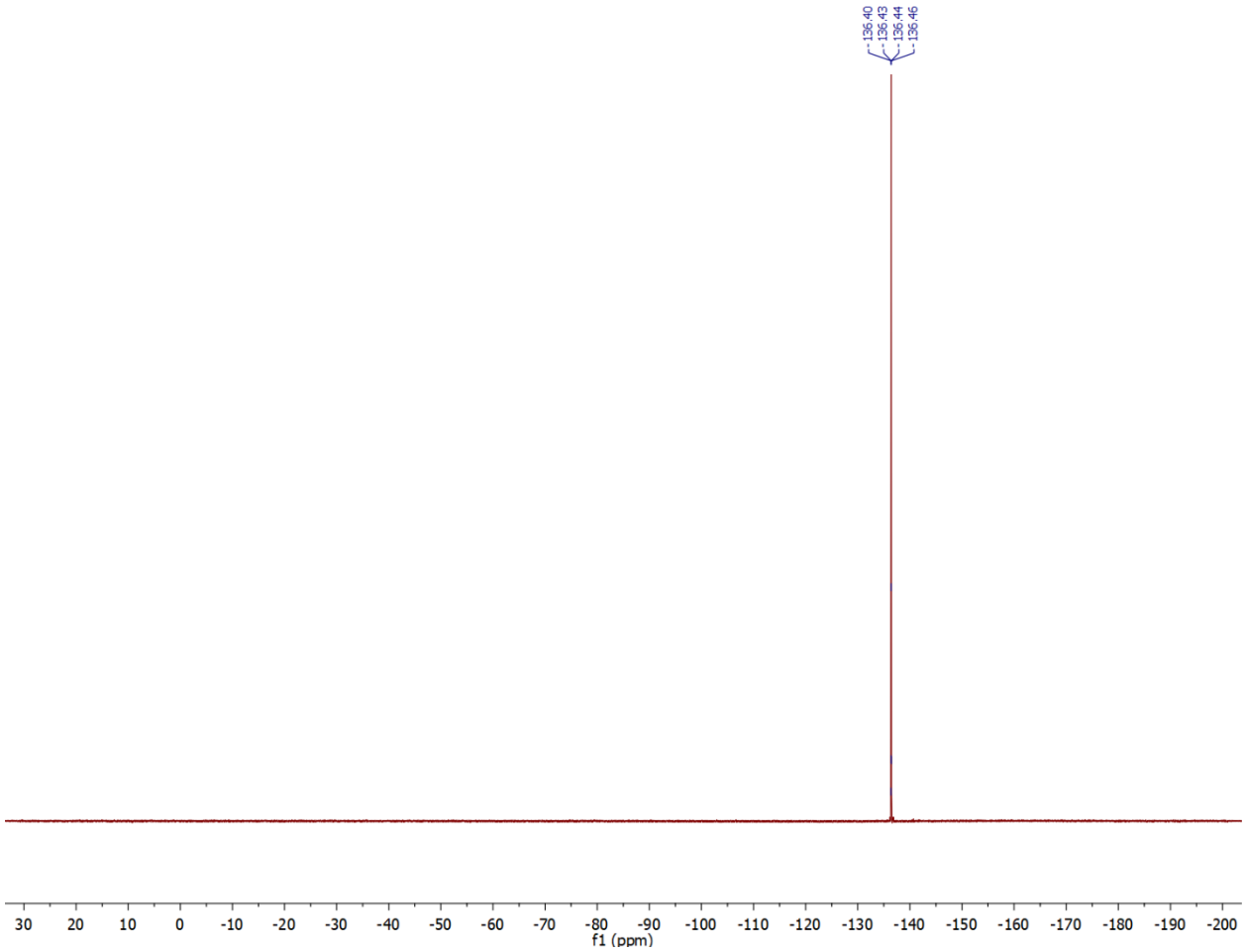
^{1}H NMR for **3F-PHPOG (3i)**

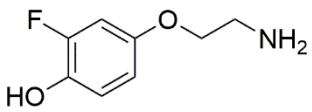


^{13}C NMR for **3F-PHPOG (3i)**



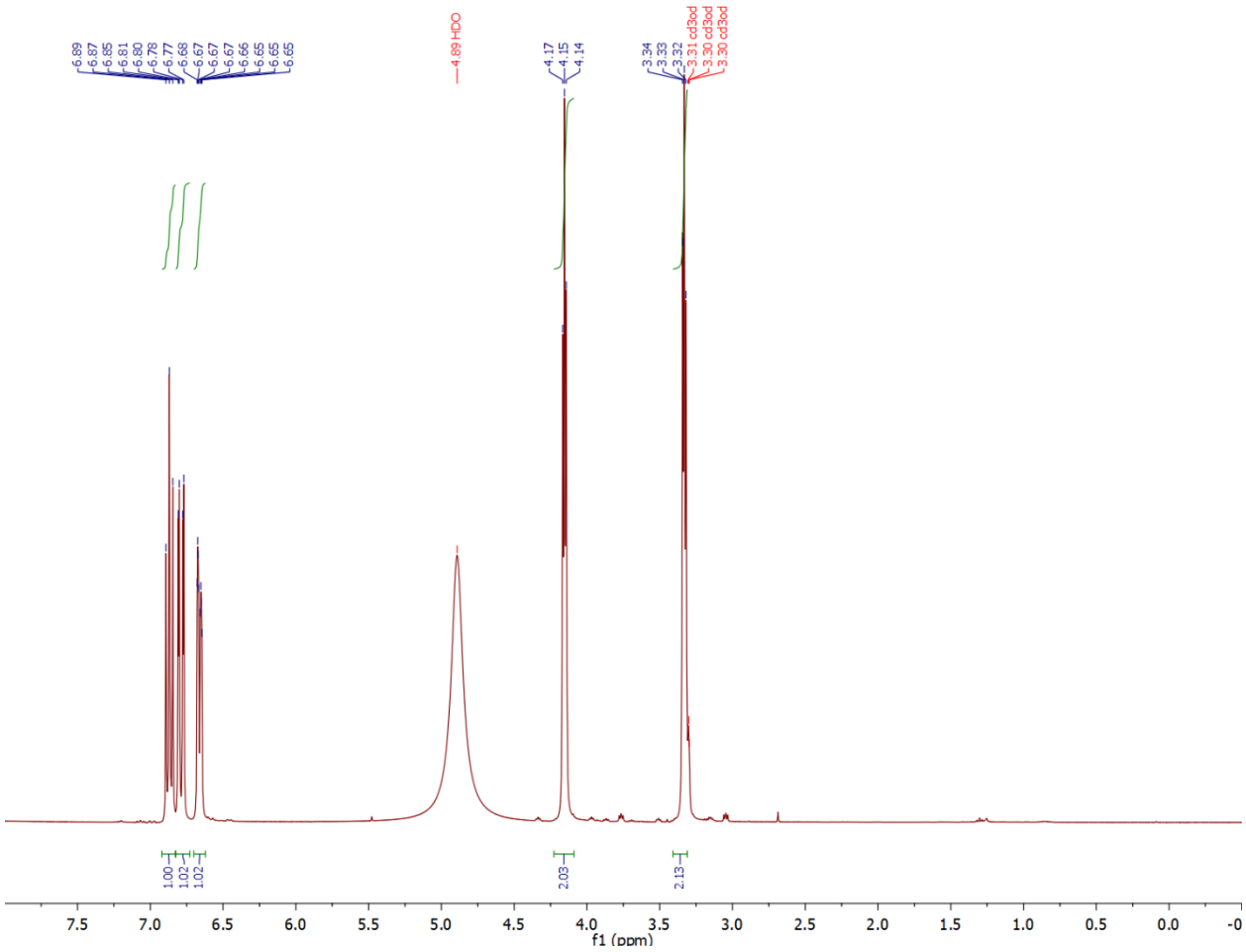
^{19}F NMR for **3F-PHPOG (3i)**



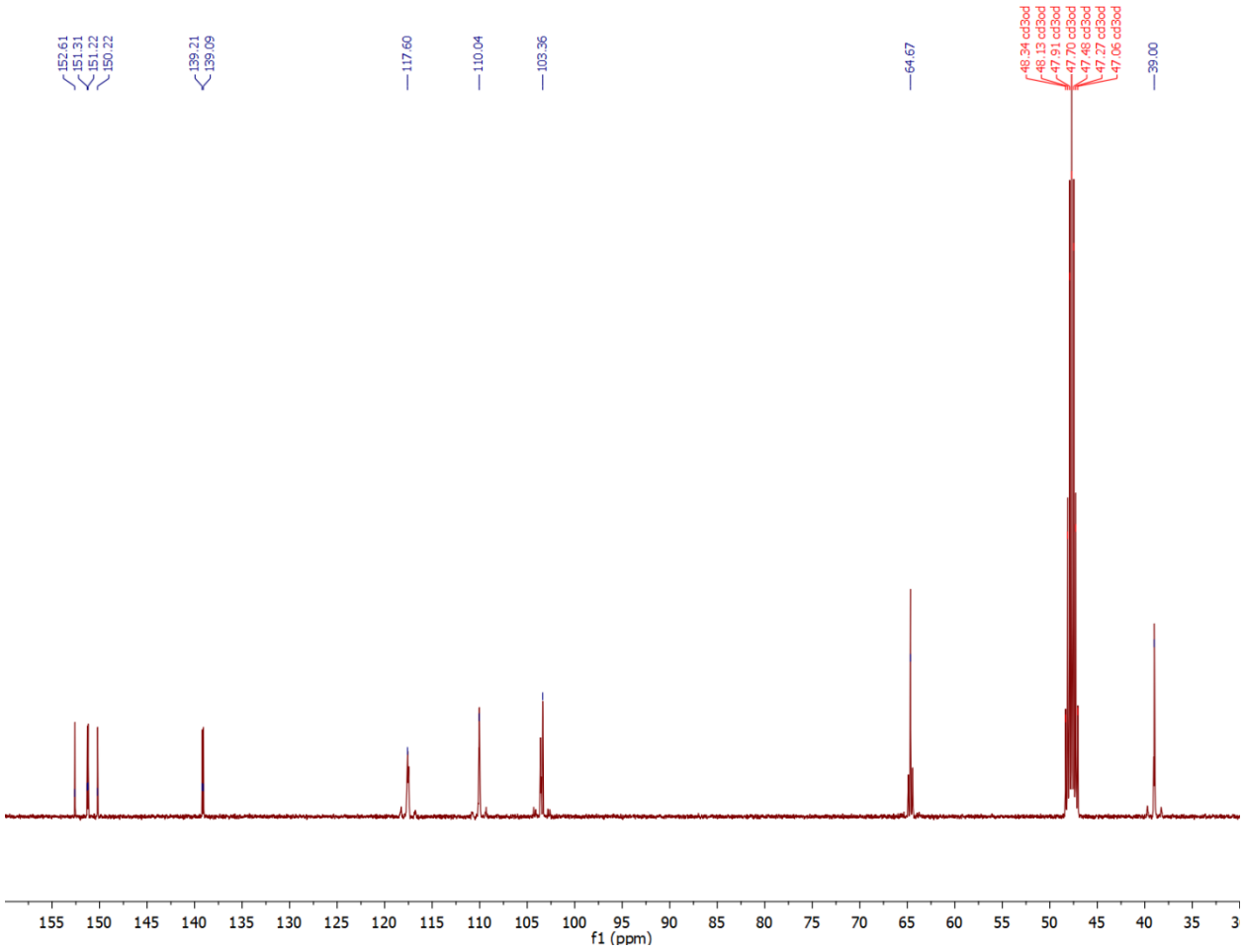


1i

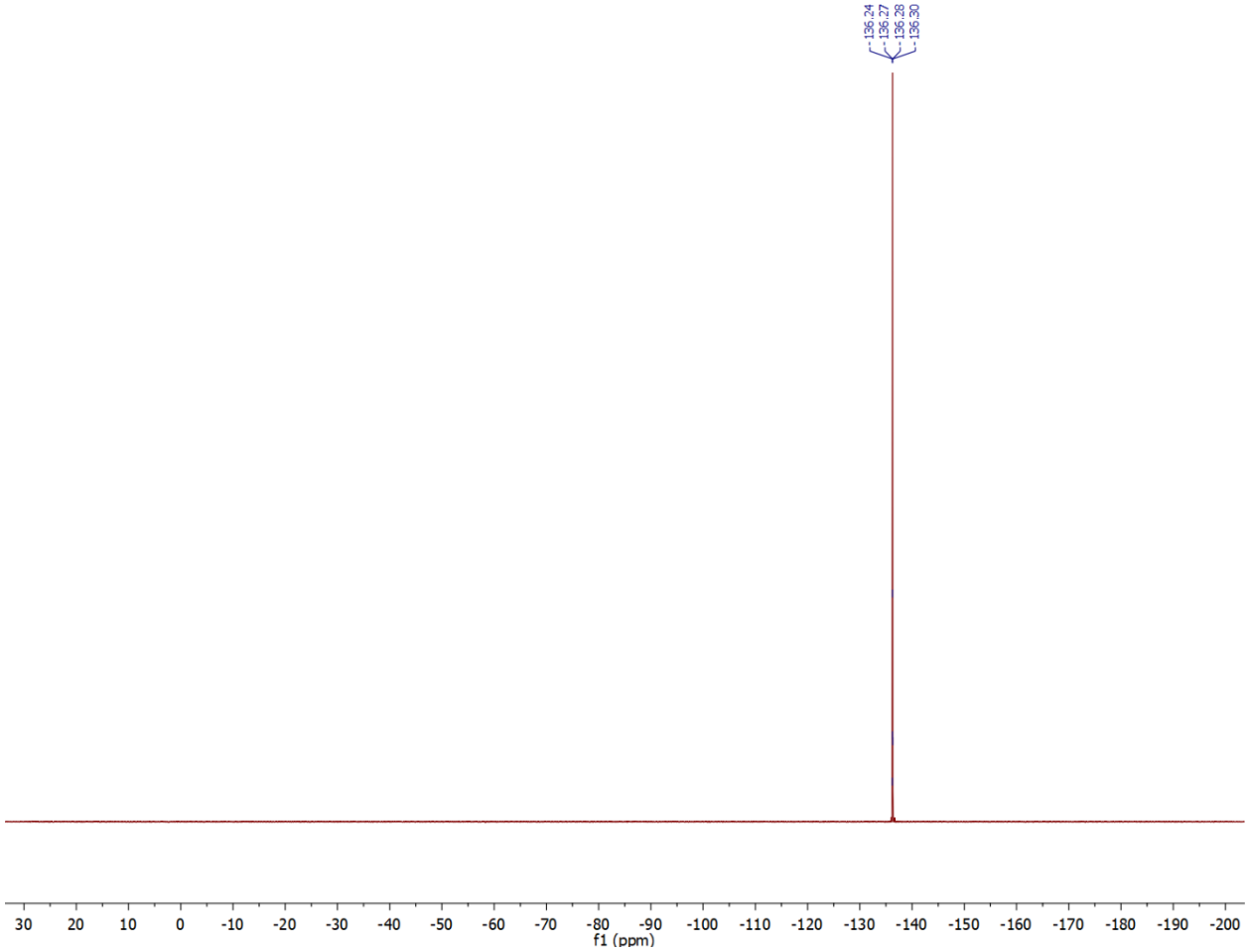
^{1}H NMR for **1i**



^{13}C NMR for **1i**

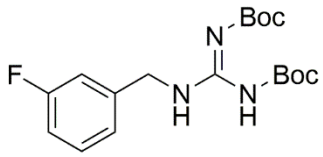


^{19}F NMR for **1i**

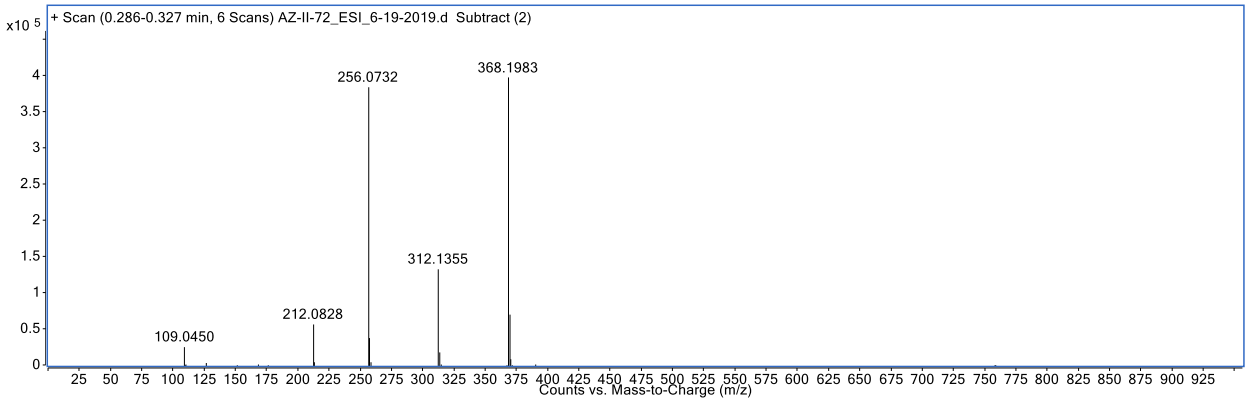


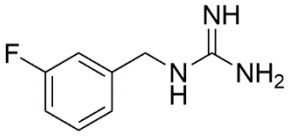
6.2 High Resolution Mass Spectra

6.2.1 MFBG

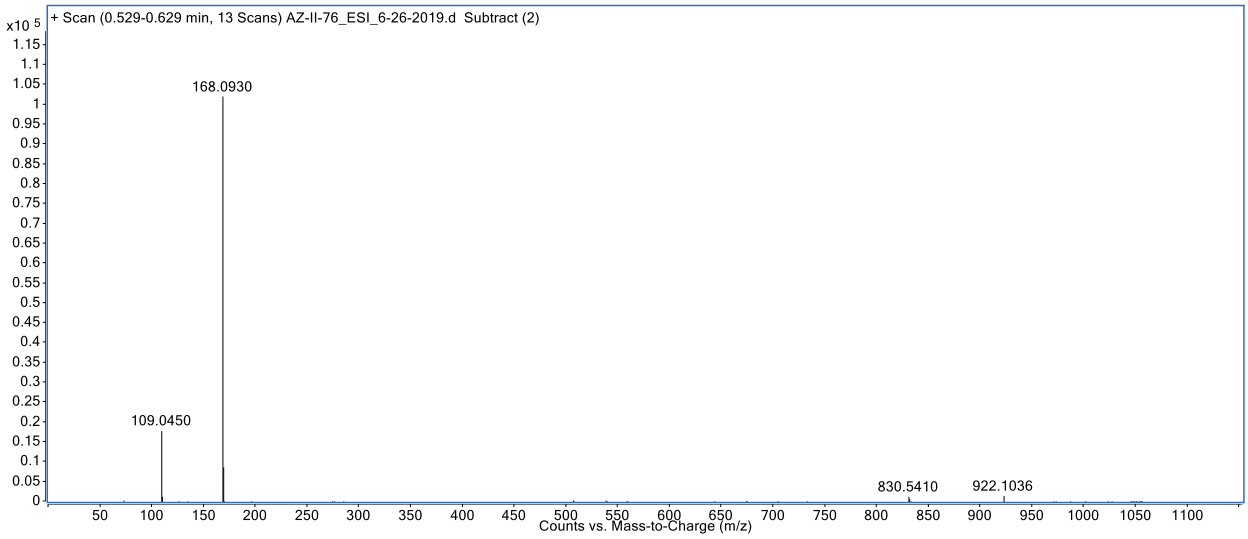


3a-Boc

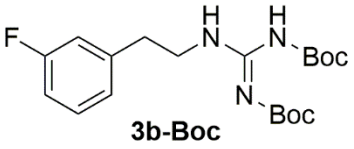




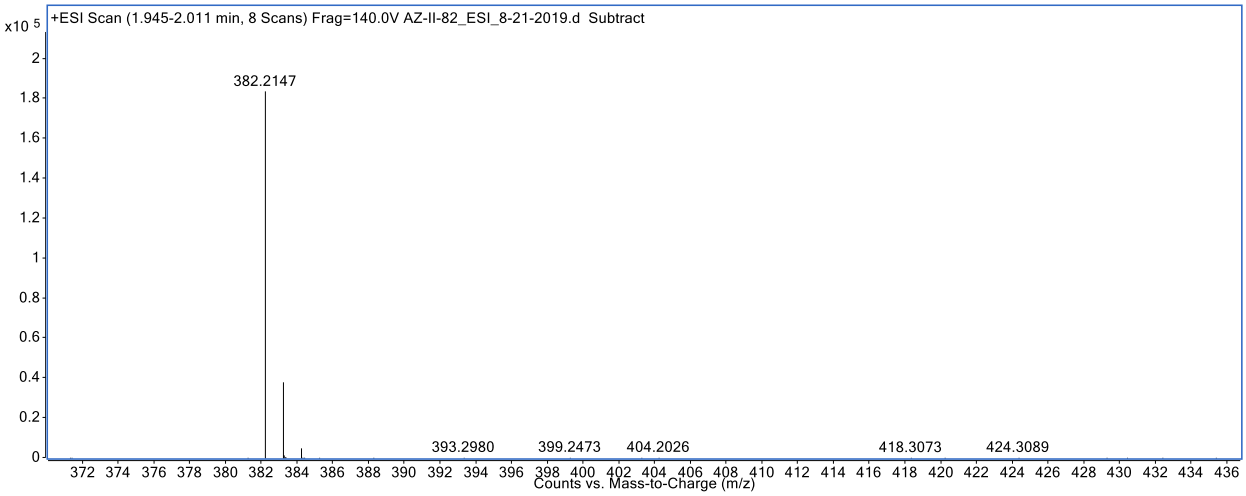
3a

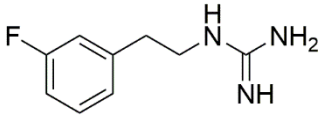


6.2.2 MFPG

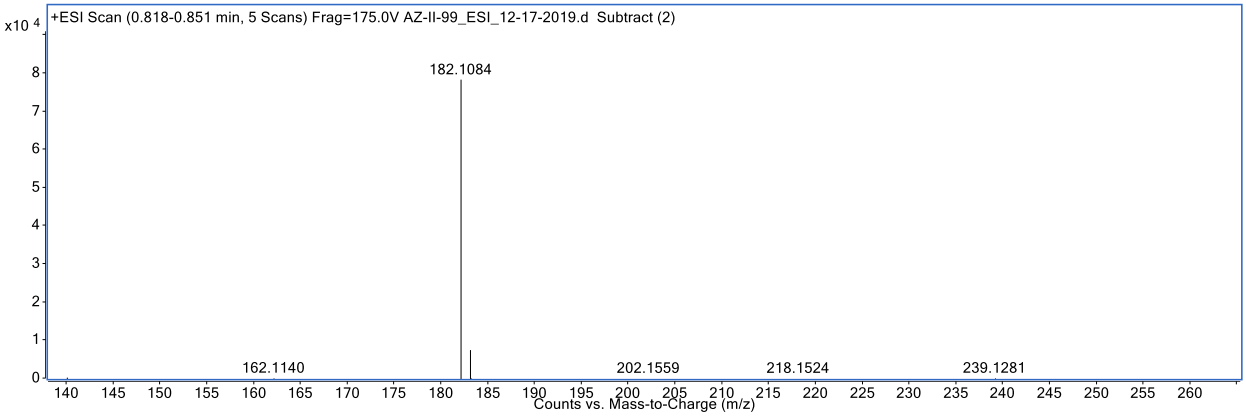


3b-Boc

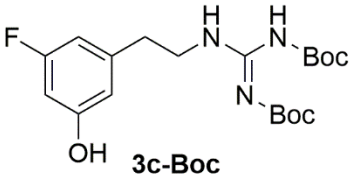




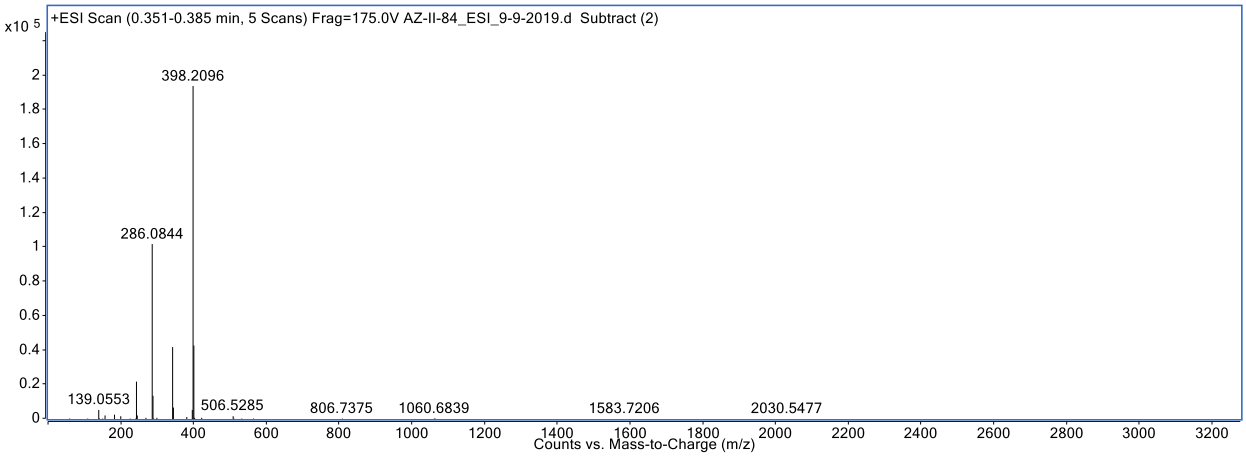
3b

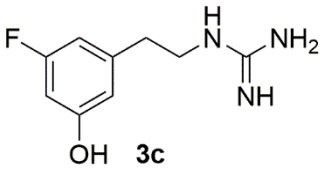


6.2.3 5F-MHPG

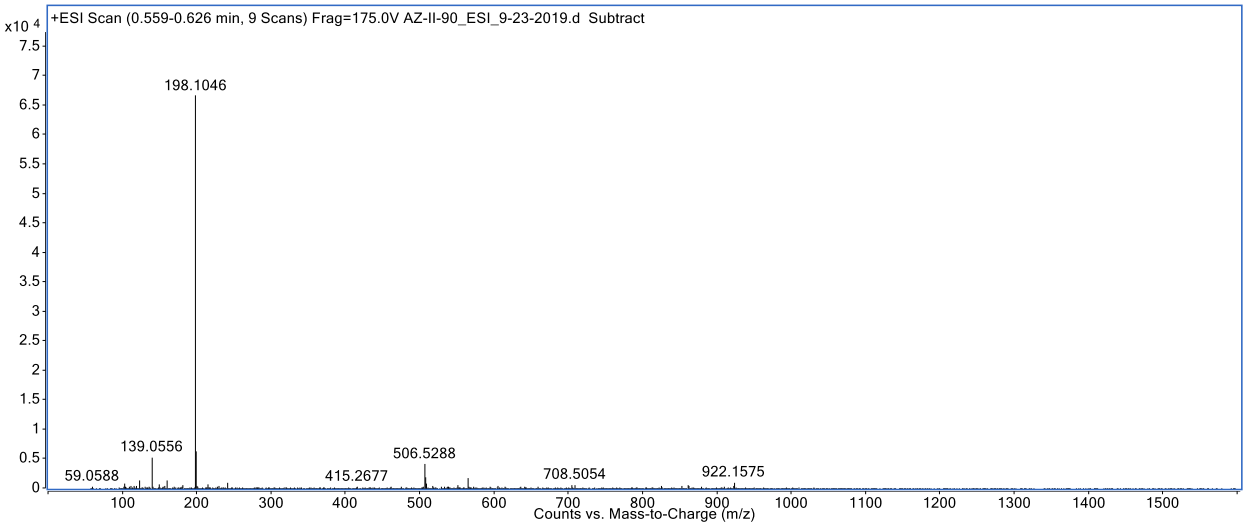


3c-Boc

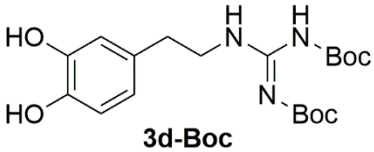




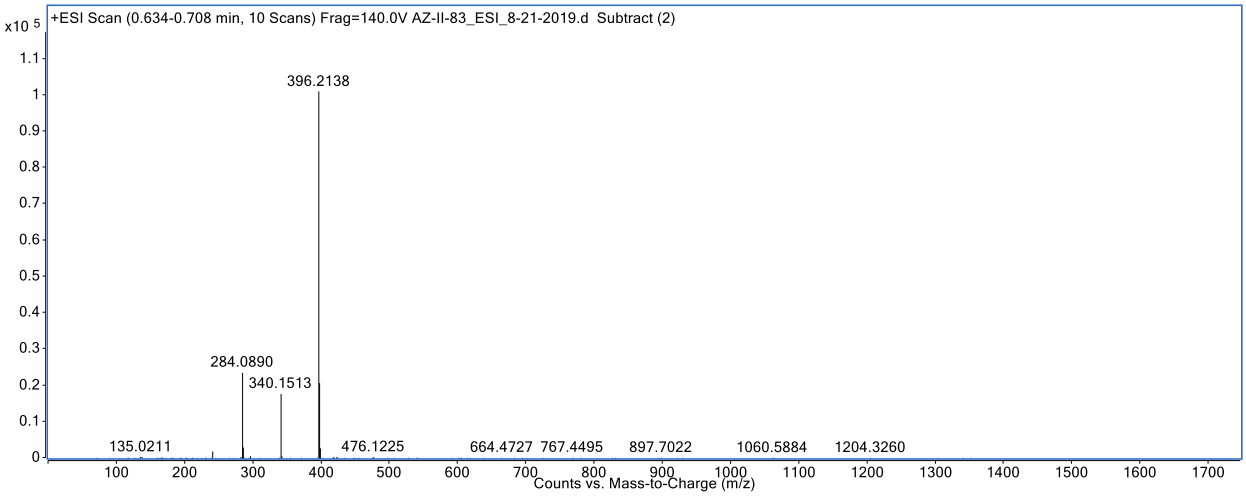
3c

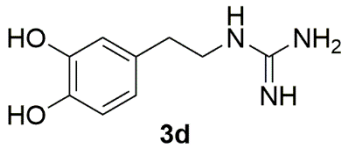


6.2.4 DOPG

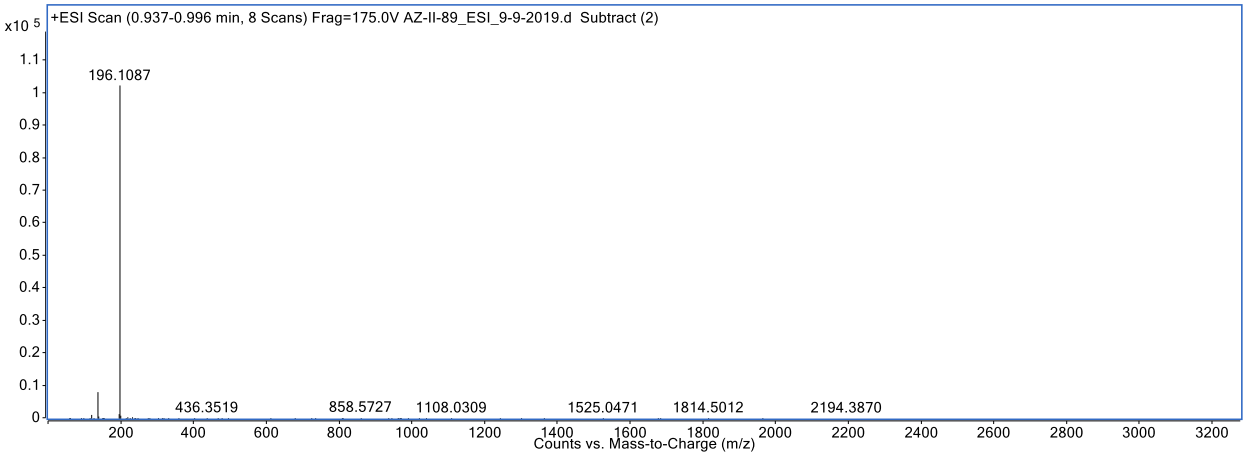


3d-Boc

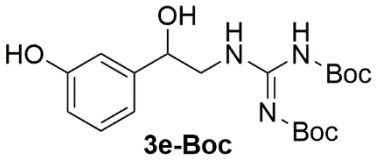




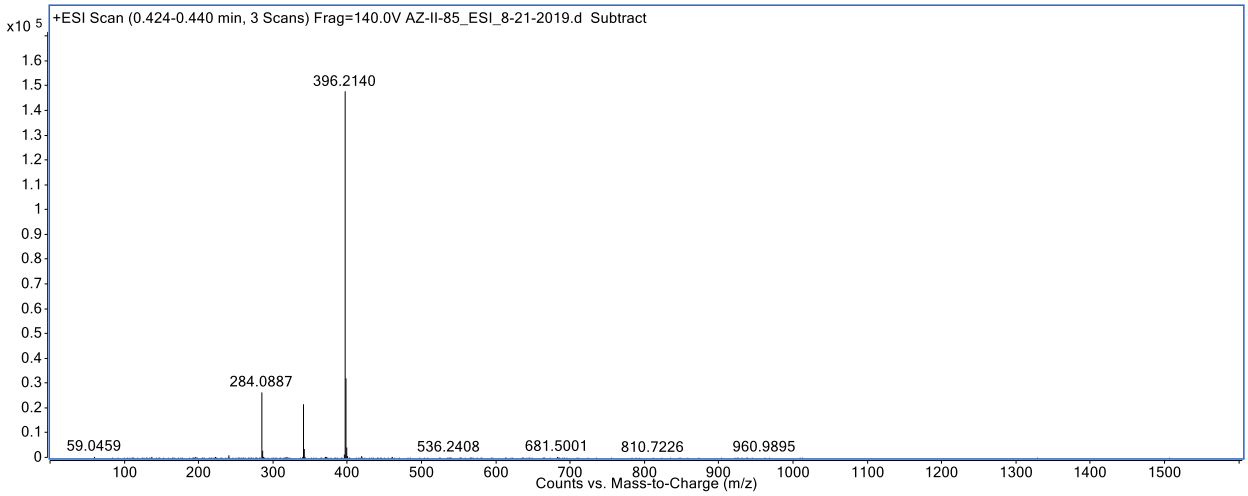
3d

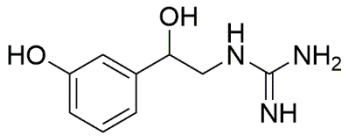


6.2.5 GMO

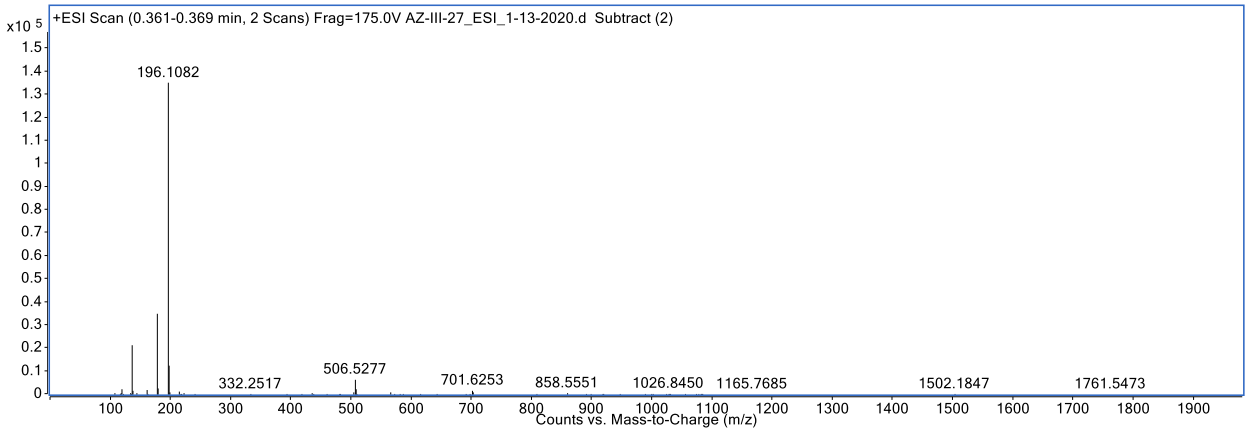


3e-Boc

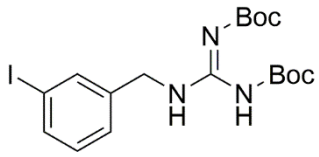




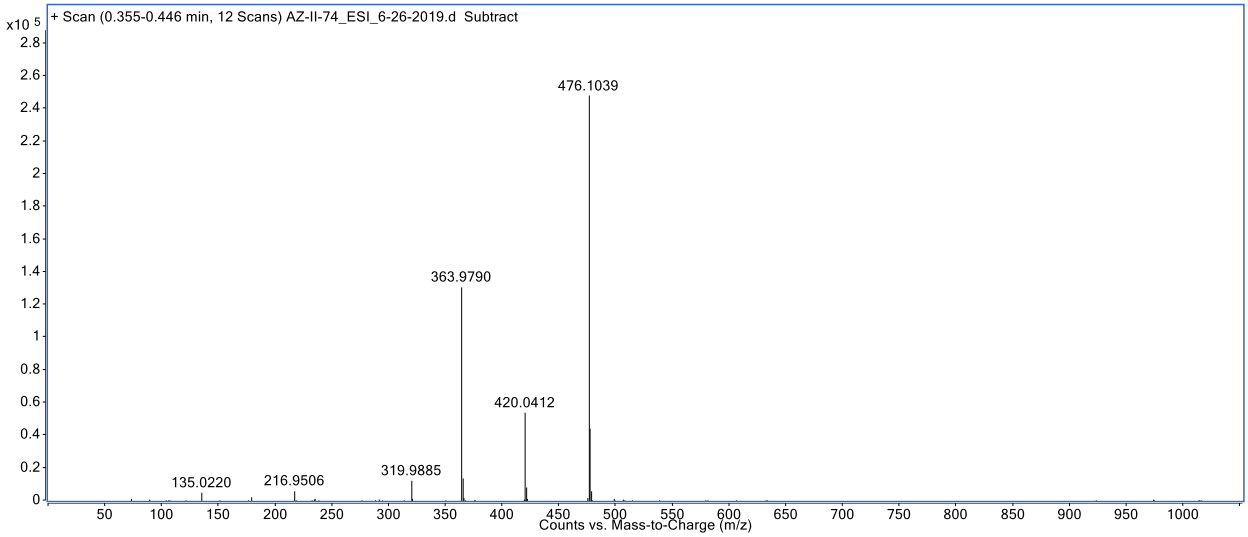
3e

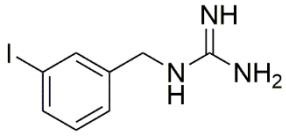


6.2.6 MIBG

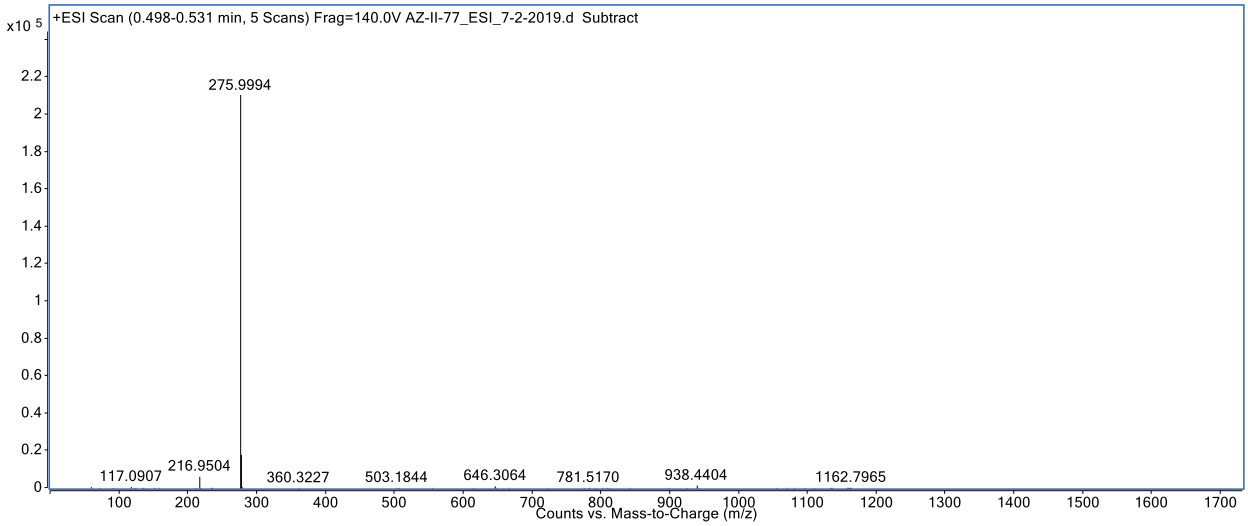


3f-Boc

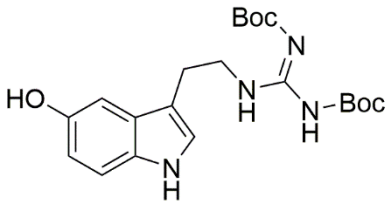




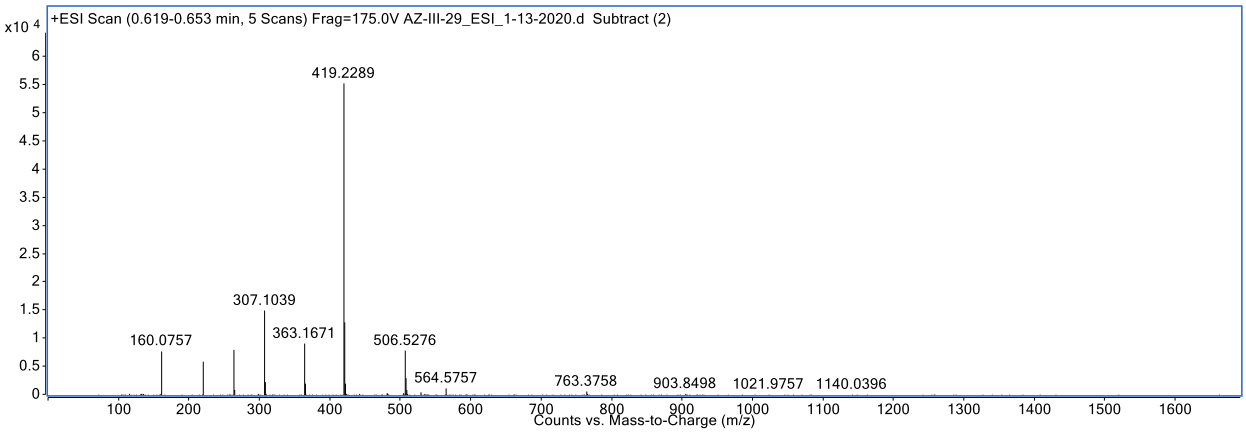
3f

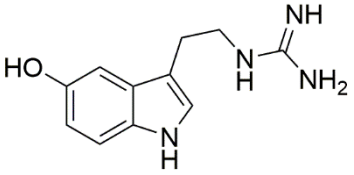


6.2.7 HTG

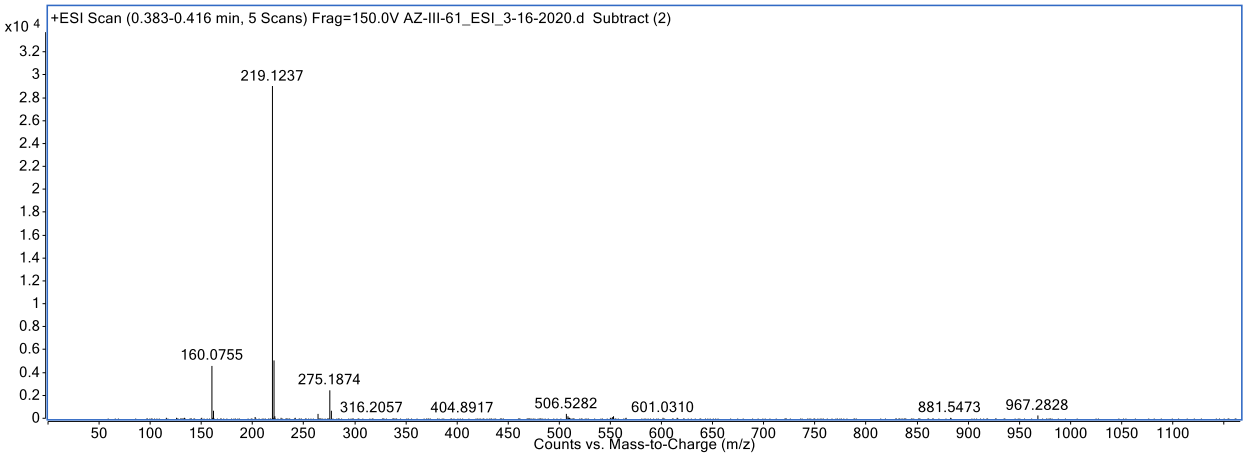


3g-Boc

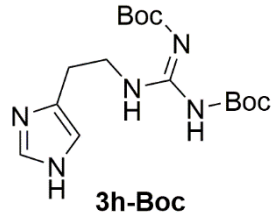




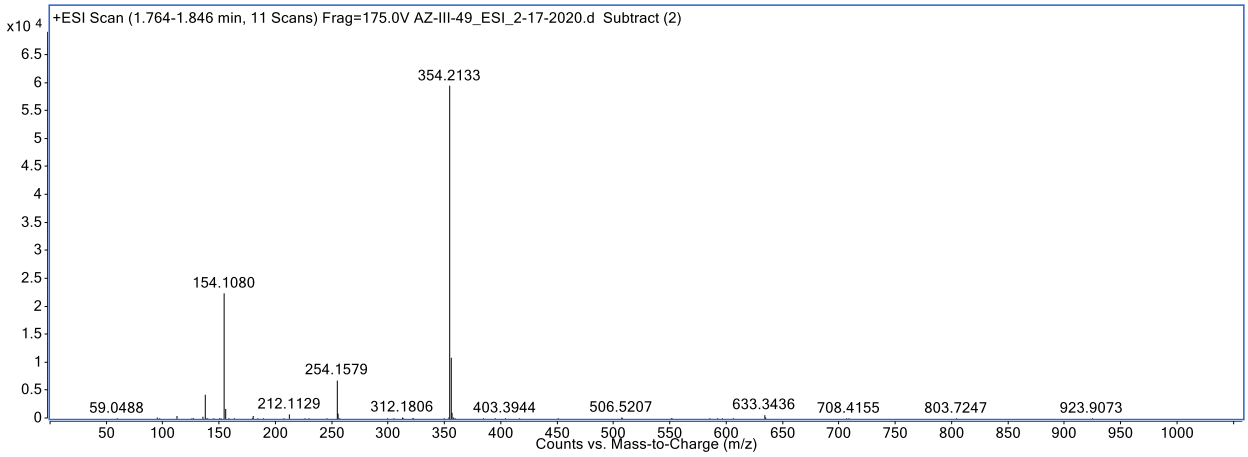
3g

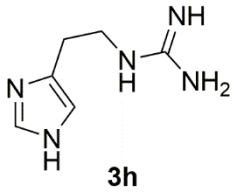


6.2.8 IEG

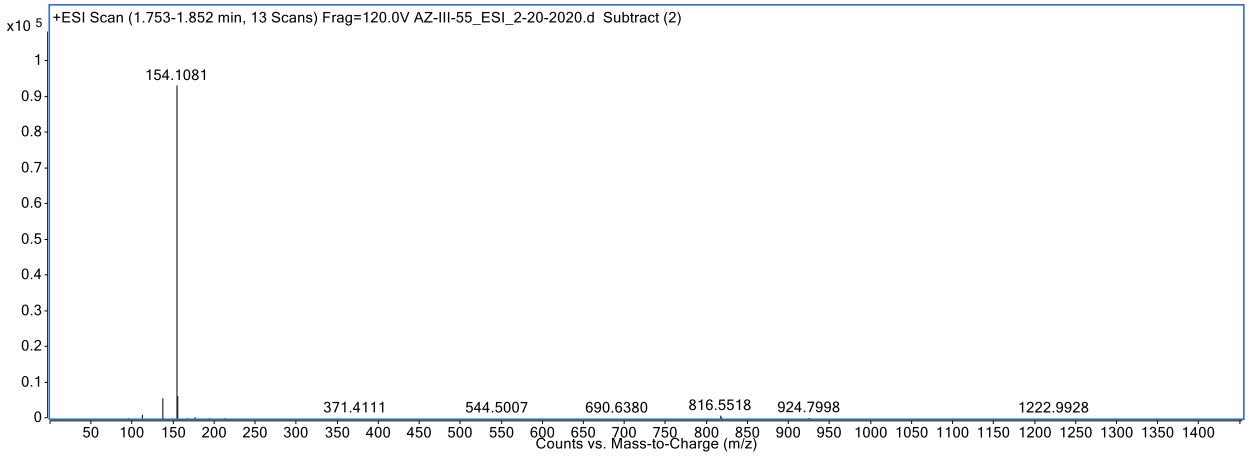


3h-Boc

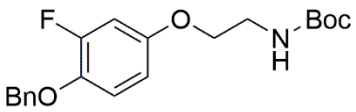




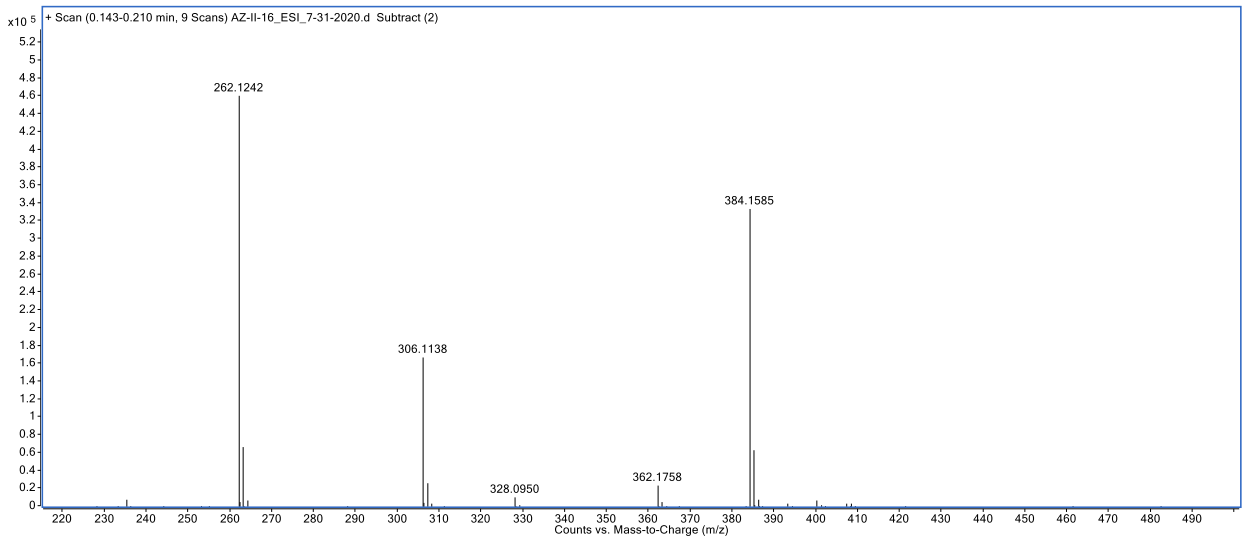
3h

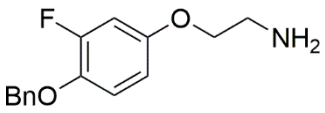


6.2.9 3F-PHPOG



5





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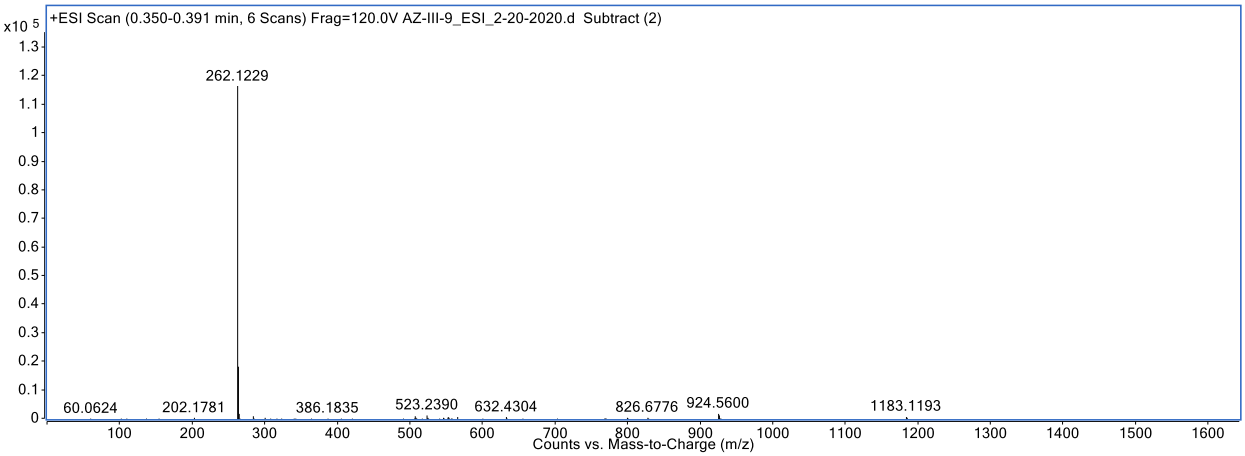
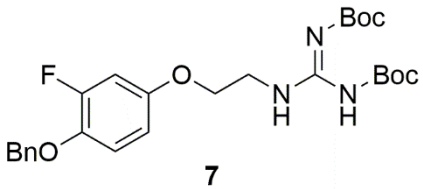
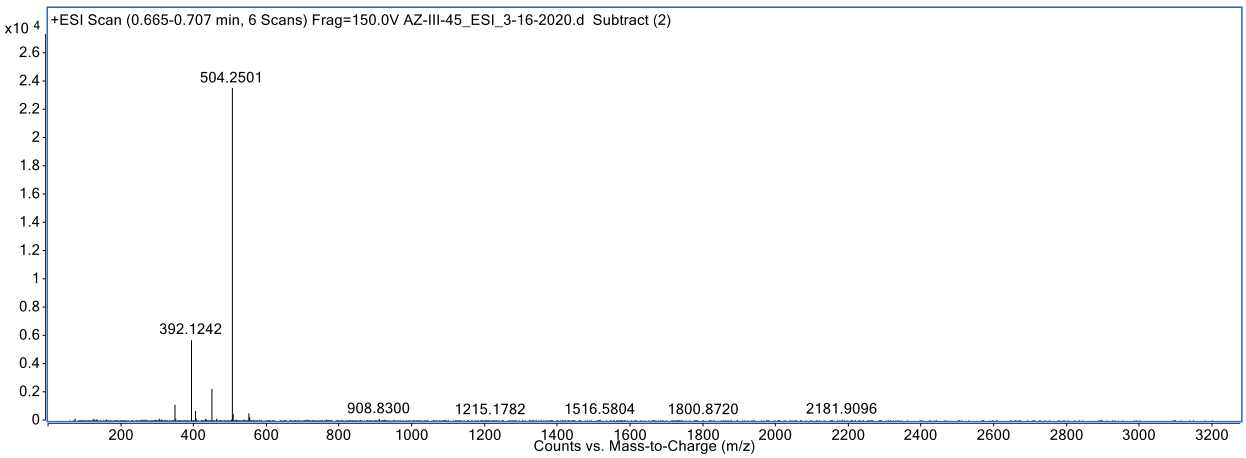
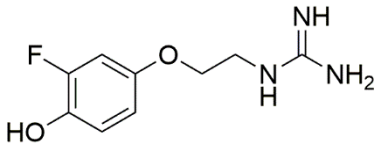


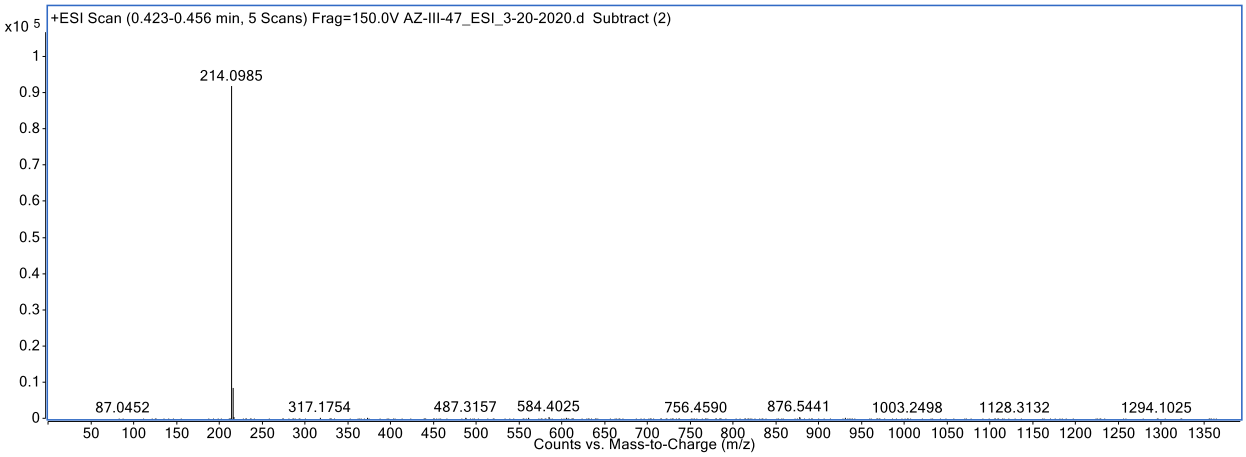

Boc
N
F
O
N
Boc
H
N
H
BnO

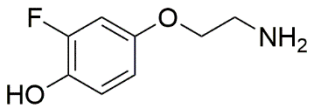
7


+ESI Scan (0.665-0.707 min, 6 Scans) Frag=150.0V AZ-III-45_ESI_3-16-2020.d Subtract (2)
x10 4
504.2501
392.1242
908.8300
1215.1782
1516.5804
1800.8720
2181.9096
Counts vs. Mass-to-Charge (m/z)

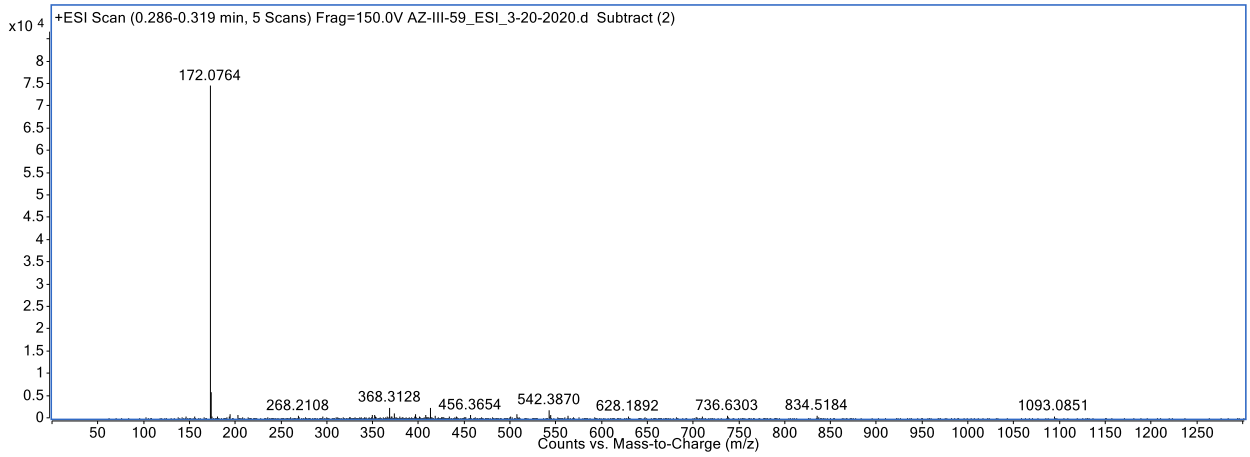

NH
F
O
N
NH2
H
HO

3F-PHPOG


+ESI Scan (0.423-0.456 min, 5 Scans) Frag=150.0V AZ-III-47_ESI_3-20-2020.d Subtract (2)
x10 5
214.0985
87.0452
317.1754
487.3157
584.4025
756.4590
876.5441
1003.2498
1128.3132
1294.1025
Counts vs. Mass-to-Charge (m/z)

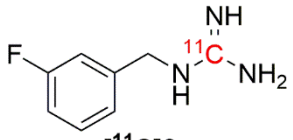

F
O
NH2
HO

1i


+ESI Scan (0.286-0.319 min, 5 Scans) Frag=150.0V AZ-III-59_ESI_3-20-2020.d Subtract (2)
x10 4
172.0764
268.2108
368.3128
456.3654
542.3870
628.1892
736.6303
834.5184
1093.0851
Counts vs. Mass-to-Charge (m/z)

6.3 Radio-HPLC

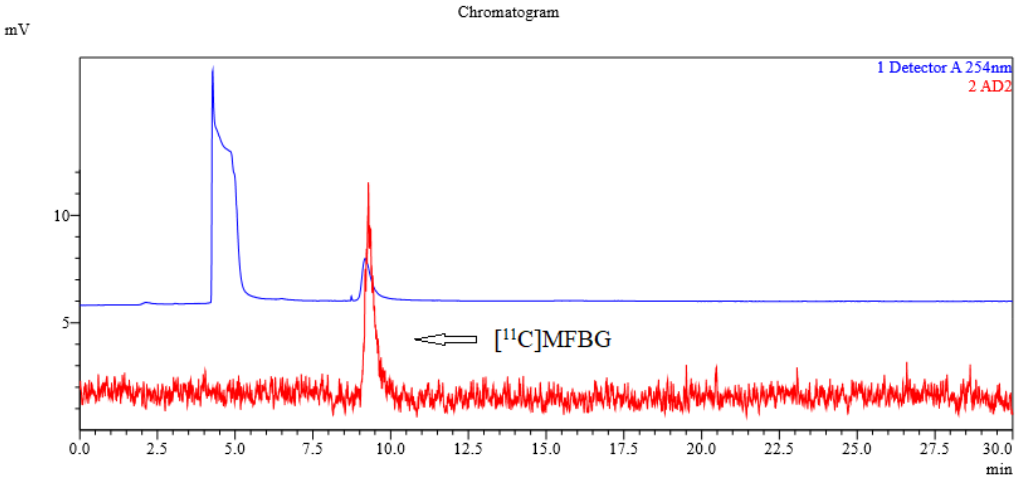
6.3.1 [^{11}C]MFBG



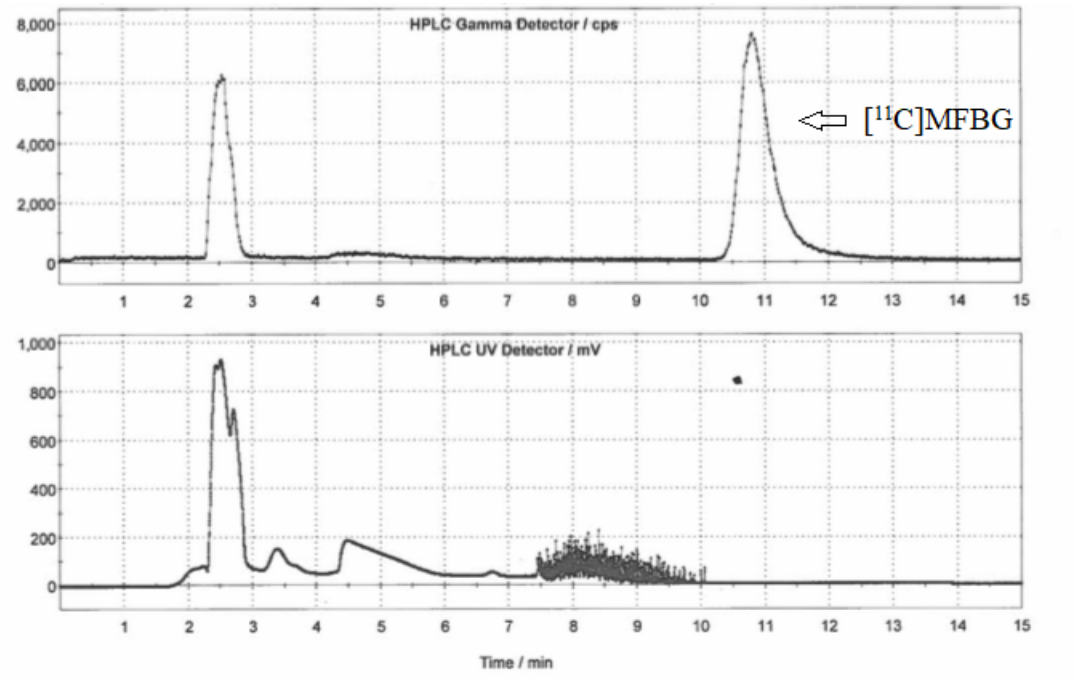
[^{11}C]3a

[^{11}C]MFBG (**[^{11}C]3a**) RAD trace overlaid with UV trace (254 nm) spiked with MFBG **3a**

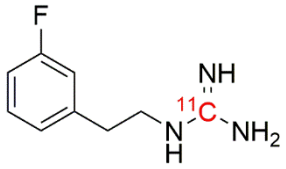
HPLC Conditions: B



[^{11}C]MFBG (**[^{11}C]3a**) preparative HPLC trace:



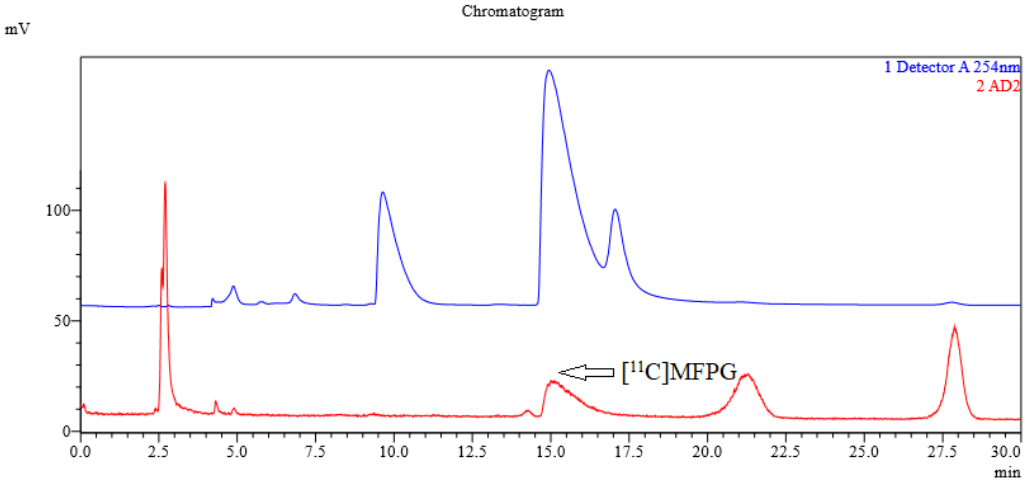
6.3.2 [^{11}C]MFPG



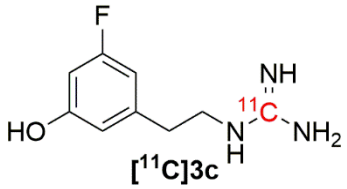
[^{11}C]3b

[^{11}C]MFPG (**[^{11}C]3b**) RAD trace overlaid with UV trace (254 nm) spiked with MFPG **3b**

HPLC Conditions: B



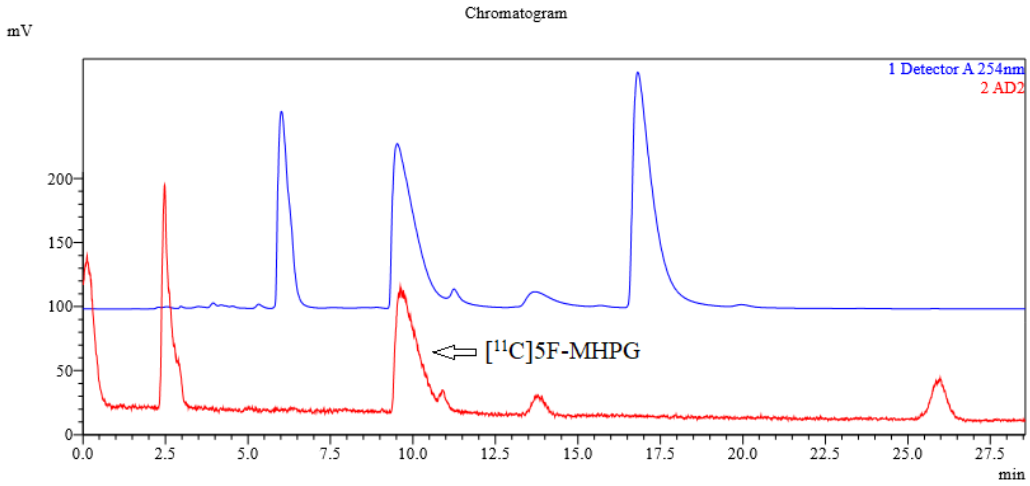
6.3.3 [^{11}C]5F-MHPG



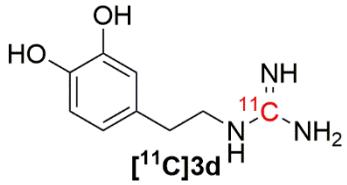
[^{11}C]3c

[^{11}C]5F-MHPG (**[^{11}C]3c**) RAD trace overlaid with UV trace (254 nm) spiked with 5F-MHPG **3c**

HPLC Conditions: A



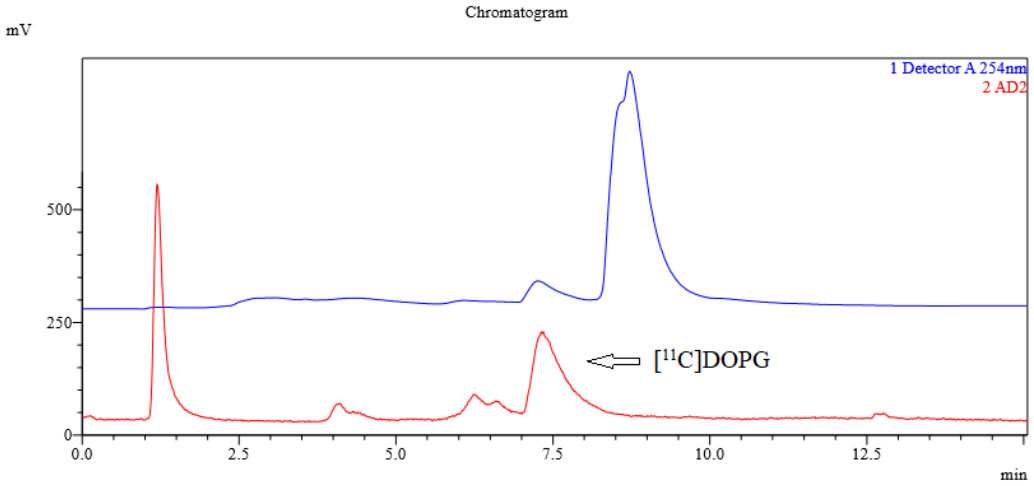
6.3.4 [^{11}C]DOPG



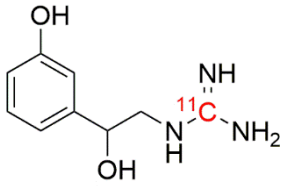
[**[^{11}C]3d**]

[^{11}C]DOPG ([**^{11}C]3d**) RAD trace overlaid with UV trace (254 nm) spiked with DOPG **3d**

HPLC Conditions: A



6.3.5 [^{11}C]GMO

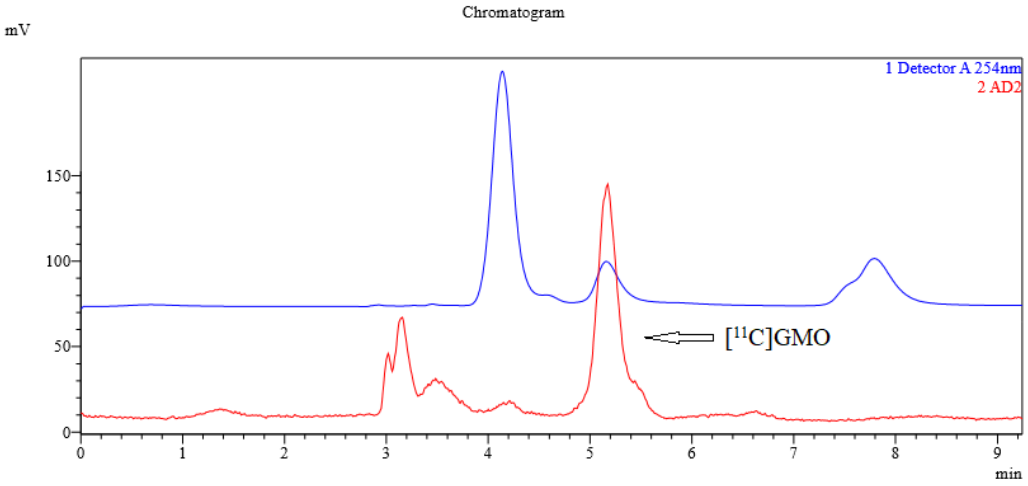


[^{11}C]3e

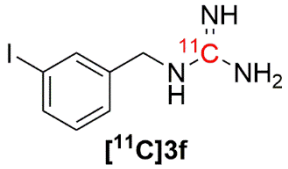
[^{11}C]GMO (**[^{11}C]3e**) RAD trace overlaid with UV trace (254 nm) spiked with GMO **3e**

HPLC Conditions:

Conditions: 10% EtOH in 60 mM NH_4OAc
Flow rate: 5 mL/min
Column: Phenomenex Synergi HydroRP 80A 250 x 10.00 mm. 10µ.



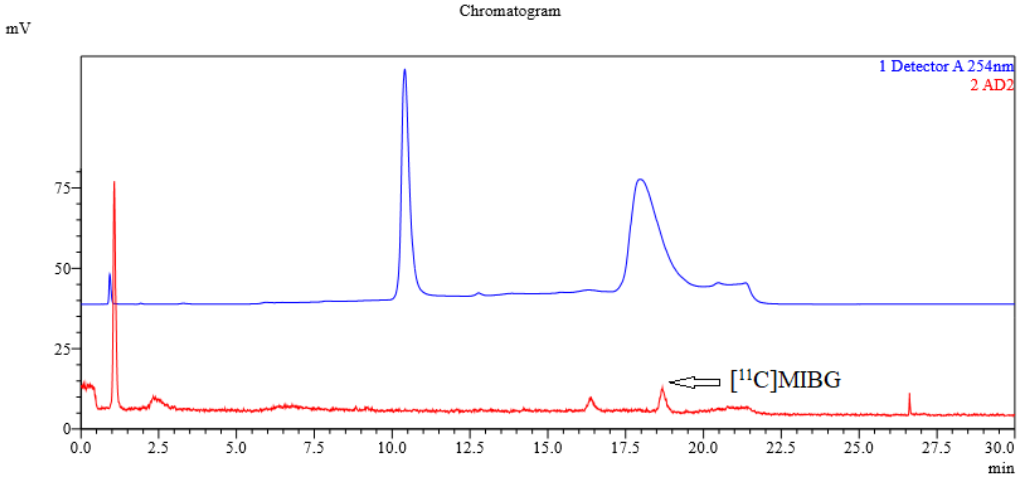
6.3.6 [^{11}C]MIBG



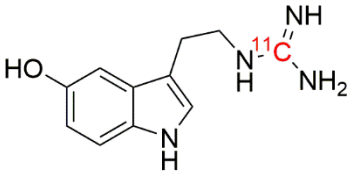
[^{11}C]3f

[^{11}C]MIBG (**[^{11}C]3f**) RAD trace overlaid with UV trace (254 nm) spiked with MIBG **3f**

HPLC Conditions: A (0-30% EtOH in 10 mM NaOAc)



6.3.7 [^{11}C]HTG

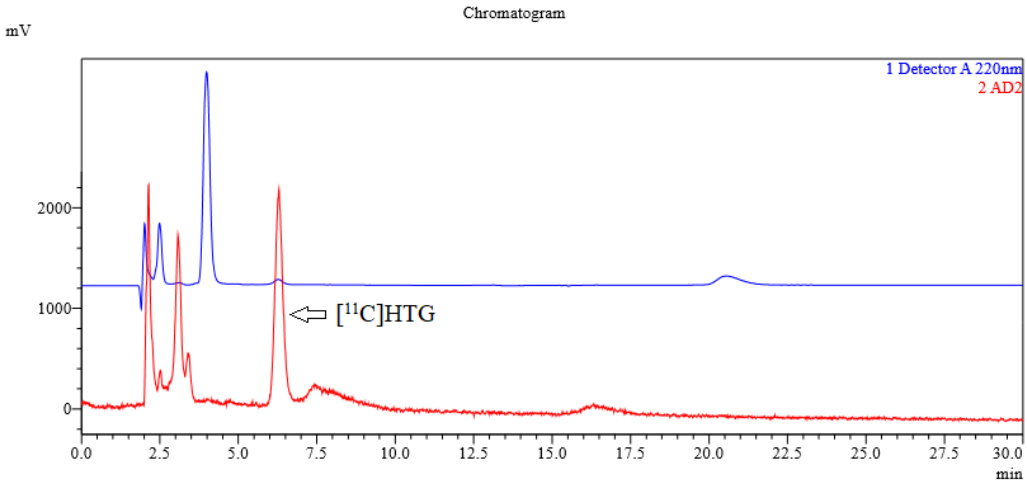


[^{11}C]3g

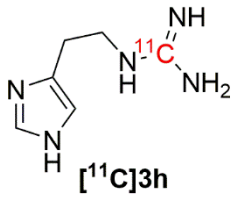
[^{11}C]HTG (**[^{11}C]3g**) RAD trace overlaid with UV trace (254 nm) spiked with HTG **3g**

HPLC Conditions:

Conditions: 10% EtOH in 60 mM NH_4OAc
Flow rate: 6 mL/min
Column: Phenomenex Synergi HydroRP 80A 250 x 10.00 mm. 10µ.



6.3.8 [^{11}C]IEG

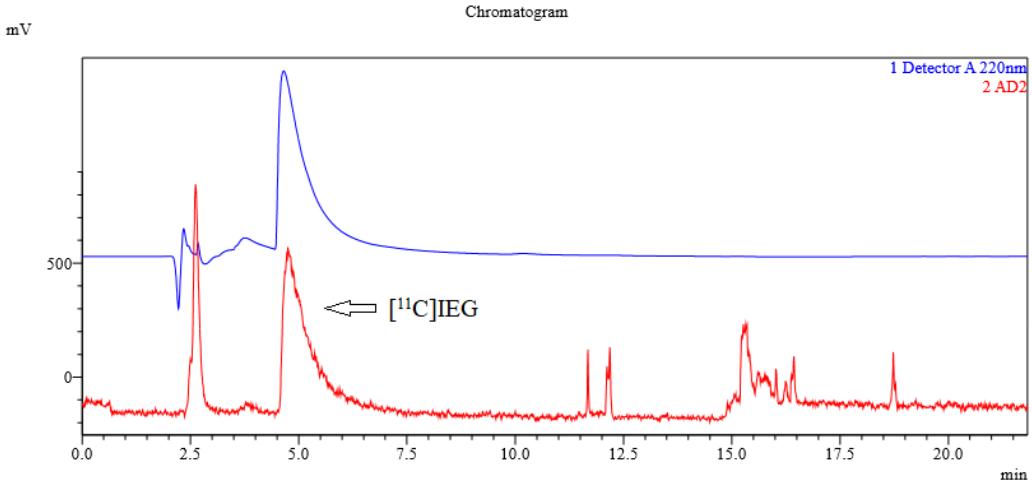


[^{11}C]3h

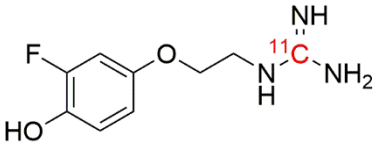
[^{11}C]IEG (**[^{11}C]3h**) RAD trace overlaid with UV trace (254 nm) spiked with IEG **3h**

HPLC Conditions:

Conditions: 2.5% EtOH in 60 mM NH_4OAc
Temperature: 40 °C
Flow rate: 1.2 mL/min
Column: Phenomenex Synergi HydroRP 80A 250 x 4.6 mm. 10µ.



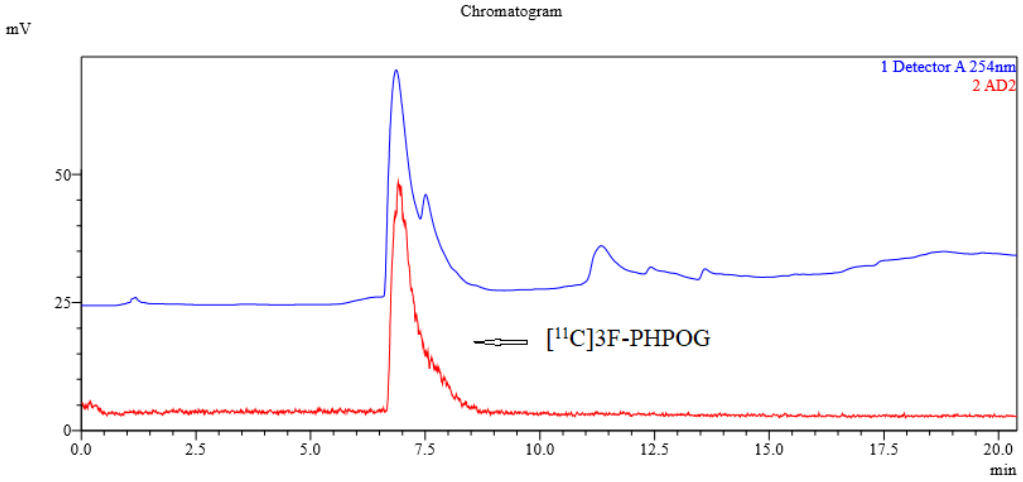
6.3.9 [^{11}C]3F-PHPOG



[^{11}C]3F-PHPOG

[^{11}C]3F-PHPOG (**[^{11}C]3i**) RAD trace overlaid with UV trace (254 nm) spiked with 3F-PHPOG **3i**

HPLC Conditions: A



[^{11}C]3F-PHPOG (**[^{11}C]3i**) Preparative HPLC: