Development of an Air-Stable Nickel Precatalyst for the Amination of Aryl Chlorides, Sulfamates, Mesylates, and Triflates

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Supporting Information

General Reagent Information

All reactions were set up on the bench top and run under a nitrogen atmosphere unless otherwise noted. All reagents and precatalyst (**2**) were weighed out in air. HPLC grade THF was purchased from Macron and purged with argon for 30 minutes and then passed through two packed columns of neutral alumina under argon pressure. HPLC grade dichloromethane was purchased from J. T. Baker and was passed through two packed columns of neutral alumina under argon pressure. Anhydrous cyclopentyl methyl ether (CPME), acetonitrile, dioxane and *tert*-butanol (*t*BuOH) were purchased from Aldrich in Sure-Seal® bottles and used as received. Lithium *tert*-butoxide, sodium *tert*-butoxide, and potassium *tert*-butoxide were purchased from Aldrich and potassium phosphate was purchased from Acros. Sodium *tert*-butoxide, potassium *tert*-butoxide, and potassium phosphate were stored in a nitrogen-filled glovebox and small amounts (3-4 g) were removed and stored in air in a desiccator filled with calcium sulfate. Lithium *tert*-butoxide was stored in air in a desiccator filled with calcium sulfate. Carbazole was purchased from Aldrich and recrystallized from toluene. 1,1'-bis(diphenylphosphene)ferrocene (dppf) and bis(triphenylphosphine)nickel(II) dichloride were purchased from Strem and used as received. Both $(Ph_3P)_2Ni(o\text{-tolyl})Cl$ (**1**) and (dppf)Ni(*o*-tolyl)Cl (**2**) were stored at room temperature under air in a desiccator filled with calcium sulfate. All other commercially available reagents were used as received without further purification unless otherwise noted.

General Analytical Information

All compounds were characterized by ^{1}H, ^{13}C, IR, and either elemental analysis or high-resolution mass spectrometry (HRMS). The ^{1}H and ^{13}C spectra are available at the end of the supporting information. NMR analyses

were performed on Varian 500 MHz, Varian 300 MHz or Bruker 400MHz instruments. Chemical shifts for ^{1}H NMR were measured relative to the residual solvent signals of C_6D_6 (7.16 ppm), $CDCl_3$ (7.26 ppm), CD_2Cl_2 (5.32 ppm) and CD_3OD (3.31 ppm). Chemical shifts for ^{13}C NMR were measured relative to the residual solvent signals of C_6D_6 (128.06 ppm), $CDCl_3$ (77.16 ppm), and CD_2Cl_2 (54.00 ppm). All ^{19}F chemical shifts are reported in δ (ppm) units relative to an external standard of $CFCl_3$ (0.00 ppm). All ^{31}P NMR chemical shifts are in δ (ppm) units relative to an external standard H_3PO_4 (0.00 ppm).

Yields refer to the isolated yield of compounds with greater than 95% purity as determined by gas chromatography (GC), ^{1}H NMR, ^{13}C NMR, and elemental analysis. The GC yields and GC conversions in Table 1 were determined from the crude reaction mixture using dodecane as the internal standard. GC analyses were performed on an Agilent 6890 gas chromatograph using a J&W DB-1 column with a FID detector. The infrared (IR) data collected were of the neat compound and were collected using instrument Thermo Scientific – Nicolet iS5 (iD5 ATR – Diamond). Elemental analysis of samples was performed by Atlantic Microlabs Inc., Norcross, GA. Flash chromatography was performed using SiliaFlash F60 silica gel from SiliCycle. In some cases, flash chromatography was performed with the aid of a Biotage SP4 instrument using silica-packed cartridges.

Synthesis of Starting Materials

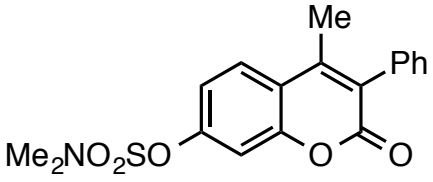
Preparation of Aryl Mesylates.

All aryl mesylates were known and synthesized according to literature procedures[1].

Preparation of Aryl Sulfamates.

4-methyl-2-oxo-3-phenyl-2*H*-chromen-7-yl dimethylsulfamate (9). To a 300 mL round bottom flask equipped with a magnetic stir-bar, was added 7-hydroxy-4-methyl-3-phenylcoumarin (2.61 g, 10.4 mmol). The flask was

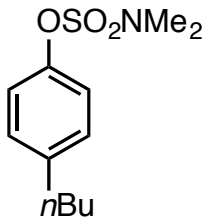
(1) (a) Fors, B. P.; Watson, D. A.; Biscoe, M. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *130*, 13552. (b) Molander, G. A.; Beaumard, F. *Org. Lett*. **2010**, *12*, 4022.



fitted with a septum and purged with nitrogen. Dichloromethane (15 mL) and DBU (3.10 mL, 20.7 mmol) were then added via syringe followed by dropwise addition of *N,N*-dimethylsulfamoyl chloride (1.17 mL, 10.9 mmol) via syringe. The reaction mixture was then allowed to stir at room temperature for 3 h. After 3 h, the reaction mixture was poured into water (50 mL) and extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated with the aid of a rotary evaporator. The crude product was purified via Biotage SP4 (silica-packed 100 g Snap cartridge; using a 0 – 50% ethyl acetate in hexanes gradient) to provide the title compound as a white solid (1.80 g, 49%), mp = 152 – 154 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.68 (m, 1H), 7.46 – 7.43 (m, 2H), 7.40 – 7.37 (m, 1H), 7.32 – 7.23 (m, 4H), 3.01 (s, 6H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.48, 153.17, 152.03, 147.18, 134.06, 129.97, 128.44, 128.34, 127.05, 126.55, 119.09, 117.86, 109.96, 38.79, 16.75. FTIR (neat, cm^{-1}): 3071.35, 2983.97, 1724.43, 1608.22, 1567.59, 1496.29, 1423.68, 1363.52, 1251.2, 1178.97, 1147.6, 1124.04, 1070.79, 1036.89, 1003.17, 987.62, 954.53, 905.26, 830.9, 813.69, 783.13, 732.02, 721.42, 700.41, 669.39, 643.79, 610.01, 557.38, 538.1. Anal. Calcd. for $C_{18}H_{17}NO_5S$: C, 60.15; H, 4.77. Found: C, 60.43; H, 4.75.

4-butylphenyl dimethylsulfamate (10). An oven-dried round bottom flask was equipped with a magnetic stir-bar and sodium hydride (60% dispersion in mineral oil, 583 mg, 14.6 mmol) was added. After fitting with a septum and purging with nitrogen, THF (35 mL) was added and the reaction mixture was cooled to 0 ˚C in an ice bath. A solution of 4-*n*-butylphenol (2.1 g, 13.9 mmol) in THF (5 mL) was then added dropwise via syringe (the septum was punctured with a second needle to vent the evolved gases) and stirred at 0˚C for 30 min. After 30 min, a solution of *N,N*-dimethylsulfamoyl chloride (2.09 g, 14.6 mmol) in THF (5 mL) was then added dropwise via syringe. The reaction mixture was then warmed to room temperature and stirred for 24 h. After 24 h, the reaction mixture was quenched with H_2O, and extracted with Et_2O and the combined organic layers were washed with aqueous 1M KOH. The organic layers were then dried over Na_2SO_4, filtered and concentrated with the aid of a rotary evaporator.



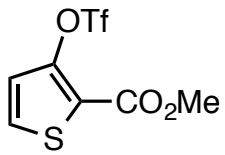
The crude residue was then purified by flash chromatography (50% CH_2Cl_2 in hexane) to give the title compound as a colorless oil (2.0 g, 56%).

^{1}H NMR (500 MHz, C_6D_6) δ 7.20 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 2.49 (s, 6H), 2.39 – 2.30 (m, 2H), 1.40 – 1.33 (m, 2H), 1.21 –1.13 (m, 2H), 0.82 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 148.94, 141.46, 129.81, 121.99, 38.31, 35.19, 33.78, 22.56, 14.11. FTIR (neat, cm^{-1}): 2956.04, 2929.77, 2858.18, 1502.13, 1458.83, 1414.71, 1367.91, 1275.69, 1195.52, 1171.66, 1148.42, 1055.24, 969.83, 857.29, 806.4, 784.39, 746.22, 682, 637.66. Anal. Calcd. for $C_{12}H_{19}NO_3S$: C, 56.01; H, 7.44. Found: C, 56.24; H, 7.65.

Preparation of Aryl Triflates

4-(diethylcarbamoyl)-2-methoxyphenyl trifluoromethanesulfonate was prepared according to the literature procedure.[2]

Methyl 3-(((trifluoromethyl)sulfonyl)oxy)thiophene-2-carboxylate (11).



To a flame dried 300 mL round bottom flask, 3-hydroxythiophene-2-carboxcylic acid methyl ester (949 mg, 6.0 mmol) was added and the flask was fitted with a septum and purged with nitrogen. Dichloromethane (12 mL) and triethylamine (1.67 mL, 12 mmol) were then added and the reaction flask was cooled to -78 ˚C in a dry ice/acetone bath. Trifluoromethanesulfonic anhydride (1.21 mL, 7.2 mmol) was then added dropwise via syringe and the reaction mixture was stirred at -78 ˚C for 1 h. The cold bath was then removed and the reaction mixture was allowed to warm to room temperature and stirred at room temperature for an additional 1 h. The reaction mixture was poured onto water (50 mL) and extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated with the aid of a rotary evaporator. The crude product was purified via flash chromatography (5% Et_2O in hexanes) to provide the title compound as a light yellow oil (1.65 g, 95%).

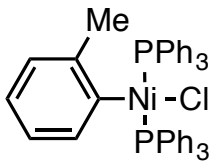
^{1}H NMR (500 MHz, C_6D_6) δ 6.71 (d, J = 5.5 Hz, 1H), 6.50 (d, J = 5.5 Hz, 1H), 3.43 (s, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 159.87, 145.64, 130.68, 123.13 (q, J = 320.7 Hz), 122.77, 122.10, 52.03. ^{19}F NMR (282 MHz, C_6D_6) δ -74.41. FTIR (neat, cm^{-1}): 3122.3, 2958.21, 1719.67, 1539.6, 1423.07,

(2) Lee, H. G.; Milner, P. J.; Buchwald, S. L. *Org. Lett.* **2013**, *15*, 5602.

1385.92, 1298.48, 1268.6, 1248.93, 1205.94, 1135.75, 1087.8, 1015.77, 1003.32, 941.59, 884.25, 855.15, 814.22, 773.85, 763.56, 656.1, 601.18. HRMS-ESI (m/z) Calcd for $C_7H_5F_3O_5S_2$ [M+Na]: 312.9423; Found: 312.9419.

Preparation of Nickel Precatalyst

[Bis(triphenylphosphine)](*o*-tolyl)chloronickel (1).

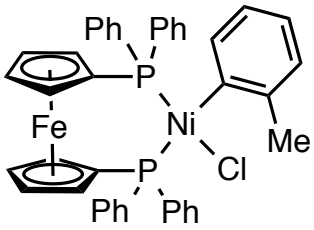


Bis(triphenylphosphine)nickel(II) dichloride (11.4 g, 17.4 mmol) was added to an oven-dried 500 mL round bottom flask equipped with a magnetic stir-bar and purged with nitrogen. THF (240 mL) was added via syringe and the reaction mixture was cooled to 0 ˚C in an ice bath. *o*-tolylmagnesium chloride (22.8 mL, 0.8 M in THF, 18.3 mmol) was then added dropwise via syringe. The reaction mixture was stirred for 15 min at 0˚C and an additional 1 h at room temperature and then was quenched with methanol (15 mL). The mixture was concentrated with the aid of a rotary evaporator and the resulting residue was triturated with the aid of sonication in methanol (450 mL) to produce a yellow suspension. The yellow suspension was filtered and the yellow solid was washed with methanol. The solid was then dissolved in CH_2Cl_2 (80 mL) and carefully filtered through a Whatman GF/D glass fiber filter to afford a homogenous orange solution that was concentrated with the aid of a rotary evaporator. The resulting orange solid was collected and triturated with pentane to afford the title compound **1** as a yellow solid (7.4 g, 60%) mp = 166 ˚C (decomposition).

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.51 – 7.11 (m, 31H), 6.34 – 6.27 (m, 2H), 5.95 (s, 1H), 2.09 (s, 3H).) ^{13}C NMR (126 MHz, CD_2Cl_2) δ 144.02, 136.17, 135.15 (t, J = 5.1 Hz), 132.28 (t, J = 21.4 Hz), 130.09, 129.59, 128.22 (t, J = 4.3 Hz), 123.15, 122.57, 26.46. ^{31}P NMR (121 MHz, CD_2Cl_2) δ 21.72. FTIR (neat, cm^{-1}): 3052.84, 1568.63, 1480.03, 1431.66, 1304.72, 1184.77, 1155.73, 1093.46, 1027.95, 852.78, 737.84, 689.06. Anal. Calcd. for $C_{43}H_{37}ClNiP_2$: C, 72.76, H, 5.25. Found: C, 72.66, H, 5.39.

[1,1'-Bis(diphenylphosphino)ferrocene](*o*-tolyl)chloronickel (2).

[Bis(triphenylphosphine)](*o*-tolyl)chloronickel (**1**) (2.95 g, 4.17 mmol) and 1,1'-Bis(diphenylphosphino)ferrocene (2.66 g, 4.80 mmol) were added to an oven-dried 500 mL round bottom flask equipped with a magnetic stir-bar



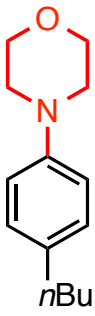
and stoppered with a rubber septum. The sealed flask was evacuated and refilled with nitrogen (this sequence was repeated a total of three times) and the THF (64 mL) was added via syringe. The orange mixture was allowed to stir at room temperature for 2 h. Pentane (144 mL) was then added via syringe and the resulting mixture was allowed to stir for 2 h to produce a yellow suspension. *Note: Addition of the correct amount of pentane is critical to facilitate the completion of the ligand exchange.* Additional pentane (100 mL) was added and the product was isolated by filtration and washed with pentane to produce an ***orange solid***. The solid was dissolved in dichloromethane (10 mL), and the resulting red suspension was carefully filtered through a Whatman GF/D glass fiber filter fitted inside a fritted filter (medium frit) to collect a *homogenous* red solution in a 300 mL round bottom flask that was then concentrated with the aid of a rotary evaporator (bath temperature was set to 25°C). The resulting residue was then triturated in a large excess of pentane with the aid of sonication to produce a yellow suspension. *Note: The filtration and trituration are crucial steps for obtaining a highly active precatalyst. However, this complex will decompose in a dichloromethane solution after an extended period of time and therefore the filtration and trituration steps must be done promptly after addition of dichloromethane.* The solid was isolated by filtration to collect the title compound as a ***yellow solid*** (2.7 g, 83%) mp = 166 – 167 °C (decomposition).

^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.28 (s, 4H), 8.08 (s, 2H), 7.54 (m, 7H), 7.36 (s, 2H), 7.29 (s, 1H), 7.09 (s, 1H), 6.86 (s, 2H), 6.70 (s, 2H), 6.53 (s, 1H), 6.40 (s, 1H), 6.20 (s, 1H), 5.25 (s, 1H), 4.64 (s,1H) 4.34 (s, 1H), 4.28 (s, 1H), 4.13 – 4.11 (m, 2H), 3.62 (s, 1H), 3.42 (s, 1H), 2.54 (s, 3H). ^{13}C NMR (126 MHz, CD_2Cl_2) Complex spectrum, see attached. ^{31}P NMR (121 MHz, CD_2Cl_2) δ 28.65 (d, J = 26.1 Hz), 11.26 (d, J = 26.0 Hz). FTIR (neat, cm^{-1}): 3046.18, 1568.59, 1481.79, 1431.62, 1305.35, 1190.43, 1162.86, 1096.72, 1037.59, 1009.94, 814.67, 733.75, 696.39, 688.23, 640.69. Anal. Calcd. for $C_{41}H_{35}ClFeNiP_2$: C, 66.58, H, 4.77. Found: C, 66.34, H, 4.85. Crystals suitable for X-ray diffraction were obtained by slow vapor diffusion of pentane onto a THF/CH_2Cl_2 solution of the complex at room temperature.

Procedures for the Nickel-catalyzed C-N Cross-coupling

General Procedure for Table 1. To an oven-dried disposable test tube (Fischer Scientific, catalog number: 1495925C) equipped with a screw-cap septum and a magnetic stir-bar (dppf)Ni(*o*-tolyl)Cl (**2**) (9.2 mg, 0.0125 mmol), dppf (6.9 mg, 0.0125 mmol), and base (0.375 mmol) were added. The reaction vessel was evacuated and backfilled with nitrogen. This sequence was repeated a total of three times. 4-*n*-butylchlorobenzene (0.042 mL, 0.25 mmol) and morpholine (0.032 mL, 0.375 mmol) were then added via syringe. Any additive, if liquid, was also added at this time. CPME (0.5 mL) was then added and the screw-cap septum was exchanged for one with an unpunctured septum under a continuous flow of nitrogen. The reaction mixture was then heated to 100 °C in a pre-heated oil bath for 15 min. After cooling to room temperature, dodecane (0.057 mL, 0.25 mmol) was added and the reaction mixture was diluted with ethyl acetate. A small aliquot was filtered through a short silica gel plug and analyzed by GC.

General Procedure A. To an oven-dried disposable test tube (Fischer Scientific, catalog number: 1495937A) equipped with a screw-cap septum and a magnetic stir-bar (dppf)Ni(*o*-tolyl)Cl (**2**) (0.05 mmol), dppf (0.05 mmol), and LiO*t*Bu (1.5 mmol) were added. Aryl halide (1 mmol) and amine (1.5 mmol), if solid, were also added at this point. The reaction vessel was then evacuated and backfilled with nitrogen. This sequence of evacuation and backfilling with nitrogen was repeated a total of three times. Aryl halide and amine, if liquid, were added, followed by MeCN (0.052 mL, 1 mmol) and CPME (2 mL). The cap was replaced with one containing an unpunctured septum under a continuous flow of nitrogen and the reaction mixture was heated to 100 °C for the specified time in a pre-heated oil bath. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through Celite eluting with additional ethyl acetate. The filtrate was then concentrated with the aid of a rotary evaporator and the residue was purified via flash chromatography.

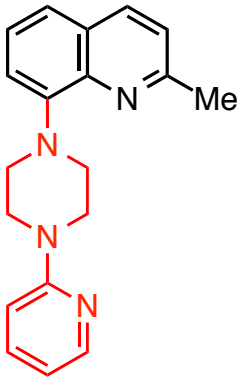


4-(4-butylphenyl)morpholine (5). Following general procedure A, a mixture of 4-*n*-butylchlorobenzene (0.169 mL, 1 mmol), morpholine (0.129 mL, 1.5 mmol), LiO*t*Bu (120 mg, 1.5 mmol), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and CPME (2 mL) was heated to 100 °C for 45 minutes. The crude product was adsorbed to silica gel and purified via

Biotage SP4 (silica-packed 50 g Snap cartridge, 0 – 5% ethyl acetate in hexanes) to provide the title compound as a orange solid (Run 1: 186 mg, (85%); Run 2: 185 mg (84%); Average Yield: 85%) mp = 37 – 39 °C.

^{1}H NMR (500 MHz, C_6D_6) δ 7.06 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.4 Hz, 2H), 3.59 – 3.57 (m, 4H), 2.78 – 2.76 (m, 4H), 2.52 (t, J = 7.7 Hz, 2H), 1.59 – 1.52 (m, 2H), 1.34 – 1.32 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 150.09, 134.31, 129.28, 116.33, 67.03, 50.01, 35.21, 34.34, 22.69, 14.25. FTIR (neat, cm^{-1}): 2957.6, 2921.49, 2858.94, 2829.22, 1610.39, 1514.1, 1444.81, 1379.73, 1363.95, 1327.79, 1301.41, 1261.04, 1230.42, 1119.59, 1068.7, 860.21, 840.53, 809.07, 730.68, 704.79, 627.09. Anal. Calcd. for $C_{14}H_{21}NO$: C, 76.67, H, 9.65. Found: C, 76.78, H, 9,51. Characterization data are in accordance with those in the literature.[3]

2-methyl-8-(4-(pyridin-2-yl)piperazin-1-yl)quinoline (6a). Following general procedure A, a mixture of 8-chloro-2-methylquinoline (178 mg, 1.0 mmol), 1-(2-pyridyl)piperazine (0.228 mL, 1.5 mmol), LiO*t*Bu (120 mg, 1.5 mmol), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1.0 mmol) and CPME (2 mL) was heated to 100 °C for 16 h. The reaction mixture was concentrated with the aid of a rotary evaporator and the crude product was purified via flash chromatography (10% ethyl acetate in hexanes with 1% triethylamine) to provide the title compound as a yellow solid (Run 1: 232 mg, (76%); Run 2: 241 mg, (79%) Average Yield: 78%), mp = 123 – 126 °C.

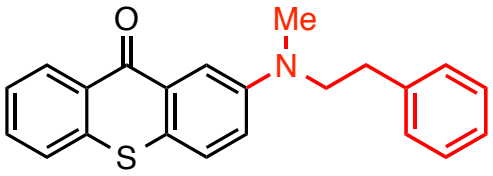


^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 – 8.24 (m, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.43 – 7.35 (m, 2H), 7.26 (d, J = 8.4 Hz, 1H), 7.13 (d, J = 6.8 Hz, 1H), 6.75 (d, J = 8.6 Hz, 1H), 6.70 – 6.60 (m, 1H), 3.89 – 3.87 (m, 4H), 3.56 – 3.54 (m, 4H), 2.75 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.86, 156.94, 148.54, 148.03, 141.99, 137.59, 136.71, 129.74, 127.79, 125.81, 121.70, 115.96, 113.41, 107.30, 51.98, 45.58, 25.97. FTIR (neat, cm^{-1}): 3000.59, 2971.61, 2846.94, 2816.98, 1592.1, 1561.28, 1481.15, 1431.86, 1383.63, 1369.87, 1352.67, 1310.8, 1232.49, 1154.39, 1118.17, 1087.67,

(3) Huang, X.; Anderson, K. W.; Zim, D.; Jiang, L.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 6653.

1024.57, 979.78, 943.62, 843.5, 772, 756.39, 737.16, 711.97, 696.6. Anal. Calcd. for $C_{19}H_{20}N_4$: C, 74.97; H, 6.62. Found: C, 74.91; H, 6.58.

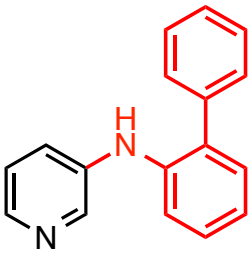
2-(methyl(phenethyl)amino)-9*H*-thioxanthen-9-one (6b). Following



general procedure A, a mixture of 2-chlorothioxanthone (247 mg, 1.0 mmol), *N*-methylphenethylamine (0.218 mL, 1.5 mmol), LiO*t*Bu (120 mg, 1.5 mmol), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1.0 mmol) and CPME (2 mL) was heated to 100 °C for 1 h. Purification via flash chromatography (0 – 10% ethyl acetate in hexanes) provided the title compound as a yellow solid (Run 1: 286 mg, (83%); Run 2: 286 mg, (83%) Average Yield: 83%), mp = 102 – 103 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, J = 8.1 Hz, 1H), 7.91 (d, J = 3.0 Hz, 1H), 7.56 (m, 2H), 7.51 – 7.38 (m, 2H), 7.33 – 7.30 (m, 2H), 7.24 – 7.20 (m, 3H), 7.09 (d, J = 7.1 Hz, 1H), 3.67 (m, 2H), 2.97 (s, 3H), 2.90 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.10, 147.52, 139.41, 137.93, 131.70, 130.09, 129.92, 128.94, 128.80, 128.69, 126.99, 126.42, 126.08, 125.65, 123.78, 118.53, 110.39, 54.73, 38.81, 32.97. FTIR (neat, cm^{-1}): 2934.14, 1626.82, 1592.04, 1493.5, 1450.64, 1433.21, 1413.04, 1383.19, 1351.28, 1332.64, 1219.48, 1193.04, 1135.51, 1116.9, 1073.79, 1033.12, 942.57, 859.05, 800.32, 737.92, 697.78. HRMS-ESI (m/z) Calcd. for $C_{22}H_{19}NOS$ [M+H]: 346.1260; Found: 346.1249.

***N*-([1,1'-biphenyl]-2-yl)pyridin-3-amine (6c).** Following general procedure

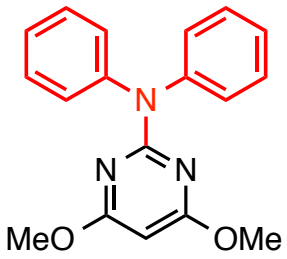


A, a mixture of 3-chloropyridine (0.095 mL, 1.0 mmol), 2-aminobiphenyl (254 mg, 1.5 mmol), LiO*t*Bu (120 mg, 1.5 mmol), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and CPME (2 mL) was heated to 100 °C for 1 h. Purification via flash chromatography (40% ethyl acetate in hexanes) provided the title compound as an off-white solid (Run 1: 233 mg, (94%); Run 2: 234 mg, (94%); Average Yield: 94%), mp = 132 – 134 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.15 (d, J = 1 Hz, 1H), 7.45 – 7.43 (m, 4H), 7.38 – 7.34 (m, 3H), 7.31 – 7.28 (m, 2H), 7.16 – 7.14 (m, 1H), 7.09 – 7.06 (m, 1H), 5.70 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ

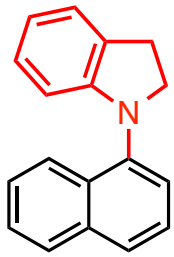
141.97, 140.45, 140.20, 139.02, 138.75, 132.59, 131.22, 129.29, 129.03, 128.46, 127.74, 123.77, 123.73, 122.35, 118.15. FTIR (neat, cm^{-1}): 3233.66, 2922, 1575.26, 1516.02, 1469.64, 1432.68, 1407.25, 1345.86, 1302.82, 1161.49, 1103.72, 1046.64, 1020.88, 1008.39, 884.83, 789.27, 778.47, 756.51, 742.69. Anal. Calcd. for $C_{17}H_{14}N_2$: C, 82.90; H, 5.73. Found: C, 82.46; H, 5.91.

4,6-dimethoxy-*N*,*N*-diphenylpyrimidin-2-amine (6d). Following general procedure A, a mixture of 2-chloro-4,6-dimethoxypyrimidine (174 mg, 1 mmol), diphenylamine (254 mg, 1.5 mmol), LiO*t*Bu (120 mg, 1.5 mmol), (dppf)Ni(*o*-tolyl)Cl (**2**) (74 mg, 0.05 mmol), dppf (55 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and CPME (2 mL) was heated to 130 °C for 16 h. The reaction mixture was filtered through a plug of Celite and eluted with additional ethyl acetate. The crude product was adsorbed to silica gel and purified via Biotage SP4 (silica-packed 50 g Snap cartridge, 0 – 50% CH_2Cl_2 in hexanes) to provide the title compound as a brown solid (Run 1: 242 mg, (78%); Run 2: 264 mg, (86%); Average Yield: 82%), mp = 154 – 155 °C.



^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.43 – 7.40 (m, 8H), 7.27 – 7.24 (m, 2H), 5.64 (s, 1H), 3.72 (s, 6H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 172.21, 161.22, 145.28, 129.09, 128.33, 125.69, 81.42, 54.0. FTIR (neat, cm^{-1}): 2948.28, 1566.38, 1491.72, 1462.15, 1423.02, 1398.31, 1362.05, 1286.48, 1241.36, 1191.31, 1156.54, 1059.79, 1000.54, 952.44, 798.79, 758.13. Anal. Calcd. for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58. Found: C, 70.24; H, 5.63.

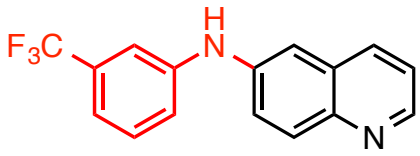
1-(naphthalen-1-yl)indoline (6e). Following general procedure A, a mixture of 1-chloronapthalene (0.136 mL, 1 mmol), indoline (0.168 mL, 1.5 mmol), LiO*t*Bu (120 mg, 1.5 mmol), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and CPME (2 mL) was heated to 100 °C for 1 h. The reaction mixture was then cooled to room temperature and diluted with Et_2O and filtered through a plug of silica gel, eluting with excess Et_2O. The filtrate was concentrated with the aid of a rotary evaporator and the crude residue was purified via flash chromatography (pentane) to provide the title compound as a white solid (Run 1: 148 mg, (60%); Run 2: 148 mg, (60%); Average Yield: 60%), mp =



80 – 83 °C.

^{1}H NMR (500 MHz, C_6D_6) δ 8.21 (d, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.30 – 7.23 (m, 3H), 7.19 (d, *J* = 7.4 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.76 (t, *J* = 7.3 Hz, 1H), 6.32 (d, *J* = 7.9 Hz, 1H), 3.54 (m, 2H), 2.80 (m, 2H). ^{13}C NMR (126 MHz, C_6D_6) δ 151.54, 142.95, 135.36, 131.05, 130.68, 128.70, 127.56, 126.51, 126.41, 126.00, 125.79, 124.90, 124.76, 119.95, 118.99, 109.67, 55.63, 29.19. FTIR (neat, cm^{-1}): 3051.94, 3026.43, 2978.58, 2947.66, 2892.19, 2867.49, 2842.32, 1604.86, 1575.09, 1482.89, 1456.1, 1398.47, 1329.65, 1297.25, 1262.55, 1222.81, 1163.19, 1117.51, 1073.03, 1050.31, 1026.62, 973.63, 947.57, 925.25, 872.16, 799.37, 765.44, 749.14, 736.11, 648.37, 641.83. Anal. Calcd. for $C_{18}H_{15}N$: C, 88.13; H, 6.16. Found: C, 88.28; H, 6.07.

***N*-(3-(trifluoromethyl)phenyl)quinolin-6-amine (6f).** Following general procedure A, a mixture of 6-chloroquinoline (164 mg, 1 mmol), 3-trifluoromethylaniline (0.187 mL, 1.5 mmol), Li*O*t*Bu* (120 mg, 1.5 mmol), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and CPME (2 mL) was heated to 100 °C for 1 h. Purification via flash chromatography (20 – 40% ethyl acetate in hexanes) provided the title compound as a white solid (Run 1: 278 mg, (97%); Run 2: 285 mg, (99%); Average Yield: 98%), mp = 170 – 172 °C.

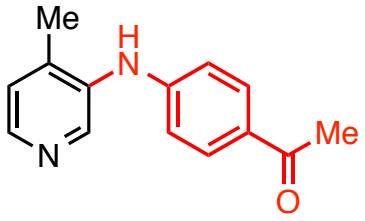


^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.05 (d, *J* = 9.0 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.50 – 7.31 (m, 5H), 7.23 (d, *J* = 7.3 Hz, 1H), 6.33 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.24, 144.71, 143.19, 140.59, 134.91, 132.21 (q, *J* = 32.3 Hz), 130.92, 130.17, 129.59, 125.19 (q, *J* = 272.6 Hz), 123.64, 121.83, 121.11, 118.31 (q, *J* = 3.3 Hz), 114.78 (q, *J* = 3.8 Hz), 111.37. ^{19}F NMR (471 MHz, $CDCl_3$) δ -63.06. FTIR (neat, cm^{-1}): 3249, 3042.68, 2941.26, 1611.79, 1591.6, 1490.31, 1330.62, 1219.51, 1161.78, 1098.6, 1069.5, 836.72, 797.57, 697.48. Anal. Calcd. for $C_{16}H_{11}F_3N_2$: C, 66.66; H, 3.85. Found: C, 66.42; H, 3.88.

General Procedure B. To a disposable test tube (Fischer Scientific, catalog number: 1495937A) equipped with a magnetic stir-bar and a screw-cap septum K_3PO_4 (3 mmol) and 3 Å molecular sieves (300 mg) were added and

the tube was flame-dried under vacuum. After cooling under vacuum, (dppf)Ni(*o*-tolyl)Cl (**2**) (0.05 mmol), dppf (0.05 mmol), were added. Aryl halide (1 mmol) and amine (1.5 mmol), if solid, were also added at this point. The reaction vessel was then evacuated and backfilled with nitrogen. This sequence of evacuation and backfilling with nitrogen was repeated a total of three times. Aryl halide and amine, if liquid, were added and followed by MeCN (1 mmol) and *t*BuOH (2 mL). The screw-cap septum was replaced with an unpunctured one under a continuous flow of nitrogen and the reaction mixture was heated to 110 °C for 16 h in a pre-heated oil bath. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a Celite plug, eluting with additional ethyl acetate. The filtrate was then concentrated with the aid of a rotary evaporator and the residue was purified by flash chromatography.

1-(4-((4-methylpyridin-3-yl)amino)phenyl)ethanone (7a). Following general procedure B, a mixture of 3-chloro-4-methylpyridine (0.110 mL, 1 mmol), 4'-aminoacetophenone (203 mg, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol),[4] 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and *t*BuOH (2 mL) was heated to 110 °C for 16 h. The reaction mixture was transferred to a separatory funnel containing water and was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated with the aid of a rotary evaporator. The crude residue was purified via flash chromatography (1 – 2% methanol in dichloromethane) to provide the title compound as a brown solid (Run 1: 189 mg, (84%); Run 2: 200 mg, (88%); Average Yield: 86%), mp = 81 – 83 °C.

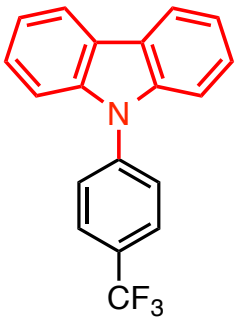


^{1}H NMR (500 MHz, C_6D_6) δ 8.54 (s, 1H), 8.27 (d, J = 3.9 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 6.68 (d, J = 4.4 Hz, 1H), 6.50 (d, J = 8.4 Hz, 3H),

(4) Although these two runs were successfully performed using 3 mmol of K_3PO_4, further experiments revealed that this substrate was sensitive to the variability in the K_3PO_4 and incomplete conversion of 3-chloro-4-methylpyridine was observed. In these cases where the standard conditions are unsuccessful, performing the reaction in accordance with general procedure A and substituting K_3PO_4 (3 mmol) for LiO*t*Bu (no 3Å MS were added) allowed for the reaction to proceed to full conversion. Alternatively, conducting the reaction using the standard conditions in general procedure C, but increasing the amount of K_3PO_4 from 3 mmol to 6 mmol also allowed for the reaction to reach completion.

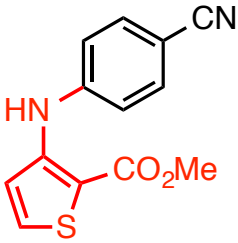
6.39 (s, 1H), 2.16 (s, 3H), 1.83 (s, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 195.41, 149.70, 146.47, 146.27, 141.90, 136.57, 130.90, 129.28, 125.96, 114.02, 25.91, 17.32. FTIR (neat, cm^{-1}): 3233.74, 3163.26, 3037.65, 2978.21, 1659.52, 1586.65, 1556.94, 1528.07, 1486.55, 1406.12, 1354.89, 1329.54, 1270.36, 1176.04, 1072.12, 1037.95, 1021.44, 954.2, 891.29, 829.43, 817.31, 811.63, 667.32, 654.52, 585.79. Anal. Calcd. for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24. Found: C, 74.20; H, 6.23.

9-(4-(trifluoromethyl)phenyl)-9*H*-carbazole (7b). Following general procedure B, a mixture of 4-chlorobenzotrifluoride (0.133 mL, 1 mmol), carbazole (250 mg, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol), 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and *t*BuOH (2 mL) was heated to 110 °C for 16 h. Purification via flash chromatography (0 – 5% ethyl acetate in hexanes) provided the title compound as a white solid (Run 1: 271 mg, (87%); Run 2: 260 mg, (84%); Average Yield: 86%), mp = 163 – 165 °C.



^{1}H NMR (500 MHz, C_6D_6) δ 8.02 (d, J = 6.6 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.29 – 7.23 (m, 4H), 7.15 – 7.11 (m, 2H), 6.95 (d, J = 8.2 Hz, 2H). ^{13}C NMR (126 MHz, C_6D_6) δ 141.18, 140.69, 129.26 (q, J = 32.4 Hz), 127.14, 127.11 (q, J = 3.8 Hz), 126.50, 125.80 (q, J = 272.1 Hz), 124.28, 121.01, 120.82, 109.92. ^{19}F NMR (282 MHz, C_6D_6) δ -62.32. FTIR (neat, cm^{-1}): 3052.97, 1612.28, 1520.47, 1489.92, 1480.01, 1451.59, 1366.64, 1319.55, 1230.17, 1167.64, 1120.23, 1104.33, 1066.16, 1017.44, 999.09, 916.73, 840.66, 748.81, 725.17, 628.09. Anal. Calcd. for $C_{19}H_{12}F_3N$: C, 73.31; H, 3.89. Found: C, 73.20; H, 3.97.

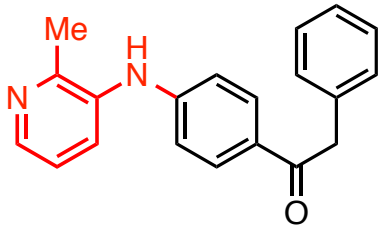
Methyl 3-((4-cyanophenyl)amino)thiophene-2-carboxylate (7c). Following general procedure B, a mixture of 4-chlorobenzonitrile (138 mg, 1 mmol), 3-aminothiophene-2-carboxcylic acid methyl ester (236 mg, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol), 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and *t*BuOH (2 mL) was heated to 110 °C for 16 h. Purification via flash chromatography (50% toluene in hexanes with 5% ethyl acetate by volume) provided the title



compound as a light yellow solid (Run 1: 224 mg, (87%); Run 2: 211 mg, (82%); Average Yield: 85%), mp = 138 – 139 °C.

^{1}H NMR (500 MHz, C_6D_6) δ 9.06 (s, 1H), 6.94 (d, J = 8.6 Hz, 2H), 6.66 (d, J = 5.4 Hz, 1H), 6.55 (d, J = 5.5 Hz, 1H), 6.36 (d, J = 8.6 Hz, 2H), 3.40 (s, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 165.33, 148.95, 145.35, 133.85, 132.22, 119.57, 118.65, 118.16, 107.21, 105.34, 51.65. FTIR (neat, cm^{-1}): 3358.8, 3108.39, 2950.84, 2218.59, 1662.44, 1580.2, 1551.9, 1510.01, 1449.05, 1428.46, 1398.7, 1255.41, 1224.67, 1170.62, 1089.59, 1034.88, 951.37, 848.43, 823.01, 771.72, 646.97, 545.43. Anal. Calcd. for $C_{13}H_{10}N_2O_2S$: C, 60.45; H, 3.90. Found: C, 60.16; H, 3.93.

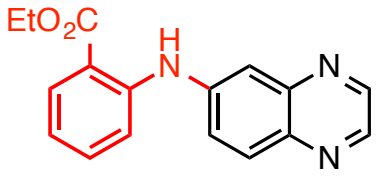
1-(4-((2-methylpyridin-3-yl)amino)phenyl)-2-phenylethanone (7d).



Following general procedure B, a mixture of 1-(4-chlorophenyl)-2-phenylethan-1-one (231 mg, 1 mmol), 2-methyl-3-aminopyridine (162 mg, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol), 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and *t*BuOH (2 mL) was heated to 110 °C for 16 h. The reaction mixture was transferred to a separatory funnel containing water and was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated with the aid of a rotary evaporator. The crude residue was purified via flash chromatography (1% methanol/6% acetone in CH_2Cl_2) to provide the title compound as a yellow solid (Run 1: 263 mg, (87%); Run 2: 263 mg, (87%); Average Yield: 87%), mp = 123 – 125 °C.

^{1}H NMR (500 MHz, C_6D_6) δ 8.28 (d, J = 5.8 Hz, 1H), 7.87 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 7.1 Hz, 2H), 7.10 (t, J = 7.6 Hz, 2H), 7.04 – 7.00 (m, 2H), 6.66 – 6.58 (m, 1H), 6.40 (d, J = 8.4 Hz, 2H), 5.50 (s, 1H), 3.94 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 195.02, 153.23, 148.79, 145.25, 136.04, 135.37, 131.29, 129.71, 129.64, 128.90, 128.86, 128.25, 128.06, 127.87, 126.87, 121.78, 114.53, 45.40, 21.02. FTIR (neat, cm^{-1}): 3350.86, 3053.88, 2892.39, 2162.39, 1659.82, 1593.87, 1570.81, 1520.31, 1434.58, 1331.28, 1232.58, 1182.15, 1116.96, 988.01, 971.19, 830.8, 818.65, 802.54, 780.41, 731.61, 719.85, 700.13. Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00. Found: C, 78.97; H, 6.07.

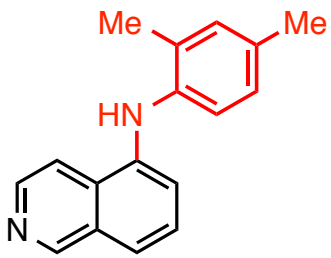
Ethyl 2-(quinoxalin-6-ylamino)benzoate (7e). Following general procedure B, a mixture of 6-chloroquinoxaline (165 mg, 1 mmol), ethyl 2-aminobenzoate (0.222 mL, 1.5 mmol), K_3PO_4 (1.274 g, 6 mmol), 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol) and dioxane (4 mL) was heated to 110 °C for 16 h. Purification via flash chromatography (20% ethyl acetate in hexanes) provided the title compound as an orange solid (Run 1: 247 mg, (84%); Run 2: 246 mg, (84%); Average Yield: 84%), mp = 77 – 79 °C.



^{1}H NMR (500 MHz, C_6D_6) δ 10.18 (s, 1H), 8.29 (d, *J* = 1.7 Hz, 1H), 8.23 (d, *J* = 1.7 Hz, 1H), 8.05 (d, *J* = 2.5 Hz, 1H), 8.01 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.14 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.01 – 6.96 (m, 1H), 6.65 – 6.59 (m, 1H), 4.03 (q, *J* = 7.1 Hz, 2H), 1.00 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 168.45, 146.16, 145.64, 145.10, 143.13, 142.80, 140.44, 134.34, 131.99, 131.00, 128.25, 128.06, 127.87, 125.74, 119.19, 115.74, 114.88, 114.52, 60.93, 14.17. FTIR (neat, cm^{-1}): 3302.08, 3260.13, 2978.93, 1680.36, 1583.91, 1518.65, 1498.89, 1452.6, 1391.56, 1316.65, 1295.67, 1231.2, 1162.26, 1132.46, 1079.26, 1024.14, 958.23, 946.19, 861.37, 824.16, 743.07, 701.62, 656.04, 599.23. Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15. Found: C, 69.88; H, 5.32.

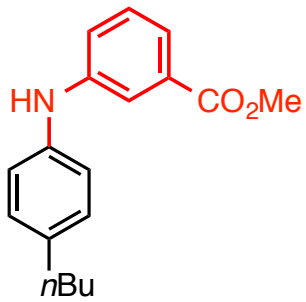
General Procedure C. To a disposable test tube (Fischer Scientific, catalog number: 1495937A) equipped with a magnetic stir-bar and a screw-cap septum K_3PO_4 (3 mmol) and powdered 3 Å molecular sieves (300 mg) were added and then the tube was flame-dried under vacuum. After cooling under vacuum, (dppf)Ni(*o*-tolyl)Cl (**2**) (0.05 mmol), dppf (0.05 mmol), (1.5 mmol) were added. Aryl electrophile (1 mmol) and amine (1.5 mmol), if solid, were also added at this point. The reaction vessel was then evacuated and backfilled with nitrogen. This sequence of evacuation and backfilling was repeated a total of three times. The aryl electrophile and amine, if liquid, were added and followed by MeCN (1 mmol) and CPME (4 mL). The cap was replaced with one containing an unpunctured septum under a continuous flow of nitrogen and the reaction mixture was heated to 110 °C for the 16 h in a pre-heated oil bath. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a Celite plug, eluting with

additional ethyl acetate. The filtrate was then concentrated with the aid of a rotary evaporator and the residue was purified by flash chromatography.



***N*-(2,4-dimethylphenyl)isoquinolin-5-amine (8a).** Following general procedure C, a mixture of isoquinolin-5-yl methanesulfonate (223 mg, 1.0 mmol), 2,4-dimethylaniline (0.185 mL, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol),[5] 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol), 3Å molecular sieves (300 mg) and CPME (4 mL) was heated to 110 °C for 16 h. Purification via flash chromatography (20 % ethyl acetate in hexanes with 10% acetone by volume) provided the title compound as a brown solid (Run 1: 222 mg, (90%), Run 2: 222 mg, (90%), Average Yield: 90%), mp = 119 – 121 °C.

^{1}H NMR (500 MHz, CD_2Cl_2) δ 9.26 (s, 1H), 8.54 (d, J = 5.9 Hz, 1H), 7.88 (d, J = 5.9 Hz, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.44 (t, J = 7.8 Hz, 1H), 7.16 (s, 1H), 7.06 – 7.02 (m, 2H), 6.96 (d, J = 7.5 Hz, 1H), 6.37 (s, 1H), 2.38 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 153.58, 143.04, 141.42, 138.94, 134.28, 132.58, 132.02, 130.49, 128.62, 128.52, 128.31, 123.46, 119.54, 115.31, 114.67, 21.37, 18.42. FTIR (neat, cm^{-1}): 3223.56, 2915.54, 1582.85, 1495.48, 1456.03, 1430.88, 1383.22, 1362.82, 1328.56, 1286.52, 1261.71, 1232.78, 1185.62, 1173.2, 1153.02, 1130.14, 1040.22, 888.57, 819.24, 800.74, 748.5, 657.61, 644.55. HRMS-ESI (m/z) Calcd for $C_{17}H_{16}N_2$ [M+H]: 249.1386; Found: 249.1405.



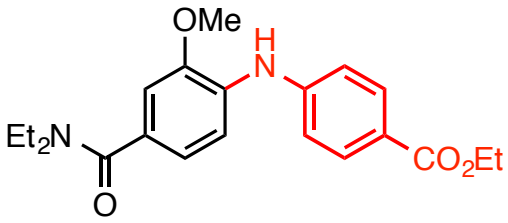
Methyl 3-((4-butylphenyl)amino)benzoate (8b). Following general procedure C, a mixture of 4-butylphenyl dimethylsulfamate (257 mg, 1.0 mmol), methyl 3-aminobenzoate (227 mg, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol), 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28

(5) Although these two runs of this substrate were performed successfully with 3 mmol of K_3PO_4, further experiments revealed that this substrate was sensitive to the amount of base in the reaction and incomplete conversion of isoquinolin-5-yl methanesulfonate was observed. In these cases where the standard conditions were unsuccessful, it was necessary to increase the amount of K_3PO_4 from 3 mmol to 6 mmol in order to achieve full conversion.

mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol), 3Å molecular sieves (300 mg) and CPME (4 mL) was heated to 110 °C for 16 h. Purification via flash chromatography (0 – 4% ethyl acetate in hexanes) provided the title compound as a brown solid (Run 1: 249 mg, (88%); Run 2: 266 mg, (94%); Average Yield: 91%), mp = 101 – 103 °C.

^{1}H NMR (500 MHz, C_6D_6) δ 7.84 – 7.81 (m, 1H), 7.71 – 7.69 (m, 1H), 7.02 (t, *J* = 7.8 Hz, 1H), 6.98 – 6.97 (m, 3H), 6.91 (d, *J* = 8.4 Hz, 2H), 5.35 (s, 1H), 3.49 (s, 3H), 2.53 – 2.33 (m, 2H), 1.53 – 1.47 (m, 2H), 1.31 – 1.24 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 167.08, 144.89, 140.33, 136.65, 131.94, 129.61, 129.52, 121.29, 120.54, 119.72, 117.99, 51.69, 35.35, 34.14, 22.68, 14.21. FTIR (neat, cm^{-1}): 3362.91, 2950.54, 2925.39, 2850.85, 1698.59, 1601.77, 1590.13, 1529.13, 1507.89, 1491.32, 1435.8, 1328.25, 1288.74, 1218.1, 1109.29, 1081.94, 994.6, 976.84, 897.39, 883.99, 848.44, 829.63, 804.81, 776.88, 752.24, 704.9, 679.37, 631.41. Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47. Found: C, 76.20; H, 7.47.

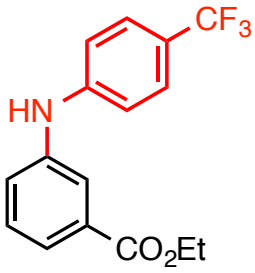
Ethyl 4-((4-(diethylcarbamoyl)-2-methoxyphenyl)amino)benzoate (8c).



Following general procedure C, a mixture of 4-(diethylcarbamoyl)-2-methoxyphenyl trifluoromethanesulfonate (355 mg, 1.0 mmol), ethyl 4-aminobenzoate (248 mg, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol), 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol), 3Å molecular sieves (300 mg) and CPME (4 mL) was heated to 110 °C for 16 h. Purification via Biotage SP4 (silica-packed 50 g Snap cartridge, 30 – 50% ethyl acetate in hexanes) provided the title compound as a light green solid (Run 1: 339 mg, (92%); Run 2: 343 mg, (93%); Average Yield: 93%), mp = 128 – 129 °C.

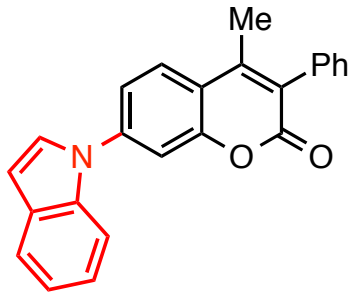
^{1}H NMR (500 MHz, C_6D_6) δ 8.13 (d, *J* = 8.7 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 1H), 7.02 (d, *J* = 1.5 Hz, 1H), 6.89 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.60 (s, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.22 (s, 7H), 1.06 (t, *J* = 7.1 Hz, 3H), 0.98 (s, 6H). ^{13}C NMR (126 MHz, C_6D_6) δ 170.67, 166.15, 149.21, 147.03, 132.39, 131.69, 130.89, 122.92, 119.58, 116.36, 115.73, 110.76, 60.43, 55.13, 41.76, 14.48, 13.80. FTIR (neat, cm^{-1}): 3280.94, 3185.74, 3076.72, 2972.91, 2937.16, 1692.65, 1589.66, 1524.67, 1457.8,

1456.18, 1428.75, 1341.82, 1309.69, 1274.05, 1247.32, 1176.37, 1107.96, 1095.68, 1025.91, 843.74, 811.61, 769.35, 757.64, 700.27. Anal. Calcd. for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07; Found: C, 67.92; H, 7.14.

Ethyl 3-((4-(trifluoromethyl)phenyl)amino)benzoate (8d). 

Following general procedure C, a mixture of ethyl 3-((methylsulfonyl)oxy)benzoate (244 mg, 1 mmol), 4-trifluoromethylaniline (0.188 mL, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol), 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (18.5 mg, 0.025 mmol), dppf (14 mg, 0.025 mmol), MeCN (0.052 mL, 1 mmol), and CPME (4 mL) was heated to 110 °C for 4 h. Purification via flash chromatography (2 – 6% ethyl acetate in hexanes) provided the title compound as a white solid (Run 1: 292 mg, (95%); Run 2: 278 mg, (90%); Average Yield: 93%), mp = 106 – 108 °C.

^{1}H NMR (500 MHz, C_6D_6) δ 7.87 – 7.70 (m, 2H), 7.27 (d, J = 8.5 Hz, 2H), 7.03 (t, J = 7.8 Hz, 1H), 6.93 (dd, J = 2.5, 1.1 Hz, 1H), 6.61 (d, J = 8.5 Hz, 2H), 5.48 (s, 1H), 4.14 (q, J = 7.2 Hz, 2H), 1.05 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 166.36, 146.39, 142.01, 132.44, 129.61, 128.66 (q, J = 270.9 Hz), 126.99 (q, J = 3.8 Hz), 123.64, 123.32, 122.63 (q, J = 32.5 Hz), 120.87, 116.05, 61.21, 14.25. ^{19}F NMR (282 MHz, C_6D_6) δ -61.37. FTIR (neat, cm^{-1}): 3354.74, 2994.82, 2906.15, 1699.64, 1606.46, 1541.18, 1486.78, 1440.51, 1402.96, 1368.12, 1305.39, 1282.88, 1213.1, 1153.38, 1102.13, 1068.39, 1027.83, 952.18, 835.16, 809.55, 749.42. The characterization data were in accordance with those reported in the literature.[1a]

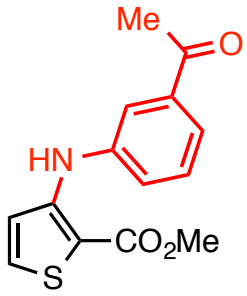
7-(1*H*-indol-1-yl)-4-methyl-3-phenyl-2*H*-chromen-2-one (8e). 

Following general procedure C, a mixture of ethyl 4-methyl-2-oxo-3-phenyl-2*H*-chromen-7-yl dimethylsulfamate (359 mg, 1.0 mmol), indole (176 mg, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol), 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol), and CPME (4 mL) was heated to 110 °C for 16 h. Purification via flash chromatography (60% toluene in hexanes with 5% Et_2O by volume) provided the title compound as an off-white solid (Run 1:

328 mg, (93%); Run 2: 322 mg, (92%); Average Yield: 93%), mp = 185 – 186 °C.

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.78 (d, *J* = 8.5 Hz, 1H), 7.73 (t, *J* = 8.0 Hz, 2H), 7.55 – 7.48 (m, 4H), 7.48 – 7.43 (m, 2H), 7.37 – 7.33 (m, 2H), 7.32 – 7.28 (m, 1H), 7.26 – 7.21 (m, 1H), 6.77 (d, *J* = 3.3 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 160.97, 154.00, 147.82, 142.58, 135.80, 135.13, 130.63, 130.43, 128.79, 128.63, 127.93, 127.08, 126.96, 123.45, 121.83, 121.57, 119.60, 118.80, 111.25, 111.07, 105.59, 16.96. FTIR (neat, cm^{-1}): 3128.47, 3107.62, 3050.76, 2925.6, 1706.31, 1599.3, 1521.65, 1452.5, 1384.89, 1356.69, 1321.66, 1295.45, 1202.99, 1148.67, 1078.43, 1061.7, 1018.12, 1000.88, 955.11, 921.27, 869.17, 812.83, 772.64, 762.4, 742.44, 735.26, 701.13, 657.67, 638.22, 622.14, 582.01, 571.9, 556.58. HRMS-ESI (m/z) Calcd for $C_{24}H_{17}NO_2$ [M+H]: 352.1332; Found: 352.1354.

Methyl 3-((3-acetylphenyl)amino)thiophene-2-carboxylate (8f).



Following general procedure C, a mixture of methyl 3-(((trifluoromethyl)sulfonyl)oxy)thiophene-2-carboxylate (290 mg, 1.0 mmol), 3'-aminoacetophenone (203 mg, 1.5 mmol), K_3PO_4 (637 mg, 3 mmol), 3 Å molecular sieves (300 mg), (dppf)Ni(*o*-tolyl)Cl (**2**) (37 mg, 0.05 mmol), dppf (28 mg, 0.05 mmol), MeCN (0.052 mL, 1 mmol), and CPME (4 mL) was heated to 110 °C for 16 h. Purification via flash chromatography (10% ethyl acetate in hexanes) provided the title compound as a light brown solid (Run 1: 268 mg, (97%); Run 2: 269 mg, (98%); Average Yield: 98%), mp = 85 – 87 °C.

^{1}H NMR (500 MHz, C_6D_6) δ 9.12 (s, 1H), 7.66 (s, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 6.95 (t, *J* = 7.8 Hz, 1H), 6.88 (dd, *J* = 7.6, 1.8 Hz, 1H), 6.82 (d, *J* = 5.5 Hz, 1H), 6.75 (d, *J* = 5.5 Hz, 1H), 3.46 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ 196.39, 165.25, 150.86, 142.12, 138.77, 132.05, 129.63, 124.01, 122.74, 119.00, 117.91, 104.41, 51.17, 26.28. FTIR (neat, cm^{-1}): 3289.04, 3113.73, 3102.16, 3052.44, 2952.67, 2922.92, 2853.02, 1677.13, 1655.43, 1595.48, 1567.08, 1488.23, 1457.75, 1456.13, 1432.79, 1384.42, 1355.94, 1250.47, 1213.8, 1094.59, 1036.3, 1024.6, 984.84, 943.77, 885.47, 840.76, 773.01, 732.29, 708.86, 679.34, 629.39, 586.11. Anal. Calcd. for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76. Found: C, 61.16; H, 4.76.

Parameters of X-ray crystallographic characterization of [1,1'-Bis(diphenylphosphino)ferrocene](*o*-tolyl)chloronickel (2).

Crystal Data

Chemical formula:	$C_{45}H_{43}ClFeNiOP_2$
Formula weight:	811.776
Crystal system:	Monoclinic
Space group:	$P2_1/n$
a:	13.9551 Å
b:	20.5372 Å
c:	14.7137 Å
α:	90.00˚
β:	118.1170˚
γ:	90.00˚
Volume (Å^3):	3719.3
Z:	4
Calculated density (g/cm^3):	1.450
Crystal Size:	0.25 x 0.25 x 0.08 mm^{-3}
Temperature (K):	100(2)
Crystal description:	Plate
Crystal color:	Gold
Radiation Type, wavelength (Å):	Mo *Kα*, 0.71073
F(000):	1688

Data Collection

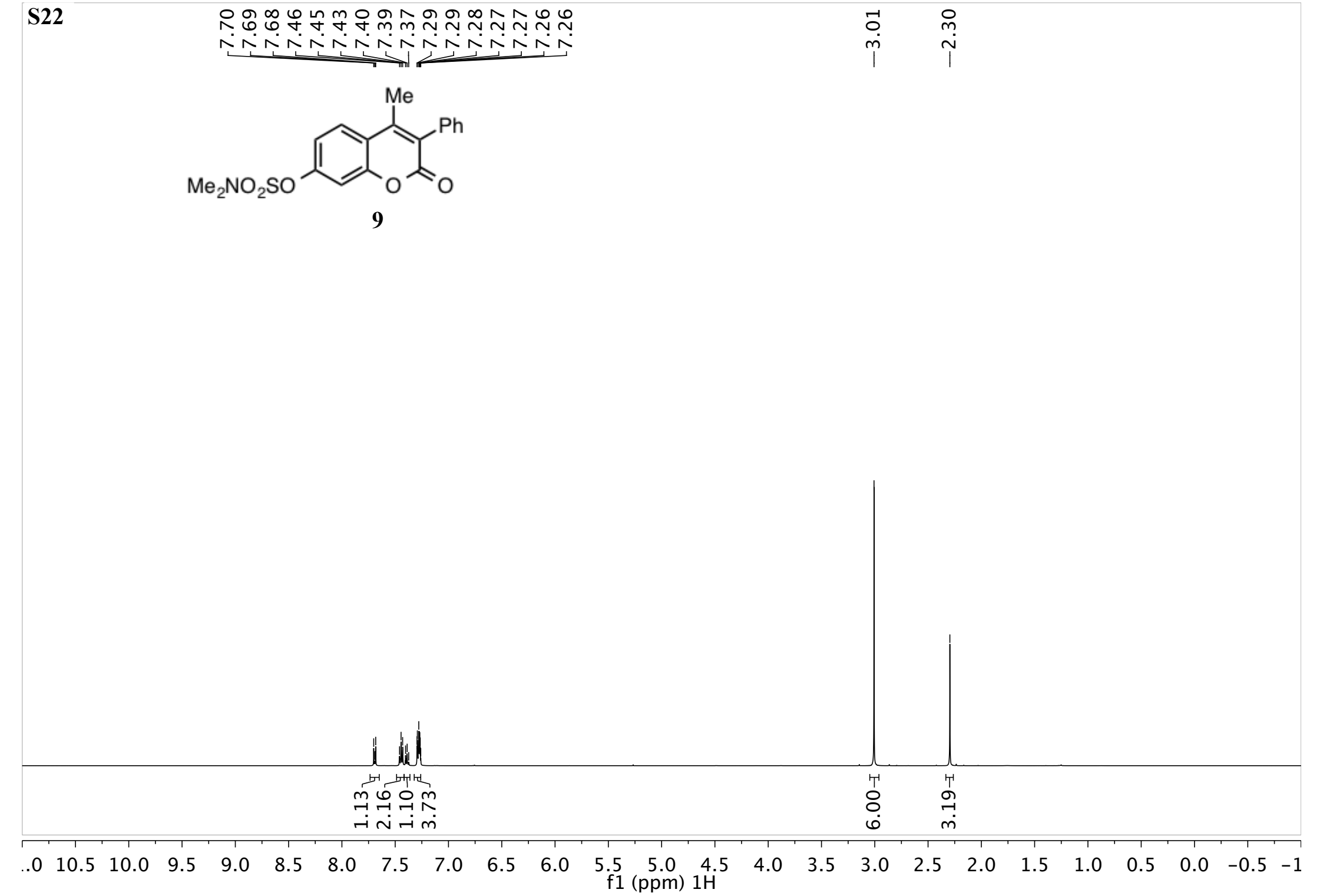
Diffractometer:	Brucker X8 Kappa DUO four-circle
Detector type:	Brucker Smart APEX2 CCD
Absorbtion correction:	multi-scan, SADABS (Sheldrick, 2009)
T_{min}, T_{max}:	0.7723, 0.9179
Absorbtion coefficient (mm^{-1}):	1.090
Reflections, total:	123956
Reflections, independent:	12525 [R(int) = 0.0387]
Reflections with I>2σI	10910
Index ranges:	$-20 \leq h \leq 20$, $-30 \leq k \leq 30$, $-21 \leq l \leq 20$
Theta range for data collection:	2.53 to 31.66˚
Completeness to theta = 31.7˚	99.5%

Refinement

Refinement Method:	Full-matrix least-squares on F^2
Final R indices [I>2σI]:	R1 = 0.0288, wR^2 = 0.0709
R indices (all data):	R1 = 0.0357, wR^2 = 0.0748
Goodness-of-fit on F_2:	1.023
Reflections/ restraints/ parameters:	12525/ 385/ 506
Hydrogen atom treatment:	constrained

Crystallographer's comments:

Highest residual density maxima are located near the THF molecule, however disorder refinement did not improve the model. The *o*-tolyl substituent on the Ni was treated as disordered over two positions, corresponding to a swiping motion in the toluene-plane and perpendicular to the Ni1-C1 bond. This treatment is only semi-satisfactory but still better than the model without tolyl-disorder. It seems likely that there is actual motion in the crystal.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7.27
7.26
7.26
3.01
2.30
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Ph
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O
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6.00
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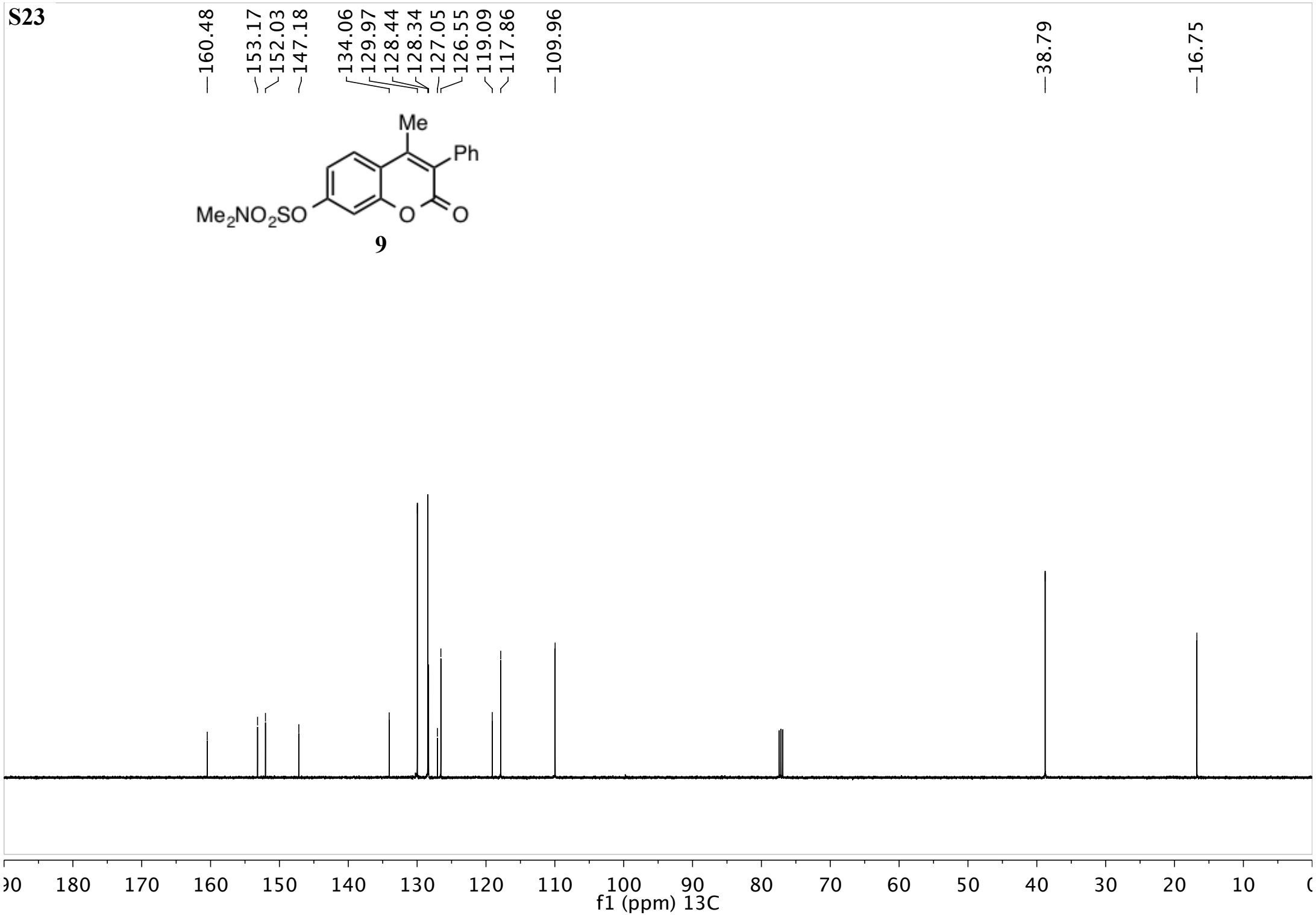
9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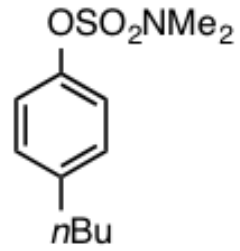
9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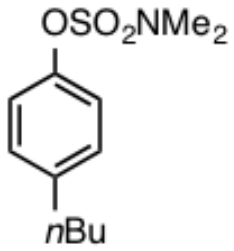
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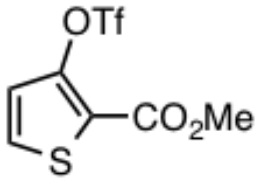
10
f1 (ppm) 13C



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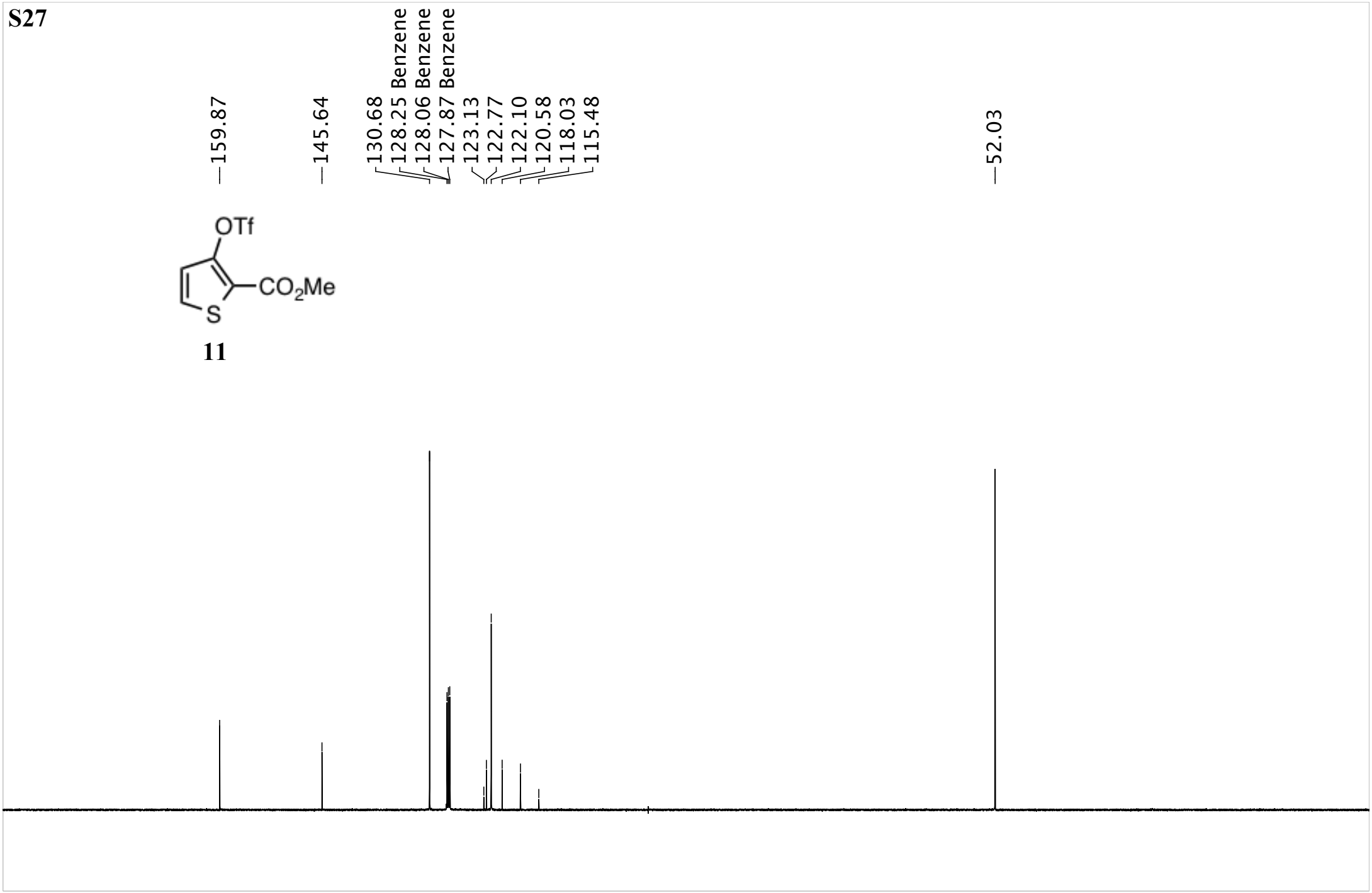
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OTf
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S
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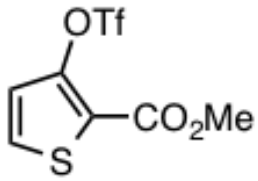
11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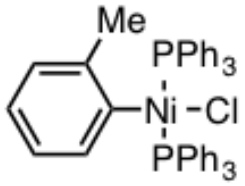
f1 (ppm) 19F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Ni
Cl
PPh3

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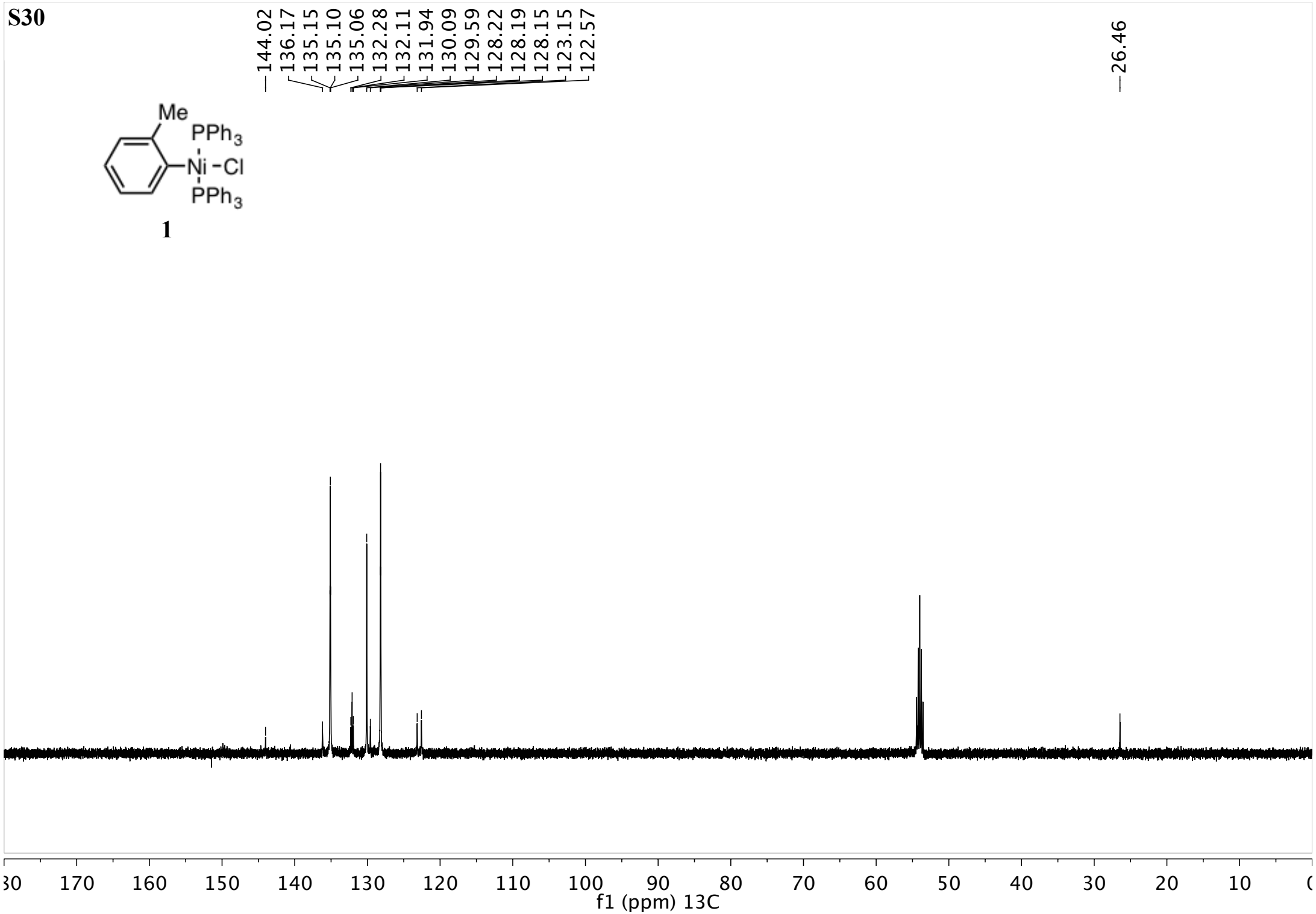
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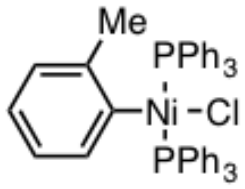
PPh3
Ni
Cl
PPh3
f1 (ppm) 13C

1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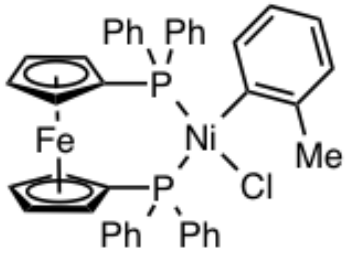
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Ni
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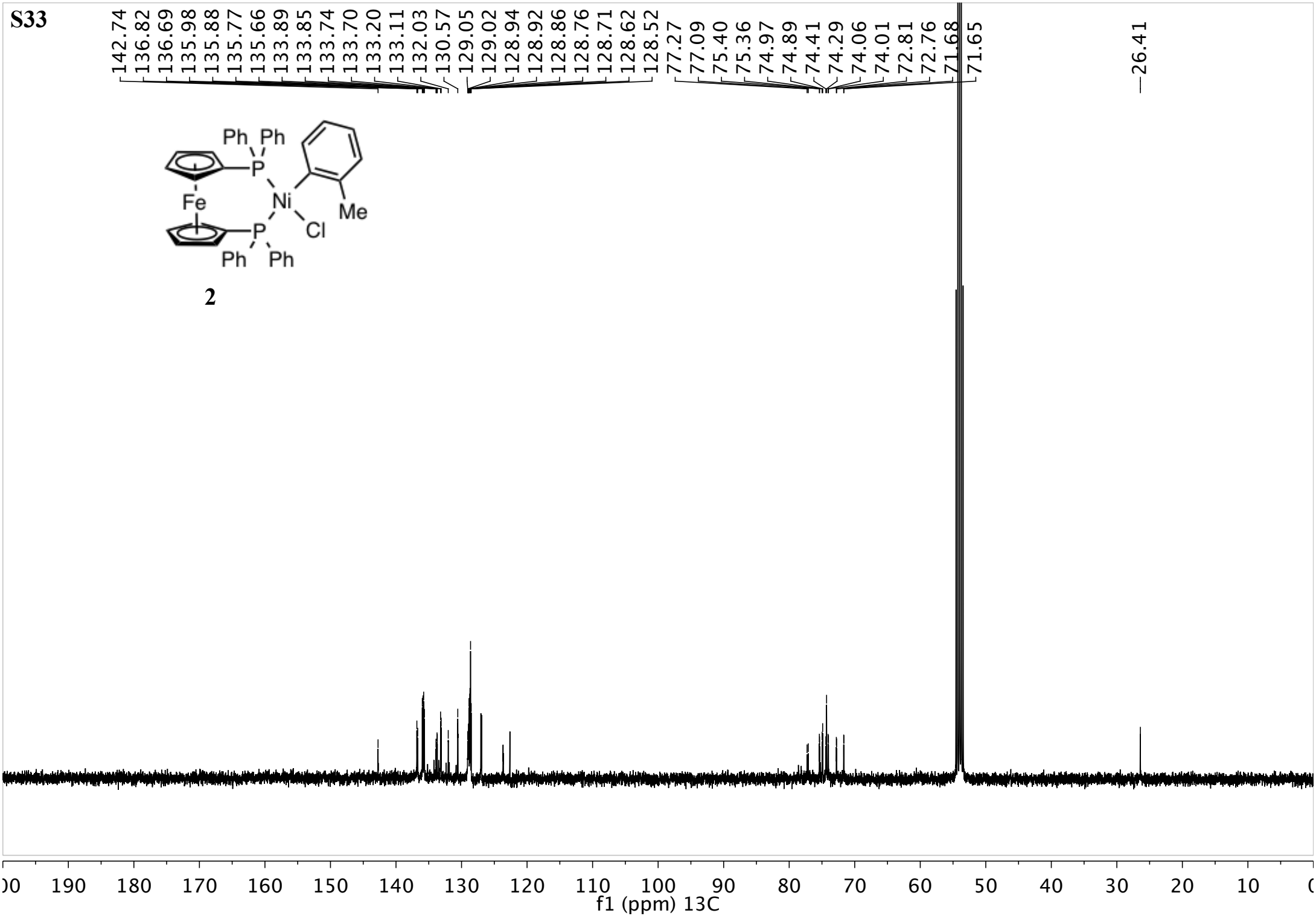
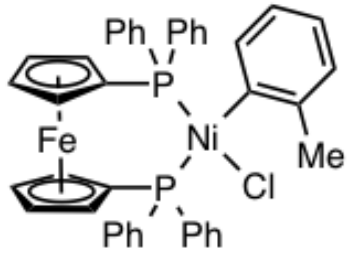
8.08
7.55
7.53
7.36
7.29
7.09
6.86
6.70
6.53
6.40
6.20
5.32
5.25
4.64
4.34
4.28
4.13
4.11
3.62
3.42
2.54
3.87
1.99
6.92
1.86
1.22
1.15
2.02
2.03
1.16
1.08
1.15
1.03
1.27
0.99
1.11
2.02
1.04
1.14
3.00
f1 (ppm) 1H

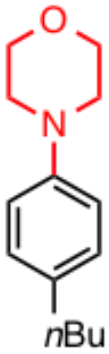

142.74
136.82
136.69
135.98
135.88
135.77
135.66
133.89
133.85
133.74
133.70
133.20
133.11
132.03
130.57
129.05
129.02
128.94
128.92
128.86
128.76
128.71
128.62
128.52
77.27
77.09
75.40
75.36
74.97
74.89
74.41
74.29
74.06
74.01
72.81
72.76
71.68
71.65
26.41
Ph
Ph
P
Fe
Ni
Me
Cl
P
Ph
Ph
f1 (ppm) 13C

2


Ph Ph
P
Fe
Ni
Me
Cl
P
Ph Ph

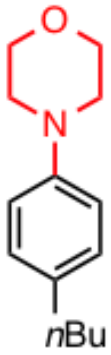
2

28.65
28.44
11.26
11.05
120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70
f1 (ppm) 31P


O
N
nBu

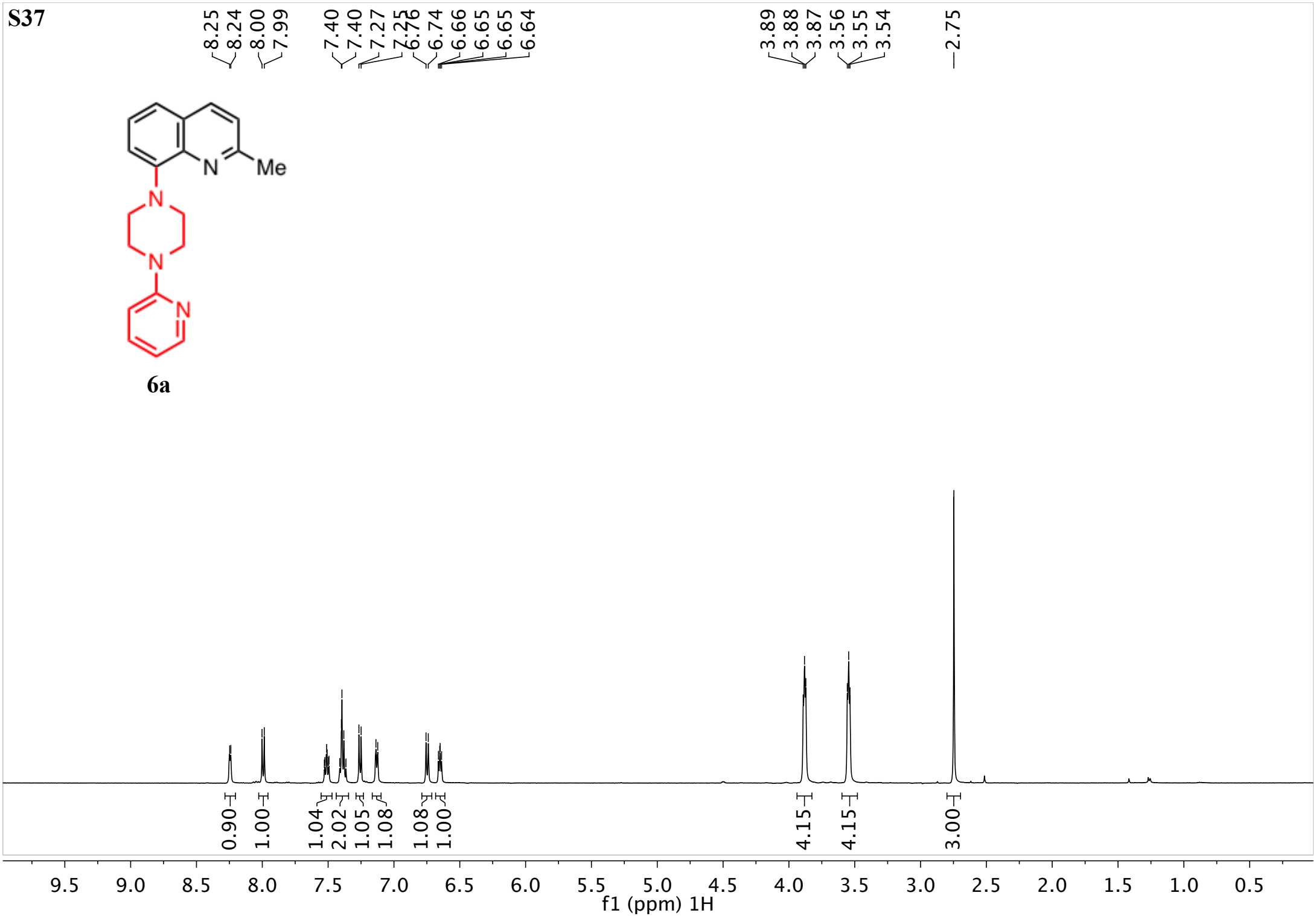
5

7.16
7.07
7.06
6.71
6.70
3.59
3.58
3.57
2.78
2.77
2.76
2.52
2.51
1.59
1.57
1.55
1.54
1.52
1.34
1.32
1.31
1.29
1.28
1.27
0.90
0.89
0.87
2.01
2.07
4.25
4.29
2.16
2.05
2.19
3.00
f1 (ppm) 1H

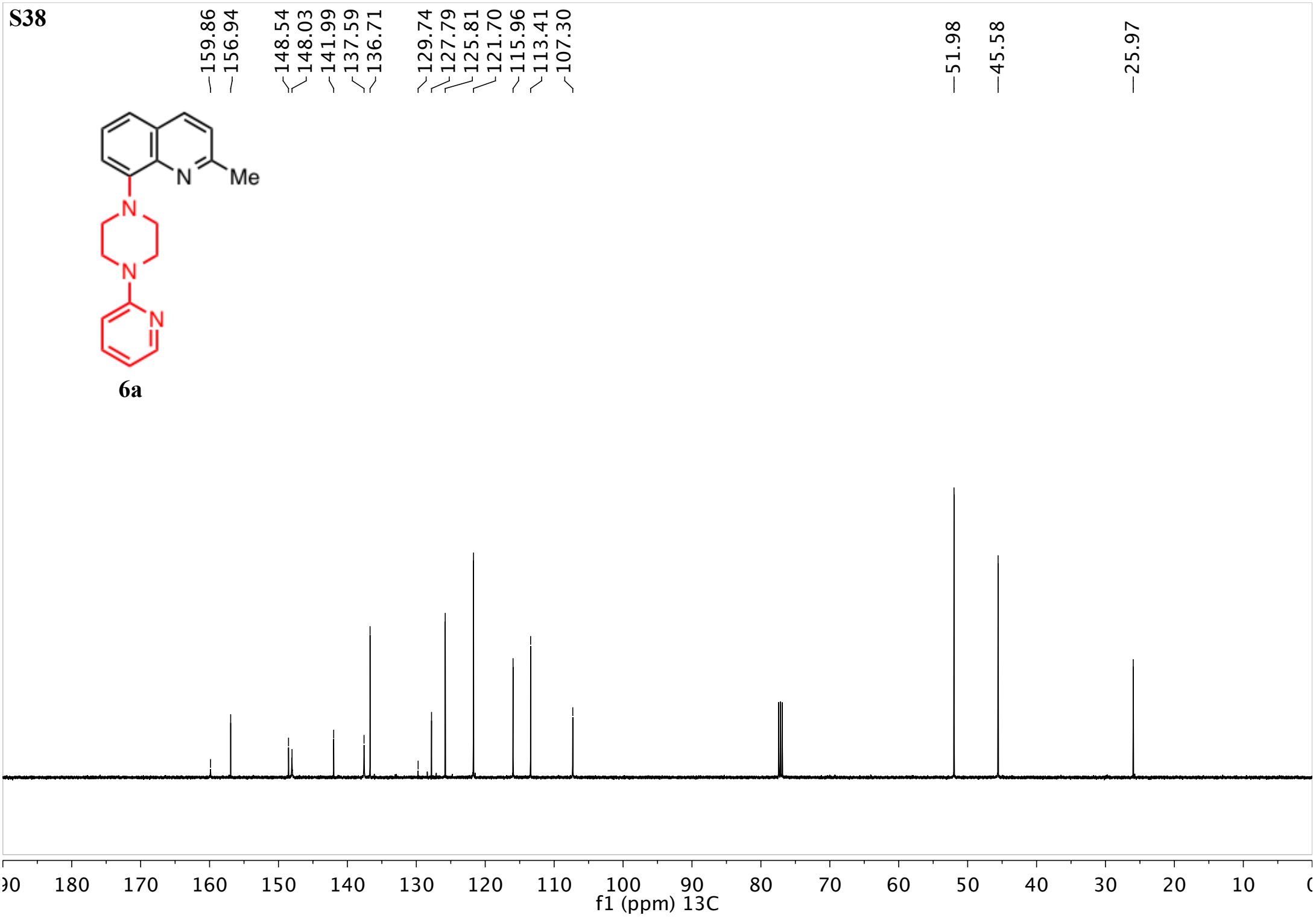

O
N
nBu

5

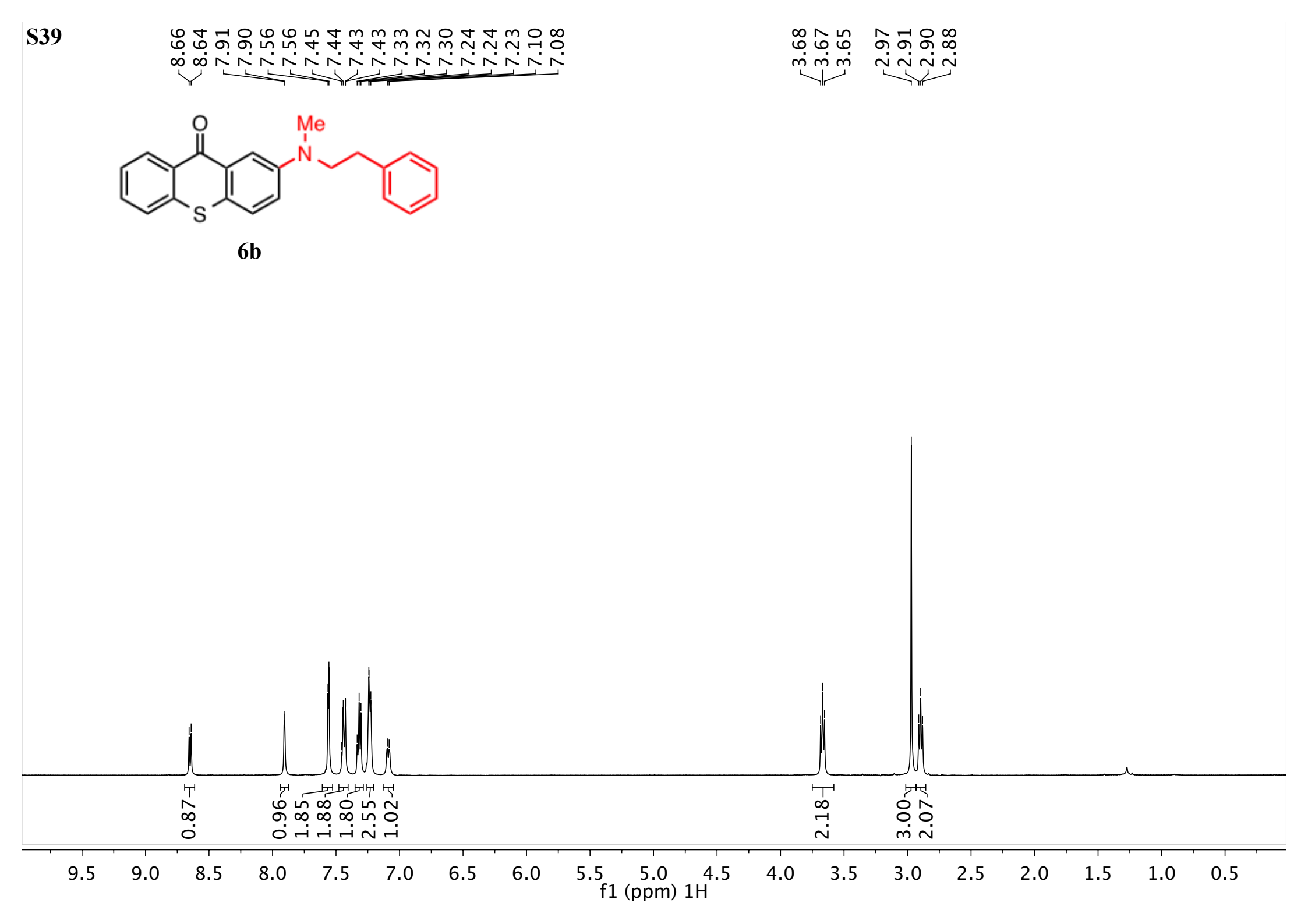
150.09
134.31
129.28
116.33
67.03
50.01
35.21
34.34
22.69
14.25
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm) 13C


8.25
8.24
8.00
7.99
7.40
7.40
7.27
7.25
6.76
6.74
6.66
6.65
6.65
6.64
3.89
3.88
3.87
3.56
3.55
3.54
2.75
N
Me
N
N
N
0.90
1.00
1.04
2.02
1.05
1.08
1.08
1.00
4.15
4.15
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm) 1H

6a

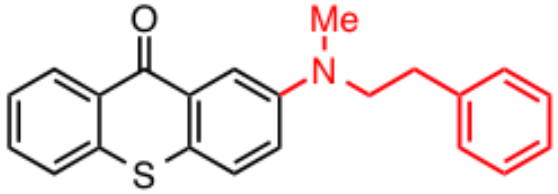

159.86
156.94
148.54
148.03
141.99
137.59
136.71
129.74
127.79
125.81
121.70
115.96
113.41
107.30
51.98
45.58
25.97
N
Me
N
N
N
f1 (ppm) 13C

6a

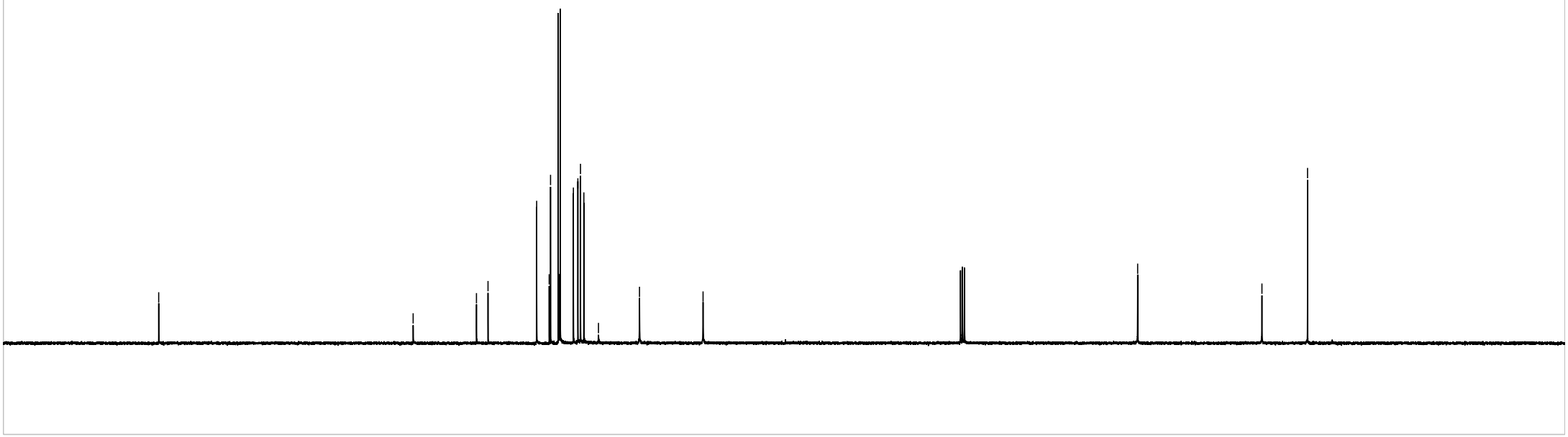

8.66
8.64
7.91
7.90
7.56
7.56
7.45
7.44
7.43
7.43
7.33
7.32
7.30
7.24
7.24
7.23
7.10
7.08
3.68
3.67
3.65
2.97
2.91
2.90
2.88
O
Me
N
S
0.87
0.96
1.85
1.88
1.80
2.55
1.02
2.18
3.00
2.07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm) 1H

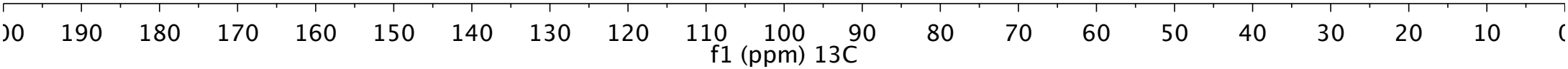
6b

180.10
147.52
131.70
129.92
128.94
128.80
128.69
126.99
126.42
126.08
125.65
110.39
54.73
38.81
32.97

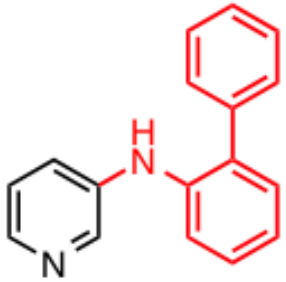


6b

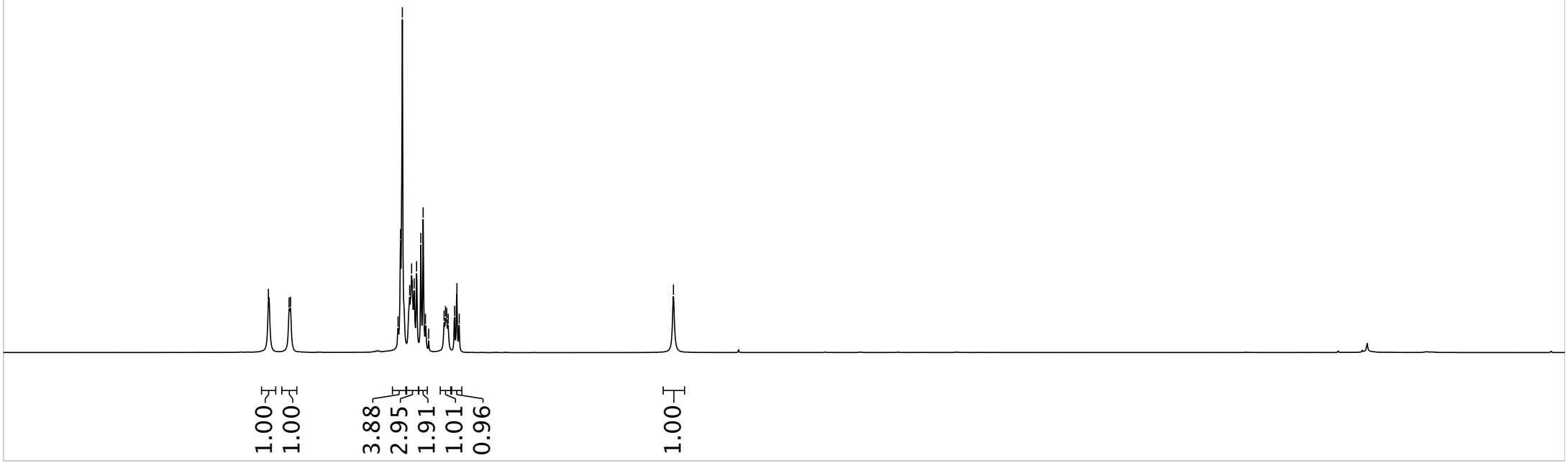


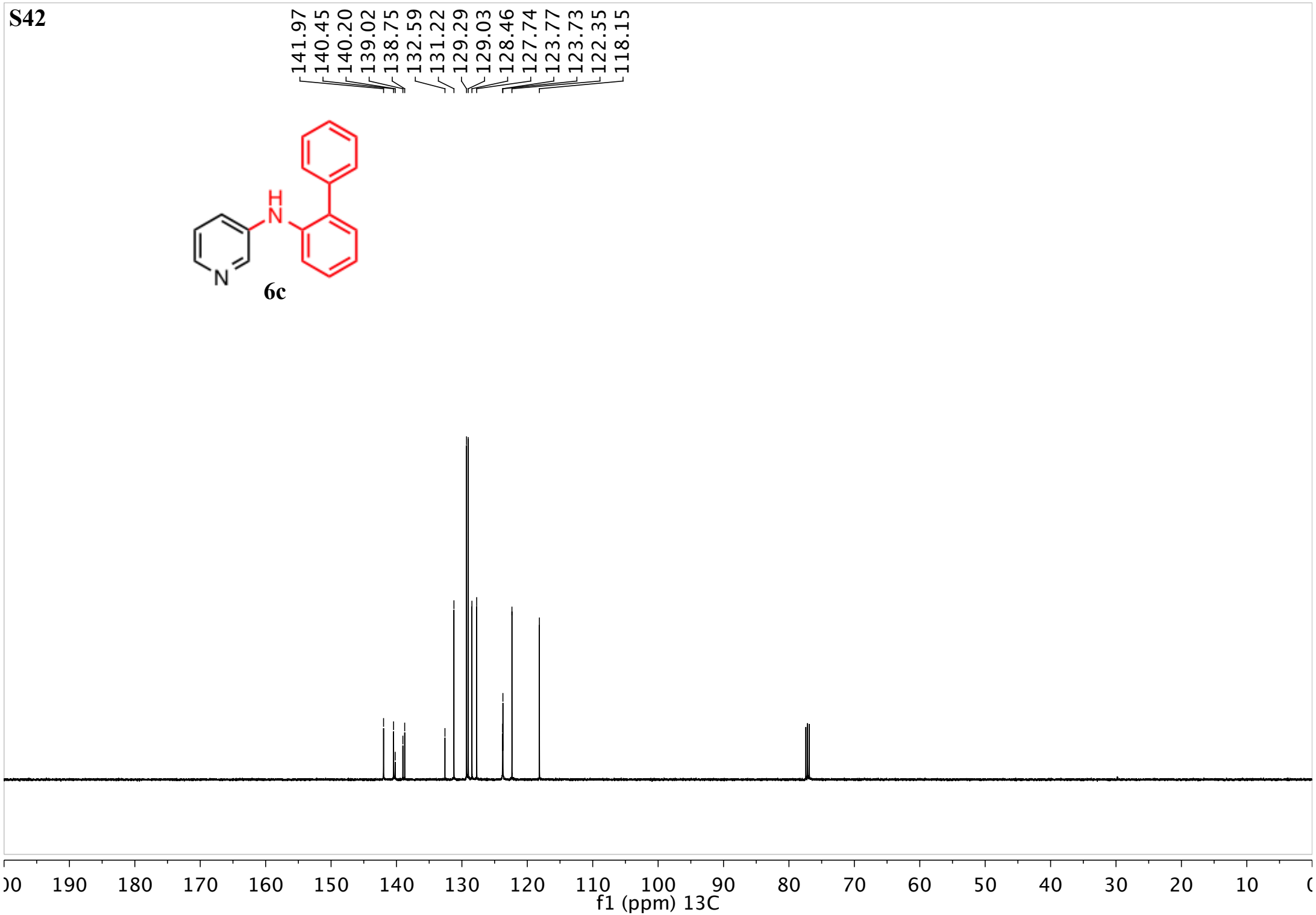



8.28
8.15
8.14
7.44
7.43
7.38
7.37
7.35
7.34
7.31
7.29
7.15
7.14
7.09
7.08
5.70


H
N
N

6c


1.00
1.00
3.88
2.95
1.91
1.01
0.96
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm) 1H

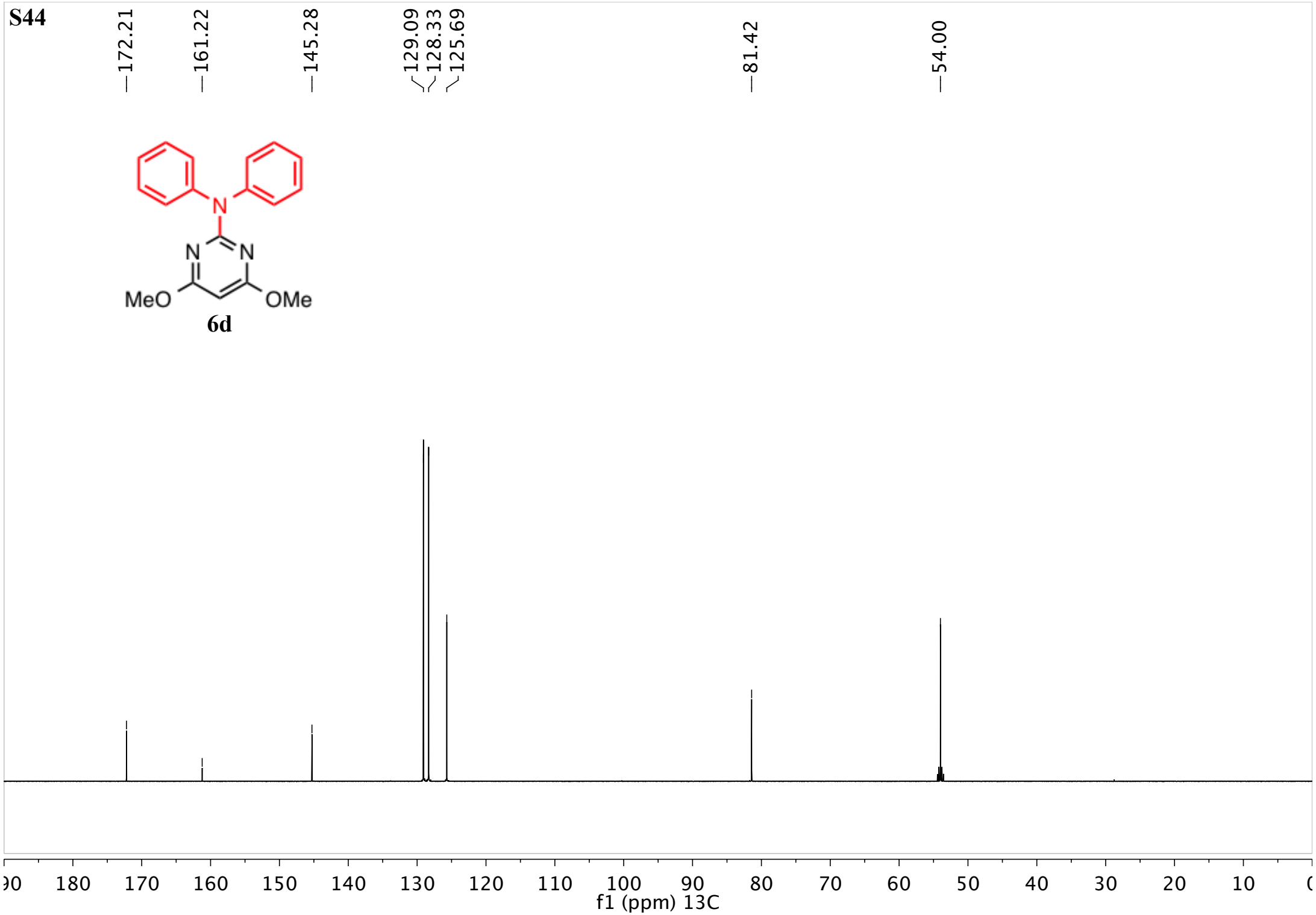

141.97
140.45
140.20
139.02
138.75
132.59
131.22
129.29
129.03
128.46
127.74
123.77
123.73
122.35
118.15
H
N
N
f1 (ppm) 13C

6c

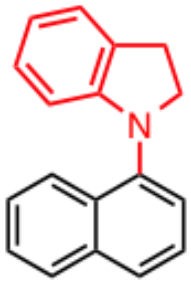

N
N
N
MeO
OMe

6d

7.43
7.42
7.40
7.27
7.25
7.24
5.64
3.72
7.78
1.96
0.86
6.00
f1 (ppm) 1H

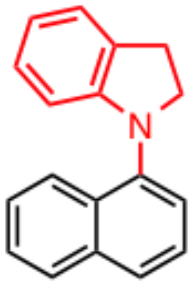

172.21
161.22
145.28
129.09
128.33
125.69
81.42
54.00
N
N
N
MeO
OMe
f1 (ppm) 13C

6d



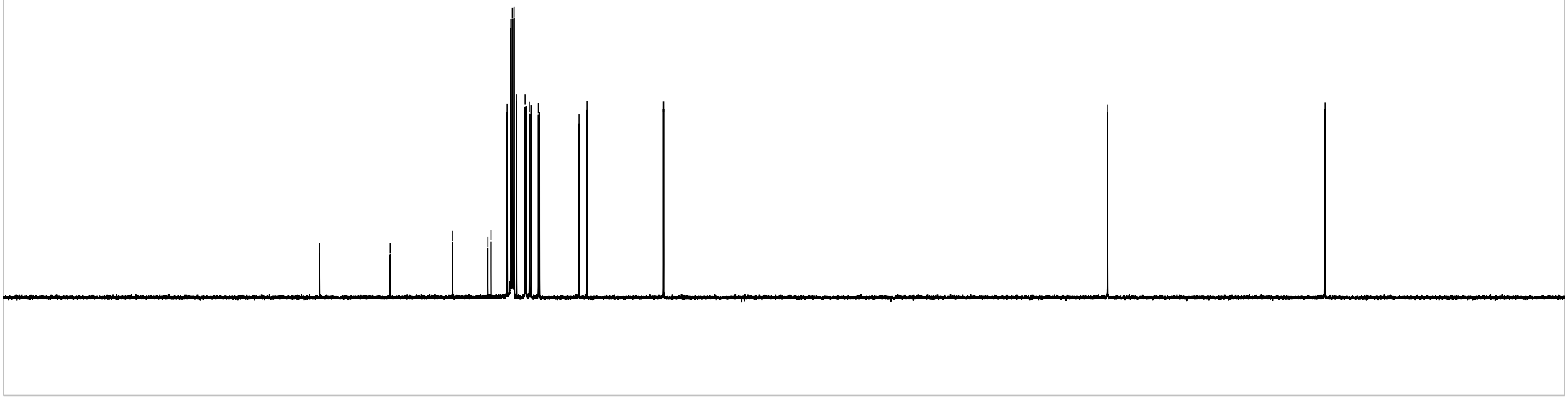
6e

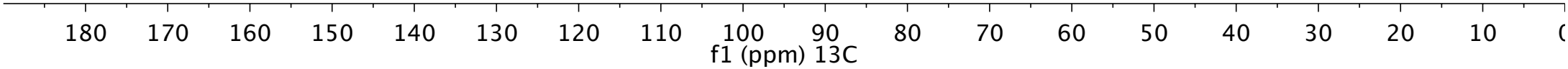
8.22
8.20
7.70
7.69
7.54
7.52
7.28
7.27
7.26
7.25
7.24
7.23
7.19
7.18
7.11
7.10
6.88
6.87
6.77
6.76
6.33
6.31
3.58
3.50
2.89
2.72
1.00
1.02
0.97
2.89
0.92
0.99
0.99
0.98
0.98
2.45
2.54
f1 (ppm) 1H

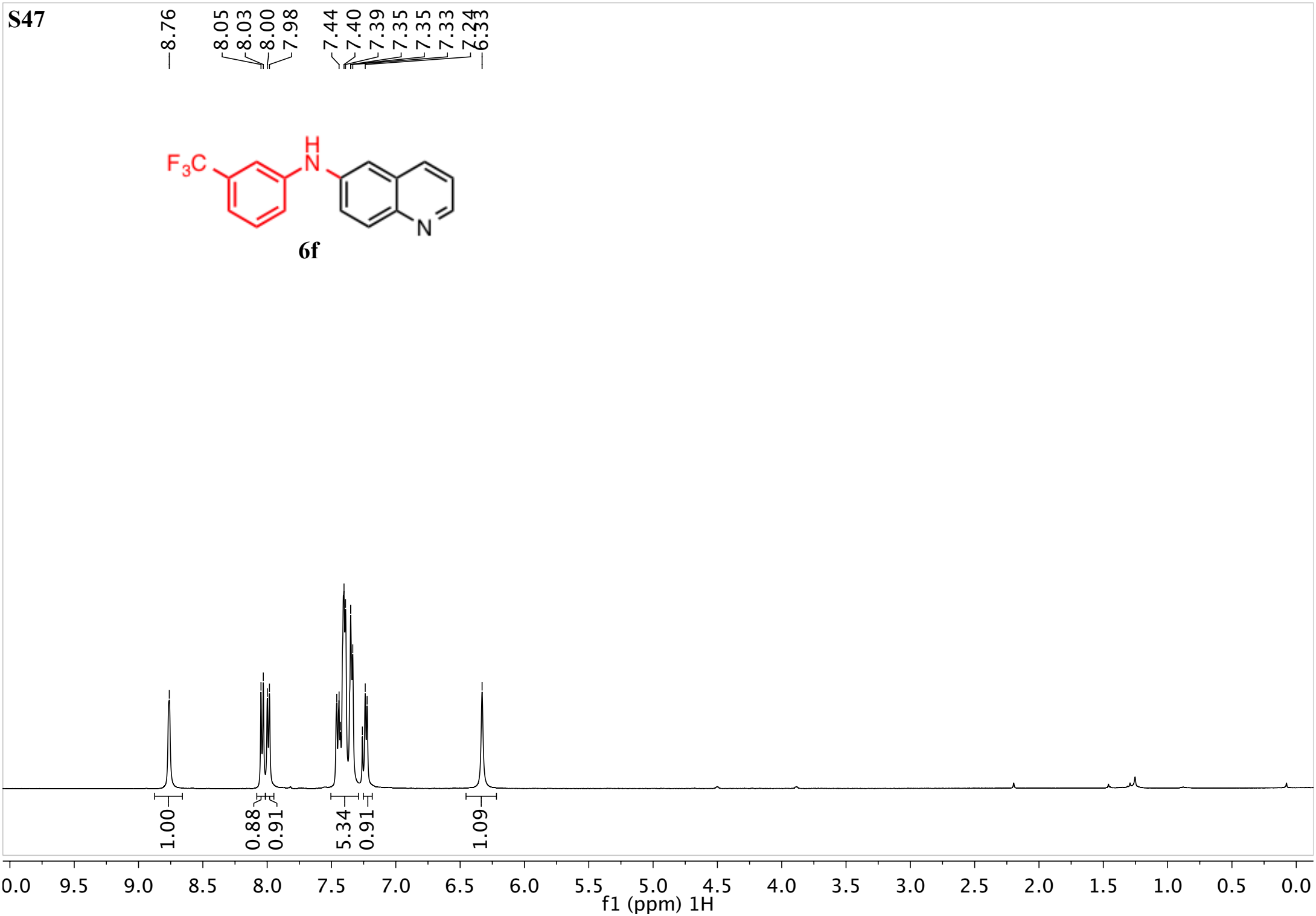


6e

151.54
142.95
128.25 Benzene
128.06 Benzene
127.87 Benzene
127.56
126.51
126.00
124.90
118.99
109.67
55.63
29.19

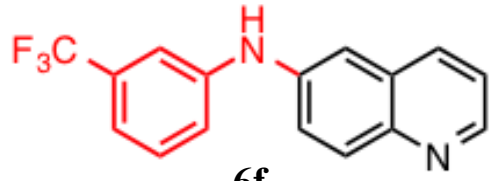




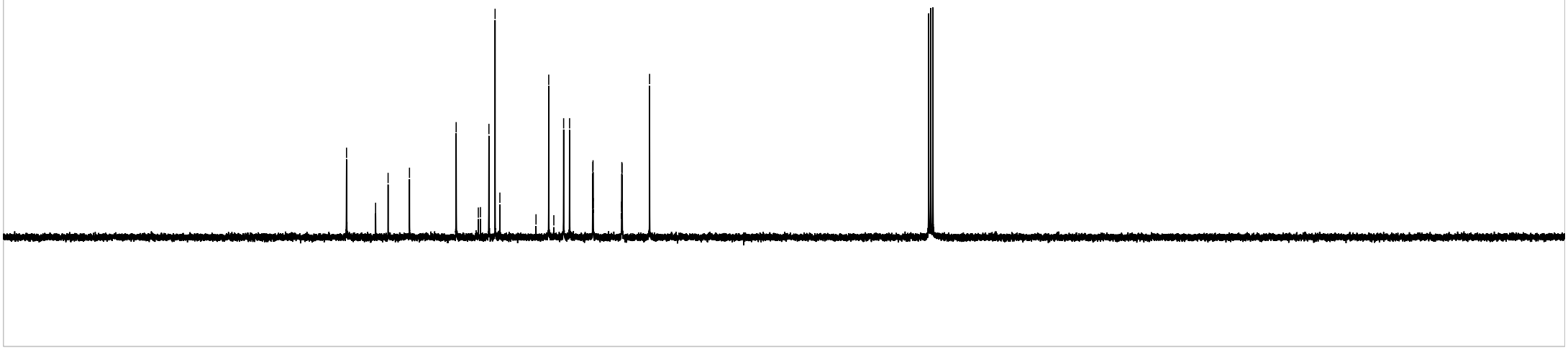

8.76
8.05
8.03
8.00
7.98
7.44
7.40
7.39
7.35
7.35
7.33
7.24
6.33
F3C
H
N
N
1.00
0.88
0.91
5.34
0.91
1.09
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm) 1H

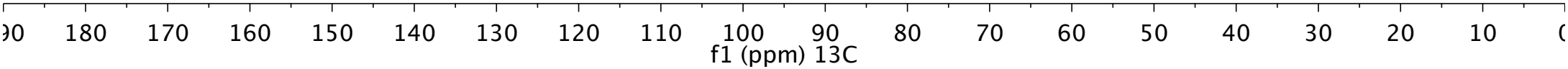
6f

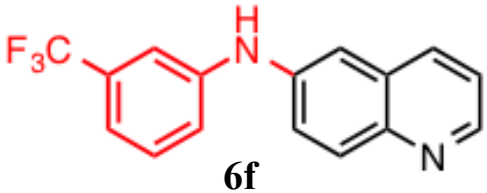
148.24
144.71
143.19
140.59
134.91
132.21
131.95
130.92
130.17
129.59
125.19
123.64
123.02
121.83
121.11
118.31
118.28
118.25
118.22
114.78
114.75
114.72
114.69
111.37



6f

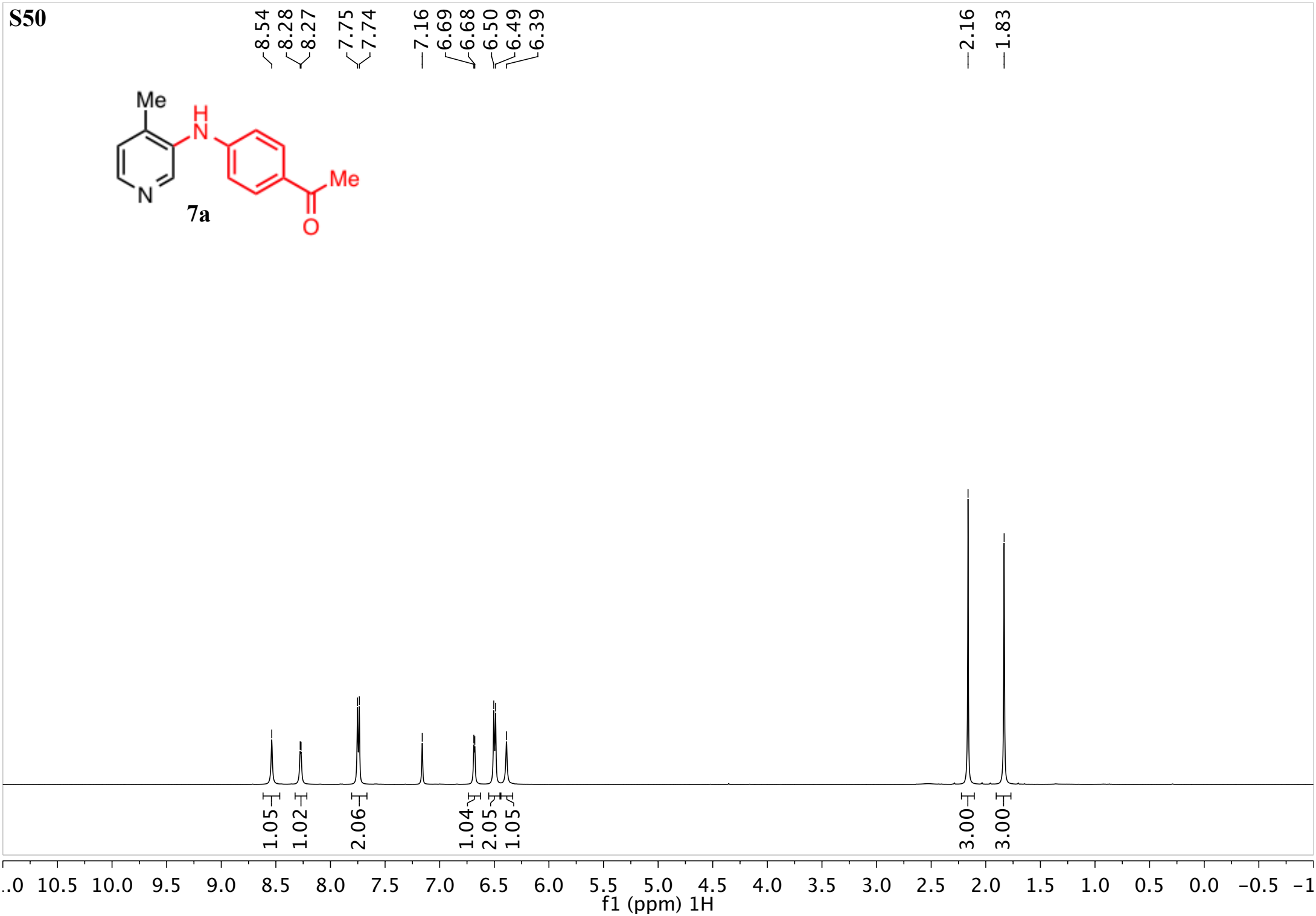




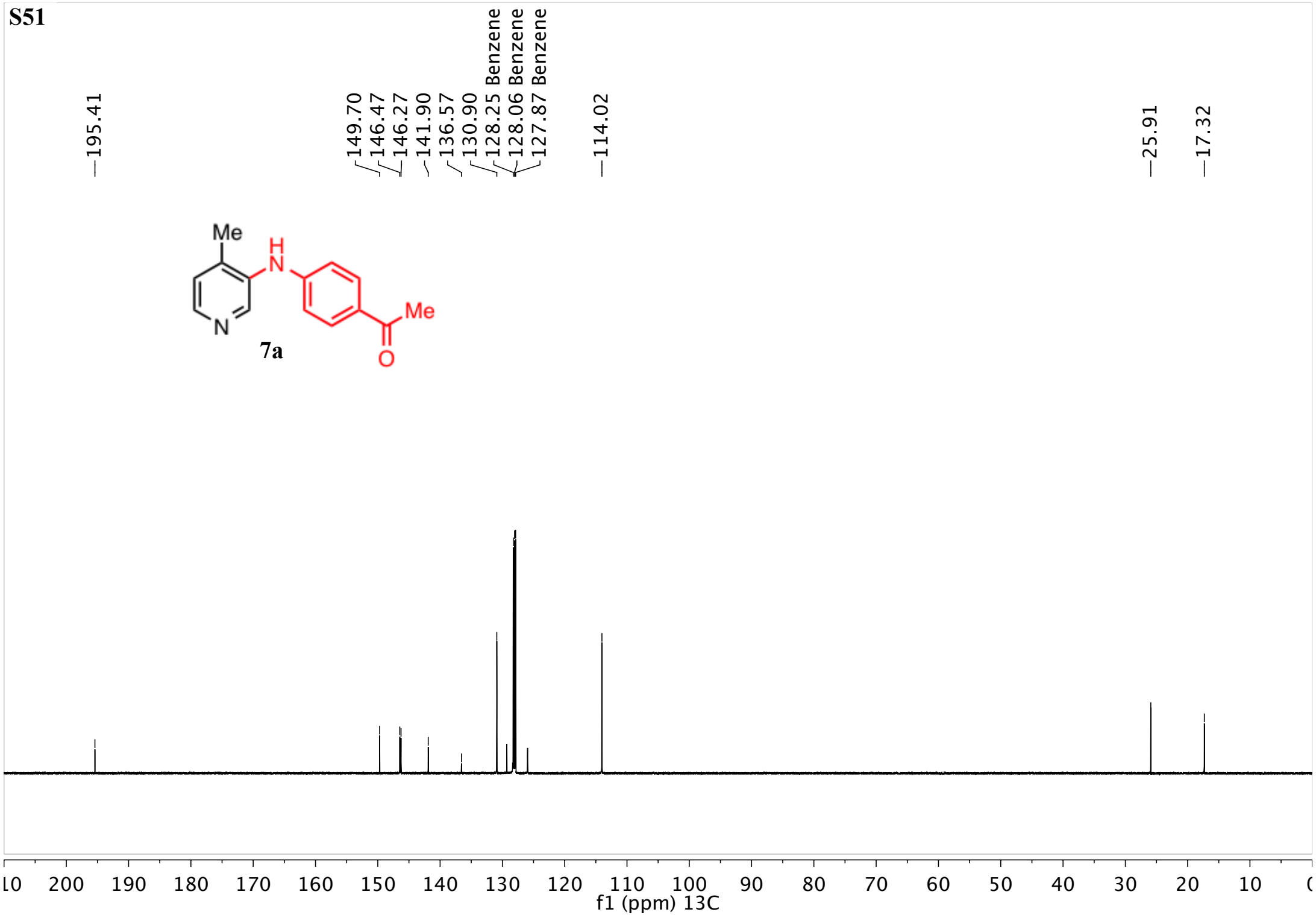

F3C
H
N
N

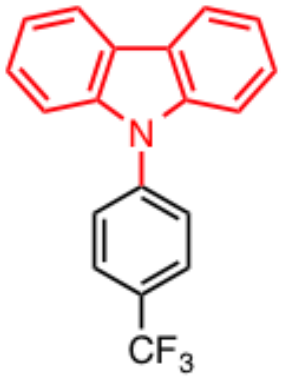
6f

-63.06
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
f1 (ppm) 19F


8.54
8.28
8.27
7.75
7.74
7.16
6.69
6.68
6.50
6.49
6.39
2.16
1.83
Me
H
N
N
Me
O
1.05
1.02
2.06
1.04
2.05
1.05
3.00
3.00
..0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm) 1H

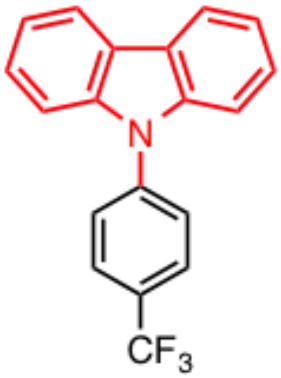
7a


195.41
149.70
146.47
146.27
141.90
136.57
130.90
128.25 Benzene
128.06 Benzene
127.87 Benzene
114.02
25.91
17.32
Me
H
N
N
Me
O
7a
f1 (ppm) 13C


N
CF3

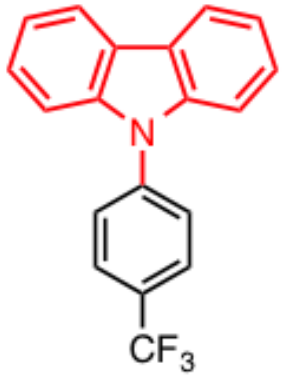
7b

8.02
8.01
7.33
7.31
7.29
7.29
7.28
7.28
7.26
7.26
7.26
7.24
7.24
7.23
7.23
7.16
7.15
7.14
7.13
6.95
6.94
1.94
1.97
4.22
2.00
2.04
f1 (ppm) 1H


N
CF3

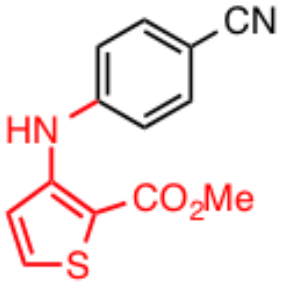
7b

141.18
140.69
128.25 Benzene
128.06 Benzene
127.87 Benzene
127.14
126.50
121.01
120.82
109.92
f1 (ppm) 13C


N
CF3

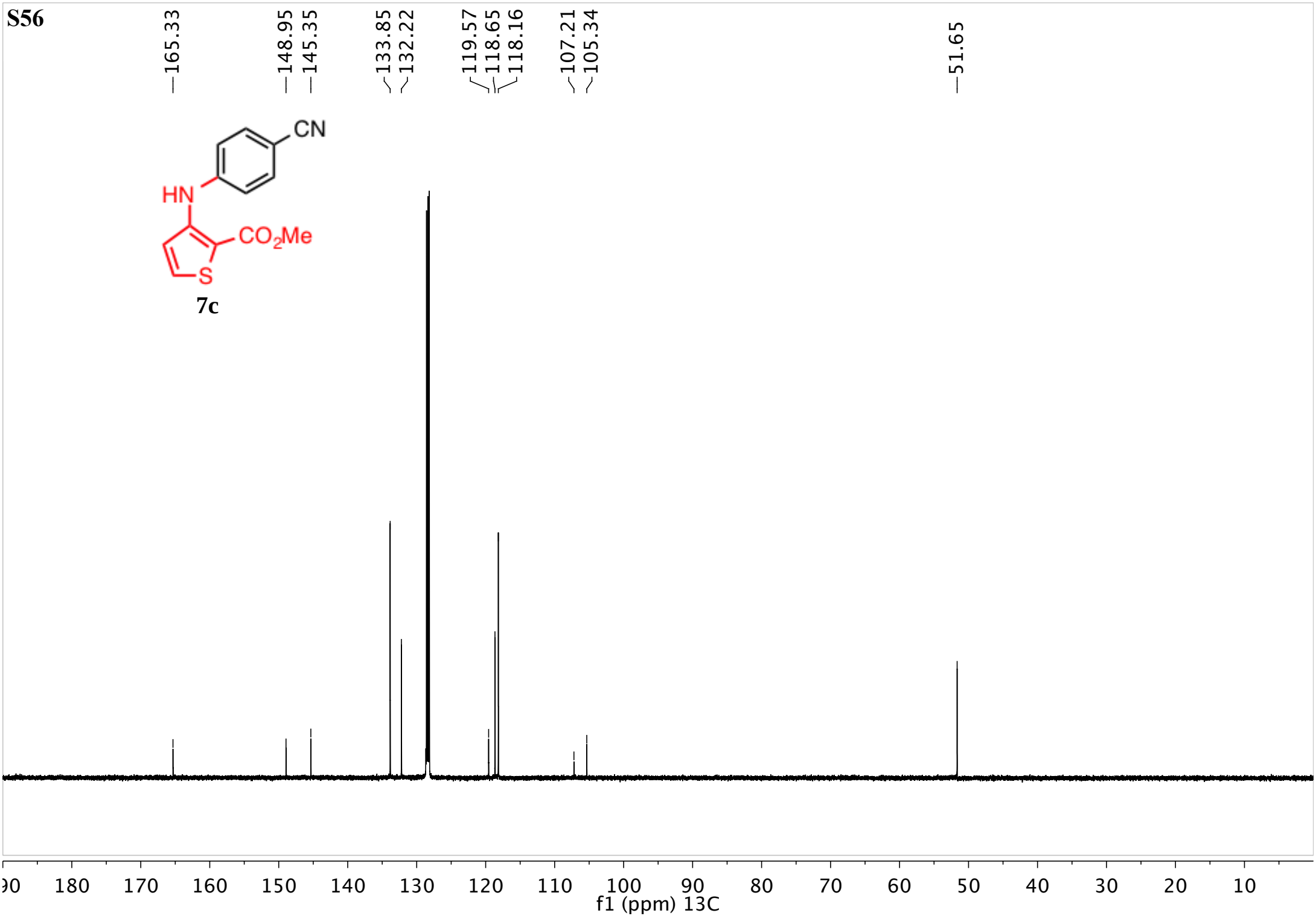
7b

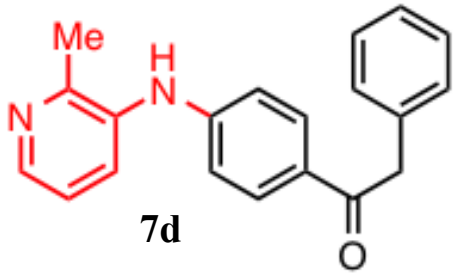
−62.32
170
150
130
110
90
70
50
30
10
−10
−30
−50
−70
−90
−110
−130
−150
−170
f1 (ppm) 19F


CN
HN
CO2Me
S

7c

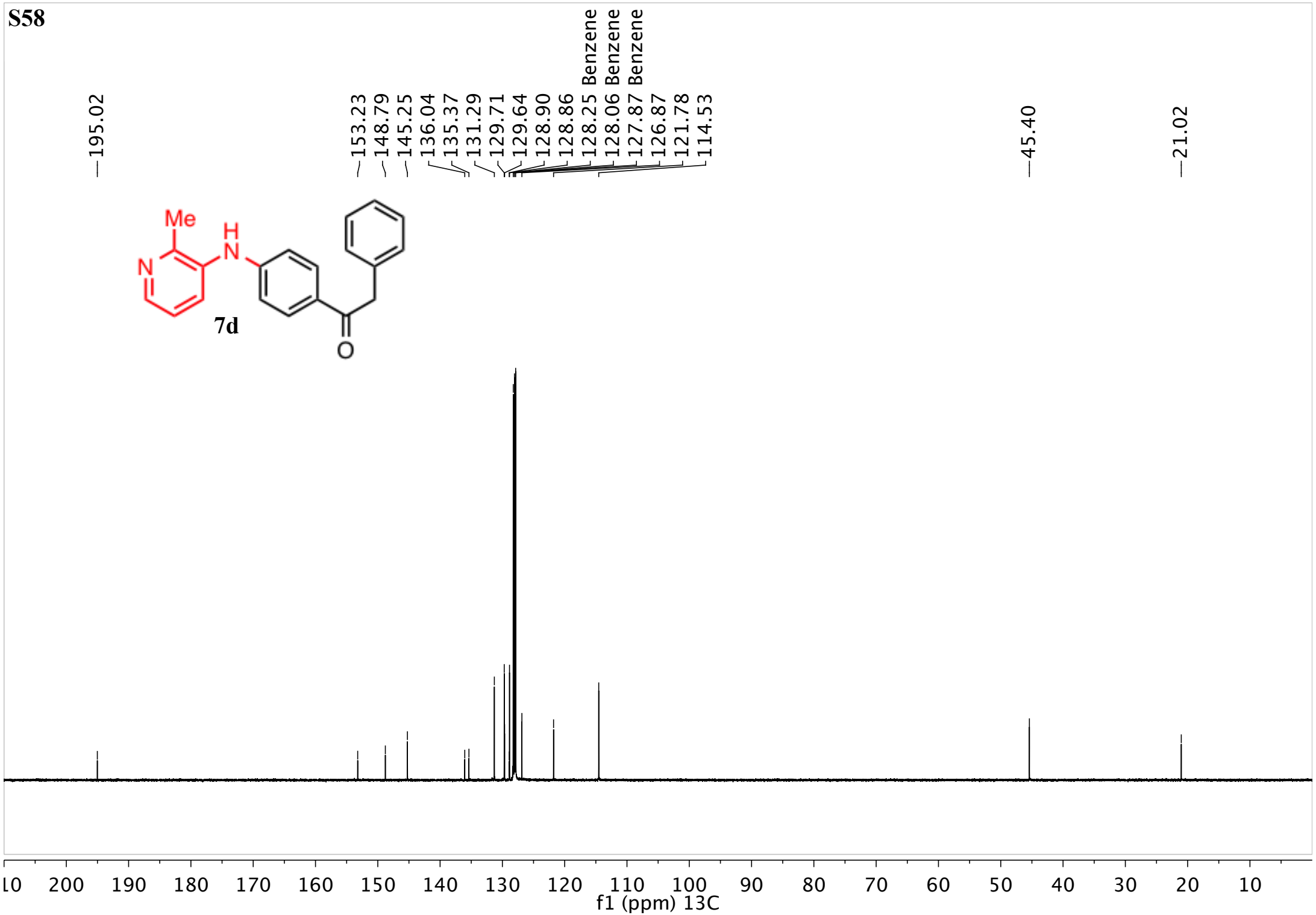
9.06
7.16
6.95
6.93
6.67
6.66
6.55
6.54
6.36
6.35
3.40
1.09
1.88
0.85
0.97
2.09
3.00
f1 (ppm) 1H

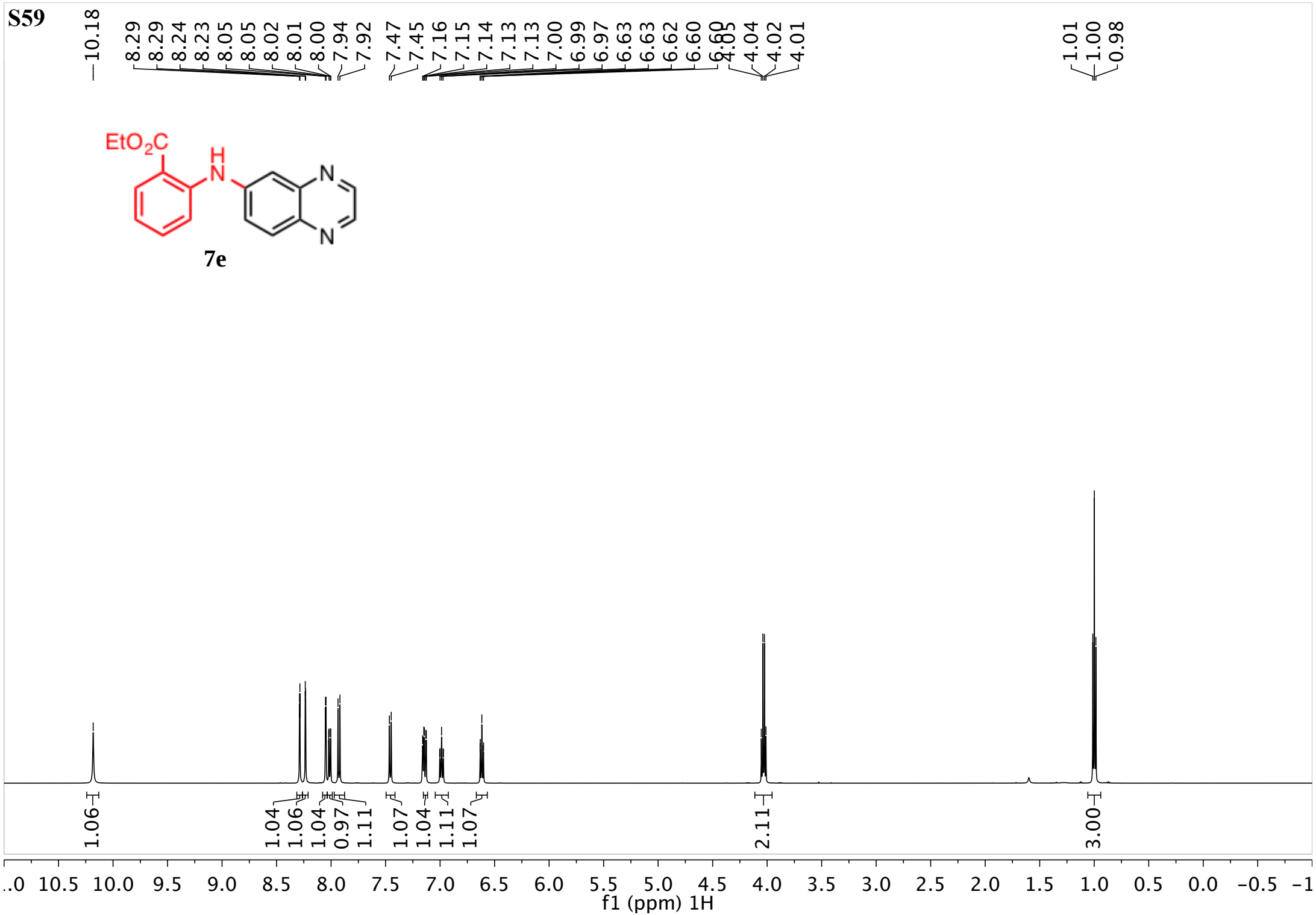

165.33
148.95
145.35
133.85
132.22
119.57
118.65
118.16
107.21
105.34
51.65
CN
HN
CO2Me
S
7c
f1 (ppm) 13C


Me
H
N
N
O

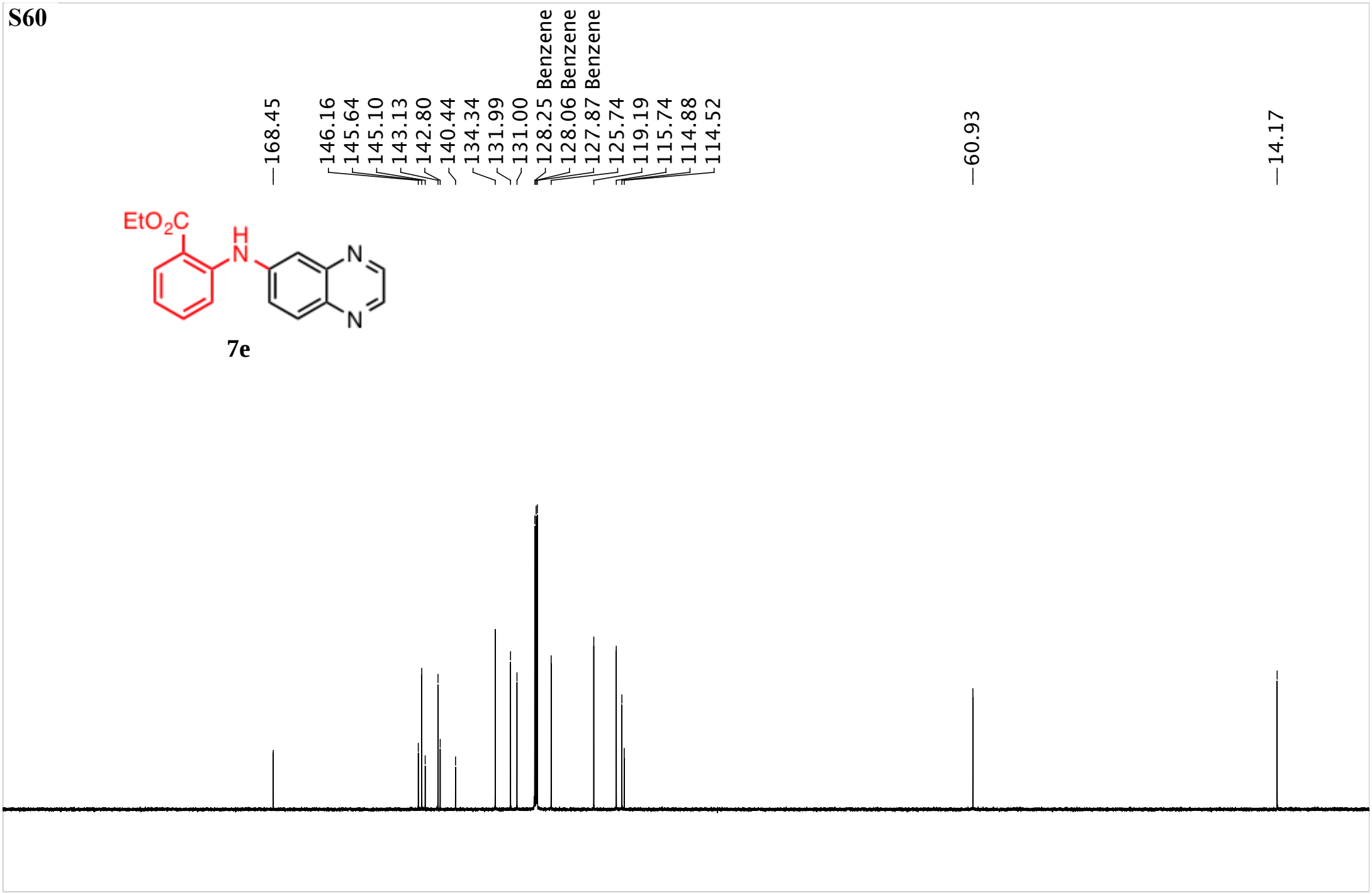
7d

8.28
8.27
7.88
7.86
7.22
7.20
7.16
7.11
7.09
7.03
7.01
6.41
6.39
5.50
3.94
2.32
1.06
2.08
1.78
2.12
2.14
1.04
2.07
1.01
1.98
3.00
f1 (ppm) 1H

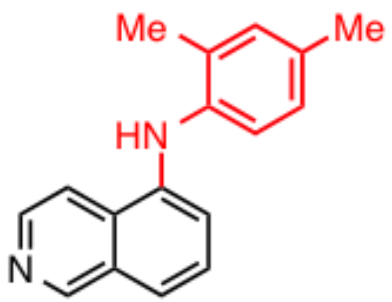

195.02
153.23
148.79
145.25
136.04
135.37
131.29
129.71
129.64
128.90
128.86
128.25 Benzene
128.06 Benzene
127.87 Benzene
126.87
121.78
114.53
45.40
21.02
Me
H
N
N
O
7d
f1 (ppm) 13C


10.18
8.29
8.29
8.24
8.23
8.05
8.05
8.02
8.01
8.00
7.94
7.92
7.47
7.45
7.16
7.15
7.14
7.13
7.13
7.00
6.99
6.97
6.63
6.63
6.62
6.60
6.60
4.05
4.04
4.02
4.01
1.01
1.00
0.98
EtO2C
H
N
N
N
1.06
1.04
1.06
1.04
0.97
1.11
1.07
1.04
1.11
1.07
2.11
3.00
f1 (ppm) 1H

7e


168.45
146.16
145.64
145.10
143.13
142.80
140.44
134.34
131.99
131.00
128.25 Benzene
128.06 Benzene
127.87 Benzene
125.74
119.19
115.74
114.88
114.52
60.93
14.17
EtO2C
H
N
N
N
f1 (ppm) 13C

7e

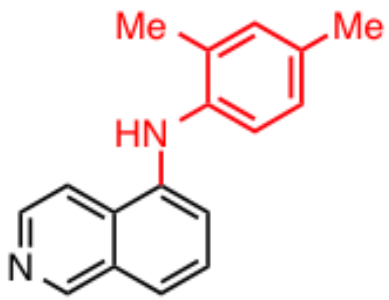

Me
Me
HN
N

8a

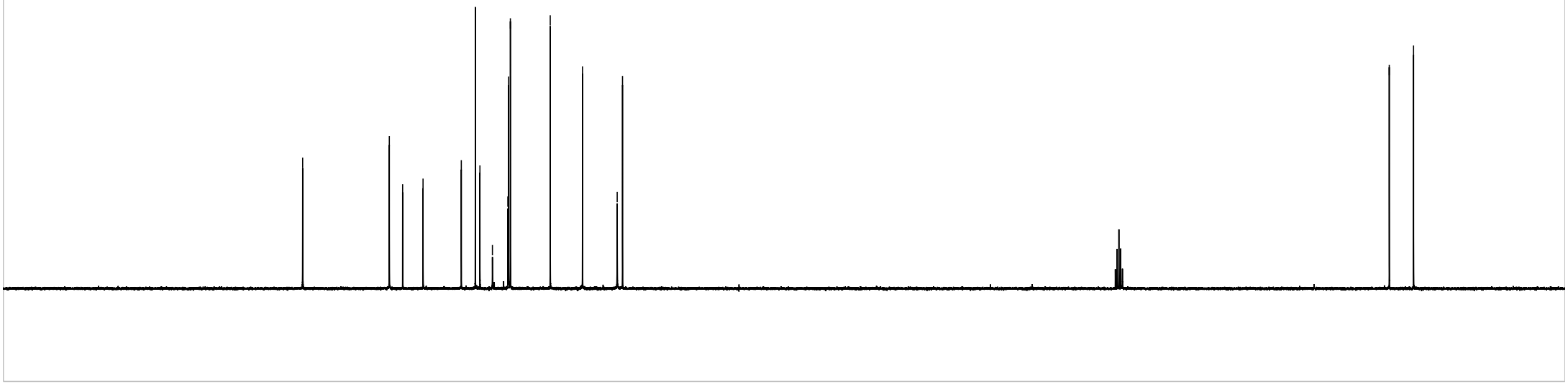
9.26
8.54
8.53
7.87
7.49
7.45
7.44
7.16
7.04
6.97
6.95
6.37
2.38
2.29
1.00
1.02
1.01
0.94
1.01
0.91
1.87
0.92
0.97
2.89
2.98
f1 (ppm) 1H

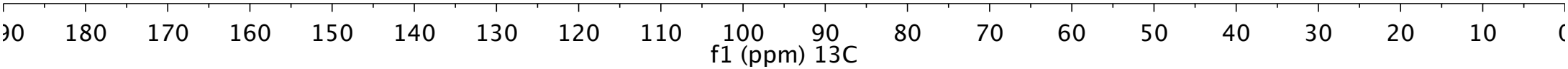
153.58
143.04
141.42
138.94
134.28
132.58
132.02
130.49
128.62
128.52
128.31
123.46
119.54
115.31
114.67

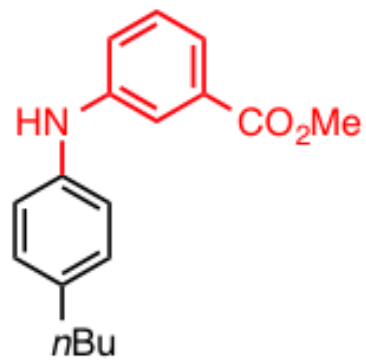
21.37
18.42



8a

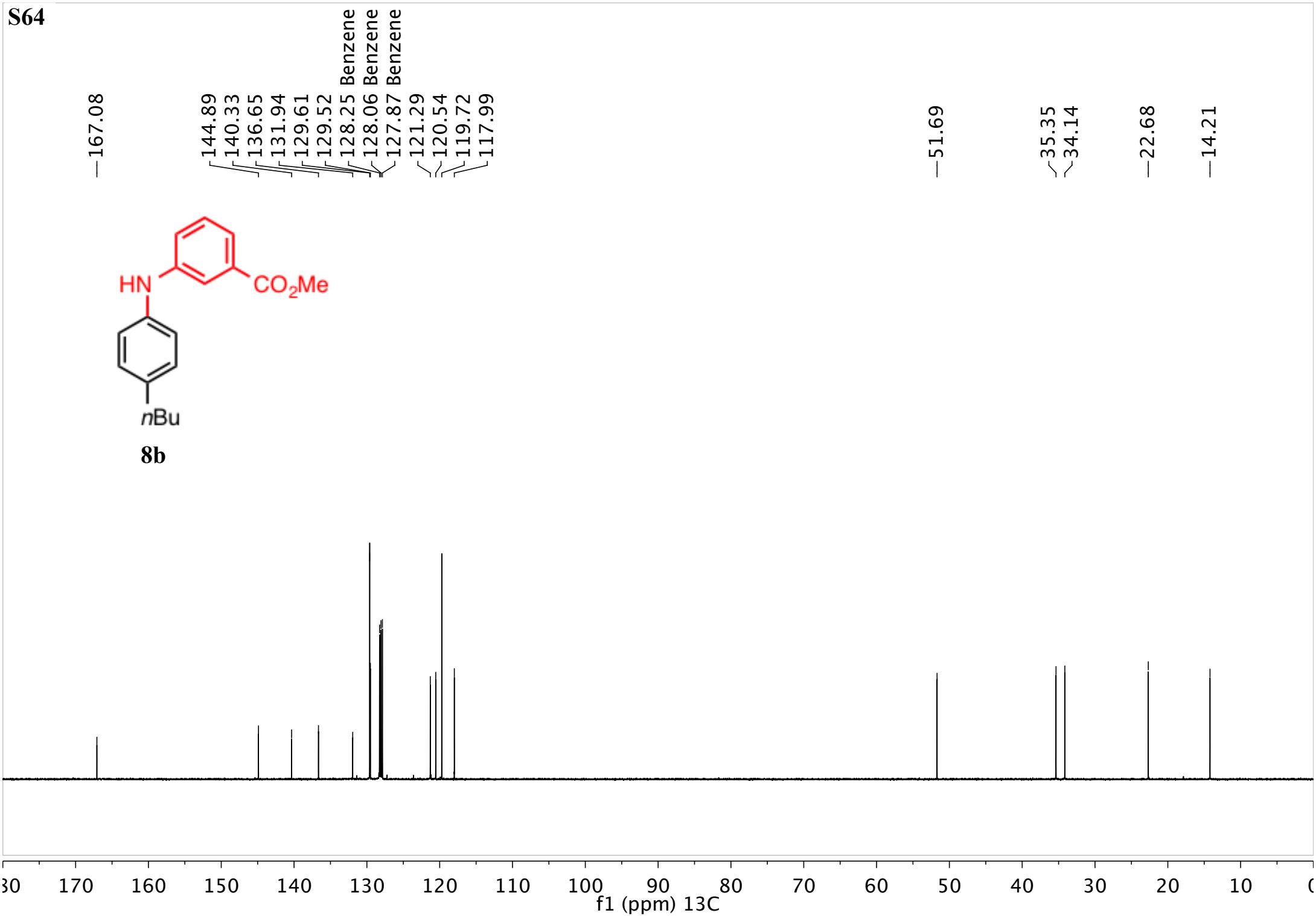




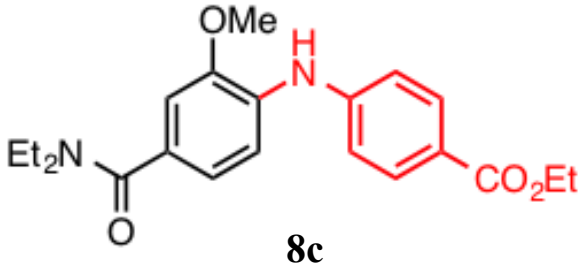

HN
CO2Me
nBu

8b

7.82
7.82
7.82
7.71
7.71
7.71
7.70
7.70
7.69
7.16
7.03
7.02
7.00
6.98
6.96
6.92
6.90
5.35
3.49
2.47
2.46
2.44
1.53
1.52
1.50
1.49
1.47
1.31
1.29
1.28
1.26
1.25
1.24
0.89
0.87
0.86
0.90
0.93
1.06
2.85
1.95
1.00
3.00
2.02
1.97
2.00
2.79
f1 (ppm) 1H

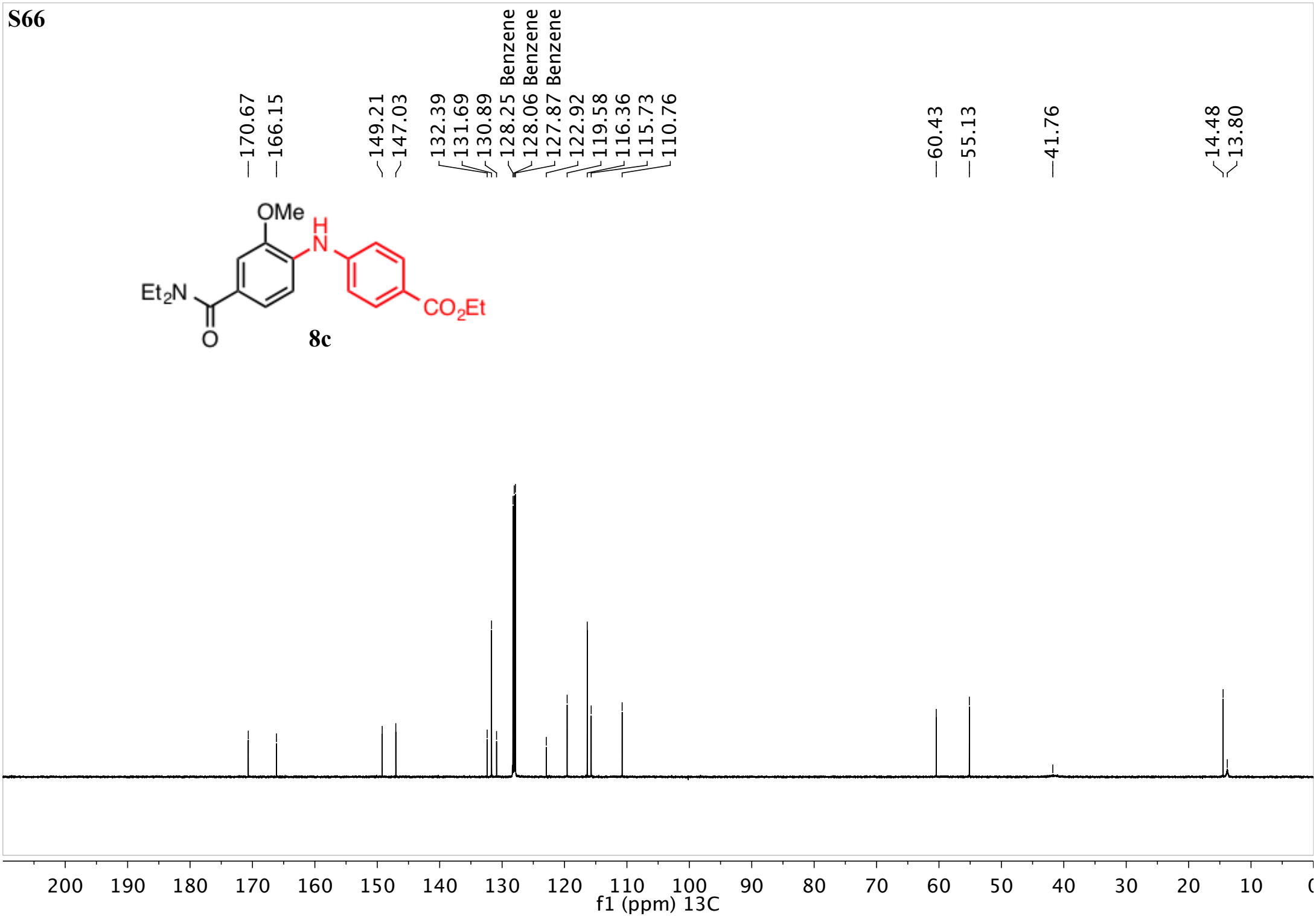

167.08
144.89
140.33
136.65
131.94
129.61
129.52
128.25 Benzene
128.06 Benzene
127.87 Benzene
121.29
120.54
119.72
117.99
51.69
35.35
34.14
22.68
14.21
HN
CO2Me
nBu
f1 (ppm) 13C

8b

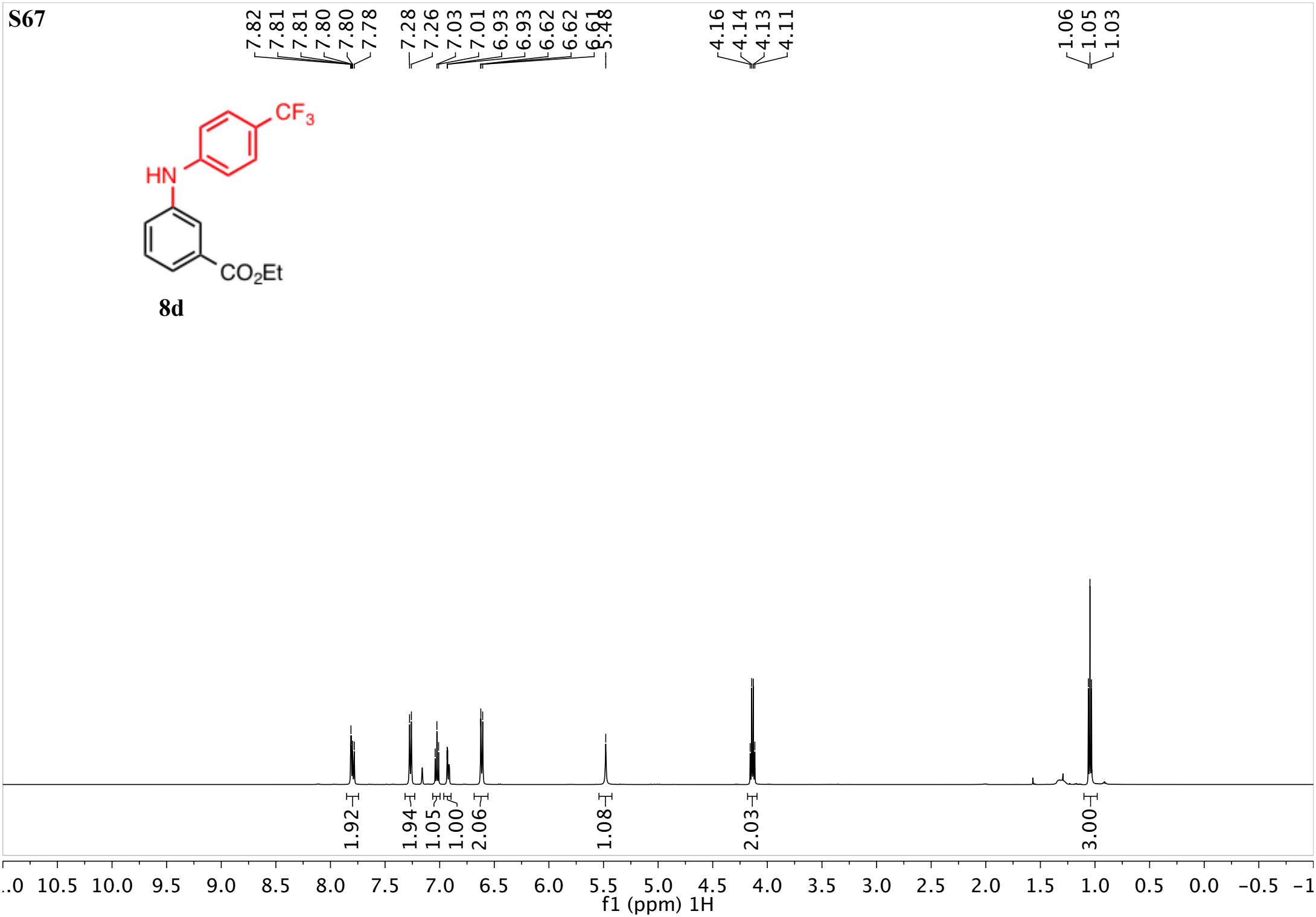

OMe
H
N
Et2N
O
CO2Et

8c

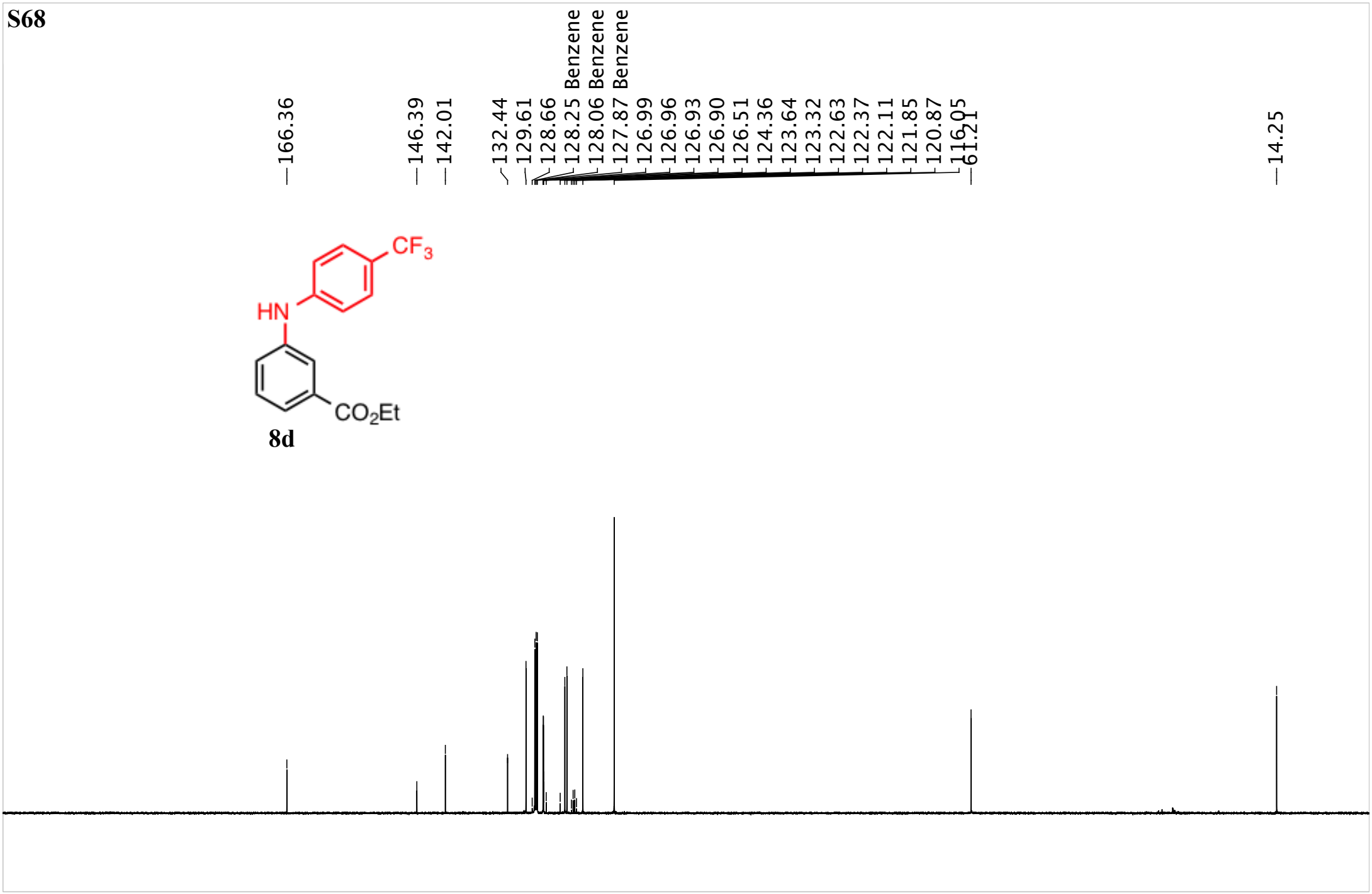
8.13
8.12
7.19
7.18
7.16
7.02
7.02
6.90
6.90
6.89
6.88
6.87
6.85
6.60
4.20
4.18
4.17
4.16
3.22
1.07
1.06
1.05
0.98
1.92
0.86
1.00
1.01
2.15
1.02
2.00
6.98
8.97
f1 (ppm) 1H


170.67
166.15
149.21
147.03
132.39
131.69
130.89
128.25 Benzene
128.06 Benzene
127.87 Benzene
122.92
119.58
116.36
115.73
110.76
60.43
55.13
41.76
14.48
13.80
OMe
H
N
Et2N
O
CO2Et
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm) 13C

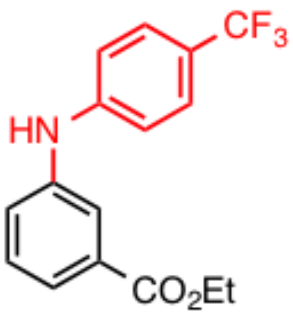
8c


7.82
7.81
7.81
7.80
7.80
7.78
7.28
7.26
7.03
7.01
6.93
6.93
6.62
6.62
6.61
5.48
4.16
4.14
4.13
4.11
1.06
1.05
1.03
CF3
HN
CO2Et
1.92
1.94
1.05
1.00
2.06
1.08
2.03
3.00
f1 (ppm) 1H

8d

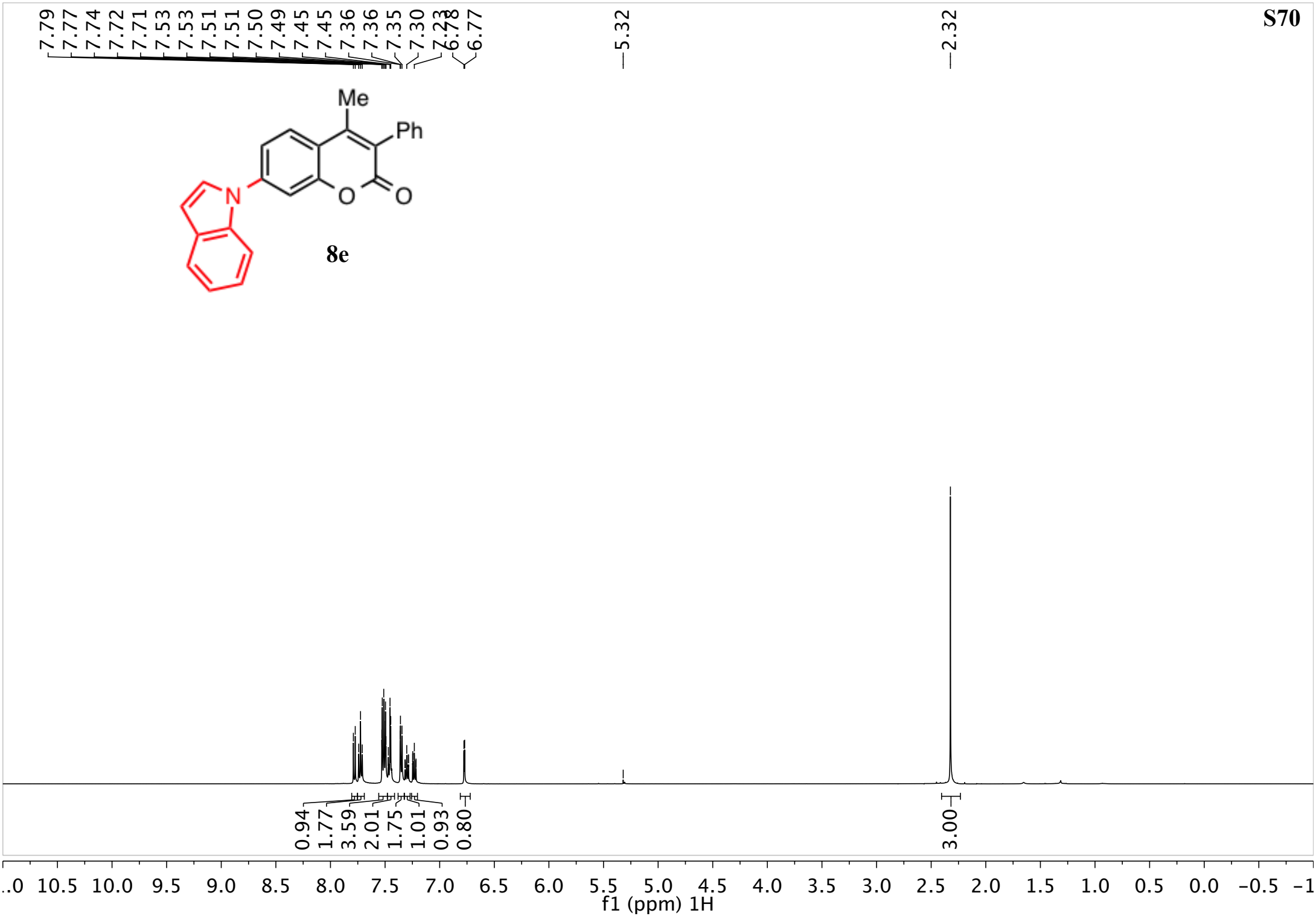

166.36
146.39
142.01
132.44
129.61
128.66
128.25 Benzene
128.06 Benzene
127.87 Benzene
126.99
126.96
126.93
126.90
126.51
124.36
123.64
123.32
122.63
122.37
122.11
121.85
120.87
116.05
61.21
14.25
CF3
HN
CO2Et
f1 (ppm) 13C

8d

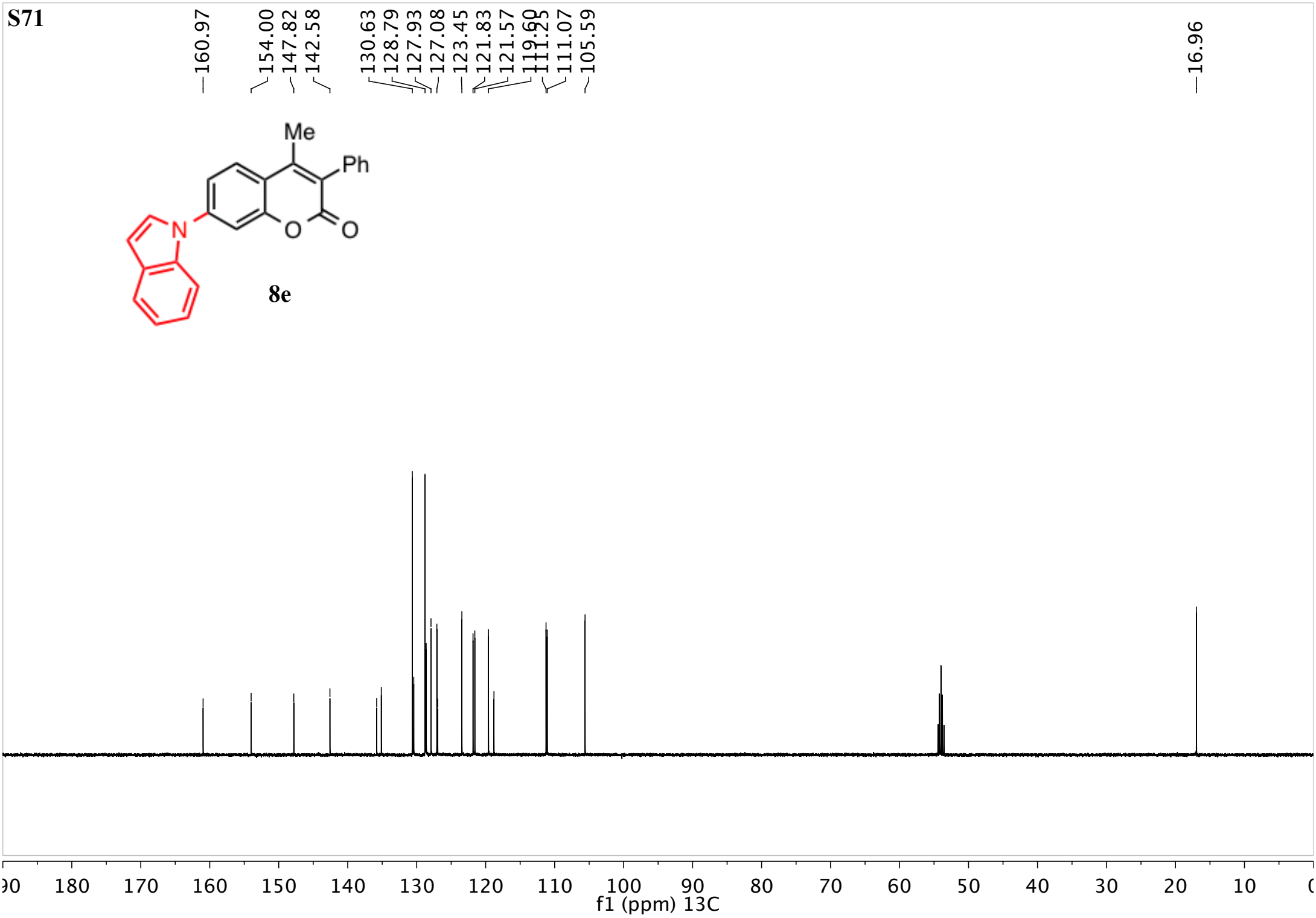

CF3
HN
CO2Et

8d

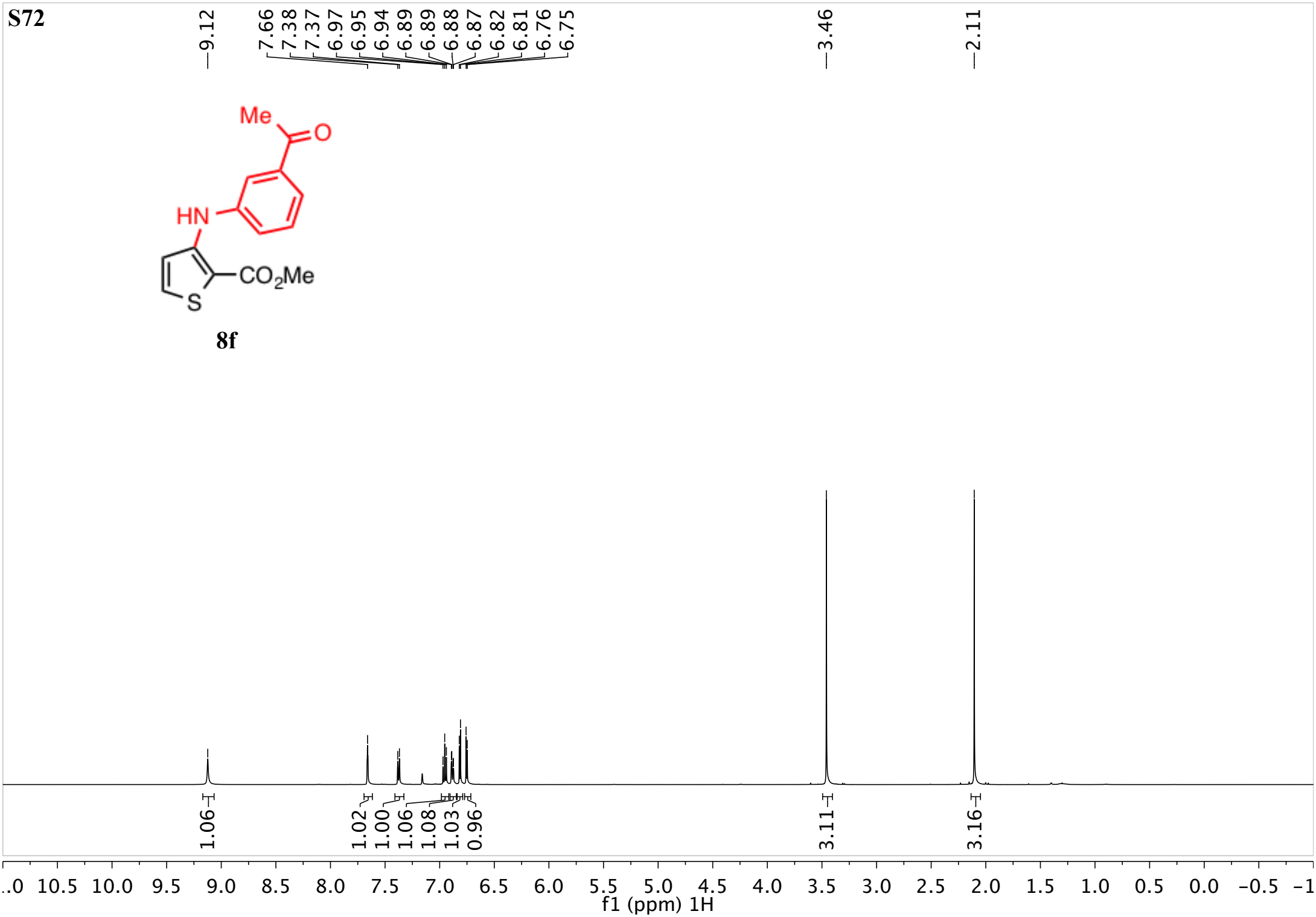
-61.37
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-17
f1 (ppm) 19F


7.79
7.77
7.74
7.72
7.71
7.53
7.53
7.51
7.51
7.50
7.49
7.45
7.45
7.36
7.36
7.35
7.30
7.23
6.78
6.77
5.32
2.32
Me
Ph
N
O
O
0.94
1.77
3.59
2.01
1.75
1.01
0.93
0.80
3.00
f1 (ppm) 1H

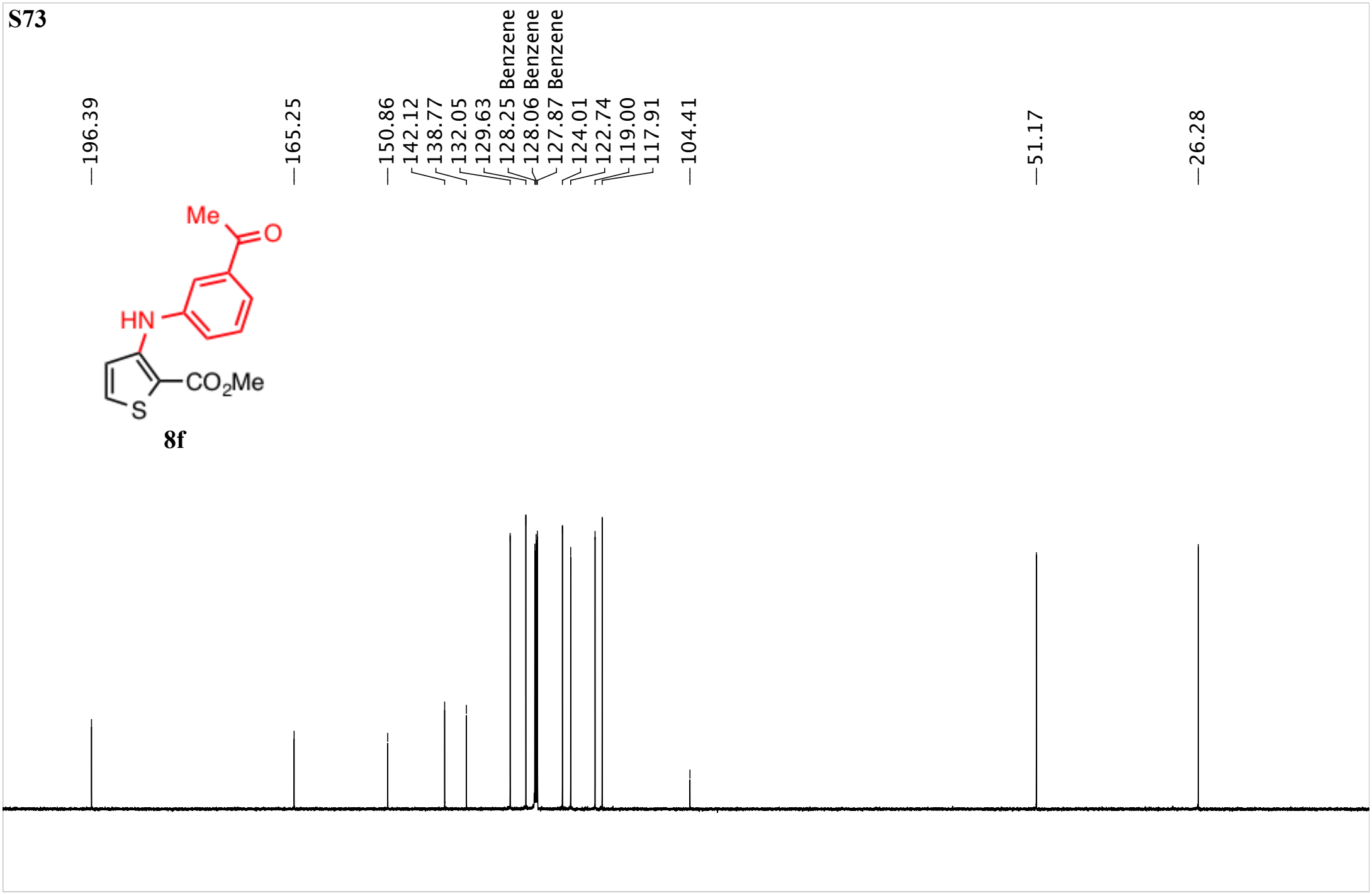
8e


160.97
154.00
147.82
142.58
130.63
128.79
127.93
127.08
123.45
121.83
121.57
119.60
111.25
111.07
105.59
16.96
Me
Ph
N
O
O
f1 (ppm) 13C

8e


9.12
7.66
7.38
7.37
6.97
6.95
6.94
6.89
6.89
6.88
6.87
6.82
6.81
6.76
6.75
3.46
2.11
Me
O
HN
CO2Me
S
1.06
1.02
1.00
1.06
1.08
1.03
0.96
3.11
3.16
f1 (ppm) 1H

8f


196.39
165.25
150.86
142.12
138.77
132.05
129.63
128.25 Benzene
128.06 Benzene
127.87 Benzene
124.01
122.74
119.00
117.91
104.41
51.17
26.28
Me
O
HN
CO2Me
S
f1 (ppm) 13C

8f