Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

SUPPLEMENTARY INFORMATION

Structural elucidation of major selective androgen receptor modulator (SARM) metabolites for doping control

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[d.] *K. L. Maddy Equine Analytical Chemistry Laboratory, School of Veterinary Medicine, University of California, Davis, CA 956161, USA*
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CONTENT

Supporting Figures

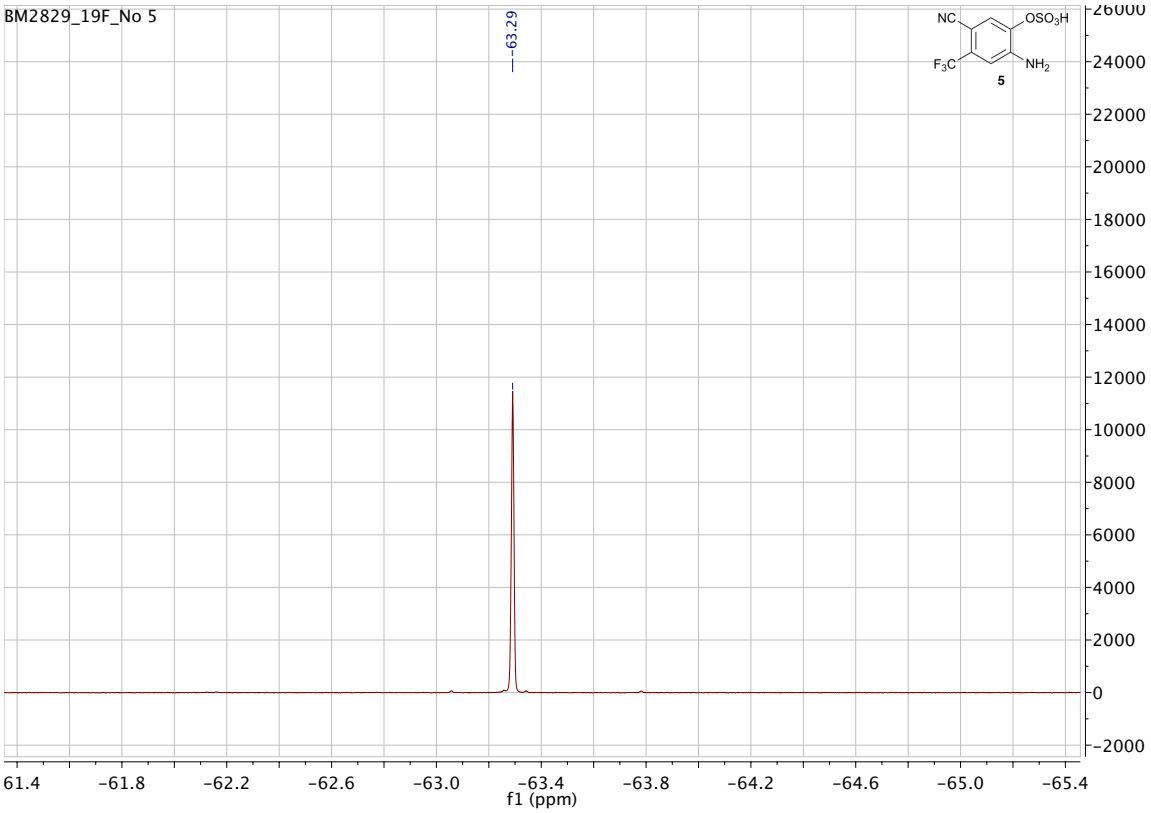


Figure S1: ^{19}F NMR spectrum of purified sulphated metabolite **5**.

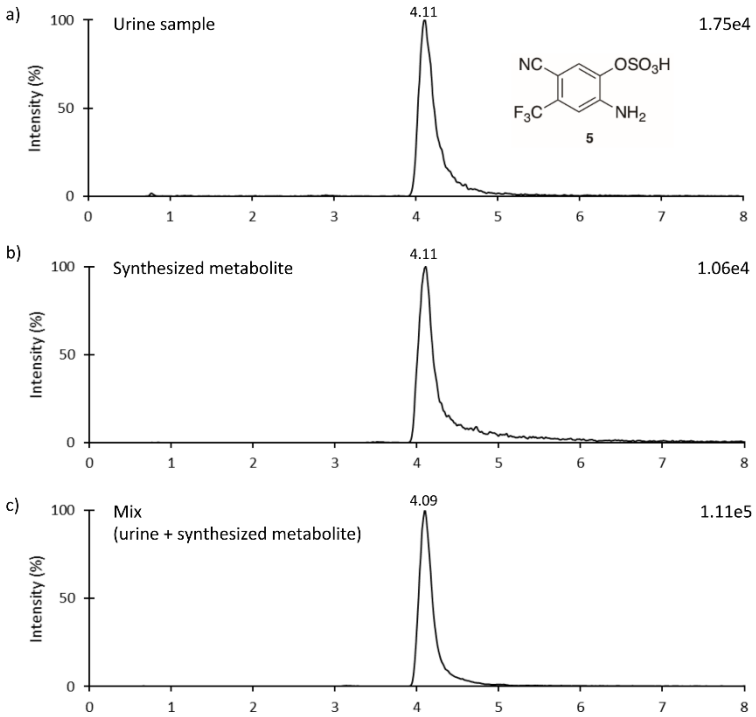


Figure S2: Retention time comparison of the urinary natural and the synthesized purified cyano SARMs-derived metabolite **5**. Extracted ion chromatograms on a C18 column for the urinary, synthesized and mixed samples (top right corner of each chromatogram: signal intensities).

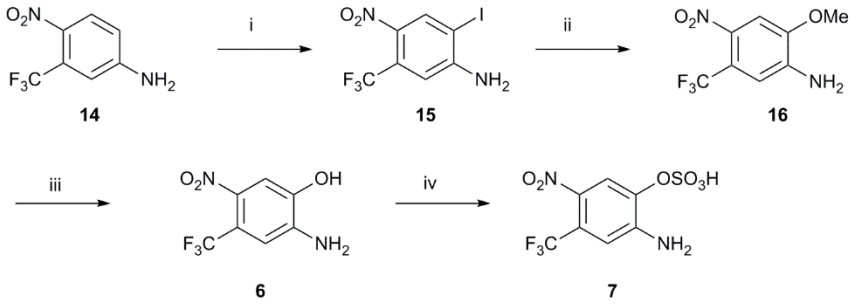


Figure S3: Synthesis of purified sulphated metabolite **7**. (i) NIS, MeOH/THF, 91%; (ii) CuI, Cs_2CO_3, 1,10-phenanthrolin-mono hydrate, MeOH, 29%; (iii) BBr_3, DCM, 40%; (iv) SO_3-NMe_3, $NaHCO_3$, NaOH, H_2O, 45%.

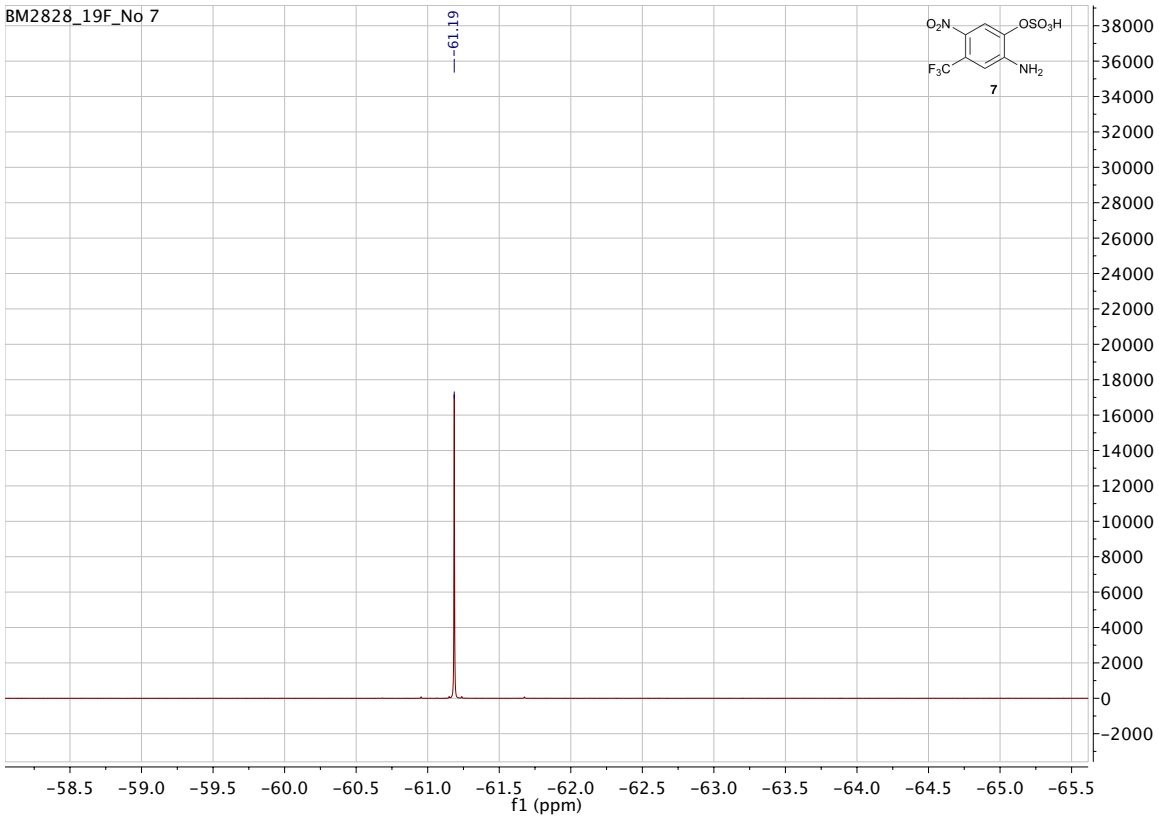


Figure S4: ^{19}F NMR spectrum of purified sulphated metabolite **7**.

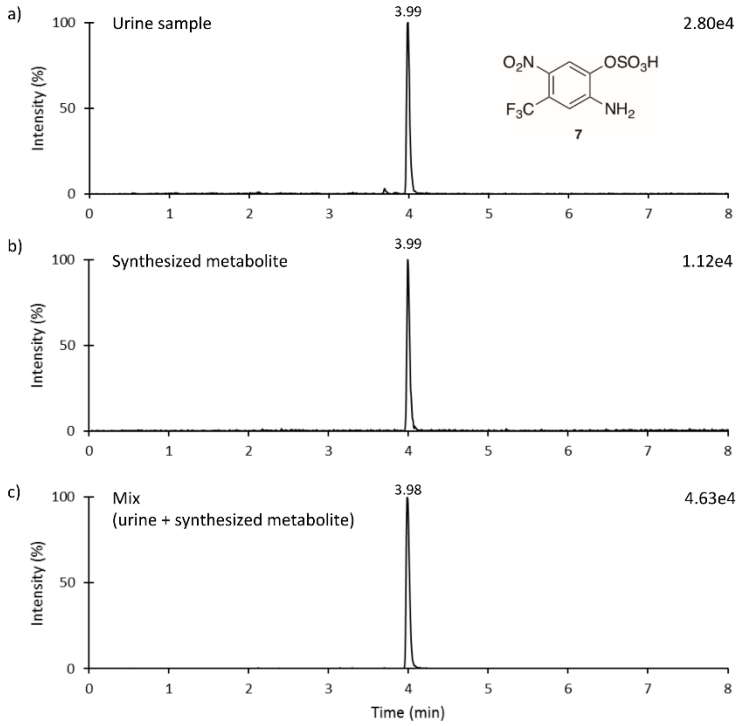


Figure S5: Comparison of the urinary natural and the synthesized purified nitro-SARMs-derived metabolite **7** (SARMs **S1**): UHPLC-MS co-injection using a C18 column for the urinary, synthesized and mixed samples (top right corner of each chromatogram: signal intensities).

General

All non-aqueous reactions were performed using flame- or oven dried glassware under an atmosphere of dry nitrogen. All reagents and solvents were purchased from Sigma-Aldrich or Fischer Scientific and were used without further purification. HPLC grade solvents were used for HPLC purification and mass spectrometry grade for UHPLC-ESI-MS analysis. Solutions were concentrated *in vacuo* on a Heidolph or a IKA rotary evaporator. Thin Layer Chromatography (TLC) was performed on silica gel 60 F-254 plates. Visualization of the developed chromatogram was performed using fluorescence quenching or staining with CAM (Cerium Ammonium Molybdate), Ninhydrin, Ehrlich reagent (4-(Dimethylamino)benzaldehyde) or Vanillin. Chromatographic purification of products was accomplished using flash column chromatography on Merck silica gel 60 (40−63 μm) or preparative reverse phase HPLC on an Agilent HPLC-1100 series system equipped with a Waters Atlantis T3 preparative column (10x100 mm, 5 μm) at a 2,5 mL/min flow rate. All synthesized compounds were ≥95% pure as determined by NMR. NMR spectra were recorded on an Agilent 400 MHz spectrometer (^{1}H NMR: 399.97 MHz, ^{13}C NMR: 100.58 MHz) or Varian 300 MHz spectrometer (^{13}C NMR: 75.43 MHz). Chemical shifts are reported in parts per million (ppm) on the δ scale from an internal standard. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectra were acquired on a SYNAPT G2-S High Definition Mass Spectrometry (HDMS) using an electrospray ionization (ESI) source with a AQCUITY UPLC I-class system and equipped with a Waters ACQUITY UPLC BEH C18 column (2.1 × 75 mm, 1.7 μm particle size) or Waters ACQUITY UPLC HSS T3 column (1.8 × 100 mm, 2.1 μm particle size).

UHPLC-MS/MS analysis

The analysis was performed on an Acquity UPLC system hyphenated with a Synapt G2 Q-TOF, both from Waters Corporation (Milford, MA, USA). The system was controlled using the MassLynx software v 4.1, also from Waters. The separation was performed on a Kinetex biphenyl column (1.7 μm, 100 x 2.1 mm) from Phenomenex (Torrance, CA, USA) and an Acquity BEH C18 column (1.7 μm, 100 x 2.1 mm) from

Waters Corporation. The mobile phase consisted of A) 0.1 % formic acid in MilliQ water and B) methanol and the flow rate was 0.5 mL/min. For the biphenyl column the column temperature was 40 °C and the gradient was 0-1 min, 5% B; 1-11 min, 5-95% B; 11-12 min, 95% B; 12 min, 95-5% B, 12-14 min, 5% B. For the C18 column, the temperature was set to 65 °C and the gradient was 0-1 min, 5% B; 1-6 min, 5-95% B; 6-8 min, 95% B; 8 min, 95-5% B, 8-10 min, 5% B.
The samples were introduced to the q-TOF using negative electrospray ionization. The capillary voltage was set to -2.50 kV and the cone voltage was 30 V. The source temperature was 120 °C, the cone gas flow 50 L/min and the desolvation gas flow 800 L/min. The instrument was operated in MSE mode, the scan range was m/z 50-1200, and the scan time was 0.2 s. In low energy mode, the collision energy was 4 V and in high energy mode the collision energy was ramped between 20-40 V. A solution of sodium formate (0.5 mM in 2-propanol:water, 90:10, v/v) was used to calibrate the instrument and a solution of leucine-encephalin (2 ng/µl in acetonitrile:0.1% formic acid in water, 50:50, v/v) was used for the lock mass correction.
To control the mass accuracy, a known standard mix consisting of leucine-enkephalin and meloxicam was analyzed before and after every sample set.

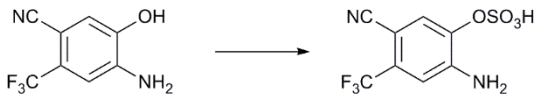
Chemical Synthesis

Synthesis of 4-amino-5-hydroxy-2-(trifluoromethyl)benzonitrile (4)

4-Amino-5-methoxy-2-(trifluoromethyl)benzonitrile **13** (35 mg, 160 µmol) was dissolved in DCM (4 mL) and BBr_3 (243 µL, 1M solution in heptane, 6 eq) was added dropwise to the reaction mixture at -78 °C. The mixture was stirred at -78 °C and slowly warmed to 25 °C within 4 h. The reaction mixture was then stirred for another 16 h at 25 °C. Upon full consumption of all starting material the reaction mixture was quenched by slow addition of MeOH (2 mL). Silica gel was added to the reaction mixture, the solvent evaporated *in vacuo* and purified by silica gel chromatography using a gradient of MeOH in DCM (1-5%) to afford 4-amino-5-hydroxy-2-(trifluoromethyl)benzonitrile **4** (11 mg, 54 µmol, 34%).

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 6.99 (s, 2H); ^{19}F NMR (376 MHz, CD_3OD) δ (ppm) = 62.29 (s, CF_3); ^{13}C NMR (100 MHz, CD_3OD) δ (ppm) = 145.7, 142.0, 125.2 (q, $^2J_{CF}$ = 31.9 Hz), 120.6 (q, $^1J_{CF}$ = 272 Hz, CF_3), 117.7, 116.9, 110.6 (q, $^3J_{CF}$ = 4.8 Hz), 94.1 (q, $^4J_{CF}$ = 2.4 Hz); HRMS (ESI -) calculated for $C_8H_4F_3N_2O^-$ $(M-H)^-$: 201.0281, found: 201.0278.

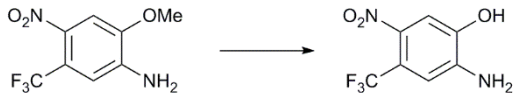
Synthesis of 2-amino-5-cyano-4-(trifluoromethyl)phenyl hydrogen sulfate (5)



$NaHCO_3$ (6.7 mg, 79 µmol, 4 eq) and a sulfur trioxide-trimethyl complex (6.9 mg, 50 µmol, 2.5 eq) were added to a solution of 4-amino-5-hydroxy-2-(trifluoromethyl)benzonitrile **4** (4.0 mg, 20 µmol) and NaOH (2.4 mg, 59 µmol, 3 eq) in water (500 µL). The mixture was heated at 40 °C and stirred for 3 days. Upon full consumption of all starting material the solvent was removed and co-evaporated with MeOH. The crude reaction mixture was subjected to HPLC purification [r.t. = 15 min, 0-5 min (0% B), 5-20 min (0-100% B) at a flow of 2.5 mL/min; buffer A = ammonium acetate 5 mM (water) and buffer B = ammonium acetate 5 mM (MeOH)] to afford 2-amino-5-cyano-4-(trifluoromethyl)phenyl hydrogen sulfate **5** (4.0 mg, 14 µmol, 72%).

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 7.69 (s, 1H), 7.12 (s, 1H); ^{19}F NMR (376 MHz, CD_3OD) δ (ppm) = 63.29 (s, CF_3); ^{13}C NMR (100 MHz, CD_3OD) δ (ppm) = 145.8, 139.8, 129.7 (q, $^2J_{CF}$ = 31.8 Hz), 127.2, 122.8 (q, $^1J_{CF}$ = 272 Hz, CF_3), 116.3, 112.3 (q, $^3J_{CF}$ = 4.8 Hz), 93.4 (q, $^4J_{CF}$ = 2.1 Hz); HRMS (ESI-) calculated for $C_8H_4F_3N_2O_4S^-$ $(M-H)^-$: 280.9849, found: 280.9844.

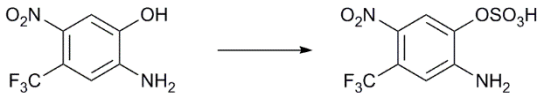
Synthesis of 2-amino-5-nitro-4-(trifluoromethyl)phenol (6)



2-Methoxy-4-nitro-5-(trifluoromethyl)aniline **16** (40 mg, 169 µmol) was dissolved in DCM (3 mL) and BBr_3 (254 µL, 1M solution in heptane, 6eq) was added dropwise into the reaction mixture at -78 °C. The mixture was stirred at -78 °C and slowly warmed to 25 °C within 4 h. The reaction mixture was then stirred for another 16 h at 25 °C. Upon full consumption of all starting material the reaction mixture was quenched by slow addition of MeOH (2 mL). Silica gel was added in the reaction mixture. The reaction mixture was evaporated. The crude material was purified by silica gel column by using gradient mixture of 1-5% of MeOH in DCM to afford 2-amino-5-nitro-4-(trifluoromethyl)phenol **6** (15 mg, 68 µmol, 40%).

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 7.44 (s, 1H), 7.02 (s, 1H); ^{19}F NMR (376 MHz, CD_3OD) δ (ppm) = 60.55 (s, CF_3); ^{13}C NMR (75 MHz, CD_3OD) δ (ppm) = 144.9, 142.4, 136.0, 123.0 (q, $^1J_{CF}$ = 271 Hz, CF_3), 117.1 (q, $^2J_{CF}$ = 33.3 Hz), 111.1, 110.6 (q, $^3J_{CF}$ = 6.4 Hz); HRMS (ESI+) calculated for $C_7H_6F_3N_2O_3^+$ $(M+H)^+$: 223.0325, found: 223.0327.

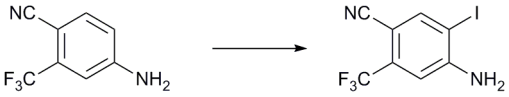
Synthesis of 2-amino-5-nitro-4-(trifluoromethyl)phenyl hydrogen sulfate (7)



Sodium bicarbonate (9.8 mg, 120 µmol, 4 eq) and a sulfur trioxide-trimethyl complex (10 mg, 73 µmol, 2.5 eq) were added to a solution of 2-amino-5-nitro-4-(trifluoromethyl)phenol **6** (6.5 mg, 29 µmol) and NaOH (3.5 mg, 88 µmol, 3 eq) in water (500 µL). Upon full consumption of all starting material the solvent was removed and co-evaporated with MeOH. The crude reaction mixture was subjected to HPLC purification [r.t.= 16 min, 0-5 min (0% buffer B), 5-20 min (0-100% buffer B); buffer A = ammonium acetate 5 mM (water) and buffer B = ammonium acetate 5 mM (MeOH)] to afford 2-amino-5-nitro-4-(trifluoromethyl)phenyl hydrogen sulfate **7** (4 mg, 10 µmol, 45%).

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 8.14 (s, 1H), 7.15 (s, 1H); ^{19}F NMR (376 MHz, CD_3OD) δ (ppm) = 61.19 (s, CF_3); ^{13}C NMR (100 MHz, CD_3OD) δ (ppm) = 146.2, 138.8, 135.1, 122.5 (q, $^1J_{CF}$ = 272 Hz, CF_3), 121.9 (q, $^2J_{CF}$ = 33.2 Hz), 120.1, 112.5 (q, $^3J_{CF}$ = 6.5 Hz); HRMS (ESI-) calculated for $C_7H_4F_3N_2O_6S^-$ $(M-H)^-$: 300.9748, found: 300.9754.

Synthesis of 4-amino-5-iodo-2-(trifluoromethyl)benzonitrile (12)



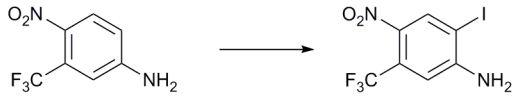
4-Amino-2-(trifluoromethyl)benzonitrile **11** (400 mg, 2.15 mmol) was dissolved in a 1:1 mixture of THF (10 mL) and methanol (10 mL). *N*-Iodosuccinimide (531 mg, 2.36 mmol, 1.1 eq) was then added, followed by addition of about 5 mol % of p-toluenesulfonic acid monohydrate (18.5 mg, 108 µmol). The solution was stirred for 16 h, then concentrated. The crude was dissolved in ethyl acetate (30 mL) and the solution was washed with water twice, then washed with brine and evaporated to afford solid. The crude product was purified by silica gel column chromatography by using gradient mixture of 10-30% EtOAc in hexane to afford 4-amino-5-iodo-2-(trifluoromethyl)benzonitrile **12** (625 mg, 2.00 mmol, 93%).

^{1}H NMR (400 MHz, (CD_3OD) δ (ppm) = 8.11 (s, 1H), 7.08 (s, 1H); ^{19}F NMR (376 MHz, $((CD_3)_2CO)$ = δ (ppm) = 63.38 (s, CF_3); ^{13}C NMR (100 MHz, $((CD_3)_2CO)$ δ (ppm) = 152.7, 145.3, 132.9 (q, $^2J_{CF}$ = 33 Hz), 122.8 (q, $^1J_{CF}$ = 272 Hz, CF_3), 115.1, 110.5 (q, $^3J_{CF}$ = 5.0 Hz), 95.9, 83.1 (q, $^4J_{CF}$ = 1.3 Hz); HRMS (ESI+) calculated for $C_8H_5F_3IN_2^+$ $(M+H)^+$: 312.9444, found: 312.9443.

Synthesis of 4-amino-5-methoxy-2-(trifluoromethyl)benzonitrile (13)[1]

4-amino-5-iodo-2-(trifluoromethyl)benzonitrile **12** (150 mg, 481 µmol), CuI (9.2 mg, 48 µmol, 0.1 eq), Cs_2CO_3 (313 mg, 961 µmol, 2 eq) and 1 ,10-phenanthrolin-mono hydrate (17 mg, 96 µmol, 0.2 eq) were mixed in 3 mL of methanol and flushed with nitrogen for 5 minutes. The reaction mixture was heated at 90 °C for 20 h. The solvent was removed and the crude product was purified by silica gel column chromatography by using gradient mixture of 10-30% EtOAc in hexane to afford 4-amino-5-methoxy-2-(trifluoromethyl)benzonitrile **13** (52 mg, 240 µmol, 50%). The analytical data of **13** perfectly agree with reference data.

Synthesis of 2-iodo-4-nitro-5-(trifluoromethyl)aniline (15)



5-Amino-2-nitrobenzotrifluoride **14** (1.00 g, 4.85 mmol) was dissolved in a 1:1 mixture of THF (10 mL) and methanol (10 mL). N-iodosuccinimide (1.20 g, 5.34 mmol, 1.1 eq) were then added, followed by addition of about 5 mol % of p-toluenesulfonic acid monohydrate (41.8 mg, 243 µmol). The solution was stirred for 16 h, then concentrated. The crude was dissolved in ethyl acetate (30 mL) and the solution was washed with water twice, then washed with brine and evaporated to afford solid. The crude product was purified by silica gel column chromatography by using gradient mixture of 10-30% EtOAc in hexane to afford 2-Iodo-4-nitro-5-(trifluoromethyl)aniline **15** (1.47 g, 4.41 mmol, 91%).

^{1}H NMR (400 MHz, (CD_3OD) δ (ppm) = 8.43 (s, 1H), 7.11 (s, 1H); ^{19}F NMR (376 MHz, CD_3OD) δ (ppm) = 61.95 (s, CF_3); ^{13}C NMR (100 MHz, CD_3OD) δ (ppm) = 153.7, 137.8, 135.5, 125.8 (q, $^2J_{CF}$ = 33 Hz), 122.3 (q, $^1J_{CF}$ = 273 Hz, CF_3), 110.7 (q, $^3J_{CF}$ = 7.0 Hz), 80.9; HR-MS (ESI+) calculated for $C_7H_3F_3IN_2O_2^-$ $(M-H)^-$: 330.9197, found: 330.9193.

Synthesis of 2-methoxy-4-nitro-5-(trifluoromethyl)aniline (16)

2-Iodo-4-nitro-5-(trifluoromethyl)aniline **15** (60 mg, 180 µmol), CuI (3.4 mg, 18 µmol, 0.1 eq), Cs_2CO_3 (118 mg, 361 µmol, 2 eq) and 1 ,10-phenanthrolin-mono hydrate (6.5 mg, 36 µmol, 0.2 eq) were mixed in 3 mL of methanol and flushed with nitrogen for 5 minutes. The reaction mixture was heated at 90 °C for 20 h. The solvent was removed and the crude product was purified by silica gel column chromatography by using gradient mixture of 10-30% EtOAc in hexane to afford 2-methoxy-4-nitro-5-(trifluoromethyl)aniline **16** (12.3 mg, 52.1 µmol, 29%) and 4-nitro-3-(trifluoromethyl)aniline (16.3 mg, 78 µmol, 43%).

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 7.61 (s, 1H), 7.05 (s, 1H), 3.97 (s, 3H, OMe); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) = 59.29 (s, CF_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 146.9, 140.9, 122.4 (q, $^1J_{CF}$ = 273 Hz, CF_3), 119.0 (q, $^2J_{CF}$ = 33.8 Hz), 111.4 (q, $^3J_{CF}$ = 6.3 Hz), 108.4, 107.6, 56.3; HRMS (ESI-) calculated for $C_8H_6F_3N_2O_3^-$ $(M-H)^-$: 235.0336, found: 235.0329.

References

1 X. Zhang, X. Li, G. F. Allan, T. Sbriscia, O. Linton, S. G. Lundeen and Z. Sui, *J. Med. Chem.*, 2007, **50**, 3857-3869.

NMR Spectra

4-Amino-5-hydroxy-2-(trifluoromethyl)benzonitrile (**4**)
^{1}H NMR, ^{13}C NMR, ^{19}F NMR

2-Amino-5-cyano-4-(trifluoromethyl)phenyl hydrogen sulfate (**5**)
^{1}H NMR, ^{13}C NMR, ^{19}F NMR

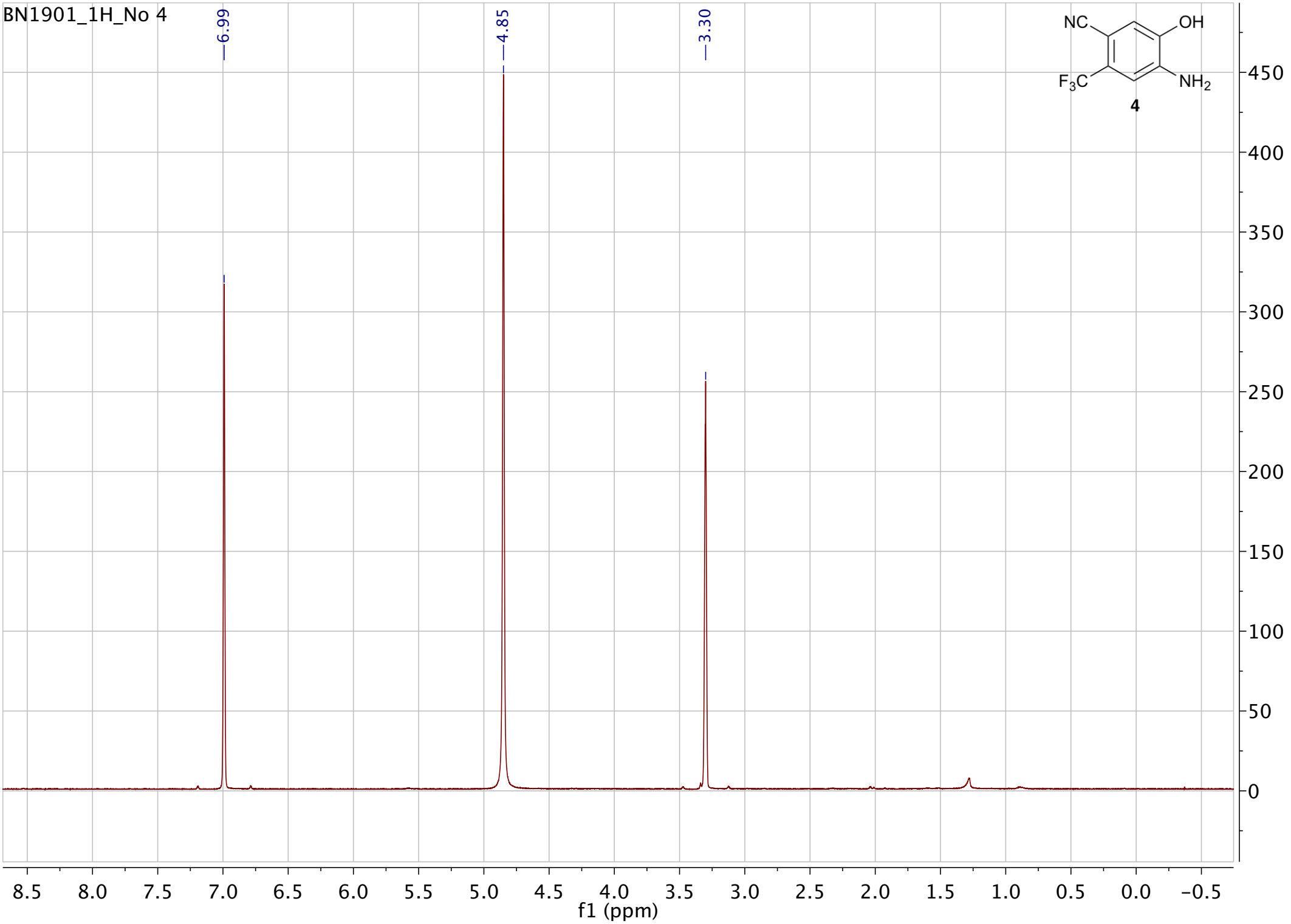
2-Amino-5-nitro-4-(trifluoromethyl)phenol (**6**)
^{1}H NMR, ^{13}C NMR, ^{19}F NMR

2-Amino-5-nitro-4-(trifluoromethyl)phenyl hydrogen sulfate (**7**)
^{1}H NMR, ^{13}C NMR, ^{19}F NMR

4-Amino-5-iodo-2-(trifluoromethyl)benzonitrile (**12**)
^{1}H NMR, ^{13}C NMR, ^{19}F NMR

2-Iodo-4-nitro-5-(trifluoromethyl)aniline (**15**)
^{1}H NMR, ^{13}C NMR, ^{19}F NMR

2-Methoxy-4-nitro-5-(trifluoromethyl)aniline (**16**)
^{1}H NMR, ^{13}C NMR, ^{19}F NMR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100
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0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
2.5
2.0
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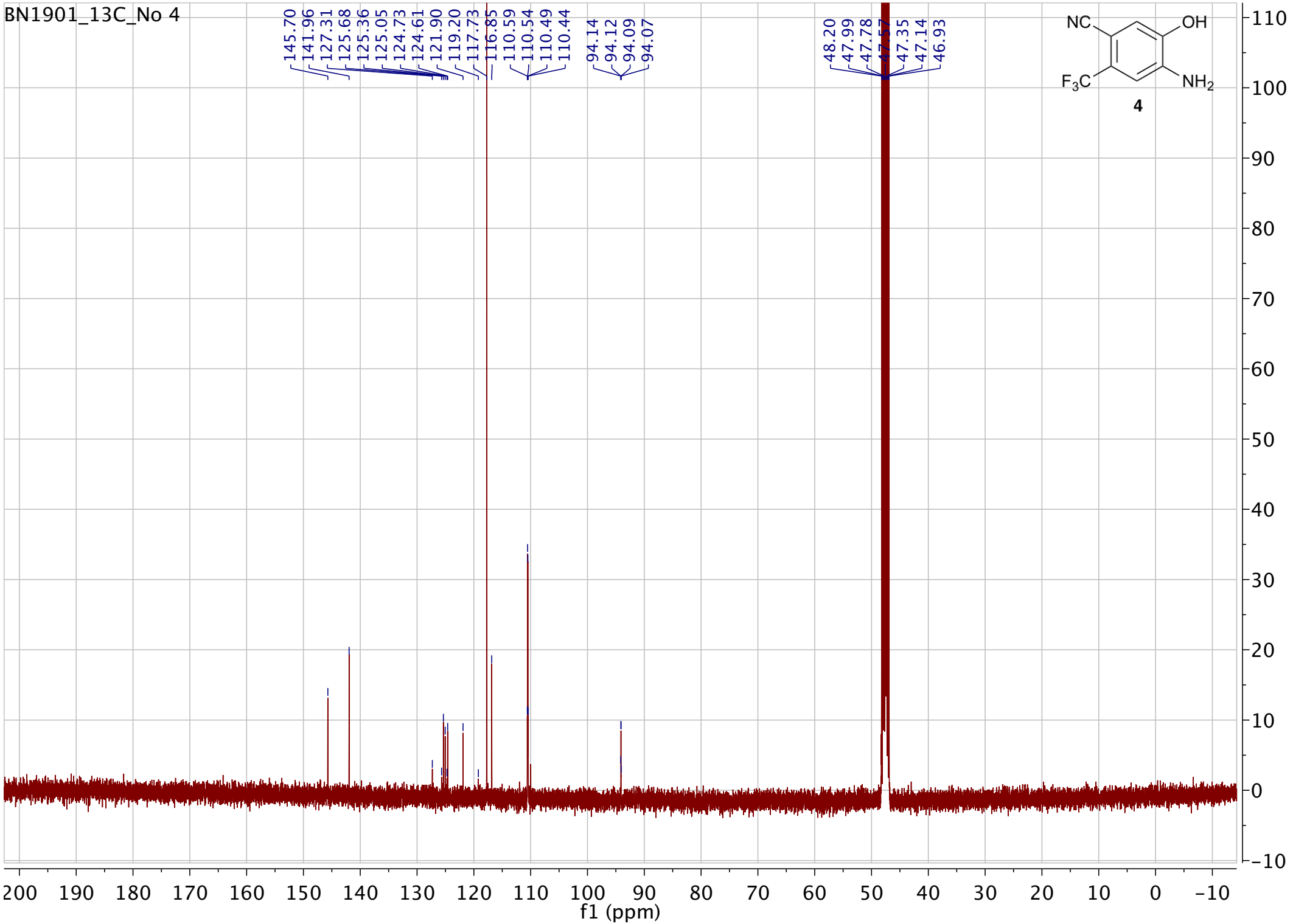
1.0
0.5
0.0
−0.5
f1 (ppm)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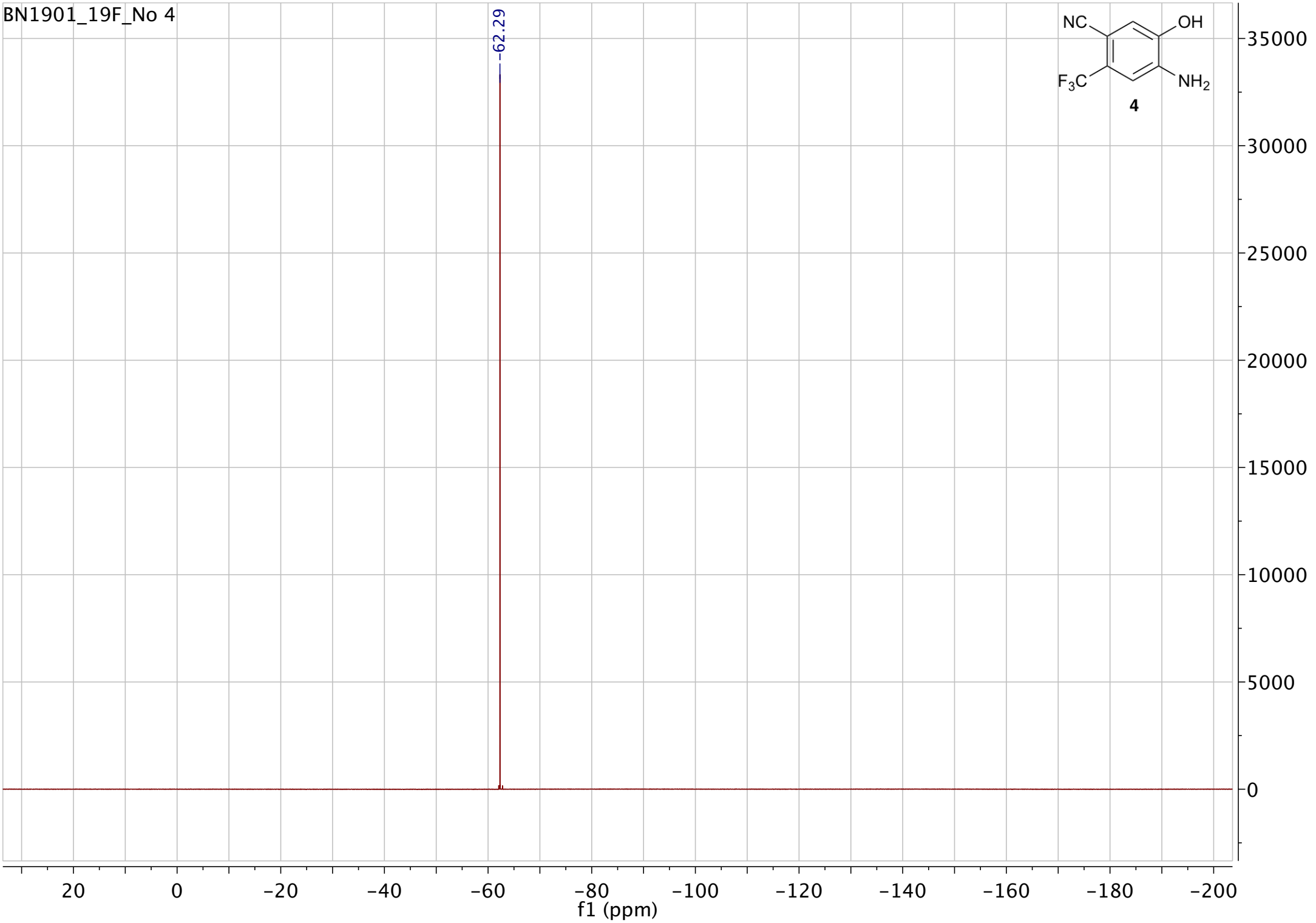
f1 (ppm)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-120
-140
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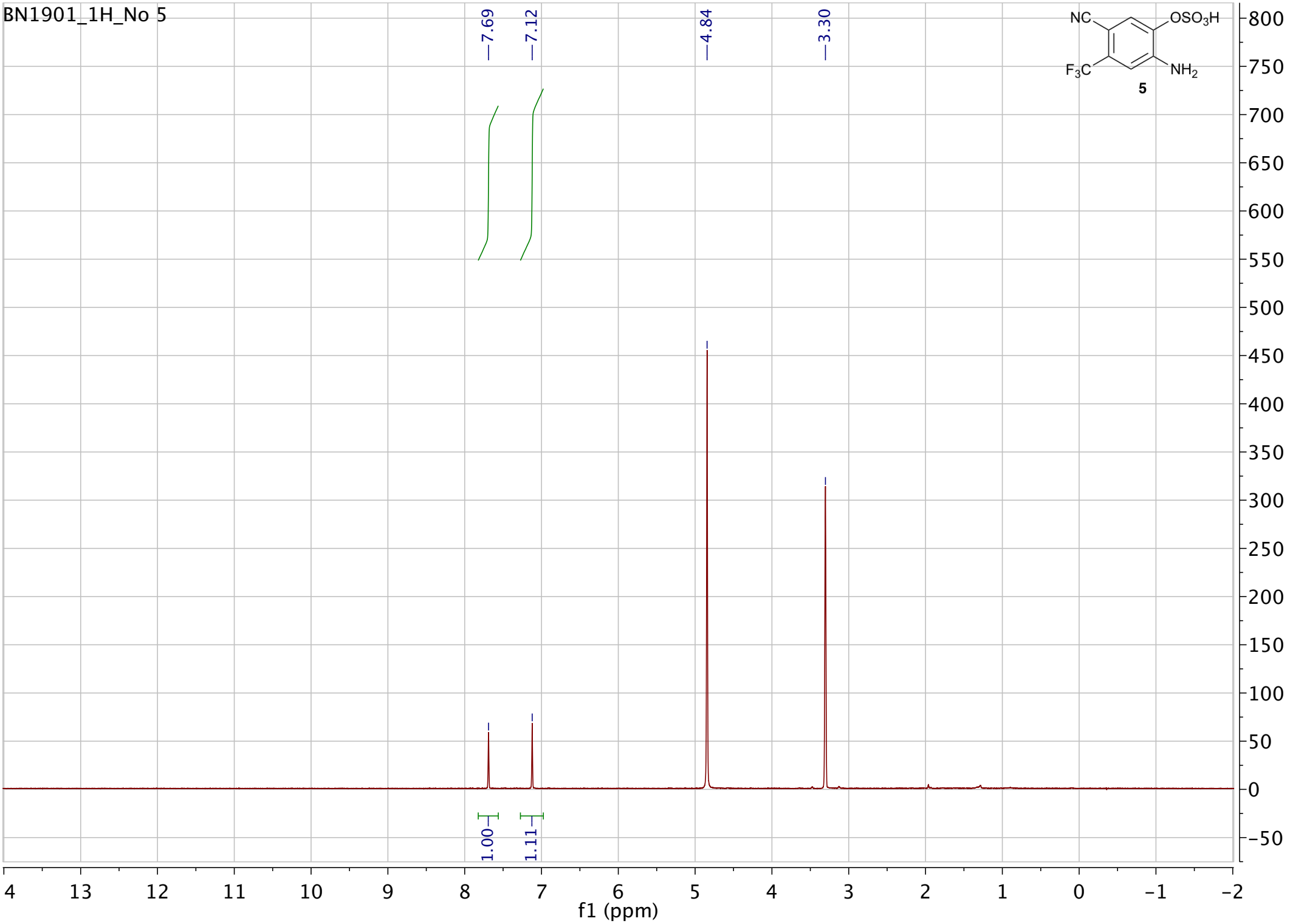
-180
-200
f1 (ppm)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f1 (ppm)

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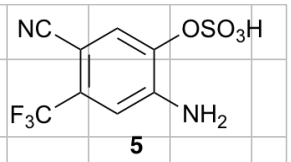
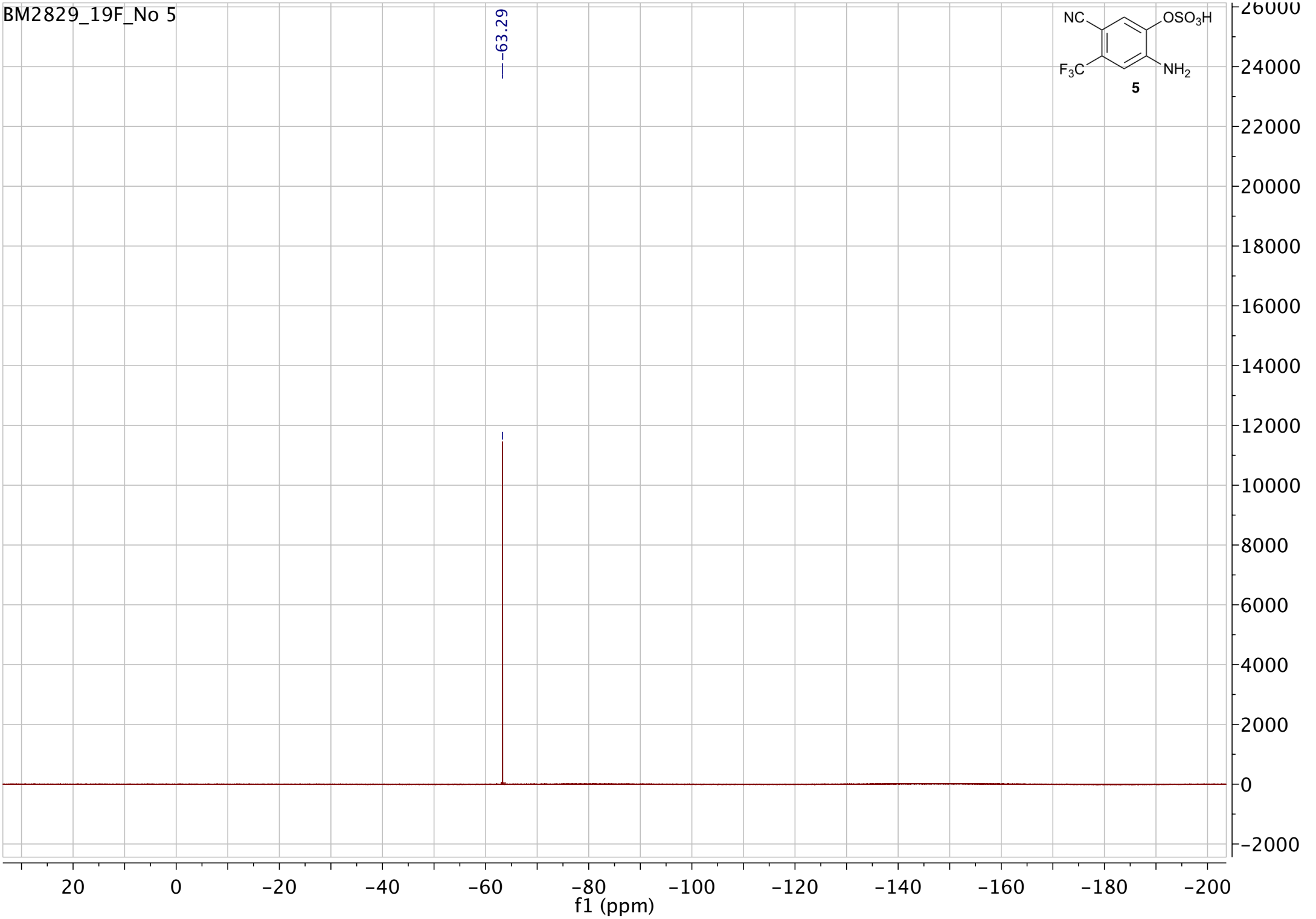


5

f1 (ppm)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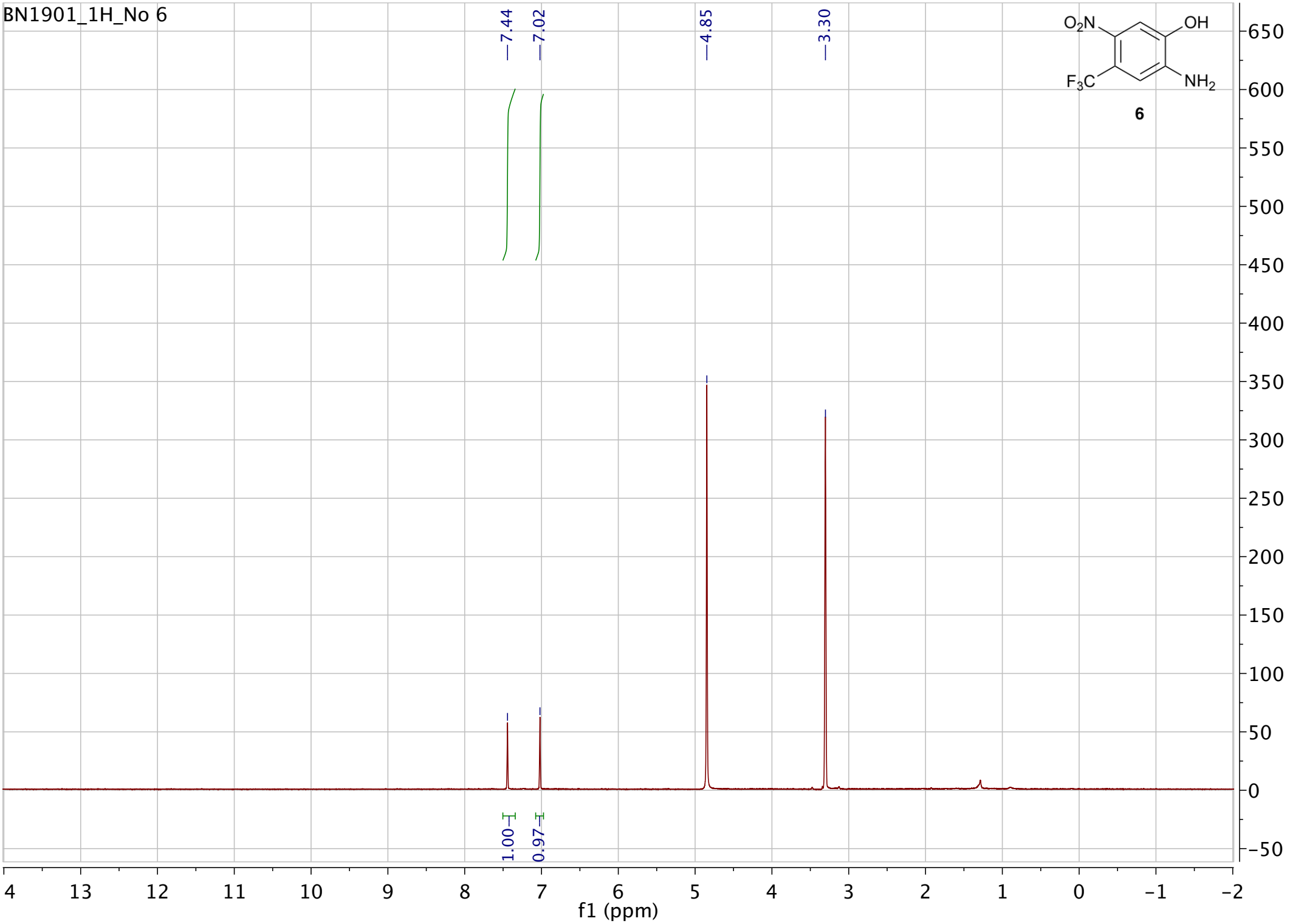
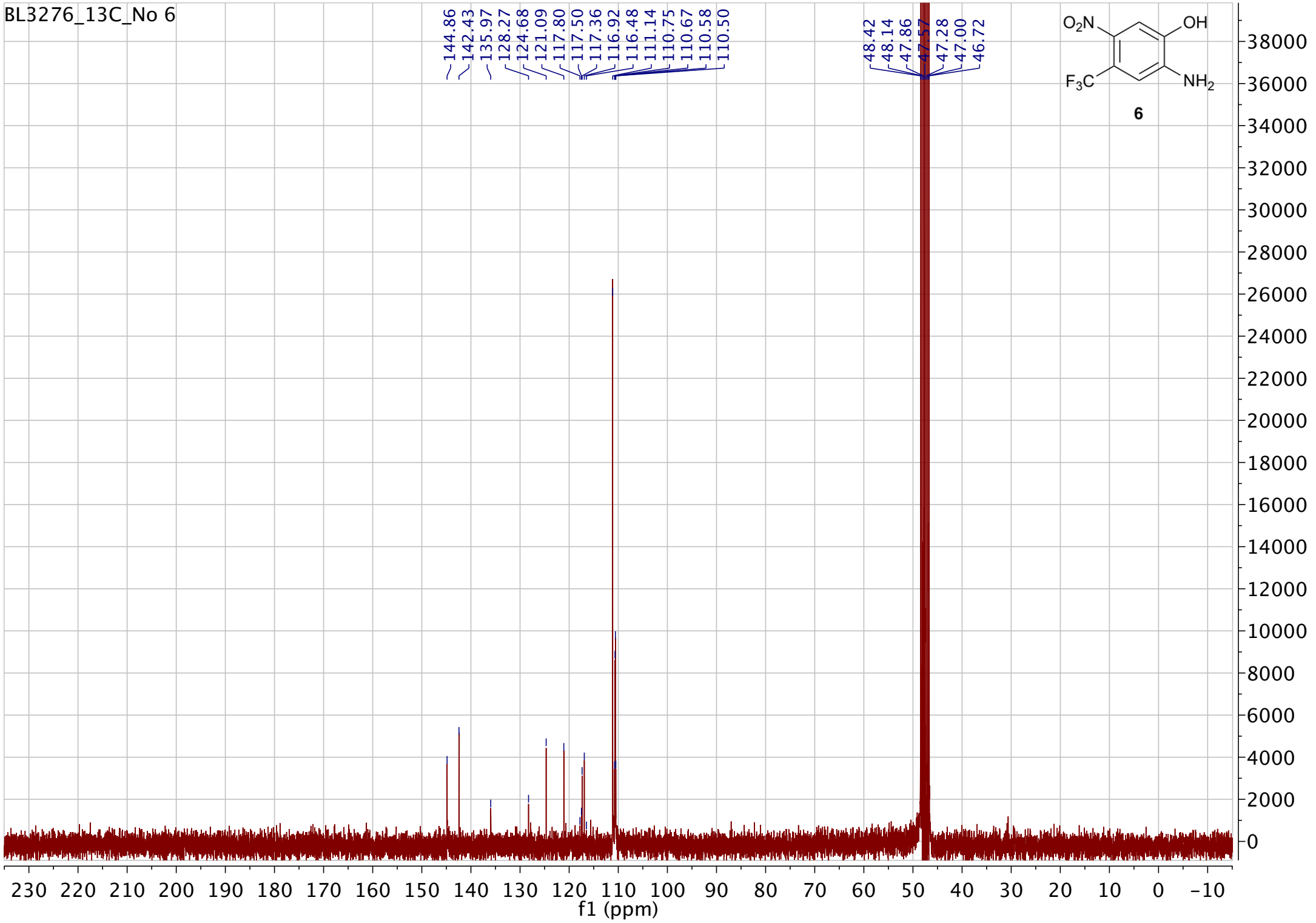
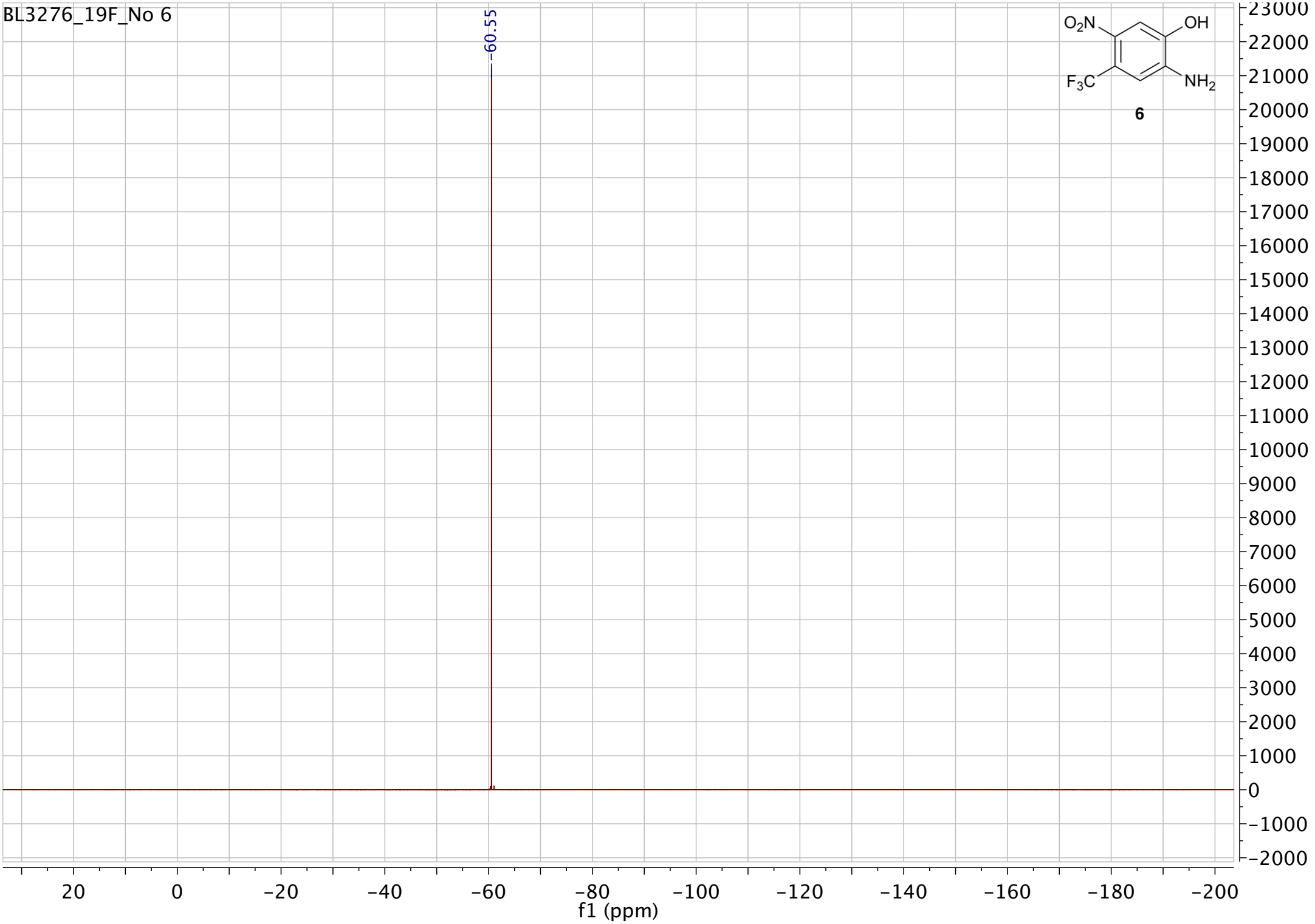
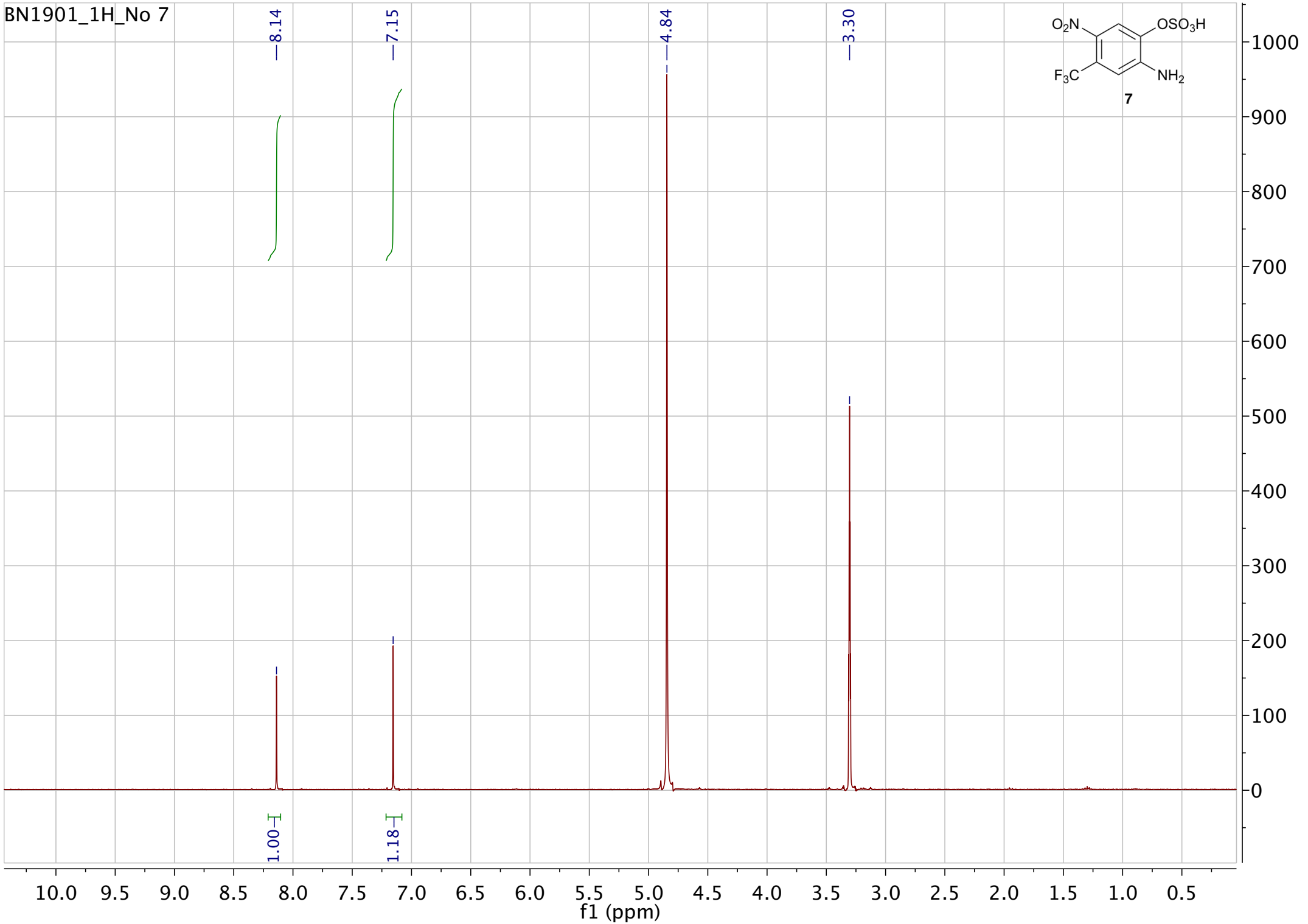
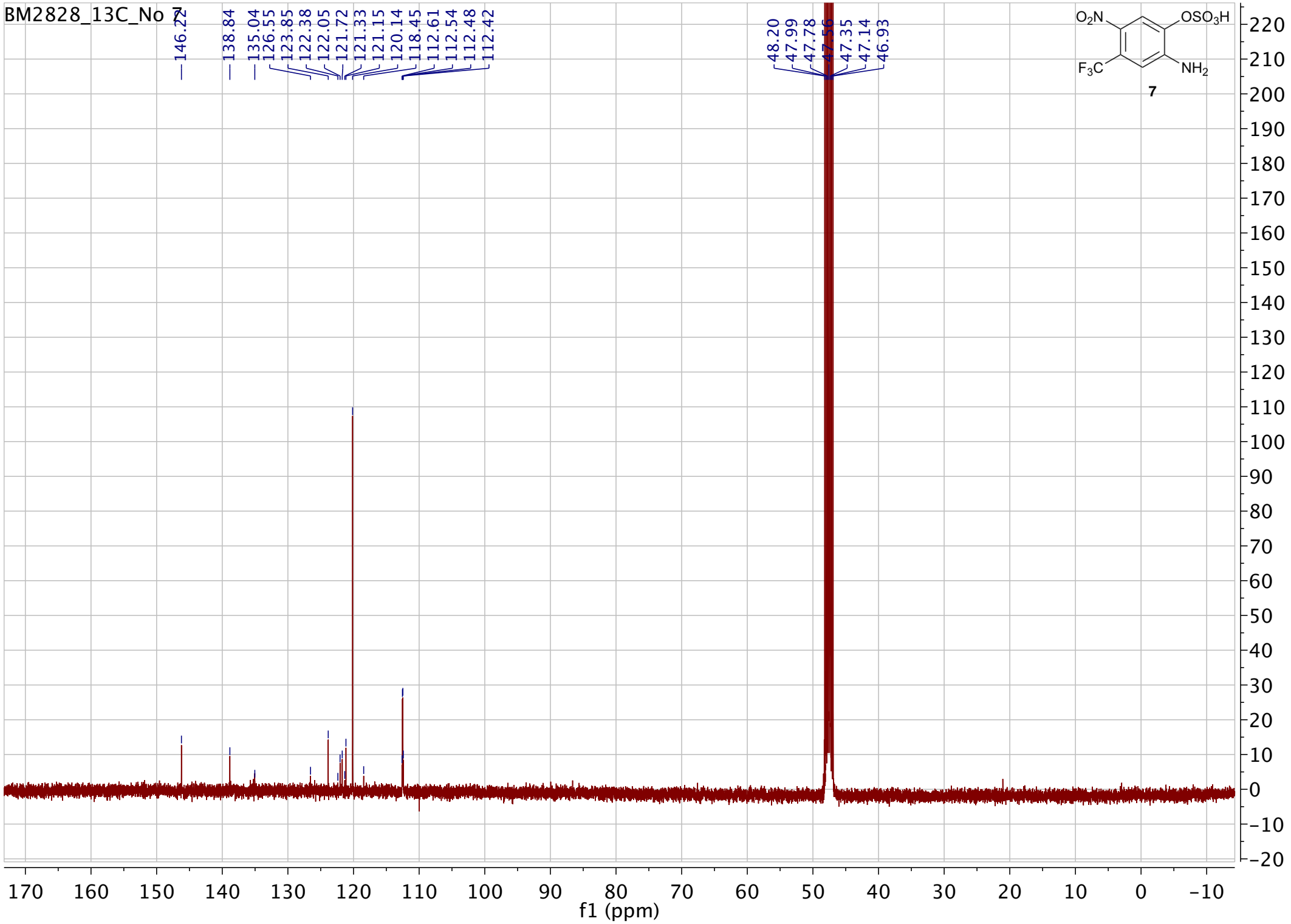
-63.29
NC
OSO3H
F3C
NH2
5
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

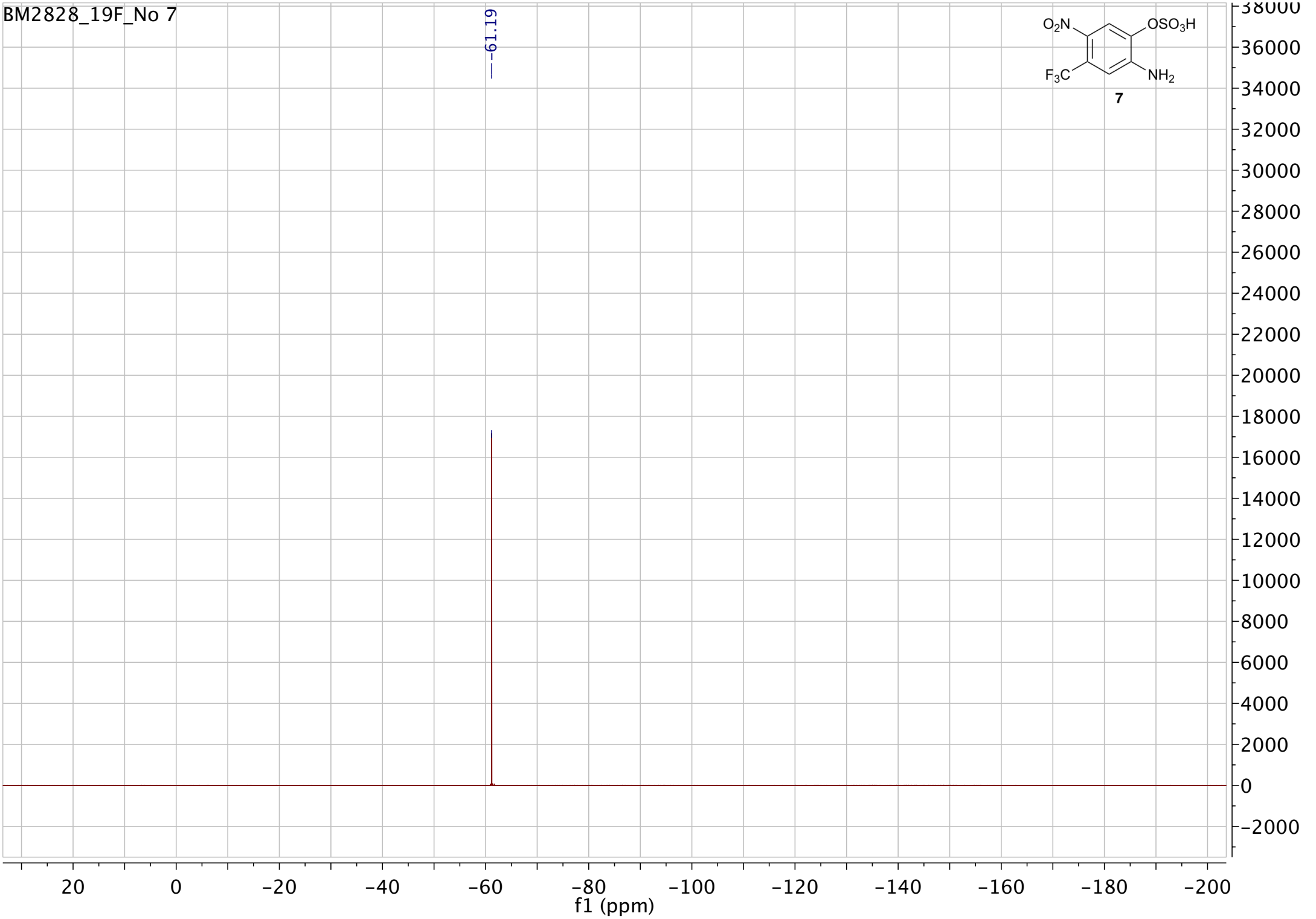

BN1901_1H_No 6
7.44
7.02
4.85
3.30
1.00
0.97
O2N
OH
F3C
NH2
6
650
600
550
500
450
400
350
300
250
200
150
100
50
0
−50
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
f1 (ppm)

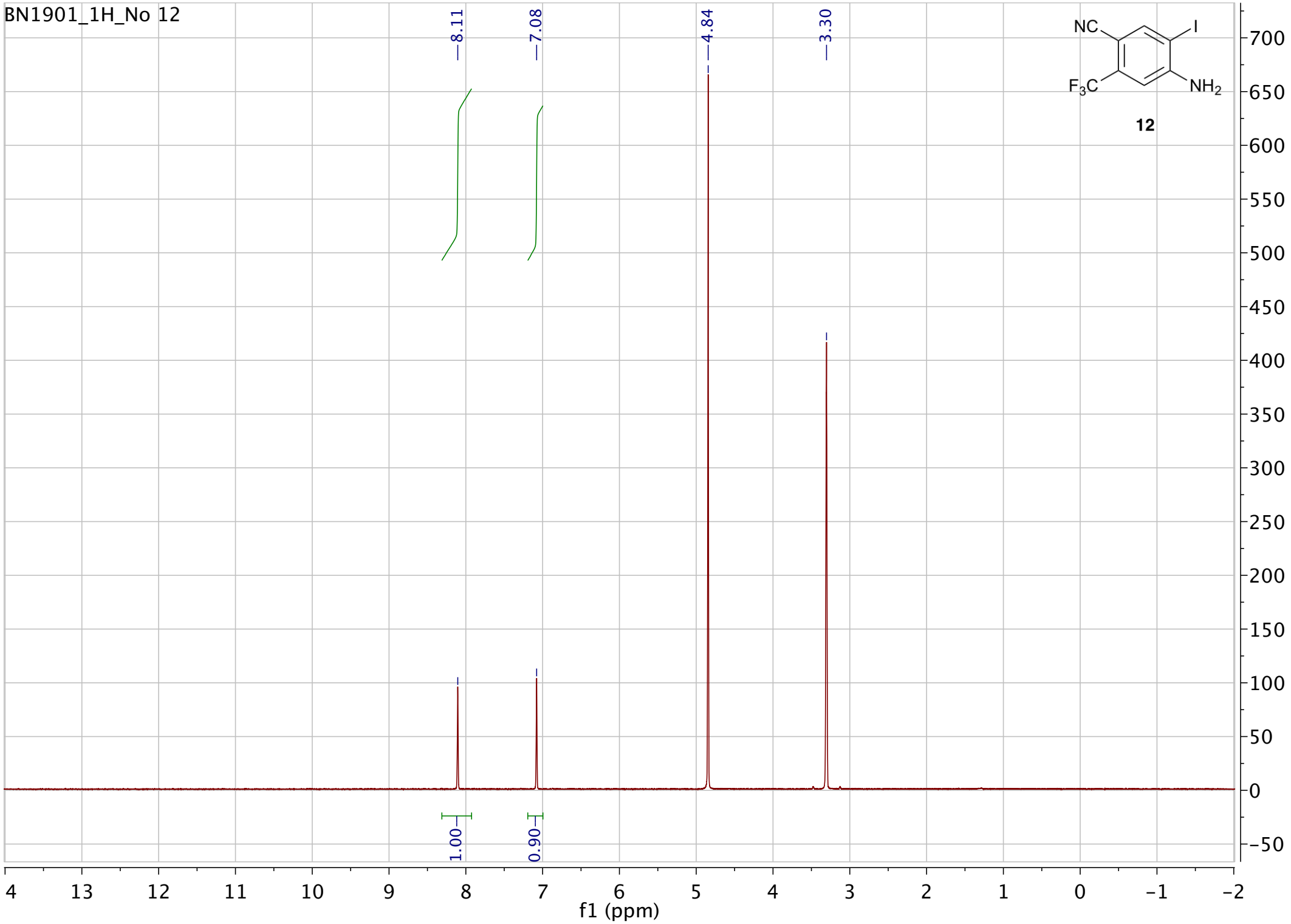

BL3276_13C_No 6
144.86
142.43
135.97
128.27
124.68
121.09
117.80
117.50
117.36
116.92
116.48
111.14
110.75
110.67
110.58
110.50
48.42
48.14
47.86
47.57
47.28
47.00
46.72
O2N
OH
F3C
NH2
6
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

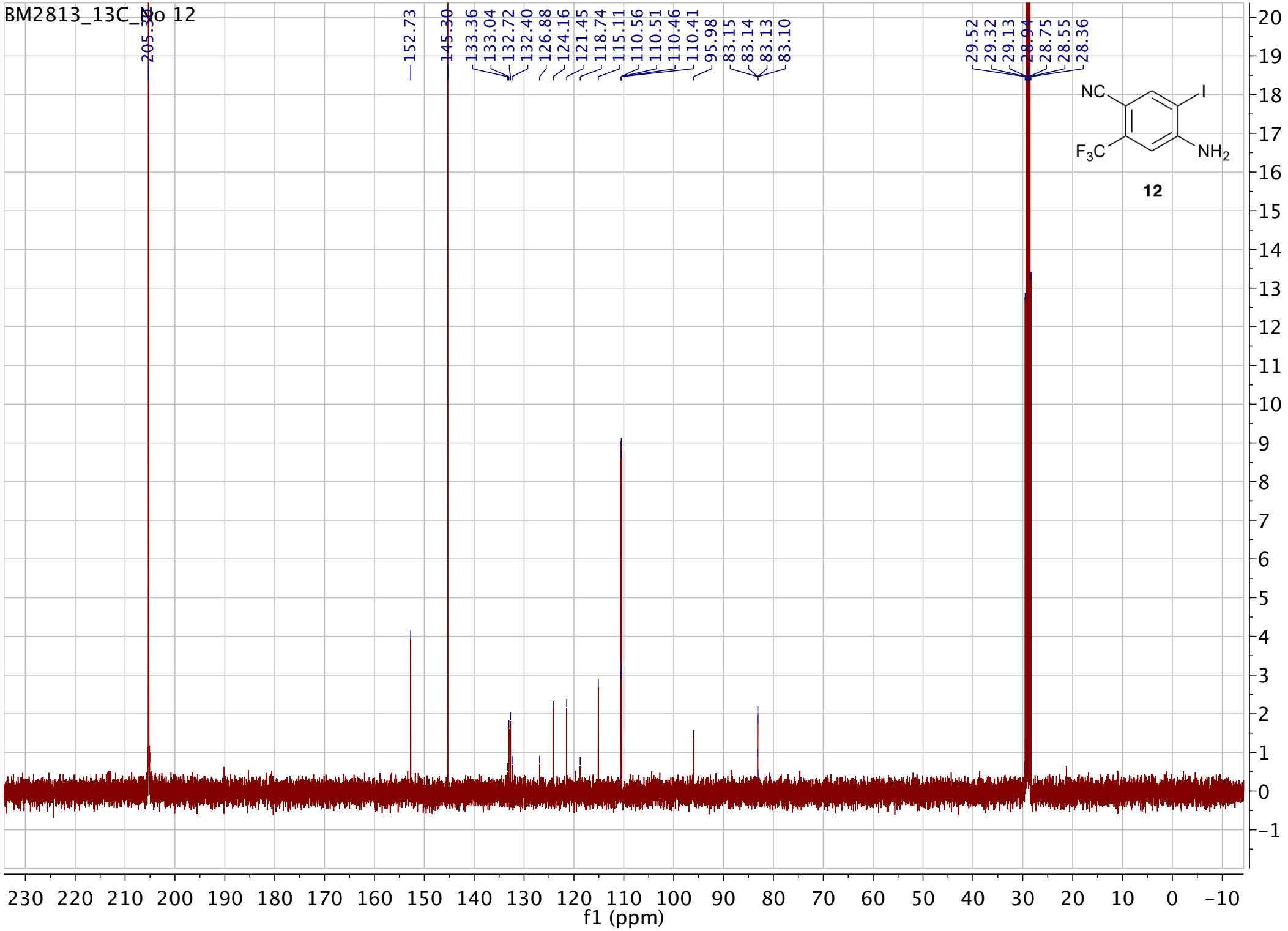

BL3276_19F_No 6
-60.55
O2N
OH
F3C
NH2
6
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

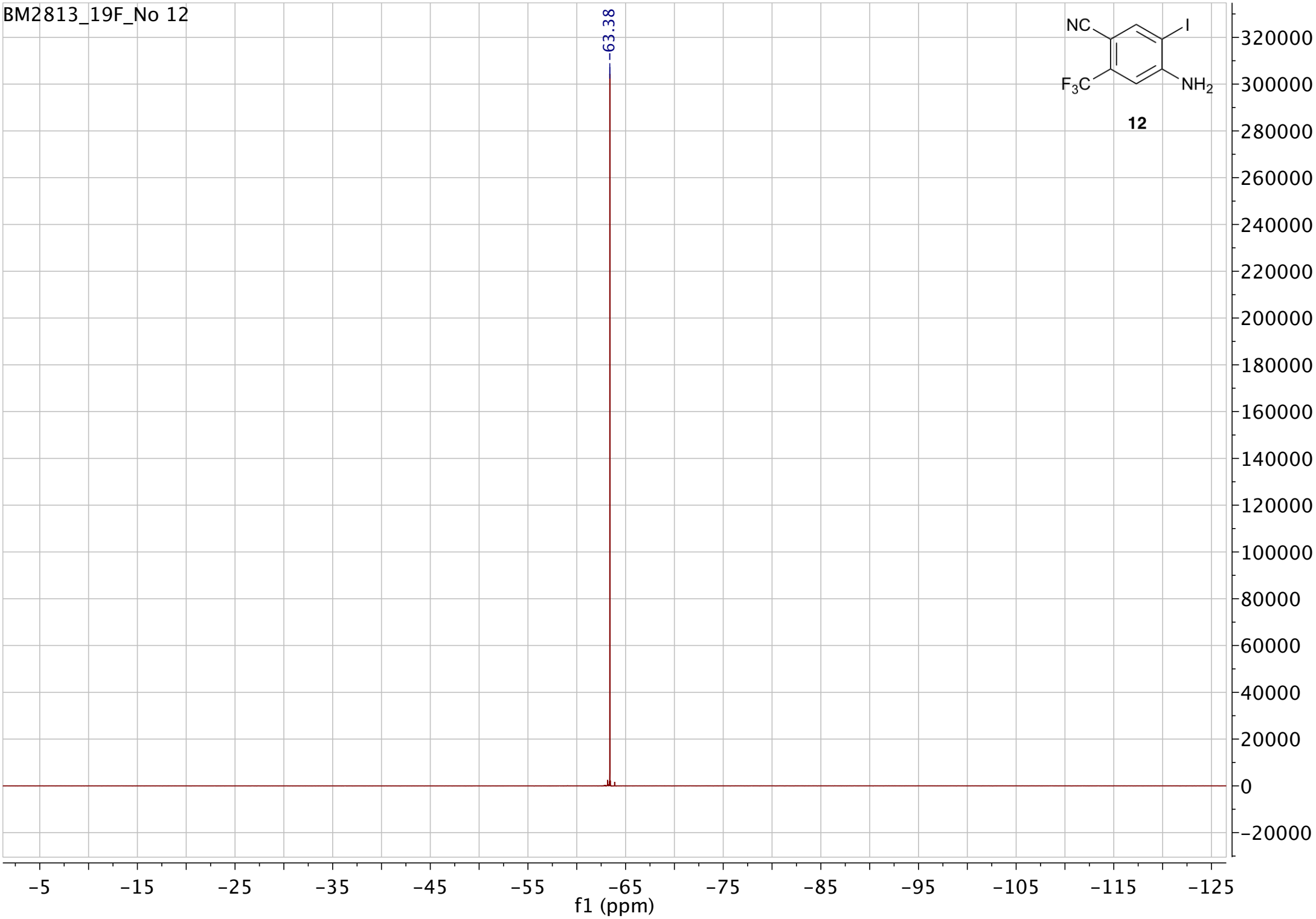

BN1901_1H_No 7
8.14
7.15
4.84
3.30
1.00
1.18
O2N
OSO3H
F3C
NH2
7
1000
900
800
700
600
500
400
300
200
100
0
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

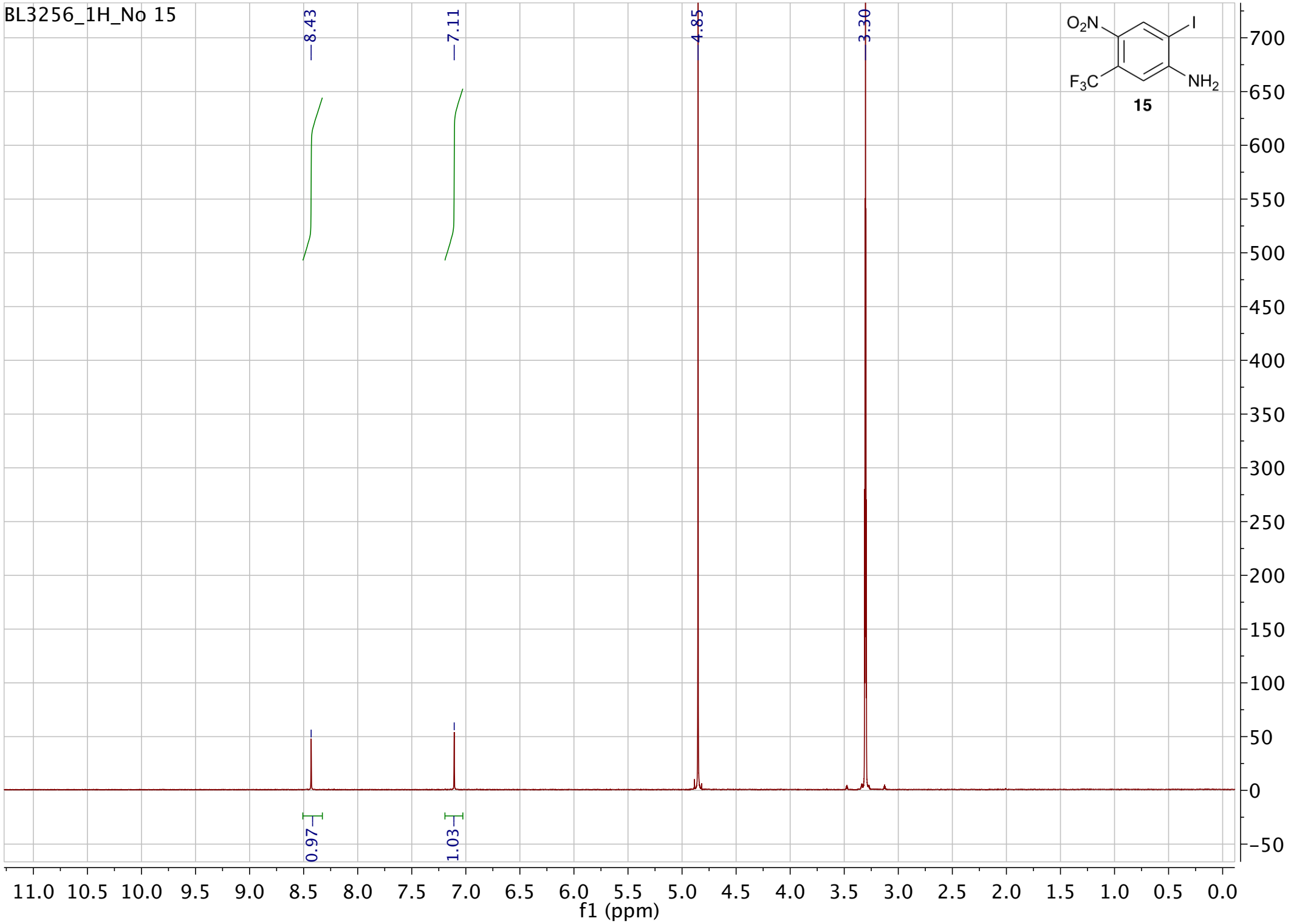

BM2828_13C_No 7
146.22
138.84
135.04
126.55
123.85
122.38
122.05
121.72
121.33
121.15
120.14
118.45
112.61
112.54
112.48
112.42
48.20
47.99
47.78
47.56
47.35
47.14
46.93
O2N
OSO3H
F3C
NH2
7
f1 (ppm)

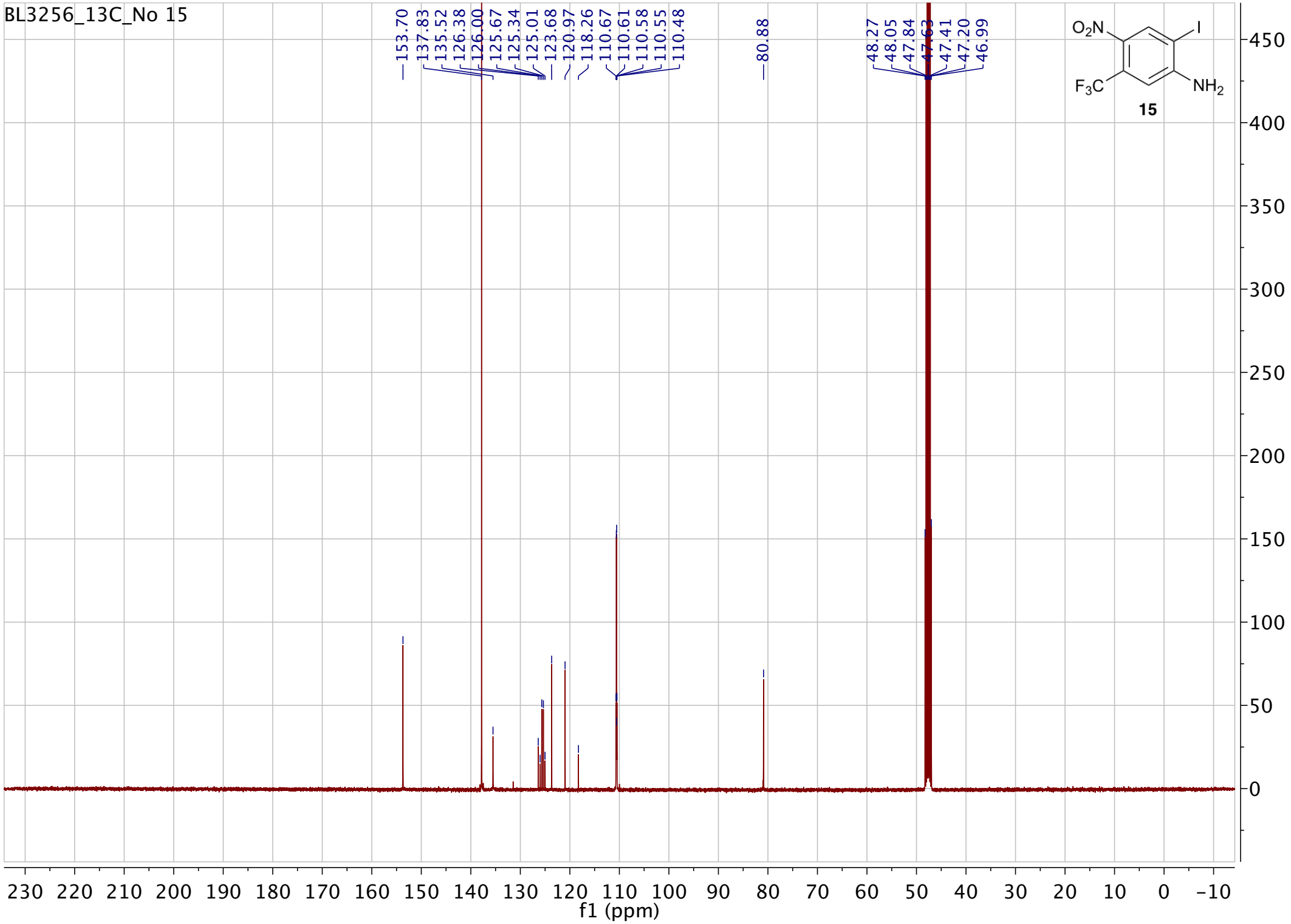

BM2828_19F_No 7
-61.19
O2N
OSO3H
F3C
NH2
7
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

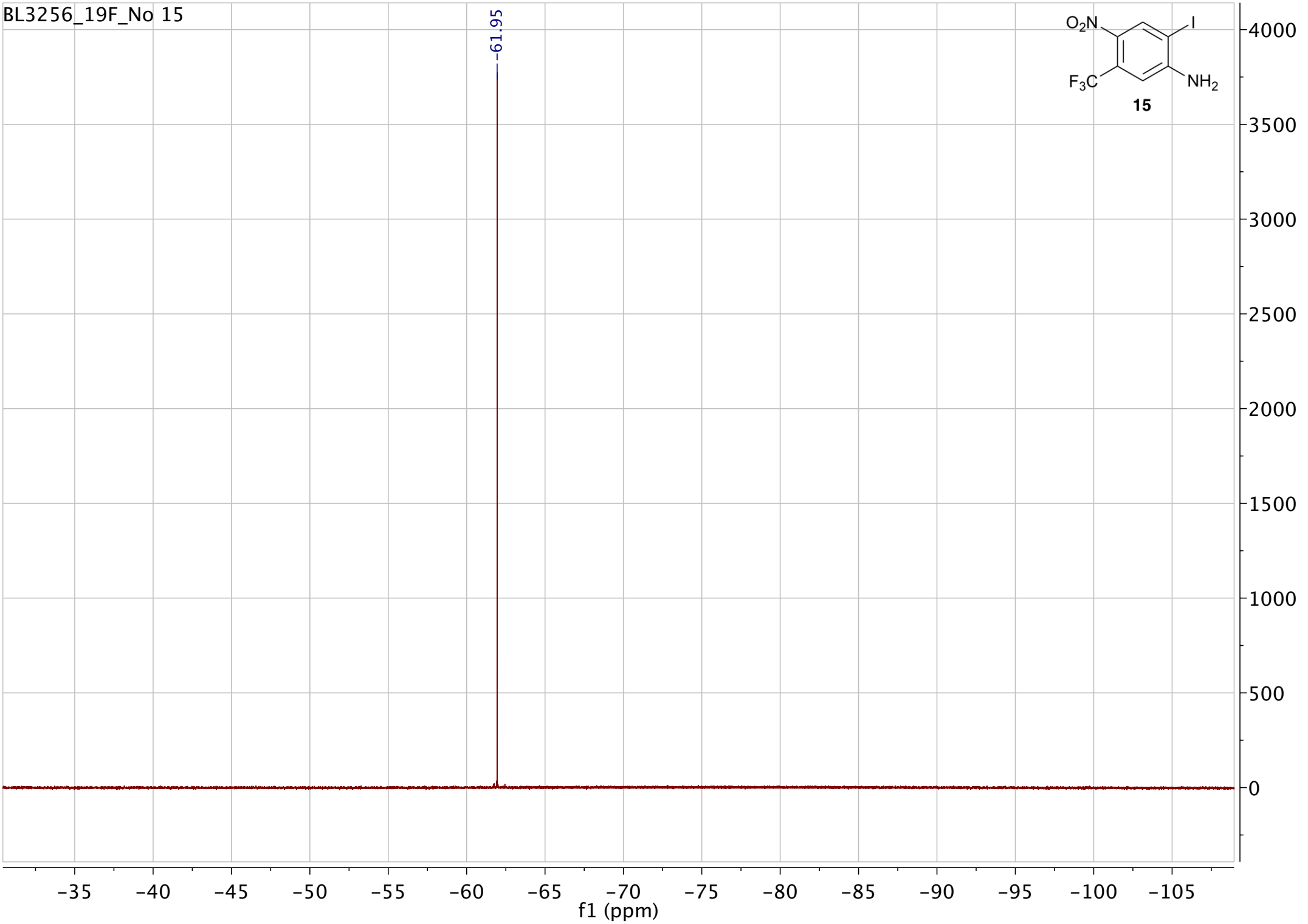

BN1901_1H_No 12
8.11
7.08
4.84
3.30
NC
I
F3C
NH2
12
1.00
0.90
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
−50
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
f1 (ppm)

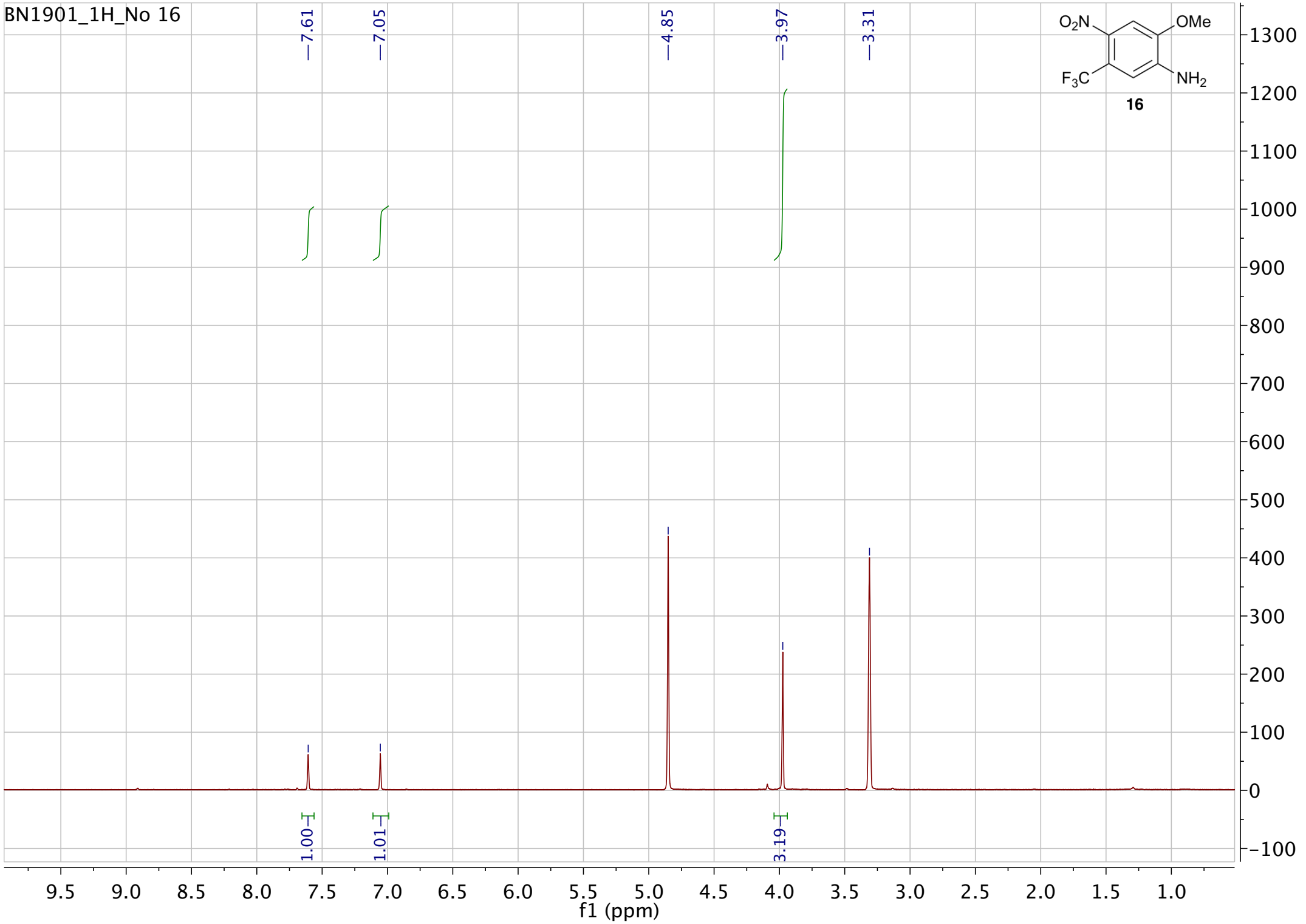

BM2813_13C_No 12
205.34
152.73
145.30
133.36
133.04
132.72
132.40
126.88
124.16
121.45
118.74
115.11
110.56
110.51
110.46
110.41
95.98
83.15
83.14
83.13
83.10
29.52
29.32
29.13
28.94
28.75
28.55
28.36
NC
I
F3C
NH2
12
f1 (ppm)

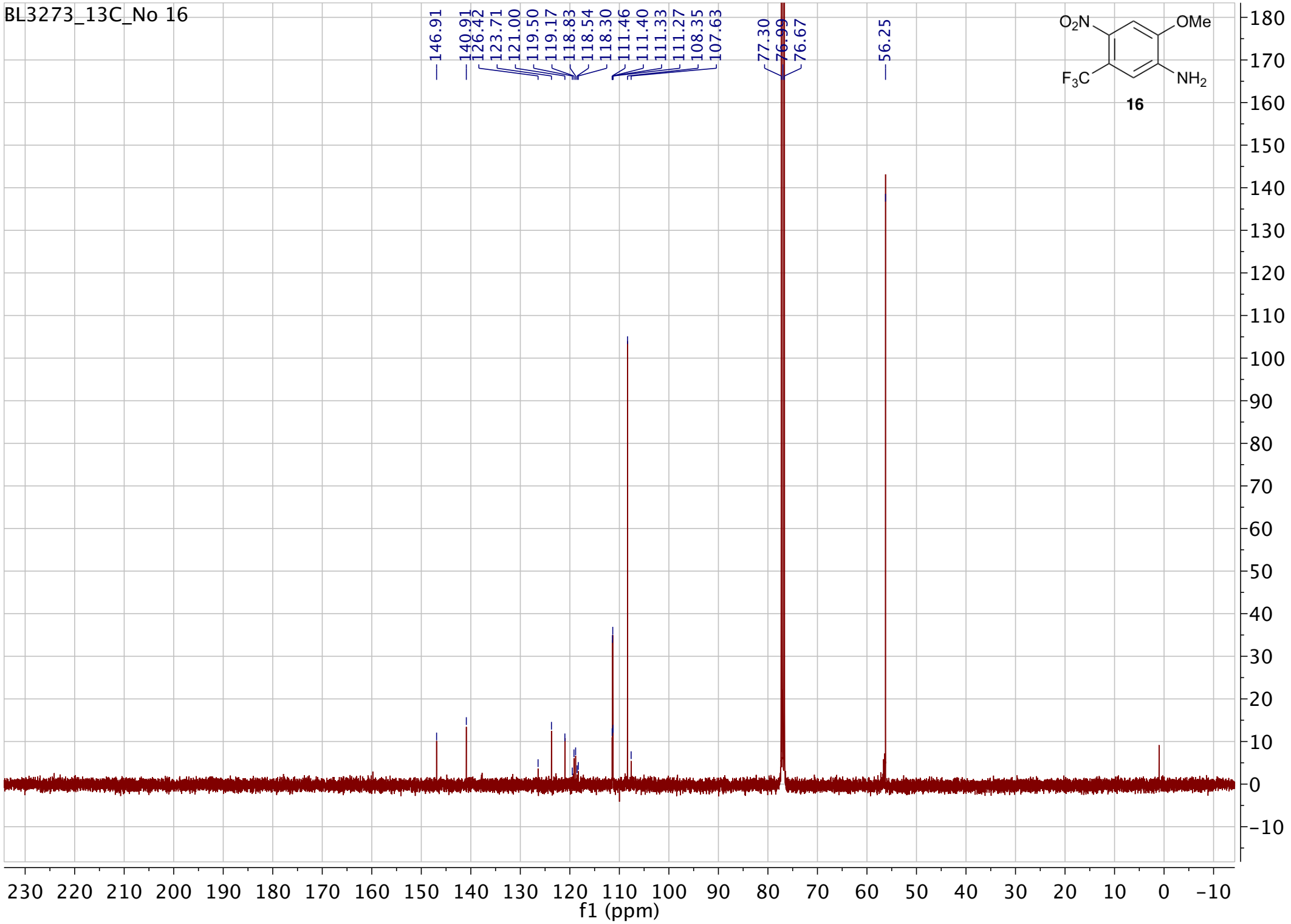

BM2813_19F_No 12
-63.38
NC
I
F3C
NH2
12
320000
300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000
-5
-15
-25
-35
-45
-55
-65
-75
-85
-95
-105
-115
-125
f1 (ppm)

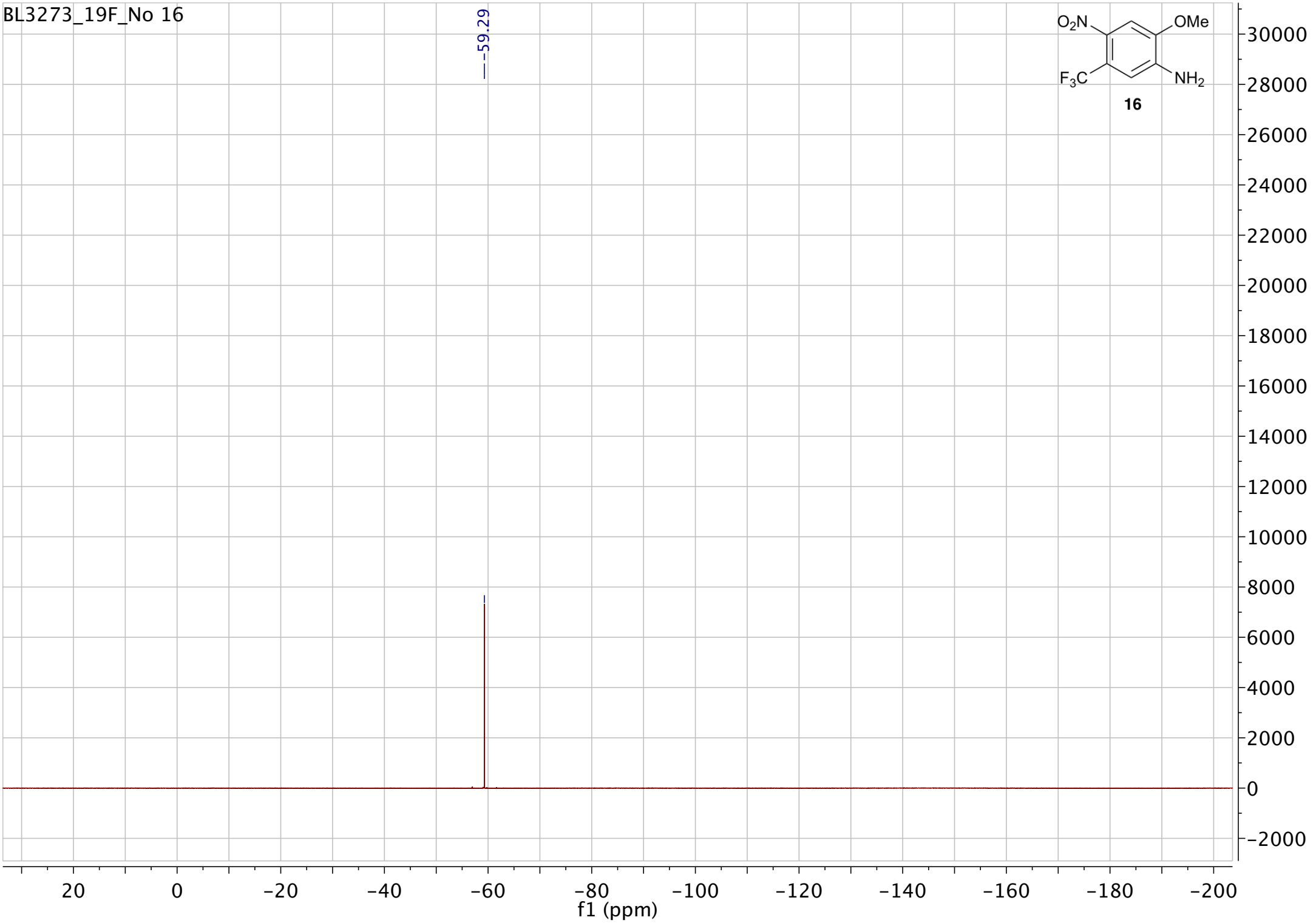

BL3256_1H_No 15
8.43
7.11
4.85
3.30
0.97
1.03
O2N
I
F3C
NH2
15
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


BL3256_13C_No 15
153.70
137.83
135.52
126.38
126.00
125.67
125.34
125.01
123.68
120.97
118.26
110.67
110.61
110.58
110.55
110.48
80.88
48.27
48.05
47.84
47.63
47.41
47.20
46.99
O2N
I
F3C
NH2
15
450
400
350
300
250
200
150
100
50
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


BL3256_19F_No 15
-61.95
O2N
I
F3C
NH2
15
4000
3500
3000
2500
2000
1500
1000
500
0
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
f1 (ppm)


BN1901_1H_No 16
7.61
7.05
4.85
3.97
3.31
1.00
1.01
3.19
O2N
OMe
F3C
NH2
16
f1 (ppm)


BL3273_13C_No 16
146.91
140.91
126.42
123.71
121.00
119.50
119.17
118.83
118.54
118.30
111.46
111.40
111.33
111.27
108.35
107.63
77.30
76.99
76.67
56.25
O2N
OMe
F3C
NH2
16
f1 (ppm)


BL3273_19F_No 16
-59.29
O2N
OMe
F3C
NH2
16
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)