

APPENDIX ONE

DEGREE OF SATURATION CONTROLLED HYDROGENATION OF COMPLEX

PYRIDINES: EXPERIMENTAL

A1.1 General Methods and Materials

Proton nuclear magnetic resonance (^1H NMR) spectra were recorded at ambient temperature on a Varian 400 MR spectrometer (400 MHz), an Agilent Inova 400 (400 MHz) spectrometer, an Agilent Inova 500 (500 MHz) spectrometer, or a Bruker AV-111 400 (400 MHz) spectrometer. Chemical shifts (δ) are reported in ppm and quoted to the nearest 0.1 ppm relative to the residual protons in CDCl_3 (7.26 ppm), CD_3OD (3.31 ppm), $(\text{CD}_3)_2\text{CO}$ (2.05 ppm), CD_3CN (1.94 ppm), D_2O (4.79 ppm), or $(\text{CD}_3)_2\text{SO}$ (2.50 ppm) and coupling constants (J) are quoted in Hertz (Hz). Data are reported as follows: Chemical shift (multiplicity, coupling constants, number of protons). Coupling constants were quoted to the nearest 0.1 Hz and multiplicity reported according to the following convention: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sext = sextet, sp = septet, m = multiplet, br = broad. Where coincident coupling constants have been observed, the apparent (app) multiplicity of the proton resonance has been reported. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at ambient temperature on a Varian 400 MR spectrometer (100 MHz), an Agilent Inova 400 (100 MHz) spectrometer, an Agilent Inova 500 spectrometer (125 MHz) or a Bruker AV-111 400 (100 MHz) spectrometer. Chemical shift (δ) was measured in ppm and quoted to the nearest 0.01 ppm relative to the residual solvent

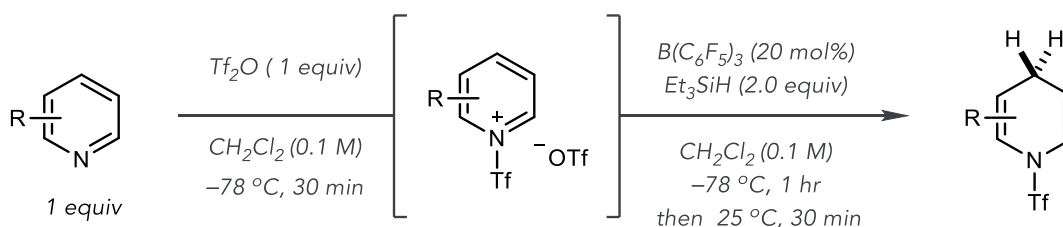
peaks in CDCl_3 (77.16 ppm), CD_3OD (49.00 ppm), $(\text{CD}_3)_2\text{CO}$ (29.84 ppm), CD_3CN (1.32 ppm), D_2O , or $(\text{CD}_3)_2\text{SO}$ (39.52 ppm).

Low-resolution mass spectra (LRMS) were measured on an Agilent 6310 Quadrupole Mass Spectrometer. High-resolution mass spectra (HRMS) were measured on an Agilent 6224 TOF LC/MS ("OTOF") interfaced to an Agilent 1200 HPLC with multi-mode (combined ESI and APCI) and Direct Analysis in Real Time (DART) sources. Infrared (IR) spectra were recorded on a Nicolet IS-50 FT-IR spectrometer as either solids or neat films, either through direct application or deposited in CHCl_3 , with absorptions reported in wavenumbers (cm^{-1}). Analytical thin layer chromatography (TLC) was performed using pre-coated Silicycle glass backed silica gel plates (Silicagel 60 F254). Manual flash column chromatography was undertaken on Silicycle silica gel Siliacflash P60 40-63 μm (230-400 mesh) under a positive pressure of air unless otherwise stated. Automated flash column chromatography was undertaken using a Teledyne Isco CombiFlash NextGen 300+ using 12 g RediSep Gold Normal-Phase Silica cartridges. Visualization was achieved using ultraviolet light (254 nm) and chemical staining with a chamber of I_2 in SiO_2 , ceric ammonium molybdate, or basic potassium permanganate solutions as appropriate. Melting points (mp) were recorded using a Büchi B-450 melting point apparatus and are reported uncorrected.

Dichloromethane, methanol, and triethylsilane were dried and distilled using standard methods. Trispentafluorophenyl borane was purchased from ChemScene and purified using standard methods until sufficiently pure by ^1H , ^{19}F , and ^{11}B NMR analysis. All other reagents were purchased at the highest commercial quality and used without further purification. Reactions were carried out under an atmosphere of nitrogen or hydrogen unless otherwise stated. All reactions were monitored by TLC, ^1H NMR spectra taken from reaction samples, and liquid

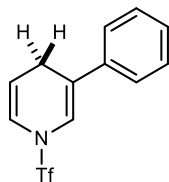
chromatography mass spectrometry (LCMS) using an Agilent 6310 Quadrupole Mass Spectrometer for MS analysis. $\text{ Tf}_2\text{O}$ (99%) was purchased from Oakwood Chemical and used without further purification but was routinely stored in a $-20\text{ }^\circ\text{C}$ fridge. Triethylsilane was purchased from Oakwood Chemical and used without purification. $[\text{Ir}(\text{cod})\text{Cl}]_2$ was purchased from Ambeed Inc. and used without further purification. 1,1'-bis(diphenylphosphino)ferrocene (dppf) was purchased from Combi-Blocks Inc and used without further purification.

General Procedure A: Preparation of 1,4-Dihydropyridines



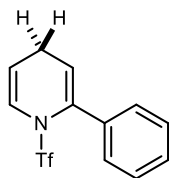
An oven-dried 8 mL vial (≤ 0.50 mmol scale) or a round bottom flask (> 0.50 mmol scale) equipped with a stir bar was charged with the heterocycle (1.0 equiv) placed under a nitrogen atmosphere (vacuum/nitrogen backfill, 3 cycles). $\text{ CH}_2\text{Cl}_2$ (0.1 M) was added, the reaction vessel cooled to $-78\text{ }^\circ\text{C}$. and $\text{ Tf}_2\text{O}$ (1.0 equiv) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes before $\text{ Et}_3\text{SiH}$ (2.0 equiv) was added dropwise via syringe followed by the $\text{ B}(\text{C}_6\text{F}_5)_3$ solution (0.2 equiv, 0.5 M solution in $\text{ CH}_2\text{Cl}_2$, freshly prepared). The reaction continued to stir at $-78\text{ }^\circ\text{C}$ for one hour. The cooling bath was removed, and the reaction warmed to room temperature with stirring (approximately 15-30 minutes). Then, the reaction solvent was removed *in vacuo* at room temperature until a minimal amount of solvent remains.

3-phenyl-1-((trifluoromethyl)sulfonyl)-1,4-dihydropyridine



Prepared according to the general reaction procedure A using freshly distilled 3-phenylpyridine (62 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The residue purified by a flash chromatography column to provide the pure title compound as a viscous colorless oil (silica gel: 100% Hexanes). (60 mg, 0.21 mmol, 52% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.30 – 7.15 (m, 5H), 6.74 (d, $J = 6.1$ Hz, 1H), 6.40 (dt, $J = 8.4, 2.3$ Hz, 1H), 5.24 – 5.15 (m, 1H), 3.11 (br, 2H). ^{19}F NMR (377 MHz, CDCl_3) δ -74.43. ^{13}C NMR (101 MHz, CDCl_3) δ 137.16, 128.48 (d, $J = 51.0$ Hz), 127.25 – 114.46 (m), 124.79, 121.23, 117.99, 109.72, 24.67.

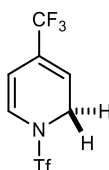
2-phenyl-1-((trifluoromethyl)sulfonyl)-1,4-dihydropyridine



Prepared according to the general reaction procedure A using freshly distilled 2-phenylpyridine (62 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The residue purified by a flash chromatography column to provide the pure title compound as a viscous colorless oil (silica gel: 100% Hexanes). (50 mg, 0.17 mmol, 43% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.46 – 7.28 (m, 5H), 6.64 (d, $J = 7.1$ Hz, 1H), 5.67 (dt, $J = 7.8, 4.0$ Hz, 1H), 5.61 (t, $J = 4.6$ Hz, 1H), 2.94 (t, $J = 4.7$ Hz, 2H). ^{19}F NMR (377 MHz, CDCl_3) δ -72.51. ^{13}C NMR (101 MHz, CDCl_3) δ 138.12,

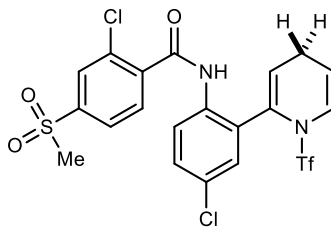
136.59, 128.31 (d, $J = 46.3$ Hz), 126.81 (d, $J = 37.2$ Hz), 124.87 – 113.57 (m), 119.02, 118.42, 23.90.

4-(trifluoromethyl)-1-((trifluoromethyl)sulfonyl)-1,2-dihydropyridine



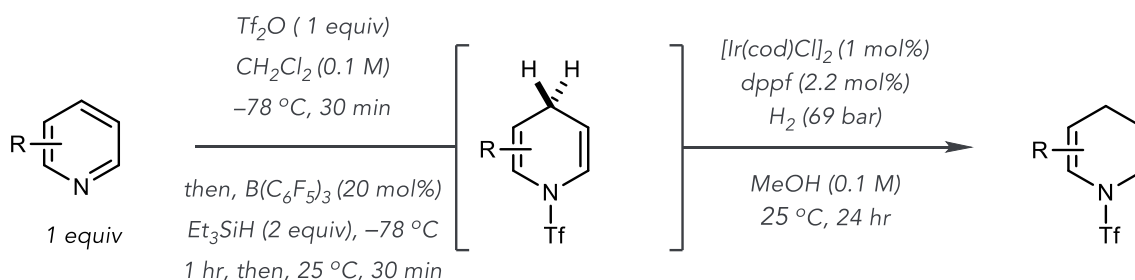
Prepared according to the general reaction procedure A using freshly distilled 2-phenylpyridine (59 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The residue purified by a flash chromatography column to provide the pure title compound as a viscous colorless oil (silica gel: 100% Hexanes). (67 mg, 0.24 mmol, 60% yield). ^1H NMR (400 MHz, CDCl_3) δ 6.53 (d, $J = 7.8$ Hz, 1H), 6.02 (tp, $J = 3.3, 1.6$ Hz, 1H), 5.63 (dd, $J = 7.9, 1.9$ Hz, 1H), 4.44 (dt, $J = 3.1, 1.6$ Hz, 2H). ^{19}F NMR (377 MHz, CDCl_3) δ -68.94 (q, $J = 2.8$ Hz), -75.47. ^{13}C NMR (101 MHz, CDCl_3) δ 134.49 – 113.98 (m), 127.59 – 120.51 (m), 127.00, 123.21, 119.08 (q, $J = 5.7$ Hz), 106.40 – 106.02 (m), 44.52. Isolated with 3% impurity.

4-(trifluoromethyl)-1-((trifluoromethyl)sulfonyl)-1,2-dihydropyridine



Prepared according to the general reaction procedure A using fresh 2-chloro-N-(4-chloro-2-(1-((trifluoromethyl)sulfonyl)-1,4-dihydropyridin-2-yl)phenyl)-4-(methylsulfonyl)benzamide (168 mg, 0.40 mmol), Ti_2O (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The residue purified by a flash chromatography column to provide the pure title compound as a viscous colorless oil (silica gel: 100% Hexanes). (42 mg, 0.08 mmol, 19% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.38 (s, 1H), 7.89 (s, 1H), 7.78 (d, $J = 2.9$ Hz, 2H), 7.72 (d, $J = 2.6$ Hz, 1H), 7.54 (dd, $J = 8.7, 2.6$ Hz, 1H), 7.36 (d, $J = 8.6$ Hz, 1H), 5.61 (q, $J = 3.5, 2.9$ Hz, 1H), 3.05 (s, 3H), 2.97 (t, $J = 4.2$ Hz, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -73.16. ^{13}C NMR (101 MHz, CDCl_3) δ 163.19, 142.80, 140.30, 135.96, 135.84, 134.34, 132.43, 130.79, 130.09, 129.09, 128.99, 125.91, 125.87, 125.01 – 115.23 (m), 122.56, 121.38, 121.35, 116.64, 44.45, 23.66.

General Procedure B: Preparation of Tetrahydropyridines



An oven-dried 8 mL vial (≤ 0.50 mmol scale) or a round bottom flask (> 0.50 mmol scale) equipped with a stir bar was charged with the heterocycle (1.0 equiv) placed under a nitrogen atmosphere (vacuum/nitrogen backfill, 3 cycles). CH_2Cl_2 (0.1 M) was added, the reaction vessel cooled to -78°C . and Ti_2O (1.0 equiv) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes before Et_3SiH (2.0 equiv) was added dropwise via syringe followed by the

B(C₆F₅)₃ solution (0.2 equiv, 0.5 M solution in CH₂Cl₂, freshly prepared). The reaction continued to stir at –78 °C for one hour. The cooling bath was removed, and the reaction warmed to room temperature with stirring (approximately 15-30 minutes). Then, the reaction solvent was removed *in vacuo* at room temperature until a minimal amount of solvent remains. The reaction mixture was then slowly dissolved in the freshly prepared [Ir(cod)Cl]₂/dppf solution in methanol and transferred to the appropriately sized vial (refer to Preparation of the [Ir(cod)Cl]₂/dppf Solution for more details). The glass vial was placed in a 150 ml stainless steel autoclave under air. The autoclave was pressurized and depressurized four times with hydrogen gas before the final pressure was set (69 bar). The reaction stirred at room temperature for 24 hours with appropriate shielding. Then, the pressure was carefully released. The reaction was concentrated *in vacuo* and isolated according to the following procedures (refer to Product Isolation Guidelines for more details).

Preparation of the [Ir(cod)Cl]₂/dppf Solution:

An oven-dried 8 mL vial (≤ 0.50 mmol scale) or a round bottom flask (> 0.50 mmol scale) equipped with a stir bar was charged with [Ir(cod)Cl]₂ (0.01 equiv) and dppf (0.022 equiv) in a glovebox under a nitrogen atmosphere. The vessel was sealed with a rubber septum in the glovebox and removed. Then, an Argon filled balloon was pierced through the septum before MeOH (0.1 M) was added. The solution stirred (500 rpm) at room temperature under Argon atmosphere for 3 hours prior to introduction of the solution described above.

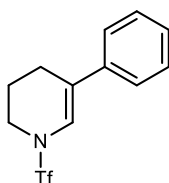
General Isolation Procedure

The reaction was dissolved in EtOAc and H₂O. The organic layer was then washed with H₂O (3x), then washed with a saturated aqueous solution of brine (1x), dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography under the stated conditions to provide the tetrahydropyridine product.

Safety Notes

High pressures of hydrogen gas have increased risk of explosion. Use caution and appropriate blast shielding and personal protection equipment.

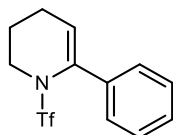
5-phe-nyl-1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydropyridine



Prepared according to the general reaction procedure B using freshly distilled 3-phenylpyridine (62 mg, 0.40 mmol), Tf₂O (67 μ L, 0.40 mmol), Et₃SiH (130 μ L, 0.8 mmol), B(C₆F₅)₃ (51 mg, 0.08 mmol), CH₂Cl₂ (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then [Ir(cod)Cl]₂ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a pale-yellow oil (silica gel: 0 to 10% EtOAc in Hexanes). (101 mg, 0.35 mmol, 87% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.27 (s, 1H), 7.27 – 7.10 (m, 3H), 6.82 (s, 1H), 3.72 – 3.65 (m, 2H), 2.45 (t, *J* = 6.6 Hz, 2H), 2.01 (p, *J* = 6.2 Hz, 1H). ¹⁹F NMR (376 MHz, CDCl₃) δ -74.59. ¹³C NMR (101 MHz,

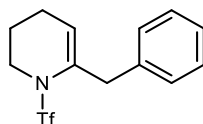
CDCl₃) δ 138.61, 128.66, 127.51, 125.03, 129.06 – 118.12 (m), 122.73, 120.02, 45.19, 23.88, 21.65.

6-phenyl-1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydropyridine



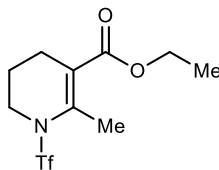
Prepared according to the general reaction procedure B using freshly distilled 2-phenylpyridine (62 mg, 0.40 mmol), Tf₂O (67 μ L, 0.40 mmol), Et₃SiH (130 μ L, 0.8 mmol), B(C₆F₅)₃ (51 mg, 0.08 mmol), CH₂Cl₂ (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then [Ir(cod)Cl]₂ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 5% EtOAc in Hexanes). (78 mg, 0.27 mmol, 67% yield). mp 60-62 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.24 (d, *J* = 5.5 Hz, 5H), 5.50 (t, *J* = 3.9 Hz, 1H), 3.78 – 3.70 (m, 2H), 2.32 – 2.23 (m, 2H), 1.97 (p, *J* = 7.0 Hz, 2H). ¹⁹F NMR (376 MHz, CDCl₃) δ -74.46. ¹³C NMR (101 MHz, CDCl₃) δ 137.97, 137.77, 128.24, 127.92, 127.07, 121.44, 123.85 – 114.83 (m), 48.76, 22.42, 22.23 (d, *J* = 1.7 Hz).

6-benzyl-1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydropyridine



Prepared according to the general reaction procedure B using freshly distilled 2-benzylpyridine (68 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a yellow oil (silica gel: 0 to 10% EtOAc in Hexanes). (53 mg, 0.17 mmol, 43% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.22 (d, $J = 14.5$ Hz, 2H), 7.12 (m, 3H), 5.08 (t, $J = 3.9$ Hz, 1H), 3.65 (s, 2H), 3.59 – 3.51 (m, 2H), 2.14 – 2.05 (m, 2H), 1.90 – 1.80 (m, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -74.49. ^{13}C NMR (101 MHz, CDCl_3) δ 137.96, 137.73, 129.03, 128.22, 127.91, 127.05, 126.55, 125 – 114.82 (m) 121.47, 48.75, 22.40, 22.20.

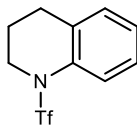
Ethyl 2-methyl-1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridine-3-carboxylate



Prepared according to the general reaction procedure B using freshly distilled ethyl 2-methylnicotinate (66 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The

reaction solvent was removed *in vacuo* at room temperature, then [Ir(cod)Cl]₂ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a colorless oil (silica gel: 0 to 15% EtOAc in Hexanes). (91 mg, 0.30 mmol, 76% yield). ¹H NMR (400 MHz, CDCl₃) δ 4.20 – 4.10 (m, 2H), 3.61 – 3.52 (m, 2H), 2.42 – 2.35 (m, 2H), 2.30 (s, 3H), 1.96 – 1.86 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). ¹⁹F NMR (376 MHz, CDCl₃) δ -75.91. ¹³C NMR (101 MHz, CDCl₃) δ 167.74, 141.75, 124.25 – 114.29 (m), 120.14, 60.92, 48.31, 24.08, 22.89, 19.49, 14.18.

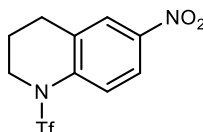
1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydroquinoline



Prepared according to the general reaction procedure B using freshly distilled quinoline (52 mg, 0.40 mmol), Tf₂O (67 μL, 0.40 mmol), Et₃SiH (130 μL, 0.8 mmol), B(C₆F₅)₃ (51 mg, 0.08 mmol), CH₂Cl₂ (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then [Ir(cod)Cl]₂ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 5% EtOAc in Hexanes). (76 mg, 0.28 mmol, 72% yield). mp 33-37 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, *J* = 8.0 Hz, 1H), 7.10 (dt, *J* = 14.6, 4.6 Hz, 3H), 3.79 (t, *J* =

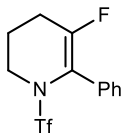
6.1 Hz, 2H), 2.79 (t, $J = 6.9$ Hz, 2H), 2.03 (p, $J = 6.6$ Hz, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.29. ^{13}C NMR (101 MHz, CDCl_3) δ 135.32, 130.93, 129.50, 126.82, 126.18, 124.47 – 115.84, 123.38, 47.98, 26.15, 23.42.

6-nitro-1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydroquinoline



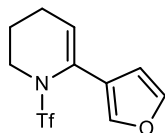
Prepared according to the general reaction procedure B using freshly distilled 6-nitroquinoline (70 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a yellow solid (silica gel: 0 to 5% EtOAc in Hexanes). (92 mg, 0.30 mmol, 74% yield). mp $46\text{--}49^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 8.04 (d, $J = 10.5$ Hz, 1H), 7.72 (d, $J = 9.9$ Hz, 1H), 3.92 (t, $J = 6.0$ Hz, 1H), 2.99 (t, $J = 6.9$ Hz, 1H), 2.21 – 2.08 (m, 1H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.05. ^{13}C NMR (101 MHz, CDCl_3) δ 144.94, 140.80, 131.35, 124.98, 125.97 – 116.22 (m), 123.53, 122.21, 48.33, 26.73, 22.68.

5-fluoro-6-phenyl-1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydropyridine



Prepared according to the general reaction procedure B using 3-fluoro-2-phenylpyridine (69 mg, 0.40 mmol), $\text{ Tf}_2\text{O}$ (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a colorless oil (silica gel: 100% Hexanes). (82 mg, 0.26 mmol, 66% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.34 – 7.20 (m, 5H), 3.72 – 3.65 (m, 2H), 2.52 – 2.44 (m, 2H), 2.13 (p, $J = 5.9$ Hz, 2H). ^{19}F NMR (377 MHz, CDCl_3) δ -74.65, -115.15. ^{13}C NMR (101 MHz, CDCl_3) δ 154.41 (d, $J = 258.1$ Hz), 131.43, 128.61, 127.93, 124.24 – 114.57 (m) 121.92, 48.47, 23.65 (d, $J = 22.9$ Hz), 23.11 (d, $J = 8.3$ Hz).

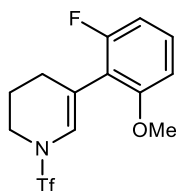
6-(furan-3-yl)-1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydropyridine



Prepared according to the general reaction procedure B using freshly distilled 2-(furan-3-yl)pyridine (58 mg, 0.40 mmol), $\text{ Tf}_2\text{O}$ (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9

mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a yellow oil (silica gel: 0 to 10% EtOAc in Hexanes) (56 mg, 0.20 mmol, 50% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.38 (s, 1H), 7.27 (s, 1H), 6.35 (s, 1H), 5.52 (t, *J* = 4.0 Hz, 2H), 3.73 – 3.66 (m, 2H), 2.28 – 2.19 (m, 2H), 1.96 (p, *J* = 7.0 Hz, 3H). ¹⁹F NMR (376 MHz, CDCl₃) δ -74.64. ¹³C NMR (101 MHz, CDCl₃) δ 142.44, 140.21, 129.54, 123.43, 124.82 – 114.82, 120.29, 110.18, 48.58, 47.51, 22.21. Isolated with 5% impurity.

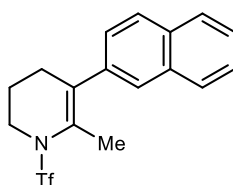
5-(2-fluoro-6-methoxyphenyl)-1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydropyridine



Prepared according to the general reaction procedure B using freshly prepared 3-(2-fluoro-6-methoxyphenyl)pyridine (81 mg, 0.40 mmol), Tf₂O (67 μL, 0.40 mmol), Et₃SiH (130 μL, 0.8 mmol), B(C₆F₅)₃ (51 mg, 0.08 mmol), CH₂Cl₂ (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then [Ir(cod)Cl]₂ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a yellow oil (silica gel: 0 to 60% EtOAc in Hexanes) (72 mg, 0.21 mmol, 53% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.17 – 7.06 (m, 1H), 6.66 – 6.56 (m, 2H), 6.45 (s, 1H), 3.71

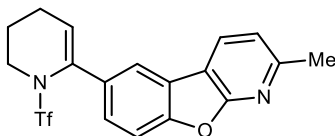
(m, 5H), 2.28 (t, $J = 6.4$ Hz, 2H), 1.97 (p, $J = 6.3$ Hz, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.08, -114.66. ^{13}C NMR (101 MHz, CDCl_3) δ 161.88, 159.45, 158.54 (d, $J = 6.7$ Hz), 128.87 (d, $J = 10.7$ Hz), 124.84 – 115.15, 123.26, 121.61, 118.38, 115.15, 114.09, 108.17 (d, $J = 23.3$ Hz), 106.51, 55.96, 45.29, 25.10, 21.65.

6-methyl-5-(naphthalen-2-yl)-1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydropyridine



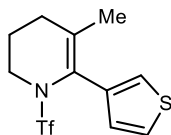
Prepared according to the general reaction procedure B using fresh 2-methyl-3-(naphthalen-2-yl)pyridine (88 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a brown solid (silica gel: 0 to 60% EtOAc in Hexanes) (100 mg, 0.28 mmol, 70% yield). mp $85\text{--}88^\circ\text{C}$ ^1H NMR (400 MHz, CDCl_3) δ 7.84 – 7.77 (m, 1H), 7.76 – 7.67 (m, 2H), 7.51 – 7.36 (m, 3H), 7.18 (d, $J = 7.0$ Hz, 1H), 3.91 – 3.70 (m, 1H), 2.42 – 2.32 (m, 1H), 2.08 (d, $J = 7.4$ Hz, 1H), 1.69 (s, 3H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.96. ^{13}C NMR (101 MHz, CDCl_3) δ 138.62, 133.84, 130.75, 128.67, 127.73, 126.62, 125.99 (d, $J = 16.3$ Hz), 125.69, 124.58, 48.75, 29.68, 23.84, 18.58.

2-methyl-6-(1-(((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridin-2-yl)benzofuro[2,3-b]pyridine



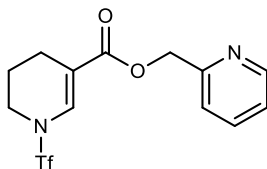
Prepared according to the general reaction procedure B using fresh 2-methyl-6-(pyridin-2-yl)benzofuro[2,3-b]pyridine (104 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (8.1 mg, 0.012 mmol) and dppf (14.7 mg, 0.026 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 60% EtOAc in Hexanes) (128 mg, 0.32 mmol, 81% yield). mp $185\text{--}188^\circ\text{C}$ ^1H NMR (400 MHz, CDCl_3) δ 8.03 (d, $J = 7.8$ Hz, 1H), 7.75 (d, $J = 9.0$ Hz, 1H), 7.33 (d, $J = 7.6$ Hz, 1H), 7.24 (t, $J = 7.6$ Hz, 1H), 7.10 (d, $J = 7.8$ Hz, 1H), 5.75 (t, $J = 3.9$ Hz, 1H), 3.96 – 3.89 (m, 2H), 2.61 (s, 3H), 2.40 – 2.31 (m, 2H), 2.09 – 1.99 (m, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -74.94. ^{13}C NMR (101 MHz, CDCl_3) δ 162.95, 156.45, 151.51, 132.47, 129.97, 127.44, 123.94 – 114.77 (m), 123.34, 122.93, 122.72, 122.63, 120.86, 118.93, 48.49, 24.49, 22.58, 22.25.

5-methyl-6-(thiophen-3-yl)-1-(((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydropyridine



Prepared according to the general reaction procedure B using fresh 3-methyl-2-(thiophen-3-yl)pyridine (70 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a tan oil (silica gel: 0 to 10% EtOAc in Hexanes) (95 mg, 0.30 mmol, 76% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.17 (dd, $J = 4.9, 2.9$ Hz, 1H), 7.12 – 7.05 (m, 1H), 6.90 (d, $J = 5.0$ Hz, 1H), 3.70 – 3.62 (m, 2H), 2.18 (t, $J = 7.1$ Hz, 2H), 2.03 – 1.92 (m, 2H), 1.58 (s, 3H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.73. ^{13}C NMR (101 MHz, CDCl_3) δ 136.46, 128.87, 128.04, 126.34, 125.18, 124.36 – 112.39 (m), 124.26, 48.46, 28.47, 23.68, 20.26.

pyridin-2-ylmethyl 1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridine-3-carboxylate



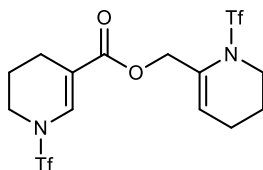
Prepared according to the general reaction procedure B using fresh pyridin-2-ylmethyl nicotinate (86 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg,

0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 50% EtOAc in Hexanes) (95 mg, 0.30 mmol, 76% yield). mp 77-78 °C ^1H NMR (400 MHz, CDCl_3) δ 8.53 (d, J = 5.4 Hz, 1H), 7.64 (d, J = 9.5 Hz, 2H), 7.28 (d, J = 7.8 Hz, 1H), 7.20 – 7.14 (m, 1H), 5.26 (s, 2H), 3.70 – 3.62 (m, 2H), 2.37 (t, J = 6.3 Hz, 2H), 1.91 (p, J = 6.3 Hz, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.14. ^{13}C NMR (101 MHz, CDCl_3) δ 165.59, 155.74, 149.45, 136.90, 133.43, 124.36 – 112.39 (m), 122.36 (d, J = 119.8 Hz), 113.52, 66.99, 45.67, 29.70, 20.68.

(1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridin-2-yl)methyl

1-

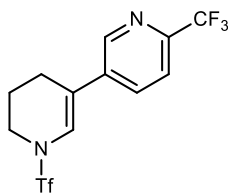
((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridine-3-carboxylate



Prepared according to the general reaction procedure B using freshly distilled ethyl 2-methylnicotinate (86 mg, 0.40 mmol), TiF_4 (134 μL , 0.80 mmol), Et_3SiH (260 μL , 1.6 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (8.1 mg, 0.012 mmol) and dppf (14.7 mg, 0.026 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a yellow oil (80 mg, 0.16 mmol, 41% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.58

(s, 1H), 5.58 (t, $J = 3.8$ Hz, 1H), 4.81 (s, 2H), 3.69 – 3.59 (m, 4H), 2.31 (t, $J = 5.4$ Hz, 2H), 2.23 – 2.14 (m, 2H), 1.97 – 1.83 (m, 4H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.23, -75.71. ^{13}C NMR (101 MHz, CDCl_3) δ 165.29, 133.90 – 121.24 (m) 133.52 (d, $J = 6.9$ Hz), 132.15, 121.75, 113.42, 113.10 – 125.72 (m), 64.54, 48.62, 45.64 (d, $J = 2.4$ Hz), 22.25, 22.11, 20.65, 20.47. Isolated with 12% dihydropyridine.

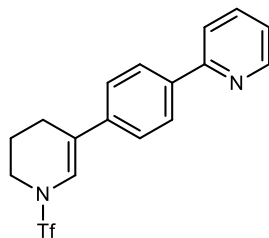
6'-(trifluoromethyl)-1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydro-3,3'-bipyridine



Prepared according to the general reaction procedure B using fresh 6-(trifluoromethyl)-3,3'-bipyridine (90 mg, 0.40 mmol), Ti_2O (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 60% EtOAc in Hexanes) (75 mg, 0.21 mmol, 52% yield). mp $59\text{--}61^\circ\text{C}$ ^1H NMR (400 MHz, CDCl_3) δ 8.63 (s, 1H), 7.73 (d, $J = 8.3$ Hz, 1H), 7.58 (d, $J = 8.3$ Hz, 1H), 6.93 (s, 1H), 3.77 – 3.69 (m, 2H), 2.49 (t, $J = 6.3$ Hz, 2H), 2.13 – 2.04 (m, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -67.78, -75.06. ^{13}C NMR (101 MHz, CDCl_3) δ 146.96, 146.61, 146.51,

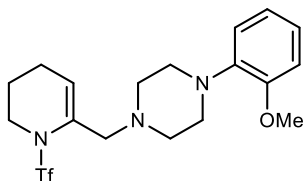
137.10, 133.24, 125.64 – 114.97 (m), 124.64 - 117.44 (m), 122.89, 120.34, 118.24 (d, $J = 9.1$ Hz), 45.13, 23.40, 21.31.

2-(4-(1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridin-3-yl)phenyl)pyridine



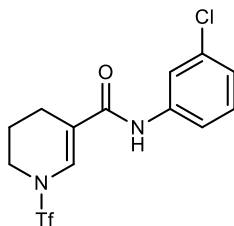
Prepared according to the general reaction procedure B using fresh 2-(4-(pyridin-3-yl)phenyl)pyridine (93 mg, 0.40 mmol), $\text{ Tf}_2\text{O}$ (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 40% EtOAc in Hexanes) (87 mg, 0.24 mmol, 59% yield). mp $113\text{--}115^\circ\text{C}$ ^1H NMR (400 MHz, CDCl_3) δ 8.60 (d, $J = 6.1$ Hz, 1H), 7.90 (d, $J = 8.5$ Hz, 2H), 7.66 (d, $J = 6.4$ Hz, 2H), 7.37 (s, 2H), 7.16 – 7.10 (m, 1H), 6.90 (s, 1H), 3.72 – 3.64 (m, 2H), 2.47 (t, $J = 7.1$ Hz, 2H), 2.01 (p, $J = 6.3$ Hz, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -74.97. ^{13}C NMR (101 MHz, CDCl_3) δ 156.67, 149.65, 139.11, 138.30, 136.89, 127.11, 125.22, 122.19 (d, $J = 5.9$ Hz), 120.46, 120.38 (d, $J = 4.7$ Hz), 45.22, 23.73, 21.60.

1-(2-methoxyphenyl)-4-((1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridin-2-yl)methyl)piperazine



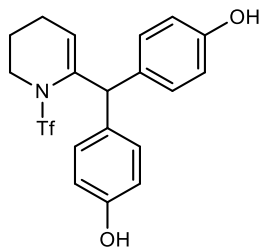
Prepared according to the general reaction procedure B using fresh 1-(2-methoxyphenyl)-4-(pyridin-2-ylmethyl)piperazine (113 mg, 0.40 mmol), Tf₂O (67 μ L, 0.40 mmol), Et₃SiH (130 μ L, 0.8 mmol), B(C₆F₅)₃ (51 mg, 0.08 mmol), CH₂Cl₂ (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then [Ir(cod)Cl]₂ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a yellow oil (silica gel: 0 to 40% EtOAc in Hexanes) (91 mg, 0.22 mmol, 54% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.00 (td, *J* = 8.1, 7.3, 2.5 Hz, 1H), 6.97 – 6.89 (m, 2H), 6.91 – 6.81 (m, 1H), 5.60 (s, 1H), 3.86 (s, 3H), 3.68 – 3.60 (m, 2H), 3.30 (s, 2H), 3.07 (s, 4H), 2.64 (s, 4H), 2.27 – 2.19 (m, 2H), 2.00 – 1.91 (m, 2H). ¹⁹F NMR (376 MHz, CDCl₃) δ -74.70. ¹³C NMR (101 MHz, CDCl₃) δ 152.28, 141.39, 133.86, 124.28 – 114.80, 122.88, 121.33, 120.97, 118.22, 111.20, 60.88, 55.35, 53.05, 50.61, 48.67, 22.74, 21.95.

N-(3-chlorophenyl)-1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridine-3-carboxamide



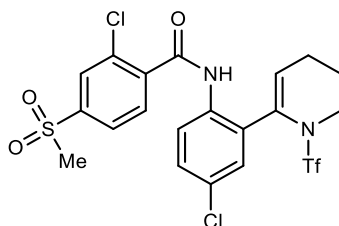
Prepared according to the general reaction procedure B using fresh N-(3-chloro-4-iodophenyl)nicotinamide (93 mg, 0.40 mmol), Tf₂O (67 μ L, 0.40 mmol), Et₃SiH (130 μ L, 0.8 mmol), B(C₆F₅)₃ (51 mg, 0.08 mmol), CH₂Cl₂ (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then [Ir(cod)Cl]₂ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a yellow oil (silica gel: 0 to 30% EtOAc in Hexanes) (114 mg, 0.31 mmol, 77% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.77 – 7.68 (m, 2H), 7.60 (s, 1H), 7.52 (s, 1H), 7.14 (dd, *J* = 8.7, 2.5 Hz, 1H), 3.76 – 3.68 (m, 2H), 2.44 (t, *J* = 6.3 Hz, 2H), 2.02 (p, *J* = 6.1 Hz, 2H). ¹⁹F NMR (377 MHz, CDCl₃) δ -75.06. ¹³C NMR (101 MHz, CDCl₃) δ 164.31, 140.18, 138.83 (d, *J* = 10.9 Hz), 129.96, 124.42 – 114.76 (m), 121.16 (d, *J* = 7.3 Hz), 120.04, 116.74, 45.42, 20.84, 20.70.

4,4'-((1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridin-2-yl)methylene)diphenol



Prepared according to the general reaction procedure B using fresh bisacodyl (111 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-tan oil (silica gel: 0 to 70% EtOAc in Hexanes) (84 mg, 0.20 mmol, 51% yield). ^1H NMR (400 MHz, CD_3CN) δ 6.98 (d, $J = 8.6$ Hz, 4H), 6.89 (s, 2H), 6.79 (d, $J = 8.6$ Hz, 4H), 5.37 (s, 1H), 5.16 (t, $J = 3.9$ Hz, 1H), 3.61 – 3.54 (m, 2H), 2.27 – 2.17 (m, 2H), 2.00 – 1.90 (m, 2H). ^{19}F NMR (376 MHz, CD_3CN) δ -76.90. ^{13}C NMR (101 MHz, CD_3CN) δ 156.17, 140.35, 133.06, 130.65, 124.11 – 114.31 (m), 117.89, 115.63, 53.63, 49.88, 22.99, 22.13.

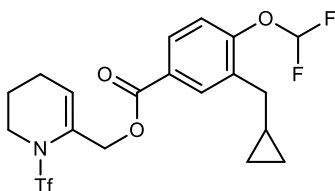
2-chloro-N-(4-chloro-2-(1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridin-2-yl)phenyl)-4-(methylsulfonyl)benzamide



Prepared according to the general reaction procedure B using fresh 2-chloro-N-(4-chloro-2-(pyridin-2-yl)phenyl)-4-(methylsulfonyl)benzamide (168 mg, 0.40 mmol), Ti_2O (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 60% EtOAc in Hexanes) (183 mg, 0.33 mmol, 82% yield). mp $97\text{--}101^\circ\text{C}$ ^1H NMR (400 MHz, CDCl_3) δ 8.19 (s, 1H), 7.95 (s, 1H), 7.83 (s, 2H), 7.61 (d, $J = 7.1$ Hz, 2H), 7.35 (d, $J = 9.0$ Hz, 1H), 5.59 (t, $J = 3.8$ Hz, 1H), 3.87 (s, 2H), 3.07 (s, 3H), 2.44 – 2.35 (m, 2H), 2.07 (t, $J = 5.6$ Hz, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -77.35. ^{13}C NMR (101 MHz, CDCl_3) δ 163.03, 143.05, 140.18, 136.96, 135.68, 134.52, 132.32 – 115.98 (m), 130.96, 129.23, 126.01, 122.98, 121.29, 48.03, 44.45, 22.45, 22.27.

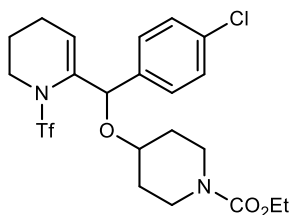
**(1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridin-2-yl)methyl
(cyclopropylmethyl)-4-(difluoromethoxy)benzoate**

3-



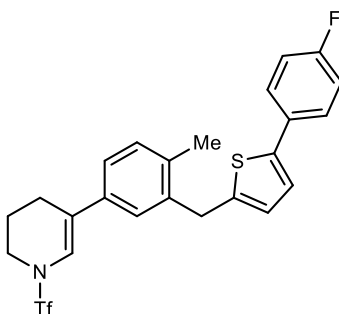
Prepared according to the general reaction procedure B using fresh pyridin-2-ylmethyl 3-(cyclopropylmethyl)-4-(difluoromethoxy)benzoate (133 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a light-yellow solid (silica gel: 0 to 40% EtOAc in Hexanes) (96 mg, 0.20 mmol, 51% yield). mp $45\text{--}47^\circ\text{C}$ ^1H NMR (400 MHz, CDCl_3) δ 7.55 (dq, $J = 3.7$, 2.0 Hz, 2H), 7.13 (d, $J = 8.7$ Hz, 1H), 6.65 (t, $J = 75.0$ Hz, 1H), 5.66 (t, $J = 3.8$ Hz, 1H), 4.97 (s, 2H), 3.85 (d, $J = 7.0$ Hz, 2H), 3.68 – 3.61 (m, 2H), 2.24 – 2.15 (m, 2H), 1.96 – 1.85 (m, 2H), 1.30 – 1.11 (m, 3H), 0.65 – 0.53 (m, 2H), 0.36 – 0.25 (m, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.55, -81.94 (d, $J = 74.9$ Hz). ^{13}C NMR (101 MHz, CDCl_3) δ 165.10, 150.17, 144.23, 132.19, 127.93, 123.34 – 115.42, 122.91, 121.78 (d, $J = 14.9$ Hz), 118.35 – 113.16, 115.75, 115.33, 74.06, 64.83, 48.68, 22.18 (d, $J = 12.0$ Hz), 10.02, 3.25.

Ethyl 4-((4-chlorophenyl)(1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridin-2-yl)methoxy)piperidine-1-carboxylate



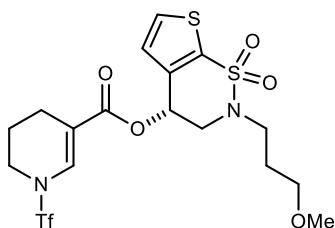
Prepared according to the general reaction procedure B using fresh ethyl 4-((4-chlorophenyl)(pyridin-2-yl)methoxy)piperidine-1-carboxylate (150 mg, 0.40 mmol), Ti_2O (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (8.1 mg, 0.012 mmol) and dppf (14.7 mg, 0.026 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a light-yellow oil (silica gel: 0 to 30% EtOAc in Hexanes) (102 mg, 0.20 mmol, 51% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.31 – 7.16 (m, 4H), 5.89 (t, $J = 4.1$ Hz, 1H), 5.40 (s, 1H), 4.04 (q, $J = 7.1$ Hz, 2H), 3.80 – 3.59 (m, 3H), 3.53 (p, $J = 4.2$ Hz, 1H), 3.15 – 2.97 (m, 3H), 2.31 – 2.10 (m, 2H), 2.04 – 1.89 (m, 1H), 1.90 – 1.81 (m, 1H), 1.81 – 1.71 (m, 1H), 1.67 (dd, $J = 10.7, 6.8$ Hz, 1H), 1.59 – 1.48 (m, 1H), 1.48 – 1.36 (m, 1H), 1.17 (t, $J = 7.1$ Hz, 3H). ^{19}F NMR (377 MHz, CDCl_3) δ -75.06. ^{13}C NMR (101 MHz, CDCl_3) δ 155.54, 138.68, 137.94, 133.86, 129.45 – 114.82, 128.97, 128.67 (d, $J = 7.3$ Hz), 121.27, 120.10, 118.04, 76.41, 61.28, 49.00, 41.12, 31.17 (d, $J = 32.0$ Hz), 22.18, 21.53, 14.69.

5-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-1-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydropyridine



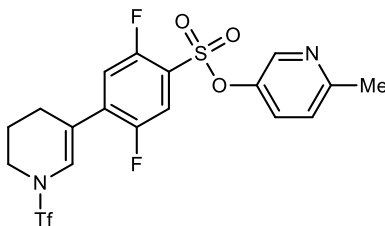
Prepared according to the general reaction procedure B using fresh 3-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyridine (144 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 20% EtOAc in Hexanes) (167 mg, 0.34 mmol, 84% yield). mp $111\text{--}115^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.36 (dd, $J = 8.8, 5.1$ Hz, 2H), 7.12 – 7.01 (m, 3H), 6.95 – 6.85 (m, 3H), 6.78 (s, 1H), 6.56 (d, $J = 3.7$ Hz, 1H), 4.02 (s, 2H), 3.66 – 3.59 (m, 2H), 2.39 (t, $J = 6.4$ Hz, 2H), 2.21 (s, 3H), 1.95 (p, $J = 6.3$ Hz, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -74.93, -115.03. ^{13}C NMR (101 MHz, CDCl_3) δ 163.37, 160.92, 141.64, 138.48, 136.61, 135.90, 130.84, 127.16 (d, $J = 8.0$ Hz), 126.11 (d, $J = 20.7$ Hz), 124.86 – 115.17, 123.58, 122.68 (d, $J = 13.8$ Hz), 119.54, 115.75 (d, $J = 21.8$ Hz), 45.21, 34.30, 23.91, 21.69, 19.17.

(R)-2-(3-methoxypropyl)-1,1-dioxido-3,4-dihydro-2H-thieno[3,2-e][1,2]thiazin-4-yl 1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridine-3-carboxylate



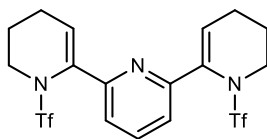
Prepared according to the general reaction procedure B using fresh (R)-2-(3-methoxypropyl)-1,1-dioxido-3,4-dihydro-2H-thieno[3,2-e][1,2]thiazin-4-yl nicotinate (153 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a light-yellow oil (silica gel: 0 to 50% EtOAc in Hexanes) (168 mg, 0.32 mmol, 81% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.58 (s, 1H), 6.83 (s, 1H), 5.79 (d, $J = 3.0$ Hz, 1H), 4.24 (dd, $J = 16.1, 4.2$ Hz, 1H), 3.80 (dd, $J = 16.0, 3.0$ Hz, 1H), 3.66 (t, $J = 6.0$ Hz, 2H), 3.54 (dt, $J = 13.7, 6.9$ Hz, 1H), 3.47 – 3.33 (m, 1H), 3.29 (d, $J = 7.0$ Hz, 2H), 3.25 (s, 5H), 2.35 – 2.27 (m, 2H), 1.92 (p, $J = 6.3$ Hz, 2H), 1.84 (q, $J = 6.1$ Hz, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.14. ^{13}C NMR (101 MHz, CDCl_3) δ 164.91, 138.40, 136.29, 134.68, 134.58, 126.24, 119.52 (q, $J = 323.3$ Hz), 112.37, 69.05, 62.16, 58.68, 51.07, 47.48, 45.65, 29.24, 20.55 (d, $J = 3.8$ Hz).

6-methylpyridin-3-yl **2,5-difluoro-4-(1-((trifluoromethyl)sulfonyl)-1,4,5,6-tetrahydropyridin-3-yl)benzenesulfonate**



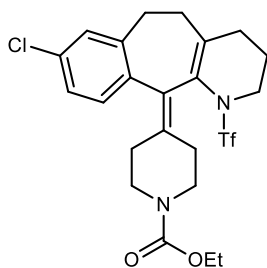
Prepared according to the general reaction procedure B using fresh 6-methylpyridin-3-yl 2,5-difluoro-4-(pyridin-3-yl)benzenesulfonate (145 mg, 0.40 mmol), TF_2O (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a light-yellow oil (silica gel: 0 to 50% EtOAc in Hexanes) (128 mg, 0.26 mmol, 64% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.12 (s, 1H), 7.45 – 7.36 (m, 2H), 7.11 (dd, $J = 9.9, 5.6$ Hz, 2H), 7.06 (s, 1H), 3.77 – 3.69 (m, 2H), 2.48 (s, 3H), 2.42 (t, $J = 6.3$ Hz, 2H), 2.04 (p, $J = 6.1$ Hz, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.01, -111.20 – -116.49 (m). ^{13}C NMR (101 MHz, CDCl_3) δ 158.07, 156.29 (dd, $J = 43.6, 2.9$ Hz), 153.76 (dd, $J = 37.6, 2.7$ Hz), 144.20, 142.30, 135.72 (dd, $J = 14.5, 8.0$ Hz), 130.21, 126.87 (d, $J = 10.2$ Hz), 124.58 – 114.91 (m), 124.18, 121.79 – 121.05 (m), 118.71 (d, $J = 30.2$ Hz), 118.13, 116.86 (dd, $J = 24.2, 4.2$ Hz), 114.91.

1,1''-bis((trifluoromethyl)sulfonyl)-1,1'',4,4'',5,5'',6,6''-octahydro-2,2':6',2''-terpyridine



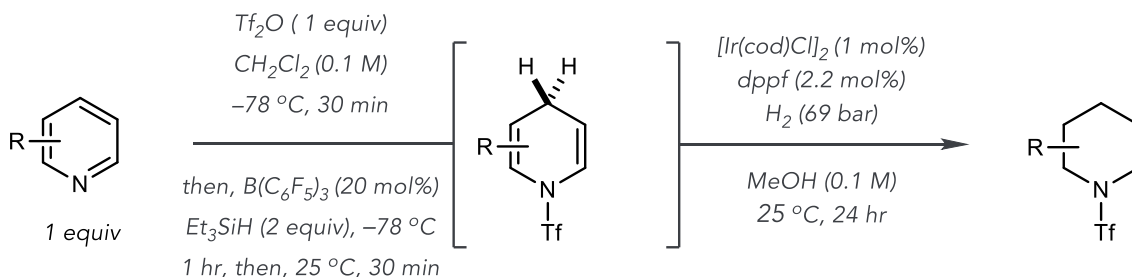
Prepared according to the general reaction procedure B using fresh 2,2':6',2''-terpyridine (93 mg, 0.40 mmol), Tf₂O (134 μ L, 0.80 mmol), Et₃SiH (260 μ L, 1.6 mmol), B(C₆F₅)₃ (51 mg, 0.08 mmol), CH₂Cl₂ (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then [Ir(cod)Cl]₂ (8.1 mg, 0.012 mmol) and dppf (14.7 mg, 0.026 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as tan solid (silica gel: 0 to 60% EtOAc in Hexanes) (101 mg, 0.20 mmol, 50% yield). mp 152-155 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.58 (t, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.3 Hz, 2H), 5.91 (d, *J* = 7.9 Hz, 2H), 3.76 – 3.69 (m, 4H), 2.37 – 2.27 (m, 4H), 2.01 (p, *J* = 6.7 Hz, 4H). ¹⁹F NMR (376 MHz, CDCl₃) δ -73.82. ¹³C NMR (101 MHz, CDCl₃) δ 154.35, 136.89, 136.69, 126.04 – 114.85 (m), 123.66, 120.63, 48.28, 22.43, 22.34.

Ethyl 4-(8-chloro-1-((trifluoromethyl)sulfonyl)-1,2,3,4,5,6-hexahydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidine-1-carboxylate



Prepared according to the general reaction procedure B using fresh ethyl 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidine-1-carboxylate (153 mg, 0.40 mmol), TiF_2O (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a viscous yellow oil (silica gel: 0 to 40% EtOAc in Hexanes) (189 mg, 0.36 mmol, 91% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.11 – 7.00 (m, 3H), 4.11 – 3.97 (m, 3H), 3.90 (s, 1H), 3.66 (m, 1H), 3.21 – 2.99 (m, 3H), 2.93 – 2.82 (m, 1H), 2.57 – 2.46 (m, 2H), 2.33 – 1.72 (m, 9H), 1.18 (t, $J = 7.1$ Hz, 3H). ^{19}F NMR (376 MHz, CDCl_3) δ -75.01, -111.20 – -116.49 (m). ^{13}C NMR (101 MHz, CDCl_3) δ 158.07, 156.29 (dd, $J = 43.6, 2.9$ Hz), 153.76 (dd, $J = 37.6, 2.7$ Hz), 144.20, 142.30, 135.72 (dd, $J = 14.5, 8.0$ Hz), 130.21, 126.87 (d, $J = 10.2$ Hz), 124.58 – 114.91 (m), 124.18, 121.79 – 121.05 (m), 118.71 (d, $J = 30.2$ Hz), 118.13, 116.86 (dd, $J = 24.2, 4.2$ Hz), 114.91.

General Procedure C: Preparation of Piperidines (Iridium-Catalyzed)



An oven-dried 8 mL vial (≤ 0.50 mmol scale) or a round bottom flask (> 0.50 mmol scale) equipped with a stir bar was charged with the heterocycle (1.0 equiv) placed under a nitrogen

atmosphere (vacuum/nitrogen backfill, 3 cycles). CH_2Cl_2 (0.1 M) was added, the reaction vessel cooled to $-78\text{ }^\circ\text{C}$. and Tf_2O (1.0 equiv) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes before Et_3SiH (2.0 equiv) was added dropwise via syringe followed by the $\text{B}(\text{C}_6\text{F}_5)_3$ solution (0.2 equiv, 0.5 M solution in CH_2Cl_2 , freshly prepared). The reaction continued to stir at $-78\text{ }^\circ\text{C}$ for one hour. The cooling bath was removed, and the reaction warmed to room temperature with stirring (approximately 15-30 minutes). Then, the reaction solvent was removed *in vacuo* at room temperature until a minimal amount of solvent remains. The reaction mixture was then dissolved in the freshly prepared $[\text{Ir}(\text{cod})\text{Cl}]_2/\text{dppf}$ solution in methanol and transferred to the appropriately sized vial (refer to Preparation of the $[\text{Ir}(\text{cod})\text{Cl}]_2/\text{dppf}$ Solution for more details). The glass vial was placed in a 150 ml stainless steel autoclave under air. The autoclave was pressurized and depressurized four times with hydrogen gas before the final pressure was set (69 bar). The reaction stirred at room temperature for 24 hours with appropriate shielding. Then, the pressure was carefully released. The reaction was concentrated *in vacuo* and isolated according to the following procedures (refer to Product Isolation Guidelines 1 for more details).

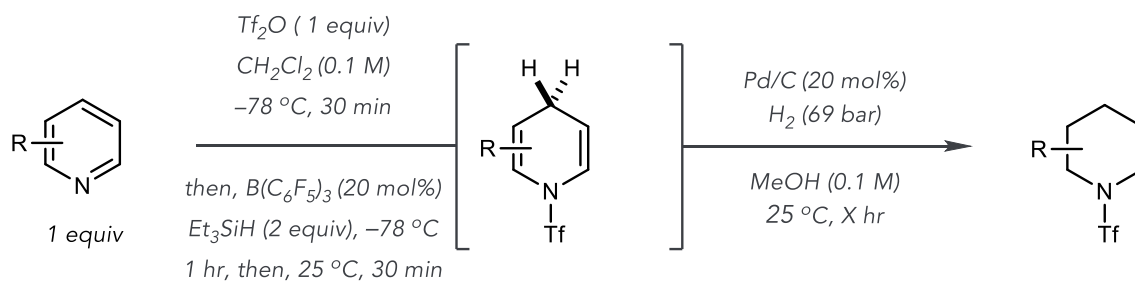
Preparation of the $[\text{Ir}(\text{cod})\text{Cl}]_2/\text{dppf}$ Solution:

An oven-dried 8 mL vial (≤ 0.50 mmol scale) or a round bottom flask (> 0.50 mmol scale) equipped with a stir bar was charged with $[\text{Ir}(\text{cod})\text{Cl}]_2$ (0.01 equiv) and dppf (0.022 equiv) in a glovebox under a nitrogen atmosphere. The vessel was sealed with a rubber septum in the glovebox and removed. Then, an Argon filled balloon was pierced through the septum before MeOH (0.1 M) was added. The solution stirred (500 rpm) at room temperature under Argon atmosphere for 3 hours prior to introduction of the solution described above.

General Isolation Procedure 1

The reaction was dissolved in EtOAc and H₂O. The organic layer was then washed with H₂O (3x), then washed with a saturated aqueous solution of brine (1x), dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography under the stated conditions to provide the piperidine product.

General Procedure D: Preparation of Piperidines (Palladium on Carbon-Catalyzed)



An oven-dried 8 mL vial (≤ 0.50 mmol scale) or a round bottom flask (> 0.50 mmol scale) equipped with a stir bar was charged with the heterocycle (1.0 equiv) placed under a nitrogen atmosphere (vacuum/nitrogen backfill, 3 cycles). CH_2Cl_2 (0.1 M) was added, the reaction vessel cooled to $-78\text{ }^\circ\text{C}$. and Tf_2O (1.0 equiv) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes before Et_3SiH (2.0 equiv) was added dropwise via syringe followed by the $\text{B}(\text{C}_6\text{F}_5)_3$ solution (0.2 equiv, 0.5 M solution in CH_2Cl_2 , freshly prepared). The reaction continued to stir at $-78\text{ }^\circ\text{C}$ for one hour. The cooling bath was removed, and the reaction warmed to room temperature with stirring (approximately 15-30 minutes). Then, the reaction solvent was removed

in vacuo at room temperature until a minimal amount of solvent remains. The reaction diluted with MeOH (0.1 M) and the Pd/C (0.2 equiv) was added. The reaction vial was capped and a balloon of hydrogen gas was bubbled through the solution while stirring (500 rpm). After the balloon is depleted, it was replaced with a fresh balloon, hovering in the headspace of the reaction. The reaction was monitored by LCMS until full conversion was observed.

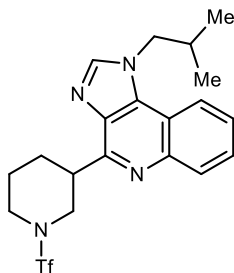
General Isolation Procedure 2

The reaction was filtered through celite to remove the palladium catalyst. Then, the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography under the stated conditions to provide the piperidine product.

Safety Notes

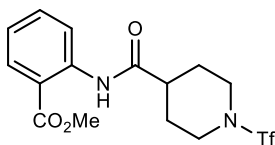
High pressures of hydrogen gas have increased risk of explosion. Use caution, appropriate blast shielding and personal protection equipment. The activated palladium species is pyrophoric and must not run dry. Dispose of the activated species after filtration as a slurried solution. In addition, on large scale (>0.5 mmol), combining the unactivated Pd/C with the concentrated reaction mixture results in a pyrophoric mixture that may spark or combust spontaneously. Adding the solvent first minimizes this risk and is advised.

1-isobutyl-4-(1-((trifluoromethyl)sulfonyl)piperidin-3-yl)-1H-imidazo[4,5-c]quinoline



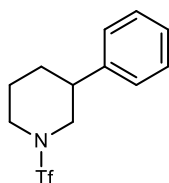
Prepared according to the general reaction procedure C using fresh 1-isobutyl-4-(pyridin-3-yl)-1H-imidazo[4,5-c]quinoline (121 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure 1. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a yellow solid (silica gel: 0 to 50% EtOAc in Hexanes) (144 mg, 0.33 mmol, 82% yield) (m.p. $138\text{--}141^\circ\text{C}$). ^1H NMR (400 MHz, CDCl_3) δ 8.20 (d, $J = 9.9$ Hz, 1H), 8.08 (d, $J = 9.8$ Hz, 1H), 7.88 (s, 1H), 7.70 – 7.63 (m, 1H), 7.59 (t, $J = 7.6$ Hz, 2H), 4.33 (d, $J = 7.4$ Hz, 3H), 4.07 (d, $J = 12.6$ Hz, 1H), 4.01 – 3.92 (m, 1H), 3.85 (t, $J = 12.6$ Hz, 1H), 3.21 (s, 1H), 2.45 – 2.31 (m, 2H), 2.11 – 1.90 (m, 3H), 1.03 (d, $J = 6.7$ Hz, 6H). ^{19}F NMR (376 MHz, CDCl_3) δ -46.86 – -92.27 (m). ^{13}C NMR (101 MHz, CDCl_3) δ 156.02, 144.33, 143.42, 136.45, 132.58, 130.69, 127.17, 126.17, 125.01 – 115.23, 119.97, 117.57, 55.14, 50.08, 47.23, 40.10, 29.39, 28.83, 25.52, 19.84.

Methyl 2-(1-((trifluoromethyl)sulfonyl)piperidine-4-carboxamido)benzoate



Prepared according to the general reaction procedure C using fresh methyl 2-(isonicotinamido)benzoate (102 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then $[\text{Ir}(\text{cod})\text{Cl}]_2$ (2.7 mg, 0.004 mmol) and dppf (4.9 mg, 0.0088 mmol) pre-stirred in MeOH (4.0 mL) at 69 bar and 25°C for 24 hours. The crude material was purified according to general isolation procedure 1. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 40% EtOAc in Hexanes) (71 mg, 0.18 mmol, 46% yield) (m.p. $100\text{--}103^\circ\text{C}$). ^1H NMR (400 MHz, CDCl_3) δ 11.23 (s, 1H), 8.62 (d, $J = 8.5$ Hz, 1H), 7.98 (d, $J = 9.8$ Hz, 1H), 7.49 (t, $J = 7.9$ Hz, 1H), 7.04 (t, $J = 7.7$ Hz, 1H), 3.95 (d, $J = 13.5$ Hz, 2H), 3.87 (s, 3H), 3.15 (d, $J = 11.8$ Hz, 2H), 2.55 – 2.43 (m, 1H), 2.06 (d, $J = 10.3$ Hz, 2H), 1.95 – 1.81 (m, 2H). ^{19}F NMR (376 MHz, CDCl_3) δ -46.86 – -92.27 (m). ^{13}C NMR (101 MHz, CDCl_3) δ 171.96, 169.01, 141.32, 134.87, 130.95, 124.90 – 115.25 (m), 122.88, 120.40, 114.95, 52.50, 46.02, 43.24, 28.31.

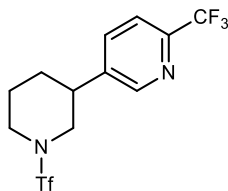
3-phenyl-1-((trifluoromethyl)sulfonyl)piperidine



Prepared according to the general reaction procedure D using freshly distilled 3-phenylpyridine (62 mg, 0.40 mmol), TiF_4 (67 μL , 0.40 mmol), Et_3SiH (130 μL , 0.8 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (51 mg, 0.08 mmol), CH_2Cl_2 (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then Pd/C (15.3 mg, 0.08 mmol, 20% Pd by wt) in MeOH

(4.0 mL) at 1 bar and 25 °C for 8 hours. The crude material was purified according to general isolation procedure 2. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as a light-yellow oil (silica gel: 0 to 10% EtOAc in Hexanes) (82 mg, 0.21 mmol, 52% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.63 (s, 1H), 7.77 – 7.64 (m, 3H), 4.05 (d, *J* = 12.6 Hz, 2H), 3.16 – 2.93 (m, 3H), 2.16 (d, *J* = 14.8 Hz, 1H), 1.99 (dt, *J* = 12.9, 2.9 Hz, 1H), 1.90 – 1.66 (m, 2H). ¹⁹F NMR (377 MHz, CDCl₃) δ -73.86 (br). ¹³C NMR (101 MHz, CDCl₃) δ 141.46, 128.83, 127.20 (d, *J* = 29.6 Hz), 124.99 – 115.35 (m), 52.74, 47.02, 42.66, 30.50, 25.60.

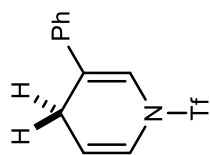
2-(trifluoromethyl)-5-(1-((trifluoromethyl)sulfonyl)piperidin-3-yl)pyridine



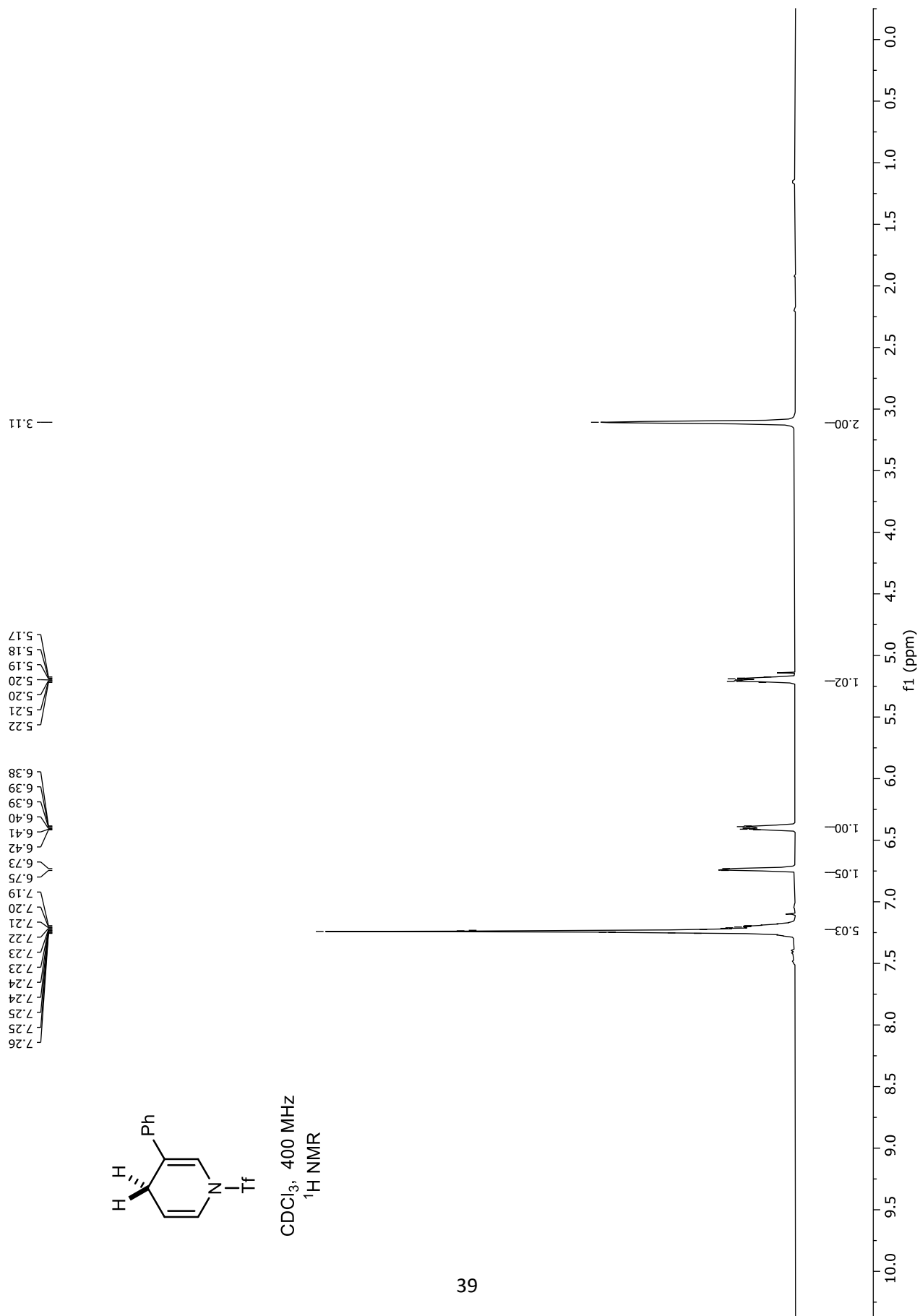
Prepared according to the general reaction procedure D using fresh 3-phenylpyridine (90 mg, 0.40 mmol), Tf₂O (67 μL, 0.40 mmol), Et₃SiH (130 μL, 0.8 mmol), B(C₆F₅)₃ (51 mg, 0.08 mmol), CH₂Cl₂ (4.0 mL) at -78°C for the dearomatization step. The reaction solvent was removed *in vacuo* at room temperature, then Pd/C (15.3 mg, 0.08 mmol, 20% Pd by wt) in MeOH (4.0 mL) at 1 bar and 25 °C for 4 hours. The crude material was purified according to general isolation procedure 2. The residue after aqueous extraction was purified by a flash chromatography column to provide the pure title compound as an off-white solid (silica gel: 0 to 20% EtOAc in Hexanes) (91 mg, 0.25 mmol, 63% yield) (m.p. 114-115 °C). ¹H NMR (400 MHz, CDCl₃) δ 8.63 (s, 1H), 7.77 – 7.64 (m, 3H), 4.05 (d, *J* = 12.6 Hz, 2H), 3.16 – 2.93 (m, 3H), 2.16 (d, *J* = 14.8 Hz, 1H), 1.99 (dt, *J* = 12.9, 2.9 Hz, 1H), 1.90 – 1.66 (m, 2H). ¹⁹F NMR (376 MHz, CDCl₃) δ -67.92, -75.11

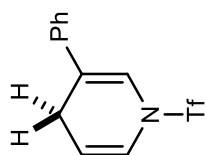
– -75.27 (br). ^{13}C NMR (101 MHz, CDCl_3) δ 149.08, 147.62, 140.04, 135.90, 124.92 - 116.68 (m), 120.59, 51.77, 46.87, 40.20, 30.28, 25.22.

^1H , ^{19}F , and ^{13}C NMR Spectra



CDCl₃, 400 MHz
¹H NMR

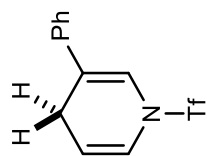




CDCl₃, 400 MHz
¹⁹F NMR

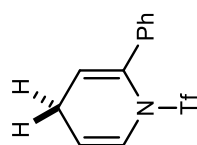
— -74.43



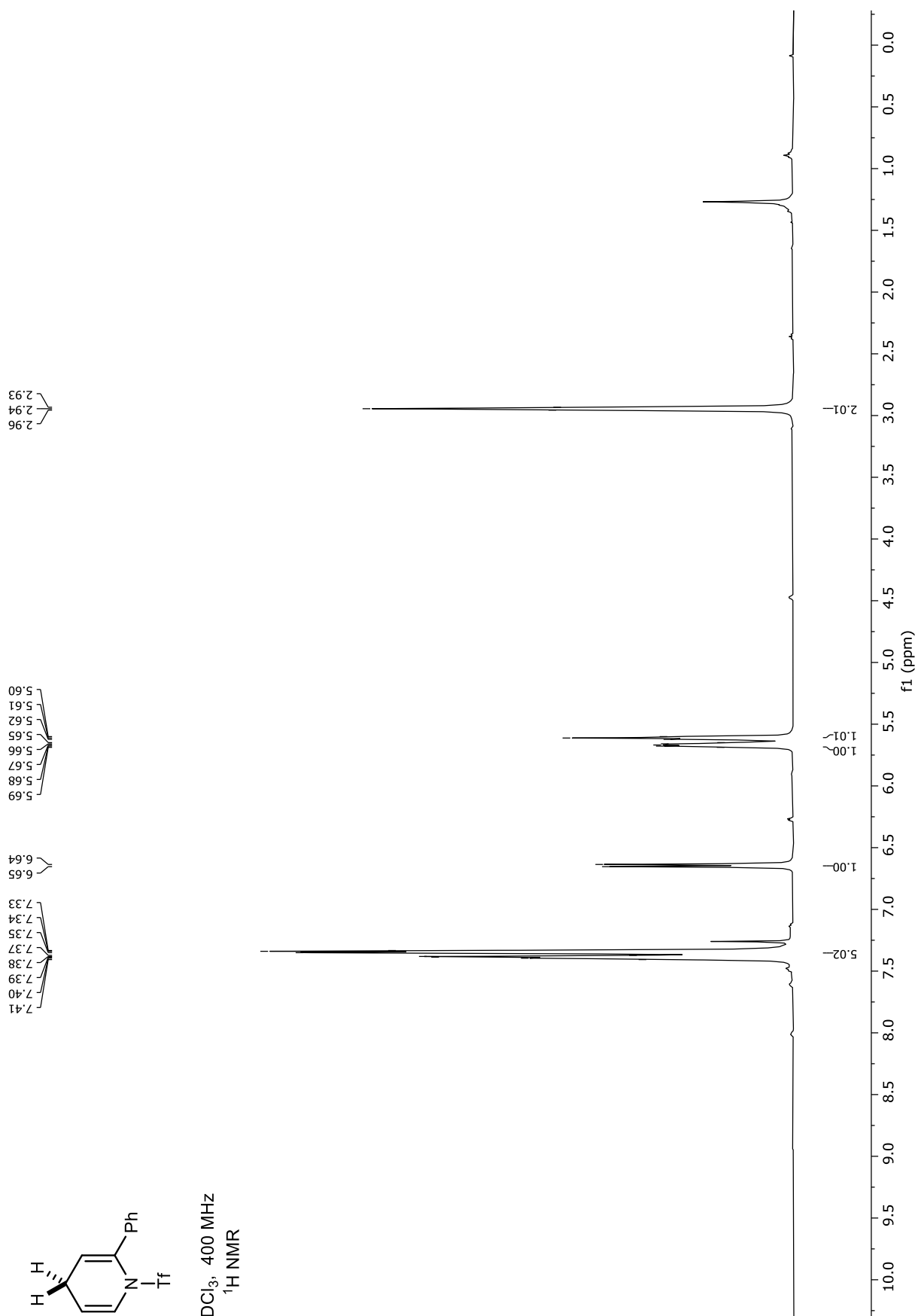


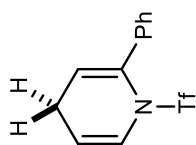
CDCl₃, 400 MHz
¹³C NMR

137.16
 128.73
 128.23
 127.25
 124.79
 121.23
 120.45
 118.31
 117.99
 114.46
 109.72
 106.02
 24.67



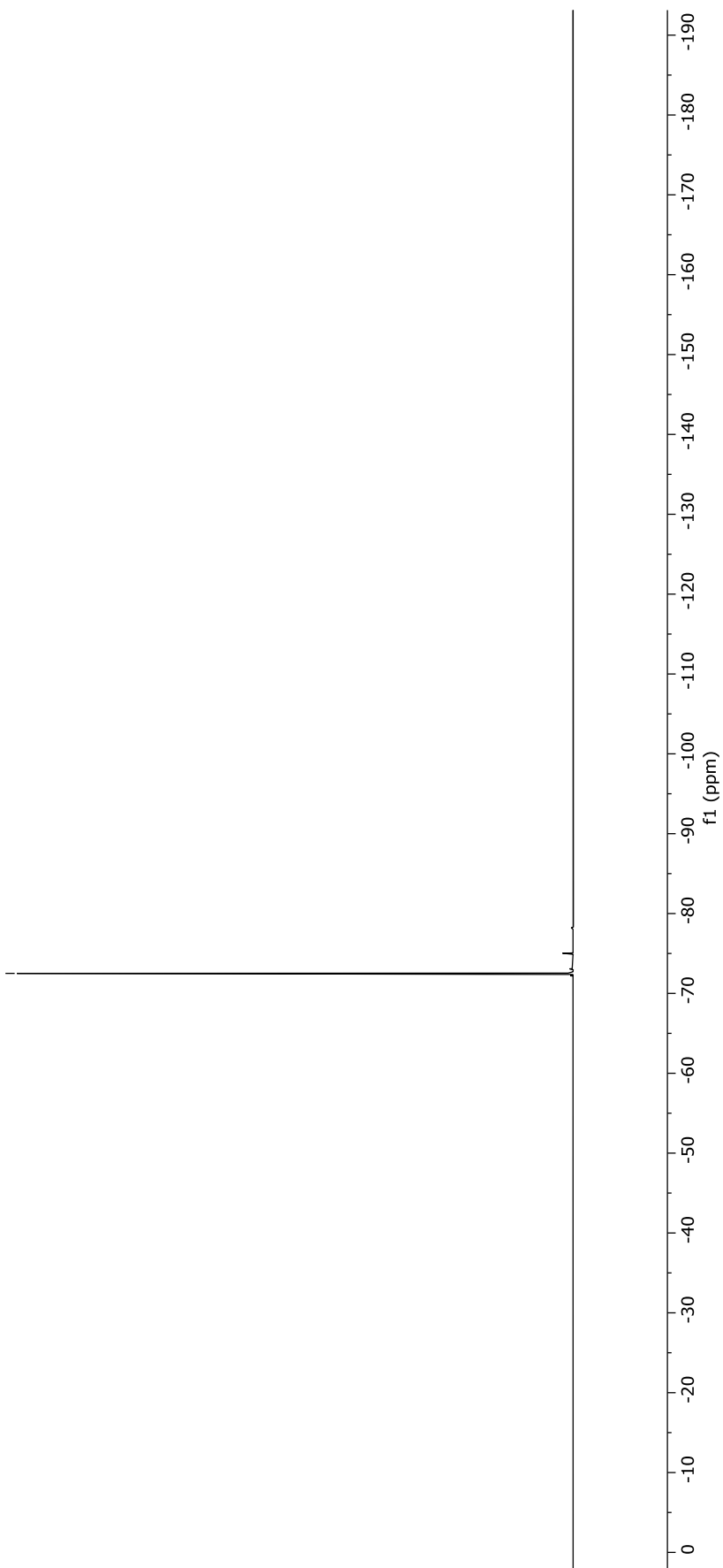
CDCl₃, 400 MHz
¹H NMR

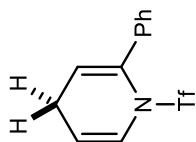




CDCl₃, 400 MHz
¹⁹F NMR

— -72.51

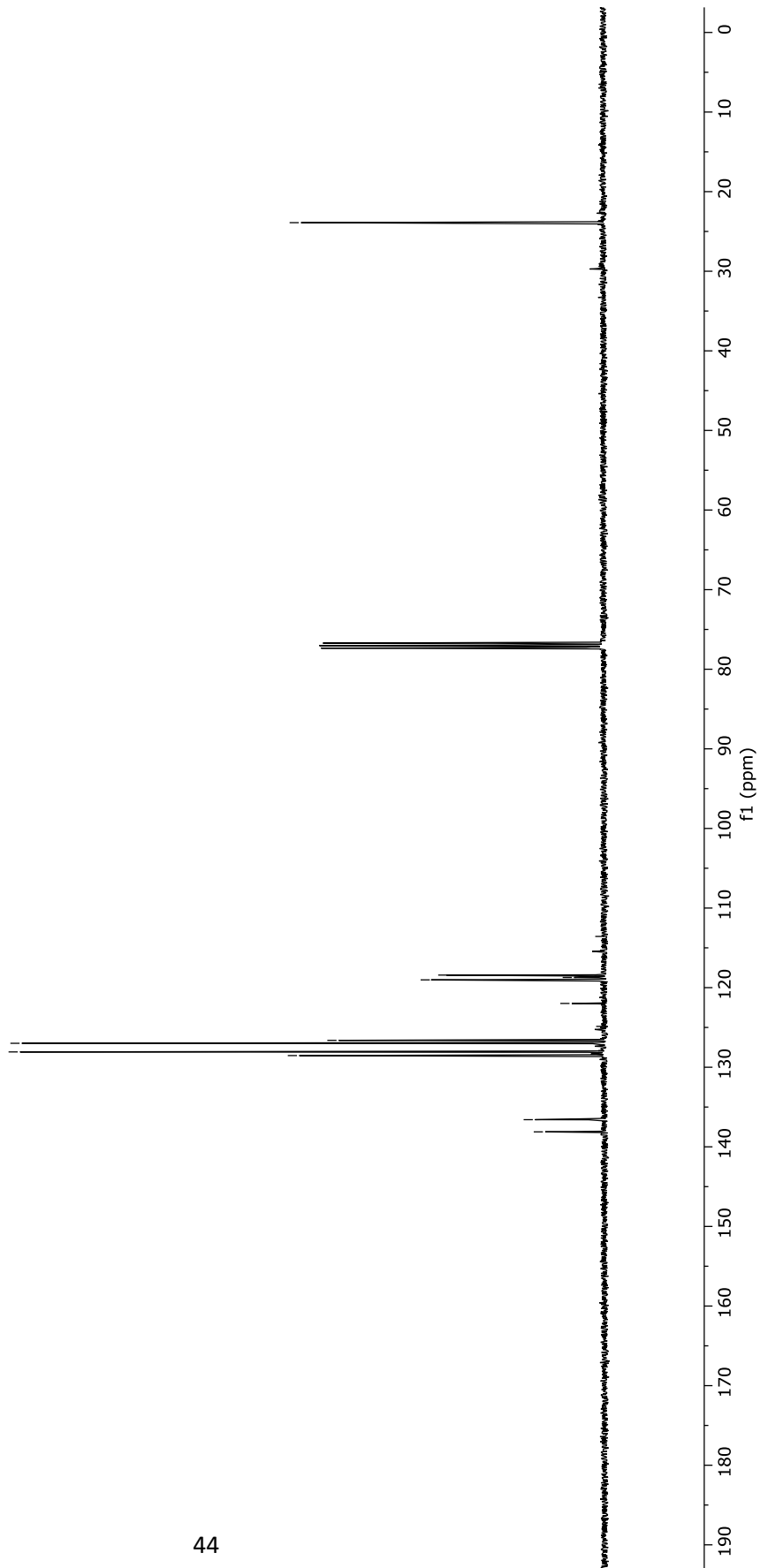


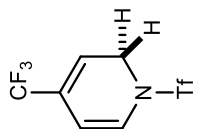


CDCl₃, 400 MHz
¹³C NMR

138.12
 136.59
 128.54
 128.08
 126.99
 126.62
 124.87
 121.99
 119.02
 118.72
 118.42
 113.57

23.90

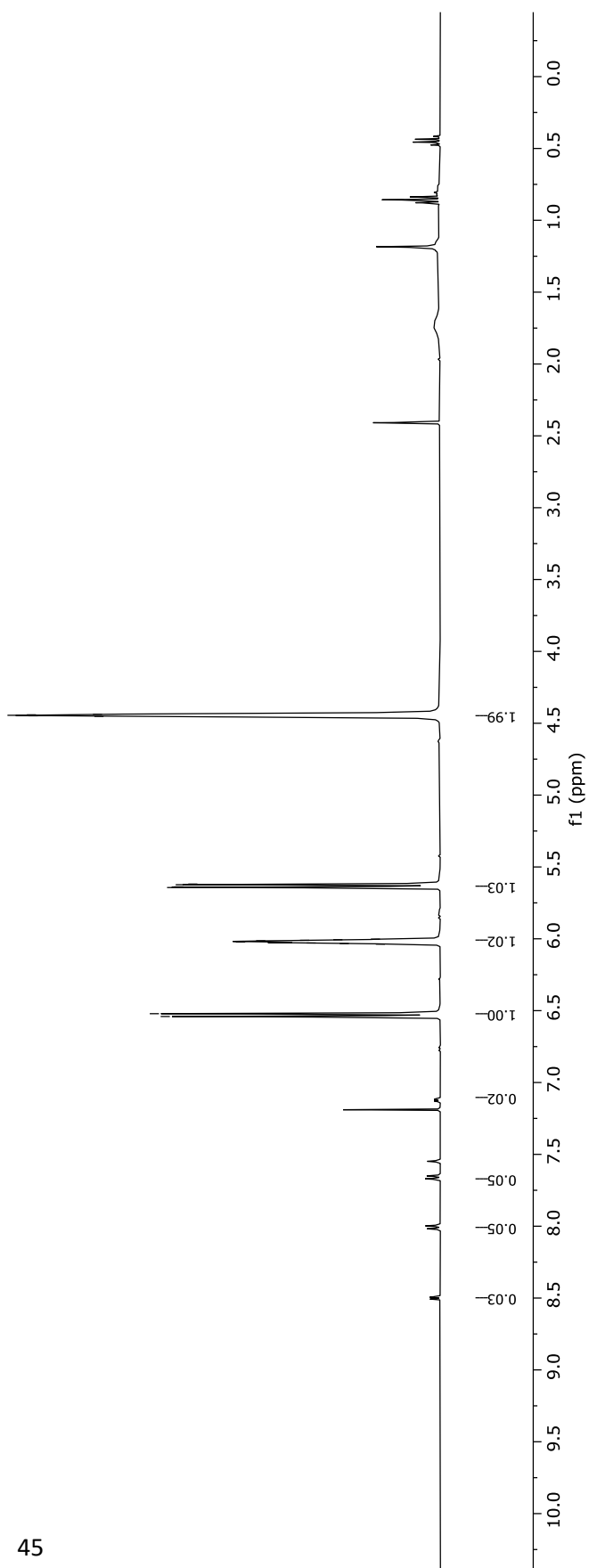


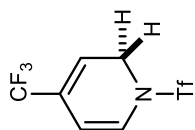


CDCl₃, 400 MHz
¹H NMR

6.54
6.52
6.04
6.03
6.03
6.02
6.01
6.01
6.01
6.00
5.64
5.64
5.62
5.62

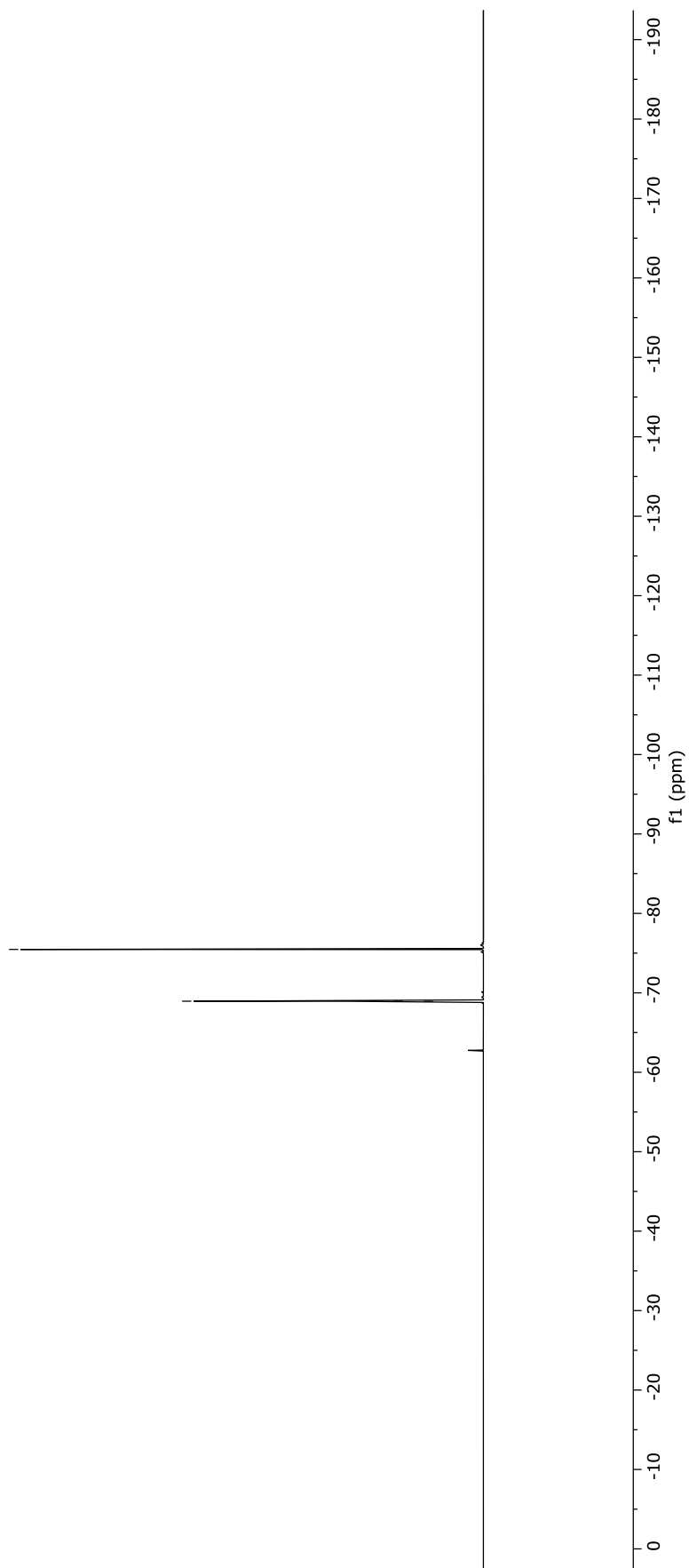
4.45
4.45
4.44
4.44
4.44
4.44

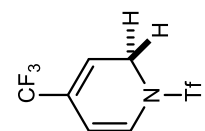




CDCl₃, 400 MHz
¹⁹F NMR

-68.93
-68.94
-68.95
-68.96
-75.47

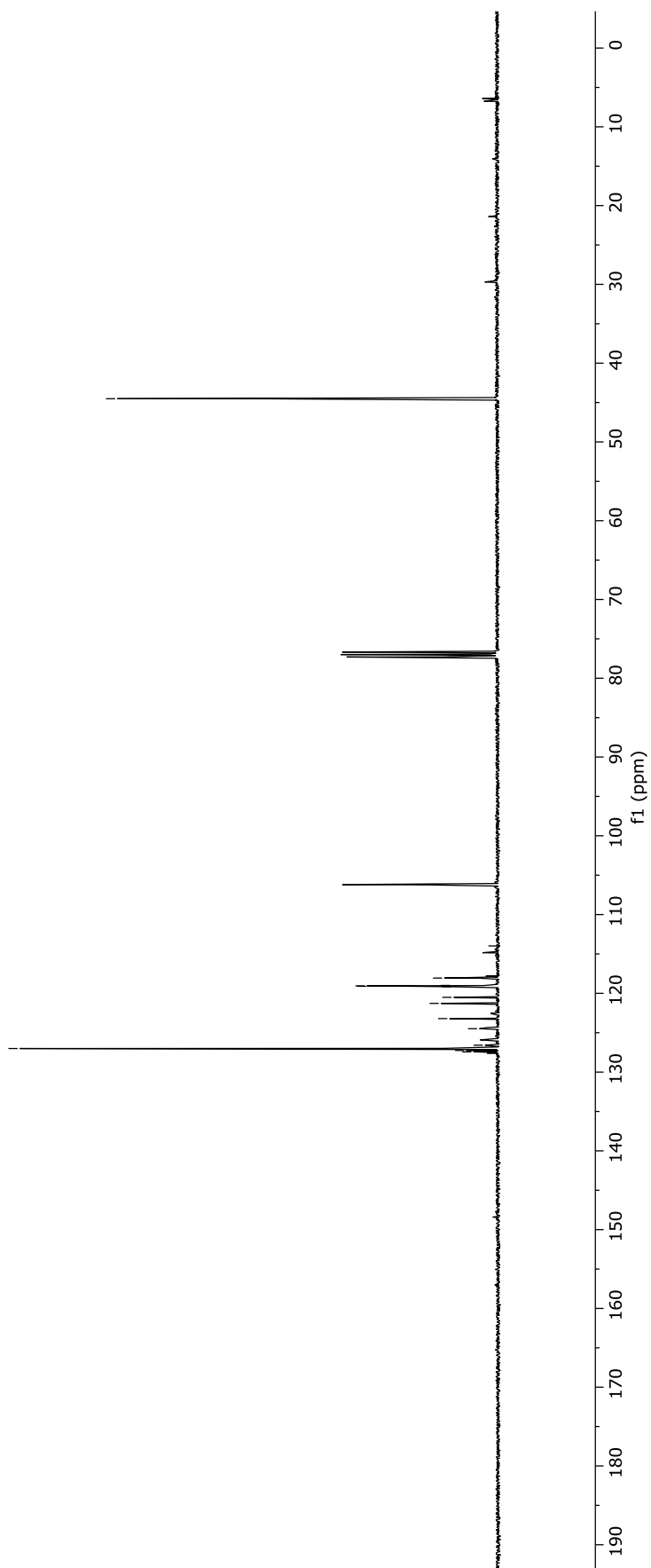


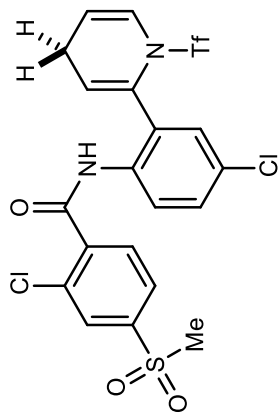


CDCl₃, 400 MHz
¹³C NMR

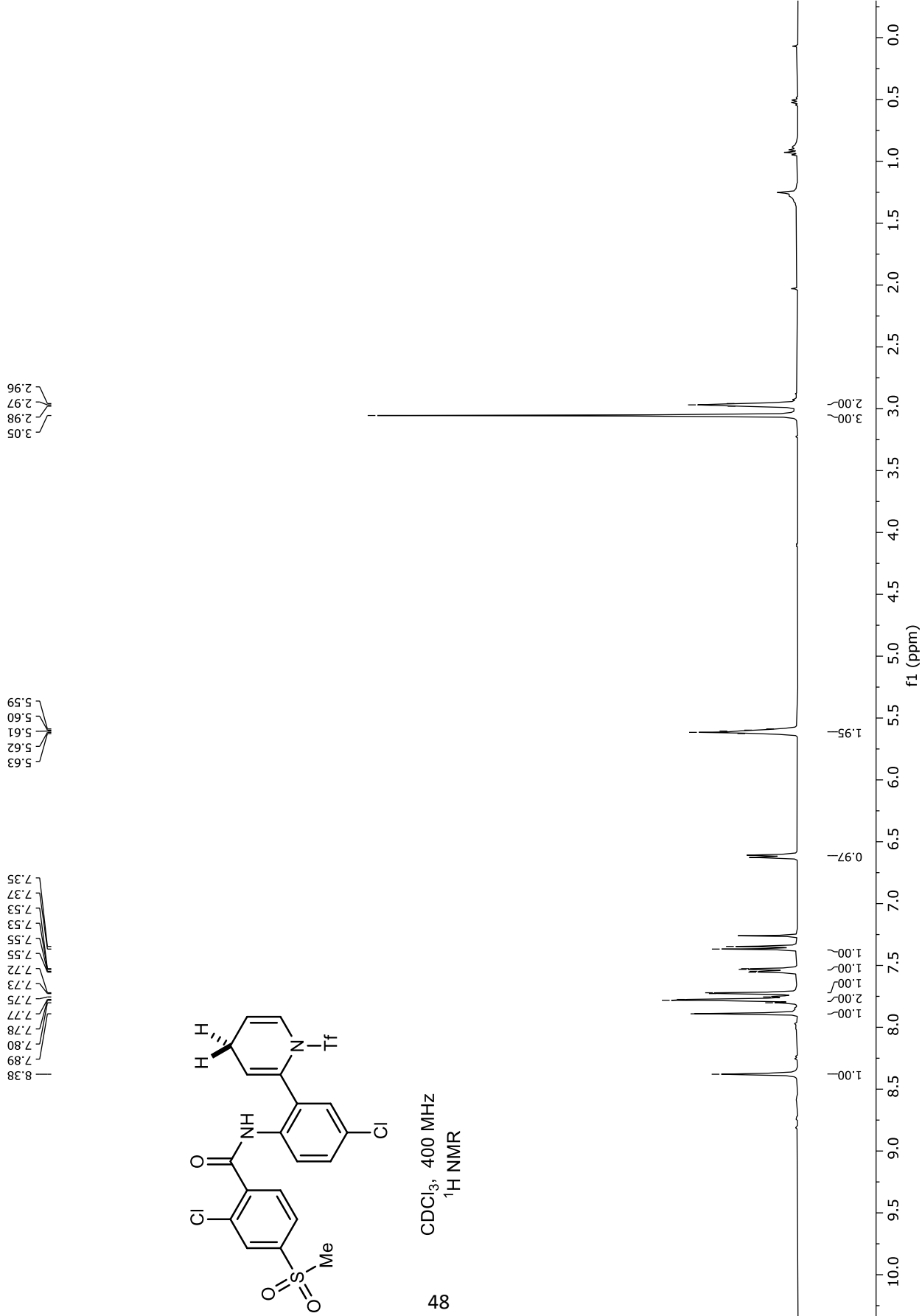
127.43
 127.25
 127.00
 126.58
 124.49
 123.21
 121.28
 120.51
 119.17
 119.11
 119.05
 119.00
 118.06
 113.98
 106.17
 106.16

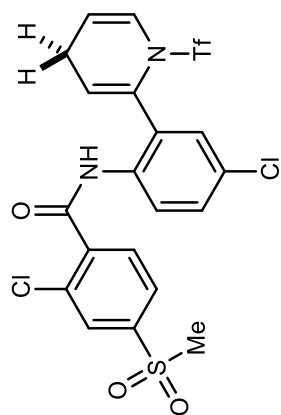
44.52





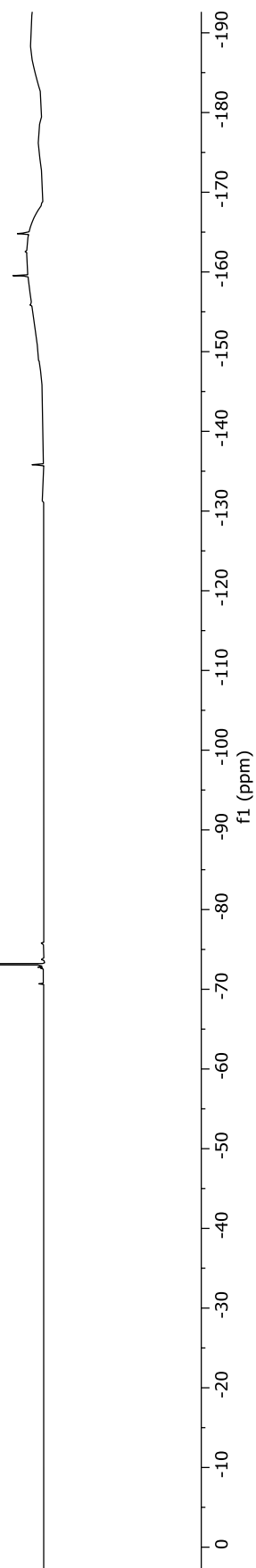
48
 CDCl₃, 400 MHz
¹H NMR

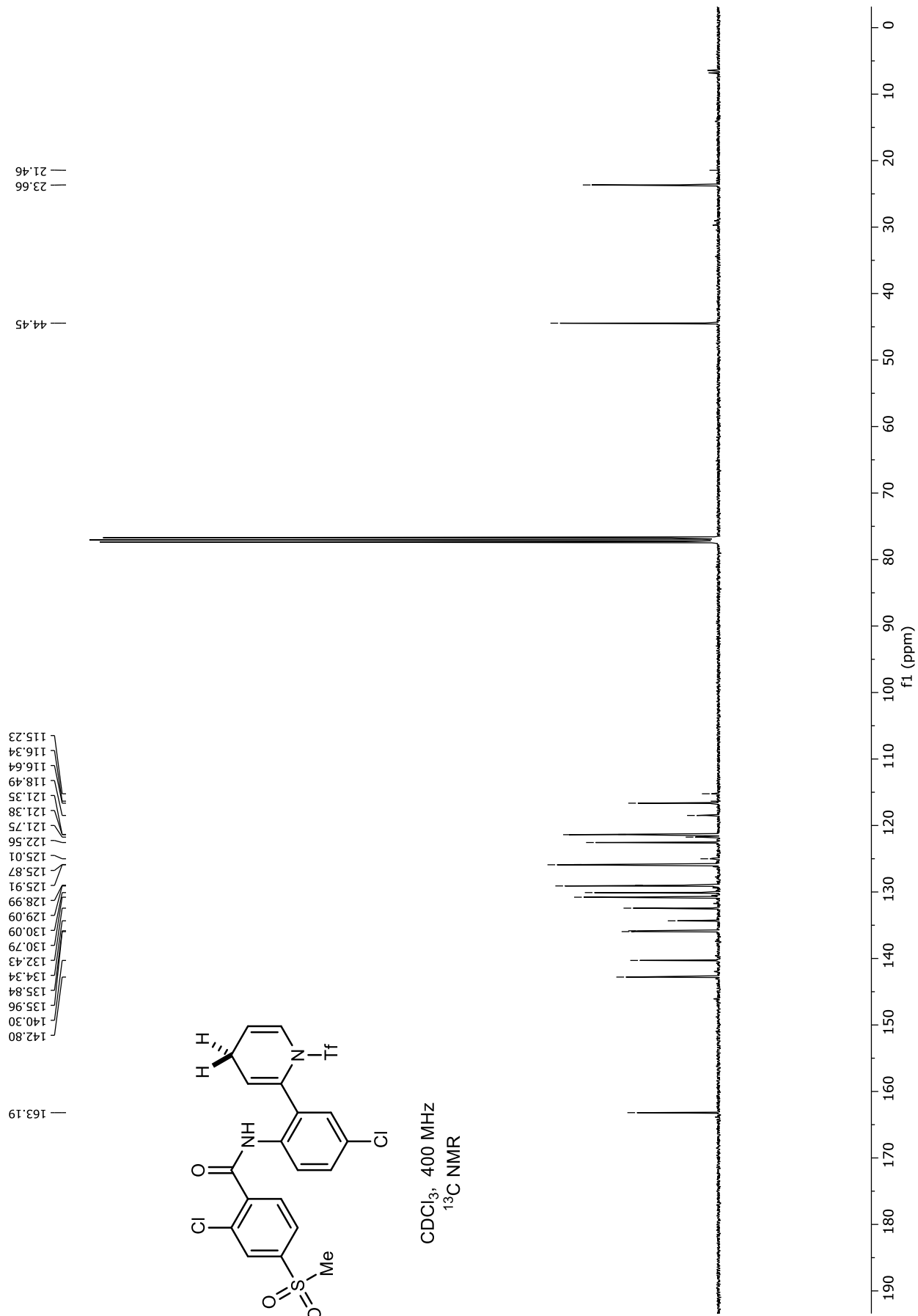


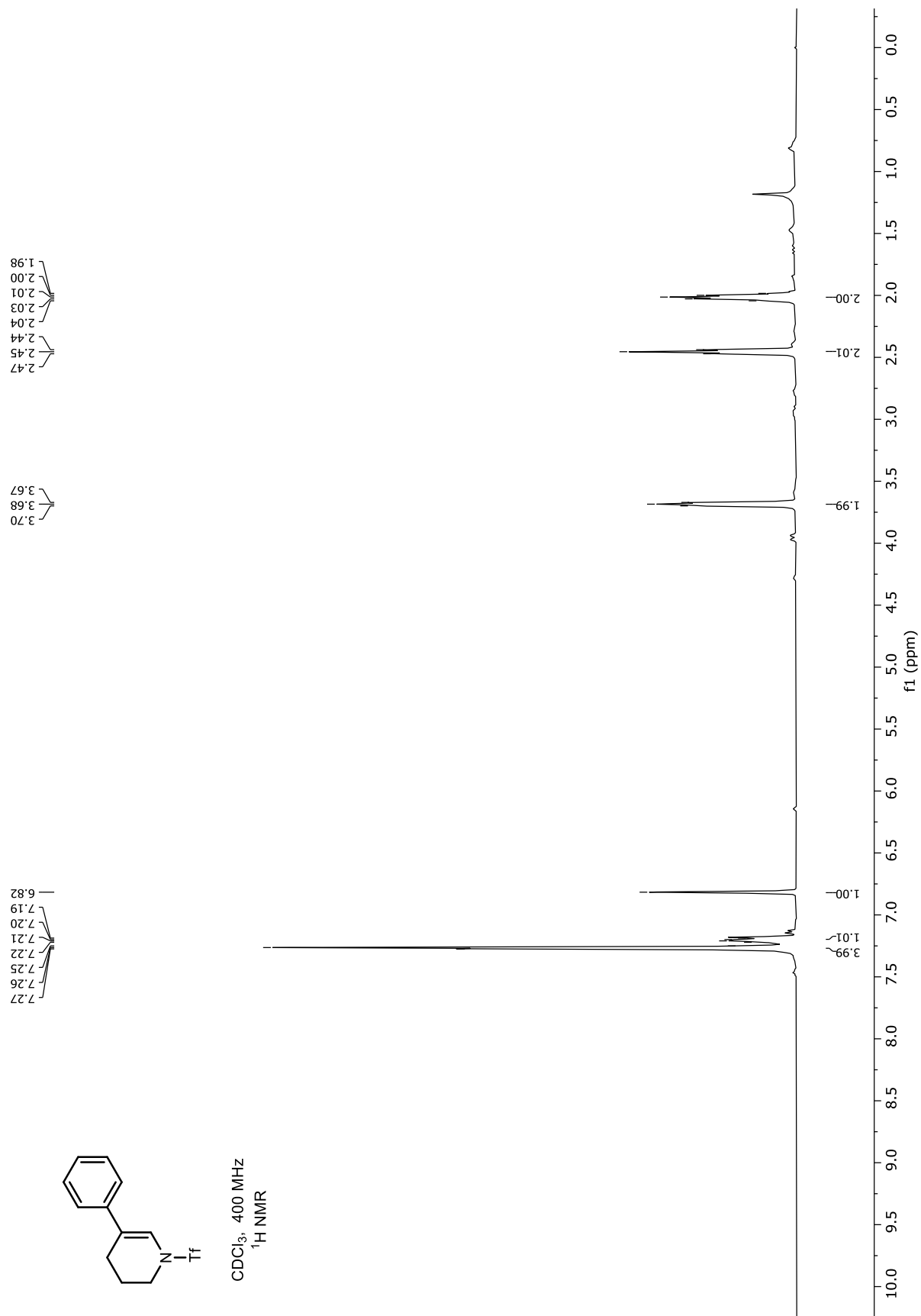


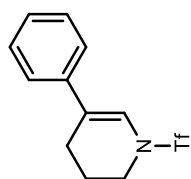
CDCl₃, 400 MHz
¹⁹F NMR

— -73.16



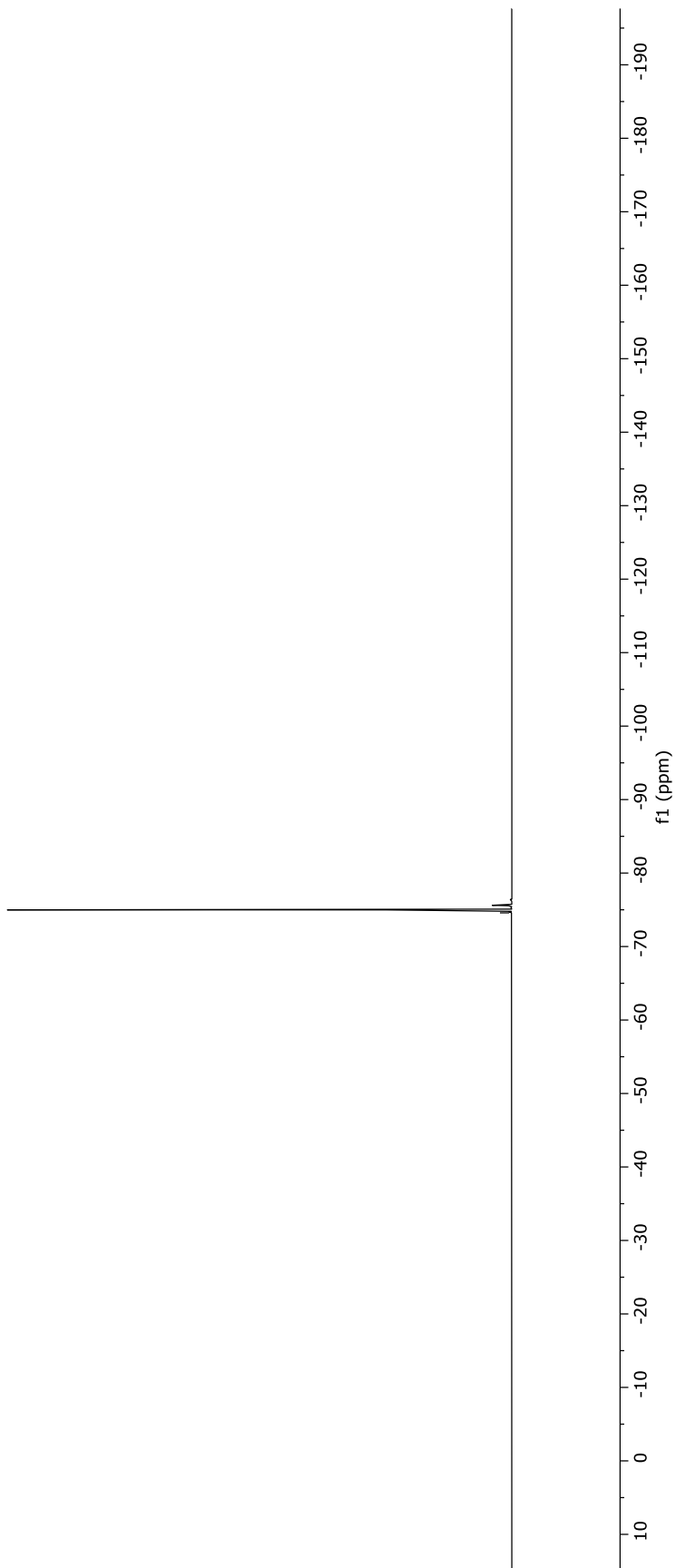


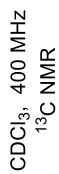
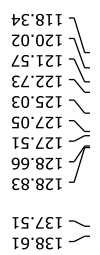


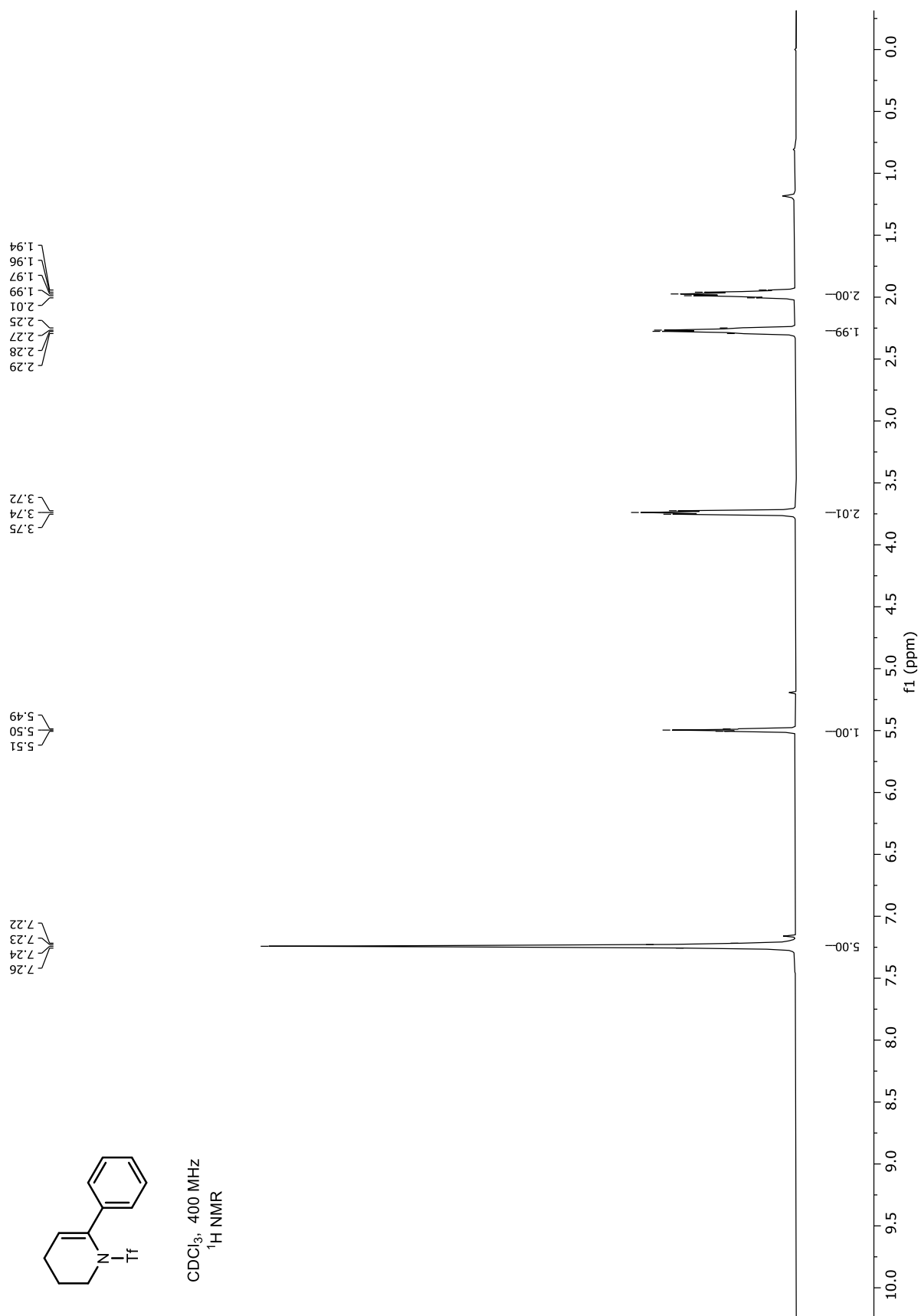


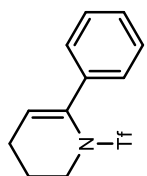
CDCl₃, 400 MHz
¹⁹F NMR

— -74.59



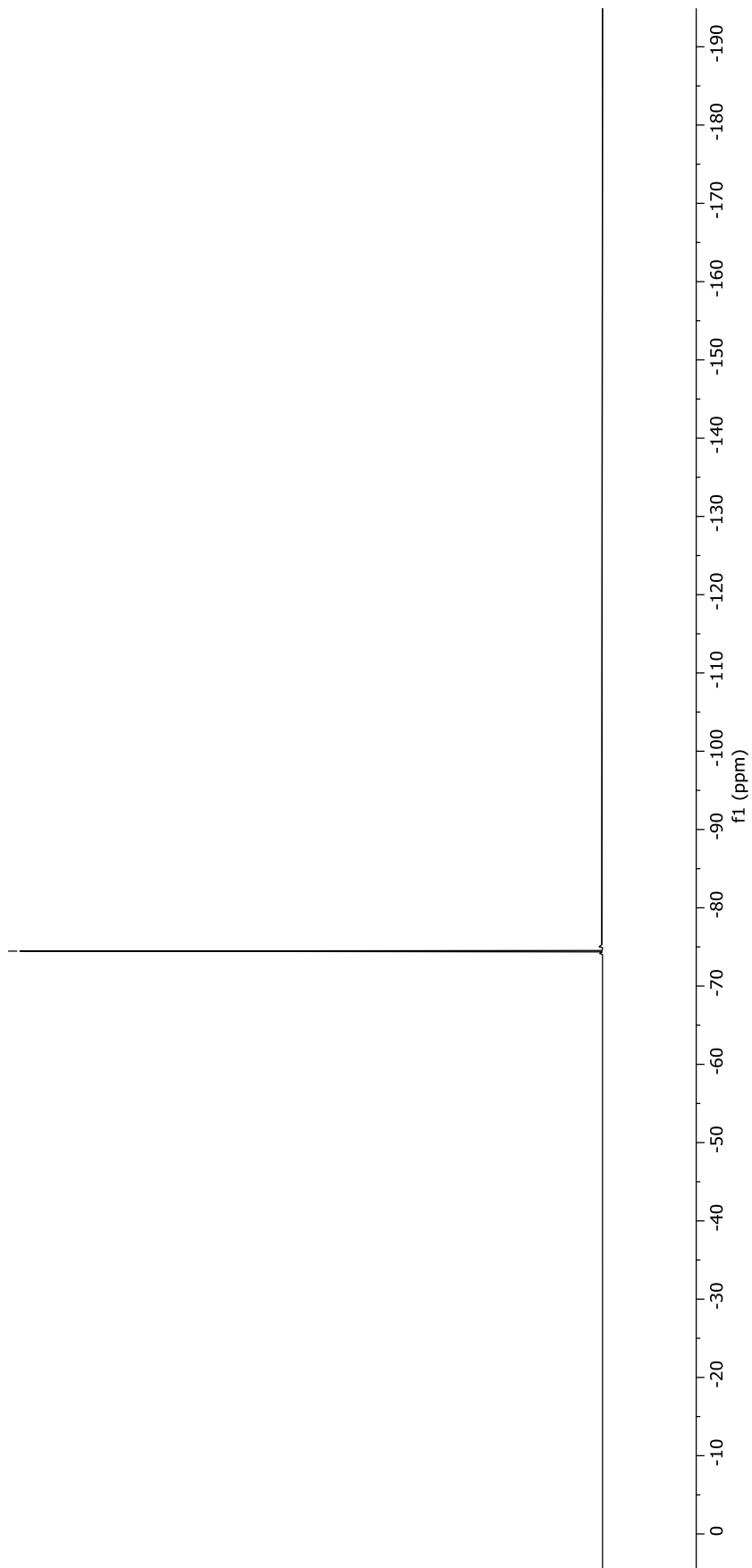






CDCl₃, 400 MHz
¹⁹F NMR

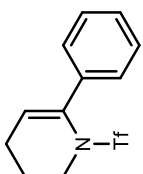
— -74.46



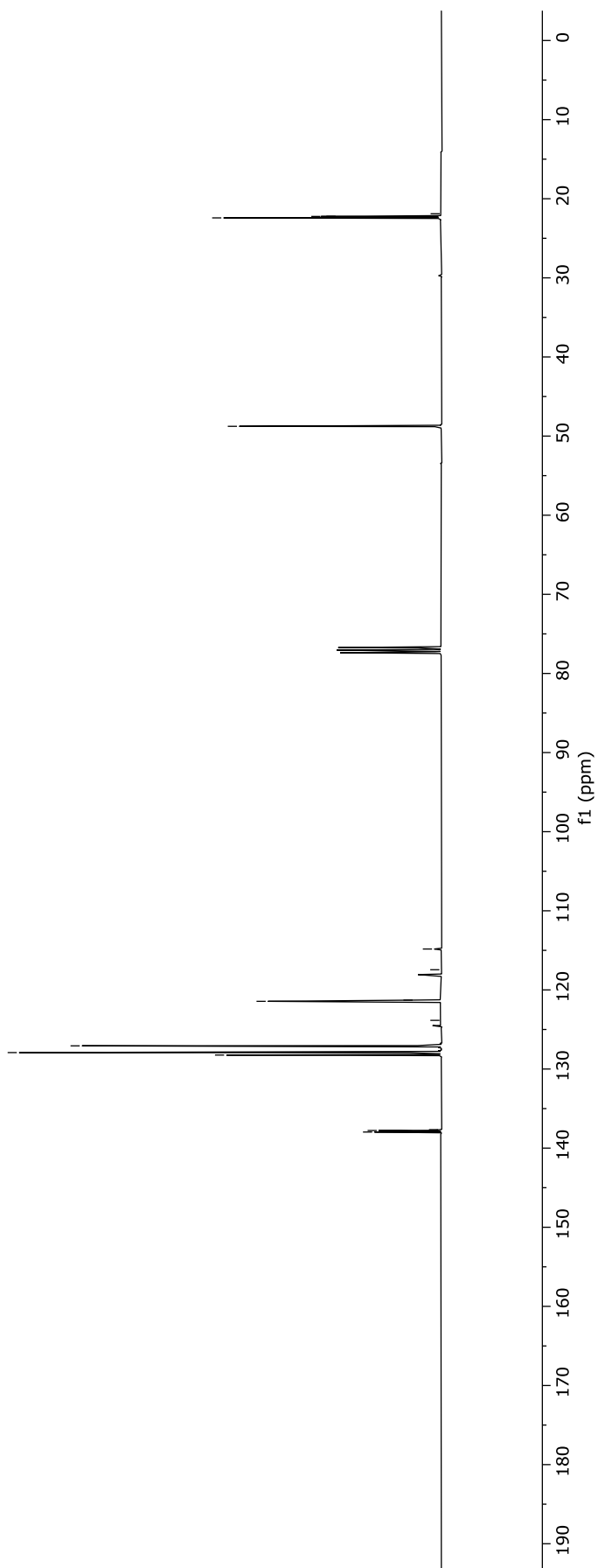
22.42
22.24
22.22
21.90

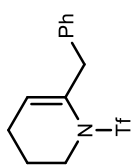
48.76

137.97
137.77
137.66
128.24
127.92
127.07
123.85
121.44
121.29
117.45
114.83



CDCl₃, 400 MHz
¹³C NMR





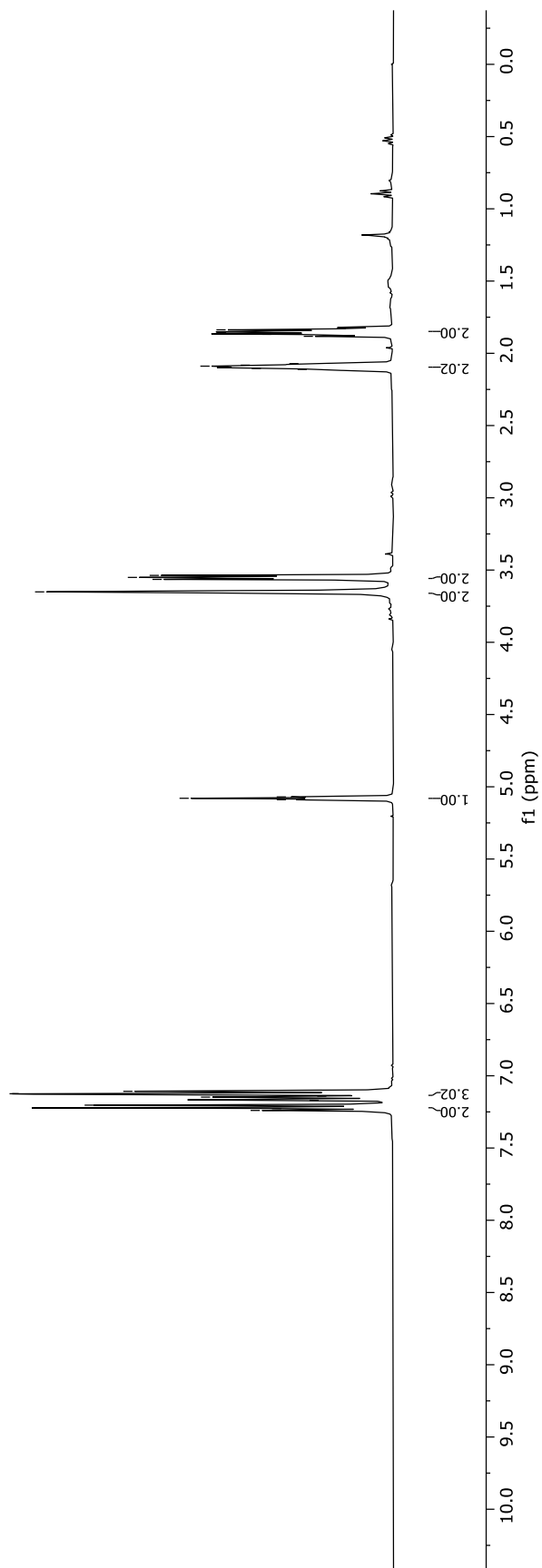
CDCl₃, 400 MHz
¹H NMR

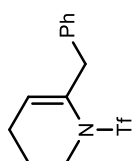
2.11
2.10
2.09
2.08
2.07
1.88
1.87
1.86
1.84
1.83

3.65
3.56
3.55
3.54

5.09
5.08
5.07

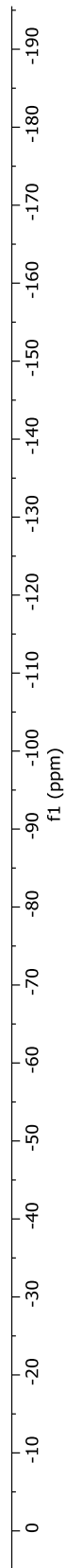
7.24
7.23
7.20
7.17
7.15
7.14
7.12
7.11

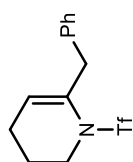




CDCl₃, 400 MHz
¹⁹F NMR

— -74.49



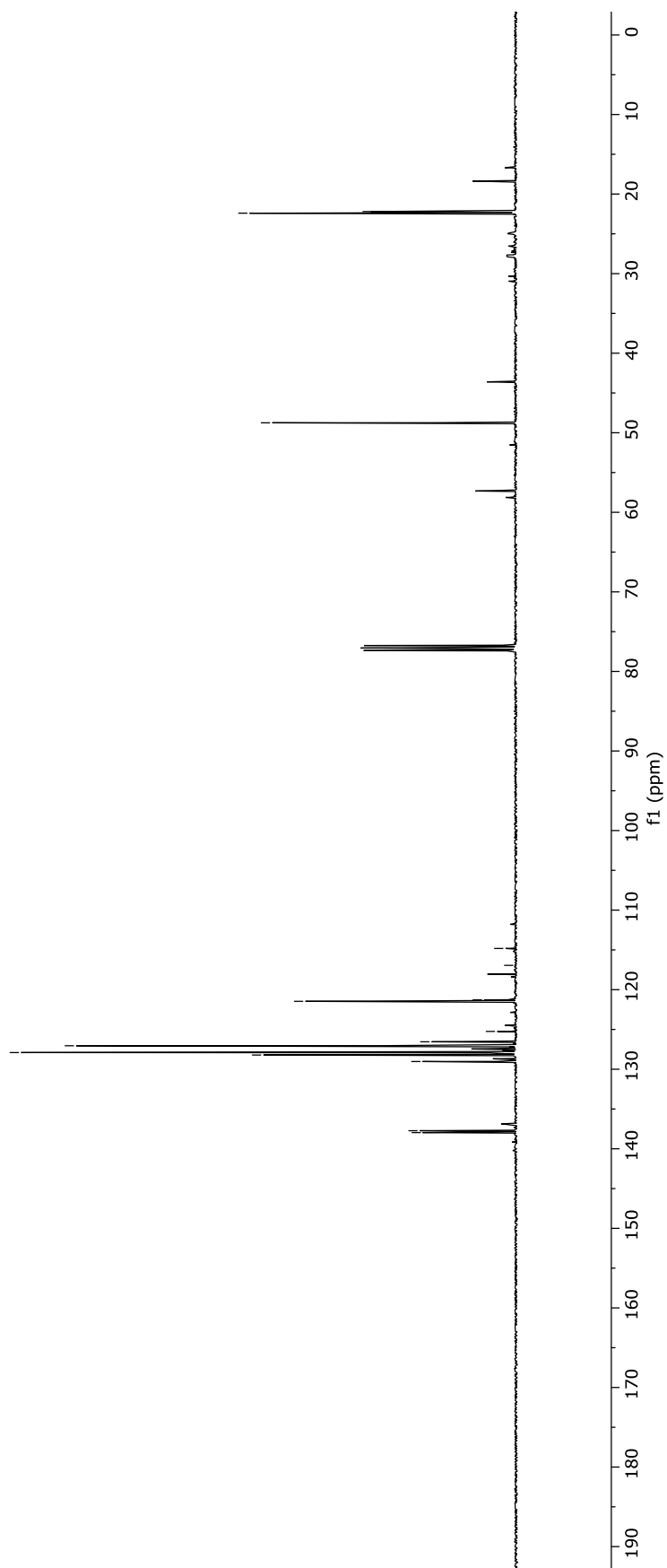


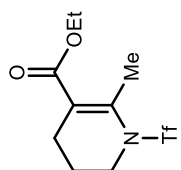
CDCl₃, 400 MHz
¹³C NMR

22.40
 22.20

48.75

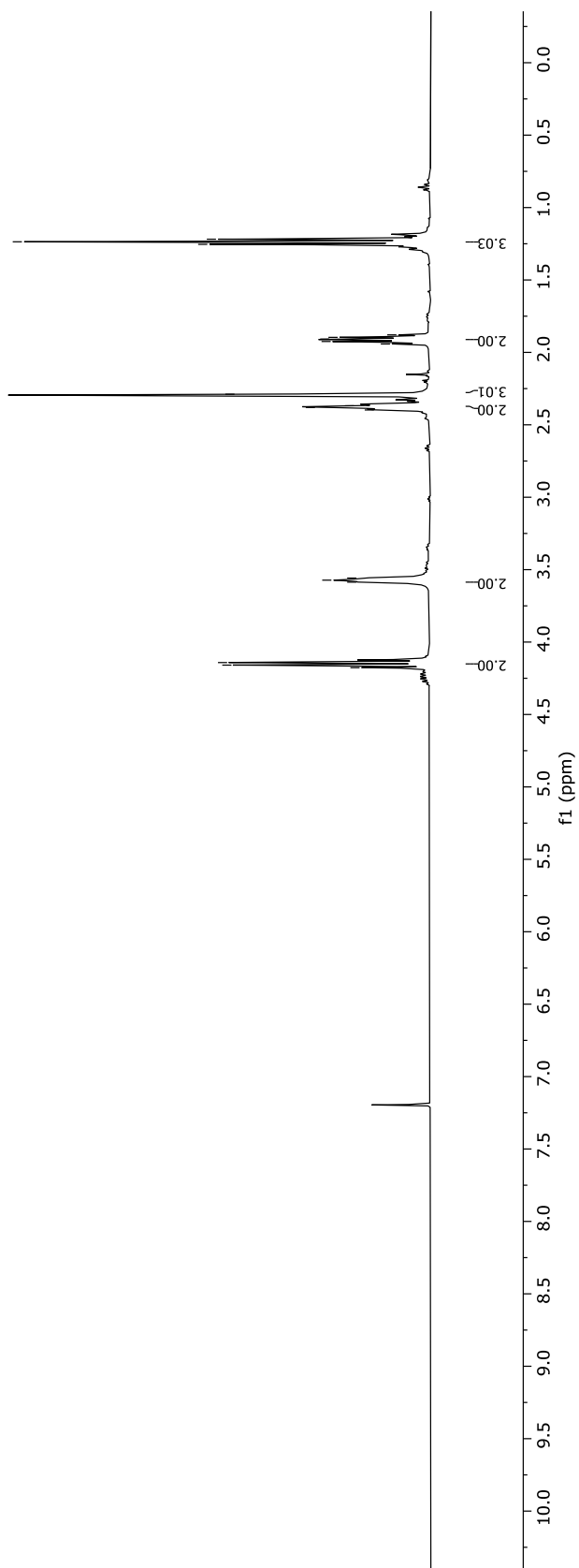
137.96
 137.73
 129.03
 128.22
 127.91
 127.05
 126.55
 125.25
 121.47
 121.28
 116.94
 114.82

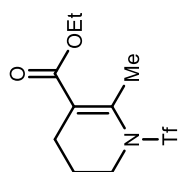




CDCl₃, 400 MHz
¹H NMR

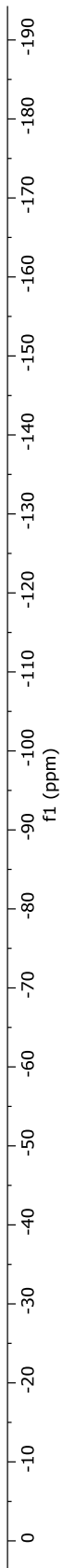
4.18, 4.16, 4.14, 4.13
 3.59, 3.57, 3.56
 2.40, 2.38, 2.37, 2.29, 1.94, 1.92, 1.91, 1.90, 1.88
 1.25, 1.24, 1.22

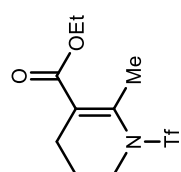




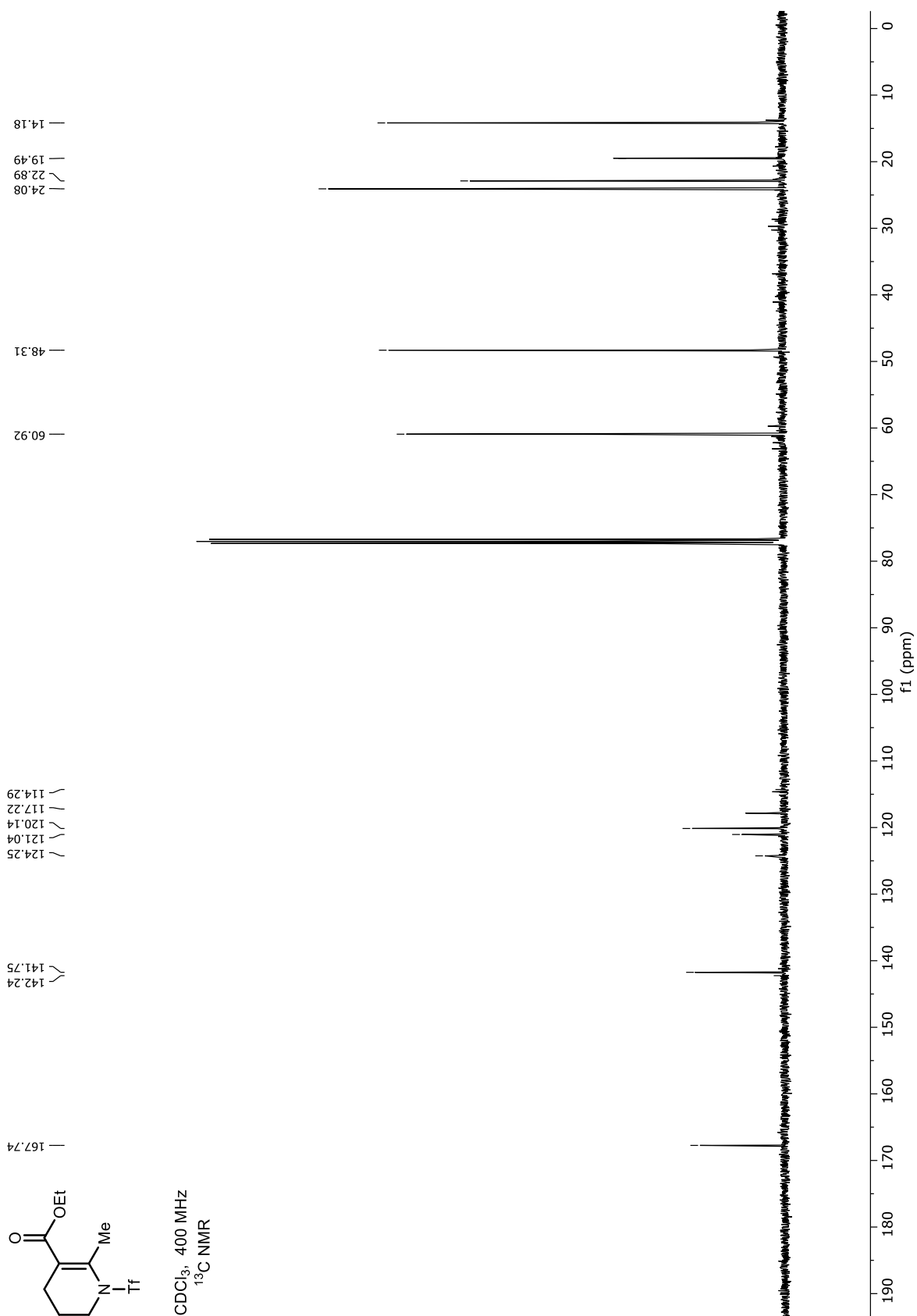
CDCl₃, 400 MHz
¹⁹F NMR

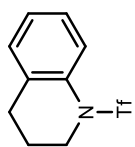
16.57, -75.91





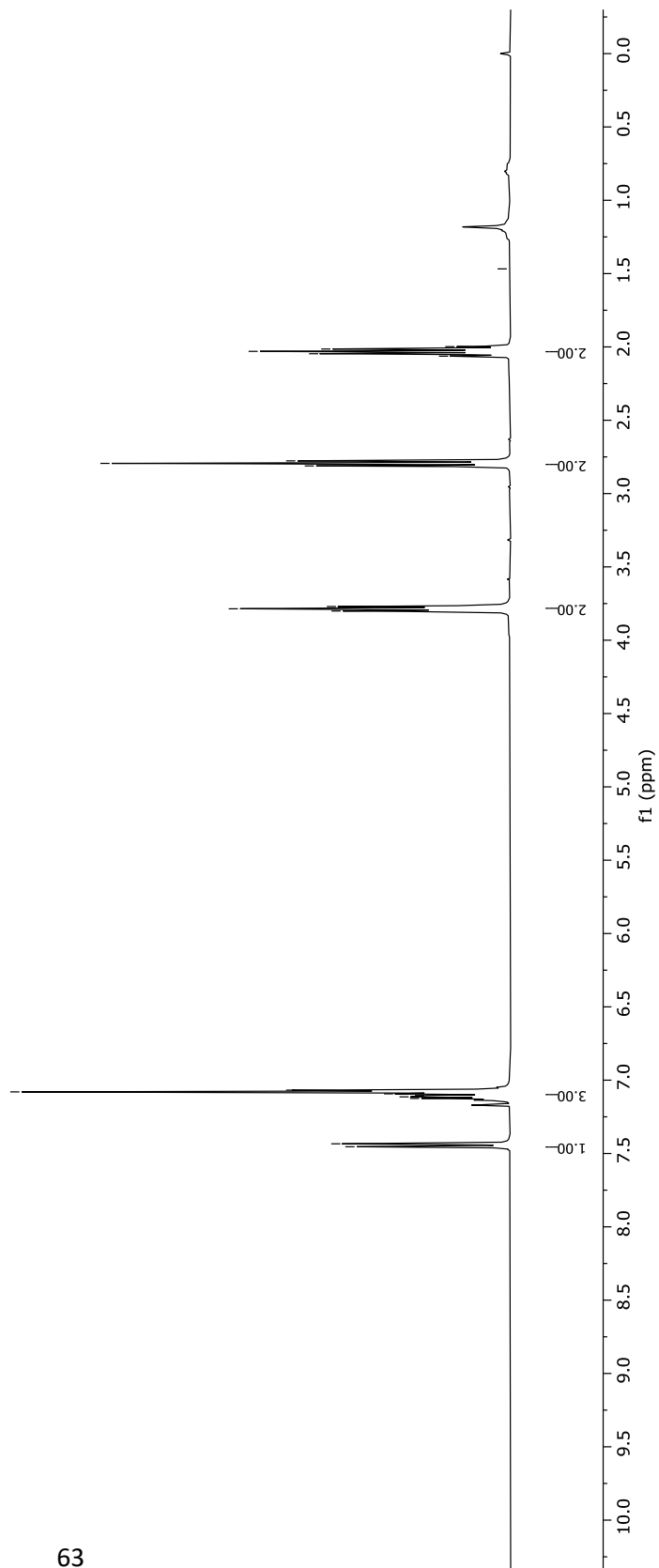
CDCl₃, 400 MHz
¹³C NMR

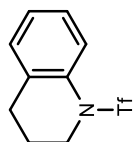




CDCl₃, 400 MHz
¹H NMR

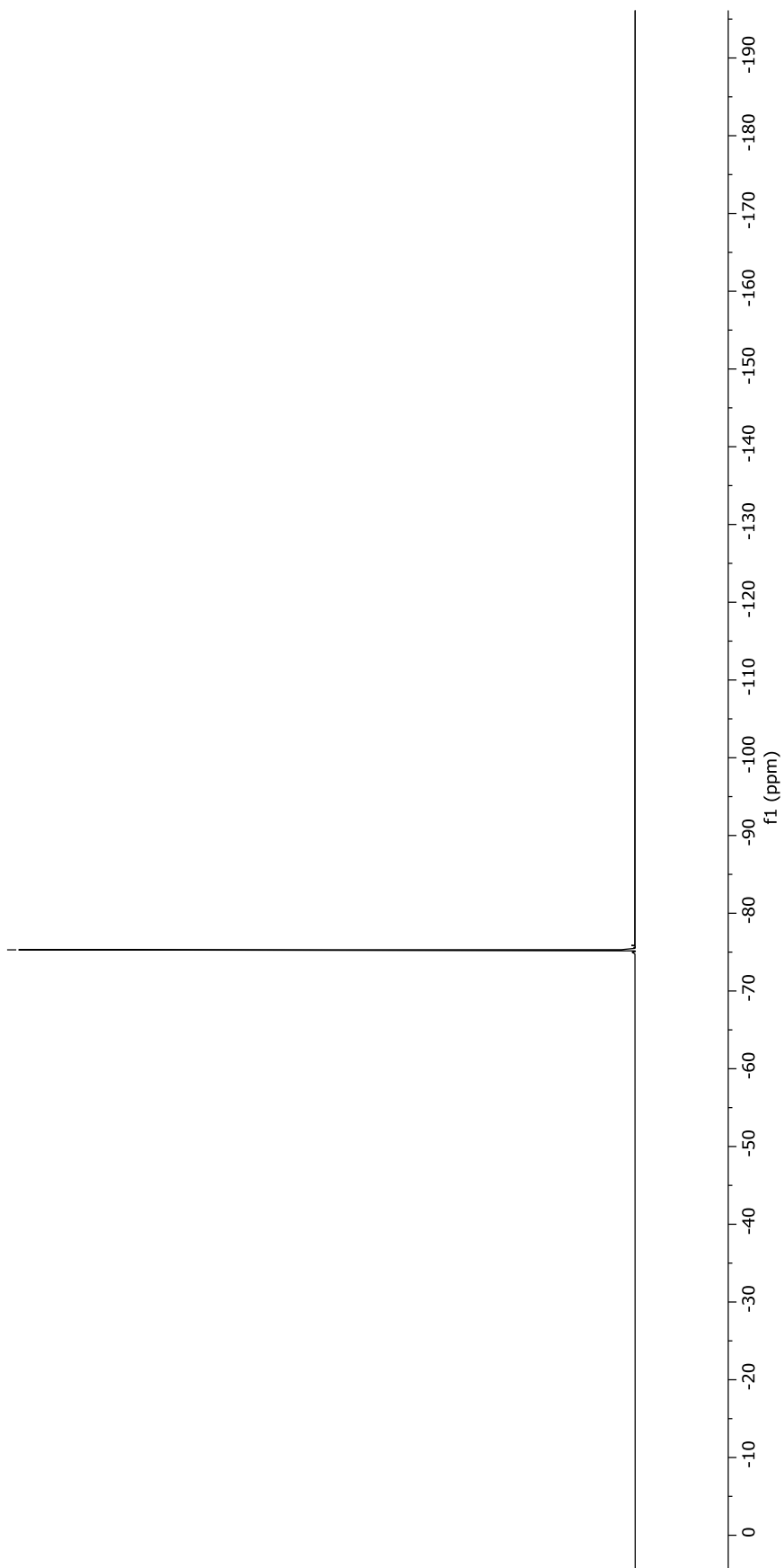
7.45
 7.43
 7.12
 7.11
 7.10
 7.09
 7.08
 7.07
 3.80
 3.79
 3.77
 2.81
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 2.78
 2.06
 2.05
 2.03
 2.01
 2.00
 1.47

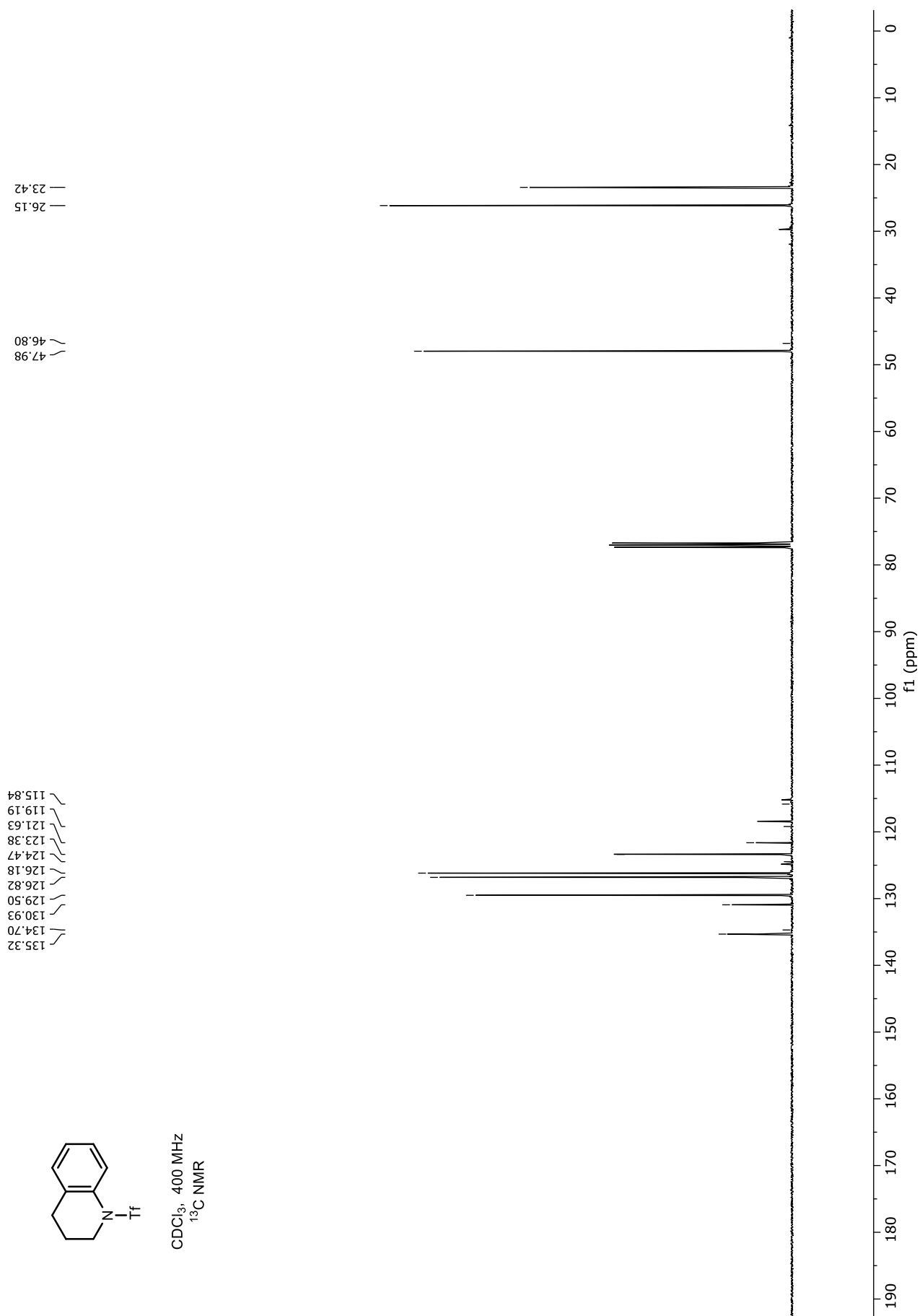




CDCl₃, 400 MHz
¹⁹F NMR

— -75.29



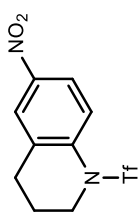


2.22
2.17
2.15
2.14
2.12

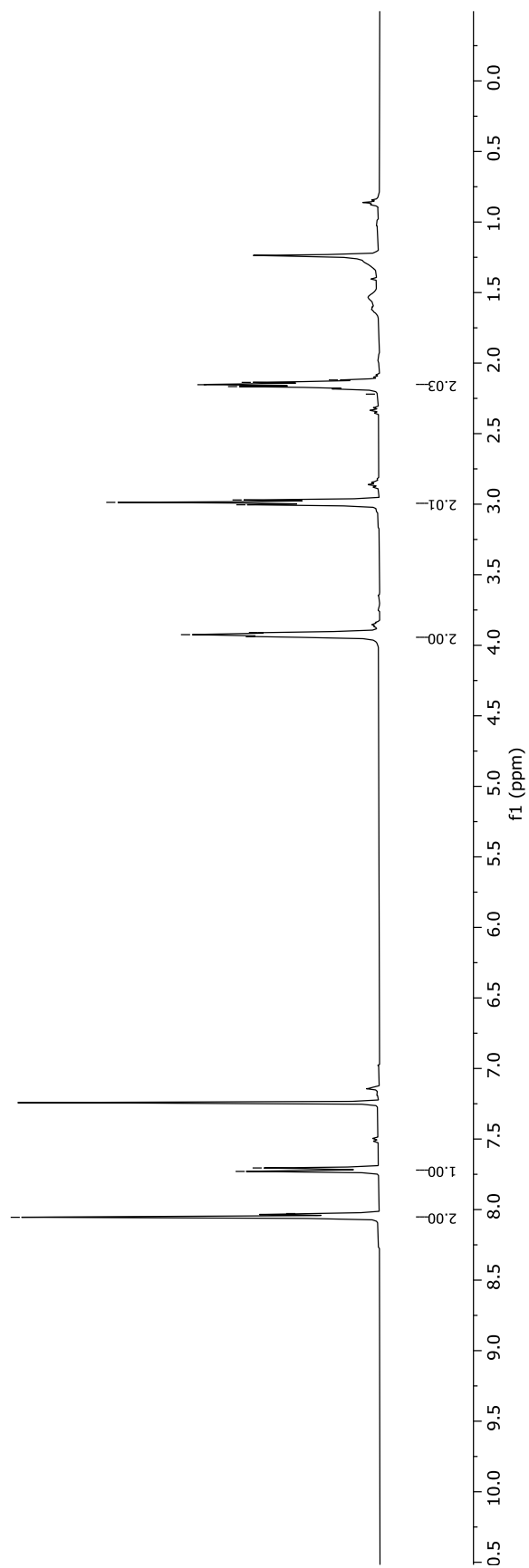
3.00
2.99
2.97

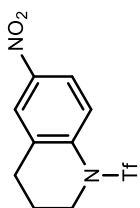
3.94
3.92
3.91

8.05
8.03
7.73
7.70



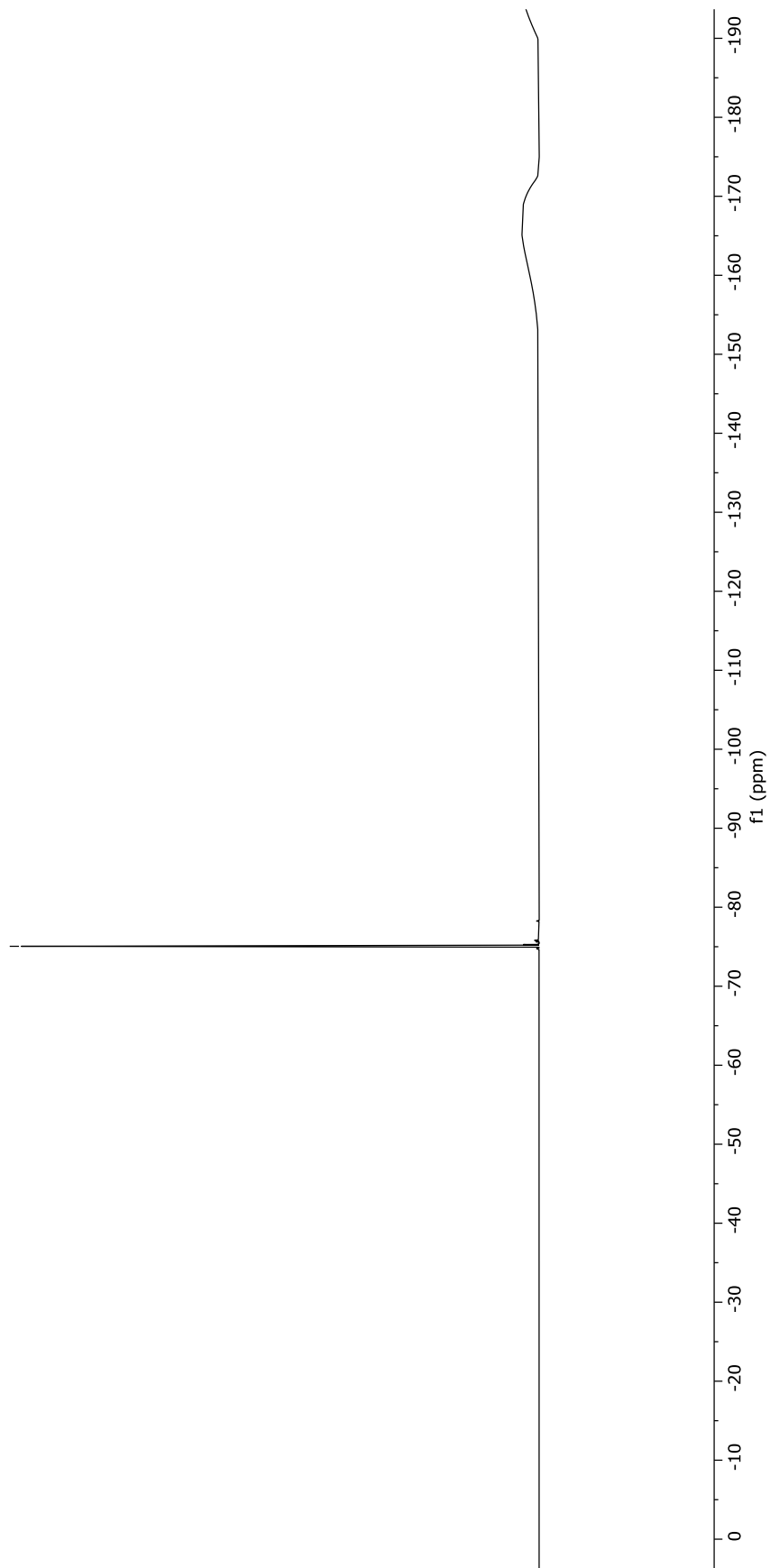
CDCl₃, 400 MHz
¹H NMR

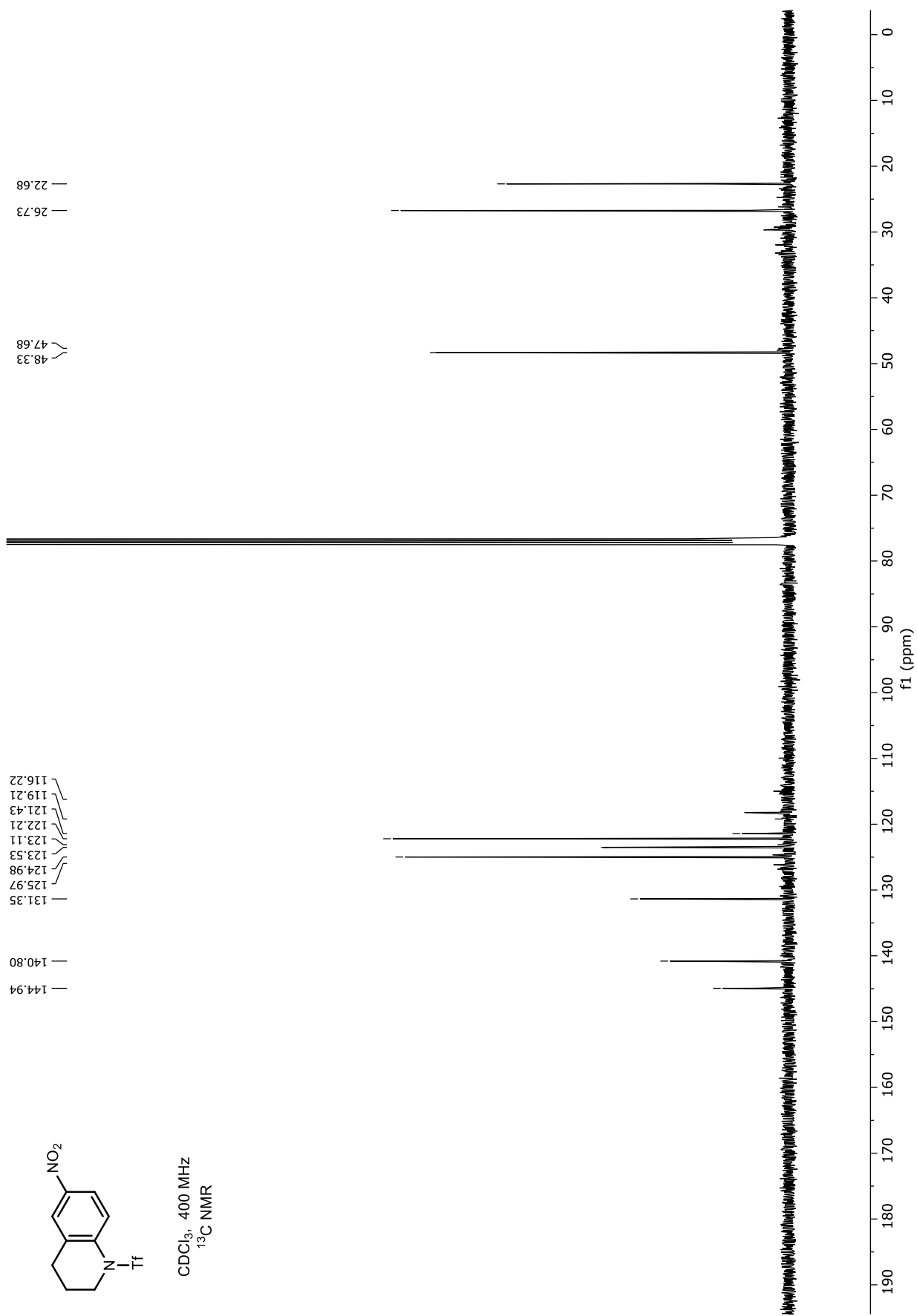


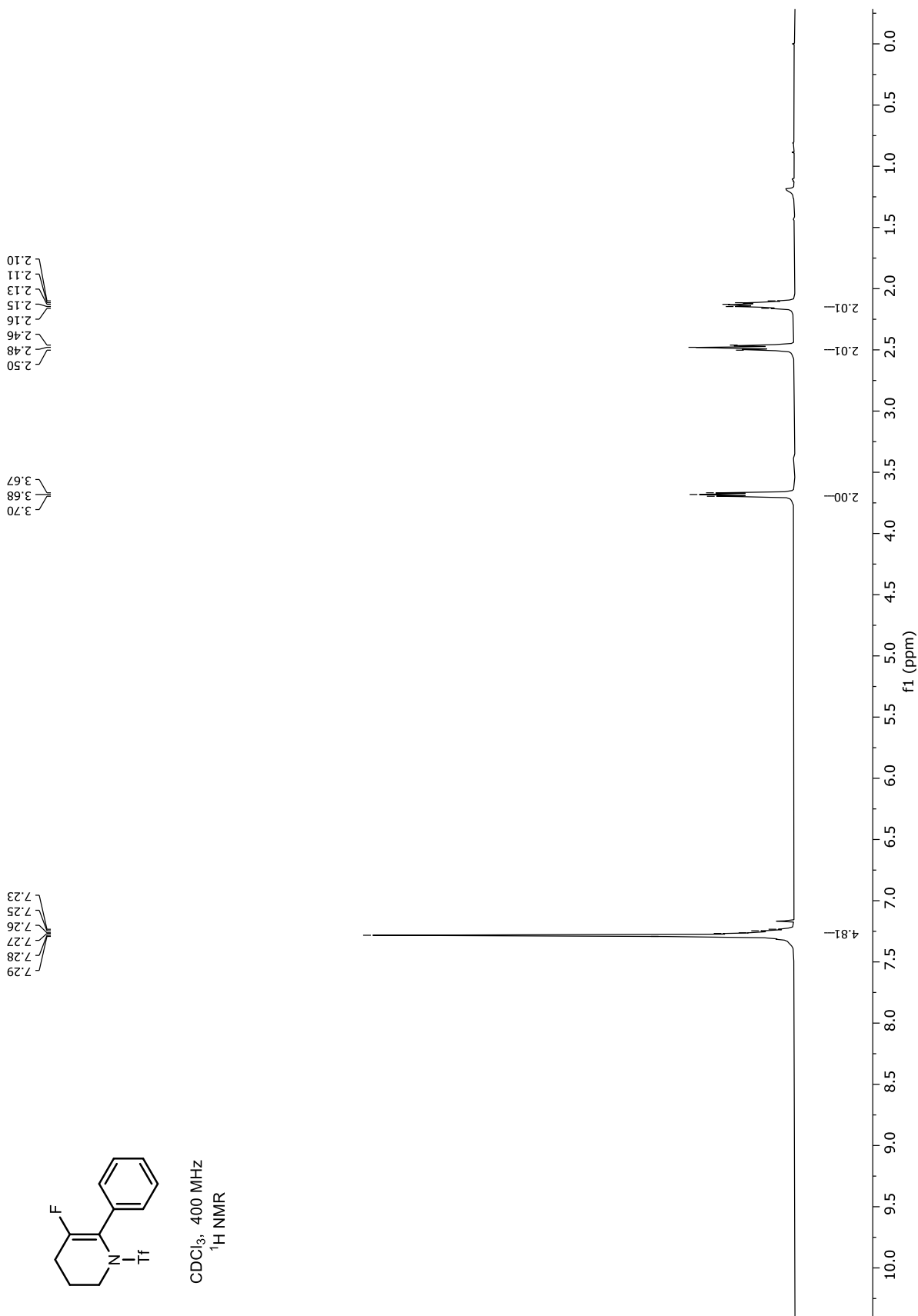


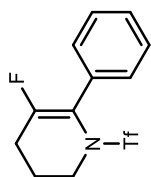
CDCl₃, 400 MHz
¹⁹F NMR

— -75.05





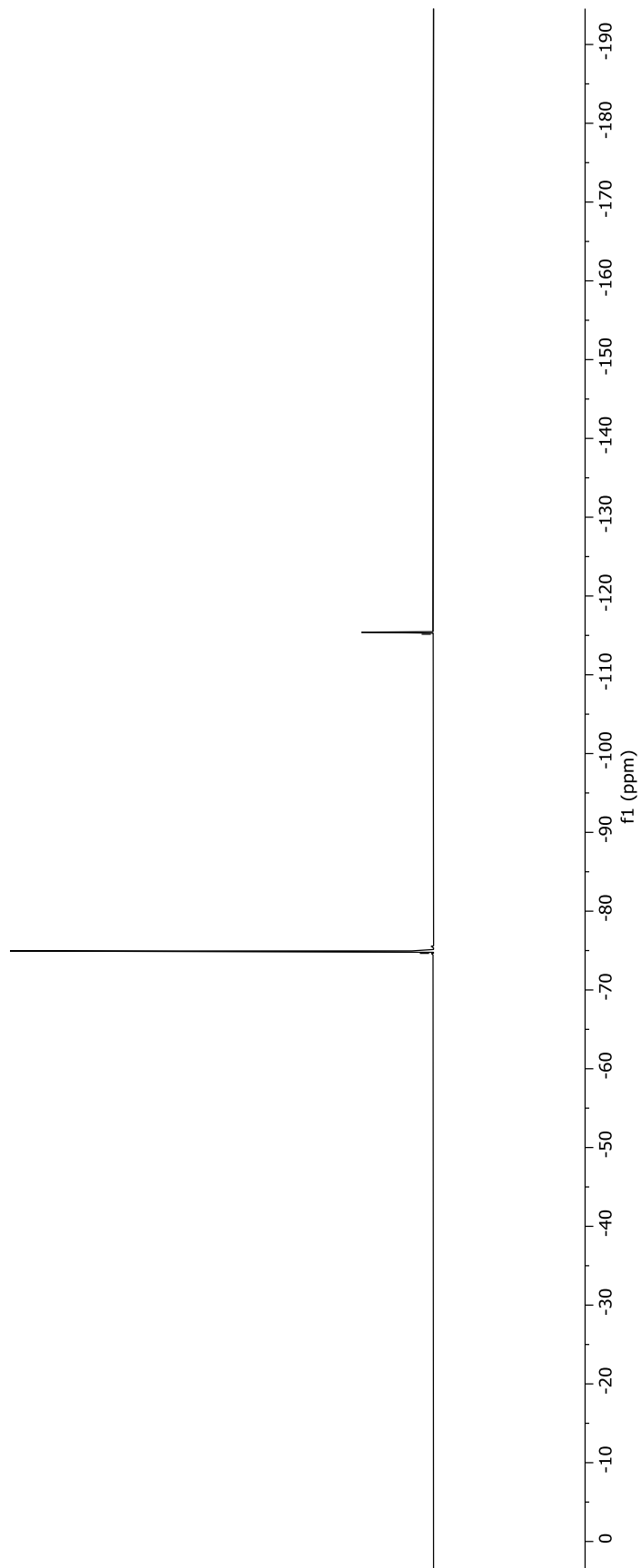


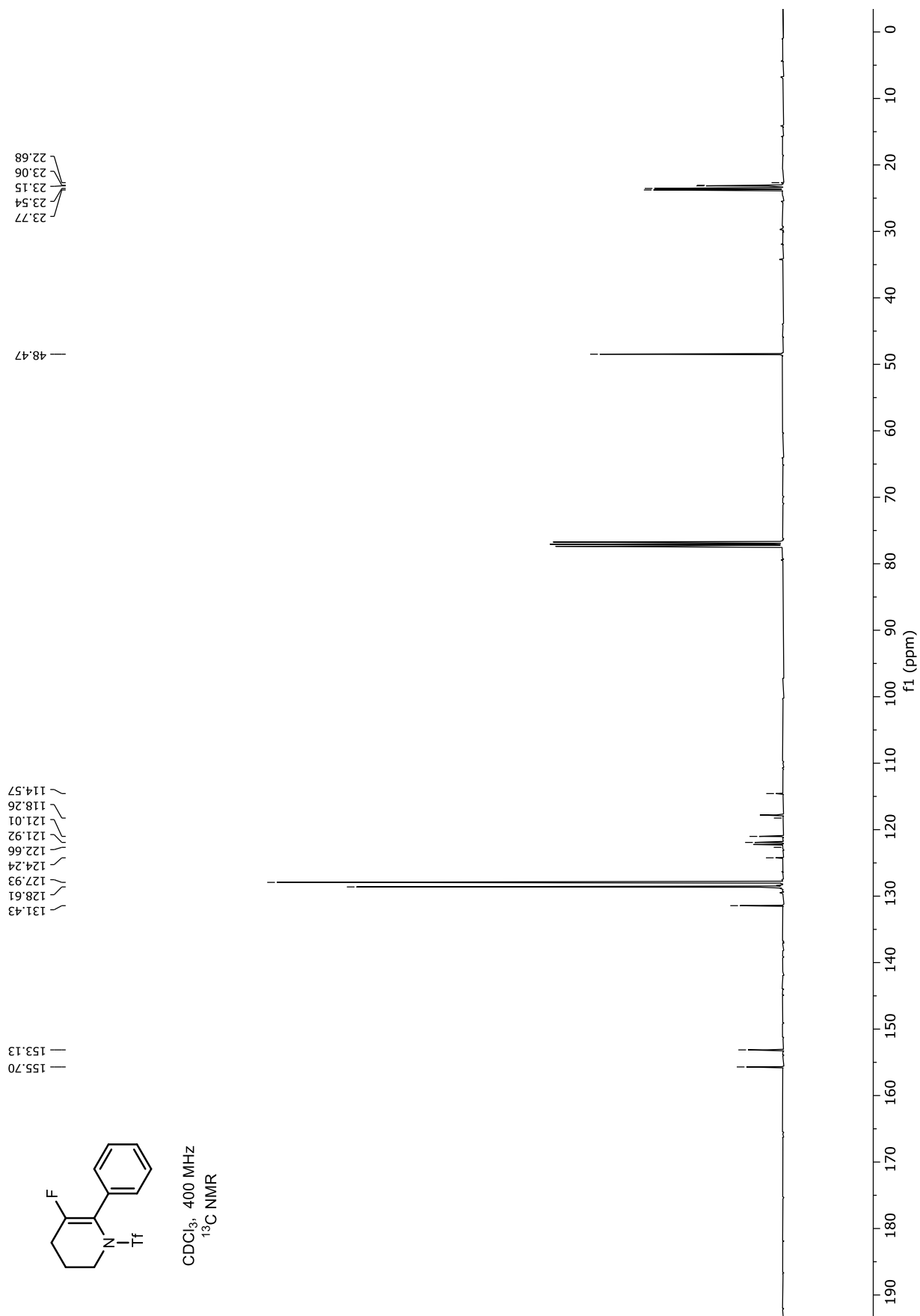


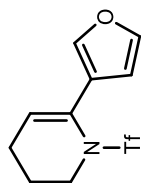
CDCl₃, 400 MHz
¹⁹F NMR

— -115.15

— -74.65







CDCl₃, 400 MHz
¹H NMR

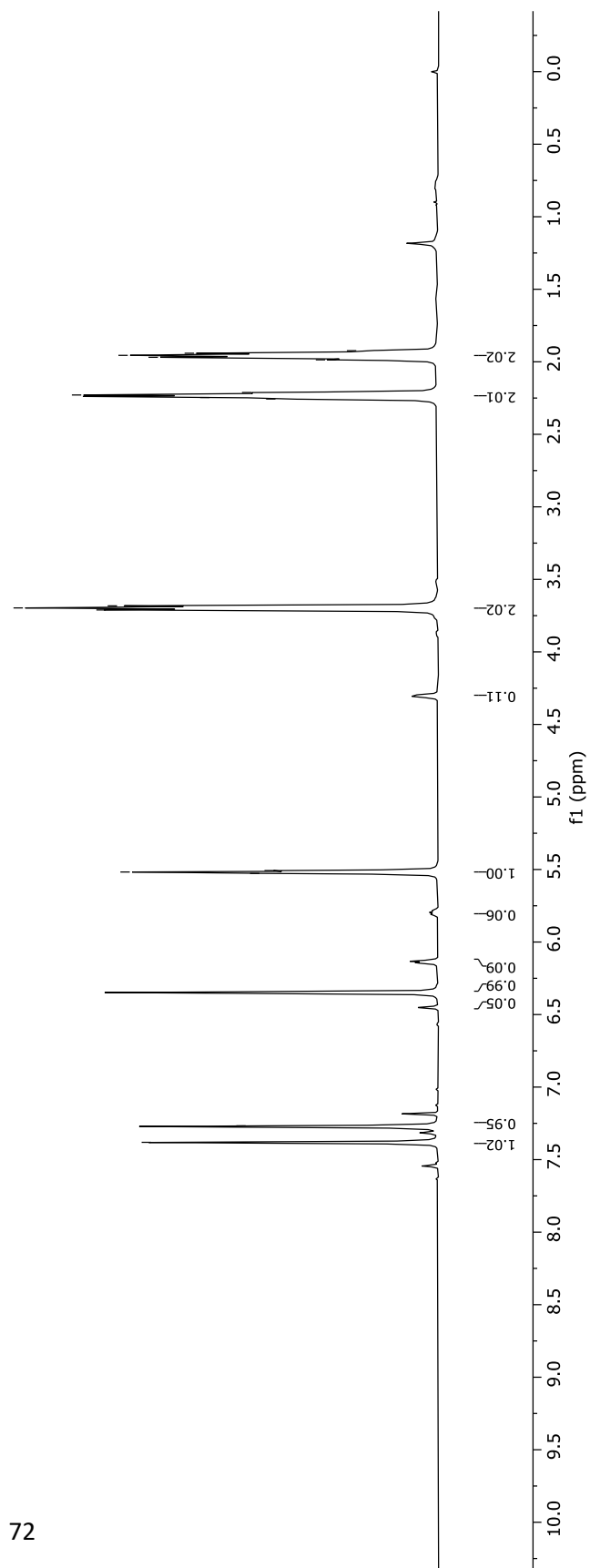
2.26
2.25
2.23
2.21
1.99
1.97
1.96
1.94
1.92

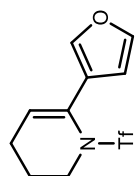
3.71
3.70
3.68

5.53
5.52
5.51

6.35

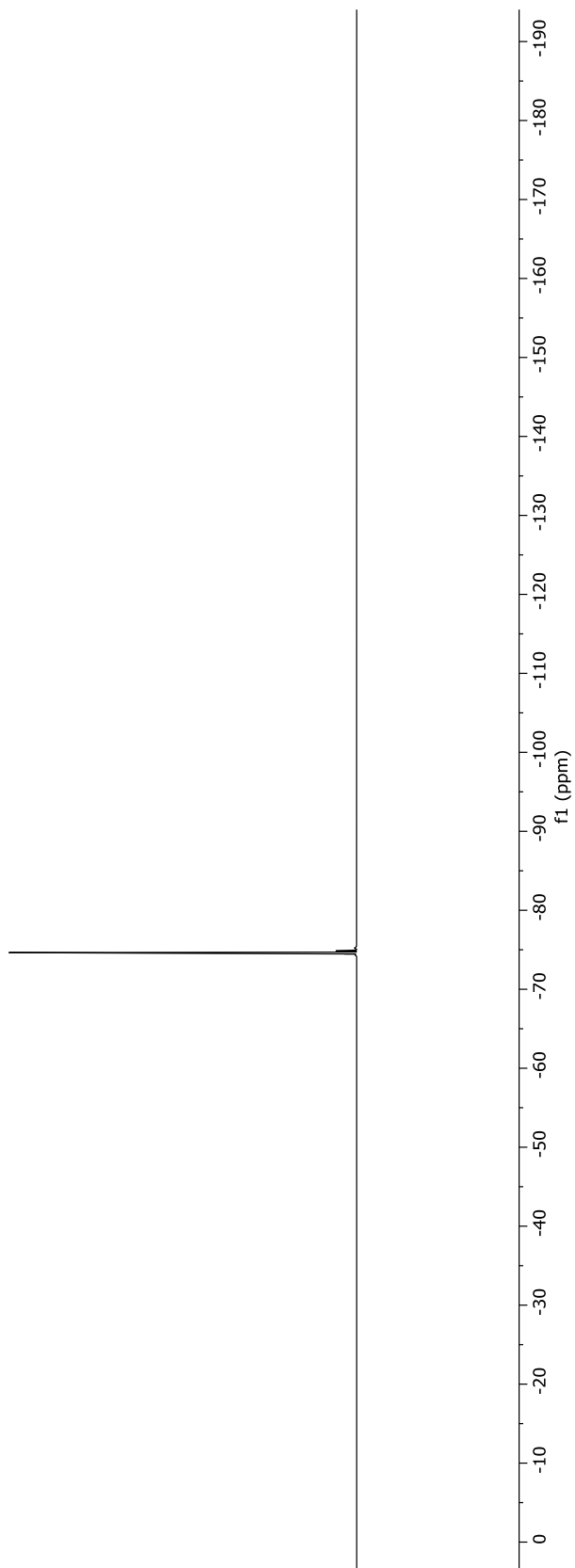
7.38
7.27

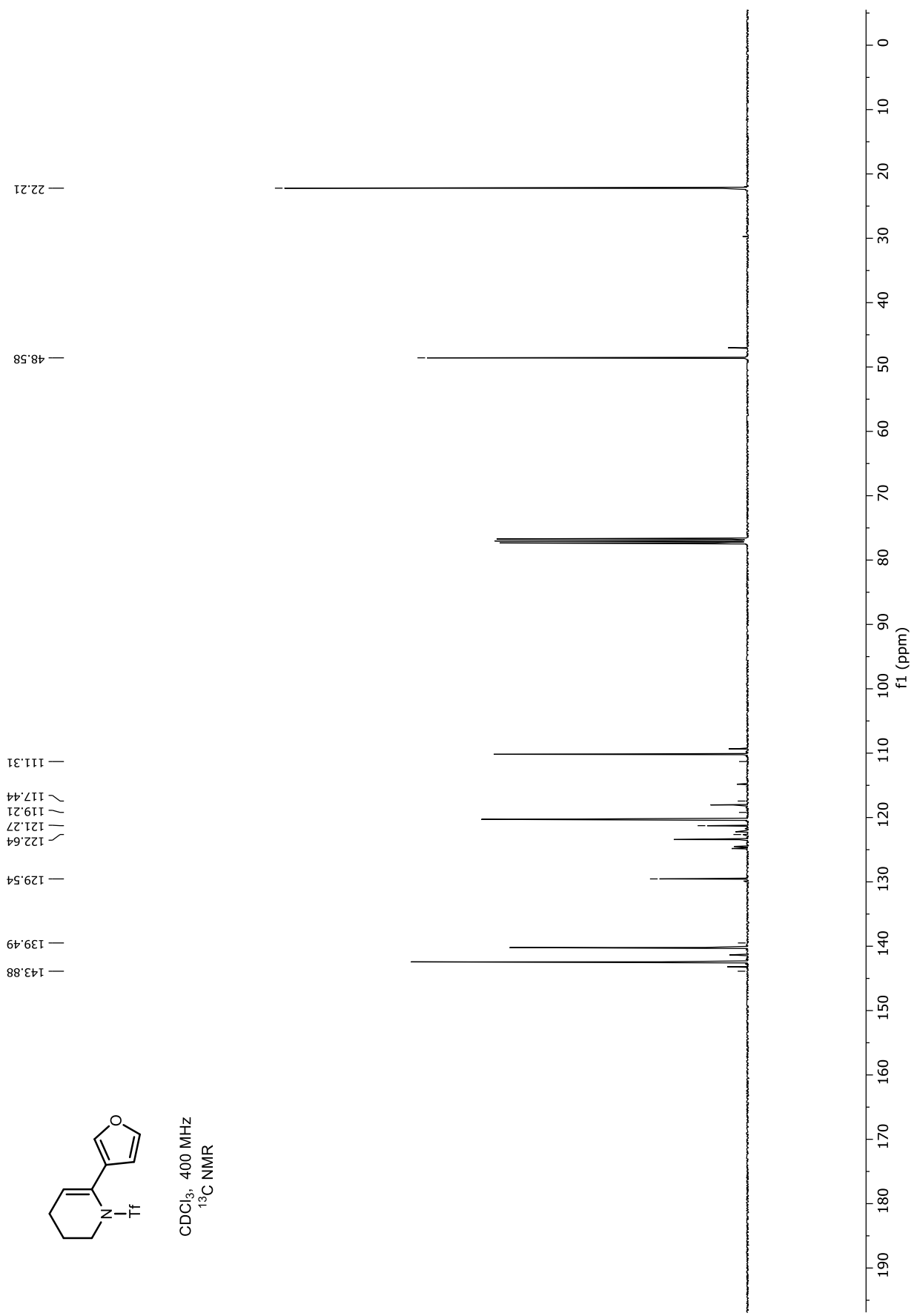


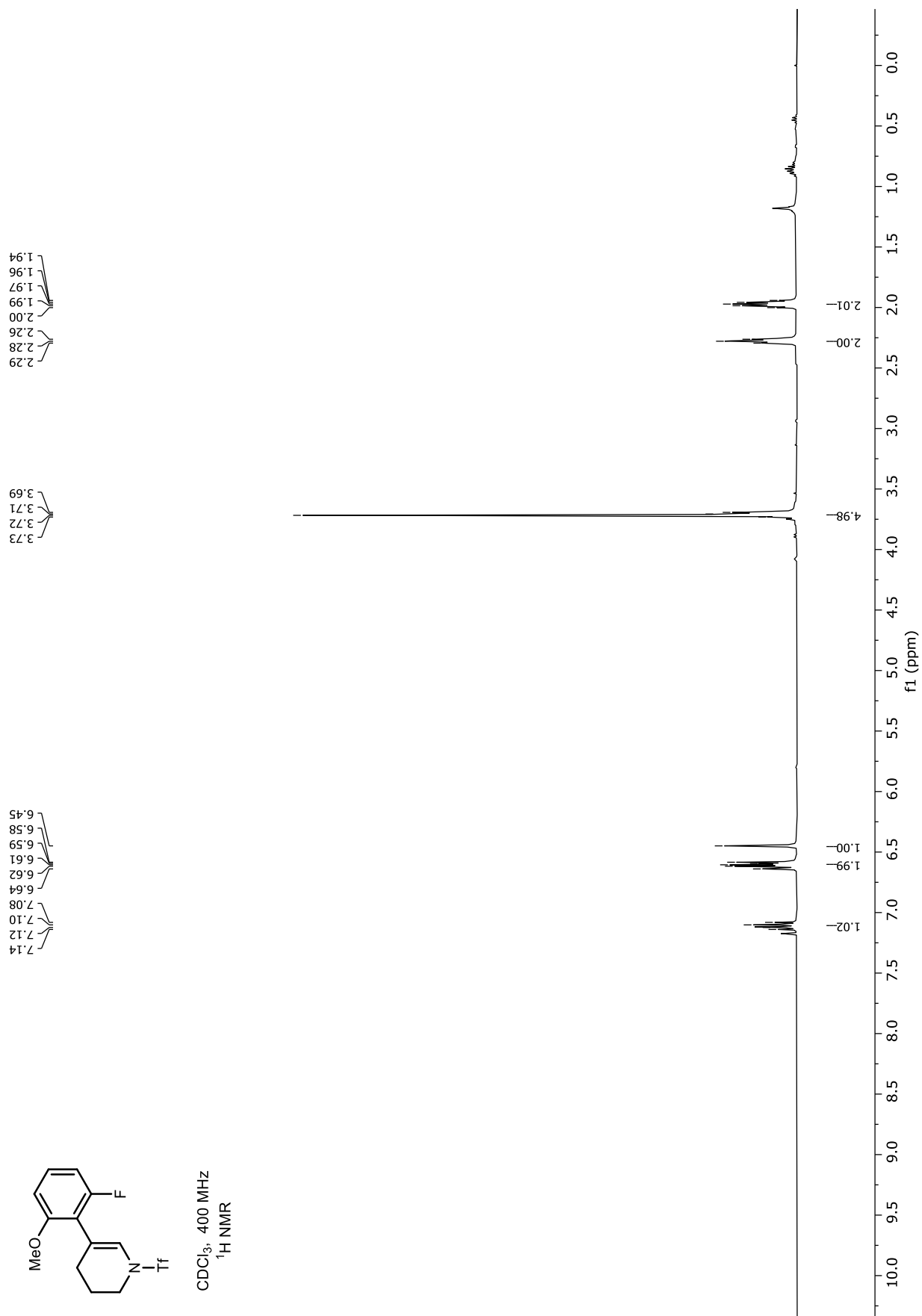


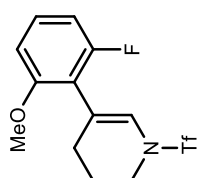
CDCl₃, 400 MHz
¹⁹F NMR

— -74.47

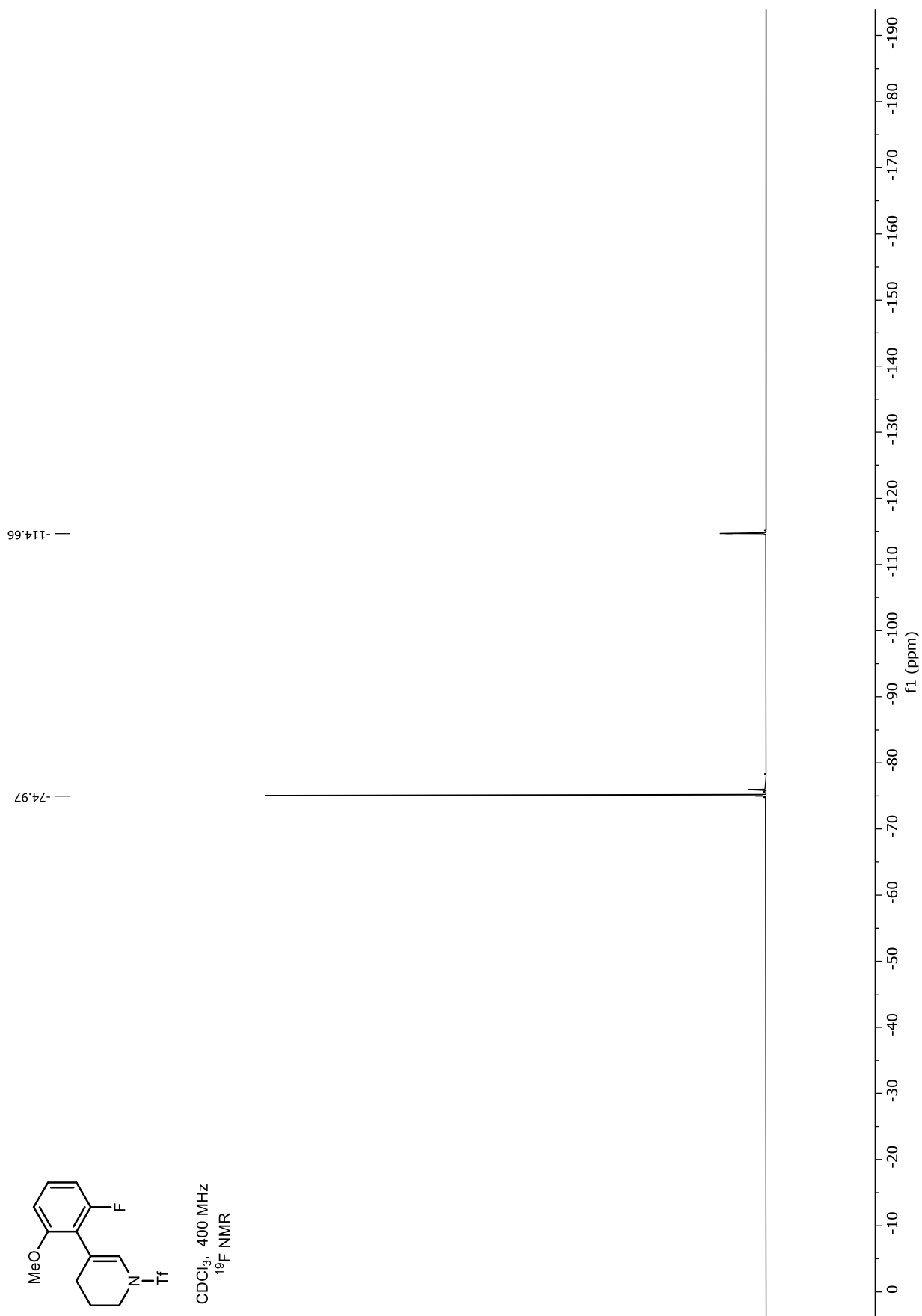


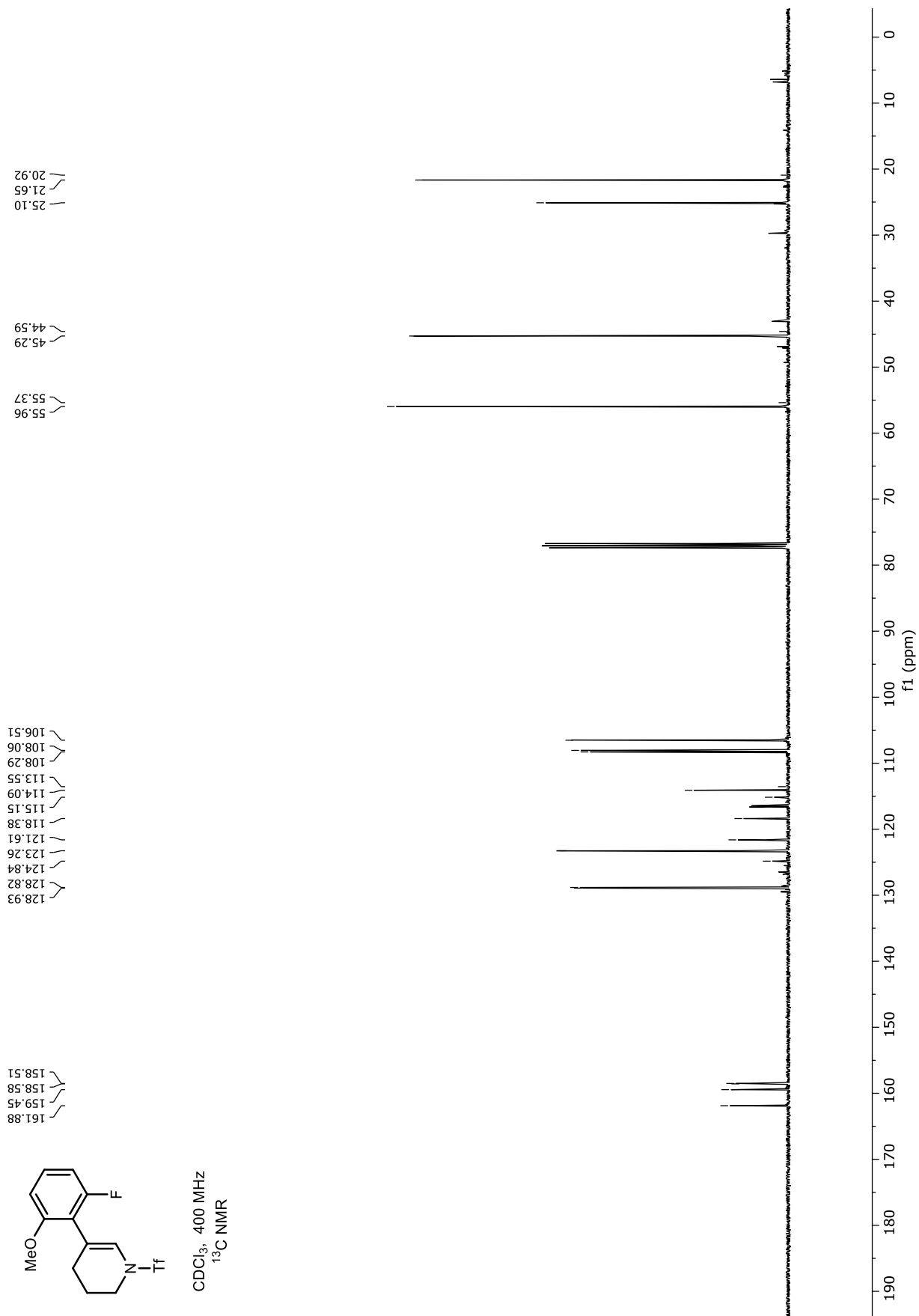


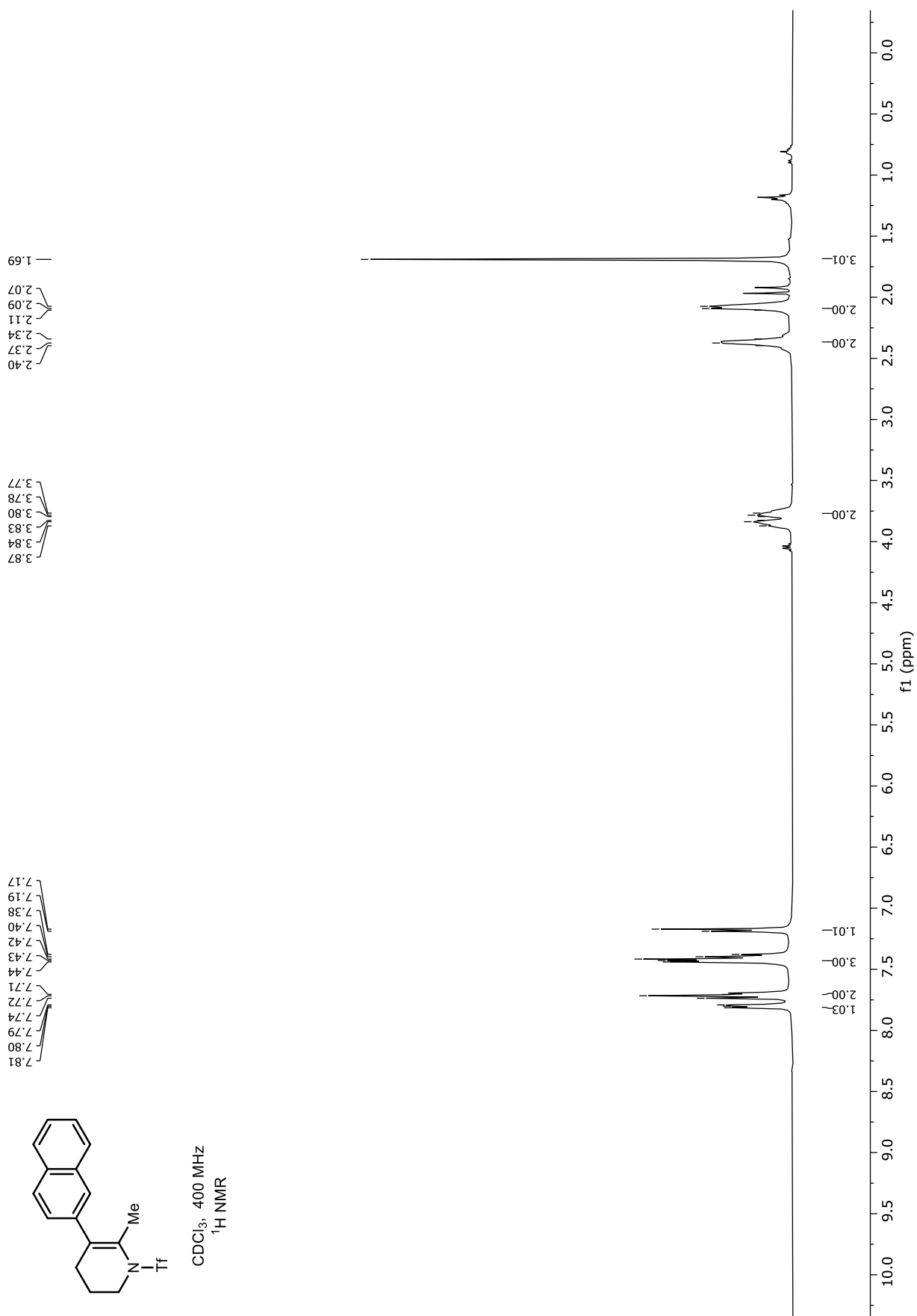


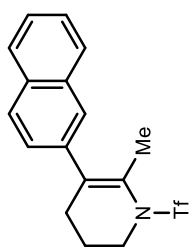


CDCl₃, 400 MHz
¹⁹F NMR





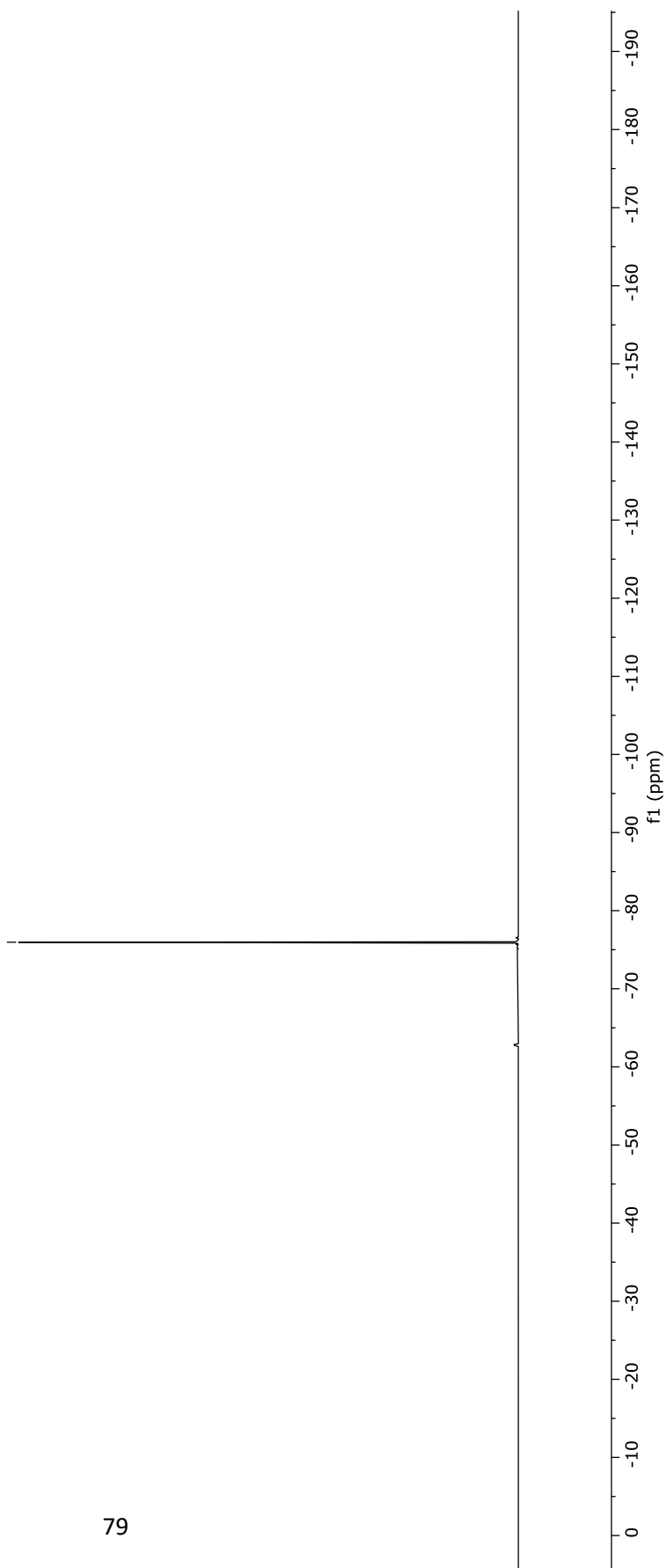


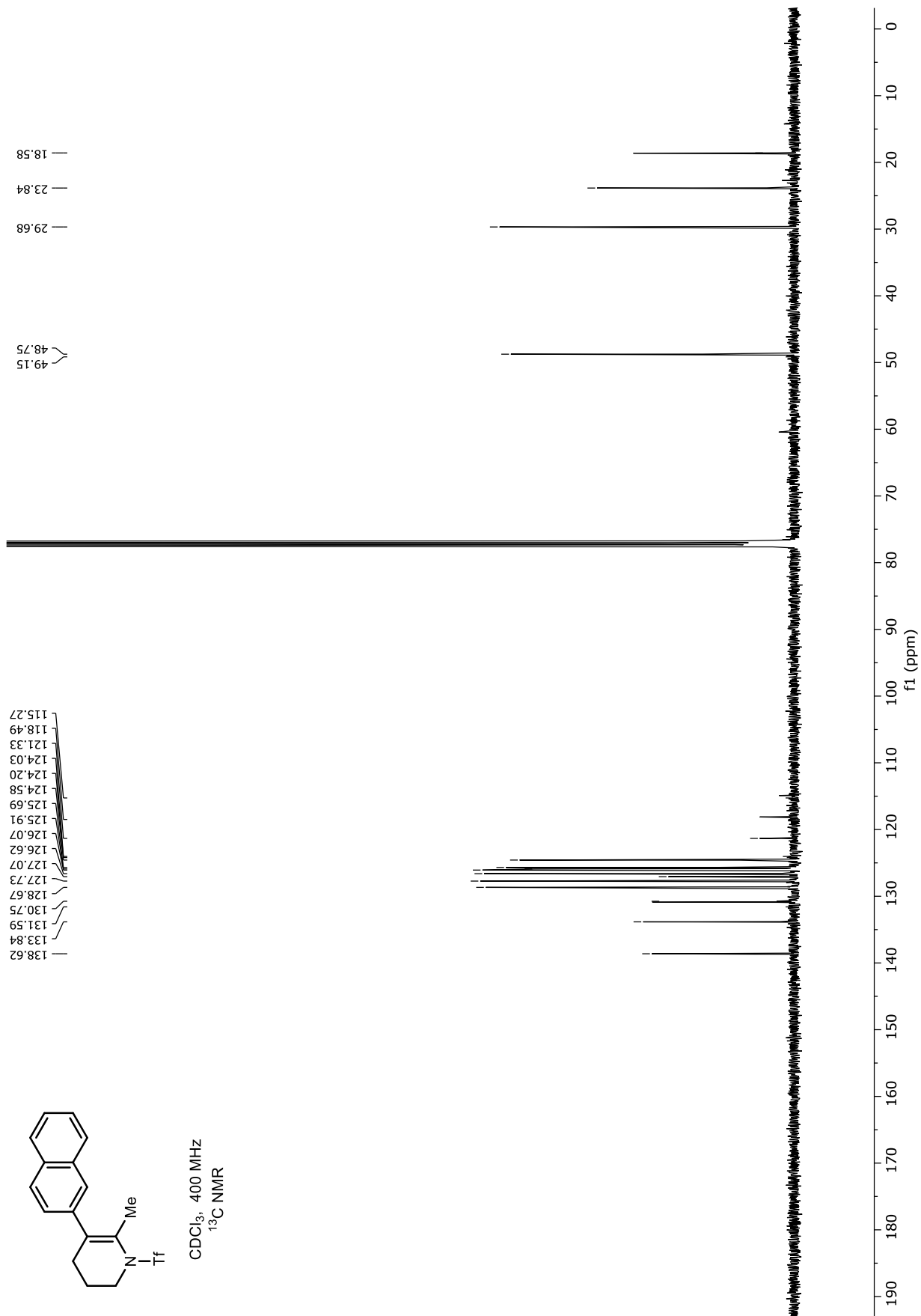


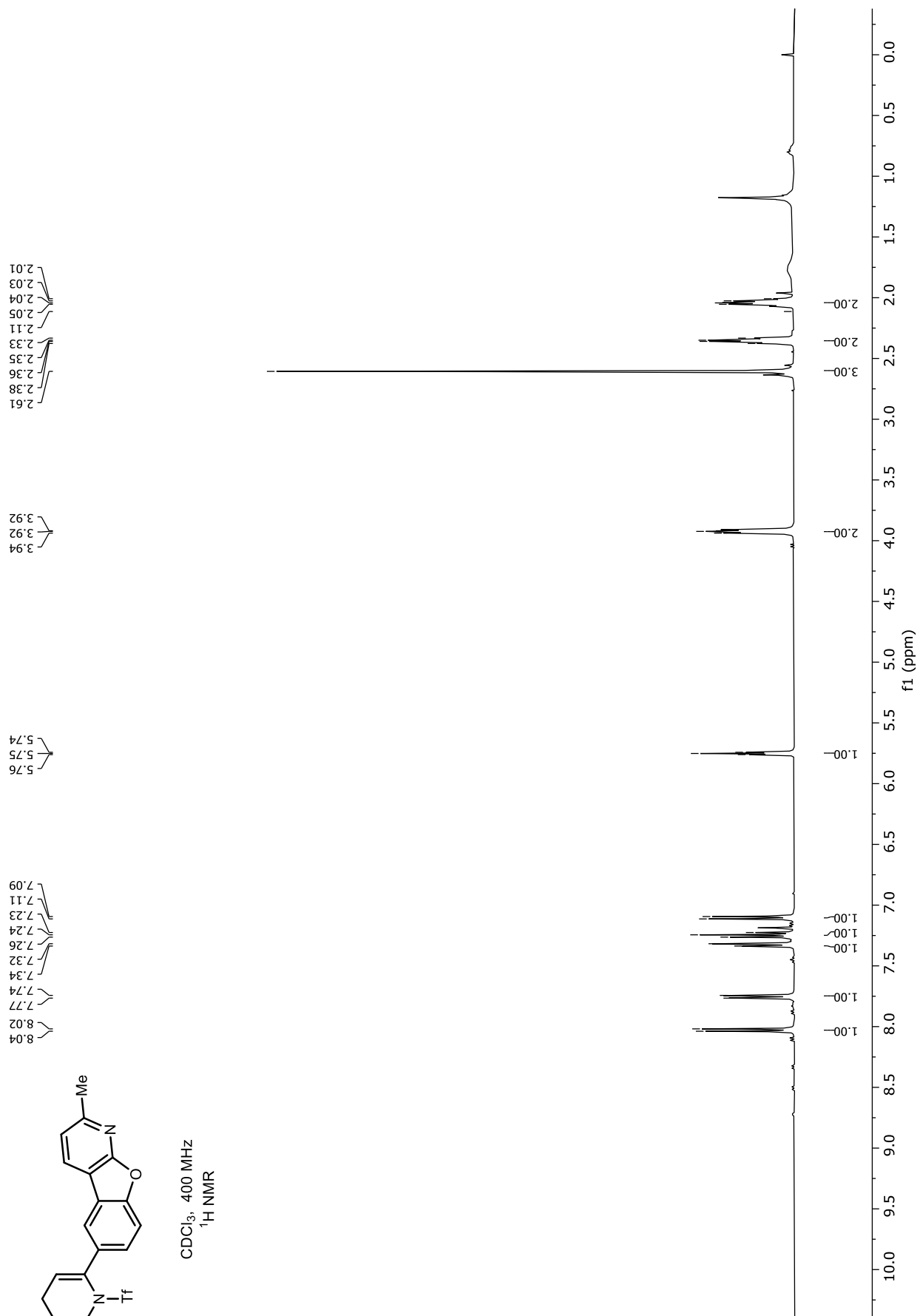
CDCl₃, 400 MHz
¹⁹F NMR

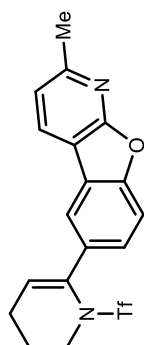
— -75.96

79



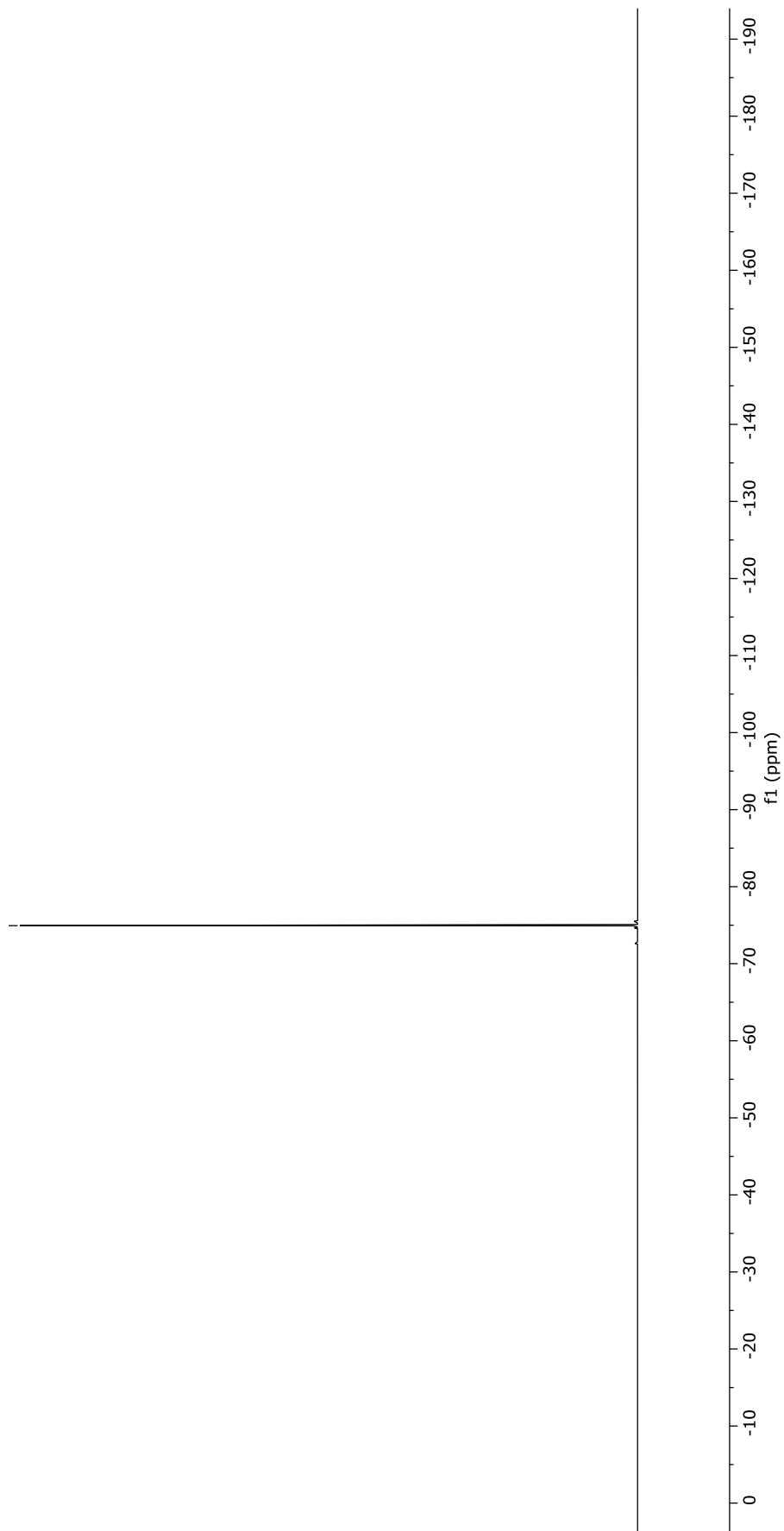


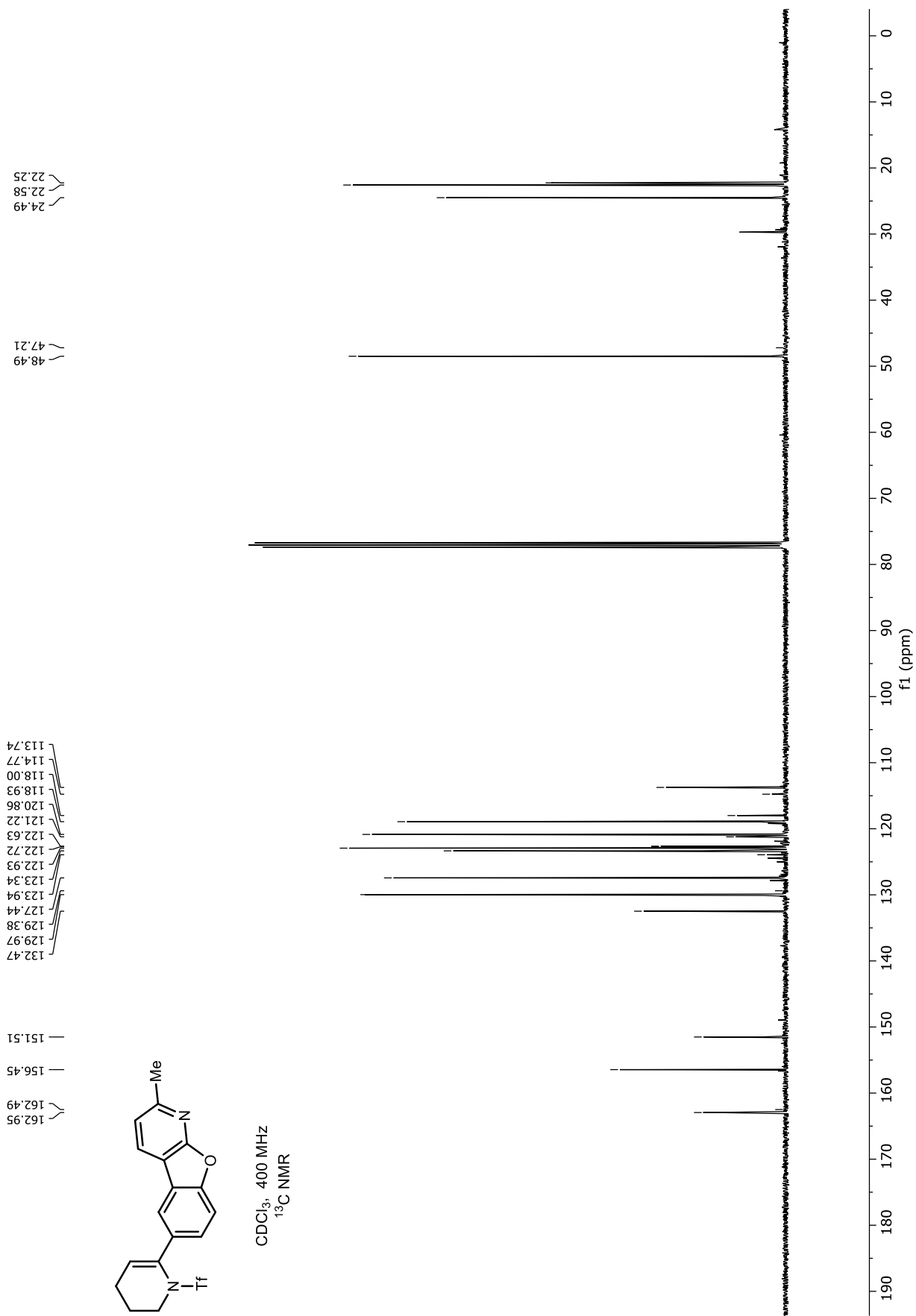


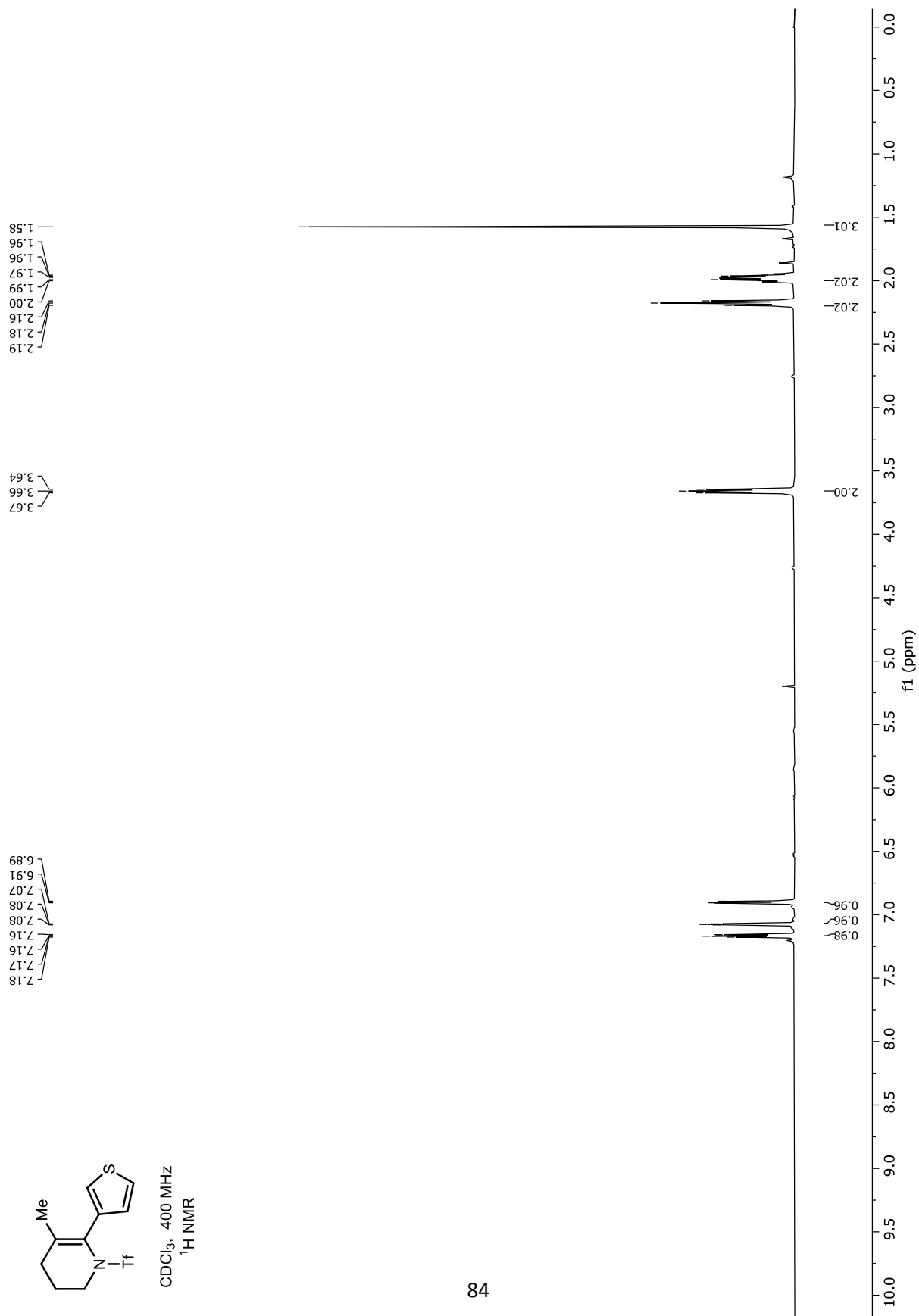


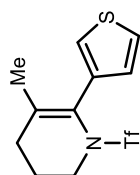
CDCl₃, 400 MHz
¹⁹F NMR

— -74.94



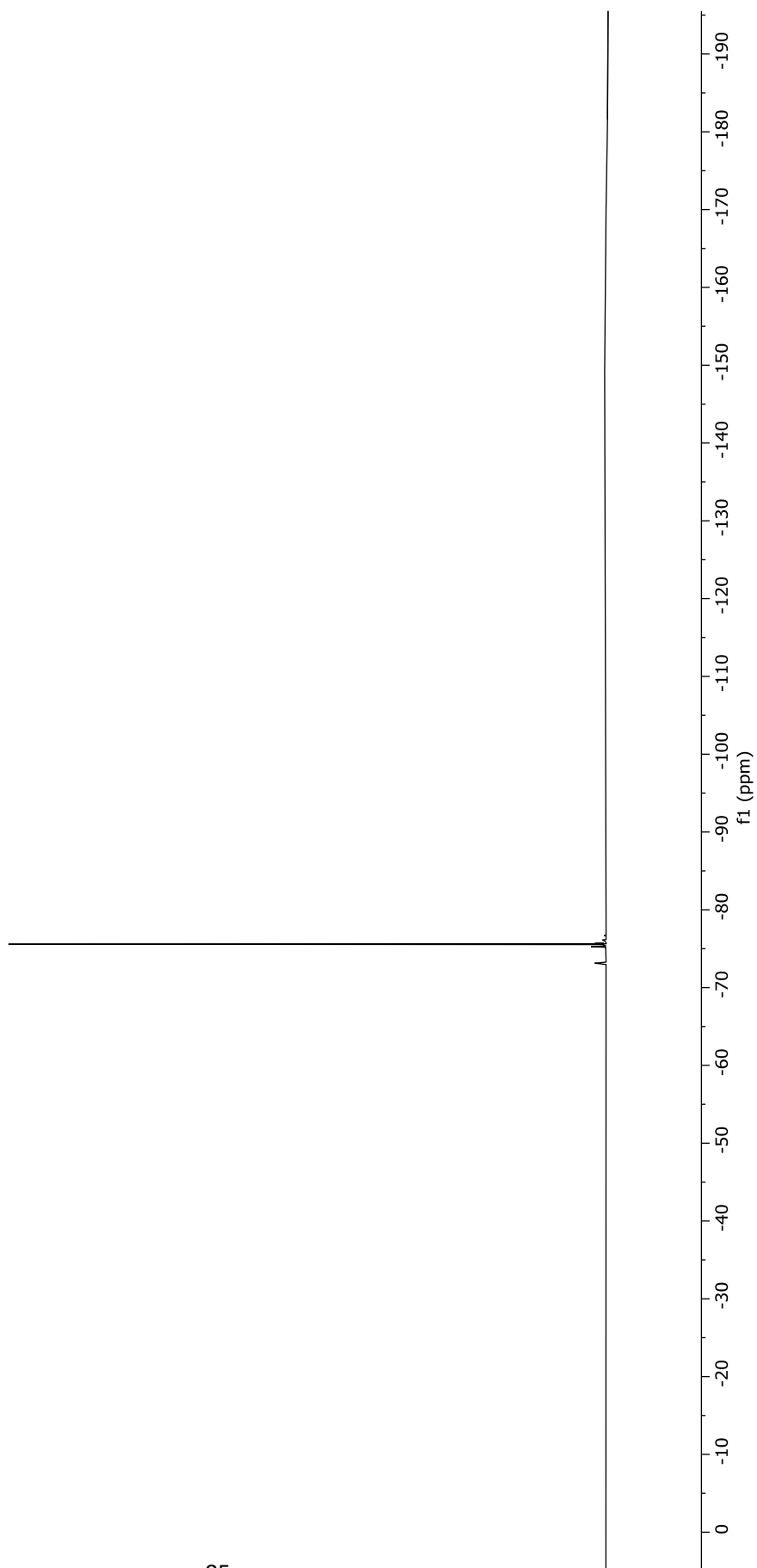


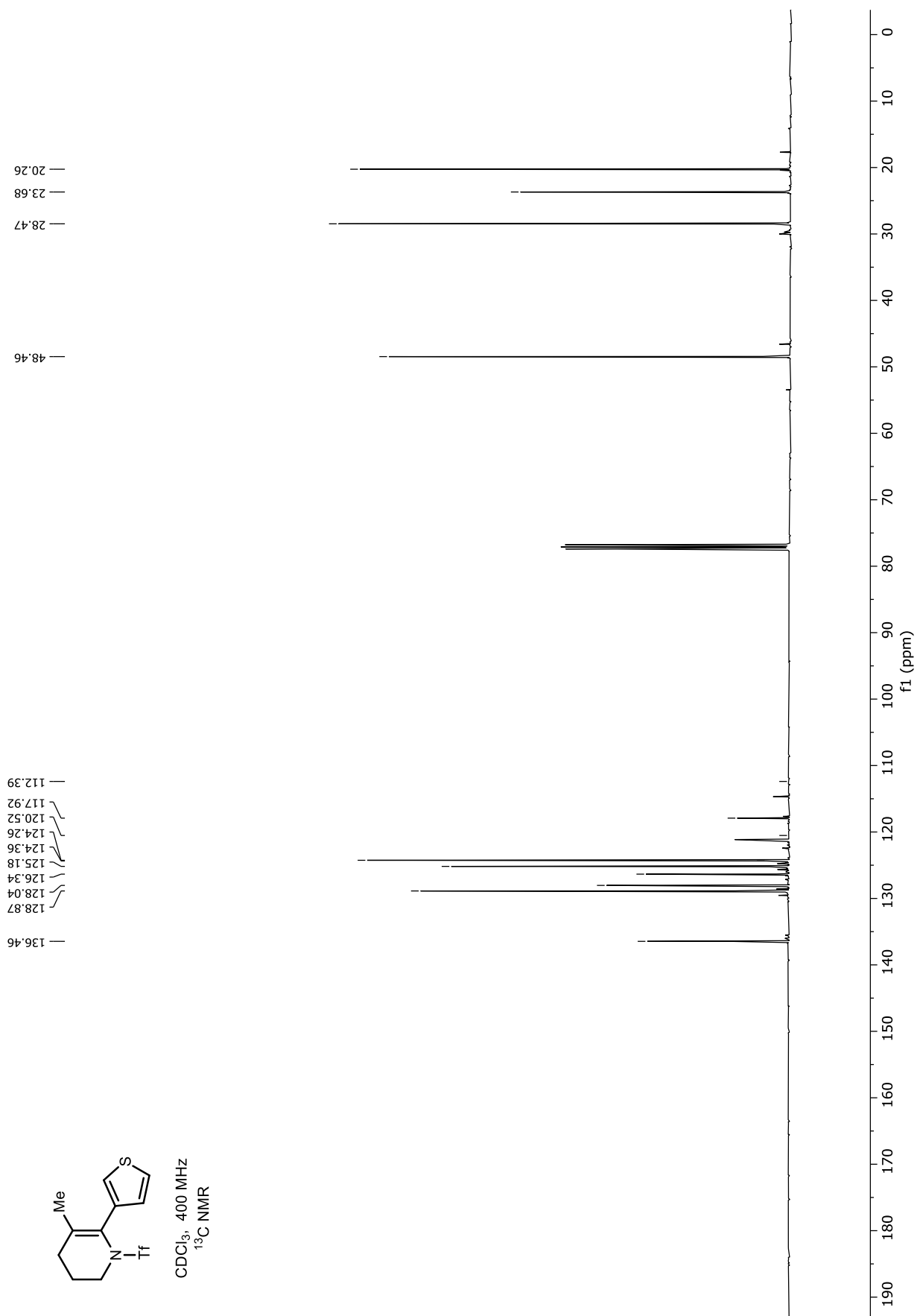


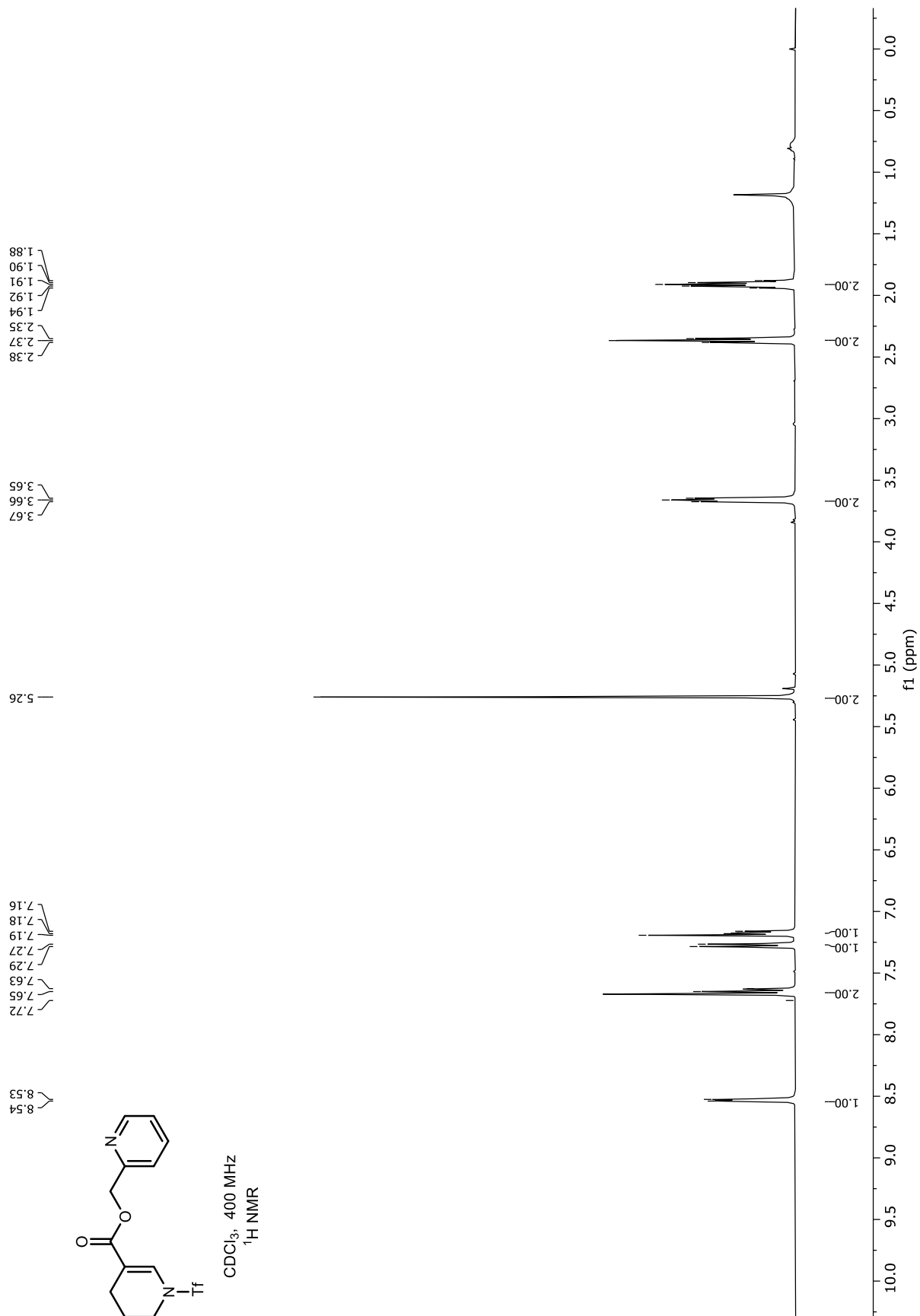


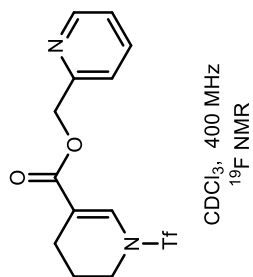
CDCl₃, 400 MHz
¹⁹F NMR

— -75.73

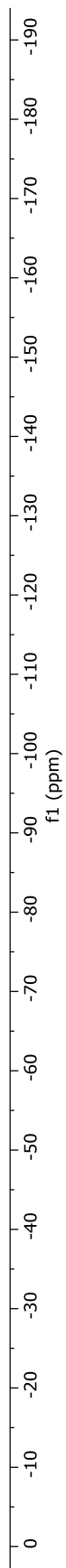


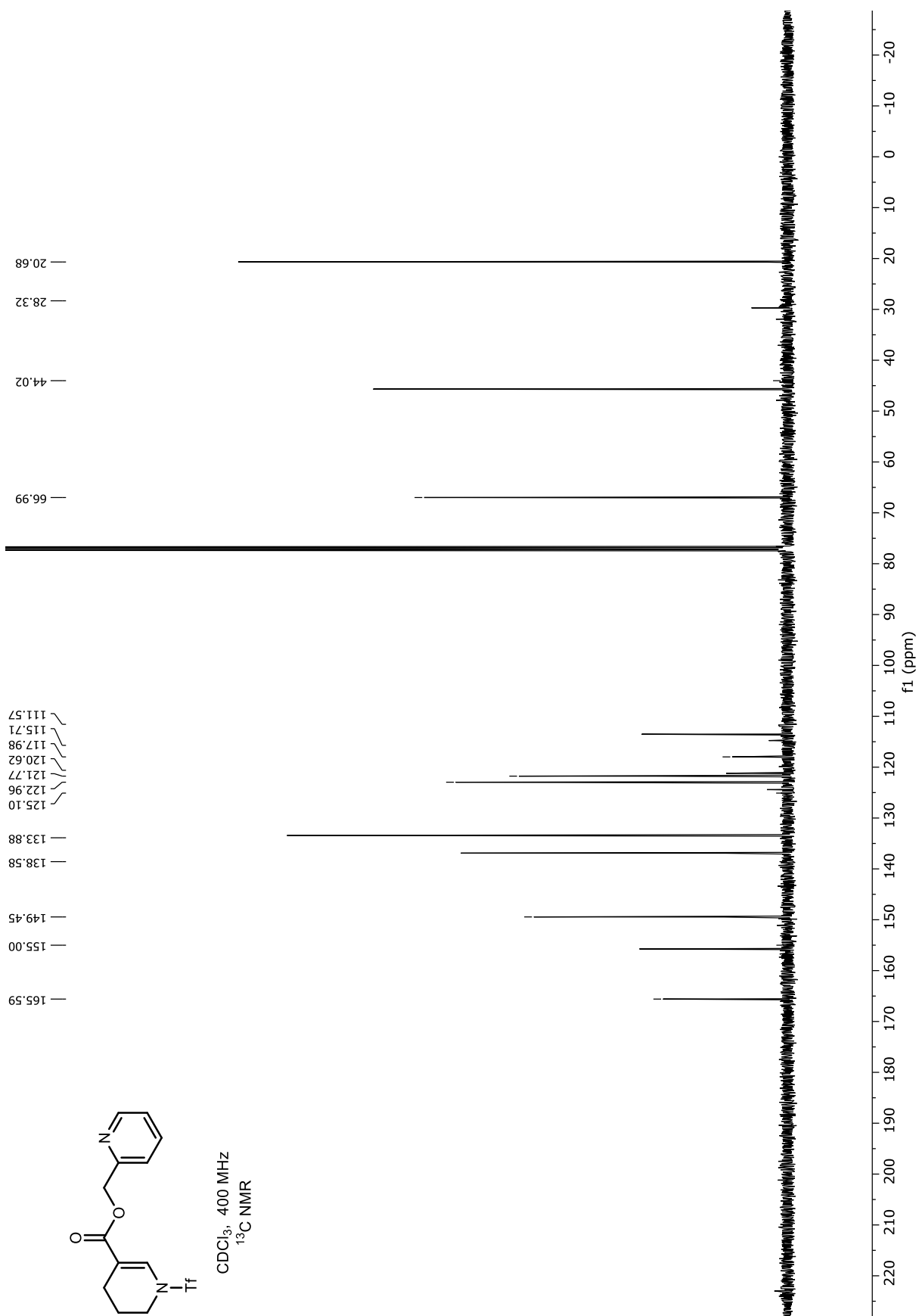


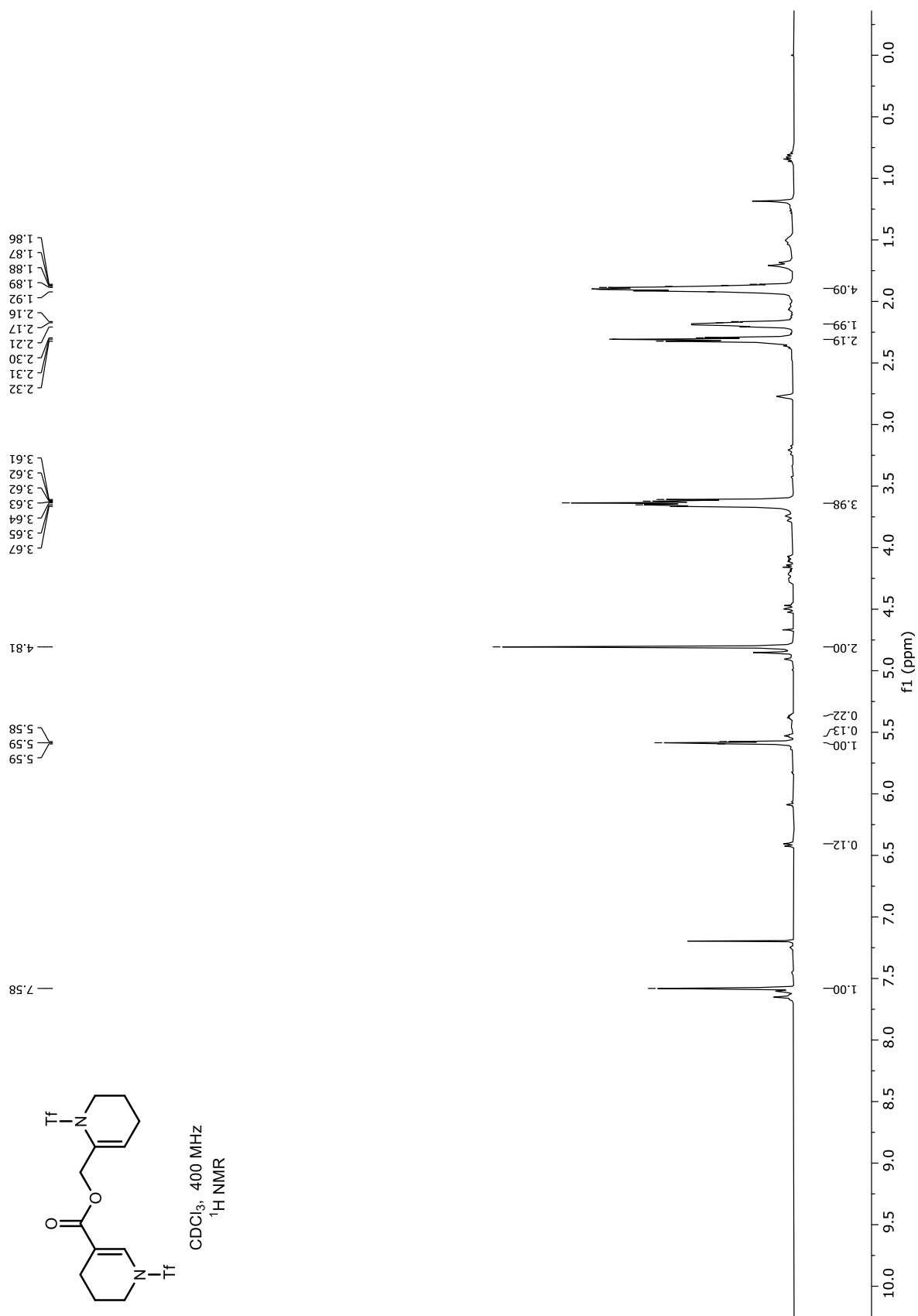




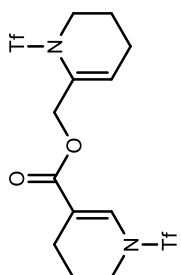
— -75.14



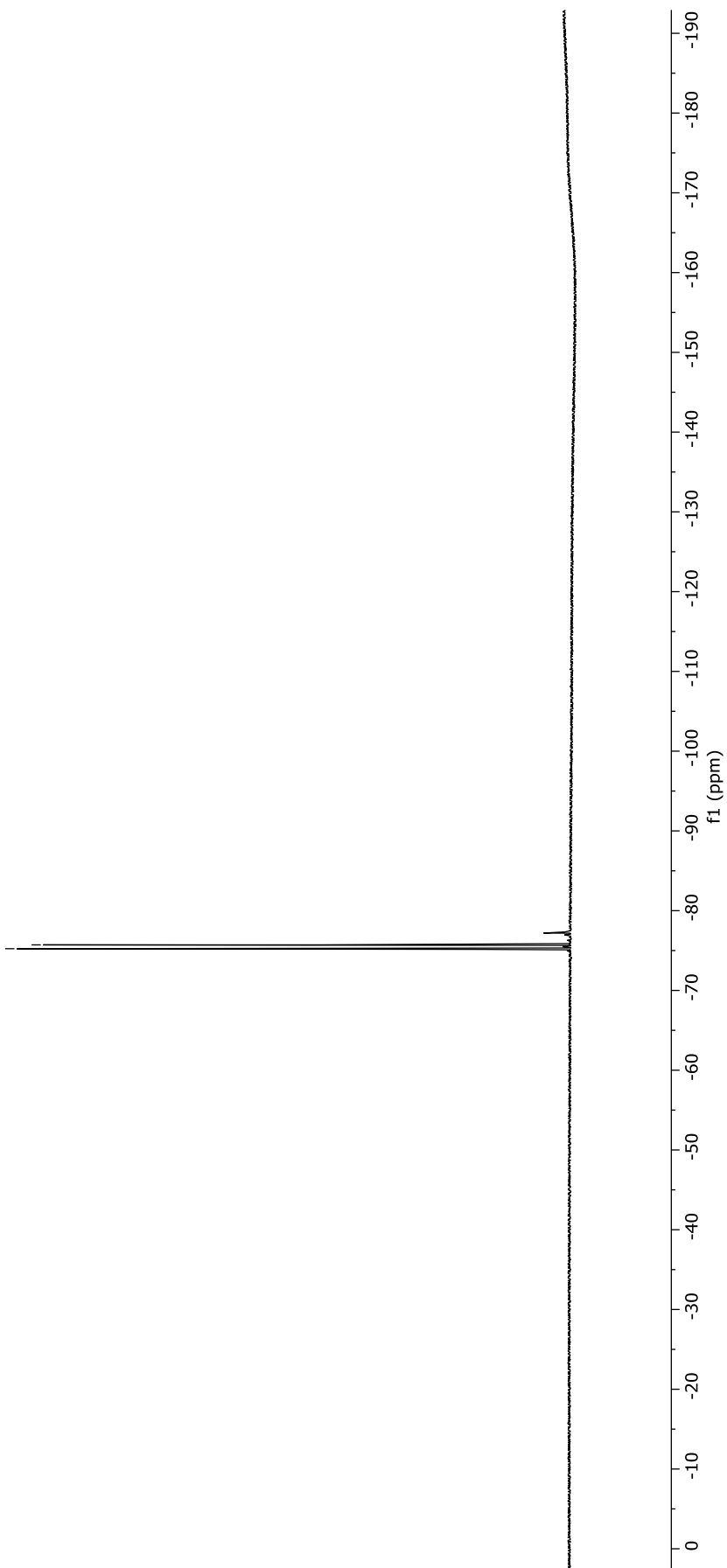


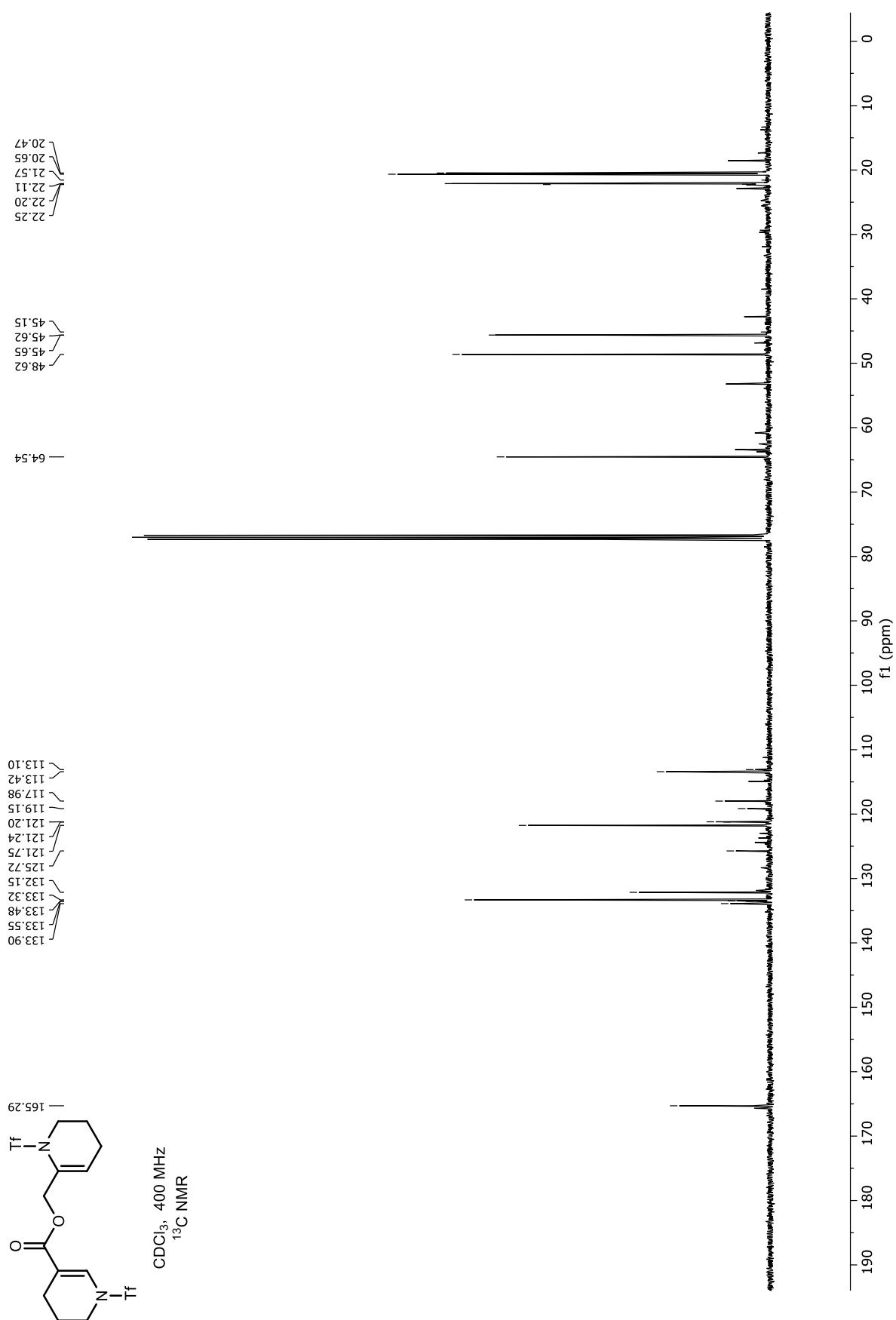


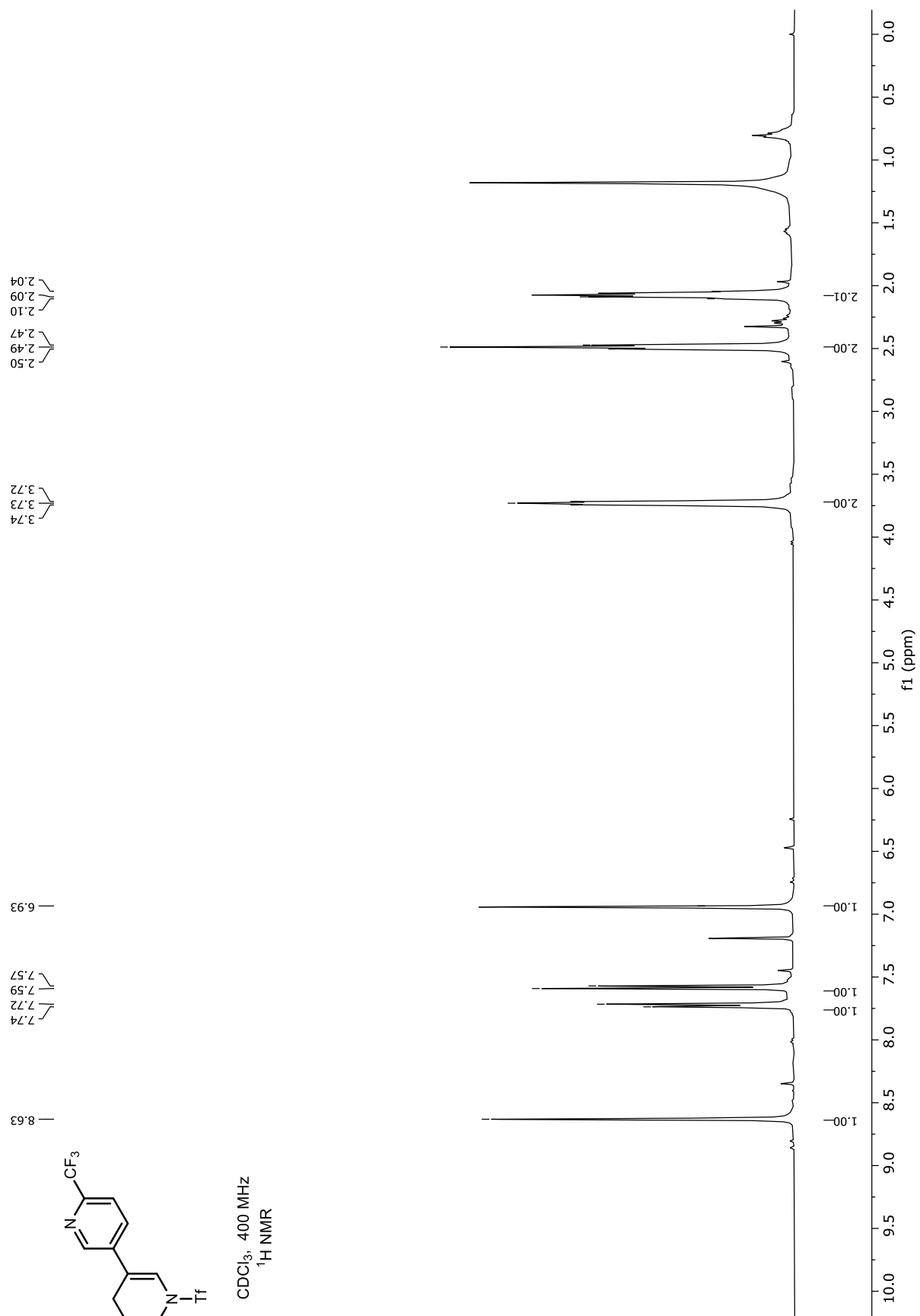
-75.23
-75.71

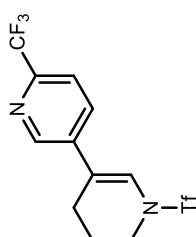


CDCl₃, 400 MHz
¹⁹F NMR



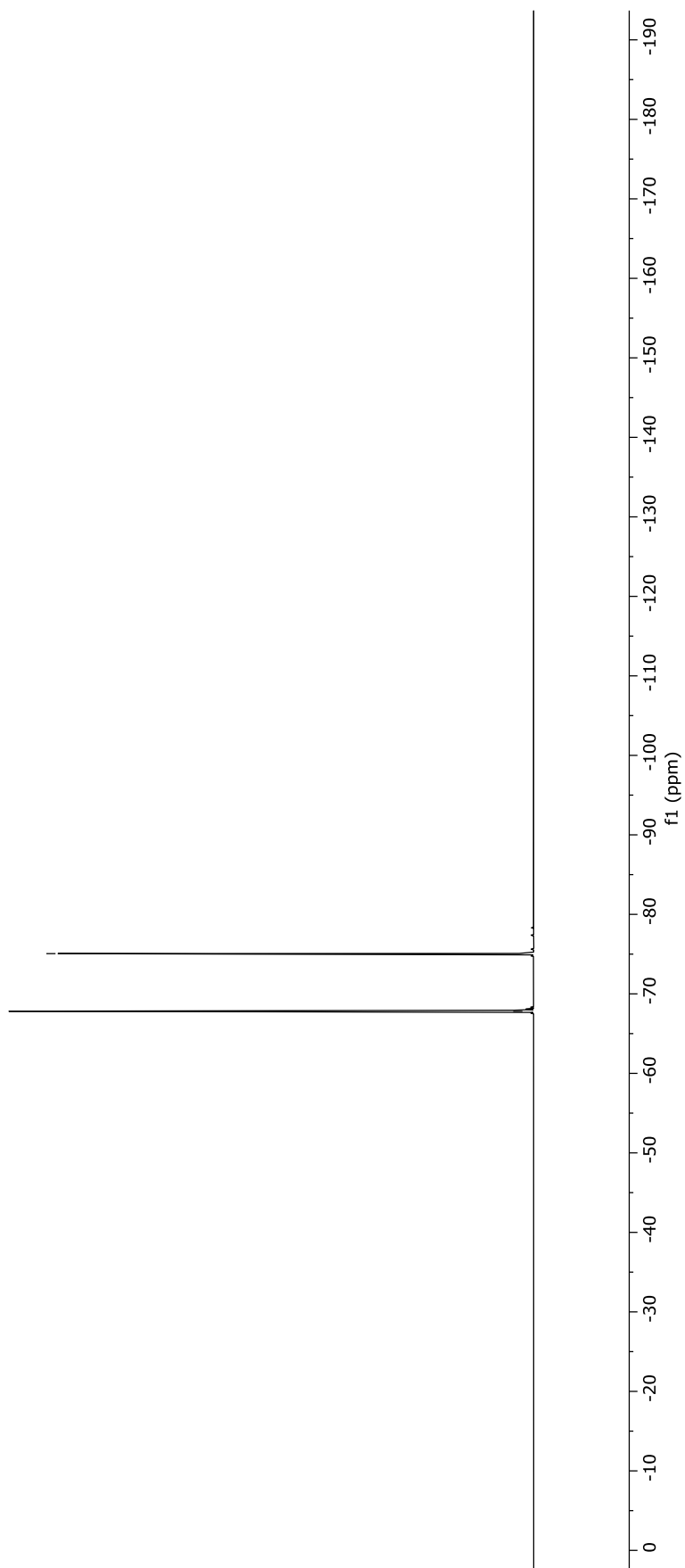


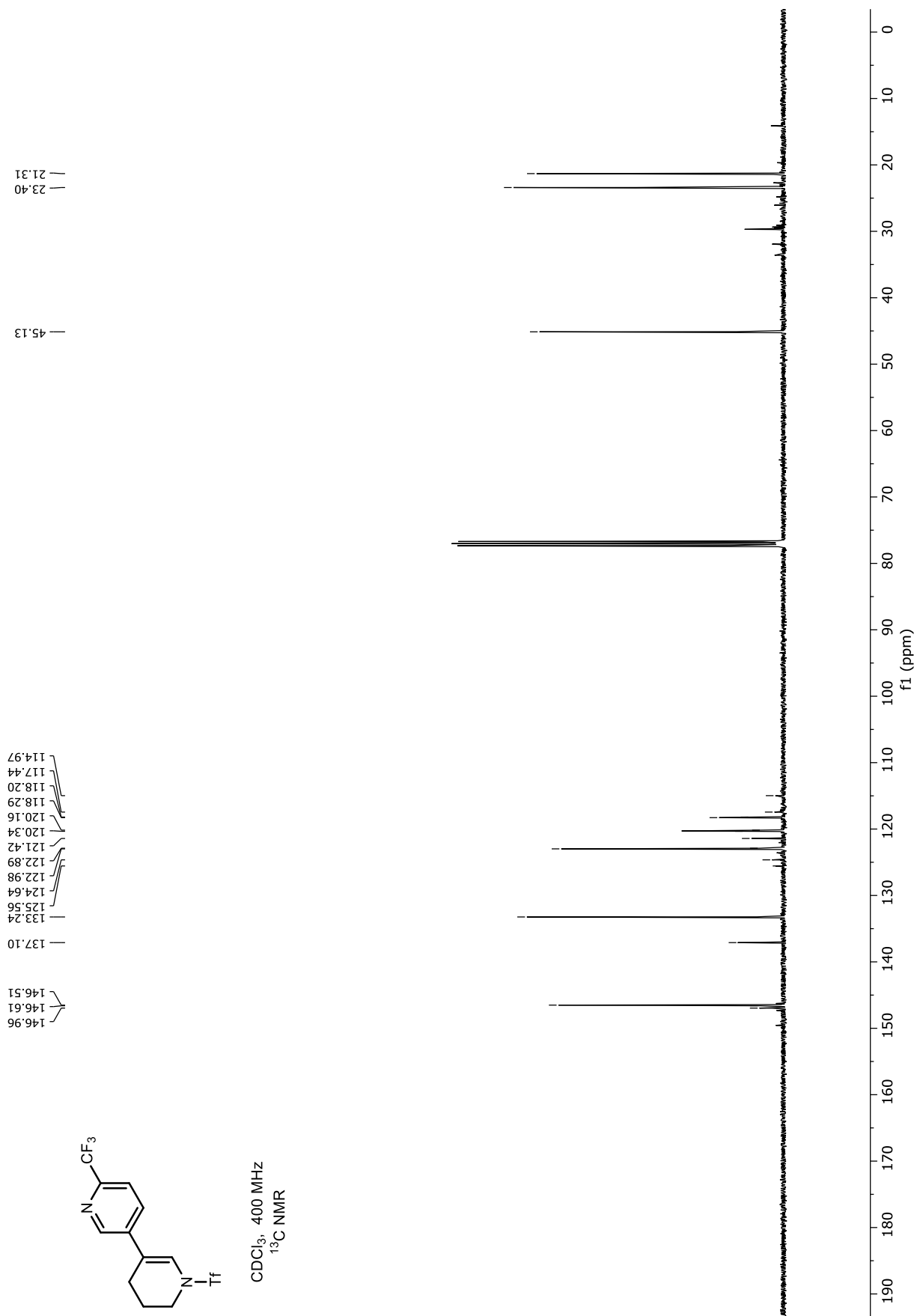




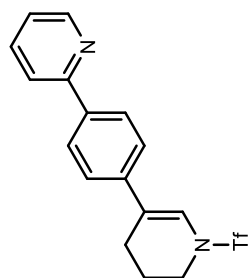
CDCl₃, 400 MHz
¹⁹F NMR

— -75.06
 — -67.78



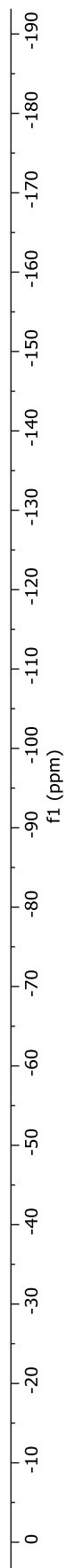


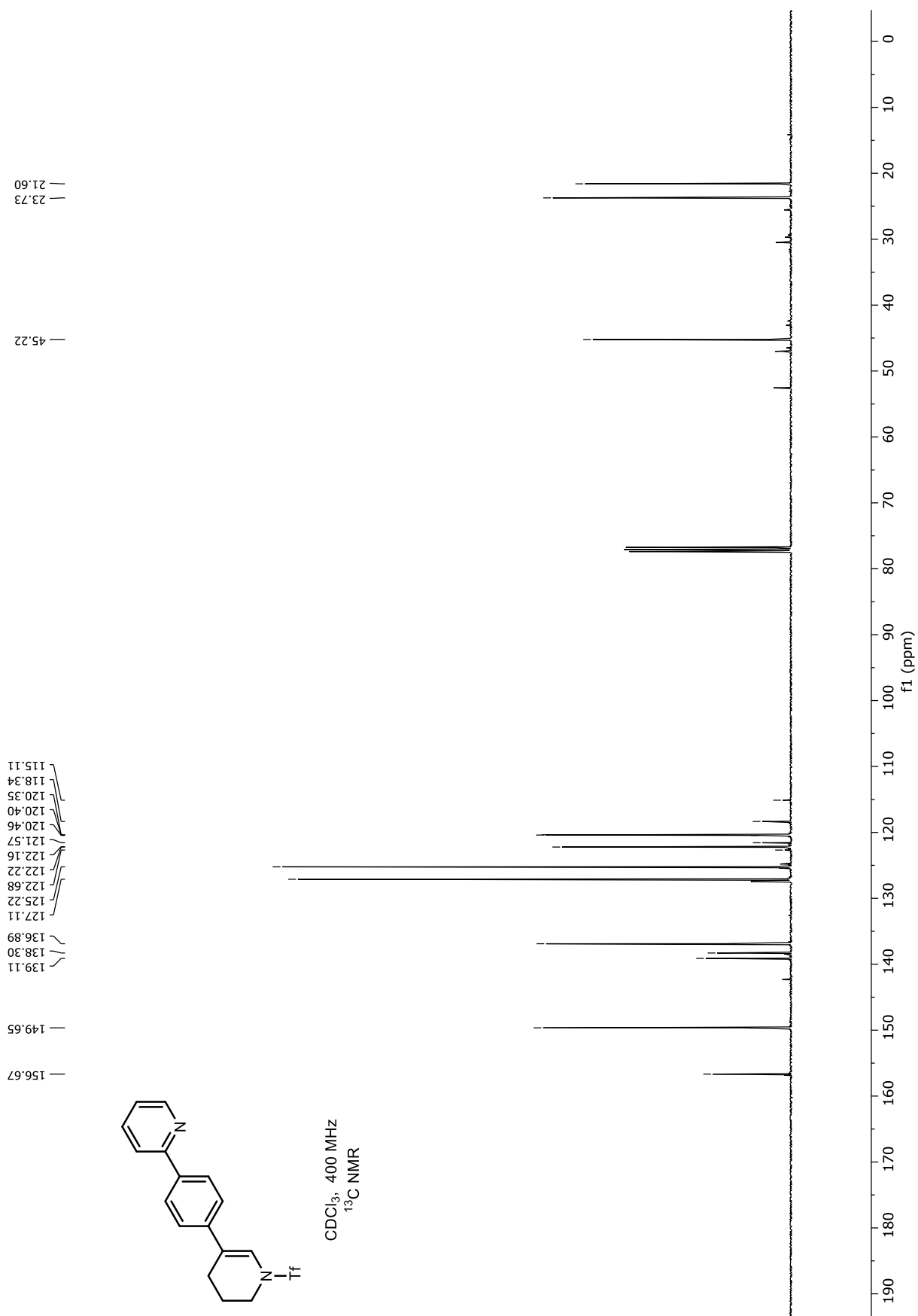


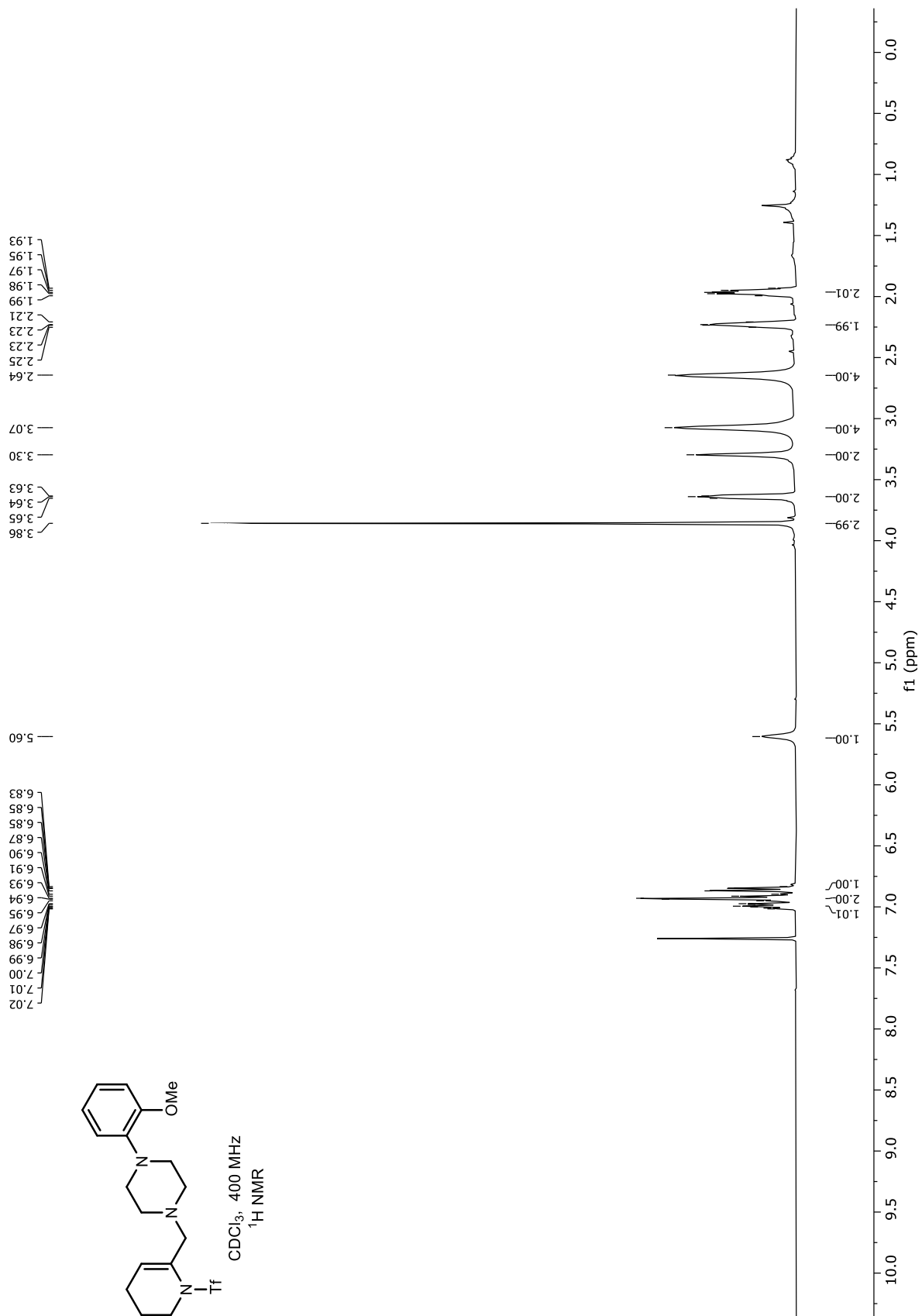


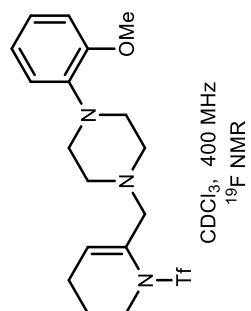
CDCl₃, 400 MHz
¹⁹F NMR

— -74.97

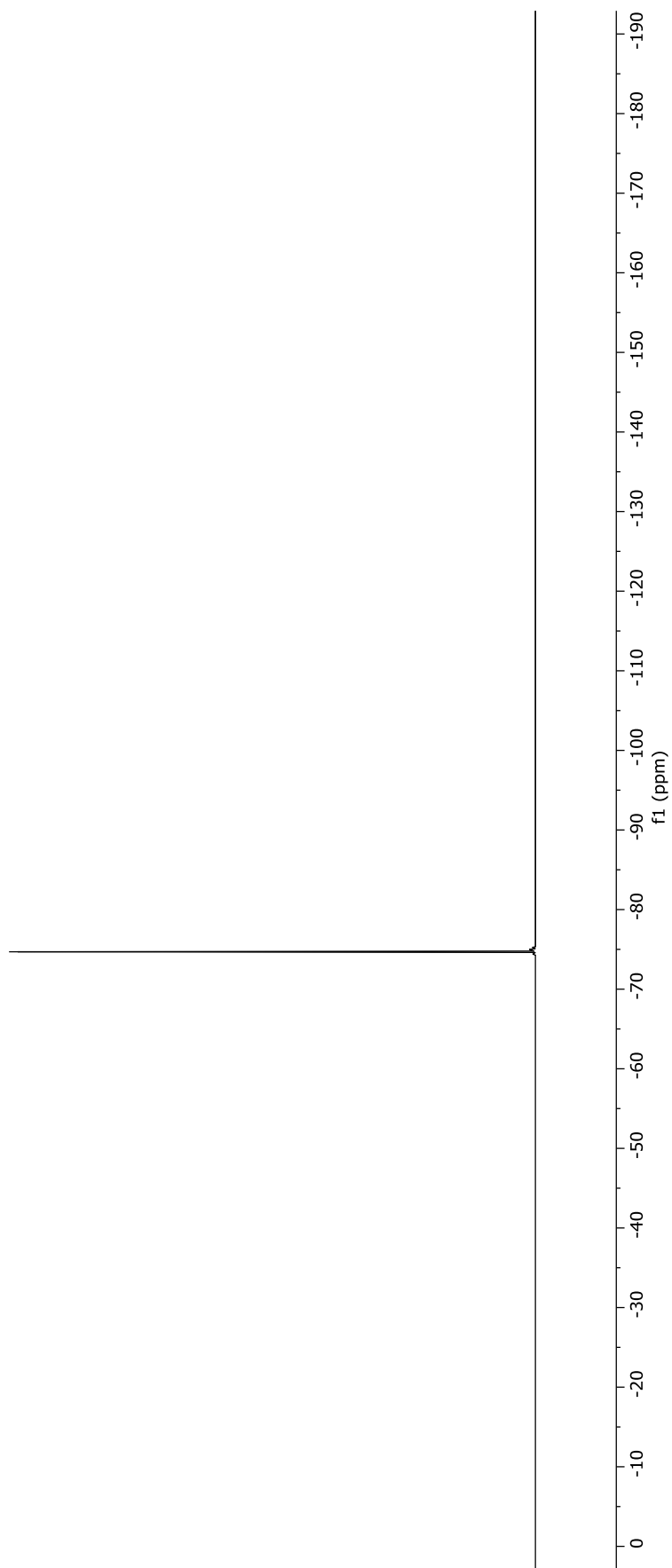


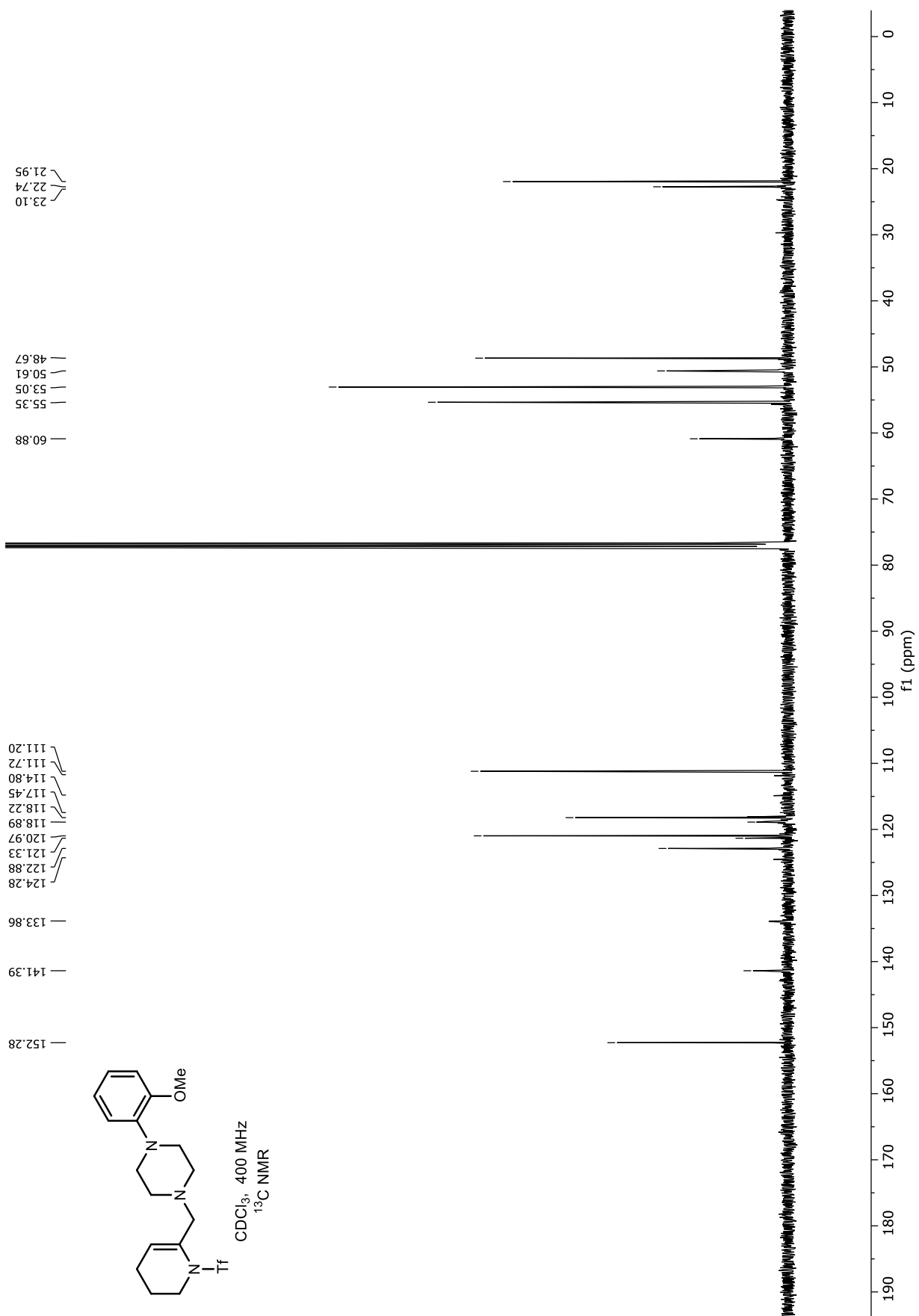


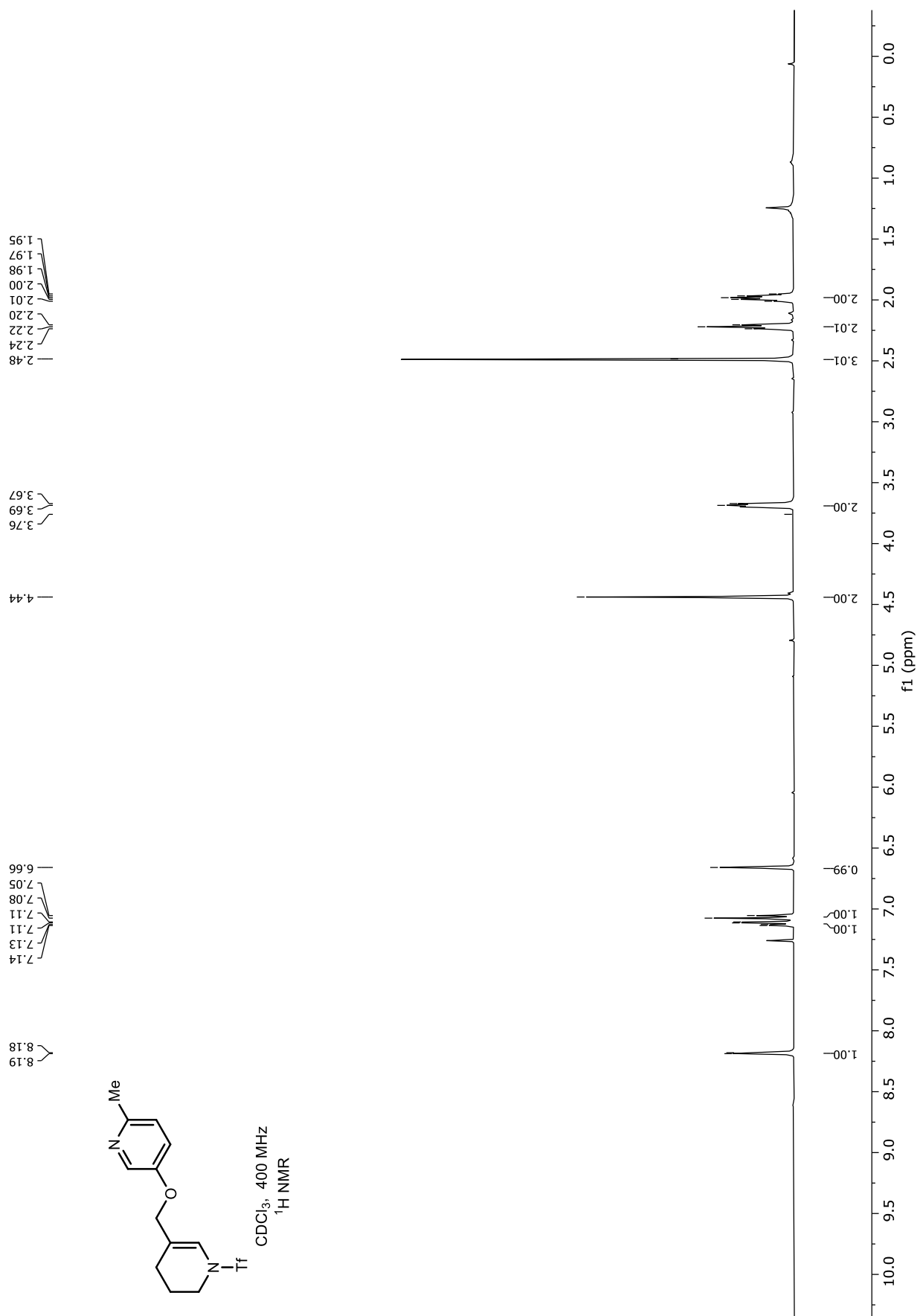


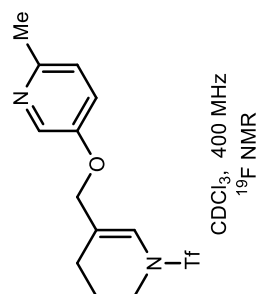


— -74.70

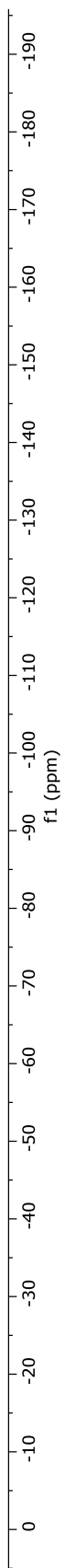
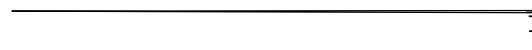


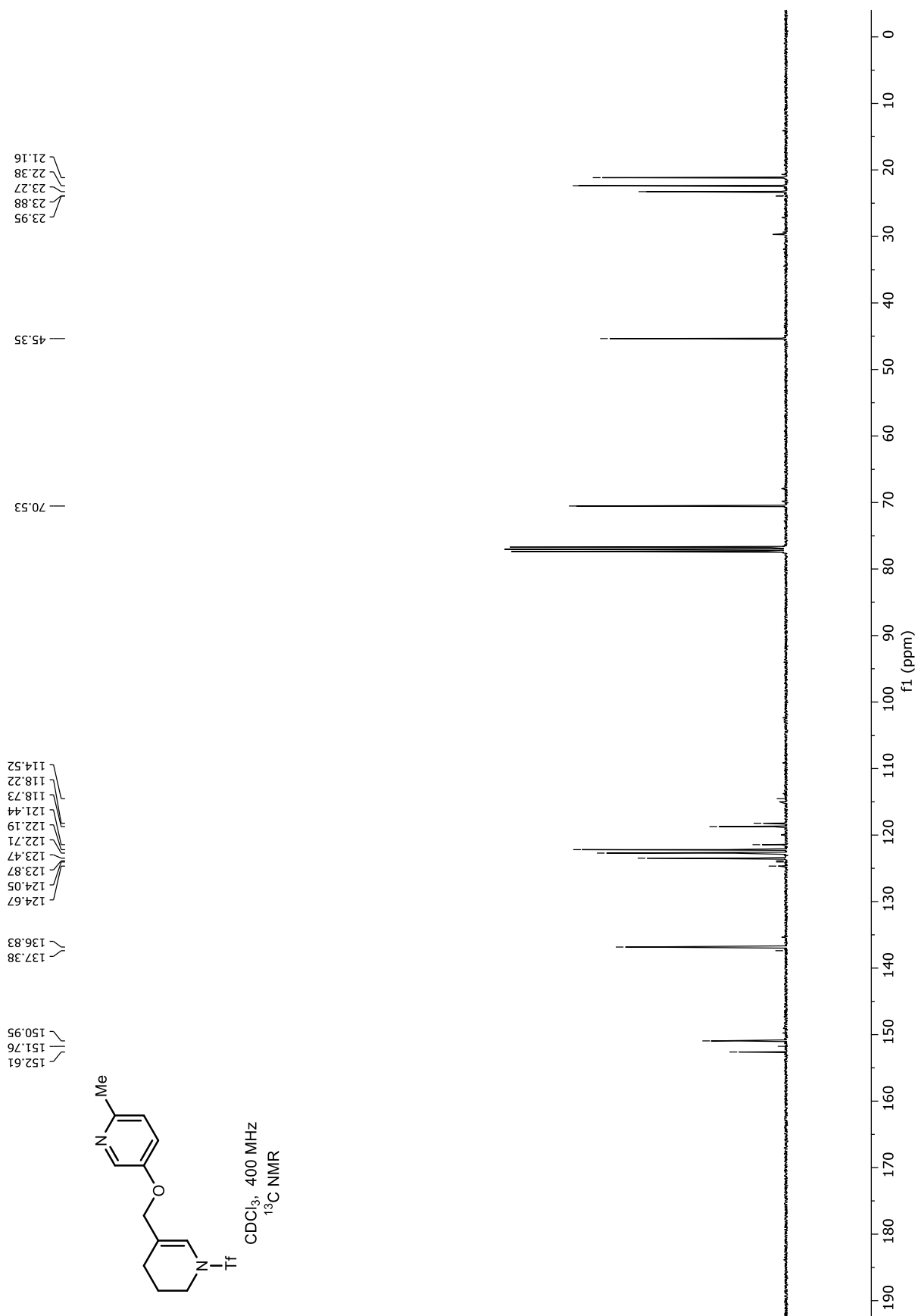


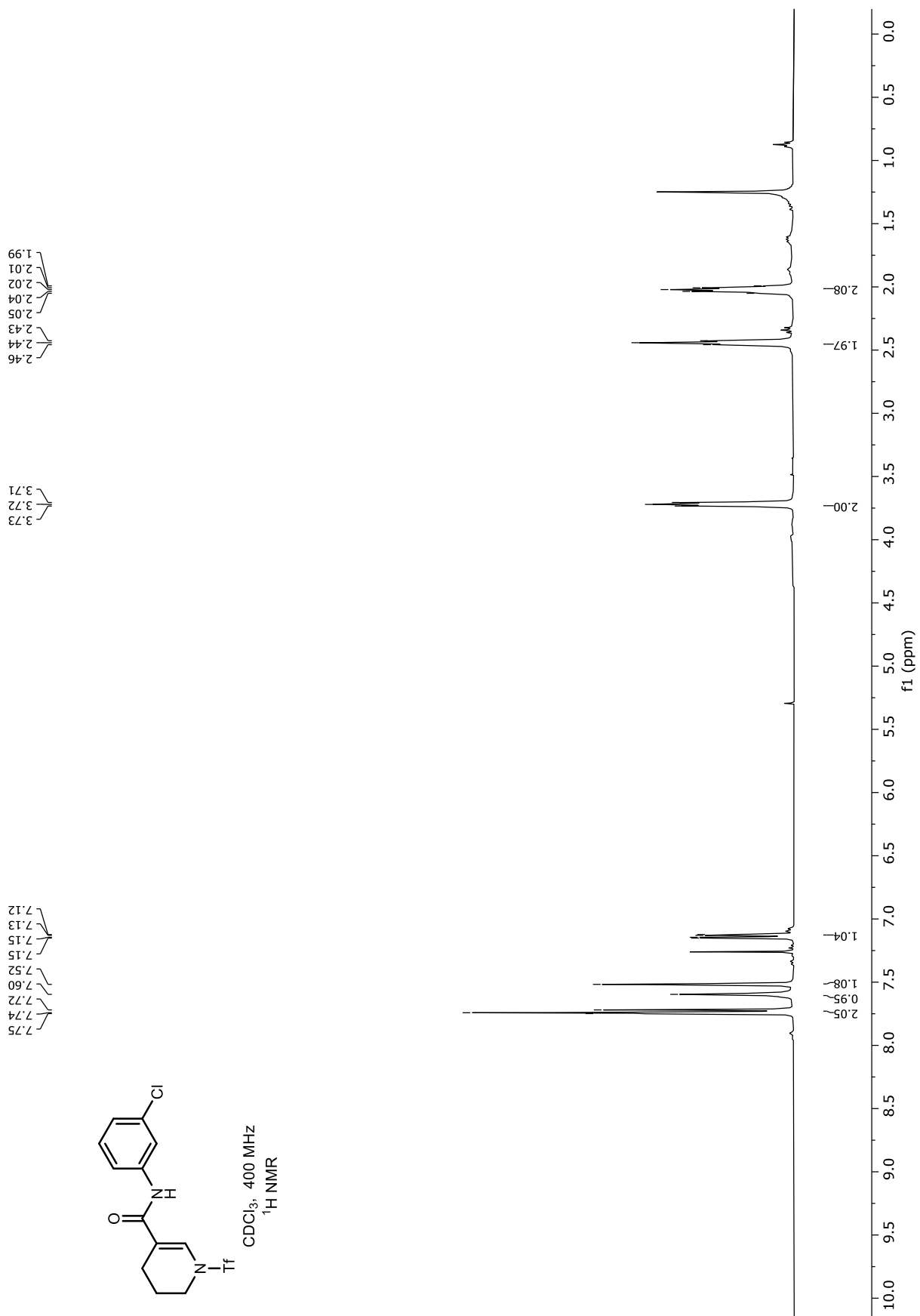




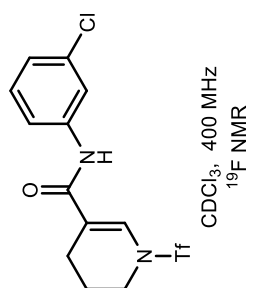
— -75.07

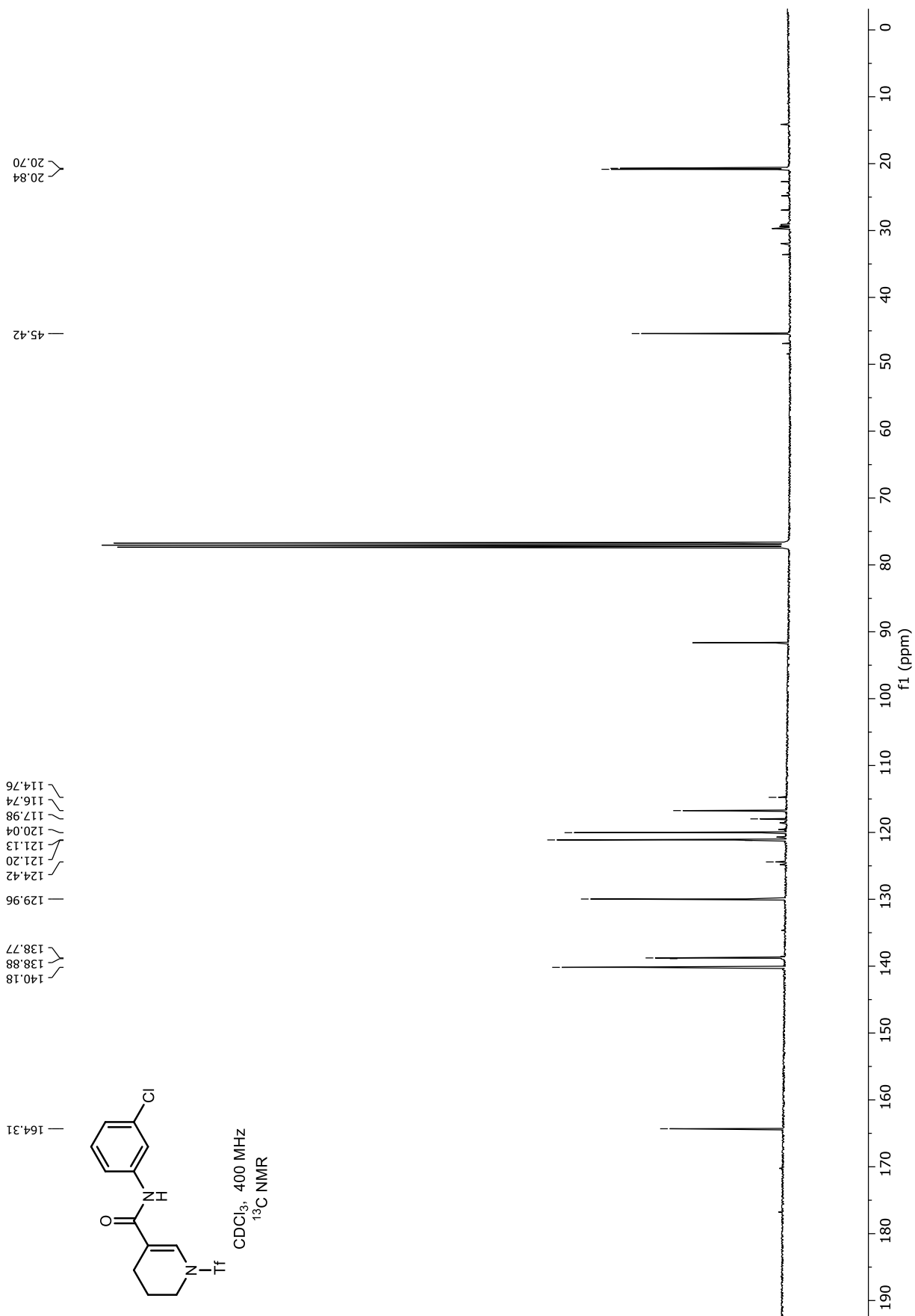


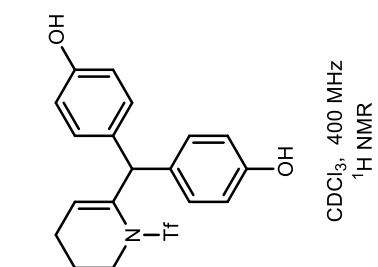




— -75.06





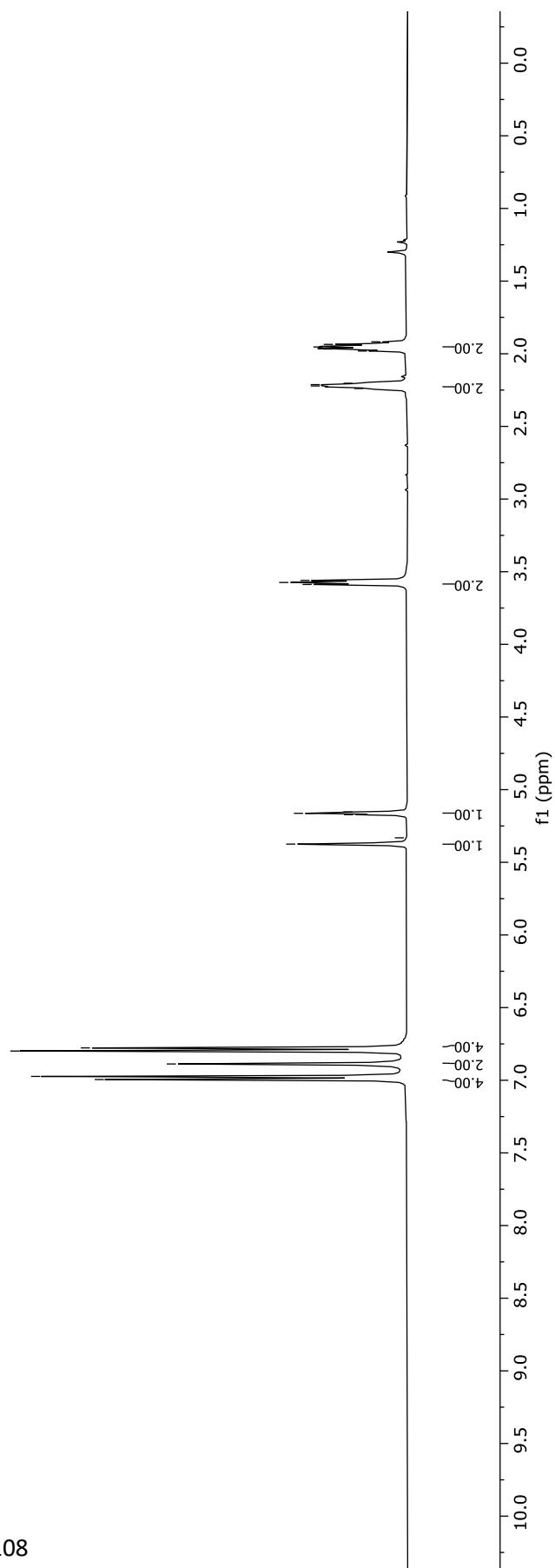


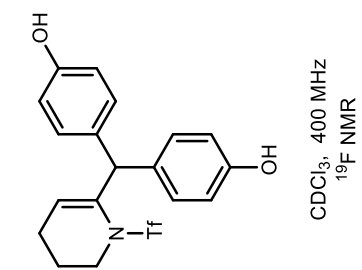
7.00
6.97
6.89
6.80
6.78

5.37
5.33
5.17
5.16
5.15

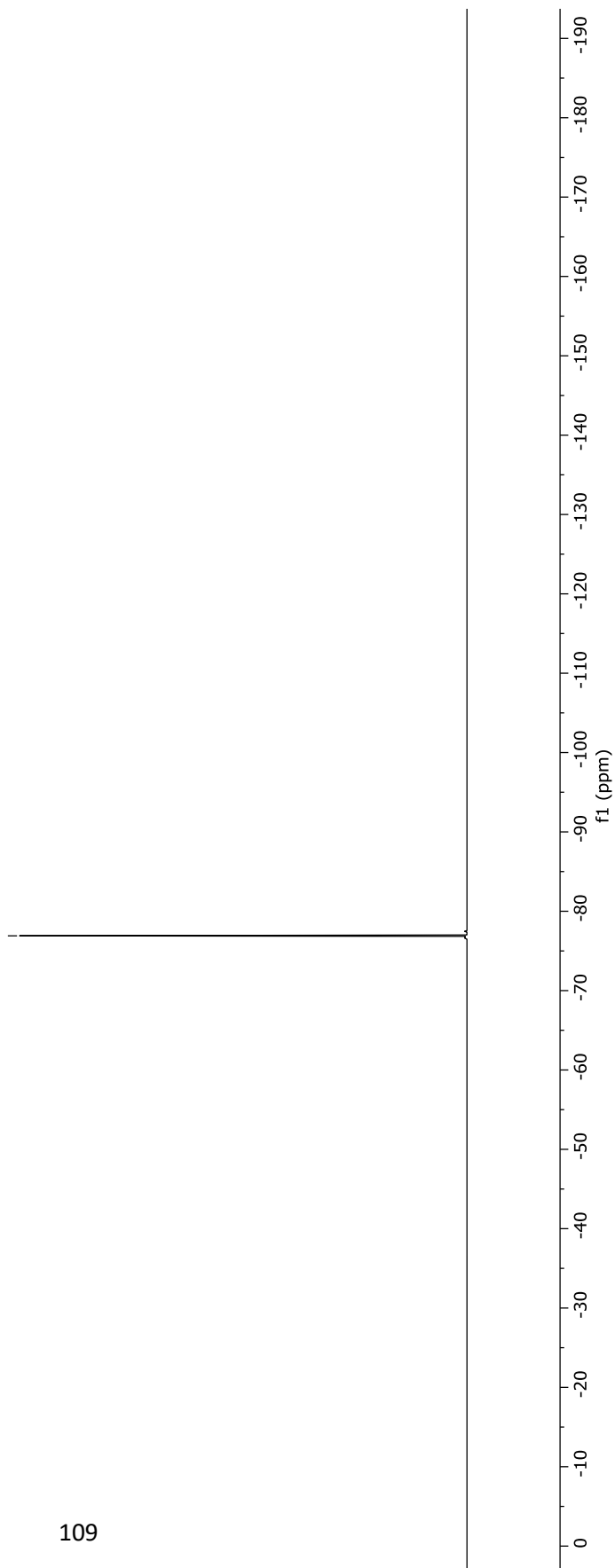
3.59
3.57
3.56

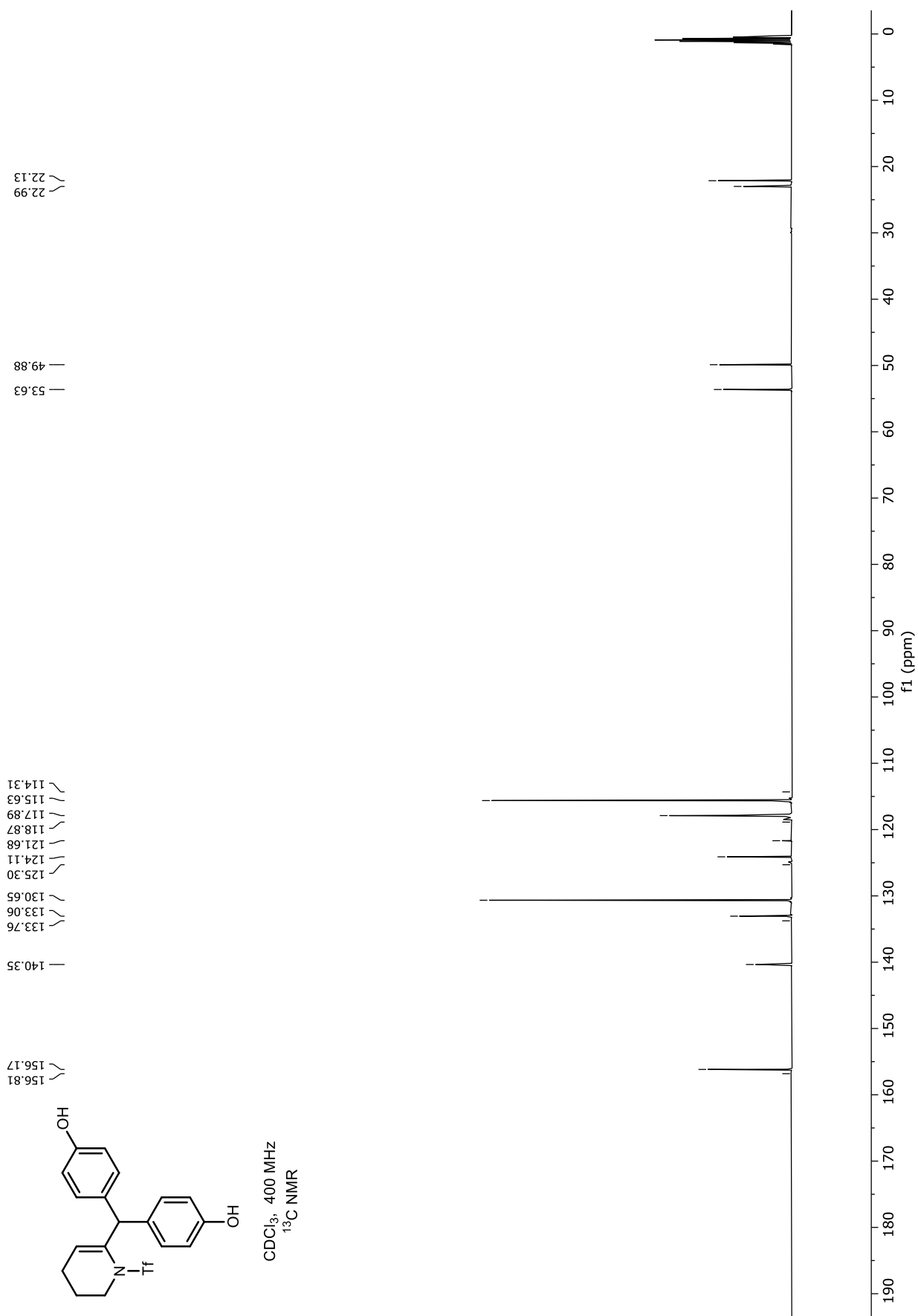
2.24
2.22
2.21
2.20
1.98
1.97
1.95
1.94
1.92

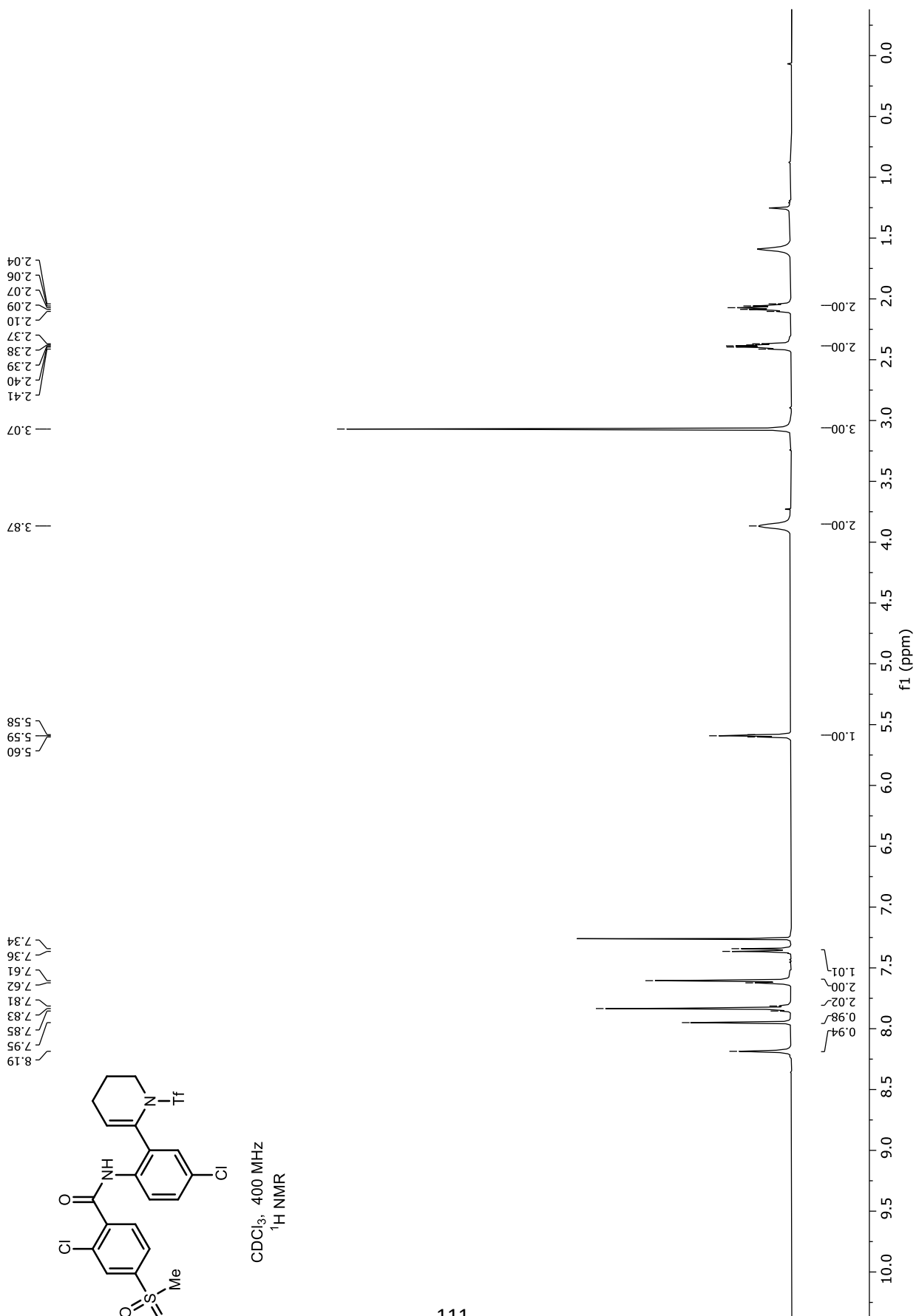


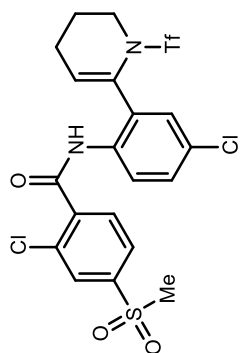


— -76.90



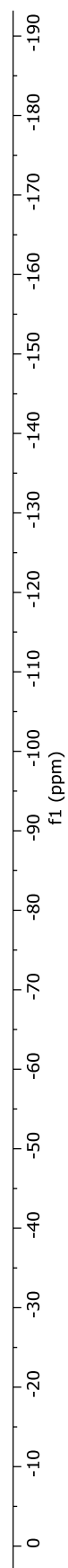


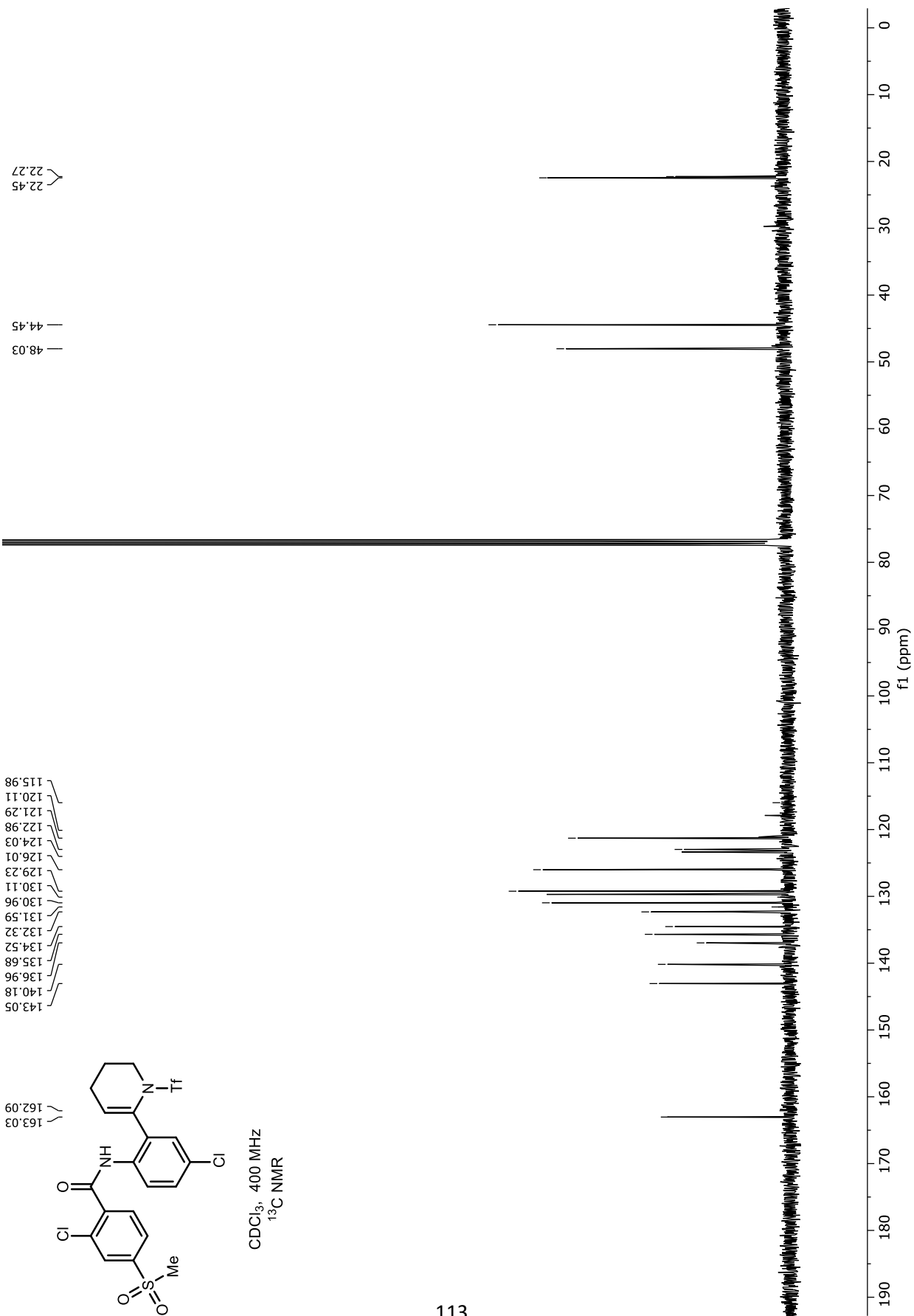


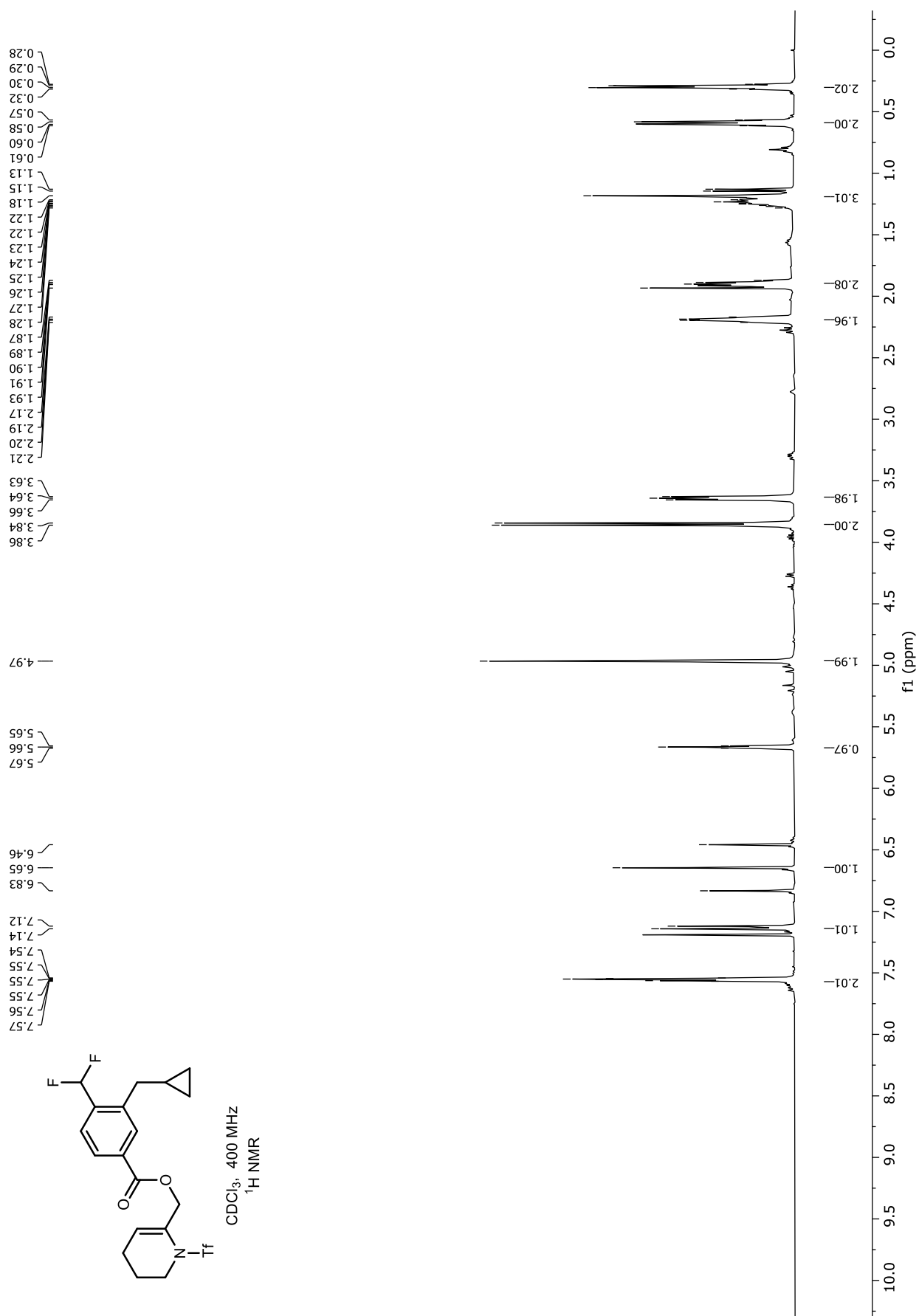


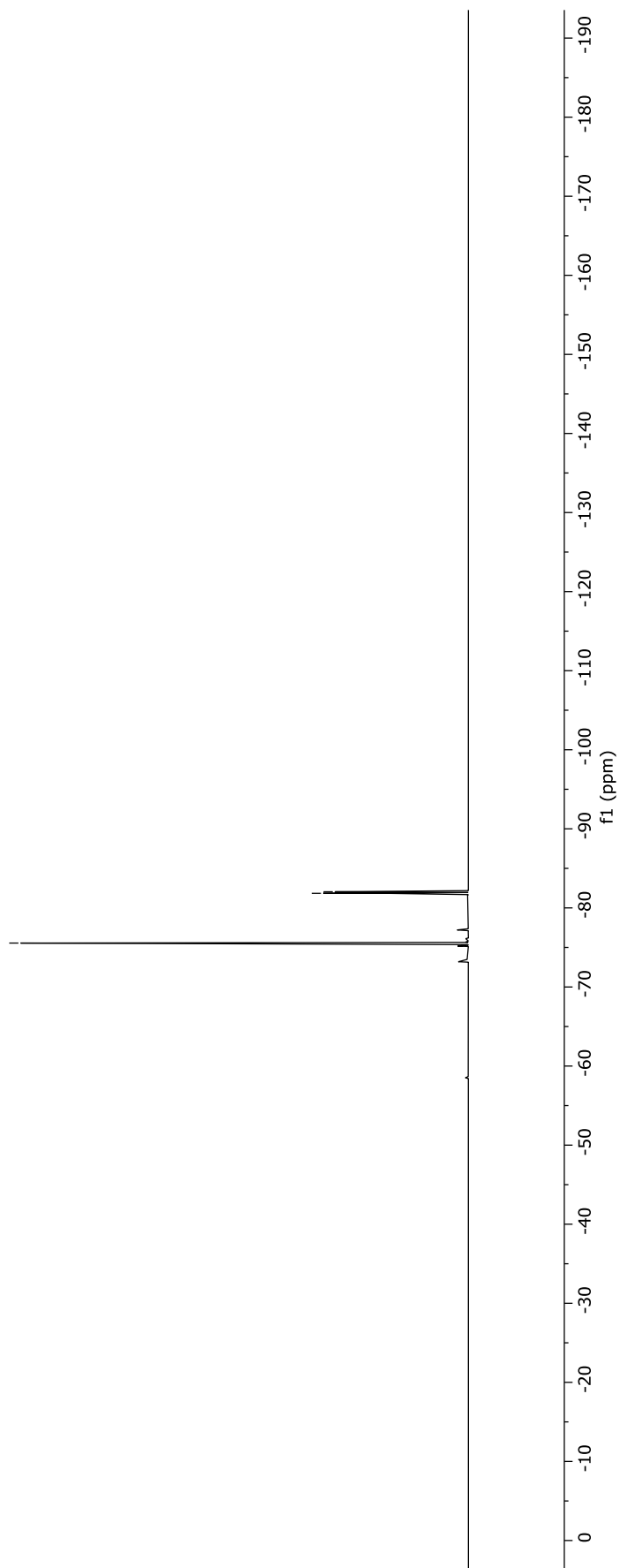
CDCl₃, 400 MHz
¹⁹F NMR

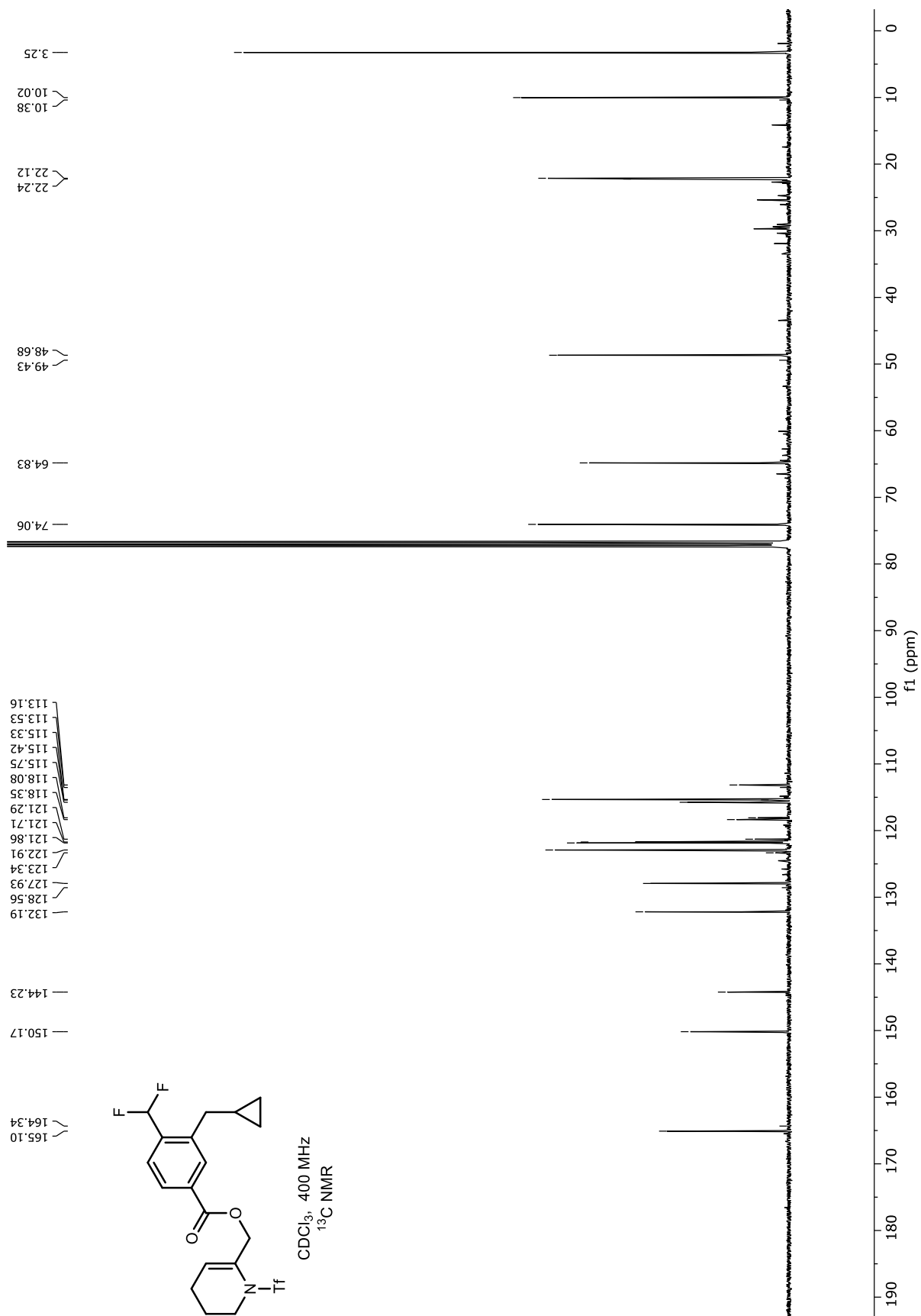
— -77.35

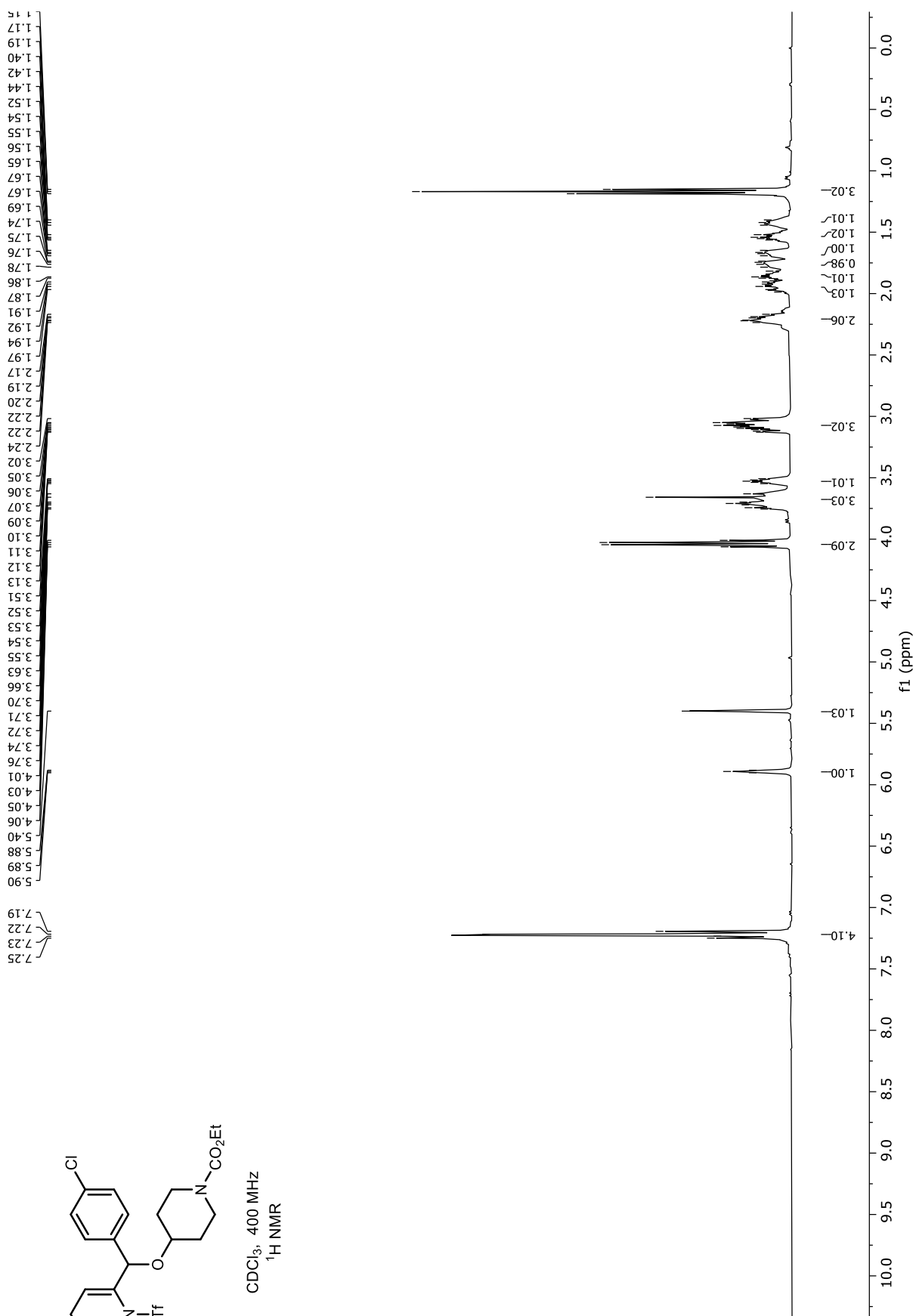


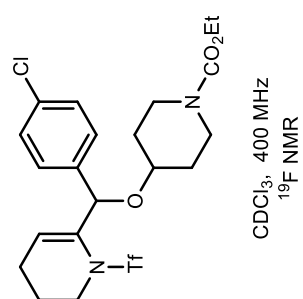




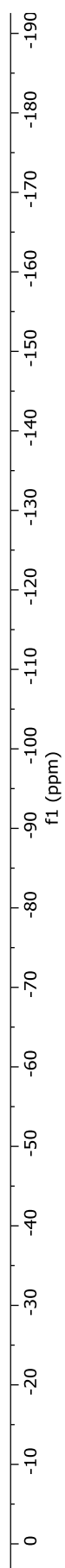


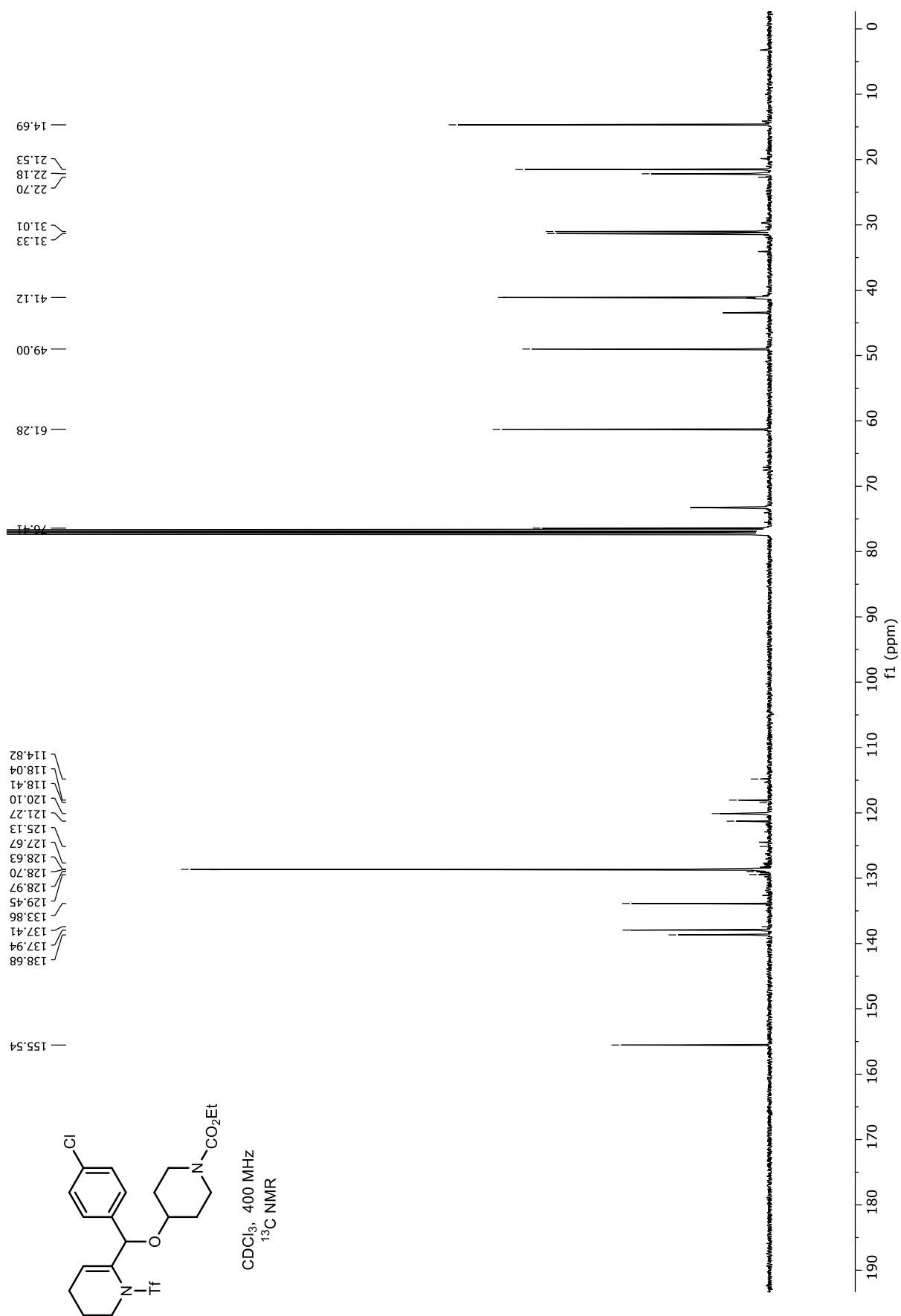


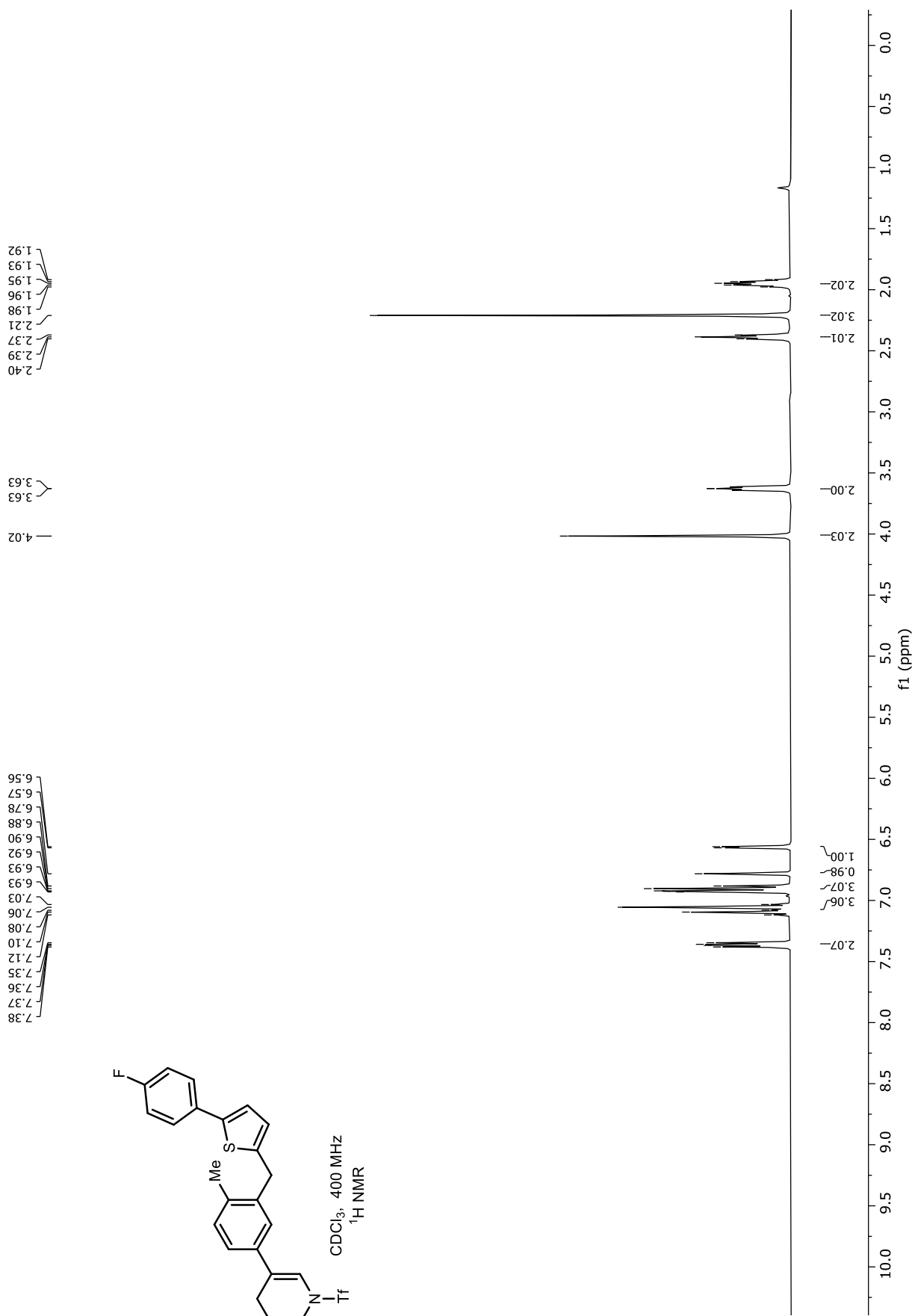


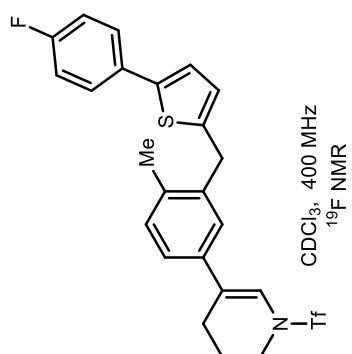


— -75.06



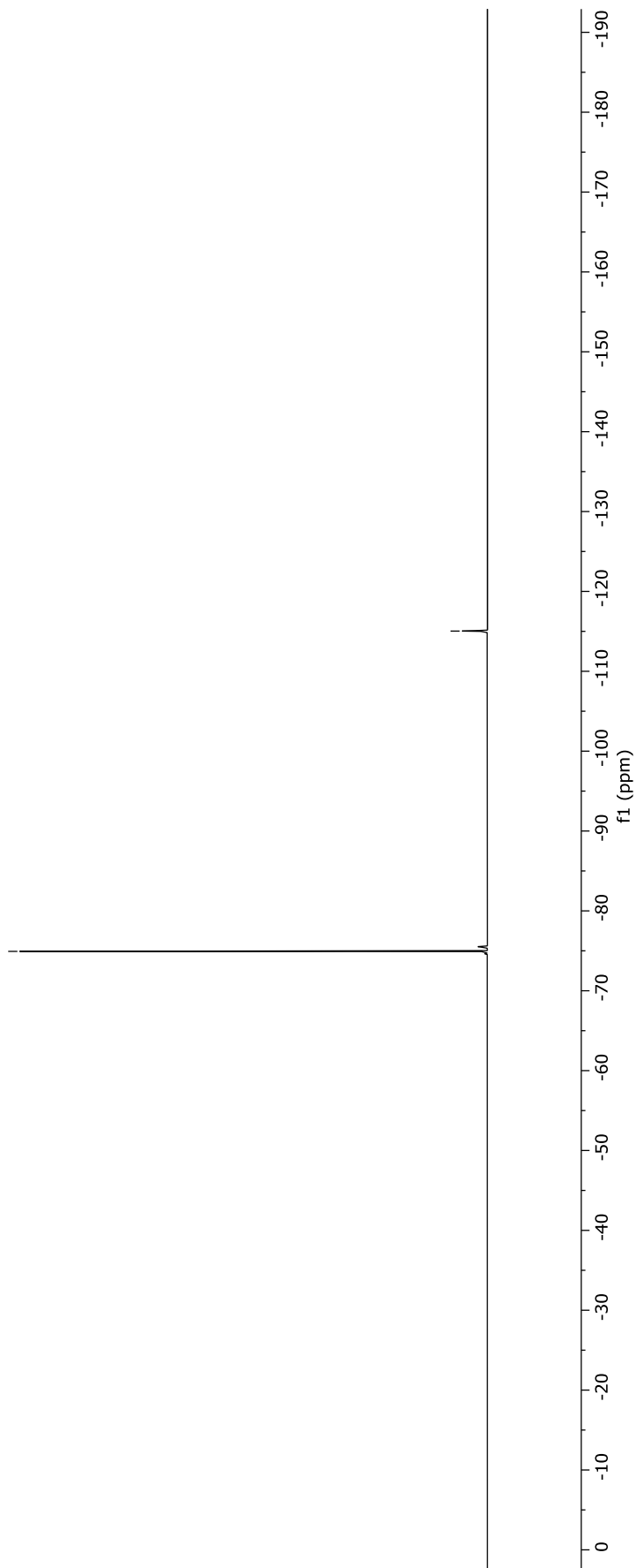


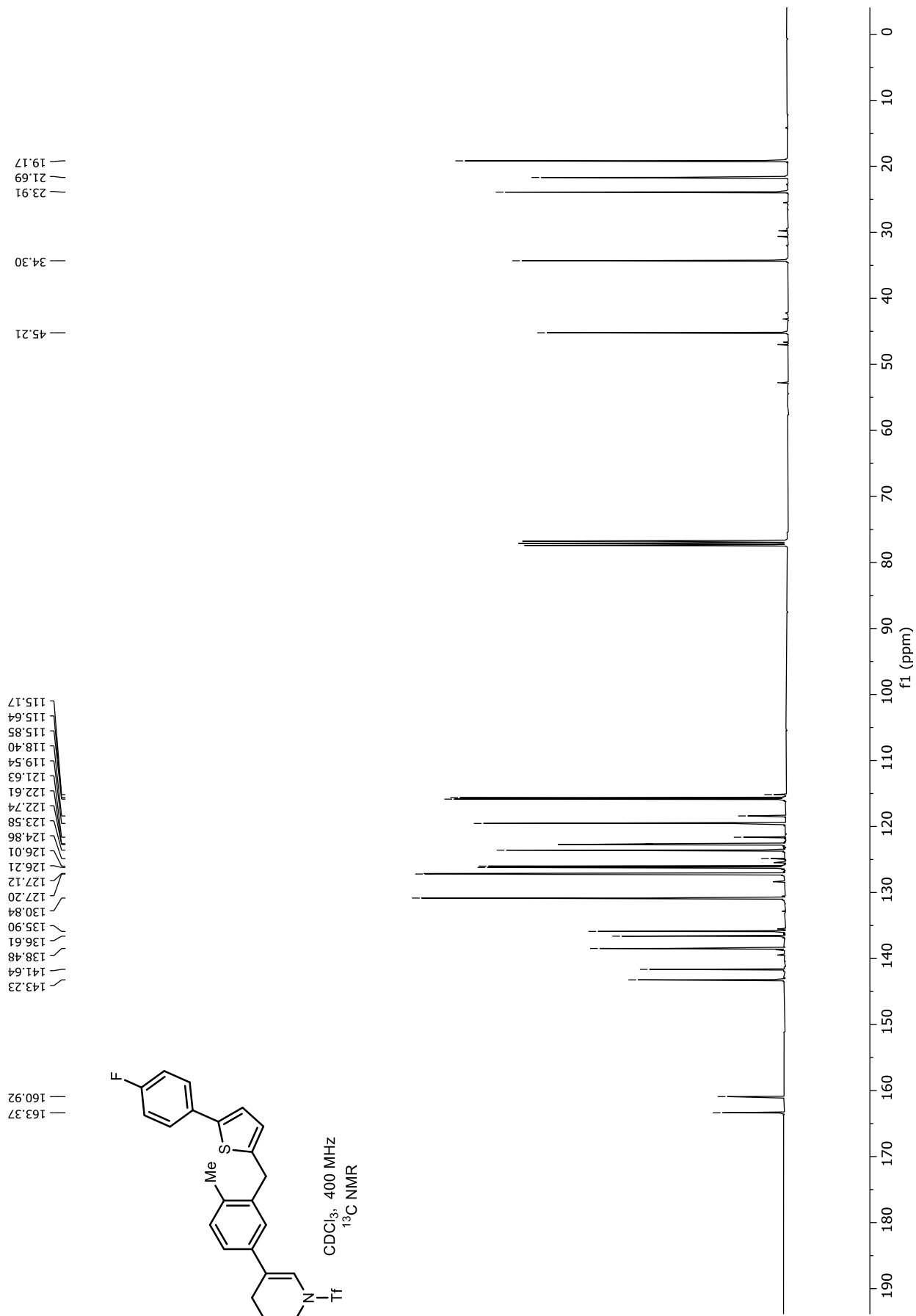


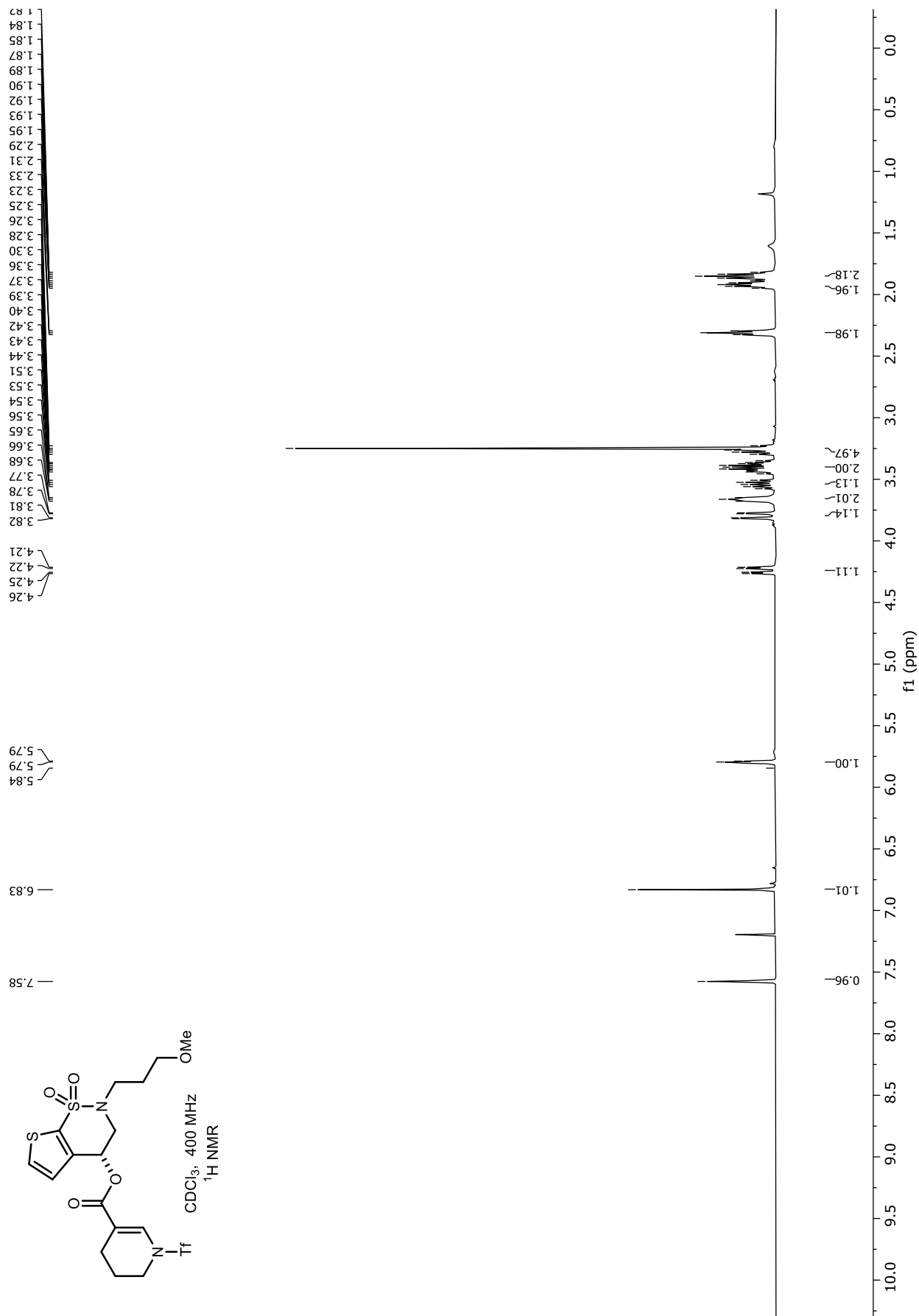


— -115.03

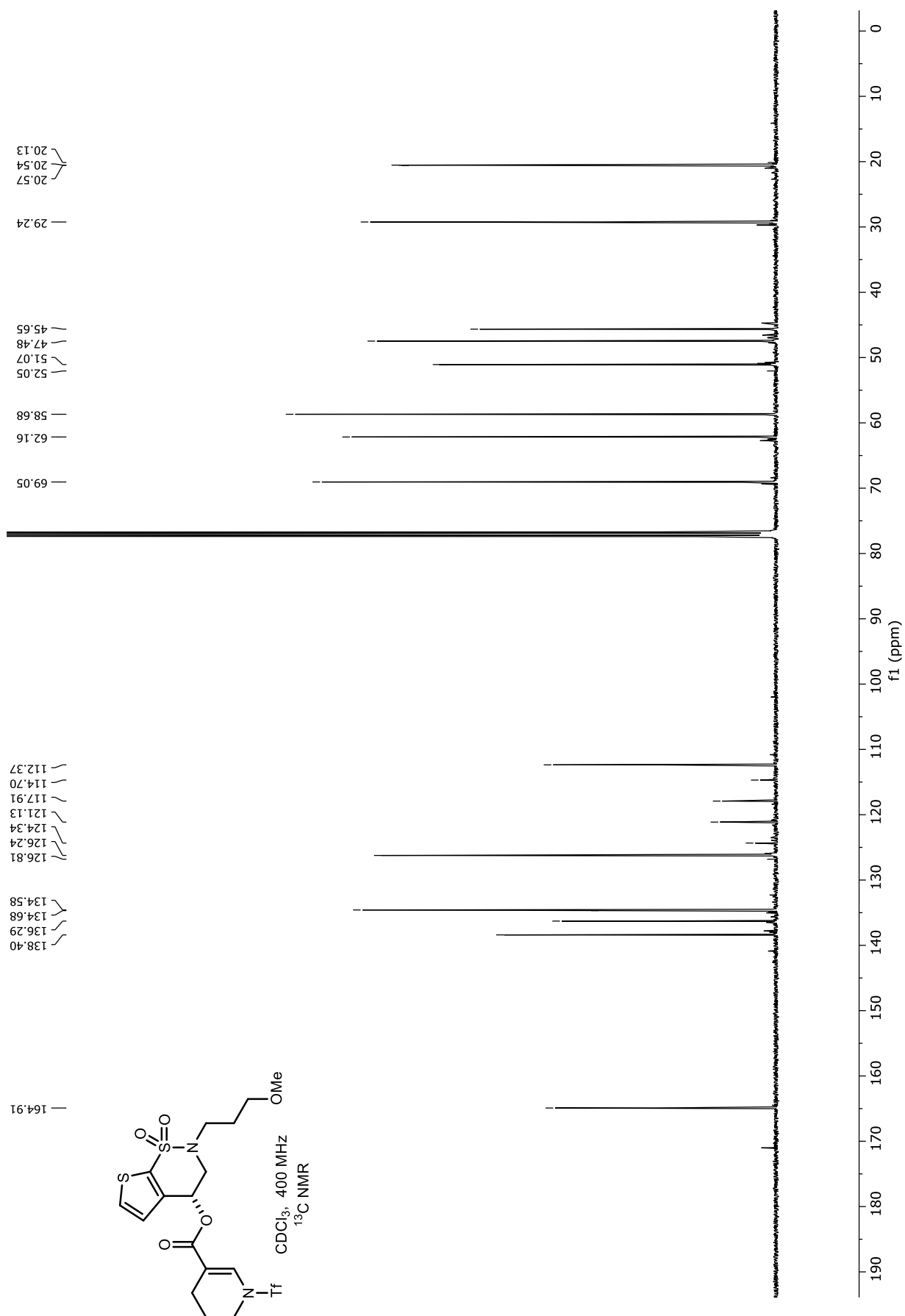
— -74.93

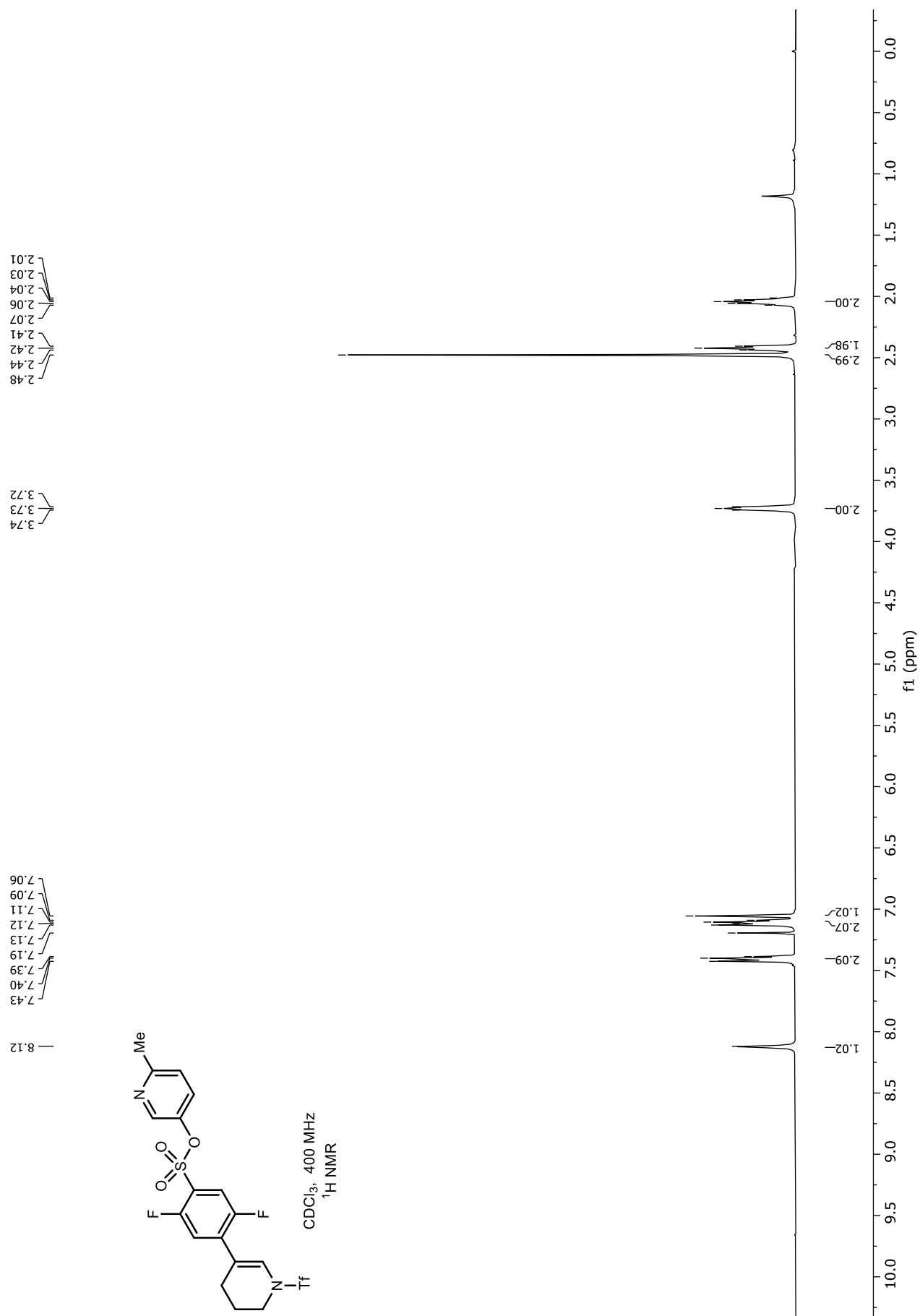


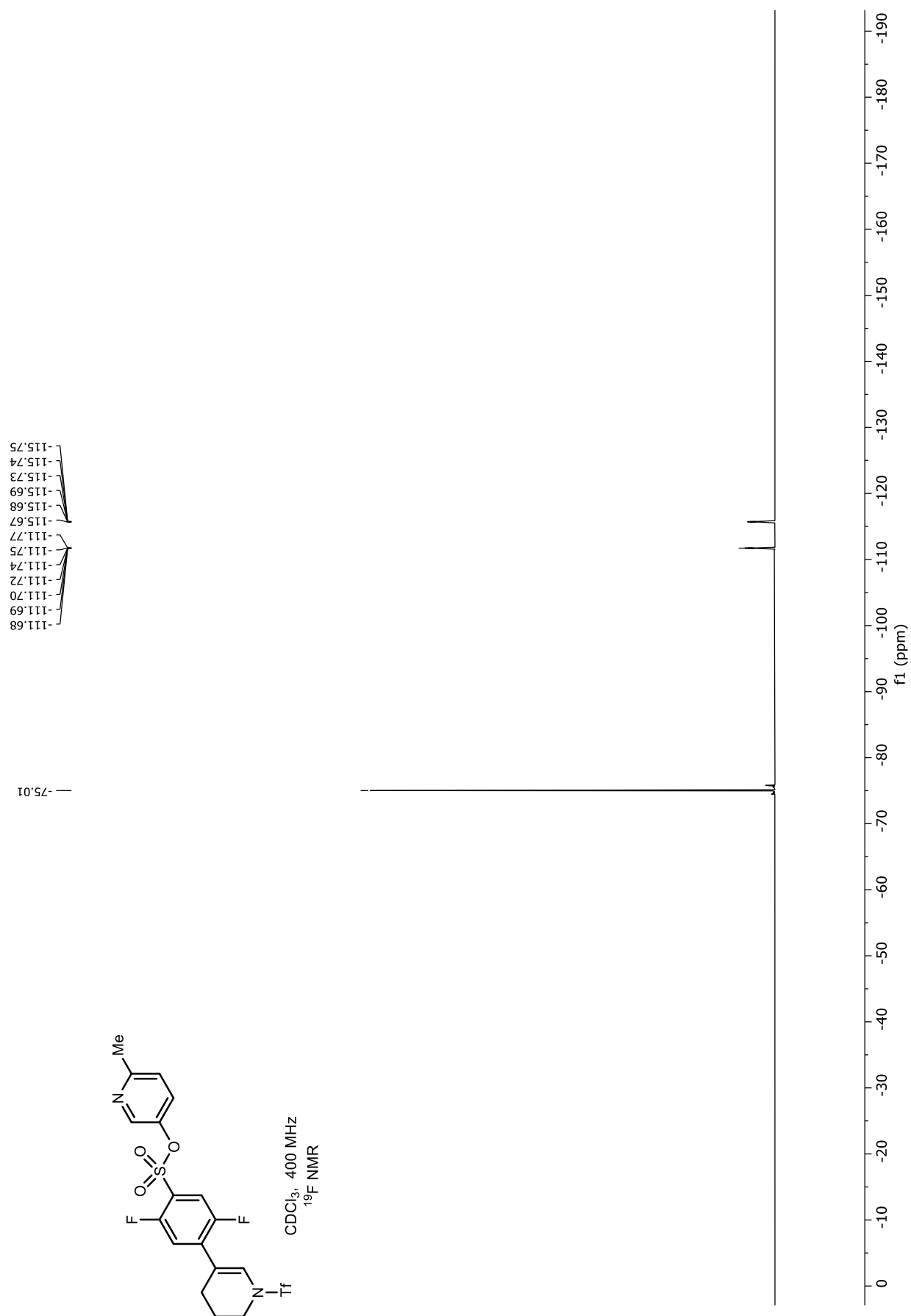


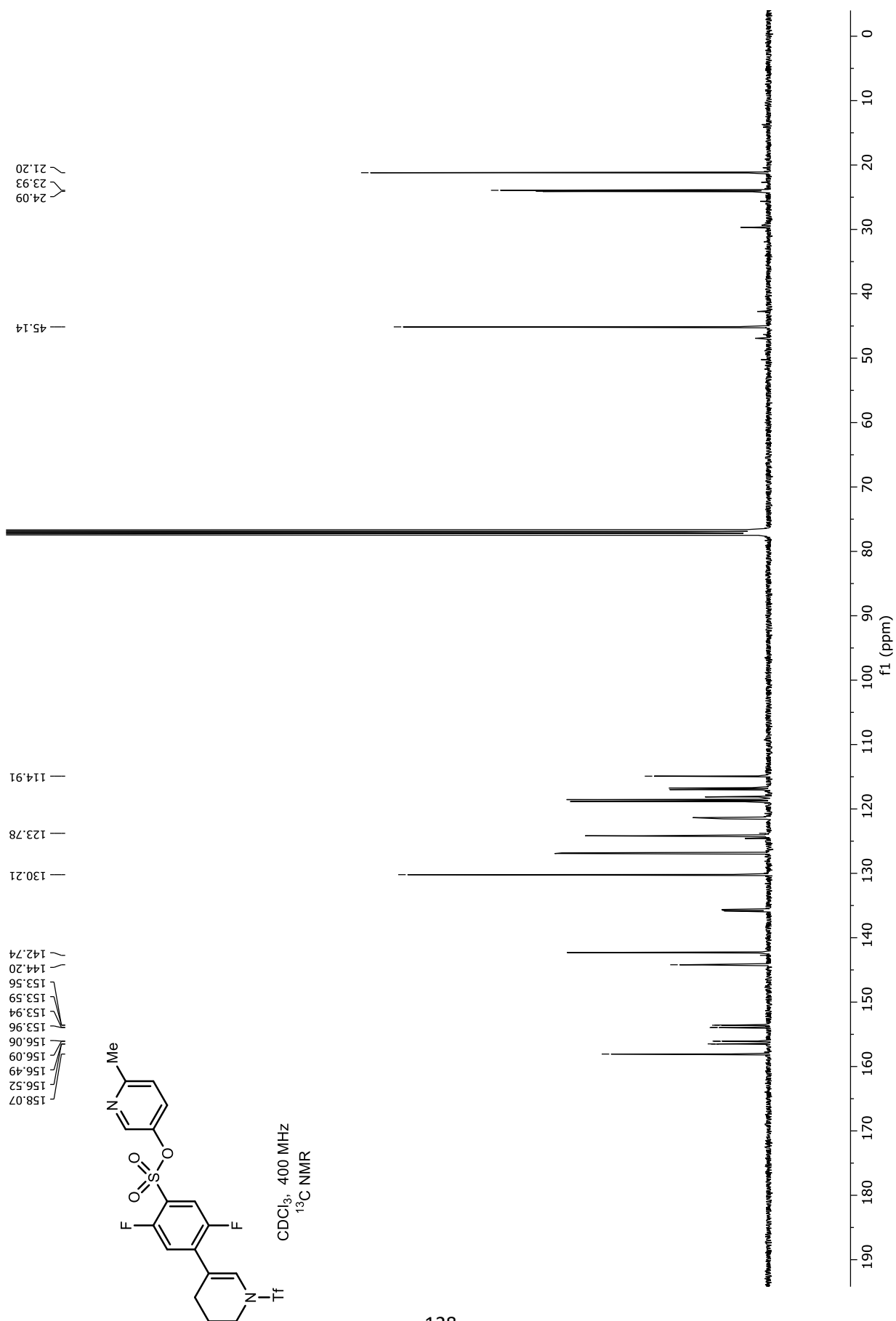


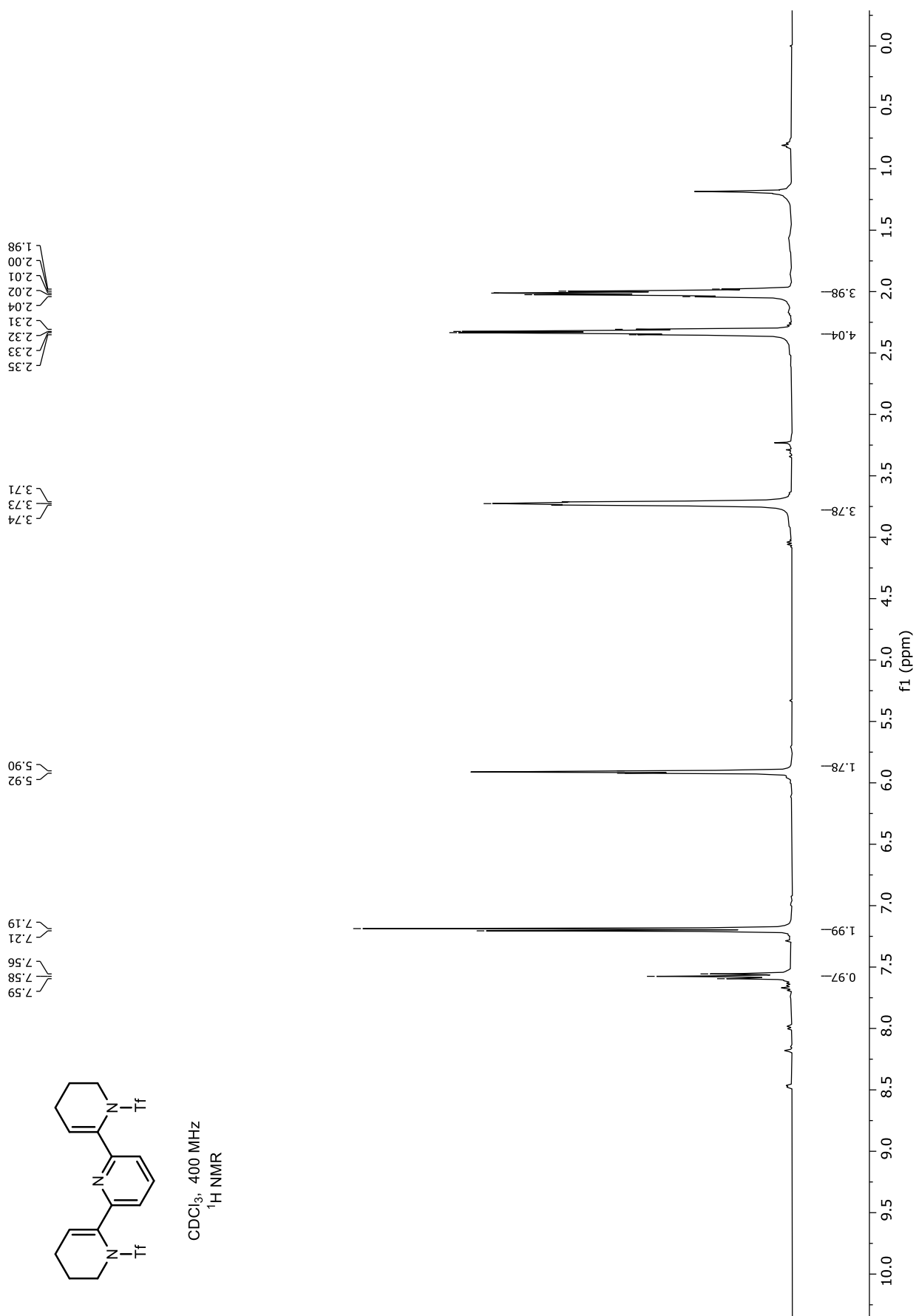


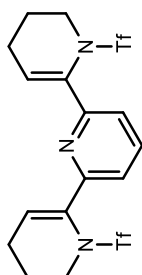






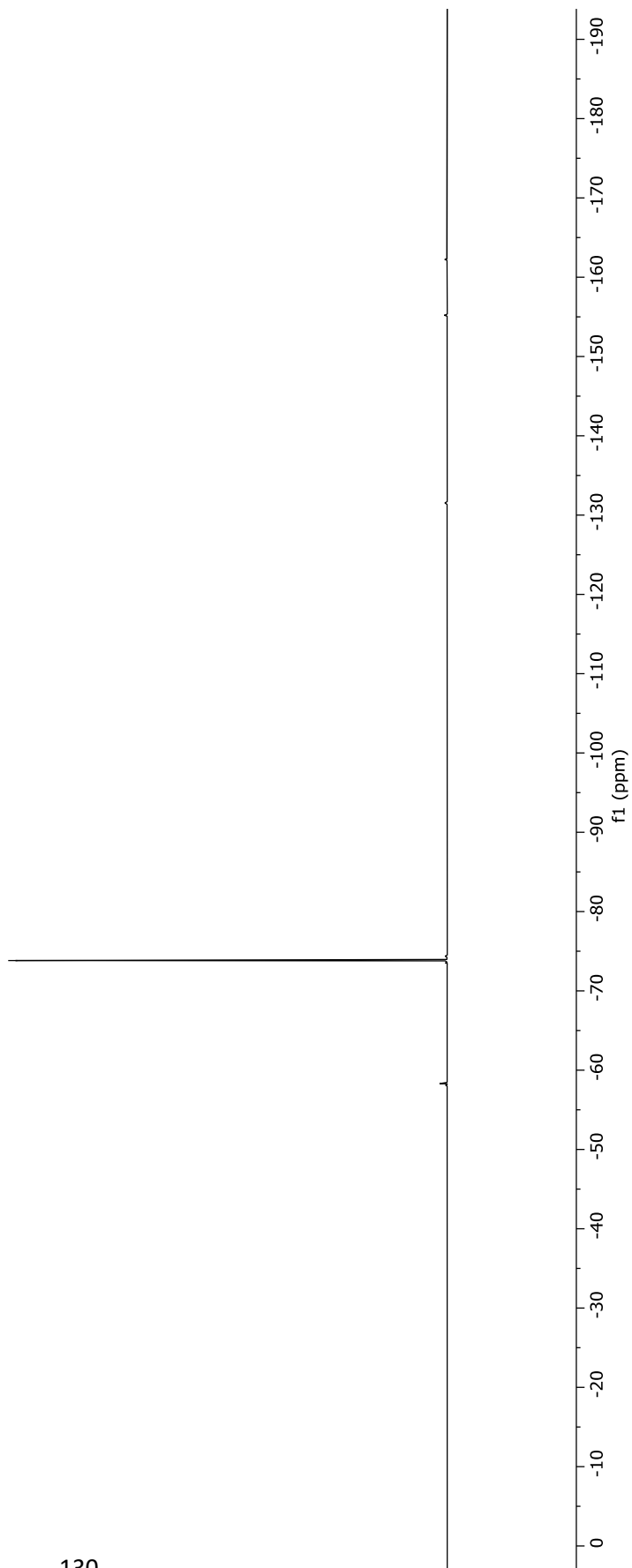


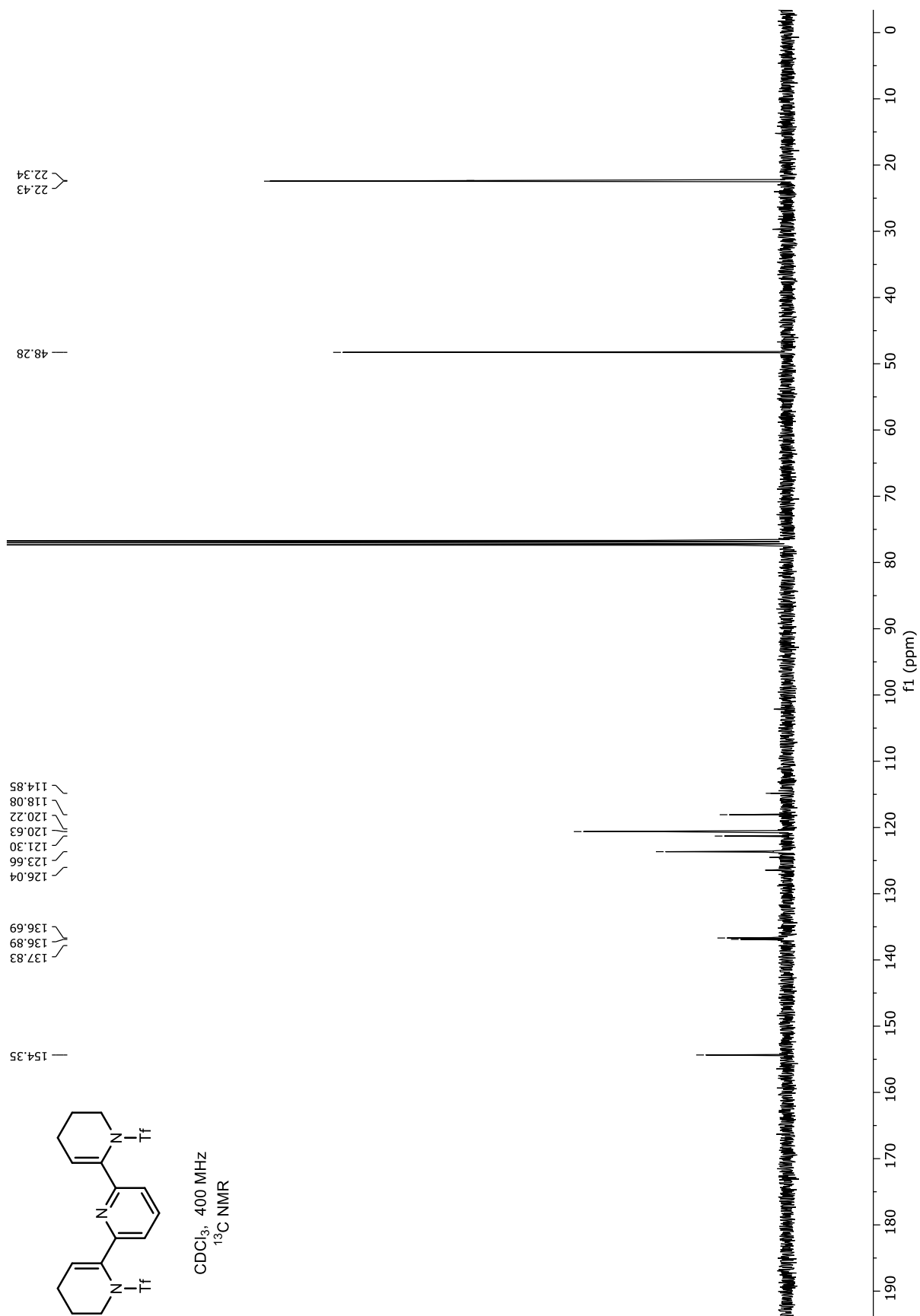


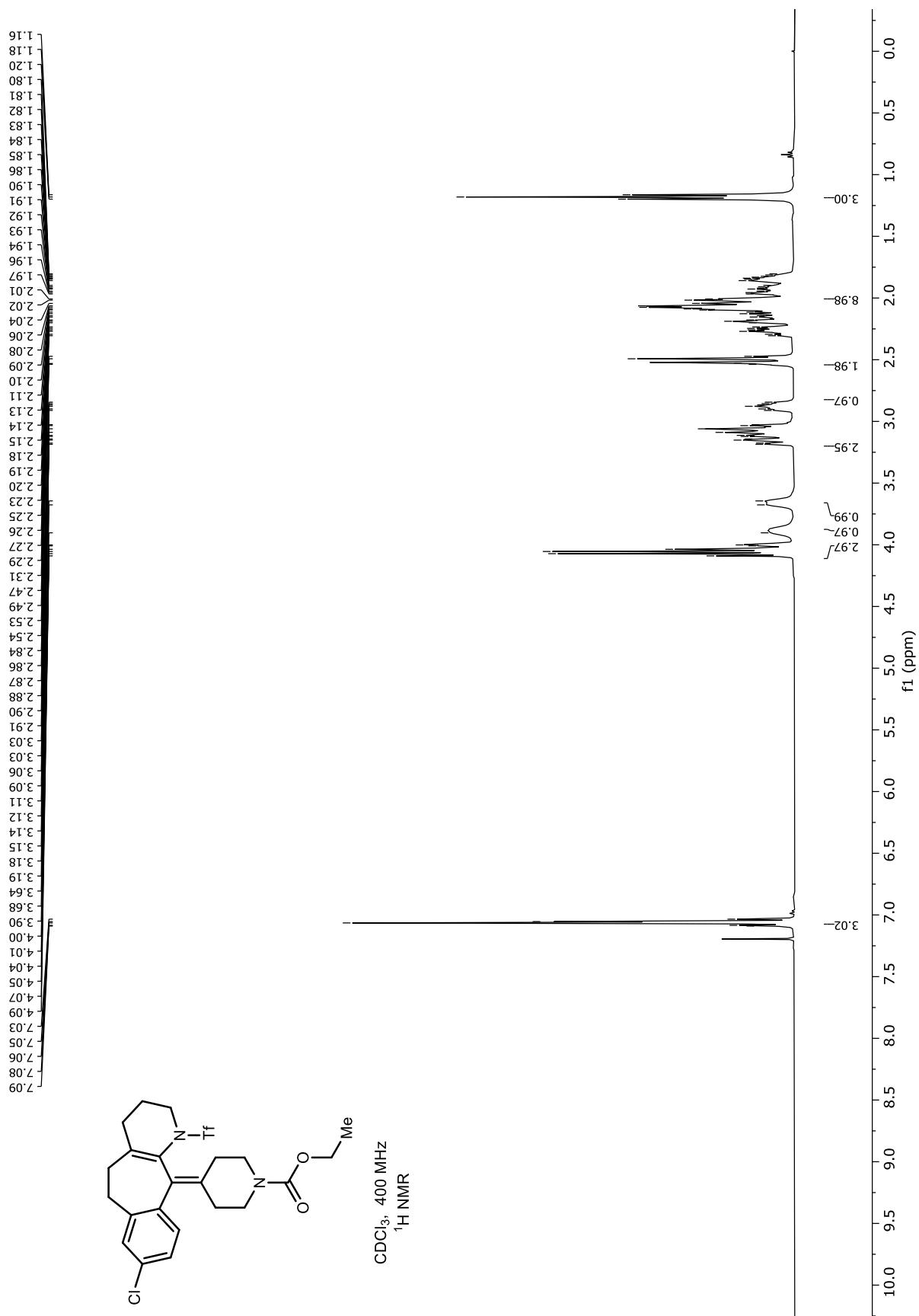


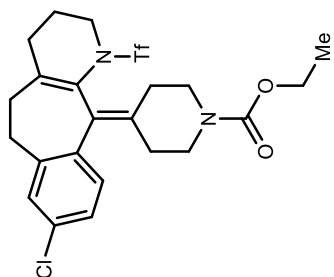
CDCl₃, 400 MHz
¹⁹F NMR

— -73.82



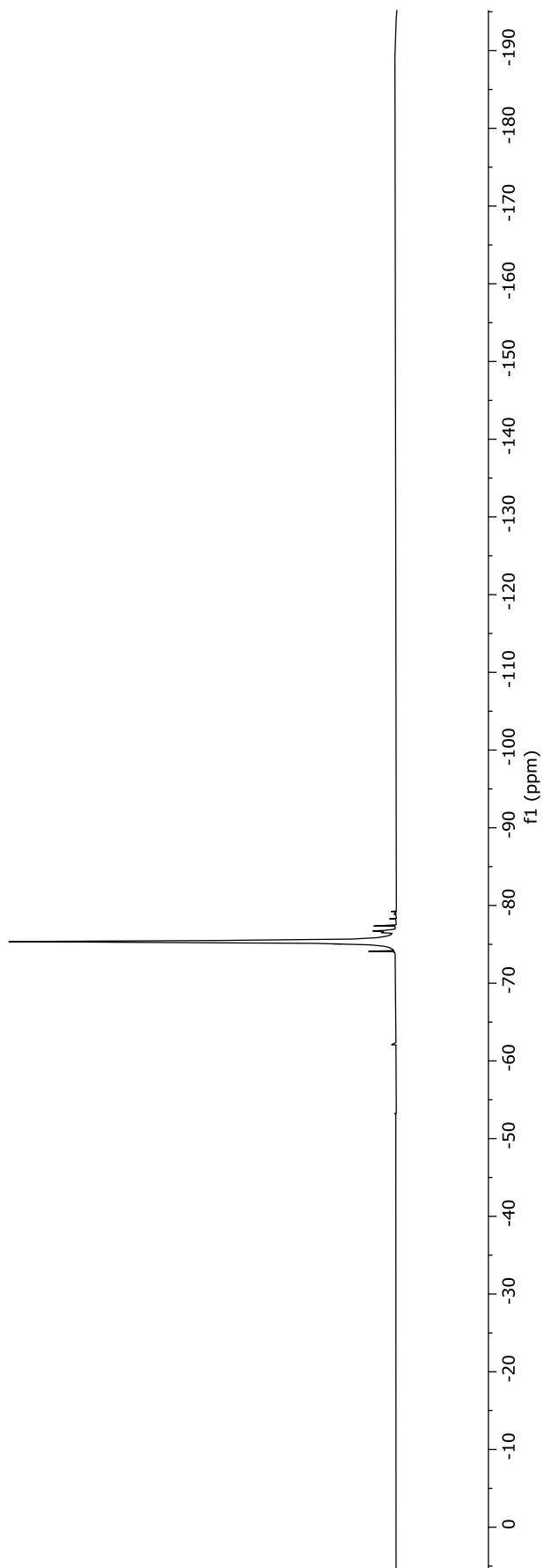


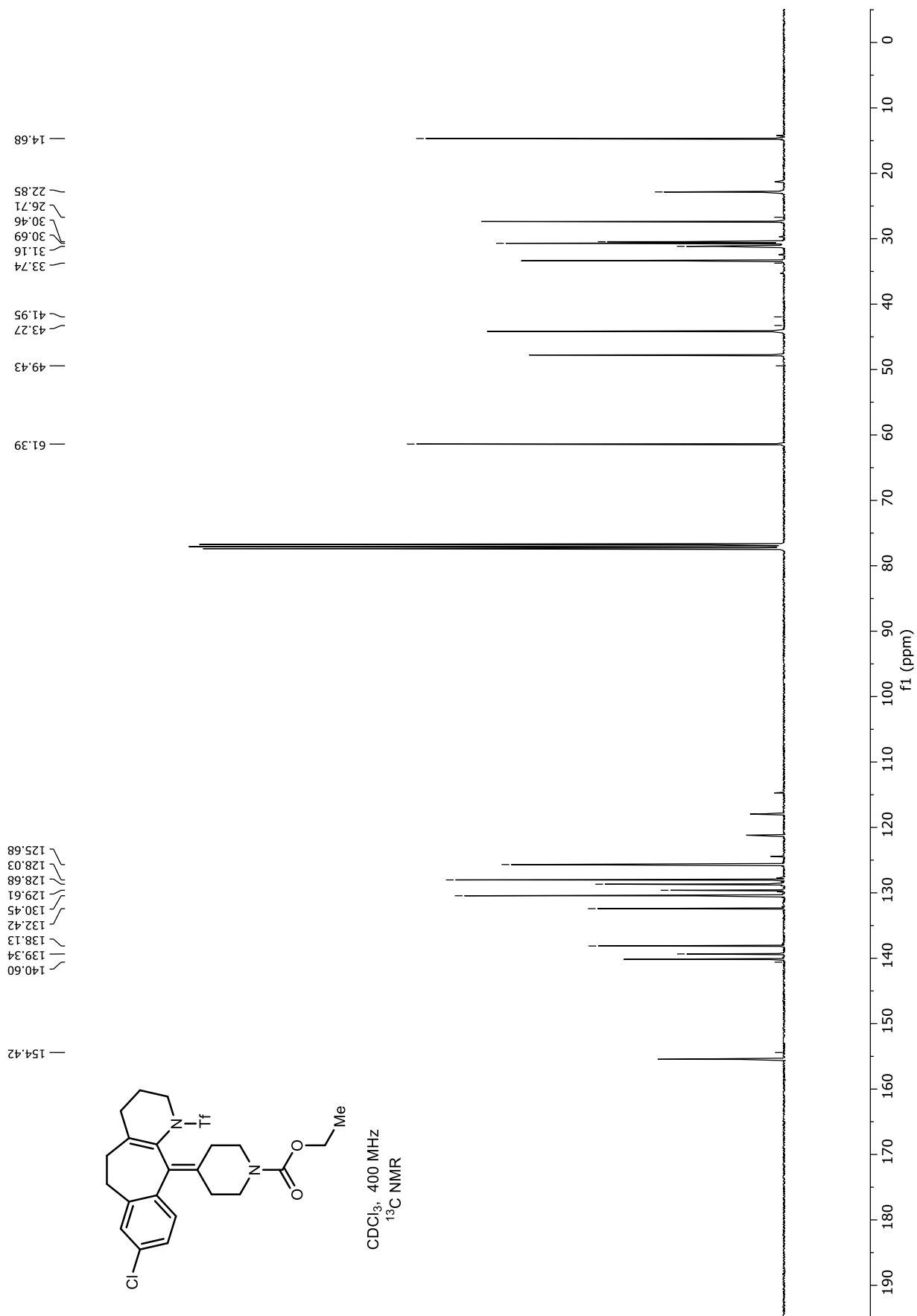


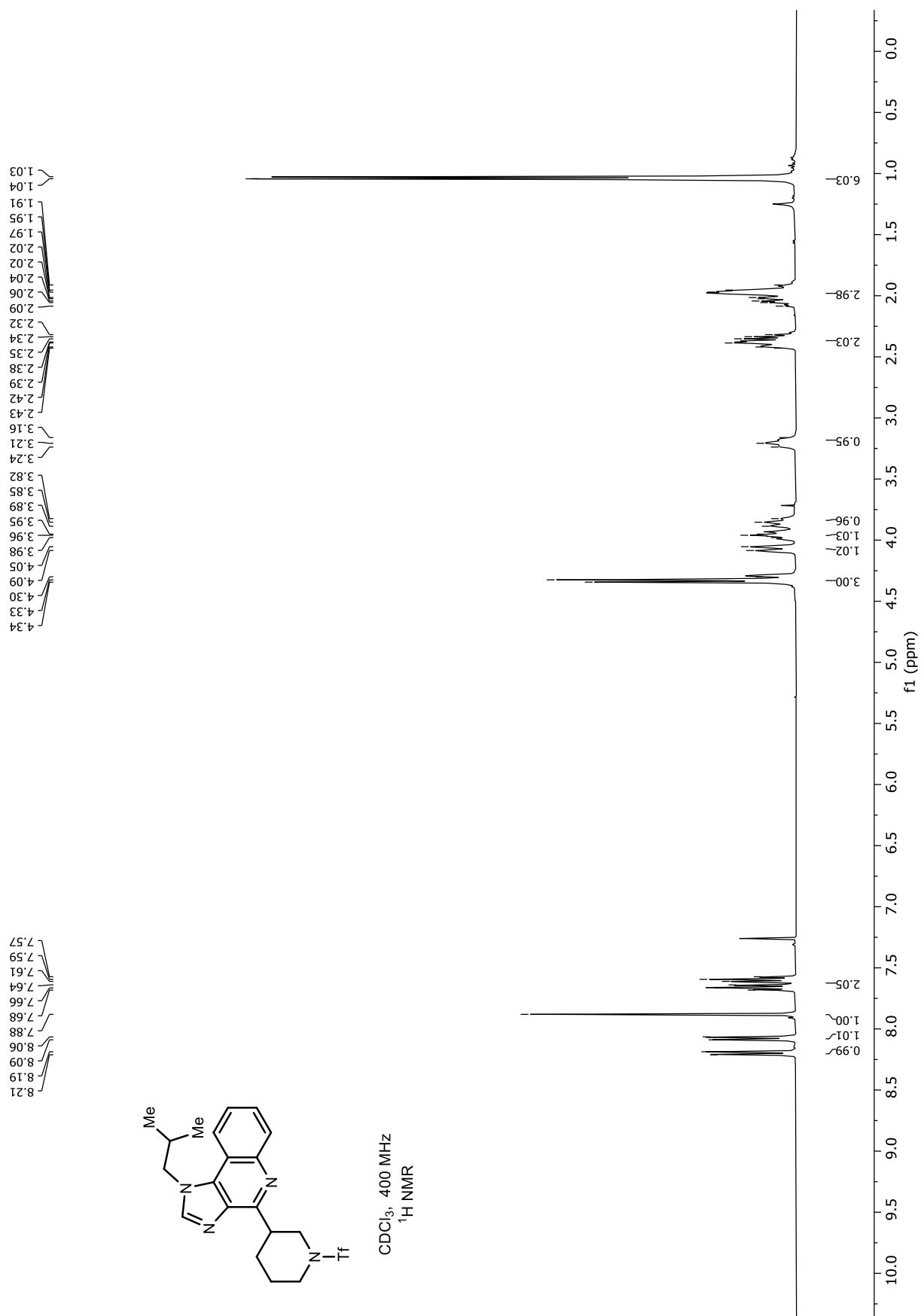


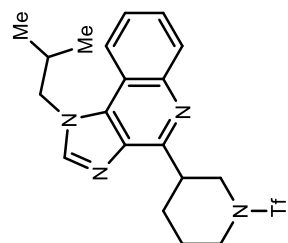
CDCl₃, 400 MHz
¹⁹F NMR

— -75.05



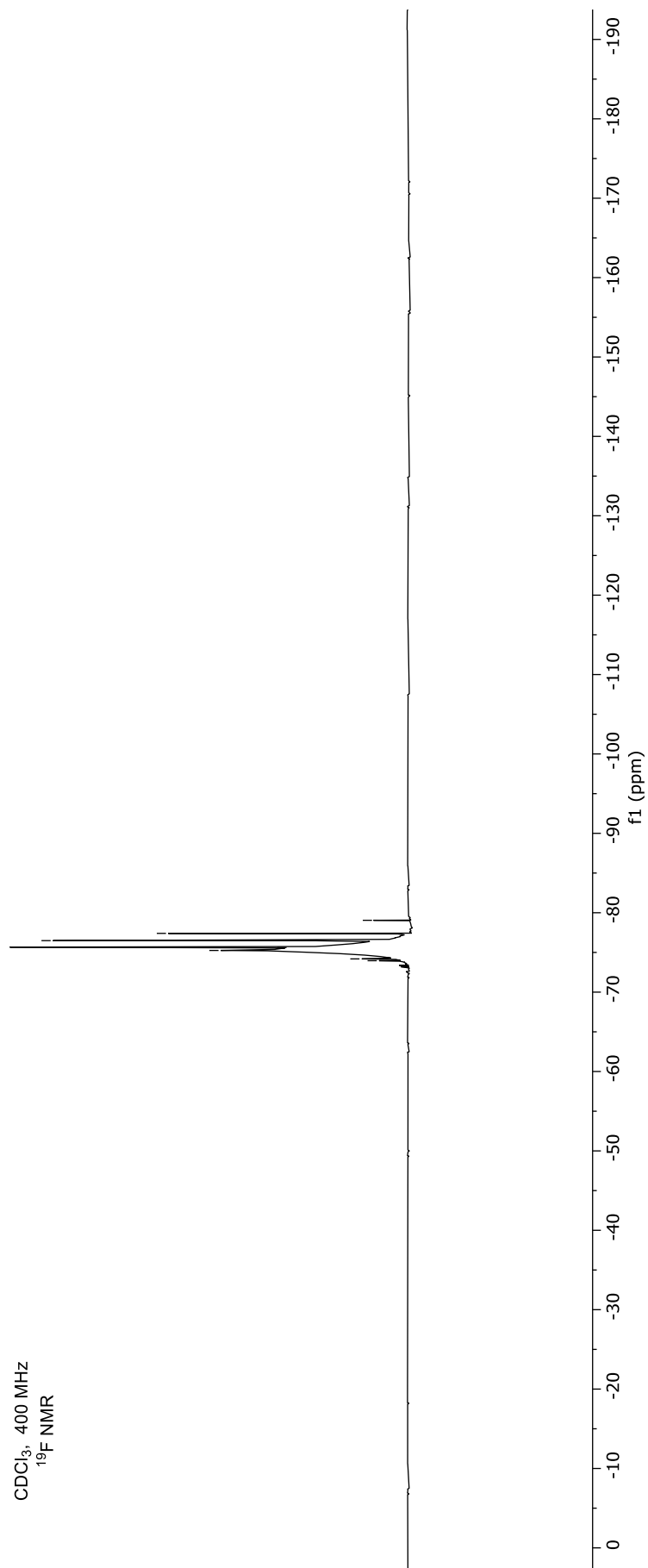


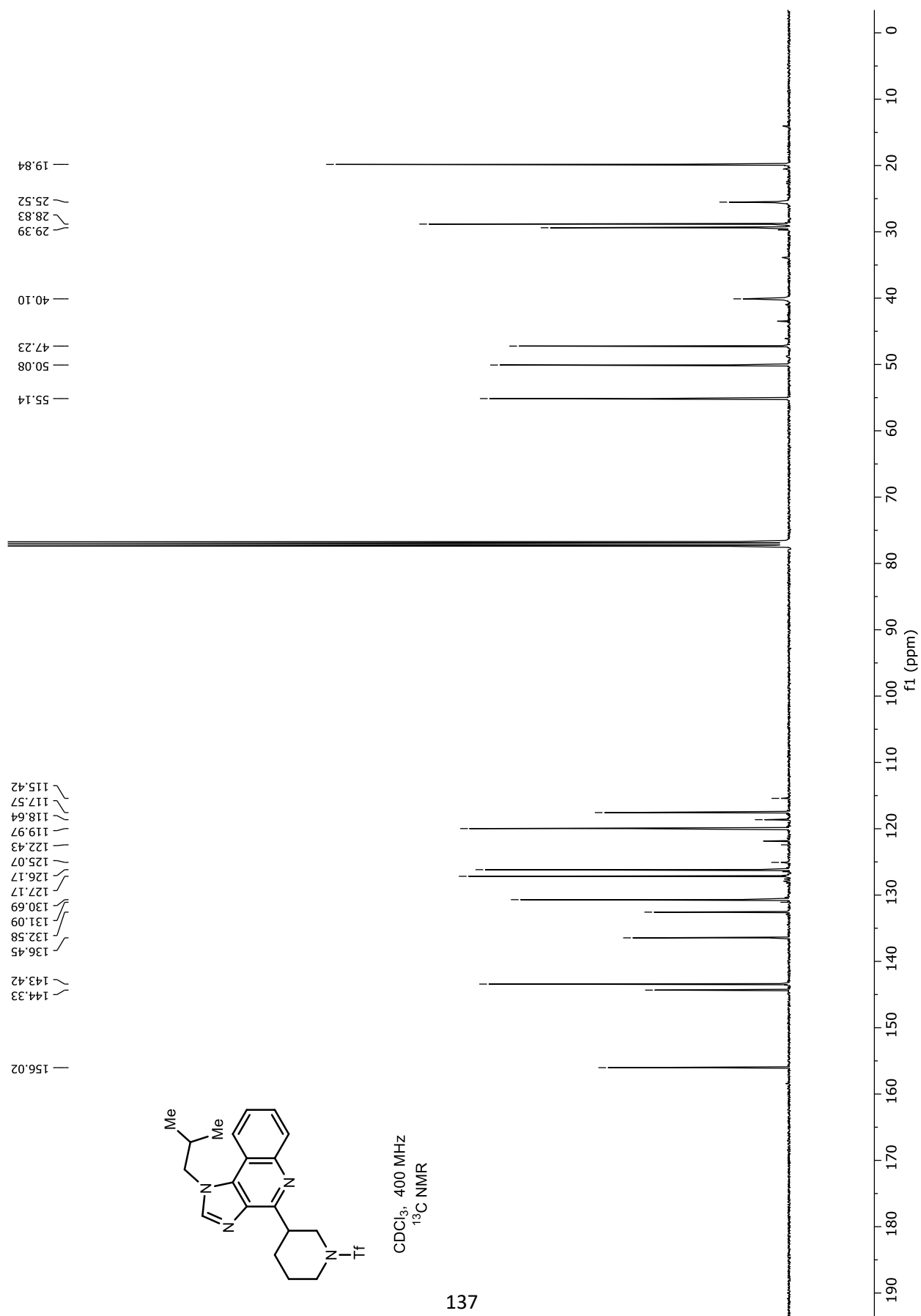


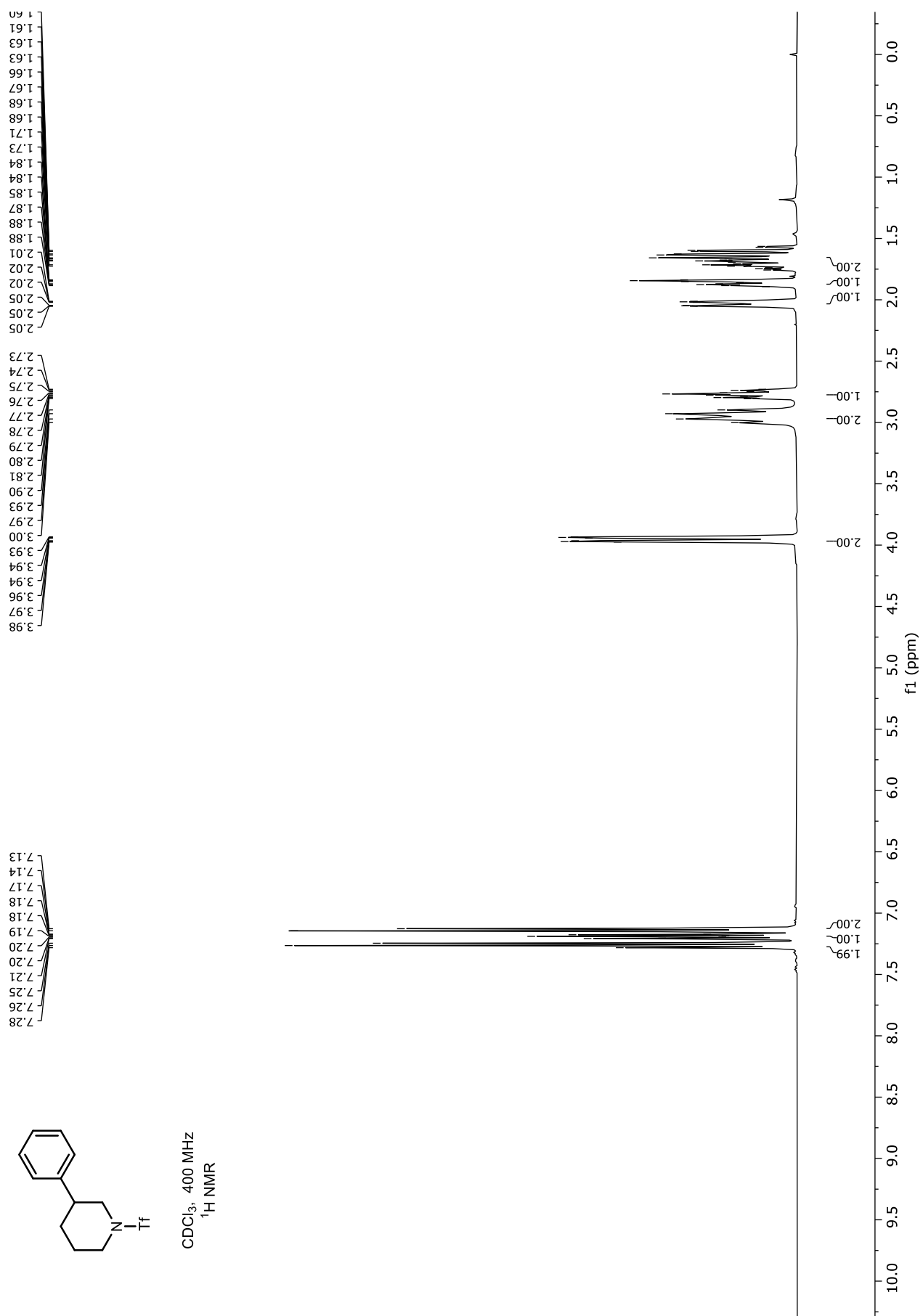


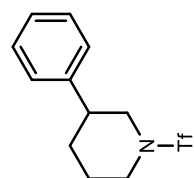
CDCl₃, 400 MHz
¹⁹F NMR

-73.96
 -74.19
 -75.25
 -75.61
 -76.48
 -77.40
 -79.05



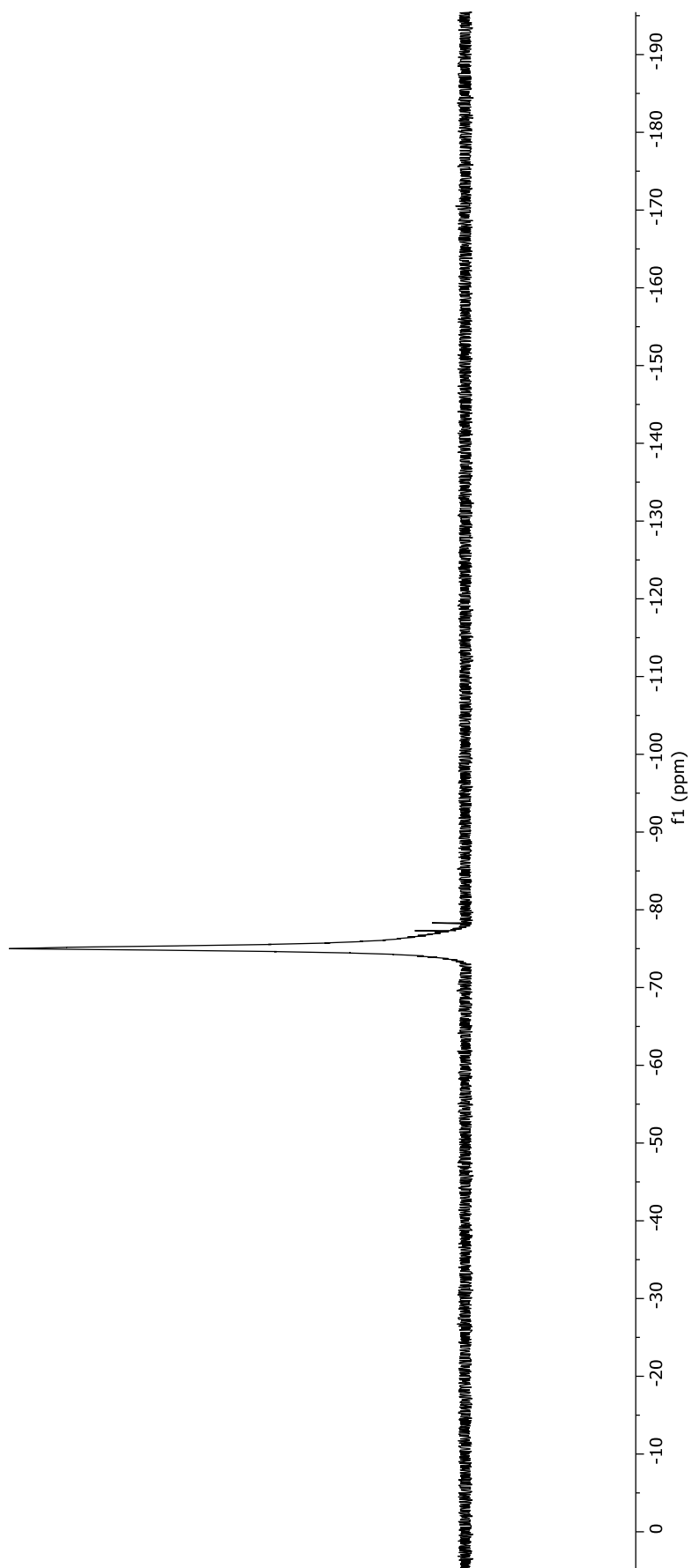


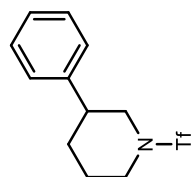




CDCl₃, 400 MHz
¹⁹F NMR

— -73.86



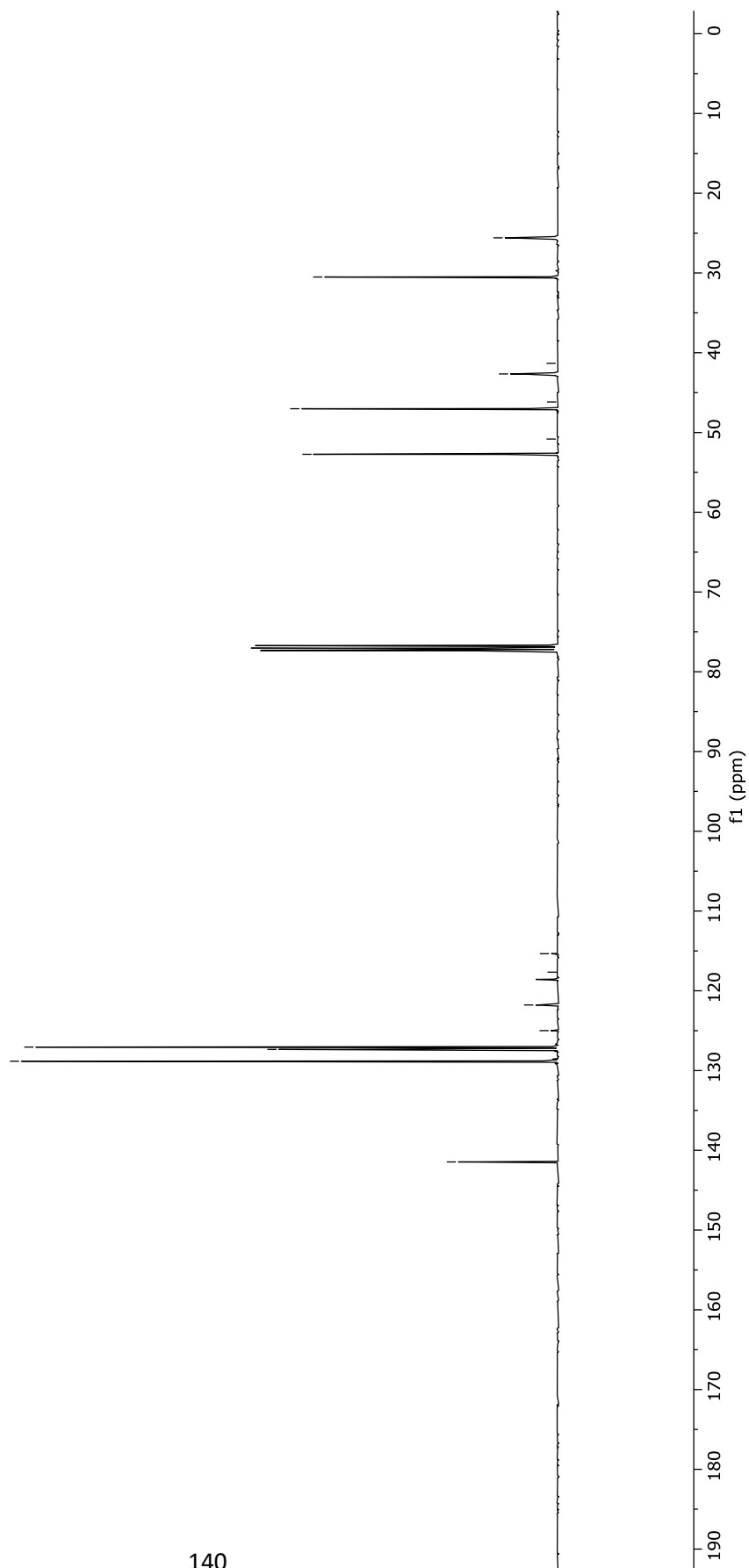


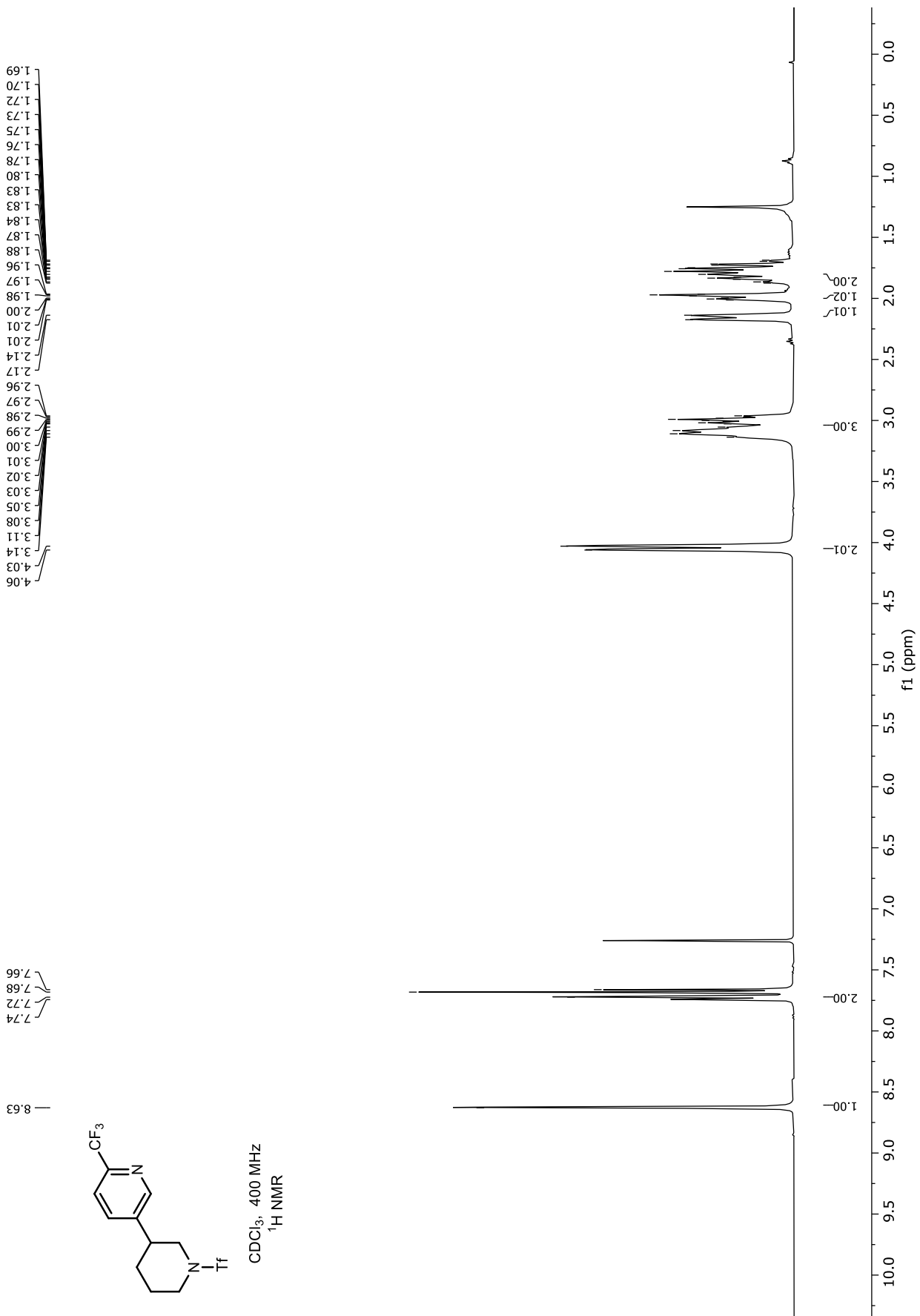
CDCl₃, 400 MHz
¹³C NMR

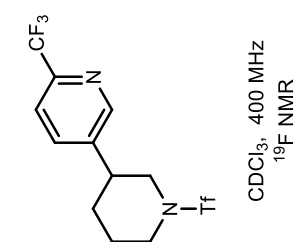
— 25.60
 — 30.50
 — 41.33
 — 42.66
 — 46.18
 — 47.02
 — 50.82
 — 52.74

— 115.35
 — 117.66
 — 121.78
 — 124.99
 — 127.06
 — 127.35
 — 128.83

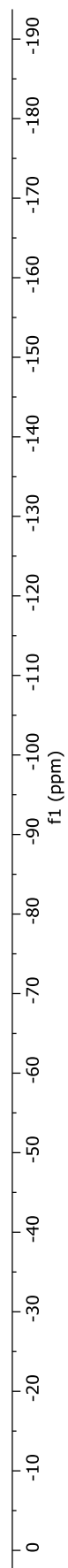
— 141.46

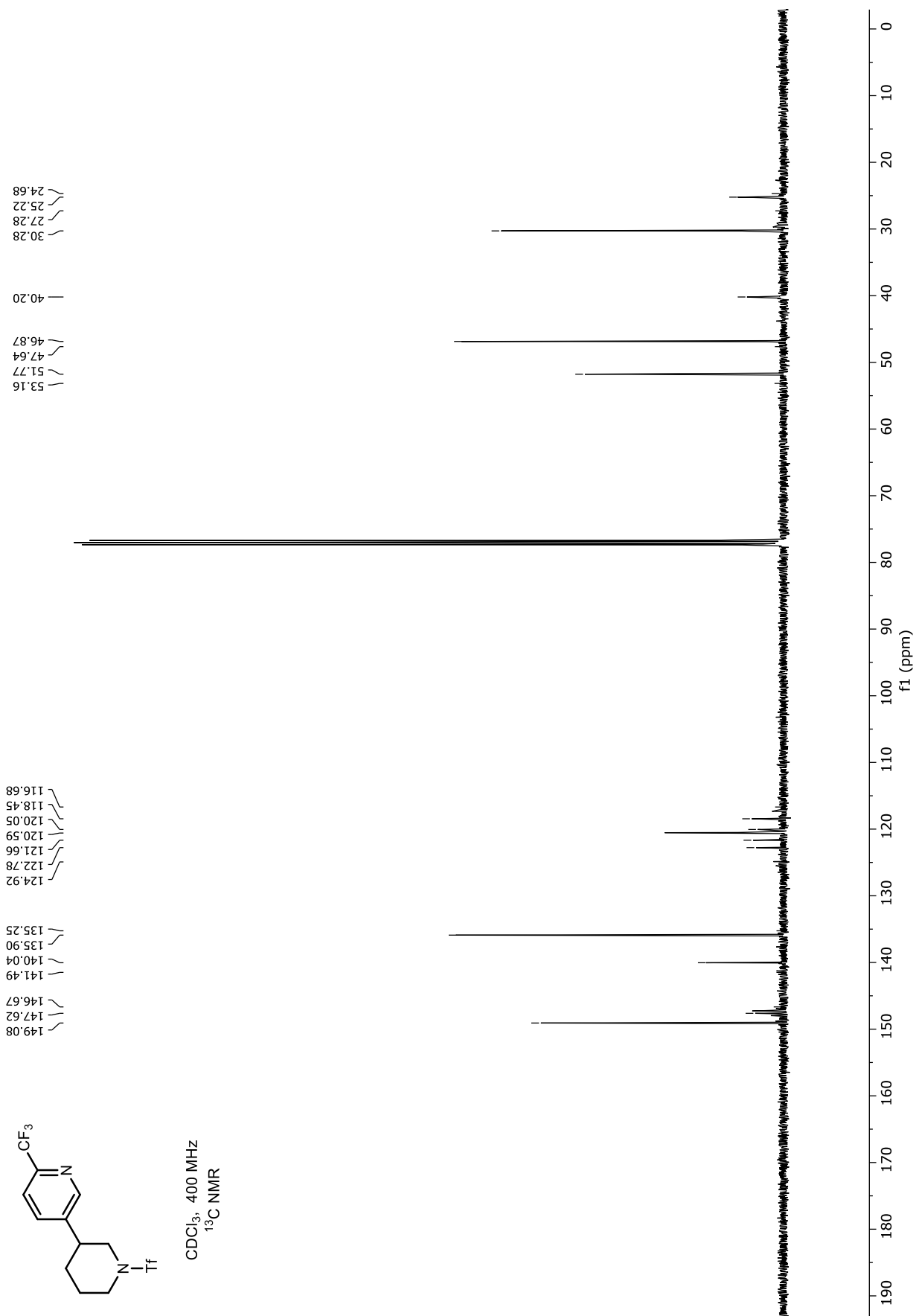


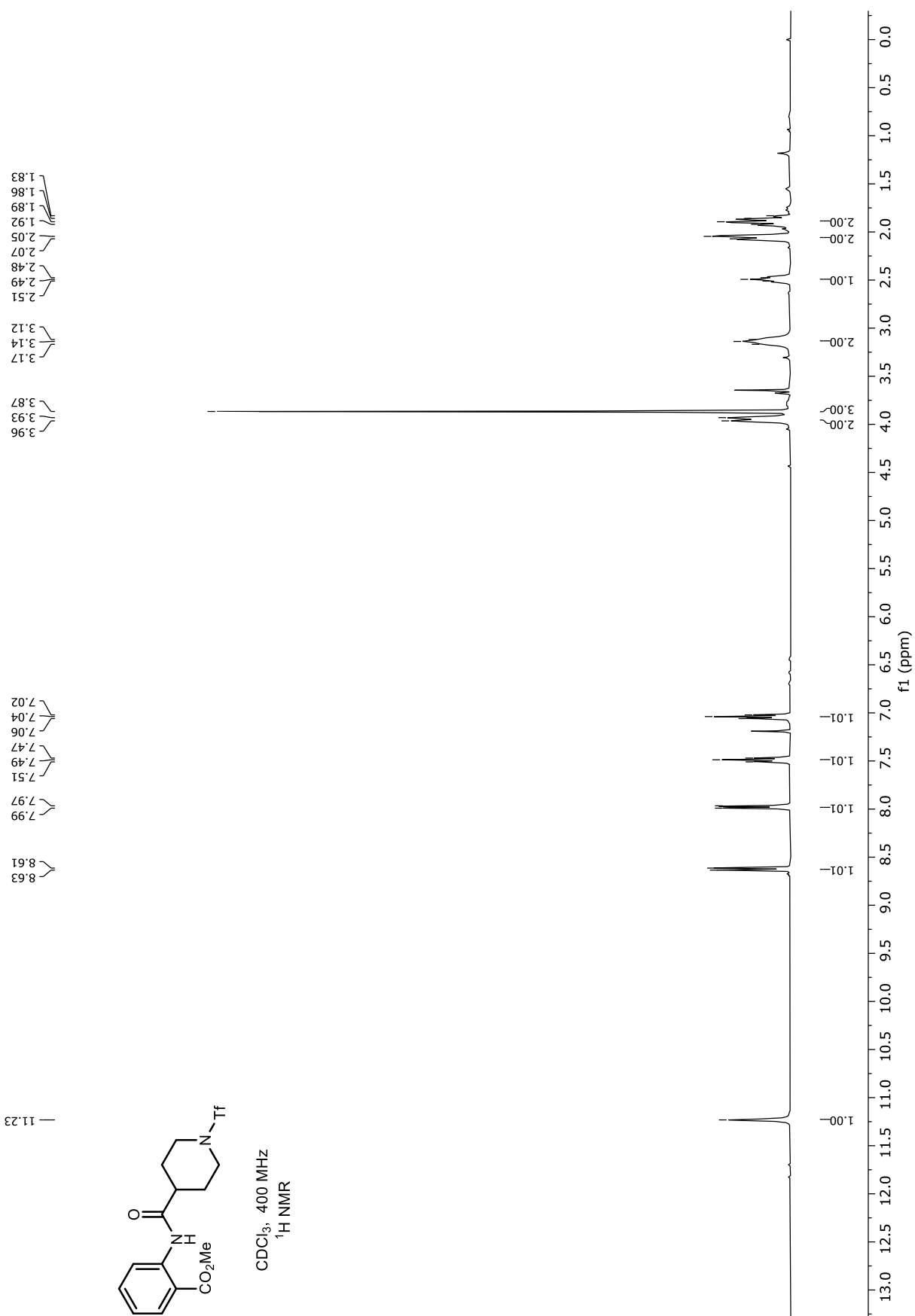


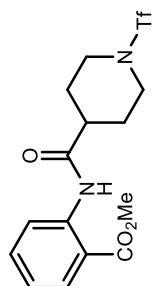


67.92
-75.05
-75.18
-75.20



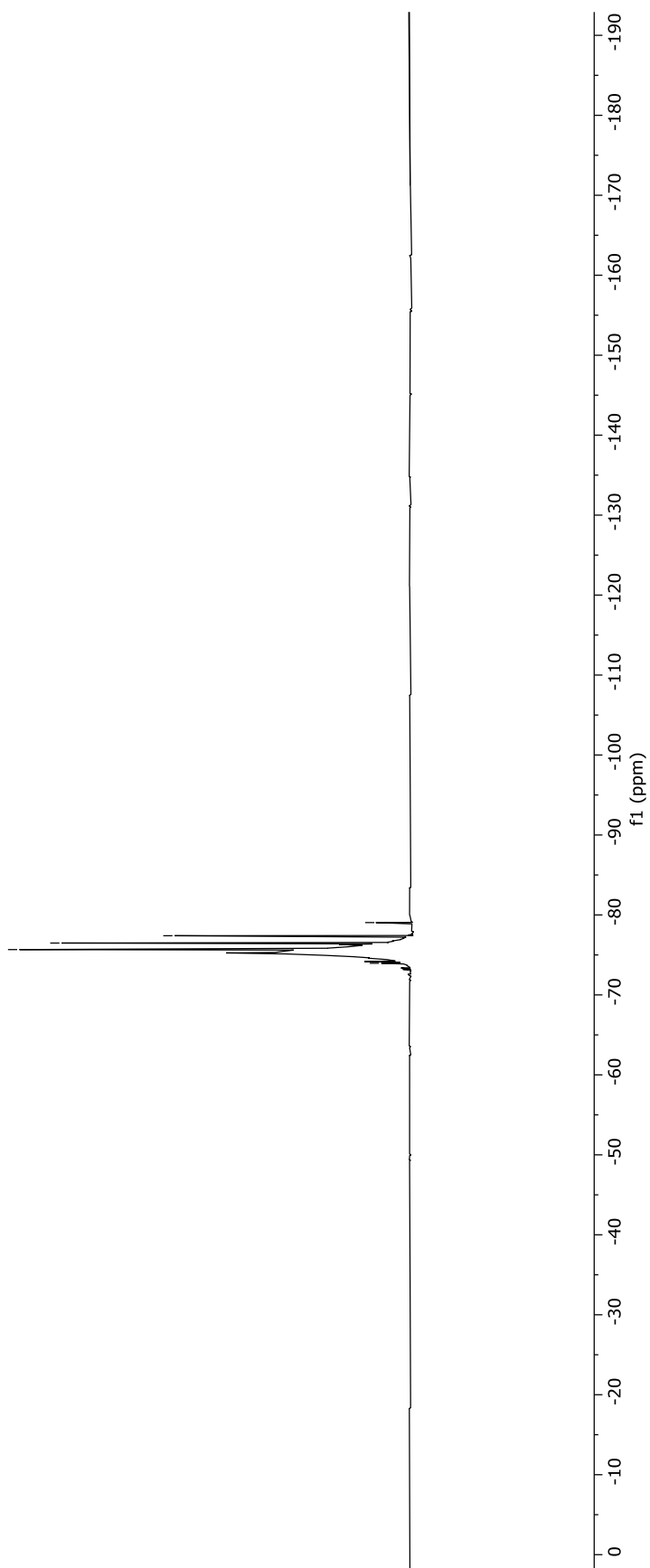


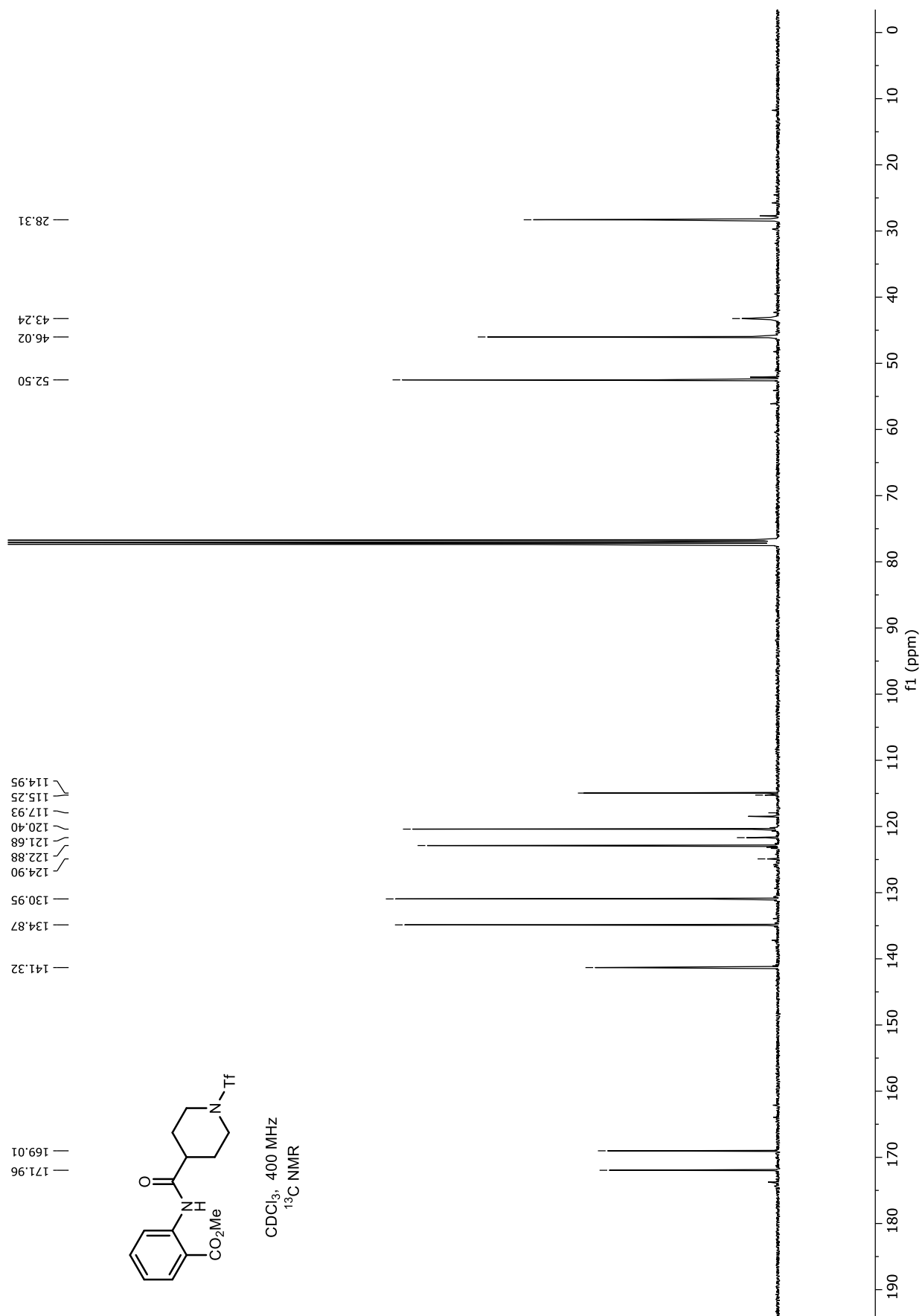




CDCl₃, 400 MHz
¹⁹F NMR

-73.96
 -75.67
 -76.48
 -77.40
 -79.05





APPENDIX TWO

A DECONSTRUCTION-RECONSTRUCTION STRATEGY FOR PYRIMIDINE

DIVERSIFICATION: EXPERIMENTAL

A2.1 General Methods and Materials

Proton nuclear magnetic resonance (^1H NMR) spectra were recorded at ambient temperature on a Varian 400 MR spectrometer (400 MHz), an Agilent Inova 400 (400 MHz) spectrometer, an Agilent Inova 500 (500 MHz) spectrometer, or a Bruker AV-111 400 (400 MHz) spectrometer. Chemical shifts (δ) are reported in ppm and quoted to the nearest 0.1 ppm relative to the residual protons in CDCl_3 (7.26 ppm), CD_3OD (3.31 ppm), $(\text{CD}_3)_2\text{CO}$ (2.05 ppm), CD_3CN (1.94 ppm), D_2O (4.79 ppm), or $(\text{CD}_3)_2\text{SO}$ (2.50 ppm) and coupling constants (J) are quoted in Hertz (Hz). Data are reported as follows: Chemical shift (multiplicity, coupling constants, number of protons). Coupling constants were quoted to the nearest 0.1 Hz and multiplicity reported according to the following convention: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sext = sextet, sp = septet, m = multiplet, br = broad. Where coincident coupling constants have been observed, the apparent (app) multiplicity of the proton resonance has been reported. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at ambient temperature on a Varian 400 MR spectrometer (100 MHz), an Agilent Inova 400 (100 MHz) spectrometer, an Agilent Inova 500 spectrometer (125 MHz) or a Bruker AV-111 400 (100 MHz) spectrometer. Chemical shift (δ) was measured in ppm and quoted to the nearest 0.01 ppm relative to the residual solvent peaks

in CDCl₃ (77.16 ppm), CD₃OD (49.00 ppm), (CD₃)₂CO (29.84 ppm), CD₃CN (1.32 ppm), D₂O, or (CD₃)₂SO (39.52 ppm).

Tetrahydrofuran (THF), toluene, hexane, diethyl ether (Et₂O), and dichloromethane (DCM) were dried and distilled using standard methods, 1,2-dichloroethane (DCE), chloroform (CHCl₃), ethanol (EtOH), and acetone were purchased anhydrous from Sigma Aldrich chemical company. All reagents were purchased at the highest commercial quality and used without further purification. Reactions were carried out under an atmosphere of nitrogen unless otherwise stated. All reactions were monitored by TLC, ¹H NMR spectra taken from reaction samples, gas chromatography (GC), and gas chromatography mass spectrometry (GCMS) using an Agilent 5977A fitted with an Agilent J&W HP – 5ms Ultra Inert Column (3m, 0.25 mm, 0.25 μm film) for MS analysis and an Agilent J&W VF (10m, 0.15 mm, 0.15 μm films) for FID analysis or liquid chromatography mass spectrometry (LCMS) using an Agilent 6310 Quadrupole Mass Spectrometer. High-resolution mass spectra (HRMS) were measured on an Agilent 6224 TOF LC/MS (“OTOF”) interfaced to an Agilent 1200 HPLC with multi-mode (combined ESI and APCI) and Direct Analysis in Real Time (DART) sources. Infrared (IR) spectra were recorded on a Nicolet IS-50 FT-IR spectrometer as either solids or neat films, either through direct application or deposited in CHCl₃, with absorptions reported in wavenumbers (cm⁻¹). Analytical thin layer chromatography (TLC) was performed using pre-coated Silicycle glass-backed silica gel plates (Silicagel 60 F254). Manual flash column chromatography was undertaken on Silicycle silica gel Siliaflash P60 40-63 mm (230-400 mesh) under a positive pressure of air unless otherwise stated. Automated flash column chromatography was undertaken using a Teledyne Isco CombiFlash NextGen 300+ using 12 g RediSep Gold Normal-Phase Silica cartridges. Visualization was

achieved using ultraviolet light (254 nm) and chemical staining with a chamber of I₂ in SiO₂, ceric ammonium molybdate, or basic potassium permanganate solutions as appropriate. Melting points (mp) were recorded using a Büchi B-450 melting point apparatus and are reported uncorrected.

A2.2 Additional Examples of N-Aryl Pyrimidinium Salts, Pyrimidine C2-Functionalizations, and Ring-Conversions

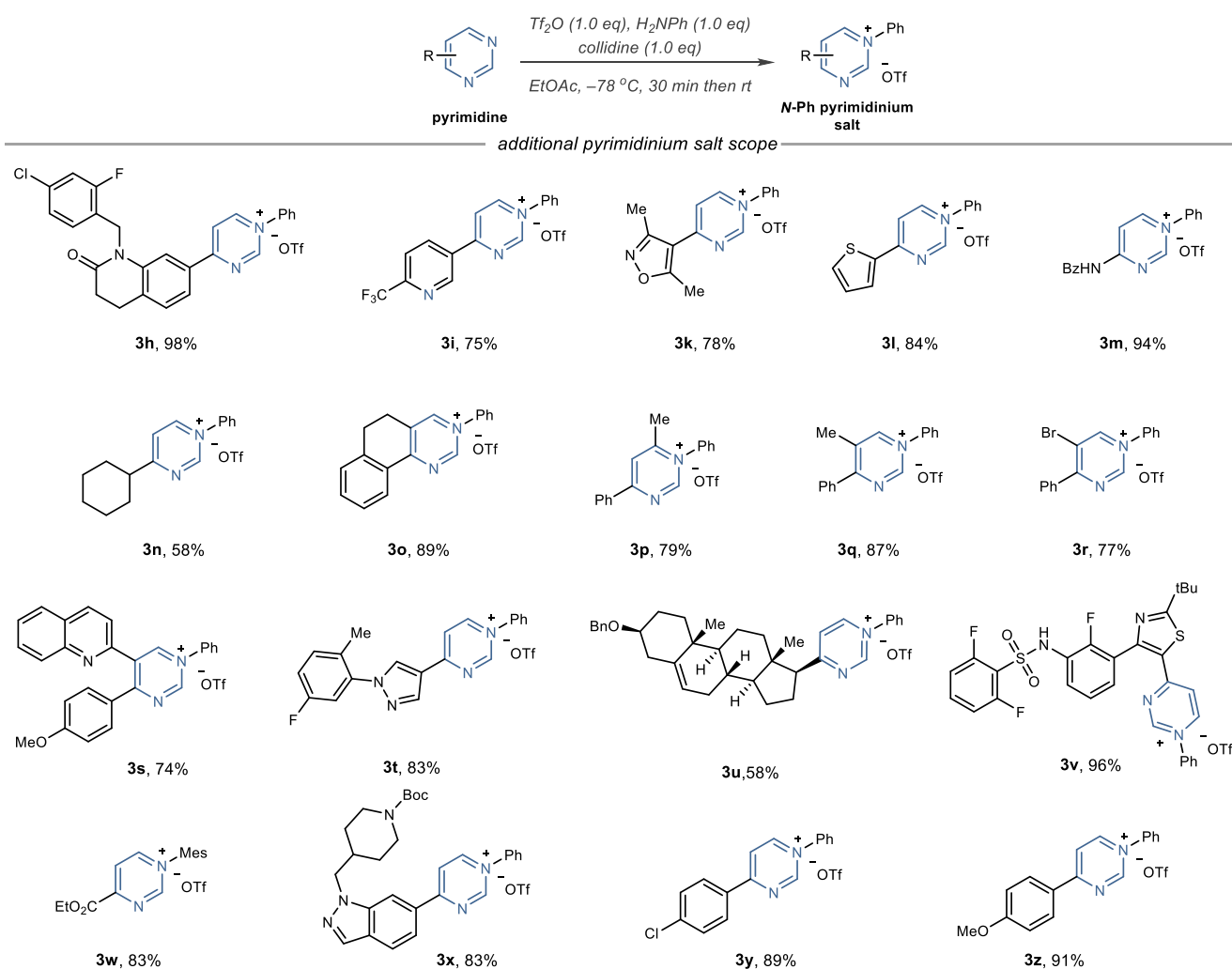


Fig. A1. Additional examples of N-aryl pyrimidinium salts. Isolated yields are shown.

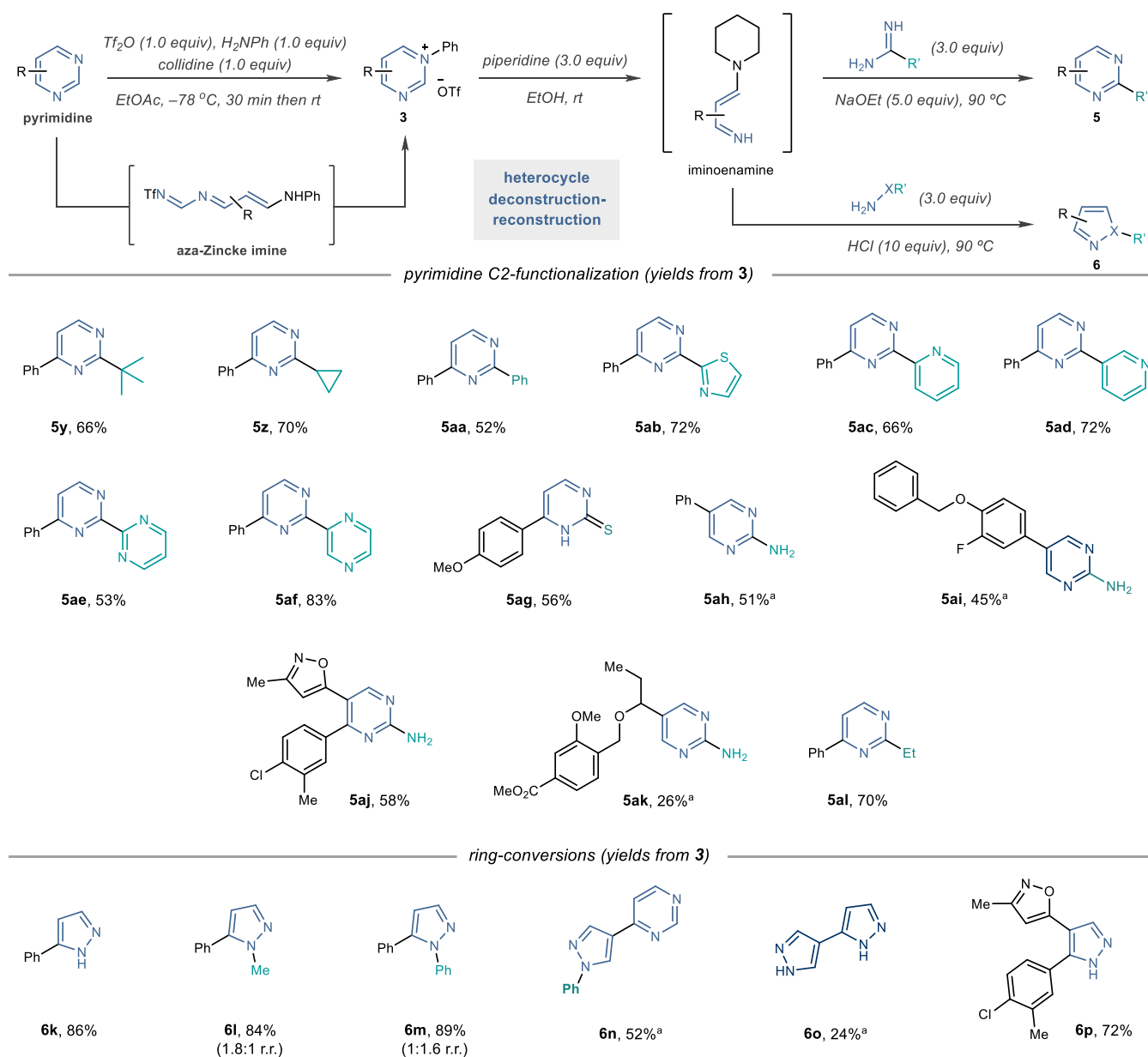
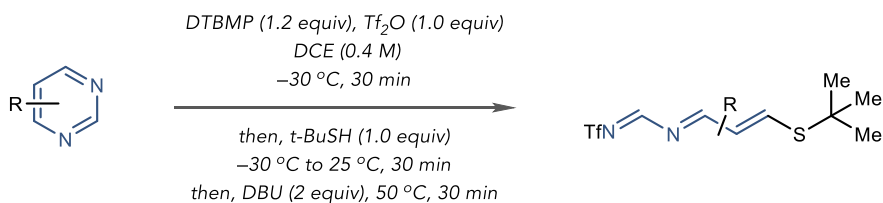


Fig. A2. Additional examples of pyrimidine C2-functionalizations and ring-conversions. Isolated yields are shown. ^aOne-pot protocol used. See “General Procedure D” or “General Procedure E” on pages 270-271 for details.

A2.3 Thiol-Ring Opening Experimental and Isolation

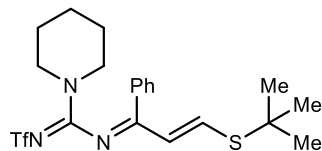


An oven-dried 8 mL vial (≤ 0.5 mmol scale) or a round bottom flask (> 0.5 mmol scale) equipped with a stir bar was charged with the pyrimidine (1.0 equiv) and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) (1.2 equiv) and placed under a nitrogen atmosphere. DCE (0.2 M) was added, the reaction vessel was cooled to –30 °C, and triflic anhydride ($\text{ Tf}_2\text{O}$) (1.0 equiv) was added dropwise. The reaction was stirred for 30 minutes before *tert*-butylthiol (1.0 equiv) was added dropwise. The reaction was warmed to room temperature and stirred for an additional 30 minutes. DBU (2 equiv) was added dropwise and the reaction was heated to 50 °C for 30 min.

Isolation Procedure: The reaction was cooled to room temperature and diluted with DCM. The crude reaction mixture was washed with water (x3) and brine (x1). The organic layer was dried with $\text{ Na}_2\text{SO}_4$ and concentrated. The resulting mixture was precipitated in pre-chilled hexanes and filtered over filter paper to afford the mostly pure thiol ring-opened product.

(E)-N-((1Z,2E)-3-(*tert*-butylthio)-1-phenylallylidene)-N'

((trifluoromethyl)sulfonyl)piperidine-1-carboximidamide



^1H NMR (400 MHz, CDCl_3) δ 7.71 – 7.64 (m, 2H), 7.56 – 7.38 (m, 4H), 6.35 (d, $J = 15.5$ Hz, 1H), 3.77 (d, $J = 5.1$ Hz, 2H), 3.34 – 3.27 (m, 2H), 1.66 (p, $J = 2.6$ Hz, 4H), 1.36 (s, 9H).

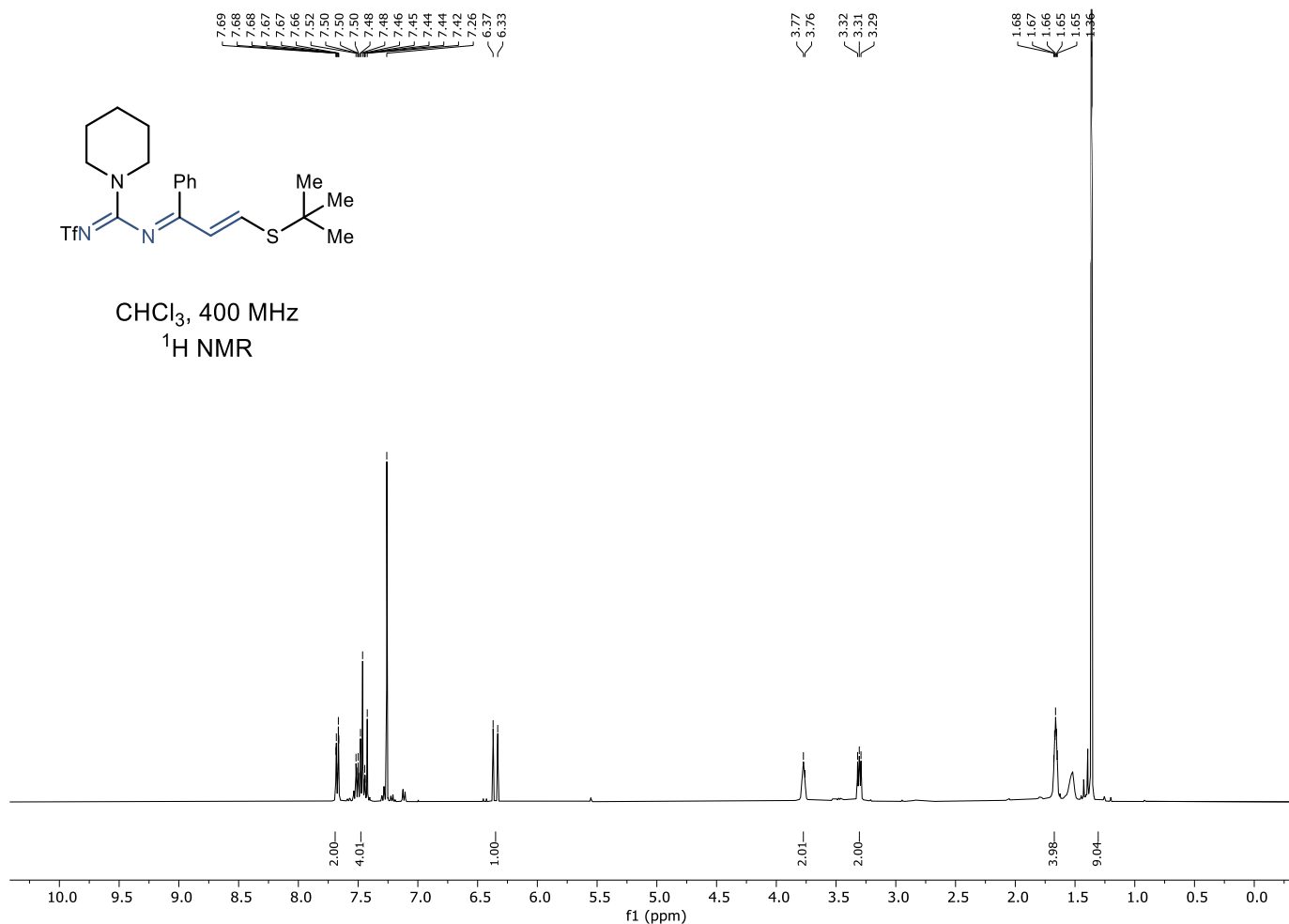
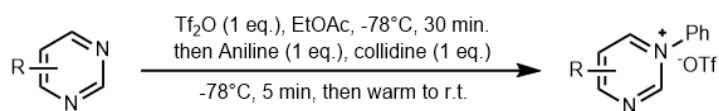


Fig. A3. Representative ^1H NMR after work-up procedure.

General Procedure A: *N*-Aryl Pyrimidinium Salt Formation



An oven-dried 8 mL vial (≤ 0.5 mmol scale) or a round bottom flask (> 0.5 mmol scale) equipped with a stir bar was charged with the pyrimidine (1.0 equiv) and placed under a nitrogen atmosphere. EtOAc (0.2 M) was added, the reaction vessel was cooled to -78 °C, and triflic anhydride ($\text{ Tf}_2\text{O}$) (1.0 equiv) was added dropwise. The reaction was stirred for 30 minutes before aniline (1.0 equiv) was added dropwise followed by collidine (1.0 equiv). The reaction was stirred for an additional 5 minutes at -78 °C. The cooling bath was removed and the reaction was allowed to warm to room temperature while stirring for approximately 30 minutes.

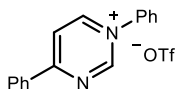
Isolation A1: The reaction was cooled to 0 °C and diluted with an equal volume Et_2O . The reaction was stirred for 15 minutes then filtered and washed with ice-cold 1:1 Et_2O :EtOAc to provide pure pyrimidinium.

Isolation A2: For products that do not precipitate with the addition of Et_2O , the reaction mixture was transferred to a separatory funnel and washed with a 0.1 M HCl solution (2x) and with brine (1x), then dried over MgSO_4 and concentrated *in vacuo*. The resulting oil was triturated with Et_2O and decanted to provide pure pyrimidinium.

Reaction Notes:

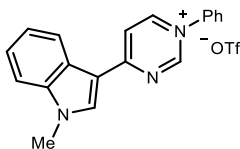
- Isolation procedure applies only to 4-substituted pyrimidines.
- Care must be taken to ensure no aniline freezes to the side of the reaction flask.
- Following aniline addition, reaction mixtures that “gel” or freeze were taken from the cooling bath and swirled by hand until aniline mixed in with the gel before returning to the cooling bath.

1,4-Diphenylpyrimidin-1-ium trifluoromethanesulfonate (3a)



Prepared according to general procedure A using 4-phenylpyrimidine (1.56 g, 10.0 mmol), EtOAc (50 mL), Tf₂O (1.68 mL, 10.0 mmol), aniline (912 μ L, 10.0 mmol), and collidine (1.32 mL, 10.0 mmol). Isolation A1 afforded the title compound as a white powder (3.62 g, 9.45 mmol, 95% yield). mp 216-220 °C; IR ν_{max} /cm⁻¹ (solid): 3102, 1622, 1589, 1417, 1256, 1146, 1030, 741, 633; ¹H NMR (400 MHz, CD₃CN) δ 9.63 – 9.57 (m, 1H), 9.15 (dd, *J* = 6.9, 2.1 Hz, 1H), 8.66 (d, *J* = 6.9 Hz, 1H), 8.46 (d, *J* = 7.2 Hz, 2H), 7.86 – 7.75 (m, 6H), 7.71 (t, *J* = 7.8 Hz, 2H); ¹³C NMR (100 MHz, CD₃CN) δ 171.28, 153.04, 151.69, 140.17, 136.35, 133.77, 132.87, 131.56, 130.86, 130.46, 125.55, 122.02 (q, *J* = 320.8 Hz), 119.53; ¹⁹F NMR (375 MHz, CD₃CN) δ -79.30; *m/z* HRMS (ESI) found [M+H]⁺ 233.1080, C₁₆H₁₃N₂⁺ requires 233.1073.

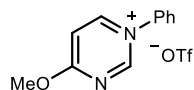
4-(1-Methyl-1H-indol-3-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3b)



Prepared according to general procedure A using 1-methyl-3-(pyrimidin-4-yl)-1H-indole (72.9 mg, 0.40 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A1 afforded the title compound as a bring-yellow solid (127 mg, 0.29 mmol, 73% yield). mp 106-109 °C; IR ν_{max} /cm⁻¹ (solid): 3103, 1630, 1549, 1253,

1221, 1028, 743, 635; ^1H NMR (400 MHz, CD_3CN) δ 9.19 (dd, $J = 2.1, 1.0$ Hz, 1H), 8.61 (s, 1H), 8.56 (dd, $J = 7.2, 2.0$ Hz, 1H), 8.54 (br, 1H), 8.07 (dd, $J = 7.3, 1.1$ Hz, 1H), 7.71 (qd, $J = 5.5, 3.7$ Hz, 5H), 7.65 – 7.59 (m, 1H), 7.50 – 7.43 (m, 2H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ 166.20, 152.16, 146.35, 141.98, 140.30, 139.98, 131.86, 131.38, 126.60, 125.52, 125.05, 124.91, 123.59, 122.0 (q, $J = 318.9$ Hz), 115.88, 112.80, 112.56, 34.91; ^{19}F NMR (375 MHz, CD_3CN) δ -79.32; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 286.1348, $\text{C}_{19}\text{H}_{16}\text{N}_3^+$ requires 286.1339.

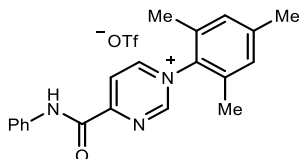
4-Methoxy-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3c)



Prepared according to general procedure A using 4-methoxypyrimidine (44.0 mg, 0.40 mmol), EtOAc (2 mL), Ti_2O (67 μL , 0.40 mmol), aniline (36 μL , 0.40 mmol), and collidine (53 μL , 0.40 mmol). Isolation A1 afforded the title compound as a white solid (84 mg, 0.25 mmol, 63% yield). mp 131-133 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3066, 1633, 1413, 1251, 1139, 1026, 838, 771, 636; ^1H NMR (400 MHz, CD_3CN) δ 9.28 (dd, $J = 2.2, 0.9$ Hz, 1H), 8.80 (dd, $J = 7.3, 2.2$ Hz, 1H), 7.83 – 7.66 (m, 5H), 7.48 (dd, $J = 7.3, 0.9$ Hz, 1H), 4.29 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ 173.54, 155.34, 151.02, 139.94, 132.30, 131.34, 125.42, 121.91 (q, $J = 320.9$ Hz), 111.69, 58.37; ^{19}F

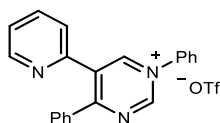
NMR (375 MHz, CD₃CN) δ -79.21; m/z HRMS (ESI) found $[M+H]^+$ 187.0873, C₁₁H₁₁N₂O⁺ requires 187.0866.

1-Mesityl-4-(phenylcarbamoyl)pyrimidin-1-ium trifluoromethanesulfonate (3d)



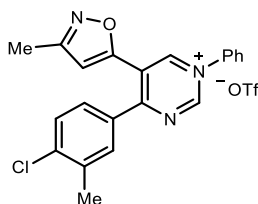
Prepared according to general procedure A using N-phenylpyrimidine-4-carboxamide (79.7 mg, 0.40 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), 2,4,6-trimethylaniline (56 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A1 afforded the title compound as a yellow powder (116 mg, 0.25 mmol, 62% yield). mp 228-231 °C; IR ν_{max} /cm⁻¹ (solid): 3273, 3034, 1682, 1521, 1447, 1258, 1142, 1029, 742, 635; ¹H NMR (400 MHz, CD₃CN) δ 10.16 (s, 1H), 9.66 (s, 1H), 9.30 (ddd, J = 6.4, 1.7, 0.7 Hz, 1H), 8.94 (dt, J = 6.4, 0.9 Hz, 1H), 7.90 – 7.83 (m, 2H), 7.52 – 7.43 (m, 2H), 7.29 (ddt, J = 7.5, 5.9, 1.0 Hz, 1H), 7.25 (s, 2H), 2.42 (s, 3H), 2.07 (s, 6H); ¹³C NMR (100 MHz, CD₃CN) δ 164.50, 158.58, 156.88, 154.70, 143.83, 137.84, 136.49, 134.39, 131.05, 130.11, 126.84, 123.64, 121.84, 122.02 (q, J = 319.1 Hz), 21.13, 17.65; ¹⁹F NMR (375 MHz, CD₃CN) δ -79.29; m/z HRMS (ESI) found $[M+H]^+$ 318.1608, C₂₀H₂₀N₃O⁺ requires 318.1601.

1,4 -Diphenyl-5-(pyridin-2-yl)pyrimidin-1-ium trifluoromethanesulfonate (3e)



Prepared according to general procedure A using 4-phenyl-5-(pyridin-2-yl)pyrimidine (700 mg, 3.00 mmol), EtOAc (15 mL), Tf₂O (504 μ L, 3.00 mmol), aniline (274 μ L, 3.00 mmol), and collidine (396 μ L, 3.00 mmol). Isolation A1 afforded the title compound as a pink powder (1.033 g, 2.25 mmol, 75% yield). mp 177-181 °C; IR ν_{max} /cm⁻¹ (solid): 3068, 3026, 1623, 1427, 1249, 1167, 1026, 746, 635; ¹H NMR (400 MHz, CD₃CN) δ 9.66 (d, *J* = 1.4 Hz, 1H), 9.32 (s, 1H), 8.70 (dd, *J* = 4.8, 1.4 Hz, 1H), 7.89 – 7.76 (m, 6H), 7.69 – 7.61 (m, 3H), 7.55 – 7.43 (m, 4H); ¹³C NMR (100 MHz, CD₃CN) δ 171.89, 152.47, 151.93, 151.59, 151.05, 139.99, 138.40, 135.52, 135.04, 134.02, 133.04, 131.61, 131.57, 129.94, 126.13, 125.77, 125.70, 122.02 (q, *J* = 321.0 Hz); ¹⁹F NMR (375 MHz, CD₃CN) δ -79.31; *m/z* HRMS (ESI) found [M+H]⁺ 310.1348, C₂₁H₁₆N₃⁺ requires 310.1339.

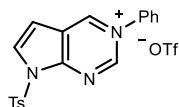
4-(4-Chloro-3-methylphenyl)-5-(3-methylisoxazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3f)



Prepared according to general procedure A using 5-(4-(4-chloro-3-methylphenyl)pyrimidin-5-yl)-3-methylisoxazole (286 mg, 1.00 mmol), EtOAc (5 mL), Tf₂O (168 μ L, 1.00 mmol), aniline (91

μL , 1.00 mmol), and collidine (132 μL , 1.00 mmol). Isolation A1 afforded the title compound as a pale-yellow powder (350 mg, 0.68 mmol, 68% yield). mp 205-209 $^{\circ}\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3073, 1616, 1589, 1426, 1250, 1164, 1049, 780, 637; ^1H NMR (400 MHz, CD_3CN) δ 9.64 (d, J = 1.8 Hz, 1H), 9.40 (d, J = 1.8 Hz, 1H), 7.87 – 7.77 (m, 5H), 7.75 (dt, J = 2.2, 0.7 Hz, 1H), 7.59 – 7.45 (m, 2H), 6.69 (s, 1H), 2.44 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ 170.22, 162.32, 161.60, 151.99, 151.96, 141.09, 139.70, 138.66, 133.77, 133.35, 133.30, 131.64, 130.85, 129.91, 125.76, 123.61, 122.02 (q, J = 318.9 Hz), 109.37, 20.13, 11.42; ^{19}F NMR (375 MHz, CD_3CN) δ -79.30; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 362.1060, $\text{C}_{21}\text{H}_{17}\text{ClN}_3\text{O}^+$ requires 362.1055.

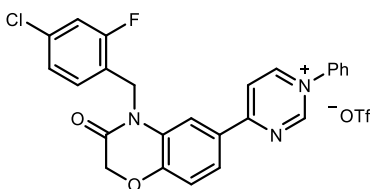
3-Phenyl-7-tosyl-7H-pyrrolo[2,3-d]pyrimidin-3-ium trifluoromethanesulfonate (3g)



Prepared according to a modified general procedure A with CH_2Cl_2 instead of EtOAc, using 7-tosyl-7H-pyrrolo[2,3-d]pyrimidine (109. mg, 0.40 mmol), CH_2Cl_2 (2 mL), Tf_2O (67 μL , 0.40 mmol), aniline (36 μL , 0.40 mmol), and collidine (53 μL , 0.40 mmol). Isolation A1 afforded the title compound as a white powder (460 mg, 0.36 mmol, 92% yield). mp 169-174 $^{\circ}\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3109, 1633, 1426, 1256, 1148, 1028, 670, 636; ^1H NMR (400 MHz, CD_3CN) δ 9.41 (d, J = 1.8 Hz, 1H), 9.32 (d, J = 1.8 Hz, 1H), 8.31 (d, J = 4.1 Hz, 1H), 8.16 (d, J = 8.5 Hz, 2H), 7.80 – 7.65 (m, 5H), 7.53 – 7.45 (m, 2H), 7.23 (d, J = 4.1 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ 151.48, 149.12, 147.82, 146.56, 141.01, 135.14, 134.05, 132.64, 131.53, 131.45,

129.70, 126.08, 122.08, 122.0 (q, $J = 318.9$ Hz), 106.78, 21.77; ^{19}F NMR (375 MHz, CD_3CN) δ -79.34. m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 350.0968, $\text{C}_{19}\text{H}_{16}\text{N}_3\text{O}_2\text{S}^+$ requires 350.0958.

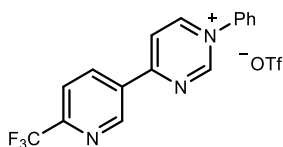
4-(4-(4-Chloro-2-fluorobenzyl)-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3h)



Prepared according to general procedure A using 4-(4-chloro-2-fluorobenzyl)-6-(pyrimidin-4-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one (147.9 mg, 0.40 mmol), EtOAc (2.00 mL), Tf_2O (67 μL , 0.40 mmol), aniline (37 μL , 0.40 mmol), and collidine (53 μL , 0.40 mmol). Isolation A2 afforded the title compound as a 2:1 mixture of triflate (^-OTf) and triflamide ($^-\text{NHTf}$) salts (233 mg, 0.39 mmol, 98% yield). Yield was calculated based on triflate salt, presumed equivalent due to <0.2% difference in product masses. mp 88-92 $^\circ\text{C}$; $\text{IR}_{\text{vmax}}/\text{cm}^{-1}$ (film): 3076, 1687, 1582, 1436, 1381, 1223, 1147, 1027, 894, 636. ^1H NMR (400 MHz, CDCl_3) δ 9.29 (dd, $J = 2.0, 1.0$ Hz, 1H), 9.19 (dd, $J = 7.0, 2.1$ Hz, 1H), 8.63 (dd, $J = 7.0, 1.0$ Hz, 1H), 8.08 (d, $J = 2.0$ Hz, 1H), 8.03 (dd, $J = 8.6, 2.0$ Hz, 1H), 7.78 – 7.68 (m, 2H), 7.63 (dd, $J = 5.3, 1.9$ Hz, 3H), 7.31 – 7.22 (m, 1H), 7.15 –

7.03 (m, 3H), 5.26 (s, 2H), 4.84 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.02, 163.38, 160.50 (d, J = 250.2 Hz), 151.79, 150.46, 138.94, 134.84 (d, J = 10.4 Hz), 132.16, 131.16, 130.43 (d, J = 4.6 Hz), 129.17, 127.40, 127.20, 125.34 (d, J = 3.5 Hz), 124.21, 121.02, 120.88, 120.57 (q, J = 318.2 Hz), 118.97, 118.77, 118.51, 116.85, 116.60, 67.56, 38.26 (d, J = 3.9 Hz). ^{19}F NMR (375 MHz, CD_3CN) δ -79.31 (s, 2F), -80.60 (s, 1F), -116.15 (t, J = 9.3 Hz, 1F). m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 446.1072, for $\text{C}_{25}\text{H}_{18}\text{ClFN}_3\text{O}_2^+$ requires 446.1066.

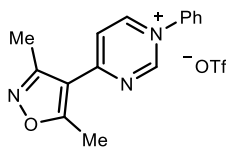
1-Phenyl-4-(6-(trifluoromethyl)pyridin-3-yl)pyrimidin-1-ium trifluoromethanesulfonate (3i)



Prepared according to general procedure A using 4-(6-(trifluoromethyl)pyridin-3-yl)pyrimidine (225 mg, 1.00 mmol), EtOAc (5 mL), Tf_2O (168 μL , 1.00 mmol), aniline (91 μL , 1.00 mmol), and collidine (132 μL , 1.0 mmol). Isolation A1 afforded the title compound as a white powder (325 mg, 0.72 mmol, 95% yield). mp 245-247 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3124, 1625, 1463, 1346, 1272, 1250, 1065, 847, 638; ^1H NMR (400 MHz, CD_3CN) δ 9.80 – 9.74 (m, 1H), 9.70 (d, J = 2.5 Hz, 1H), 9.34 (dd, J = 6.8, 1.9 Hz, 1H), 8.98 (dd, J = 8.4, 2.2 Hz, 1H), 8.83 (dd, J = 6.8, 1.1 Hz, 1H), 8.14 (dd, J = 8.4, 0.9 Hz, 1H), 7.83 (s, 5H). ^{13}C NMR (100 MHz, CDCl_3) δ 172.87, 157.94 (d, J = 5.1 Hz), 157.47, 156.83, 156.48, 155.84 (d, J = 6.4 Hz), 144.51 (d, J = 6.7 Hz), 144.33, 137.61, 137.21, 136.04, 131.14 - 121.42 (m), 126.82, 125.67, 125.50. ^{19}F NMR (375 MHz,

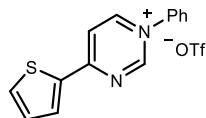
CD₃CN) δ -68.92, -79.33. HRMS (ESI) found $[M+H]^+$ 302.0955, for C₁₇H₁₁F₆N₃O₃S⁺ requires 302.0900.

4-(3,5-Dimethylisoxazol-4-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3k)



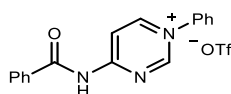
Prepared according to general procedure A using 3,5-dimethyl-4-(pyrimidin-4-yl)isoxazole (526 mg, 3.00 mmol), EtOAc (15 mL), Tf₂O (504 μ L, 3.00 mmol), aniline (273 μ L, 3.00 mmol), and collidine (396 μ L, 3.0 mmol). Isolation A1 afforded the title compound as a white powder (3.62 g, 9.45 mmol, 95% yield). mp 175-178 °C; IR ν_{max} /cm⁻¹ (solid): 2358, 2049, 1586, 1274, 1226, 1151, 782, 639, 556; ¹H NMR (400 MHz, CD₃CN) δ 9.56 (s, 1H), 9.10 (dd, J = 6.9, 2.1 Hz, 1H), 8.25 (d, J = 7.0 Hz, 1H), 7.80 (s, 5H), 2.89 (s, 3H), 2.63 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 182.15, 169.68, 165.12, 157.16, 155.50, 144.61, 138.35, 135.96, 131.14 - 121.42 (m), 129.98, 124.79 (d, J = 5.1 Hz), 119.17, 19.31, 17.07. ¹⁹F NMR (375 MHz, CD₃CN) δ -79.28; HRMS (ESI) found $[M+H]^+$ 252.1220, for C₁₆H₁₄F₃N₃O₄S⁺ requires 252.1209.

1-Phenyl-4-(thiophen-2-yl)pyrimidin-1-ium trifluoromethanesulfonate (3l)



Prepared according to general procedure A using 4-(thiophen-2-yl)pyrimidine (60.0 mg, 0.37 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A1 afforded the title compound as a white powder (120 mg, 0.31 mmol, 84% yield). mp 177-180 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3123, 1626, 1415, 1253, 1146, 1032, 770, 712, 636; ¹H NMR (400 MHz, CD₃CN) δ 9.37 (dd, J = 2.0, 1.1 Hz, 1H), 8.94 (dd, J = 7.0, 2.0 Hz, 1H), 8.43 – 8.35 (m, 2H), 8.18 (dd, J = 5.0, 1.1 Hz, 1H), 7.79 – 7.71 (m, 5H), 7.44 (dd, J = 5.0, 4.0 Hz, 1H); ¹³C NMR (100 MHz, CD₃CN) δ 165.40, 153.26, 150.46, 141.12, 140.22, 139.69, 137.34, 132.70, 132.07, 131.55, 125.38, 122.08 (q, J = 321.0 Hz), 117.45; ¹⁹F NMR (375 MHz, CD₃CN) δ -79.29; m/z HRMS (ESI) found $[M+H]^+$ 239.0645, C₁₄H₁₁N₂S⁺ requires 239.0637.

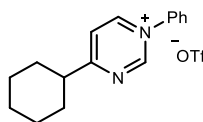
4-Benzamido-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3m)



Prepared according to general procedure A using N-(pyrimidin-4-yl)benzamide (79.7 mg, 0.40 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A1 afforded the title compound as an opaque white solid (160 mg, 37.6 mmol, 94% yield). mp 181-183 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3387, 3098, 1704, 1632, 1514, 1430, 1247, 1141, 1030, 634. ¹H NMR (400 MHz, CD₃CN) δ 10.56 (s, 1H), 9.29 (dd, J = 2.1, 1.0 Hz,

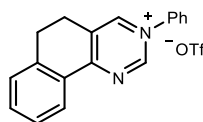
1H), 8.93 (dd, $J = 7.5, 2.1$ Hz, 1H), 8.80 (dd, $J = 7.5, 1.0$ Hz, 1H), 8.12 – 7.98 (m, 2H), 7.73 (m, 6H), 7.61 (t, $J = 7.8$ Hz, 2H); ^{13}C NMR (100 MHz, CD_3CN) δ 168.22, 163.13, 153.60, 151.60, 140.11, 134.93, 132.82, 132.37, 131.42, 129.79, 129.66, 125.36, 121.97 (q, $J = 320.8$ Hz), 111.49; ^{19}F NMR (375 MHz, CD_3CN) δ -79.20; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 267.1133, $\text{C}_{17}\text{H}_{14}\text{N}_3\text{O}^+$ requires 267.1140.

4-Cyclohexyl-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3n)



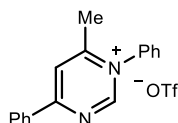
Prepared according to general procedure A using 4-cyclohexylpyrimidine (64.9 mg, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 μL , 0.40 mmol), aniline (36 μL , 0.40 mmol), and collidine (53 μL , 0.40 mmol). Isolation A1 afforded the title compound as a pale-yellow flaky powder (90.3 mg, 0.23 mmol, 58% yield). mp 137-141 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3066, 2936, 2855, 1623, 1255, 1154, 1028, 760, 636; ^1H NMR (400 MHz, CD_3CN) δ 9.55 (d, $J = 0.8$ Hz, 1H), 9.08 (dd, $J = 6.7, 2.0$ Hz, 1H), 8.14 (dd, $J = 6.7, 1.1$ Hz, 1H), 7.77 (d, $J = 1.1$ Hz, 5H), 3.16 (tt, $J = 11.7, 3.4$ Hz, 1H), 2.06 (ddd, $J = 12.9, 3.2, 1.5$ Hz, 2H), 1.93 (t, $J = 3.4$ Hz, 1H), 1.82 (ddt, $J = 12.8, 3.4, 1.7$ Hz, 1H), 1.68 (qd, $J = 12.3, 3.1$ Hz, 2H), 1.52 (qt, $J = 12.7, 3.2$ Hz, 2H), 1.39 (tt, $J = 12.5, 3.4$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 185.96, 152.81, 151.26, 140.30, 132.79, 131.47, 125.63, 122.61, 121.97 (q, $J = 319.0$ Hz), 47.48, 32.11, 26.34, 26.11; ^{19}F NMR (375 MHz, CD_3CN) δ -79.32; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 239.1548, $\text{C}_{16}\text{H}_{19}\text{N}_2^+$ requires 239.1543.

3-Phenyl-5,6-dihydrobenzo[h]quinazolin-3-ium trifluoromethanesulfonate (3o)



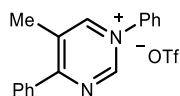
Prepared according to general procedure A using 5,6-dihydrobenzo[h]quinazoline (72.9 mg, 0.40 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A1 afforded the title compound as a white powder (146 mg, 0.37 mmol, 89% yield). mp 179-182 °C; IR ν_{max} /cm⁻¹ (solid): 3043, 1624, 1432, 1258, 1028, 758, 635; ¹H NMR (400 MHz, CD₃CN) δ 9.55 (d, J = 0.8 Hz, 1H), 9.08 (dd, J = 6.7, 2.0 Hz, 3H), 8.14 (dd, J = 6.7, 1.1 Hz, 3H), 7.77 (d, J = 1.1 Hz, 8H), 3.16 (tt, J = 11.7, 3.4 Hz, 3H), 2.06 (ddd, J = 12.9, 3.2, 1.5 Hz, 5H), 1.93 (t, J = 3.4 Hz, 2H), 1.82 (ddt, J = 12.8, 3.4, 1.7 Hz, 2H), 1.68 (qd, J = 12.3, 3.1 Hz, 6H), 1.52 (qt, J = 12.7, 3.2 Hz, 6H), 1.39 (tt, J = 12.5, 3.4 Hz, 3H); ¹³C NMR (100 MHz, CD₃CN) δ 167.18, 151.48, 148.71, 143.75, 140.38, 136.70, 132.73, 132.70, 131.56, 130.47, 130.20, 129.21, 128.76, 125.44, 122.03 (q, J = 320.9 Hz), 26.56, 24.86; ¹⁹F NMR (375 MHz, CD₃CN) δ -79.32; m/z HRMS (ESI) found [M+H]⁺ 239.1548, C₁₆H₁₉N₂⁺ requires 239.1543

6-Methyl-1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (3p)



Prepared according to general procedure A using 6-methyl-4-phenylpyrimidine (68 μ L, 0.40 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A1 afforded the title compound as an off-white solid (126 mg, 0.32 mmol, 79% yield). mp 202-204 °C. IR_v_{max}/cm⁻¹ (solid): 3060, 1623, 1261, 1145, 1028, 739, 639; ¹H NMR (400 MHz, CDCl₃) δ 9.08 (s, 1H), 8.49 (s, 1H), 8.41 – 8.34 (m, 2H), 7.76 – 7.69 (m, 6H), 7.63 – 7.54 (m, 2H), 2.68 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.04, 163.65, 151.86, 136.91, 134.90, 132.91, 132.15, 130.92, 129.74, 129.69, 126.17, 125.00 (q, *J* = 320.8 Hz), 120.05, 21.59. ¹⁹F NMR (376 MHz, CDCl₃) δ -78.31. *m/z* HRMS (ESI) found [M+H]⁺ 247.1239, C₁₈H₁₅F₃N₂O₃S⁺ requires 247.1230.

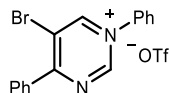
5-Methyl-1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (3q)



Prepared according to general procedure A using 4-phenyl-5-methylpyrimidine (106 mg, 0.62 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A1 afforded the title compound as a peach-colored powder (215 mg, 0.54 mmol, 87% yield). mp 209-213 °C; IR ν _{max}/cm⁻¹ (solid): 3074, 3035, 1624, 1438, 1255, 1137, 1032, 764, 690, 636; ¹H NMR (400 MHz, CD₃CN) δ 9.51 (d, *J* = 1.9 Hz, 1H), 9.10 (dd, *J* = 1.9, 0.9 Hz, 1H), 8.01 – 7.87 (m, 2H), 7.79 (s, 5H), 7.76 – 7.71 (m, 1H), 7.71 – 7.63 (m, 2H), 2.70 (s, 3H); ¹³C NMR (100 MHz, CD₃CN) δ 173.15, 152.30, 149.96, 140.06, 135.79, 133.61, 133.47,

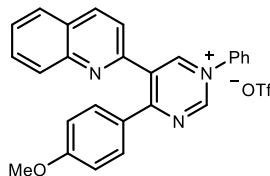
132.96, 131.61, 131.03, 130.00, 125.57, 122.06 (q, $J = 320.9$ Hz), 18.27; ^{19}F NMR (375 MHz, CD_3CN) δ -79.31; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+ 247.1238$, $\text{C}_{17}\text{H}_{15}\text{N}_2^+$ requires 247.1230.

5-Bromo-1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (3r)



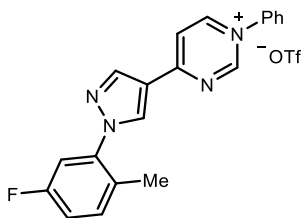
Prepared according to general procedure A using 4-phenyl-5-bromopyrimidine (235.1 mg, 1.00 mmol), EtOAc (5 mL), Tf_2O (168 μL , 1.00 mmol), aniline (91 μL , 1.00 mmol), and collidine (132 μL , 1.00 mmol). Isolation A1 afforded the title compound as a white powder (355 mg, 0.77 mmol, 77% yield). mp 238-241 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3060, 3003, 1612, 1587, 1439, 1279, 1253, 1225, 1032, 763, 636; ^1H NMR (400 MHz, CD_3CN) δ 9.62 (d, $J = 1.7$ Hz, 1H), 9.50 (d, $J = 1.7$ Hz, 1H), 8.16 – 8.09 (m, 2H), 7.85 – 7.76 (m, 6H), 7.70 (ddt, $J = 8.3, 6.5, 1.3$ Hz, 2H); ^{13}C NMR (100 MHz, CD_3CN) δ 172.28, 154.35, 150.73, 139.28, 135.17, 134.56, 133.34, 131.62, 131.28, 129.91, 125.72, 122.01 (d, $J = 320.7$ Hz), 119.81; ^{19}F NMR (375 MHz, CD_3CN) δ -79.27; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+ 311.0187$, $\text{C}_{16}\text{H}_{12}\text{BrN}_2^+$ requires 311.0178.

4-(4-Methoxyphenyl)-1-phenyl-5-(quinolin-2-yl)pyrimidin-1-ium trifluoromethanesulfonate (3s)



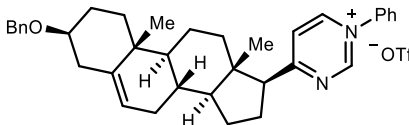
Prepared according to general procedure A using 2-(4-(4-methoxyphenyl)pyrimidin-5-yl)quinoline (125 mg, 0.40 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A2 afforded the title compound as a bright-orange glass (139 mg, 0.26 mmol, 74% yield). mp 95-99 °C; IR ν_{max} /cm⁻¹ (solid): 3062, 1584, 1425, 1252, 1174, 1028, 760, 635; ¹H NMR (400 MHz, CD₃CN) δ 9.55 (d, J = 1.9 Hz, 1H), 9.31 (d, J = 1.9 Hz, 1H), 8.35 (d, J = 8.5 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 8.05 – 7.95 (m, 1H), 7.89 – 7.84 (m, 1H), 7.83 – 7.69 (m, 8H), 7.51 (d, J = 8.5 Hz, 1H), 6.95 (d, J = 9.0 Hz, 2H), 3.84 (s, 3H); ¹³C NMR (100 MHz, CD₃CN) δ 170.30, 165.48, 152.95, 152.16, 150.58, 149.30, 139.92, 138.46, 134.60, 133.59, 132.78, 131.61, 131.50, 130.21, 129.07, 129.04, 128.60, 127.11, 125.61, 122.59, 121.94 (q, J = 319.0 Hz), 115.64, 56.52; ¹⁹F NMR (375 MHz, CD₃CN) δ -79.14; m/z HRMS (ESI) found [M+H]⁺ 390.1610, C₂₆H₂₀N₃O⁺ requires 390.1601.

4-(1-(5-Fluoro-2-methylphenyl)-1H-pyrazol-4-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (1t)



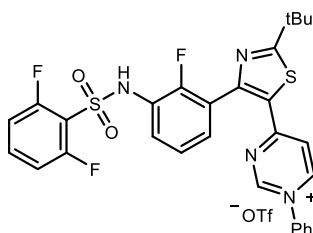
Prepared according to general procedure A using 4-(1-(5-fluoro-2-methylphenyl)-1H-pyrazol-4-yl)pyrimidine (254.3 mg, 1.0 mmol), EtOAc (5 mL), Tf₂O (168 μL, 1.0 mmol), aniline (91 μL, 1.0 mmol), and collidine (132 μL, 1.0 mmol). Isolation A2 afforded the title compound as a red solid (396 mg, 0.83 mmol, 83% yield). mp 150-154 °C; IR ν_{max} /cm⁻¹ (film): 3109, 3055, 1574, 1507, 1269, 1142, 1032; ¹H NMR (400 MHz, CD₃CN) δ 9.41 (d, J = 2.0 Hz, 1H), 8.96 (dd, J = 7.0, 2.0 Hz, 1H), 8.88 (d, J = 0.7 Hz, 1H), 8.62 – 8.59 (s, 1H), 8.31 (dd, J = 7.0, 1.1 Hz, 1H), 7.75 (s, 5H), 7.47 (dd, J = 8.6, 6.1 Hz, 1H), 7.31 (dd, J = 9.1, 2.7 Hz, 1H), 7.25 (td, J = 8.5, 2.7 Hz, 1H), 2.28 (s, 3H); ¹³C NMR (100 MHz, CD₃CN) δ 166.08, 161.66 (d, J = 244.1 Hz), 153.33, 150.54, 142.78, 140.33, 140.23 (d, J = 10.1 Hz), 136.84, 133.95 (d, J = 8.6 Hz), 132.63, 131.53, 130.62 (d, J = 3.6 Hz), 125.43, 122.05 (q, J = 319.0 Hz), 121.18, 118.40, 117.41 (d, J = 20.9 Hz), 114.09 (d, J = 24.7 Hz), 17.62; ¹⁹F NMR (375 MHz, CD₃CN) δ -79.31 (3F), -117.10 – -117.27 (q, J = 6.9 Hz, 1F); *m/z* HRMS (ESI) found [M+H]⁺ 331.1359, C₂₀H₁₆FN₄⁺ requires 331.1354.

4-((3S,8S,9S,10R,13S,14S,17S)-3-(Benzyloxy)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (1u)



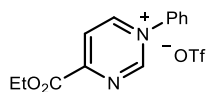
Prepared according to a modified general procedure A using 4-((3S,8S,9S,10R,13S,14S,17S)-3-(benzyloxy)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)pyrimidine (177.1 mg, 0.4 mmol), CH₂Cl₂ (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A1 afforded the title compound as a single diastereomer (white powder, 155 mg, 0.23 mmol, 58% yield). mp 214-218 °C; IR ν_{max} /cm⁻¹ (film): 2936, 1627, 1427, 1255, 1030, 736, 637; ¹H NMR (400 MHz, CD₃CN) δ 9.50 (s, 1H), 8.95 (dd, J = 6.7, 2.0 Hz, 1H), 8.03 (d, J = 6.7 Hz, 1H), 7.84 – 7.63 (m, 5H), 7.34 (d, J = 4.0 Hz, 4H), 7.28 (ddd, J = 8.7, 5.3, 3.5 Hz, 1H), 5.39 (dt, J = 4.1, 1.9 Hz, 1H), 4.54 (s, 2H), 3.25 (td, J = 10.3, 4.7 Hz, 2H), 2.63 – 2.50 (m, 1H), 2.43 (ddd, J = 13.1, 4.7, 2.4 Hz, 1H), 2.29 – 2.17 (m, 1H), 2.11 (d, J = 1.2 Hz, 2H), 2.10 – 2.02 (m, 1H), 1.92 – 1.83 (m, 2H), 1.79 (dt, J = 11.7, 3.3 Hz, 1H), 1.72 – 1.64 (m, 1H), 1.62 (d, J = 7.1 Hz, 1H), 1.59 – 1.54 (m, 1H), 1.53 – 1.43 (m, 4H), 1.16 – 1.05 (m, 2H), 1.03 (s, 3H), 0.64 (s, 3H); ¹³C NMR (100 MHz, CD₃CN) δ 182.72, 152.04, 150.12, 142.13, 140.50, 140.28, 132.85, 131.52, 129.19, 128.49, 128.22, 125.63, 123.92, 122.07 (q, J = 318.9 Hz), 122.00, 79.26, 70.28, 59.99, 58.13, 50.97, 49.35, 39.86, 38.24, 38.03, 37.74, 33.10, 32.54, 29.17, 25.77, 25.52, 21.60, 19.77, 13.31; ¹⁹F NMR (375 MHz, CD₃CN) δ -79.33; *m/z* HRMS (ESI) found [M+H]⁺ 519.3376, C₃₆H₄₃N₂O⁺ requires 519.3370.

4-(2-(*Tert*-butyl)-4-(3-((2,6-difluorophenyl)sulfonamido)-2-fluorophenyl)thiazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (1v)



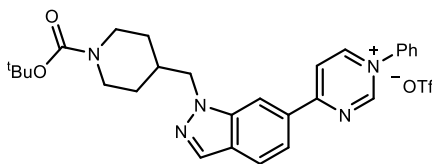
Prepared according to a modified general procedure A with CH₂Cl₂ instead of EtOAc, and *N*-{3-(2-(tert-butyl)-5-(pyrimidin-4-yl)thiazol-4-yl)-2-fluorophenyl}-2,6-difluorobenzenesulfonamide (1.00 g, 2.00 mmol), CH₂Cl₂ (10 mL), Tf₂O (336 μL, 2.00 mmol), aniline (182 μL, 1.00 mmol), and collidine (264 μL, 2.00 mmol). Following Isolation A2, the crude material was dissolved in MeOH (10 mL) and NaOTf (688 mg, 4.00 mmol), stirred for 30 minutes at room temperature, and concentrated *in vacuo*. The resulting solid was dissolved in CH₂Cl₂ (50 mL) and filtered. The filtrate was concentrated to afford the title compound as a brown crystalline solid (1.40 g, 1.92 mmol, 96% yield). Product decomposes above 125°C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3097, 2967, 1622, 1468, 1250, 1164, 1029, 771, 636; ¹H NMR (400 MHz, CDCl₃) δ 9.23 (s, 1H), 8.98 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.69 (s, 1H), 7.85 – 7.70 (m, 3H), 7.67 – 7.57 (m, 4H), 7.52 (t, *J* = 6.6 Hz, 1H), 7.42 (tt, *J* = 8.4, 5.9 Hz, 1H), 7.31 – 7.22 (m, 1H), 6.89 (t, *J* = 9.0 Hz, 2H), 5.29 (s, 1H), 1.49 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 190.26, 163.94, 159.47 (dd, *J* = 257.7, 3.5 Hz), 153.64, 150.92, 150.59 (d, *J* = 17.3 Hz), 139.11, 135.05 (t, *J* = 11.3 Hz), 131.83, 130.82, 130.46, 127.96 (d, *J* = 152.5 Hz), 125.62 (d, *J* = 4.1 Hz), 124.79 (d, *J* = 13.0 Hz), 124.27, 122.88 (d, *J* = 13.2 Hz), 122.00 (q, *J* = 329.9 Hz), 121.98, 118.80, 118.24, 117.51 (t, 15.2 Hz), 113.17 (dd, *J* = 23.0, 3.5 Hz), 38.93, 30.50; ¹⁹F NMR (376 MHz, CDCl₃) δ -78.33 (3F), -107.14 (t, *J* = 9.0 Hz, 2F), -124.76 (1F); *m/z* HRMS (ESI) found [M+H]⁺ 581.1297, C₂₉H₂₄F₃N₄O₂S₂⁺ requires 581.1287.

4-(Ethoxycarbonyl)-1-mesitylpyrimidin-1-ium trifluoromethanesulfonate (3w)



Prepared according to a modified general procedure A using ethyl pyrimidine-4-carboxylate (304 mg, 2.00 mmol), EtOAc (10.0 mL), Tf₂O (336 μL, 2.00 mmol), 2,4,6-trimethylaniline (281 μL, 2.00 mmol), and collidine (264 μL, 2.00 mmol). The reaction was held at -78 °C for an additional 30 minutes, followed by the addition of trifluoromethanesulfonic acid (177 μL, 2.00 mmol), then warming to room temperature. Isolation A2 afforded the title compound as a yellow powder (340 mg, 0.81 mmol, 40% yield). mp 179-183 °C; IR ν_{max} /cm⁻¹ (solid): 3096, 1735, 1663, 1320, 1261, 1149, 1032, 636; ¹H NMR (400 MHz, CD₃CN) δ 9.64 (s, 1H), 9.33 (dd, J = 6.4, 1.7 Hz, 1H), 8.83 (dd, J = 6.4, 1.1 Hz, 1H), 7.23 (s, 2H), 4.57 (q, J = 7.1 Hz, 2H), 2.41 (s, 3H), 2.04 (s, 6H), 1.45 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CD₃CN) δ 162.66, 161.65, 157.07, 155.57, 143.87, 134.26, 131.06, 125.74, 121.98 (q, J = 320.7 Hz), 65.06, 21.12, 17.60, 14.21, 1.24; ¹⁹F NMR (375 MHz, CD₃CN) δ -79.31; *m/z* HRMS (ESI) found 271.1449, [M+H]⁺ C₁₆H₁₉N₂O₂⁺ requires 271.1441.

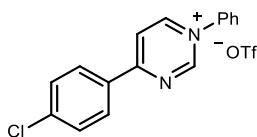
4-(1-((1-(Tert-butoxycarbonyl)piperidin-4-yl)methyl)-1H-indazol-6-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (1x)



Prepared according to general procedure A using tert-butyl 4-((6-(pyrimidin-4-yl)-1H-indazol-1-yl)methyl)piperidine-1-carboxylate (177.1 mg, 0.45 mmol), EtOAc (2.25 mL), Tf₂O (76 μL, 0.45 mmol), aniline (41 μL, 0.45 mmol), and collidine (60 μL, 0.45 mmol). Isolation A2 afforded the

title compound as a 3:1 mixture of triflate (^-OTf) and triflamide ($^-\text{NHTf}$) salts (219 mg, 0.35 mmol, 78% yield). Yield was calculated based on triflate salt, presumed equivalent due to <0.2% difference in product masses. mp 96-101 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3054, 2985, 1679, 1626, 1427, 1264, 1030, 895, 703, 638. ^1H NMR (400 MHz, CD_3CN) δ 9.59 (s, 1H), 9.17 – 9.09 (m, 1H), 8.79 – 8.74 (m, 1H), 8.72 (s, 1H), 8.21 – 8.10 (m, 2H), 8.07 – 7.99 (m, 1H), 7.79 (s, 5H), 4.46 (d, J = 6.4 Hz, 2H), 4.03 (d, J = 13.4 Hz, 2H), 2.66 (s, 2H), 2.42 – 2.02 (m, 3H), 1.53 (d, J = 13.3 Hz, 2H), 1.41 (s, 9H), 1.34 – 1.12 (m, 2H). ^{13}C NMR (100 MHz, CD_3CN) δ 171.84, 155.43, 152.94, 151.41, 141.14, 140.23, 134.33, 132.99, 131.67, 131.44, 128.63, 125.62, 123.69, 121.22, 120.77 (q, J = 318.1 Hz) 119.85, 113.64, 79.75, 55.04, 43.09, 38.10, 30.42, 28.58. ^{19}F NMR (375 MHz, CD_3CN) δ -79.31 (s, 2F), -80.60 (s, 1F), -116.15 (t, J = 9.3 Hz, 1F). m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 470.2557, for $\text{C}_{28}\text{H}_{32}\text{N}_5\text{O}_2^+$ requires 470.2551.

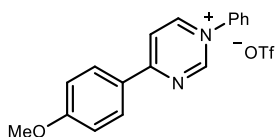
4-(4-Chlorophenyl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3y)



Prepared according to general procedure A using 4-(4-chlorophenyl)pyrimidine (76.3 mg, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 μL , 0.40 mmol), aniline (36 μL , 0.40 mmol), and collidine (53 μL , 0.40 mmol). Isolation A1 afforded the title compound as a white powder (149 mg, 0.36 mmol, 89% yield). mp 194-198 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3125, 3071, 1628, 1588, 1274, 1261, 1152, 1032, 773, 637; ^1H NMR (400 MHz, CD_3CN) δ 9.60 (d, J = 1.9 Hz, 1H), 9.16 (dd, J = 7.0, 2.0 Hz, 1H), 8.64 (d, J = 6.9 Hz, 1H), 8.43 (d, J = 8.6 Hz, 2H), 7.78 (s, 5H), 7.72 (d, J = 8.7 Hz, 2H); ^{13}C

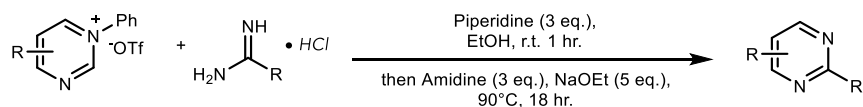
NMR (100 MHz, CD₃CN) δ 169.97, 153.01, 151.90, 142.22, 140.10, 132.83, 132.47, 131.95, 131.50, 130.97, 125.50, 121.9 (q, J = 319.0, 119.58); ¹⁹F NMR (375 MHz, CD₃CN) δ -79.14; m/z HRMS (ESI) found $[M+H]^+$ 267.0690, C₁₆H₁₂ClN₂⁺ requires 267.0684.

4-(4-Methoxyphenyl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3z)



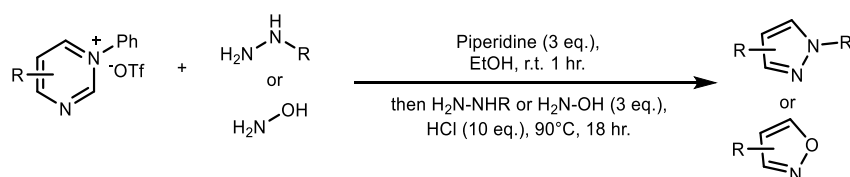
Prepared according to general procedure A using 4-(4-methoxyphenyl)pyrimidine (74.5 mg, 0.4 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), and collidine (53 μ L, 0.40 mmol). Isolation A1 afforded the title compound as a yellow powder (150 mg, 0.36 mmol, 91% yield). mp 176-178 °C; IR ν_{max} /cm⁻¹ (solid): 3082, 1585, 1465, 1430, 1257, 1150, 1028, 833, 771, 633; ¹H NMR (400 MHz, CD₃CN) δ 9.44 (d, J = 2.0 Hz, 1H), 8.96 (dd, J = 7.2, 2.0 Hz, 1H), 8.47 (t, J = 8.2 Hz, 3H), 7.75 (s, 5H), 7.22 (d, J = 9.0 Hz, 2H), 3.96 (s, 3H); ¹³C NMR (100 MHz, CD₃CN) δ 169.95, 166.96, 152.54, 150.34, 140.10, 133.04, 132.50, 131.43, 125.91, 125.31, 121.9 (q, J = 319.3 Hz), 118.26, 116.38, 56.72; ¹⁹F NMR (375 MHz, CD₃CN) δ -79.11; m/z HRMS (ESI) found $[M+H]^+$ 263.1187, C₁₇H₁₅N₂O⁺ requires 263.1179.

General Procedure B: Pyrimidine C2-Functionalization



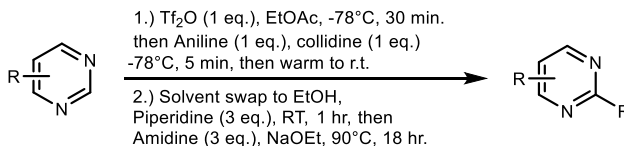
An oven dried 8 mL vial (≤ 0.5 mmol scale) or a round bottom flask (> 0.5 mmol scale) equipped with a stir bar was charged with the pyrimidinium salt (1.0 equiv), EtOH (0.2 M), and piperidine (3.0 equiv). The reaction was stirred for 60 minutes at 25 °C before amidine (3.0 equiv, HCl salt or free amidine) was added followed by NaOEt (5.0 equiv, 21% soln. in EtOH). The reaction was heated to 90 °C for 18 hours. After cooling to room temperature, the reaction was diluted with EtOAc and H₂O, then extracted into EtOAc (3x). The combined organic extract was washed with brine (1x) and dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

General Procedure C: Pyrimidine Ring-Contraction



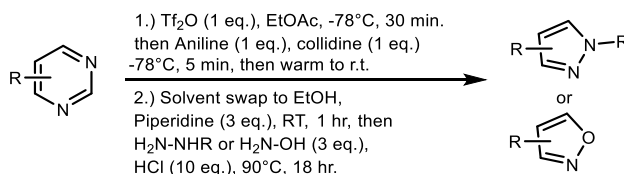
An oven dried 8 mL vial (≤ 0.5 mmol scale) or a round bottom flask (> 0.5 mmol scale) equipped with a stir bar was charged with the pyrimidinium salt (1.0 equiv), EtOH (0.2 M), and piperidine (3.0 equiv). The reaction was stirred for 60 minutes at 25 °C before hydrazine (3.0 equiv) or hydroxylamine HCl (3.0 equiv) was added followed by concentrated HCl (10 equiv). The reaction was heated to 90 °C for 18 hours. After cooling to room temperature, the reaction was quenched with sat. NaHCO₃, then extracted into EtOAc (3x). The combined organic extract was washed with brine (1x) and dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

General Procedure D: One-Pot Pyrimidine C2-Functionalization



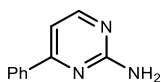
An oven dried 8 mL vial (≤ 0.5 mmol scale) or a round bottom flask (> 0.5 mmol scale) equipped with a stir bar was charged with the pyrimidine (1.0 equiv) and placed under a nitrogen atmosphere. EtOAc (0.2 M) was added, the reaction vessel cooled to -78°C and Tf_2O (1.0 equiv) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes before aniline (1.0 equiv) was added dropwise followed by collidine (1.0 equiv). The reaction was stirred for a further 5 minutes at -78°C . The cooling bath was removed and the reaction was allowed to warm to room temperature while stirring for approximately 30 minutes. The reaction was then concentrated with a gentle stream of air (< 0.5 mmol scale) or *in vacuo* at 40°C (> 0.5 mmol scale). Then EtOH (0.2 M) and piperidine (3.0 equiv) were added. The reaction was stirred for 60 minutes before amidine (3.0 equiv, HCl salt or free amidine) was added followed by NaOEt (5.0 equiv, 21% soln. in EtOH). The reaction was heated to 90°C for 18 hours. After cooling to room temperature, the reaction was diluted with EtOAc and H_2O , then extracted into EtOAc (3x). The combined organic extract was washed (1x) with brine and dried (MgSO_4), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

General Procedure E: One-Pot Pyrimidine Ring-Contraction



An oven dried 8 mL vial (≤ 0.5 mmol scale) or a round bottom flask (> 0.5 mmol scale) equipped with a stir bar was charged with the pyrimidine (1.0 equiv) and placed under a nitrogen atmosphere. EtOAc (0.2 M) was added, the reaction vessel cooled to -78 °C and Ti_2O (1.0 equiv) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes before aniline (1.0 equiv) was added dropwise followed by collidine (1.0 equiv). The reaction was stirred for a further 5 minutes at -78 °C. The cooling bath was removed and the reaction was allowed to warm to room temperature while stirring for approximately 30 minutes. The reaction was then concentrated with a gentle stream of air (< 0.5 mmol scale) or *in vacuo* at 40 °C (> 0.5 mmol scale). Then EtOH (0.2 M) and piperidine (3.0 equiv) were added. The reaction was stirred for 60 minutes before hydrazine (3.0 equiv) or hydroxylamine HCl (3.0 equiv) was added followed by concentrated HCl (10 equiv). The reaction was heated to 90 °C for 18 hours. After cooling to room temperature, the reaction was quenched with sat. NaHCO_3 , then extracted into EtOAc (3x). The combined organic extract was washed (1x) with brine and dried (MgSO_4), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

4-Phenylpyrimidin-2-amine (5a)

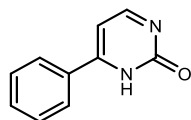


Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μL , 1.20 mmol), guanidine hydrochloride (115 mg, 1.20 mmol), and NaOEt (747 μL , 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 10-30% EtOAc

in hexanes with 1% AcOH modifier) to provide the title compound as a pale-yellow powder (57 mg, 0.33 mmol, 83% yield).

To demonstrate comparable yield in a one-pot procedure, **1a** was also prepared according to general procedure D using 4-phenylpyrimidine (62.5 mg, 0.40 mmol), EtOAc (2 mL), Tf₂O (67 μ L, 0.40 mmol), aniline (36 μ L, 0.40 mmol), collidine (54 μ L, 0.40 mmol). Then, solvent was exchanged for EtOH (2 mL) and piperidine (119 μ L, 1.20 mmol), guanidine hydrochloride (115 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH) were added. The crude material was purified by flash chromatography (silica gel: 1:60:39 AcOH:EtOAc:hexanes) to provide the title compound as a pale yellow powder (48 mg, 0.27 mmol, 70% yield). mp 162-165 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3264, 3149, 2405, 1654, 1553, 1461, 819, 766; ¹H NMR (400 MHz, CDCl₃) δ 8.35 (d, *J* = 5.3 Hz, 1H), 8.17 – 7.81 (m, 2H), 7.66 – 7.42 (m, 3H), 7.05 (d, *J* = 5.3 Hz, 1H), 5.17 (s, 2H); ¹³C NMR (100 MHz, (CD₃)₂SO) δ 164.24, 164.07, 159.51, 137.48, 130.93, 129.15, 127.15, 106.28; *m/z* HRMS (DART) found [M+H]⁺ 172.0879, C₁₀H₁₀N₃⁺ requires 172.0869. Spectra matched literature values.¹³

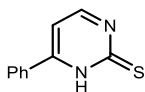
6-Phenylpyrimidin-2(1H)-one (5b)



Prepared according to a modified general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), pyrrolidine (164 μ L, 2.00 mmol), and stirred for 18 hours at room temperature before adding urea (91.3 mg, 1.20 mmol), and NaOEt

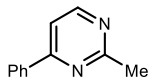
(747 μ L, 2.00 mmol, as a 21% soln. in EtOH). Following the reaction, AcOH (229 μ L, 4.00 mmol) was added at room temperature and saturated NaHCO_3 was added until the pH = 8. The aqueous layer was extracted with CH_2Cl_2 . The crude material washed with warm Et_2O and filtered to provide the title compound as a brown powder (17 mg, 0.10 mmol, 25% yield). Decomposed above 230 $^\circ\text{C}$; ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{SO}$) δ 11.91 (s, 1H), 8.14 – 8.07 (d, 2H), 8.05 (d, J = 6.4 Hz, 1H), 7.68 – 7.49 (m, 3H), 6.99 (d, J = 6.5 Hz, 1H). m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 173.0716, $\text{C}_{10}\text{H}_8\text{N}_2\text{O}^+$ requires 173.0709. Spectra matched literature values.¹⁴

6-Phenylpyrimidine-2(1H)-thione (5c)



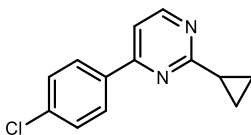
Prepared according to a modified general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), thiourea (91.3 mg, 1.20 mmol), and NaOEt (747 μ L, 2.0 mmol, as a 21% soln. in EtOH). Following the reaction, AcOH (229 μ L, 4.00 mmol) was added at room temperature and saturated NaHCO_3 was added until the pH = 8. The aqueous layer was extracted with 3:1 CH_2Cl_2 :isopropanol. The crude material was purified by flash chromatography (silica gel: 1:40:59 AcOH:EtOAc:hexanes) to provide the title compound as a brown powder (40 mg, 0.21 mmol, 53% yield). Material decomposes above 275 $^\circ\text{C}$; ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{SO}$) δ 8.77 (d, J = 5.3 Hz, 1H), 8.08 (d, J = 7.0 Hz, 2H), 7.92 (d, J = 5.3 Hz, 1H), 7.61 – 7.50 (m, 1H), 7.47 (dd, J = 8.3, 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{SO}$) δ 168.63, 164.20, 159.83, 135.57, 132.22, 129.54, 127.51, 114.68. Spectra matched literature values.¹⁵

2-Methyl-4-phenylpyrimidine (5d)



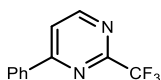
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), acetamidine hydrochloride (114 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:40:59 AcOH:EtOAc:hexanes) to afford the title compound as a 17:1 mixture of title compound: 4-phenylpyrimidine (orange solid, 49 mg, 0.29 mmol, 72% yield). mp 43-46 $^{\circ}$ C; IR ν_{max} /cm $^{-1}$ (solid): 3060, 2925, 1573, 1547, 1428, 1314, 840, 792, 752, 699; ^1H NMR (400 MHz, CDCl_3) δ 8.64 (d, J = 5.3 Hz, 1H), 8.05 (dd, J = 6.7, 3.1 Hz, 2H), 7.55 – 7.43 (m, 4H), 2.79 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.41, 164.05, 157.45, 136.94, 130.81, 128.95, 127.18, 113.93, 26.32; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 171.0924, $\text{C}_{11}\text{H}_{11}\text{N}_2^+$ requires 171.0917. Spectra matched literature values.¹⁶

4-(4-Chlorophenyl)-2-cyclopropylpyrimidine (5e)



Prepared according to general procedure B using 4-(4-chlorophenyl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (167 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), cyclopropanecarboximidamide hydrochloride (145 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 0-12% EtOAc in hexanes) to provide the title compound as a brown oil (60 mg, 0.26 mmol, 65% yield). mp 69-72 $^{\circ}$ C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3065, 3007, 1599, 1542, 1453, 1104, 1014, 915, 856, 867, 791; ^1H NMR (400 MHz, CDCl_3) δ 8.55 (d, J = 5.3 Hz, 1H), 7.98 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 5.3 Hz, 1H), 2.29 (tt, J = 8.4, 4.7 Hz, 1H), 1.19 (dt, J = 6.2, 3.3 Hz, 2H), 1.11 – 1.01 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.27, 162.18, 157.45, 136.94, 135.40, 129.06, 128.34, 113.10, 18.37, 10.85; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 231.0700, $\text{C}_{13}\text{H}_{12}\text{ClN}_2^+$ requires 231.0684.

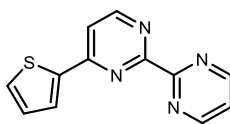
4-Phenyl-2-(trifluoromethyl)pyrimidine (5f)



Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), trifluoroacetamidine (135 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 0-20% EtOAc in hexanes) to provide the title compound as a white solid (66 mg, 0.30 mmol, 75% yield). mp 44-47 $^{\circ}$ C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3070, 1583, 1336, 1202, 1136, 873, 767, 688; ^1H NMR (400 MHz, CDCl_3) δ 8.87 (d, J = 5.3 Hz, 1H), 8.15 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 5.3 Hz, 1H), 7.71 – 7.13

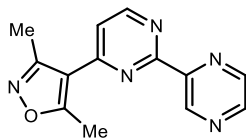
(m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.27, 158.33, 157.00 (q, $J = 36.4$ Hz), 135.00, 132.07, 129.22, 127.44, 122.47-115.61 (q, $J = 275.8$ Hz), 118.28; ^{19}F NMR (375 MHz, CDCl_3) δ -70.52; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 255.0639, $\text{C}_{11}\text{H}_8\text{F}_3\text{N}_2^+$ requires 225.0634. Spectra matched literature values.¹⁷

4-(Thiophen-2-yl)-2,2'-bipyrimidine (5g)



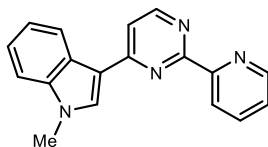
Prepared according to general procedure B using 1-phenyl-4-(thiophen-2-yl)pyrimidin-1-ium trifluoromethanesulfonate (108 mg, 0.28 mmol), EtOH (1.40 mL), piperidine (82 μL , 0.84 mmol), 2-amidinopyrimidine hydrochloride (132 mg, 0.84 mmol), and NaOEt (517 μL , 1.40 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:99 $\text{Et}_3\text{N}:\text{EtOAc}$ followed by 1:19:20:60 $\text{Et}_3\text{N}:\text{hexanes}:\text{EtOAc}:\text{EtOH}$) to provide the title compound as a yellow solid (32 mg, 0.13 mmol, 49% yield). mp 180-183 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3066, 3045, 1555, 1426, 1379, 760; ^1H NMR (400 MHz, CDCl_3) δ 9.00 (d, $J = 4.9$ Hz, 2H), 8.90 (d, $J = 5.3$ Hz, 1H), 7.91 – 7.85 (m, 1H), 7.62 (d, $J = 5.3$ Hz, 1H), 7.57 – 7.50 (m, 1H), 7.40 (t, $J = 4.8$ Hz, 1H), 7.15 (dd, $J = 5.0, 3.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.78, 162.72, 160.20, 158.18, 157.99, 141.71, 130.65, 128.52, 128.35, 121.34, 115.37; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 241.0555, $\text{C}_{12}\text{H}_9\text{N}_4\text{S}^+$ requires 241.0542.

3,5-Dimethyl-4-(2-(pyrazin-2-yl)pyrimidin-4-yl)isoxazole (5h)



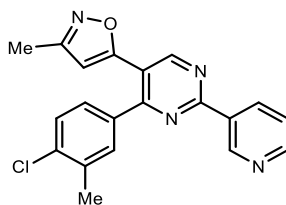
Prepared according to general procedure B using 4-(3,5-dimethylisoxazol-4-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (160.5 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), pyrazine-2-carboximidamide hydrochloride (190.3 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:99 AcOH:EtOAc followed by 1:50:25:25 AcOH:hexanes:EtOAc:EtOH) to provide the title compound as a pale-yellow solid (71 mg, 0.28 mmol, 70% yield). mp 173-177 $^{\circ}$ C; IR ν_{max} /cm $^{-1}$ (film): 3047, 1605, 1564, 1422, 1375, 1012, 845, 713, 678; ^1H NMR (400 MHz, CDCl_3) δ 9.70 (d, J = 1.6 Hz, 1H), 8.97 (d, J = 5.3 Hz, 1H), 8.81 – 8.76 (m, 1H), 8.70 (d, J = 2.4 Hz, 1H), 7.40 (d, J = 5.3 Hz, 1H), 2.77 (s, 3H), 2.58 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.65, 162.27, 158.97, 158.63, 158.61, 150.09, 145.90, 145.31, 144.68, 118.15, 113.88, 13.70, 12.46; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 254.1043, $\text{C}_{13}\text{H}_{12}\text{N}_5\text{O}^+$ requires 254.1036.

1-Methyl-3-(2-(pyridin-2-yl)pyrimidin-4-yl)-1H-indole (5i)



Prepared according to general procedure B using 4-(1-Methyl-1H-indol-3-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (174 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), picolinimidamide hydrochloride (189 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:99 Et₃N:EtOAc followed by 1:75:24 Et₃N:EtOAc:EtOH) to provide the title compound as a brown solid (63 mg, 0.22 mmol, 55% yield). mp 89-94 °C; IR ν_{max} /cm⁻¹ (solid): 3066, 3048, 2927, 2191, 1576, 1389, 1230, 720; ¹H NMR (400 MHz, CDCl₃) δ 8.85 – 8.81 (m, 1H), 8.75 (d, *J* = 5.4 Hz, 1H), 8.61 (d, *J* = 7.9 Hz, 1H), 8.49 (dd, *J* = 7.3, 2.2 Hz, 1H), 7.89 – 7.82 (m, 2H), 7.47 (d, *J* = 5.4 Hz, 1H), 7.37 (ddd, *J* = 7.7, 4.8, 1.2 Hz, 1H), 7.34 – 7.29 (m, 3H), 3.79 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.38, 161.93, 157.16, 155.57, 149.94, 138.01, 136.84, 131.75, 125.98, 124.61, 123.46, 122.80, 121.73, 121.60, 114.94, 113.52, 109.96, 33.35; *m/z* HRMS (DART) found [M+H]⁺ 287.1303, C₁₈H₁₅N₄⁺ requires 287.1291.

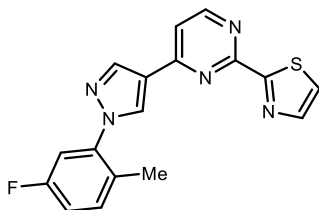
5-(4-(4-Chloro-3-methylphenyl)-2-(pyridin-3-yl)pyrimidin-5-yl)-3-methylisoxazole (5j)



Prepared according to general procedure B using 4-(4-chloro-3-methylphenyl)-5-(3-methylisoxazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (205 mg, 0.40 mmol), piperidine (118 μ L, 1.20 mmol), EtOH (2 mL), nicotinimidamide hydrochloride (145 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The residue was purified by

flash chromatography (silica gel: 60% EtOAc in hexanes. A second column was needed (70% EtOAc in hexanes) to provide the pure title compound as a yellow solid (59 mg, 0.16 mmol, 40% yield). mp 142-144 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3359, 3146, 1659, 1592, 1412, 1044, 819, 703. ^1H NMR (400 MHz, CDCl_3) δ 9.65 (s, 1H), 9.04 (s, 1H), 8.68 (dd, $J = 12.4, 6.4$ Hz, 2H), 7.46 (d, $J = 1.8$ Hz, 1H), 7.39 – 7.30 (m, 2H), 7.26 – 7.19 (m, 1H), 5.86 (s, 1H), 2.36 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 164.98, 163.09 (d, $J = 36.4$ Hz), 160.25, 157.58, 152.01, 150.29, 136.89 (d, $J = 14.2$ Hz), 135.82, 135.51, 135.50, 132.25, 131.42, 129.31, 128.95, 127.59, 123.46, 118.58, 105.17, 20.17, 11.49; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 363.1017, $\text{C}_{20}\text{H}_{15}\text{ClN}_4\text{O}^+$ requires 363.0934.

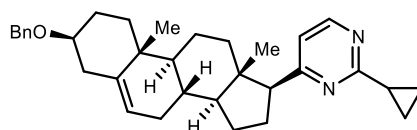
2-(4-(1-(5-Fluoro-2-methylphenyl)-1H-pyrazol-4-yl)pyrimidin-2-yl)thiazole (5k)



Prepared according to general procedure B using 4-(1-(5-fluoro-2-methylphenyl)-1H-pyrazol-4-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (192.2 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μL , 1.20 mmol), thiazole-2-carboximidamide hydrochloride (196.4 mg, 1.20 mmol), and NaOEt (747 μL , 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:2:97 AcOH:MeOH: CH_2Cl_2) to provide the title compound as a pink solid (87 mg, 0.26 mmol, 64% yield). mp 81-85 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3076, 1580, 1527, 1430, 1249, 875, 776; ^1H NMR (400 MHz, CDCl_3) δ 8.75 (d,

$J = 5.3$ Hz, 1H), 8.40 (s, 1H), 8.29 (s, 1H), 8.02 (d, $J = 3.1$ Hz, 1H), 7.51 (d, $J = 3.2$ Hz, 1H), 7.41 (d, $J = 5.2$ Hz, 1H), 7.35 – 7.24 (m, 1H), 7.12 (dd, $J = 8.8, 2.7$ Hz, 1H), 7.06 (td, $J = 8.3, 2.7$ Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3); ^{19}F NMR (375 MHz, CDCl_3) δ -115.36 (q, $J = 8.1$ Hz); m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 338.0873, $\text{C}_{17}\text{H}_{13}\text{FN}_5\text{S}^+$ requires 338.0870.

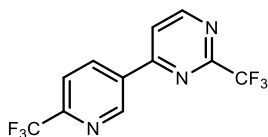
4-((3S,8S,9S,10R,13S,14S,17S)-3-(Benzyloxy)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2-cyclopropylpyrimidine (5l)



Prepared according to general procedure B using 4-((3S,8S,9S,10R,13S,14S,17S)-3-(benzyloxy)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (134 mg, 0.20 mmol), EtOH (1 mL), piperidine (60 μL , 0.60 mmol), cyclopropanecarboximidamide hydrochloride (72.4 mg, 0.60 mmol), and NaOEt (374 μL , 1.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 25% EtOAc in hexanes) to provide the title compound as a pale-yellow solid (51 mg, 0.11 mmol, 53% yield). mp 92-97 $^{\circ}\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2932, 2903, 1574, 1551, 1435, 1113, 730; ^1H NMR (400 MHz, CDCl_3) δ 8.38 (d, $J = 5.2$ Hz, 1H), 7.40 – 7.30 (m, 4H), 7.29 – 7.19 (m, 1H), 6.83 (d, $J = 5.3$ Hz, 1H), 5.39 – 5.34 (m, 1H), 4.56 (s, 2H), 3.29 (tt, $J = 11.3, 4.5$ Hz, 1H), 2.69 (t, $J = 9.4$ Hz, 1H), 2.43 (tt, $J = 7.9, 4.0$ Hz, 2H), 2.29 (ddt, $J = 13.7, 10.5, 2.7$ Hz, 1H), 2.17-2.23 (m, 1H), 2.04 (dtd, $J = 13.6, 4.9, 2.3$ Hz,

1H), 2.00 – 1.91 (m, 1H), 1.91 – 1.83 (m, 2H), 1.83 – 1.73 (m, 2H), 1.62 (dd, J = 10.5, 2.7 Hz, 1H), 1.59 – 1.51 (m, 3H), 1.49 (d, J = 4.6 Hz, 1H), 1.37 (ddd, J = 13.1, 8.2, 3.8 Hz, 3H), 1.24 (dt, J = 10.1, 5.9 Hz, 1H), 1.15 – 1.08 (m, 2H), 1.06 (d, J = 3.7 Hz, 1H), 1.01-1.03 (m, 1H), 1.00 (s, 3H), 0.47 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.08, 169.86, 155.64, 141.16, 139.15, 128.45, 127.65, 127.50, 121.47, 117.46, 78.61, 70.03, 57.88, 57.01, 50.39, 45.21, 39.26, 38.16, 37.38, 37.10, 32.26, 32.06, 28.53, 24.79, 24.40, 20.90, 19.52, 18.27, 13.02, 10.63, 10.59; *m/z* HRMS (ESI) found [M+H]⁺ 483.3379, C₃₃H₄₃N₂O⁺ requires 483.3370.

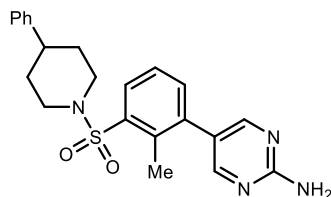
2-(Trifluoromethyl)-4-(6-(trifluoromethyl)pyridin-3-yl)pyrimidine (5m)



Prepared according to general procedure B using 1-phenyl-2-(trifluoromethyl)-4-(6-(trifluoromethyl)pyridin-3-yl)pyrimidin-1-ium trifluoromethanesulfonate (160 mg, 0.35 mmol), EtOH (1.8 mL), piperidine (104 μL, 1.05 mmol), trifluoroacetamidine (118 mg, 1.05 mmol), and NaOEt (654 μL, 1.75 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:39:60 AcOH:EtOAc:hexanes) to provide the title compound as an orange solid (41 mg, 0.14 mmol, 40% yield). mp 89-94 °C; IR *v*_{max}/cm⁻¹ (solid): 3312, 3158, 1645, 1590, 1512, 1485, 1224, 798, 697; ¹H NMR (400 MHz, CDCl₃) δ 9.40 (s, 1H), 9.06 (d, J = 5.3 Hz, 1H), 8.71 (dd, J = 8.3, 2.2 Hz, 1H), 8.00 (d, J = 5.2 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 161.70, 159.53, 157.69 (q, J = 37.2 Hz), 150.76 (q, J = 35.3 Hz), 148.79, 136.82, 133.67, 121.01 (q, J = 2.8 Hz), 120.90, 120.57 (q, J = 180.4 Hz), 119.01; ¹⁹F NMR

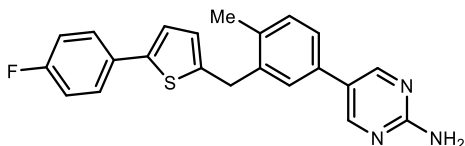
(375 MHz, CDCl₃) δ -68.17 (s, 3F), -70.61 (s, 3F); m/z HRMS (ESI) found $[M+H]^+$ 294.0460, C₁₁H₆F₆N₃⁺ requires 294.0460.

5-(2-Methyl-3-((4-phenylpiperidin-1-yl)sulfonyl)phenyl)pyrimidin-2-amine (5n)



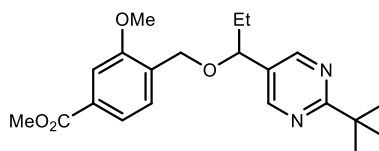
Prepared according to a modified general procedure D using 5-(2-methyl-3-((4-phenylpiperidin-1-yl)sulfonyl)phenyl)pyrimidine (79 mg, 0.20 mmol), Tf₂O (34 μ L, 0.20 mmol), *p*-NO₂ aniline (28.0 mg, 0.20 mmol), collidine (25 μ L, 0.20 mmol), EtOAc (1 mL), then piperidine (59 μ L, 0.60 mmol), EtOH (1 mL), guanidine hydrochloride (382 mg, 4.00 mmol) and NaOEt (428 μ L, 1.00 mmol, as a 21% soln. in EtOH). The residue was purified by flash chromatography (silica gel: 3% MeOH in dichloromethane) to provide the pure title compound as an off-white solid (31 mg, 0.076 mmol, 38% yield). mp 215-217 °C. IR_{max}/cm⁻¹ (film): 3675, 2988, 2337, 2161, 1622, 1482, 1161, 1067, 561. ¹H NMR (400 MHz, CDCl₃) δ 8.21 (s, 2H), 7.96 (t, *J* = 4.7 Hz, 1H), 7.33 (d, *J* = 4.5 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.11 (d, *J* = 7.0 Hz, 3H), 5.19 (s, 2H), 3.88 – 3.79 (m, 2H), 2.80 (td, *J* = 12.5, 2.8 Hz, 2H), 2.57 (dt, *J* = 12.4, 3.7 Hz, 1H), 2.52 (s, 3H), 1.90 – 1.81 (m, 2H), 1.71 (qd, *J* = 12.6, 4.3 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 162.16, 158.23, 144.88, 138.50, 138.01, 136.20, 134.66, 130.19, 128.64, 126.71, 125.93, 124.50, 45.94, 42.12, 32.91, 17.66. m/z HRMS (ESI) found 409.1721, $[M+H]^+$ for C₂₂H₂₄N₄O₂S⁺ requires 409.1698.

5-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyrimidin-2-amine (5o)



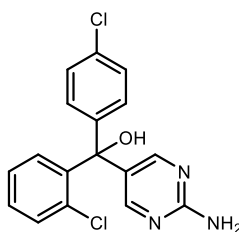
Prepared according to a modified general procedure D using 5-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyrimidine (144 mg, 0.40 mmol), TiCl_4 (67 μL , 0.40 mmol), *p*- NO_2 aniline (56.0 mg, 0.40 mmol), collidine (53 μL , 0.40 mmol), EtOAc (2 mL), then piperidine (118 μL , 1.20 mmol), EtOH (2 mL), guanidine hydrochloride (472 mg, 8.00 mmol) and NaOEt (747 μL , 2.00 mmol, as a 21% soln. in EtOH). The residue was purified by flash chromatography (silica gel: 70% EtOAc in hexanes) to provide the pure title compound as an off-white solid (114 mg, 0.30 mmol, 76% yield). mp 120-122 $^\circ\text{C}$. IR $_{\text{max}}$ /cm $^{-1}$ (film): 3657, 2988, 2358, 2161, 2050, 1506, 1065, 644, 576. ^1H NMR (400 MHz, CDCl_3) δ 8.56 (s, 2H), 7.64 – 7.54 (m, 2H), 7.50 (d, J = 2.1 Hz, 1H), 7.40 (dd, J = 7.8, 2.1 Hz, 1H), 7.34 – 7.25 (m, 1H), 7.23 – 7.08 (m, 3H), 6.84 (dt, J = 3.6, 1.1 Hz, 1H), 5.53 (s, 2H), 4.24 (s, 2H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 163.40, 160.94, 157.32, 154.78, 142.45, 141.93, 139.57, 137.61, 134.10, 132.22, 131.60, 127.88, 127.18 (d, J = 8.0 Hz), 126.26, 125.41, 122.75, 115.87, 34.12, 19.33. ^{19}F NMR (375 MHz, CDCl_3) δ -114.94 (dq, J = 9.0, 4.5 Hz). m/z HRMS (ESI) found 376.1313, $[\text{M}+\text{H}]^+$ for $\text{C}_{22}\text{H}_{18}\text{FN}_3\text{S}^+$ requires 376.1283.

Methyl 4-((1-(2-(tert-butyl)pyrimidin-5-yl)propoxy)methyl)-3-methoxybenzoate (5p)



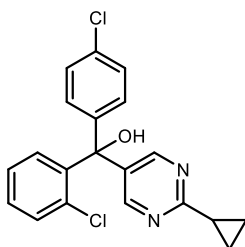
Prepared according to a modified general procedure D using methyl 3-methoxy-4-((1-(pyrimidin-5-yl)propoxy)methyl)benzoate (50.2 mg, 0.16 mmol), TiF_4 (27 μL , 0.16 mmol), *p*- NO_2 aniline (21.8 mg, 0.16 mmol), collidine (21 μL , 0.16 mmol), EtOAc (0.8 mL), then piperidine (47 μL , 0.48 mmol), MeOH (0.8 mL), pivalimidamide hydrochloride (216 mg, 1.60 mmol), and NaOMe (42.7 mg, 0.80 mmol). The residue was purified by flash chromatography (silica gel: 15% EtOAc in hexanes) to provide the pure title compound as a yellow oil (22 mg, 0.06 mmol, 38% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2958, 1720, 1587, 1432, 1288, 1230, 1103, 1036, 760; ^1H NMR (400 MHz, CDCl_3) δ 8.62 (s, 2H), 7.64 (d, J = 7.8 Hz, 1H), 7.51 – 7.44 (m, 2H), 4.46 (s, 2H), 4.28 (t, J = 6.5 Hz, 1H), 3.90 (s, 3H), 3.82 (s, 3H), 1.92 (dp, J = 14.6, 7.4 Hz, 1H), 1.82 – 1.67 (dp, J = 14.1, 7.2 Hz, 1H), 1.41 (s, 9H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.89, 167.06, 156.74, 155.49, 131.90, 131.55, 130.61, 128.39, 122.11, 110.81, 79.59, 65.99, 55.51, 52.29, 39.34, 30.85, 29.77, 10.08; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 373.2124, $\text{C}_{21}\text{H}_{29}\text{N}_2\text{O}_4^+$ requires 373.2122.

(2-Aminopyrimidin-5-yl)(2-chlorophenyl)(4-chlorophenyl)methanol (5q)



Prepared according to a modified general procedure D using (2-chlorophenyl)(4-chlorophenyl)(pyrimidin-5-yl)methanol (132 mg, 0.40 mmol), Tf₂O (67 μ L, 0.40 mmol), *p*-NO₂ aniline (56.0 mg, 0.40 mmol), collidine (53 μ L, 0.40 mmol), EtOAc (2 mL), then piperidine (118 μ L, 1.20 mmol), EtOH (2 mL), guanidine hydrochloride (472 mg, 8.00 mmol) and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The residue was purified by flash chromatography (silica gel: 80% EtOAc in hexanes) to provide the pure title compound as an off-white solid (46 mg, 0.13 mmol, 33% yield). mp 78-80 °C. IR_{ν_{max}}/cm⁻¹ (film): 3292, 3157, 1669, 1605, 1496, 1483, 1266, 1131, 813, 693. ¹H NMR (400 MHz, CDCl₃) δ 8.03 (s, 2H), 7.35 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.30 – 7.19 (m, 3H), 7.16 – 7.07 (m, 3H), 6.79 (dd, *J* = 7.9, 1.8 Hz, 1H), 5.27 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 162.16, 157.90, 143.00, 141.86, 133.88, 132.81, 131.77, 130.75, 129.87, 128.85, 128.53, 128.28, 126.91, 79.76. *m/z* HRMS (ESI) found [M+H]⁺ 346.0514, for C₁₇H₁₃Cl₂N₃O⁺ requires 346.0514.

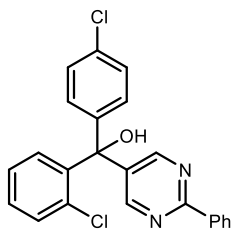
(2-Chlorophenyl)(4-chlorophenyl)(2-cyclopropylpyrimidin-5-yl)methanol (5r)



Prepared according to a modified general procedure D using (2-chlorophenyl)(4-chlorophenyl)(pyrimidin-5-yl)methanol (132 mg, 0.40 mmol), Tf₂O (67 μ L, 0.40 mmol), *p*-NO₂ aniline (56.0 mg, 0.40 mmol), collidine (53 μ L, 0.40 mmol), EtOAc (2 mL), then piperidine (118

μL , 1.20 mmol), EtOH (2 mL), cyclopropanecarboximidamide hydrochloride (960 mg, 8.00 mmol), and NaOEt (747 μL , 2.00 mmol, as a 21% soln. in EtOH). The residue was purified by flash chromatography (silica: 0-30% EtOAc in hexanes. A second column was needed (30% dichloromethane in hexanes)) to provide the pure title compound as a viscous yellow oil (57 mg, 0.15 mmol, 38% yield). IR $_{\text{max}}/\text{cm}^{-1}$ (film): 3168, 1545, 1454, 1190, 1013, 904, 757, 728. ^1H NMR (400 MHz, CDCl_3) δ 8.33 (s, 2H), 7.36 (d, J = 8.0 Hz, 1H), 7.26 (d, J = 8.6 Hz, 3H), 7.11 (dd, J = 12.7, 8.1 Hz, 3H), 6.71 (d, 1H), 4.39 (s, 1H), 2.19 (td, J = 8.6, 8.1, 4.1 Hz, 1H), 1.13 – 0.98 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 171.06, 156.15, 142.46, 141.30, 134.79, 134.12, 132.73, 131.85, 130.70, 130.09, 128.79, 128.67, 127.02, 79.75, 17.83, 11.25 (d, J = 3.8 Hz). m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 371.0724, $\text{C}_{20}\text{H}_{16}\text{Cl}_2\text{N}_2\text{O}^+$ requires 371.0718.

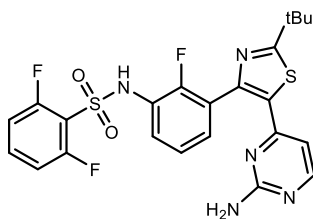
(2-Chlorophenyl)(4-chlorophenyl)(2-phenylpyrimidin-5-yl)methanol (5s)



Prepared according to a modified general procedure D using (2-chlorophenyl)(4-chlorophenyl)(pyrimidin-5-yl)methanol (132 mg, 0.40 mmol), TiF_2O (67 μL , 0.40 mmol), $p\text{-NO}_2$ aniline (56.0 mg, 0.40 mmol), collidine (53 μL , 0.40 mmol), EtOAc (2 mL), then piperidine (118 μL , 1.20 mmol), EtOH (2 mL), benzimidamide hydrochloride (626 mg, 4.00 mmol), and NaOEt (747 μL , 2.00 mmol, as a 21% soln. in EtOH). The residue was purified by flash chromatography (silica gel: 20% EtOAc in hexanes. A second column was needed (0 to 10% EtOAc in hexanes))

to provide the pure title compound as a viscous yellow oil (45 mg, 0.11 mmol, 28% yield). IR_{max}/cm⁻¹ (film): 1651, 1579, 1428, 1163, 1045, 736, 694. ¹H NMR (400 MHz, CDCl₃) δ 8.59 (s, 2H), 8.38 (dd, *J* = 6.8, 3.1 Hz, 2H), 7.54 – 7.34 (m, 4H), 7.27 (dd, *J* = 9.0, 2.8 Hz, 3H), 7.22 – 7.08 (m, 3H), 6.75 (d, *J* = 7.9 Hz, 1H), 4.39 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 163.62, 156.65, 142.45, 141.33, 137.04, 135.84, 134.19, 132.78, 131.89, 130.97, 130.79, 130.13, 128.89, 128.72, 128.63, 128.23, 127.06, 79.88. *m/z* HRMS (ESI) found [M+H]⁺ 407.0724, C₂₃H₁₆Cl₂N₂O⁺ requires 407.0718.

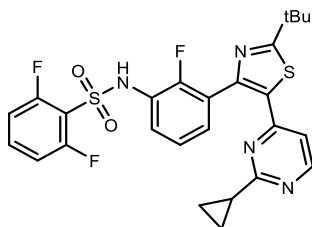
Dabrafenib (5t)



Prepared according to a modified general procedure D, heated to 70 °C instead of 90 °C. Used *N*-{3-(2-(*tert*-butyl)-5-(pyrimidin-4-yl)thiazol-4-yl)-2-fluorophenyl}-2,6-difluorobenzenesulfonamide (126 mg, 0.25 mmol), EtOAc (1.25 mL), Tf₂O (42 μL, 0.25 mmol), aniline (23 μL, 0.25 mmol), collidine (33 μL, 0.25 mmol), then EtOH (1.25 mL), piperidine (75 μL, 0.75 mmol), guanidine hydrochloride (71.6 mg, 0.75 mmol), and NaOEt (467 μL, 1.25 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:60:39 AcOH:EtOAc:hexanes) to provide the title compound as a white powder (84 mg, 0.16 mmol, 64% yield). mp 162-165 °C; IR *v*_{max}/cm⁻¹ (solid): 3467, 3366, 2964, 1612, 1573, 1459, 1356, 1165, 1010, 795, 633; ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, *J* = 5.3 Hz, 1H), 7.49 – 7.38

(m, 1H), 7.31 (ddd, $J = 14.5, 8.5, 6.0$ Hz, 1H), 7.21 – 7.11 (m, 1H), 7.10 – 6.98 (m, 1H), 6.79 (t, $J = 9.0$ Hz, 2H), 5.96 (d, $J = 5.3$ Hz, 1H), 5.30 (s, 2H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3 , one drop $(\text{CD}_3)_2\text{SO}$ added for solubility) δ 182.33, 162.81, 159.50 (dd, $J = 257.7, 3.6$ Hz), 158.80, 158.31, 152.33 (d, $J = 250.5$ Hz), 145.88, 134.74 (t, $J = 11.0$ Hz), 133.77, 128.47, 125.52, 124.84 – 124.54 (m, 2C), 124.27 (d, $J = 14.3$ Hz), 117.73 (t, $J = 15.7$ Hz), 112.93 (dd, $J = 22.9, 3.7$ Hz), 107.11, 37.86, 30.60; ^{19}F NMR (375 MHz, CDCl_3) δ -106.80 (dt, $J = 9.9, 4.8$ Hz, 2F), -128.81 (td, $J = 7.0, 3.6$ Hz, 1F); m/z HRMS (DART) found $[\text{M}+\text{H}]^+ 520.1089$, $\text{C}_{23}\text{H}_{21}\text{F}_3\text{N}_5\text{O}_2\text{S}_2^+$ requires 520.1083. Spectra matched literature values.¹⁸

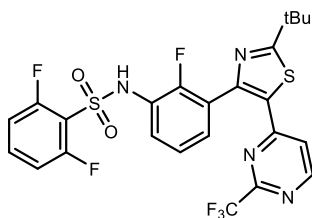
***N*-(3-(2-(*Tert*-butyl)-5-(2-cyclopropylpyrimidin-4-yl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (5u)**



Prepared according to a modified general procedure D, heated to 70 °C instead of 90 °C. Used *N*-(3-(2-(*tert*-butyl)-5-(pyrimidin-4-yl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (126 mg, 0.25 mmol), EtOAc (1.25 mL), TiF_2O (42 μL , 0.25 mmol), aniline (23 μL , 0.25 mmol), collidine (33 μL , 0.25 mmol), then EtOH (1.25 mL), piperidine (75 μL , 0.75 mmol), cyclopropanecarboximidamide hydrochloride (90.4 mg, 0.75 mmol), and NaOEt (467. μL , 1.25 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:40:59 AcOH:EtOAc:hexanes) to provide the title compound as a

peach-colored powder (83 mg, 0.15 mmol, 61% yield). mp 213-216 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 2964, 2747, 1568, 1568, 1355, 1171, 1002, 792, 633; ^1H NMR (400 MHz, CDCl_3) δ 8.25 (d, J = 5.4 Hz, 1H), 7.72 (td, J = 7.7, 1.7 Hz, 1H), 7.49 (tt, J = 8.5, 5.9 Hz, 1H), 7.39 (s, 1H), 7.30 (ddd, J = 8.1, 6.5, 1.7 Hz, 1H), 7.24 – 7.18 (m, 1H), 6.97 (t, J = 8.7 Hz, 2H), 6.54 (d, J = 5.4 Hz, 1H), 2.19 (tt, J = 7.2, 5.7 Hz, 1H), 1.47 (d, J = 0.8 Hz, 9H), 1.07 – 0.98 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 183.38, 172.27, 159.76 (dd, J = 259.8, 3.4 Hz), 157.74, 156.78, 150.67 (d, J = 247.8 Hz), 146.02, 135.29 (t, J = 11.0 Hz), 133.88, 127.96 (d, J = 2.3 Hz), 125.29 (d, J = 4.5 Hz), 124.46 (dd, J = 54.7, 13.3 Hz), 122.73, 116.88, 113.33, 113.24, 113.08 (dd, J = 229.9, 3.6 Hz), 38.10, 30.72, 18.06, 10.95; ^{19}F NMR (375 MHz, CDCl_3) δ -106.86 (dt, J = 9.7, 4.5 Hz, 2F), -130.42 (tt, J = 7.1, 3.8 Hz, 1F); m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 545.1302, $\text{C}_{26}\text{H}_{24}\text{F}_3\text{N}_4\text{O}_2\text{S}_2^+$ requires 545.1287.

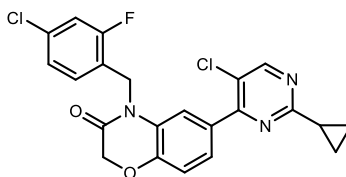
***N*-(3-(2-(*Tert*-butyl)-5-(2-(trifluoromethyl)pyrimidin-4-yl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (5v)**



Prepared according to a modified general procedure D, heated to 70 °C instead of 90 °C. Used *N*-(3-(2-(*tert*-butyl)-5-(pyrimidin-4-yl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (126 mg, 0.25 mmol), EtOAc (1.25 mL), TiF_2O (42 μL , 0.25 mmol), aniline (23 μL , 0.25 mmol), collidine (33 μL , 0.25 mmol), then EtOH (1.25 mL), piperidine (75

μL , 0.75 mmol), trifluoroacetamidine (85.0 mg, 0.75 mmol), and NaOEt (467 μL , 1.25 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 30% EtOAc in hexanes. A second column was needed (0.25:10:89.75 Et₃N:EtOAc:CH₂Cl₂)) to provide the title compound as a white powder (33 mg, 0.06 mmol, 23% yield). mp 207-211 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3068, 2964, 2922, 1613, 1578, 1442, 1418, 1360, 1159, 1006, 816; ¹H NMR (400 MHz, (CD₃)₂CO) δ 8.78 (d, J = 5.4 Hz, 1H), 7.74 – 7.61 (m, 2H), 7.53 (ddd, J = 8.0, 6.4, 1.7 Hz, 1H), 7.36 (td, J = 7.9, 1.0 Hz, 1H), 7.31 – 7.24 (m, 1H), 7.20 – 7.09 (m, 2H), 1.48 (s, 9H); ¹³C NMR (100 MHz, (CD₃)₂CO) δ 185.15, 160.43 (dd, J = 256.2, 3.9 Hz), 160.10, 159.92, 157.00 (d, J = 36.3 Hz), 153.46 (d, J = 250.0 Hz), 149.02, 136.52 (t, J = 11.2 Hz), 132.81, 129.56 (d, J = 2.3 Hz), 127.32, 126.44 (d, J = 13.1 Hz), 126.04 (d, J = 4.6 Hz), 124.77 (d, J = 13.7 Hz), 120.54 (q, J = 273.4 Hz), 119.85, 118.82 (t, J = 16.4 Hz), 114.08 (dd, J = 23.3, 3.7 Hz), 38.99, 30.82; ¹⁹F NMR (375 MHz, (CD₃)₂CO) δ -71.12 (3F), -108.04 (ddd, J = 9.2, 6.0, 3.5 Hz, 2F), -126.37 (tt, J = 6.4, 3.0 Hz, 1F); m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 573.0858, C₂₄H₁₉F₆N₄O₂S₂⁺ requires 573.0848.

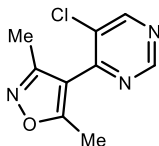
6-(5-Chloro-2-cyclopropylpyrimidin-4-yl)-4-(4-chloro-2-fluorobenzyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (5w)



An oven dried 8 mL vial equipped with a stir bar was charged with 4-(4-(4-chloro-2-fluorobenzyl)-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)-1-phenylpyrimidin-1-ium

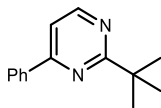
trifluoromethanesulfonate (119.2 mg, 0.20 mmol), and placed under a nitrogen atmosphere. Then EtOH (1.0 mL, 0.2M) and piperidine (60 μ L, 0.60 mmol, 3 equiv) were added. The reaction was stirred for 60 minutes before trifluoroacetic acid (46 μ L, 0.60 mmol, 3 equiv) and *N*-chlorosuccinimide (80.1 mg, 0.60 mmol, 3 equiv) was added. The reaction was stirred for an additional 30 minutes before cyclopropanecarboximidamide hydrochloride (72.3 mg, 0.60 mmol, 3 equiv) was added, followed by NaOEt (672 μ L, 1.80 mmol, 9.0 equiv, 21% soln. in EtOH). The reaction was heated to 90 °C for 18 hours. After cooling to room temperature, the reaction was diluted with EtOAc and H₂O, then extracted into EtOAc (3x). The combined organic extract was washed (1x) with brine and dried (MgSO₄), filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel: 0 to 35% EtOAc in hexanes. A second column was required (0 to 3% EtOAc in CH₂Cl₂)) to provide the pure title compound as a white solid (46 mg, 0.10 mmol, 52% yield). IR_{max}/cm⁻¹ (film): 3088, 1676, 1530, 1389, 1279, 1060, 906, 824. ¹H NMR (400 MHz, CDCl₃) δ 8.50 (s, 1H), 7.62 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 7.20 – 6.83 (m, 4H), 5.22 (s, 2H), 4.80 (s, 2H), 2.23 (tt, *J* = 7.7, 5.1 Hz, 1H), 1.21 – 0.71 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 170.31, 164.57, 160.26 (d, *J* = 248.2 Hz), 160.07, 157.64, 146.94, 134.50 (d, *J* = 10.2 Hz), 130.90, 129.33 (d, *J* = 4.7 Hz), 127.97, 126.10, 125.23 (d, *J* = 3.6 Hz), 125.03, 121.46 (d, *J* = 14.2 Hz), 117.02, 116.80, 116.77, 116.56, 67.73, 38.28 (d, *J* = 4.7 Hz), 17.91, 11.26; ¹⁹F NMR (375 MHz, CDCl₃) δ -115.49 (dd, *J* = 9.8, 7.6 Hz). *m/z* HRMS (DART) found 444.0659, [M+H]⁺ for C₂₂H₁₇Cl₂FN₃O₂⁺ requires 444.0676

4-(5-Chloropyrimidin-4-yl)-3,5-dimethylisoxazole (5x)



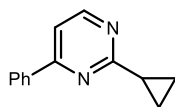
An oven dried 8 mL vial equipped with a stir bar was charged with 4-(3,5-dimethylisoxazol-4-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (160 mg, 0.40 mmol), and placed under a nitrogen atmosphere. Then EtOH (2.0 mL, 0.2 M) and piperidine (120 μ L, 1.2 mmol, 3 equiv) were added. The reaction was stirred for 60 minutes before trifluoroacetic acid (88 μ L, 1.2 mmol, 3 equiv) and *N*-chlorosuccinimide (160 mg, 1.2 mmol, 3 equiv) was added. The reaction was stirred for an additional 30 minutes before formamidine hydrochloride (96 mg, 1.2 mmol, 3 equiv) was added followed by NaOEt (1.34 mL, 3.6 mmol, 9.0 equiv, 21% soln. in EtOH). The reaction was heated to 90 °C for 18 hours. After cooling to room temperature, the reaction was diluted with EtOAc and H₂O, then extracted into EtOAc (3x). The combined organic extract was washed (1x) with brine and dried (MgSO₄), filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel: 70% EtOAc in hexanes) to provide the pure title compound as a light orange solid (22 mg, 0.10 mmol, 40% yield). mp 85-87 °C. IR_ν_{max}/cm⁻¹ (film): 2970, 2323, 2184, 1979, 1729, 1391, 1066, 788, 561. ¹H NMR (400 MHz, CDCl₃) δ 9.08 (s, 1H), 8.76 (s, 1H), 2.37 (s, 3H), 2.24 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.96, 158.91, 157.38, 156.41, 156.13, 130.38, 112.73, 12.82, 10.88. *m/z* HRMS (ESI) found 210.0430, [M+H]⁺ for C₉H₈ClN₃O⁺ requires 210.0434.

2-(*Tert*-butyl)-4-phenylpyrimidine (5y)



Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), 2,2-dimethylpropanimidamide hydrochloride (164 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 2.5% EtOAc in hexanes) to provide the title compound as a clear oil (55.6 mg, 0.26 mmol, 66% yield). mp 32-34 $^{\circ}$ C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 2975, 2952, 1566, 1544, 1448, 1362, 1177, 768, 694; ^1H NMR (400 MHz, CDCl_3) δ 8.72 (d, J = 5.2 Hz, 1H), 8.27 – 7.79 (m, 2H), 7.70 – 7.09 (m, 4H), 1.50 (d, J = 1.5 Hz, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 177.38, 162.99, 157.21, 137.30, 130.72, 128.87, 127.13, 113.32, 39.64, 29.70; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 213.1394, $\text{C}_{14}\text{H}_{17}\text{N}_2^+$ requires 213.1386.¹⁹

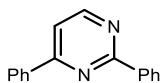
2-Cyclopropyl-4-phenylpyrimidine (5z)



Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), cyclopropanecarboximidamide hydrochloride (145 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica

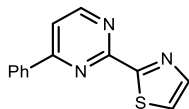
gel: 0-10% EtOAc in hexanes) to provide the title compound as a pale-yellow oil (55 mg, 0.28 mmol, 70% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3007, 1568, 1546, 1359, 1262, 916, 836, 763, 691; ^1H NMR (400 MHz, CDCl_3) δ 8.56 (d, $J = 5.3$ Hz, 1H), 8.06 (dd, $J = 6.8, 3.0$ Hz, 2H), 7.47 (d, $J = 3.2$ Hz, 3H), 7.40 (d, $J = 5.3$ Hz, 1H), 2.32 (tt, $J = 8.1, 4.7$ Hz, 1H), 1.22 (dt, $J = 4.7, 3.2$ Hz, 2H), 1.17 – 0.84 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.13, 163.46, 157.28, 137.02, 130.73, 128.85, 127.08, 113.43, 18.40, 10.76; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 197.1119, $\text{C}_{13}\text{H}_{13}\text{N}_2^+$ requires 197.1073. Spectra matched literature values.²⁰

2,4-Diphenylpyrimidine (5aa)



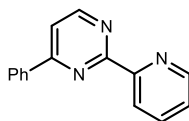
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μL , 1.20 mmol), benzamidine hydrochloride (188 mg, 1.20 mmol), and NaOEt (747 μL , 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 0-5% EtOAc in hexanes) to provide the title compound as a white solid (48 mg, 0.21 mmol, 52% yield). mp 70-72 $^{\circ}\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3065, 3034, 1541, 1423, 1379, 745, 687; ^1H NMR (400 MHz, CDCl_3) δ 8.84 (d, $J = 5.3$ Hz, 1H), 8.67 – 8.50 (m, 2H), 8.32 – 8.11 (m, 2H), 7.60 (d, $J = 5.3$ Hz, 1H), 7.57 – 7.51 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 164.61, 163.86, 157.88, 137.93, 136.99, 131.00, 130.76, 128.97, 128.59, 128.35, 127.24, 114.54; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 223.1145, $\text{C}_{16}\text{H}_{13}\text{N}_2^+$ requires 223.1073. Spectra matched literature values.²¹

2-(4-Phenylpyrimidin-2-yl)thiazole (5ab)



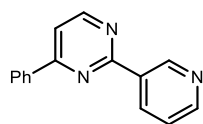
Prepared according to a modified general procedure B heating to 60 °C instead of 90 °C. 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), thiazole-2-carboximidamide hydrochloride (196 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:70:29 AcOH:EtOAc:hexanes) to provide the title compound as a pale-brown solid (69 mg, 0.29 mmol, 72% yield). mp 88-92 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3075, 1570, 1500, 1430, 1309, 1110, 760, 692, 682; ^1H NMR (400 MHz, CDCl_3) δ 8.85 (d, $J = 5.2$ Hz, 1H), 8.19 (dd, $J = 6.7, 3.1$ Hz, 1H), 8.06 (d, $J = 3.1$ Hz, 1H), 7.67 (d, $J = 5.3$ Hz, 1H), 7.60 – 7.41 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.28, 164.51, 159.64, 158.35, 145.12, 135.79, 131.44, 129.01, 127.32, 123.04, 116.13; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 240.0616, $\text{C}_{13}\text{H}_{10}\text{N}_3\text{S}^+$ requires 240.0590. Spectra matched literature values.²²

4-Phenyl-2-(pyridin-2-yl)pyrimidine (5ac)



Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), picolinimidamide hydrochloride (189 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:70:29 Et₃N:EtOAc:hexanes followed by 1:75:24 Et₃N:EtOAc:EtOH) to provide the title compound as a brown oil (62 mg, 0.26 mmol, 66% yield). IR ν_{max} /cm⁻¹ (film): 3059, 1560, 1543, 1420, 1382, 753, 691, 627; ¹H NMR (400 MHz, CDCl₃) δ 8.91 (d, J = 5.2 Hz, 1H), 8.85 – 8.75 (m, 1H), 8.61 (d, J = 8.0 Hz, 1H), 8.29 – 7.94 (m, 2H), 7.82 (td, J = 7.7, 1.8 Hz, 1H), 7.63 (d, J = 5.3 Hz, 1H), 7.54 – 7.32 (m, 3H), 7.35 (ddd, J = 7.5, 4.7, 1.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 164.21, 163.61, 158.51, 155.01, 150.06, 136.85, 136.56, 131.11, 128.96, 127.27, 124.86, 123.66, 115.80; m/z HRMS (DART) found [M+H]⁺ 234.1081, C₁₅H₁₂N₃⁺ requires 234.1026. Spectra matched literature values.¹⁷

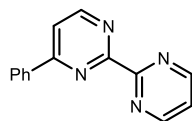
4-Phenyl-2-(pyridin-3-yl)pyrimidine (5ad)



Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), 3-amidinopyridine hydrochloride (189. mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 30-50%

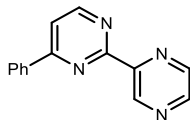
EtOAc in hexanes) to provide the title compound as a pink powder (68 mg, 0.29 mmol, 72% yield). mp 89-91 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3040, 2921, 1580, 1559, 1543, 1369, 1189, 1020, 758, 685, 614; ^1H NMR (400 MHz, CDCl_3) δ 9.75 (s, 1H), 8.84 – 8.73 (m, 2H), 8.70 (d, J = 4.8 Hz, 1H), 8.19 – 8.02 (m, 2H), 7.56 (d, J = 5.4 Hz, 1H), 7.53 – 7.43 (m, 3H), 7.38 (dd, J = 8.0, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.95, 162.80, 157.95, 151.35, 150.02, 136.44, 135.51, 133.31, 131.22, 129.00, 127.16, 123.33, 115.07; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 234.1019, $\text{C}_{15}\text{H}_{12}\text{N}_3^+$ requires 234.1026. Spectra matched literature values.²¹

4-Phenyl-2,2'-bipyrimidine (5ae)



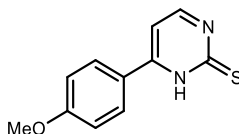
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μL , 1.20 mmol), 2-amidinopyrimidine hydrochloride (190 mg, 1.20 mmol), and NaOEt (747 μL , 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:70:29 $\text{Et}_3\text{N}:\text{EtOAc}:\text{hexanes}$ followed by 1:75:24 $\text{Et}_3\text{N}:\text{EtOAc}:\text{EtOH}$) to provide the title compound as a yellow solid (50 mg, 0.21 mmol, 53% yield). mp 122-125 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3073, 2923, 1556, 1419, 1376, 828, 760, 692, 632; ^1H NMR (400 MHz, CDCl_3) δ 8.96 (d, J = 4.9 Hz, 3H), 8.18 – 8.08 (m, 2H), 7.73 (d, J = 5.2 Hz, 1H), 7.51 – 7.40 (m, 3H), 7.35 (t, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.37, 162.92, 162.73, 158.39, 157.97, 136.41, 131.18, 128.98, 127.56, 121.30, 117.12; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 235.0981, $\text{C}_{14}\text{H}_{11}\text{N}_4^+$ requires 235.0983.

4-Phenyl-2-(pyrazin-2-yl)pyrimidine (5af)



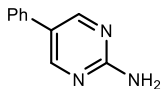
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), pyrazine-2-carboximidamide hydrochloride (190 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:49:50 Et₃N:EtOAc:hexanes followed by 1:75:24 Et₃N:EtOAc:hexanes) to provide the title compound as a pale yellow solid (78 mg, 0.33 mmol, 83% yield). mp 97-99 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3056, 1578, 1563, 1541, 1451, 1367, 1323, 1142, 1015, 767, 687; ¹H NMR (400 MHz, CDCl₃) δ 9.88 (d, J = 1.5 Hz, 1H), 9.00 (d, J = 5.3 Hz, 1H), 8.87 – 8.75 (m, 1H), 8.72 (s, 1H), 8.39 – 8.01 (m, 2H), 7.78 (d, J = 5.3 Hz, 1H), 7.67 – 7.48 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.31, 162.03, 158.56, 150.14, 145.53, 145.43, 144.34, 135.99, 131.36, 129.01, 127.22, 116.28; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 235.0996, C₁₄H₁₁N₄⁺ requires 235.0978.

6-(4-Methoxyphenyl)pyrimidine-2(1H)-thione (5ag)



Prepared according to a modified general procedure B using 4-(4-methoxyphenyl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (165 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), thiourea (91.3 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). Upon completion, AcOH (200 μ L, 3.50 mmol) was added to the reaction mixture at room temperature. The product was filtered and washed with ice-cold EtOH to provide the title compound as a yellow solid (49 mg, 0.23 mmol, 56% yield). mp 219-225 $^{\circ}$ C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 2889, 1583, 1436, 1264, 1157, 1024, 794; ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{SO}$) δ 13.52 (s, 1H), 8.26 – 8.09 (m, 2H), 8.00 (d, J = 6.6 Hz, 1H), 7.38 (d, J = 6.7 Hz, 1H), 7.09 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{SO}$) δ 181.14, 165.65, 163.30, 146.85, 130.47, 127.80, 114.90, 105.31, 56.00; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 219.0596, $\text{C}_{11}\text{H}_{11}\text{N}_2\text{OS}^+$ requires 219.0587.

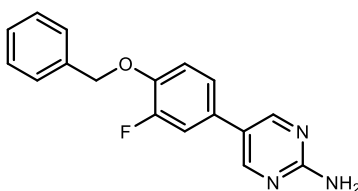
5-Phenylpyrimidin-2-amine (5ah)



Prepared according to general procedure D using 5-phenylpyrimidine (62.5 mg, 0.40 mmol), TiF_2O (67 μ L, 0.40 mmol), *para*-nitro (*p*- NO_2) aniline (56 mg, 0.40 mmol), collidine (53 μ L, 0.40 mmol), EtOAc (2 mL), piperidine (118 μ L, 1.20 mmol), EtOH (2 mL), guanidine hydrochloride

(764 mg, 8.00 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The residue was purified by flash chromatography (silica gel: 1:55:44 AcOH:EtOAc:hexanes) to provide the pure title compound as an off-white solid (35 mg, 0.21 mmol, 51% yield). mp 161-164 $^{\circ}$ C. ^1H NMR (400 MHz, CDCl_3) δ 8.53 (s, 2H), 7.51 – 7.40 (m, 4H), 7.35 (t, J = 7.0 Hz, 1H), 5.52 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.39, 156.50, 135.30, 129.17, 127.57, 126.05, 124.89; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 172.0869, $\text{C}_{10}\text{H}_{10}\text{N}_3^+$ requires 172.0869. Spectra matched literature values.²³

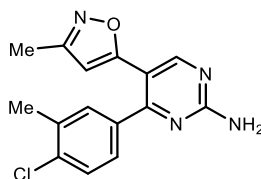
5-(4-(Benzyloxy)-3-fluorophenyl)pyrimidin-2-amine (5ai)



Prepared according to a modified general procedure D using 5-(4-(benzyloxy)-3-fluorophenyl)pyrimidine (112 mg, 0.400 mmol), TiF_4 (67 μ L, 0.40 mmol), *p*- NO_2 aniline (56 mg, 0.40 mmol), collidine (53 μ L, 0.40 mmol), EtOAc (2 mL), piperidine (118 μ L, 1.20 mmol), EtOH (2 mL), guanidine hydrochloride (472 mg, 8.00 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The residue was purified by flash chromatography (silica gel: 60% EtOAc in hexanes) to provide the pure title compound as an off-white solid (53 mg, 0.18 mmol, 45% yield). mp 78-80 $^{\circ}$ C. IR $_{\text{max}}$ /cm $^{-1}$ (solid): 3318, 3183, 1615, 1555, 1471, 1091, 820, 756; ^1H NMR (400 MHz, CDCl_3) δ 8.38 (s, 2H), 7.43 – 7.35 (m, 2H), 7.35 – 7.29 (m, 2H), 7.29 – 7.23 (m, 1H), 7.21 – 7.09 (m, 1H), 7.05 (dd, J = 8.4, 2.7 Hz, 1H), 6.98 (t, J = 8.4 Hz, 1H), 5.23 (s, 2H), 5.10 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.08, 156.18, 154.47, 152.01, 146.30 (d, J = 10.9 Hz), 136.33,

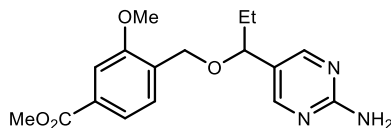
128.69, 128.23, 127.44, 123.81 (d, $J = 2.2$ Hz), 121.72 (d, $J = 3.6$ Hz), 116.38 (d, $J = 2.5$ Hz), 114.04 (d, $J = 19.3$ Hz), 71.51. ^{19}F NMR (375 MHz, CDCl_3) δ -132.44 (dd, $J = 11.8, 8.3$ Hz). m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 296.1198, $\text{C}_{17}\text{H}_{14}\text{FN}_3\text{O}^+$ requires 296.1199.

4-(4-Chloro-3-methylphenyl)-5-(3-methylisoxazol-5-yl)pyrimidin-2-amine (5aj)



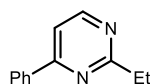
Prepared according to general procedure B using 4-(4-chloro-3-methylphenyl)-5-(3-methylisoxazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (205 mg, 0.40 mmol), piperidine (118 μL , 1.20 mmol), EtOH (2 mL), guanidine hydrochloride (71.0 mg, 1.20 mmol), and NaOEt (747 μL , 2.00 mmol, as a 21% soln. in EtOH). The residue was purified by flash chromatography (silica gel: 60% EtOAc in hexanes. A second column was needed (70% EtOAc in hexanes)) to provide the pure title compound as a light-yellow solid (69 mg, 0.23 mmol, 58% yield). mp 181-183 $^{\circ}\text{C}$. $\text{IR}_{\text{max}}/\text{cm}^{-1}$ (solid): 3361, 3148, 1660, 1577, 1476, 1045, 820, 739. ^1H NMR (400 MHz, CDCl_3) δ 8.57 (s, 1H), 7.28 (d, $J = 8.3$ Hz, 2H), 7.08 (d, $J = 10.5$ Hz, 1H), 5.74 (s, 2H), 5.53 (s, 1H), 2.31 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 166.01, 164.89, 162.71, 159.97, 158.91, 136.63, 136.28, 135.96, 130.81, 129.16, 127.10, 111.12, 103.15, 20.09, 11.46. m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 301.0861, $\text{C}_{20}\text{H}_{15}\text{ClN}_4\text{O}^+$ requires 301.0778.

Methyl 4-((1-(2-aminopyrimidin-5-yl)propoxy)methyl)-3-methoxybenzoate (5ak)



Prepared according to a modified general procedure D using methyl 3-methoxy-4-((1-(pyrimidin-5-yl)propoxy)methyl)benzoate (63.3 mg, 0.20 mmol), TiF_2O (34 μL , 0.20 mmol), *p*- NO_2 -aniline (27.6 mg, 0.20 mmol), collidine (26 μL , 0.20 mmol), EtOAc (1 mL), then piperidine (60 μL , 0.60 mmol), MeOH (1 mL), guanidine hydrochloride (382 mg, 4.00 mmol), and NaOMe (54.0 mg, 1.00 mmol). The residue was purified by flash chromatography (silica gel: 1:70:29 AcOH:EtOAc:hexanes). A second column was needed (70 to 100% EtOAc in hexanes) to provide the pure title compound as a white solid (17 mg, 0.05 mmol, 26% yield). mp 124-128 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3319, 3172, 2967, 1717, 1283, 1228, 1077, 761; ^1H NMR (400 MHz, CDCl_3) δ 8.26 (s, 2H), 7.64 (d, J = 7.8 Hz, 1H), 7.51 – 7.44 (m, 2H), 5.25 (s, 2H), 4.58 – 4.33 (m, 2H), 4.12 (t, J = 6.8 Hz, 1H), 3.91 (s, 3H), 3.83 (s, 3H), 1.92 (dp, J = 14.5, 7.3 Hz, 1H), 1.70 (dp, J = 14.1, 7.2 Hz, 1H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.13, 162.99, 157.53, 156.74, 132.18, 130.47, 128.25, 124.85, 122.11, 110.81, 79.56, 65.37, 55.52, 52.29, 30.68, 10.22; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 332.1609, $\text{C}_{17}\text{H}_{22}\text{N}_3\text{O}_4^+$ requires 332.1605.

2-Ethyl-4-phenylpyrimidine (5al)



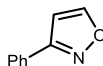
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), propionimidamide hydrochloride (130 mg, 1.20 mmol), and NaOEt (747 μ L, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 25% EtOAc in hexanes) to provide the title compound as a clear oil (52 mg, 0.28 mmol, 70% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2972, 1569, 1546, 1432, 840, 764, 690, 627; ^1H NMR (400 MHz, CDCl_3) δ 8.66 (d, $J = 5.3$ Hz, 1H), 8.11 – 8.05 (m, 2H), 7.79 – 6.76 (m, 4H), 3.05 (q, $J = 7.6$ Hz, 2H), 1.43 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.38, 163.87, 157.50, 137.08, 130.77, 128.92, 127.17, 113.95, 32.85, 12.68; m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 185.1078, $\text{C}_{12}\text{H}_{13}\text{N}_2^+$ requires 185.1078.

3-Phenylisoxazole and 5-phenylisoxazole (6a)



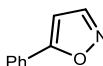
Prepared according to general procedure C using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), hydroxylamine hydrochloride (139 mg, 1.20 mmol), and concentrated aqueous HCl (333 μ L, 4.00 mmol). Crude NMR showed 22% of 3-phenyl and 53% of 5-phenyl isoxazole relative to triphenylmethane internal standard. The crude material was purified by flash chromatography (silica gel: 10% hexanes in toluene) to provide pure regioisomers.

3-Phenylisoxazole (6a, minor)



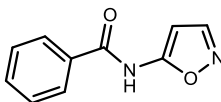
Clear oil (6.00 mg, 0.04 mmol, 10%). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3124, 3063, 2927, 1552, 1457, 1395, 1123, 878, 762, 699; ^1H NMR (400 MHz, CDCl_3) δ 8.46 (d, $J = 1.7$ Hz, 1H), 7.94 – 7.73 (m, 2H), 7.53 – 7.40 (m, 3H), 6.67 (d, $J = 1.7$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.54, 158.89, 130.06, 128.97, 128.83, 126.93, 102.47. Spectra matched literature values.²⁴

5-Phenylisoxazole (6a, major)



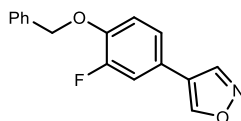
Clear oil (30 mg, 0.21 mmol, 52%). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3062, 1571, 1458, 1197, 817, 794, 761, 689; ^1H NMR (400 MHz, CDCl_3) δ 8.28 (d, $J = 1.9$ Hz, 1H), 7.84 – 7.71 (m, 2H), 7.49 – 7.37 (m, 3H), 6.51 (d, $J = 1.9$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.45, 150.92, 130.29, 129.09, 127.36, 125.95, 98.75. Spectra matched literature values.²⁵

N-(Isoxazol-5-yl)benzamide (6b)



Prepared according to a modified general procedure C using 4-benzamido-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (170 mg, 0.40 mmol), EtOH (2.00 mL), piperidine (119 μ L, 1.20 mmol), hydroxylamine hydrochloride (83.4 mg, 1.20 mmol), and concentrated aqueous HCl (333 μ L, 4.00 mmol) at 40 °C. The crude material was purified by flash chromatography (silica gel: 0-35% EtOAc in hexanes) to provide the title compound as a white solid (46 mg, 0.25 mmol, 61% yield). mp 134-137 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3243, 3216, 3130, 3054, 3006, 1687, 1527, 1499, 1272, 773, 686; ^1H NMR (400 MHz, CDCl_3) δ 9.66 (s, 1H), 8.16 (d, J = 1.9 Hz, 1H), 7.92 (d, J = 7.3 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H), 6.52 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.61, 160.71, 152.00, 132.98, 132.42, 128.96, 127.61, 88.59; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 189.0667, $\text{C}_{10}\text{H}_9\text{N}_2\text{O}_2^+$ requires 189.0659.

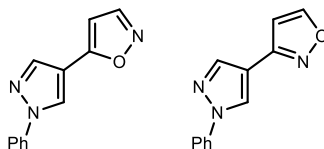
4-(4-(Benzyloxy)-3-fluorophenyl)isoxazole (6c)



Prepared according to a modified general procedure E using 5-(4-(benzyloxy)-3-fluorophenyl)pyrimidine (112 mg, 0.40 mmol), TiF_4 (67 μ L, 0.40 mmol), $p\text{-NO}_2$ aniline (56.0 mg, 0.40 mmol), collidine (53 μ L, 0.40 mmol), EtOAc (2 mL), piperidine (118 μ L, 1.20 mmol), EtOH (2 mL), hydroxylamine hydrochloride (559 mg, 8.00 mmol), and concentrated HCl (333 μ L, 4.00 mmol). The residue was purified by flash chromatography (silica gel: 80% EtOAc in hexanes. A second column was needed (15% EtOAc in hexanes)) to provide the pure title compound as a yellow solid (43 mg, 0.16 mmol, 40% yield). mp 102-104 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid):

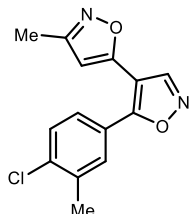
1603, 1513, 1283, 1262, 1114, 986, 811, 753, 703; ^1H NMR (400 MHz, CDCl_3) δ 8.51 (s, 1H), 8.40 (s, 1H), 7.40 – 7.34 (m, 2H), 7.34 – 7.29 (m, 2H), 7.29 – 7.23 (m, 1H), 7.19 – 7.10 (m, 1H), 7.09 – 7.02 (m, 1H), 6.95 (t, $J = 8.5$ Hz, 1H), 5.09 (s, 2H). ^{19}F NMR (375 MHz, CDCl_3) δ -132.36 (dd, $J = 11.8, 8.3$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 154.31, 153.07, 151.85, 147.83, 146.53 (d, $J = 10.7$ Hz), 136.20, 128.71, 128.28, 127.45, 122.30 (d, $J = 3.6$ Hz), 116.31 (d, $J = 2.4$ Hz), 114.68, 114.49, 71.46. m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 270.2727, $\text{C}_{16}\text{H}_{12}\text{FNO}_2^+$ requires 270.2754.

5-(1-Phenyl-1H-pyrazol-4-yl)isoxazole and 3-(1-phenyl-1H-pyrazol-4-yl)isoxazole (6d, major and minor)



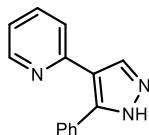
Prepared according to general procedure E using 4-(1-phenyl-1H-pyrazol-4-yl)pyrimidine (**6n**) (88.9 mg, 0.40 mmol), EtOAc (2 mL), TiF_2O (67 μL , 0.40 mmol), aniline (36 μL , 0.40 mmol), collidine (53 μL , 0.40 mmol), then EtOH (2 mL), hydroxylamine hydrochloride (139 mg, 2.00 mmol), and concentrated aqueous HCl (333 μL , 10.0 mmol). The crude material was purified by flash chromatography (silica gel: 1:29:70 AcOH:EtOAc:hexanes) to provide the title compounds as a 1:3 mixture of 3-(1-phenyl-1H-pyrazol-4-yl)isoxazole: 5-(1-phenyl-1H-pyrazol-4-yl)isoxazole (tan solid, 44 mg, 0.21 mmol, 52% yield). mp 131-134°C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3111, 3055, 1633, 1598, 1501, 1471, 1374, 1214, 1203, 955, 865, 749, 688; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 212.0827, $\text{C}_{12}\text{H}_{10}\text{N}_3\text{O}^+$ requires 212.0818.

4-(4-Chloro-3-methylphenyl)-3'-methyl-3,5'-biisoxazole (6e)



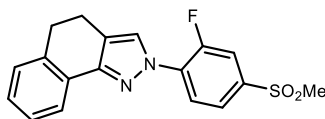
Prepared according to general procedure C using 4-(4-chloro-3-methylphenyl)-5-(3-methylisoxazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (205 mg, 0.40 mmol), piperidine (118 μ L, 1.20 mmol), EtOH (2 mL), hydroxylamine hydrochloride (83.0 mg, 1.20 mmol), and concentrated HCl (333 μ L, 4.00 mmol). The residue was purified by flash chromatography (silica gel: 80% dichloromethane in hexanes) to provide the pure title compound as a tan solid (80 mg, 0.30 mmol, 73% yield). mp 69-72 $^{\circ}$ C. IR $_{\text{max}}$ /cm $^{-1}$ (solid): 2922, 1650, 1416, 1152, 1045, 922, 781, 674. ^1H NMR (400 MHz, CDCl_3) δ 8.48 (s, 1H), 7.62 (s, 1H), 7.51 (d, J = 8.3 Hz, 1H), 7.40 (d, J = 8.3 Hz, 1H), 6.16 (s, 1H), 2.38 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 164.64, 159.55, 159.24, 149.04, 136.59, 136.14, 129.17, 128.70, 125.47, 123.89, 103.80, 101.72, 19.12, 10.38. m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 275.7075; $\text{C}_{14}\text{H}_{11}\text{ClN}_2\text{O}_2^+$ requires 275.7040.

2-(5-Phenyl-1H-pyrazol-4-yl)pyridine (6f)



Prepared according to general procedure C using 1,4-diphenyl-5-(pyridin-2-yl)pyrimidin-1-ium trifluoromethanesulfonate (184 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), hydrazine hydrate (58 μ L, 1.20 mmol), and concentrated aqueous HCl (333 μ L, 4.00 mmol). The crude material was purified by flash chromatography (silica gel: 50-100% EtOAc in hexanes) to provide the title compound as a white solid (80 mg, 0.36 mmol, 90% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3139, 2919, 1590, 1509, 1429, 768, 726, 696; ^1H NMR (400 MHz, CDCl_3) δ 8.64 – 8.48 (m, 1H), 7.92 (s, 1H), 7.47 (qd, $J = 3.9, 1.8$ Hz, 3H), 7.34 – 7.23 (m, 3H), 7.14 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.11 – 7.01 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 152.72, 149.51, 145.55, 136.23, 135.15, 131.71, 128.72, 128.62, 128.47, 122.52, 121.21, 119.71; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 222.1049, $\text{C}_{14}\text{H}_{12}\text{N}_3^+$ requires 222.1026.

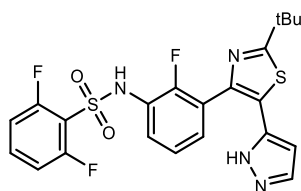
1-(3-Fluoro-4-(methylsulfonyl)phenyl)-4,5-dihydro-1H-benzo[g]indazole (6g)



Prepared according to general procedure C using 3-phenyl-5,6-dihydrobenzo[h]quinazolin-3-ium trifluoromethanesulfonate (163 mg, 0.40 mmol), piperidine (118 μ L, 1.20 mmol), EtOH (2 mL), (3-fluoro-4-(methylsulfonyl)phenyl)hydrazine (245 mg, 0.40 mmol), and concentrated HCl (333 μ L, 4.00 mmol). The residue was purified by flash chromatography (silica gel: 30% EtOAc in

hexanes. A second column was needed (29:70:1 EtOAc:hexanes:NEt₃) to provide the pure title compound as an orange solid (56. mg, 0.16 mmol, 41% yield). mp 145-146 °C. IR_{max}/cm⁻¹ (solid): 3359, 2921, 1515, 1414, 1312, 1233, 1140, 760, 607. ¹H NMR (400 MHz, CDCl₃) δ 7.83 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.75 (dt, *J* = 8.4, 6.9 Hz, 2H), 7.59 (s, 1H), 7.24 (d, *J* = 8.6 Hz, 1H), 7.12 (dd, *J* = 15.0, 1.4 Hz, 1H), 6.98 (td, *J* = 7.6, 1.5 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 3.07 (s, 3H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.71 (t, *J* = 7.4 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 157.55, 154.96, 141.78 (d, *J* = 5.9 Hz), 139.76, 137.19, 133.98 (d, *J* = 11.9 Hz), 129.79, 128.90, 128.13, 126.77, 126.27, 124.11 (d, *J* = 4.3 Hz), 121.42, 120.39, 116.77 (d, *J* = 22.9 Hz), 44.48, 30.33, 19.69. ¹⁹F NMR (375 MHz, CDCl₃) δ -115.70. *m/z* HRMS (ESI) found [M+H]⁺ 343.0920, C₁₈H₁₅FN₂O₂S⁺ requires 343.0916.

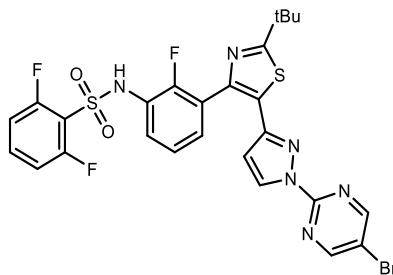
***N*-(3-(2-(*Tert*-butyl)-5-(1H-pyrazol-5-yl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (6h)**



Prepared according to general procedure C using 4-(2-(*tert*-butyl)-4-(3-((2,6-difluorophenyl)sulfonamido)-2-fluorophenyl)thiazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (183 mg, 0.25 mmol), EtOH (1.25 mL), piperidine (75 μL, 0.75 mmol), hydrazine hydrate (36 μL, 0.75 mmol), and concentrated aqueous HCl (208 μL, 1.25 mmol). The crude material was purified by flash chromatography (silica gel: 55% EtOAc in hexanes) to

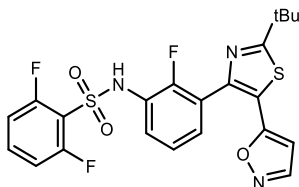
provide the title compound as a white solid (106 mg, 0.22 mmol, 86% yield). mp 211-214 °C; ; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3246, 3154, 2934, 1614, 1589, 1470, 1356, 1185, 1005, 788, 758; ^1H NMR (400 MHz, CD_3CN) δ 11.10 (s, 1H), 8.37 (s, 1H), 7.65 – 7.51 (m, 2H), 7.43 (d, $J = 2.4$ Hz, 1H), 7.28 (ddd, $J = 8.2, 6.4, 1.9$ Hz, 1H), 7.21 (td, $J = 7.8, 0.9$ Hz, 1H), 7.07 (t, $J = 8.8$ Hz, 2H), 5.55 (d, $J = 2.4$ Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, CD_3CN) δ 179.82, 160.45 (dd, $J = 257.7, 3.8$ Hz), 154.00 (d, $J = 248.7$ Hz), 143.33, 136.92 (t, $J = 11.3$ Hz), 131.07 (br), 130.66 (d, $J = 2.8$ Hz), 129.14, 127.01, 125.76 (d, $J = 14.9$ Hz), 125.53 (d, $J = 4.7$ Hz), 124.84 (d, $J = 13.5$ Hz), 117.75 (t, $J = 15.9$ Hz), 114.17 (dd, $J = 23.1, 3.6$ Hz), 103.31, 79.10, 38.41, 30.91; ^{19}F NMR (375 MHz, CD_3CN) δ -108.50 (d, $J = 5.6$ Hz, 2F), -127.69 (1F); m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 493.1028, $\text{C}_{22}\text{H}_{20}\text{F}_3\text{N}_4\text{O}_2\text{S}_2^+$ requires 493.0974.

***N*-(3-(5-(1-(5-Bromopyrimidin-2-yl)-1H-pyrazol-3-yl)-2-(*tert*-butyl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (6i)**



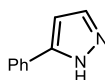
Prepared according to general procedure C using 4-(2-(*tert*-butyl)-4-(3-((2,6-difluorophenyl)sulfonamido)-2-fluorophenyl)thiazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (183 mg, 0.25 mmol), EtOH (1.25 mL), piperidine (75 μ L, 0.75 mmol), 5-bromo-2-hydrazinopyrimidine (142 mg, 0.75 mmol), and concentrated aqueous HCl (208 μ L, 1.25 mmol). The crude material was purified by flash chromatography (1:49:50 AcOH: EtOAc: hexanes) followed by a preparative TLC (2% MeOH in dichloromethane) to provide the title compound as a white fluffy solid (77 mg, 0.12 mmol, 47% yield). mp 215-221 $^{\circ}$ C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3069, 2957, 1613, 1518, 1420, 1171, 1004, 784, 634; ^1H NMR (400 MHz, CDCl_3) δ 8.52 (s, 2H), 7.72 (d, J = 1.7 Hz, 1H), 7.49 (dddd, J = 10.2, 8.4, 6.6, 2.3 Hz, 2H), 7.17 (s, 1H), 7.05 – 6.88 (m, 4H), 6.40 (d, J = 1.7 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 181.78, 159.74 (dd, J = 258.2, 3.5 Hz), 158.86, 158.57, 154.84, 150.05 (d, J = 248.9 Hz), 146.00 (d, J = 1.9 Hz), 142.32, 135.16 (t, J = 11.1 Hz), 134.53 (d, J = 1.4 Hz), 127.55 (d, J = 2.8 Hz), 124.59 (d, J = 12.5 Hz), 124.47 (d, J = 4.5 Hz), 123.14 (d, J = 13.2 Hz), 121.09, 117.37, 116.79 (t, J = 15.2 Hz), 113.19 (dd, J = 23.1, 3.7 Hz), 112.59, 38.01, 30.81; ^{19}F NMR (375 MHz, CDCl_3) δ -106.92 – -107.03 (m, 2F), -132.07 (tt, J = 7.0, 3.6 Hz, 1F); m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 649.0300, $\text{C}_{26}\text{H}_{21}\text{BrF}_3\text{N}_6\text{O}_2\text{S}_2^+$ requires 649.029

***N*-(3-(2-(*Tert*-butyl)-5-(isoxazol-5-yl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (6j)**



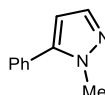
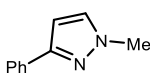
Prepared according to general procedure C using 4-(2-(*tert*-butyl)-4-(3-((2,6-difluorophenyl)sulfonamido)-2-fluorophenyl)thiazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (183 mg, 0.25 mmol), EtOH (1.25 mL), piperidine (75 μ L, 0.75 mmol), hydroxylamine hydrochloride (52.1 mg, 0.75 mmol), and concentrated aqueous HCl (208 μ L, 1.25 mmol). The crude material was purified by flash chromatography (silica gel: 35% EtOAc in hexanes) to provide the title compound as a 16:1 mixture of regioisomers (88 mg, 0.18 mmol, 70% yield). Reported spectra are of major isomer. mp 144-147 $^{\circ}$ C; IR ν_{max} /cm $^{-1}$ (solid): 3081, 1609, 1584, 1461, 1365, 1170, 1004, 792, 634; ^1H NMR (400 MHz, CDCl_3) δ 8.12 (d, J = 1.9 Hz, 1H), 7.70 (td, J = 7.8, 1.7 Hz, 1H), 7.50 (tt, J = 8.5, 5.9 Hz, 1H), 7.30 (ddd, J = 8.1, 6.5, 1.8 Hz, 1H), 7.19 (td, J = 8.0, 1.0 Hz, 1H), 6.99 (t, J = 8.7 Hz, 2H), 5.80 (d, J = 1.9 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 182.82, 159.83 (dd, J = 259.8, 3.5 Hz), 159.02, 151.00 (d, J = 247.5 Hz), 150.70, 146.01, 135.41 (t, J = 11.1 Hz), 128.15 (d, J = 2.5 Hz), 125.13 (d, J = 4.5 Hz), 124.76 (d, J = 12.5 Hz), 123.23 (d, J = 13.5 Hz), 123.14, 120.59, 116.94 (t, J = 15.3 Hz), 113.31 (dd, J = 23.2, 3.6 Hz), 100.42, 38.24, 30.79; ^{19}F NMR (376 MHz, CDCl_3) δ -106.87 (2F), -130.10 (1F); m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 494.0826, $\text{C}_{22}\text{H}_{19}\text{F}_3\text{N}_3\text{O}_3\text{S}_2^+$ requires 494.0814.

5-Phenyl-1H-pyrazole (6k)



Prepared according to general procedure C using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.400 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), hydrazine hydrate (53 μ L, 1.20 mmol), and concentrated aqueous HCl (333 μ L, 4.00 mmol). The crude material was purified by flash chromatography (silica gel: 1:50:49 Et₃N:EtOAc:hexanes) to provide the title compound as a white powder (50 mg, 0.35 mmol, 86% yield). mp 72-74 °C; IR ν_{max} /cm⁻¹ (solid): 3105, 3065, 2957, 2847, 1498, 1469, 1444, 1095, 958, 826, 755, 690; ¹H NMR (400 MHz, CDCl₃) δ 12.06 (s, 1H), 7.77 (d, J = 7.0 Hz, 2H), 7.61 (d, J = 2.2 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.37 – 7.29 (m, 1H), 6.62 (d, J = 2.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 149.22, 133.25, 132.21, 128.81, 128.06, 125.89, 102.68; m/z HRMS (DART) found [M+H]⁺ 145.0799, C₉H₉N₂⁺ requires 145.0760. Spectra matched literature values.⁸

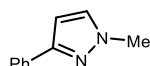
1-Methyl-3-phenyl-1H-pyrazole and 1-methyl-5-phenyl-1H-pyrazole (6l)



Prepared according to general procedure C using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), methylhydrazine (63 μ L, 1.20 mmol), and concentrated aqueous HCl (333 μ L, 4.00 mmol). Crude

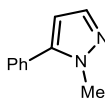
NMR showed 30% of 3-phenyl- and 52% of 5-phenyl-1-methyl-1H-pyrazole relative to triphenylmethane internal standard. The crude material was purified by flash chromatography (silica gel: 15% EtOAc in toluene) to provide pure regioisomers.

1-Methyl-3-phenyl-1H-pyrazole (6l, minor)



Yellow solid (12 mg, 0.07 mmol, 19%). mp 45-57 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.80 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 2.3 Hz, 1H), 7.32 – 7.27 (m, 1H), 6.54 (d, *J* = 2.3 Hz, 1H), 3.95 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 151.61, 133.56, 131.37, 128.62, 127.55, 125.54, 102.85, 39.05. Spectra matched literature values.²⁶

1-Methyl-5-phenyl-1H-pyrazole (6l, major)



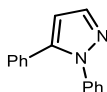
Yellow oil (23 mg, 0.15 mmol, 37%). ¹H NMR (400 MHz, CDCl₃) δ 7.51 (d, *J* = 1.9 Hz, 1H), 7.48 – 7.34 (m, 5H), 6.30 (d, *J* = 1.9 Hz, 1H), 3.89 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 143.58, 138.53, 130.79, 128.77, 128.68, 128.43, 106.05, 37.49. Spectra matched literature values.²⁷

1,5-Diphenyl-1H-pyrazole and 1,3-diphenyl-1H-pyrazole (6m)



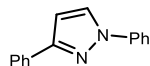
Prepared according to general procedure C using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 μ L, 1.20 mmol), phenylhydrazine (118 μ L, 1.20 mmol), and concentrated aqueous HCl (333 μ L, 4.00 mmol). The crude material was purified by flash chromatography (silica gel: 0-10% EtOAc in toluene) to provide pure regioisomers.

1,5-Diphenyl-1H-pyrazole (6m, minor)



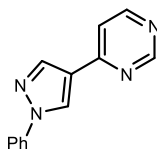
Orange solid (27 mg, 0.12 mmol, 30%). mp 79-82 $^{\circ}$ C IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3061, 2922, 1598, 1504, 1359, 1045, 954, 749, 684; ^1H NMR (400 MHz, CDCl_3) δ 7.96 (d, J = 2.5 Hz, 1H), 7.95 – 7.89 (m, 2H), 7.78 (dt, J = 7.8, 1.2 Hz, 2H), 7.51 – 7.40 (m, 4H), 7.37 – 7.32 (m, 1H), 7.32 – 7.27 (m, 1H), 6.79 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 152.94, 140.26, 133.14, 129.43, 128.66, 128.04, 127.99, 126.34, 125.85, 119.07, 105.04; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 221.1129, $\text{C}_{15}\text{H}_{13}\text{N}_2^+$ requires 221.1073. Spectra matched literature values.⁸

1,3-Diphenyl-1H-pyrazole (6m, major)



Brown solid (43 mg, 0.20 mmol, 49%). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3960, 2998, 1592, 1499, 1450, 1378, 756, 687; ^1H NMR (400 MHz, CDCl_3) δ 7.64 (d, $J = 1.9$ Hz, 1H), 7.27 – 7.19 (m, 8H), 7.15 (ddd, $J = 5.0, 4.3, 2.8$ Hz, 2H), 6.42 (d, $J = 1.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.08, 140.24, 140.06, 130.56, 128.93, 128.79, 128.50, 128.27, 127.50, 125.25, 107.88; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 221.1124, $\text{C}_{15}\text{H}_{13}\text{N}_2^+$ requires 221.1073. Spectra matched literature values.²⁸

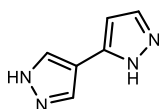
4-(1-Phenyl-1H-pyrazol-4-yl)pyrimidine (6n)



Prepared according to a modified general procedure E using 2,4,6-trimethylaniline instead of aniline. Used 4-5'-bipyrimidine (158 mg, 1.00 mmol), EtOAc (5 mL), Ti_2O (168 μL , 1.00 mmol), 2,4,6-trimethylaniline (421 μL , 1.20 mmol), collidine (132 μL , 1.00 mmol), then EtOH (2 mL), phenylhydrazine (295 μL , 5.00 mmol), and concentrated aqueous HCl (833 μL , 10.0 mmol). The crude material was purified by flash chromatography (silica gel: 0.5:1:98.5 AcOH:MeOH: CH_2Cl_2) to provide the title compound as an orange solid (115 mg, 0.52 mmol, 52% yield). mp 106-112°C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3054, 2922, 1584, 1505, 1388, 1284, 1180, 967, 951, 755, 687, 658; ^1H NMR (400 MHz, CDCl_3) δ 9.15 (d, $J = 1.4$ Hz, 1H), 8.68 (d, $J = 5.3$ Hz, 1H), 8.61 (s, 1H), 8.24 (s, 1H), 7.75 (d, $J = 7.5$ Hz, 2H), 7.54 – 7.46 (m, 3H), 7.36 (t, $J = 7.4$ Hz,

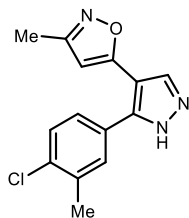
1H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.88, 158.70, 156.87, 139.94, 139.63, 129.77, 127.61, 127.11, 122.91, 119.58, 116.54; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 233.0989, $\text{C}_{13}\text{H}_{11}\text{N}_4^+$ requires 223.0978.

1'H, 2H-3,4'-Bipyrazole (6o)



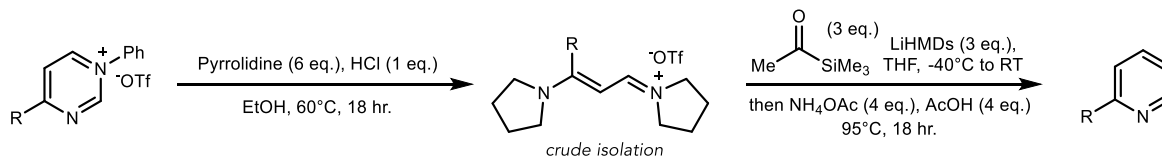
Prepared according to a modified general procedure E using 2,4,6-trimethylaniline instead of aniline. Used 4-5'-bipyrimidine (126 mg, 0.80 mmol), EtOAc (4 mL), Ti_2O (270 μL , 1.60 mmol), 2,4,6-trimethylaniline (450 μL , 3.20 mmol), collidine (212 μL , 1.60 mmol), then EtOH (4 mL), hydrazine hydrate (194 μL , 4.00 mmol), and concentrated aqueous HCl (666 μL , 8.00 mmol). The crude material was purified by flash chromatography (silica gel: 1:10:89 AcOH:MeOH: CH_2Cl_2) to provide the title compound as a pale-brown solid (25 mg, 0.19 mmol, 24% yield). mp 233-236 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (solid): 3122, 3038, 2884, 2232, 1605, 1373, 765; ^1H NMR (400 MHz, MeOD) δ 7.93 (s, 2H), 7.59 (d, $J = 2.2$ Hz, 1H), 6.46 (d, $J = 2.2$ Hz, 1H); ^{13}C NMR (HCl salt, 100 MHz, D_2O and 1 equiv. aqueous HCl for solubility) δ 139.63, 134.13, 132.67, 109.08, 104.07; m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 135.0661, $\text{C}_6\text{H}_7\text{N}_4^+$ requires 135.0665.

5-(4-(4-Chloro-3-methylphenyl)-1H-pyrazol-3-yl)-3-methylisoxazole (6p)



Prepared according to general procedure C using 4-(4-chloro-3-methylphenyl)-5-(3-methylisoxazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (205 mg, 0.40 mmol), piperidine (118 μ L, 1.20 mmol), EtOH (2 mL), hydrazine hydrate (38 μ L, 1.20 mmol), and concentrated HCl (333 μ L, 4.00 mmol). The residue was purified by flash chromatography (silica gel: 20 to 100% EtOAc in hexanes) to provide the pure title compound as a tan solid (79 mg, 0.29 mmol, 72% yield). mp 100-104 $^{\circ}$ C. IR $_{\text{max}}$ /cm $^{-1}$ (solid): 3166, 3119, 2936, 1623, 1436, 1413, 1045, 918, 784, 729. ^1H NMR (400 MHz, CDCl_3) δ 7.90 (s, 1H), 7.34 (dd, J = 11.3, 3.1 Hz, 2H), 7.25 (d, J = 2.0 Hz, 1H), 5.85 (s, 1H), 2.34 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 163.62, 160.05, 136.76, 135.53, 134.26, 133.51, 130.89, 129.48, 128.98, 127.22, 108.26, 100.53, 20.09, 11.45. m/z HRMS (DART) found $[\text{M}+\text{H}]^+$ 274.0743, $\text{C}_{14}\text{H}_{12}\text{ClN}_3\text{O}^+$ requires 274.0669.

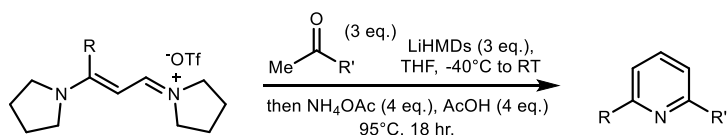
General Procedure F: Vinamidium Formation and Pyridine Formation



An oven dried 8 mL vial (≤ 0.5 mmol scale) or a round bottom flask (> 0.5 mmol scale) equipped with a stir bar was charged with the pyrimidinium salt (1.0 equiv), EtOH (0.2 M), HCl (1.0 equiv, 4.0M in Dioxane), and pyrrolidine (6.0 equiv). The reaction was stirred for 18 hours at 60 $^{\circ}$ C. Next, the reaction was concentrated *in vacuo* and diluted with a 1:3 solution of isopropyl alcohol

(iPrOH):CH₂Cl₂ and washed with a 0.1M aqueous solution of HCl (2x). The aqueous layer was extracted with iPrOH:CH₂Cl and the combined organic extract was washed with brine (1x) and dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was dissolved in a minimal amount of CH₂Cl₂ and added dropwise to a stirring solution of 1:3 Et₂O:hexanes, then chilled in a -20 °C freezer (approx. 1 hour) and decanted to provide crude vinamidinium salt. In a separate flask, acetyltrimethylsilane (3.0 equiv) was added to THF (0.2M) and cooled to -40 °C before adding lithium bis(trimethylsilyl)amide (LiHMDS, 3.0 equiv). The reaction was stirred for 30 minutes before adding vinamidinium (a minimal amount of THF can be used to dissolve the vinamidinium salt if unable to transfer as a solid), then warmed to room temperature under ambient. Next, NH₄OAc (4 equiv) and acetic acid (4 equiv) were added, and the reaction was heated to 95 °C for 18 hours. After cooling to room temperature, the reaction was quenched with sat. NaHCO₃, extracted into EtOAc (3x). The combined organic extract was washed with water (1x), brine (1x), and dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

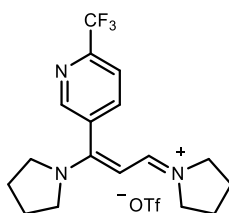
General Procedure G: Pyridine Formation from Isolated Vinamidinium Salt



An oven dried 8 mL vial (≤ 0.5 mmol scale) or a round bottom flask (> 0.5 mmol scale) equipped with a stir bar was charged with the ketone or acetyltrimethylsilane (3.0 equiv) was added to THF (0.2M) and cooled to -40 °C before adding lithium bis(trimethylsilyl)amide (LiHMDS, 3.0 equiv). The reaction was stirred for 30 minutes before adding vinamidinium (1.0 equiv), then warmed to room temperature under ambient. Next, NH₄OAc (4 equiv) and acetic acid (4 equiv) were added, and the reaction was heated to 95 °C for 18 hours. After cooling to room temperature, the reaction

was quenched with sat. NaHCO₃, extracted into EtOAc (3x). The combined organic extract was washed with water (1x), brine (1x), and dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

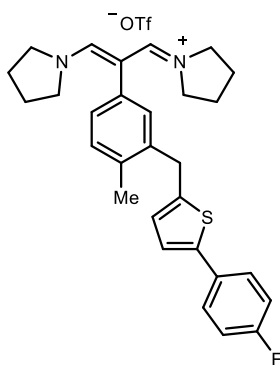
(Z)-1-(3-(Pyrrolidin-1-yl)-3-(6-(trifluoromethyl)pyridin-3-yl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate



An oven dried 8 mL vial equipped with a stir bar was charged with 1-phenyl-4-(6-(trifluoromethyl)pyridin-3-yl)pyrimidin-1-ium trifluoromethanesulfonate (180 mg, 0.40 mmol, 1 equiv), and placed under a nitrogen atmosphere. Then EtOH (2.0 mL, 0.2 M), concentrated aqueous HCl (33 μ L, 0.40 mmol, 1 equiv), and pyrrolidine (100 μ L, 2.4 mmol, 6 equiv) were added. The reaction was heated to 60 °C for 18 hours. After cooling to room temperature, the reaction was concentrated and dissolved in a minimal amount of CH₂Cl₂ (1 mL). The crude reaction was added to an equal volume of 3:1 hexanes:Et₂O. The precipitate was filtered, then purified by flash chromatography (silica gel: 1:6:93 AcOH:MeOH:CH₂Cl₂) to provide the pure title compound as a pale yellow solid (80 mg, 0.17 mmol, 43% yield). mp 100-102 °C. IR_ν_{max}/cm⁻¹ (film): 2979, 1620, 1556, 1450, 1332, 1260, 1139, 1030, 637. ¹H NMR (400 MHz, CDCl₃) δ 8.59 (d, J = 2.1 Hz, 1H), 8.32 (dd, J = 8.0, 2.3 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 6.88 (d, J = 11.9 Hz, 1H), 5.38 (d, J = 12.0 Hz, 1H), 3.87 (dt, J = 14.3, 6.9 Hz, 1H), 3.63 (dq, J = 11.1, 6.1, 5.4 Hz,

3H), 3.46 (p, $J = 6.9$ Hz, 2H), 3.21 (ddt, $J = 40.0, 13.1, 7.0$ Hz, 2H), 2.27 – 1.83 (m, 8H). ^{13}C NMR (100 MHz, CDCl_3) δ 163.33, 156.15, 148.16, 139.27, 121.39, 119.43 – 149.47 (m), 95.02, 54.55, 53.09, 50.80, 48.91, 25.21, 24.84 (d, $J = 2.4$ Hz), 24.72. m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 324.1735, for $\text{C}_{18}\text{H}_{21}\text{F}_6\text{N}_3\text{O}_3\text{S}^+$ requires 324.1682.

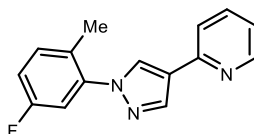
(Z)-1-(2-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-3-(pyrrolidin-1-yl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate



An oven dried round bottom flask equipped with a stir bar was charged with 5-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyrimidine (1.0 g, 2.8 mmol, 1.0 equiv) and placed under a nitrogen atmosphere. EtOAc (0.2 M) was added, the reaction vessel cooled to -78 °C and Ti_2O (465 μL , 2.8 mmol, 1.0 equiv) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes before 4-(trifluoromethyl)aniline (350 μL , 2.8 mmol, 1.0 equiv) was added dropwise followed by collidine (382 μL , 2.8 mmol, 1.0 equiv). The reaction was stirred for a further 5 minutes at -78 °C. The cooling bath was removed and the reaction was allowed to warm to room temperature while stirring for approximately 30 minutes. The reaction was then concentrated *in vacuo* at 40 °C. Then EtOH (0.2 M) and pyrrolidine (1.4 mL, 16.6 mmol, 6.0 equiv) were added. The reaction was heated to 60 °C for 18 hours. After cooling to room temperature, the reaction was concentrated and dissolved in a minimal amount of CH_2Cl_2 (1 mL).

The crude reaction was added to an equal volume of 3:1 hexanes:Et₂O. The precipitate was filtered, then purified by flash chromatography (silica gel: 6% MeOH in CH₂Cl₂) to provide the pure title compound as a red solid (861 mg, 1.41 mmol, 51% yield). mp 188-189 °C. IR_{max}/cm⁻¹ (solid): 2928, 2323, 1980, 1569, 1510, 1424, 1223, 1144, 1028, 636. ¹H NMR (400 MHz, CDCl₃) δ 8.13 (s, 2H), 7.47 – 7.38 (m, 2H), 7.14 (d, J = 7.8 Hz, 1H), 7.08 (d, J = 2.0 Hz, 1H), 7.06 – 6.98 (m, 4H), 6.75 – 6.69 (m, 1H), 4.13 (s, 2H), 3.82 (t, J = 6.8 Hz, 4H), 2.70 – 2.61 (m, 4H), 2.38 (s, 3H), 1.85 – 1.67 (m, 8H); ¹³C NMR (100 MHz, CDCl₃) δ 160.25, 142.89, 141.84, 138.33, 137.25, 133.64, 131.18, 130.86, 130.53 (d, J = 3.3 Hz), 130.13, 126.99 (d, J = 8.0 Hz), 126.07, 122.71, 115.99, 115.77, 106.40, 56.37, 49.35, 33.96, 25.96, 23.73, 19.36; ¹⁹F NMR (375 MHz, CDCl₃) δ -78.24 (3F), -114.53 (ddd, J = 13.9, 8.3, 5.6 Hz, 1F); *m/z* HRMS (ESI) found [M+H]⁺ 459.2289, for C₃₀H₃₂F₄N₂O₃S₂⁺ requires 459.2265.

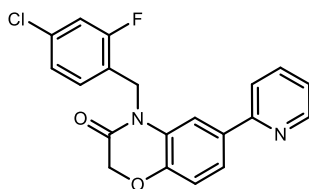
2-(1-(5-Fluoro-2-methylphenyl)-1H-pyrazol-4-yl)pyridine (7a)



Prepared according to general procedure F using 4-(1-(5-fluoro-2-methylphenyl)-1H-pyrazol-4-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (144 mg, 0.30 mmol), EtOH (1.5 mL), HCl (75 μL, 0.30 mmol), pyrrolidine (150 μL, 1.80 mmol), acetyltrimethylsilane (148 μL, 0.90 mmol), LiHMDS (0.9 mL, 0.90 mmol), THF (1.5 mL), NH₄OAc (92.5 mg, 1.20 mmol), AcOH (69 μL, 1.20 mmol). The crude material was purified by flash chromatography (silica gel: 0-50% EtOAc in hexanes) to provide the pure title compound as a brown oil (37 mg, 0.15 mmol, 49% yield). IR_{max}/cm⁻¹ (film): 3033, 2910, 1598, 1507, 1415, 1253, 1229, 1112, 828, 635; ¹H NMR (400 MHz, CDCl₃) δ 8.59 (d, J = 4.9 Hz, 1H), 8.19 (s, J = 1.4 Hz, 2H), 7.71 (tt, J = 7.7, 1.7 Hz,

1H), 7.54 (d, J = 7.9 Hz, 1H), 7.29 (dd, J = 8.5, 6.3 Hz, 1H), 7.20 – 7.12 (m, 2H), 7.06 (tt, J = 8.3, 2.0 Hz, 1H), 2.30 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.98 (d, J = 246.0 Hz), 151.61, 149.87, 140.40 (d, J = 9.5 Hz), 138.93, 136.81, 132.58 (d, J = 8.5 Hz), 129.19, 128.99 (d, J = 3.6 Hz), 124.65, 121.61, 119.87, 115.54 (d, J = 20.7 Hz), 113.29 (d, J = 24.0 Hz); ¹⁹F NMR (375 MHz, CDCl₃) δ -115.76 (q, J = 7.8 Hz); *m/z* HRMS (ESI) found [M+H]⁺ 254.1098, for C₁₅H₁₃FN₃⁺ requires 254.1088.

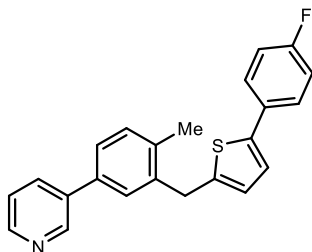
4-(4-Chloro-2-fluorobenzyl)-6-(pyridin-2-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one (7b)



Prepared according to general procedure F using 4-(4-chloro-2-fluorobenzyl)-6-(1-phenyl-1H-pyrimidin-4-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one trifluoromethanesulfonate (238 mg, 0.4 mmol), EtOH (2 mL), HCl (100 μL, 0.4 mmol), pyrrolidine (197 μL, 2.4 mmol), acetyltrimethylsilane (197 μL, 1.20 mmol), LiHMDS (1.2 mL, 1.20 mmol), THF (2.0 mL), NH₄OAc (123 mg, 1.60 mmol), AcOH (92 μL, 1.60 mmol). The crude material was purified by flash chromatography (silica gel: 0-40% EtOAc in hexanes) to provide the pure title compound as a pale-orange solid (56 mg, 0.15 mmol, 38% yield). mp 152-156 °C; IR_{max}/cm⁻¹ (film): 3085, 1607, 1580, 1488, 1420, 1378, 1273, 891, 777, 582. ¹H NMR (400 MHz, CDCl₃) δ 8.67 – 8.54 (m, 1H), 7.71 (td, J = 7.8, 1.8 Hz, 1H), 7.63 (d, J = 7.5 Hz, 2H), 7.55 (dd, J = 8.1, 1.0 Hz, 1H), 7.22 – 6.99 (m, 5H), 5.27 (s, 3H), 4.75 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 164.76, 160.37 (d, J = 249.5 Hz), 156.18, 149.80, 146.14, 136.92, 134.72, 134.37 (d, J = 10.0 Hz), 129.69 (d, J = 4.7 Hz), 128.50, 125.19 (d, J = 3.6 Hz), 122.99, 122.17, 121.79 (d, J = 14.5 Hz), 119.95, 117.49,

116.50 (d, $J = 25.1$ Hz), 113.90, 67.79, 38.08 (d, $J = 4.5$ Hz); ^{19}F NMR (375 MHz, CDCl_3) δ - 115.52 (t, $J = 3.8$ Hz); m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 369.0816, for $\text{C}_{20}\text{H}_{15}\text{ClFN}_2\text{O}_2^+$ requires 369.0801.

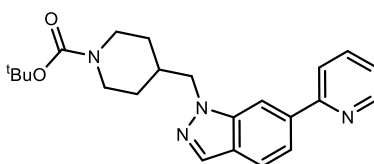
3-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyridine (7c)



Prepared according to modified general procedure G using (Z)-1-(2-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-3-(pyrrolidin-1-yl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate (122 mg, 0.20 mmol), acetyltrimethylsilane (33 μL , 0.20 mmol), LiHMDS (200 μL , 0.20 mmol), THF (1.0 mL), NH_4OAc (62 mg, 0.80 mmol), AcOH (46 μL , 0.80 mmol). The crude material was purified by flash column chromatography (silica gel: 0 to 40% EtOAc:Hexanes) to provide the pure title compound as a tan solid (51 mg, 0.14 mmol, 72% yield). mp 51-60 $^\circ\text{C}$. IR $_{\text{max}}$ /cm $^{-1}$ (film): 2921, 2218, 1571, 1472, 1423, 1230, 906, 799, 728. ^1H NMR (400 MHz, CDCl_3) δ 8.77 (d, $J = 2.4$ Hz, 1H), 8.49 (dd, $J = 4.9, 1.8$ Hz, 1H), 7.78 (dt, $J = 8.0, 2.1$ Hz, 1H), 7.43 – 7.30 (m, 4H), 7.30 – 7.11 (m, 2H), 7.00 – 6.90 (m, 3H), 6.64 (d, $J = 3.7$ Hz, 1H), 4.12 (s, 2H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.36, 160.91, 148.19 (d, $J = 3.6$ Hz), 142.90, 141.76, 139.07, 136.54, 136.44, 135.78, 134.26, 131.28, 130.76, 128.17, 127.16 (d, $J = 8.0$ Hz), 126.14, 125.61, 123.55, 122.73, 115.74 (d, $J = 21.8$ Hz), 34.20, 19.26; ^{19}F

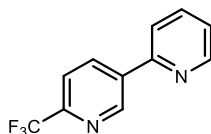
NMR (375 MHz, CDCl₃) δ -115.07 (tt, J = 8.3, 5.2 Hz); m/z HRMS (ESI) found $[M+H]^+$ 360.1222, for C₂₃H₁₈FNS⁺ requires 360.1222.

Tert-butyl 4-((6-(pyridin-2-yl)-1H-indazol-1-yl)methyl)piperidine-1-carboxylate (7d)



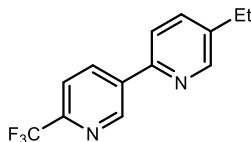
Prepared according to general procedure F using 4-(1-((1-(tert-butoxycarbonyl)piperidin-4-yl)methyl)-1H-indazol-6-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (214 mg, 0.35 mmol), EtOH (1.7 mL), HCl (86 μ L, 0.35 mmol), pyrrolidine (170 μ L, 2.07 mmol), acetyltrimethylsilane (170 μ L, 1.04 mmol), LiHMDS (1.0 mL, 1.04 mmol), THF (1.7 mL), NH₄OAc (106 mg, 1.38 mmol), AcOH (79 μ L, 1.38 mmol). The crude material was purified by flash chromatography (silica gel: 0-60% EtOAc in hexanes) to provide the pure title compound as a brown oil (49 mg, 0.13 mmol, 36% yield). mp 60-64 °C; IR_{max}/cm⁻¹ (film): 3050, 2976, 2930, 1681, 1587, 1425, 1289, 1159, 965, 840. ¹H NMR (400 MHz, CDCl₃) δ 8.74 (d, J = 4.5 Hz, 1H), 8.09 (s, 1H), 8.02 (s, 1H), 7.81 (dd, J = 9.0, 6.5 Hz, 3H), 7.72 (dd, J = 8.4, 1.4 Hz, 1H), 7.30 – 7.27 (m, 1H), 4.33 (d, J = 7.2 Hz, 2H), 4.09 (s, 2H), 2.64 (t, J = 12.5 Hz, 2H), 2.23 (dq, J = 11.3, 7.5, 3.5 Hz, 1H), 1.56 (d, J = 13.7 Hz, 2H), 1.43 (s, 9H), 1.33 – 1.18 (m, 2H); ¹³C NMR (100 MHz, CD₃CN) δ 157.97, 155.38, 150.59, 141.42, 138.47, 137.98, 133.51, 125.17, 123.45, 122.03, 121.88, 120.63, 108.62, 79.61, 54.63, 44.18, 38.01, 30.45, 28.55. m/z HRMS (ESI) found $[M+H]^+$ 393.2298, for C₂₃H₂₉N₄O₂⁺ requires 393.2285.

6'-(Trifluoromethyl)-2,3'-bipyridine (7e)



Prepared according to general procedure G using (Z)-1-(3-(pyrrolidin-1-yl)-3-(6-(trifluoromethyl)pyridin-3-yl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate (144 mg, 0.30 mmol), acetyltrimethylsilane (148 μ L, 0.90 mmol), LiHMDS (1.5 mL, 0.90 mmol), THF (1.5 mL), NH_4OAc (92.5 mg, 1.20 mmol), AcOH (69 μ L, 1.20 mmol). The crude material was purified by flash column chromatography (silica gel: 30% EtOAc in hexanes) to provide the pure title compound as a tan solid (35 mg, 0.14 mmol, 72% yield). mp 66-68 $^{\circ}\text{C}$. IR $_{\text{max}}$ /cm $^{-1}$ (film): 2956, 2360, 1589, 1435, 1335, 1247, 1098, 1016, 740. ^1H NMR (400 MHz, CDCl_3) δ 9.29 (d, J = 2.5 Hz, 1H), 8.76 (dt, J = 4.9, 1.5 Hz, 1H), 8.51 (dd, J = 8.2, 2.4 Hz, 1H), 7.89 – 7.76 (m, 3H), 7.35 (ddd, J = 6.6, 4.9, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 153.25, 150.38, 148.35, 137.47, 137.23, 135.66, 123.67, 122.98, 120.98, 120.45 (q, J = 2.8 Hz); ^{19}F NMR (375 MHz, CDCl_3) δ -67.82. m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 225.0643, for $\text{C}_{11}\text{H}_7\text{F}_3\text{N}_2^+$ requires 225.0639. Spectra matched literature values.²⁹

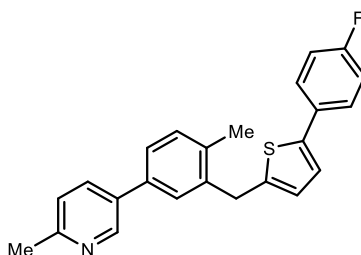
5-Ethyl-6'-(trifluoromethyl)-2,3'-bipyridine (7f)



An oven dried 8 mL vial equipped with a stir bar was charged lithium diisopropylamine (2M in hexanes) (300 μ L, 0.6 mmol, 3.0 equiv) in THF (0.28M) and cooled to 0 $^{\circ}\text{C}$. (E)-2-butyldiene-1,1-dimethylhydrazine (80 μ L, 0.6 mmol, 3.0 equiv) was added dropwise. The reaction was stirred

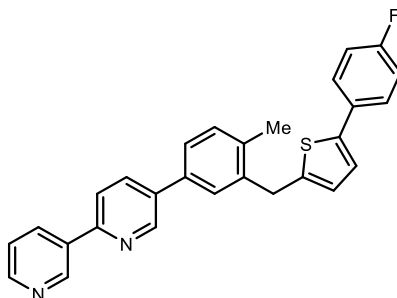
for 1 hour before adding (Z)-1-(3-(pyrrolidin-1-yl)-3-(6-(trifluoromethyl)pyridin-3-yl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate (122 mg, 0.2 mmol, 1.0 equiv), then warmed to room temperature with stirring for 1 hour. Next, NH₄OAc (4 equiv) and acetic acid (4 equiv) were added, and the reaction stirred at room temperature for 1 hour. The reaction was then heated to 95 °C for 18 hours. After cooling to room temperature, the reaction was quenched with sat. NaHCO₃, extracted into EtOAc (3x). The combined organic extract was washed with water (1x), brine (1x), and dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography (silica gel: 0 to 20% EtOAc:Hexanes) to provide the pure title compound as a yellow solid (33 mg, 0.13 mmol, 65% yield). mp 57-59 °C. IR_ν_{max}/cm⁻¹ (film): 2970, 2933, 1583, 1474, 1265, 1175, 1137, 1089, 1014, 735, 703; ¹H NMR (400 MHz, CDCl₃) δ 9.27 (d, J = 2.3 Hz, 1H), 8.60 (d, J = 3.0 Hz, 1H), 8.49 (dd, J = 8.1, 2.9 Hz, 1H), 7.80 – 7.69 (m, 2H), 7.66 (dd, J = 8.1, 2.3 Hz, 1H), 2.73 (q, J = 7.6 Hz, 2H), 1.31 (t, J = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 150.75, 150.18, 148.41 - 147.20 (m), 139.65, 137.53, 136.46, 135.33, 120.60, 120.42 (q, J = 2.7 Hz), 25.89, 15.20; ¹⁹F NMR (375 MHz, CDCl₃) δ -67.78; *m/z* HRMS (ESI) found [M+H]⁺ 253.0946, for C₁₃H₁₁F₃N₂⁺ requires 253.0952.

5-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-2-methylpyridine (7g)



Prepared according to modified general procedure G using (Z)-1-(2-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-3-(pyrrolidin-1-yl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate (122 mg, 0.20 mmol), acetone (15 μ L, 0.20 mmol), LiHMDS (200 μ L, 0.20 mmol), THF (1.0 mL), NH_4OAc (62 mg, 0.80 mmol), AcOH (46 μ L, 0.80 mmol). The crude material was purified by flash column chromatography (silica gel: 0 to 40% EtOAc:Hexanes) to provide the pure title compound as an orange oil (46 mg, 0.12 mmol, 61% yield). $\text{IR}_{\text{max}}/\text{cm}^{-1}$ (film): 3015, 2921, 1596, 1509, 1478, 1254, 1231, 1097, 820, 731; ^1H NMR (400 MHz, CDCl_3) δ 8.64 (d, J = 2.8 Hz, 1H), 7.68 (dd, J = 8.0, 2.4 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.37 – 7.28 (m, 2H), 7.23 – 7.16 (m, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.01 – 6.89 (m, 3H), 6.64 (dt, J = 3.6, 1.3 Hz, 1H), 4.12 (s, 2H), 2.51 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.35, 160.90, 157.00, 147.43, 142.98, 141.72, 138.96, 136.13, 135.91, 134.58, 133.49, 131.19, 127.99, 127.15 (d, J = 8.0 Hz), 126.12, 125.41, 123.12, 122.72, 115.73 (d, J = 21.8 Hz), 34.20, 24.10, 19.23; ^{19}F NMR (375 MHz, CDCl_3) δ -115.10 (td, J = 8.7, 4.5 Hz); m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 374.1375, for $\text{C}_{24}\text{H}_{20}\text{FNS}^+$ requires 374.1378.

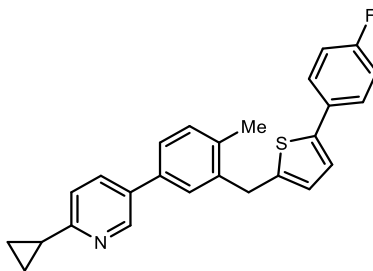
5-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-2,3'-bipyridine (7h)



Prepared according to modified general procedure G using (Z)-1-(2-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-3-(pyrrolidin-1-yl)allylidene)pyrrolidin-1-

ium trifluoromethanesulfonate (122 mg, 0.20 mmol), 1-(pyridin-3-yl)ethan-1-one (15 μ L, 0.20 mmol), LiHMDS (200 μ L, 0.20 mmol), THF (1.0 mL), NH_4OAc (62 mg, 0.80 mmol), AcOH (46 μ L, 0.80 mmol). The crude material was purified by flash column chromatography (silica gel: 0 to 70% EtOAc:Hexanes) to provide the pure title compound as an tan solid (63 mg, 0.14 mmol, 72% yield). mp 125-127 $^{\circ}\text{C}$. $\text{IR}_{\text{max}}/\text{cm}^{-1}$ (film): 3015, 2921, 1595, 1478, 1445, 1254, 1232, 1179, 903, 820; ^1H NMR (400 MHz, CDCl_3) δ 9.24 (s, 1H), 8.95 (d, J = 2.5 Hz, 1H), 8.66 (d, J = 3.4 Hz, 1H), 8.36 (dt, J = 8.0, 2.0 Hz, 1H), 7.97 (dd, J = 8.3, 2.4 Hz, 1H), 7.81 (d, J = 8.3 Hz, 1H), 7.54 – 7.45 (m, 4H), 7.42 (dd, J = 8.0, 4.8 Hz, 1H), 7.32 (d, J = 7.8 Hz, 1H), 7.08 – 6.97 (m, 3H), 6.74 (d, J = 3.5 Hz, 1H), 4.22 (s, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.37, 160.91, 153.26, 149.92, 148.40, 148.19, 142.79, 141.81, 139.20, 136.76, 135.49, 135.26, 135.07, 134.17, 131.36, 130.76 (d, J = 3.6 Hz), 128.00, 127.16 (d, J = 8.0 Hz), 126.21, 125.47, 123.65, 122.75, 120.37, 115.64, 34.19, 19.30; ^{19}F NMR (375 MHz, CDCl_3) δ -114.99 (dp, J = 8.3, 4.2 Hz); m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 437.1485, for $\text{C}_{28}\text{H}_{21}\text{FN}_2\text{S}^+$ requires 437.1487.

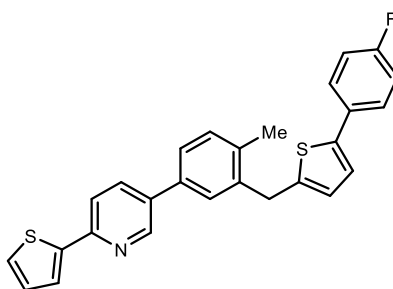
2-Cyclopropyl-5-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyridine
(7i)



Prepared according to modified general procedure G using (Z)-1-(2-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-3-(pyrrolidin-1-yl)allylidene)pyrrolidin-1-

ium trifluoromethanesulfonate (122 mg, 0.20 mmol), cyclopropyl ketone (20 μ L, 0.20 mmol), LiHMDS (200 μ L, 0.20 mmol), THF (1.0 mL), NH_4OAc (62 mg, 0.80 mmol), AcOH (46 μ L, 0.80 mmol). The crude material was purified by flash column chromatography (silica gel: 0 to 20% EtOAc:Hexanes) to provide the pure title compound as a white solid (50 mg, 0.13 mmol, 65% yield). mp 66-68 $^{\circ}\text{C}$. $\text{IR}_{\text{max}}/\text{cm}^{-1}$ (film): 3015, 2921, 1595, 1509, 1478, 1254, 1213, 1097, 820, 733; ^1H NMR (400 MHz, CDCl_3) δ 8.66 (dd, $J = 2.4, 0.9$ Hz, 1H), 7.71 (dd, $J = 8.1, 2.4$ Hz, 1H), 7.55 – 7.45 (m, 2H), 7.45 – 7.34 (m, 2H), 7.17 (dd, $J = 8.1, 0.9$ Hz, 1H), 7.08 – 6.97 (m, 3H), 6.71 (dd, $J = 3.6, 1.1$ Hz, 1H), 4.18 (s, 2H), 2.37 (s, 3H), 2.12 – 2.01 (m, 1H), 1.09 – 0.96 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.35, 161.57, 160.90, 147.58, 142.98, 141.72, 138.94, 135.92, 134.14, 133.16, 131.15, 127.86, 127.15 (d, $J = 8.0$ Hz), 126.14, 125.29, 122.72, 121.08, 115.83, 115.62, 34.17, 19.22, 16.91, 9.88; ^{19}F NMR (375 MHz, CDCl_3) δ -115.14 (m); m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 400.1526, for $\text{C}_{26}\text{H}_{22}\text{FNS}^+$ requires 400.1535.

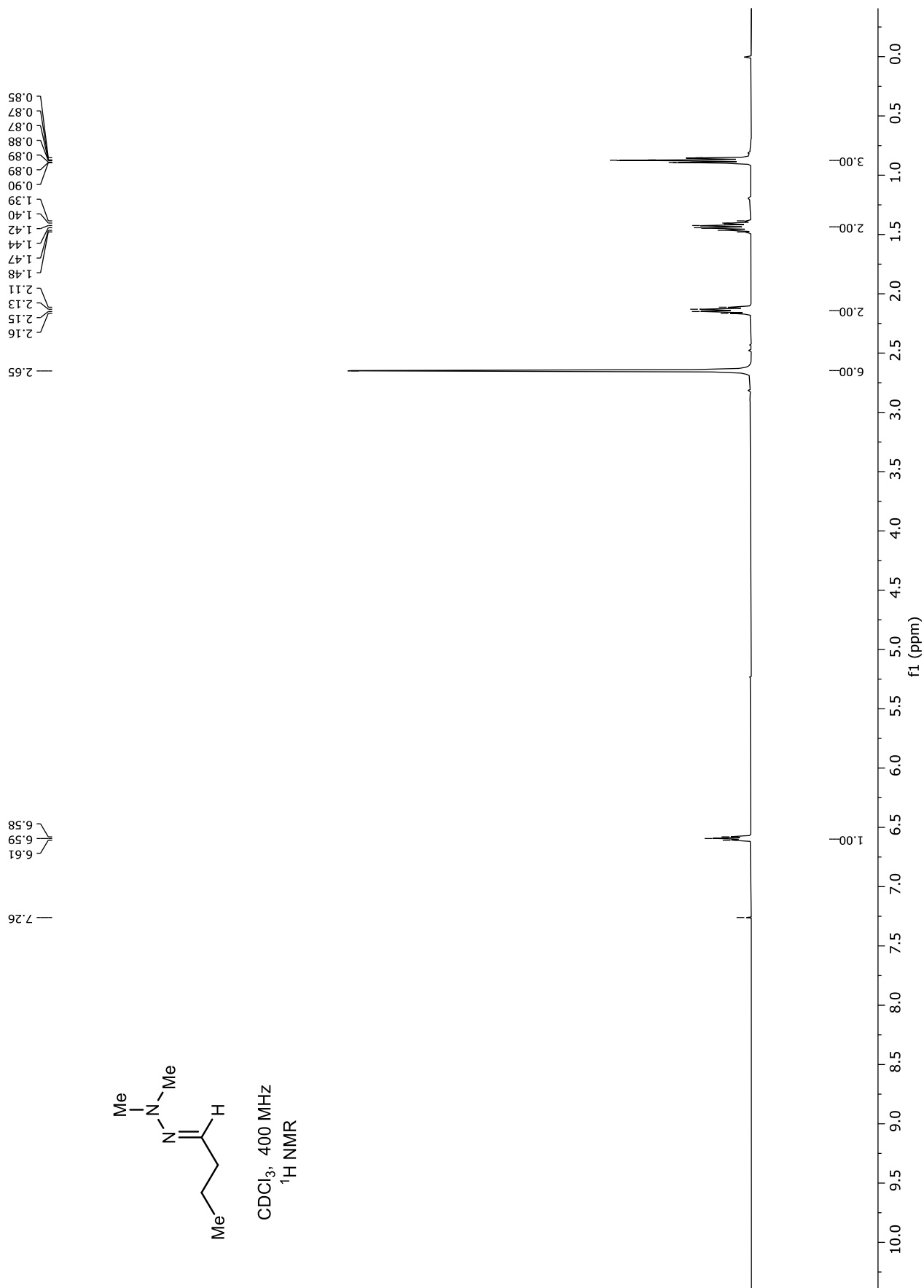
5-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-2-(thiophen-2-yl)pyridine (7j)

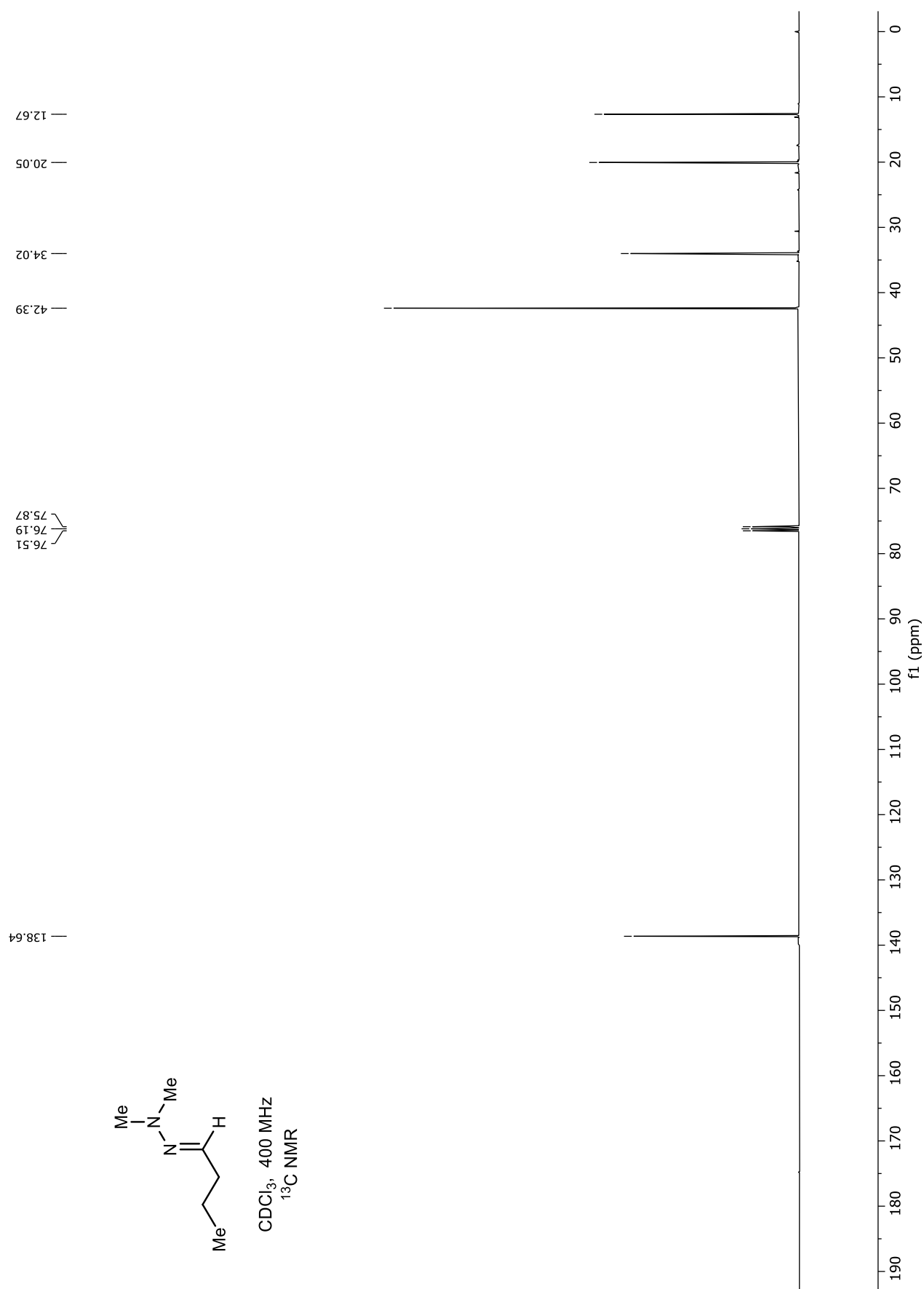


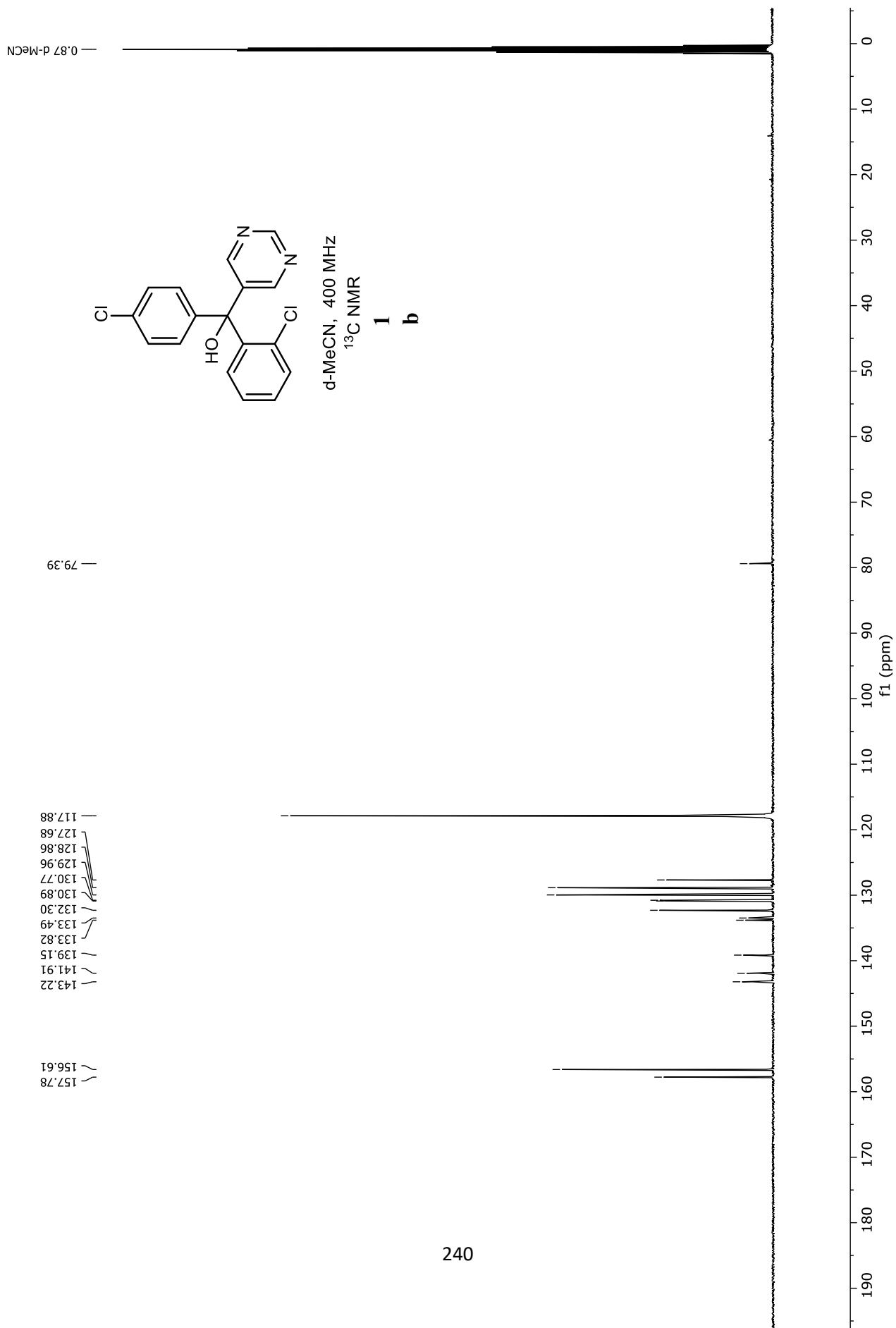
Prepared according to modified general procedure G using (Z)-1-(2-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-3-(pyrrolidin-1-yl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate (122 mg, 0.20 mmol), 1-(thiophen-2-yl)ethan-1-one (22 μ L, 0.20

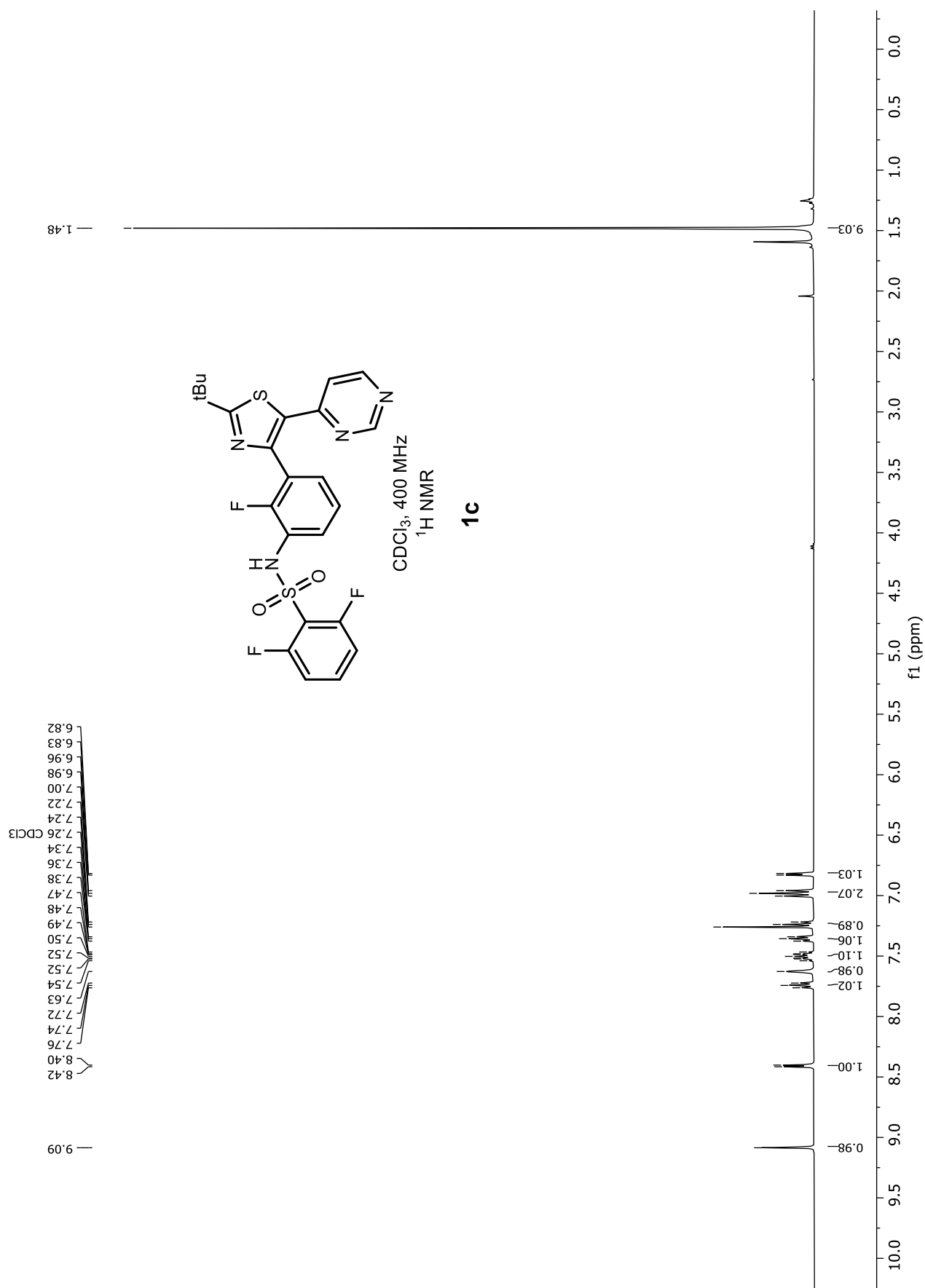
mmol), LiHMDS (200 μ L, 0.20 mmol), THF (1.0 mL), NH_4OAc (62 mg, 0.80 mmol), AcOH (46 μ L, 0.80 mmol). The crude material was purified by flash column chromatography (silica gel: 0 to 20% EtOAc:hexanes) to provide the pure title compound as yellow solid (49 mg, 0.11 mmol, 55% yield). $\text{IR}_{\text{vmax}}/\text{cm}^{-1}$ (film): 3053, 3001, 1509, 1472, 1264, 895, 802, 723, 703, 659; ^1H NMR (400 MHz, CDCl_3) δ 8.80 (d, J = 2.5 Hz, 1H), 7.87 (dd, J = 8.3, 2.5 Hz, 1H), 7.70 (d, J = 8.3 Hz, 1H), 7.60 (d, J = 3.9 Hz, 1H), 7.53 – 7.38 (m, 5H), 7.33 – 7.24 (m, 1H), 7.16 – 7.10 (m, 1H), 7.09 – 6.99 (m, 3H), 6.74 (d, J = 3.8 Hz, 1H), 4.21 (s, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.37, 160.91, 151.21, 147.81, 144.64, 142.83, 141.80, 139.13, 136.46, 135.49, 134.77, 134.50, 131.29, 130.79 (d, J = 3.6 Hz), 128.14, 127.68 (d, J = 18.2 Hz), 127.21, 126.22, 125.26, 124.50, 122.76, 118.67, 115.74 (d, J = 21.8 Hz), 34.17, 19.29; ^{19}F NMR (375 MHz, CDCl_3) δ -115.10 (td, J = 8.7, 4.5 Hz). m/z HRMS (ESI) found $[\text{M}+\text{H}]^+$ 442.1092, for $\text{C}_{27}\text{H}_{21}\text{FNS}_2^+$ requires 442.1094.

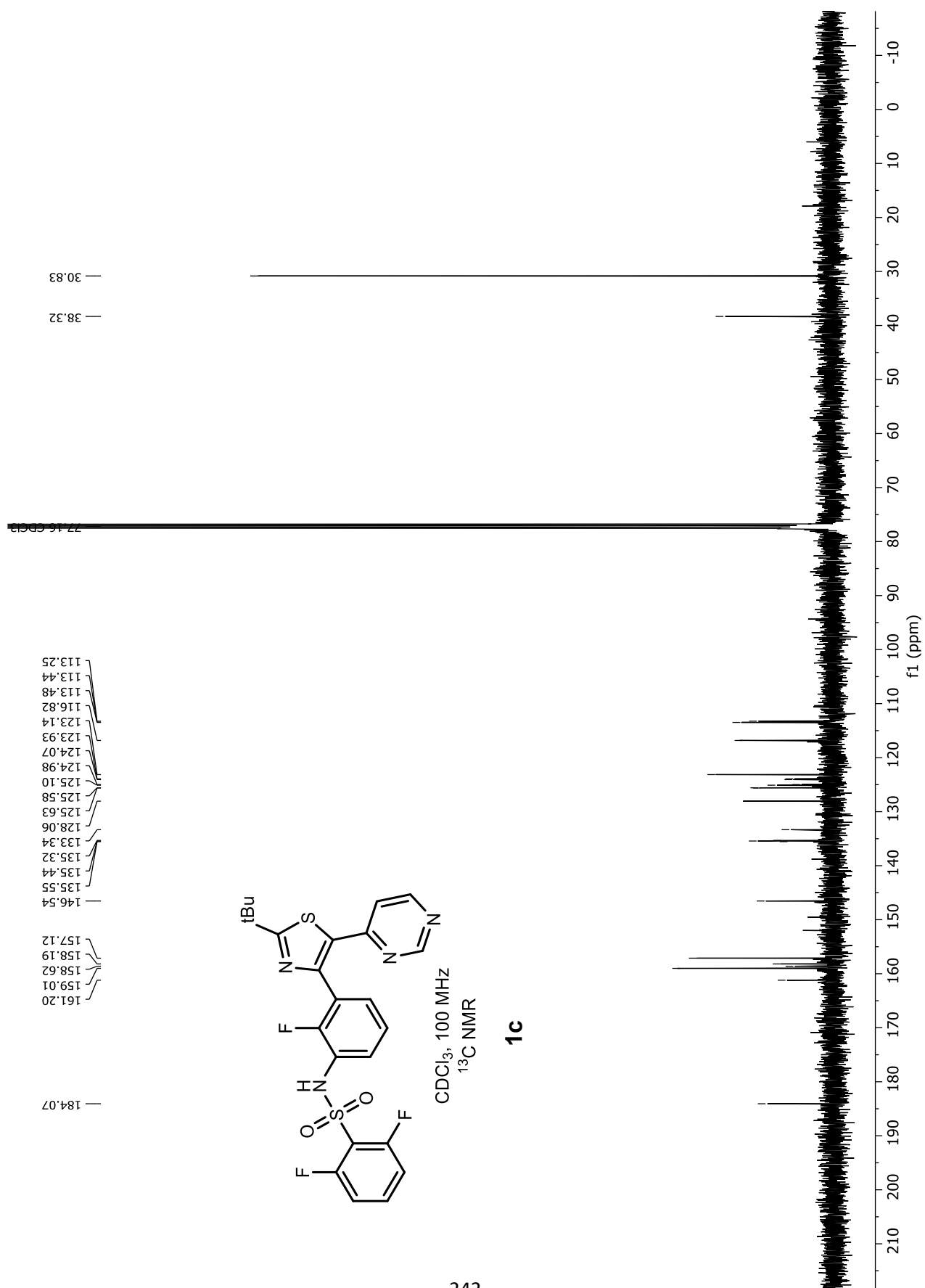
^1H , ^{19}F , and ^{13}C NMR Spectra

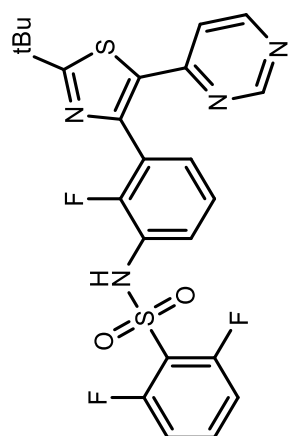






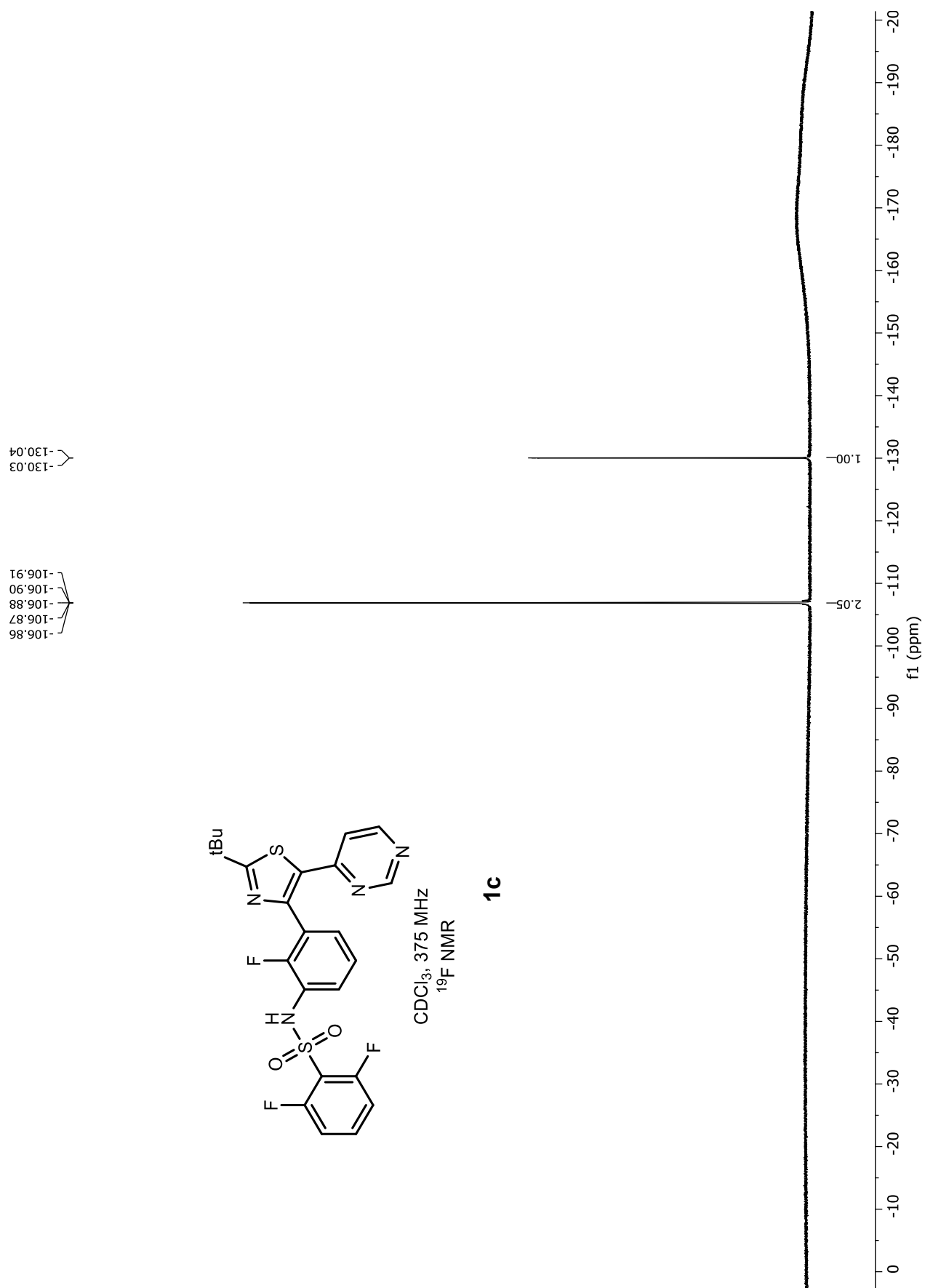


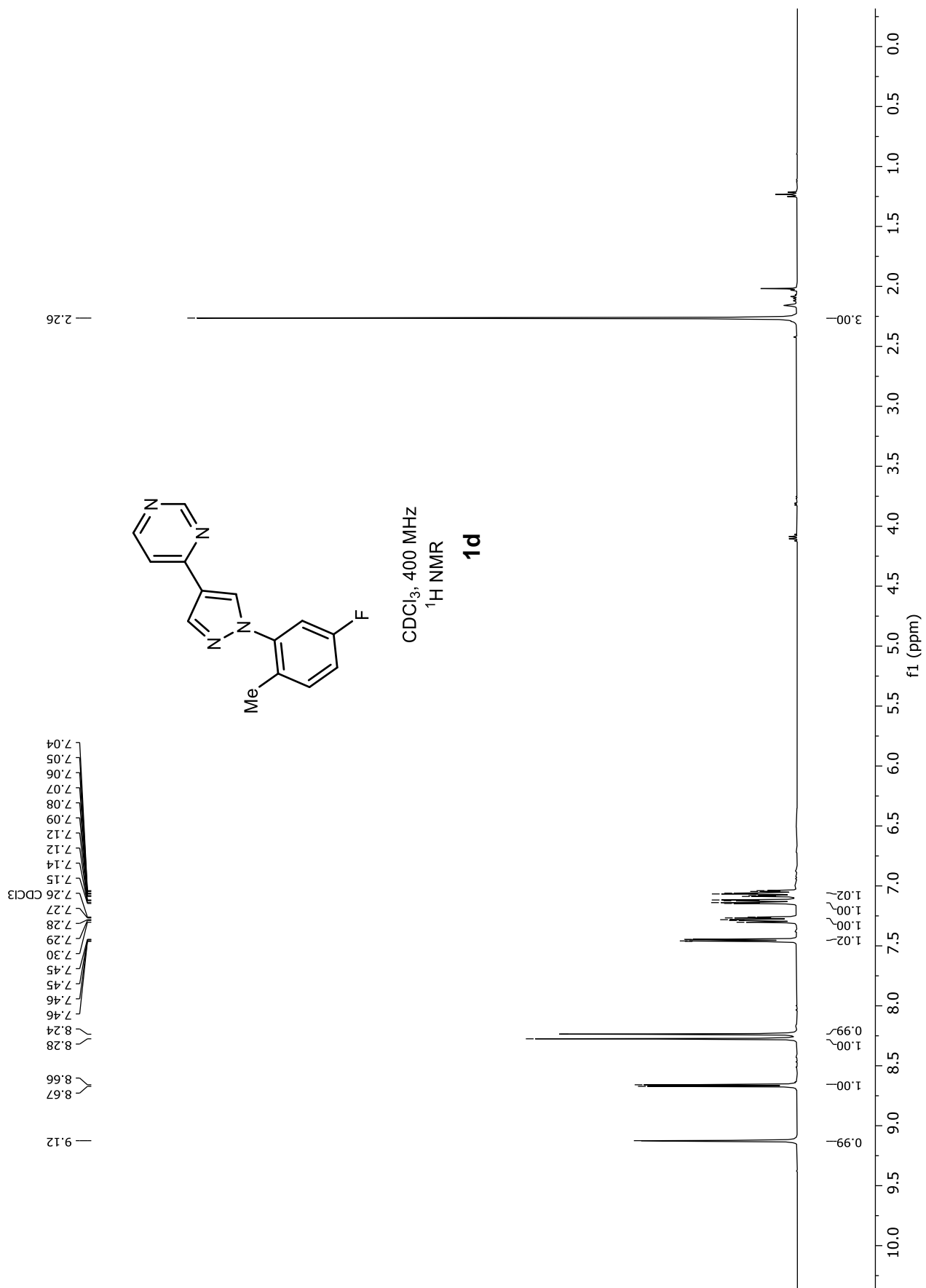


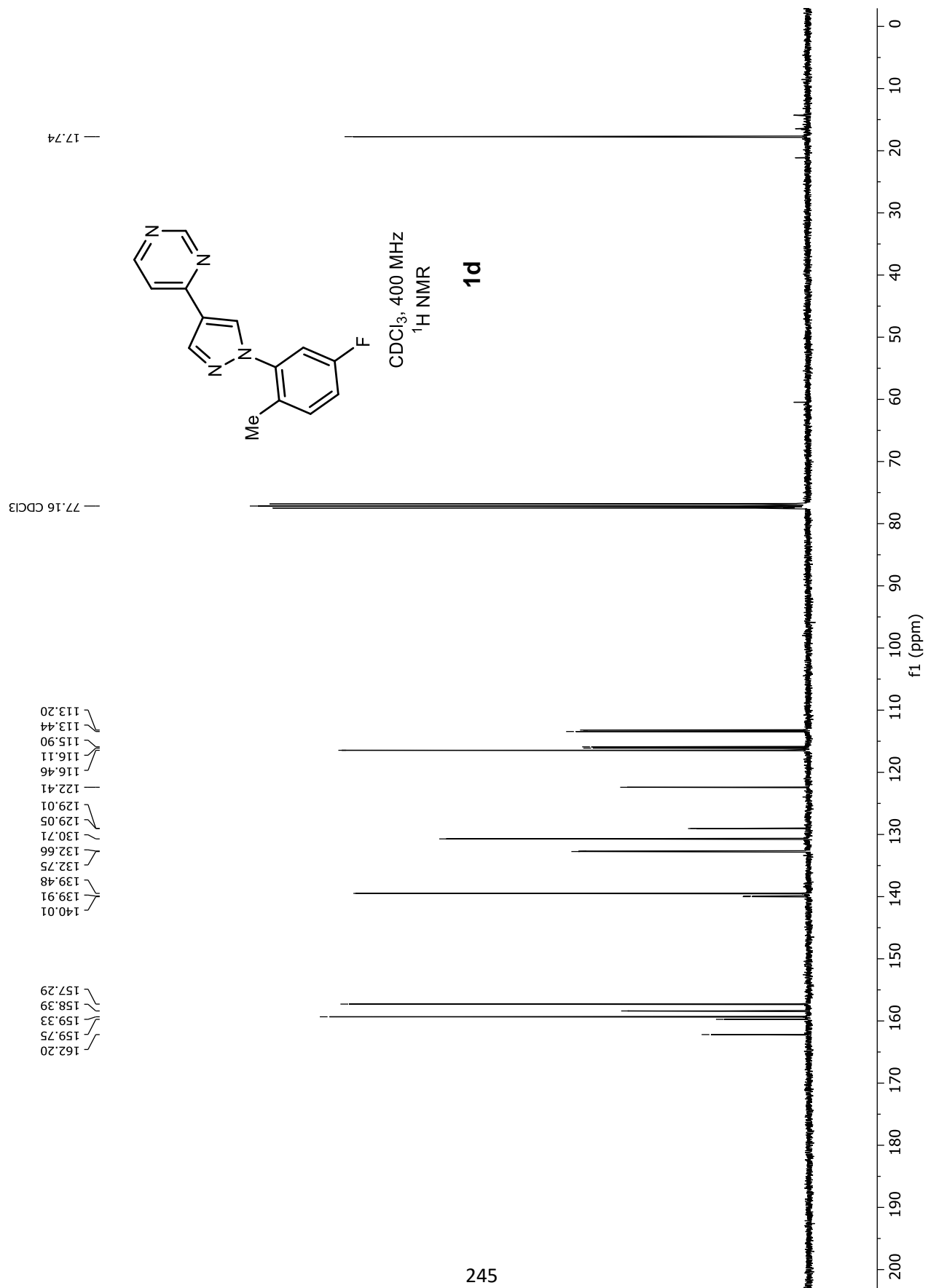


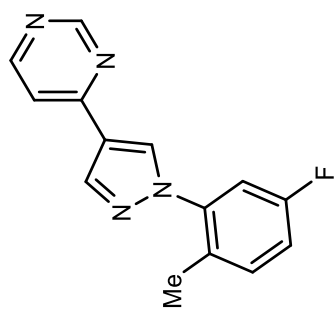
CDCl₃, 375 MHz
¹⁹F NMR

1c





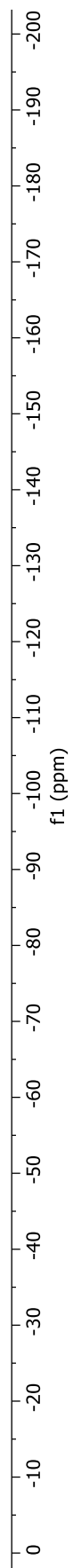


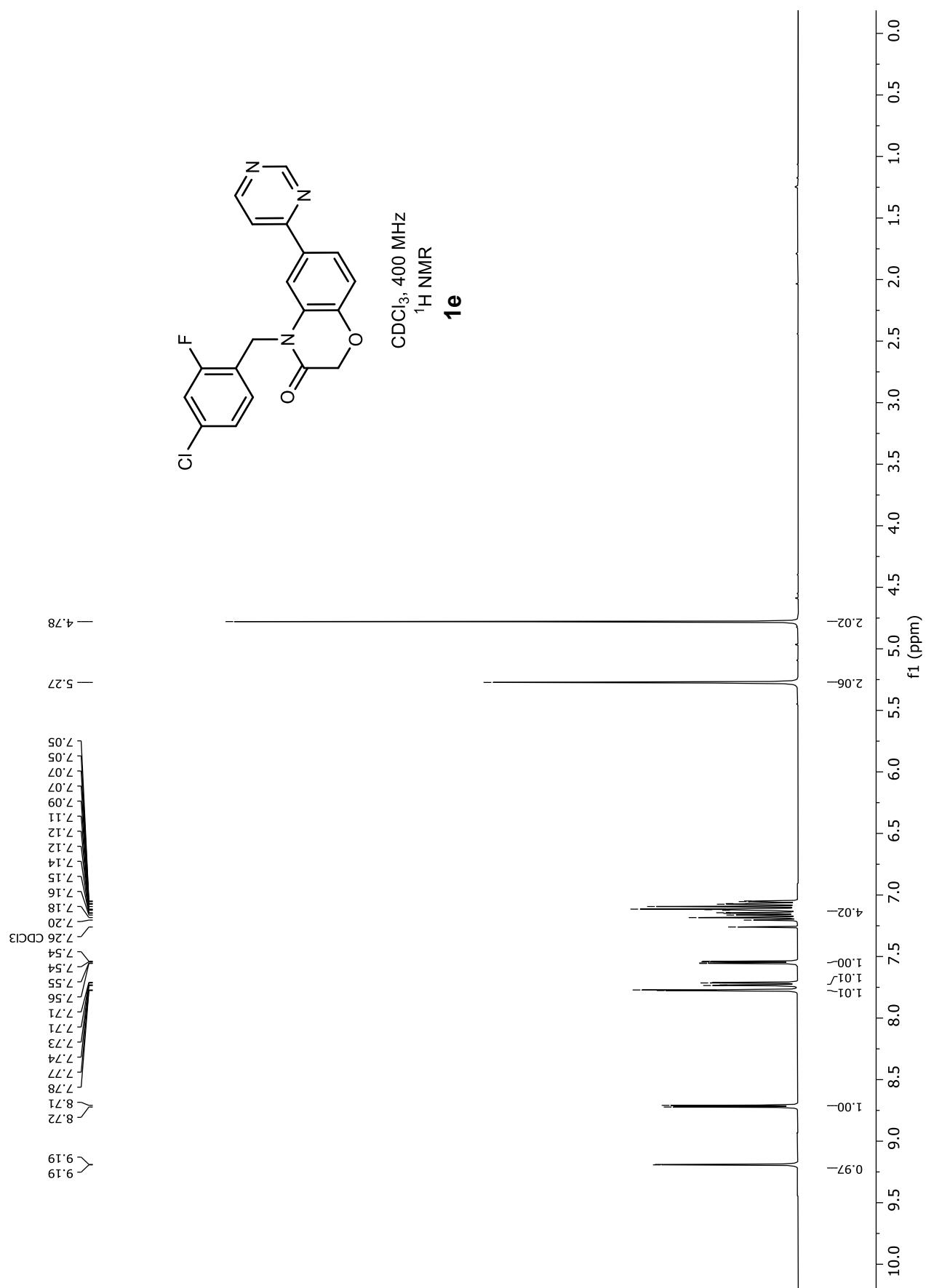


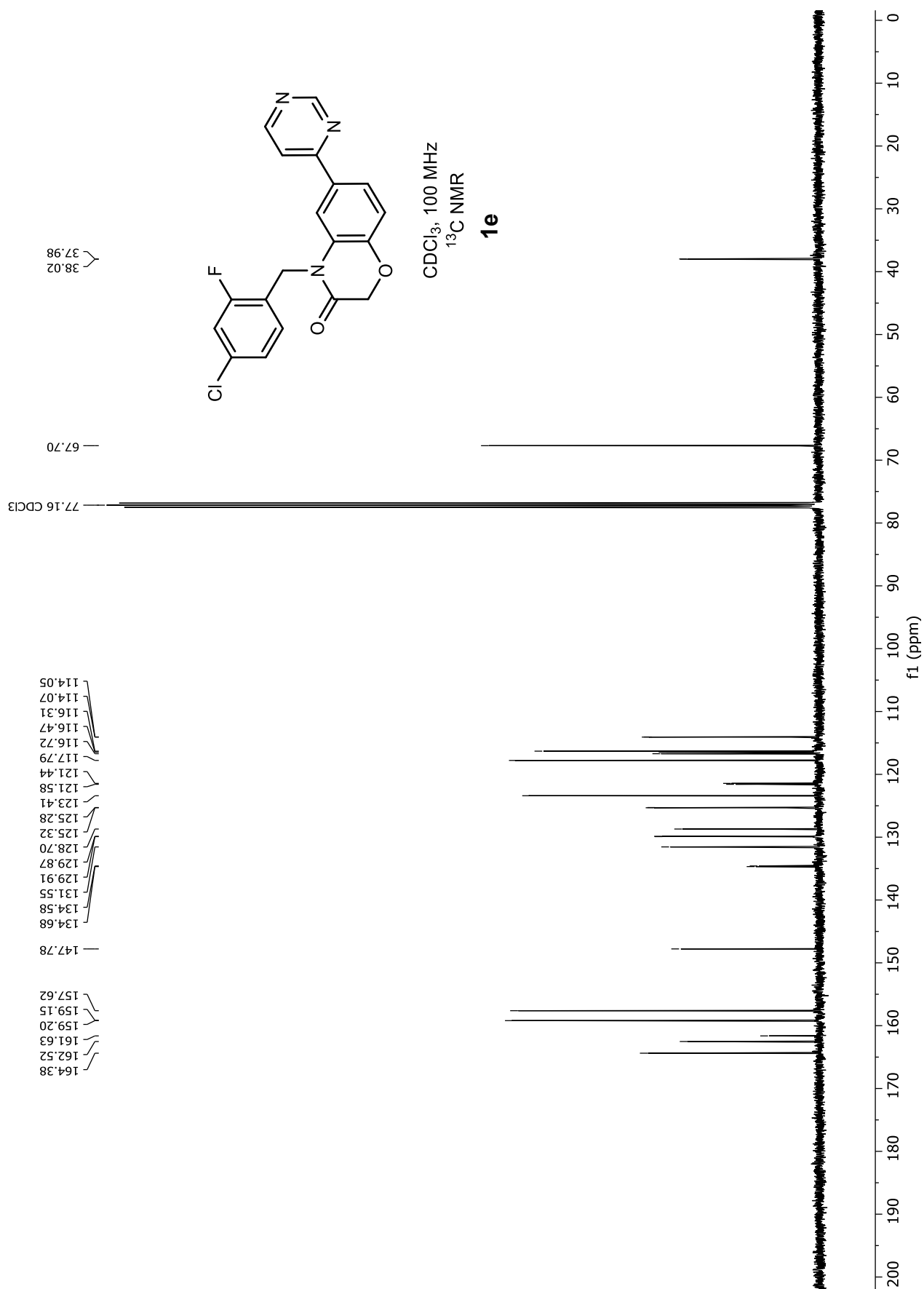
CDCl₃, 375 MHz
¹⁹F NMR

1d

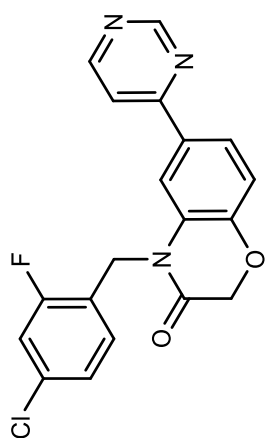
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 -115.40
 -115.38
 -115.36







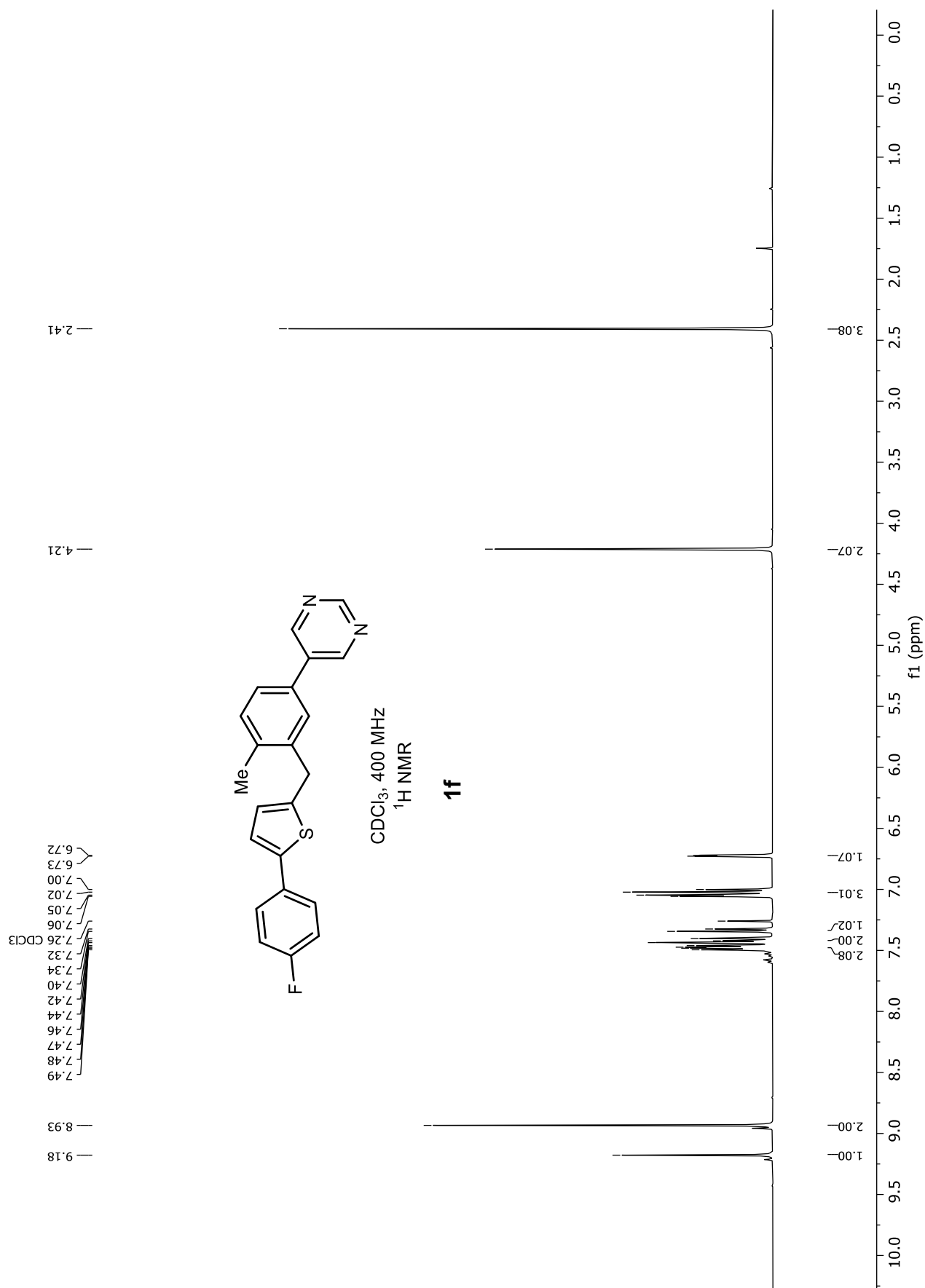
-115.53
-115.56
-115.58

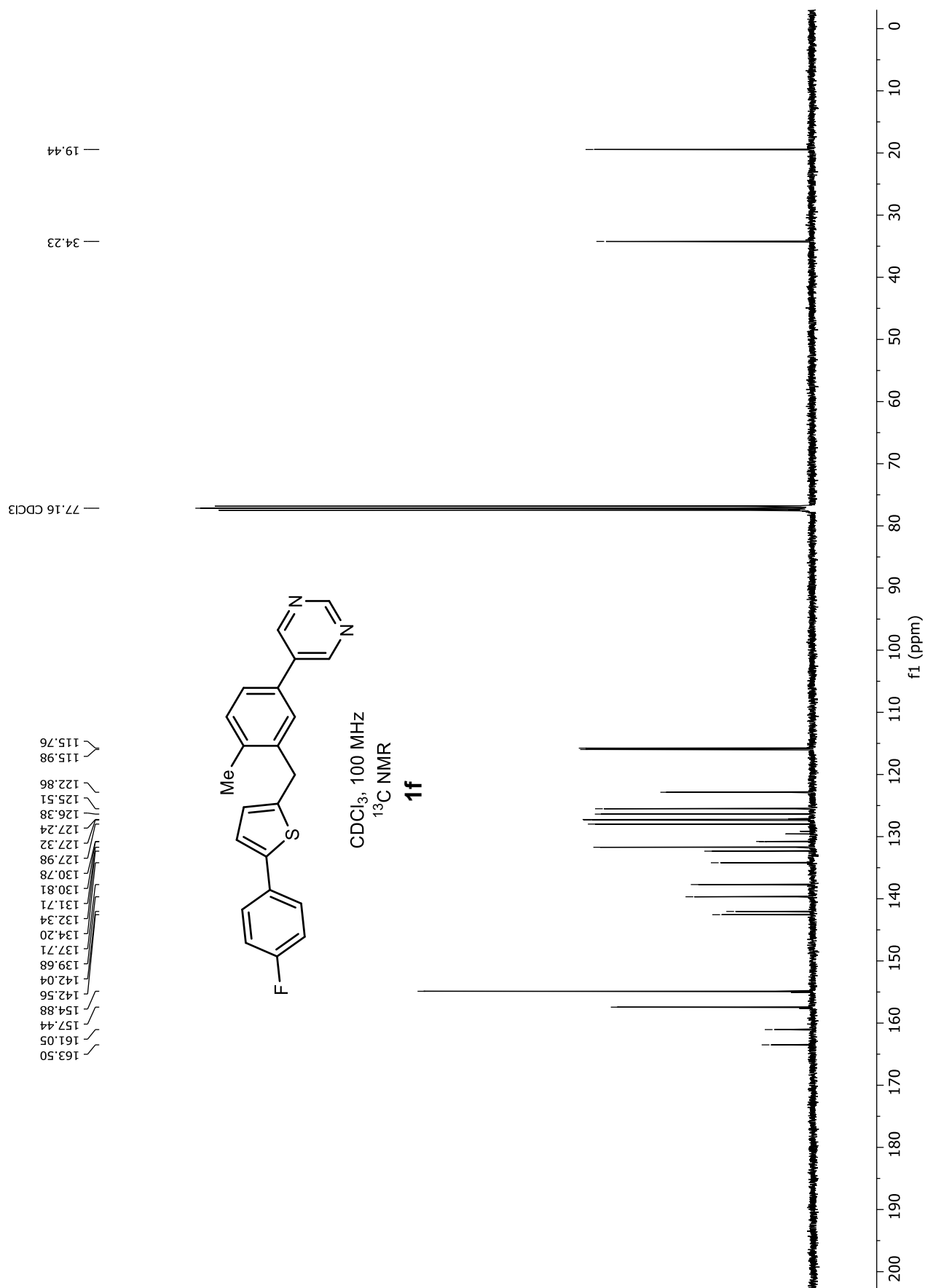


CDCl₃, 375 MHz
¹⁹F NMR

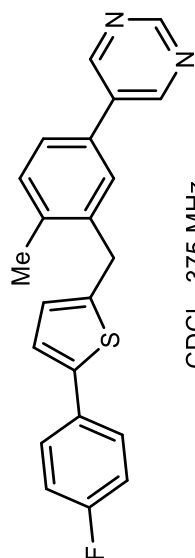
1e

f1 (ppm)





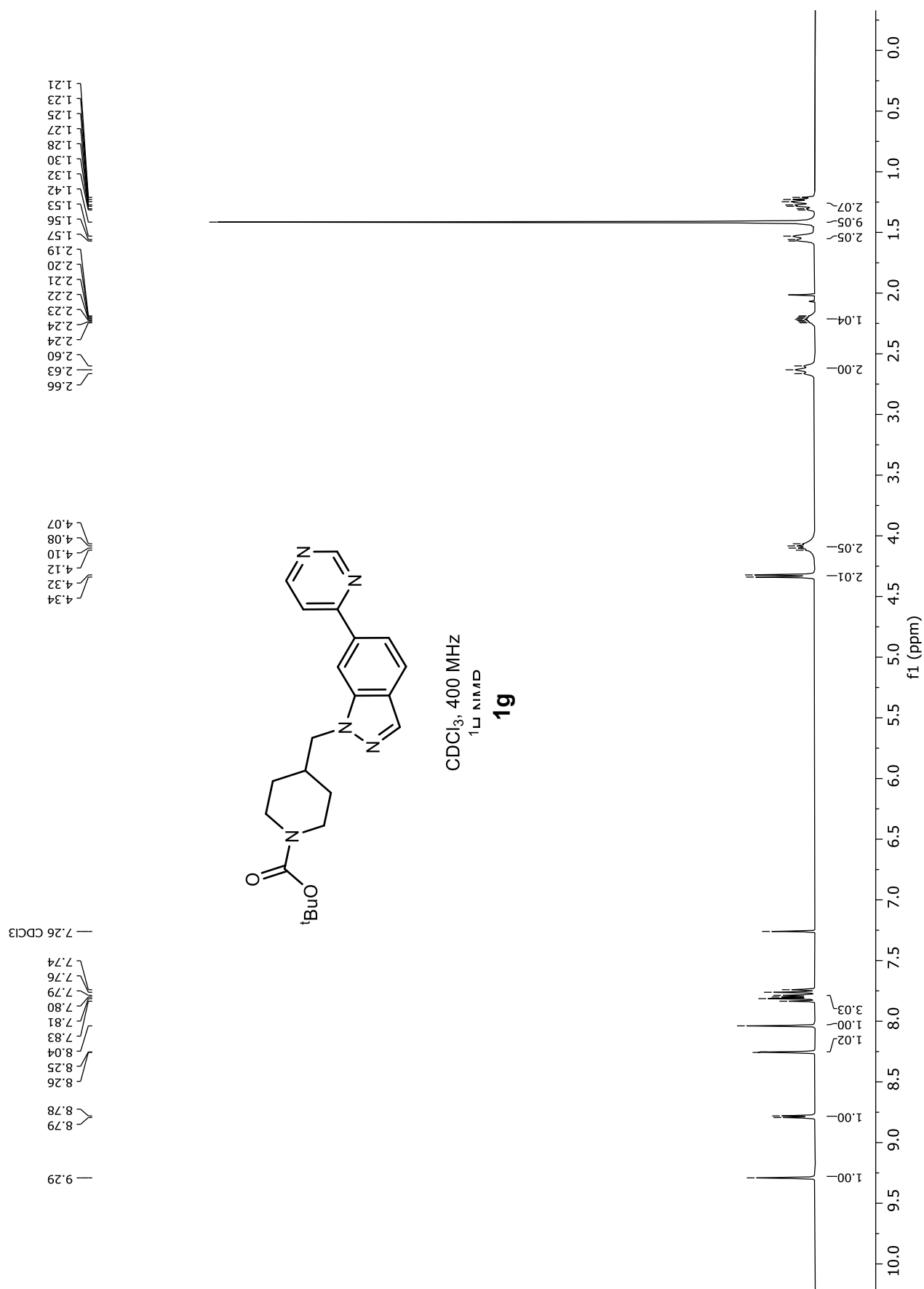
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-114.90
-114.91
-114.92
-114.93
-114.95

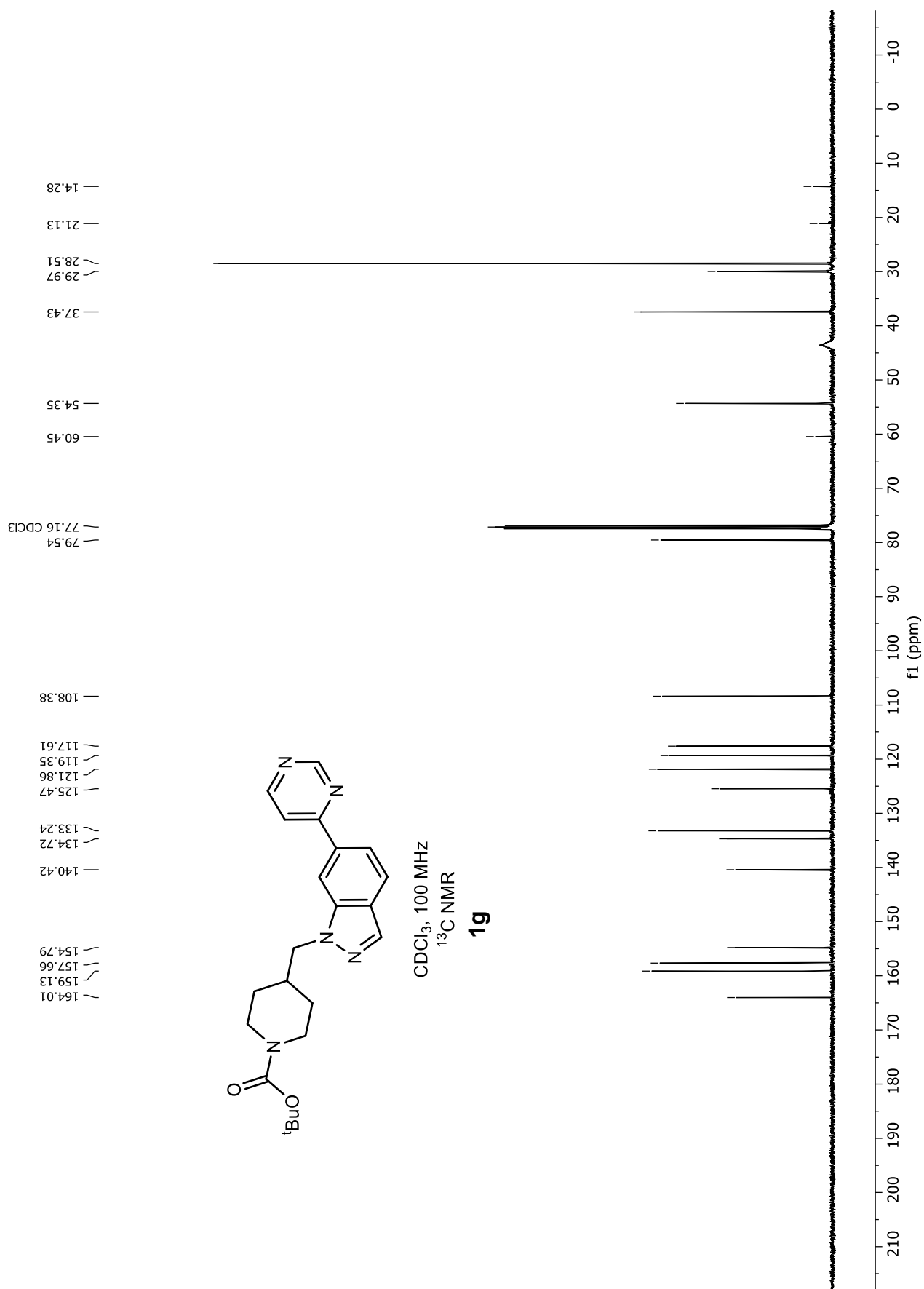


CDCl₃, 375 MHz
101.62444

1f

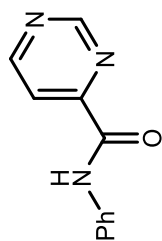
f1 (ppm)



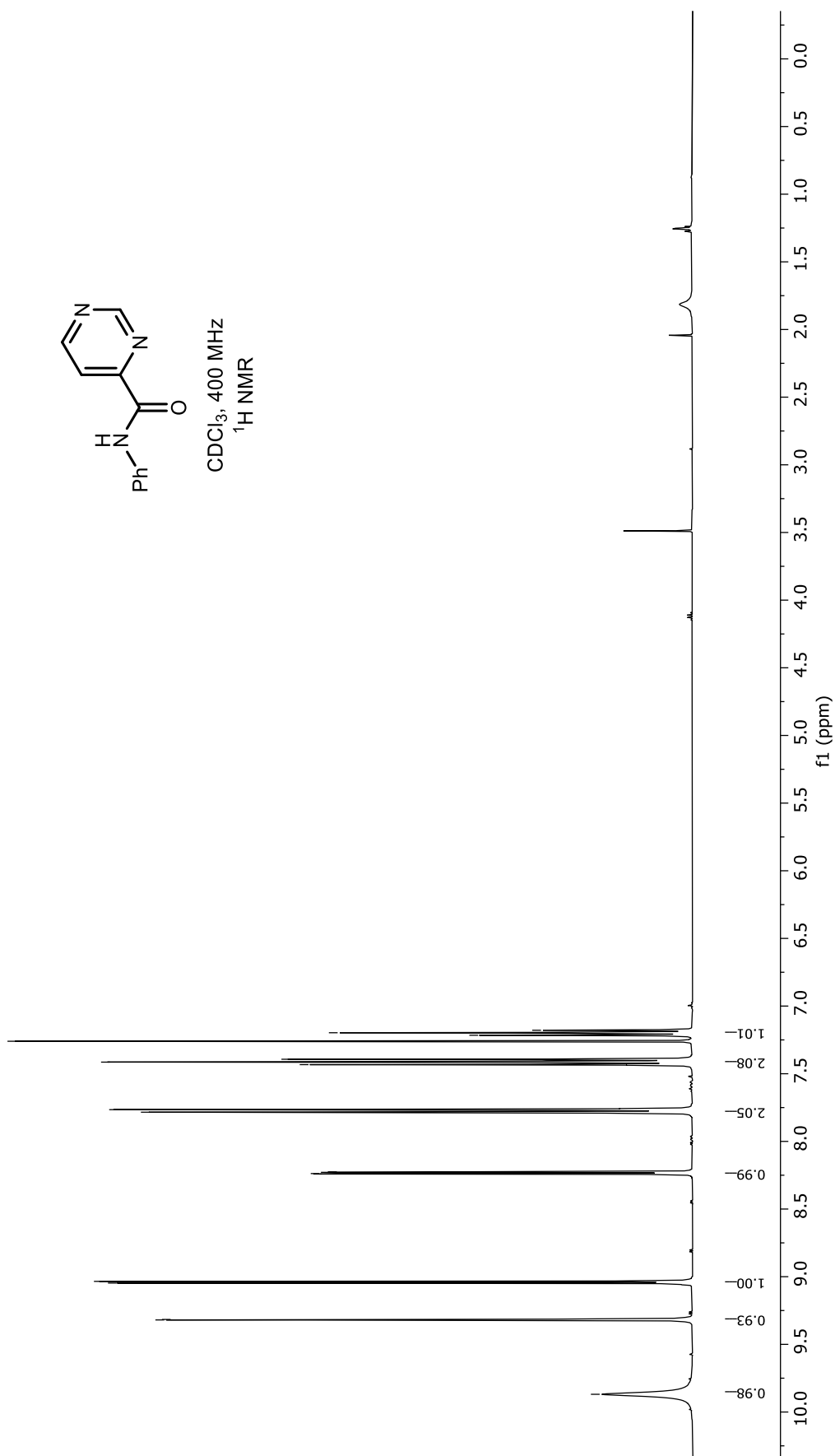


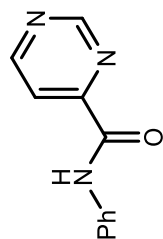
9.87
9.32
9.32
9.05
9.03
8.24
8.23
8.23
7.78
7.77
7.43
7.41
7.39
7.26
7.22
7.20
7.18

CDCl₃

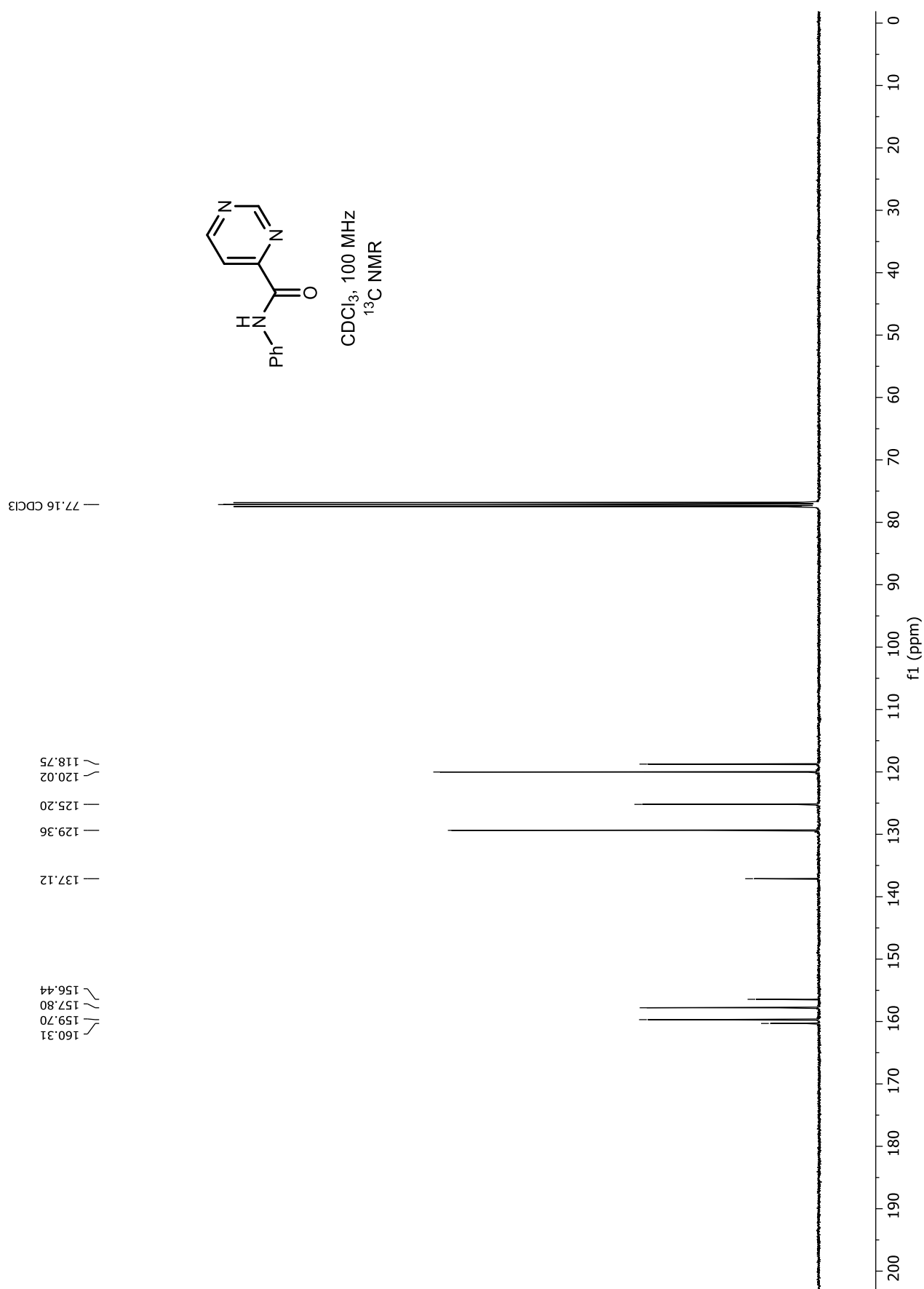


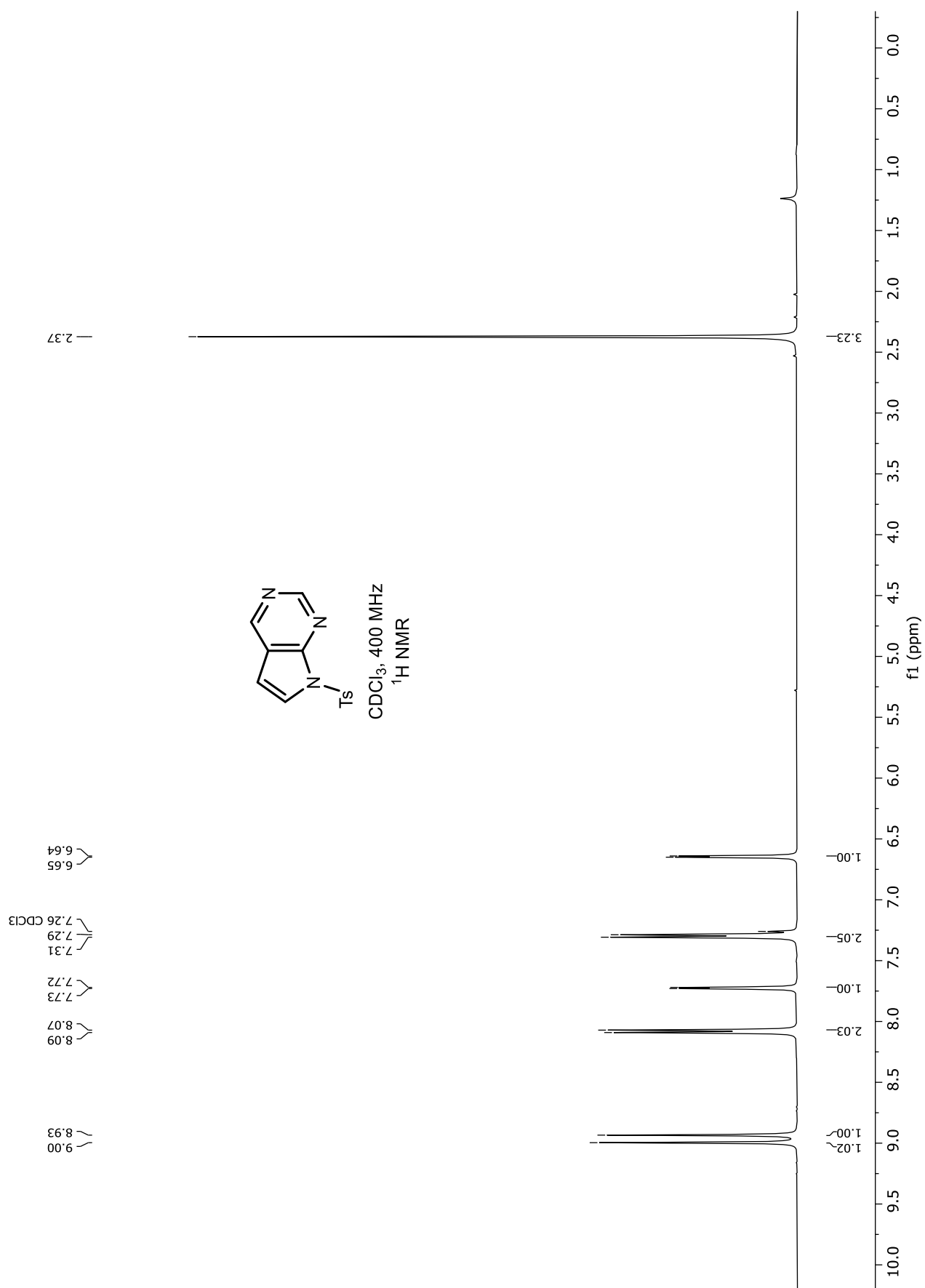
CDCl₃, 400 MHz
¹H NMR

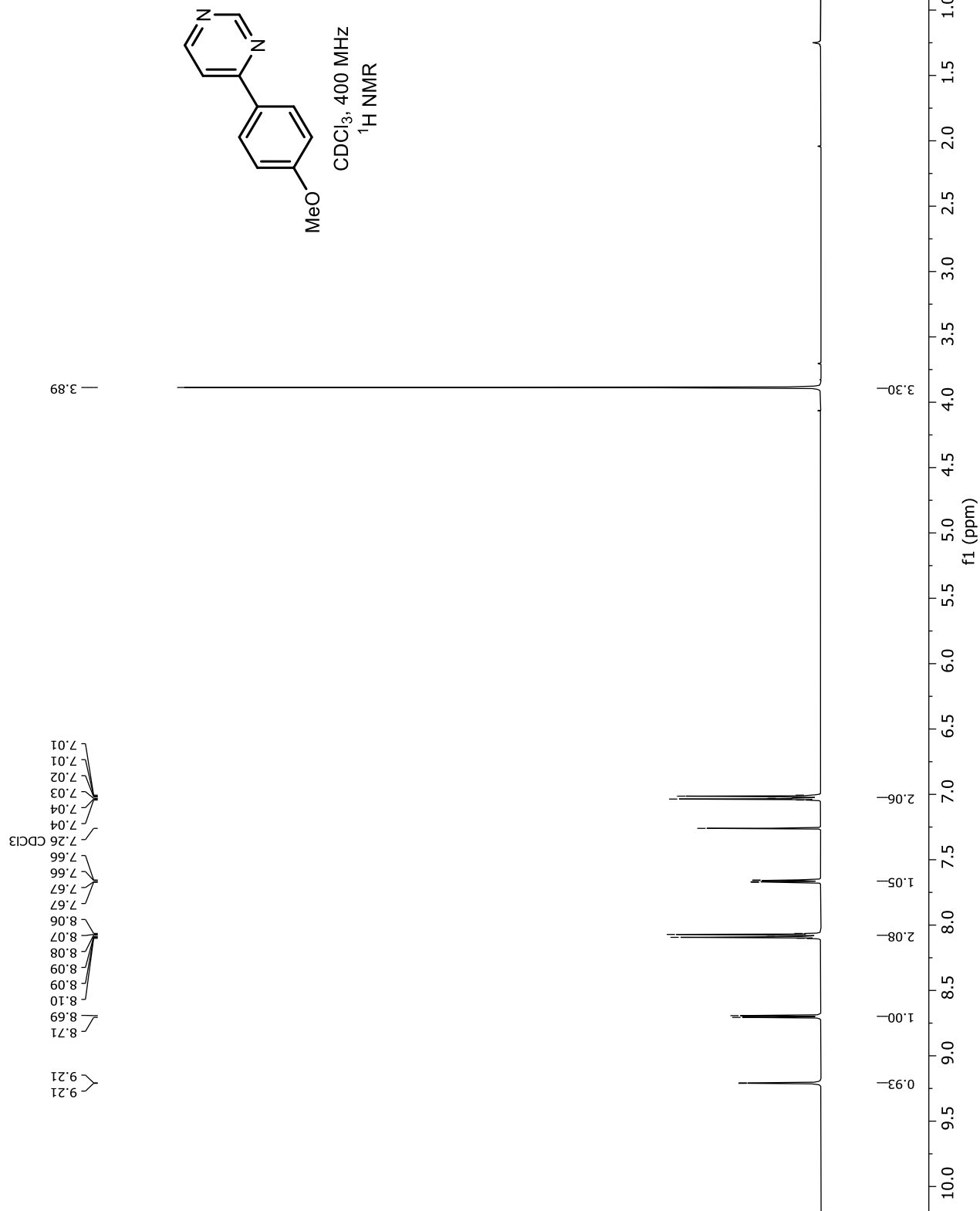




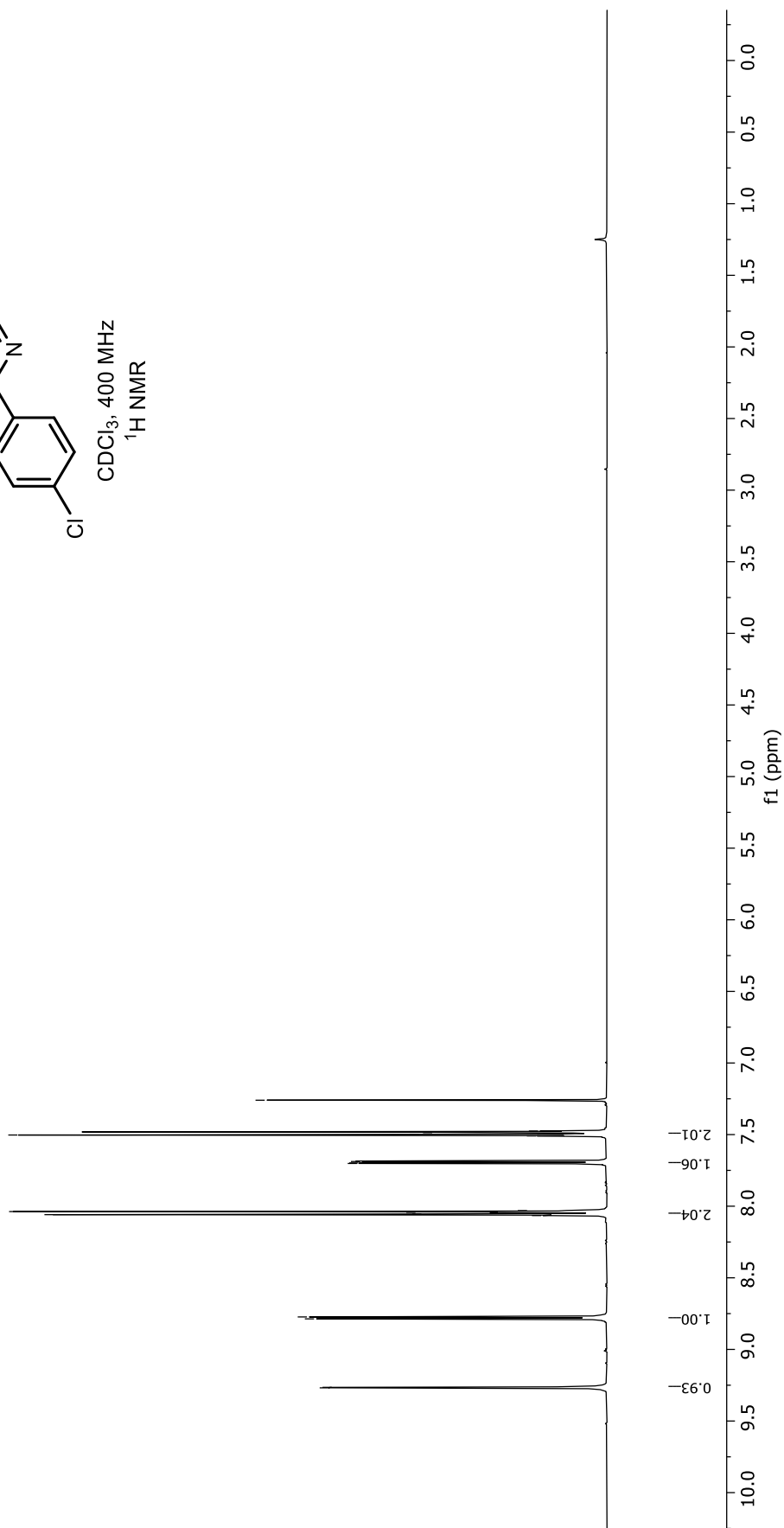
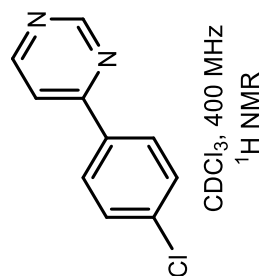
CDCl₃, 100 MHz
¹³C NMR



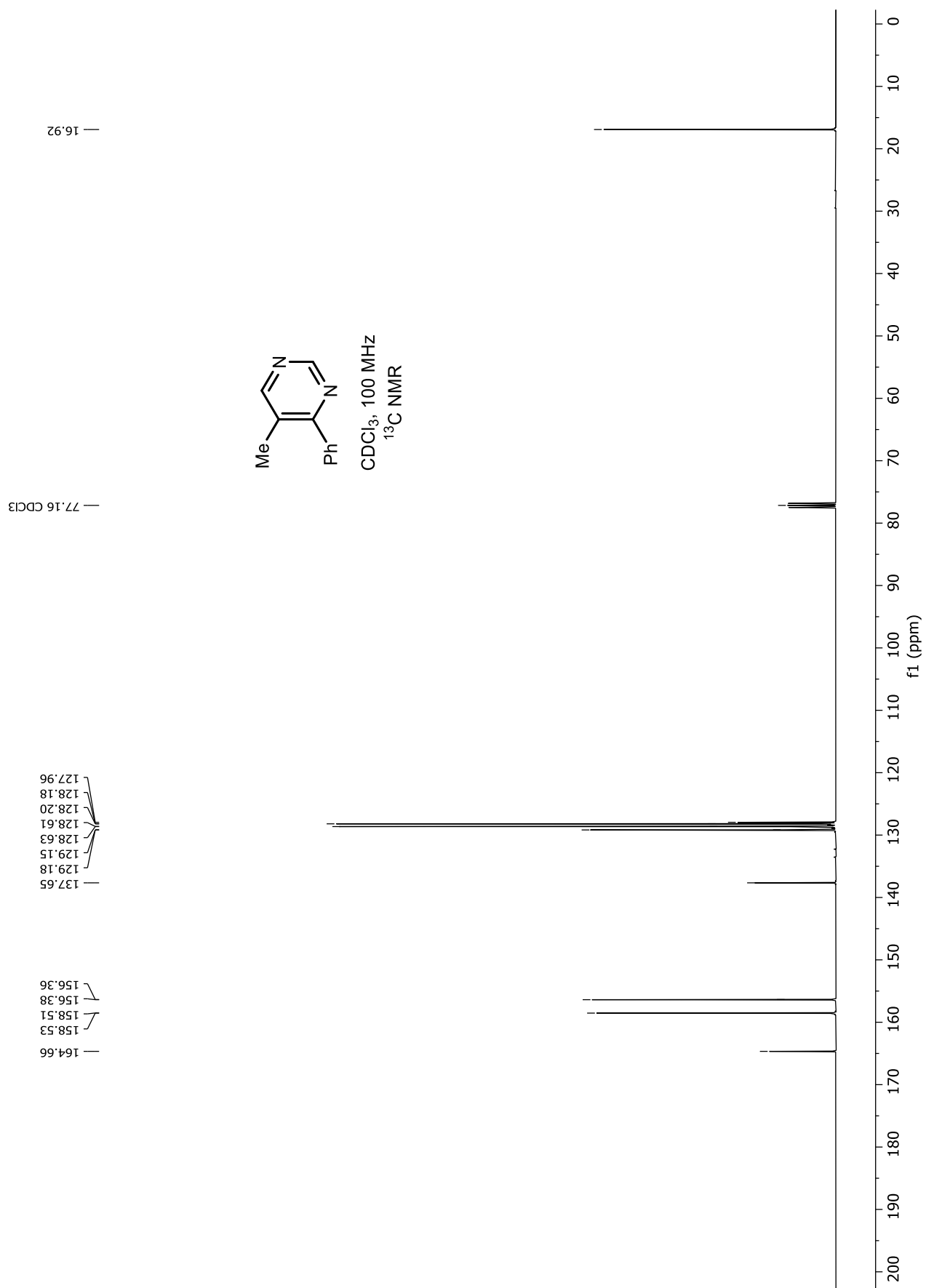


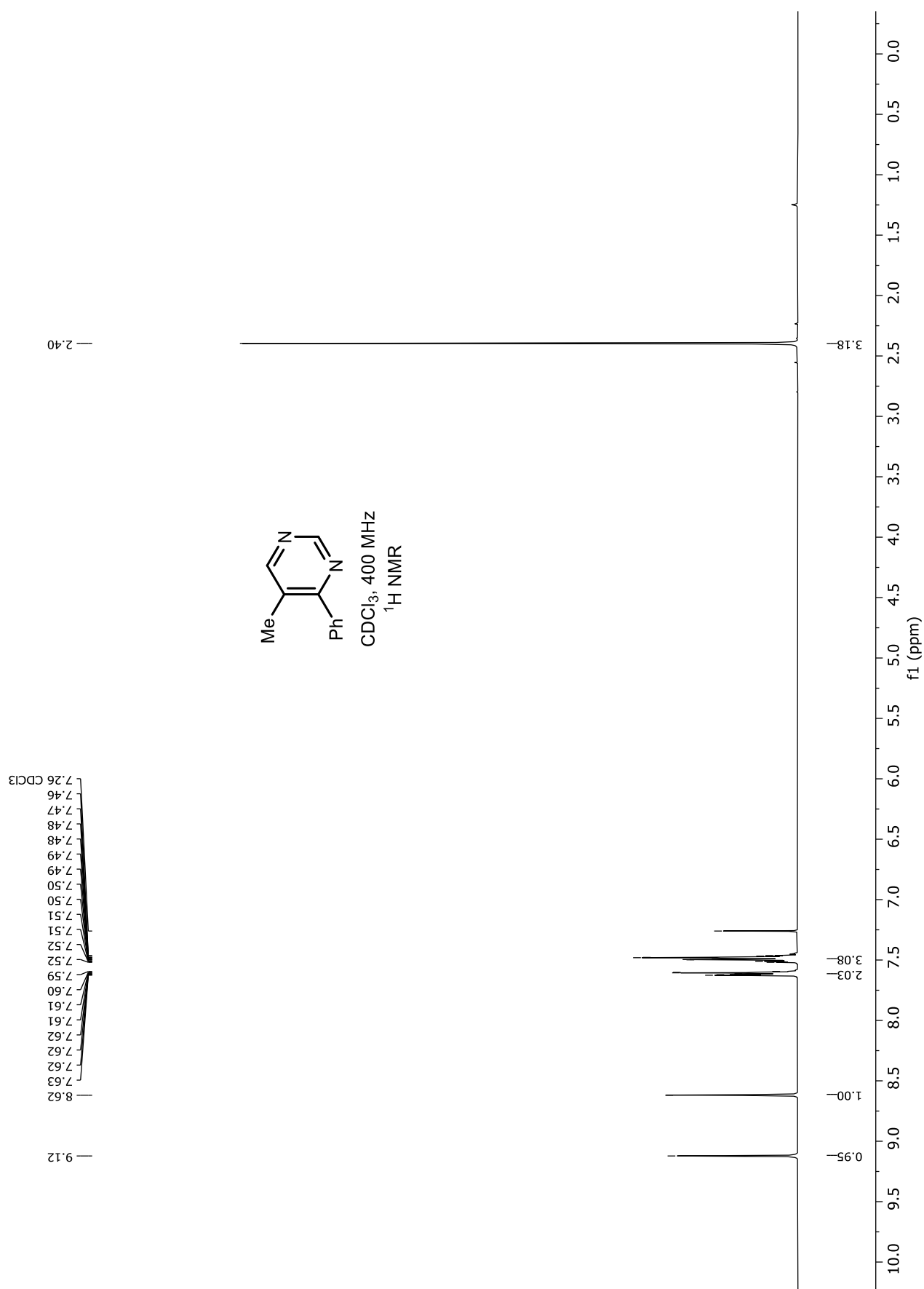


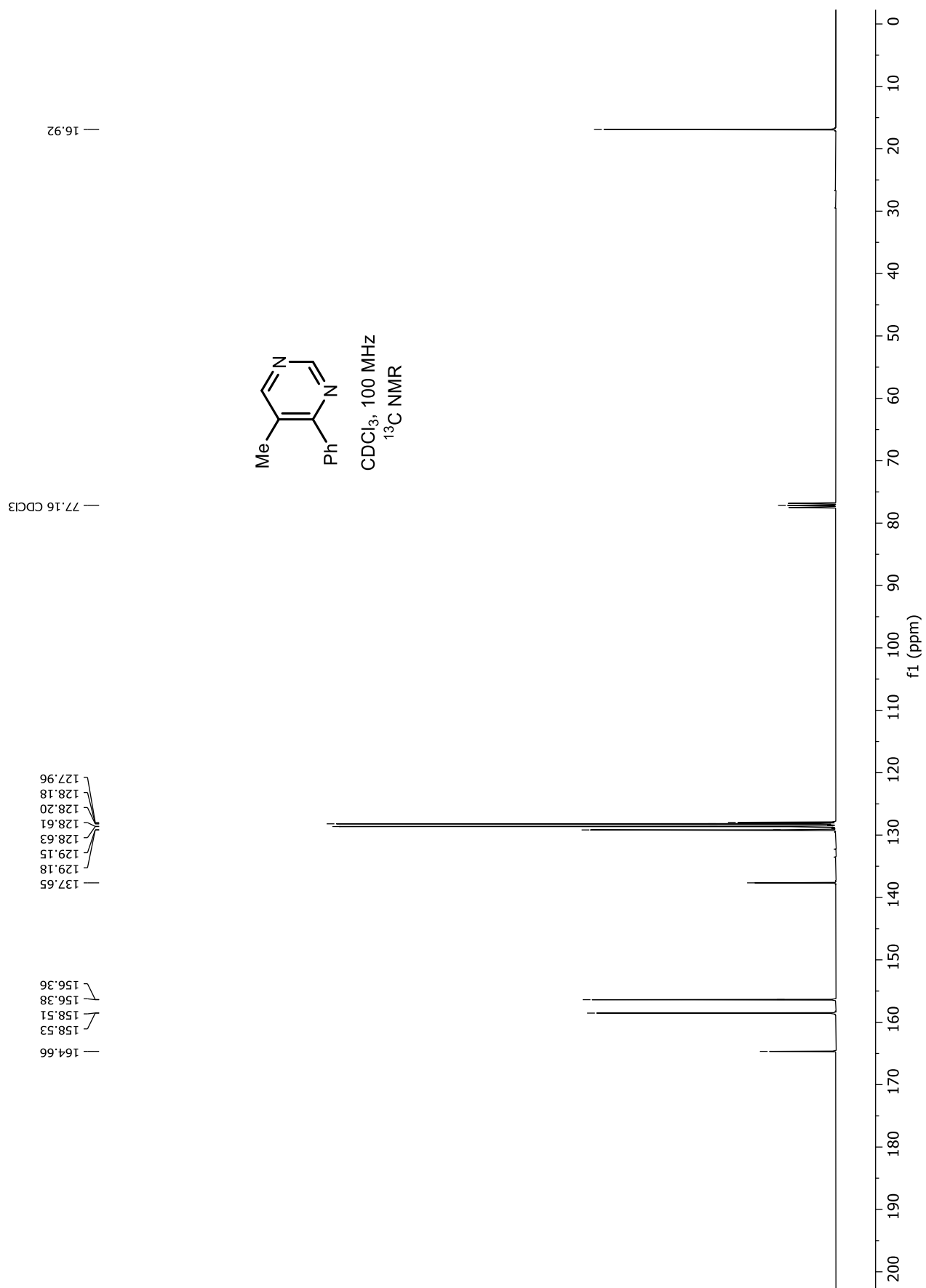
9.27
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 8.05
 8.04
 8.04
 8.03
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 7.70
 7.69
 7.68
 7.51
 7.50
 7.50
 7.49
 7.48
 7.47
 7.26 CDCl₃





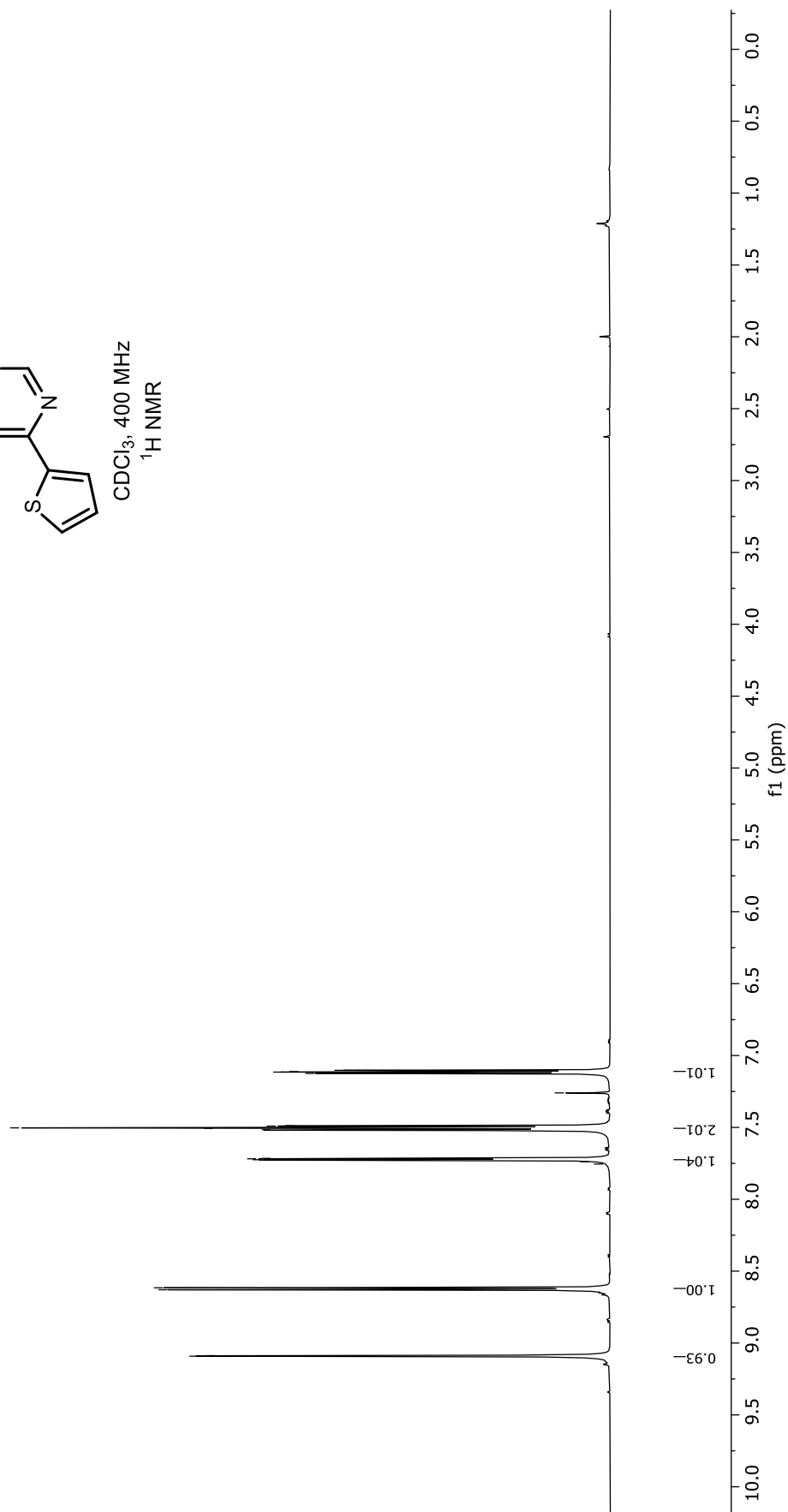
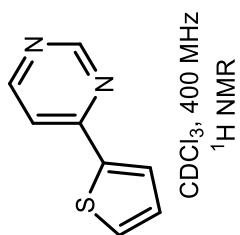


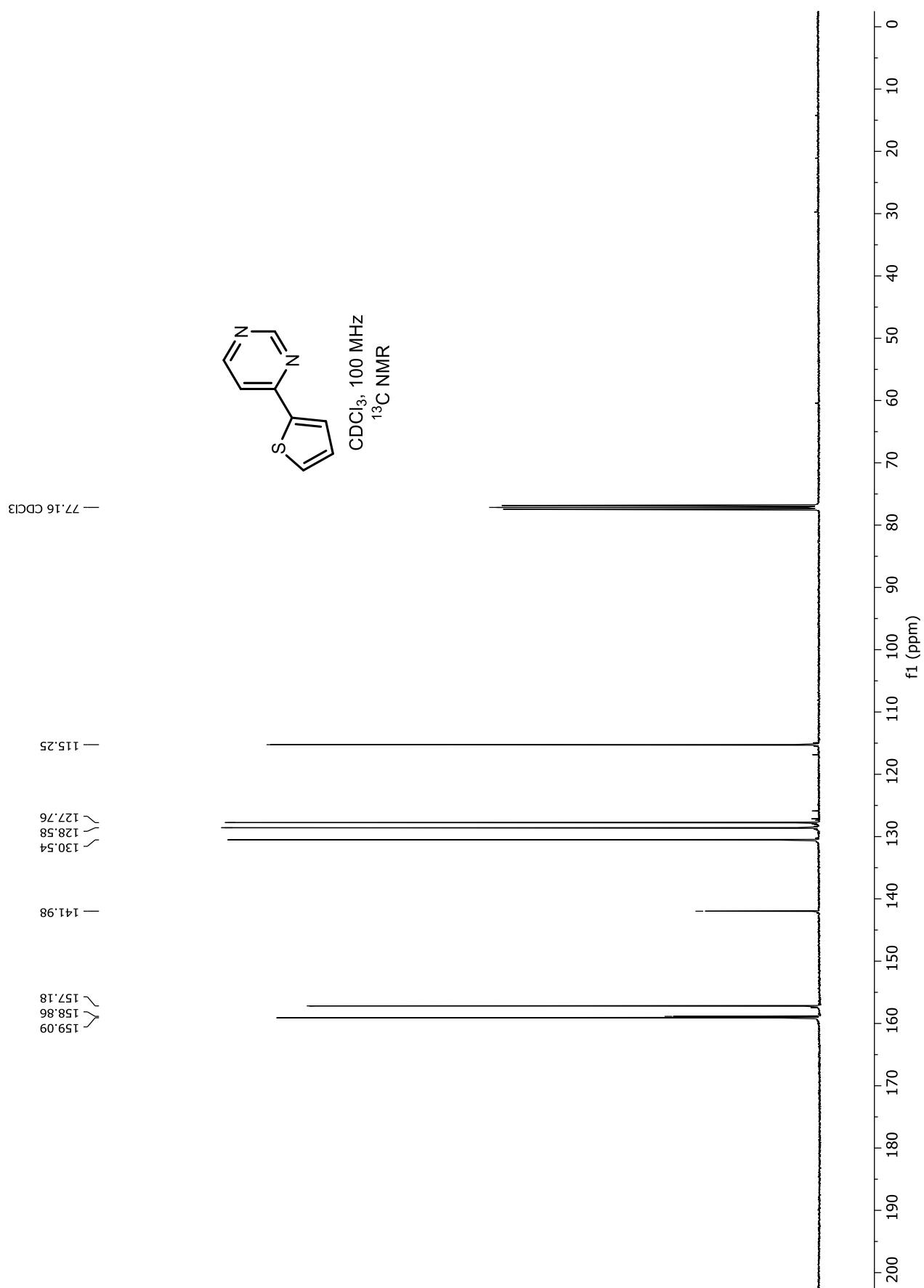


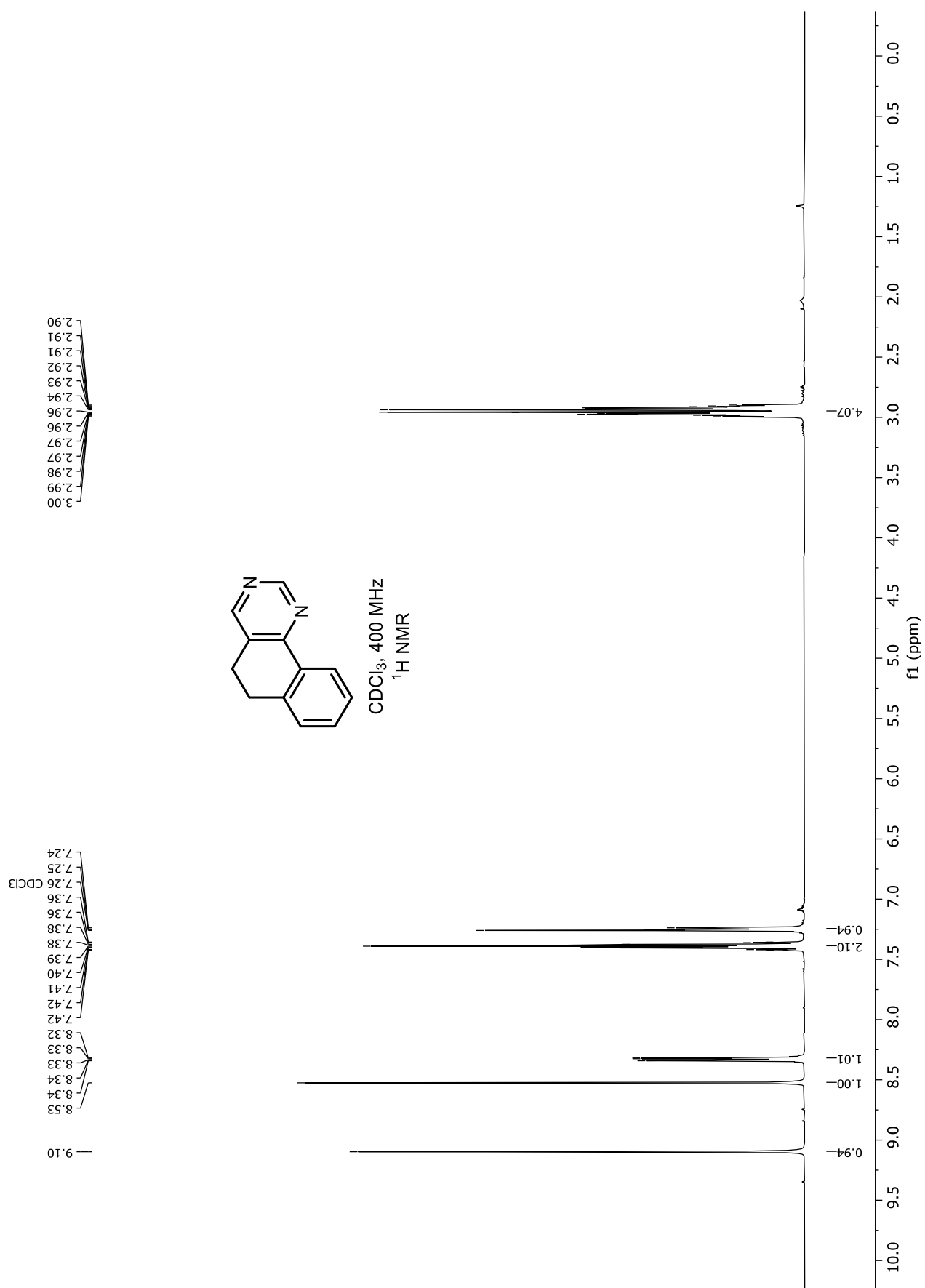


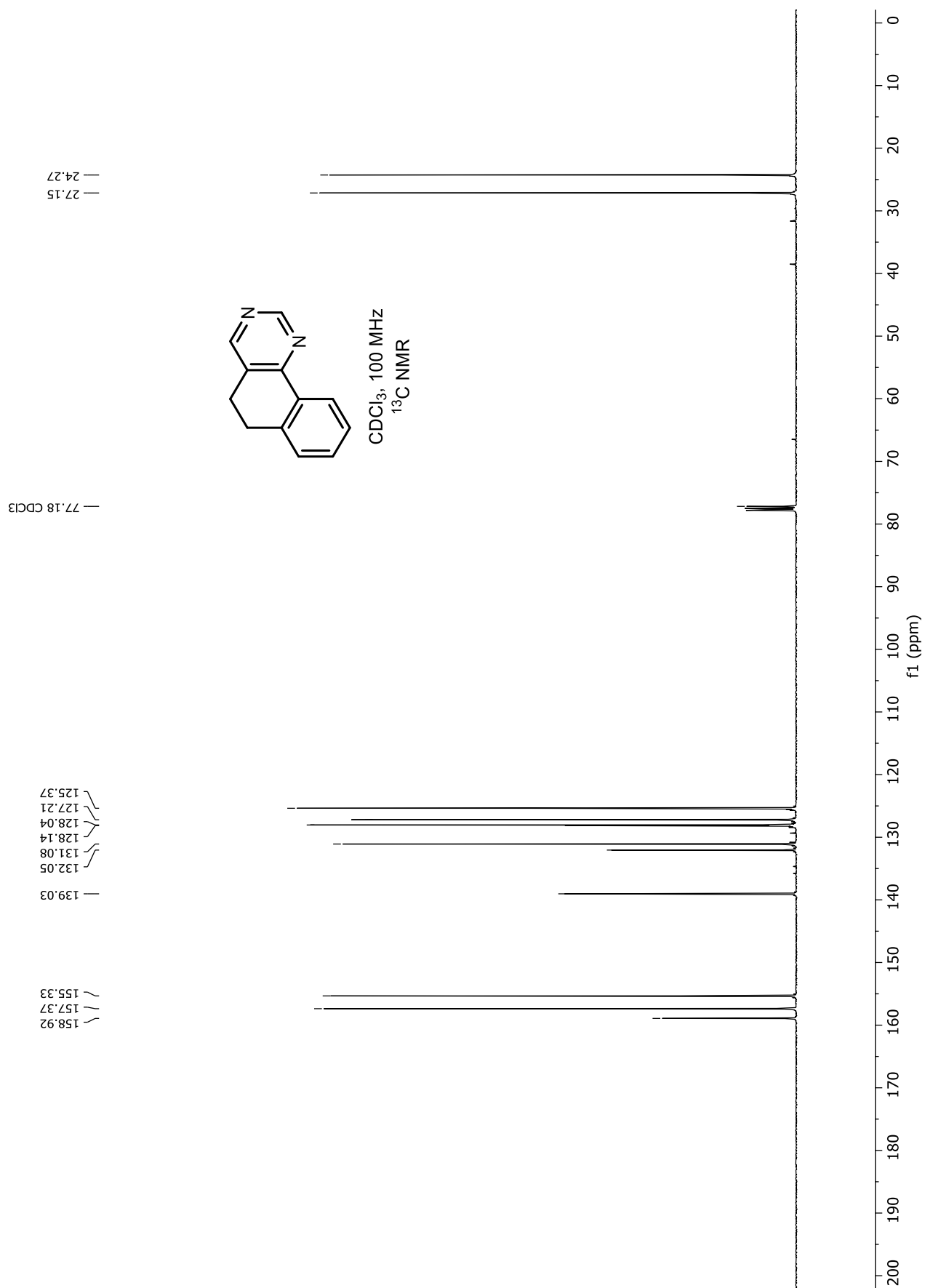
9.09
9.09
8.63
8.62
7.76
7.74
7.73
7.72
7.72
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7.49
7.49
7.26
7.12
7.12
7.11
7.10

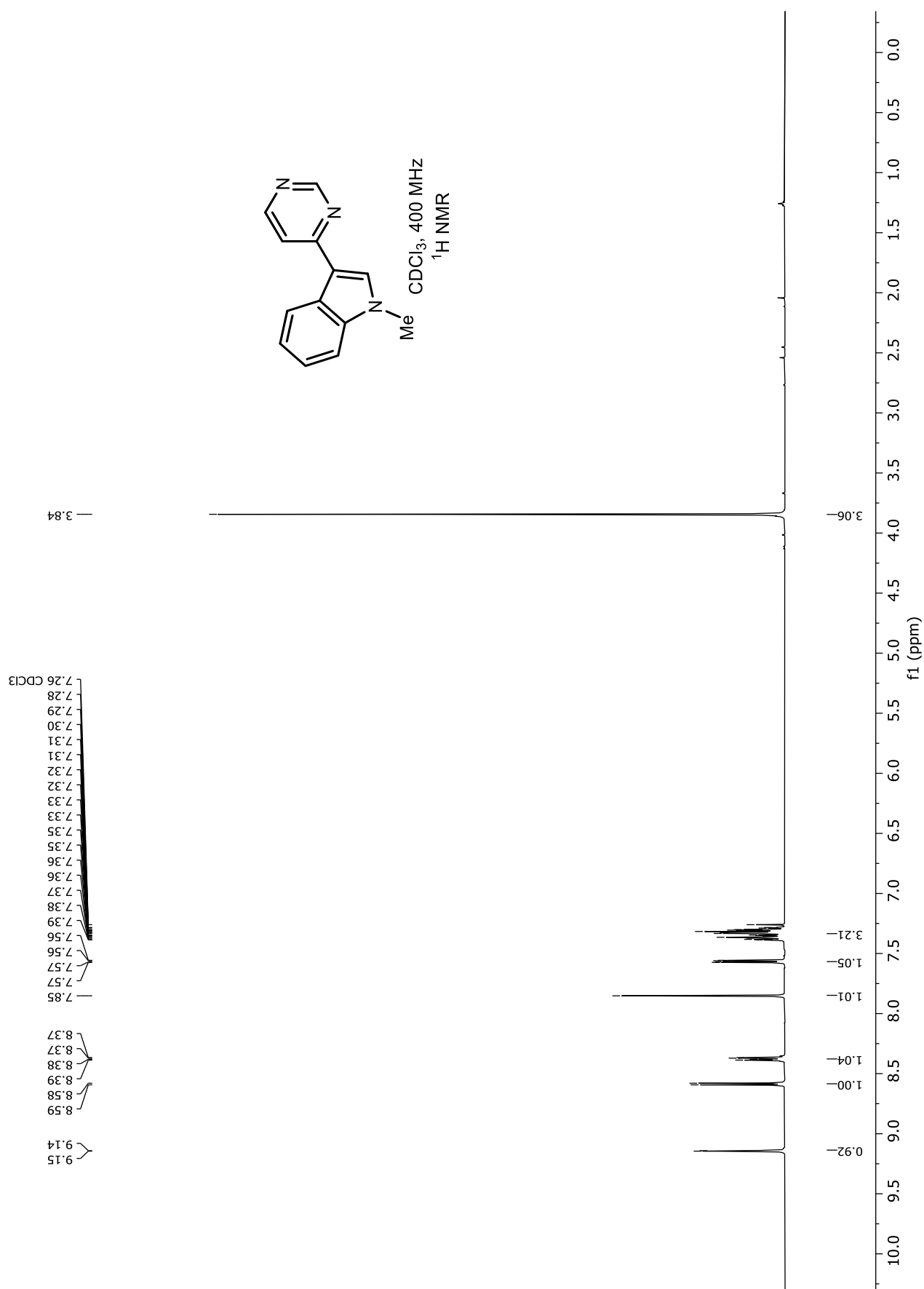
CDCl₃

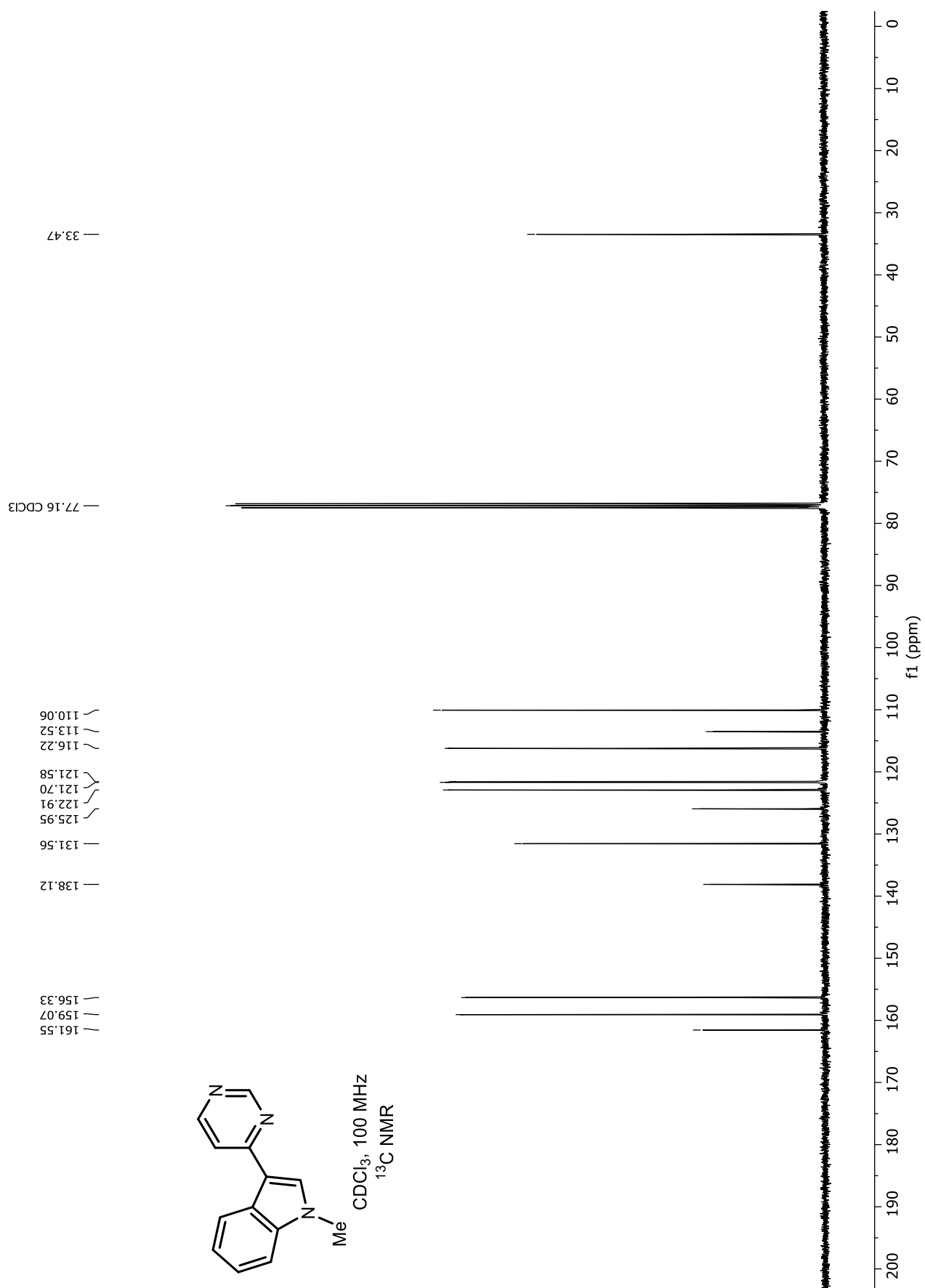


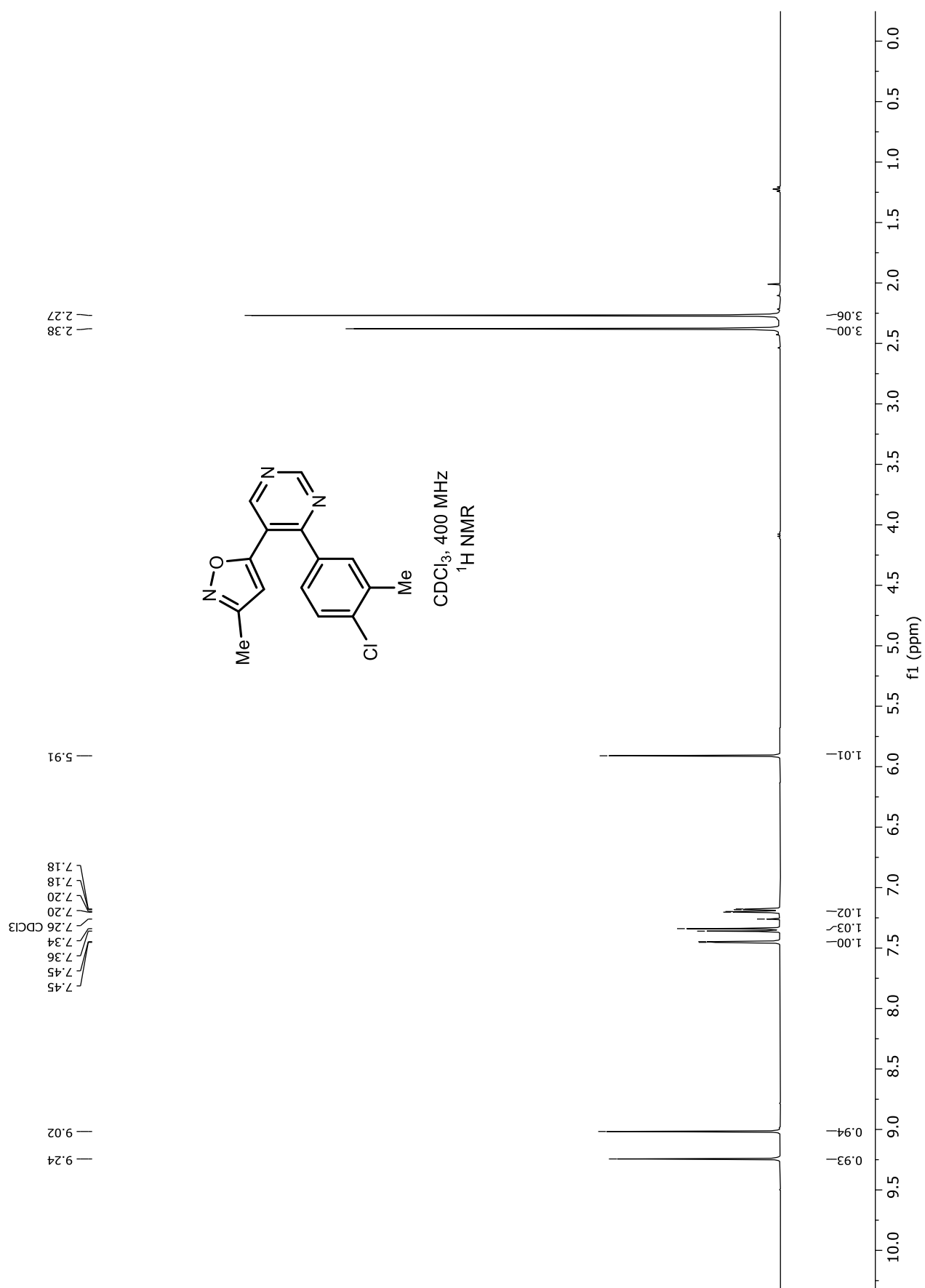


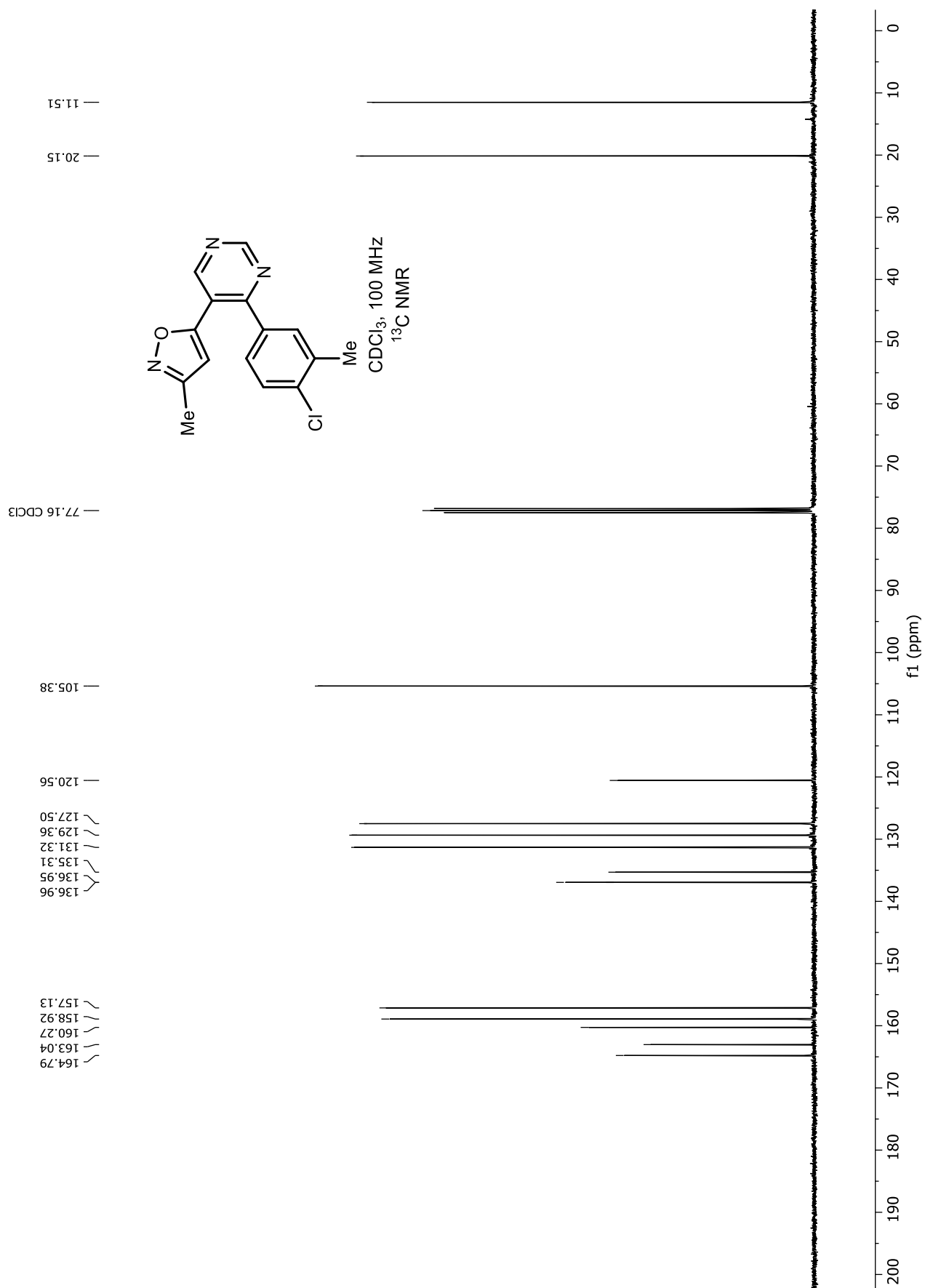


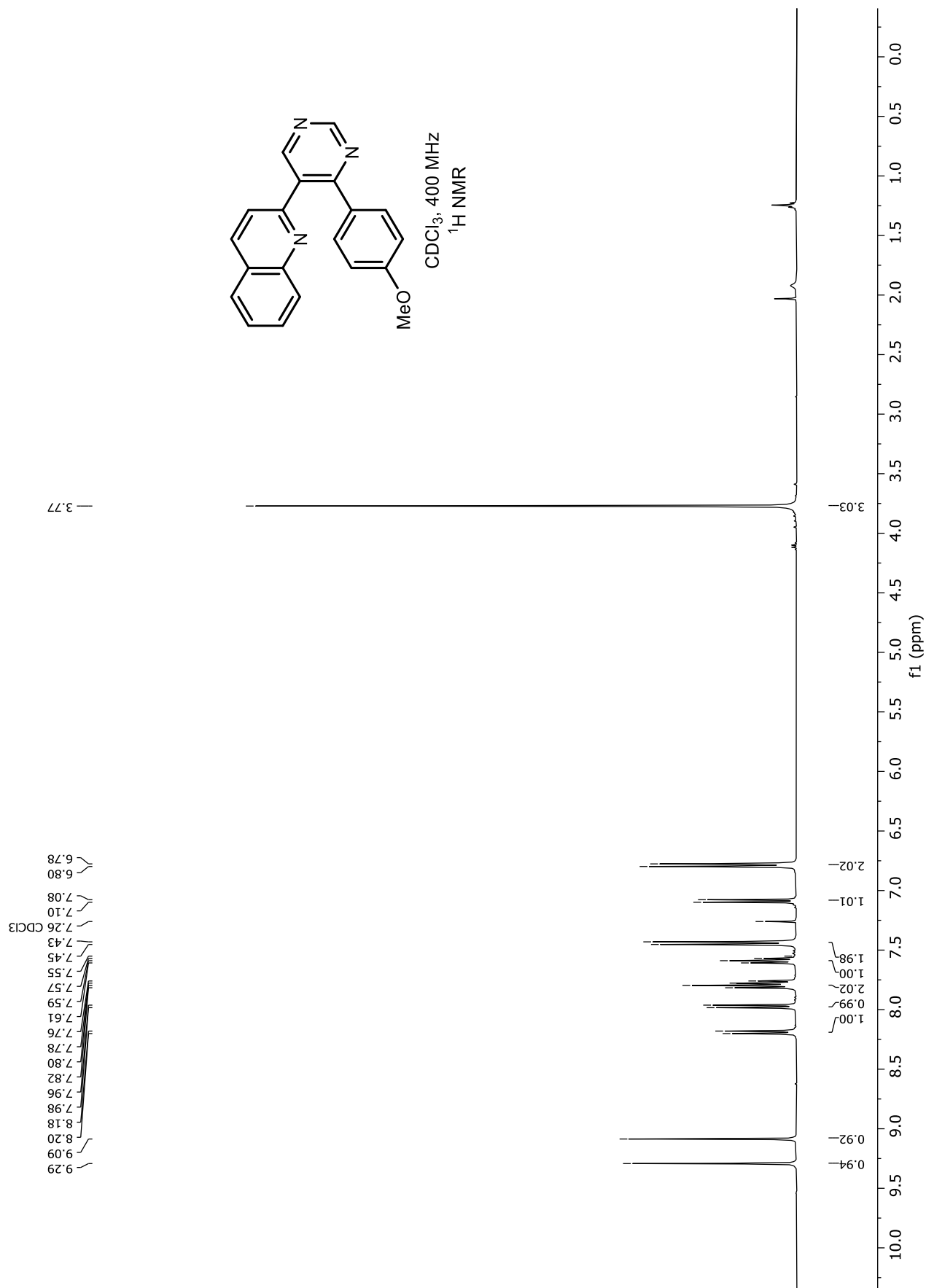


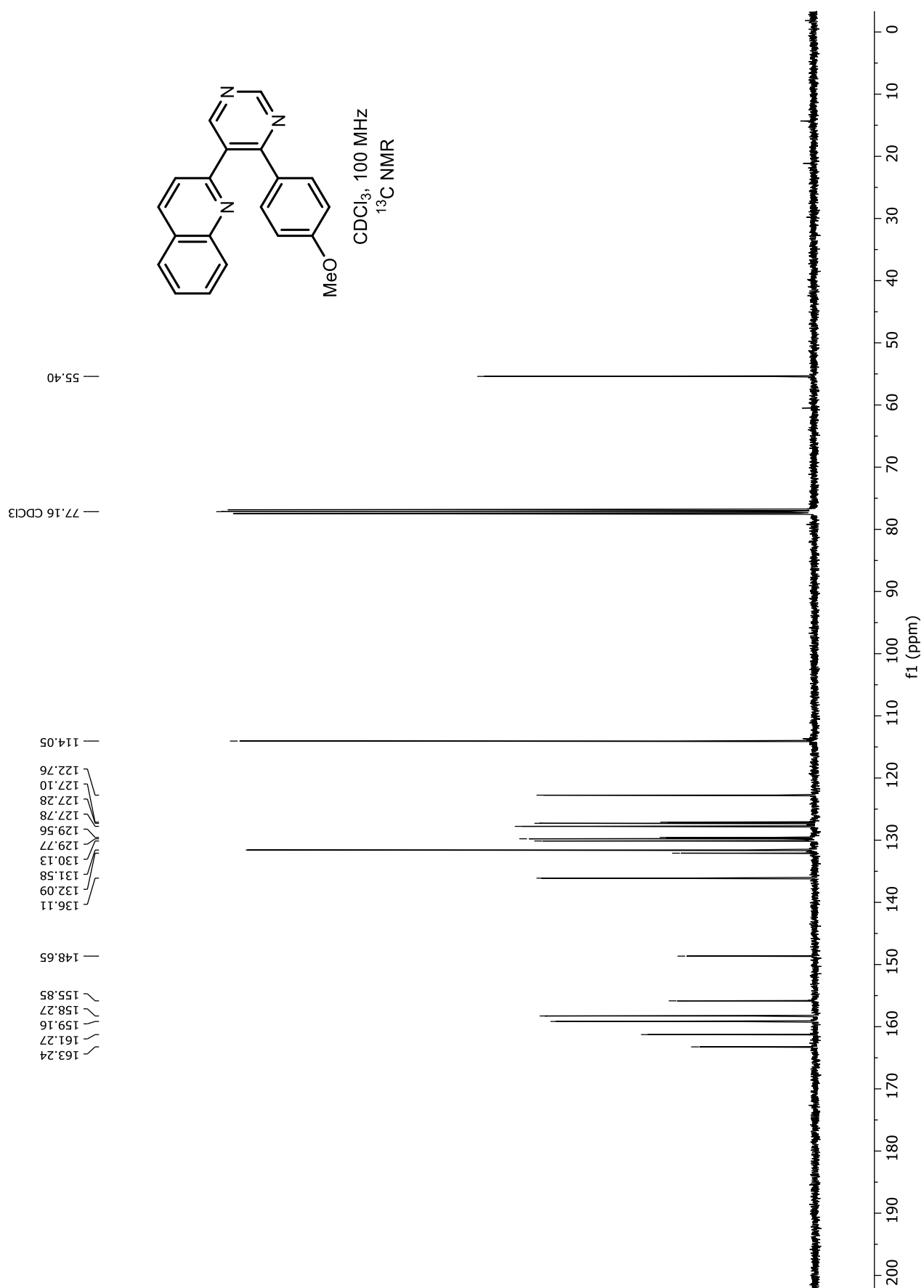




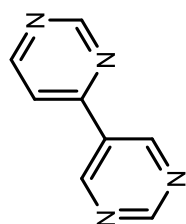




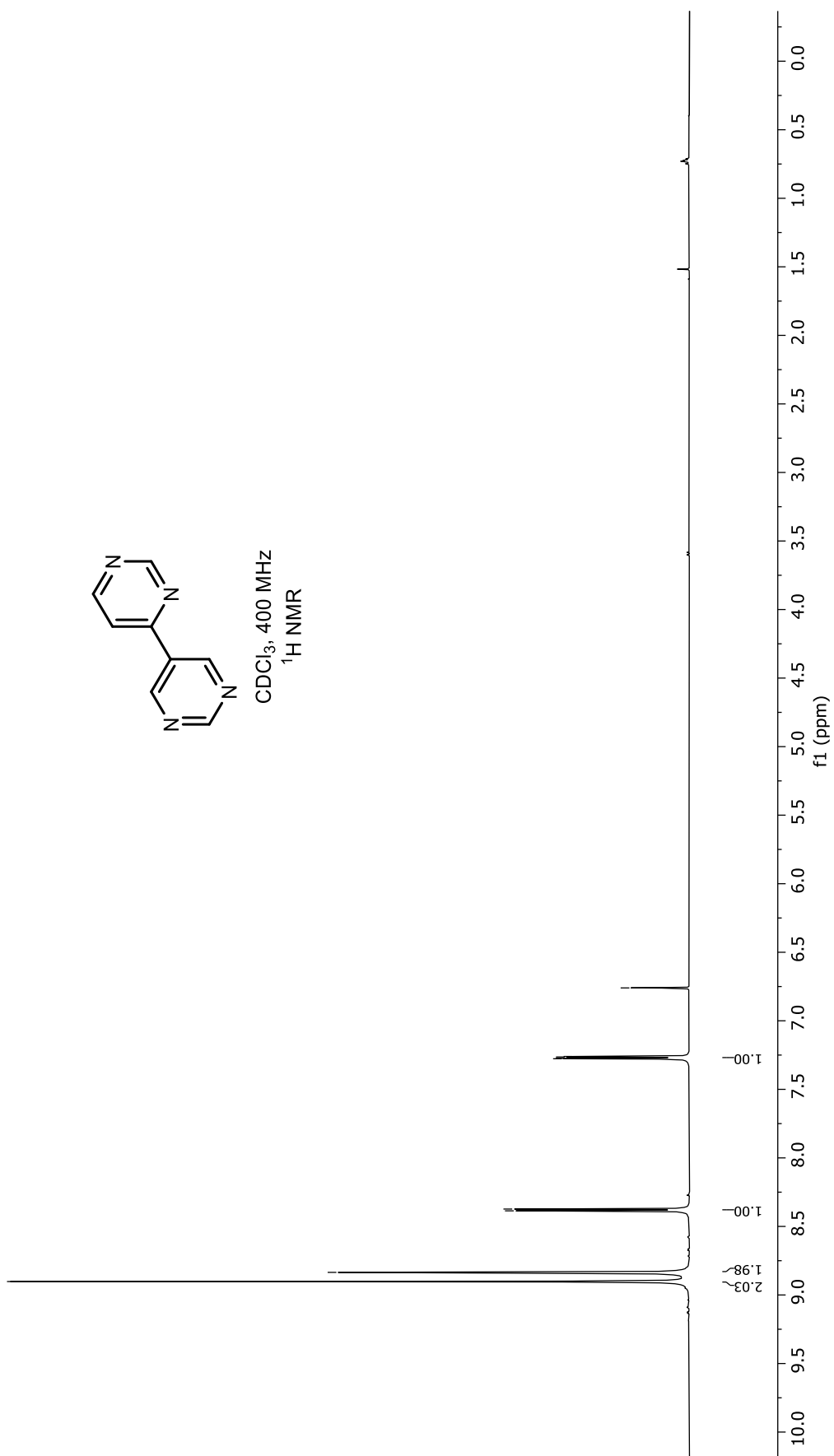


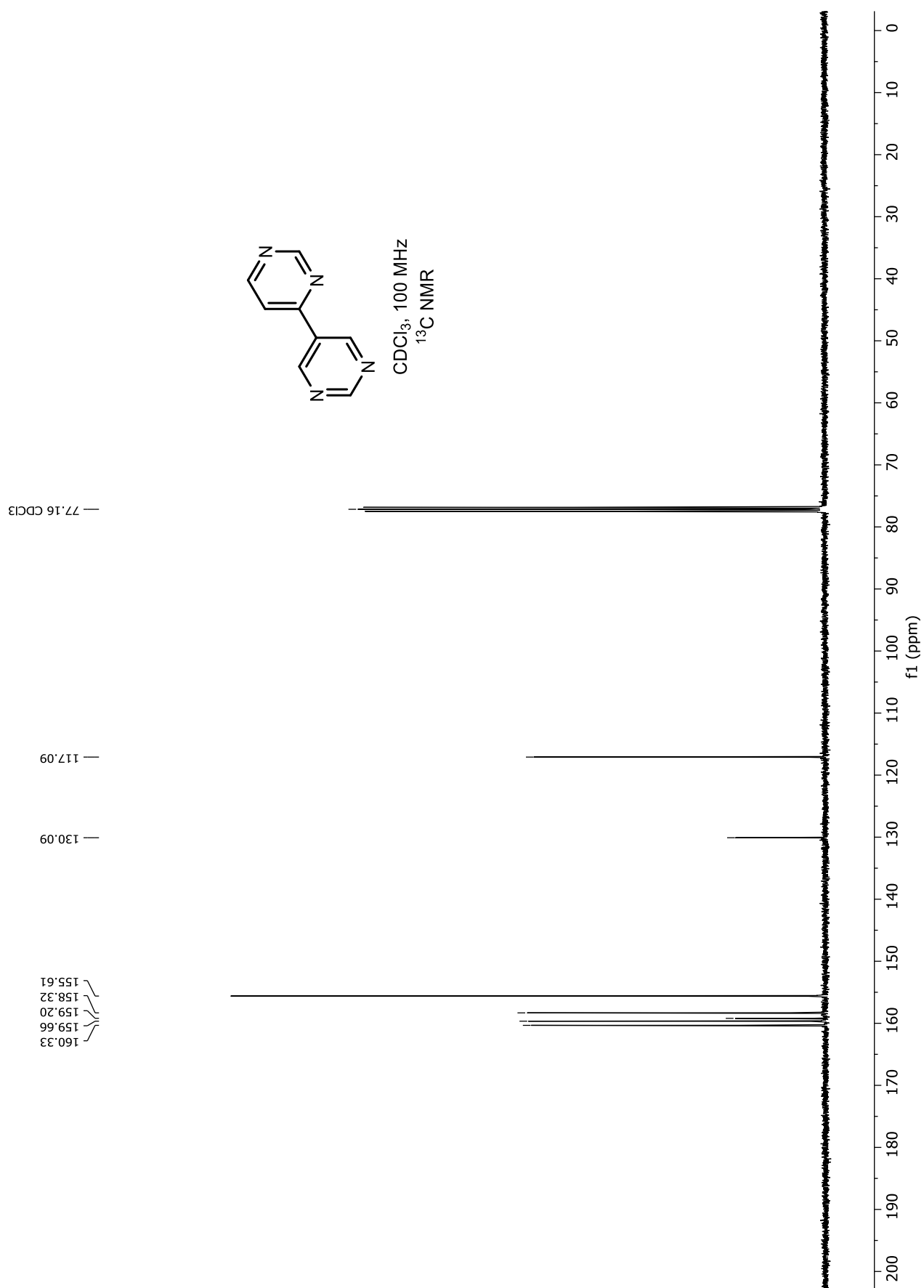


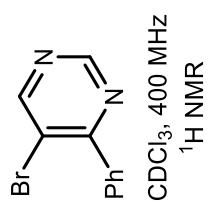
8.90
8.84
8.39
8.37
7.28
7.27
7.26
7.26
6.76



CDCl₃, 400 MHz
¹H NMR

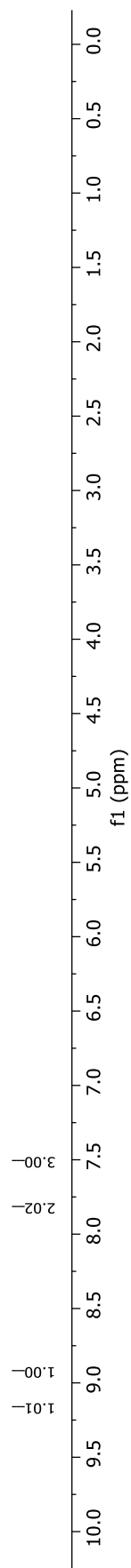


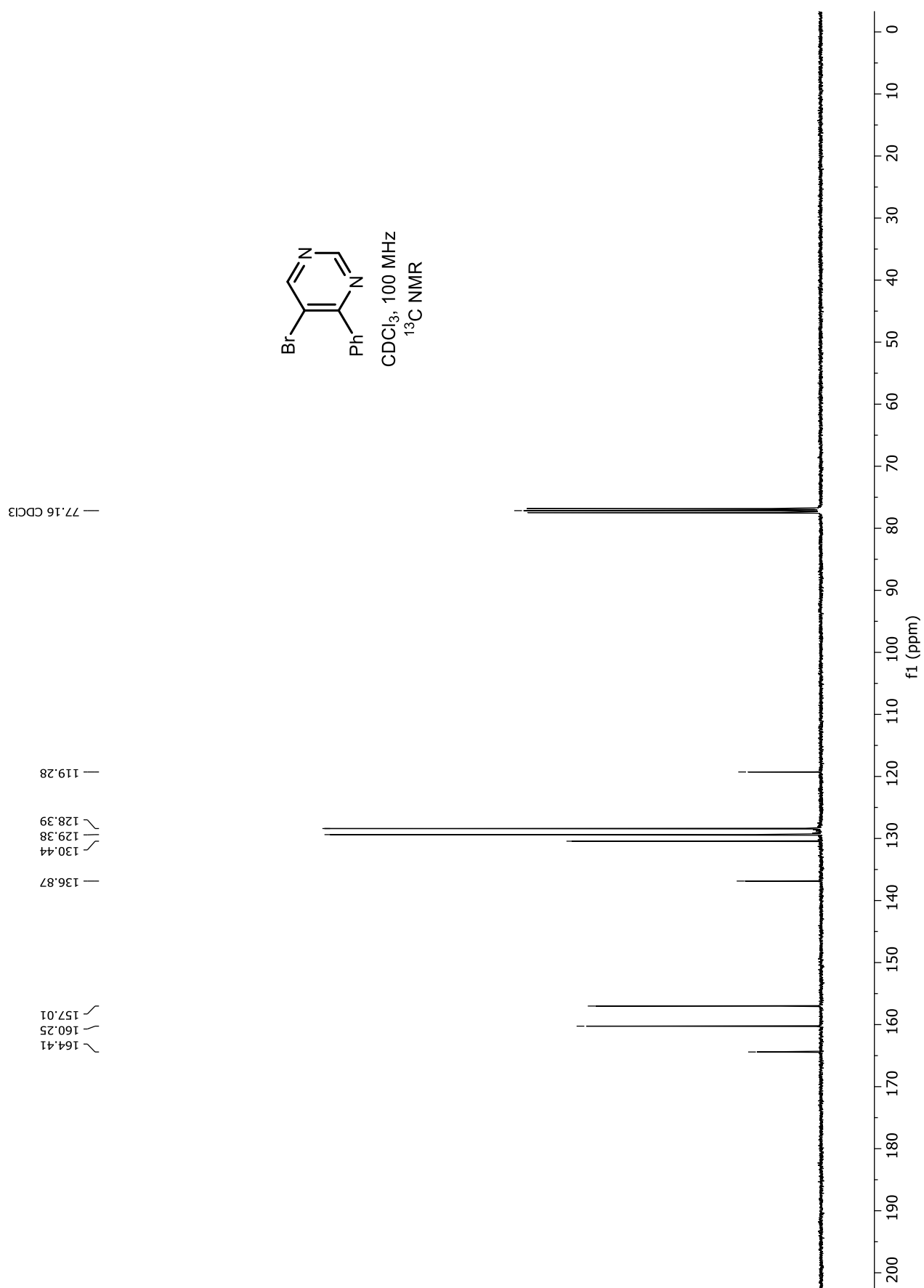
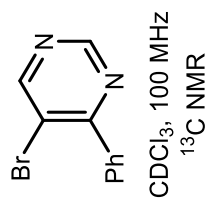


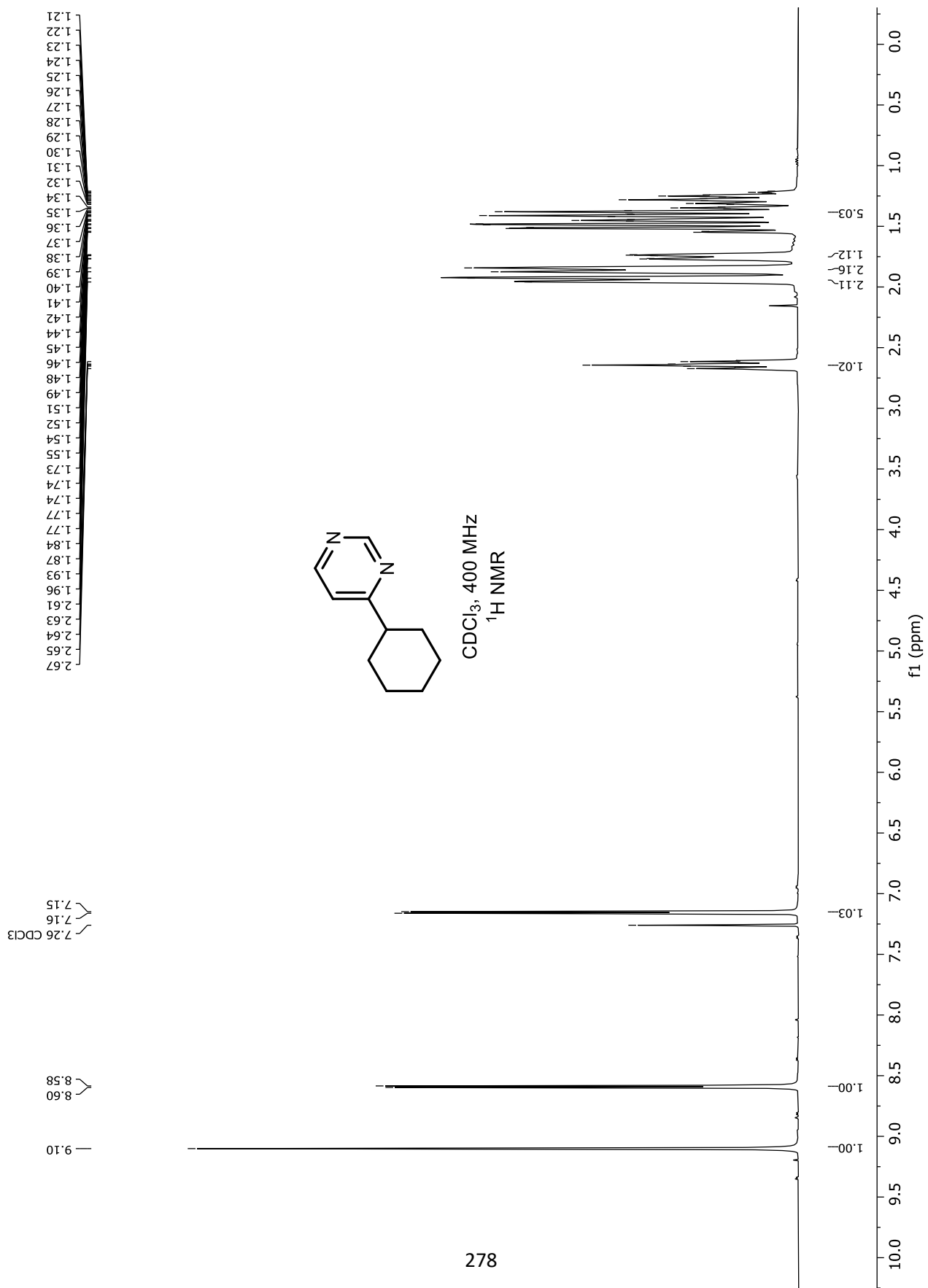


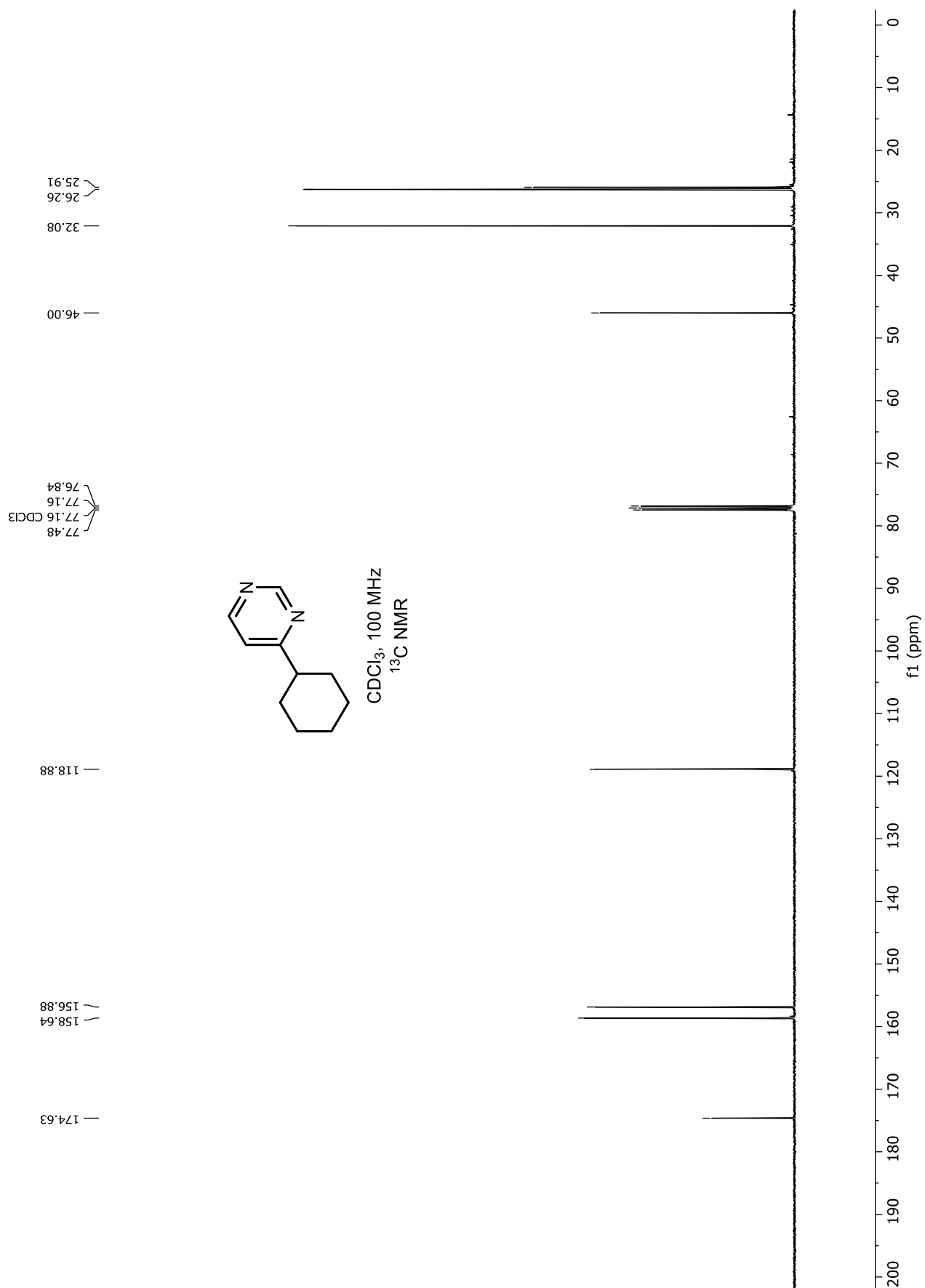
7.83
 7.82
 7.81
 7.80
 7.80
 7.51
 7.51
 7.50
 7.26 CDCl₃

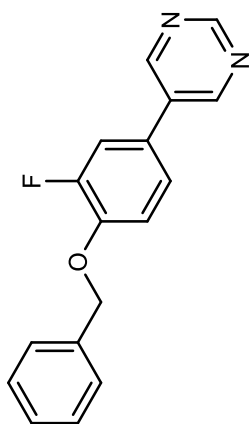
9.16
 8.92











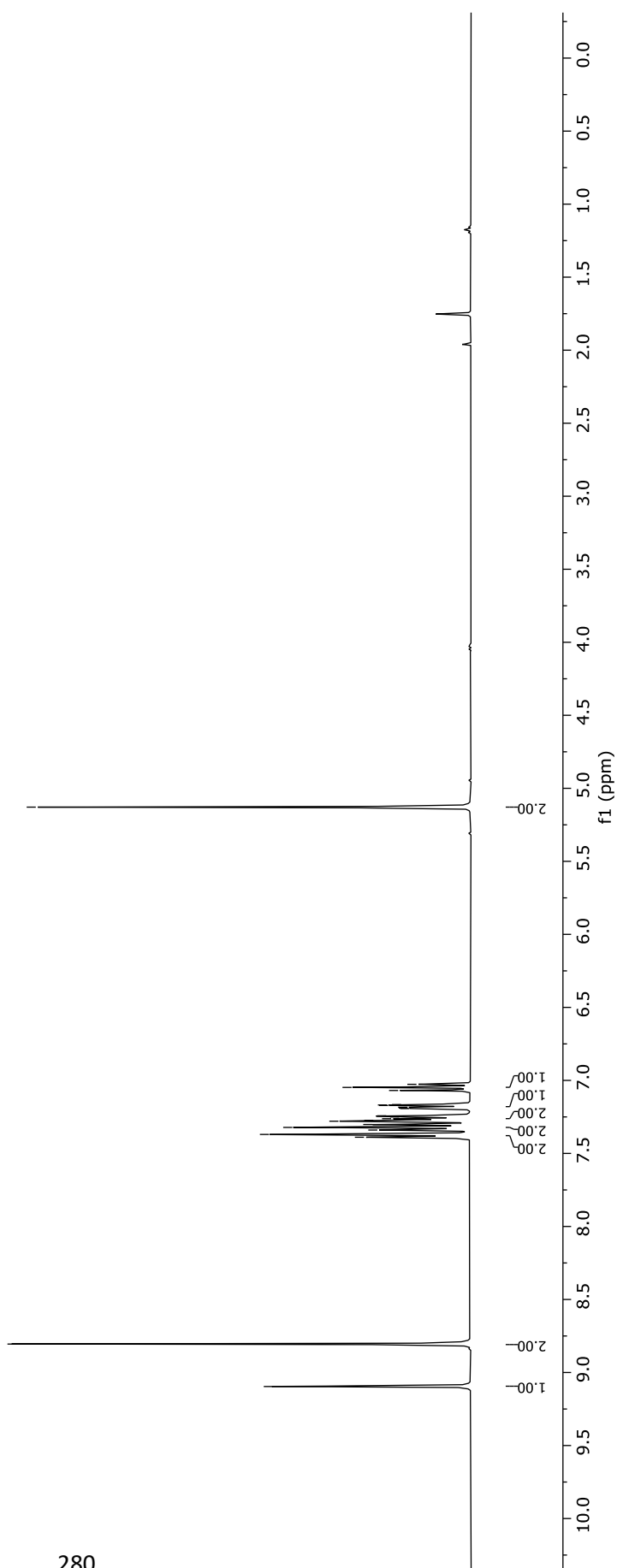
CDCl₃, 400 MHz
¹H NMR

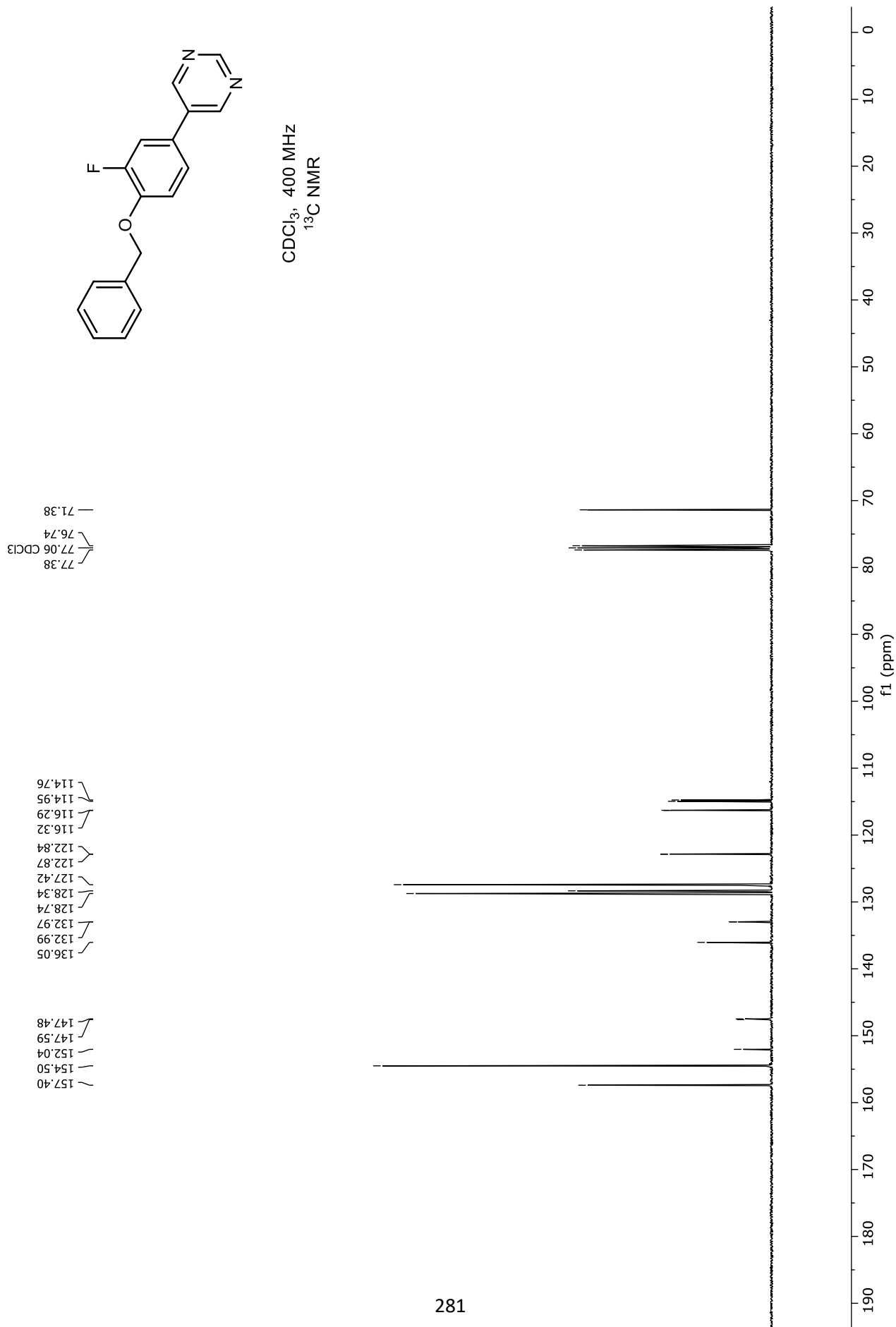
— 5.13

7.39
7.37
7.34
7.32
7.30
7.28
7.27
7.26
7.25
7.24
7.19
7.19
7.18
7.17
7.17
7.07
7.05
7.03

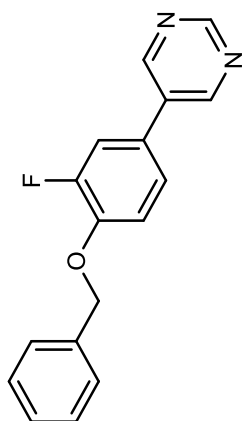
— 8.81

— 9.10

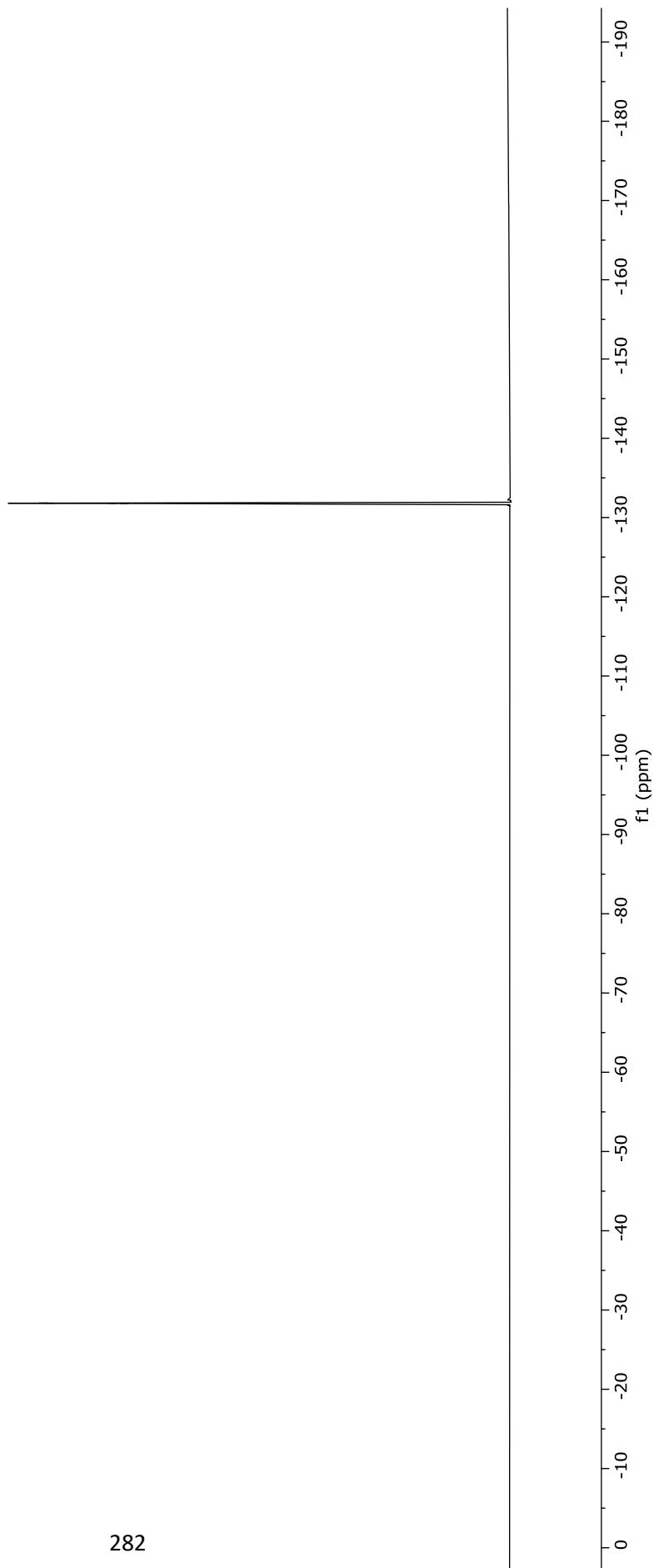


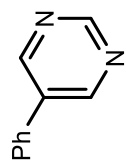


-131.77
-131.80
-131.81
-131.83



CDCl₃, 400 MHz
¹⁹F NMR

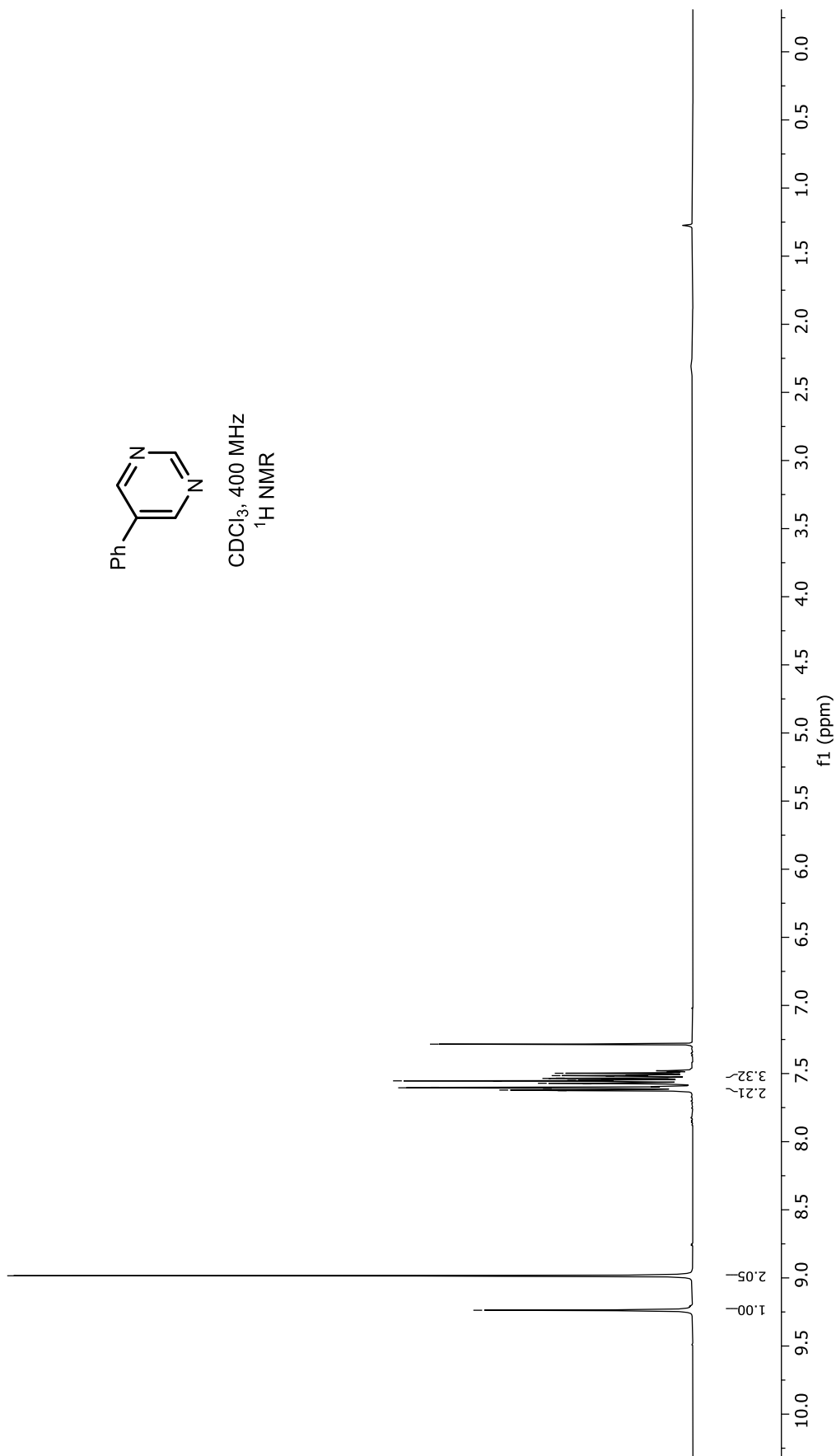


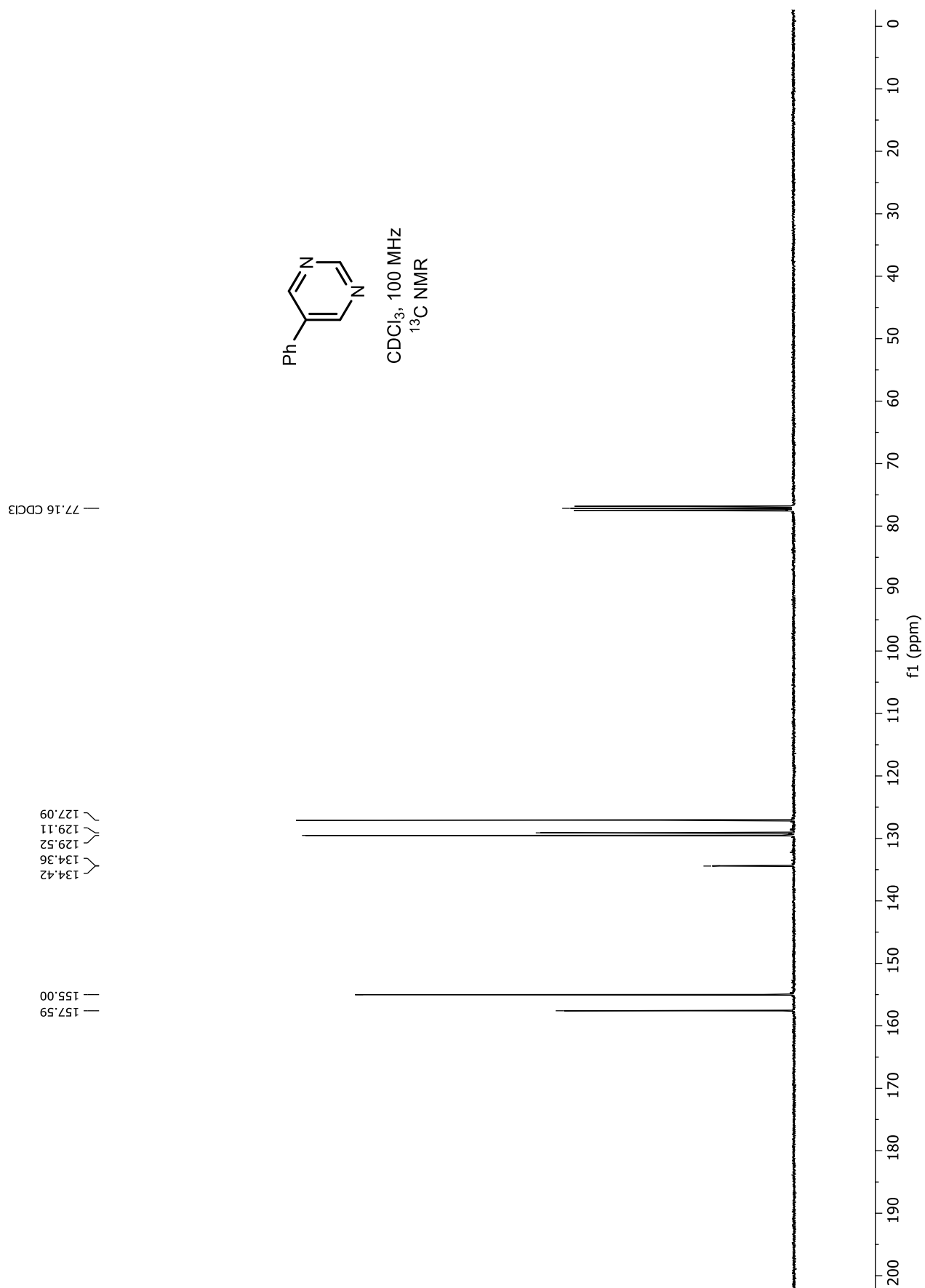
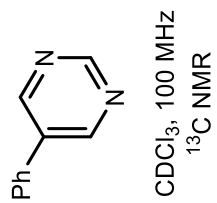


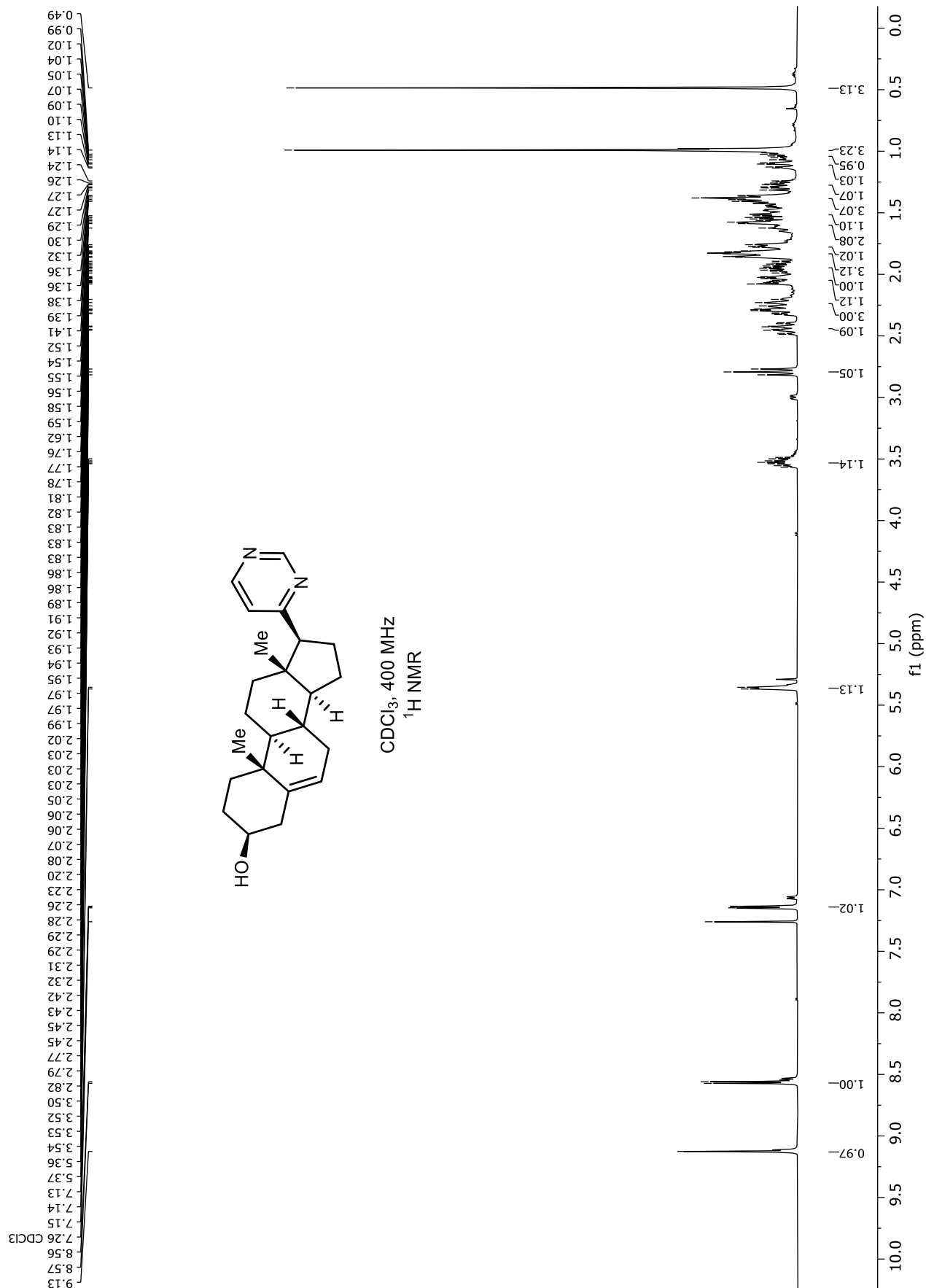
CDCl₃, 400 MHz
¹H NMR

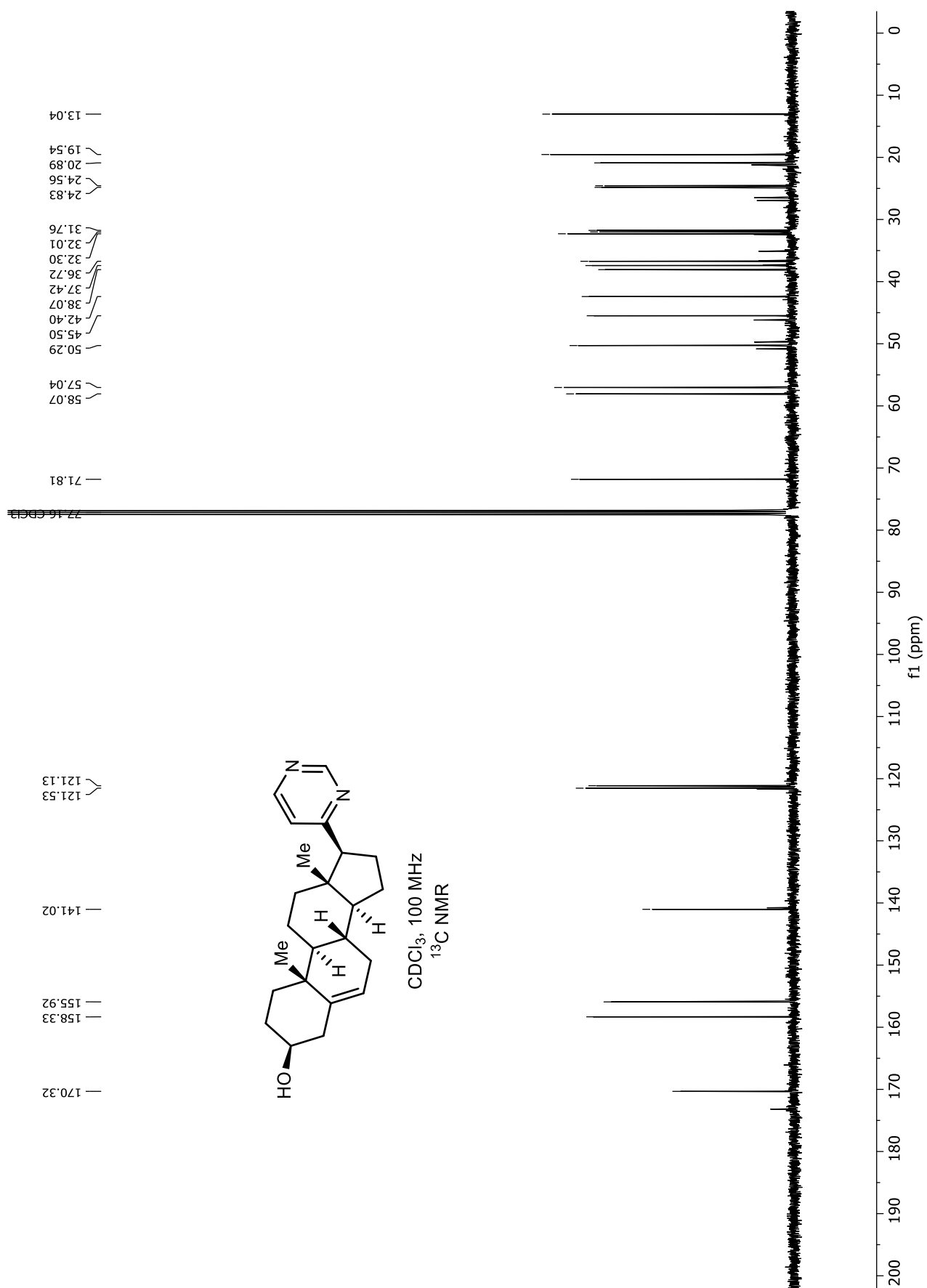
7.28 CDCl₃
 7.50
 7.52
 7.52
 7.53
 7.54
 7.54
 7.55
 7.55
 7.56
 7.57
 7.57
 7.60
 7.60
 7.61
 7.62
 7.63

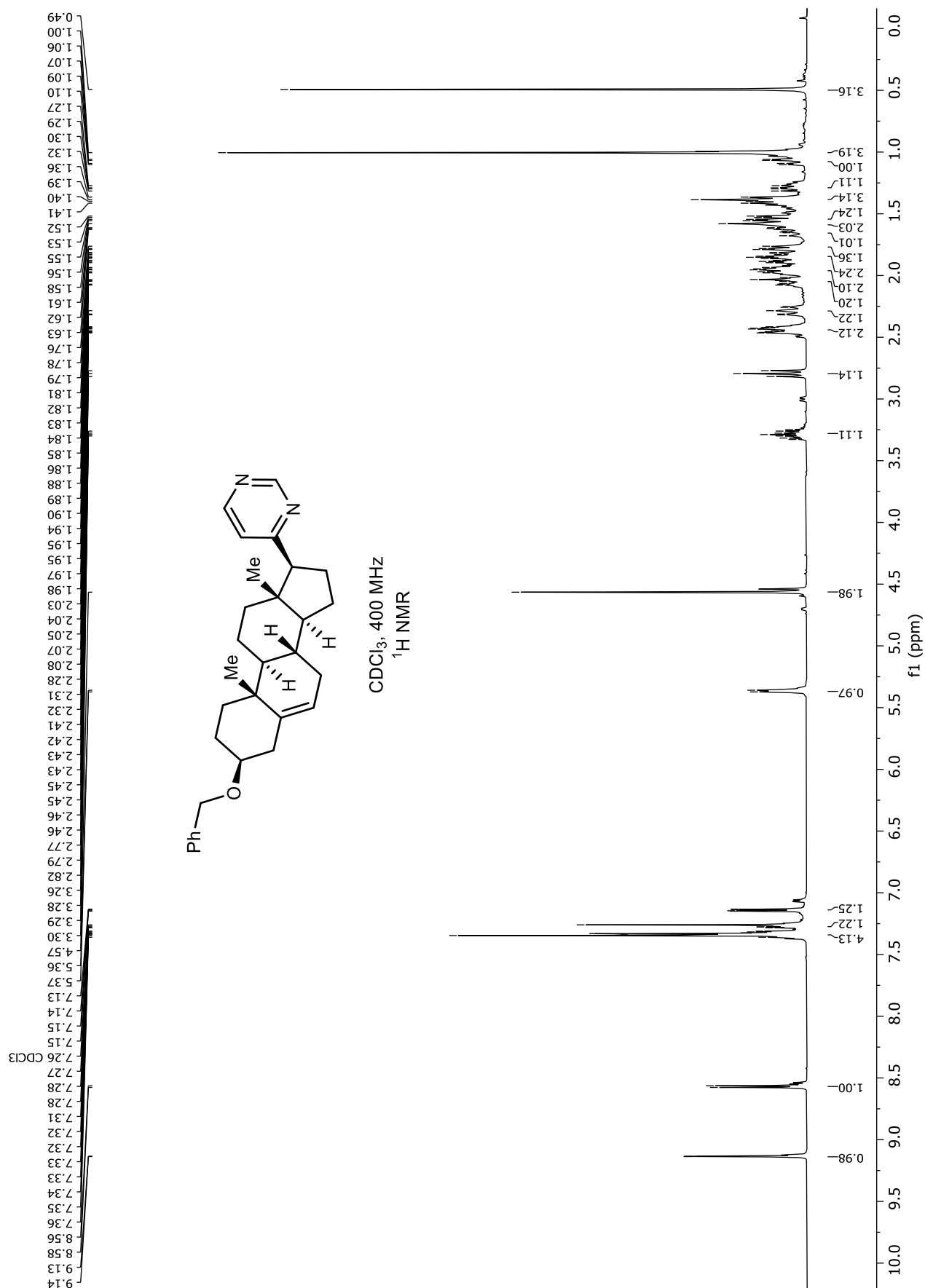
9.24
 8.98

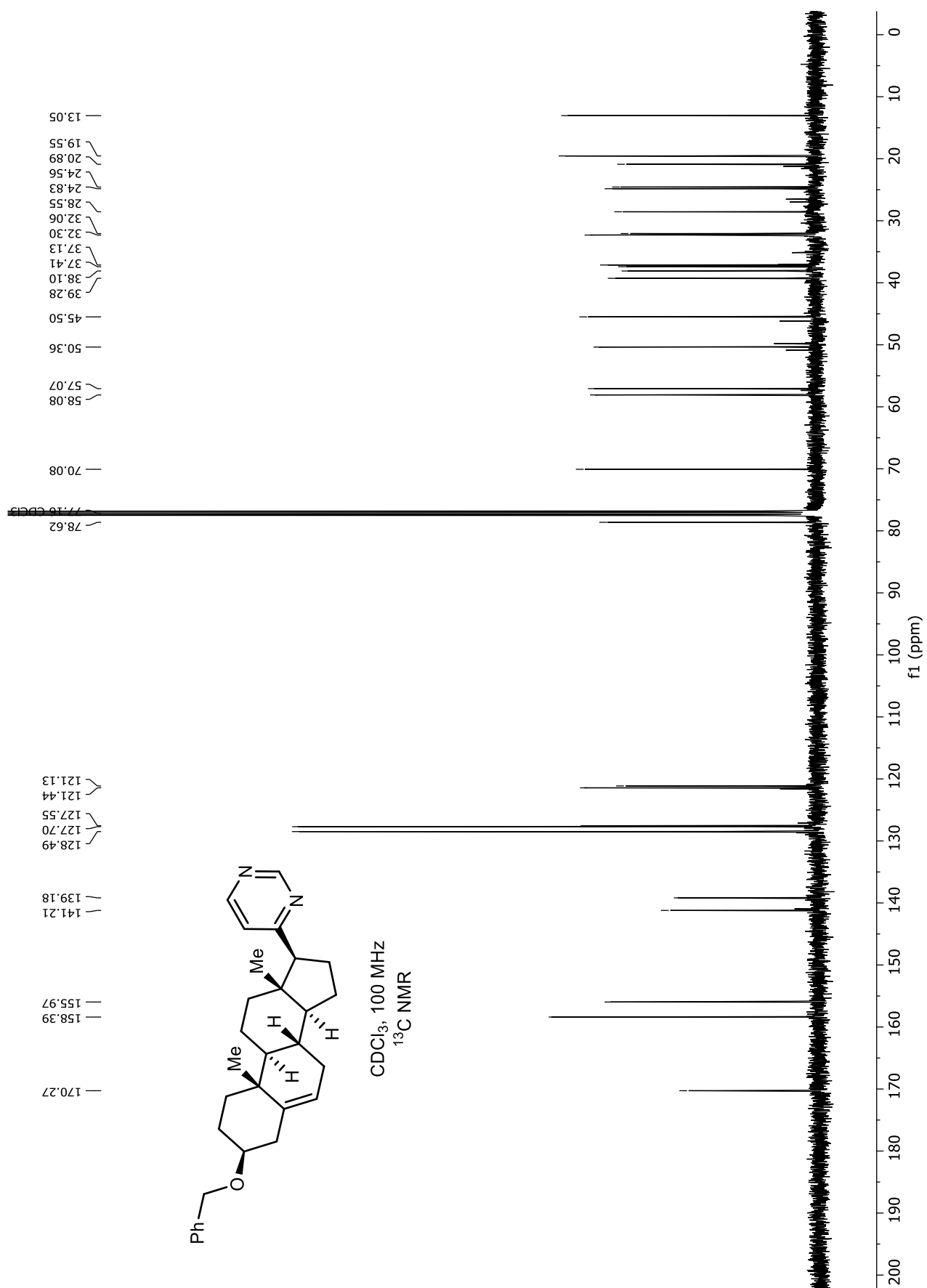


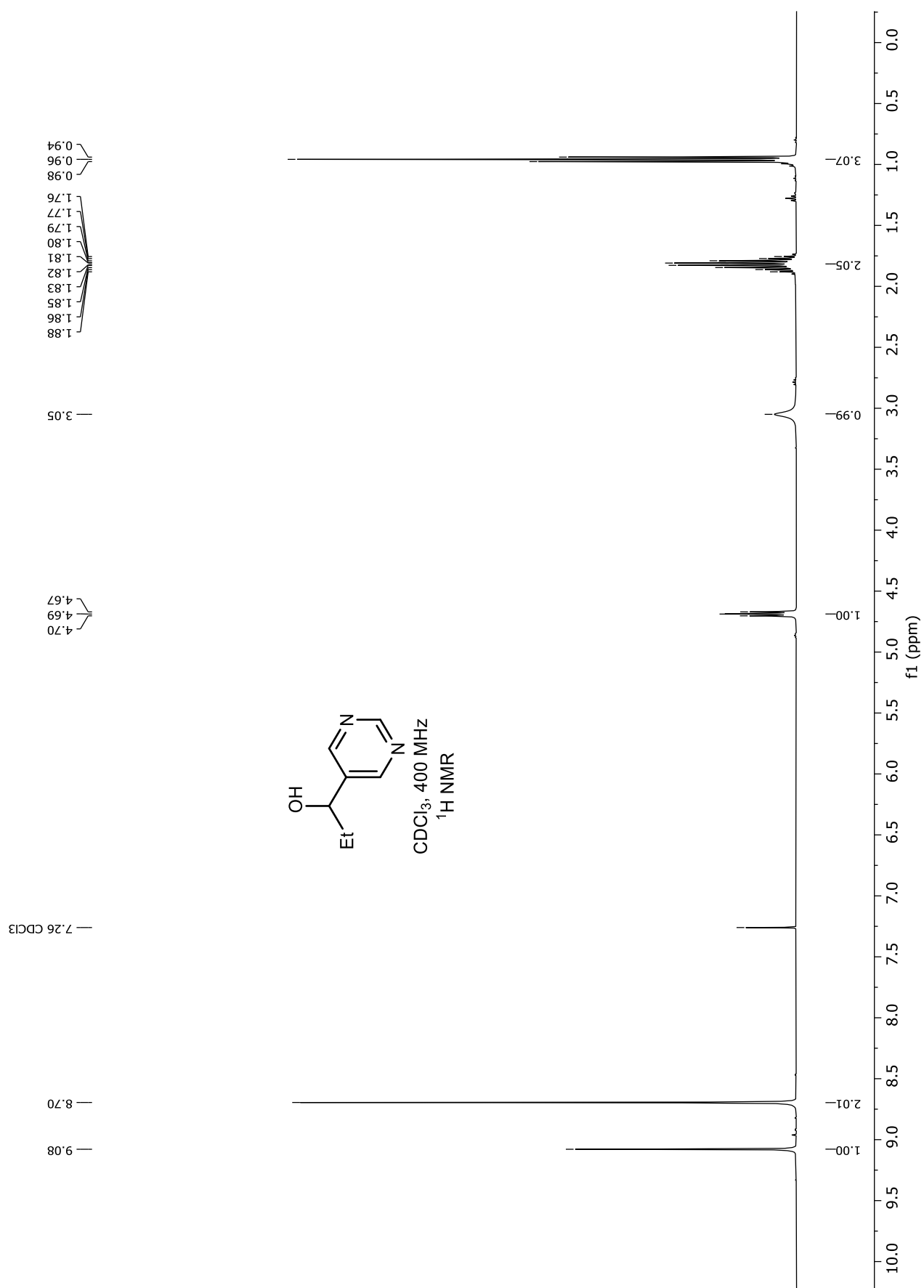
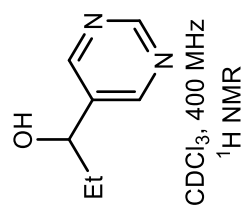


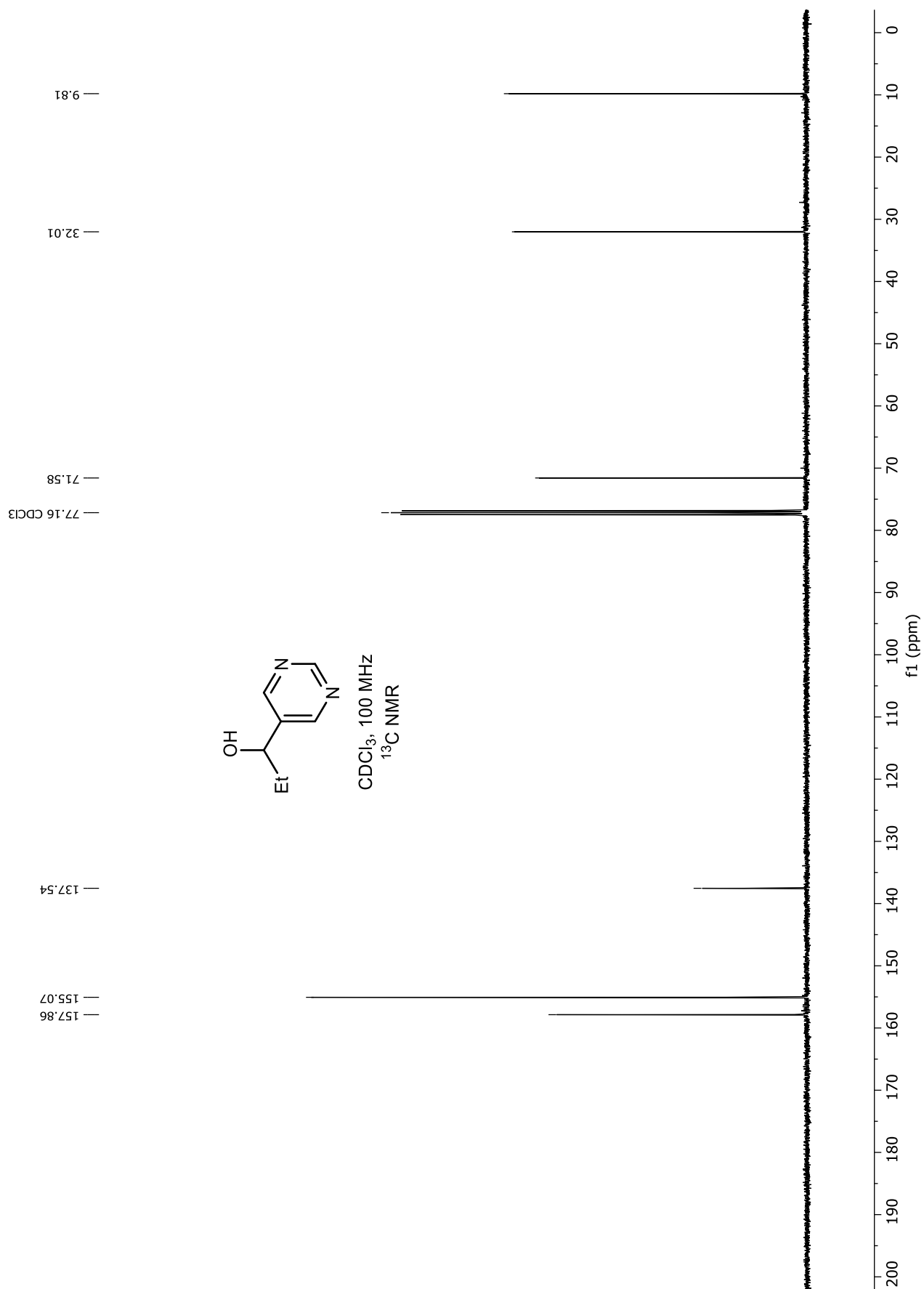


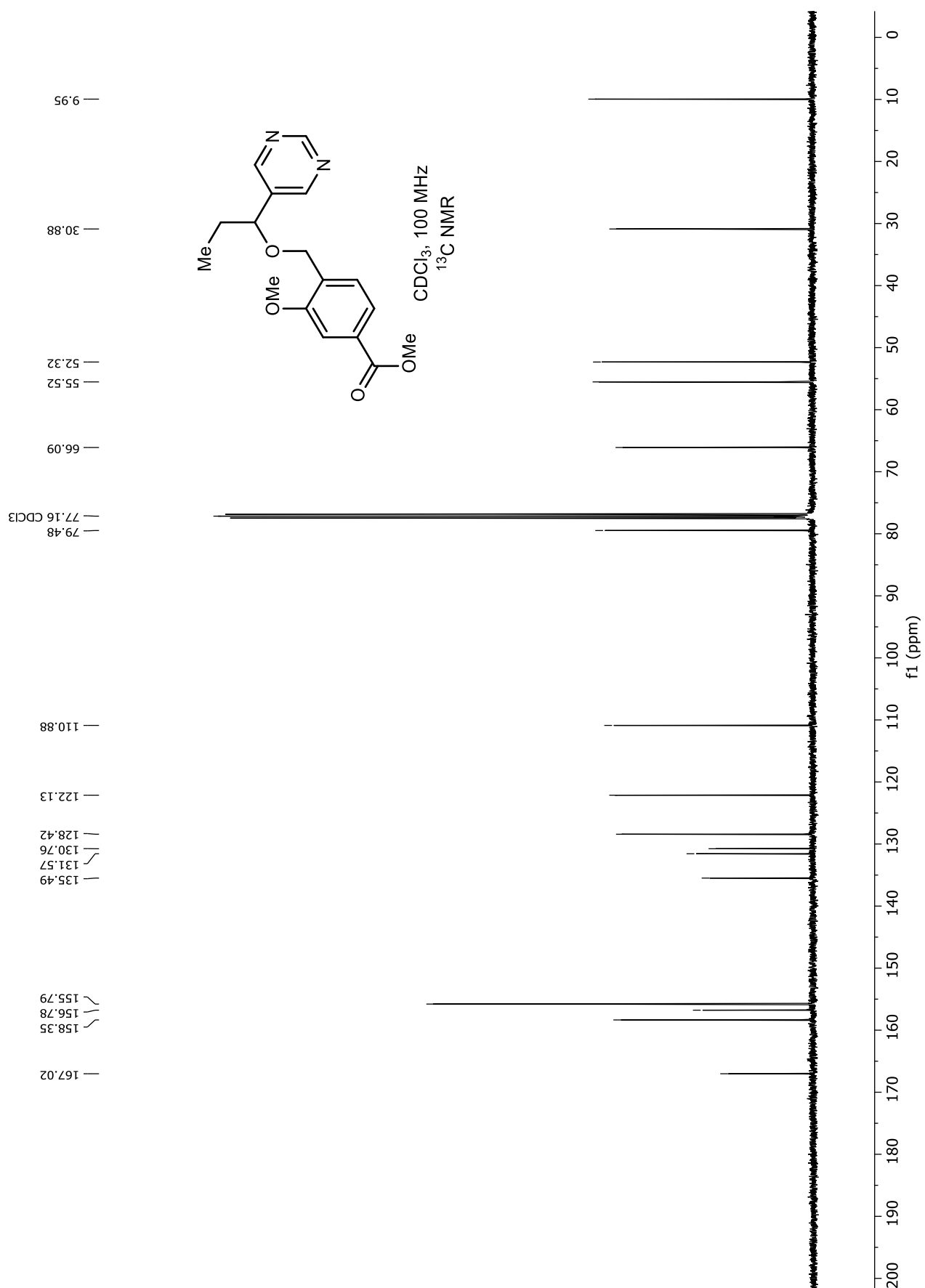








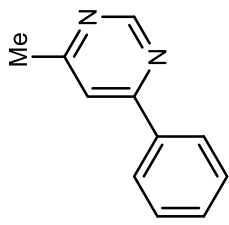




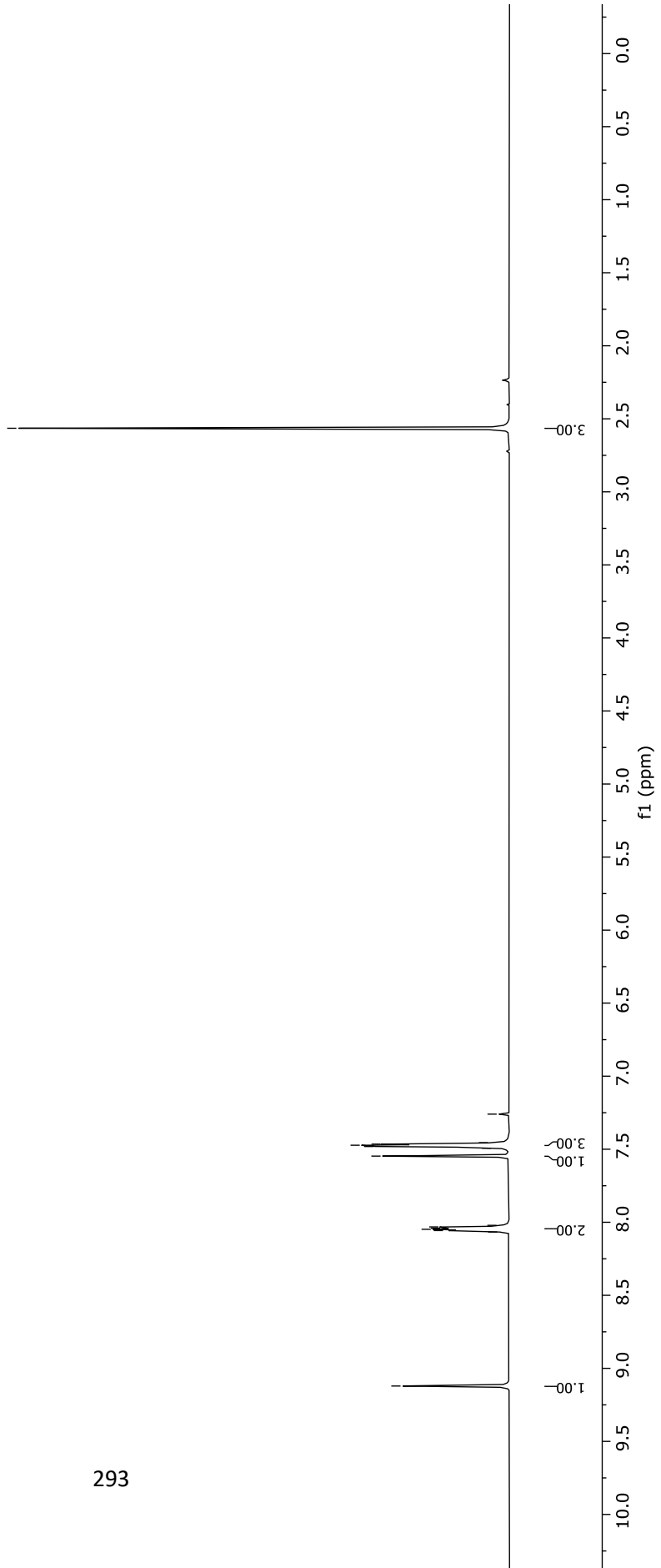
8.07
8.06
8.05
8.04
8.03
8.02
7.55
7.49
7.48
7.47
7.46
7.46
7.26

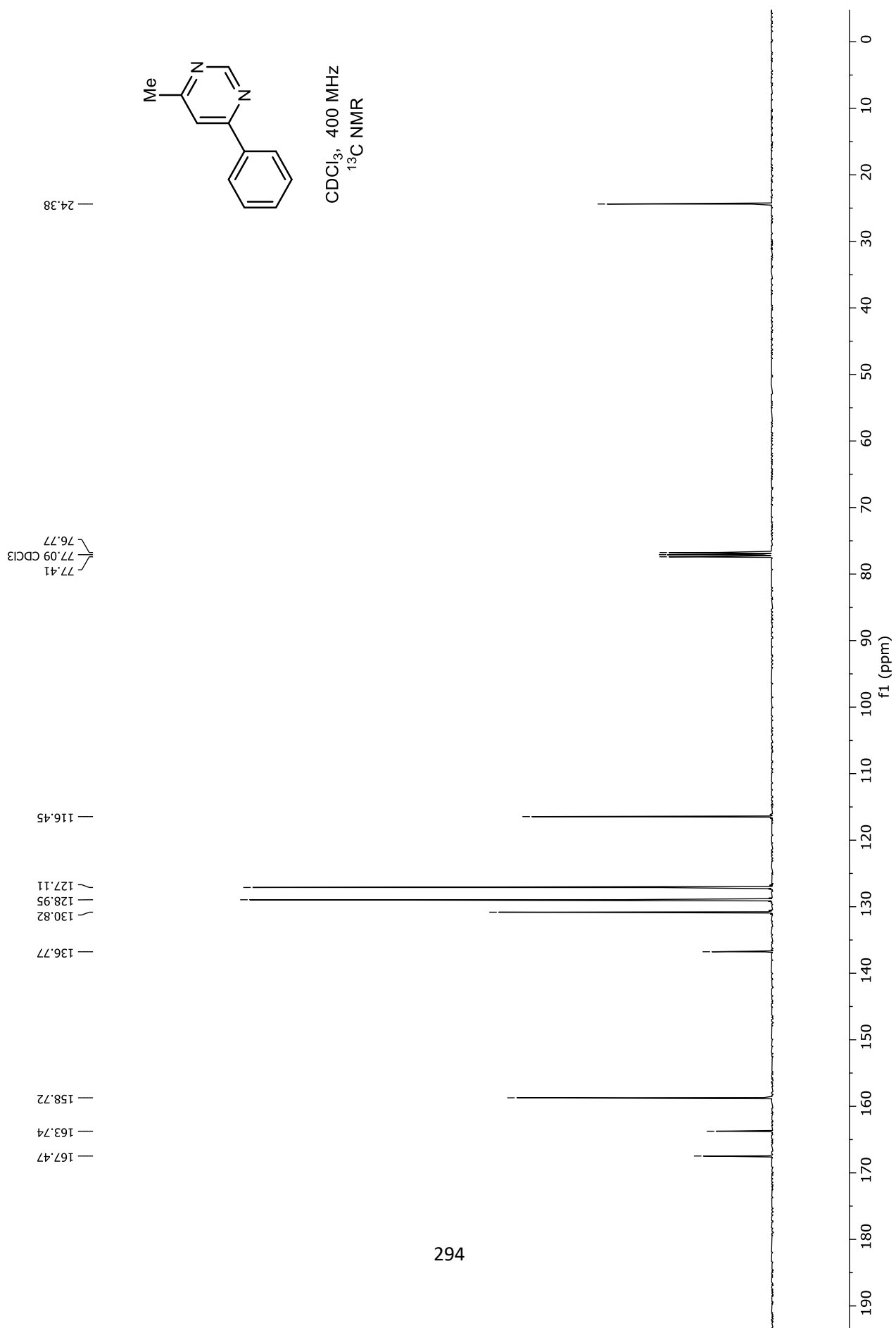
— 2.56

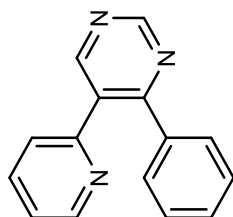
— 9.12



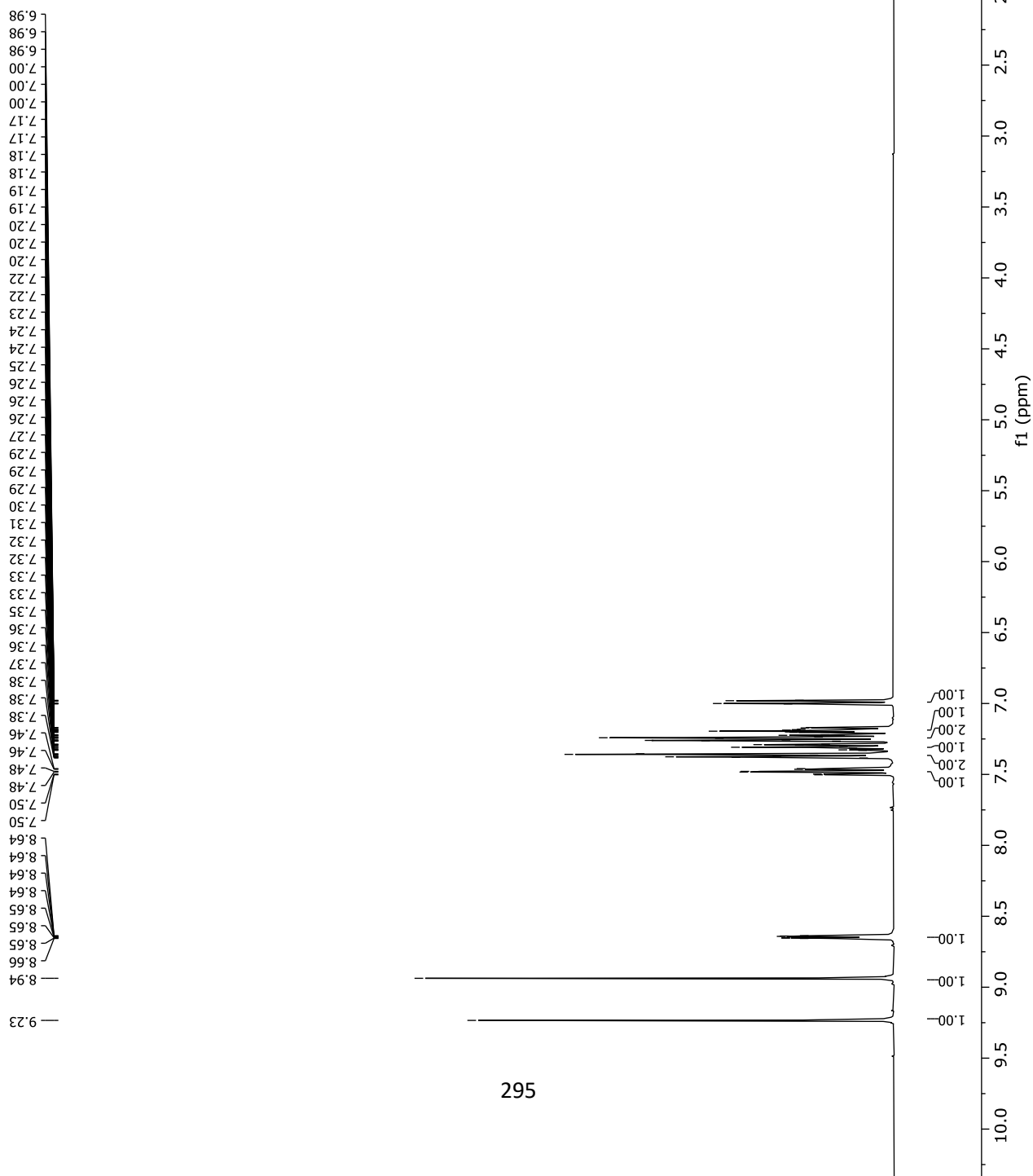
CDCl₃, 400 MHz
¹H NMR

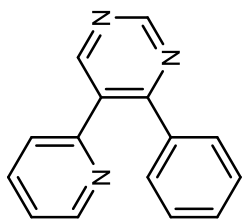






CDCI₃, 400 MHz
¹H NMR



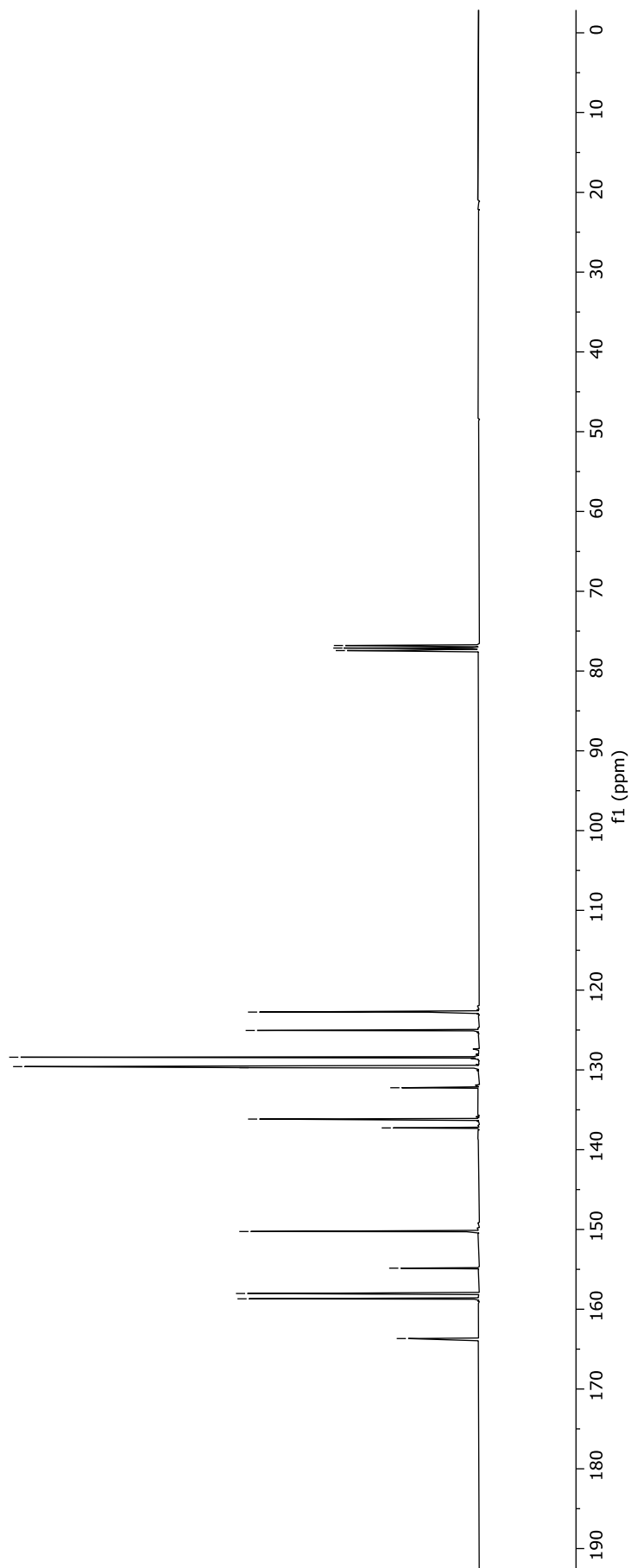


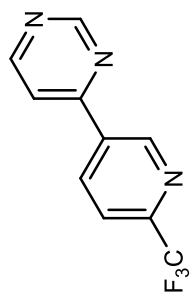
CDCl₃, 400 MHz
¹H NMR

77.44
 77.12 CDCl₃
 76.80

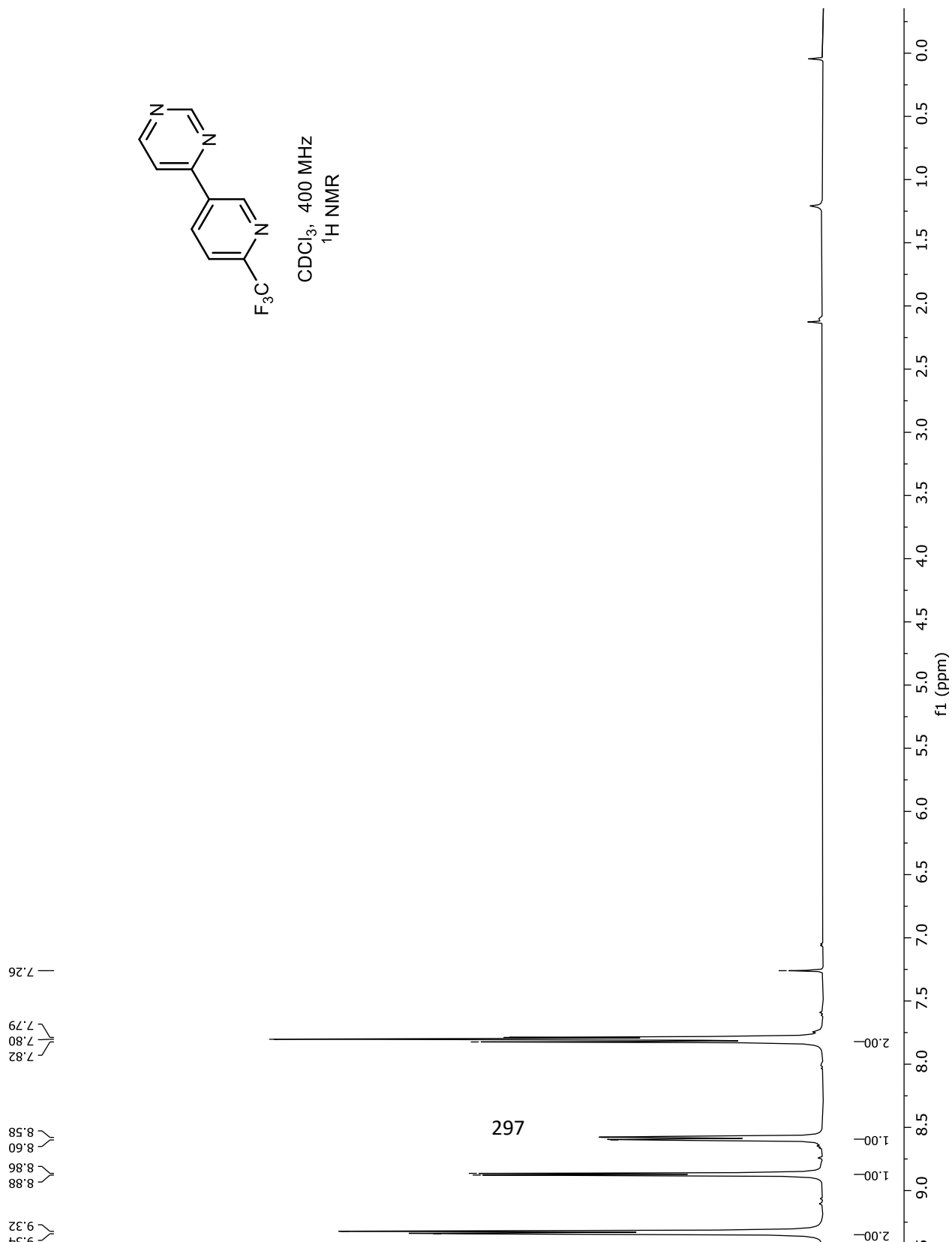
137.27
 136.16
 132.24
 129.72
 129.59
 128.41
 125.06
 122.75

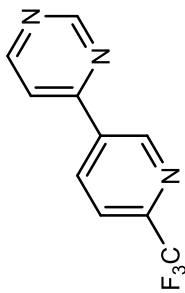
163.68
 158.69
 158.03
 154.85
 150.26



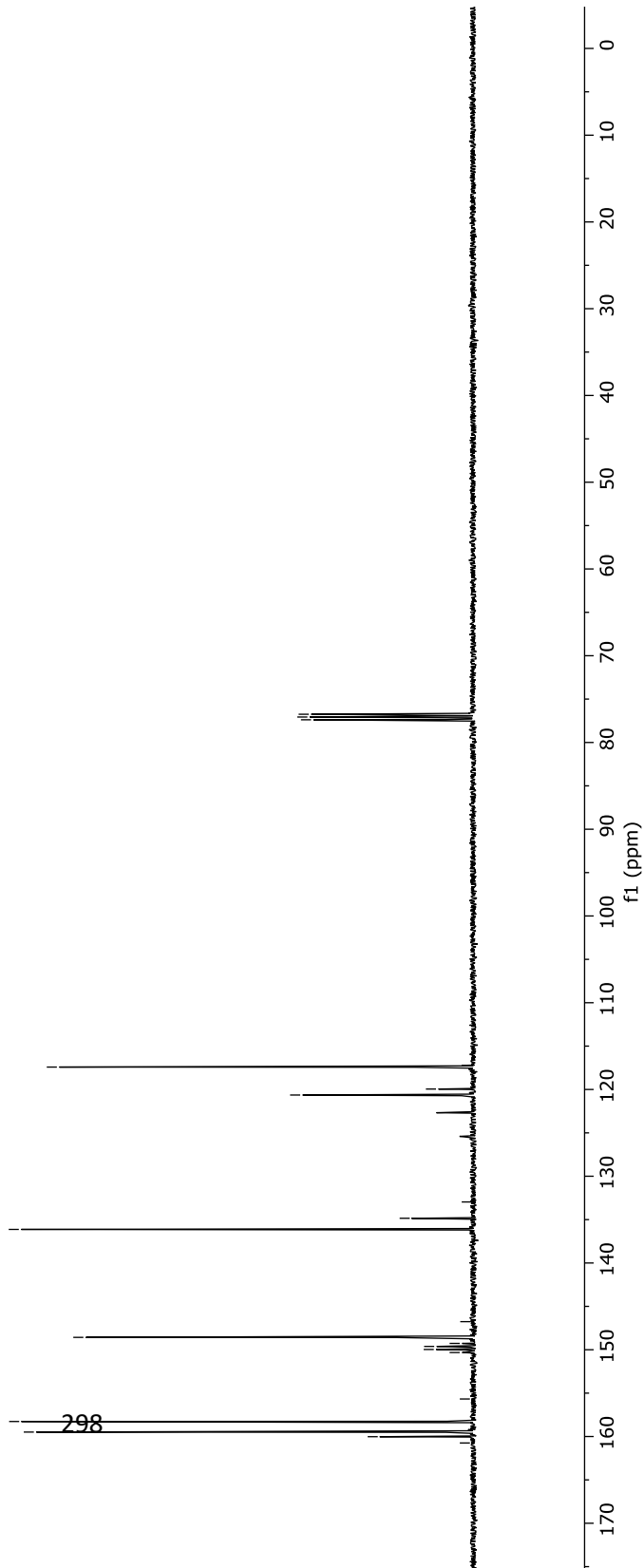


CDCl₃, 400 MHz
¹H NMR





CDCl_3 , 400 MHz
 ^{13}C NMR



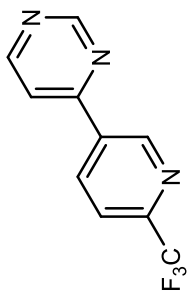
77.38
 77.07
 76.75

120.64
 120.61
 119.95
 117.42

136.13
 134.85
 132.97

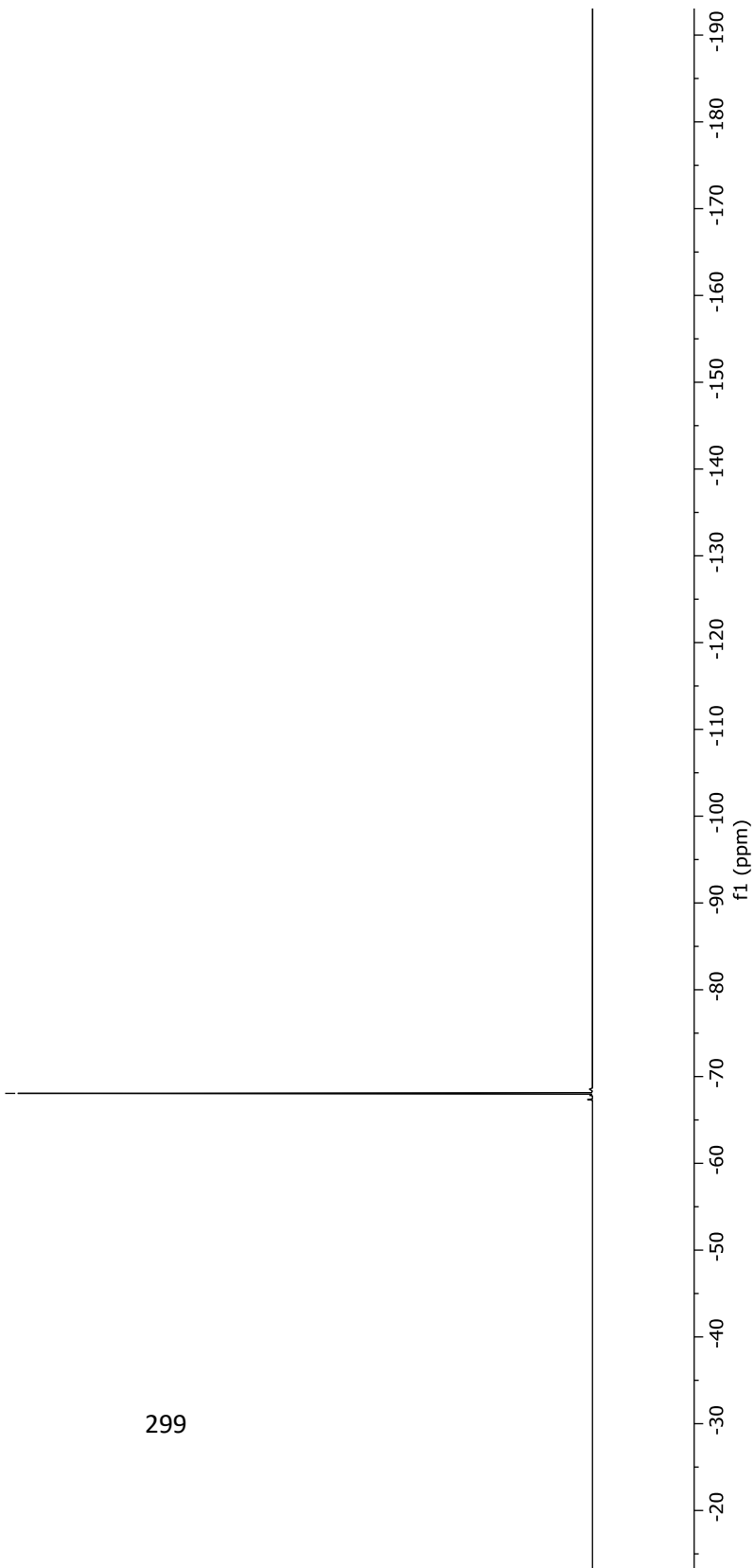
146.76
 148.57
 149.27
 149.62
 149.97
 150.32
 155.68
 158.27
 159.49
 160.02
 160.75

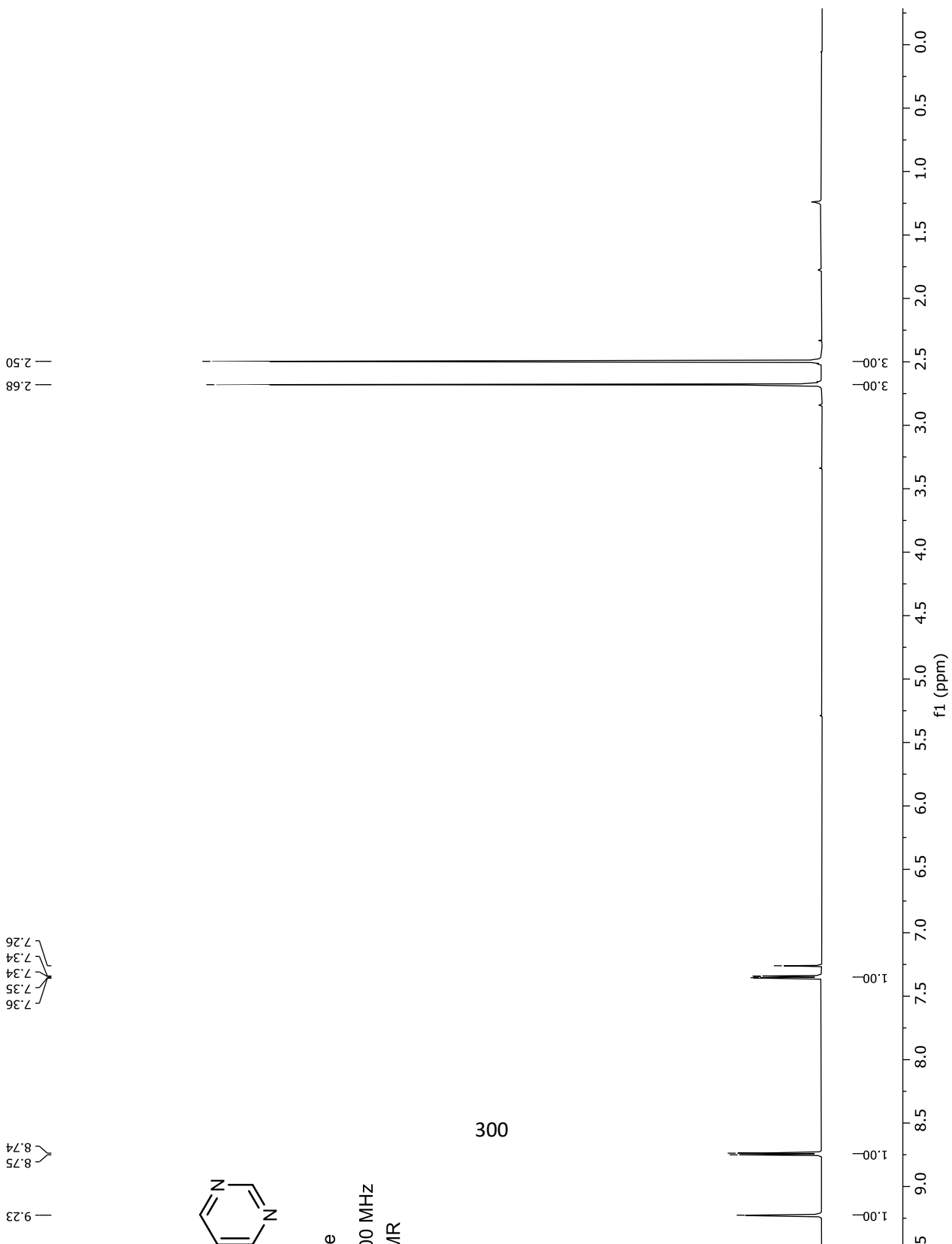
298

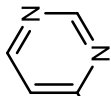


CDCl₃, 400 MHz
¹⁹F NMR

90'89- —



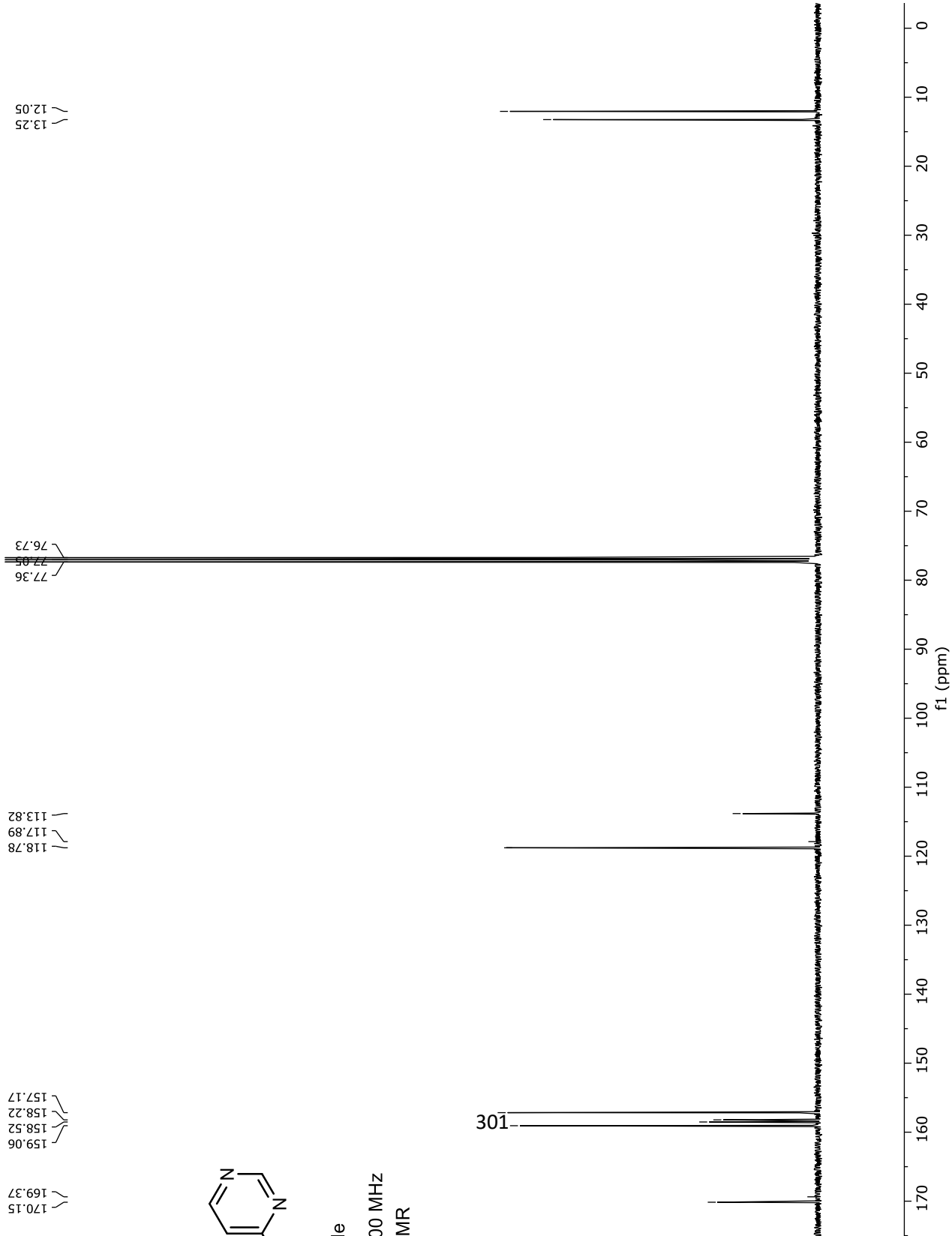




le

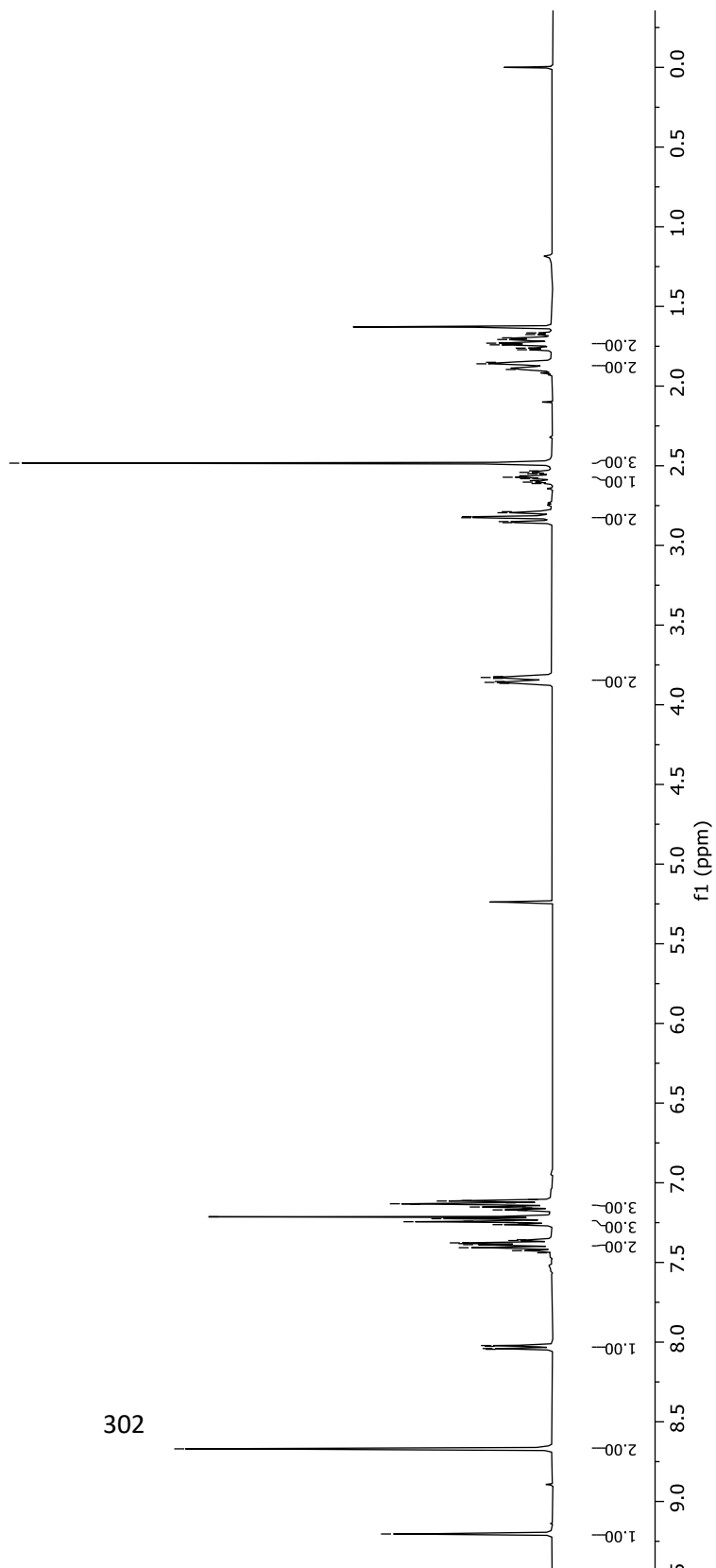
00 MHz

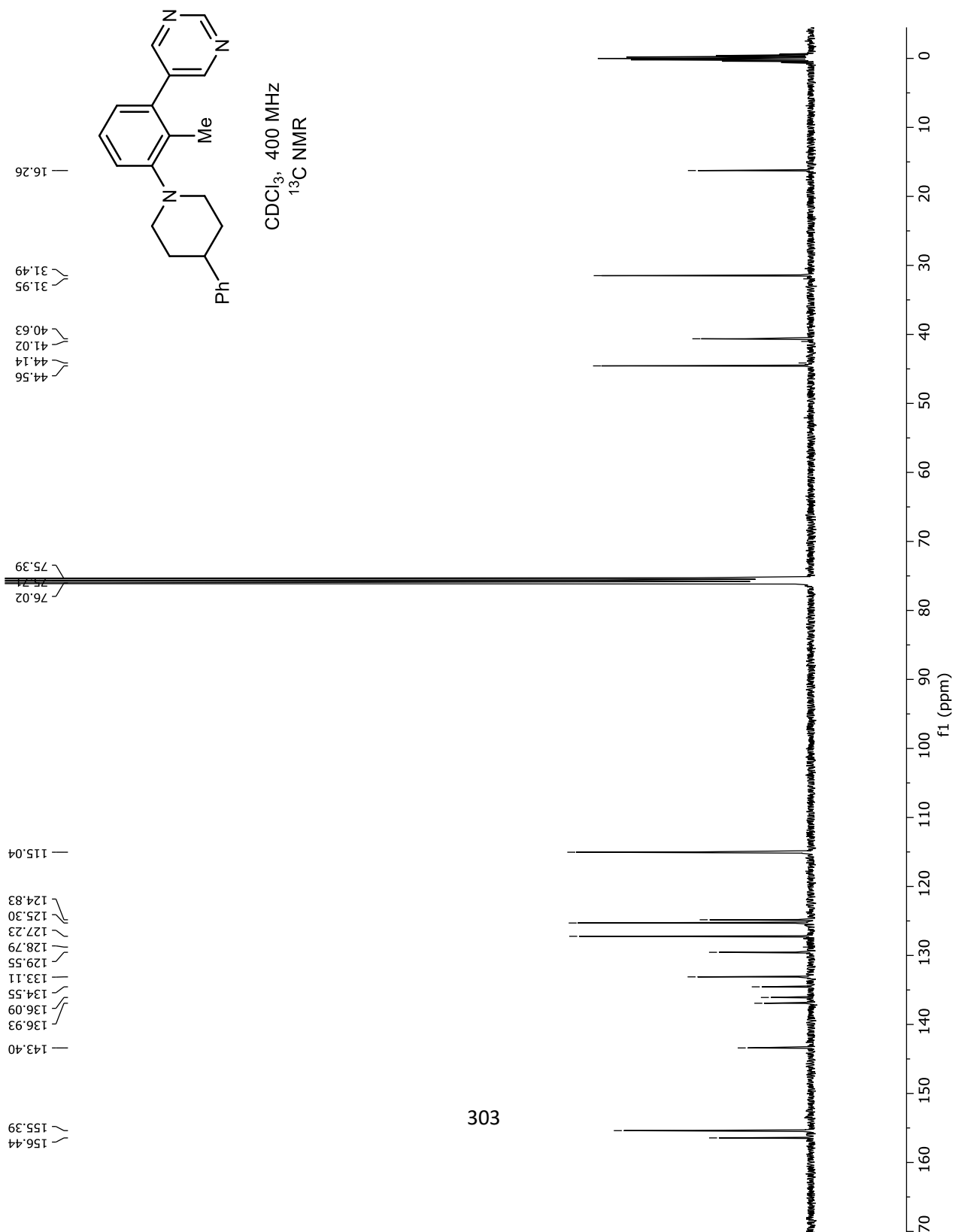
MR

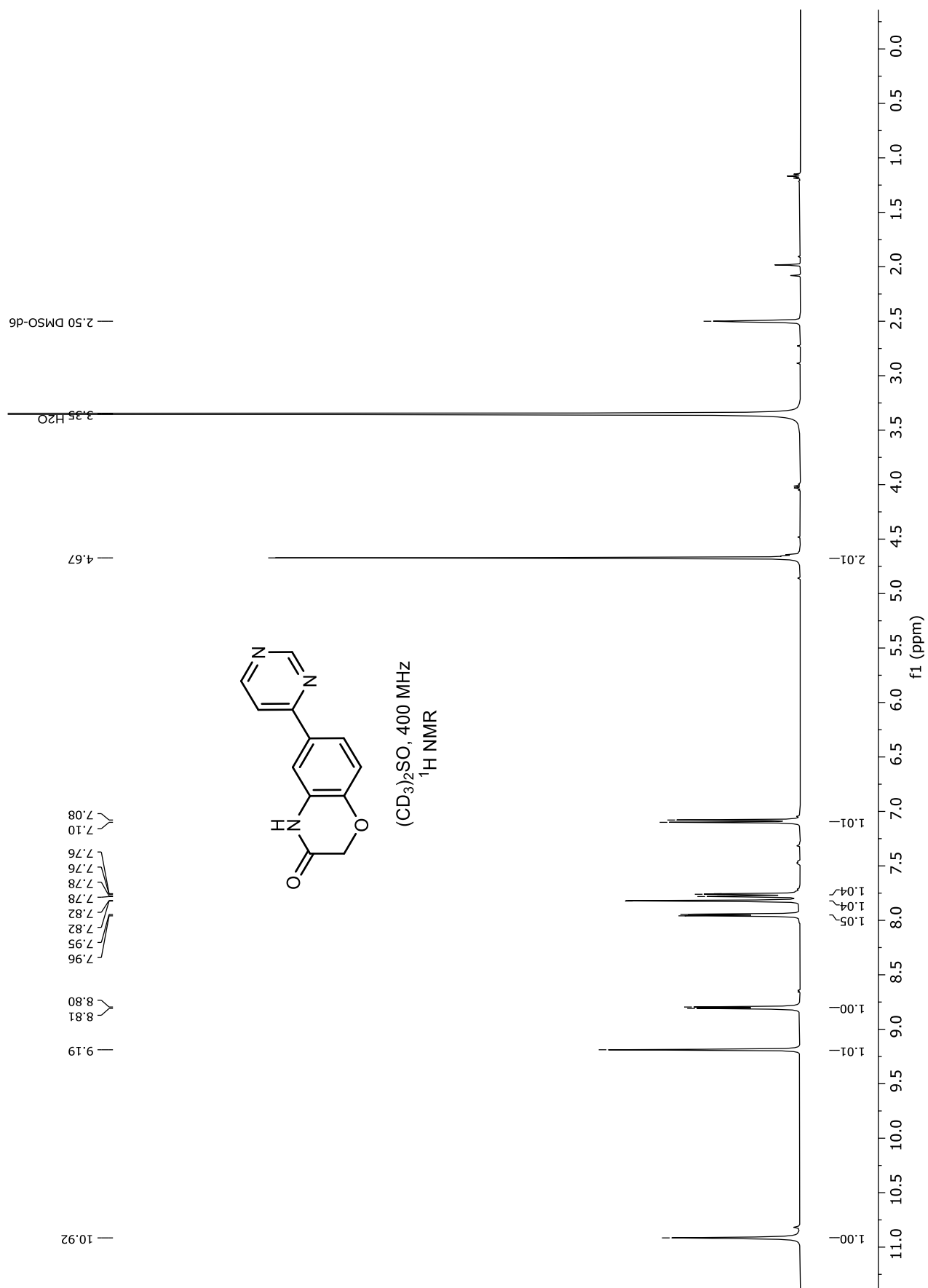


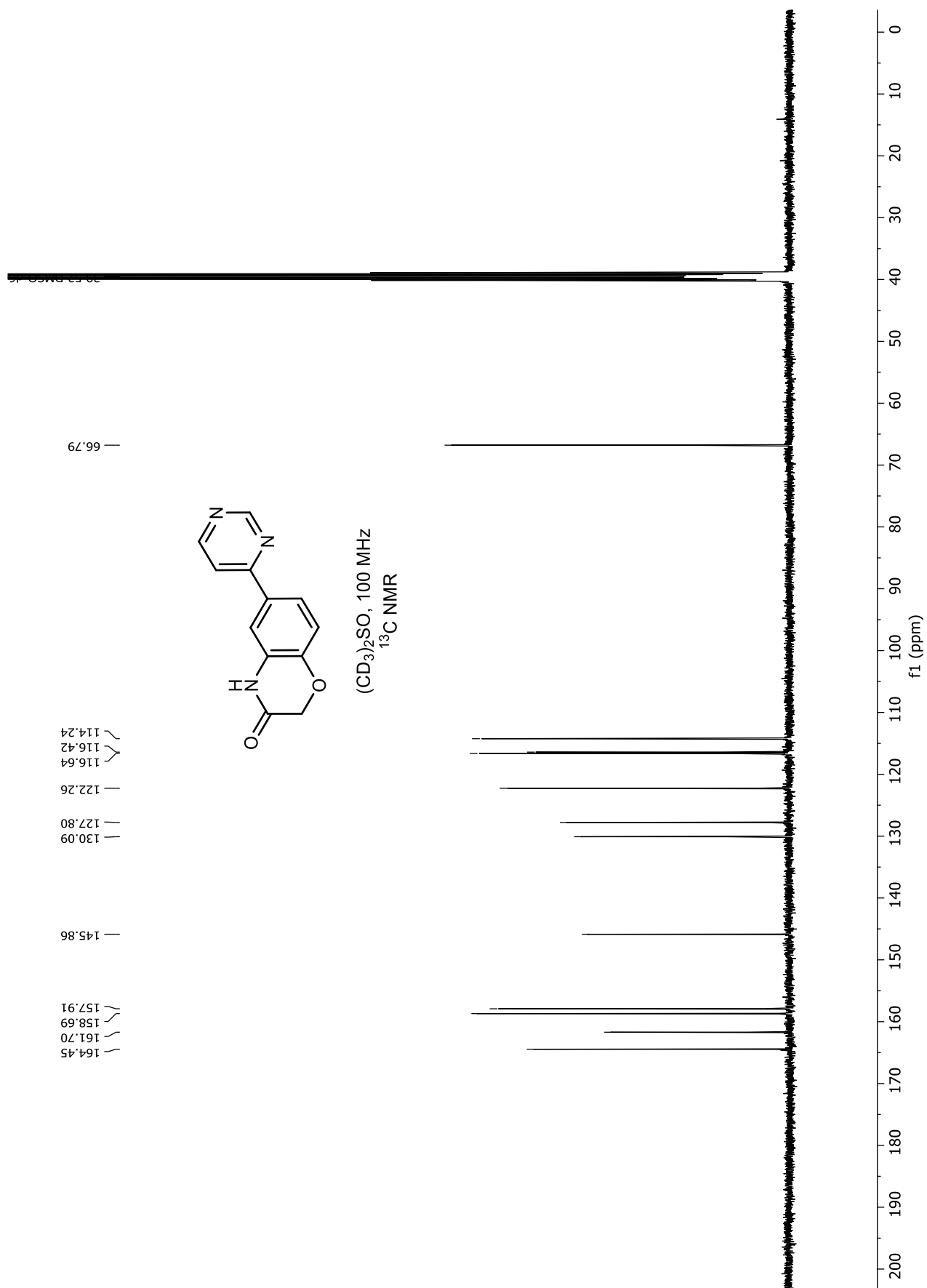


CDCl₃, 400 MHz
 ^1H NMR

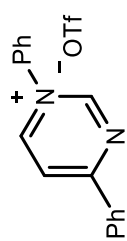








— 1.94 CD3CN
— 2.19 H2O

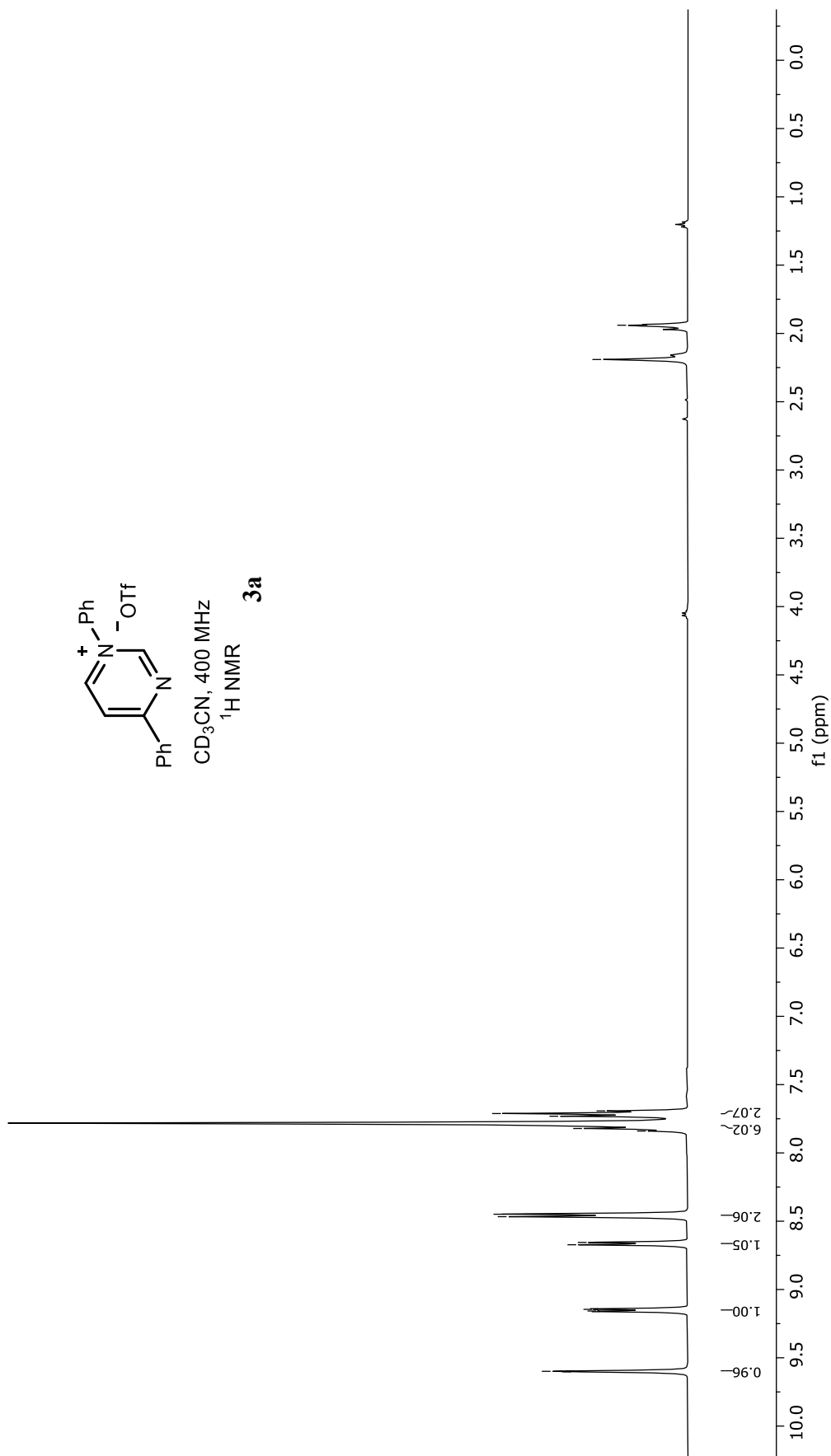


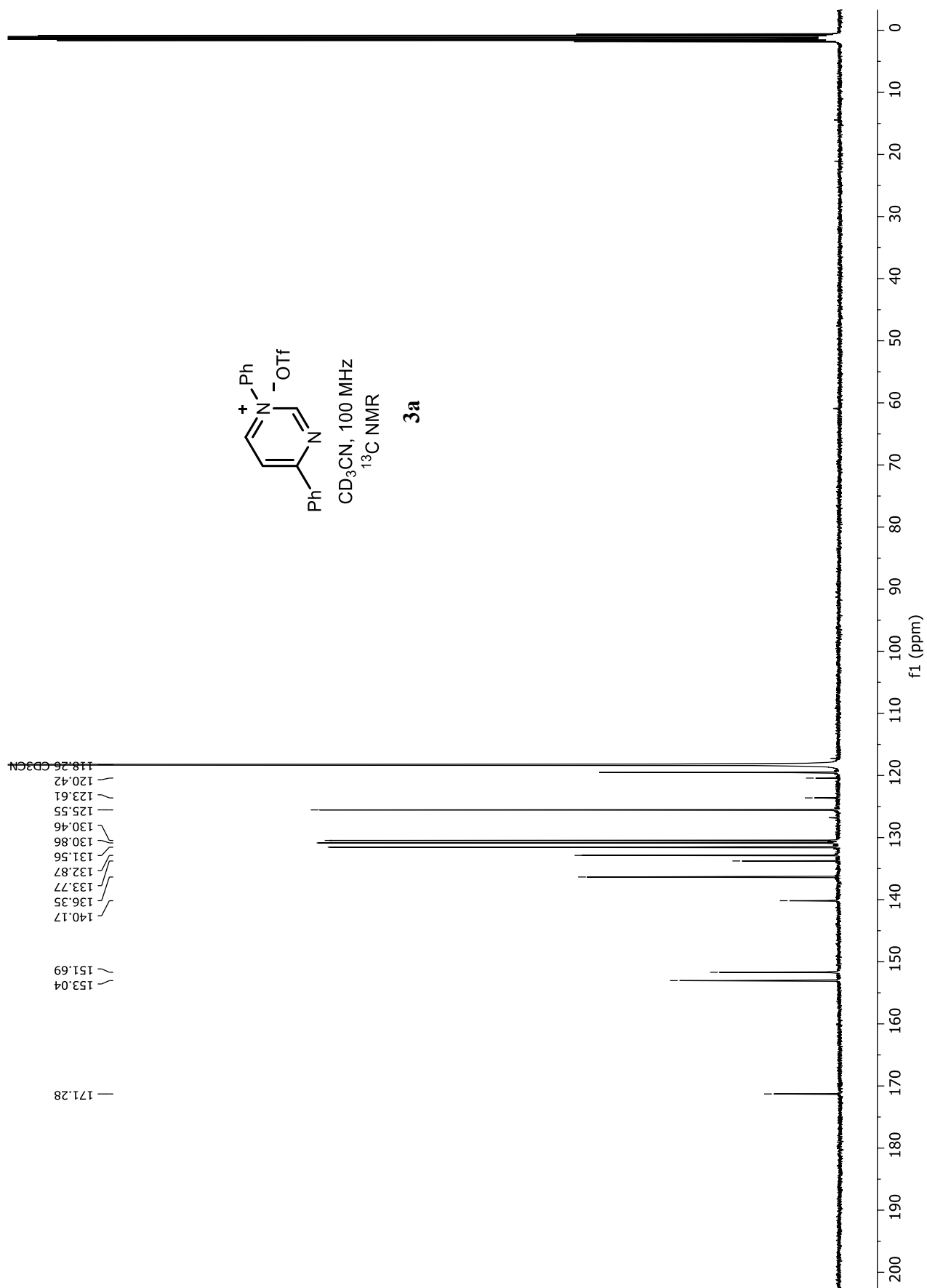
CD₃CN, 400 MHz

¹H NMR

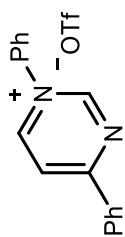
3a

7.69
7.71
7.73
7.78
7.82
7.84
8.45
8.47
8.66
8.67
9.14
9.15
9.16
9.60
9.60



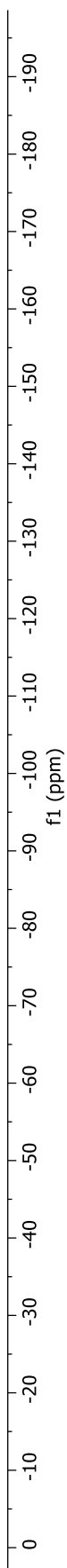


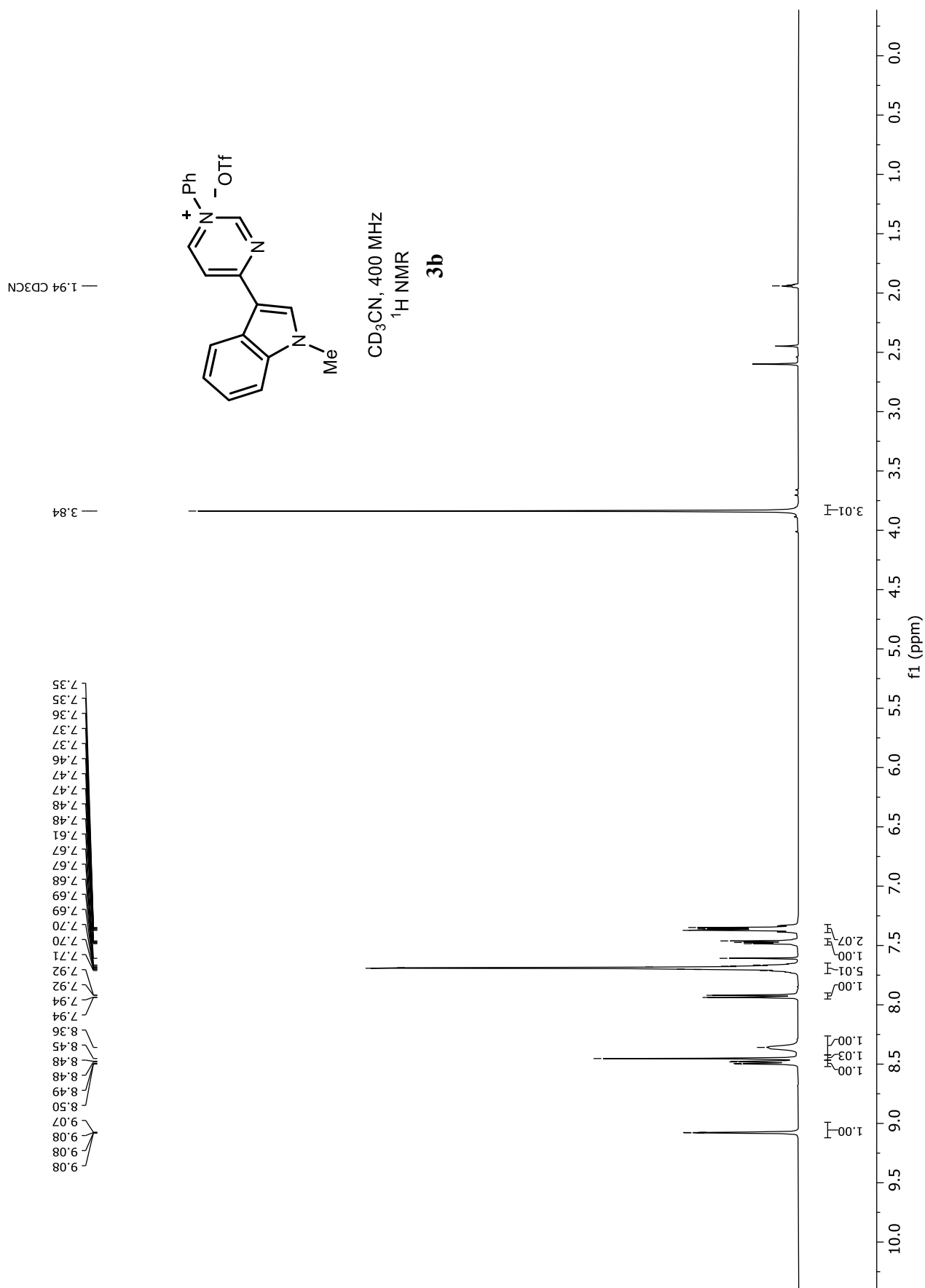
— -79.30



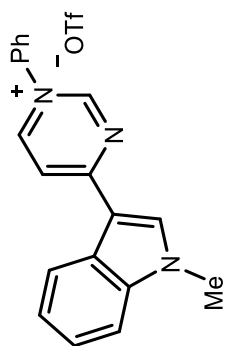
CD₃CN, 375 MHz
¹⁹F NMR

3a



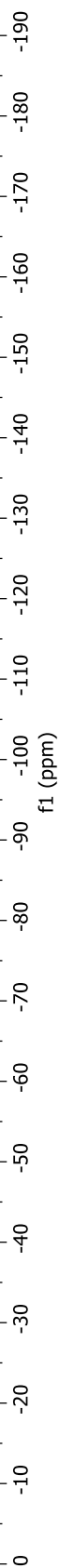


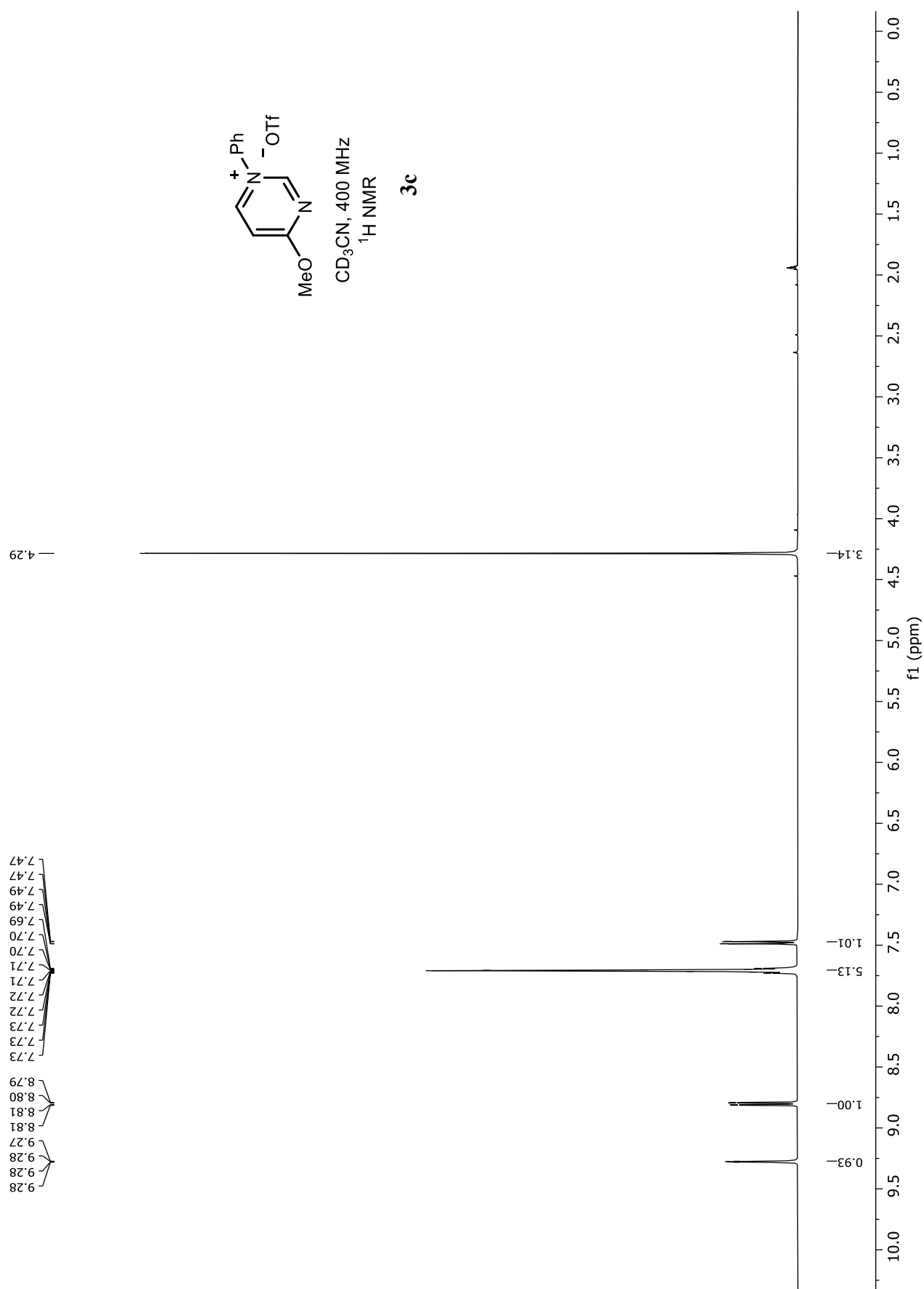
— -79.32

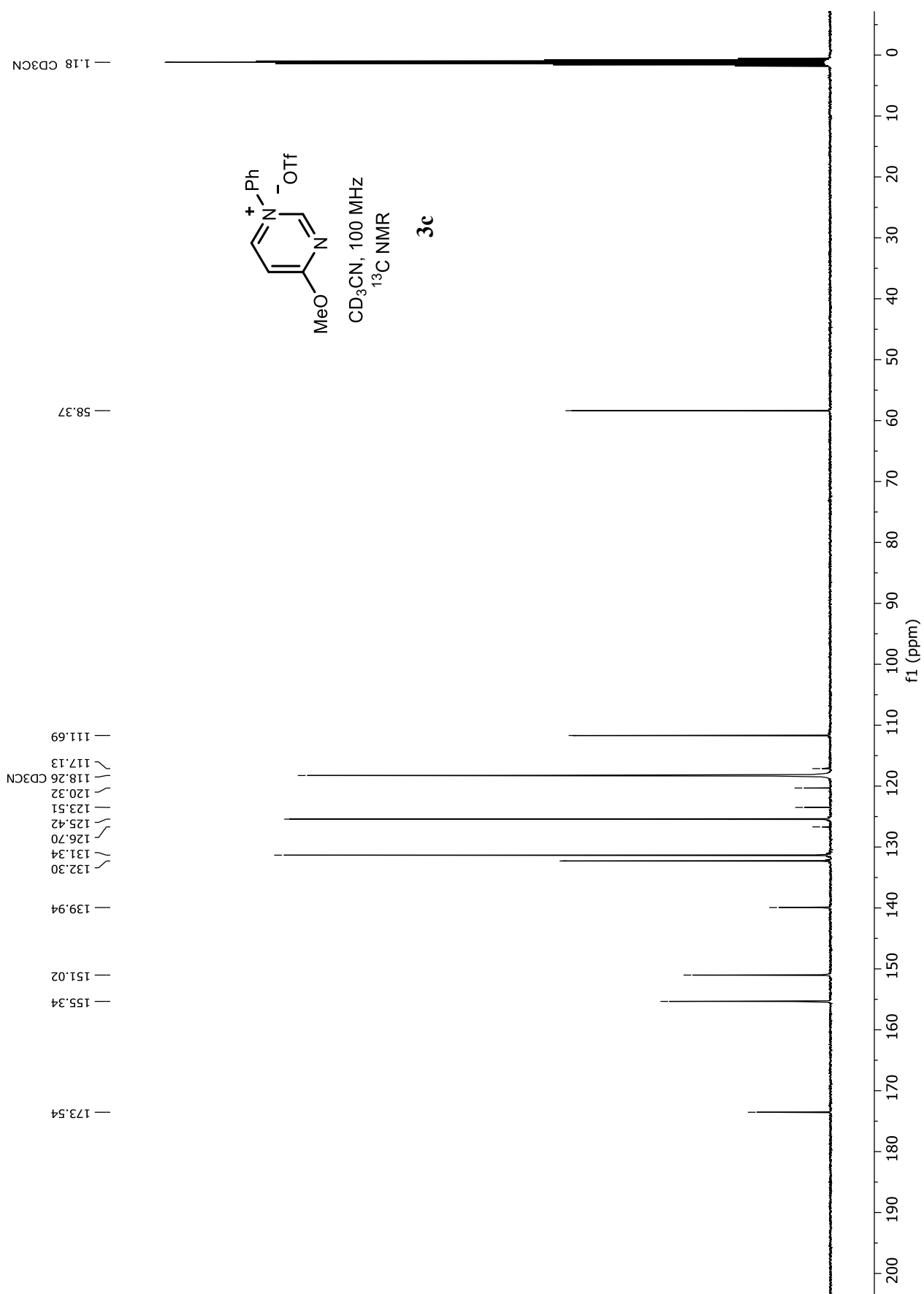


CD₃CN, 375 MHz
¹⁹F NMR

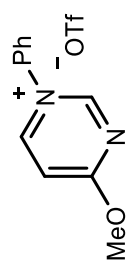
3b





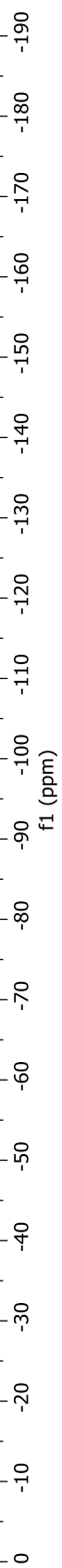


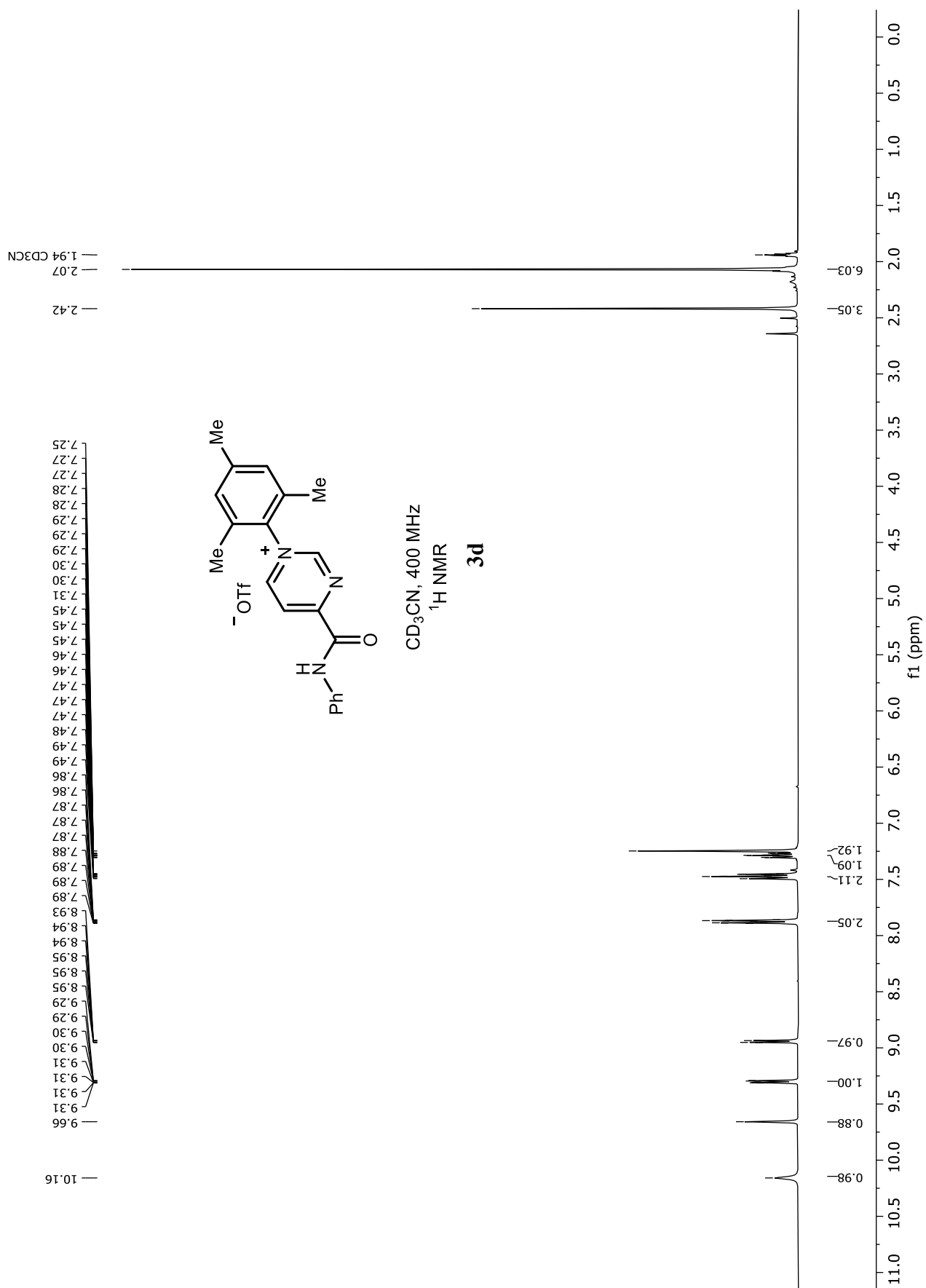
— -79.21



CD₃CN, 375 MHz
¹⁹F NMR

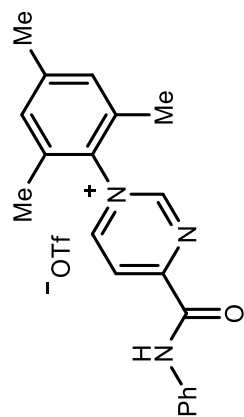
3c





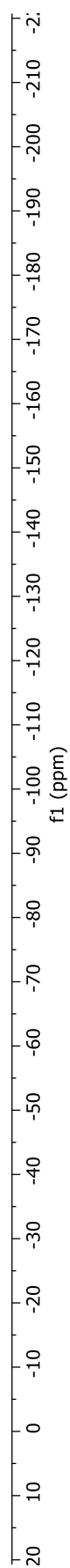


— -79.29

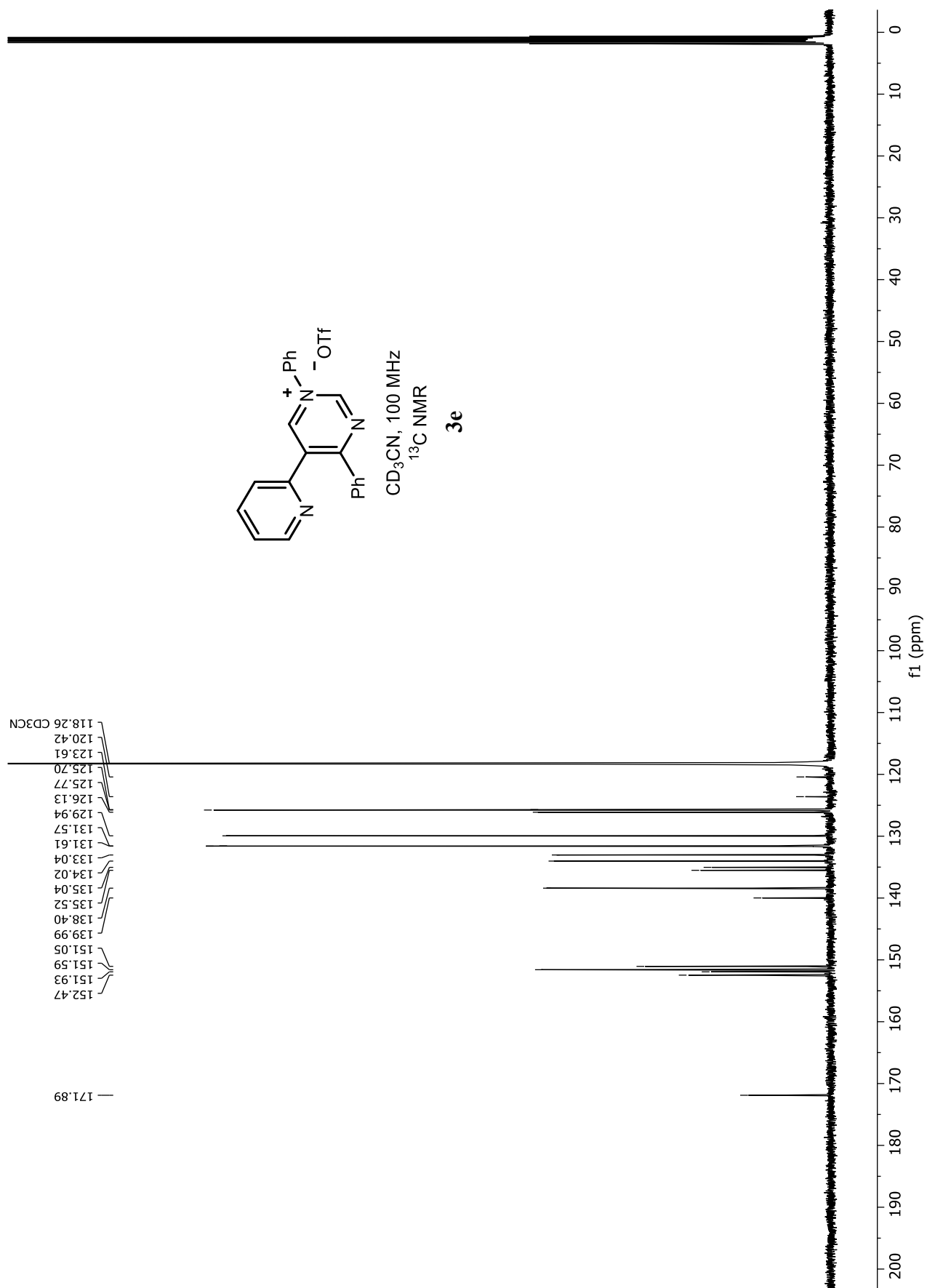


CD₃CN, 375 MHz
¹⁹F NMR

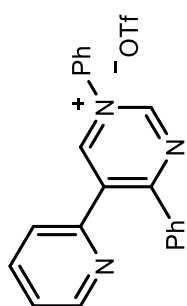
3d





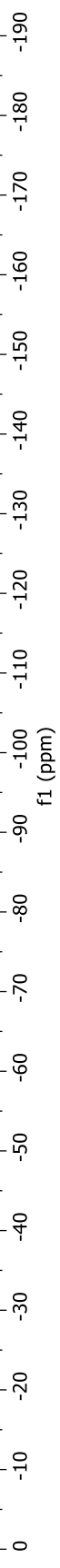


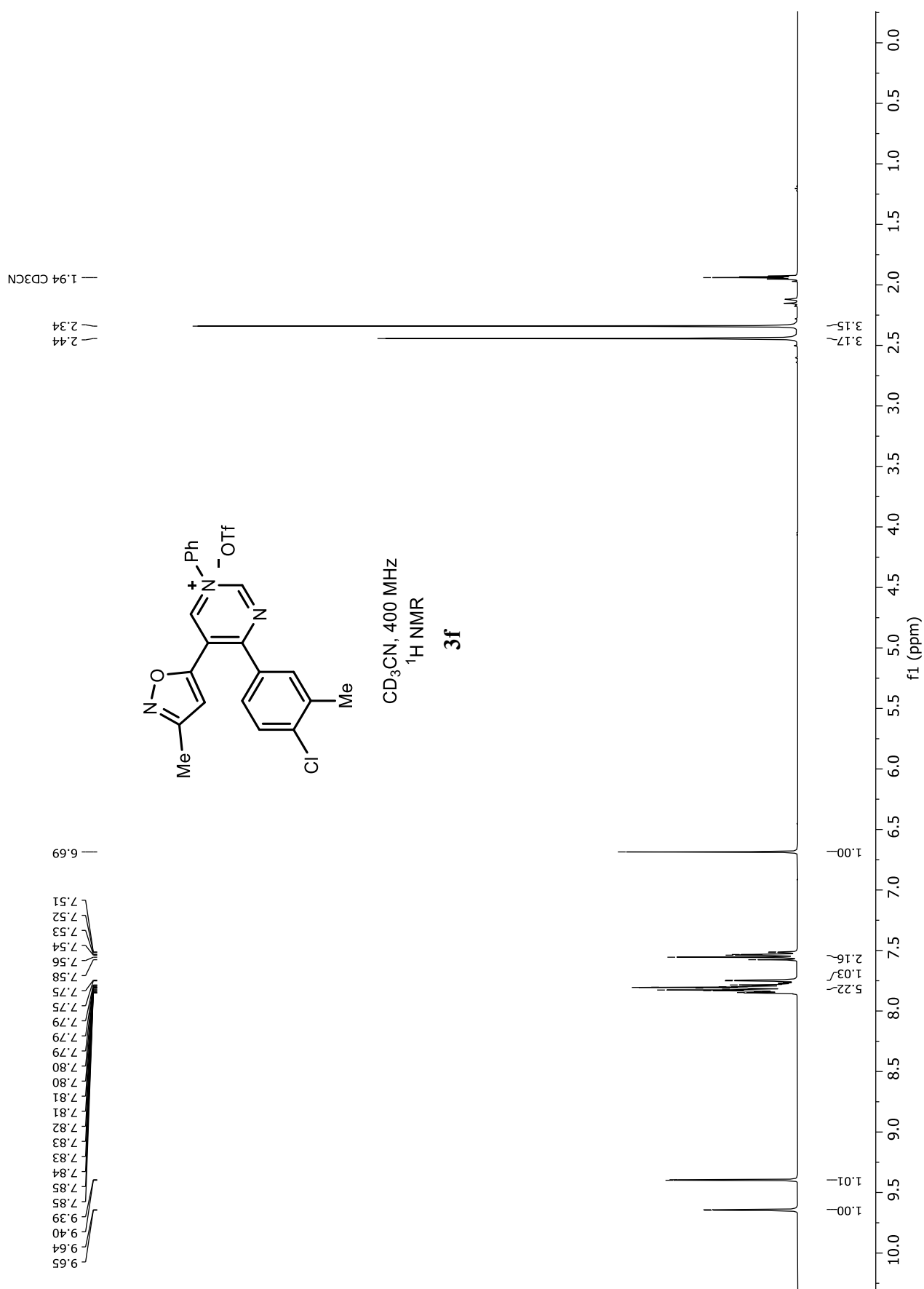
— -79.31

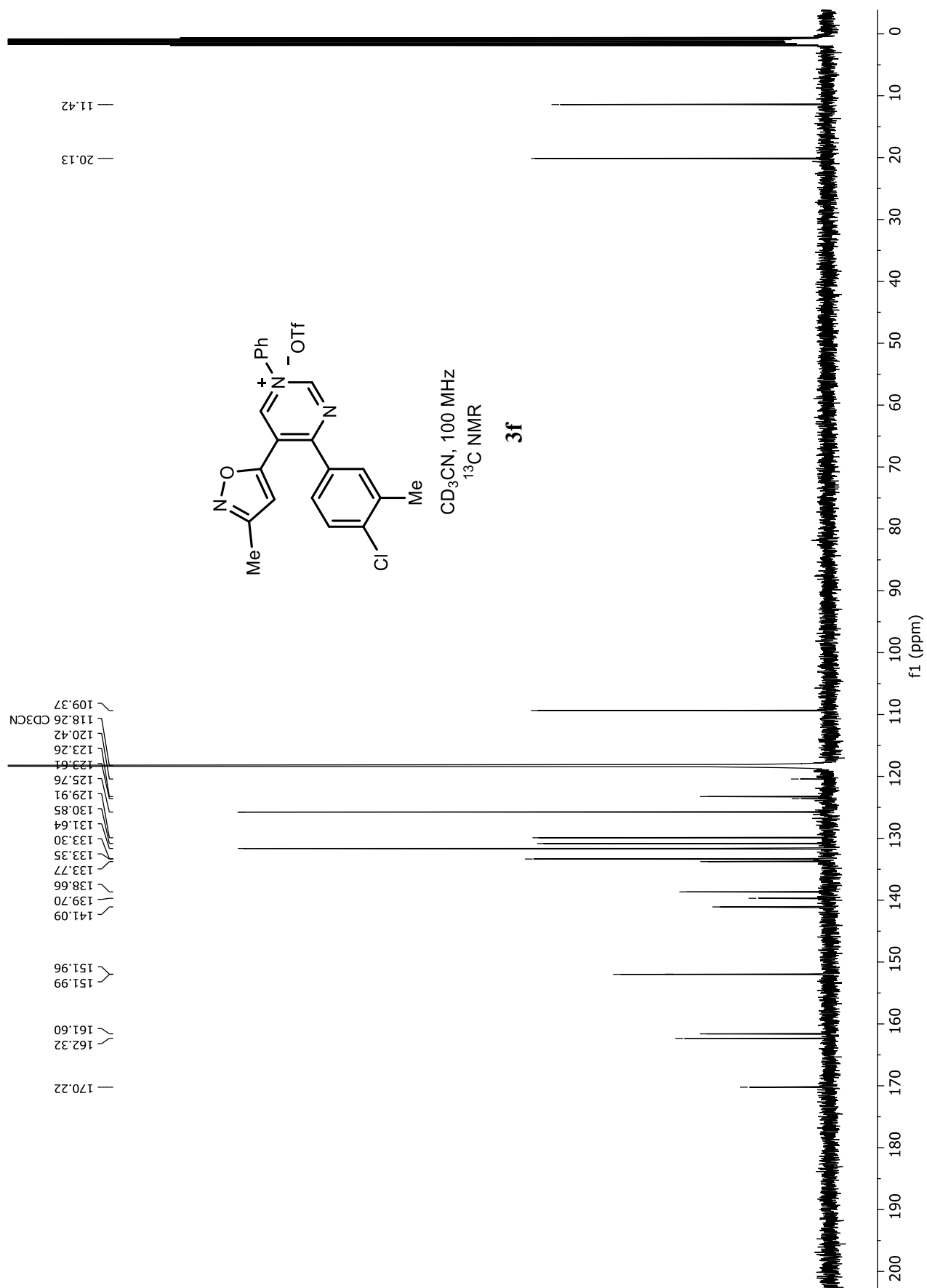


CD₃CN, 375 MHz
¹⁹F NMR

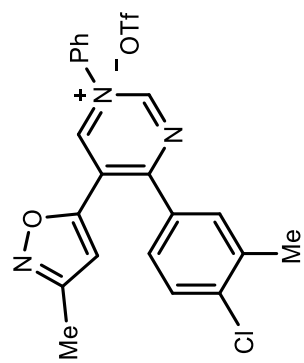
3e





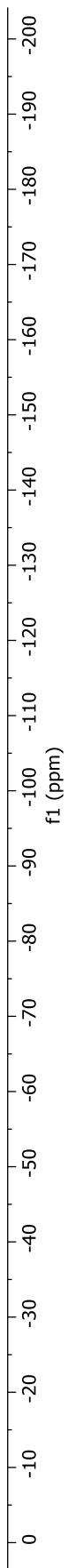


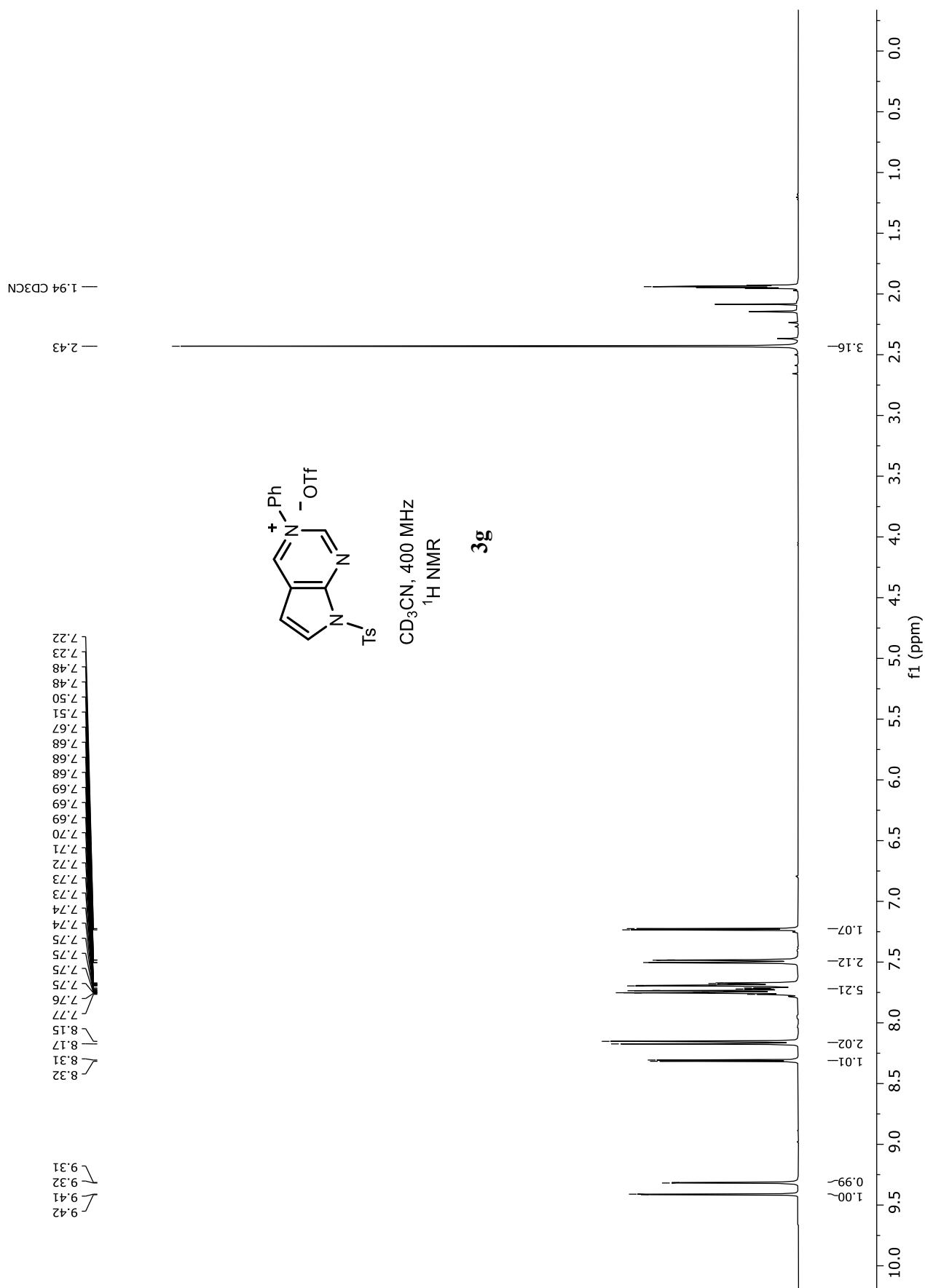
— -79.30

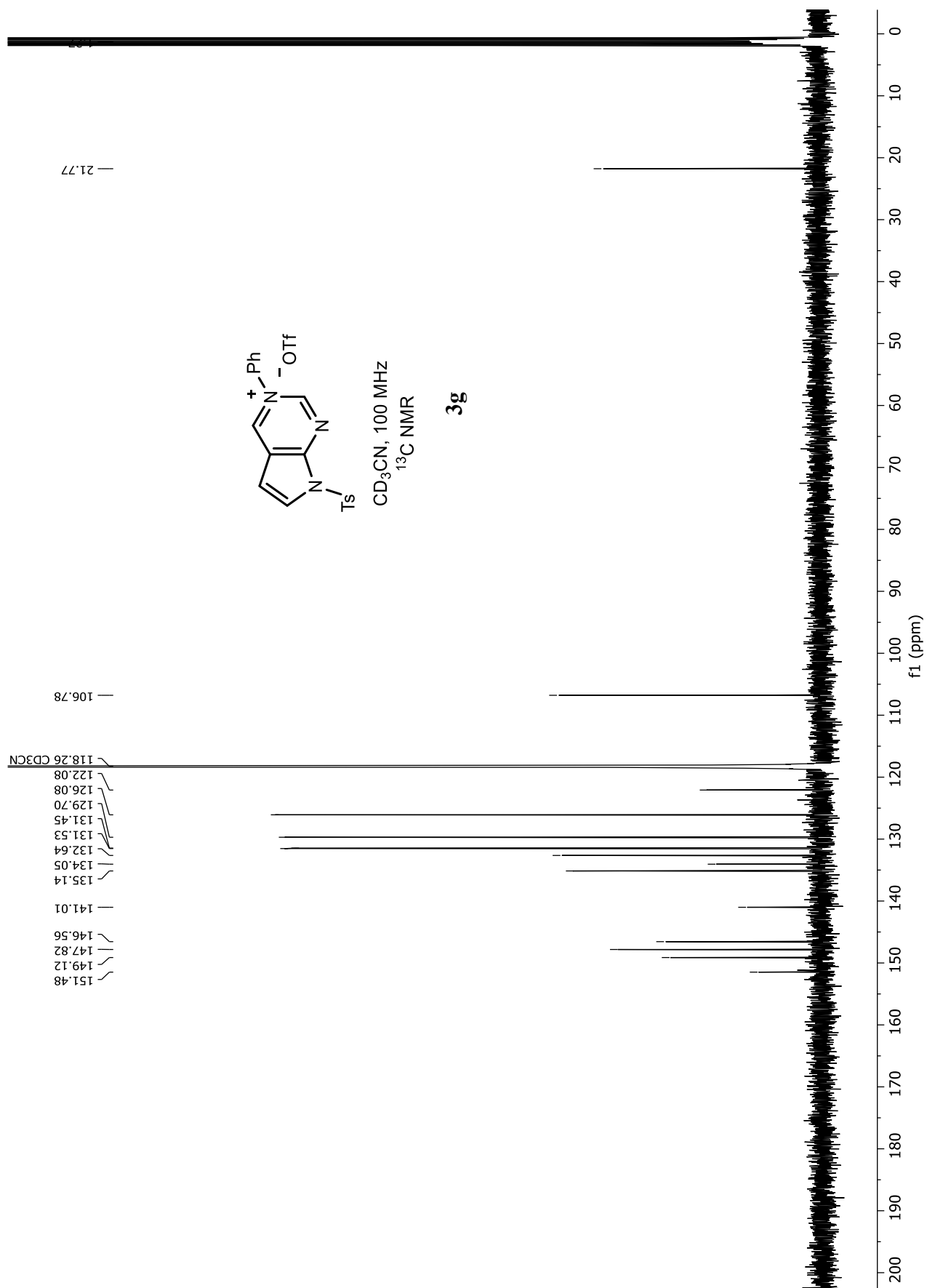


CD₃CN, 375 MHz
¹⁹F NMR

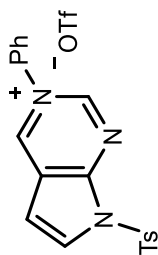
3f







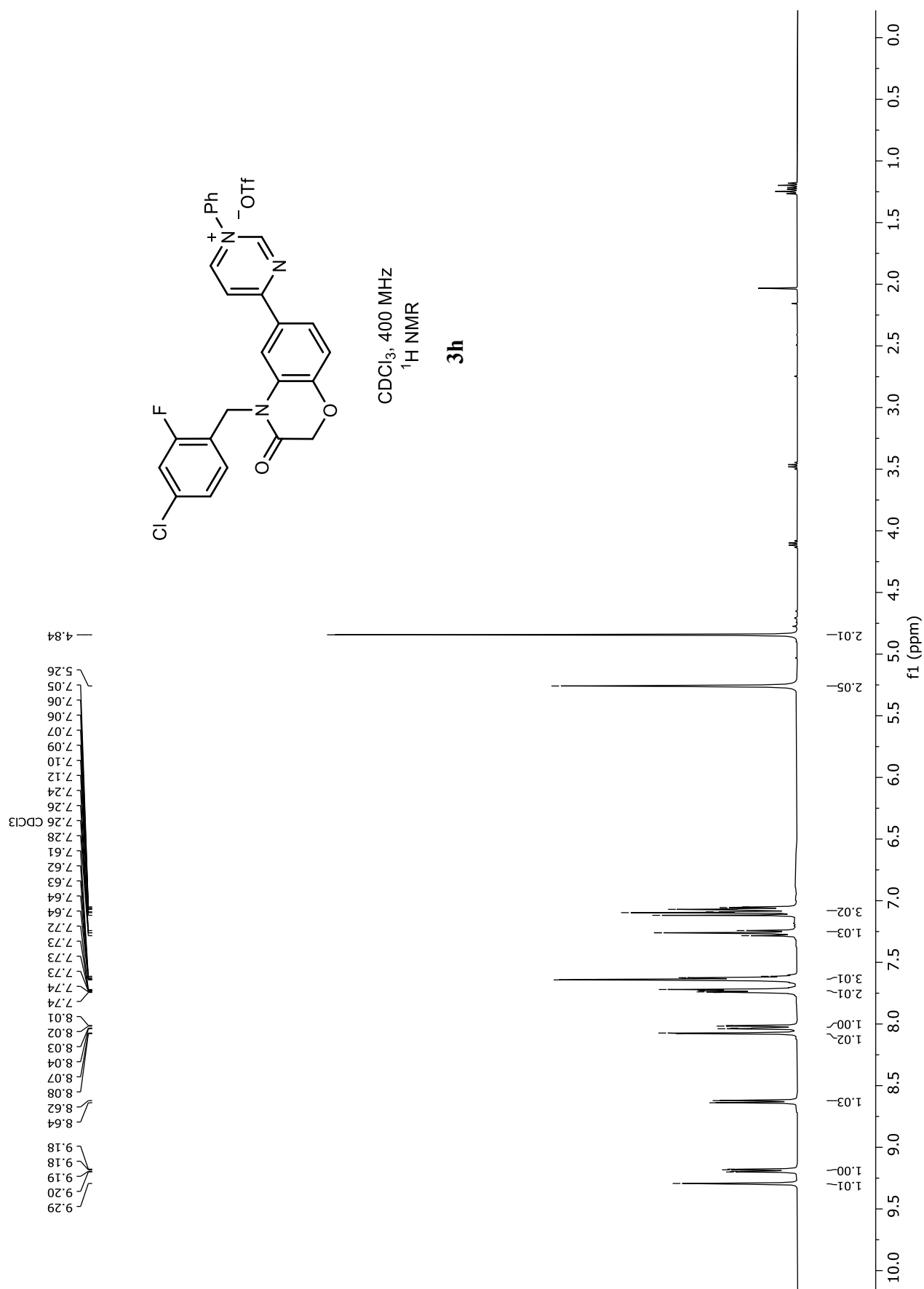
— -79.34

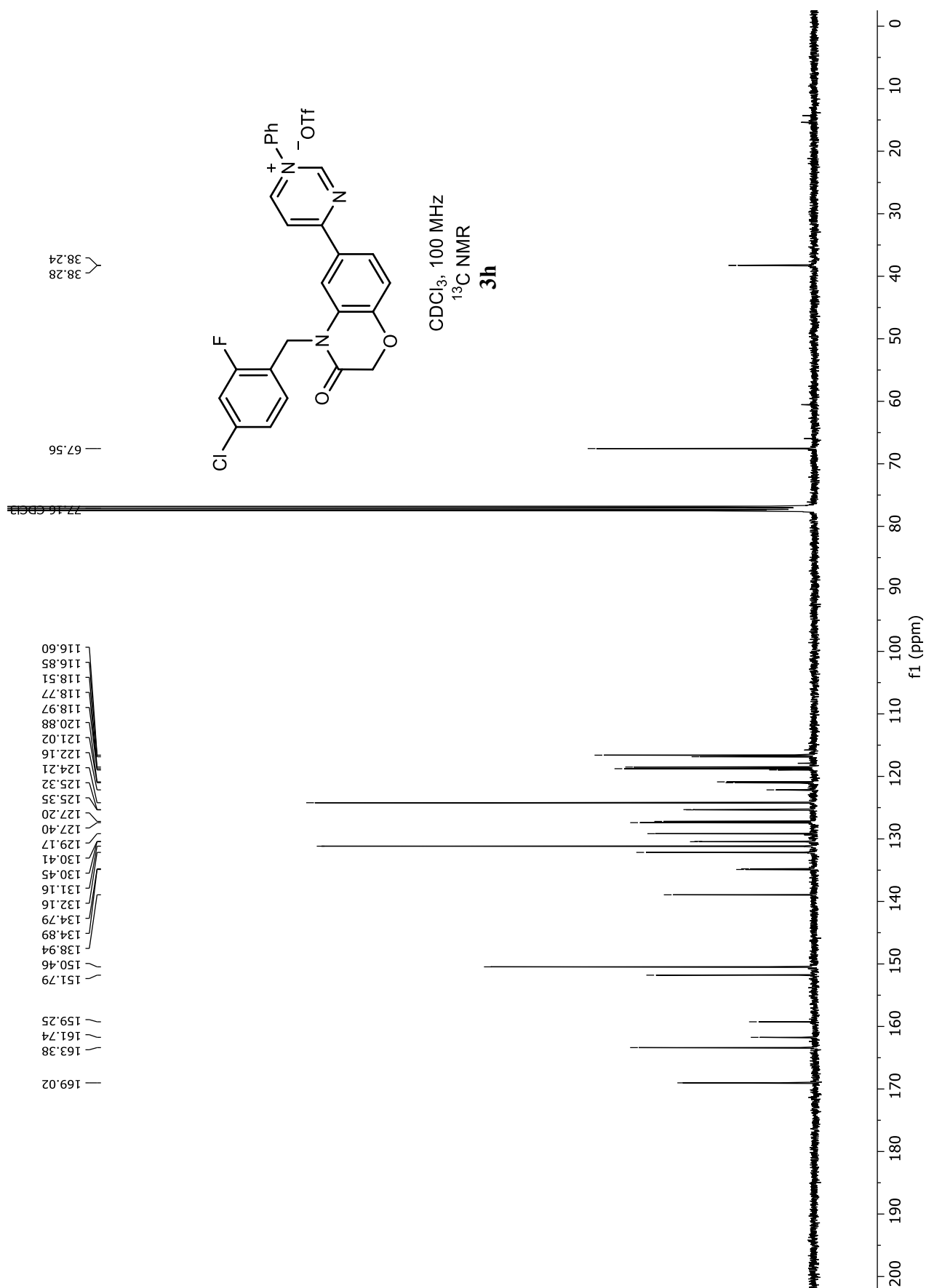


CD₃CN, 375 MHz
¹⁹F NMR

3g

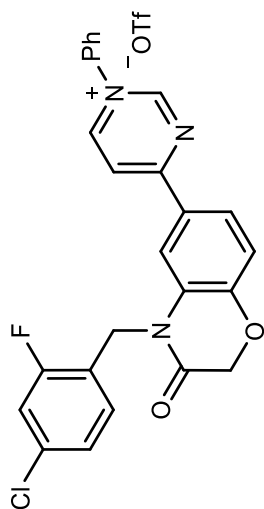
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)





-116.13
-116.15
-116.18

-79.31
-80.60



CD₃CN, 375 MHz
¹⁹F NMR
3h

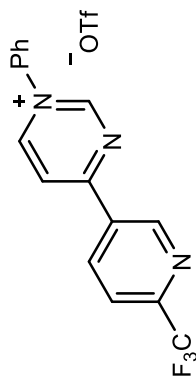
2.05
1.01
1.00

f1 (ppm)

1.98
1.97
1.97
1.96
1.96

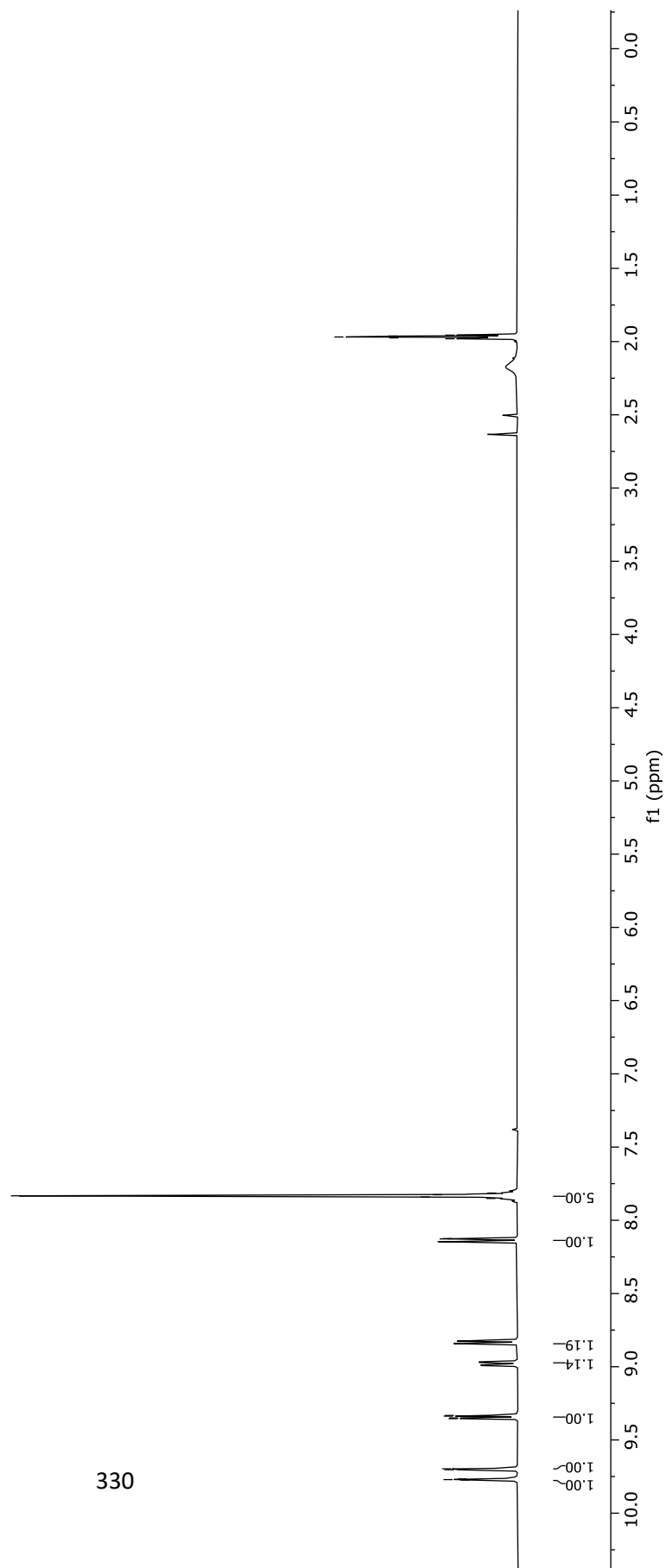
8.15
8.15
8.13
8.13
7.85
7.84
7.83
7.83
7.81

9.77
9.77
9.70
9.70
9.35
9.35
9.34
9.33

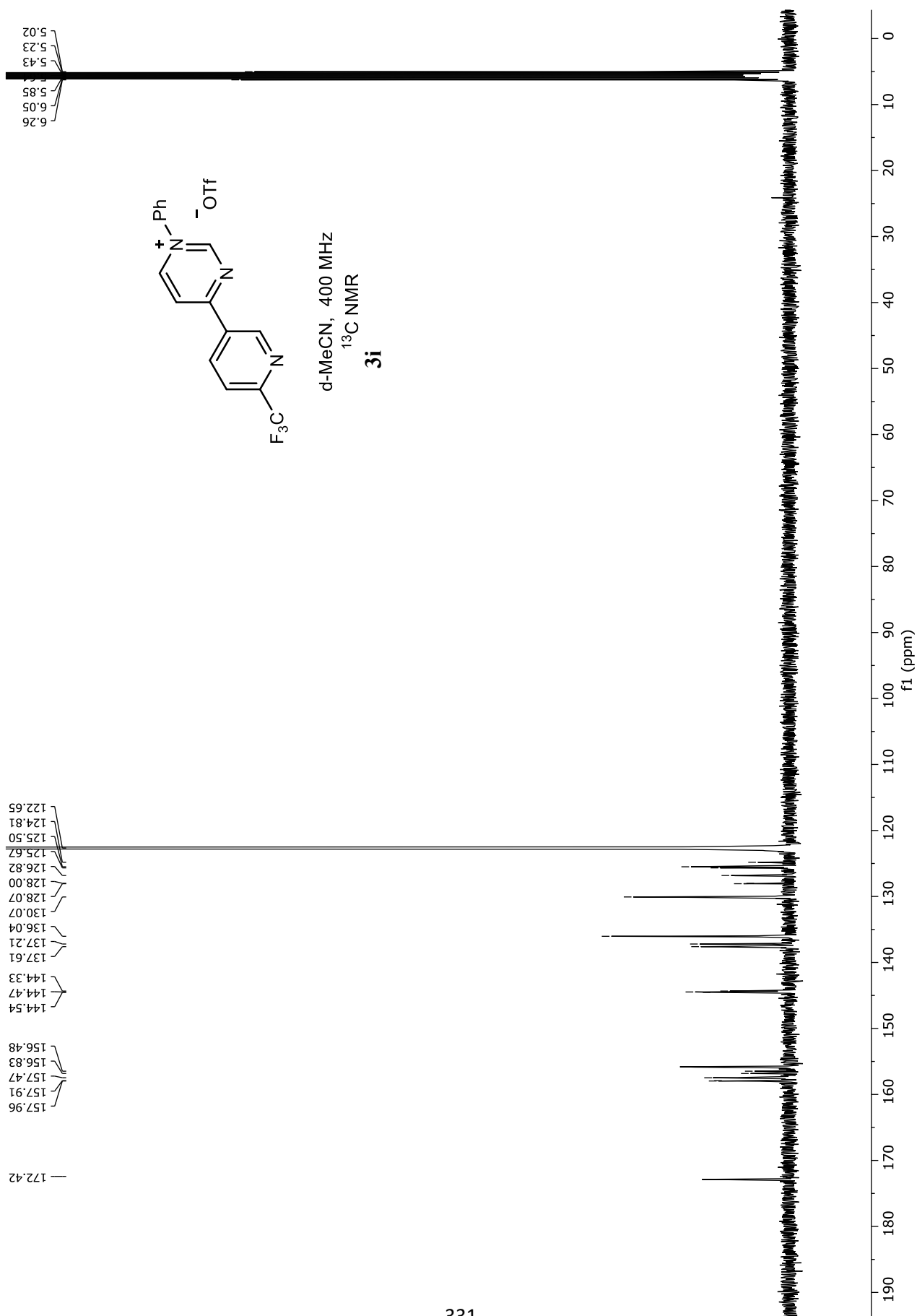


d-MeCN, 400 MHz
¹H NMR

3i

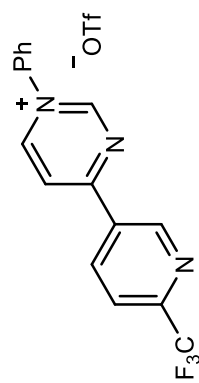


330



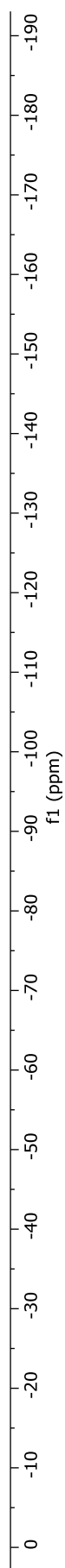
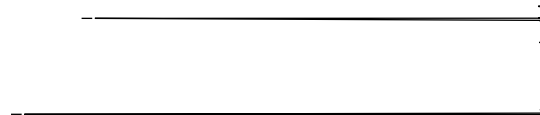
— -68.92

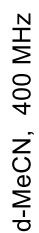
— -79.33



d-MeCN, 400 MHz
¹⁹F NMR

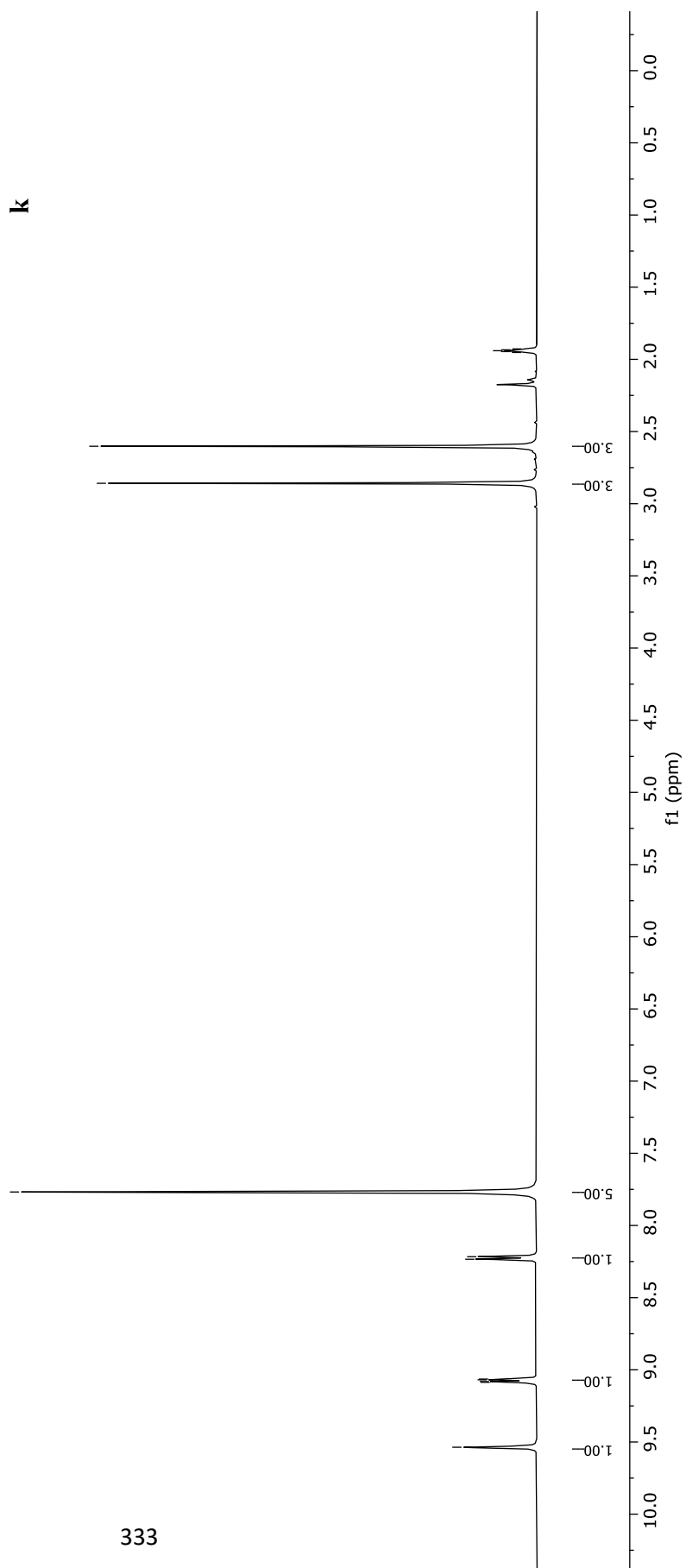
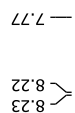
3i

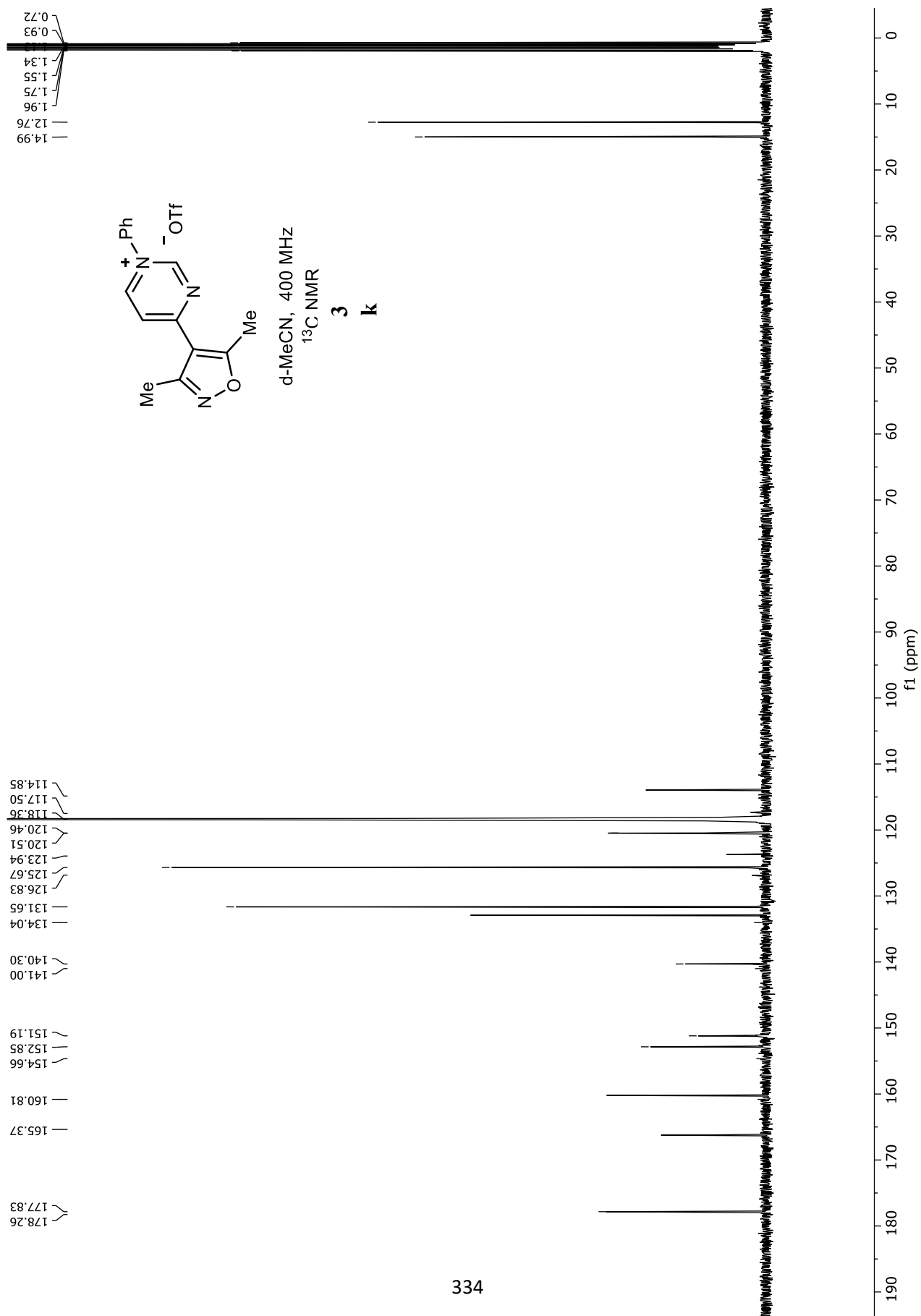




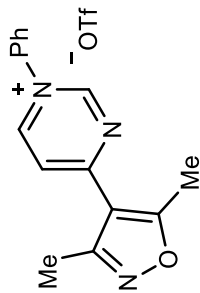
111111

k





— -79.28



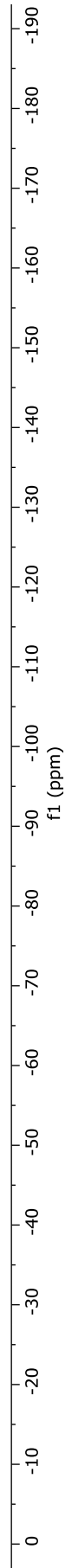
d-MeCN, 400 MHz

¹⁹F NMR

335

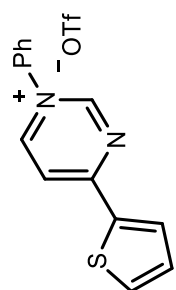
3

k



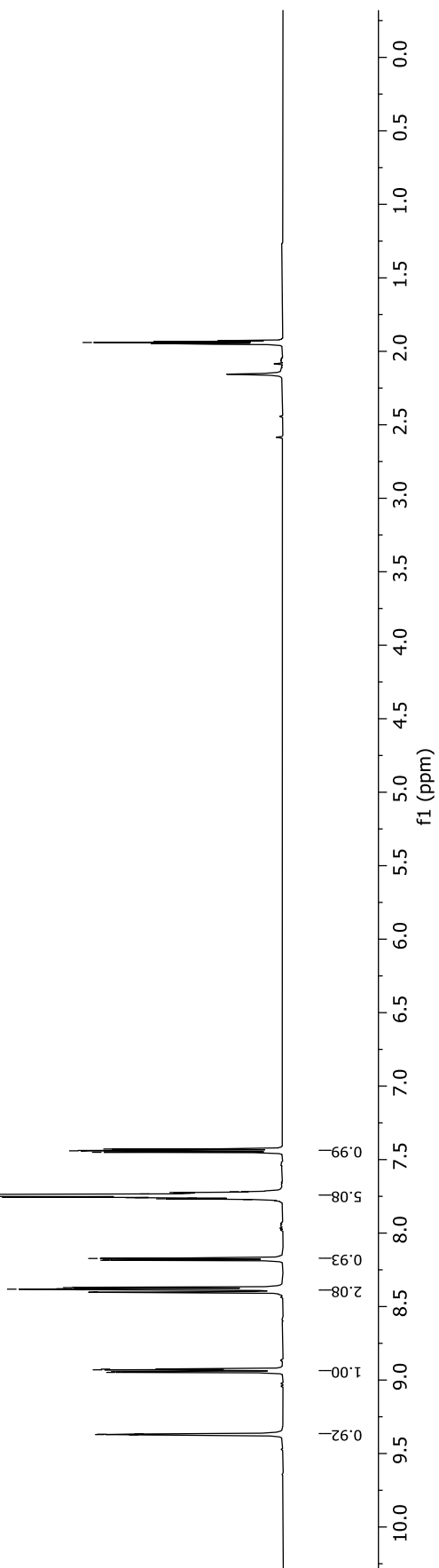
— 1.94 CD3CN

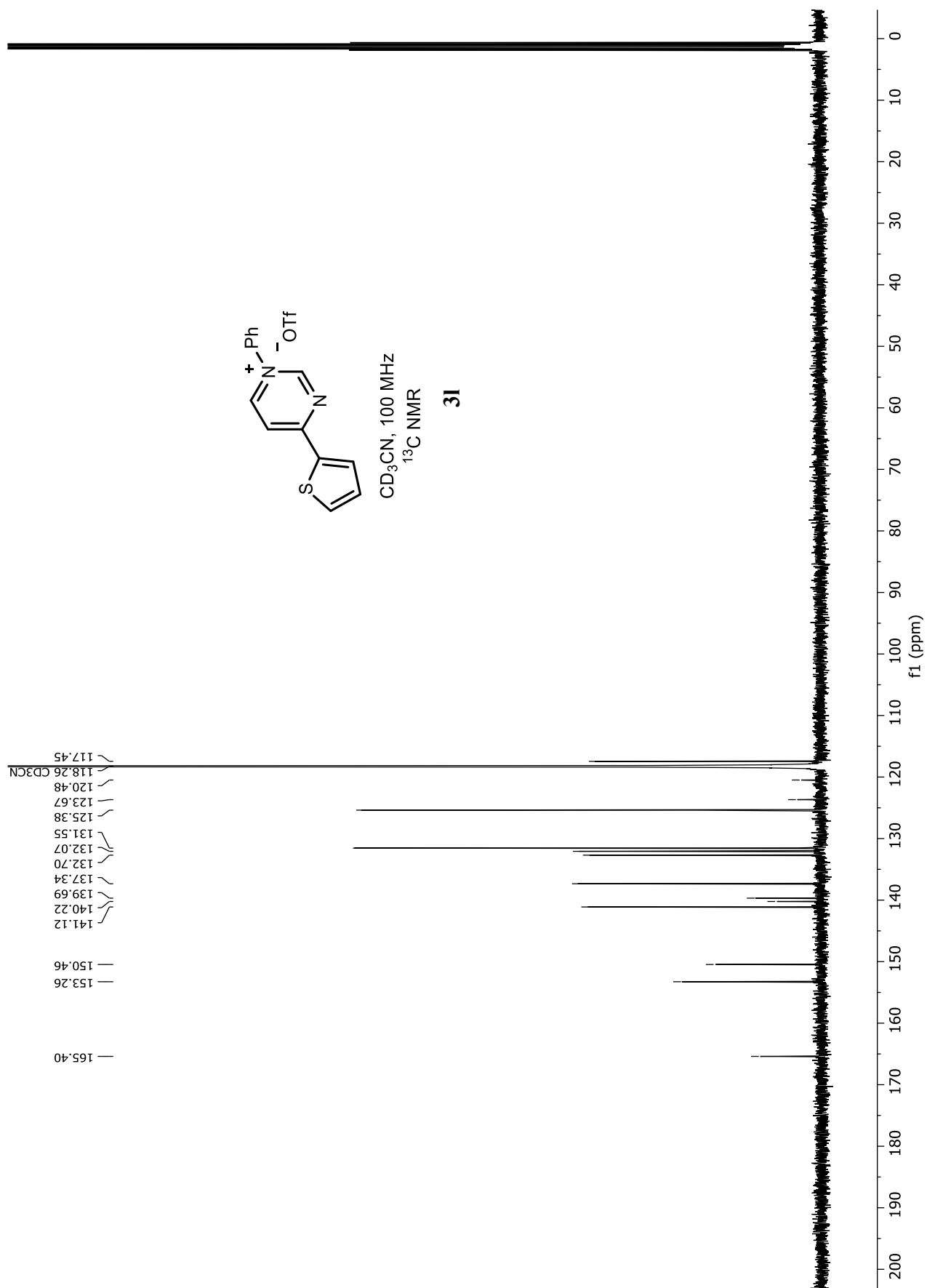
9.37
9.37
9.37
8.95
8.94
8.93
8.40
8.40
8.39
8.38
8.38
8.38
8.37
8.37
8.19
8.18
8.17
8.17
7.77
7.77
7.76
7.76
7.75
7.74
7.74
7.73
7.73
7.73
7.72
7.72
7.45
7.44
7.44
7.43



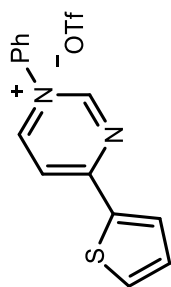
CD₃CN, 400 MHz
¹H NMR

3l





— -79.29



CD₃CN, 375 MHz
¹⁹F NMR

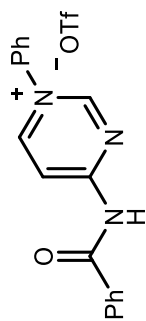
3I

338

0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190

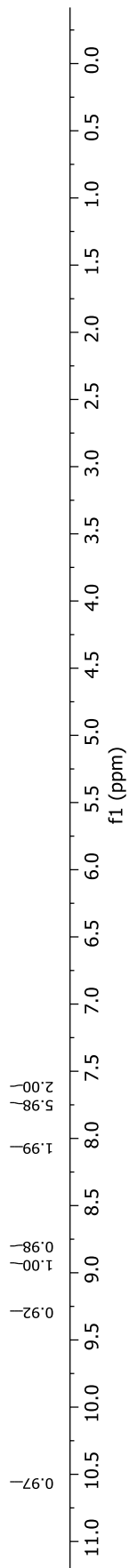
f1 (ppm)

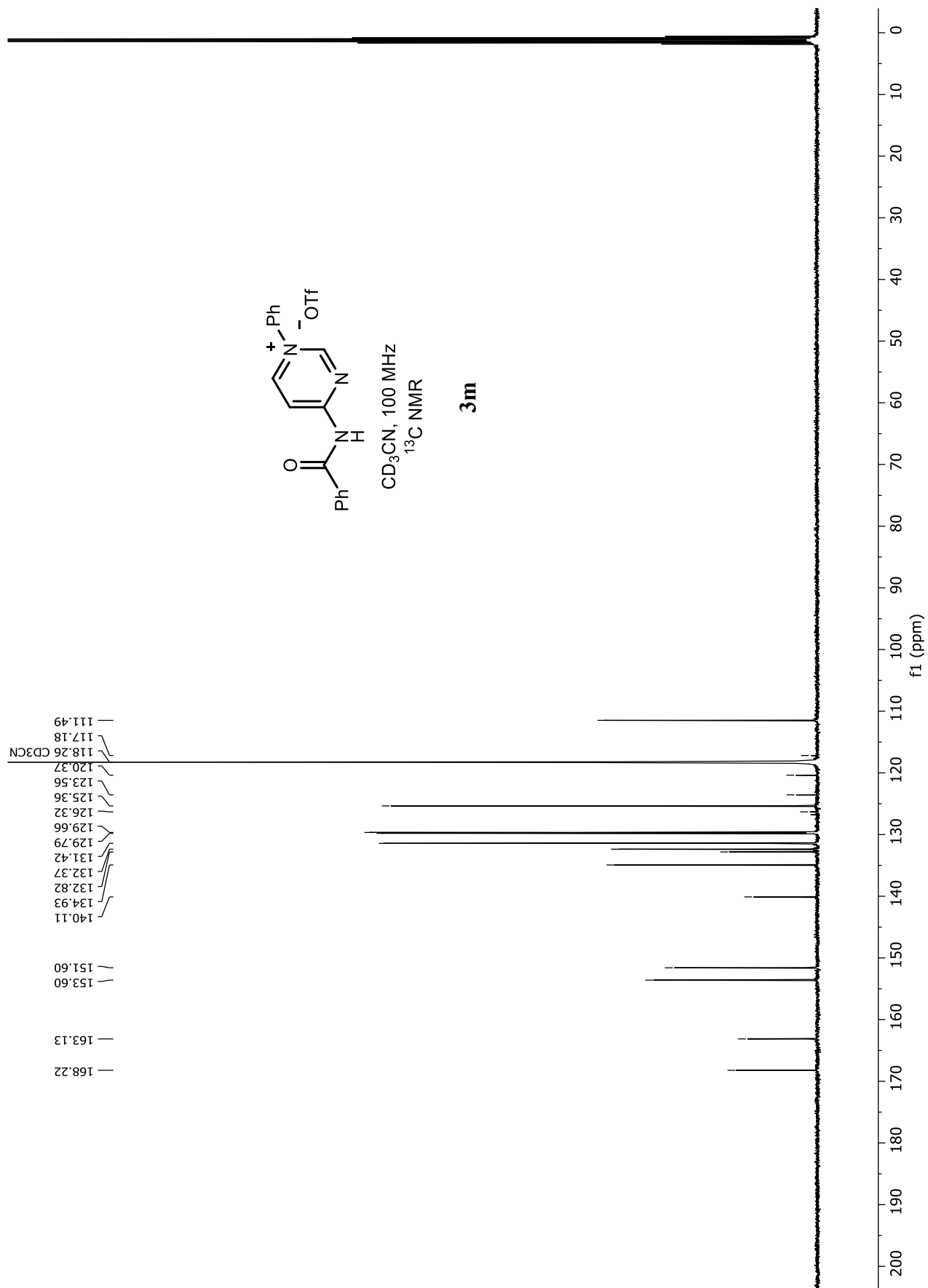
10.56 —
9.30
9.29
9.29
8.94
8.94
8.92
8.92
8.81
8.81
8.79
8.79
8.08
8.07
8.07
8.06
8.05
8.05
7.76
7.75
7.75
7.73
7.72
7.72
7.71
7.63
7.62
7.61
7.59
7.59



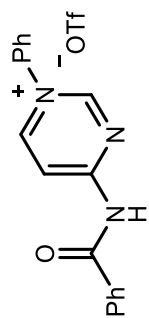
CD₃CN, 400 MHz
¹H NMR

3m





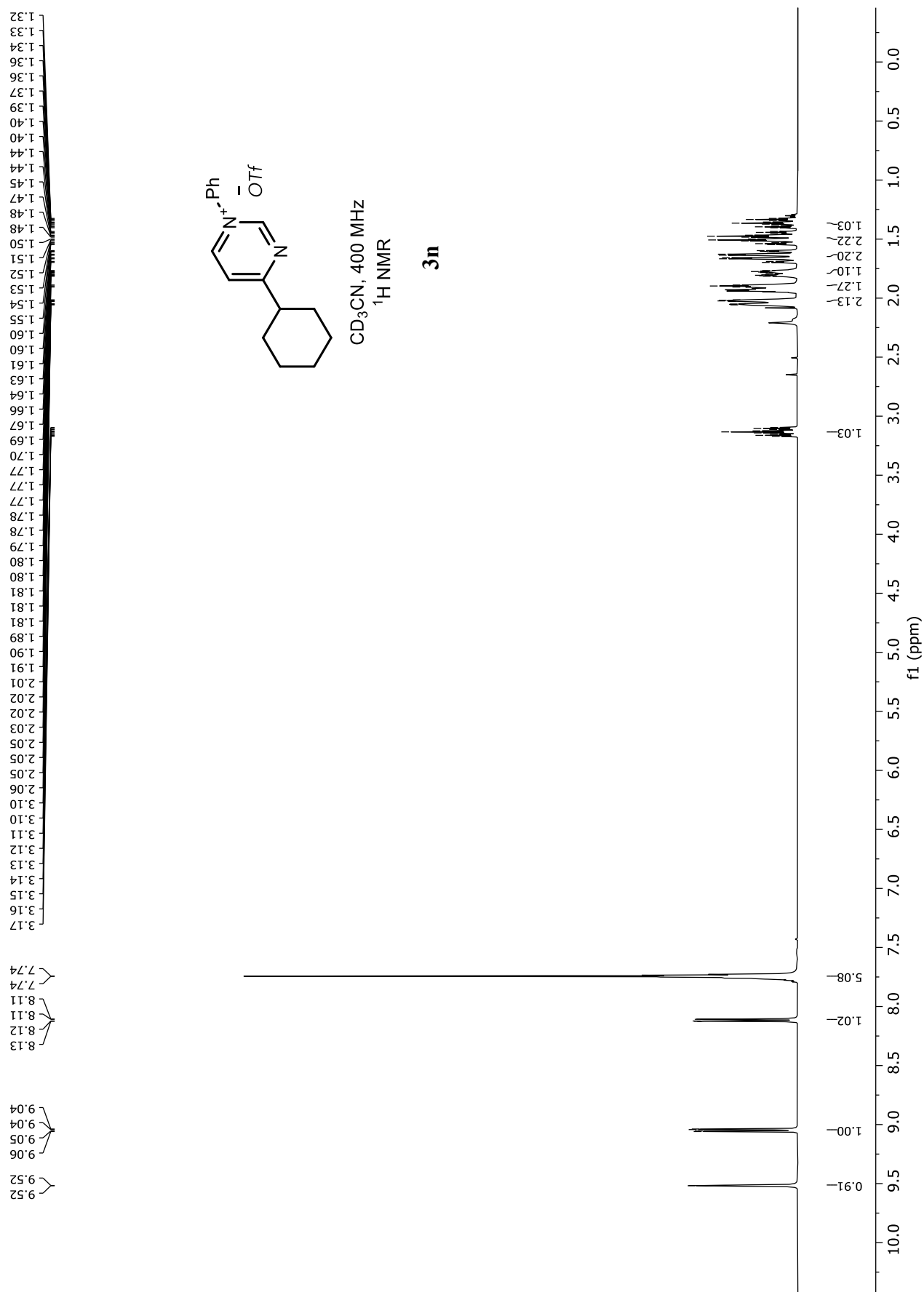
— -79.20

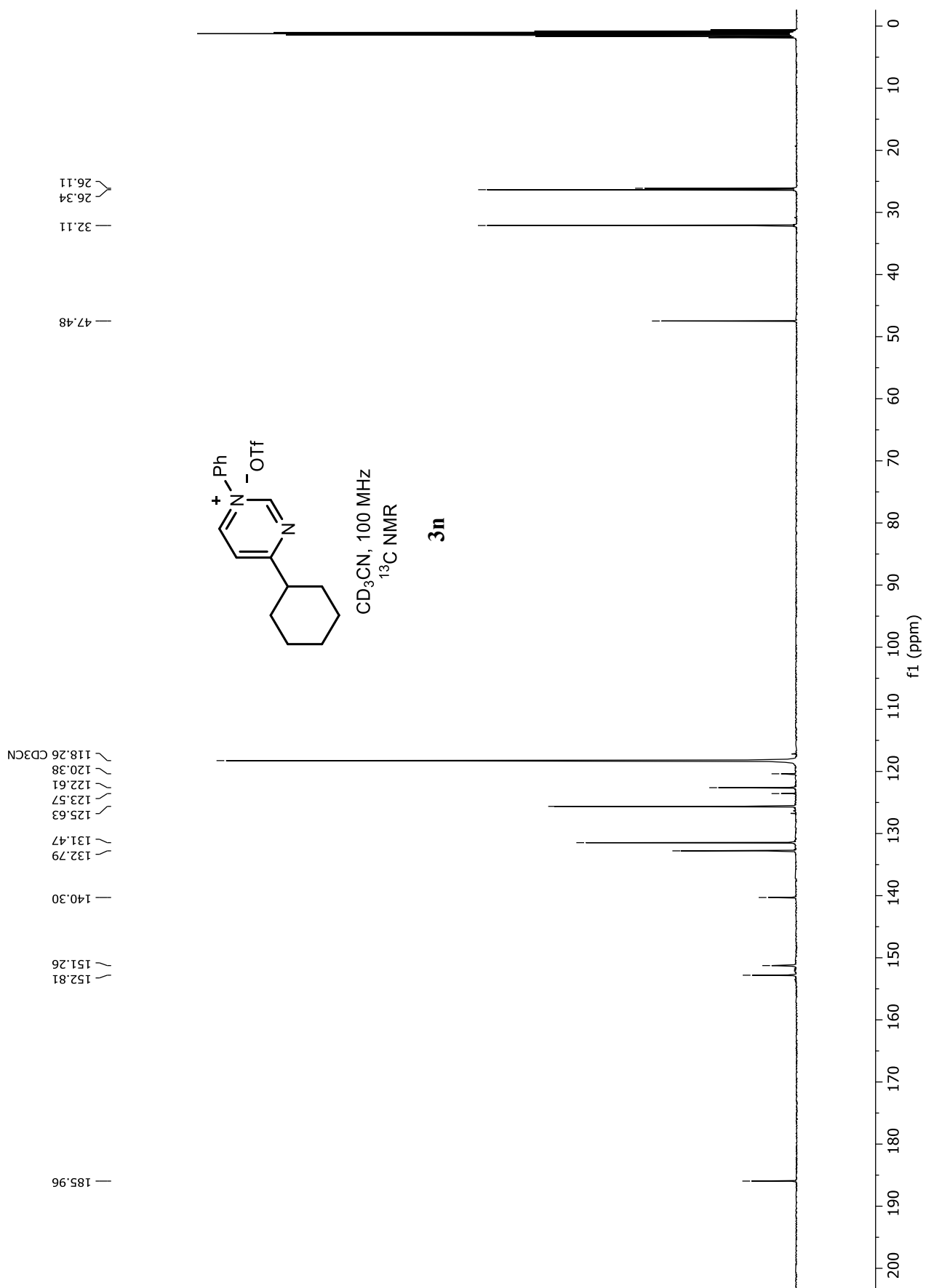


CD₃CN, 375 MHz
¹⁹F NMR

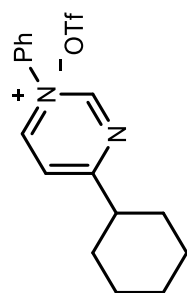
3m

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





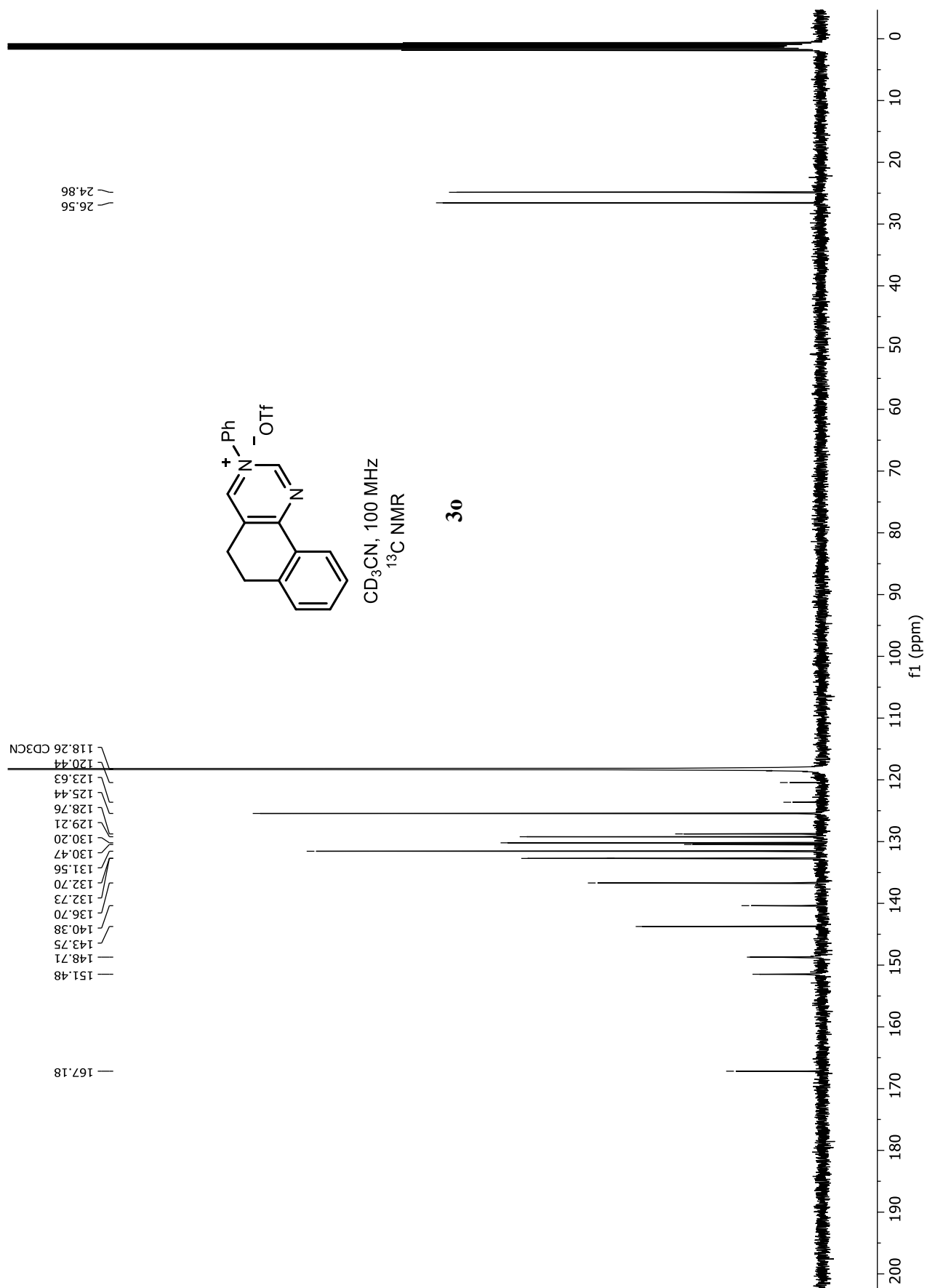
— -79.32



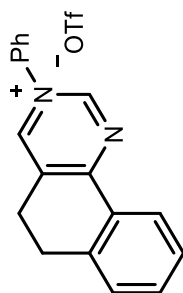
CD₃CN, 375 MHz
¹⁹F NMR

3n

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



— -79.28

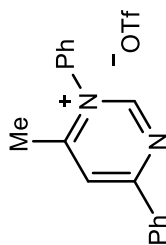


CD₃CN, 375 MHz
¹⁹F NMR

30

0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190

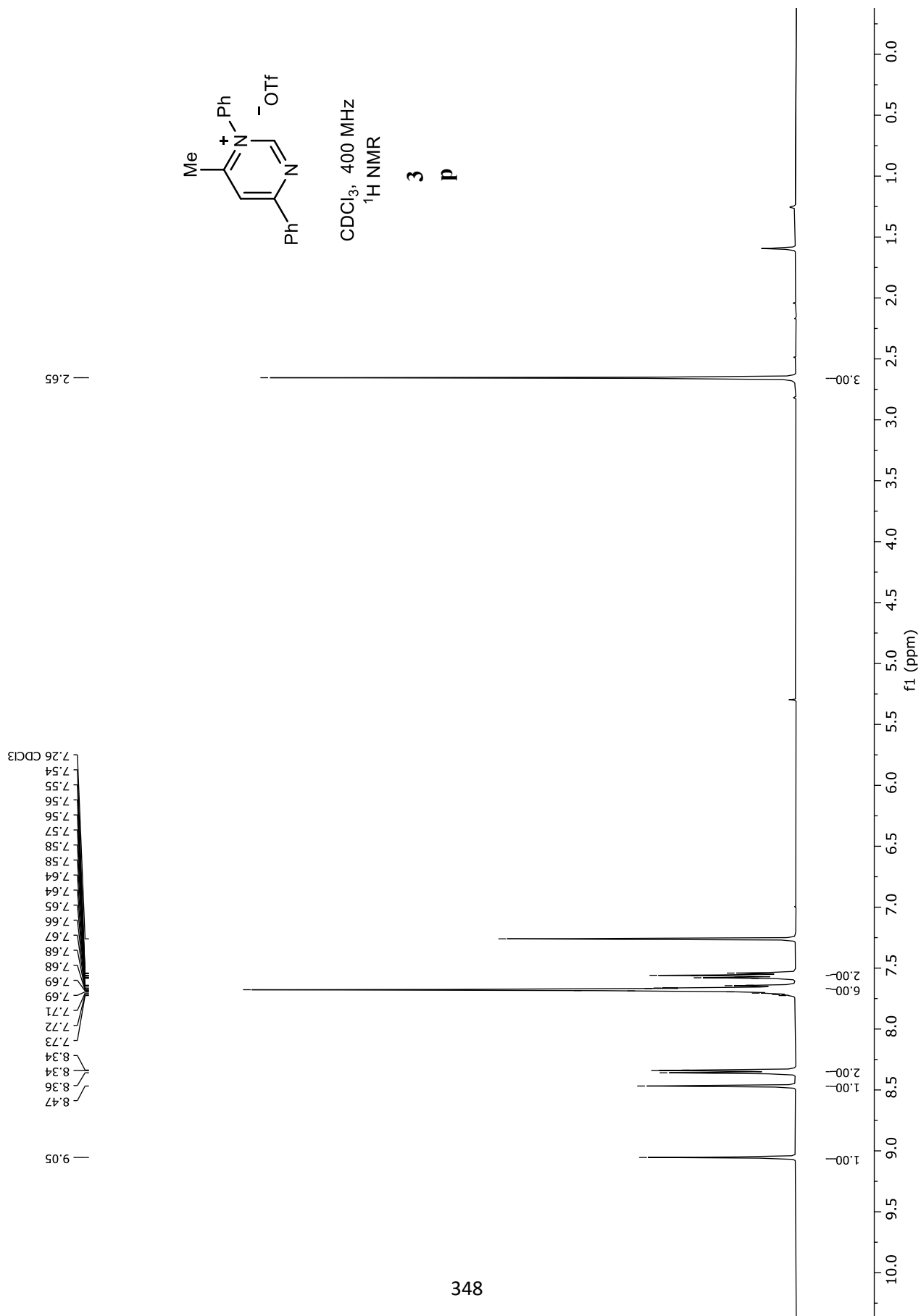
f1 (ppm)

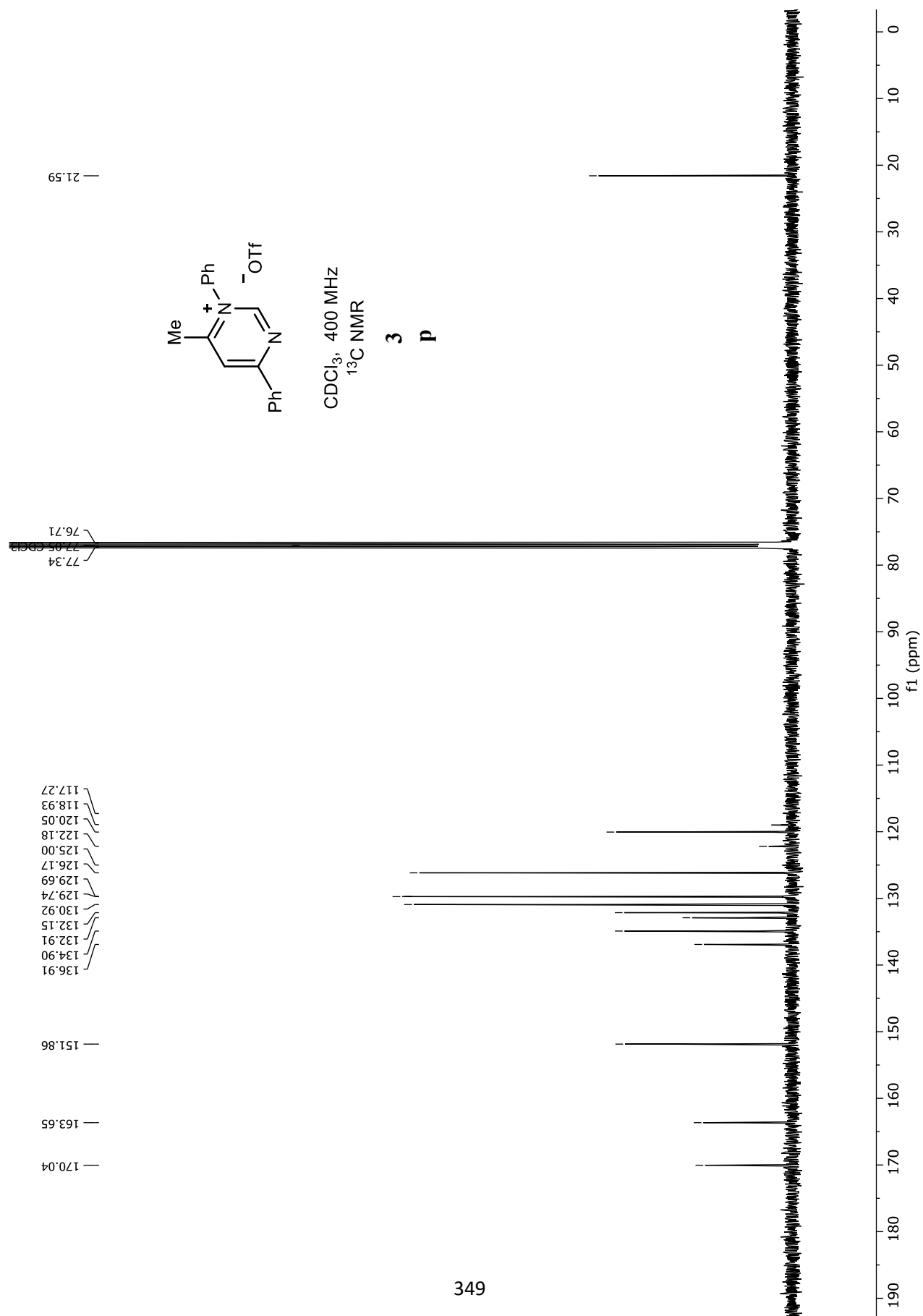


CDCl₃, 400 MHz
¹H NMR

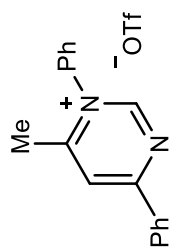
3

p





— -78.31

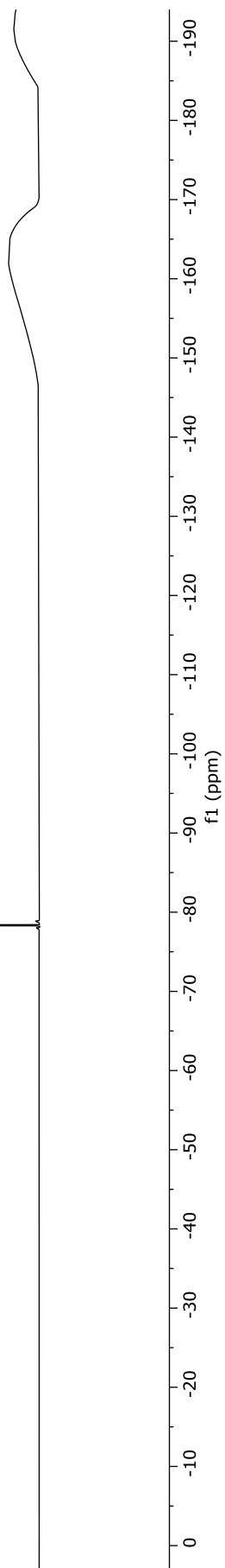


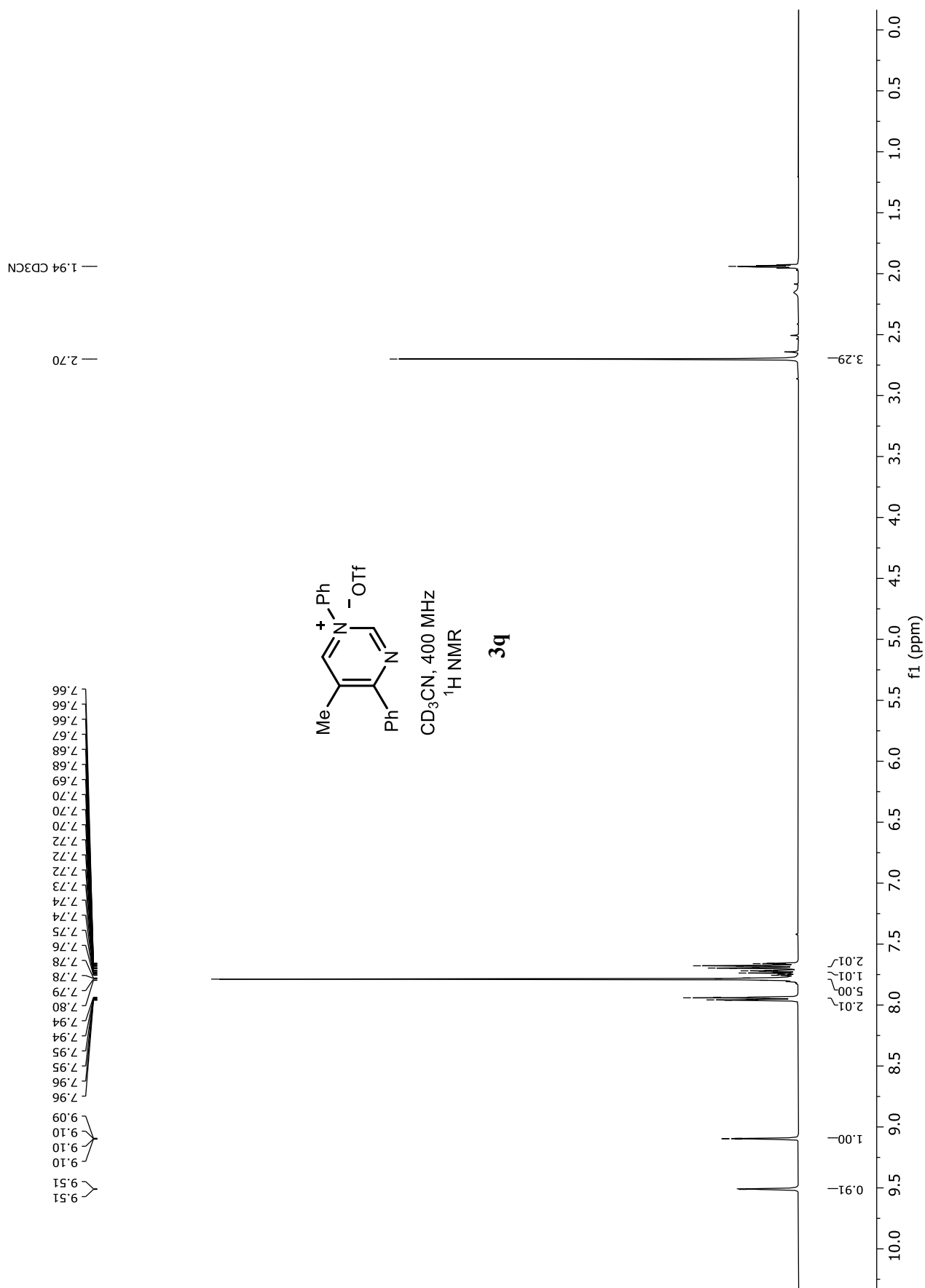
CDCl₃, 400 MHz
¹⁹F NMR

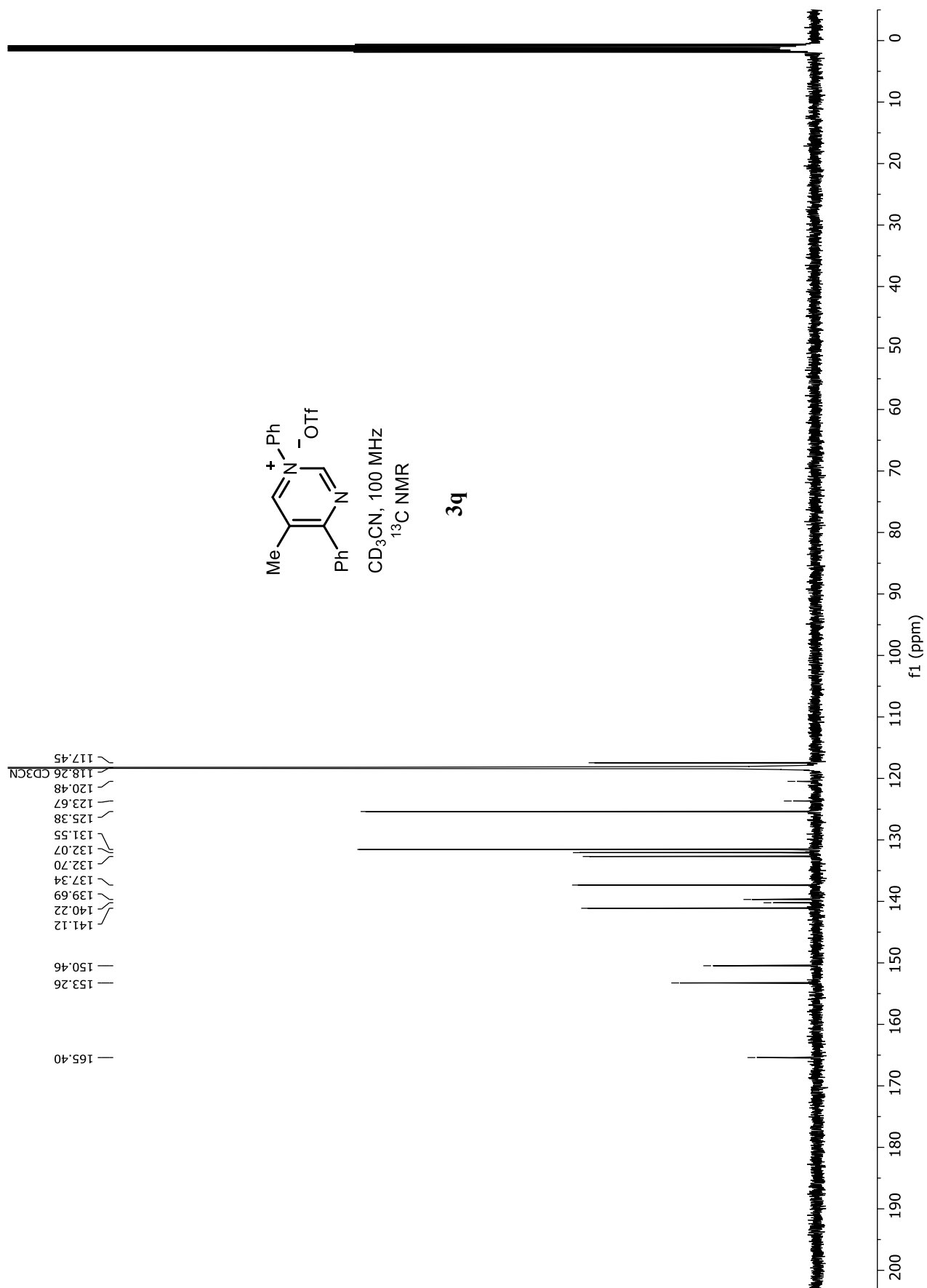
3

p

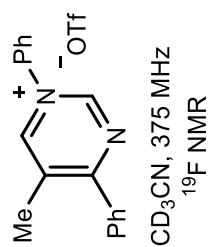
350





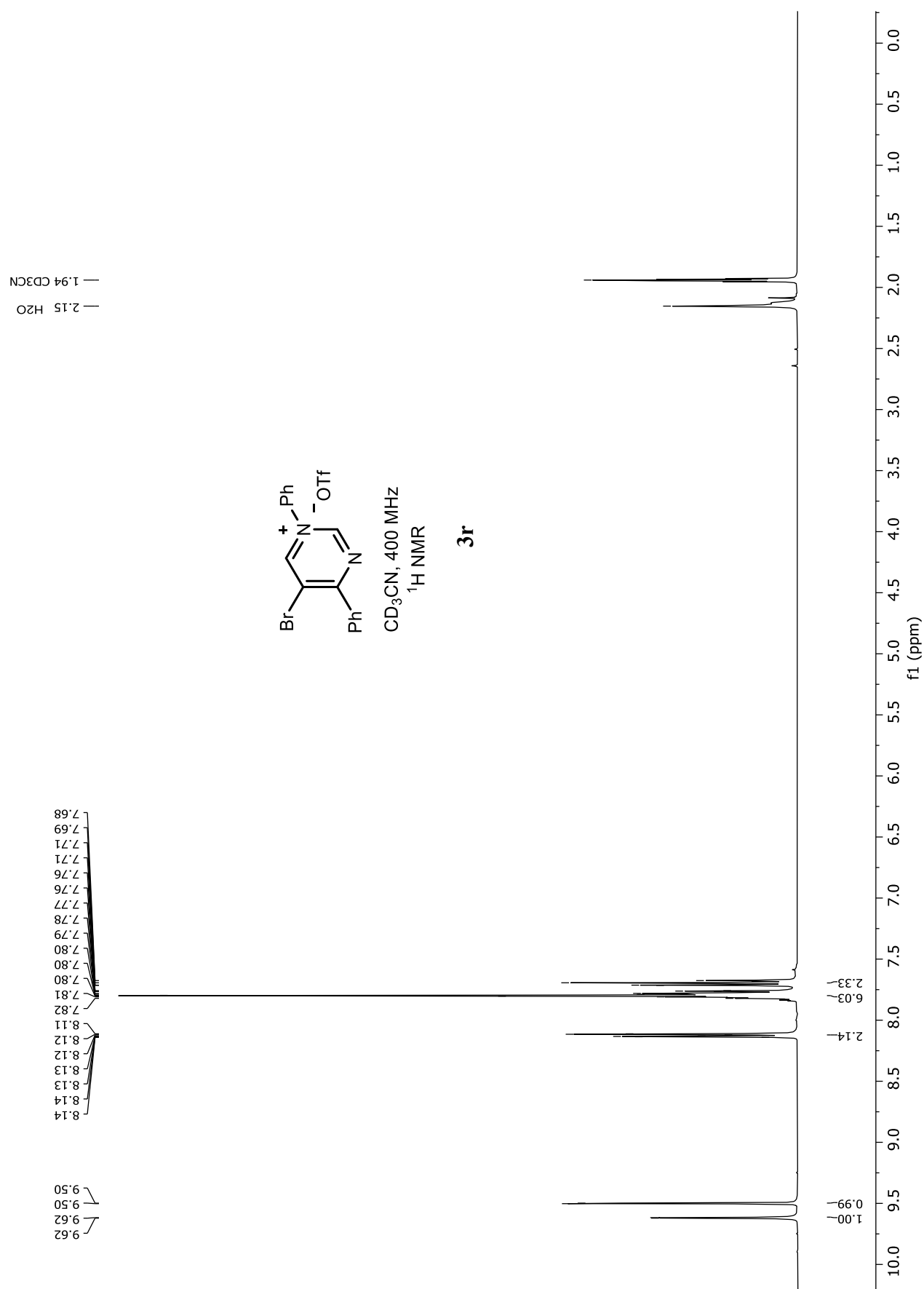


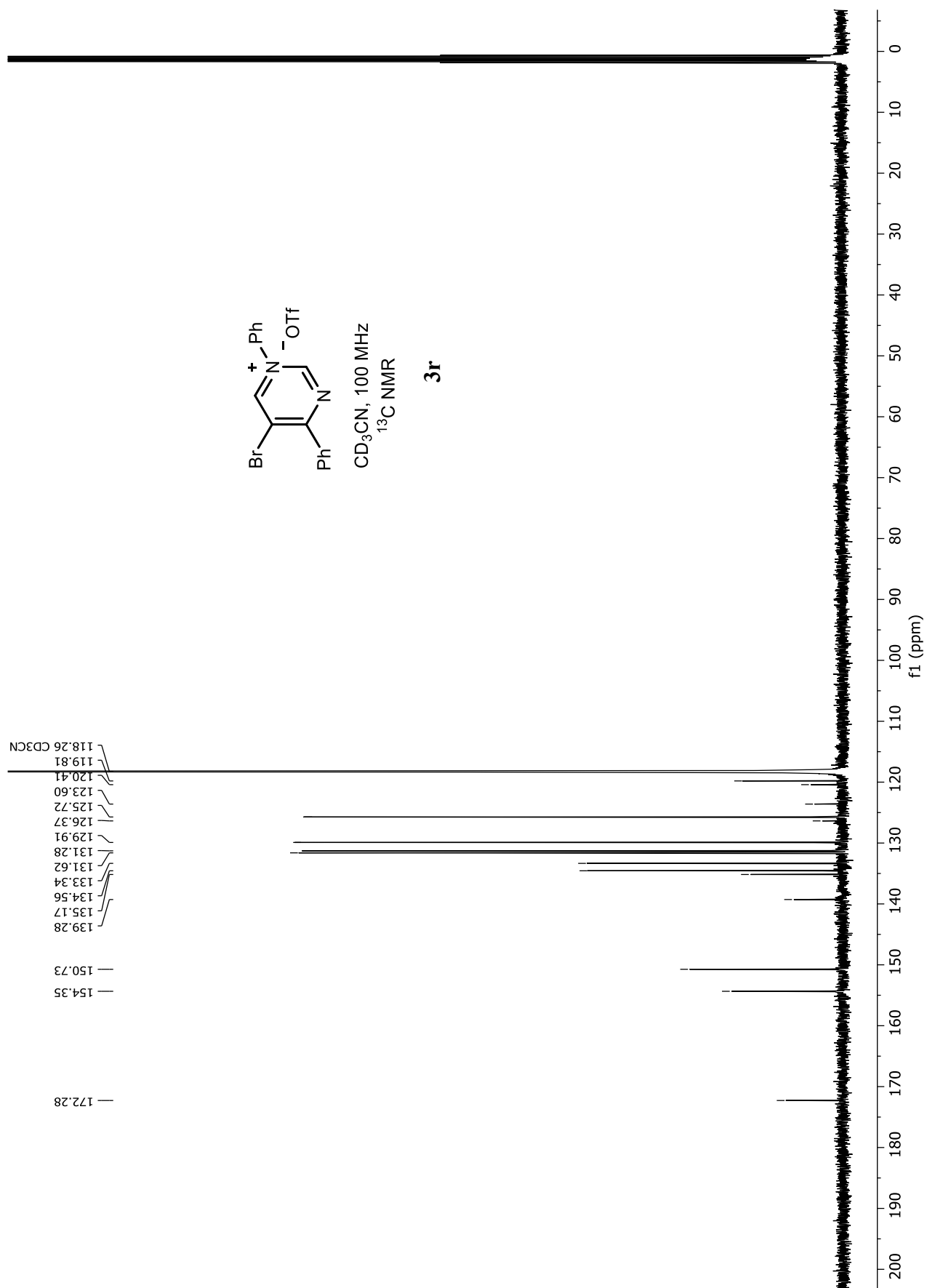
— -79.31



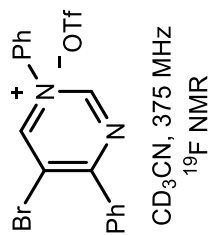
3q

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



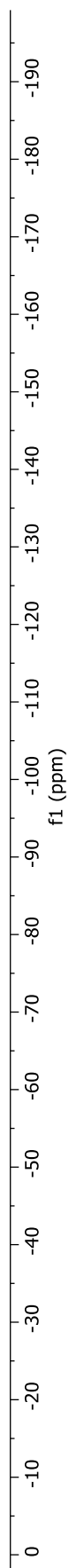


— -79.27



356

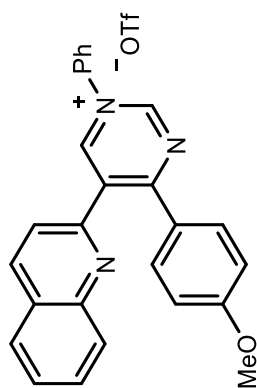
3r



— 1.94 CD3CN

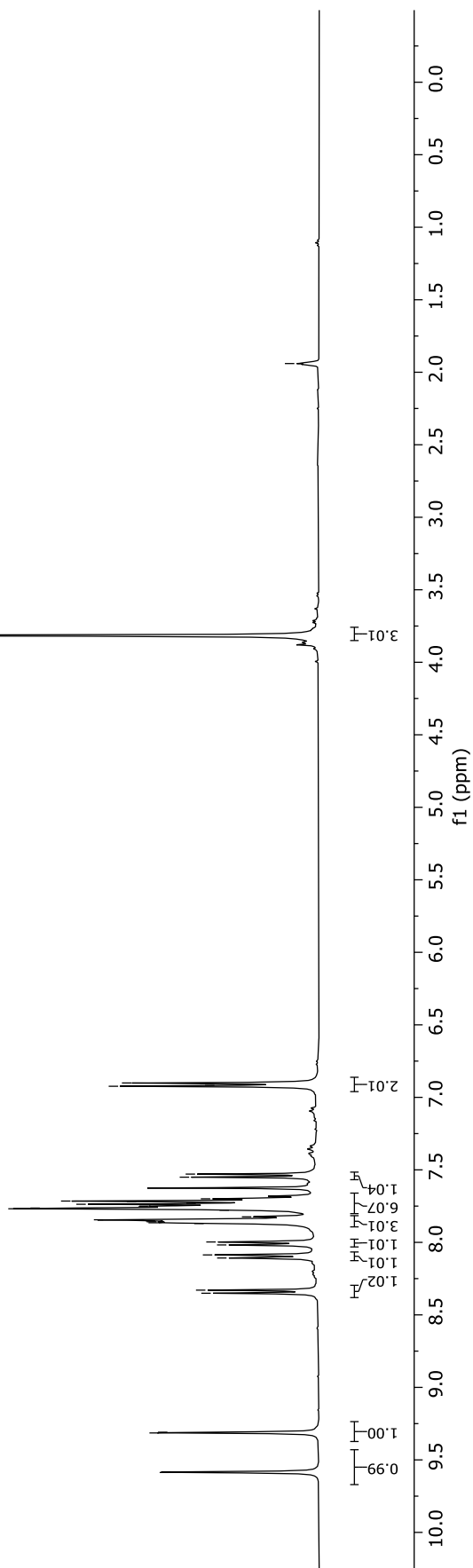
9.59
9.58
9.31
9.31
8.35
8.33
8.11
8.09
8.02
8.00
7.87
7.86
7.86
7.85
7.84
7.82
7.78
7.77
7.76
7.75
7.75
7.74
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7.72
7.72
7.70
7.55
7.53
6.92
6.92
6.91
6.90

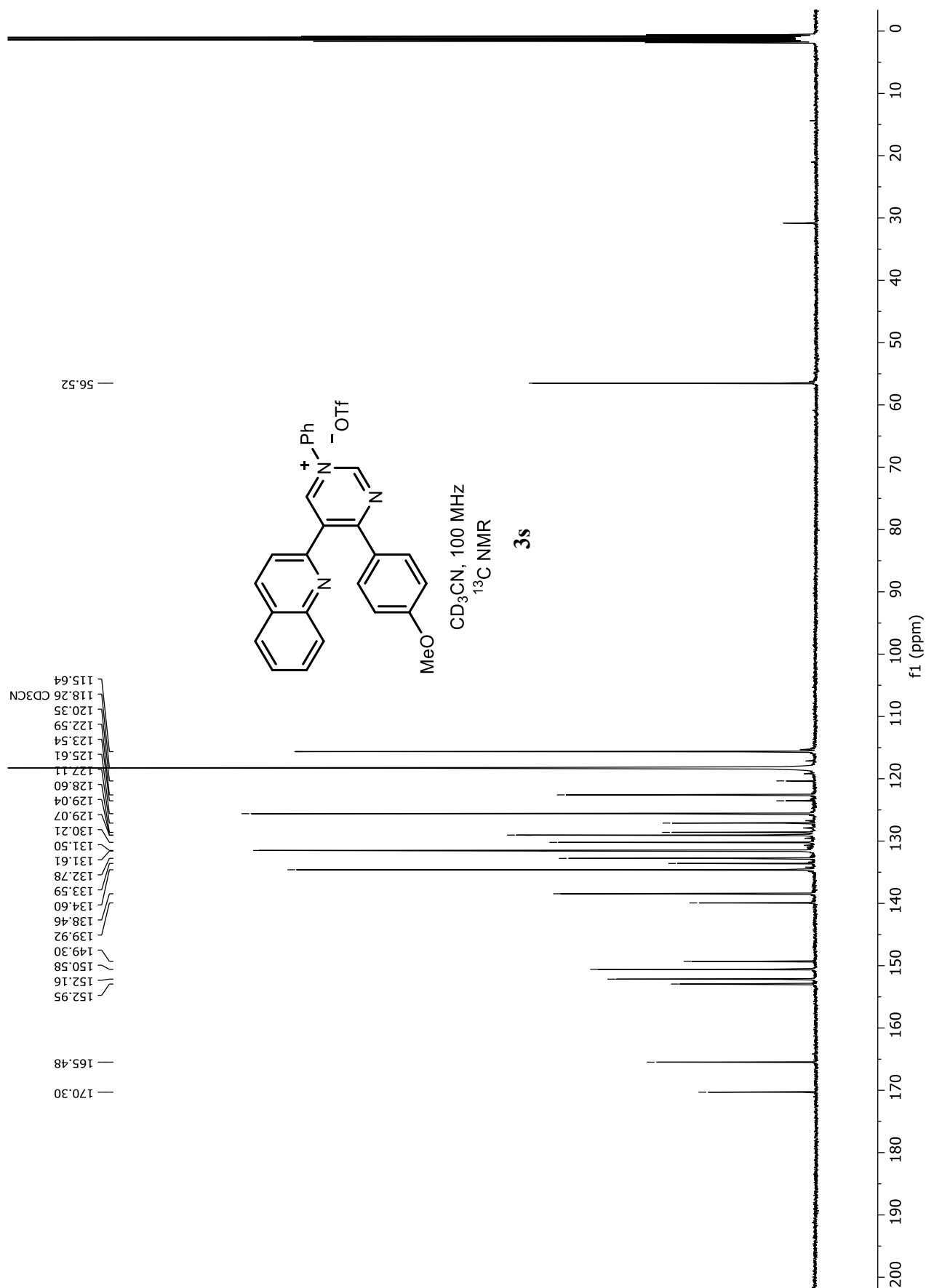
— 3.82



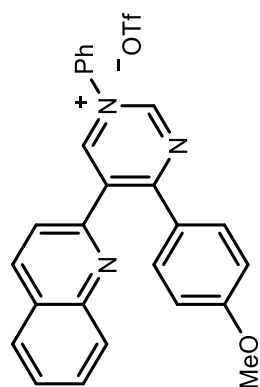
CD₃CN, 400 MHz
¹H NMR

3s



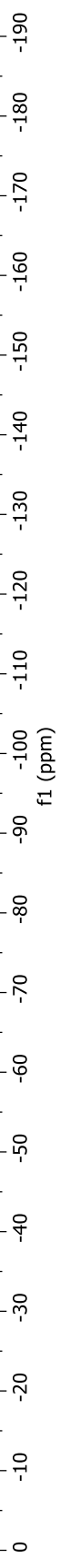


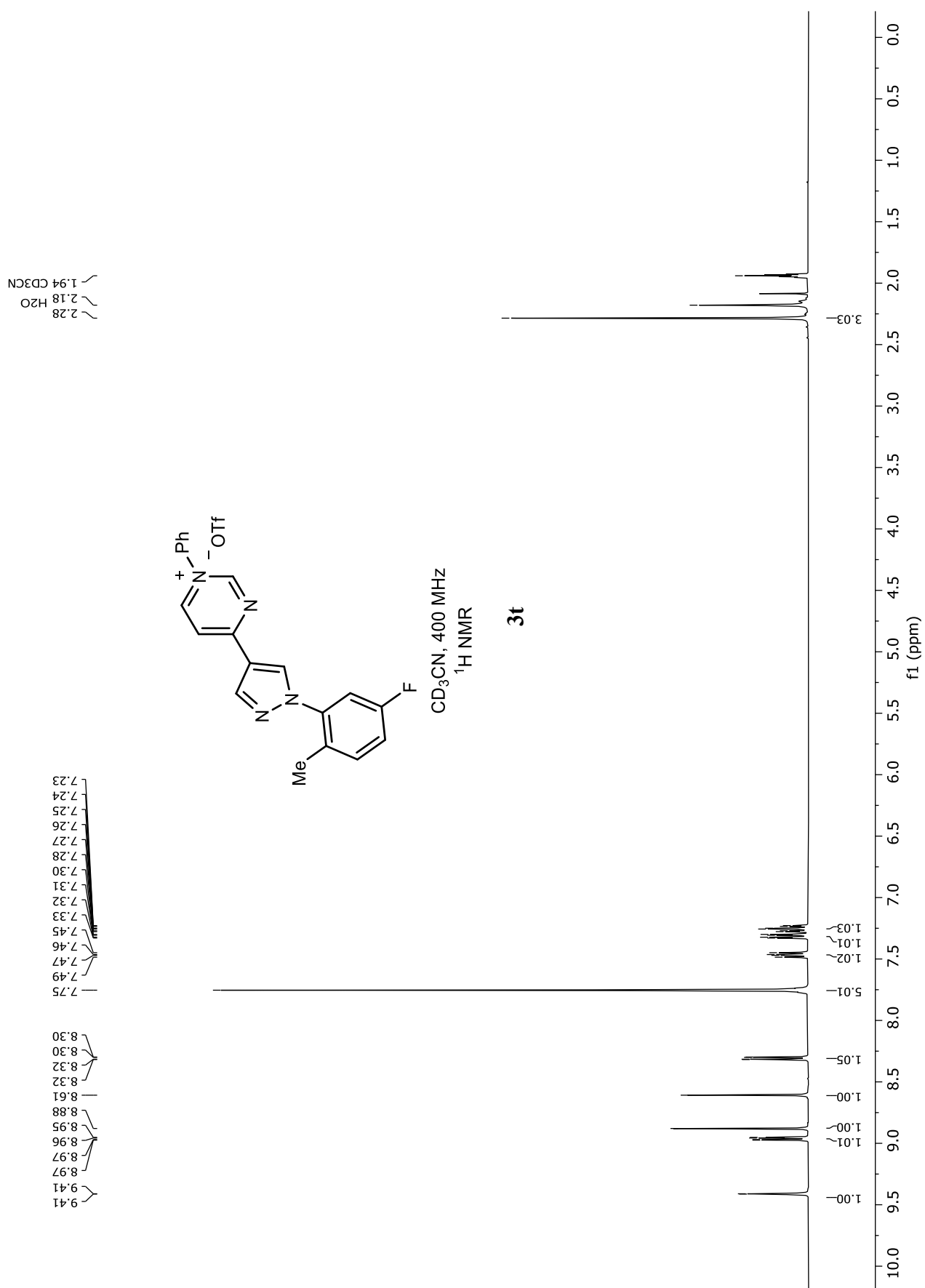
— -79.14

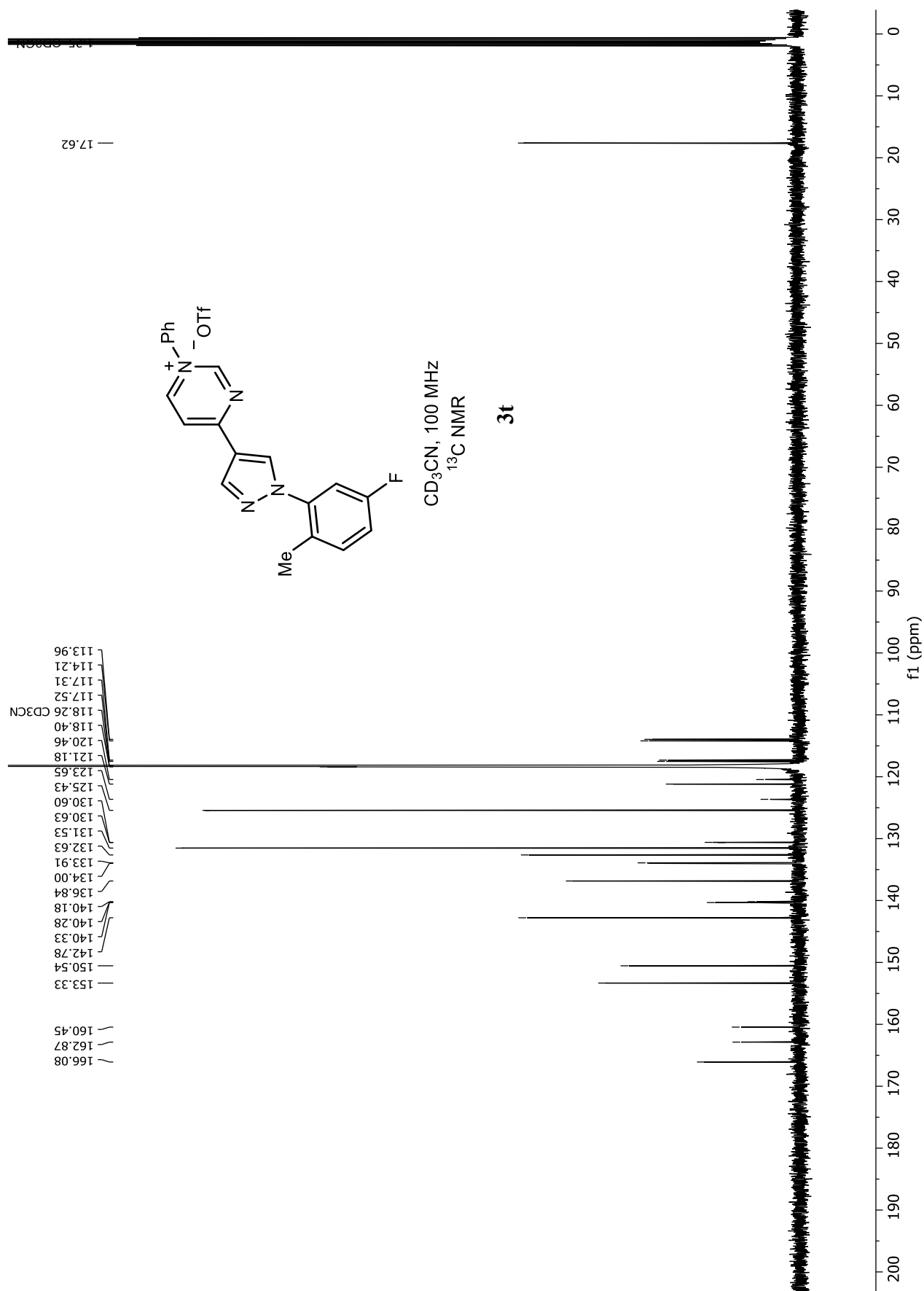


CD₃CN, 375 MHz
¹⁹F NMR

3s

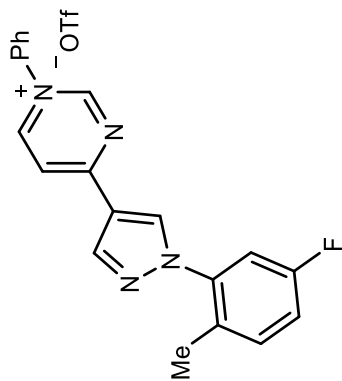






-117.13
-117.16
-117.17
-117.19

-79.31



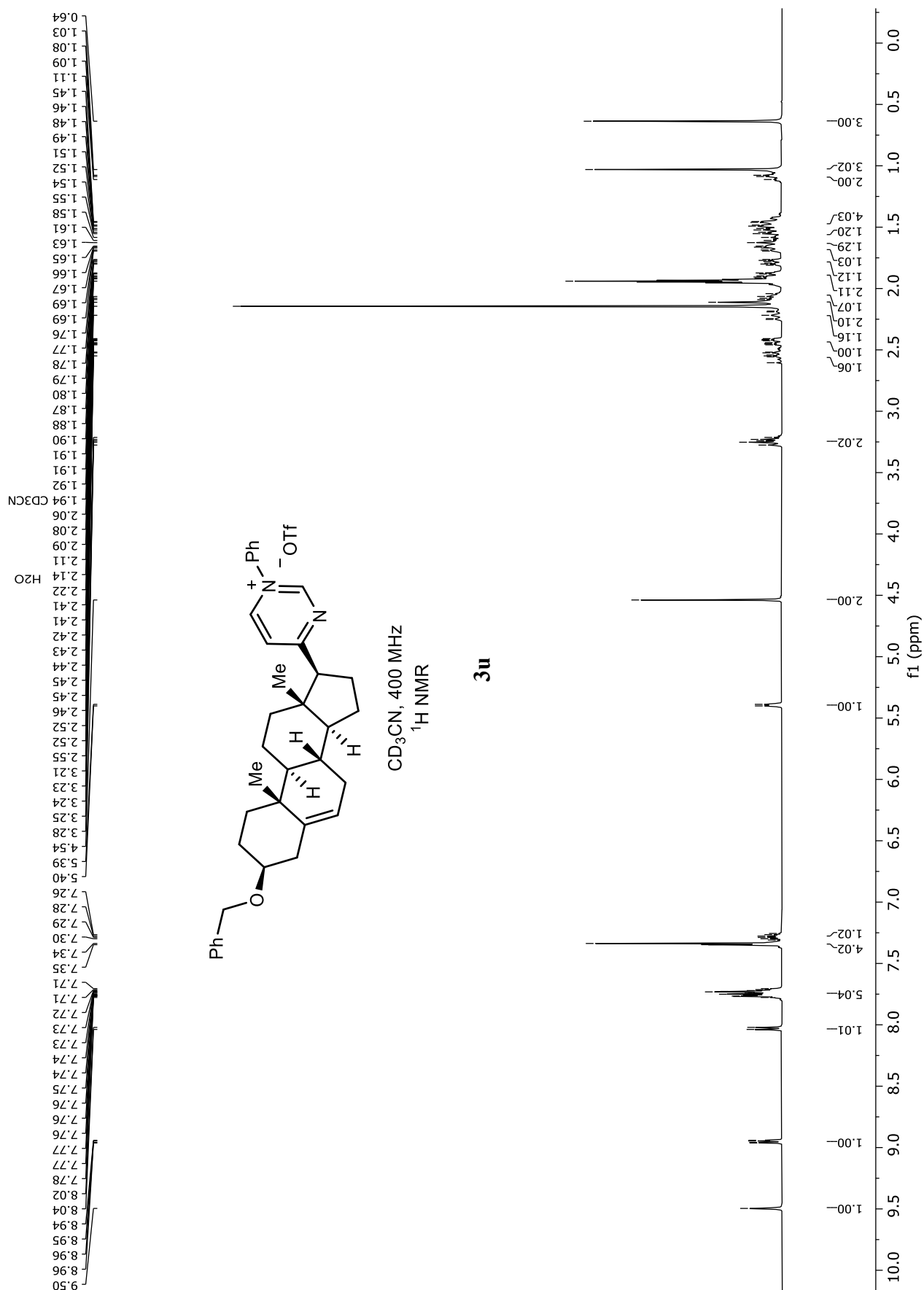
CD₃CN, 375 MHz
¹⁹F NMR

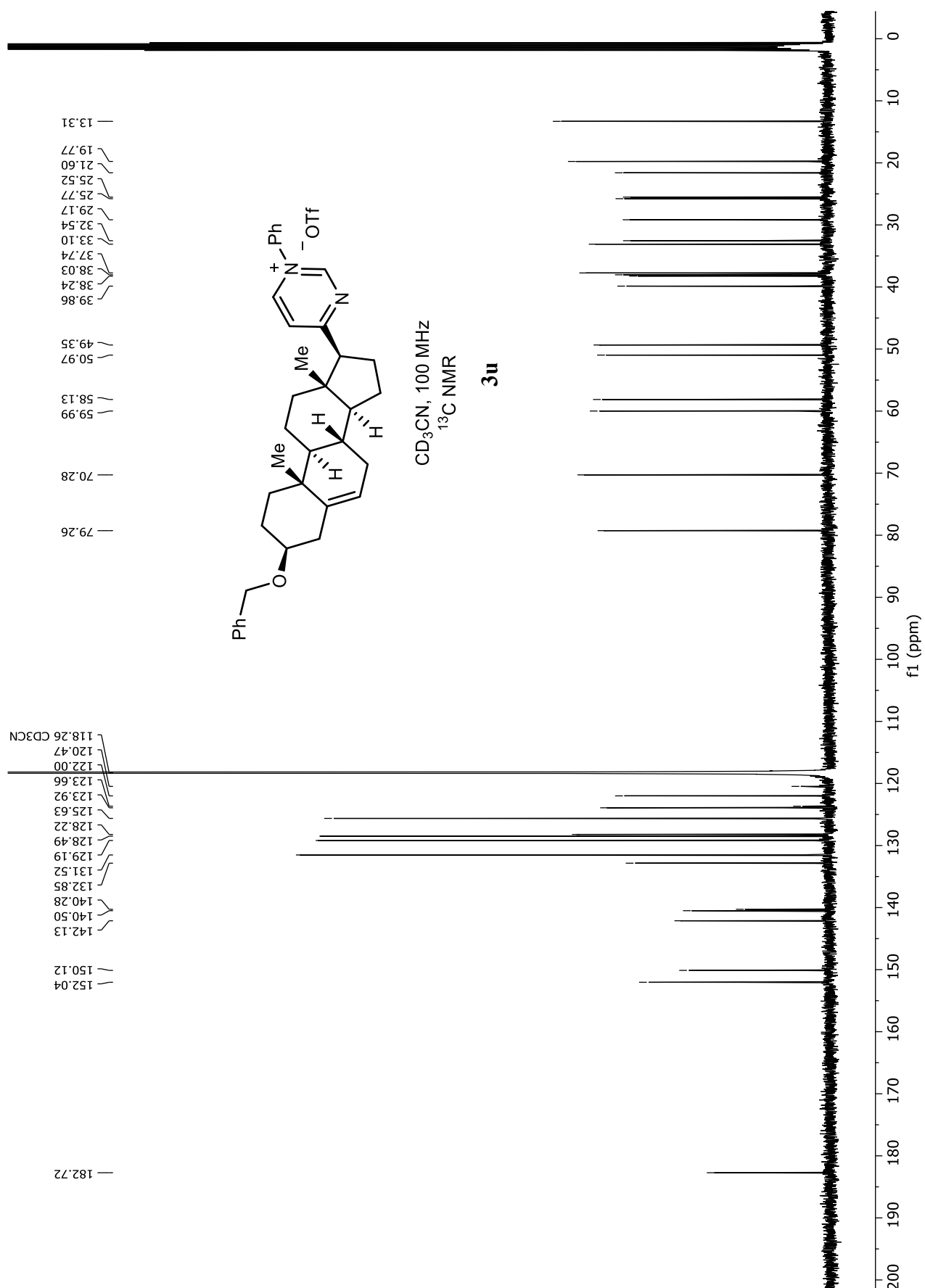
3t

1.09

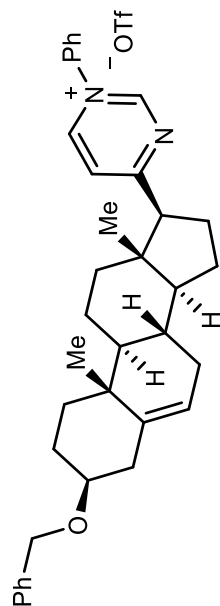
f1 (ppm)

3.00





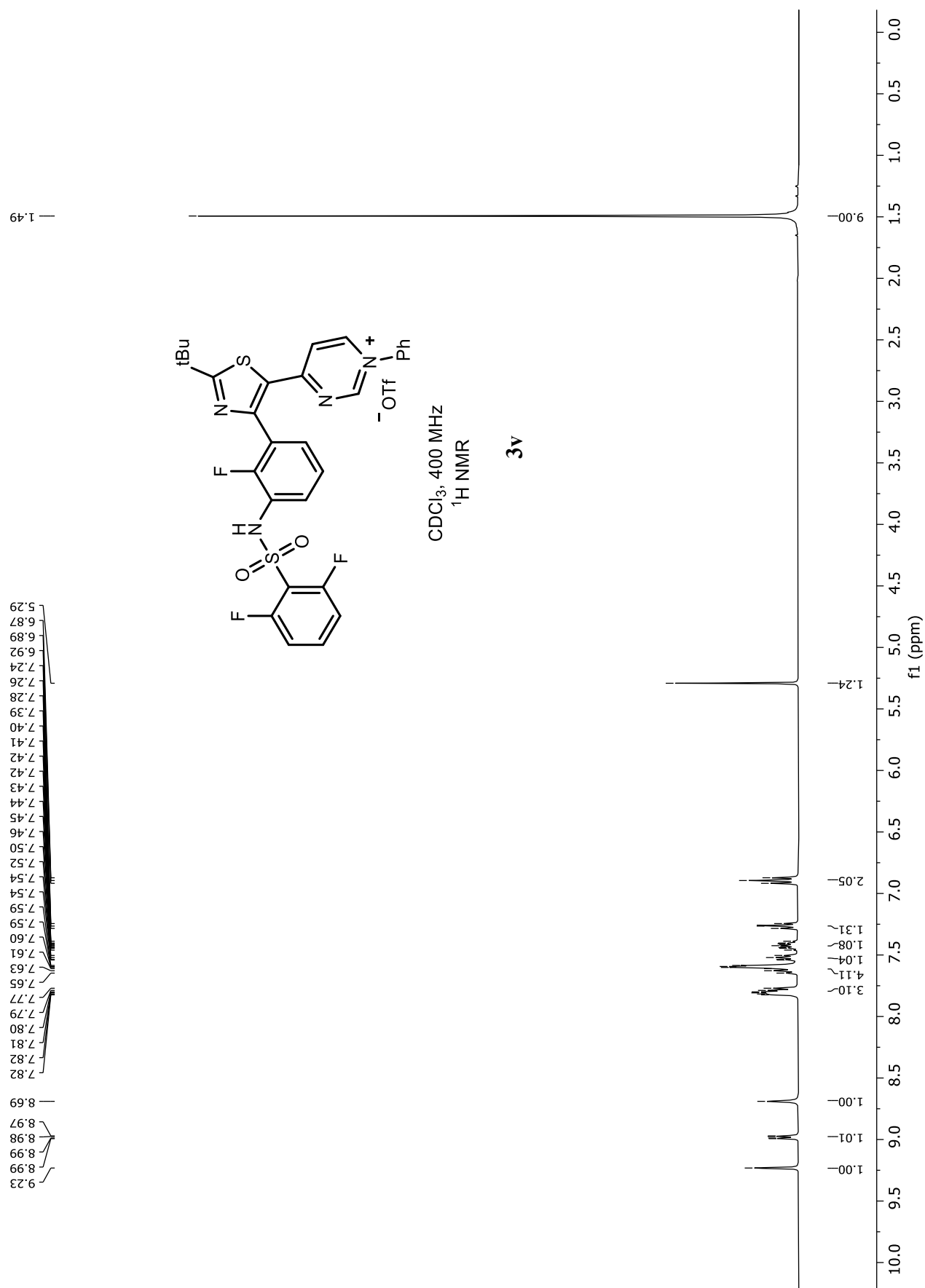
— -79.33

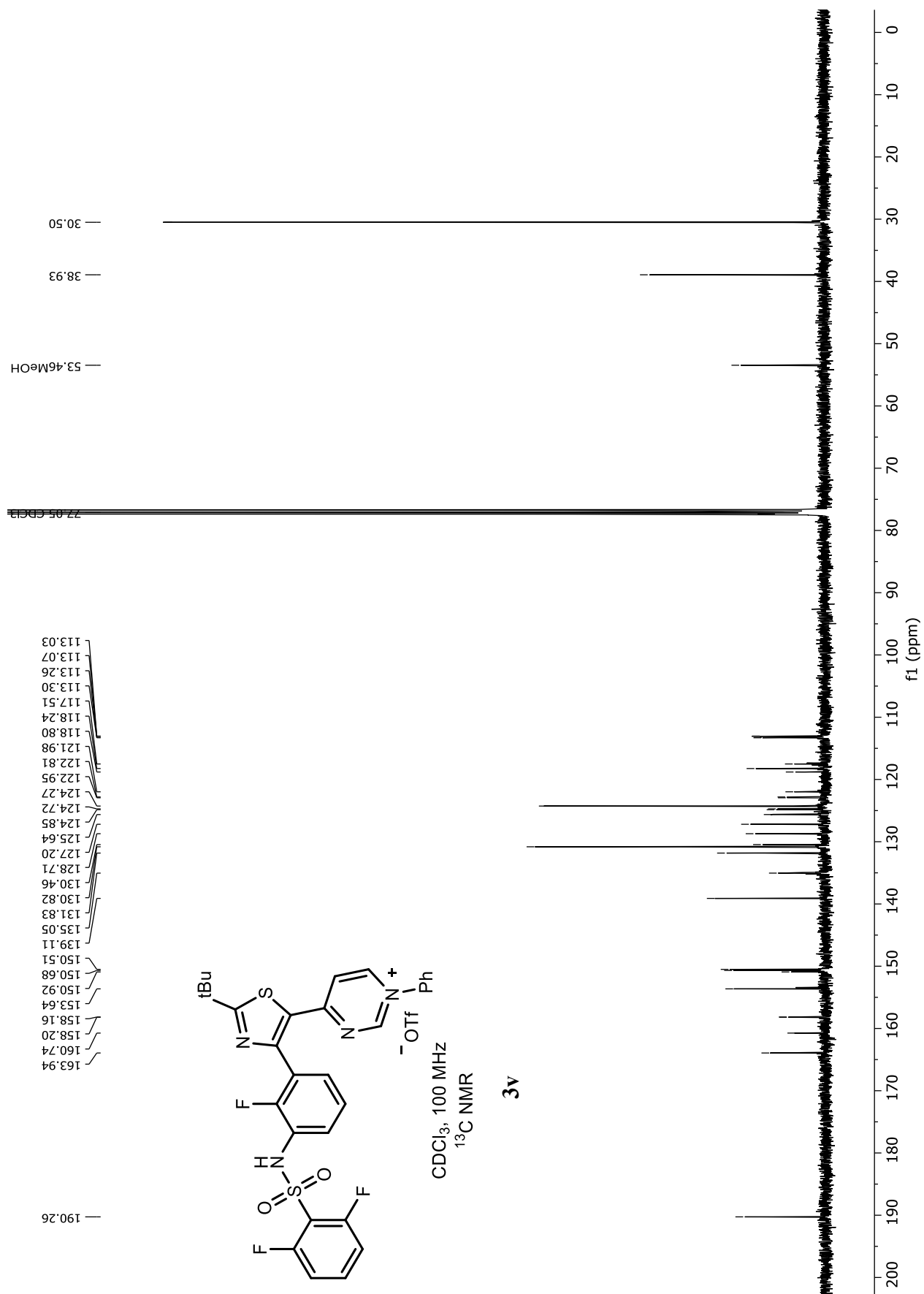


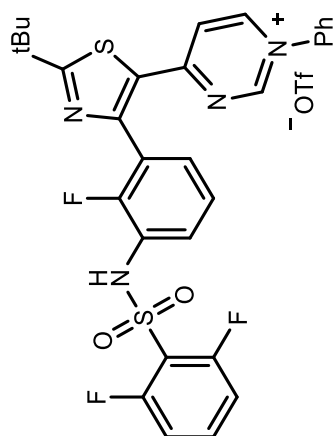
CD₃CN, 375 MHz
¹⁹F NMR

3u

f1 (ppm)





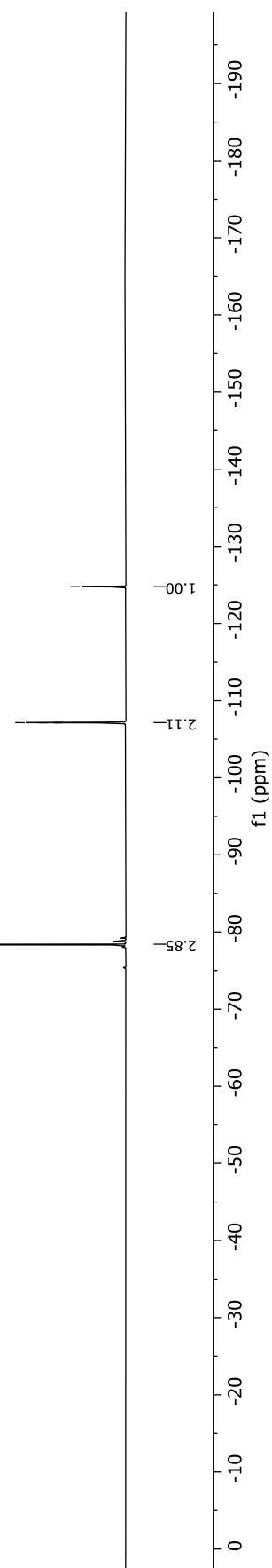


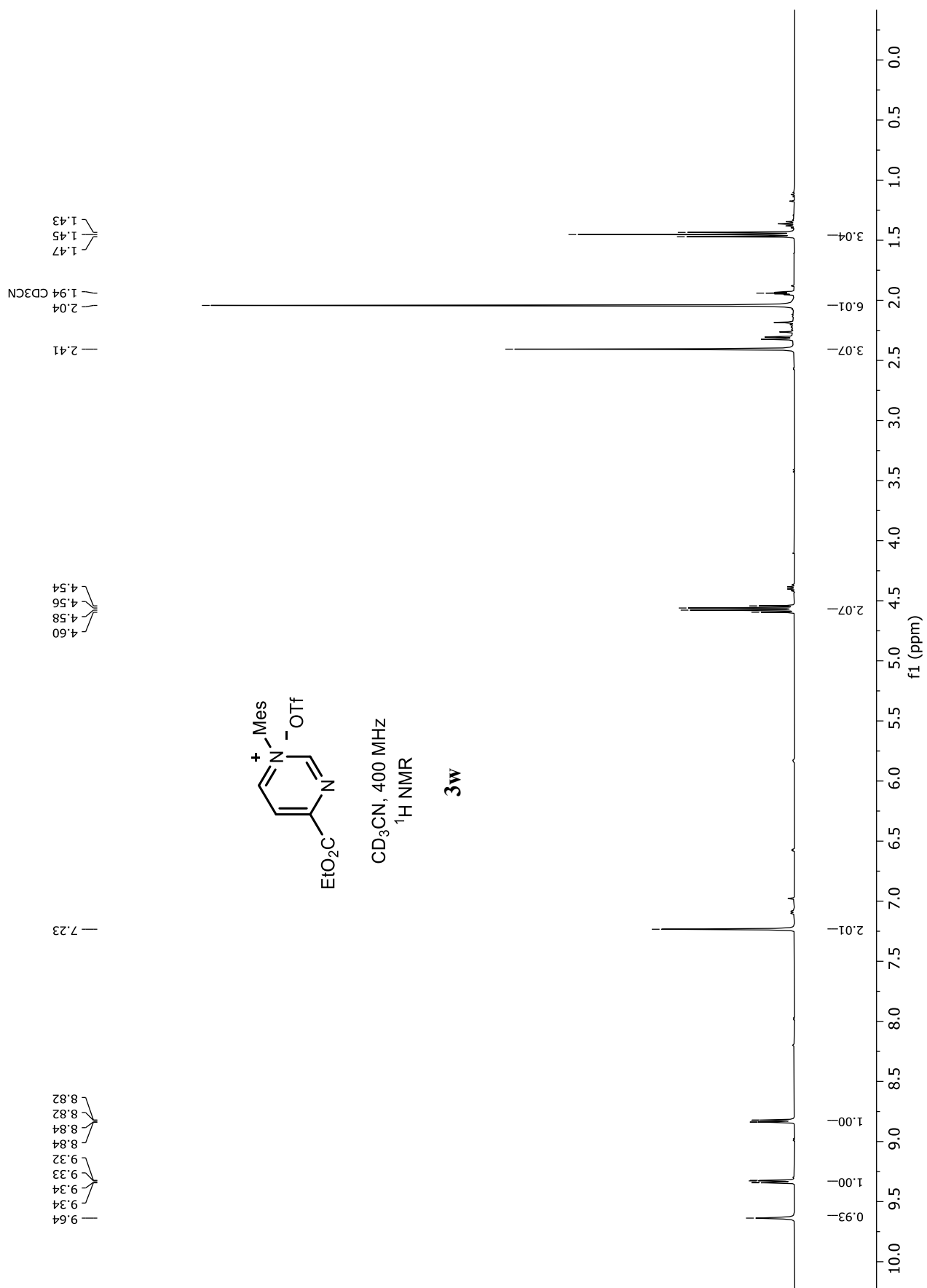
CDCl₃, 375 MHz
¹⁹F NMR

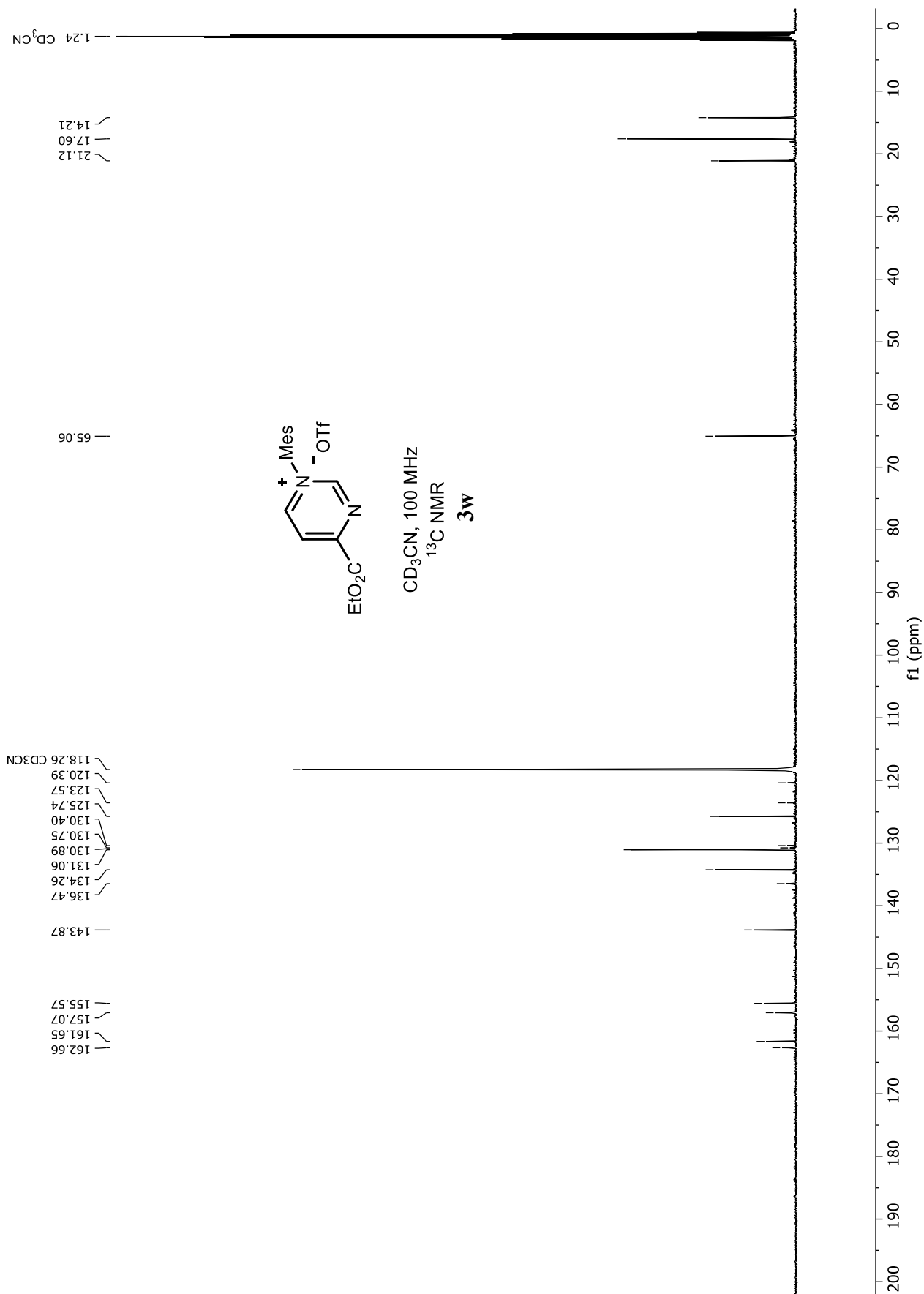
3v

— -124.76
 — -107.16
 — -107.14
 — -107.12
 — -107.11

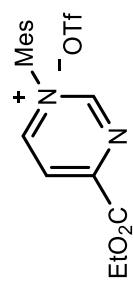
— -78.33





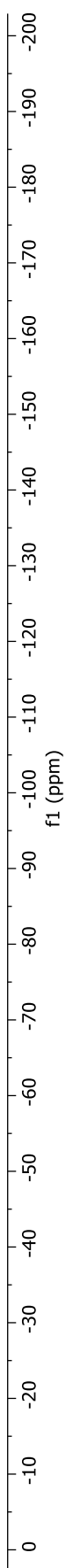


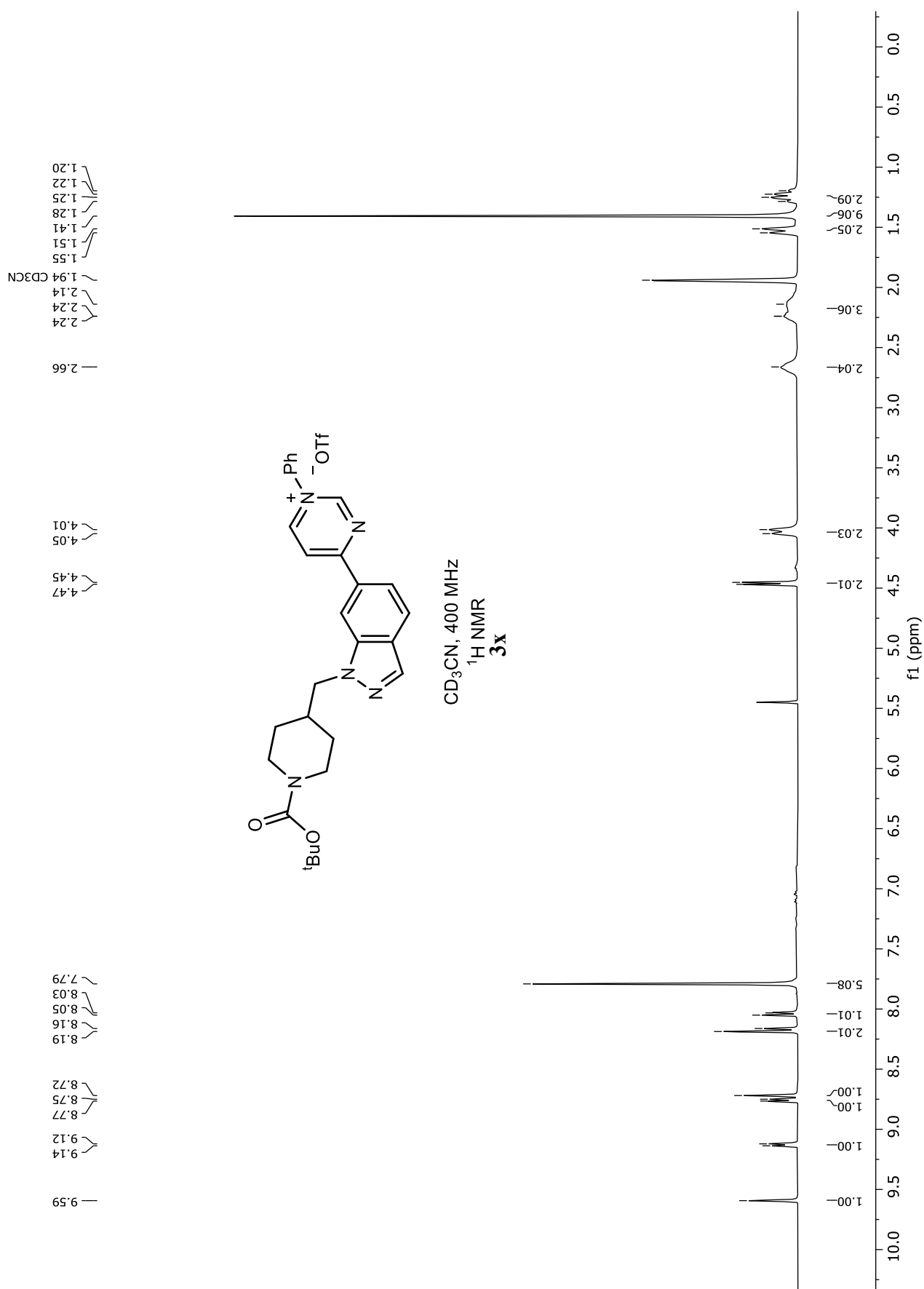
— -79.31

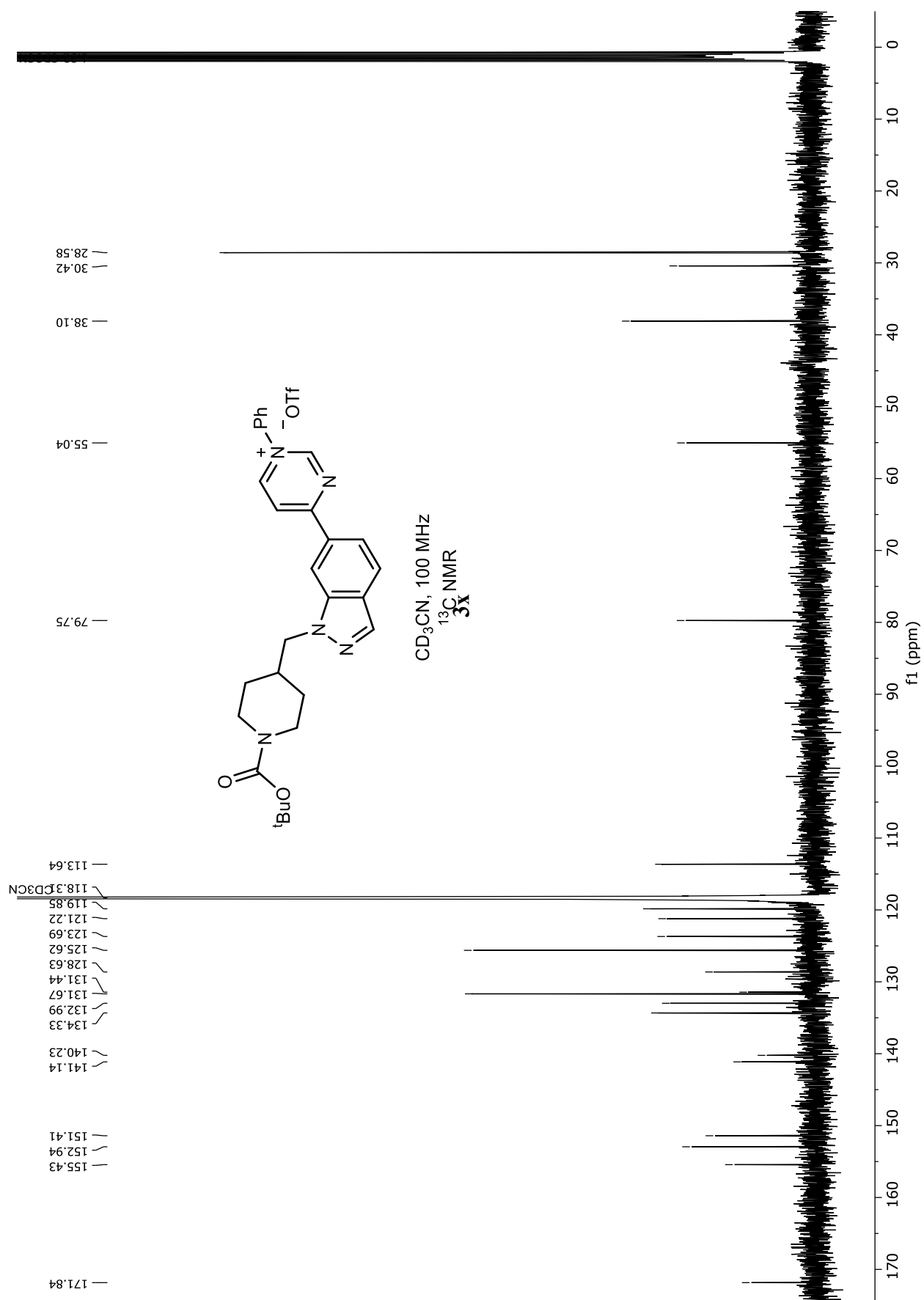


CD₃CN, 375 MHz
¹⁹F NMR

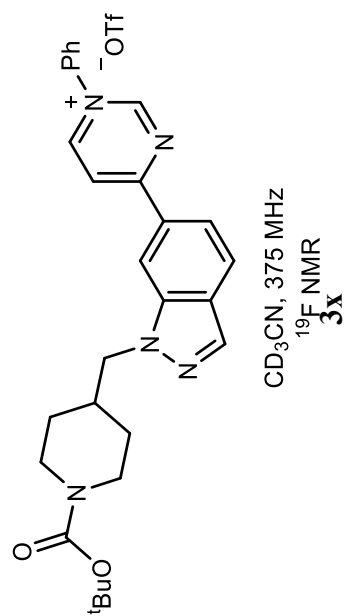
3w





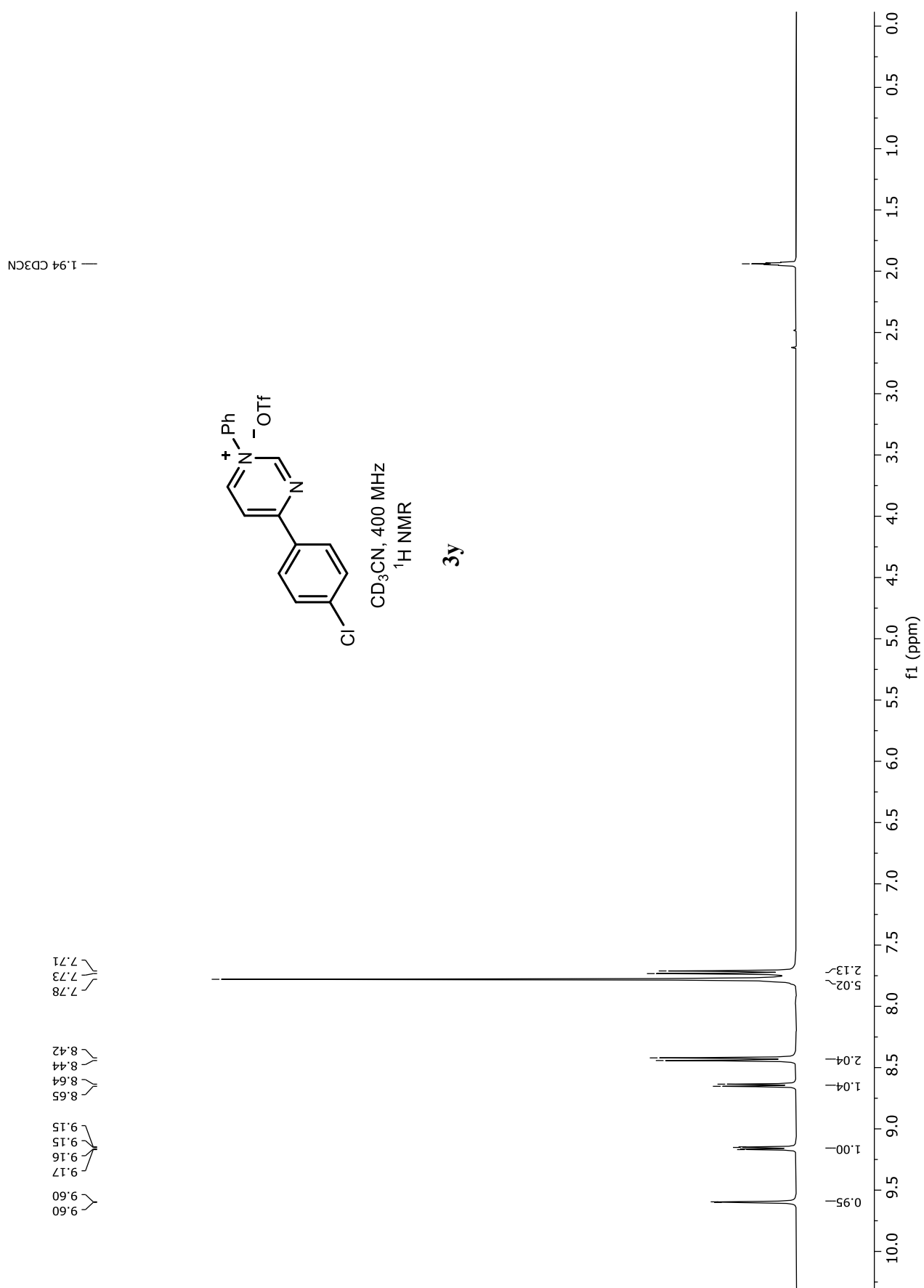


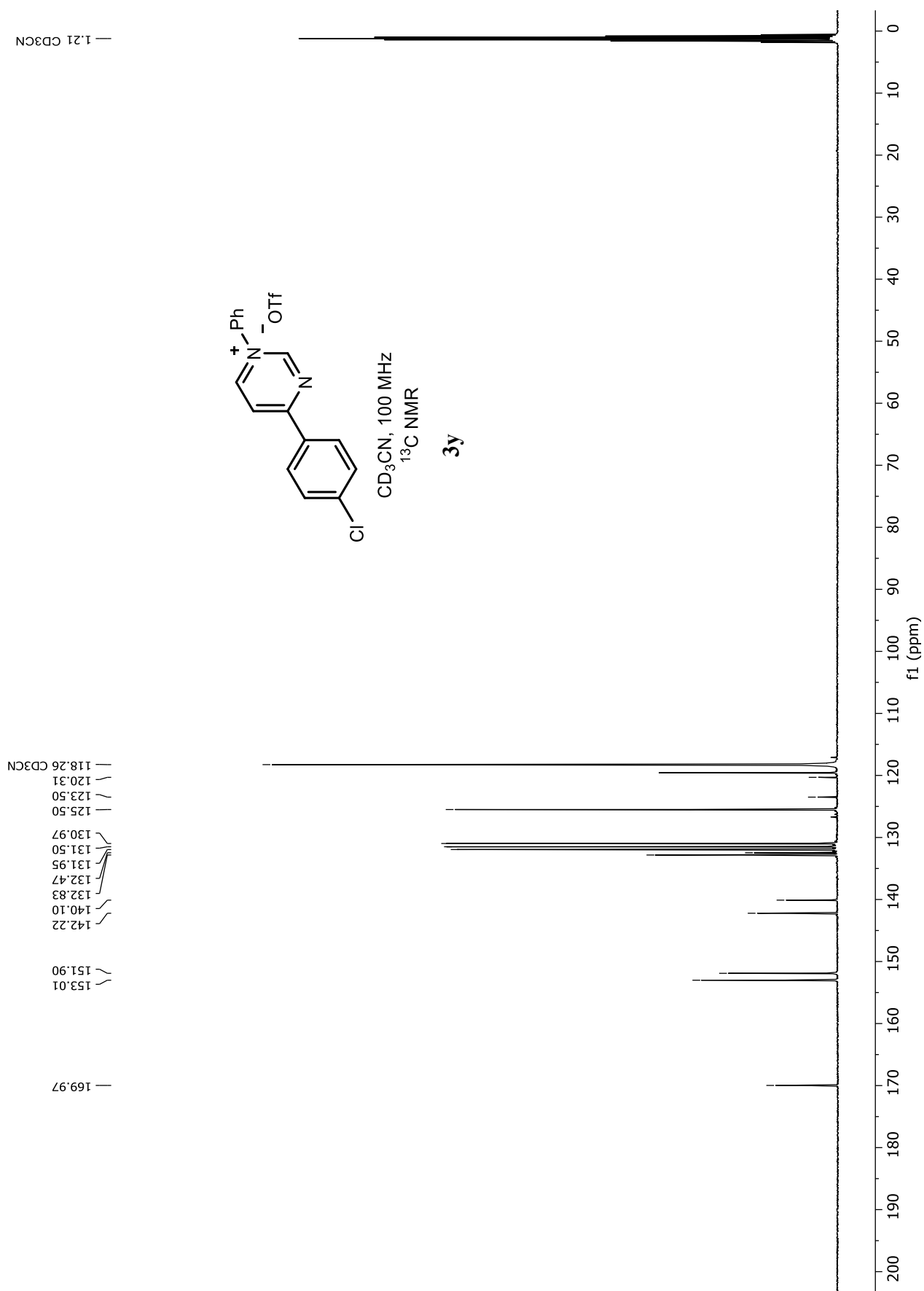
~ -80.61
~ -79.31



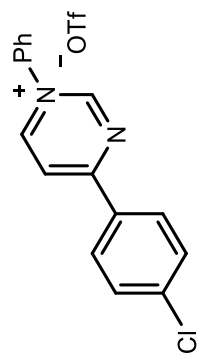
2.27
0.72

f1 (ppm)



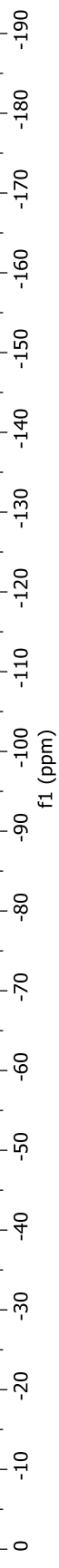


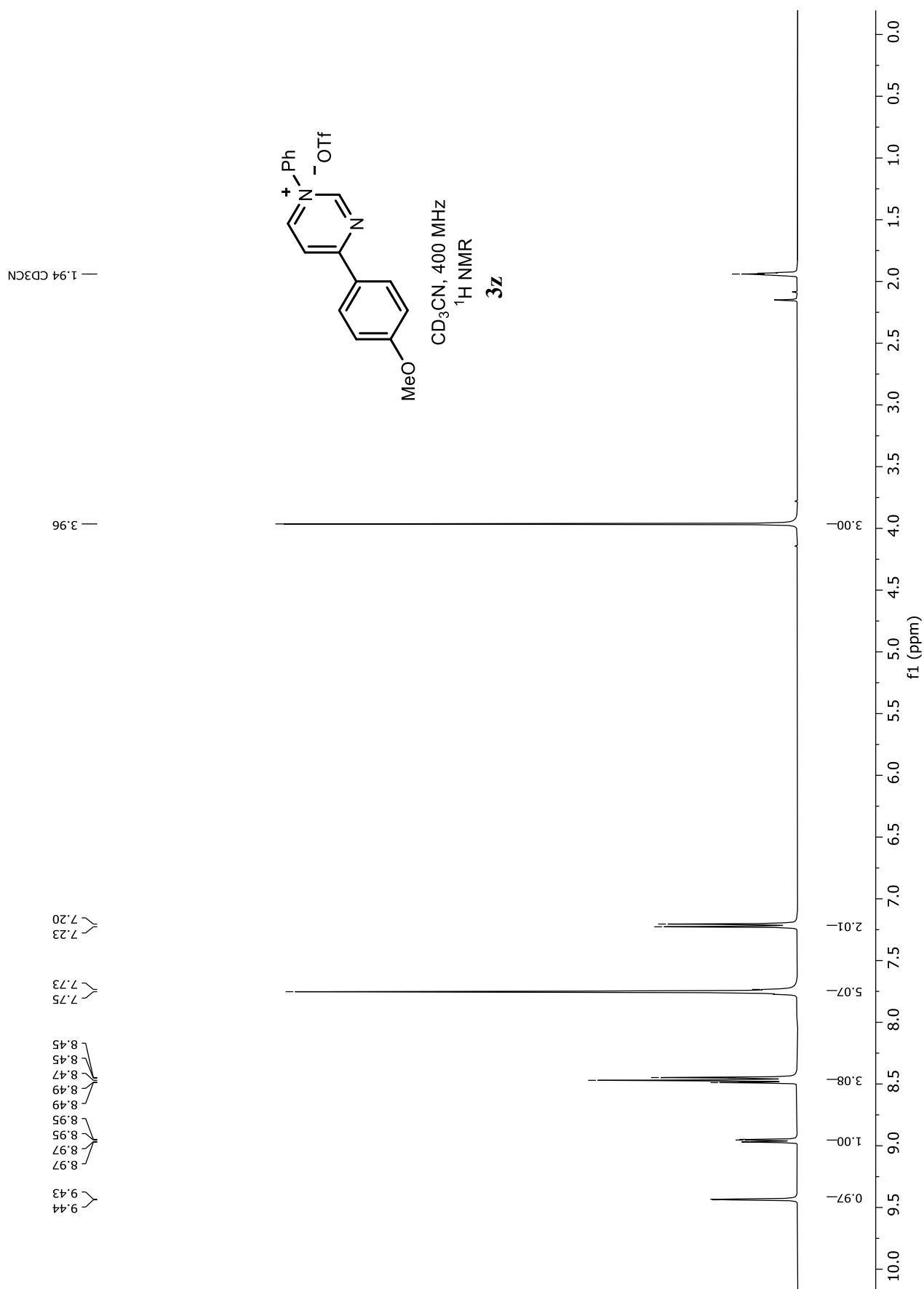
— -79.14

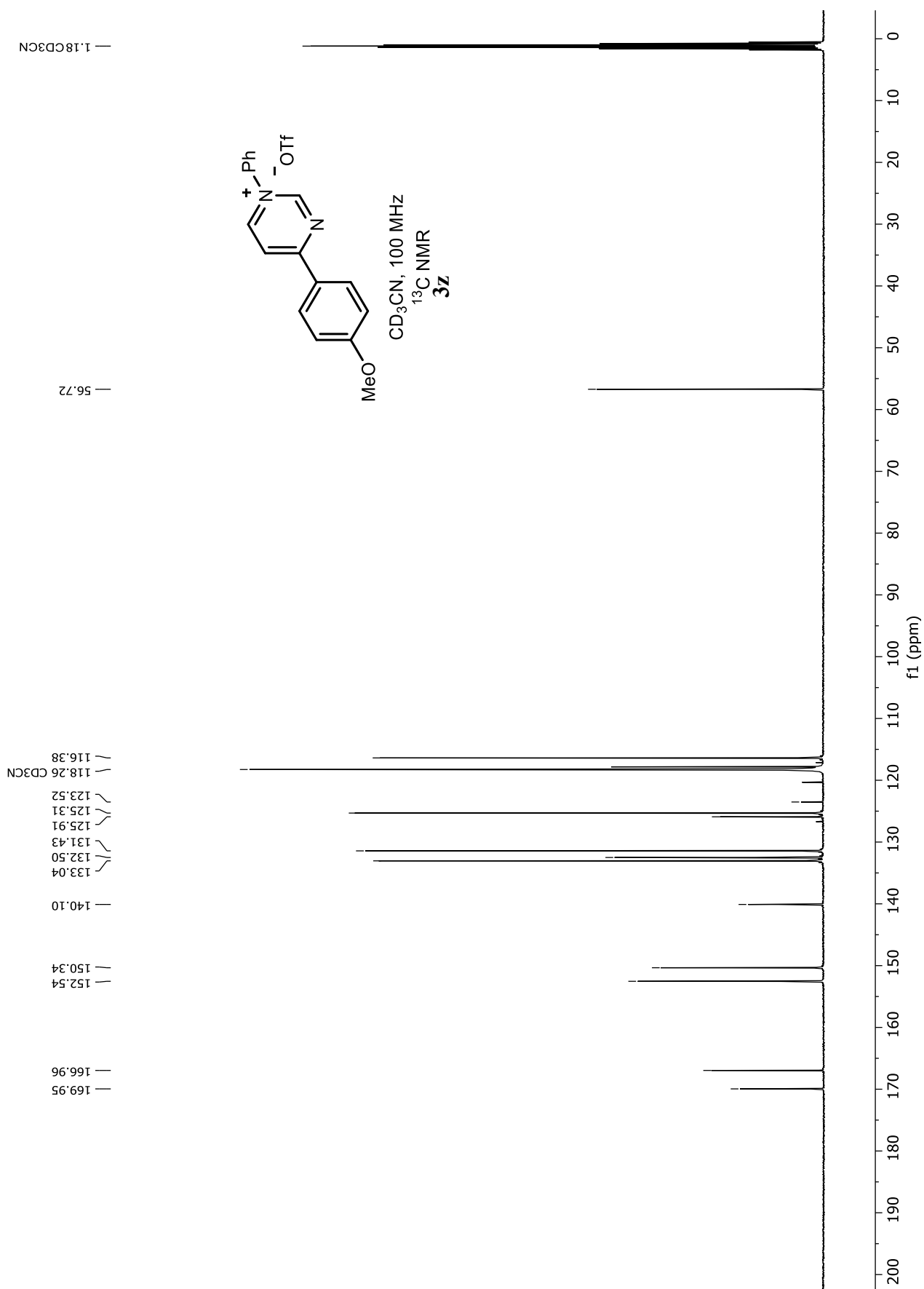


CD₃CN, 375 MHz
¹⁹F NMR

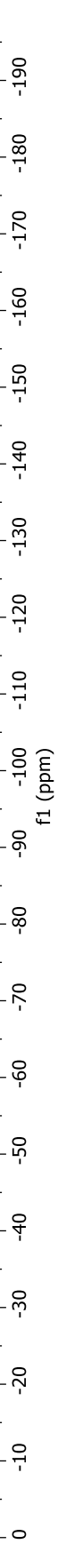
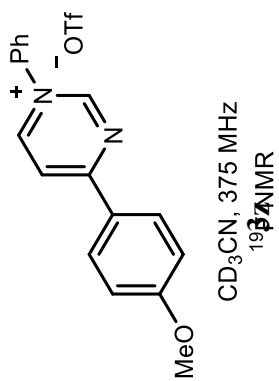
3y

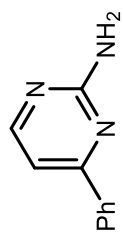






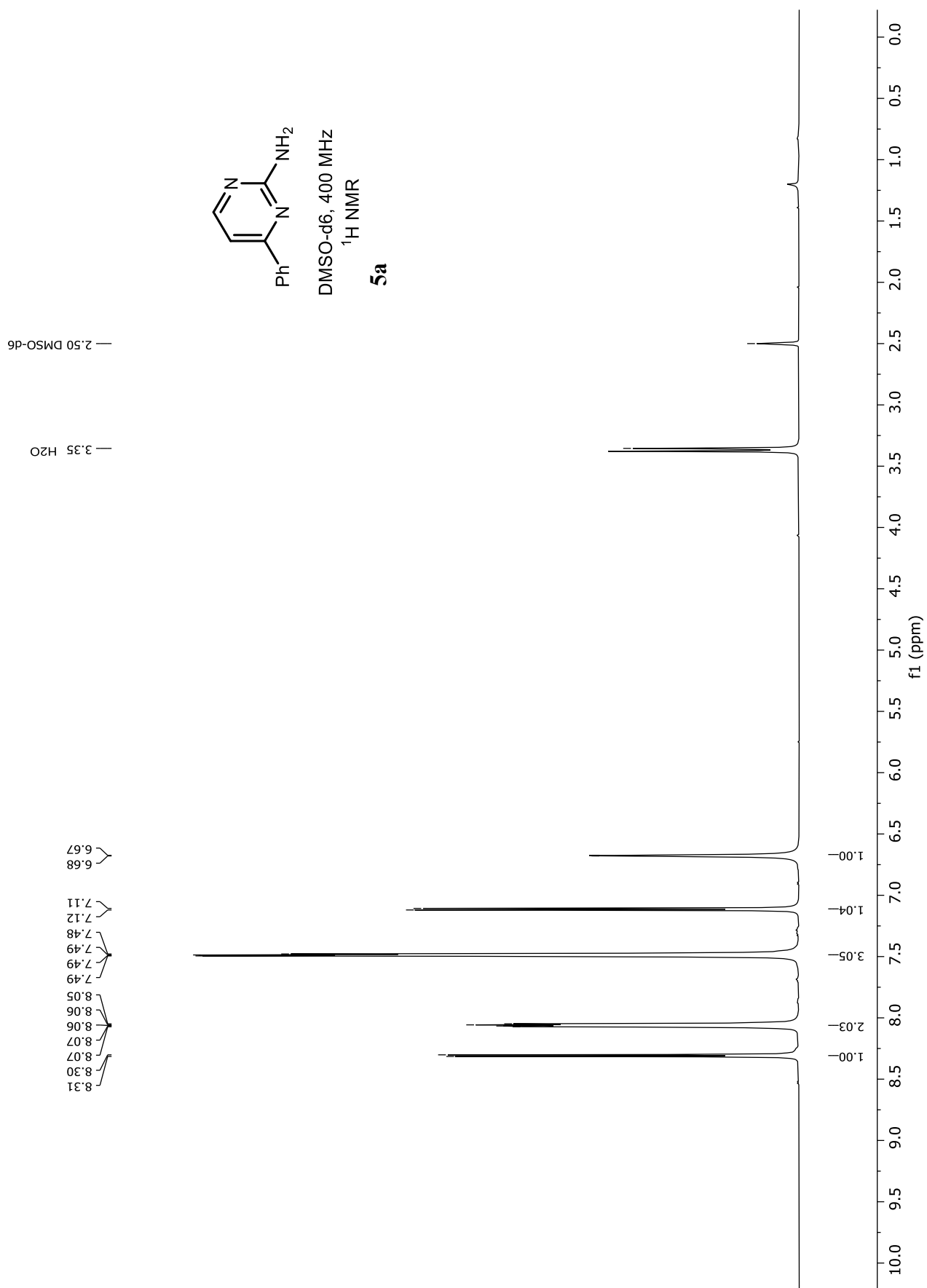
— -79.11

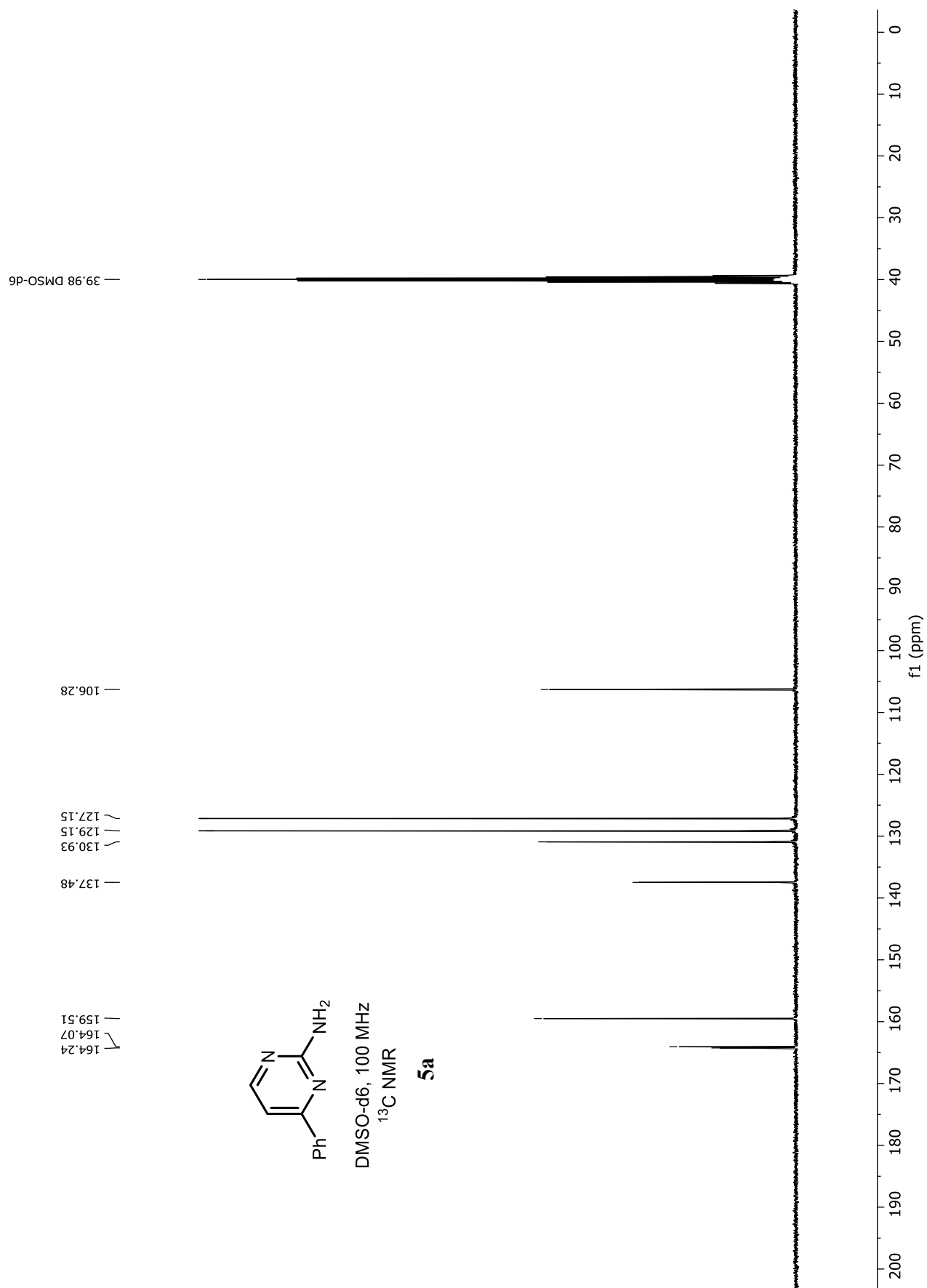


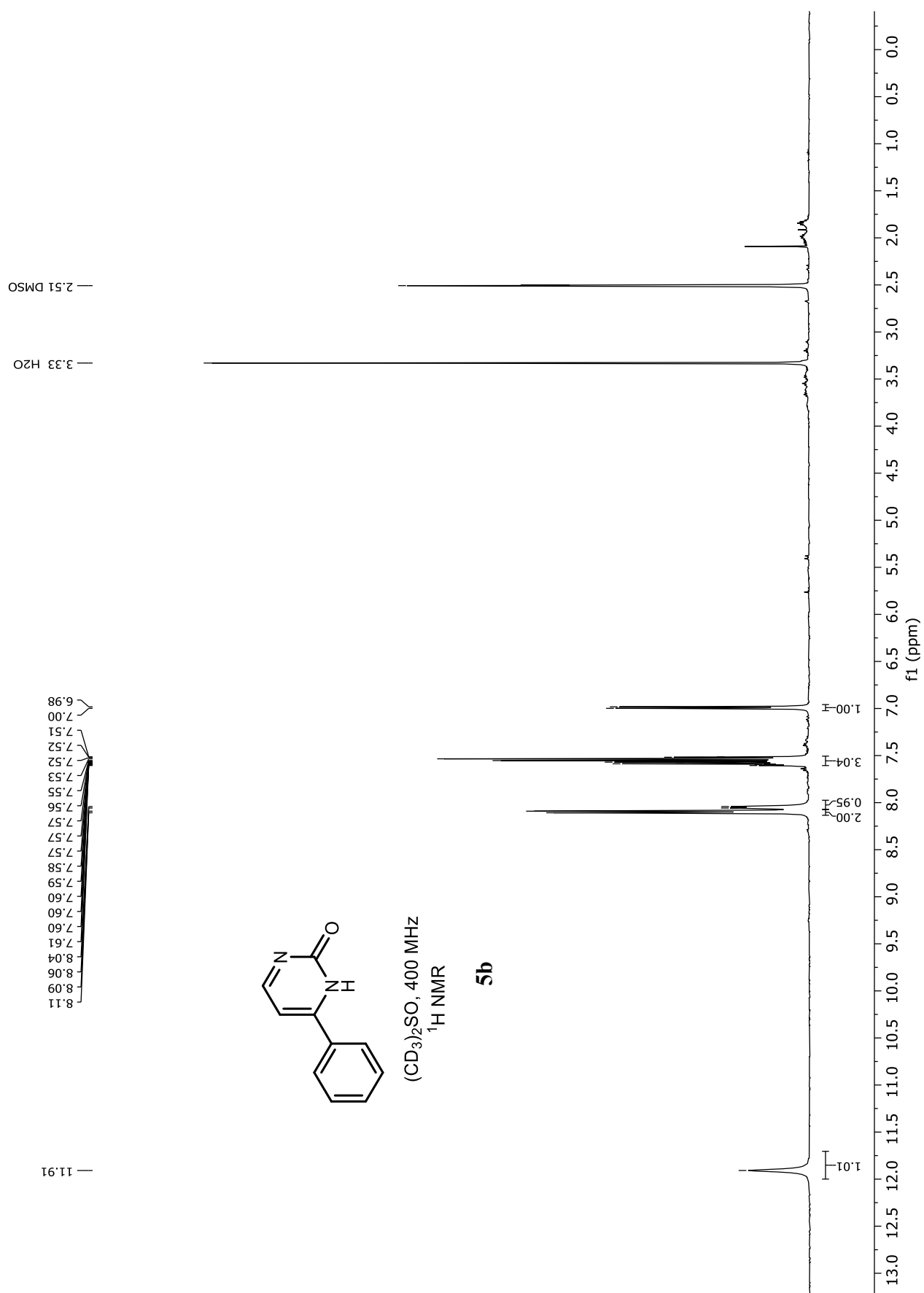


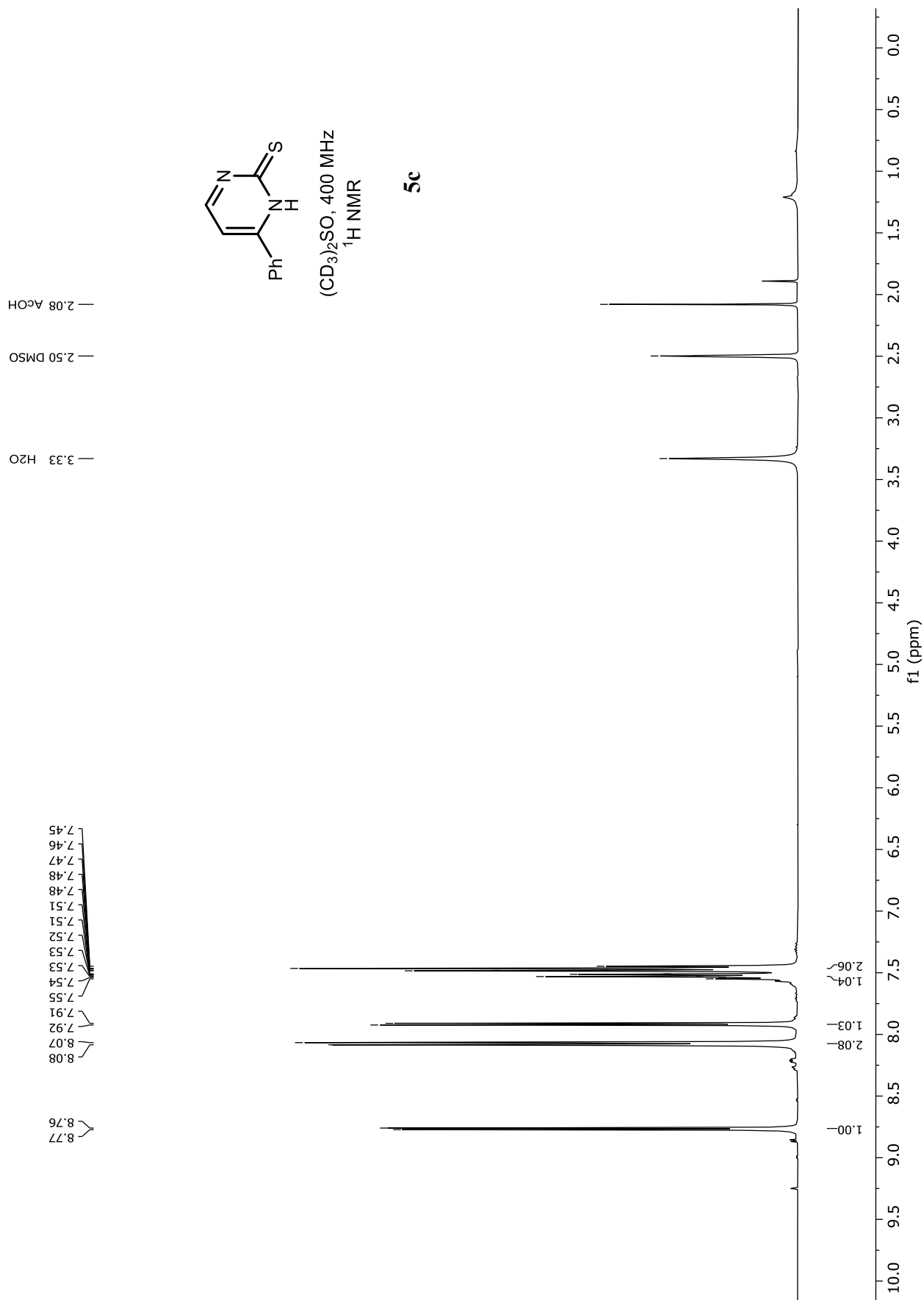
DMSO-d₆, 400 MHz
¹H NMR

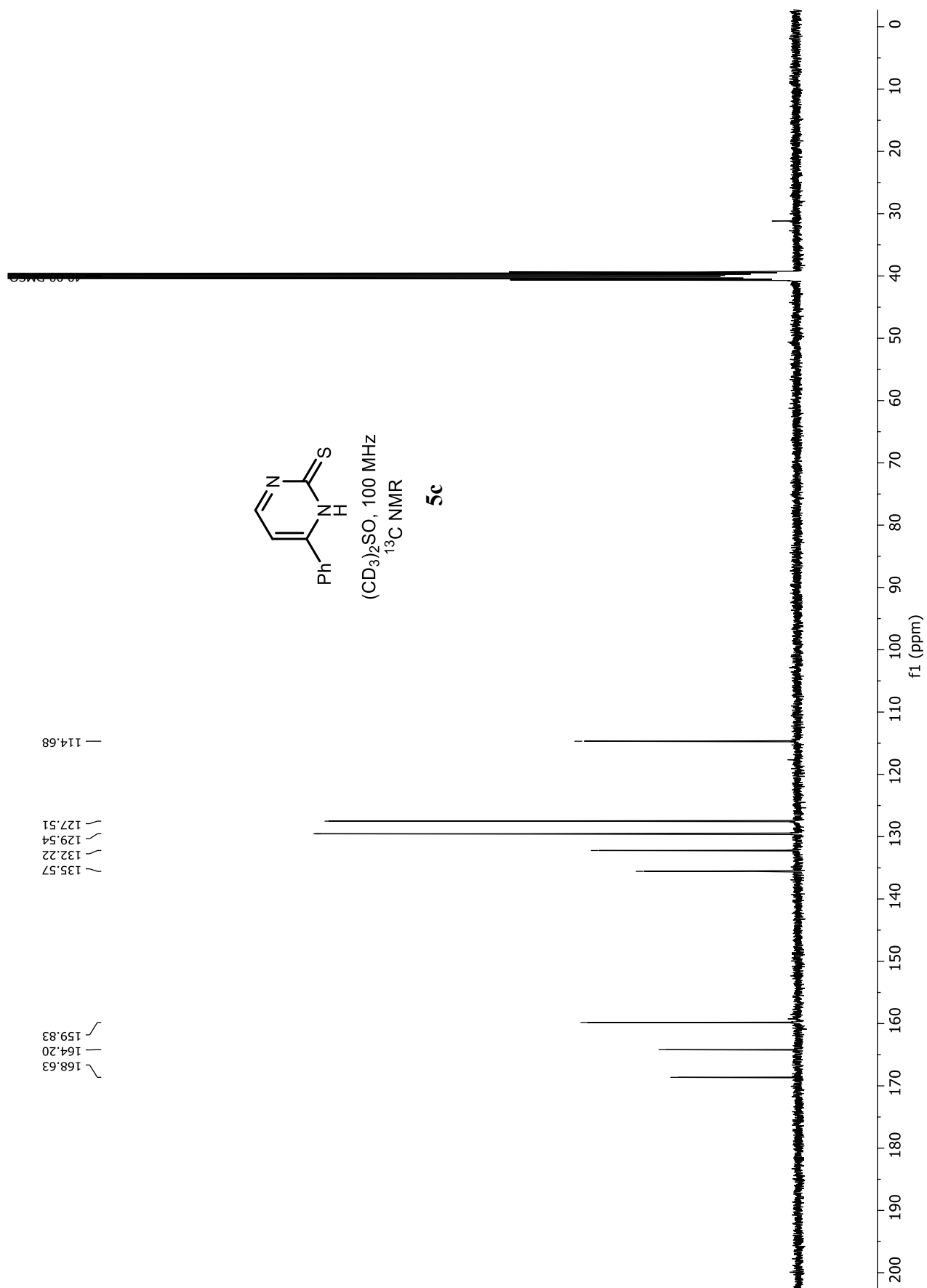
5a

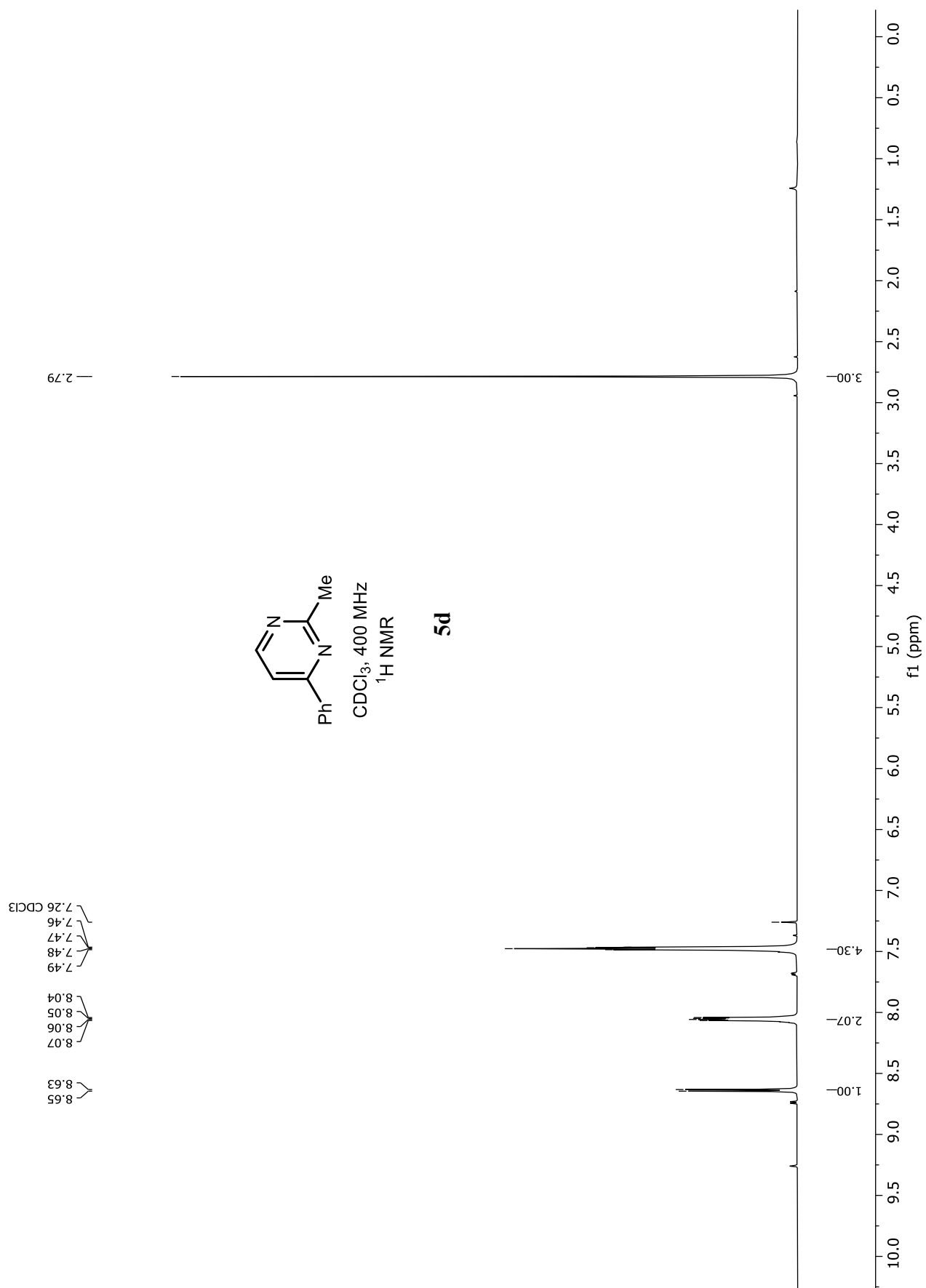


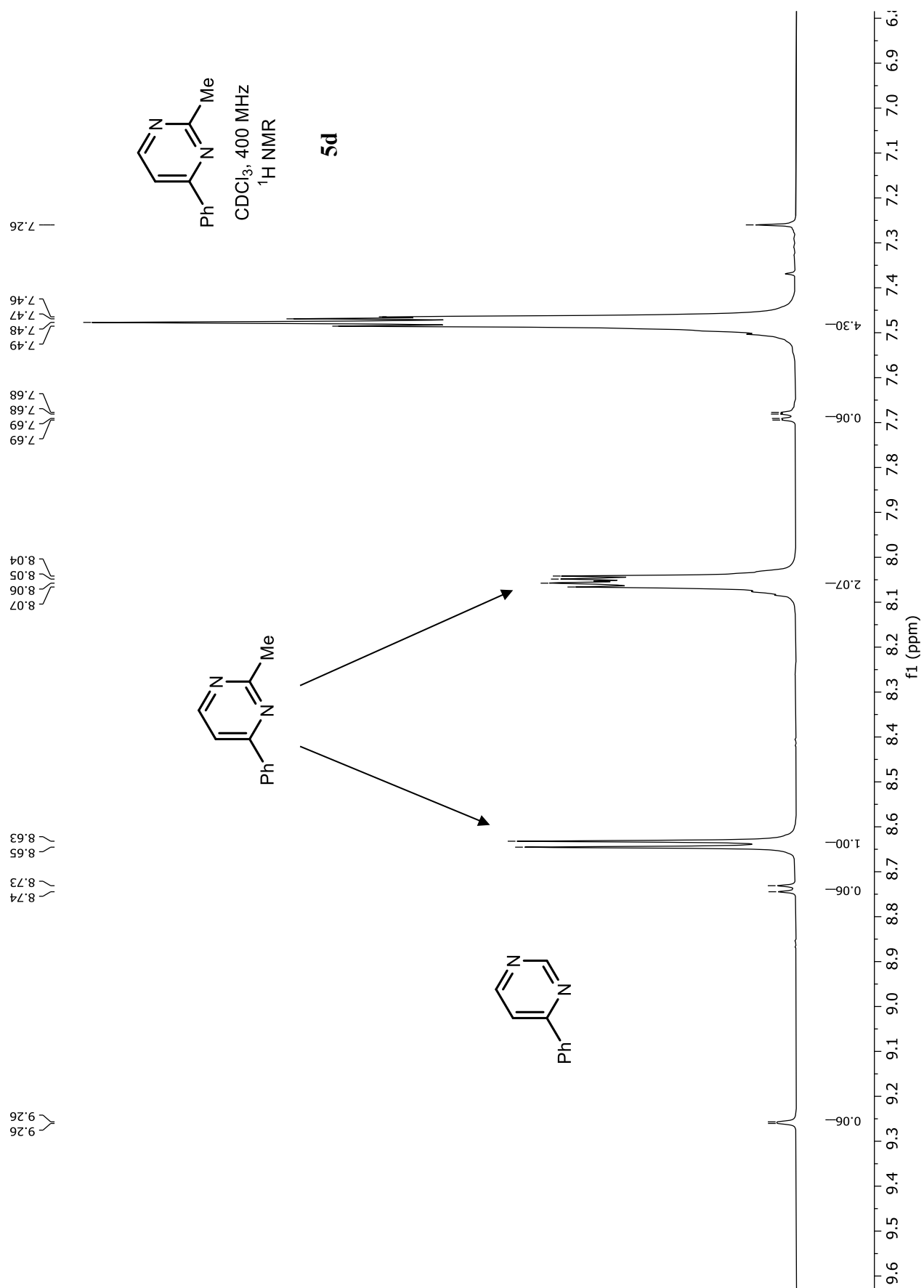


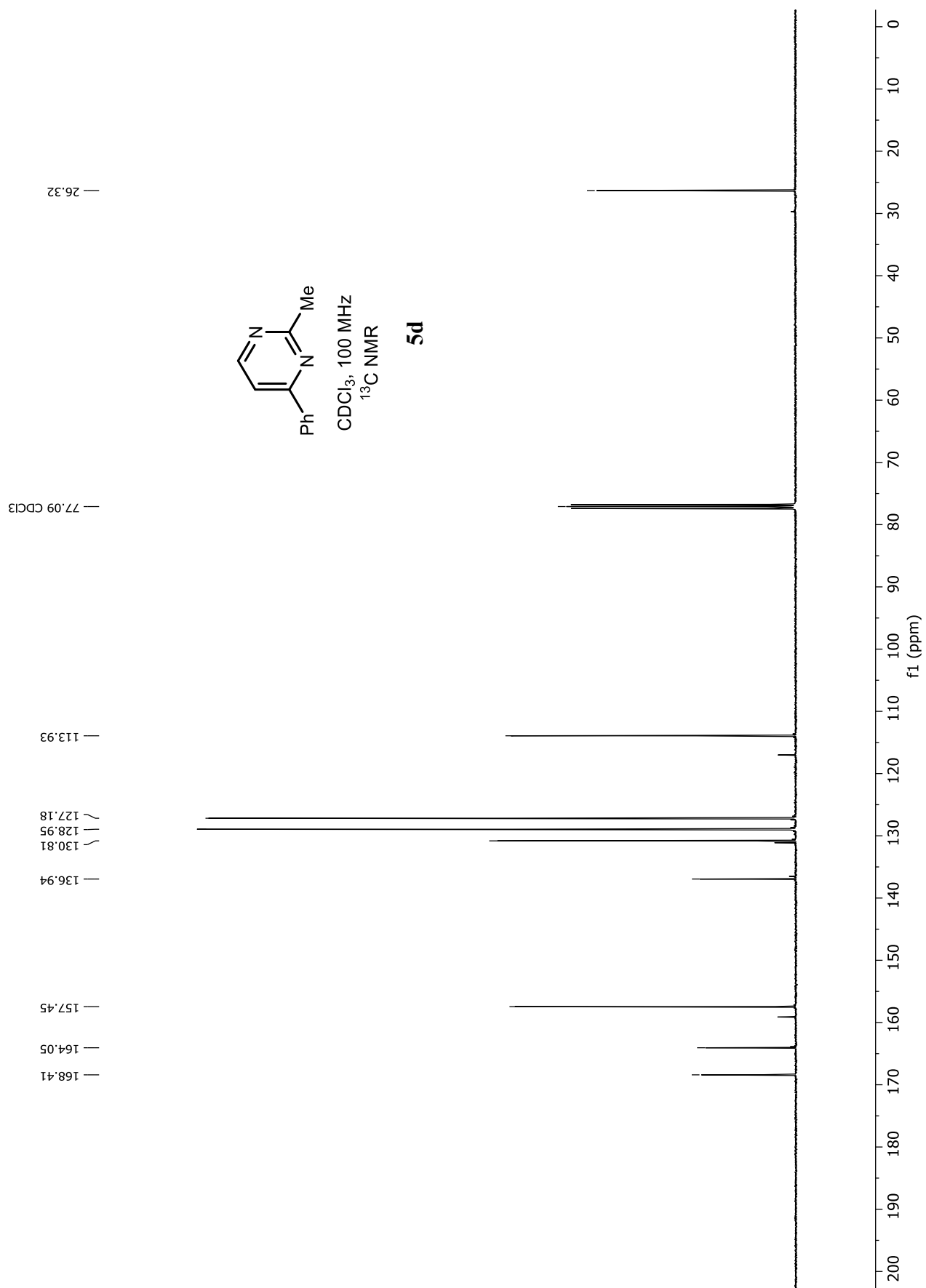


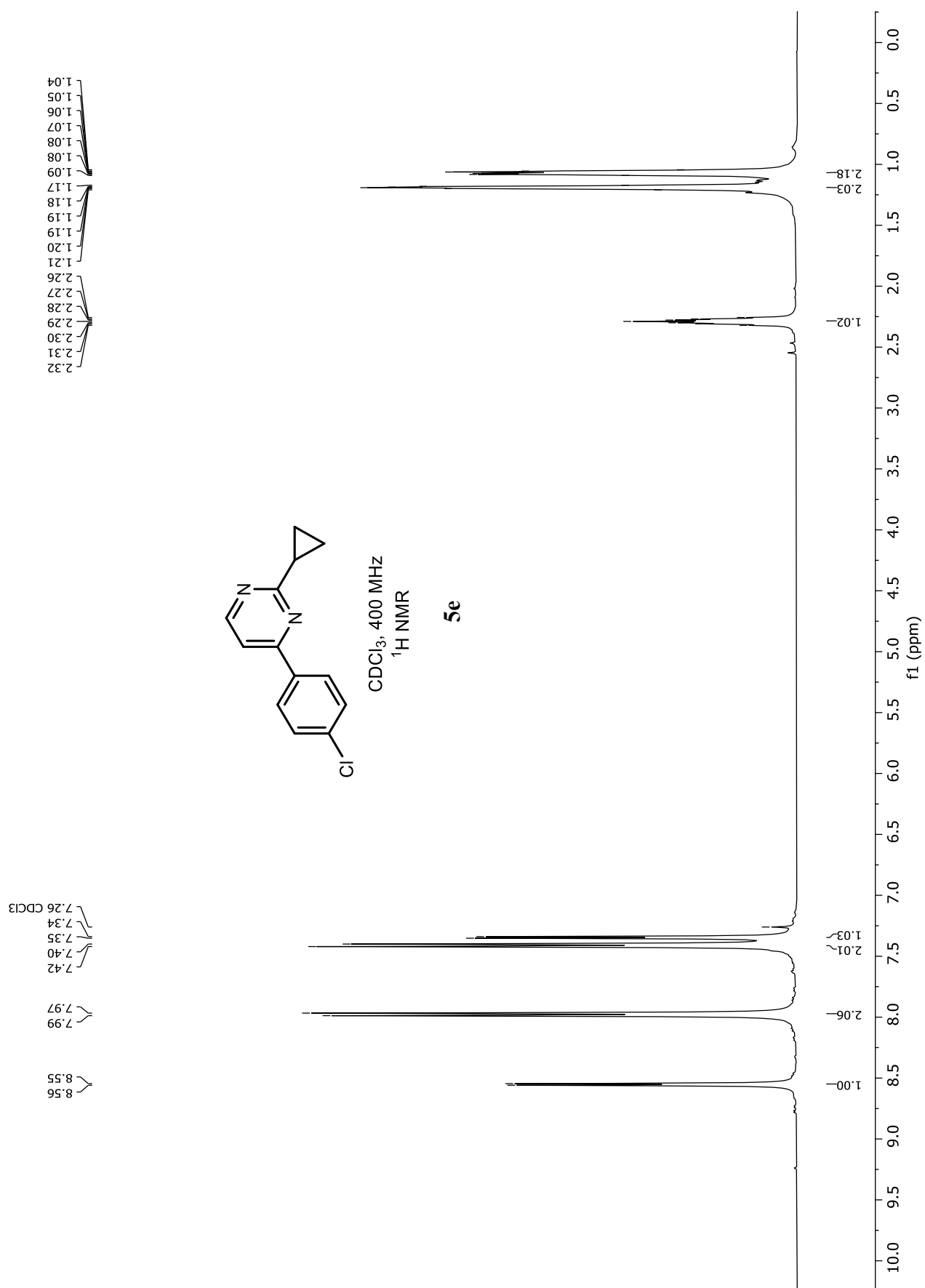




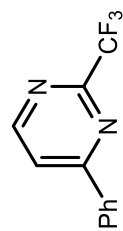






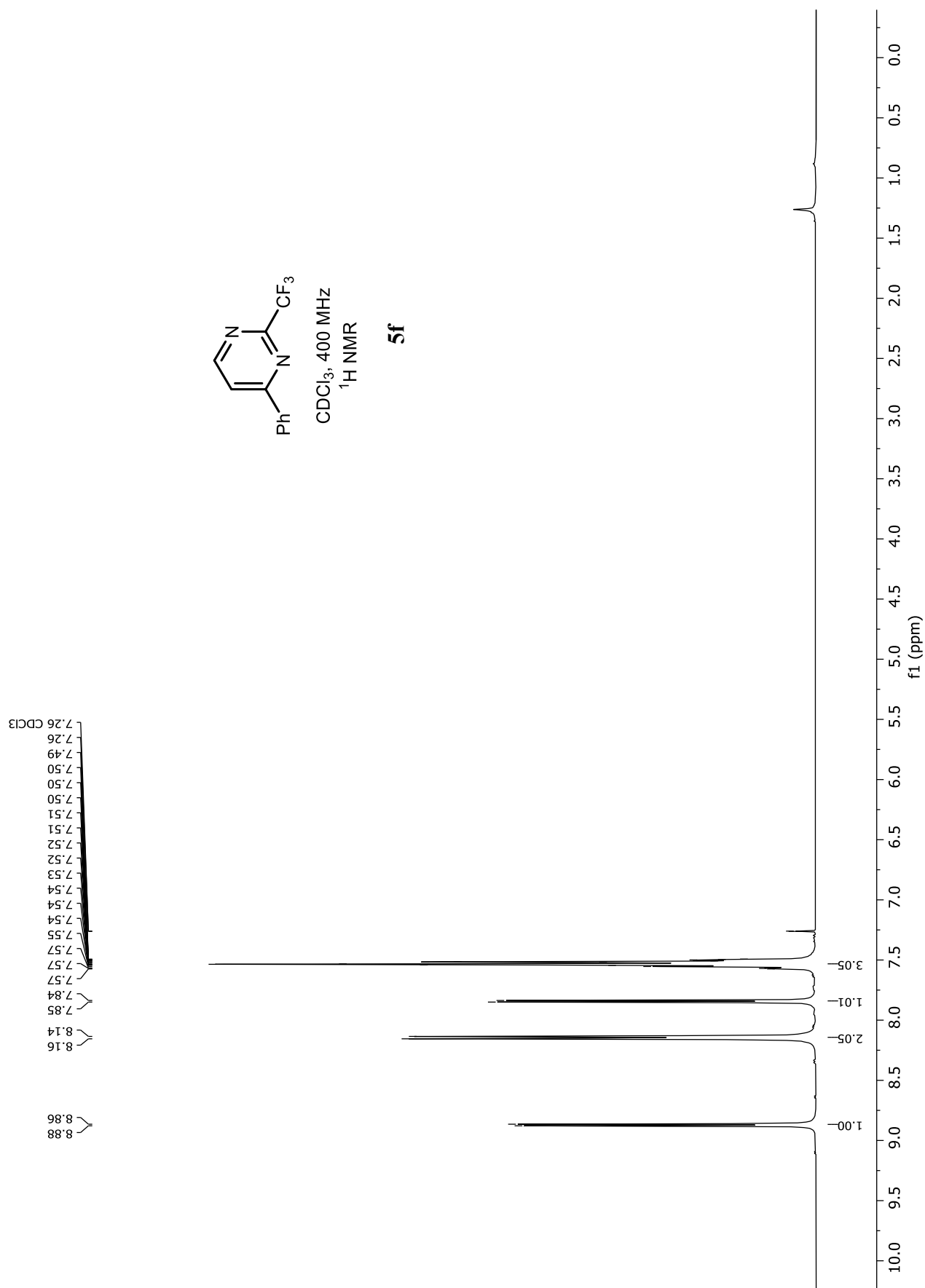


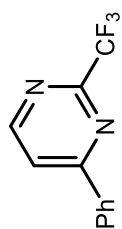




CDCl₃, 400 MHz
¹H NMR

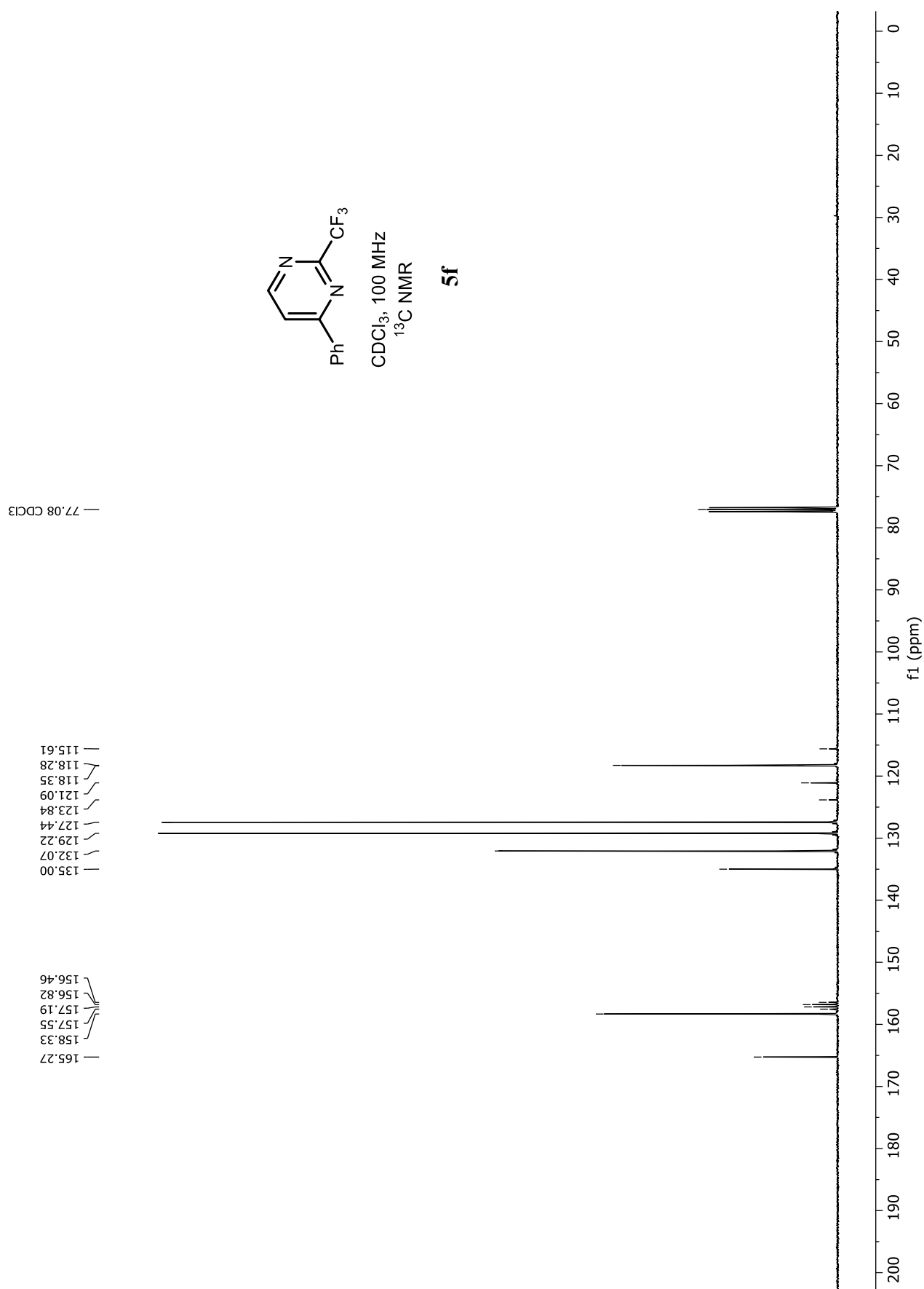
5f

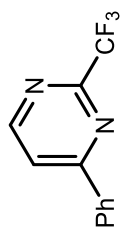




CDCl₃, 100 MHz
¹³C NMR

5f

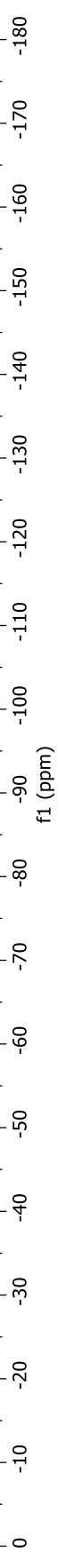




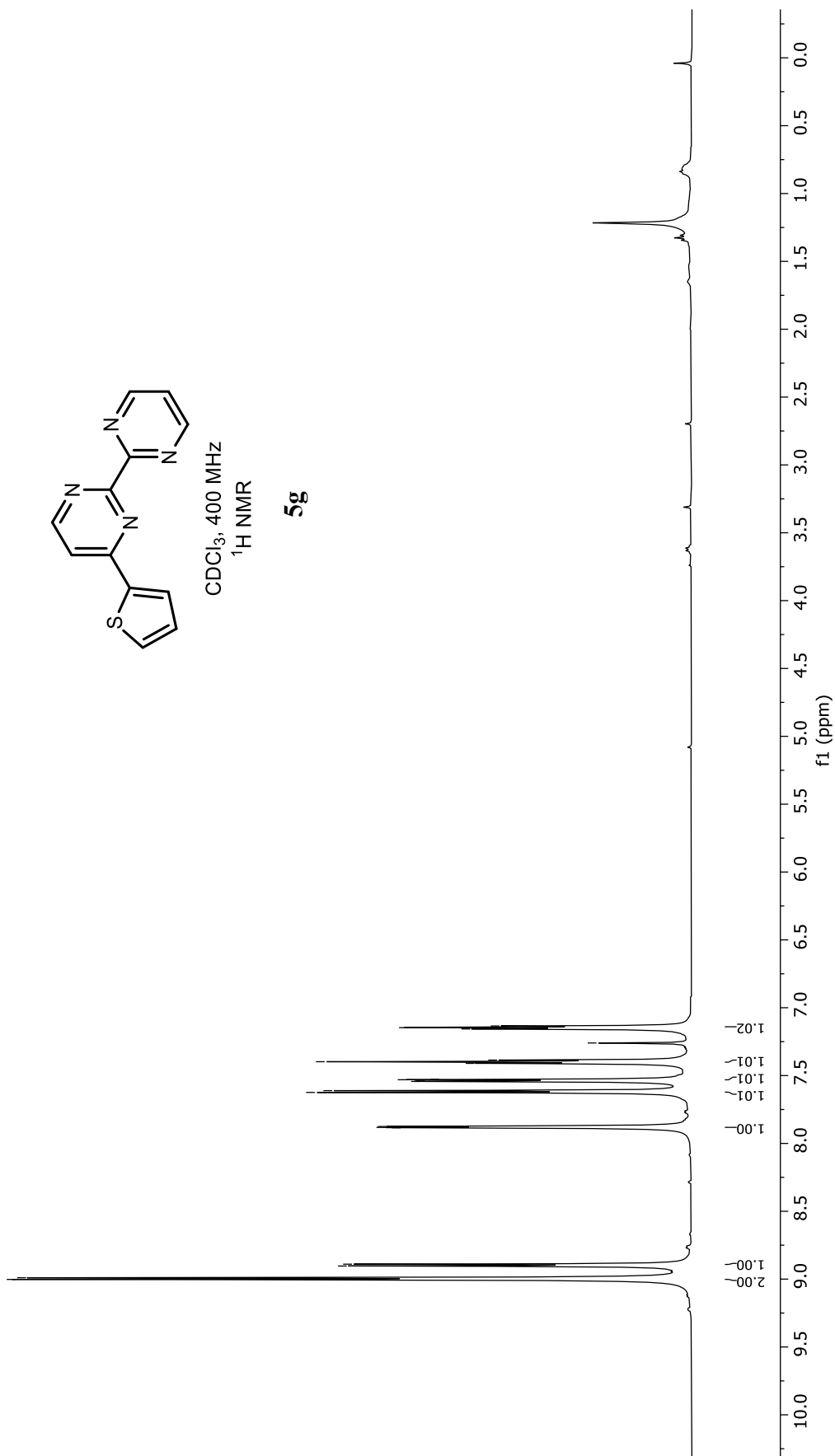
CDCl₃, 375 MHz
¹⁹F NMR

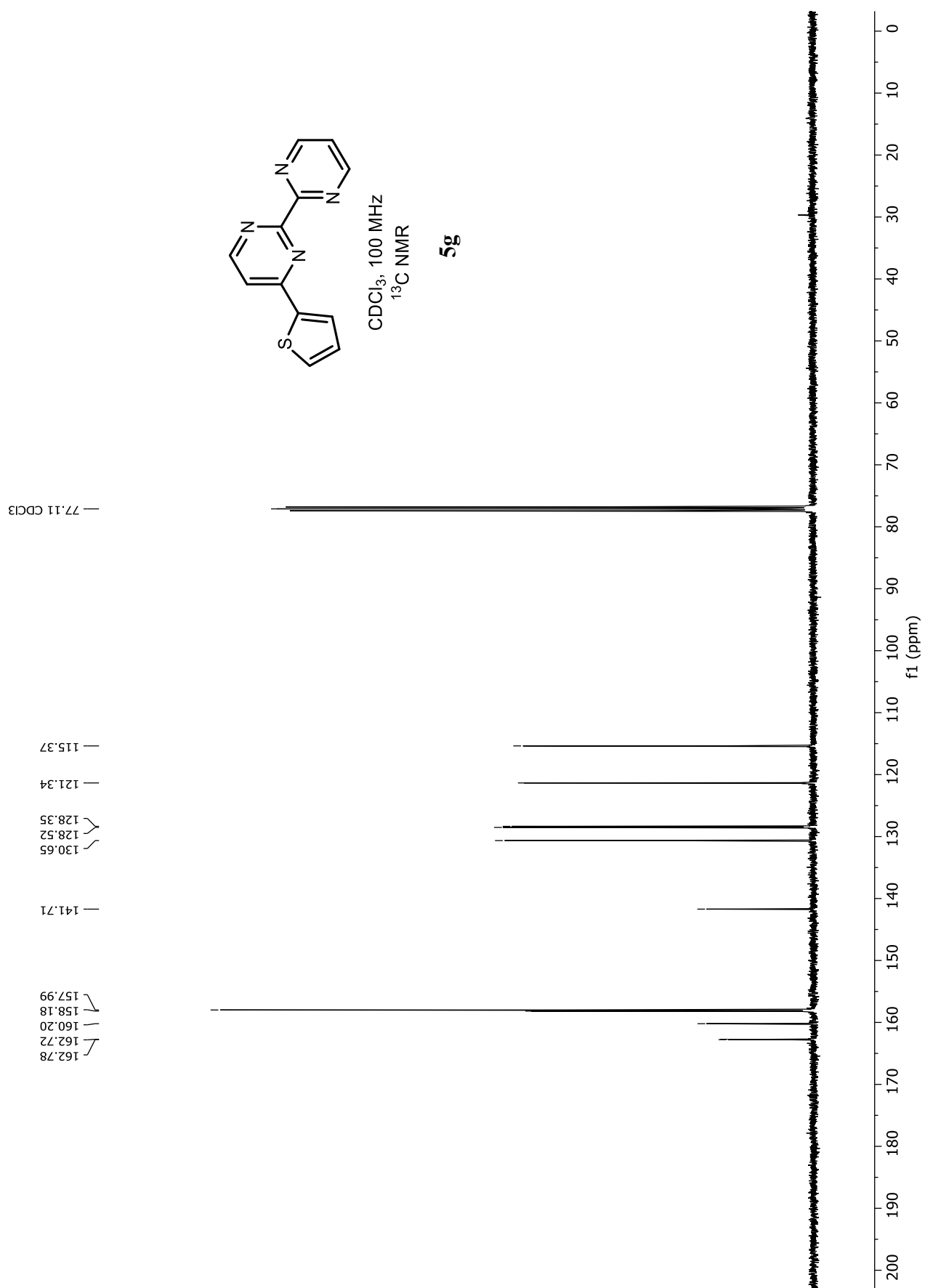
5f

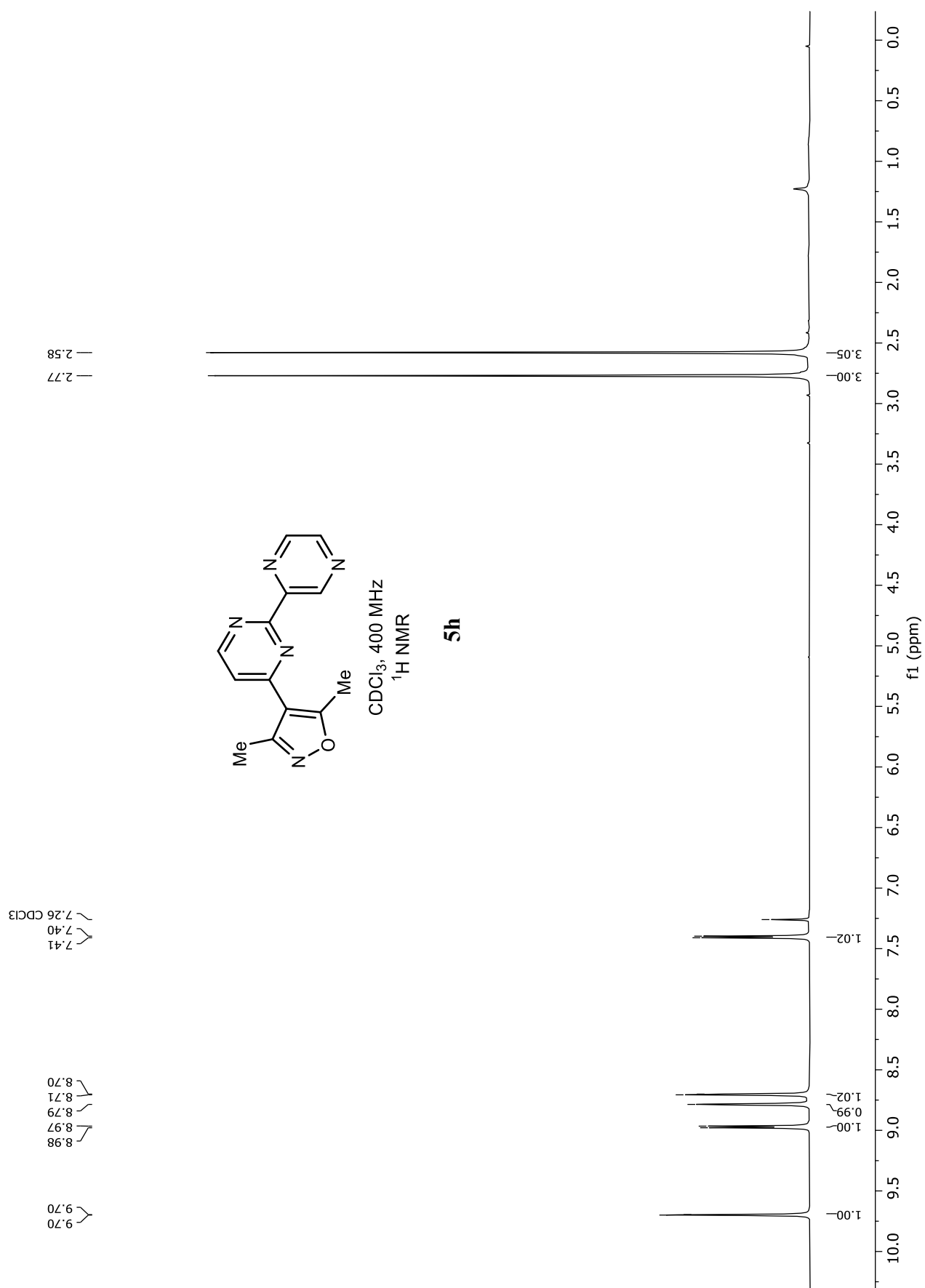
— -70.52

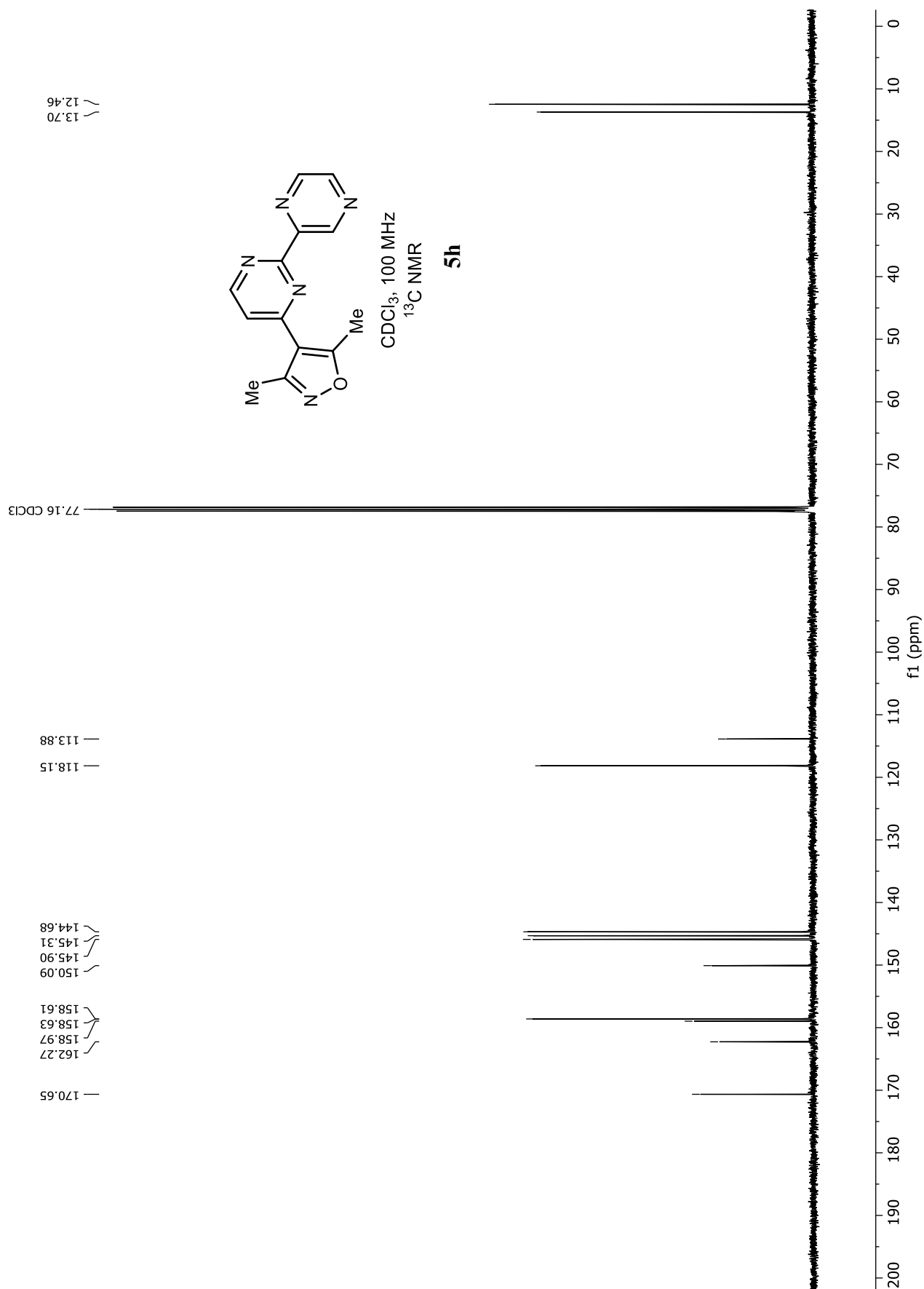


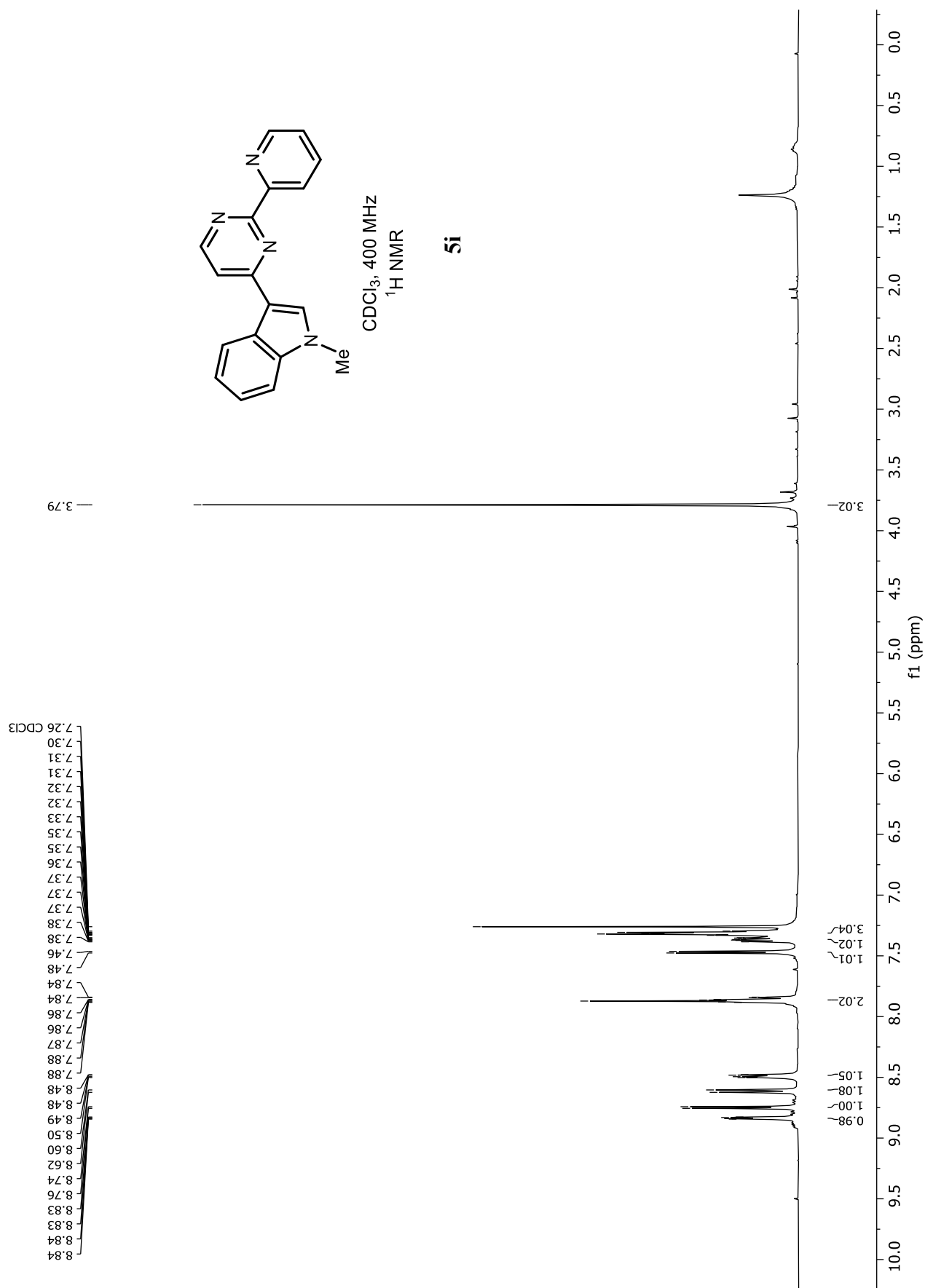
9.00
8.99
8.90
8.89
7.88
7.88
7.88
7.62
7.61
7.54
7.54
7.53
7.53
7.41
7.40
7.39
7.26 CDCl₃
7.16
7.15
7.14
7.13

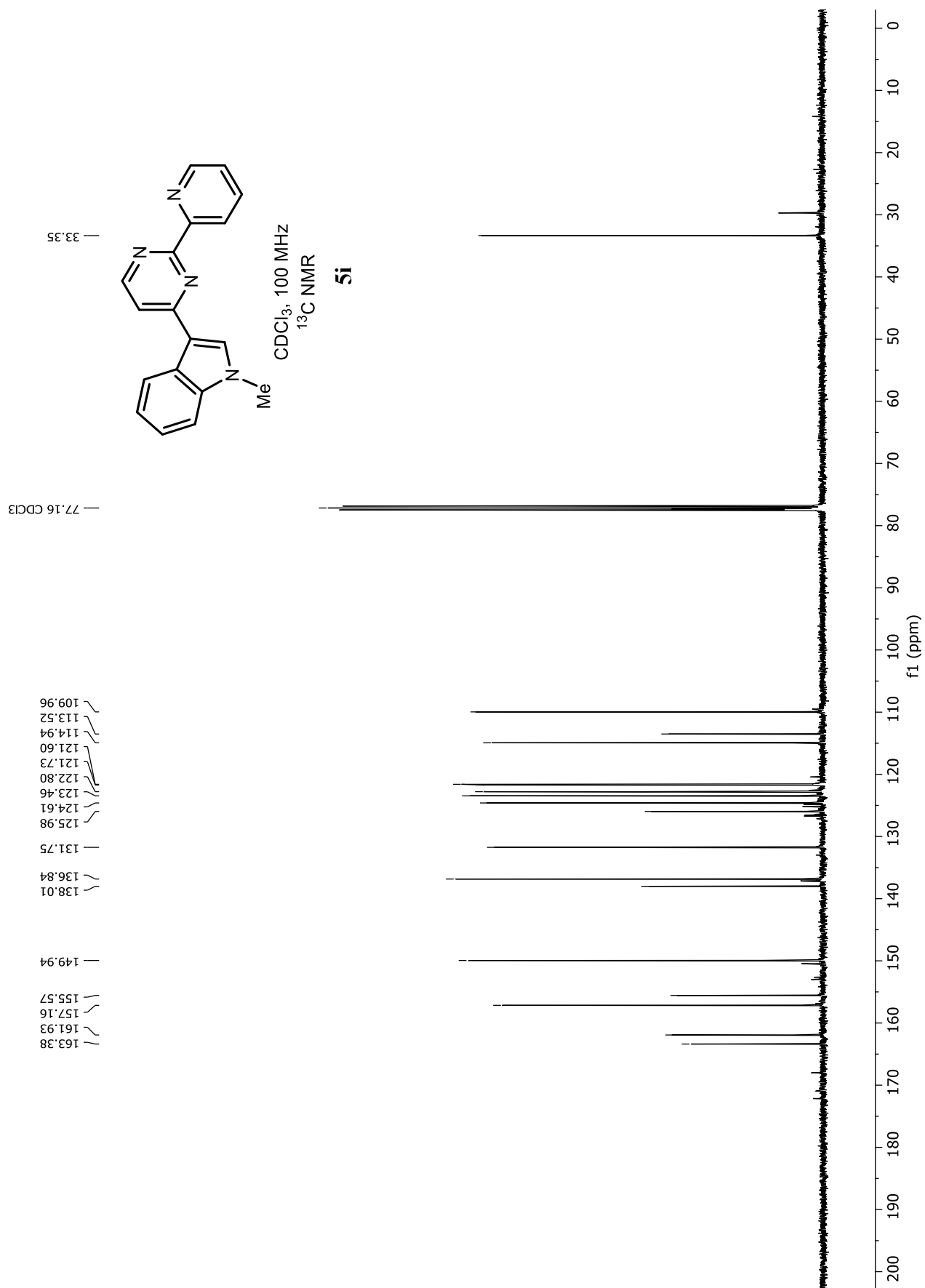


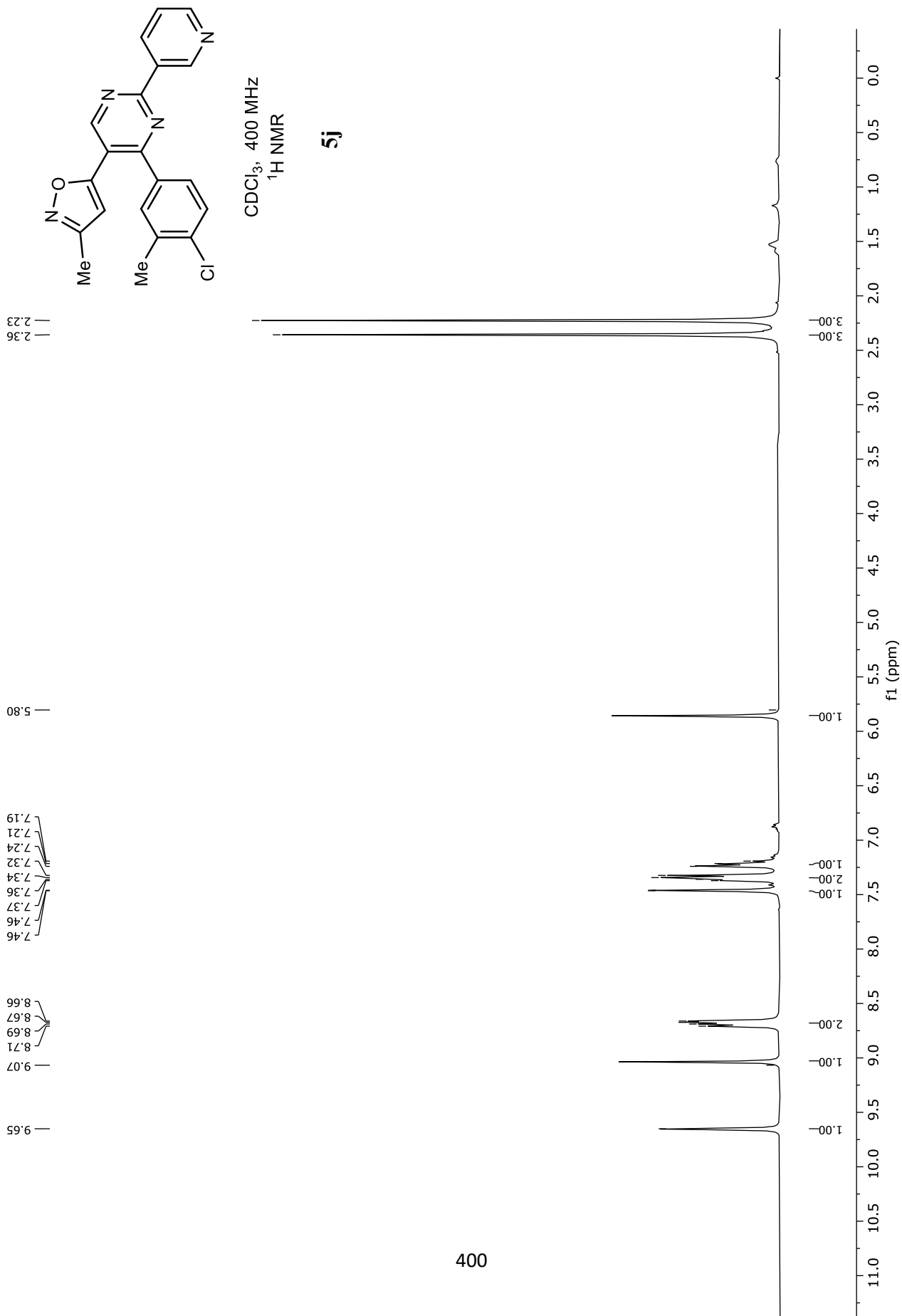


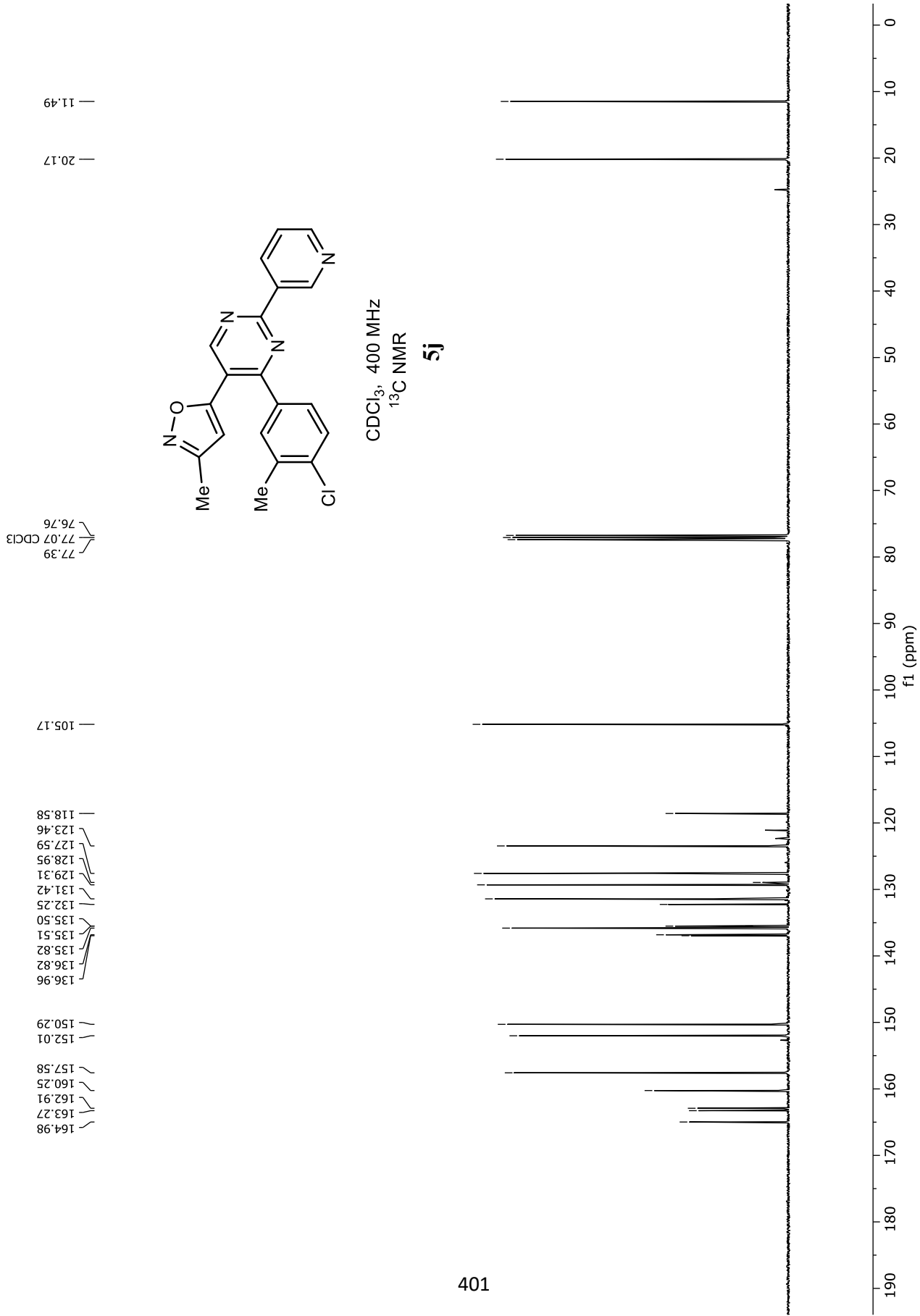


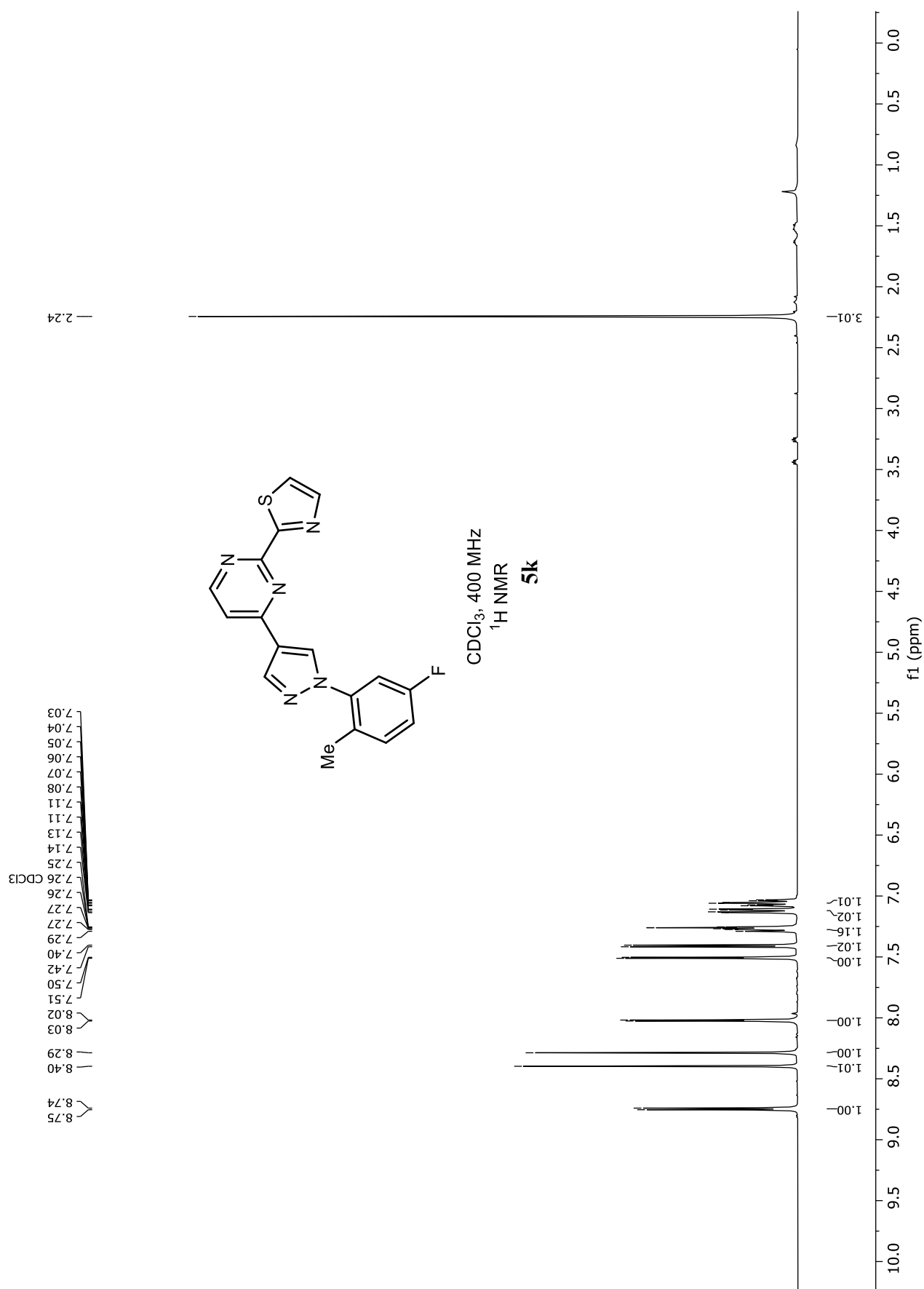


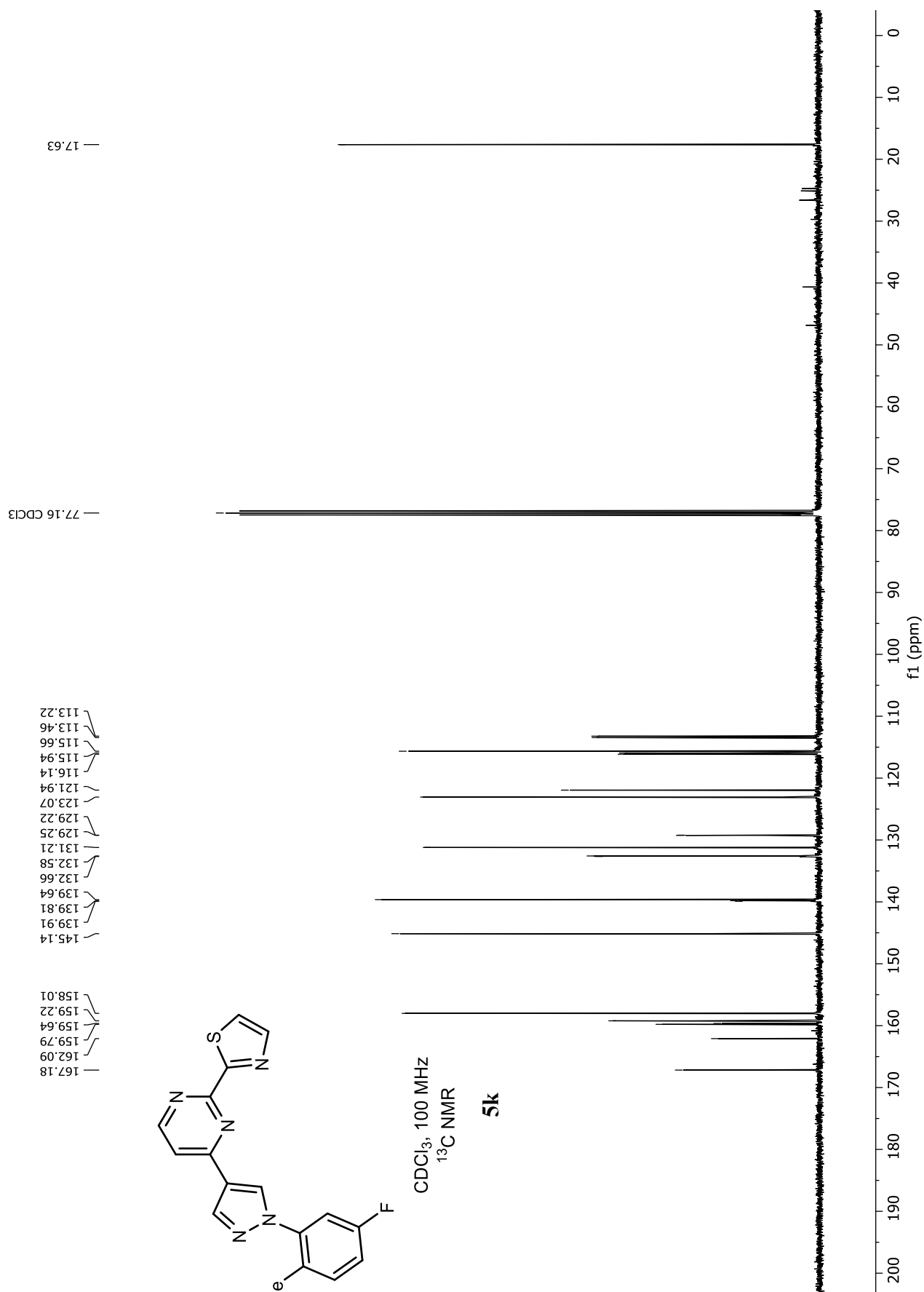


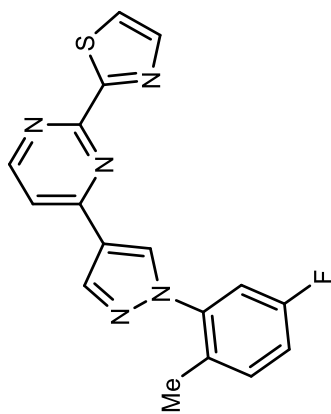








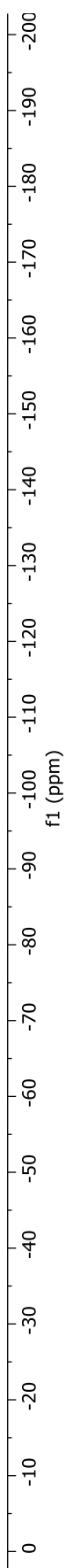


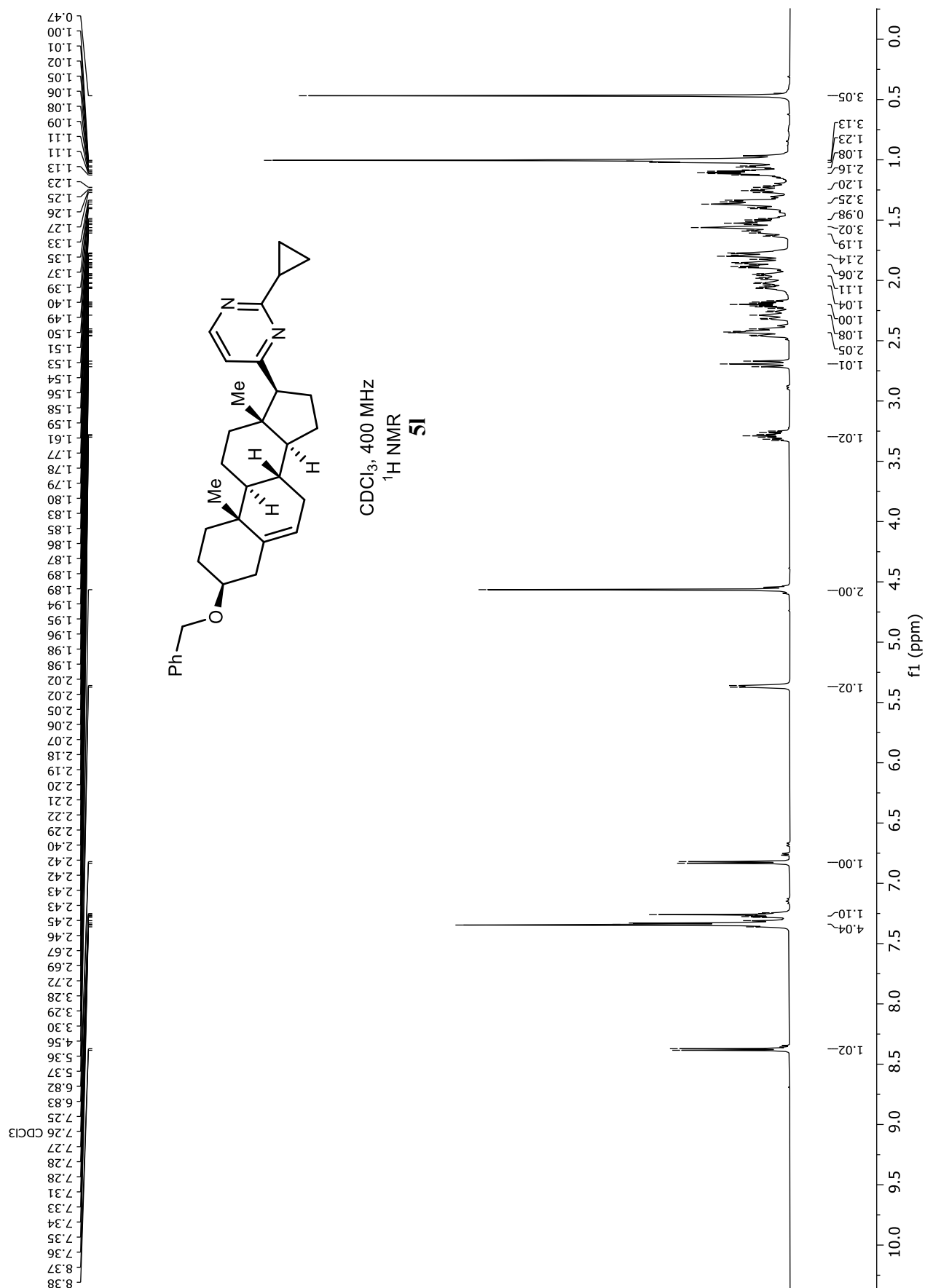


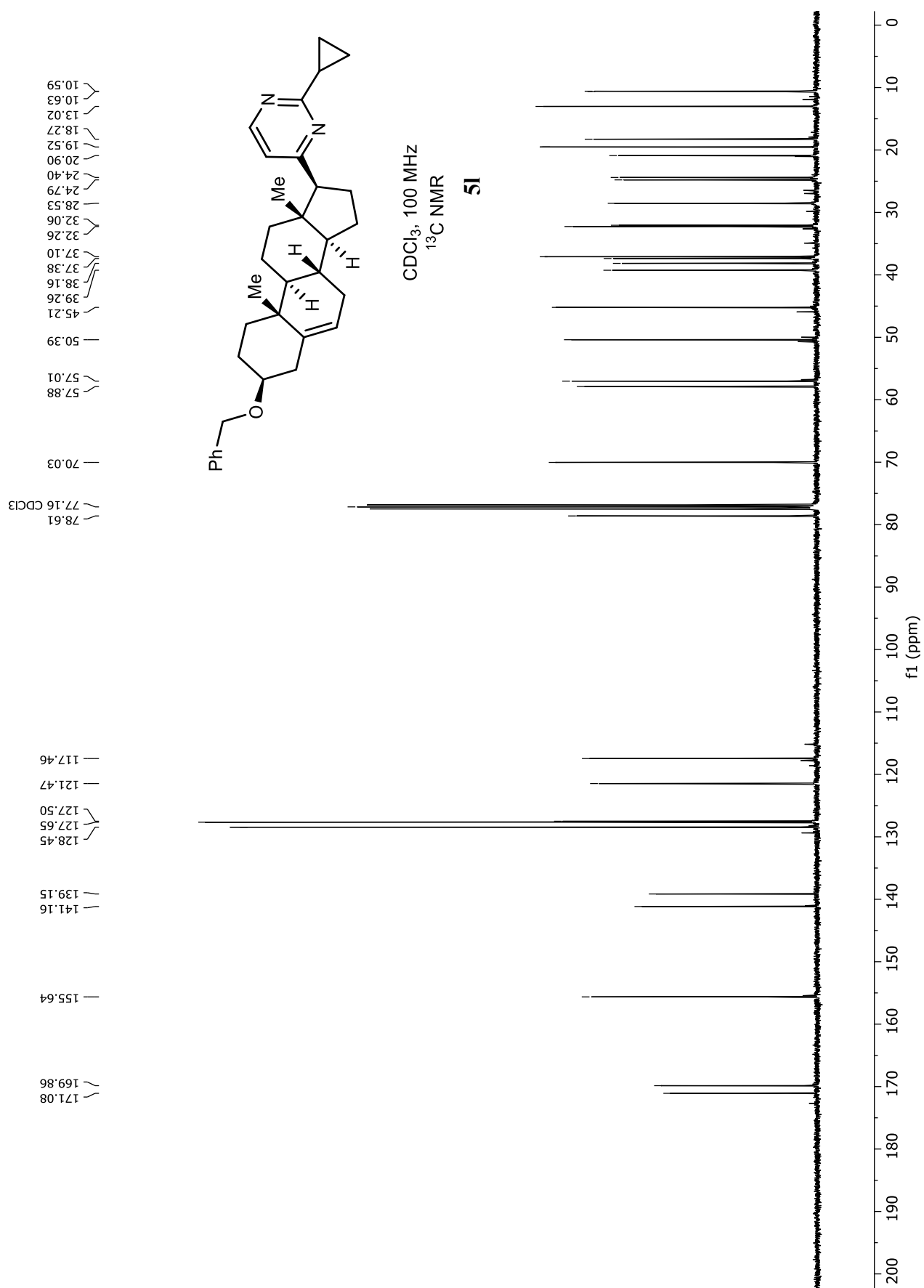
CDCl₃, 375 MHz
¹⁹F NMR

5k

-115.39
 -115.37
 -115.35
 -115.33

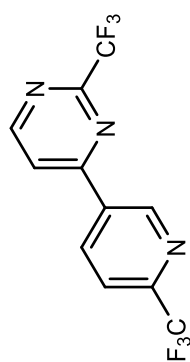






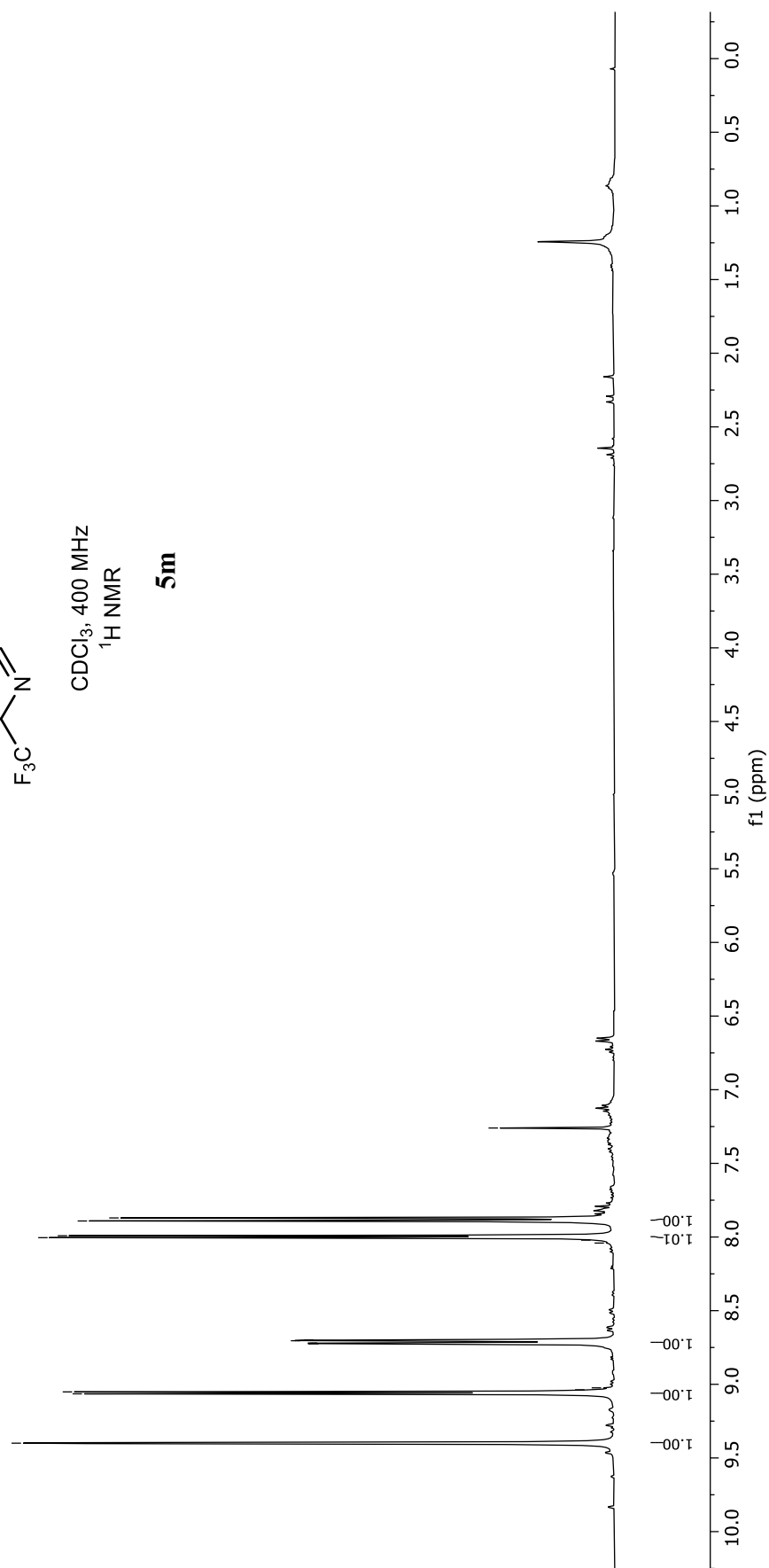
— 7.26 CDCl₃

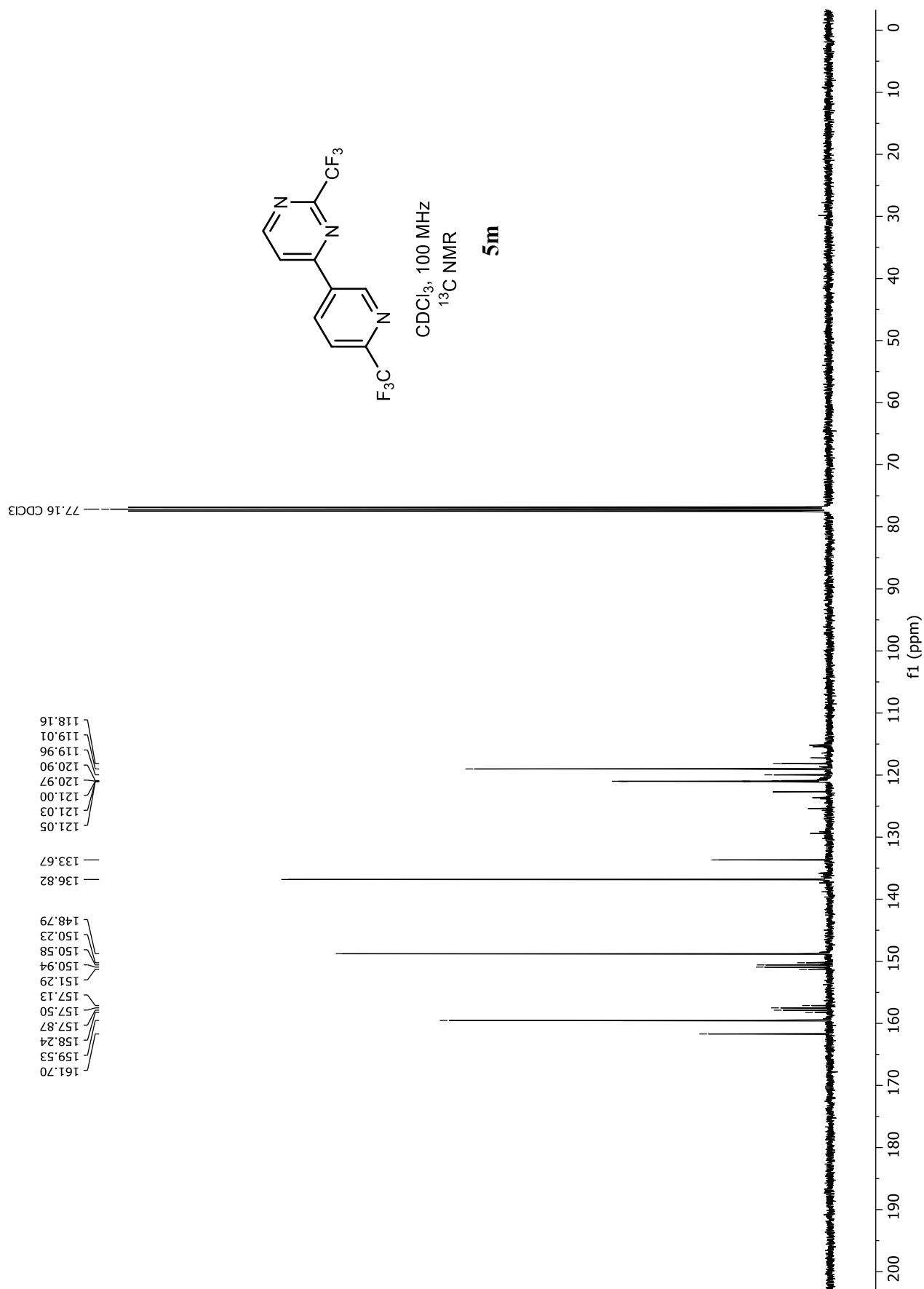
9.40
9.06
9.05
9.04
9.02
8.72
8.72
8.70
8.70
8.04
8.02
8.00
7.99
7.89
7.87



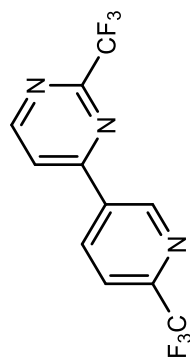
CDCl₃, 400 MHz
¹H NMR

5m





— -68.17
— -70.61

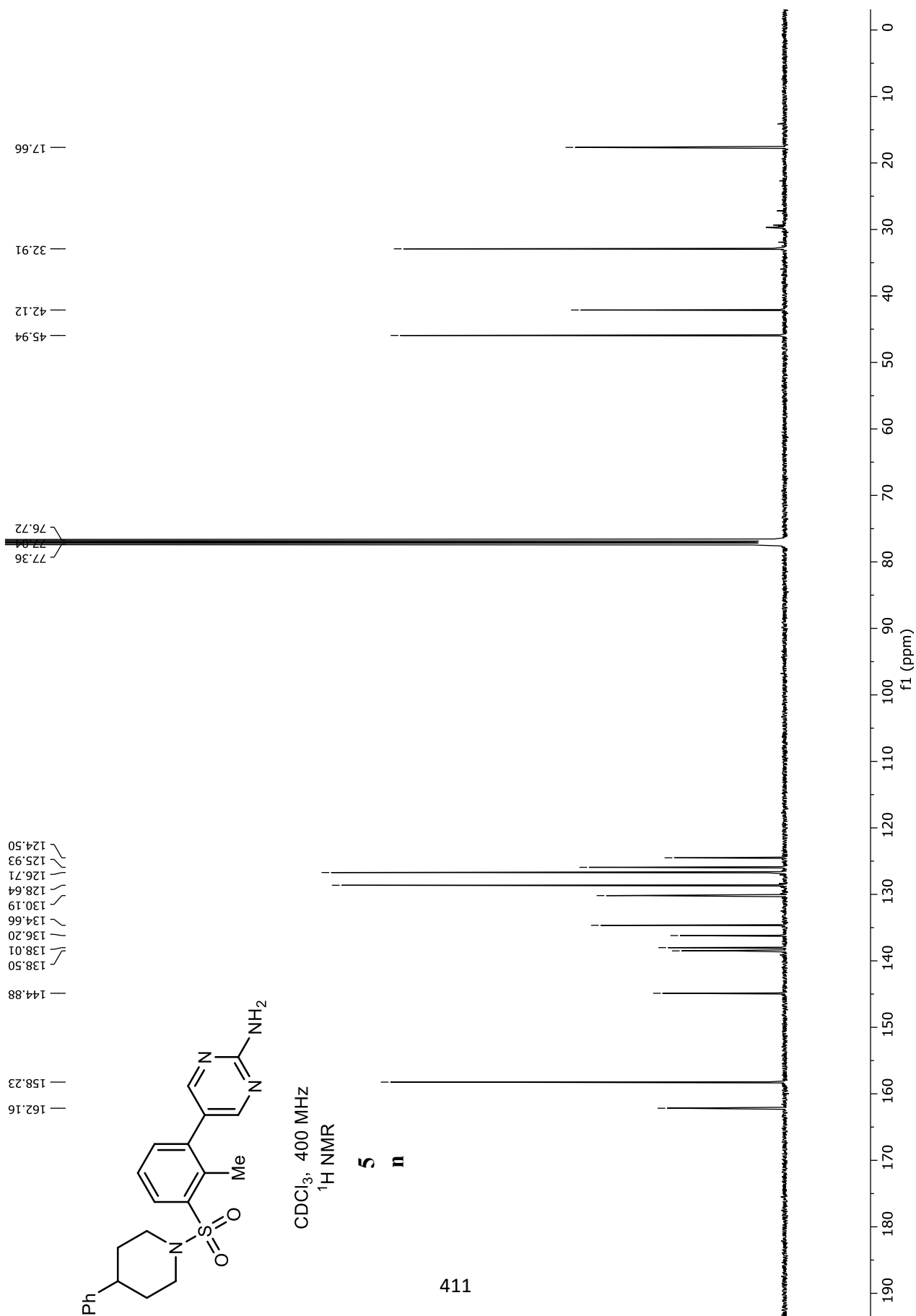


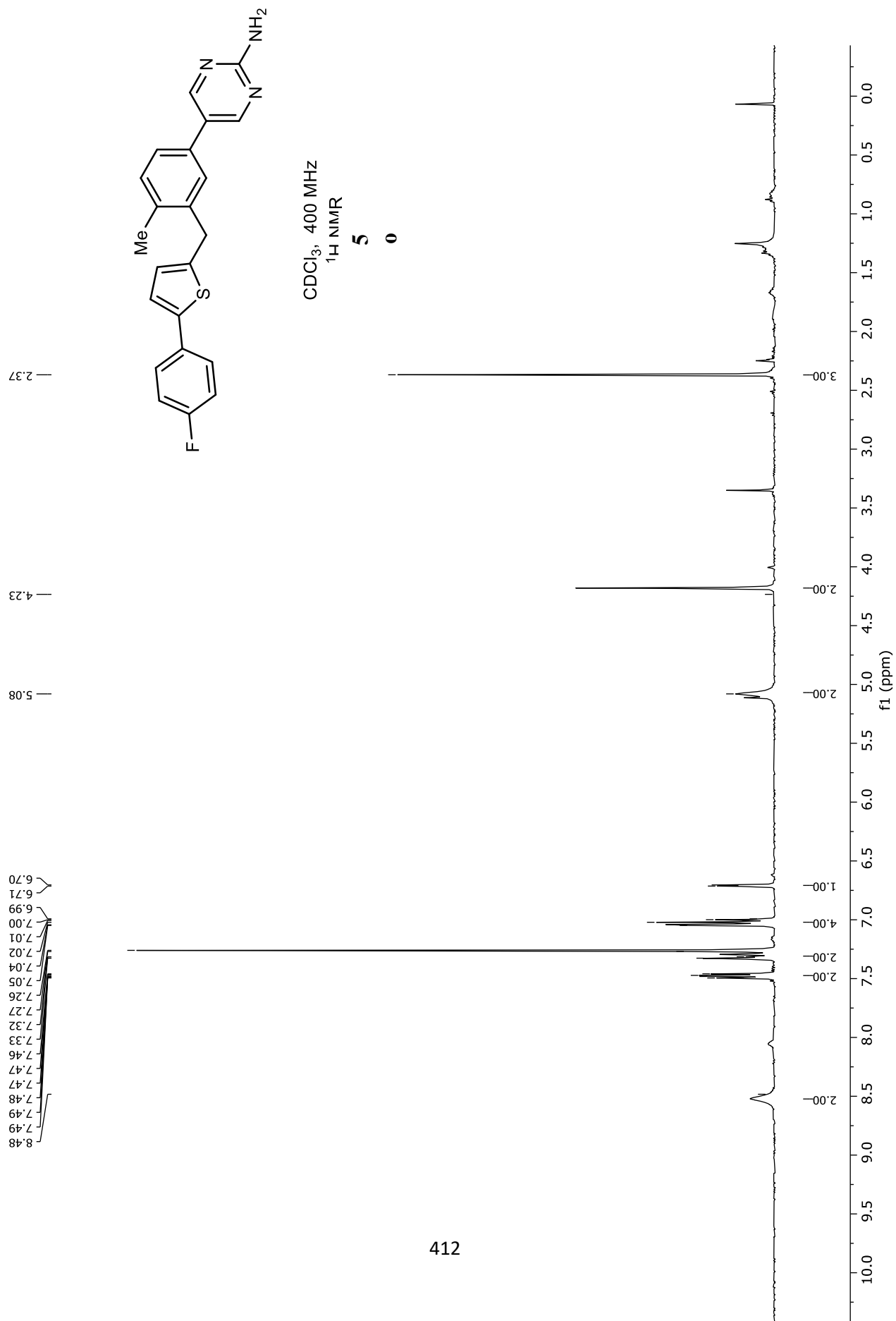
CDCl₃, 375 MHz
¹⁹F NMR

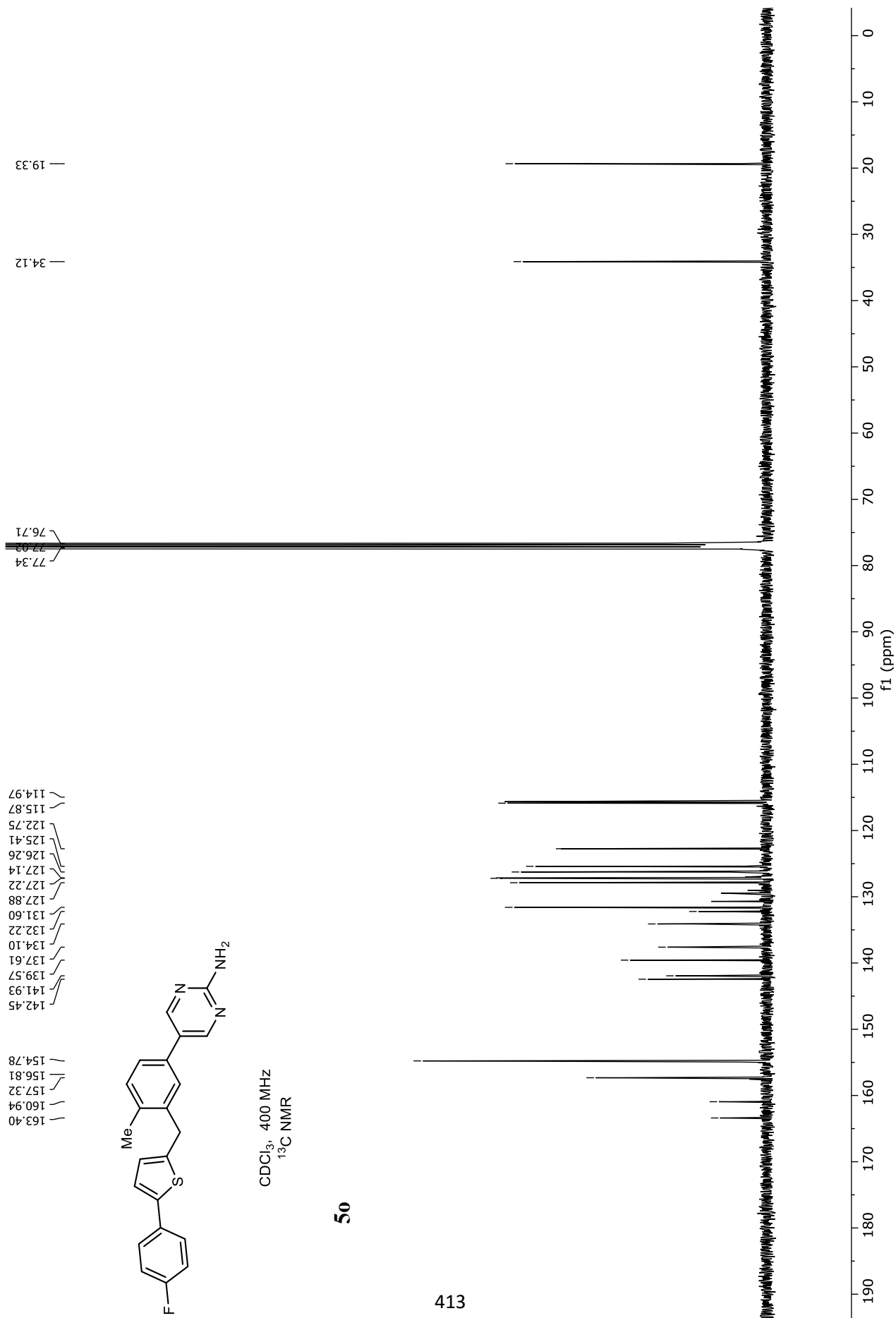
5m

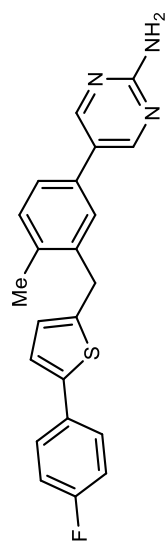
3.02
3.00

f1 (ppm)









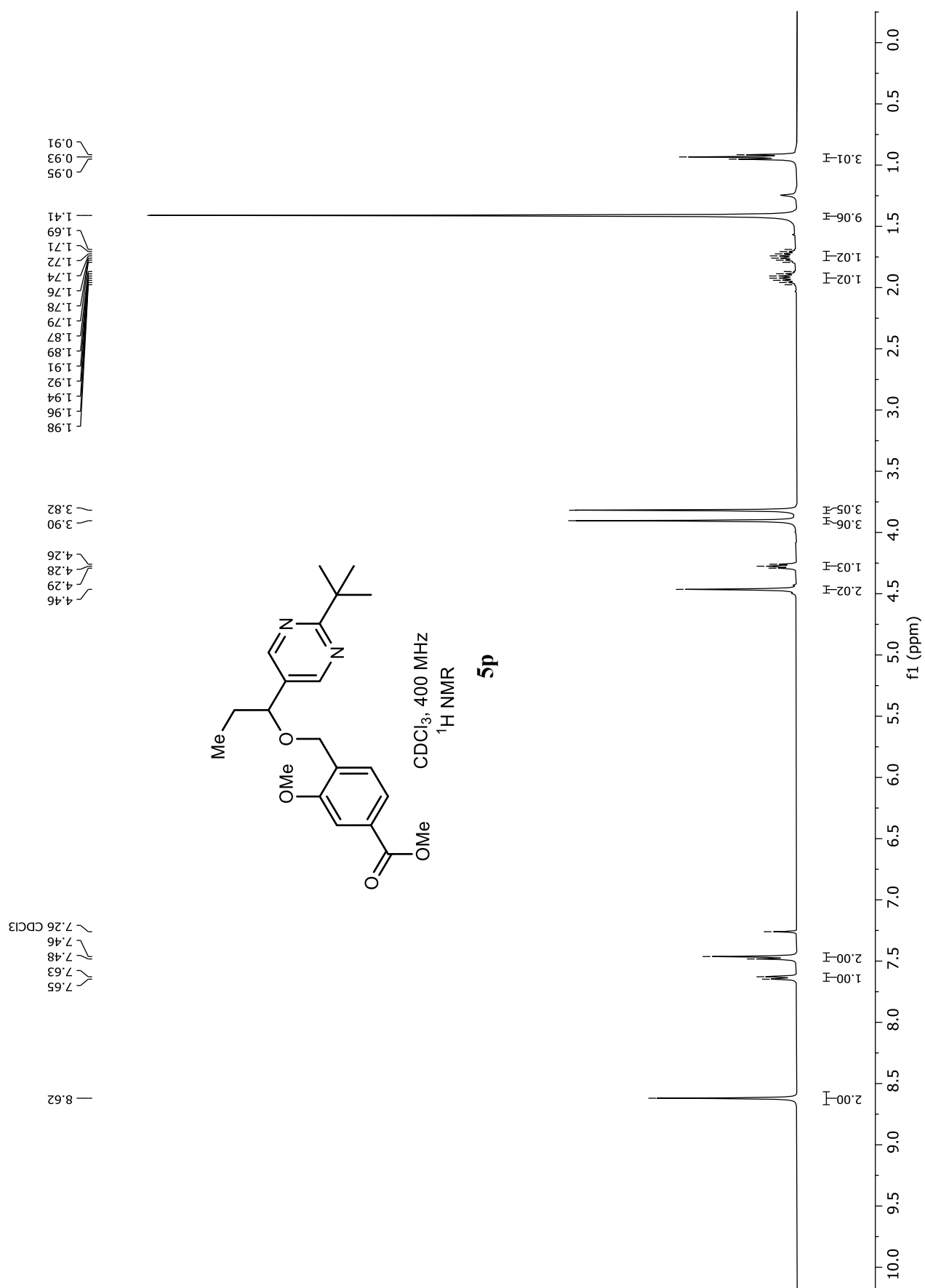
CDCl₃, 400 MHz
¹⁹F NMR

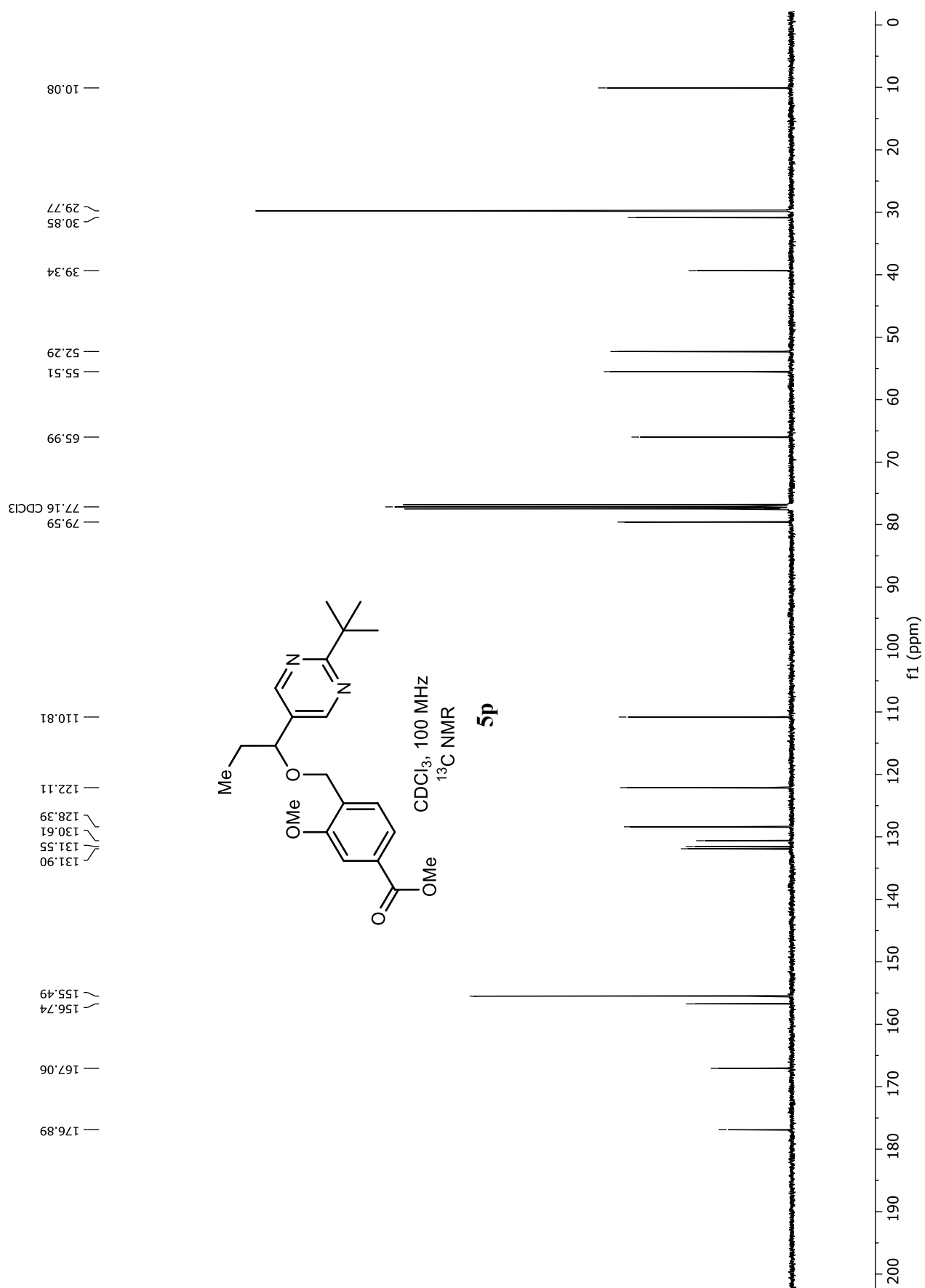
50

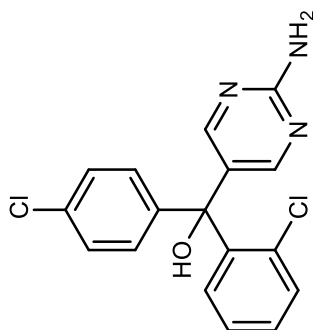
-114.89
-114.91
-114.92
-114.93
-114.94
-114.96
-114.97
-115.00

414







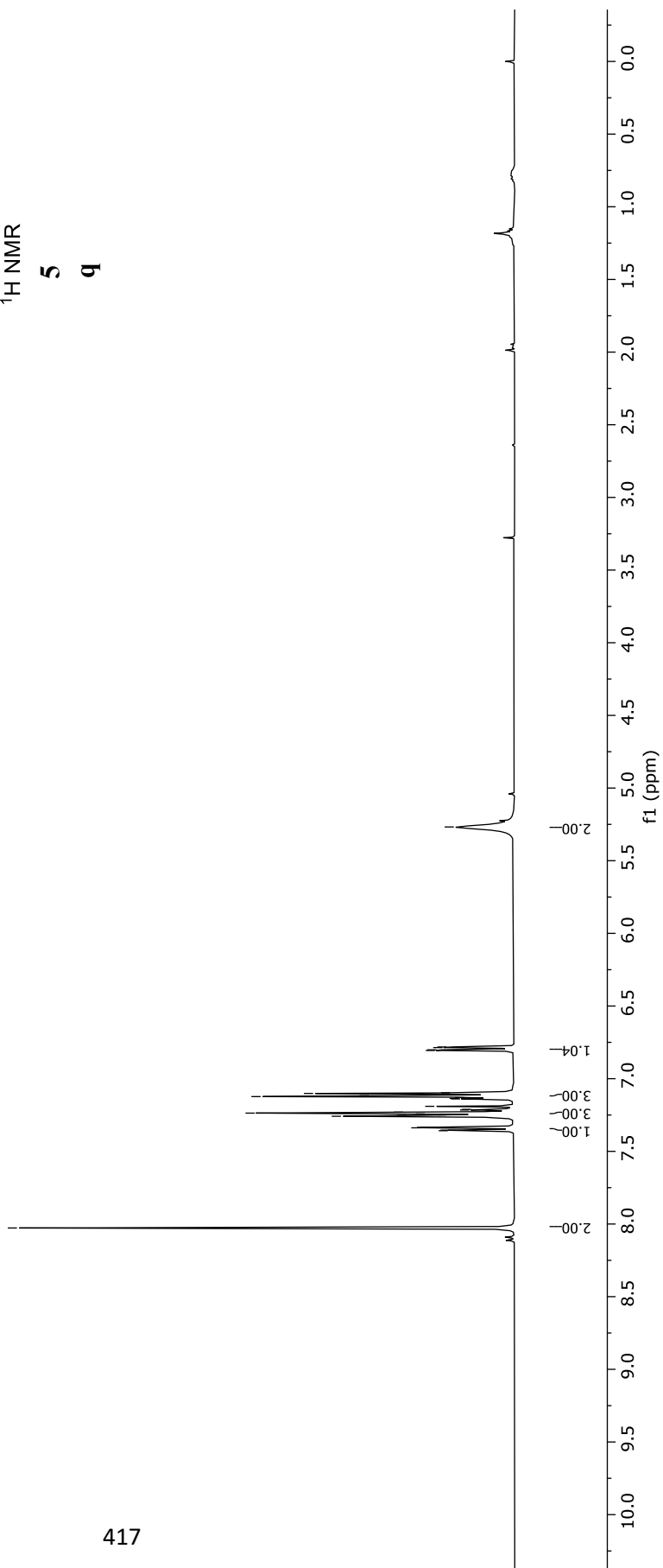


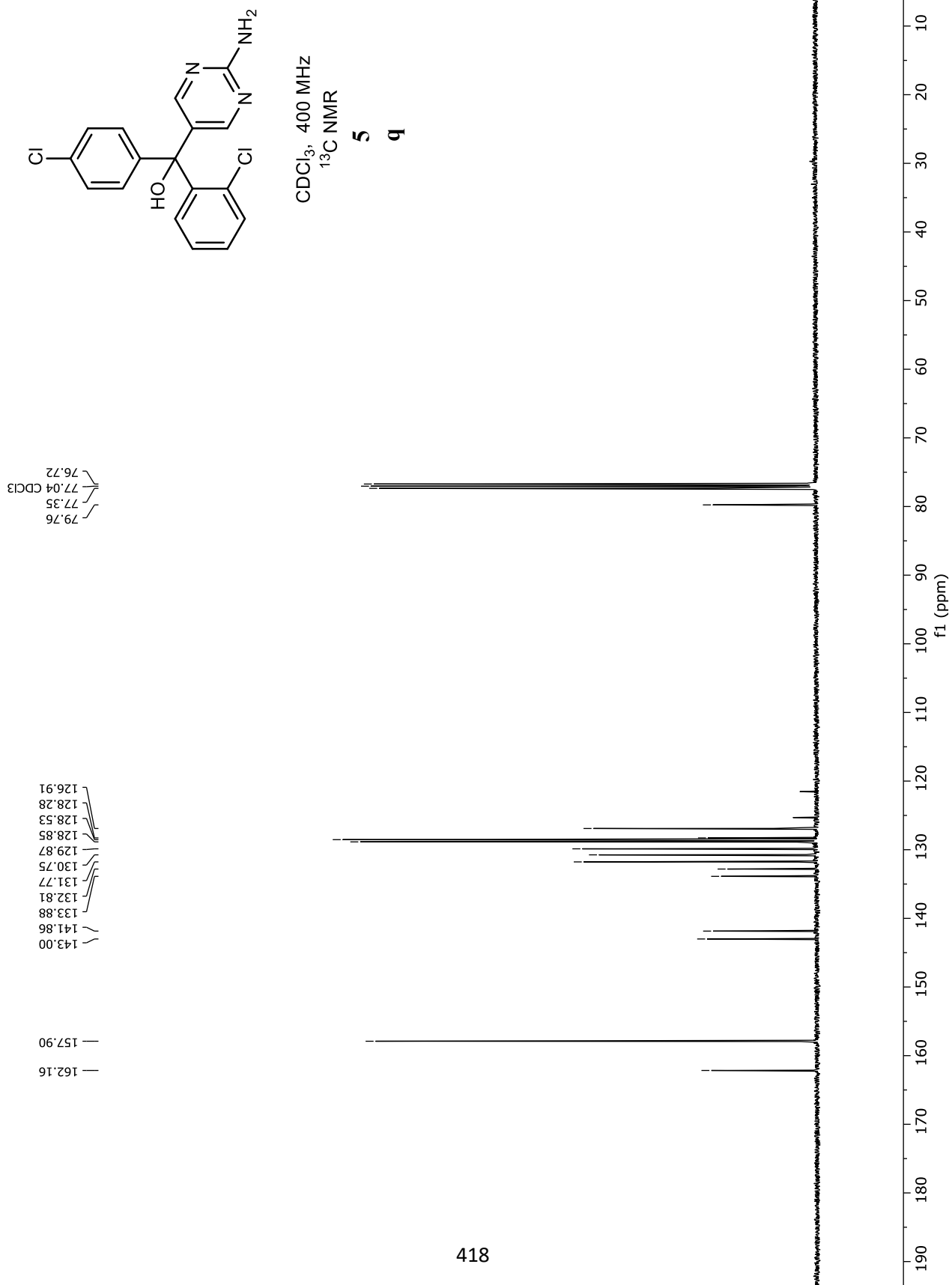
CDCl₃, 400 MHz
¹H NMR

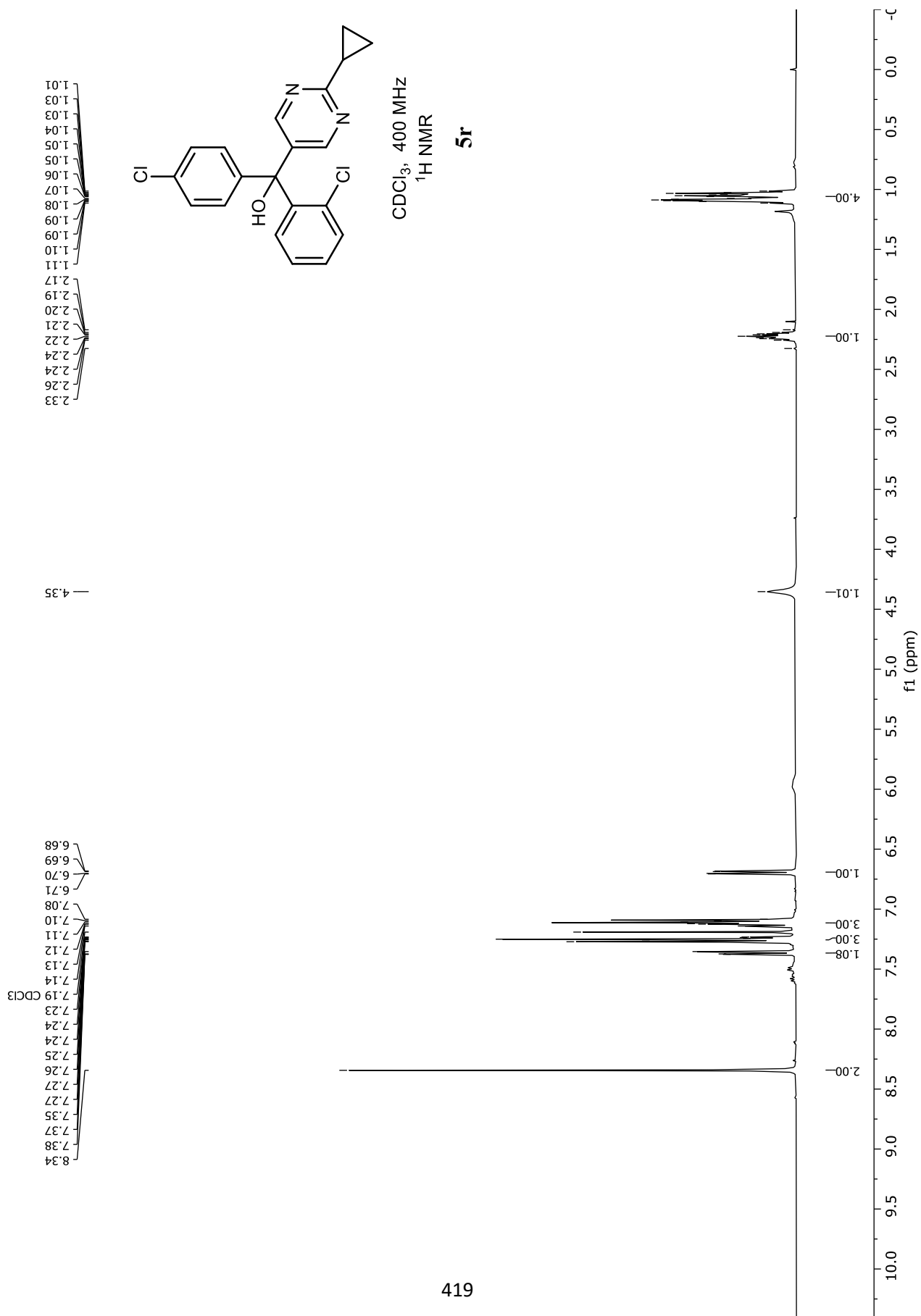
5 q

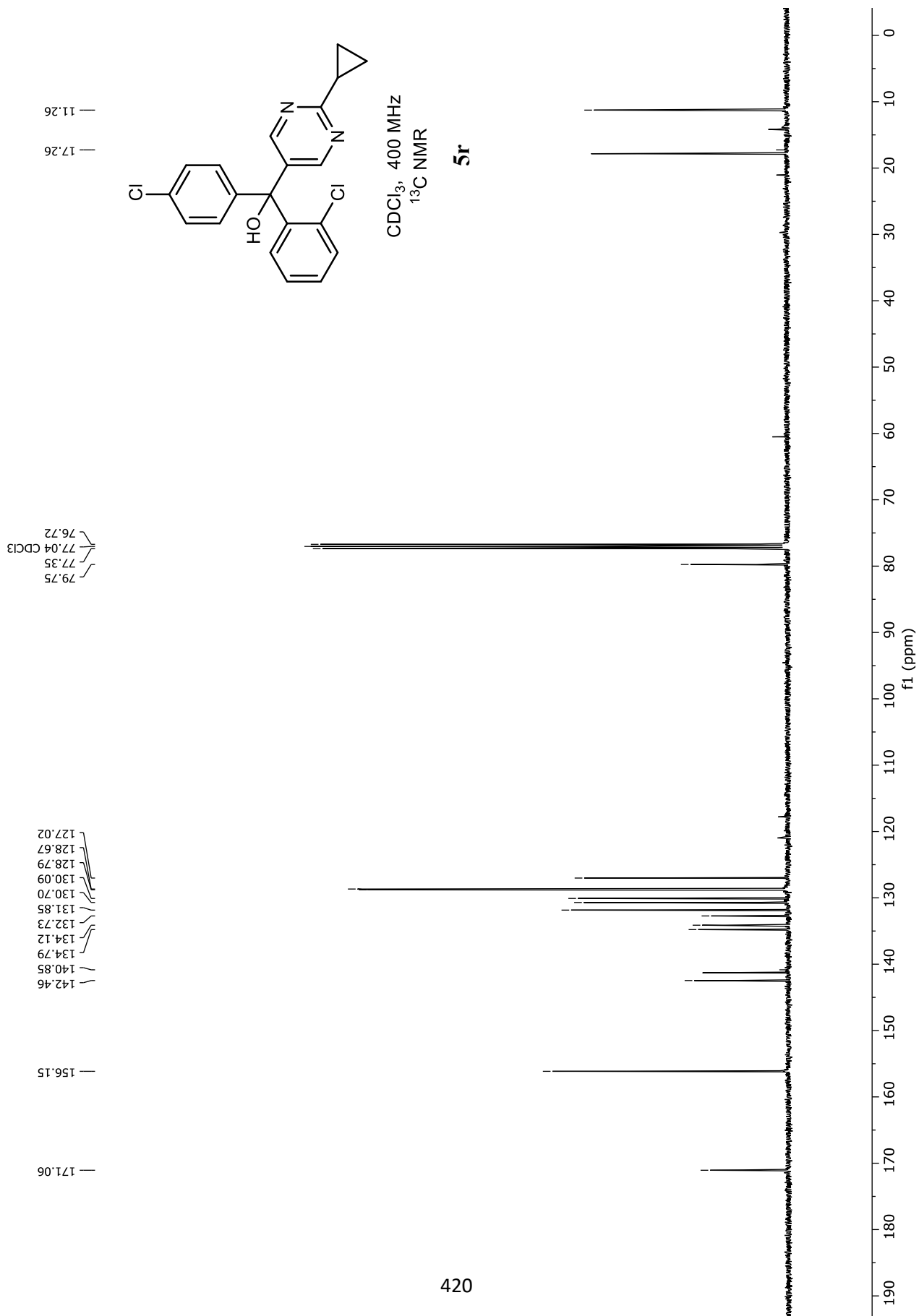
5.27

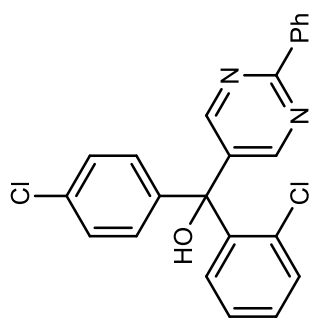
8.03
7.36
7.35
7.34
7.33
7.26
7.25
7.25
7.24
7.24
7.23
7.22
7.21
7.19
7.14
7.14
7.13
7.12
7.12
7.11
7.10
7.10
6.81
6.80
6.79
6.78





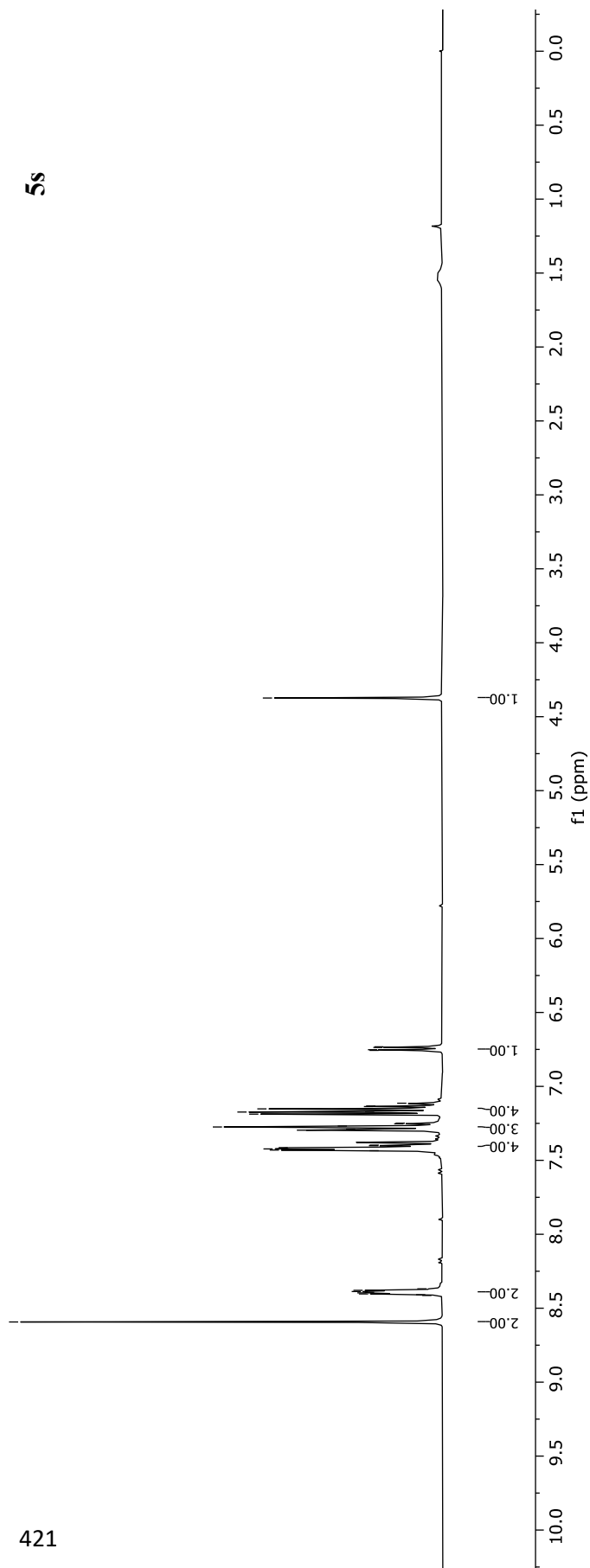
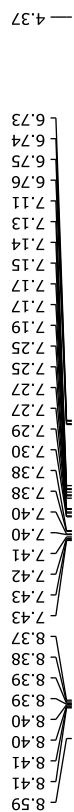


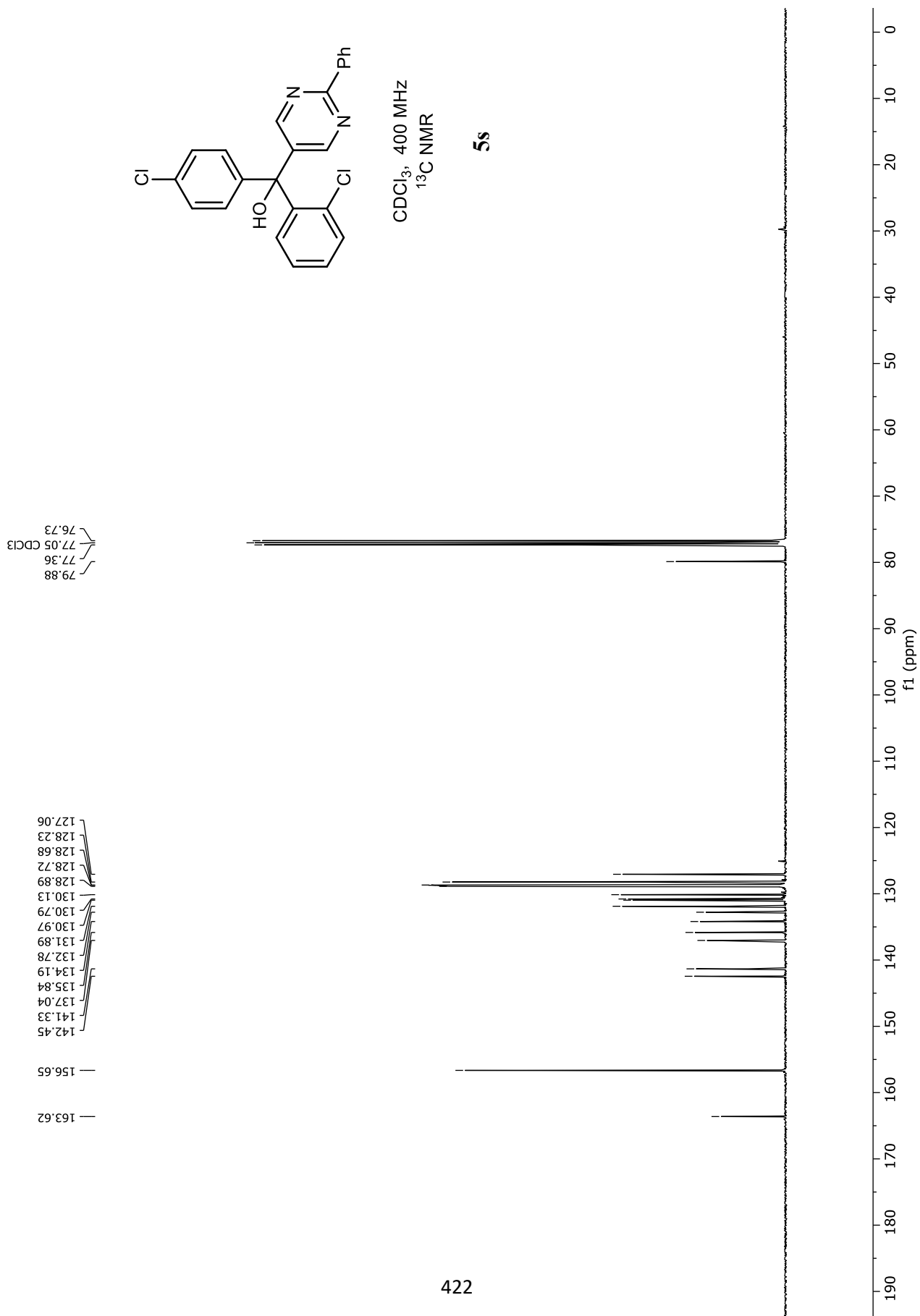


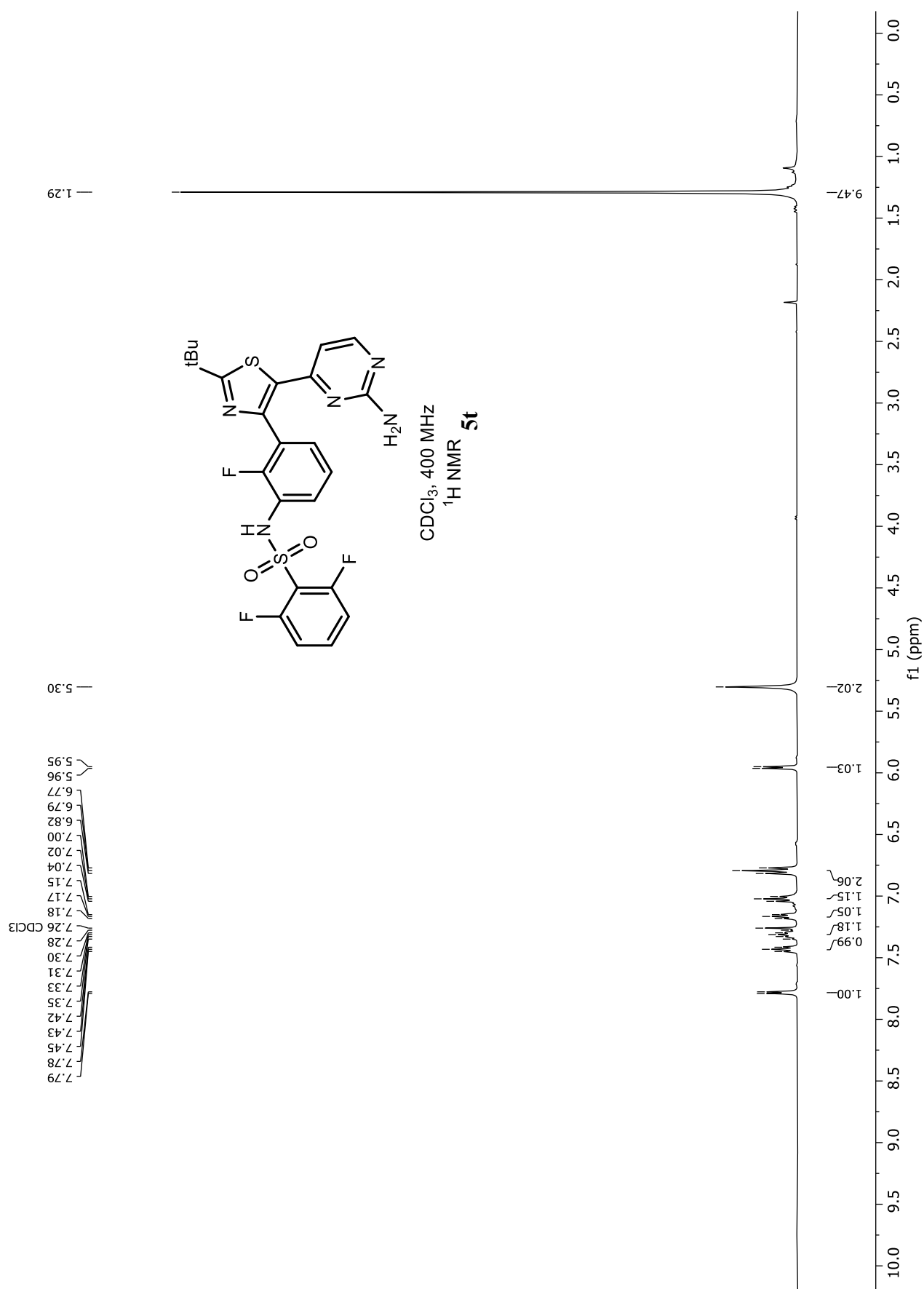


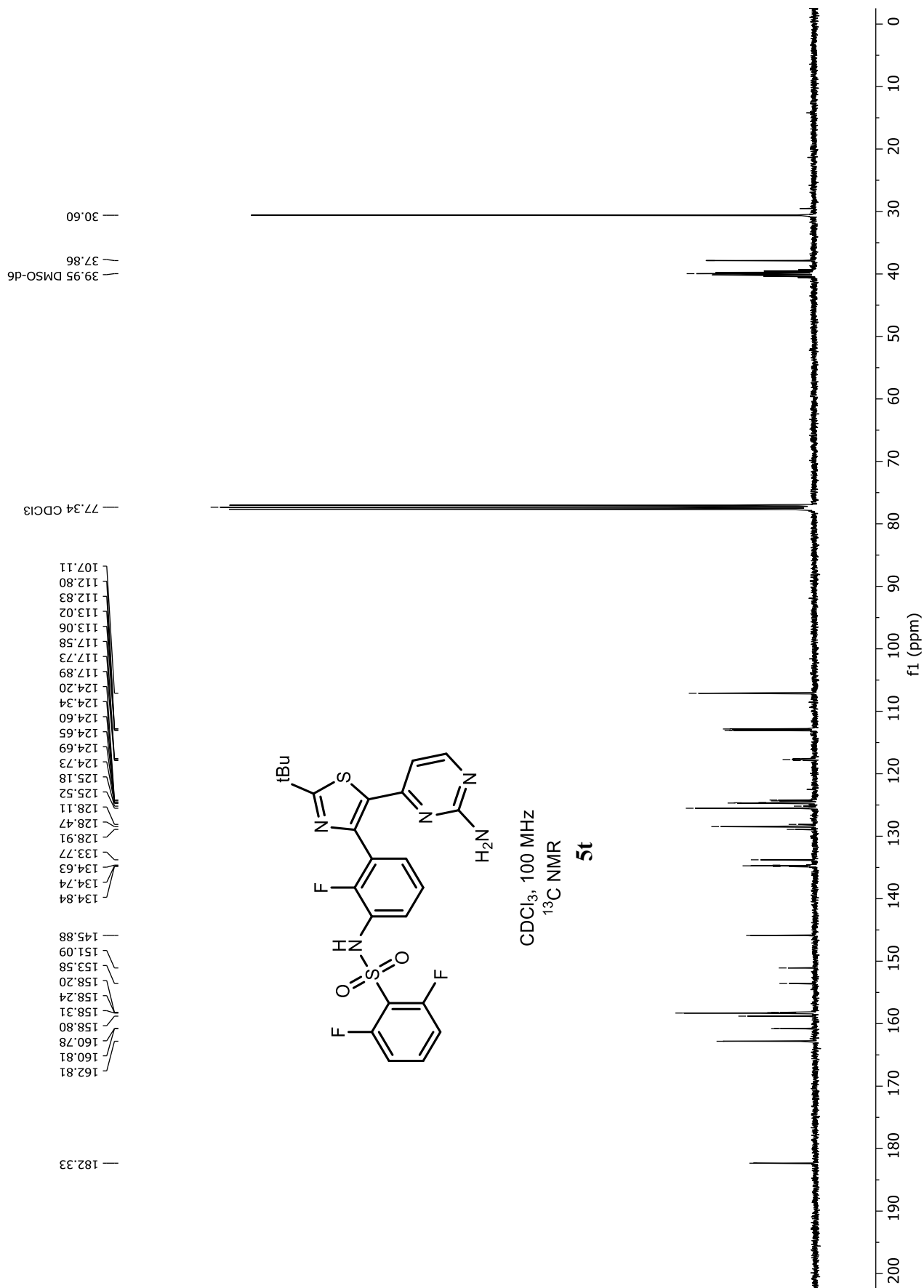
CDCl₃, 400 MHz
¹H NMR

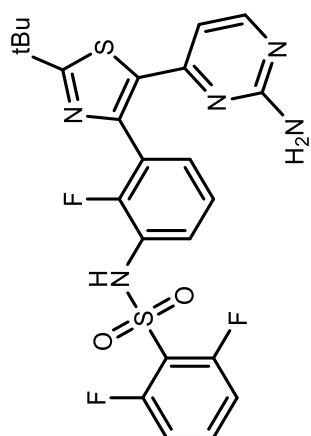
5s







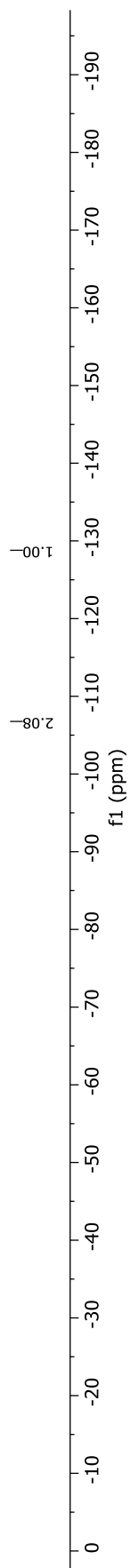


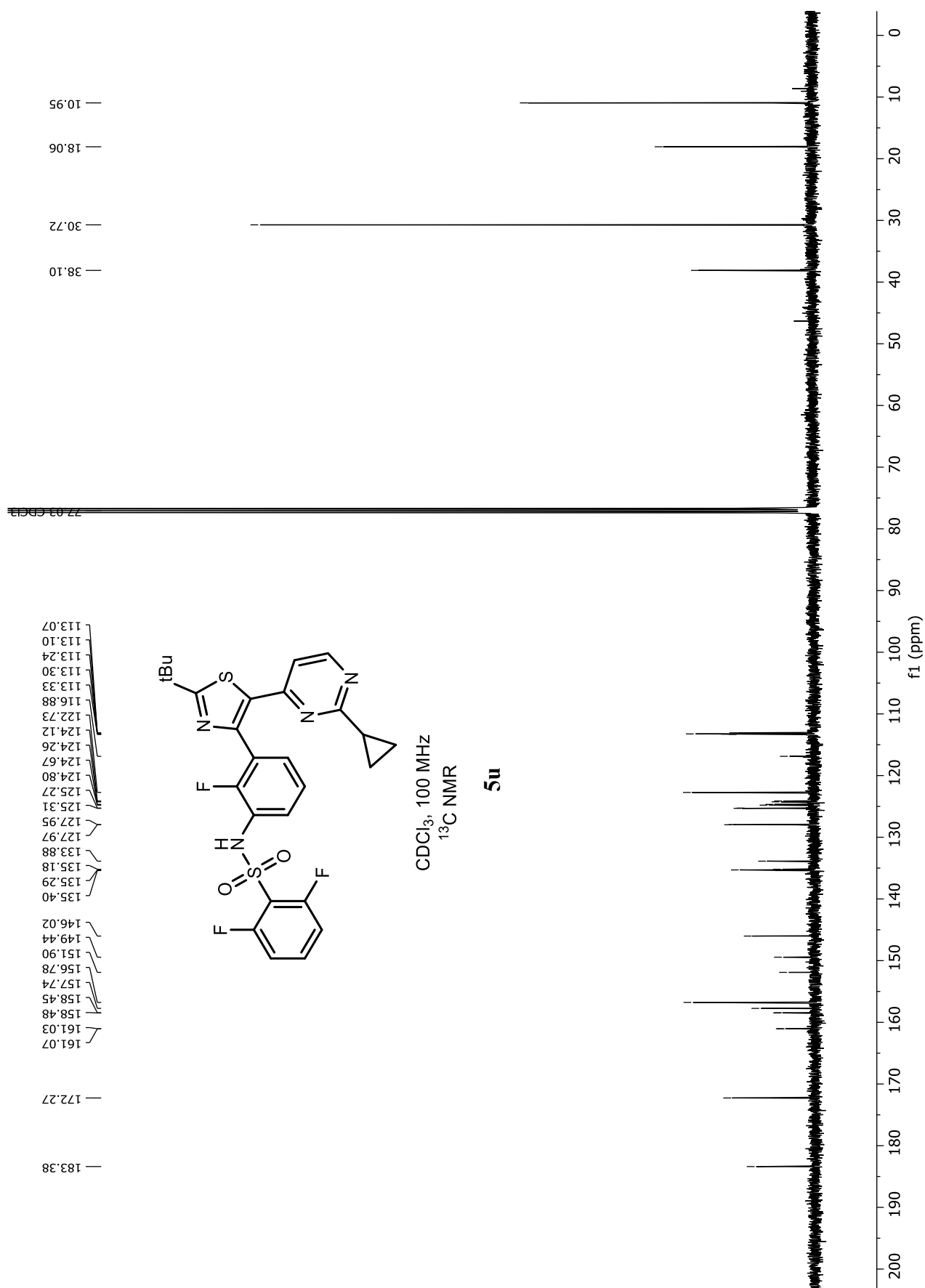


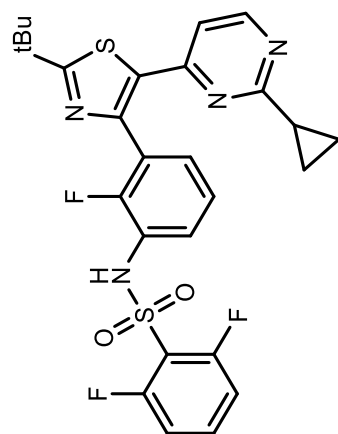
CDCl₃, 375 MHz
¹⁹F NMR

5t

-106.77
-106.79
-106.80
-106.81
-106.83
-106.87
-106.88
-128.77
-128.78
-128.79
-128.80
-128.81
-128.82
-128.83



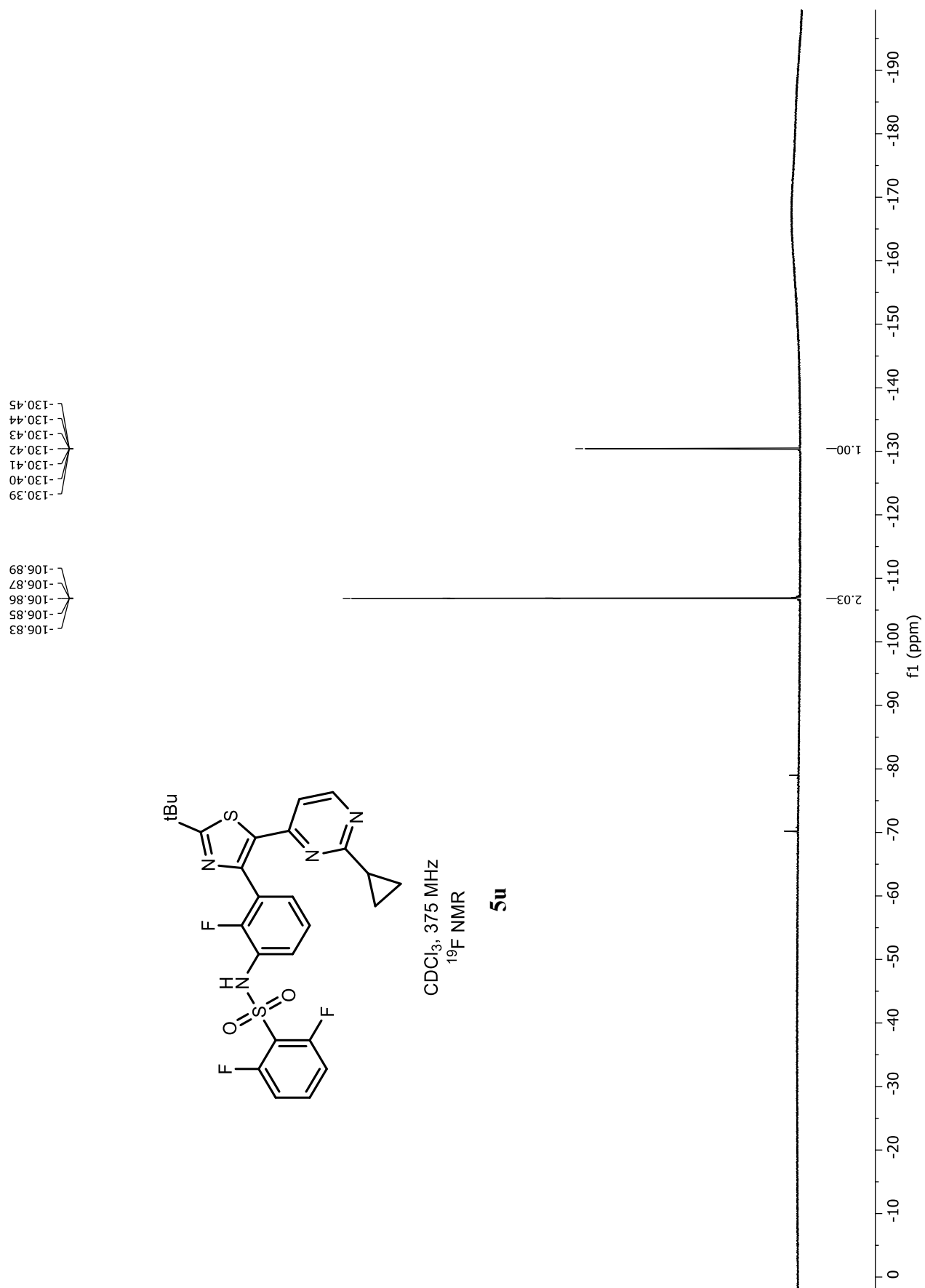


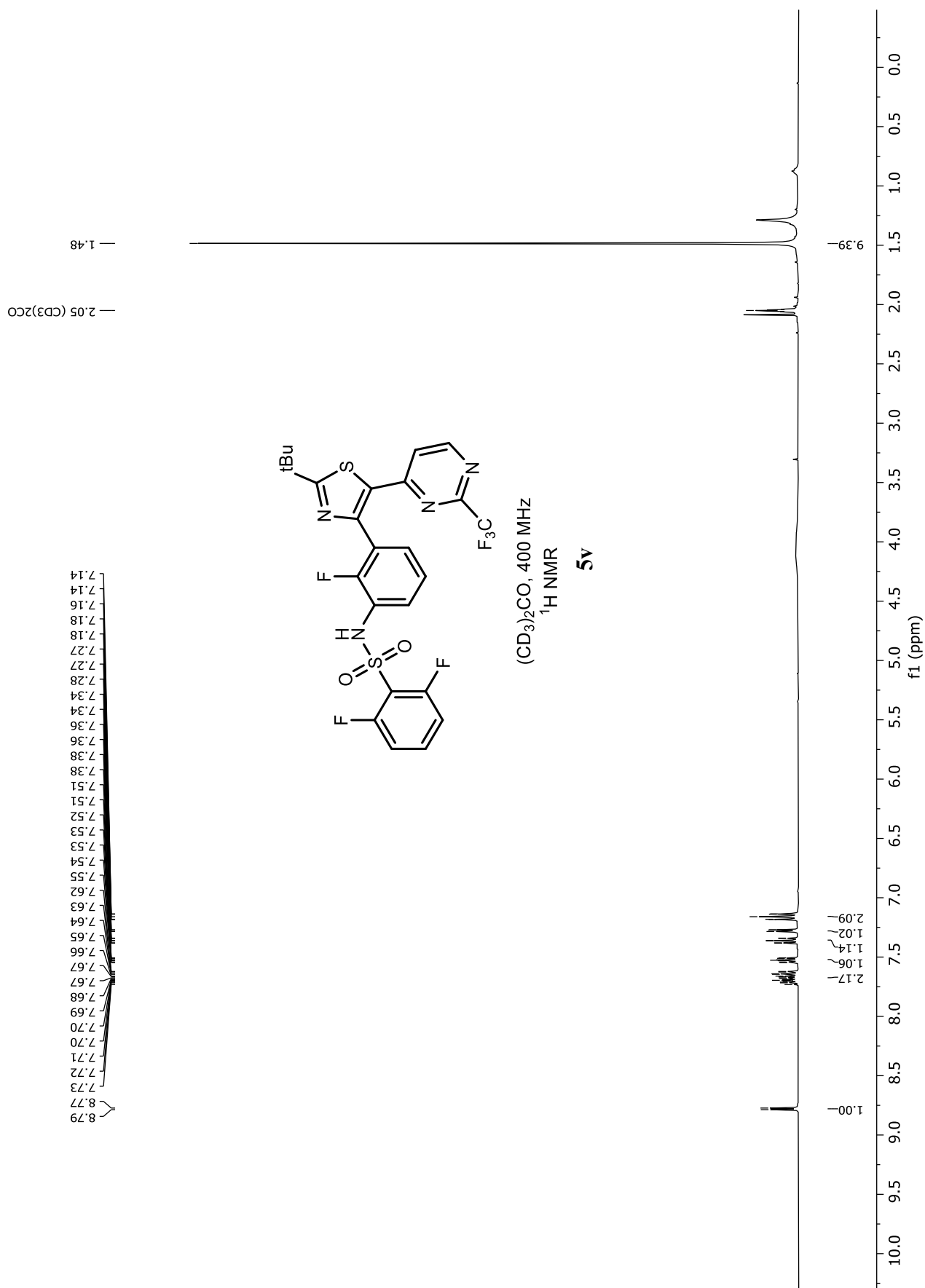


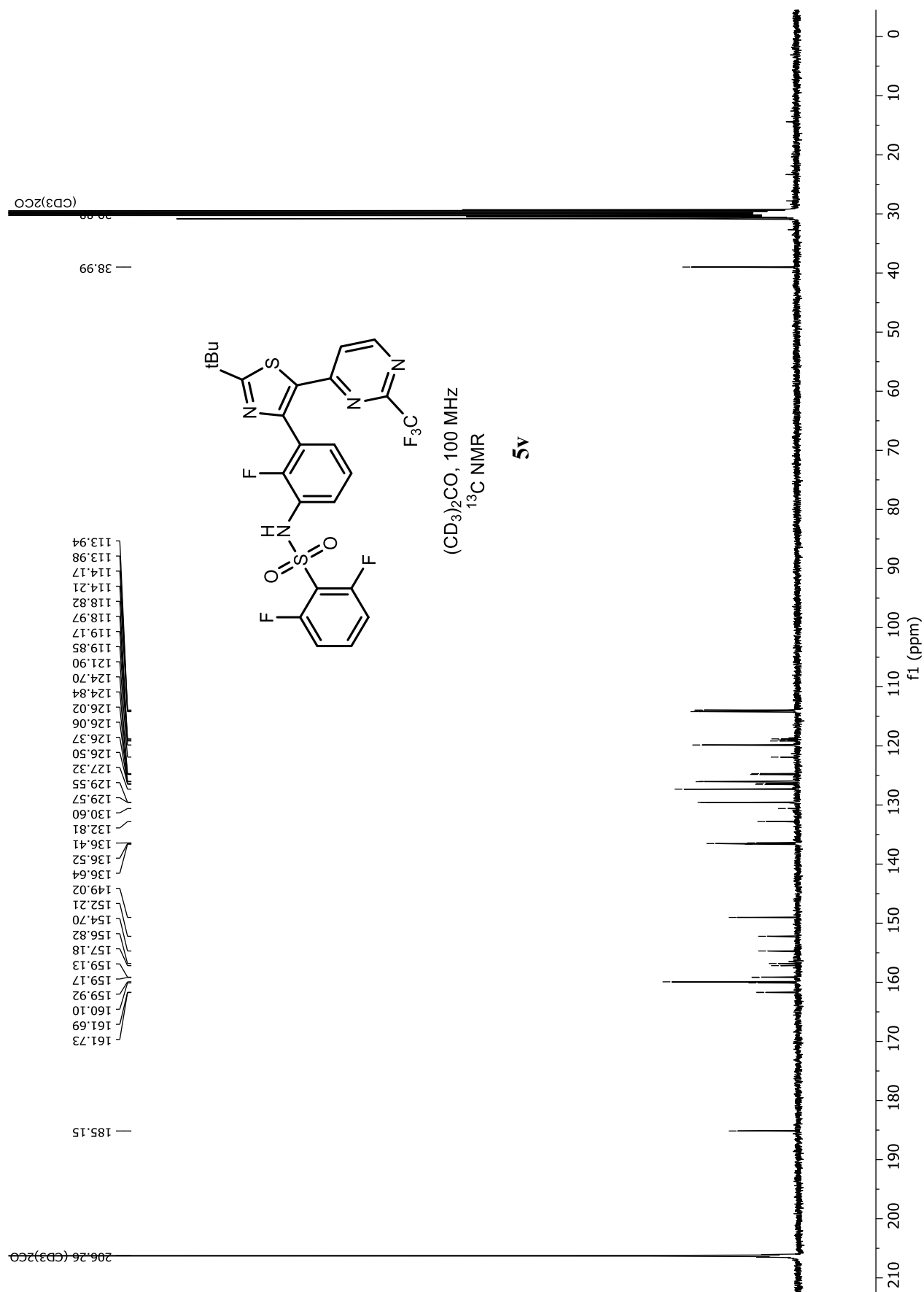
CDCl₃, 375 MHz

¹⁹F NMR

5u

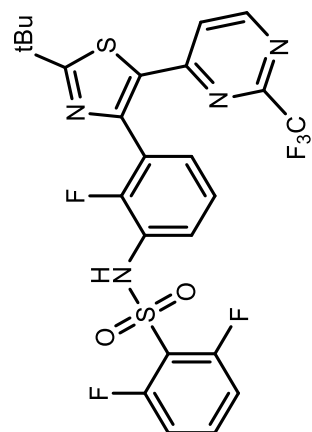






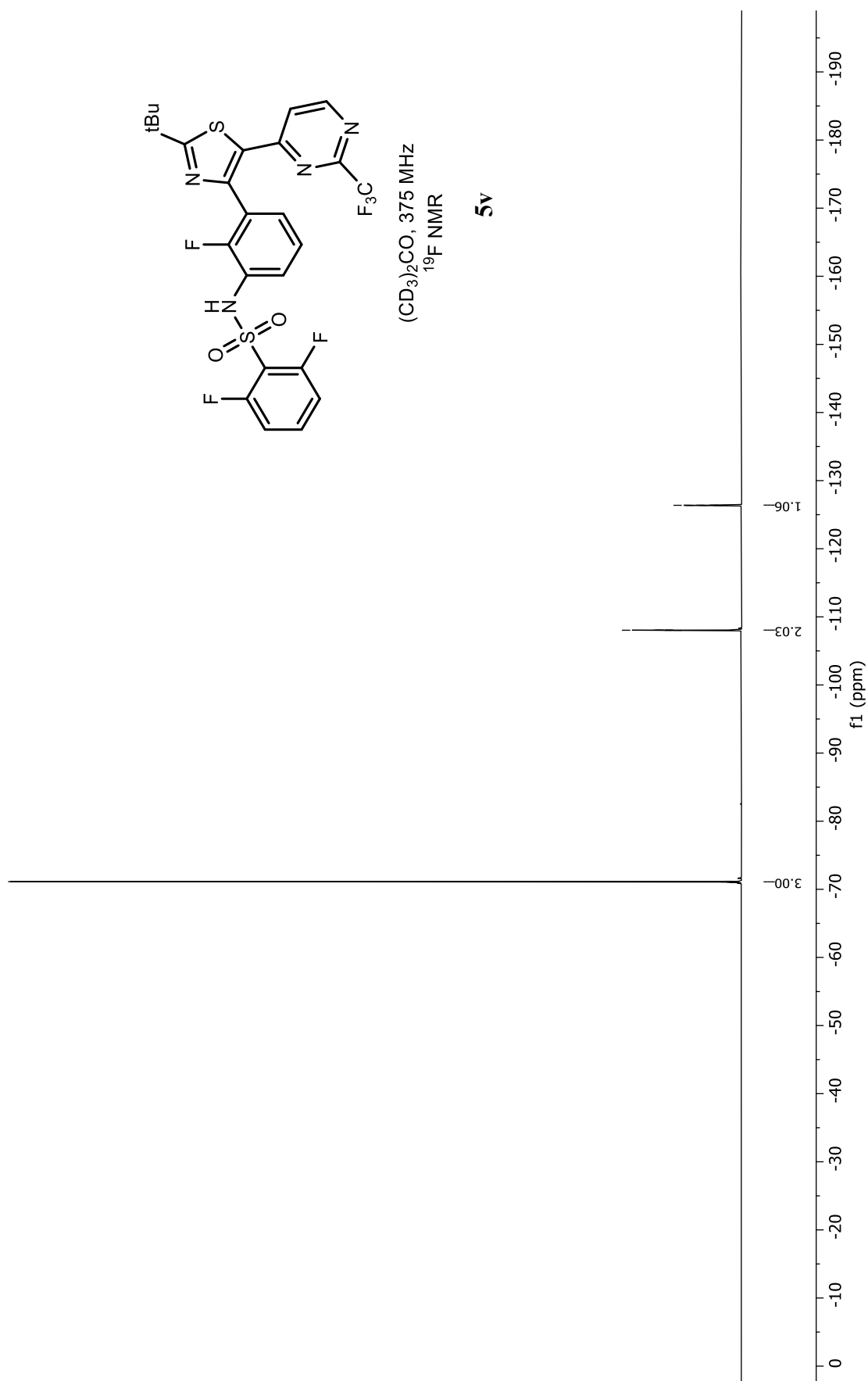
-108.01
-108.02
-108.03
-108.04
-108.04
-108.05
-108.06
-126.35
-126.36
-126.37
-126.37
-126.38
-126.39
-126.40

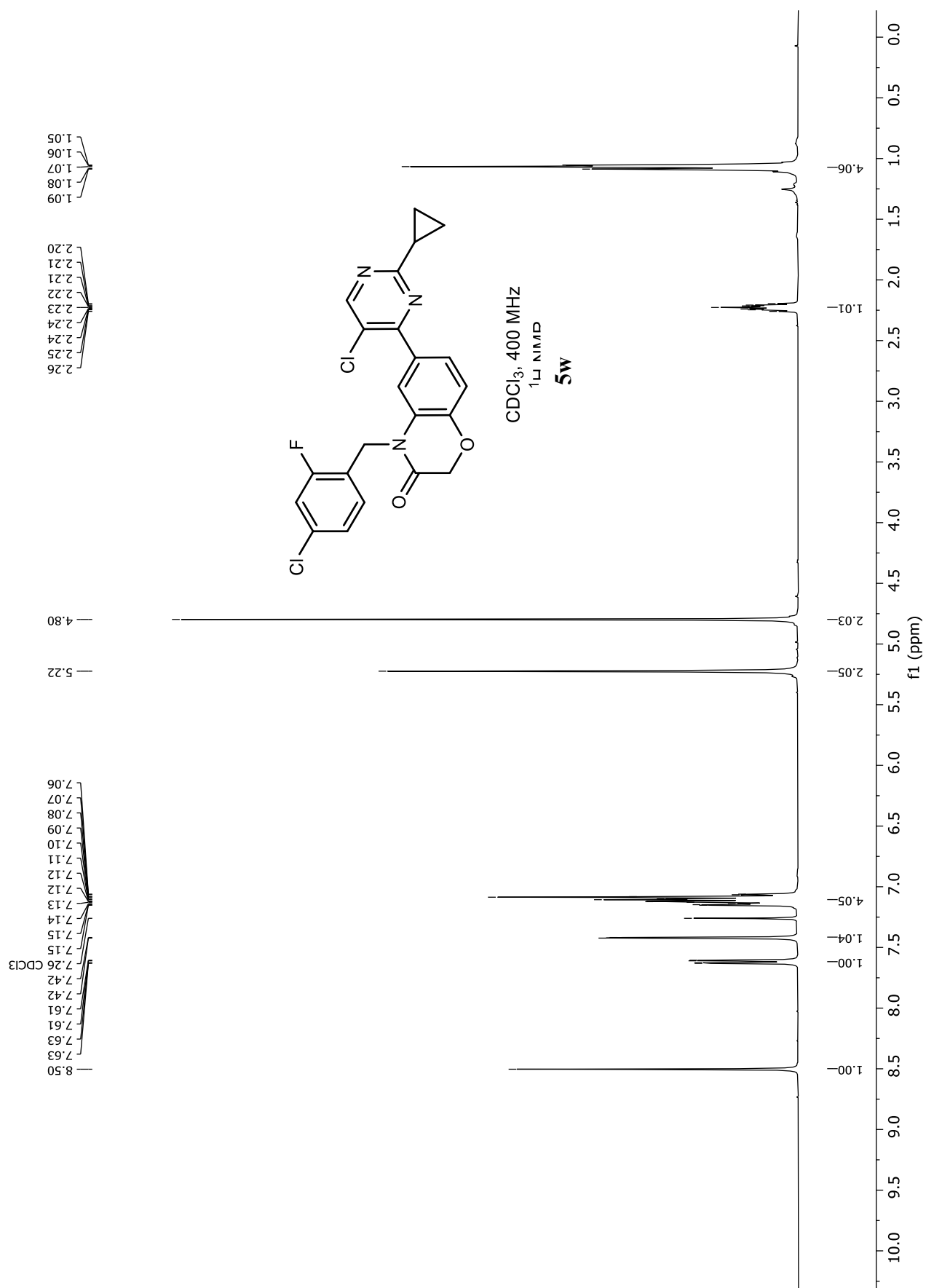
-70.98
-71.04
-71.06
-71.07
-71.08
-71.09
-71.10
-71.12
-71.15
-71.16
-71.17
-71.18

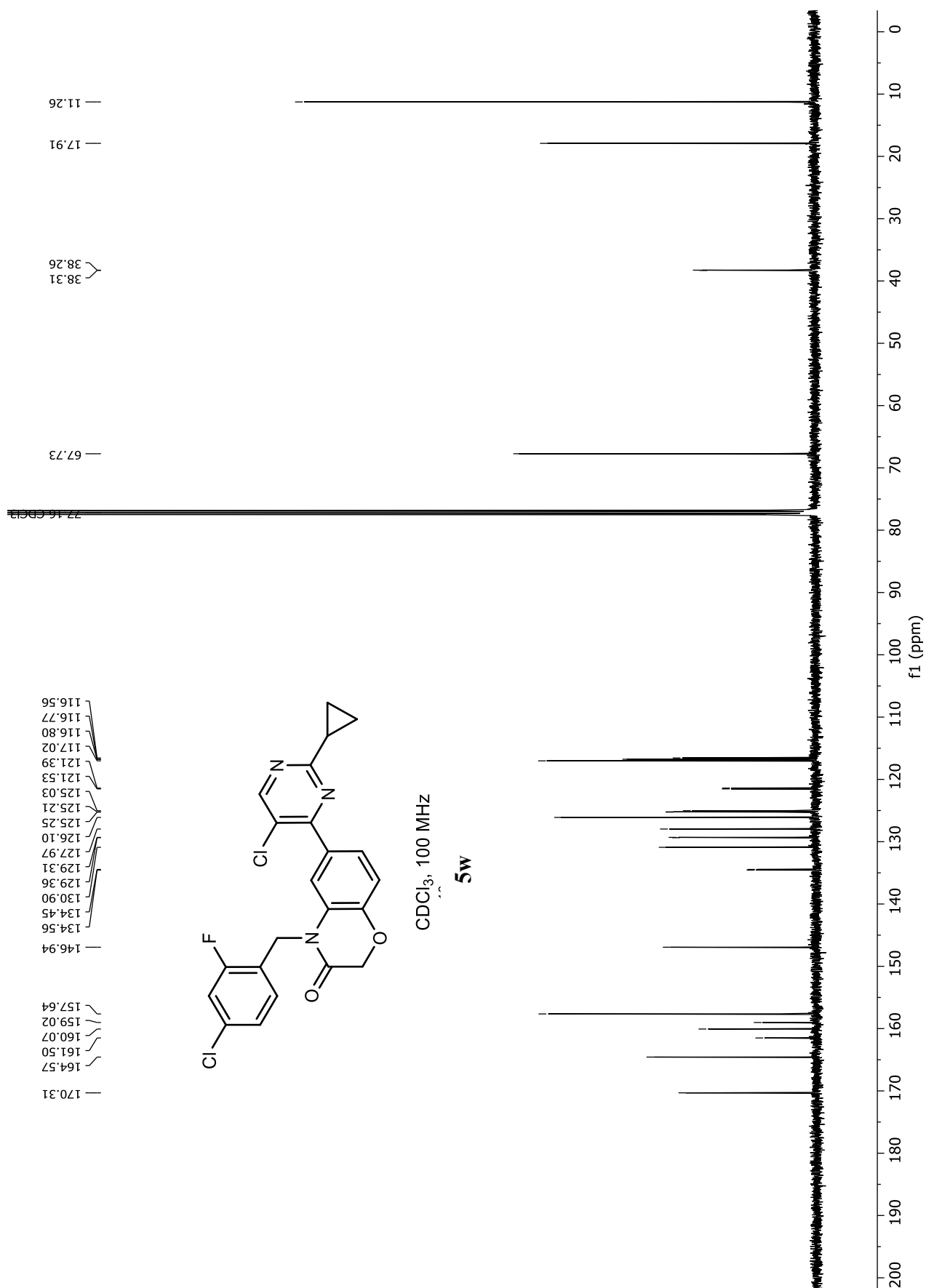


(CD₃)₂CO, 375 MHz
¹⁹F NMR

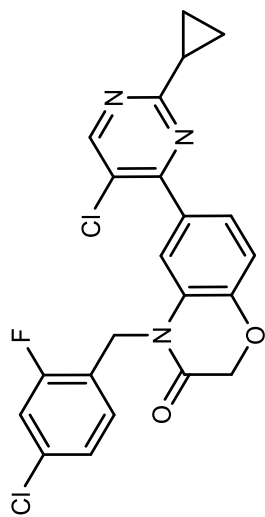
5v





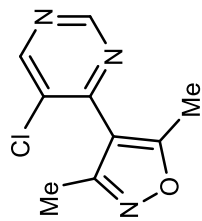


-115.46
-115.48
-115.49
-115.51



CDCI₃, 375 MHz
19F NMR
5w

f1 (ppm)



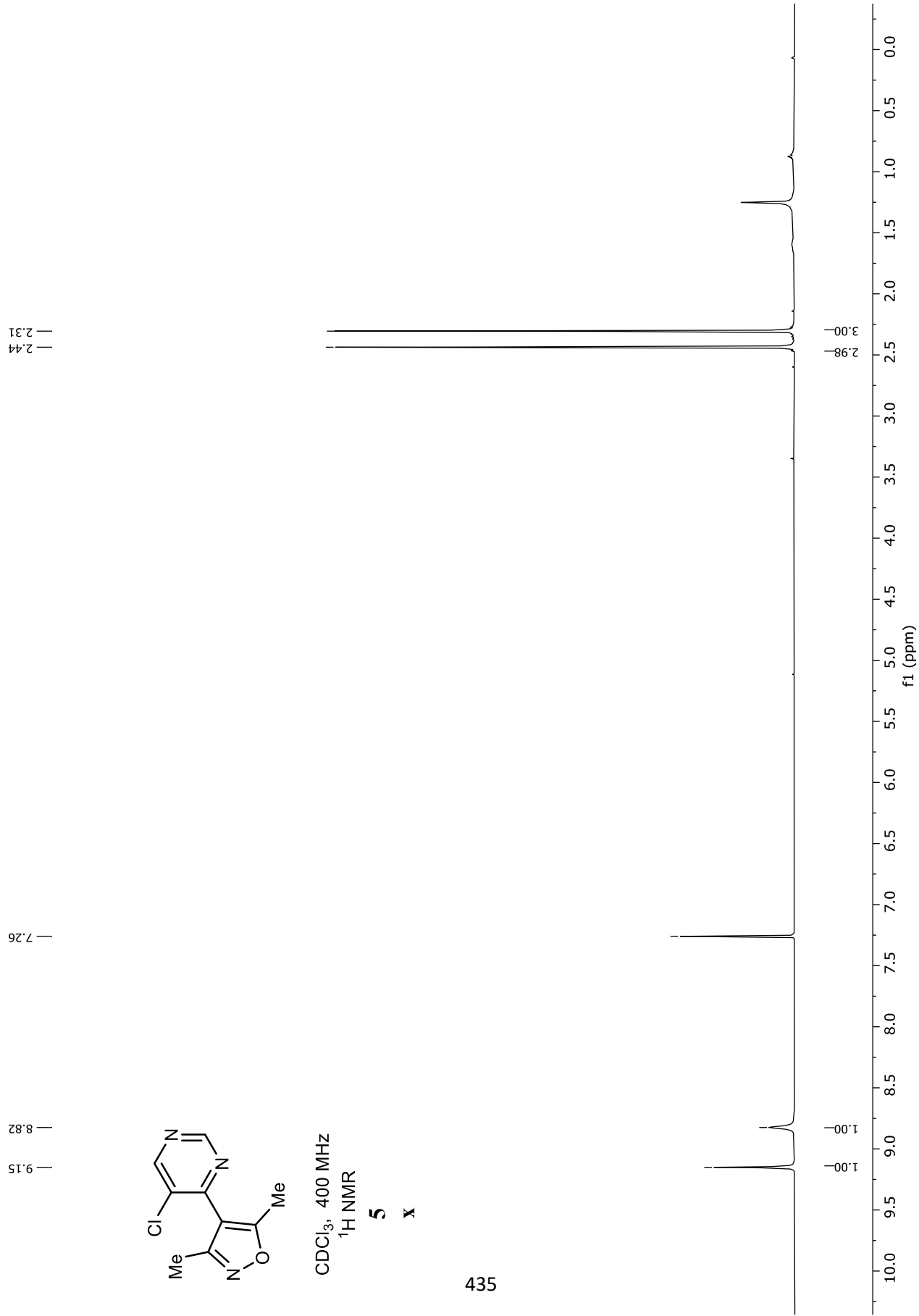
CDCl₃, 400 MHz

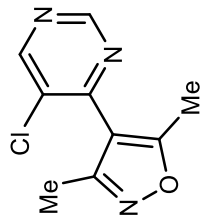
¹H NMR

5

x

435

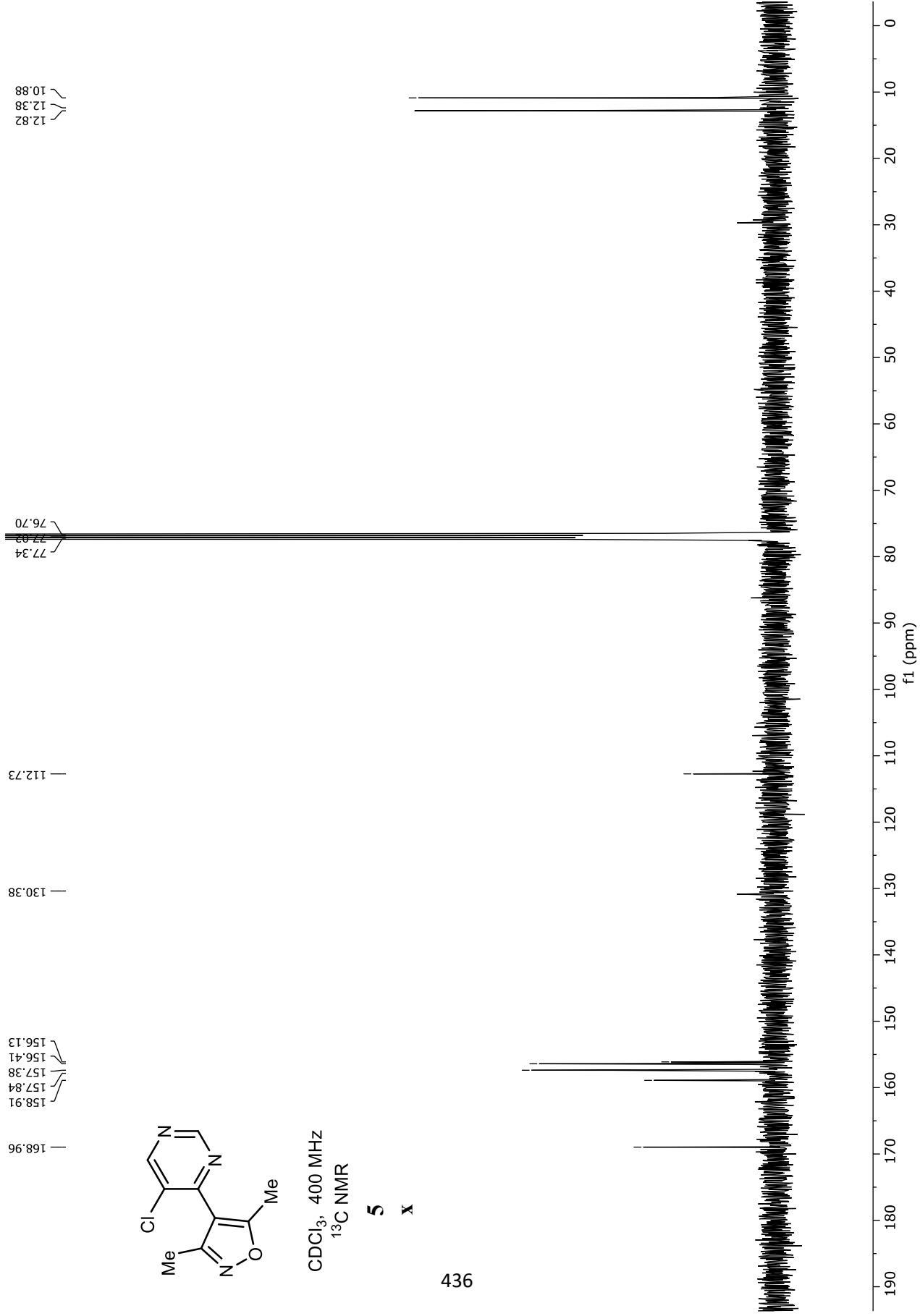


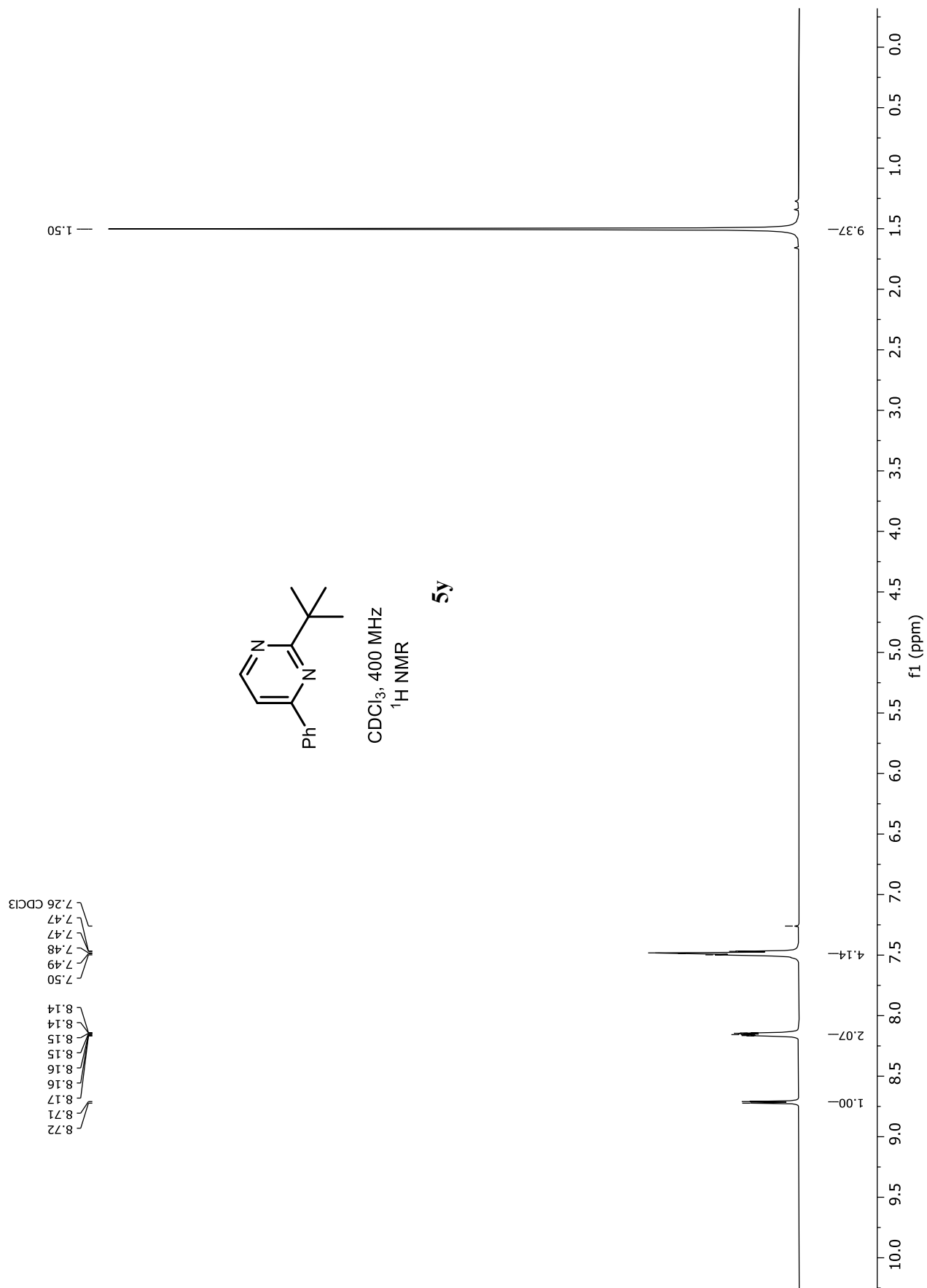


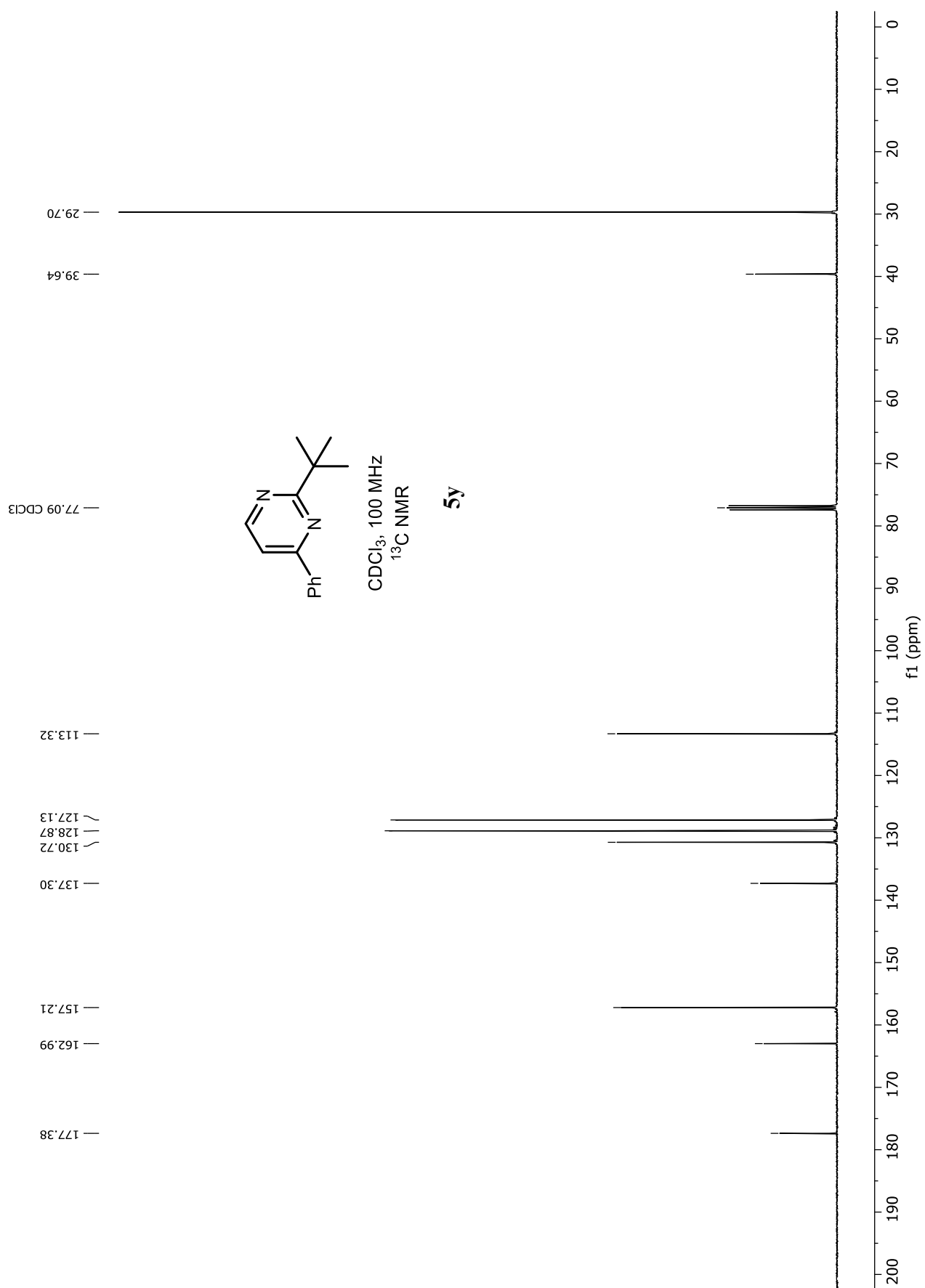
CDCl₃, 400 MHz
¹³C NMR

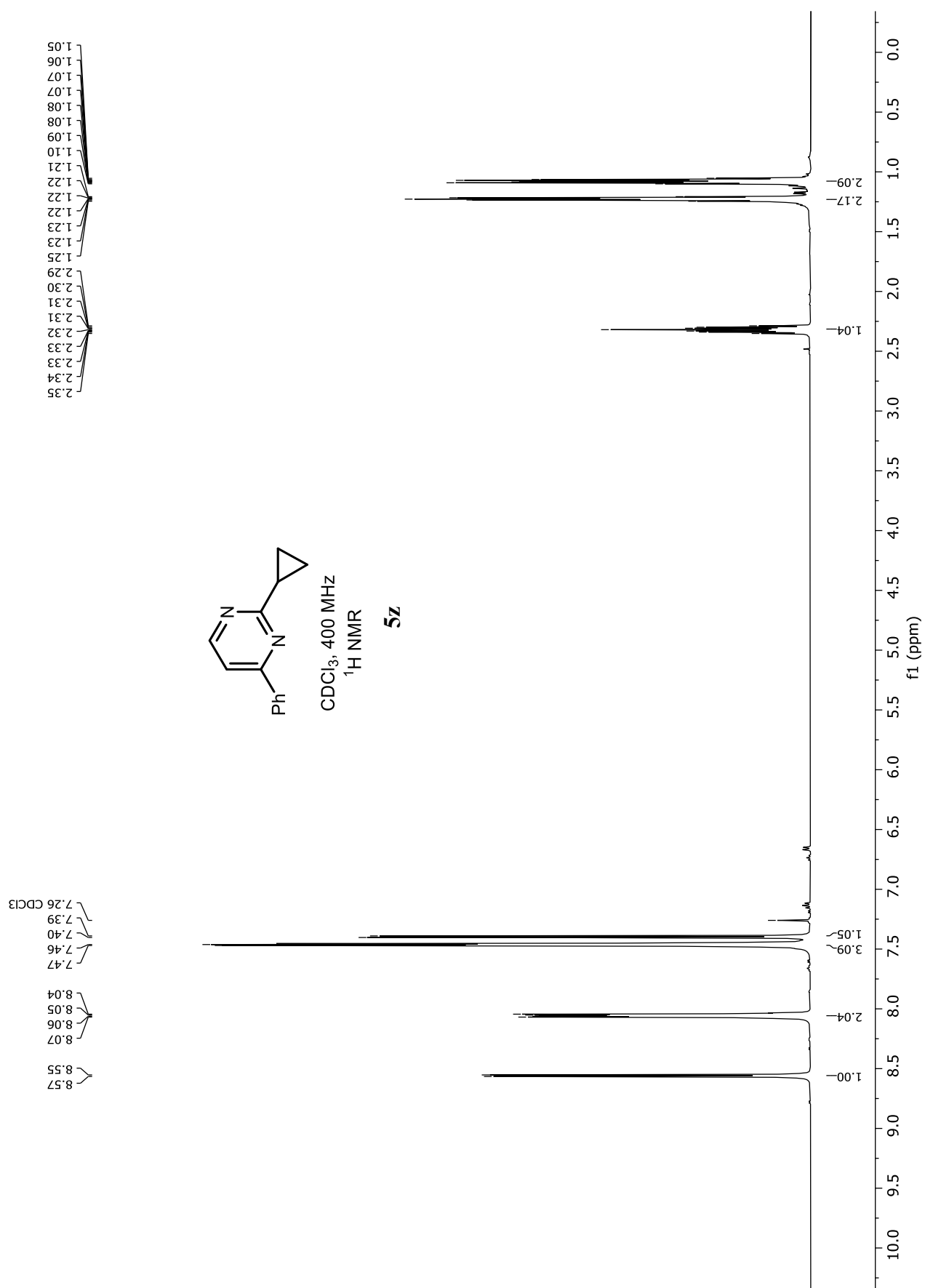
5
 x

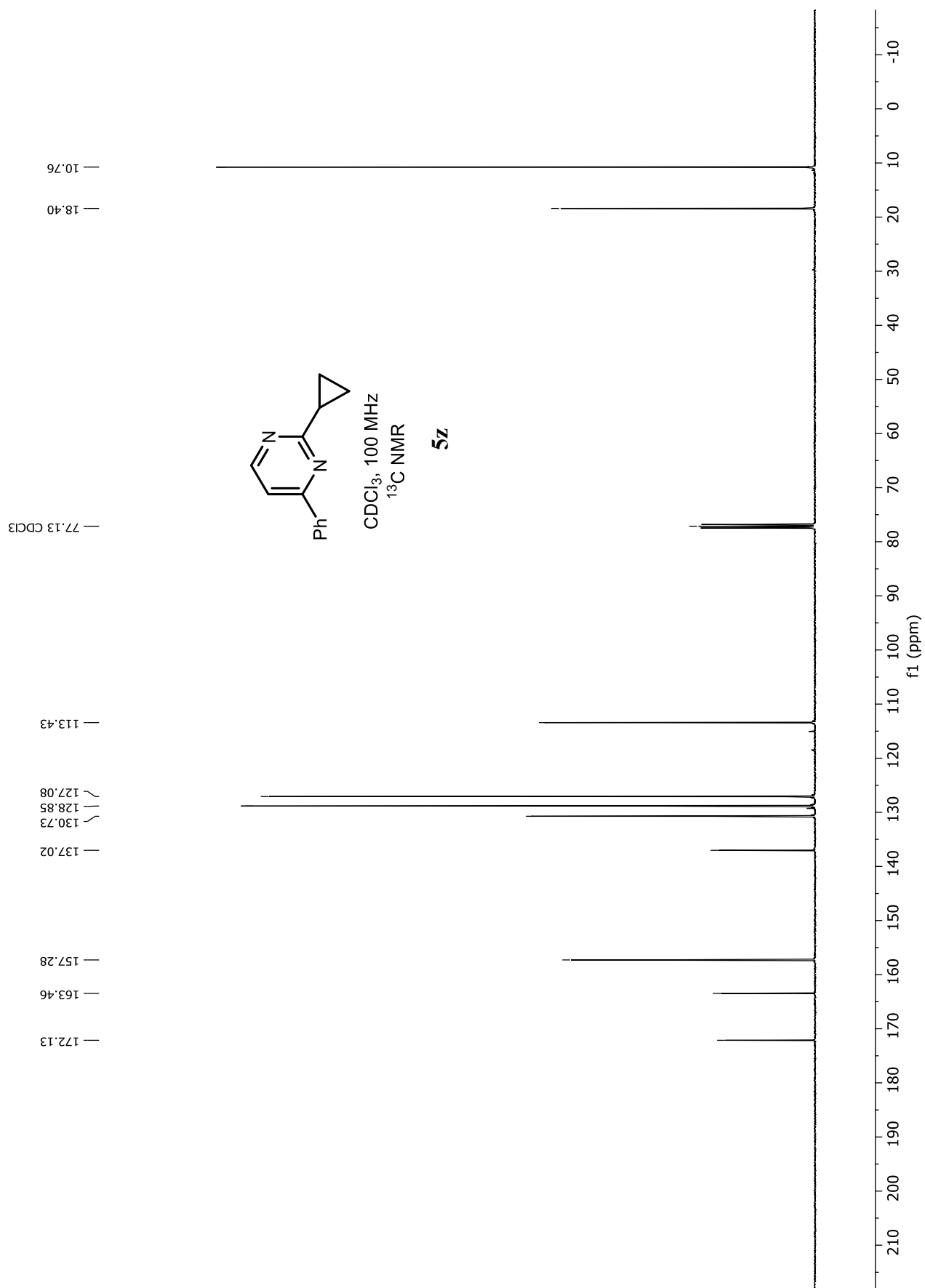
436

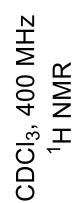




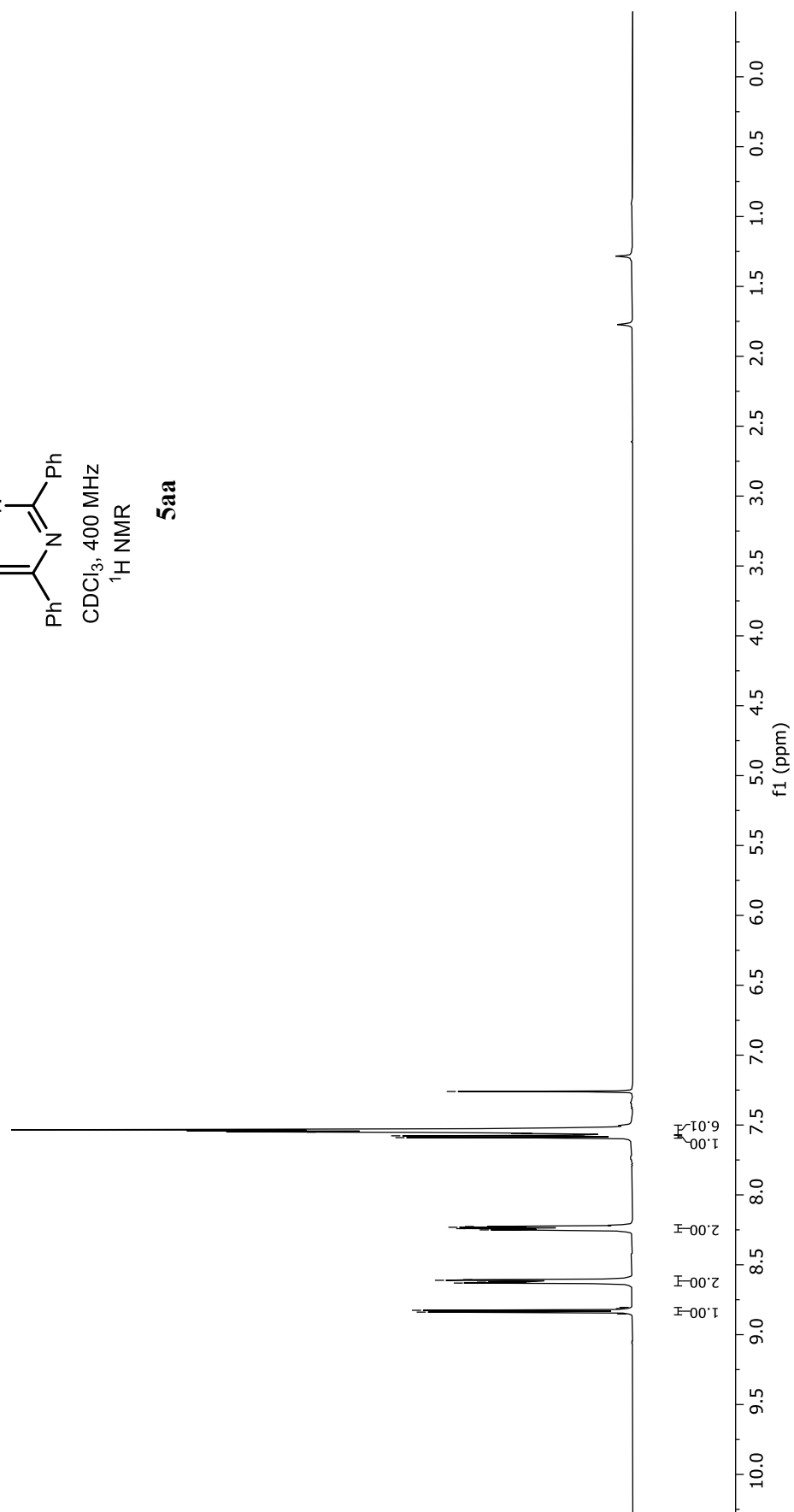
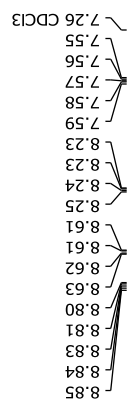


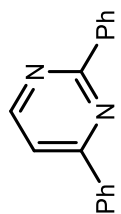






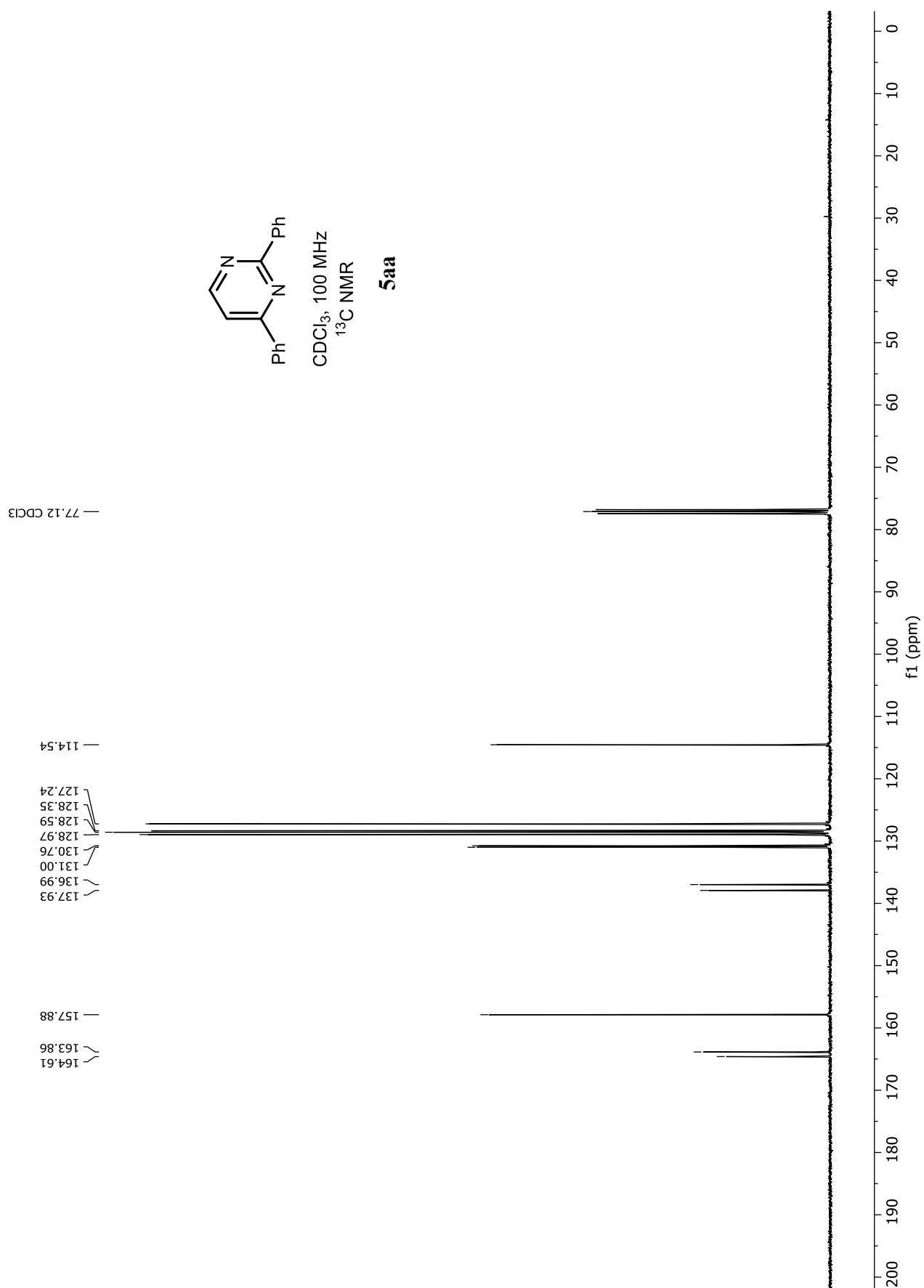
441



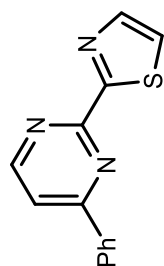


CDCl₃, 100 MHz
¹³C NMR

5aa

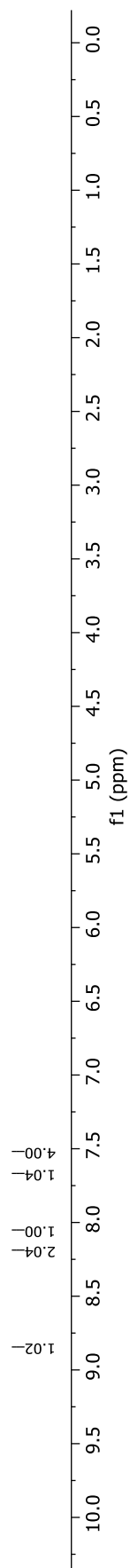


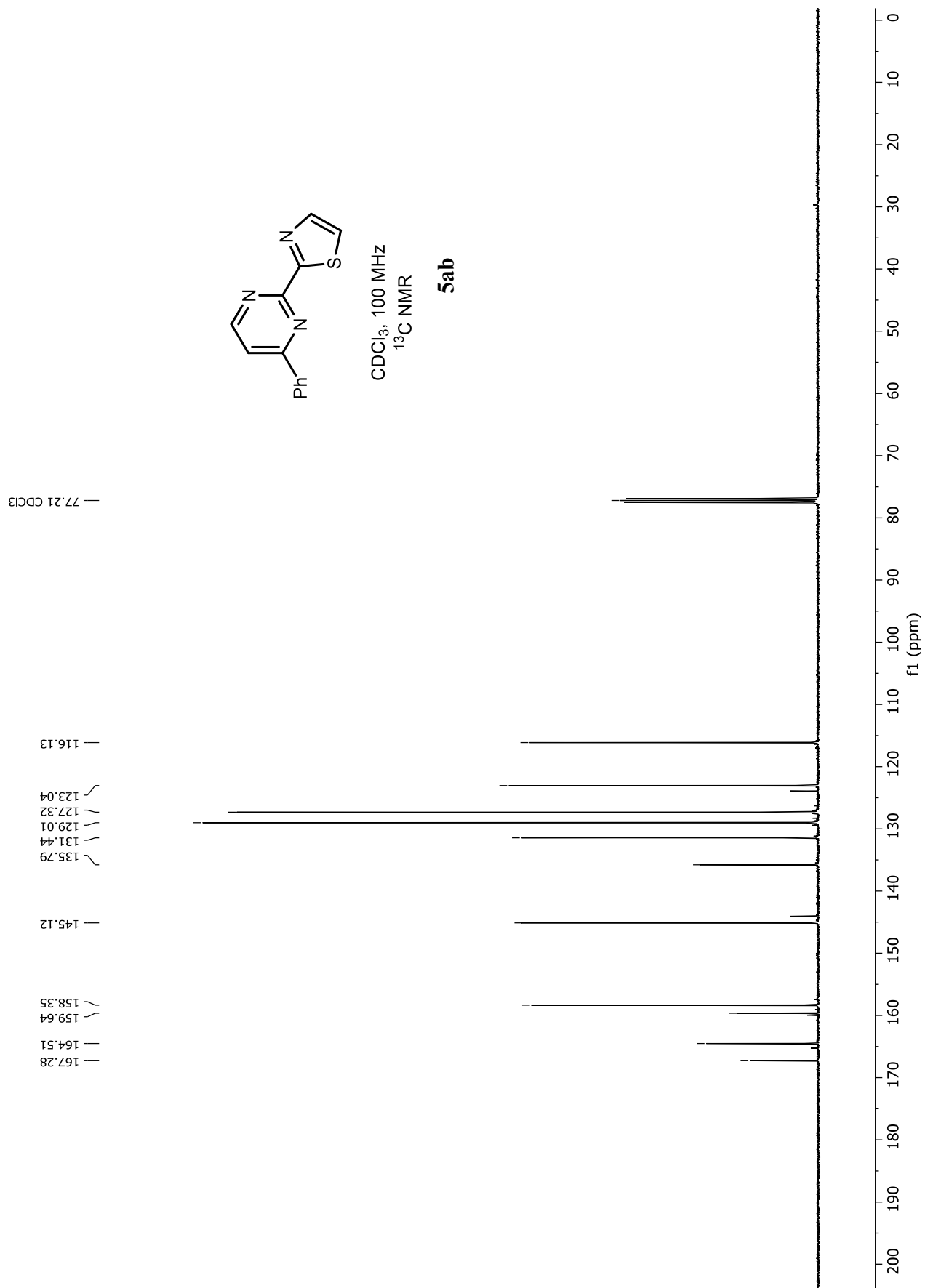
8.85
8.84
8.20
8.19
8.18
8.17
8.06
8.05
7.67
7.66
7.53
7.52
7.51
7.51
7.50
7.26 CDCl₃



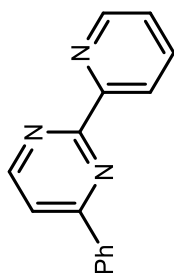
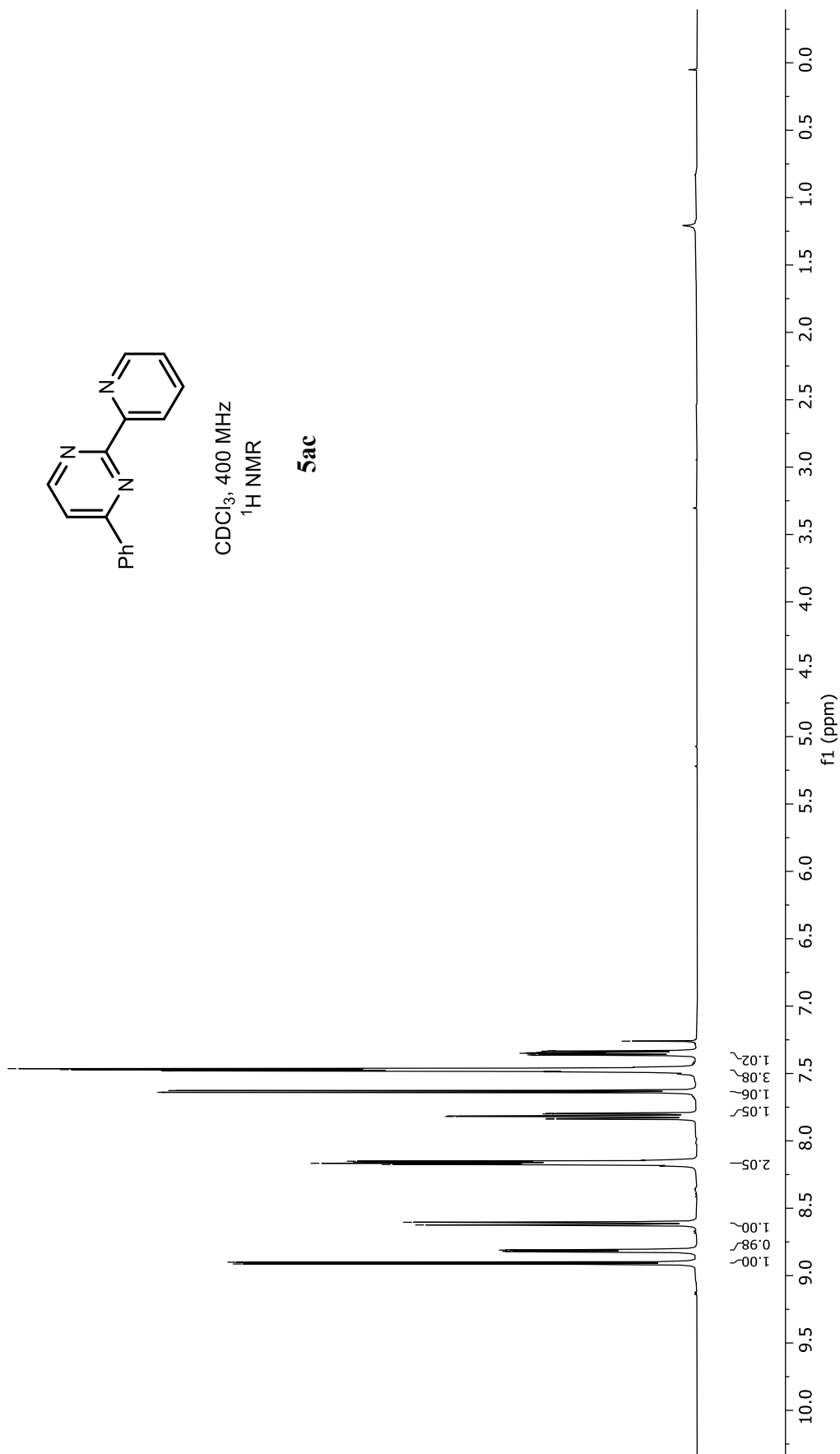
CDCl₃, 400 MHz
¹H NMR

5ab



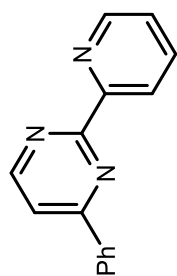


8.91
8.90
8.82
8.82
8.81
8.81
8.81
8.62
8.60
8.18
8.17
8.16
8.16
8.15
7.84
7.83
7.82
7.81
7.80
7.80
7.64
7.63
7.48
7.47
7.46
7.37
7.36
7.35
7.35
7.34
7.33
7.33
7.26 CDCl₃



CDCl₃, 400 MHz
¹H NMR

5ac



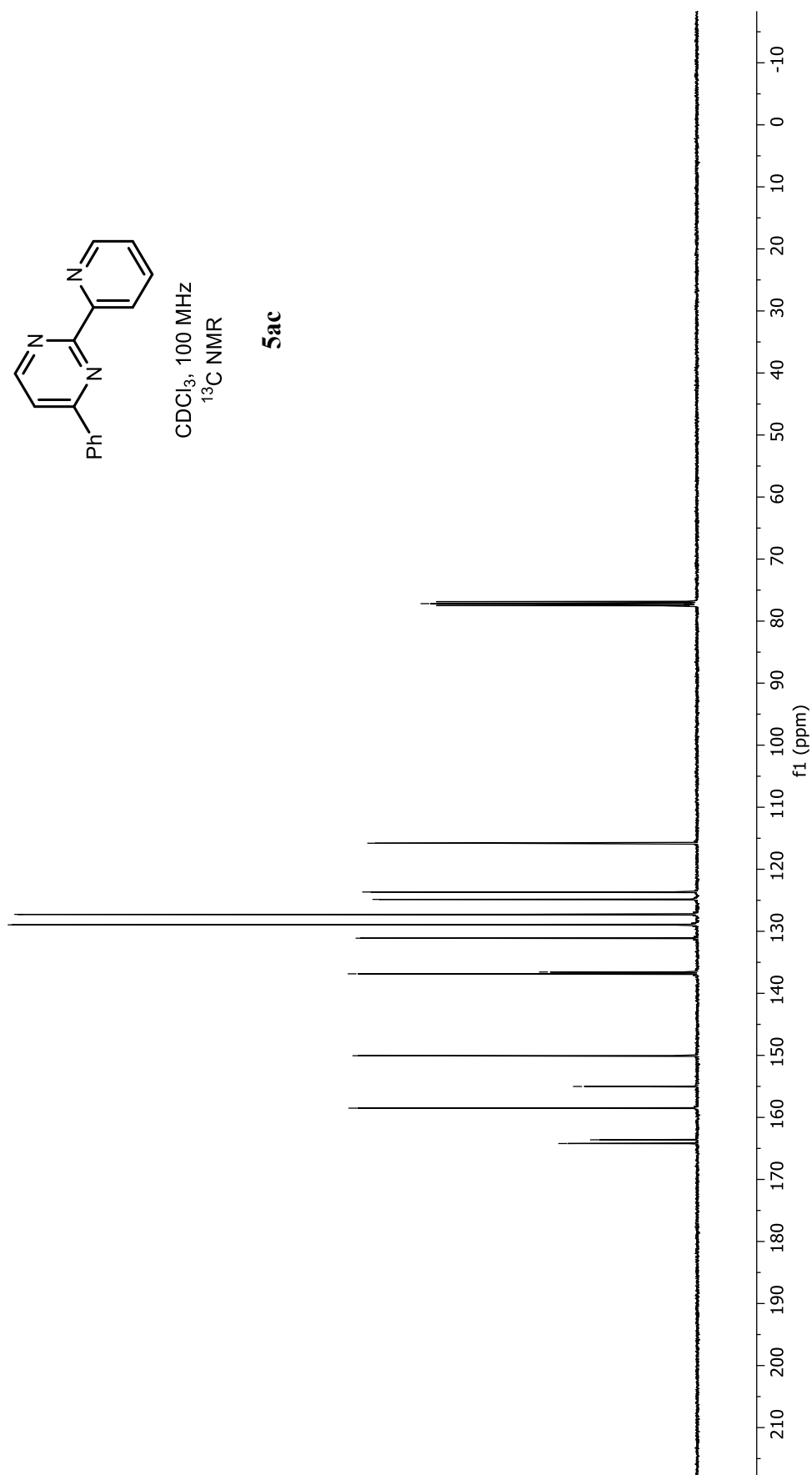
CDCl₃, 100 MHz
¹³C NMR

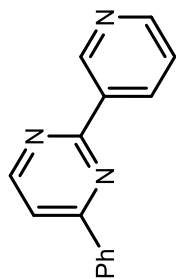
5ac

— 77.18 CDCl₃

115.80
 123.66
 124.86
 127.27
 128.96
 131.11
 136.56
 136.85

150.06
 155.01
 158.51
 163.61
 164.21

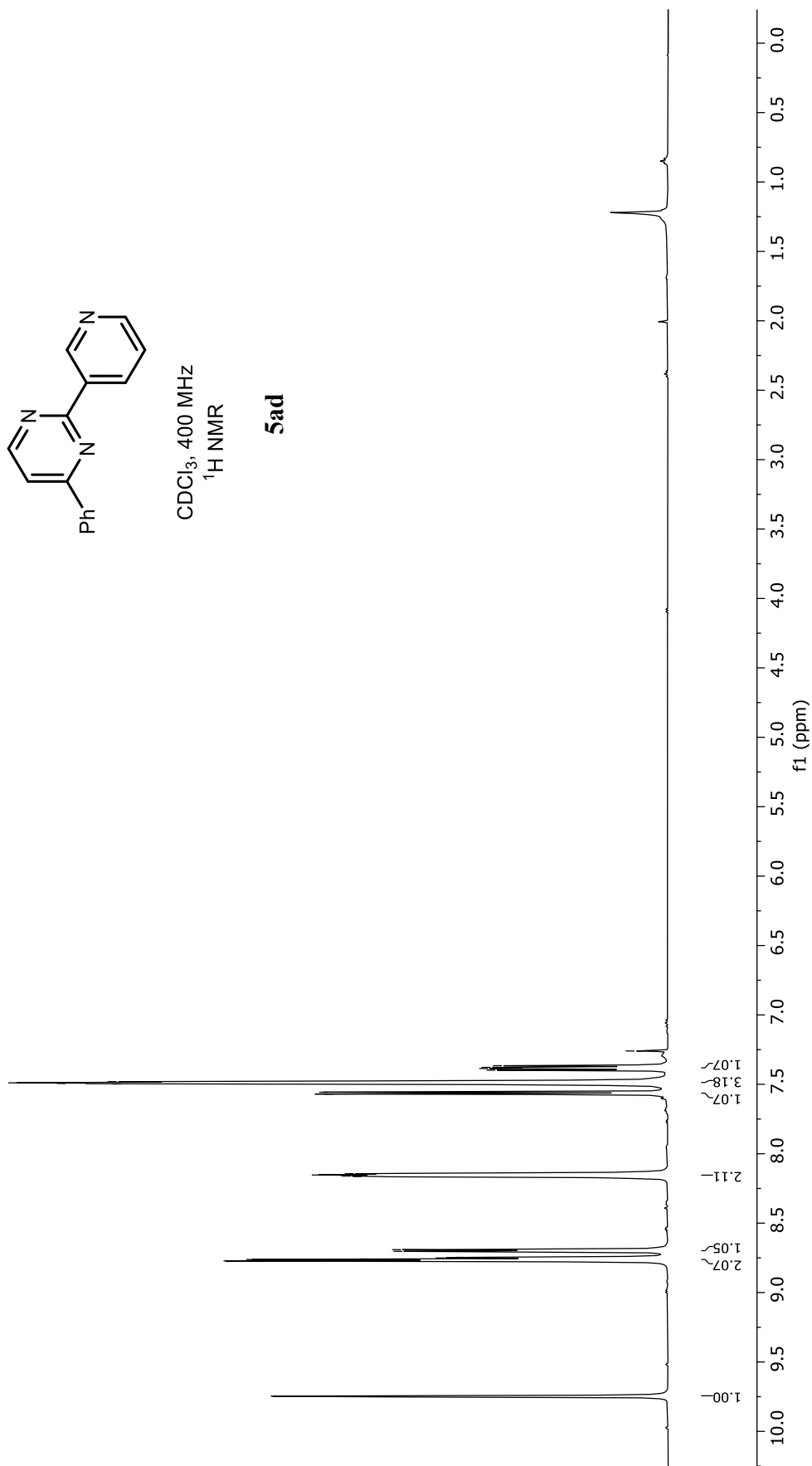


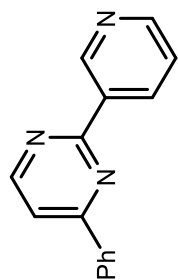


CDCl₃, 400 MHz
¹H NMR

5ad

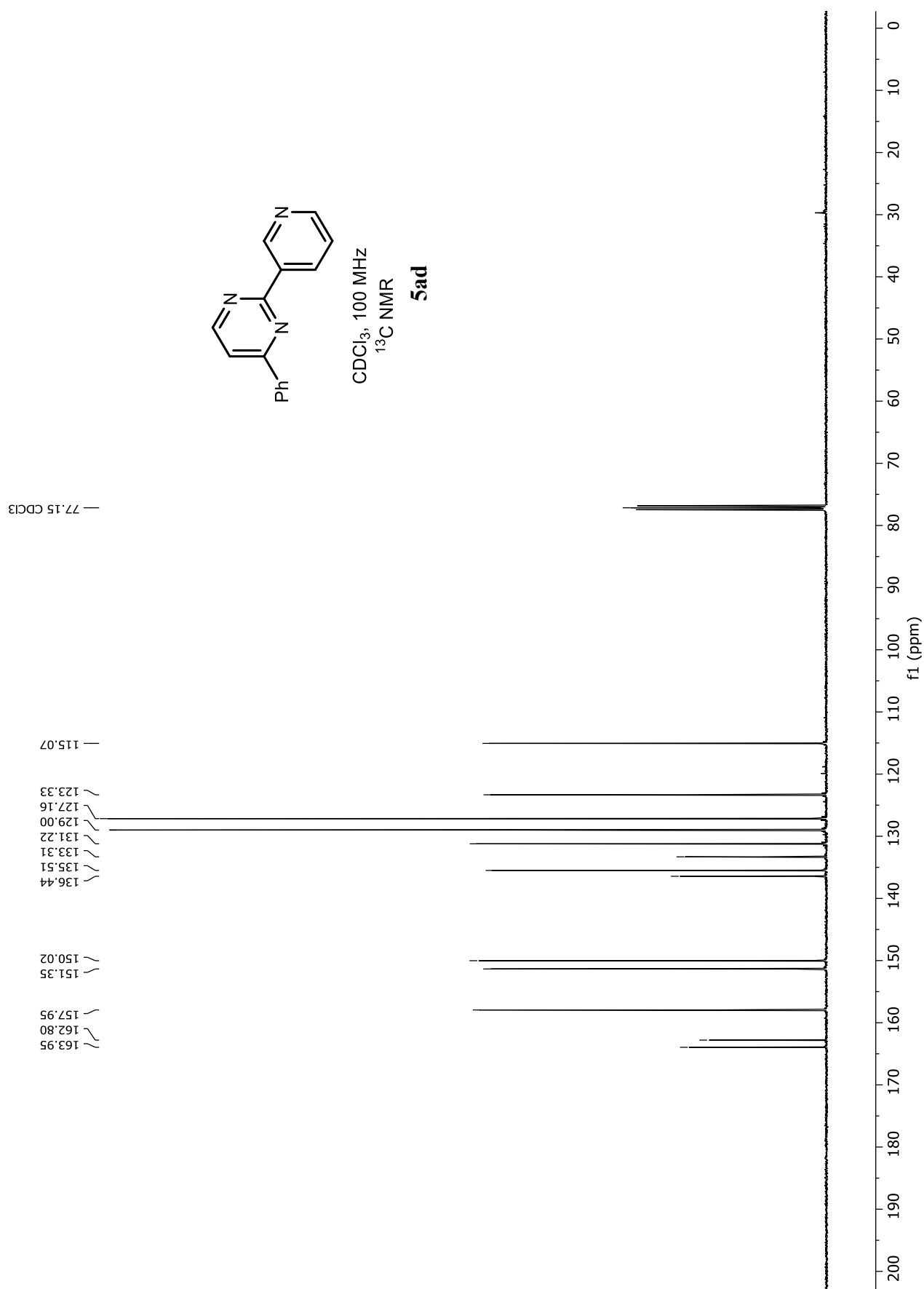
9.75
 8.78
 8.77
 8.76
 8.75
 8.75
 8.70
 8.69
 8.16
 8.16
 8.16
 8.15
 8.15
 8.14
 7.57
 7.56
 7.50
 7.49
 7.49
 7.49
 7.48
 7.40
 7.39
 7.38
 7.37
 7.26 CDCl₃

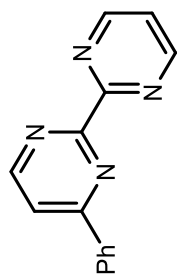




CDCl₃, 100 MHz
¹³C NMR

5ad

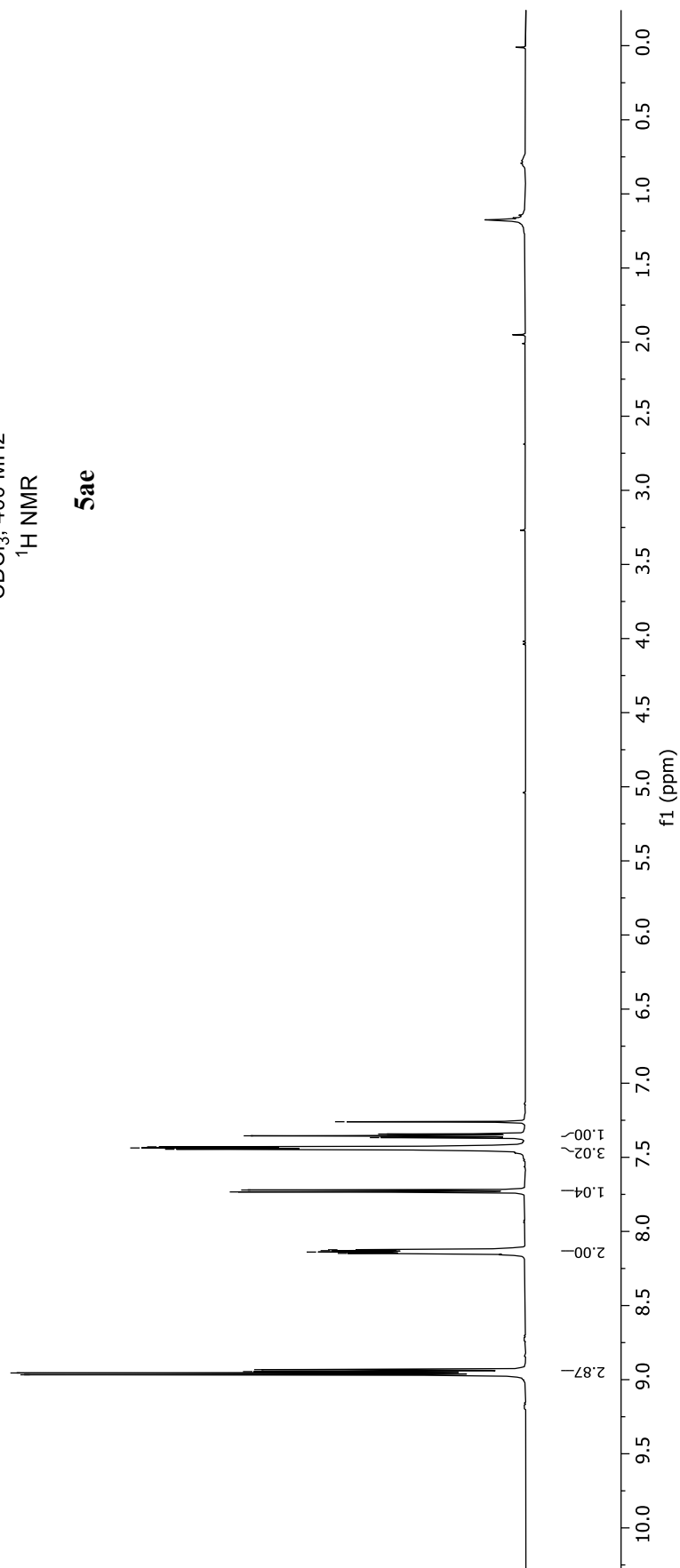


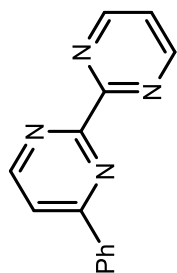


CDCl₃, 400 MHz
¹H NMR

5ae

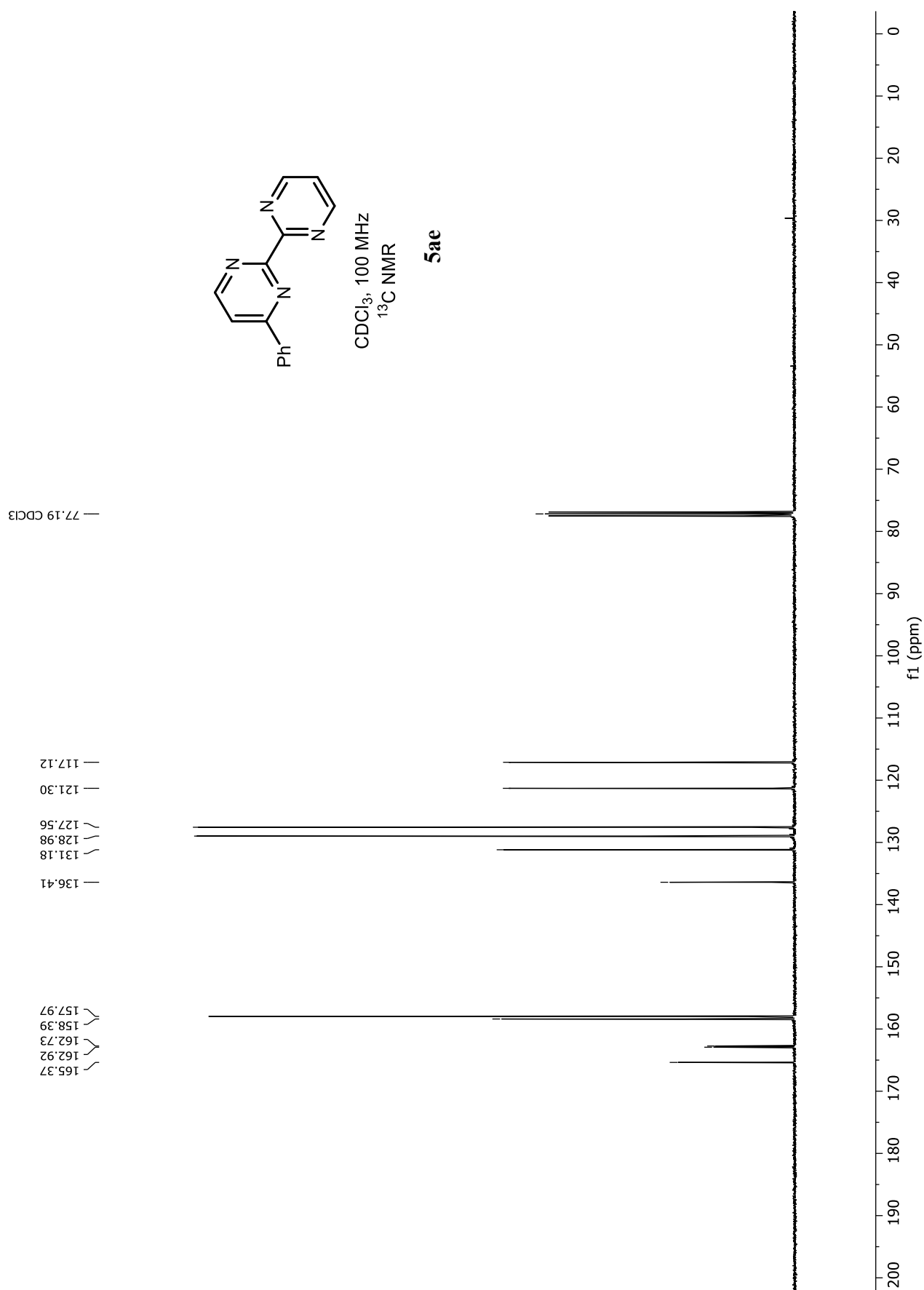
8.97
8.95
8.95
8.93
8.15
8.14
8.13
8.13
8.12
7.73
7.72
7.45
7.44
7.43
7.37
7.35
7.34
7.26 CDCl₃

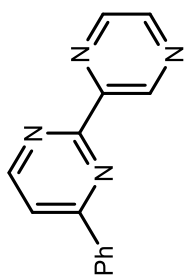




CDCl₃, 100 MHz
¹³C NMR

5ae



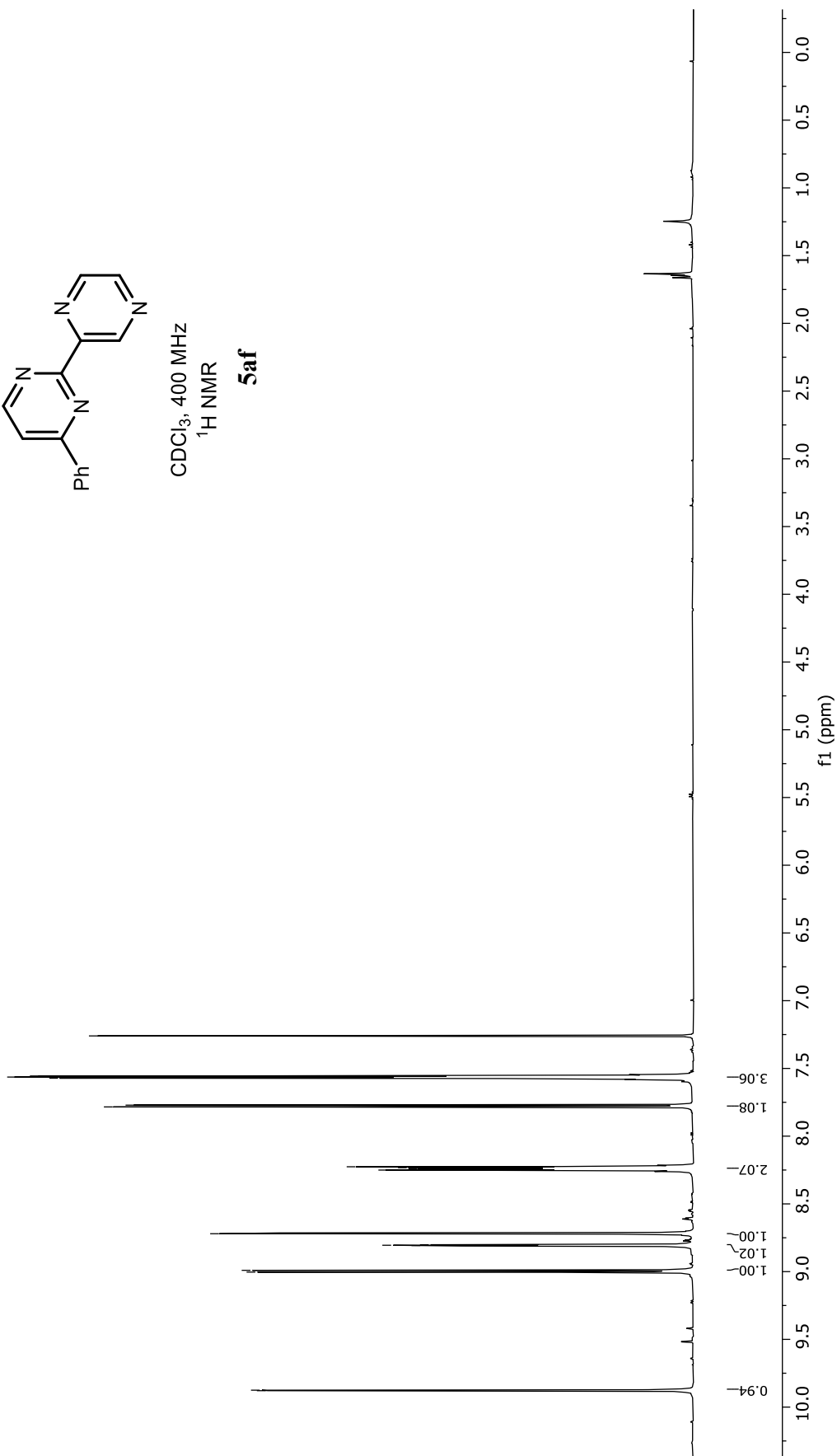


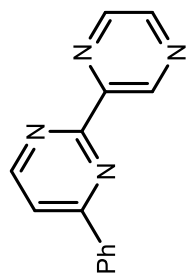
CDCl₃, 400 MHz
¹H NMR

5af

9.00
 8.99
 8.81
 8.81
 8.80
 8.72
 8.25
 8.24
 8.24
 8.23
 8.23
 7.78
 7.77
 7.57
 7.56
 7.56
 — 7.26 CDCl₃

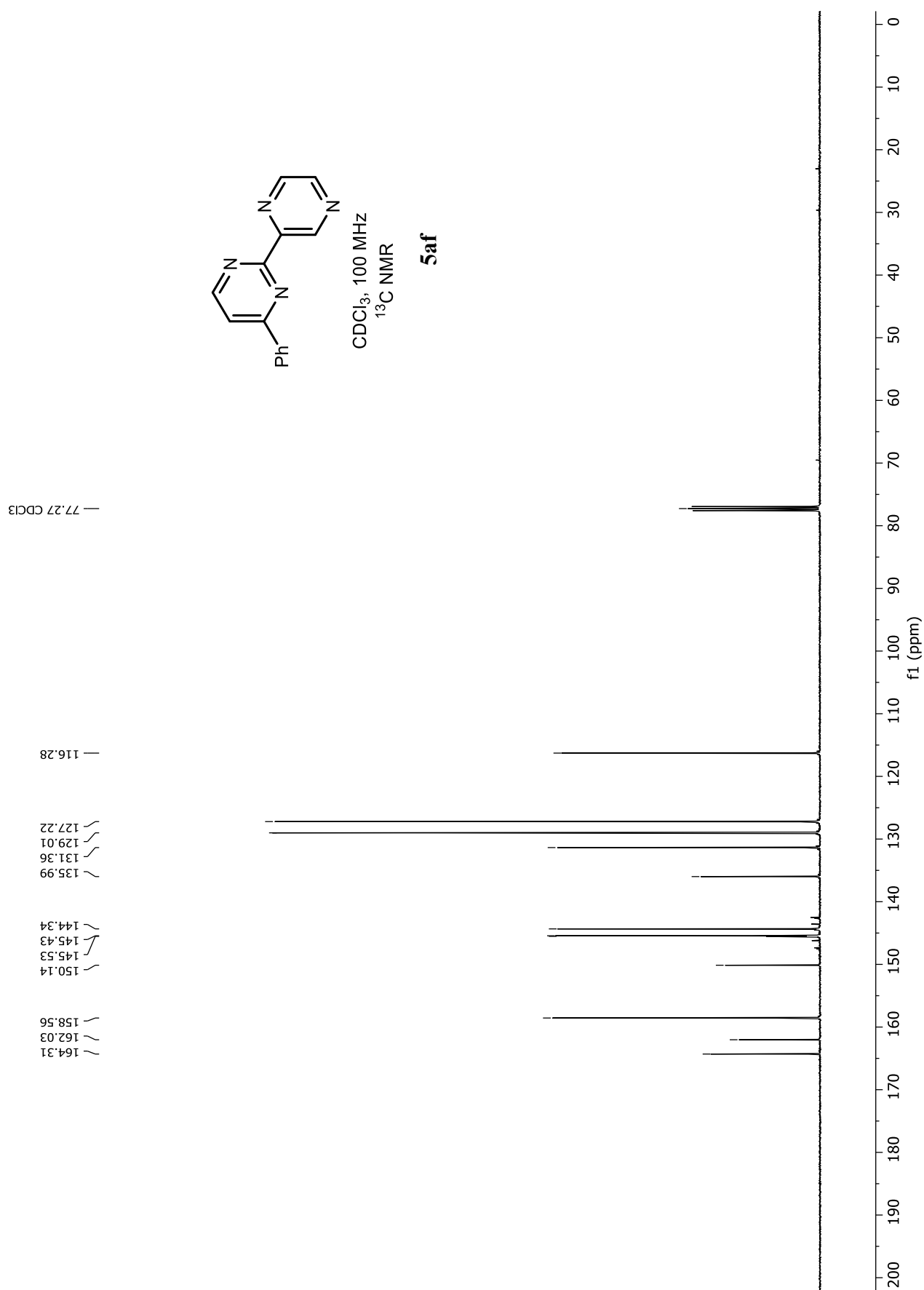
9.88

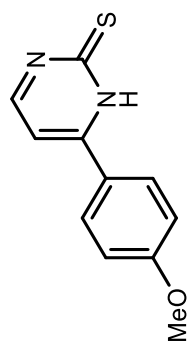




CDCl₃, 100 MHz
¹³C NMR

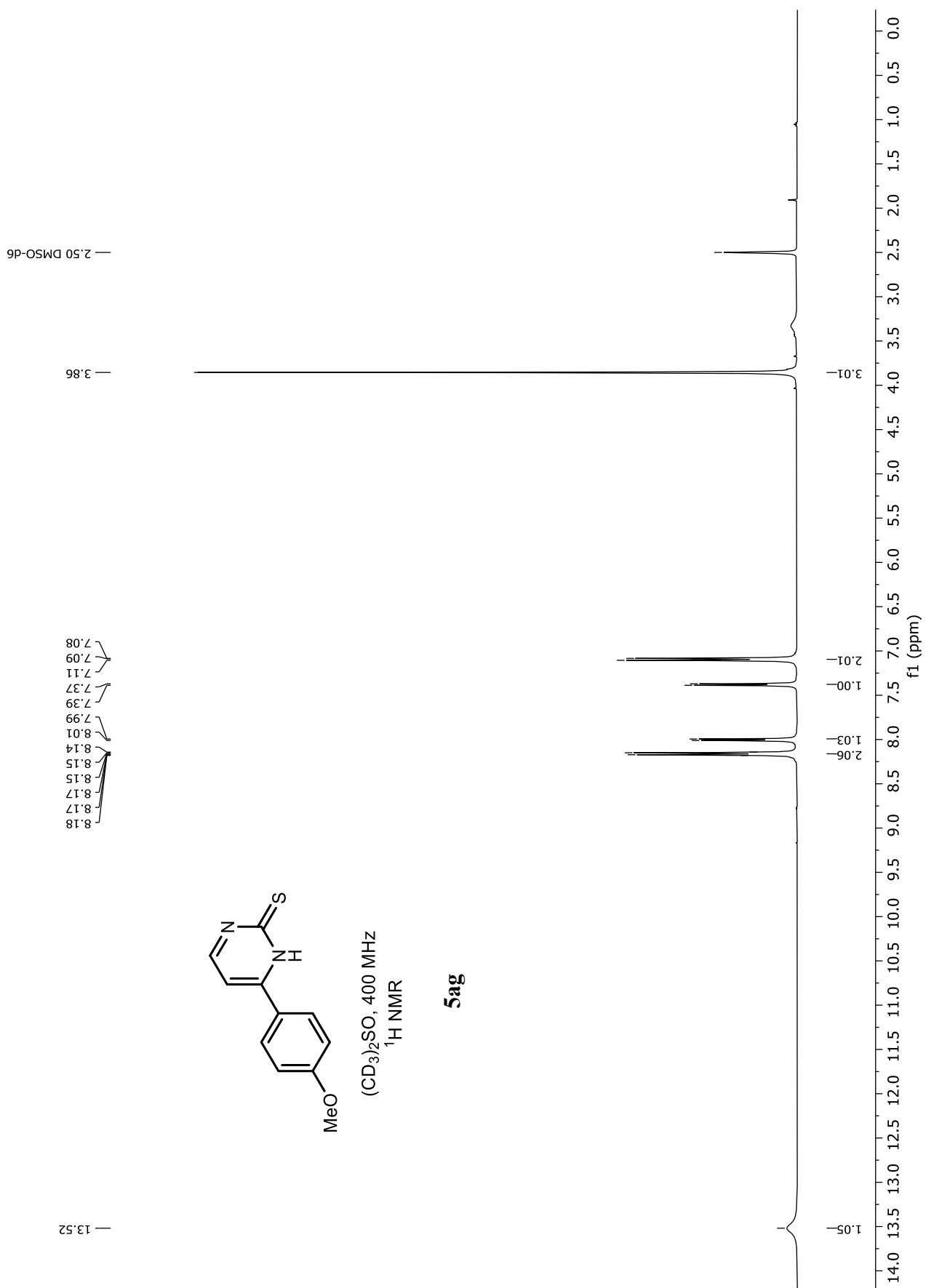
5af

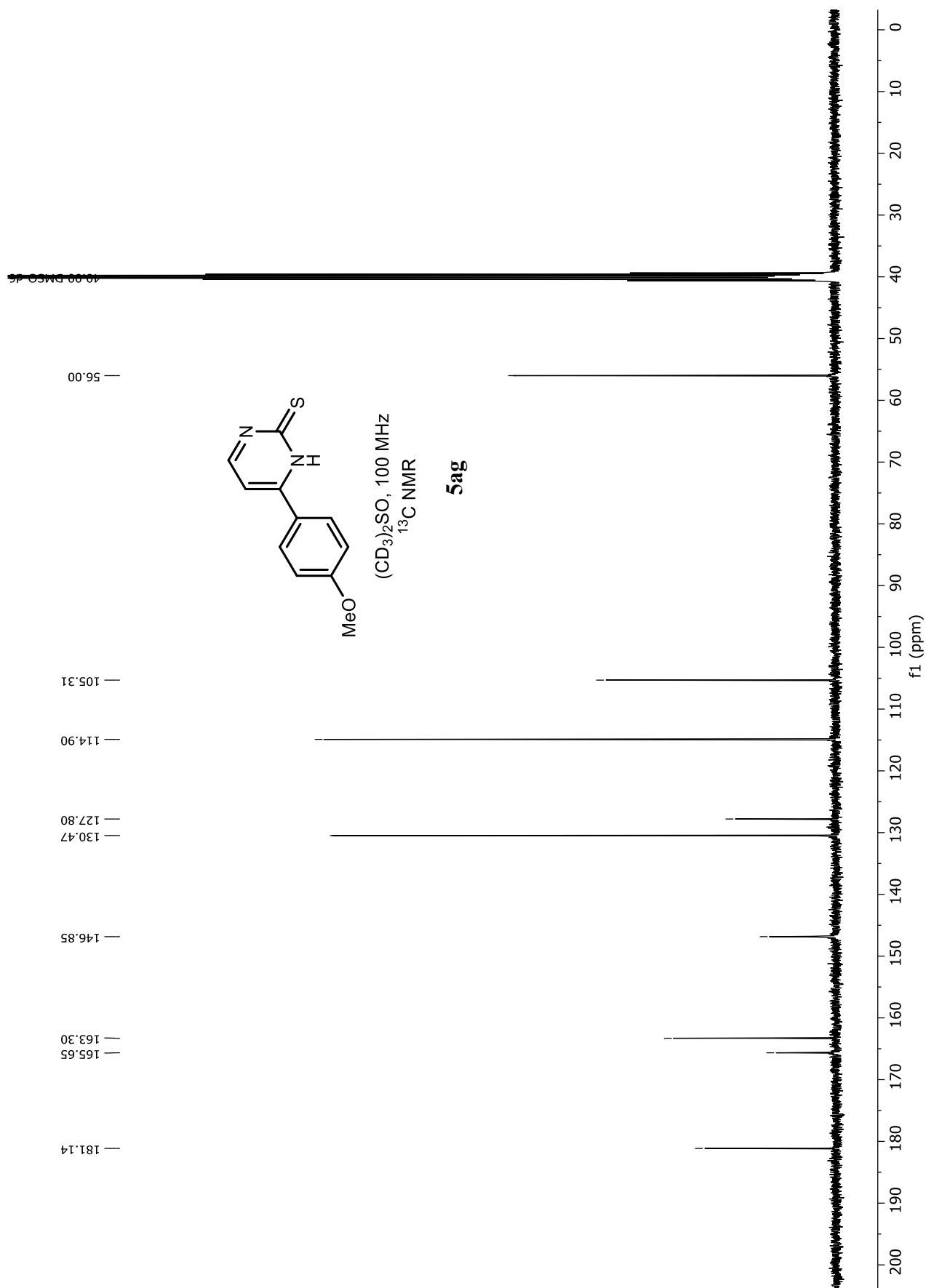


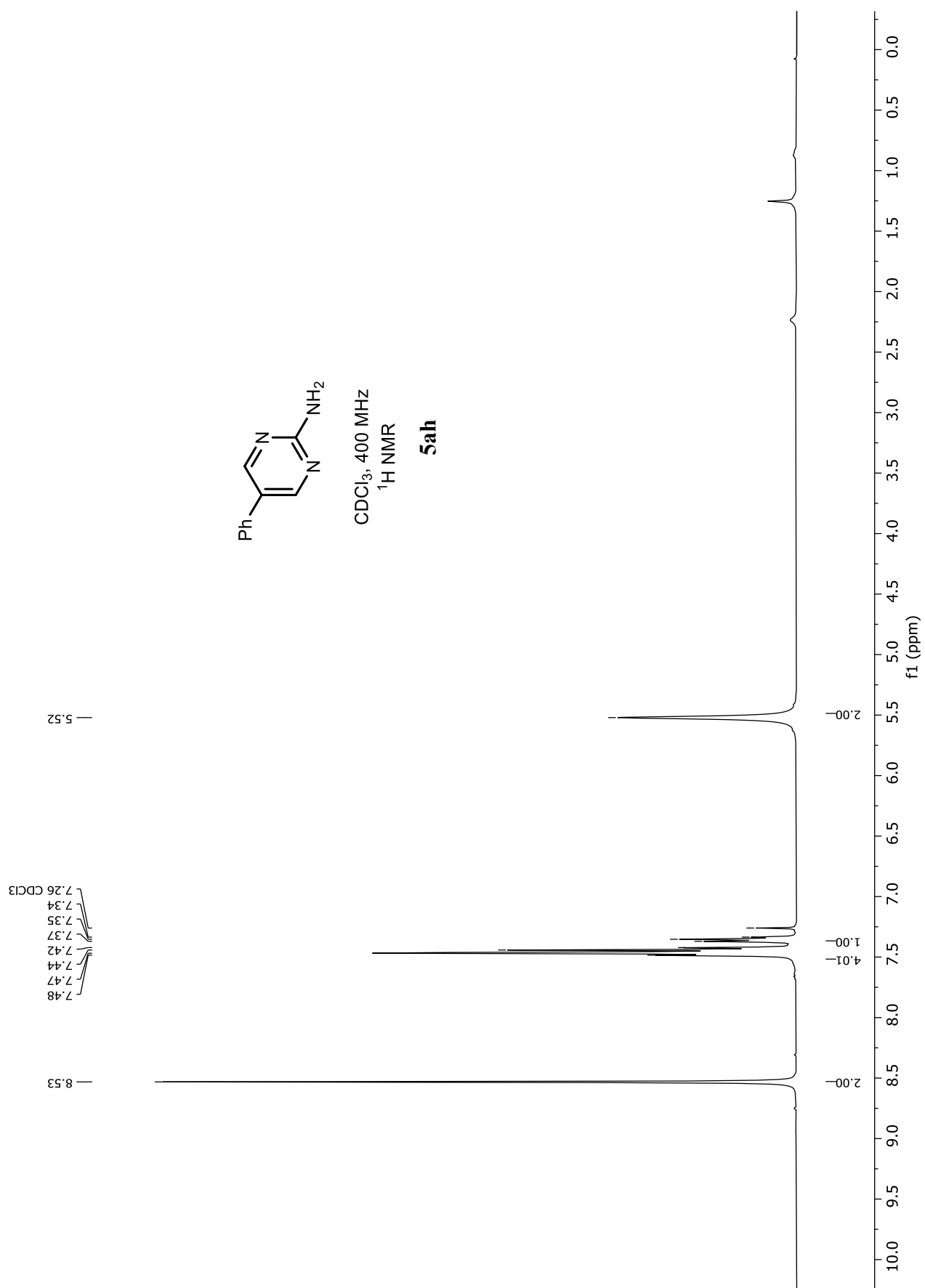


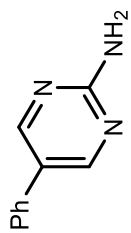
(CD₃)₂SO, 400 MHz
¹H NMR

5ag



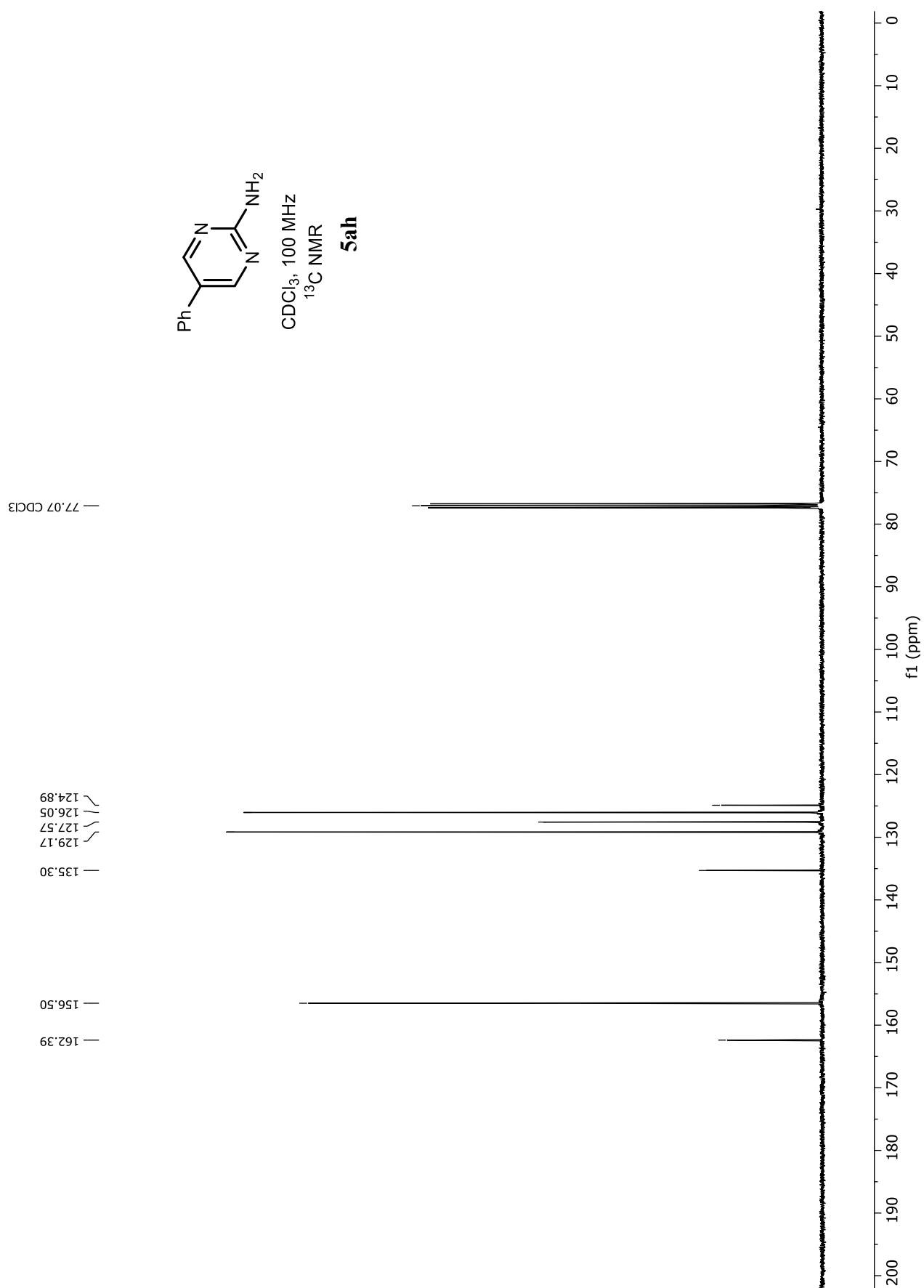


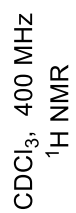




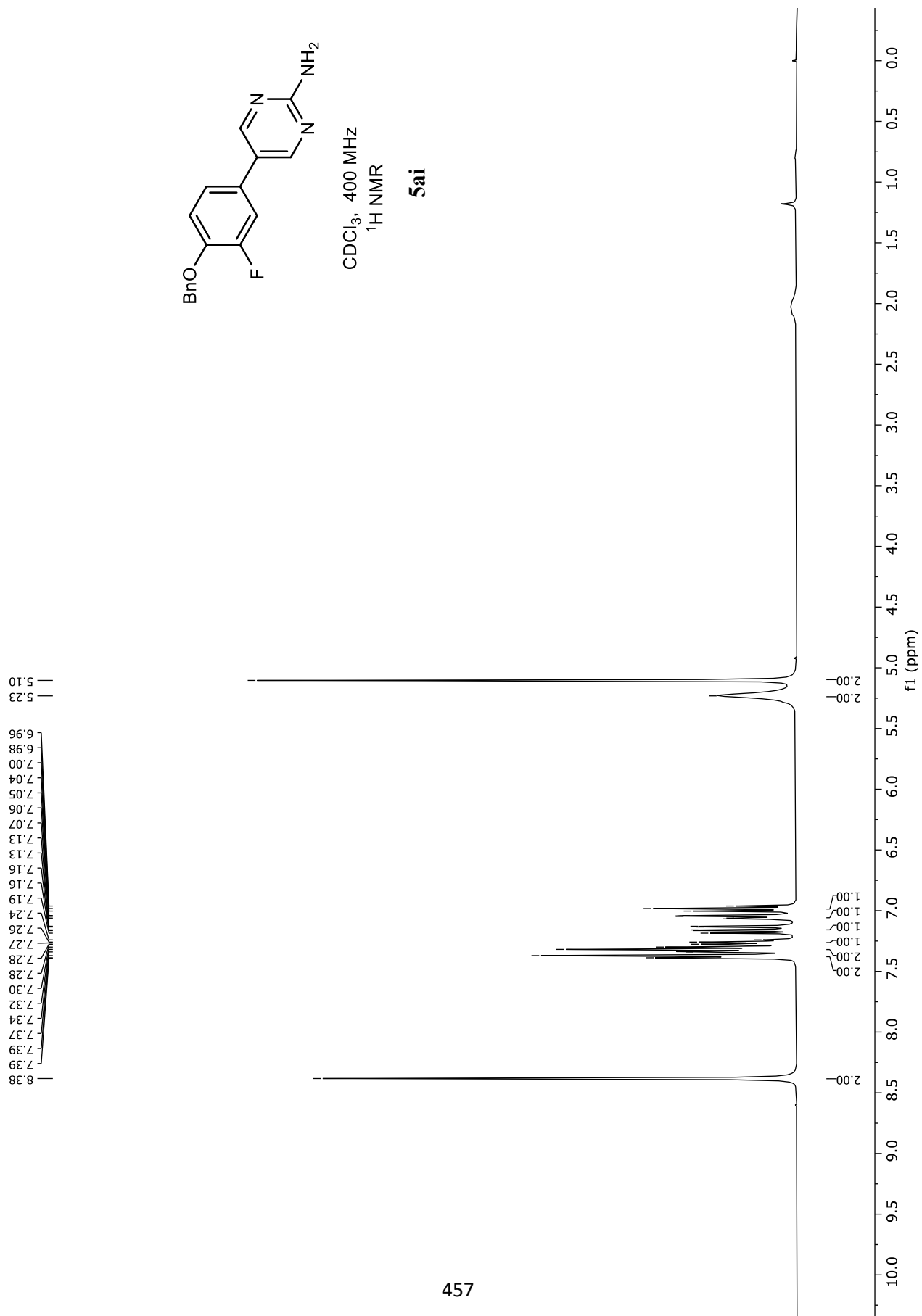
CDCl₃, 100 MHz
¹³C NMR

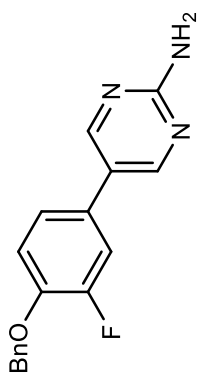
5ah





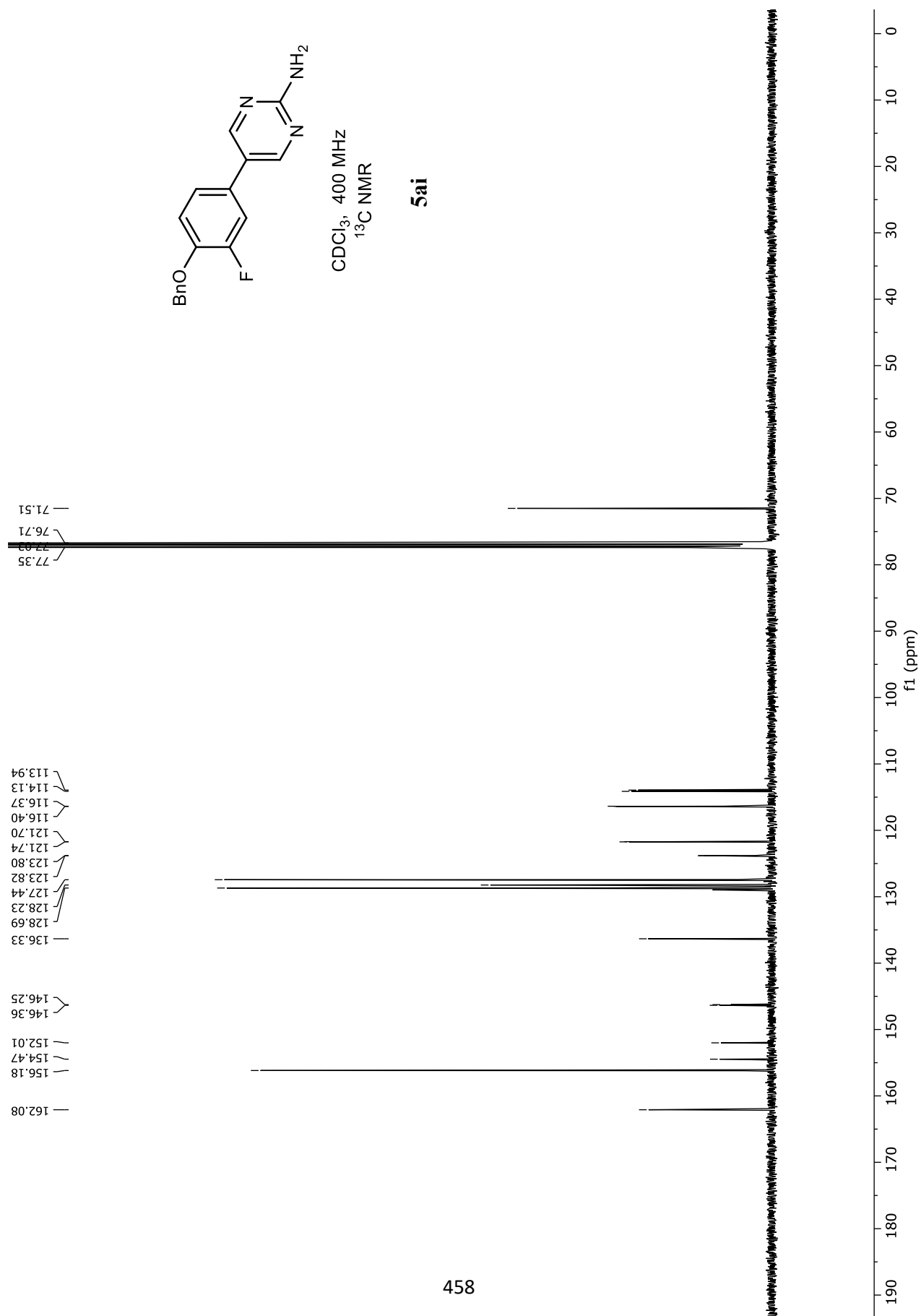
457



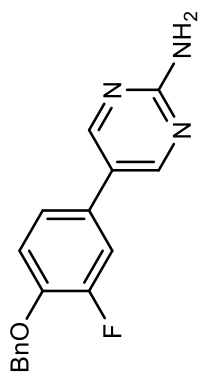


CDCl₃, 400 MHz
¹³C NMR

5ai



-132.41
-132.43
-132.44
-132.46



CDCl₃, 400 MHz
¹⁹F NMR

5ai

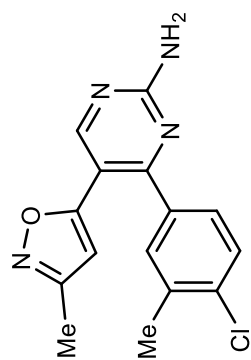


— 2.38
— 2.22

— 5.81
— 5.59

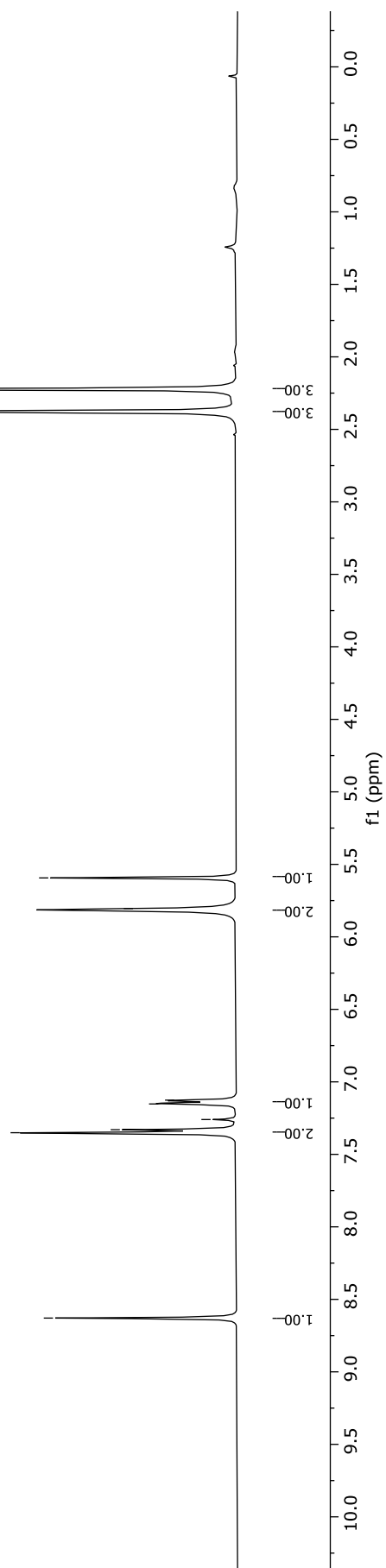
7.35
7.33
7.26
7.15
7.13

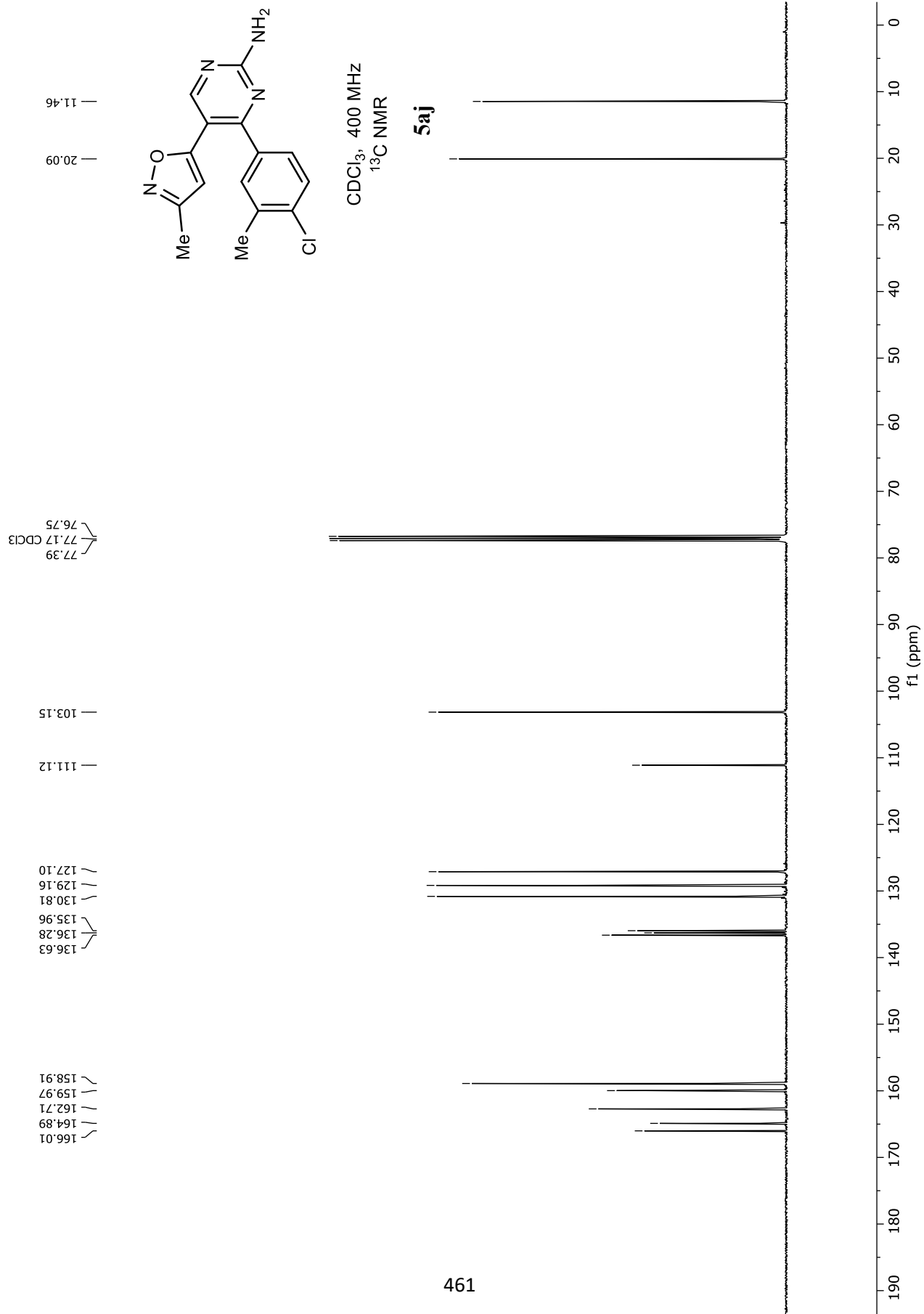
— 8.63

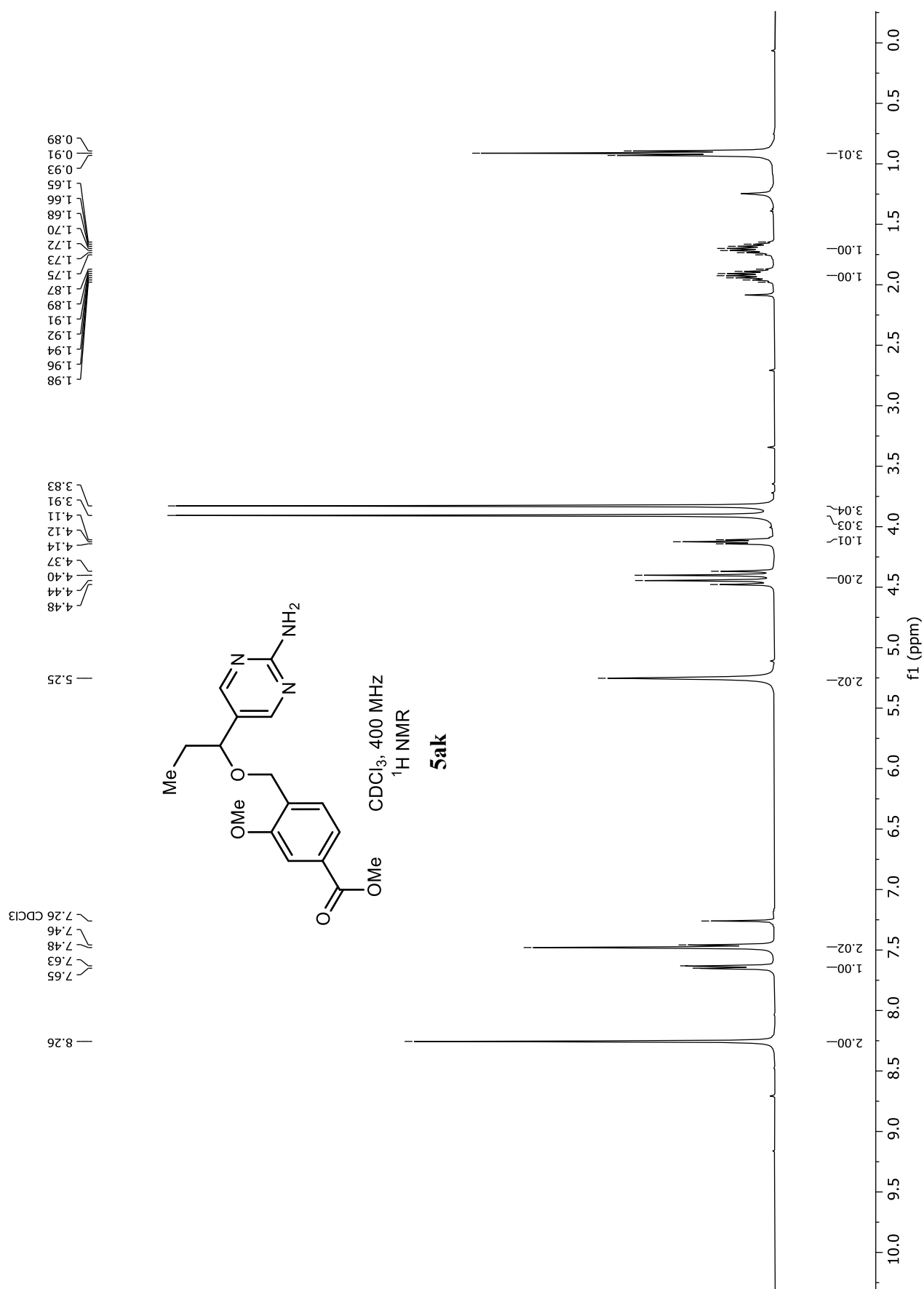


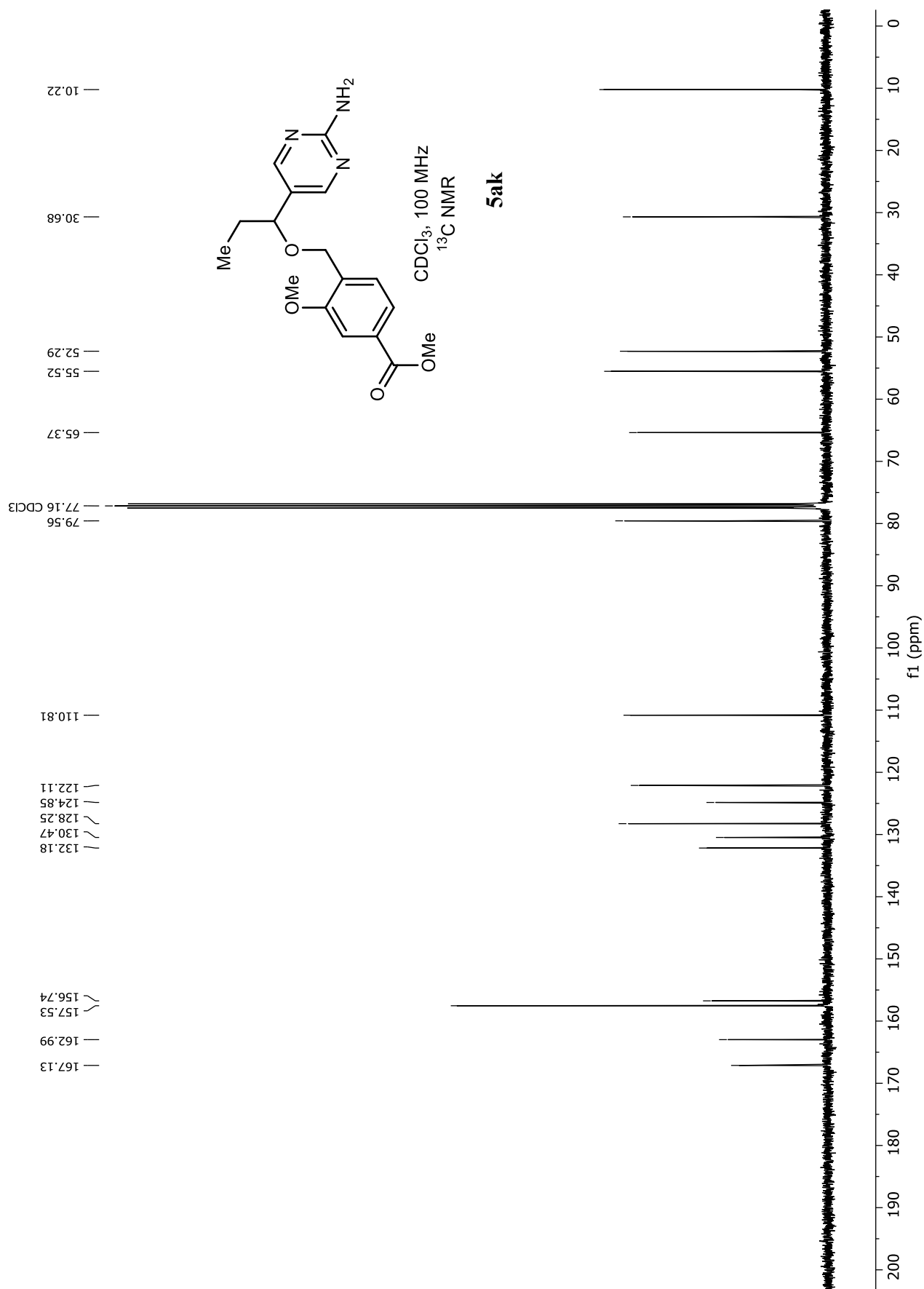
CDCl₃, 400 MHz
¹H NMR

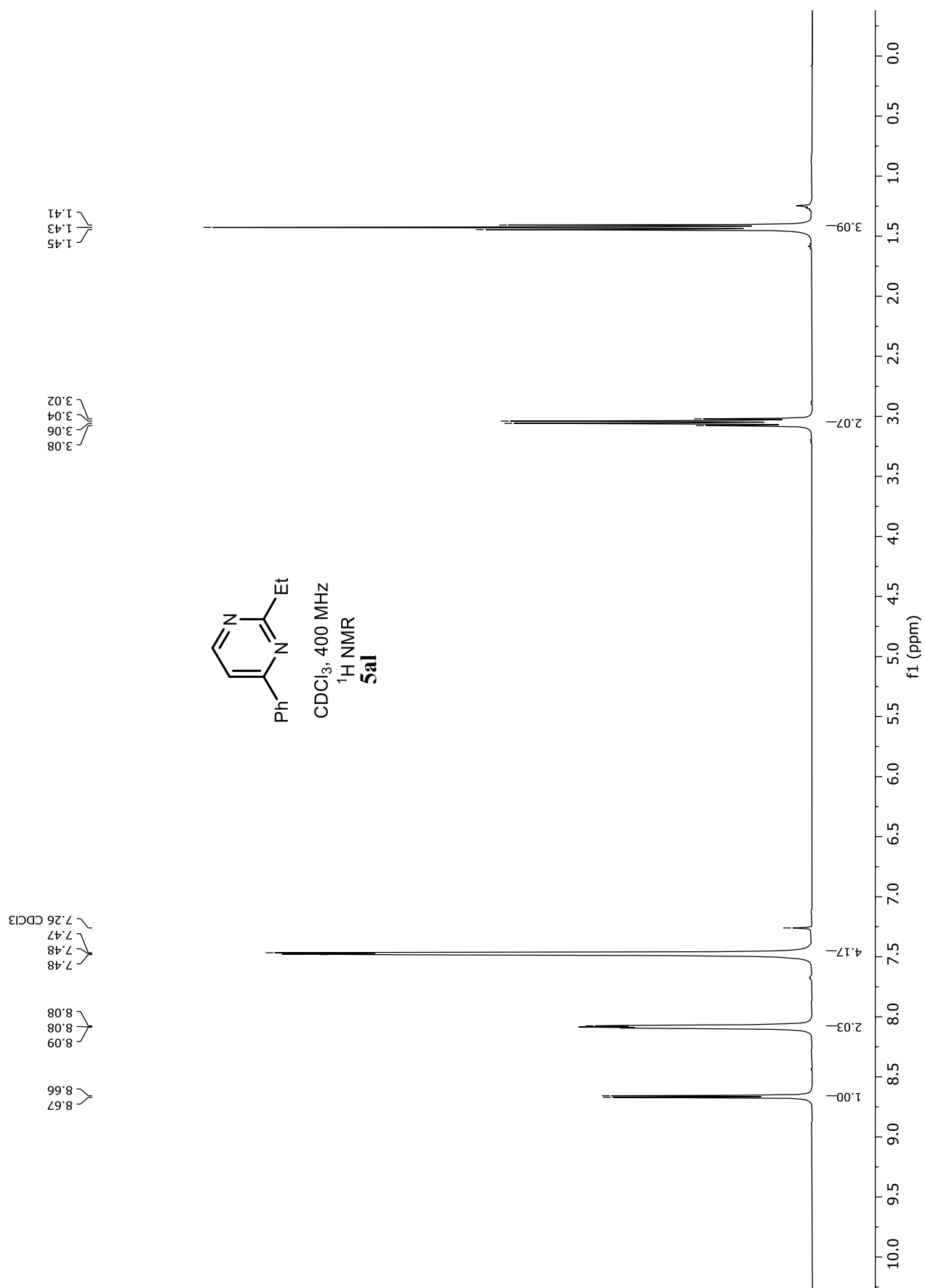
5aj

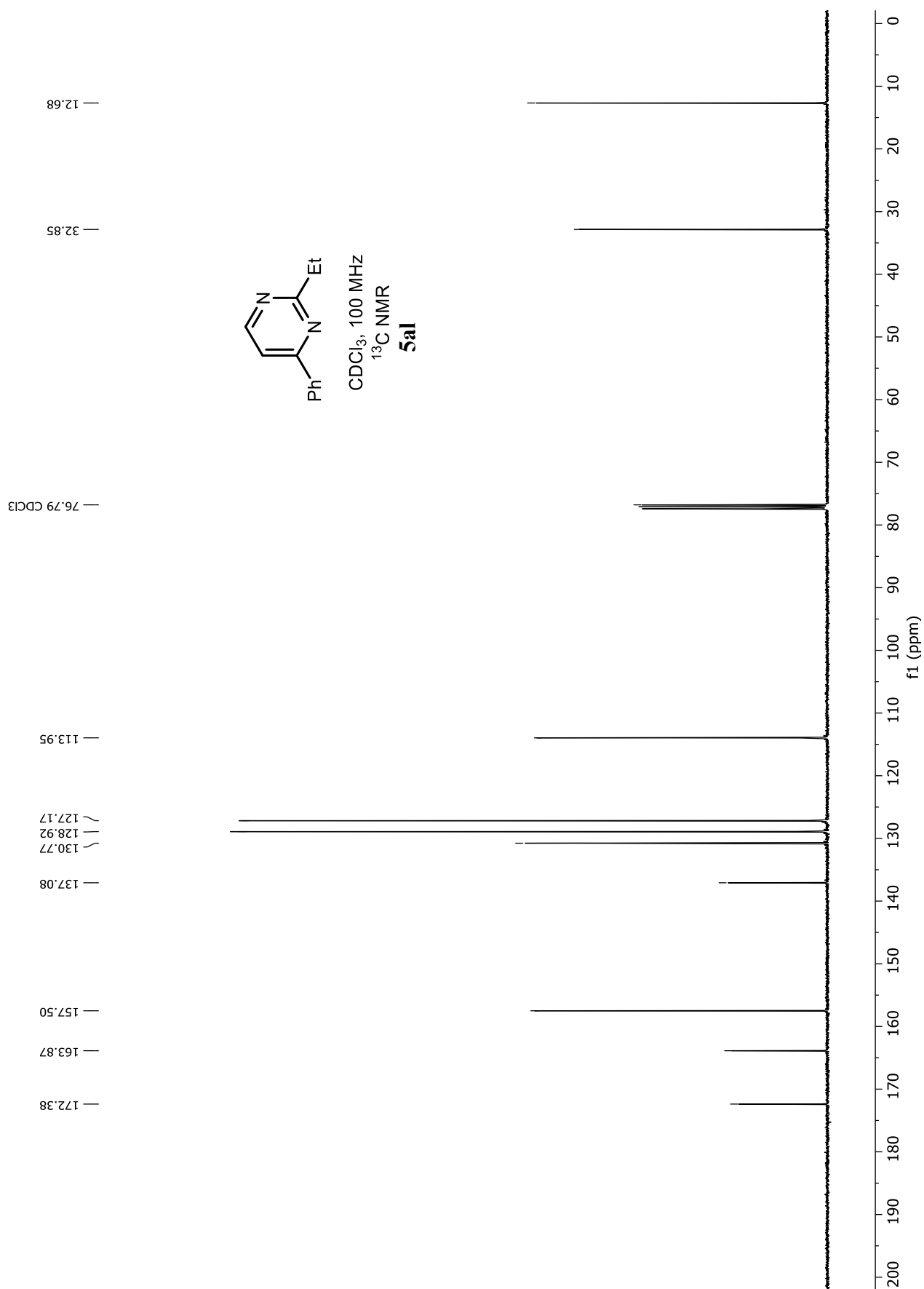


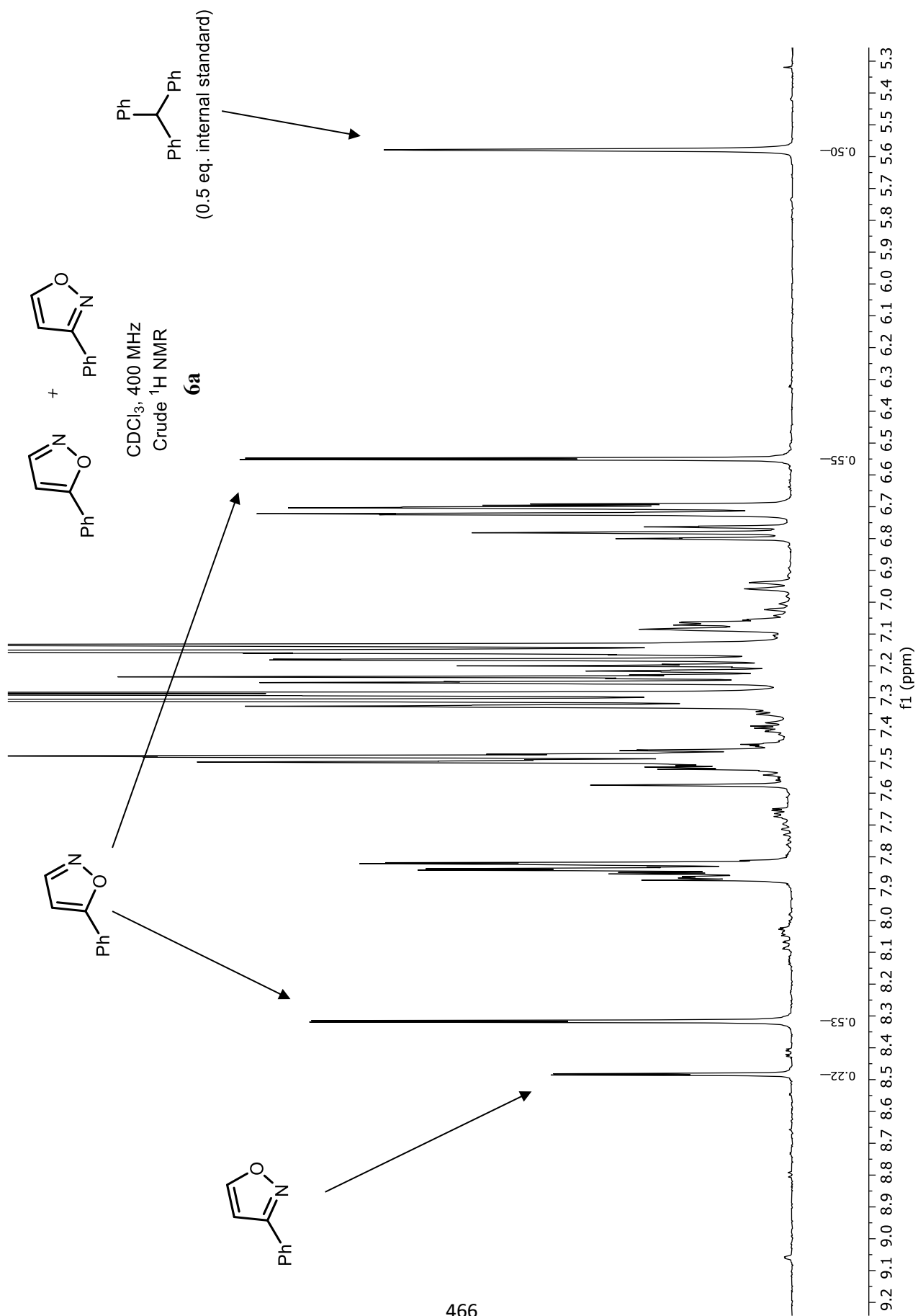


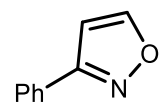










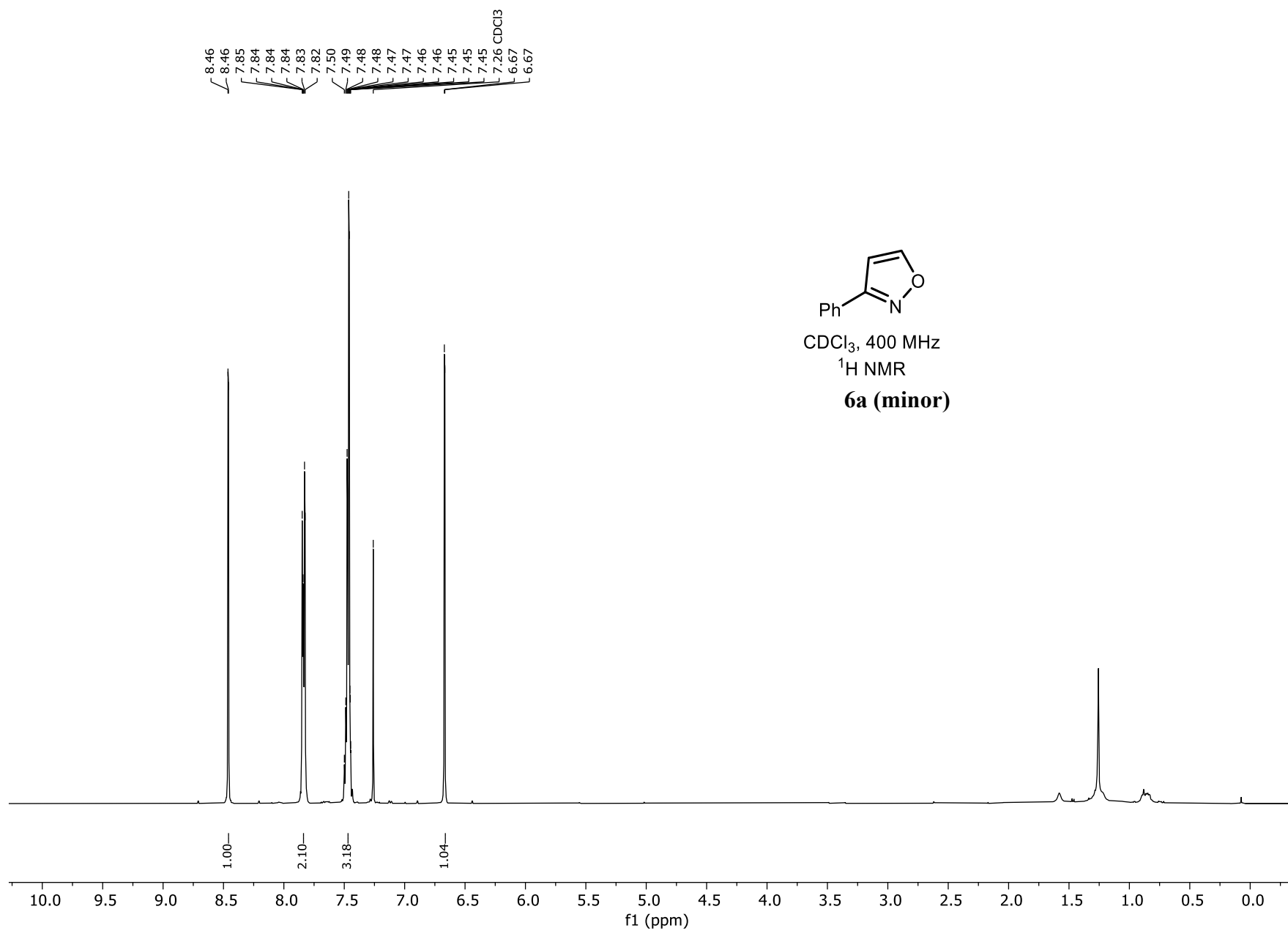


CDCl₃, 400 MHz

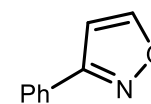
¹H NMR

6a (minor)

467

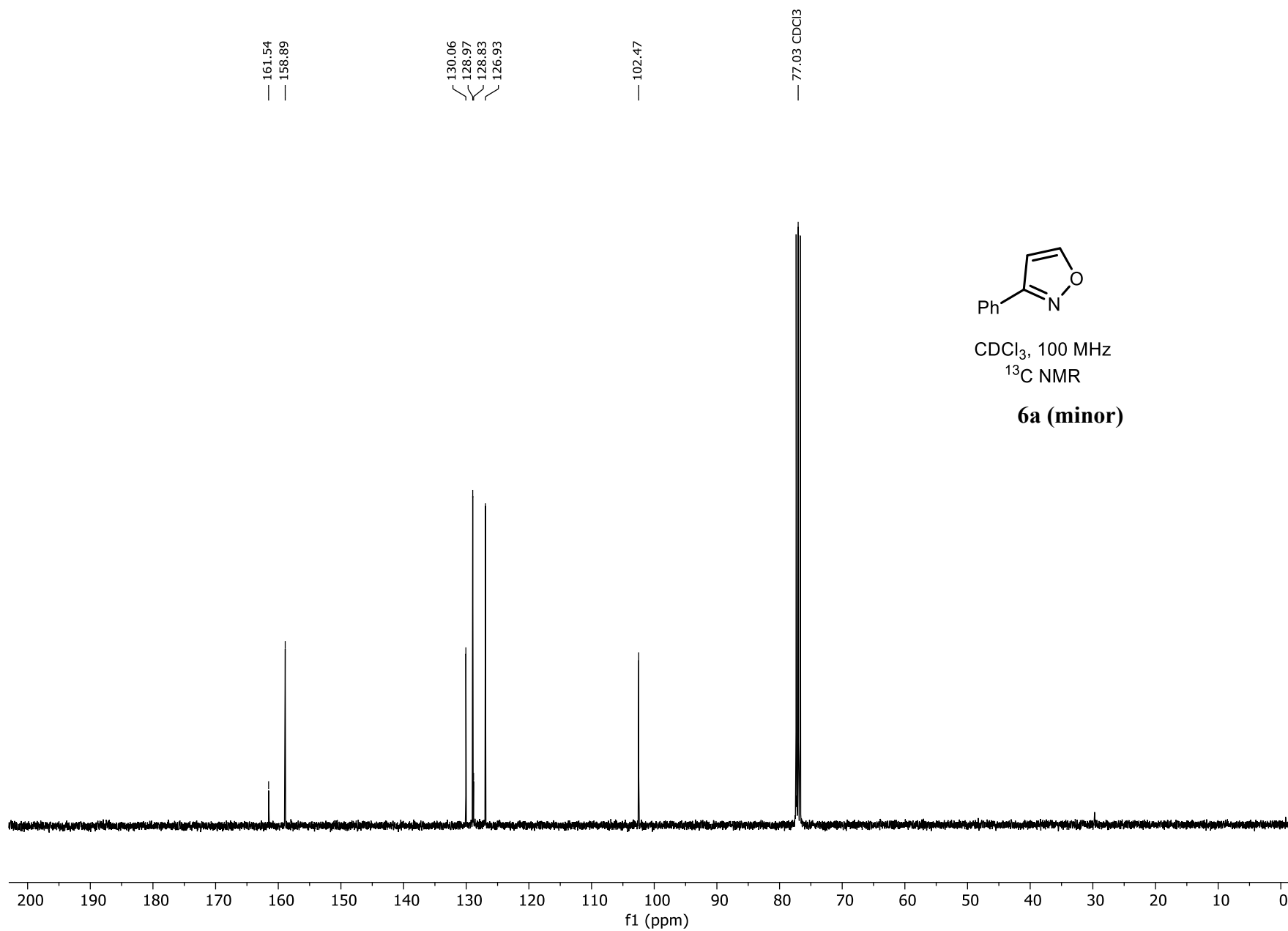


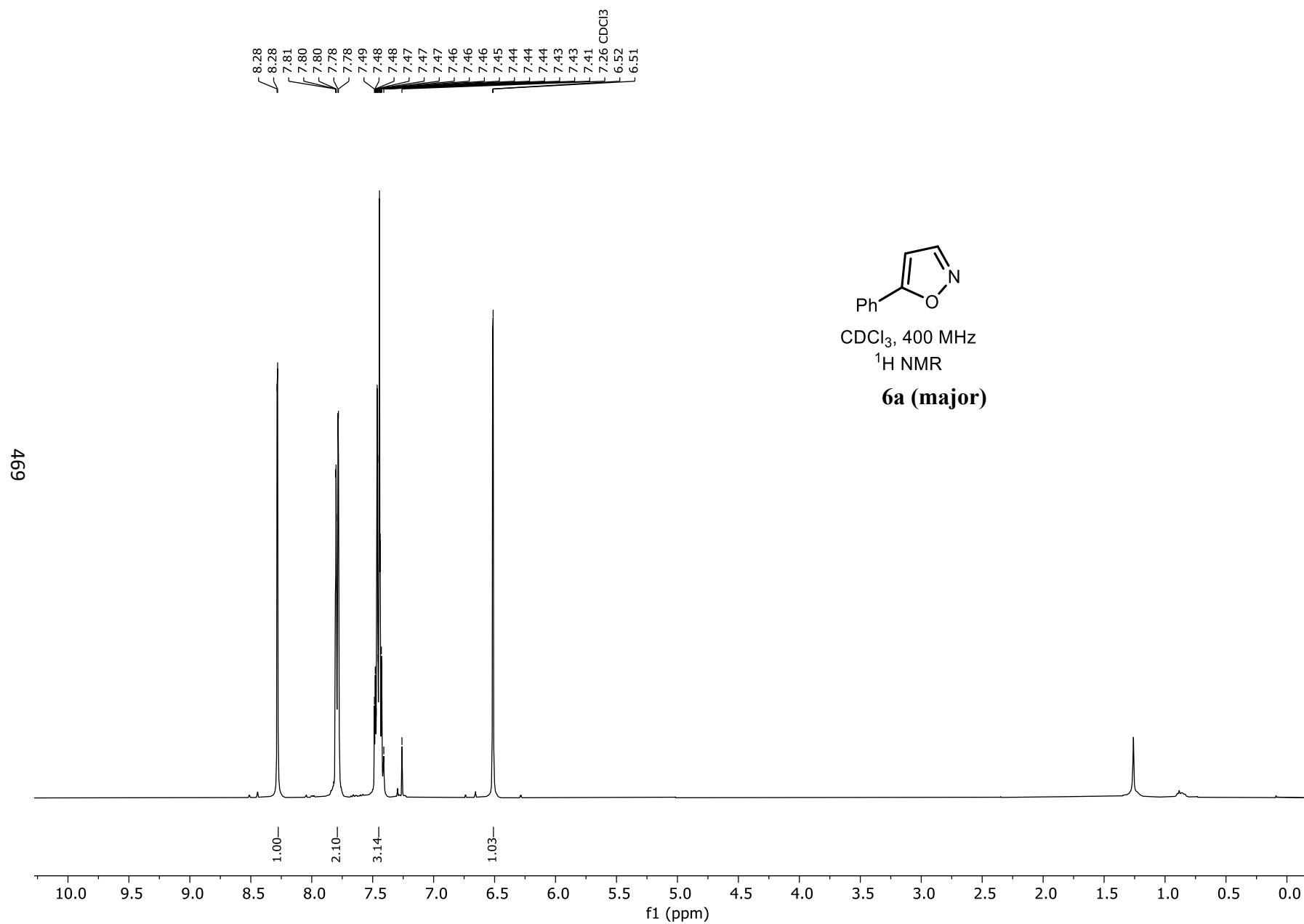
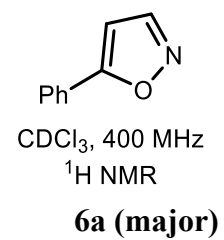
468

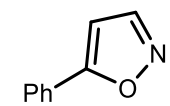


CDCl₃, 100 MHz
¹³C NMR

6a (minor)

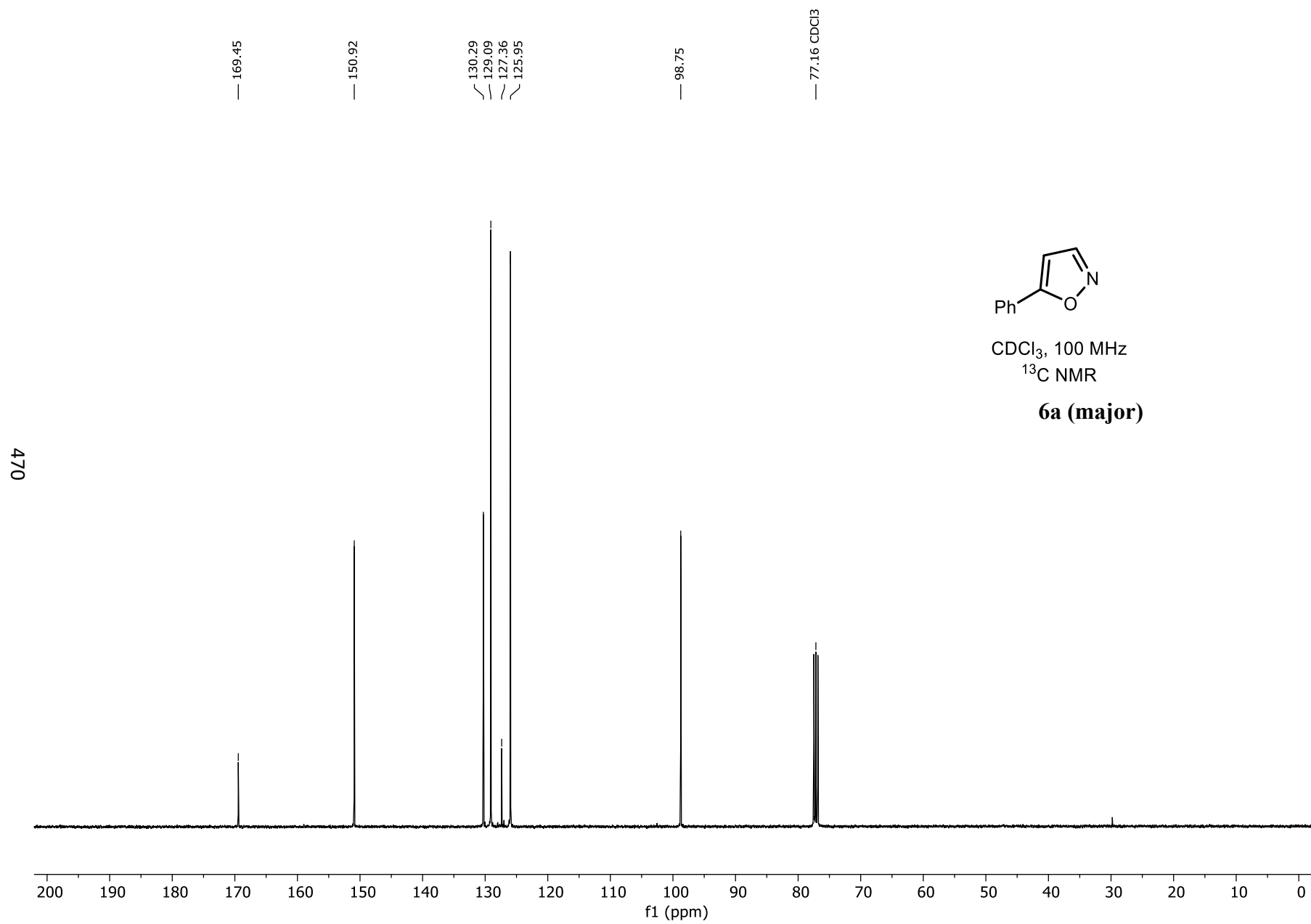


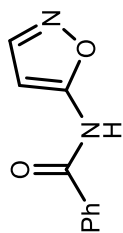




CDCl₃, 100 MHz
¹³C NMR

6a (major)



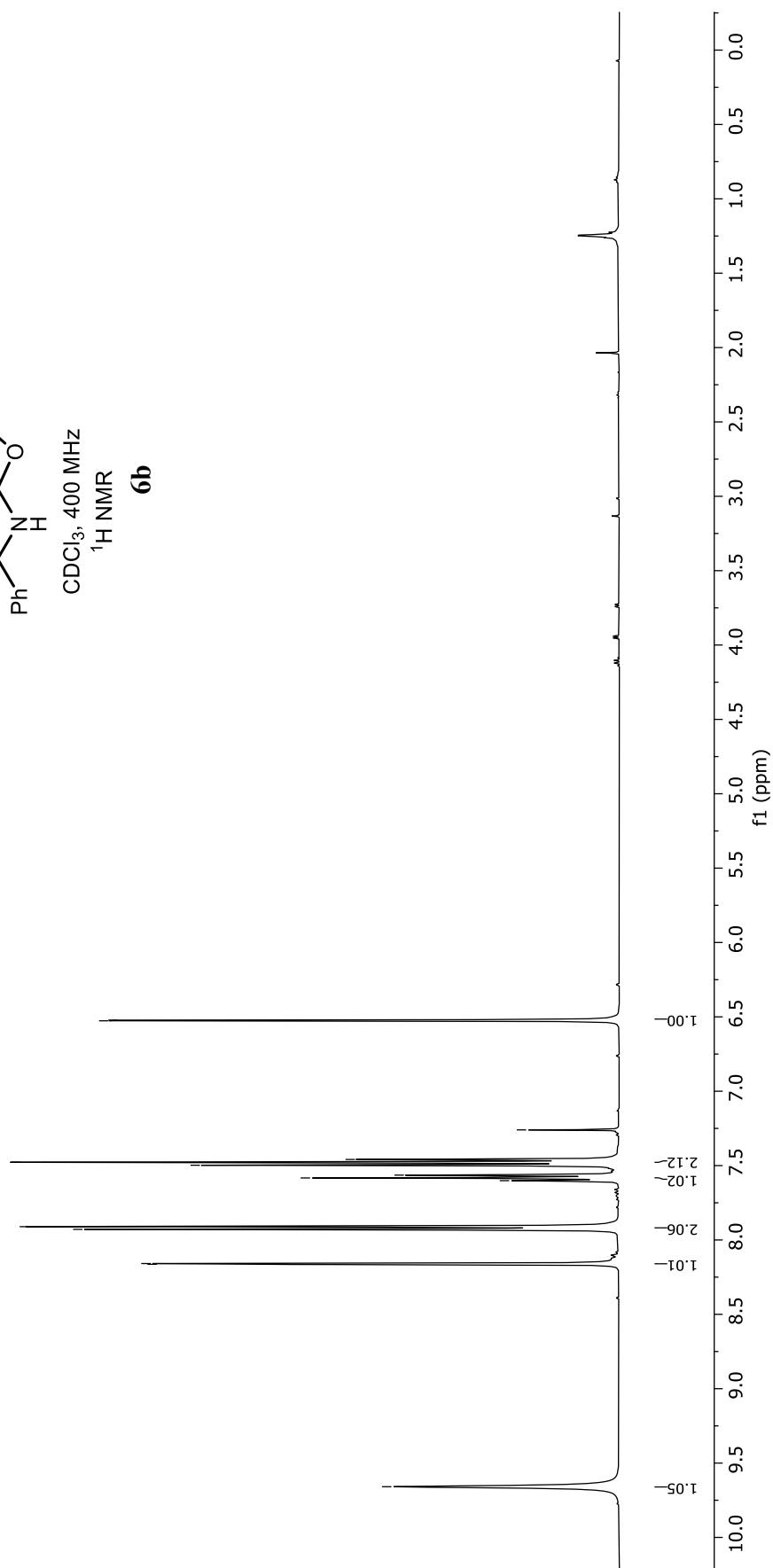


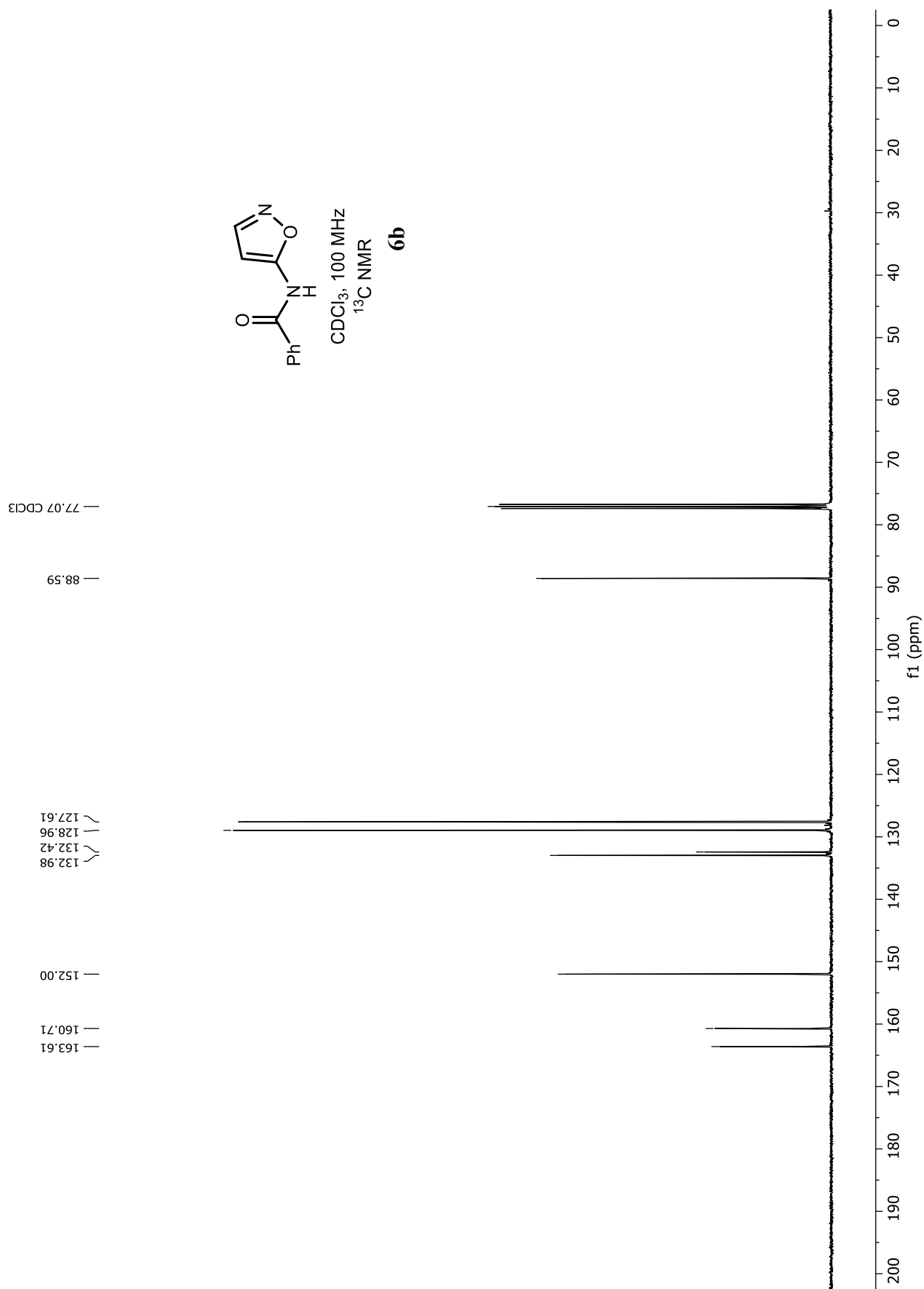
CDCl₃, 400 MHz
¹H NMR

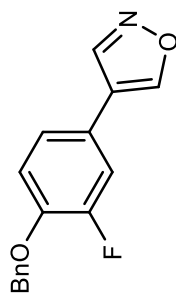
6b

8.16
 8.16
 7.93
 7.91
 7.60
 7.58
 7.56
 7.50
 7.48
 7.46
 7.26 CDCl₃
 6.53
 6.52

9.66







CDCl₃, 400 MHz
¹H NMR

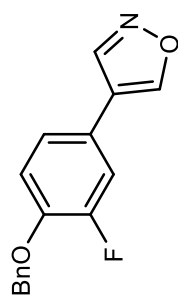
6c

8.51
8.40
7.38
7.38
7.36
7.34
7.33
7.33
7.32
7.31
7.30
7.30
7.28
7.28
7.27
7.26
7.24
7.18
7.15
7.14
7.12
7.11
7.07
7.07
7.05
7.05
7.04
6.97
6.95
6.93
5.09

2.00
f1 (ppm)

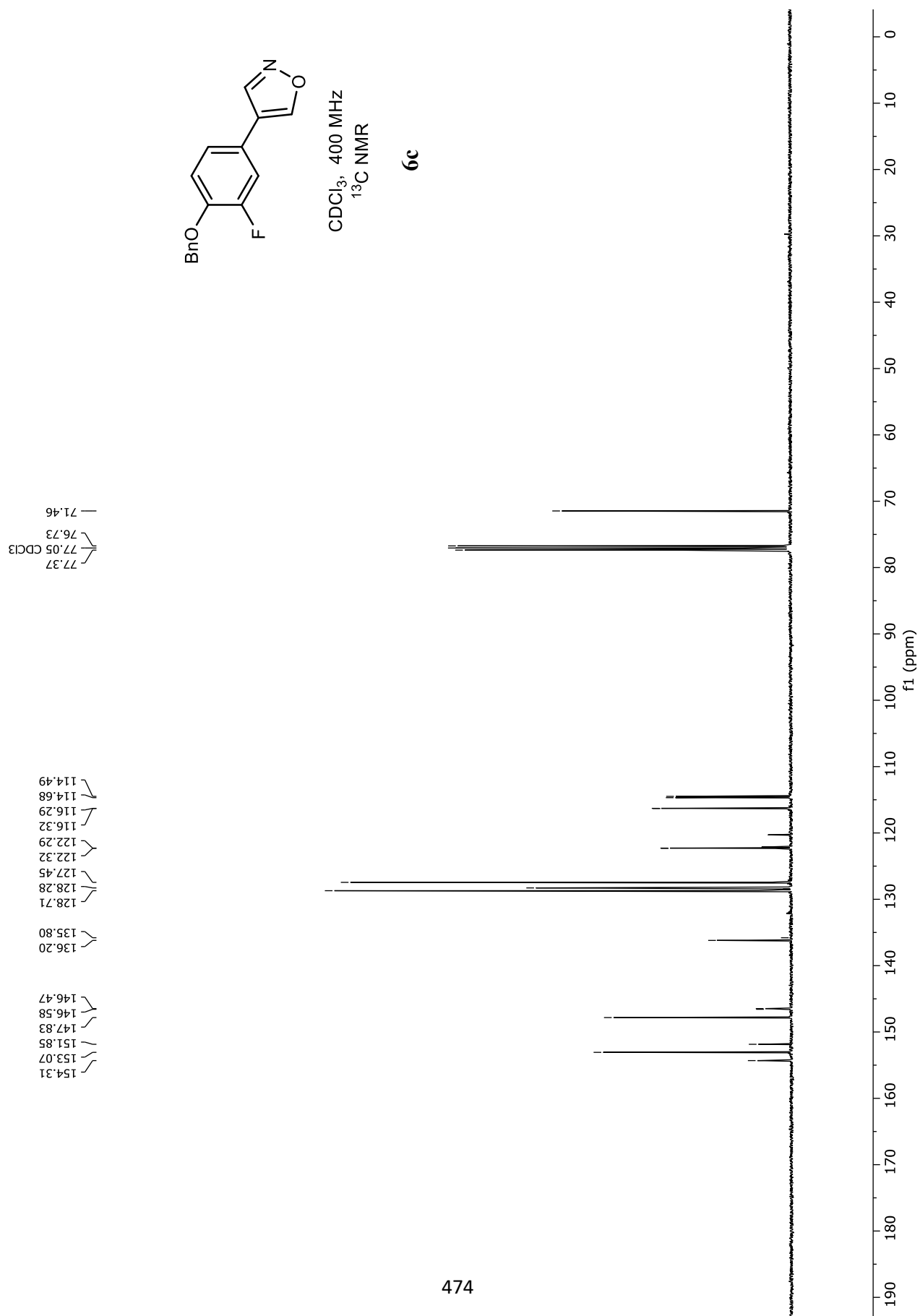
2.00
2.00
1.00
1.00
1.00
1.00
1.00

1.00
1.00

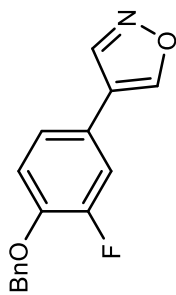


CDCl₃, 400 MHz
¹³C NMR

6c



-132.39
-132.37
-132.36
-132.33



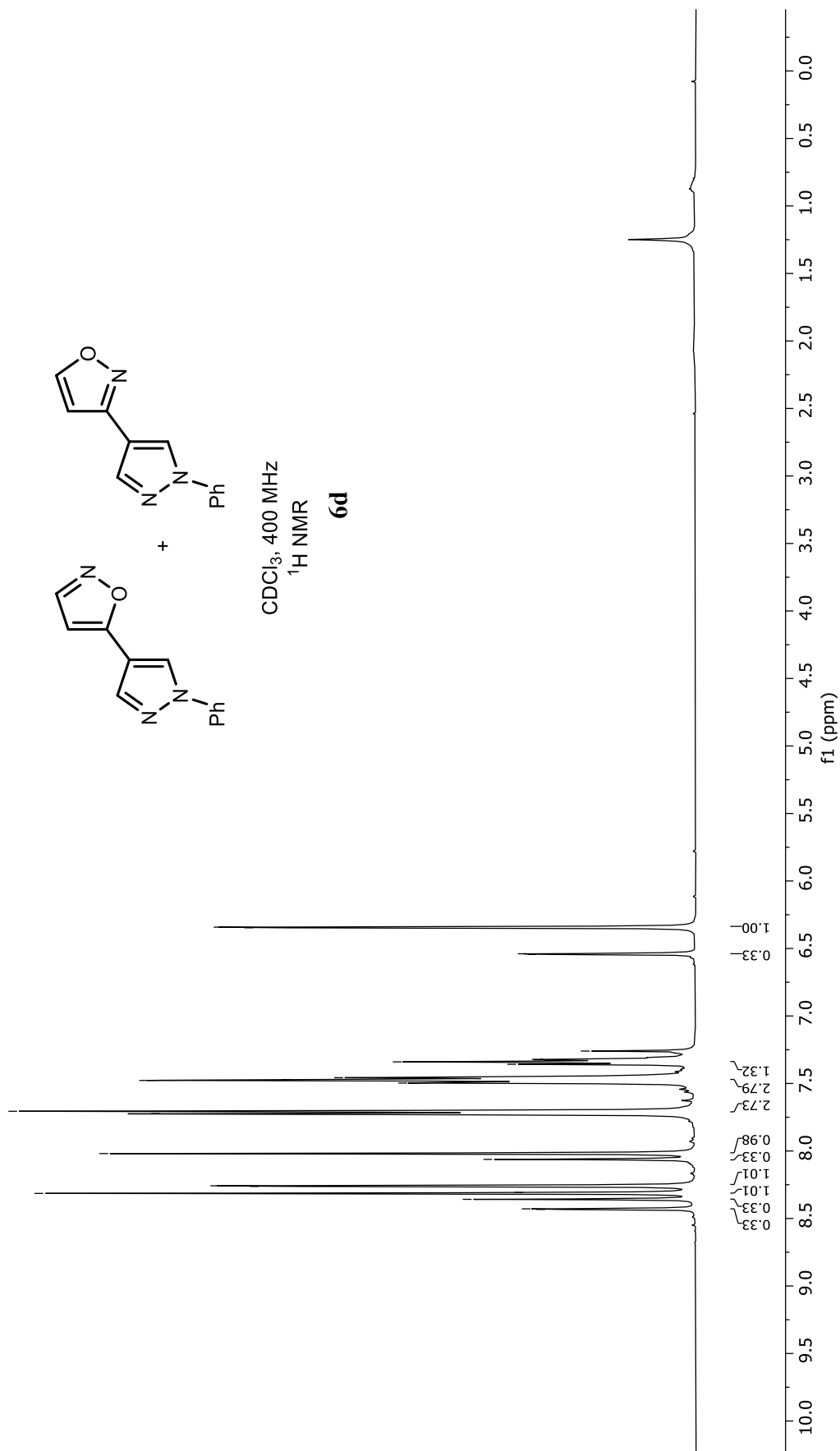
CDCl_3 , 400 MHz
 ^{19}F NMR

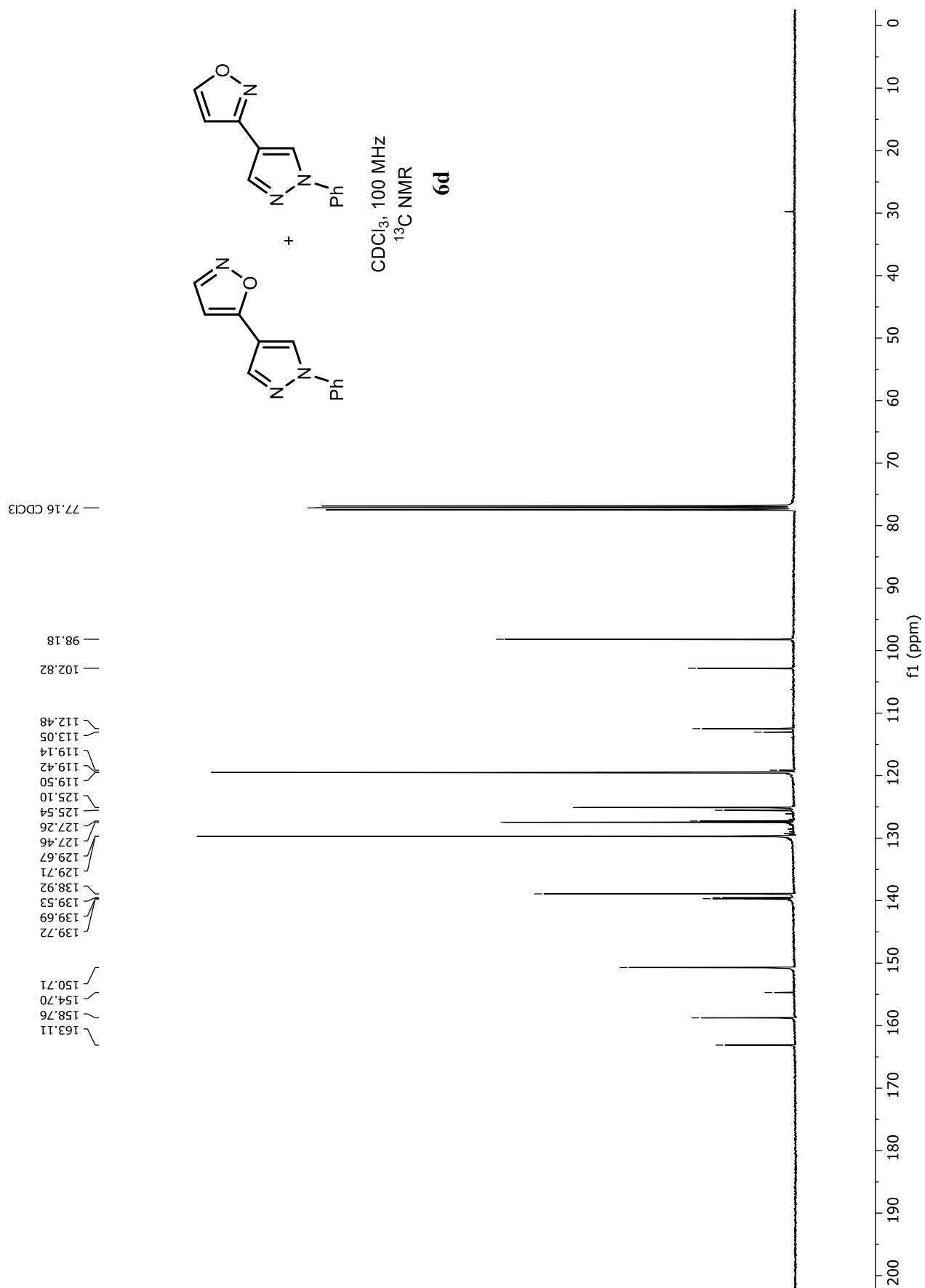
6c

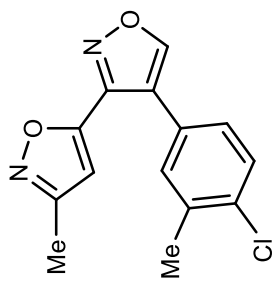


0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

8.43
8.43
8.36
8.31
8.31
8.26
8.26
8.06
8.02
7.72
7.71
7.50
7.48
7.47
7.46
7.36
7.34
7.33
7.32
7.26 CDCl₃
6.54
6.54
6.35
6.34

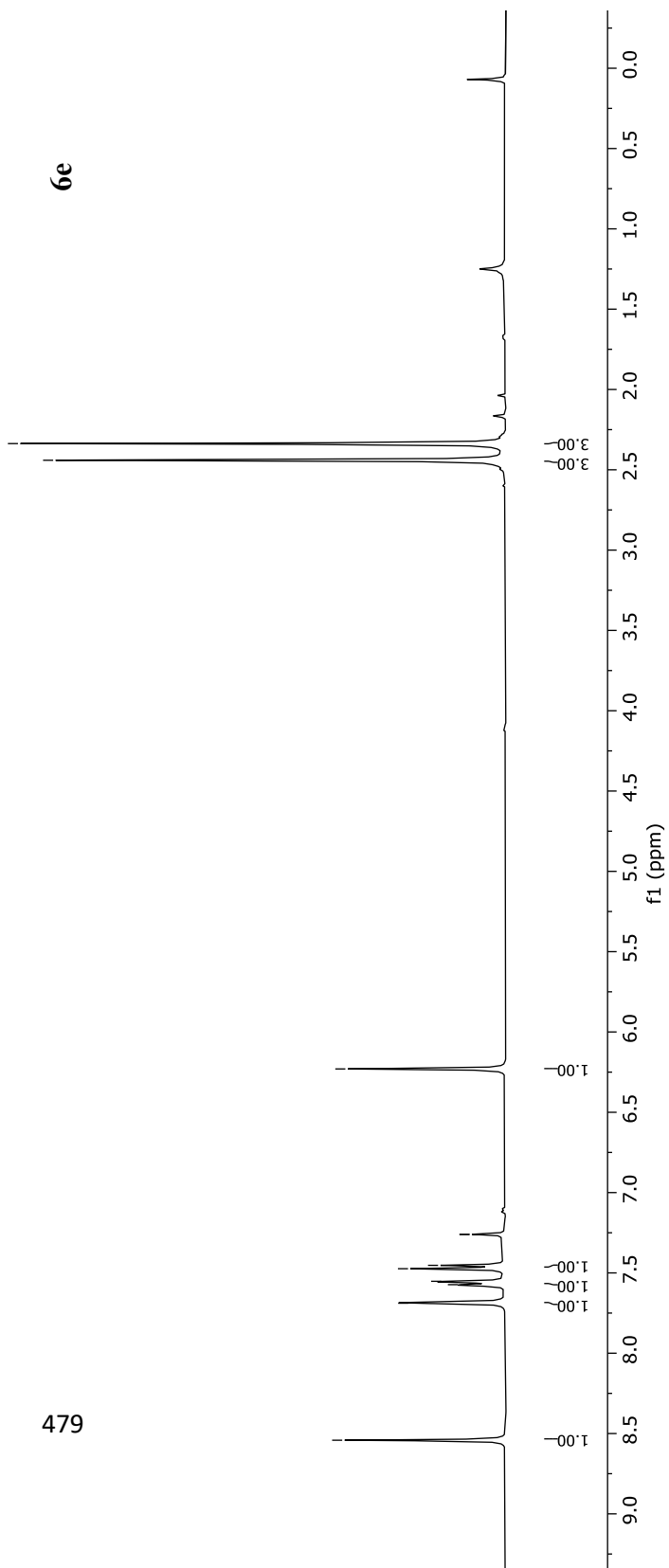
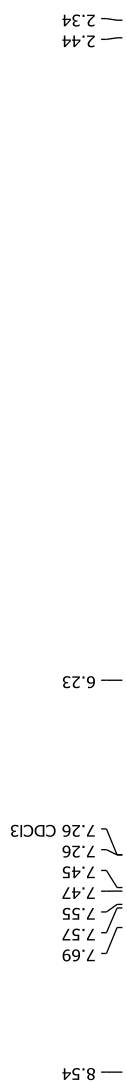


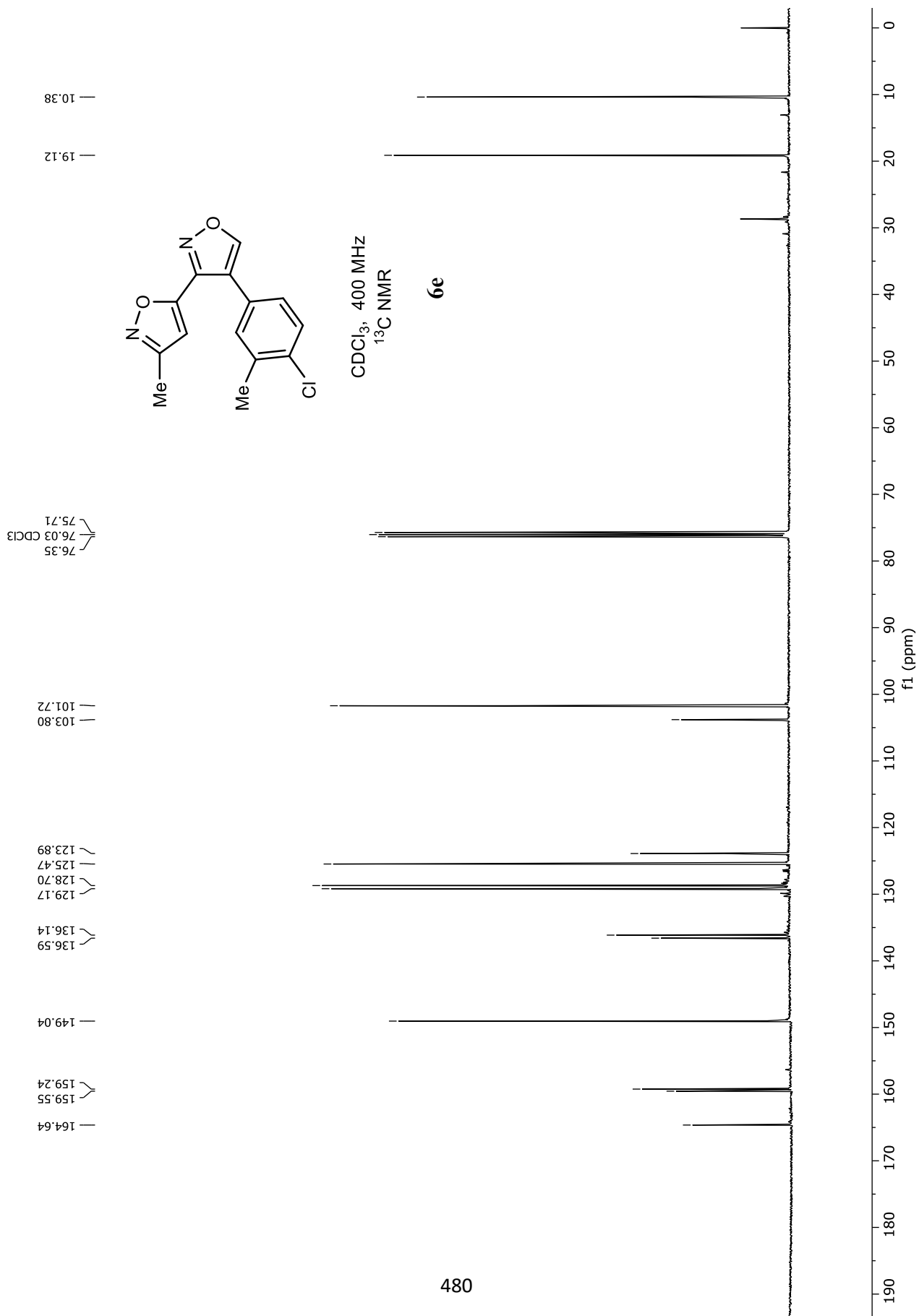


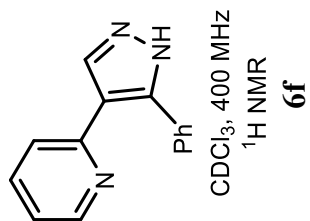


CDCl₃, 400 MHz
¹H NMR

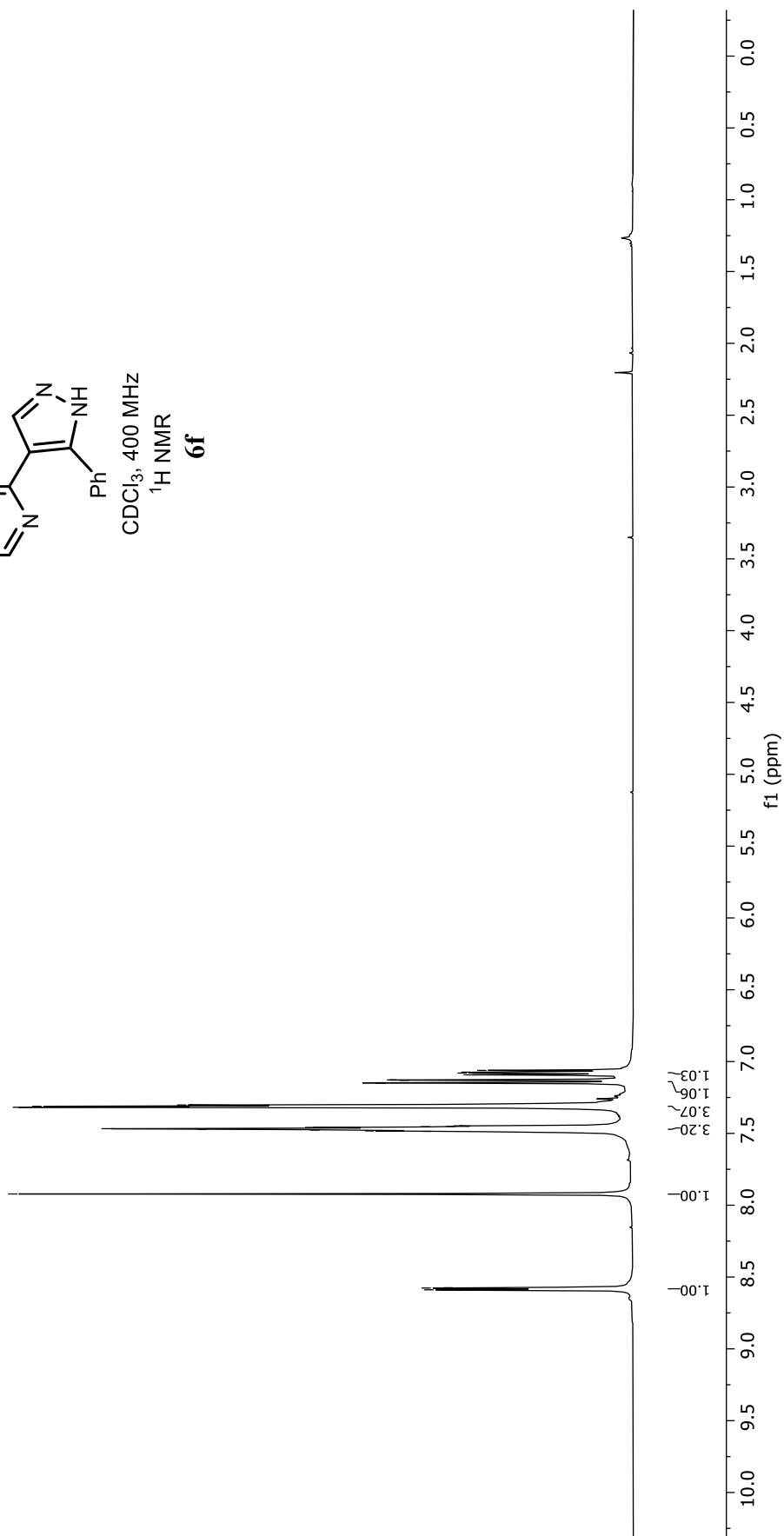
6e

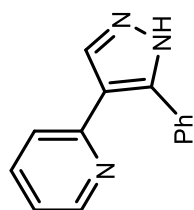






8.59
 8.59
 8.59
 8.58
 8.58
 8.57
 7.92
 7.49
 7.48
 7.48
 7.47
 7.46
 7.45
 7.45
 7.45
 7.32
 7.32
 7.31
 7.30
 7.15
 7.15
 7.13
 7.13
 7.09
 7.09
 7.08
 7.07
 7.06



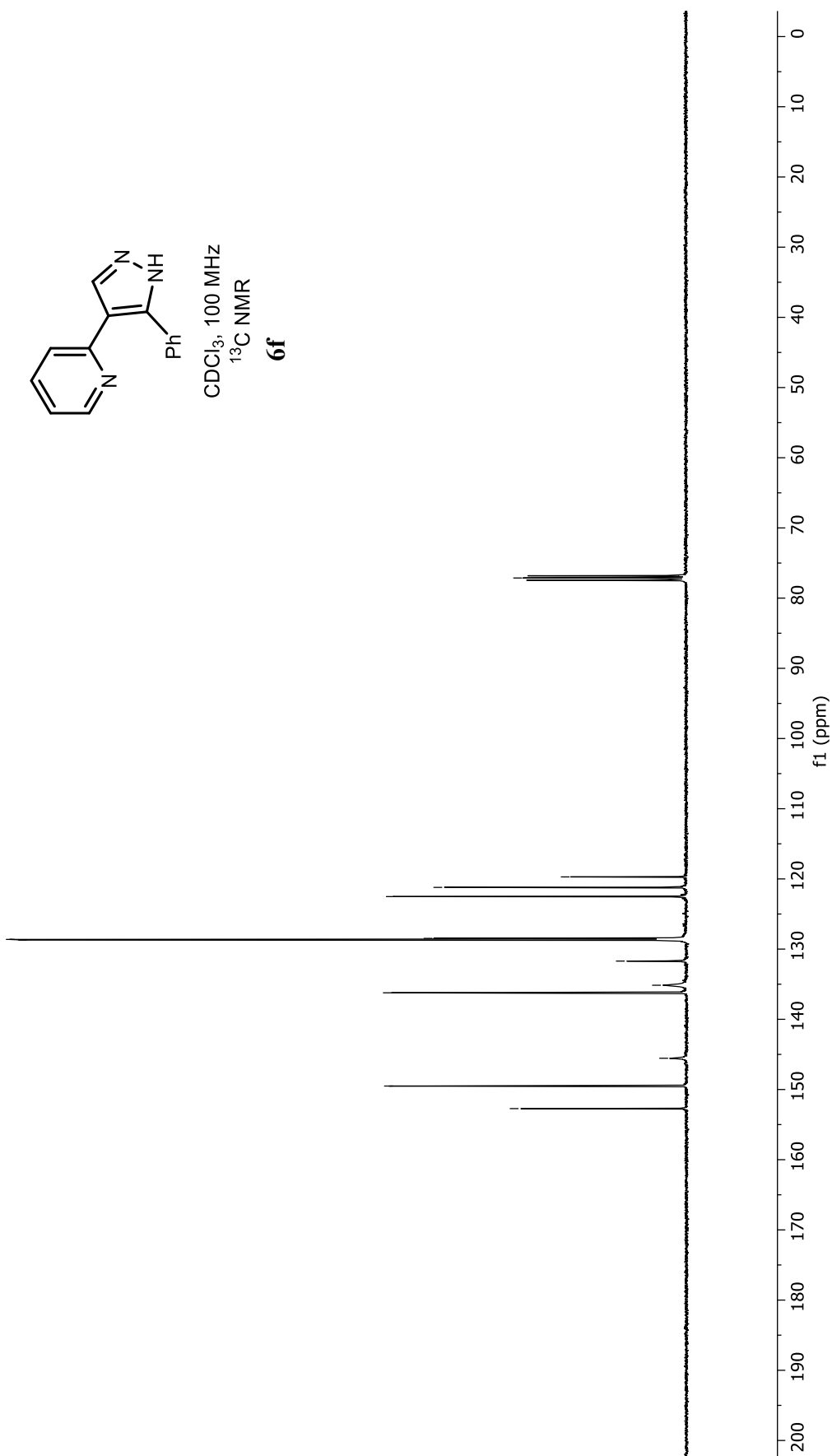


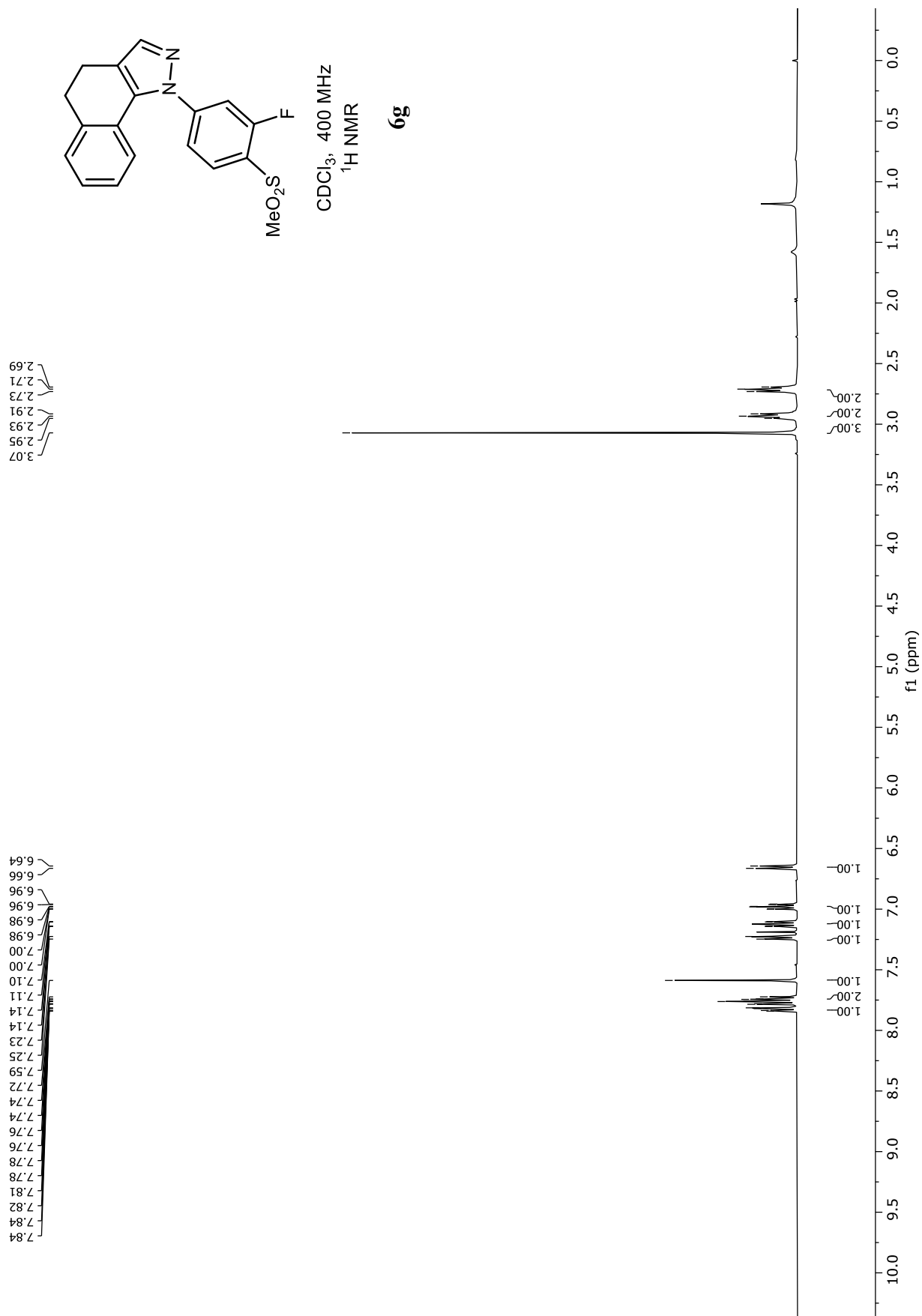
CDCl₃, 100 MHz
¹³C NMR

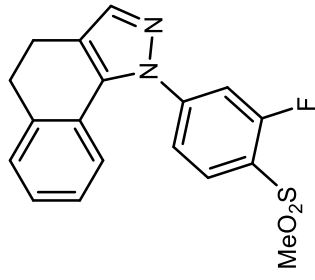
6f

— 77.13 CDCl₃

152.72
 149.51
 145.55
 136.23
 135.15
 131.71
 128.72
 128.62
 128.47
 122.52
 121.21
 119.71

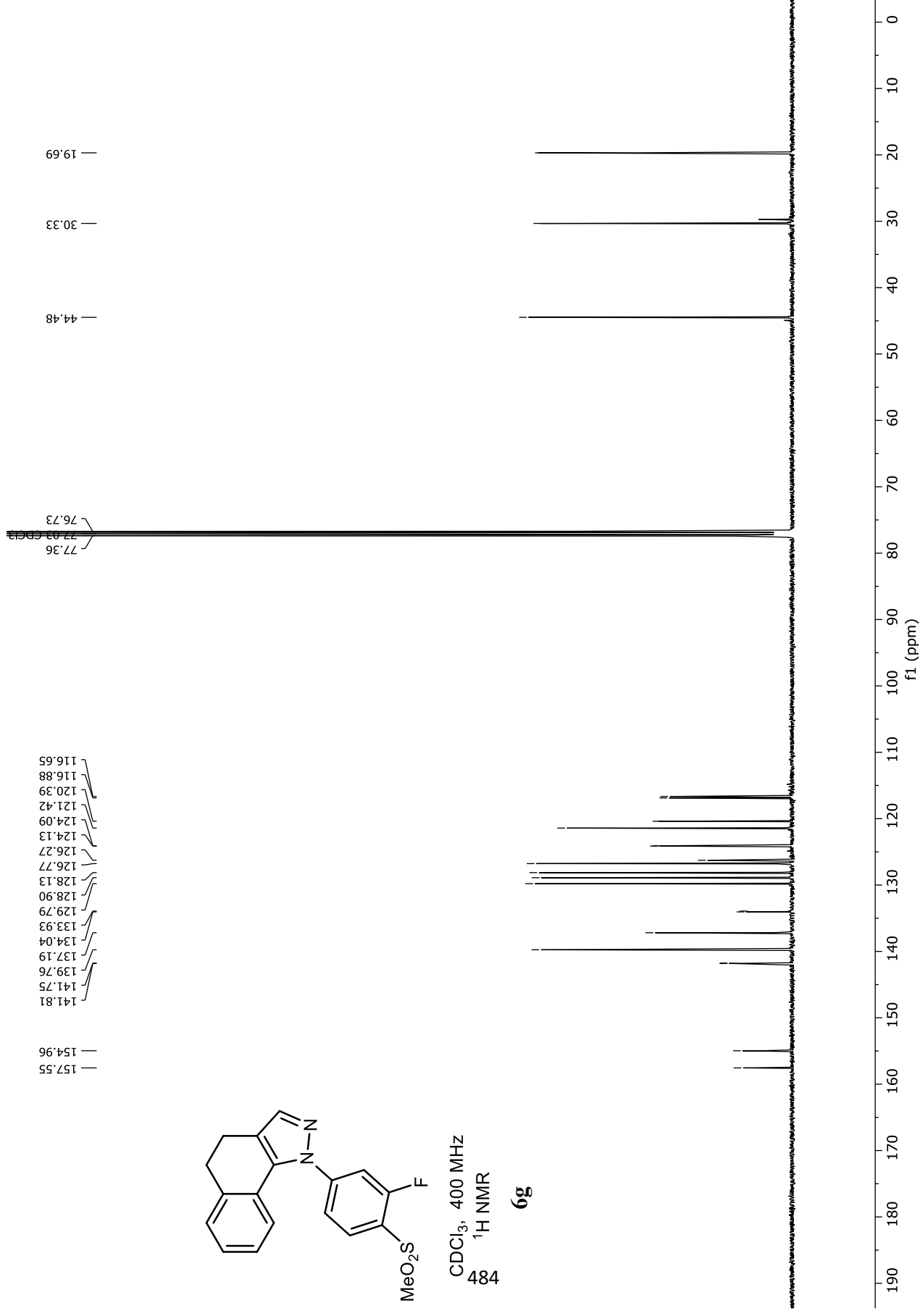




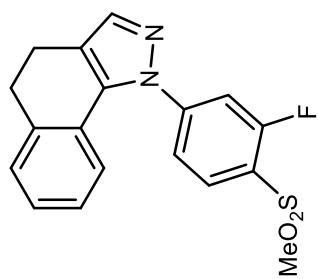


CDCl₃, 400 MHz
¹H NMR

6g



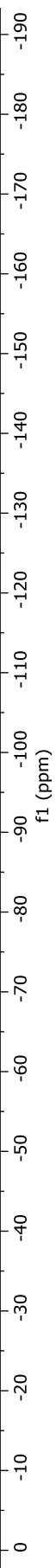
— -115.70

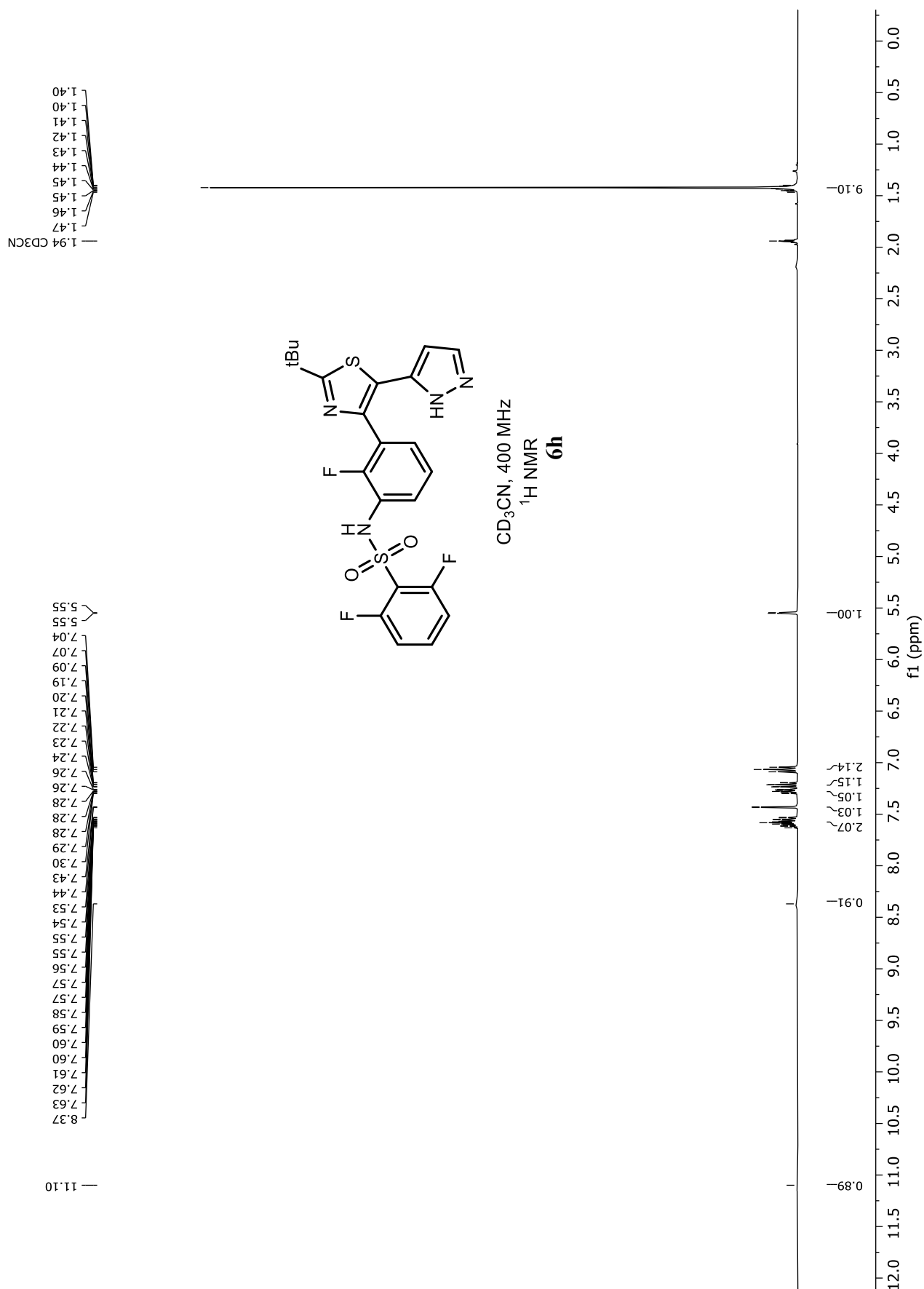


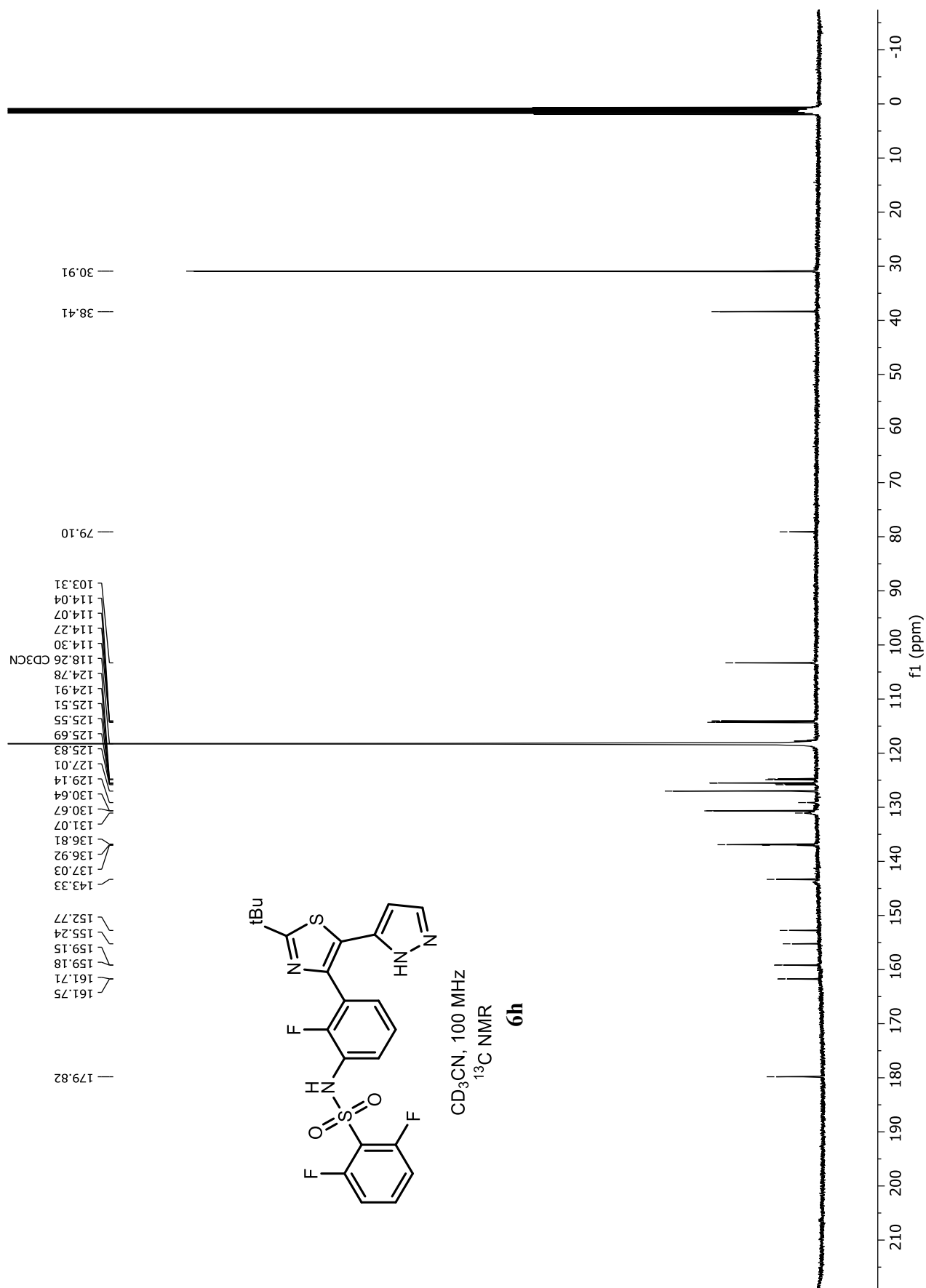
CDCl₃, 400 MHz
¹H NMR

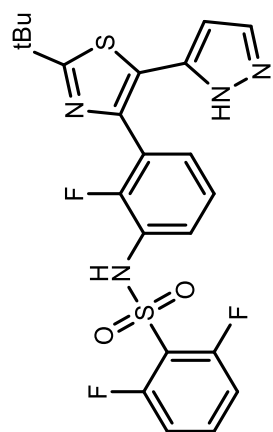
6g

485





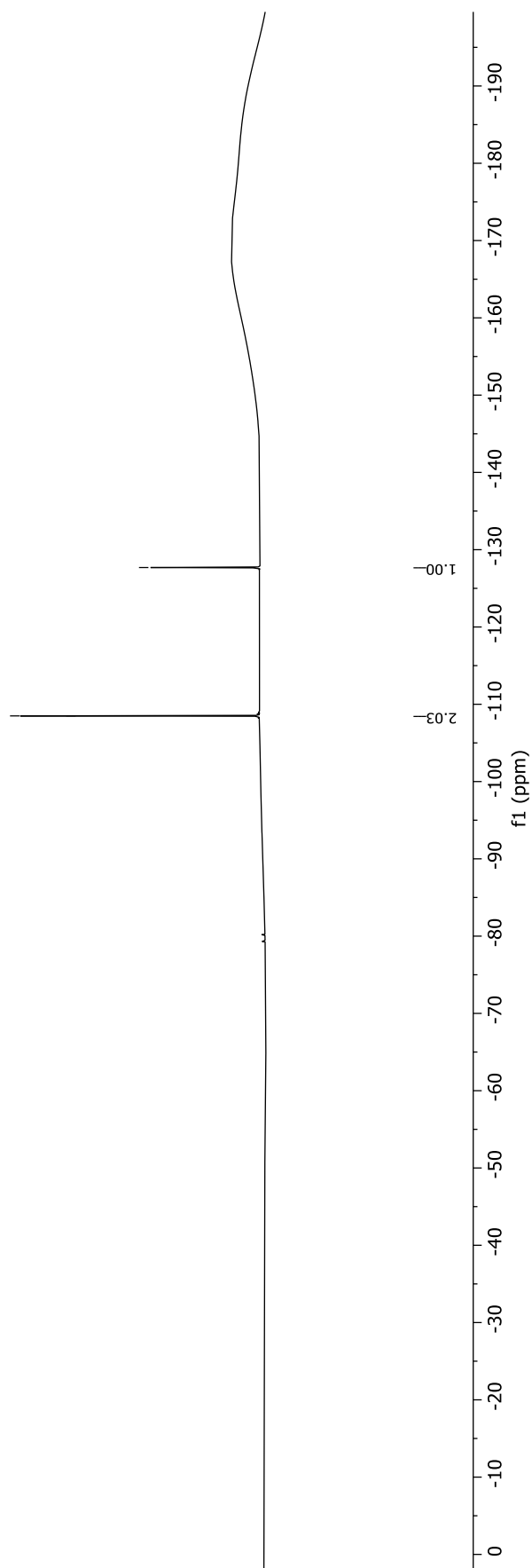


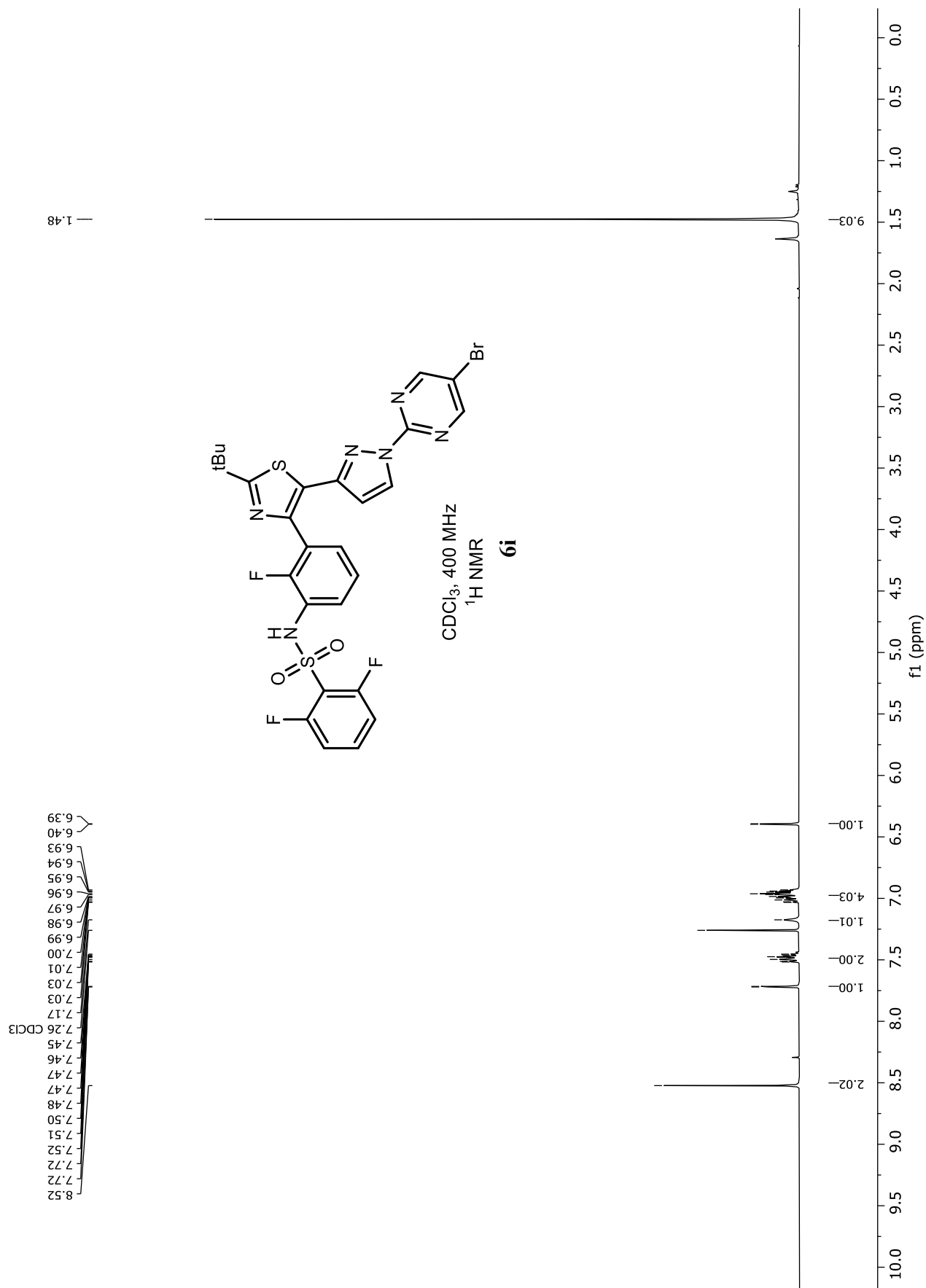


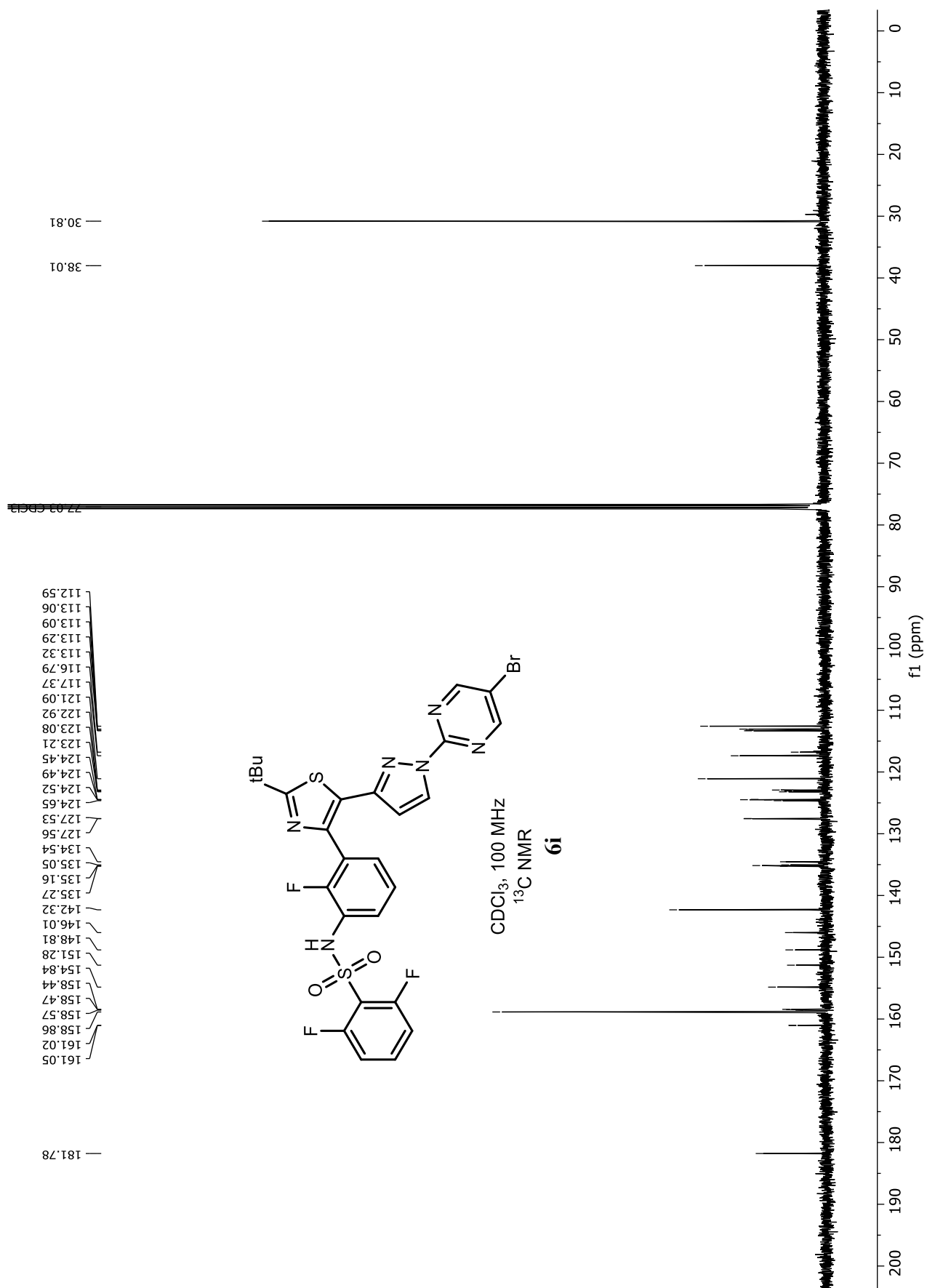
CD₃CN, 375 MHz
¹⁹F NMR

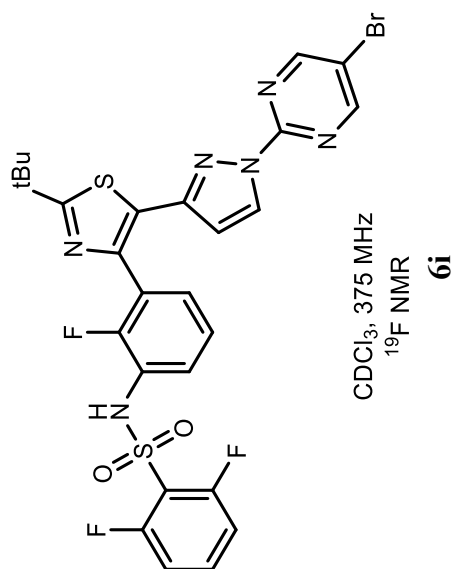
6h

— -108.49
 — -108.51
 — -127.69









CDCl₃, 375 MHz

¹⁹F NMR

6i

-132.04
-132.05
-132.06
-132.07
-132.08
-132.09
-132.10

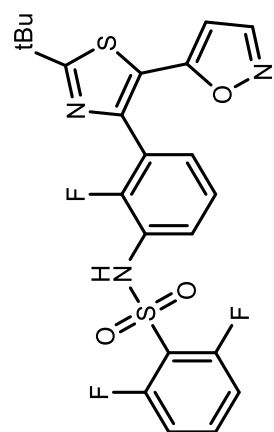
-106.95
-106.96
-106.97
-106.99
-107.00

1.00

2.05

f1 (ppm)

8.12
8.11
7.73
7.72
7.71
7.70
7.69
7.68
7.54
7.52
7.51
7.50
7.49
7.48
7.48
7.46
7.32
7.32
7.30
7.30
7.30
7.29
7.28
7.26
7.21
7.21
7.19
7.19
7.17
7.17
7.01
6.99
6.97
5.80
5.80
CDCl₃

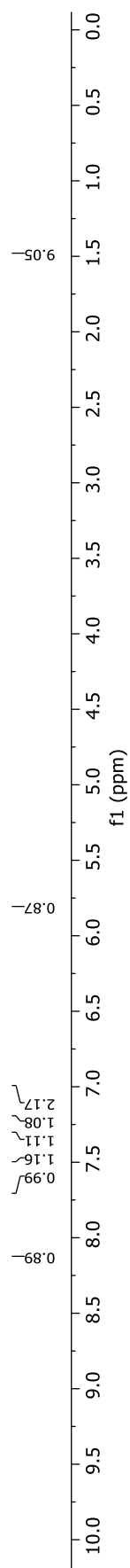


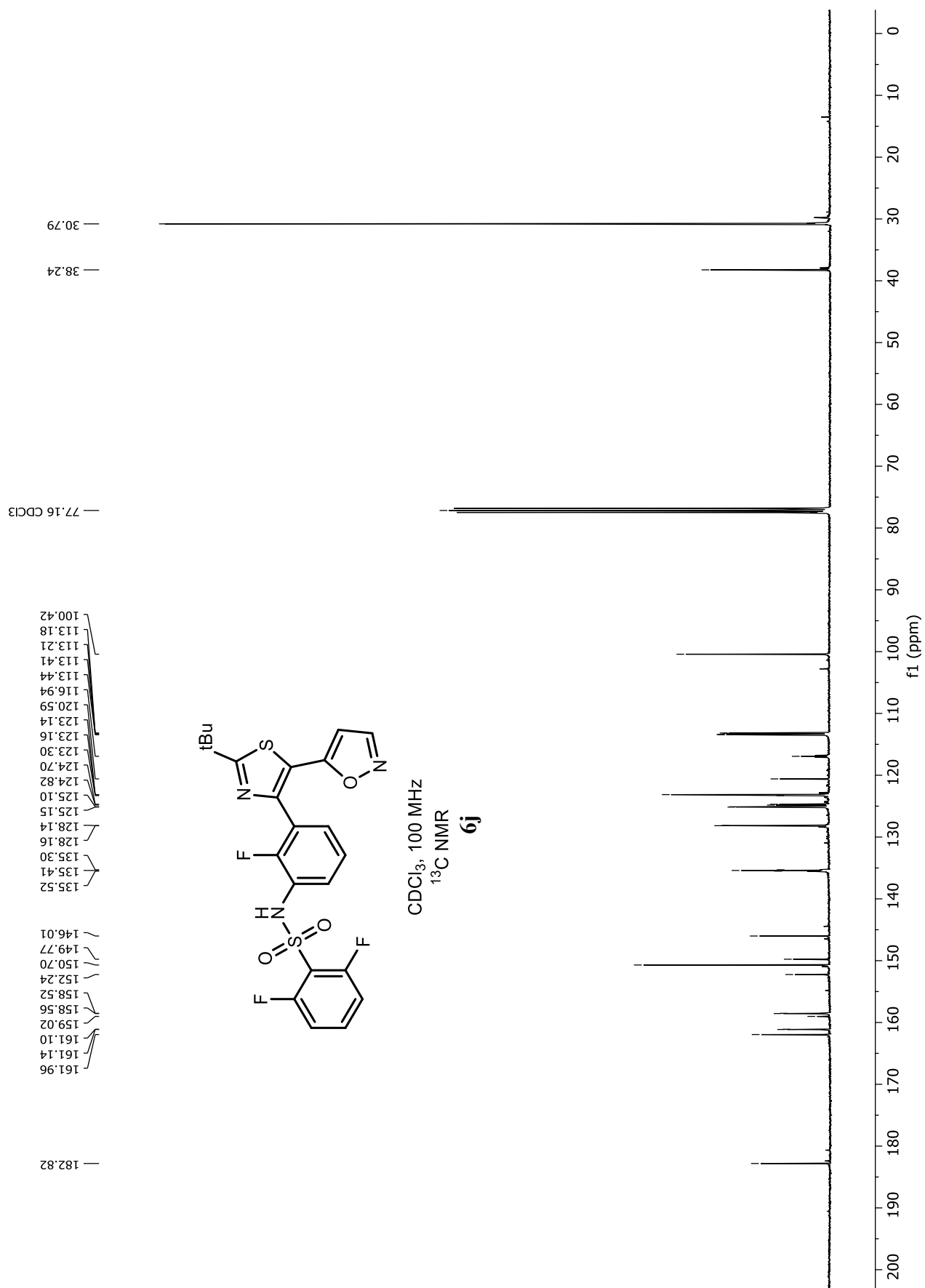
CDCl₃, 400 MHz

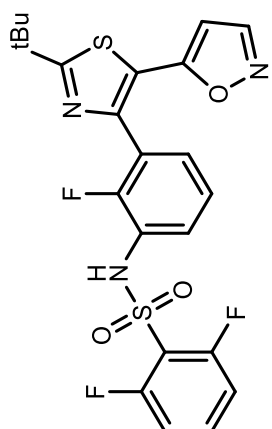
¹H NMR

6j

1.48

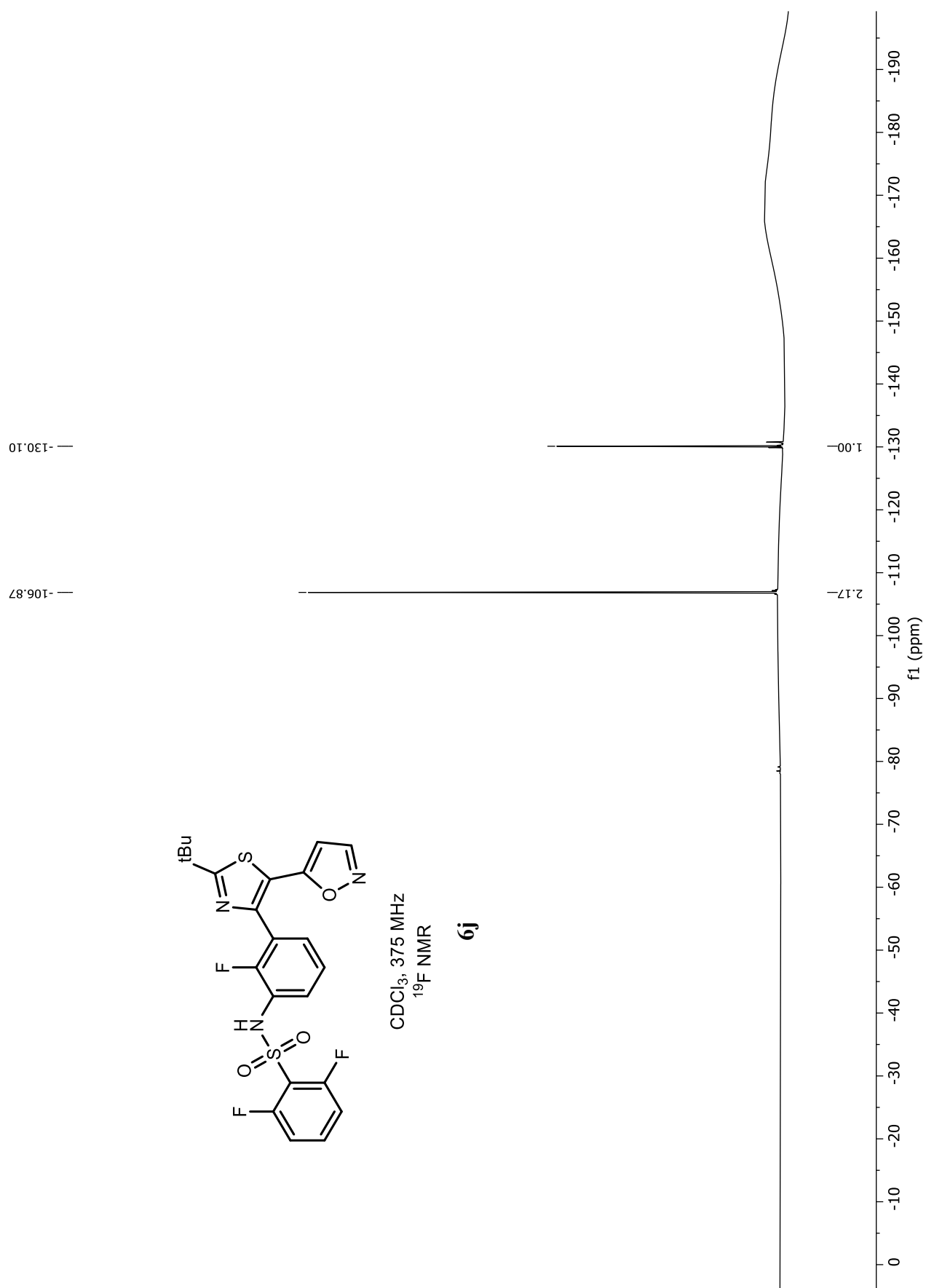


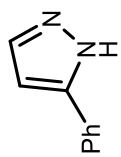




CDCl₃, 375 MHz
¹⁹F NMR

6j





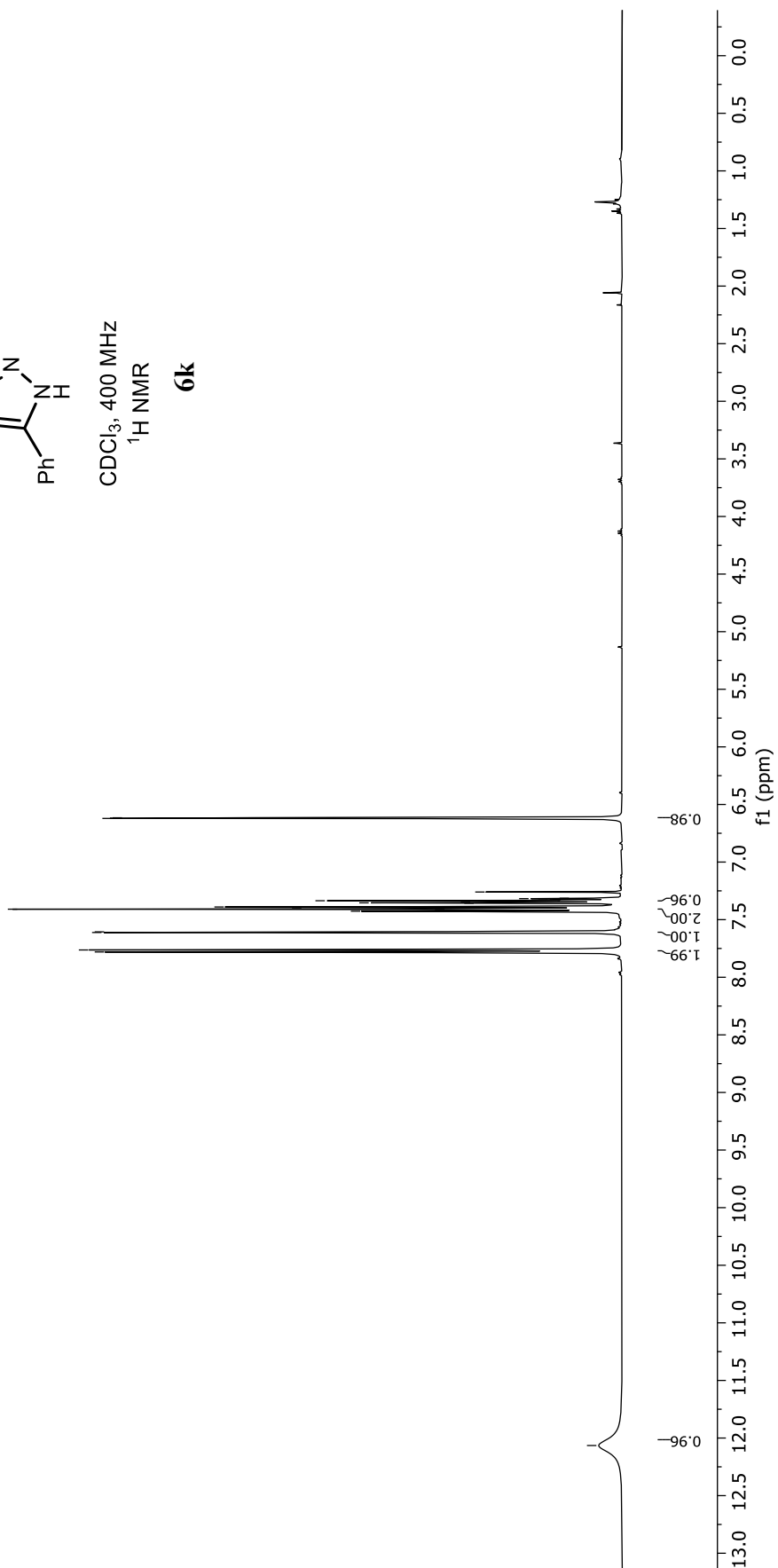
CDCl₃, 400 MHz

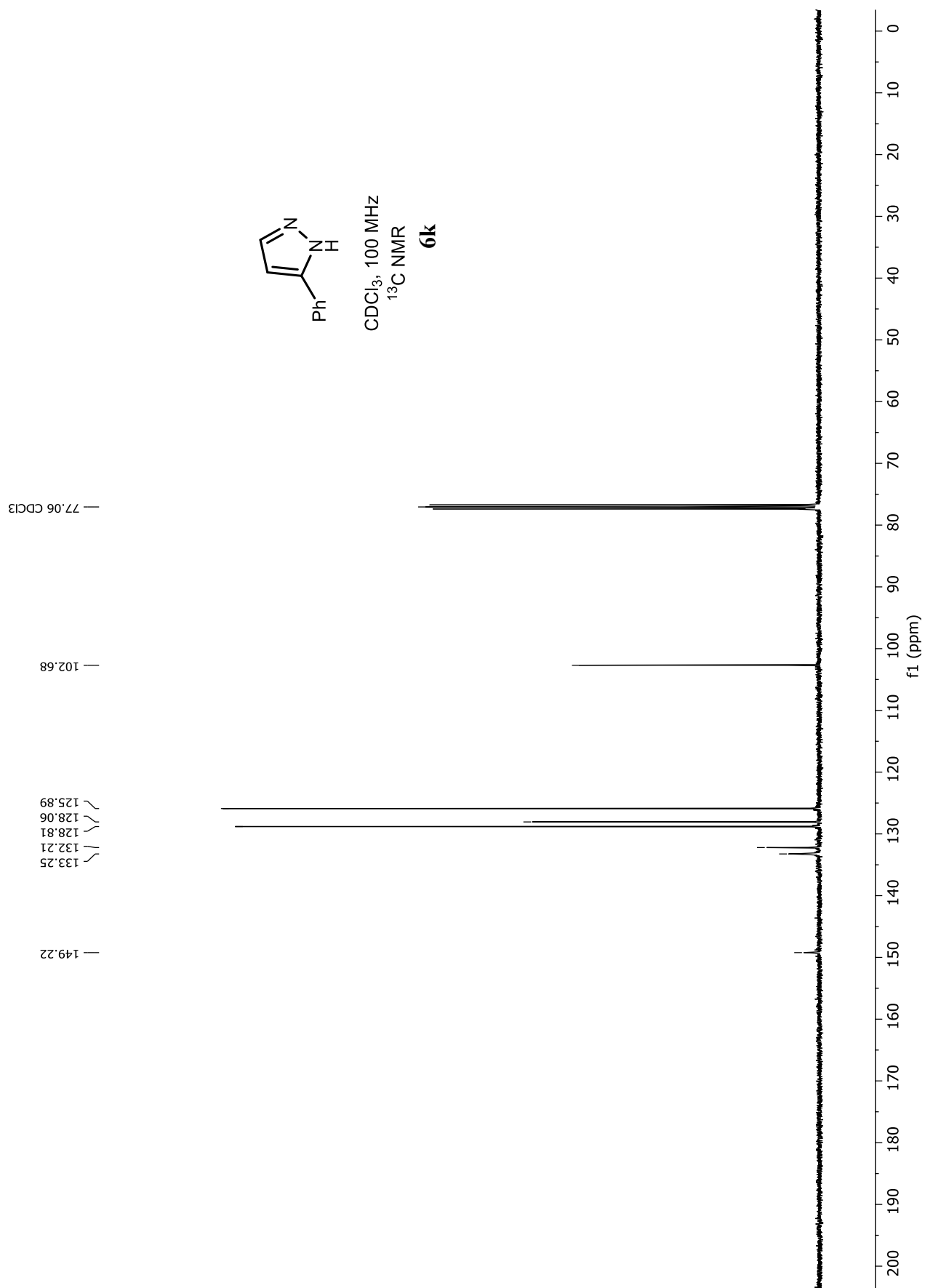
¹H NMR

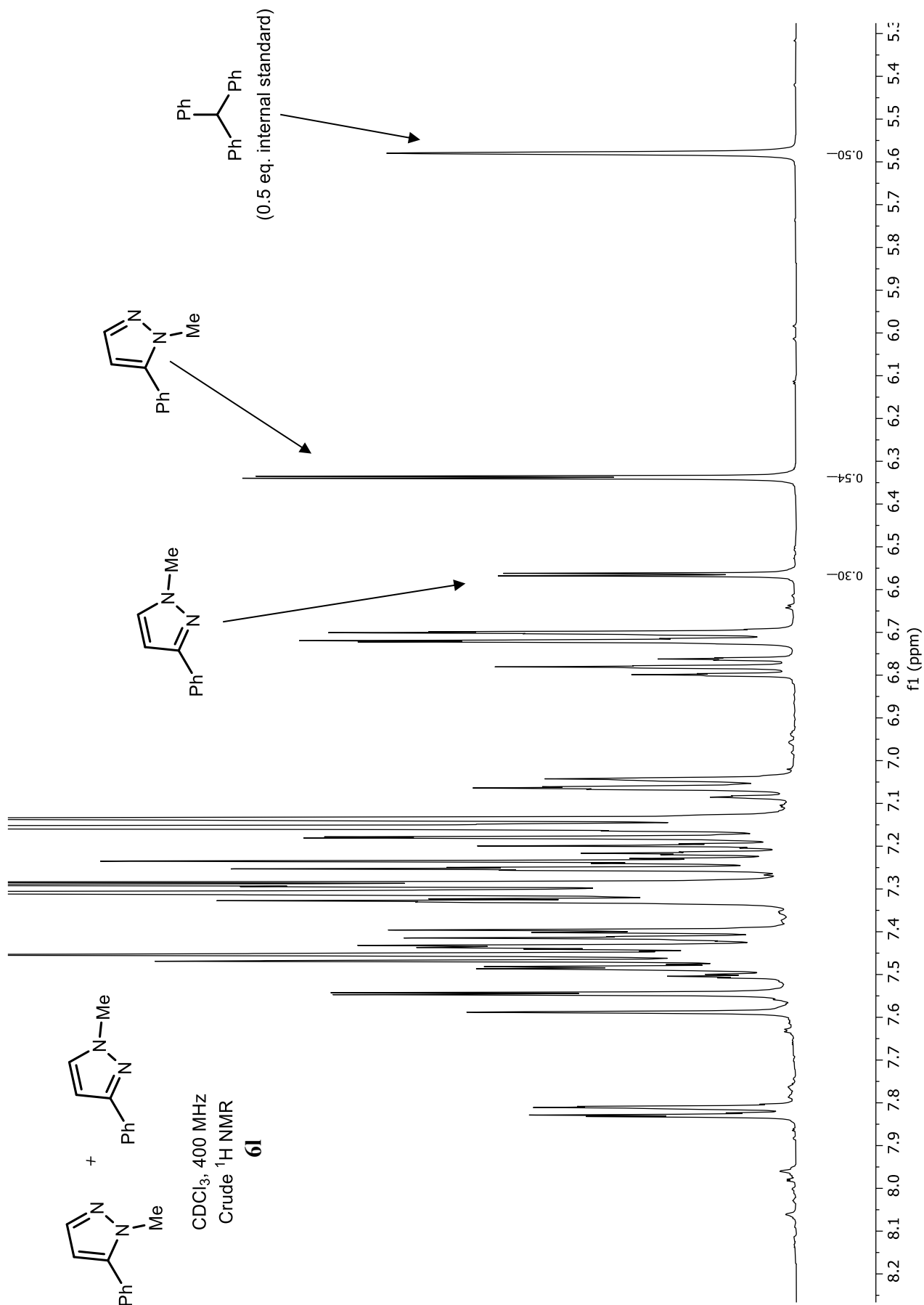
6k

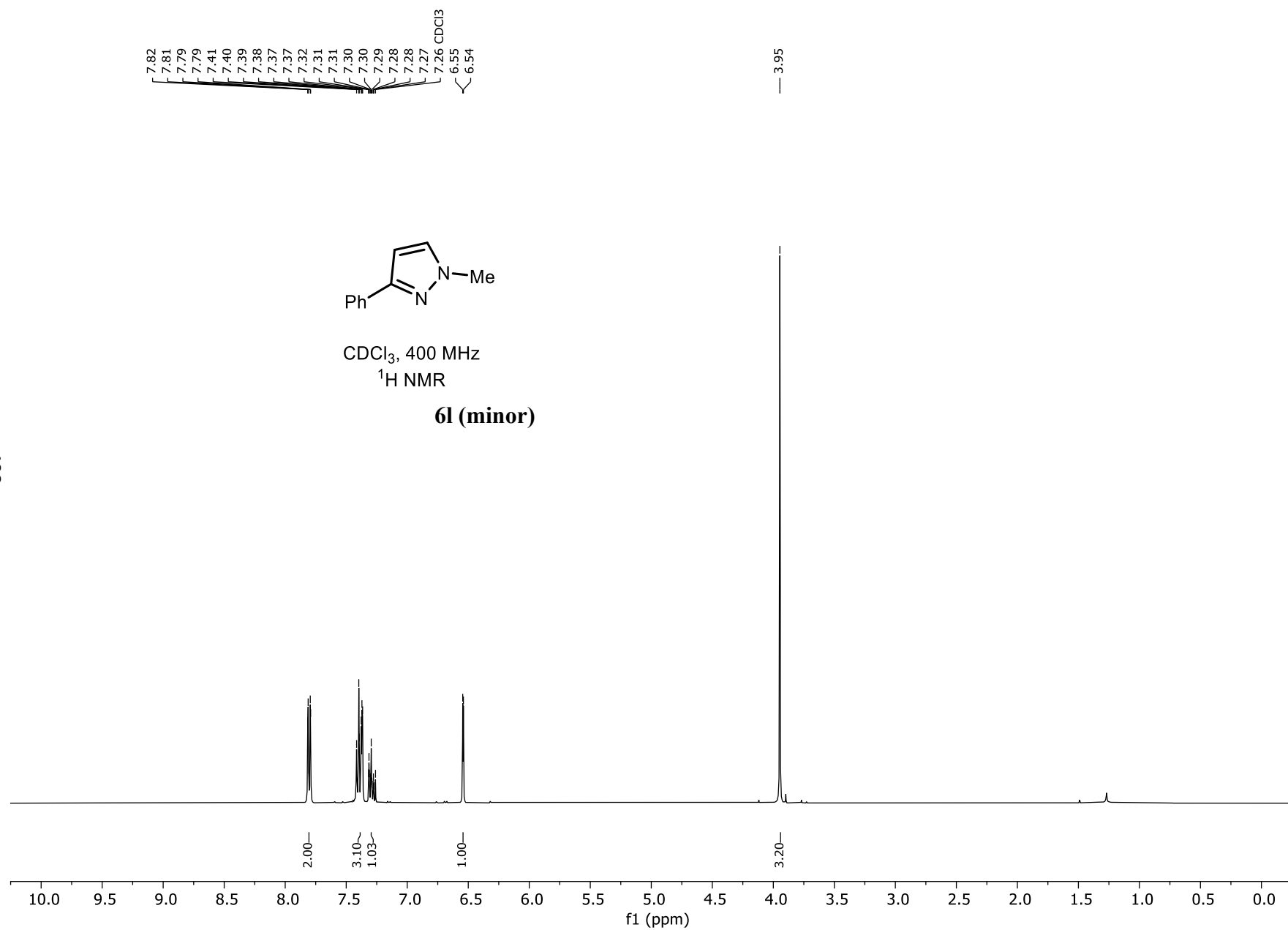
7.78
7.76
7.61
7.61
7.43
7.43
7.42
7.41
7.41
7.40
7.39
7.39
7.39
7.36
7.35
7.35
7.34
7.33
7.32
7.32
7.31
7.26 CDCl₃
6.62
6.62

— 12.06

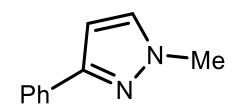
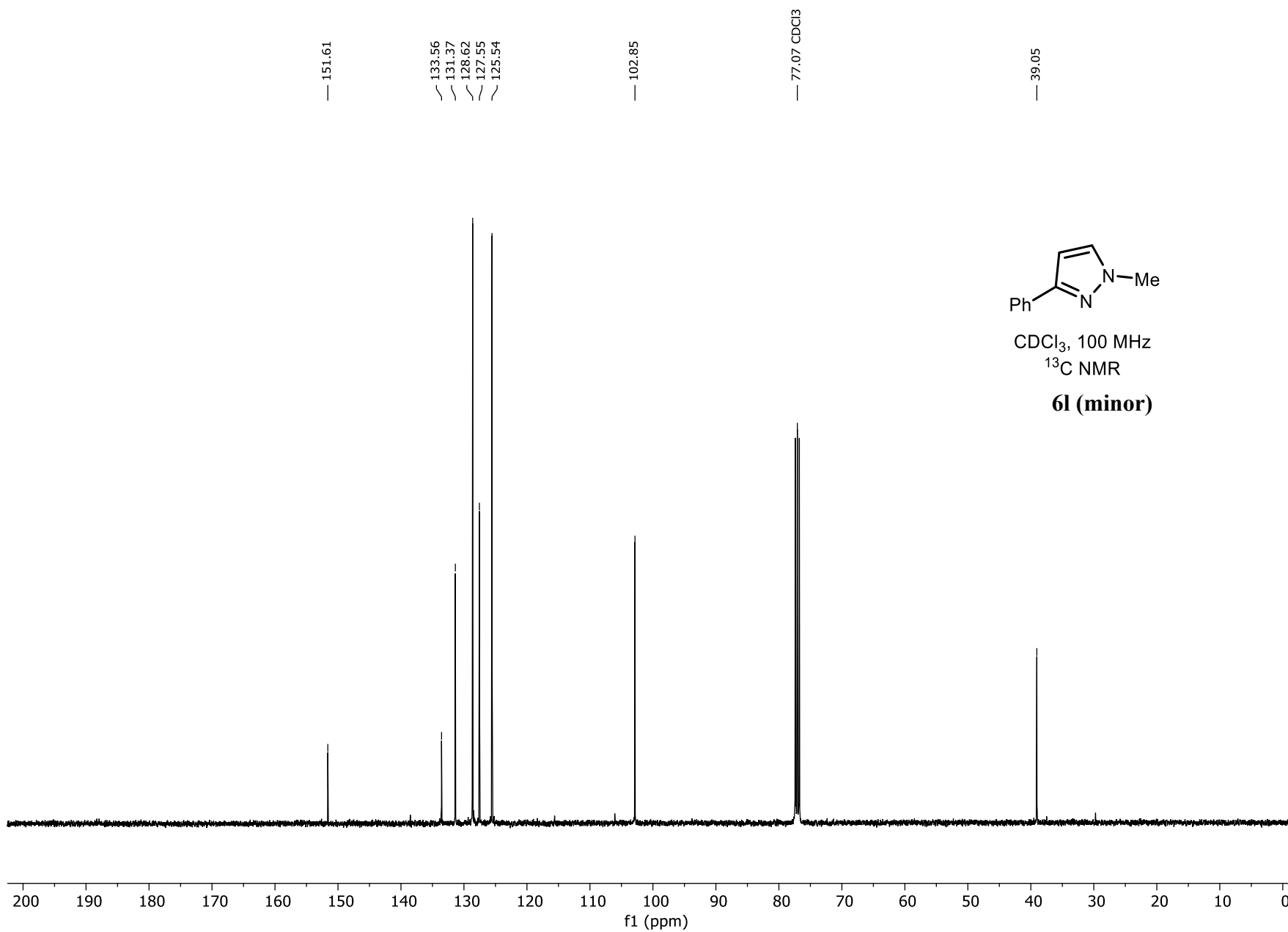




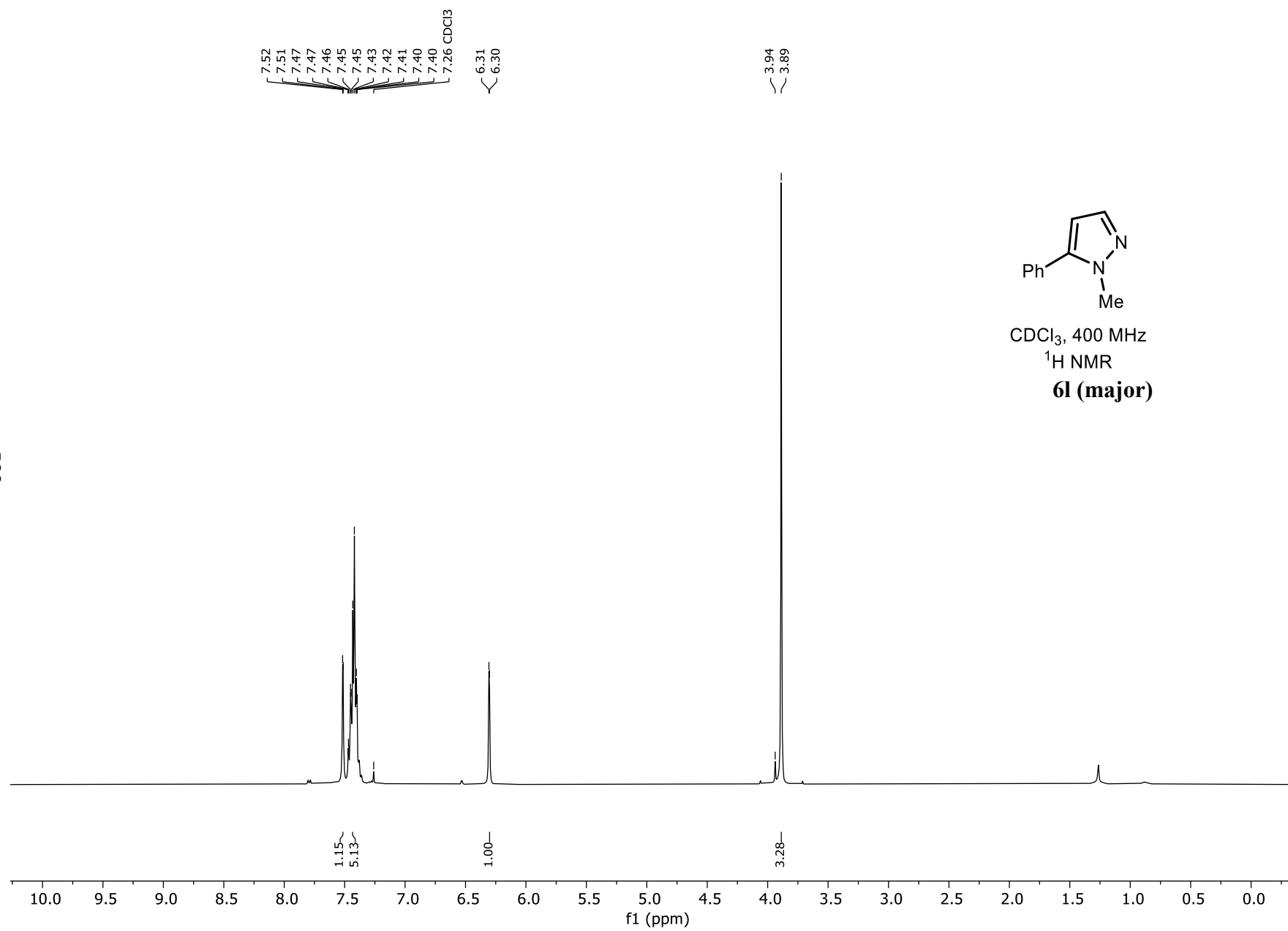


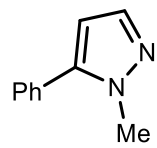


499



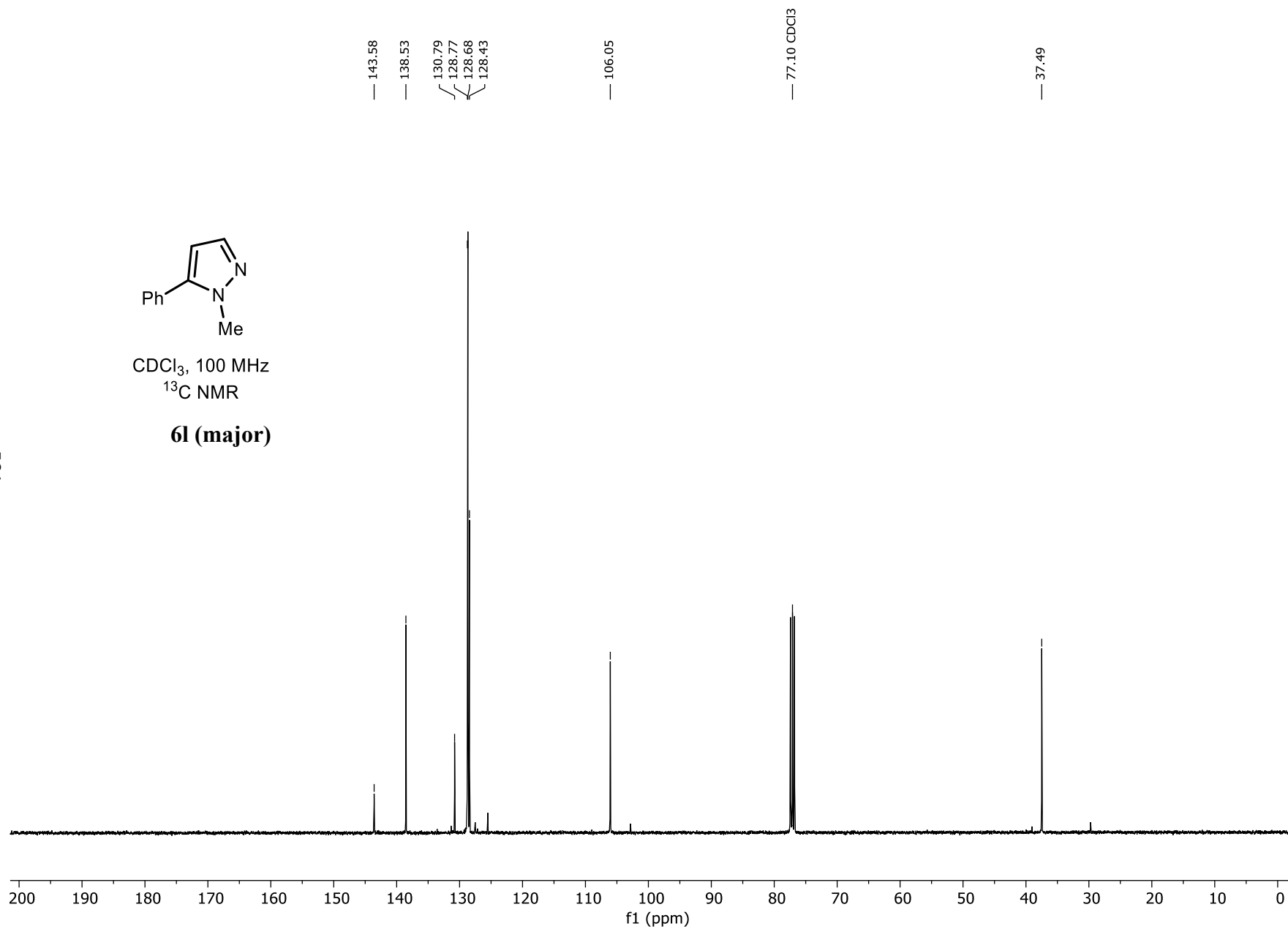
500

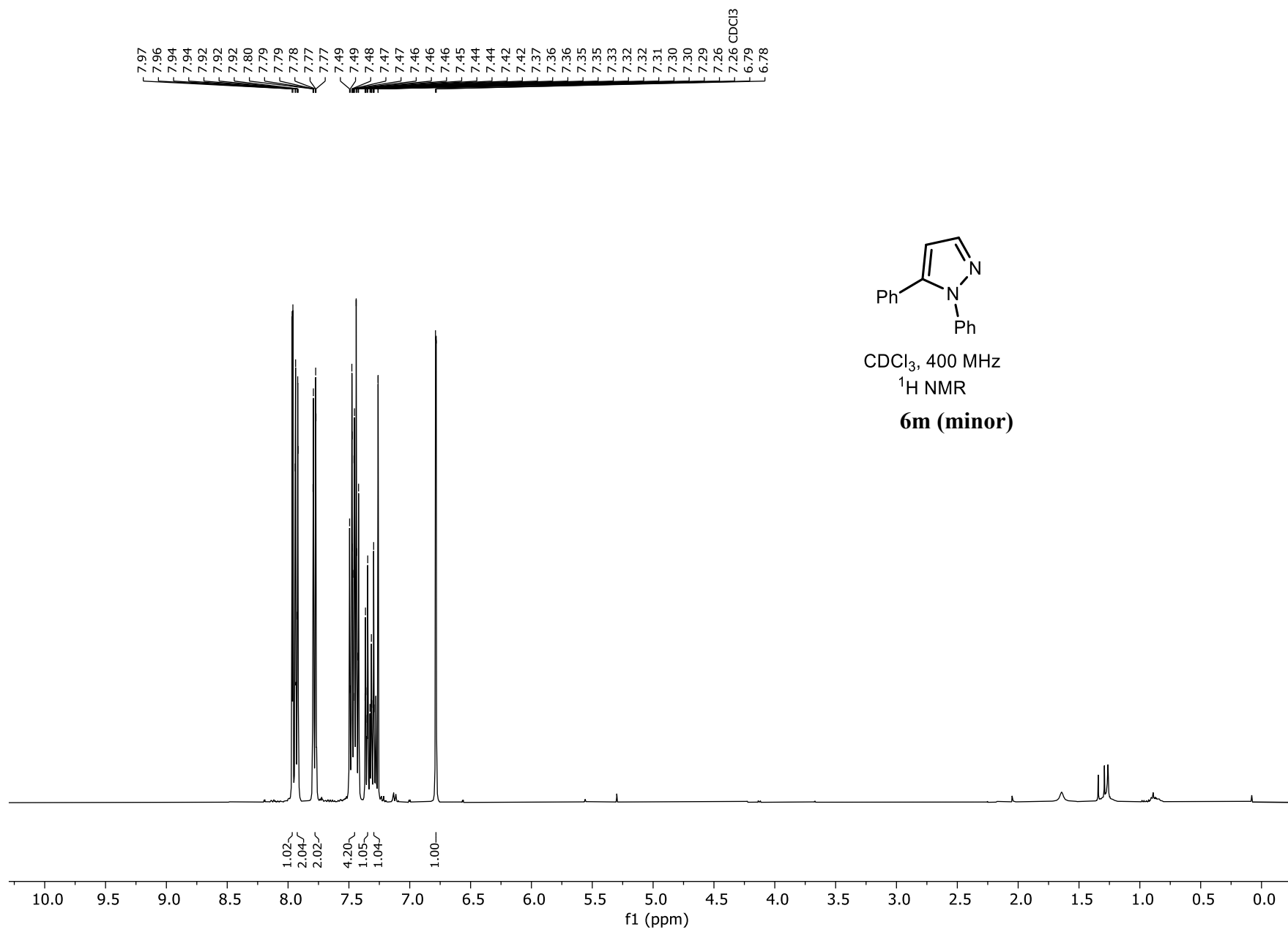




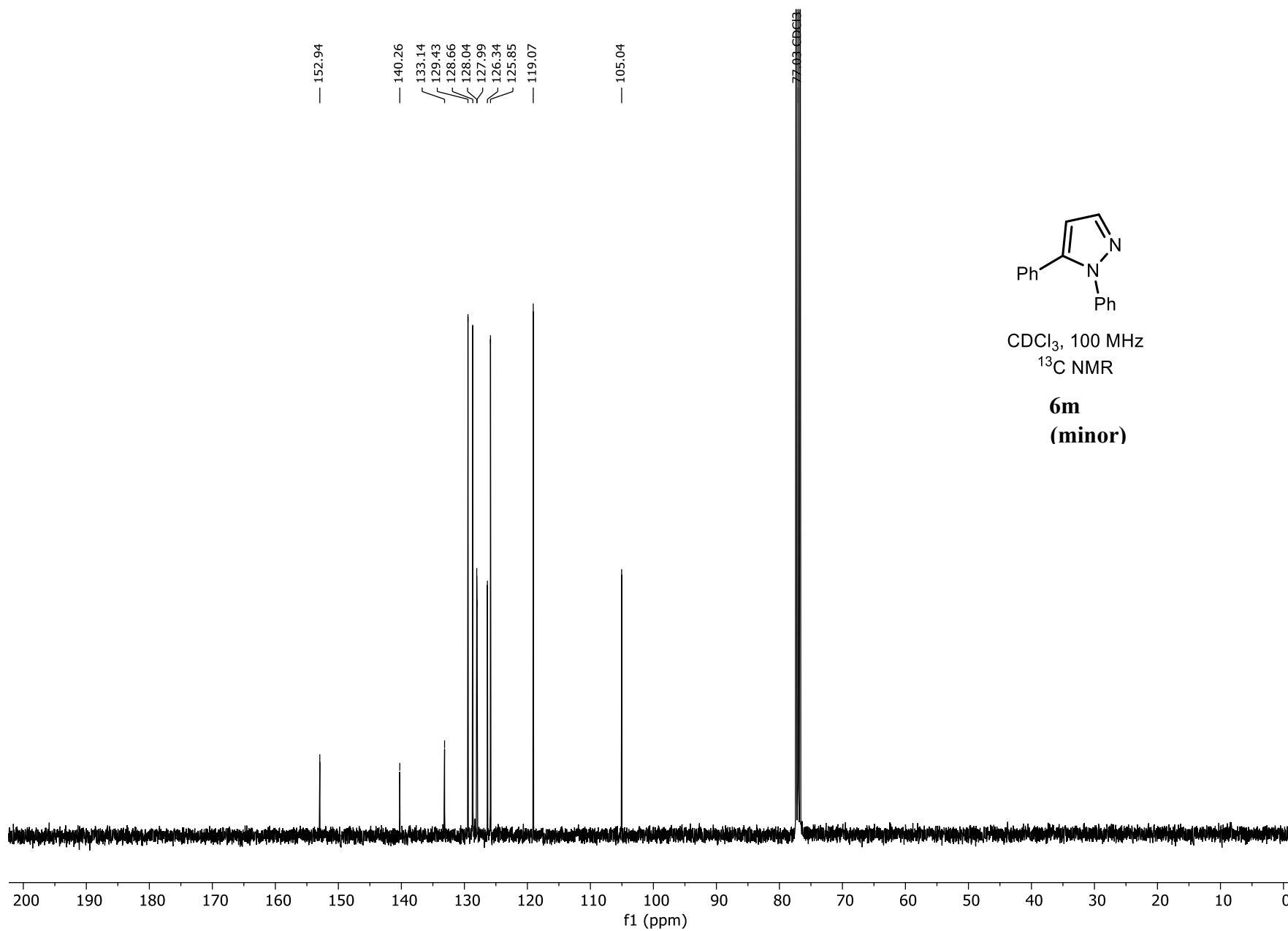
CDCl₃, 100 MHz
¹³C NMR

6l (major)

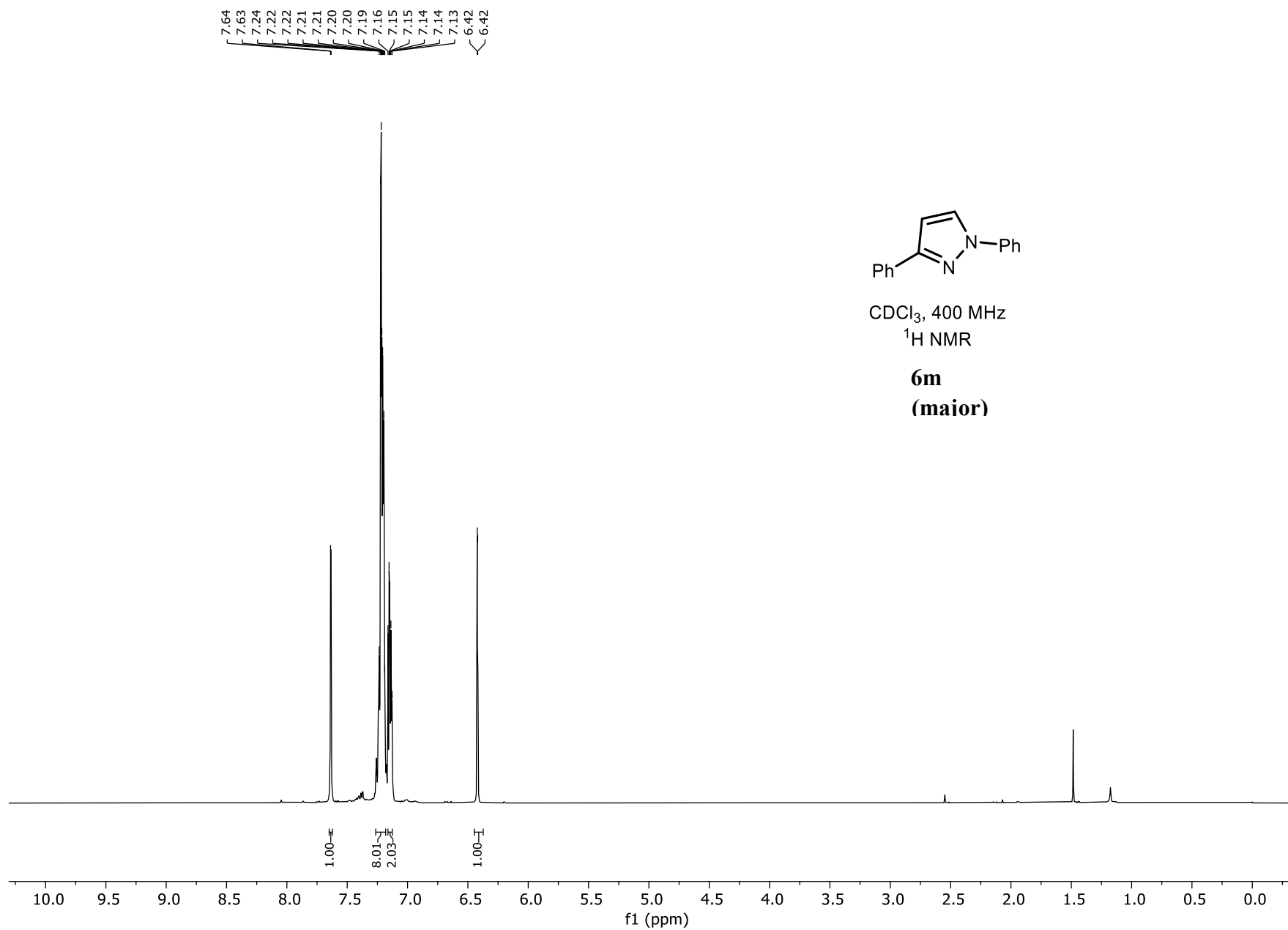


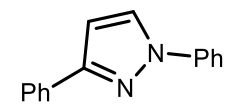


503



504



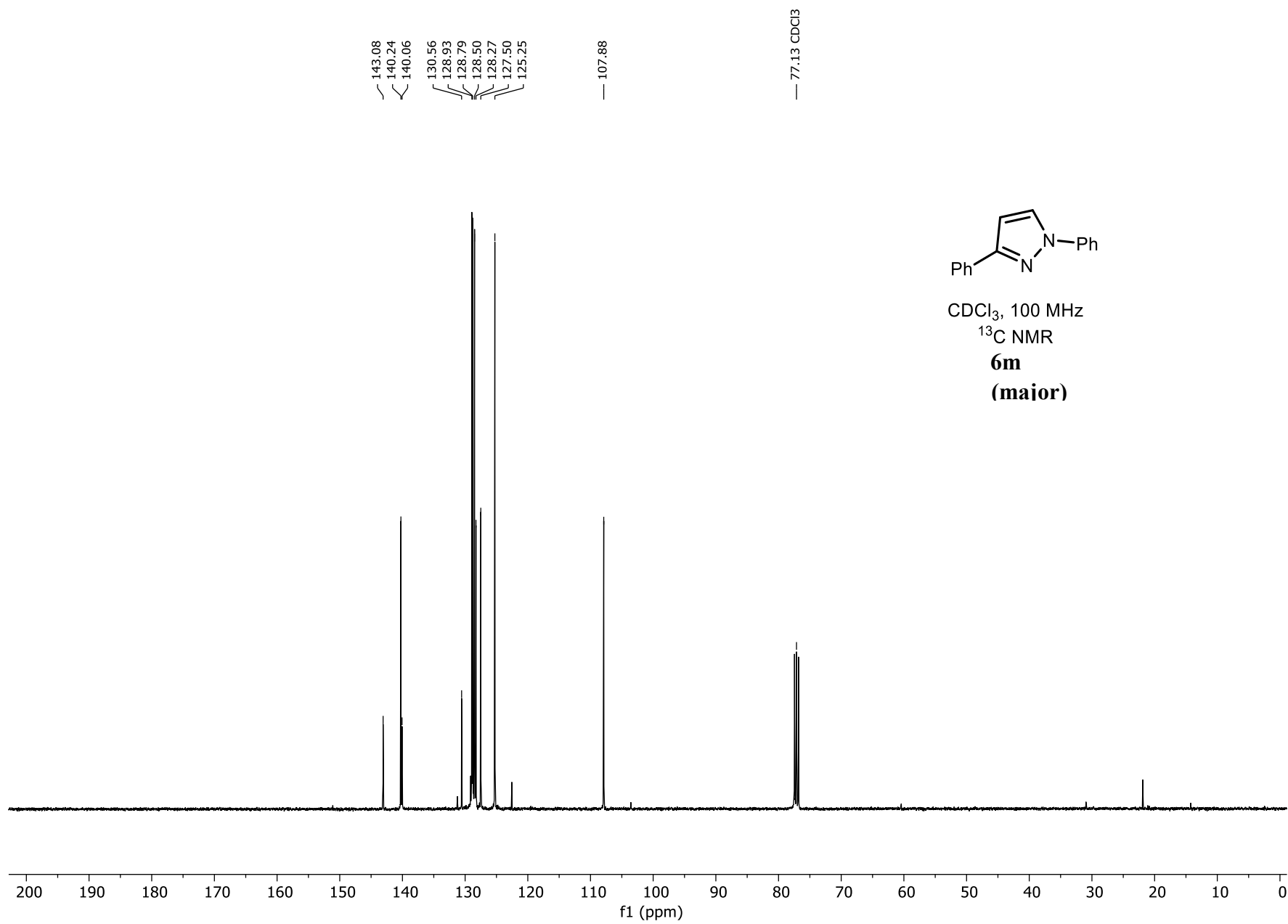


CDCl₃, 100 MHz

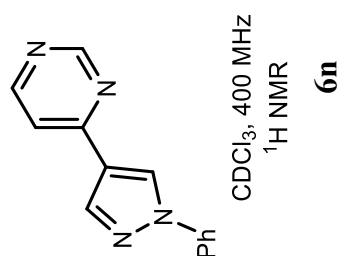
¹³C NMR

6m

(major)

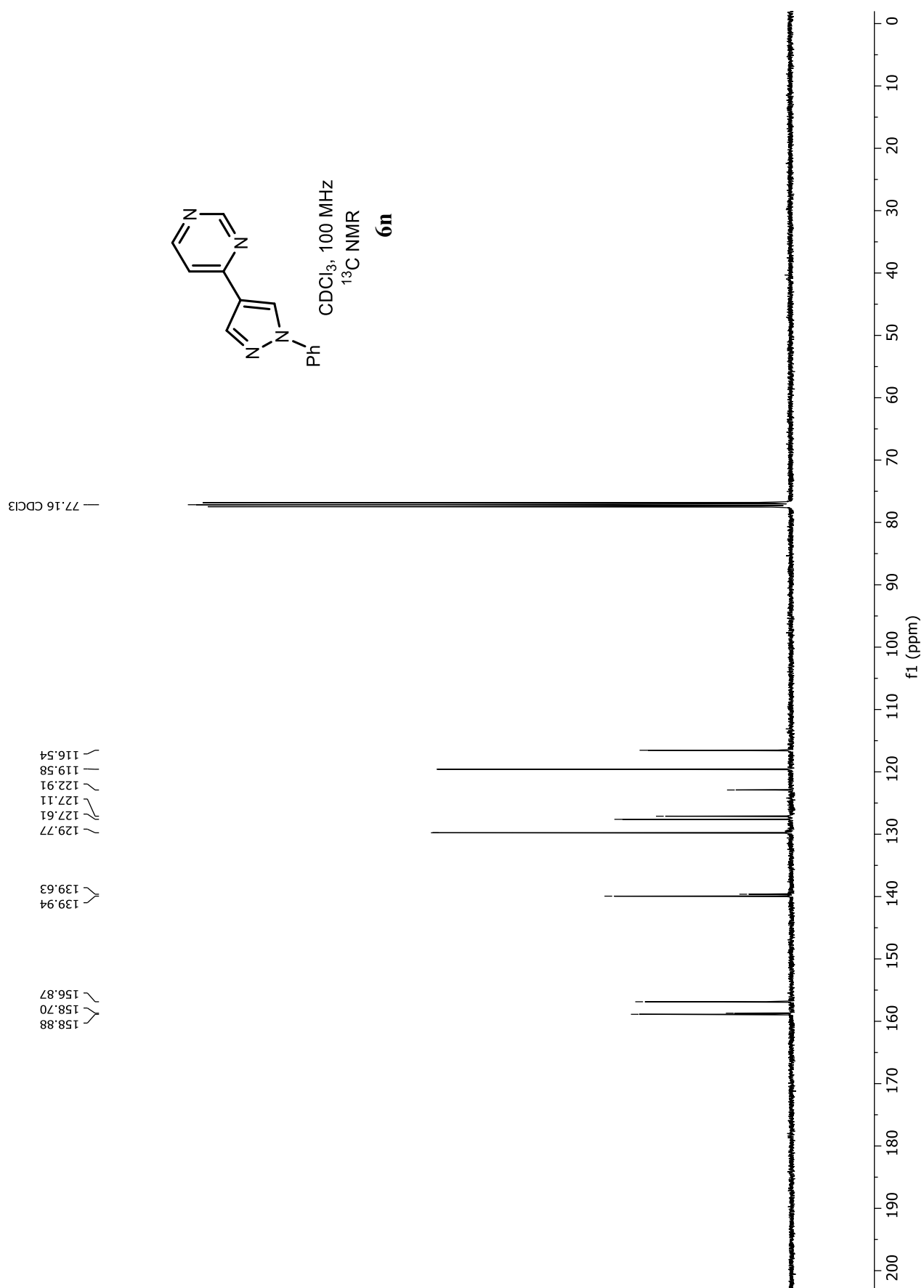


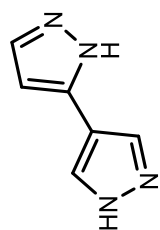
9.15
 8.69
 8.68
 8.61
 8.24
 7.76
 7.74
 7.52
 7.51
 7.50
 7.49
 7.48
 7.38
 7.36
 7.34
 7.26 CDCl₃



1.02
 1.01
 1.00
 0.97
 2.02
 3.12
 1.01

f1 (ppm)





CD₃OD, 400 MHz
¹H NMR

60

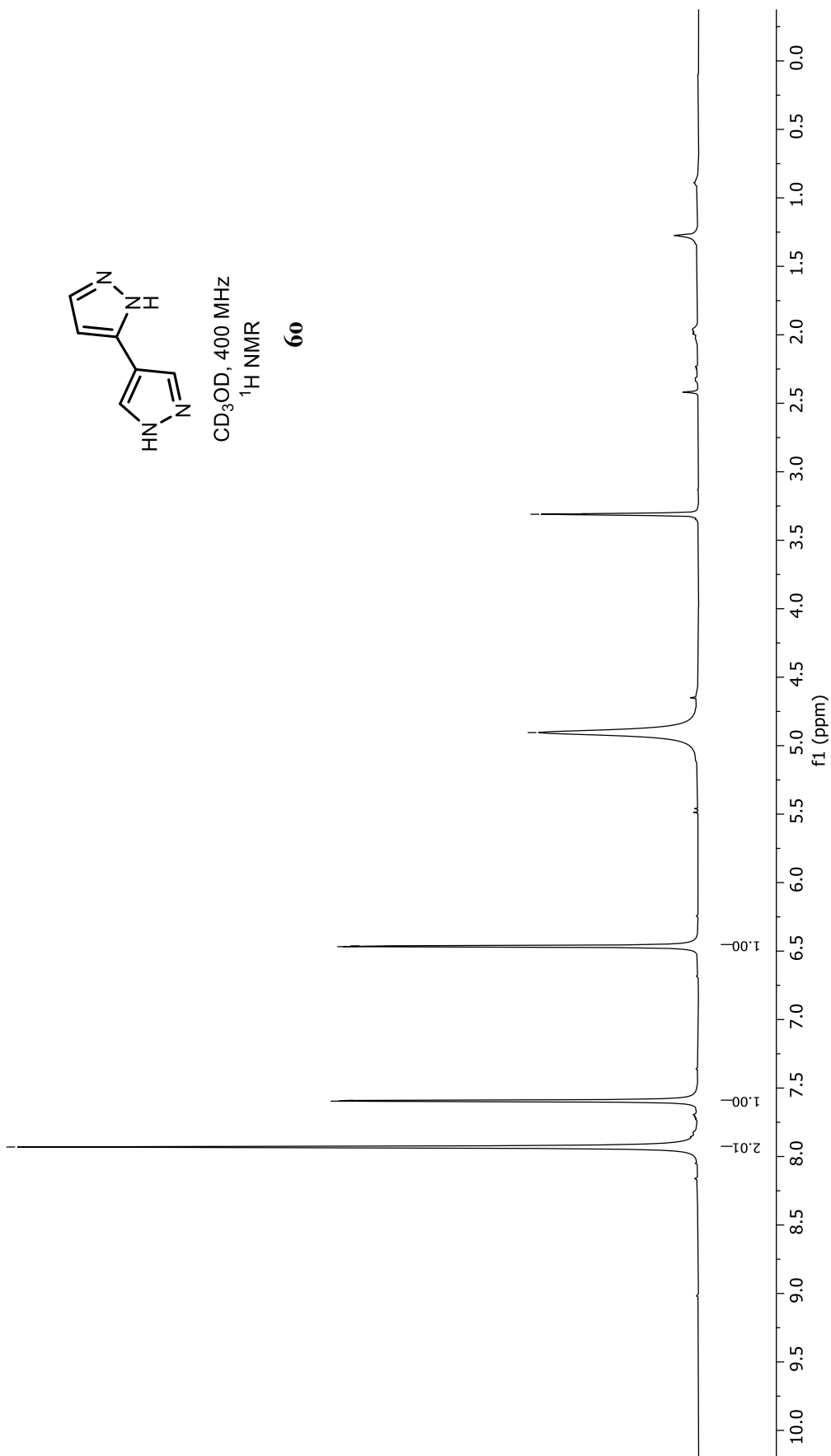
— 3.31 DMSO-d₆

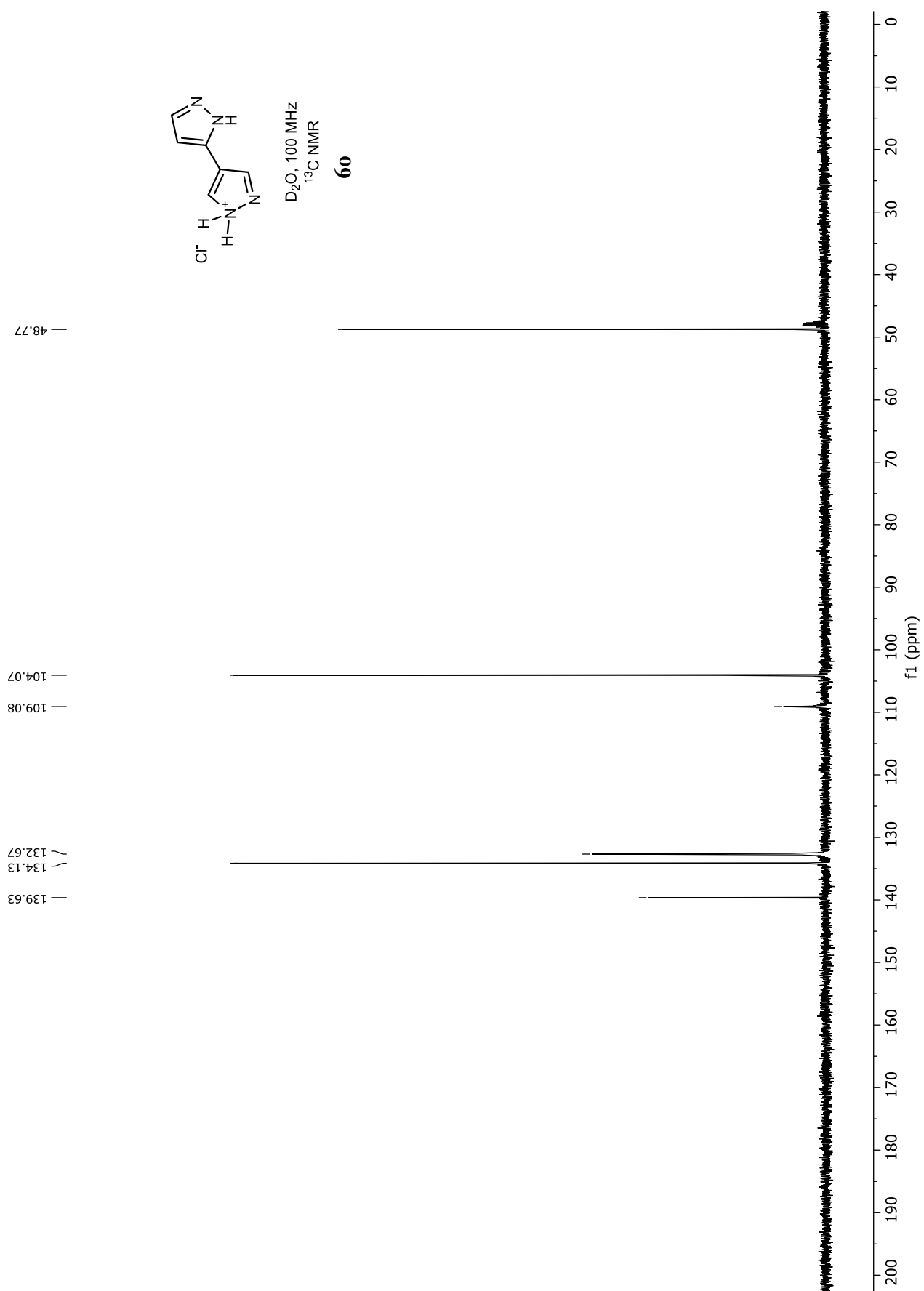
— 4.90 H₂O

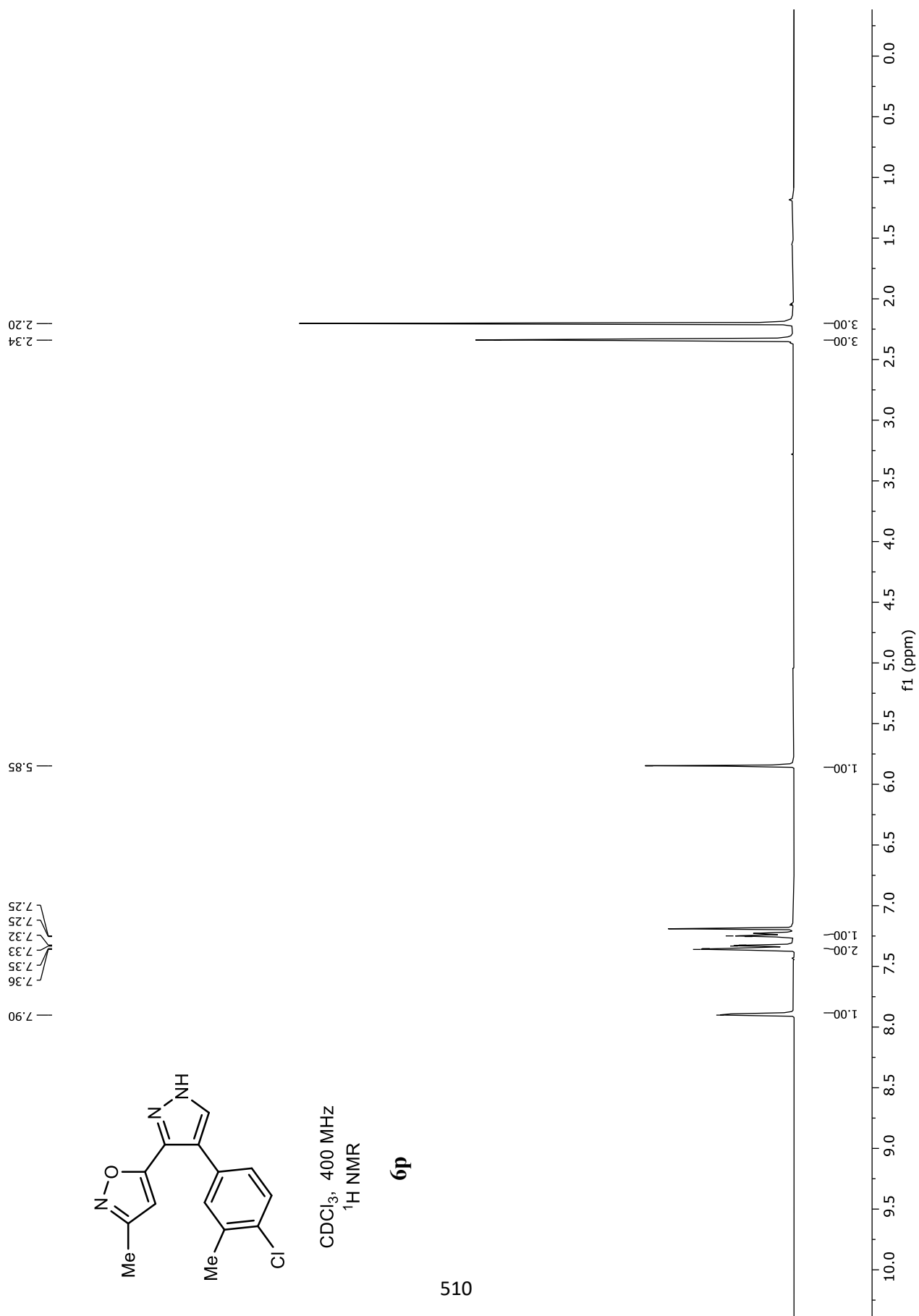
6.47
 6.46

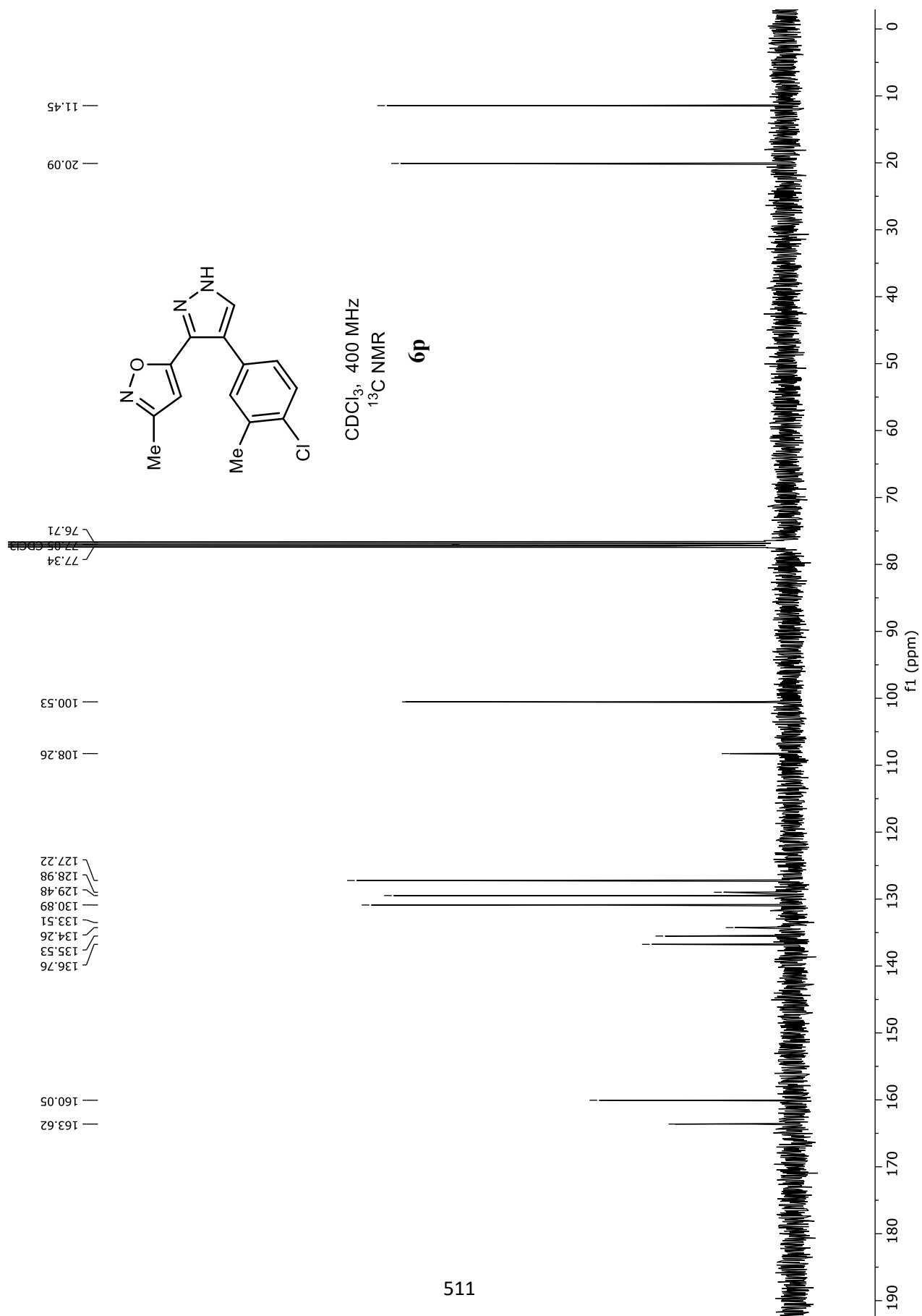
7.59
 7.60

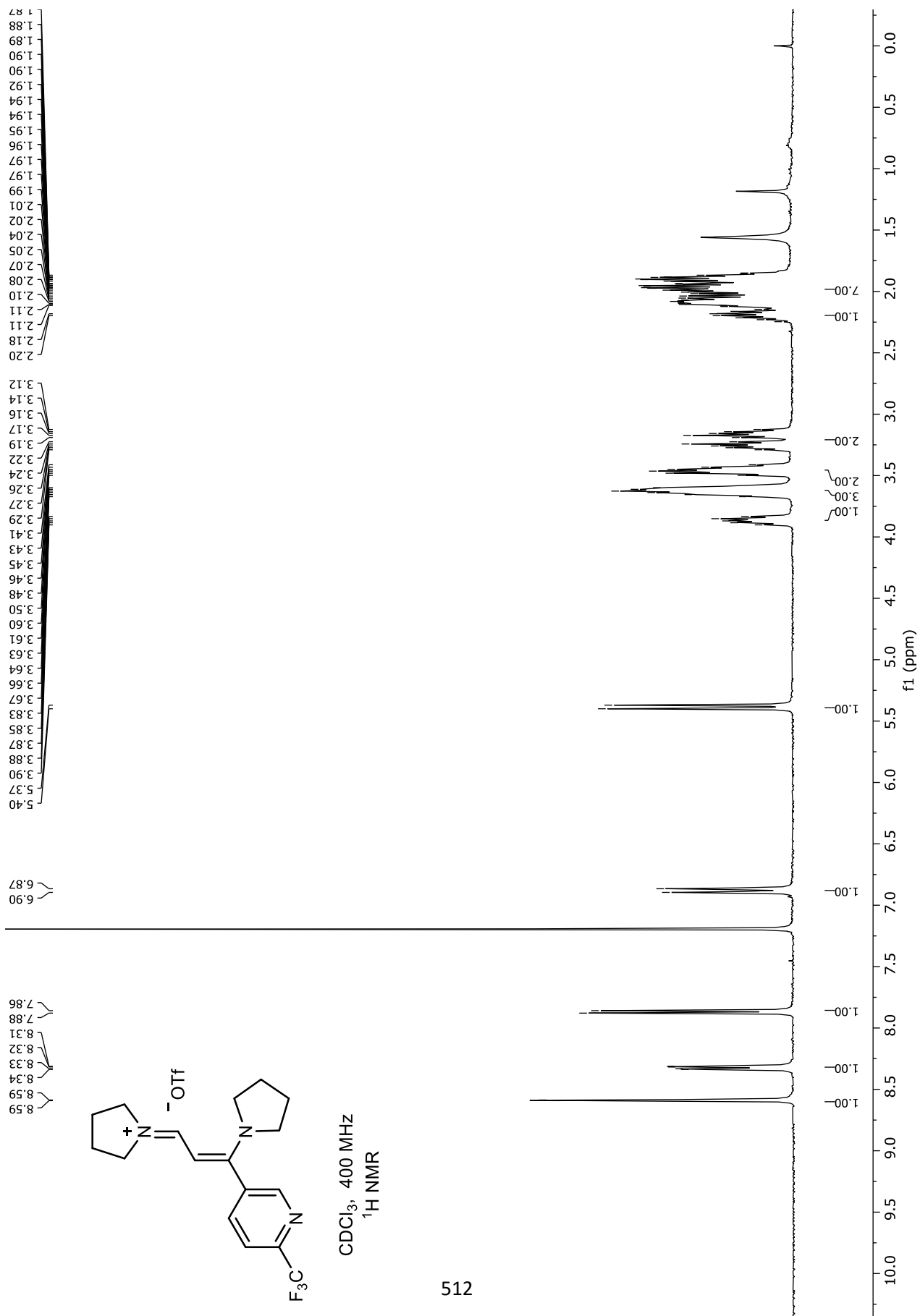
— 7.93

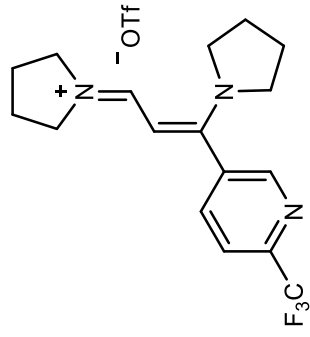








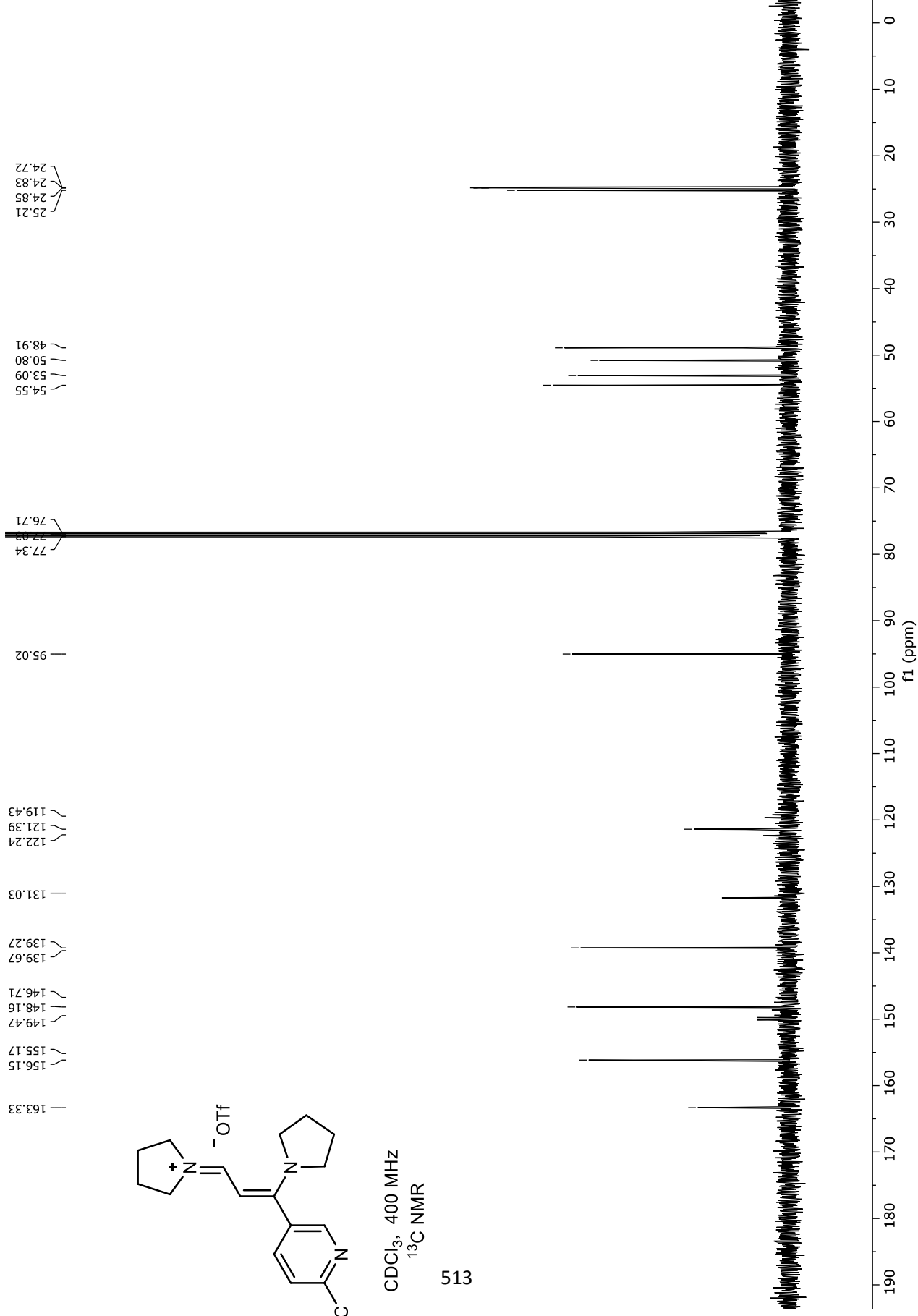




CDCl₃, 400 MHz

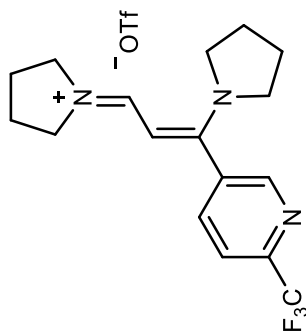
¹³C NMR

513



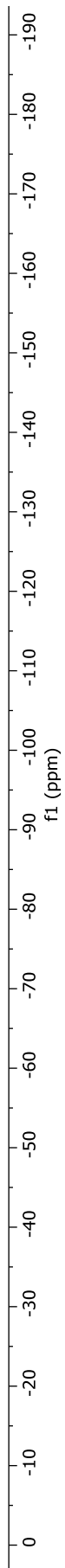
— -78.32

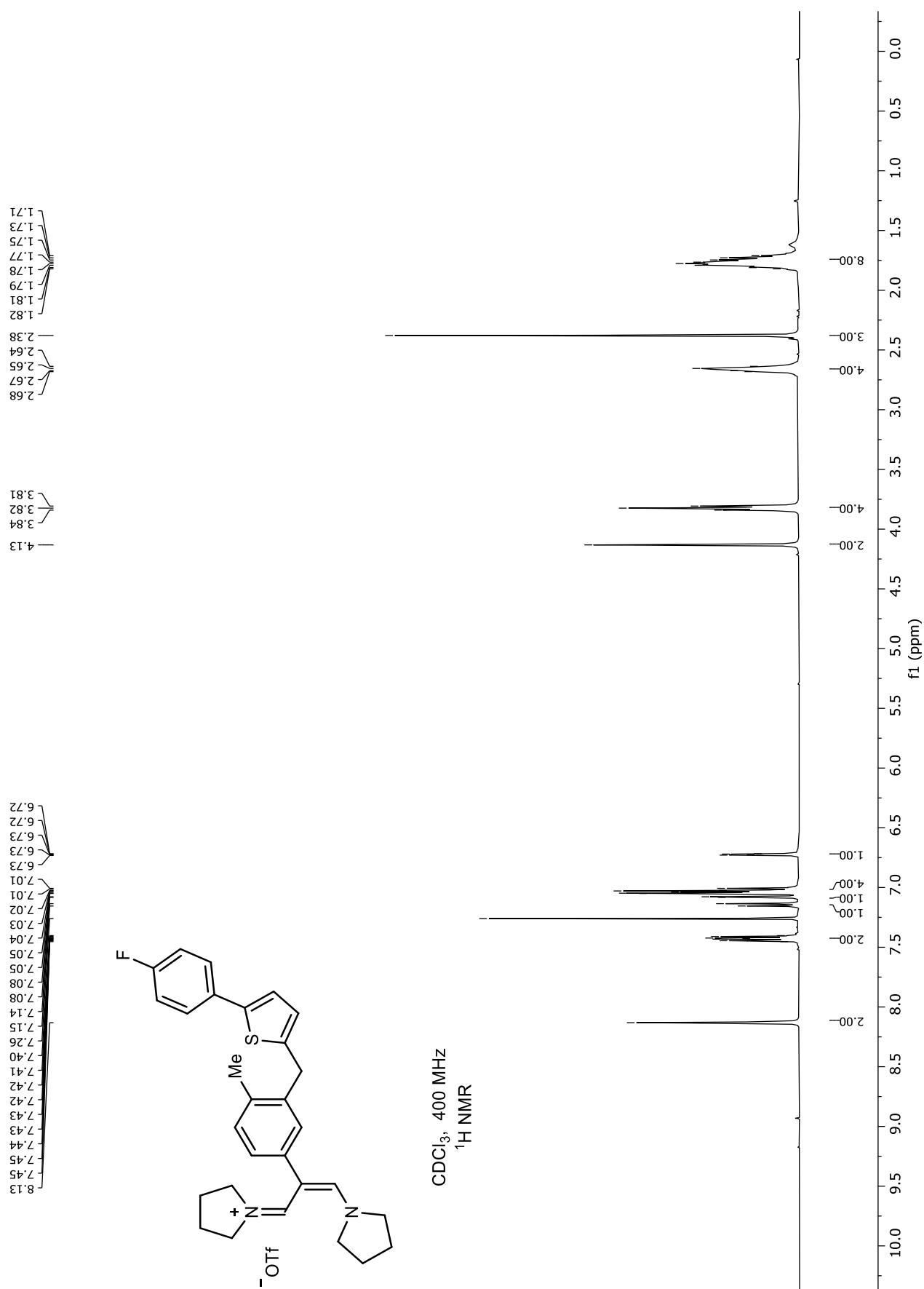
— -68.15

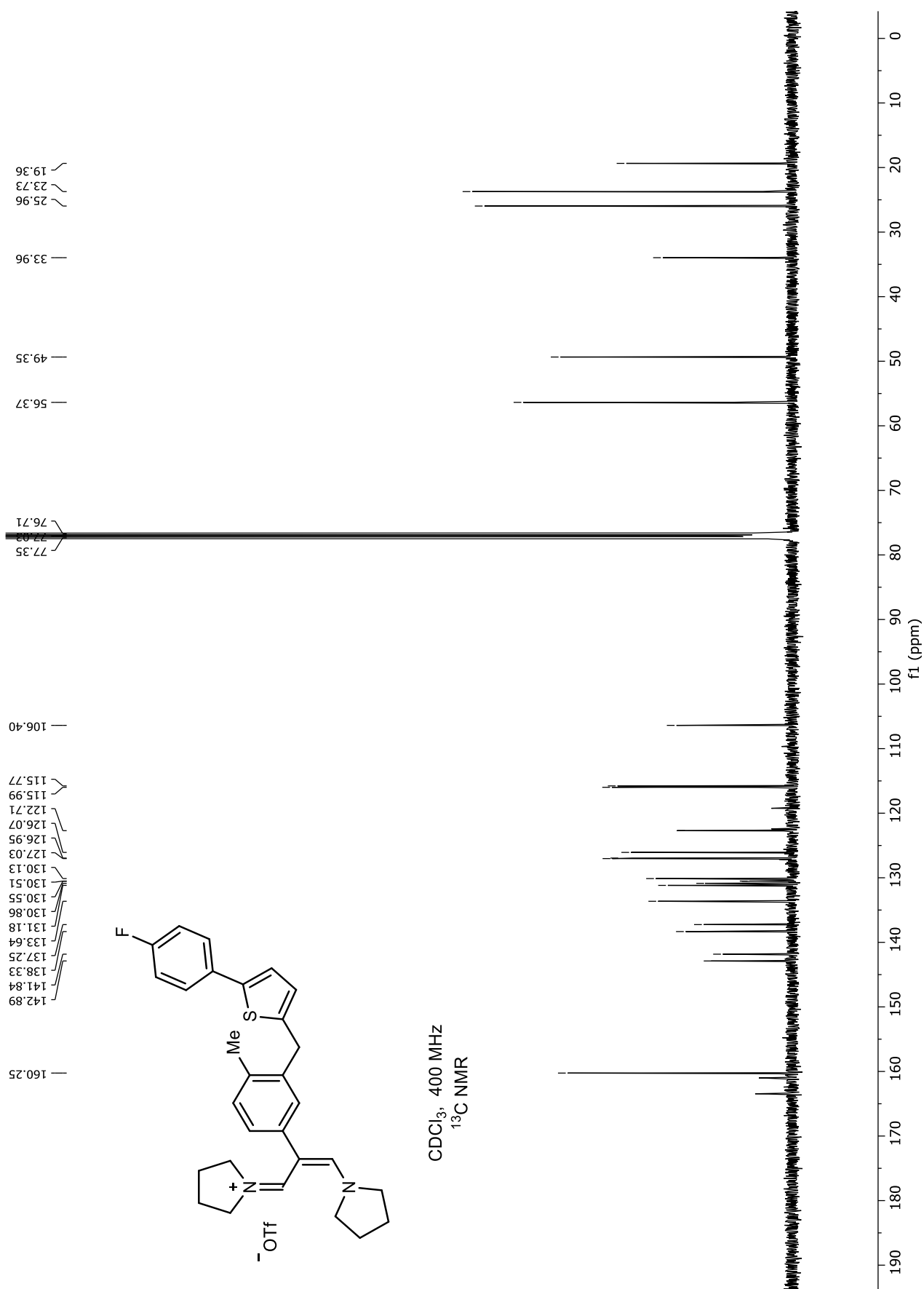


CDCl₃, 400 MHz
¹⁹F NMR

514

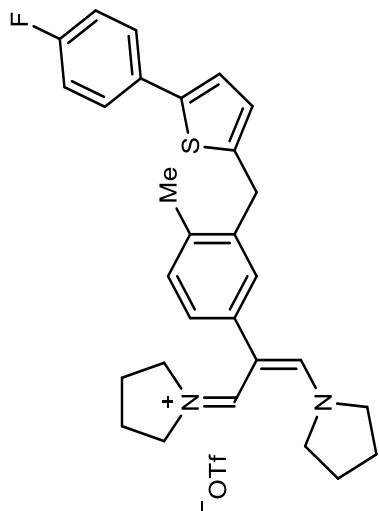






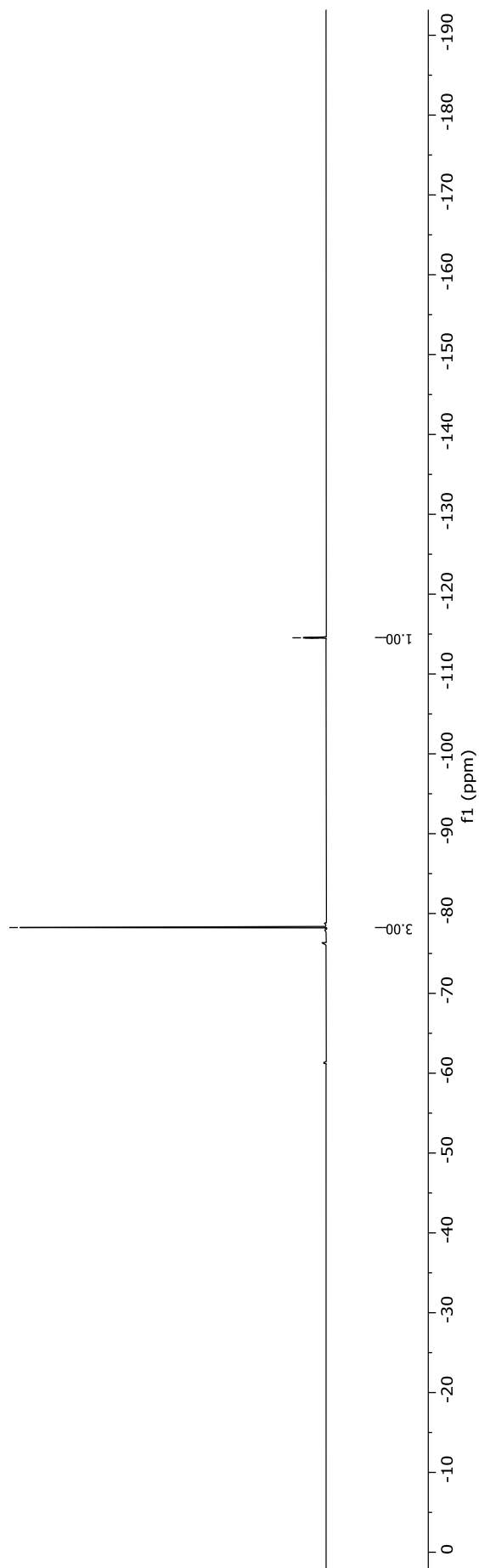
-114.50
-114.51
-114.52
-114.53
-114.55
-114.55
-114.57

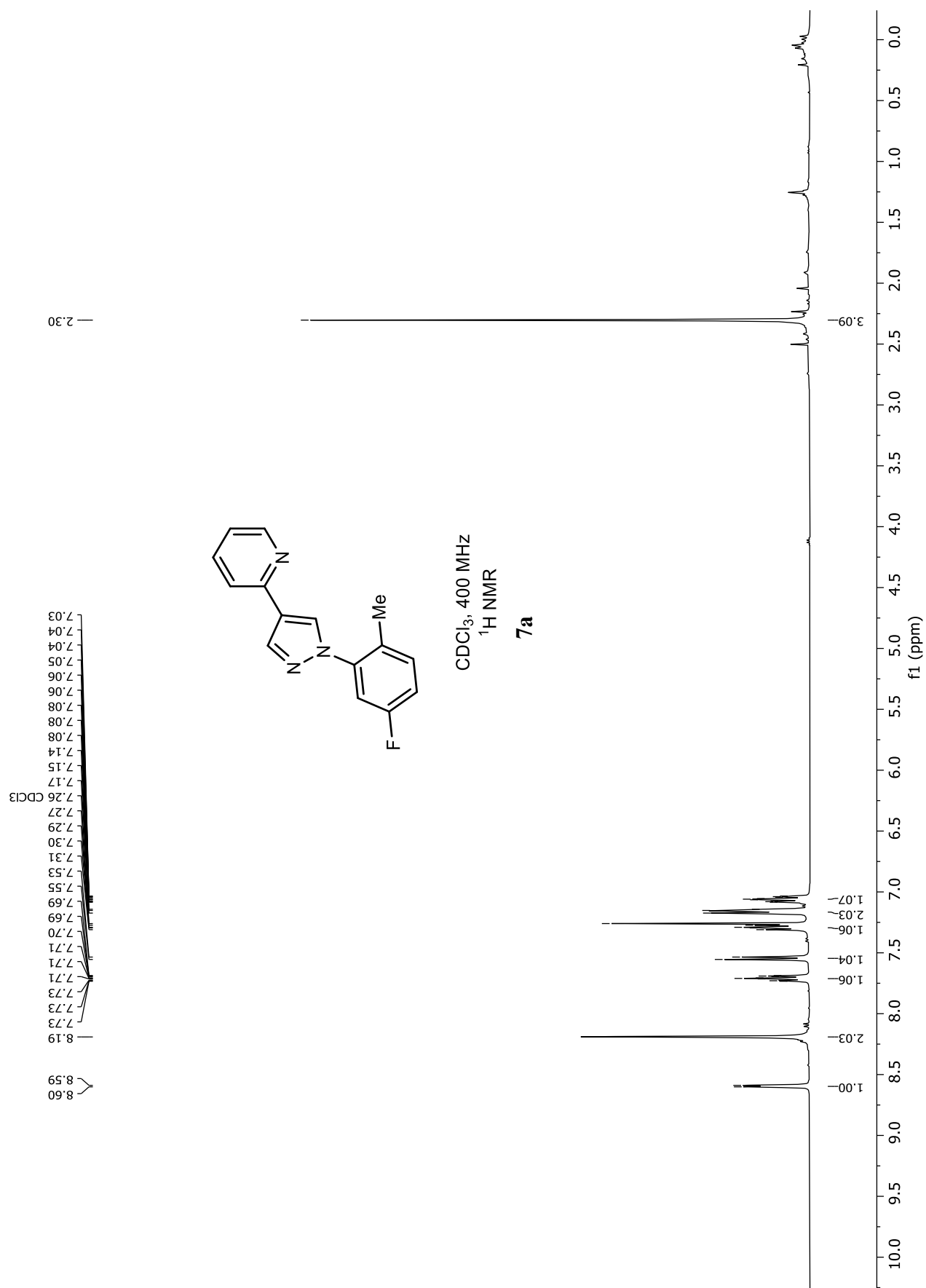
-78.24

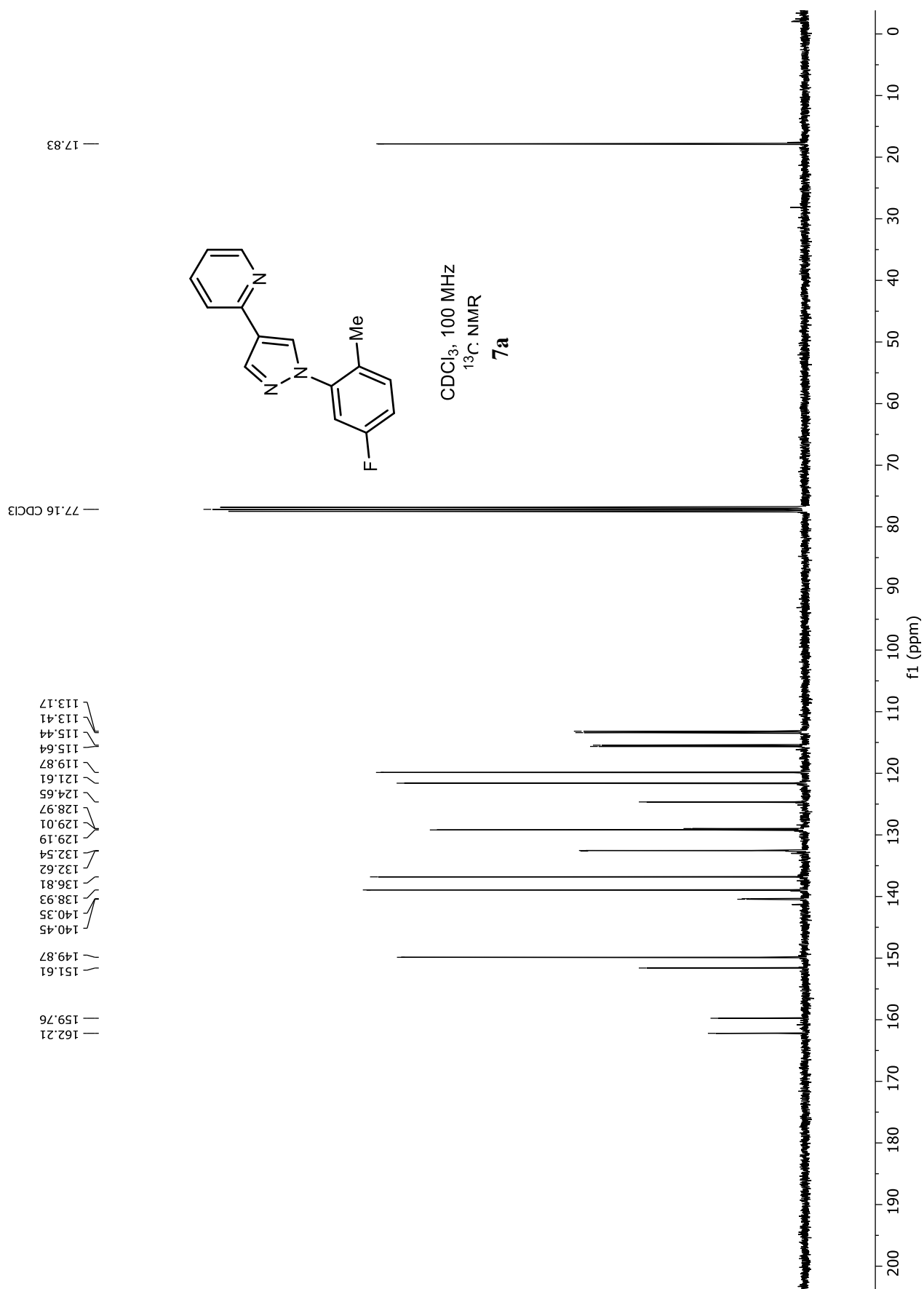


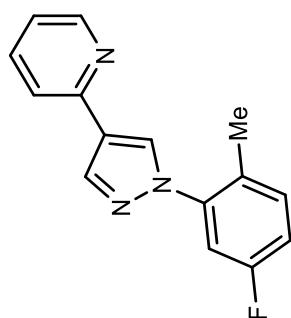
CDCl_3 , 400 MHz
 ^{19}F NMR

517







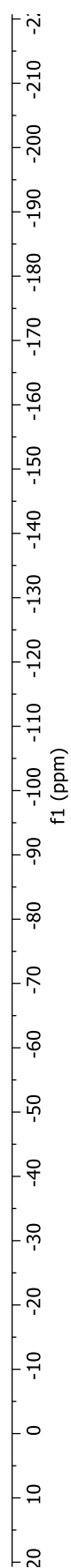


CDCl₃, 375 MHz

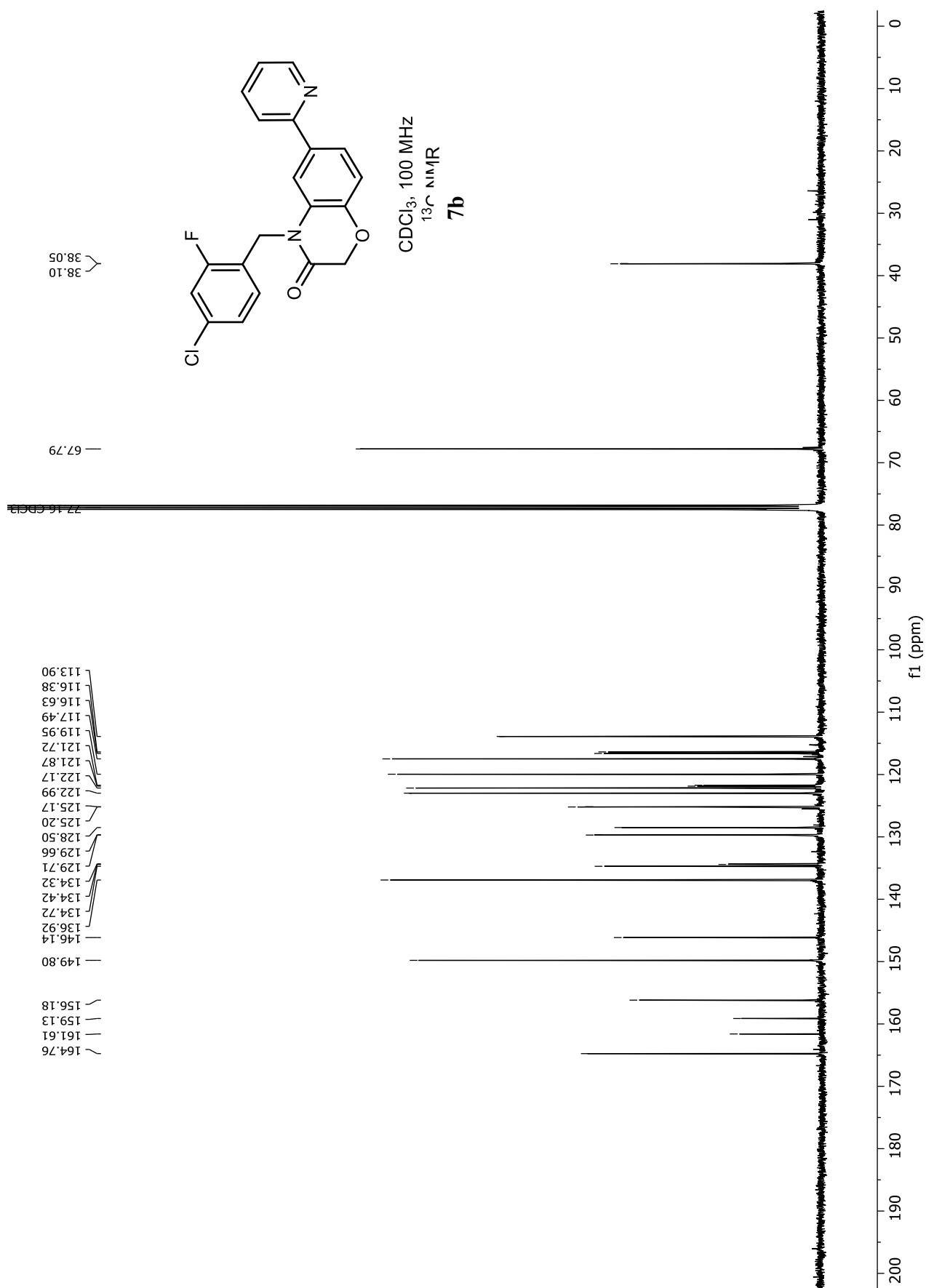
¹⁹F NMR

7a

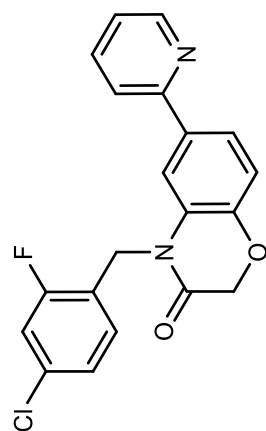
-115.73
-115.75
-115.77
-115.79







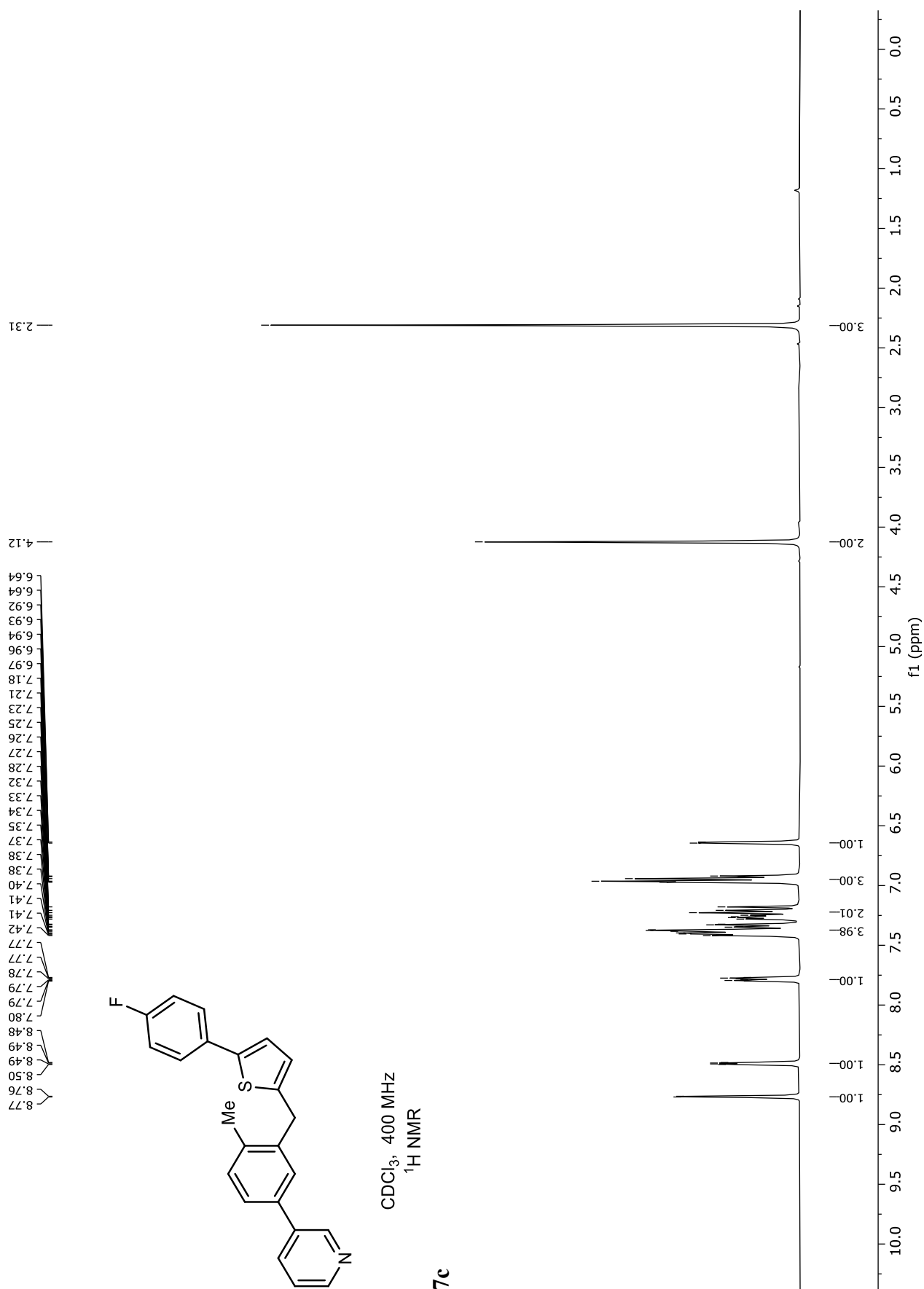
-115.49
-115.52
-115.54



CDCl₃, 375 MHz
¹⁹F NMR

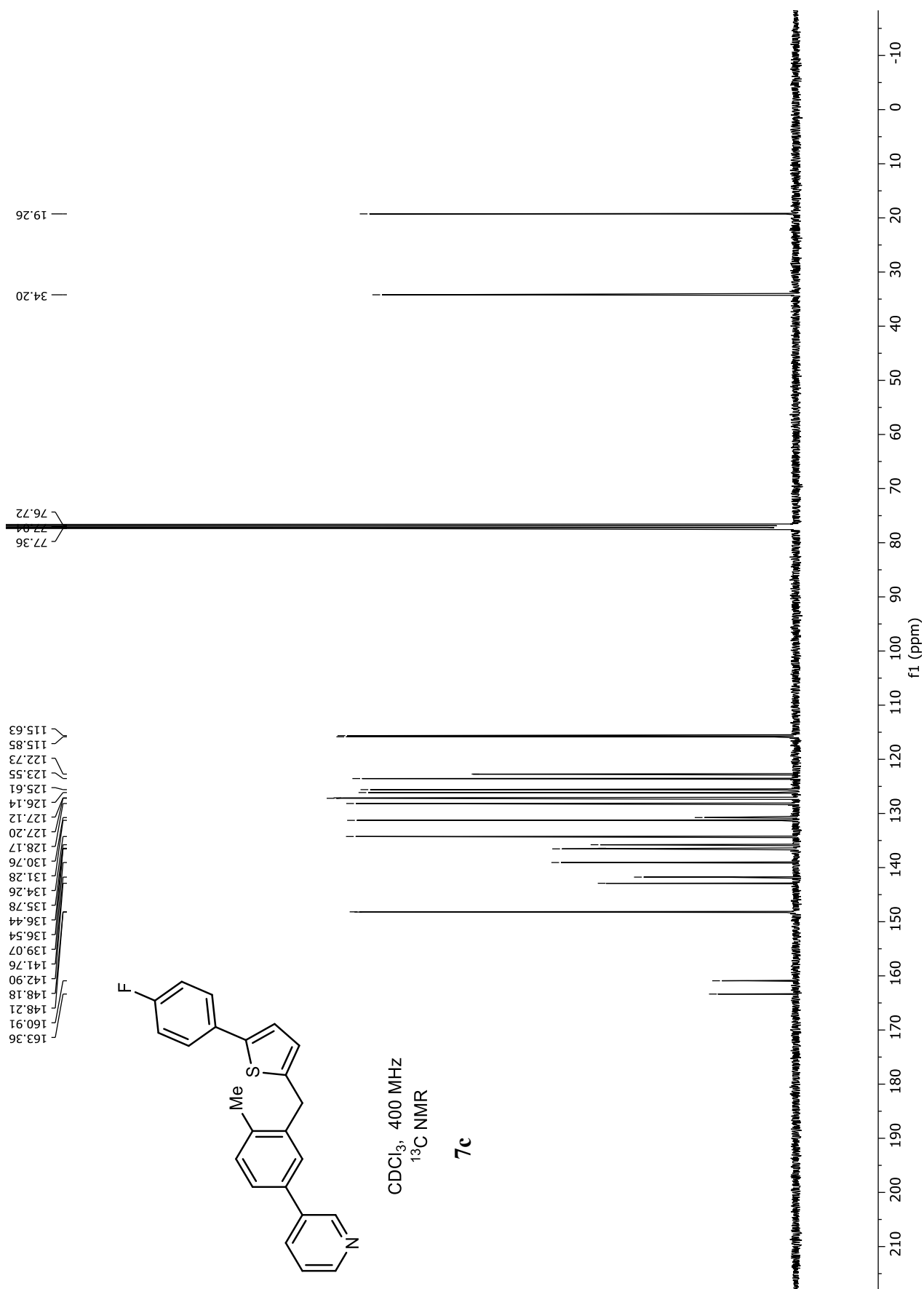
7b

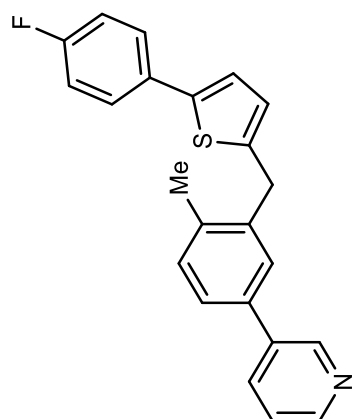
f1 (ppm)



7c

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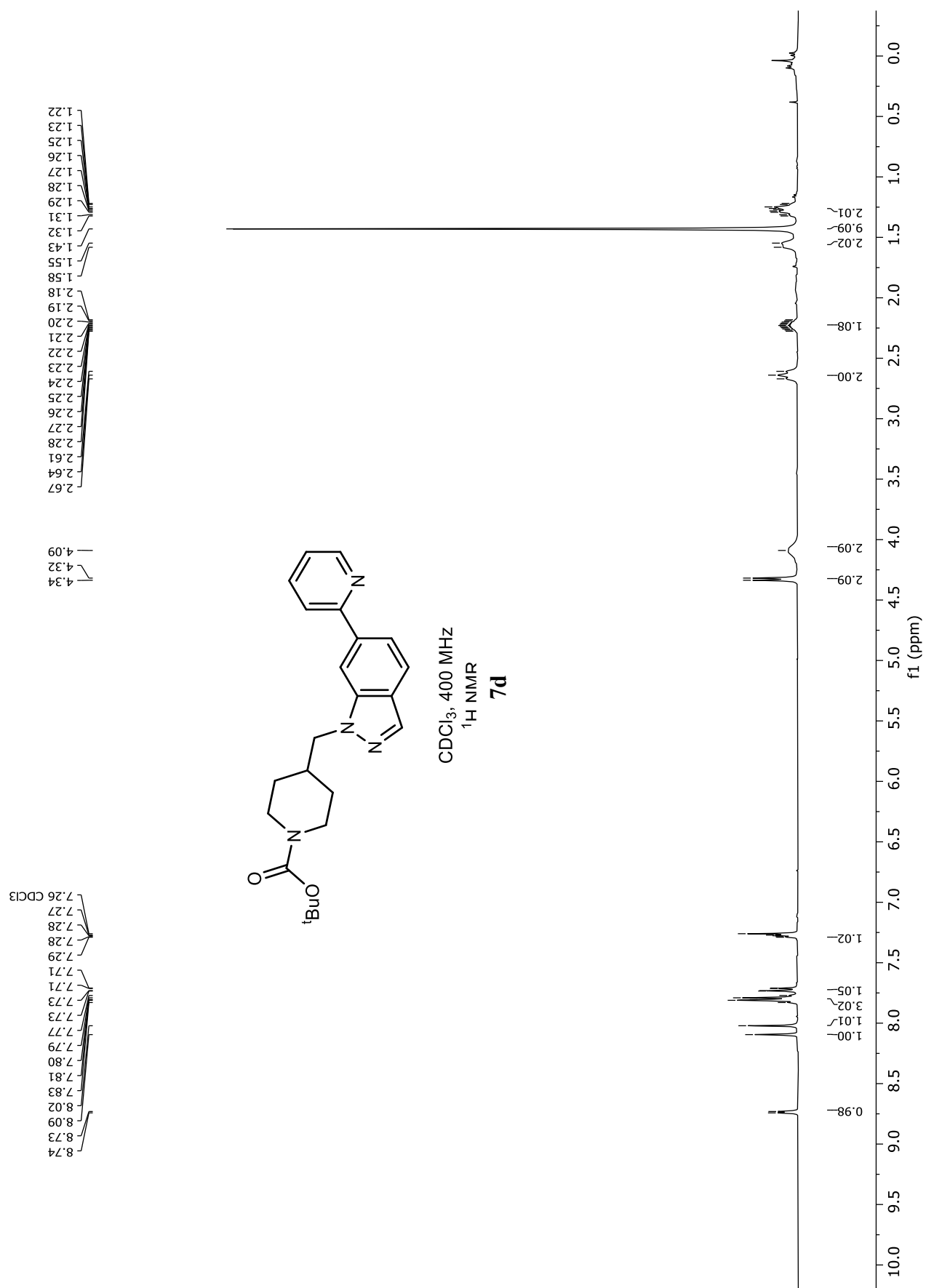


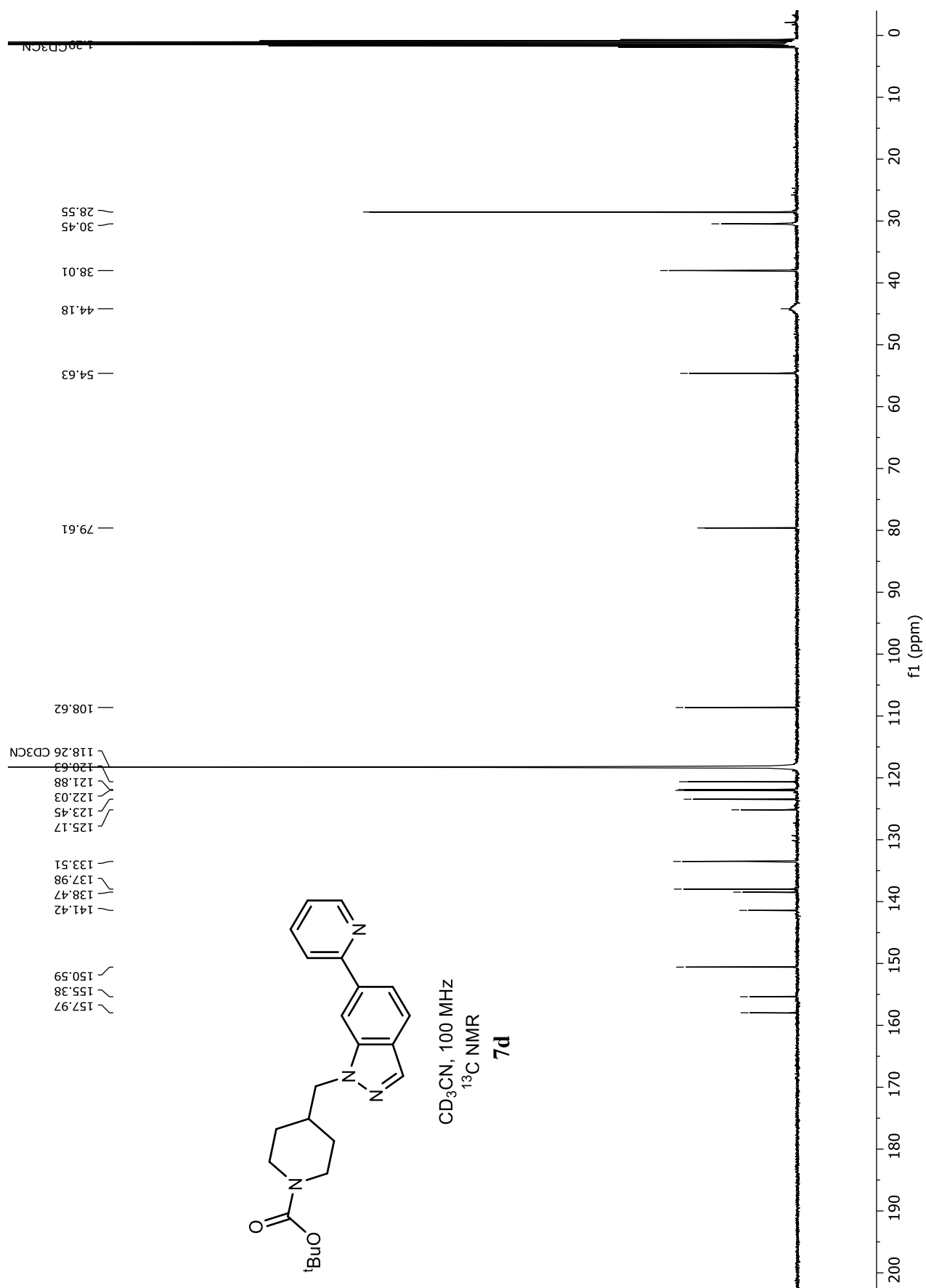
CDCl₃, 400 MHz
¹⁹F NMR

7c

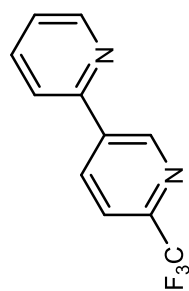
-115.11
 -115.09
 -115.08
 -115.08
 -115.07
 -115.06
 -115.06
 -115.05
 -115.03





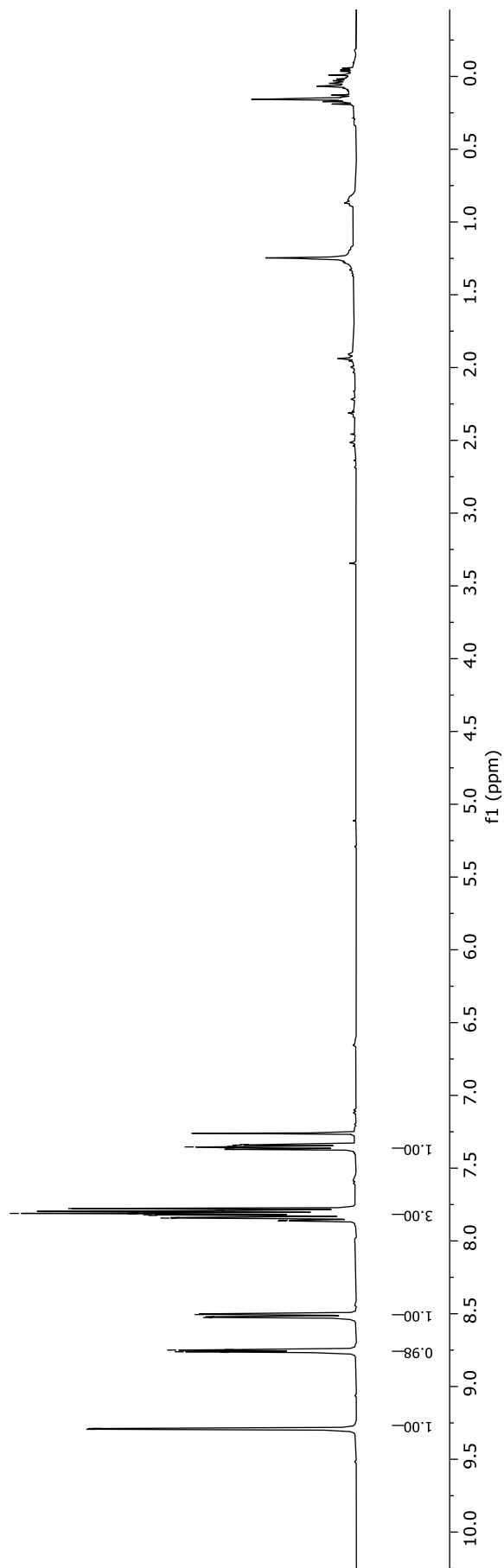


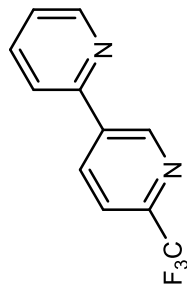
9.29
 9.29
 8.77
 8.76
 8.76
 8.75
 8.75
 8.53
 8.52
 8.52
 8.51
 8.50
 7.86
 7.86
 7.84
 7.84
 7.82
 7.82
 7.81
 7.81
 7.80
 7.79
 7.78
 7.37
 7.37
 7.37
 7.36
 7.35
 7.35
 7.34
 7.34



CDCl₃, 400 MHz
¹H NMR

7e





CDCl₃, 400 MHz
¹³C NMR

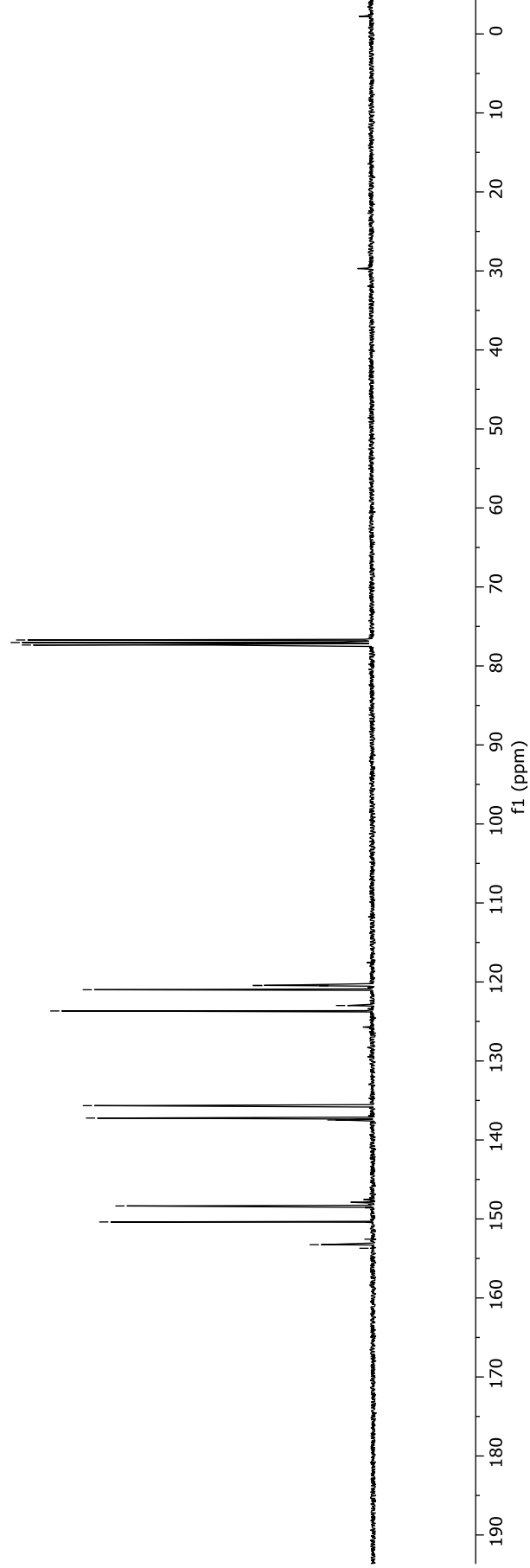
7e

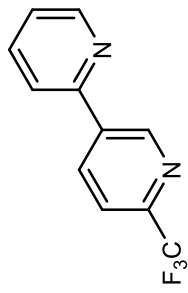
530

153.71
 153.25
 152.56
 150.38
 148.35

137.47
 137.23
 135.66
 123.67
 122.98
 120.98
 120.49
 120.46
 120.43
 120.41

77.35
 77.03
 76.71



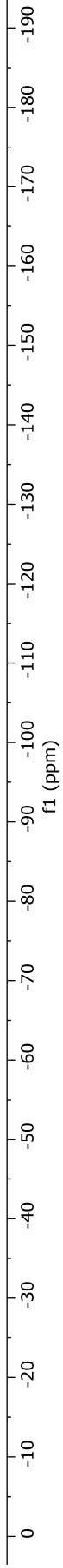


CDCl₃, 400 MHz
¹⁹F NMR

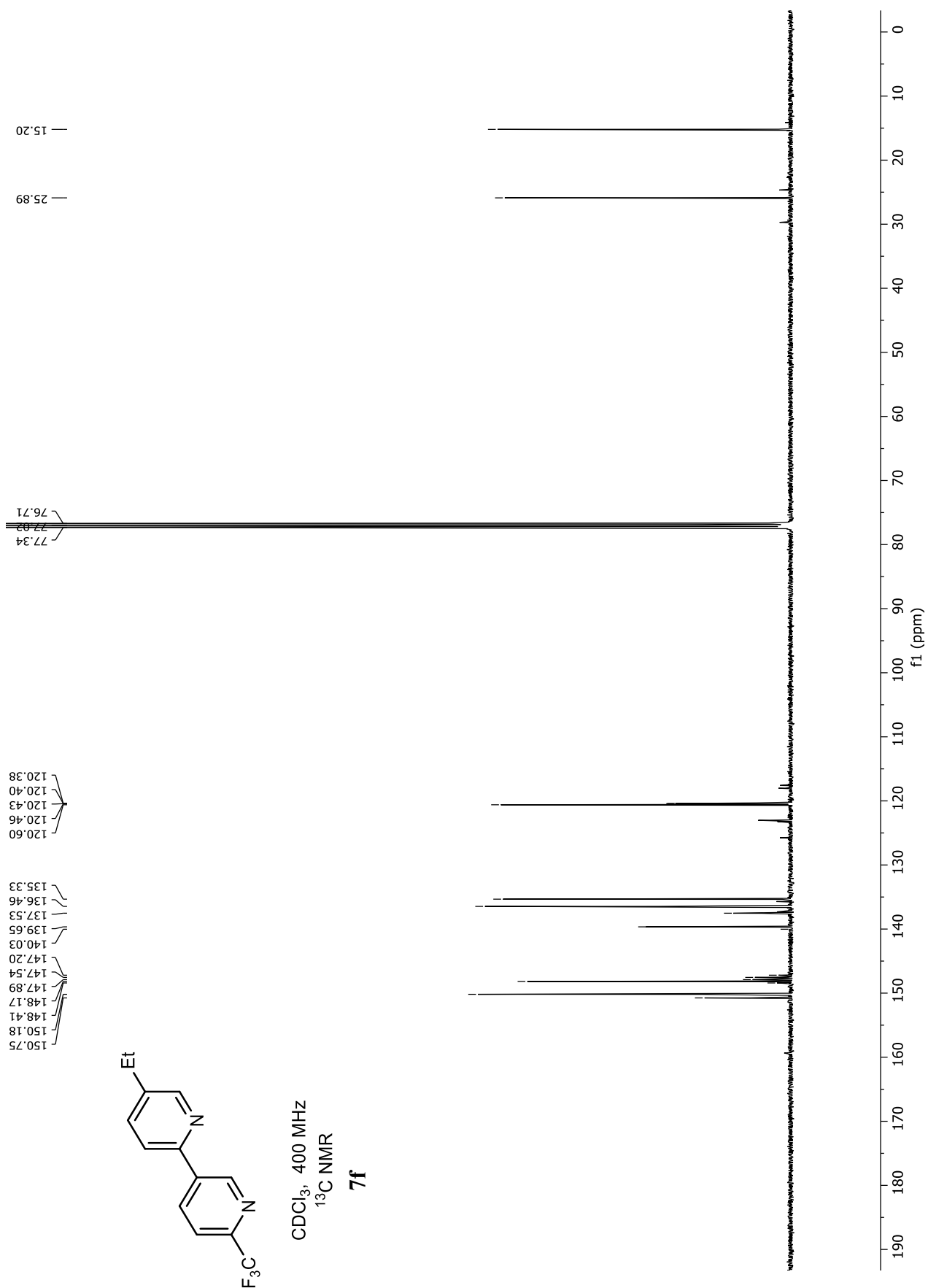
531

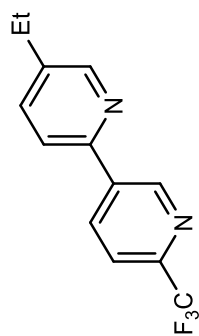
7e

— -67.82







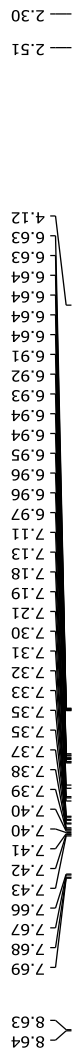


CDCl₃, 400 MHz
¹⁹F NMR

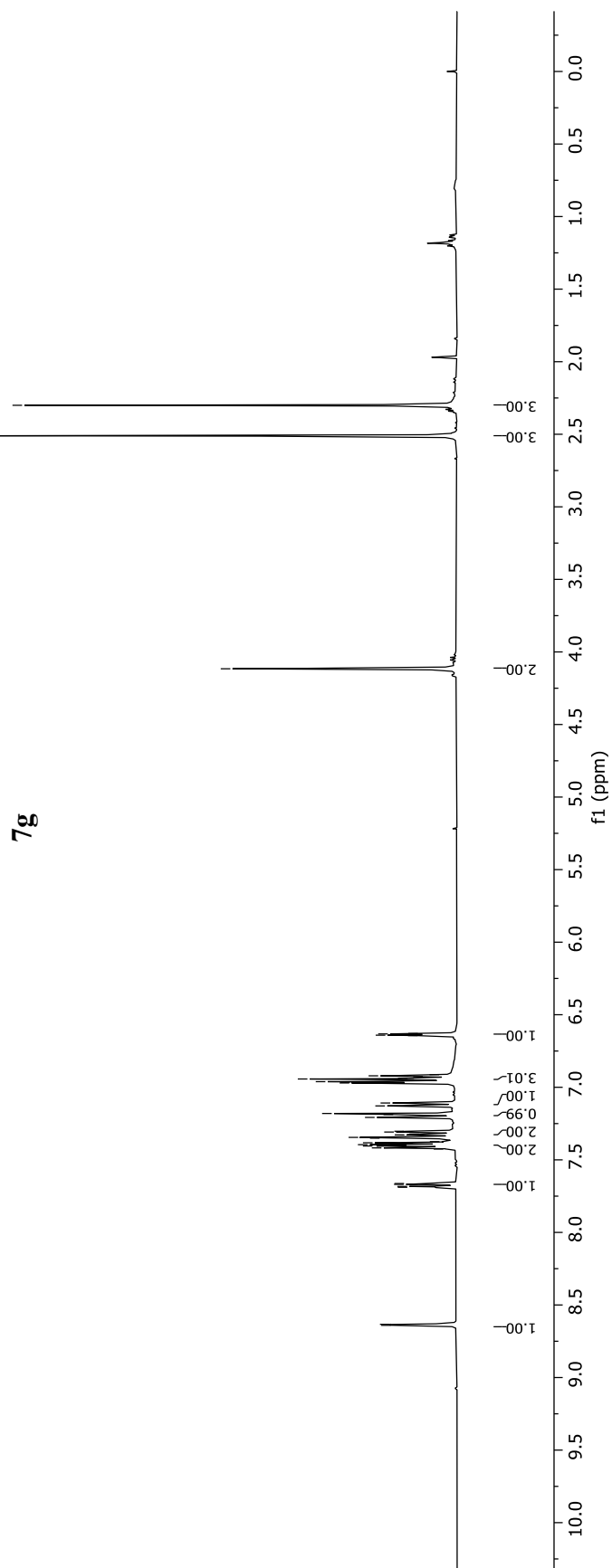
7f

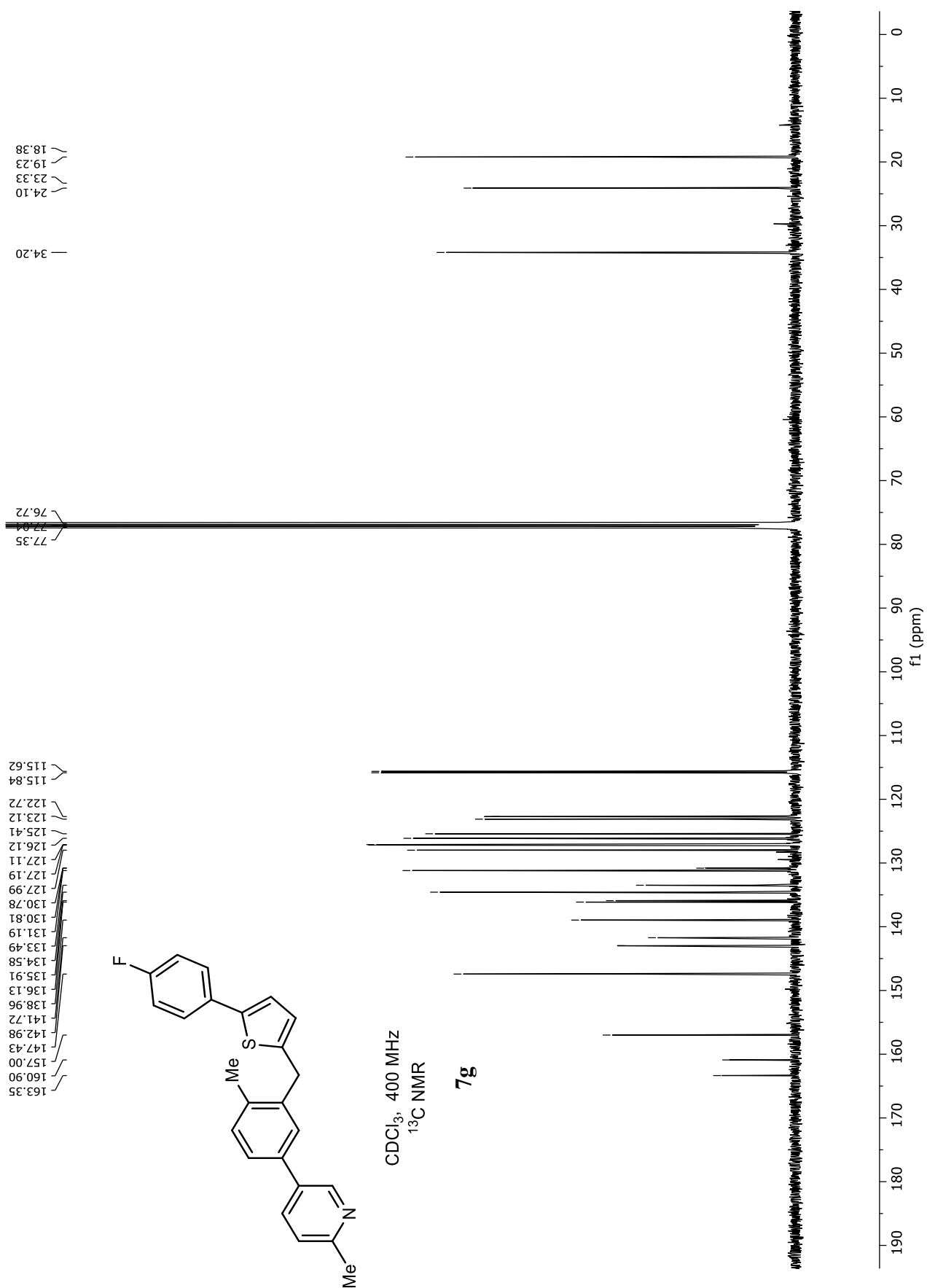
— -67.78

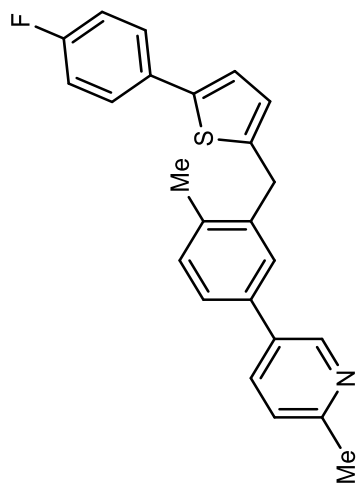




CDCl₃, 400 MHz
¹H NMR



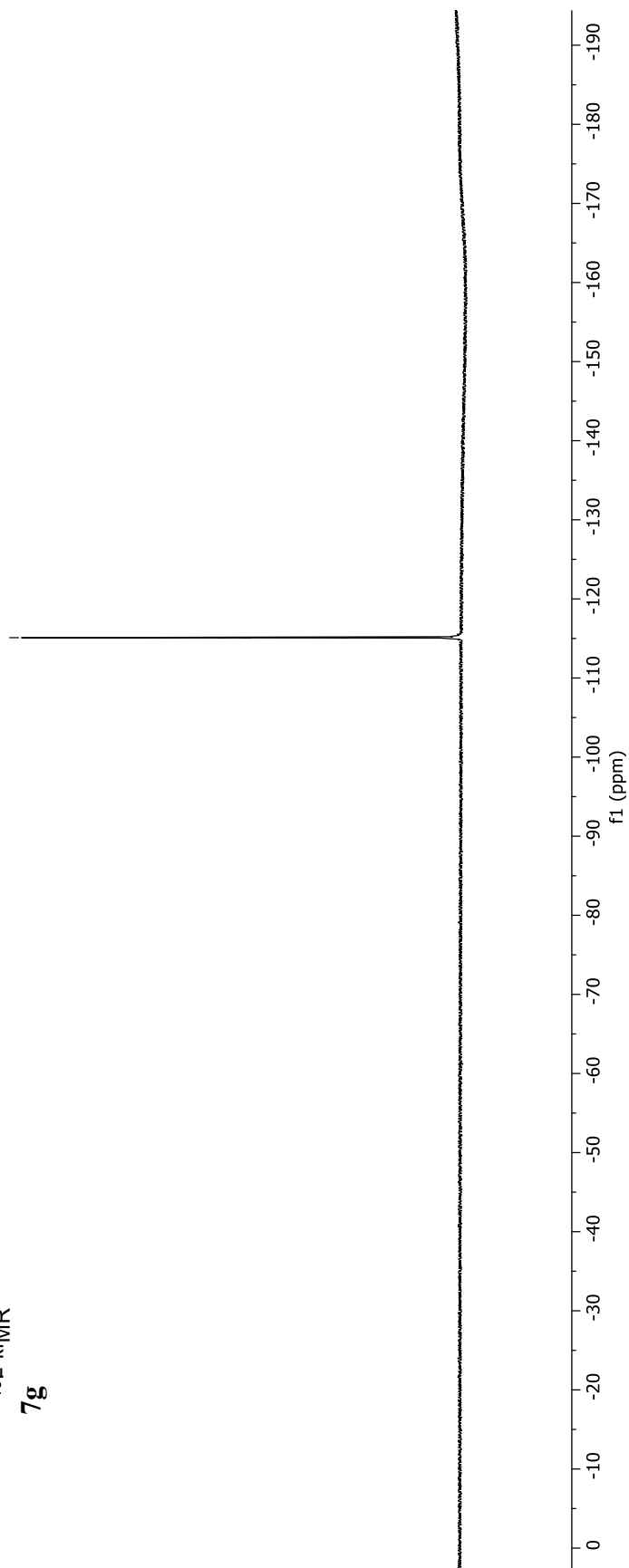


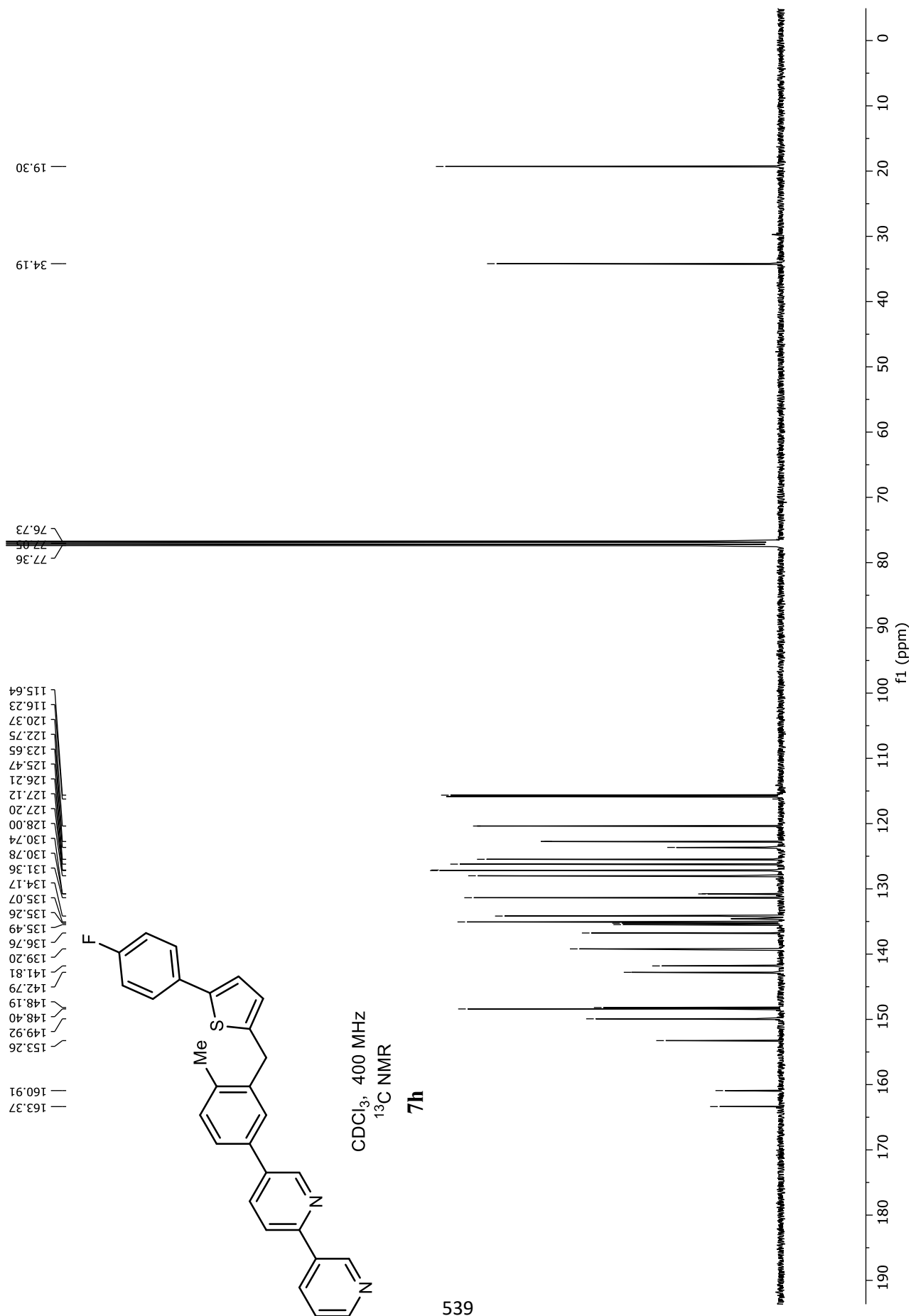


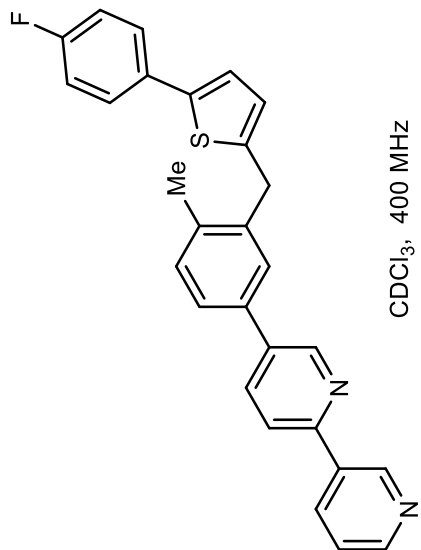
CDCl₃, 400 MHz
¹⁹F NMR

7g

-115.06
-115.08
-115.08
-115.10
-115.11
-115.12
-115.13







CDCl₃, 400 MHz
¹⁹F NMR

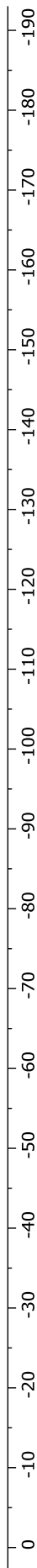
7h

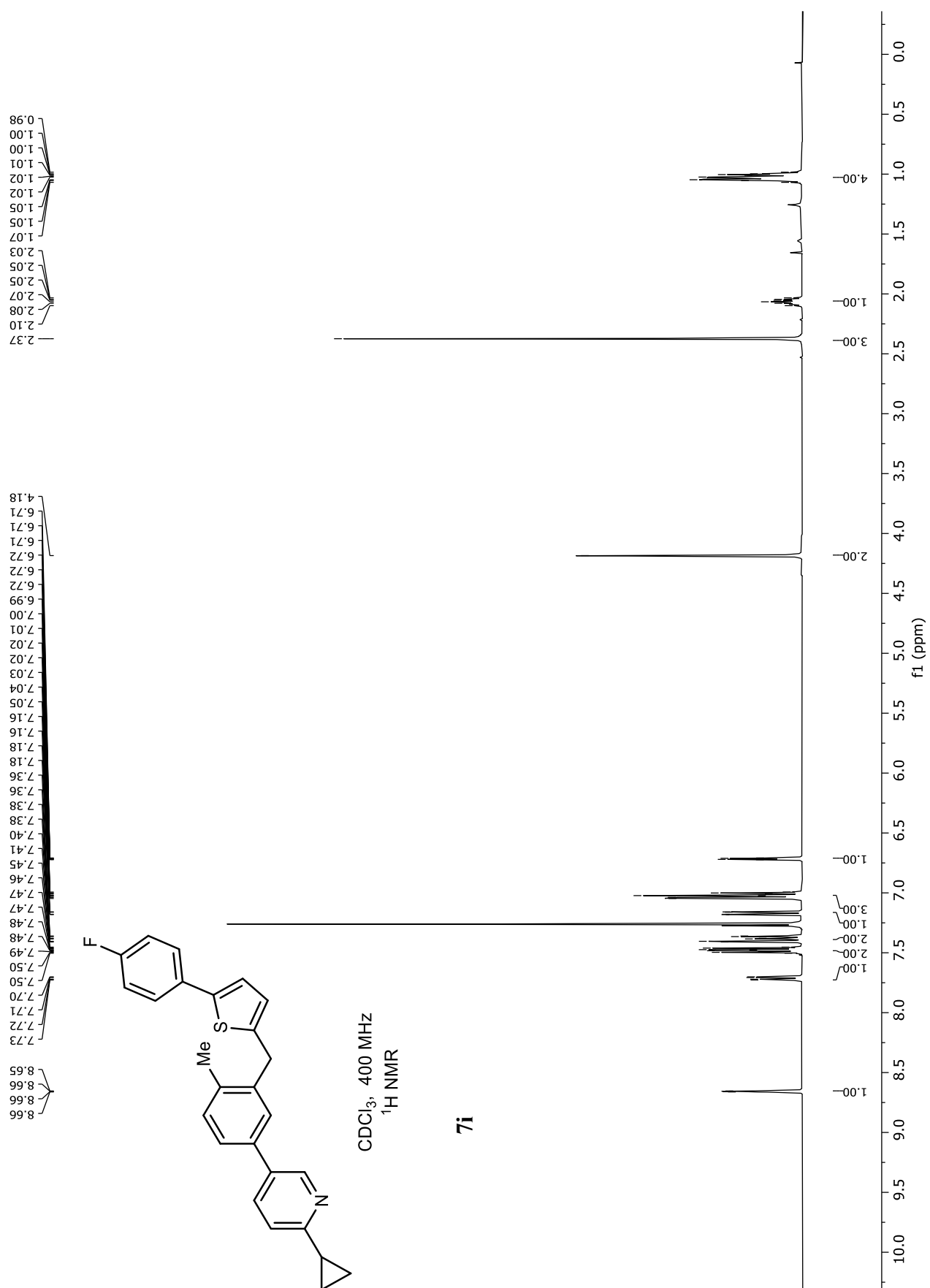
540

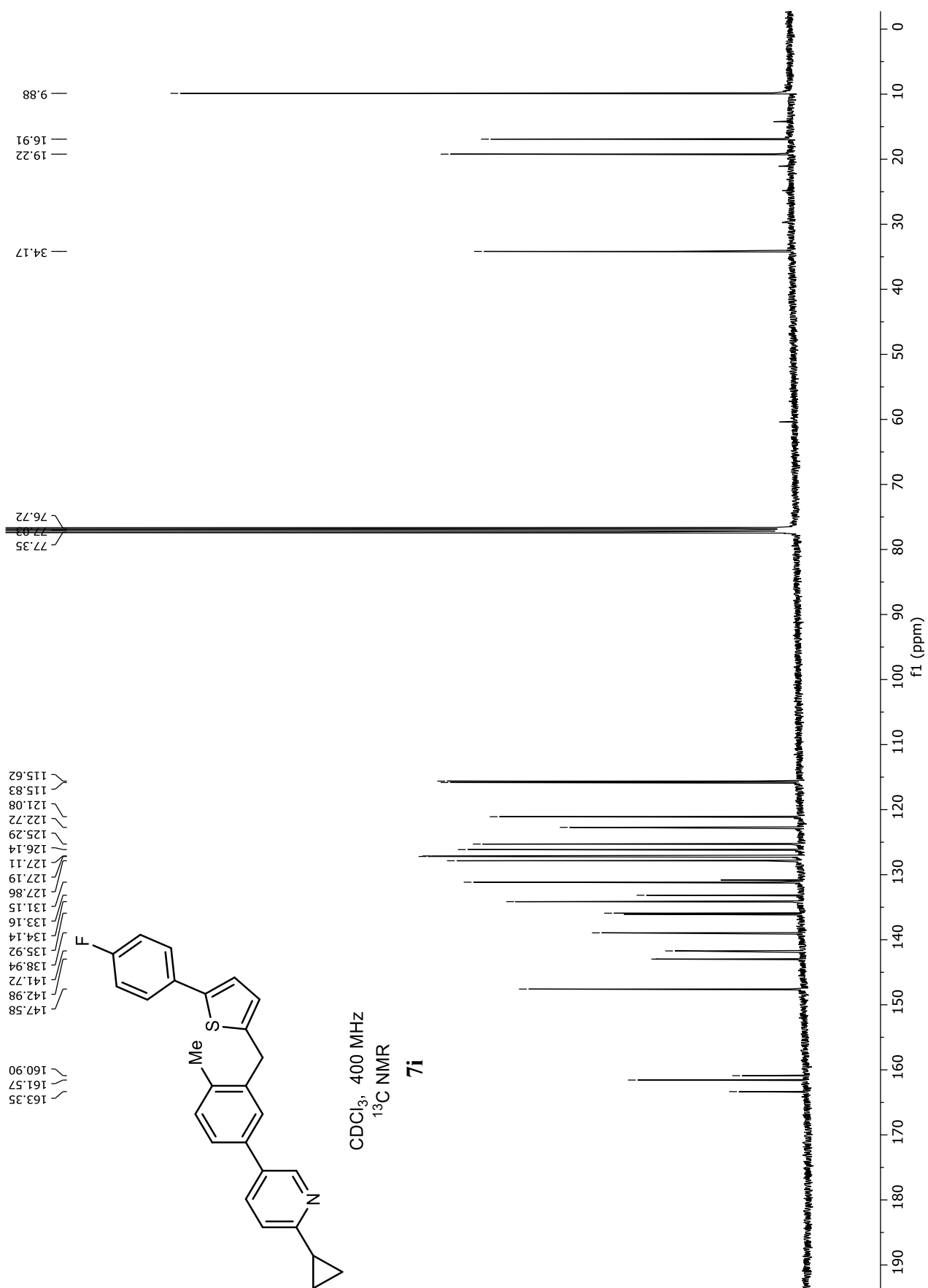
-114.94
-114.96
-114.97
-114.98
-114.99
-115.00
-115.01
-115.03



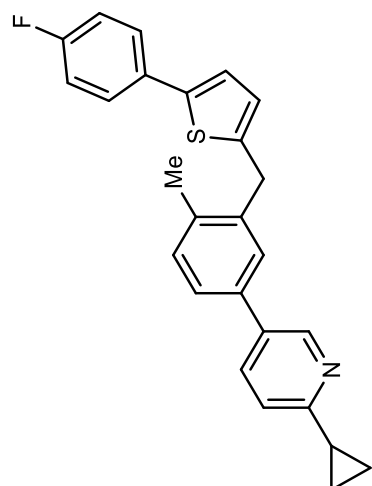
f1 (ppm)







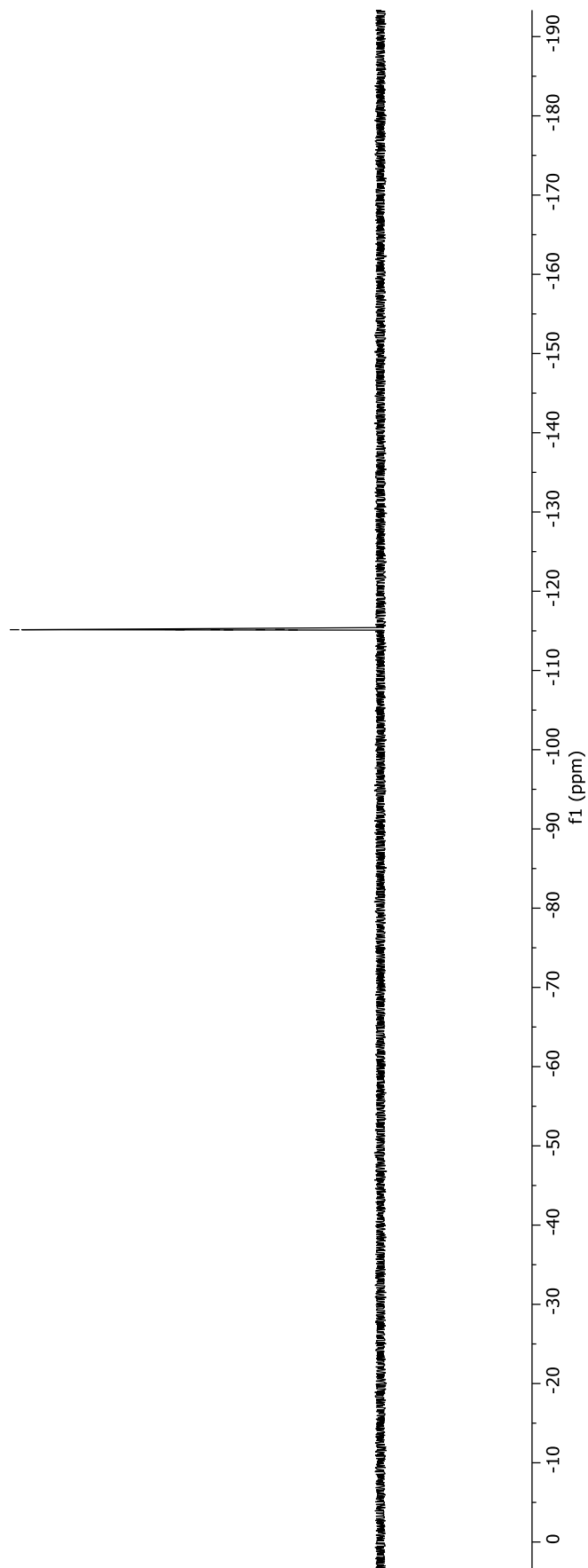
-115.11
-115.12
-115.13
-115.14
-115.15
-115.16
-115.17
-115.18

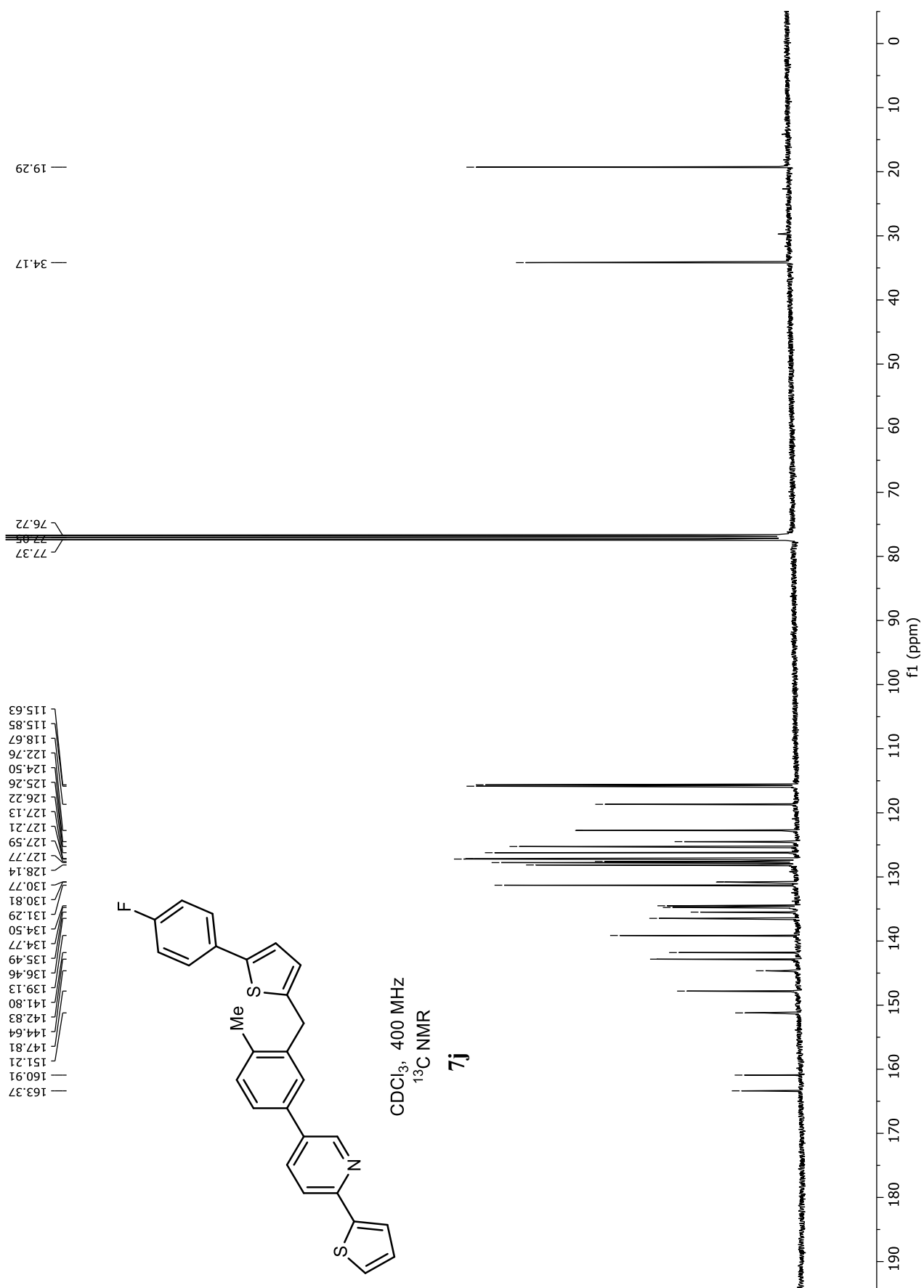


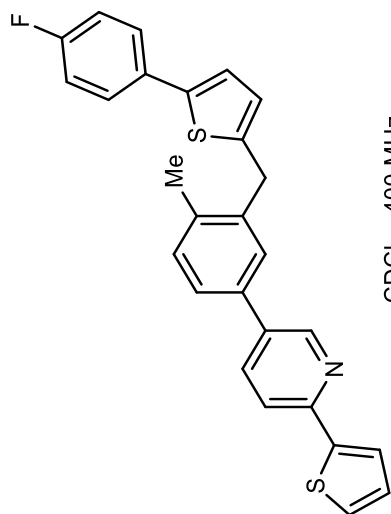
CDCl₃, 400 MHz
¹⁹F NMR

7i

543







CDCl₃, 400 MHz
¹⁹F NMR

7j

-115.13
 -115.11
 -115.11
 -115.10
 -115.09
 -115.08
 -115.08
 -115.07
 -115.05

