An Improved Catalyst System for the Pd-Catalyzed Fluorination of (Hetero)Aryl Triflates

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EXPERIMENTAL SUPPORTING INFORMATION

Procedures

General Procedures. Anhydrous, oxygen-free toluene was obtained by passage through activated alumina columns followed by an argon sparge. Cyclohexane, pentane, and *t*butyl methyl ether (TBME) were purchased from Aldrich in Sure-Seal™ bottles and sparged with argon before use. CD_2Cl_2 and tol-d_8 were purchased in sealed ampules from Cambridge Isotopes. $CDCl_3$ and CD_3OD were purchased from Cambridge Isotopes. Cesium fluoride (99.9%) was purchased from Strem and dried at 200 °C under high vacuum for 24 h. The dried CsF was then transferred to a nitrogen-filled glovebox where it was thoroughly ground using an oven-dried mortar and pestle. The finely ground CsF was then filtered through a 45 μm stainless-steel sieve (purchased from Cole Parmer) to obtain CsF with particle size of < 45 μm. Preparations of **1**[1] and **2**[2] have been previously described; the **1** used in this work was received as a gift from Dr. Naoyuki Hoshiya (MIT), for which we are grateful. The preparation of **3**[3] has been previously described; the **3** used in this work was received as a gift from Mr. Nicholas Bruno (MIT), for which

we are grateful. [(1,5-COD)Pd($CH_2TMS)_2$] was prepared according to the literature[4] or using the procedure described below and stored at –20 °C when not in use. All other reagents were purchased from commercial sources and used without further purification. Compounds were analyzed by ^{1}H, ^{13}C, ^{31}P, ^{19}F NMR, and IR, as well as by elemental analysis in some cases. All ^{19}F NMR yields stated for fluorination reactions are calculated from ^{19}F NMR spectra relative to an internal standard of 1-fluoronaphthalene. ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL 300 MHz or Varian Inova 500 MHz spectrometers and were calibrated using residual solvent as an internal reference. ^{19}F and $^{31}P\{^{1}H\}$ spectra were recorded on a Varian XL 300 MHz or Varian Inova 500 MHz spectrometer. ^{19}F NMR spectra were calibrated to an external standard of $PhCF_3$ (δ –63.72 ppm). All ^{19}F and ^{31}P NMR are proton decoupled. ^{31}P NMR spectra were calibrated to an external standard of *aq*. H_3PO_4 (δ 0.0 ppm). The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, pt = pseudotriplet, q = quartet, p = pentet, m = multiplet. IR spectra were recorded on a Thermo Scientific Nicolet iS5 Fourier Transform IR Spectrometer.

General procedure for Table 1: These reactions were set up following the literature procedure.[5] In a nitrogen-filled glovebox, cesium fluoride (46 mg, 0.30 mmol, 3.0 eq.), **1** or **2** (0.0060 mmol, 0.060 eq.), aryl triflate (0.10 mmol, 1.00 eq.), Pd source (0.0040 mmol, 0.040 eq., 4% "Pd"), and toluene (1.0 mL) were added (in this order) to an oven-dried reaction tube equipped with a stir bar. The tube was capped, removed from the glovebox, placed in an oil bath that had been pre-heated to 120 °C, and allowed to stir vigorously for 14 h. At this time, the reaction mixture was cooled to room temperature

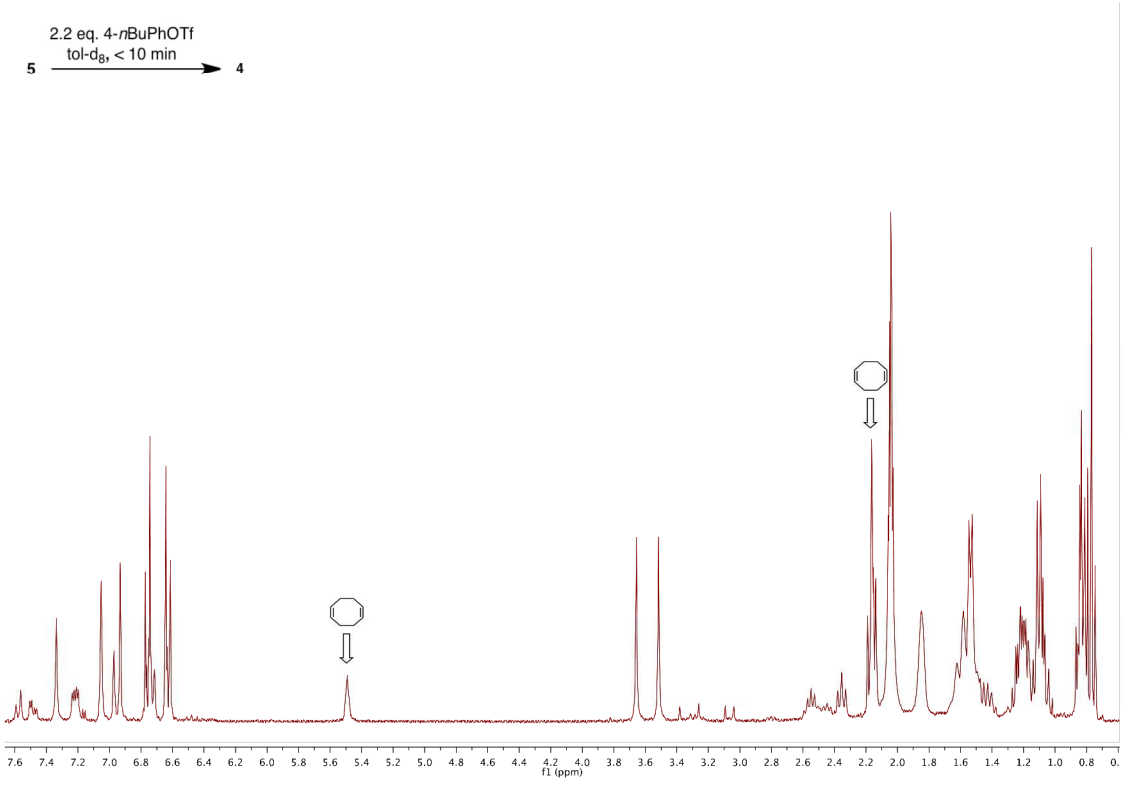
and 1-fluoronaphthalene was added. The reaction mixture was analyzed directly by ^{19}F NMR (300 MHz) for conversion and yield.

General procedure for reactions set up with 3, 4, and 5 (Table 1): In a nitrogen-filled glovebox, cesium fluoride (46 mg, 0.30 mmol, 3.0 eq.), catalyst (4% "Pd"), aryl triflate (0.10 mmol, 1.0 eq.), and toluene (1.0 mL) were added (in this order) to an oven-dried reaction tube equipped with a stir bar. The tube was capped, removed from the glovebox, placed in an oil bath that had been pre-heated to 120 °C, and allowed to stir vigorously for 14 h. At this time, the reaction mixture was cooled to room temperature and 1-fluoronaphthalene was added. The reaction mixture was analyzed directly by ^{19}F NMR (300 MHz) for conversion and yield.

General procedure for inhibition experiments: In a nitrogen-filled glovebox, cesium fluoride (46 mg, 0.30 mmol, 3.0 eq.), **2** (3.9 mg, 0.0060 mmol, 0.060 eq.), aryl triflate (0.10 mmol, 1.0 eq.), $[(cinnamyl)PdCl]_2$ (1.0 mg, 0.0020 mmol, 0.020 eq.) , alkene (dba or 1,5-COD) (0.010 mmol, 0.10 eq.) and toluene (1.0 mL) were added (in this order) to an oven-dried reaction tube equipped with a stir bar. The tube was capped, removed from the glovebox, placed in an oil bath that had been pre-heated to 120 °C, and allowed to stir vigorously for 14 h. At this time, the reaction mixture was cooled to room temperature and 1-fluoronaphthalene was added. The reaction mixture was analyzed directly by ^{19}F NMR (300 MHz) for conversion and yield.

P**rocedure for reaction between 5 and 4-*n*BuPhOTf:** In a nitrogen-filled glovebox, **5**

(16 mg, 0.010 mmol, 1.0 eq.) was suspended in tol-d_8 (1.0 mL) in an oven-dried screw-cap NMR tube. 4-*n*BuPhOTf (6.3 mg, 0.022 mmol, 2.2 eq.) was then added, and the NMR tube was capped and removed from the glovebox. After <10 min at room temperature, complete conversion of **5** to **4** was observed by ^{31}P NMR (121 MHz), and 0.5 eq. of 1,5-cyclooctadiene could be detected by ^{1}H NMR integration (300 MHz, tol-d_8). The reaction mixture was also homogenous and red in color.

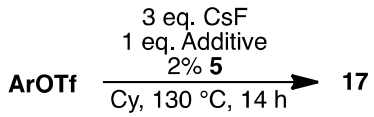


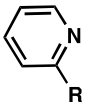
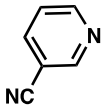
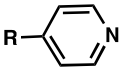
Procedure to estimate the air stability of 5. In a nitrogen-filled glovebox, **5** (20 mg, 0.013 mmol, 1.0 eq.) was weighed out in a vial and then removed from the glovebox. The vial was placed uncapped on the benchtop for a period of 24 h. The vial was transferred back to the glovebox and suspended in tol-d_8 (1.8 mL). 4-*n*BuPhOTf (7.80 mg, 0.028 mmol, 2.2 eq.) was added, and the vial was vigorously shaken for 10 min. At

this point the mixture turned homogeneous and red in color. Then, 1,3,5-trimethoxybenzene (2.10 mg, 0.013 mmol, 1.0 eq.) in tol-d_8 (0.2 mL) was added, and the reaction mixture was analyzed by ^{31}P (121 MHz) and ^{1}H (300 MHz) NMR. By ^{31}P NMR, the only signals observed were at δ 113 ppm (**4**) and a weak signal at δ 55 ppm for an unidentified species. By ^{1}H NMR, an 83% yield of **4** was observed; the spectrum was very similar to that shown above for the reaction conducted with material stored in a glovebox.

General procedure for "robustness screen" (Table S1): In a nitrogen-filled glovebox, cesium fluoride (46 mg, 0.30 mmol, 3.0 eq.), **5** (3.2 mg, 0.0020 mmol, 0.020 eq.), and cyclohexane (1.0 mL) were added to an oven-dried reaction tube equipped with a stir bar. The reaction mixture was stirred at room temperature for 1 min, at which time δ-tocopherol triflate (54 mg, 0.10 mmol, 1.0 eq.) was added in one portion, followed by the indicated additive (0.10 mmol, 1.0 eq.). The tube was capped, removed from the glovebox, placed in an oil bath that had been pre-heated to 130 °C, and allowed to stir vigorously for 14 h. At this time, the reaction mixture was cooled to room temperature and 1-fluoronaphthalene was added. The reaction mixture was analyzed directly by ^{19}F NMR (300 MHz) for conversion and yield.

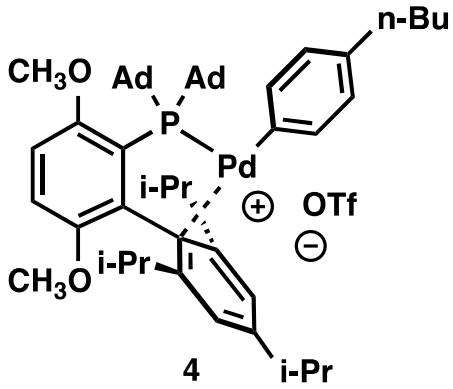
Table S1. Effect of nitrogen-containing additives on the conversion of □-tocopherol triflate to 15.[a]



Entry	Additive		Conversion	ArF Yield (α:β)
1	None		100%	80% (>20:1)
2			80%	15% (n.d.)
3		R = Me	80%	28% (n.d.)
		R = NMe_2	100%	68% (10:1)
		R = CN	30%	<5%
4			40%	<5%
5		R = NMe_2	40%	<5%
		R = CN	30%	<5%
6			100%	<5%
7			100%	35% (n.d.)
8			100%	44% (10:1)
9			100%	46% (6:1)
10			50%	<5%
11			100%	77% (>20:1)
12	Bu_3N		100%	75% (>20:1)

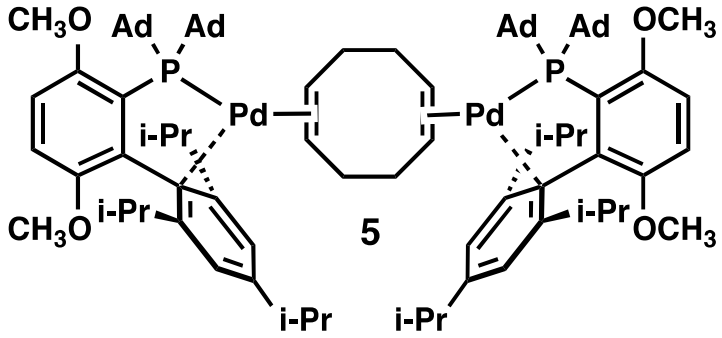
Complexes

Modified Preparation of [(1,5-cyclooctadiene)Pd($CH_2TMS)_2$]: This procedure is a slight modification of the previously reported synthesis.[4] [(1,5-cyclooctadiene)$PdCl_2$] (2.00 g, 7.01 mmol, 1.00 eq.) was added to an oven-dried 200 mL roundbottom flask. The flask was placed under high vacuum and then back-filled with argon. Ether (60.0 mL) was added, and the reaction mixture was cooled to 0 °C using an ice bath. Then, 1M trimethylsilylmethylmagnesium chloride solution in ether (17.5 mL, 17.5 mmol, 2.50 eq.) was added dropwise over 10 min., after which time the reaction mixture was allowed to stir at 0 °C for an additional 20 min. Acetone (4.0 mL) was added, resulting in formation of a black precipitate, and the reaction mixture was stirred at 0 °C for 5 min. before being placed under high vacuum to remove the solvent at 0 °C. Once the solvent was fully evaporated, the flask was opened to air and pentane (2 x 50.0 mL) was added, and the resulting non-homogenous solution was filtered in air through a tightly packed plug of celite into a second 200 mL roundbottom flask that had been placed in an ice water bath. After a final washing of the celite plug with pentane (50.0 mL), the flask was placed under high vacuum to evaporate the solvent at 0 °C. The flask was transferred to a nitrogen-filled glovebox and [(1,5-cyclooctadiene)Pd($CH_2TMS)_2$] (1.97 g, 5.06 mmol, 72%) was isolated as a light gray solid. The ^1H and ^{13}C NMR spectra of the obtained material are identical to those reported in the literature.[4]



Prepared following the literature procedure for making oxidative addition complexes of biaryl phosphine ligands.[6] In a nitrogen-filled glovebox, AdBrettPhos (641 mg, 1.00 mmol, 1.00 eq.) was suspended in pentane (10 mL). To this suspension was added [(COD)Pd($CH_2TMS)_2$] (389 mg, 1.00 mmol, 1.00 eq.) in one portion, followed by 4-*n*butylphenyl triflate (565 mg, 2.00 mmol, 2.00 eq.). The non-homogenous mixture was stirred vigorously at room temperature for 48 h, during which time a bright yellow solid precipitated from solution. At this time, the non-homogenous mixture was filtered though a fine sintered glass frit. The filter cake was washed with pentane (20 mL) and dried under vacuum to yield **4** (937 mg, 91%) as a yellow solid. ^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.29 (d, J = 9 Hz, 1H), 7.15-7.73 (m, 3H), 7.10-7.14 (m, 2H), 6.81 (d, J = 8 Hz, 2H), 3.92 (s, 3H), 3.77 (s, 3H), 2.57 (septet, J = 7 Hz, 2H), 2.50 (t, J = 8 Hz, 2H), 2.35 (septet, J = 6 Hz, 1H), 2.00-2.09 (bs, 12H), 1.90-1.98 (bs, 6H), 1.63-1.69 (bs, 12H), 1.49-1.56 (m, 7H), 1.22-1.34 (m, 4H), 1.08-1.14 (m, 5H), 0.79-0.92 (m, 9H) ppm; ^{13}C NMR (125 MHz, CD_2Cl_2): δ 154.5, 153.0, 152.9, 150.5, 148.5, 148.4, 141.4, 139.3, 135.3, 135.2, 132.3, 132.2, 128.8, 127.9, 127.8, 117.5, 117.4, 116.3, 116.0, 113.9, 55.3, 55.1, 47.5, 47.4, 41.8, 36.3, 35.0, 34.5, 34.2, 34.0, 31.7, 29.6, 29.5, 25.5, 23.7, 22.7, 22.5, 22.5, 22.2, 14.2, 14.1 ppm (observed complexity is due to C-P coupling); ^{31}P NMR (121 MHz, CD_2Cl_2): δ

113.2 ppm; ^{19}F NMR (470 MHz, CD_2Cl_2): δ –79.3 ppm. Anal. Calcd. for: $C_{54}H_{74}O_5F_3PPdS$: C, 62.99 , H, 7.24; found C, 61.19, H, 7.29.

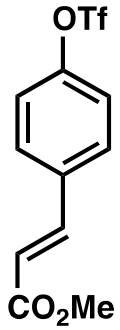


5

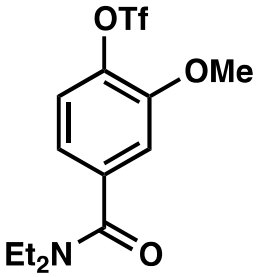
In a nitrogen-filled glovebox, AdBrettPhos (1.28 g, 2.00 mmol, 1.00 eq.) and [(COD)Pd($CH_2TMS)_2$] (778 mg, 2.00 mmol, 1.00 eq.) were suspended in pentane (30.0 mL). The reaction mixture was stirred vigorously at room temperature for 48 h, during which time a pale yellow solid precipitated from solution. At this time, the non-homogenous mixture was filtered though a sintered glass frit. The filter cake was washed with pentane (3 x 10 mL) to yield **5** (1.56 g, 96%) as a pale yellow solid. When dodecane was added to the filtrate as an internal standard, 11%, of 1,3-COD and 33% of 1,5-COD were detected, respectively, by GC analysis (upon comparison to a standard curve). A third species, which we assumed was 1,4-COD and had an identical response factor to that of 1,5-COD, was also present (9%).[7] IR (neat): 2950, 2900, 2847, 1575, 1456, 1418, 1375, 1342, 1301, 1291, 1157, 1090, 1048, 1015, 930, 866, 804, 748, 715, 617 cm^{-1}. **5** is almost completely insoluble in cyclohexane, pentane, toluene, benzene, THF, Et_2O, 1,2-dimethoxyethane, cyclopentyl methyl ether, methyl *t*-butyl ether, DMSO, DMF, and acetone. **5** is unstable in chlorinated solvents, pyridine, and methanol.

Phenols and Aryl Triflates

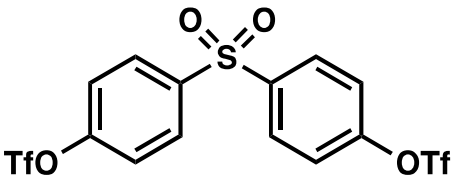
Unless specified otherwise, aryl triflates were prepared from the corresponding phenols following the method of Ritter.[8] Aryl nonaflates were prepared *via* the same method using perfluorobutanesulfonyl fluoride in place of triflic anhydride. *p*-Coumaric acid methyl ester,[9] *N*-(4-hydroxyphenyl)-*N*-methylacetamide,[10] and 3-hydroxyquinoline[11] were prepared according to the literature. Unless specified otherwise, all other phenols were purchased from commercial sources. The triflates derived from estrone,[8] δ-tocopherol,[8] 4-methylumbelliferone,[12] 4-chloro-3,5-dimethylphenol,[13] and 8-trifluoromethyl-4-quinolinol,[14] have been previously described.



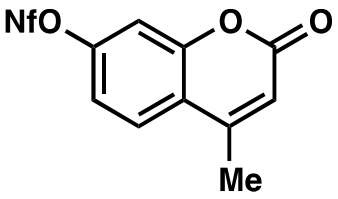
White solid. Melting Point: 33-34 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, J = 15 Hz, 1H), 7.56-7.60 (m, 2H), 7.27-7.31 (m, 2H), 6.44 (d, J = 16 Hz, 1H), 3.75 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9, 150.4, 142.5, 136.0, 129.9, 122.0, 120.1, 118.8 (q, J = 319 Hz), 52.0 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ –73.1 ppm. IR: 2960, 1704, 1641, 1598, 1504, 1423, 1326, 1248, 1216, 1198, 1173, 1135, 1019, 977, 947, 880, 844, 832, 775, 750, 739, 704, 687, 609, 593 cm^{-1}. Anal. Calcd. for $C_{11}H_9F_3O_5S$: C, 42.58, H, 2.92; found C, 42.80 , H, 2.87.



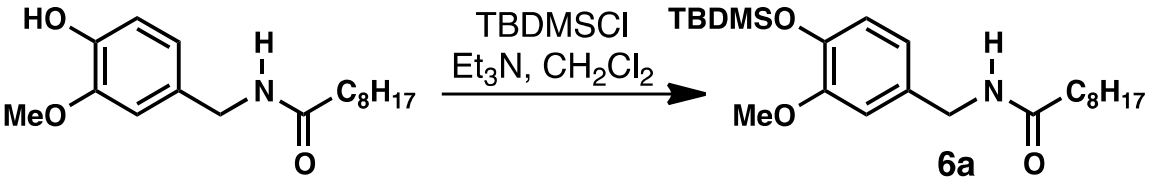
Yellow solid. Melting Point: 40 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (d, J = 8 Hz, 1H), 7.05 (d, J = 2 Hz, 1H), 6.95 (dd, J = 8, 2 Hz, 1H), 3.90 (s, 3H), 3.52 (bs, 2H), 3.24 (bs, 2H), 1.23 (bs, 3H), 1.13 (bs, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.5, 151.7, 139.1, 138.5, 122.6, 118.6, 118.8 (q, J = 319 Hz), 111.8, 56.4, 43.5, 39.5, 14.3, 12.9 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ –74.5 ppm. IR: 2977, 2941, 1630, 1601, 1502, 1463, 1420, 1295, 1265, 1248, 1202, 1137, 1107, 1029, 882, 817, 760, 609 cm^{-1}. Anal. Calcd. for $C_{13}H_{16}F_3NO_5S$: C, 43.94 , H, 4.54; found C, 44.06, H, 4.56.



White crystalline solid. Melting Point: 121 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (dd, J = 9, 1 Hz, 4H), 7.46 (dd, J = 9, 1 Hz, 4H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.8, 141.1, 130.6, 123.0, 118.7 (q, J = 319 Hz) ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ– □□□□□□ IR (neat): 3104, 1583, 1486, 1429, 1406, 1326, 1291, 1251, 1205, 1133, 1103, 1014, 878, 841, 725, 658 cm^{-1}. Anal. Calcd. for $C_{14}H_8O_8F_6S_3$: C, 32.69, H, 1.57; found C, 32.83, H, 1.57.

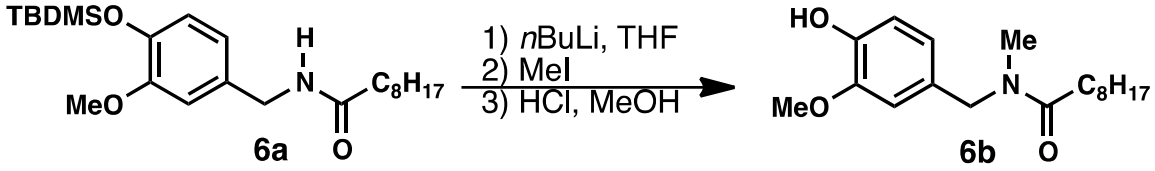


Fluffy white crystalline solid. Melting Point: 95 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 9 Hz, 1H), 7.22-7.27 (m, 2H), 6.33 (s, 1H), 2.45 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.6, 154.2, 151.4, 151.1, 126.5, 120.1, 117.5, 116.0, 110.6, 18.8 ppm (the signals for the C_4F_9 group are omitted due to complex C-F coupling); ^{19}F NMR (470 MHz, $CDCl_3$): δ –81.1, –108.9, –121.2, –126.2 ppm. IR (neat): 3082, 1722, 1629, 1603, 1433, 1384, 1350, 1235, 1194, 1138, 1112, 1068, 1030, 1015, 977, 899, 839, 825, 806, 732, 696, 629, 581 cm^{-1}. Anal. Calcd. for $C_{14}H_7O_5F_9S$: C, 36.69, H, 1.54; found C, 36.83, H, 1.43.



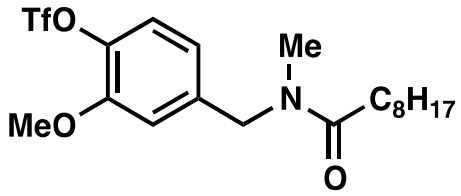
To a solution of nonivamide (1.47 g, 5.00 mmol, 1.00 eq.) in CH_2Cl_2 (20 mL) was added triethylamine (0.84 mL, 6.00 mmol, 1.20 eq.), followed by *t*butyldimethylsilyl chloride (829 mg, 5.50 mmol, 1.10 eq.). The reaction mixture was then vigorously stirred under an inert atmosphere for 14 h. At this time, the reaction mixture was quenched with water (20 mL) and the organic and aqueous phases were separated. The aqueous phase was extracted with ethyl acetate (3 x 20 mL), and the organic extracts were combined and dried over $MgSO_4$. After concentration, the crude product was purified by flash chromatography (1:4 EtOAc:hexanes → 1:3 EtOAc:hexanes) to yield **6a** (2.01 g, 99%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.78 (dd, J = 8, 2 Hz, 1H), 6.75-6.77 (m, 1H), 6.68-6.71 (m, 1H), 5.71 (bs, 1H), 4.35 (d, J = 5 Hz, 2H), 3.78 (s, 3H), 2.20 (t, J = 7

Hz, 2H), 1.65 (p, J = 8 Hz, 2H), 1.23-1.31 (m, 10H), 0.98 (s, 9H), 0.87 (t, J = 7 Hz, 3H), 0.14 (s, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1, 151.3, 144.7, 132.1, 121.1, 120.4, 112.1, 55.7, 43.7, 37.1, 32.1, 29.6, 29.4, 26.1, 25.9, 22.9, 22.6, 18.7, 14.3, –4.4 ppm. IR (in $CHCl_3$): 3289, 2927, 2856, 1642, 1512, 1464, 1418, 1281, 1250, 1233, 1157, 1126, 1039, 898, 839, 781 cm^{-1}.



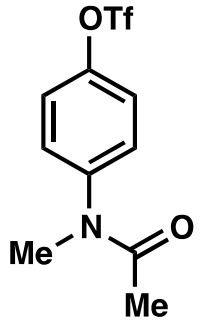
A solution of **6a** (1.45 g, 3.60 mmol, 1.00 eq.) in anhydrous THF (20 mL) was cooled to –78 °C. 2.50 M solution of *n*BuLi in hexane (1.56 mL, 3.90 mmol, 1.10 eq.) was added dropwise, and the reaction mixture was allowed to stir for 1 h at –78 °C. At this time, iodomethane (0.331 mL, 5.30 mmol, 1.50 eq.) was added. The reaction mixture was warmed to room temperature over 1 h, and then allowed to stir at room temperature for an addition 8 h. The reaction was then quenched with saturated *aq*. NH_4Cl (20 mL). The organic and aqueous phases were separated, and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). After concentration, the crude product was dissolved in methanol (10 mL) and 2.0 M hydrochloric acid (0.1 mL) was added. The mixture was heated to 60 °C and stirred at this temperature for 2 h. The reaction mixture was cooled to room temperature, the solvent was removed, and the resulting oil was quenched with saturated *aq*. $NaHCO_3$ (10 mL) and diluted with ethyl acetate (20 mL). The organic and aqueous phases were separated, and the aqueous phase was extracted with ethyl acetate (2 x 20 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography to yield **6b** (887 mg, 81% over two steps) as a colorless oil. **6b** exists as a 1.5:1 mixture of rotamers in solution. ^{1}H NMR

(500 MHz, $CDCl_3$): major rotamer: δ 6.84 (d, J = 8 Hz, 1H), 6.80 (s, 1H), 6.72 (d, J = 8 Hz, 1H), 5.66 (bs, 1H), 4.50 (s, 2H), 3.86 (s, 3H), 2.89 (s, 3H), 2.33-2.39 (m, 2H), 1.64-1.68 (m, 2H), 1.25-1.30 (m, 10H), 0.85-0.89 (m, 3H) ppm; minor rotamer: δ 6.90 (d, J = 8 Hz, 1H), 6.66 (d, J = 8 Hz, 1H), 6.61 (s, 1H), 4.45 (s, 2H), 3.87 (s, 3H), 2.92 (s, 3H), 2.33-2.39 (m, 2H), 1.64-1.68 (m, 2H), 1.25-1.30 (m, 10H), 0.85-0.89 (m, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.4, 146.9, 145.1, 129.7, 121.4, 119.4, 114.8, 114.1, 110.9, 108.7, 56.1, 53.3, 50.7, 34.7, 33.8, 33.4, 32.0, 29.7, 29.6, 29.3, 25.7, 25.4, 22.8, 14.2 ppm (observed complexity is due to the presence of two rotamers in solution). IR (in $CHCl_3$): 3950, 3010, 2927, 2855, 1627, 1464, 1456, 1432, 1402, 1273, 1238, 1215, 1152, 1125, 1037 cm^{-1}.

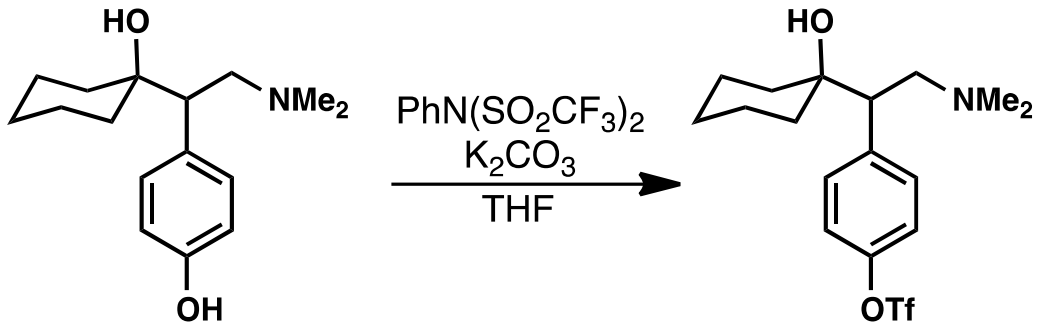


Thick yellow oil. This compound exists as a 2.5:1 mixture of rotamers in solution. ^1H NMR (500 MHz, $CDCl_3$): major rotamer: δ 7.11 (d, J = 8 Hz, 1H), 6.92 (d, J = 2 Hz, 1H), 6.79 (dd, J = 8, 2 Hz, 1H), 4.54 (s, 2H), 3.84 (s, 3H), 2.93 (s, 3H), 2.35 (t, J = 8 Hz, 2H), 1.59-1.68 (m, 2H), 1.18-1.36 (m, 10H), 0.81-0.88 (m, 3H) ppm; minor rotamer: δ 7.17 (d, J = 8 Hz, 1H), 6.77 (s, 1H), 6.74 (d, J = 9 Hz, 1H), 4.51 (s, 2H), 3.86 (s, 3H), 2.92 (s, 3H), 2.30 (t, J = 8 Hz, 2H), 1.59-1.68 (m, 2H), 1.18-1.36 (m, 10H), 0.81-0.88 (m, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.6, 173.5, 151.9, 151.5, 139.6, 138.8, 137.9, 122.9, 122.3, 120.1, 120.0, 118.3, 117.5, 112.8, 110.7, 56.2, 56.2, 53.0, 50.6, 35.1, 34.0, 33.5, 33.1, 31.9, 31.8, 29.5, 29.5, 29.5, 29.2, 29.2, 25.4, 25.2, 22.7, 22.7, 14.1, 14.1 ppm (observed complexity is due to the presence of two rotamers in solution); ^{19}F NMR (470

MHz, $CDCl_3$): δ –74.1 ppm (major rotamer), δ –74.1 ppm (minor rotamer). IR (neat): 2925, 2855, 1645, 1601, 1504, 1464, 1419, 1285, 1248, 1203, 1139, 1104, 1032, 875, 704, 614 cm^{-1}. Anal. Calcd. for $C_{19}H_{28}O_5F_3NS$: C, 51.92, H, 6.42; found C, 52.03, H, 6.34.

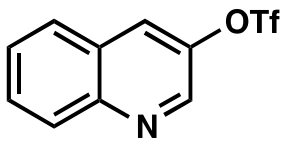


White crystalline solid. Melting Point: 70 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 7.30 (d, J = 9 Hz, 2H), 7.27 (d, J = 8 Hz, 2H), 3.23 (s, 3H), 1.85 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 148.6, 144.9, 129.5, 123.2, 119.1 (q, J = 319 Hz), 37.6, 22.9 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –73.1 ppm. IR (neat): 3108, 3062, 3045, 1648, 1594, 1500, 1421, 1389, 1354, 1298, 1248, 1200, 1130, 1087, 1021, 978, 886, 868, 828, 784, 757, 641, 607 cm^{-1}. Anal. Calcd. for $C_{10}H_{10}O_4F_3NS$: C, 40.41, H, 3.39; found C, 40.62, H, 3.42.



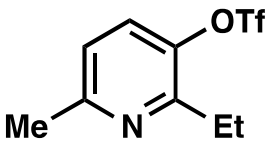
A 20 mL reaction tube was charged with desvenlafaxine (793 mg, 3.01 mmol, 1.00 eq.), *N*-phenyl-bis(trifluoromethanesulfonimide) (1.18 g, 3.31 mmol, 1.10 eq.), and K_2CO_3 (832 mg, 6.02 mmol, 2.00 eq.). The tube was evacuated under high vacuum and

backfilled with nitrogen. This procedure was repeated a total of three times. THF (10 mL) was added, and the heterogeneous mixture was stirred at 70 °C for 12 h. At this time the mixture was cooled to room temperature and filtered through a pad of Celite, eluting with EtOAc (50 mL). After concentration, the crude product was purified by flash chromatography (hexanes → EtOAc →1:20 acetone:EtOAc → 1:10 acetone:EtOAc → 1:20 MeOH:CH_2Cl_2 → 1:10 MeOH:CH_2Cl_2) to yield desvenlafaxine triflate (1.10 g, 92%) as a white solid. Melting Point: 90 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21 (d, J = 9 Hz, 2H), 7.17 (d, J = 9 Hz, 2H), 5.86 (bs, 1H), 3.28 (pt, J = 12 Hz, 1H), 3.03 (dd, J = 13 Hz, 3 Hz, 1H), 2.29-2.35 (m, 7H), 1.63-1.77 (m, 3H), 1.47-1.60 (m, 3H), 1.34-1.42 (m, 1H), 1.22 (ptd, J = 12, 4 Hz, 1H), 0.81-0.97 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.4, 141.5, 131.0, 120.9, 118.8 (q, J = 319 Hz), 74.1, 60.9, 52.1, 45.6, 38.3, 31.4, 26.0, 21.6, 21.3ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –73.2 ppm. IR: 3148 (broad), 2943, 2861, 2832, 2780, 1502, 1469, 1420, 1404, 1250, 1200, 1140, 1041, 1013, 968, 877, 852, 776, 745, 733, 606 cm^{-1}. Anal. Calcd. for: $C_{10}H_{24}O_4F_3NS$: C, 51.63 , H, 6.12; found C, 51.67, H, 6.05.

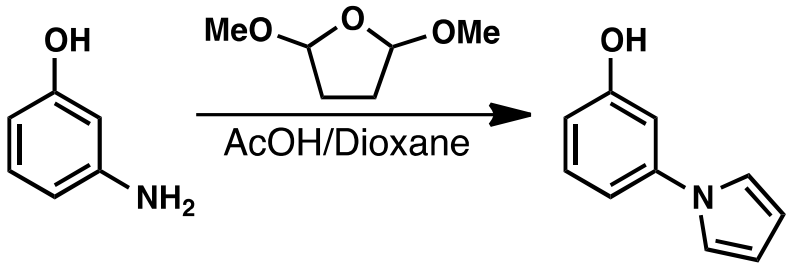


Off-white crystalline solid. Melting Point: 38 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.84 (d, J = 3 Hz, 1H), 8.17 (d, J = 9 Hz, 1H), 8.08 (d, J = 3 Hz, 1H), 7.86 (d, J = 9 Hz, 1H), 7.78-7.82 (m, 1H), 7.64 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.2, 143.8, 143.3, 130.8, 129.8, 128.5, 128.1, 127.7, 127.0, 118.9 (q, J = 319 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ –72.8 ppm. IR (neat): 3065, 1601, 1505, 1421, 1329, 1243, 1204, 1131,

1114, 971, 912, 903, 850, 829, 785, 758, 751, 700, 645, 603 cm^{-1}. Anal. Calcd. for: $C_{10}H_6O_3F_3NS$: C, 43.33 , H, 2.18; found C, 43.58, H, 2.21.

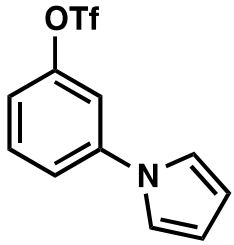


Pale yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ 7.43 (d, J = 8 Hz, 1H), 7.05 (d, J = 9 Hz, 1H), 2.87 (q, J = 8 Hz, 2H), 2.54 (s, 3H), 1.30 (t, J = 8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.3, 155.3, 143.0, 129.1, 122.1, 118.7 (q, J = 318 Hz), 25.9, 24.2, 12.8 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –74.1 ppm. IR: 2978, 2942, 2884, 1592, 1455, 1422, 1250, 1207, 1137, 1097, 910, 865, 824, 714, 697, 644, 627 cm^{-1}. Anal. Calcd. for $C_9H_{10}F_3NO_3S$: C, 40.15 , H, 3.74; found C, 40.44, H, 3.73.

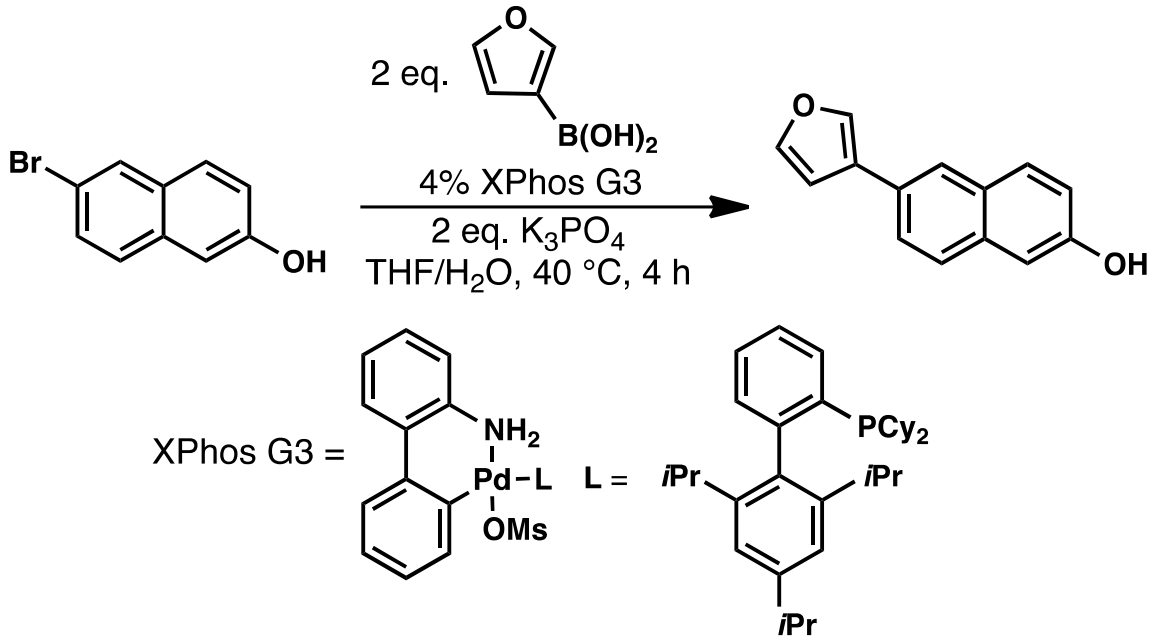


3-aminophenol (1.09 g, 11.0 mmol, 1.10 eq.) and 2,5-dimethoxytetrahydrofuran (1.30 mL, 10.0 mmol, 1.00 eq.) were dissolved in dioxane (6 mL) in a two-neck roundbottom flask equipped with a reflux condenser. Acetic acid (4 mL) was added, and the reaction mixture was stirred at reflux for 6 h, during which time the reaction solution turned dark brown. The reaction mixture was cooled to room temperature and the solvent was removed. The resulting brown sludge was partitioned between CH_2Cl_2 (100 mL) and water (100 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 100 mL). The non-homogenous organic layers were combined, dried over $MgSO_4$, and filtered to give a homogenous solution. The solvent was removed with the

aid of a rotary evaporator, and the crude product was purified by flash chromatography (1:4 EtOAc:hexanes) to yield 3-(1*H*-pyrrol-1-yl)phenol (848 mg, 53%) as a light brown solid. Melting point: 62-64 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (pt, J = 8 Hz, 1H), 7.09 (td, J = 2, 1 Hz, 2H), 6.98-7.01 (m, 1H), 6.86 (td, J = 2, 1 Hz, 1H), 6.69-6.72 (m, 1H), 6.38 (td, J = 2, 1 Hz, 2H), 5.29 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 142.0, 130.7, 119.4, 113.0, 112.6, 110.5, 107.8 ppm. IR (neat): 2800-3500 (broad), 1615, 1591, 1513, 1483, 1398, 1336, 1296, 1203, 1172, 1131, 1091, 1078, 1065, 1024, 952, 847, 769, 714 cm^{-1}.

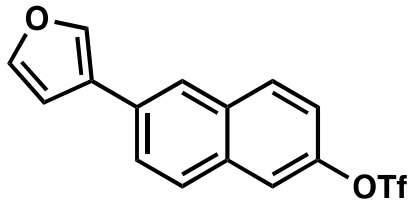


White crystalline solid. Melting Point: 46 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (pt, J = 8 Hz, 1H), 7.43 (d, J = 8 Hz, 1H), 7.32 (s, 1H), 7.16 (d, J = 8 Hz, 1H), 7.10 (s, 2H), 6.41 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.2, 142.4, 131.3, 120.0, 119.3, 118.9 (q, J = 319 Hz), 118.0, 113.5, 111.7 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ –73.1 ppm. IR (neat): 3134, 3077, 1614, 1589, 1505, 1417, 1338, 1318, 1249, 1197, 1138, 1087, 1069, 1027, 952, 878, 856, 796, 781, 761, 730, 647 cm^{-1}. Anal. Calcd. for $C_{11}H_8O_3NS$: C, 45.36, H, 2.77; found C, 45.92, H, 2.68.

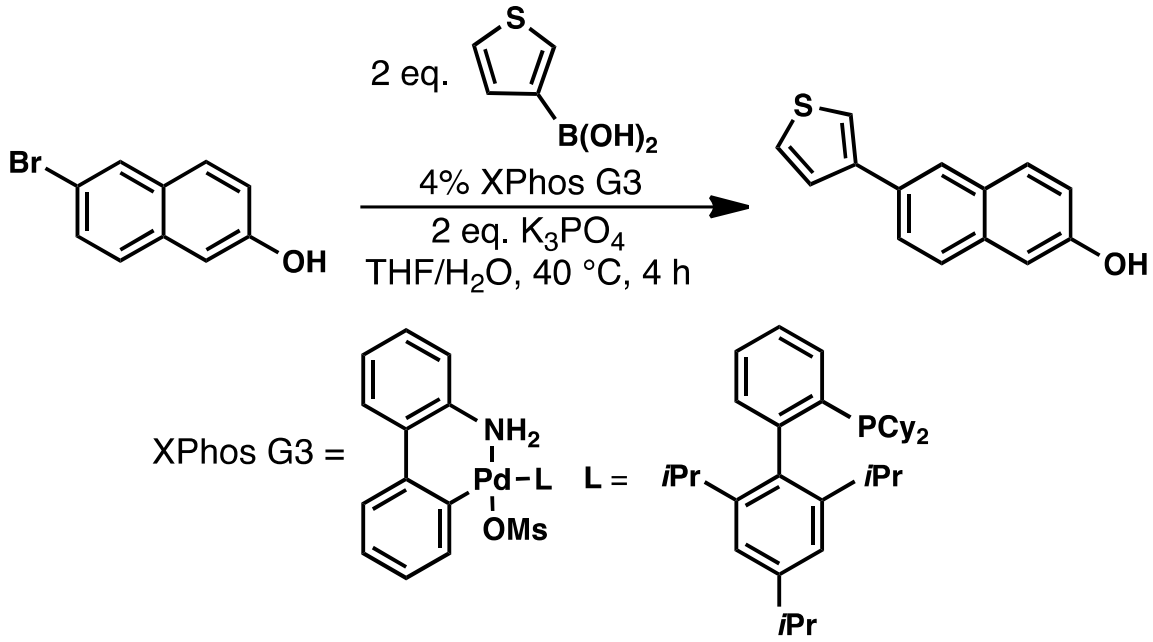


Procedure adapted from the literature.[15] 2-bromo-6-hydroxynaphthalene (892 mg, 4.00 mmol, 1.00 eq.), 3-furanyl boronic acid (896 mg, 8.00 mmol, 2.00 eq.), and XPhos G3[15] (136 mg, 0.160 mmol, 0.0400 eq.) were added to a roundbottom flask equipped with a stir bar. The flask was capped with a septum. Next, the flask was evacuated under high vacuum and backfilled with nitrogen. This procedure was repeated a total of three times. THF (8 mL) and degassed 2 M *aq*. K_3PO_4 (16.0 mL, 8.00 mmol, 2.00 eq.) were then added, and then hole in the septum was covered with teflon tape. The reaction mixture was stirred at 40 °C for 4 h. Upon completion of the reaction, the reaction mixture was cooled to room temperature, quenched with saturated *aq*. NH_4Cl (40 mL), and diluted with Et_2O (40 mL). The two phases were separated, and the aqueous phase was extracted with Et_2O (4 x 40 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. Purification by flash chromatography (1:10 EtOAc:hexanes → 1:5 EtOAc: hexanes) yielded 6-(furan-3-yl)-2-hydroxynaphthalene (776 mg, 92%) as a light brown powder. Melting Point: 169 °C. ^{1}H NMR (500 MHz, CD_3OD): δ 7.93 (dd, J = 2, 1 Hz,

1H), 7.85-7.87 (m, 1H), 7.70 (d, J = 9 Hz, 1H), 7.62 (d, J = 9 Hz, 1H), 7.58 (d, J = 2 Hz, 2H), 7.56 (dd, J = 3, 2 Hz, 1H), 7.09 (d, J = 3 Hz, 1H), 7.07 (dd, J = 9, 3 Hz, 1H), 6.87 (dd, J = 1, 1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.4, 145.0, 139.8, 135.5, 130.4, 130.1, 128.3, 128.0, 127.8, 125.7, 124.7, 119.6, 109.9, 109.6 ppm. IR (neat): 3436 (broad), 3140, 3125, 1635, 1619, 1519, 1475, 1287, 1202, 1150, 1135, 1051, 897, 888, 867, 813, 782 cm^{-1}.

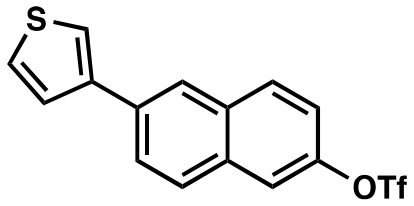


White solid. Melting Point: 72 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.82-7.90 (m, 3H), 7.68-7.74 (m, 2H), 7.54-7.57 (m, 1H), 7.37 (dd, J = 9, 3 Hz, 1H), 6.82-6.84 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.1, 144.3, 139.5, 132.9, 132.5, 131.5, 130.6, 128.8, 126.4, 126.1, 124.0, 120.3, 119.3, 119.1 (q, J = 319 Hz), 109.9 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ –73.2 ppm. IR (neat): 3132, 1608, 1470, 1419, 1397, 1210, 1184, 1163, 1130, 1109, 1054, 1016, 969, 947, 885, 871, 846, 815, 785, 743, 715, 709, 695, 644, 594 cm^{-1}.



Procedure adapted from the literature.[15] 2-bromo-6-hydroxynaphthalene (892 mg, 4.00 mmol, 1.00 eq.), 3-thienyl boronic acid (1.06 g, 8.00 mmol, 2.00 eq.), and XPhos G3[15] (136 mg, 0.160 mmol, 0.0400 eq.) were added to a roundbottom flask equipped with a stir bar. The flask was capped with a septum. Next, the flask was evacuated under high vacuum and backfilled with nitrogen. This procedure was repeated a total of three times. THF (8 mL) and degassed 2 M *aq*. K_3PO_4 (16.0 mL, 8.00 mmol, 2.00 eq.) were then added, and then hole in the septum was covered with teflon tape. The reaction mixture was stirred at 40 °C for 4 h. Upon completion of the reaction, the reaction mixture was cooled to room temperature, quenched with saturated *aq*. NH_4Cl (40 mL), and diluted with Et_2O (40 mL). The two phases were separated, and the aqueous phase was extracted with Et_2O (3 x 40 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. Purification by flash chromatography (1:10 EtOAc:hexanes → 1:5 EtOAc: hexanes) yielded 6-(thiophen-3-yl)-2-hydroxynaphthalene 756 mg, 84%) as a light brown powder. Melting Point: 195 °C. ^{1}H NMR (500 MHz, CD_3OD): δ 7.97 (s, 1H), 7.60-7.74

(m, 4H), 7.53 (dt, J = 5, 1 Hz, 1H), 7.46 (ddd, J = 5, 3, 1 Hz, 1H), 7.05-7.10 (m, 2H) ppm; ^{13}C NMR (125 MHz, CD_3OD): δ 156.5, 143.7, 135.5, 131.8, 130.7, 130.1, 127.8, 127.2, 127.1, 126.2, 125.4, 120.6, 119.7, 109.8 ppm. IR (neat): 3249 (broad), 3094, 1630, 1603, 1575, 1516, 1479, 1456, 1398, 1305, 1247, 1202, 1148, 1090, 965, 885, 868, 813, 776, 764 cm^{-1}.

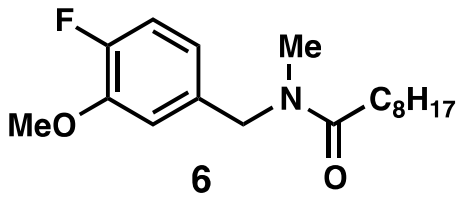


White solid. Melting Point: 110 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.93 (d, J = 9 Hz, 1H), 7.89 (d, J = 9 Hz, 1H), 7.84 (dd, J = 9, 2 Hz, 1H), 7.74 (d, J = 3 Hz, 1H), 7.61 (dd, J = 3, 1 Hz, 1H), 7.52 (dd, J = 6, 1 Hz, 1H), 7.46 (dd, J = 5, 3 Hz, 1H), 7.38 (dd, J = 9, 3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.1, 141.6, 134.7, 132.8, 132.5, 130.8, 128.7, 126.9, 126.4, 124.7, 121.5, 120.2, 119.2, 117.7 ppm (the signal corresponding to the *C*F_3 group could not be readily observed); ^{19}F NMR (470 MHz, $CDCl_3$): δ –73.1 ppm. IR (neat): 3099, 1602, 1508, 1473, 1421, 1360, 1204, 1133, 1109, 963, 935, 883, 848, 809, 778, 712, 672, 636, 604, 584 cm^{-1}. Anal. Calcd. for $C_{15}H_9O_3F_3S_2$: C, 50.27, H, 2.53; found C, 50.21, H, 2.36.

Aryl Fluorides

General Procedure using 5: In a nitrogen-filled glovebox, cesium fluoride (456 mg, 3.00 mmol, 3.00 eq.), **5** (1-2%), and solvent (10 mL) were added to an oven-dried reaction tube equipped with a stir bar. The reaction mixture was stirred at room temperature for 1 min, at which time the aryl triflate (1.00 mmol, 1.00 eq.) was added in

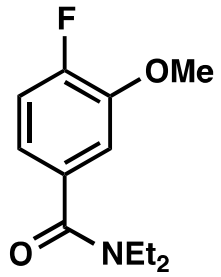
one portion. The tube was capped, removed from the glovebox, placed in an oil bath that had been pre-heated to the desired reaction temperature, and allowed to vigorously stir at that temperature for 14 h (the stirring rate should be maintained at over 1000 rpm for optimal results). The reaction mixtures typically turned dark red during this period, and no significant formation of Pd nanoparticles was observed, although the reaction mixture remained non-homogenous due to the poor solubility of CsF and CsOTf in organic solvents. At this time, the reaction mixture was cooled to room temperature and passed through a plug of celite, eluting with Et_2O or EtOAc (40 mL). The solvent was removed with the aid of a rotary evaporator and the resulting crude products were purified directly by flash chromatography. All isolated yields are an average of two runs.



6

Following the general procedure, CsF (228 mg, 1.50 mmol, 3.00 eq.), N-methylnonivamide triflate (220 mg, 0.500 mmol, 1.00 eq.), **5** (12.0 mg, 0.00750 mmol, 0.0150 eq., "3% Pd"), and toluene (5 mL) were combined and heated at 130 °C. The crude product mixture was purified by flash chromatography (1:3 EtOAc:hexanes → 1:2 EtOAc:hexanes) to yield fluoro-deoxy-*N*-methylnonivamide (132 mg, 85%) as a yellow oil. **6** exists as a 2:1 mixture of rotamers in solution. ^{1}H NMR (500 MHz, $CDCl_3$): major rotamer: δ 6.95 (dd, J = 12, 7 Hz, 1H), 6.85 (dd, J = 8, 2 Hz, 1H), 6.68-6.72 (m, 1H), 4.49 (s, 2H), 3.82 (s, 3H), 2.88 (s, 3H), 2.30-2.35 (m, 2H), 1.61-1.67 (m, 2H), 1.20-1.32 (m, 10H), 0.81-0.85 (m, 3H) ppm; minor rotamer: δ 7.01 (dd, J = 11, 8 Hz), 6.68-6.72 (m, 1H), 6.62-6.66 (m, 1H), 4.45 (s, 2H), 3.83 (s, 3H), 2.89 (s, 3H), 2.30-2.35 (m, 2H), 1.61-

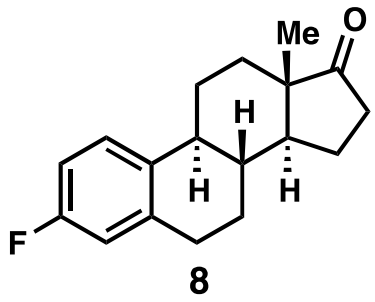
1.67 (m, 2H), 1.20-1.32 (m, 10H), 0.81-0.85 (m, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.6, 173.3, 152.7, 150.8, 148.1, 147.8, 147.7, 134.1, 134.1, 133.2, 133.1, 120.4, 120.3, 118.5, 118.4, 116.4, 116.2, 115.8, 115.6, 113.2, 113.2, 111.2, 111.2, 56.2, 56.2, 53.0, 50.4, 34.8, 33.8, 33.6, 33.1, 31.9, 31.8, 29.7, 29.5, 29.5, 29.5, 29.4, 29.2, 29.2, 25.5, 25.2, 22.7, 14.1, 14.1 ppm (observed complexity is due to C-F coupling and the presence of two rotamers in solution); ^{19}F NMR (470 MHz, $CDCl_3$): δ –137.7 ppm (major rotamer), δ –137.1 ppm (minor rotamer). Coalesence of the two sets of ^{1}H NMR (500 MHz, DMSO-d_6) signals was observed between 70 °C and 80 °C (see attached). The assignation of the multiplet signal at δ 6.68-6.72 as containing signals for both the major and minor rotamers was confirmed by a ^{1}H-^{1}H COSY NMR experiment (see attached), which showed coupling between this signal and the signals for the N-C*H*$_2$-Ar protons present in both rotamers. IR (neat): 2954, 2923, 2854, 1643, 1610, 1516, 1464, 1417, 1280, 1216, 1150, 1119, 1032, 922, 808, 785, 730 cm^{-1}.



7

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 4-(diethylcarbamoyl)-2-methoxyphenyl triflate (355 mg, 1.00 mmol, 1.00 eq.), **5** (16.0 mg, 0.0100 mmol, 0.0100 eq., "2% Pd"), and toluene (10 mL) were combined and heated at 100 °C. The crude product mixture was purified by flash chromatography (1:2 EtOAc:hexanes → 1:1 EtOAc:hexanes) to yield *N*,*N*-diethyl-4-fluoro-3-

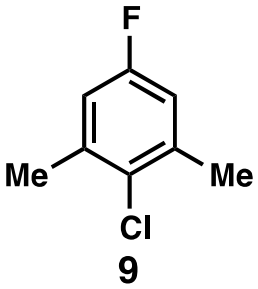
methoxybenzamide (205 mg, 91%) as an amber oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.00 (dd, J = 11, 8 Hz, 1H), 6.95 (dd, J = 8, 2 Hz, 1H), 6.81-6.85 (m, 1H), 3.83 (s, 3H), 3.44 (bs, 2H), 3.2 (bs, 2H), 1.16 (bs, 3H), 1.07 (bs, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 152.8 (d, J = 247 Hz), 147.7 (d, J = 11 Hz), 133.7 (d, J = 4 Hz), 118.9 (d, J = 7 Hz), 115.9 (d, J = 19 Hz), 112.2 (d, J = 2 Hz), 56.3, 43.4 (bs), 39.5 (bs), 14.4 (bs), 13.1 (bs) ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –134.1 ppm. IR (neat): 2973, 2937, 1627, 1605, 1518, 1461, 1426, 1316, 1290, 1263, 1213, 1165, 1119, 1092, 1030, 920, 819, 787, 727, 609 cm^{-1}.



8

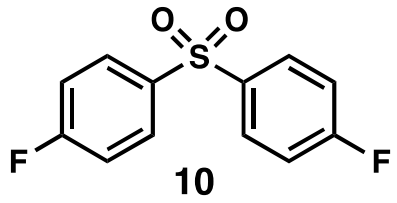
Following the general procedure, CsF (228 mg, 1.50 mmol, 3.00 eq.), estrone triflate (201 mg, 0.500 mmol, 1.00 eq.), **5** (8.0 mg, 0.0050 mmol, 0.010 eq., "2% Pd"), and cyclohexane (5 mL) were combined and heated at 120 °C. The crude product mixture was purified by flash chromatography (1:10 EtOAc:hexanes → 1:5 EtOAc:hexanes) to yield fluoro-deoxyestrone (97.4 mg, 70%) as a white solid. Melting Point: 179–180 °C (Lit. 178–180 °C).[17] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (dd, J = 9, 6 Hz, 1H), 6.83 (ptd, J = 9, 3 Hz, 1H), 6.78 (dd, J = 10 Hz, 3 Hz), 2.87-2.92 (m, 2H), 2.50 (dd, J = 20, 9 Hz, 1H), 2.34-241 (m, 1H), 2.22-2.27 (m, 1H), 1.94-2.18 (m, 4H), 1.40-1.67 (m, 6H), 0.91 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 220.7, 161.1 (d, J = 243 Hz), 138.8 (d, J = 7 Hz), 135.4 (d, J = 3 Hz), 126.9 (d, J = 8 Hz), 115.2 (d, J = 20 Hz), 112.6 (d, J = 21 Hz), 50.4, 48.0, 44.1, 38.2, 35.9, 31.6, 29.6, 26.4, 26.0, 21.7, 13.9 ppm; ^{19}F NMR (282 MHz,

$CDCl_3$): δ –118.4 ppm. Contaminated with ~4% of a compound with ^{19}F NMR shift of δ –117.6 ppm, which is likely a regioisomer of the desired compound. IR (neat): 3043, 2927, 2866, 1739, 1610, 1585, 1494, 1451, 1427, 1419, 1404, 1377, 1230, 1211, 1148, 1052, 1008, 916, 907, 889, 816, 784 cm^{-1}. These spectra are consistent with those reported in the literature.[8]



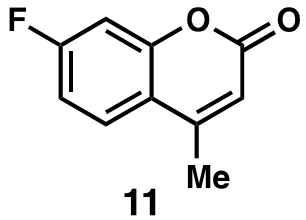
9

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 4-chloro-3,5-dimethylphenyltrifluoromethanesulfonate (289 mg, 1.00 mmol, 1.00 eq.), **5** (16.0 mg, 0.0100 mmol, 0.0100 eq., "2% Pd"), and toluene (10 mL) were combined and heated at 110 °C for 14 h. The crude product mixture was purified by flash chromatography (pentane) to yield 1-chloro-4-fluoro-2,6-dimethylbenzene (133 mg, 84%) as colorless oil. Contaminated with <5% toluene. ^1H NMR (500 MHz, $CDCl_3$): δ 6.81 (d, J = 9 Hz, 2H), 2.37 (s, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.7 (d, J = 243 Hz), 138.2 (d, J = 8 Hz), 129.6 (d, J = 3 Hz), 115.3 (d, J = 22 Hz), 21.1 (d, J = 1 Hz) ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –118.0 (t, J = 9 Hz) ppm. IR (neat): 2957, 1607, 1579, 1467, 1437, 1412, 1312, 1137, 1063, 1022, 856, 730, 697, 627 cm^{-1}. Note: This compound should not be placed under high vacuum due to its volatility.



10

Following the general procedure, CsF (456 mg, 3.00 mmol, 6.00 eq.), 4,4'-sulfonylbis(phenyltrifluoromethanesulfonate) (257 mg, 0.500 mmol, 1.00 eq.), **5** (24.0 mg, 0.0150 mmol, 0.0300 eq., "6% Pd"), and toluene (5 mL) were combined and heated at 130 °C for 14 h. The crude product mixture was purified by flash chromatography (1:10 EtOAc:hexanes → 1:5 EtOAc:hexanes) to yield 4,4'-sulfonylbis(fluorobenzene) (104 mg, 82%) as white crystalline solid. Melting Point: 98 °C (Lit. 97-98 °C).[18] ^{1}H (500 MHz, $CDCl_3$): δ 7.92-7.96 (m, 4H), 7.15-7.20 (m, 4H) ppm; ^{13}C (125 MHz, $CDCl_3$): δ 165.6 (d, J = 255 Hz), 137.6 (d, J = 3 Hz), 130.5 (d, J = 10 Hz), 116.8 (d, J = 23 Hz) ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ –104.2 ppm. IR (neat): 3104, 3068, 3041, 1587, 1491, 1407, 1323, 1291, 1234, 1154, 1099, 1070, 833, 813, 712, 676 cm^{-1}. These spectra are consistent with those reported in the literature.[19]

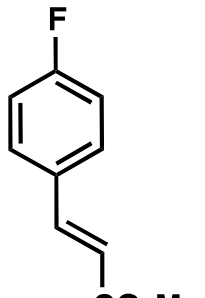


11

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 4-methylumbelliferone triflate (308 mg, 1.00 mmol, 1.00 eq.), **5** (16.0 mg, 0.0100 mmol, 0.0100 eq., "2% Pd"), and toluene (10 mL) were combined and heated at 110 °C. The crude product mixture was purified by flash chromatography (1:5 EtOAc:hexanes → 1:3 EtOAc:hexanes) to yield 7-fluoro-4-methyl-coumarin (164 mg, 92%) as a pale yellow solid. Melting Point: 130 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56–7.59 (m, 1H), 6.99–

7.04 (m, 2H), 6.22 (s, 1H), 2.42 (d, J = 1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.5 (d, J = 252 Hz), 160.5, 154.8 (d, J = 13 Hz), 152.1 (d, J = 1 Hz), 126.4 (d, J = 10 Hz), 116.8 (d, J = 3 Hz), 114.0 (d, J = 3 Hz), 112.3 (d, J = 23 Hz), 104.6 (d, J = 25 Hz), 18.9 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –106.2 ppm. IR (neat): 3083, 3060, 2919, 1713, 1609, 1575, 1501, 1418, 1383, 1370, 1272, 1143, 1122, 1067, 1015, 978, 873, 809, 797, 747, 705, 623 cm^{-1}. These spectra are consistent with those reported in the literature.[20]

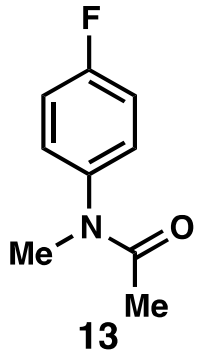
Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 4-methylumbelliferone nonaflate (458 mg, 1.00 mmol, 1.00 eq.), **5** (16.6 mg, 0.0100 mmol, 0.0100 eq.), and toluene (10 mL) were combined and heated at 110 °C. The crude product mixture was purified by flash chromatography (1:5 EtOAc:hexanes → 1:3 EtOAc:hexanes) to yield 7-fluoro-4-methyl-coumarin (158 mg, 89%) as a pale yellow solid. The spectra obtained for this compound are identical with those reported in the previous entry and are consistent with those reported in the literature.[20]



12

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), (*E*)-methyl 3-(4-(triflate)phenyl)acrylate (310 mg, 1.00 mmol, 1.00 eq.), **5** (16.0 mg, 0.0100 mmol, 0.0100 eq., "2% Pd"), and toluene (10 mL) were combined and heated at 80 °C. The crude product mixture was purified by flash chromatography (hexanes → 1:10 EtOAc:hexanes)

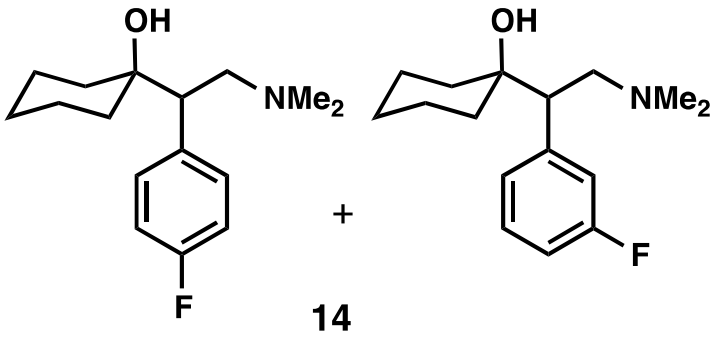
to yield (*E*)-methyl 3-(4-fluorophenyl)acrylate (166 mg, 92%) as a pale yellow solid. Melting Point: 45 °C (Lit. 45–47 °C).[16] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J = 16 Hz, 1H), 7.43-7.48 (m, 2H), 7.00-7.05 (m, 2H), 6.31 (d, J = 16 Hz, 1H), 3.75 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 163.9 (d, J = 250 Hz), 143.5 (d, J = 1 Hz), 130.6, 130.0 (d, J = 8 Hz), 117.5, 116.1 (d, J = 23 Hz), 51.7 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –109.9 ppm. IR (neat): 3036, 2956, 1705, 1632, 1599, 1509, 1435, 1317, 1282, 1223, 1202, 1171, 1160, 1005, 939, 832, 782 cm^{-1}. These spectra are consistent with those reported in the literature.[16] This compound should not be placed under high vacuum due to its predilection towards sublimation.



13

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 4-(*N*-methylacetamido)phenyl trifllate (297 mg, 1.00 mmol, 1.00 eq.), **5** (32.0 mg, 0.0200 mmol, 0.0200 eq., 4% Pd"), and cyclohexane (10 mL) were combined and heated at 120 °C. The crude product mixture was purified by flash chromatography (1:1 EtOAc:hexanes) to yield *N*-(4-fluorophenyl)-*N*-methylacetamide (119 mg, 71%) as a yellow solid. Melting Point: 64–66 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.10-7.15 (m, 2H), 7.02-7.07 (m, 2H), 3.18 (s, 3H), 1.80 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 161.7 (d, J = 236 Hz), 140.7, 128.9 (d, J = 9 Hz), 116.7 (d, J = 23 Hz), 37.2, 22.4 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –113.9 ppm. IR (neat): 3072, 3047, 3012, 2933,

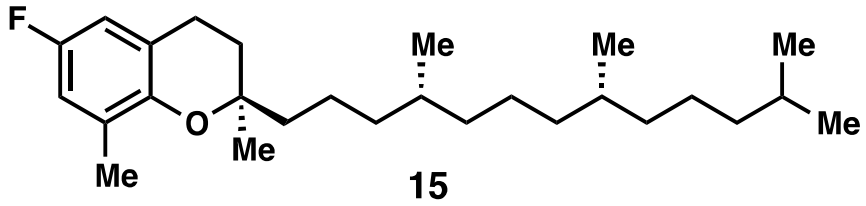
1659, 1502, 1417, 1385, 1305, 1218, 1160, 1142, 1086, 974, 844, 815, 731, 587, 557 cm^{-1}. Anal. Calcd. for $C_9H_{10}ONF$: C, 64.66, H, 6.03; found, 64.97, H, 6.19.



14

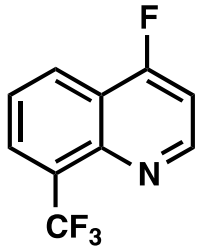
Following the general procedure, CsF (228 mg, 1.50 mmol, 3.00 eq.), desvenlaflaxine triflate (198 mg, 0.500 mmol, 1.00 eq.), **5** (24.0 mg, 0.0150 mmol, 0.0300 eq., "6% Pd"), and toluene (5 mL) were combined and heated at 130 °C. The crude product mixture was purified by flash chromatography (1st column (silica gel): EtOAc → MeOH:CH_2Cl_2 1:20 →1:10 →1:7; 2nd column (alumina): EtOAc:hexanes 1:10 → 1:5 → 1:3) to yield **16** (178 mg, 67%) as a white solid. **14** was obtained as a 3:1 mixture of regioisomers by ^{19}F NMR. Melting Point: 91-95 °C. ^1H NMR (500 MHz, $CDCl_3$): major regioisomer: δ 7.07 (dd, J = 7, 2 Hz, 2H), 6.94 (pt, J = 9 Hz, 2H), 3.25 (pt, J = 13 Hz, 1H), 2.94-3.00 (m, 1H), 2.28-2.32 (m, 7H), 0.79-1.88 (m, 10H) ppm; minor regioisomer: δ 7.18-7.27 (m, 2H), 7.11 (d, J = 7 Hz, 1H), 6.80-6.92 (m, 1H), 3.28-3.35 (m, 1H), 2.28-2.32 (m, 7H), 0.79-1.88 (m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): complex spectrum due to C-F coupling and presence of two regioisomers, see attached; ^{19}F NMR (282 MHz, $CDCl_3$): major regioisomer: δ –116.5 ppm; minor regioisomer: δ –113.7 ppm. IR (neat): 3135 (broad), 2981, 2929, 2859, 2828, 2782, 1606, 1587, 1511, 1464, 1445, 1323, 1370, 1249, 1037, 1011, 969, 903, 876, 849 cm^{-1}. The assignation of the desired product to the major regioisomer was made based on the resemblance of the ^1H and ^{13}C NMR spectra of the

major product to a *para*-substituted aromatic system, and that of the minor regioisomer to a *meta*-substituted aromatic system. In addition, the ^{19}F NMR shift for the major regioisomer is upfield from that of the minor regioisomer, which is consistent with the electron-donating group being *para* to the fluorine atom in the major regioisomer and *meta* in the minor regioisomer.



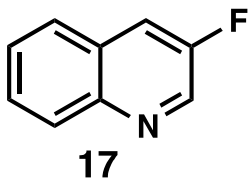
15

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), δ-tocopherol triflate (535 mg, 1.00 mmol, 1.00 eq.), **5** (24.0 mg, 0.0150 mmol, 0.0150 eq., "3% Pd"), and cyclohexane (10 mL) were combined and heated at 130 °C. The crude product mixture was purified by flash chromatography (hexanes) to yield fluoro-deoxy-δ-tocopherol (352 mg, 88%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.70 (dd, J = 9, 3 Hz, 1H), 6.61 (dd, J = 9, 2 Hz, 1H), 2.68-2.79 (m, 2H), 2.17 (s, 3H), 1.74-1.84 (m, 2H), 1.04-1.64 (m, 27H), 0.86-0.92 (m, 11H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.9 (d, J = 235 Hz), 148.0 (d, J = 2 Hz), 127.9 (d, J = 8 Hz), 121.5 (d, J = 8 Hz), 115.1 (d, J = 22 Hz), 112.4 (d, J = 22 Hz), 76.1, 40.1, 39.6, 37.6, 37.6, 37.6, 37.5, 33.0, 32.8, 31.3, 28.2, 25.0, 24.6, 24.3, 22.9, 22.8, 22.7, 21.1, 19.9, 19.8 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –126.7 ppm. Contaminated with ~5% of a compound with ^{19}F NMR shift of δ –129.1 ppm, which is likely a regioisomer of the desired compound. IR (neat): 2925, 2867, 1743, 1377, 1219, 1126, 1046, 990, 931, 915, 856, 735, 711 cm^{-1}. These spectra are consistent with those reported in the literature.[8]



16

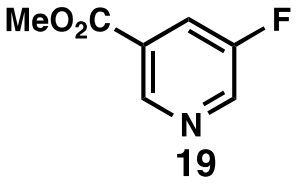
Following the general procedure, CsF (228 mg, 1.50 mmol, 3.00 eq.), 8-(trifluoromethyl)quinolin-4-yl trifllate (173 mg, 0.500 mmol, 1.00 eq.), **5** (8.0 mg, 0.0050 mmol, 0.010 eq., "2% Pd"), and toluene (5 mL) were combined and heated at 90 °C. The crude product mixture was purified by flash chromatography (hexanes → 1:10 EtOAc:hexanes) to yield 4-fluoro-8-trifluoromethylquinoline (94 mg, 87%) as a white solid. Melting Point: 97 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.98 (dd, J = 9, 5 Hz, 1H), 8.23 (d, J = 9 Hz, 1H), 8.09 (d, J = 7 Hz, 1H), 7.60 (pt, J = 8 Hz, 1H), 7.17 (dd, J = 9, 5 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): Complex spectra due to C-F coupling; ^{19}F NMR (282 MHz, $CDCl_3$): δ –60.8, –111.4 ppm. IR (neat): 3064, 1631, 1609, 1577, 1504, 1479, 1423, 1312, 1294, 1263, 1231, 1214, 1129, 1096, 1071, 883, 861, 821, 805, 768, 717 cm^{-1}. Anal. Calcd. for $C_{10}H_5NF_4$: C, 55.83, H, 2.34; found C, 56.09, H, 2.40. This compound should not be placed under high vacuum due to its predilection towards sublimation.



17

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 3-quinolinyl triflate (277 mg, 1.00 mmol, 1.00 eq.), **5** (32.0 mg, 0.0200 mmol, 0.0200 eq., "4% Pd"), and toluene (10 mL) were combined and heated at 120 °C. The crude product mixture was purified by flash chromatography (hexanes →1:10 EtOAc:hexanes) to yield 3-

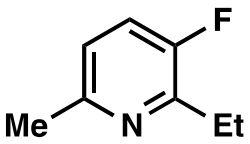
fluoroquinoline (103 mg, 70%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.77 (d, J = 3 Hz, 1H), 8.08 (d, J = 9 Hz, 1H), 7.66-7.72 (m, 2H), 7.62 (pt, J = 8 Hz, 1H), 7.50 (d, J = 8 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.2 (d, J = 255 Hz), 145.4 (d, J = 2 Hz), 141.5 (d, J = 28 Hz), 129.7, 128.7, 127.8 (d, J = 6 Hz), 127.4 (d, J = 5 Hz), 118.5 (d, J = 16 Hz) ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –128.5 ppm. IR (neat): 3059, 1611, 1497, 1464, 1426, 1336, 1270, 1210, 1154, 1138, 983, 889, 857, 779, 749, 709, 610 cm^{-1}. These spectra are consistent with those reported in the literature.[21] This compound should not be placed under high vacuum due to its volatility.



19

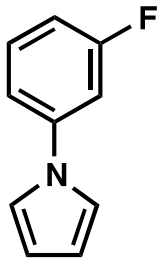
Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), methyl 5-triflatonicotinate (285 mg, 1.00 mmol, 1.00 eq.), **5** (32.0 mg, 0.0200 mmol, 0.0200 eq., "4% Pd"), and toluene (10 mL) were combined and heated at 130 °C. The crude product mixture was purified by flash chromatography (1:5 EtOAc:hexanes → 1:3 EtOAc:hexanes) to yield methyl 5-fluoronicotinate (68 mg, 44%) as an off-white solid. Melting Point: 51 °C (Lit. 48 °C).[22] ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.01 (s, 1H), 8.62 (d, J = 4 Hz, 1H), 7.94-7.98 (m, 1H), 3.94 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7 (d, J = 2 Hz), 159.2 (d, J = 257 Hz), 146.7 (d, J = 4 Hz), 142.2 (d, J = 23 Hz), 127.4 (d, J = 3 Hz), 123.7 (d, J = 19 Hz), 52.8 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –126.3 ppm. IR (neat): 3062, 2967, 1723, 1599, 1571, 1446, 1440, 1417, 1308, 1294, 1215, 1162, 1093, 1018, 973, 940, 901, 796, 767, 689, 688 cm^{-1}. These spectra are consistent with those

reported in the literature.[22] This compound should not be placed under high vacuum due to its predilection for sublimation.



20

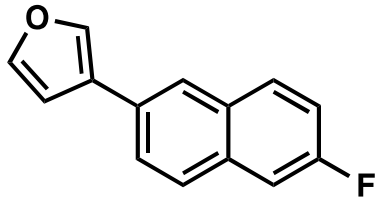
Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 2-ethyl-6-methyl-3-triflatopyridine (269 mg, 1.00 mmol, 1.00 eq.), **5** (32.0 mg, 0.0200 mmol, 0.0200 eq., "4% Pd"), and toluene (10 mL) were combined and heated at 130 °C. The crude product mixture was purified by flash chromatography (pentane → 1:10 Et_2O/pentane → 1:5 Et_2O/pentane) to yield methyl 2-ethyl-3-fluoro-6-methylpyridine (89 mg, 64%) as a sweet-smelling colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15 (pt, J = 9 Hz, 1H), 6.91 (dd, J = 9, 3 Hz, 1H), 2.80 (qd, J = 8, 2 Hz, 1H), 2.47 (s, 3H), 1.23 (t, J = 8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.0 (d, J = 250 Hz), 153.3 (d, J = 5 Hz), 150.6 (d, J = 16 Hz), 122.7 (d, J = 20 Hz), 121.7 (d, J = 3 Hz), 25.3 (d, J = 2 Hz), 23.8 (d, J = 2 Hz), 13.2 (d, J = 2 Hz) ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –132.6 ppm. IR (neat): 2974, 2938, 2878, 1598, 1466, 1238, 1155, 1120, 1050, 909, 820, 733 cm^{-1}. This compound should not be placed under high vacuum due to its volatility.



21

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 3-(1*H*-pyrrol-1-yl)phenyl triflate (291 mg, 1.00 mmol, 1.00 eq.), **5** (24.0 mg, 0.0150 mmol, 0.0150 eq.,

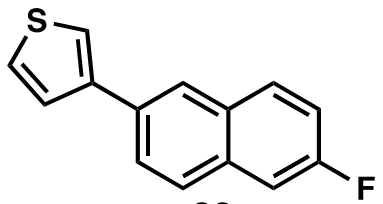
"3% Pd"), and toluene (10 mL) were combined and heated at 120°C. The crude product mixture was purified by flash chromatography (1:40 EtOAc:hexanes → 1:20 EtOAc:hexanes → 1:10 EtOAc:hexanes) to yield 1-(3-fluorophenyl)-1*H*-pyrrole (115 mg, 71%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (dd, J = 16, 9 Hz, 1H), 7.22 (dd, J = 9, 2 Hz, 1H), 7.11-7.17 (m, 3H), 6.95-7.00 (m, 1H), 6.41-6.42 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (d, J = 245 Hz), 142.2 (d, J = 10 Hz), 130.9 (d, J = 10 Hz), 119.3, 115.8, 112.4 (d, J = 21 Hz), 111.1, 107.8 (d, J = 25 Hz) ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –111.5 ppm. IR (neat): 3106, 3075, 1612, 1598, 1503, 1479, 1455, 1342, 1316, 1251, 1172, 1160, 1107, 1066, 1025, 954, 844, 775, 719, 680 cm^{-1}. Anal. Calcd. for $C_{10}H_8NF_6$: C, 74.52, H, 5.00; found C, 73.48, H, 5.09. The sensitivity of this pyrrole-containing compound is likely responsible for the discrepancy in elemental analysis.



22

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 6-(furan-3-yl)-2-naphthyl triflate (342 mg, 1.00 mmol, 1.00 eq.), **5** (16.0 mg, 0.0100 mmol, 0.0100 eq., "2% Pd"), and toluene (10 mL) were combined and heated at 100 °C. The crude product mixture was purified by flash chromatography (hexanes) to yield 6-(furan-3-yl)-2-fluoronaphthalene (193 mg, 91%) as an off-white solid. Melting Point: 99-101 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.75-7.87 (m, 3H), 7.65 (d, J = 9 Hz, 1H), 7.56-7.58 (m, 1H), 7.47 (dd, J = 10, 3 Hz, 1H), 7.30 (td, J = 9, 3 Hz, 1H), 6.84 (dd, J = 2, 2 Hz,

1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.6 (d, J = 244 Hz), 144.0, 138.9, 133.2 (d, J = 9 Hz), 130.8, 130.2 (d, J = 9 Hz), 129.2 (d, J = 3 Hz), 127.9 (d, J = 5 Hz), 126.3, 125.6, 124.0 (d, J = 1 Hz) 116.7 (d, J = 25 Hz), 110.9 (d, J = 20 Hz), 108.9, 99.8 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –115.3 ppm. Contaminated with ~2% of a compound with ^{19}F NMR shift of δ –114.7 ppm, which is likely a regioisomer of the desired compound. IR (neat): 3133, 1610, 1559, 1514, 1501, 1474, 1365, 1249, 1237, 1198, 1164, 1142, 1092, 1052, 971, 891, 881, 814, 782, 740, 632 cm^{-1}. Anal. Calcd. for $C_{14}H_9OF$: C, 79.23, H, 4.27; found C, 78.98, H, 4.17.



23

Following the general procedure, CsF (456 mg, 3.00 mmol, 3.00 eq.), 6-(thiophen-3-yl)-2-naphthyl triflate (358 mg, 1.00 mmol, 1.00 eq.), **5** (16.0 mg, 0.0100 mmol, 0.0100 eq., "2% Pd"), and toluene (10 mL) were combined and heated at 130 °C. The crude product mixture was purified by flash chromatography (hexanes) to yield 6-(thiophen-3-yl)-2-fluoronaphthalene (203 mg, 89%) as a white solid. Melting Point: 147 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.76-7.86 (m, 3H), 7.55-7.57 (m, 1H), 7.52 (dd, J = 5, 1 Hz, 1H), 7.43-7.49 (m, 2H), 7.30 (td, J = 9, 3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.7 (d, J = 245 Hz), 142.0, 133.3 (d, J = 9 Hz), 132.7 (d, J = 3 Hz), 130.8 (d, J = 1 Hz), 130.5 (d, J = 9 Hz), 127.9 (d, J = 5 Hz), 126.6, 126.5, 126.2 (d, J = 1 Hz), 124.8 (d, J = 1 Hz), 120.7, 116.8 (d, J = 25 Hz), 110.9 (d, J = 20 Hz) ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ –115.0 ppm. Contaminated with ~3% of a compound with ^{19}F NMR shift of δ –114.6 ppm, which is likely a regioisomer of the desired compound. IR (neat):

3095, 1602, 1575, 1507, 1500, 1407, 1364, 1234, 1205, 1189, 1140, 1116, 1092, 967, 871, 810, 777, 727, 623 cm^{-1}. Anal. Calcd. for $C_{14}H_9FS$: C, 73.66, H, 3.97; found C, 73.97, H, 4.21.

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7. Although to our knowledge the isomerization of alkenes in the presence of a Pd(0) species has never been reported, isomerization in the presence of Pd(II) species is well-known. In this case the isomerization could be mediated by a Pd(II) species present before reductive elimination of $(TMSCH_2)_2$. However, at this time it is unclear exactly what is the mechanism of 1,5-COD isomerization to 1,4- and 1,3-COD.

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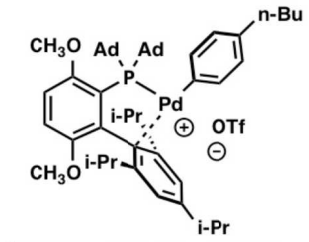
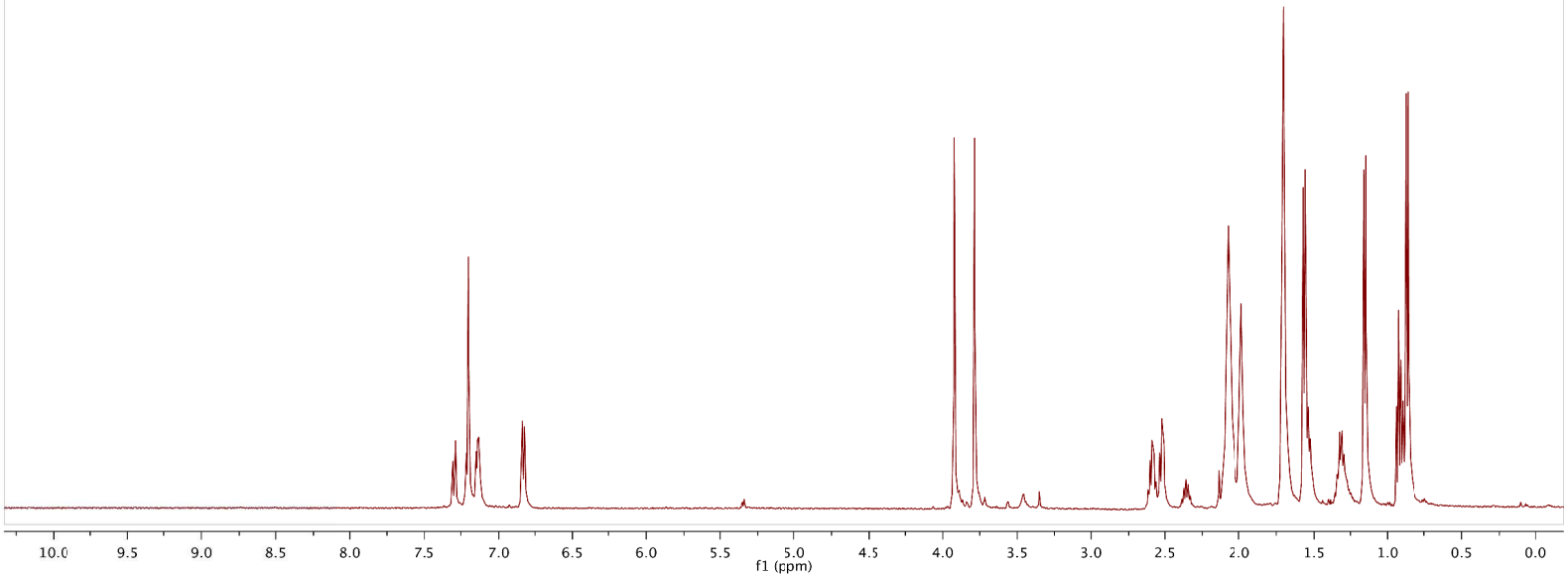
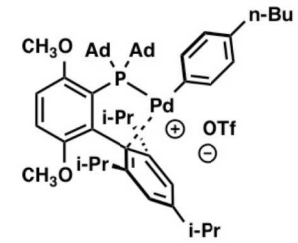


^{1}H NMR, 500 MHz, CD_2Cl_2

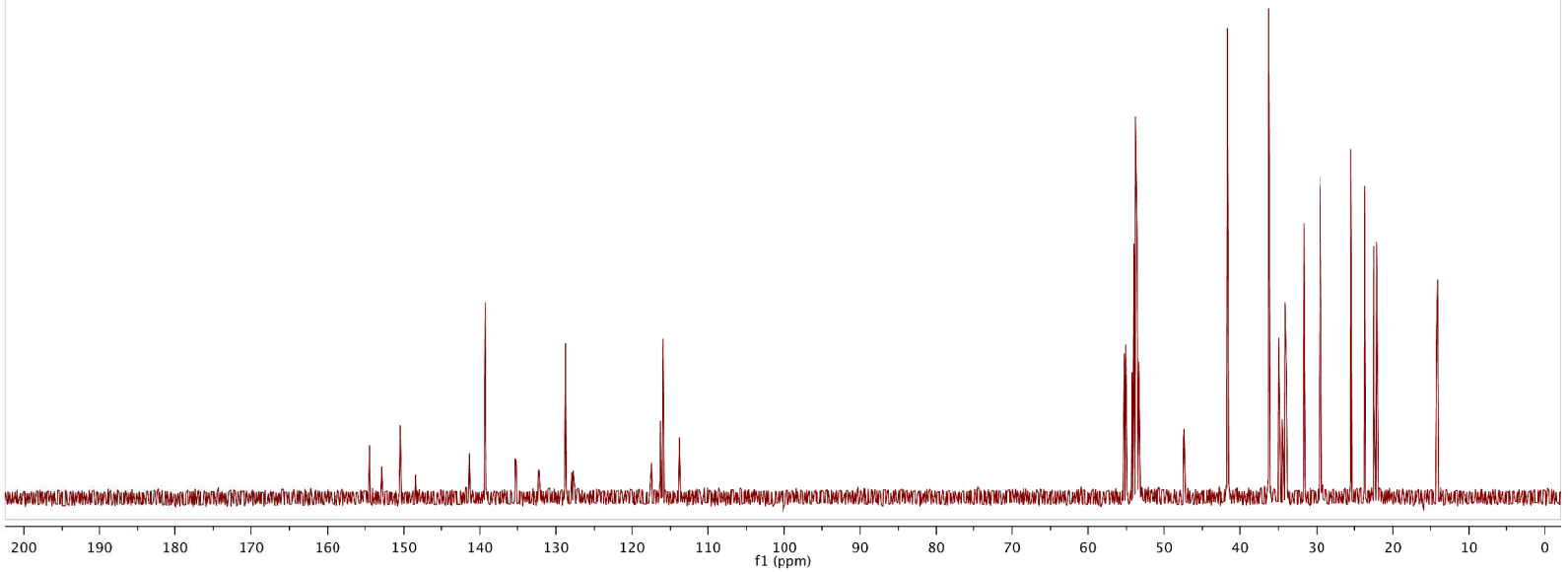
4

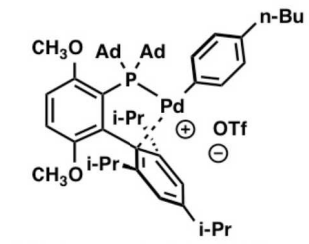




^{13}C NMR, 125 MHz, CD_2Cl_2

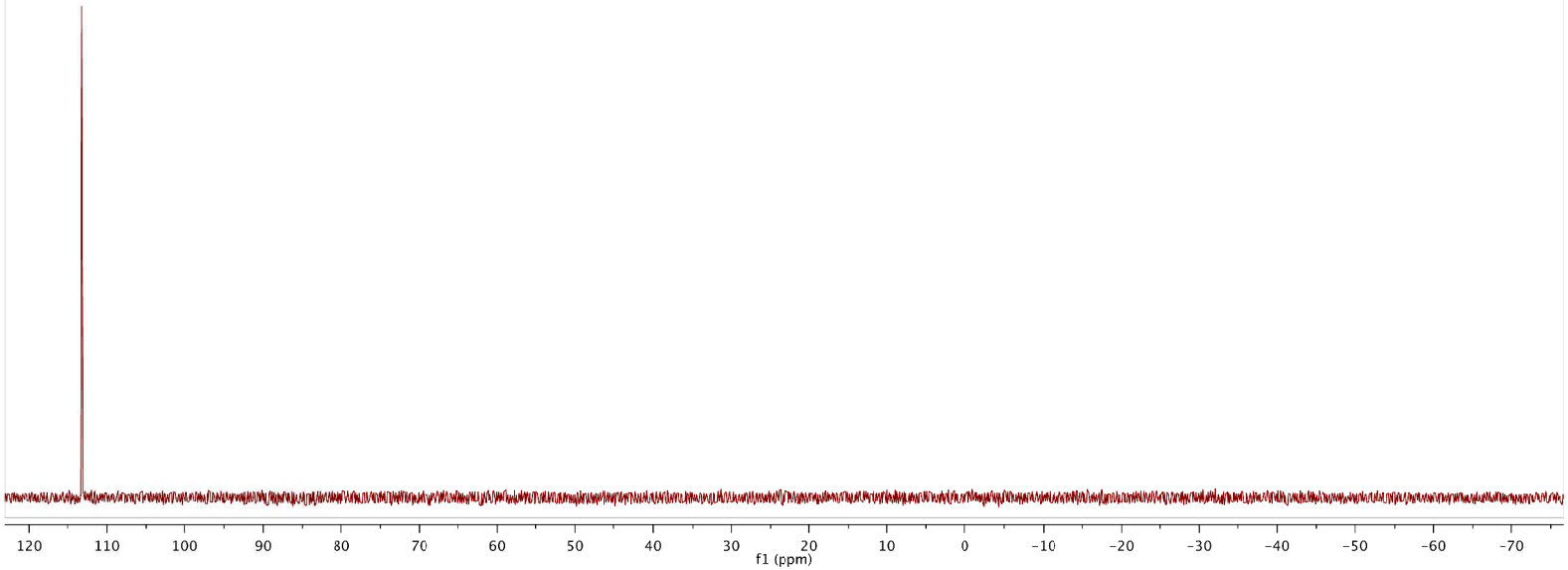
4

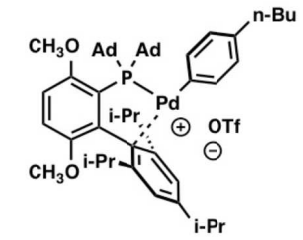




^{31}P NMR, 121 MHz, CD_2Cl_2

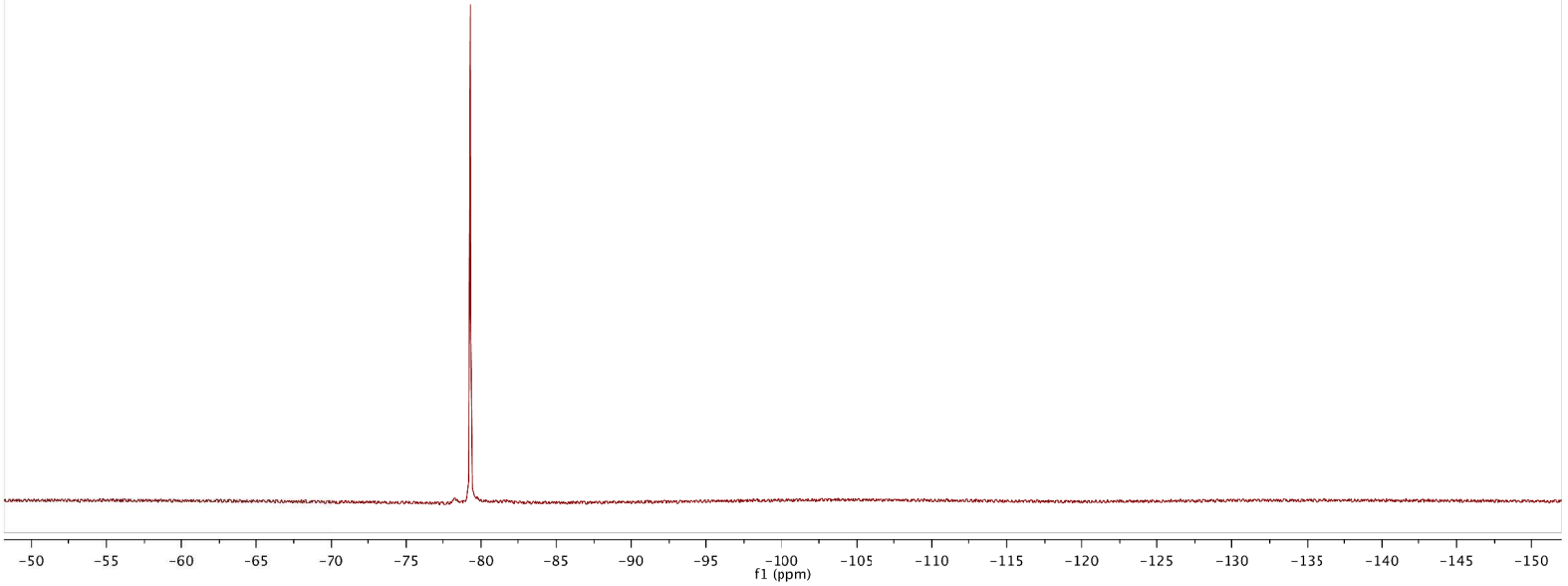
4

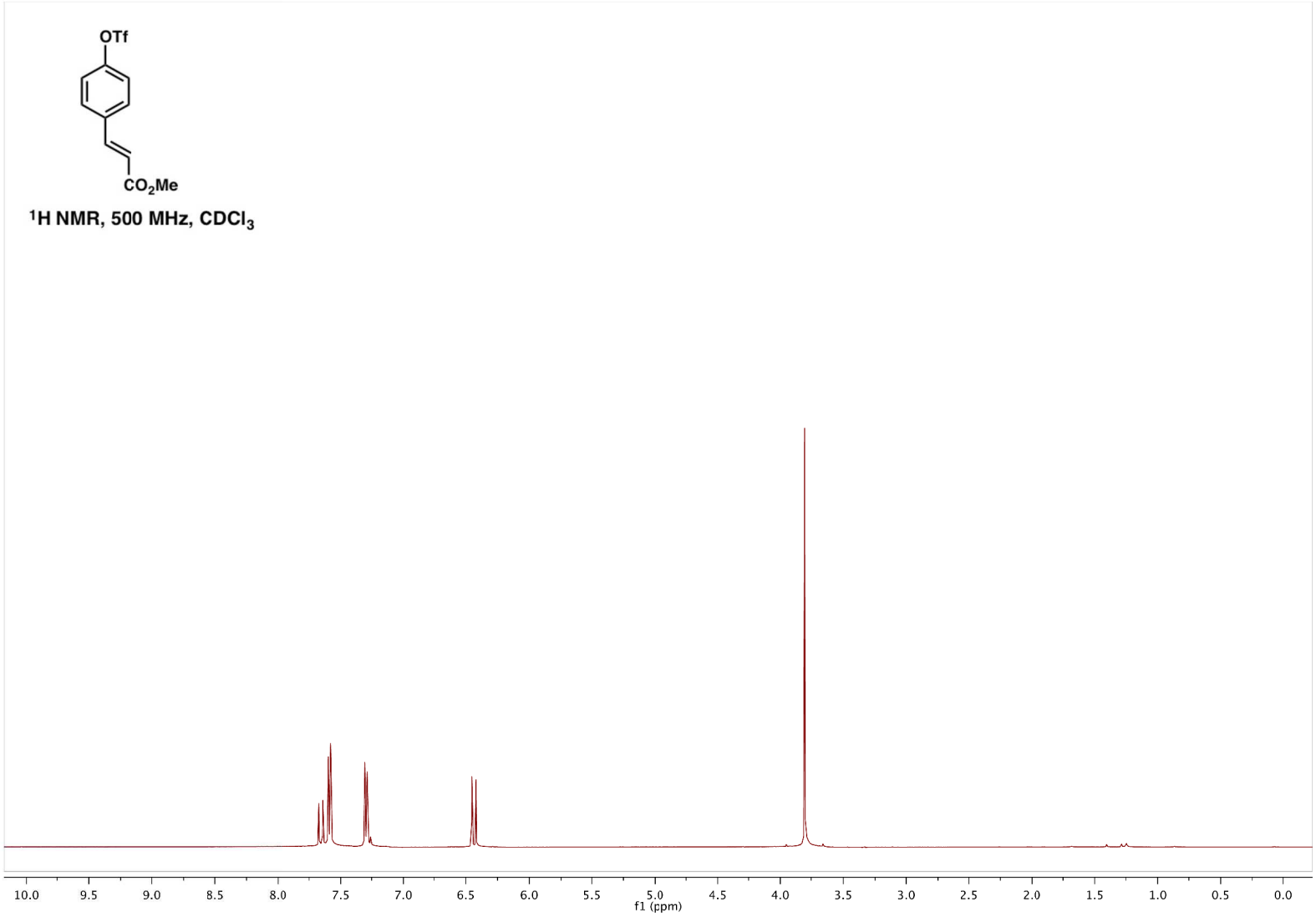




^{19}F NMR, 470 MHz, CD_2Cl_2

4

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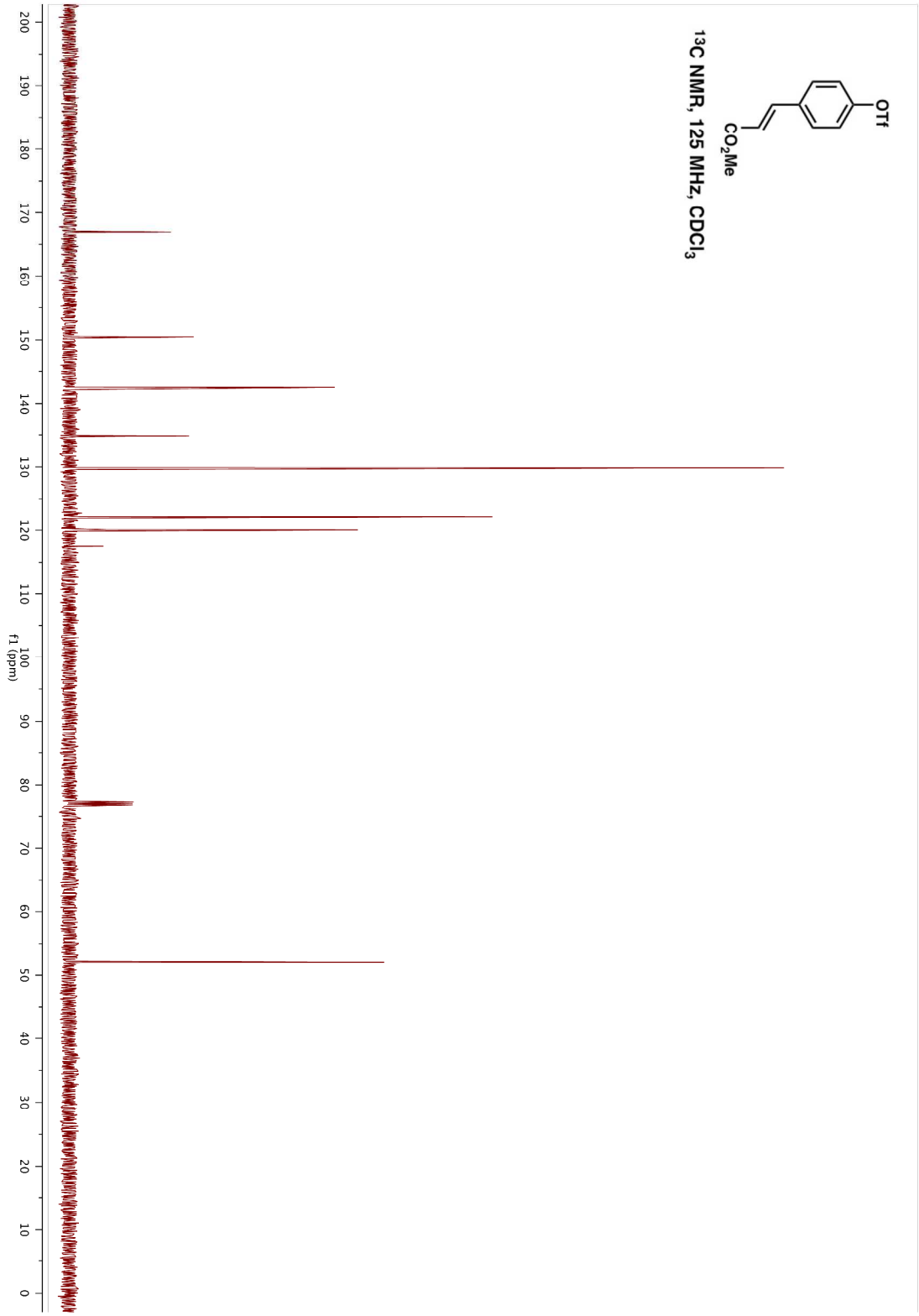
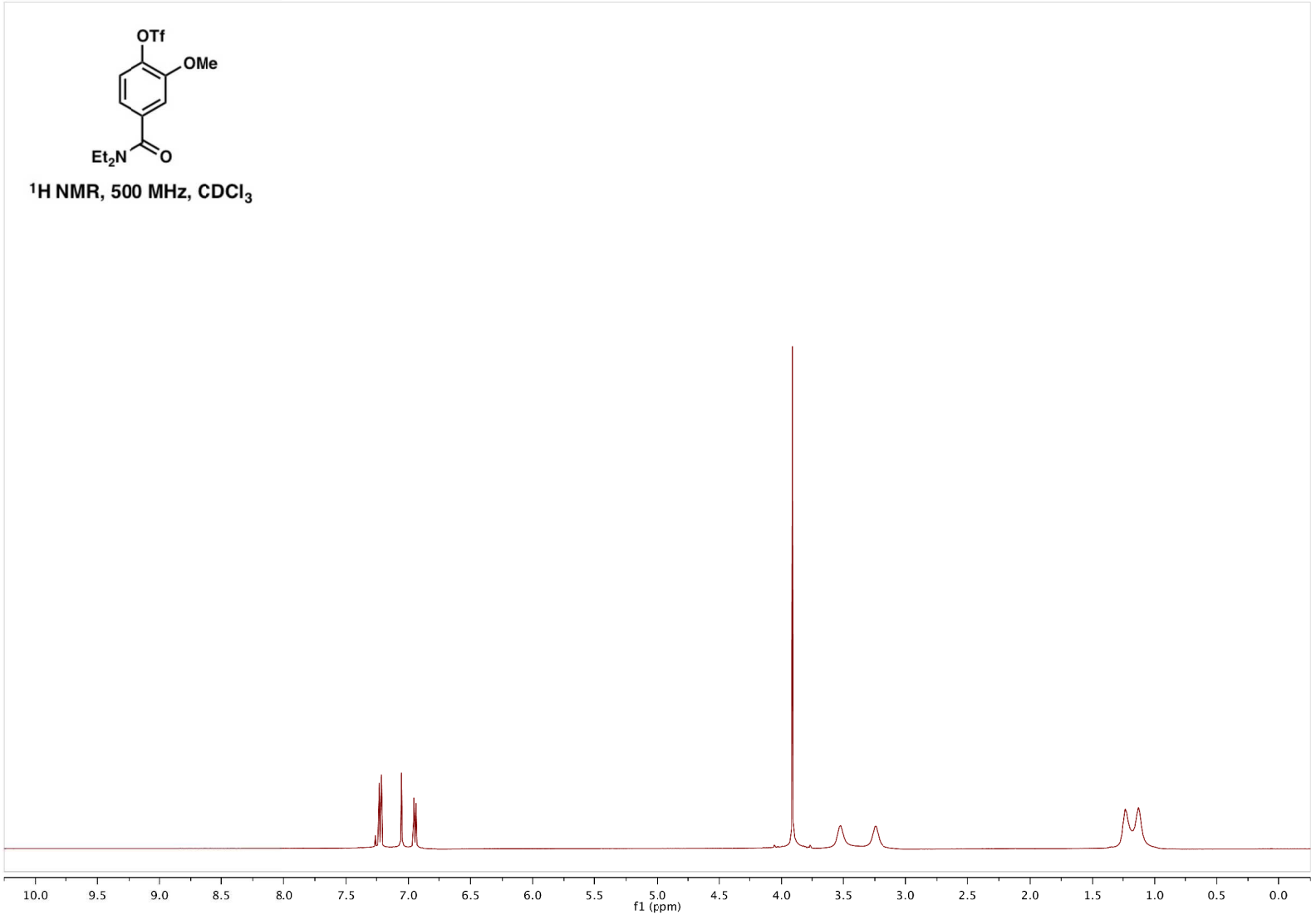
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OTf
CO2Me
13C NMR, 125 MHz, CDCl3
f1 (ppm)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OMe
Et2N
O
1H NMR, 500 MHz, CDCl3
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9.5
9.0
8.5
8.0
7.5
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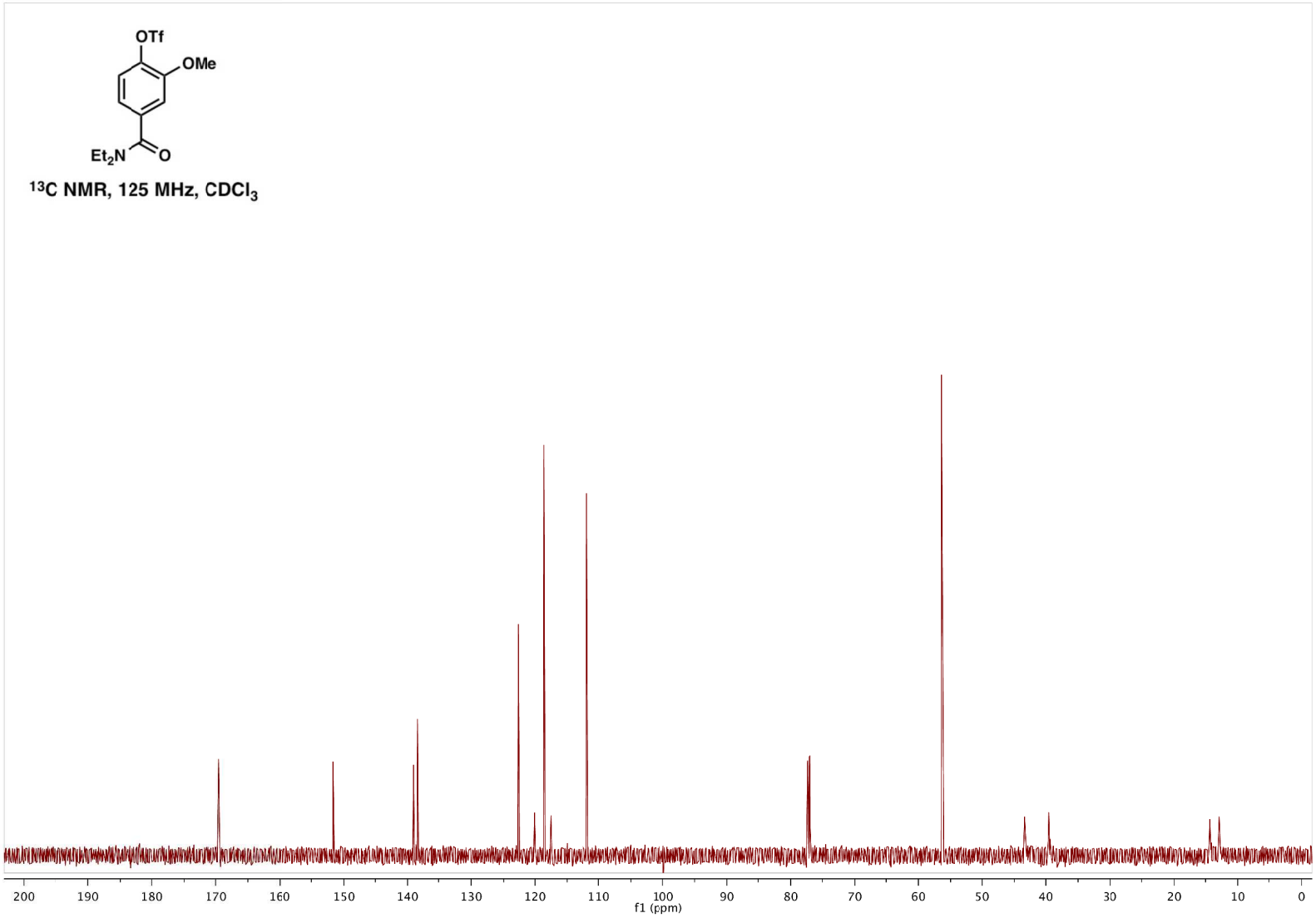
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OTf
OMe
Et2N
O
13C NMR, 125 MHz, CDCl3
200
190
180
170
160
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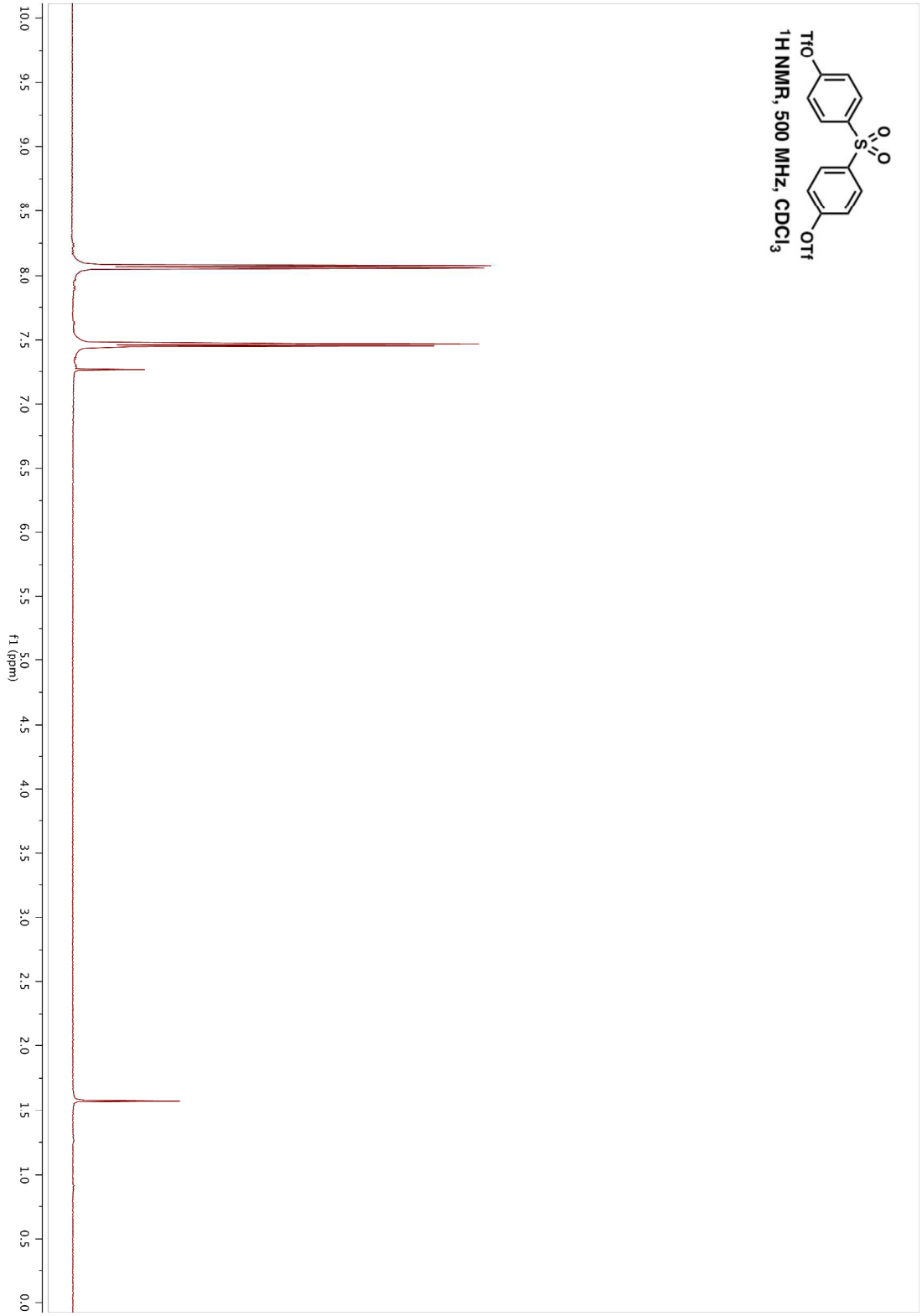
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


TfO
OTf
O
O
S
1H NMR, 500 MHz, CDCl3
f1 (ppm)
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9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
3.0
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2.0
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1.0
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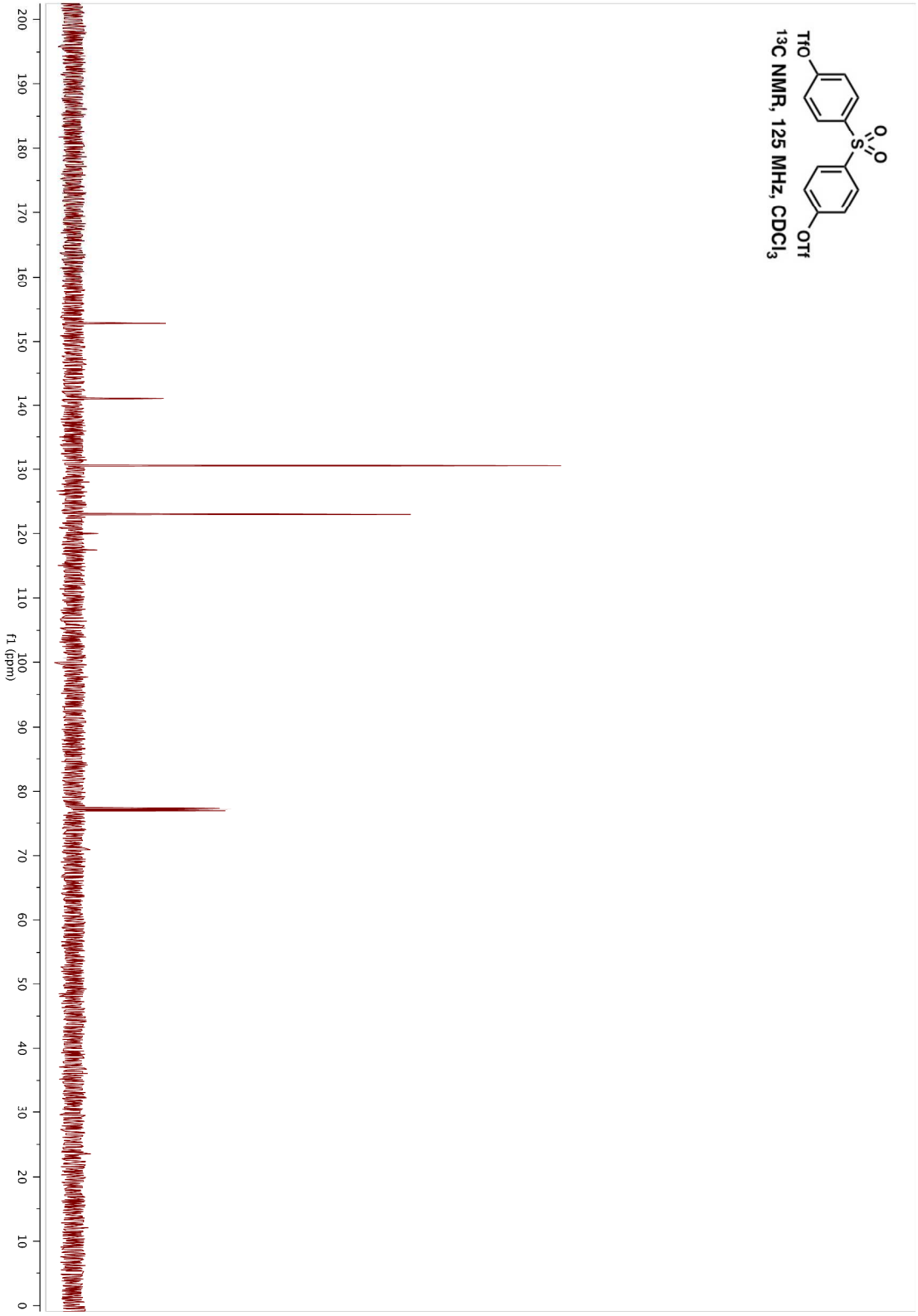
0.0


TfO
OTf
^{13}C NMR, 125 MHz, CDCl$_3$
f1 (ppm)
200
190
180
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120
110
100
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80
70
60
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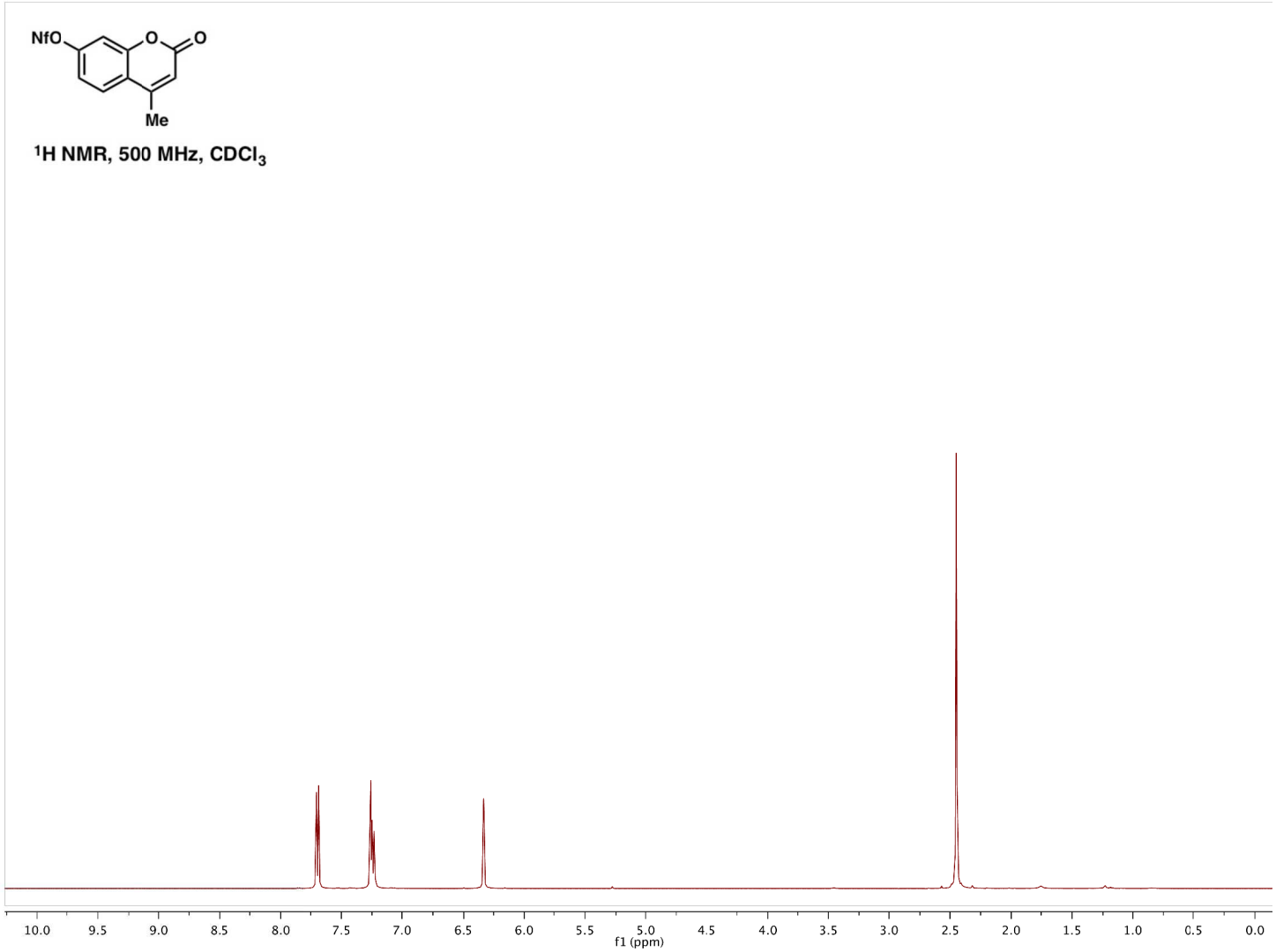
30
20
10
0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O
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Me
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6.5
6.0
5.5
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1.0
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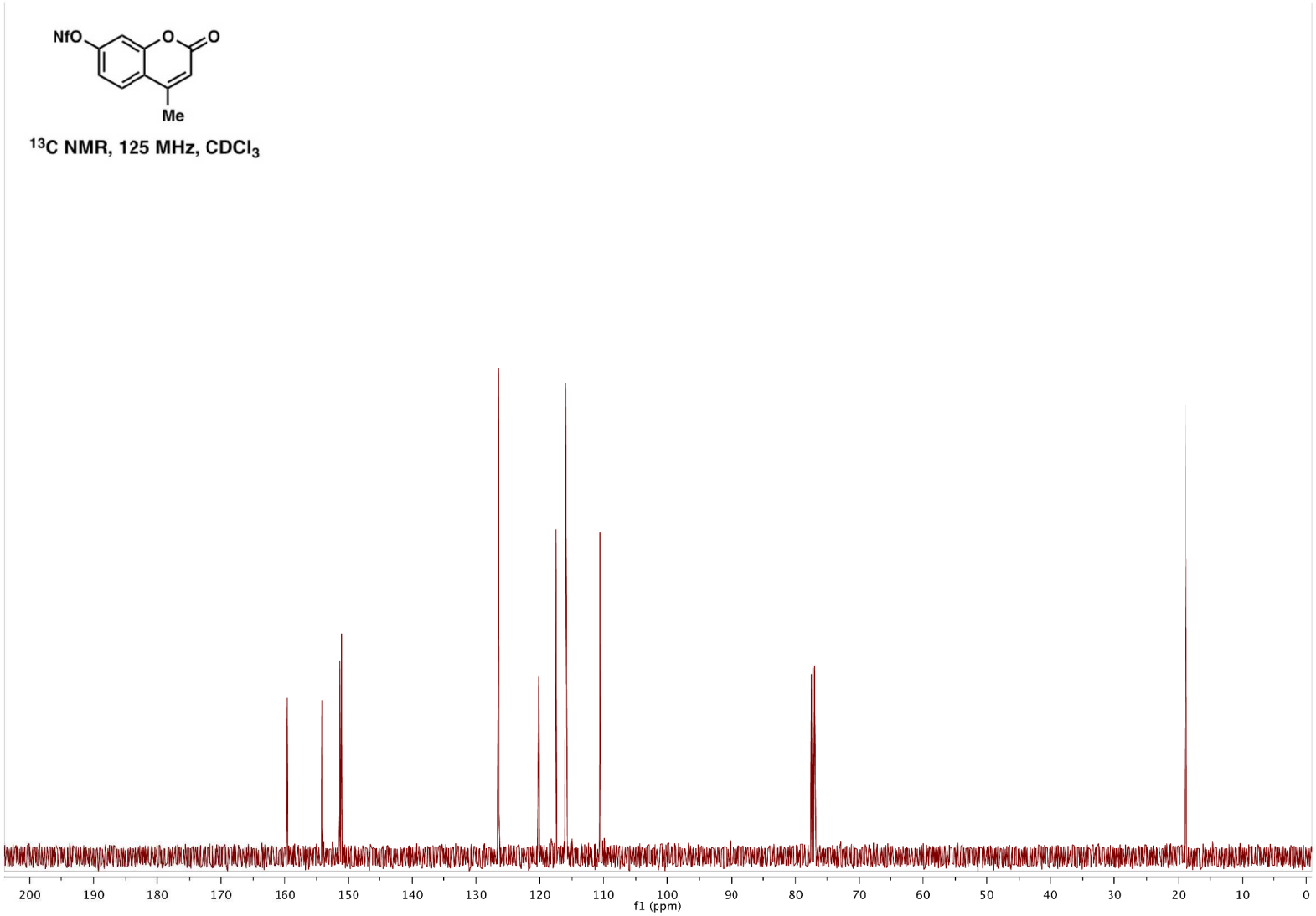
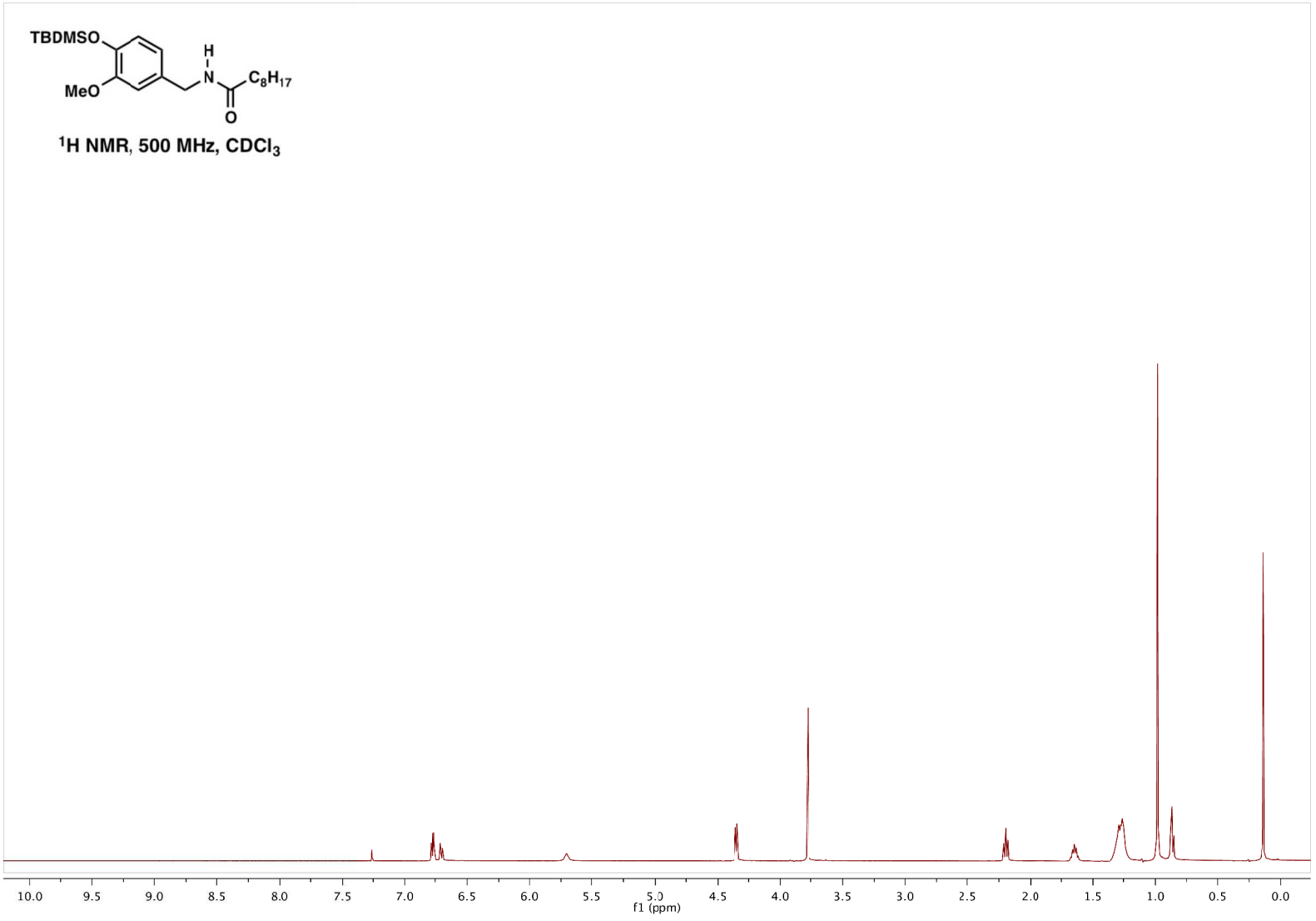
0.0
f1 (ppm)


NfO
O
O
Me
^{13}C NMR, 125 MHz, CDCl$_3$
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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MeO
H
N
O
C_8H_{17}
^{1}H NMR, 500 MHz, CDCl$_3$
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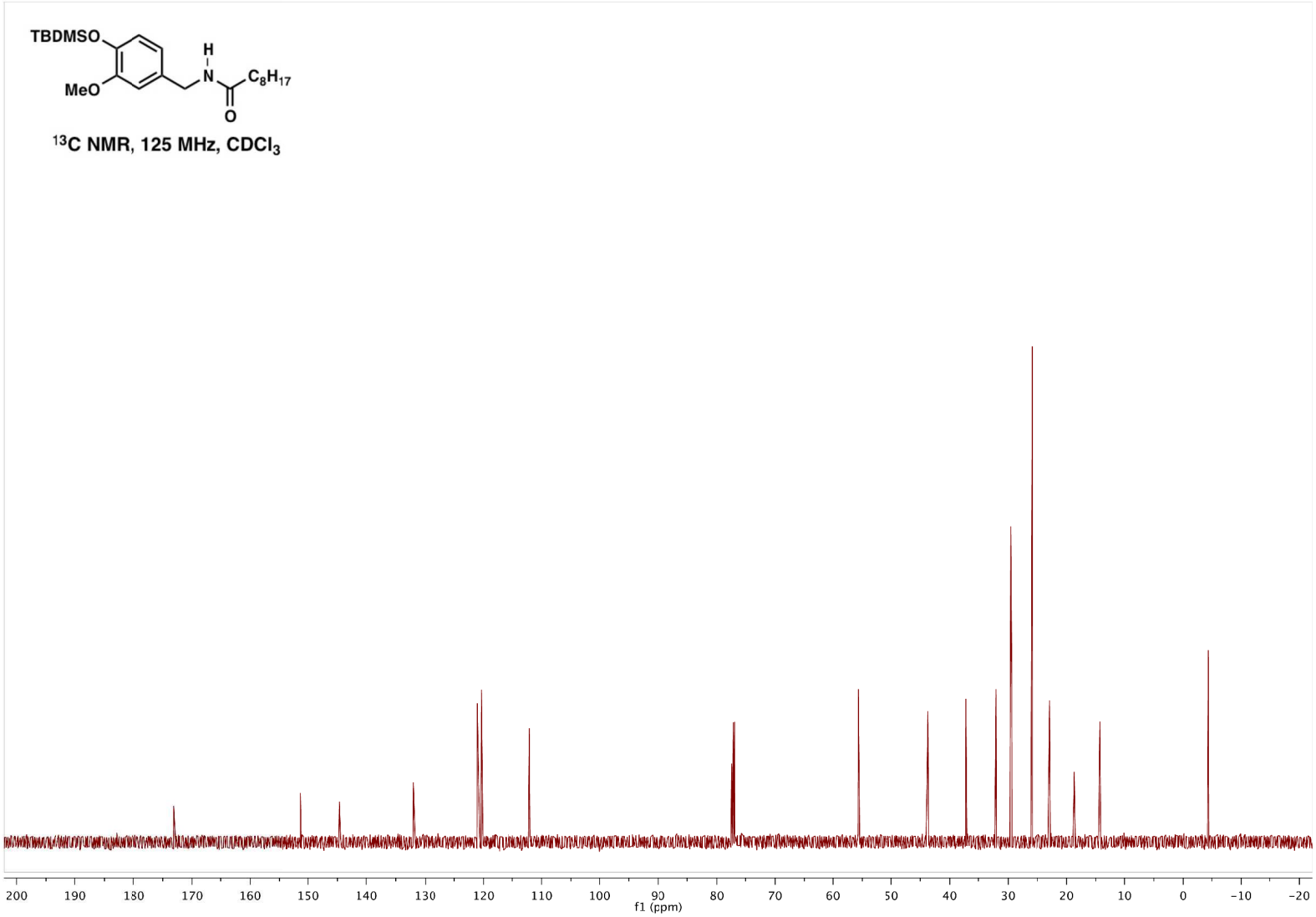
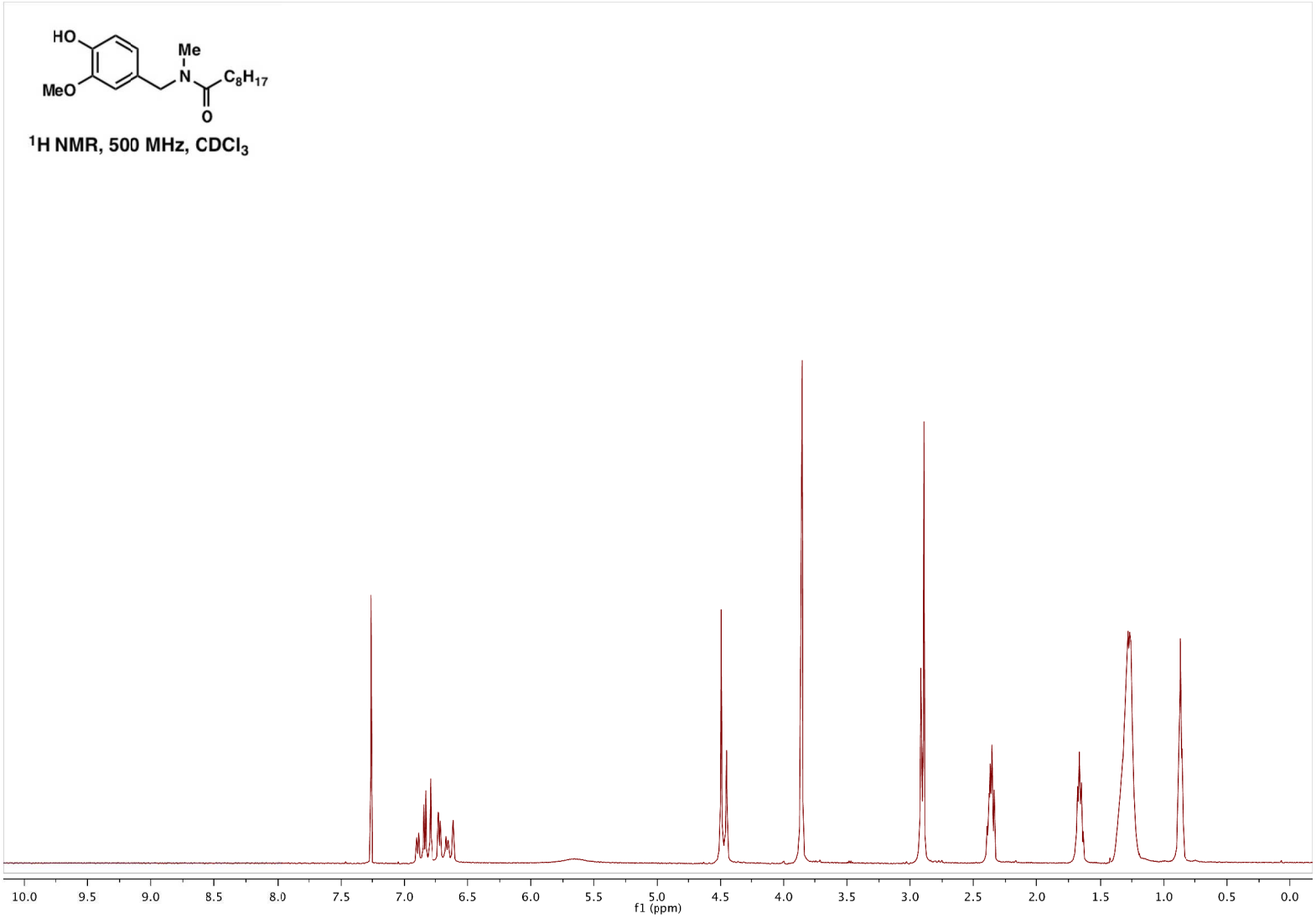
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


TBDMSO
MeO
H
N
O
C_8H_{17}
^{13}C NMR, 125 MHz, $CDCl_3$
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
f1 (ppm)


HO
MeO
Me
N
C8H17
O
1H NMR, 500 MHz, CDCl3
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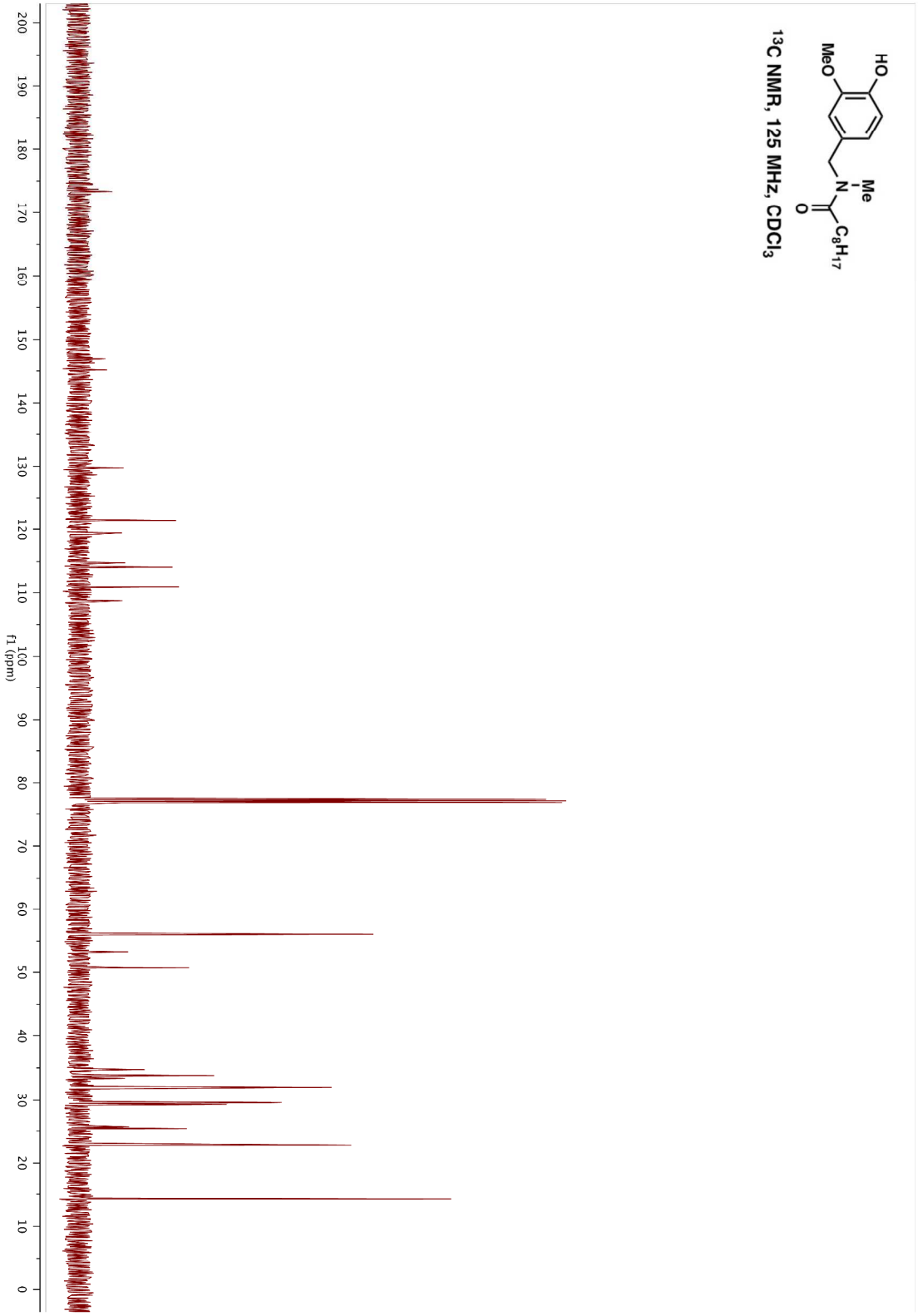
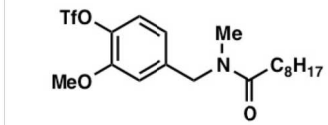
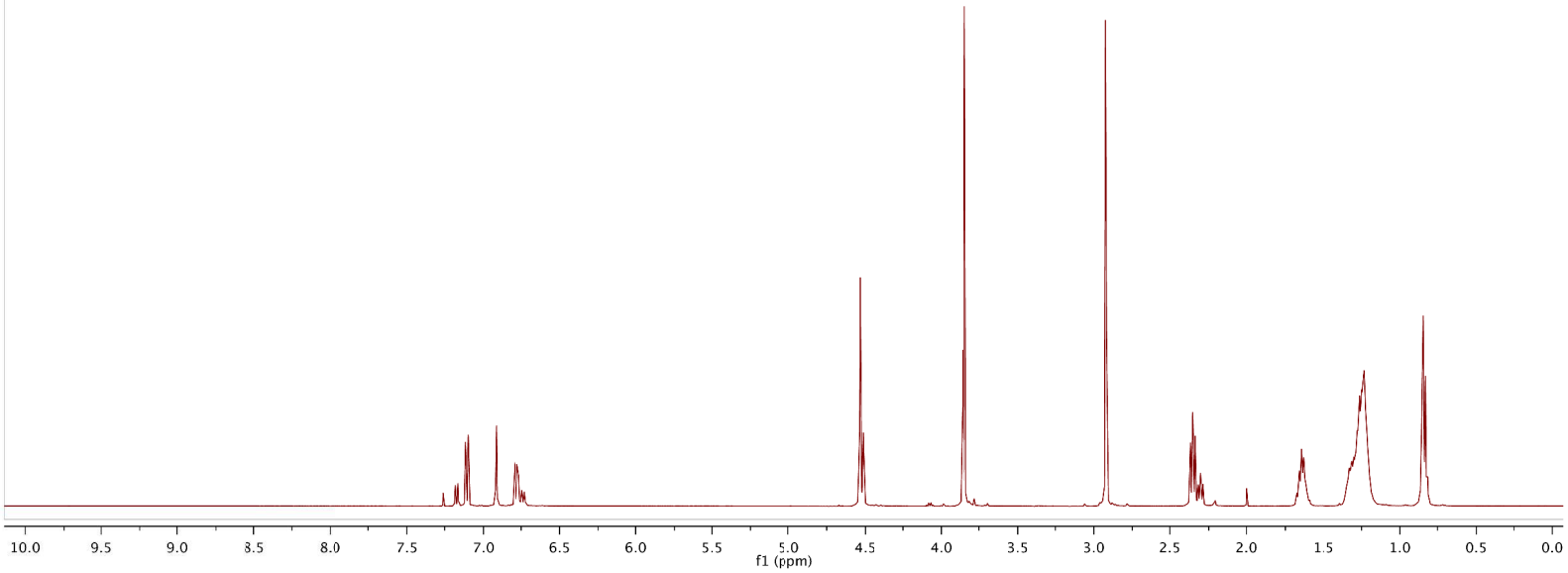
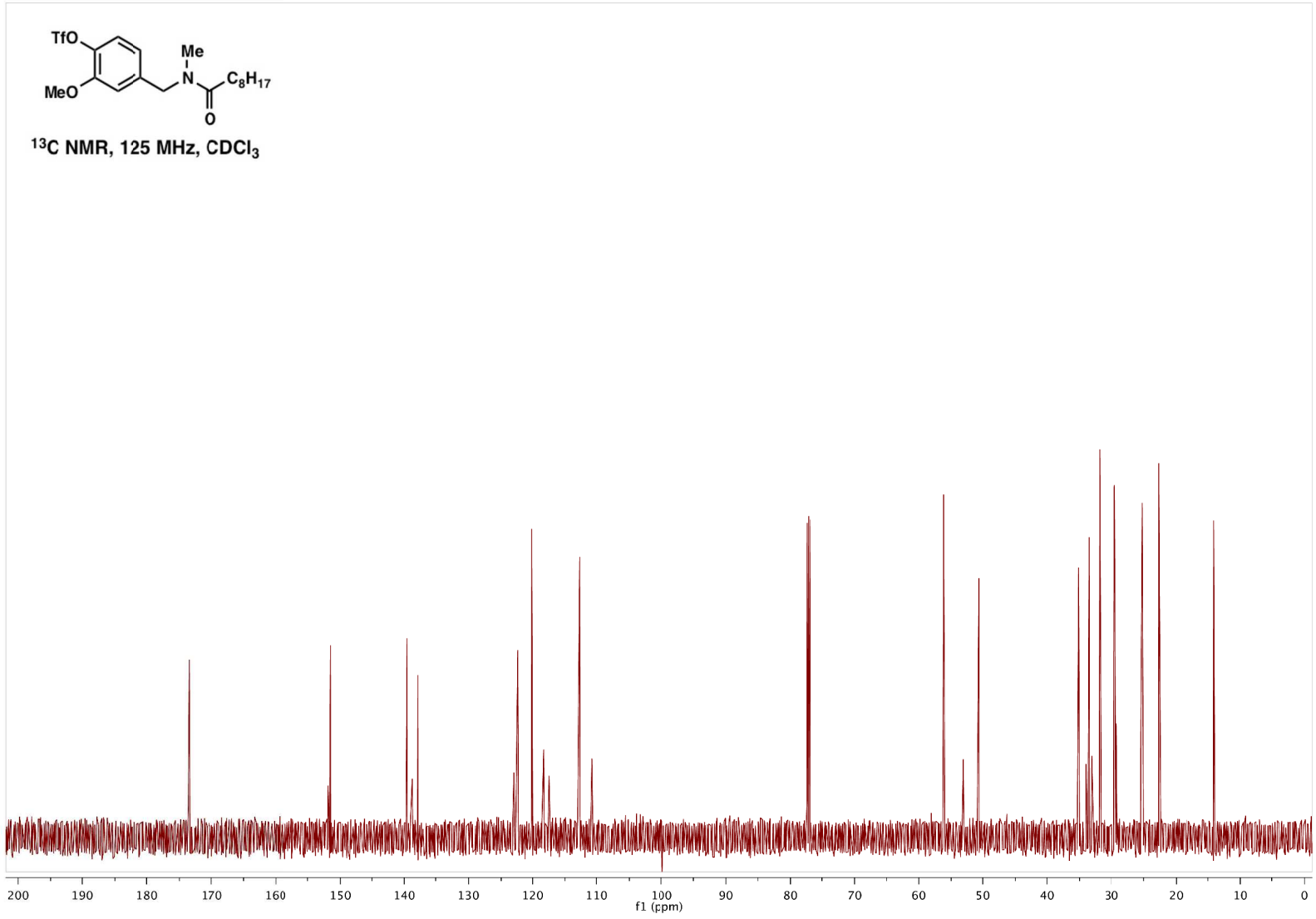
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

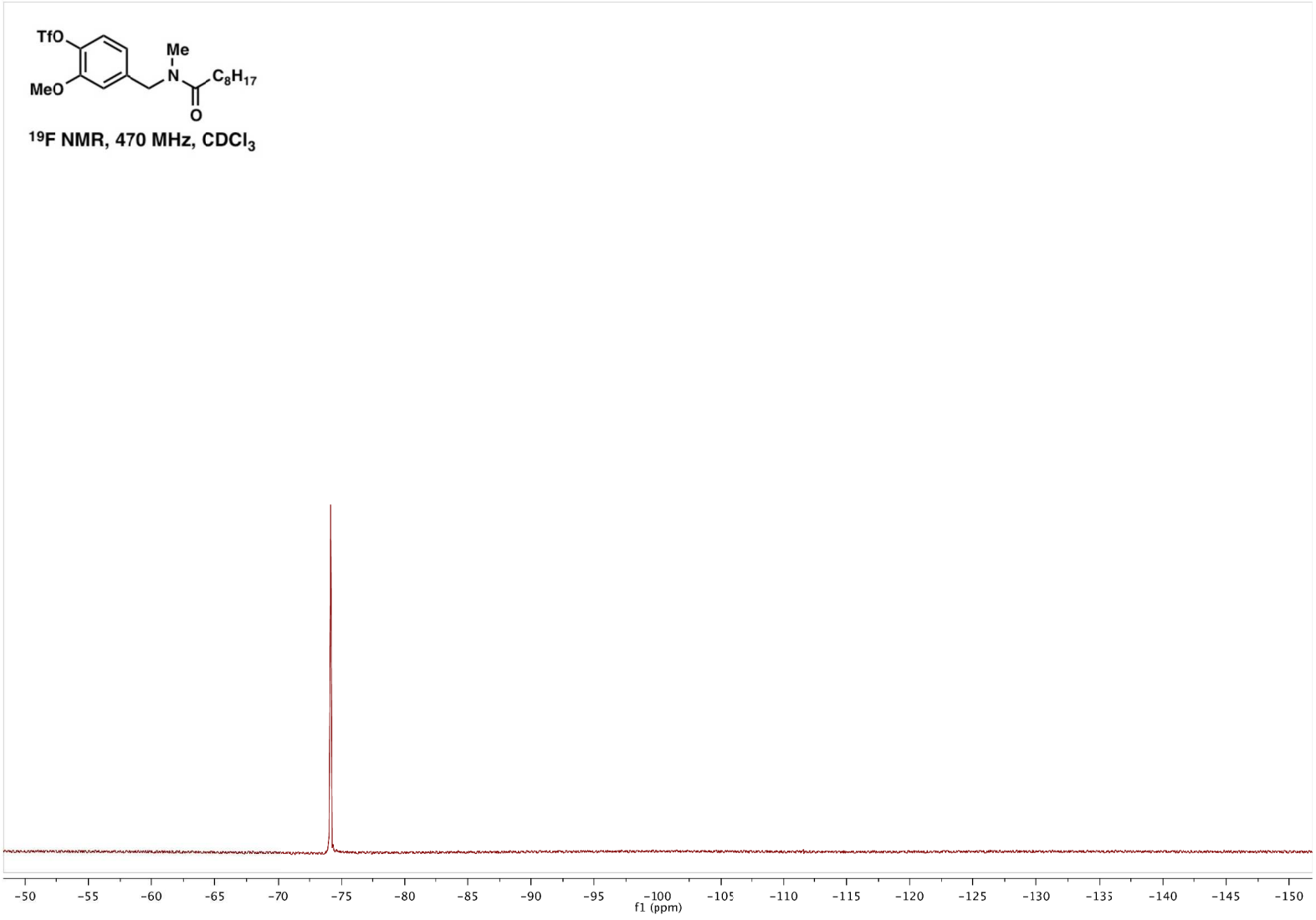

HO
MeO
Me
N
O
C8H17
13C NMR, 125 MHz, CDCl3
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

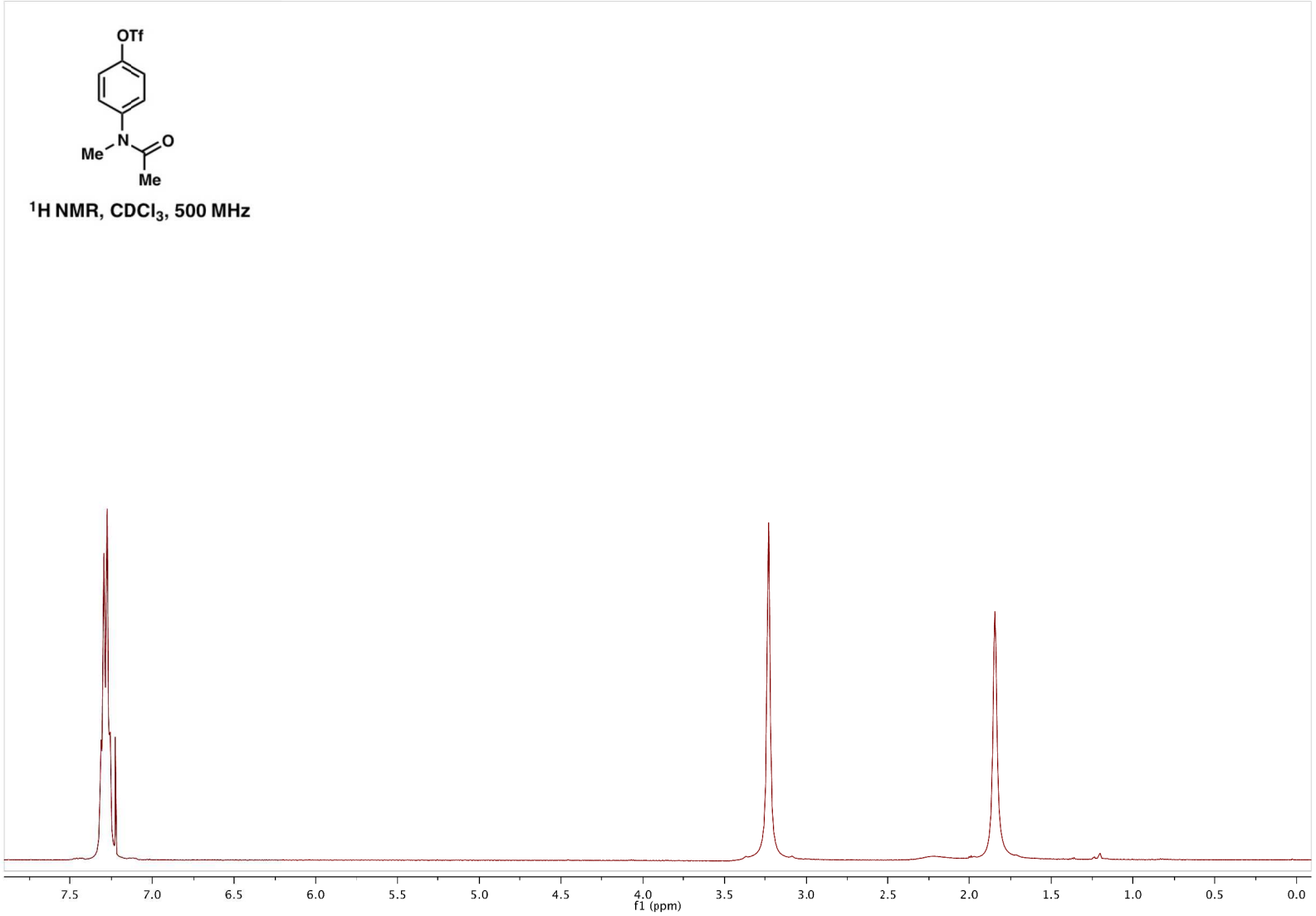


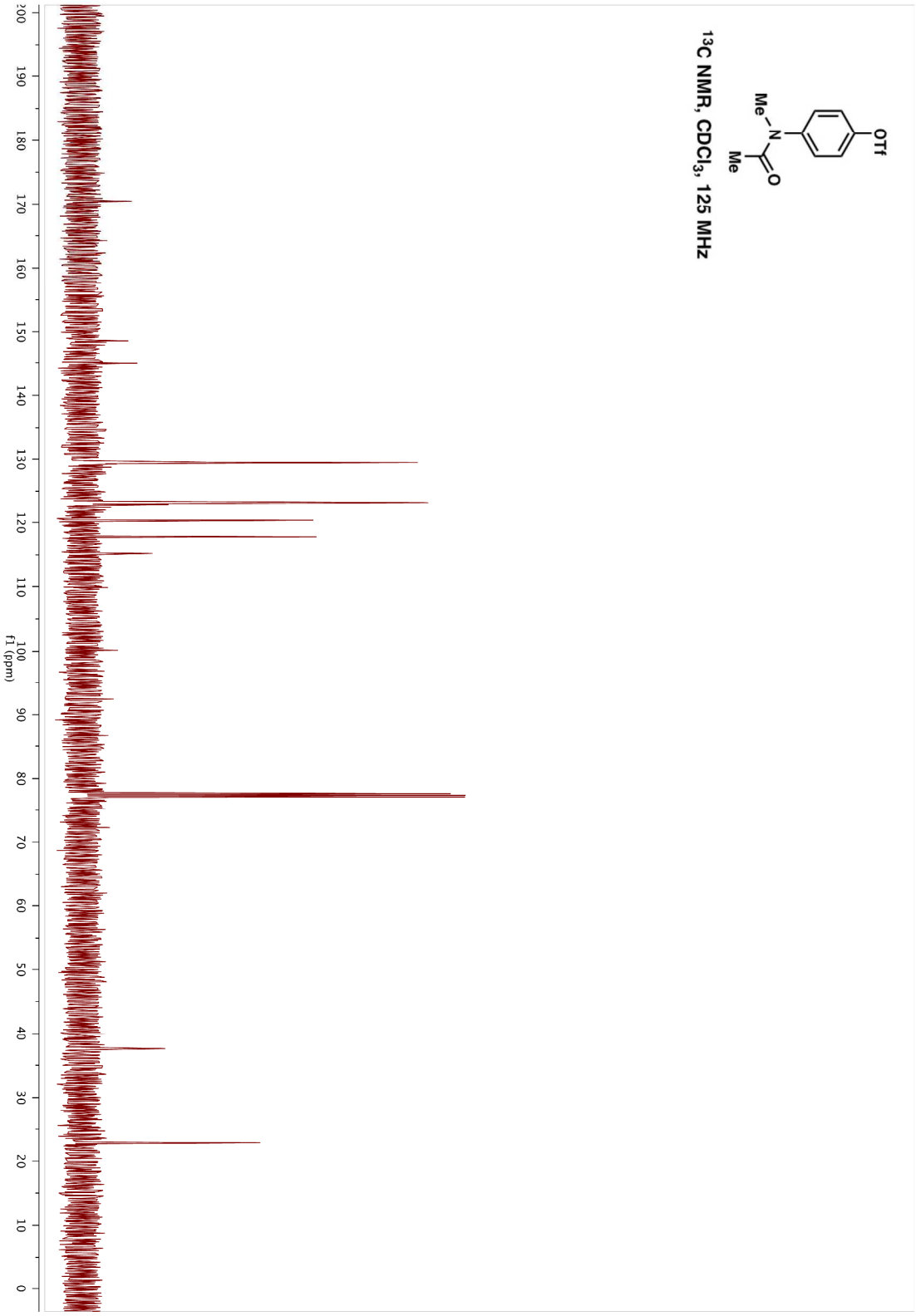
^{1}H NMR, 500 MHz, $CDCl_3$

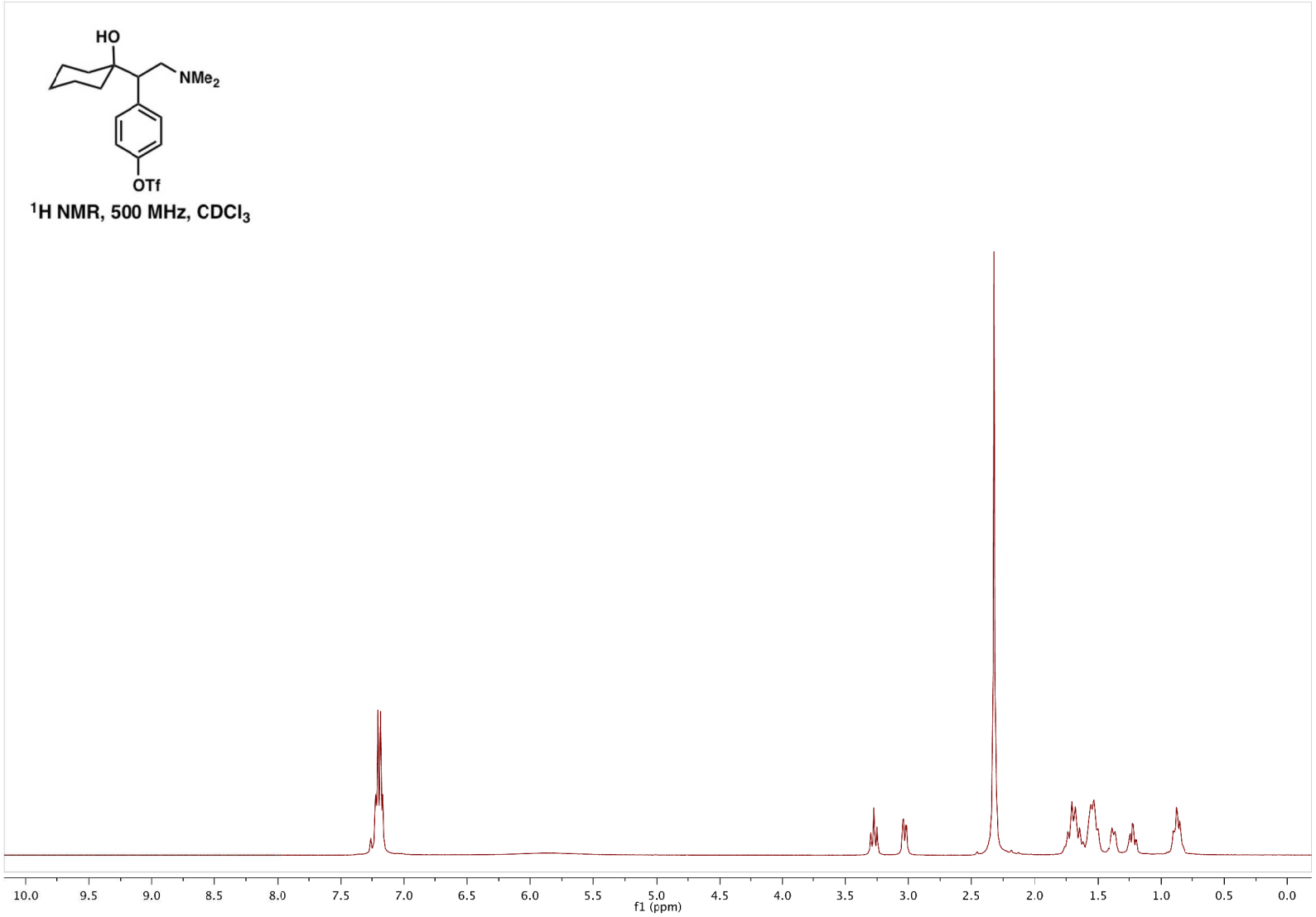


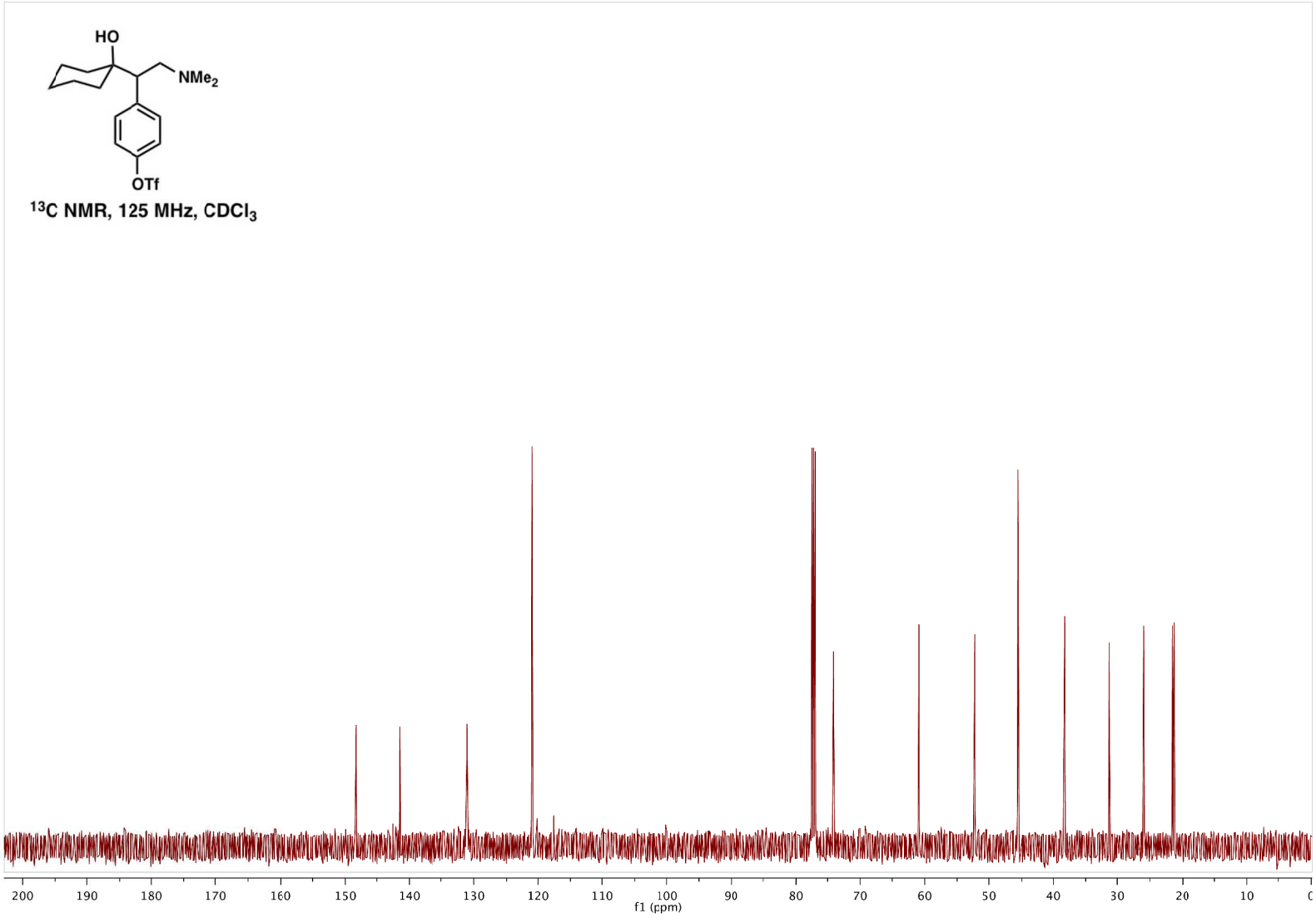

TfO
MeO
Me
N
C8H17
O
13C NMR, 125 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

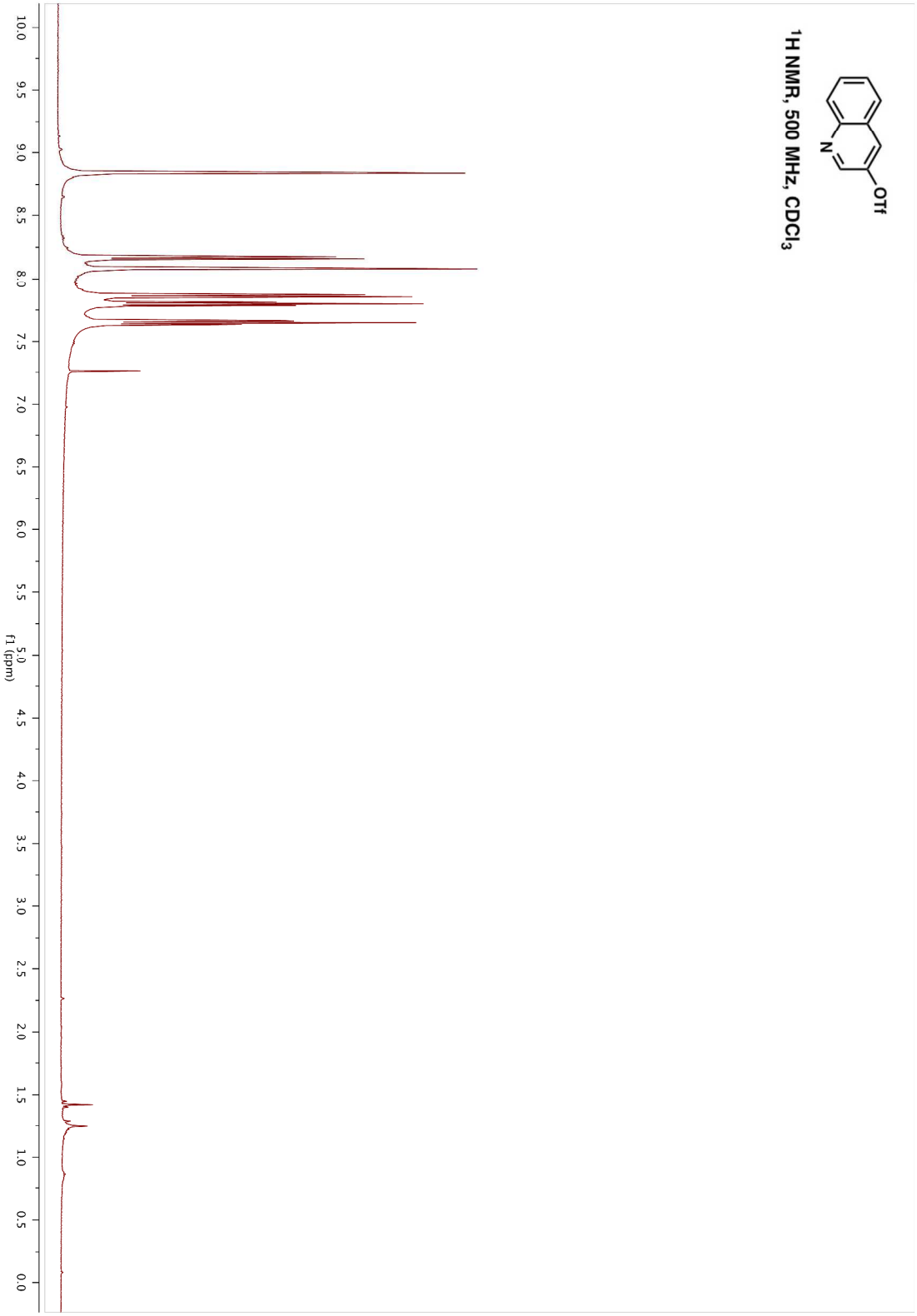

TfO
MeO
Me
N
C8H17
O
19F NMR, 470 MHz, CDCl3
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
f1 (ppm)

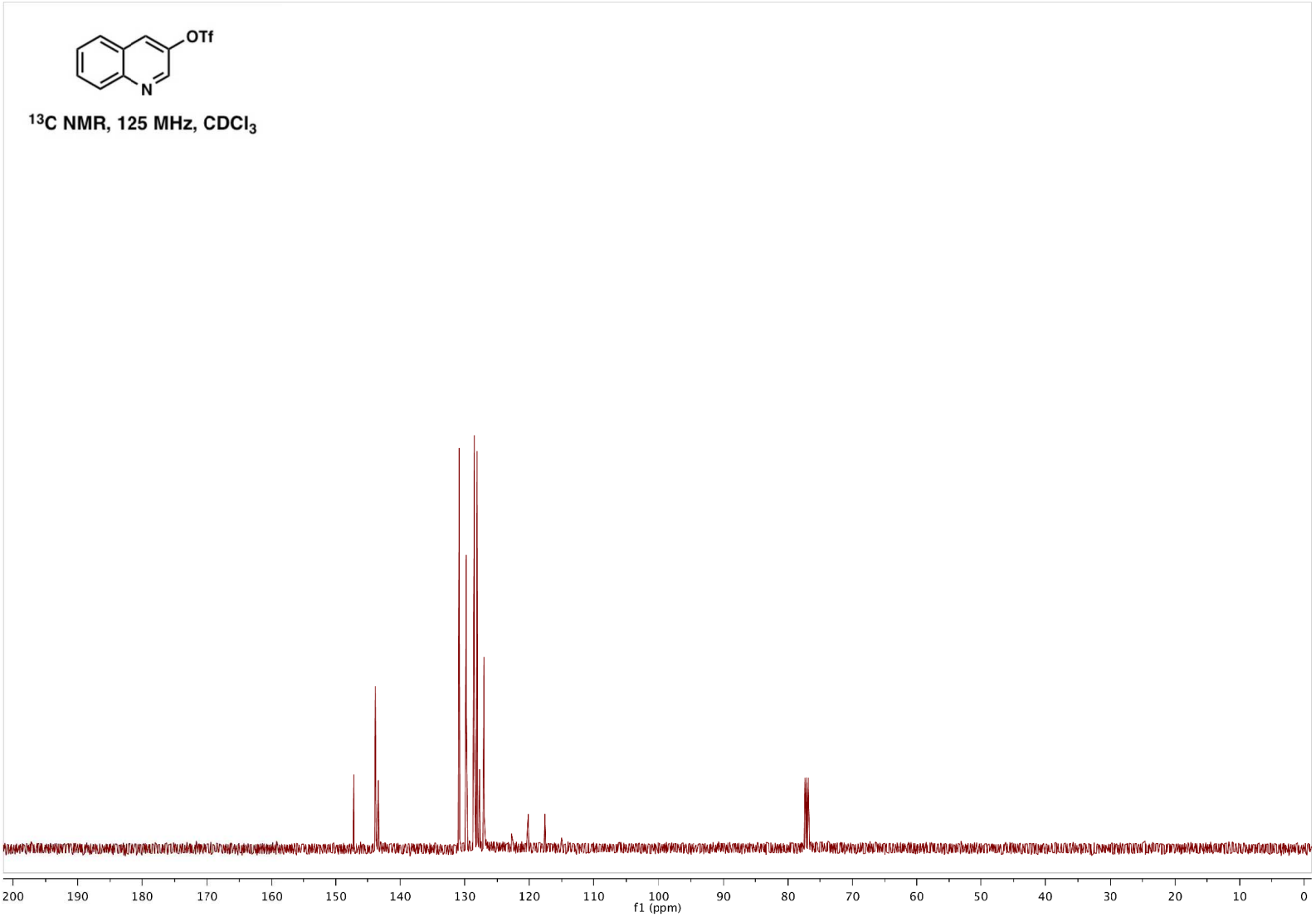

OTf
Me
N
O
Me
^{1}H NMR, $CDCl_3$, 500 MHz
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
f1 (ppm)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

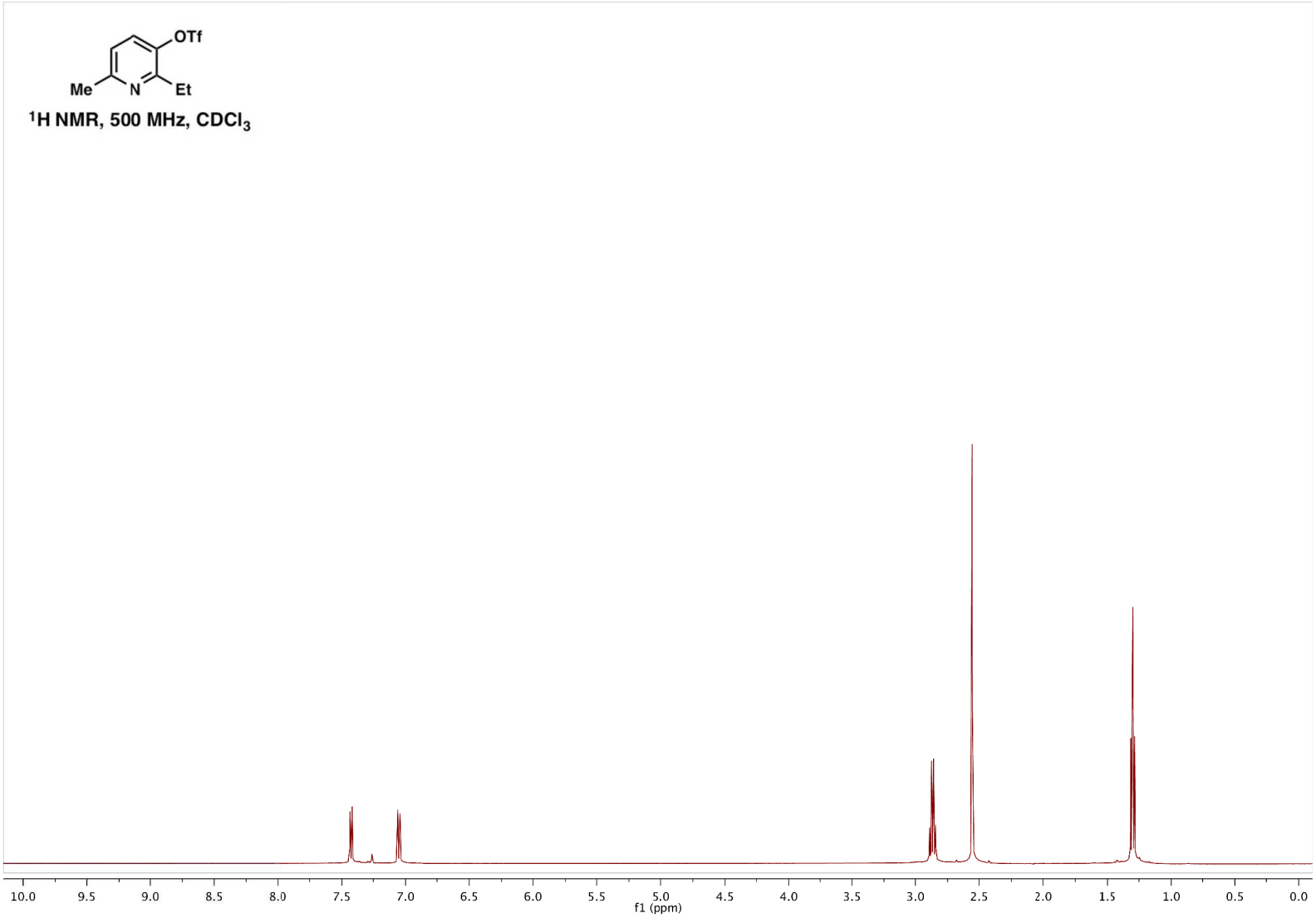

OTf
Me
N
Me
O
^{13}C NMR, $CDCl_3$, 125 MHz
f1 (ppm)

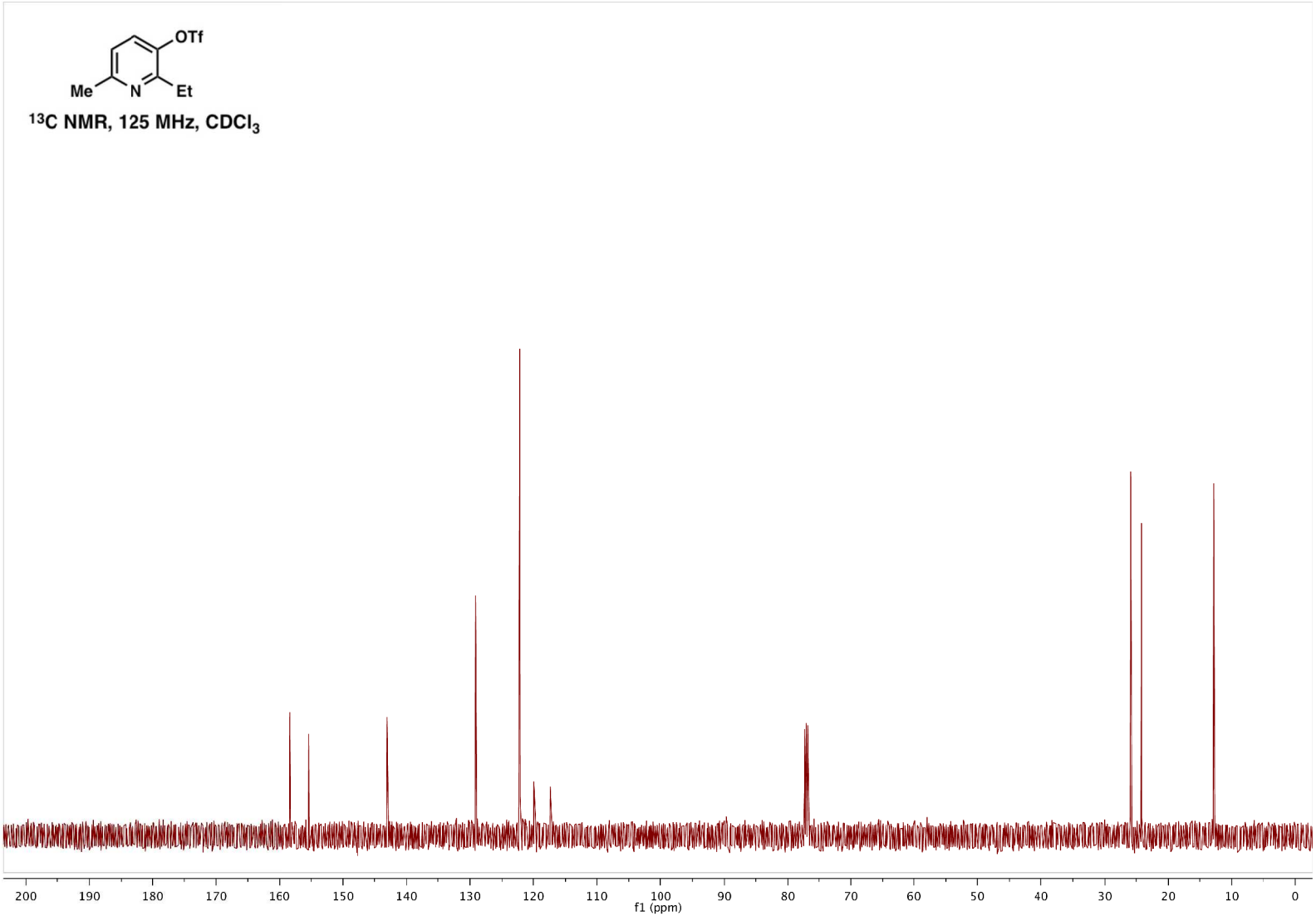

HO
NMe2
OTf
1H NMR, 500 MHz, CDCl3
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

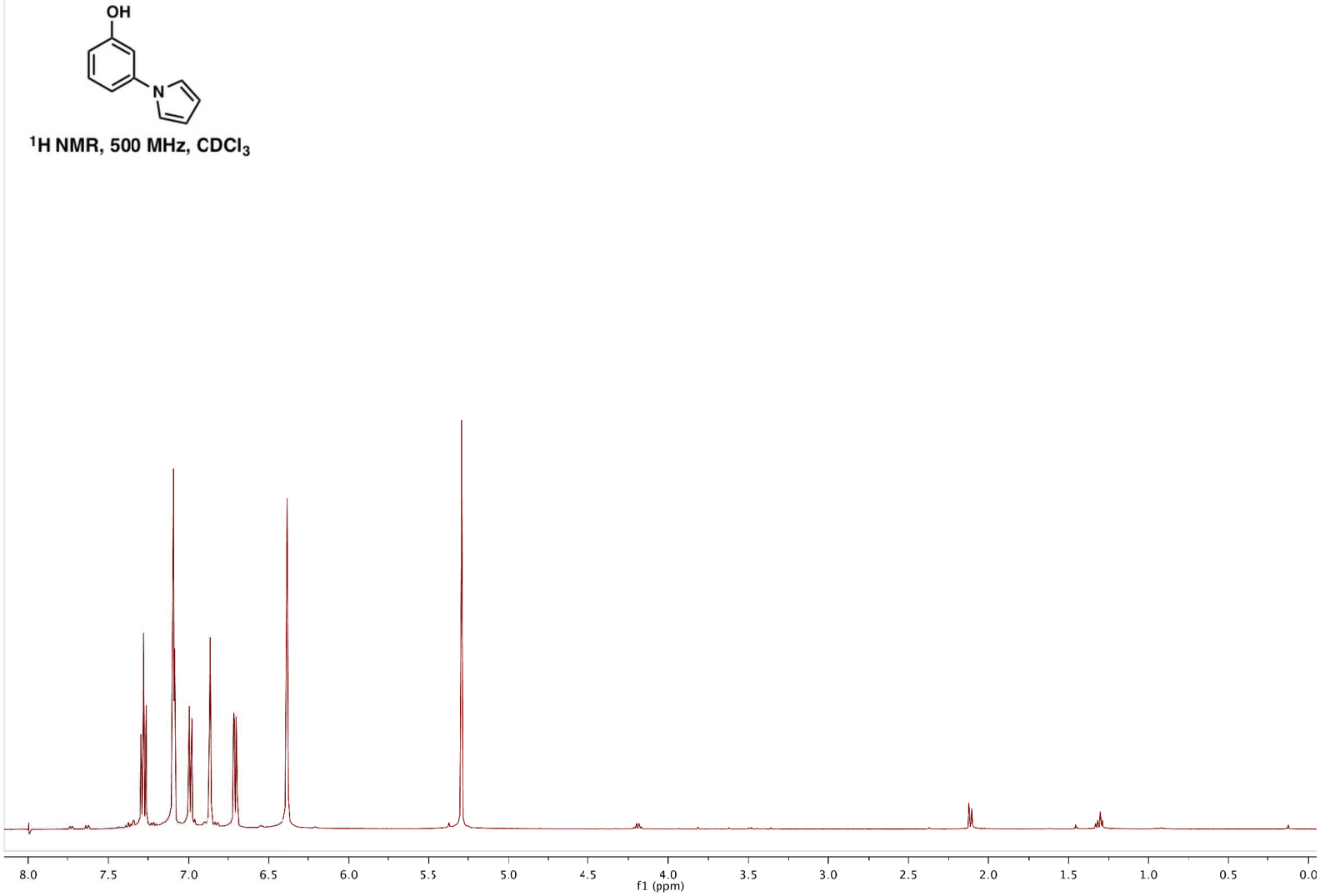

HO
NMe2
OTf
13C NMR, 125 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

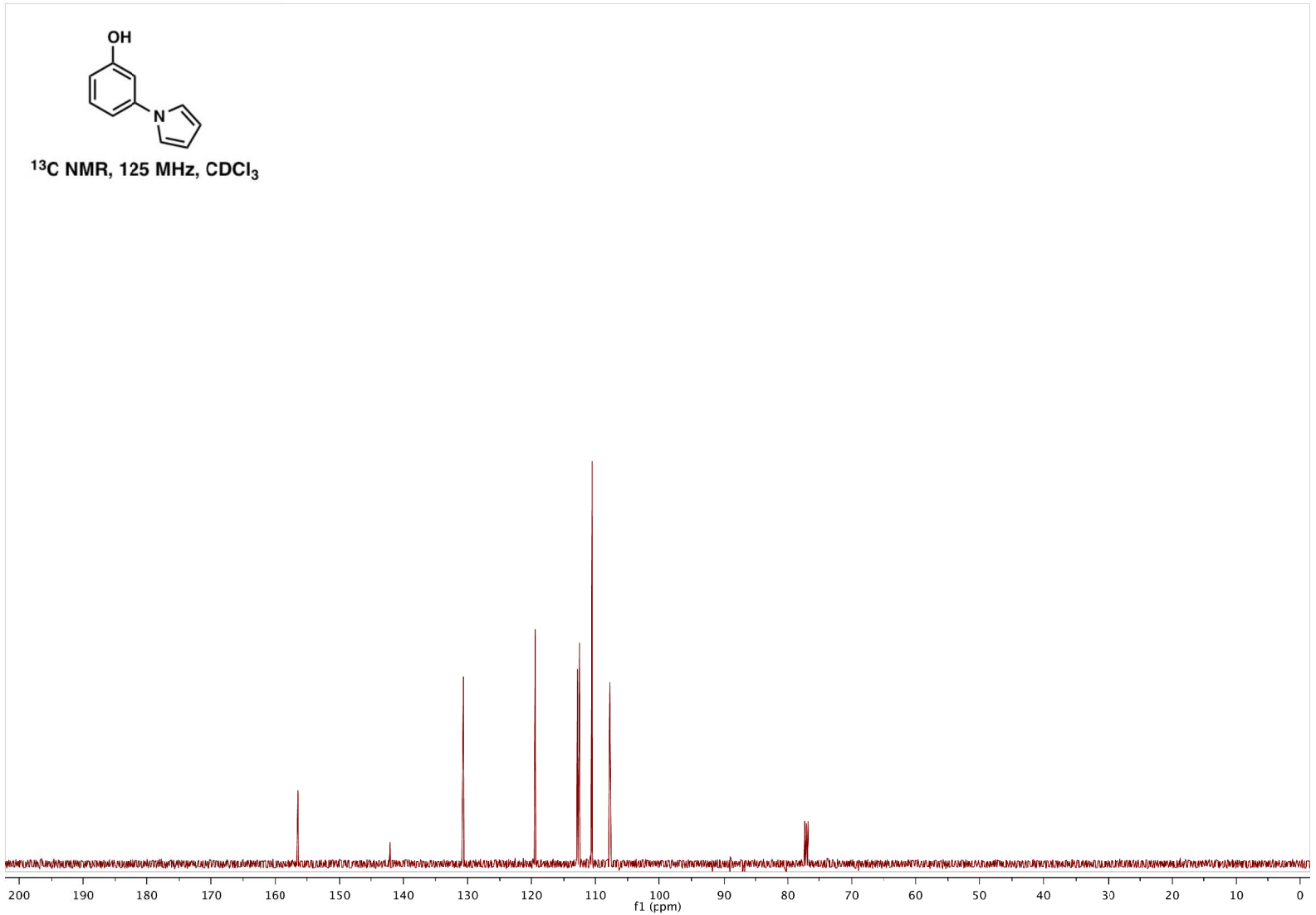

OTf
N
^{1}H NMR, 500 MHz, $CDCl_3$
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

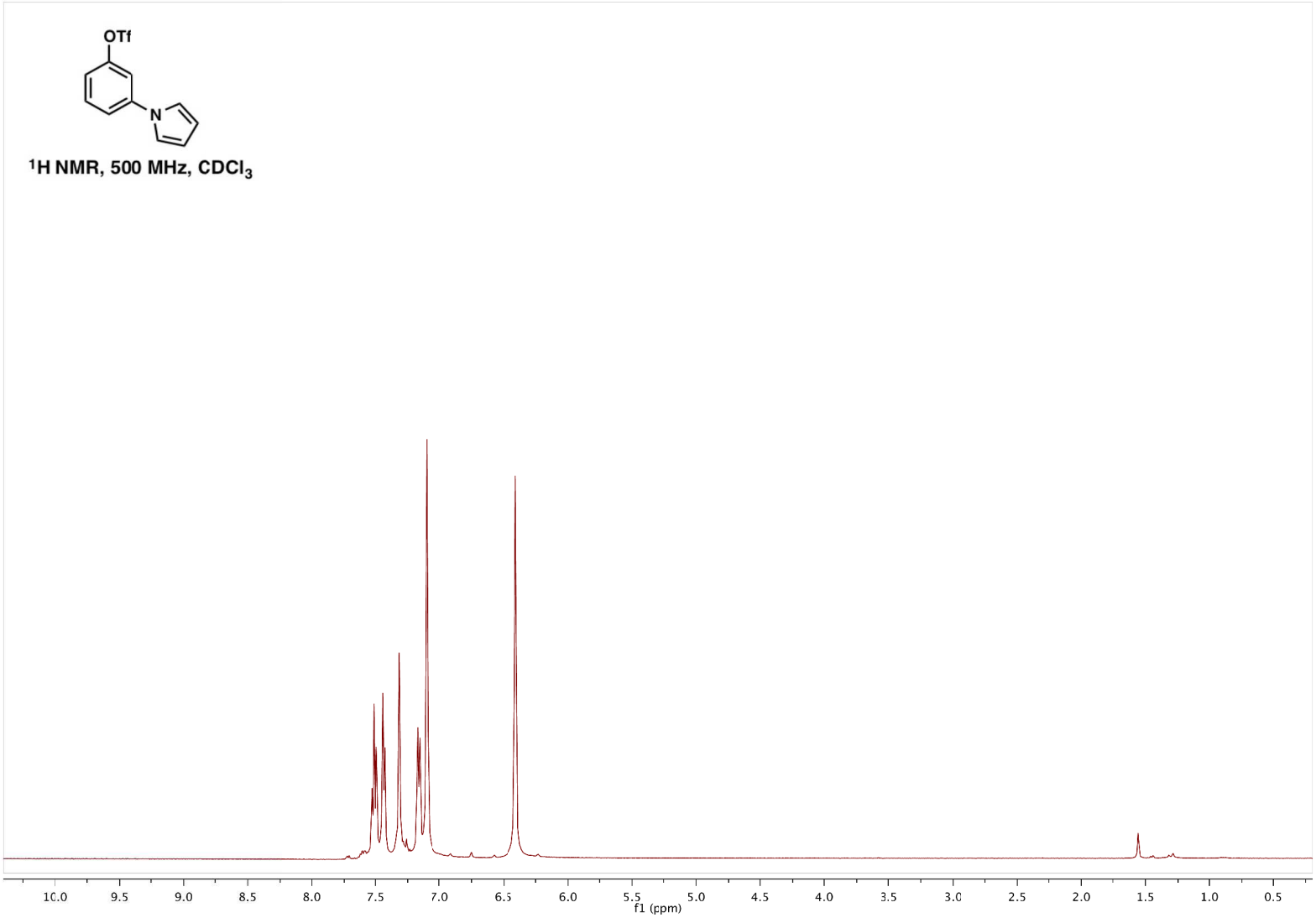

OTf
N
13C NMR, 125 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

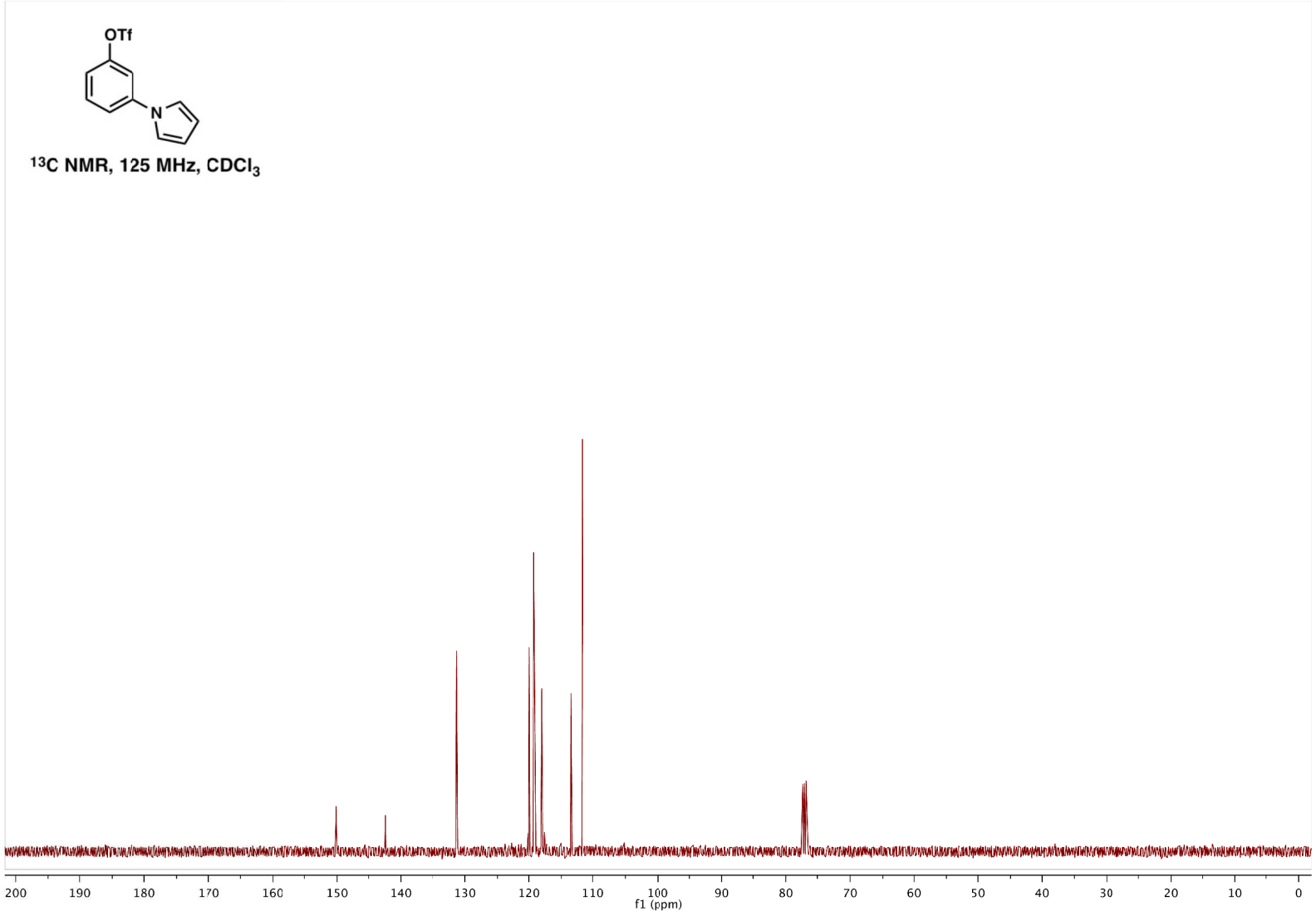

OTf
Me
N
Et
1H NMR, 500 MHz, CDCl3
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

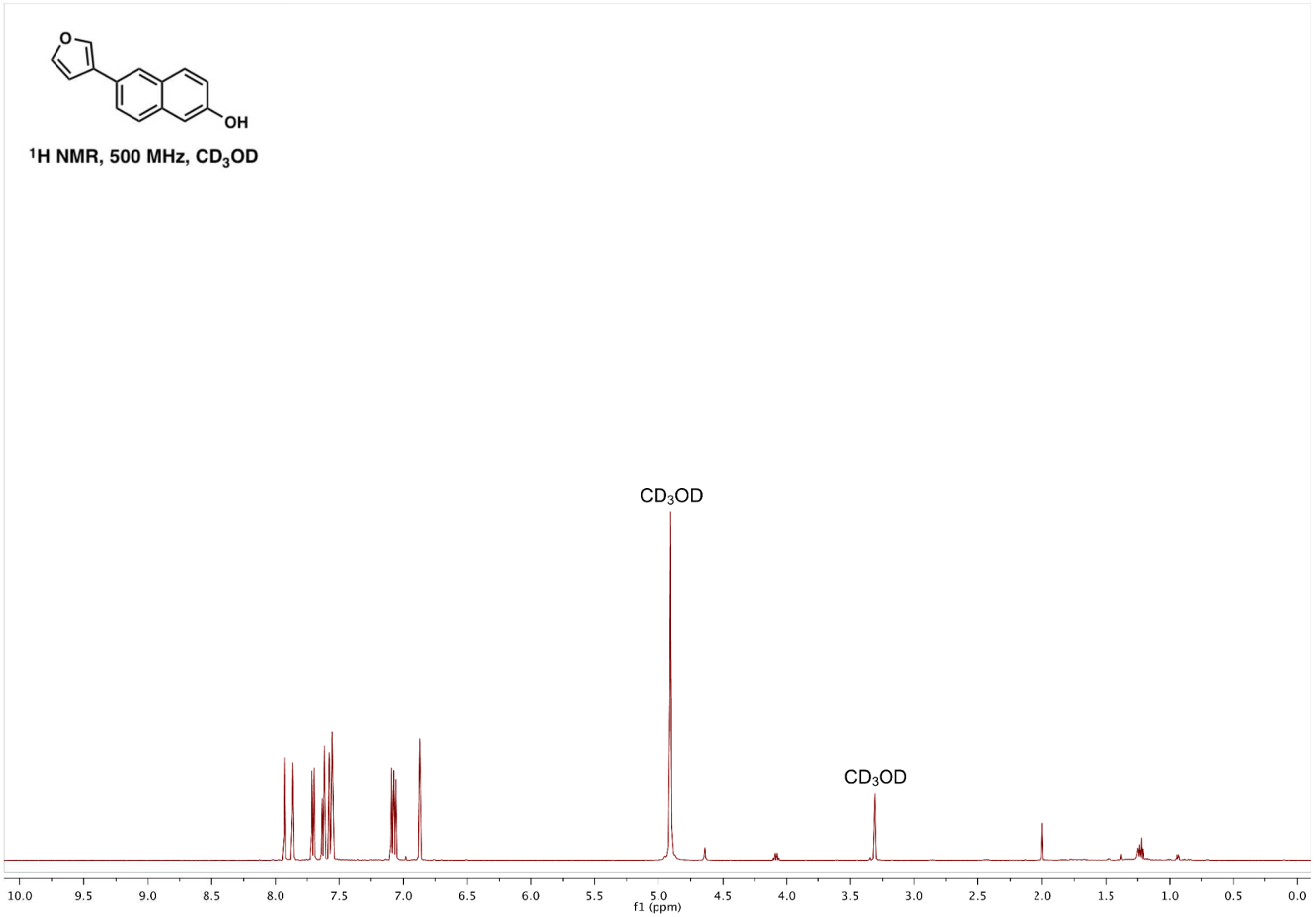

OTf
Me
N
Et
13C NMR, 125 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

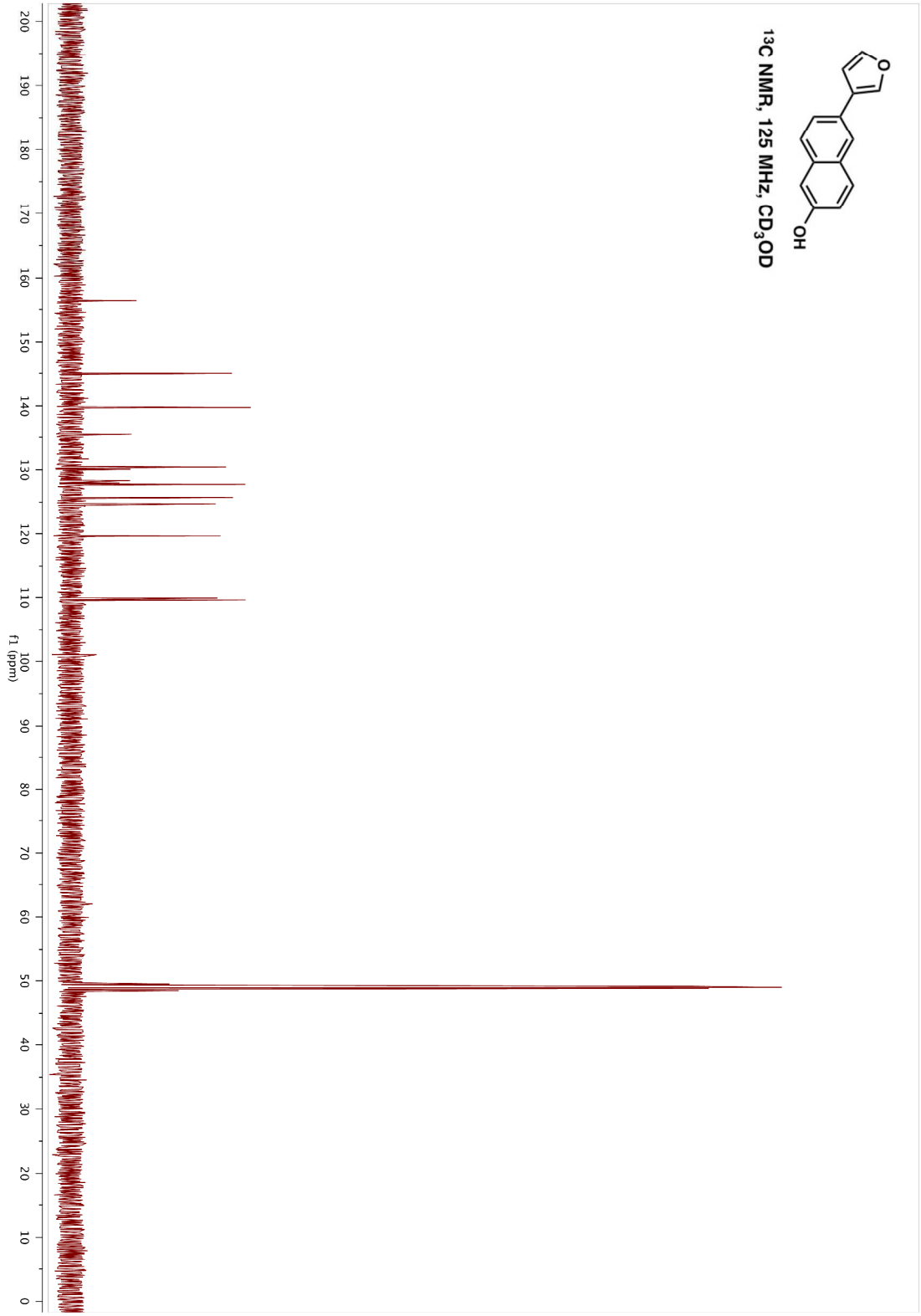

OH
N
^{1}H NMR, 500 MHz, CDCl$_3$
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

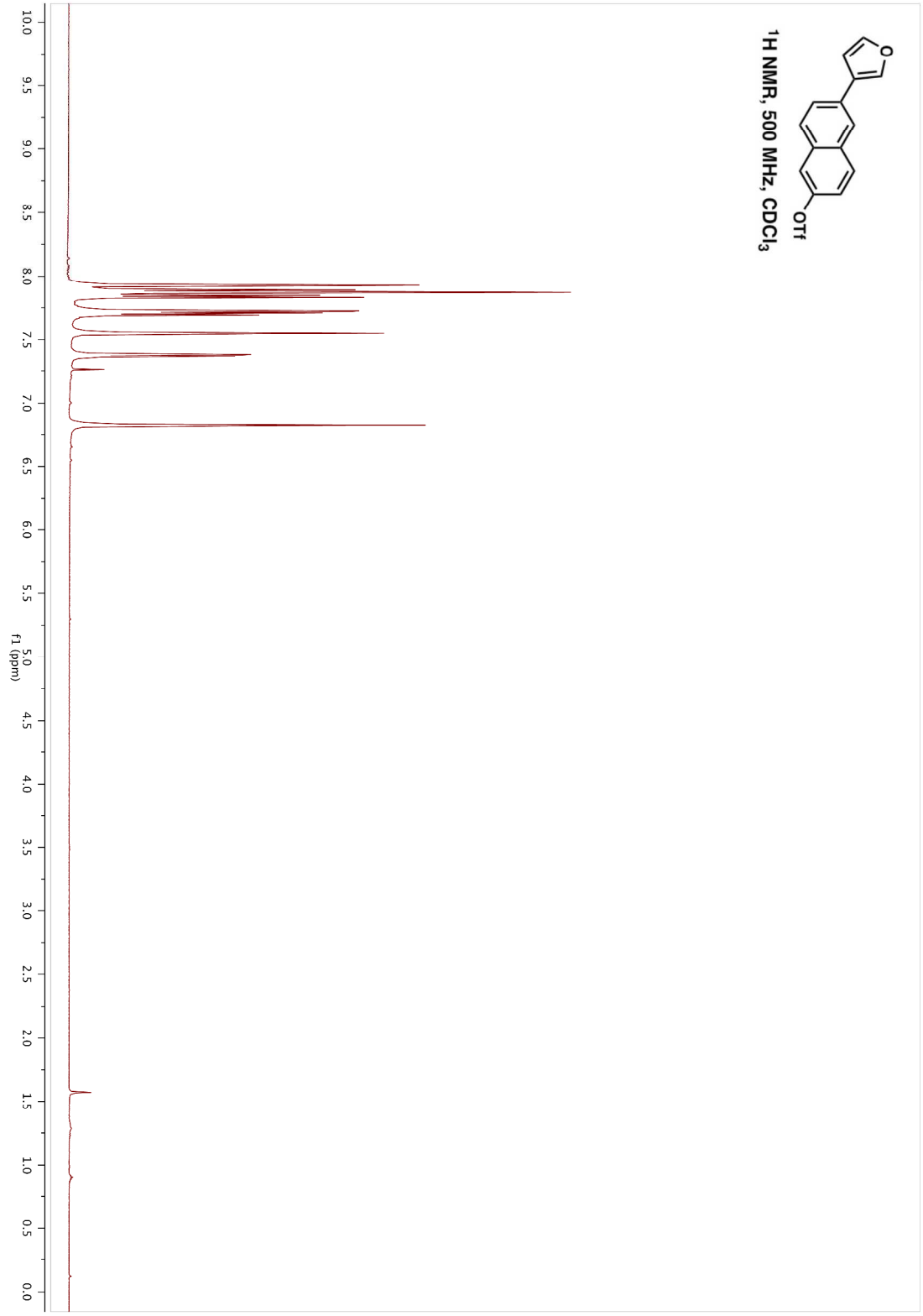

OH
N
^{13}C NMR, 125 MHz, $CDCl_3$
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

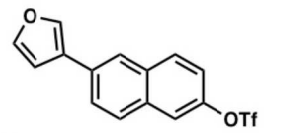

OTf
N
^{1}H NMR, 500 MHz, $CDCl_3$
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


OTf
N
^{13}C NMR, 125 MHz, CDCl$_3$
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

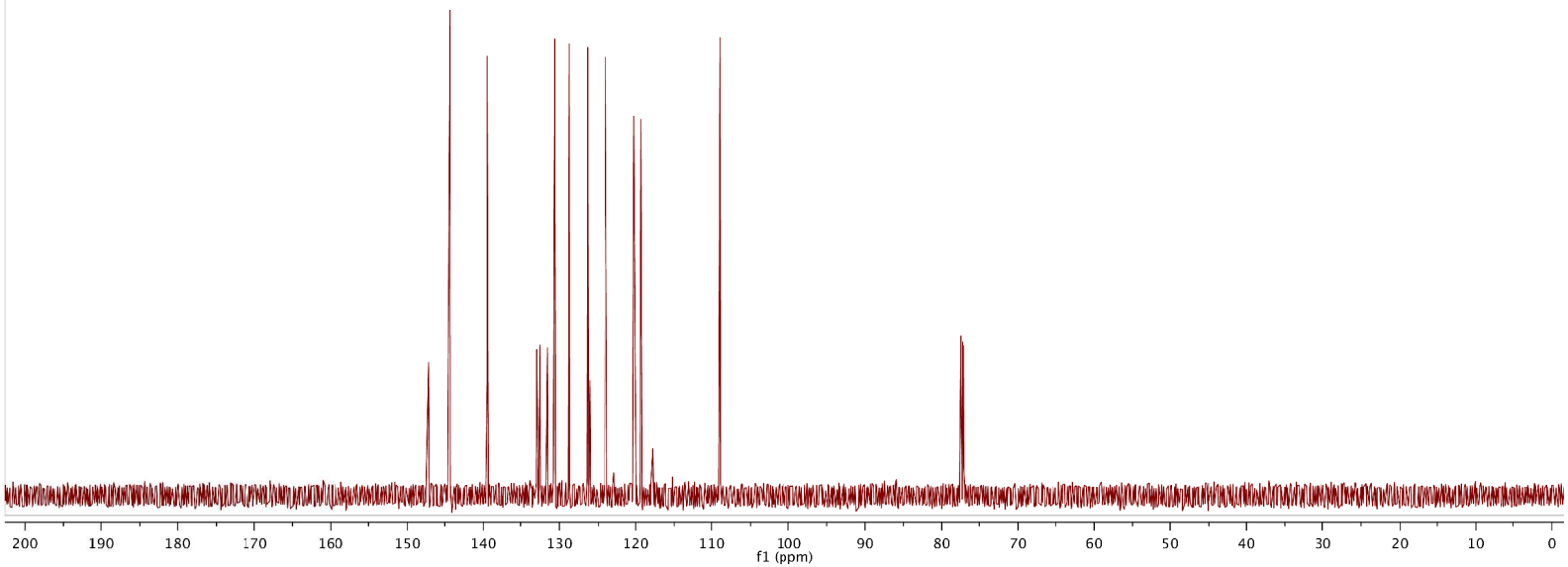

O
OH
^{1}H NMR, 500 MHz, CD_3OD
CD_3OD
CD_3OD
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

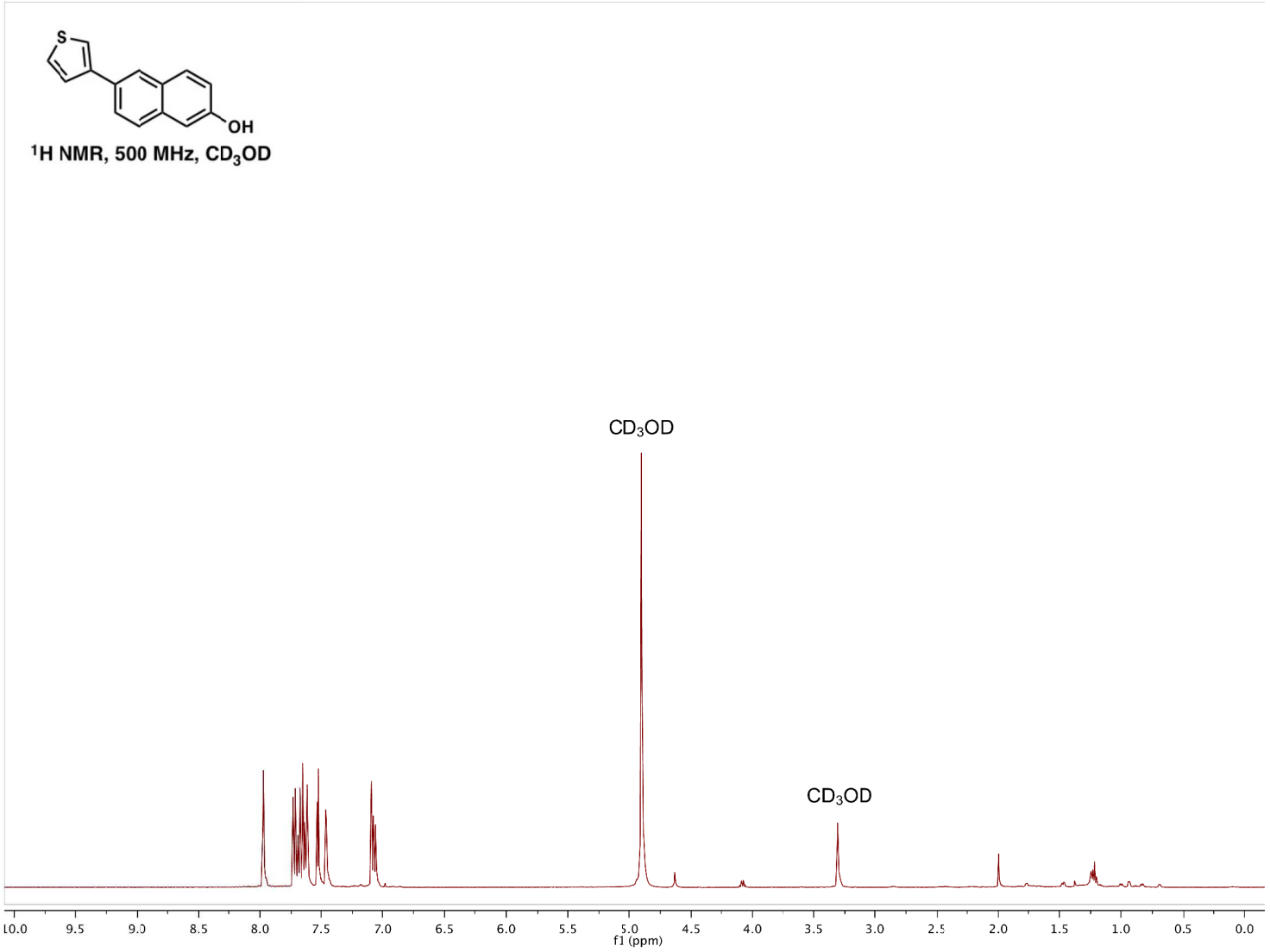

^{13}C NMR, 125 MHz, CD_3OD
OH
O
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

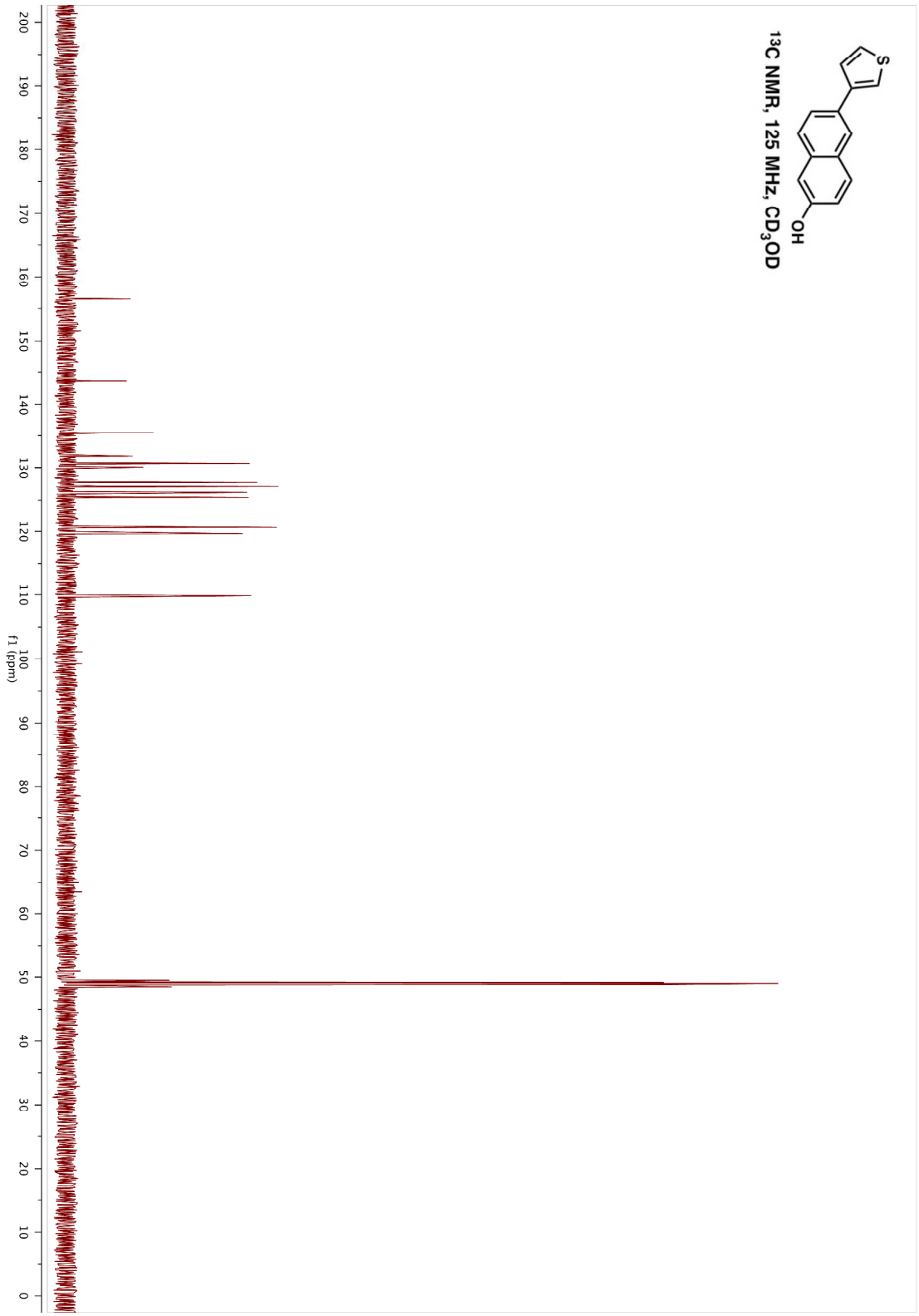

OTf
^{1}H NMR, 500 MHz, CDCl$_3$
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

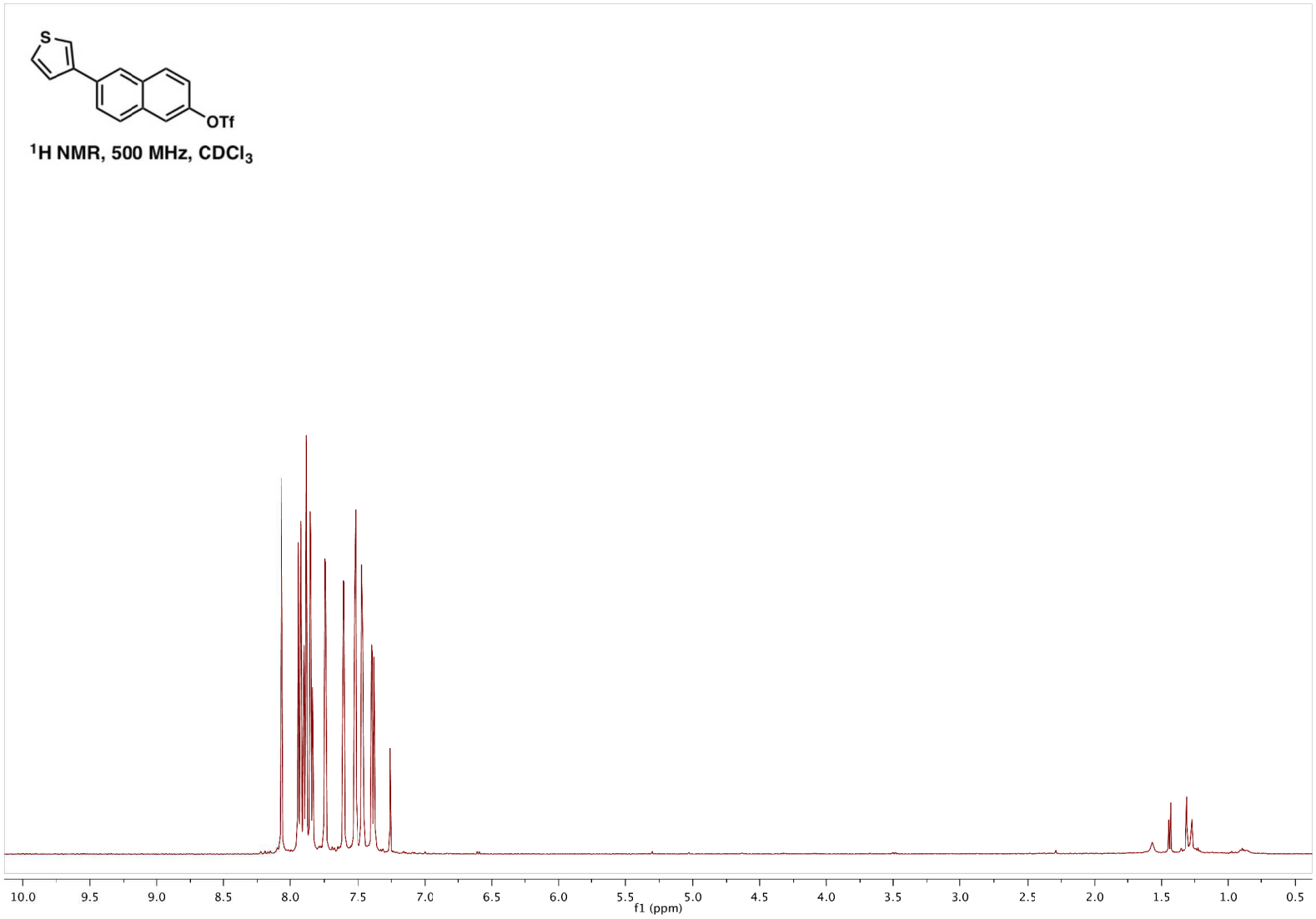


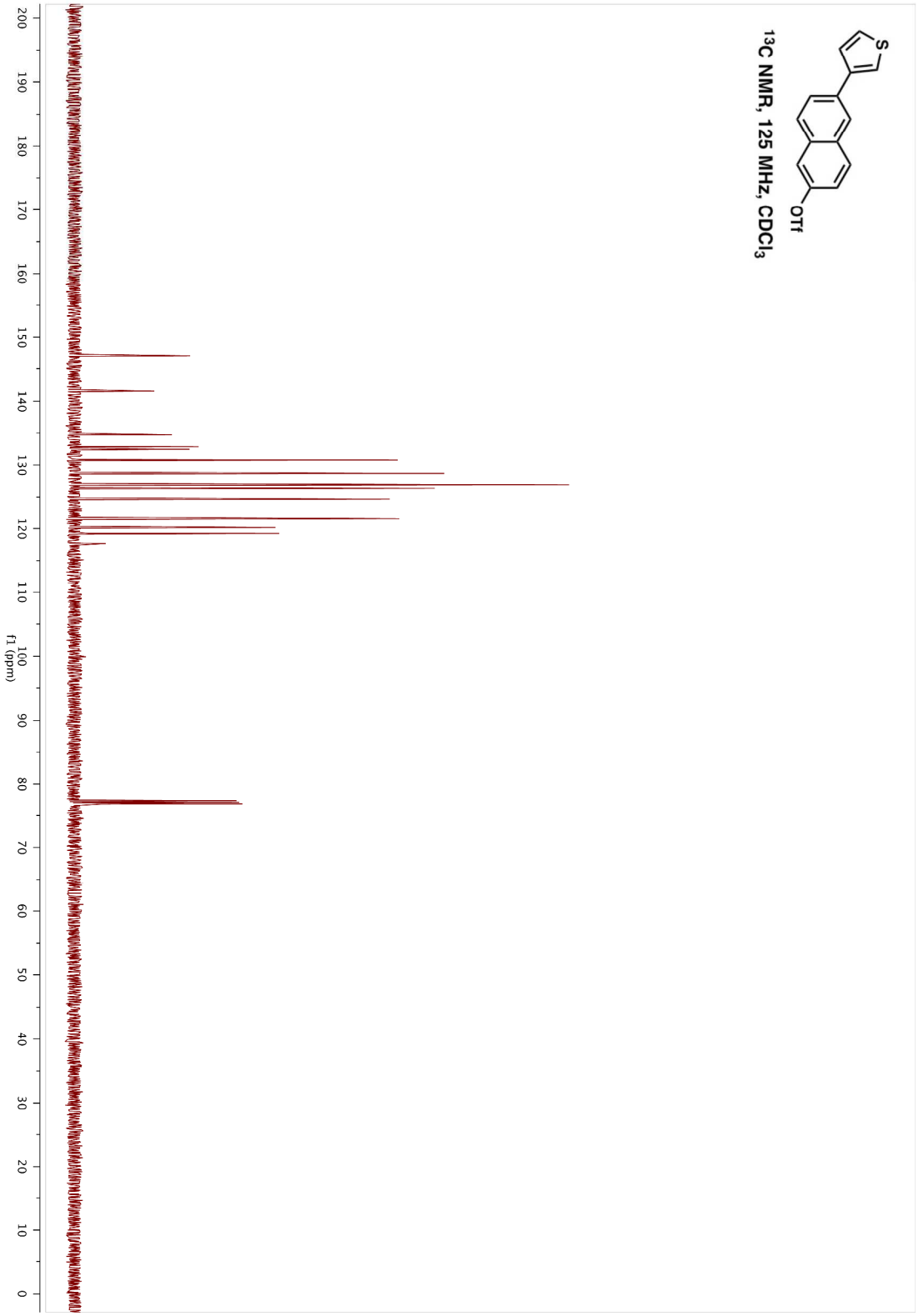
^{13}C NMR, 125 MHz, $CDCl_3$

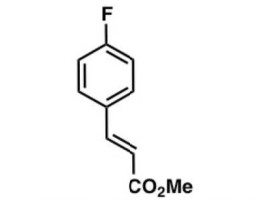



S
OH
^{1}H NMR, 500 MHz, CD_3OD
CD_3OD
CD_3OD
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


^{13}C NMR, 125 MHz, CD_3OD
S
OH
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

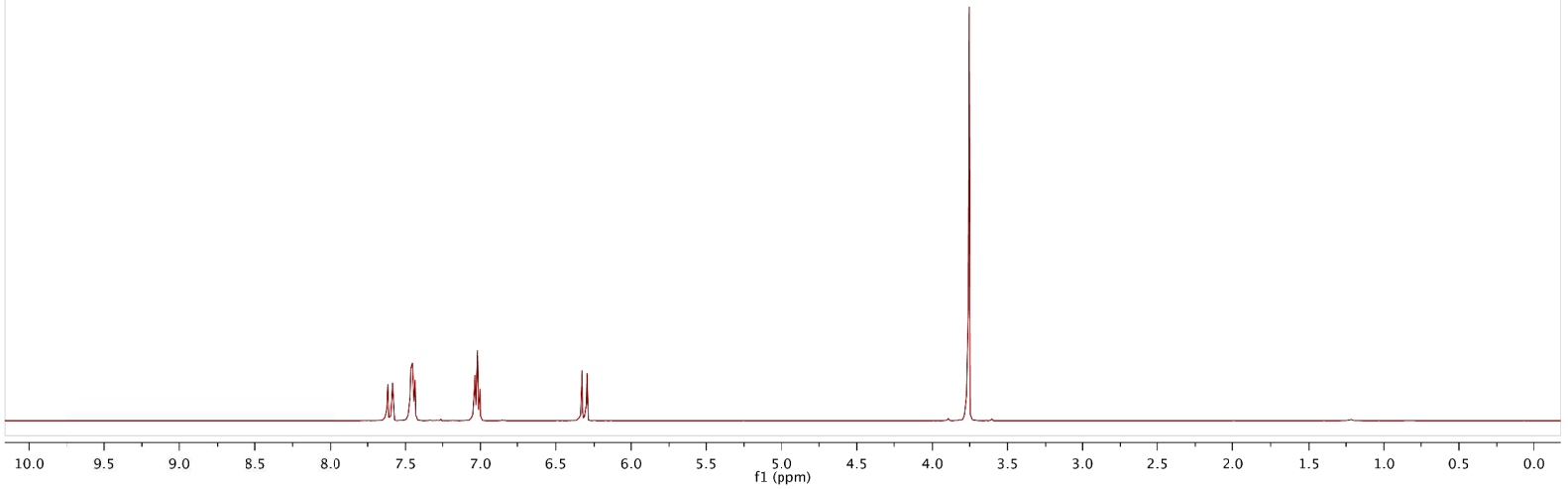

S
OTf
^{1}H NMR, 500 MHz, CDCl$_3$
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

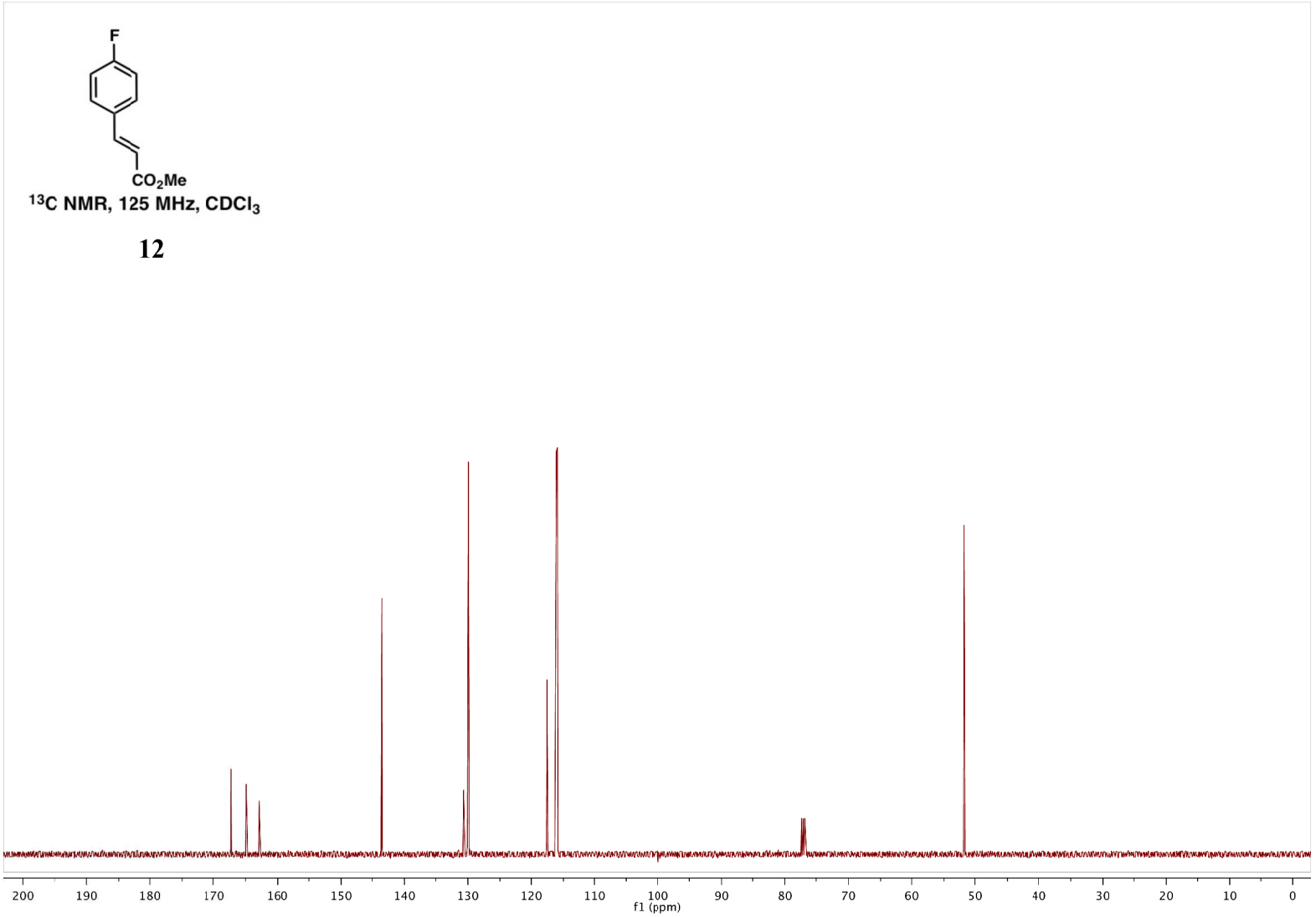

S
OTf
^{13}C NMR, 125 MHz, CDCl$_3$
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

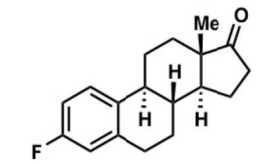


^{1}H NMR, 500 MHz, $CDCl_3$

12

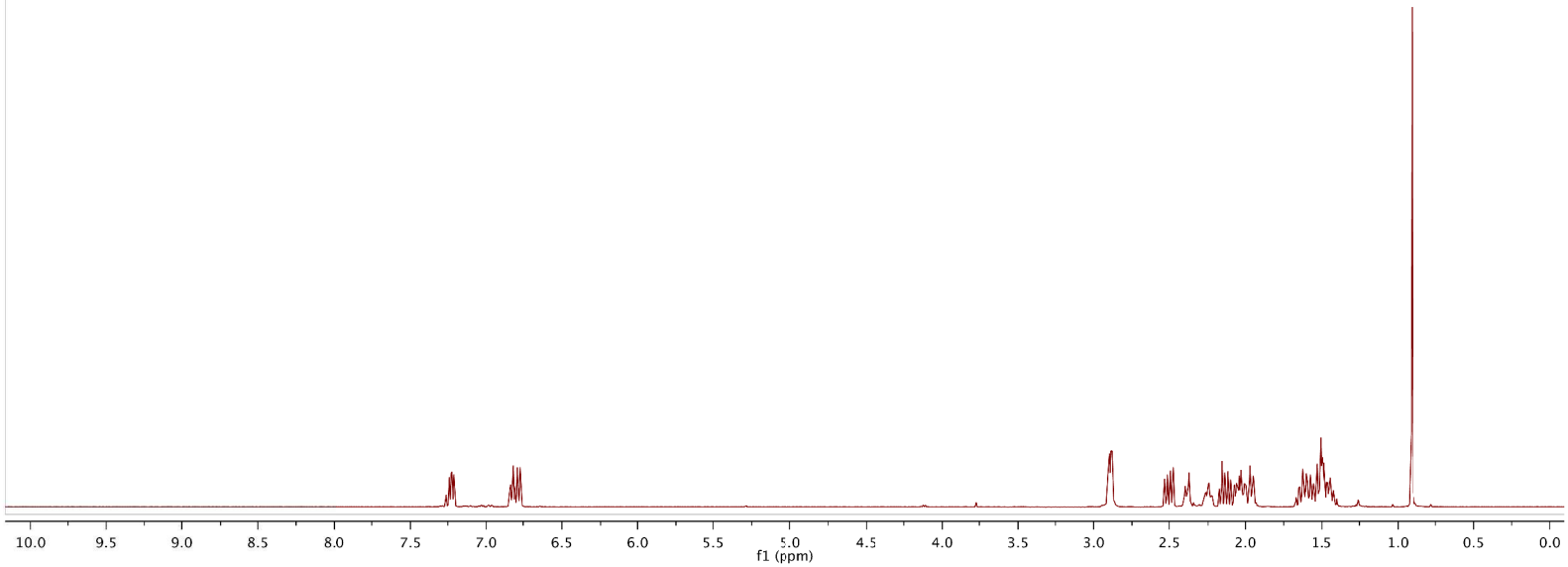


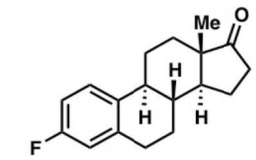

F
CO2Me
13C NMR, 125 MHz, CDCl3
12
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



^{1}H NMR, 500 MHz, $CDCl_3$

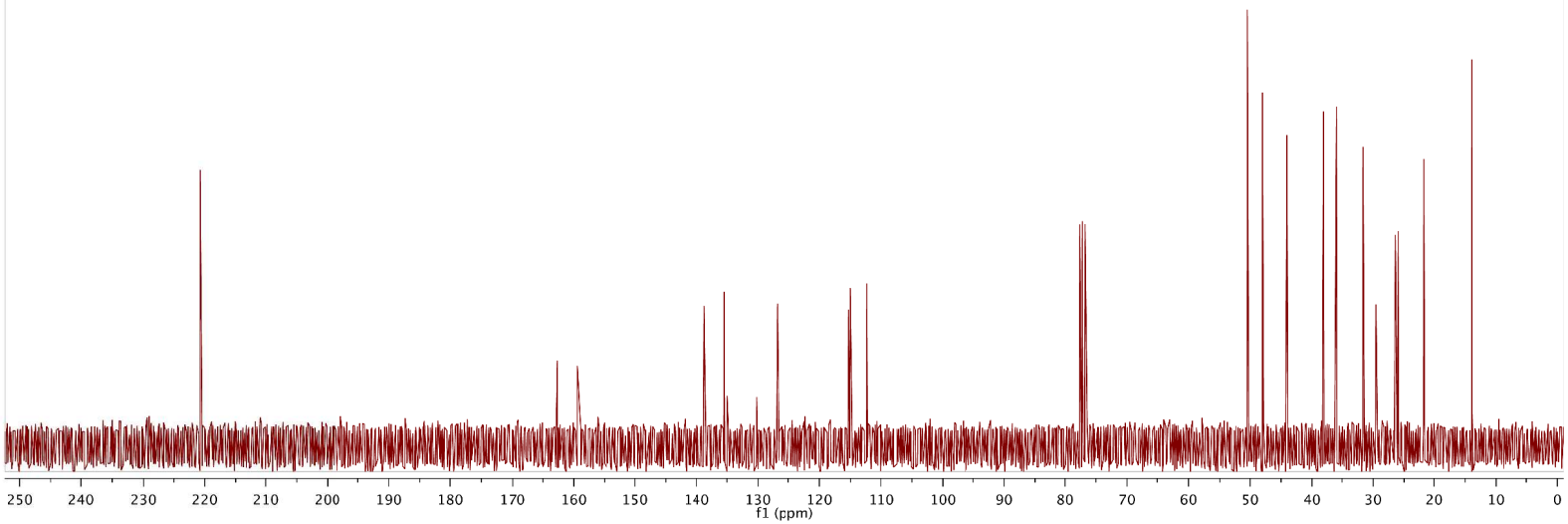
8

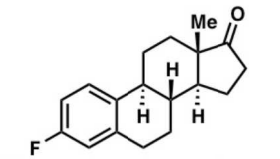




^{13}C NMR, 75 MHz, $CDCl_3$

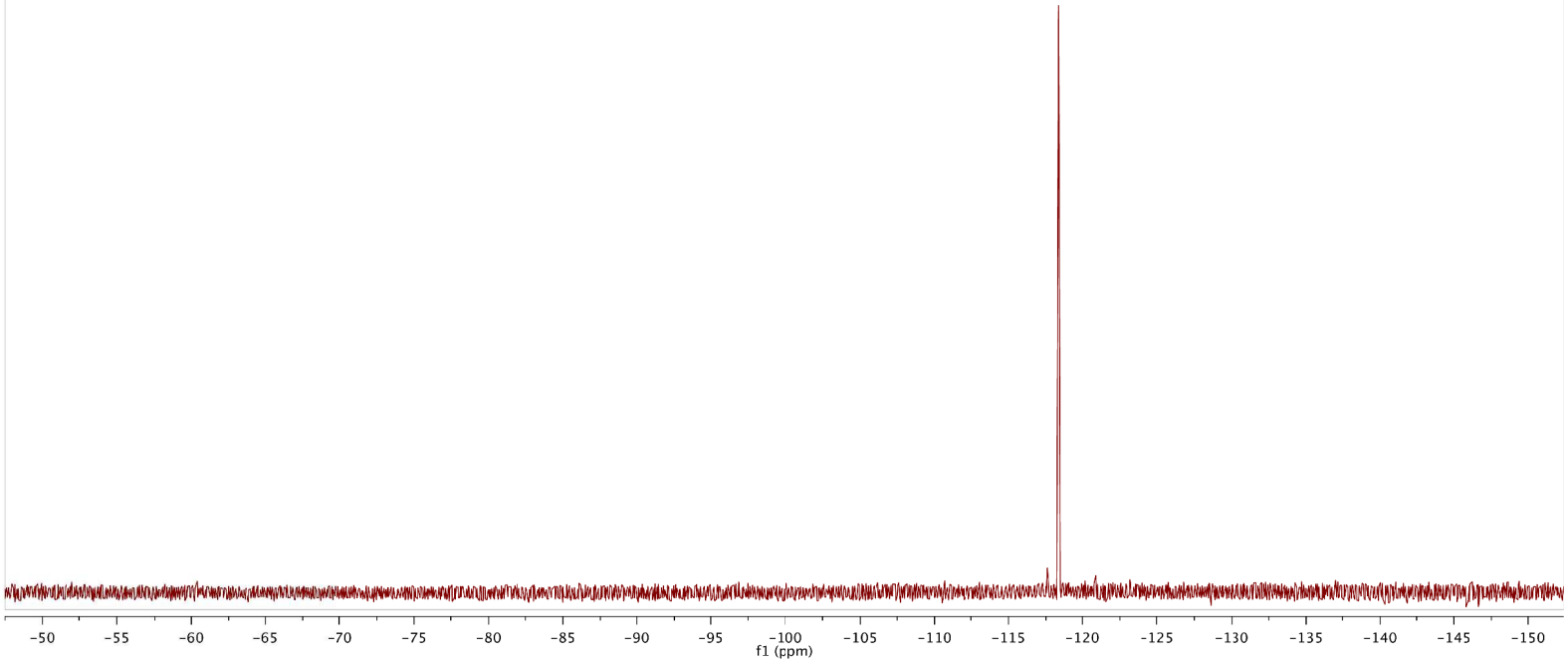
8

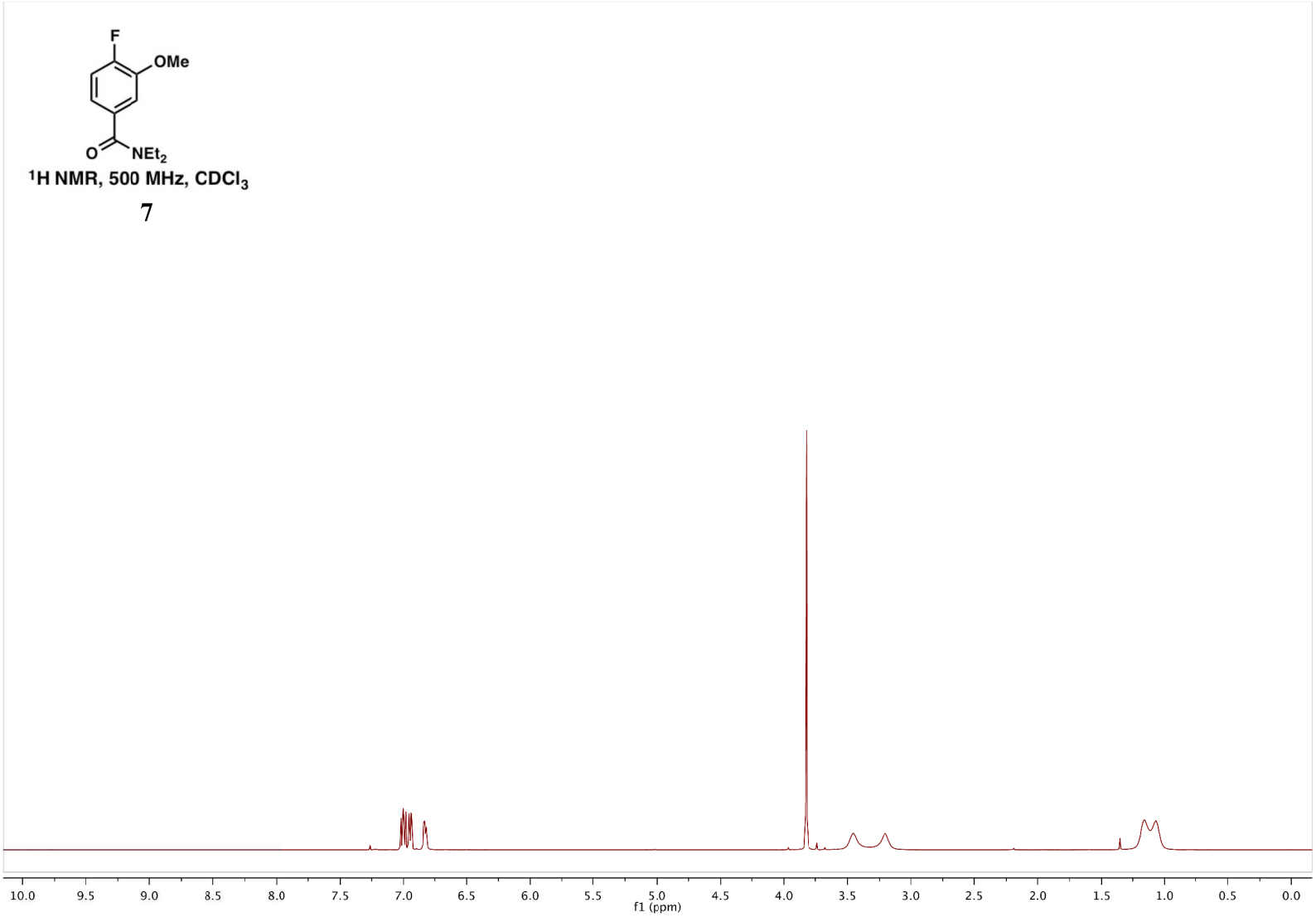


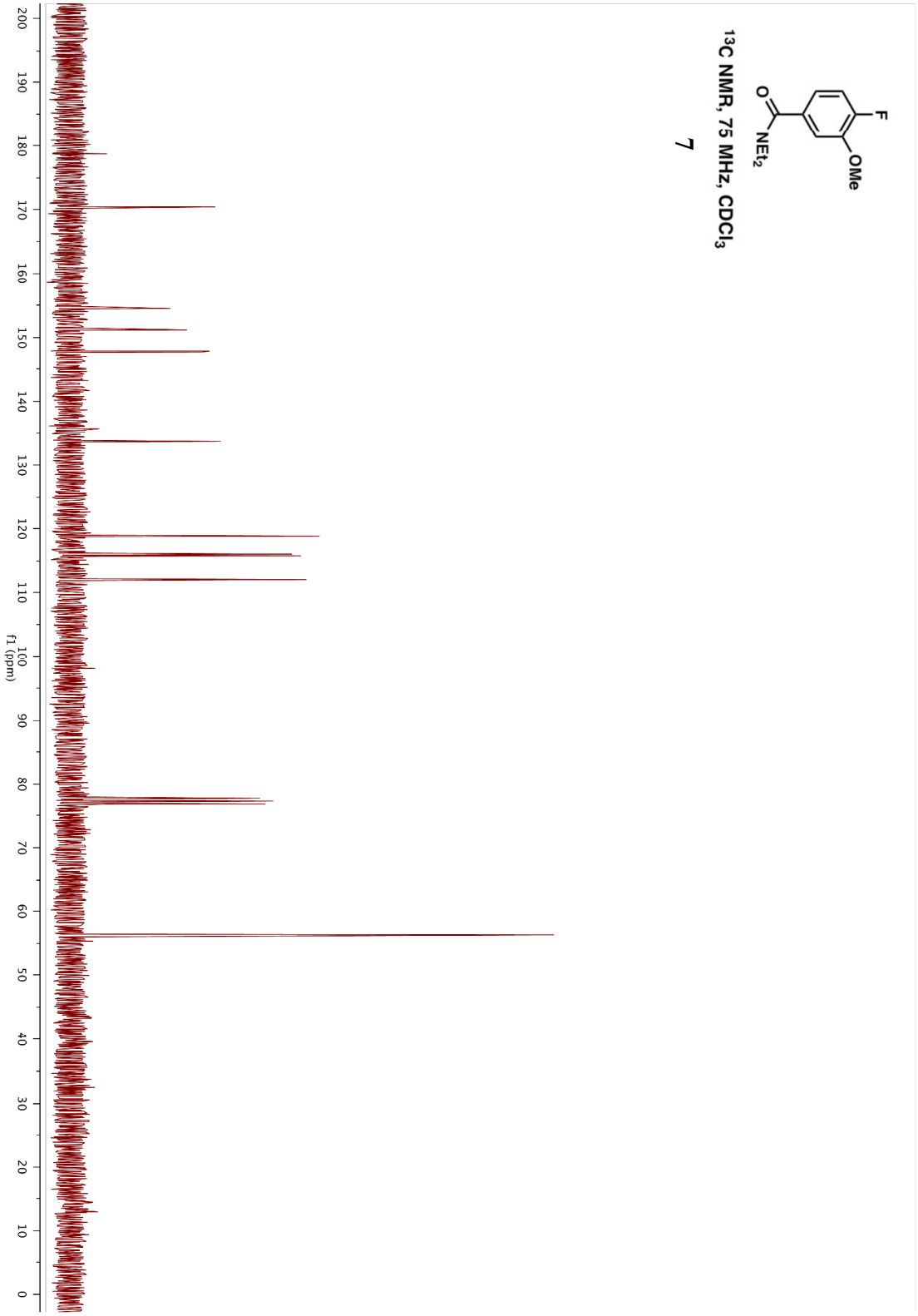


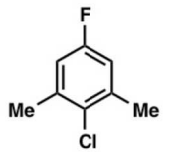
^{19}F NMR, 282 MHz, $CDCl_3$

8



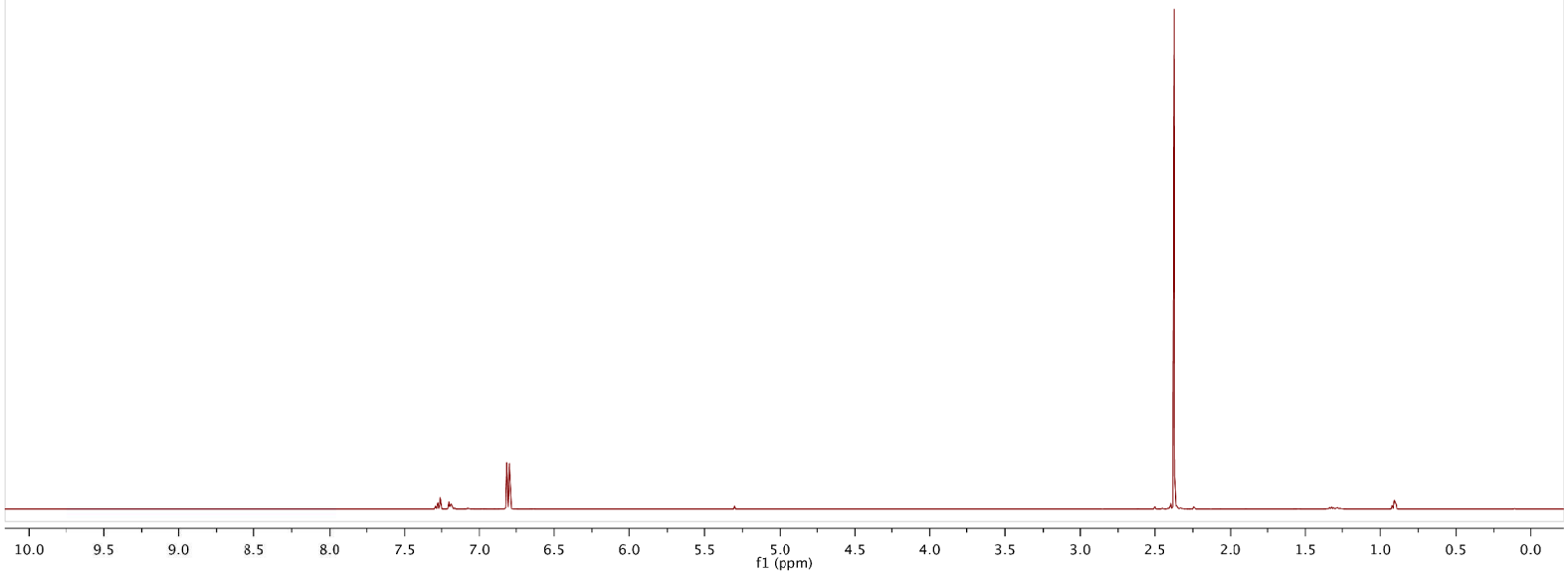

F
OMe
O
NEt2
1H NMR, 500 MHz, CDCl3
7
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

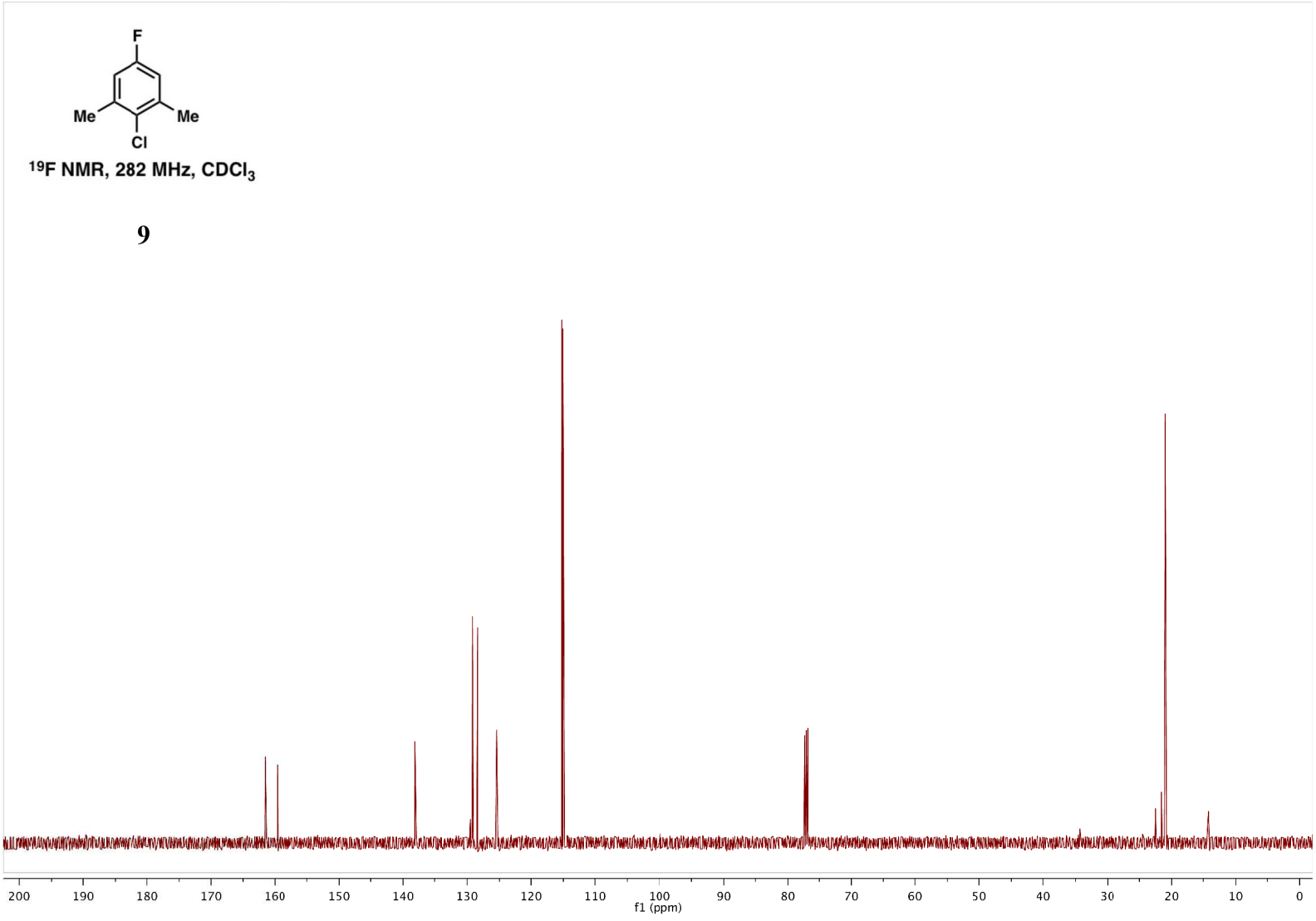

F
OMe
O
NEt2
13C NMR, 75 MHz, CDCl3
7
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

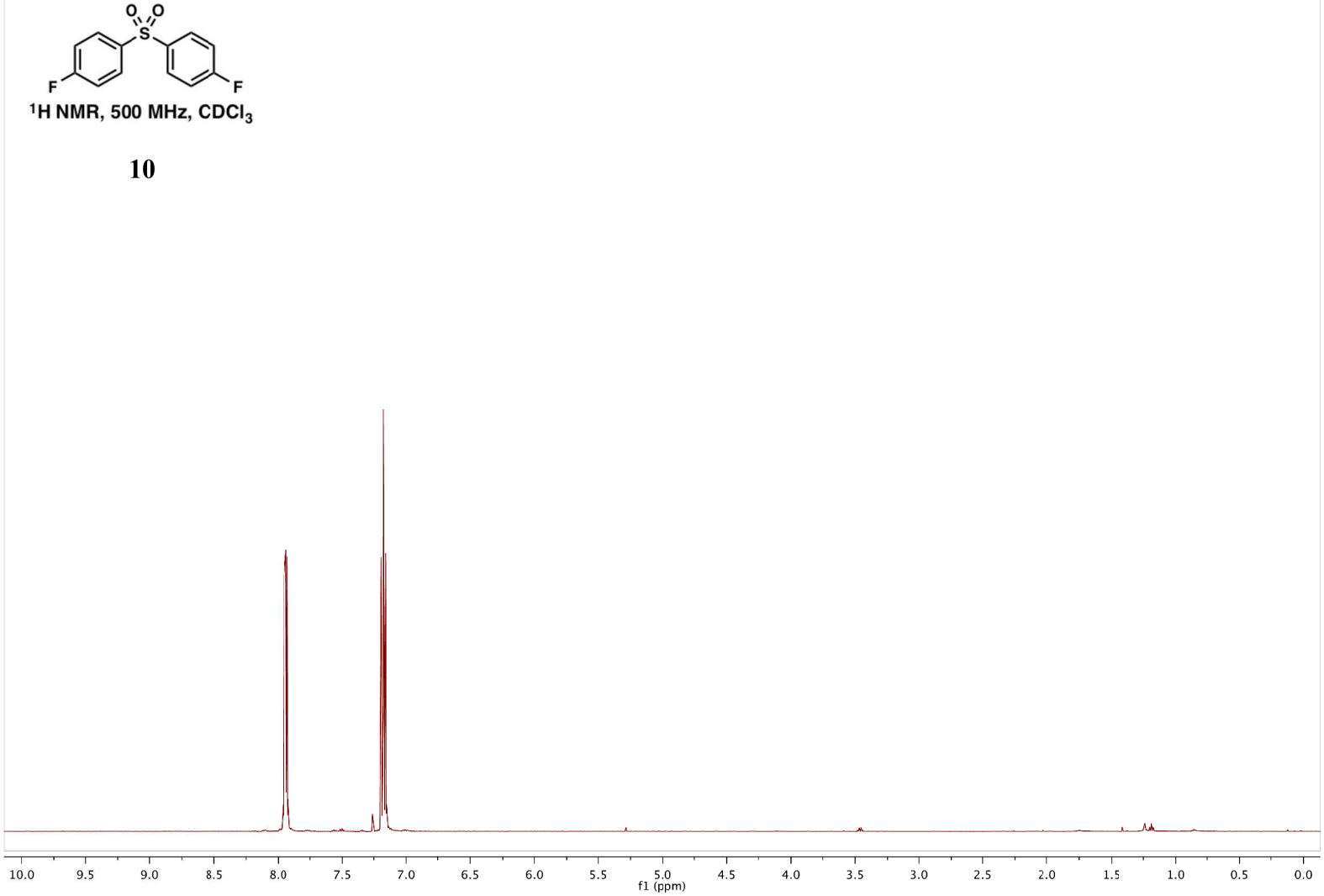


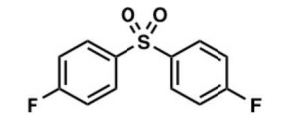
^{1}H NMR, 500 MHz, $CDCl_3$

9



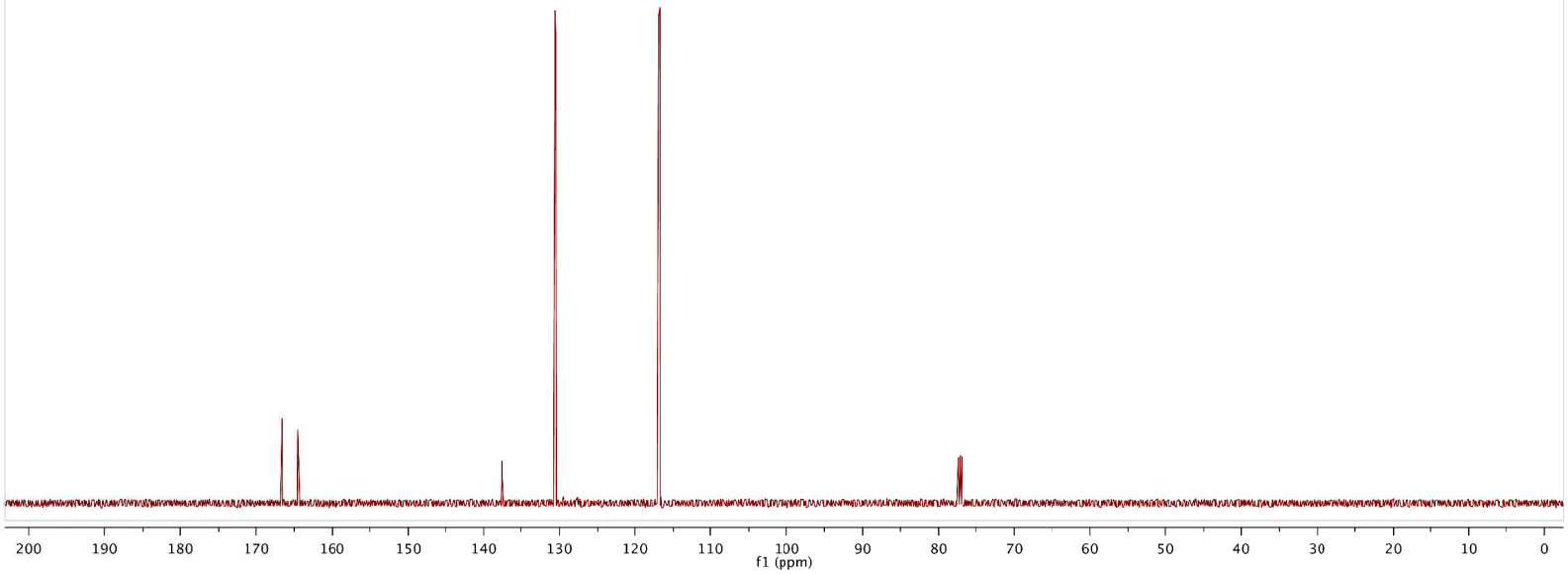

F
Me
Me
Cl
19F NMR, 282 MHz, CDCl3
9
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

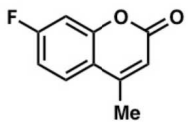

F
F
^{1}H NMR, 500 MHz, CDCl$_3$
10
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



^{13}C NMR, 125 MHz, $CDCl_3$

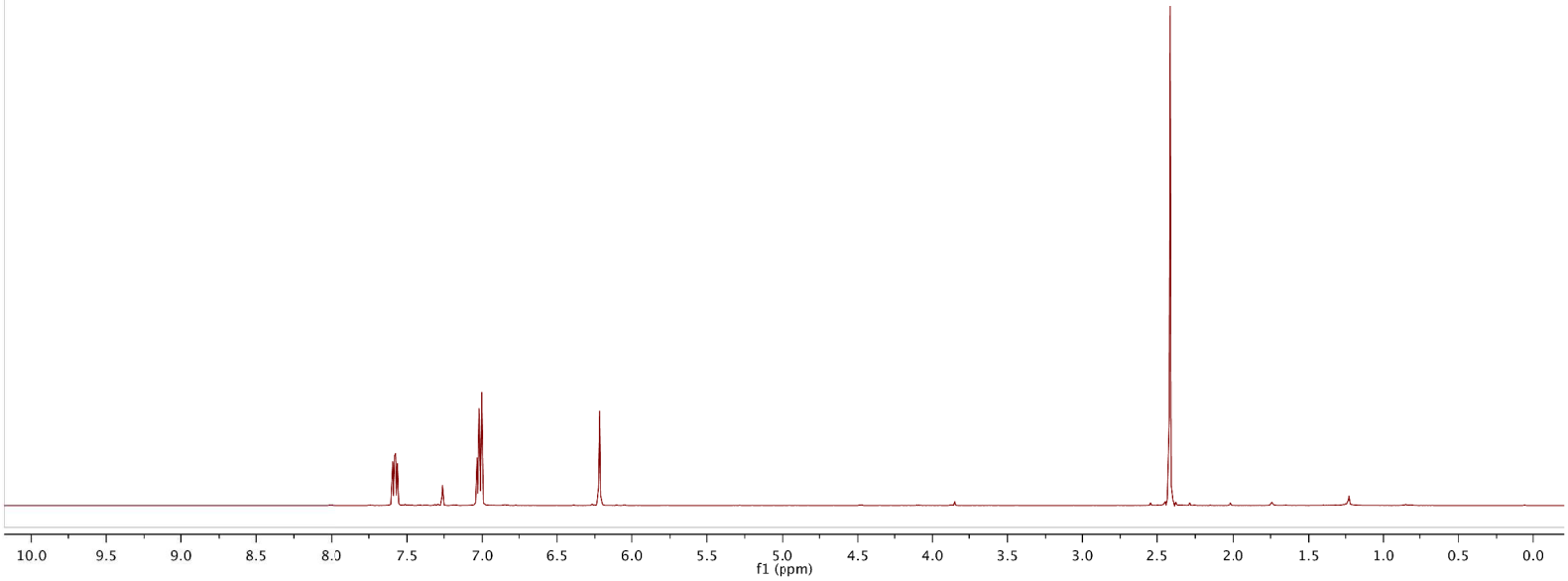
10

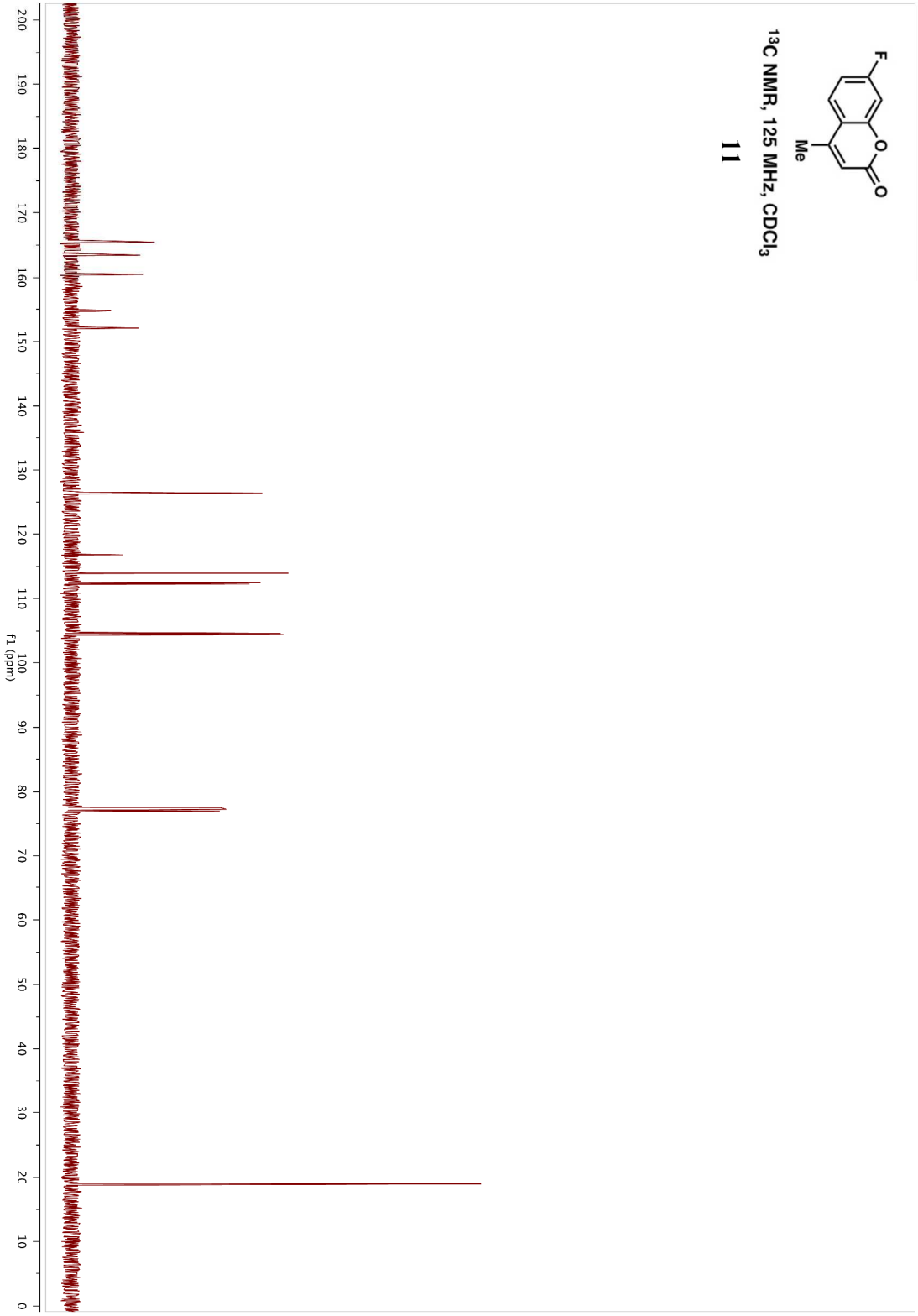


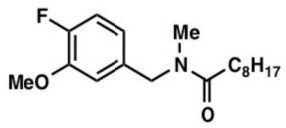


^{1}H NMR, 500 MHz, $CDCl_3$

11

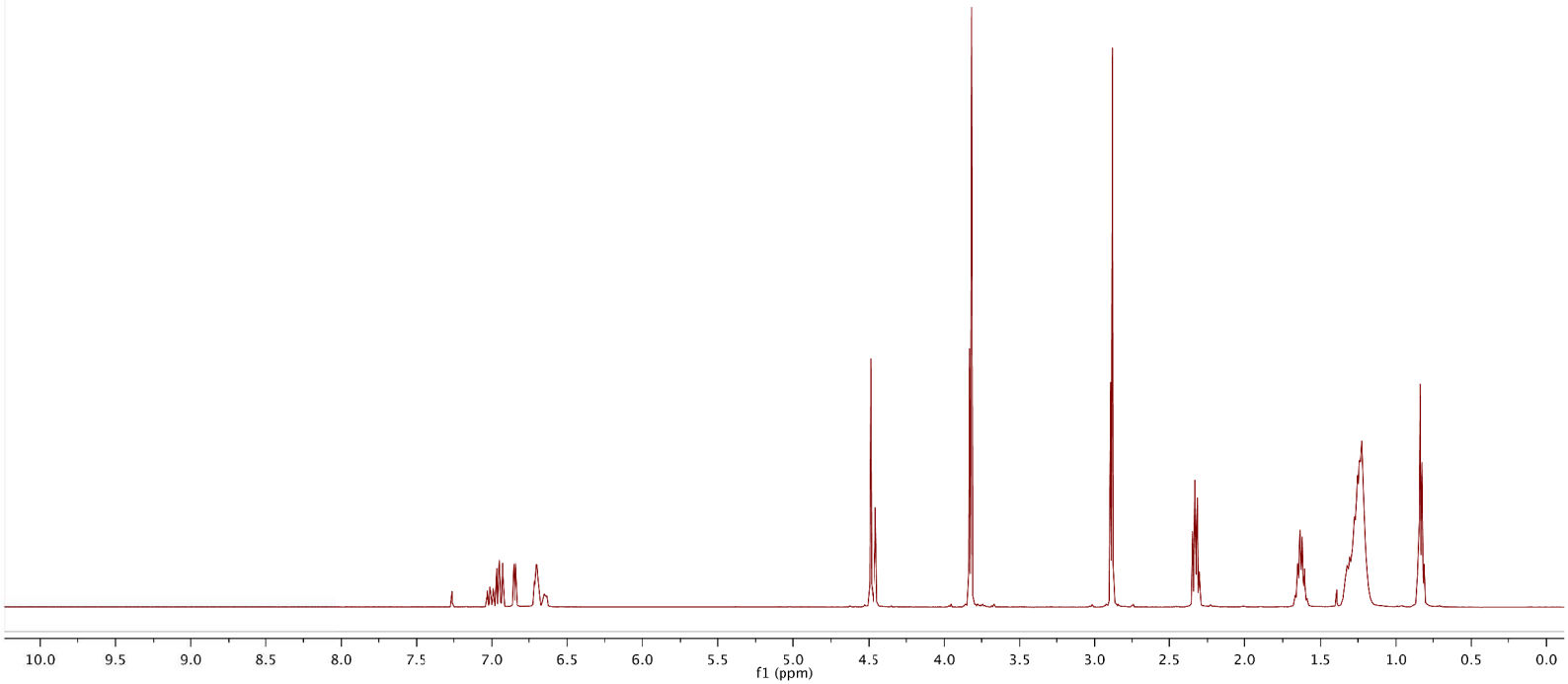


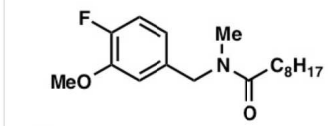

F
O
O
Me
^{13}C NMR, 125 MHz, CDCl$_3$
11
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



^{1}H NMR, 500 MHz, $CDCl_3$

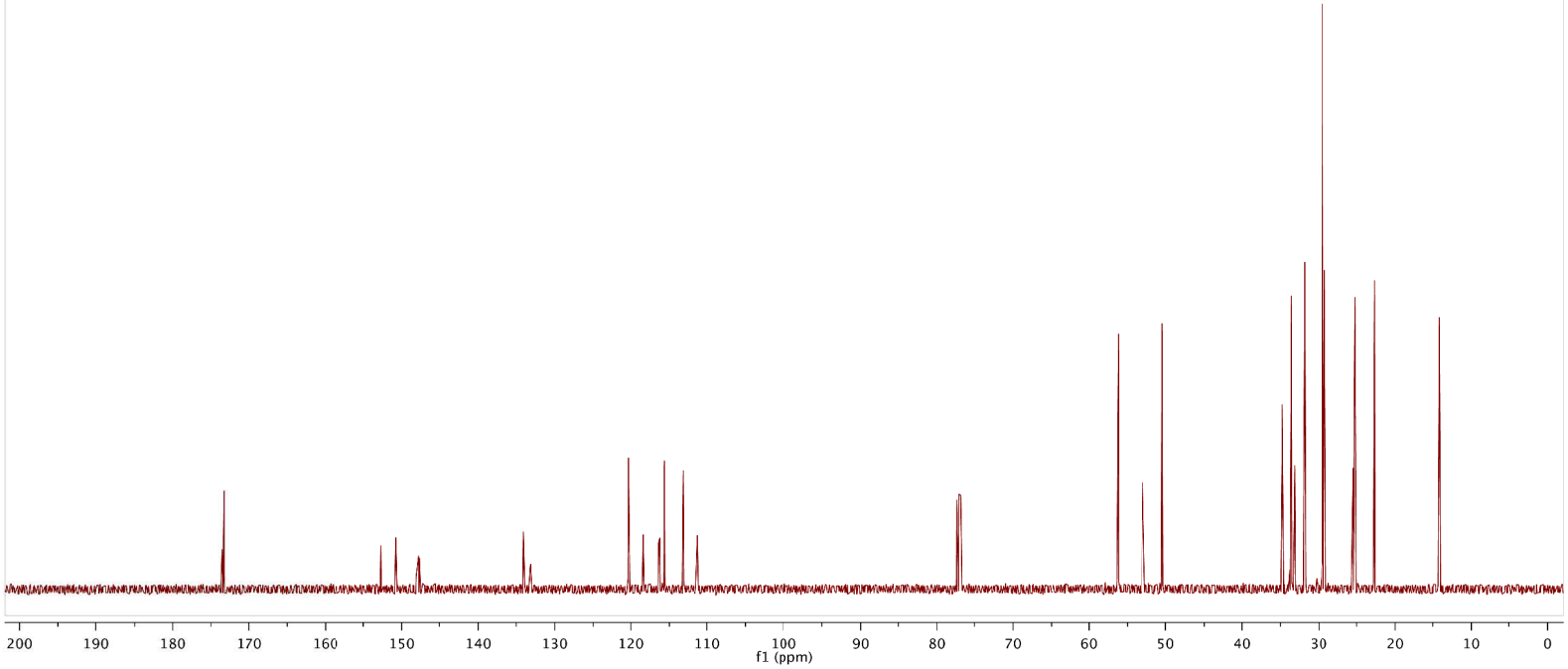
6

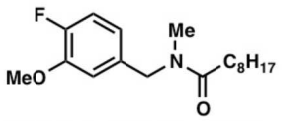




^{13}C NMR, 125 MHz, $CDCl_3$

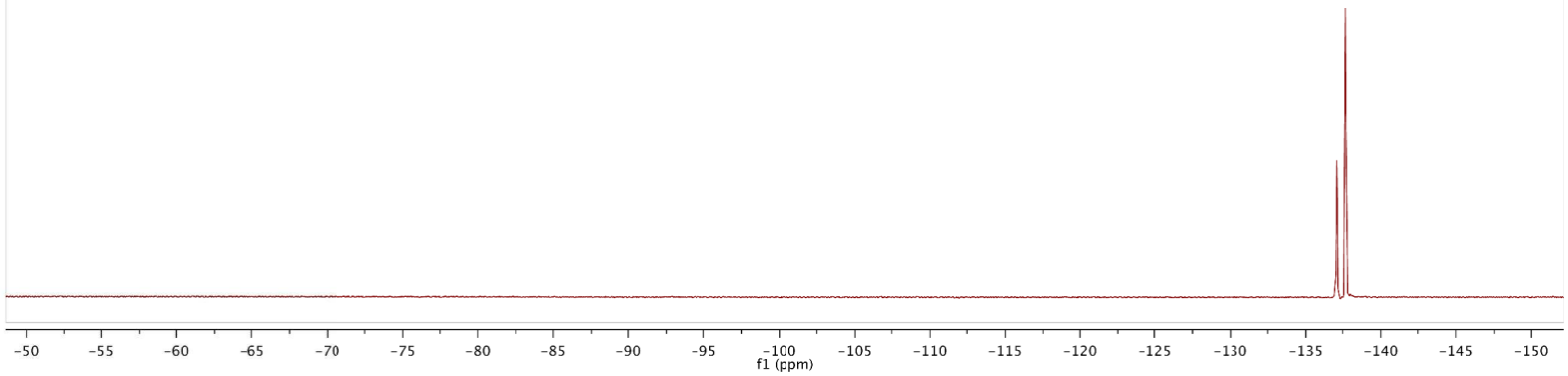
6



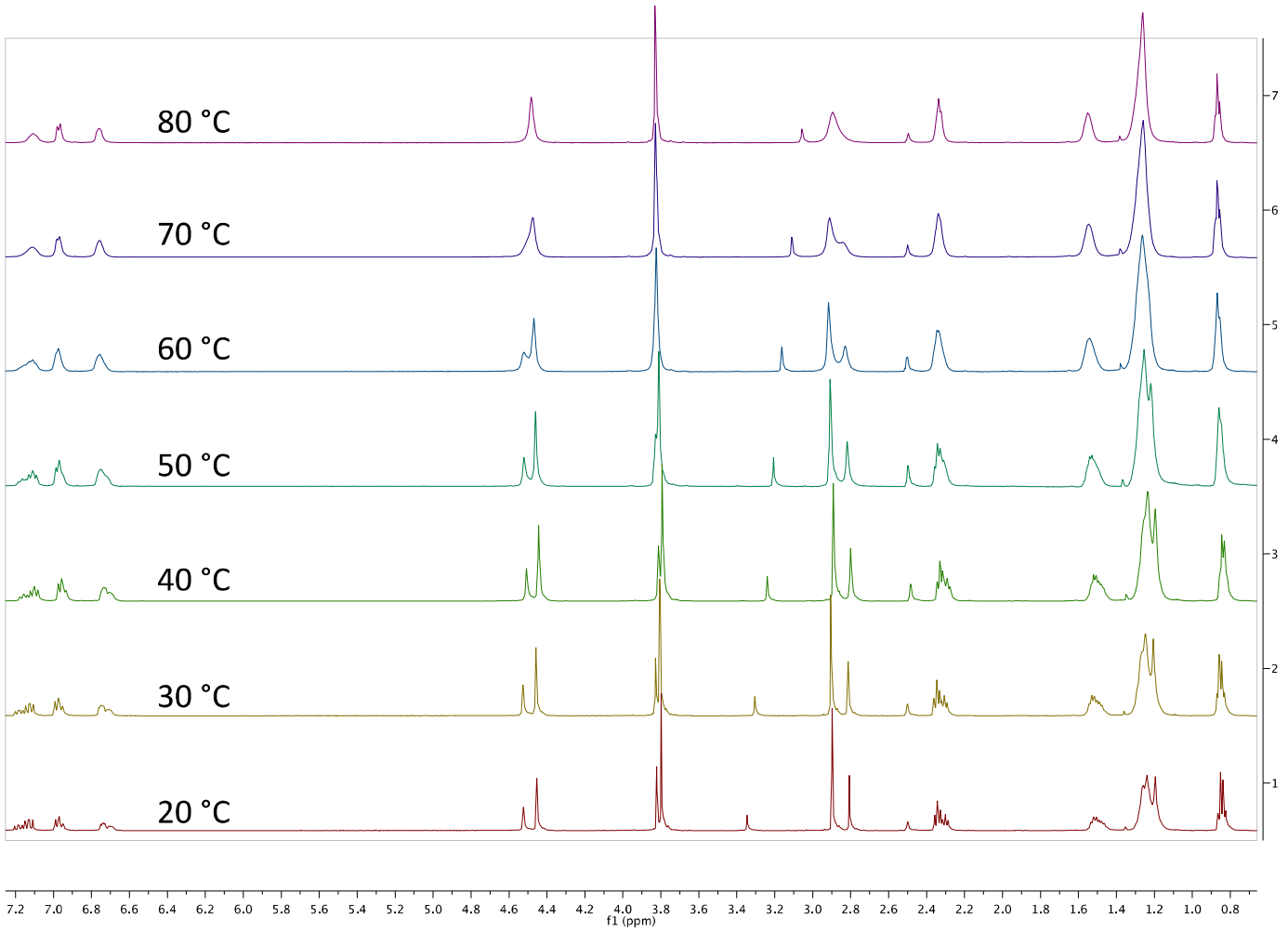


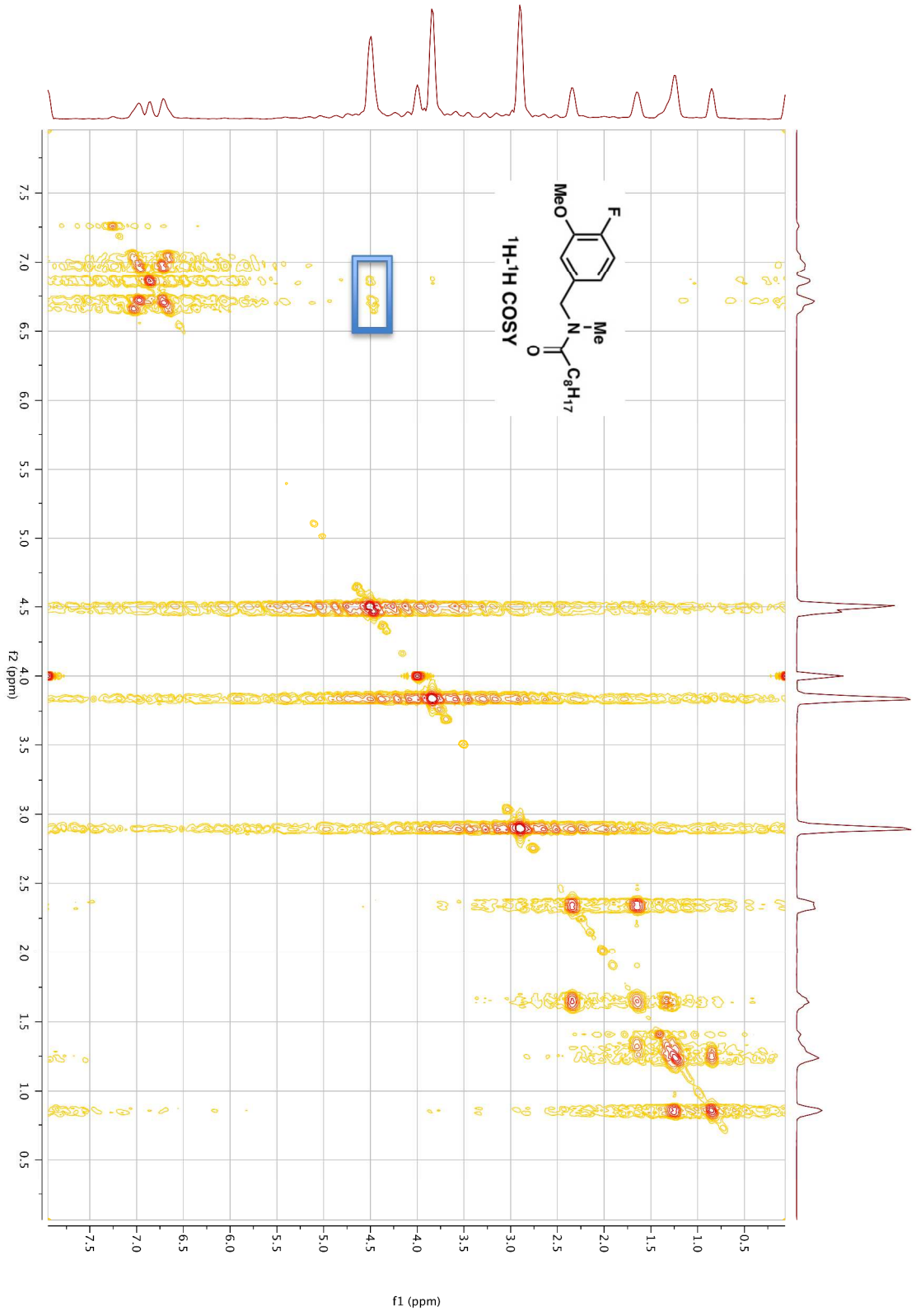
^{19}F NMR, 470 MHz, $CDCl_3$

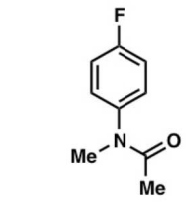
6



6

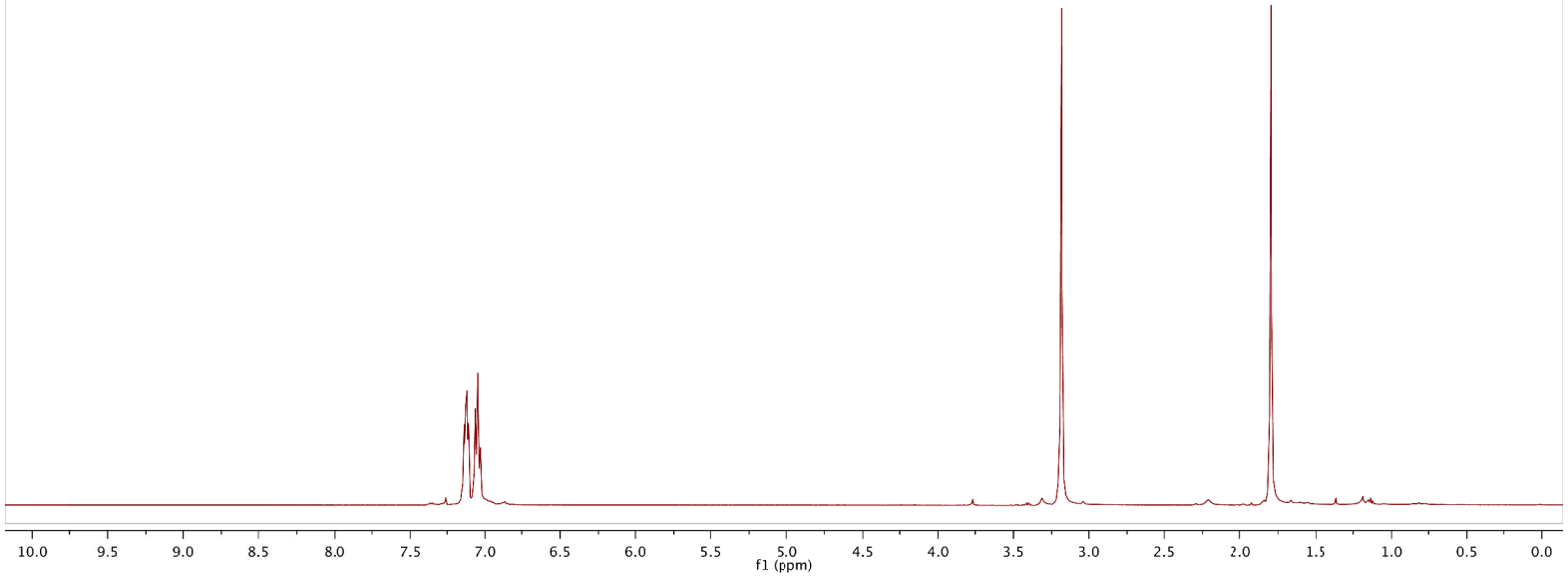

80 °C
70 °C
60 °C
50 °C
40 °C
30 °C
20 °C
7
6
5
4
3
2
1
7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8
f1 (ppm)

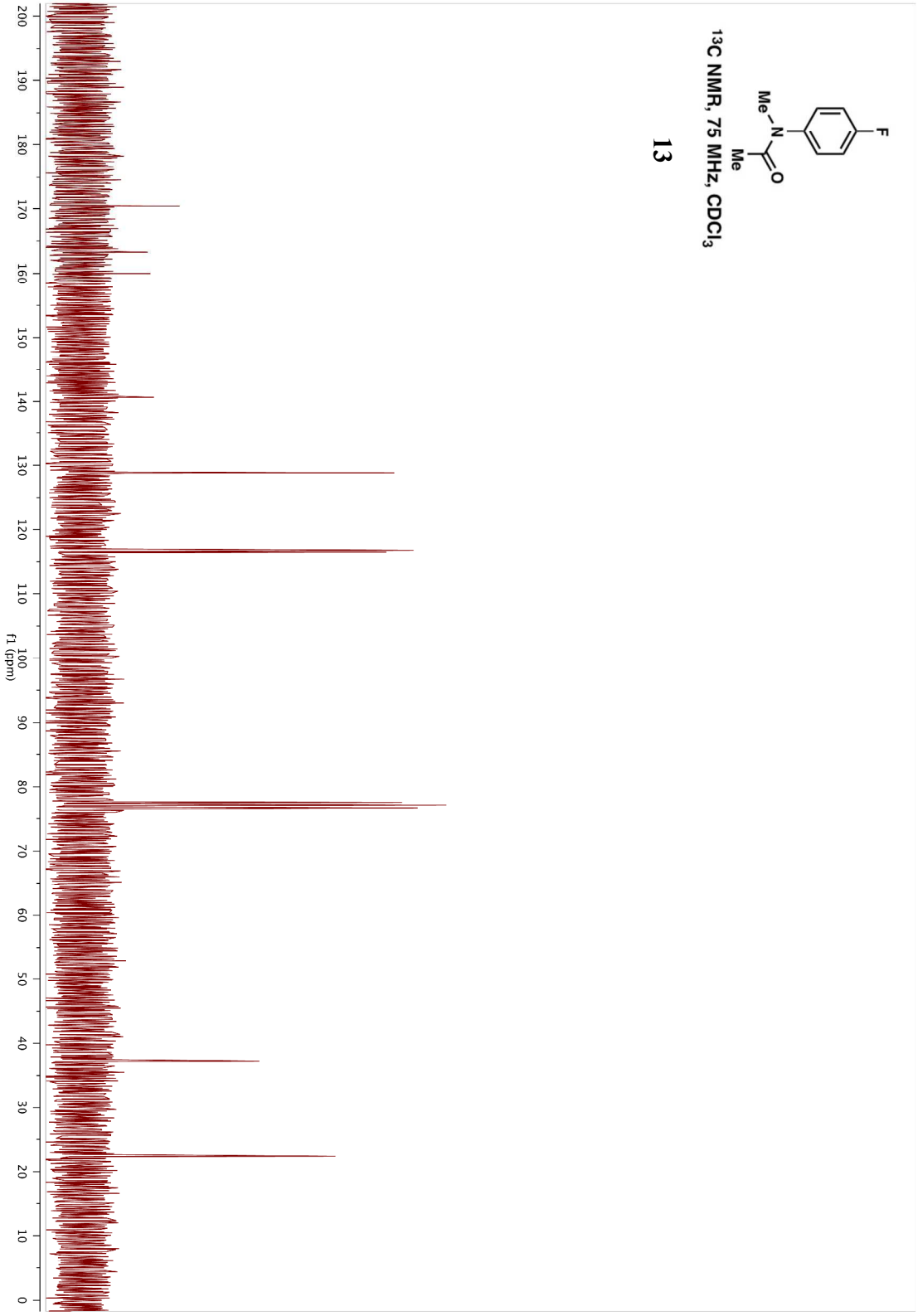

^{1}H-^{1}H COSY
MeO
F
Me
N
O
C_8H_{17}
f2 (ppm)
f1 (ppm)

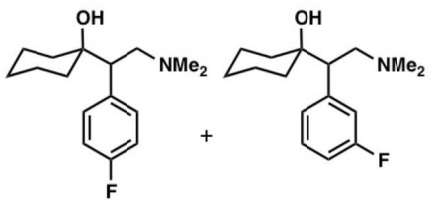


^{1}H NMR, 500 MHz, $CDCl_3$

13

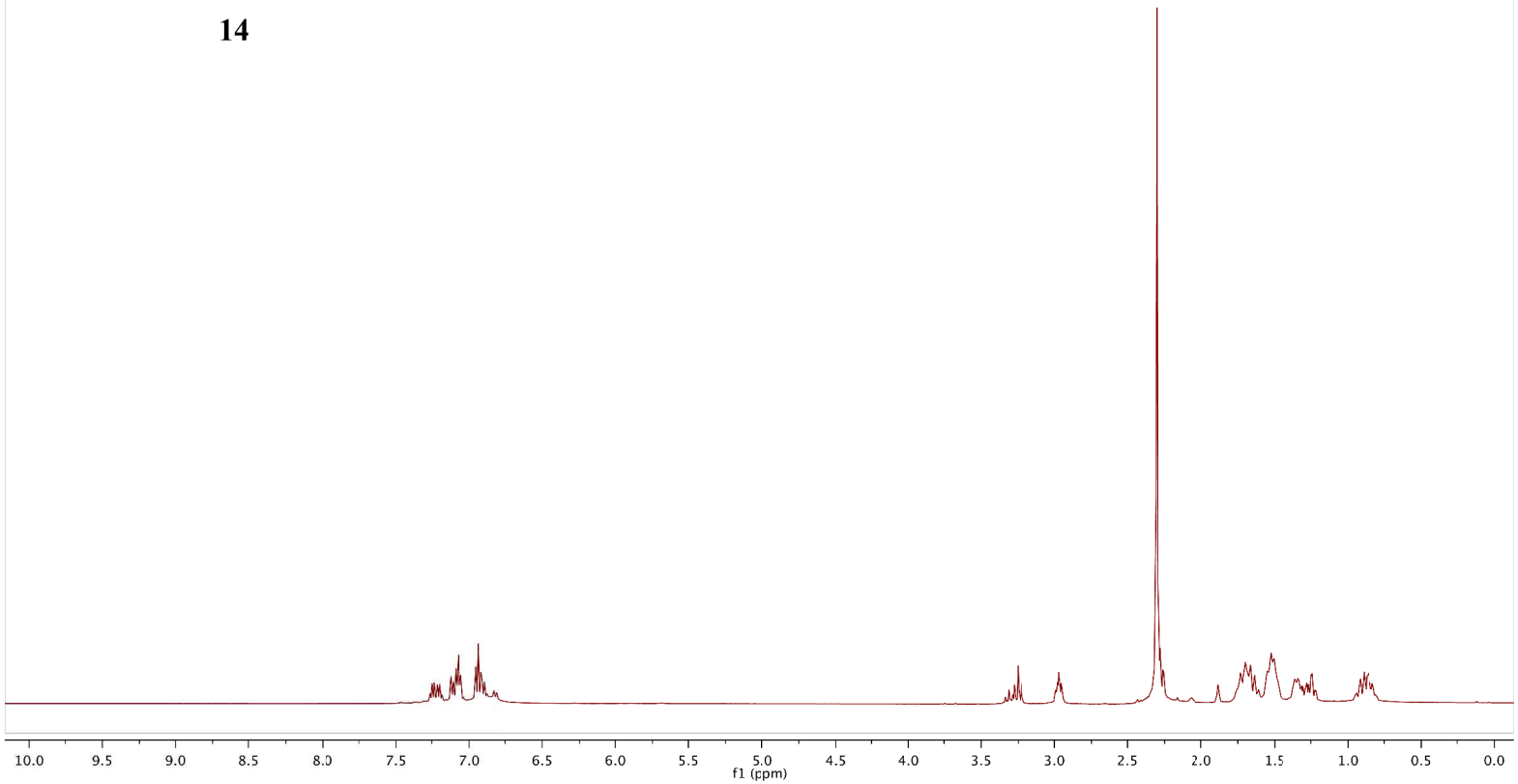


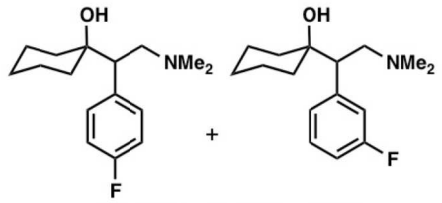

F
Me
N
O
Me
13
^{13}C NMR, 75 MHz, CDCl$_3$
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



^{1}H NMR, 500 MHz, $CDCl_3$

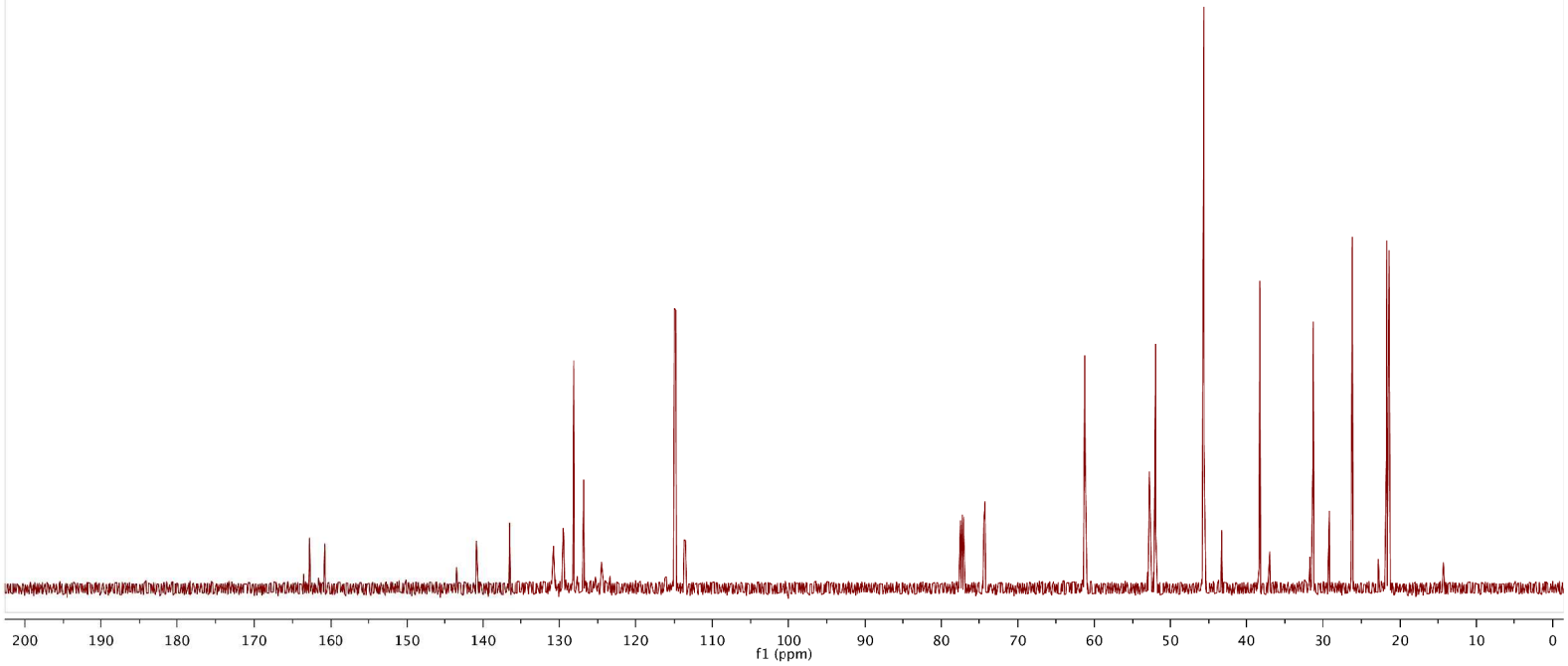
14

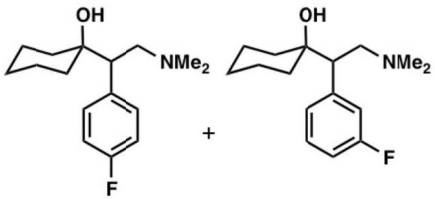




^{13}C NMR, 125 MHz, $CDCl_3$

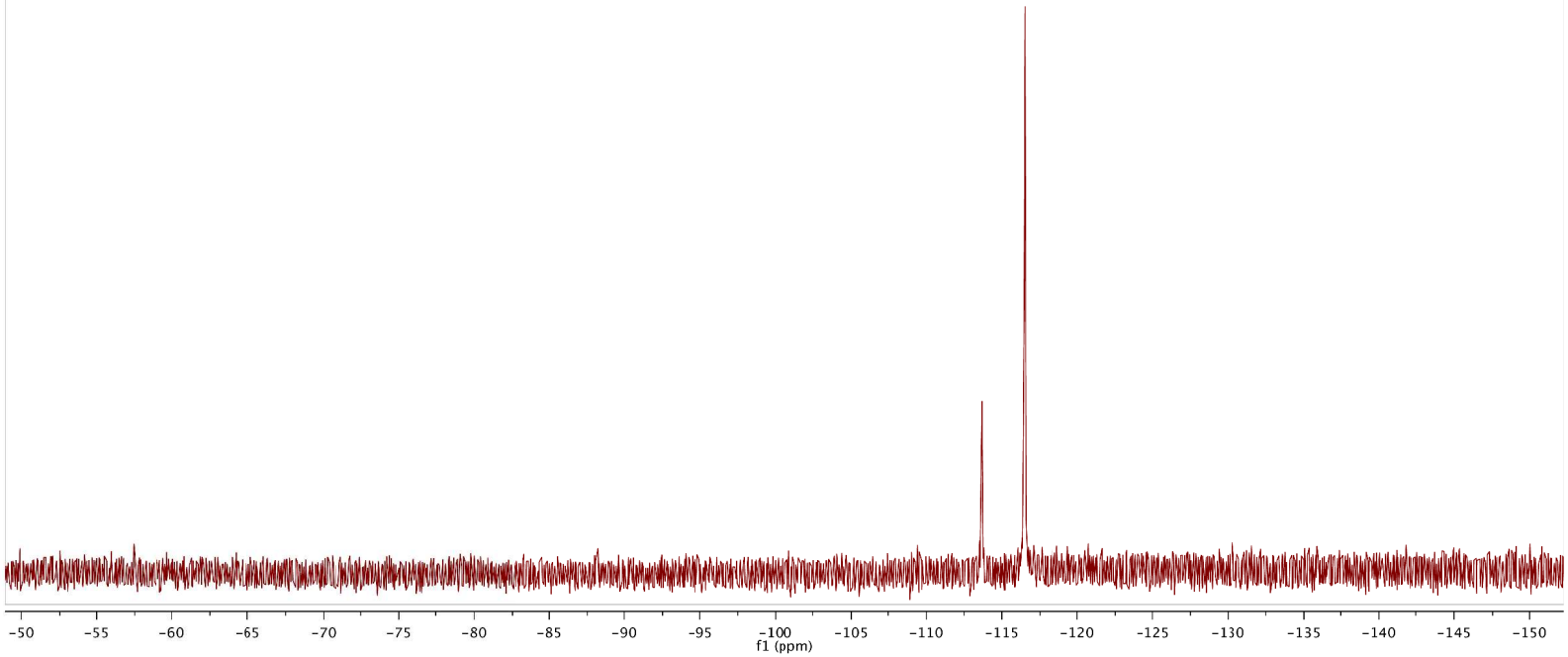
14

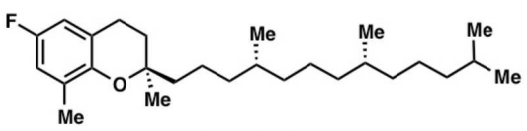




^{19}F NMR, 282 MHz, $CDCl_3$

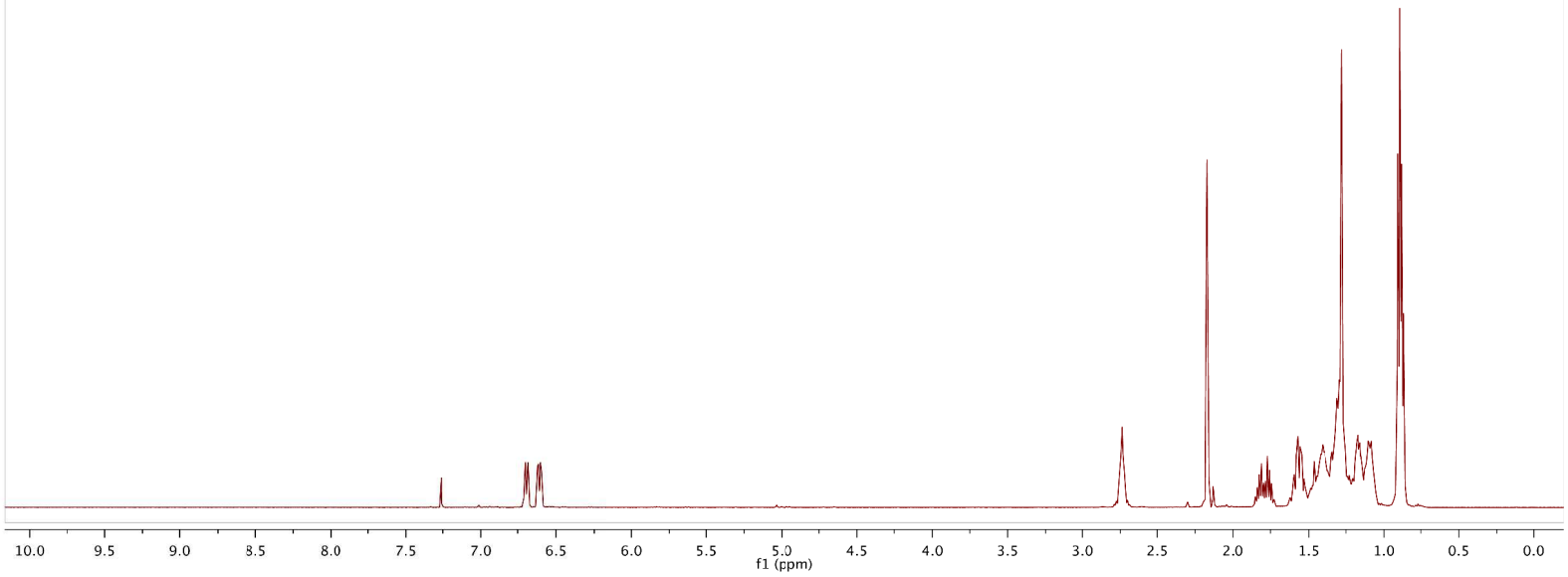
14

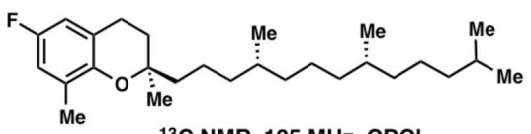




^{1}H NMR, 500 MHz, $CDCl_3$

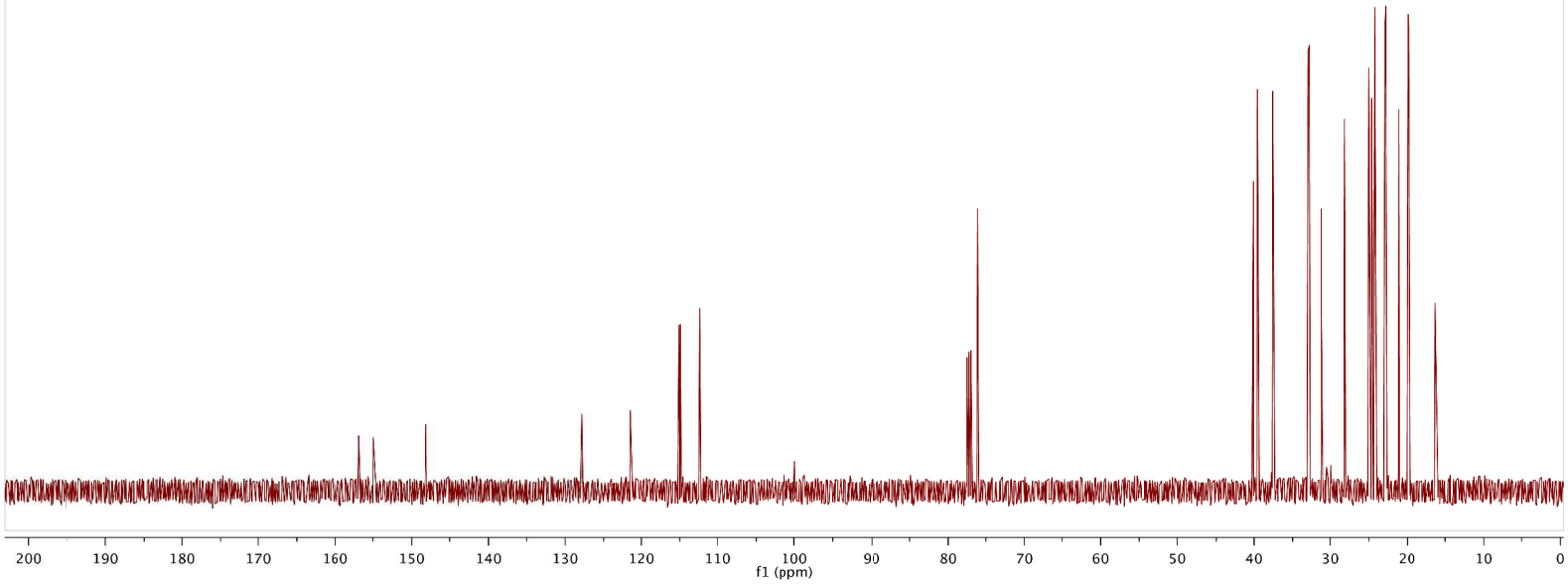
15

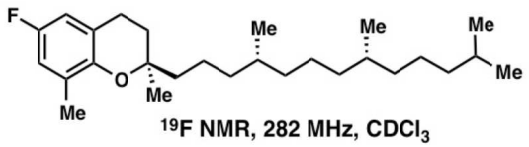




^{13}C NMR, 125 MHz, $CDCl_3$

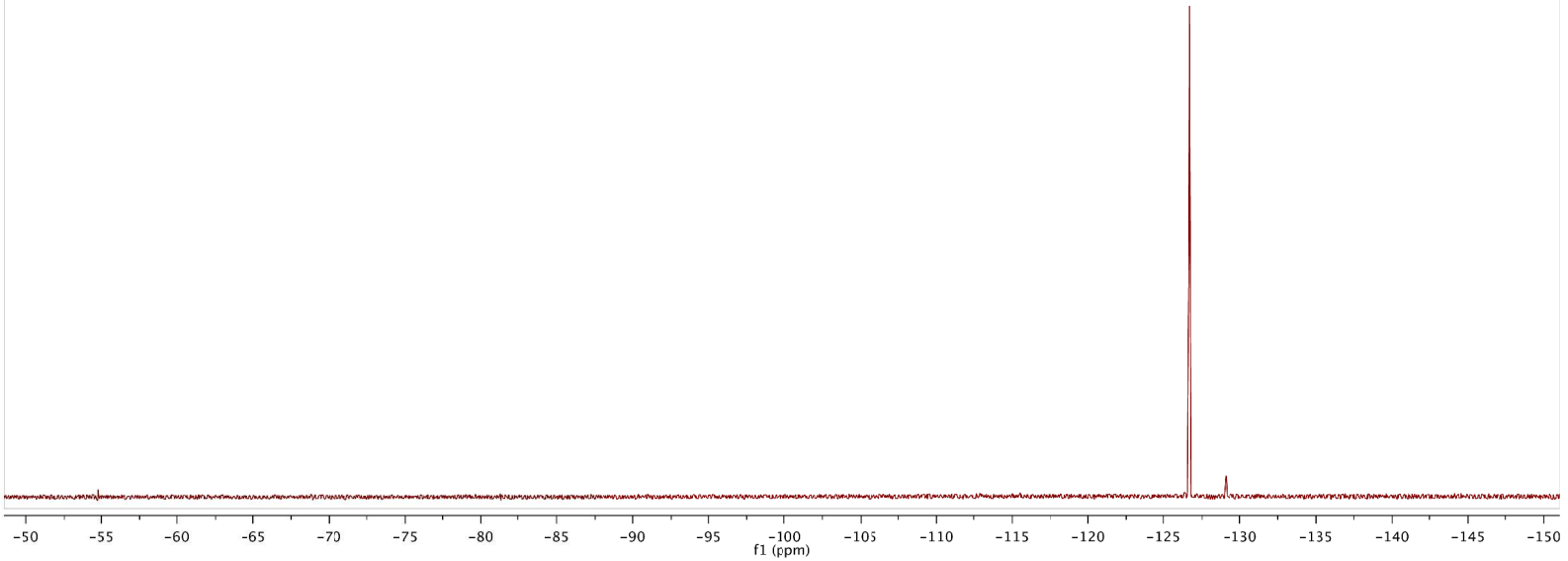
15

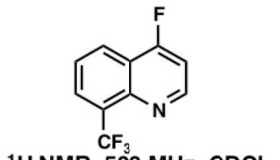




^{19}F NMR, 282 MHz, $CDCl_3$

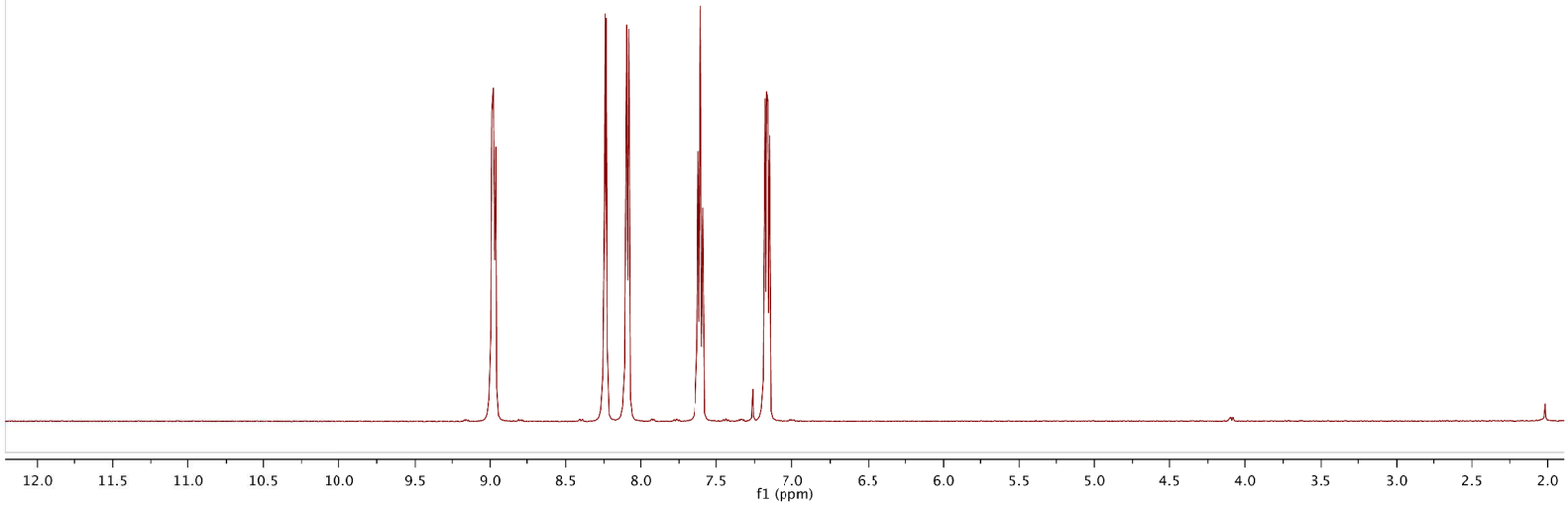
15

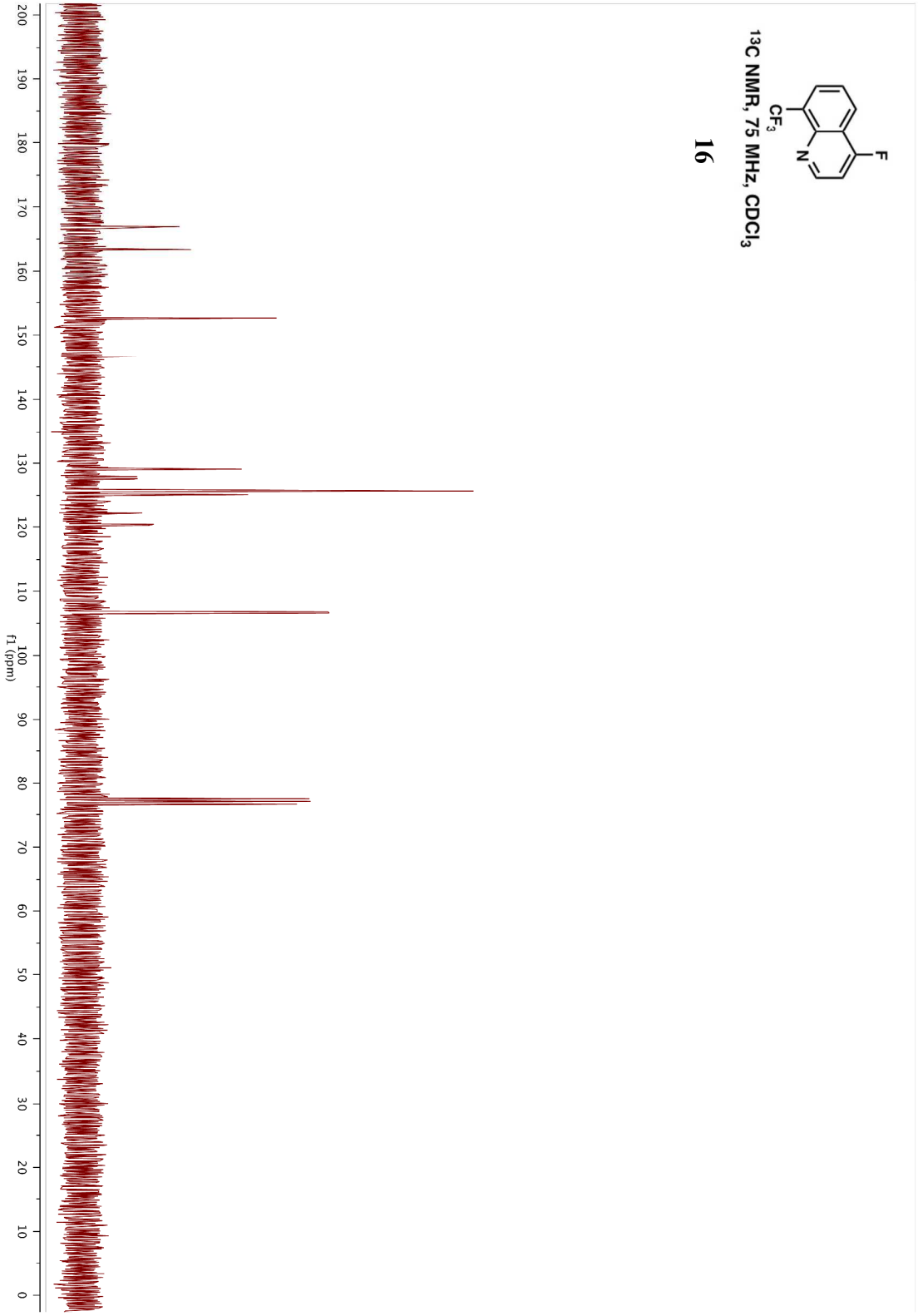


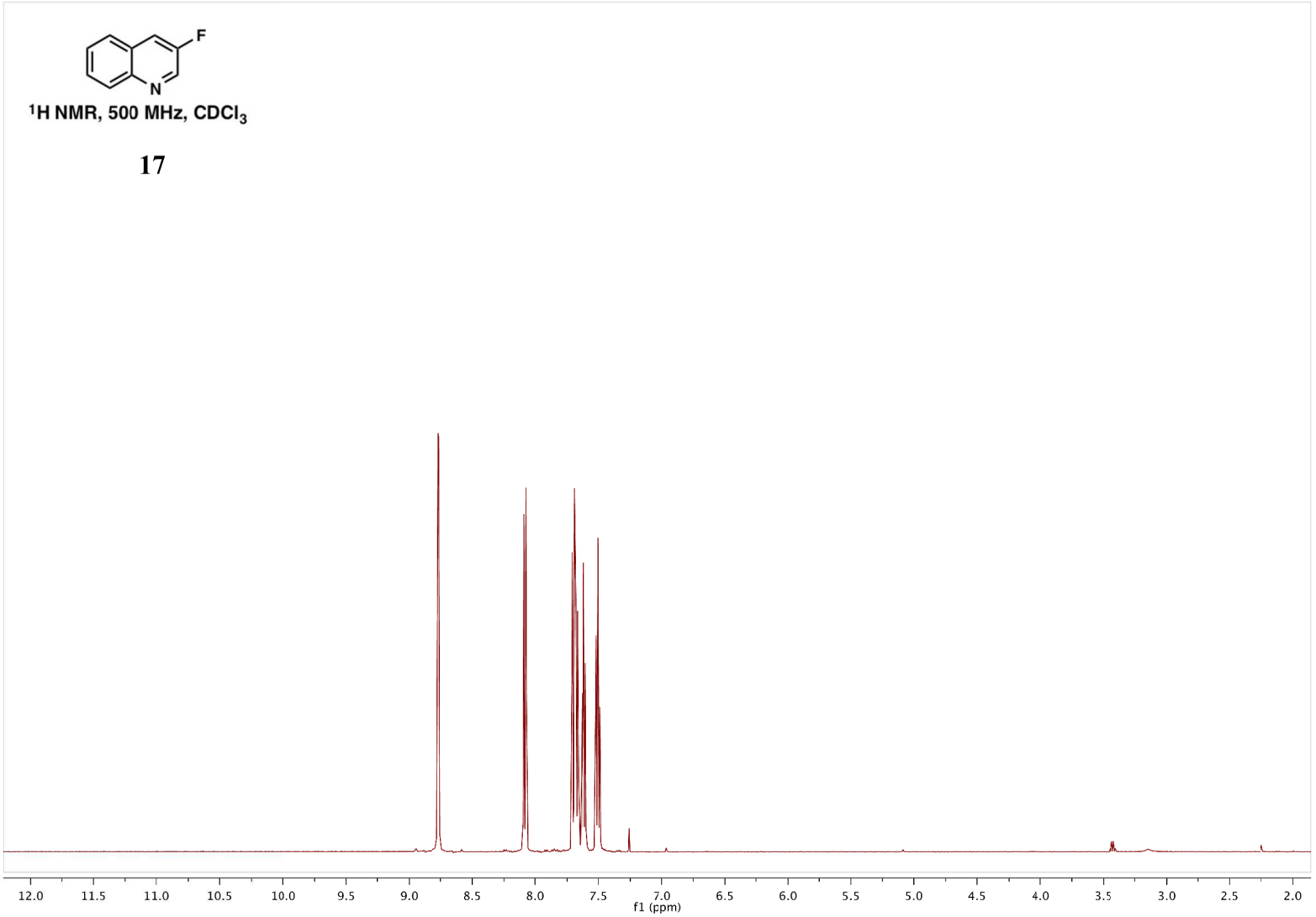


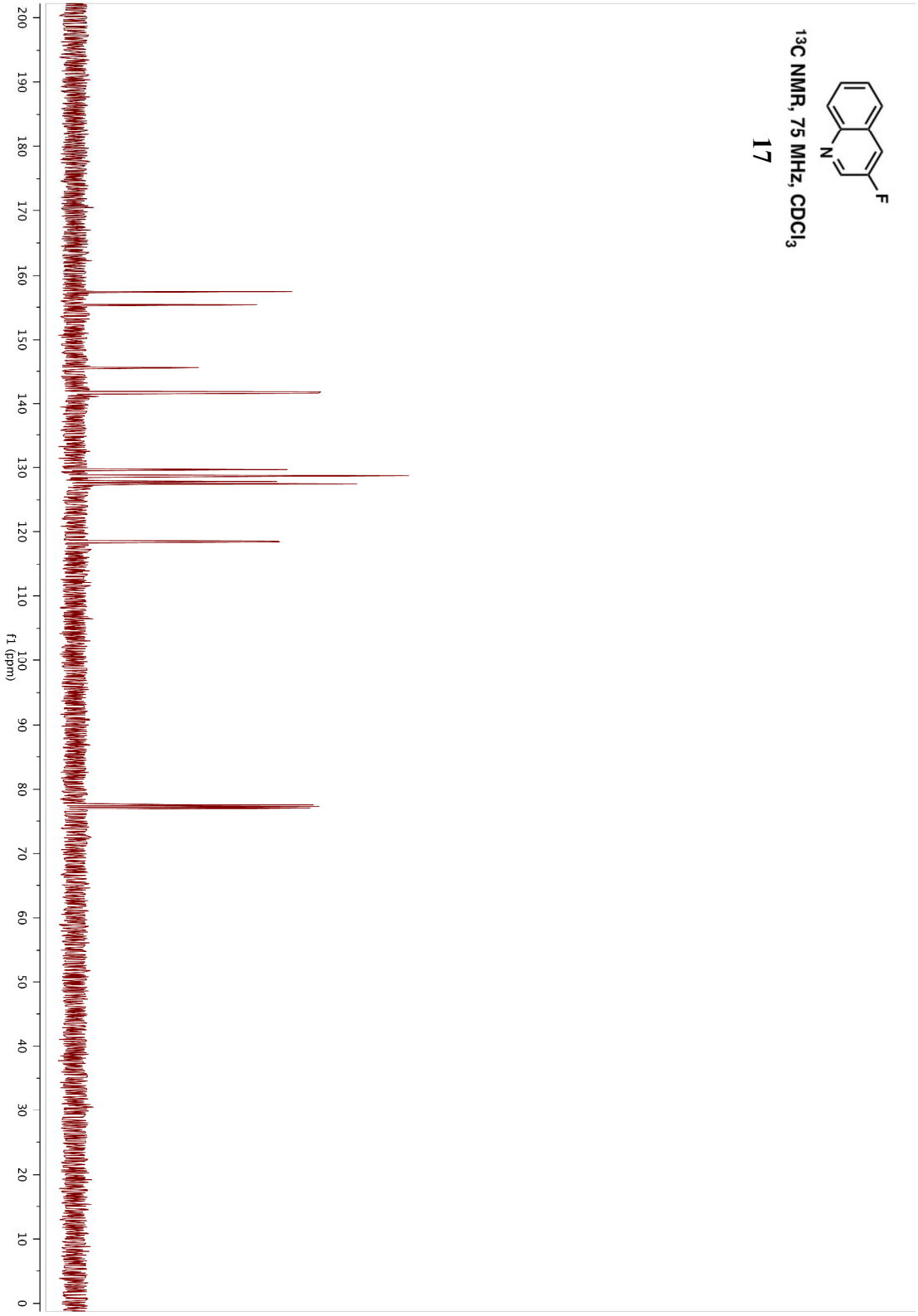
^{1}H NMR, 500 MHz, $CDCl_3$

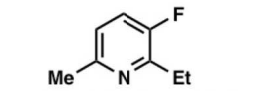
16




16
^{13}C NMR, 75 MHz, CDCl$_3$
CF$_3$
F
N
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

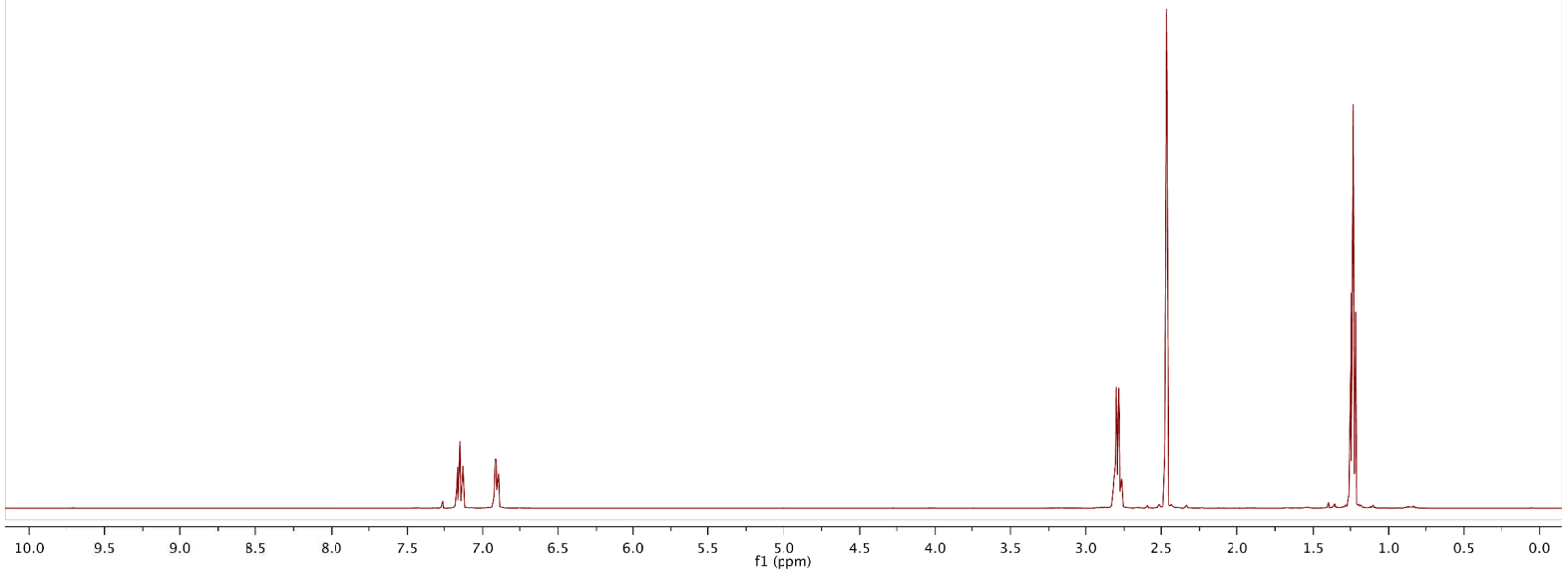

F
N
1H NMR, 500 MHz, CDCl3
17
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

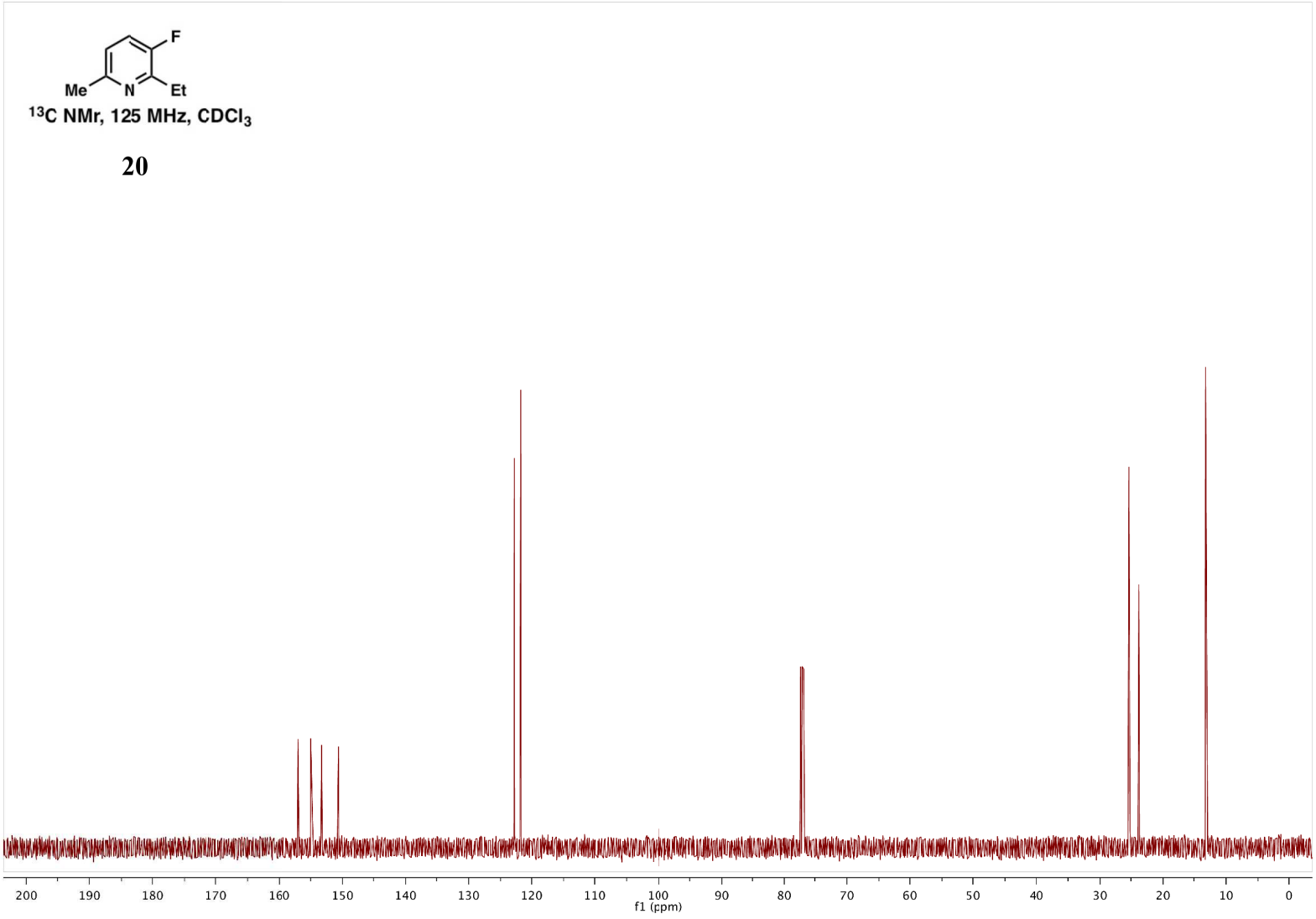

^{13}C NMR, 75 MHz, CDCl$_3$
17
F
N
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

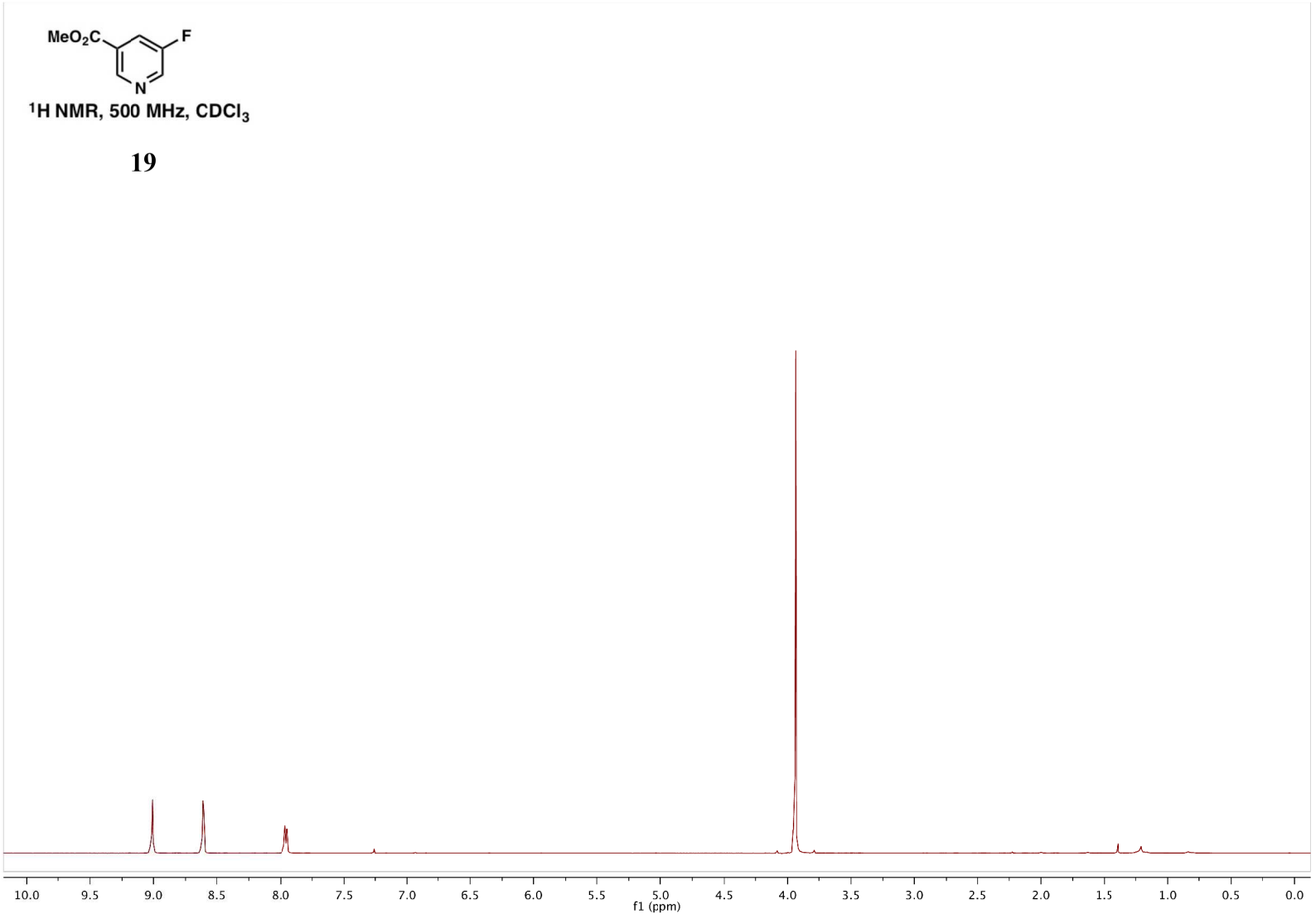


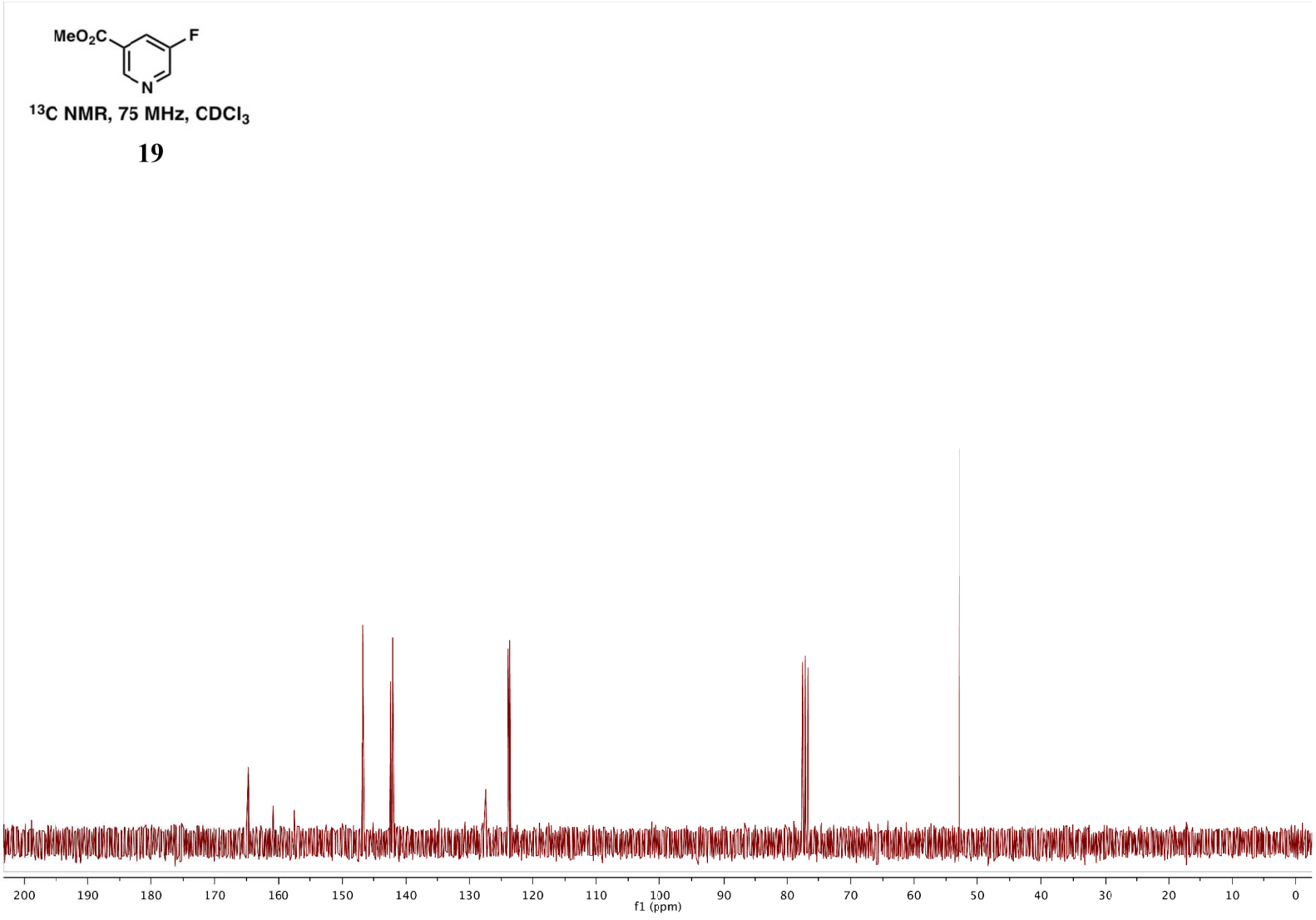
^{1}H NMr, 500 MHz, $CDCl_3$

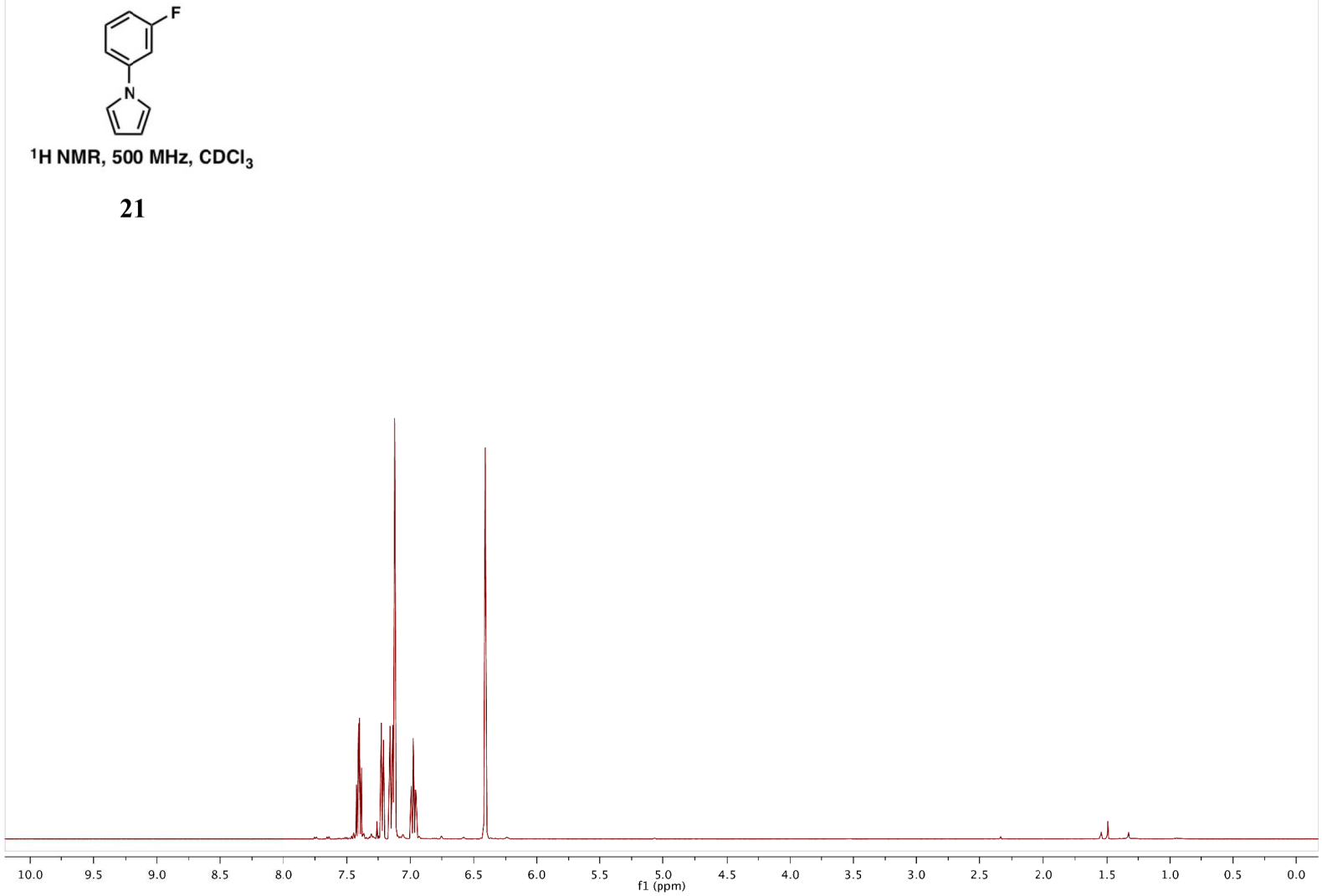
20

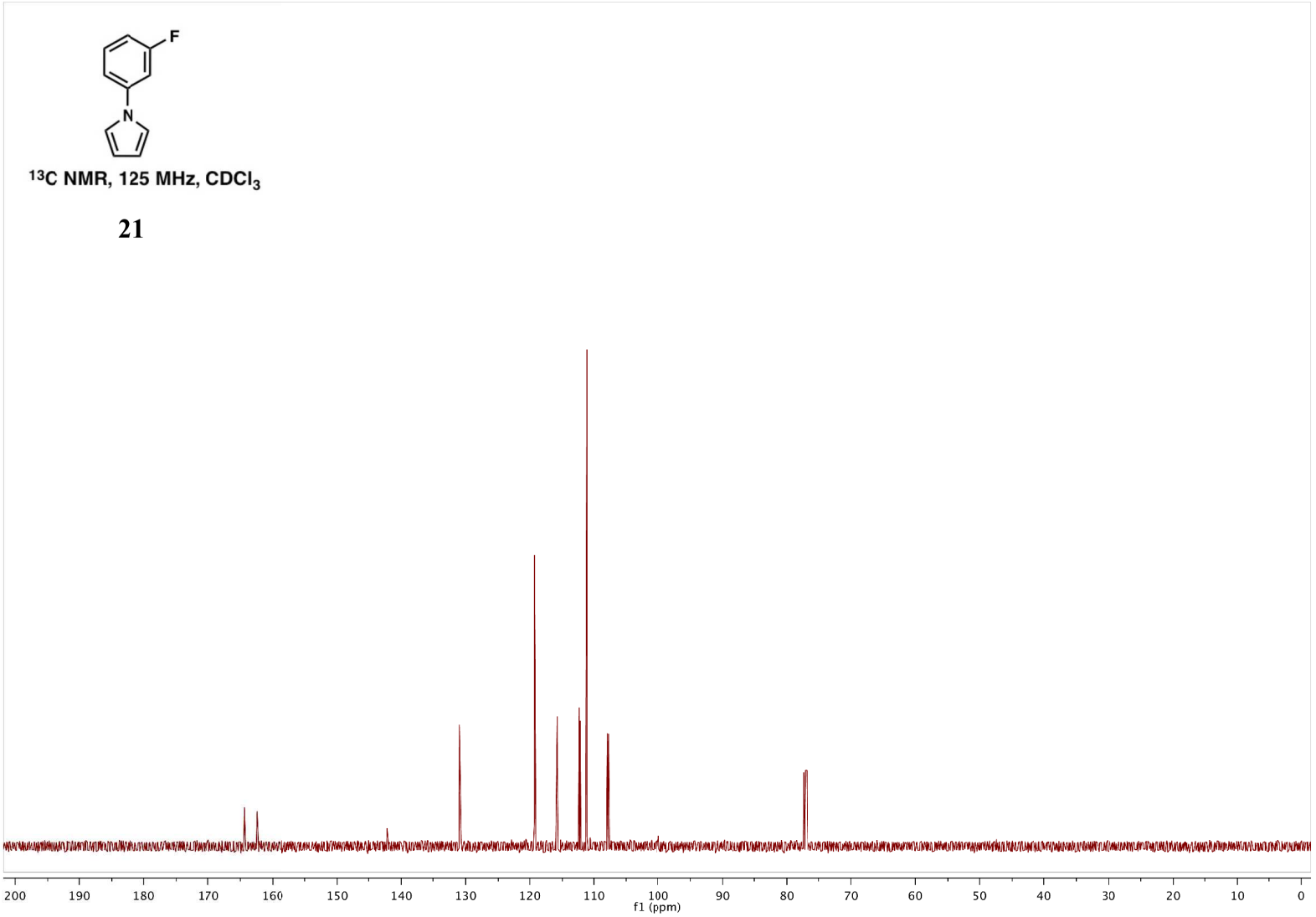


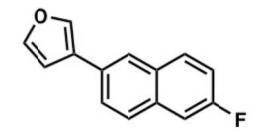

F
Me
N
Et
^{13}C NMr, 125 MHz, $CDCl_3$
20
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


MeO2C
F
N
1H NMR, 500 MHz, CDCl3
19
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


MeO2C
F
N
13C NMR, 75 MHz, CDCl3
19
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

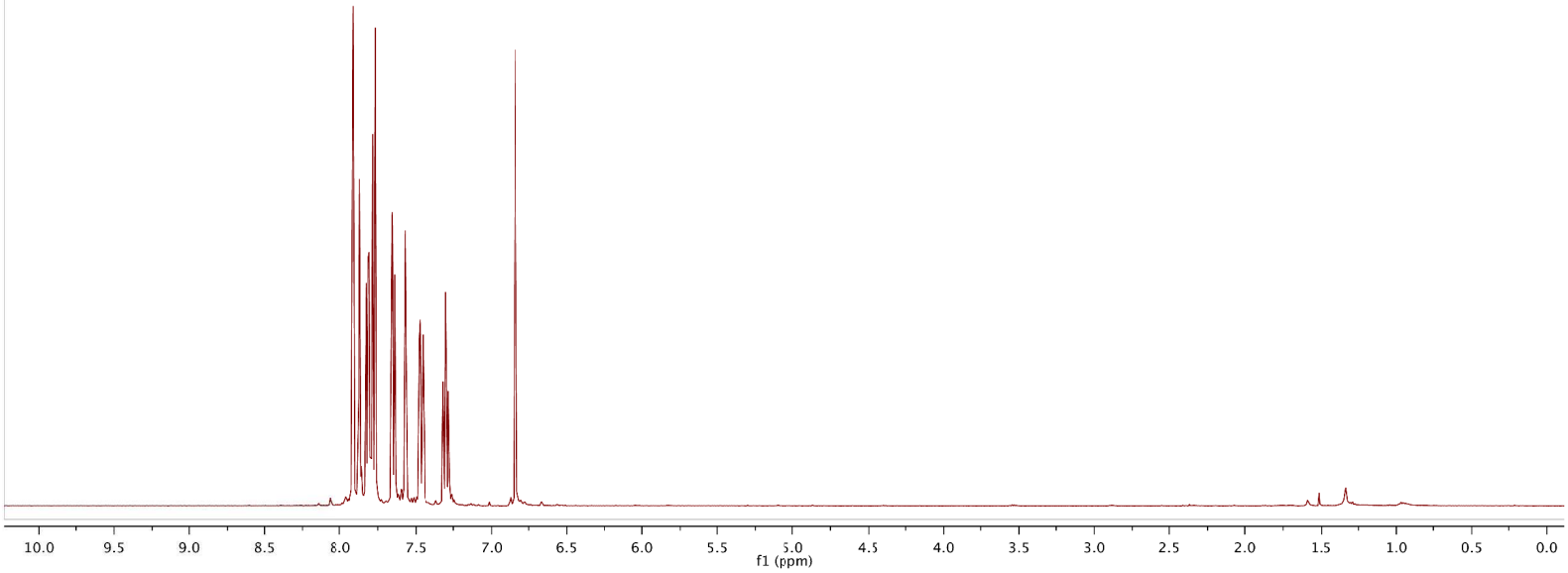

F
N
^{1}H NMR, 500 MHz, CDCl$_3$
21
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

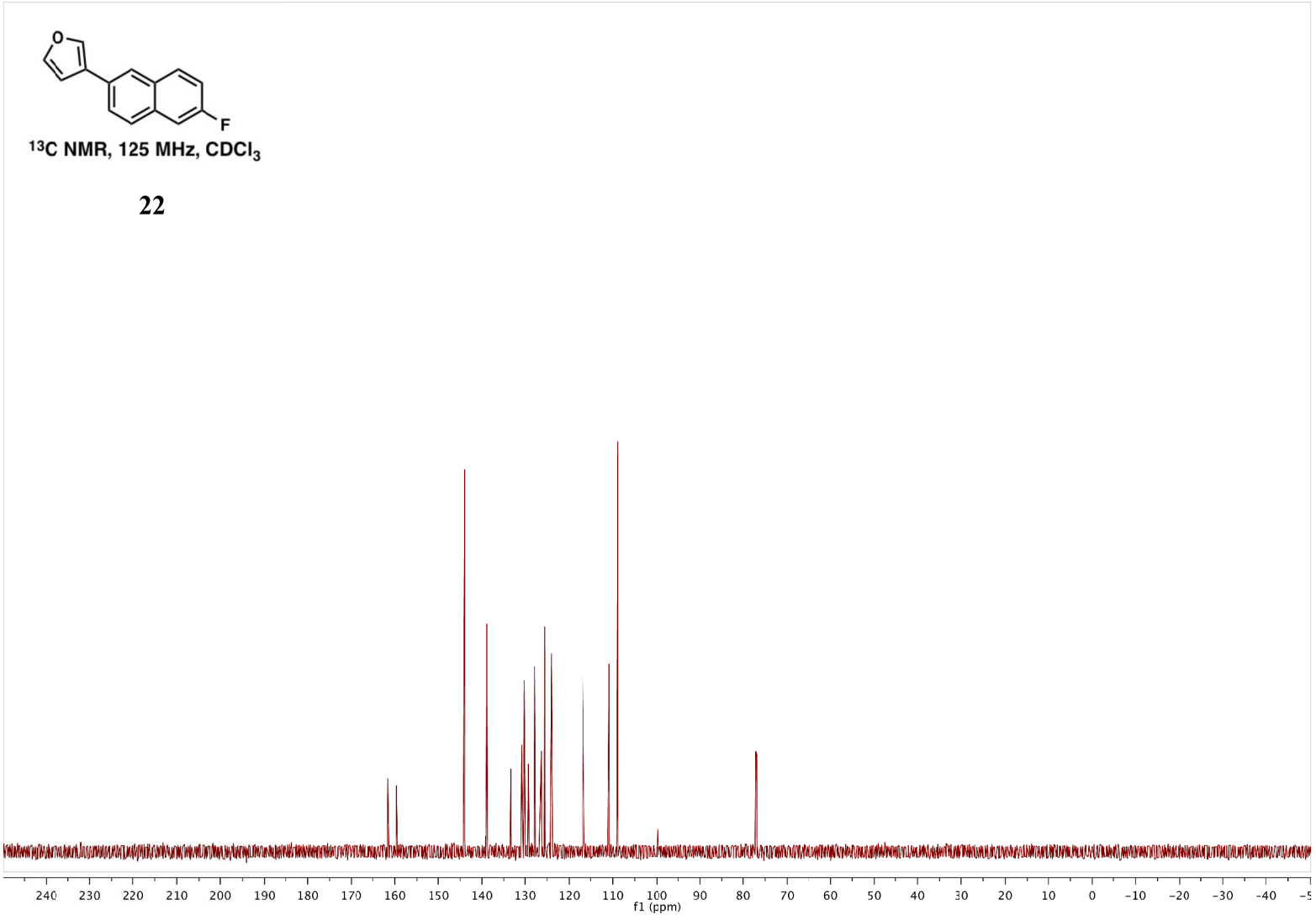

F
N
^{13}C NMR, 125 MHz, CDCl$_3$
21
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

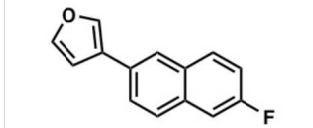


^{1}H NMR, 500 MHz, $CDCl_3$

22

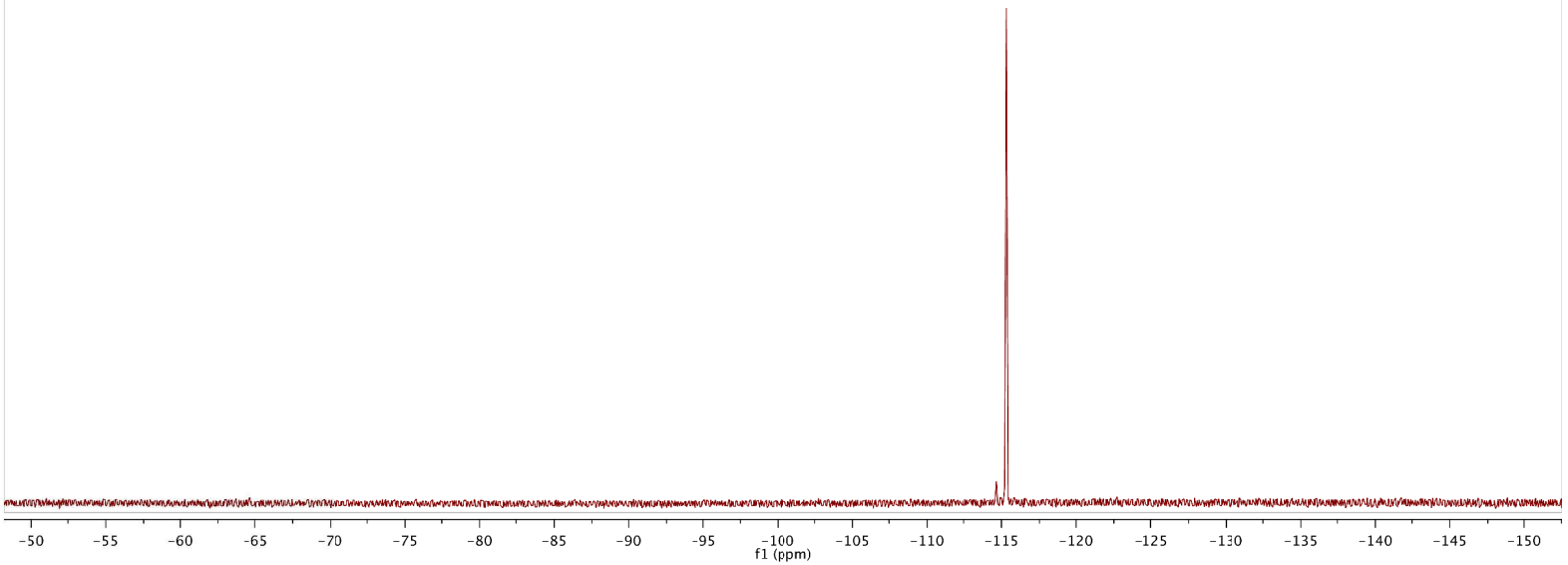


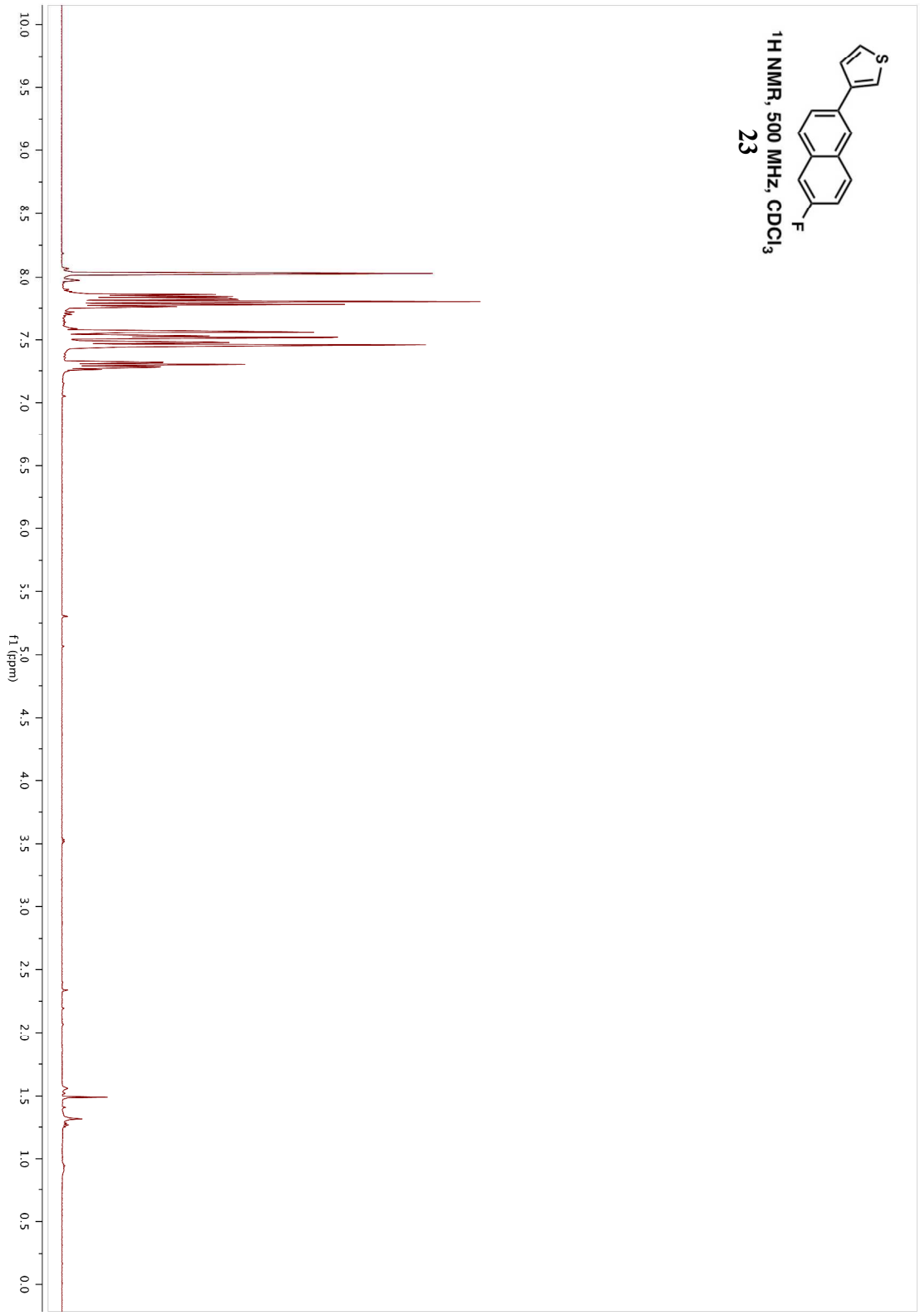

O
F
^{13}C NMR, 125 MHz, CDCl$_3$
22
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20 −30 −40
f1 (ppm)

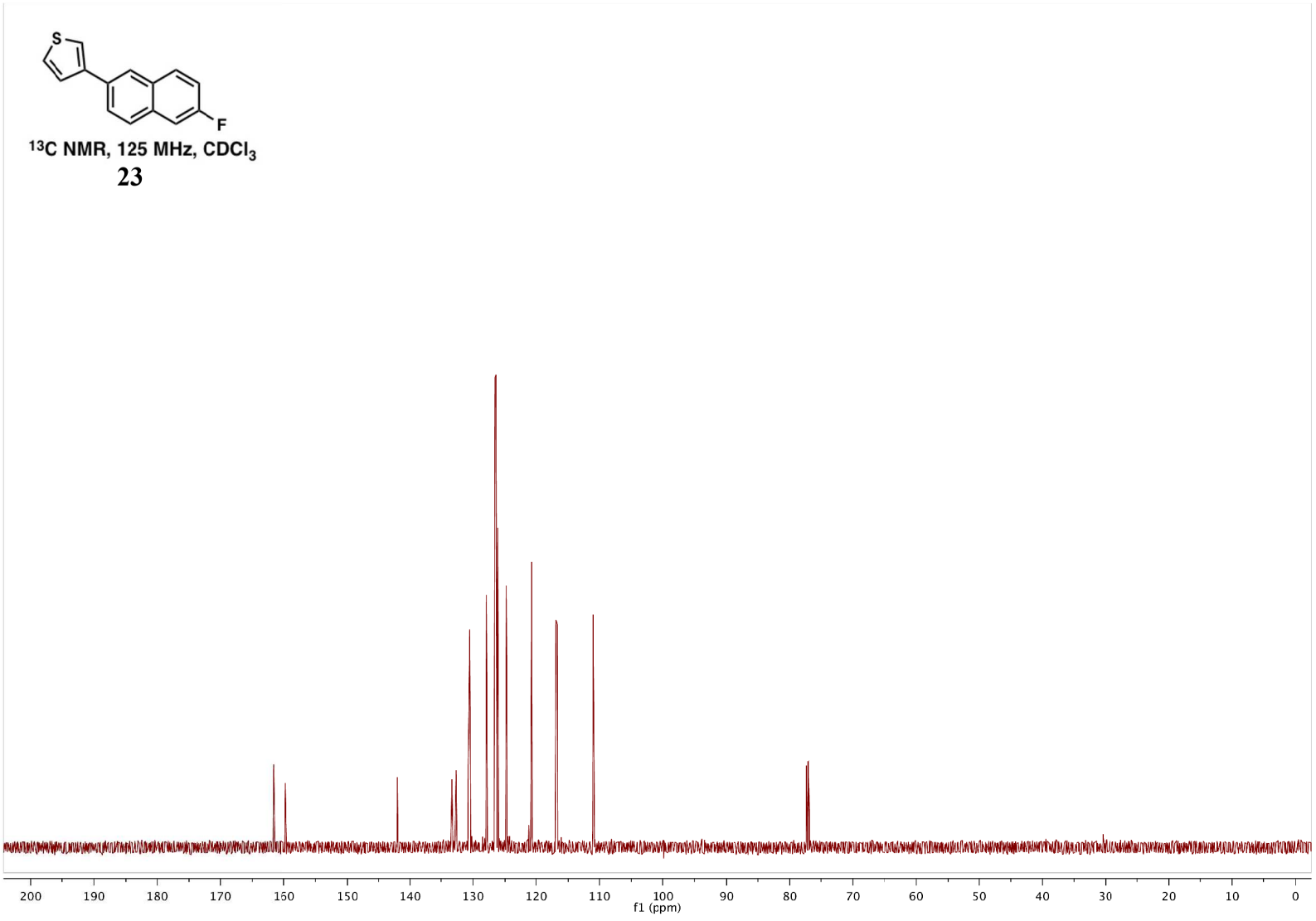


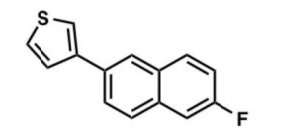
^{19}F NMR, 470 MHz, $CDCl_3$

22




S
F
^{1}H NMR, 500 MHz, CDCl$_3$
23
f1 (ppm)
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


S
F
^{13}C NMR, 125 MHz, CDCl$_3$
23
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



^{19}F NMR, 470 MHz, $CDCl_3$

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