

# Synthesis of Aryl Sulfonamides via Palladium-Catalyzed Chlorosulfonylation of Arylboronic Acids

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## I. General Information

### A) General Reagent Information:

Unless otherwise stated, all reactions were set-up on the bench top and carried out under an argon atmosphere. Anhydrous acetone was purchased from Acros Organics, and this solvent was degassed by sparging with N<sub>2</sub> for one h. All other solvents were purified and dried by passage through successive alumina and Q5 reactant-packed columns on a solvent purification system. Sulfuryl chloride, phenol, pyridine, and *N,N*-diisopropylethylamine were purchased from Aldrich Chemical Co. and used as received. Anhydrous Na<sub>2</sub>CO<sub>3</sub> was received from VWR. The arylboronic acid substrates were purchased from Frontier Scientific, Combi-Blocks, and Aldrich and used as received without further purification. Ligand PhDavePhos (**L3**) was purchased from Strem, and *tert*-BuDavePhos (**L2**) was obtained from Aldrich. CPhos (**L4**)<sup>1</sup> and precatalysts of **P1**, **P2**, **P6**, and **P7** were synthesized according to literature procedures.<sup>2</sup> Compounds were purified by flash chromatography using Silicycle SiliaFlashP60 (230-400 mesh) silica gel.

### B) General Analytical Information:

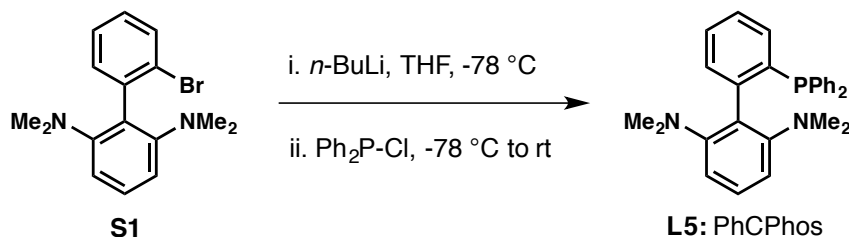
All compounds (starting materials and products) were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, <sup>31</sup>P NMR (when applicable), <sup>19</sup>F NMR (when applicable), IR spectroscopy, melting point (when applicable), and elemental analysis or mass spectrometry. The <sup>1</sup>H, <sup>13</sup>C, <sup>31</sup>P, and <sup>19</sup>F NMR spectra can be found in Section III of the supporting information. <sup>1</sup>H, <sup>13</sup>C, <sup>31</sup>P, and <sup>19</sup>F NMR were recorded on Varian 300 MHz, Varian 500 MHz or Bruker 400 MHz spectrometers. The spectra were calibrated according to residual solvent peaks (CDCl<sub>3</sub>: 7.26 ppm for <sup>1</sup>H NMR and 77.0 ppm for <sup>13</sup>C NMR; CD<sub>2</sub>Cl<sub>2</sub>: 5.32 ppm for <sup>1</sup>H NMR and 53.84 ppm for <sup>13</sup>C NMR), an external reference (H<sub>3</sub>PO<sub>4</sub>: 0 ppm for <sup>31</sup>P), or an internal reference (CF<sub>3</sub>Ph: -63.7 ppm for <sup>19</sup>F). The <sup>13</sup>C, and <sup>31</sup>P NMR spectra were obtained with <sup>1</sup>H decoupling, and the <sup>19</sup>F NMR spectra were obtained without <sup>1</sup>H decoupling. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent. IR spectra were obtained on a Thermo Scientific iD5 ATR Nicolet iS5 FT-IR spectrometer. Elemental analyses were carried out by Atlantic Microlab, Inc., Norcross, GA. ESI-MS spectra were recorded on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS). Melting points (m.p.) were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatographic (GC) analyses were performed on an Agilent 7890A instrument (FID detector) using a J&W DB-1 column (10m, 0.1 mm I.D.). Reactions were monitored by GC and thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) or Fluka aluminum oxide/TLC-cards using UV light as a visualizing agent.

<sup>1</sup> Han, C.; Buchwald, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 7532.

<sup>2</sup> Bruno, N. C.; Tudge, M. T.; Buchwald, S. L. *Chem. Sci.* **2013**, *4*, 916.

## II. Experimental Procedures and Characterization Data.

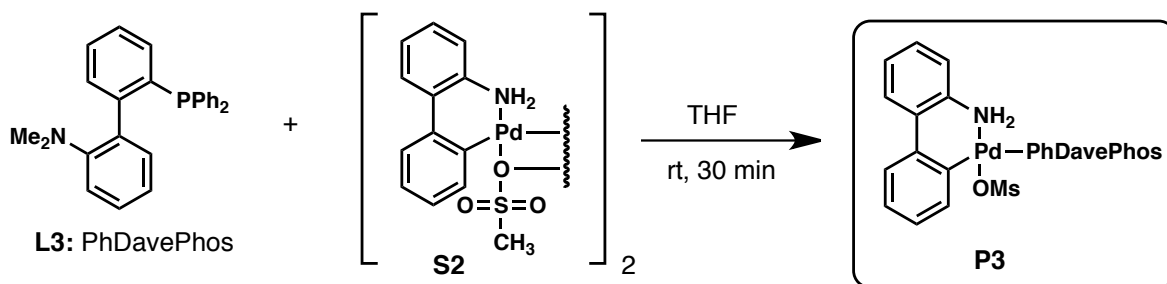
### A) Synthesis of PhCPhos (L5):



**2'-(Diphenylphosphino)-6-methoxy-N,N-dimethylbiphenyl-2-amine (L5):** The starting material, 2'-bromo-6-methoxy-N,N-dimethylbiphenyl-2-amine (**S1**), was synthesized according to a procedure reported by Han and Buchwald.<sup>1</sup> An oven-dried 250 mL round-bottom flask, which was equipped with a magnetic stir bar and fitted with a Teflon septum, was charged with **S1** (4.58 g, 14.35 mmol, 1.0 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times). THF (58.0 mL) was added via syringe and the solution was cooled to -78 °C. n-Butyllithium (2.5 M solution in hexanes, 6.06 mL, 15.1 mmol, 1.05 equiv) was added dropwise via syringe over 15 min and the resulting mixture was stirred at -78 °C for 45 min. Chlorodicyclohexylphosphine (2.85 mL, 15.1 mmol, 1.05) was then added dropwise via syringe over 15 min. The reaction mixture was stirred at -78 °C for 2 h and then allowed to slowly warm to room temperature overnight (~ 12 h). The reaction was quenched by addition of methanol (~1.0 mL), filtered through a pad of SiO<sub>2</sub> topped with a layer of Celite, and eluted with ethyl acetate (300 mL). The filtrate was concentrated *in vacuo* to afford a yellow solid. Recrystallization from dichloromethane and methanol provided the title compound as a white solid (5.13 g, 84% yield); mp = 134-136 °C.

<sup>1</sup>**H NMR** (300 MHz, CDCl<sub>3</sub>) δ 7.56 – 7.38 (m, 3H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.32 – 7.21 (m, 11H), 6.88 (d, *J* = 8.0 Hz, 2H), 2.22 (s, 12H). <sup>13</sup>**C NMR** (75 MHz, CDCl<sub>3</sub>) δ 153.0, 145.8, 145.3, 140.3, 140.1, 136.5, 136.4, 136.3, 136.2, 133.1, 132.9, 132.4, 132.3, 129.9, 129.8, 128.9, 128.6, 127.9, 127.8, 127.4, 126.3, 113.3, 43.4 (Observed complexity due to C—P splitting). <sup>31</sup>**P NMR** (121 MHz, CDCl<sub>3</sub>) δ -13.8. **IR** (neat, cm<sup>-1</sup>): 2934, 2824, 2778, 1573, 1462, 1432, 1293, 1163, 1088, 1043, 1005, 935, 808, 768, 742, 694, 570. **Anal.** Calculated for C<sub>16</sub>H<sub>19</sub>BrN<sub>2</sub>: C, 79.22; H, 6.89. Found C, 79.34; H, 6.94.

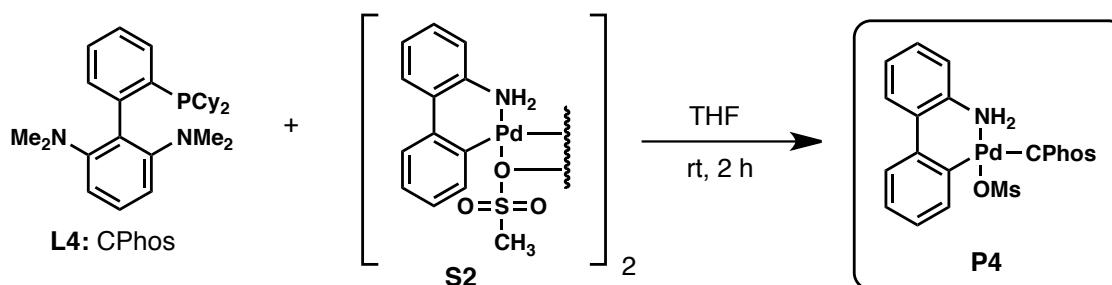
### B) Synthesis of Pd-Precatalysts P3-P5:



**PhDavePhos (L3) Palladacyclic Precatalyst, P3:** An oven-dried flask equipped with a magnetic stir bar was charged with μ-mesylate dimer **S2** (370 mg, 0.5 mmol, 0.50 equiv) and PhDavePhos (389 mg, 1.0 mmol, 1.0 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous THF (4 mL) was then added via syringe. After the mixture was allowed to stir for 30 min at room temperature, the stir bar was removed and ~90% of solvent was removed under vacuum at room temperature. The residue was then triturated with pentane, and the resulting yellow

crystals were isolated via filtration and further dried under vacuum. Precatalyst **P3** was obtained as an inseparable mixture of two phosphorous-containing compounds (0.71g total, 94% yield).

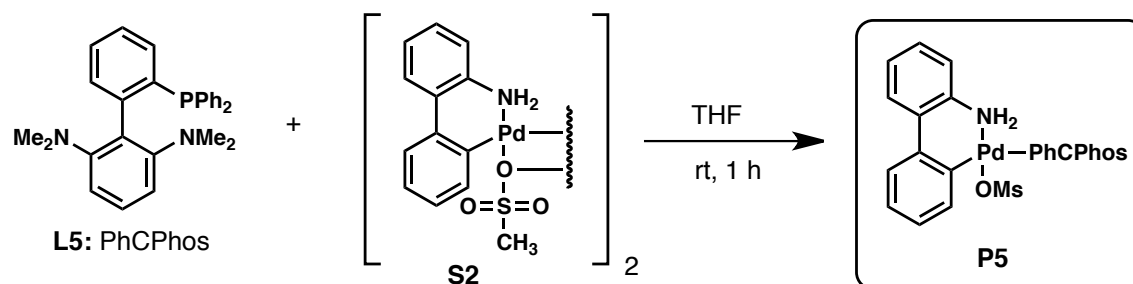
**<sup>1</sup>H NMR** (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 8.00 (ddt, *J* = 11.7, 6.1, 1.7 Hz, 2H), 7.86 – 7.49 (m, 4H), 7.50 – 6.76 (m, 18H), 6.63 (td, *J* = 7.4, 6.7, 1.3 Hz, 1H), 6.18 – 5.93 (m, 1H), 3.49 (d, *J* = 11.1 Hz, 1H), 3.07 (s, 1H), 2.57 (s, 6H), 2.39 (s, 3H). **<sup>13</sup>C NMR** (75 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 154.2, 148.3, 147.9, 147.6, 139.6, 137.5, 137.3, 137.3, 136.6, 136.5, 135.1, 134.9, 134.3, 133.5, 133.4, 133.1, 132.4, 132.2, 131.6, 130.9, 130.8, 130.6, 130.0, 129.9, 129.09, 128.4, 128.3, 128.1, 128.0, 127.9, 127.5, 127.3, 127.2, 126.4, 125.6, 121.3, 120.7, 117.3, 43.7, 39.5, 34.3. (Observed complexity due to C—P splitting). **<sup>31</sup>P NMR** (121 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 40.5, 35.5. **IR** (neat, cm<sup>-1</sup>): 3050, 1575, 1493, 1434, 1421, 1191, 1157, 1096, 1035, 1020, 1001, 946, 737, 693, 616, 569, 557.



**CPhos (L4) Palladacyclic Precatalyst, P4:**<sup>3</sup> An oven-dried flask equipped with a magnetic stir bar was charged with  $\mu$ -mesylate dimer **S2** (1.85 g, 5.0 mmol, 0.50 equiv) and CPhos (2.19 mg, 1.0 mmol, 1.0 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous THF (20 mL) was then added via syringe. After the mixture was allowed to stir for 2 h min at room temperature, the stir bar was removed from the vessel and the reaction mixture was transferred to a scintillation vial. The majority of solvent was removed under vacuum at room temperature until ~10% of the initial volume remained. The residue was then triturated with pentane. The resulting yellow solid was isolated via filtration and further dried under vacuum to afford 4.03 g of **P4** (98% yield). This compound is light sensitive, and so it was stored in a scintillation vial wrapped with aluminum foil.

**<sup>1</sup>H NMR** (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.81 (t, *J* = 8.1 Hz, 1H), 7.67 (t, *J* = 7.7, 1H), 7.56 – 7.29 (m, 4H), 7.29 – 6.94 (m, 9H), 5.44 (d, *J* = 9.7 Hz, 1H), 2.78 – 2.58 (m, 1H), 2.57-2.19 (m, 2H), 2.51 (s, 6H), 2.39 (s, 3H), 2.30 (s, 6H), 2.10 – 1.59 (m, 6H), 1.58 – 1.16 (m, 9H), 1.07-0.79 (m, 4H), 0.45 – 0.11 (m, 1H). **<sup>13</sup>C NMR** (126 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 159.4, 154.9, 146.2, 146.1, 142.7, 140.4, 139.3, 137.4, 137.3, 135.0, 134.6, 134.2, 133.8, 132.1, 128.3, 127.7, 127.0, 126.9, 125.6, 120.9, 113.2, 113.0, 111.7, 68.1, 44.9, 43.8, 39.6, 37.38, 37.2, 37.0, 36.9, 31.1, 30.3, 30.2, 29.9, 29.6, 28.4, 27.6, 27.2, 26.3, 26.3, 26.0, 26.0 (Observed complexity due to C—P splitting). **<sup>31</sup>P NMR** (121 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 40.8. **IR** (neat, cm<sup>-1</sup>): 2928, 2852, 1569, 1491, 1421, 1211, 1191, 1164, 1131, 1034, 1018, 1002, 780, 758, 737, 555.

<sup>3</sup> The CPhos precatalyst (**P4**) is currently available from Aldrich.

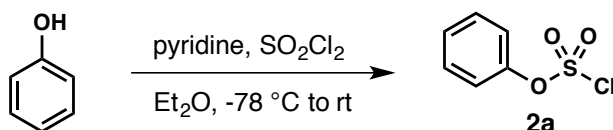


**PhCPhos (L5) Palladacyclic Precatalyst, P5:** An oven-dried flask equipped with a magnetic stir bar was charged with  $\mu$ -mesylate dimer **S2** (591 mg, 0.80 mmol, 0.50 equiv) and PhCPhos (678 mg, 1.6 mmol, 1.0 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous THF (6.5 mL) was then added via syringe. After the mixture was allowed to stir for 1 h at room temperature, the stir bar was removed from the vessel and the reaction mixture was transferred to a scintillation vial. The majority of solvent was removed under vacuum at room temperature until ~10% of the initial volume remained. The residue was then triturated with pentane. The resulting yellow solid was isolated via filtration and further dried under vacuum to afford 1.27 g of **P5** (quantitative yield).

**$^1\text{H}$  NMR** (300 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  7.86 (t,  $J$  = 8.1 Hz, 1H), 7.65 – 7.48 (m, 4H), 7.47 – 7.03 (m, 16H), 7.00 (t,  $J$  = 7.3 Hz, 1H), 6.89 (dd,  $J$  = 8.1, 0.9 Hz, 1H), 6.67 (dddd,  $J$  = 8.0, 7.2, 1.7, 0.9 Hz, 1H), 6.37 (ddd,  $J$  = 7.6, 6.3, 1.1 Hz, 1H), 6.03 (dd,  $J$  = 10.7, 4.9 Hz, 1H), 2.73–2.61 (m, 1H), 2.69 (s, 6H), 2.31 (s, 3H), 1.88 (s, 6H).  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  156.9, 155.2, 146.0, 145.7, 145.1, 140.1, 138.8, 137.9, 137.8, 136.7, 136.0, 135.8, 135.2, 134.7, 134.3, 134.2, 134.0, 132.8, 132.4, 132.2, 131.5, 131.3, 130.2, 129.5, 128.9, 128.8, 128.7, 128.5, 128.4, 128.2, 128.1, 127.9, 127.6, 127.0, 126.7, 125.7, 121.2, 113.8, 113.2, 112.1, 44.7, 43.2, 39.5 (Observed complexity due to C—P splitting).  **$^{31}\text{P}$  NMR** (121 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  40.2. **IR** (neat,  $\text{cm}^{-1}$ ): 3286, 2942, 1571, 1492, 1434, 1424, 1226, 1175, 1160, 1091, 1035, 1019, 1001, 793, 771, 748, 697, 614, 572.

### C) Preparation of Aryl Chlorosulfates (2a–2c):

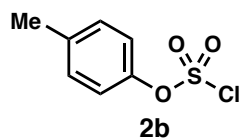
#### Representative Procedure:



**Phenyl chlorosulfate (2a):** An oven-dried 500 mL round-bottom flask equipped with a large stir bar was charged with phenol (9.5 g, 100 mmol, 1.0 equiv). The vessel was evacuated and backfilled with nitrogen (this process was repeated a total of 3 times). Anhydrous  $\text{Et}_2\text{O}$  (125 mL) and pyridine (8.09 mL, 100 mmol, 1.0 equiv) were then added via syringe and the solution was cooled to  $-78\text{ }^\circ\text{C}$ . A separate oven-dried 200 mL round-bottom flask was evacuated and backfilled with nitrogen (this process was repeated a total of 3 times). Anhydrous  $\text{Et}_2\text{O}$  (125 mL) was added to the 200 mL flask via syringe, and the flask was placed in a separate dry ice/acetone bath and allowed to cool to  $-78\text{ }^\circ\text{C}$ . Neat sulfonyl chloride (8.36 mL, 100 mmol, 1.0 equiv) was then added via syringe to the 200 mL flask at  $-78\text{ }^\circ\text{C}$  (the addition of neat  $\text{SO}_2\text{Cl}_2$  to anhydrous  $\text{Et}_2\text{O}$  is exothermic and will cause the  $\text{Et}_2\text{O}$  to evaporate if not performed at lower temperatures). The cooled solution of  $\text{SO}_2\text{Cl}_2$  in  $\text{Et}_2\text{O}$  was transferred slowly (over 20 min) via canula to the vigorously stirred solution of phenol and pyridine at  $-78\text{ }^\circ\text{C}$ . (**Note:** Stirring becomes difficult as the pyridinium salt is formed, and so periodic swirling of the reaction flask by hand may be required. We

observed no problems with stirring when an IKA RCT Basic stir plate was used, however). After stirring for 2 h at -78 °C, no additional dry ice was added to the cooling bath and the reaction mixture was allowed to slowly warm to room temperature overnight. The crude reaction mixture was filtered through a pad of celite, and the reaction flask was washed with additional Et<sub>2</sub>O (100-200 mL). The filtrate was then concentrated and the resulting residue was purified immediately via SiO<sub>2</sub> flash chromatography (0-3% EtOAc in hexanes) to afford **2a** as a colorless oil (16.19 g, 84 % yield).

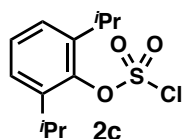
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.53-7.37 (m, 5H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 150.0, 130.2, 128.8, 121.6. **IR** (neat, cm<sup>-1</sup>): 1586, 1485, 1410, 1197, 1172, 1131, 1023, 913, 875, 774, 657, 685, 611, 584. **EI-MS** (*m/z*): 192 [M]<sup>+</sup>.



**4-Methylphenyl chlorosulfate (2b):** Following the representative procedure for the preparation of **2a**, the title compound was prepared using *p*-cresol (5.34 g, 50 mmol, 1.0 equiv), pyridine (4.1 mL, 50 mmol, 1.0 equiv), and sulfonyl chloride (4.18 mL, 50 mmol, 1.0 equiv). The crude product was purified by flash column chromatography (0-1% EtOAc in hexanes) to afford **2b** as a clear, colorless oil (9.5

g, 92% yield).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 7.28 (s, 4H), 2.40 (s, 3H). **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 148.0, 139.0, 130.7, 121.4, 21.0. **IR** (neat, cm<sup>-1</sup>): 1500, 1411, 1199, 1175, 1132, 1018, 880, 823, 802, 720, 692, 639, 591, 576. **EI-MS** (*m/z*): 206 [M]<sup>+</sup>.



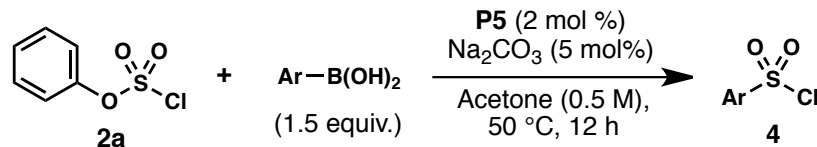
**2,6-Diisopropylphenyl chlorosulfate (2c):** Following the representative procedure for the preparation of **2a**, the title compound was prepared using 2,6-diisopropylphenol (9.55 mL, 50 mmol, 1.0 equiv), pyridine (4.1 mL, 50 mmol, 1.0 equiv), and sulfonyl chloride (4.18 mL, 50 mmol, 1.0 equiv). The crude product was purified by flash column chromatography (0-1% EtOAc in hexanes) to afford **2c** as a clear, colorless oil

(10.1 g, 73% yield).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.33 (dd, *J* = 8.2, 7.1 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 2H), 3.43 (m, 2H), 1.27 (d, *J* = 6.8 Hz, 12H). **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 147.0, 141.8, 128.9, 125.2, 27.76, 23.6. **IR** (neat, cm<sup>-1</sup>): 1406, 1387, 1192, 1129, 1071, 1045, 889, 864, 799, 767, 744, 618, 571. **EI-MS** (*m/z*): 276 [M]<sup>+</sup>.

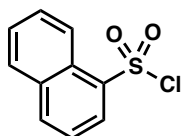
## D) Preparation of Arylsulfonyl Chlorides (4c-j)

### Generation Procedure A:



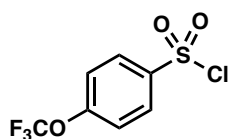
An oven-dried test tube equipped with a magnetic stir bar was charged with **P5** (0.02 mmol, 2 mol%), Na<sub>2</sub>CO<sub>3</sub> (5.3 mg, 0.05 mmol, 5 mol%), and the arylboronic acid (1.5 mmol, 1.5 equiv) and the tube was sealed with a Teflon screw-cap septum. The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous acetone (2.0 mL) was then added via syringe. After the mixture was allowed to stir for ~3 min at room temperature, neat phenyl chlorosulfate (133 μL, 1.0 mmol, 1.0 equiv) was added. The vessel was then placed in a preheated oil bath and the reaction mixture was allowed to stir at the desired temperature for 12 h. After the reaction mixture was allowed to cool to room temperature, it was diluted with EtOAc and filtered through a pad of silica gel topped with a layer of

celite, which was washed with additional EtOAc. The filtrate was concentrated and the resulting residue was purified by flash chromatography (using a Biotage Isolera Four system with a SNAP 25 g cartridge) to afford the desired sulfonyl chloride.



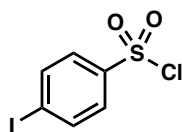
**Naphthalene-1-sulfonyl chloride (4c):** Following *General Procedure A*, the title compound was prepared using 1-naphthaleneboronic acid (258 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 60 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 0-5% EtOAc in hexanes) to afford **4c** as a white solid (200 mg, 88% yield); mp = 60-62 °C (lit.<sup>4</sup> 64-67 °C).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 8.79 (d, *J* = 8.6 Hz, 1H), 8.37 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 8.3, 1H), 7.81 (ddd, *J* = 8.6, 6.9, 1.4 Hz, 1H), 7.70 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.60 (dd, *J* = 7.9 Hz, *J* = 7.9 Hz, 1H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>) δ 139.3, 137.0, 134.3, 129.4, 129.3, 129.2, 127.6, 127.2, 123.9, 123.8. **IR** (neat, cm<sup>-1</sup>): 1592, 1504, 1365, 1346, 1169, 1136, 966, 830, 800, 760, 736, 673, 619, 572, 559. **HRMS-ESI** (*m/z*) [*M* + NH<sub>4</sub>]<sup>+</sup> Calcd. for C<sub>10</sub>H<sub>7</sub>ClO<sub>2</sub>S, 244.0194; found, 244.0196.



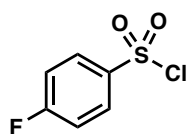
**4-(Trifluoromethoxy)benzenesulfonyl chloride (4d):** Following *General Procedure A*, the title compound was prepared using 4-trifluoromethoxyphenylboronic acid (309 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 60 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 0-3% EtOAc in hexanes) to afford **4d** as a colorless oil (173 mg, 66% yield).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 8.18 – 8.05 (m, 2H), 7.44 (d, *J* = 7.8 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>) δ 154.1 (q, *J* = 1.9), 142.2, 129.7, 120.4 (q, *J* = 260.8), 121.3. **<sup>19</sup>F NMR** (282 MHz, CDCl<sub>3</sub>) δ -57.8. **IR** (neat, cm<sup>-1</sup>): 1589, 1493, 1381, 1254, 1207, 1156, 1082, 1015, 840, 808, 688, 667, 583, 559. **HRMS-ESI** (*m/z*) [*M* + NH<sub>4</sub>]<sup>+</sup> Calcd. for C<sub>7</sub>H<sub>4</sub>ClF<sub>3</sub>O<sub>3</sub>S, 277.9860; found, 277.9868.



**4-Iodobenzenesulfonyl chloride (4e):** Following *General Procedure A*, the title compound was prepared using 4-iodophenylboronic acid (372 mg, 1.5 mmol). (**Note:** Stirring was difficult during the first 1-2 h of this reaction, and so an IKA RCT Basic stir plate was used to facilitate stirring). The reaction was judged as complete by TLC and GC after 12 h at 55 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, (0-7% EtOAc in hexanes) to afford **4e** as a white solid (183 mg, 64%); mp = 83-86 °C (lit.<sup>4</sup> 80-82 °C).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 8.00 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 8.8 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>) δ 144.0, 139.3, 128.3, 104.0. **IR** (neat, cm<sup>-1</sup>): 1560, 1369, 1176, 1157, 1076, 1051, 1005, 834, 813, 729, 694, 581, 551. **HRMS-ESI** (*m/z*) [*M* + NH<sub>4</sub>]<sup>+</sup> Calcd. for C<sub>6</sub>H<sub>4</sub>ClIO<sub>2</sub>S, 319.9004; found, 319.9020.

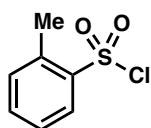


**4-Fluorobenzenesulfonyl chloride (4f):** Following *General Procedure A*, the title compound was prepared using 4-fluorophenylboronic acid (210 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 70 °C. The crude product

<sup>4</sup> Melting point listed on Sigma-Aldrich website.

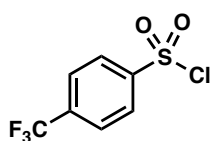
was purified by flash column chromatography (Biotage, 25g SNAP column, 0-4% EtOAc in hexanes) to afford **4f** as a yellow solid (165 mg, 85% yield); mp = 33-36 °C (lit.<sup>4</sup> 29-31 °C; lit.<sup>5</sup> 34 °C).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.13 – 8.02 (m, 2H), 7.38 – 7.21 (m, 2H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 166.6 (d, *J* = 259.8), 140.5 (d, *J* = 3.2 Hz), 130.4 (d, *J* = 10.1 Hz), 117.4 (d, *J* = 23.2 Hz). <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>) δ -99.6. IR (neat, cm<sup>-1</sup>): 1587, 1491, 1409, 1377, 1294, 1242, 1178, 1156, 1081, 838, 816, 706, 658, 561. HRMS-ESI (*m/z*) [*M* + NH<sub>4</sub>]<sup>+</sup> Calcd. for C<sub>6</sub>H<sub>4</sub>ClFO<sub>2</sub>S, 211.9943; found, 211.9946.



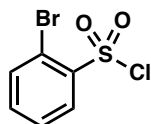
**2-Methylbenzenesulfonyl chloride (4g):** Following *General Procedure A*, the title compound was prepared using 2-methylphenylboronic acid (204 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 50 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 0-6% EtOAc in hexanes) to afford **4g** as a colorless oil (143 mg, 75% yield). Note: The chemical shifts in the <sup>1</sup>H NMR spectrum of **4g** were consistent with those in the <sup>1</sup>H NMR spectrum of an authentic sample obtained from Sigma-Aldrich.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.07 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.76 – 7.52 (m, 1H), 7.48 – 7.31 (m, 2H), 2.79 (s, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 143.2, 138.3, 135.5, 133.6, 129.0, 127.0, 20.5. IR (neat, cm<sup>-1</sup>): 1471, 1365, 1280, 1173, 1131, 1057, 1036, 806, 757, 700, 686, 577, 558. HRMS-ESI (*m/z*) [*M* + NH<sub>4</sub>]<sup>+</sup> Calcd. for C<sub>7</sub>H<sub>7</sub>ClO<sub>2</sub>S, 208.0194; found, 208.0198.



**4-Trifluoromethylbenzenesulfonyl chloride (4h):** Following *General Procedure A*, the title compound was prepared using 4-trifluorophenylboronic acid (285 mg, 1.5 mmol) and Na<sub>2</sub>CO<sub>3</sub> (10.6 mg, 0.1 mmol, 10 mol%). The reaction was judged as complete by TLC and GC after 12 h at 70 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 0-4% EtOAc in hexanes) to afford **4h** as a off-white solid (131 mg, 54% yield); mp = 30-32 °C (lit.<sup>6</sup> oil). Note: Compound **4h** undergoes significant decomposition upon purification with SiO<sub>2</sub> gel. The chemical shifts in the <sup>1</sup>H NMR spectrum of **4h** were consistent with those obtained from an authentic sample from Sigma-Aldrich.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.20 (d, *J* = 8.2 Hz, 2H), 7.92 (d, *J* = 8.3 Hz, 2H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 147.1 (app d, *J* = 1.4 Hz), 136.7 (q, *J* = 33.6 Hz), 127.6, 127.0 (q, *J* = 3.7 Hz), 122.7 (q, *J* = 273.4 Hz). <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>) δ -63.5. IR (neat, cm<sup>-1</sup>): 1407, 1382, 1319, 1174, 1135, 1109, 1061, 1016, 842, 711, 600, 578, 557. EI-MS (*m/z*): 244 [*M*]<sup>+</sup>.



**2-Bromobenzenesulfonyl chloride (4i):** Following *General Procedure A*, the title compound was prepared using 2-bromophenylboronic acid (301 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 55 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 3-10% EtOAc in hexanes) to afford **4i** as a yellow solid (202 mg, 79% yield); mp = 50-52 °C (lit.<sup>4</sup> 49-52 °C; lit.<sup>7</sup> 45-48 °C).

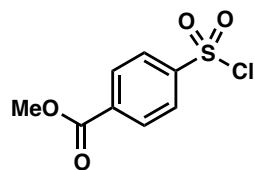
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.23 – 8.12 (m, 1H), 7.91 – 7.79 (m, 1H), 7.64 – 7.49 (m, 2H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 143.2, 136.7, 136.2, 131.0, 128.3, 120.9. IR (neat, cm<sup>-1</sup>): 1567, 1445, 1429, 1369, 1252, 1179, 1098, 1021, 759, 735, 694, 646, 573, 551. HRMS-ESI (*m/z*) [*M* + H]<sup>+</sup> Calcd. for C<sub>6</sub>H<sub>4</sub>BrClO<sub>2</sub>S, 254.8877; found, 254.8890.

<sup>5</sup> Bahrami, K.; Khodaei, M.M.; Khaledian, D. *Tetrahedron Lett.* **2012**, 53, 354.

<sup>6</sup> Pu, Y.; Christesen, A.; Ku, Y. *Tetrahedron Lett.* **2010**, 51, 418.

<sup>7</sup> Hogan, P.J.; Cox, B.G. *Org. Proc. Res. Dev.* **2009**, 13, 875.



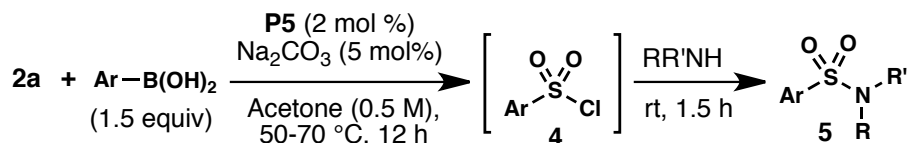


**4-(Methoxycarbonyl)benzenesulfonyl chloride (4j):** Following *General Procedure A*, the title compound was prepared using 4-methoxycarbonylphenylboronic acid (270 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 60 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 2-7% EtOAc in hexanes) to afford **4j** as a slightly pink solid (152 mg, 65% yield); mp =

73-76 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 8.28 (d, *J* = 8.9 Hz, 2H), 8.12 (d, *J* = 8.9 Hz, 2H), 3.99 (s, 3H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>) δ 165.1, 147.6, 136.3, 131.1, 127.3, 53.2. **IR** (neat, cm<sup>-1</sup>): 1725, 1435, 1400, 1377, 1280, 1188, 1168, 1106, 1011, 966, 866, 832, 758, 733, 684, 582, 560. **HRMS-ESI** (*m/z*) [*M* + NH<sub>4</sub>]<sup>+</sup> Calcd. for C<sub>8</sub>H<sub>7</sub>ClO<sub>4</sub>S, 252.0092; found, 252.0101.

## E) Preparation of Aryl Sulfonamides (5a-5o)



### Generation Procedure B: Preparation of Sulfonamides Derived from Secondary Amines.

Following *General Procedure A*, a mixture of **P5** (15.9 mg, 0.02 mmol, 2 mol%), Na<sub>2</sub>CO<sub>3</sub> (5.3 mg, 0.05 mmol, 5 mol%), arylboronic acid (1.5 mmol, 1.5 equiv), and phenyl chlorosulfate (133 μL, 1.0 mmol, 1.0 equiv) in anhydrous acetone (2.0 mL) was stirred at the desired temperature for 12 h. After the reaction mixture was allowed to cool to room temperature, it was placed under a positive atmosphere of argon and anhydrous THF (1.0 mL) was added via syringe (additional THF was not added to reactions in which a commercially available 2.0 M solution of Me<sub>2</sub>NH in THF was used). The reaction mixture was cooled to 0 °C and the desired secondary amine (2.2 mmol, 2.2 equiv) was then added to the vigorously stirred solution of crude sulfonyl chloride. After stirring for 5 min at 0 °C, the reaction vessel was removed from the ice bath, allowed to warm to room temperature, and stirred for 1.5 h. The reaction mixture was then diluted with EtOAc and filtered through a pad of silica gel topped with a layer of celite, which was washed with additional EtOAc. The filtrate was concentrated and the resulting residue was purified by flash chromatography (using a Biotage Isolera Four system with a SNAP 25 g cartridge) to afford the desired sulfonamide.

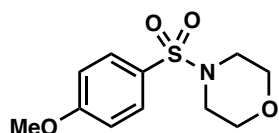
### Generation Procedure C: Preparation of Sulfonamides Derived from Primary Amines.

Following *General Procedure A*, a mixture of **P5** (15.9 mg, 0.02 mmol, 2 mol%), Na<sub>2</sub>CO<sub>3</sub> (5.3 mg, 0.05 mmol, 5 mol%), arylboronic acid (1.5 mmol, 1.5 equiv), and phenyl chlorosulfate (133 μL, 1.0 mmol, 1.0 equiv) in anhydrous acetone (2.0 mL) was stirred at the desired temperature for 12 h. After the mixture was allowed to cool to room temperature, the reaction mixture was placed under a positive atmosphere of argon and anhydrous THF (1.0 mL) was added via syringe. The reaction was cooled to 0 °C and the desired primary amine (3.0 mmol, 3.0 equiv or 2.2 mmol, 2.0 equiv) was then added to the vigorously stirred solution of crude sulfonyl chloride. After stirring for 5 min at 0 °C, the reaction vessel was removed from the ice bath, allowed to warm to room temperature, and stirred for 1.5 h at this temperature.

The reaction mixture was then diluted with EtOAc and filtered through a pad of silica gel topped with a layer of celite, which was washed with additional EtOAc. The filtrate was concentrated and the resulting residue was purified by flash chromatography (using a Biotage Isolera Four system with a SNAP 25 g cartridge) to afford the desired sulfonamide.

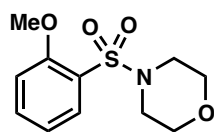
#### Generation Procedure D: Preparation of Sulfonamides Derived from Anilines.

Following *General Procedure A*, a mixture of **P5** (15.9 mg, 0.02 mmol, 2 mol%), Na<sub>2</sub>CO<sub>3</sub> (5.3 mg, 0.05 mmol, 5 mol%), arylboronic acid (1.5 mmol, 1.5 equiv), and phenyl chlorosulfate (133  $\mu$ L, 1.0 mmol, 1.0 equiv) in anhydrous acetone (2.0 mL) was stirred at the desired temperature for 12 h. The reaction mixture was allowed to cool to room temperature, placed under a positive atmosphere of argon, and then cooled to 0 °C. The desired aniline (1.2 mmol, 1.2 equiv.) and pyridine (0.245 mL, 3.0 mmol, 3.0 equiv) were then added successively to the vigorously stirred solution of the crude sulfonyl chloride at 0 °C. After stirring for 30 min at 0 °C, the reaction vessel was removed from the ice bath, allowed to warm to room temperature, and stirred for 5 h at this temperature. The reaction mixture was then diluted with EtOAc and filtered through a pad of silica gel topped with a layer of celite, which was washed with additional EtOAc. The filtrate was concentrated and the resulting residue was purified by flash chromatography (using a Biotage Isolera Four system with a SNAP 25 g cartridge) to afford the desired sulfonamide.



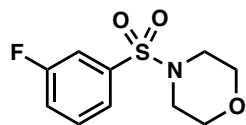
**4-Methoxybenzenesulfonylmorpholide (5a):** Following *General Procedure B*, the title compound was prepared using 4-methoxyphenylboronic acid (228 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 50 °C for 12 h. Morpholine (192  $\mu$ L, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-50% EtOAc in hexanes) to afford **5a** as a white solid (0.246 g, 96% yield); mp = 110-111 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.72-7.61 (m, 2H), 7.04-6.99 (m, 2H), 3.88 (s, 3H), 3.76-3.72 (m, 4H), 2.99-2.96 (m, 4H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  163.0, 129.8, 126.3, 114.1, 65.8, 55.5, 45.8. **IR** (neat, cm<sup>-1</sup>): 3103, 2928, 2847, 1598, 1578, 1499, 1439. **Anal.** Calcd. for C<sub>11</sub>H<sub>15</sub>NO<sub>4</sub>S: C, 51.35; H, 5.88; N, 5.44. Found C, 51.38; H, 5.96.



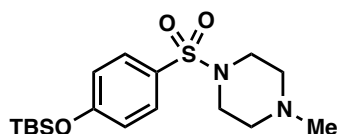
**2-Methoxybenzenesulfonylmorpholide (5b):** Following *General Procedure B*, the title compound was prepared using 2-methoxyphenylboronic acid (228 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 50 °C for 12 h. Morpholine (192  $\mu$ L, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-45% EtOAc in hexanes) to afford **5b** as a white solid (0.245 g, 79% yield); mp = 86.0-86.5 °C.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.83 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.49 (ddd, *J* = 8.3, 7.4, 1.8 Hz, 1H), 7.07 – 6.88 (m, 2H), 3.88 (s, 3H), 3.74 – 3.56 (m, 4H), 3.22 – 3.08 (m, 4H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  157.0, 134.8, 131.8, 125.7, 120.4, 112.4, 66.7, 56.0, 46.0. **IR** (neat, cm<sup>-1</sup>): 2968, 2921, 2863, 1592, 1579, 1480, 1465, 1447, 1433, 1342, 1331, 1325, 1279, 1262, 1155, 1141, 1114, 1078, 1062, 1044, 1016, 944, 924, 858, 768, 758, 735, 614, 588, 573, 567, 565. **Anal.** Calcd. for C<sub>11</sub>H<sub>15</sub>NO<sub>4</sub>S: C, 51.35; H, 5.88. Found C, 51.54; H, 5.80.



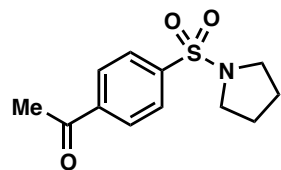
**3-Fluorobenzenesulfonylmorpholide (5c):** Following *General Procedure B*, the title compound was prepared using 3-fluorophenylboronic acid (210 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 70 °C for 12 h. Morpholine (192  $\mu$ L, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-30% EtOAc in hexanes) to afford the product as a white solid (0.161 g, 66% yield); mp = 112.2-113.2 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.59-7.51 (m, 2H), 7.49-7.44 (m, 1H), 7.39-7.30 (m, 1H), 3.77-3.73 (m, 4H), 3.04-3.00 (m, 4H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  162.4 (d,  $J$  = 252.0 Hz), 137.2 (d,  $J$  = 6.5 Hz), 130.9 (d,  $J$  = 7.8 Hz), 123.5 (d,  $J$  = 3.4 Hz), 120.2 (d,  $J$  = 21.2 Hz), 115.0 (d,  $J$  = 24.2 Hz), 65.9, 45.9. **<sup>19</sup>F NMR** (376.5 MHz, CDCl<sub>3</sub>)  $\delta$  -109.4 (s, 1F). **IR** (neat, cm<sup>-1</sup>): 2917, 2863, 1589, 1475, 1392, 1346, 1329, 1294, 1272, 1261, 1220, 1155, 1112, 1088. **Anal.** Calculated for C<sub>10</sub>H<sub>10</sub>FN<sub>2</sub>O<sub>3</sub>S: C, 48.97; H, 4.93. Found C, 48.98; H, 4.82.



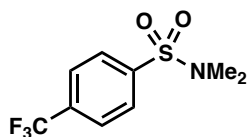
**1-Methylpiperazine-4-(4-(*tert*-butyldimethylsilyloxy)benzenesulfonamide (5d):** Following a modification of *General Procedure B*, the title compound was prepared using 4-(*tert*-butyldimethylsilyloxy)phenyl boronic acid (378 mg, 1.5 mmol) and **P5**. The cross-coupling reaction was carried out at 50 °C for 12 h. Following complete chlorosulfonylation, the reaction was cooled to 0 °C, and DIPEA (0.348 mL, 2 mmol, 2.0 equiv) and 1-Methylpiperazine (0.135 mL, 1.2 mmol, 1.0 equiv) were added successively. After 5 min, the reaction vessel was removed from the ice bath and stirred for 1.5 h at rt. The mixture was then diluted with EtOAc and filtered through a plug of SiO<sub>2</sub>, using 30% MeOH in EtOAc as the eluent. The product was purified by flash column chromatography (Biotage, 25g SNAP column, 50-100% EtOAc in hexanes, followed by 15% MeOH in EtOAc) to afford **5d** as a yellow solid (0.301 g, 81% yield); mp = 70-73 °C. **Note:** Compound **5d** was characterized immediately following purification because it undergoes rapid desilylation to form the corresponding free phenol.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.63 (d,  $J$  = 9.0 Hz, 2H), 6.92 (d,  $J$  = 8.9 Hz, 2H), 3.02 (br s, 4H), 2.55 – 2.40 (m, 4H), 2.27 (s, 3H), 0.98 (s, 9H), 0.23 (s, 6H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  159.7, 129.8, 127.4, 120.1, 53.9, 45.8, 45.6, 25.4, 18.1, -4.50. **IR** (neat, cm<sup>-1</sup>): 2934, 2856, 2794, 2765, 1590, 1490, 1472, 1405, 1384, 1371, 1342, 1329, 1285, 1252, 1167, 1152, 1144, 1098, 1065, 890, 854, 825, 783, 758, 666, 631, 610, 581, 575, 563, 557. **Anal.** Calcd. for C<sub>17</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub>SSi: C, 55.10; H, 8.16. Found C, 55.07; H, 8.09.



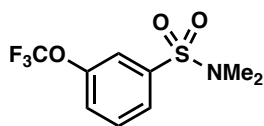
**Pyrrolidine-4-Acetylbenzenesulfonamide (5e):** Following *General Procedure B*, the title compound was prepared using 4-acetylphenylboronic acid (246 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 60 °C for 12 h. Pyrrolidine (181  $\mu$ L, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 10-50% EtOAc in hexanes) to afford **5e** as a white solid (0.187 g, 74% yield); mp = 143.5-144.5 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.09 (d,  $J$  = 8.8 Hz, 2H), 7.93 (d,  $J$  = 8.8 Hz, 2H), 3.53 – 3.03 (m, 4H), 2.66 (s, 3H), 1.84 – 1.72 (m, 4H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  196.8, 140.7, 139.8, 128.7, 127.5, 47.8, 26.7, 25.1. **IR** (neat, cm<sup>-1</sup>): 3096, 2968, 2873, 1692, 1595, 1396, 1292, 1006, 774, 1066, 958, 852, 774, 748, 725, 634. **Anal.** Calcd. for C<sub>12</sub>H<sub>15</sub>NO<sub>3</sub>S: C, 56.90; H, 5.97. Found C, 56.86; H, 5.81.



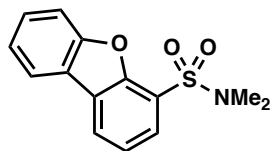
***N,N*-dimethyl-4-(trifluoromethyl)benzenesulfonamide (5f):** Following *General Procedure B*, the title compound was prepared using 4-trifluorophenylboronic acid (285 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 70 °C for 12 h. Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 3-15% EtOAc in hexanes) to afford **5f** as a yellow solid (0.153 g, 60% yield); mp = 80.5-81.5 °C.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.92 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.2 Hz, 2H), 2.75 (s, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 139.4, 134.3 (q, *J* = 33.0 Hz), 128.1, 126.2 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 272.9 Hz), 37.8. <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ -63.2. IR (neat, cm<sup>-1</sup>): 1458, 1407, 1337, 1325, 1314, 1296, 1148, 1110, 1092, 1015, 947, 840, 788, 742, 692, 596, 582, 574, 566. Anal. Calcd. for C<sub>9</sub>H<sub>10</sub>F<sub>3</sub>NO<sub>2</sub>S: C, 42.69; H, 3.98. Found C, 42.87; H, 3.94.



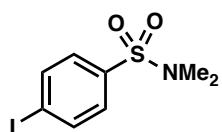
***N,N*-dimethyl-3-(trifluoromethoxy)benzenesulfonamide (5g):** Following *General Procedure B*, the title compound was prepared using 3-trifluoromethoxyphenylboronic acid (309 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 65 °C for 12 h. Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 2-15% EtOAc in hexanes) to afford **5g** as a white solid (0.219, 81% yield); mp = 46.0-48.0 °C.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.71 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.50 – 7.42 (m, 1H), 2.73 (s, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 149.2 (q, *J* = 2.0 Hz), 137.5, 130.7, 125.3, 125.0 (q, *J* = 1.0 Hz), 120.21 (q, *J* = 258.8 Hz), 120.16 (q, *J* = 1.1 Hz), 37.8. <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ -58.1 (s, 3F). IR (neat, cm<sup>-1</sup>): 1473, 1458, 1437, 1337, 1307, 1280, 1256, 1221, 1204, 1179, 1143, 1094, 1082, 1050, 1000, 950, 919, 682. Anal. Calcd. for C<sub>9</sub>H<sub>10</sub>F<sub>3</sub>NO<sub>3</sub>S: C, 40.15; H, 3.74. Found C, 40.26; H, 3.66.



***N,N*-dimethyl-4-dibenzofuransulfonamide (5h):** Following *General Procedure B*, the title compound was prepared using dibenzofuran-4-boronic acid (318 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 60 °C for 12 h and **P1** as the catalyst. (**Note:** Stirring was difficult during the first 1-2 h of the chlorosulfonylation reaction, and so an IKA RCT Basic stir plate was used to facilitate stirring). Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 3-18% EtOAc in hexanes) to afford **5h** as a white solid (0.178 g, 65% yield); mp = 146.5-147.5 °C.

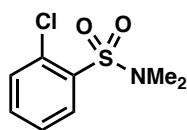
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.17 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.00 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H), 7.91 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.72 – 7.63 (m, 1H), 7.59 – 7.38 (m, 3H), 2.90 (s, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.3, 151.6, 128.3, 128.0, 126.5, 125.5, 123.7, 122.8, 122.7, 121.1, 120.9, 112.2, 37.8. IR (neat, cm<sup>-1</sup>): 1469, 1441, 1418, 1354, 1339, 1188, 1161, 1154, 1111, 1059, 960, 637, 582, 577. Anal. Calcd. for C<sub>14</sub>H<sub>13</sub>NO<sub>3</sub>S: C, 61.07; H, 4.76. Found C, 60.81; H, 4.79.



***N,N*-dimethyl-4-iodobenzenesulfonamide (5i):** Following *General Procedure B*, the title compound was prepared using 4-iodophenylboronic acid (372 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 55 °C for 12 h. (**Note:** Stirring was difficult during the first 1-2 h of the chlorosulfonylation reaction, and so an IKA RCT Basic stir plate was used to facilitate stirring).

Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 3-10% EtOAc in hexanes) to afford **5i** as a white solid (0.231 g, 74% yield); mp = 134-135 °C.

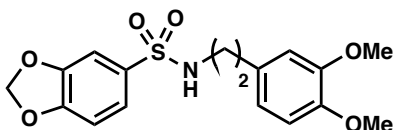
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 7.90 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 2H), 2.71 (s, 6H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 138.3, 135.3, 129.1, 100.2, 37.9. **IR** (neat, cm<sup>-1</sup>): 3079, 1567, 1466, 1450, 1387, 1341, 1328, 1271, 1257, 1180, 1163, 1088. **Anal.** Calcd. for C<sub>8</sub>H<sub>10</sub>INO<sub>2</sub>S: C, 30.88; H, 3.24. Found C, 31.15; H, 3.08. **HRMS-ESI** (*m/z*) [*M* + *H*]<sup>+</sup> Calcd. for C<sub>8</sub>H<sub>10</sub>IO<sub>2</sub>S, 311.9550; found, 311.9548.



***N,N*-dimethyl-2-chlorobenzenesulfonamide (5j):** Following *General Procedure B*, the title compound was prepared using 2-chlorophenylboronic acid (235 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 60 °C for 12 h.

Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (3-15% EtOAc in hexanes) to afford **5j** as a white solid (0.141 g, 64% yield); mp = 40.0-41.8 °C.

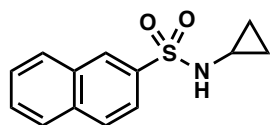
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.05 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.55 – 7.45 (m, 2H), 7.39 (ddd, *J* = 7.9, 7.1, 1.6 Hz, 1H), 2.88 (s, 6H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 135.9, 133.5, 132.1, 132.0, 126.9, 37.3. (**Note:** only 6 carbon signals for **5j** resolve in the <sup>13</sup>C spectrum). **IR** (neat, cm<sup>-1</sup>): 3090, 2872, 1569, 1450, 1346, 1256, 1160, 1106, 1041, 954, 754, 713, 690, 654, 578. **Anal.** Calcd. for C<sub>8</sub>H<sub>10</sub>ClNO<sub>2</sub>S: C, 43.74; H, 4.54. Found C, 43.99; H, 4.68.



***N*-[2-(3,4-dimethoxyphenyl)ethyl]-1,3-benzodioxole-5-sulfonamide (5k):** Following *General Procedure C*, the title compound was prepared using 3,4-methylenedioxyphenylboronic acid (249 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried

out at 50 °C for 12 h. 3,4-Dimethoxyphenethylamine (373 μL, 2.2 mmol) was used as the primary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 20% EtOAc in hexanes) to afford **5k** as a white solid (282.4 mg, 77% yield; 266.8 mg, 73% yield); mp = 118-120 °C.

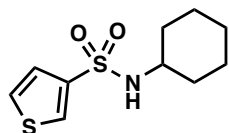
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.36 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.15 (d, *J* = 1.9 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.63 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.57 (d, *J* = 2.0 Hz, 1H), 6.07 (s, 2H), 4.55 – 4.25 (m, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.19 (app q, *J* = 6.6 Hz, 2H), 2.71 (t, *J* = 6.8 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 151.1, 148.9, 148.1, 147.7, 132.9, 130.1, 122.6, 120.6, 111.6, 111.1, 107.9, 107.1, 102.2, 55.8, 55.7, 44.3, 35.2. **IR** (neat, cm<sup>-1</sup>): 3231, 2931, 1594, 1512, 1501, 1483, 1471, 1356, 1328, 1255, 1231, 1174, 1147, 1137, 1111, 1069, 1022, 936, 909, 858, 846, 830, 764, 727, 709, 667, 634, 618, 602, 573, 561, 558, 551. **Anal.** Calcd. for C<sub>17</sub>H<sub>19</sub>NO<sub>6</sub>S: C, 55.88; H, 5.24. Found C, 55.59; H, 5.31.



***N*-cyclopropylnaphthalene-2-sulfonamide (5l):** Following *General Procedure C*, the title compound was prepared using 2-naphthaleneboronic acid (258 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 50 °C for 12 h. Cyclopropylamine (208 μL, 3.0 mmol) was used as the primary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-30% EtOAc in hexanes) to afford **5l** as a white solid (0.21 g, 85% yield); mp = 99.5-101.0 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 8.50 (s, 1H), 8.08 – 7.76 (m, 4H), 7.75 – 7.52 (m, 2H), 5.04 (br s, 1H), 2.31–2.23 (m, 1H), 0.66-0.53 (m, 4H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>) δ 136.4, 134.7, 132.0, 129.3, 129.1,

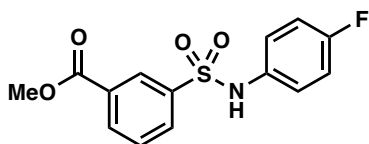
128.7, 128.7, 127.8, 127.4, 122.4, 24.2, 5.99. **IR** (neat,  $\text{cm}^{-1}$ ): 3279, 1591, 1502, 1455, 1406, 1366, 1306, 1226, 1160, 967, 884, 751, 694, 640, 567. **Anal.** Calcd. for  $\text{C}_{13}\text{H}_{13}\text{NO}_2\text{S}$ : C, 63.13; H, 5.30. Found C, 63.05; H, 5.33.



**N-cyclohexylthiophene-3-sulfonamide (5m):** Following of the *General Procedure C*, the title compound was prepared using 3-thiopheneboronic acid (192 mg, 1.5 mmol) and **P4** (16.1 mg, 0.02 mmol, 2 mol%). The chlorosulfonylation reaction was carried out at 55 °C for 12 h. Cyclohexylamine (343  $\mu\text{L}$ , 3.0 mmol) was used as the primary amine to form the desired sulfonamide. The crude product

was purified by flash column chromatography (Biotage, 25g SNAP column, 5-25% EtOAc in hexanes) to afford **5m** as a white solid (0.171 g, 70% yield); mp = 94.0-95.0 °C.

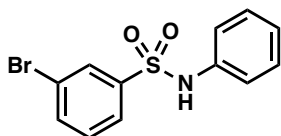
**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (dd,  $J$  = 3.1, 1.3 Hz, 1H), 7.41 (dd,  $J$  = 5.1, 3.1 Hz, 1H), 7.35 (dd,  $J$  = 5.1, 1.3 Hz, 1H), 4.49 (d,  $J$  = 7.8 Hz, 1H), 3.33 – 3.02 (m, 1H), 1.90 – 1.39 (m, 5H), 1.37 – 1.03 (m, 5H).  **$^{13}\text{C}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  141.5, 129.9, 127.9, 125.5, 52.8, 33.8, 25.1, 24.6. **IR** (neat,  $\text{cm}^{-1}$ ): 3264, 3106, 2932, 2854, 1448, 1312, 1297, 1209, 927, 998, 927, 891, 881, 815, 800, 729, 698, 641, 629, 597. **Anal.** Calcd. for  $\text{C}_{10}\text{H}_{15}\text{NO}_2\text{S}_2$ : C, 48.95; H, 6.16. Found C, 49.08; H, 6.20.



**Methyl 3-(N-(4-fluorophenyl)sulfamoyl)benzoate (5n):** Following *General Procedure D*, the title compound was prepared using 3-methoxycarbonylphenylboronic acid (270 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 60 °C for 12 h. 4-Fluoroaniline (114  $\mu\text{L}$ , 1.2 mmol) was used as the aniline to form the

desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-25% EtOAc in hexanes) to afford **5n** as an off-white solid (0.239 g, 77% yield); mp = 104.8-105.8 °C.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.53 – 8.38 (m, 1H), 8.20 (ddd,  $J$  = 7.8, 1.7, 1.2 Hz, 1H), 7.89 (ddd,  $J$  = 7.9, 1.9, 1.2 Hz, 1H), 7.58 – 7.46 (m, 1H), 7.31 (s, 1H), 7.11 – 7.02 (m, 2H), 6.97 – 6.87 (m, 2H), 3.91 (s, 3H).  **$^{13}\text{C}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.5, 160.7 (d,  $J$  = 246 Hz), 139.3, 133.8, 131.9 (d,  $J$  = 2.96), 131.3, 131.2, 129.3, 128.3, 124.7 (d,  $J$  = 9.0 Hz), 116.2 (d,  $J$  = 22.8 Hz), 52.7.  **$^{19}\text{F}$  NMR** (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -115.8. **IR** (neat,  $\text{cm}^{-1}$ ): 3239, 1728, 1505, 1437, 1336, 1309, 1292, 1259, 1232, 1204, 1191, 1170, 1156, 1124, 1098, 1085, 1076, 1014, 965, 856, 831, 814, 751, 678, 639, 589, 575. **Anal.** Calcd. for  $\text{C}_{14}\text{H}_{12}\text{FNO}_4\text{S}$ : C, 54.36; H, 3.91. Found C, 54.49; H, 3.91.

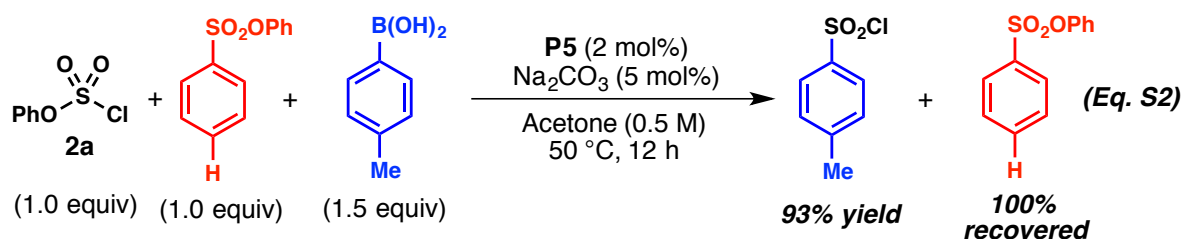
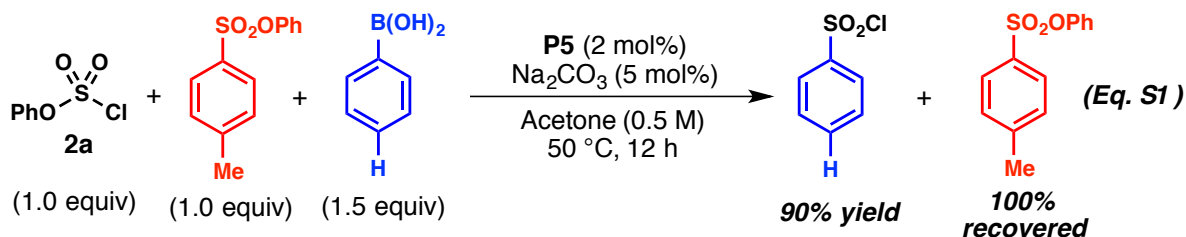


**3-Bromo-N-phenylbenzenesulfonamide (5o):** Following *General Procedure D*, the title compound was prepared using 3-bromophenylboronic acid (301 mg, 1.5 mmol) and **P5**. The cross-coupling reaction was carried out at 55 °C for 12 h. Aniline (109  $\mu\text{L}$ , 1.2 mmol) was used as the aniline to form the desired sulfonamide. The crude product was purified by flash column chromatography

(Biotage, 25g SNAP column, 5-25% EtOAc in hexanes) to afford **5o** as a yellow solid (0.253 g; 81% yield); mp = 104.5-105.5 °C.

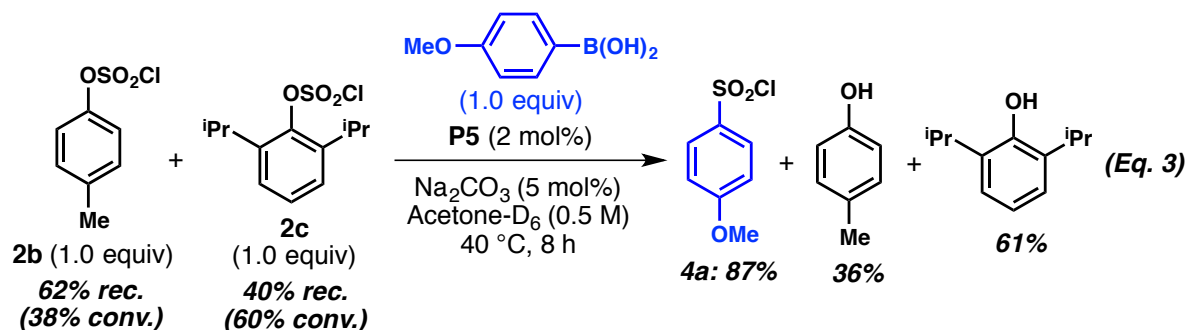
**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.92 (s, 1H), 7.66 (d,  $J$  = 8 Hz, 2H), 7.33-7.24 (m, 3H), 7.19-7.13 (m, 1H), 7.09-7.05 (m, 2H), 6.68 (br s, 1H).  **$^{13}\text{C}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  140.6, 136.0, 135.8, 130.5, 130.0, 129.4, 125.7, 125.7, 122.9, 121.8. **IR** (neat,  $\text{cm}^{-1}$ ): 3259, 1600, 1571, 1481, 1463, 1339, 1298, 1154, 1096, 1086, 920, 902, 785, 767, 752, 619, 580, 573, 558. **Anal.** Calcd. for  $\text{C}_{12}\text{H}_{10}\text{BrNO}_2\text{S}$ : C, 46.17; H, 3.23. Found C, 46.32; H, 3.22.

**F) Control Experiments: To confirm that sulfonate esters are not converted to sulfonyl chlorides:**



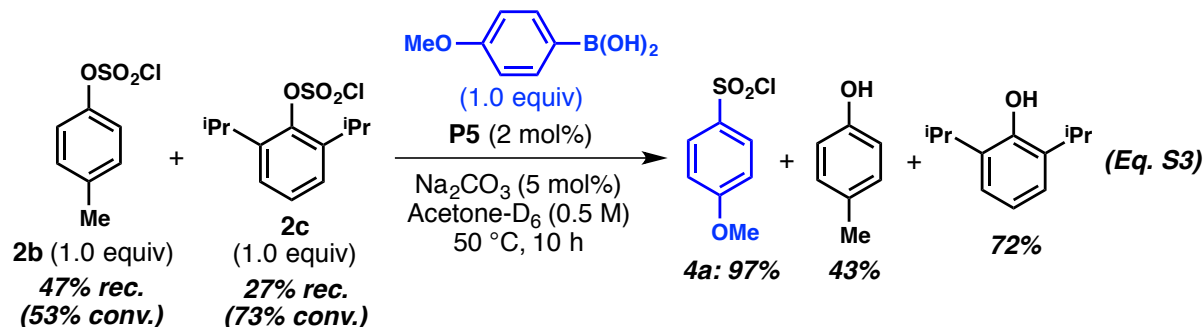
Two separate oven-dried test tubes, each equipped with a magnetic stir bar, were charged with **P5** (7.94 mg, 0.01 mmol, 2 mol%),  $\text{Na}_2\text{CO}_3$  (2.65 mg, 0.025 mmol, 5 mol%), either phenylboronic acid (for Eq. S1, 93 mg, 0.75 mmol, 1.5 equiv) or 4-methylphenylboronic acid (for Eq. S2, 104 mg, 0.75 mmol, 1.5 equiv), and either phenyl tosylate (for Eq. S1, 124 mg, 0.5 mmol, 1.0 equiv) or phenyl benzenesulfonate (for Eq. S2, 117 mg, 0.5 mmol, 1.0 equiv). The tubes were sealed with a Teflon screw-cap septum. The vessels were evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous acetone (1.0 mL) was then added via syringe. After the mixtures were allowed to stir for ~3 min at room temperature, neat phenyl chlorosulfate (66  $\mu\text{L}$ , 0.5 mmol, 1.0 equiv) was added. The vessels were then placed in a preheated oil bath at 50 °C and the reaction mixtures were allowed to stir for 12 h. After the reaction mixtures were allowed to cool to room temperature, an internal standard was added (tetradecane) and the mixtures were diluted with EtOAc and filtered through a short plug of silica gel. The crude reaction mixtures were analyzed by GC and the results are shown in Equations S1 and S2. In each case, 100% of the phenyl sulfonate ester was recovered while the sulfonyl chloride derived from the arylboronic acid was formed in near quantitative yield, thus demonstrating that the sulfonate esters are not converted to the corresponding sulfonyl chlorides under these conditions.

### G) Competition Experiments Between **2b** and **2c**:



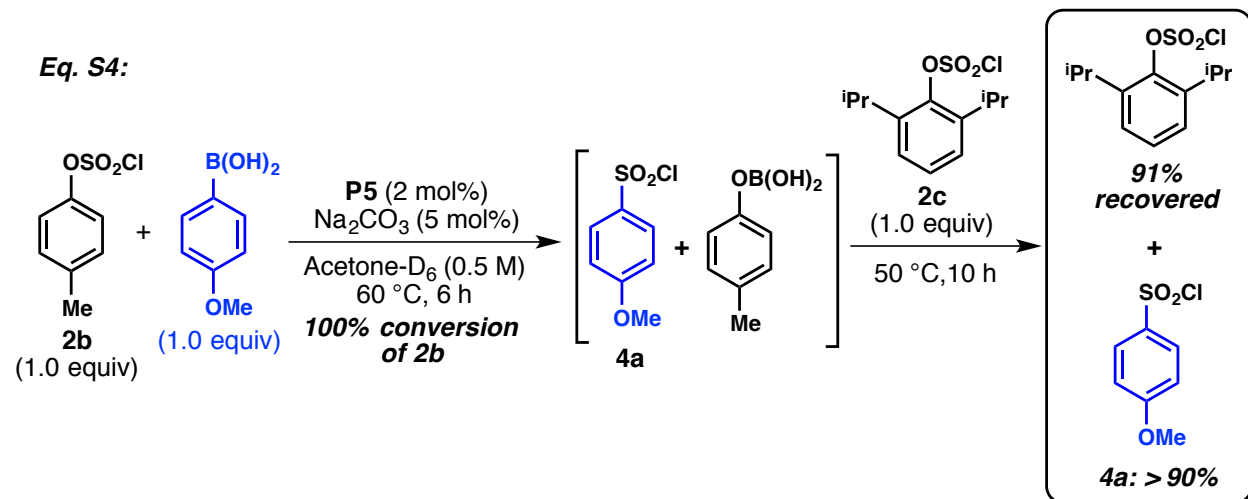
An oven-dried test tube equipped with a magnetic stir bar was charged with **P5** (0.01 mmol, 2 mol%),  $\text{Na}_2\text{CO}_3$  (2.65 mg, 0.025 mmol, 5 mol%), and the 4-methoxyphenylboronic acid (76 mg, 0.5 mmol, 1.0 equiv), and the tube was sealed with a Teflon screw-cap septum. The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and deuterated acetone- $\text{D}_6$  (1.0 mL) was then added via syringe. After the mixture was allowed to stir for ~3 min at room temperature, neat **2b** (75.4  $\mu\text{L}$ , 0.5 mmol, 1.0 equiv) and **2c** (116  $\mu\text{L}$ , 0.5 mmol, 1.0 equiv) were added sequentially. The vessel was then placed in a preheated oil bath at 40 °C and the reaction mixture was allowed to stir for 8 h. After the reaction mixture was allowed to cool to room temperature, an internal standard (1,3,5-trimethoxybenzene, 28.03 mg) was added. A small aliquot (~0.2 mL) of the crude reaction mixture was filtered through a short plug of  $\text{SiO}_2$  (~1.5 cm in a pipette with a cotton filter), which was further washed with  $\text{CD}_3\text{Cl}$  (~0.6 mL). The resulting yellow solution was then analyzed by  $^1\text{H}$  NMR (see spectrum on page 91). Because both **2b** and **2c** are converted to the same sulfonyl chloride product (**4a**, 87% NMR yield), the amounts of recovered **2b** (40%) and **2c** (62%) were quantified along with the corresponding phenol byproducts. The NMR data show that **2c** undergoes higher conversion to **4a**, which suggests that the more sterically hindered substrate (**2c**) is slightly more reactive than **2b**.

**Note:** The integrals of the benzylic protons of **2c** and 2,6-diisopropylphenol were used to calculate the NMR yields of these compounds, but these signals overlap to a small degree in the  $^1\text{H}$  NMR spectrum on page 91. The benzylic protons signals completely resolve from one another if the crude reaction mixture is first filtered through a short plug of  $\text{SiO}_2$ , concentrated and then dissolved in  $\text{CD}_3\text{Cl}$ . However, **2b** is volatile, and a significant amount of this compound is removed upon concentrating the sample; therefore, this workup procedure was not used to prepare the NMR sample used to analyze the substrate and product distributions of Eq. 3. To show an example of a spectrum in which the signals of **2c** and 2,6-diisopropylphenol are completely differentiated from one another, we included the  $^1\text{H}$  NMR spectrum of the crude reaction mixture of Eq. S3 below (see spectrum on page 92). In order to promote full conversion of the arylboronic acid to **4a**, the reaction depicted in Eq. S3 was conducted at 50 °C for 10 h, but under otherwise identical conditions to those depicted in Eq. 3.

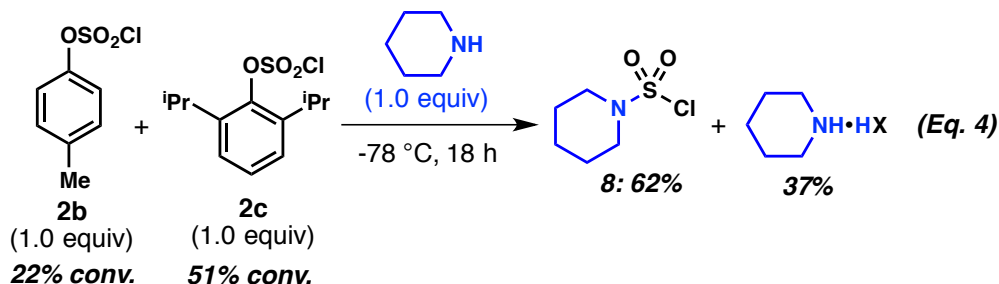




The control experiment below (Eq. S4) was performed to show that **2c** is not converted to **2b** during the competition experiments (Eq. 3 and Eq. S3). First, substrate **2b** was subjected to the chlorosulfonylation conditions in the absence of **2c**. Following complete conversion of **2b** to the sulfonyl chloride (**4a**), substrate **2c** was then added and the reaction mixture was allowed to stir at 50 °C for 10 h. Analysis by <sup>1</sup>H NMR showed 91% recovery of **2c**, 0% recovery of **2b**, and > 90% NMR yield of **4a**.

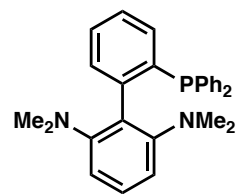


#### H) Competition Experiment with Piperidine:



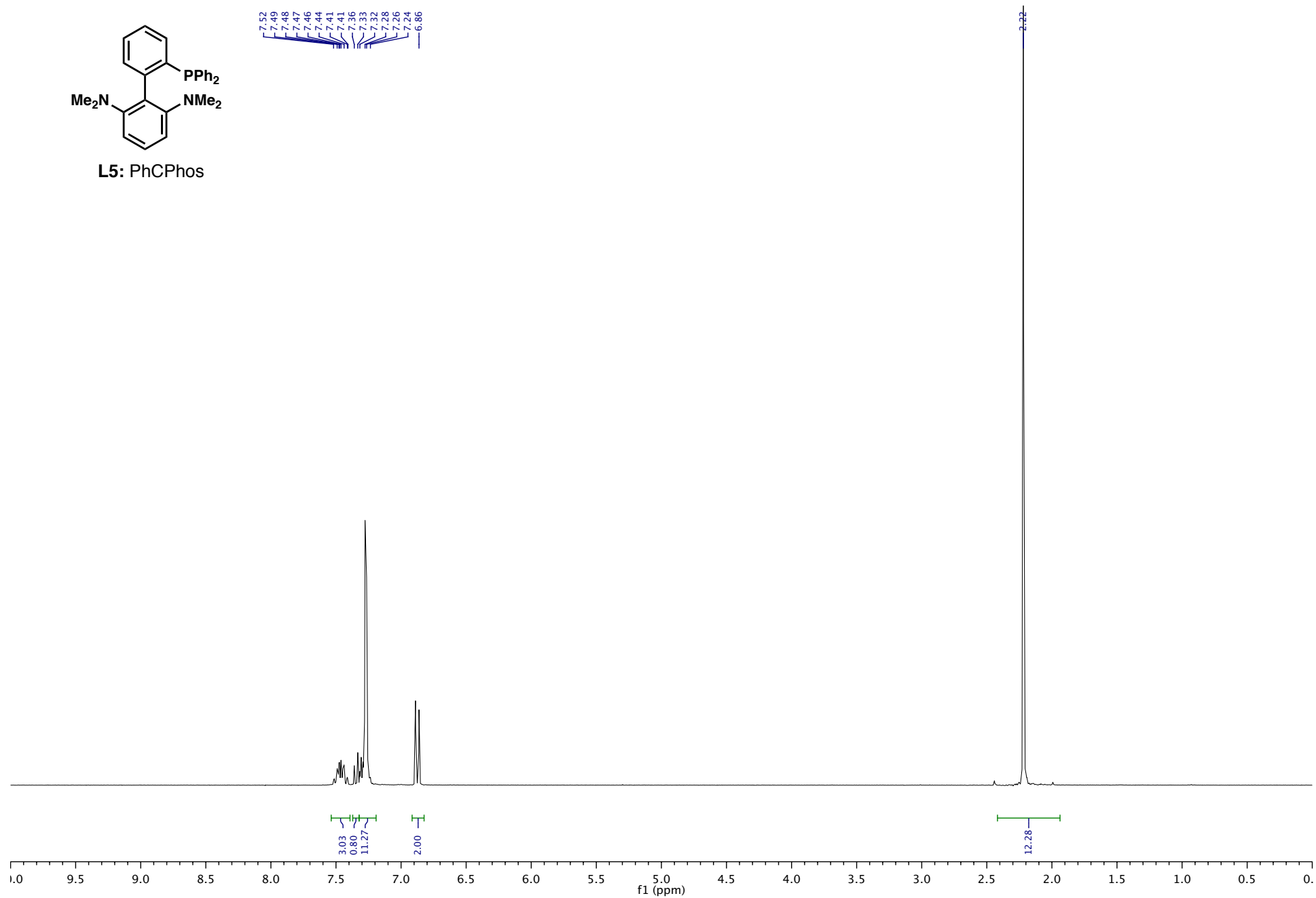
An oven-dried test tube equipped with a magnetic stir bar was sealed with a Teflon screw-cap septum. The vessel was evacuated and backfilled with N<sub>2</sub> (this process was repeated a total of 3 times), and neat **2b** (75.4 μL, 0.5 mmol, 1.0 equiv), neat **2c** (116 μL, 0.5 mmol, 1.0 equiv), and CD<sub>2</sub>Cl<sub>2</sub> (2.0 mL) were added under a N<sub>2</sub> atmosphere. The vessel was allowed to cool to -78 °C in a dry ice/acetone bath, and a solution of piperidine (50 μL, 0.5 mmol, 1.0 equiv) in CD<sub>2</sub>Cl<sub>2</sub> (0.5 mL) was added slowly via syringe (over 2 min) along the inner wall of the vessel. The reaction mixture was stirred for 18 h at -78 °C. Immediately after the reaction mixture was allowed to warm to room temperature, an internal standard (1,3,5-trimethoxybenzene, 28.03 mg) was added, and a small aliquot (~0.2 mL) of the crude reaction mixture was diluted with CD<sub>3</sub>Cl (~0.6 mL) and analyzed by <sup>1</sup>H NMR (see spectrum on page 93). **Note:** The signals of the sulfamoyl chloride (**8**) and the piperidinium salt overlap in the <sup>1</sup>H NMR spectrum. Therefore, a separate aliquot (~0.2 mL) of the crude reaction mixture was filtered through a short plug of SiO<sub>2</sub> (~1.5 cm in a pipette with a cotton filter) to remove the piperidinium salt. The filter was further washed with CD<sub>3</sub>Cl (~0.6 mL) and the combined filtrate was analyzed by <sup>1</sup>H NMR (see expanded region on page 93). Because both **2b** and **2c** are converted to the same sulfamoyl chloride product (**8**), the amounts of recovered **2b** and **2c** were quantified. The NMR data show that a larger amount of the sterically hindered substrate (**2c**) is consumed than **2b**. In addition, **2b** and **2c** react with piperidine to form the corresponding sulfamoyl chloride (**8**), demonstrating that S-O bond cleavage is also favored in the absence of a palladium catalyst.

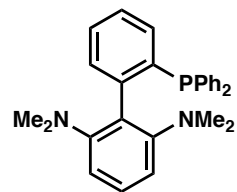
### III. $^1\text{H}$ , $^{13}\text{C}$ , $^{19}\text{F}$ , and $^{31}\text{P}$ NMR Spectra.



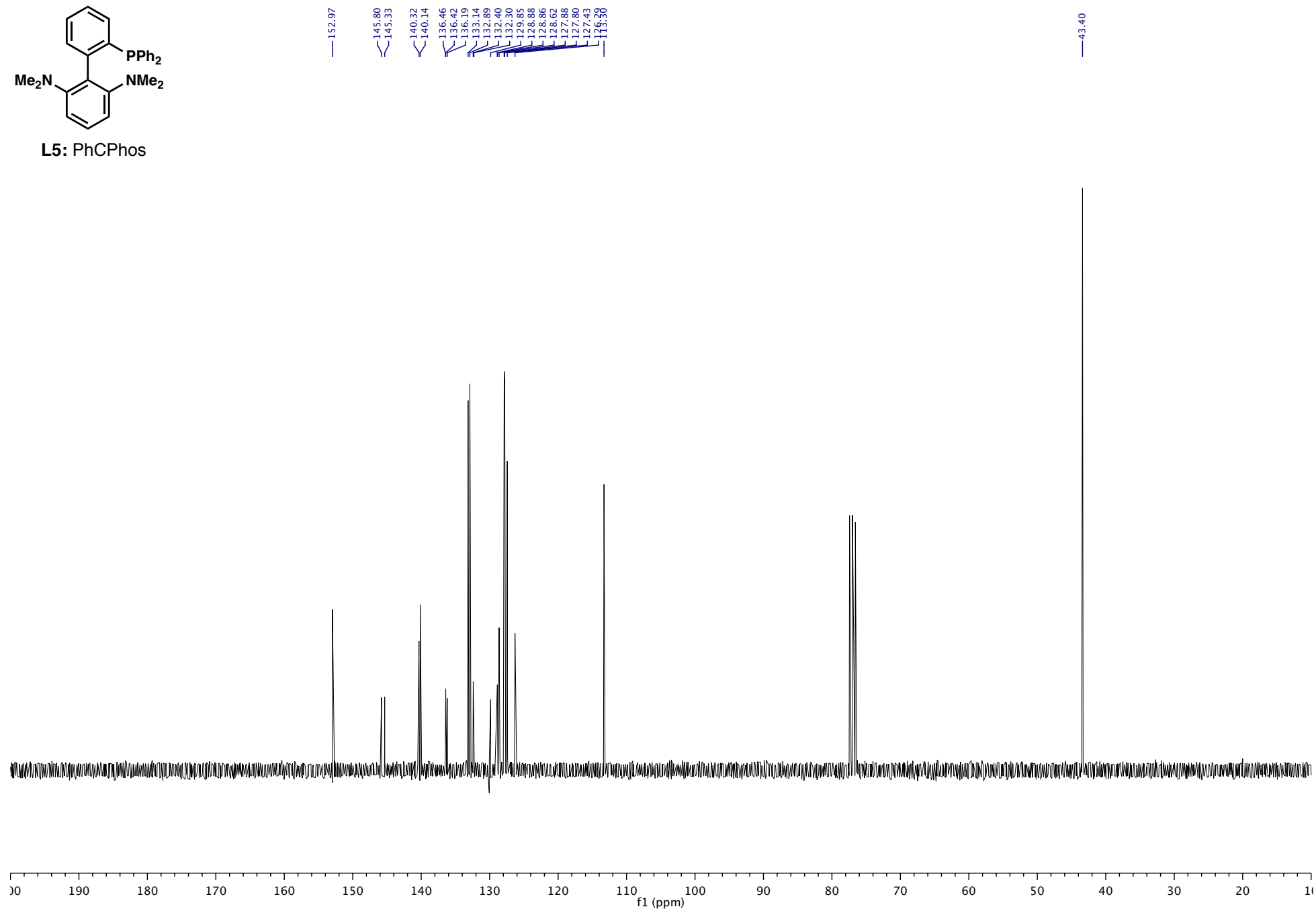
L5: PhCPhos

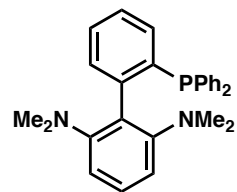
7.52  
7.49  
7.48  
7.47  
7.46  
7.44  
7.41  
7.41  
7.36  
7.33  
7.32  
7.28  
7.26  
7.24  
6.86



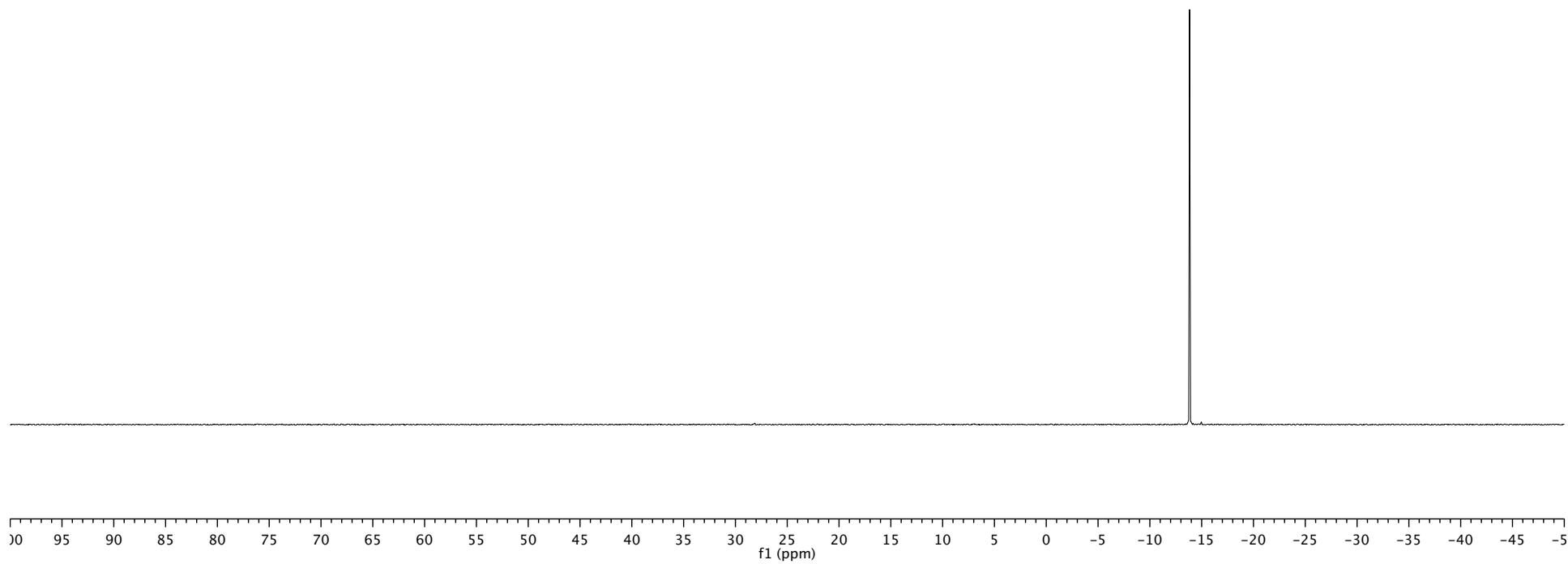


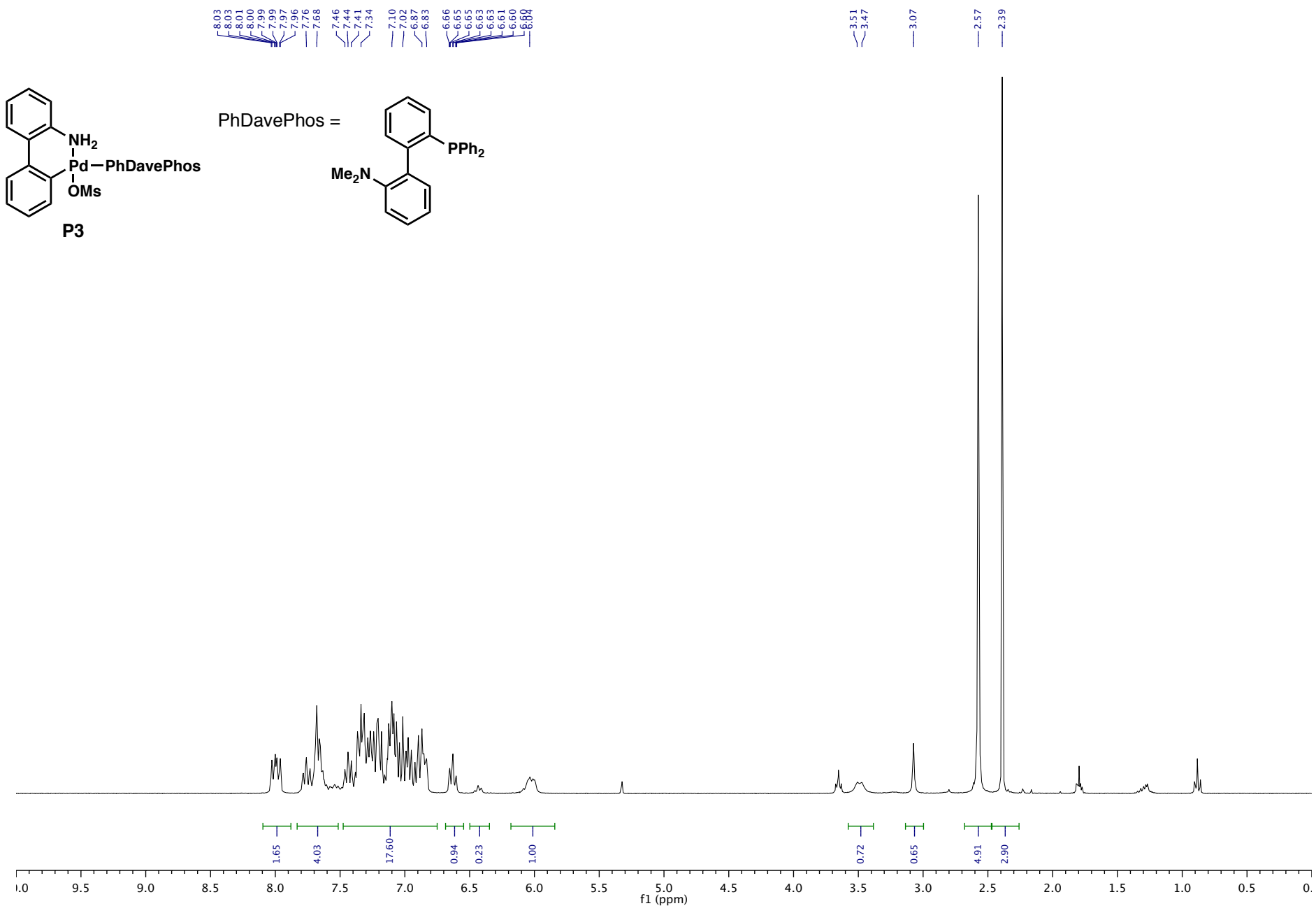
L5: PhCPhos

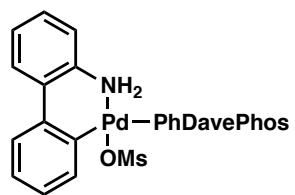




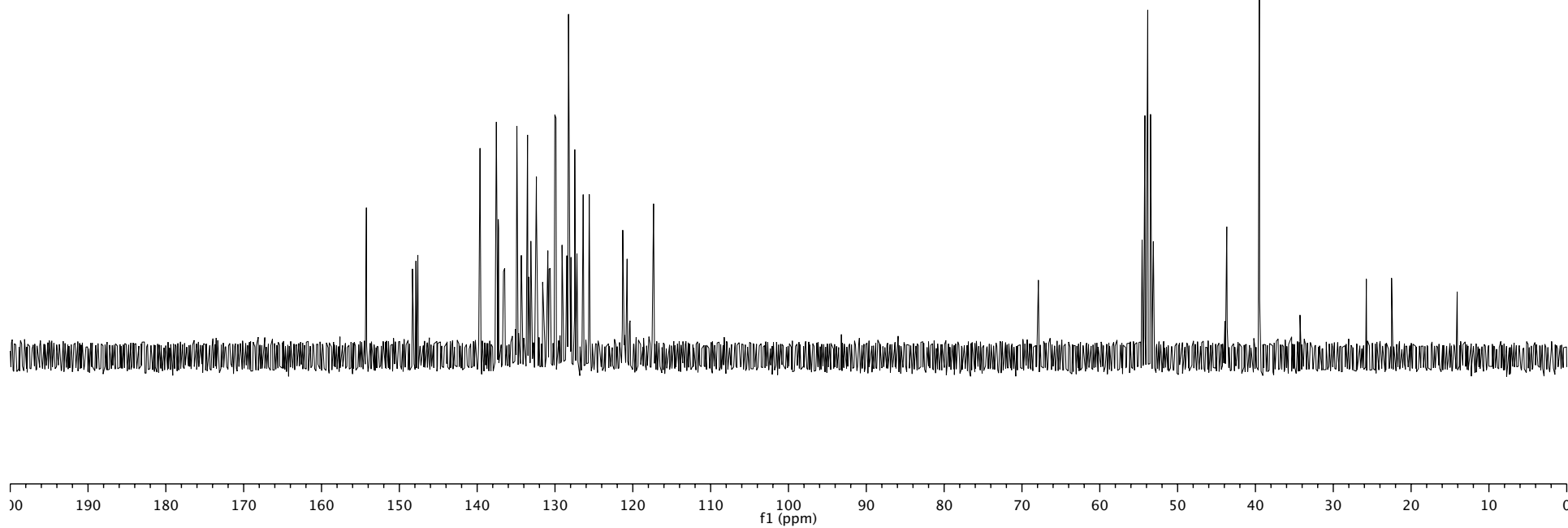
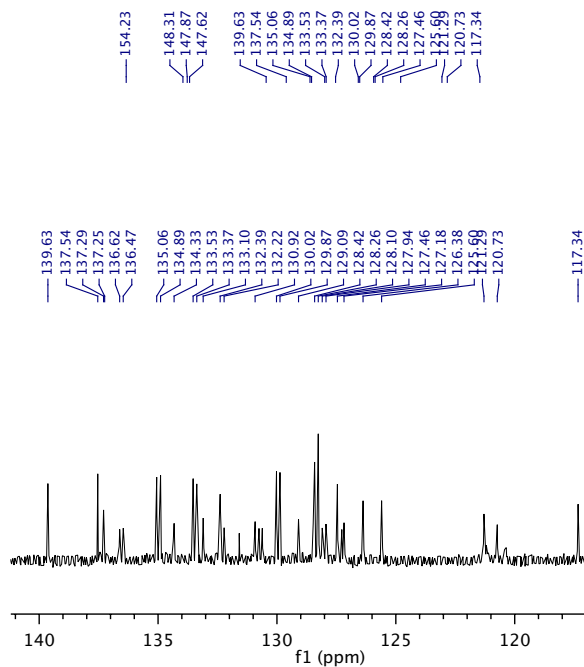
L5: PhCPhos

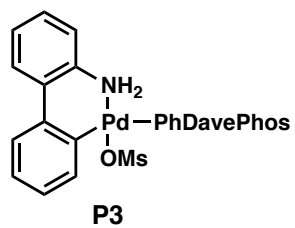




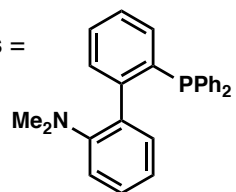


**P3**



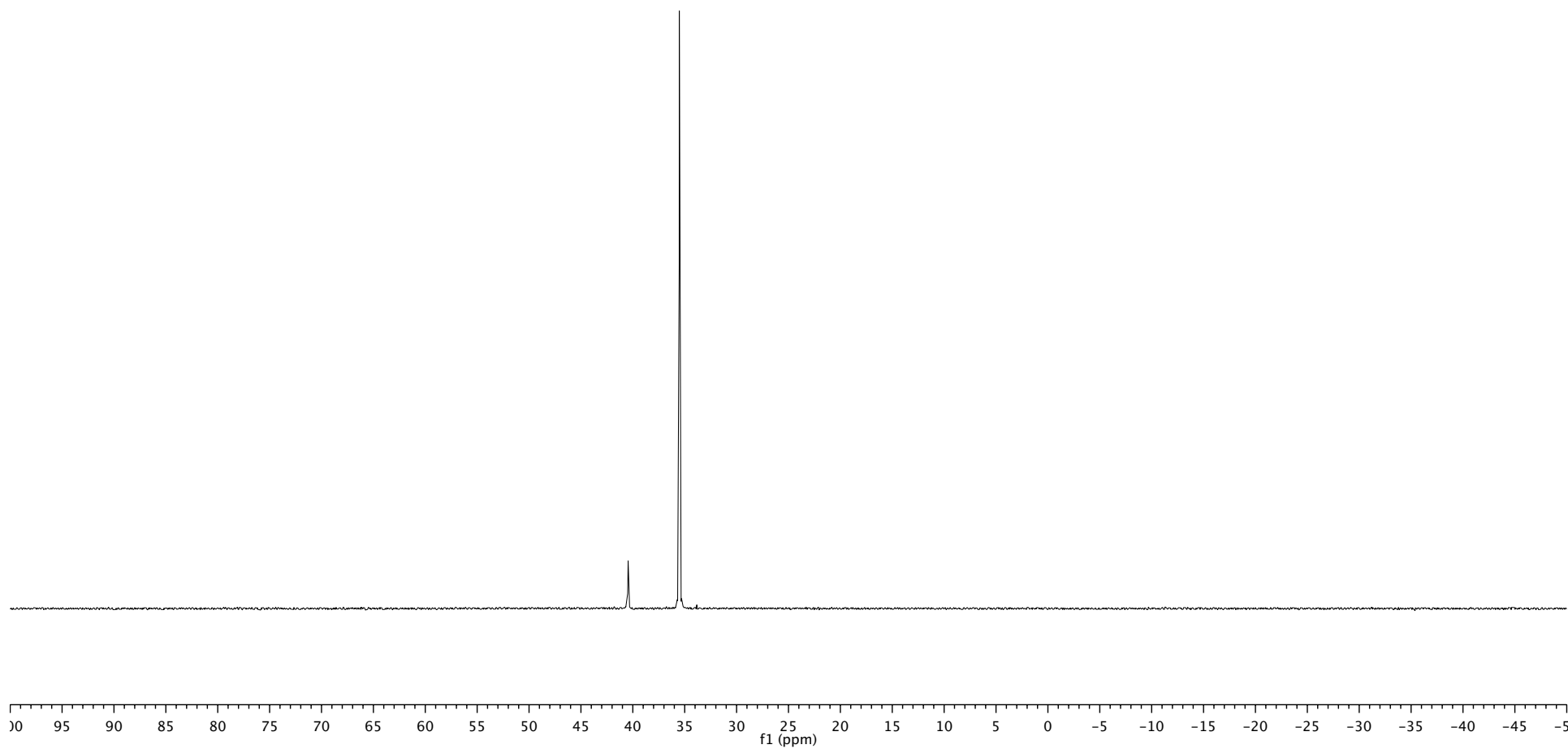


PhDavePhos =

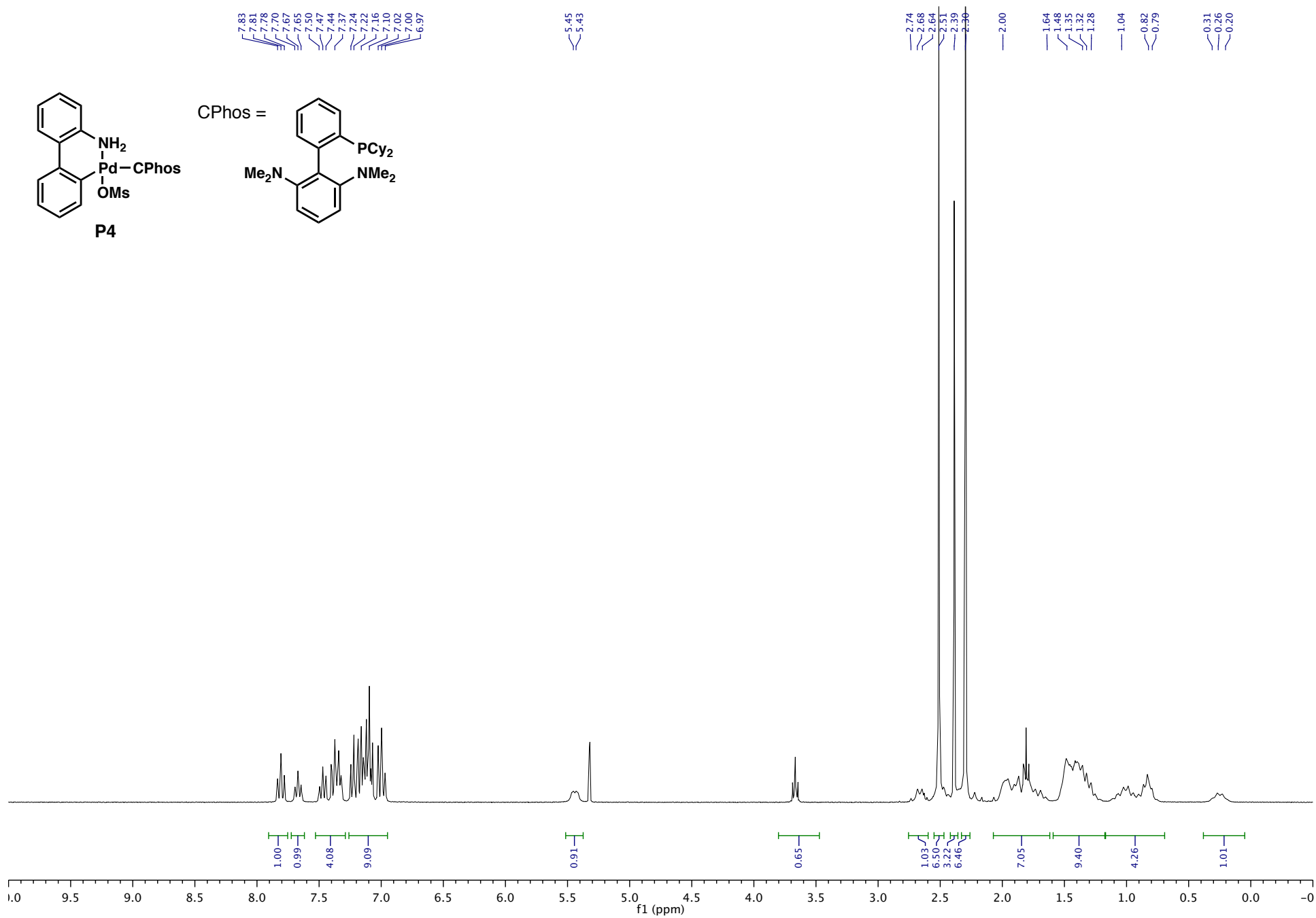


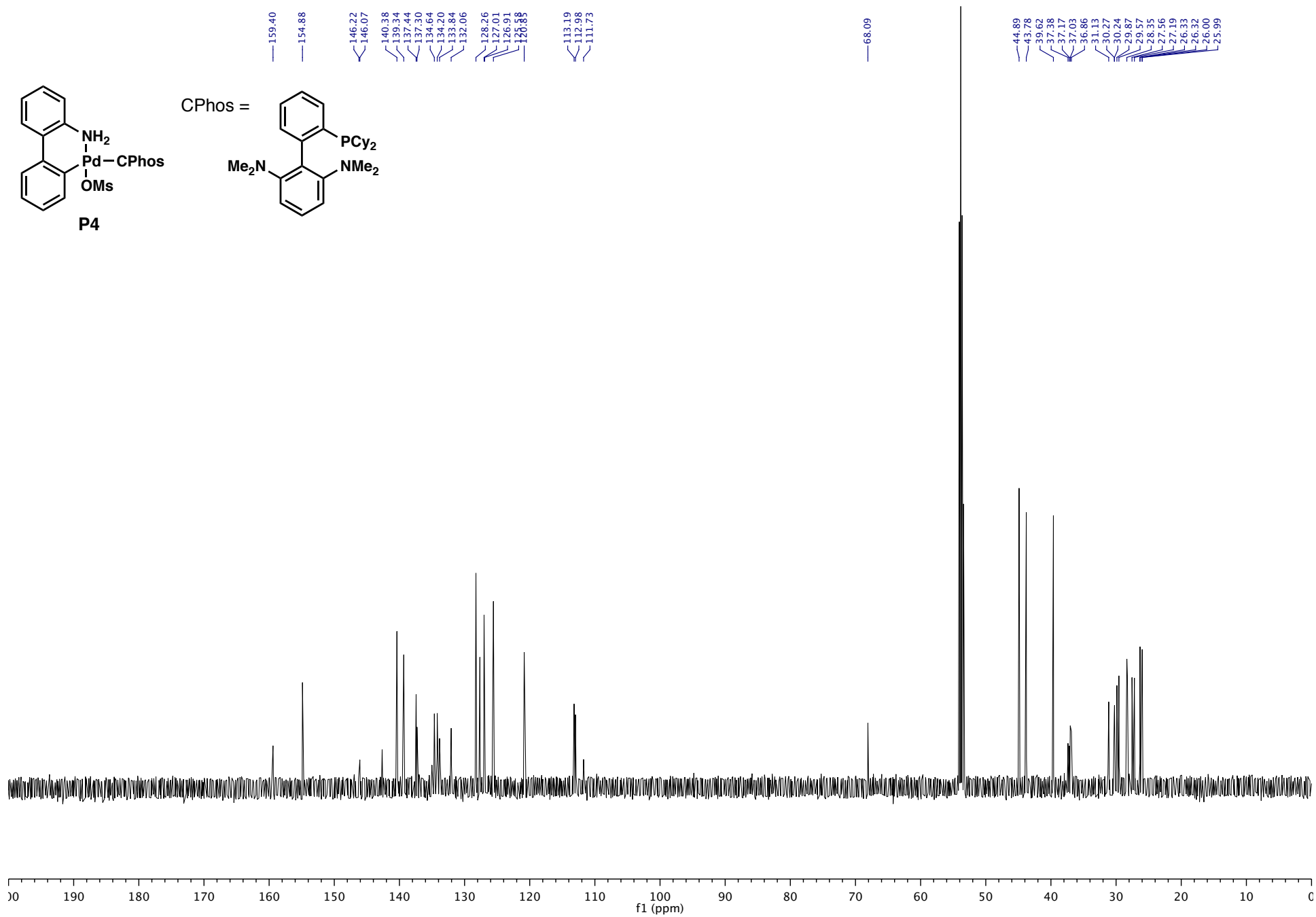
— 40.45

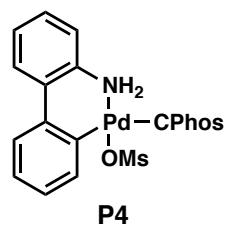
— 35.52



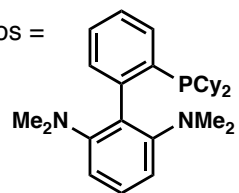




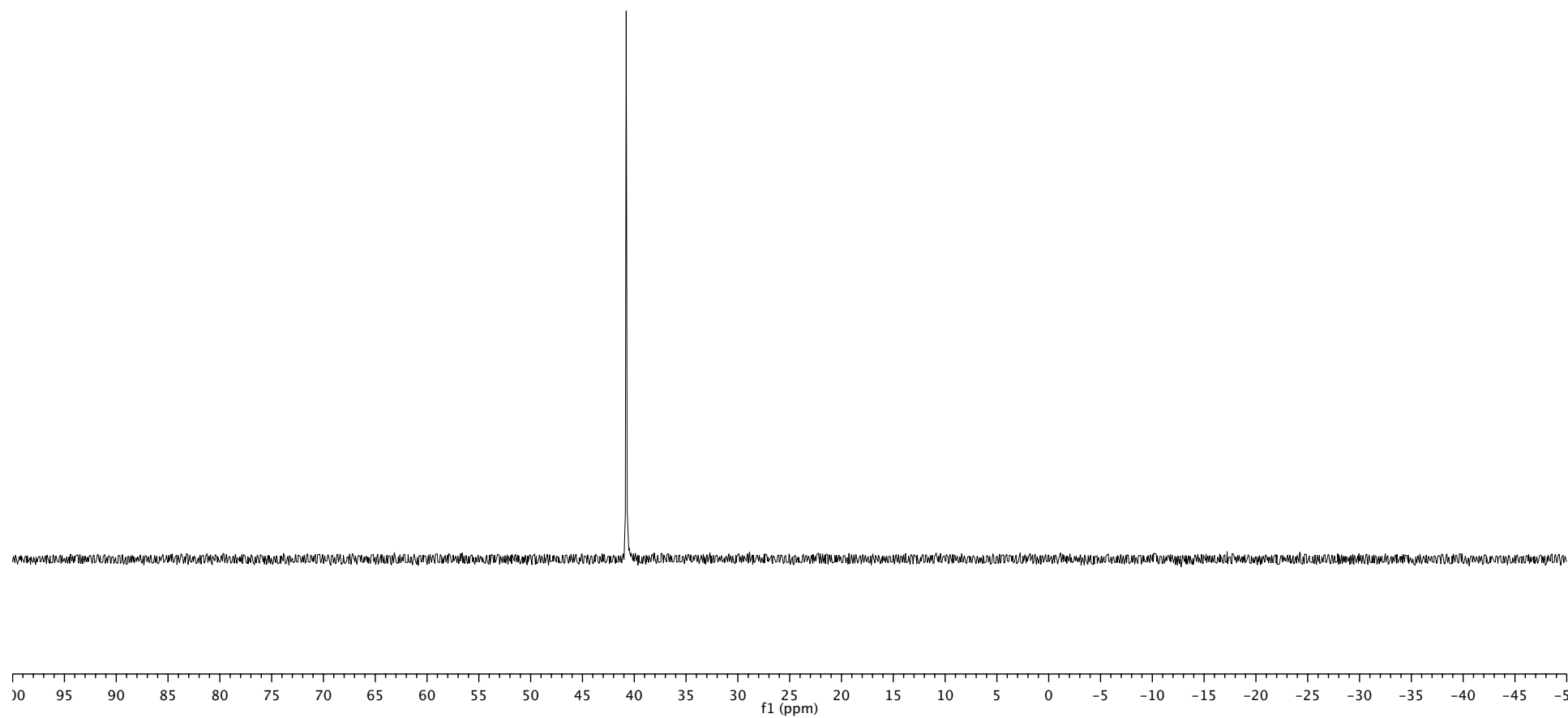


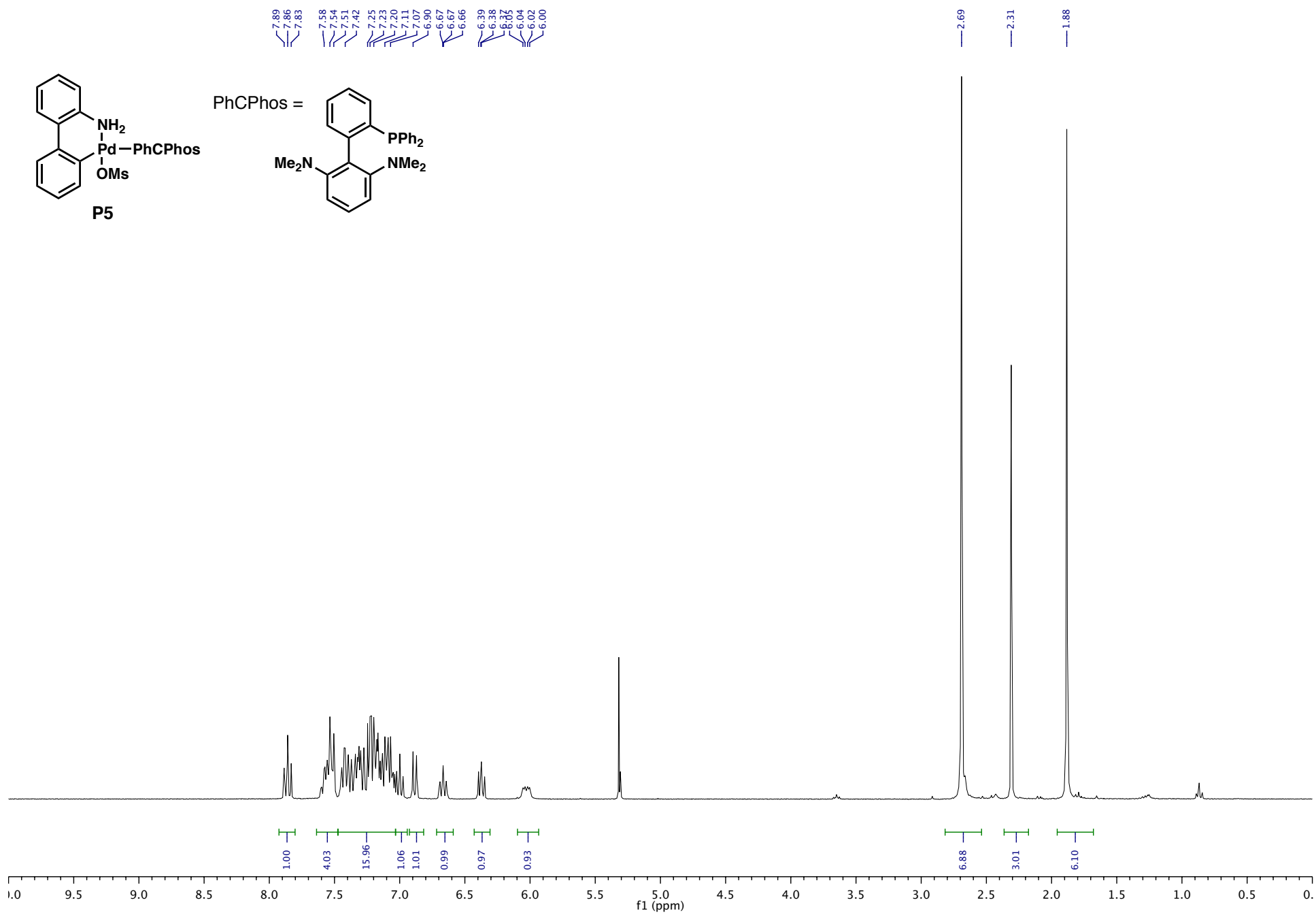


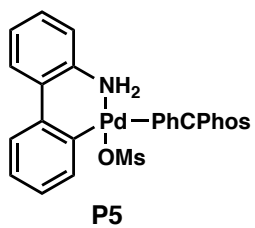
CPhos =



— 40.78





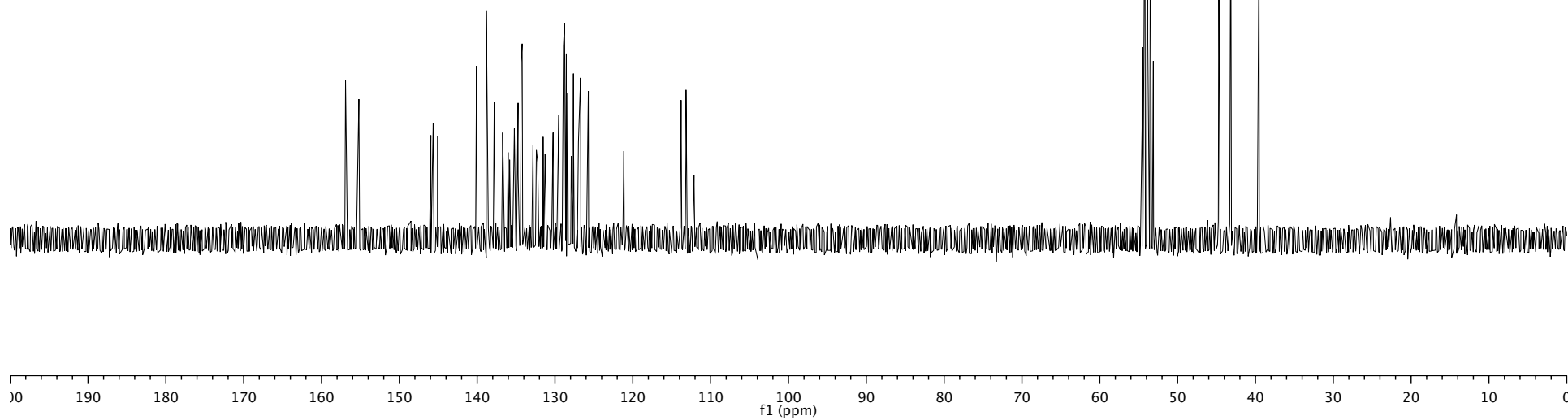
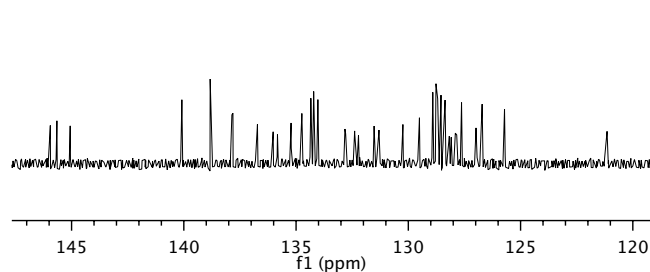


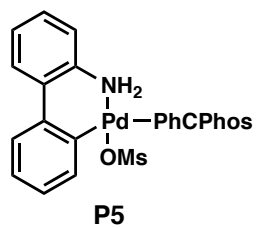
156.91  
155.20

145.95  
145.65  
145.07  
140.09  
138.83  
134.34  
134.20  
134.03  
128.91  
128.69  
128.54  
128.36  
127.63  
126.71  
125.72  
121.15  
113.79  
113.16  
112.13

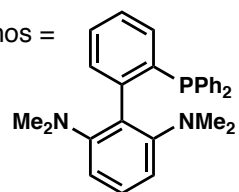
44.71  
43.17  
39.54

145.95  
145.65  
145.07  
140.09  
138.83  
137.86  
137.81  
137.72  
136.72  
136.02  
135.83  
135.23  
134.74  
134.34  
134.20  
134.03  
132.79  
132.39  
132.22  
131.49  
131.31  
130.24  
129.50  
128.91  
128.82  
128.69  
128.54  
128.36  
128.17  
128.09  
127.91  
127.63  
127.00  
126.71  
125.72  
121.15

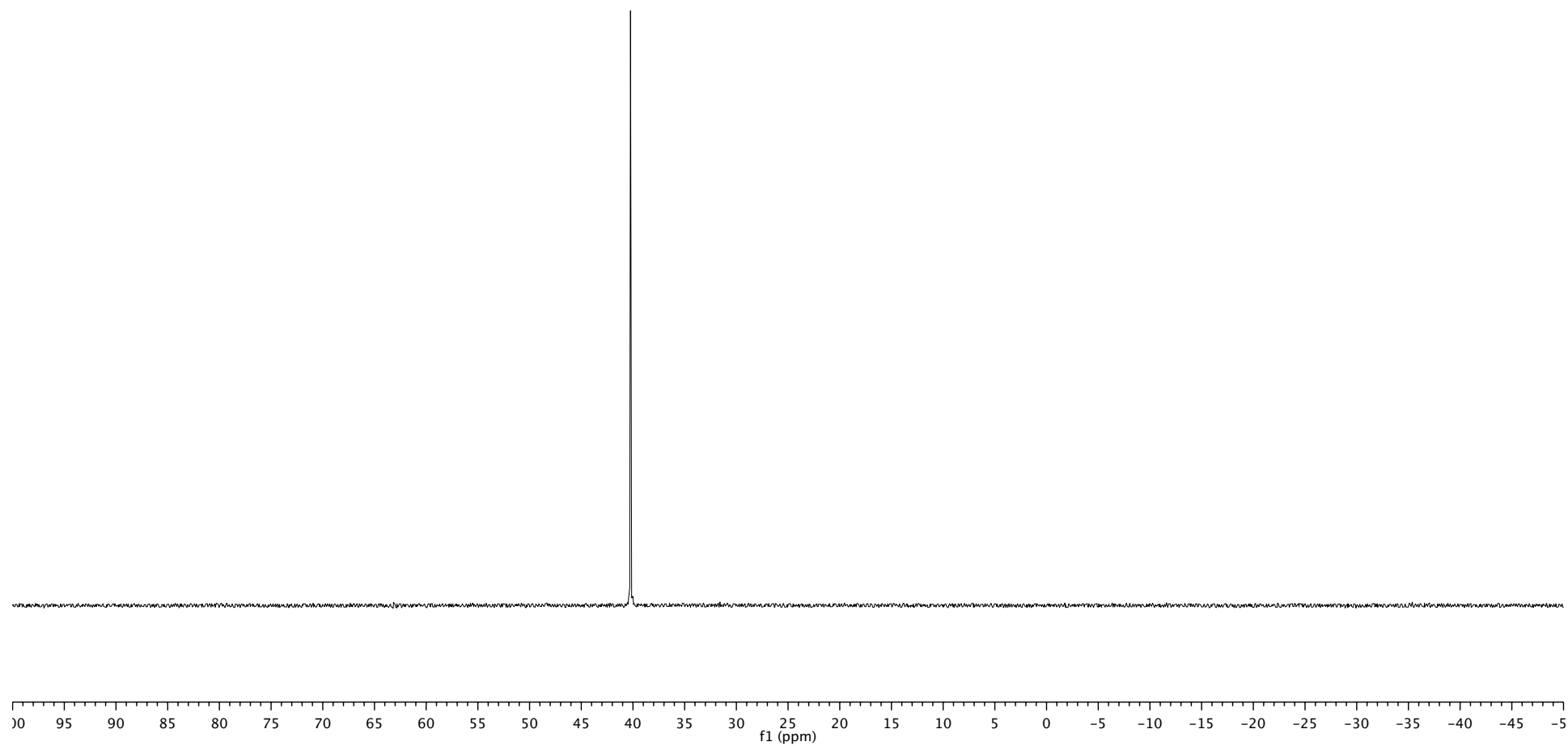


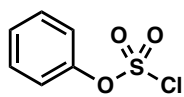


PhCPhos =



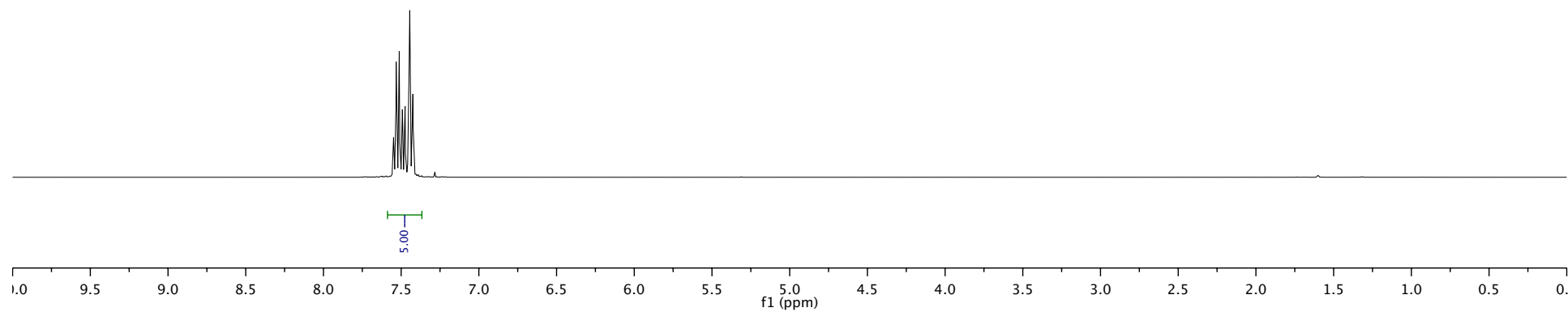
40.24

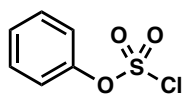




2a

7.55  
7.35  
7.33  
7.31  
7.44  
7.42  
7.42



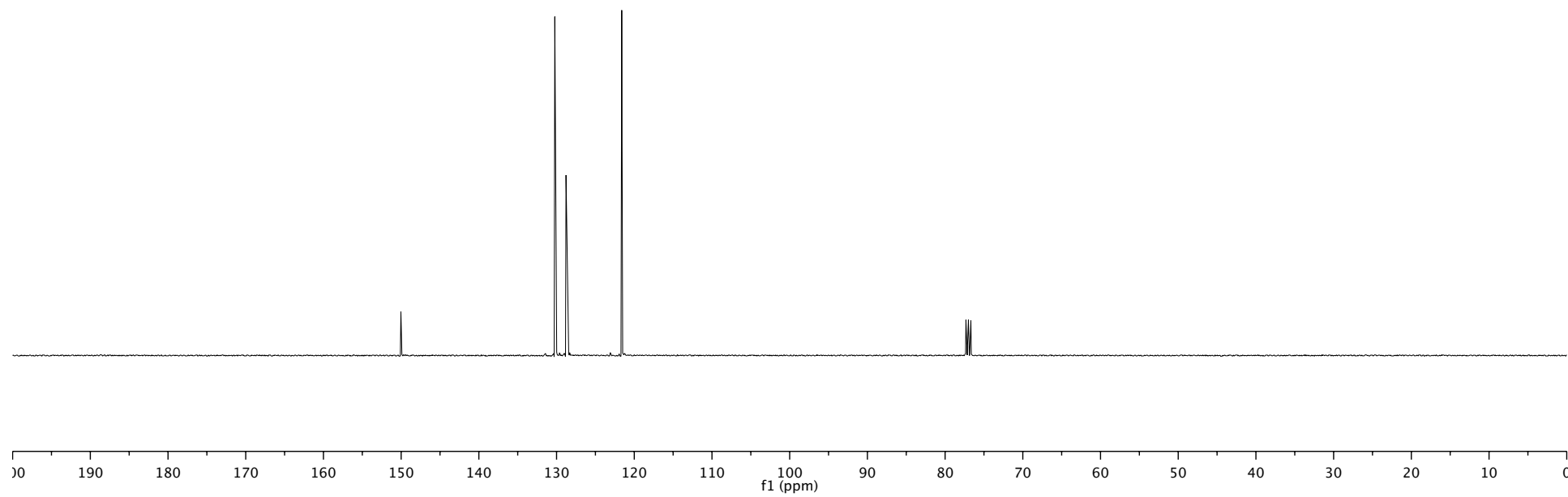


**2a**

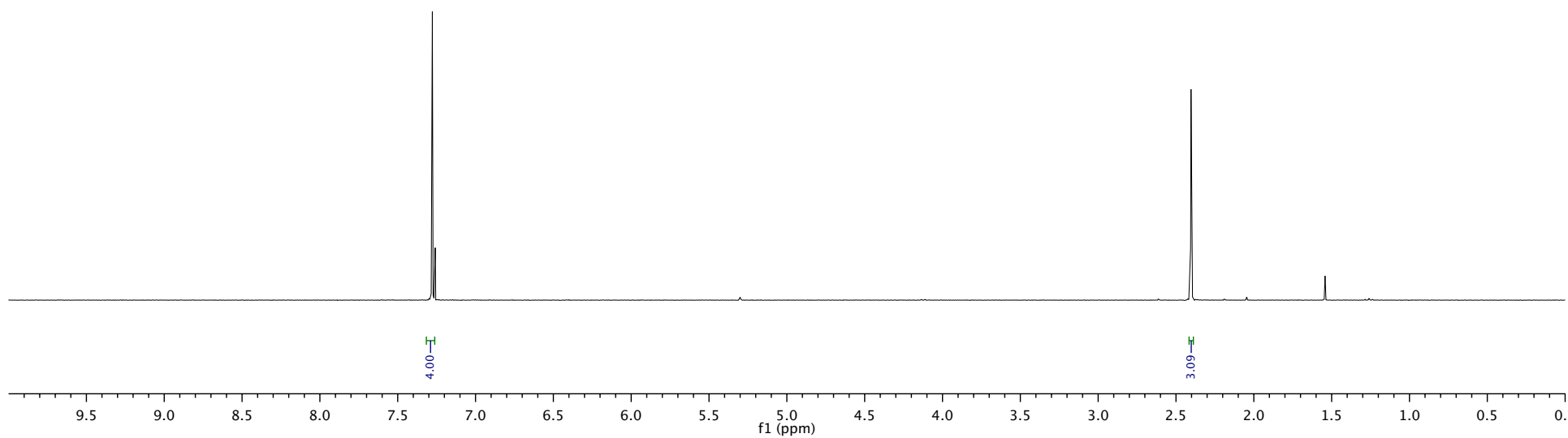
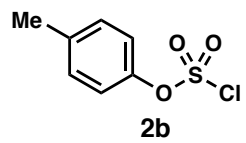
150.03

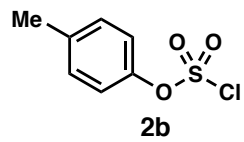
130.23  
128.78

121.61









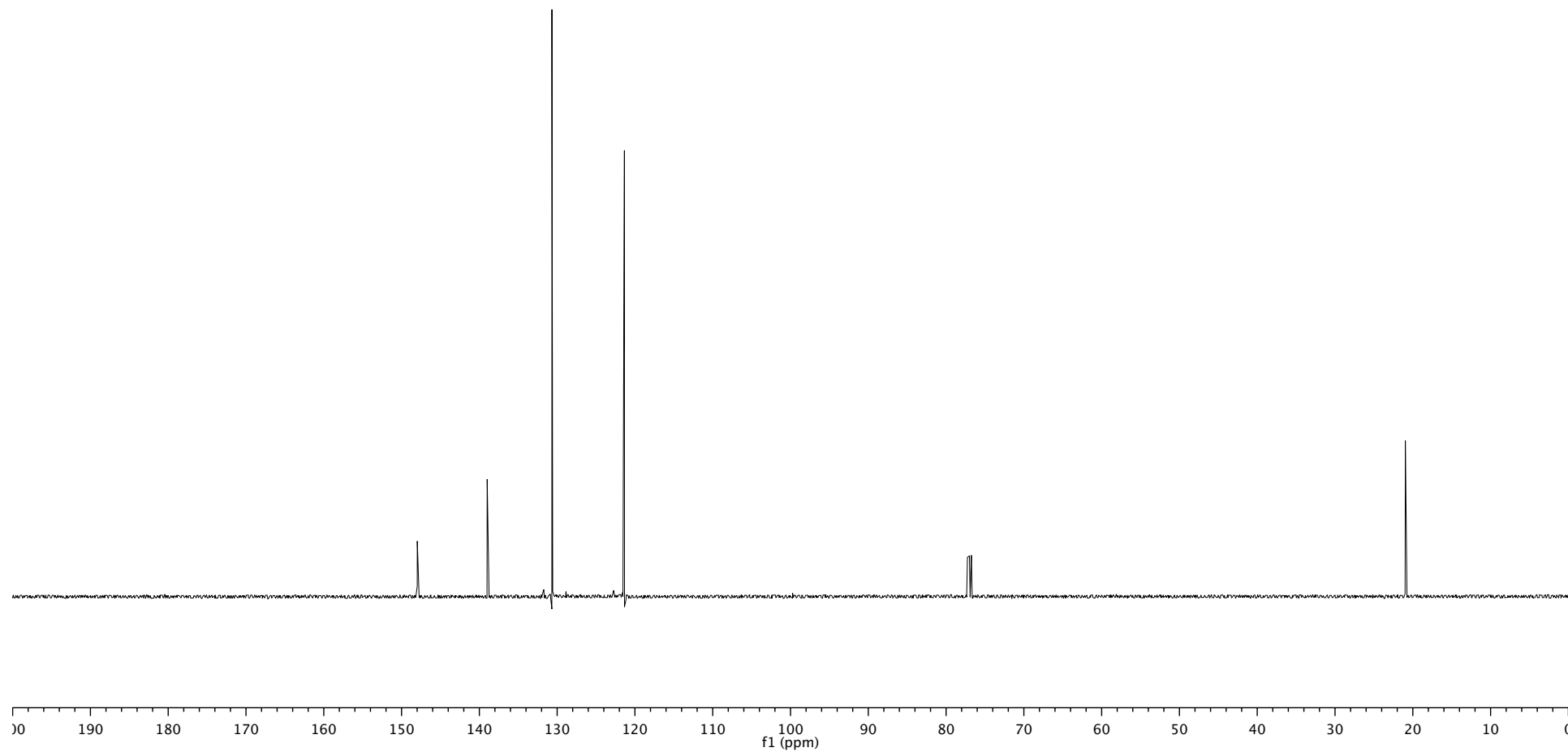
147.98

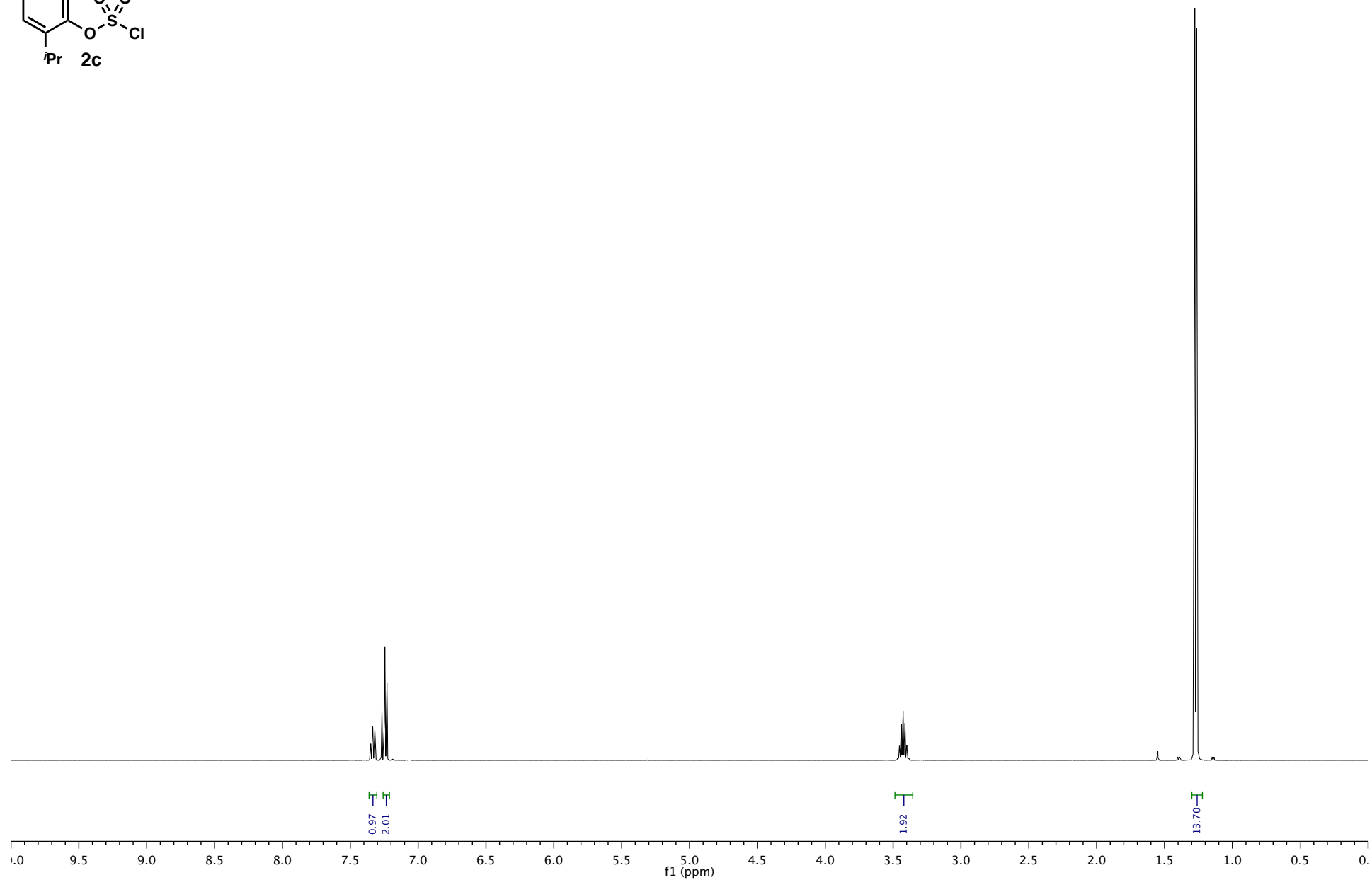
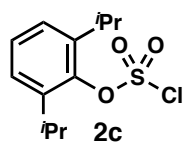
138.99

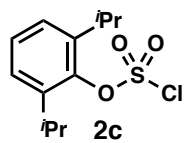
130.67

121.35

20.96







— 146.97

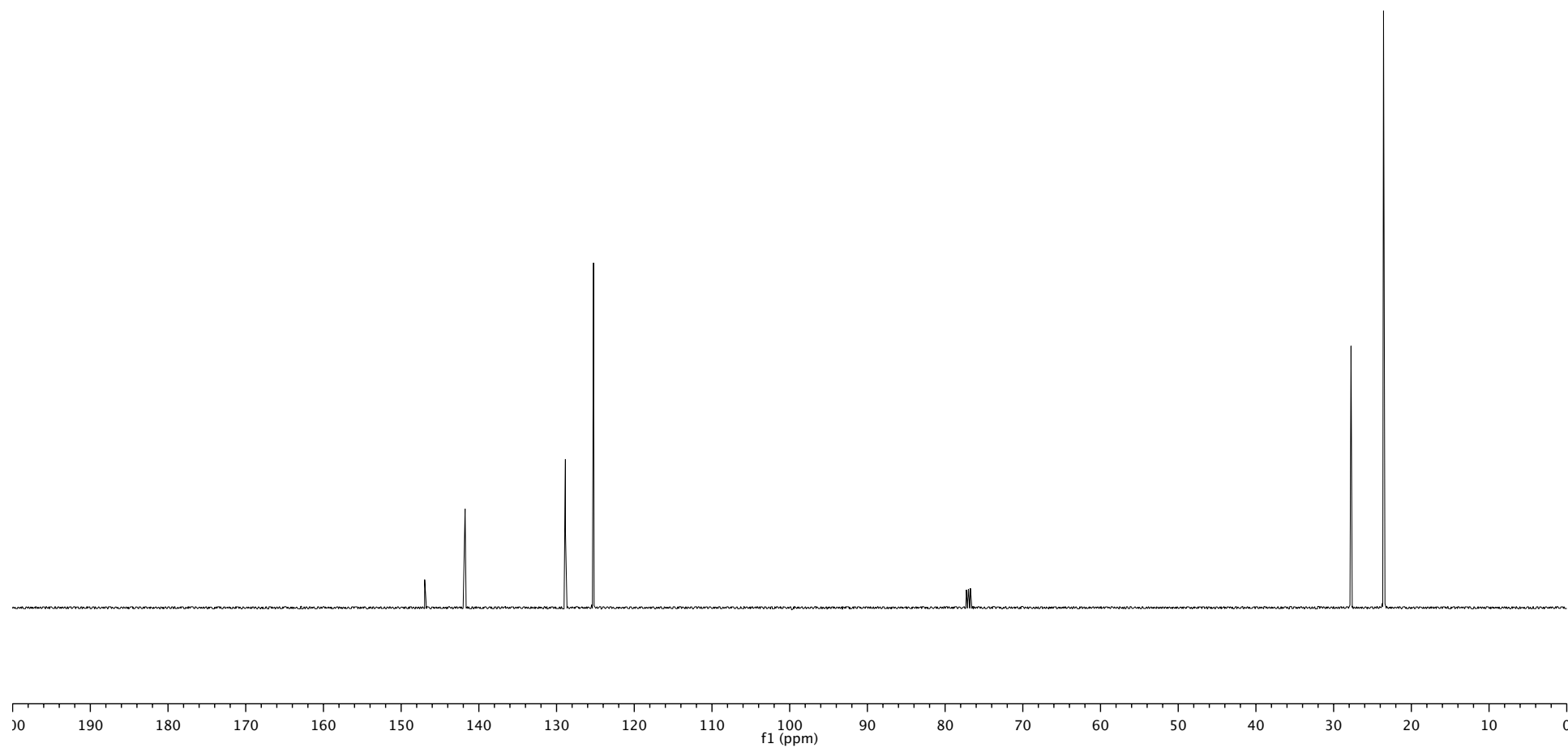
— 141.77

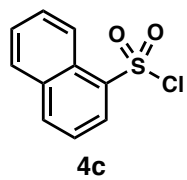
— 128.86

— 125.24

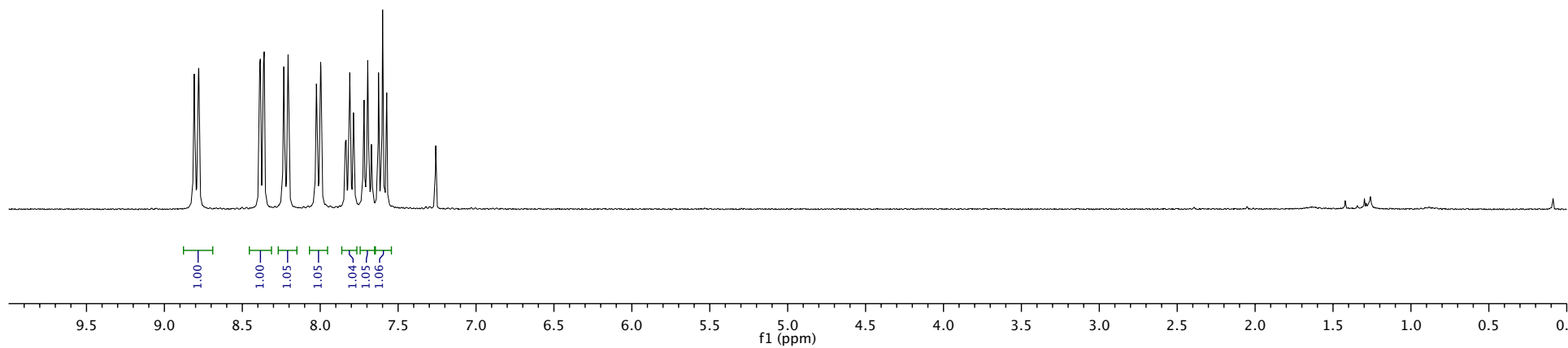
— 27.76

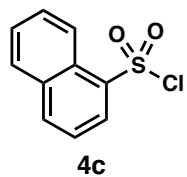
— 23.58



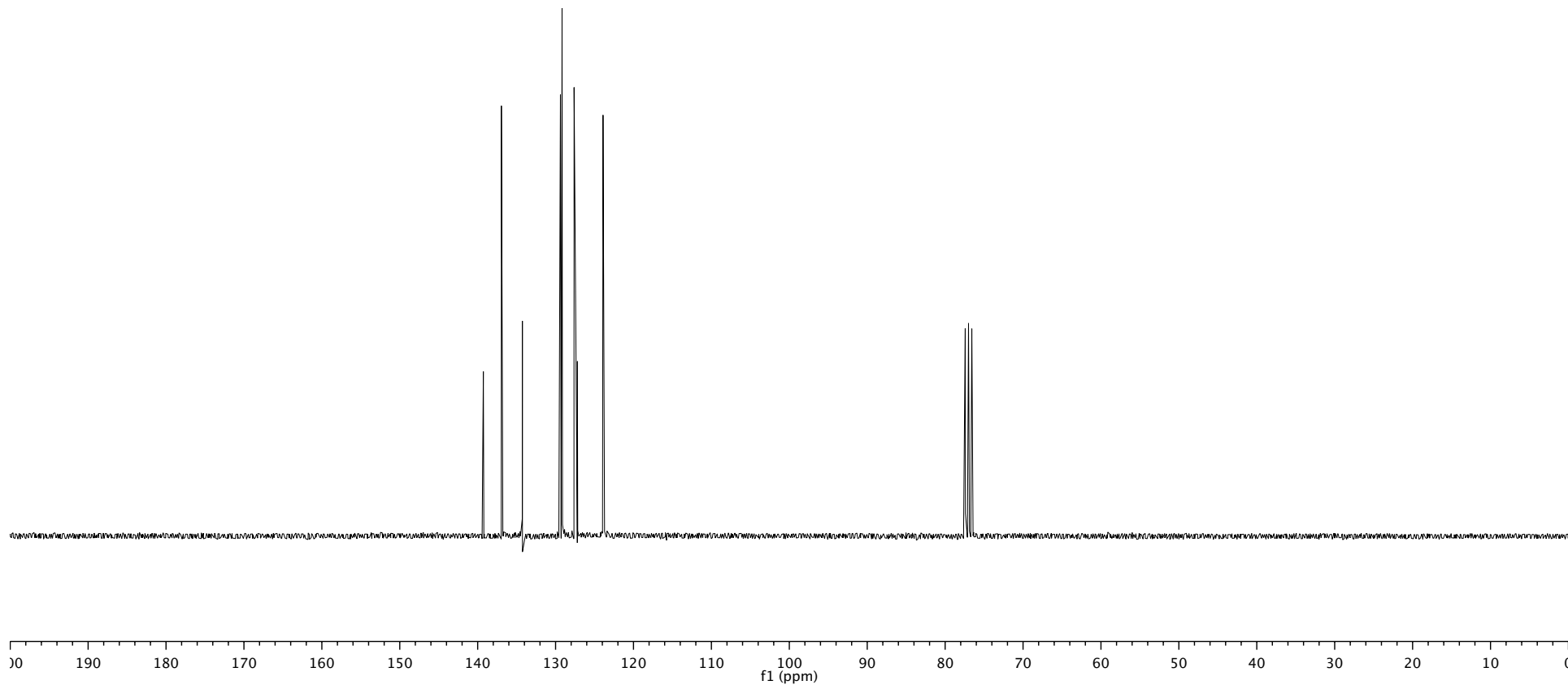


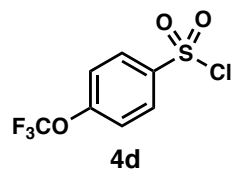
8.81  
 8.81  
 8.78  
 8.78  
 8.39  
 8.38  
 8.36  
 8.36  
 8.21  
 8.02  
 8.00  
 7.84  
 7.83  
 7.82  
 7.81  
 7.80  
 7.79  
 7.78  
 7.72  
 7.72  
 7.70  
 7.70  
 7.69  
 7.67  
 7.67  
 7.63  
 7.60  
 7.57





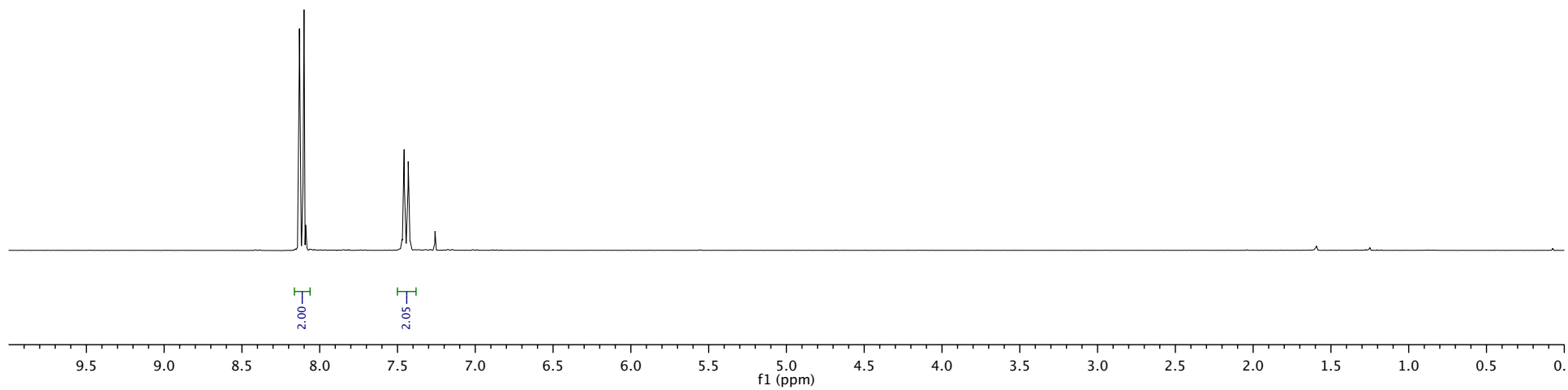
139.27  
136.96  
134.26  
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129.26  
129.17  
127.63  
127.20  
123.91  
123.79

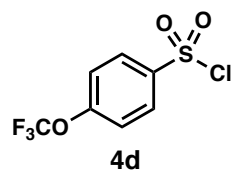




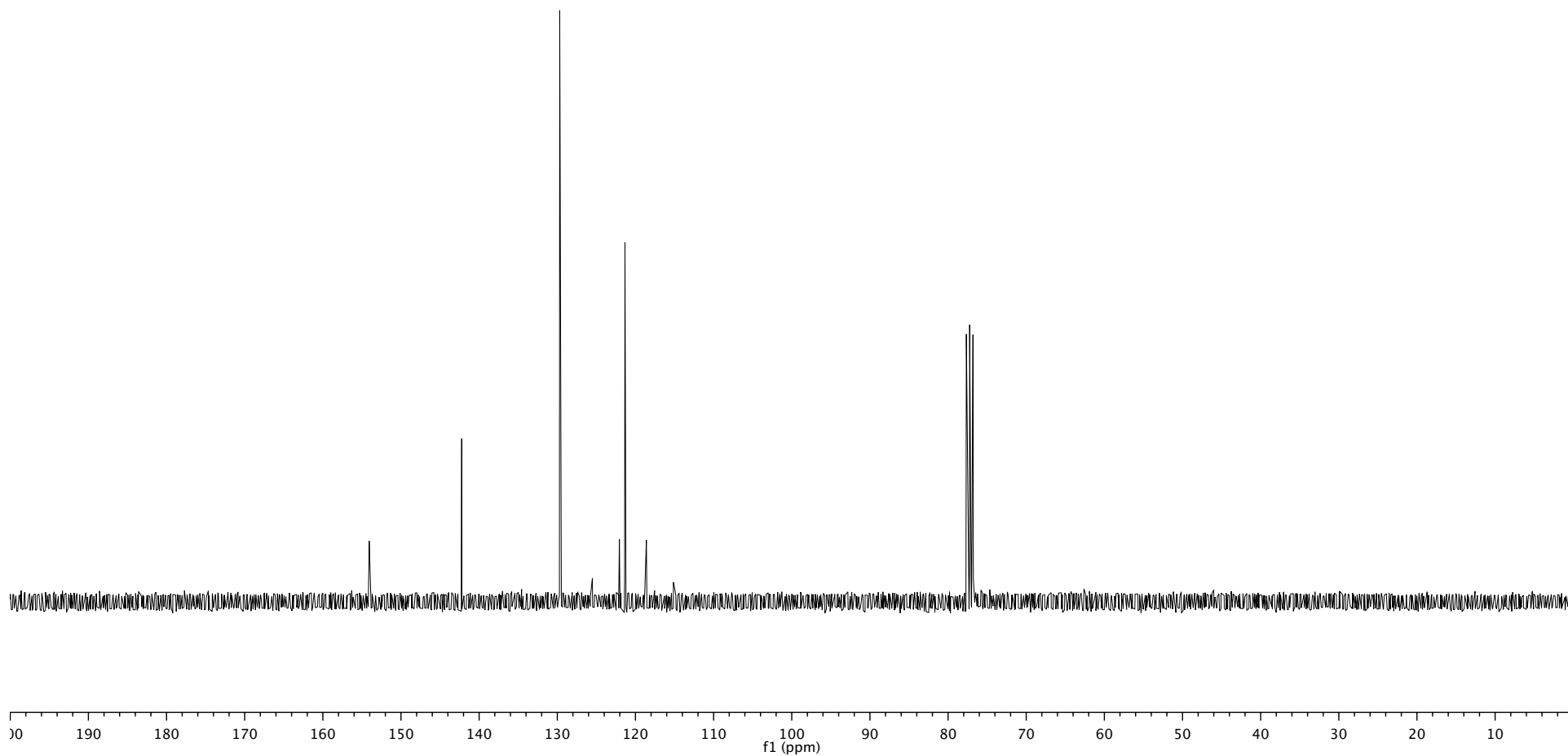
8.14  
8.13  
8.12  
8.11  
8.10  
8.09

7.46  
7.43

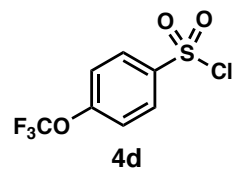




154.11  
 154.09  
 154.06  
 154.04  
 142.23  
 129.69  
 125.51  
 122.06  
 121.38  
 121.36  
 121.34  
 121.32

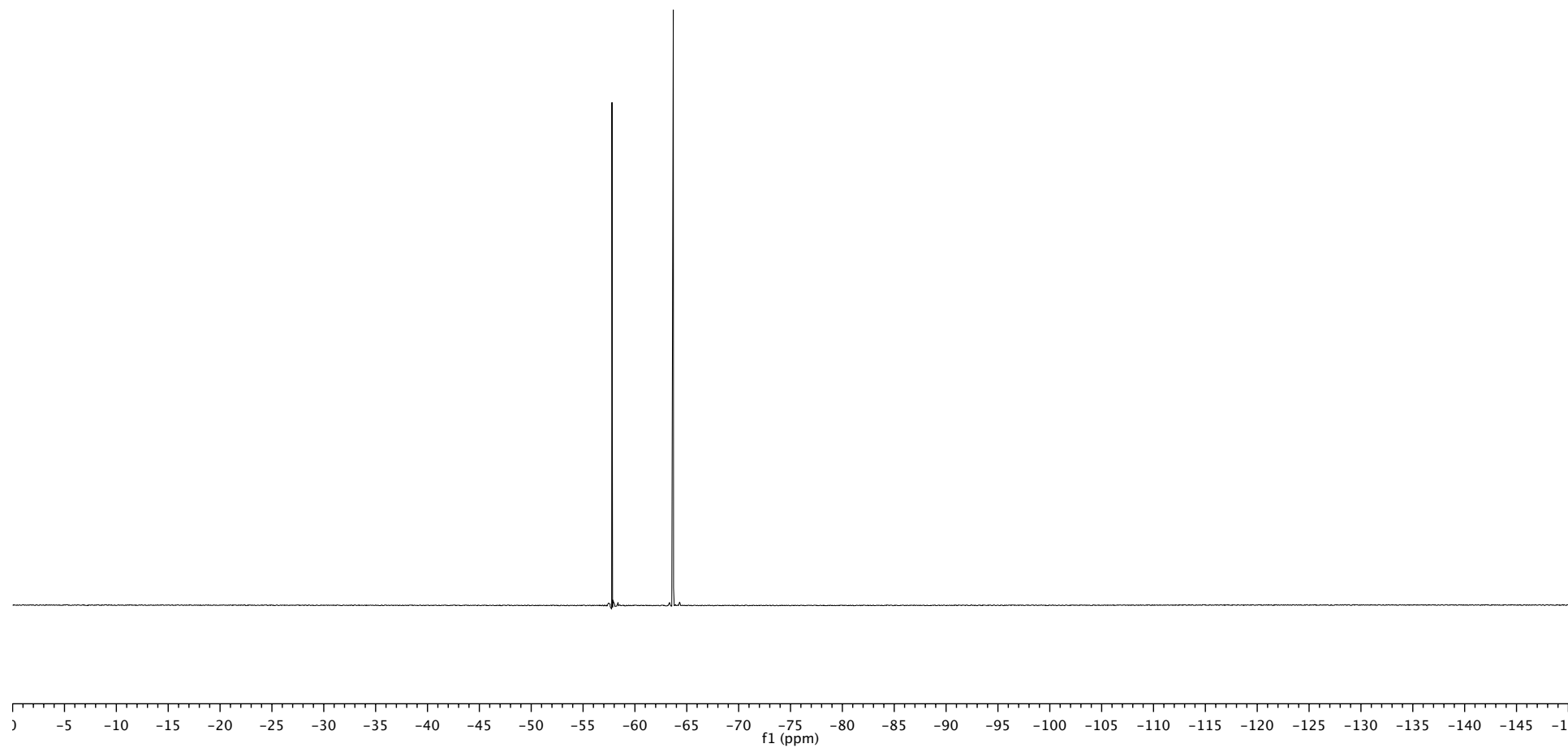


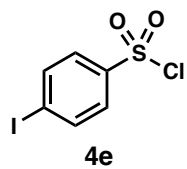




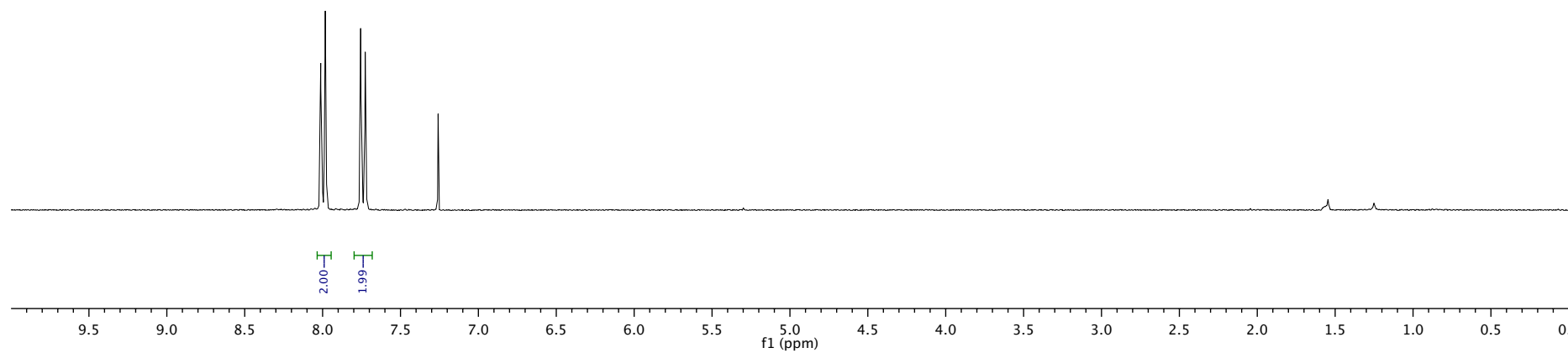
— -57.79

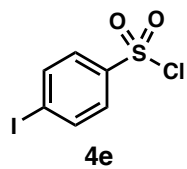
— -63.70 CF3Ph



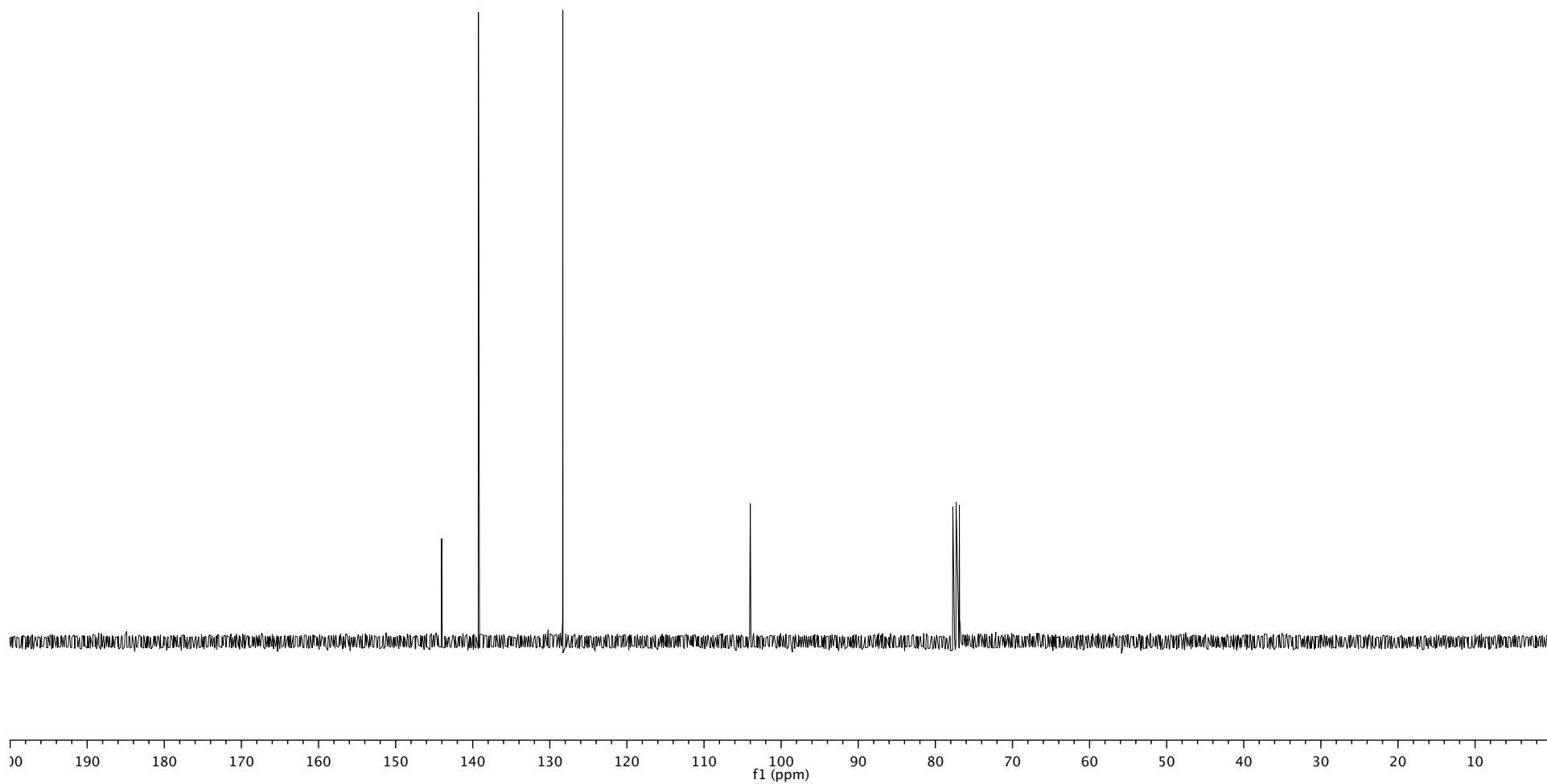


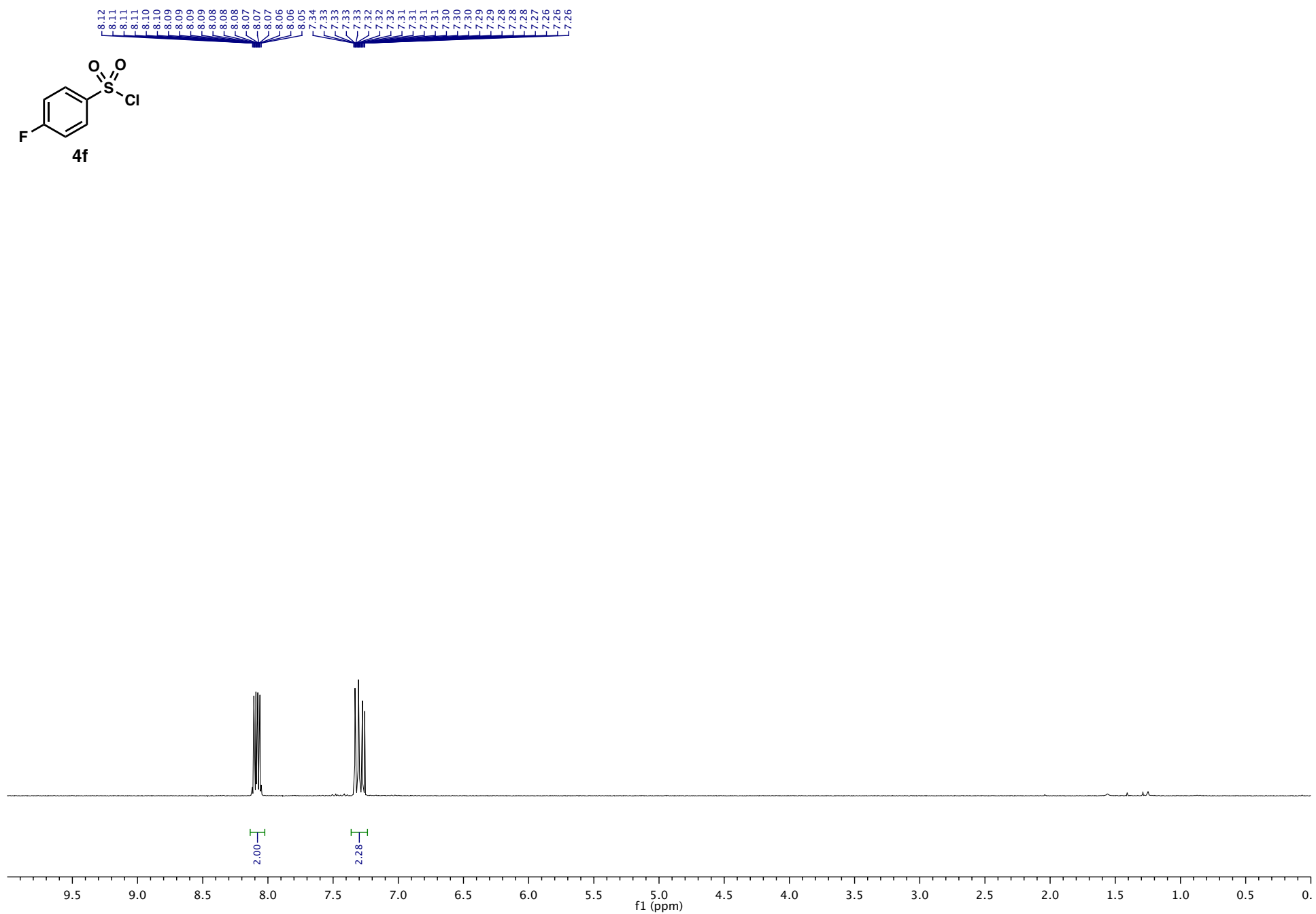
8.01  
7.98  
7.76  
7.73

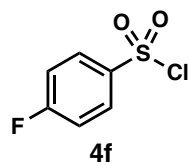




— 144.03  
— 139.26  
— 128.32  
— 104.00







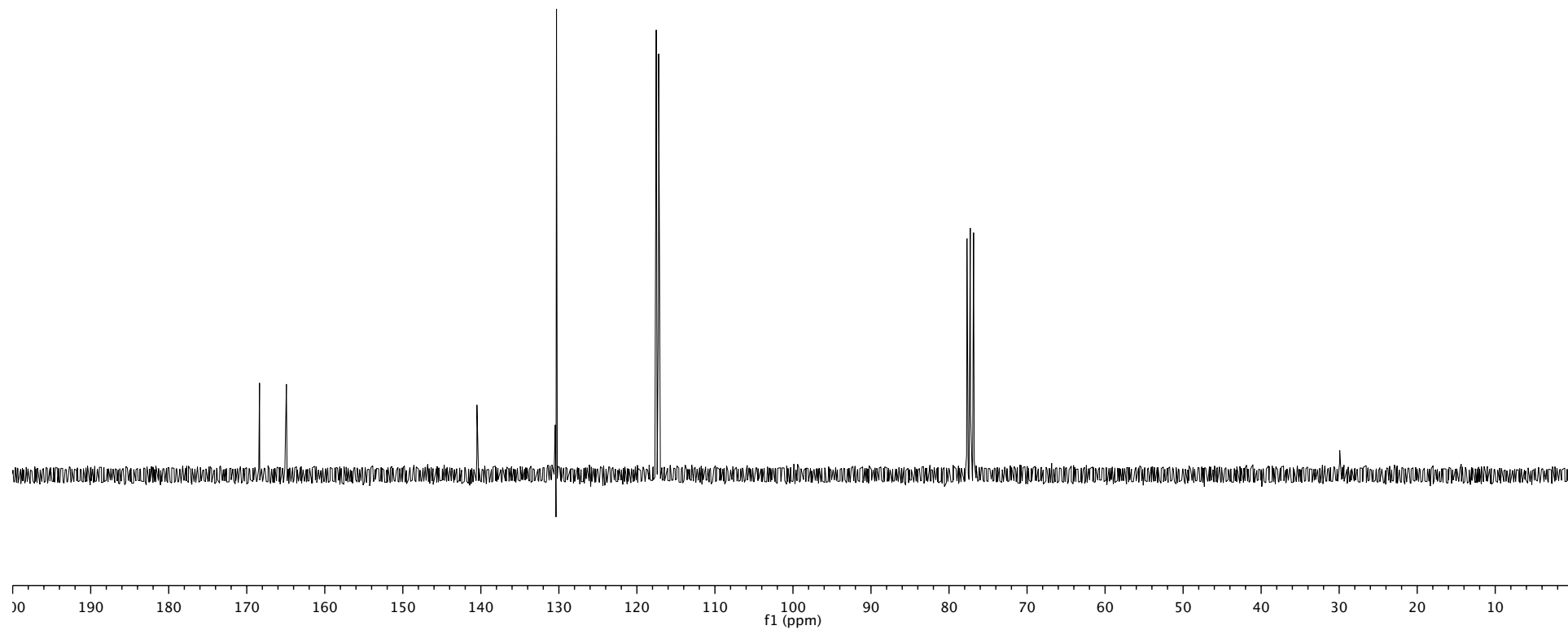
168.36

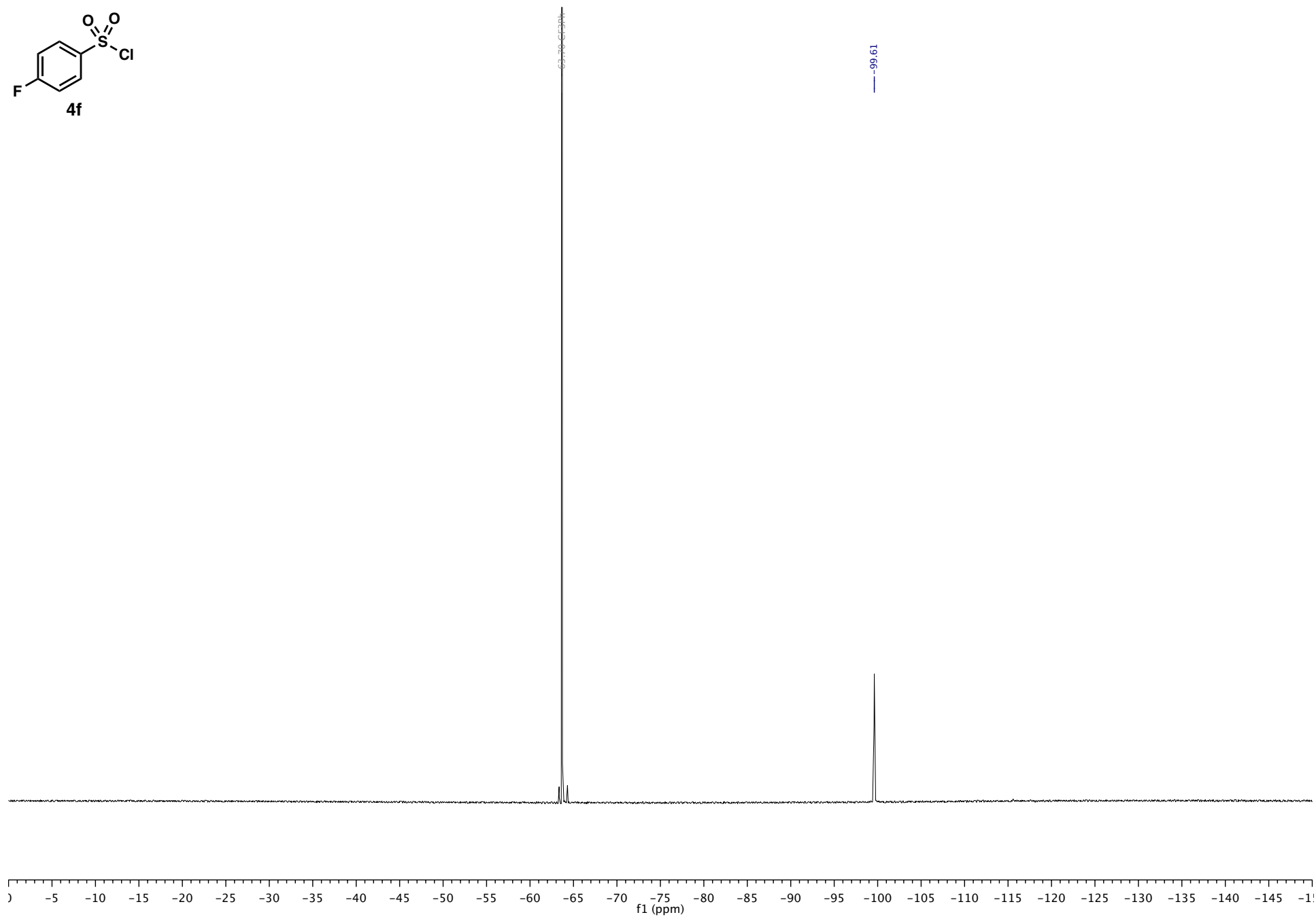
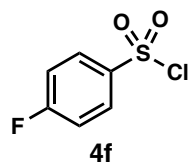
164.92

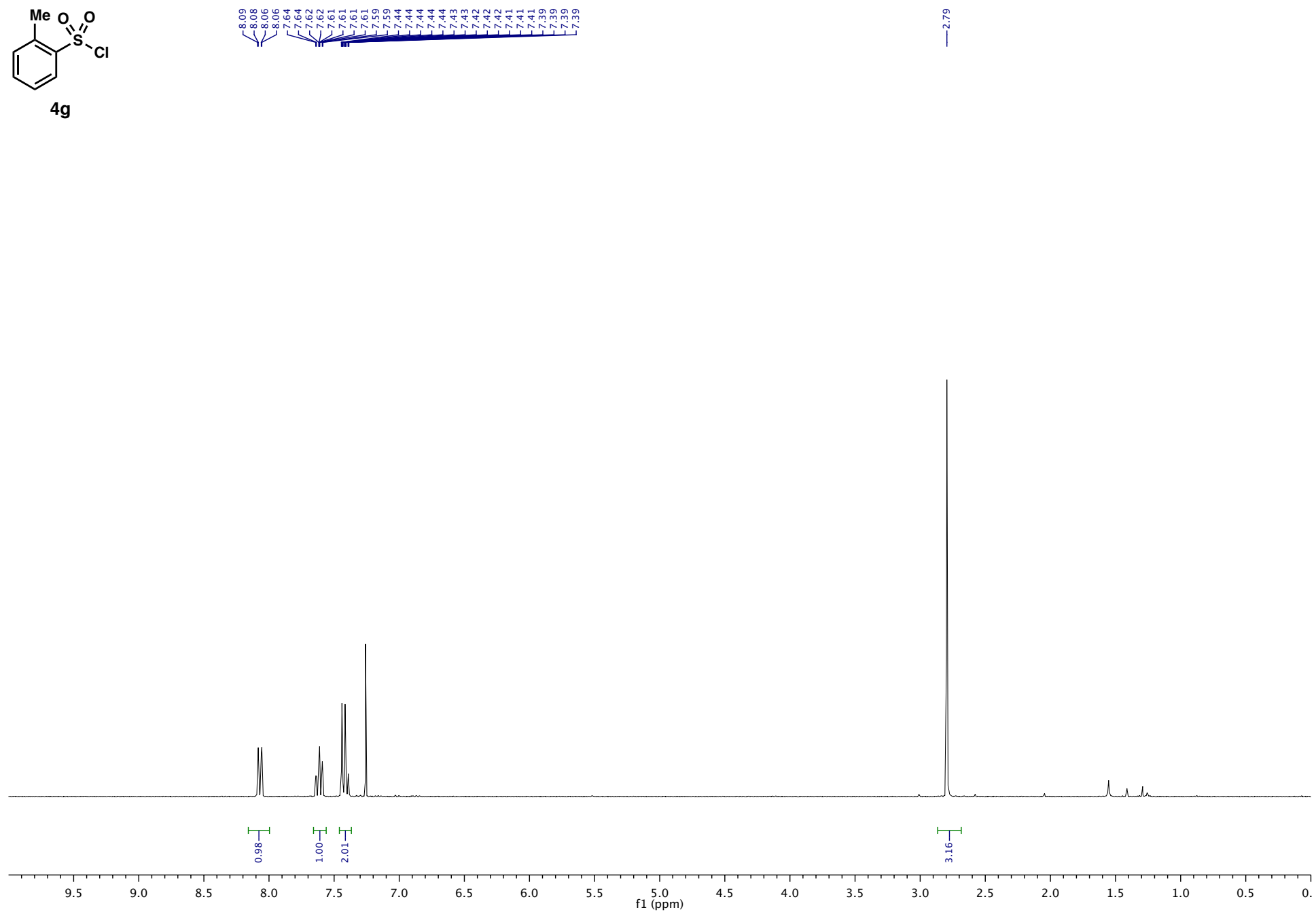
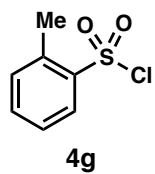
140.50  
140.46

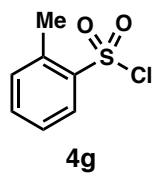
130.44  
130.31

117.52  
117.22



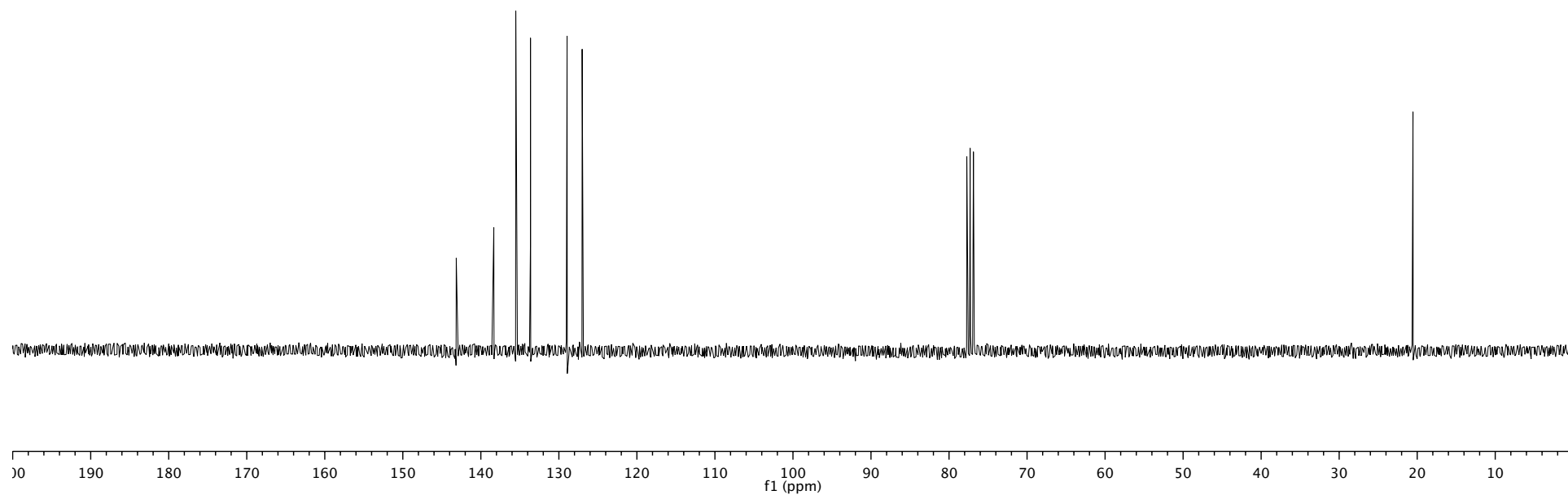




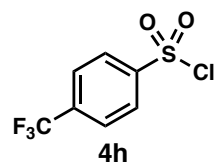


— 143.15  
 ~ 138.34  
 ~ 135.52  
 ~ 133.63  
 — 128.95  
 — 127.02

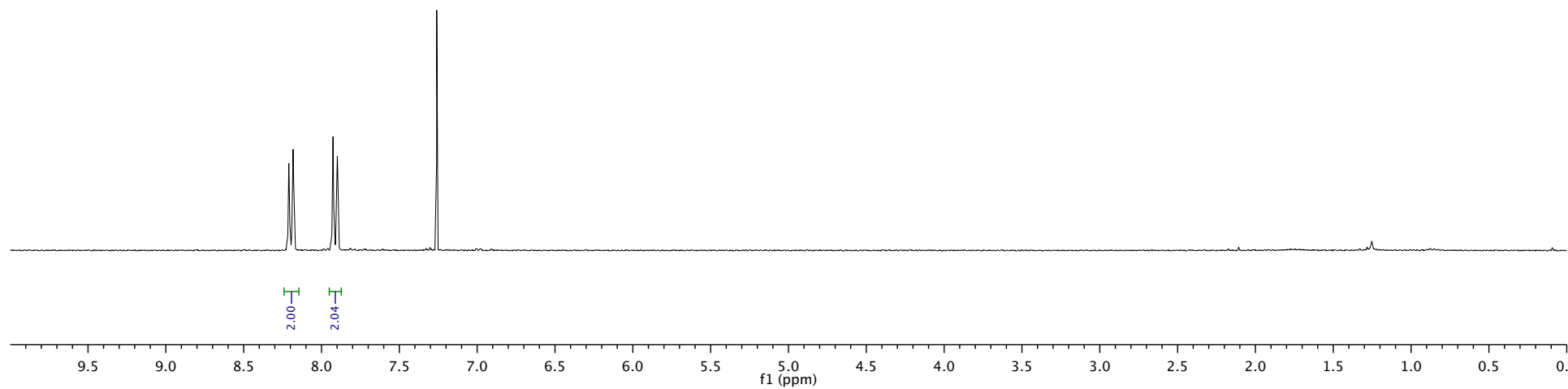
— 20.54

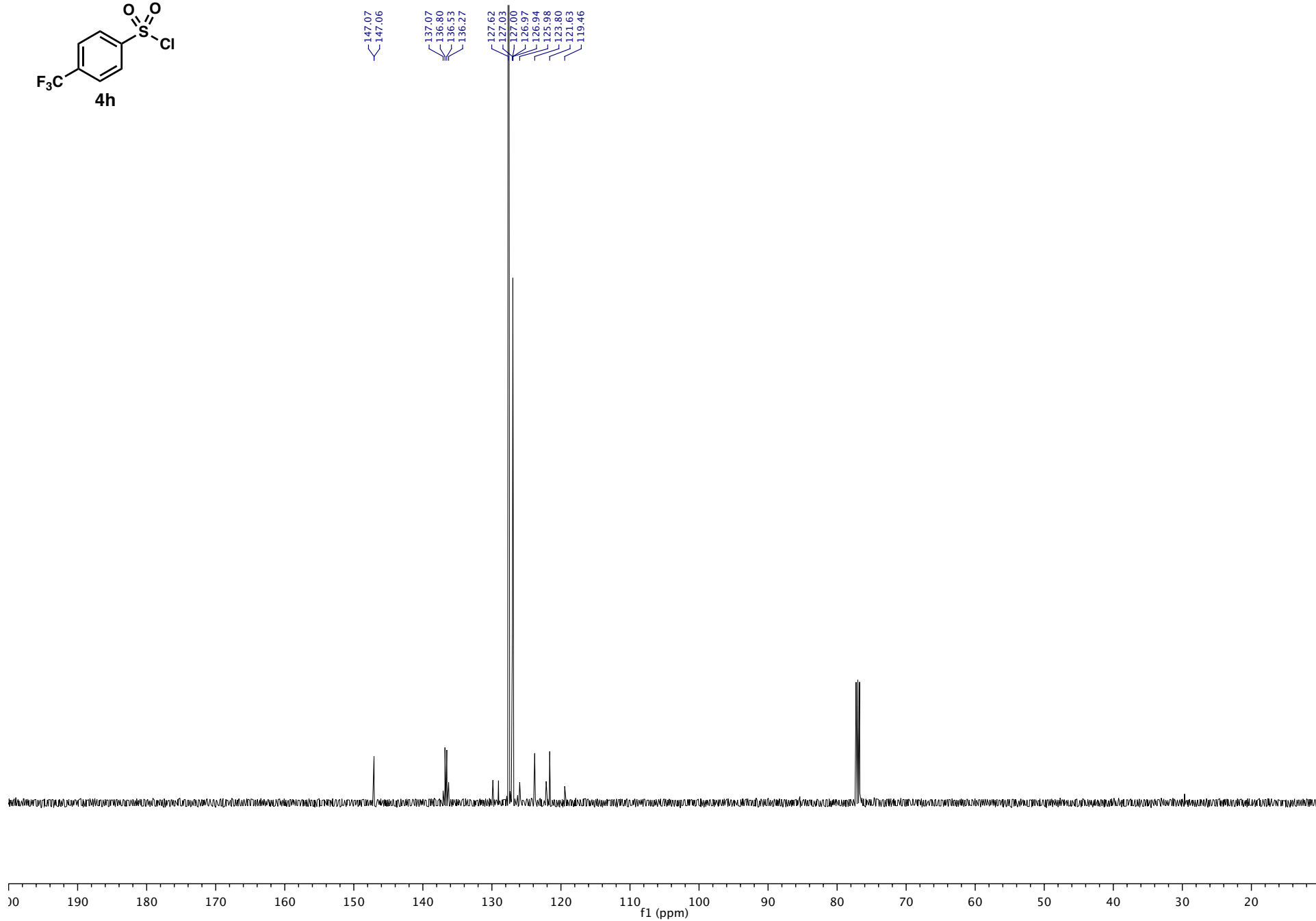
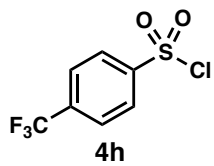


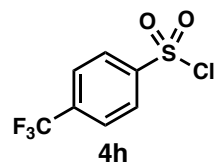




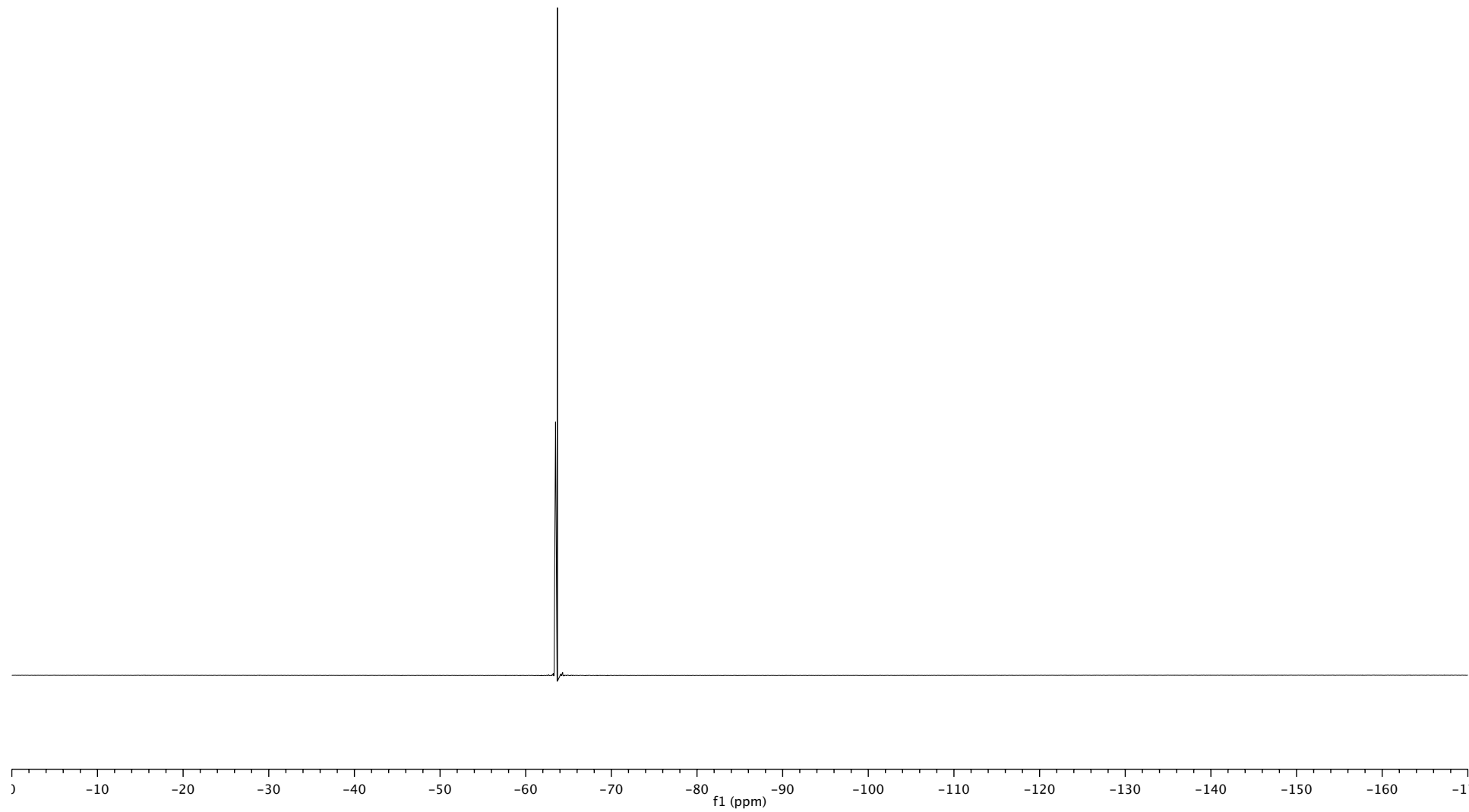
8.21  
8.18  
7.93  
7.90

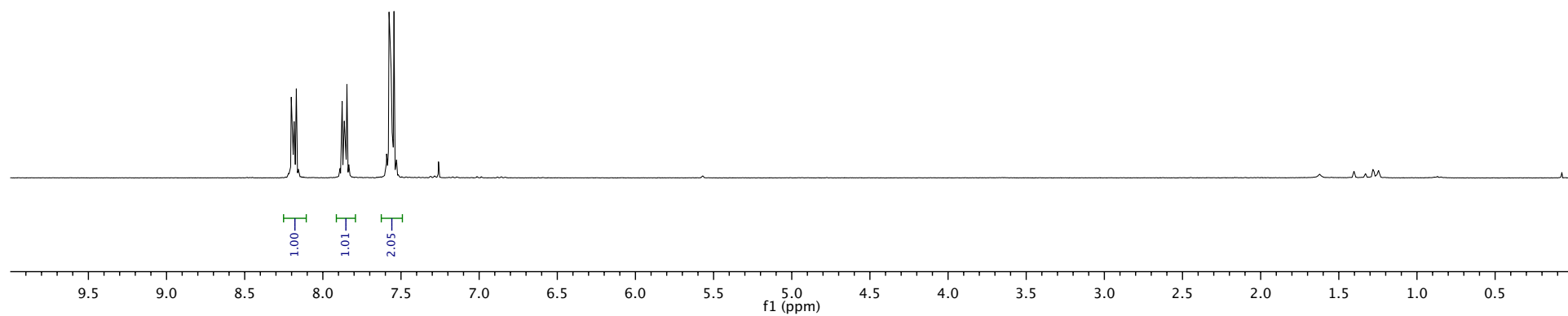
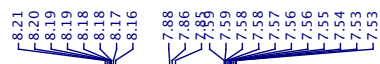
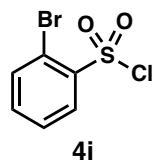


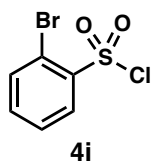




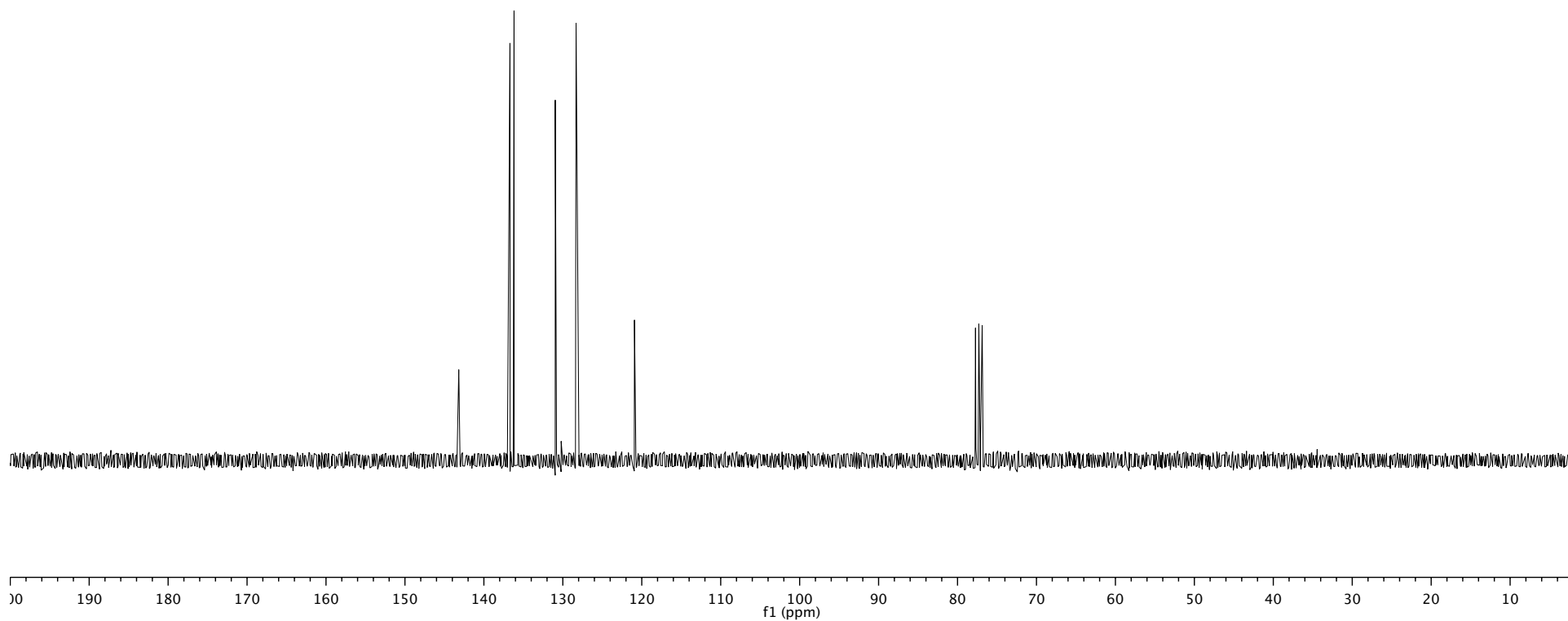
$\sim 63.48$   
 $\sim 63.70$  CF<sub>3</sub>Ph

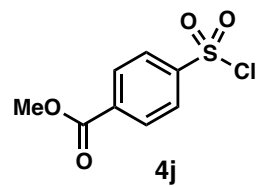






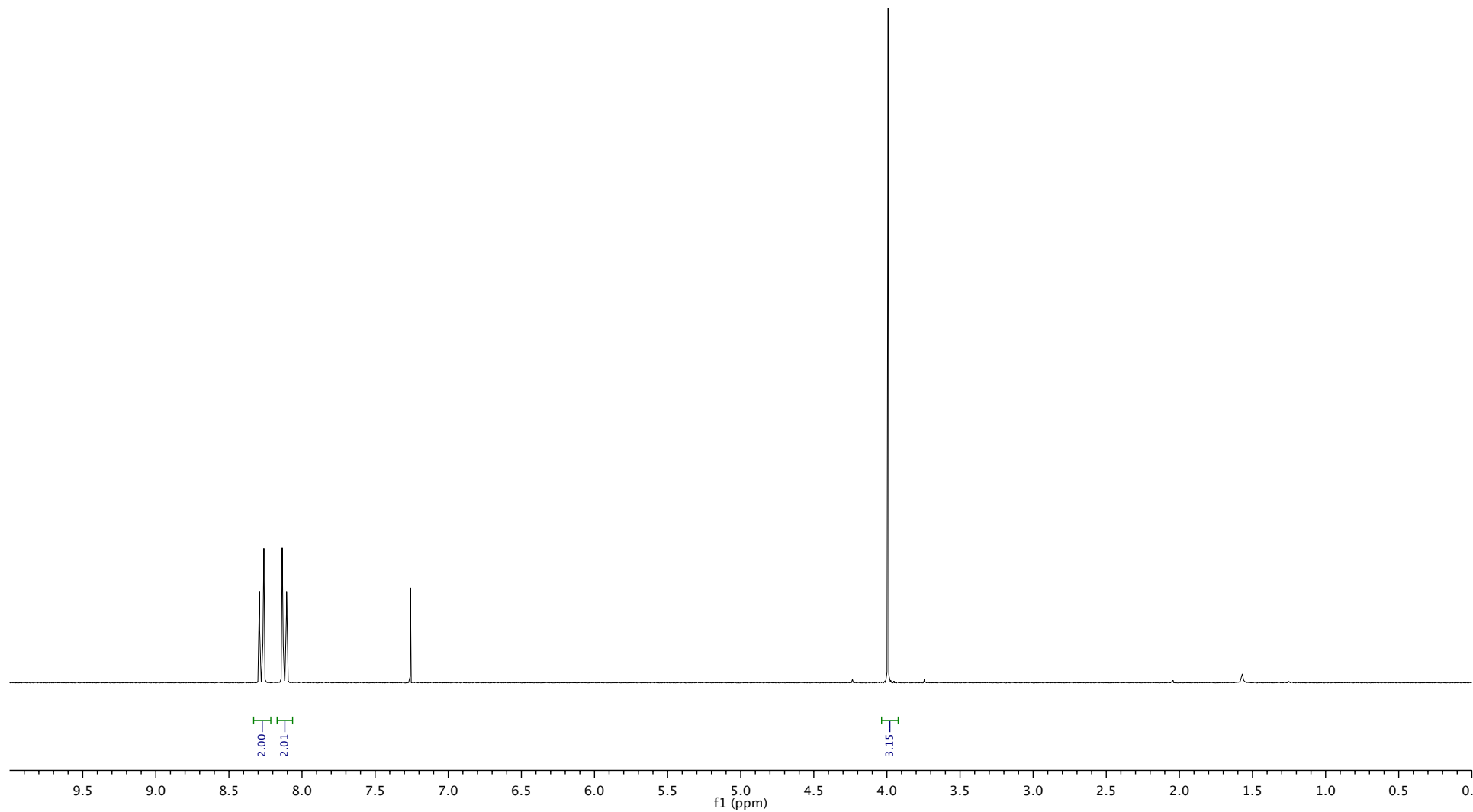
143.18  
 136.70  
 136.18  
 130.96  
 128.32  
 120.93

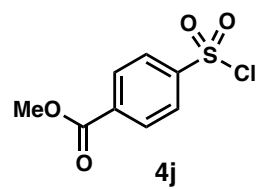




8.29  
8.26  
8.14  
8.11

3.99





— 165.10

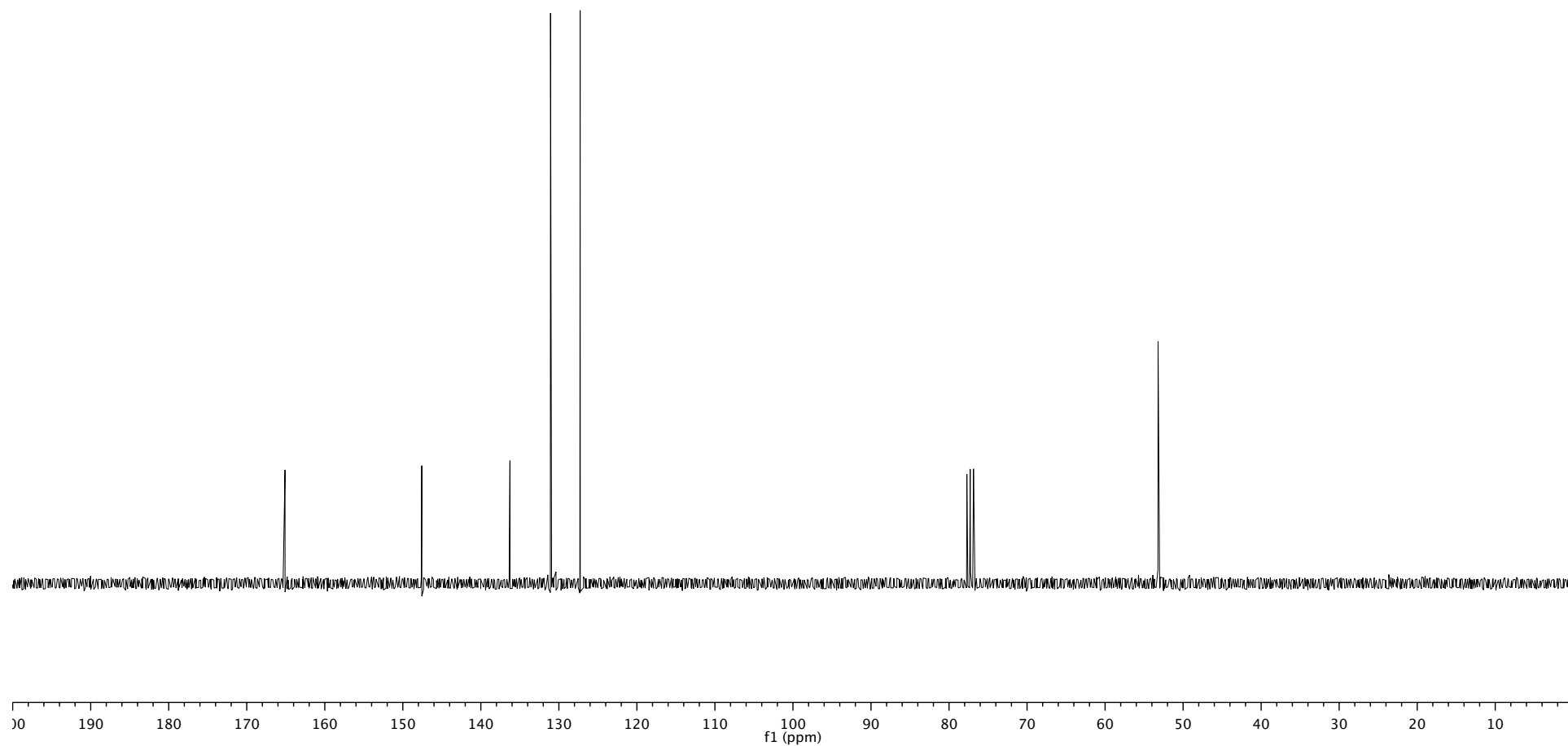
— 147.57

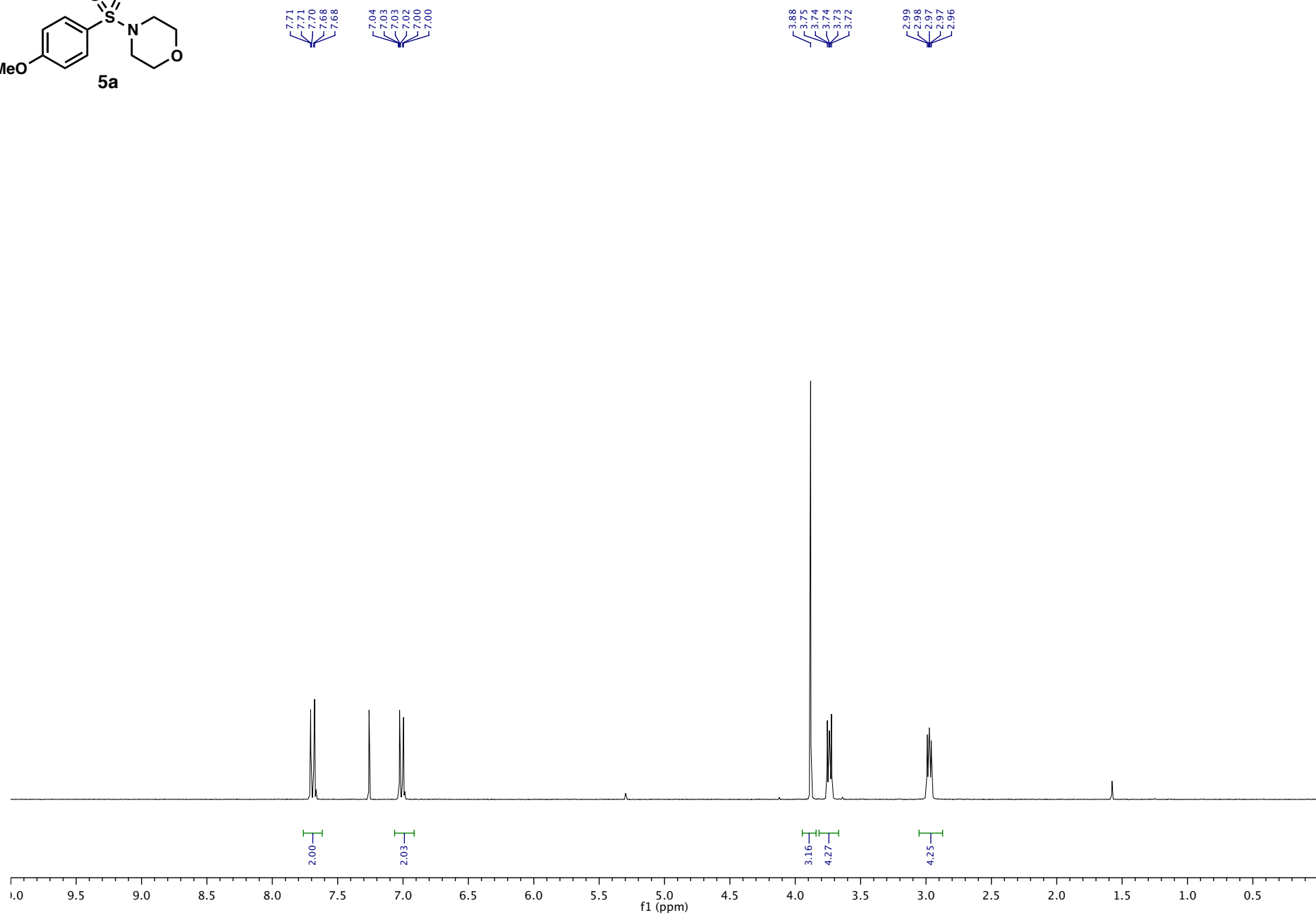
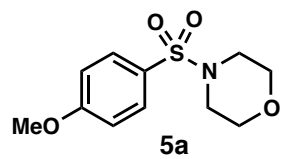
— 136.27

— 131.07

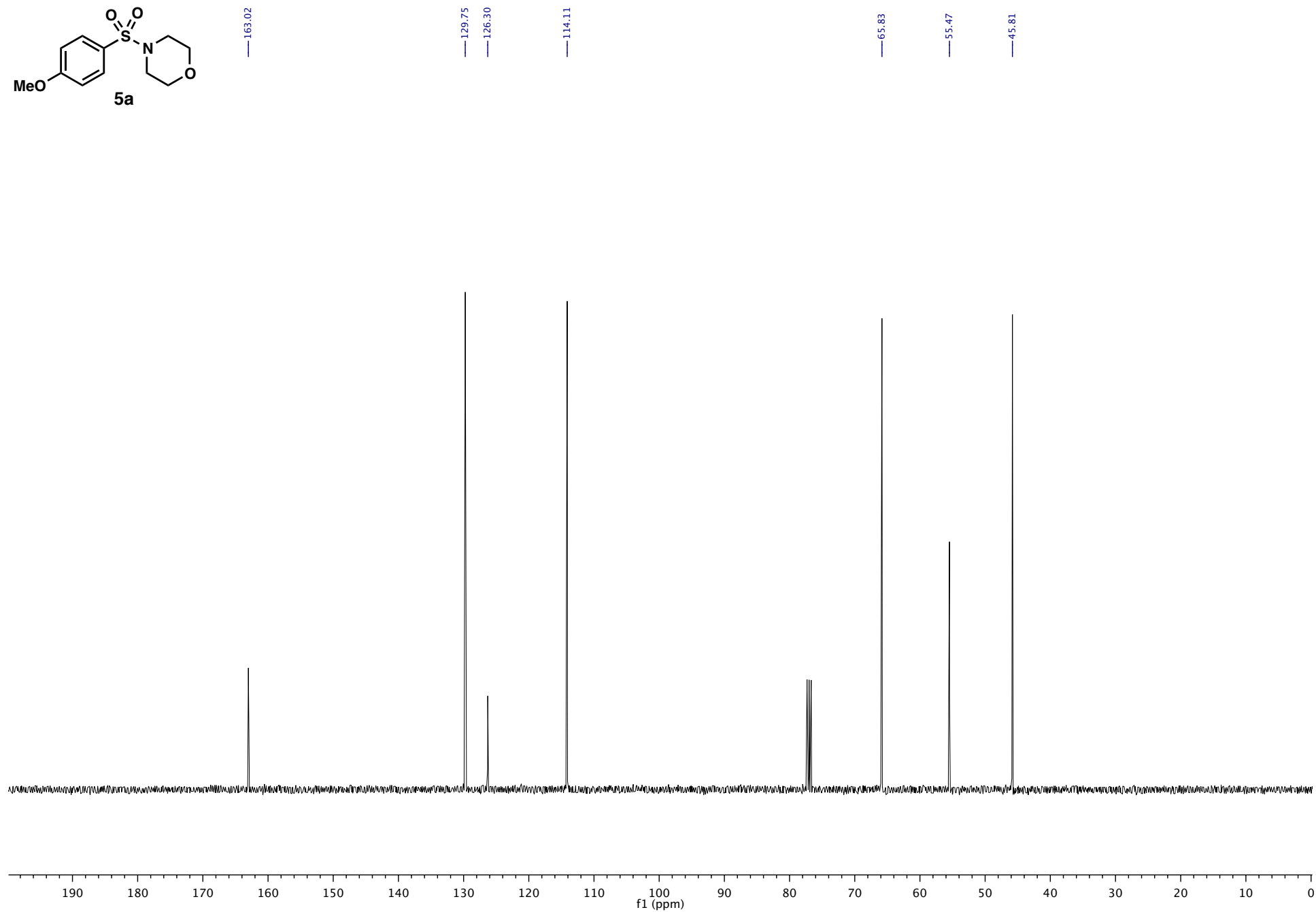
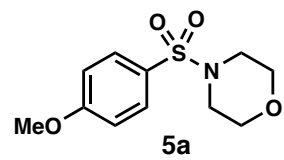
— 127.27

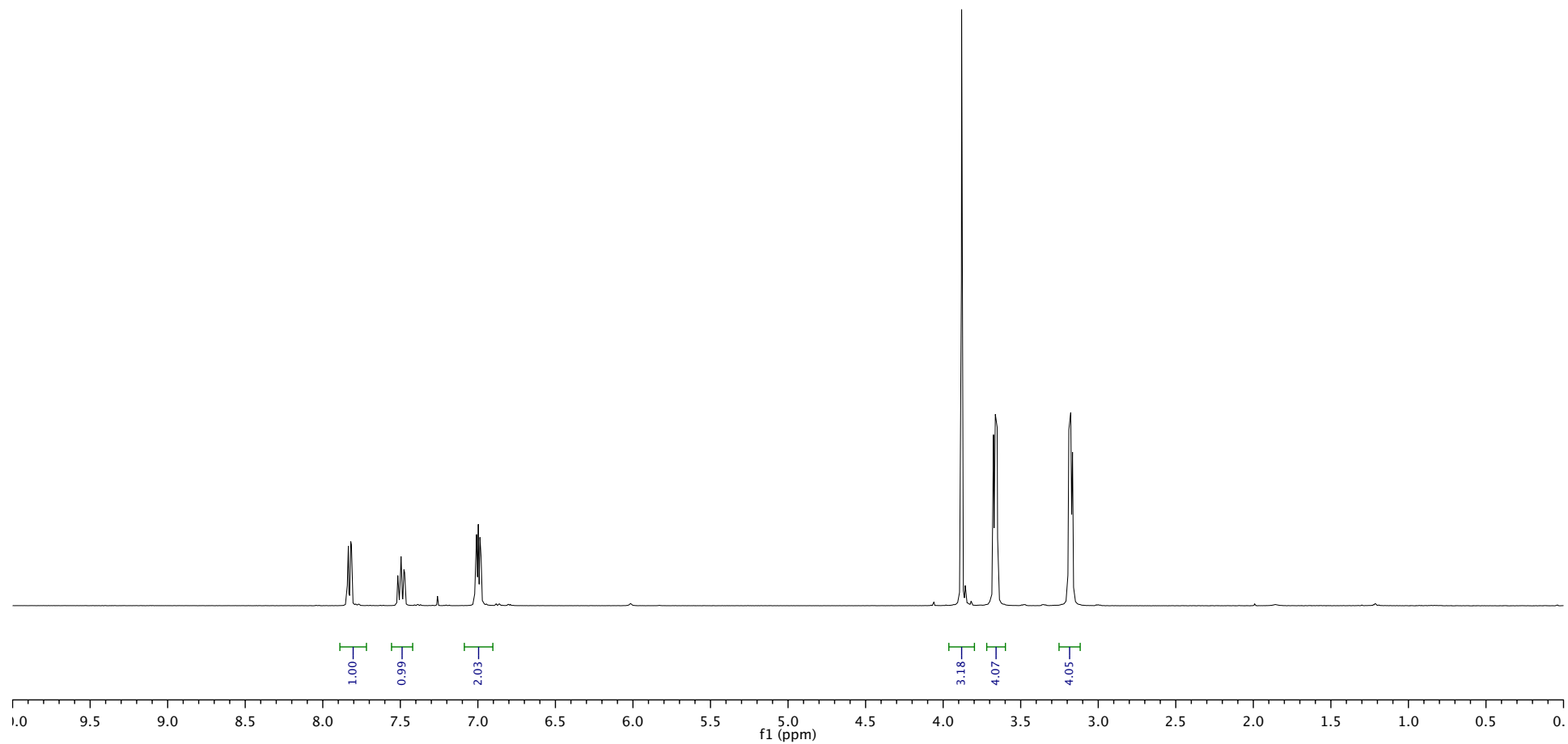
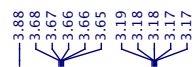
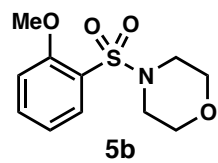
— 53.21

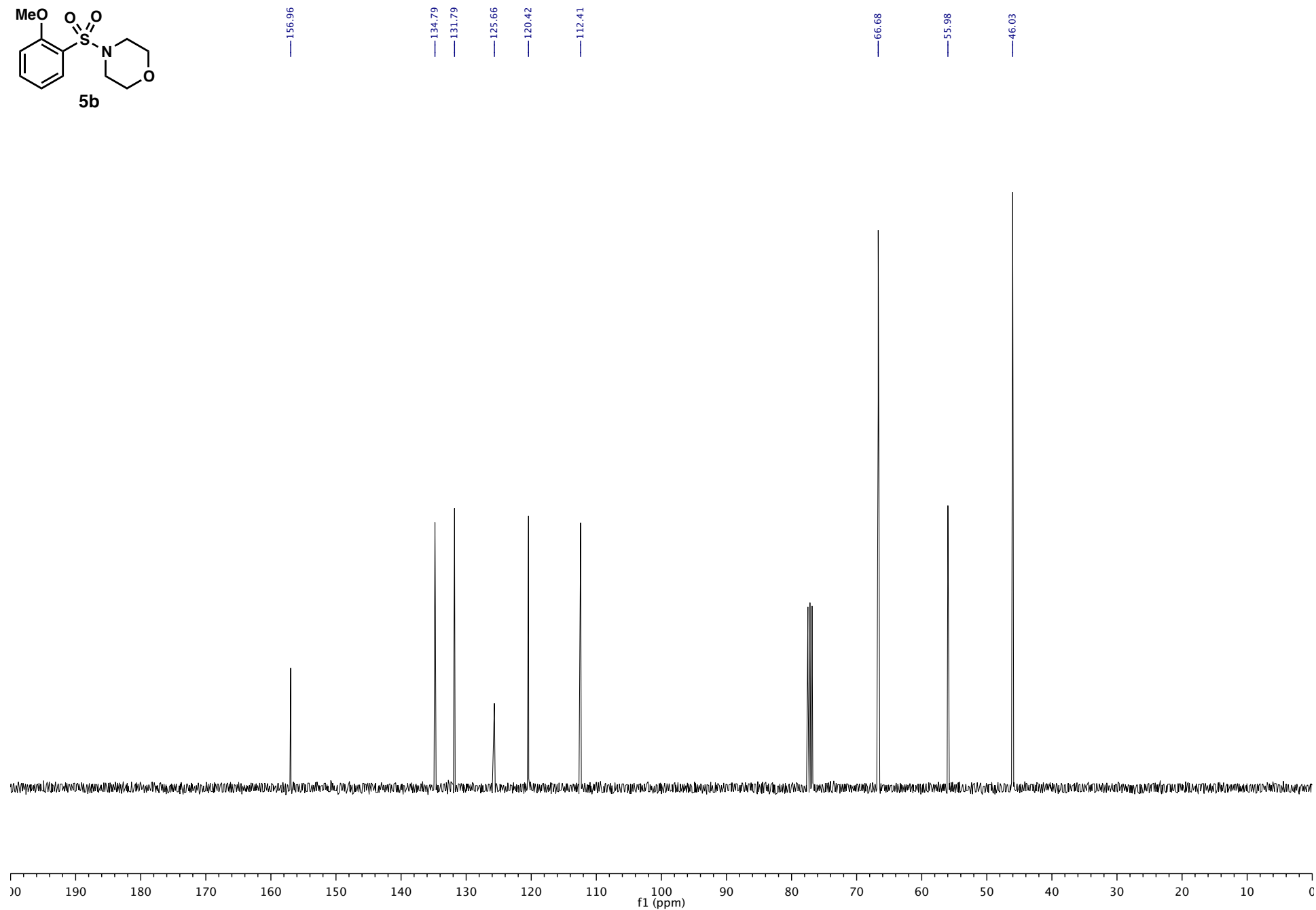
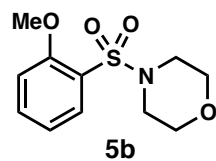


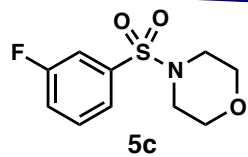








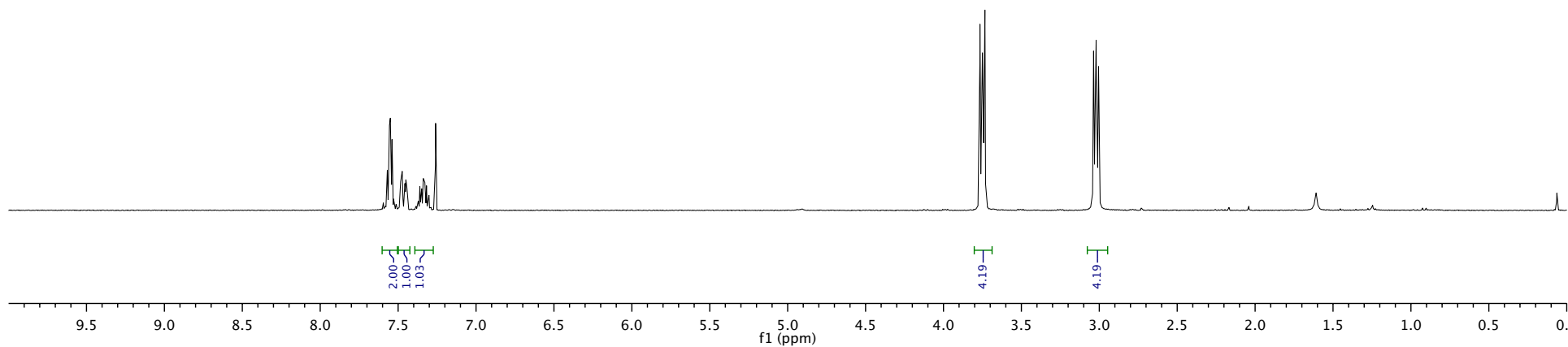


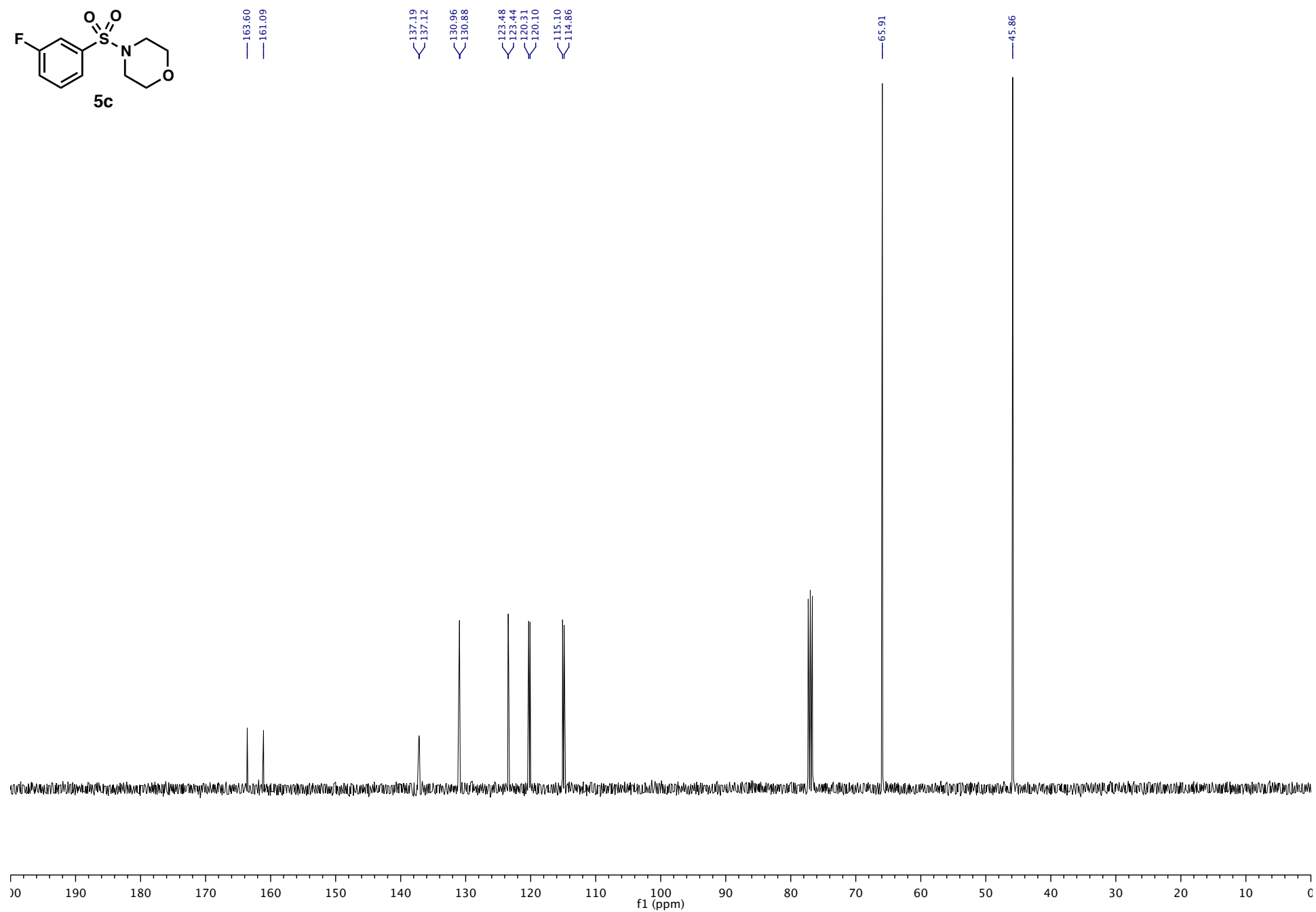
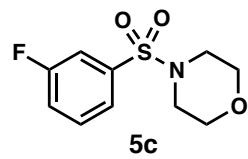


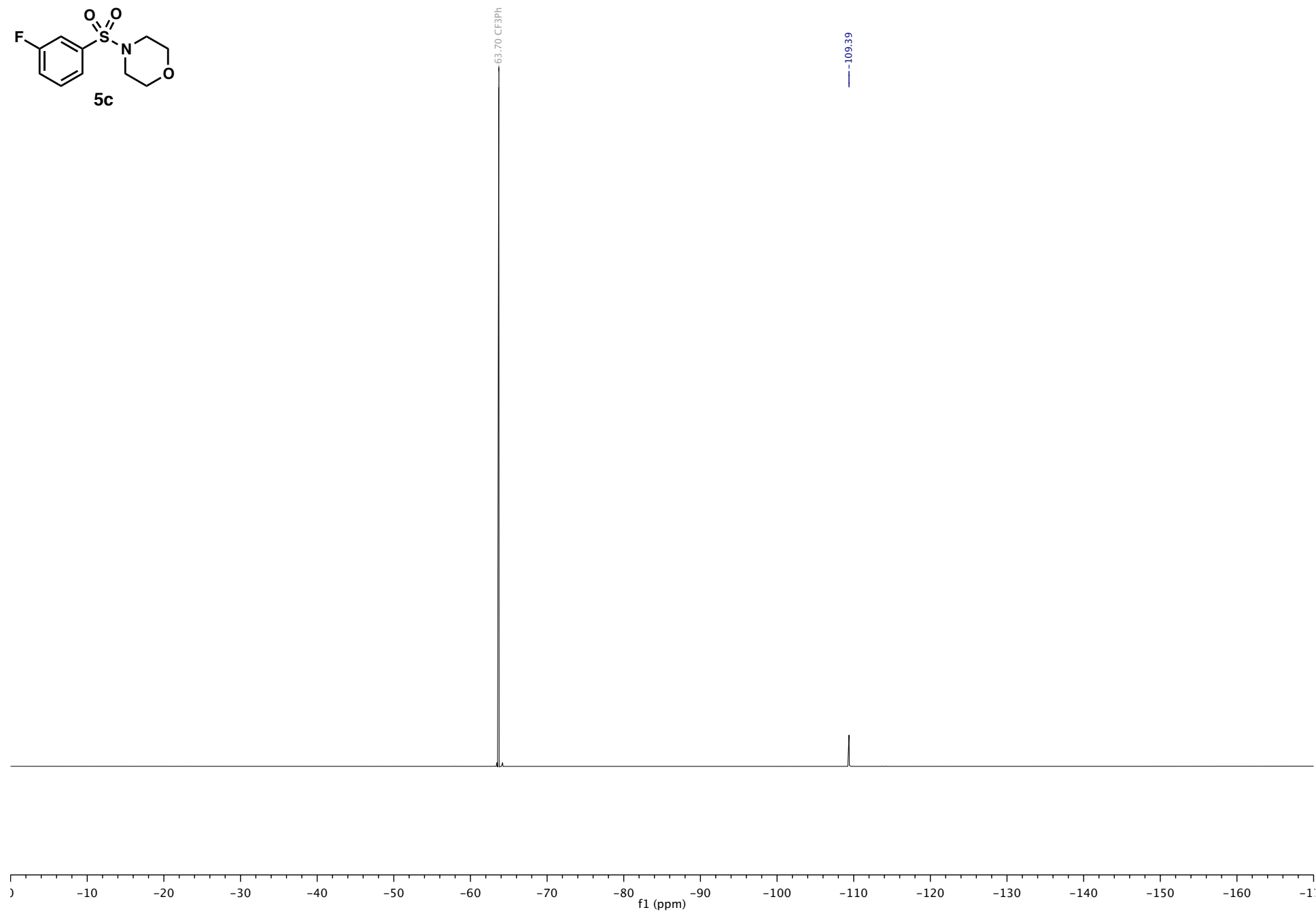
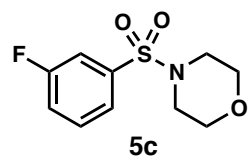
7.57  
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7.49  
7.48  
7.48  
7.47  
7.47  
7.46  
7.46  
7.45  
7.45  
7.45  
7.44  
7.44  
7.37  
7.36  
7.36  
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7.32  
7.32  
7.31  
7.30

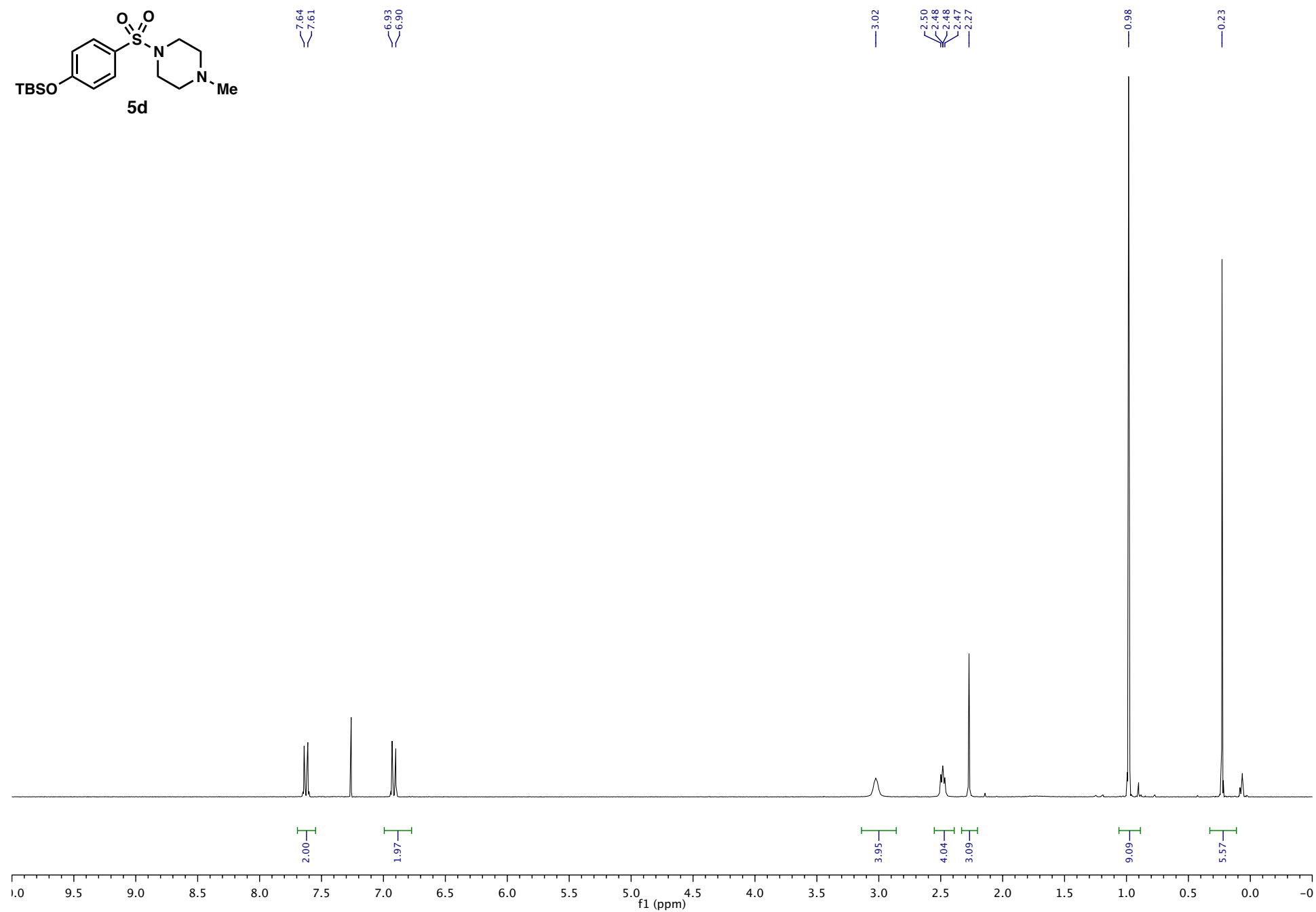
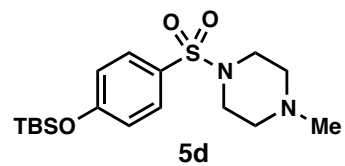
3.77  
3.76  
3.75  
3.74  
3.73

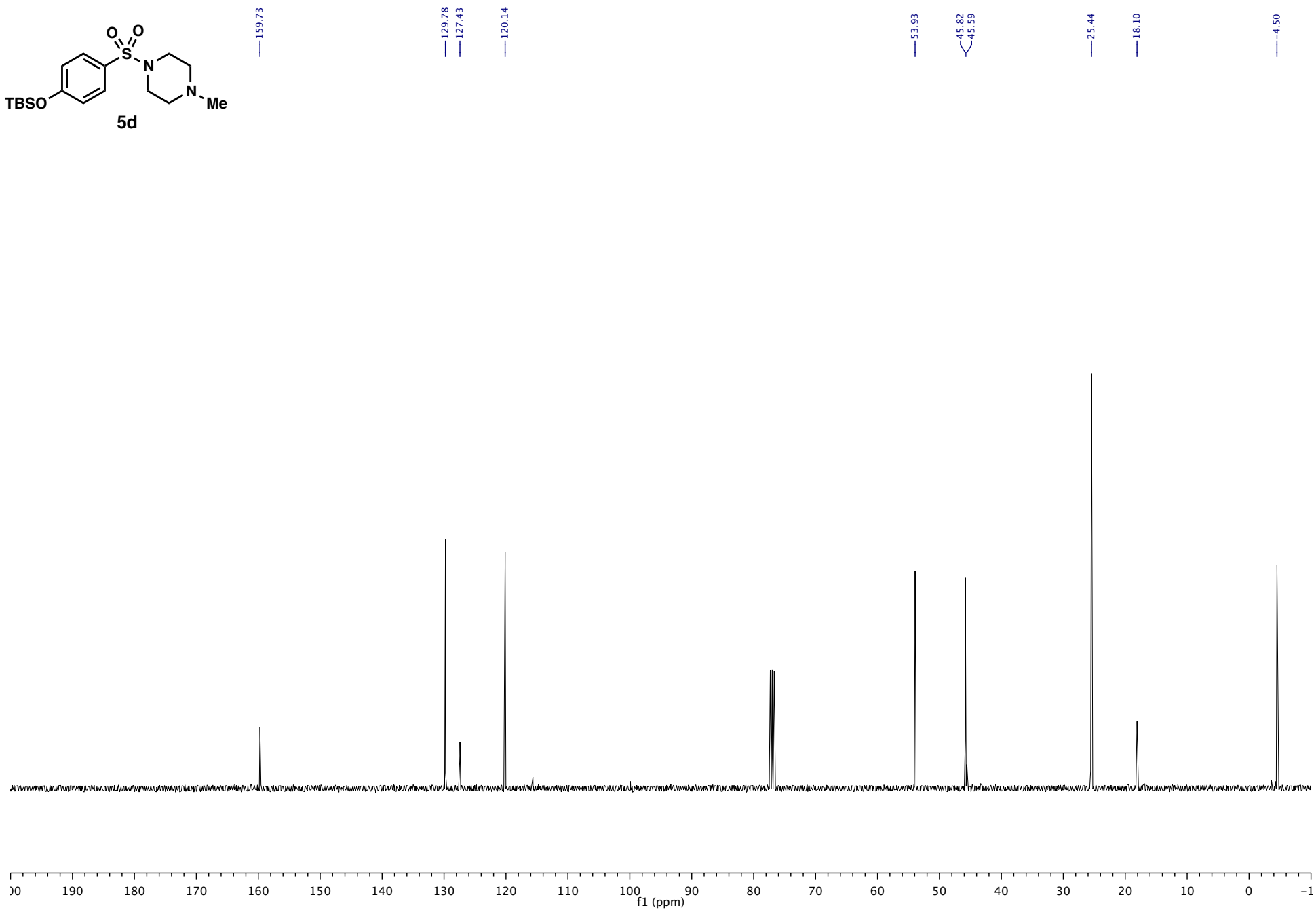
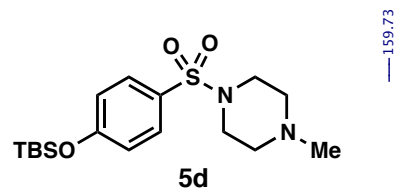
3.04  
3.03  
3.02  
3.01  
3.00



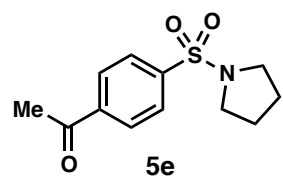










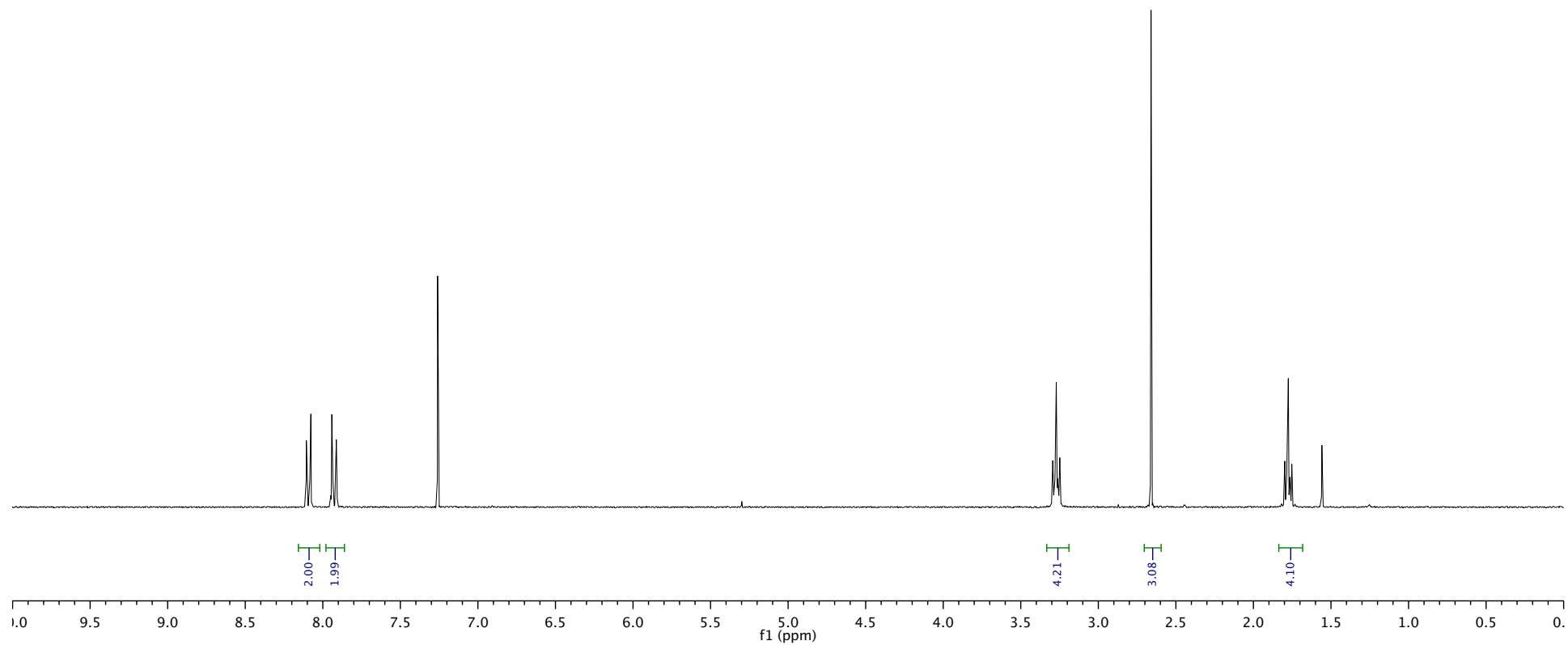


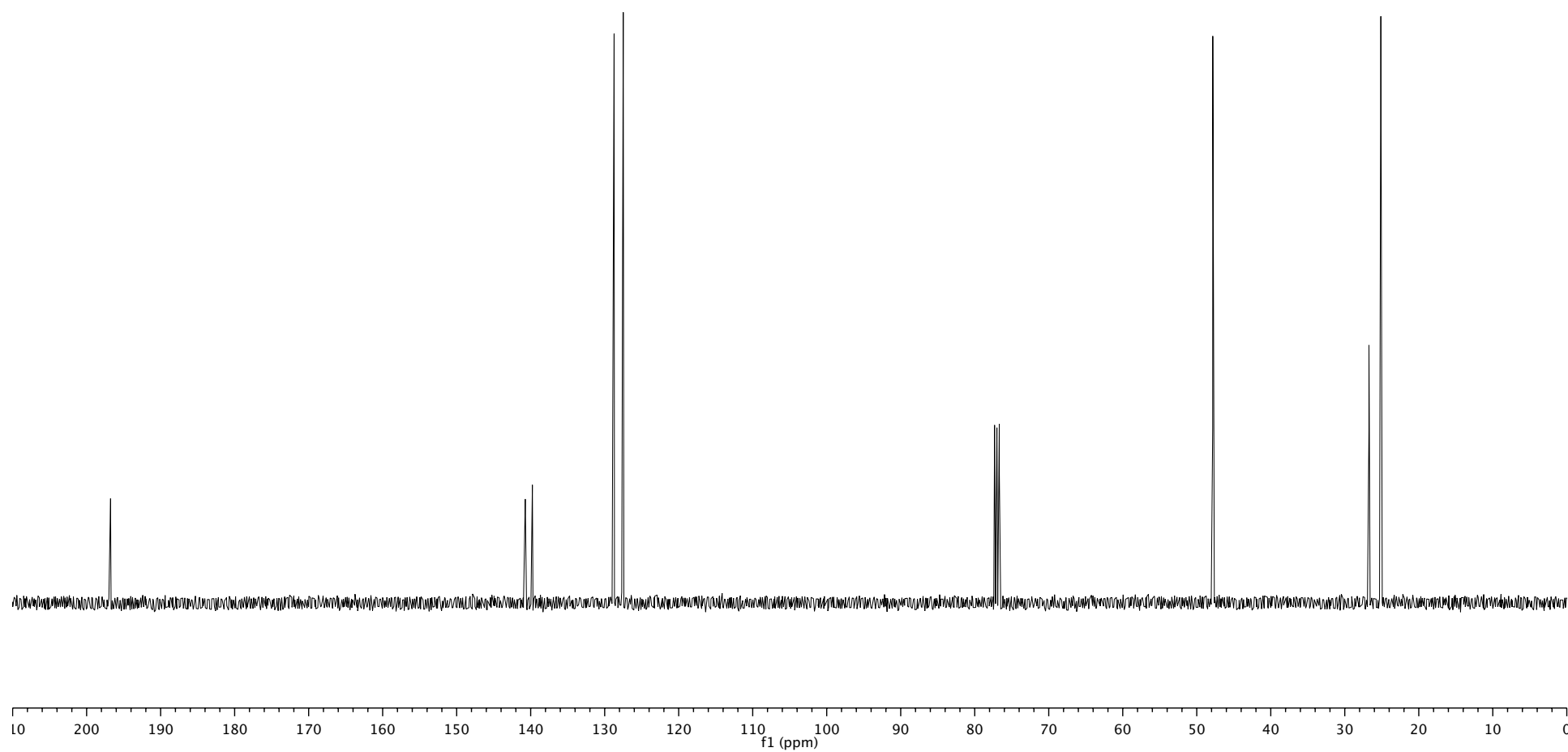
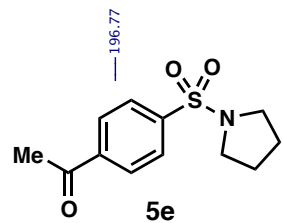
8.11  
8.08  
7.94  
7.91

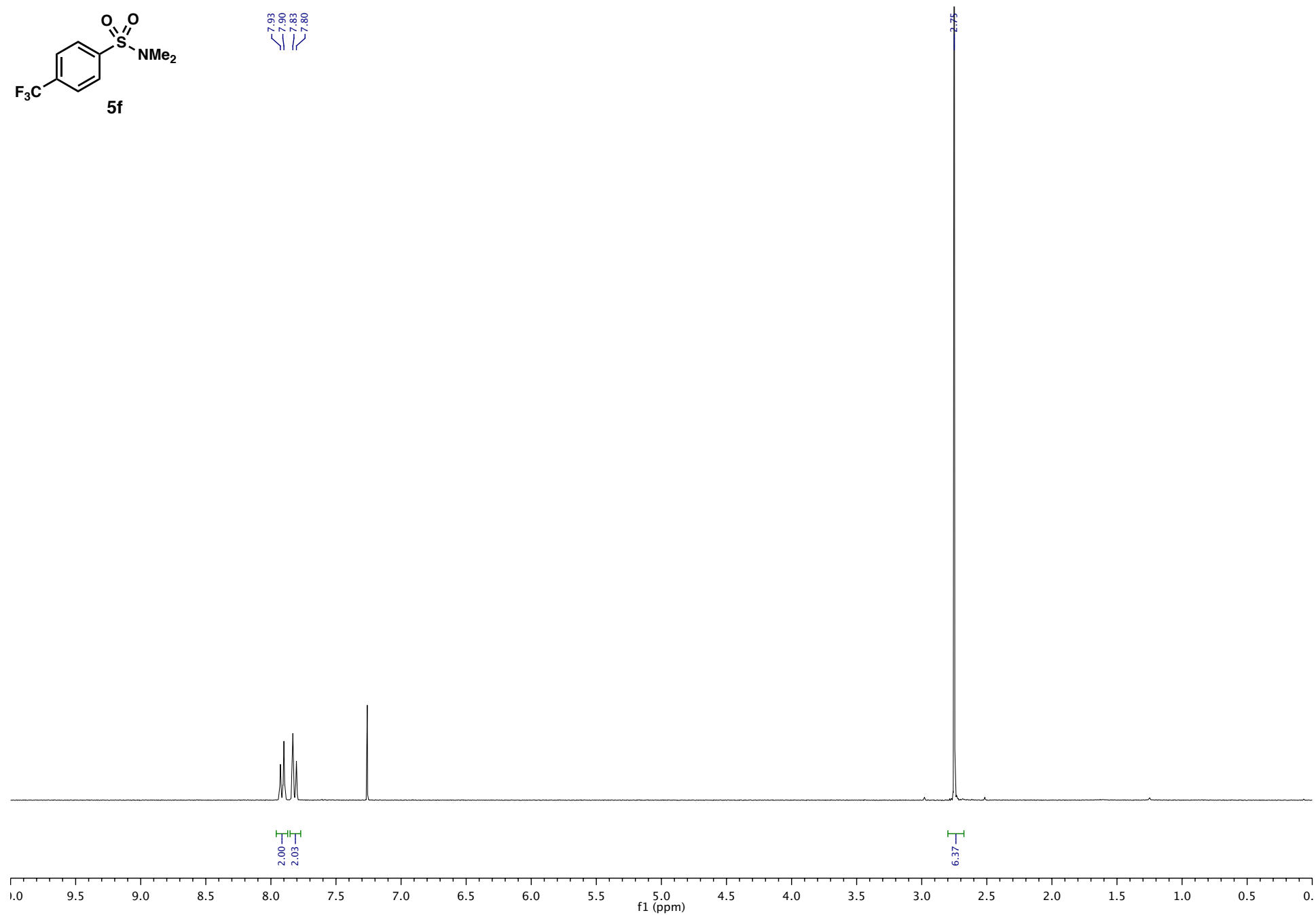
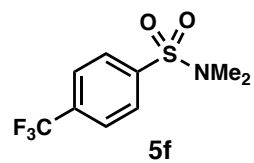
3.29  
3.28  
3.26  
3.27  
3.26  
3.25

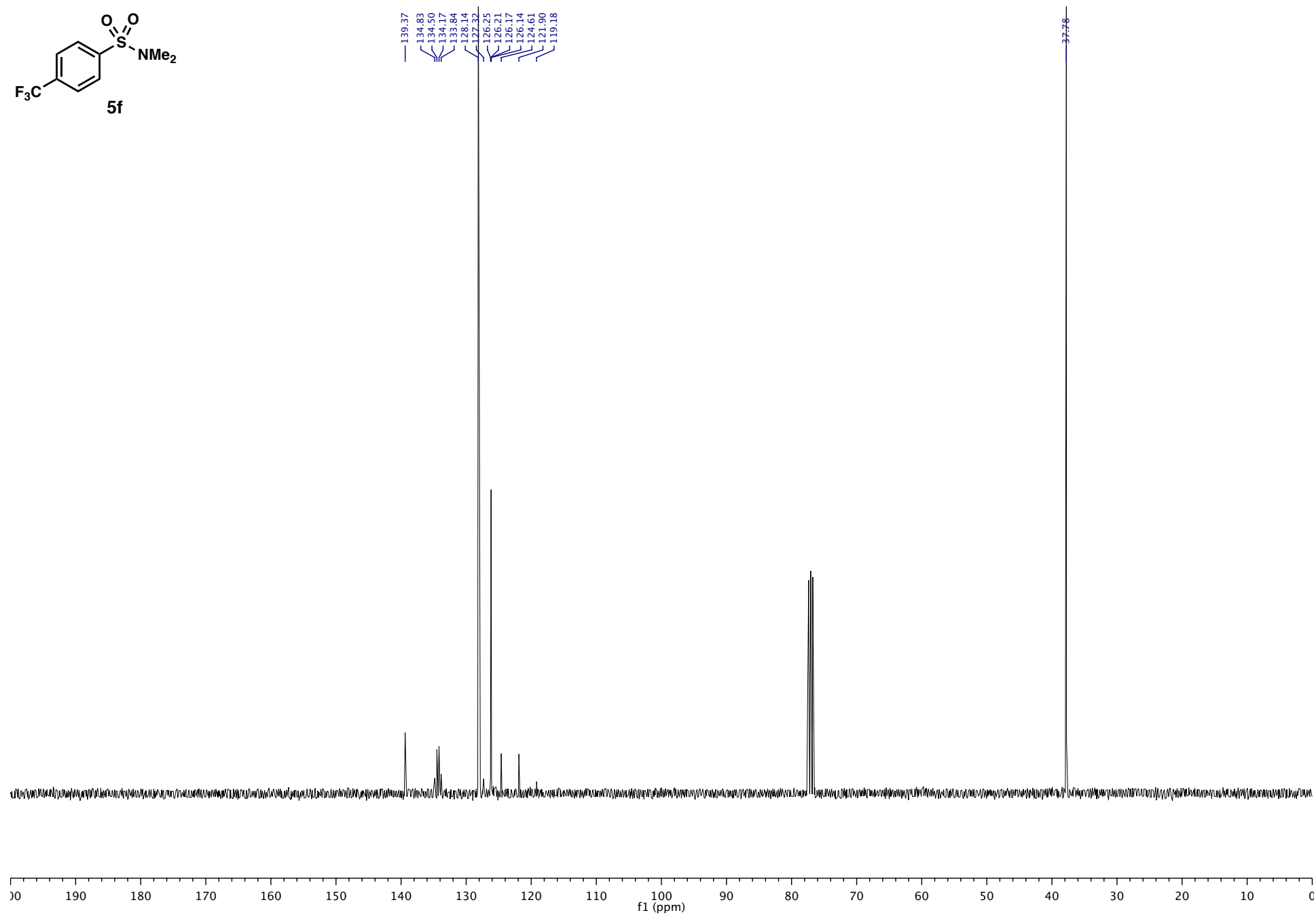
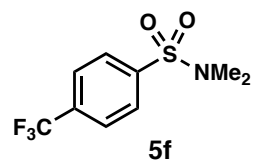
2.66

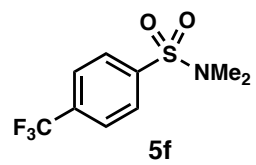
1.80  
1.79  
1.78  
1.78  
1.77  
1.76  
1.75



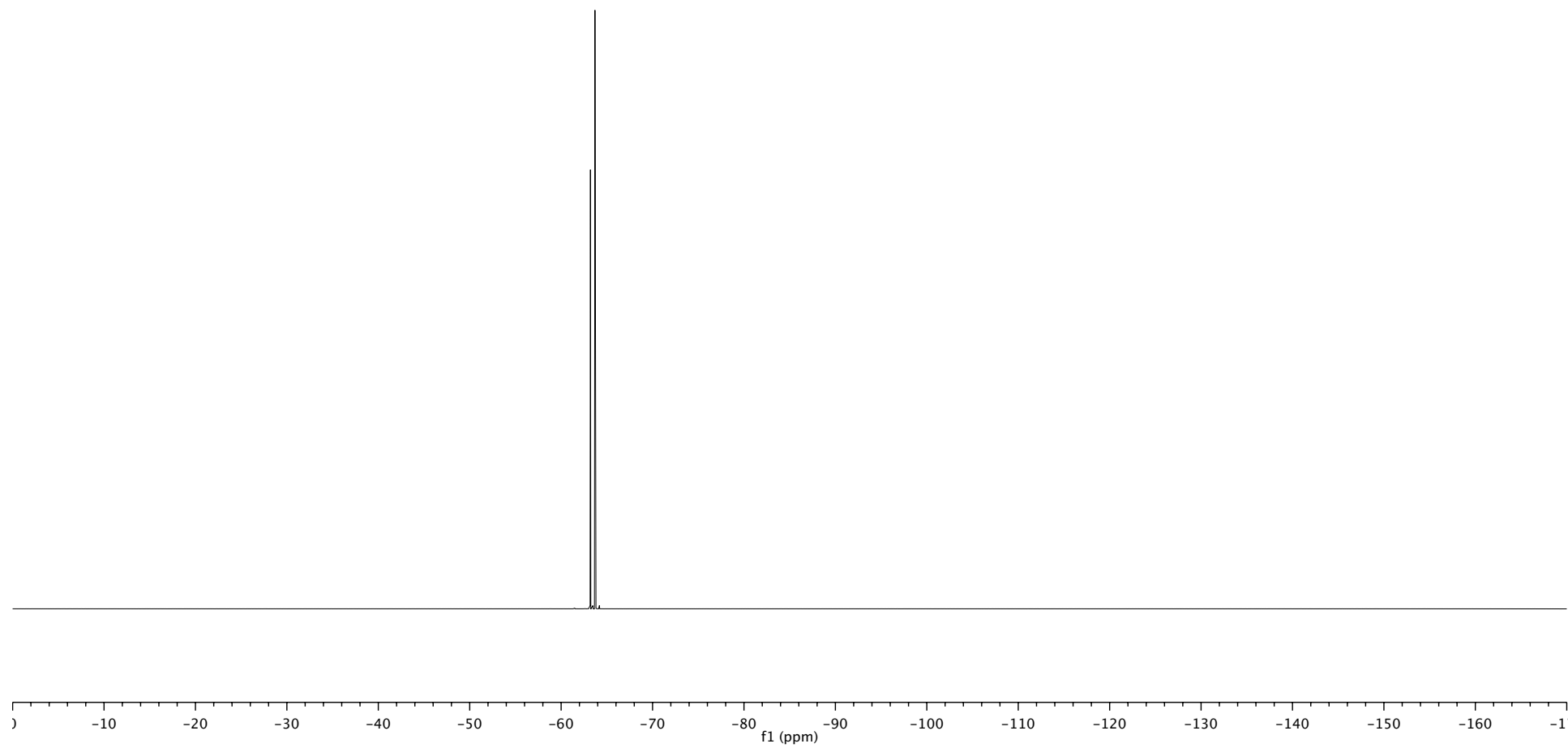




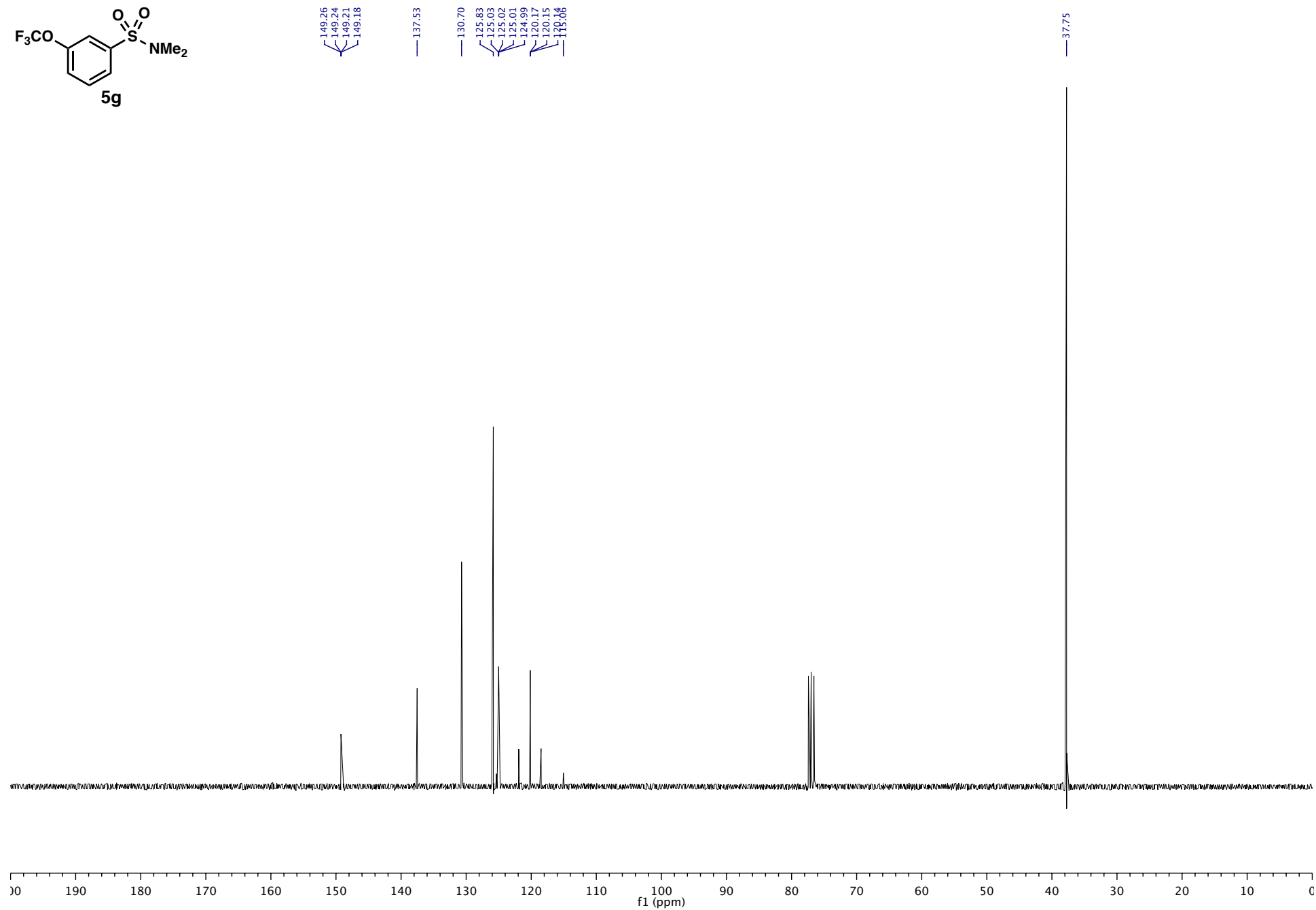
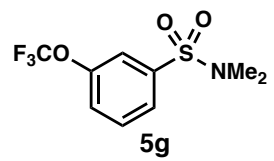


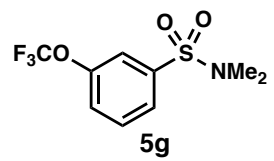


-63.21  
 -63.70 CF<sub>3</sub>ph



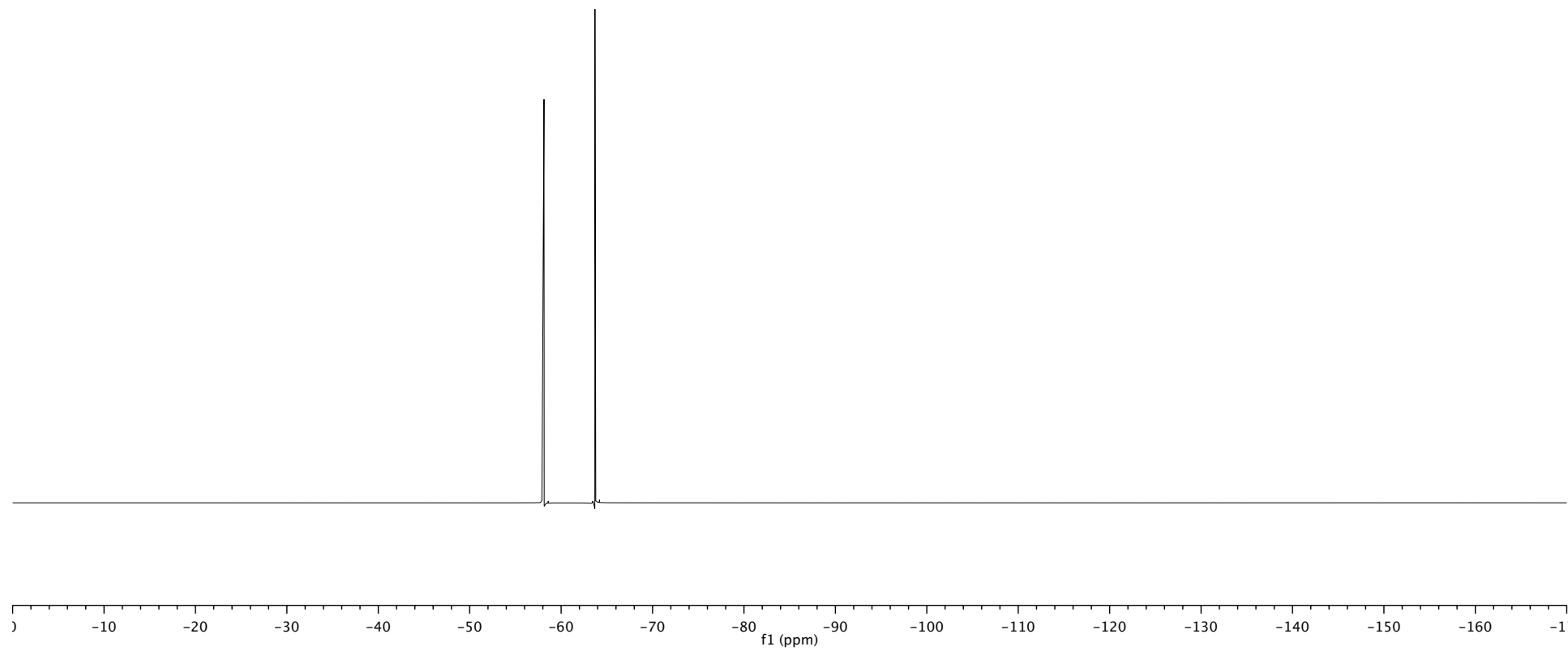




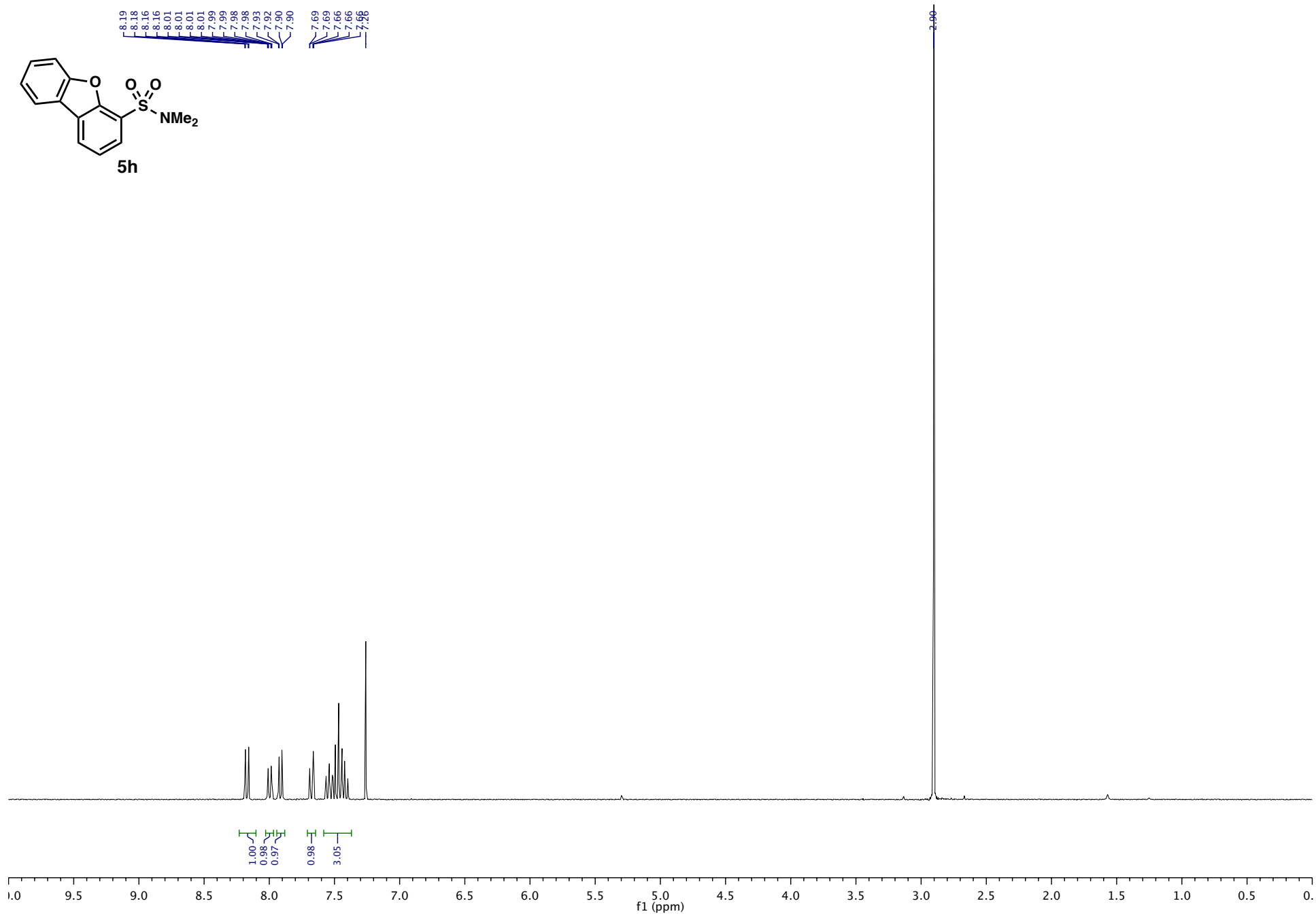


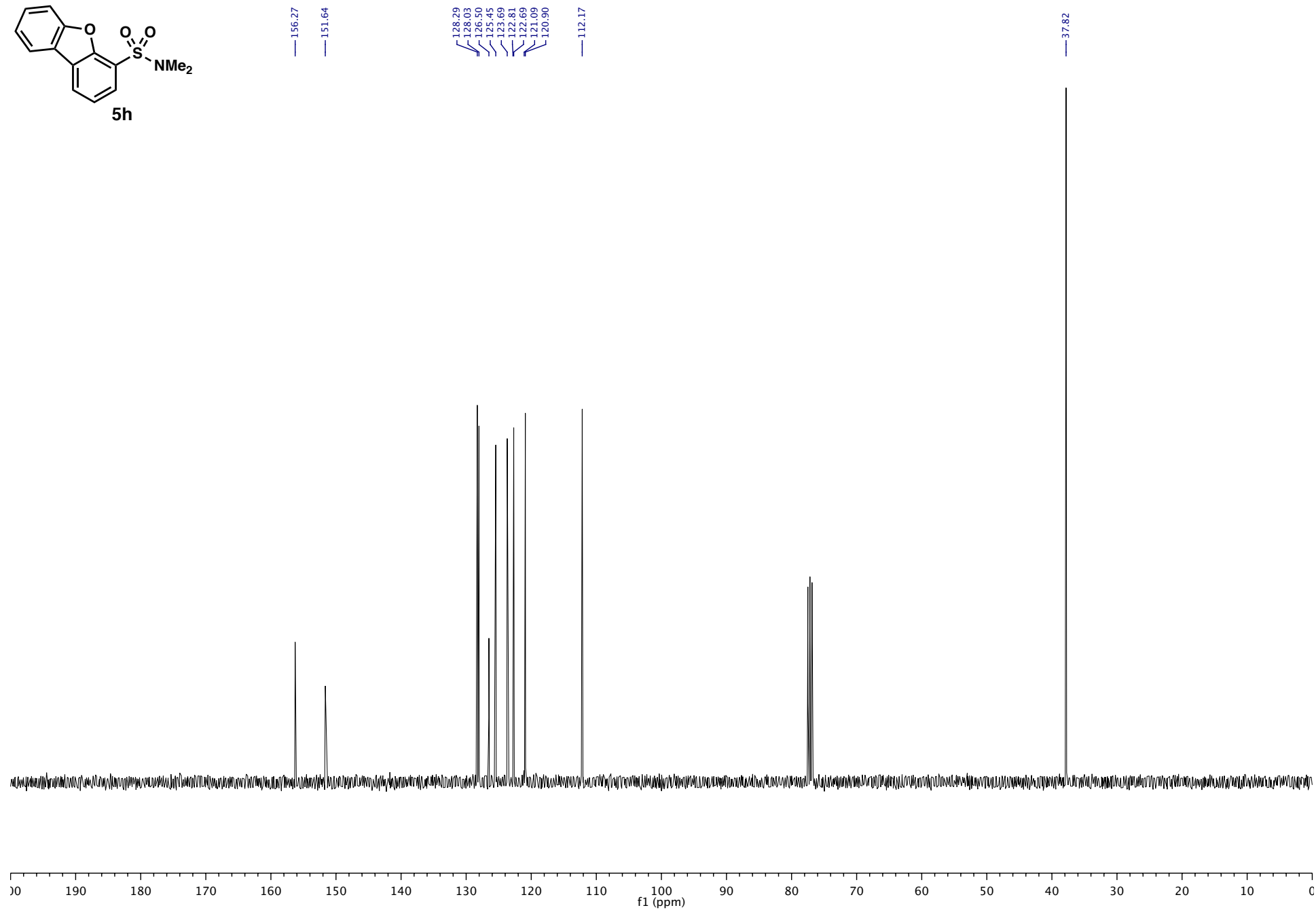
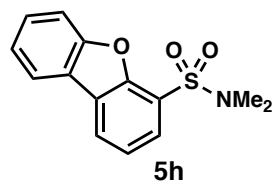
— -58.13

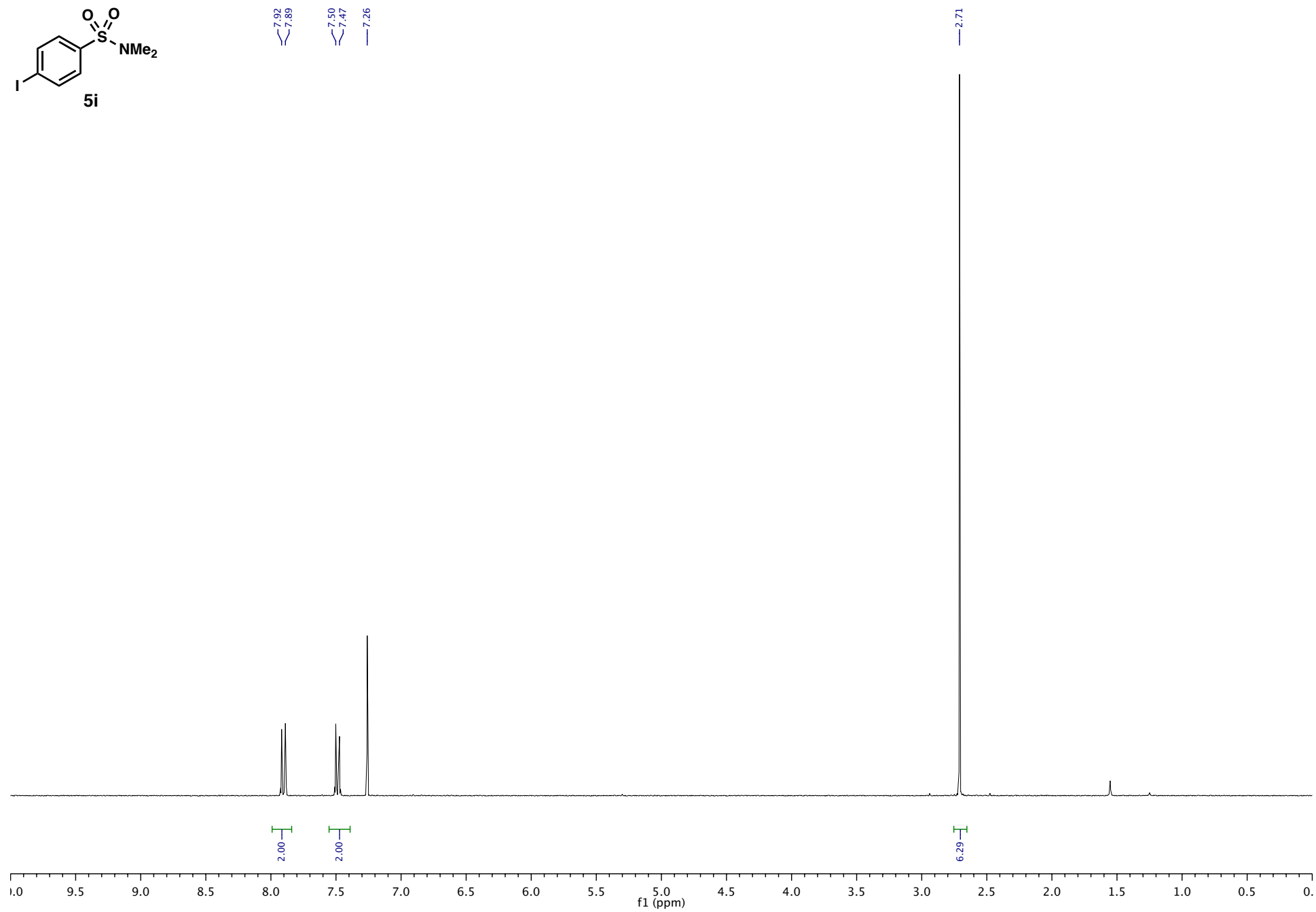
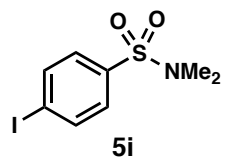
— -63.70 CF3Ph

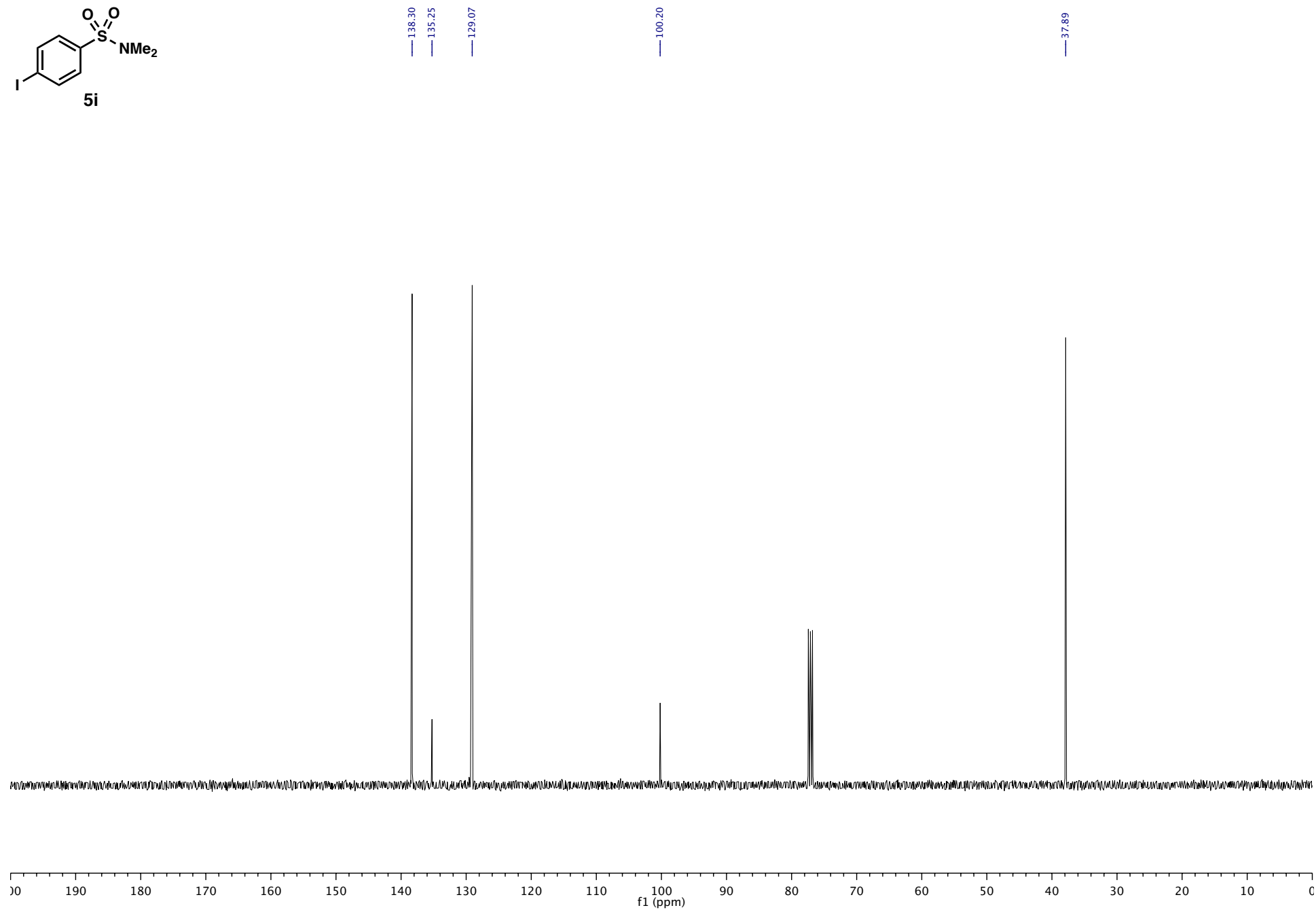
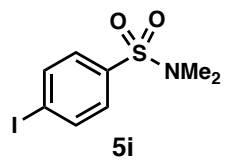


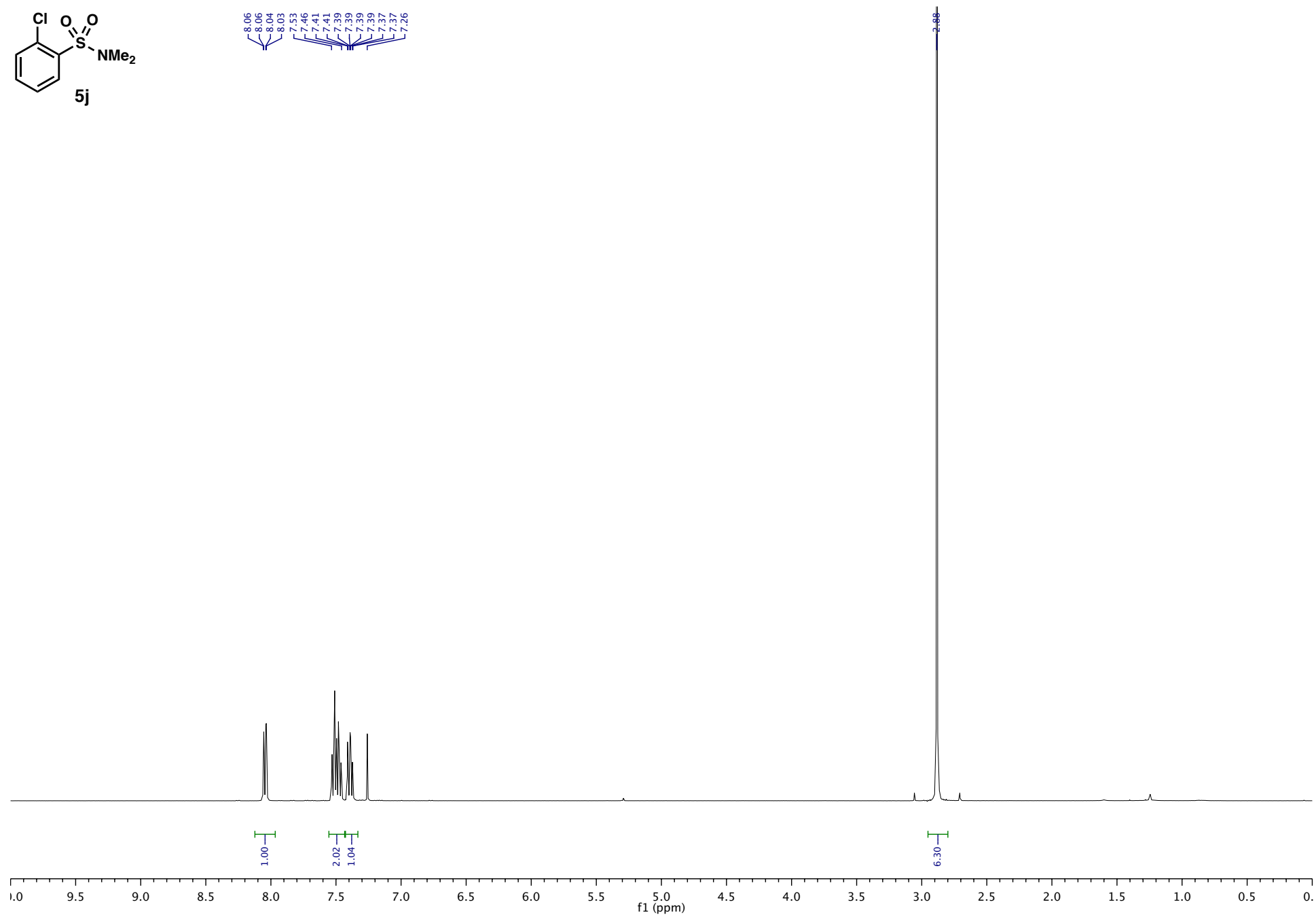
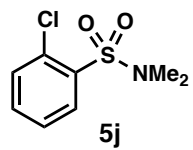


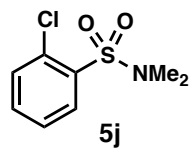






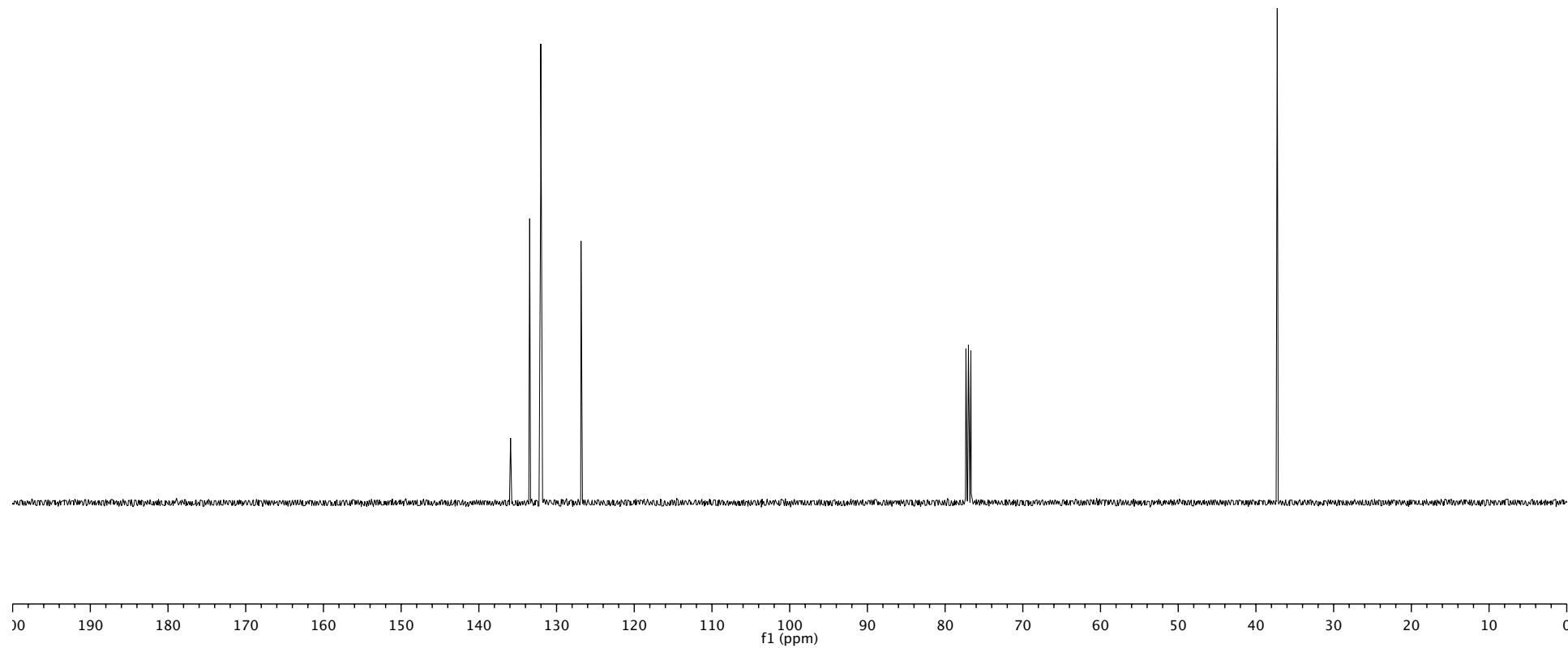


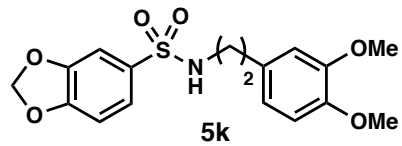




135.92  
133.46  
132.10  
132.04  
126.85

37.26





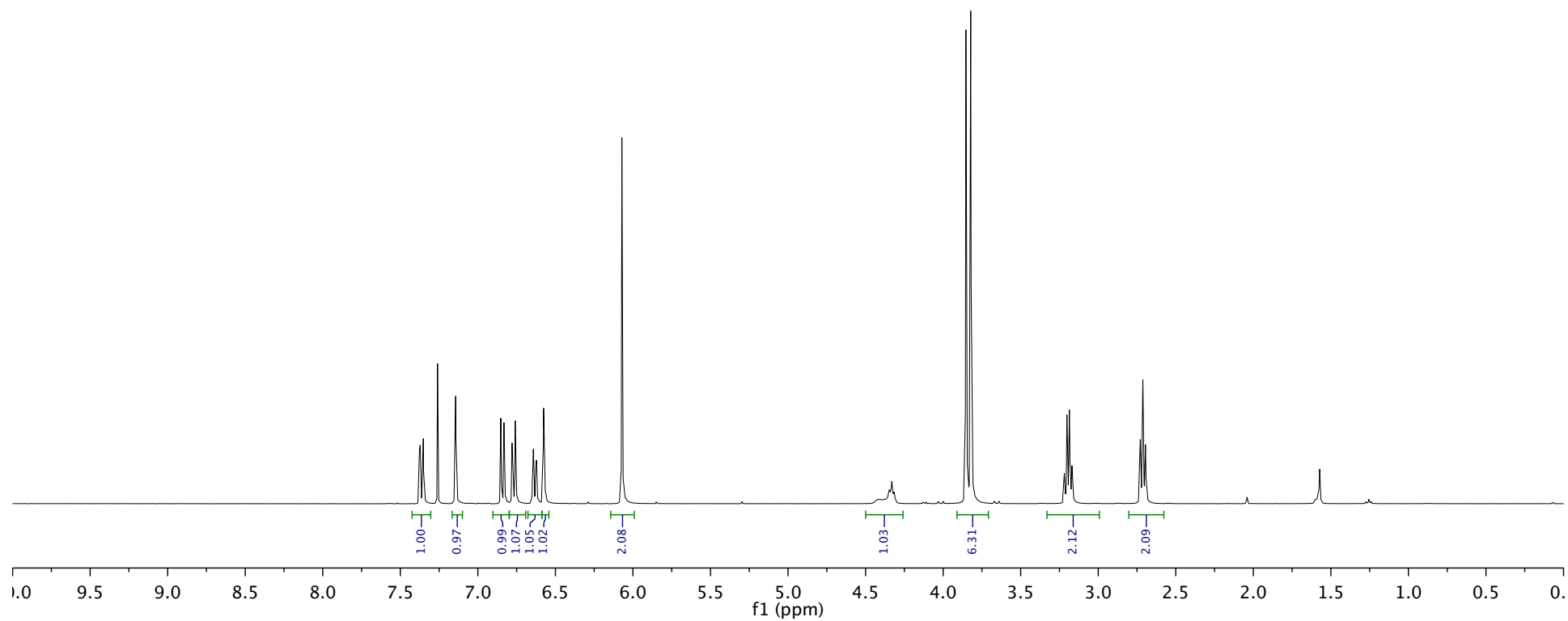
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 7.356  
 7.352  
 7.148  
 7.143  
 6.852  
 6.831  
 6.779  
 6.759  
 6.647  
 6.642  
 6.627  
 6.622  
 6.576  
 6.571  
 — 6.071

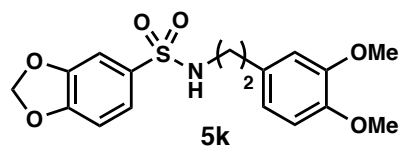
4.410  
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 4.315

3.853  
 3.822

3.219  
 3.202  
 3.186  
 3.169

2.729  
 2.712  
 2.695





151.14  
148.87  
148.07  
147.68

132.85  
130.05

122.59  
120.64

111.56  
111.14  
107.93  
107.08

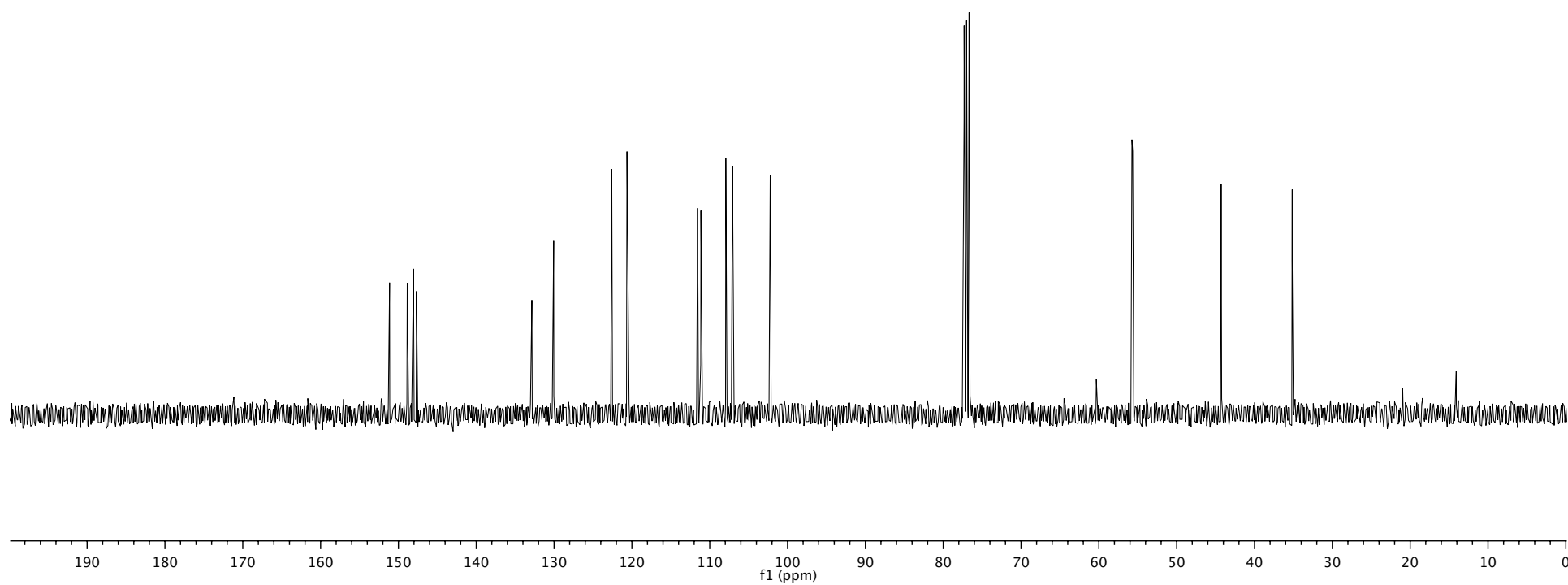
102.23

77.00

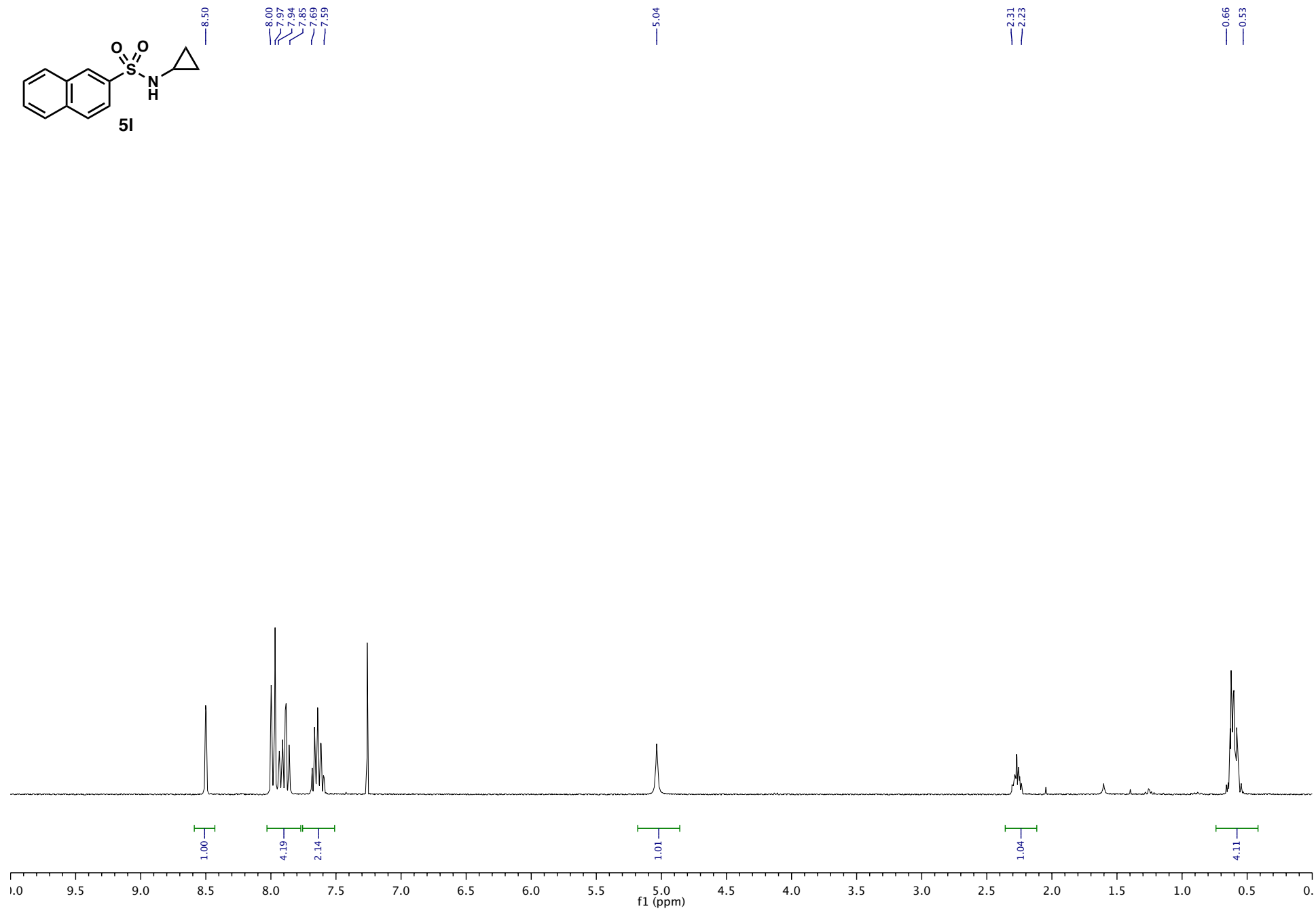
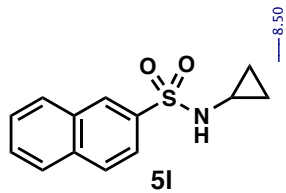
55.75  
55.65

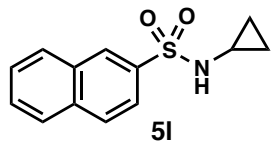
44.28

35.16





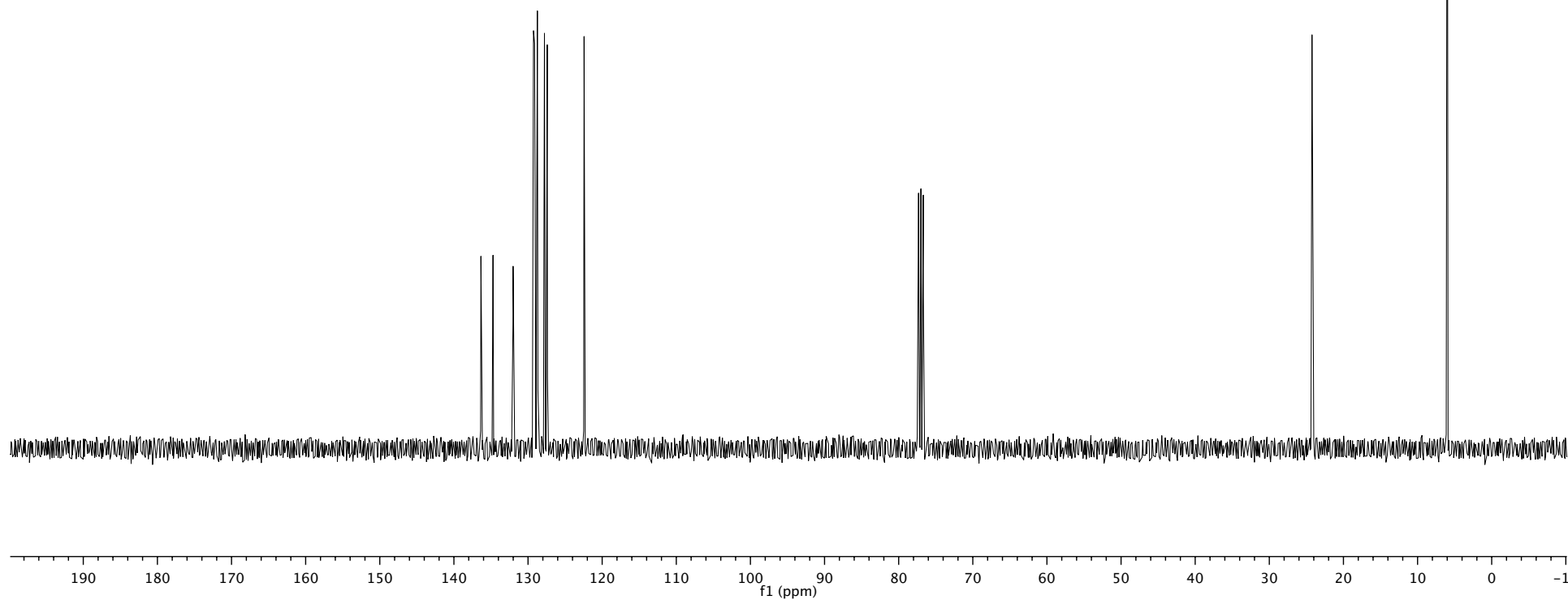


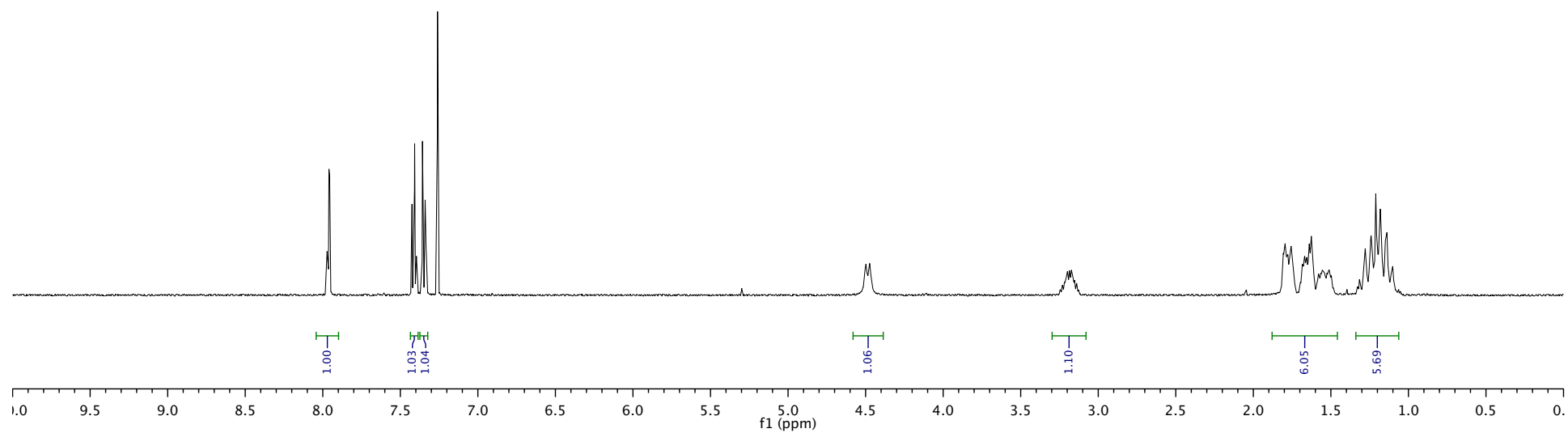
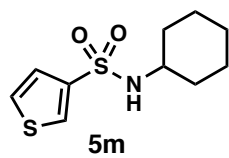


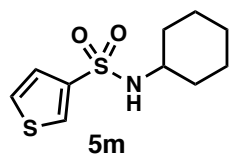
136.36  
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132.01  
129.26  
129.12  
128.74  
128.70  
127.79  
127.40  
122.44

24.24

5.99







141.48

129.91

127.91

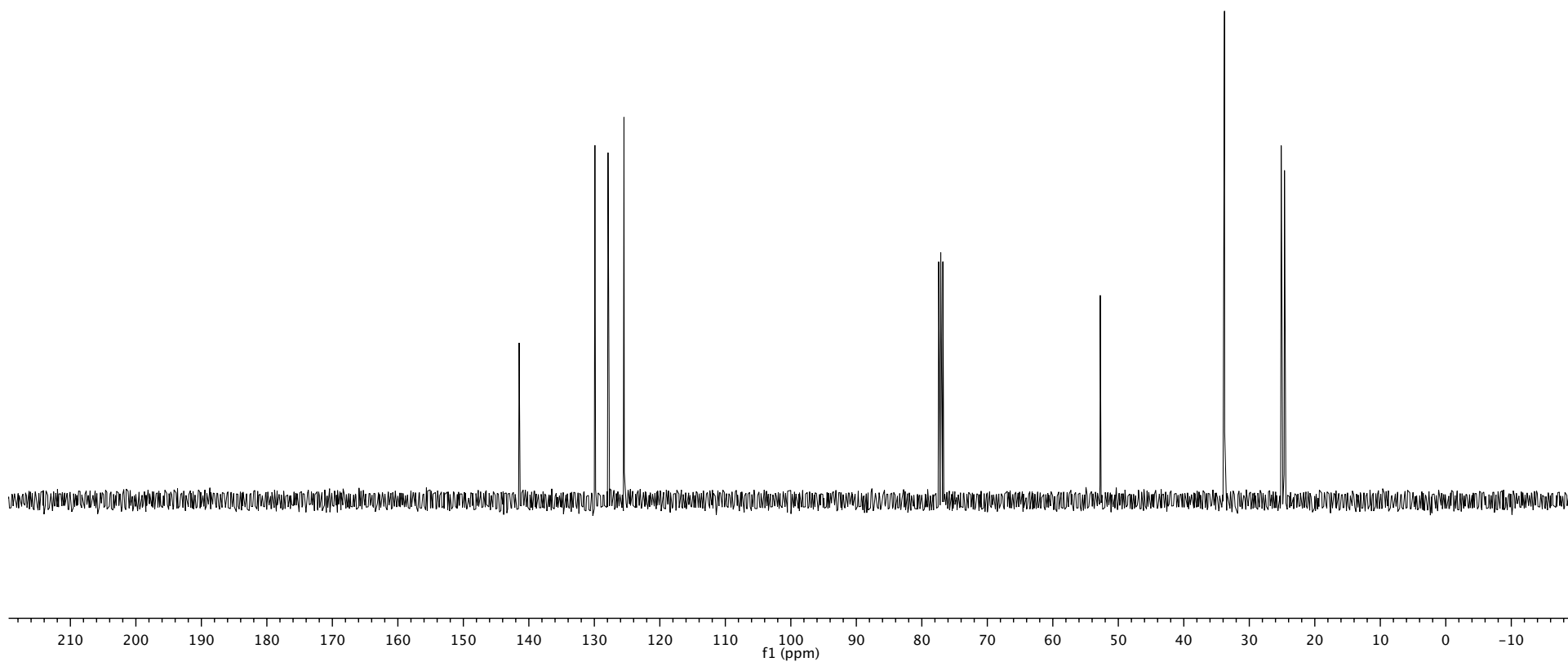
125.47

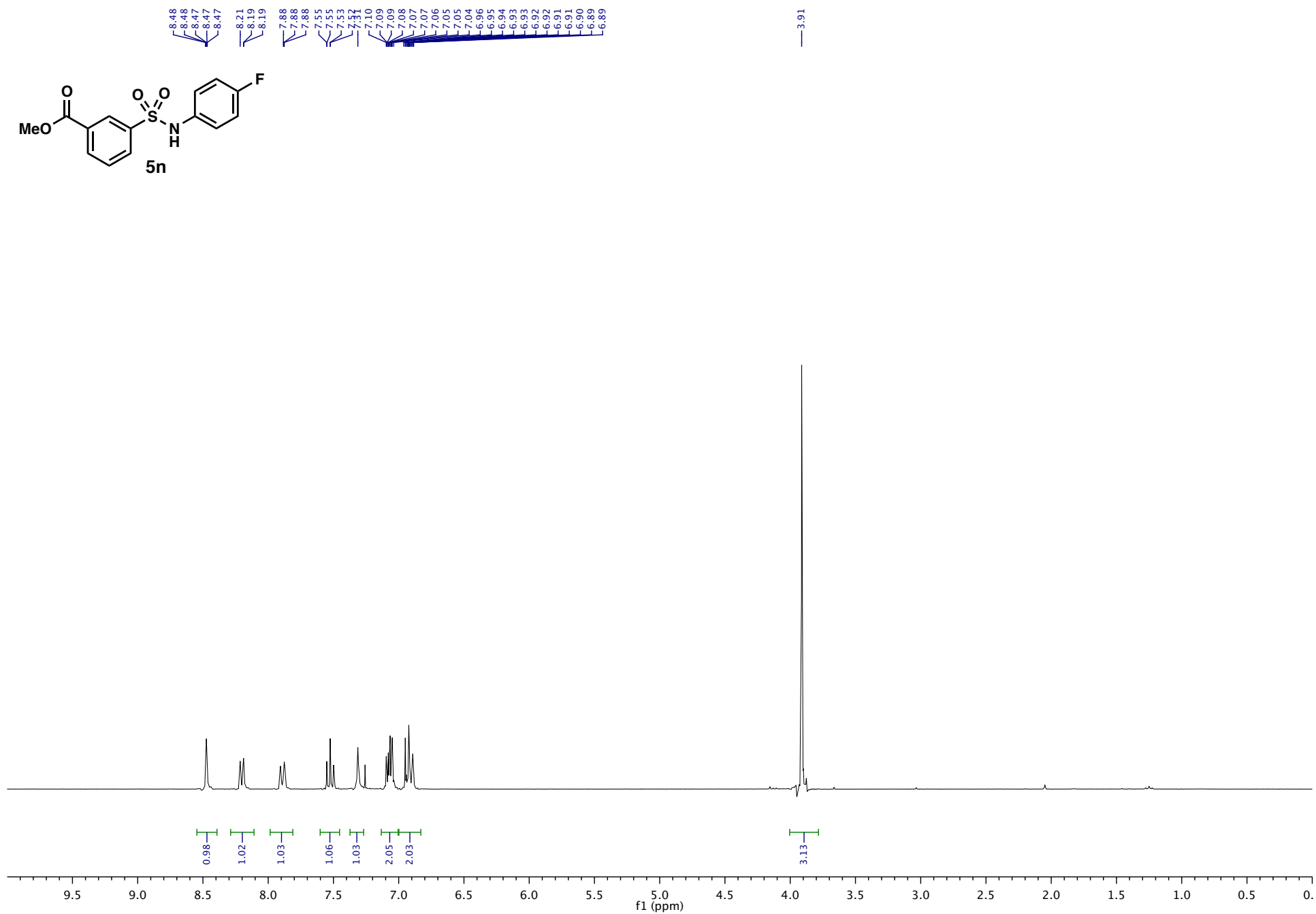
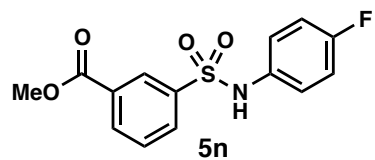
52.76

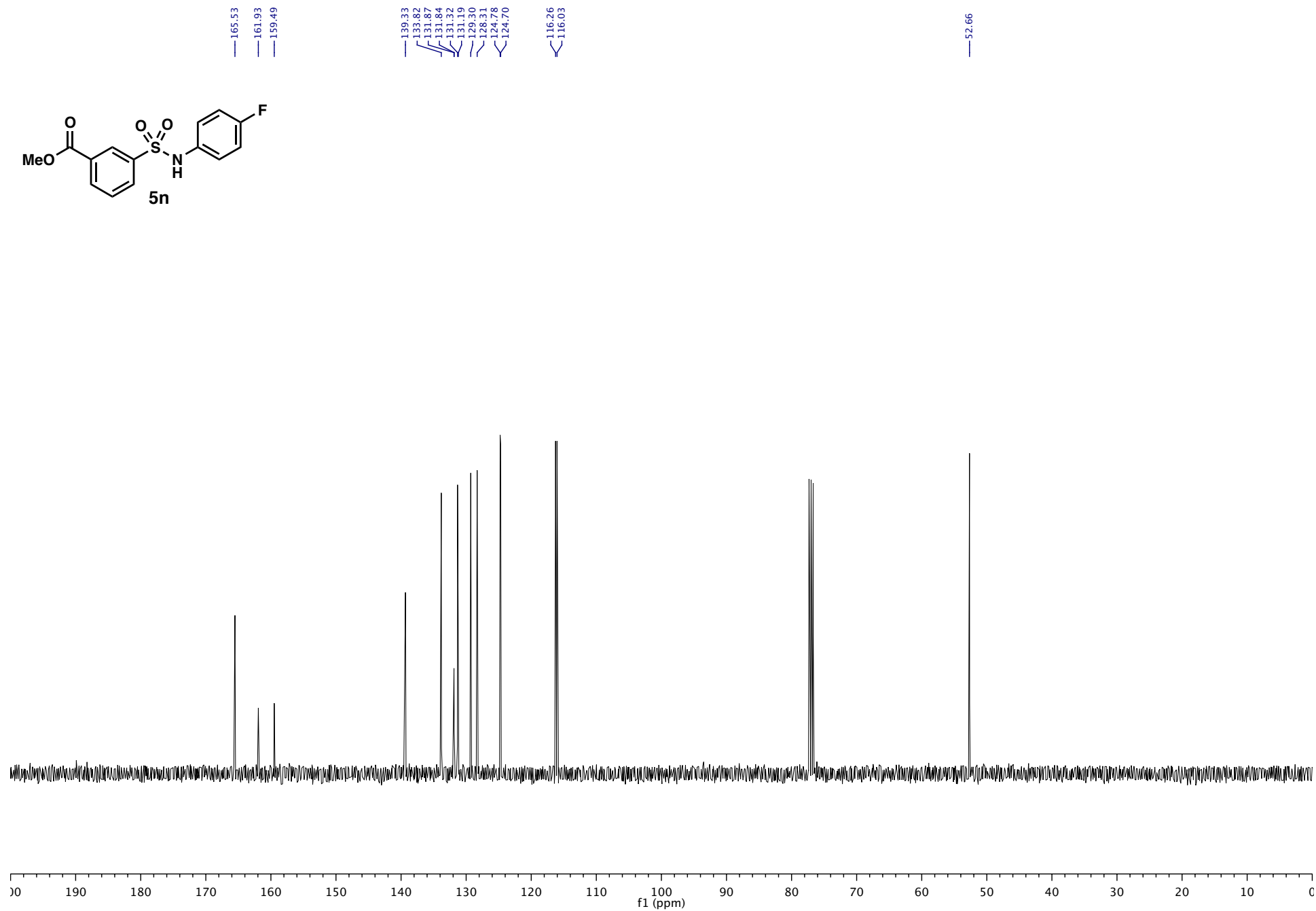
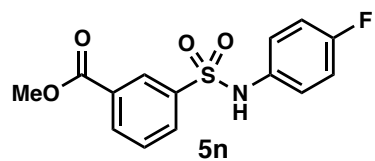
33.79

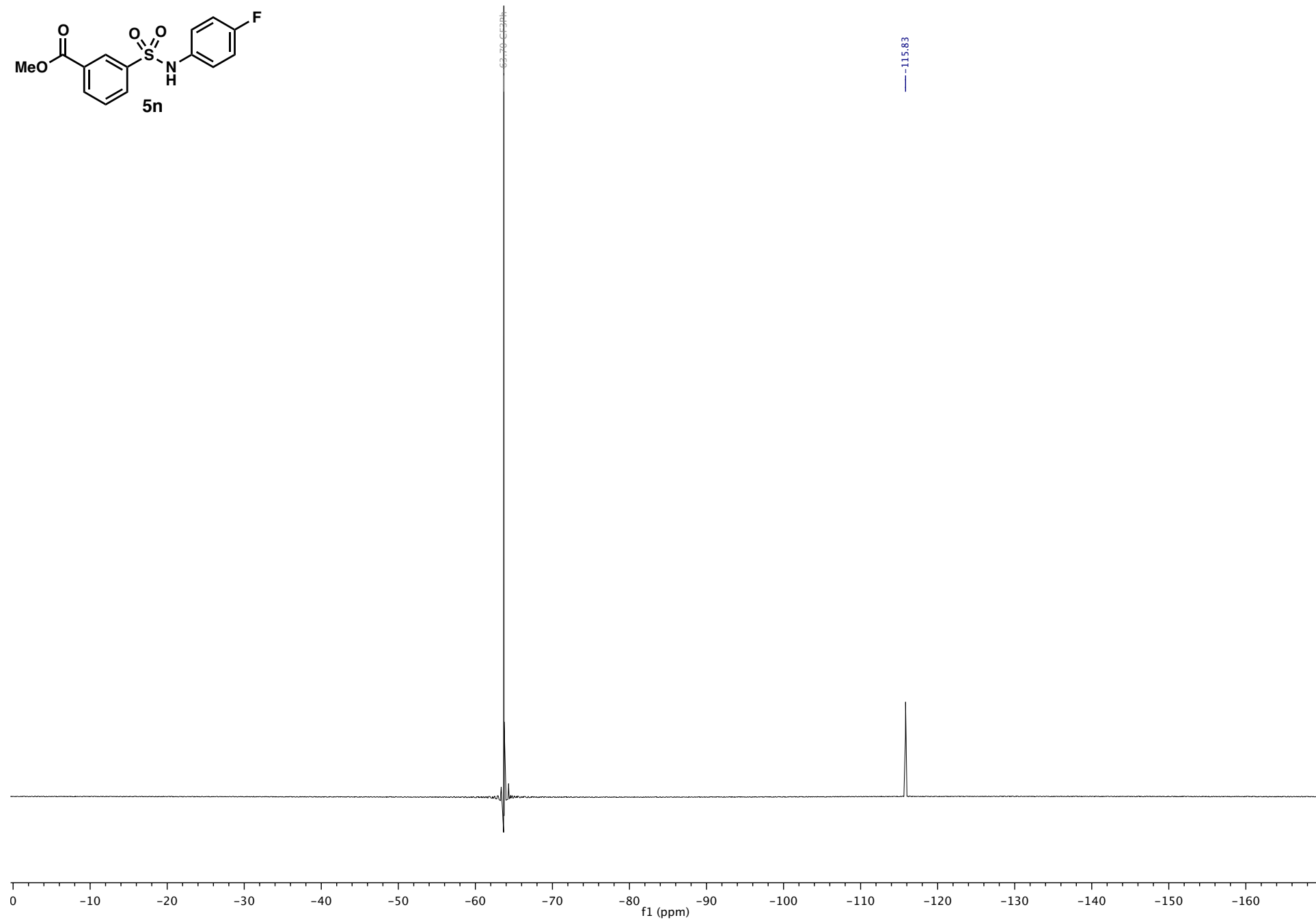
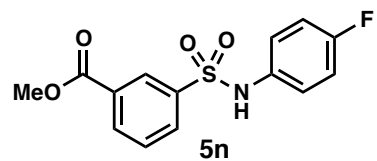
25.13

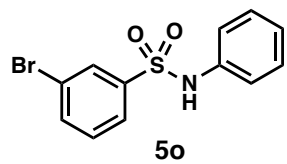
24.62



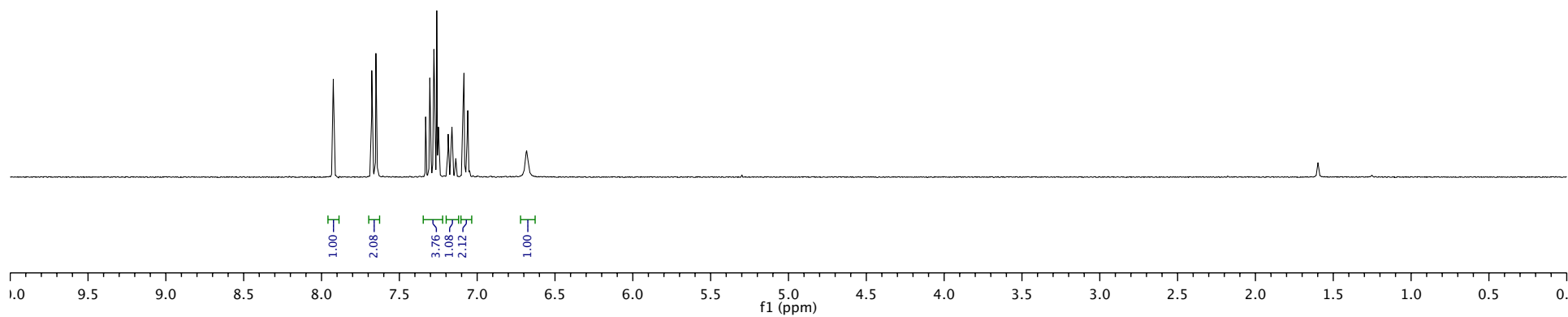




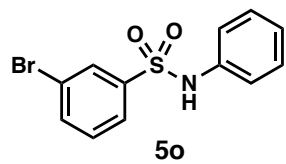




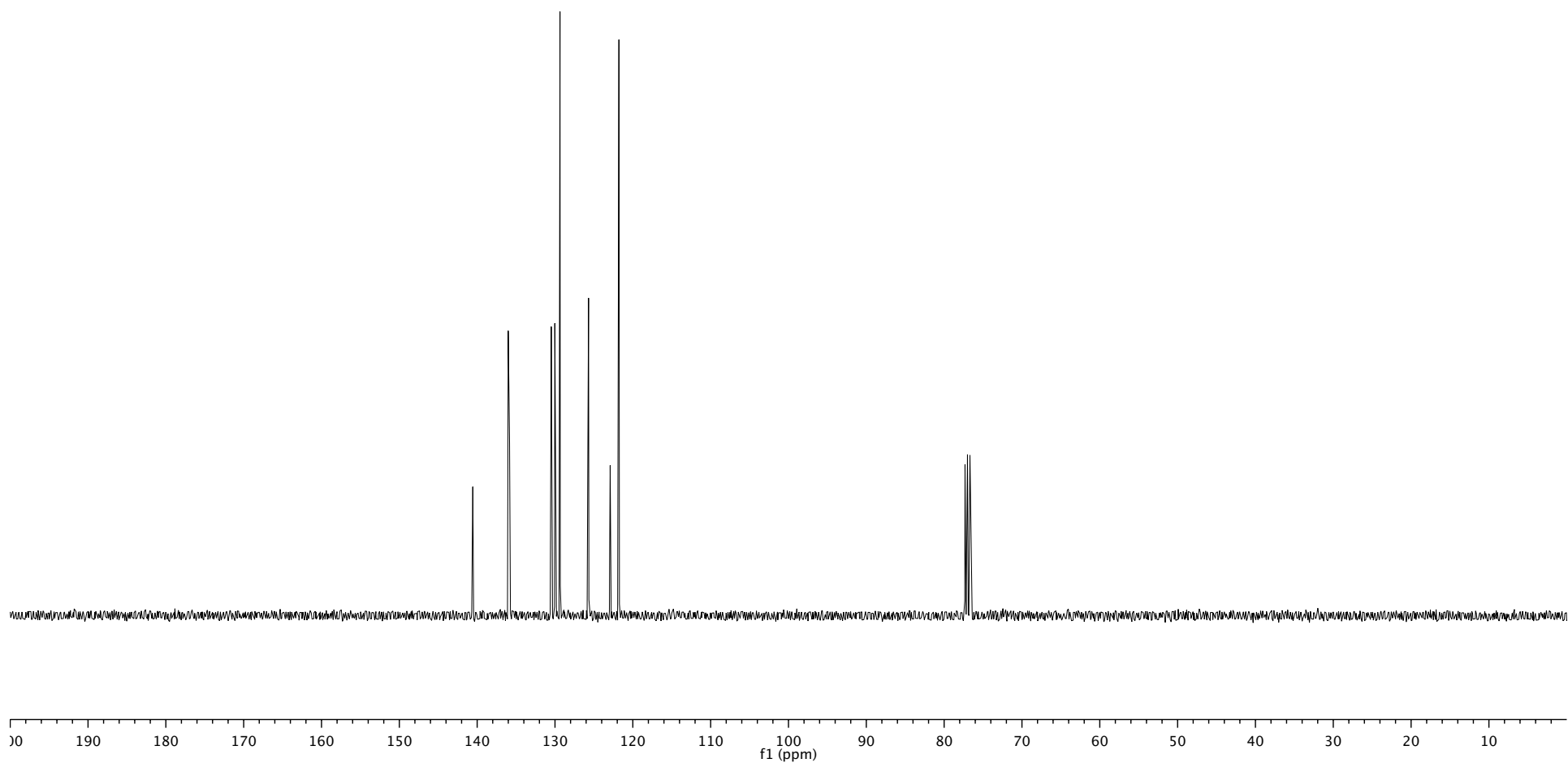
7.92  
7.68  
7.65  
7.33  
7.24  
7.19  
7.13  
7.09  
7.05  
6.68



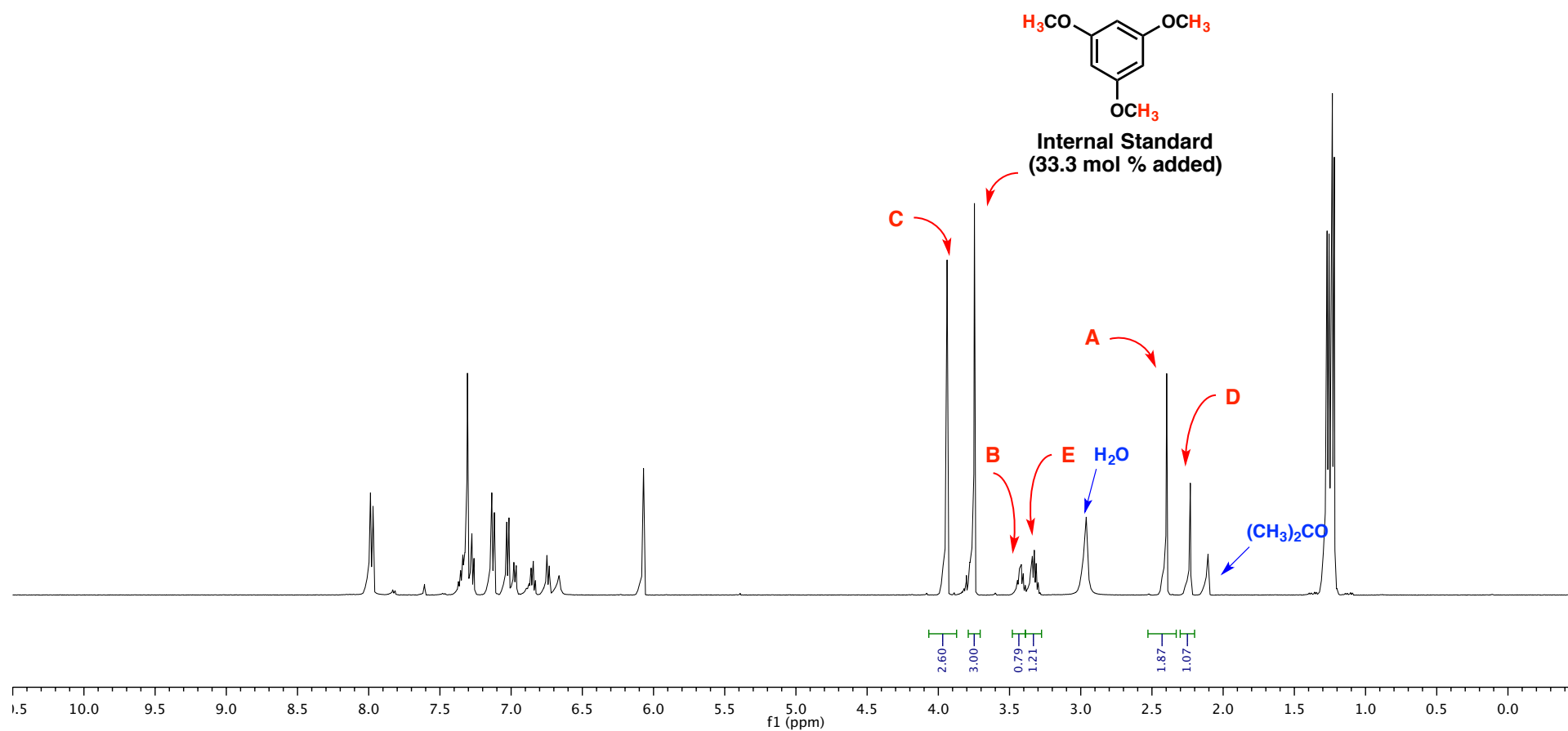
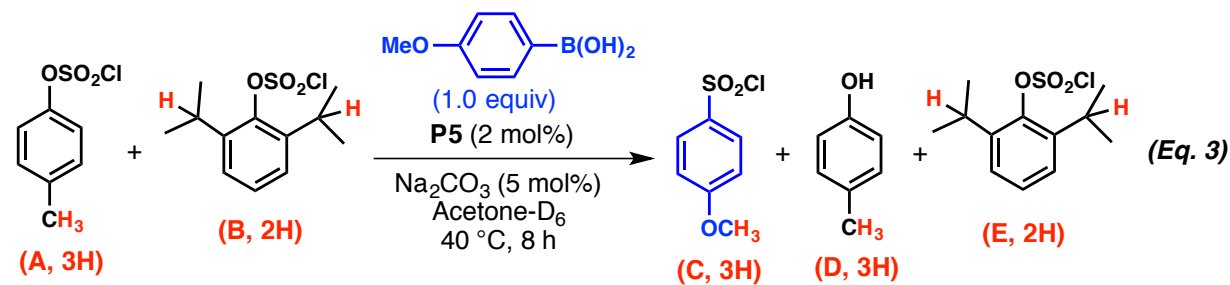




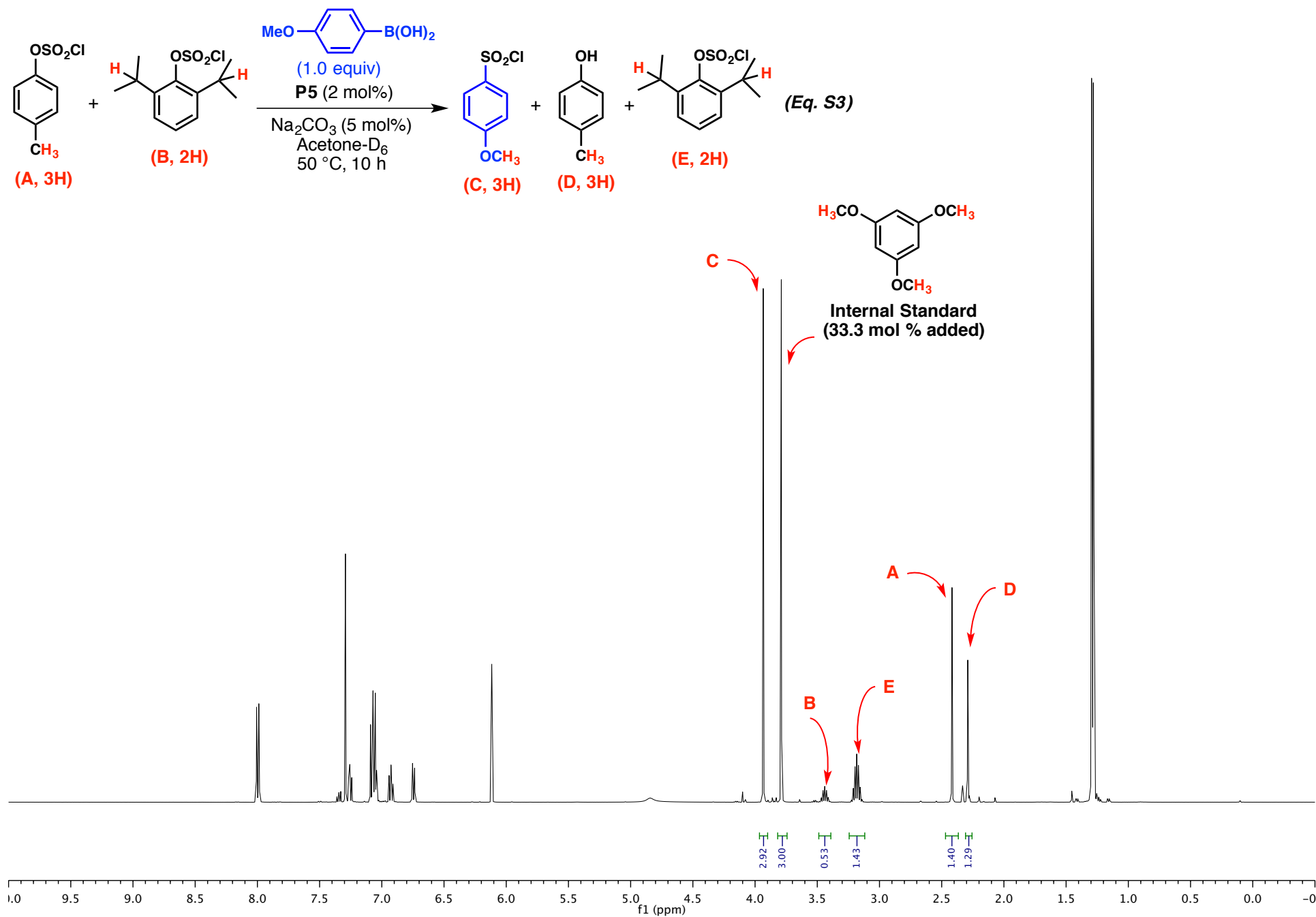
140.57  
136.01  
135.84  
130.48  
130.02  
129.36  
125.71  
125.69  
122.91  
121.78



<sup>1</sup>H NMR analysis of crude reaction mixture of Equation 3.



<sup>1</sup>H NMR analysis of crude reaction mixture of Equation S3 (crude reaction mixture filtered through SiO<sub>2</sub>, concentrated, and dissolved in CDCl<sub>3</sub>)



<sup>1</sup>H NMR analysis of crude reaction mixture of Eq. 4 (Expanded signal **C** taken from spectrum recorded after piperidinium salt removed via SiO<sub>2</sub> filtration)

