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Supplementary information

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Supplementary Information

A Deconstruction-Reconstruction Strategy for Pyrimidine Diversification

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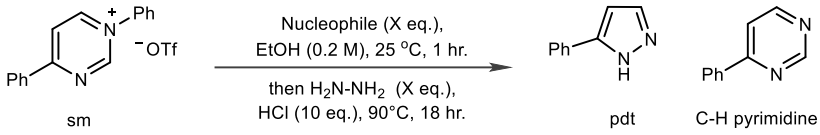
1. General Information:

Proton nuclear magnetic resonance (^{1}H 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), $(CD_3)_2CO$ (2.05 ppm), CD_3CN (1.94 ppm), D_2O (4.79 ppm), or $(CD_3)_2SO$ (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), $(CD_3)_2CO$ (29.84 ppm), CD_3CN (1.32 ppm), D_2O, or $(CD_3)_2SO$ (39.52 ppm).

Tetrahydrofuran (THF), toluene, hexane, diethyl ether (Et_2O), and dichloromethane (DCM) were dried and distilled using standard methods, 1,2-dichloroethane (DCE), chloroform ($CHCl_3$), 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, ^{1}H 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 $CHCl_3$, 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 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 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.

2. Optimization Studies:

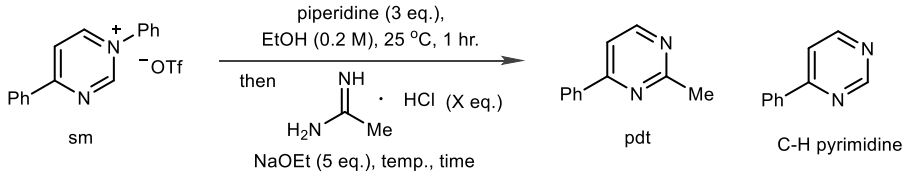
Table S1. Optimization of ring-contraction of *N*-aryl pyrimidinium **3a** to azoles.



entry	nucleophile ID	nucleophile equiv	hydrazine equiv	C-H pyrimidine	pdt
1	NaOH	3	3	n.d.	83
2	NaOH	5	3	n.d.	88
3	NaOH	3	5	n.d.	92
4	NaOH	5	5	n.d.	87
5	piperidine	3	3	01	92
6	piperidine	3	5	01	88

Yields determined by ^{1}H NMR using triphenylmethane as an internal standard.

Table S2. Optimization of C2-functionalization of *N*-aryl pyrimidinium **3a**.

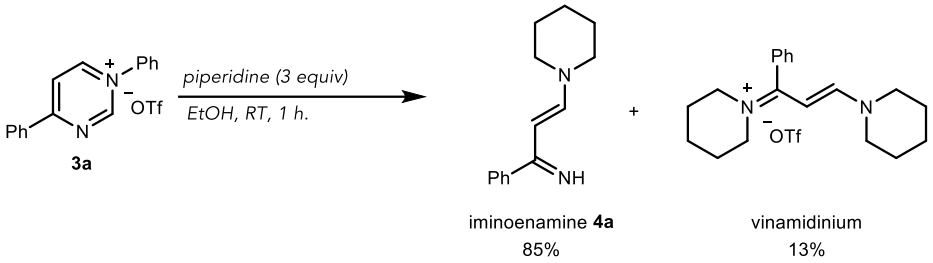


entry	amidine equiv	temperature (°C)	time (hr.)	C-H pyrimidine	pdt
1	1.5	90	18	03	32
2	3	90	18	06	72
3	5	90	18	16	65
4	3	50	18	05	38
5	3	70	18	05	54
6	3	90	1	04	38
7	3	90	5	04	51

Yields determined by ^{1}H NMR using triphenylmethane as an internal standard.

3. Cleavage of N-Aryl Pyrimidinium Salt Example

Scheme 1. Cleavage of **3a** to iminoenamine **4a** and vinamidinium byproduct.



Yields determined by ^{1}H NMR using mesitylene as an internal standard.

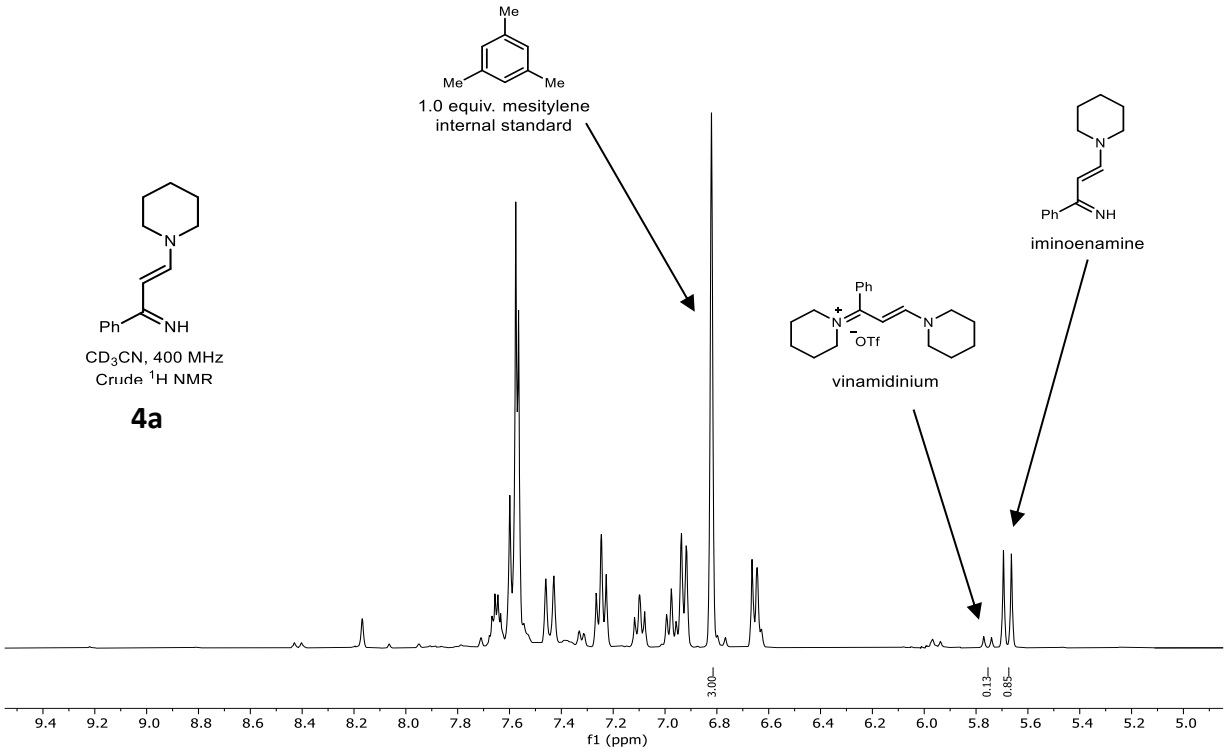


Fig. S1. Representative crude ^{1}H NMR of iminoenamine **4a** and minor vinamidinium byproduct using mesitylene as an internal standard.

4. Problematic Substrates for *N*-Aryl Pyrimidinium Formation and Subsequent Functionalizations:

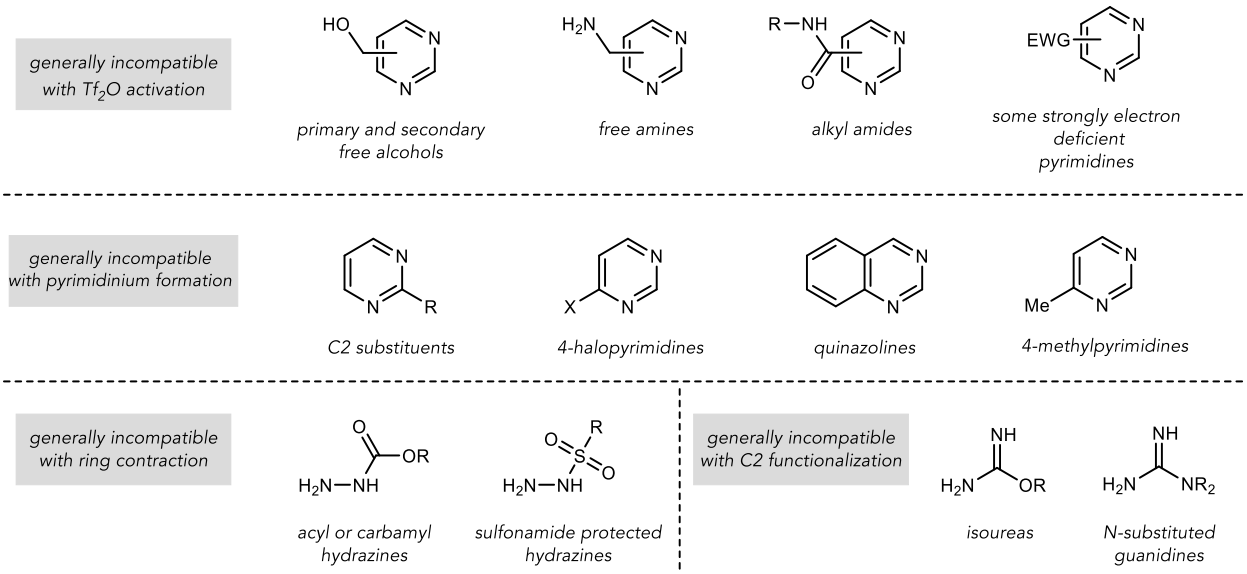


Fig. S2. Problematic substrates for *N*-aryl pyrimidinium formation and subsequent functionalization.

- Substrates with free alcohols, amines, and alkyl amides undergo competitive triflylation or unwanted side-reactivity with Tf_2O. As such, free alcohols or amines should generally be protected prior to reaction. Strongly electron-deficient pyrimidines do not efficiently form *N*-Tf pyrimidiniums and therefore do not undergo subsequent steps.
- Certain classes of pyrimidines did not undergo salt formation or resulted in low yields. For example, C2-substituted pyrimidines gave low yields of products. The reasons for this outcome are unclear at present. When we tested quinazolines, we observed trace amounts of the corresponding quinazolinium salt. The majority of the mass balance was unreacted starting material, with minor amounts of ring-opened species and other cyclic dearomatized adducts. At present the reasons for this reaction outcome are unclear and note that other fused systems are compatible such as deazapurines. In the case of 4-methylpyrimidines, we observed a number of unknown side-reactions. *N*Tf formation acidifies the C-H bonds on the methyl substituent and could potentially lead to unwanted deprotonation. Note that reactions can proceed for other alkyl groups indicating that this phenomena is specific for a 4-methyl substituent.
- Protected hydrazines, such as *N*-acyl- and *N*-sulfonylhydrazines result in N-H pyrazoles, indicating cleavage of those groups during recyclization.
- When we tested isoureas and *N*-substituted guanidines in the recyclization step, we observed primarily 2-NH_2-pyrimidine products. Our current hypothesis is that condensation of these groups onto the iminoenamine intermediates liberates NH_3 into the reaction mixture. Subsequent displacement of the 2-substituent occurs resulting in 2-NH_2-pyrimidines.

5. Ring-Opening, Cleavage, and Functionalization of 5-Substituted Pyrimidines:

In cases where a 5-substituted pyrimidine is employed, *N*-aryl pryimidiniums do not form in appreciable yield. Instead, mixtures of various ring-opened (and ring-cleaved) products form (observed via ^{1}H NMR and LCMS). However, in a one-pot procedure, this mixture of intermediates readily converts to C2-functionalized products. In addition to C2-functionalization, ring-contraction also occurs from this reaction mixture yielding isoxazoles and pyrazoles. This mixture is summarized below using C2-amination of 5-phenyl pyrimidine (**5ah**) as an example:

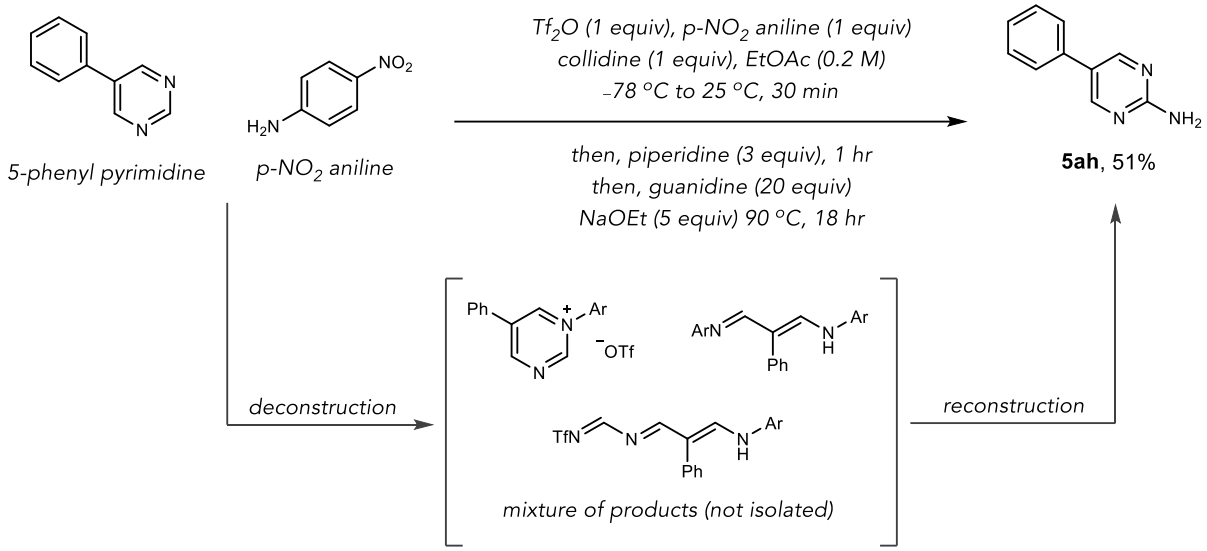


Fig. S3. C2-amination of 5-phenyl pyrimidine from mixtures of intermediates.

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

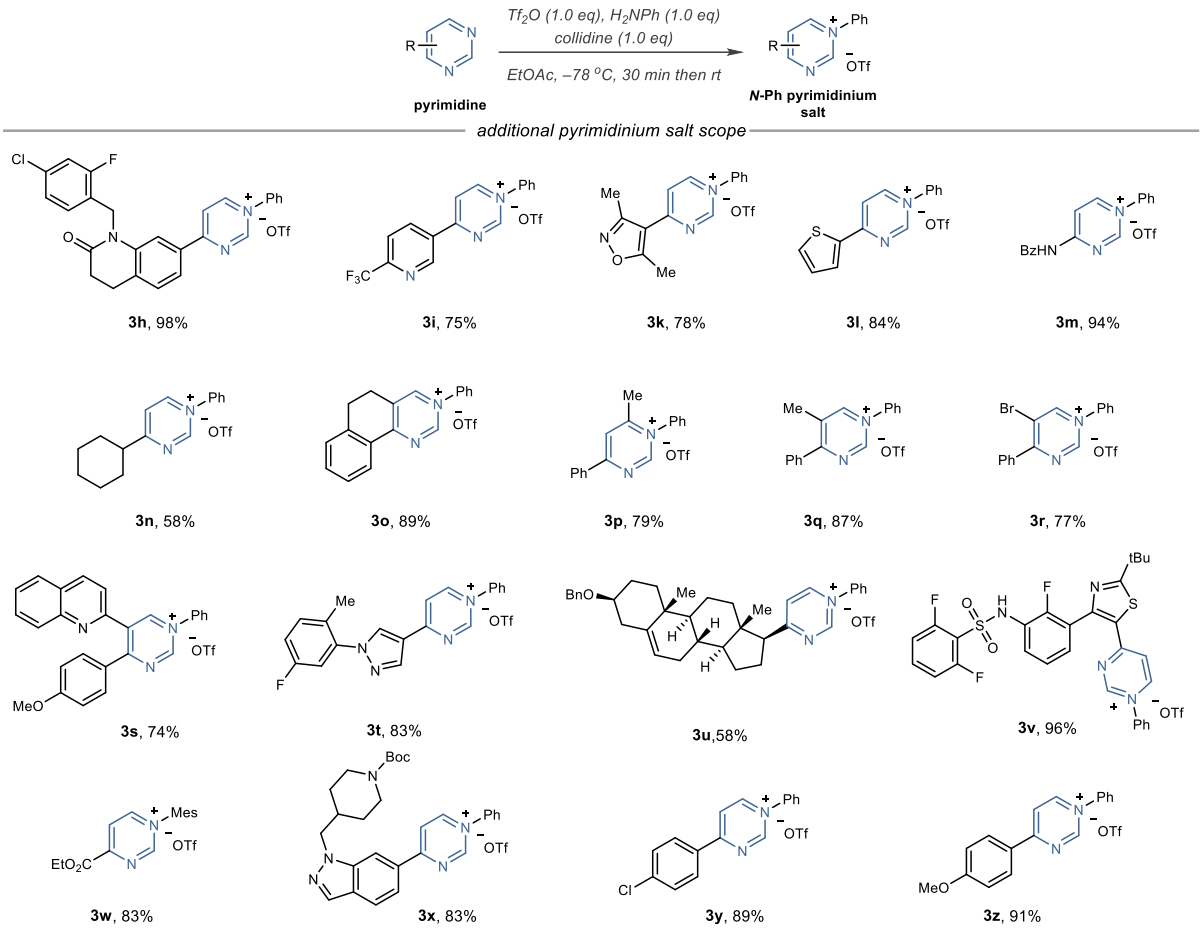


Fig. S4. Additional examples of N-aryl pyrimidinium salts. Isolated yields are shown.

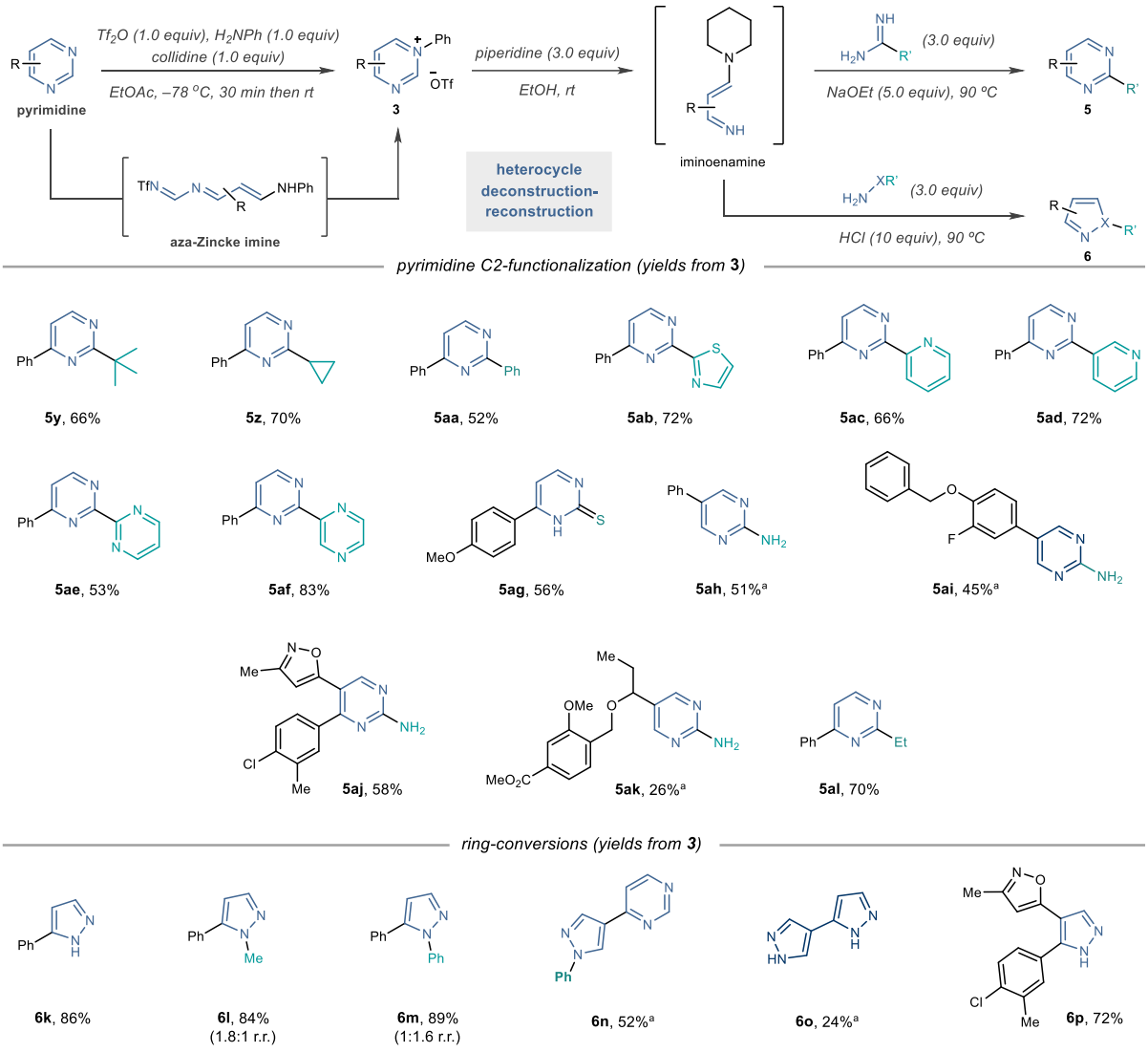


Fig. S5. Additional examples of pyrimidine C2-functionalizations and ring-conversions. Isolated yields are shown. [a]One-pot protocol used. See "General Procedure D" or "General Procedure E" on pages S34-35 for details.

7. Guide for Atom Incorporation in Pyrimidine to Pyridine Conversions

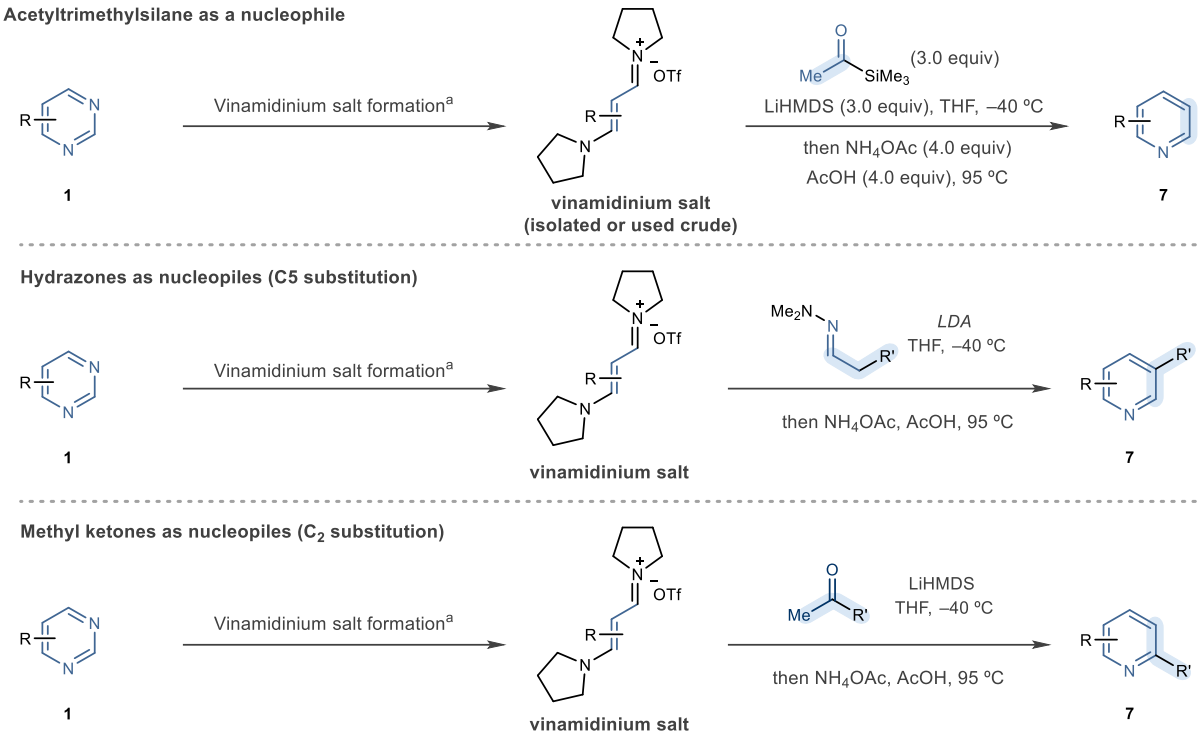
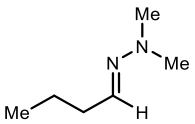


Fig. S6. Guide for atom incorporation in pyrimidine to pyridine conversion. Blue highlights indicate atoms incorporated into pyridine molecules. [a]Vinamidinium salt formation performed one-pot from pyrimidines or in two steps with pyrimidinium salt intermediates. See pgs. S65-72 for details.

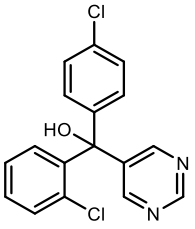
8. Preparation of Heterocyclic Starting Materials.

(E)-2-butylidene-1,1-dimethylhydrazine



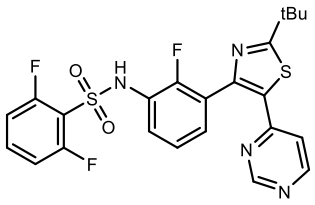
An oven dried round bottom flask equipped with a stir bar and reflux condenser was charged 1,1-dimethylhydrazine (1.5 mL, 20.0 mmol, 1.0 equiv) and butyraldehyde (1.8 mL, 20.0 mmol, 1.0 equiv) in hexanes (0.5 M) under a N_2 atmosphere. The reaction was heated to 70 ºC for 18 hours. After cooling to room temperature, the reaction was gently concentrated *in vacuo* at 40 ºC. The residual oil was purified by vacuum distillation (118-120 ºC) to afford the pure title compound as a yellow oil (1.62 g, 14.2 mmol, 71% yield). IRυ_{max}/cm^{-1} (film): 2957, 2872, 2781, 1608, 1467, 1255, 1137, 1025, 1025, 1012, 810. ^{1}H NMR (400 MHz, CDCl3) δ 6.59 (t, J = 5.6 Hz, 1H), 2.65 (s, 6H), 2.14 (q, J = 6.5 Hz, 2H), 1.50 – 1.38 (m, 2H), 0.93 – 0.83 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.64, 42.39, 34.02, 20.05, 12.67. *m/z* HRMS (ESI) found $[M+H]^+$ 253.0946, for $C_6H_{14}N_2^+$ requires 253.0952.

(2-Chlorophenyl)(4-chlorophenyl)(pyrimidin-5-yl)methanol (1b)



Prepared according to a modified reported procedure.[1] An oven-dried 500 mL round bottom flask equipped with a stir bar was charged with 5-bromopyrimidine (4.77 g, 30.0 mmol) and (2-chlorophenyl)(4-chlorophenyl)methanone (7.53 g, 30.0 mmol) and subjected to three cycles of vacuum/nitrogen backfill. THF (111 mL) was charged to the flask and cooled to –78 ˚C for 10 minutes. *n*-BuLi (18.8 mL, 30 mmol, 1.6 M in hexanes) was added dropwise. After the addition was completed, the reaction mixture warmed to 25 ºC and stirred for an additional 10 minutes. The reaction mixture was cooled to –20 ˚C and water (300 mL) was slowly added. The organic solvent was separated and concentrated *in vacuo.* The residue was dissolved in hot toluene (50 ˚C, 75 mL) and successively washed with a 0.5 M solution of HCl until neutral pH was obtained. The combined organic layers were washed with water (3x), dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel: 50% EtOAc in hexanes) to provide the pure title compound as a light-yellow solid (2.67 g, 8.1 mmol, 27% yield). mp 168-170 °C. ^{13}C NMR (100 MHz, CD_3CN) δ 157.78, 156.61, 143.22, 141.91, 139.15, 133.82, 133.49, 132.30, 130.83 (d, J = 11.9 Hz), 129.96, 128.86, 127.68, 117.88, 79.39. *m/z* HRMS (DART) found $[M+H]^+$ 331.0389, $C_{17}H_{12}Cl_2N_2O^+$ requires 331.0327. Spectra matched literature values. Spectra matched literature values.[1]

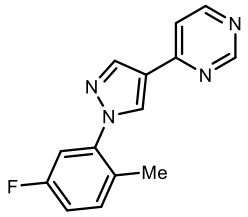
N-{3-(2-(*Tert*-butyl)-5-(pyrimidin-4-yl)thiazol-4-yl)-2-fluorophenyl}-2,6-difluorobenzenesulfonamide (1c)



Prepared according to a modified reported procedure.[2] Under a nitrogen atmosphere, an oven-dried 250 mL round bottom flask was charged with methyl 3-{(2,6-difluorophenyl)sulfonamido}-2-fluorobenzoate (5.00 g, 14.5 mmol) and anhydrous THF (10 mL). The mixture was cooled to 0 °C, and then a 1.25 M solution of lithium bis(trimethylsilyl)amide (LiHMDS) in THF (39.4 mL, 50.0 mmol) was added dropwise via syringe. The mixture was stirred for 10 minutes at 0 °C, then a solution of 4-methylpyrimidine (1.60 mL, 17.4 mmol) in anhydrous THF (30 mL) was added dropwise. The mixture was warmed to 23 °C over 1 hour. The volume of the mixture was reduced to half *in vacuo*, then 100 mL 6 N aqueous hydrochloric acid (HCl) was added. The aqueous layer was separated and washed with EtOAc (100 mL). The aqueous layer was then basified with saturated aqueous sodium carbonate (150 mL) and extracted with EtOAc (100 mL × 3). The combined organic layers were washed with brine (150 mL) and concentrated in vacuo. The residue was triturated with a solvent mixture of EtOAc/Et_2O (1:1 (v/v)), transferred into an oven-dried 250 mL round bottom flask, and dissolved in *N*,*N*-dimethylacetamide (100 mL). To the stirred mixture, *N*-chlorosuccinimide (1.55 g, 11.6 mmol) was added in one portion. The mixture

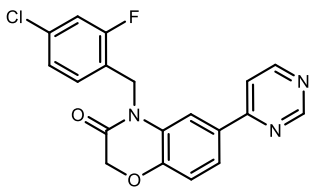
was stirred at room temperature for 18 hours, then 2,2-dimethylpropanethioamide (1.36 g, 11.6 mmol) was added. The reaction vessel was sealed with a rubber septum, and the mixture was heated to 65 °C while stirring for 16 hours. The reaction mixture was cooled to room temperature and diluted with water (200 mL). The mixture was extracted with EtOAc (3x) and the combined organic layers were washed with water and brine, dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 50% EtOAc in hexanes) afforded the title compound as a white solid (3.82 g, 7.6 mmol, 52% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.41 (d, *J* = 5.4 Hz, 1H), 7.74 (td, *J* = 7.8, 1.7 Hz, 1H), 7.63 (s, 1H), 7.50 (tt, *J* = 8.3, 5.9 Hz, 1H), 7.36 (ddd, *J* = 8.1, 6.5, 1.7 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 6.98 (t, *J* = 9.0 Hz, 2H), 6.82 (d, *J* = 5.4 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.07, 159.89 (dd, *J* = 258.3, 3.4 Hz), 159.01, 158.19, 157.12, 150.76 (d, J= 246.8 Hz), 146.54, 135.44 (t, *J* = 11.2 Hz), 133.34, 128.05 (d, *J* = 1.96 Hz), 125.60 (d, *J* = 4.4 Hz), 125.04 (d, *J* = 12.5 Hz), 124.00 (d, *J* = 13.9 Hz), 123.14, 117.10, 116.82, 113.35 (dd, *J* = 228.4, 3.5 Hz), 38.32, 30.83; ^{19}F NMR (375 MHz, $CDCl_3$) δ -106.88 (dt, *J* = 9.6, 4.3 Hz, 2F), -130.04 (d, *J* = 2.9 Hz, 1F). Spectra matched literature values.[2]

4-(1-(5-Fluoro-2-methylphenyl)-1H-pyrazol-4-yl)pyrimidine (1d)



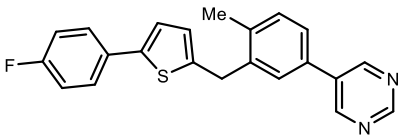
To an oven dried 50 mL three-neck flask equipped with a stir bar was charged 4-methylpyrimidine (457 µL, 5.0 mmol), DMF (1.63 mL, 10.5 mmol), and chloroform (5 mL). The flask was equipped with a nitrogen inlet and an outlet needle into 2M aqueous NaOH. The reaction vessel was cooled to –10 ˚C before slowly adding triphosgene (1.04 g, 3.5 mmol) portion-wise over 2 hours. When all of the triphosgene was added, the ice bath was removed and the solution warmed to 35 ˚C. When the solution began to cool, chloroform was removed *in vacuo*, and the red gum was triturated with 10 mL EtOAc. Next was added water (7.00 mL) and $NaHCO_3$ (87.5 mg, 1.10 mmol), and the mixture was stirred for 5 minutes. To the resulting solution was added 5-fluoro-2-methylphenylhydrazine hydrochloride (1.06 g, 6.00 mmol), and additional $NaHCO_3$ (840 mg, 10.0 mmol) was added slowly. Once the $NaHCO_3$ was added, the reaction was stirred at room temperature for 1 hour. Next, the reaction was diluted with water and extracted with EtOAc. The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 10-100% EtOAc in hexanes) afforded the title compound as a pink solid (826 mg, 3.25 mmol, 65% yield). mp 131-133 ˚C; IR ν_{max}/cm^{-1} (film): 3089, 3051, 1591, 1511, 1372, 974, 832, 721; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.67 (d, J = 5.3 Hz, 1H), 8.28 (s, 1H), 8.24 (s, 1H), 7.45 (dd, J = 5.4, 1.4 Hz, 1H), 7.28 (dd, J = 8.5, 5.9 Hz, 1H), 7.13 (dd, J = 8.8, 2.7 Hz, 1H), 7.06 (td, J = 8.3, 2.7 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.20, 159.75, 158.39, 158.31 (d, J = 205.6 Hz), 139.96 (d, J = 9.7 Hz), 139.48, 132.71 (d, J = 8.4 Hz), 130.71, 129.03 (d, J = 3.6 Hz), 122.41, 116.46, 116.00 (d, J = 20.7 Hz), 113.32 (d, J = 24.1 Hz), 17.74; ^{19}F NMR (375 MHz, $CDCl_3$) 19F NMR (375 MHz, $CDCl_3$) δ -115.39 (q, J = 8.3 Hz); *m/z* HRMS (ESI) found $[M+H]^+$ 255.1045, $C_{14}H_{12}FN_4^+$ requires 255.1041.

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



An oven dried 100 mL round bottom flask equipped with a stir bar was charged with 6-(Pyrimidin-4-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one (795 mg, 3.5 mmol) and was subjected to three cycles of vacuum/nitrogen backfill. DMF (15 mL) was added and the mixture was cooled to 0 °C before adding NaH (168 mg, 4.2 mmol, 60% suspension on mineral oil) and stirring for 30 minutes under ambient conditions. The reaction was again cooled to 0 °C for the addition of 4-chloro-2-fluorobenzyl bromide (1.17 g, 5.3 mmol). The reaction was stirred at room temperature for 18 hours before solvent was removed *in vacuo*. The resulting oil was diluted with water and extracted with EtOAc (2x) The combined organic layers were washed with brine, dried ($MgSO_4$), filtered over a frit, and concentrated in vacuo. Flash column chromatography (silica gel: 60% EtOAc in hexanes) afforded the title compound as an pale yellow solid (928 mg, 2.5 mmol, 72% yield). mp 160-165 °C. IRυ_{max}/cm-1 (film): 3053, 2900, 2161, 1979, 1575, 1467, 1381, 1264, 1065, 733. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (d, J = 1.4 Hz, 1H), 8.72 (d, J = 5.4 Hz, 1H), 7.77 (d, J = 2.0 Hz, 1H), 7.72 (dd, J = 8.4, 2.0 Hz, 1H), 7.55 (dd, J = 5.4, 1.4 Hz, 1H), 7.23 – 6.69 (m, 4H), 5.27 (s, 2H), 4.78 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.38, 162.52, 161.63, 159.15, 158.41 (d, J = 158.8 Hz), 147.78, 134.63 (d, J = 10.2 Hz), 131.55, 129.89 (d, J = 4.7 Hz), 128.70, 125.30 (d, J = 3.6 Hz), 123.41, 121.51 (d, J = 14.3 Hz), 117.79, 116.59 (d, J = 25.1 Hz), 116.31, 114.06 (d, J = 2.1 Hz), 67.70, 38.00 (d, J = 4.4 Hz). ^{19}F NMR (375 MHz, $CDCl_3$) δ -115.56 (t, J = 8.9 Hz). HRMS (ESI) found $[M+H]^+$ 370.0766, for $C_{19}H_{14}ClFN_3O_2^+$ requires 370.0753.

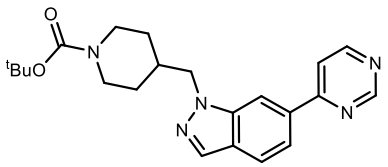
5-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyrimidine (1f)



An oven dried 150 mL pressure tube equipped with a stir bar was charged with 2-(5-bromo-2-methylbenzyl)-5-(4-fluorophenyl)thiophene (3.61 g, 10.0 mmol), Na_2CO_3 (2.12 g, 20.0 mmol), $Pd(dppf)Cl_2$ (366 mg, 0.5 mmol), and pyrimidin-5-ylboronic acid (1.40 mg, 11.0 mmol) and was subjected to three cycles of vacuum/nitrogen backfill. H_2O (25 mL) and degassed 1,4-dioxane (25 mL) were charged to the tube and the mixture was heated at 80 °C for 18 hours, then cooled to room temperature and diluted with EtOAc. The reaction mixture was filtered through a celite pad before the aqueous layer was extracted with EtOAc (2x). The combined organic layers were dried ($MgSO_4$), filtered over a frit, and concentrated in vacuo. Flash column chromatography (silica gel: 20-60% EtOAc in hexanes) afforded the title compound as an off-white solid (3.26 g, 9.0 mmol, 90% yield). mp 106-109 °C. IRυ_{max}/cm^{-1} (film): 3033, 2910, 1573, 1507, 1415, 1229, 828, 728, 635. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.93 (s, 2H), 7.48 (dd, J = 8.5, 5.3 Hz, 2H), 7.45 – 7.37 (m, 2H), 7.33 (d, J = 7.8

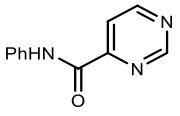
Hz, 1H), 7.08 – 6.99 (m, 3H), 6.72 (d, J = 2.4 Hz, 1H), 4.21 (s, 2H), 2.41 (s, 3H). ^{19}F NMR (375 MHz, $CDCl_3$) δ -114.92 (td, J = 8.7, 4.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.28 (d, J = 246.9 Hz), 157.44, 154.88, 142.56, 142.04, 139.68, 137.71, 134.20, 132.34, 131.71, 130.80 (d, J = 3.4 Hz), 127.98, 127.28 (d, J = 7.9 Hz), 126.38, 125.51, 122.86, 115.87 (d, J = 21.8 Hz), 34.23, 19.44. HRMS (ESI) found $[M+H]^+$ 361.1191, for $C_{22}H_{18}FN_2S^+$ requires 361.1169.

Tert-butyl 4-((6-(pyrimidin-2-yl)-1H-indazol-1-yl)methyl)piperidine-1-carboxylate (1g)



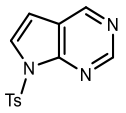
An oven dried 150 mL pressure tube equipped with a stir bar was charged with 4-chloropyrimidine hydrochloride (1.51 g, 10.0 mmol), Na_2CO_3 (3.12 g, 30.0 mmol), $Pd(dppf)Cl_2$ (366 mg, 0.5 mmol), and (1H-indazol-6-yl)boronic acid (2.26g, 14.0 mmol) and was subjected to three cycles of vacuum/nitrogen backfill. H_2O (25 mL) and degassed 1,4-dioxane (25 mL) were charged to the tube and the mixture was heated at 80 °C for 18 hours, then cooled to room temperature and diluted with water. The mixture was extracted with CH_2Cl_2 (2x). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered over a frit, and concentrated in vacuo. Flash column chromatography (silica gel: 1:90:9 AcOH:EtOAc:hexanes) afforded crude 6-(pyrimidin-4-yl)-1H-indazole as a pink solid (186 mg, 0.9 mmol, 9% yield). Next, the whole batch was carried forward and added to a 25-mL oven dried round bottom flask. Cs_2CO_3 (606 mg, 1.9 mmol), and tert-butyl 4-(bromomethyl)piperidine-1-carboxylate (311 mg, 1.1 mmol) were added and subjected to three cycles of vacuum/nitrogen backfill. DMF (4 mL) was charged to the flask and the mixture was heated at 60 °C for 18 hours, then cooled to room temperature and diluted with water. The mixture was extracted with EtOAc (2x). Note: Brine was needed to break the emulsion. The combined organic layers were dried ($MgSO_4$), filtered over a frit, and concentrated in vacuo. Flash column chromatography (silica gel: 90% EtOAc in hexanes) afforded the title compound as a white solid (196 g, 0.5 mmol, 54% yield, 5% yield overall). mp 53-56 °C. IRυ_{max}/cm-1 (film): 2973, 2928, 1574, 1459, 1387, 1246, 1158. 1058, 836, 768. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.79 (d, J = 5.3 Hz, 1H), 8.25 (d, J = 1.7 Hz, 1H), 8.04 (s, 1H), 7.92 – 7.54 (m, 3H), 4.33 (d, J = 7.1 Hz, 2H), 4.09 (q, J = 7.0 Hz, 2H), 2.63 (t, J = 12.8 Hz, 2H), 2.22 (ddd, J = 11.5, 7.6, 3.8 Hz, 1H), 1.63 – 1.47 (m, 2H), 1.42 (s, 9H), 1.35 – 1.12 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.01, 159.13, 157.66, 154.79, 140.42, 134.72, 133.24, 125.47, 121.86, 119.35, 117.61, 108.38, 79.54, 60.45, 54.35, 37.43, 29.97, 28.51, 21.13, 14.28; HRMS (ESI) found $[M+H]^+$ 394.2243, for $C_{22}H_{28}N_5O_2^+$ requires 394.2238.

***N*-Phenylpyrimidine-4-carboxamide**



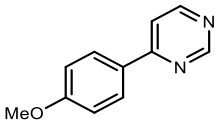
An oven-dried 50 mL round-bottom flask equipped with a stir bar was charged with pyrimidine-4-carboxylic acid (1.24 g, 10.0 mmol), N,N-diisopropylethylamine (DIPEA) (5.2 mL, 30.0 mmol), (3-dimethylamino-propyl)-ethyl-carbodiimide hydrochloride (3.10 g, 20.0 mmol), 3-benzotriazol-1-ol monohydrate (2.70 g, 20.0 mmol), aniline (1.37 mL, 15.0 mmol), and was subjected to three cycles of vacuum/nitrogen backfill. THF (30 mL) was added and the mixture was stirred at room temperature for 40 hours. The reaction mixture was concentrated *in vacuo*, then diluted with water and extracted with EtOAc (3x). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 10-40% EtOAc in hexanes) afforded the title compound as a pink solid (1.49 g, 7.5 mmol, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 9.32 (d, *J* = 1.4 Hz, 1H), 9.04 (d, *J* = 5.0 Hz, 1H), 8.23 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.77 (d, *J* = 7.4 Hz, 2H), 7.41 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.31, 159.70, 157.80, 156.44, 137.12, 129.36, 125.20, 120.02, 118.75. Spectra matched literature values.[3]

7-Tosyl-7H-pyrrolo[2,3-d]pyrimidine



An oven-dried 50 mL round bottom flask equipped with a stir bar was charged with 7H-pyrrolo[2,3-d]pyrimidine (119 mg, 1.00 mmol) and subjected to three cycles of vacuum/nitrogen backfill. Acetone (10 mL) was added and the mixture was cooled to 0 ˚C. NaOH (800 µL, 1.60 mmol, 2 M solution in water) and 4-toluenesulfonyl chloride (229 mg, 1.20 mmol) were added and the mixture was allowed to warm to room temperature and stirred for 2 hours. The reaction mixture was concentrated *in vacuo*, then diluted with water and filtered. The resulting purple solid was purified by flash column chromatography (silica gel: 25-100% EtOAc in hexanes) afforded the title compound as a tan powder (182 mg, 0.67 mmol, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.93 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 4.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.64 (d, *J* = 4.0 Hz, 1H), 2.37 (s, 3H); *m/z* HRMS (DART) found $[M+H]^+$ 274.0724, $C_{13}H_{12}N_3O_2S^+$ requires 274.0645. Spectra matched literature values.[4]

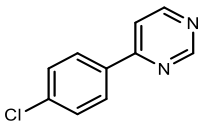
4-(4-Methoxyphenyl)pyrimidine



An oven-dried 70 mL pressure tube equipped with a stir bar was charged with 4-chloropyrimidine hydrochloride (377 mg, 2.50 mmol), Cs_2CO_3 (2.85 g, 8.75 mmol), $Pd(PPh_3)_4$ (114 mg, 0.125 mmol), DIPEA (653 µL, 3.75 mmol), (4-methoxyphenyl)boronic acid (418 mg, 2.75 mmol), and was subjected to three cycles of vacuum/nitrogen backfill. Degassed H_2O (12.5 mL) and degassed dimethoxyethane (12.5 mL) were charged to the tube and the mixture was heated at 90 ˚C for 24 hours, then cooled to room temperature and diluted with water. The aqueous layer was extracted with CH_2Cl_2 (2x), and the combined organics were washed with brine. The combined organic layers were dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 20-60% EtOAc in hexanes) afforded the title compound as a white powder (240 mg, 1.29 mmol, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (d, *J* = 1.4 Hz, 1H), 8.70 (d, *J* = 5.4 Hz, 1H), 8.13 –

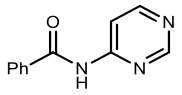
8.04 (m, 2H), 7.66 (dd, *J* = 5.5, 1.4 Hz, 1H), 7.07 – 6.98 (m, 2H), 3.89 (s, 3H); *m/z* HRMS (DART) found $[M+H]^+$ 187.0943, $C_{11}H_{11}N_2O^+$ requires 187.0866. Spectra matched literature values.[5]

4-(4-Chlorophenyl)pyrimidine



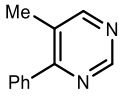
Prepared according to a previously reported protocol.[6] An oven-dried 150-mL pressure tube equipped with a stir bar was charged with 4′-chloroacetophenone (648 µL, 5.00 mmol), $CH(OEt)_3$ (2.50 mL, 15.0 mmol), NH_4OAc (771 g, 10.0 mmol), $ZnCl_2$ (61.0 mg, 0.50 mmol), and toluene (10 mL). Nitrogen was bubbled through the reaction mixture for 30 minutes, then sealed under nitrogen. The solution was heated to 100 ˚C for 40 hours. Upon completion, the reaction was quenched with excess saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3x). The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica gel: 10-50% EtOAc in hexanes) to afford the title compound as a white powder (372 mg, 1.95 mmol, 39% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (d, *J* = 1.4 Hz, 1H), 8.78 (d, *J* = 5.4 Hz, 1H), 8.09 – 8.00 (m, 2H), 7.69 (dd, *J* = 5.4, 1.5 Hz, 1H), 7.54 – 7.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.80, 159.21, 157.70, 137.56, 134.99, 129.41, 128.53, 116.84. Spectra matched literature values.[6]

N-(Pyrimidin-4-yl)benzamide



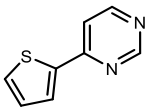
An oven-dried 100 mL round bottom flask equipped with a stir bar was charged with 4-aminopyrimidine (238 mg, 2.50 mmol) and placed under a nitrogen atmosphere. CH_2Cl_2 (16.7 mL) was added, and the suspension was cooled to 0 ˚C before adding triethylamine (697 µL, 5.00 mmol) and benzoyl chloride (290 µL, 2.50 mmol). The reaction was allowed to warm to room temperature and stirred for 3 hours before quenching with saturated $NaHCO_3$. The organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (2x), and the combined organics were washed with brine. The combined organic layers were dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 50-100% EtOAc in hexanes) afforded the title compound as a white powder (242 mg, 1.21 mmol, 49% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.70 (d, *J* = 5.9 Hz, 2H), 8.37 (d, *J* = 5.8 Hz, 1H), 7.96 – 7.89 (m, 2H), 7.67 – 7.60 (m, 1H), 7.60 – 7.50 (m, 2H); *m/z* HRMS (DART) found $[M+H]^+$ 200.0804, $C_{11}H_{10}N_3O^+$ requires 200.0818. Spectra matched literature values.[7]

5-Methyl-4-phenylpyrimidine



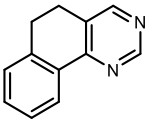
An oven-dried 150-mL pressure tube equipped with a stir bar was charged with propiophenone (664 µL, 5.00 mmol), $CH(OEt)_3$ (2.50 mL, 15.0 mmol), NH_4OAc (771 mg, 10.0 mmol), $ZnCl_2$ (61.0 mg, 0.50 mmol), and toluene (10 mL). Nitrogen was bubbled through the reaction mixture for 30 minutes, then sealed under nitrogen. The solution was heated to 100 ˚C for 18 hours. Upon completion, the reaction was quenched with excess saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3x). The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica gel: 10-50% EtOAc in hexanes) to afford the title compound as a clear oil (106 mg, 0.62 mmol, 12% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.62 (d, *J* = 0.8 Hz, 1H), 7.66 – 7.56 (m, 2H), 7.54 – 7.42 (m, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.66, 158.53, 156.38, 137.65, 129.18, 128.63, 128.20, 127.96, 16.92. Spectra matched literature values.[6]

4-(Thiophen-2-yl)pyrimidine



An oven-dried 150-mL pressure tube equipped with a stir bar was charged with 2-acetylthiophene (540 µL, 5.00 mmol), $CH(OEt)_3$ (2.50 mL, 15.0 mmol), NH_4OAc (771 mg, 10.0 mmol), $ZnCl_2$ (68.0 mg, 0.500 mmol), and toluene (10 mL). Nitrogen was bubbled through the reaction mixture for 30 minutes, then sealed under nitrogen. The solution was heated to 100 ˚C for 40 hours. Upon completion, the reaction was quenched with excess saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3x). The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica gel: 10-50% EtOAc in hexanes) to afford the title compound as a yellow solid (60 mg, 0.37 mmol, 7% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 1.5 Hz, 1H), 8.62 (d, *J* = 5.4 Hz, 1H), 7.72 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.50 (ddd, *J* = 6.0, 5.2, 1.3 Hz, 2H), 7.11 (dd, *J* = 5.0, 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.09, 158.86, 157.18, 141.98, 130.54, 128.58, 127.76, 115.25. Spectra matched literature values. [6]

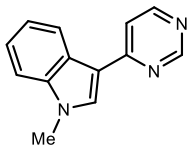
5,6-Dihydrobenzo[h]quinazoline



An oven-dried 150-mL[8] pressure tube equipped with a stir bar was charged with α-tetralone (1.33 mL, 10.0 mmol), $CH(OEt)_3$ (5.00 mL, 30.0 mmol), NH_4OAc (1.54 g, 20.0 mmol), $ZnCl_2$ (136 mg, 0.10 mmol), and toluene (20 mL). Nitrogen was bubbled through the reaction mixture for 30 minutes, then sealed under nitrogen. The solution was heated to 100 ˚C for 40 hours. Upon completion, the reaction was quenched with excess saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3x). The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica gel: 10-50% EtOAc in hexanes) to afford the title compound as a yellow solid (60 mg, 0.37 mmol, 7% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.53 (s, 1H), 8.37 – 8.28 (m, 1H), 7.45 – 7.33 (m, 2H), 7.25

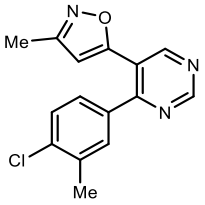
(d, J = 6.0 Hz, 1H), 3.02 – 2.88 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.92, 157.37, 155.33, 139.03, 132.05, 131.08, 128.14, 128.04, 127.21, 125.37, 27.15, 24.27; Spectra matched literature values.[6]

1-Methyl-3-(pyrimidin-4-yl)-1H-indole



An oven-dried 100 mL round bottom flask equipped with a stir bar was charged with 3-acetylindole (1.59 g, 10.0 mmol) and placed under a nitrogen atmosphere. THF (20 mL) was added, and the suspension was cooled to 0 ˚C before adding NaH (800 mg, 20.0 mmol, 60% dispersion in mineral oil). The resulting suspension was stirred for 30 minutes before adding iodomethane (1.25 mL, 20.0 mmol). The reaction was stirred for 30 min, then removed THF *in vacuo* and quenched with water (40 mL) and extracted with EtOAc (2x), and the combined organics were washed with brine. The combined organic layers were dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. To the resulting oil hexanes (15 mL) was added and the resulting solid was filtered. The resulting white solid was transferred to an oven-dried 150 mL pressure tube equipped with a stir bar and was charged with $CH(OEt)_3$ (4.50 mL, 26.4 mmol), NH_4Oac (1.40 g, 13.2 mmol), $ZnCl_2$ (120 mg, 0.88 mmol), and toluene (18 mL). After sparging with nitrogen, the reaction flask was capped and heated to 100 ˚C for 40 hours. Upon completion, the reaction was quenched with excess saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3x). The combined organic extracts were washed with brine and dried ($MgSO_4$) filtered over a frit and concentrated *in vacuo*. Flash column chromatography (silica gel: 50-100% EtOAc in hexanes) afforded the title compound as a brown solid (208 mg, 0.99 mmol, 10% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (d, J = 1.5 Hz, 1H), 8.59 (d, J = 5.5 Hz, 1H), 8.42 – 8.33 (m, 1H), 7.85 (s, 1H), 7.57 (dd, J = 5.5, 1.4 Hz, 1H), 7.42 – 7.26 (m, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.55, 159.07, 156.33, 138.12, 131.56, 125.95, 122.91, 121.70, 121.58, 116.22, 113.52, 110.06, 33.47. Spectra matched literature values.[8]

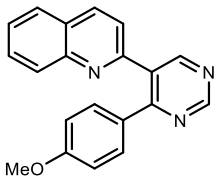
5-(4-(4-Chloro-3-methylphenyl)pyrimidin-5-yl)-3-methylisoxazole



To an oven-dried 250 mL round bottom flask equipped with a stir bar under a nitrogen atmosphere was charged diisopropylamine (2.82 mL, 20.0 mmol) and THF (20 mL). The solution was cooled to –78 ˚C before adding n-butyllithium (n-BuLi) (13.8 mL, 22.0 mmol, 1.6 M in hexanes) dropwise and stirred for 30 minutes. To the solution was added 3,5-dimethylisoxazole (1.96 mL, 20.0 mmol) and stirred for 1 hour before adding a solution of 4-chloro-3-methylbenzonitrile (3.03 g, 20.0 mmol) in THF (7 mL) and stirring for an additional hour The reaction was allowed to warm to room temperature for 1 hour, then quenched with water (150 mL) and extracted with EtOAc (2x), and the combined organics were washed with brine. The combined organic layers were dried

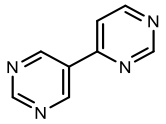
($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. The resulting material was recrystallized in 2:1 hexanes:EtOAc (10 mL) and chilled in a –20 ˚C freezer before filtering. The resulting tan solid was transferred to an oven-dried 100 mL round bottom flask equipped with a condenser and stir bar was charged with $CH(OEt)_3$ (6.50 mL, 39.0 mmol), NH_4OAc (2.00 g, 26.0 mmol), $ZnCl_2$ (177 mg, 3.90 mmol), and toluene (26 mL). After sparging with nitrogen, the reaction was heated to 100 ˚C for 20 hours. Upon completion, the reaction was quenched with excess saturated $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic extracts were washed with brine and dried ($MgSO_4$) filtered over a frit and concentrated *in vacuo*. Flash column chromatography (silica gel: 0-30% EtOAc in hexanes) afforded the title compound as a tan solid (2.17 g, 7.60 mmol, 38% yield). mp 98-100 ˚C; IR ν_{max}/cm^{-1} (film): 3118, 1615, 1567, 1436, 1413, 1043, 822, 657; ^1H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 9.02 (s, 1H), 7.45 (d, *J* = 2.2 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.19 (dd, *J* = 8.3, 2.2 Hz, 1H), 5.91 (s, 1H), 2.38 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.79, 163.04, 160.27, 158.92, 157.13, 136.96, 136.95, 135.31, 131.32, 129.36, 127.50, 120.56, 105.38, 20.15, 11.51; *m/z* HRMS (DART) found $[M+H]^+$ 286.0746, $C_{15}H_{13}ClN_3O^+$ requires 286.0742.

2-(4-(4-Methoxyphenyl)pyrimidin-5-yl)quinoline



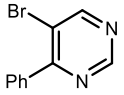
To an oven-dried 100 mL round bottom flask equipped with a stir bar under a nitrogen atmosphere was charged diisopropylamine (1.41 mL, 10.0 mmol) and THF (10 mL). The solution was cooled to –78 ˚C before adding *n*-BuLi (6.90 mL, 11.0 mmol, 1.6 M in hexanes) dropwise and stirred for 30 minutes. To the solution was added quinaldine (1.35 mL, 10.0 mmol) and stirred for 1 hour before adding a solution of 4-methoxybenzonitrile (1.33 g, 10.0 mmol) in THF (5 mL) and stirring for 1 hour. The reaction was allowed to warm to room temperature for an additional hour, then quenched with water (75 mL) and extracted with EtOAc (2x). The combined organic layers were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. The resulting material was recrystallized in EtOAc (8 mL) and chilled in a 0 ˚C freezer before filtering. The resulting bright yellow solid was transferred to an oven-dried 100 mL round bottom flask equipped with a condenser and stir bar was charged with $CH(OEt)_3$ (3.30 mL, 20.0 mmol), NH_4OAc (1.02 g, 13.2 mmol), $ZnCl_2$ (90.0 mg, 0.66 mmol), and toluene (13 mL). After sparging with nitrogen, the reaction was heated to 100 ˚C for 20 hours. Upon completion, the reaction was quenched with excess saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3x). The combined organic extracts were washed with brine and dried ($MgSO_4$) filtered over a frit and concentrated *in vacuo*. Flash column chromatography (silica gel: 20-70% EtOAc in hexanes) afforded the title compound as an orange solid (1.32 g, 4.20 mmol, 42% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 9.09 (s, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.84 – 7.74 (m, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 1H), 6.79 (d, *J* = 8.7 Hz, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.24, 161.27, 159.16, 158.27, 155.85, 148.65, 136.11, 132.09, 131.58, 130.13, 129.77, 129.56, 127.78, 127.28, 127.10, 122.76, 114.05, 55.40. Spectra matched literature values.[6]

4,5'-Bipyrimidine



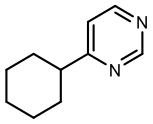
To an oven-dried 100 mL round bottom flask equipped with a stir bar was charged 5-bromopyrimidine (795 mg, 5.00 mmol) and placed under a nitrogen atmosphere. THF (25 mL) was added, then cooled to –100 °C in a methanol-liquid nitrogen bath. *n*-BuLi (3.13 mL, 5.00 mmol, 1.6 M in hexanes) was added dropwise and the reaction was stirred for 30 minutes before a solution of pyrimidine (394 µL, 5.00 mmol) in THF (5 mL) was added. The reaction mixture was stirred at –100 °C for 10 minutes before allowing the solution to warm to room temperature for 1 hour. Water (25 mL) was then added and stirred for 15 min before adding $KMnO_4$ (790 mg, 5.00 mmol) and stirring for an additional 15 minutes. The mixture was concentrated to one-half the original volume *in vacuo* before diluting with CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Flash column chromatography (silica gel: 50-100% EtOAc in hexanes) afforded the title compound as a white fluffy solid (266 mg, 1.68 mmol, 34% yield). mp 152-157 °C; IR ν_{max}/cm^{-1} (solid): 3056, 2358, 1569, 1388, 1193, 838, 778, 713, 629; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 2H), 8.84 (s, 2H), 8.38 (d, *J* = 5.3 Hz, 1H), 7.27 (dd, *J* = 5.3, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.33, 159.66, 159.20, 158.32, 155.61, 130.09, 117.09; *m/z* HRMS (DART) found $[M+H]^+$ 159.0670, $C_8H_7N_4^+$ requires 159.0665.

5-Bromo-4-phenylpyrimidine



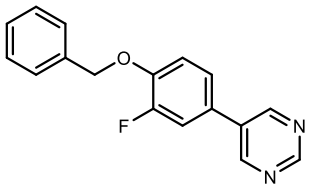
Prepared according to a modified reported procedure.[9] To an oven-dried 100 mL round bottom flask equipped with a stir bar was charged 4-phenylpyrimidine (781 mg, 5.00 mmol) and placed under a nitrogen atmosphere. CH_2Cl_2 (25 mL) was added, the reaction vessel cooled to –78 ºC and Tf_2O (841 µL, 5.00 mmol) was added dropwise. The reaction was stirred for 30 minutes before dibenzylamine (961 µL, 5.00 mmol) was added dropwise as a solution (1.00 M in CH_2Cl_2) followed by collidine (661 µL, 5.00 mmol). The reaction was stirred for a further 30 minutes at –78 ºC. The cooling bath was removed, and the reaction was allowed to warm to room temperature while stirring for approximately 30 minutes. *N*-Bromosuccinimide (890 mg, 5.00 mmol) and trifluoroacetic acid (383 µL, 5.00 mmol) were added, and the reaction was stirred at room temperature for 1 hour. Then, NH_4OAc (3.85g, 50.0 mmol) and EtOH (50 mL) were added and the reaction was heated to 60 ºC for 2 hours. After cooling to room temperature, the reaction was concentrated *in vacuo* and diluted with H_2O, then extracted into CH_2Cl_2 (3x). The organic extract was dried ($MgSO_4$), filtered, and concentrated down. Flash column chromatography (silica gel: 15% Et_2O in hexanes) afforded the title compound as a pale-yellow solid (523 mg, 2.22 mmol, 45% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.92 (s, 1H), 7.86 – 7.76 (m, 2H), 7.57 – 7.45 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.41, 160.25, 157.01, 136.87, 130.44, 129.38, 128.39, 119.28. Spectra matched literature values.[9]

4-Cyclohexylpyrimidine



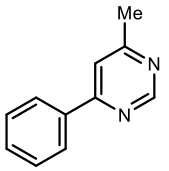
An oven-dried 150-mL pressure tube equipped with a stir bar was charged with cyclohexyl methyl ketone (1.38 mL, 10.0 mmol), $CH(OEt)_3$ (5.00 mL, 30.0 mmol), NH_4OAc (1.54 g, 20.0 mmol), $ZnCl_2$ (136 mg, 0.10 mmol), and toluene (20 mL). Nitrogen was bubbled through the reaction mixture for 30 minutes, then sealed under nitrogen. The solution was heated to 100 ˚C for 40 hours. Flash column chromatography (silica gel: 40% EtOAc in hexanes) afforded the title compound as a pale-yellow oil (293 mg, 1.81 mmol, 18% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.59 (d, J = 5.2 Hz, 1H), 7.15 (d, J = 5.2 Hz, 1H), 2.78 – 2.52 (m, 1H), 1.94 (d, J = 12.5 Hz, 2H), 1.86 (d, J = 12.6 Hz, 2H), 1.80 – 1.68 (m, 2H), 1.57 – 1.19 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.63, 158.64, 156.88, 118.88, 46.00, 32.08, 26.26, 25.91; Spectra matched literature values.[6]

5-(4-(Benzyloxy)-3-fluorophenyl)pyrimidine



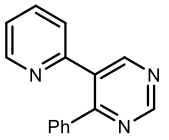
Prepared according to a modified reported procedure.[10] An oven-dried pressure tube equipped with a stir bar was charged with 5-iodopyrimidine (827 mg, 4.00 mmol), (4-(benzyloxy)-3-fluorophenyl)boronic acid (1.47 g, 6.00 mmol), Pd/C (10% w/w) (140 mg, 1.32 mmol), K_2CO_3 (8.50 g, 40.0 mmol) and subjected to three cycles of vacuum/nitrogen backfill. Degassed EtOH and water (3:1; 0.125 M) were charged to the tube and sealed under nitrogen. The mixture was heated to 80 ℃ for 18 hours, then cooled to room temperature. The reaction was filtered over celite and diluted with EtOAc (150 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried with Na_2SO_4, filtered over a frit, and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel: 30% EtOAc in hexanes) to provide the pure title compound as a white solid (634 mg, 2.26 mmol, 57% yield). mp 114 - 115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.81 (s, 2H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.22 (m, 2H), 7.22 – 7.14 (m, 1H), 7.05 (t, *J* = 8.4 Hz, 1H), 5.13 (s, 2H).). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.40, 154.50, 152.04, 147.53 (d, *J* = 10.7 Hz), 136.05, 132.98 (d, *J* = 2.0 Hz), 128.74, 128.34, 127.42, 122.86 (d, *J* = 3.6 Hz), 116.31 (d, *J* = 2.4 Hz), 114.85 (d, *J* = 19.4 Hz), 71.38. ^{19}F NMR (376 MHz, $CDCl_3$) δ -131.80 (dd, *J* = 12.1, 8.0 Hz). Spectra matched literature values.[11]

4-Methyl-6-phenylpyrimidine



An oven-dried pressure tube equipped with a stir bar was charged with 4-chloro-6-phenylpyrimidine (1.00 g, 7.80 mmol), phenyl boronic acid (1.10 g, 9.40 mmol), $Pd(Ph_3)Cl_2$ (56.0 mg, 0.08 mmol), K_2CO_3 (2 M in H_20) (17.0 g, 160 mmol) and subjected to three cycles of vacuum/nitrogen backfill. Degassed dioxane (0.4 M) was charged to the tube and sealed under nitrogen. The mixture was heated to 90 ºC for 18 hours, then cooled to room temperature. The reaction was filtered over celite and diluted with EtOAc (300 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried with Na_2SO_4, filtered over a frit, and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel: 10% hexanes in acetone) to provide the pure title compound as a white solid (1.31 g, 7.72 mmol, 99% yield). mp 38 - 40 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.07 (dd, *J* = 6.4, 3.5 Hz, 2H), 7.57 (s, 1H), 7.54 – 7.46 (m, 3H), 2.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.47, 163.74, 158.72, 136.77, 130.82, 128.95, 127.11, 116.45, 24.38. Spectra matched literature values.[8]

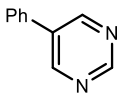
4-Phenyl-5-(pyridin-2-yl)pyrimidine



To an oven-dried 100 mL round bottom flask equipped with a stir bar under a nitrogen atmosphere was charged diisopropylamine (706 mL, µL, 5.00 mmol) and THF (5 mL). The solution was cooled to –78 ˚C before adding *n*-BuLi (3.40 mL, 5.50 mmol, 1.6 M in hexanes) dropwise and stirred for 30 minutes. To the solution was added 4-methylpyridine (494 µL, 5.00 mmol) and stirred for 1 hour before adding a solution of benzonitrile (515 µL, 5.00 mmol) in THF (2.5 mL) and stirring for 1 hour. The reaction was allowed to warm to room temperature for 1 hour then quenched with water (50 mL) and extracted with EtOAc (2x). The combined organic layers were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. The resulting material was recrystallized in 3:1 hexanes:EtOAc (8 mL) and chilled in a –20 ˚C freezer before filtering. The resulting bright yellow solid was transferred to an oven-dried 100 mL round bottom flask equipped with a condenser and stir bar and was charged with $CH(OEt)_3$ (1.40 mL, 2.75 mmol), NH_4Oac (424 mg, 5.50 mmol), $ZnCl_2$ (38 mg, 0.28 mmol), and toluene (6 mL). After sparging with nitrogen, the reaction was heated to 100 ˚C for 48 hours. Upon completion, the reaction was quenched with excess saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3x). The combined organic extracts were washed with brine and dried ($MgSO_4$) filtered over a frit and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel: 30% EtOAc in hexanes) to provide the pure title compound as a tan solid (3.0 g, 12.8 mmol, 15% yield). mp 100-102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (s, 1H), 8.94 (s, 1H), 8.65 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.48 (td, *J* = 7.8, 1.9 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.35 – 7.27 (m, 1H),

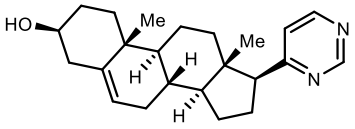
7.27 – 7.22 (m, 2H), 7.22 – 7.15 (m, 1H), 6.99 (dt, *J* = 7.9, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.68, 158.69, 158.03, 154.85, 150.26, 137.27, 136.16, 132.24, 129.65 (d, *J* = 13.4 Hz), 128.41, 125.06, 122.75. Spectra matched literature values.[6]

5-Phenylpyrimidine



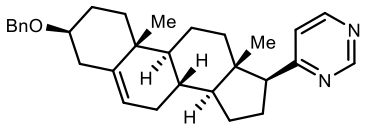
An oven-dried 150 mL pressure tube equipped with a stir bar was charged with 5-bromopyrimidine (1.59 g, 10.0 mmol), K_2CO_3 (2.76 g, 20.0 mmol), $Pd(OAc)_2$ (112 mg, 0.50 mmol), triphenylphosphine (524 mg, 2.00 mmol), phenylboronic acid (1.71 g, 14.0 mmol) and subjected to three cycles of vacuum/nitrogen backfill. Degassed H_2O (25 mL) and degassed dimethoxyethane (25 mL) were charged to the tube and the mixture was heated at 80 ˚C for 18 hours, then cooled to room temperature and diluted with EtOAc. The reaction mixture was filtered through a celite pad before the aqueous layer was extracted with EtOAc (2x). The combined organic layers were dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 10-60% EtOAc in hexanes) afforded the title compound as a yellow oil (1.39 g, 8.9 mmol, 89% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.98 (s, 2H), 7.64 – 7.58 (m, 2H), 7.58 – 7.39 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.33, 159.66, 159.20, 158.32, 155.61, 130.09, 117.09; Spectra matched literature values.[10]

(3S,8S,9S,10R,13S,14S,17S)-10,13-Dimethyl-17-(pyrimidin-4-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-ol



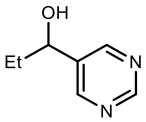
To an oven dried 50 mL pressure tube equipped with a stir bar was added pregnenolone (2.22g, 7.00 mmol), NH_4OAc (1.08g, 14.0 mmol), and NH_4I (102 mg, 0.70 mmol) and subjected to three cycles of vacuum/nitrogen backfill. *N*,*N*-dimethylformamide dimethyl acetal (2.80 mL, 21.0 mmol) was added and the suspension was heated to 120 ˚C for 6 hours. Upon completion, as monitored by TLC, the mixture was concentrated *in vacuo* and diluted with water, then extracted with EtOAc. The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 80-100% EtOAc in hexanes) afforded the title compound as a 6:1 mixture of diastereomers (white solid, 974 mg, 2.76 mmol, 40% yield). Reported spectroscopy are of the major diastereomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.57 (d, J = 5.3 Hz, 1H), 7.22 – 7.05 (m, 1H), 5.36 (tt, J = 5.8, 2.2 Hz, 1H), 3.53 (tt, J = 11.2, 4.5 Hz, 1H), 2.79 (t, J = 9.5 Hz, 1H), 2.54 – 2.37 (m, 1H), 2.35 – 2.16 (m, 3H), 2.10 – 2.00 (m, 1H), 1.94 (dtd, J = 13.4, 9.3, 5.9 Hz, 1H), 1.89 – 1.79 (m, 3H), 1.79 – 1.73 (m, 1H), 1.68 – 1.55 (m, 2H), 1.56 – 1.52 (m, 1H), 1.42 – 1.35 (m, 3H), 1.28 (ddd, J = 12.3, 10.2, 6.9 Hz, 1H), 1.15 – 1.06 (m, 1H), 1.06 – 1.01 (m, 1H), 0.99 (s, 3H), 0.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.32, 158.33, 155.92, 141.02, 121.53, 121.13, 71.81, 58.07, 57.04, 50.29, 45.50, 42.40, 38.07, 37.42, 36.72, 32.30, 32.01, 31.76, 24.83, 24.56, 20.89, 19.54, 13.04. Spectra matched literature values.[12]

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



To an oven-dried 50 mL round bottom flask equipped with a stir bar was added (3S,8S,9S,10R,13S,14S,17S)-10,13-dimethyl-17-(pyrimidin-4-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-ol (970 mg, 2.75 mmol) and dissolved in THF (8.4 mL, 0.33M). The tube was subjected to three cycles of vacuum/nitrogen backfill and cooled to 0 ˚C before adding sodium hydride (116 mg, 3.00 mmol, 60% dispersion in mineral oil). The solution was stirred at 0 ˚C for 30 minutes before adding benzyl bromide (392 µL, 3.30 mmol). The solution was heated to 50 ˚C for 18 hours. Next, the reaction mixture was quenched with water, then extracted with CH_2Cl_2. The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 0-80% EtOAc in hexanes) afforded the title compound as a white solid (974 mg, 2.76 mmol, 40% yield). The 6:1 mixture of diastereomers from the starting material was retained. Reported spectroscopy are of the major diastereomer. mp 156-163 ˚C; IR ν_{max}/cm^{-1} (solid): 2940, 1579, 1386, 1096, 731, 694; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (d, J = 1.4 Hz, 1H), 8.57 (d, J = 5.3 Hz, 1H), 7.42 – 7.30 (m, 4H), 7.28 (t, J = 2.7 Hz, 1H), 7.14 (dd, J = 5.2, 1.4 Hz, 1H), 5.41 – 5.28 (m, 1H), 4.57 (s, 2H), 3.29 (tt, J = 11.4, 4.6 Hz, 1H), 2.79 (t, J = 9.5 Hz, 1H), 2.44 (ddt, J = 13.2, 4.9, 2.1 Hz, 2H), 2.28 (ddd, J = 13.6, 10.9, 2.7 Hz, 1H), 2.11 – 2.01 (m, 1H), 2.00 – 1.92 (m, 2H), 1.91 – 1.81 (m, 2H), 1.78 (dd, J = 7.9, 2.6 Hz, 1H), 1.74 – 1.63 (m, 1H), 1.63 – 1.57 (m, 2H), 1.54 (dd, J = 10.5, 4.3 Hz, 1H), 1.45 – 1.33 (m, 3H), 1.33 – 1.26 (m, 1H), 1.08 (dd, J = 13.7, 3.8 Hz, 1H), 1.00 (s, 3H), 0.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.27, 158.39, 155.97, 141.21, 139.18, 128.49, 127.70, 127.55, 121.44, 121.13, 78.62, 70.08, 58.08, 57.07, 50.36, 45.50, 39.28, 38.10, 37.41, 37.13, 32.30, 32.06, 28.55, 24.83, 24.56, 20.89, 19.55, 13.05; *m/z* HRMS (ESI) found $[M+H]^+$ 443.3061, $C_{30}H_{39}N_2O^+$ requires 443.3057.

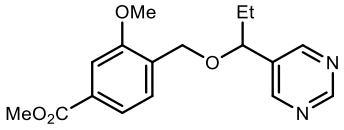
1-(Pyrimidin-5-yl)propan-1-ol



To an oven-dried 100 mL round bottom flask equipped with a stir bar was added pyrimidine-5-carboxaldehyde (757 mg, 7.00 mmol) and subjected to three cycles of vacuum/nitrogen backfill. Next was added THF (15.6 mL, 0.45M), the solution was cooled to -70 ˚C, and ethylmagnesium bromide (2.8 mL, 8.40 mmol, 3M solution in Et_2O) was added dropwise over 5 minutes. The reaction was allowed to warm to room temperature over 1 hour, then cooled to 0 ˚C and quenched with EtOH (7 mL). Next was added 2M aqueous HCl until pH = 7. The resulting solution was diluted with water and extracted with EtOAc. The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 50-100% EtOAc in hexanes) afforded the title compound as a clear oil (177 mg, 1.28 mmol, 18% yield). ^{1}H NMR

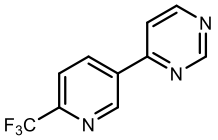
(400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.70 (s, 2H), 4.69 (dd, J = 7.2, 5.8 Hz, 1H), 3.05 (s, 1H), 2.16 – 1.51 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.86, 155.07, 137.54, 71.58, 32.01, 9.81.

Methyl 3-methoxy-4-((1-(pyrimidin-5-yl)propoxy)methyl)benzoate



To an oven-dried 50 mL round bottom flask equipped with a stir bar was added 1-(pyrimidin-5-yl)propan-1-ol (166 mg, 1.20 mmol). The flask was placed under a nitrogen atmosphere before dissolving in DMF (3.5 mL, 0.33M). The solution was cooled to 0 ˚C and sodium hydride (120 mg, 2.50 mmol, 60% dispersion in mineral oil) was added portion-wise over 1 minute. The reaction was stirred at 0 ˚C for 30 minutes before adding methyl 4-(bromomethyl)-3-methoxybenzoate (622 mg, 2.40 mmol) and tetrabutylammonium iodide (22 mg, 0.05 mmol). The reaction was stirred at 0 ˚C for 2 hours before quenching with water, then extracting with EtOAc (3x). The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 0-80% EtOAc in hexanes) afforded the title compound as a white solid (276 mg, 0.87 mmol, 73% yield). mp 71-75 ˚C; IR ν_{max}/cm^{-1} (film): 2935, 2876, 1711, 1579, 1435, 1409, 1283, 1087, 731; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.70 (s, 2H), 7.65 (dd, J = 7.8, 1.5 Hz, 1H), 7.51 – 7.44 (m, 2H), 4.52 – 4.40 (m, 2H), 4.32 (dd, J = 7.2, 5.9 Hz, 1H), 3.91 (s, 3H), 3.82 (s, 3H), 1.93 (dt, J = 13.9, 7.3 Hz, 1H), 1.84 – 1.69 (m, 1H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.02, 158.35, 156.78, 155.79, 135.49, 131.57, 130.76, 128.42, 122.13, 110.88, 79.48, 66.09, 55.52, 52.32, 30.88, 9.95; *m/z* HRMS (ESI) found $[M+H]^+$ 317.1492, $C_{17}H_{21}N_2O_4^+$ requires 317.1496.

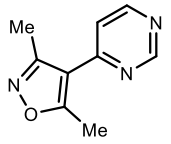
4-(6-(Trifluoromethyl)pyridin-3-yl)pyrimidine



An oven dried 8 mL vial equipped with a stir bar was charged with 2-chloro-4-(6-(trifluoromethyl)pyridin-3-yl)pyrimidine (1.51 g, 5.80 mmol, 1 equiv) and Pd/C (117 mg, 0.58 mmol, 0.1 equiv). EtOH (13.8 mL, 0.42 M) and triethylamine (1.61 mL, 11.6 mmol, 2 equiv) was added. The reaction vial was capped, and a double-skinned balloon of hydrogen gas was bubbled through the solution while stirring (550 rpm). After the balloon was depleted, it was replaced with a fresh, double-skinned balloon filled with hydrogen gas hovering in the headspace of the vial. The reaction was monitored by LCMS until full conversion of the starting material and intermediates was observed. The balloon was removed, and the reaction mixture was filtered through Celite and concentrated in vacuo. Flash chromatography (silica gel: 60% EtOAc in hexanes) to provide the pure title compound as an off-white solid (791 mg, 3.51 mmol, 61% yield). mp 84-86 °C. IRυ_{max}/cm^{-1} (film): 1582, 1340, 1179, 1066, 838, 777, 559, 525. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (d, J = 7.8 Hz, 2H), 8.83 (d, J = 5.4 Hz, 1H), 8.54 (d, J = 8.1 Hz, 1H), 7.76 (t, J = 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.02, 159.49, 158.27, 149.79 (q, J = 35.2 Hz),

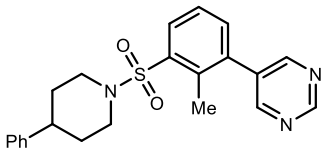
148.57, 136.13, 134.85, 120.63 (d, J = 2.8 Hz), 119.95, 117.42. ^{19}F NMR (375 MHz, $CDCl_3$) δ -68.06. *m/z* HRMS (ESI) found $[M+H]^+$ 226.0598, for $C_{10}H_6F_3N_3^+$ requires 226.0592.

3,5-Dimethyl-4-(pyrimidin-4-yl)isoxazole



An oven dried 8 mL vial equipped with a stir bar was charged with 4-(2-chloropyrimidin-4-yl)-3,5-dimethylisoxazole (516 mg, 2.47 mmol, 1 equiv) and Pd/C (50 mg, 0.25 mmol, 0.1 equiv). EtOH (6.0 mL, 0.42 M) and triethylamine (688 μL, 4.94 mmol, 2 equiv) was added. The reaction vial was capped, and a double-skinned balloon of hydrogen gas was bubbled through the solution while stirring (550 rpm). After the balloon was depleted, it was replaced with a fresh, double-skinned balloon filled with hydrogen gas hovering in the headspace of the vial. The reaction was monitored by LCMS until full conversion of the starting material and intermediates was observed. The balloon was removed, and the reaction mixture was filtered through Celite and concentrated in vacuo. Flash chromatography (silica gel: 60:40 EtOAc:Hexanes) to provide the pure title compound as an off-white solid (791 mg, 3.51 mmol, 61% yield). mp 86-87 °C. IRυ_{max}/cm^{-1} (film): 3675,2988, 2900, 1571, 1336, 1182, 799. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.69 (d, J = 5.3 Hz, 1H), 7.29 (dd, J = 5.4, 1.5 Hz, 1H), 2.62 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.15, 159.06, 158.52, 158.22, 157.17, 118.78, 113.82, 13.25, 12.05. *m/z* HRMS (ESI) found $[M+H]^+$ 176.0820, for $C_9H_9N_3O^+$ requires 176.0824.

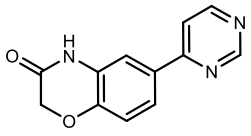
5-(2-Methyl-3-((4-phenylpiperidin-1-yl)sulfonyl)phenyl)pyrimidine



An oven dried 150 mL pressure tube equipped with a stir bar was charged with 1-((3-chloro-2-methylphenyl)sulfonyl)-4-phenylpiperidine (2.45 g, 7.0 mmol), Na_2CO_3 (2.34 g, 22.1 mmol), $Pd(OAc)_2$ (367 mg, 0.34 mmol), triphenylphosphine (367 mg, 1.4 mmol), and pyrimidin-5-ylboronic acid (868 mg, 7.0 mmol) and was subjected to three cycles of vacuum/nitrogen backfill. Degassed H_2O (1 mL) and degassed dimethoxyethane (6 mL) were charged to the tube and the mixture was heated at 80 °C for 18 hours, then cooled to room temperature and diluted with EtOAc. The reaction mixture was filtered through a celite pad before the aqueous layer was extracted with EtOAc (2x). The combined organic layers were dried ($MgSO_4$), filtered over a frit, and concentrated in vacuo. Flash column chromatography (silica gel: 70:30 EtOAc:hexanes) afforded the title compound as a tan solid (184 mg, 0.47 mmol, 12% yield). mp 165-167 °C. IRυ_{max}/cm-1 (film): 3292, 3157, 1669, 1605, 1496, 1483, 1266, 1131, 813, 693. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.67 (s, 2H), 8.03 (dd, J = 7.5, 1.9 Hz, 1H), 7.45 – 7.34 (m, 2H), 7.28 – 7.20 (m, 3H), 7.20 – 7.08 (m, 3H), 3.84 (dt, J = 12.3, 2.3 Hz, 2H), 2.82 (td, J = 12.4, 2.6 Hz, 2H), 2.57 (tt, J = 12.3, 3.7 Hz, 1H), 2.48 (s, 3H), 1.95 – 1.85 (m, 2H), 1.72 (qd, J = 12.3, 4.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.44, 155.39, 143.40, 136.93, 136.09, 134.55, 133.11, 129.55, 127.23, 125.30,

124.83, 115.04, 44.56, 40.63, 31.49, 16.26. HRMS (ESI) found $[M+H]^+$ 394.1610, for $C_{22}H_{23}N_3O_2S^+$ requires 394.1589.

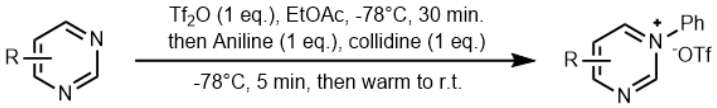
6-(Pyrimidin-4-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one



To an oven dried 50 mL round bottom flask equipped with a stir bar and condenser was added 6-acetyl-2H-1,4-benzoxazin-3(4H)-one (1.91 g, 10.0 mmol), NH_4OAc (1.54g, 20.0 mmol), and NH_4I (145 mg, 1.00 mmol) and subjected to three cycles of vacuum/nitrogen backfill. *N*,*N*-Dimethylformamide dimethyl acetal (4.0 mL, 30.0 mmol) was added and the suspension was heated to 120 ˚C for 18 hours. Upon completion, the mixture was concentrated *in vacuo* and diluted with water, then extracted with EtOAc. The combined organic extracts were washed with brine and dried ($MgSO_4$), filtered over a frit, and concentrated *in vacuo*. Flash column chromatography (silica gel: 0-2% MeOH in EtOAc) afforded the title compound as a pale-yellow solid (800 mg, 3.5 mmol, 35% yield). mp 258-262 °C. IRυ_{max}/cm-1 (film): 3075, 2974, 1610, 1575, 1498, 1385, 1057, 810, 704, 666. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.92 (s, 1H), 9.19 (s, 1H), 8.80 (d, J = 5.4 Hz, 1H), 8.11 – 7.89 (m, 1H), 7.82 (d, J = 2.0 Hz, 1H), 7.77 (dd, J = 8.4, 2.1 Hz, 1H), 7.09 (d, J = 8.4 Hz, 1H), 4.67 (s, 2H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 164.45, 161.70, 158.69, 157.91, 145.86, 130.09, 127.80, 122.26, 116.64, 116.42, 114.24, 66.79; HRMS (ESI) found $[M+H]^+$ 228.0769, for $C_{12}H_{10}N_3O_2^+$ requires 228.0768.

9. General Procedure for *N*-Aryl Pyrimidinium Salt Formation:

General Procedure A (*N*-Phenyl Pyrimidinium 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 ºC, and triflic anhydride (Tf_2O) (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 ºC. 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 ºC 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.

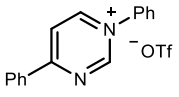
Isolation A2: For products that do not precipitate with the addition of Et_2O, the reaction mixture was transferred to a separatory funnel and washed with a 0.1 M HCl solution (2x) and with brine (1x), then dried over $MgSO_4$ and concentrated *in vacuo*. The resulting oil was triturated with Et_2O and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

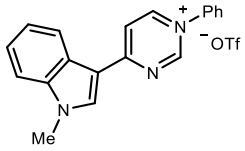
10. Preparation of *N*-Aryl Pyrimidinium Salts:

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



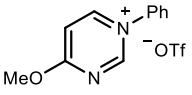
Prepared according to general procedure A using 4-phenylpyrimidine (1.56 g, 10.0 mmol), EtOAc (50 mL), Tf_2O (1.68 mL, 10.0 mmol), aniline (912 µL, 10.0 mmol), and collidine (1.32 mL, 10.0 mmol). Isolation A1 afforded the title compound as a white powder (3.62 g, 9.45 mmol, 95% yield). mp 216-220 °C; IR ν_{max}/cm^{-1} (solid): 3102, 1622, 1589, 1417, 1256, 1146, 1030, 741, 633; ^1H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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; ^{19}F NMR (375 MHz, CD_3CN) δ -79.30; *m/z* HRMS (ESI) found $[M+H]^+$ 233.1080, $C_{16}H_{13}N_2^+$ requires 233.1073.

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



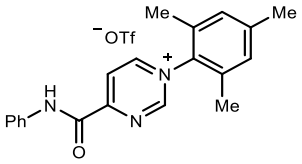
Prepared according to general procedure A using 1-methyl-3-(pyrimidin-4-yl)-1H-indole (72.9 mg, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), and collidine (53 µL, 0.40 mmol). Isolation A1 afforded the title compound as a bring-yellow solid (127 mg, 0.29 mmol, 73% yield). 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 $[M+H]^+$ 286.1348, $C_{19}H_{16}N_3^+$ requires 286.1339.

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



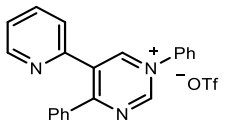
Prepared according to general procedure A using 4-methoxypyrimidine (44.0 mg, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), and collidine (53 µL, 0.40 mmol). Isolation A1 afforded the title compound as a white solid (84 mg, 0.25 mmol, 63% yield). mp 131-133 ˚C; IR ν_{max}/cm^{-1} (solid): 3066, 1633, 1413, 1251, 1139, 1026, 838, 771, 636; ^{1}H 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, CD_3CN) δ -79.21; *m/z* HRMS (ESI) found $[M+H]^+$ 187.0873, $C_{11}H_{11}N_2O^+$ 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), Tf_2O (67 µL, 0.40 mmol), 2,4,6-trimethylaniline (56 µL, 0.40 mmol), and collidine (53 µL, 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; ^{1}H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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; ^{19}F NMR (375 MHz, CD_3CN) δ -79.29; *m/z* HRMS (ESI) found $[M+H]^+$ 318.1608, $C_{20}H_{20}N_3O^+$ requires 318.1601.

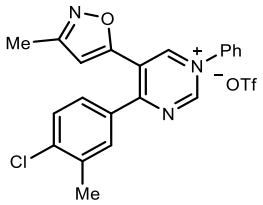
1,4 -Diphenyl-5-(pyridin-2-yl)pyrimidin-1-ium trifluoromethanesulfonate (3e)



Prepared according to general procedure A using 4-phenyl-5-(pyridin-2-yl)pyrimidine (700 mg, 3.00 mmol), EtOAc (15 mL), Tf_2O (504 µL, 3.00 mmol), aniline (274 µL, 3.00 mmol), and collidine (396 µL, 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; ^{1}H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) δ 171.89, 152.47, 151.93, 151.59, 151.05, 139.99, 138.40, 135.52, 135.04,

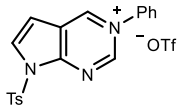
134.02, 133.04, 131.61, 131.57, 129.94, 126.13, 125.77, 125.70, 122.02 (q, J = 321.0 Hz); ^{19}F NMR (375 MHz, CD_3CN) δ -79.31; *m/z* HRMS (ESI) found $[M+H]^+$ 310.1348, $C_{21}H_{16}N_3^+$ requires 310.1339.

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



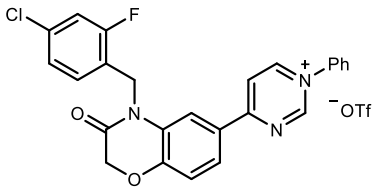
Prepared according to general procedure A using 5-(4-(4-chloro-3-methylphenyl)pyrimidin-5-yl)-3-methylisoxazole (286 mg, 1.00 mmol), EtOAc (5 mL), Tf_2O (168 µL, 1.00 mmol), aniline (91 µL, 1.00 mmol), and collidine (132 µL, 1.00 mmol). Isolation A1 afforded the title compound as a pale-yellow powder (350 mg, 0.68 mmol, 68% yield). mp 205-209 ˚C; IR ν_{max}/cm^{-1} (solid): 3073, 1616, 1589, 1426, 1250, 1164, 1049, 780, 637; ^{1}H 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 $[M+H]^+$ 362.1060, $C_{21}H_{17}ClN_3O^+$ requires 362.1055.

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



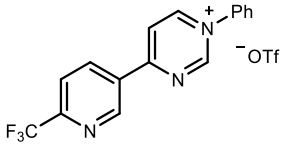
Prepared according to a modified general procedure A with CH_2Cl_2 instead of EtOAc, using 7-tosyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (109. mg, 0.40 mmol), CH_2Cl_2 (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), and collidine (53 µL, 0.40 mmol). Isolation A1 afforded the title compound as a white powder (460 mg, 0.36 mmol, 92% yield). mp 169-174 ˚C; IR ν_{max}/cm^{-1} (solid): 3109, 1633, 1426, 1256, 1148, 1028, 670, 636; ^{1}H 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 $[M+H]^+$ 350.0968, $C_{19}H_{16}N_3O_2S^+$ 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)



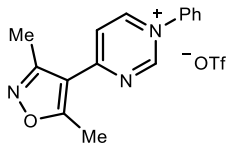
Prepared according to general procedure A using 4-(4-chloro-2-fluorobenzyl)-6-(pyrimidin-4-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one (147.9 mg, 0.40 mmol), EtOAc (2.00 mL), Tf_2O (67 µL, 0.40 mmol), aniline (37 µL, 0.40 mmol), and collidine (53 µL, 0.40 mmol). Isolation A2 afforded the title compound as a 2:1 mixture of triflate ($^-$OTf) and triflamide ($^-$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 $^\circ$C; IRυ_{max}/cm^{-1} (film): 3076, 1687, 1582, 1436, 1381, 1223, 1147, 1027, 894, 636. ^{1}H 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 $[M+H]^+$ 446.1072, for $C_{25}H_{18}ClFN_3O_2^+$ requires 446.1066.

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



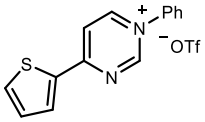
Prepared according to general procedure A using 4-(6-(trifluoromethyl)pyridin-3-yl)pyrimidine (225 mg, 1.00 mmol), EtOAc (5 mL), Tf_2O (168 µL, 1.00 mmol), aniline (91 µL, 1.00 mmol), and collidine (132 µL, 1.0 mmol). Isolation A1 afforded the title compound as a white powder (325 mg, 0.72 mmol, 95% yield). mp 245-247 $^\circ$C; IR ν_{max}/cm^{-1} (solid): 3124, 1625, 1463, 1346, 1272, 1250, 1065, 847, 638; ^{1}H 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, CD_3CN) δ -68.92, -79.33. HRMS (ESI) found $[M+H]^+$ 302.0955, for $C_{17}H_{11}F_6N_3O_3S^+$ requires 302.0900.

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



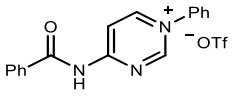
Prepared according to general procedure A using 3,5-dimethyl-4-(pyrimidin-4-yl)isoxazole (526 mg, 3.00 mmol), EtOAc (15 mL), Tf_2O (504 µL, 3.00 mmol), aniline (273 µL, 3.00 mmol), and collidine (396 µL, 3.0 mmol). Isolation A1 afforded the title compound as a white powder (3.62 g, 9.45 mmol, 95% yield). mp 175-178 ˚C; IR ν_{max}/cm^{-1} (solid): 2358, 2049, 1586, 1274, 1226, 1151, 782, 639, 556; ^1H NMR (400 MHz, CD_3CN) 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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. ^{19}F NMR (375 MHz, CD_3CN) δ -79.28; HRMS (ESI) found $[M+H]^+$ 252.1220, for $C_{16}H_{14}F_3N_3O_4S^+$ 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), 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 (120 mg, 0.31 mmol, 84% yield). mp 177-180 ˚C; IR ν_{max}/cm^{-1} (solid): 3123, 1626, 1415, 1253, 1146, 1032, 770, 712, 636; ^1H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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; ^{19}F NMR (375 MHz, CD_3CN) δ -79.29; *m/z* HRMS (ESI) found $[M+H]^+$ 239.0645, $C_{14}H_{11}N_2S^+$ requires 239.0637.

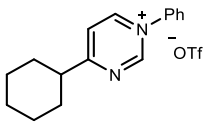
4-Benzamido-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3m)



Prepared according to general procedure A using N-(pyrimidin-4-yl)benzamide (79.7 mg, 0.40 mmol), EtOAc (2 mL), 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 an opaque white solid (160 mg, 37.6 mmol, 94% yield). mp 181-183 ˚C; IR ν_{max}/cm^{-1} (film): 3387, 3098, 1704, 1632, 1514, 1430, 1247, 1141, 1030, 634. ^1H NMR (400 MHz, CD_3CN) 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,

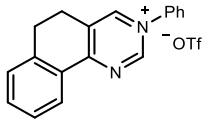
140.11, 134.93, 132.82, 132.37, 131.42, 129.79, 129.66, 125.36, 121.97 (q, *J* = 320.8 Hz), 111.49; ^{19}F NMR (375 MHz, CD_3CN) δ -79.20; *m/z* HRMS (ESI) found $[M+H]^+$ 267.1133, $C_{17}H_{14}N_3O^+$ requires 267.1140.

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



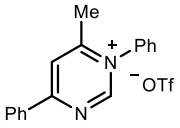
Prepared according to general procedure A using 4-cyclohexylpyrimidine (64.9 mg, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), and collidine (53 µL, 0.40 mmol). Isolation A1 afforded the title compound as a pale-yellow flaky powder (90.3 mg, 0.23 mmol, 58% yield). mp 137-141 ˚C; IR ν_{max}/cm^{-1} (solid): 3066, 2936, 2855, 1623, 1255, 1154, 1028, 760, 636; ^{1}H 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 $[M+H]^+$ 239.1548, $C_{16}H_{19}N_2^+$ requires 239.1543.

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



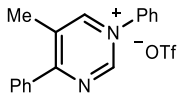
Prepared according to general procedure A using 5,6-dihydrobenzo[*h*]quinazoline (72.9 mg, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), and collidine (53 µL, 0.40 mmol). Isolation A1 afforded the title compound as a white powder (146 mg, 0.37 mmol, 89% yield). mp 179-182 ˚C; IR ν_{max}/cm^{-1} (solid): 3043, 1624, 1432, 1258, 1028, 758, 635; ^{1}H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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; ^{19}F NMR (375 MHz, CD_3CN) δ -79.32; *m/z* HRMS (ESI) found $[M+H]^+$ 239.1548, $C_{16}H_{19}N_2^+$ requires 239.1543

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



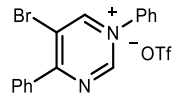
Prepared according to general procedure A using 6-methyl-4-phenylpyrimidine (68 µL, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), and collidine (53 µL, 0.40 mmol). Isolation A1 afforded the title compound as an off-white solid (126 mg, 0.32 mmol, 79% yield). mp 202-204 °C. IRυ_{max}/cm^{-1} (solid): 3060, 1623, 1261, 1145, 1028, 739, 639; ^{1}H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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. ^{19}F NMR (376 MHz, $CDCl_3$) δ -78.31. *m/z* HRMS (ESI) found $[M+H]^+$ 247.1239, $C_{18}H_{15}F_3N_2O_3S^+$ requires 247.1230.

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



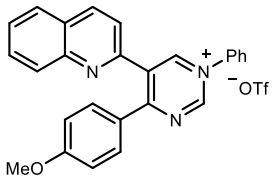
Prepared according to general procedure A using 4-phenyl-5-methylpyrimidine (106 mg, 0.62 mmol), EtOAc (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), and collidine (53 µL, 0.40 mmol). Isolation A1 afforded the title compound as a peach-colored powder (215 mg, 0.54 mmol, 87% yield). mp 209-213 °C; IR ν_{max}/cm^{-1} (solid): 3074, 3035, 1624, 1438, 1255, 1137, 1032, 764, 690, 636; ^{1}H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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 $[M+H]^+$ 247.1238, $C_{17}H_{15}N_2^+$ requires 247.1230.

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



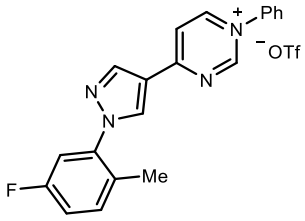
Prepared according to general procedure A using 4-phenyl-5-bromopyrimidine (235.1 mg, 1.00 mmol), EtOAc (5 mL), Tf_2O (168 µL, 1.00 mmol), aniline (91 µL, 1.00 mmol), and collidine (132 µL, 1.00 mmol). Isolation A1 afforded the title compound as a white powder (355 mg, 0.77 mmol, 77% yield). mp 238-241 °C; IR ν_{max}/cm^{-1} (solid): 3060, 3003, 1612, 1587, 1439, 1279, 1253, 1225, 1032, 763, 636; ^{1}H 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 $[M+H]^+$ 311.0187, $C_{16}H_{12}BrN_2^+$ requires 311.0178.

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



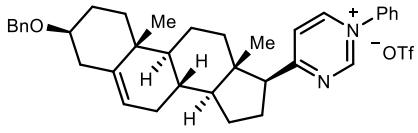
Prepared according to general procedure A using 2-(4-(4-methoxyphenyl)pyrimidin-5-yl)quinoline (125 mg, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), and collidine (53 µL, 0.40 mmol). Isolation A2 afforded the title compound as a bright-orange glass (139 mg, 0.26 mmol, 74% yield). mp 95-99 °C; IR ν_{max}/cm^{-1} (solid): 3062, 1584, 1425, 1252, 1174, 1028, 760, 635; ^1H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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; ^{19}F NMR (375 MHz, CD_3CN) δ -79.14; *m/z* HRMS (ESI) found $[M+H]^+$ 390.1610, $C_{26}H_{20}N_3O^+$ requires 390.1601.

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



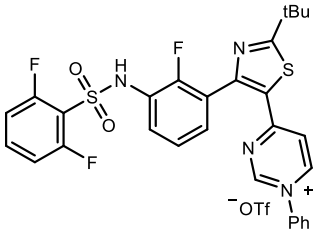
Prepared according to general procedure A using 4-(1-(5-fluoro-2-methylphenyl)-1H-pyrazol-4-yl)pyrimidine (254.3 mg, 1.0 mmol), EtOAc (5 mL), Tf_2O (168 µL, 1.0 mmol), aniline (91 µL, 1.0 mmol), and collidine (132 µL, 1.0 mmol). Isolation A2 afforded the title compound as a red solid (396 mg, 0.83 mmol, 83% yield). mp 150-154 °C; IR ν_{max}/cm^{-1} (film): 3109, 3055, 1574, 1507, 1269, 1142, 1032; ^1H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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; ^{19}F NMR (375 MHz, CD_3CN) δ -79.31 (3F), -117.10 – -117.27 (q, J = 6.9 Hz, 1F); *m/z* HRMS (ESI) found $[M+H]^+$ 331.1359, $C_{20}H_{16}FN_4^+$ 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), 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 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; ^{1}H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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; ^{19}F NMR (375 MHz, CD_3CN) δ -79.33; *m/z* HRMS (ESI) found $[M+H]^+$ 519.3376, $C_{36}H_{43}N_2O^+$ requires 519.3370.

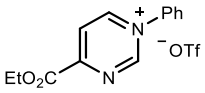
4-(2-(*Tert*-butyl)-4-(3-((2,6-difluorophenyl)sulfonamido)-2-fluorophenyl)thiazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (1v)



Prepared according to a modified general procedure A with CH_2Cl_2 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), CH_2Cl_2 (10 mL), Tf_2O (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 CH_2Cl_2 (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 ν_{max}/cm^{-1} (solid): 3097, 2967, 1622, 1468, 1250, 1164, 1029, 771, 636; ^{1}H NMR (400 MHz, $CDCl_3$) 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),

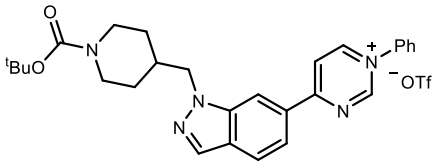
6.89 (t, *J* = 9.0 Hz, 2H), 5.29 (s, 1H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.26, 163.94, 159.47 (dd, *J* = 257.7, 3.5 Hz), 153.64, 150.92, 150.59 (d, *J* = 17.3 Hz), 139.11, 135.05 (t, *J* = 11.3 Hz), 131.83, 130.82, 130.46, 127.96 (d, *J* = 152.5 Hz), 125.62 (d, *J* = 4.1 Hz), 124.79 (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; ^{19}F NMR (376 MHz, $CDCl_3$) δ -78.33 (3F), -107.14 (t, *J* = 9.0 Hz, 2F), -124.76 (1F); *m/z* HRMS (ESI) found $[M+H]^+$ 581.1297, $C_{29}H_{24}F_3N_4O_2S_2^+$ 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), Tf_2O (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; ^{1}H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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; ^{19}F NMR (375 MHz, CD_3CN) δ -79.31; *m/z* HRMS (ESI) found 271.1449, $[M+H]^+$ $C_{16}H_{19}N_2O_2^+$ requires 271.1441.

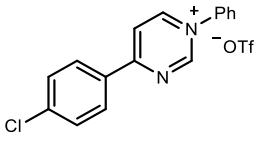
4-(1-((1-(Tert-butoxycarbonyl)piperidin-4-yl)methyl)-1H-indazol-6-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (1x)



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), Tf_2O (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 ($^-$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; IRυ_{max}/cm^{-1} (film): 3054, 2985, 1679, 1626, 1427, 1264, 1030, 895, 703, 638. ^{1}H 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,

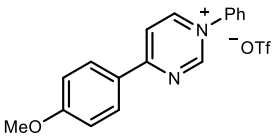
43.09, 38.10, 30.42, 28.58. ^{19}F NMR (375 MHz, CD_3CN) δ -79.31 (s, 2F), -80.60 (s, 1F), -116.15 (t, J = 9.3 Hz, 1F). *m/z* HRMS (ESI) found $[M+H]^+$ 470.2557, for $C_{28}H_{32}N_5O_2^+$ requires 470.2551.

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 ν_{max}/cm^{-1} (solid): 3125, 3071, 1628, 1588, 1274, 1261, 1152, 1032, 773, 637; ^{1}H 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, CD_3CN) 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); ^{19}F NMR (375 MHz, CD_3CN) δ -79.14; *m/z* HRMS (ESI) found $[M+H]^+$ 267.0690, $C_{16}H_{12}ClN_2^+$ requires 267.0684.

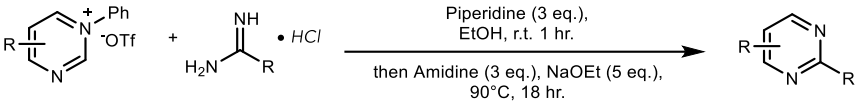
4-(4-Methoxyphenyl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (3z)



Prepared according to general procedure A using 4-(4-methoxyphenyl)pyrimidine (74.5 mg, 0.4 mmol), EtOAc (2 mL), 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 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; ^{1}H NMR (400 MHz, CD_3CN) 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); ^{13}C NMR (100 MHz, CD_3CN) 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; ^{19}F NMR (375 MHz, CD_3CN) δ -79.11; *m/z* HRMS (ESI) found $[M+H]^+$ 263.1187, $C_{17}H_{15}N_2O^+$ requires 263.1179.

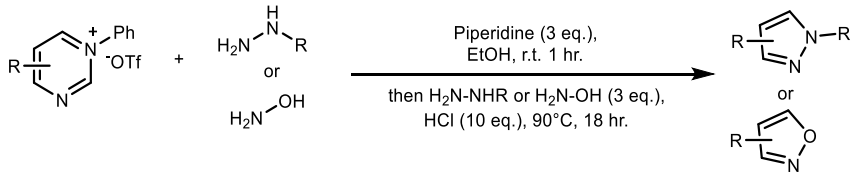
11. General Procedures for Pyrimidine C2-Functionalization and Ring-Conversion:

General Procedure B (Pyrimidine C2-Functionalization from Pyrimidinium 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 pyrimidinium salt (1.0 equiv), EtOH (0.2 M), and piperidine (3.0 equiv). The reaction was stirred for 60 minutes at 25 ºC 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 ºC 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 with brine (1x) and dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

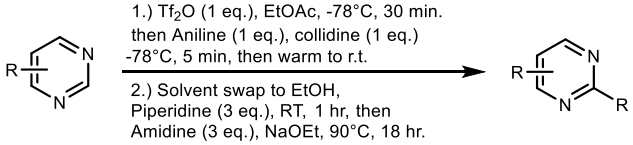
General Procedure C (Pyrimidine Ring-Conversion from Pyrimidinium Salt)



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 pyrimidinium salt (1.0 equiv), EtOH (0.2 M), and piperidine (3.0 equiv). The reaction was stirred for 60 minutes at 25 ºC 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 ºC 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 with brine (1x) and dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

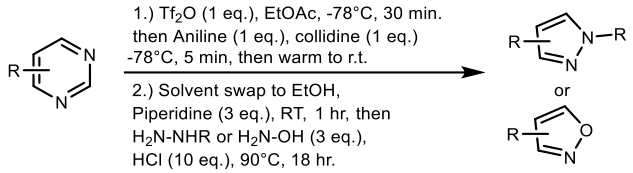
One-pot Pyrimidine Ring-Conversions

General Procedure D (One-Pot C2-Functionalizations from Pyrimidine)



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 ºC 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 ºC. 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 ºC (> 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 ºC 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.

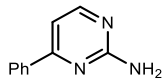
General Procedure E (One-Pot Ring-Conversions from Pyrimidine)



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 ºC 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 ºC. 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 ºC (> 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 ºC 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.

12. C2-Functionalization and Ring-Conversion of Pyrimidines:

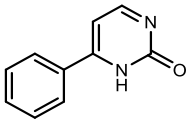
4-Phenylpyrimidin-2-amine (5a)



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).

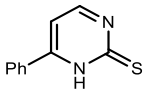
To demonstrate comparable yield in a one-pot procedure, **1a** was also prepared according to general procedure D using 4-phenylpyrimidine (62.5 mg, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), collidine (54 µL, 0.40 mmol). Then, solvent was exchanged for EtOH (2 mL) and 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) 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 ν_{max}/cm^{-1} (solid): 3264, 3149, 2405, 1654, 1553, 1461, 819, 766; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) 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, $C_{10}H_{10}N_3^+$ requires 172.0869. Spectra matched literature values.[13]

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



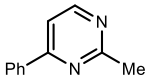
Prepared according to a modified general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), pyrrolidine (164 µL, 2.00 mmol), and stirred for 18 hours at room temperature before adding urea (91.3 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). Following the reaction, AcOH (229 µL, 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 °C; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) 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 $[M+H]^+$ 173.0716, $C_{10}H_8N_2O^+$ requires 173.0709. Spectra matched literature values.[14]

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



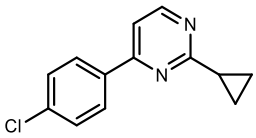
Prepared according to a modified general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), thiourea (91.3 mg, 1.20 mmol), and NaOEt (747 µL, 2.0 mmol, as a 21% soln. in EtOH). Following the reaction, AcOH (229 µL, 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 ˚C; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) 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, $(CD_3)_2SO$) 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 µL, 1.20 mmol), acetamidine hydrochloride (114 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: 1:40:59 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 ˚C; IR ν_{max}/cm^{-1} (solid): 3060, 2925, 1573, 1547, 1428, 1314, 840, 792, 752, 699; ^{1}H 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 $[M+H]^+$ 171.0924, $C_{11}H_{11}N_2^+$ requires 171.0917. Spectra matched literature values.[16]

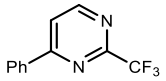
4-(4-Chlorophenyl)-2-cyclopropylpyrimidine (5e)



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 µL, 1.20 mmol), cyclopropanecarboximidamide hydrochloride (145 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: 0-12% EtOAc in hexanes) to provide the title compound as a brown oil (60 mg, 0.26 mmol, 65% yield). mp 69-72 ˚C; IR ν_{max}/cm^{-1} (solid): 3065, 3007, 1599, 1542, 1453, 1104, 1014, 915, 856, 867, 791; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 5.3

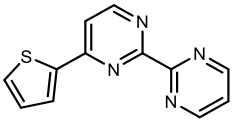
Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 5.3 Hz, 1H), 2.29 (tt, *J* = 8.4, 4.7 Hz, 1H), 1.19 (dt, *J* = 6.2, 3.3 Hz, 2H), 1.11 – 1.01 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.27, 162.18, 157.45, 136.94, 135.40, 129.06, 128.34, 113.10, 18.37, 10.85; *m/z* HRMS (DART) found $[M+H]^+$ 231.0700, $C_{13}H_{12}ClN_2^+$ requires 231.0684.

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



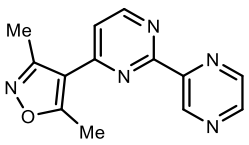
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), trifluoroacetamidine (135 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 0-20% EtOAc in hexanes) to provide the title compound as a white solid (66 mg, 0.30 mmol, 75% yield). mp 44-47 °C; IR ν_{max}/cm^{-1} (solid): 3070, 1583, 1336, 1202, 1136, 873, 767, 688; ^{1}H 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 $[M+H]^+$ 255.0639, $C_{11}H_8F_3N_2^+$ requires 225.0634. Spectra matched literature values.[17]

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



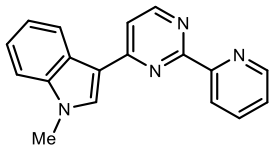
Prepared according to general procedure B using 1-phenyl-4-(thiophen-2-yl)pyrimidin-1-ium trifluoromethanesulfonate (108 mg, 0.28 mmol), EtOH (1.40 mL), piperidine (82 µL, 0.84 mmol), 2-amidinopyrimidine hydrochloride (132 mg, 0.84 mmol), and NaOEt (517 µL, 1.40 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:99 Et_3N:EtOAc followed by 1:19:20:60 Et_3N:hexanes:EtOAc:EtOH)) to provide the title compound as a yellow solid (32 mg, 0.13 mmol, 49% yield). mp 180-183 °C; IR ν_{max}/cm^{-1} (solid): 3066, 3045, 1555, 1426, 1379, 760; ^{1}H 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 $[M+H]^+$ 241.0555, $C_{12}H_9N_4S^+$ requires 241.0542.

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



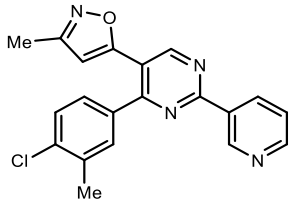
Prepared according to general procedure B using 4-(3,5-dimethylisoxazol-4-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (160.5 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), pyrazine-2-carboximidamide hydrochloride (190.3 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:99 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 °C; IR ν_{max}/cm^{-1} (film): 3047, 1605, 1564, 1422, 1375, 1012, 845, 713, 678; ^{1}H 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 $[M+H]^+$ 254.1043, $C_{13}H_{12}N_5O^+$ 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 µL, 1.20 mmol), picolinimidamide hydrochloride (189 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: 1:99 Et_3N:EtOAc followed by 1:75:24 Et_3N: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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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, $C_{18}H_{15}N_4^+$ requires 287.1291.

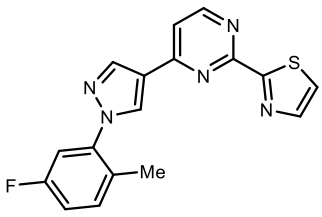
5-(4-(4-Chloro-3-methylphenyl)-2-(pyridin-3-yl)pyrimidin-5-yl)-3-methylisoxazole (5j)



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 µL, 1.20 mmol), EtOH (2 mL), nicotinimidamide hydrochloride (145 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 yellow solid (59 mg, 0.16 mmol,

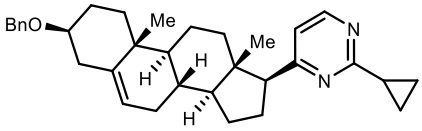
40% yield). mp 142-144 °C. IRυ_{max}/cm^{-1} (solid): 3359, 3146, 1659, 1592, 1412, 1044, 819, 703. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 9.04 (s, 1H), 8.68 (dd, *J* = 12.4, 6.4 Hz, 2H), 7.46 (d, *J* = 1.8 Hz, 1H), 7.39 – 7.30 (m, 2H), 7.26 – 7.19 (m, 1H), 5.86 (s, 1H), 2.36 (s, 3H), 2.23 (s, 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 $[M+H]^+$ 363.1017, $C_{20}H_{15}ClN_4O^+$ 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-pyrazo l-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 ν_{max}/cm^{-1} (film): 3076, 1580, 1527, 1430, 1249, 875, 776; ^{1}H NMR (400 MHz, $CDCl_3$) 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 $[M+H]^+$ 338.0873, $C_{17}H_{13}FN_5S^+$ requires 338.0870.

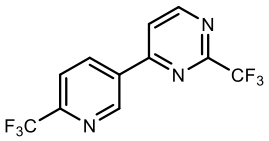
4-((3S,8S,9S,10R,13S,14S,17S)-3-(Benzyloxy)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2-cyclopropylpyrimidine (5l)



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 ˚C; IR ν_{max}/cm^{-1} (film): 2932, 2903, 1574, 1551, 1435, 1113, 730; ^{1}H 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,

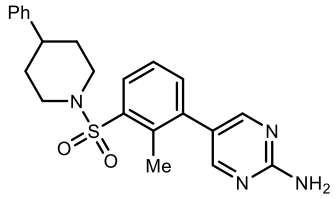
4.5 Hz, 1H), 2.69 (t, J = 9.4 Hz, 1H), 2.43 (tt, J = 7.9, 4.0 Hz, 2H), 2.29 (ddt, J = 13.7, 10.5, 2.7 Hz, 1H), 2.17-2.23 (m, 1H), 2.04 (dtd, J = 13.6, 4.9, 2.3 Hz, 1H), 2.00 – 1.91 (m, 1H), 1.91 – 1.83 (m, 2H), 1.83 – 1.73 (m, 2H), 1.62 (dd, J = 10.5, 2.7 Hz, 1H), 1.59 – 1.51 (m, 3H), 1.49 (d, J = 4.6 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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, $C_{33}H_{43}N_2O^+$ 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 ν_{max}/cm^{-1} (solid): 3312, 3158, 1645, 1590, 1512, 1485, 1224, 798, 697; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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; ^{19}F NMR (375 MHz, CDCl3) δ -68.17 (s, 3F), -70.61 (s, 3F); *m/z* HRMS (ESI) found $[M+H]^+$ 294.0460, $C_{11}H_6F_6N_3^+$ requires 294.0460.

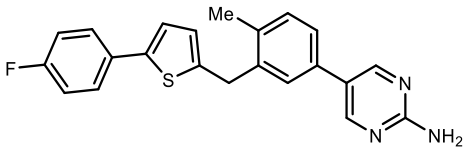
5-(2-Methyl-3-((4-phenylpiperidin-1-yl)sulfonyl)phenyl)pyrimidin-2-amine (5n)



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), Tf_2O (34 µL, 0.20 mmol), *p*-NO_2 aniline (28.0 mg, 0.20 mmol), collidine (25 µL, 0.20 mmol), EtOAc (1 mL), then piperidine (59 µL, 0.60 mmol), EtOH (1 mL), guanidine hydrochloride (382 mg, 4.00 mmol) and NaOEt (428 µL, 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. IRυ_{max}/cm^{-1} (film): 3675, 2988, 2337, 2161, 1622, 1482, 1161, 1067, 561. ^{1}H NMR (400 MHz, $CDCl_3$) 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 =

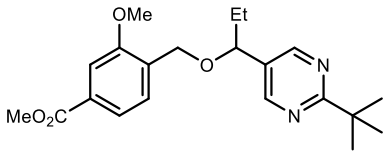
12.5, 2.8 Hz, 2H), 2.57 (dt, J = 12.4, 3.7 Hz, 1H), 2.52 (s, 3H), 1.90 – 1.81 (m, 2H), 1.71 (qd, J = 12.6, 4.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.16, 158.23, 144.88, 138.50, 138.01, 136.20, 134.66, 130.19, 128.64, 126.71, 125.93, 124.50, 45.94, 42.12, 32.91, 17.66. *m/z* HRMS (ESI) found 409.1721, $[M+H]^+$ for $C_{22}H_{24}N_4O_2S^+$ requires 409.1698.

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



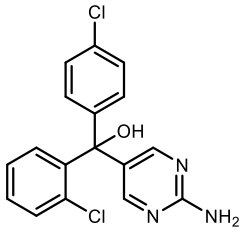
Prepared according to a modified general procedure D using 5-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyrimidine (144 mg, 0.40 mmol), Tf_2O (67 μL, 0.40 mmol), *p*-NO_2 aniline (56.0 mg, 0.40 mmol), collidine (53 μL, 0.40 mmol), EtOAc (2 mL), then piperidine (118 μL, 1.20 mmol), EtOH (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 °C. IRυ_{max}/cm^{-1} (film): 3657, 2988, 2358, 2161, 2050, 1506, 1065, 644, 576. ^{1}H 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, $[M+H]^+$ for $C_{22}H_{18}FN_3S^+$ requires 376.1283.

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



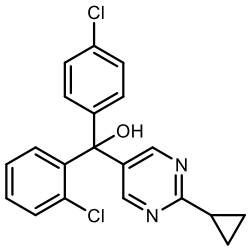
Prepared according to a modified general procedure D using methyl 3-methoxy-4-((1-(pyrimidin-5-yl)propoxy)methyl)benzoate (50.2 mg, 0.16 mmol), Tf_2O (27 μL, 0.16 mmol), *p*-NO_2 aniline (21.8 mg, 0.16 mmol), collidine (21 μL, 0.16 mmol), EtOAc (0.8 mL), then piperidine (47 μL, 0.48 mmol), MeOH (0.8 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 ν_{max}/cm^{-1} (film): 2958, 1720, 1587, 1432, 1288, 1230, 1103, 1036, 760; ^{1}H 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 $[M+H]^+$ 373.2124, $C_{21}H_{29}N_2O_4^+$ requires 373.2122.

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



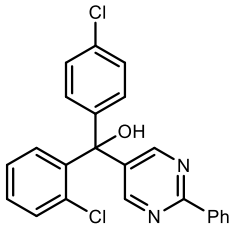
Prepared according to a modified general procedure D using (2-chlorophenyl)(4-chlorophenyl)(pyrimidin-5-yl)methanol (132 mg, 0.40 mmol), Tf_2O (67 µL, 0.40 mmol), *p*-NO_2 aniline (56.0 mg, 0.40 mmol), collidine (53 µL, 0.40 mmol), EtOAc (2 mL), then piperidine (118 µL, 1.20 mmol), EtOH (2 mL), guanidine 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: 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. IRυ_{max}/cm^{-1} (film): 3292, 3157, 1669, 1605, 1496, 1483, 1266, 1131, 813, 693. ^{1}H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{17}H_{13}Cl_2N_3O^+$ requires 346.0514.

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



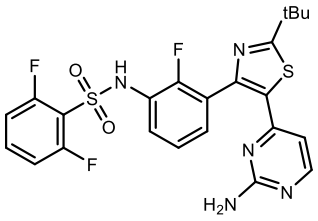
Prepared according to a modified general procedure D using (2-chlorophenyl)(4-chlorophenyl)(pyrimidin-5-yl)methanol (132 mg, 0.40 mmol), Tf_2O (67 µL, 0.40 mmol), *p*-NO_2 aniline (56.0 mg, 0.40 mmol), collidine (53 µL, 0.40 mmol), EtOAc (2 mL), then piperidine (118 µL, 1.20 mmol), EtOH (2 mL), cyclopropanecarboximidamide 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). IRυ_{max}/cm^{-1} (film): 3168, 1545, 1454, 1190, 1013, 904, 757, 728. ^{1}H 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 $[M+H]^+$ 371.0724, $C_{20}H_{16}Cl_2N_2O^+$ 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), Tf_2O (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), 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). IRυ_{max}/cm^{-1} (film): 1651, 1579, 1428, 1163, 1045, 736, 694. ^{1}H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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, $C_{23}H_{16}Cl_2N_2O^+$ requires 407.0718.

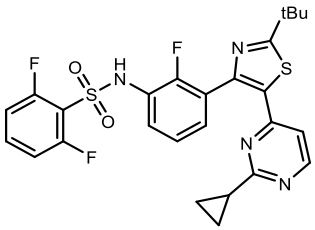
Dabrafenib (5t)



Prepared according to a modified general procedure D, heated to 70 ºC instead of 90 ºC. 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), Tf_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), 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 ν_{max}/cm^{-1} (solid): 3467, 3366, 2964, 1612, 1573, 1459, 1356, 1165, 1010, 795, 633; ^{1}H NMR (400 MHz, $CDCl_3$) 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 $(CD_3)_2SO$ 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*

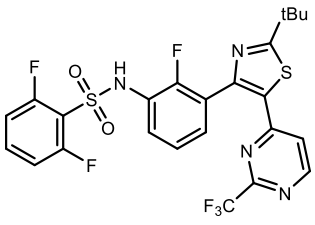
HRMS (DART) found $[M+H]^+$ 520.1089, $C_{23}H_{21}F_3N_5O_2S_2^+$ requires 520.1083. Spectra matched literature values.[18]

_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 ºC instead of 90 ºC. 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), Tf_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 ν_{max}/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 $[M+H]^+$ 545.1302, $C_{26}H_{24}F_3N_4O_2S_2^+$ requires 545.1287.

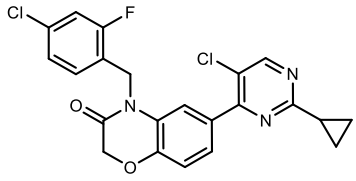
_N_-(3-(2-(*Tert*-butyl)-5-(2-(trifluoromethyl)pyrimidin-4-yl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (5v)



Prepared according to a modified general procedure D, heated to 70 ºC instead of 90 ºC. 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), Tf_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,

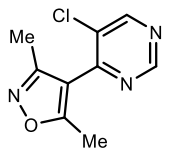
1.25 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 30% EtOAc in hexanes. A second column was needed (0.25:10:89.75 Et_3N:EtOAc:CH_2Cl_2)) to provide the title compound as a white powder (33 mg, 0.06 mmol, 23% yield). mp 207-211 °C; IR ν_{max}/cm^{-1} (solid): 3068, 2964, 2922, 1613, 1578, 1442, 1418, 1360, 1159, 1006, 816; ^{1}H NMR (400 MHz, $(CD_3)_2CO$) 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); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) 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; ^{19}F NMR (375 MHz, $(CD_3)_2CO$) 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 $[M+H]^+$ 573.0858, $C_{24}H_{19}F_6N_4O_2S_2^+$ 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)



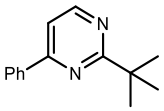
An oven dried 8 mL vial equipped with a stir bar was charged with 4-(4-(4-chloro-2-fluorobenzyl)-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (119.2 mg, 0.20 mmol), and placed under a nitrogen atmosphere. Then EtOH (1.0 mL, 0.2M) and piperidine (60 μL, 0.60 mmol, 3 equiv) were added. The reaction was stirred for 60 minutes before trifluoroacetic acid (46 μL, 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 μL, 1.80 mmol, 9.0 equiv, 21% soln. in EtOH). The reaction was heated to 90 ºC 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 residue was purified by flash chromatography (silica gel: 0 to 35% EtOAc in hexanes. A second column was required (0 to 3% EtOAc in CH_2Cl_2)) to provide the pure title compound as a white solid (46 mg, 0.10 mmol, 52% yield). IRυ_{max}/cm^{-1} (film): 3088, 1676, 1530, 1389, 1279, 1060, 906, 824. ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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; ^{19}F NMR (375 MHz, $CDCl_3$) δ -115.49 (dd, J = 9.8, 7.6 Hz). *m/z* HRMS (DART) found 444.0659, $[M+H]^+$ for $C_{22}H_{17}Cl_2FN_3O_2^+$ requires 444.0676

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



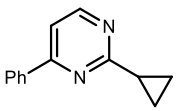
An oven dried 8 mL vial equipped with a stir bar was charged with 4-(3,5-dimethylisoxazol-4-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (160 mg, 0.40 mmol), and placed under a nitrogen atmosphere. Then EtOH (2.0 mL, 0.2 M) and piperidine (120 µL, 1.2 mmol, 3 equiv) were added. The reaction was stirred for 60 minutes before trifluoroacetic acid (88 µL, 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 ºC 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 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. IRυ_{max}/cm^{-1} (film): 2970, 2323, 2184, 1979, 1729, 1391, 1066, 788, 561. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.76 (s, 1H), 2.37 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_9H_8ClN_3O^+$ requires 210.0434.

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



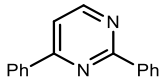
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), 2,2-dimethylpropanimidamide hydrochloride (164 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 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 ˚C; IR ν_{max}/cm^{-1} (solid): 2975, 2952, 1566, 1544, 1448, 1362, 1177, 768, 694; ^{1}H 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 $[M+H]^+$ 213.1394, $C_{14}H_{17}N_2^+$ requires 213.1386.[19]

2-Cyclopropyl-4-phenylpyrimidine (5z)



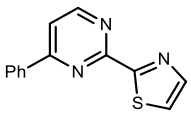
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), cyclopropanecarboximidamide hydrochloride (145 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 0-10% EtOAc in hexanes) to provide the title compound as a pale-yellow oil (55 mg, 0.28 mmol, 70% yield). IR ν_{max}/cm^{-1} (film): 3007, 1568, 1546, 1359, 1262, 916, 836, 763, 691; ^{1}H 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 $[M+H]^+$ 197.1119, $C_{13}H_{13}N_2^+$ requires 197.1073. Spectra matched literature values.[20]

2,4-Diphenylpyrimidine (5aa)



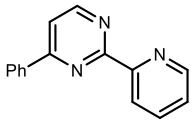
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), benzamidine hydrochloride (188 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified 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 ˚C; IR ν_{max}/cm^{-1} (solid): 3065, 3034, 1541, 1423, 1379, 745, 687; ^{1}H 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 $[M+H]^+$ 223.1145, $C_{16}H_{13}N_2^+$ requires 233.1073. Spectra matched literature values.[21]

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



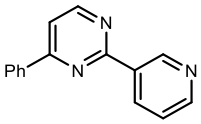
Prepared according to a modified general procedure B heating to 60 ºC instead of 90 ºC. 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), thiazole-2-carboximidamide hydrochloride (196 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:70:29 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 ν_{max}/cm^{-1} (solid): 3075, 1570, 1500, 1430, 1309, 1110, 760, 692, 682; ^{1}H 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 $[M+H]^+$ 240.0616, $C_{13}H_{10}N_3S^+$ requires 240.0590. Spectra matched literature values.[22]

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



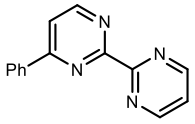
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), picolinimidamide hydrochloride (189 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:70:29 Et_3N:EtOAc:hexanes followed by 1:75:24 Et_3N: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, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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, $C_{15}H_{12}N_3^+$ 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 µL, 1.20 mmol), 3-amidinopyridine hydrochloride (189. 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: 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 ν_{max}/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 $[M+H]^+$ 234.1019, $C_{15}H_{12}N_3^+$ requires 234.1026. Spectra matched literature values.[21]

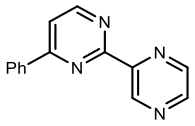
4-Phenyl-2,2'-bipyrimidine (5ae)



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 Et_3N:EtOAc:hexanes followed by 1:75:24 Et_3N:EtOAc:EtOH) to provide the

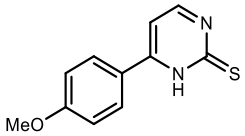
title compound as a yellow solid (50 mg, 0.21 mmol, 53% yield). mp 122-125 °C; IR ν_{max}/cm^{-1} (solid): 3073, 2923, 1556, 1419, 1376, 828, 760, 692, 632; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, *J* = 4.9 Hz, 3H), 8.18 – 8.08 (m, 2H), 7.73 (d, *J* = 5.2 Hz, 1H), 7.51 – 7.40 (m, 3H), 7.35 (t, *J* = 4.8 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 $[M+H]^+$ 235.0981, $C_{14}H_{11}N_4^+$ requires 235.0983.

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



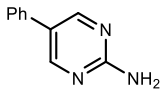
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), pyrazine-2-carboximidamide hydrochloride (190 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 1:49:50 Et_3N:EtOAc:hexanes followed by 1:75:24 Et_3N:EtOAc:hexanes) to provide the title compound as a pale yellow solid (78 mg, 0.33 mmol, 83% yield). mp 97-99 °C; IR ν_{max}/cm^{-1} (solid): 3056, 1578, 1563, 1541, 1451, 1367, 1323, 1142, 1015, 767, 687; ^1H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $[M+H]^+$ 235.0996, $C_{14}H_{11}N_4^+$ requires 235.0978.

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



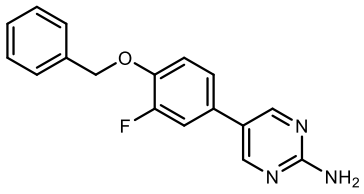
Prepared according to a modified general procedure B using 4-(4-methoxyphenyl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (165 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), thiourea (91.3 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). Upon completion, AcOH (200 µL, 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 °C; IR ν_{max}/cm^{-1} (solid): 2889, 1583, 1436, 1264, 1157, 1024, 794; ^1H NMR (400 MHz, $(CD_3)_2SO$) 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, $(CD_3)_2SO$) δ 181.14, 165.65, 163.30, 146.85, 130.47, 127.80, 114.90, 105.31, 56.00; *m/z* HRMS (DART) found $[M+H]^+$ 219.0596, $C_{11}H_{11}N_2OS^+$ requires 219.0587.

5-Phenylpyrimidin-2-amine (5ah)



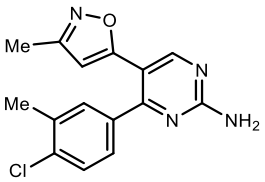
Prepared according to general procedure D using 5-phenylpyrimidine (62.5 mg, 0.40 mmol), Tf_2O (67 µL, 0.40 mmol), *para*-nitro (*p*-NO_2) aniline (56 mg, 0.40 mmol), collidine (53 µL, 0.40 mmol), EtOAc (2 mL), piperidine (118 µL, 1.20 mmol), EtOH (2 mL), guanidine hydrochloride (764 mg, 8.00 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The residue was purified by flash chromatography (silica gel: 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 °C. ^{1}H 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 $[M+H]^+$ 172.0869, $C_{10}H_{10}N_3^+$ requires 172.0869. Spectra matched literature values.[23]

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



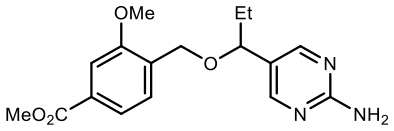
Prepared according to a modified general procedure D using 5-(4-(benzyloxy)-3-fluorophenyl)pyrimidine (112 mg, 0.400 mmol), Tf_2O (67 µL, 0.40 mmol), *p*-NO_2 aniline (56 mg, 0.40 mmol), collidine (53 µL, 0.40 mmol), EtOAc (2 mL), piperidine (118 µL, 1.20 mmol), EtOH (2 mL), guanidine hydrochloride (472 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: 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 °C. IRυ_{max}/cm^{-1} (solid): 3318, 3183, 1615, 1555, 1471, 1091, 820, 756; ^{1}H 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 $[M+H]^+$ 296.1198, $C_{17}H_{14}FN_3O^+$ requires 296.1199.

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



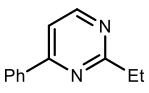
Prepared according to general procedure B using 4-(4-chloro-3-methylphenyl)-5-(3-methylisoxazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (205 mg, 0.40 mmol), piperidine (118 µL, 1.20 mmol), EtOH (2 mL), guanidine hydrochloride (71.0 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% 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 °C. IRυ_{max}/cm^{-1} (solid): 3361, 3148, 1660, 1577, 1476, 1045, 820, 739. ^{1}H 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 $[M+H]^+$ 301.0861, $C_{20}H_{15}ClN_4O^+$ 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), Tf_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 ˚C; IR ν_{max}/cm^{-1} (film): 3319, 3172, 2967, 1717, 1283, 1228, 1077, 761; ^{1}H 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 $[M+H]^+$ 332.1609, $C_{17}H_{22}N_3O_4^+$ requires 332.1605.

2-Ethyl-4-phenylpyrimidine (5al)



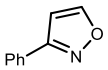
Prepared according to general procedure B using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), propionimidamide hydrochloride (130 mg, 1.20 mmol), and NaOEt (747 µL, 2.00 mmol, as a 21% soln. in EtOH). The crude material was purified by flash chromatography (silica gel: 25% EtOAc in hexanes) to provide the title compound as a clear oil (52 mg, 0.28 mmol, 70% yield). IR ν_{max}/cm^{-1} (film): 2972, 1569, 1546, 1432, 840, 764, 690, 627; ^{1}H 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 $[M+H]^+$ 185.1078, $C_{12}H_{13}N_2^+$ requires 185.1078.

3-Phenylisoxazole and 5-phenylisoxazole (6a)

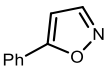
Prepared according to general procedure C using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), hydroxylamine hydrochloride (139 mg, 1.20 mmol), and concentrated aqueous HCl (333 µL, 4.00 mmol). Crude NMR showed 22% of 3-phenyl and 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)



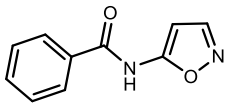
Clear oil (6.00 mg, 0.04 mmol, 10%). IR ν_{max}/cm^{-1} (film): 3124, 3063, 2927, 1552, 1457, 1395, 1123, 878, 762, 699; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 1.7 Hz, 1H), 7.94 – 7.73 (m, 2H), 7.53 – 7.40 (m, 3H), 6.67 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.54, 158.89, 130.06, 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 ν_{max}/cm^{-1} (film): 3062, 1571, 1458, 1197, 817, 794, 761, 689; ^{1}H 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]

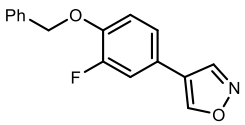
N-(Isoxazol-5-yl)benzamide (6b)



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 µL, 1.20 mmol), hydroxylamine hydrochloride (83.4 mg, 1.20 mmol), and concentrated aqueous HCl (333 µL, 4.00 mmol) at 40 ˚C.

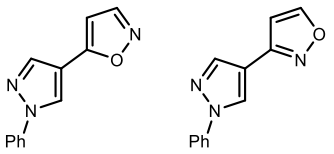
The crude material was purified by flash chromatography (silica gel: 0-35% EtOAc in hexanes) to provide the title compound as a white solid (46 mg, 0.25 mmol, 61% yield). mp 134-137 °C; IR ν_{max}/cm^{-1} (solid): 3243, 3216, 3130, 3054, 3006, 1687, 1527, 1499, 1272, 773, 686; ^{1}H NMR (400 MHz, $CDCl_3$) 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 $[M+H]^+$ 189.0667, $C_{10}H_9N_2O_2^+$ requires 189.0659.

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



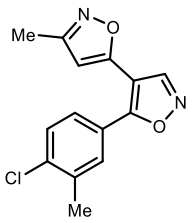
Prepared according to a modified general procedure E using 5-(4-(benzyloxy)-3-fluorophenyl)pyrimidine (112 mg, 0.40 mmol), Tf_2O (67 µL, 0.40 mmol), *p*-NO_2 aniline (56.0 mg, 0.40 mmol), collidine (53 µL, 0.40 mmol), EtOAc (2 mL), piperidine (118 µL, 1.20 mmol), EtOH (2 mL), hydroxylamine hydrochloride (559 mg, 8.00 mmol), and concentrated HCl (333 µL, 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. IRυ_{max}/cm^{-1} (solid): 1603, 1513, 1283, 1262, 1114, 986, 811, 753, 703; ^{1}H 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 $[M+H]^+$ 270.2727, $C_{16}H_{12}FNO_2^+$ requires 270.2754.

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



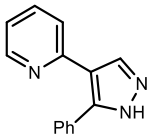
Prepared according to general procedure E using 4-(1-phenyl-1H-pyrazol-4-yl)pyrimidine (**6n**) (88.9 mg, 0.40 mmol), EtOAc (2 mL), Tf_2O (67 µL, 0.40 mmol), aniline (36 µL, 0.40 mmol), collidine (53 µL, 0.40 mmol), then EtOH (2 mL), hydroxylamine hydrochloride (139 mg, 2.00 mmol), and concentrated aqueous 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 ν_{max}/cm^{-1} (solid): 3111, 3055, 1633, 1598, 1501, 1471, 1374, 1214, 1203, 955, 865, 749, 688; *m/z* HRMS (DART) found $[M+H]^+$ 212.0827, $C_{12}H_{10}N_3O^+$ requires 212.0818.

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



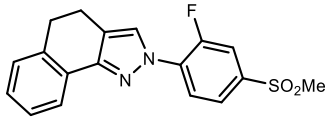
Prepared according to general procedure C using 4-(4-chloro-3-methylphenyl)-5-(3-methylisoxazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (205 mg, 0.40 mmol), piperidine (118 µL, 1.20 mmol), EtOH (2 mL), hydroxylamine hydrochloride (83.0 mg, 1.20 mmol), and concentrated HCl (333 µL, 4.00 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 °C. IRυ_{max}/cm^{-1} (solid): 2922, 1650, 1416, 1152, 1045, 922, 781, 674. ^{1}H 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 $[M+H]^+$ 275.7075; $C_{14}H_{11}ClN_2O_2^+$ requires 275.7040.

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



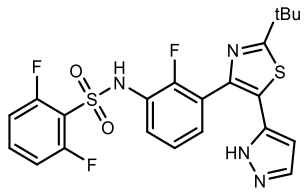
Prepared according to general procedure C using 1,4-diphenyl-5-(pyridin-2-yl)pyrimidin-1-ium trifluoromethanesulfonate (184 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), hydrazine hydrate (58 µL, 1.20 mmol), and concentrated aqueous HCl (333 µL, 4.00 mmol). The crude material was purified 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 ν_{max}/cm^{-1} (film): 3139, 2919, 1590, 1509, 1429, 768, 726, 696; ^{1}H 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 $[M+H]^+$ 222.1049, $C_{14}H_{12}N_3^+$ requires 222.1026.

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



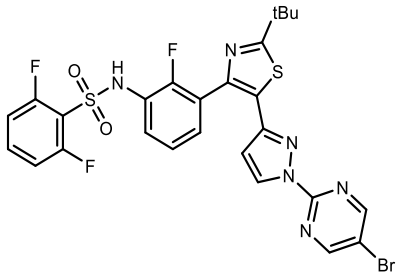
Prepared according to general procedure C using 3-phenyl-5,6-dihydrobenzo[h]quinazolin-3-ium trifluoromethanesulfonate (163 mg, 0.40 mmol), piperidine (118 µL, 1.20 mmol), EtOH (2 mL), (3-fluoro-4-(methylsulfonyl)phenyl)hydrazine (245 mg, 0.40 mmol), and concentrated HCl (333 µL, 4.00 mmol). The residue was purified by flash chromatography (silica gel: 30% EtOAc in hexanes. A second column was needed (29:70:1 EtOAc:hexanes:NEt_3)) to provide the pure title compound as an orange solid (56. mg, 0.16 mmol, 41% yield). mp 145-146 °C. IRυ_{max}/cm^{-1} (solid): 3359, 2921, 1515, 1414, 1312, 1233, 1140, 760, 607. ^{1}H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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. ^{19}F NMR (375 MHz, $CDCl_3$) δ -115.70. *m/z* HRMS (ESI) found $[M+H]^+$ 343.0920, $C_{18}H_{15}FN_2O_2S^+$ requires 343.0916.

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



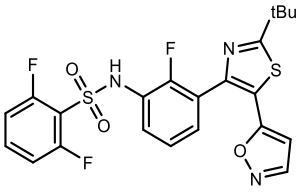
Prepared according to general procedure C using 4-(2-(*tert*-butyl)-4-(3-((2,6-difluorophenyl)sulfonamido)-2-fluorophenyl)thiazol-5-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (183 mg, 0.25 mmol), EtOH (1.25 mL), piperidine (75 µL, 0.75 mmol), hydrazine hydrate (36 µL, 0.75 mmol), and concentrated 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 ν_{max}/cm^{-1} (solid): 3246, 3154, 2934, 1614, 1589, 1470, 1356, 1185, 1005, 788, 758; ^{1}H 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 $[M+H]^+$ 493.1028, $C_{22}H_{20}F_3N_4O_2S_2^+$ 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 µL, 0.75 mmol), 5-bromo-2-hydrazinopyrimidine (142 mg, 0.75 mmol), and concentrated aqueous HCl (208 µL, 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 ˚C; IR ν_{max}/cm^{-1} (solid): 3069, 2957, 1613, 1518, 1420, 1171, 1004, 784, 634; ^{1}H 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 $[M+H]^+$ 649.0300, $C_{26}H_{21}BrF_3N_6O_2S_2^+$ requires 649.029

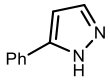
***N*-(3-(2-(*Tert*-butyl)-5-(isoxazol-5-yl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (6j)**



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 µL, 0.75 mmol), hydroxylamine hydrochloride (52.1 mg, 0.75 mmol), and concentrated aqueous HCl (208 µL, 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 ˚C; IR ν_{max}/cm^{-1} (solid): 3081, 1609, 1584, 1461, 1365, 1170, 1004, 792, 634; ^{1}H 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

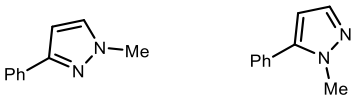
Hz), 159.02, 151.00 (d, *J* = 247.5 Hz), 150.70, 146.01, 135.41 (t, *J* = 11.1 Hz), 128.15 (d, *J* = 2.5 Hz), 125.13 (d, *J* = 4.5 Hz), 124.76 (d, *J* = 12.5 Hz), 123.23 (d, *J* = 13.5 Hz), 123.14, 120.59, 116.94 (t, *J* = 15.3 Hz), 113.31 (dd, *J* = 23.2, 3.6 Hz), 100.42, 38.24, 30.79; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.87 (2F), -130.10 (1F); *m/z* HRMS (DART) found $[M+H]^+$ 494.0826, $C_{22}H_{19}F_3N_3O_3S_2^+$ requires 494.0814.

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



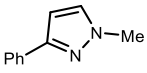
Prepared according to general procedure C using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.400 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), hydrazine hydrate (53 µL, 1.20 mmol), and concentrated aqueous HCl (333 µL, 4.00 mmol). The crude material was purified by flash chromatography (silica gel: 1:50:49 Et_3N: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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.22, 133.25, 132.21, 128.81, 128.06, 125.89, 102.68; *m/z* HRMS (DART) found $[M+H]^+$ 145.0799, $C_9H_9N_2^+$ requires 145.0760. Spectra matched literature values.[8]

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



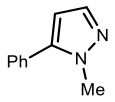
Prepared according to general procedure C using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), methylhydrazine (63 µL, 1.20 mmol), and concentrated aqueous HCl (333 µL, 4.00 mmol). Crude NMR showed 30% of 3-phenyl- and 52% of 5-phenyl-1-methyl-1H-pyrazole 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)



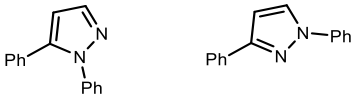
Yellow solid (12 mg, 0.07 mmol, 19%). mp 45-57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 2.3 Hz, 1H), 7.32 – 7.27 (m, 1H), 6.54 (d, *J* = 2.3 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.61, 133.56, 131.37, 128.62, 127.55, 125.54, 102.85, 39.05. Spectra matched literature values.[26]

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



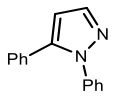
Yellow oil (23 mg, 0.15 mmol, 37%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 1.9 Hz, 1H), 7.48 – 7.34 (m, 5H), 6.30 (d, *J* = 1.9 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.58, 138.53, 130.79, 128.77, 128.68, 128.43, 106.05, 37.49. Spectra matched literature values.[27]

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



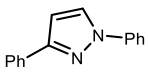
Prepared according to general procedure C using 1,4-diphenylpyrimidin-1-ium trifluoromethanesulfonate (153 mg, 0.40 mmol), EtOH (2 mL), piperidine (119 µL, 1.20 mmol), phenylhydrazine (118 µL, 1.20 mmol), and concentrated aqueous HCl (333 µL, 4.00 mmol). The crude material was purified by flash chromatography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

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



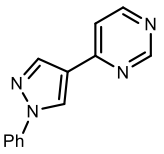
Orange solid (27 mg, 0.12 mmol, 30%). mp 79-82 ˚C IR ν_{max}/cm^{-1} (solid): 3061, 2922, 1598, 1504, 1359, 1045, 954, 749, 684; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 2.5 Hz, 1H), 7.95 – 7.89 (m, 2H), 7.78 (dt, *J* = 7.8, 1.2 Hz, 2H), 7.51 – 7.40 (m, 4H), 7.37 – 7.32 (m, 1H), 7.32 – 7.27 (m, 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 $[M+H]^+$ 221.1129, $C_{15}H_{13}N_2^+$ requires 221.1073. Spectra matched literature values.[8]

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



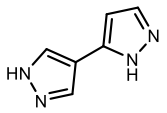
Brown solid (43 mg, 0.20 mmol, 49%). IR ν_{max}/cm^{-1} (solid): 3960, 2998, 1592, 1499, 1450, 1378, 756, 687; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 1.9 Hz, 1H), 7.27 – 7.19 (m, 8H), 7.15 (ddd, *J* = 5.0, 4.3, 2.8 Hz, 2H), 6.42 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.08, 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 $[M+H]^+$ 221.1124, $C_{15}H_{13}N_2^+$ requires 221.1073. Spectra matched literature values.[28]

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



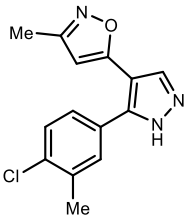
Prepared according to a modified general procedure E using 2,4,6-trimethylaniline instead of aniline. Used 4-5'-bipyrimidine (158 mg, 1.00 mmol), EtOAc (5 mL), Tf_2O (168 µL, 1.00 mmol), 2,4,6-trimethylaniline (421 µL, 1.20 mmol), collidine (132 µL, 1.00 mmol), then EtOH (2 mL), phenylhydrazine (295 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 ν_{max}/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 $[M+H]^+$ 233.0989, $C_{13}H_{11}N_4^+$ 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), Tf_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˚C; IR ν_{max}/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 $[M+H]^+$ 135.0661, $C_6H_7N_4^+$ requires 135.0665.

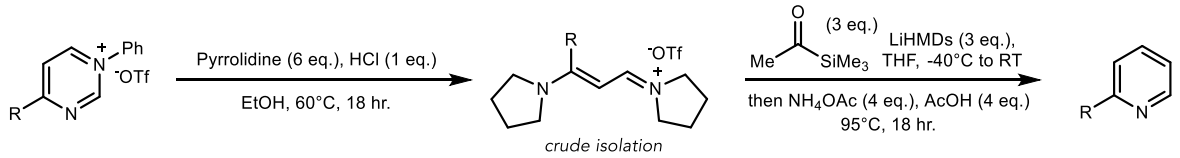
5-(4-(4-Chloro-3-methylphenyl)-1H-pyrazol-3-yl)-3-methylisoxazole (6p)



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 μL, 1.20 mmol), EtOH (2 mL), hydrazine hydrate (38 μL, 1.20 mmol), and concentrated HCl (333 μL, 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 °C. IRυ_{max}/cm^{-1} (solid): 3166, 3119, 2936, 1623, 1436, 1413, 1045, 918, 784, 729. ^{1}H 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 $[M+H]^+$ 274.0743, $C_{14}H_{12}ClN_3O^+$ requires 274.0669.

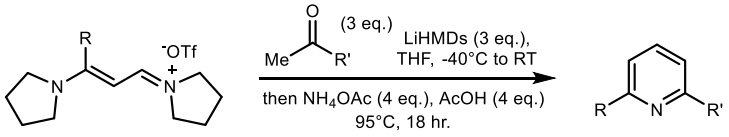
13. General Procedures for Vinamidinium Formation and Pyridine Conversion

General Procedure G (Pyridine Formation from Pyrimidinium 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 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 ºC. Next, the reaction was concentrated *in vacuo* and diluted with a 1:3 solution of isopropyl alcohol (iPrOH):CH_2Cl_2 and washed with a 0.1M aqueous solution of HCl (2x). The aqueous layer was extracted with iPrOH:CH_2Cl and the combined organic extract was washed with brine (1x) and dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude material was dissolved in a minimal amount of CH_2Cl_2 and added dropwise to a stirring solution of 1:3 Et_2O:hexanes, then chilled in a -20 ºC 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 ºC 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, NH_4OAc (4 equiv) and acetic acid (4 equiv) were added, and the reaction was heated to 95 ºC for 18 hours. After cooling to room temperature, the reaction was quenched with sat. $NaHCO_3$, extracted into EtOAc (3x). The combined organic extract was washed with water (1x), brine (1x), and dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

General Procedure H (Pyridine Formation from Vinamidinium Salt)

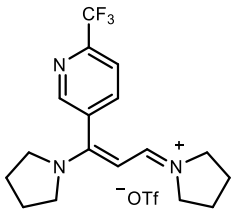


An oven dried 8 mL vial (≤ 0.5 mmol scale) or a round bottom flask (> 0.5 mmol scale) equipped with a stir bar was charged with the ketone or acetyltrimethylsilane (3.0 equiv) was added to THF (0.2M) and cooled to -40 ºC before adding lithium bis(trimethylsilyl)amide (LiHMDS, 3.0 equiv). The reaction was stirred for 30 minutes before adding vinamidinium (1.0 equiv), then warmed to room temperature under ambient. Next, NH_4OAc (4 equiv) and acetic acid (4 equiv) were added, and the reaction was heated to 95 ºC for 18 hours. After cooling to

room temperature, the reaction was quenched with sat. $NaHCO_3$, extracted into EtOAc (3x). The combined organic extract was washed with water (1x), brine (1x), and dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude material was purified with flash column chromatography.

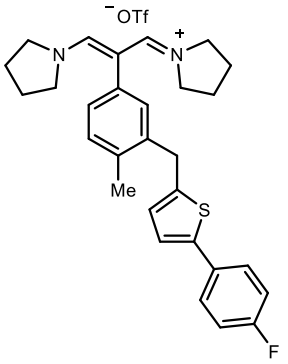
14. Vinamidinium and Pyridine Formation from Pyrimidines and Pyrimidinium Salts

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



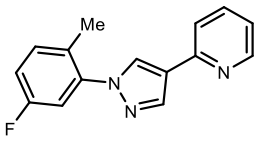
An oven dried 8 mL vial equipped with a stir bar was charged with 1-phenyl-4-(6-(trifluoromethyl)pyridin-3-yl)pyrimidin-1-ium trifluoromethanesulfonate (180 mg, 0.40 mmol, 1 equiv), and placed under a nitrogen atmosphere. Then EtOH (2.0 mL, 0.2 M), concentrated aqueous HCl (33 µL, 0.40 mmol, 1 equiv), and pyrrolidine (100 µL, 2.4 mmol, 6 equiv) were added. The reaction was heated to 60 ºC 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:Et_2O. The precipitate was filtered, then purified by flash chromatography (silica gel: 1:6:93 AcOH:MeOH:CH_2Cl_2) to provide the pure title compound as a pale yellow solid (80 mg, 0.17 mmol, 43% yield). mp 100-102 °C. IRυ_{max}/cm^{-1} (film): 2979, 1620, 1556, 1450, 1332, 1260, 1139, 1030, 637. ^{1}H NMR (400 MHz, $CDCl_3$) 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 $[M+H]^+$ 324.1735, for $C_{18}H_{21}F_6N_3O_3S^+$ 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



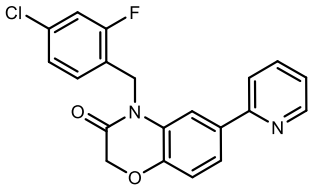
An oven dried round bottom flask equipped with a stir bar was charged with 5-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyrimidine (1.0 g, 2.8 mmol, 1.0 equiv) and placed under a nitrogen atmosphere. EtOAc (0.2 M) was added, the reaction vessel cooled to –78 ºC and Tf_2O (465 µL, 2.8 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 ºC. 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 ºC. Then EtOH (0.2 M) and pyrrolidine (1.4 mL, 16.6 mmol, 6.0 equiv) were added. The reaction was heated to 60 ºC 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:Et_2O. The precipitate was filtered, then purified by flash chromatography (silica gel: 6% MeOH in CH_2Cl_2) to provide the pure title compound as a red solid (861 mg, 1.41 mmol, 51% yield). mp 188-189 °C. IRυ_{max}/cm^{-1} (solid):2928, 2323, 1980, 1569, 1510, 1424, 1223, 1144, 1028, 636. ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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; ^{19}F NMR (375 MHz, $CDCl_3$) 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 $C_{30}H_{32}F_4N_2O_3S_2^+$ requires 459.2265.

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



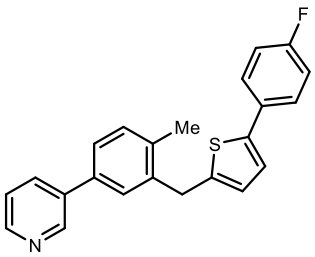
Prepared according to general procedure G using 4-(1-(5-fluoro-2-methylphenyl)-1H-pyrazol-4-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (144 mg, 0.30 mmol), EtOH (1.5 mL), HCl (75 µL, 0.30 mmol), pyrrolidine (150 µL, 1.80 mmol), acetyltrimethylsilane (148 µL, 0.90 mmol), LiHMDS (0.9 mL, 0.90 mmol), THF (1.5 mL), NH_4OAc (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). IRυ_{max}/cm^{-1} (film): 3033, 2910, 1598, 1507, 1415, 1253, 1229, 1112, 828, 635; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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); ^{19}F NMR (375 MHz, $CDCl_3$) δ -115.76 (q, J = 7.8 Hz); *m/z* HRMS (ESI) found $[M+H]^+$ 254.1098, for $C_{15}H_{13}FN_3^+$ requires 254.1088.

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



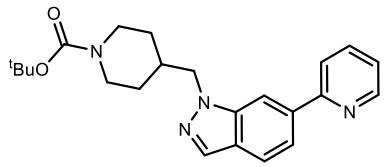
Prepared according to general procedure G using 4-(4-chloro-2-fluorobenzyl)-6-(1-phenyl-1l4-pyrimidin-4-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one trifluoromethanesulfonate (238 mg, 0.4 mmol), EtOH (2 mL), HCl (100 µL, 0.4 mmol), pyrrolidine (197 µL, 2.4 mmol), acetyltrimethylsilane (197 µL, 1.20 mmol), LiHMDS (1.2 mL, 1.20 mmol), THF (2.0 mL), NH_4OAc (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; IRυ_{max}/cm^{-1} (film): 3085, 1607, 1580, 1488, 1420, 1378, 1273, 891, 777, 582. ^{1}H NMR (400 MHz, $CDCl_3$) 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, 32H), 4.75 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $[M+H]^+$ 369.0816, for $C_{20}H_{15}ClFN_2O_2^+$ requires 369.0801.

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



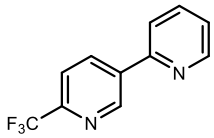
Prepared according to modified general procedure H using (Z)-1-(2-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-3-(pyrrolidin-1-yl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate (122 mg, 0.20 mmol), acetyltrimethylsilane (33 µL, 0.20 mmol), LiHMDS (200 µL, 0.20 mmol), THF (1.0 mL), 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 °C. IRυ_{max}/cm^{-1} (film): 2921, 2218, 1571, 1472, 1423, 1230, 906, 799, 728. ^{1}H 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, $CDCl_3$) δ -115.07 (tt, J = 8.3, 5.2 Hz); *m/z* HRMS (ESI) found $[M+H]^+$ 360.1222, for $C_{23}H_{18}FNS^+$ requires 360.1222.

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



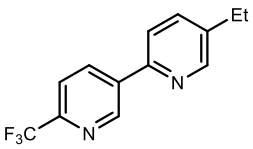
Prepared according to general procedure G using 4-(1-((1-(tert-butoxycarbonyl)piperidin-4-yl)methyl)-1H-indazol-6-yl)-1-phenylpyrimidin-1-ium trifluoromethanesulfonate (214 mg, 0.35 mmol), EtOH (1.7 mL), HCl (86 µL, 0.35 mmol), pyrrolidine (170 µL, 2.07 mmol), acetyltrimethylsilane (170 µL, 1.04 mmol), LiHMDS (1.0 mL, 1.04 mmol), THF (1.7 mL), NH_4OAc (106 mg, 1.38 mmol), AcOH (79 µL, 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; IRυ_{max}/cm^{-1} (film): 3050, 2976, 2930, 1681, 1587, 1425, 1289, 1159, 965, 840. ^{1}H NMR (400 MHz, $CDCl_3$) 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 (dqd, 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); ^{13}C NMR (100 MHz, CD_3CN) 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 $C_{23}H_{29}N_4O_2^+$ requires 393.2285.

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



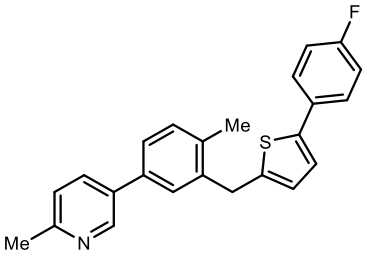
Prepared according to general procedure H using (Z)-1-(3-(pyrrolidin-1-yl)-3-(6-(trifluoromethyl)pyridin-3-yl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate (144 mg, 0.30 mmol), acetyltrimethylsilane (148 µL, 0.90 mmol), LiHMDS (1.5 mL, 0.90 mmol), THF (1.5 mL), NH_4OAc (92.5 mg, 1.20 mmol), AcOH (69 µL, 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 °C. IRυ_{max}/cm^{-1} (film): 2956, 2360, 1589, 1435, 1335, 1247, 1098, 1016, 740. ^{1}H 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 $[M+H]^+$ 225.0643, for $C_{11}H_7F_3N_2^+$ 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 µL, 0.6 mmol, 3.0 equiv) in THF (0.28M) and cooled to 0 ºC. (E)-2-butylidene-1,1-dimethylhydrazine (80 µL, 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, NH_4OAc (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 ºC for 18 hours. After cooling to room temperature, the reaction was quenched with sat. $NaHCO_3$, extracted into EtOAc (3x). The combined organic extract was washed with water (1x), brine (1x), and dried ($MgSO_4$), 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. IRυ_{max}/cm^{-1} (film): 2970, 2933, 1583, 1474, 1265, 1175, 1137, 1089, 1014, 735, 703; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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; ^{19}F NMR (375 MHz, $CDCl_3$) δ -67.78; *m/z* HRMS (ESI) found $[M+H]^+$ 253.0946, for $C_{13}H_{11}F_3N_2^+$ requires 253.0952.

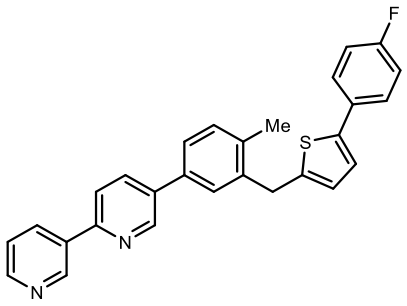
5-(3-((5-(4-Fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-2-methylpyridine (7g)



Prepared according to modified general procedure H 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 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 an orange oil (46 mg, 0.12 mmol, 61% yield). IRυ_{max}/cm^{-1} (film): 3015, 2921, 1596, 1509, 1478, 1254, 1231, 1097, 820, 731; ^{1}H 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,

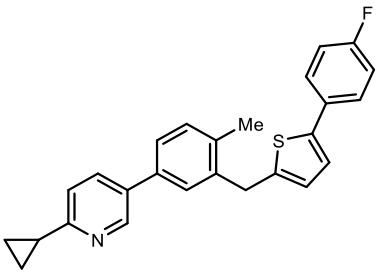
134.58, 133.49, 131.19, 127.99, 127.15 (d, J = 8.0 Hz), 126.12, 125.41, 123.12, 122.72, 115.73 (d, J = 21.8 Hz), 34.20, 24.10, 19.23; ^{19}F NMR (375 MHz, $CDCl_3$) δ -115.10 (td, J = 8.7, 4.5 Hz); *m/z* HRMS (ESI) found $[M+H]^+$ 374.1375, for $C_{24}H_{20}FNS^+$ requires 374.1378.

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



Prepared according to modified general procedure H 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 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 70% EtOAc:Hexanes) to provide the pure title compound as an tan solid (63 mg, 0.14 mmol, 72% yield). mp 125-127 °C. IRυ_{max}/cm^{-1} (film): 3015, 2921, 1595, 1478, 1445, 1254, 1232, 1179, 903, 820; ^{1}H 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, CDCl3) 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 $[M+H]^+$ 437.1485, for $C_{28}H_{21}FN_2S^+$ requires 437.1487.

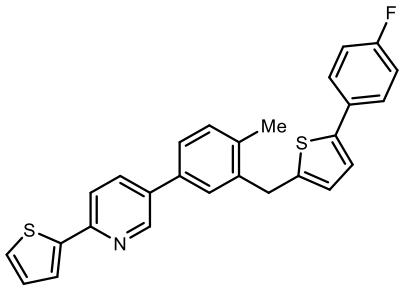
2-Cyclopropyl-5-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)pyridine (7i)



Prepared according to modified general procedure H 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), cyclopropylanone (20 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 20% EtOAc:Hexanes) to provide the pure title compound as a white solid (50 mg, 0.13 mmol, 65% yield). mp 66-68 °C. IRυ_{max}/cm^{-1} (film): 3015, 2921, 1595, 1509, 1478, 1254, 1213, 1097, 820, 733; ^{1}H 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 $[M+H]^+$ 400.1526, for $C_{26}H_{22}FNS^+$ 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 H 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 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 20% EtOAc:hexanes) to provide the pure title compound as yellow solid (49 mg, 0.11 mmol, 55% yield). IRυ_{max}/cm^{-1} (film): 3053, 3001, 1509, 1472, 1264, 895, 802, 723, 703, 659; ^{1}H 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 $[M+H]^+$ 442.1092, for $C_{27}H_{21}FNS_2^+$ requires 442.1094.

15. Computational Details:

Computational methods

Gaussian 16 revision C.01[30] was employed for all density functional theory (DFT) calculations, using an "ultrafine" pruned (99,590) grid for numerical integration of the exchange-correlation functional and its derivatives. The range-separated dispersion-corrected ωB97X-D[31,32] functional and the 6-31+G(d,p)[33–37] basis set was used to optimize all stationary point geometries.[38] Vibrational frequency calculations were used to confirm stationary points as minima or first-order saddle points on the potential energy surface (PES) and to obtain quasi-harmonic rigid-rotor/harmonic oscillator thermochemical corrections with the *GoodVibes*[39] program. Where

possible, Intrinsic reaction coordinate (IRC) calculations[40] were carried out to ensure that the intermediates (**Int**) of the different pathways connected to their corresponding transition structure (**TS**).

Energies were refined with single-point energy calculations at the ωB97X-D/def2-TZVP level. In all cases, the calculations included the integral equation formalism variant of the polarizable continuum model (IEF-PCM)[41–44] with the SMD[45] solvation model (solvent=ethyl ethanoate) to account for solvent effects.

Conformational sampling (due to rotations about single bonds) of ground state (**GS**) and transition state (**TS**) structures was performed using a combination of RDKit (with the MMFF force field) and manual sampling.[46] These different conformers are described in the text (in order of their relative stability) by appending a number after each name (*e.g.*, _1, _2, _3, *etc.*). Representations in the main text and Supporting Information refer to the most stable conformation found for each step. Gibbs free energy (G) values of all the energy profiles correspond to the Boltzmann weighted G of all the conformers found in each step (G_{av}).

Visualization settings have been made openly accessible.[47] Atomic charges, Wiberg bond orders,[48] and Fukui indices were computed using natural population analysis (NPA) with *NBO 7.0*,[49] interfaced to *Gaussian 16*. Nucleus Independent Chemical Shift (NICS) calculations were performed at the B3LYP/6-311+G(d,p) level of theory for select transition structures to assess aromaticity[50].

Thermochemistry with *GoodVibes*

Quasi-harmonic corrections were introduced to the computed vibrational entropies using a frequency cut-off value of 100.0 cm^{-1} with GoodVibes, following the approach proposed by Grimme[51] at 195.15 K (–78 °C). Also, a correction for the change in standard state from gas phase at 1 atm to a 1 M solution was applied.[52] A few GS calculations showed persistent imaginary frequencies smaller than 50 cm^{-1}. These imaginary frequencies were inverted to obtain thermochemical contributions.[53] After conformational sampling, duplicate structures at the DFT level were automatically excluded using Goodvibes. Boltzmann weighted Gibbs energies (G_{av}) are quoted throughout, which include considerations of molecular point group and entropies of mixing.[54–57]

Thermochemical data including absolute energies, zero-point energies (ZPE), and T·S, among other parameters, at the ωB97X-D/6-31+G(d,p) level, as well as the absolute energies, corrected final G and relative G obtained after ωB97X-D/def2-TZVP single point energy calculations, are tabulated in the separate *Pyrimidinium_Goodvibes.dat* file. Optimized geometries presented in this work can be found in the separate *Pyrimidinium.xyz* file.

PES for 4Ph-pyrimidine and aniline reacting at C6

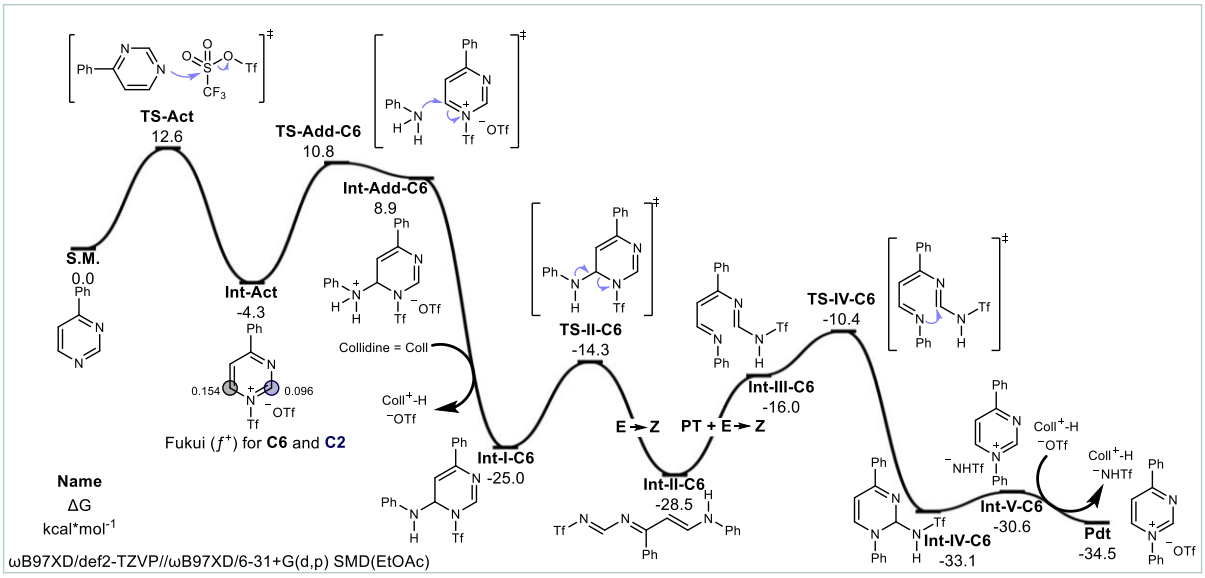


Fig. S7. Computed PES for the reaction between 4-phenyl-pyrimidine, triflic anhydride, and aniline reacting at the C6 position of the pyrimidine. (E→Z indicates isomerization, PT indicates proton transfer). Relative Gibbs energies shown in kcal*mol^{-1}.

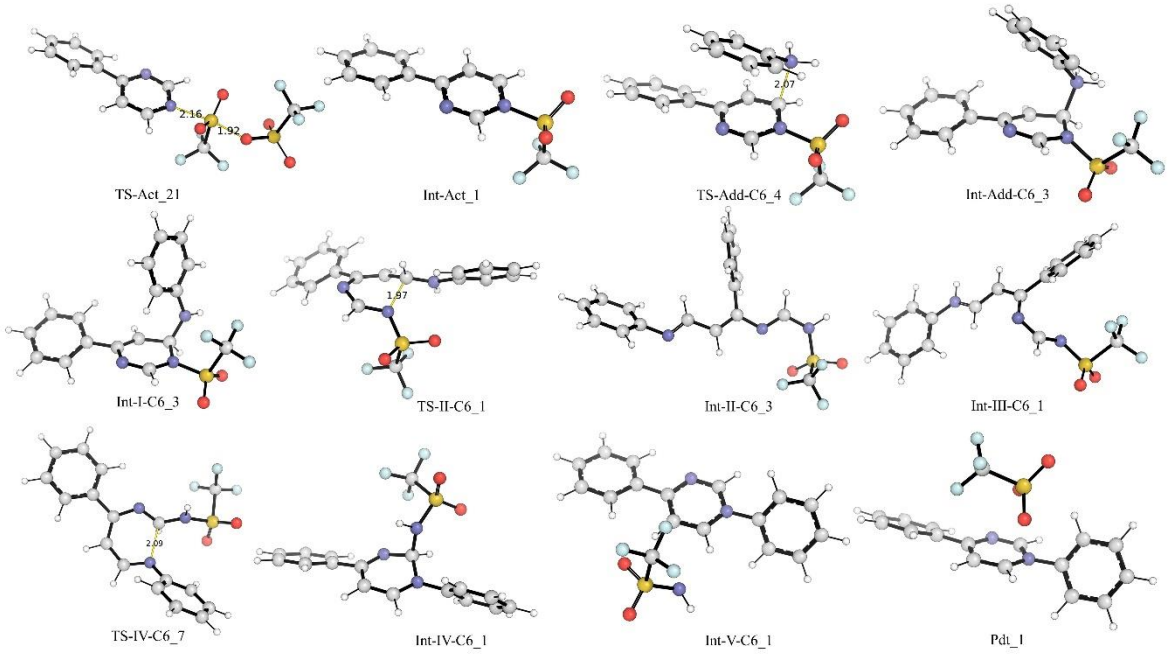


Fig. S8. Most stable conformers of stationary points along the PES for the reaction between 4-phenyl-pyrimidine, triflic anhydride, and aniline reacting at the C6 position of the pyrimidine.

PES for 4Ph-pyrimidine and aniline reacting at C2

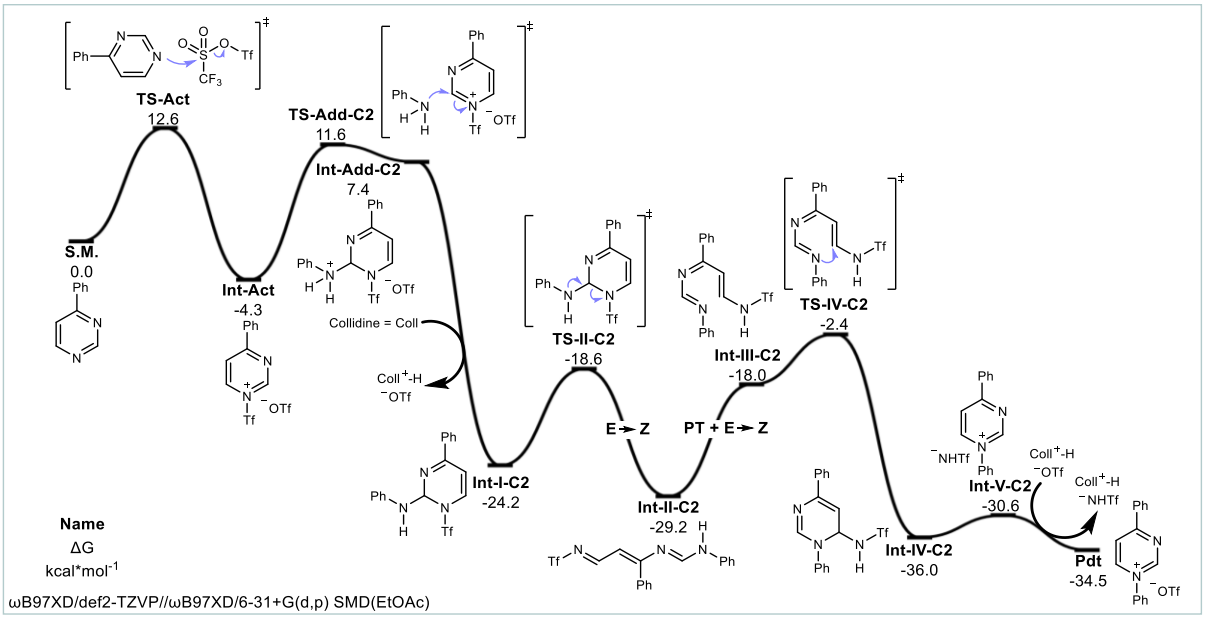


Fig. S9. Computed PES for the reaction between 4-phenyl-pyrimidine, triflic anhydride, and aniline reacting at the C2 position of the pyrimidine. Relative Gibbs energies shown in kcal*mol^{-1}.

Nucleophilic addition of aniline at the pyrimidine's C2 position is kinetically less favorable and leads to an unproductive cyclization pathway (**TS-IV** is comparatively high in energy in relation to the regioisomeric pathway). This observation is consistent across all pyrimidine substrate models. We conducted computational investigations to consider whether deprotonation of Int-Add, rather than C–N bond formation in TS-Add-C6, contributes to the regioselectivity of the transformation. These studies show that the Int-Add/collidine complex is not a stable minimum on the Potential Energy Surface (PES): upon geometry optimization, proton transfer occurs and the complex evolves directly to Int-I/protonated collidine, which lies downhill in energy by more than 30 kcal/mol downhill. This behavior was replicated in geometry optimizations with both M06-2X and B3LYP-D3(BJ) functionals. Since there is no energetic barrier for the deprotonation step, there are no transition structures on the PES between Int-Add and Int-I. We therefore believe that this deprotonation process happens at, or close to, the diffusion limit.

In ethyl acetate at -78 °C, we estimate the diffusion rate constant to be around 1.2 x 1010 mol-1s-1 (based on the solvent's viscosity at the reaction temperature, 0.358 cP, and the Stokes–Einstein equation), which in turn is comparable (from Transition State Theory) to a theoretical Gibbs energy of activation for the subsequent deprotonation step of 2.3 kcal/mol.[58] This is roughly comparable to the reverse reaction leading back to the starting materials. These results, suggest that deprotonation may additionally contribute to the regioselectivity of this transformation – however, the absence of any transition structures for this step on the PES, make these contributions difficult to quantify.

NICS(0)$_{zz}$ calculations

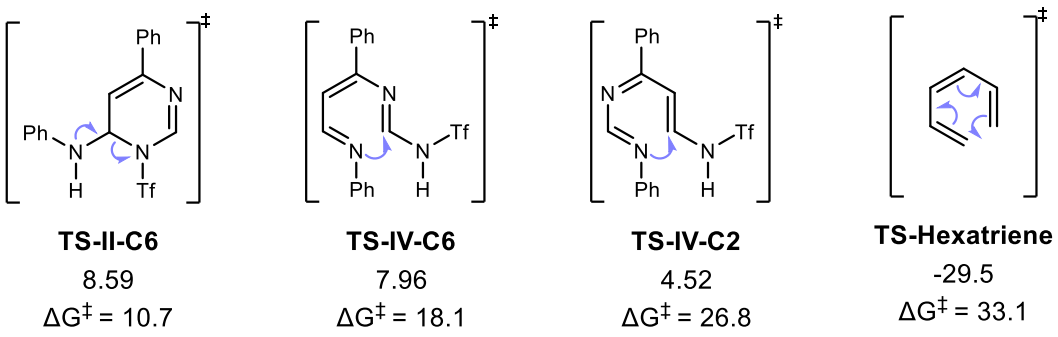


Fig. S10. NICS(0)$_{zz}$ (Nucleus Independent Chemical Shift) calculations performed at the B3LYP/6-311+G(d,p) level of theory on the most stable conformer. The electrocyclization of trans-hexatriene is shown for reference.

PES for 4CO_2Me-pyrimidine and aniline at C6 and C2

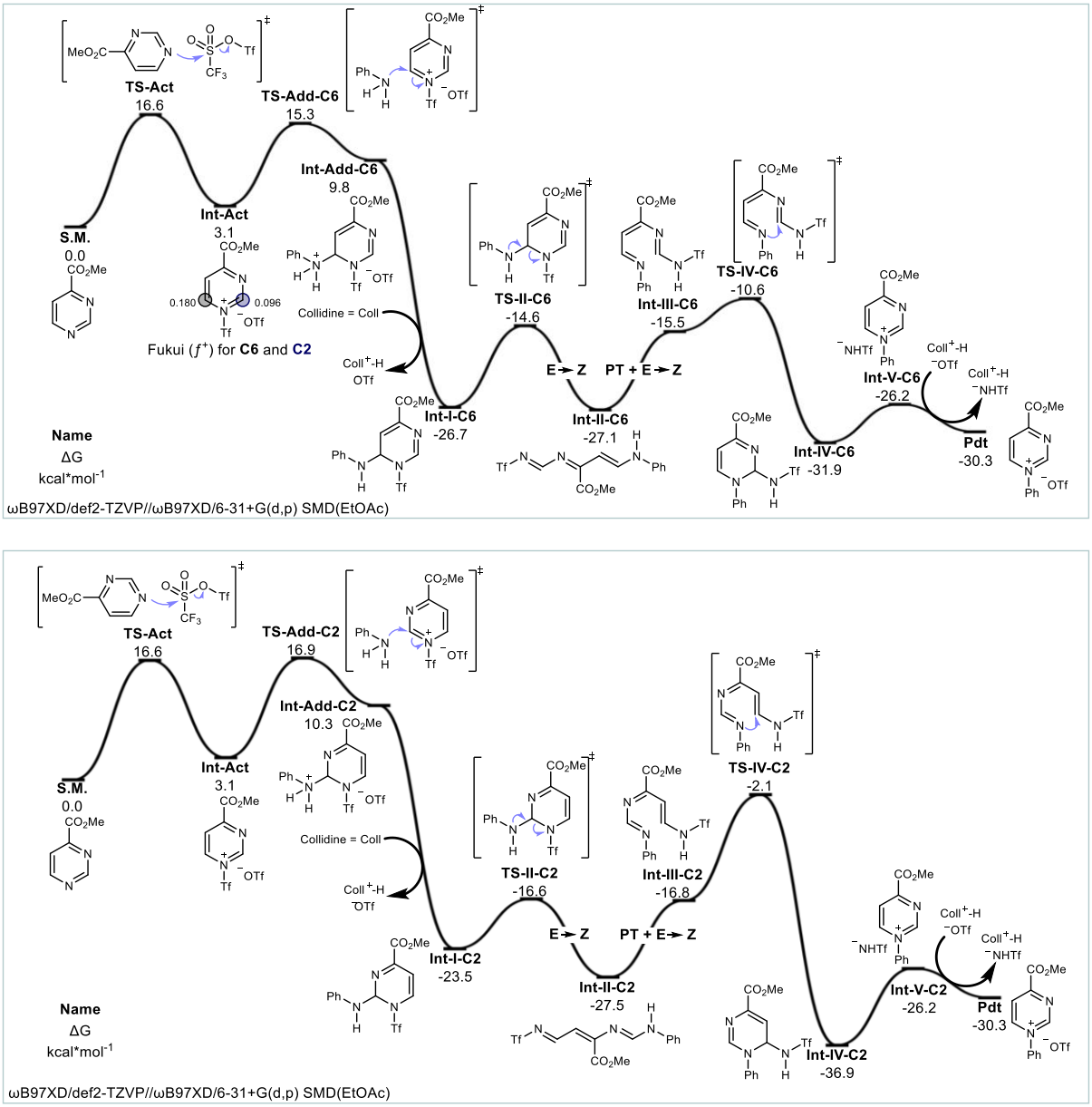


Fig. S11. Computed PES for the reaction between 4-CO_2Me-pyrimidine, triflic anhydride, and aniline reacting at the C6 and C2 position of the pyrimidine. Relative Gibbs energies shown in kcal*mol^{-1}. Of note is the instability of the product relative to **Int-IV**.

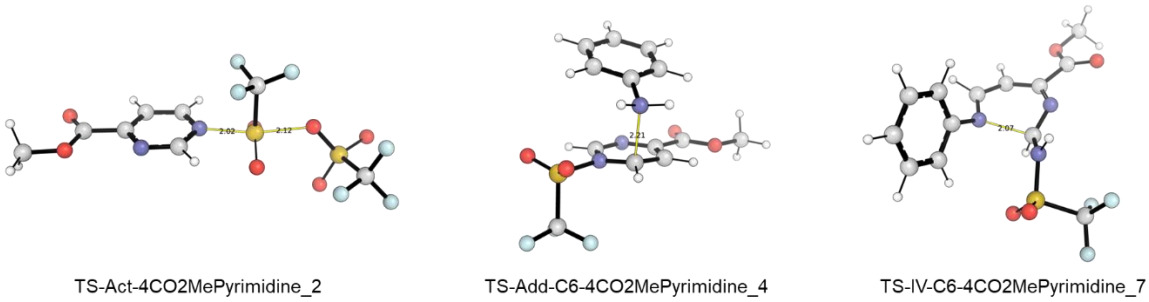


Fig. S12. Most stable conformers of TS along the PES for the reaction between 4-CO_2Me-pyrimidine, triflic anhydride, and aniline reacting at the C6 position of the pyrimidine.

PES for 4Me-Pyrimidine and Aniline C6 and C2

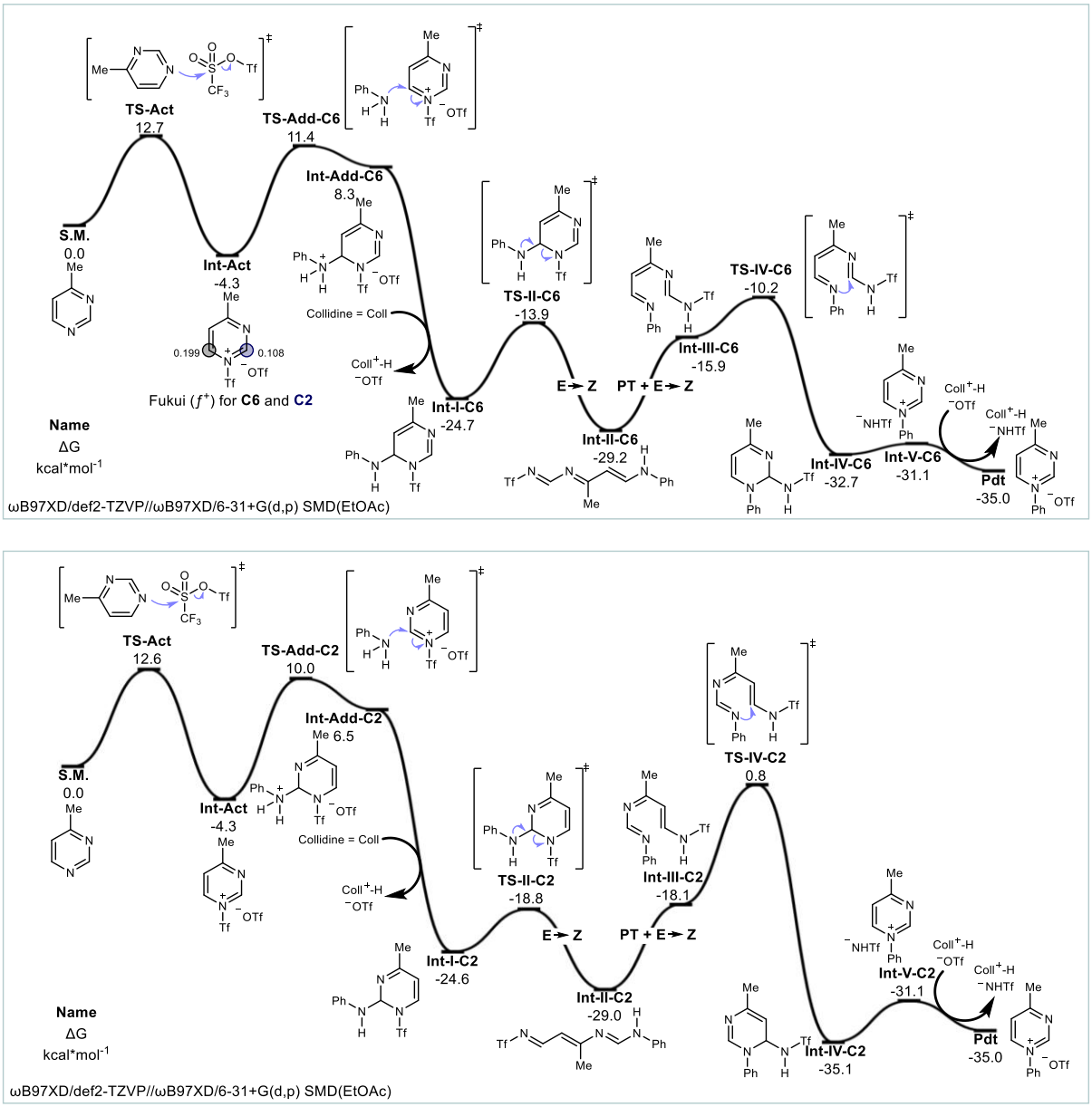


Fig. S13. Computed PES for the mechanism of the reaction between 4-Me-pyrimidine, triflic anhydride, and aniline reacting at the C6 and C2 position of the pyrimidine. Relative Gibbs energies shown in kcal*mol^{-1}. Addition at the C2 position of the pyrimidine is kinetically favored but subsequently leads to an unproductive cyclization pathway.

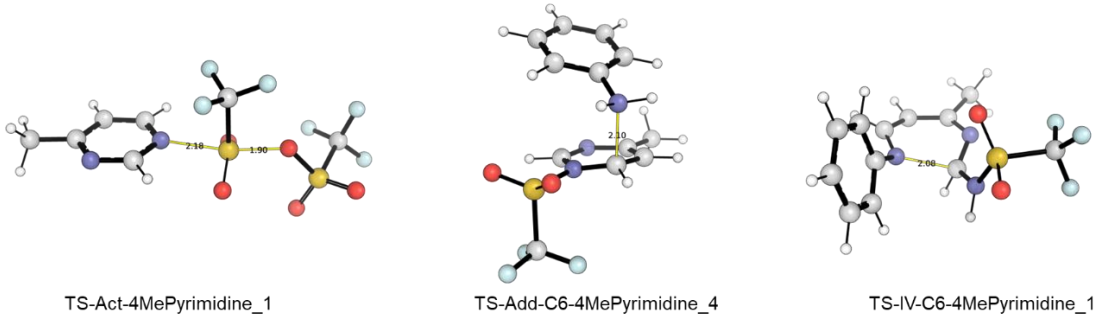


Fig. S14. Most stable conformers of TS along the PES for the reaction between 4-Me-pyrimidine, triflic anhydride, and aniline reacting at the C6 position of the pyrimidine.

Collidine triflylation

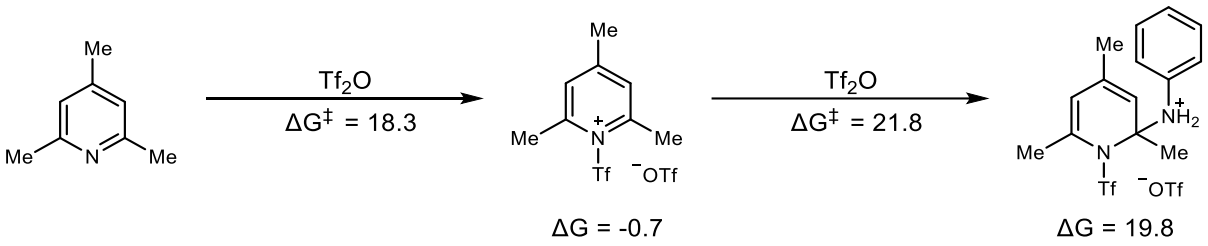


Fig. S15. Computed activation barriers for the reaction of collidine, triflic anhydride, and aniline. Relative Gibbs energies shown in kcal*mol^{-1}.

Triflimide triflylation

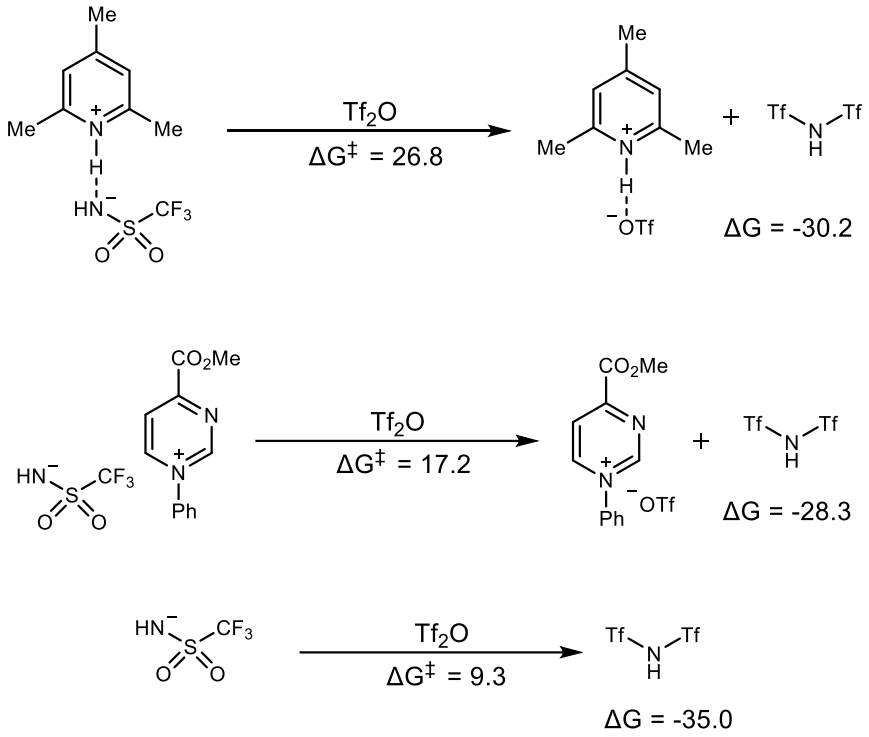


Fig. S16. Computed activation barriers for the reaction of various forms of the triflamide anion and triflic anhydride to form bistriflamide. Relative Gibbs energies shown in kcal*mol^{-1}. These reactions are competitive with substrate activation and indicate that this pathway might lead to unproductive consumption of triflic anhydride.

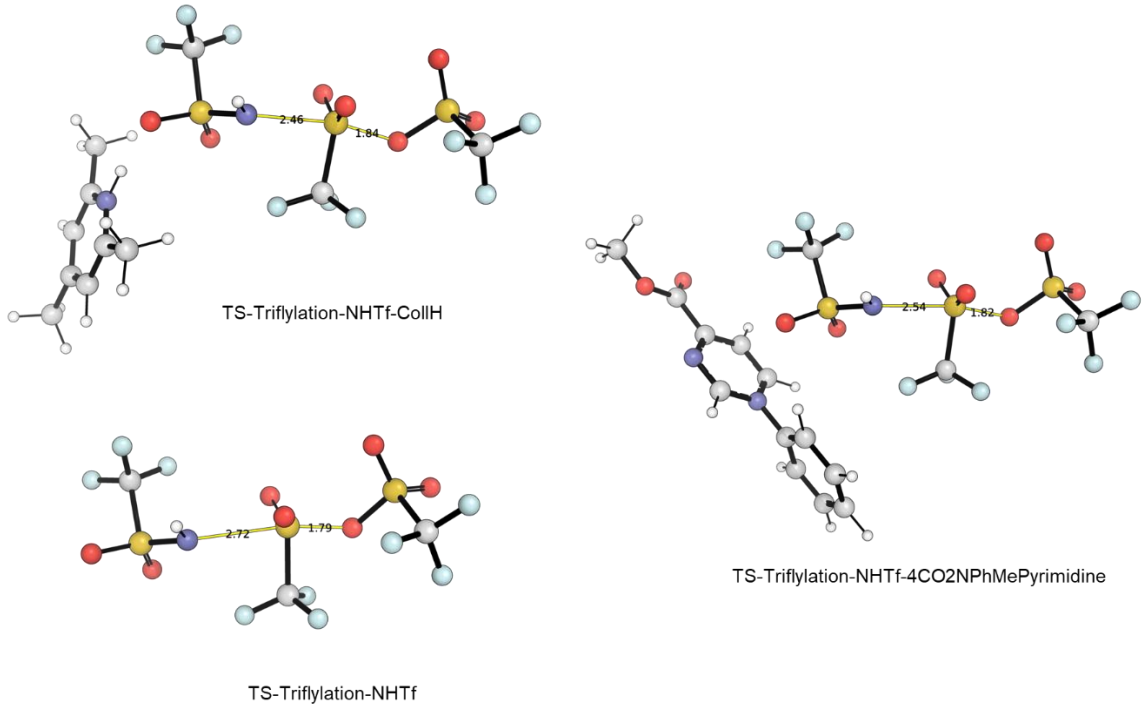
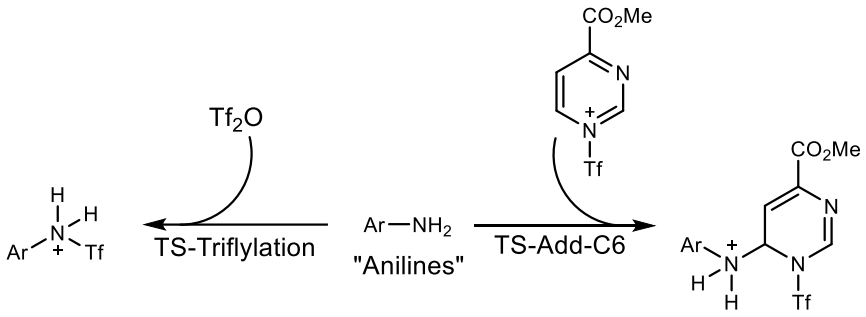


Fig. S17. Representative structures for the reaction of various forms of the triflamide anion and triflic anhydride to form bistriflamide.

Aniline triflylation



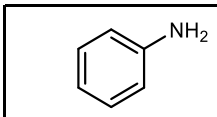
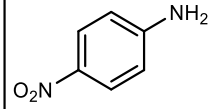
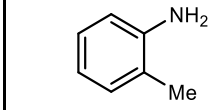
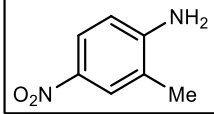
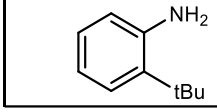
Anilines	TS-Triflation	TS-Addition-C6
	15.8	15.3
	22.0	22.6
	15.0	15.5
	22.0	23.2
	17.2	14.9

Table S3. Computed activation barriers for the reaction of various substituted anilines and triflic anhydride and the competing addition to 4-CO_2Me pyrimidine. Relative Gibbs energies shown in kcal*mol^{-1}.

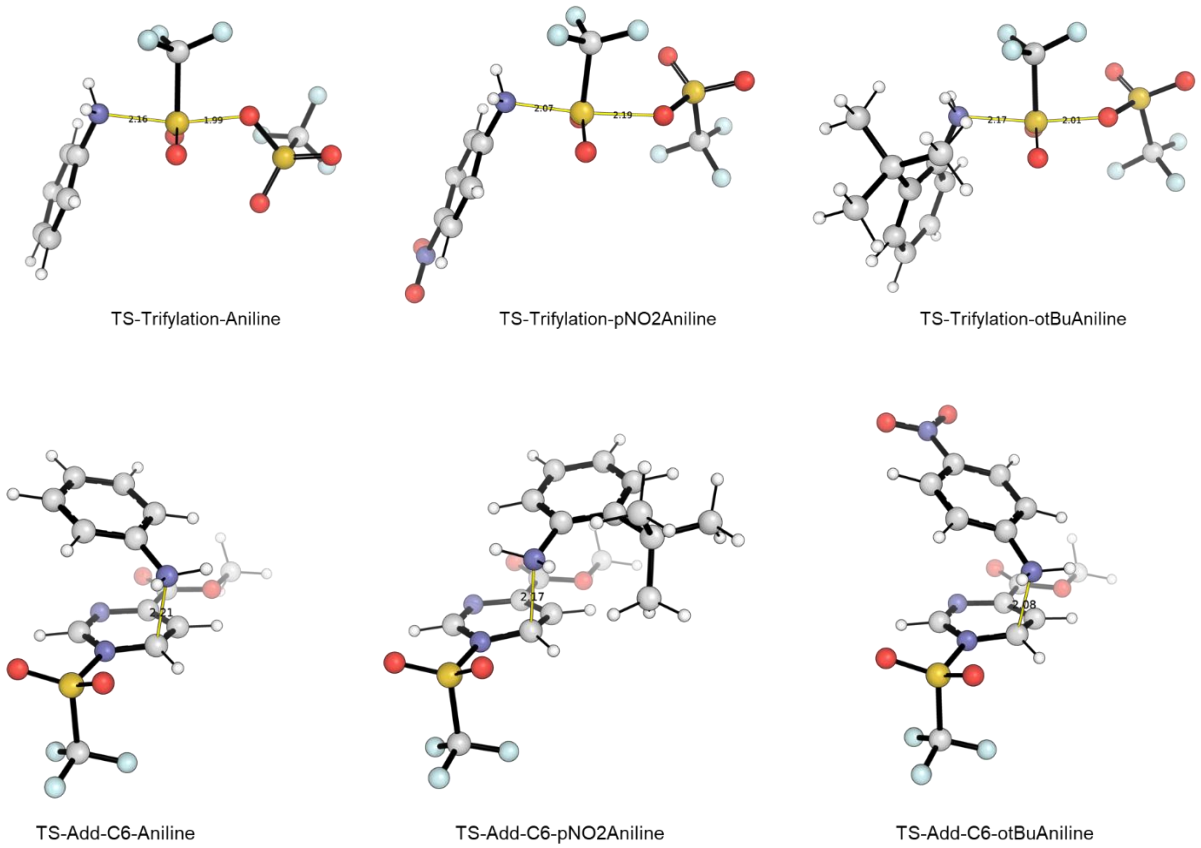


Fig. S18. Representative structures for the reaction of various substituted anilines and triflic anhydride and the competing addition to 4-CO_2Me pyrimidine.

Substituent effect on cyclization barrier

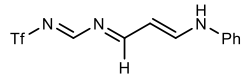
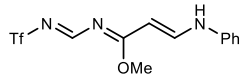
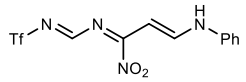
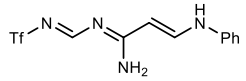
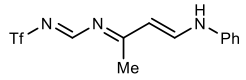
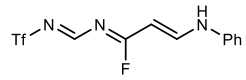
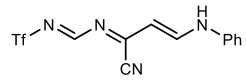
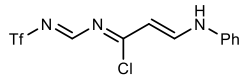
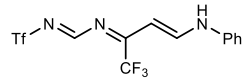
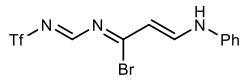
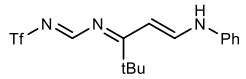
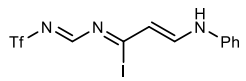
Int-II	TS-IV $\Delta G^{\ddagger}$	A-Value	σ-para	NBO Charge C4 @ Int-II	NBO Charge C4 @ TS-IV
	22.7	0.00	0.00	0.183	0.089
	19.4	0.60	-0.27	0.656	0.561
	14.5	1.10	0.78	0.413	0.300
	26.5	1.60	-0.66	0.494	0.444
	18.0	1.70	-0.17	0.397	0.290
	19.4	0.15	0.06	0.699	0.632
	15.3	0.17	0.66	0.212	0.112
	18.2	0.43	0.23	0.338	0.250
	12.7	2.10	0.54	0.255	0.145
	17.1	0.38	0.23	0.286	0.195
	17.4	4.00	-0.20	0.447	0.316
	18.5	0.43	0.18	0.223	0.127

Table S4. Computed cyclization barrier (TS-IV, kcal*mol^{-1}) for differently substituted pyrimidines. A values and Hammett σ_{para} values for the 4-position substituent[58,59] ωB97X-D/def2-TZVP//ωB97X-D/6-31+G(d,p) NBO charges at the C4 carbon of Int-II, and in the fifth column, NBO charges at the C4 carbon of TS-IV.

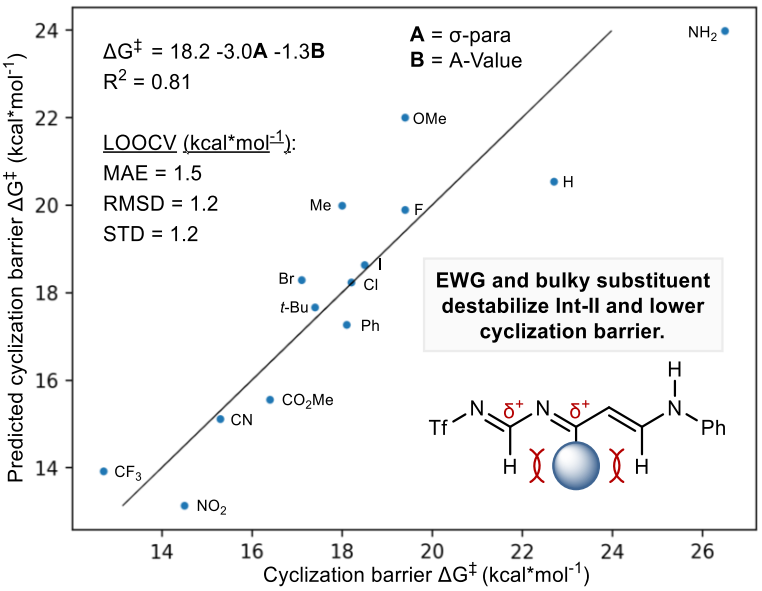
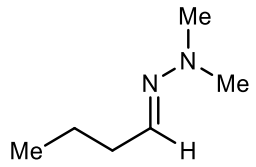


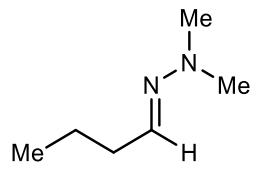
Fig. S19. Bivariate linear regression model correlating cyclization barrier with substituent steric (A-value), and electronic (σ_{para}) descriptors. No feature selection was performed. The values of features were scaled using sklearn's StandardScaler tool. Leave One Out Cross Validation (LOOCV) was performed using sklearn's LeaveOneOut tool. The code used to generate the graph in this figure is available in supplementary material as a Jupyter notebook.

(BivariateLinearRegression_Pyrimidinium.ipynb)

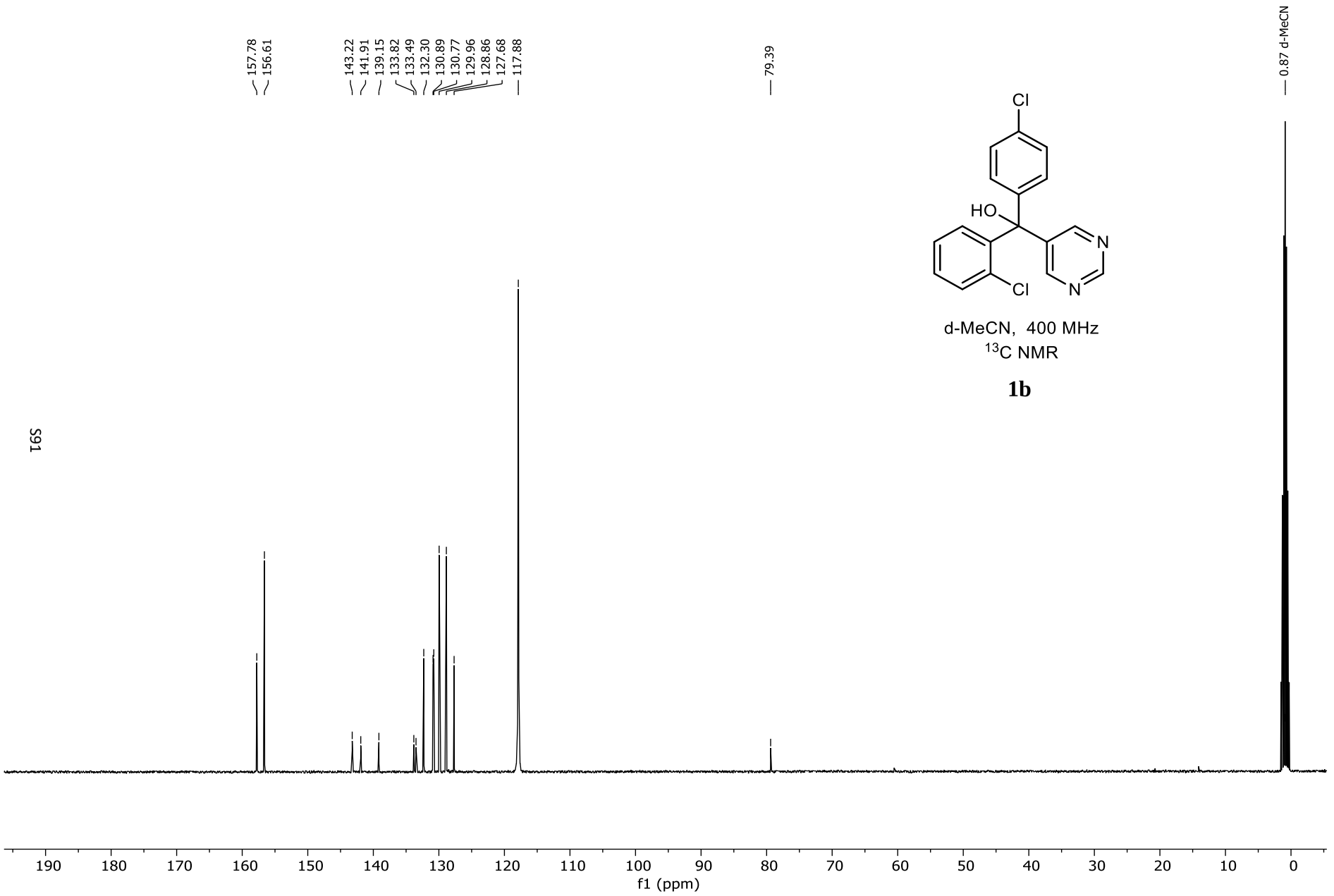
16. NMR Data (^{1}H, ^{13}C, and ^{19}F spectra):

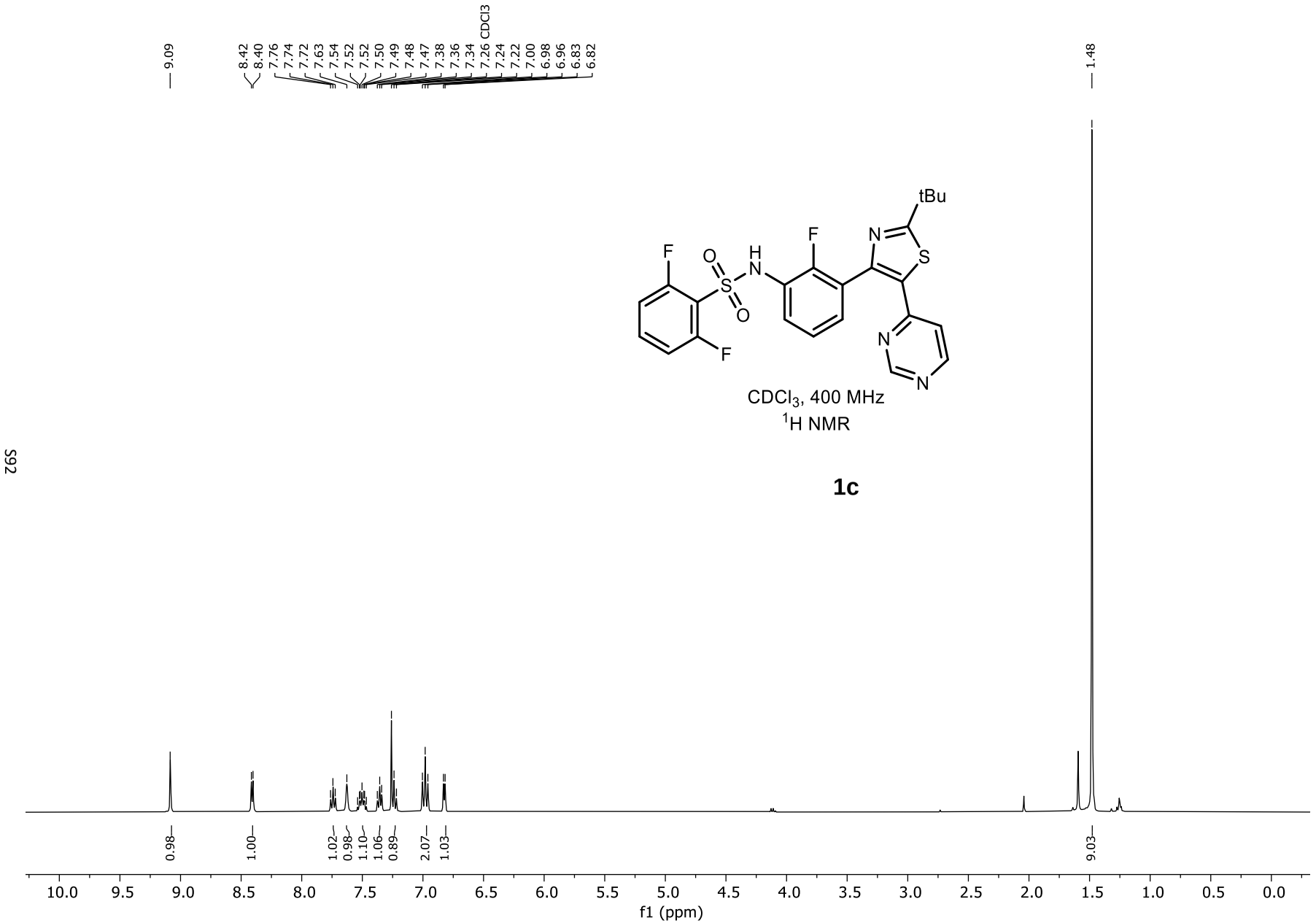


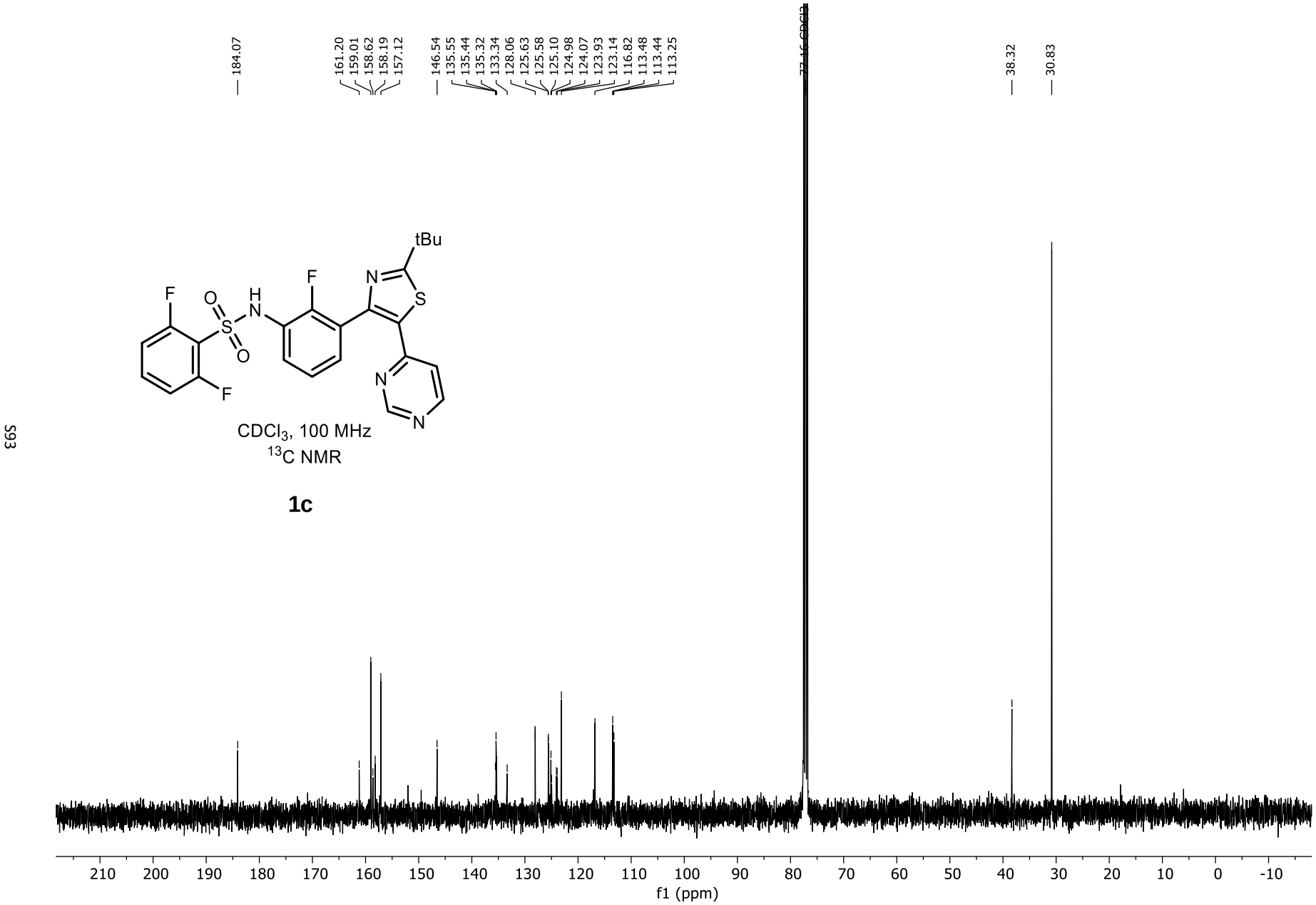
$CDCl_3$, 400 MHz
^1H NMR

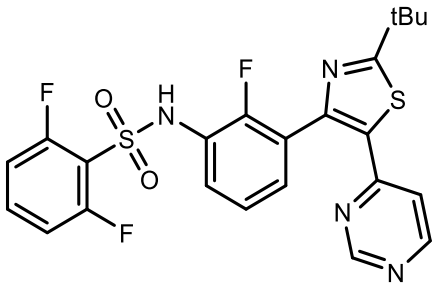


$CDCl_3$, 400 MHz
^{13}C NMR


157.78
156.61
143.22
141.91
139.15
133.82
133.49
132.30
130.89
130.77
129.96
128.86
127.68
117.88
79.39
0.87 d-MeCN
Cl
HO
N
N
Cl
d-MeCN, 400 MHz
13C NMR
1b
f1 (ppm)


9.09
8.42
8.40
7.76
7.74
7.72
7.63
7.54
7.52
7.52
7.50
7.49
7.48
7.47
7.38
7.36
7.34
7.26 CDCl3
7.24
7.22
7.00
6.98
6.96
6.83
6.82
1.48
tBu
F
O
H
N
F
N
S
S
O
F
N
N
CDCl3, 400 MHz
1H NMR
1c
0.98
1.00
1.02
0.98
1.10
1.06
0.89
2.07
1.03
9.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

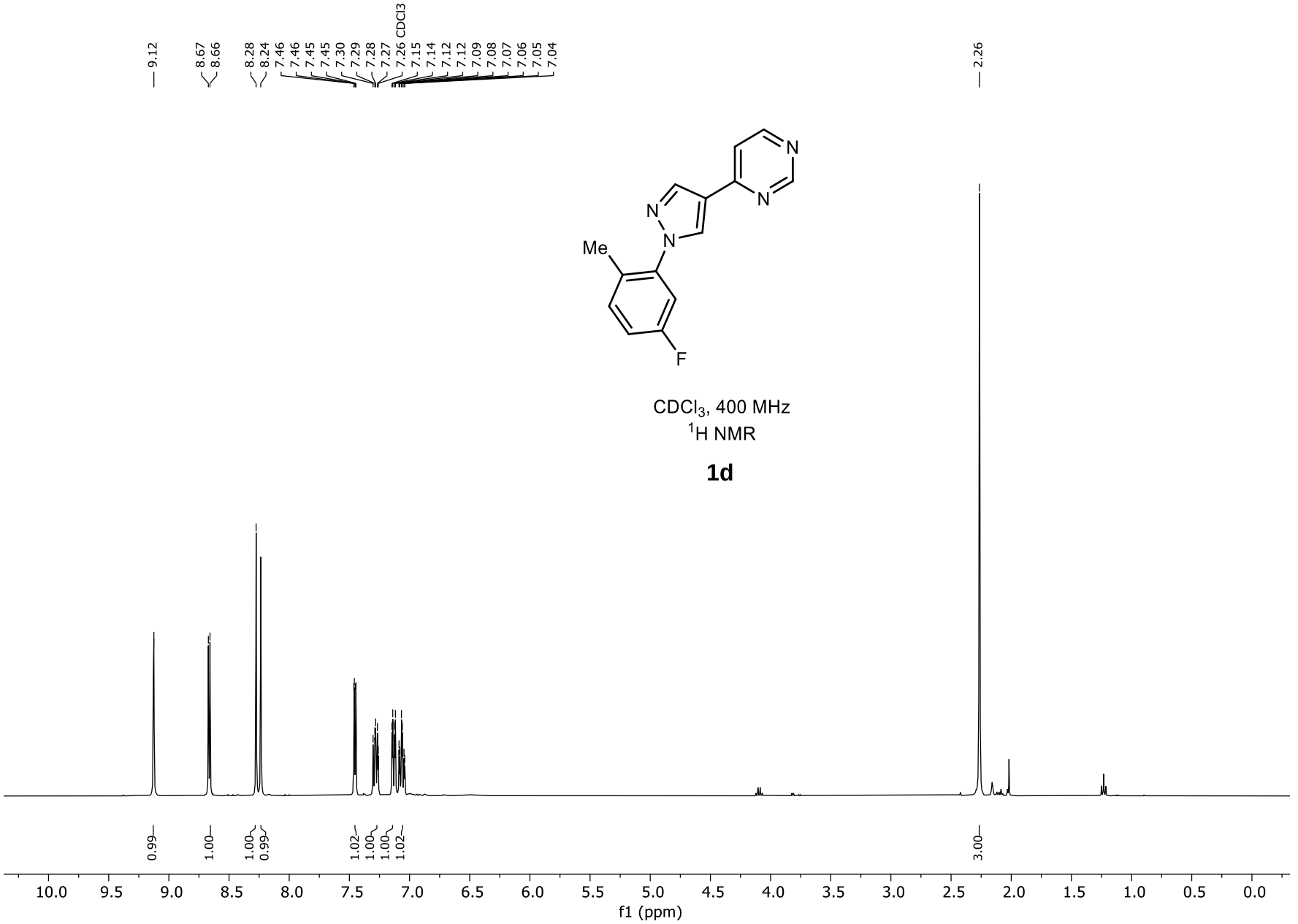

184.07
161.20
159.01
158.62
158.19
157.12
146.54
135.55
135.44
135.32
133.34
128.06
125.63
125.58
125.10
124.98
124.07
123.93
123.14
116.82
113.48
113.44
113.25
77.16 CDCl3
38.32
30.83
tBu
F
O
H
N
S
F
N
S
O
F
N
N
CDCl3, 100 MHz
13C NMR
1c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

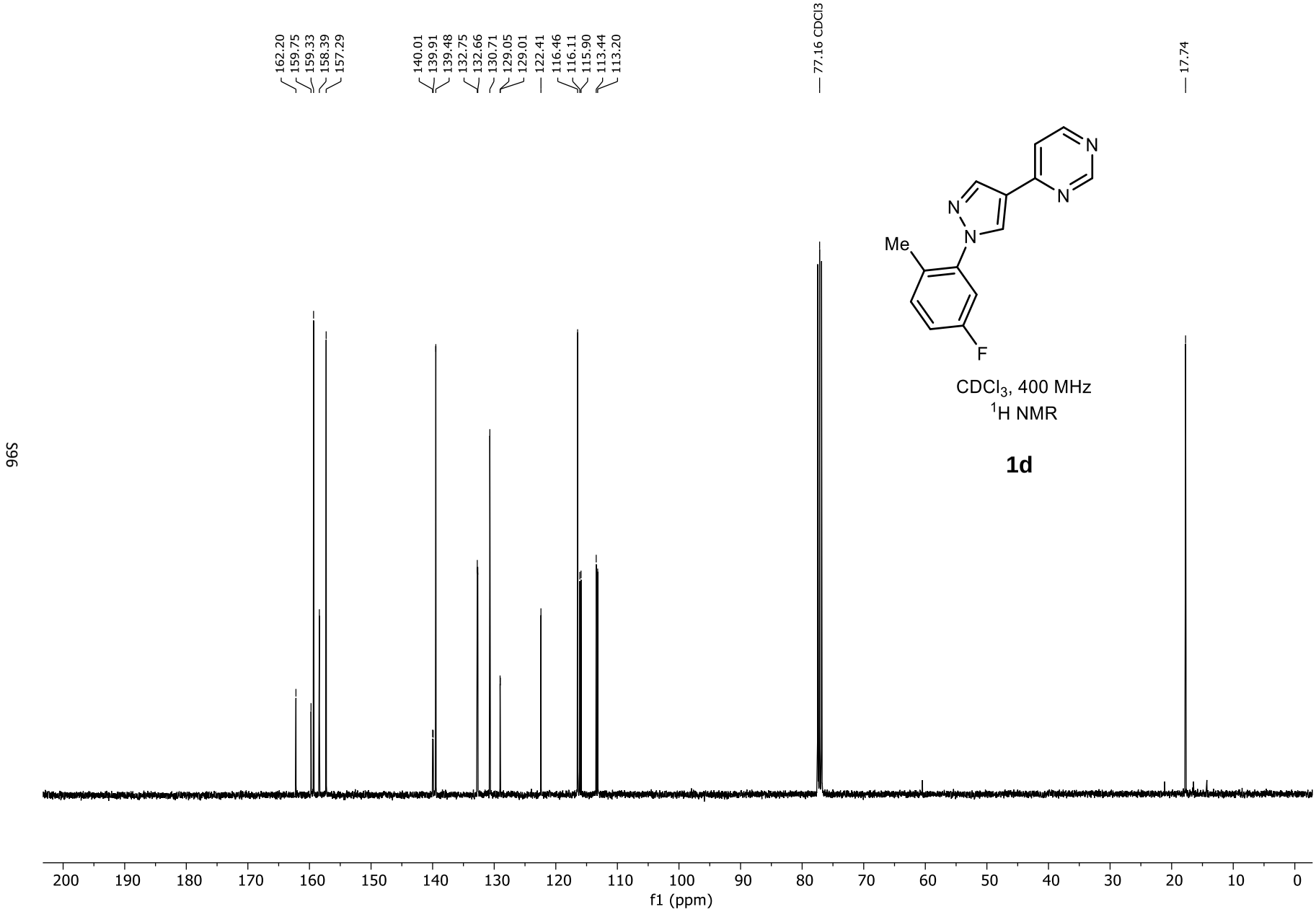


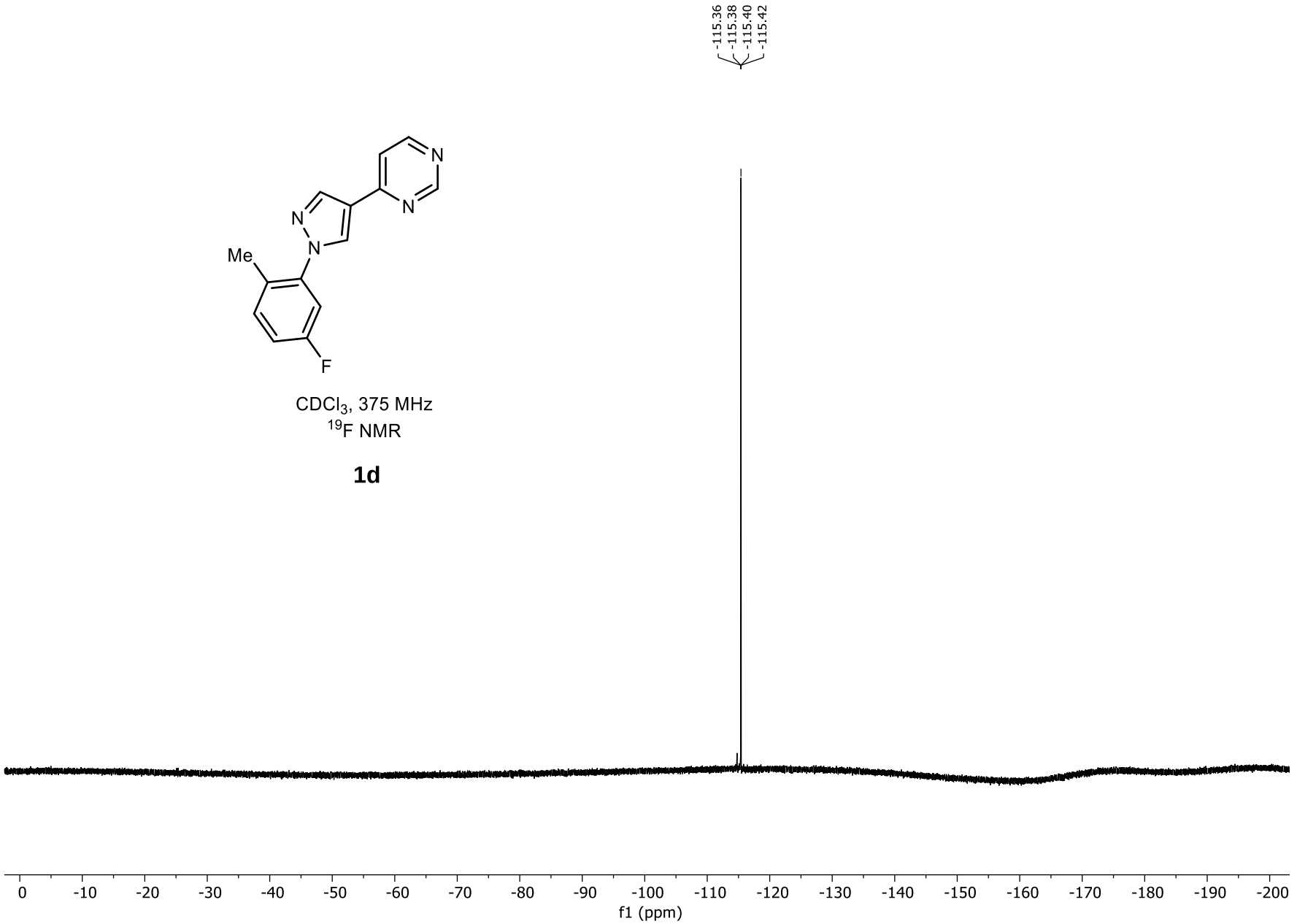
$CDCl_3$, 375 MHz

^{19}F NMR

1c

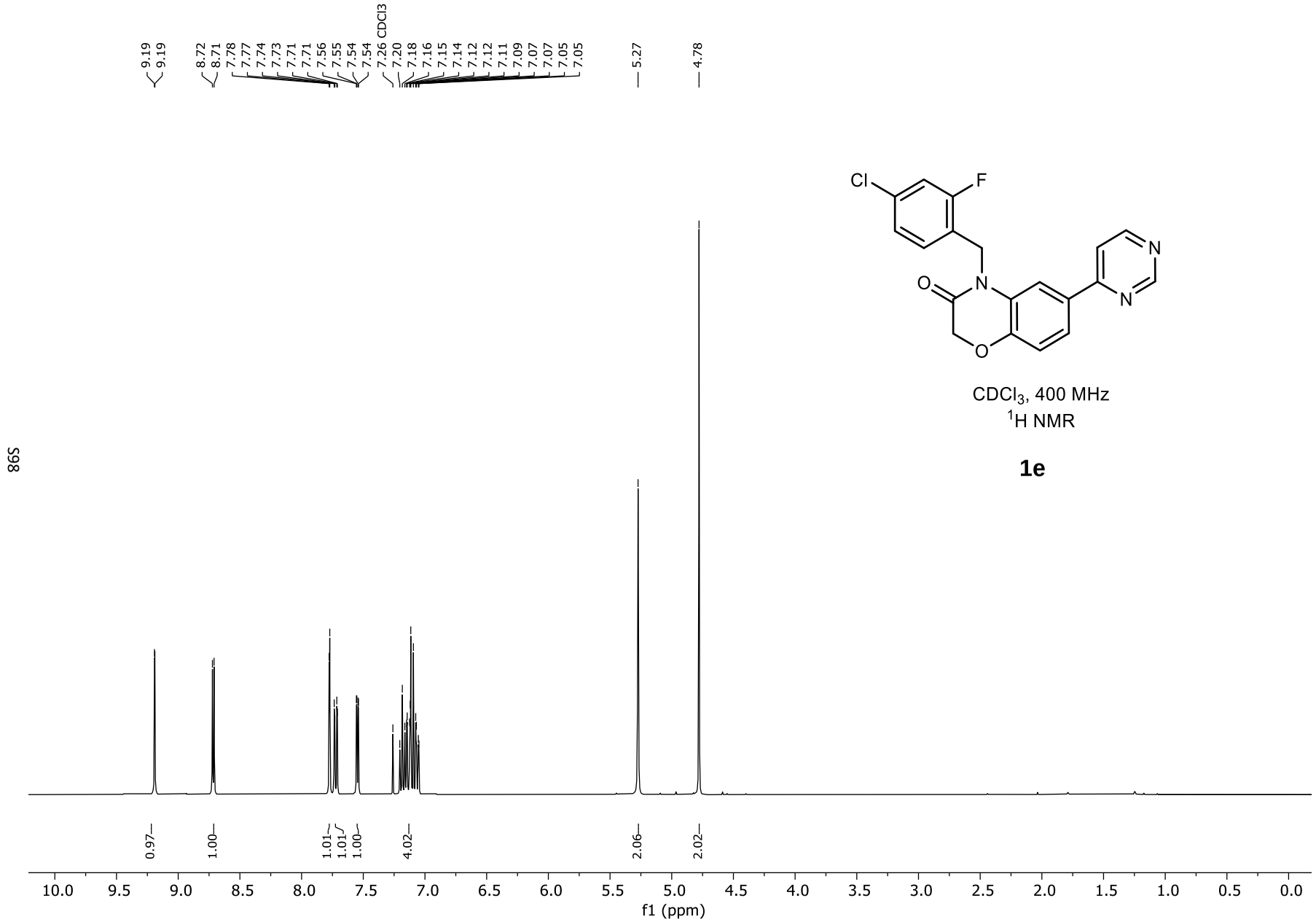

9.12
8.67
8.66
8.28
8.24
7.46
7.46
7.45
7.45
7.30
7.29
7.28
7.27
7.26 CDCl3
7.15
7.14
7.12
7.12
7.09
7.08
7.07
7.06
7.05
7.04
2.26
N
N
N
N
Me
F
CDCl3, 400 MHz
1H NMR
1d
0.99
1.00
1.00
0.99
1.02
1.00
1.00
1.02
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

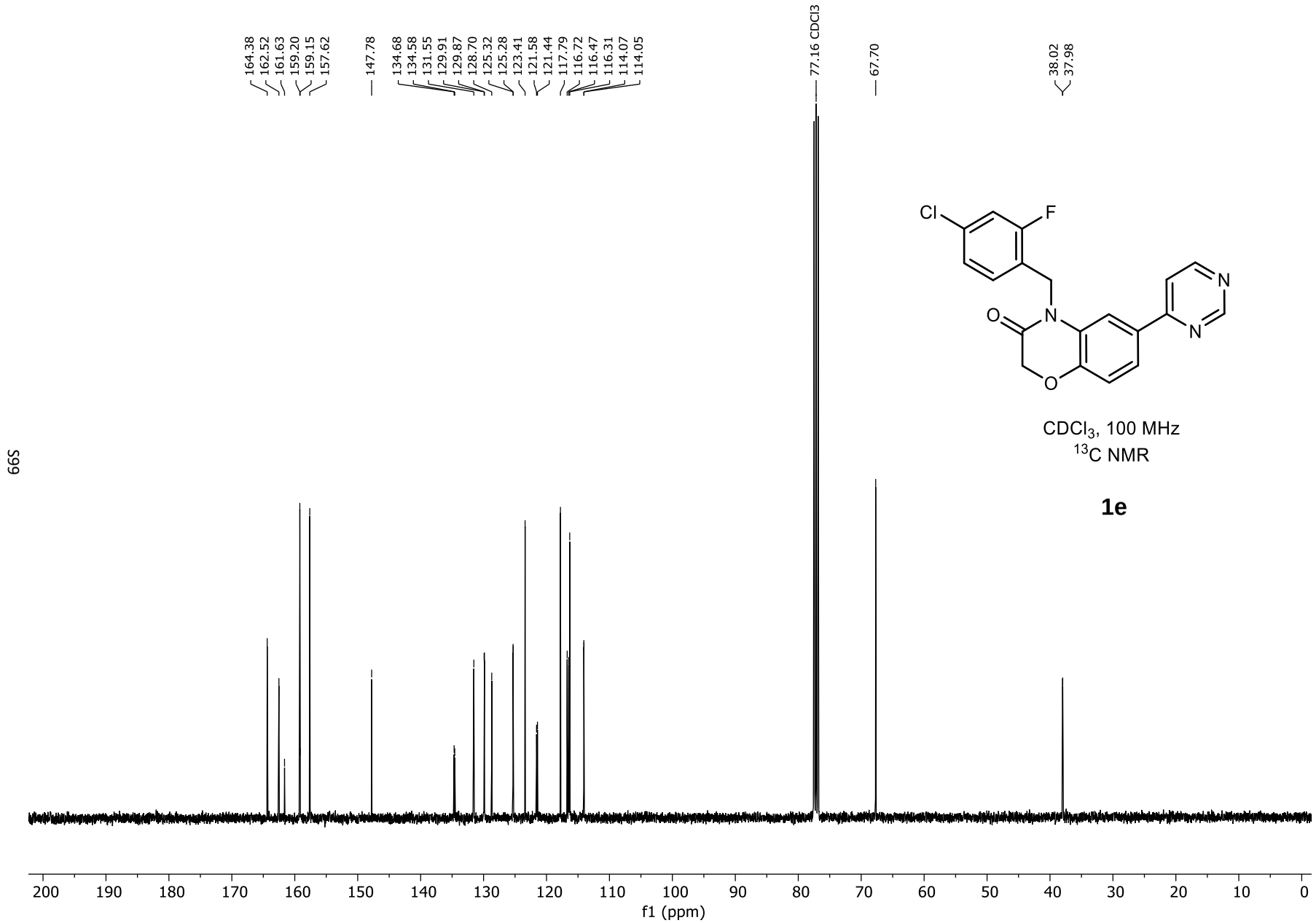

162.20
159.75
159.33
158.39
157.29
140.01
139.91
139.48
132.75
132.66
130.71
129.05
129.01
122.41
116.46
116.11
115.90
113.44
113.20
77.16 CDCl3
17.74
N
N
N
N
Me
F
CDCl3, 400 MHz
1H NMR
1d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

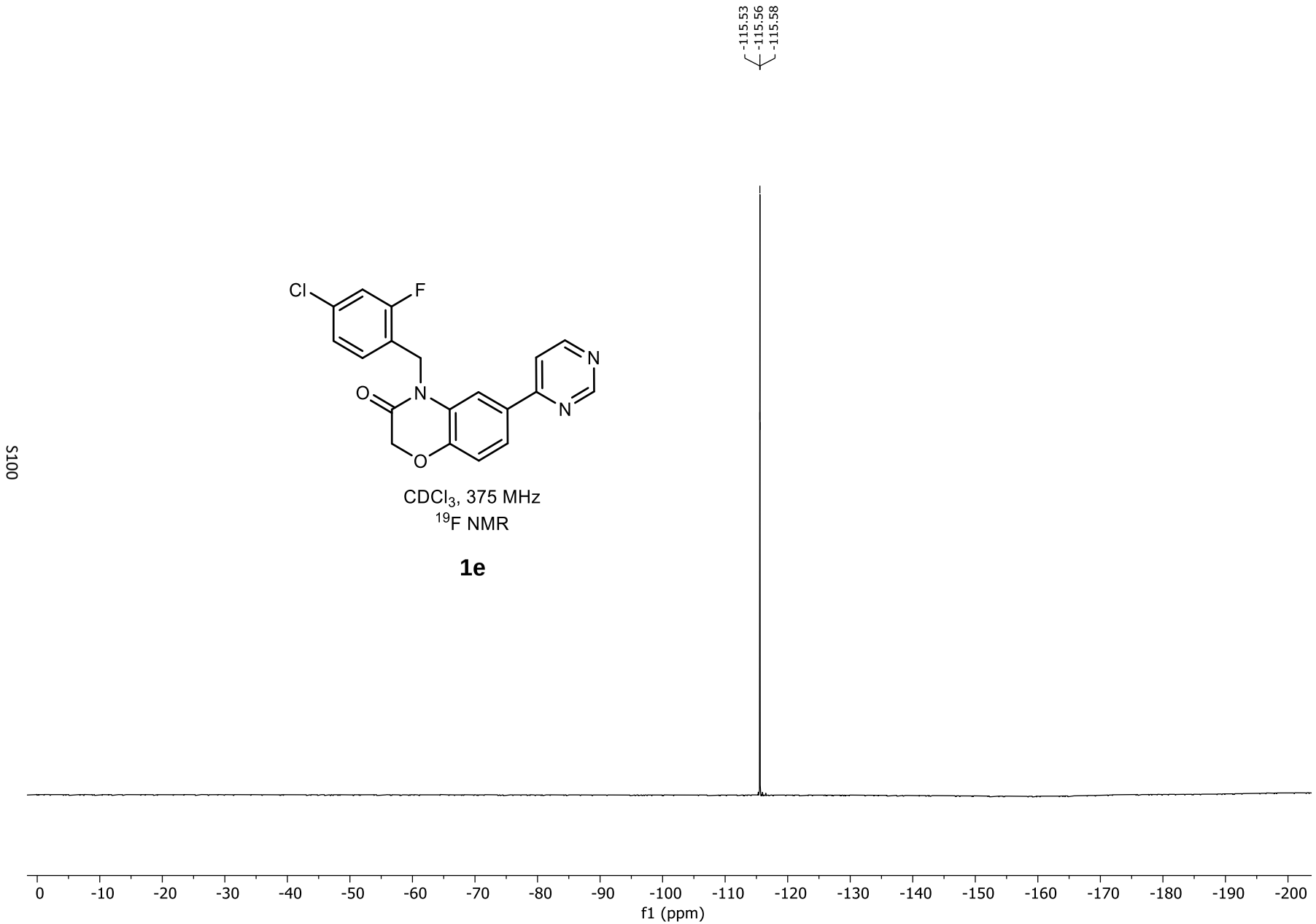


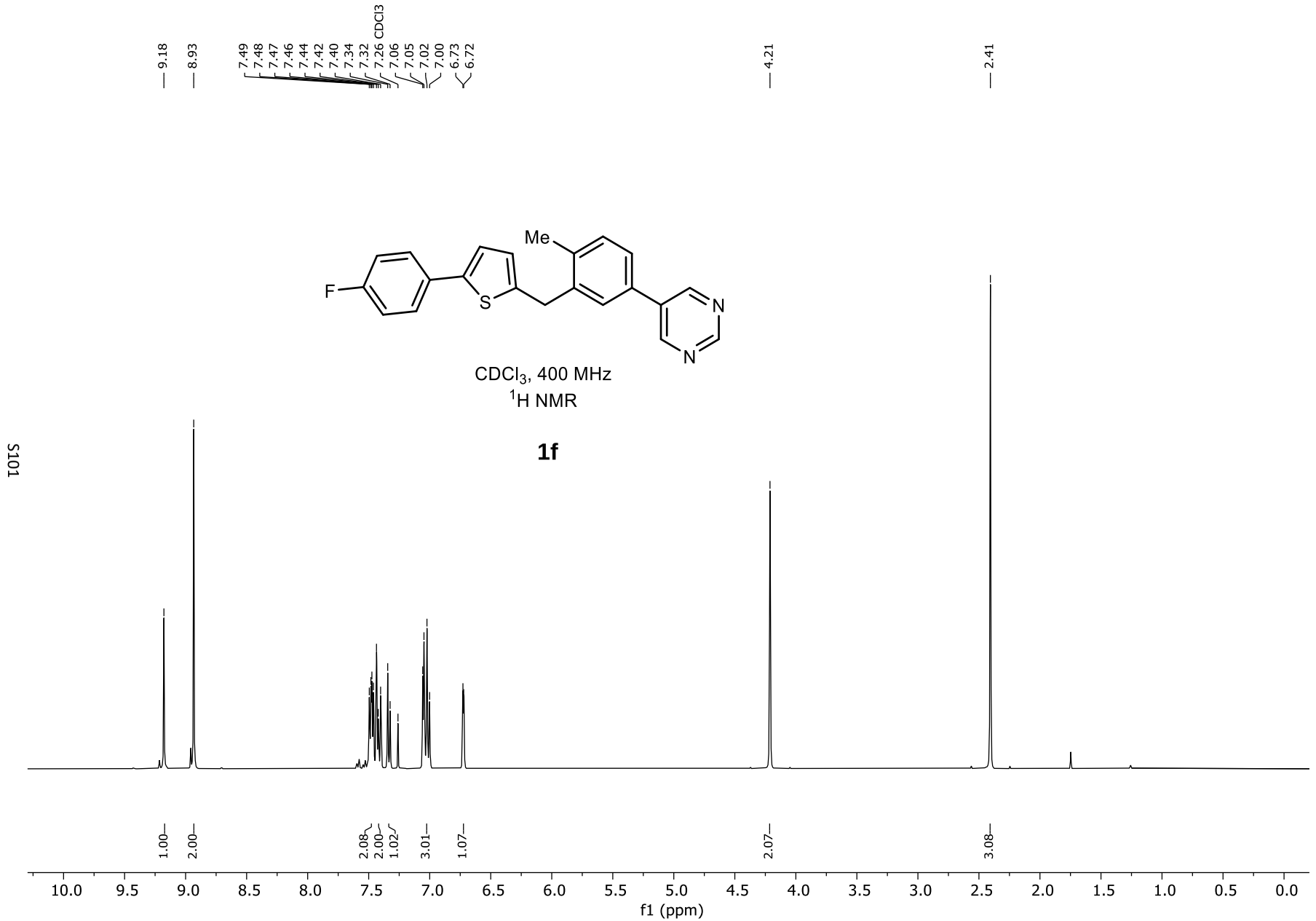
$CDCl_3$, 375 MHz
^{19}F NMR

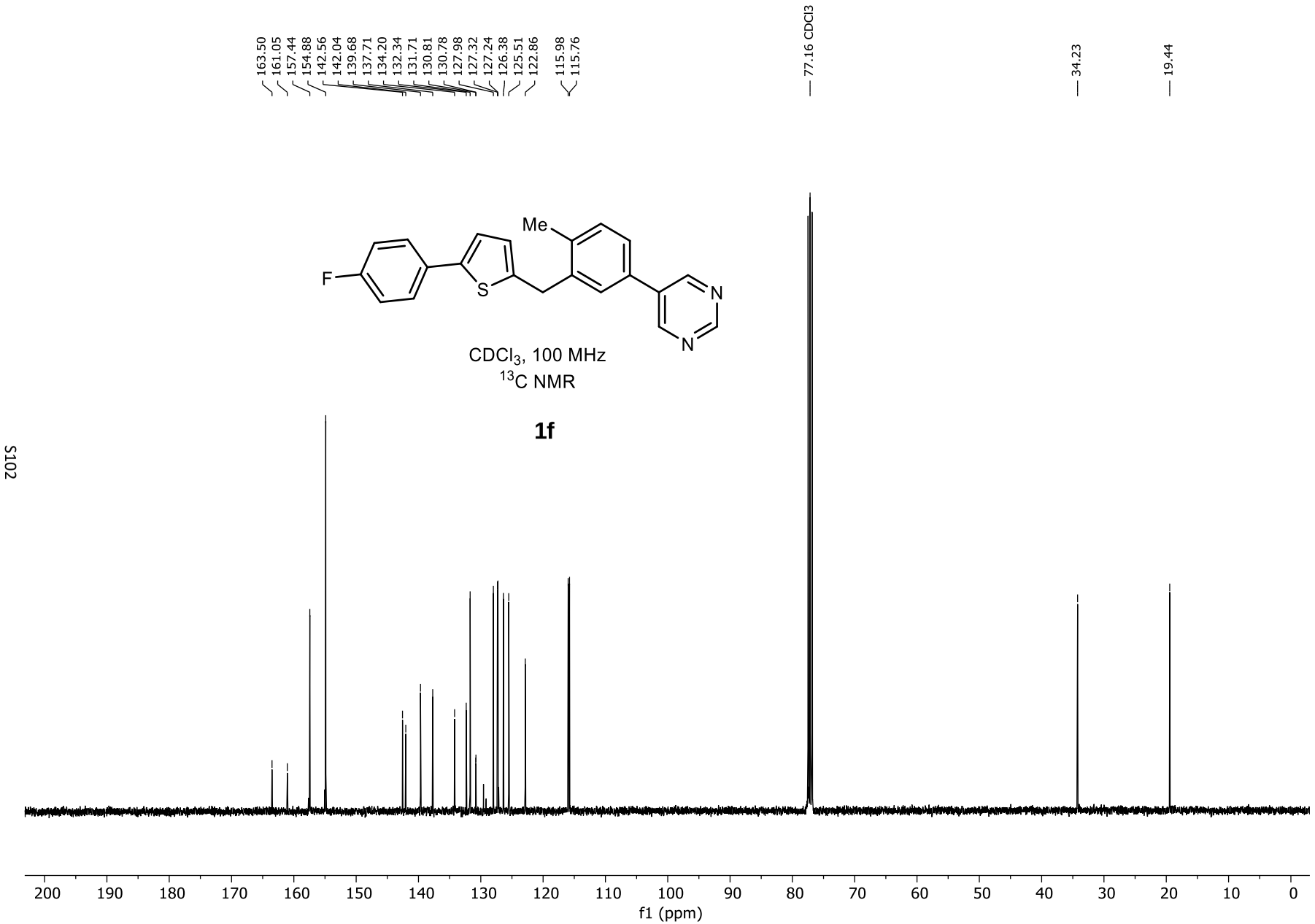
1d


9.19
9.19
8.72
8.71
7.78
7.77
7.74
7.73
7.71
7.71
7.56
7.55
7.54
7.54
7.26 CDCl3
7.20
7.18
7.16
7.15
7.14
7.12
7.12
7.11
7.09
7.07
7.07
7.05
7.05
5.27
4.78
Cl
F
O
N
N
N
O
CDCl3, 400 MHz
1H NMR
1e
S98
0.97
1.00
1.01
1.01
1.00
4.02
2.06
2.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

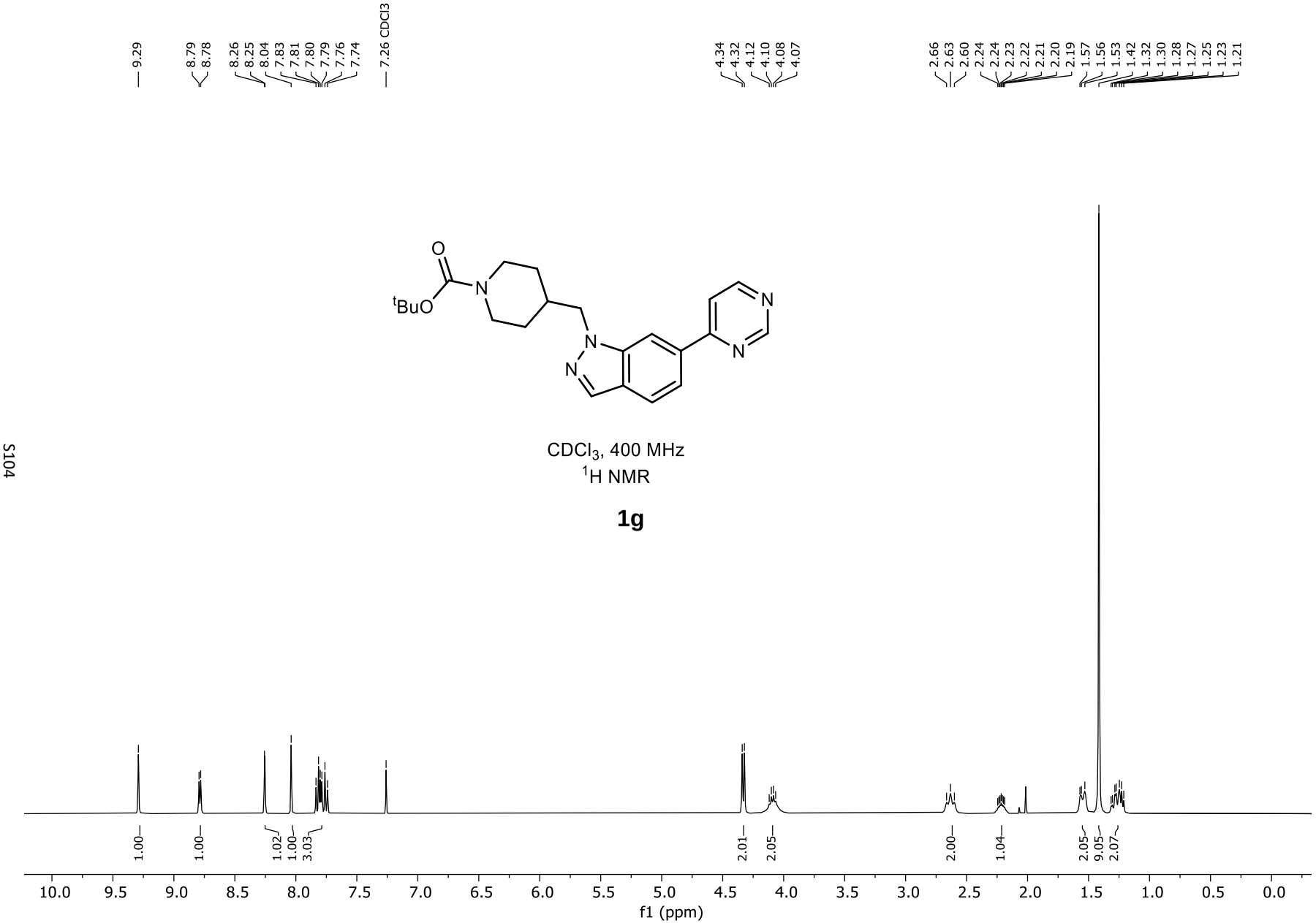

164.38
162.52
161.63
159.20
159.15
157.62
147.78
134.68
134.58
131.55
129.91
129.87
128.70
125.32
125.28
123.41
121.58
121.44
117.79
116.72
116.47
116.31
114.07
114.05
77.16 CDCl3
67.70
38.02
37.98
Cl
F
N
O
N
O
N
CDCl3, 100 MHz
13C NMR
1e
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

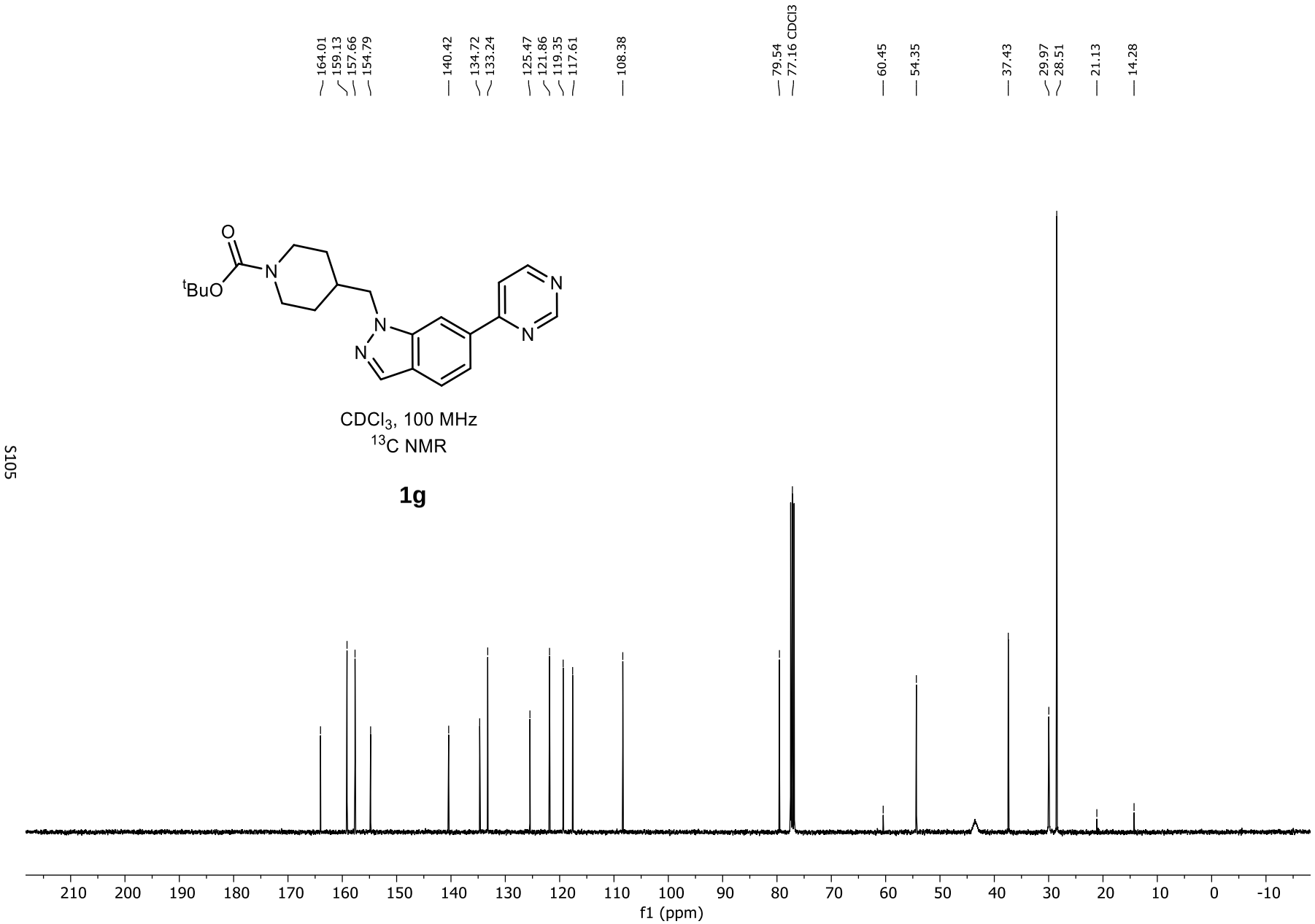

-115.53
-115.56
-115.58
Cl
F
O
N
N
N
O
S100
CDCl3, 375 MHz
19F NMR
1e
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

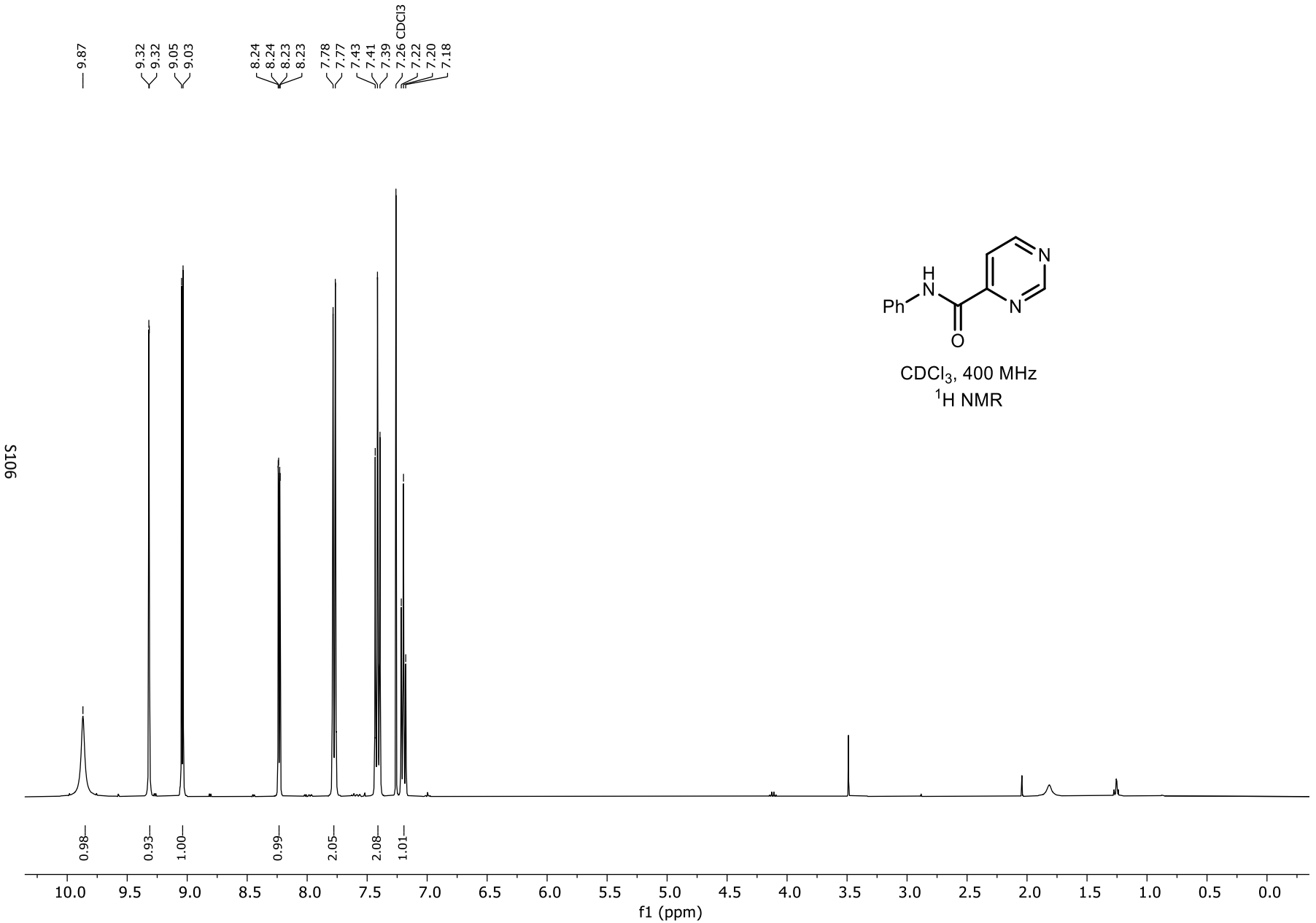

9.18
8.93
7.49
7.48
7.47
7.46
7.44
7.42
7.40
7.34
7.32
7.26 CDCl3
7.06
7.05
7.02
7.00
6.73
6.72
4.21
2.41
Me
F
S
N
N
CDCl3, 400 MHz
1H NMR
1f
S101
1.00
2.00
2.08
2.00
1.02
3.01
1.07
2.07
3.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

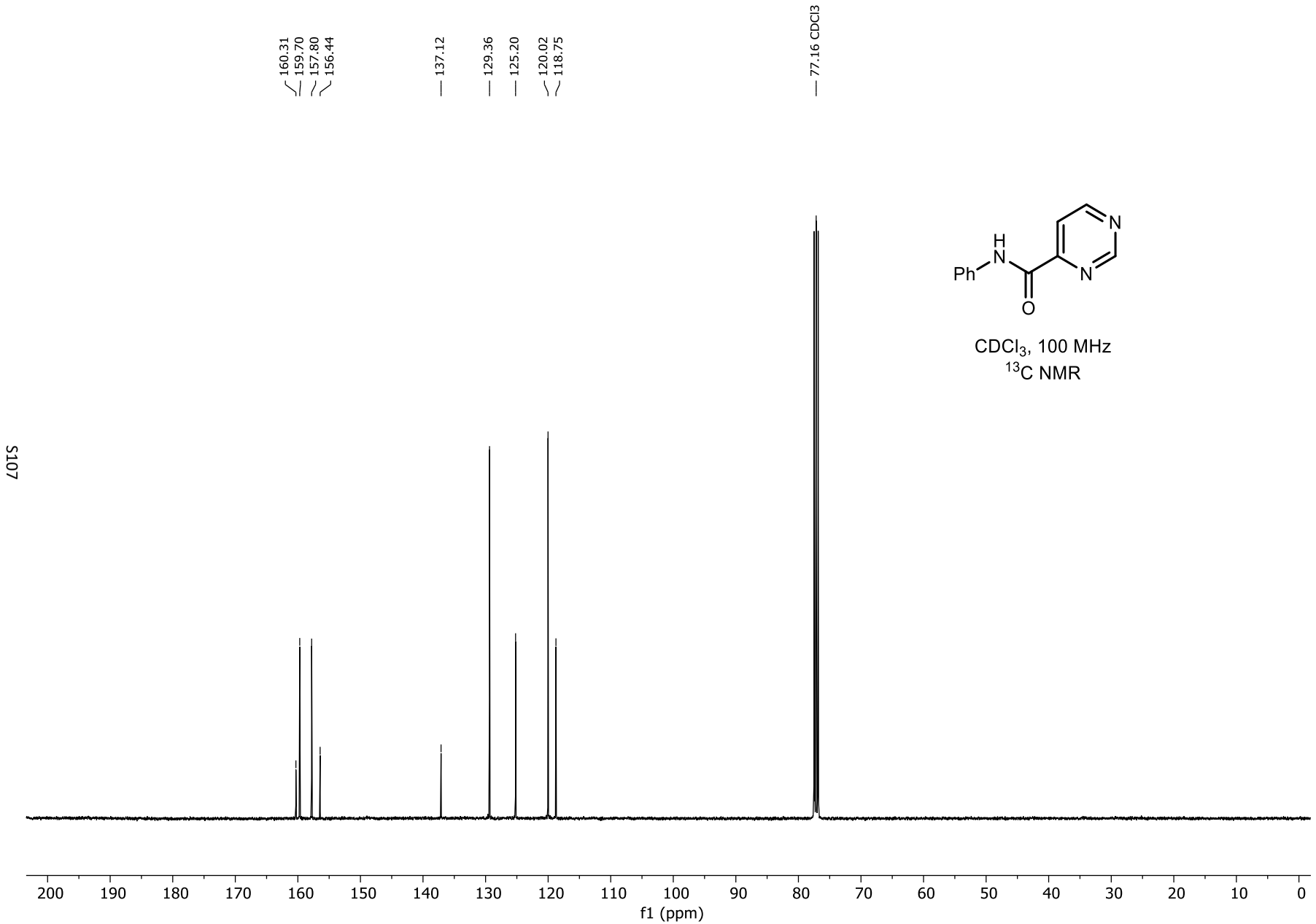

163.50
161.05
157.44
154.88
142.56
142.04
139.68
137.71
134.20
132.34
131.71
130.81
130.78
127.98
127.32
127.24
126.38
125.51
122.86
115.98
115.76
77.16 CDCl3
34.23
19.44
Me
F
S
N
N
CDCl3, 100 MHz
13C NMR
1f
S102
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

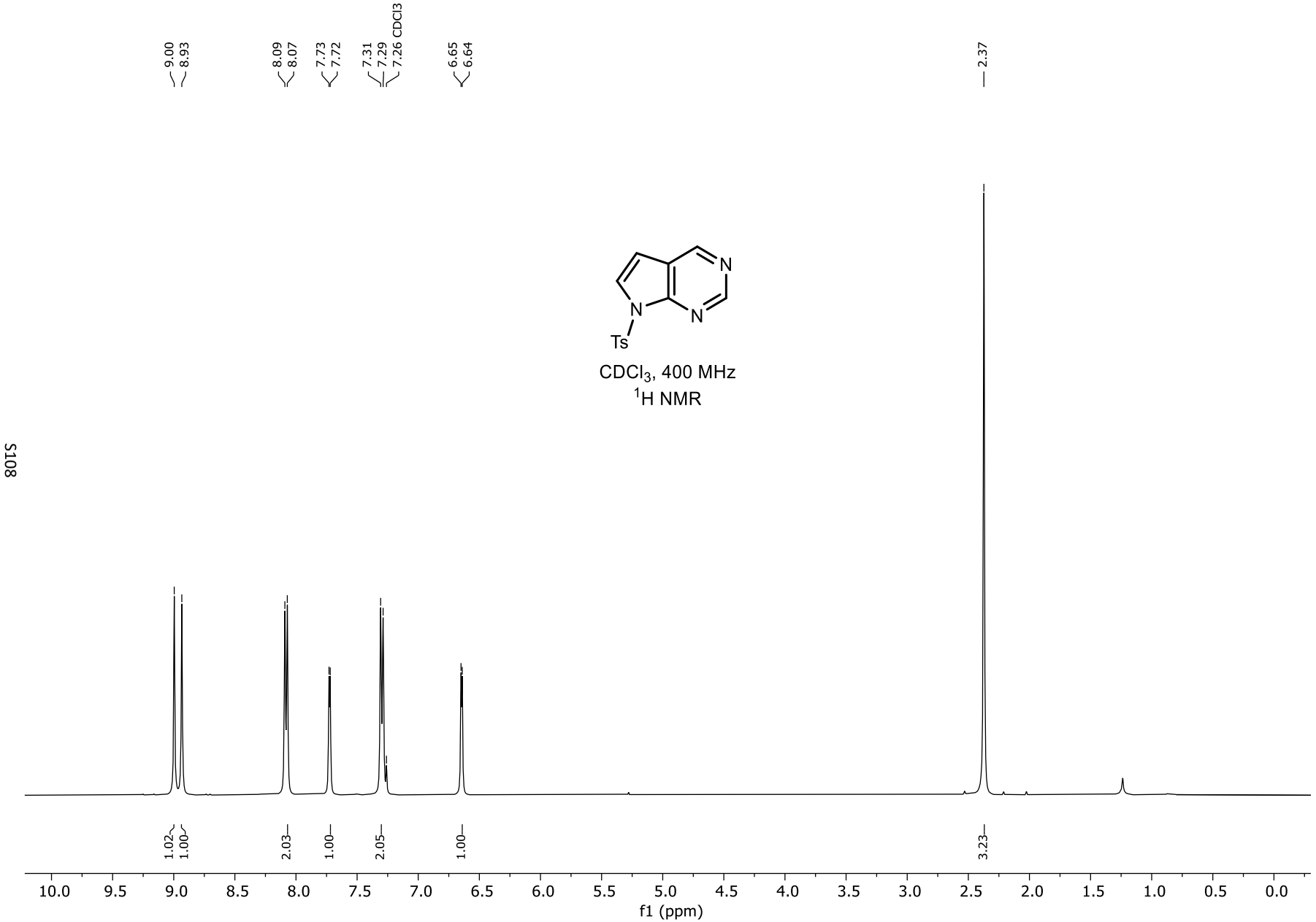

-114.87
-114.89
-114.90
-114.91
-114.92
-114.93
-114.95
Me
F
S
N
N
CDCl3, 375 MHz
19F NMR
1f
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

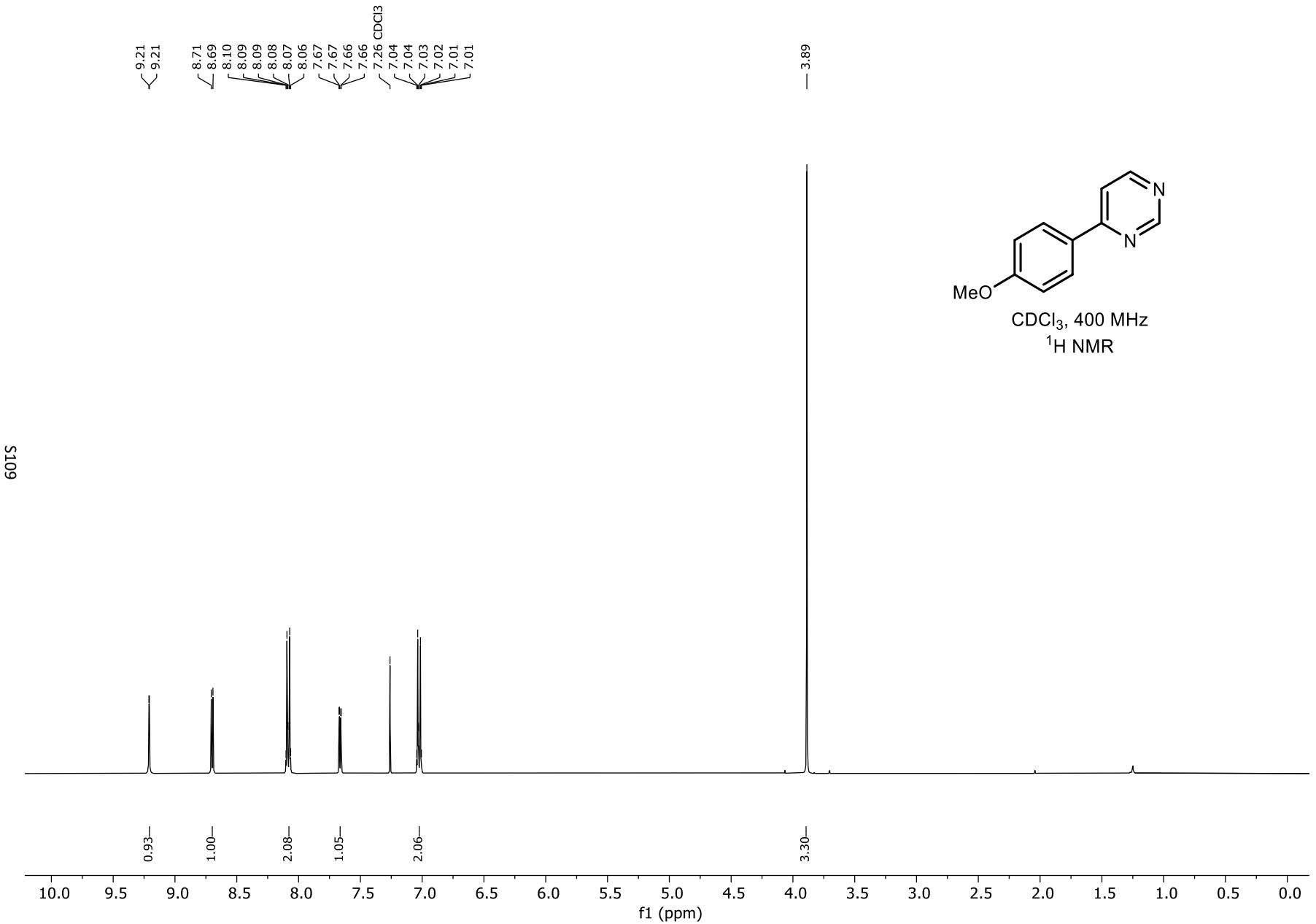

9.29
8.79
8.78
8.26
8.25
8.04
7.83
7.81
7.80
7.79
7.76
7.74
7.26 CDCl3
4.34
4.32
4.12
4.10
4.08
4.07
2.66
2.63
2.60
2.24
2.23
2.22
2.21
2.20
2.19
1.57
1.56
1.53
1.42
1.32
1.30
1.28
1.27
1.25
1.23
1.21
O
tBuO
N
N
N
N
N
CDCl3, 400 MHz
1H NMR
1g
1.00
1.00
1.02
1.00
3.03
2.01
2.05
2.00
1.04
2.05
9.05
2.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

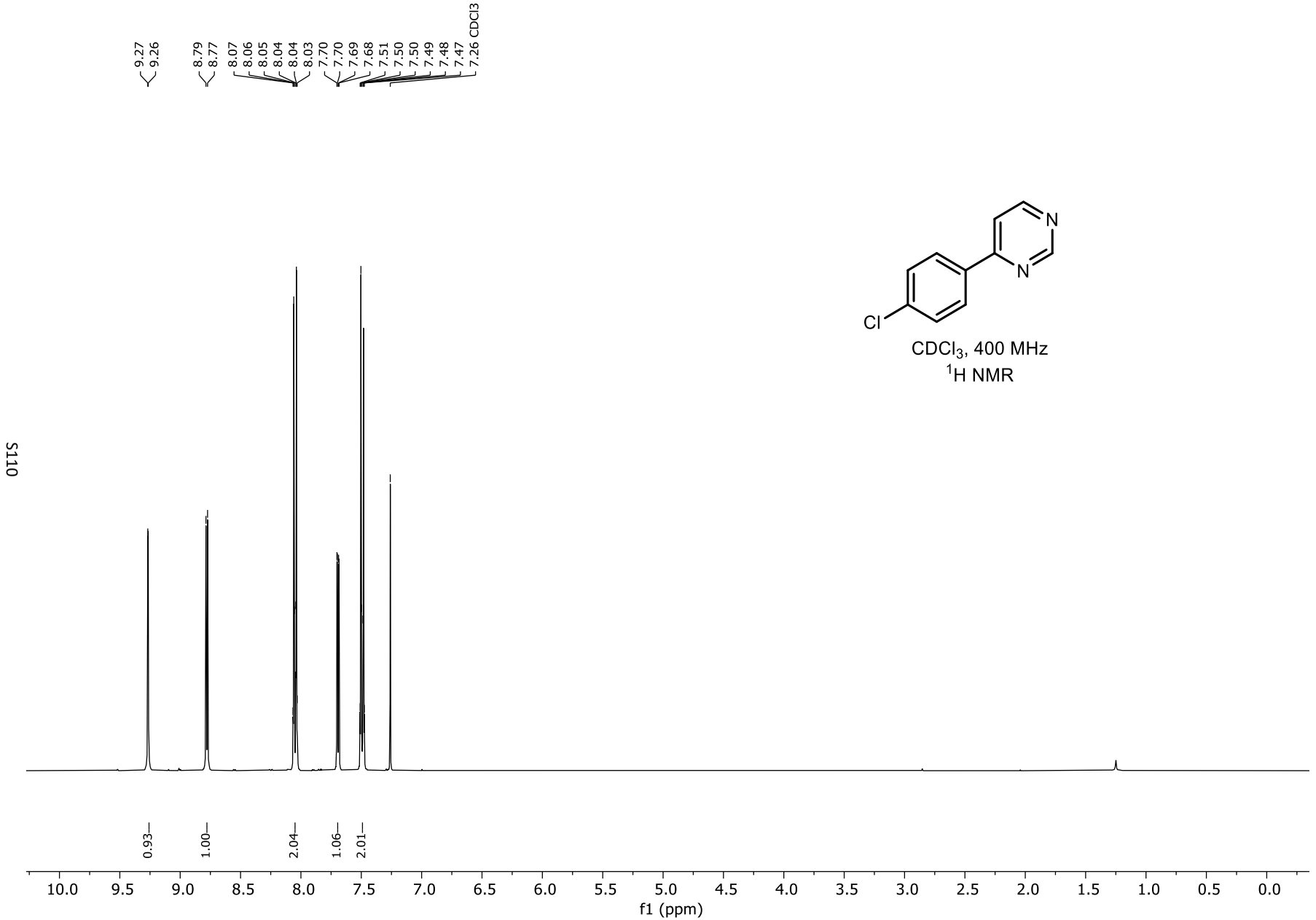

164.01
159.13
157.66
154.79
140.42
134.72
133.24
125.47
121.86
119.35
117.61
108.38
79.54
77.16 CDCl3
60.45
54.35
37.43
29.97
28.51
21.13
14.28
O
tBuO
N
N
N
N
N
CDCl3, 100 MHz
13C NMR
1g
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

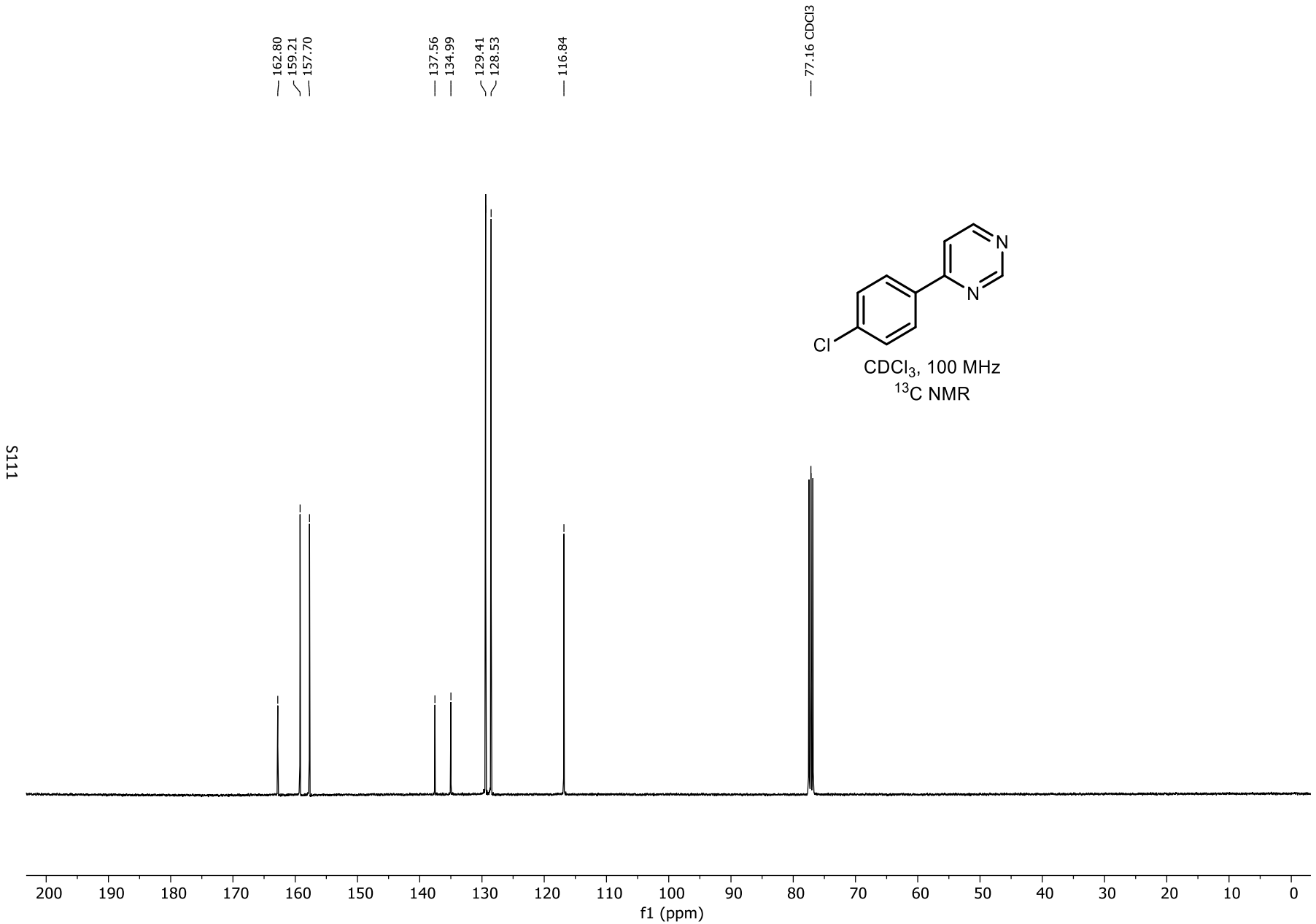

9.87
9.32
9.32
9.05
9.03
8.24
8.24
8.23
8.23
7.78
7.77
7.43
7.41
7.39
7.26 CDCl3
7.22
7.20
7.18
S106
0.98
0.93
1.00
0.99
2.05
2.08
1.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
Ph
H
N
N
N
O
CDCl3, 400 MHz
1H NMR

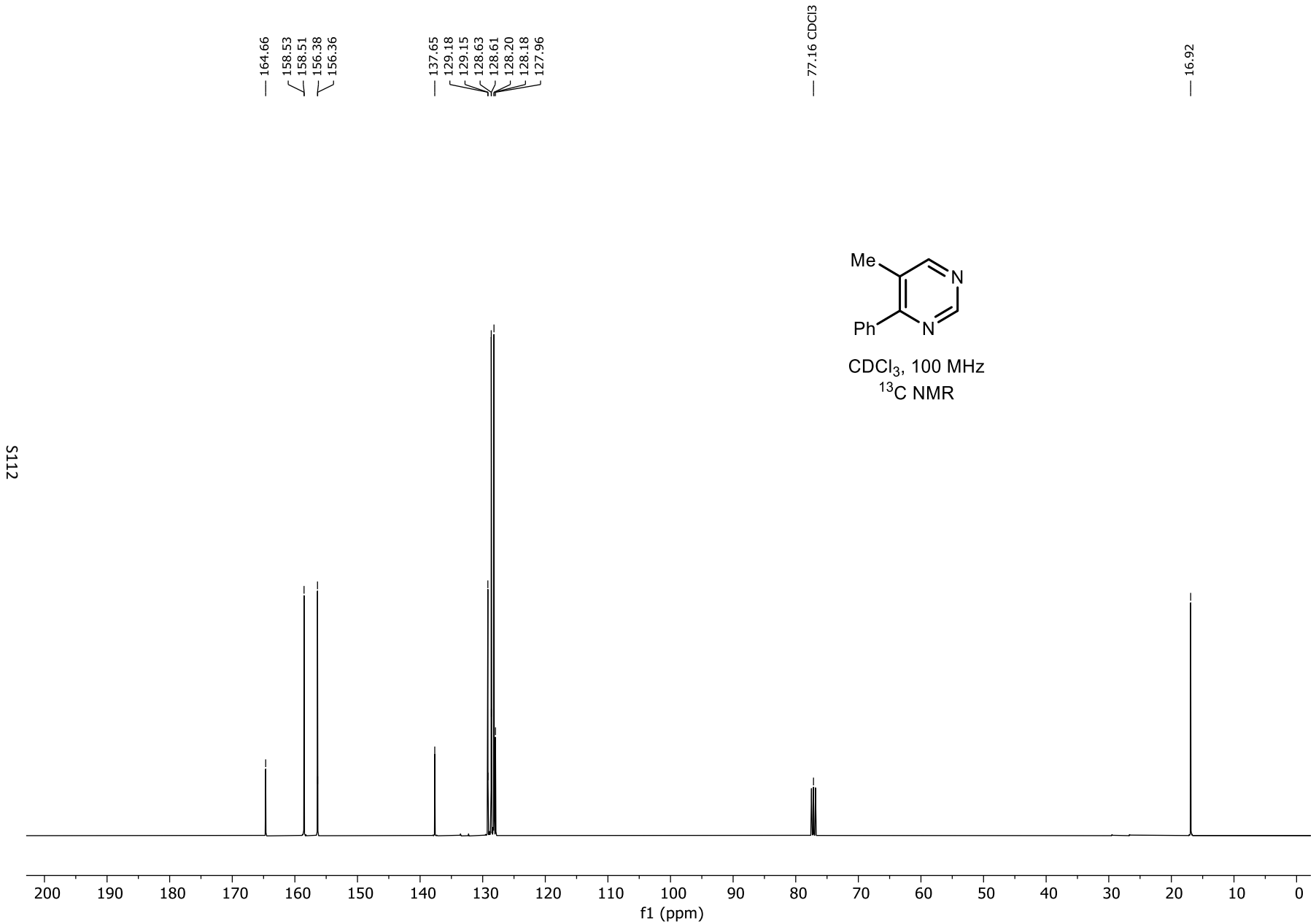

160.31
159.70
157.80
156.44
137.12
129.36
125.20
120.02
118.75
77.16 CDCl3
Ph
N
H
N
N
O
CDCl3, 100 MHz
13C NMR
S107
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

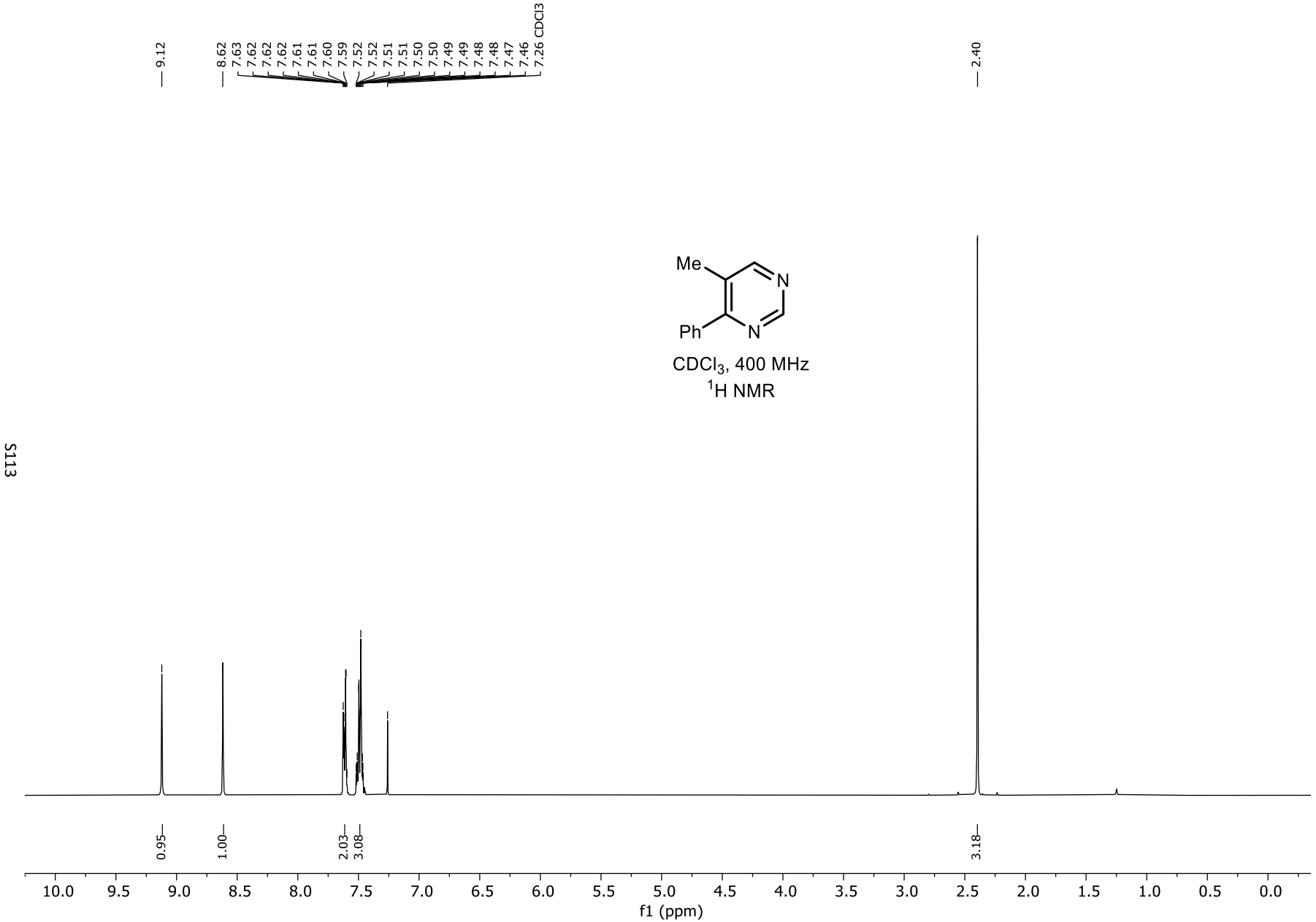

9.00
8.93
8.09
8.07
7.73
7.72
7.31
7.29
7.26 CDCl3
6.65
6.64
2.37
N
N
N
Ts
CDCl3, 400 MHz
1H NMR
1.02
1.00
2.03
1.00
2.05
1.00
3.23
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

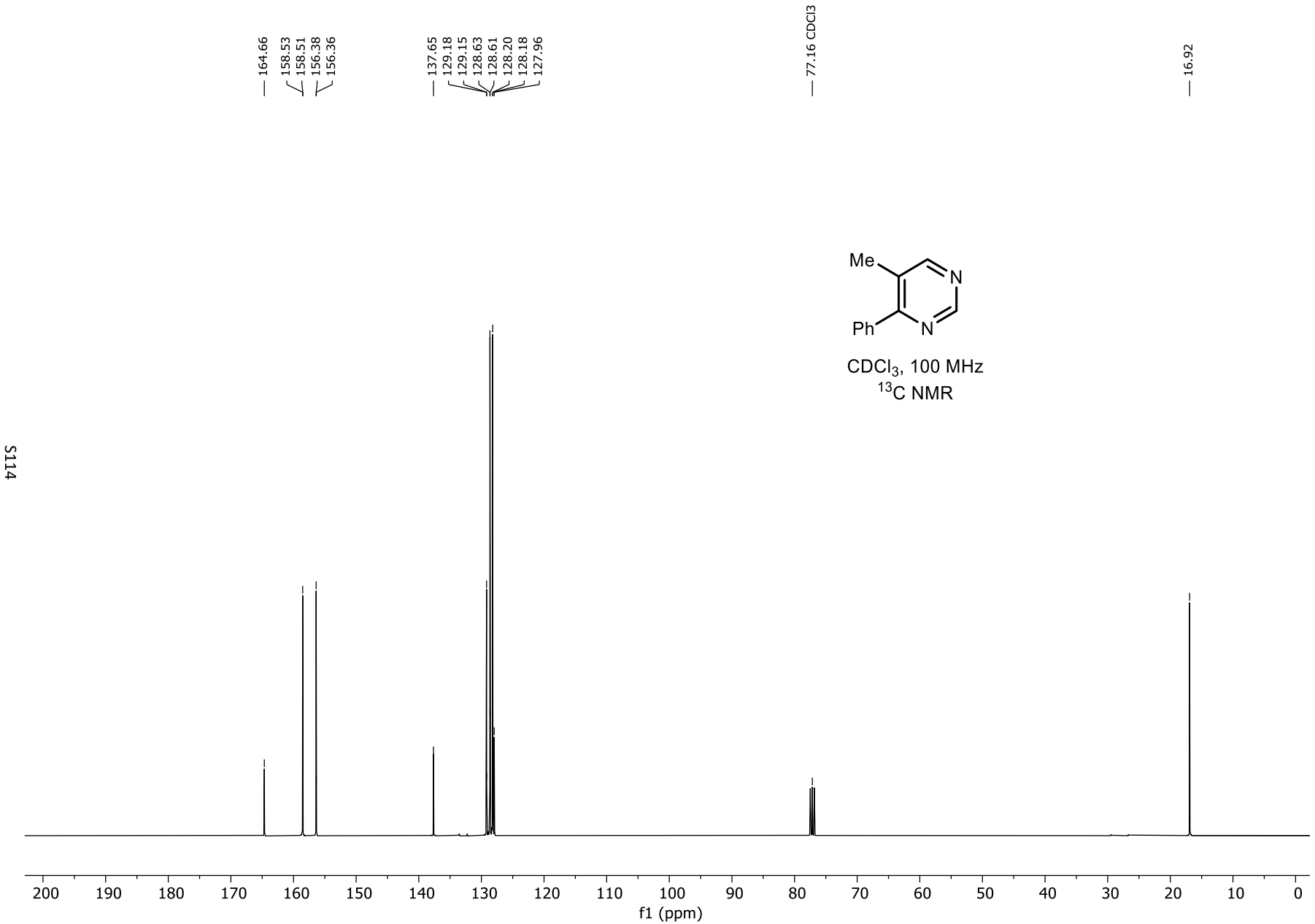

9.21
9.21
8.71
8.69
8.10
8.09
8.09
8.08
8.07
8.06
7.67
7.67
7.66
7.66
7.26 CDCl3
7.04
7.04
7.03
7.02
7.01
7.01
3.89
N
N
MeO
CDCl3, 400 MHz
1H NMR
S109
0.93
1.00
2.08
1.05
2.06
3.30
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

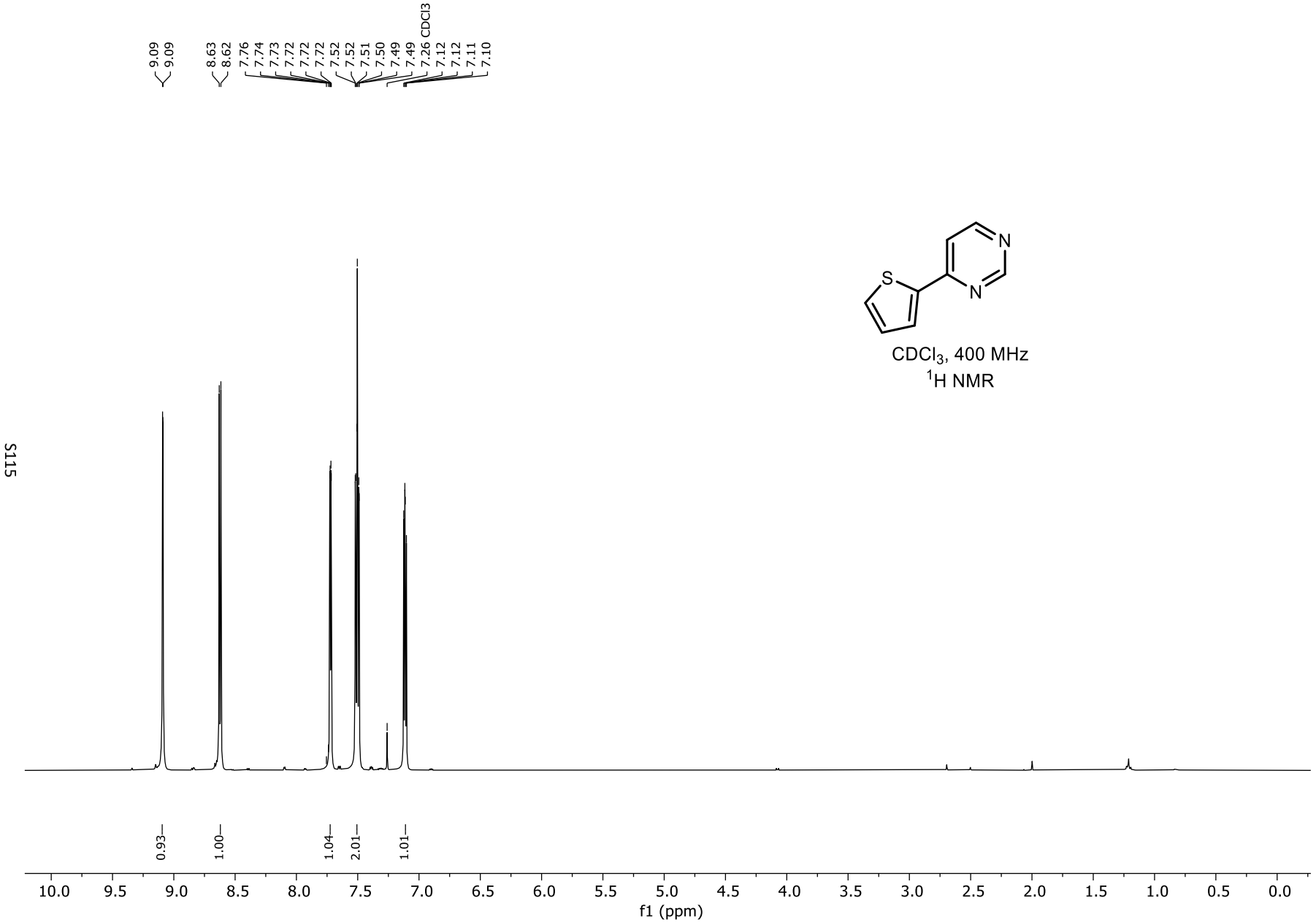

9.27
9.26
8.79
8.77
8.07
8.06
8.05
8.04
8.04
8.03
7.70
7.70
7.69
7.68
7.51
7.50
7.50
7.49
7.48
7.47
7.26 CDCl3
N
N
Cl
CDCl3, 400 MHz
1H NMR
S110
0.93
1.00
2.04
1.06
2.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

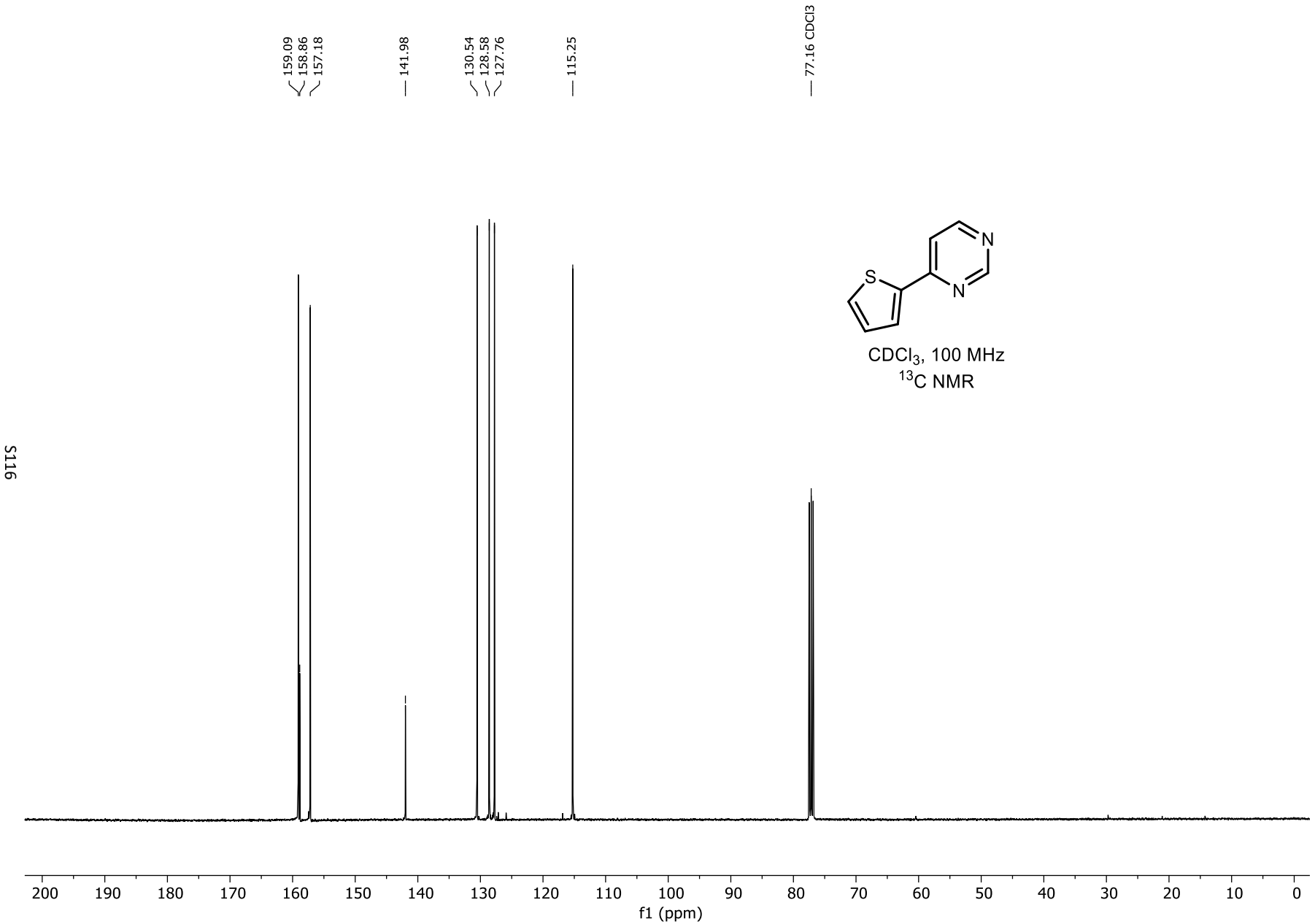

162.80
159.21
157.70
137.56
134.99
129.41
128.53
116.84
77.16 CDCl3
N
N
Cl
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

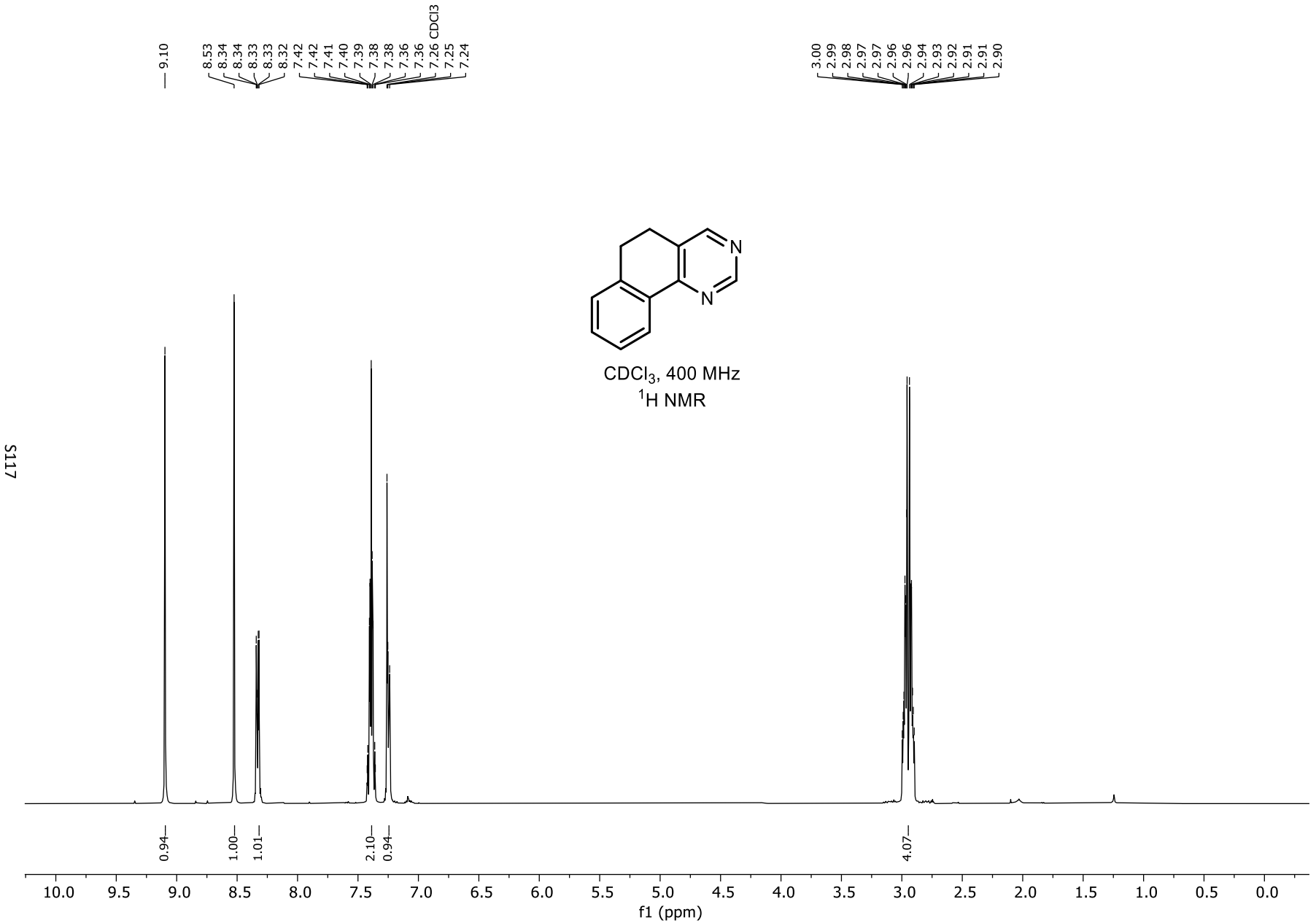

164.66
158.53
158.51
156.38
156.36
137.65
129.18
129.15
128.63
128.61
128.20
128.18
127.96
77.16 CDCl3
16.92
Me
N
Ph
N
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

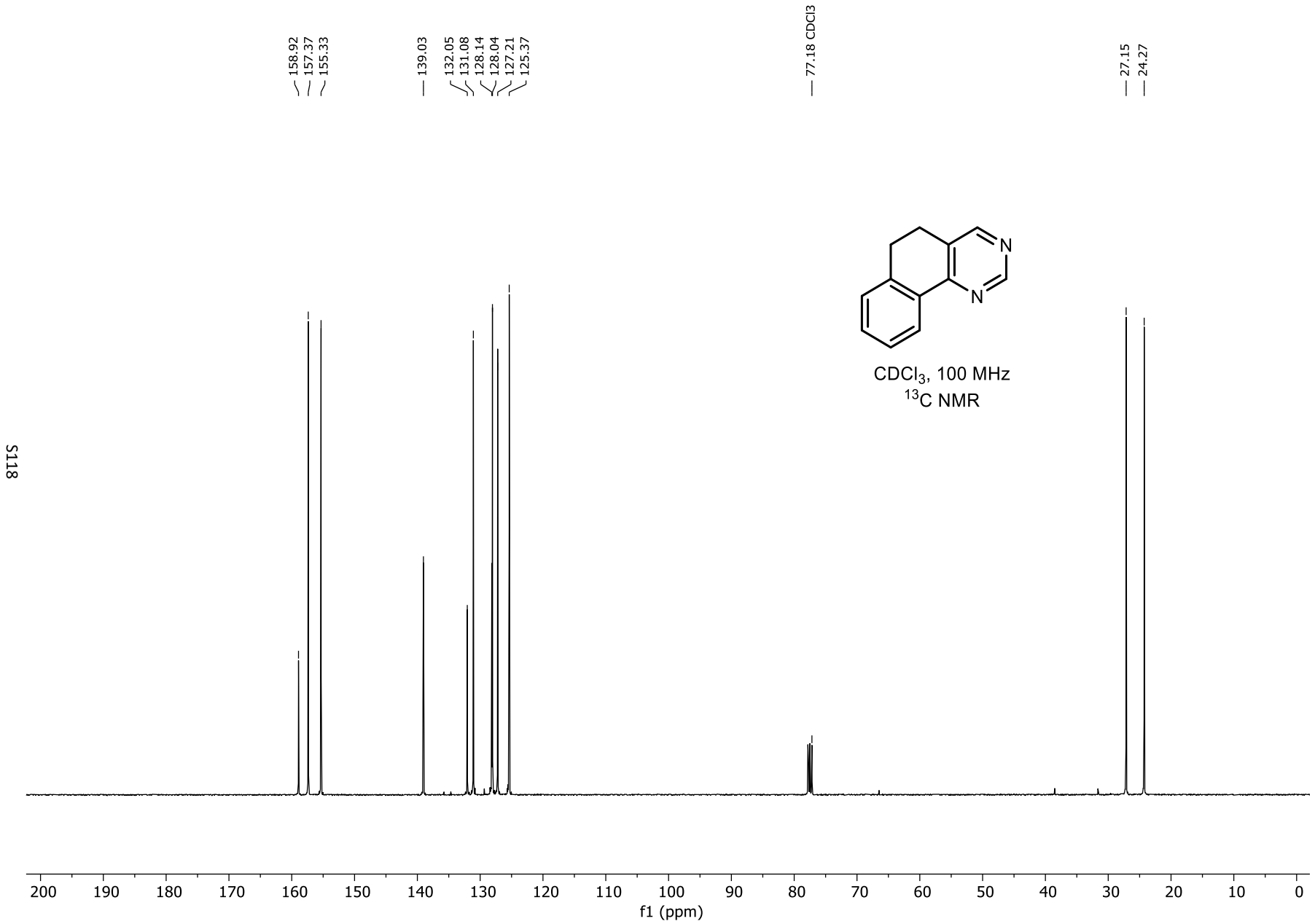

9.12
8.62
7.63
7.62
7.62
7.62
7.61
7.61
7.60
7.59
7.52
7.52
7.51
7.51
7.50
7.50
7.49
7.49
7.48
7.48
7.47
7.46
7.26 CDCl3
2.40
Me
N
Ph
N
CDCl3, 400 MHz
1H NMR
0.95
1.00
2.03
3.08
3.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

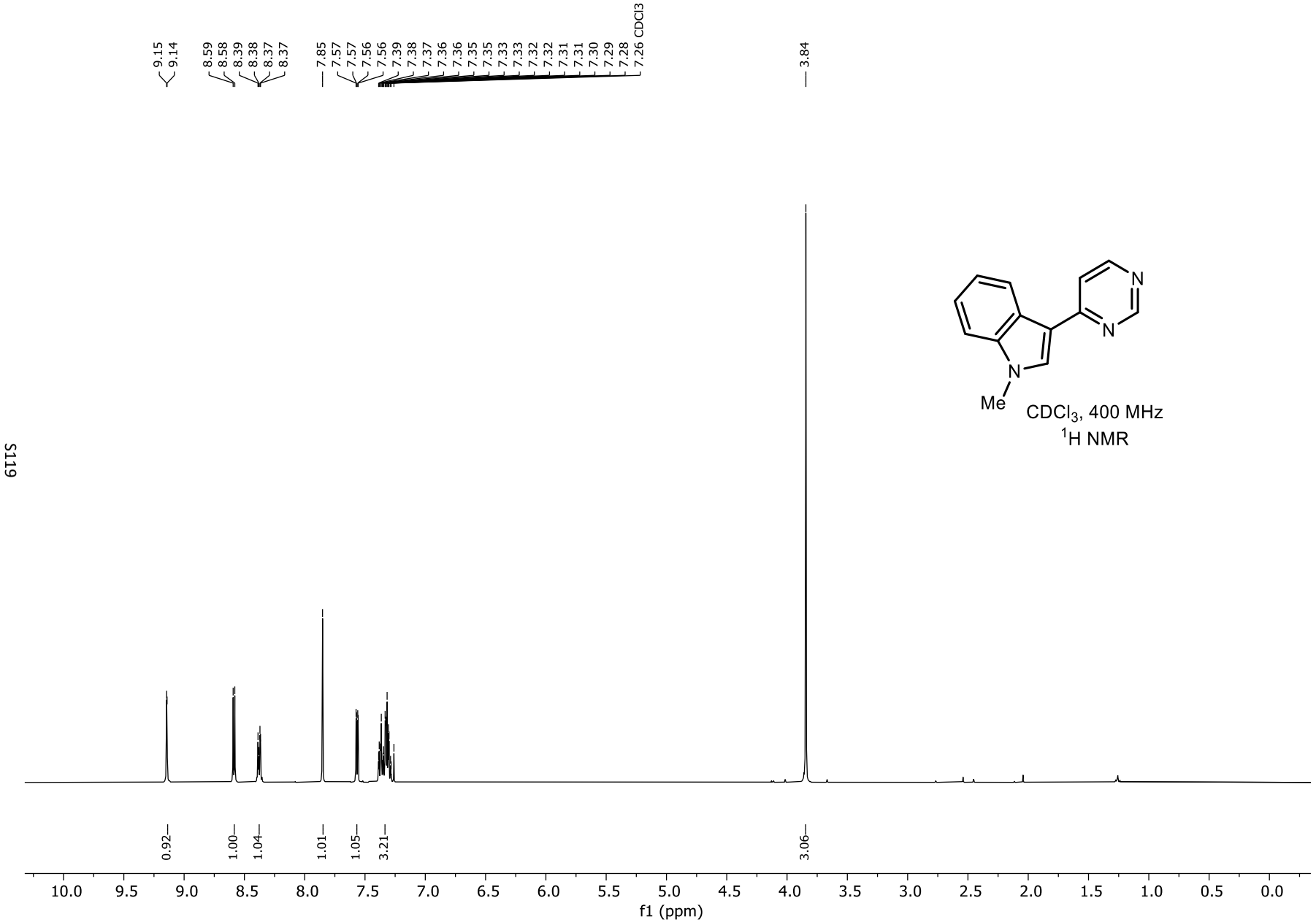

164.66
158.53
158.51
156.38
156.36
137.65
129.18
129.15
128.63
128.61
128.20
128.18
127.96
77.16 CDCl3
16.92
Me
N
Ph
N
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

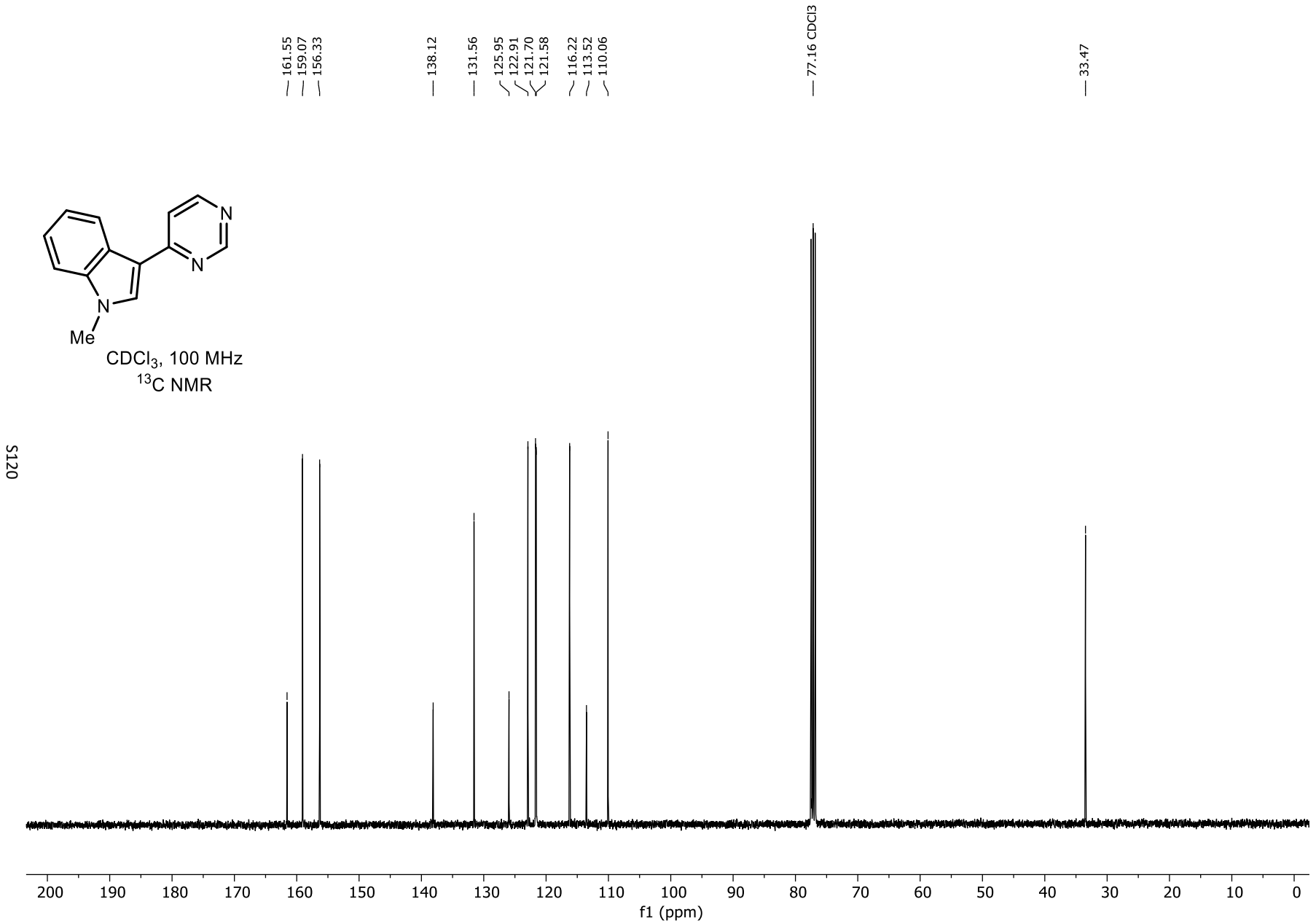

9.09
9.09
8.63
8.62
7.76
7.74
7.73
7.72
7.72
7.72
7.52
7.52
7.51
7.50
7.49
7.49
7.26 CDCl3
7.12
7.12
7.11
7.10
N
S
N
CDCl3, 400 MHz
1H NMR
S115
0.93
1.00
1.04
2.01
1.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

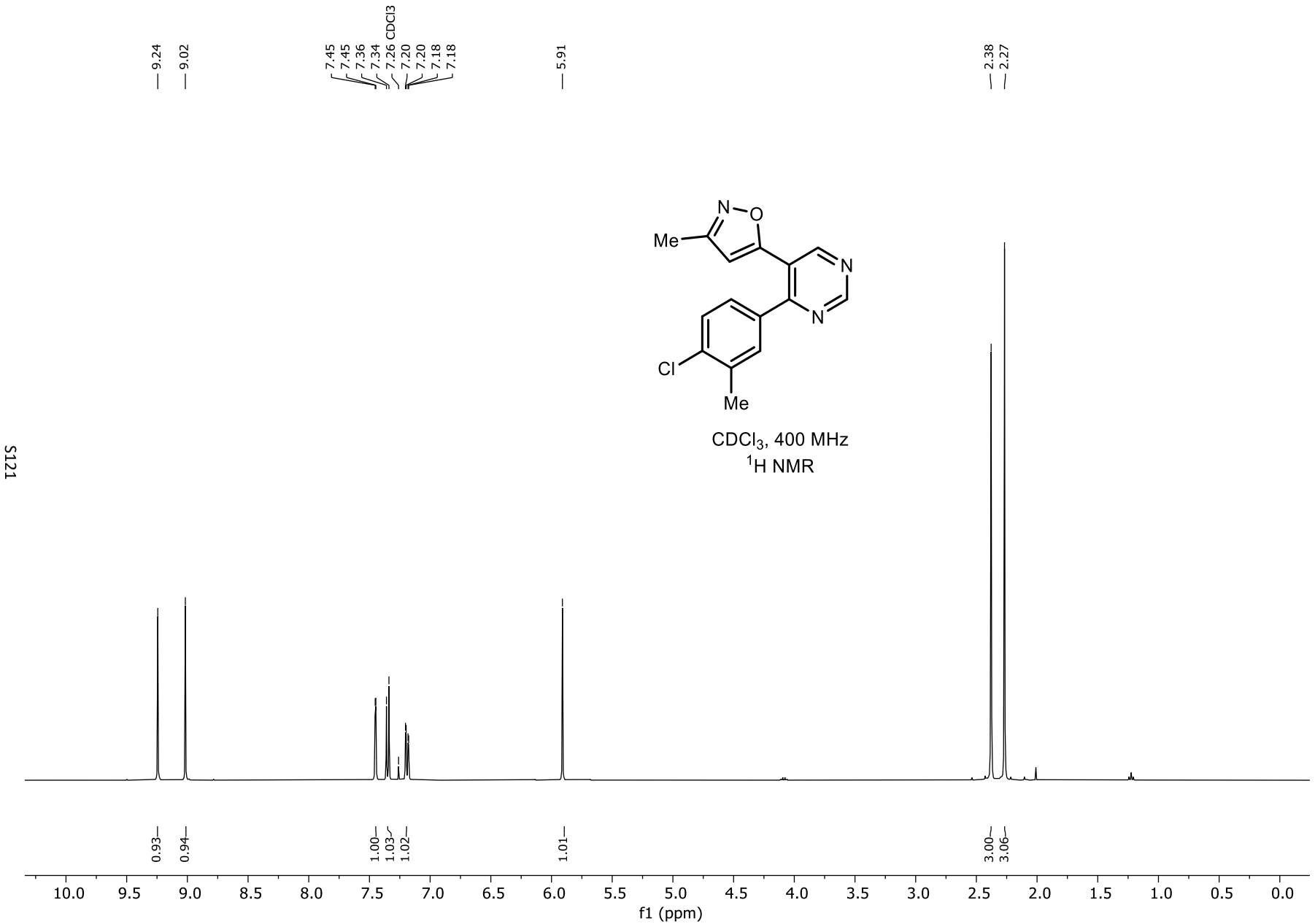

159.09
158.86
157.18
141.98
130.54
128.58
127.76
115.25
77.16 CDCl3
S
N
N
CDCl3, 100 MHz
13C NMR
S116
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

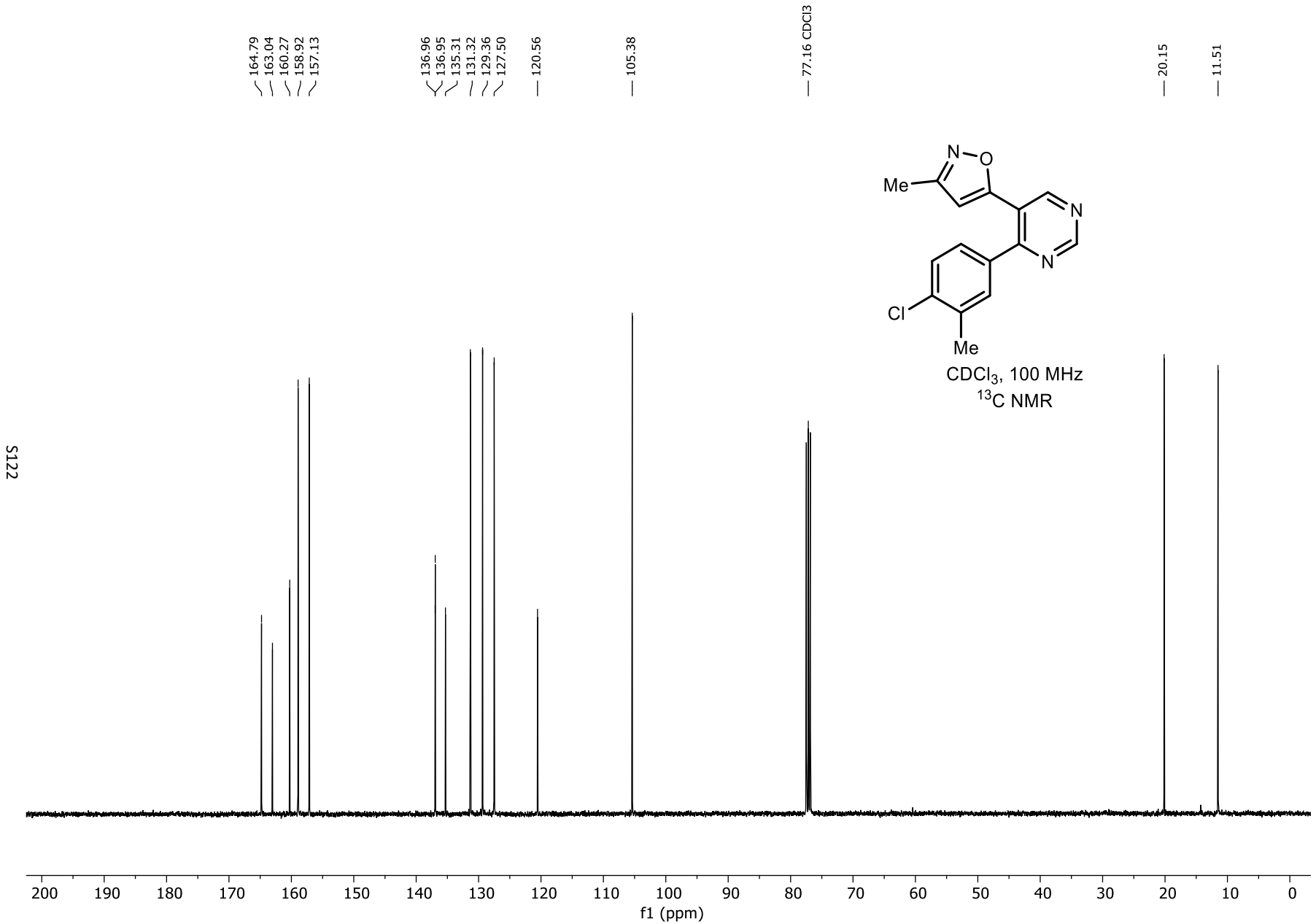

9.10
8.53
8.34
8.34
8.33
8.33
8.32
7.42
7.42
7.41
7.40
7.39
7.38
7.38
7.36
7.26 CDCl3
7.25
7.24
3.00
2.99
2.98
2.97
2.97
2.96
2.96
2.94
2.93
2.92
2.91
2.91
2.90
N
N
CDCl3, 400 MHz
1H NMR
0.94
1.00
1.01
2.10
0.94
4.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

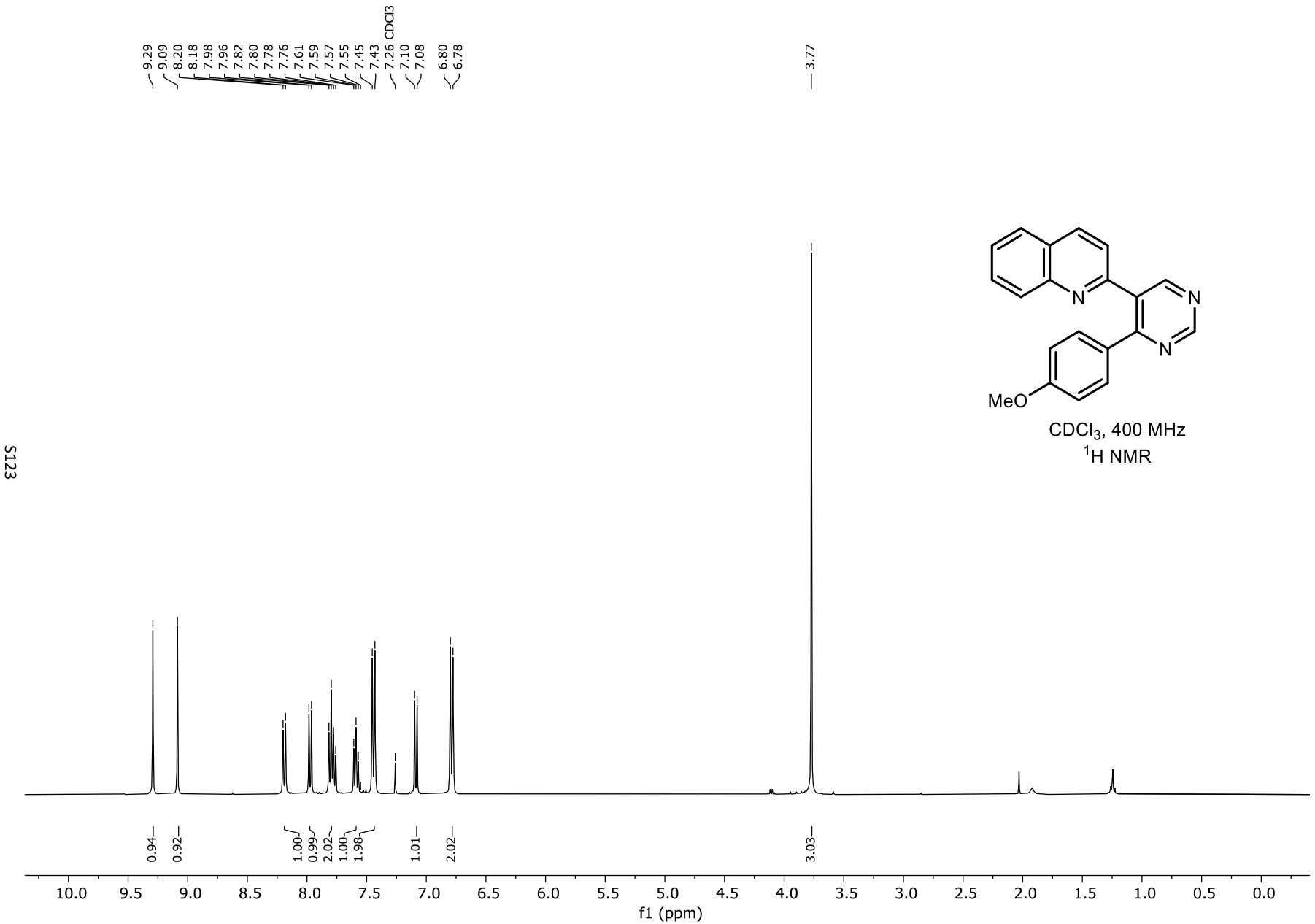

158.92
157.37
155.33
139.03
132.05
131.08
128.14
128.04
127.21
125.37
77.18 CDCl3
27.15
24.27
N
N
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

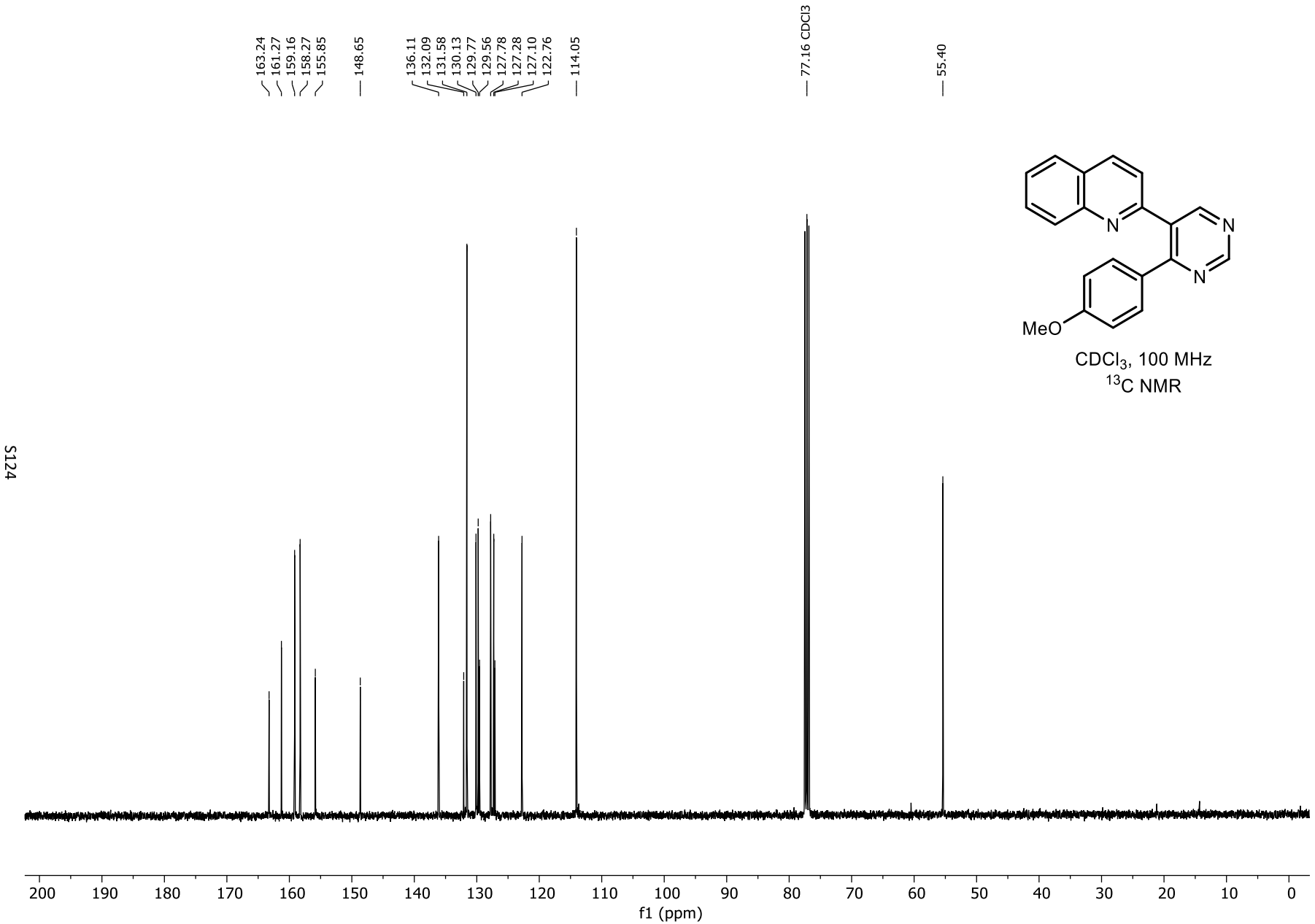

9.15
9.14
8.59
8.58
8.39
8.38
8.37
8.37
7.85
7.57
7.57
7.56
7.56
7.39
7.38
7.37
7.36
7.36
7.35
7.35
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.29
7.28
7.26 CDCl3
3.84
N
N
N
Me
CDCl3, 400 MHz
1H NMR
0.92
1.00
1.04
1.01
1.05
3.21
3.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

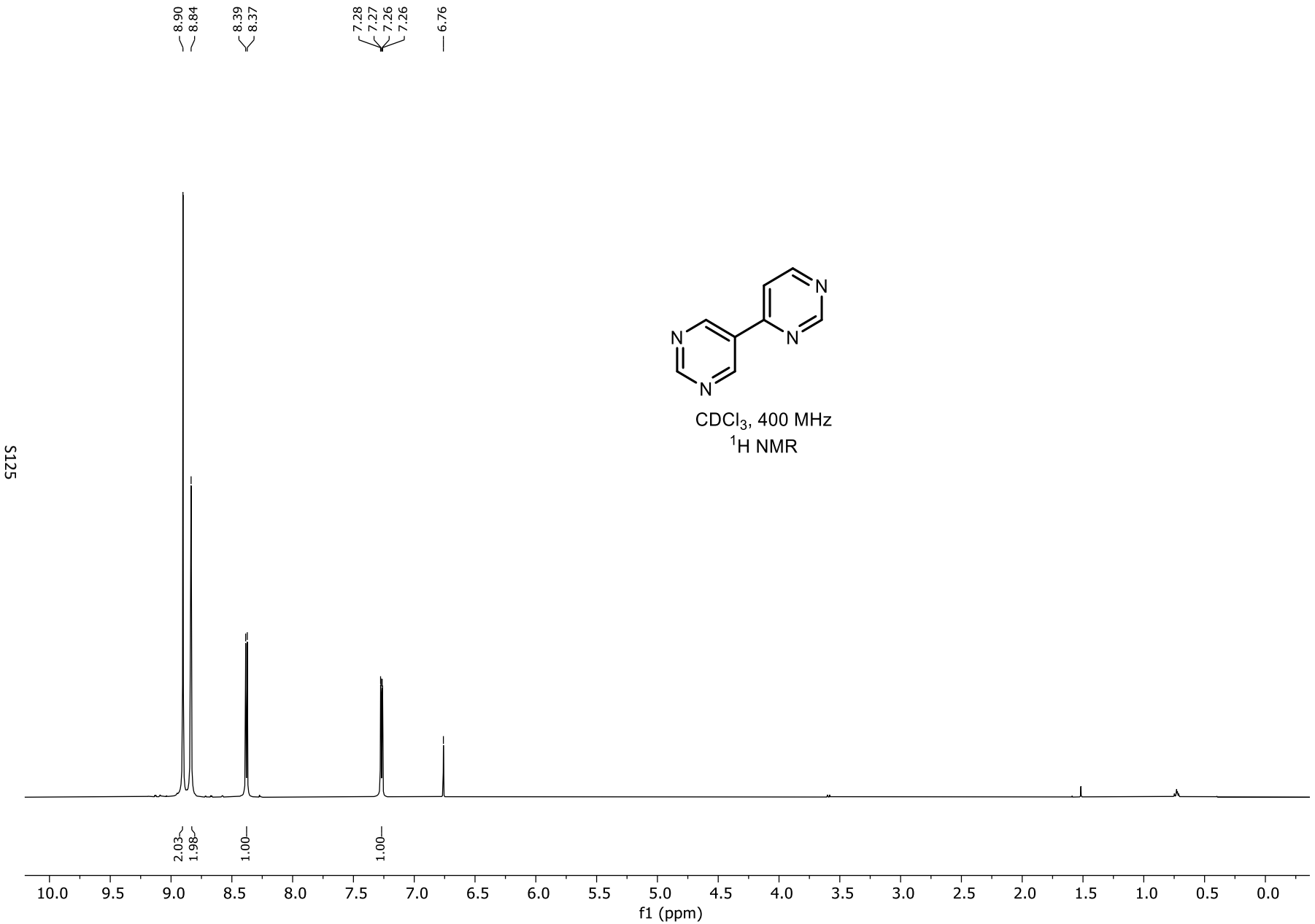

161.55
159.07
156.33
138.12
131.56
125.95
122.91
121.70
121.58
116.22
113.52
110.06
77.16 CDCl3
33.47
N
N
N
Me
CDCl3, 100 MHz
13C NMR
S120
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

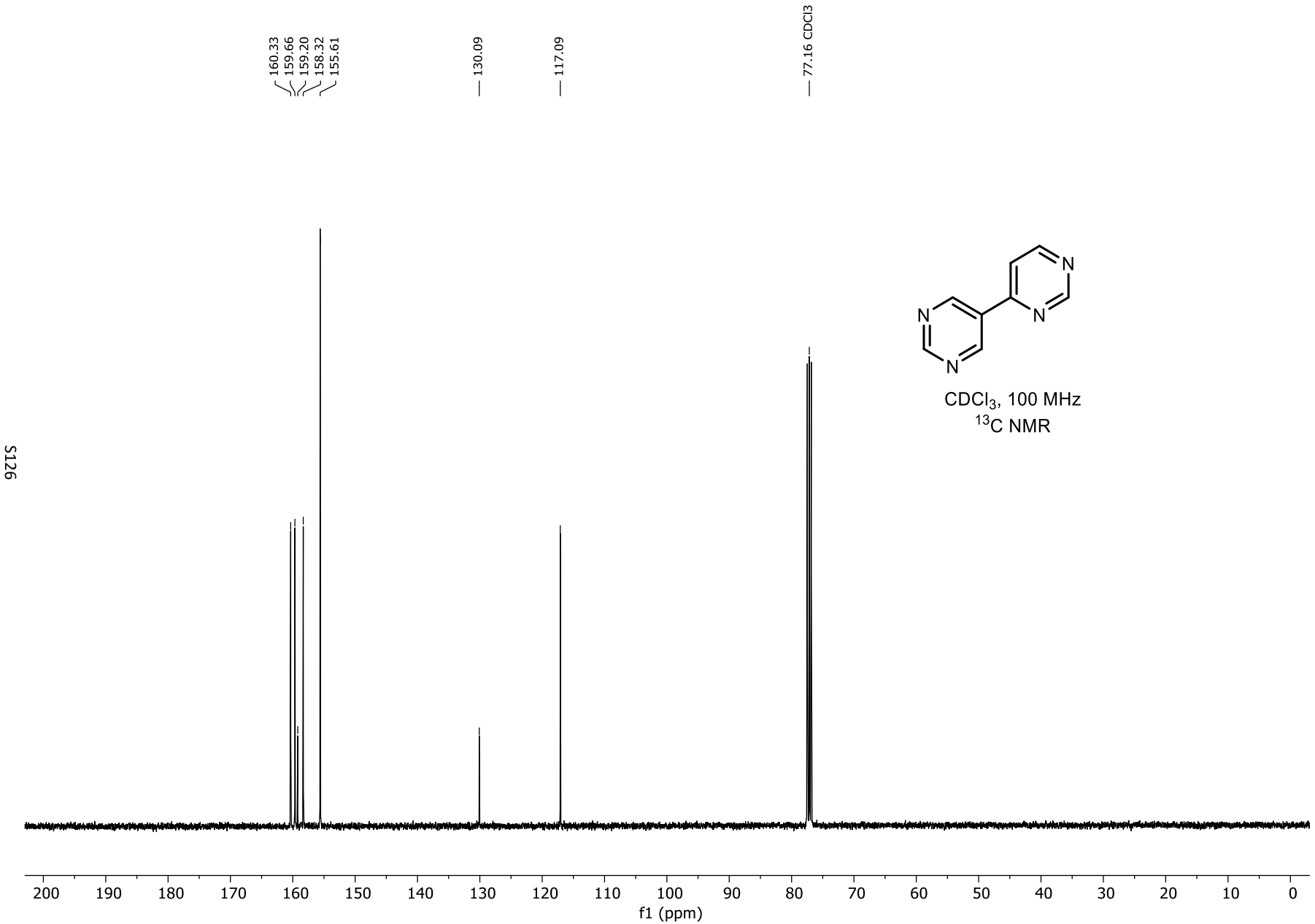

9.24
9.02
7.45
7.45
7.36
7.34
7.26 CDCl3
7.20
7.18
7.18
5.91
2.38
2.27
N
O
Me
N
N
Cl
Me
CDCl3, 400 MHz
1H NMR
0.93
0.94
1.00
1.03
1.02
1.01
3.00
3.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

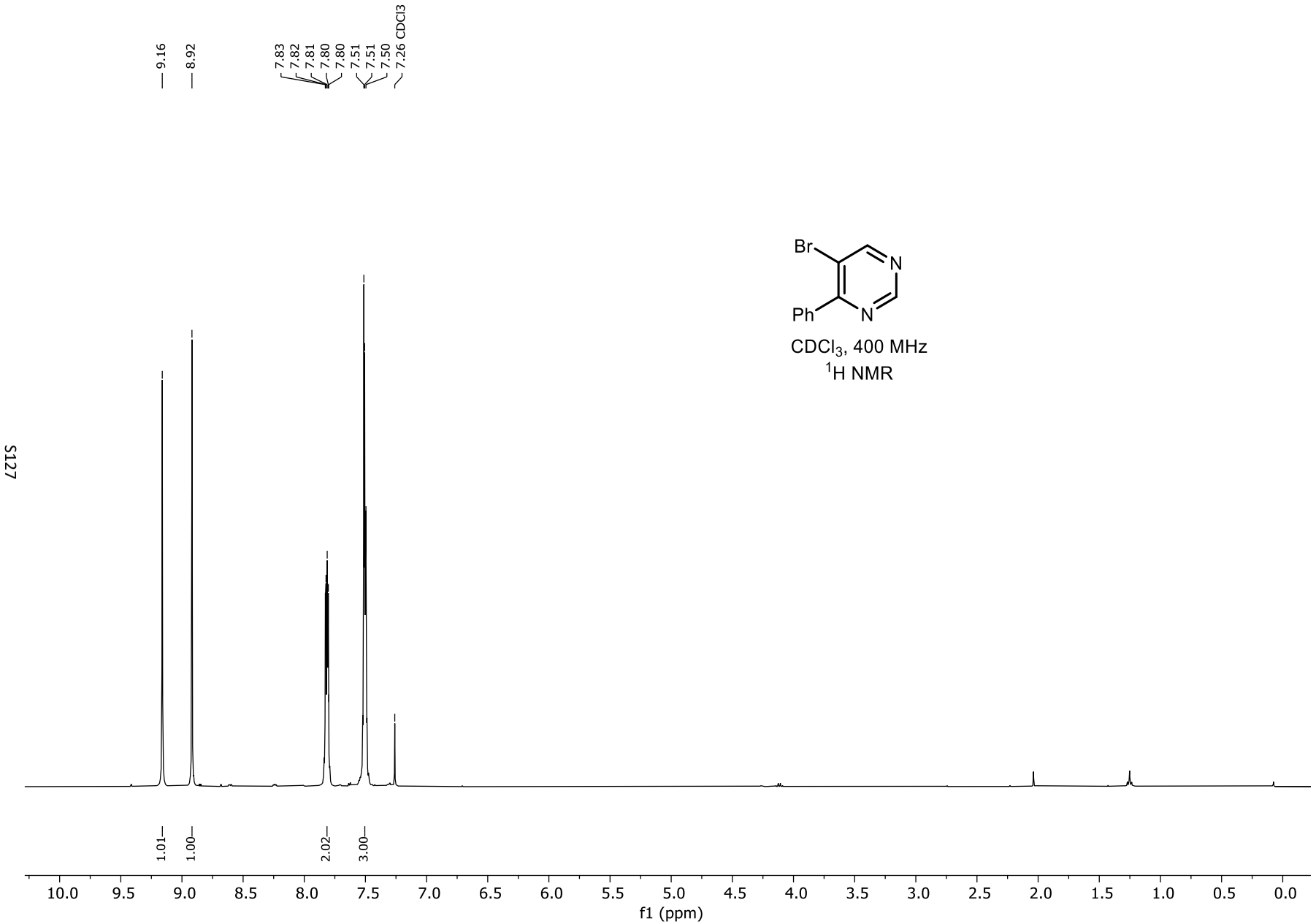

164.79
163.04
160.27
158.92
157.13
136.96
136.95
135.31
131.32
129.36
127.50
120.56
105.38
77.16 CDCl3
20.15
11.51
N
O
Me
N
N
Cl
Me
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

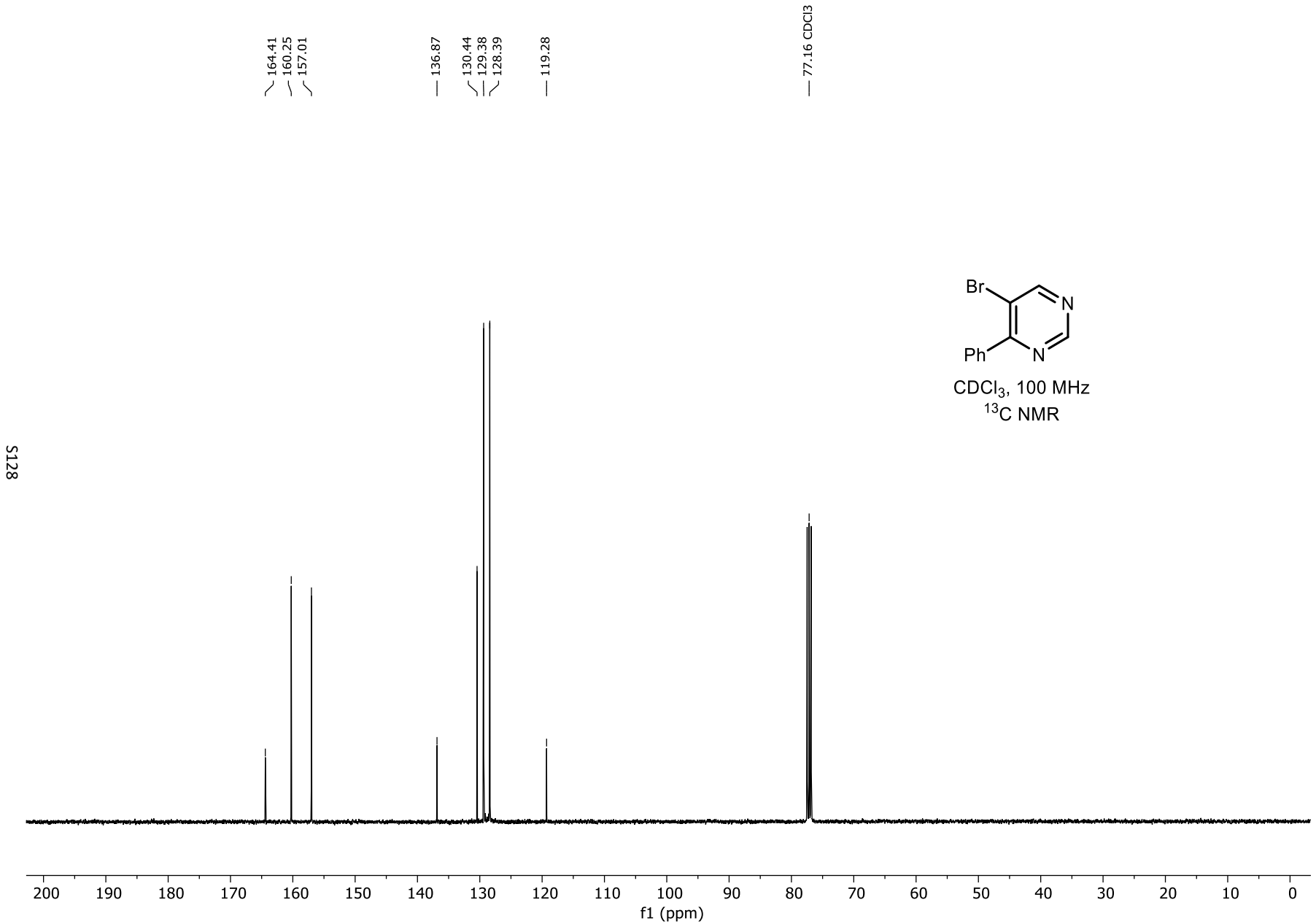

9.29
9.09
8.20
8.18
7.98
7.96
7.82
7.80
7.78
7.76
7.61
7.59
7.57
7.55
7.45
7.43
7.26 CDCl3
7.10
7.08
6.80
6.78
3.77
N
N
N
MeO
CDCl3, 400 MHz
1H NMR
0.94
0.92
1.00
0.99
2.02
1.00
1.98
1.01
2.02
3.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

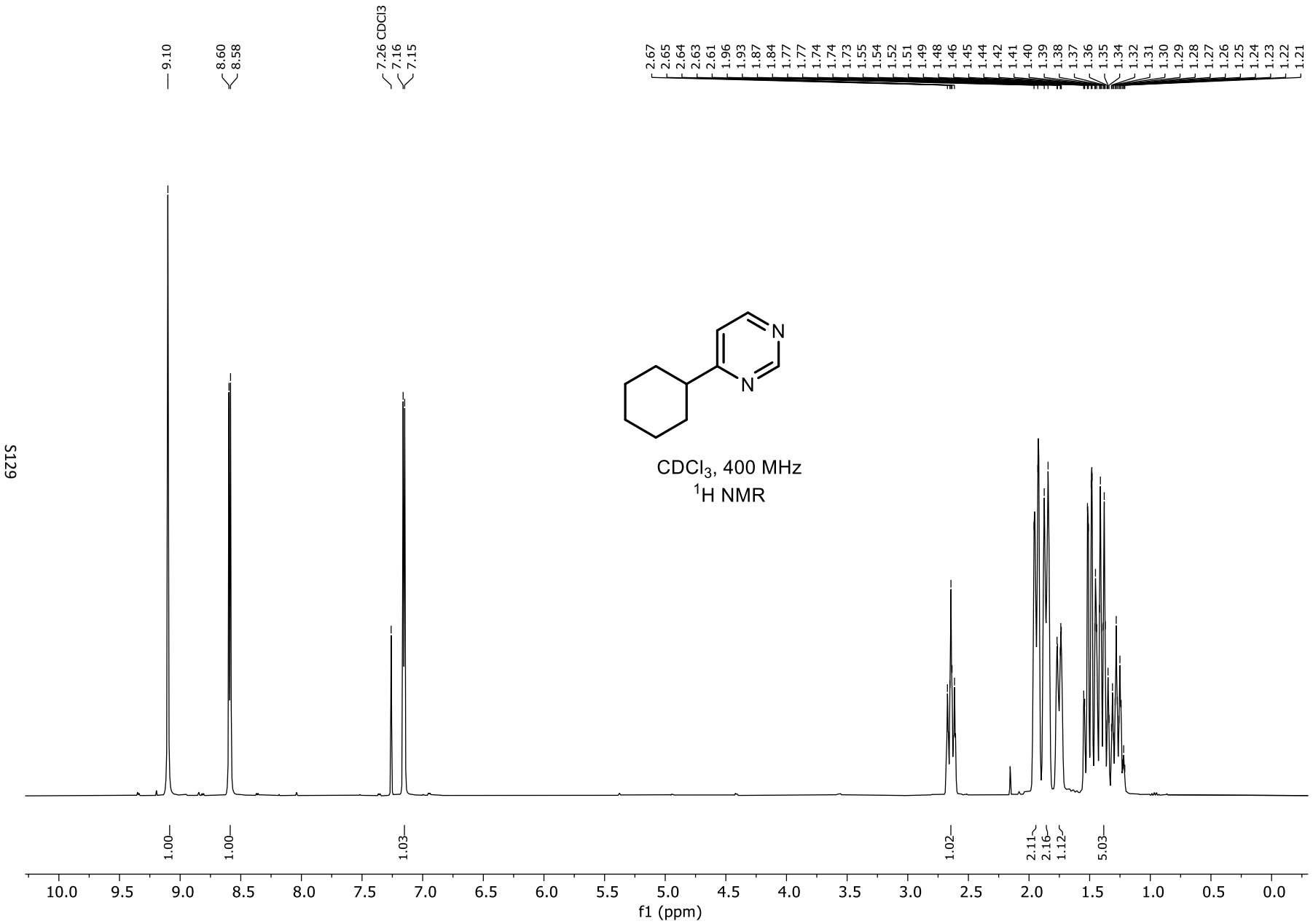

163.24
161.27
159.16
158.27
155.85
148.65
136.11
132.09
131.58
130.13
129.77
129.56
127.78
127.28
127.10
122.76
114.05
77.16 CDCl3
55.40
N
N
N
MeO
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

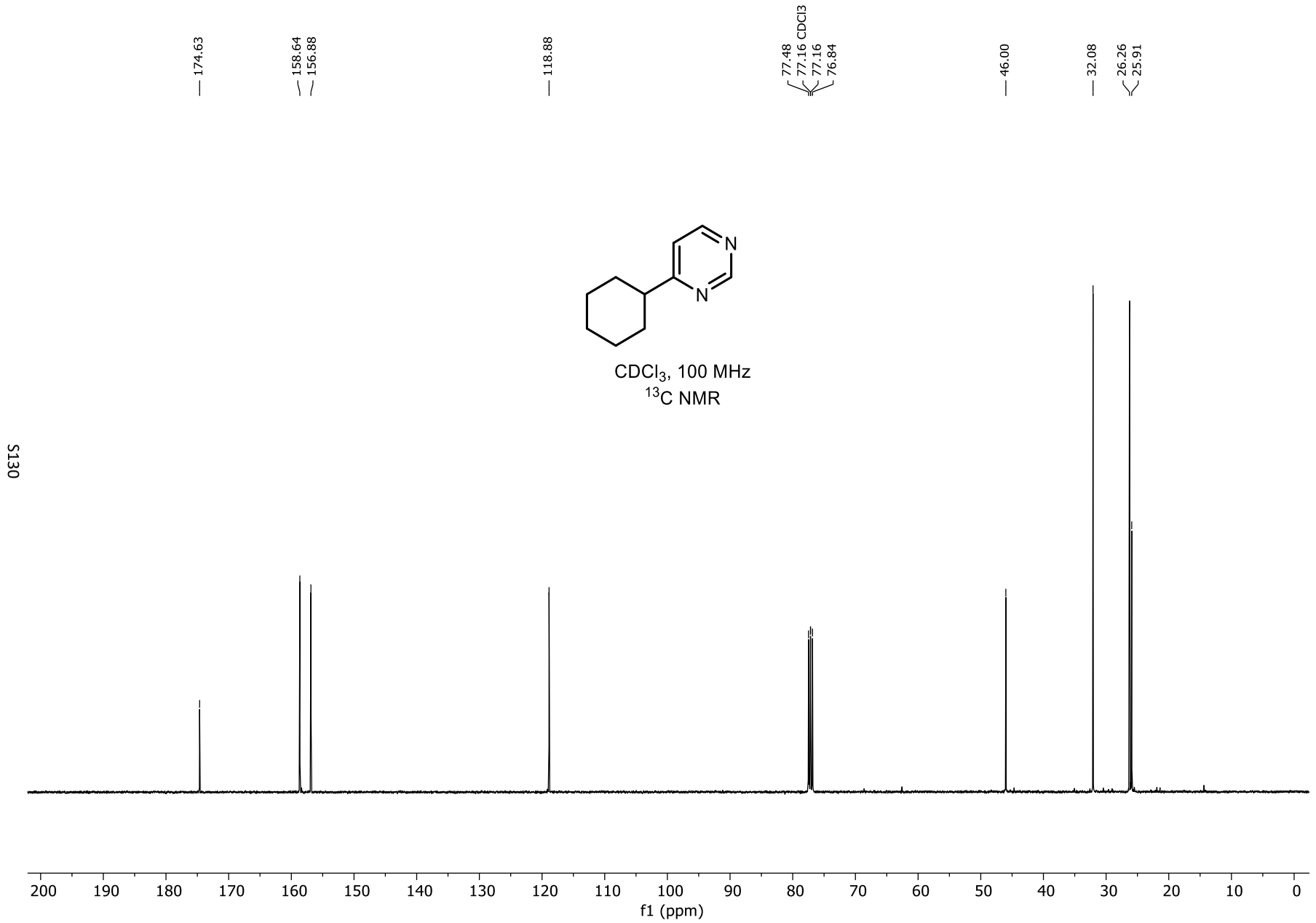

8.90
8.84
8.39
8.37
7.28
7.27
7.26
7.26
6.76
N
N
N
N
CDCl3, 400 MHz
1H NMR
2.03
1.98
1.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

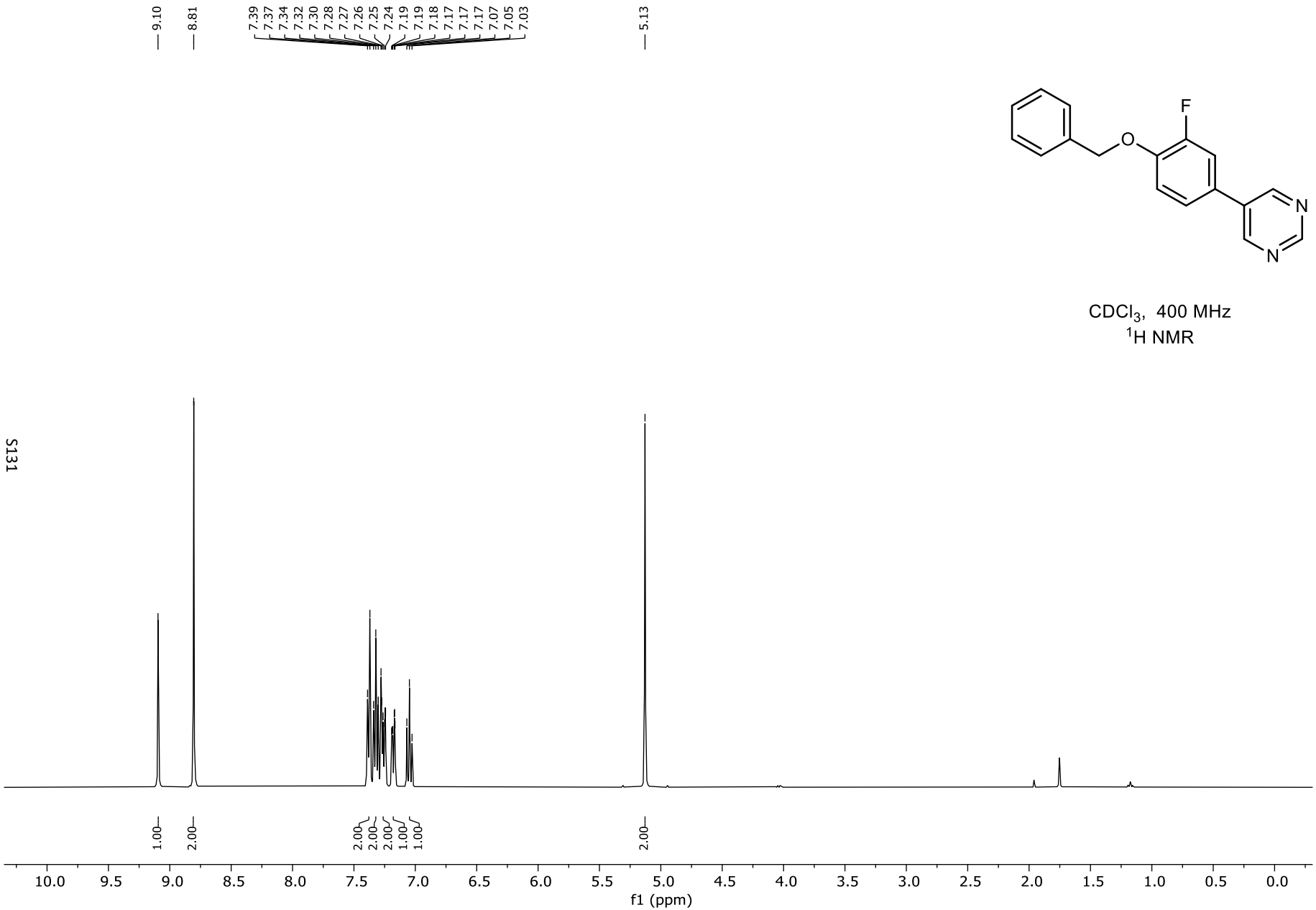

160.33
159.66
159.20
158.32
155.61
130.09
117.09
77.16 CDCl3
N
N
N
N
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

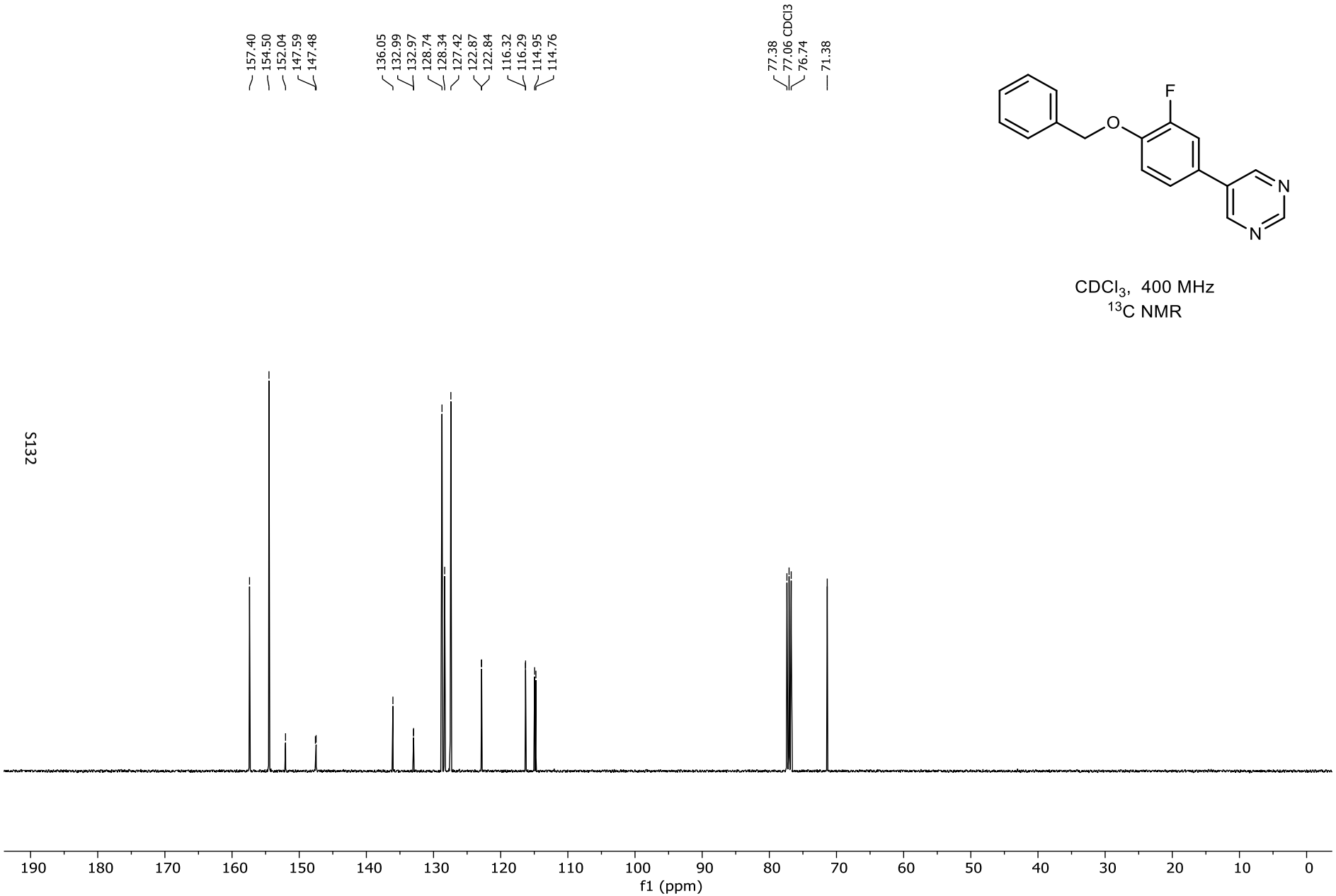

9.16
8.92
7.83
7.82
7.81
7.80
7.80
7.51
7.51
7.50
7.26 CDCl3
Br
N
Ph
N
CDCl3, 400 MHz
1H NMR
1.01
1.00
2.02
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

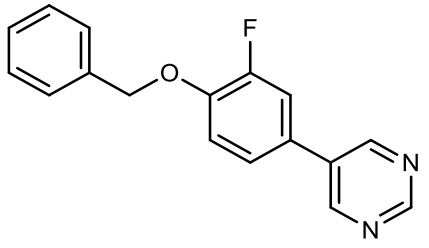

164.41
160.25
157.01
136.87
130.44
129.38
128.39
119.28
77.16 CDCl3
Br
N
Ph
N
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.10
8.60
8.58
7.26 CDCl3
7.16
7.15
2.67
2.65
2.64
2.63
2.61
1.96
1.93
1.87
1.84
1.77
1.77
1.74
1.74
1.73
1.55
1.54
1.52
1.51
1.49
1.48
1.46
1.45
1.44
1.42
1.41
1.40
1.39
1.38
1.37
1.36
1.35
1.34
1.32
1.31
1.30
1.29
1.28
1.27
1.26
1.25
1.24
1.23
1.22
1.21
N
N
CDCl3, 400 MHz
1H NMR
S129
1.00
1.00
1.03
1.02
2.11
2.16
1.12
5.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


174.63
158.64
156.88
118.88
77.48
77.16 CDCl3
77.16
76.84
46.00
32.08
26.26
25.91
N
N
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.10
8.81
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
7.17
7.07
7.05
7.03
5.13
F
O
N
N
CDCl3, 400 MHz
1H NMR
S131
1.00
2.00
2.00
2.00
2.00
1.00
1.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


157.40
154.50
152.04
147.59
147.48
136.05
132.99
132.97
128.74
128.34
127.42
122.87
122.84
116.32
116.29
114.95
114.76
77.38
77.06 CDCl3
76.74
71.38
F
O
N
N
CDCl3, 400 MHz
13C NMR
S132
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

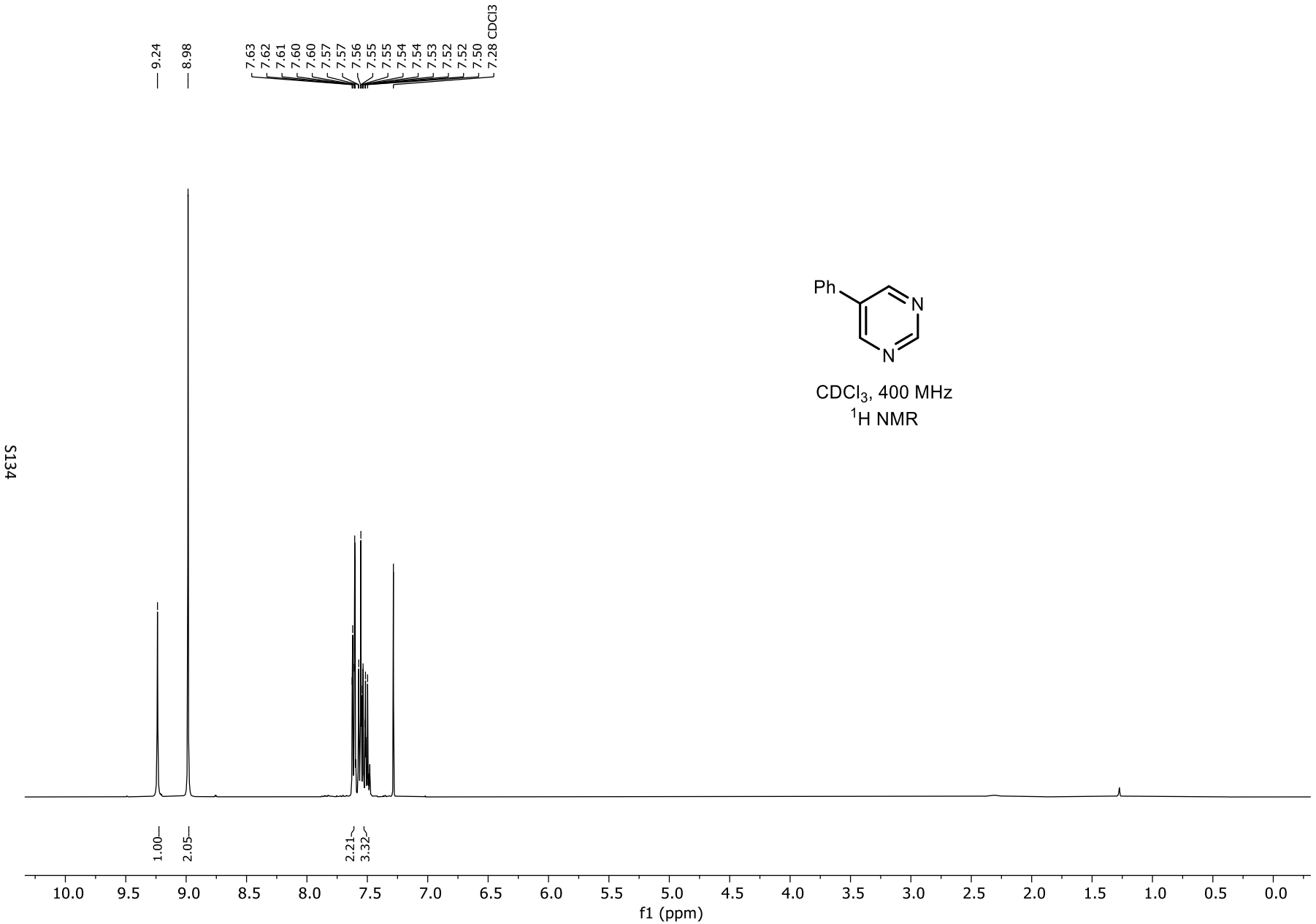


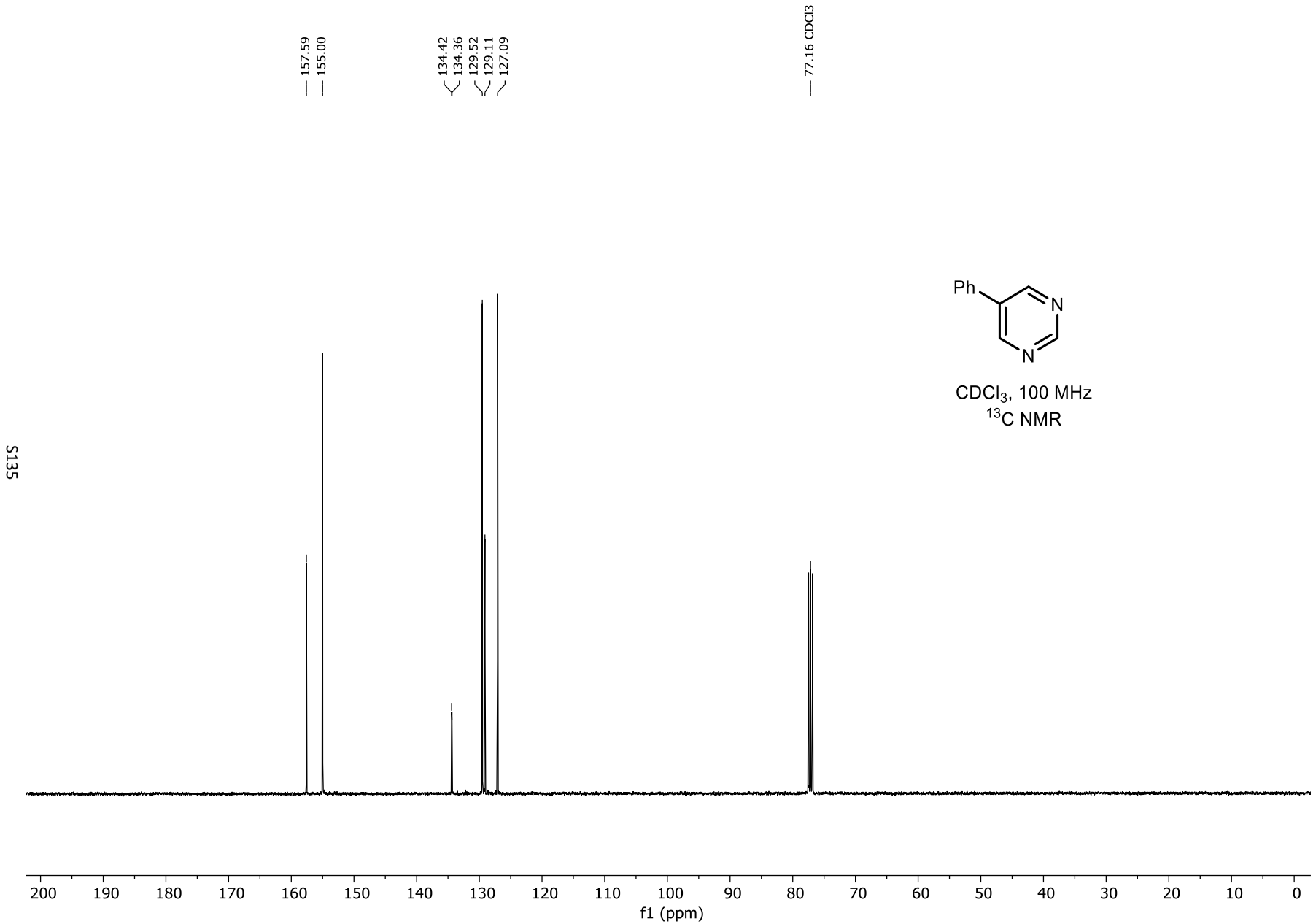
$CDCl_3$, 400 MHz
^{19}F NMR

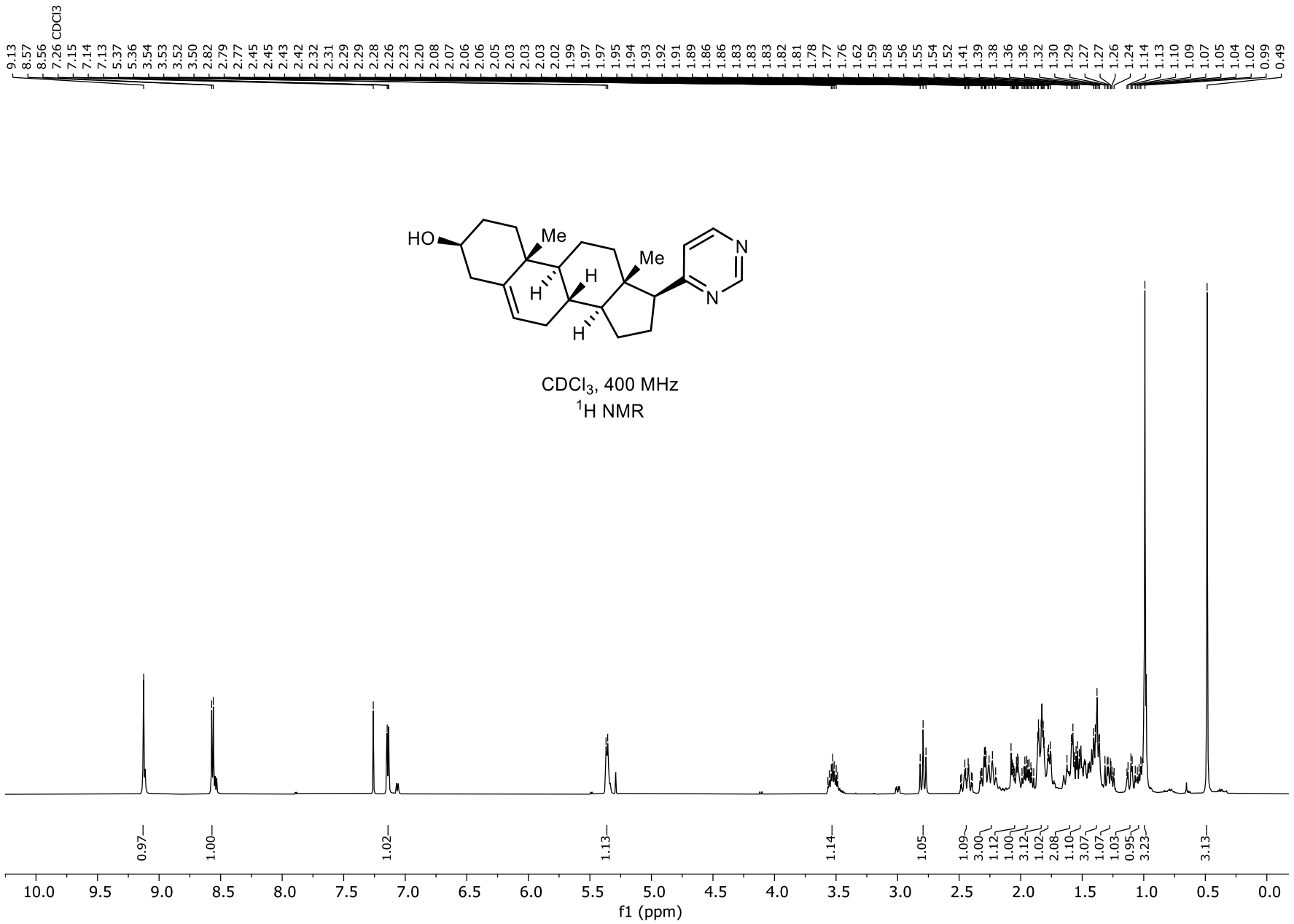
-131.77
-131.80
-131.81
-131.83

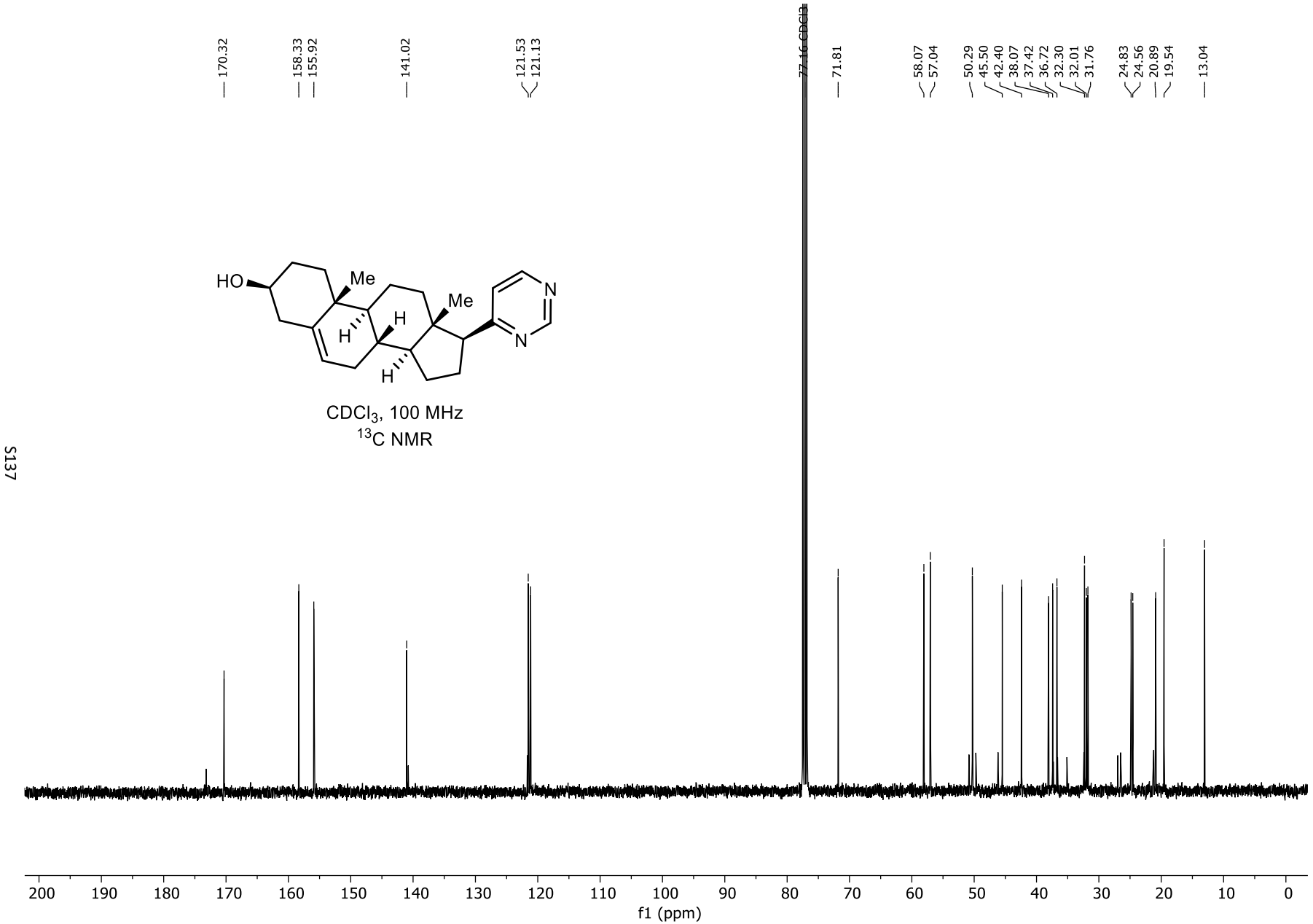
S133

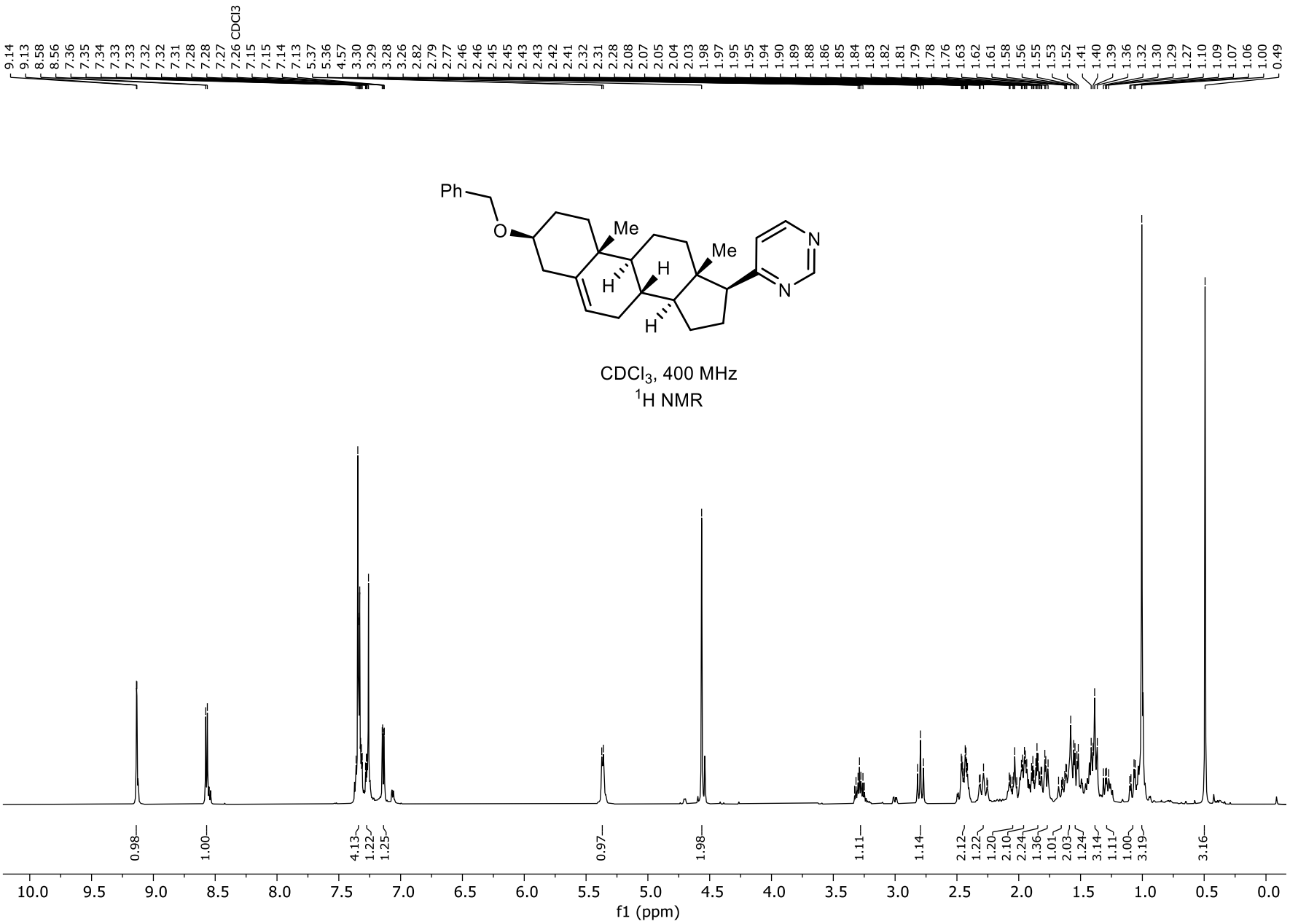
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

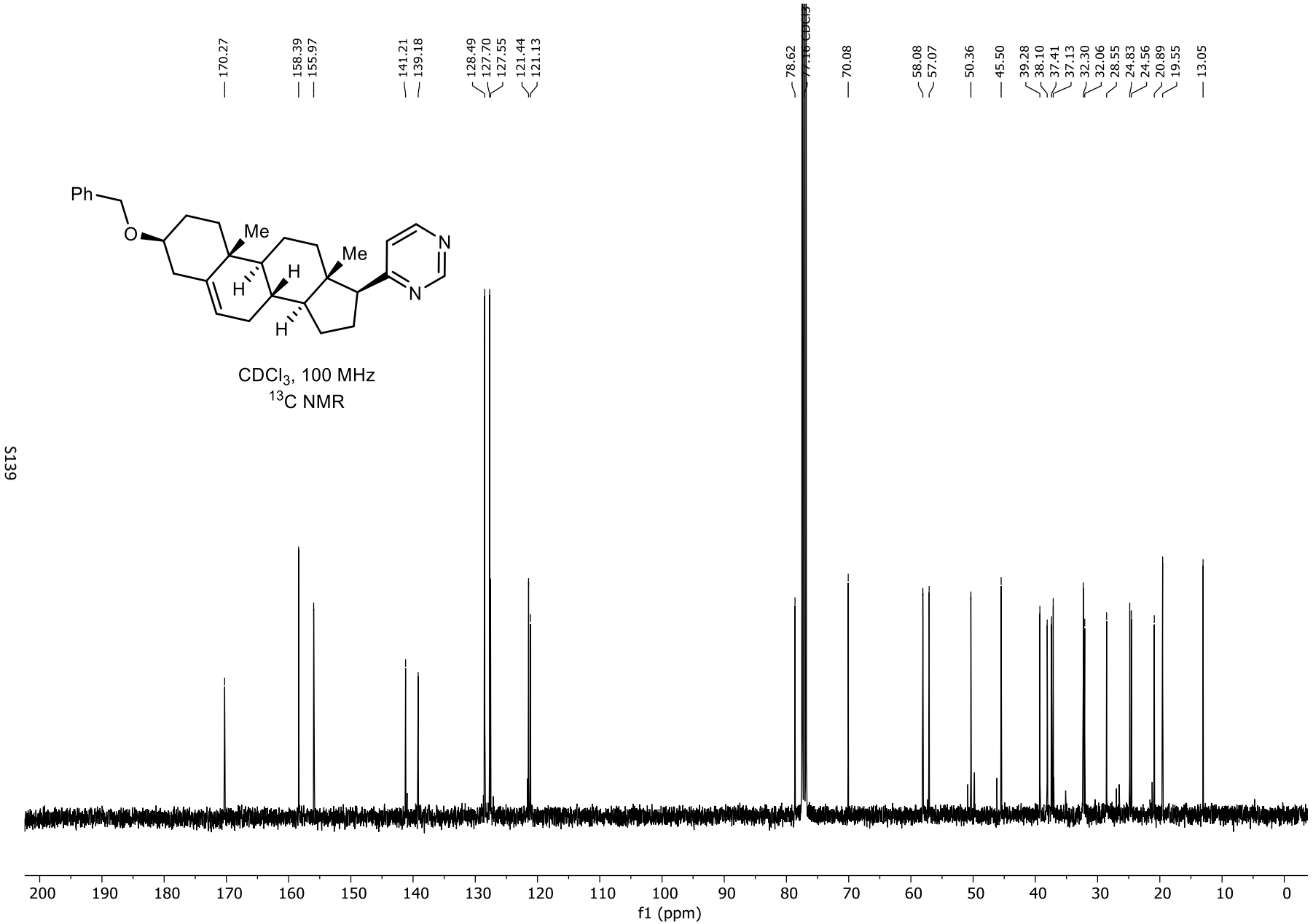

9.24
8.98
7.63
7.62
7.61
7.60
7.60
7.57
7.57
7.56
7.55
7.55
7.54
7.54
7.53
7.52
7.52
7.50
7.28 CDCl3
Ph
N
N
CDCl3, 400 MHz
1H NMR
1.00
2.05
2.21
3.32
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

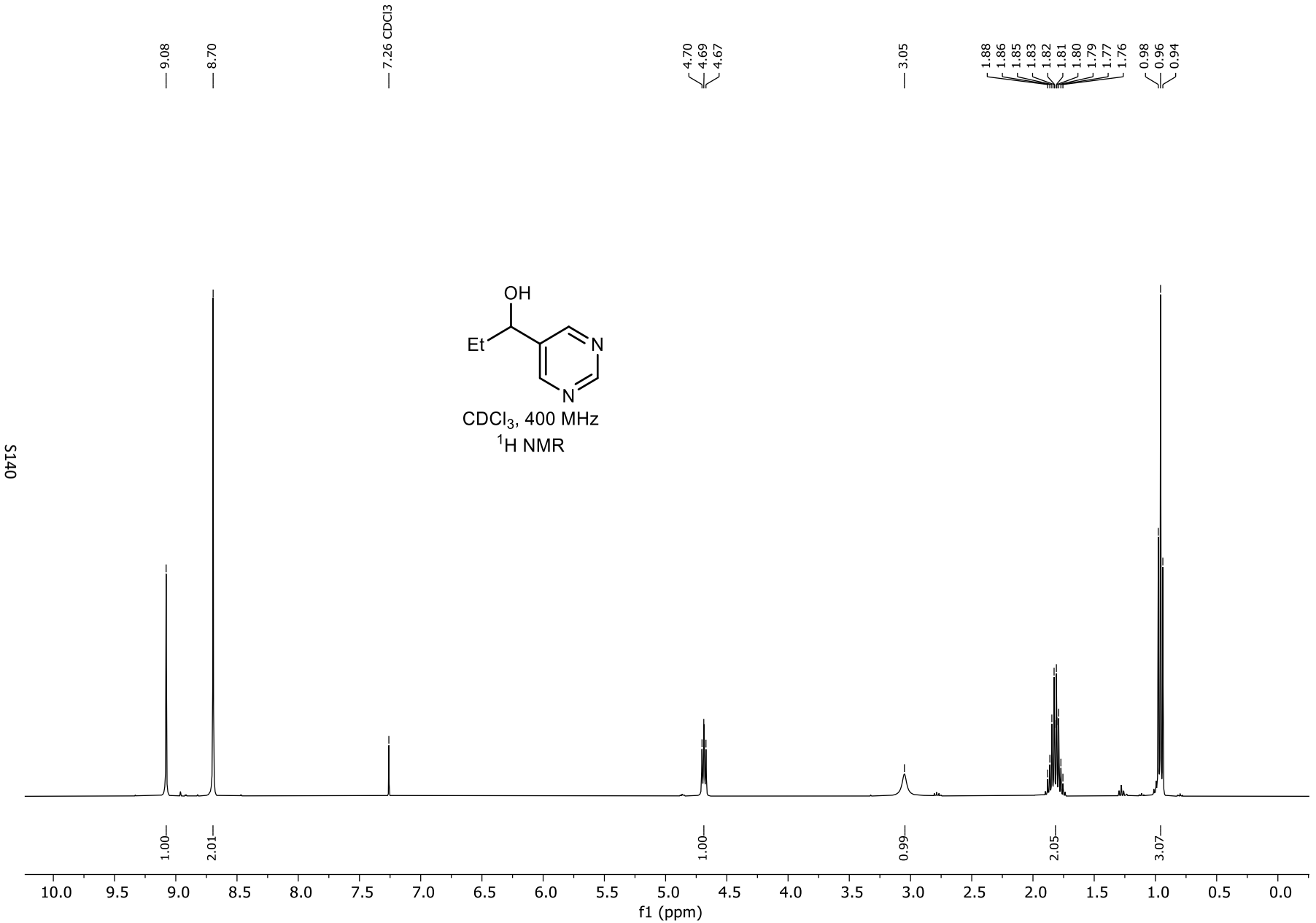

157.59
155.00
134.42
134.36
129.52
129.11
127.09
77.16 CDCl3
Ph
N
N
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

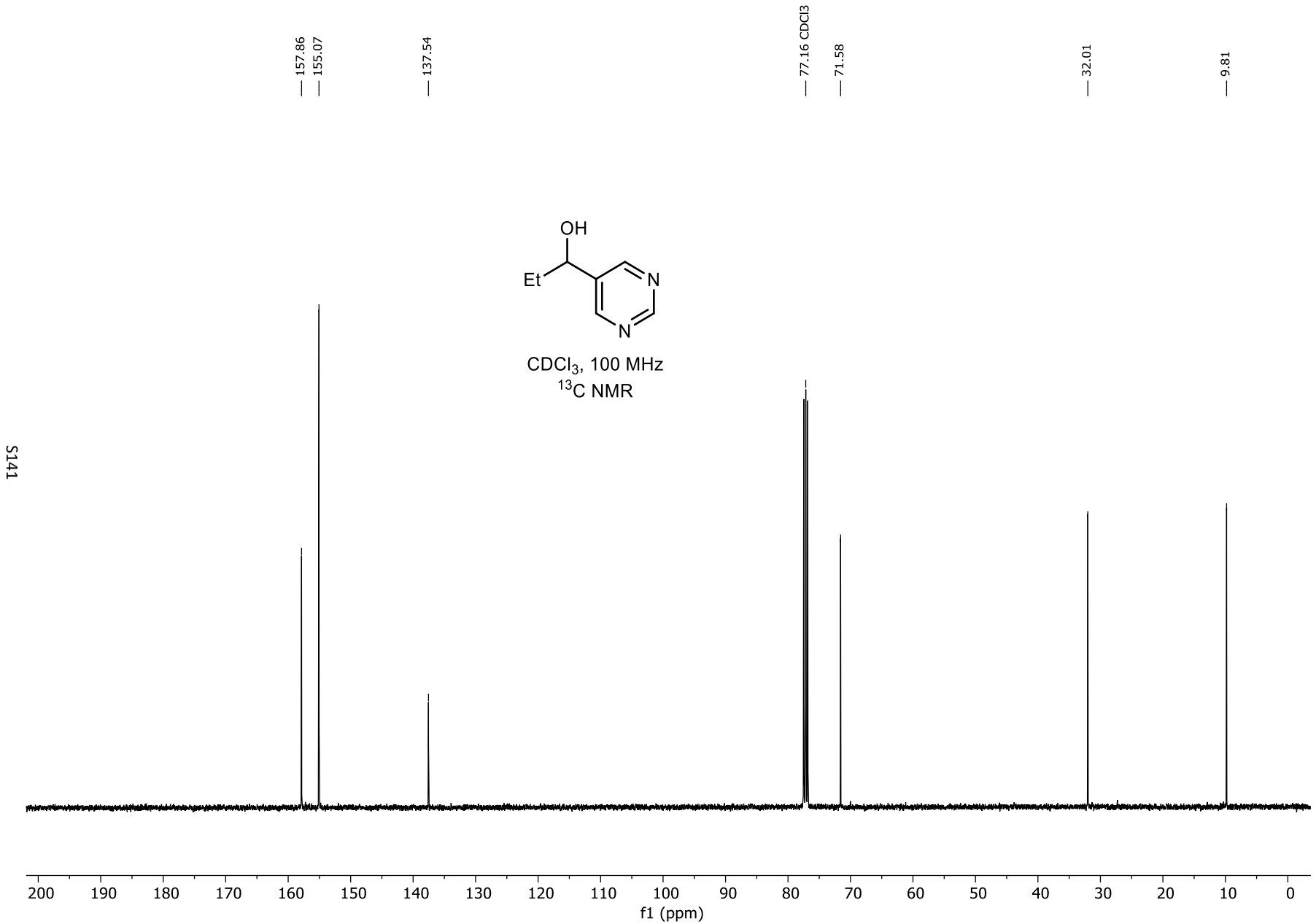

9.13 8.57 8.56 CDCl3 7.26 7.15 7.14 7.13 5.37 5.36 3.54 3.53 3.52 3.50 2.82 2.79 2.77 2.45 2.45 2.43 2.42 2.32 2.31 2.29 2.29 2.28 2.26 2.23 2.20 2.08 2.07 2.06 2.06 2.05 2.03 2.03 2.03 2.02 1.99 1.97 1.97 1.95 1.94 1.93 1.92 1.91 1.89 1.86 1.86 1.83 1.83 1.83 1.82 1.81 1.78 1.77 1.76 1.62 1.59 1.58 1.56 1.55 1.54 1.52 1.41 1.39 1.38 1.36 1.36 1.32 1.30 1.29 1.27 1.27 1.26 1.24 1.14 1.13 1.10 1.09 1.07 1.05 1.04 1.02 0.99 0.49
HO
Me
Me
H
H
H
N
N
CDCl3, 400 MHz
1H NMR
0.97
1.00
1.02
1.13
1.14
1.05
1.09
3.00
1.12
1.00
3.12
1.02
2.08
1.10
3.07
1.07
1.03
0.95
3.23
3.13
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

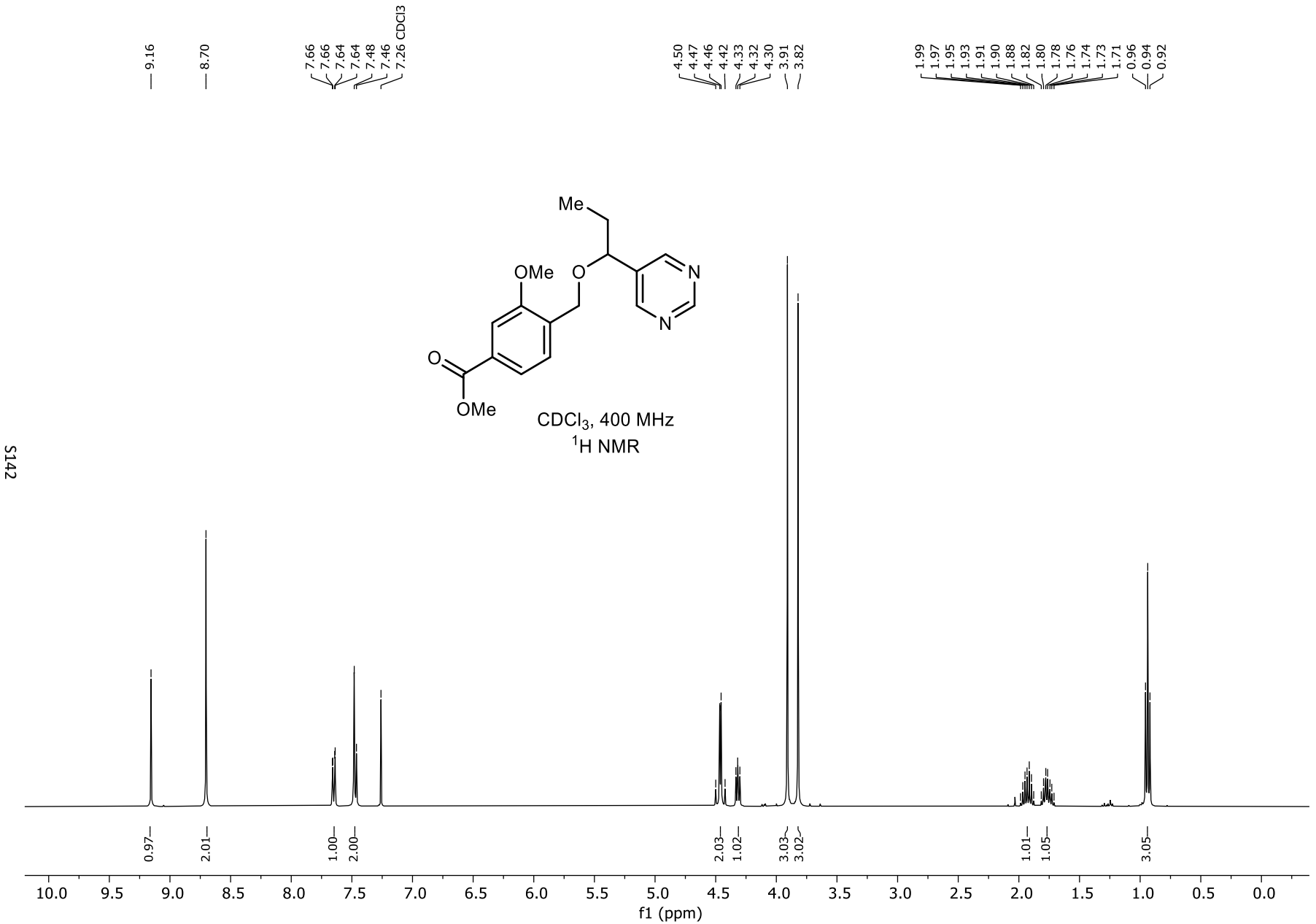

170.32
158.33
155.92
141.02
121.53
121.13
77.16 CDCl3
71.81
58.07
57.04
50.29
45.50
42.40
38.07
37.42
36.72
32.30
32.01
31.76
24.83
24.56
20.89
19.54
13.04
HO
Me
Me
H
H
H
N
N
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

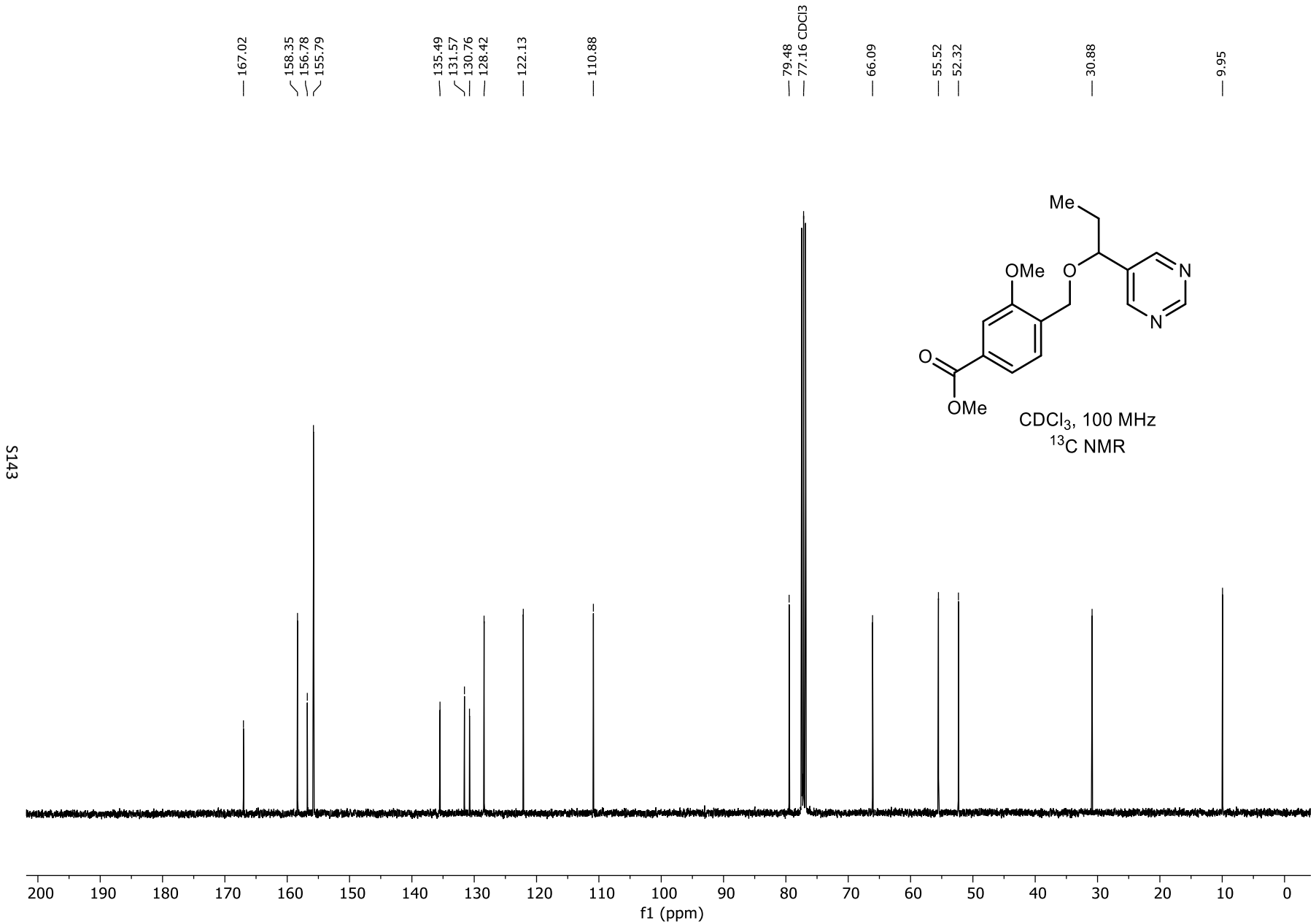

9.14 9.13 8.58 8.56 7.36 7.35 7.34 7.33 7.33 7.32 7.32 7.31 7.28 7.28 7.27 7.26 CDCl3 7.15 7.15 7.14 7.13 5.37 5.36 4.57 3.30 3.29 3.28 3.26 2.82 2.79 2.77 2.46 2.46 2.45 2.45 2.43 2.43 2.42 2.41 2.32 2.31 2.28 2.08 2.07 2.05 2.04 2.03 1.98 1.97 1.95 1.95 1.94 1.90 1.89 1.88 1.86 1.85 1.84 1.83 1.82 1.81 1.79 1.78 1.76 1.63 1.62 1.61 1.58 1.56 1.55 1.53 1.52 1.41 1.40 1.39 1.36 1.32 1.30 1.29 1.27 1.10 1.09 1.07 1.06 1.00 0.49
Ph
O
Me
Me
H
H
H
N
N
CDCl3, 400 MHz
1H NMR
S138
0.98
1.00
4.13
1.22
1.25
0.97
1.98
1.11
1.14
2.12
1.22
1.20
2.10
2.24
1.36
1.01
2.03
1.24
3.14
1.11
1.00
3.19
3.16
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

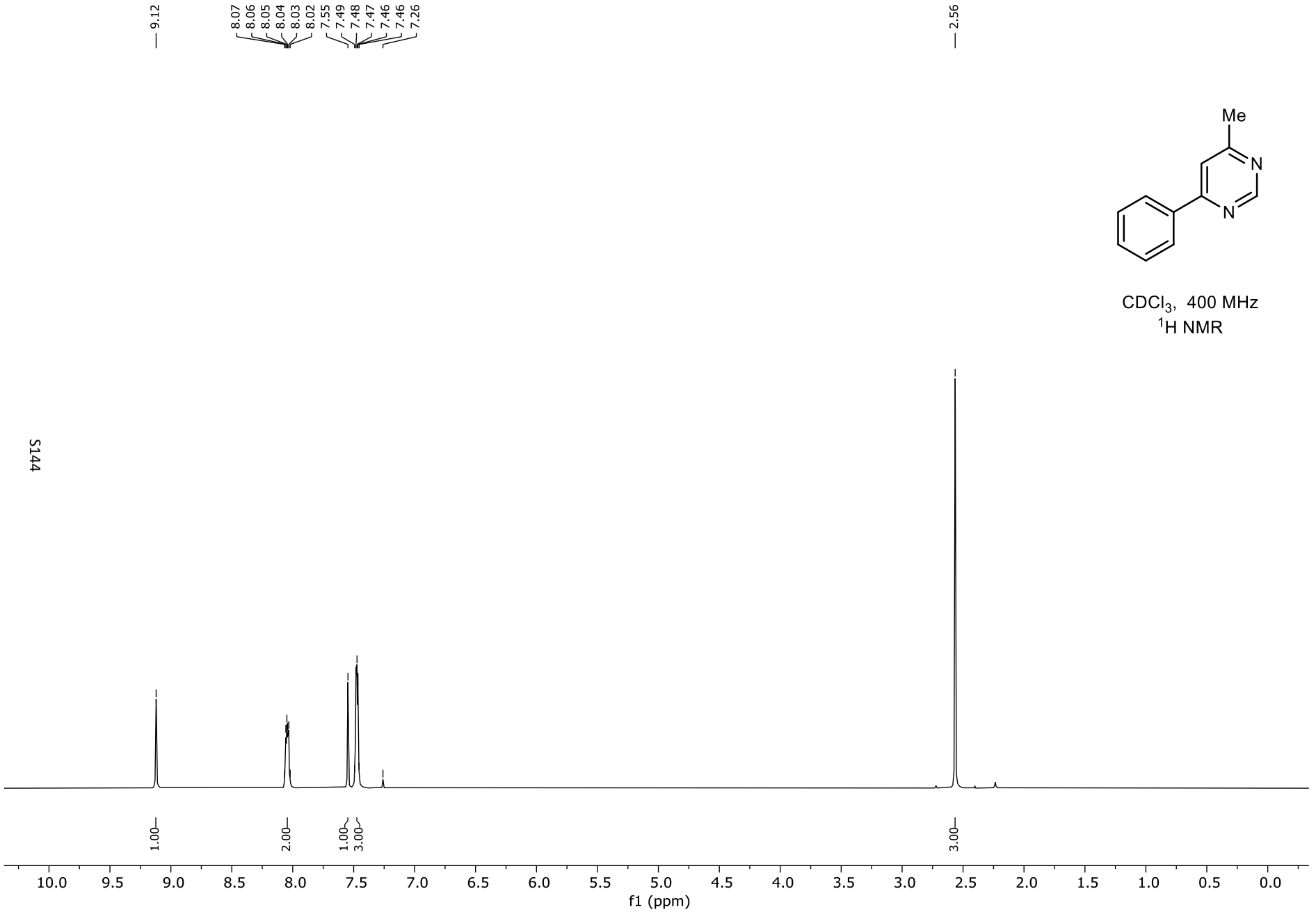

170.27
158.39
155.97
141.21
139.18
128.49
127.70
127.55
121.44
121.13
78.62
77.16 CDCl3
70.08
58.08
57.07
50.36
45.50
39.28
38.10
37.41
37.13
32.30
32.06
28.55
24.83
24.56
20.89
19.55
13.05
Ph
O
Me
Me
H
H
H
N
N
CDCl3, 100 MHz
13C NMR
f1 (ppm)

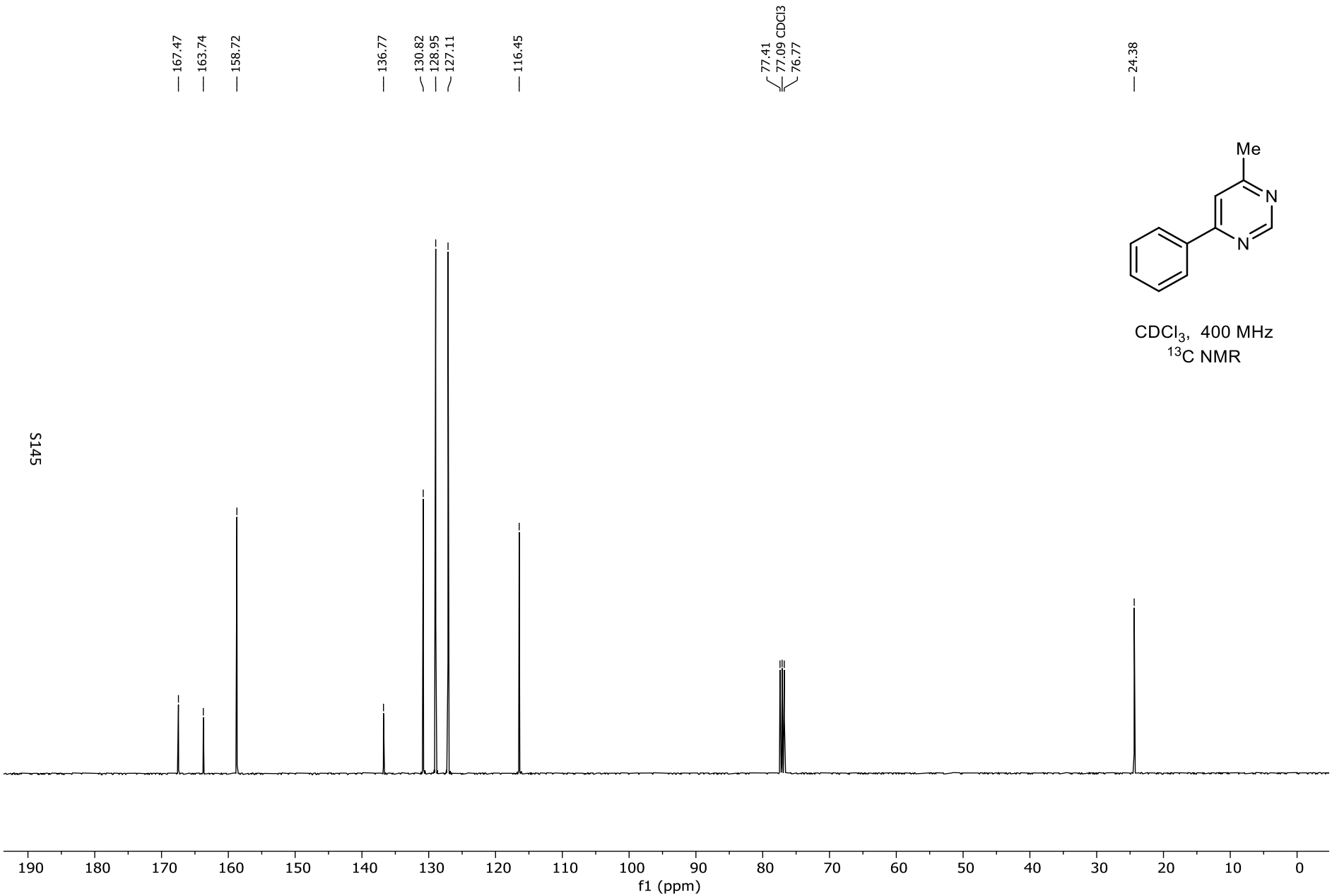

9.08
8.70
7.26 CDCl3
4.70
4.69
4.67
3.05
1.88
1.86
1.85
1.83
1.82
1.81
1.80
1.79
1.77
1.76
0.98
0.96
0.94
OH
Et
N
N
CDCl3, 400 MHz
1H NMR
1.00
2.01
1.00
0.99
2.05
3.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

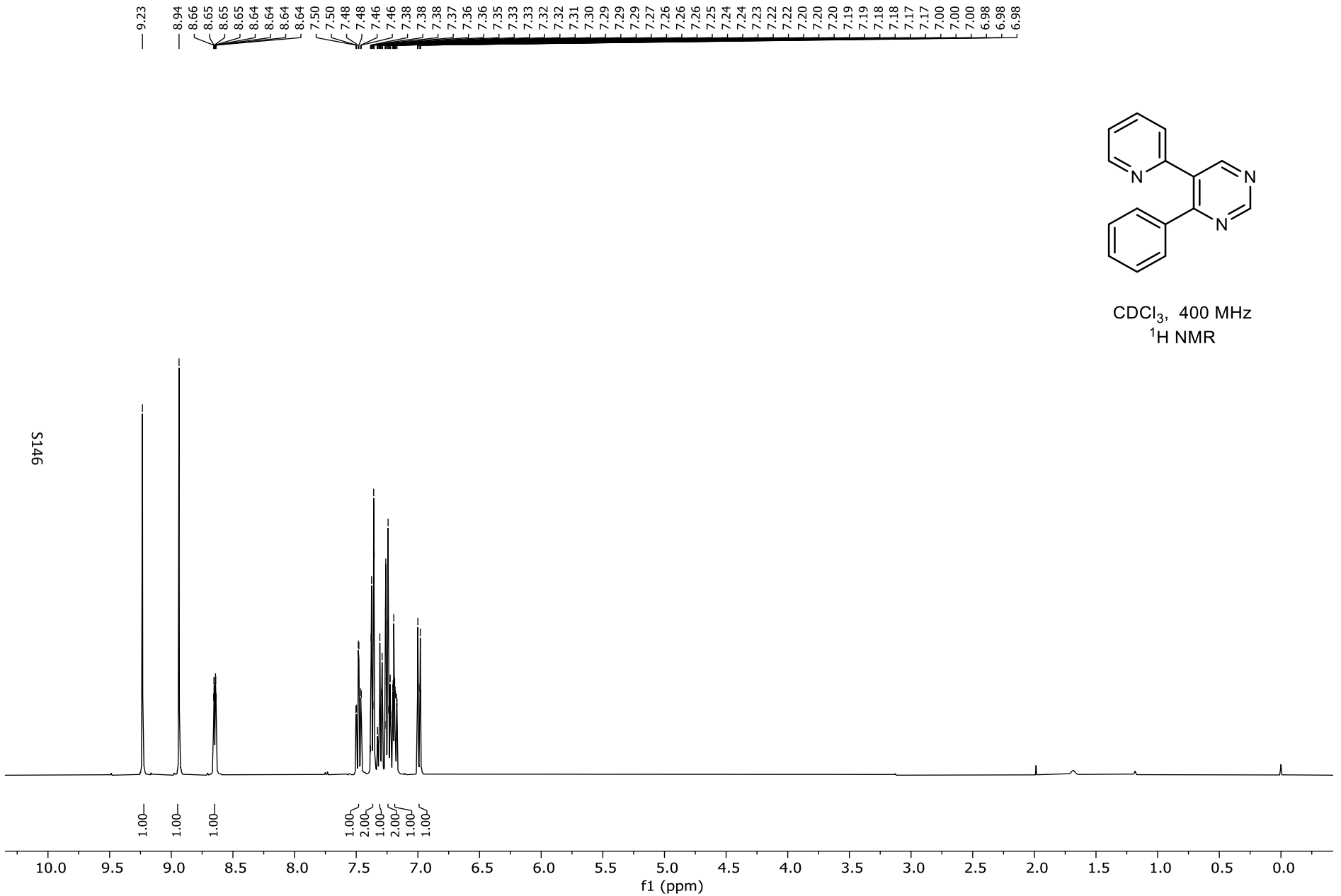

157.86
155.07
137.54
77.16 CDCl3
71.58
32.01
9.81
OH
Et
N
N
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

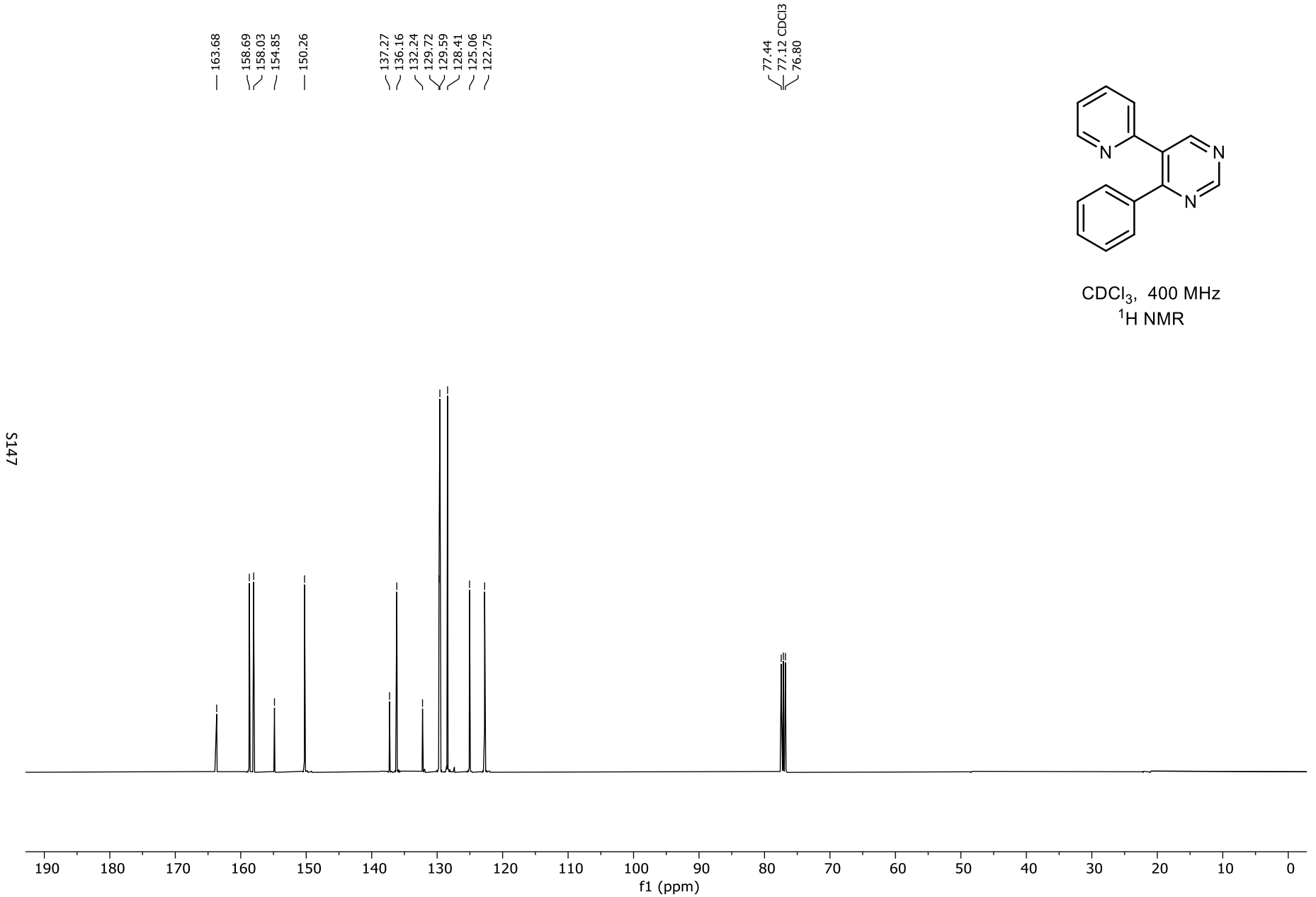

9.16
8.70
7.66
7.66
7.64
7.64
7.48
7.46
7.26 CDCl3
4.50
4.47
4.46
4.42
4.33
4.32
4.30
3.91
3.82
1.99
1.97
1.95
1.93
1.91
1.90
1.88
1.82
1.80
1.78
1.76
1.74
1.73
1.71
0.96
0.94
0.92
Me
OMe
O
N
N
O
OMe
CDCl3, 400 MHz
1H NMR
0.97
2.01
1.00
2.00
2.03
1.02
3.03
3.02
1.01
1.05
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

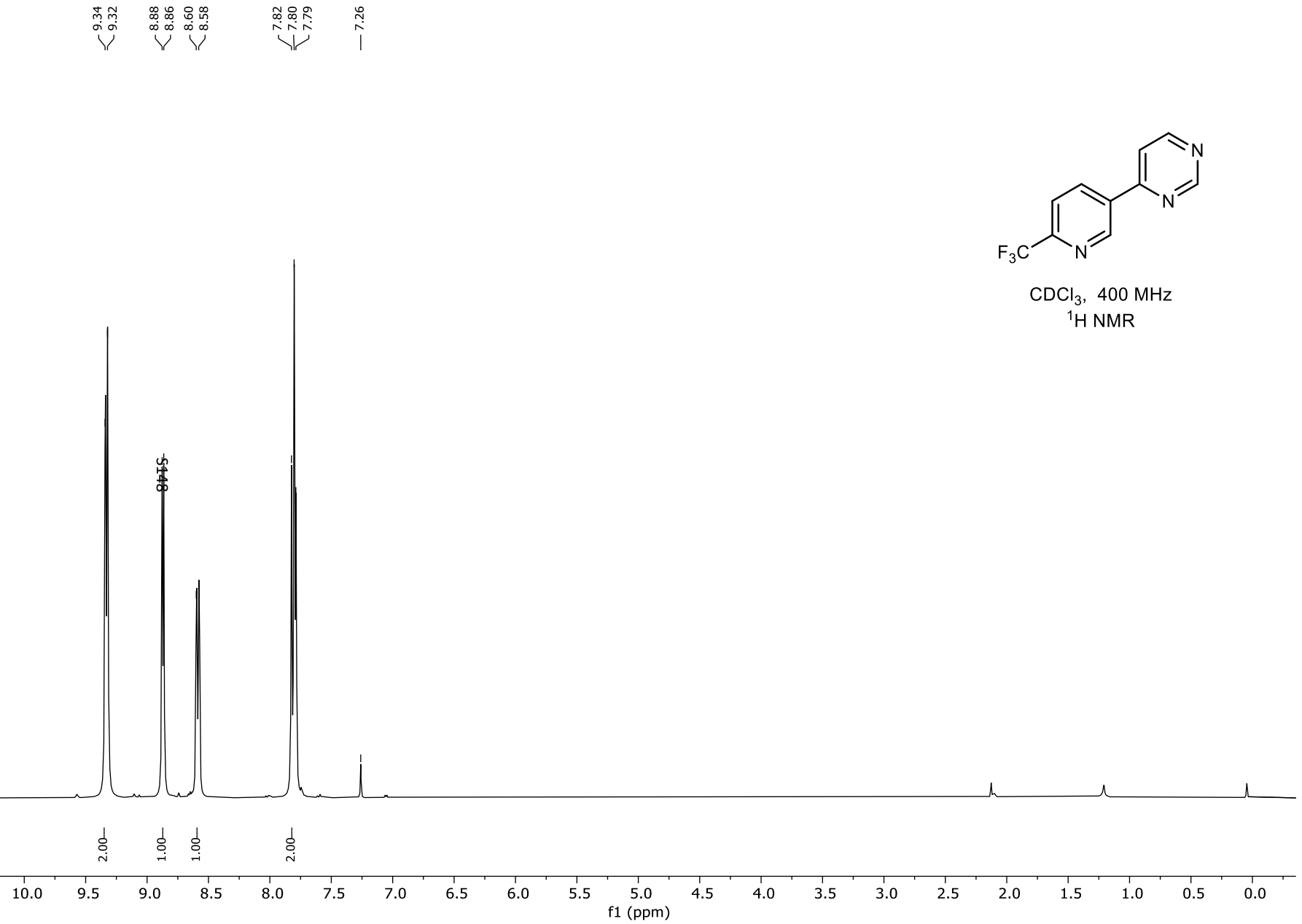

167.02
158.35
156.78
155.79
135.49
131.57
130.76
128.42
122.13
110.88
79.48
77.16 CDCl3
66.09
55.52
52.32
30.88
9.95
Me
OMe
O
N
N
O
OMe
CDCl3, 100 MHz
13C NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.12
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
Me
N
N
CDCl3, 400 MHz
1H NMR
1.00
2.00
1.00
3.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

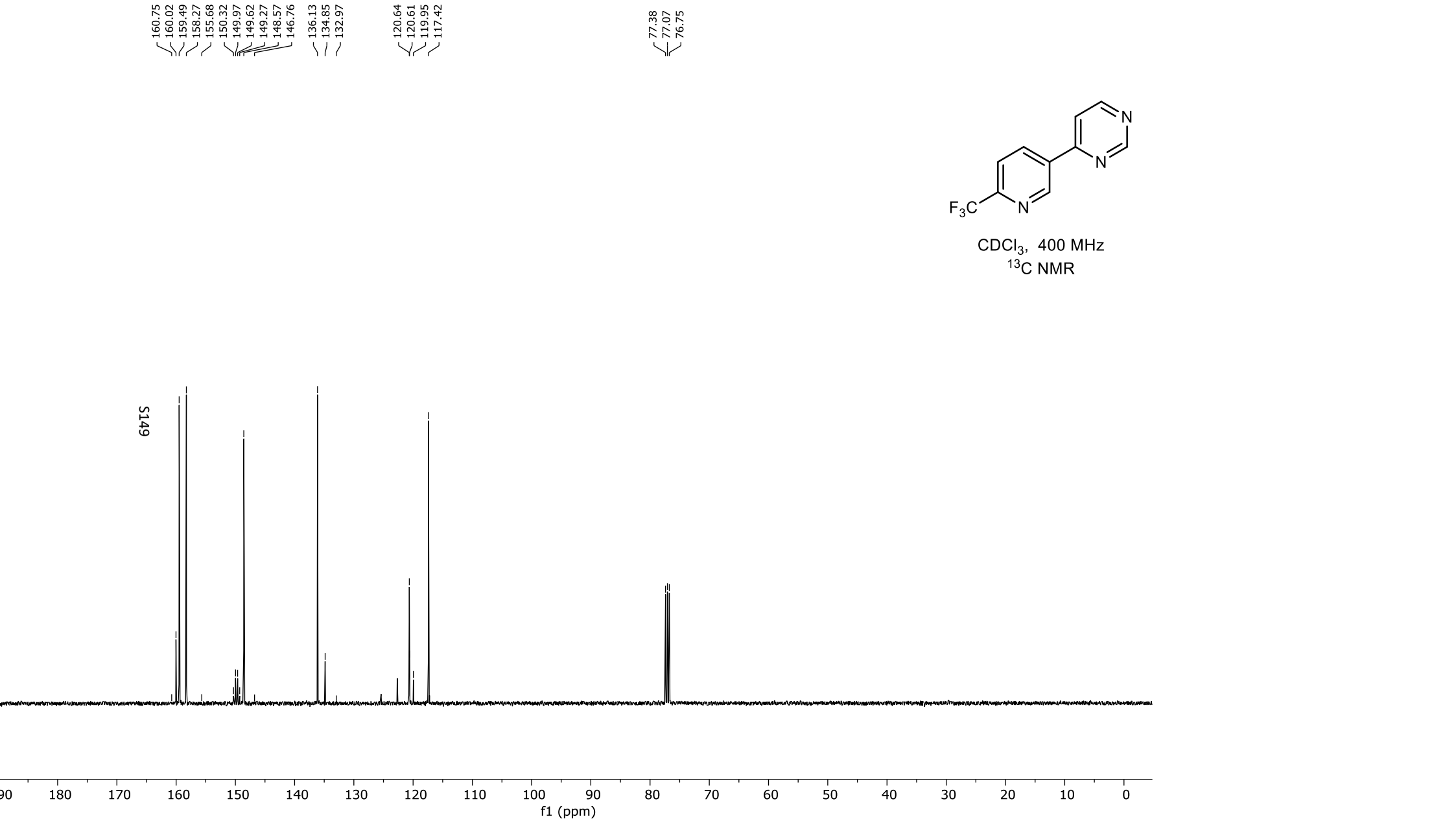

167.47
163.74
158.72
136.77
130.82
128.95
127.11
116.45
77.41
77.09 CDCl3
76.77
24.38
Me
N
N
CDCl3, 400 MHz
13C NMR
S145
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

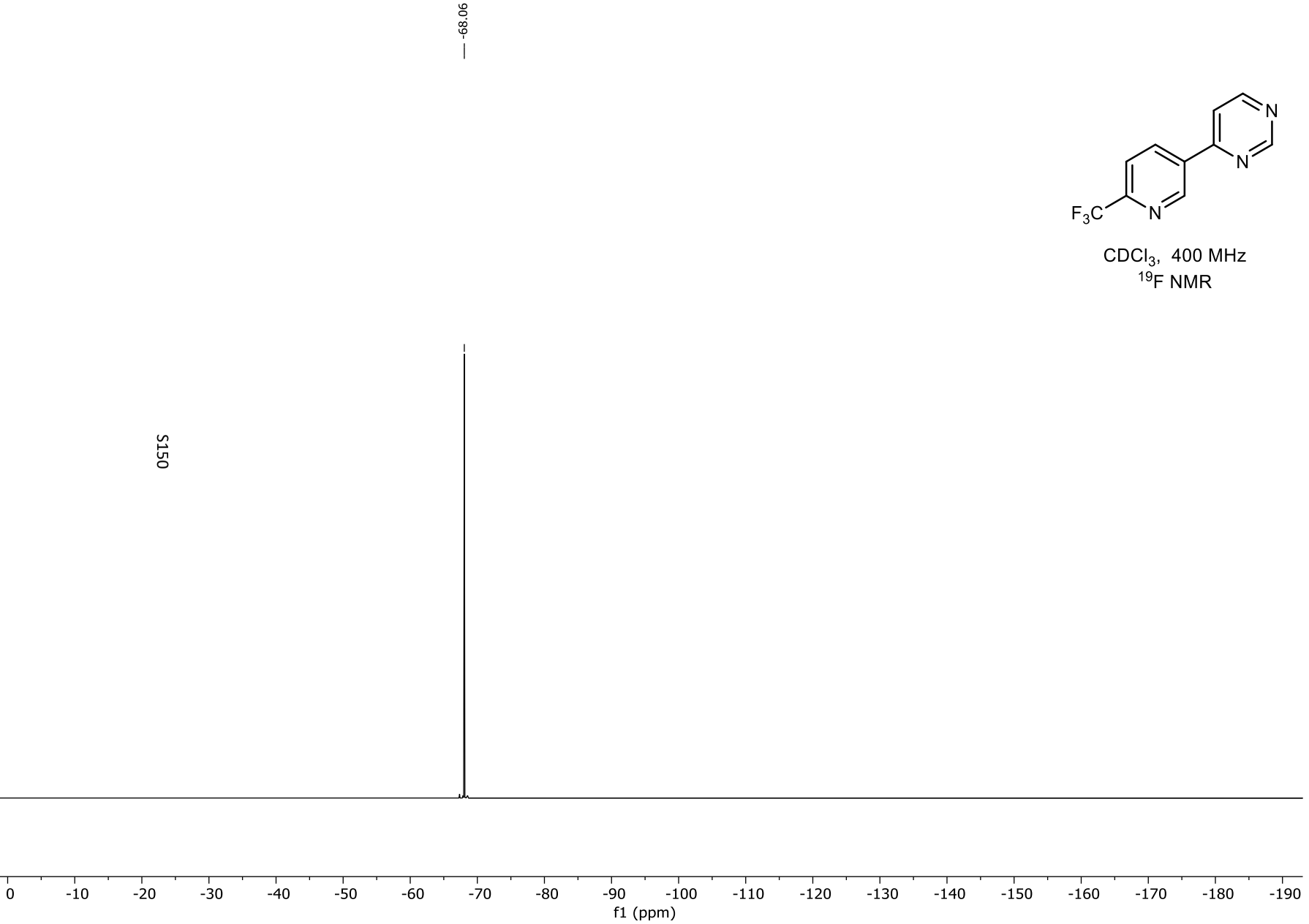

9.23
8.94
8.66
8.65
8.65
8.65
8.64
8.64
8.64
8.64
7.50
7.50
7.48
7.48
7.46
7.46
7.38
7.38
7.38
7.37
7.36
7.36
7.35
7.33
7.33
7.32
7.32
7.31
7.30
7.29
7.29
7.29
7.27
7.26
7.26
7.26
7.25
7.24
7.24
7.23
7.22
7.22
7.20
7.20
7.20
7.19
7.19
7.18
7.18
7.17
7.17
7.00
7.00
7.00
6.98
6.98
6.98
N
N
N
CDCl3, 400 MHz
1H NMR
S146
1.00
1.00
1.00
1.00
2.00
1.00
2.00
1.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


163.68
158.69
158.03
154.85
150.26
137.27
136.16
132.24
129.72
129.59
128.41
125.06
122.75
77.44
77.12 CDCl3
76.80
N
N
N
CDCl3, 400 MHz
1H NMR
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

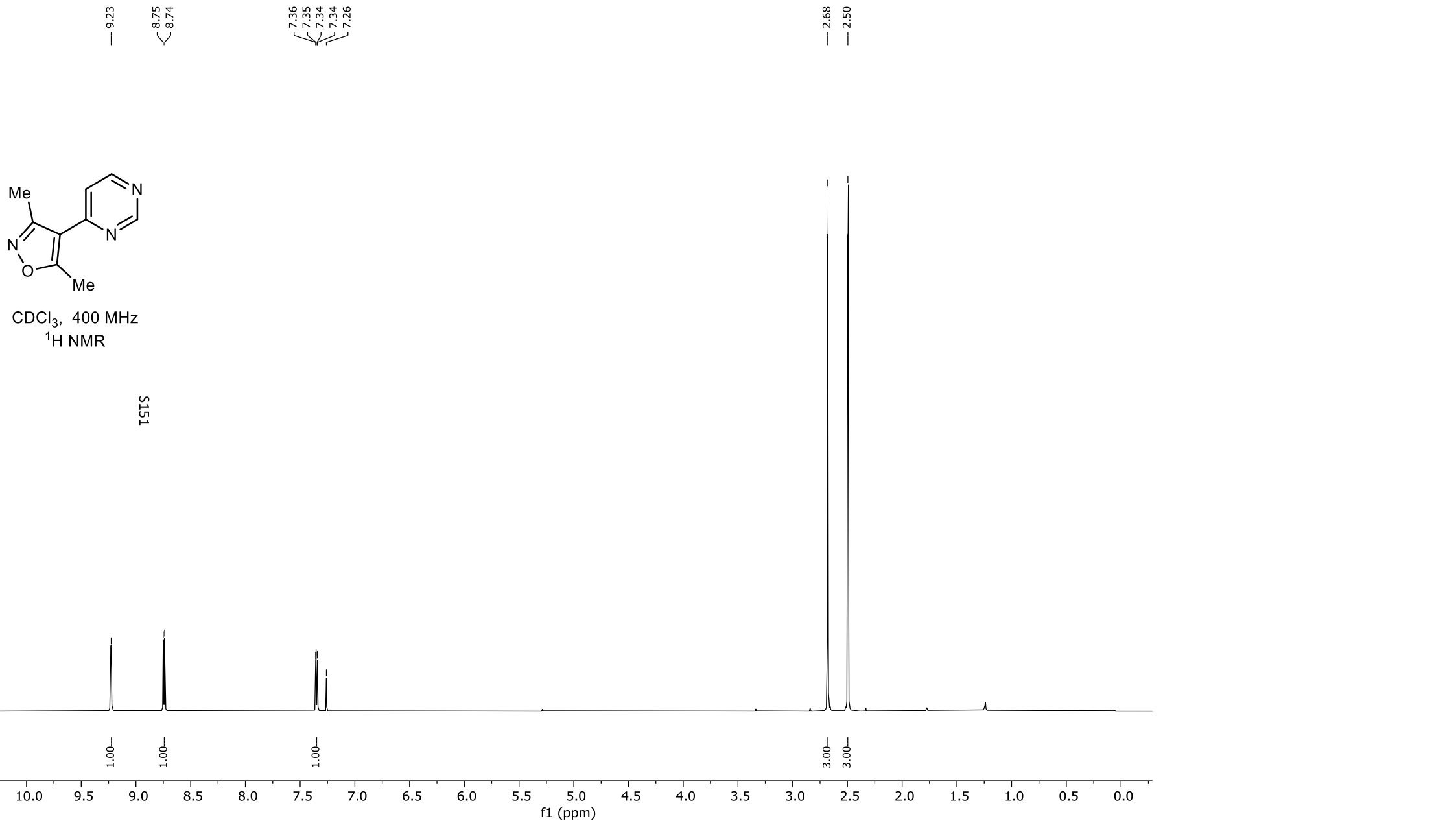


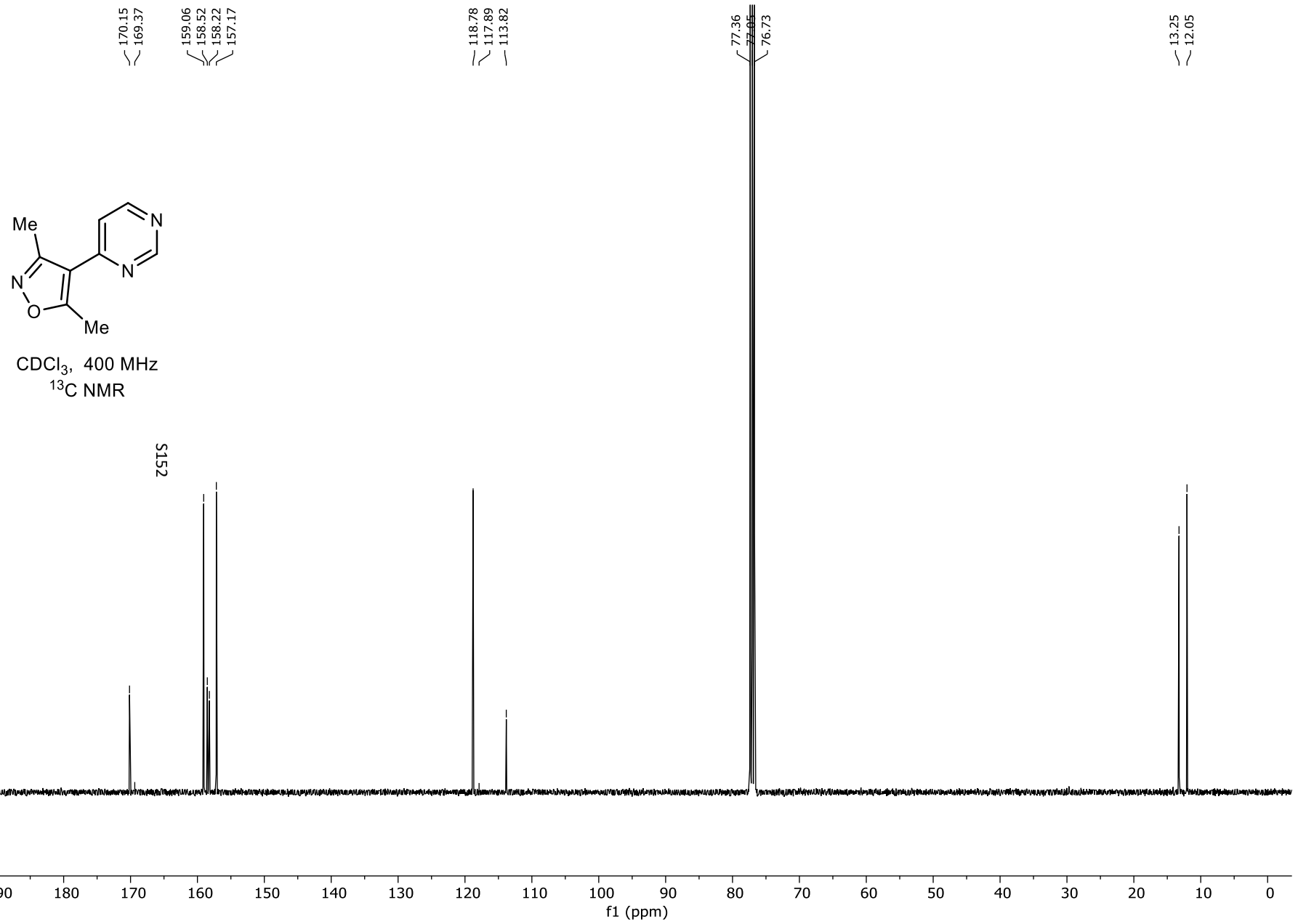
$CDCl_3$, 400 MHz
^1H NMR

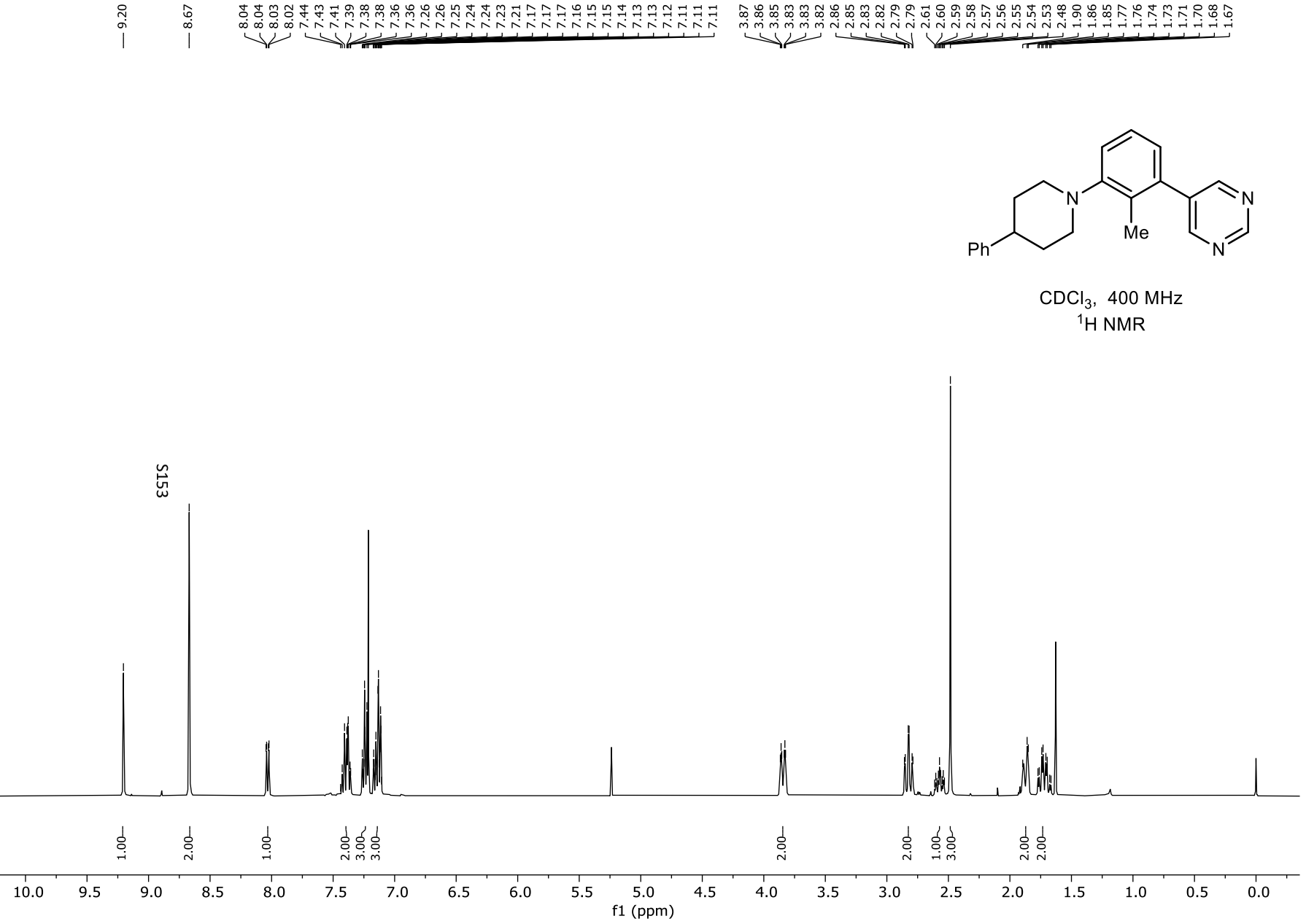

160.75
160.02
159.49
158.27
155.68
150.32
149.97
149.62
149.27
148.57
146.76
136.13
134.85
132.97
120.64
120.61
119.95
117.42
77.38
77.07
76.75
S149
N
N
F3C
N
CDCl3, 400 MHz
13C NMR
f1 (ppm)



$CDCl_3$, 400 MHz
^{19}F NMR

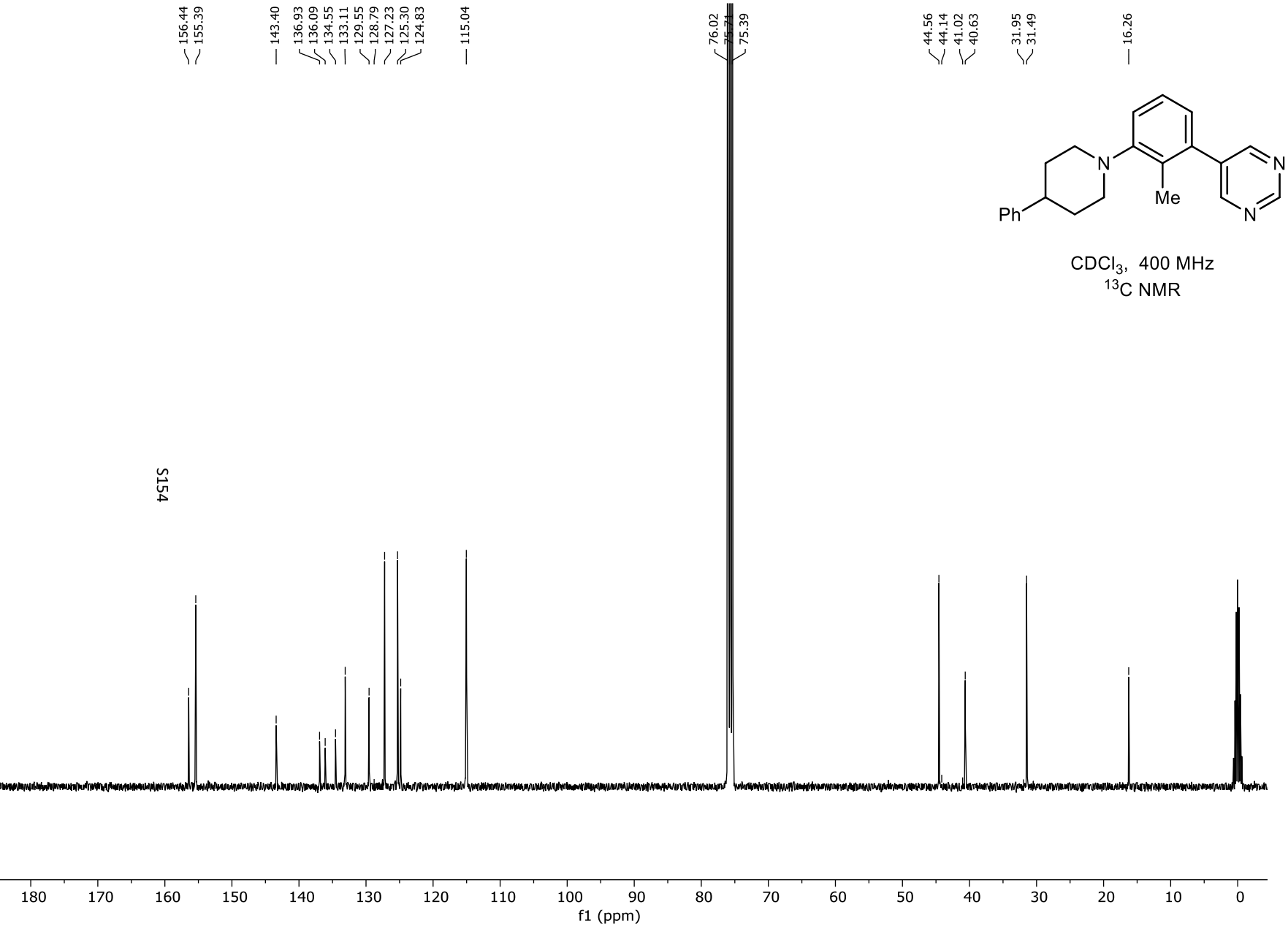

9.23
8.75
8.74
7.36
7.35
7.34
7.34
7.26
2.68
2.50
Me
N
N
N
O
Me
CDCl3, 400 MHz
1H NMR
S151
1.00
1.00
1.00
3.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

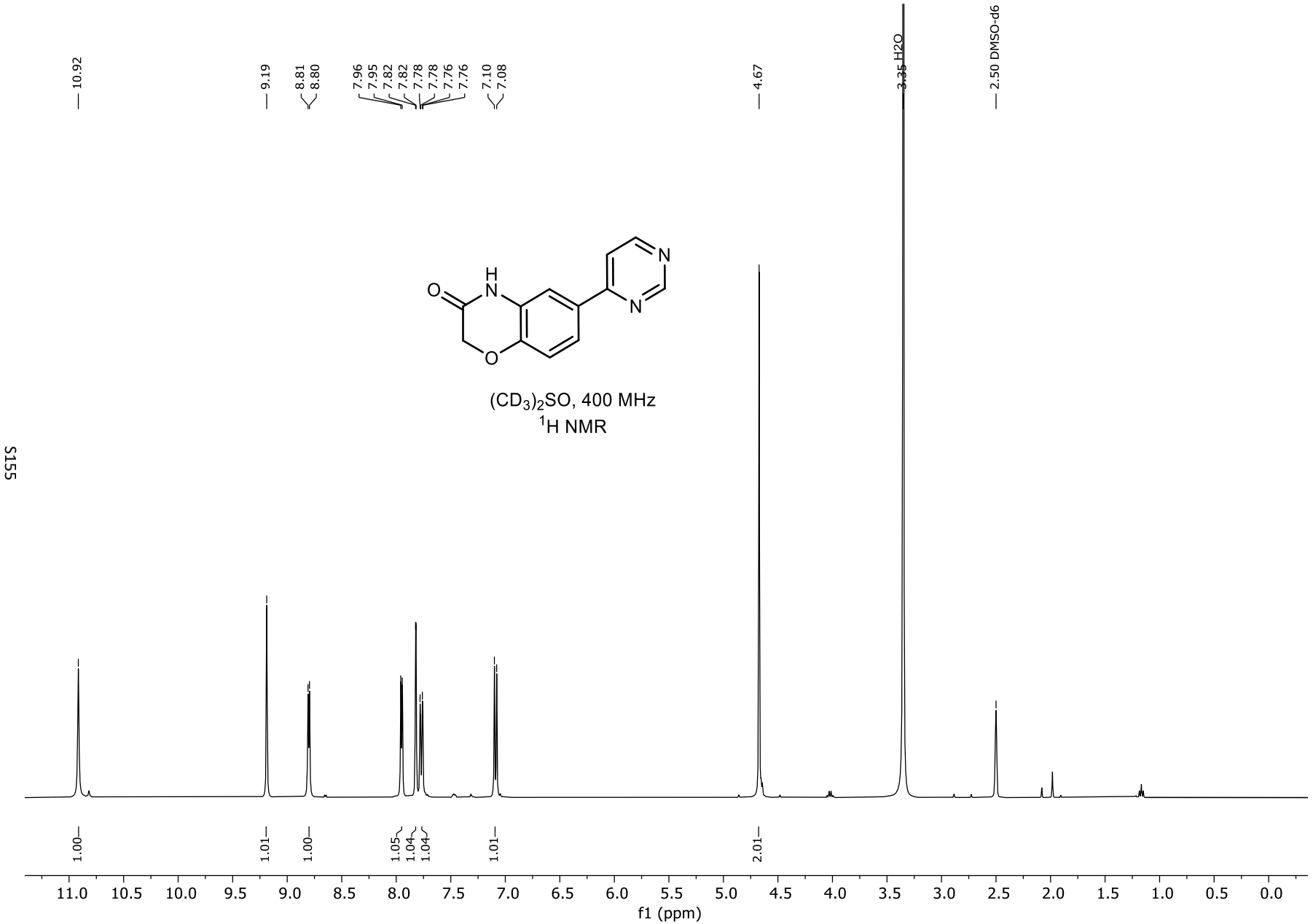

170.15
169.37
159.06
158.52
158.22
157.17
118.78
117.89
113.82
77.36
77.05
76.73
13.25
12.05
Me
N
N
N
O
Me
CDCl3, 400 MHz
13C NMR
S152
f1 (ppm)

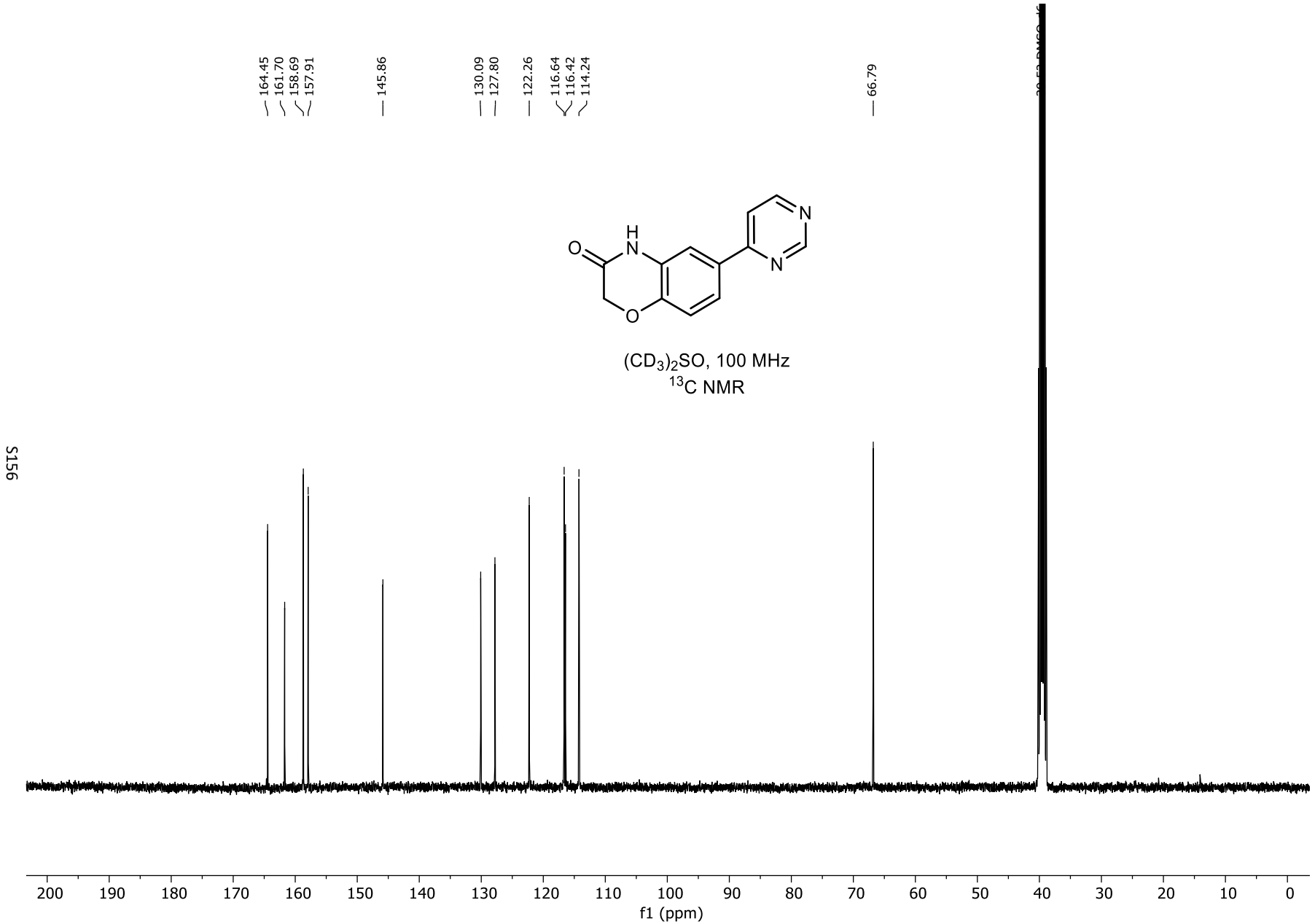


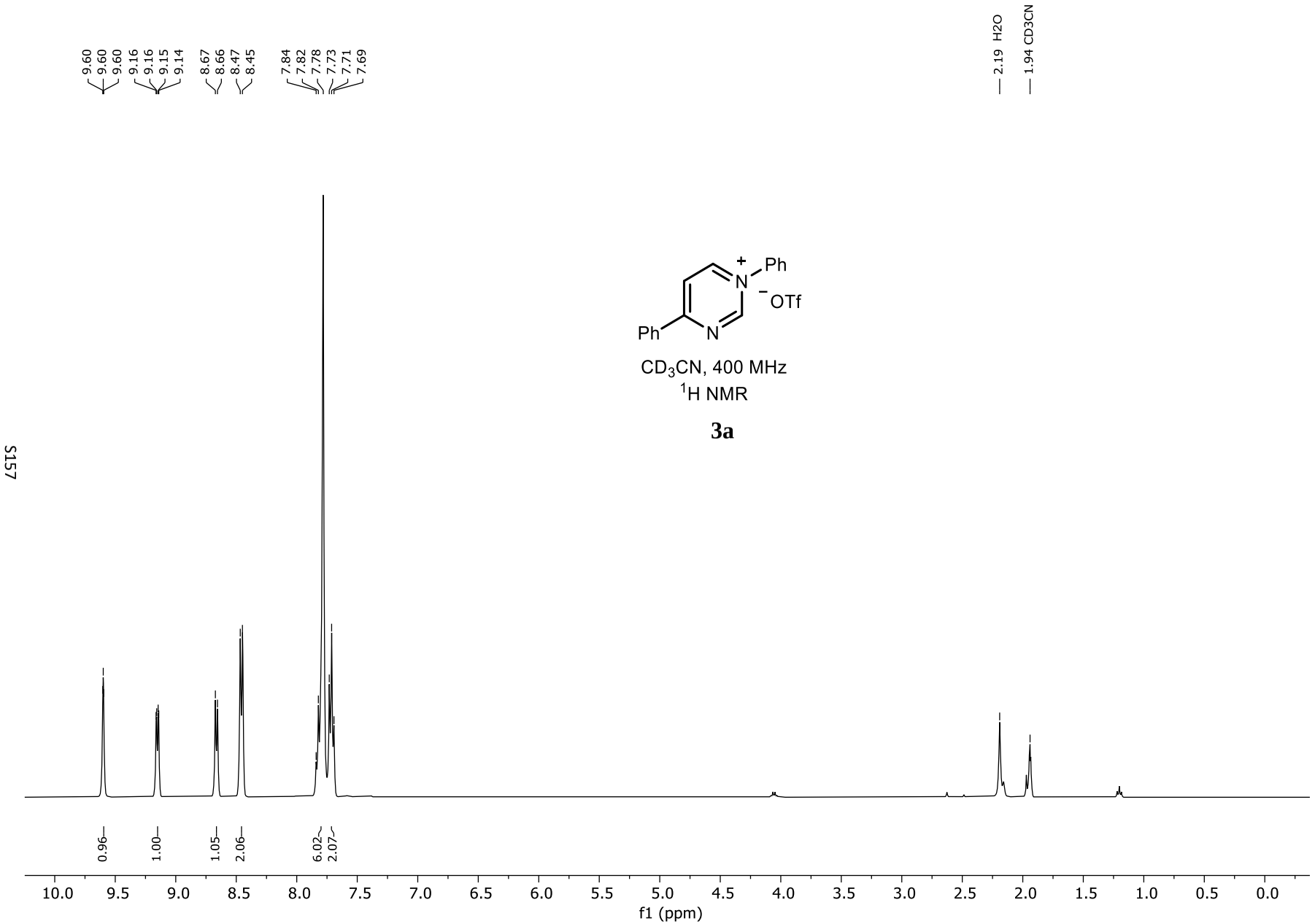
$CDCl_3$, 400 MHz

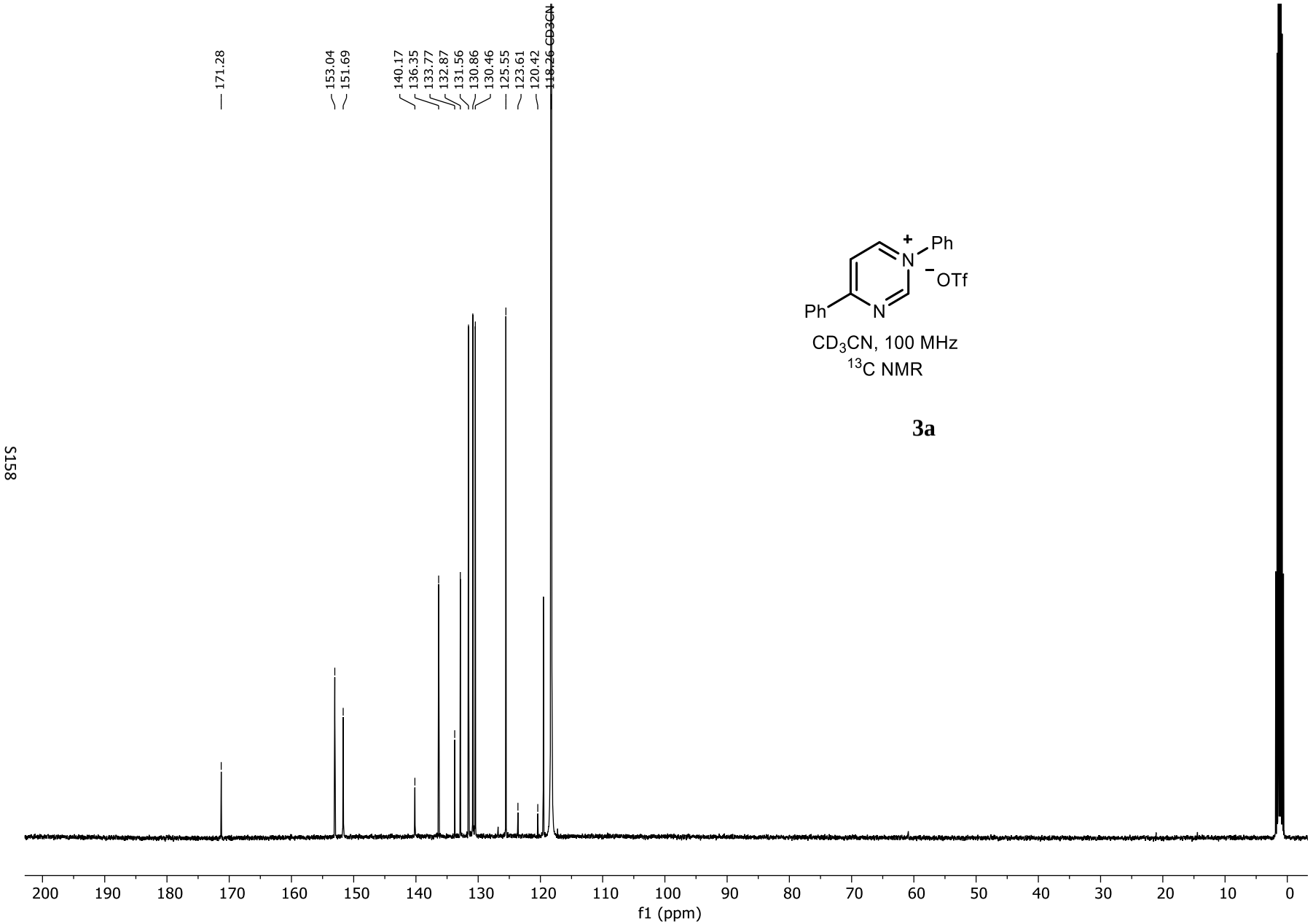
^1H NMR

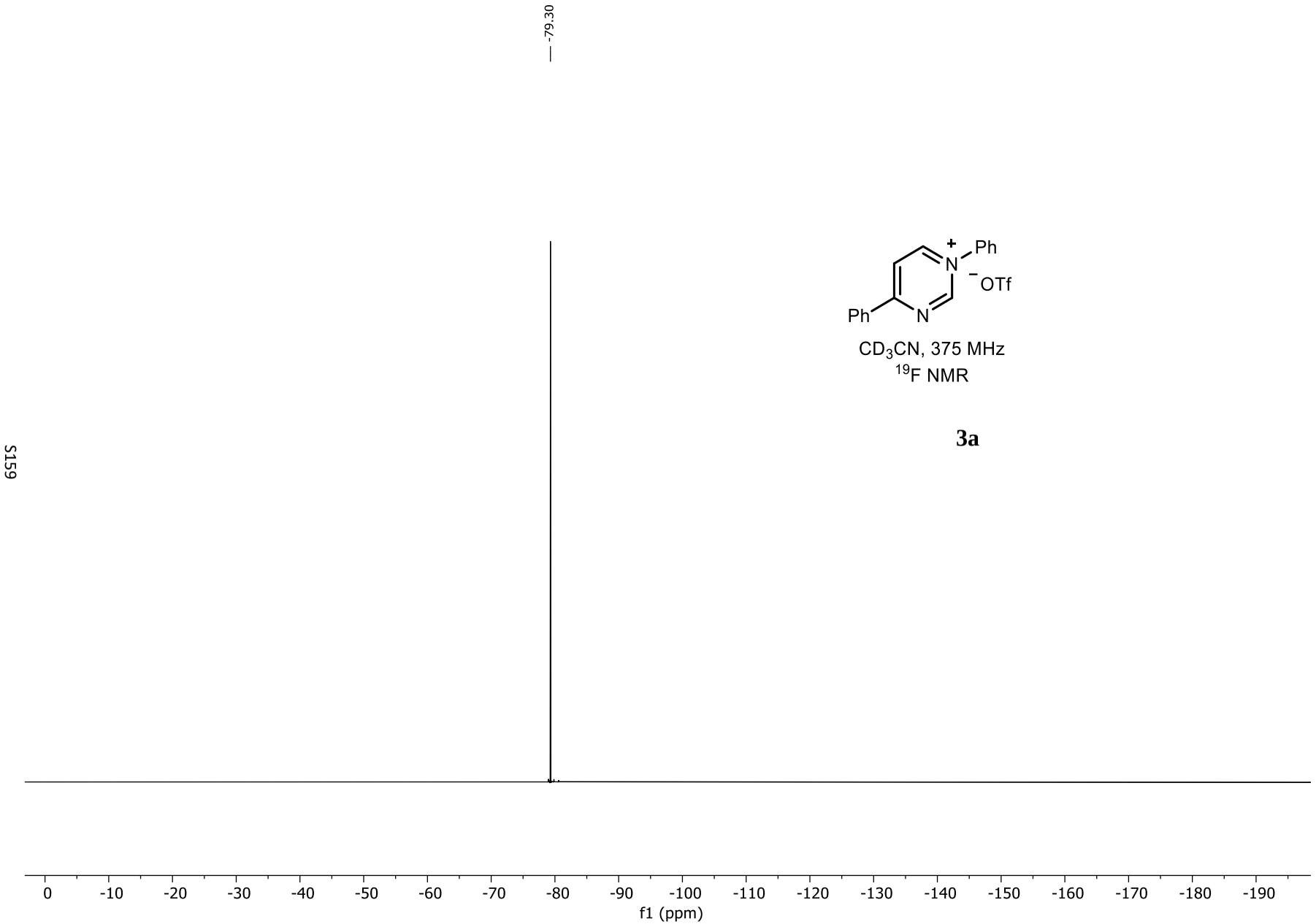

156.44
155.39
143.40
136.93
136.09
134.55
133.11
129.55
128.79
127.23
125.30
124.83
115.04
76.02
75.71
75.39
44.56
44.14
41.02
40.63
31.95
31.49
16.26
S154
N
N
N
Me
Ph
CDCl3, 400 MHz
13C NMR
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

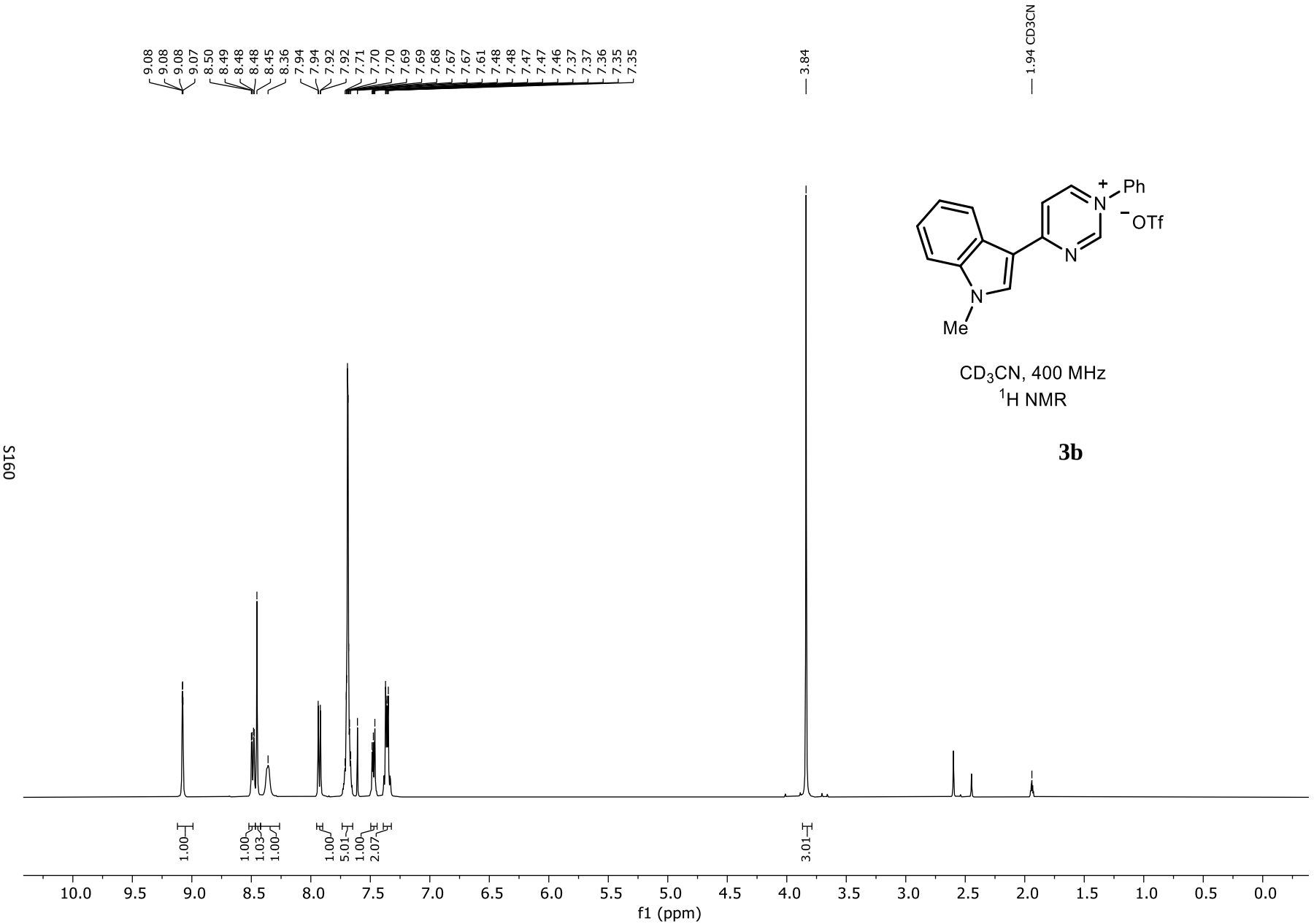

10.92
9.19
8.81
8.80
7.96
7.95
7.82
7.78
7.78
7.76
7.76
7.10
7.08
4.67
3.35 H2O
2.50 DMSO-d6
O
H
N
N
N
O
(CD3)2SO, 400 MHz
1H NMR
1.00
1.01
1.00
1.05
1.04
1.04
1.01
2.01
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

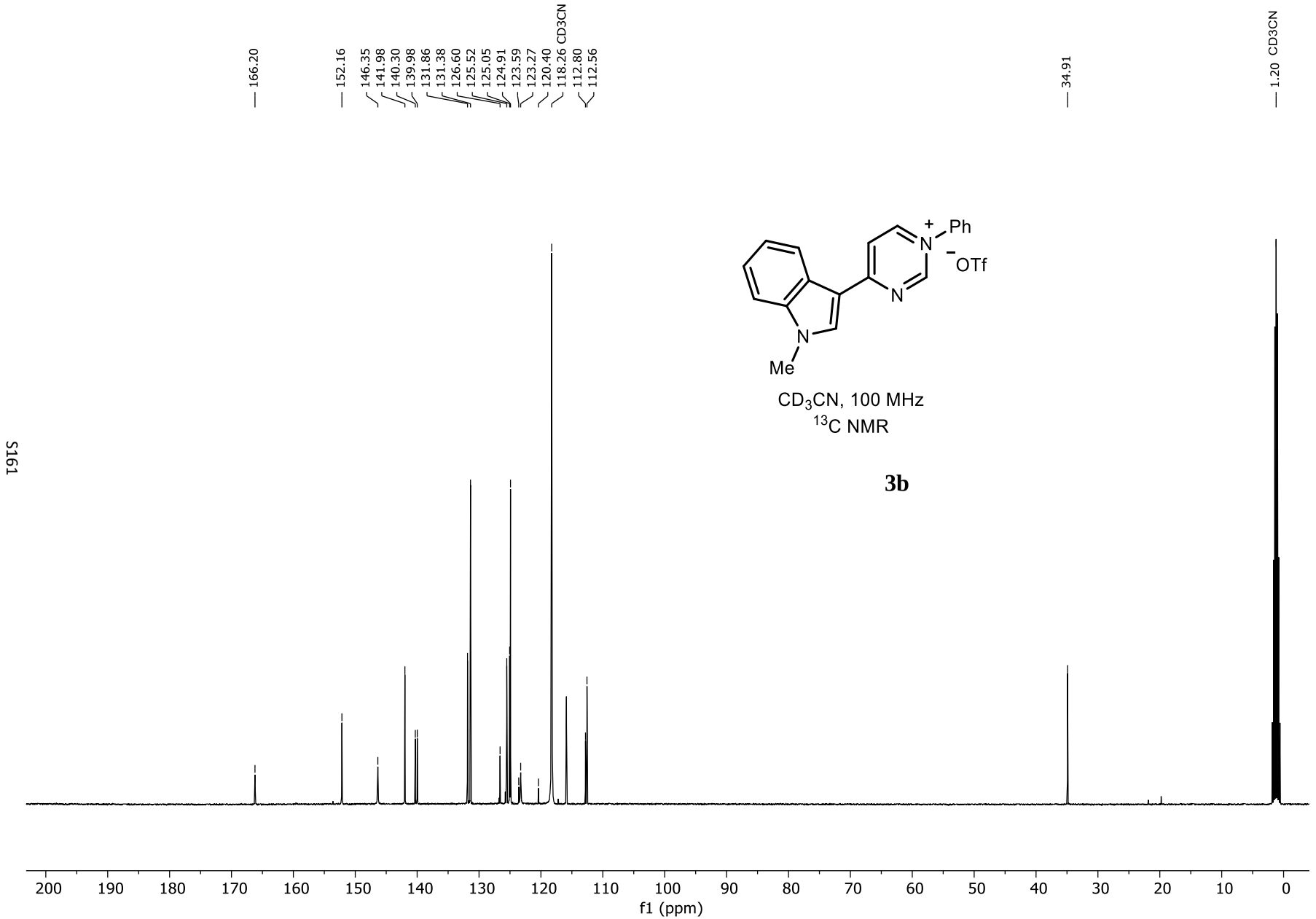

164.45
161.70
158.69
157.91
145.86
130.09
127.80
122.26
116.64
116.42
114.24
66.79
H
N
O
O
N
N
(CD3)2SO, 100 MHz
13C NMR
S156
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

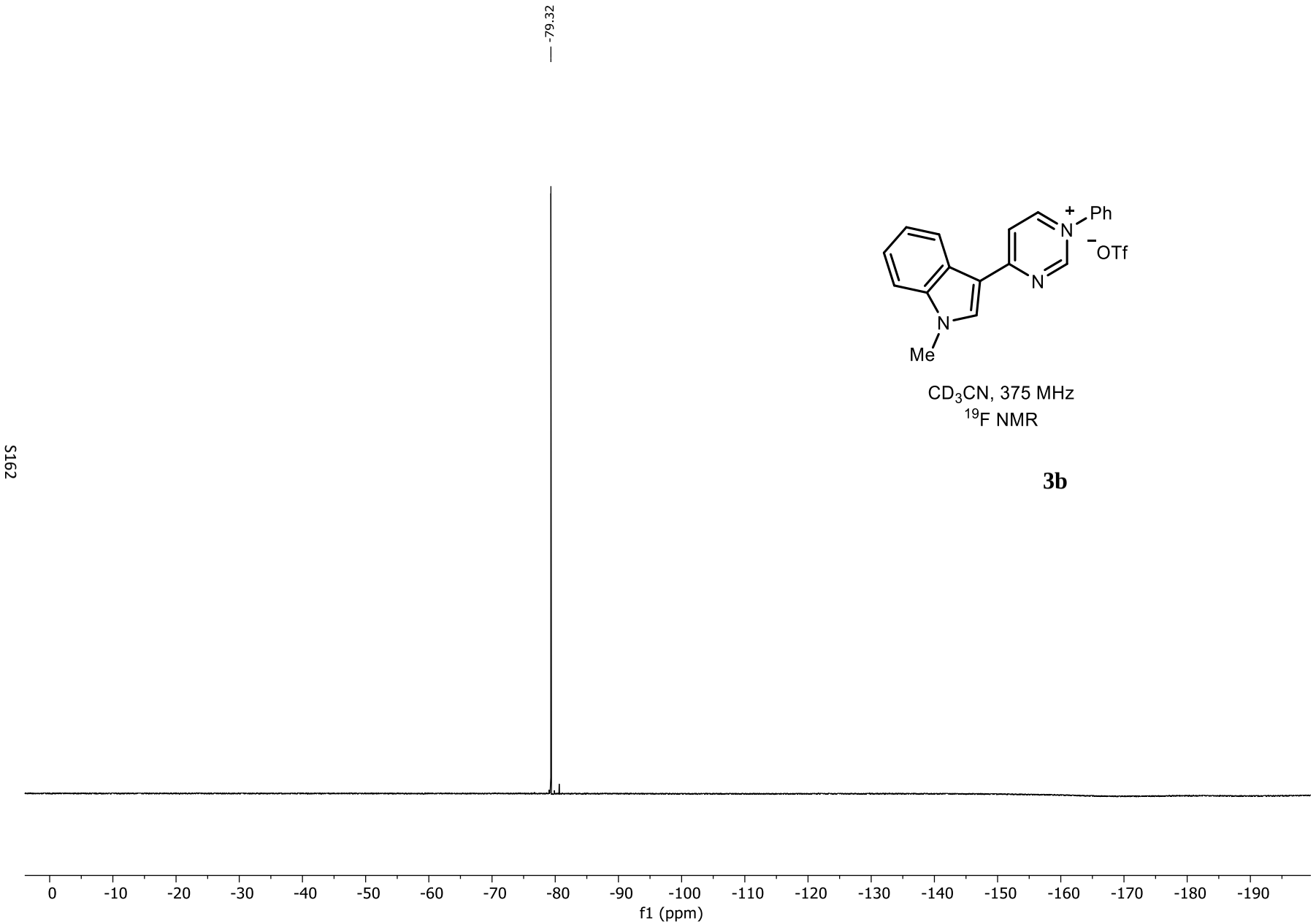

9.60
9.60
9.60
9.16
9.16
9.15
9.14
8.67
8.66
8.47
8.45
7.84
7.82
7.78
7.73
7.71
7.69
2.19 H2O
1.94 CD3CN
Ph
N
OTf
Ph
N
CD3CN, 400 MHz
1H NMR
3a
S157
0.96
1.00
1.05
2.06
6.02
2.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


171.28
153.04
151.69
140.17
136.35
133.77
132.87
131.56
130.86
130.46
125.55
123.61
120.42
118.26 CD3CN
Ph
N
OTf
Ph
N
CD3CN, 100 MHz
13C NMR
3a
S158
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-79.30
Ph
N
OTf
Ph
N
CD3CN, 375 MHz
19F NMR
3a
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

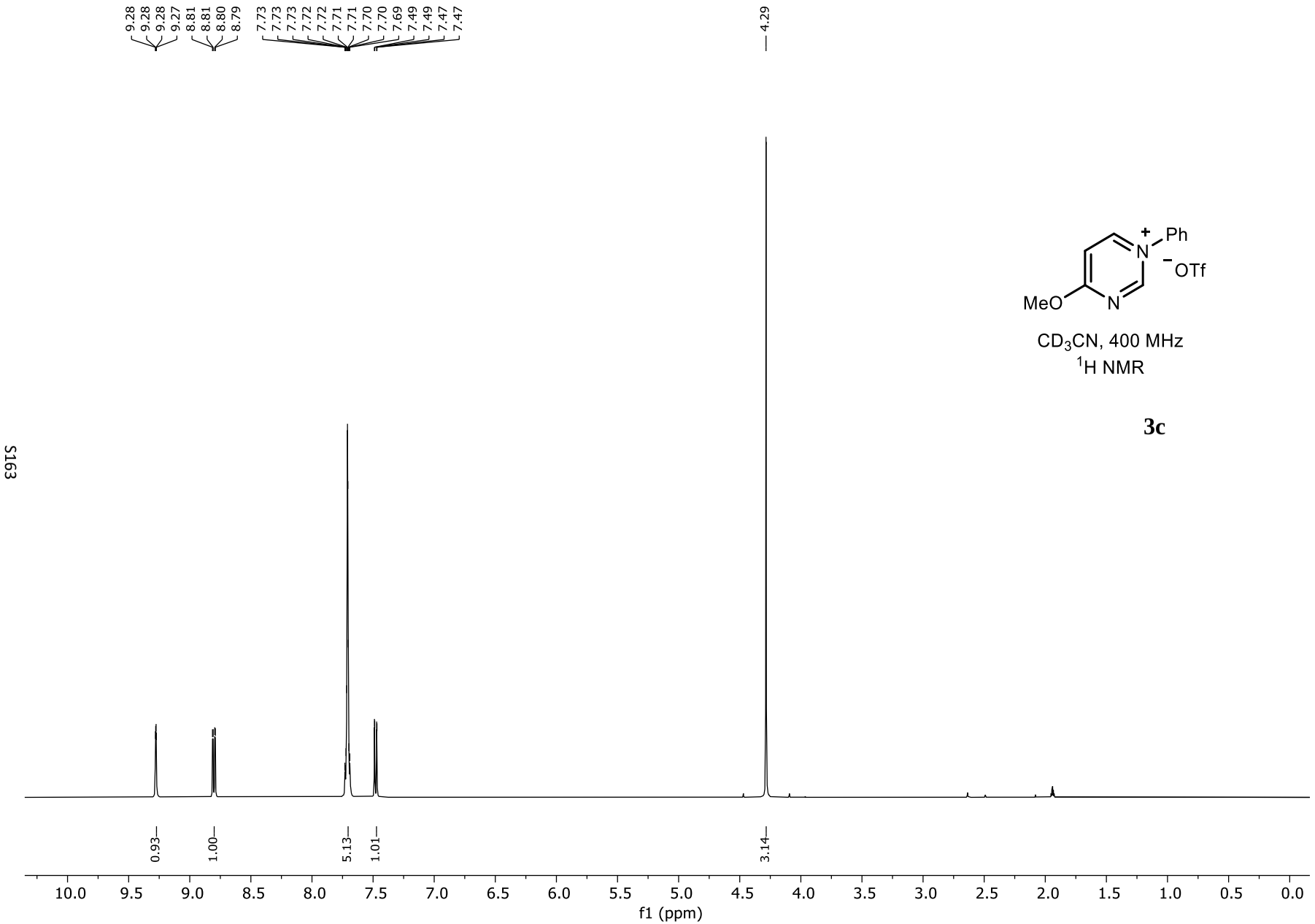

9.08
9.08
9.08
9.07
8.50
8.49
8.48
8.48
8.48
8.45
8.36
7.94
7.94
7.92
7.92
7.71
7.70
7.70
7.69
7.69
7.68
7.67
7.67
7.61
7.48
7.48
7.47
7.47
7.46
7.37
7.37
7.36
7.35
7.35
3.84
1.94 CD3CN
Ph
OTf
N
N
N
Me
CD3CN, 400 MHz
1H NMR
3b
1.00
1.00
1.03
1.00
1.00
5.01
1.00
2.07
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

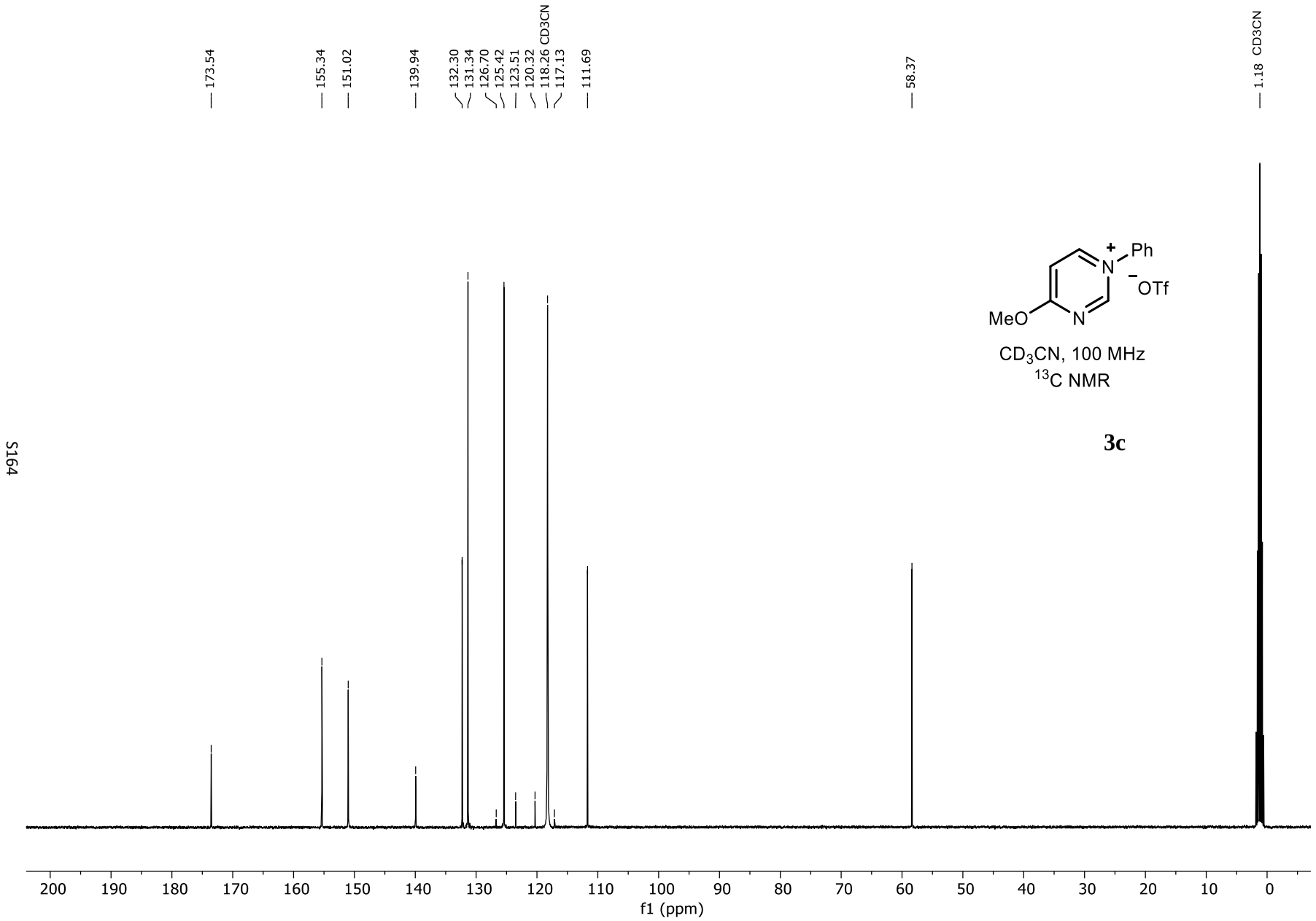

166.20
152.16
146.35
141.98
140.30
139.98
131.86
131.38
126.60
125.52
125.05
124.91
123.59
123.27
120.40
118.26 CD3CN
112.80
112.56
34.91
1.20 CD3CN
Ph
OTf
N
N
N
Me
CD3CN, 100 MHz
13C NMR
3b
S161
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

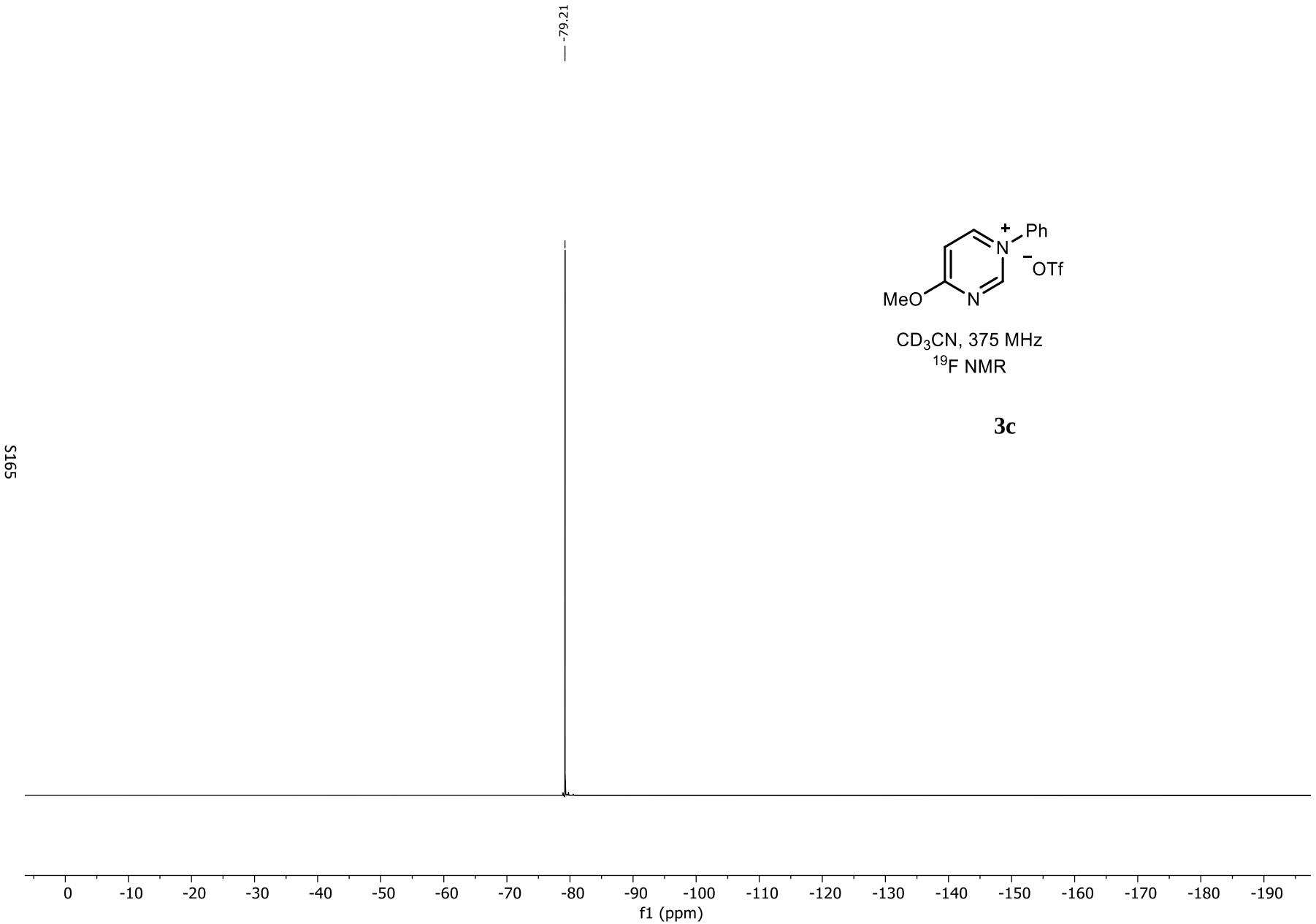


CD_3CN, 375 MHz
^{19}F NMR

3b

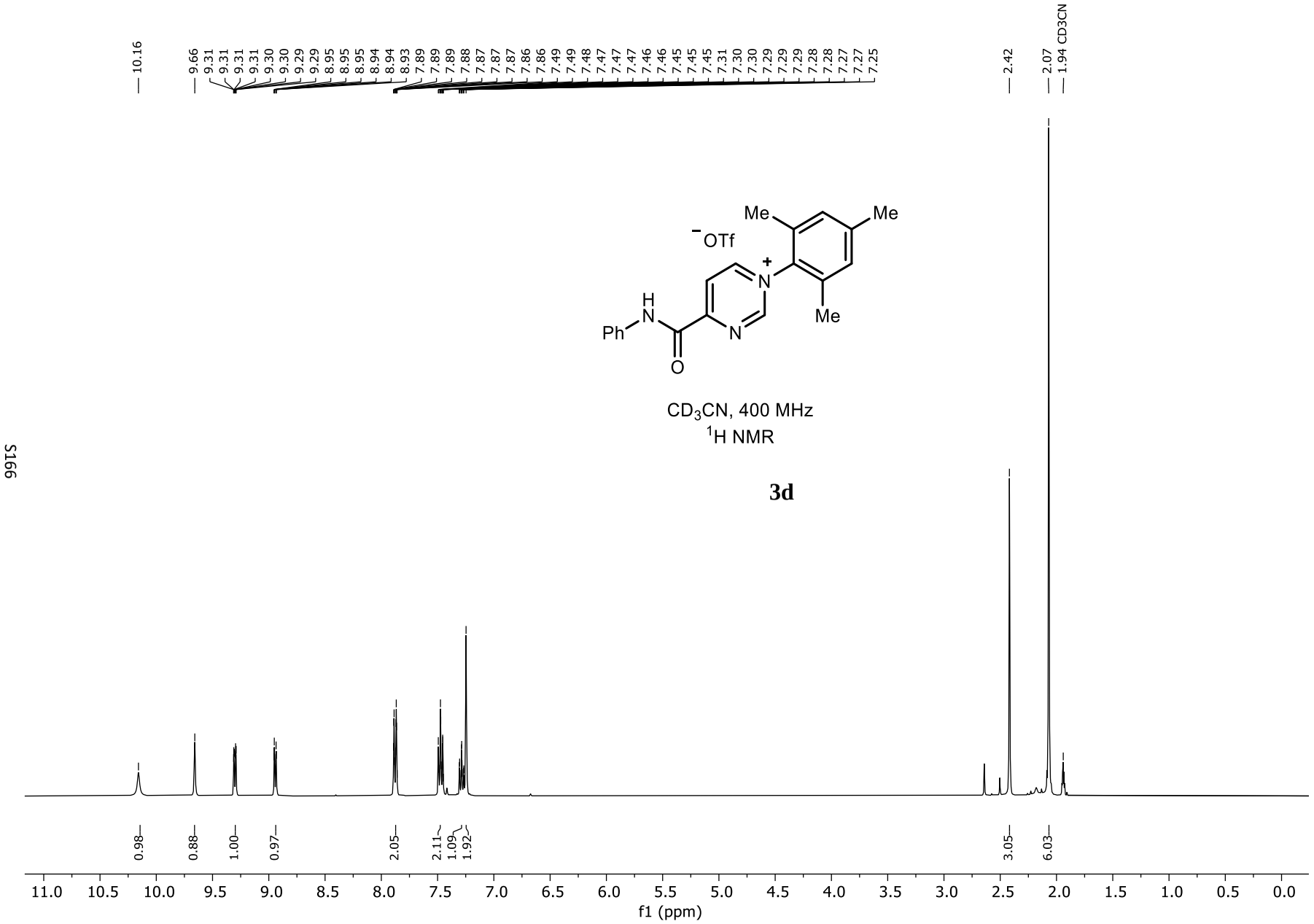

9.28
9.28
9.28
9.27
8.81
8.81
8.80
8.79
7.73
7.73
7.73
7.72
7.72
7.71
7.71
7.70
7.70
7.69
7.49
7.49
7.47
7.47
4.29
Ph
N
OTf
MeO
N
CD3CN, 400 MHz
1H NMR
3c
S163
0.93
1.00
5.13
1.01
3.14
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

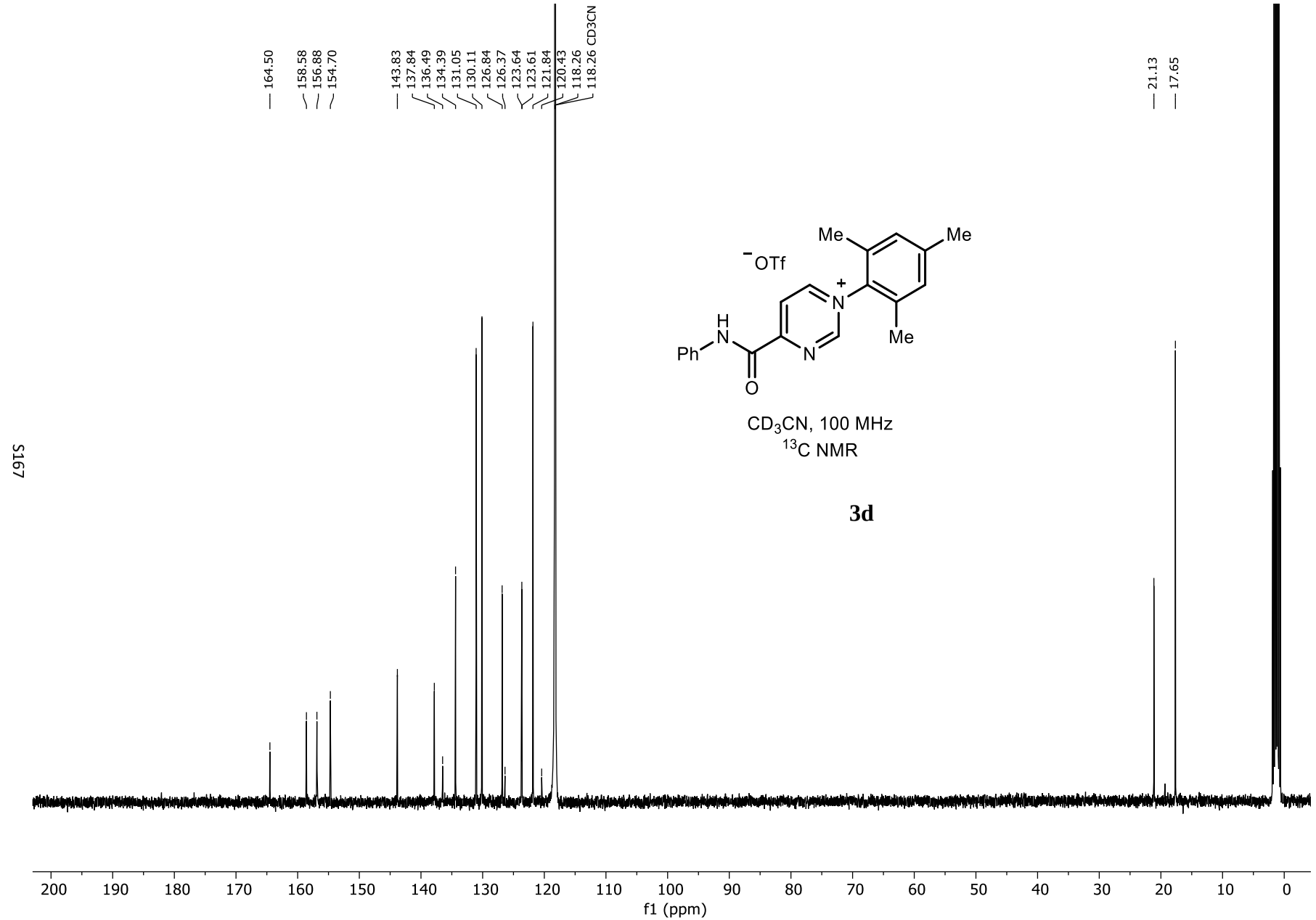

173.54
155.34
151.02
139.94
132.30
131.34
126.70
125.42
123.51
120.32
118.26 CD3CN
117.13
111.69
58.37
1.18 CD3CN
Ph
N
OTf
MeO
N
CD3CN, 100 MHz
13C NMR
3c
f1 (ppm)

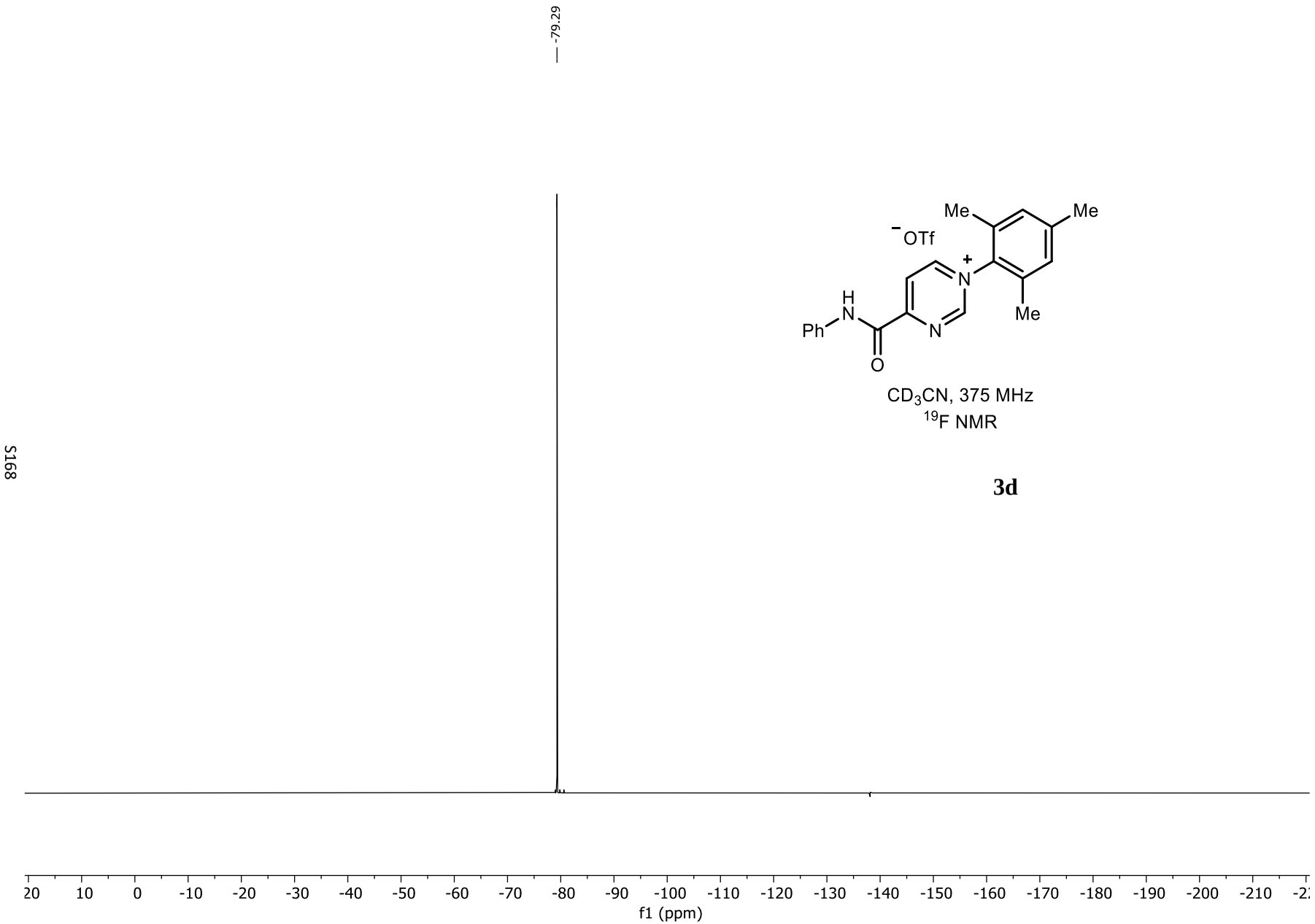


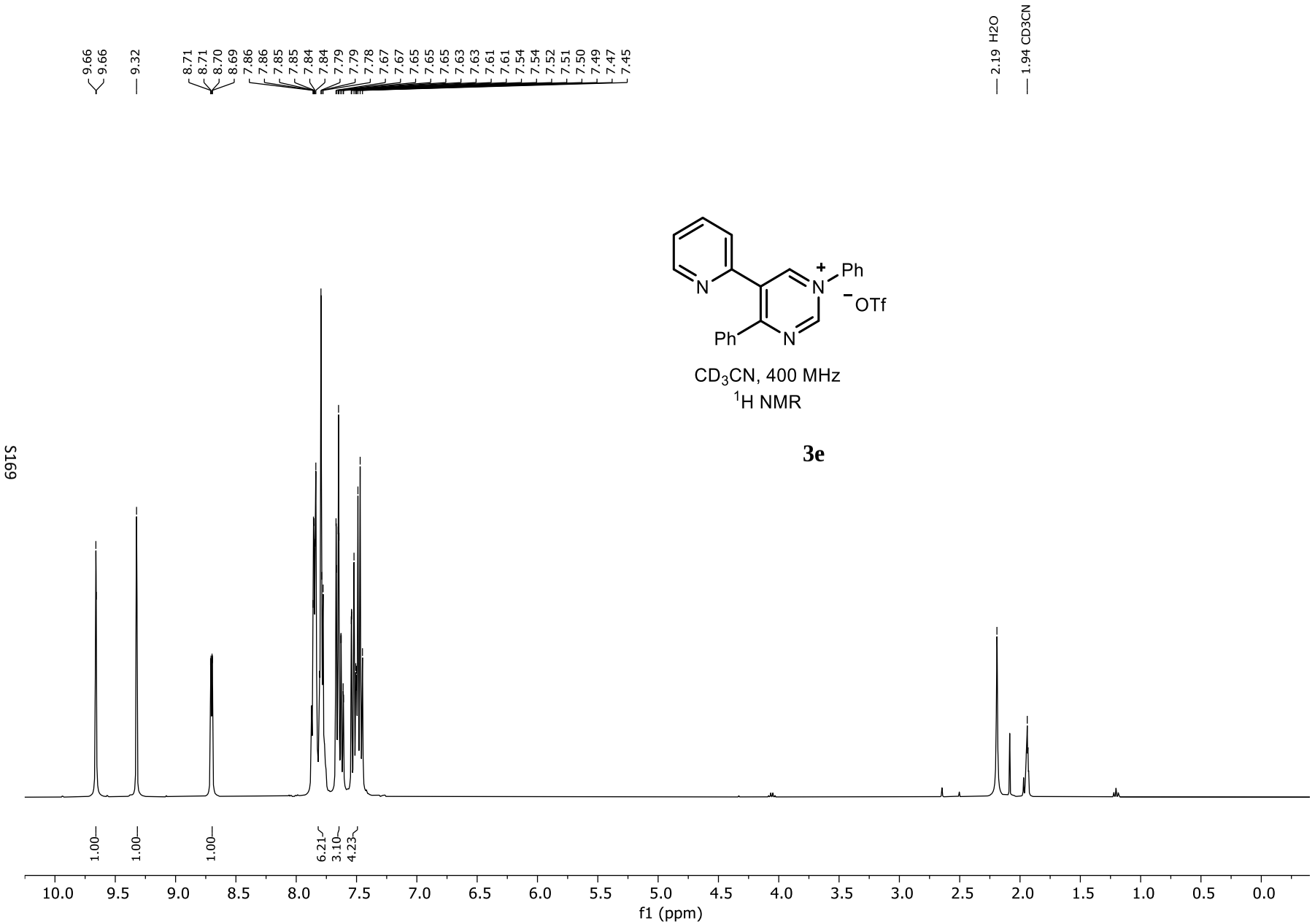
CD_3CN, 375 MHz
^{19}F NMR

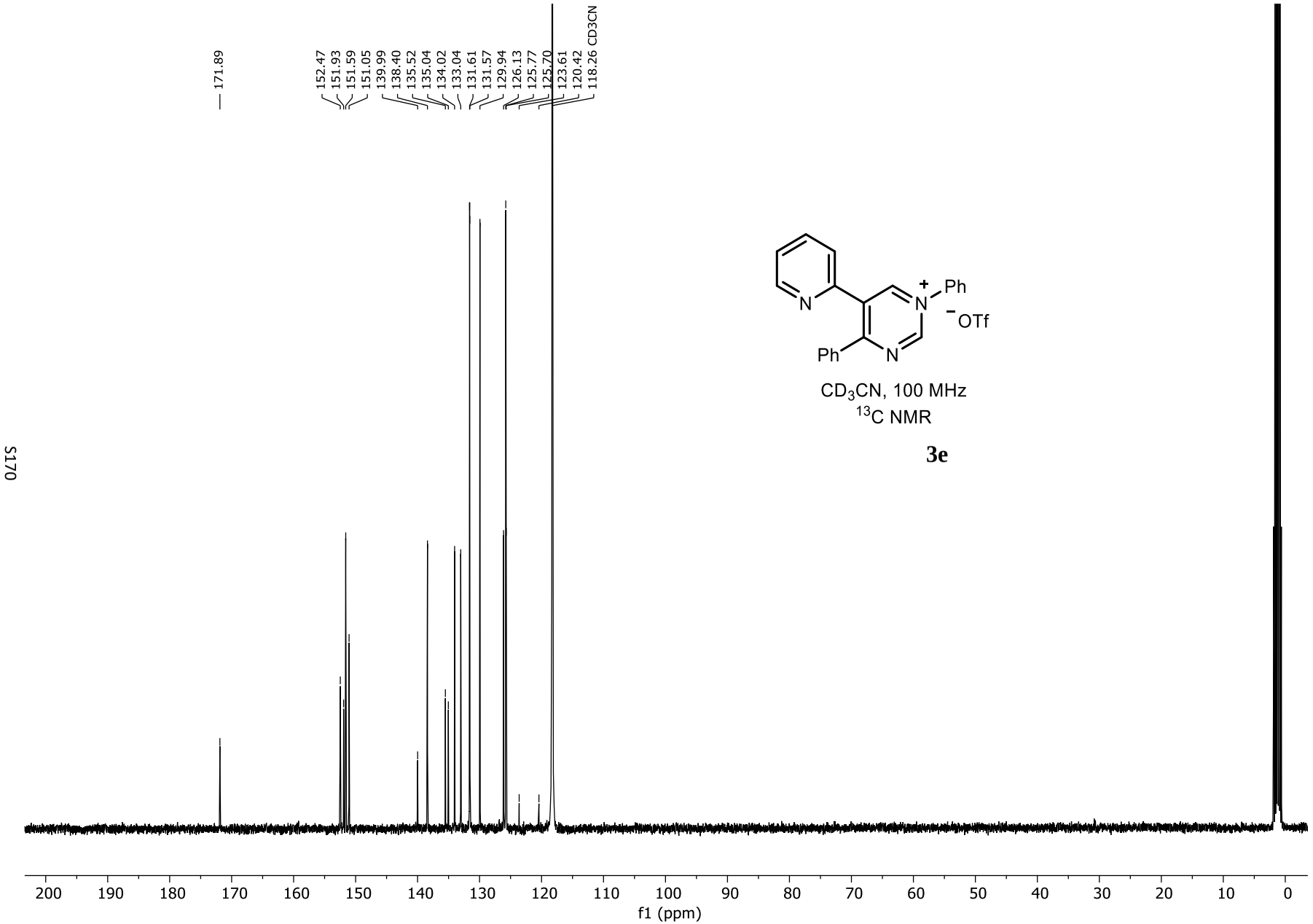
3c

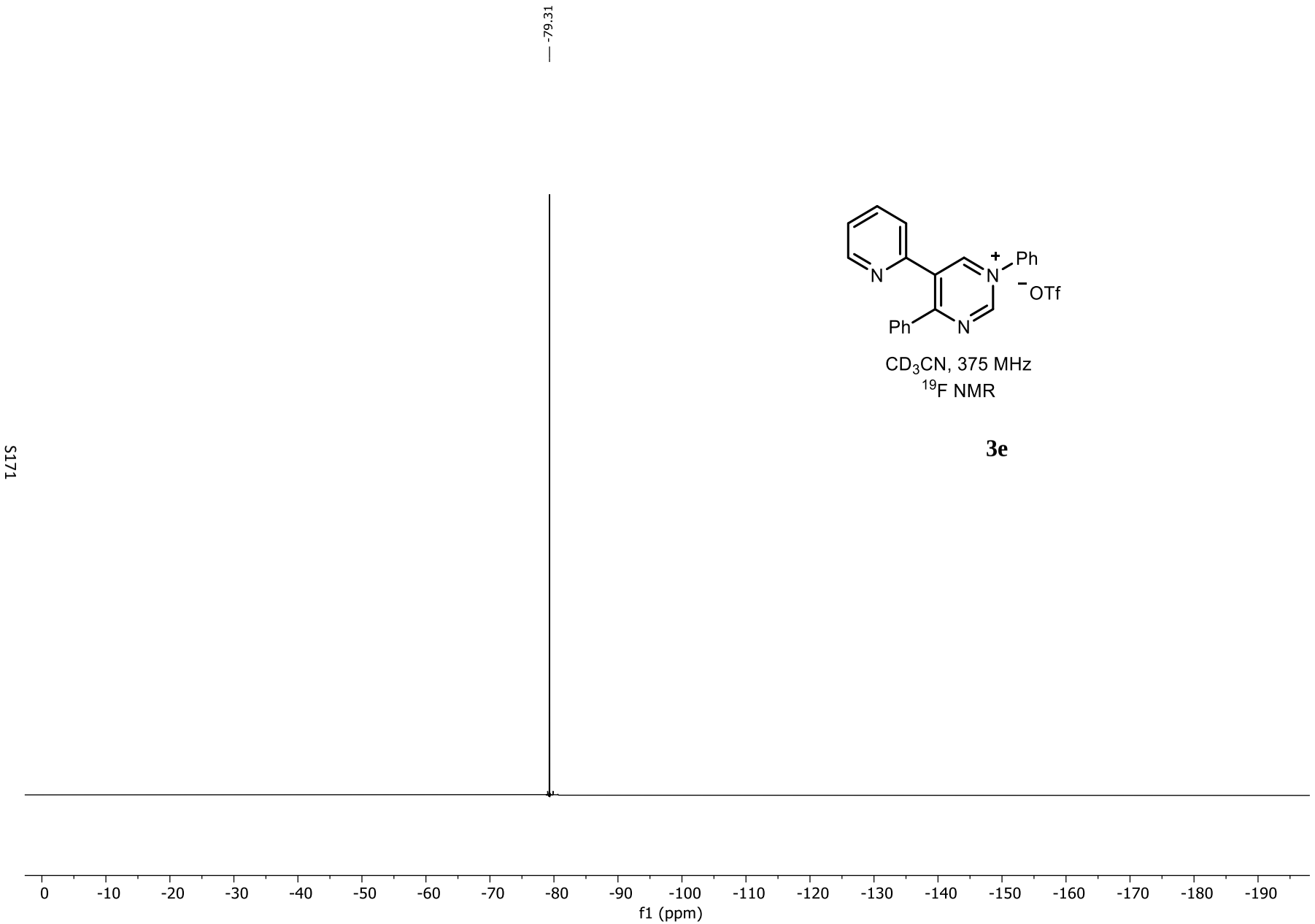

10.16
9.66
9.31
9.31
9.31
9.30
9.30
9.29
9.29
8.95
8.95
8.95
8.94
8.94
8.93
7.89
7.89
7.89
7.88
7.87
7.87
7.87
7.86
7.86
7.49
7.49
7.48
7.47
7.47
7.47
7.46
7.46
7.45
7.45
7.45
7.31
7.30
7.30
7.29
7.29
7.29
7.28
7.28
7.27
7.27
7.25
2.42
2.07
1.94 CD3CN
Me
Me
OTf
N
H
N
Ph
N
Me
O
CD3CN, 400 MHz
1H NMR
3d
0.98
0.88
1.00
0.97
2.05
2.11
1.09
1.92
3.05
6.03
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


164.50
158.58
156.88
154.70
143.83
137.84
136.49
134.39
131.05
130.11
126.84
126.37
123.64
123.61
121.84
120.43
118.26
118.26 CD3CN
21.13
17.65
Me
Me
Me
OTf
N
H
N
Ph
N
O
CD3CN, 100 MHz
13C NMR
3d
f1 (ppm)


-79.29
Me
Me
OTf
N
H
N
Ph
N
Me
O
CD3CN, 375 MHz
19F NMR
3d
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

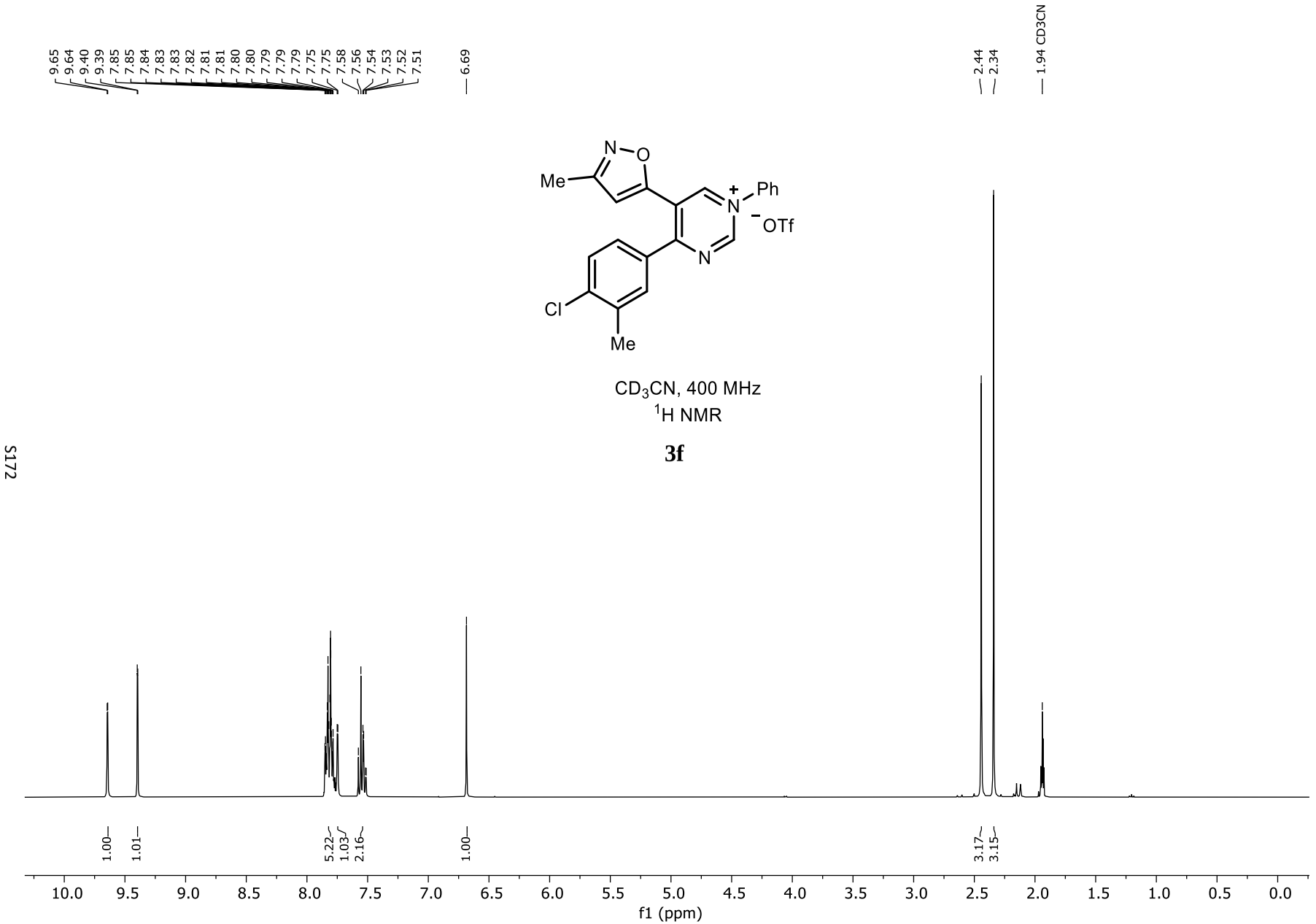

9.66
9.66
9.32
8.71
8.71
8.70
8.69
7.86
7.86
7.85
7.85
7.84
7.84
7.79
7.79
7.78
7.67
7.67
7.65
7.65
7.65
7.63
7.63
7.61
7.61
7.54
7.54
7.52
7.51
7.50
7.49
7.47
7.45
2.19 H2O
1.94 CD3CN
Ph
N
N
OTf
Ph
N
CD3CN, 400 MHz
1H NMR
3e
S169
1.00
1.00
1.00
6.21
3.10
4.23
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

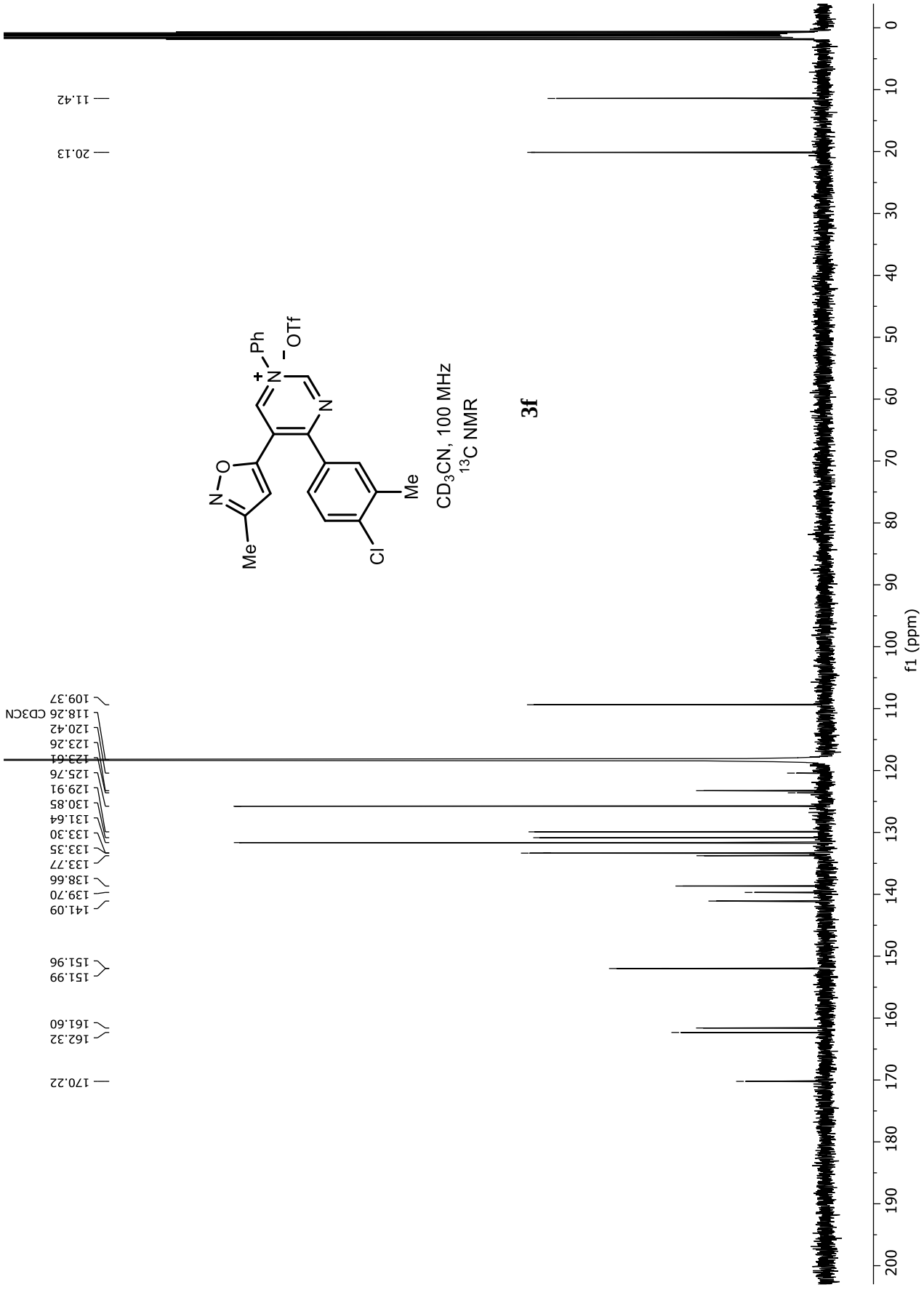

171.89
152.47
151.93
151.59
151.05
139.99
138.40
135.52
135.04
134.02
133.04
131.61
131.57
129.94
126.13
125.77
125.70
123.61
120.42
118.26 CD3CN
Ph
N
N
OTf
Ph
N
CD3CN, 100 MHz
13C NMR
3e
f1 (ppm)

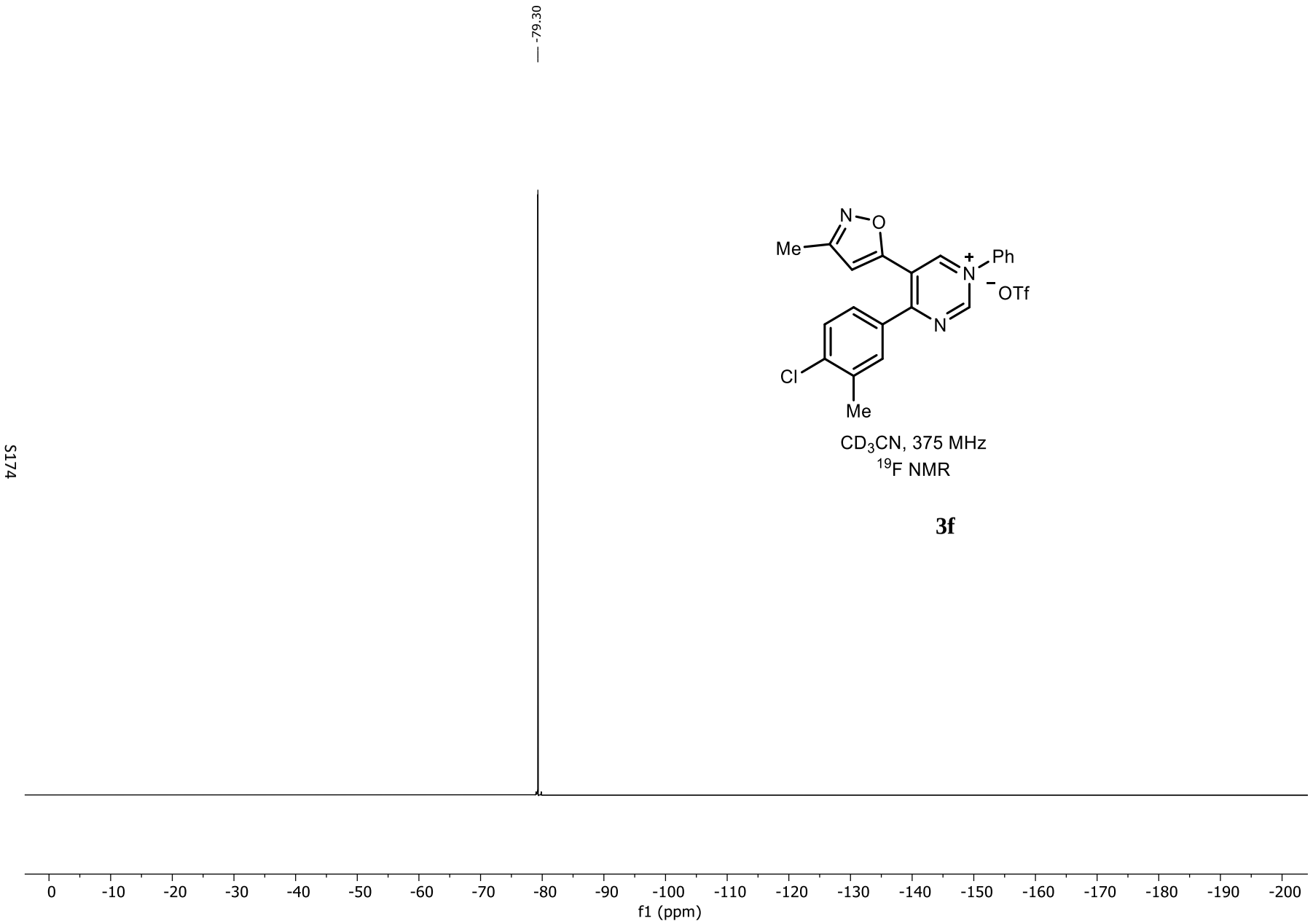


CD_3CN, 375 MHz
^{19}F NMR

3e

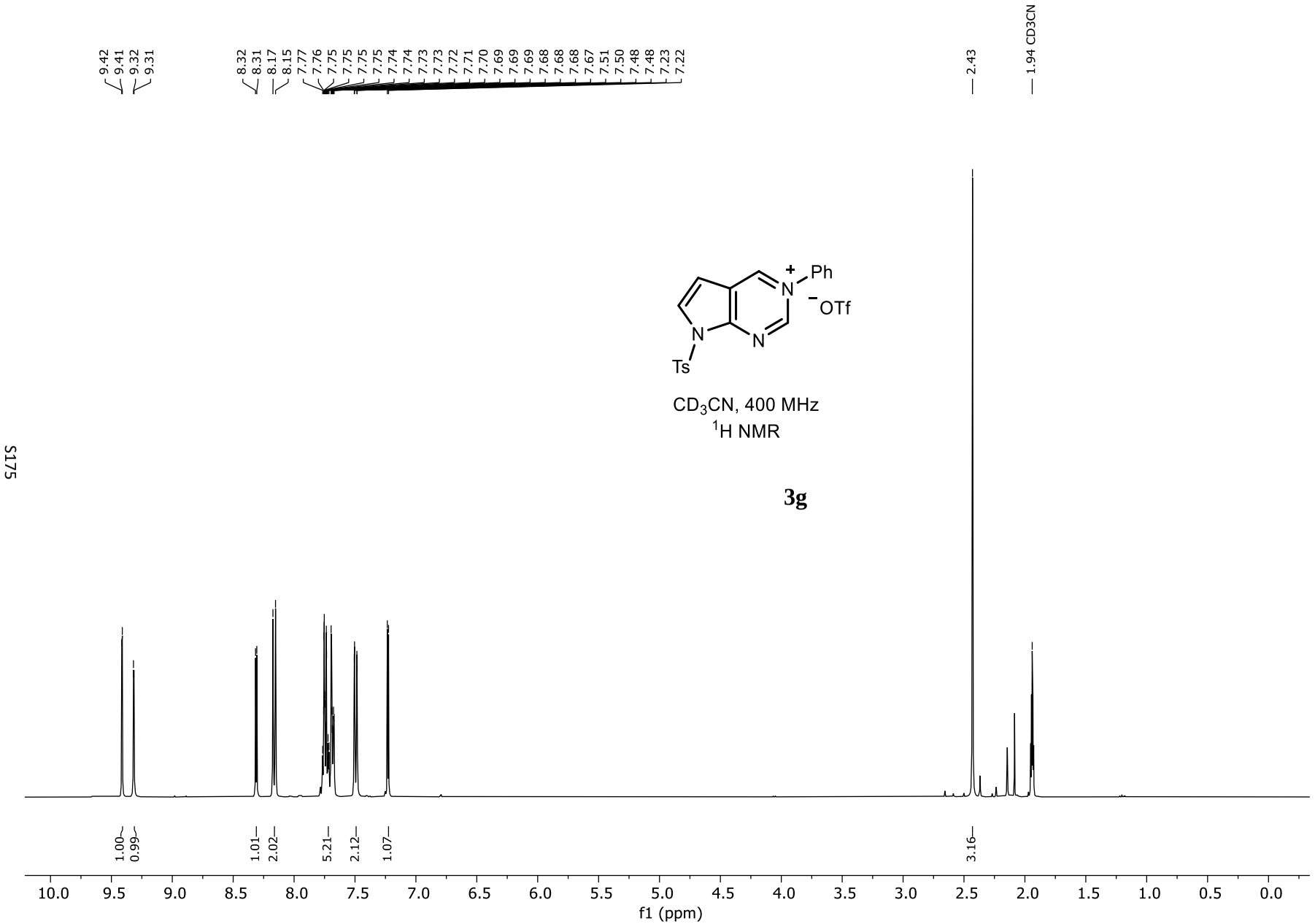

9.65
9.64
9.40
9.39
7.85
7.85
7.84
7.83
7.83
7.82
7.81
7.81
7.80
7.80
7.79
7.79
7.79
7.75
7.75
7.58
7.56
7.54
7.53
7.52
7.51
6.69
2.44
2.34
1.94 CD3CN
Me
N
O
Ph
N
OTf
N
Cl
Me
CD3CN, 400 MHz
1H NMR
3f
1.00
1.01
5.22
1.03
2.16
1.00
3.17
3.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

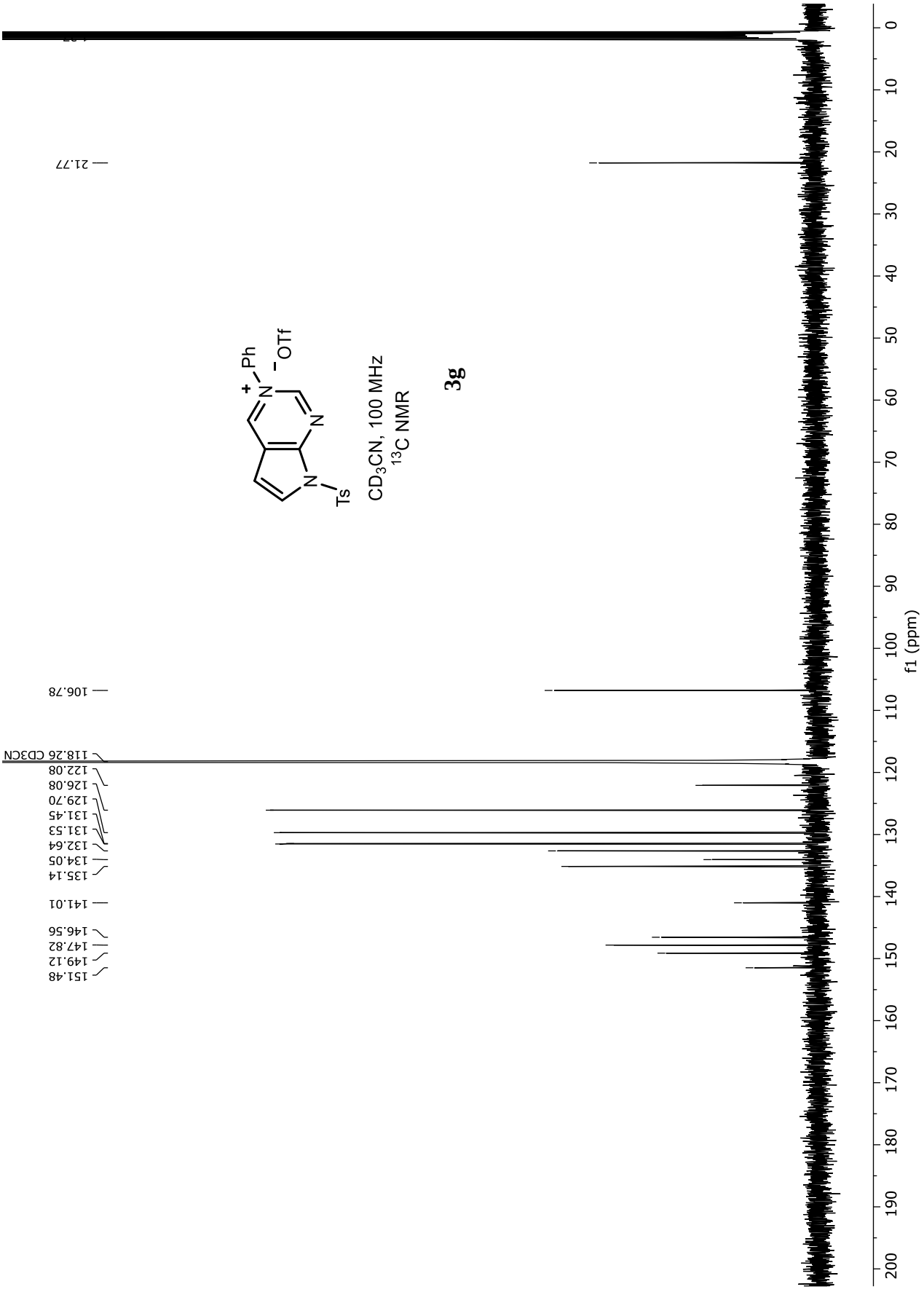

3f
CD3CN, 100 MHz
13C NMR
Ph
OTf
Me
Cl
Me
11.42
20.13
109.37
118.26 CD3CN
120.42
123.26
123.61
125.76
129.91
130.85
131.64
133.30
133.35
133.77
138.66
139.70
141.09
151.96
151.99
161.60
162.32
170.22
f1 (ppm)

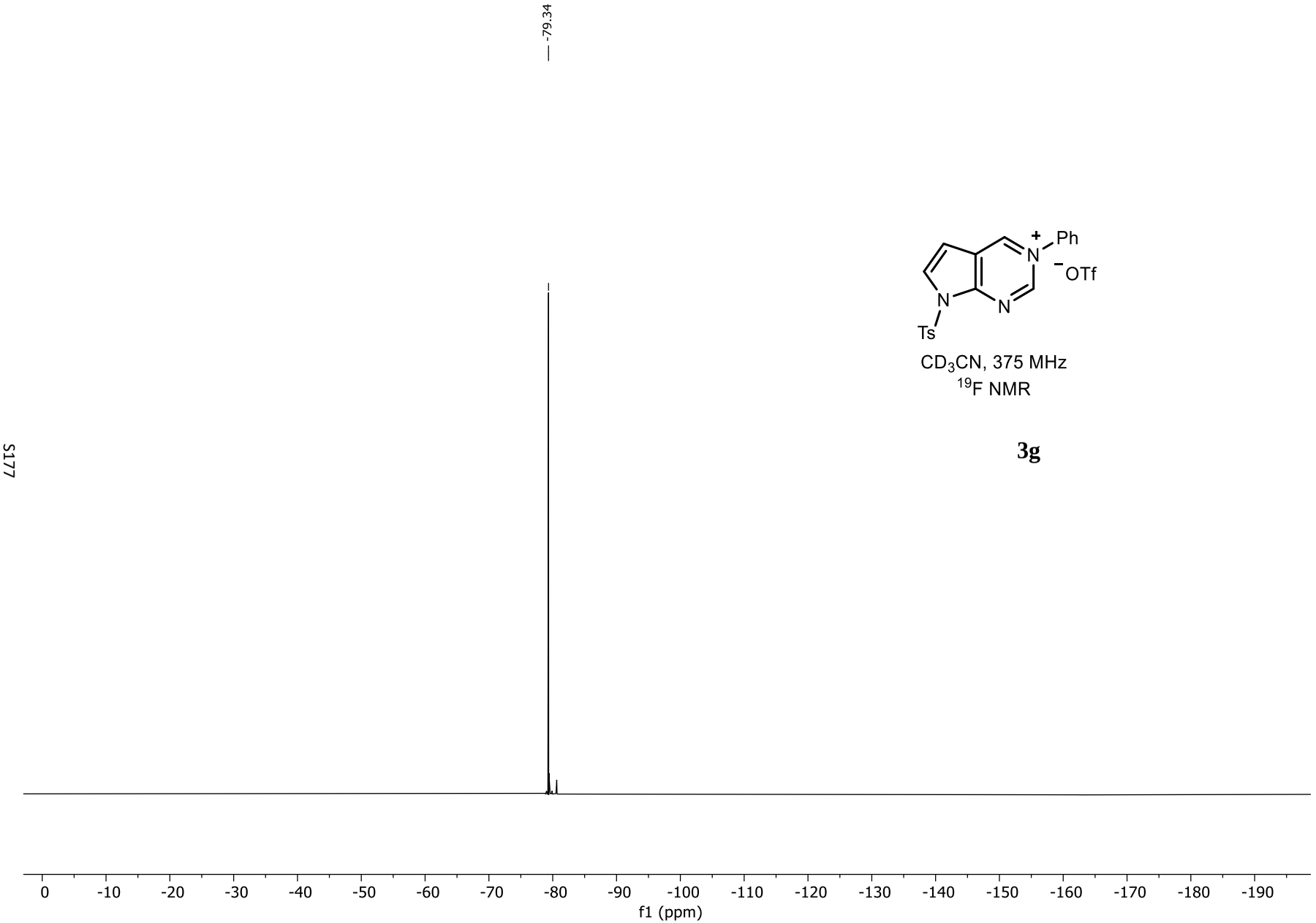


CD_3CN, 375 MHz
^{19}F NMR

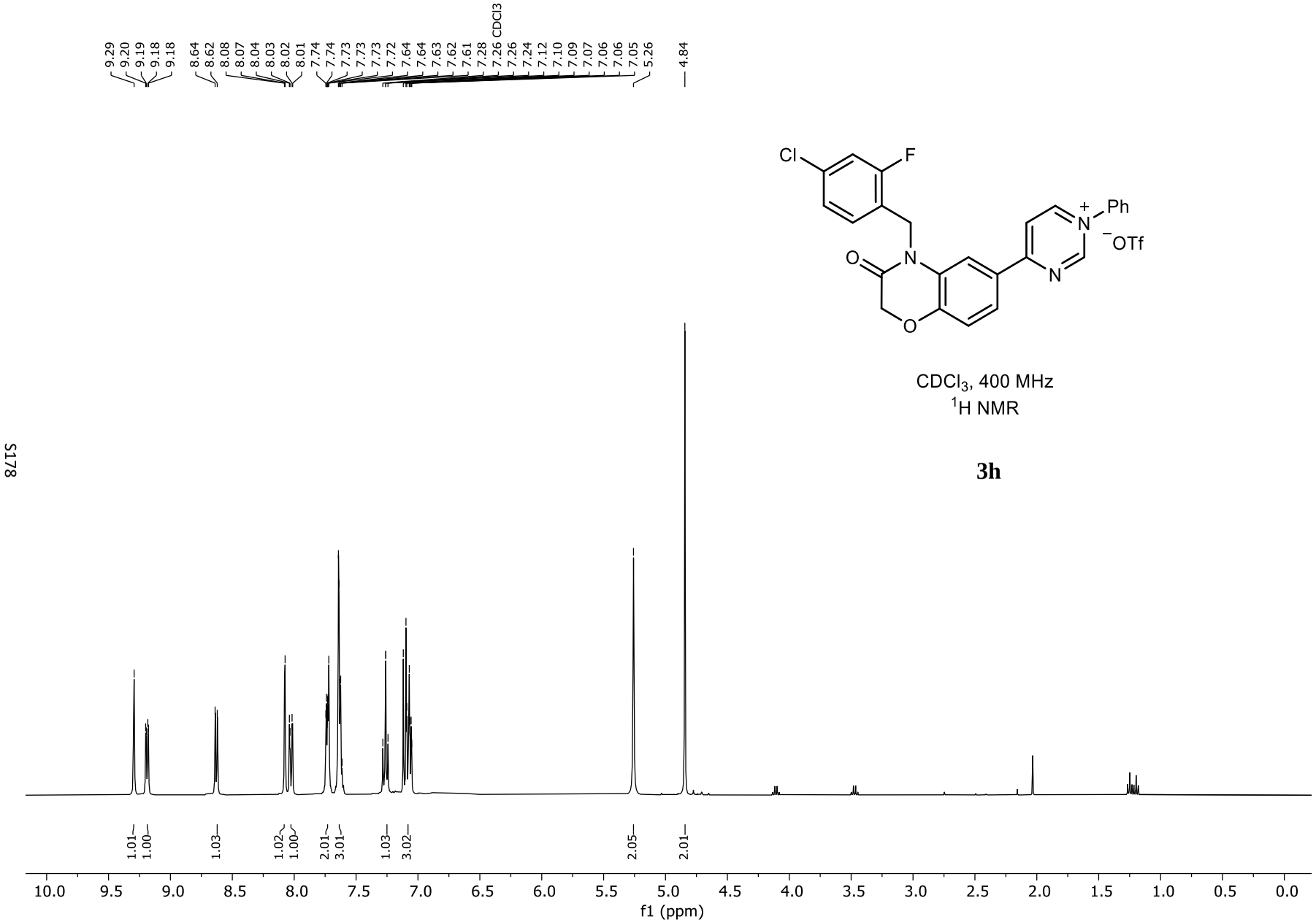
3f

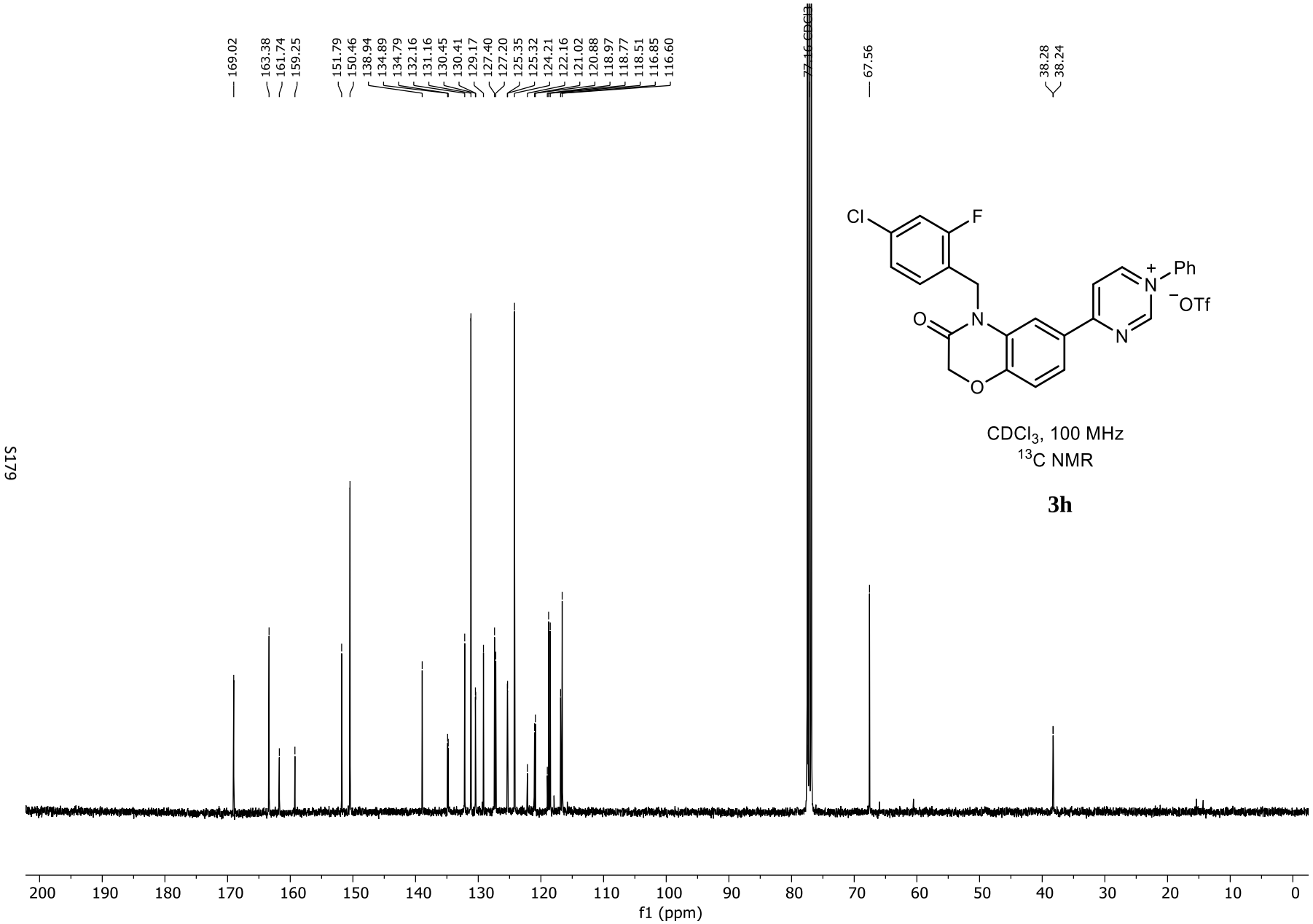

9.42
9.41
9.32
9.31
8.32
8.31
8.17
8.15
7.77
7.76
7.75
7.75
7.75
7.75
7.74
7.74
7.73
7.73
7.72
7.71
7.70
7.69
7.69
7.69
7.68
7.68
7.68
7.67
7.51
7.50
7.48
7.48
7.23
7.22
2.43
1.94 CD3CN
Ph
OTf
N
N
N
Ts
CD3CN, 400 MHz
1H NMR
3g
1.00
0.99
1.01
2.02
5.21
2.12
1.07
3.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

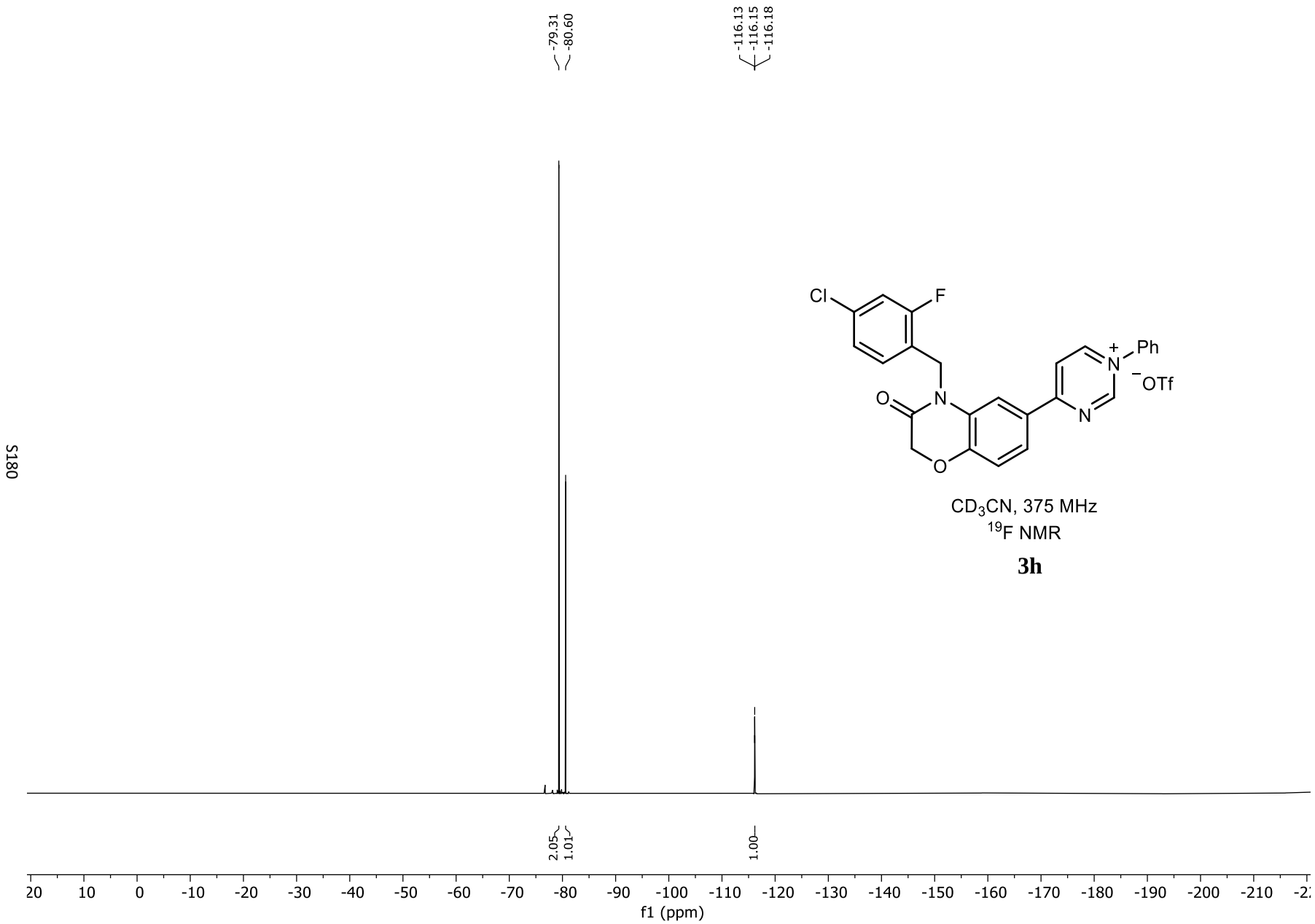

21.77
106.78
118.26 CD3CN
122.08
126.08
129.70
131.45
131.53
132.64
134.05
135.14
141.01
146.56
147.82
149.12
151.48
Ph
OTf
Ts
CD3CN, 100 MHz
13C NMR
3g
f1 (ppm)


-79.34
Ph
N
OTf
N
N
Ts
CD3CN, 375 MHz
19F NMR
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

3g


9.29
9.20
9.19
9.18
9.18
8.64
8.62
8.08
8.07
8.04
8.03
8.02
8.01
7.74
7.74
7.73
7.73
7.73
7.72
7.64
7.64
7.63
7.62
7.61
7.28
7.26 CDCl3
7.26
7.24
7.12
7.10
7.09
7.07
7.06
7.06
7.05
5.26
4.84
Cl
F
O
N
N
+
N
Ph
−
OTf
O
CDCl3, 400 MHz
1H NMR
3h
1.01
1.00
1.03
1.02
1.00
2.01
3.01
1.03
3.02
2.05
2.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

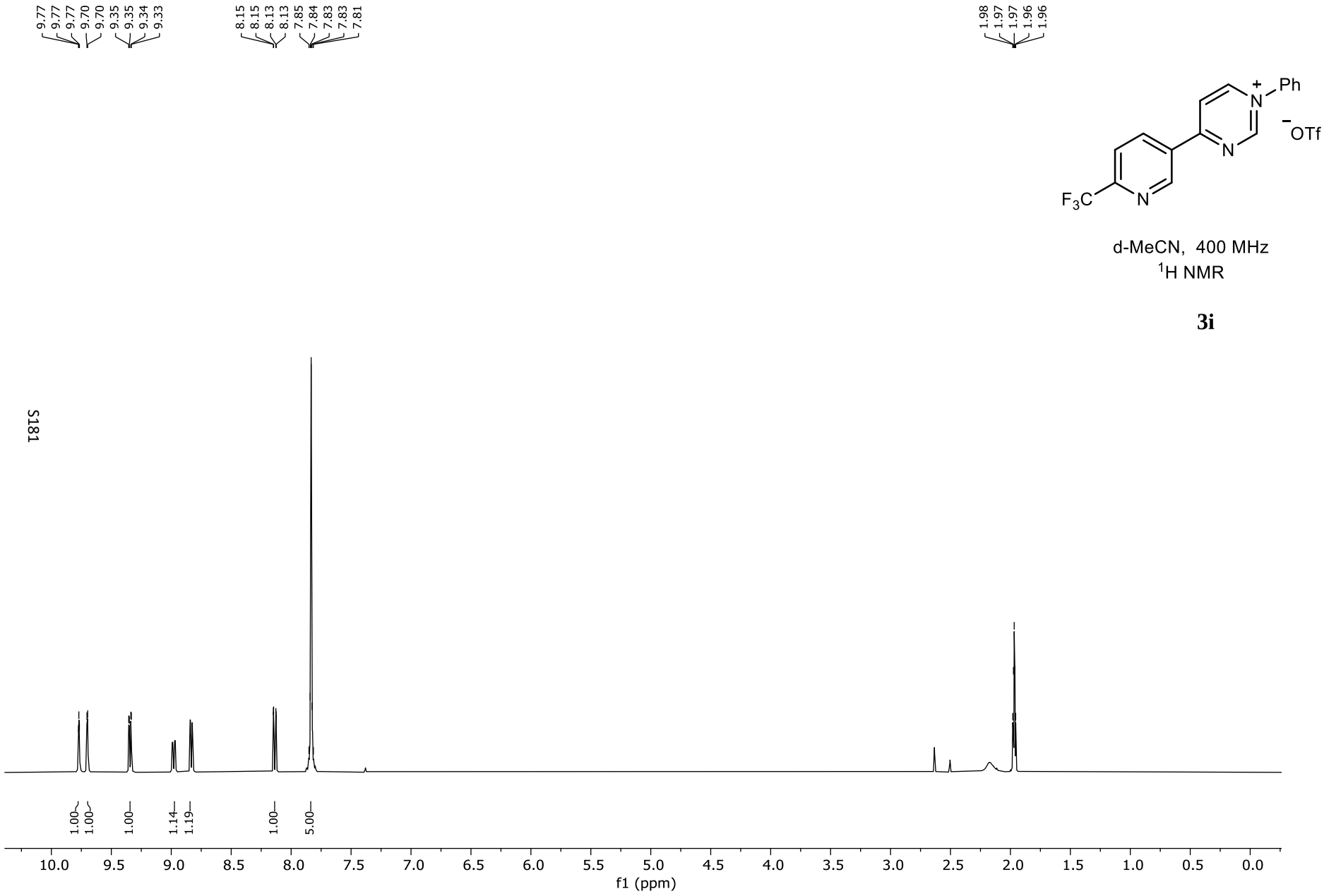

169.02
163.38
161.74
159.25
151.79
150.46
138.94
134.89
134.79
132.16
131.16
130.45
130.41
129.17
127.40
127.20
125.35
125.32
124.21
122.16
121.02
120.88
118.97
118.77
118.51
116.85
116.60
77.16 CDCl3
67.56
38.28
38.24
Cl
F
O
N
O
N
+
N
Ph
−
OTf
CDCl3, 100 MHz
13C NMR
3h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

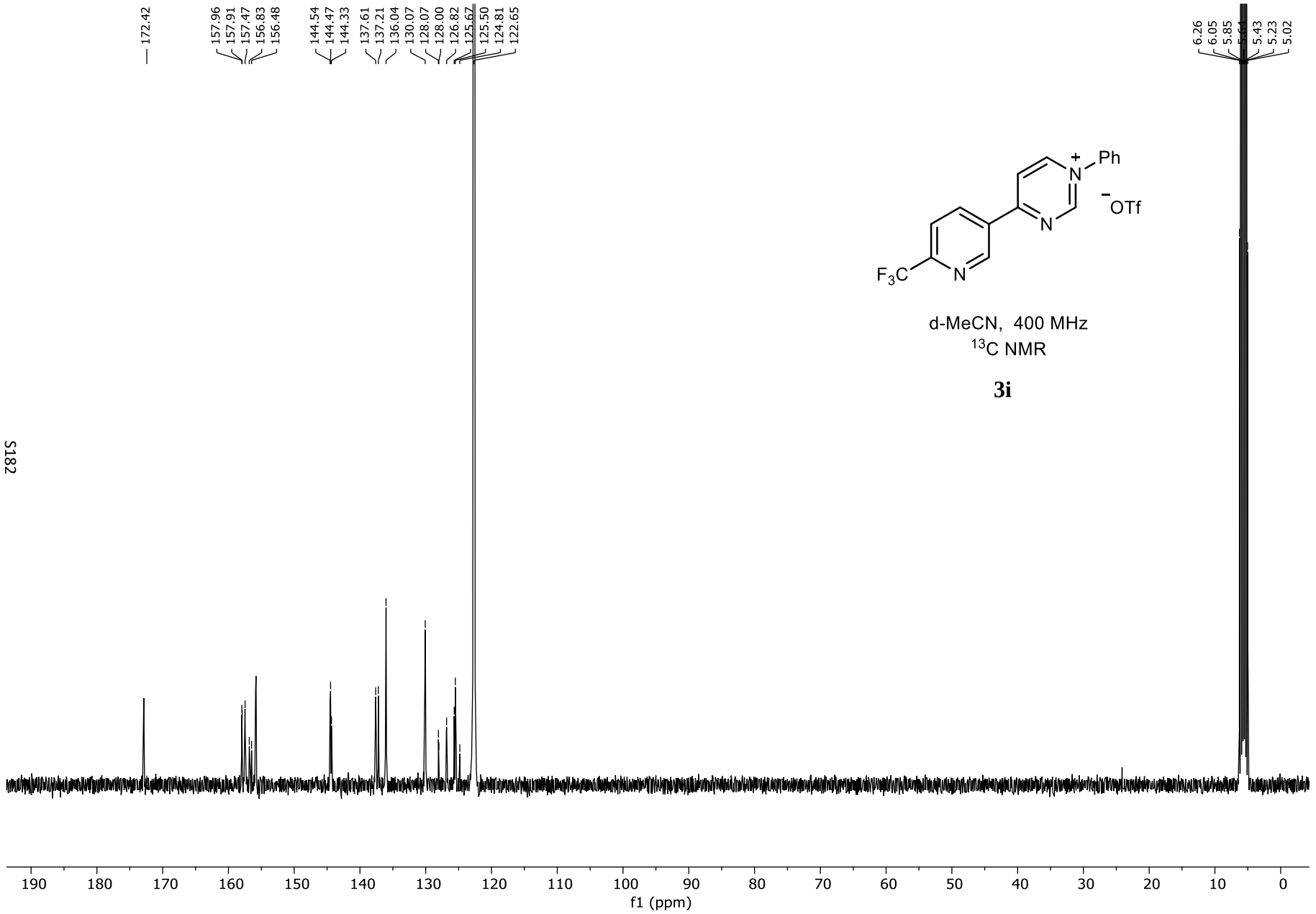


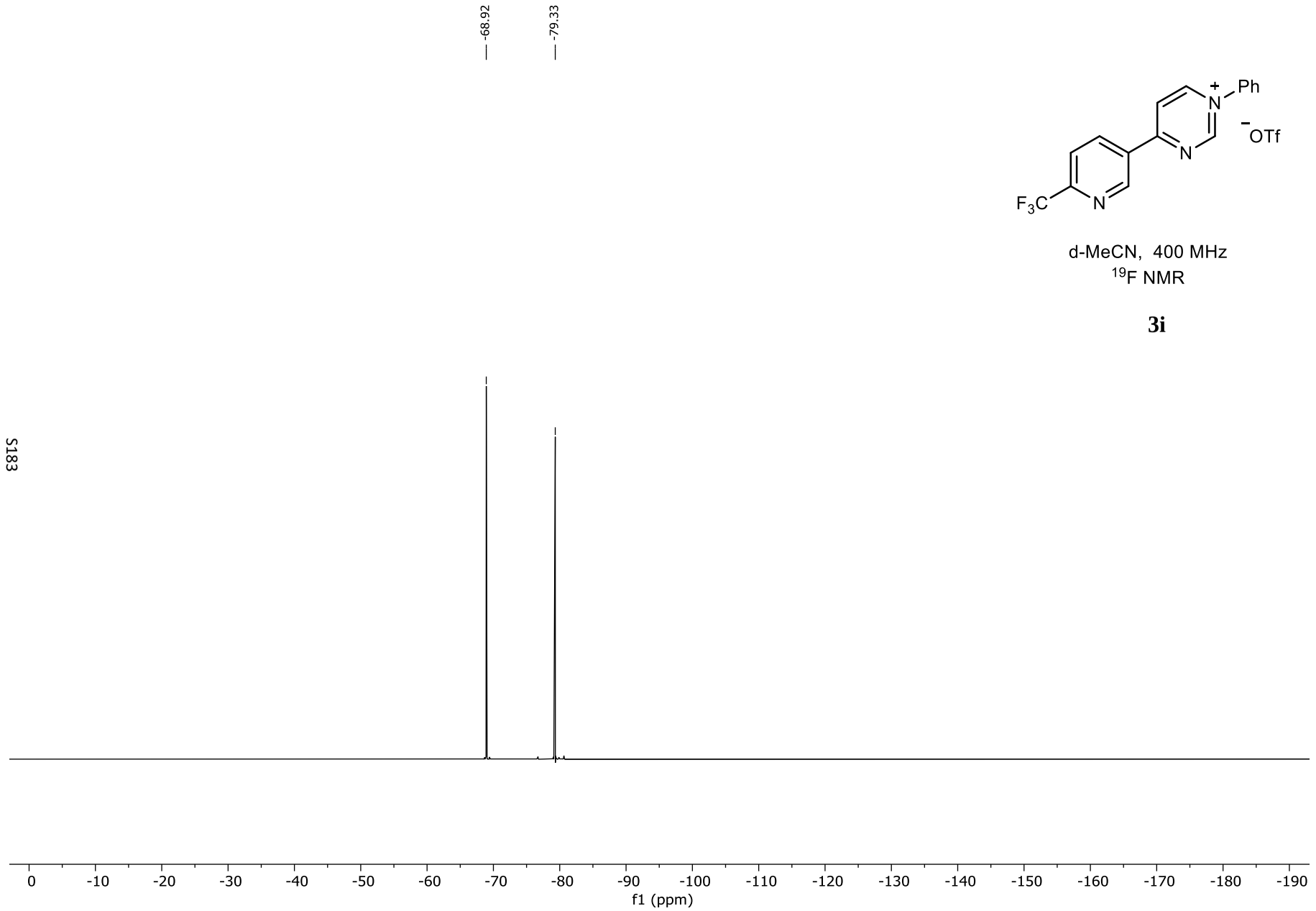
CD_3CN, 375 MHz

^{19}F NMR

3h

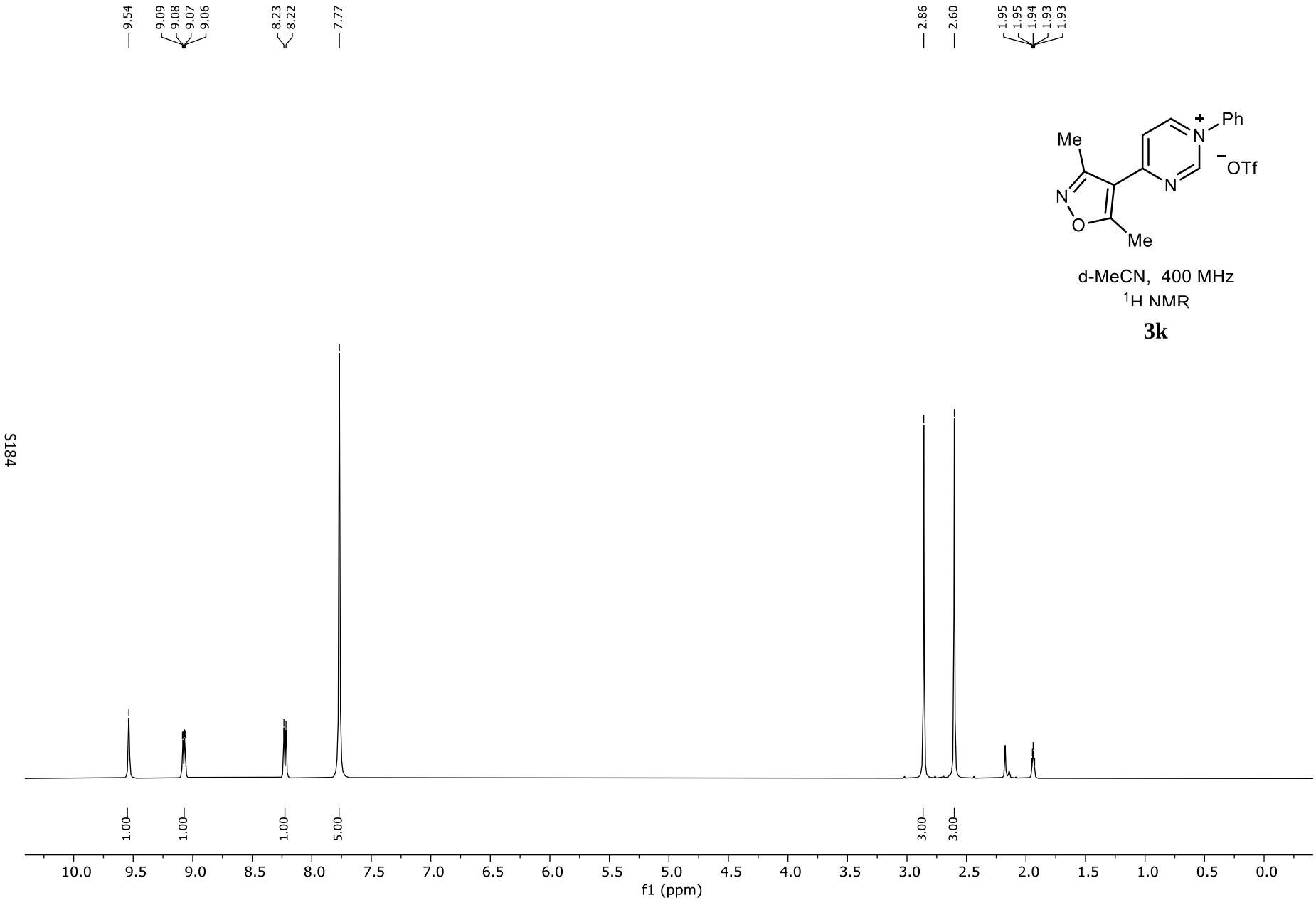

9.77
9.77
9.77
9.70
9.70
9.35
9.35
9.34
9.33
8.15
8.15
8.13
8.13
7.85
7.84
7.83
7.83
7.81
1.98
1.97
1.97
1.96
1.96
Ph
N
OTf
N
F3C
d-MeCN, 400 MHz
1H NMR
3i
S181
1.00
1.00
1.00
1.14
1.19
1.00
5.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

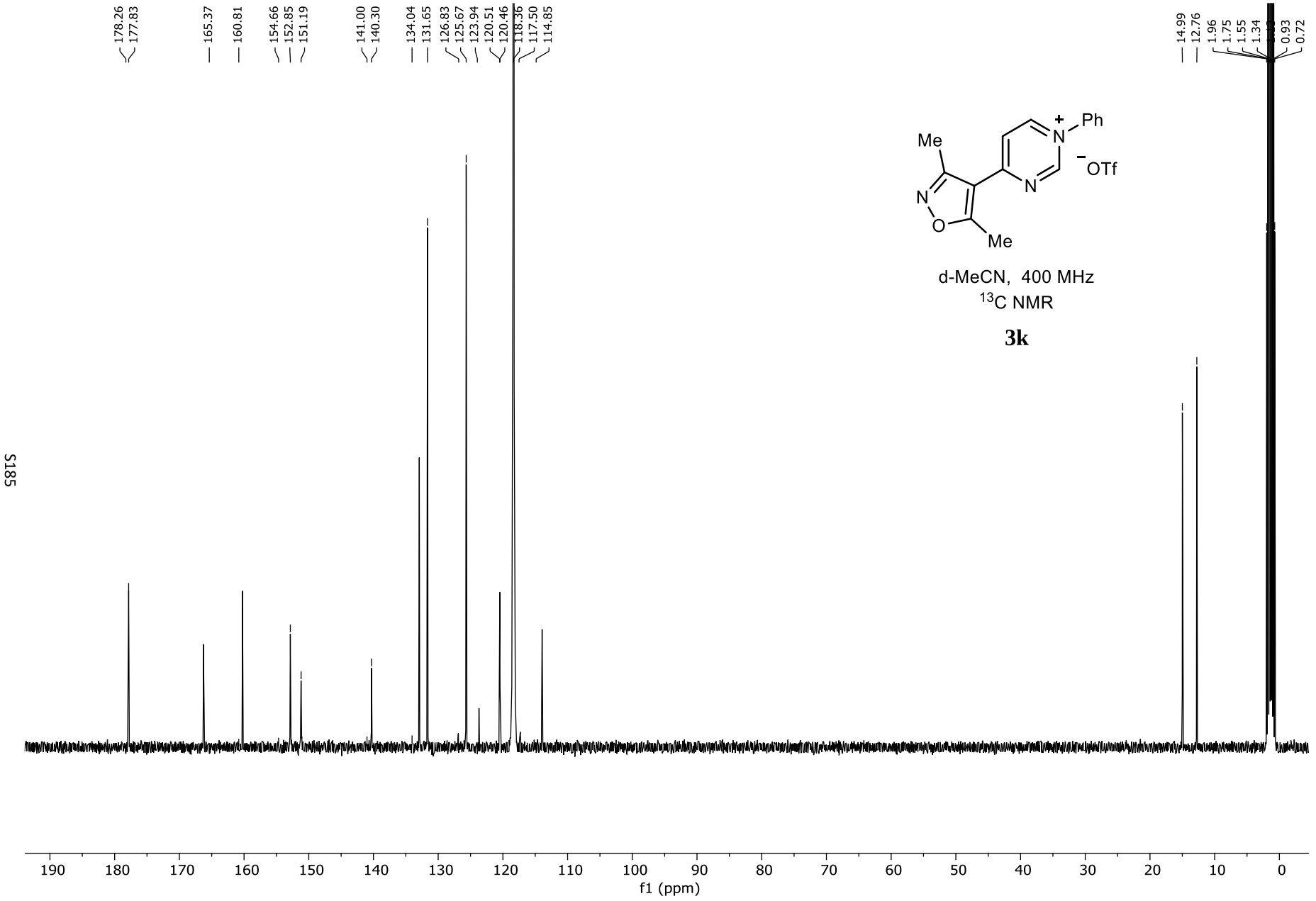

172.42
157.96
157.91
157.47
156.83
156.48
144.54
144.47
144.33
137.61
137.21
136.04
130.07
128.07
128.00
126.82
125.67
125.50
124.81
122.65
6.26
6.05
5.85
5.43
5.23
5.02
Ph
N
OTf
N
F3C
d-MeCN, 400 MHz
13C NMR
3i
f1 (ppm)

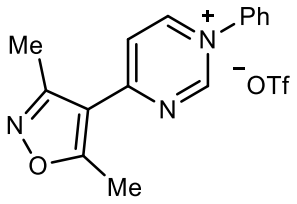


d-MeCN, 400 MHz
^{19}F NMR

3i


9.54
9.09
9.08
9.07
9.06
8.23
8.22
7.77
2.86
2.60
1.95
1.95
1.94
1.93
1.93
Me
N
Ph
OTf
N
N
O
Me
d-MeCN, 400 MHz
1H NMR
3k
S184
1.00
1.00
1.00
5.00
3.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

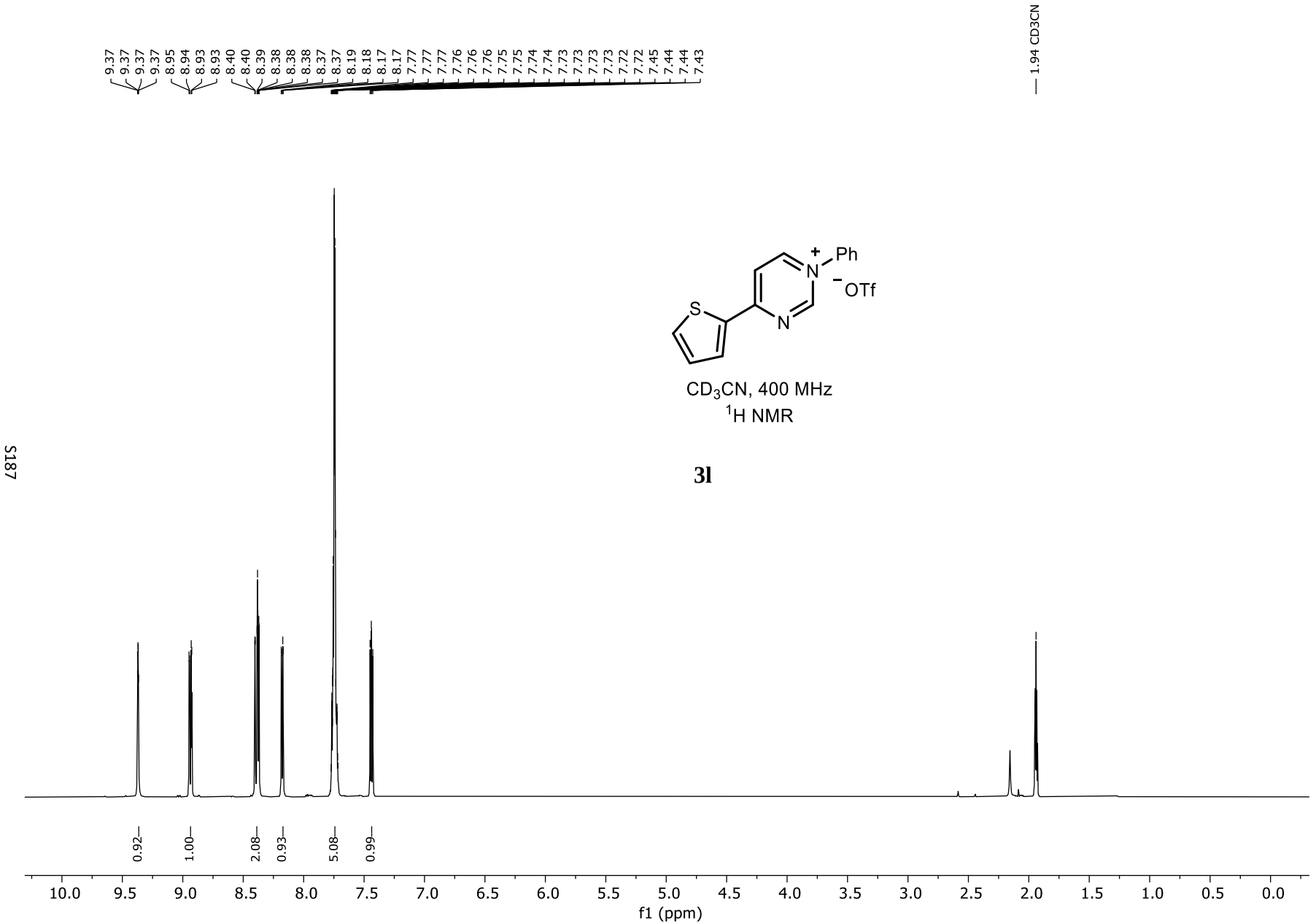

178.26
177.83
165.37
160.81
154.66
152.85
151.19
141.00
140.30
134.04
131.65
126.83
125.67
123.94
120.51
120.46
118.36
117.50
114.85
14.99
12.76
1.96
1.75
1.55
1.34
0.93
0.72
Me
N
O
Me
N
N
+
Ph
−
OTf
d-MeCN, 400 MHz
13C NMR
3k
S185
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

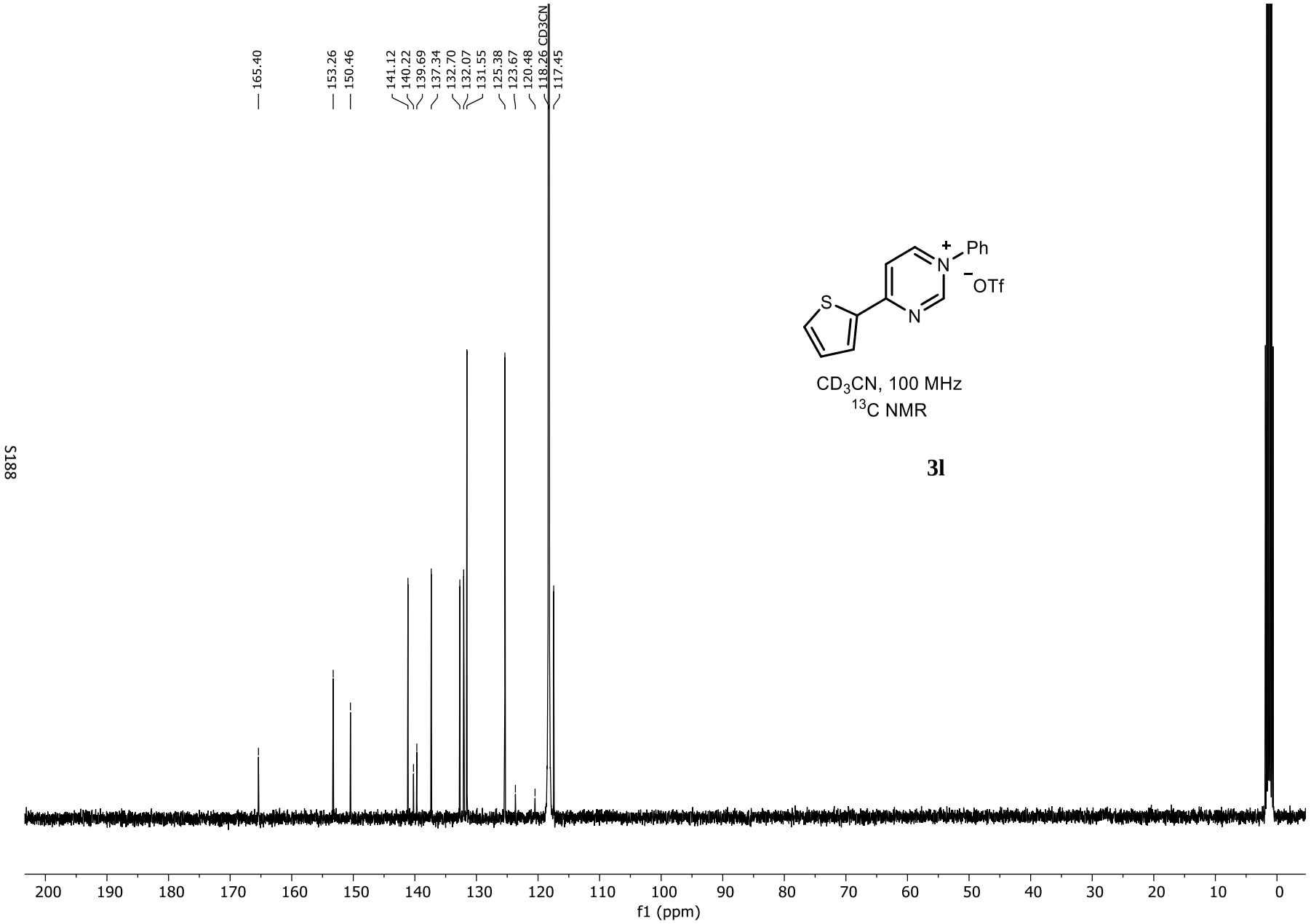


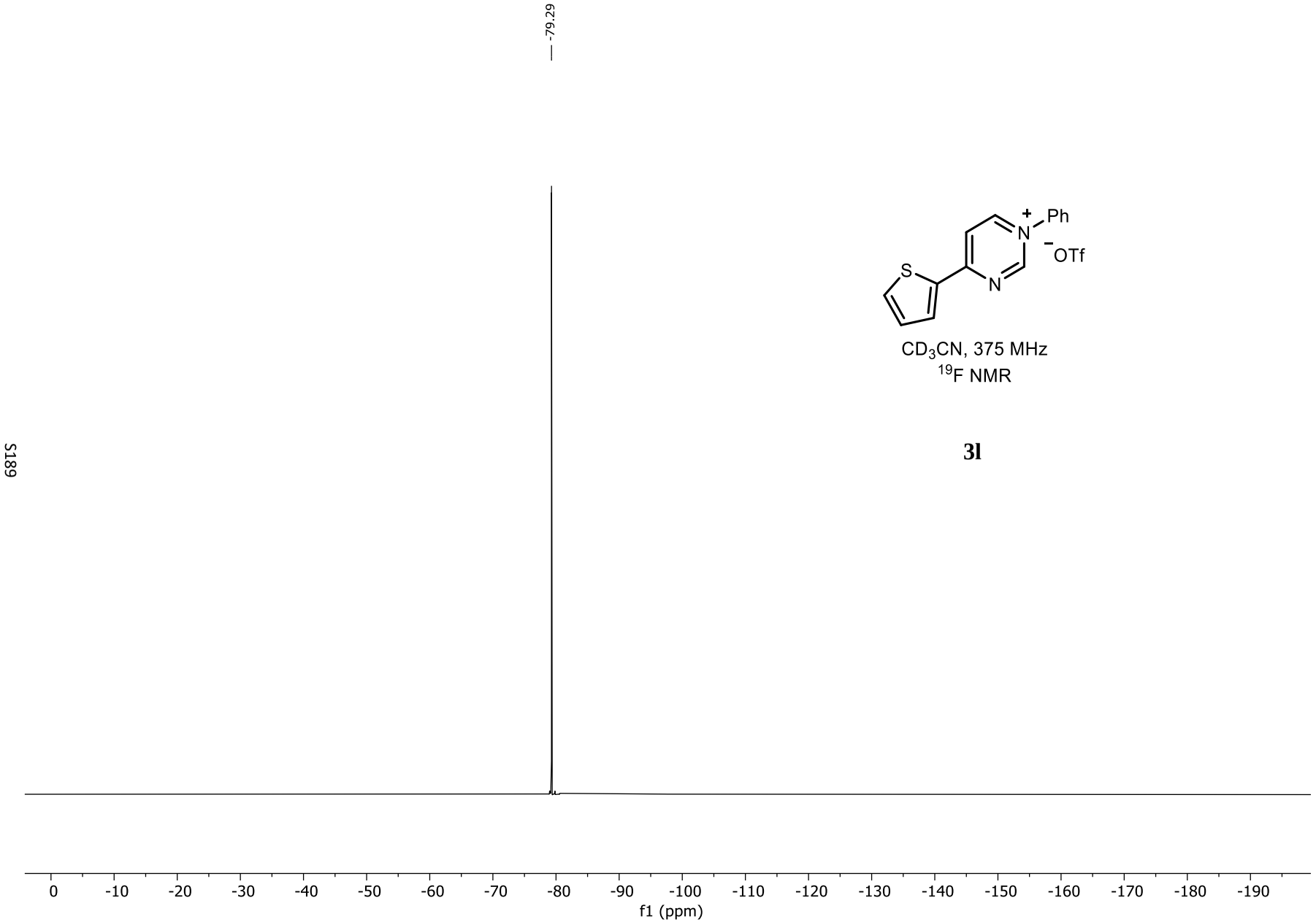
d-MeCN, 400 MHz

^{19}F NMR

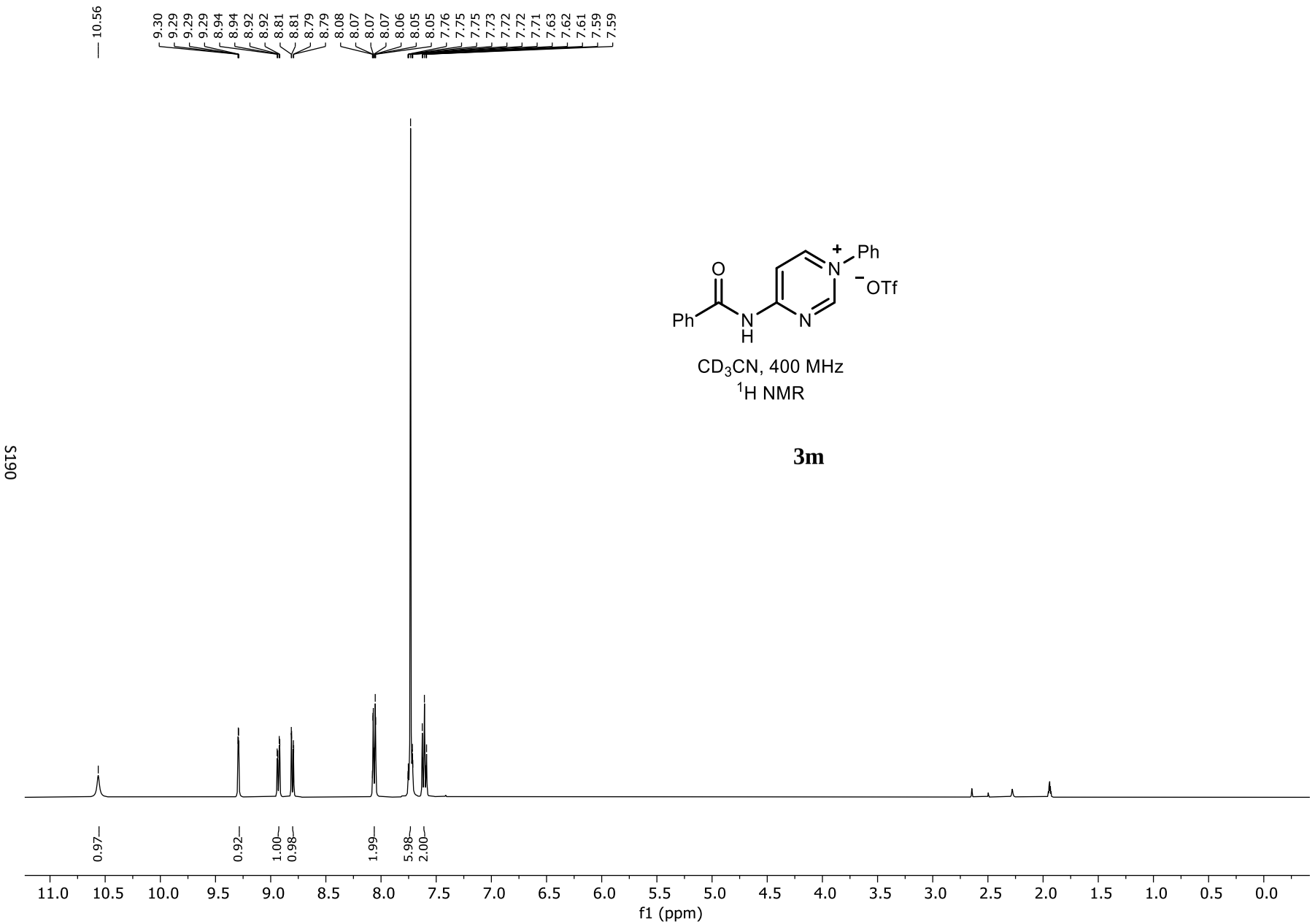
3k

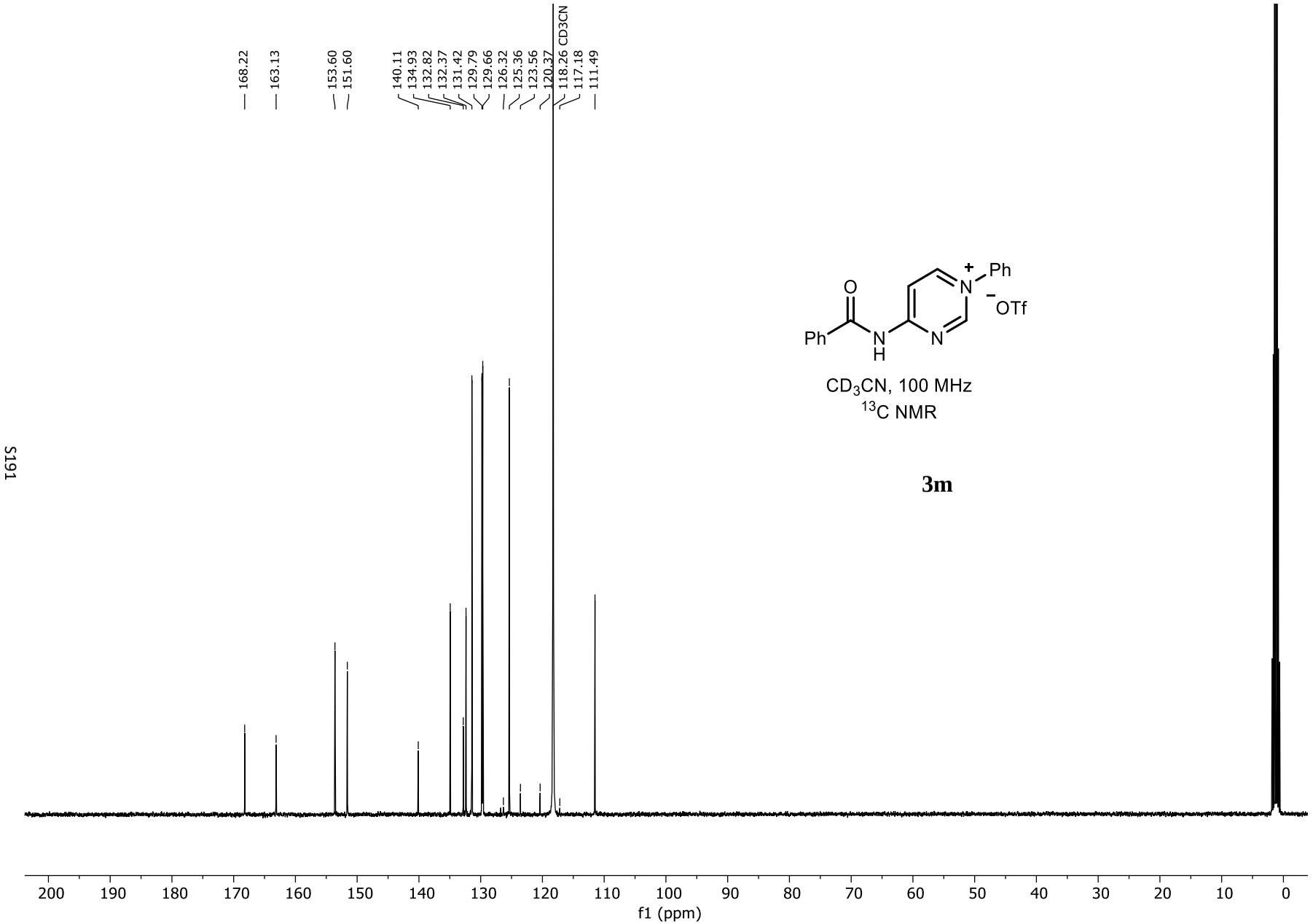

9.37
9.37
9.37
8.95
8.94
8.93
8.93
8.40
8.40
8.39
8.38
8.38
8.38
8.37
8.37
8.19
8.18
8.17
8.17
7.77
7.77
7.77
7.76
7.76
7.76
7.75
7.75
7.74
7.74
7.73
7.73
7.73
7.73
7.72
7.72
7.45
7.44
7.44
7.43
1.94 CD3CN
Ph
N
OTf
S
N
CD3CN, 400 MHz
1H NMR
3l
S187
0.92
1.00
2.08
0.93
5.08
0.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

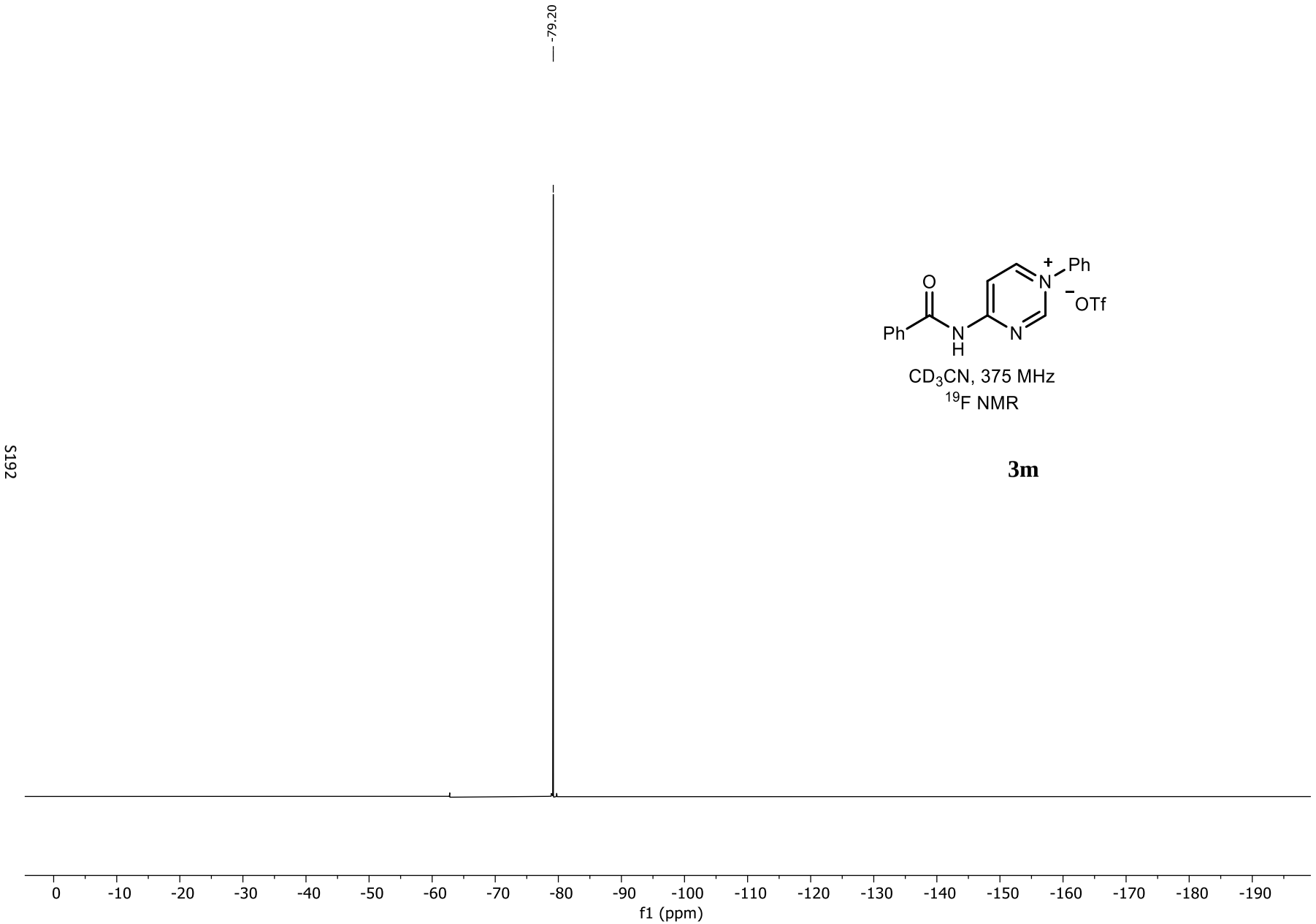

165.40
153.26
150.46
141.12
140.22
139.69
137.34
132.70
132.07
131.55
125.38
123.67
120.48
118.26 CD3CN
117.45
Ph
N
OTf
S
N
CD3CN, 100 MHz
13C NMR
3l
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-79.29
Ph
N
OTf
S
N
CD3CN, 375 MHz
19F NMR
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

3l


10.56
9.30
9.29
9.29
9.29
8.94
8.94
8.92
8.92
8.92
8.81
8.81
8.79
8.79
8.08
8.07
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
Ph
N
O
Ph
N
H
N
OTf
CD3CN, 400 MHz
1H NMR
3m
S190
0.97
0.92
1.00
0.98
1.99
5.98
2.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

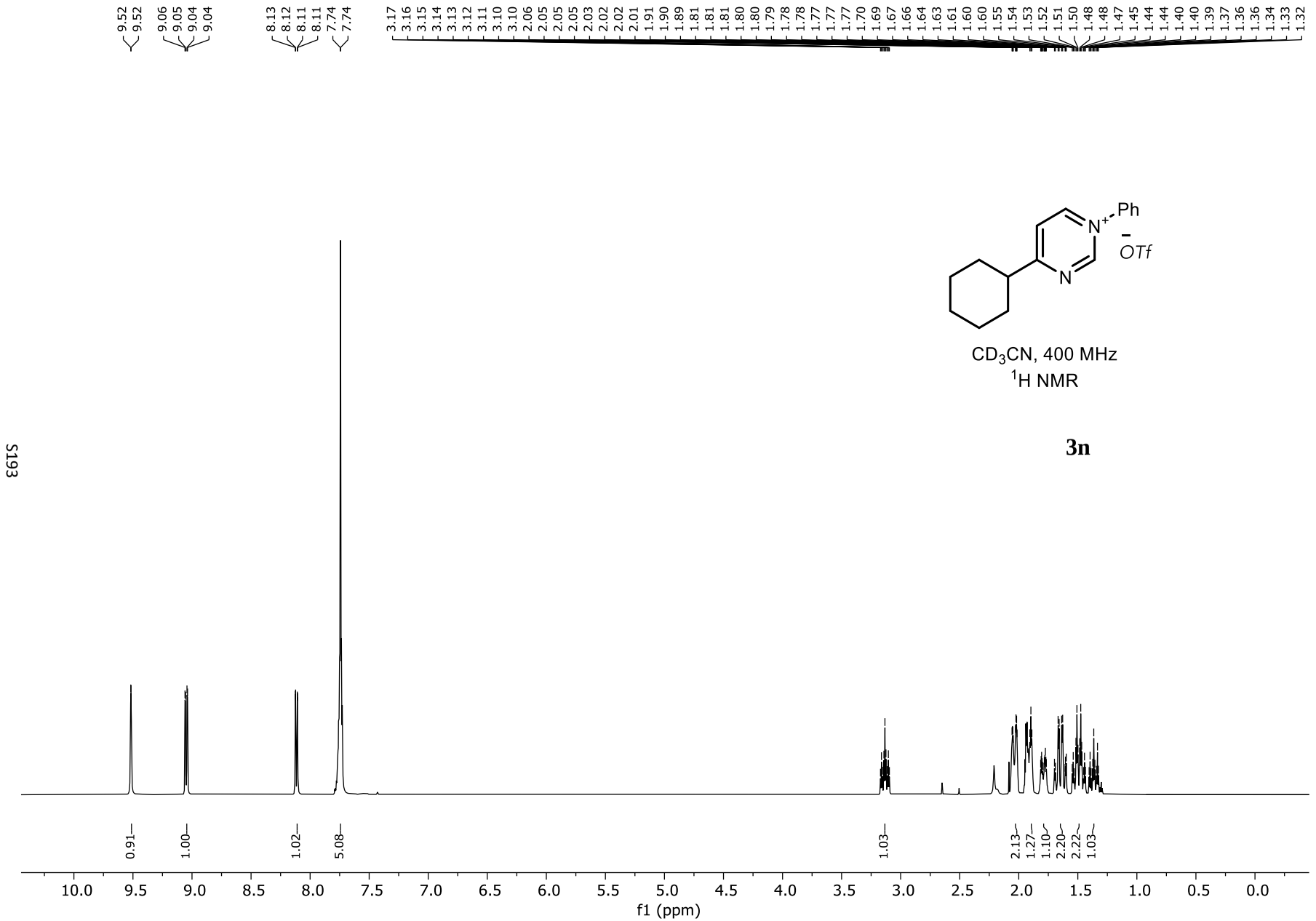

168.22
163.13
153.60
151.60
140.11
134.93
132.82
132.37
131.42
129.79
129.66
126.32
125.36
123.56
120.37
118.26 CD3CN
117.18
111.49
O
Ph
N
H
N
N
Ph
OTf
CD3CN, 100 MHz
13C NMR
3m
f1 (ppm)

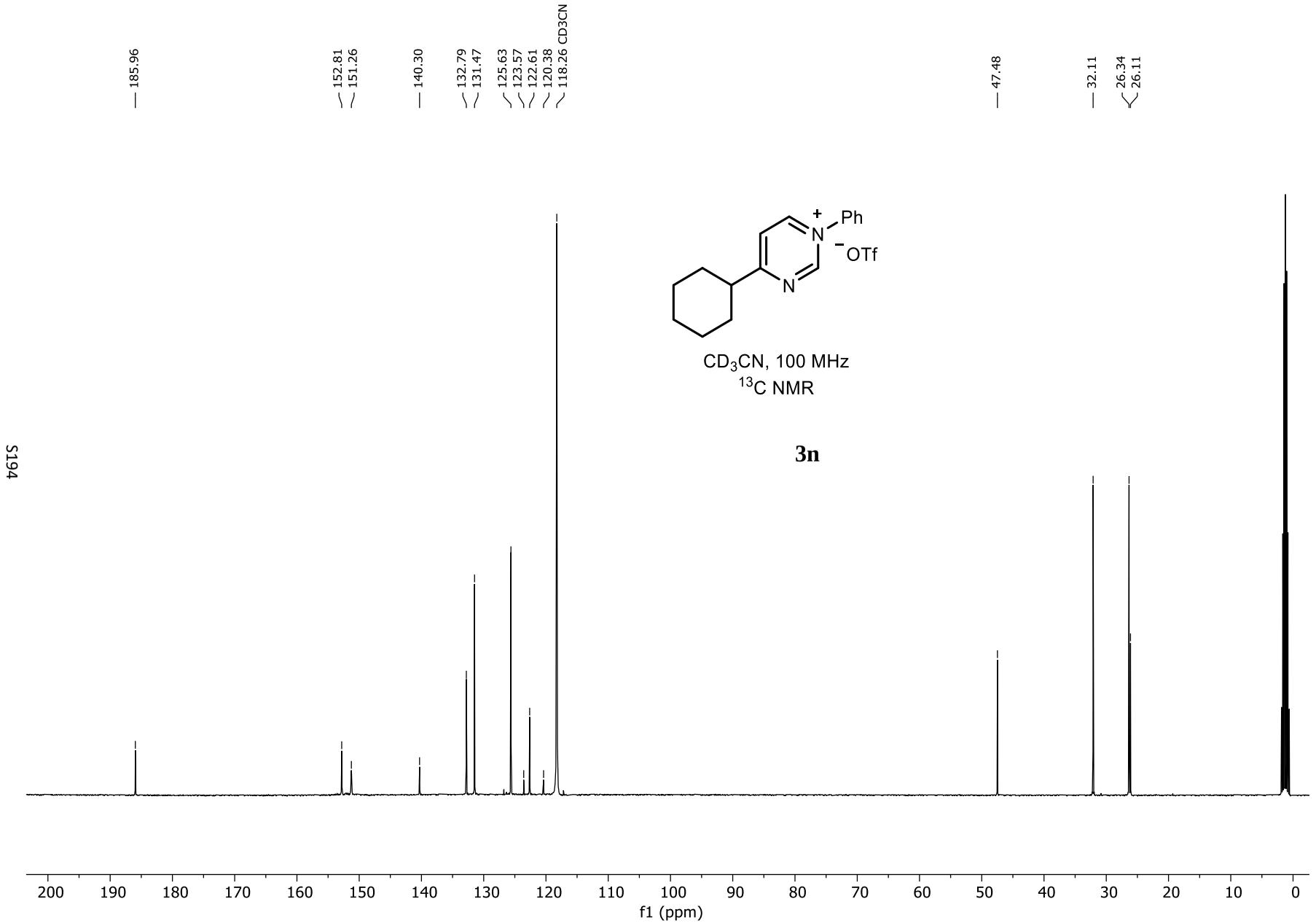


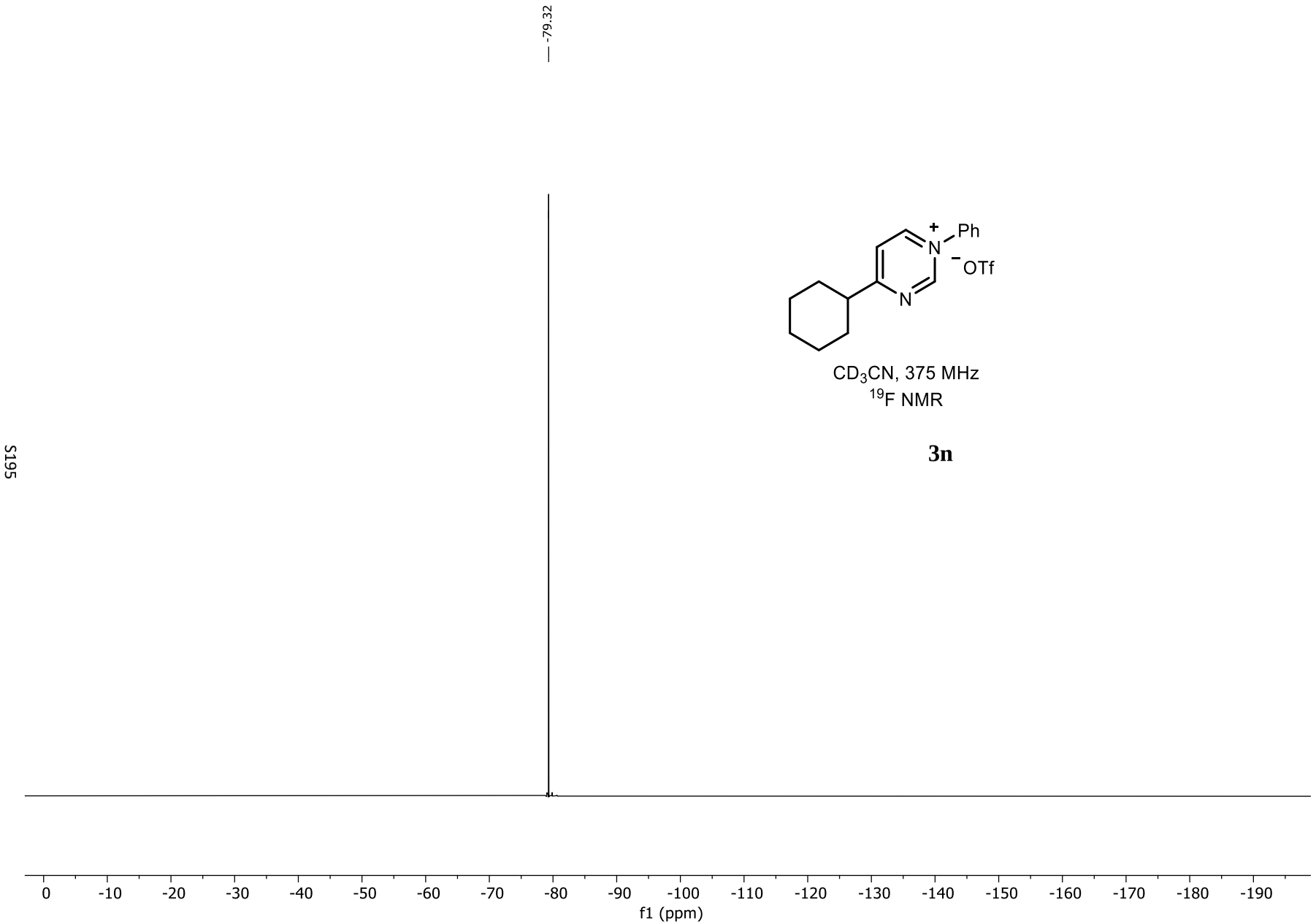
CD_3CN, 375 MHz

^{19}F NMR

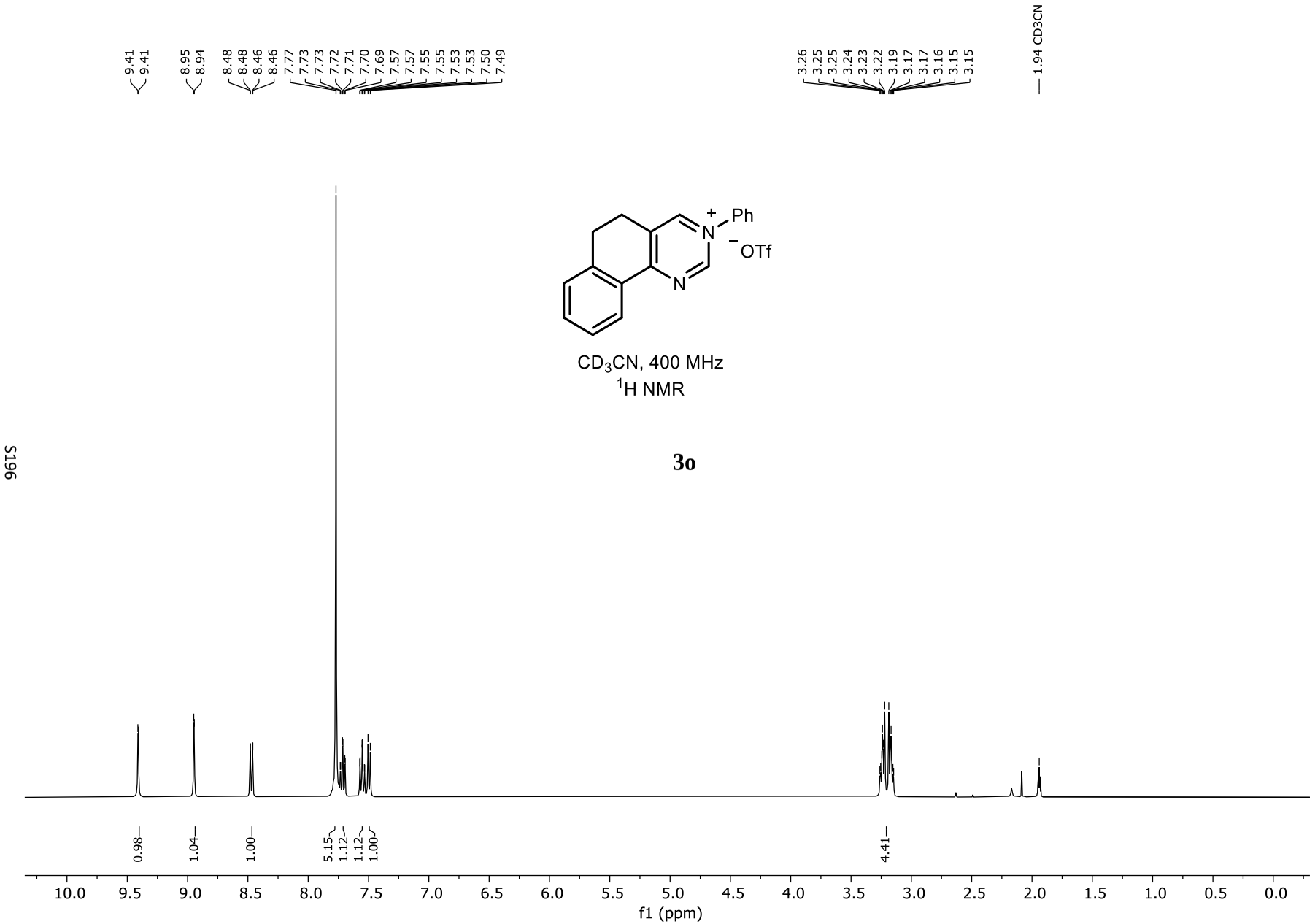
3m

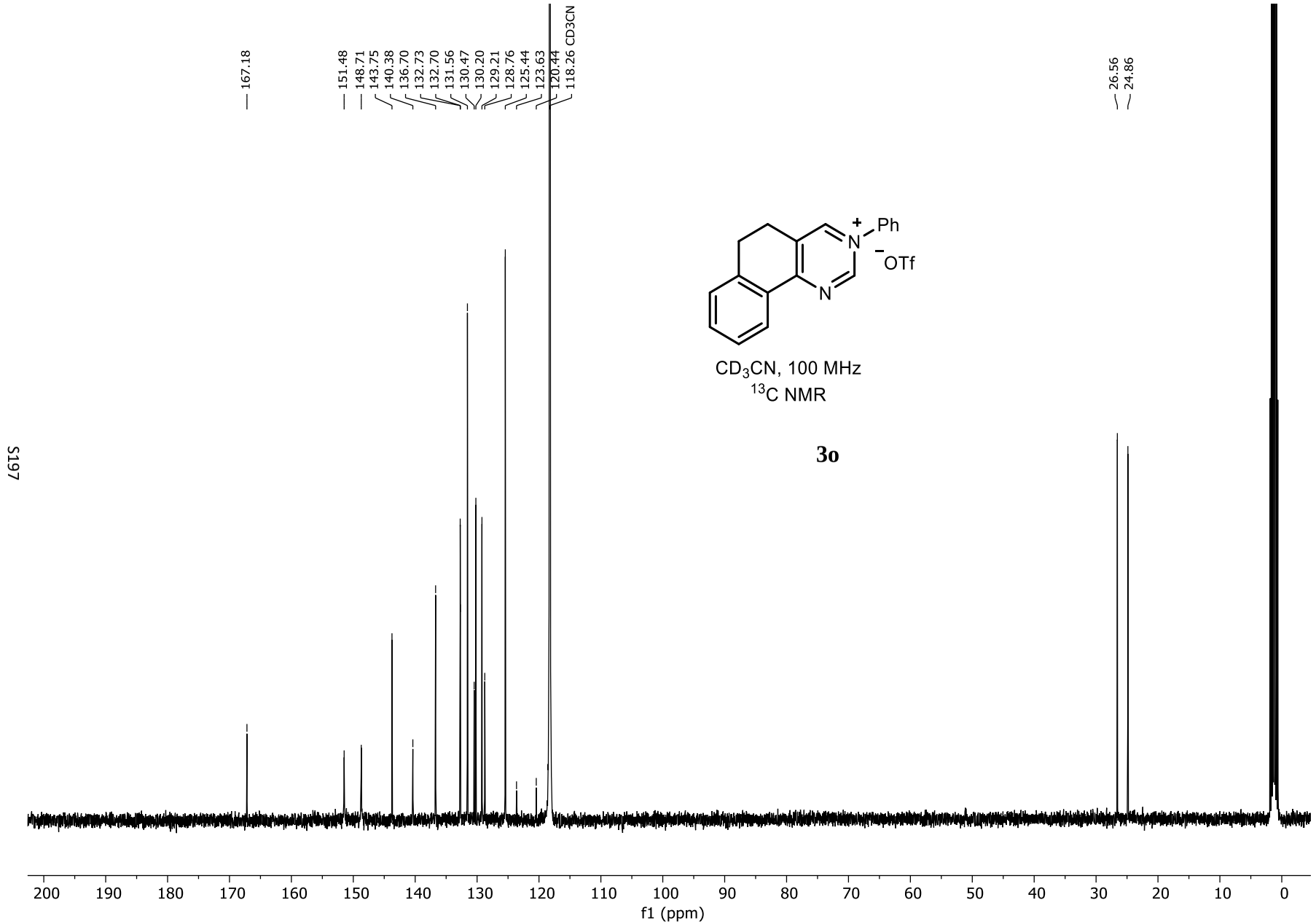

9.52 9.52 9.06 9.05 9.04 9.04 8.13 8.12 8.11 8.11 7.74 7.74
3.17 3.16 3.15 3.14 3.13 3.12 3.11 3.10 3.10 2.06 2.05 2.05 2.05 2.03 2.02 2.02 2.01 1.91 1.90 1.89 1.81 1.81 1.81 1.80 1.80 1.79 1.78 1.78 1.77 1.77 1.77 1.70 1.69 1.67 1.66 1.64 1.63 1.61 1.60 1.60 1.55 1.54 1.53 1.52 1.51 1.50 1.48 1.48 1.47 1.45 1.44 1.44 1.40 1.40 1.39 1.37 1.36 1.36 1.34 1.33 1.32
Ph
N+
OTf
N
CD3CN, 400 MHz
1H NMR
3n
S193
0.91 1.00 1.02 5.08 1.03 2.13 1.27 1.10 2.20 2.22 1.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


185.96
152.81
151.26
140.30
132.79
131.47
125.63
123.57
122.61
120.38
118.26 CD3CN
47.48
32.11
26.34
26.11
Ph
N
OTf
N
CD3CN, 100 MHz
13C NMR
3n
S194
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-79.32
Ph
N
OTf
N
CD3CN, 375 MHz
19F NMR
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

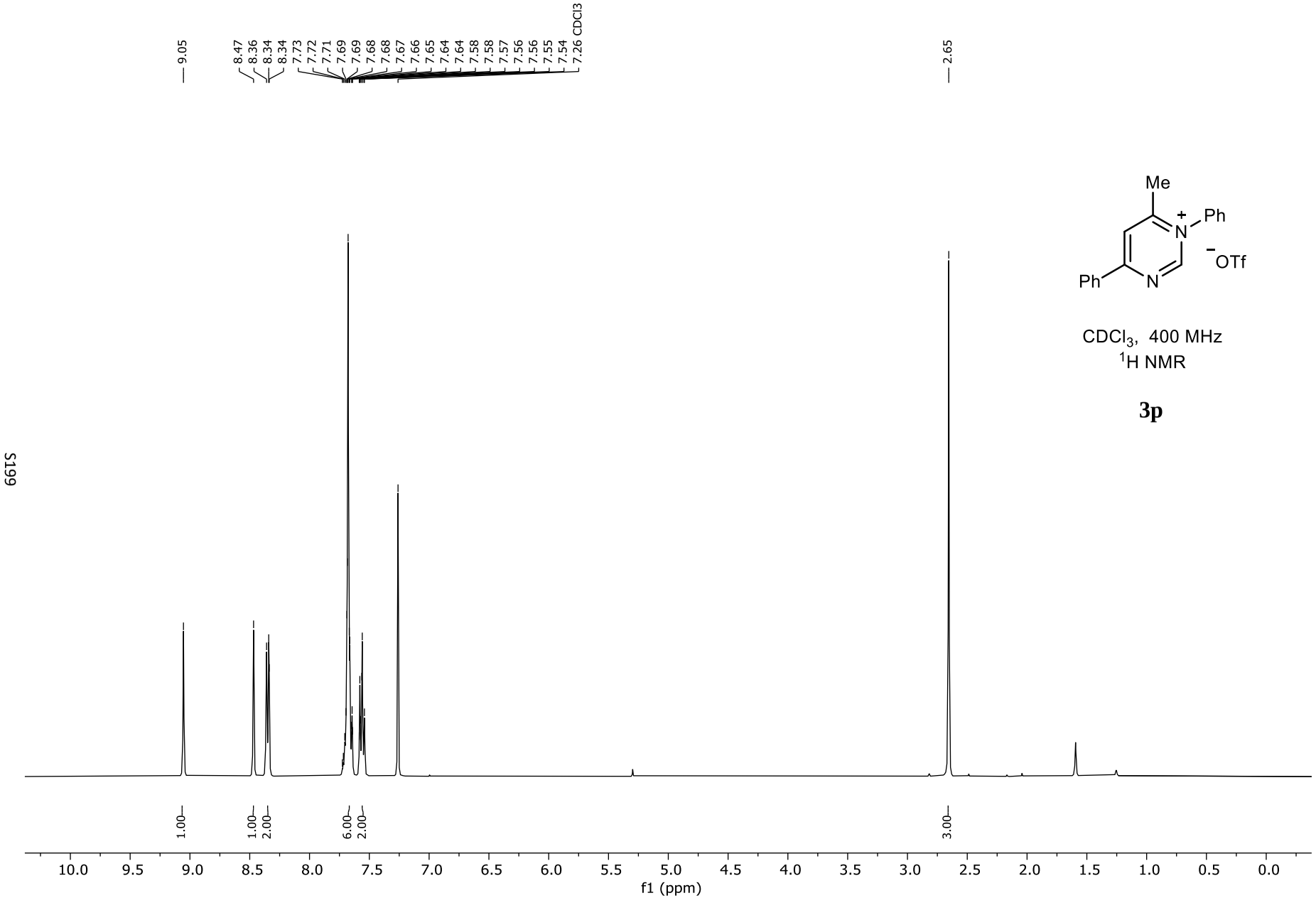
3n

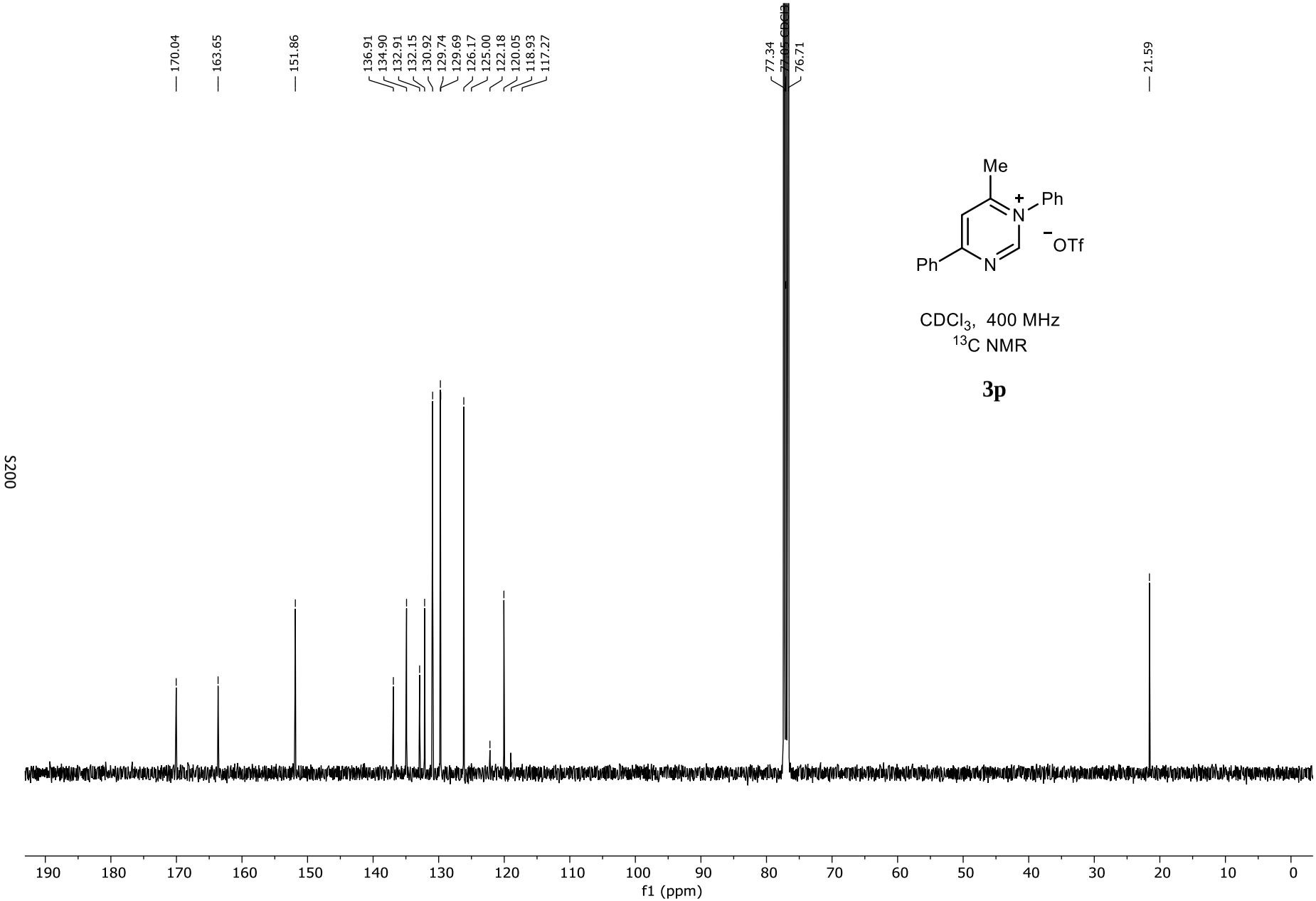

9.41
9.41
8.95
8.94
8.48
8.48
8.46
8.46
7.77
7.73
7.73
7.72
7.71
7.70
7.69
7.57
7.57
7.55
7.55
7.53
7.53
7.50
7.49
3.26
3.25
3.25
3.24
3.23
3.22
3.19
3.17
3.17
3.16
3.15
3.15
1.94 CD3CN
Ph
N
OTf
N
CD3CN, 400 MHz
1H NMR
3o
0.98
1.04
1.00
5.15
1.12
1.12
1.00
4.41
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


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
123.63
120.44
118.26 CD3CN
26.56
24.86
Ph
N
OTf
N
CD3CN, 100 MHz
13C NMR
3o
f1 (ppm)

CD_3CN, 375 MHz
^{19}F NMR

3o


9.05
8.47
8.36
8.34
8.34
7.73
7.72
7.71
7.69
7.69
7.68
7.68
7.67
7.66
7.65
7.64
7.64
7.58
7.58
7.57
7.56
7.56
7.55
7.54
7.26 CDCl3
2.65
Me
Ph
N
OTf
Ph
N
CDCl3, 400 MHz
1H NMR
3p
S199
1.00
1.00
2.00
6.00
2.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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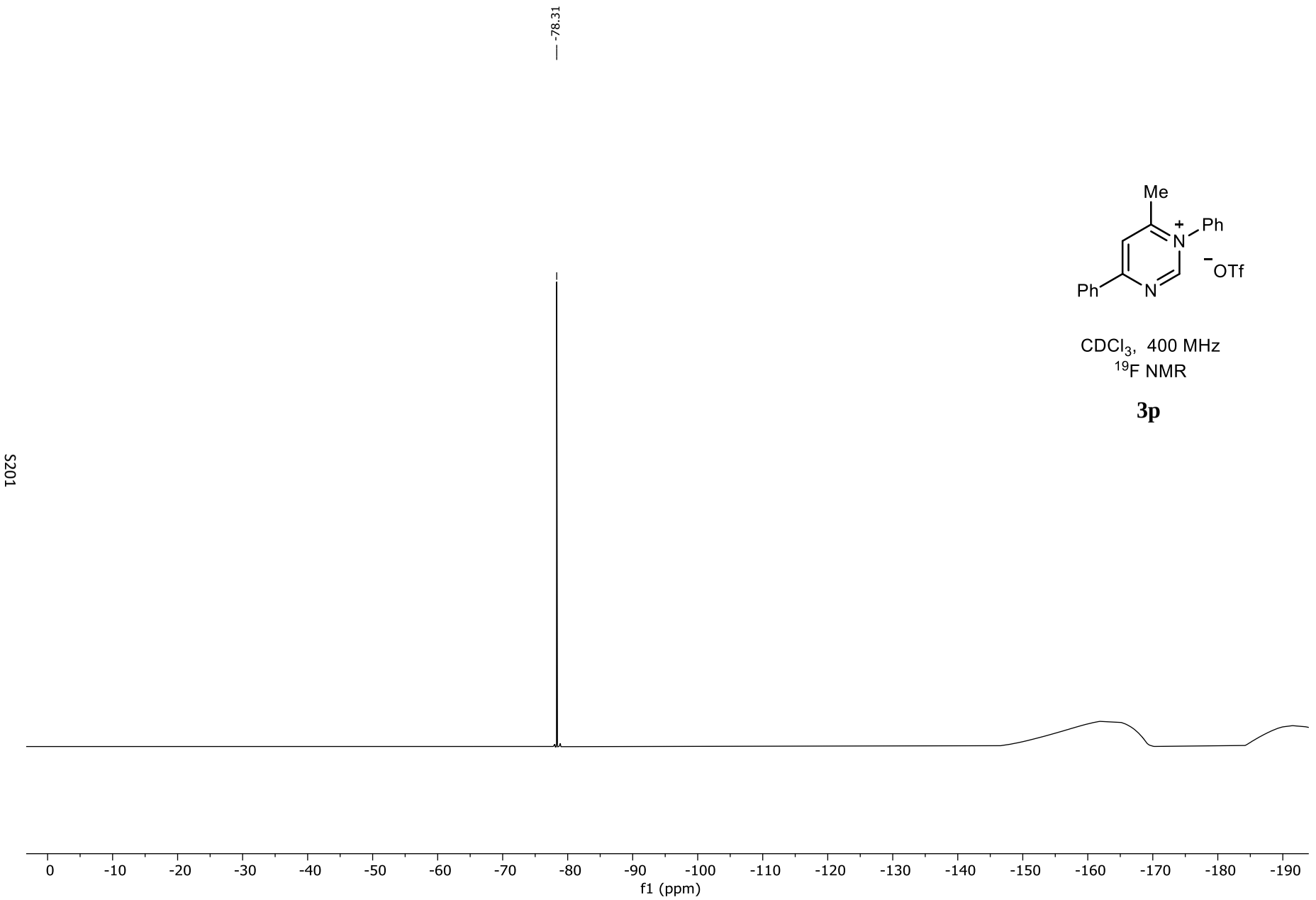
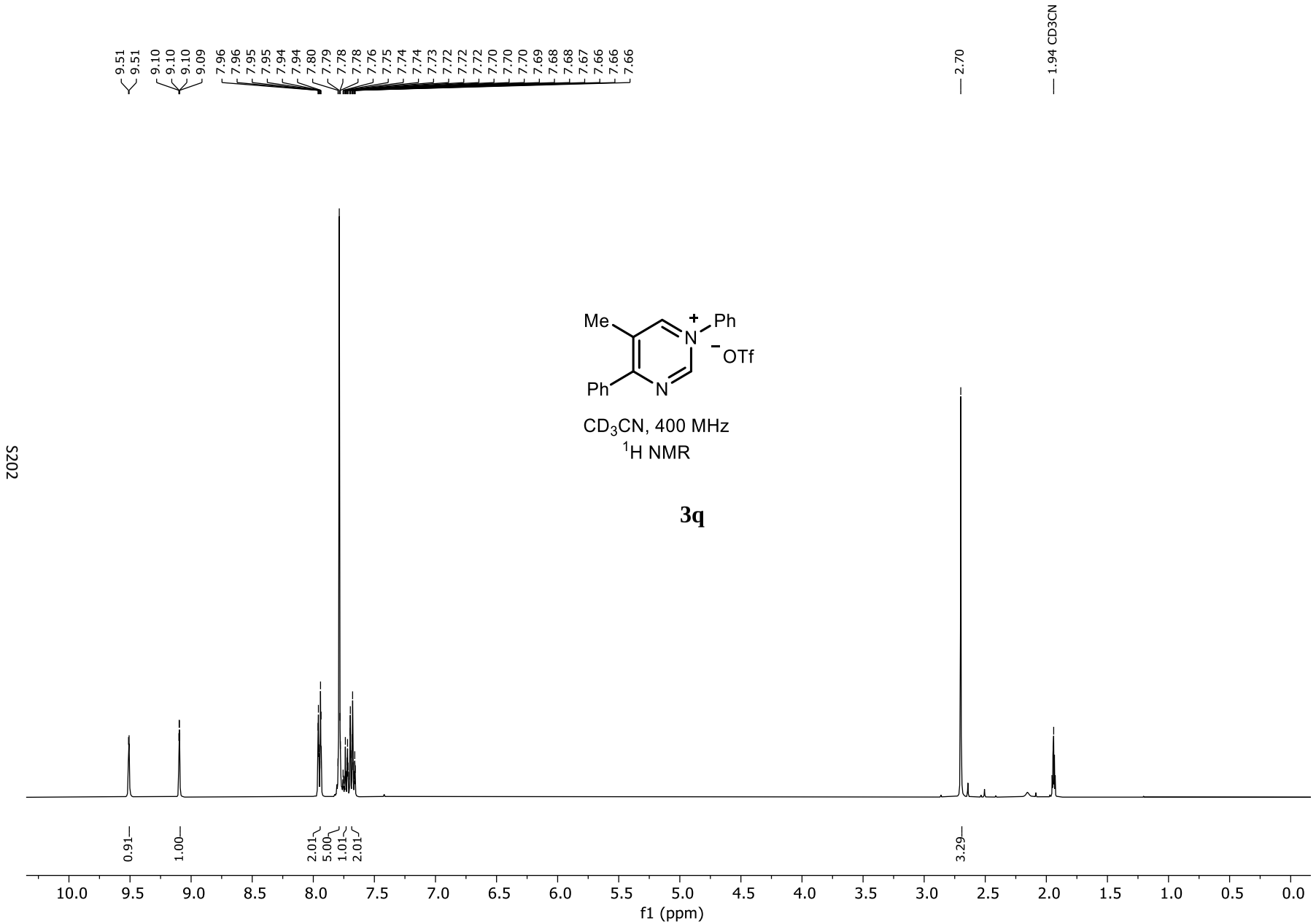
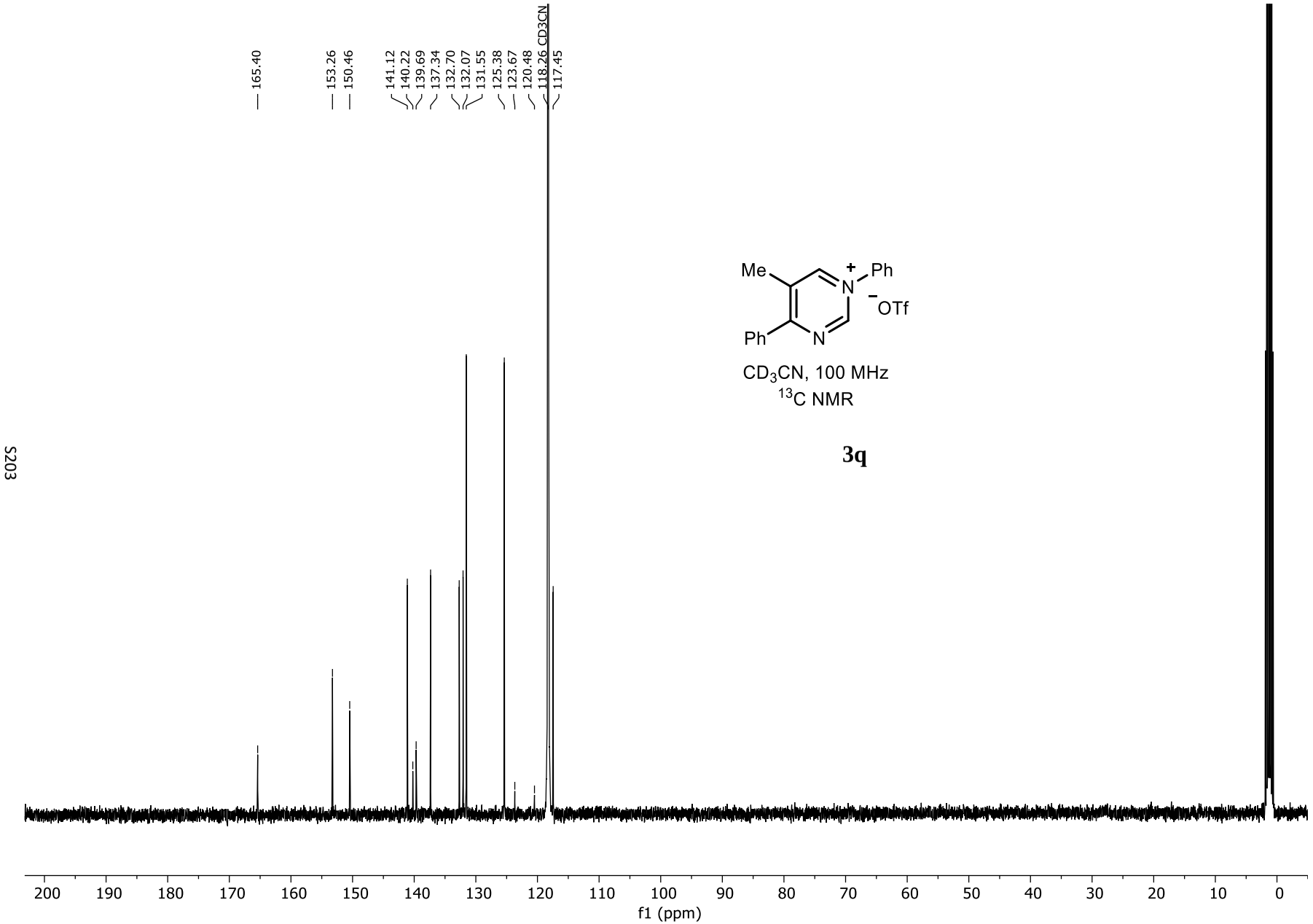
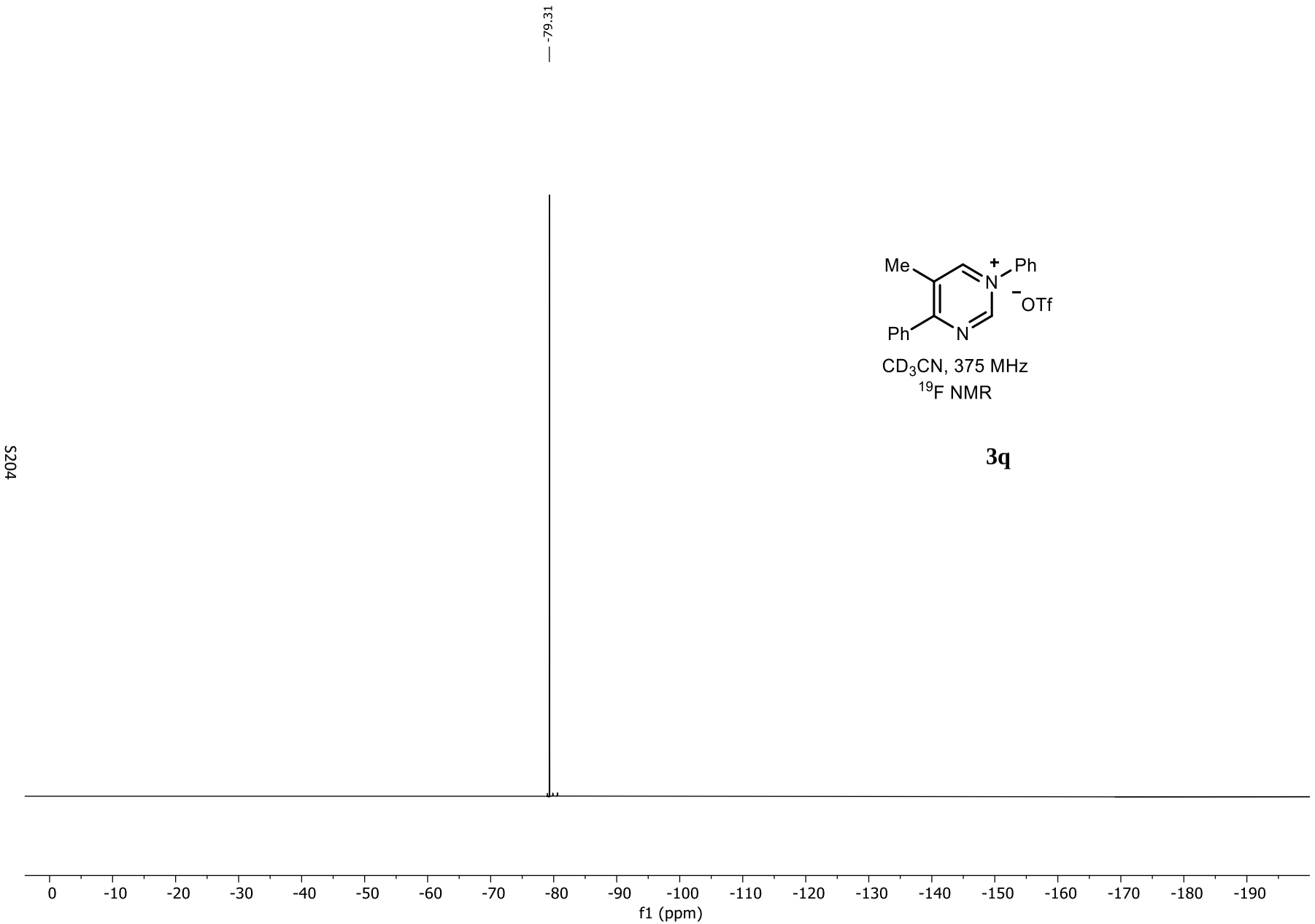
163.65
151.86
136.91
134.90
132.91
132.15
130.92
129.74
129.69
126.17
125.00
122.18
120.05
118.93
117.27
77.34
76.71
21.59
Me
Ph
N
OTf
Ph
N
CDCl3, 400 MHz
13C NMR
3p
S200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

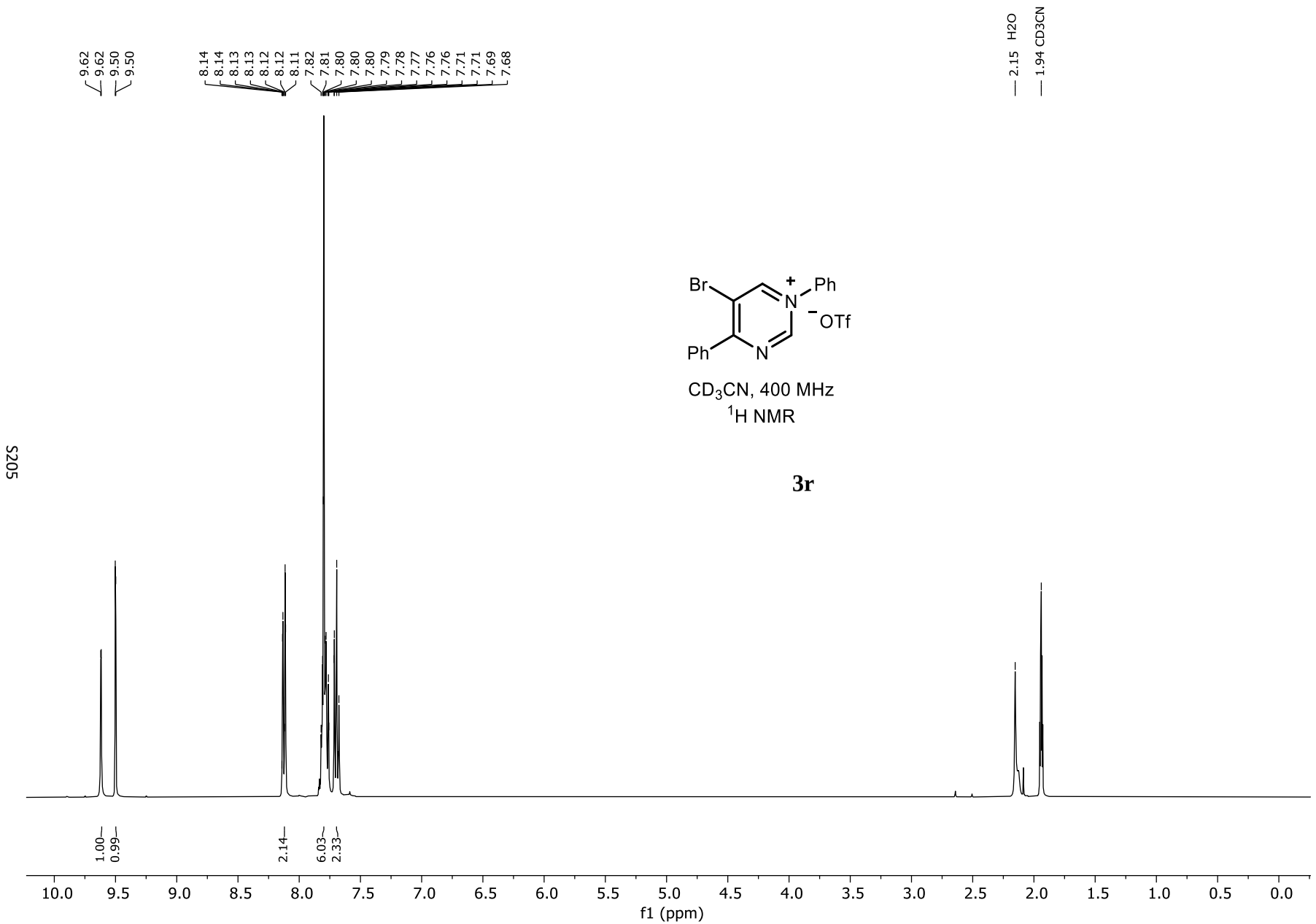

-78.31
Me
Ph
N
OTf
Ph
N
CDCl3, 400 MHz
19F NMR
3p
S201
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

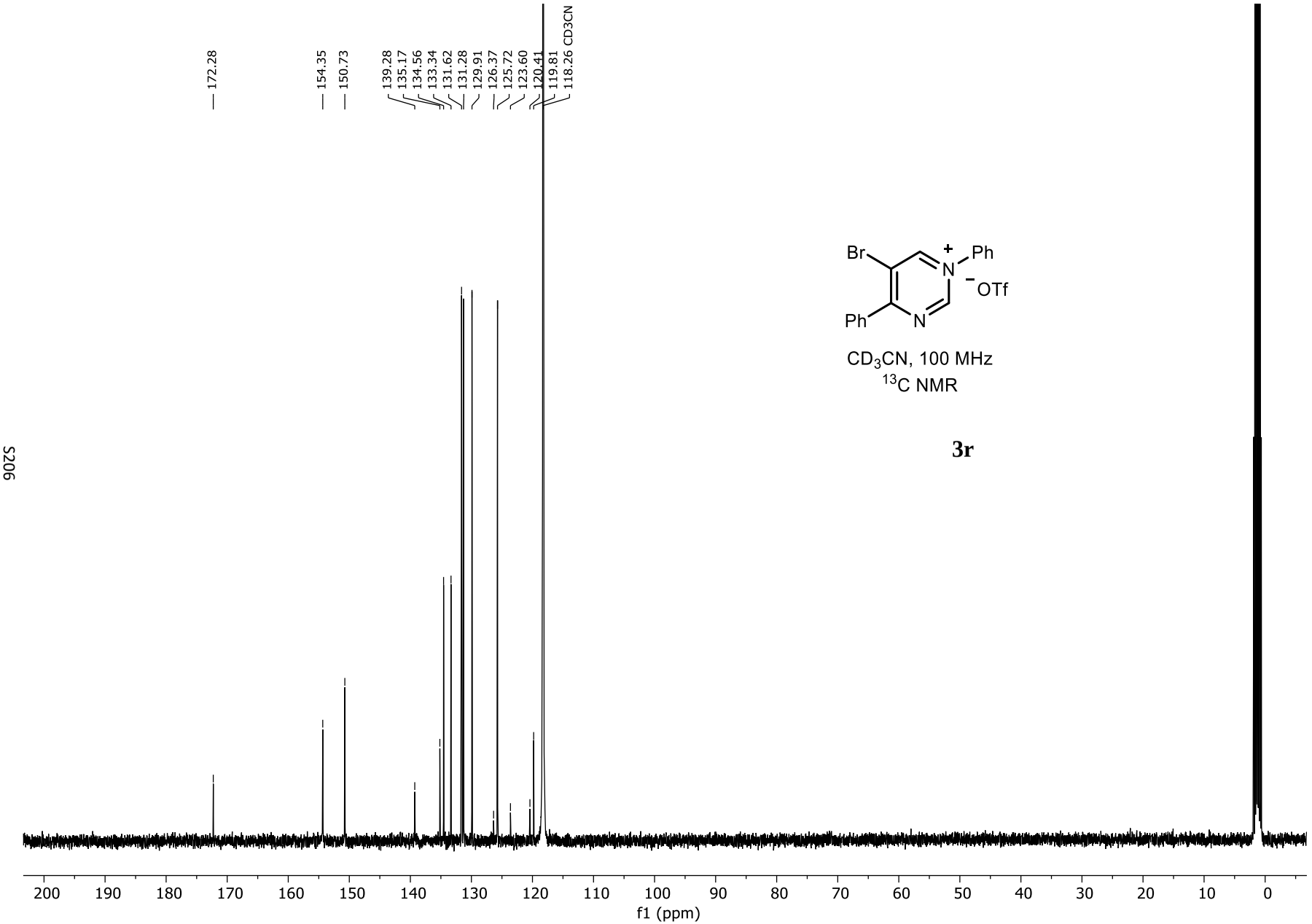

9.51
9.51
9.10
9.10
9.10
9.09
7.96
7.96
7.95
7.95
7.94
7.94
7.80
7.79
7.78
7.78
7.76
7.75
7.74
7.74
7.73
7.72
7.72
7.72
7.70
7.70
7.70
7.69
7.68
7.68
7.67
7.66
7.66
7.66
2.70
1.94 CD3CN
Me
Ph
N
OTf
Ph
N
CD3CN, 400 MHz
1H NMR
3q
S202
0.91
1.00
2.01
5.00
1.01
2.01
3.29
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

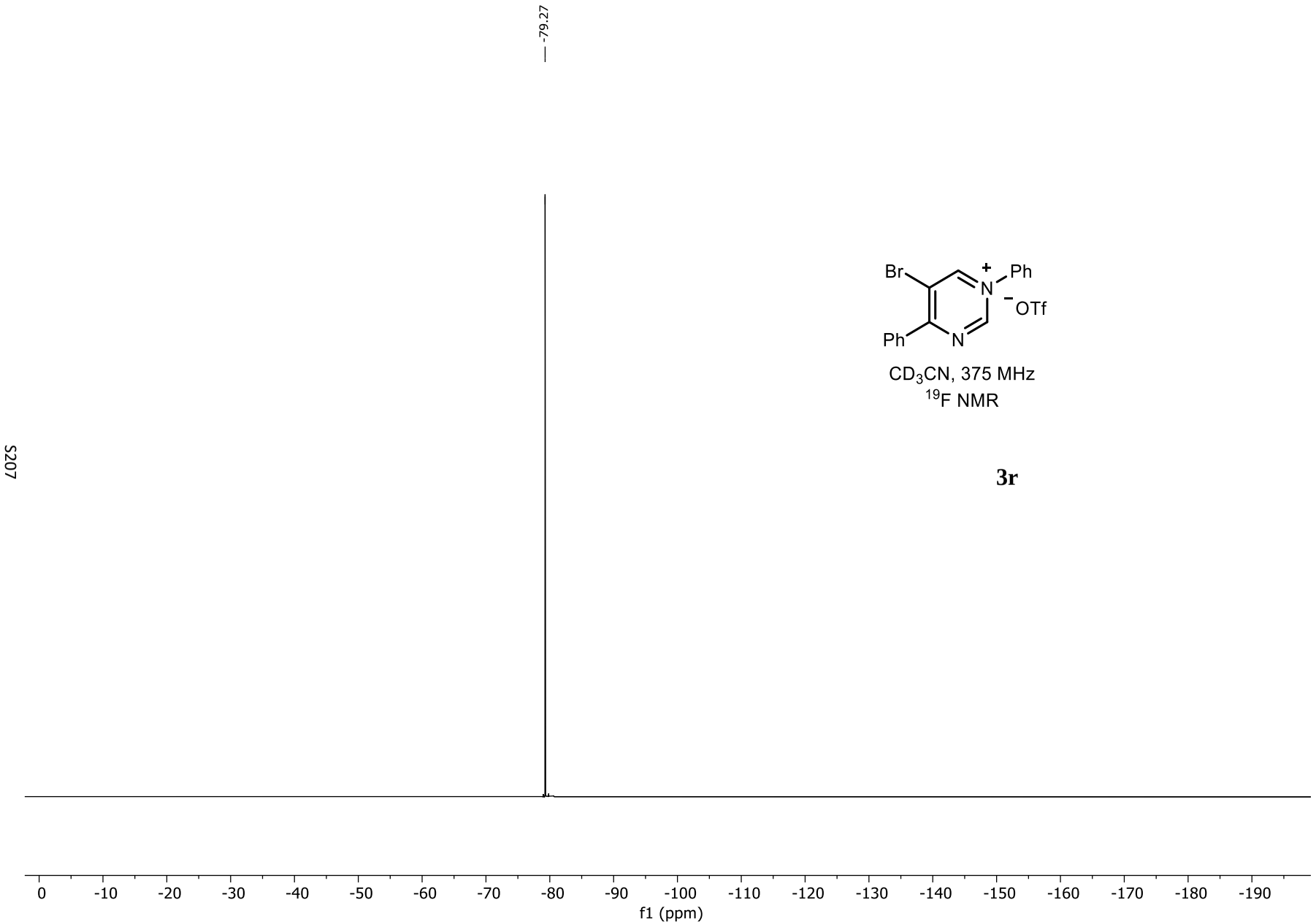

165.40
153.26
150.46
141.12
140.22
139.69
137.34
132.70
132.07
131.55
125.38
123.67
120.48
118.26 CD3CN
117.45
Me
Ph
N
OTf
Ph
N
CD3CN, 100 MHz
13C NMR
3q
S203
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-79.31
Me
Ph
N
OTf
Ph
N
CD3CN, 375 MHz
19F NMR
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

3q


9.62
9.62
9.50
9.50
8.14
8.14
8.13
8.13
8.12
8.12
8.11
7.82
7.81
7.80
7.80
7.80
7.79
7.78
7.77
7.76
7.76
7.71
7.71
7.69
7.68
2.15 H2O
1.94 CD3CN
S205
Br
Ph
N
OTf
Ph
N
CD3CN, 400 MHz
1H NMR
3r
1.00
0.99
2.14
6.03
2.33
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

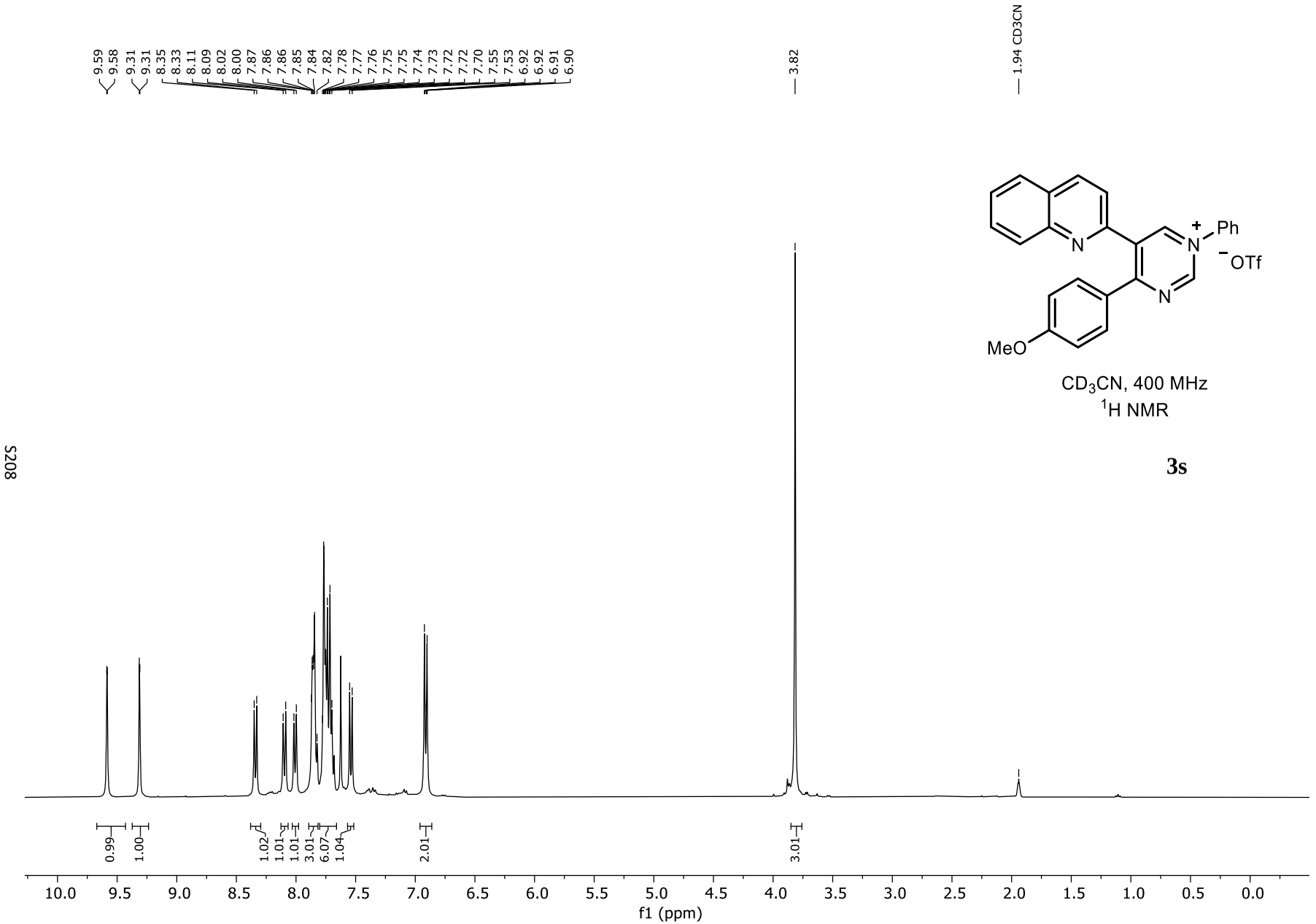

172.28
154.35
150.73
139.28
135.17
134.56
133.34
131.62
131.28
129.91
126.37
125.72
123.60
120.41
119.81
118.26 CD3CN
Br
Ph
N
OTf
Ph
N
CD3CN, 100 MHz
13C NMR
3r
S206
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



CD_3CN, 375 MHz

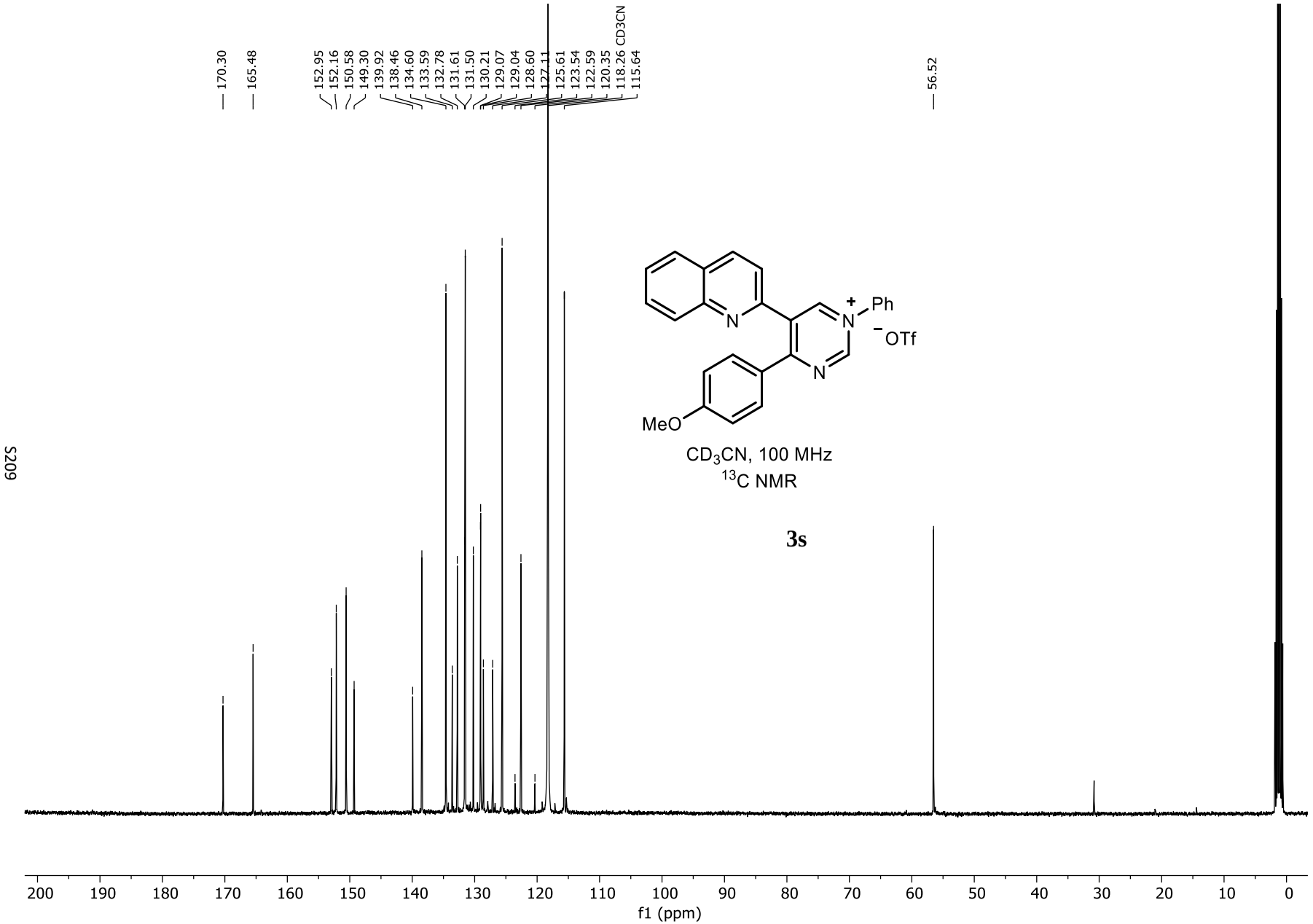
^{19}F NMR

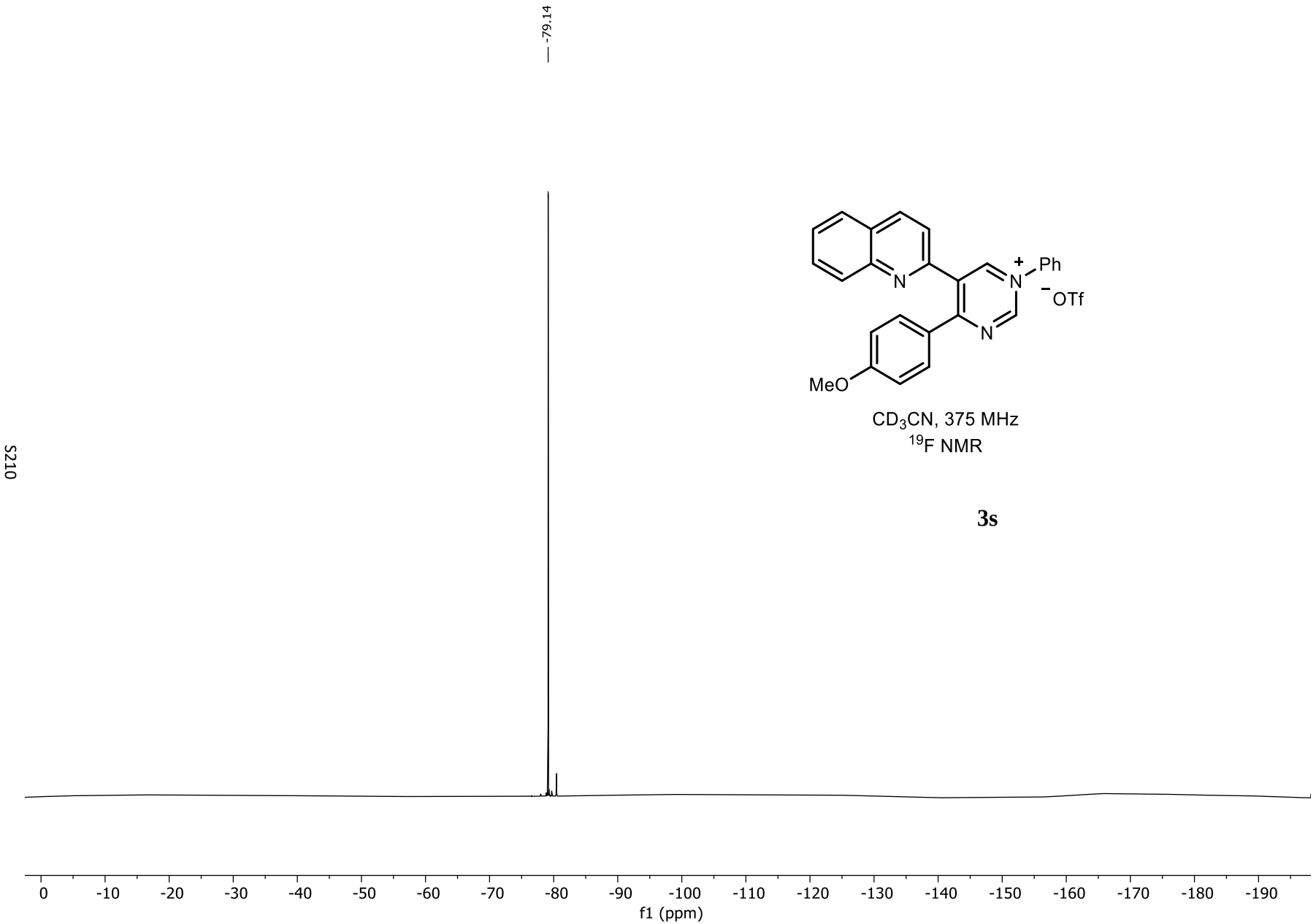
3r



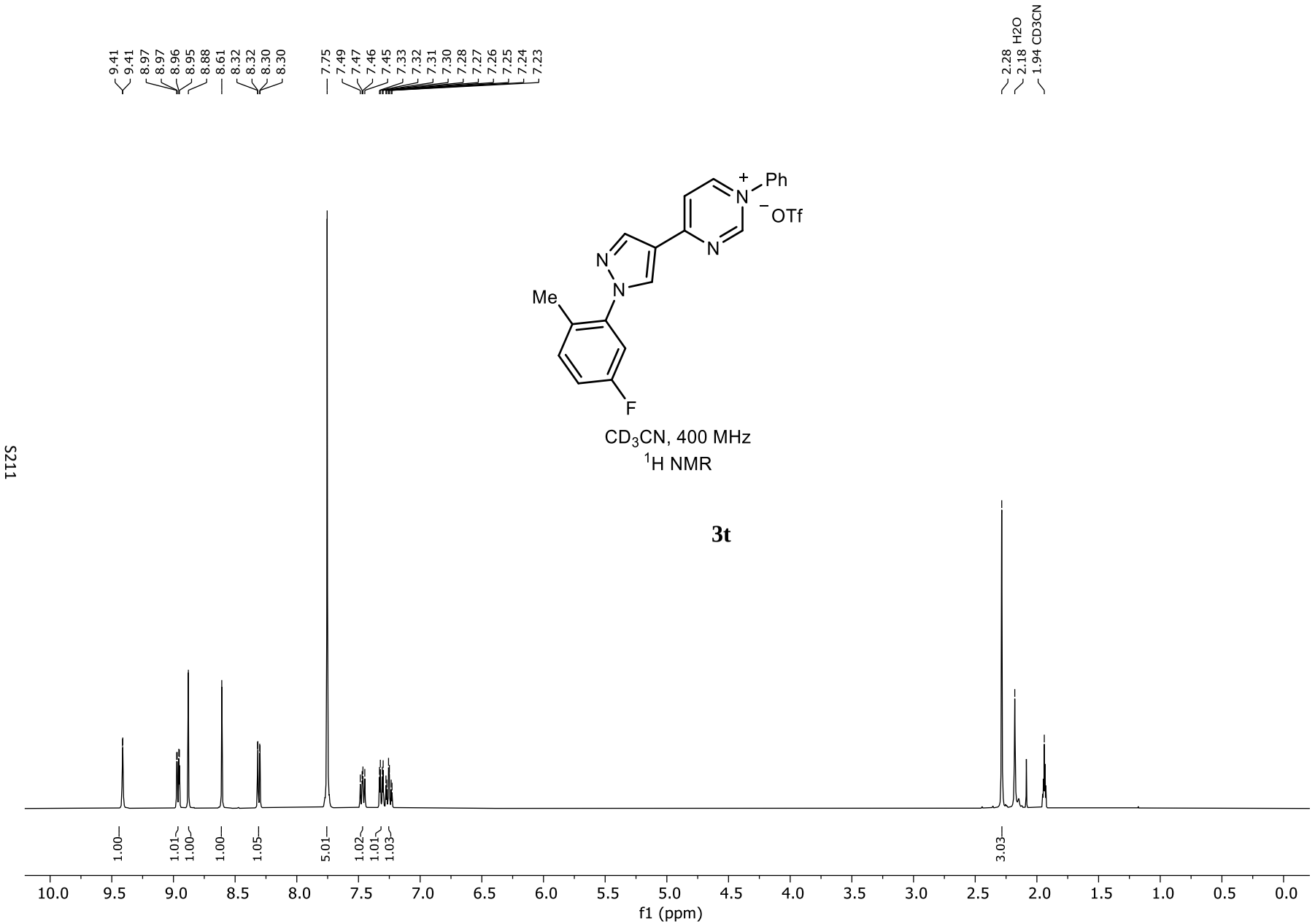
CD_3CN, 400 MHz
^1H NMR

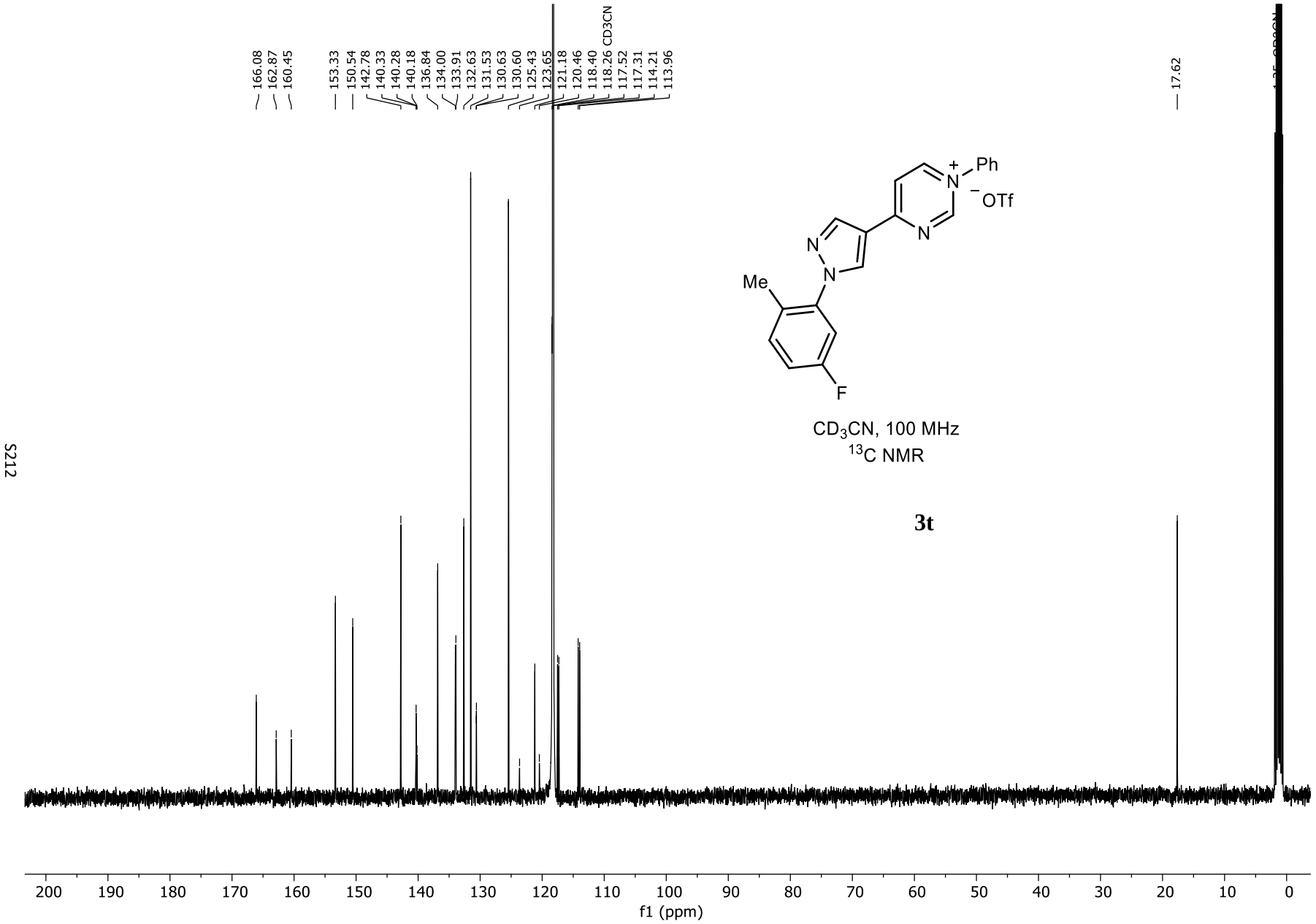
3s

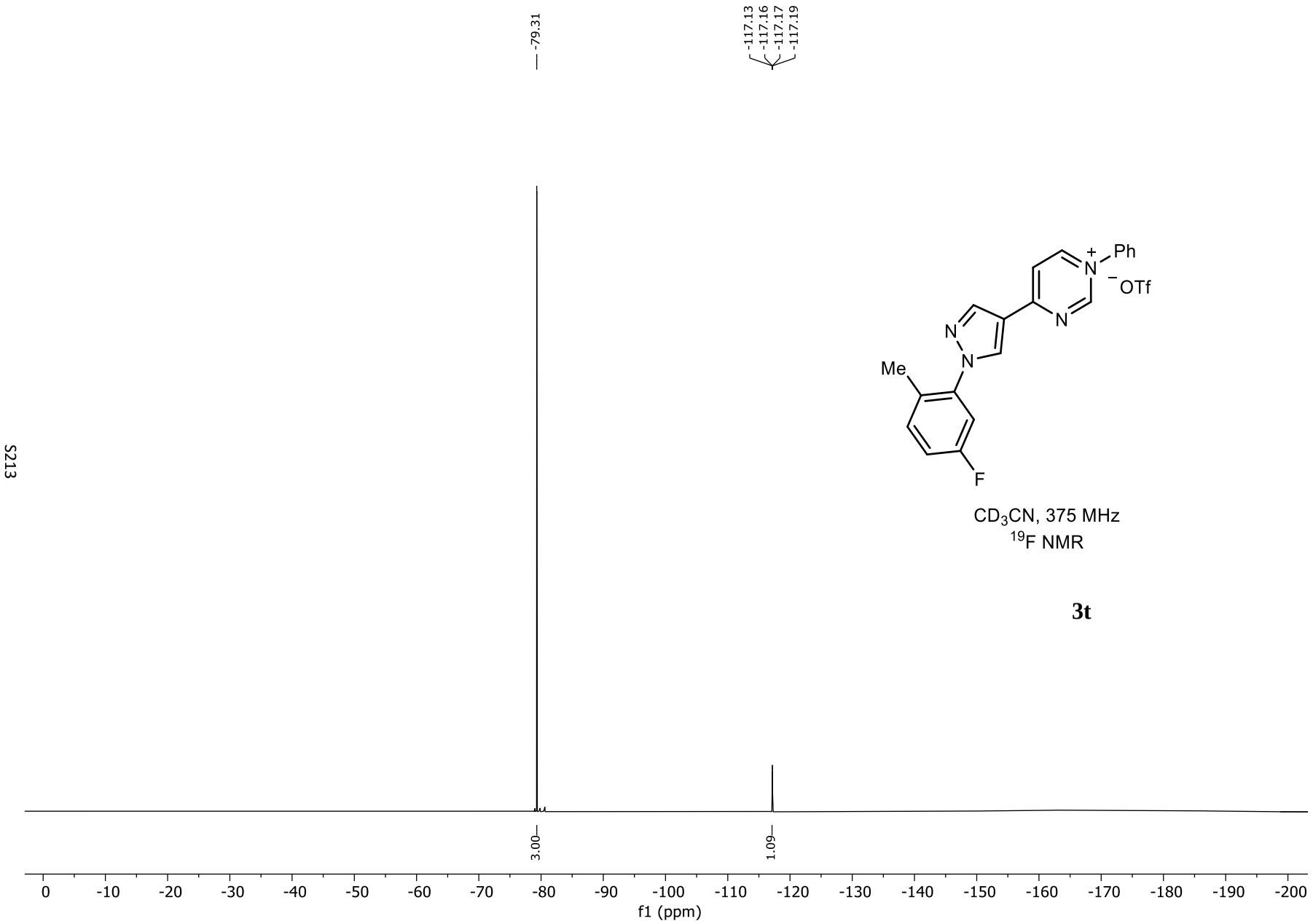

170.30
165.48
152.95
152.16
150.58
149.30
139.92
138.46
134.60
133.59
132.78
131.61
131.50
130.21
129.07
129.04
128.60
127.11
125.61
123.54
122.59
120.35
118.26 CD3CN
115.64
56.52
Ph
OTf
MeO
CD3CN, 100 MHz
13C NMR
3s
S209
f1 (ppm)


-79.14
Ph
OTf
MeO
N
N
N
CD3CN, 375 MHz
19F NMR
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

3s

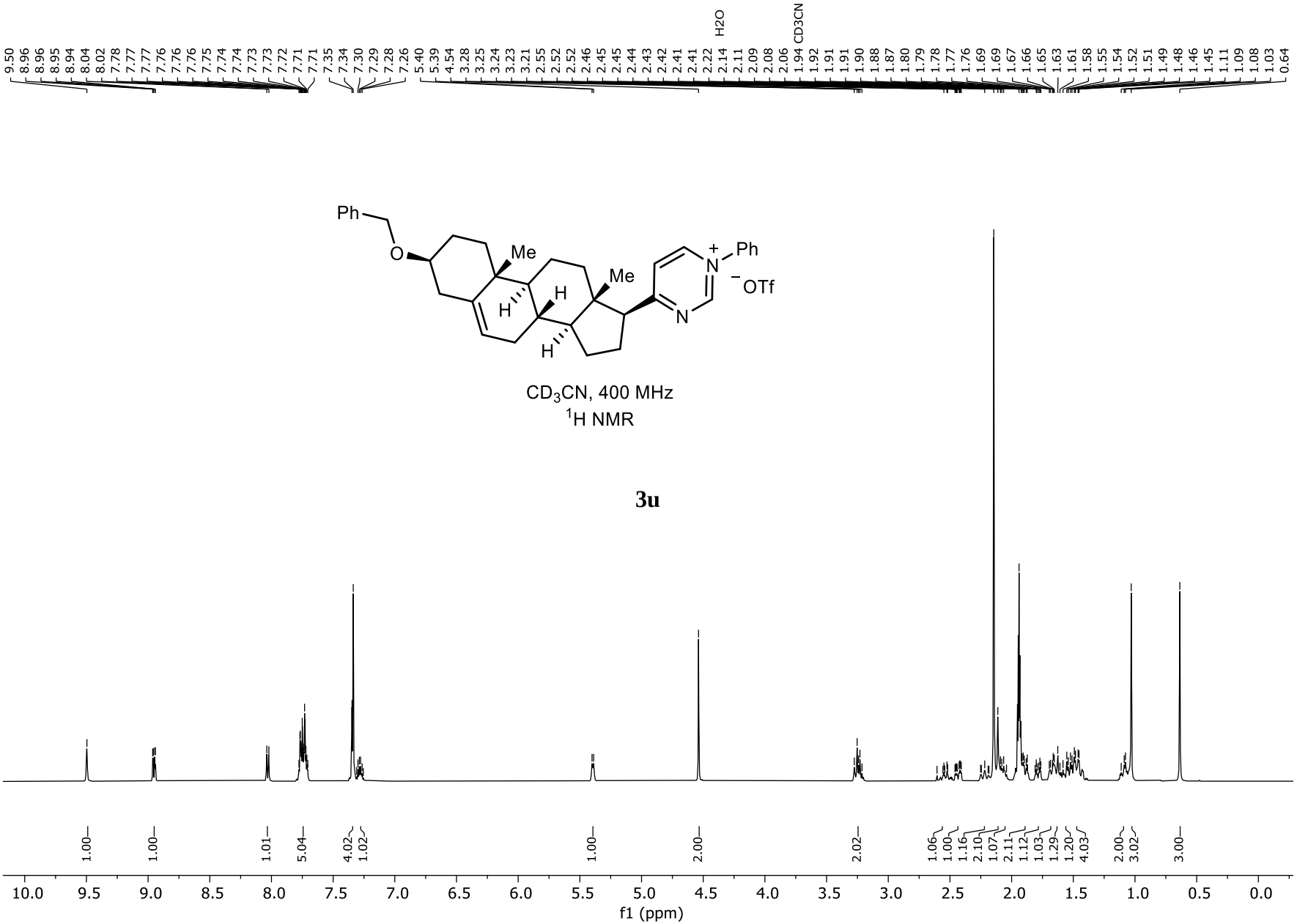

9.41
9.41
8.97
8.97
8.96
8.95
8.88
8.61
8.32
8.32
8.30
8.30
7.75
7.49
7.47
7.46
7.45
7.33
7.32
7.31
7.30
7.28
7.27
7.26
7.25
7.24
7.23
2.28 H2O
2.18
1.94 CD3CN
Ph
N
OTf
N
N
N
Me
F
CD3CN, 400 MHz
1H NMR
3t
1.00
1.01
1.00
1.00
1.05
5.01
1.02
1.01
1.03
3.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

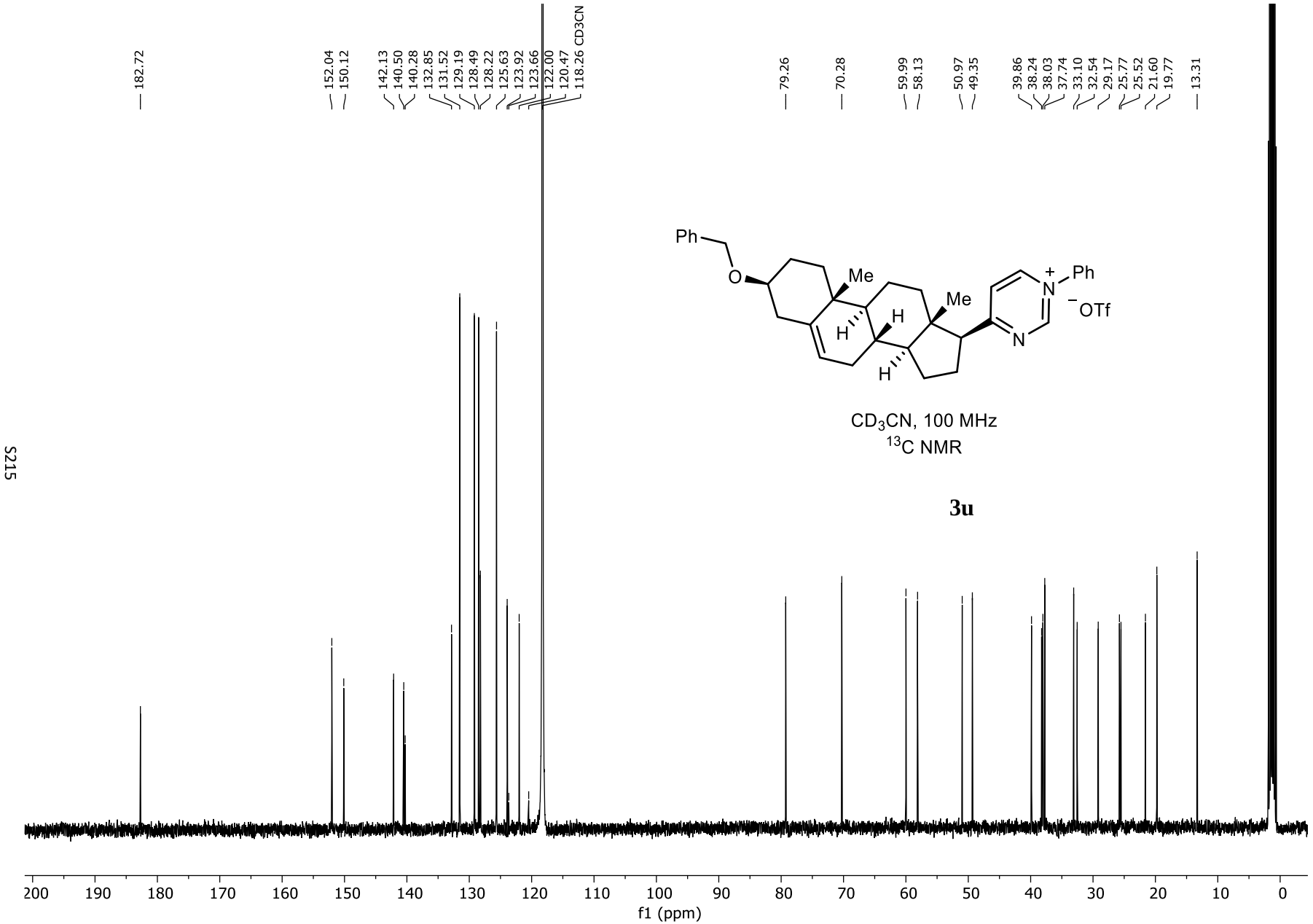

166.08
162.87
160.45
153.33
150.54
142.78
140.33
140.28
140.18
136.84
134.00
133.91
132.63
131.53
130.63
130.60
125.43
123.65
121.18
120.46
118.40
118.26 CD3CN
117.52
117.31
114.21
113.96
17.62
1.35
Ph
N
+
OTf
N
N
N
Me
F
CD3CN, 100 MHz
13C NMR
3t
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

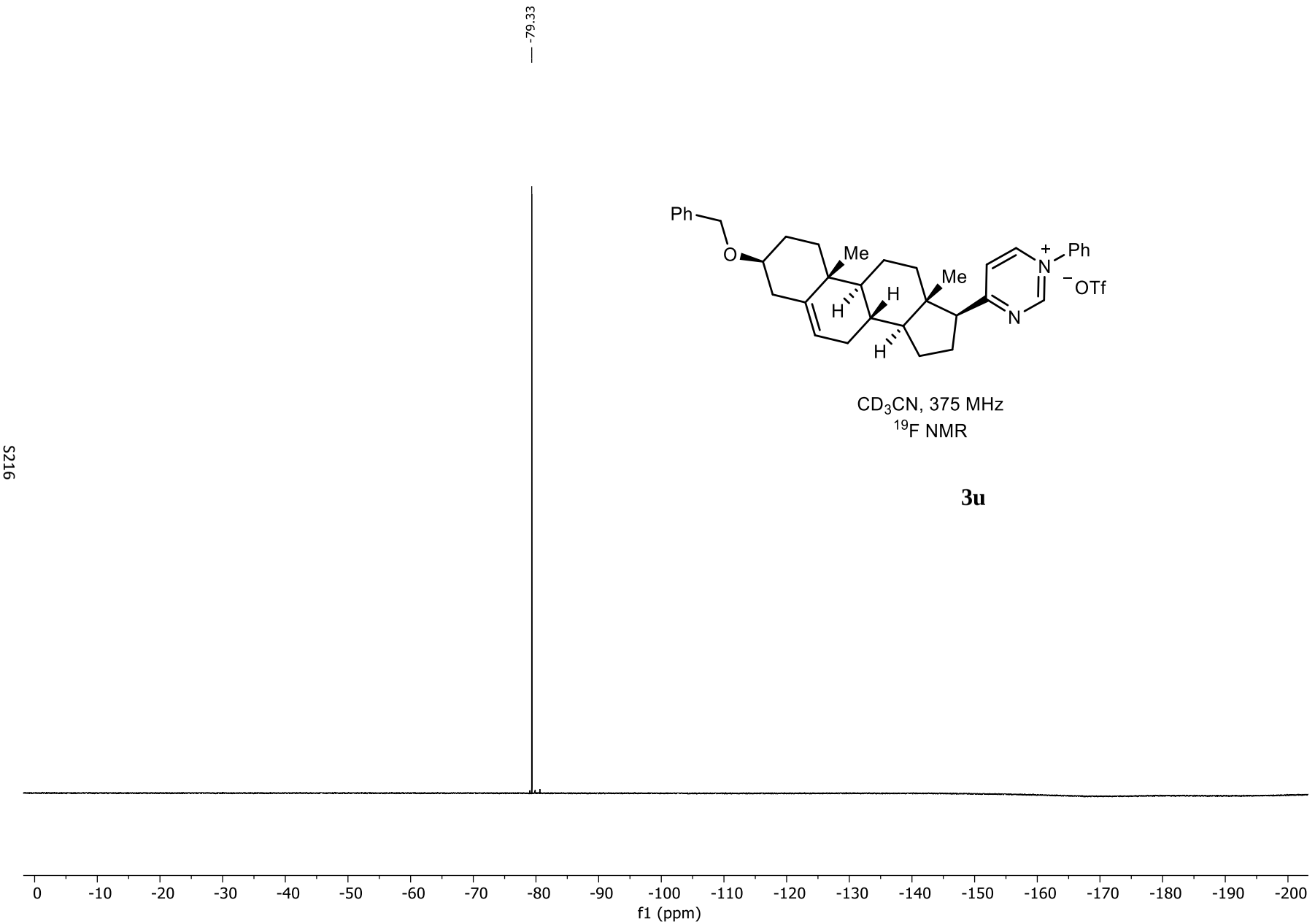


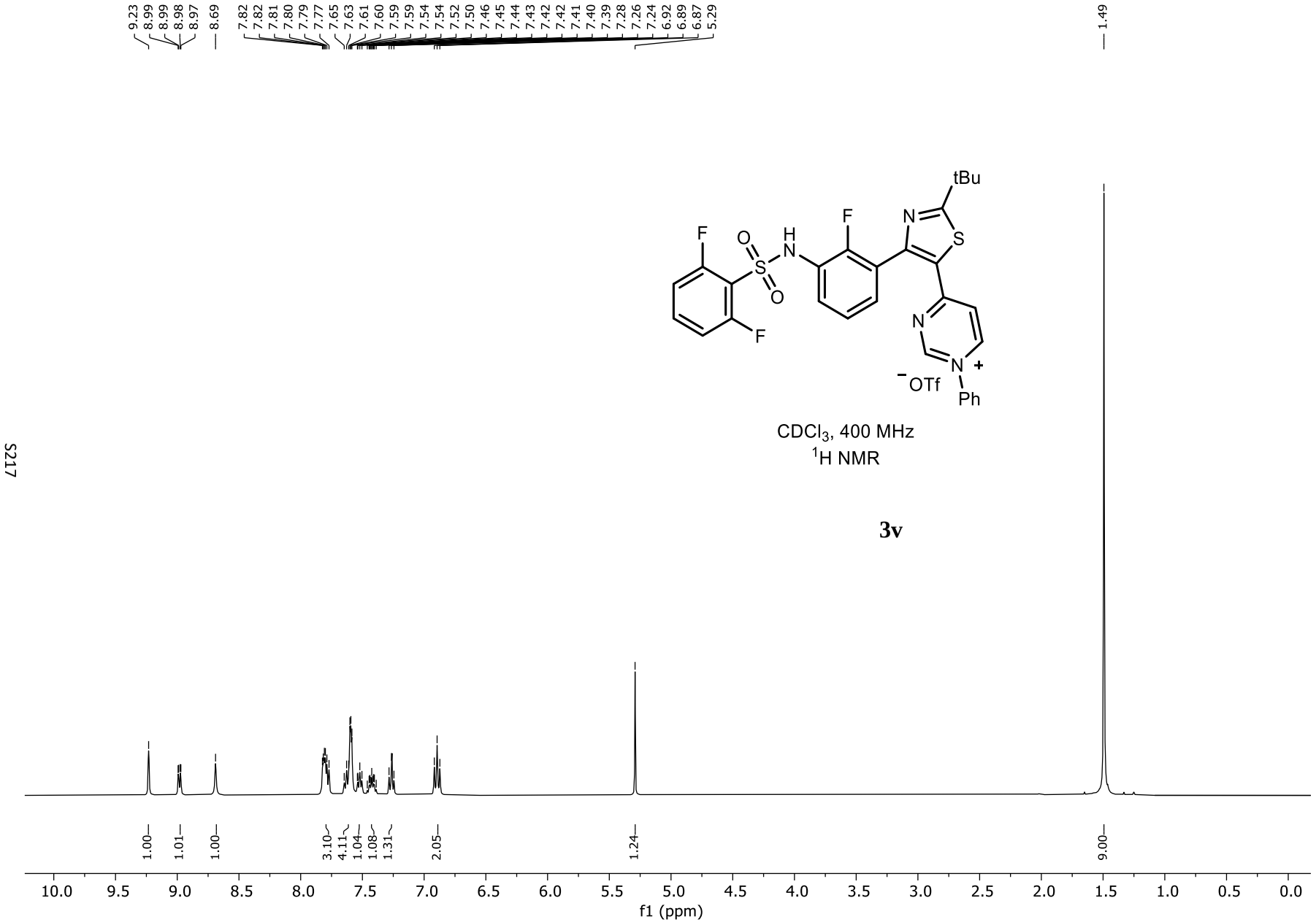
CD_3CN, 375 MHz
^{19}F NMR

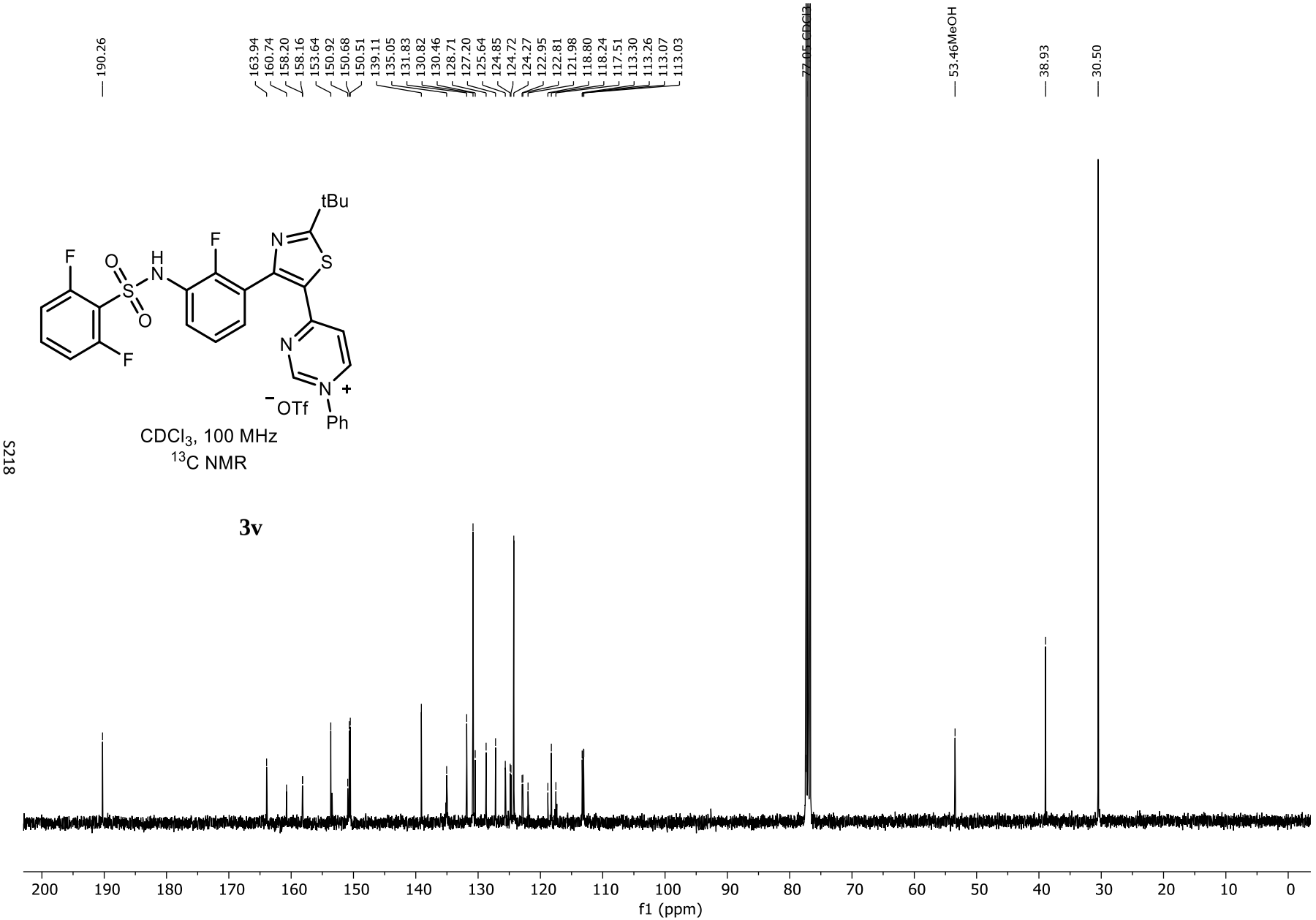
3t

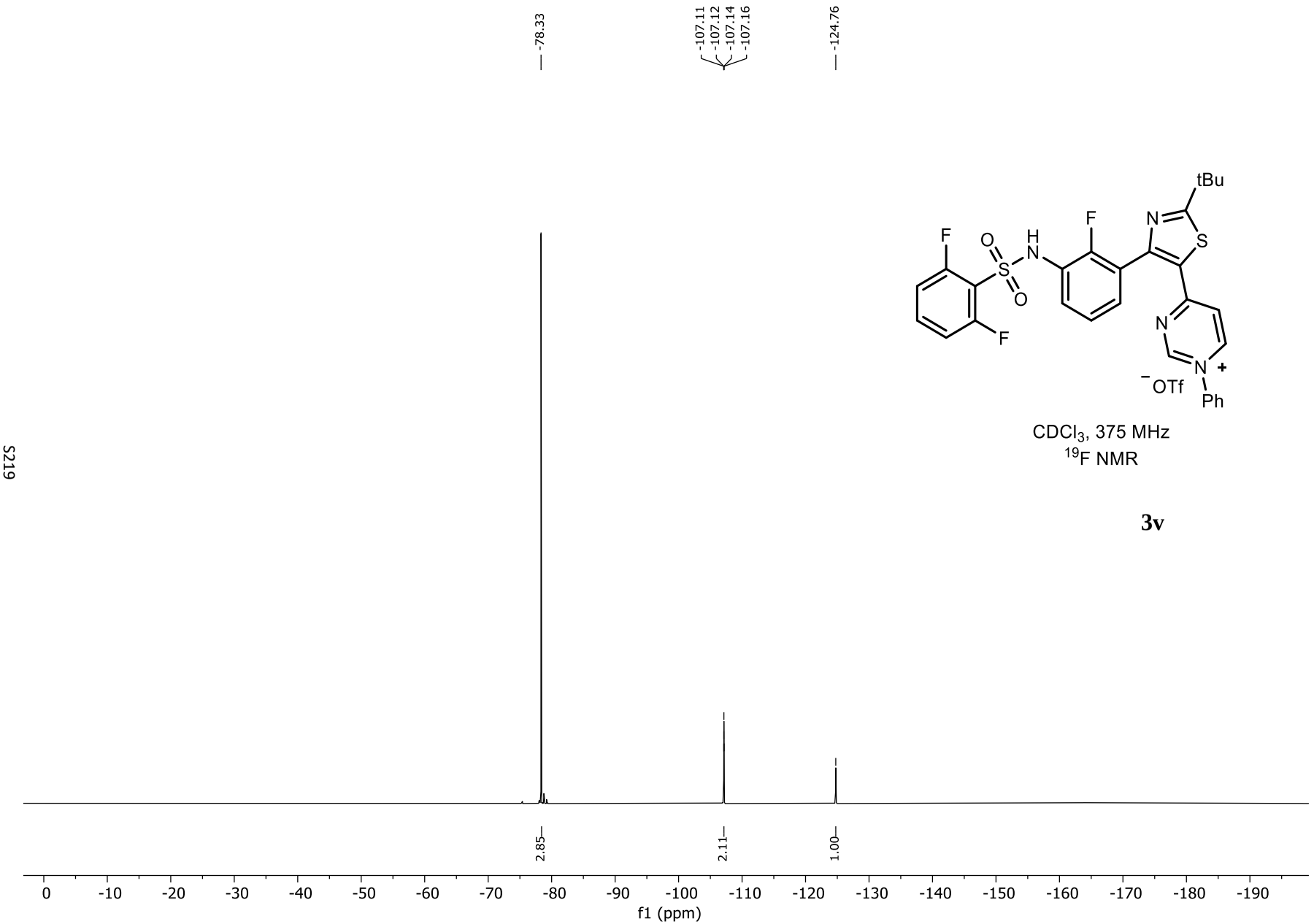

9.50 8.96 8.96 8.95 8.94 8.04 8.02 7.78 7.77 7.77 7.76 7.76 7.76 7.75 7.74 7.74 7.73 7.73 7.72 7.71 7.71 7.35 7.34 7.30 7.29 7.28 7.26 5.40 5.39 4.54 3.28 3.25 3.24 3.23 3.21 2.55 2.52 2.52 2.46 2.45 2.45 2.44 2.43 2.42 2.41 2.41 2.22 2.14 2.11 2.09 2.08 2.06 1.94 1.92 1.91 1.91 1.90 1.88 1.87 1.80 1.79 1.78 1.77 1.76 1.69 1.69 1.67 1.66 1.65 1.63 1.61 1.58 1.55 1.54 1.52 1.51 1.49 1.48 1.46 1.45 1.11 1.09 1.08 1.03 0.64
H2O
CD3CN
Ph
O
Me
H
H
H
Me
N
+
Ph
−
OTf
CD3CN, 400 MHz
1H NMR
3u
1.00 1.00 1.01 5.04 4.02 1.02 1.00 2.00 2.02 1.06 1.00 1.16 2.10 1.07 2.11 1.12 1.03 1.29 1.20 4.03 2.00 3.02 3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


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
123.66
122.00
120.47
118.26 CD3CN
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
Ph
O
Me
H
H
Me
H
N
+
N
Ph
−
OTf
CD3CN, 100 MHz
13C NMR
3u
S215
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-79.33
Ph
O
Me
H
H
Me
+
N
Ph
−
OTf
N
CD3CN, 375 MHz
19F NMR
3u
S216
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)


9.23
8.99
8.99
8.98
8.97
8.69
7.82
7.82
7.81
7.80
7.79
7.77
7.65
7.63
7.61
7.60
7.59
7.59
7.54
7.54
7.52
7.50
7.46
7.45
7.44
7.43
7.42
7.42
7.41
7.40
7.39
7.28
7.26
7.24
6.92
6.89
6.87
5.29
1.49
tBu
F
O
H
N
F
N
S
S
O
F
N
N
+
OTf
Ph
CDCl3, 400 MHz
1H NMR
3v
1.00
1.01
1.00
3.10
4.11
1.04
1.08
1.31
2.05
1.24
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

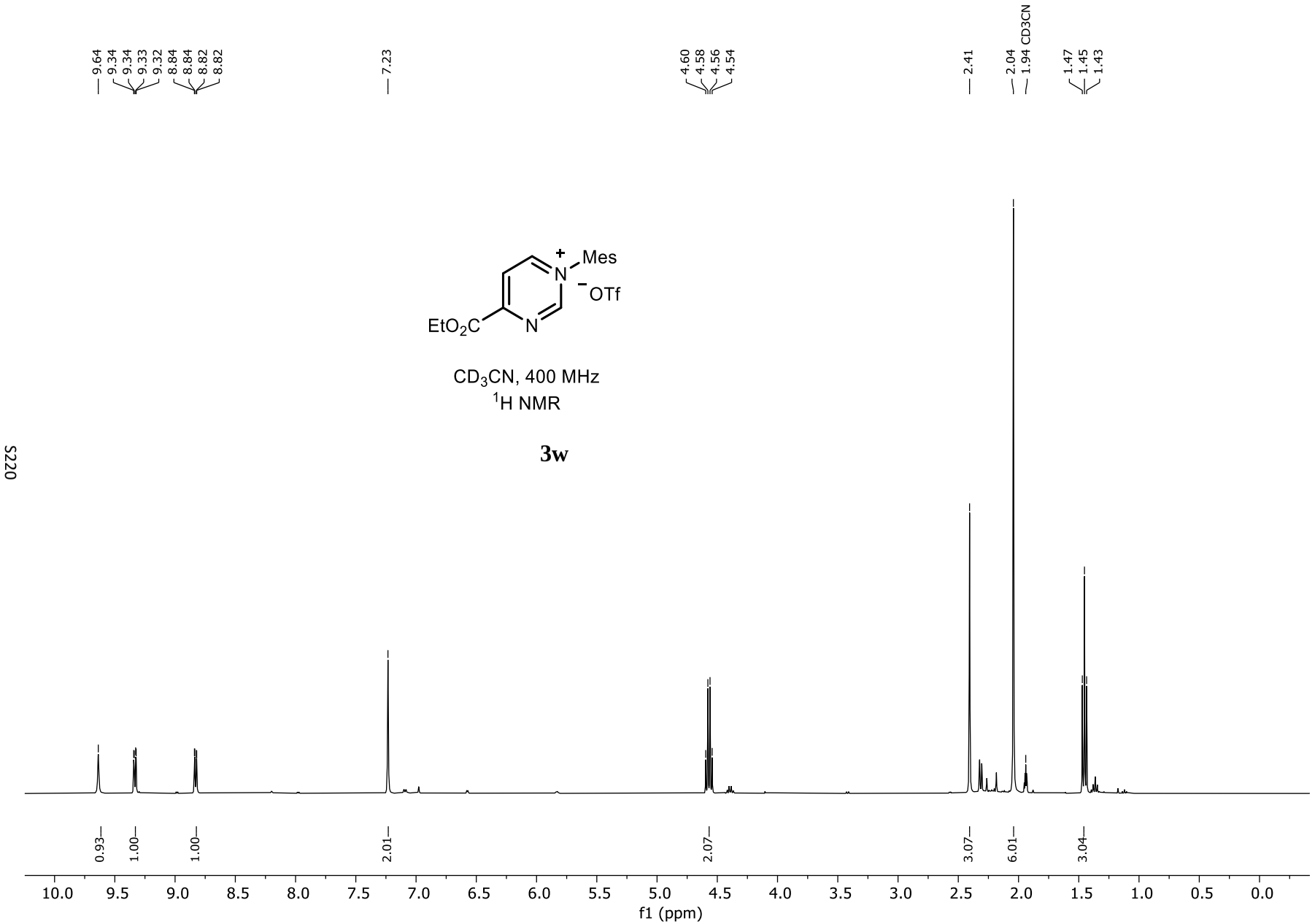

190.26
163.94
160.74
158.20
158.16
153.64
150.92
150.68
150.51
139.11
135.05
131.83
130.82
130.46
128.71
127.20
125.64
124.85
124.72
124.27
122.95
122.81
121.98
118.80
118.24
117.51
113.30
113.26
113.07
113.03
77.05 CDCl3
53.46MeOH
38.93
30.50
tBu
F
N
S
O
H
N
F
F
O
S
O
N
N
+
N
Ph
OTf
CDCl3, 100 MHz
13C NMR
3v
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

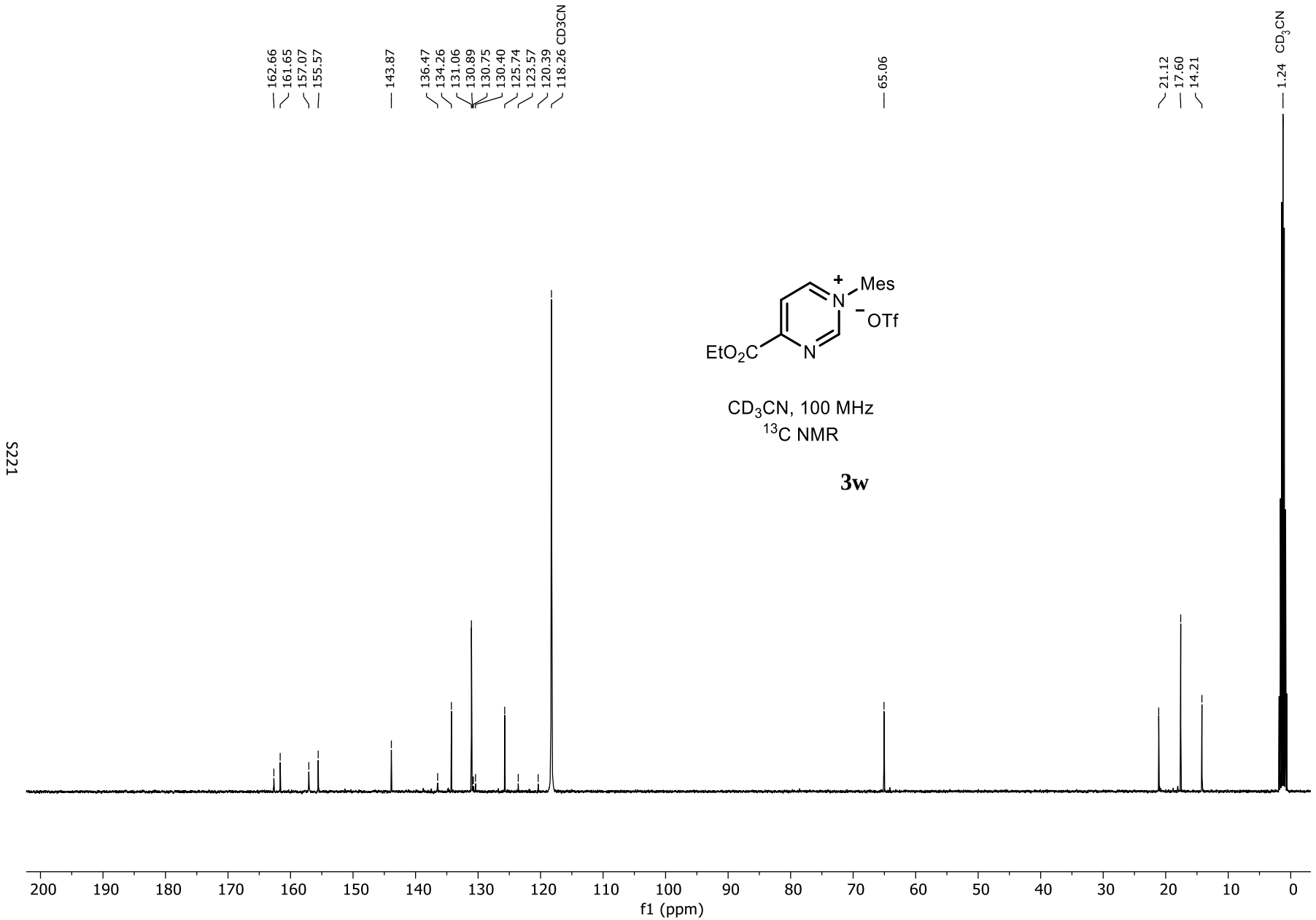


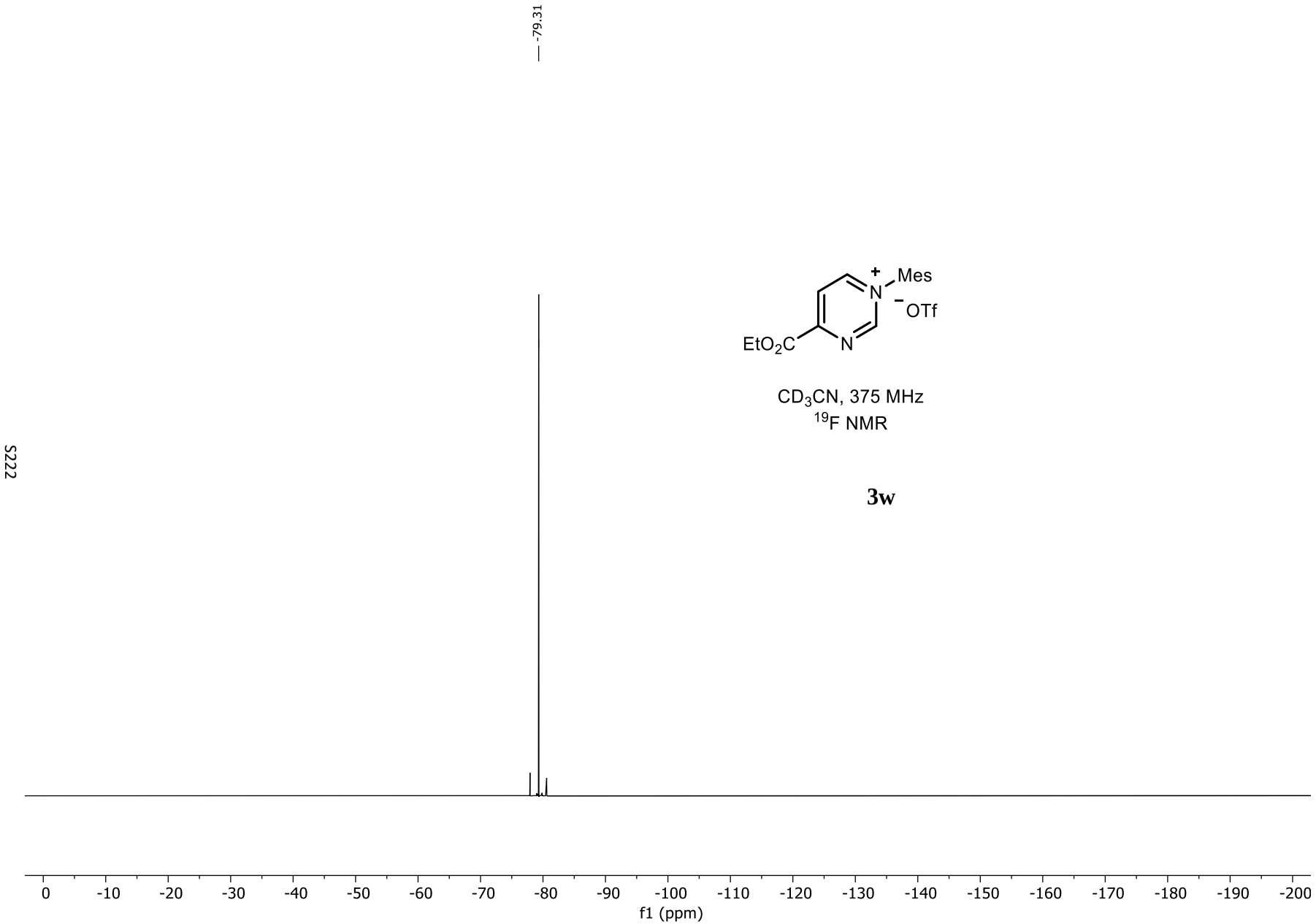
$CDCl_3$, 375 MHz

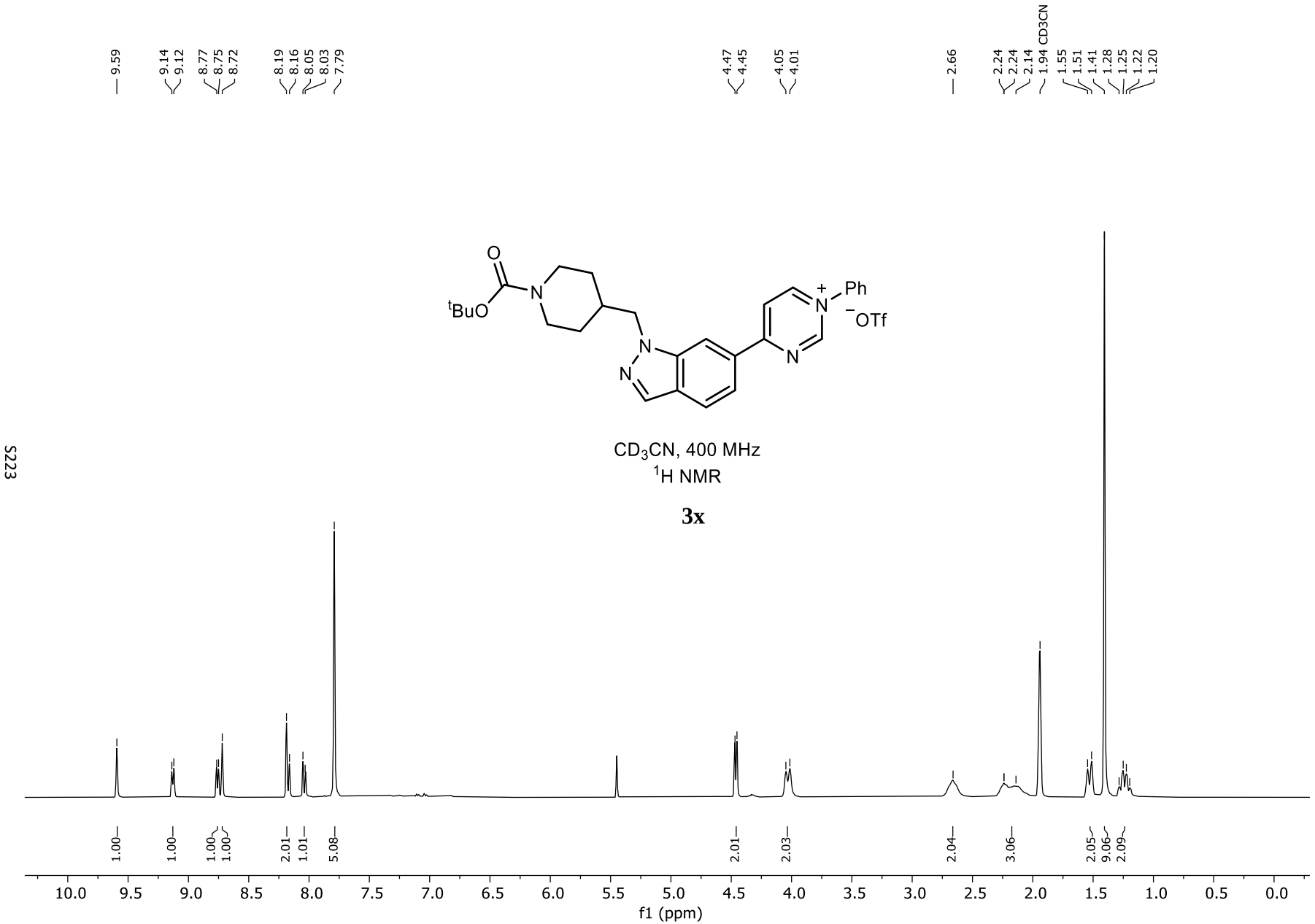
^{19}F NMR

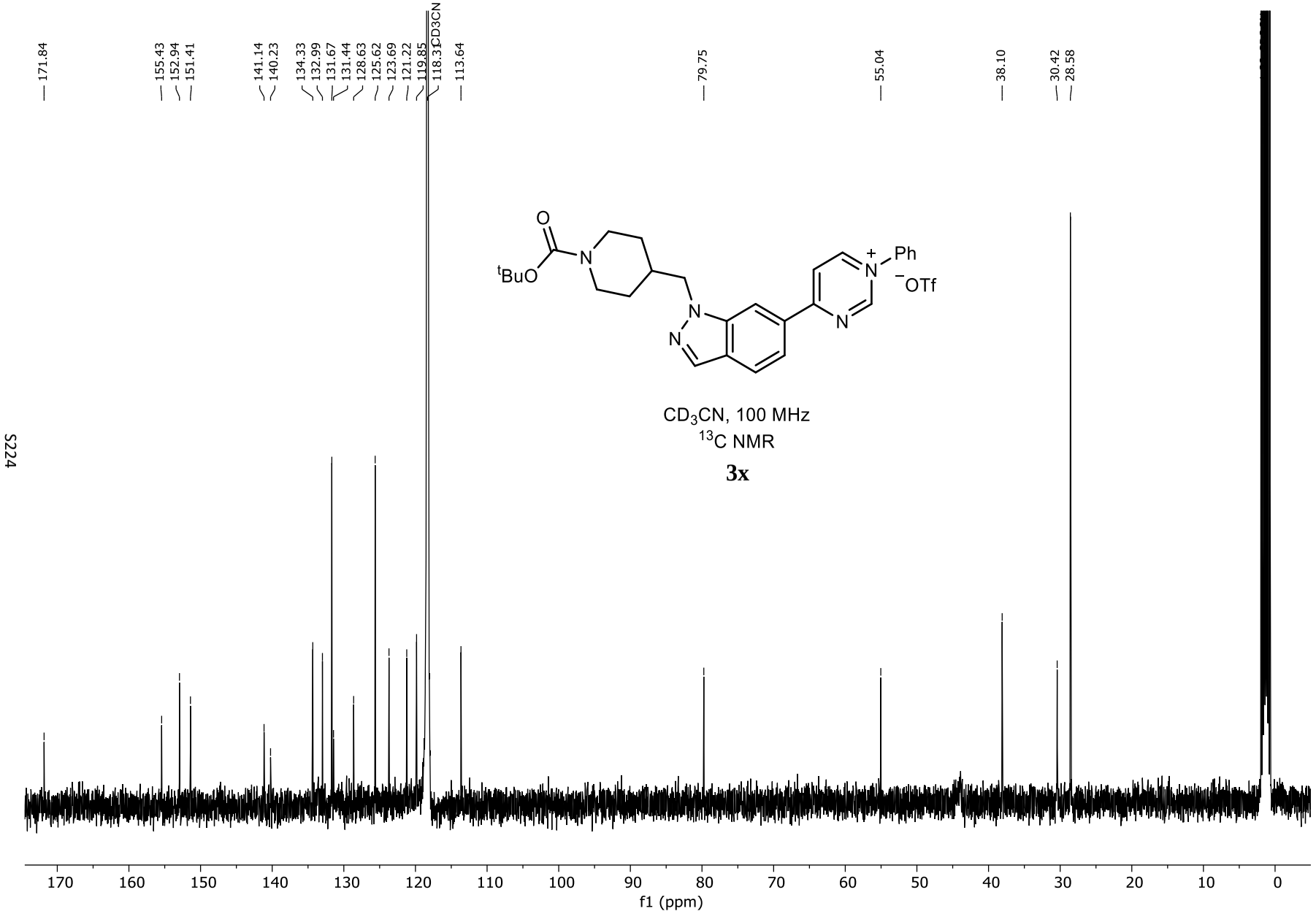
3v

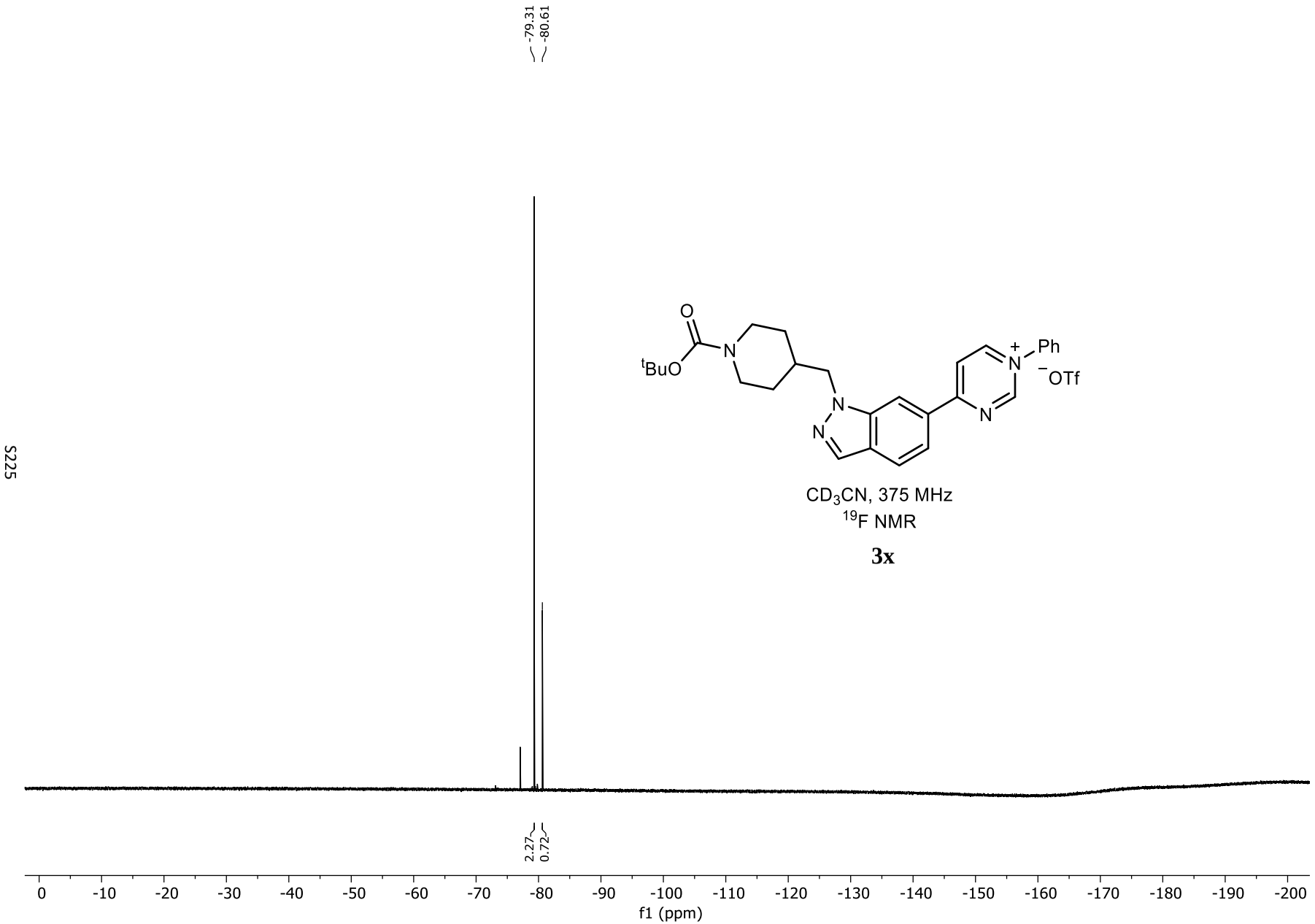

9.64
9.34
9.34
9.33
9.32
8.84
8.84
8.82
8.82
7.23
4.60
4.58
4.56
4.54
2.41
2.04
1.94 CD3CN
1.47
1.45
1.43
Mes
OTf
EtO2C
N
CD3CN, 400 MHz
1H NMR
3w
S220
0.93
1.00
1.00
2.01
2.07
3.07
6.01
3.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

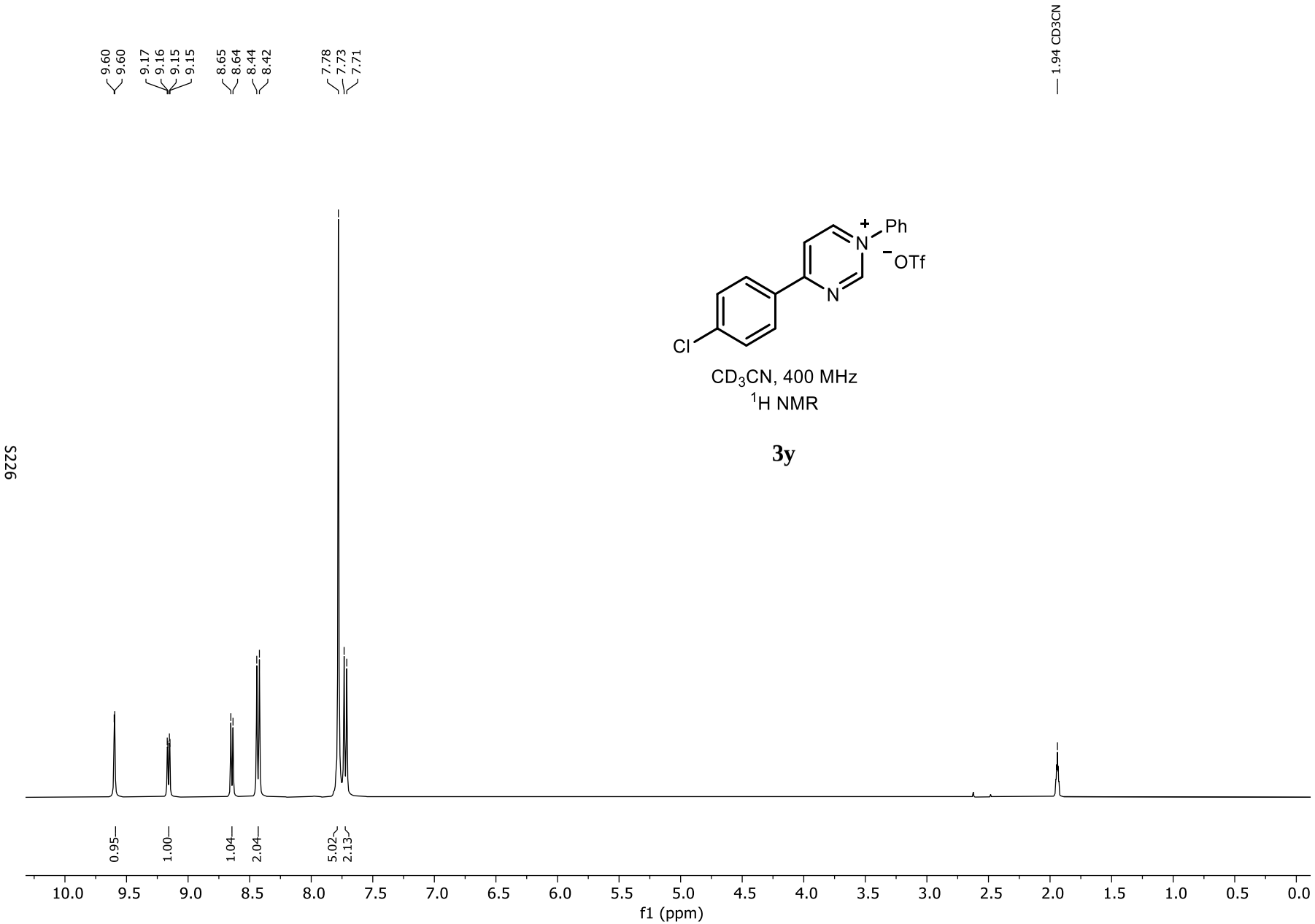

162.66
161.65
157.07
155.57
143.87
136.47
134.26
131.06
130.89
130.75
130.40
125.74
123.57
120.39
118.26 CD3CN
65.06
21.12
17.60
14.21
1.24 CD3CN
Mes
N
OTf
EtO2C
N
CD3CN, 100 MHz
13C NMR
3w
f1 (ppm)

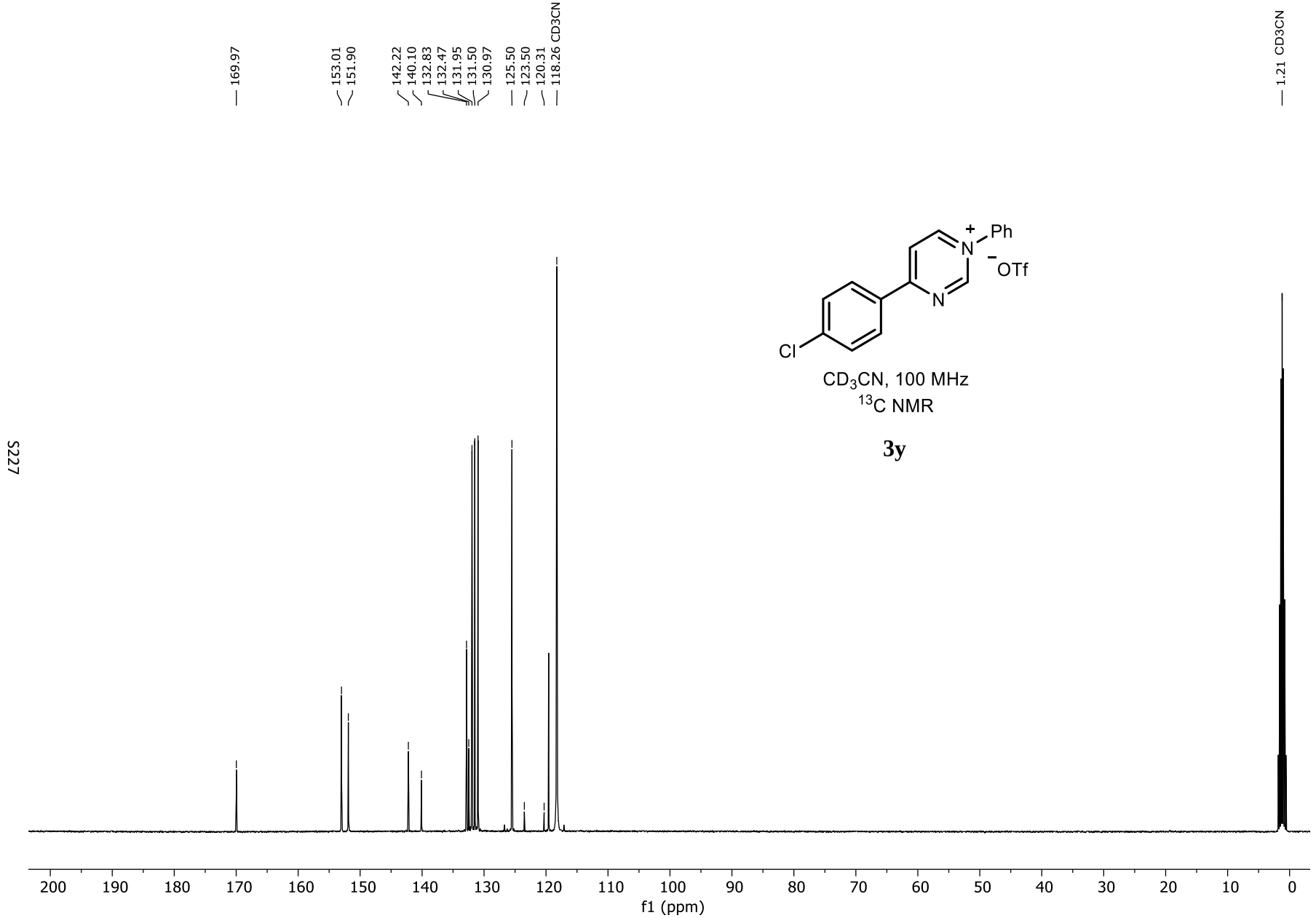

-79.31
Mes
OTf
EtO2C
N
CD3CN, 375 MHz
19F NMR
3w
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

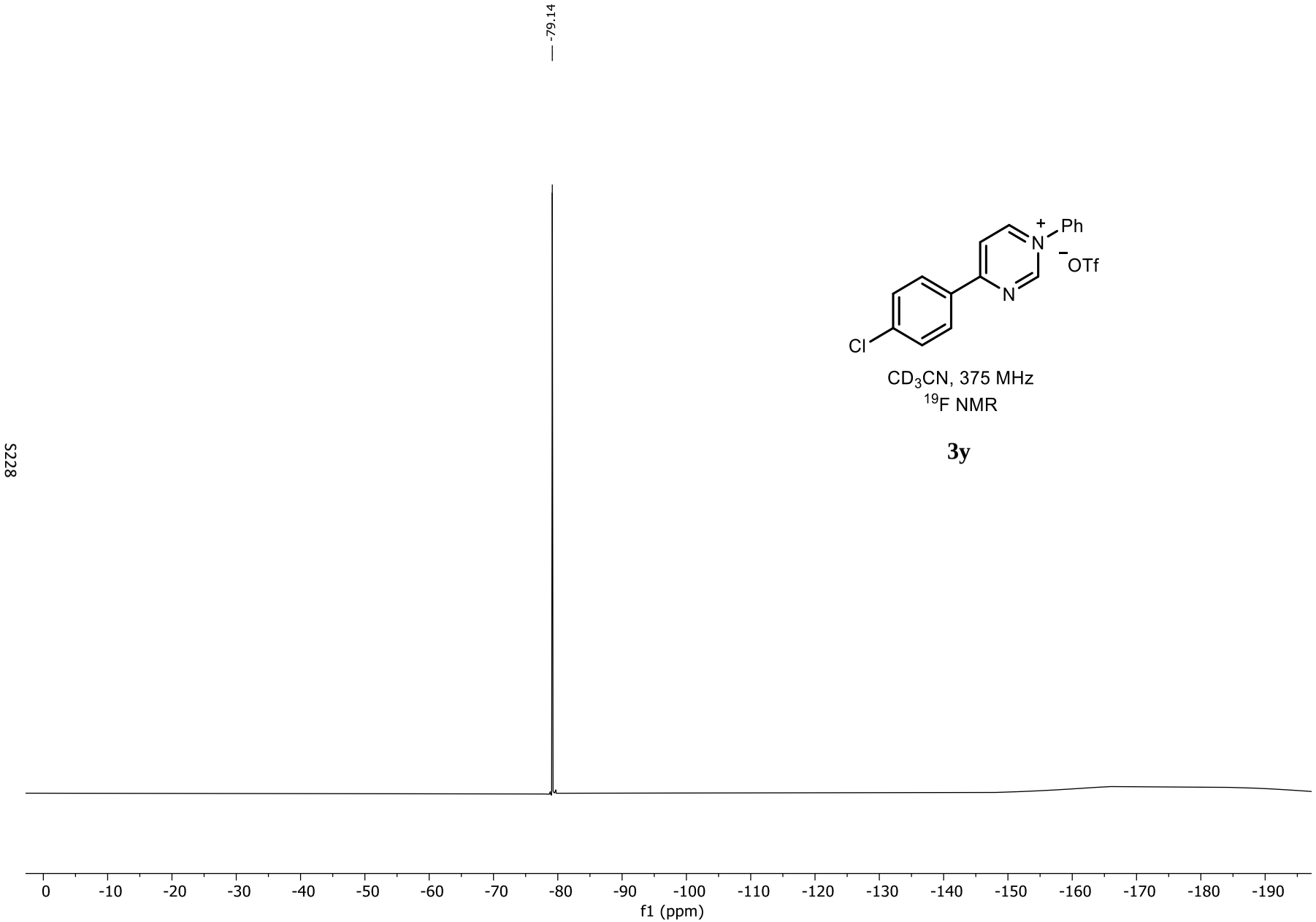

9.59
9.14
9.12
8.77
8.75
8.72
8.19
8.16
8.05
8.03
7.79
4.47
4.45
4.05
4.01
2.66
2.24
2.24
2.14
1.94 CD3CN
1.55
1.51
1.41
1.28
1.25
1.22
1.20
O
tBuO
N
N
N
N
+
Ph
−
OTf
CD3CN, 400 MHz
1H NMR
3x
1.00
1.00
1.00
1.00
2.01
1.01
5.08
2.01
2.03
2.04
3.06
2.05
9.06
2.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


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
119.85
118.31
CD3CN
113.64
79.75
55.04
38.10
30.42
28.58
O
tBuO
N
N
N
N
+
Ph
OTf
CD3CN, 100 MHz
13C NMR
3x
S224
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-79.31
-80.61
O
tBuO
N
N
N
N
+
N
Ph
−
OTf
CD3CN, 375 MHz
19F NMR
3x
2.27
0.72
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

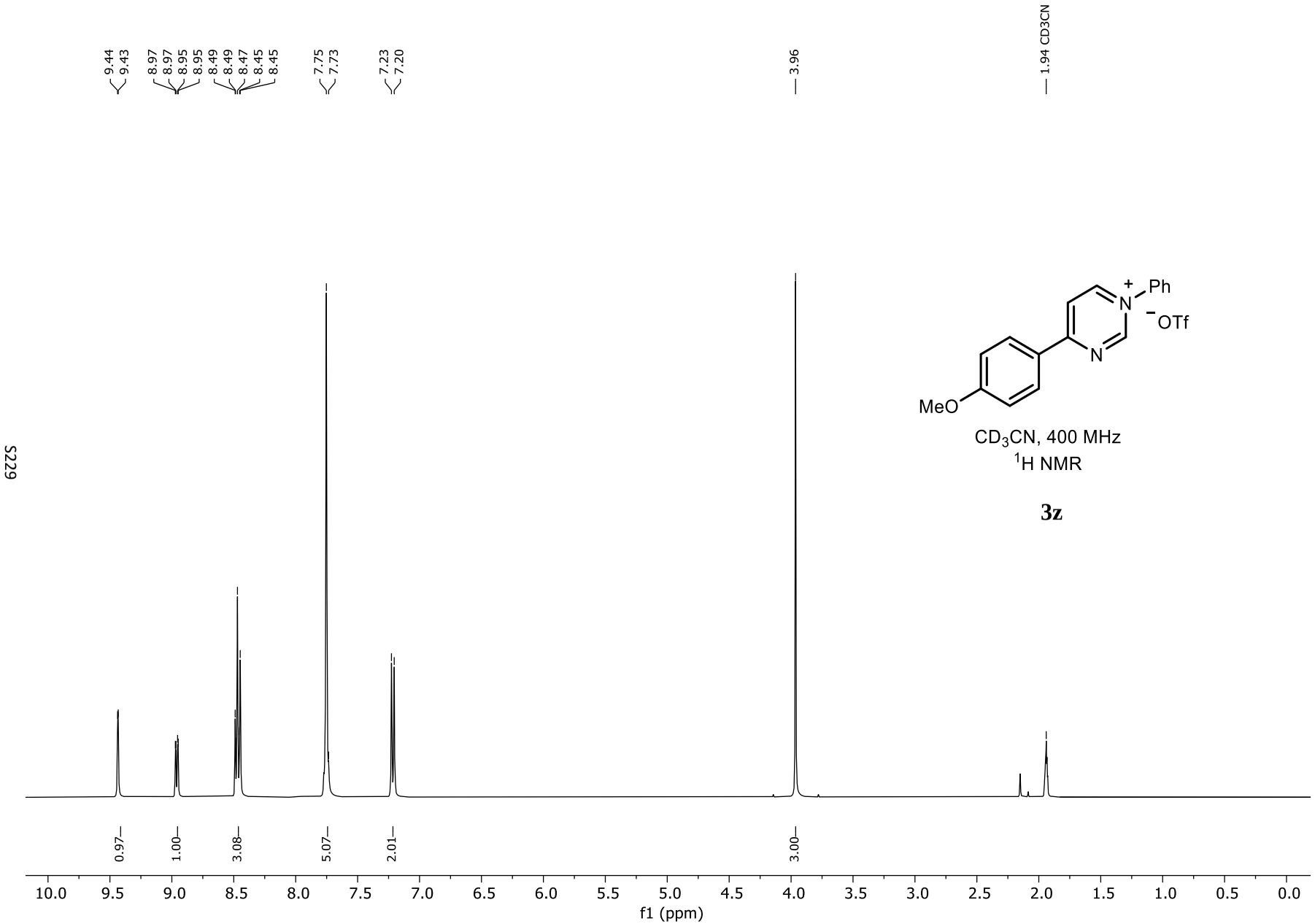

9.60
9.60
9.17
9.16
9.15
9.15
8.65
8.64
8.44
8.42
7.78
7.73
7.71
1.94 CD3CN
Ph
N
OTf
N
Cl
CD3CN, 400 MHz
1H NMR
3y
S226
0.95
1.00
1.04
2.04
5.02
2.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

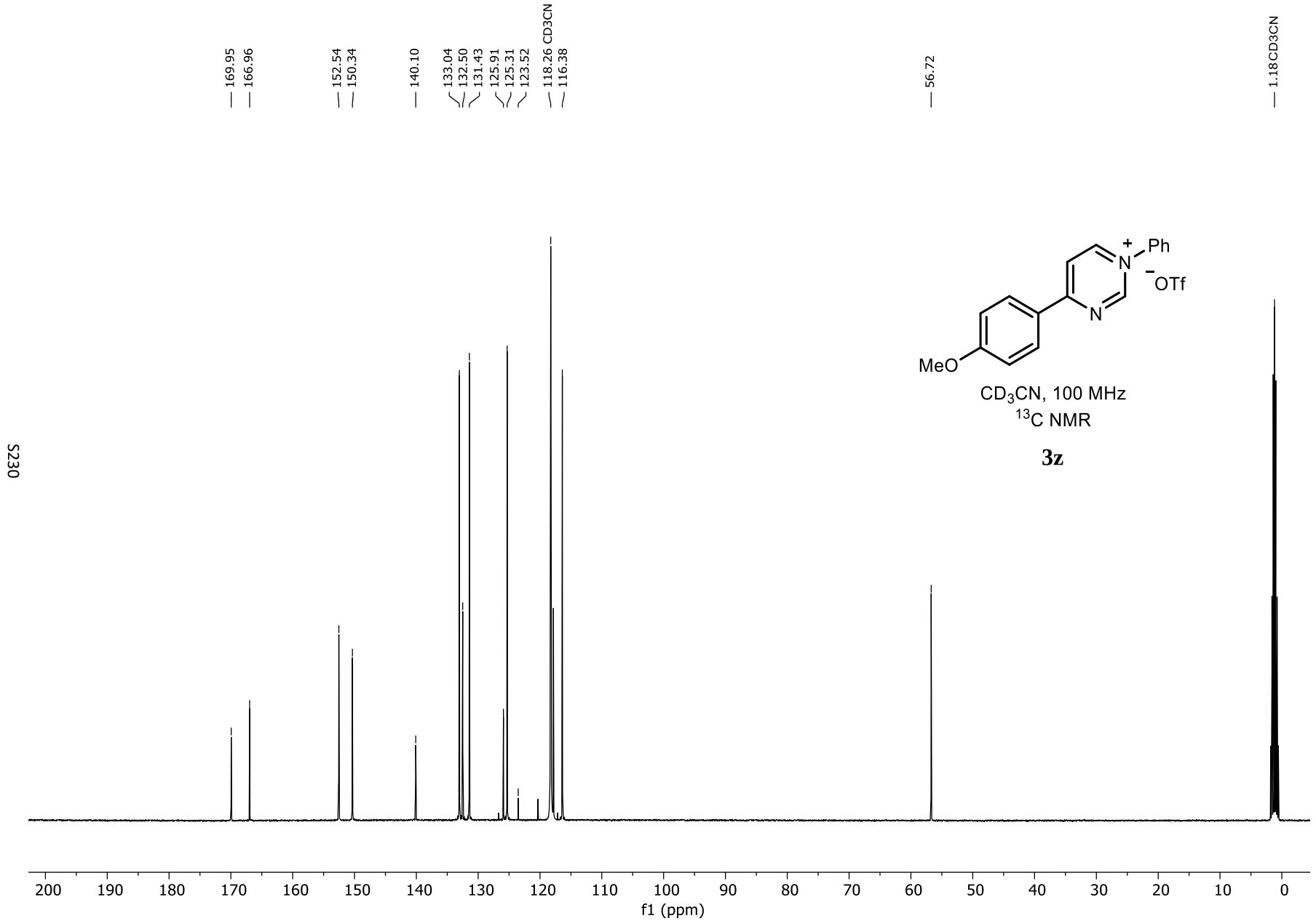

169.97
153.01
151.90
142.22
140.10
132.83
132.47
131.95
131.50
130.97
125.50
123.50
120.31
118.26 CD3CN
1.21 CD3CN
Ph
N
OTf
N
Cl
CD3CN, 100 MHz
13C NMR
3y
S227
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

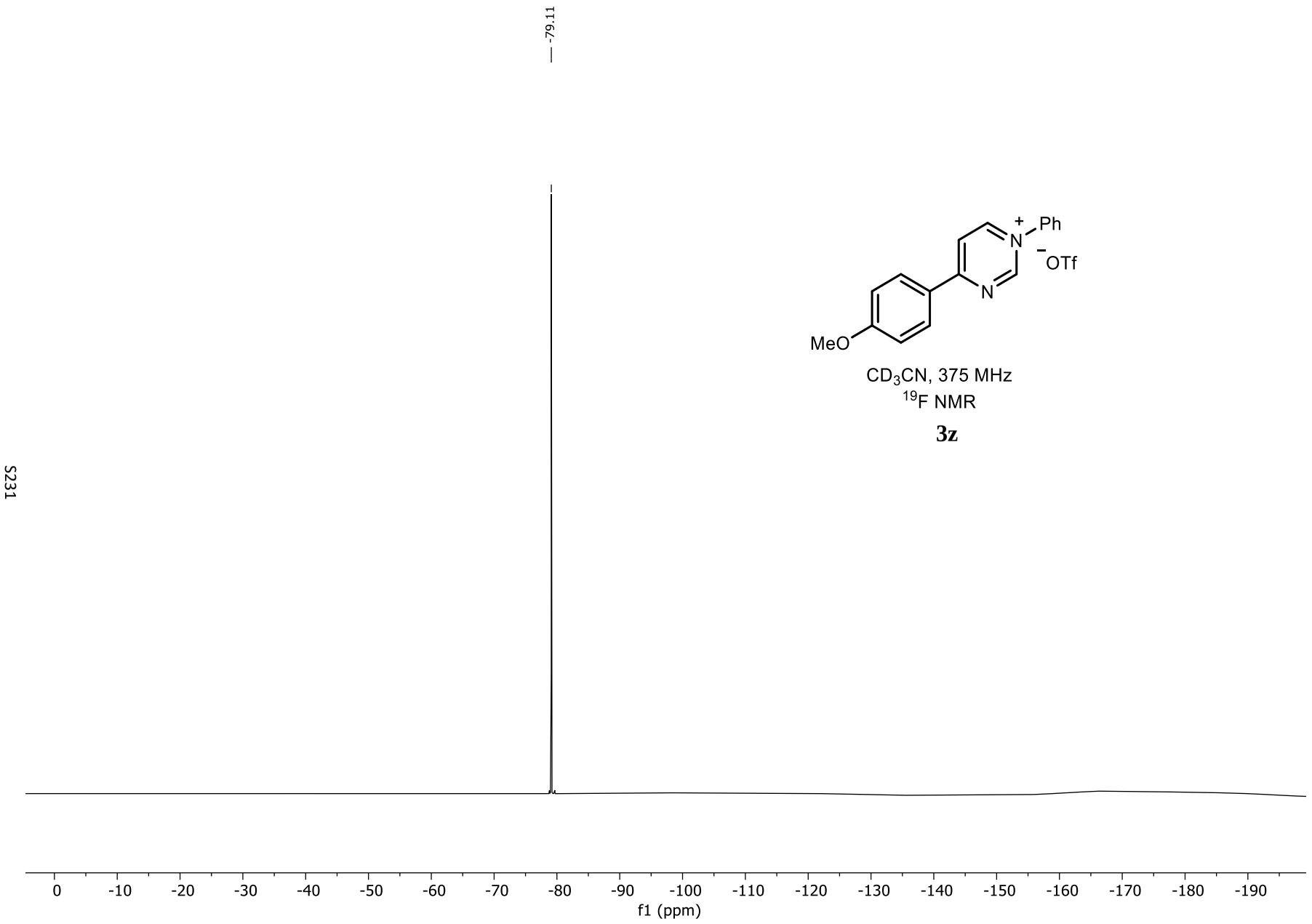


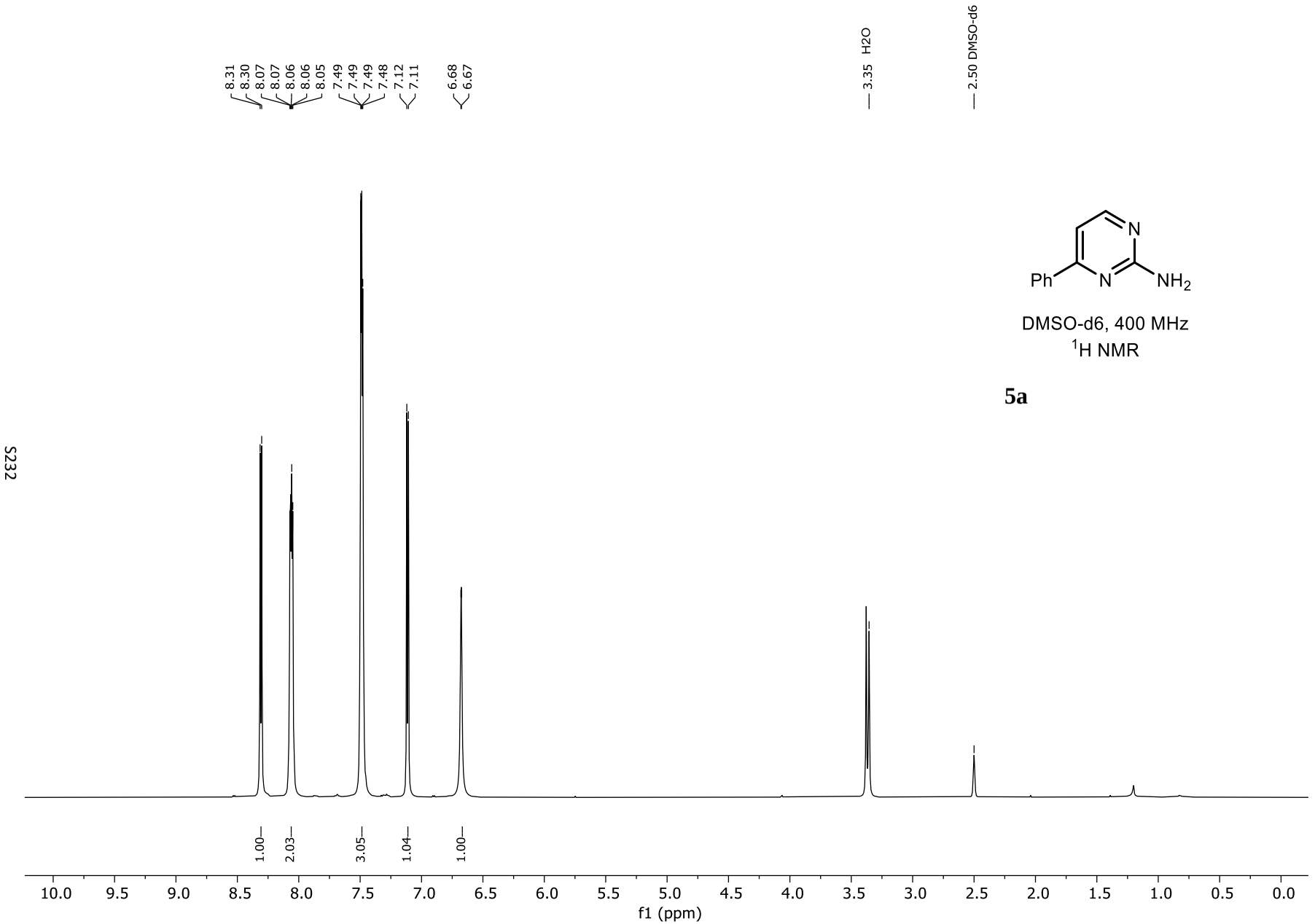
CD_3CN, 375 MHz
^{19}F NMR

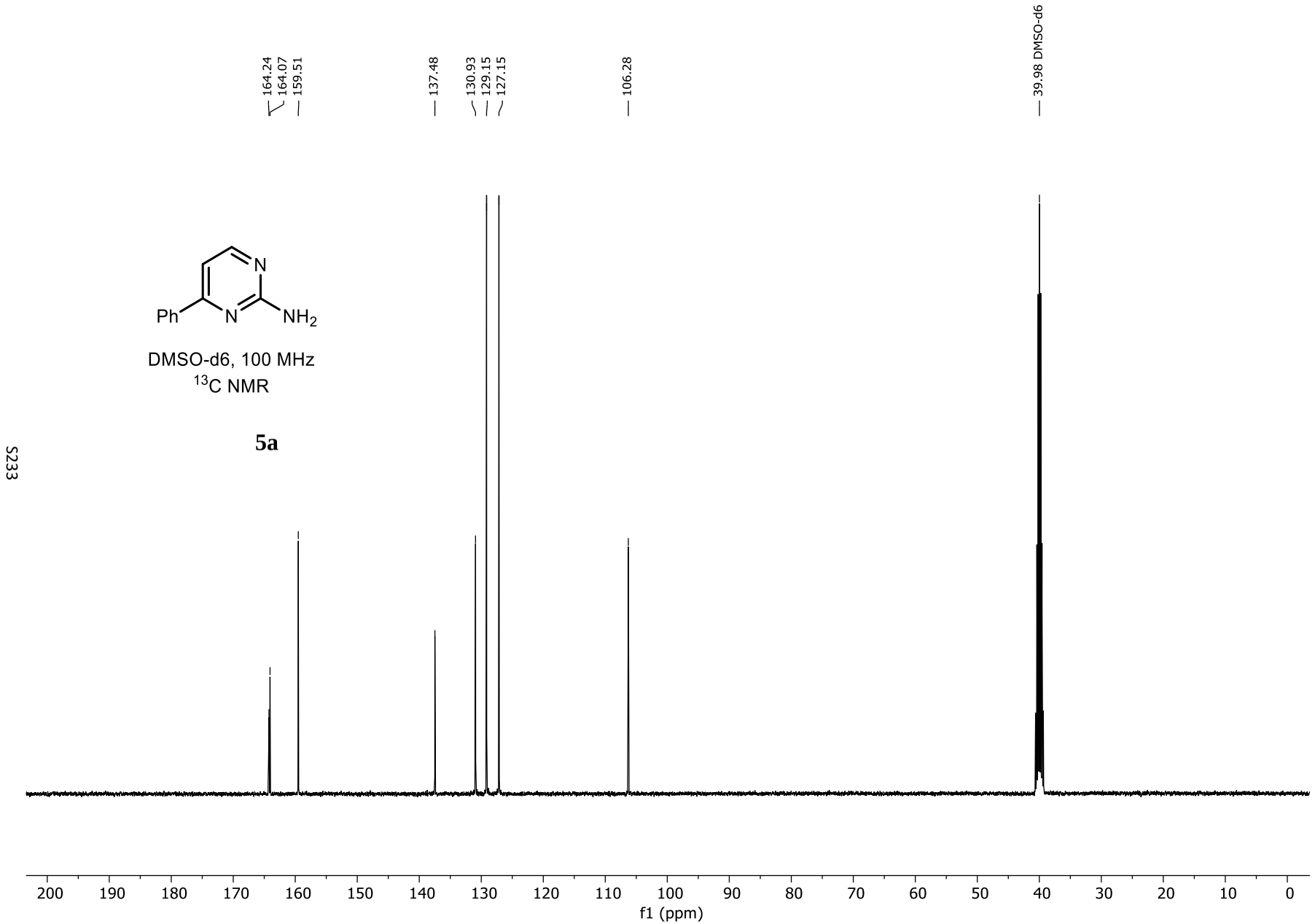
3y

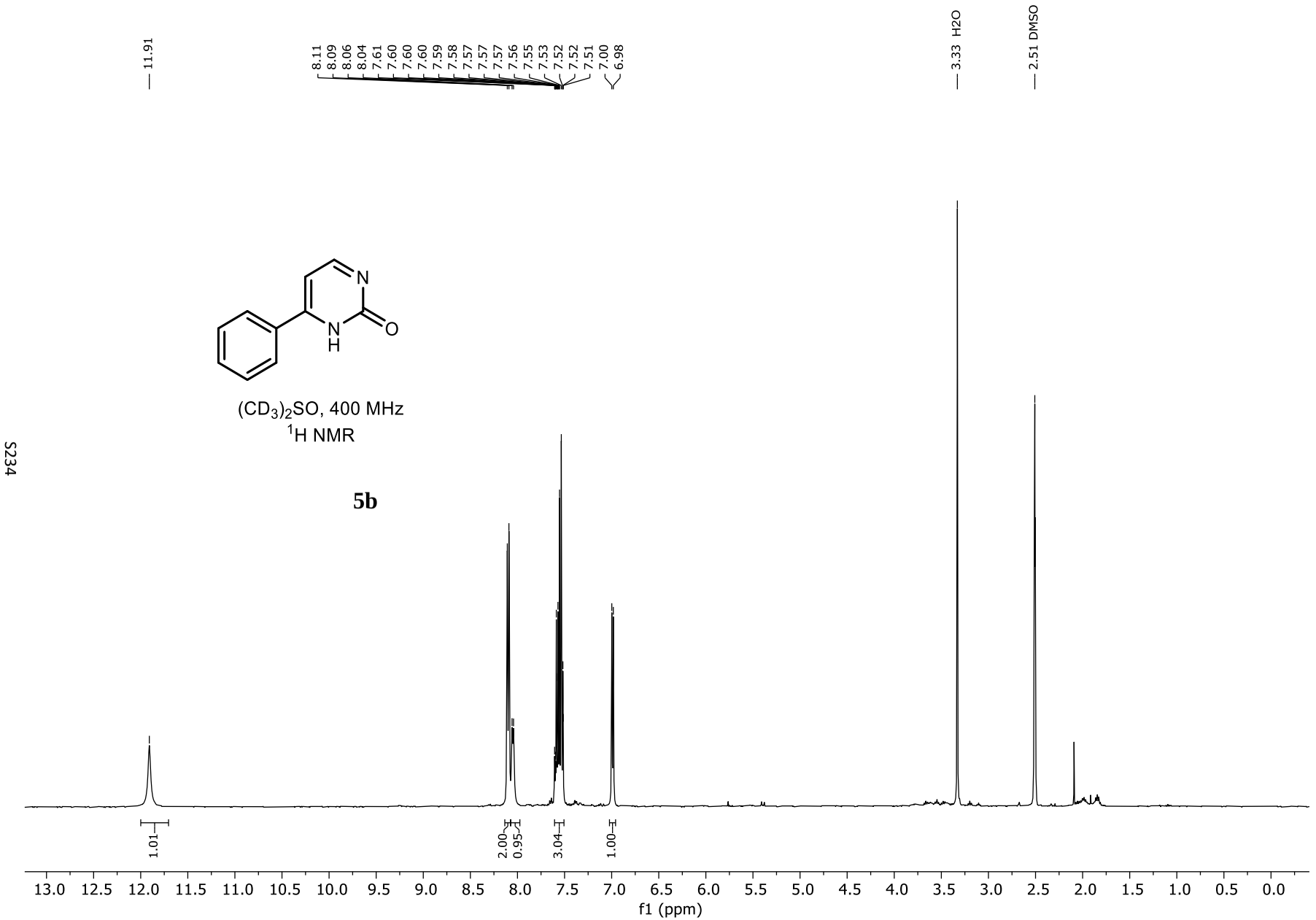

9.44
9.43
8.97
8.97
8.95
8.95
8.49
8.49
8.47
8.45
8.45
7.75
7.73
7.23
7.20
3.96
1.94 CD3CN
S229
Ph
N
OTf
N
MeO
CD3CN, 400 MHz
1H NMR
3z
0.97
1.00
3.08
5.07
2.01
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

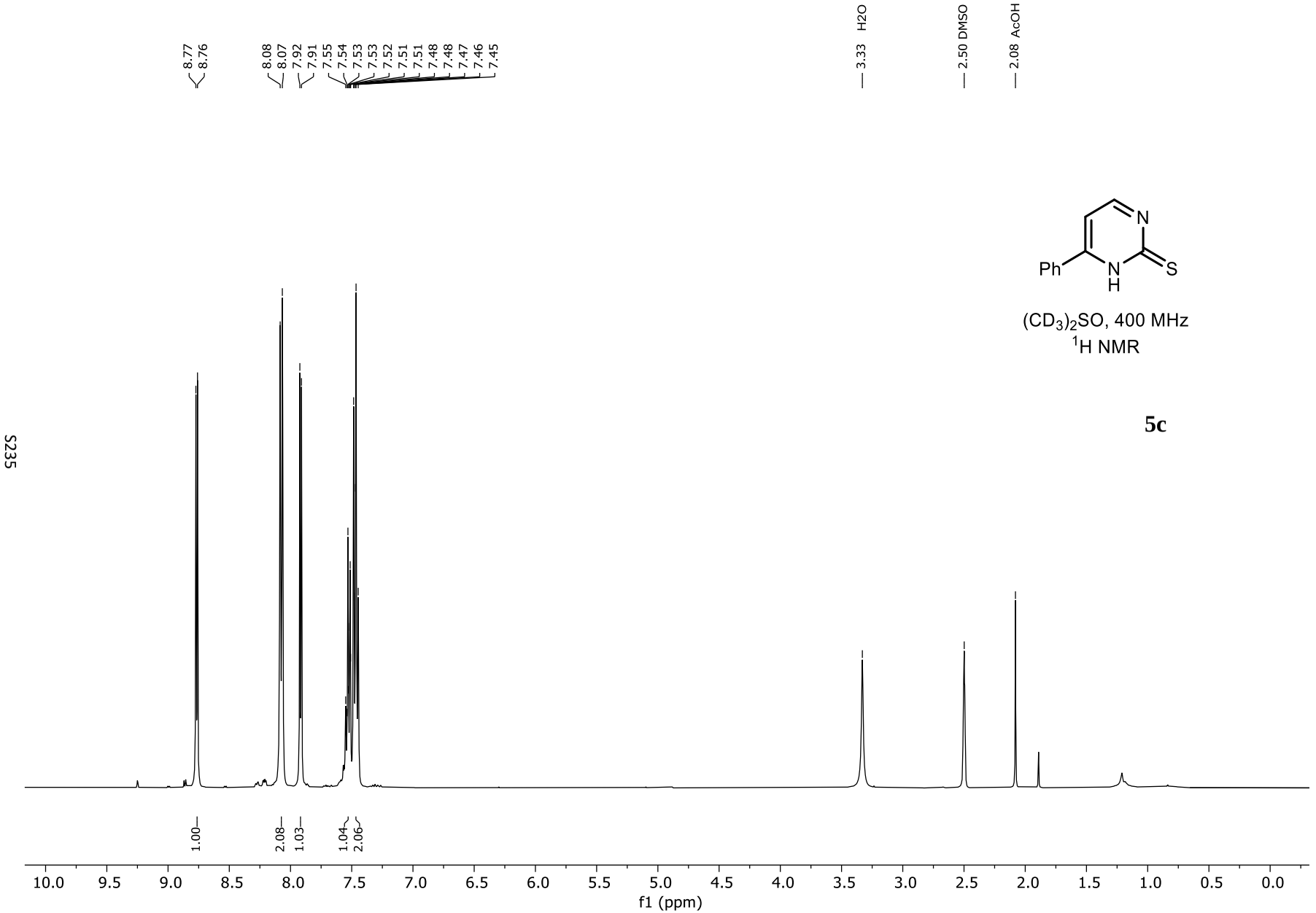

169.95
166.96
152.54
150.34
140.10
133.04
132.50
131.43
125.91
125.31
123.52
118.26 CD3CN
116.38
56.72
1.18 CD3CN
Ph
N
OTf
N
MeO
CD3CN, 100 MHz
13C NMR
3z
S230
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

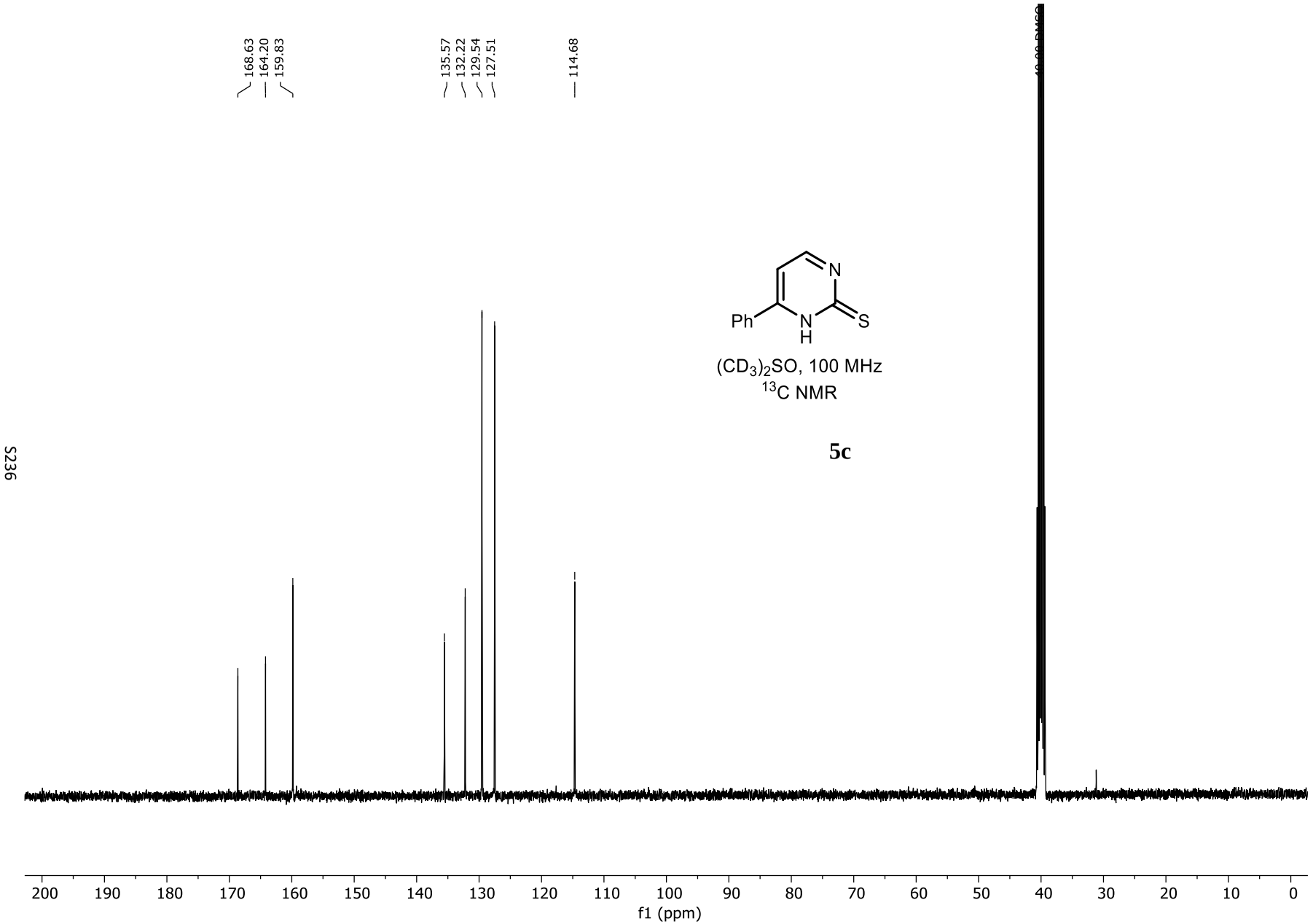

-79.11
Ph
N
OTf
N
MeO
CD3CN, 375 MHz
19F NMR
3z
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

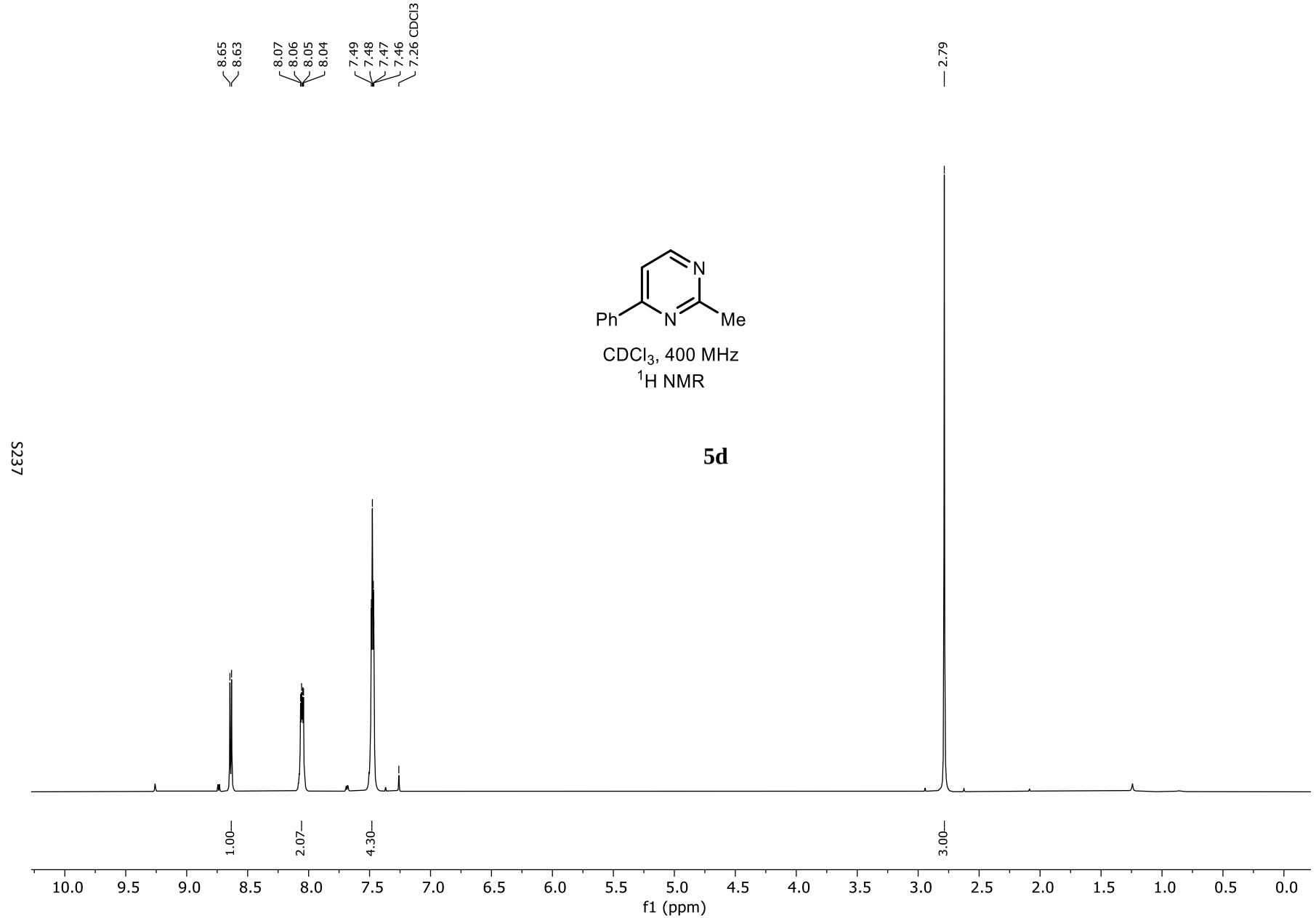

8.31
8.30
8.07
8.07
8.06
8.06
8.05
7.49
7.49
7.49
7.48
7.12
7.11
6.68
6.67
3.35 H2O
2.50 DMSO-d6
Ph
N
N
NH2
DMSO-d6, 400 MHz
1H NMR
5a
S232
1.00
2.03
3.05
1.04
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


164.24
164.07
159.51
137.48
130.93
129.15
127.15
106.28
39.98 DMSO-d6
Ph
N
N
NH2
DMSO-d6, 100 MHz
13C NMR
5a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

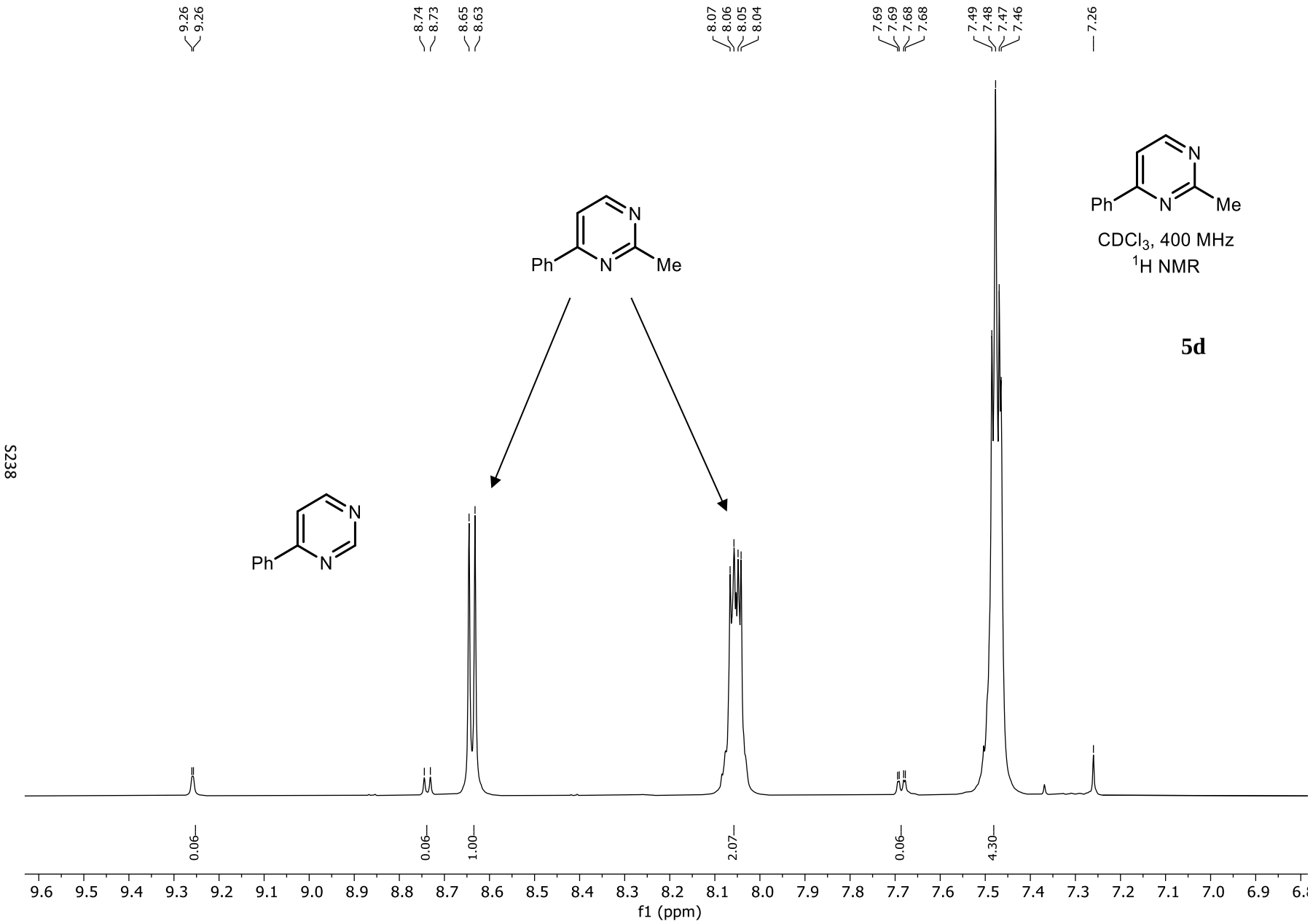

11.91
8.11
8.09
8.06
8.04
7.61
7.60
7.60
7.60
7.59
7.58
7.57
7.57
7.57
7.56
7.55
7.53
7.52
7.52
7.51
7.00
6.98
3.33 H2O
2.51 DMSO
N
N
H
O
(CD3)2SO, 400 MHz
1H NMR
5b
1.01
2.00
0.95
3.04
1.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

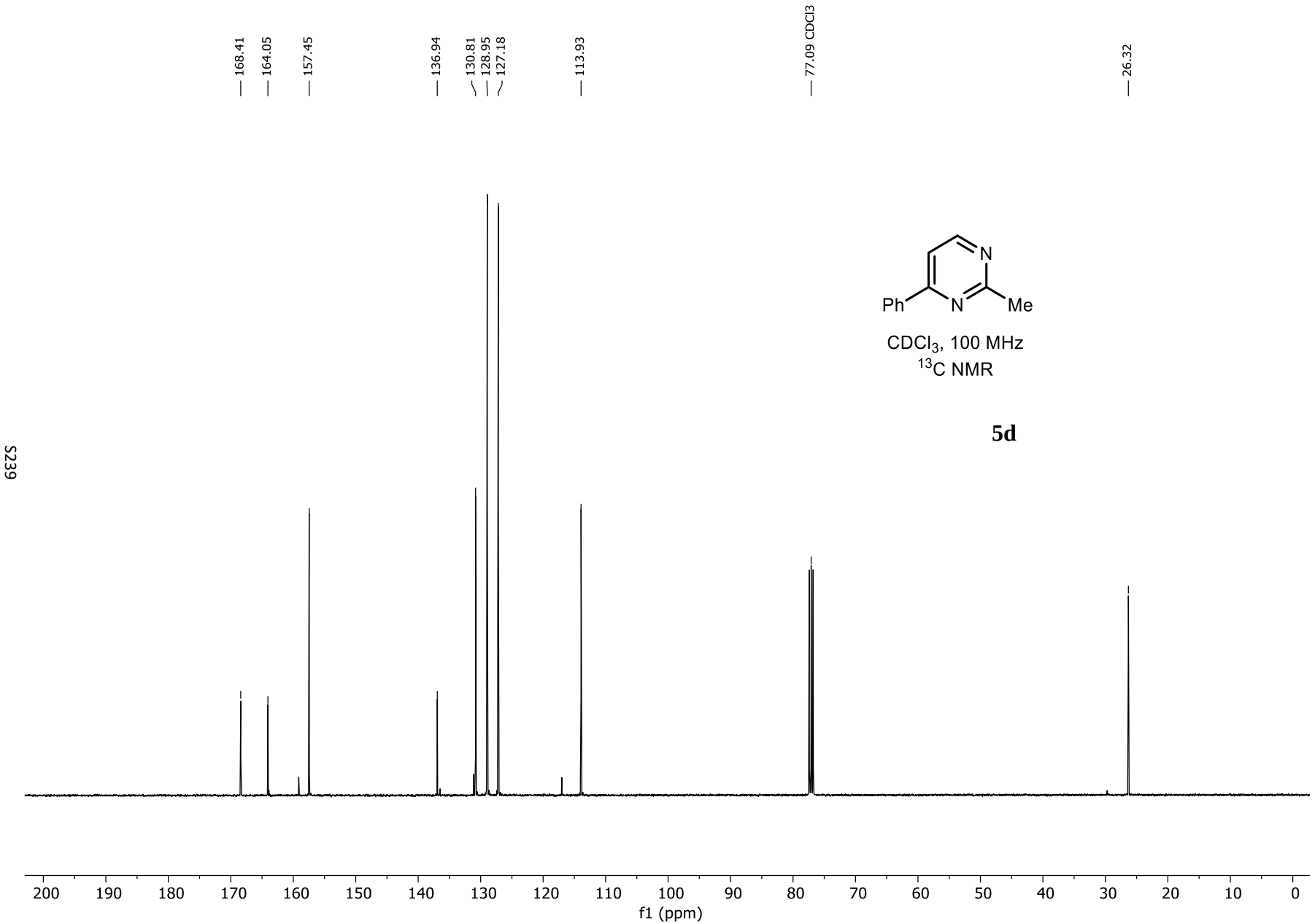

8.77
8.76
8.08
8.07
7.92
7.91
7.55
7.54
7.53
7.53
7.52
7.51
7.51
7.48
7.48
7.47
7.46
7.45
3.33 H2O
2.50 DMSO
2.08 AcOH
N
Ph
N
H
S
(CD3)2SO, 400 MHz
1H NMR
5c
S235
1.00
2.08
1.03
1.04
2.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

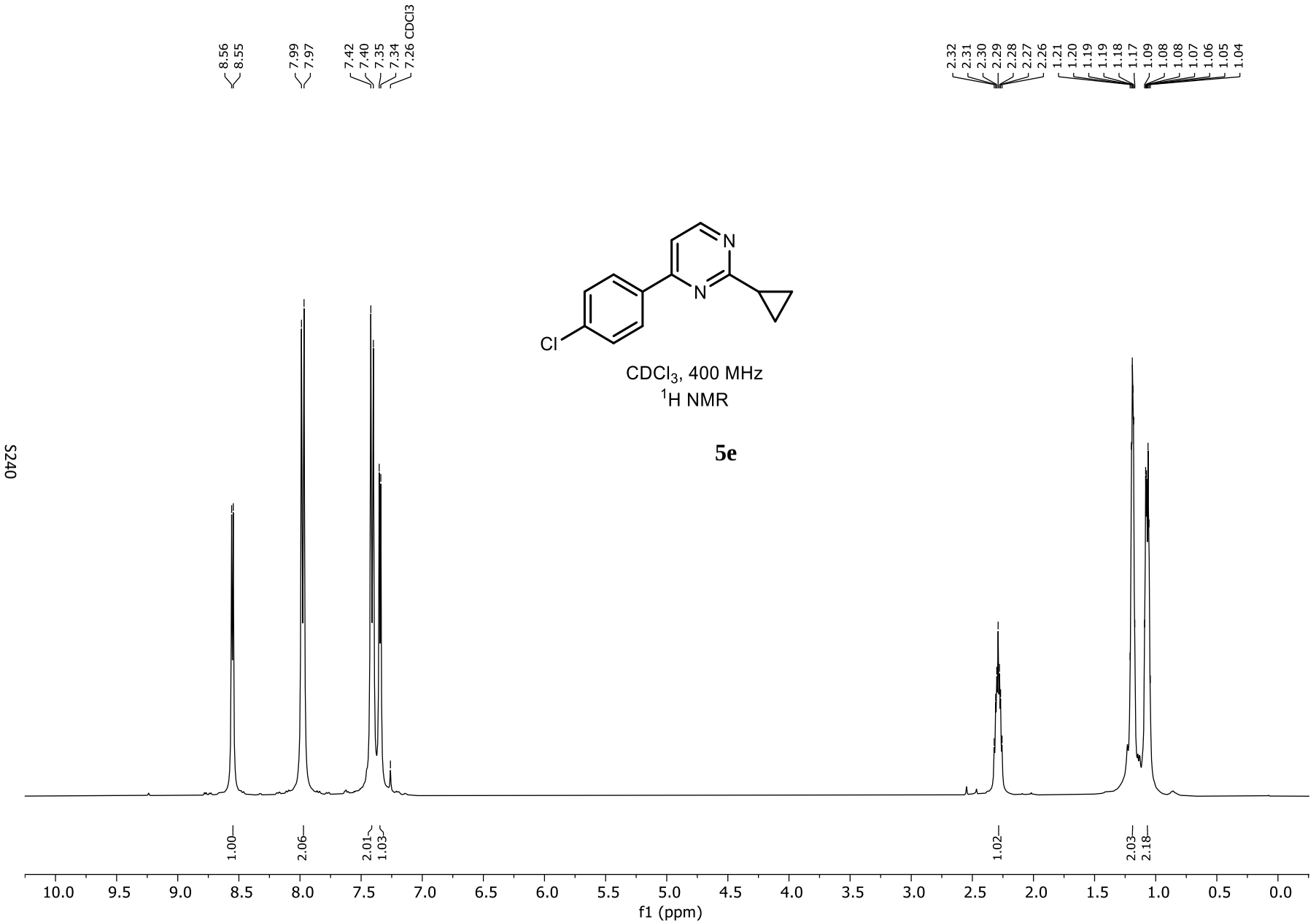

168.63
164.20
159.83
135.57
132.22
129.54
127.51
114.68
N
Ph
N
H
S
(CD3)2SO, 100 MHz
13C NMR
5c
f1 (ppm)

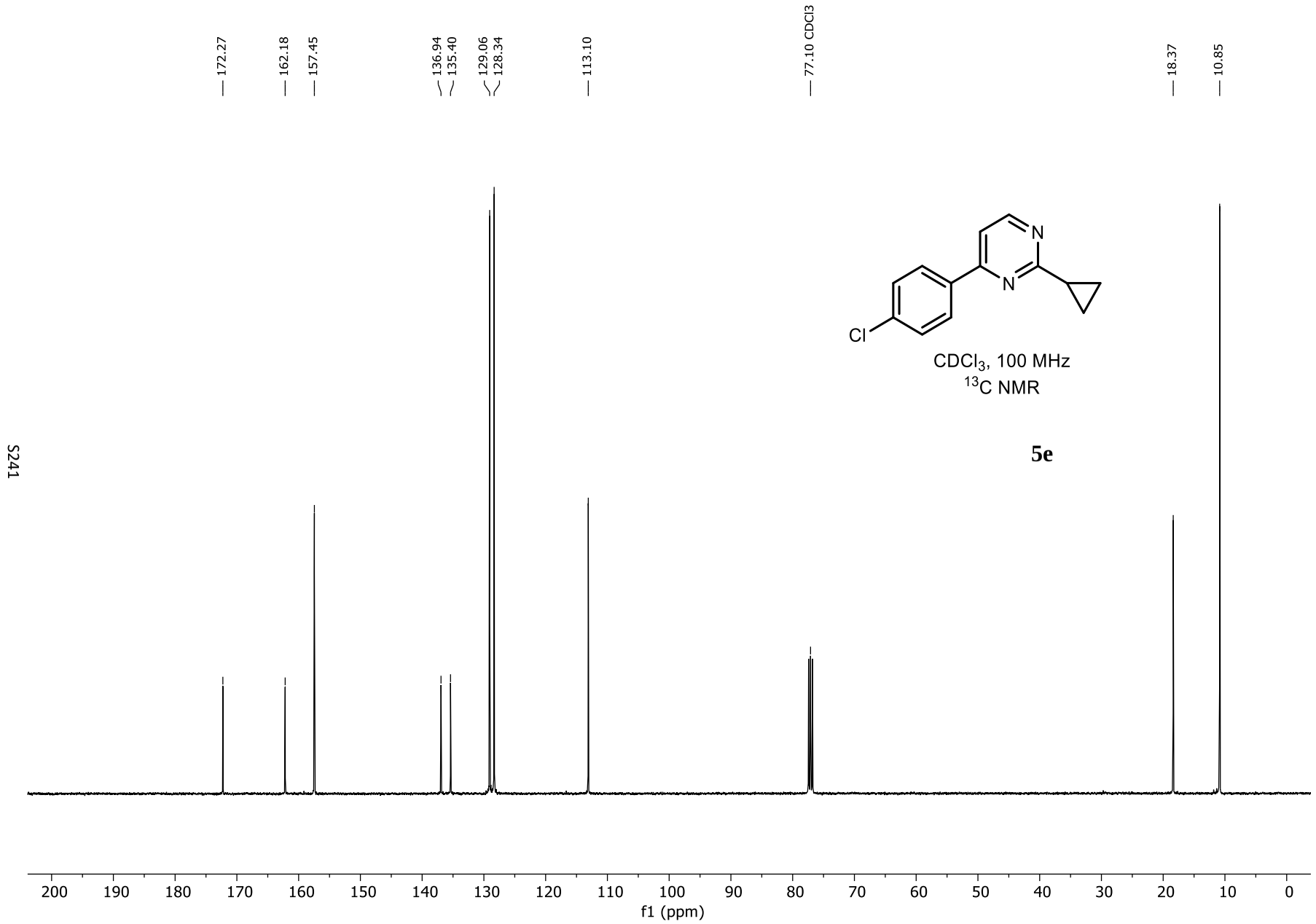

8.65
8.63
8.07
8.06
8.05
8.04
7.49
7.48
7.47
7.46
7.26 CDCl3
2.79
N
Ph
N
Me
CDCl3, 400 MHz
1H NMR
1.00
2.07
4.30
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

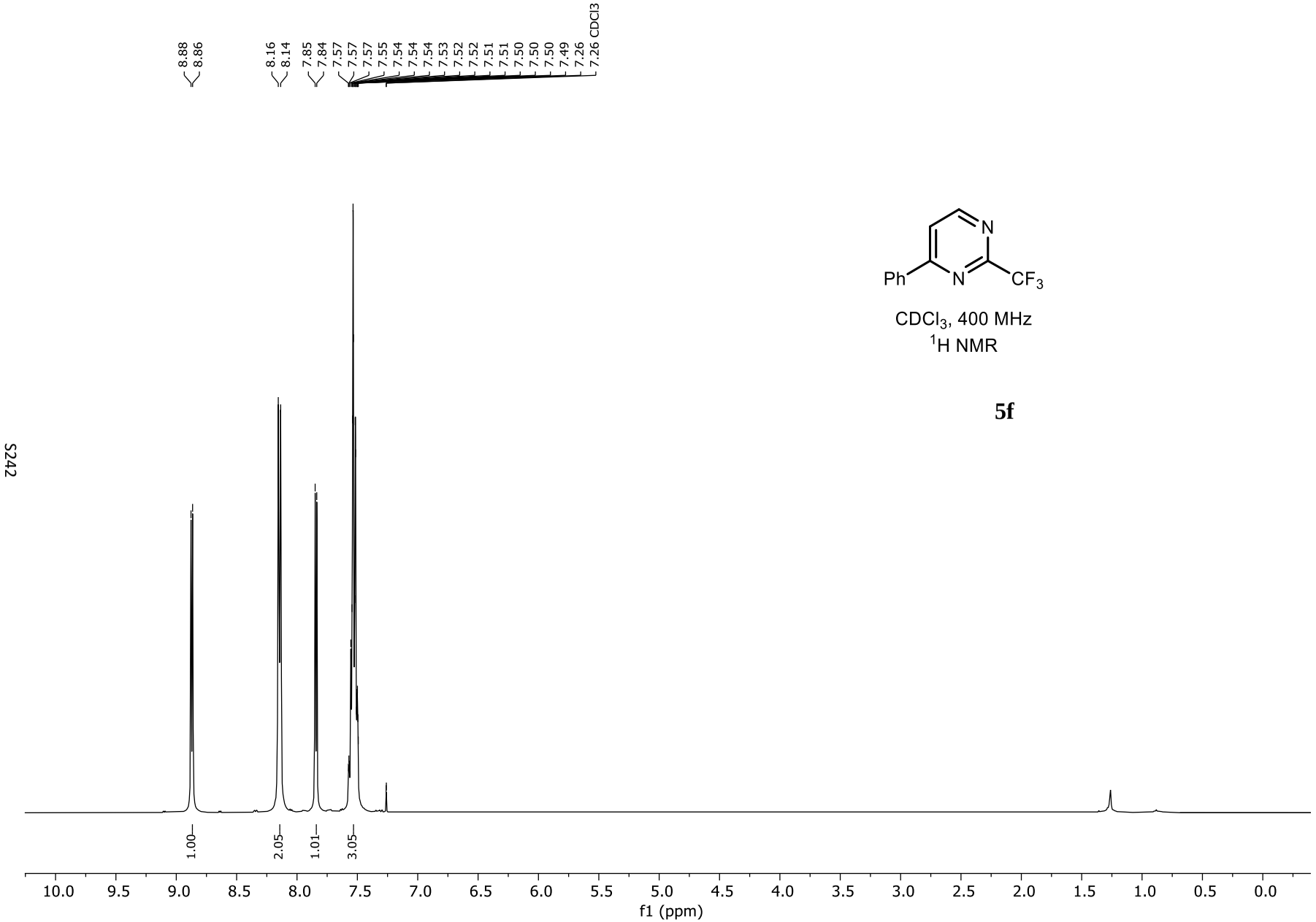
5d

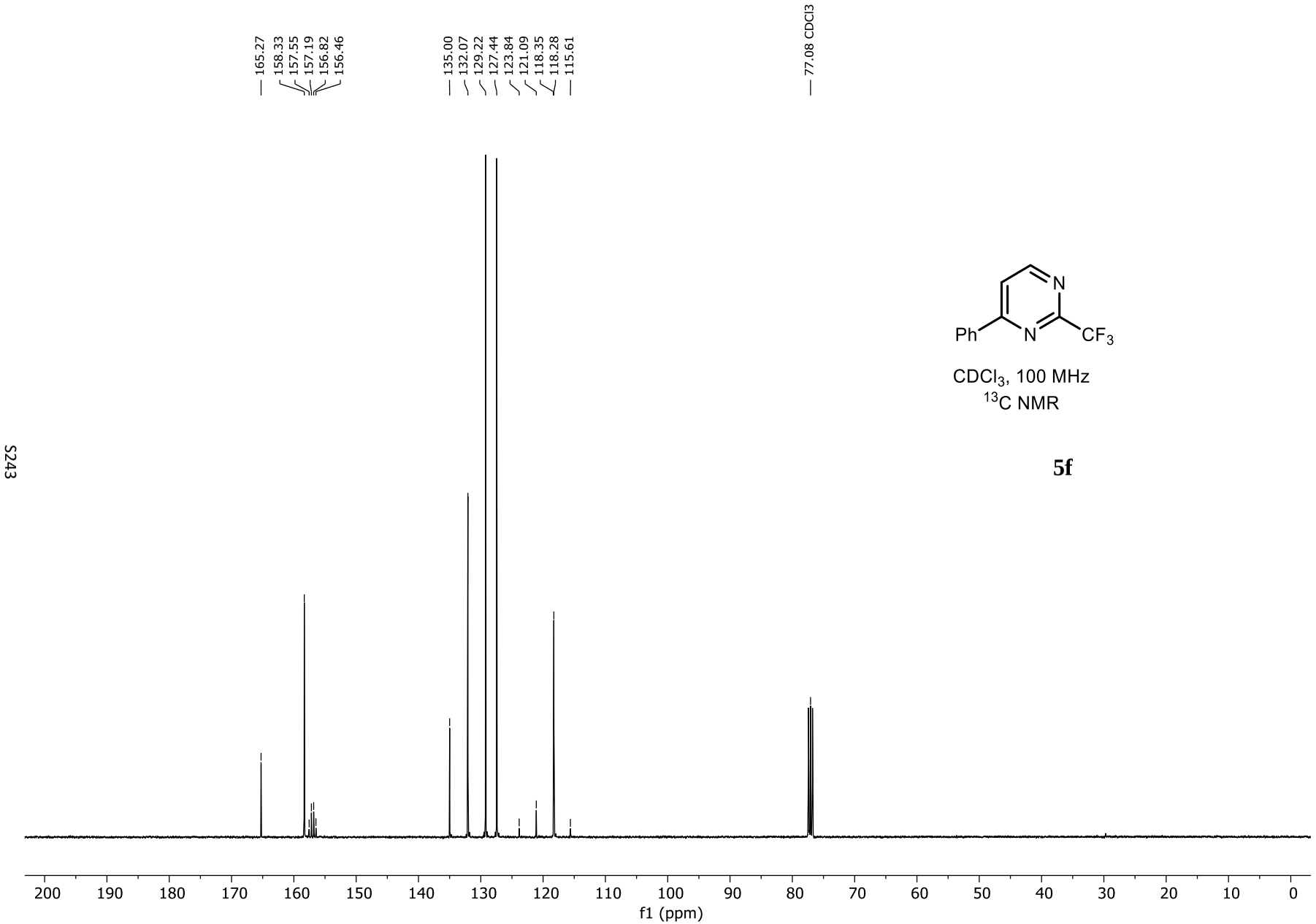

9.26
9.26
8.74
8.73
8.65
8.63
8.07
8.06
8.05
8.04
7.69
7.69
7.68
7.68
7.49
7.48
7.47
7.46
7.26
Ph
N
N
Me
Ph
N
N
CDCl3, 400 MHz
1H NMR
5d
0.06
0.06
1.00
2.07
0.06
4.30
f1 (ppm)


168.41
164.05
157.45
136.94
130.81
128.95
127.18
113.93
77.09 CDCl3
26.32
N
Ph
N
Me
CDCl3, 100 MHz
13C NMR
5d
S239
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

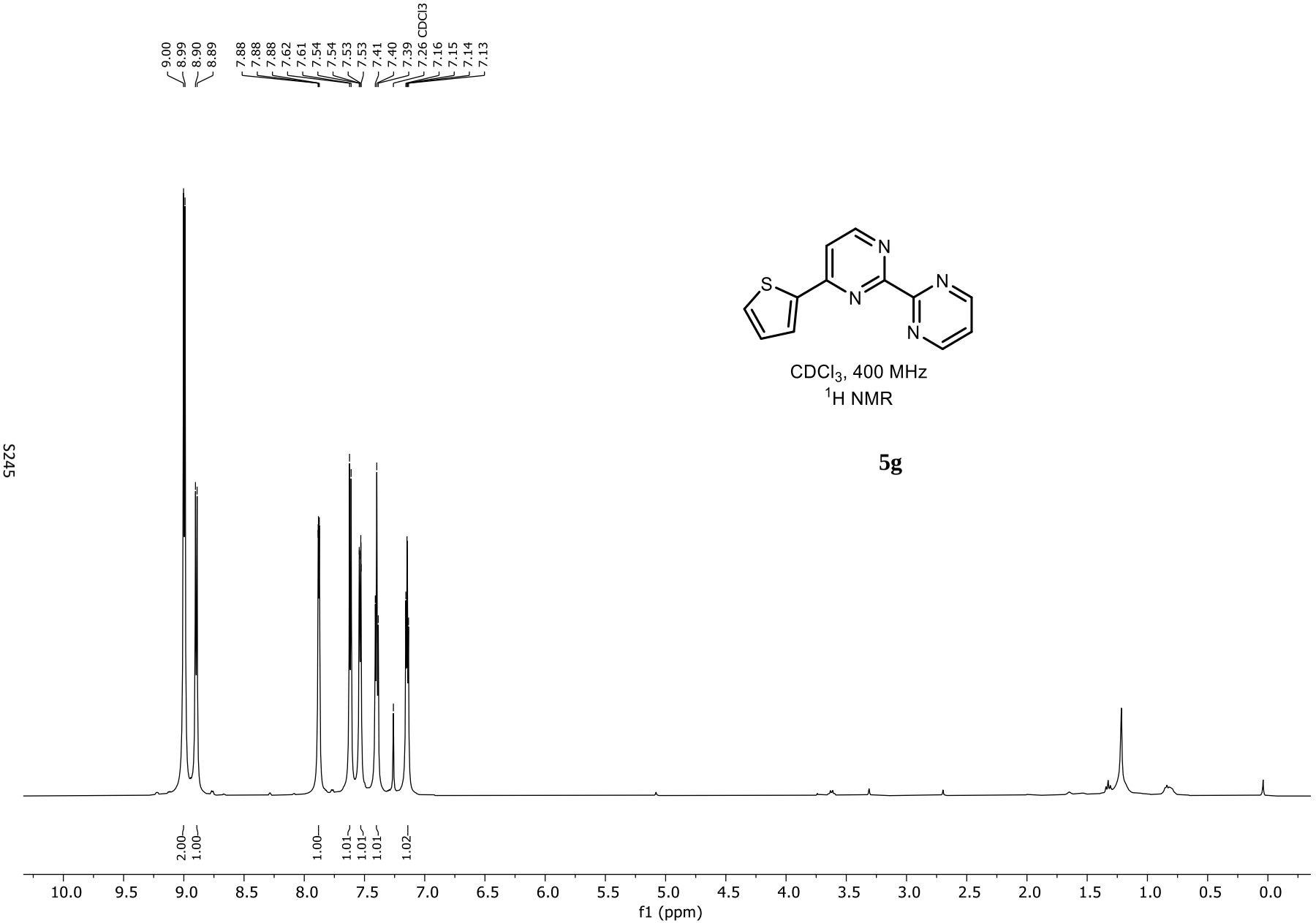

8.56
8.55
7.99
7.97
7.42
7.40
7.35
7.34
7.26 CDCl3
2.32
2.31
2.30
2.29
2.28
2.27
2.26
1.21
1.20
1.19
1.19
1.18
1.17
1.09
1.08
1.08
1.07
1.06
1.05
1.04
N
N
Cl
CDCl3, 400 MHz
1H NMR
5e
S240
1.00
2.06
2.01
1.03
1.02
2.03
2.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


172.27
162.18
157.45
136.94
135.40
129.06
128.34
113.10
77.10 CDCl3
18.37
10.85
N
N
Cl
CDCl3, 100 MHz
13C NMR
5e
S241
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.88
8.86
8.16
8.14
7.85
7.84
7.57
7.57
7.57
7.55
7.54
7.54
7.54
7.53
7.52
7.52
7.51
7.51
7.50
7.50
7.50
7.49
7.26
7.26 CDCl3
N
Ph
N
CF3
CDCl3, 400 MHz
1H NMR
5f
1.00
2.05
1.01
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

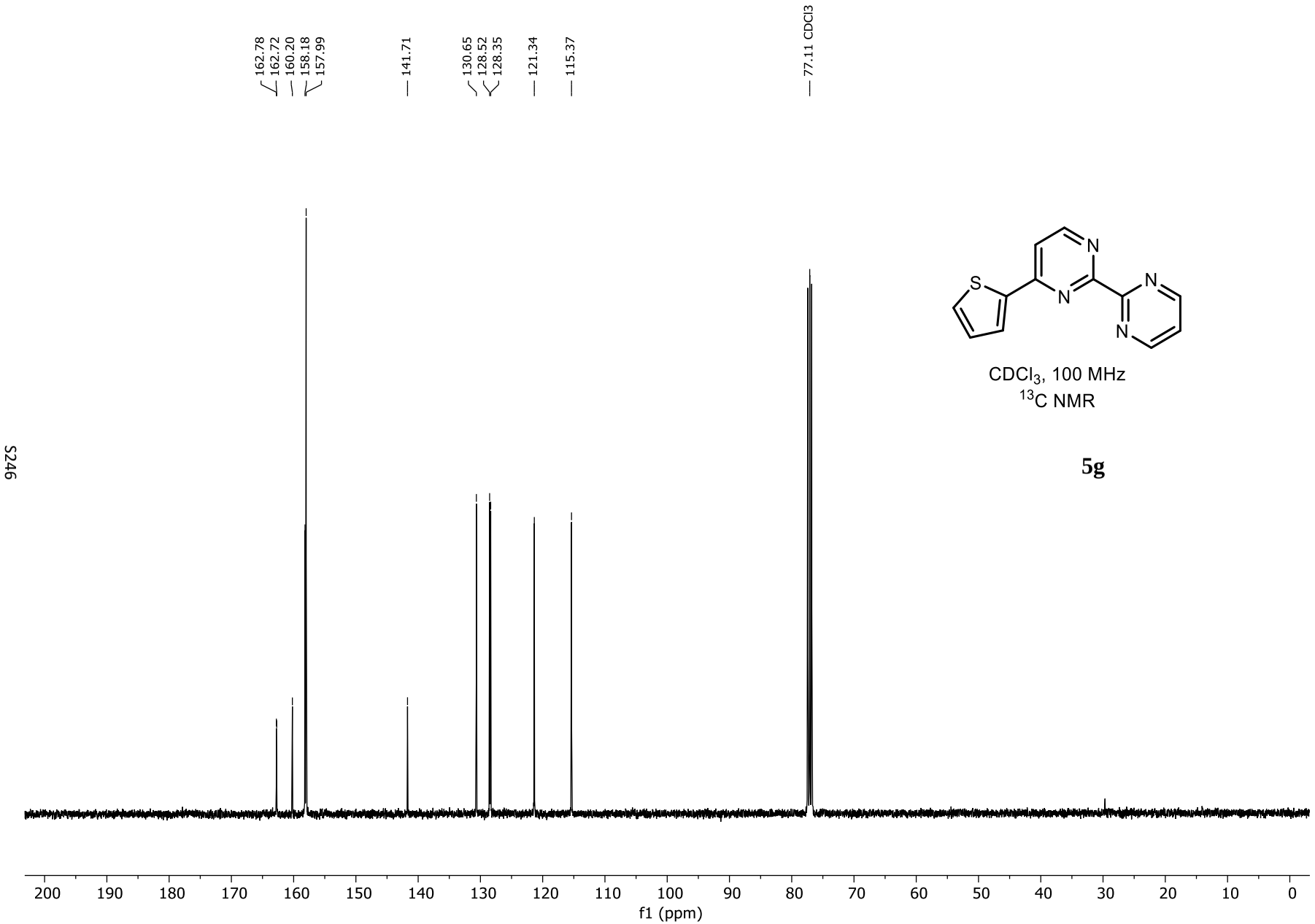

165.27
158.33
157.55
157.19
156.82
156.46
135.00
132.07
129.22
127.44
123.84
121.09
118.35
118.28
115.61
77.08 CDCl3
Ph
N
N
CF3
CDCl3, 100 MHz
13C NMR
5f
f1 (ppm)

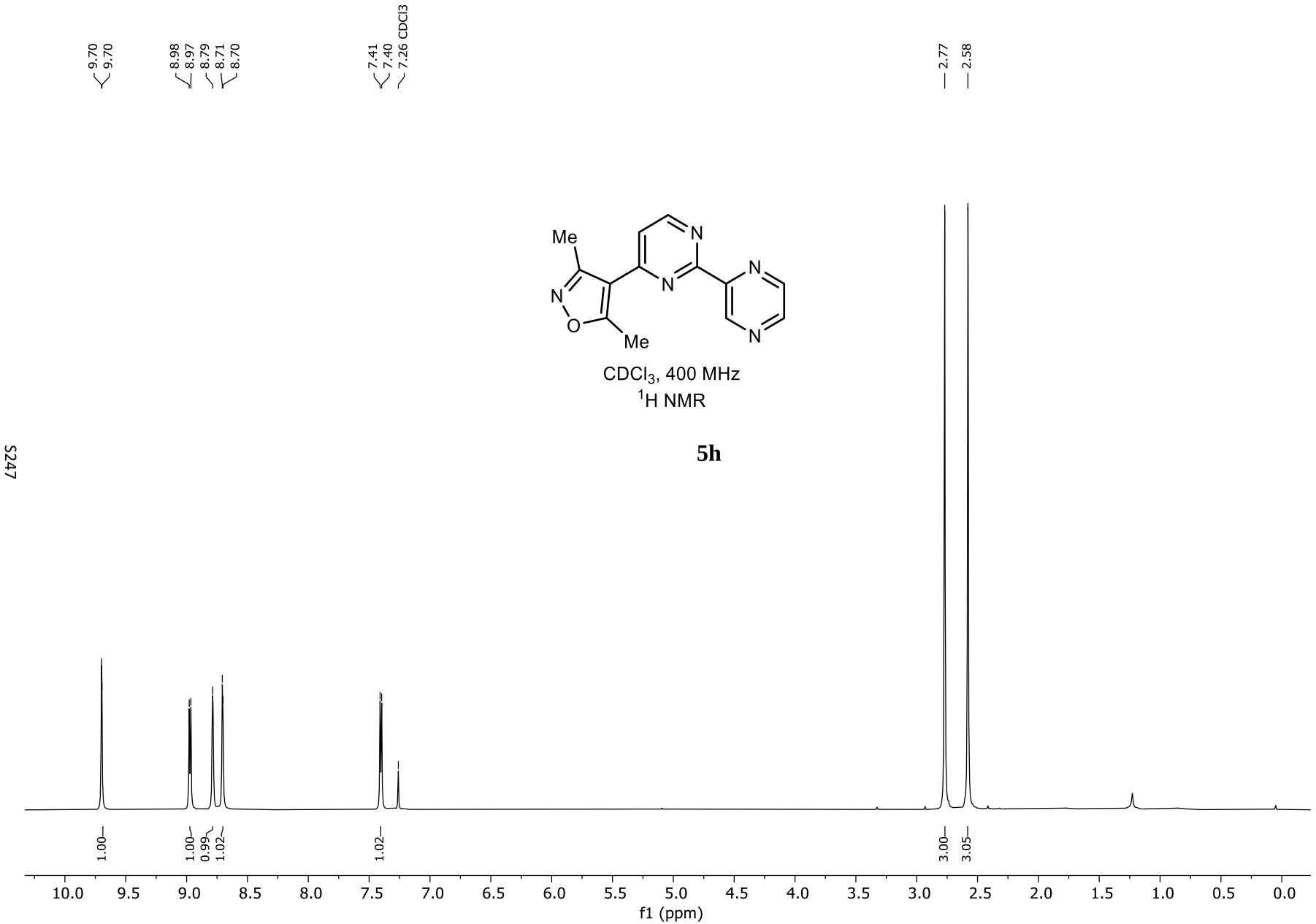

-70.52
Ph
N
N
CF3
CDCl3, 375 MHz
19F NMR
5f
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)



$CDCl_3$, 400 MHz
^1H NMR

5g

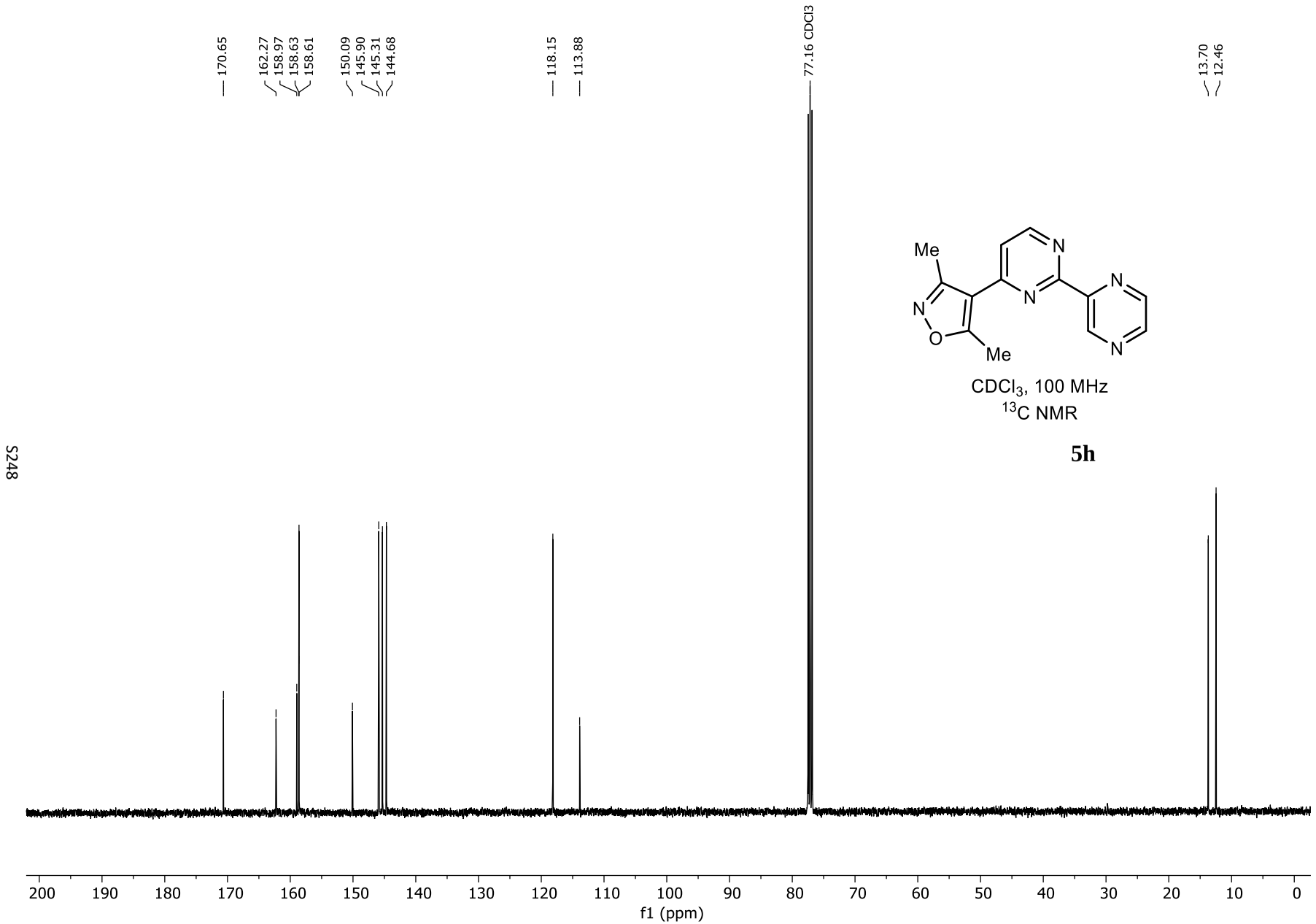

162.78
162.72
160.20
158.18
157.99
141.71
130.65
128.52
128.35
121.34
115.37
77.11 CDCl3
S
N
N
N
N
CDCl3, 100 MHz
13C NMR
5g
f1 (ppm)

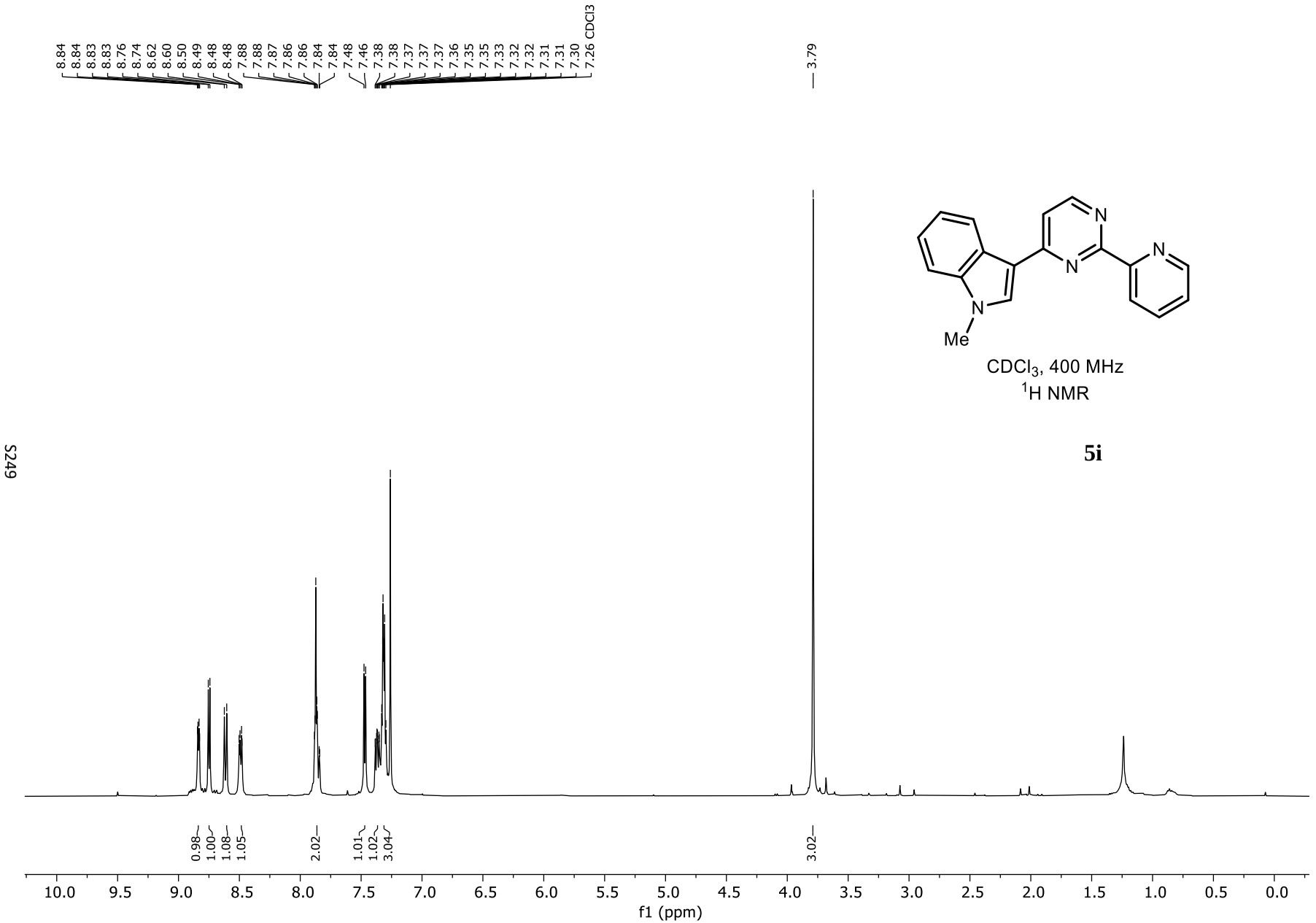


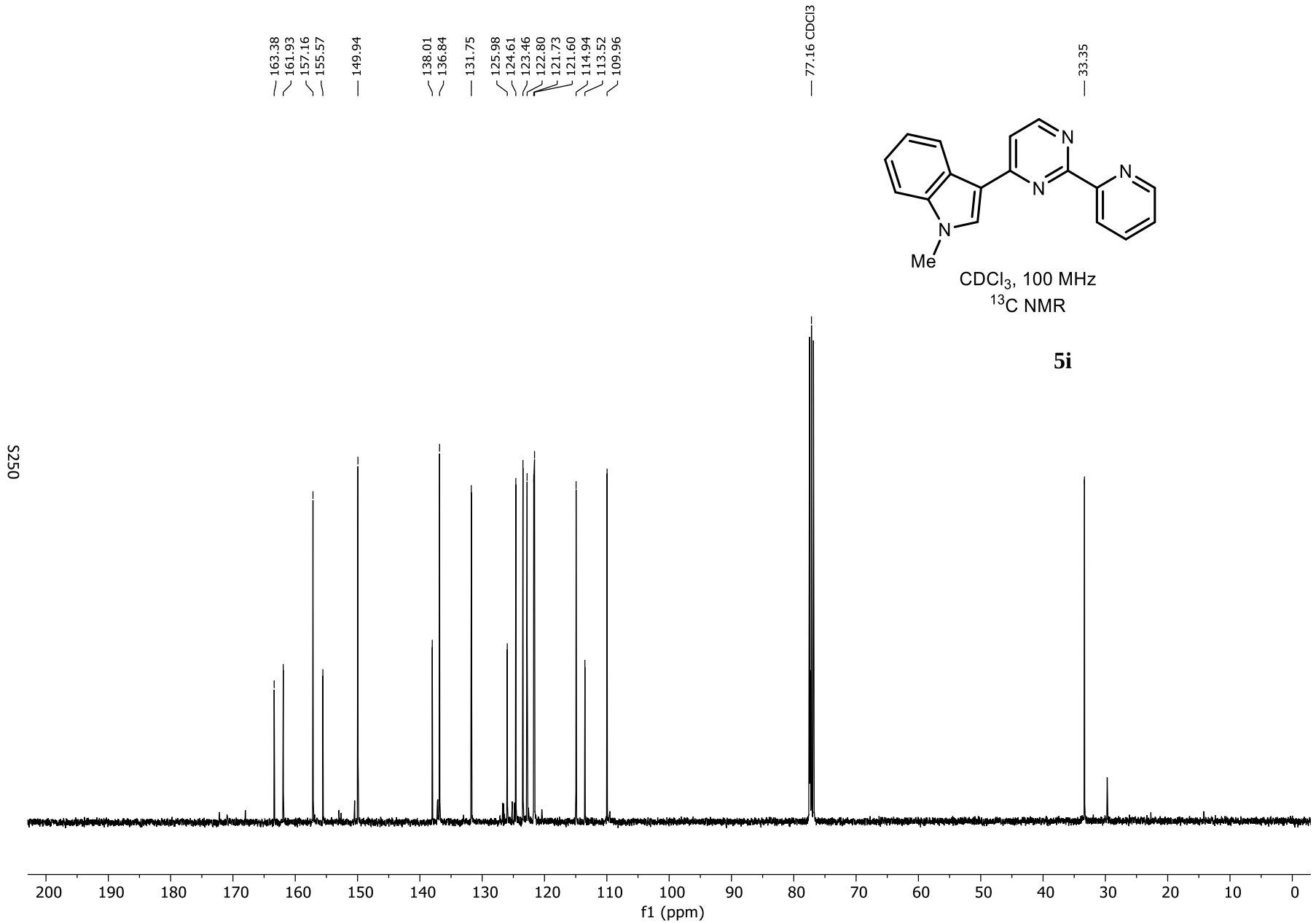
$CDCl_3$, 400 MHz

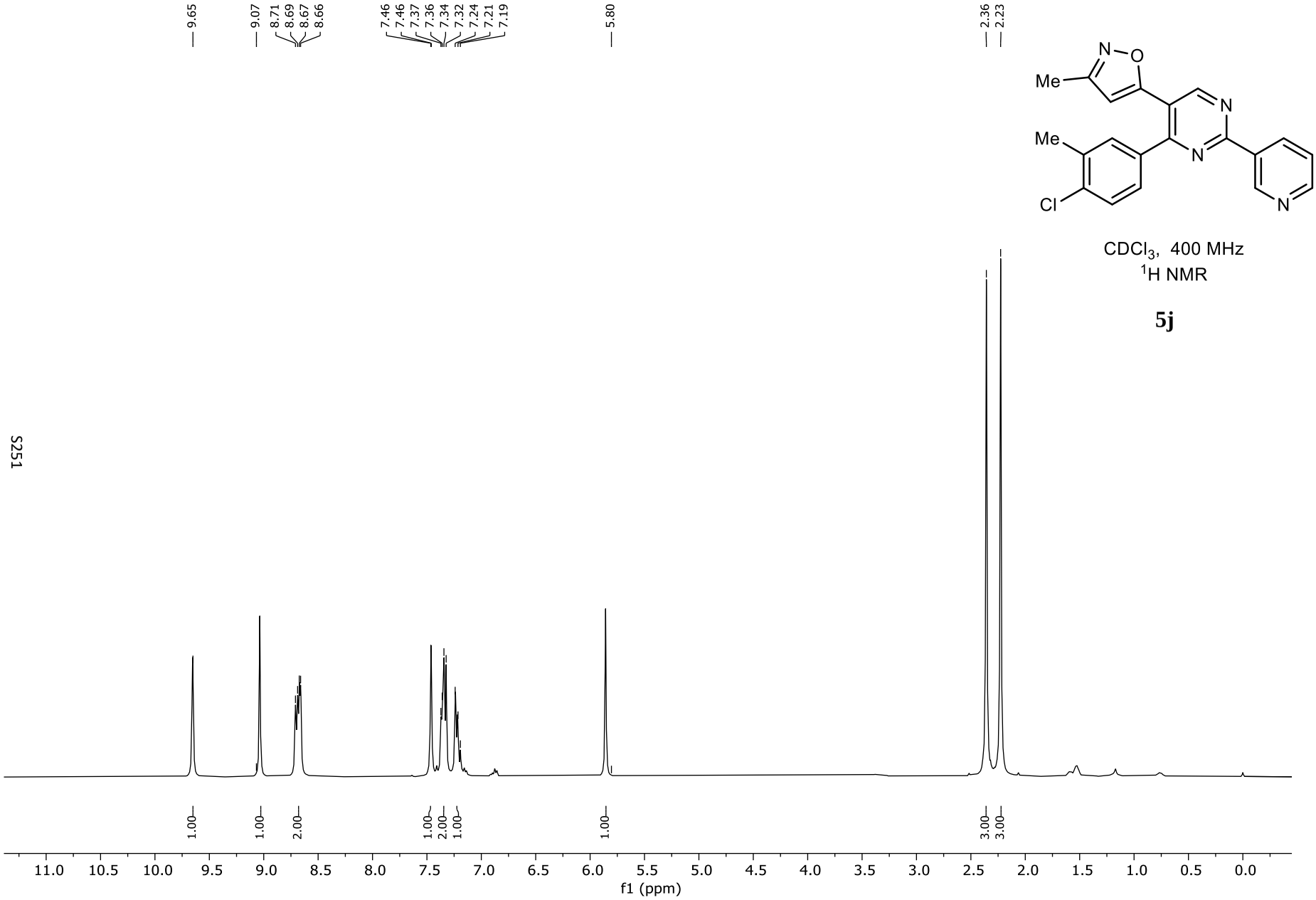
^1H NMR

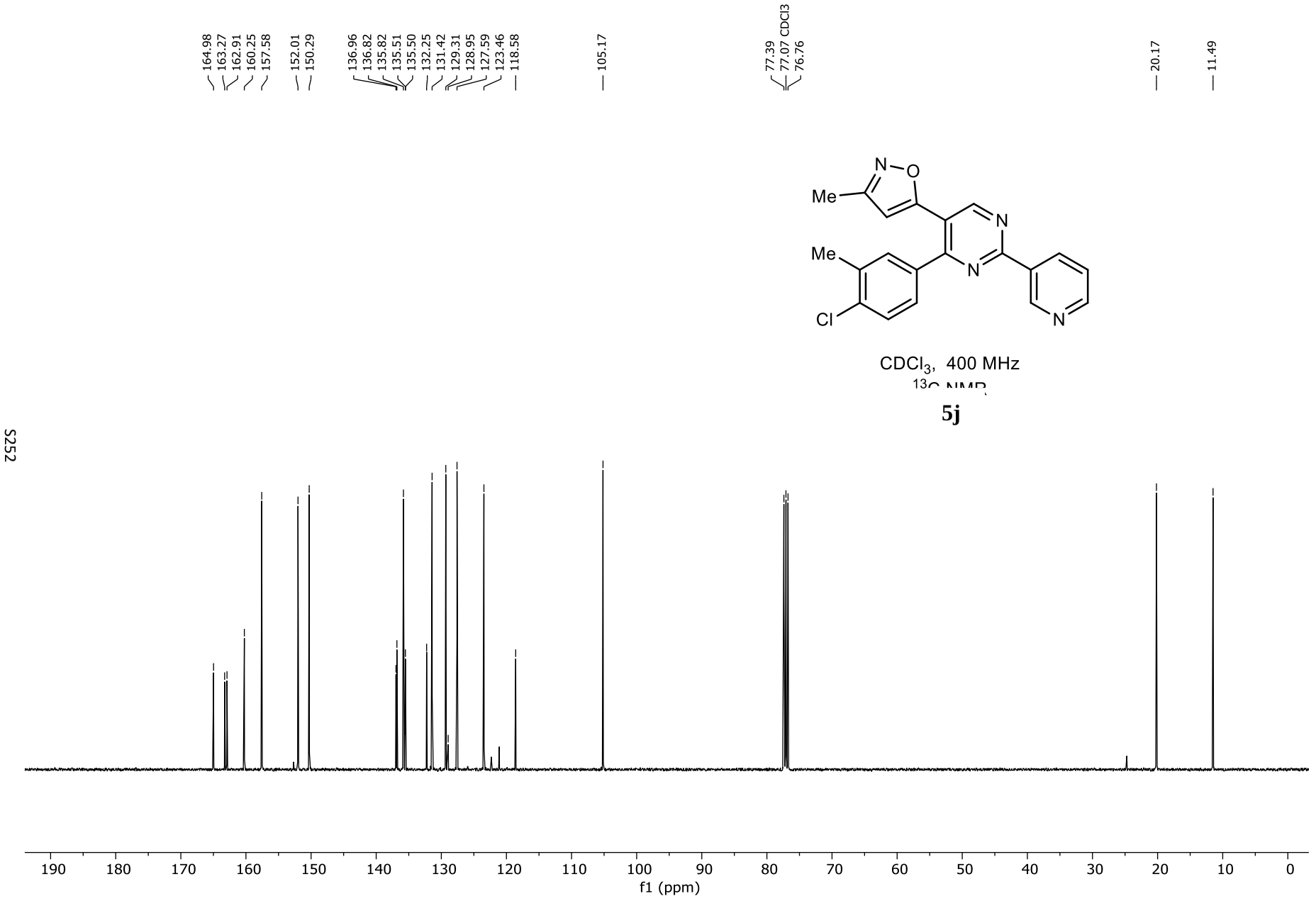
5h

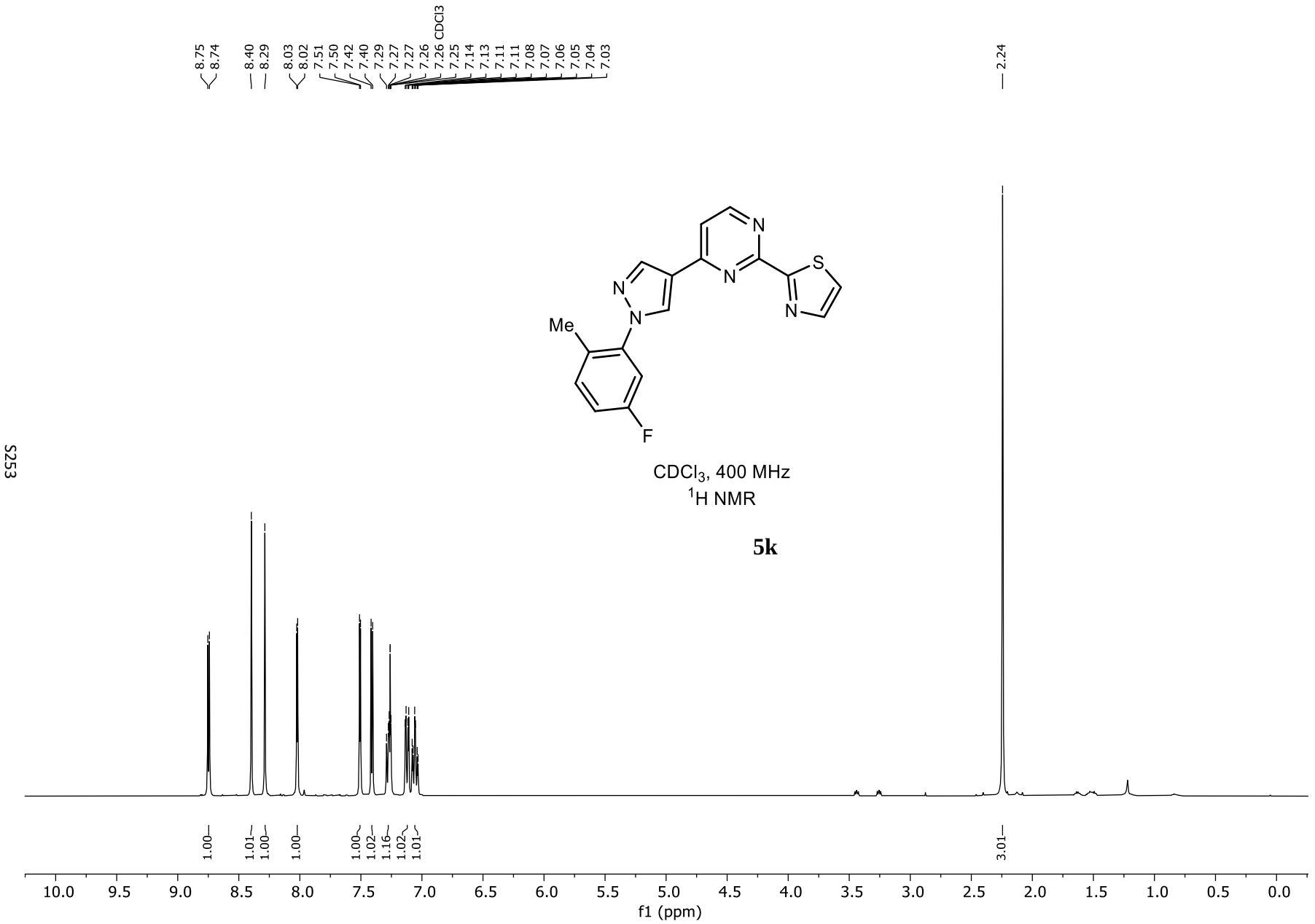

170.65
162.27
158.97
158.63
158.61
150.09
145.90
145.31
144.68
118.15
113.88
77.16 CDCl3
13.70
12.46
Me
N
N
N
N
O
Me
CDCl3, 100 MHz
13C NMR
5h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

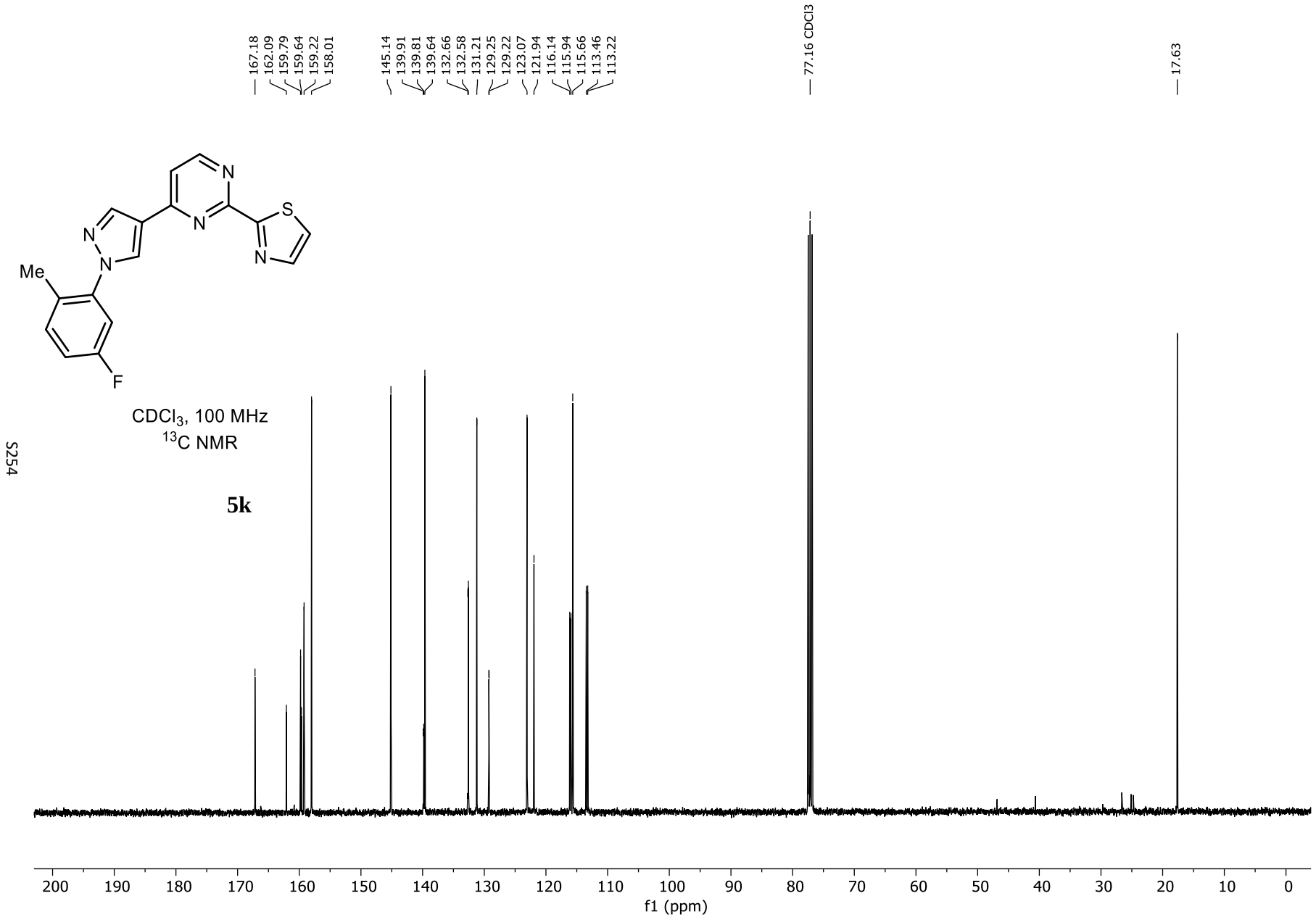

8.84
8.84
8.83
8.83
8.76
8.74
8.62
8.60
8.50
8.49
8.48
8.48
7.88
7.87
7.86
7.86
7.84
7.84
7.48
7.46
7.38
7.38
7.37
7.37
7.37
7.36
7.35
7.35
7.33
7.32
7.32
7.31
7.31
7.30
7.26 CDCl3
3.79
N
N
N
N
Me
CDCl3, 400 MHz
1H NMR
5i
S249
0.98
1.00
1.08
1.05
2.02
1.01
1.02
3.04
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

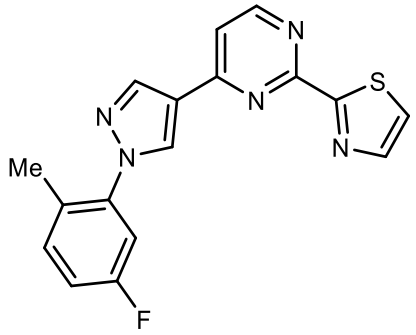

163.38
161.93
157.16
155.57
149.94
138.01
136.84
131.75
125.98
124.61
123.46
122.80
121.73
121.60
114.94
113.52
109.96
77.16 CDCl3
33.35
N
N
N
N
Me
CDCl3, 100 MHz
13C NMR
5i
S250
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.65
9.07
8.71
8.69
8.67
8.66
7.46
7.46
7.37
7.36
7.34
7.32
7.24
7.21
7.19
5.80
2.36
2.23
Me
N
O
N
Me
N
Cl
N
CDCl3, 400 MHz
1H NMR
5j
S251
1.00
1.00
2.00
1.00
2.00
1.00
1.00
3.00
3.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


164.98
163.27
162.91
160.25
157.58
152.01
150.29
136.96
136.82
135.82
135.51
135.50
132.25
131.42
129.31
128.95
127.59
123.46
118.58
105.17
77.39
77.07 CDCl3
76.76
20.17
11.49
Me
Me
Cl
N
O
N
N
N
CDCl3, 400 MHz
13C NMR
5j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.75
8.74
8.40
8.29
8.03
8.02
7.51
7.50
7.42
7.40
7.29
7.27
7.27
7.26 CDCl3
7.25
7.14
7.13
7.11
7.11
7.08
7.07
7.06
7.05
7.04
7.03
2.24
N
N
S
N
N
N
Me
F
CDCl3, 400 MHz
1H NMR
5k
S253
1.00
1.01
1.00
1.00
1.00
1.02
1.16
1.02
1.01
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

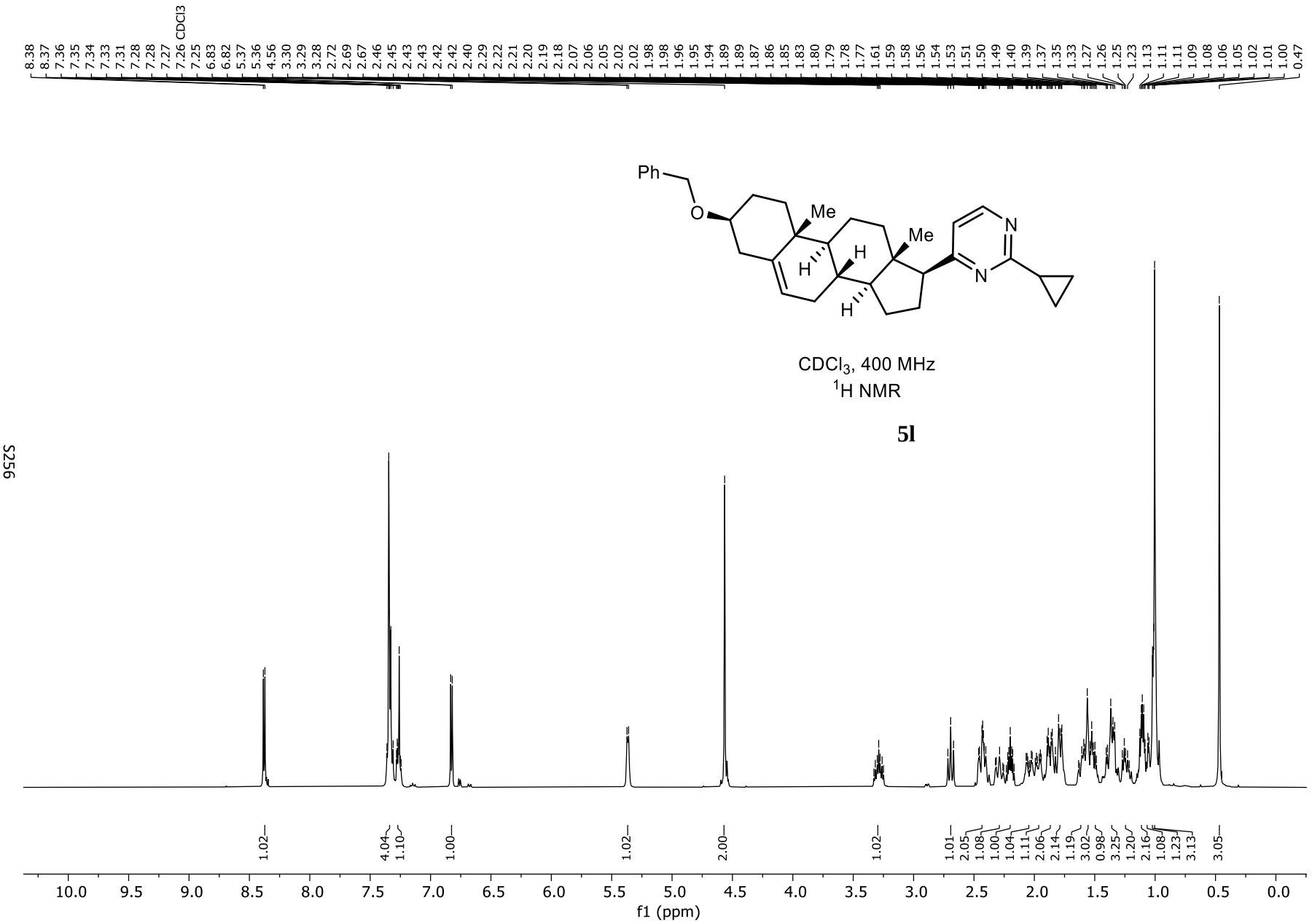

167.18
162.09
159.79
159.64
159.22
158.01
145.14
139.91
139.81
139.64
132.66
132.58
131.21
129.25
129.22
123.07
121.94
116.14
115.94
115.66
113.46
113.22
77.16 CDCl3
17.63
N
N
S
N
N
N
Me
F
CDCl3, 100 MHz
13C NMR
5k
S254
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

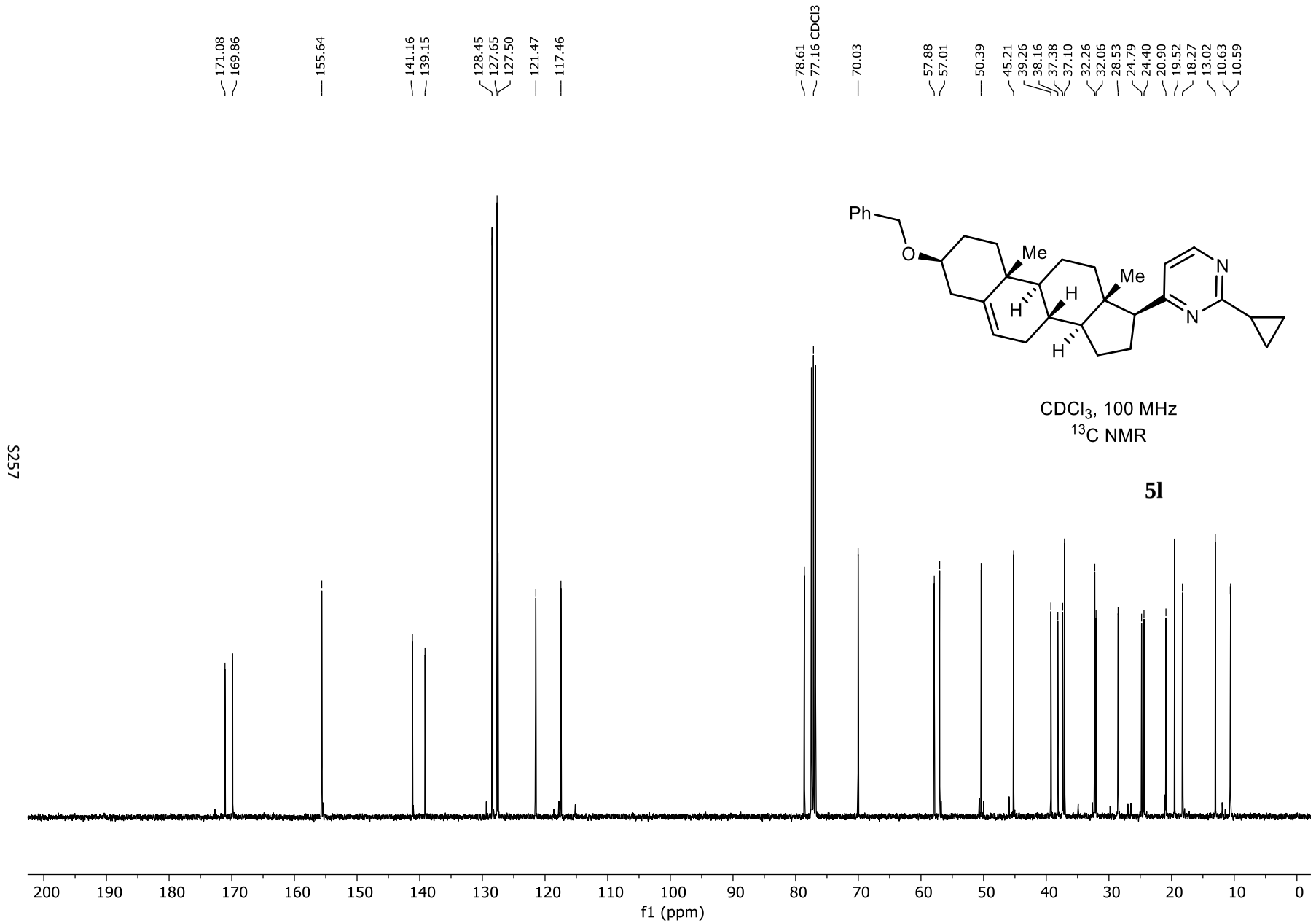


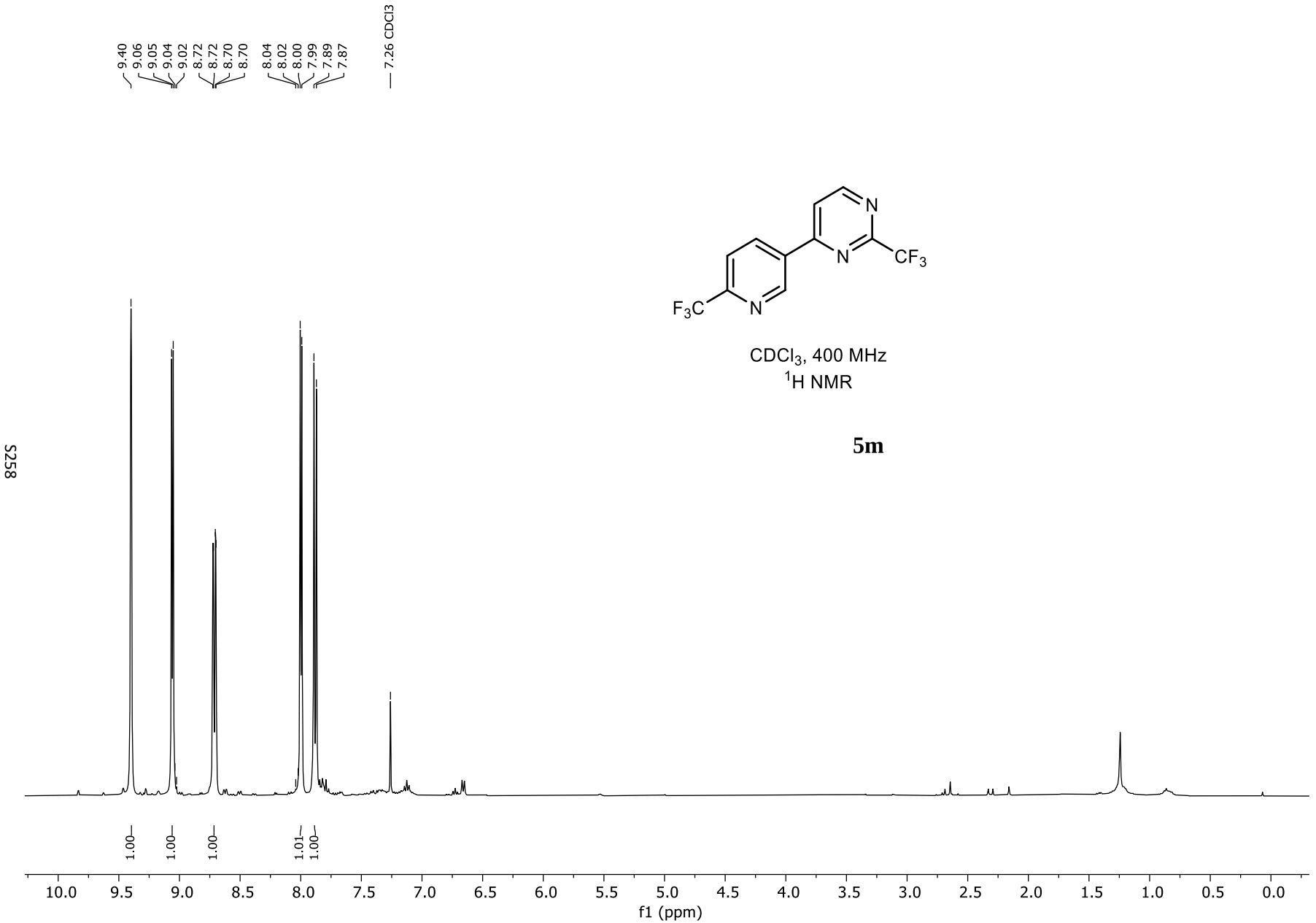
$CDCl_3$, 375 MHz

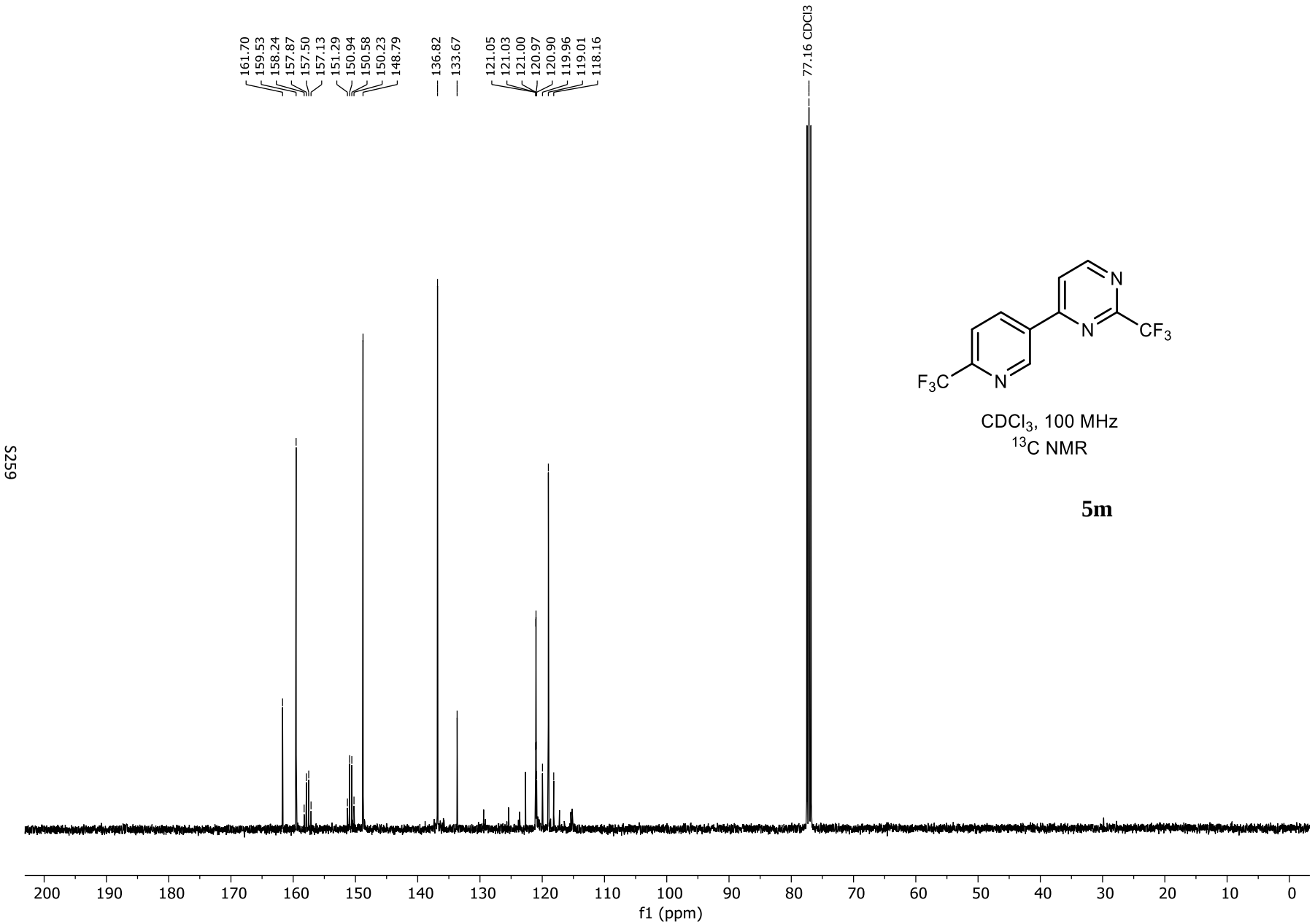
^{19}F NMR

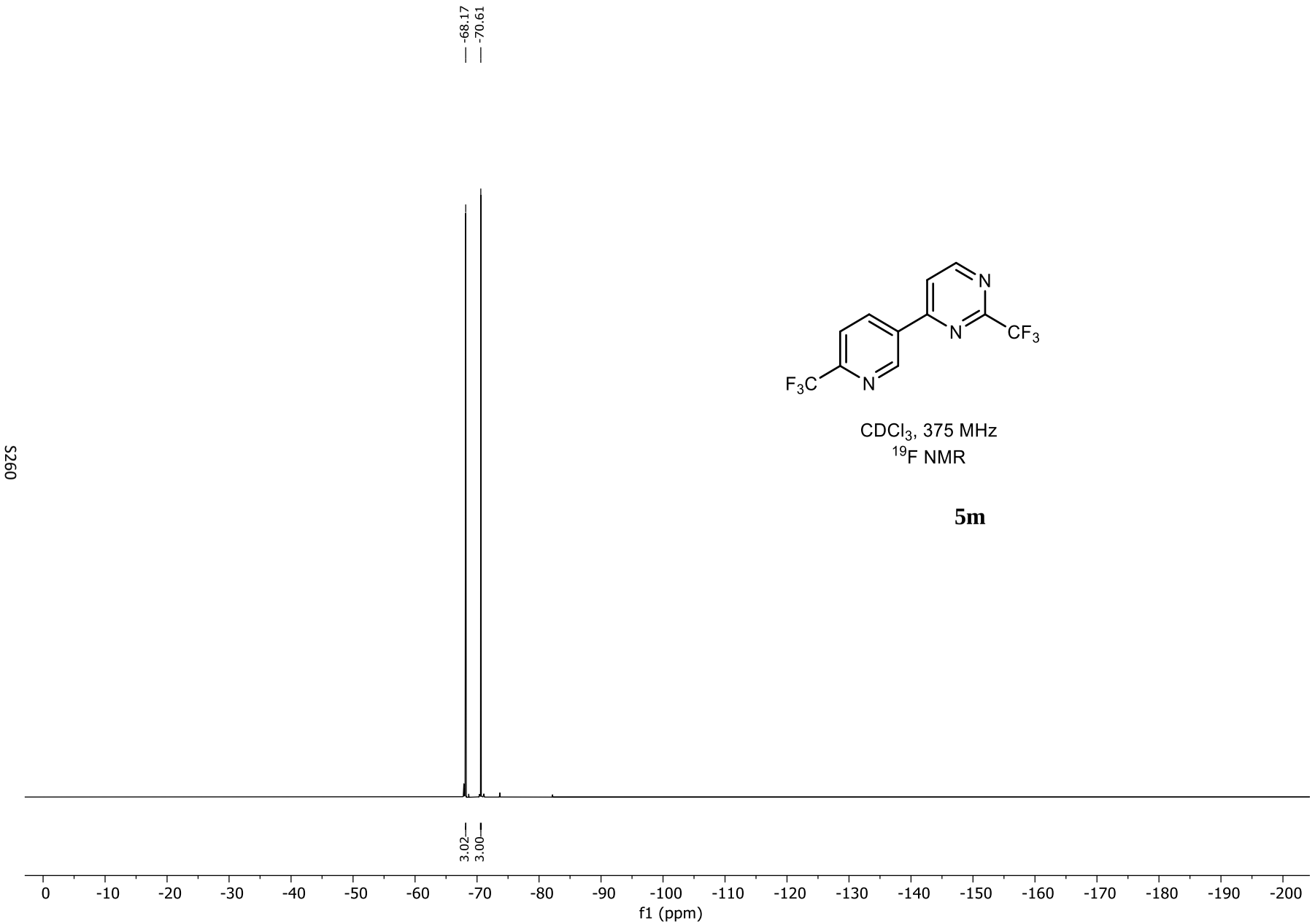
5k

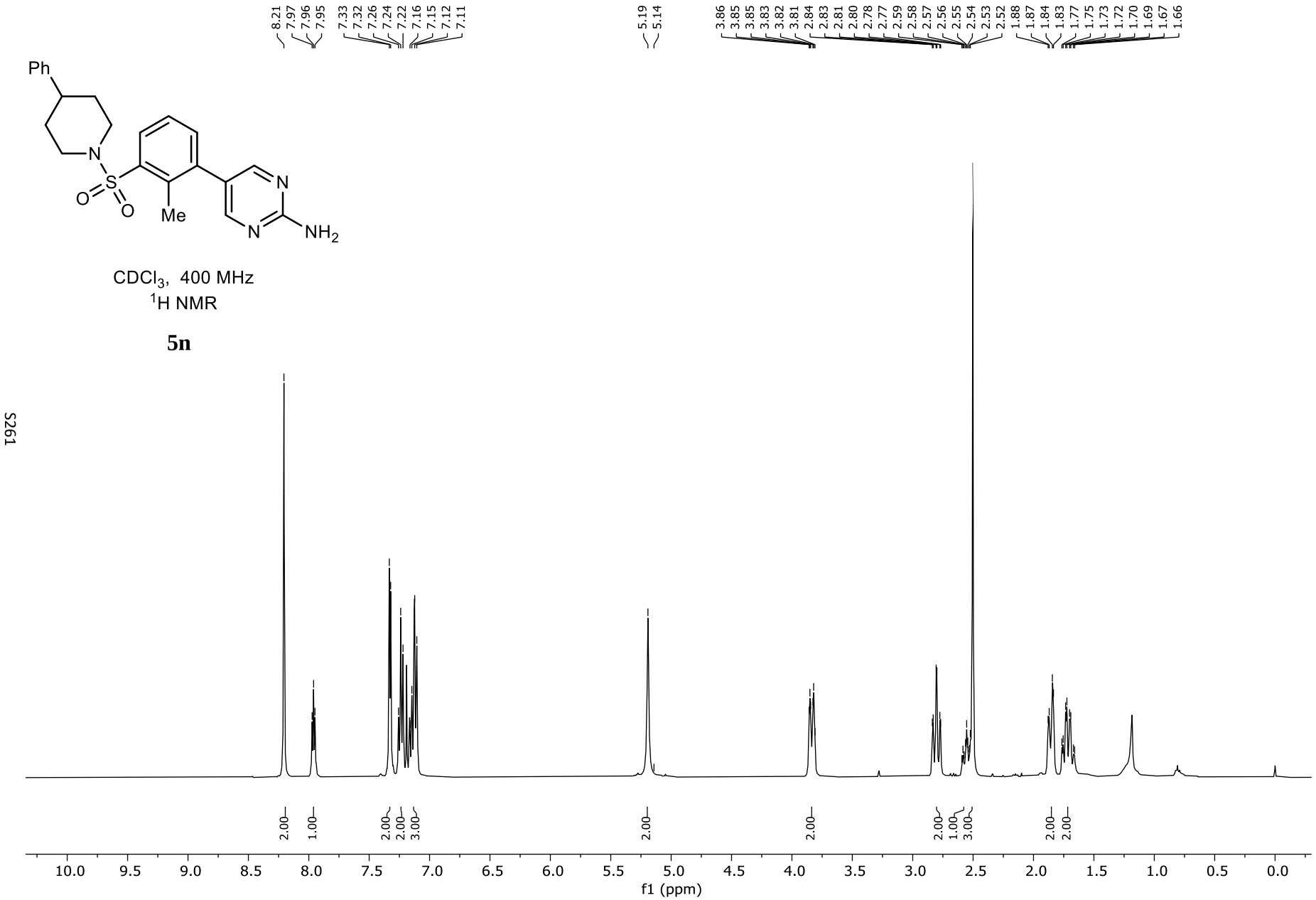

8.38 8.37 7.36 7.35 7.34 7.33 7.31 7.28 7.28 7.27 CDCl3 7.26 7.25 6.83 6.82 5.37 5.36 4.56 3.30 3.29 3.28 2.72 2.69 2.67 2.46 2.45 2.43 2.43 2.42 2.42 2.40 2.29 2.22 2.21 2.20 2.19 2.18 2.07 2.06 2.05 2.02 2.02 1.98 1.98 1.96 1.95 1.94 1.89 1.89 1.87 1.86 1.85 1.83 1.80 1.79 1.78 1.77 1.61 1.59 1.58 1.56 1.54 1.53 1.51 1.50 1.49 1.40 1.39 1.37 1.35 1.33 1.27 1.26 1.25 1.23 1.13 1.11 1.11 1.09 1.08 1.06 1.05 1.02 1.01 1.00 0.47
Ph
O
Me
Me
H
H
H
N
N
CDCl3, 400 MHz
1H NMR
5l
S256
1.02
4.04
1.10
1.00
1.02
2.00
1.02
1.01
2.05
1.08
1.00
1.04
1.11
2.06
2.14
1.19
3.02
0.98
3.25
1.20
2.16
1.08
1.23
3.13
3.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

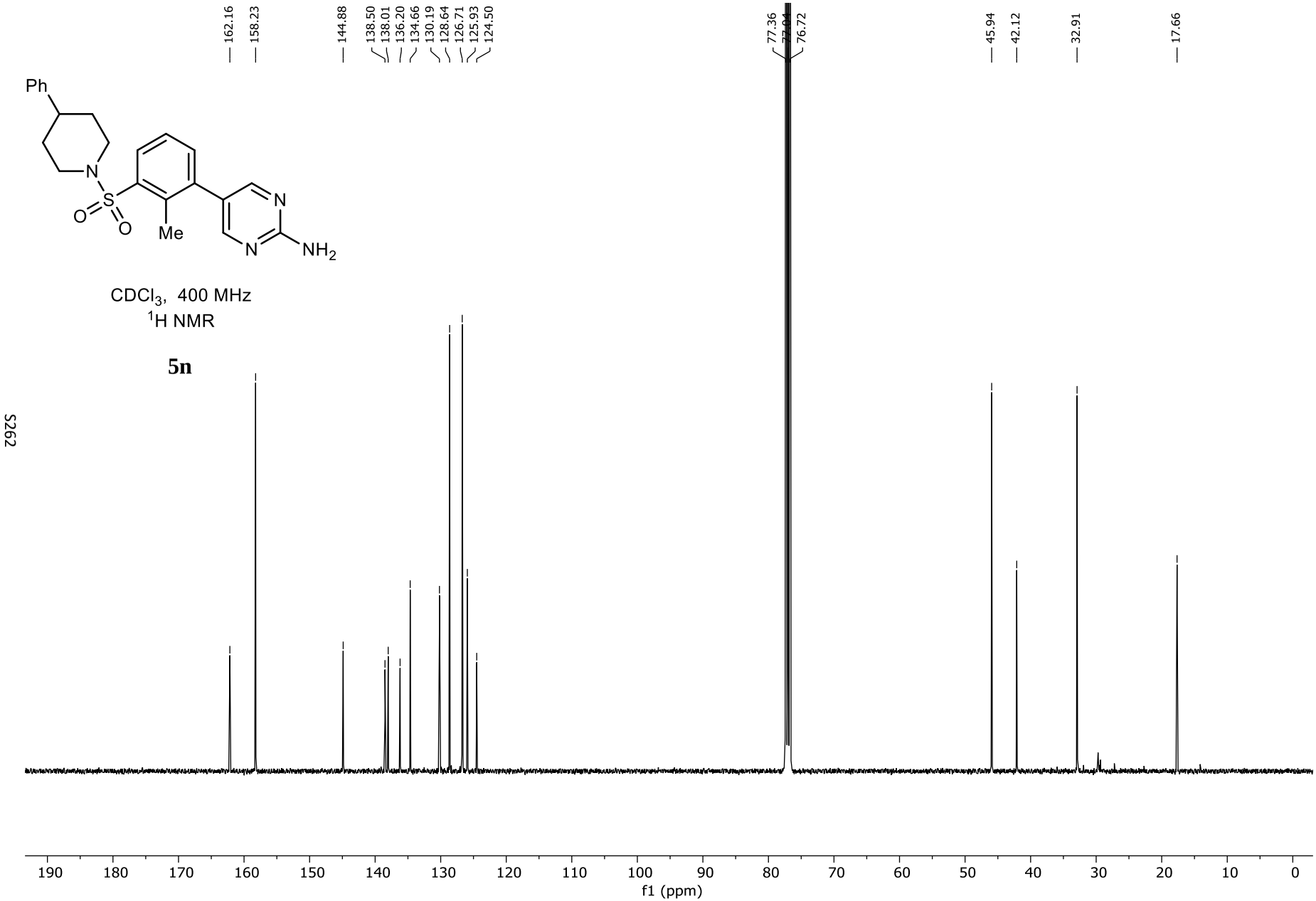

171.08
169.86
155.64
141.16
139.15
128.45
127.65
127.50
121.47
117.46
78.61
77.16 CDCl3
70.03
57.88
57.01
50.39
45.21
39.26
38.16
37.38
37.10
32.26
32.06
28.53
24.79
24.40
20.90
19.52
18.27
13.02
10.63
10.59
Ph
O
Me
Me
H
H
H
N
N
CDCl3, 100 MHz
13C NMR
5l
S257
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

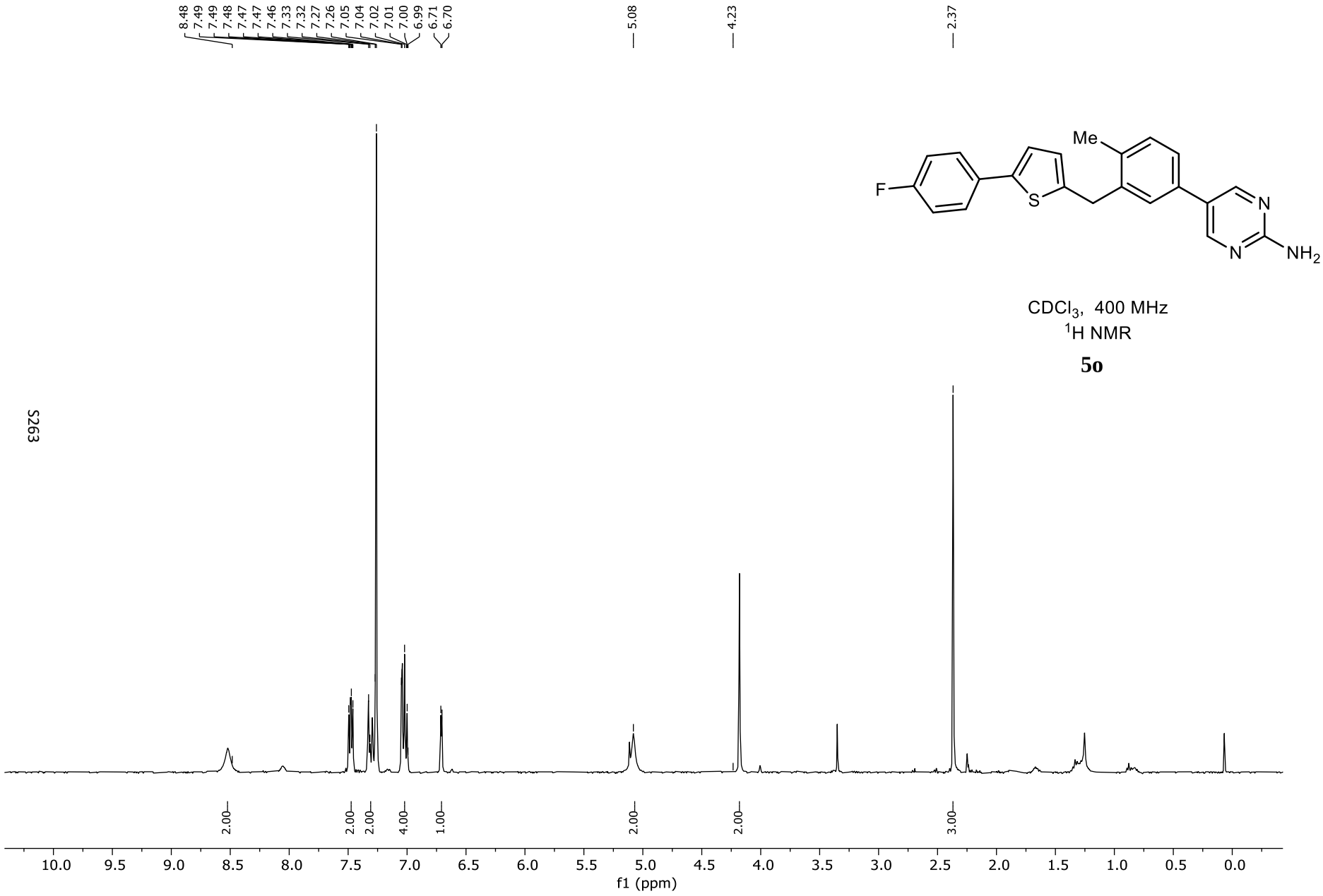

9.40
9.06
9.05
9.04
9.02
8.72
8.72
8.70
8.70
8.04
8.02
8.00
7.99
7.89
7.87
7.26 CDCl3
N
N
CF3
F3C
N
CDCl3, 400 MHz
1H NMR
5m
S258
1.00
1.00
1.00
1.01
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

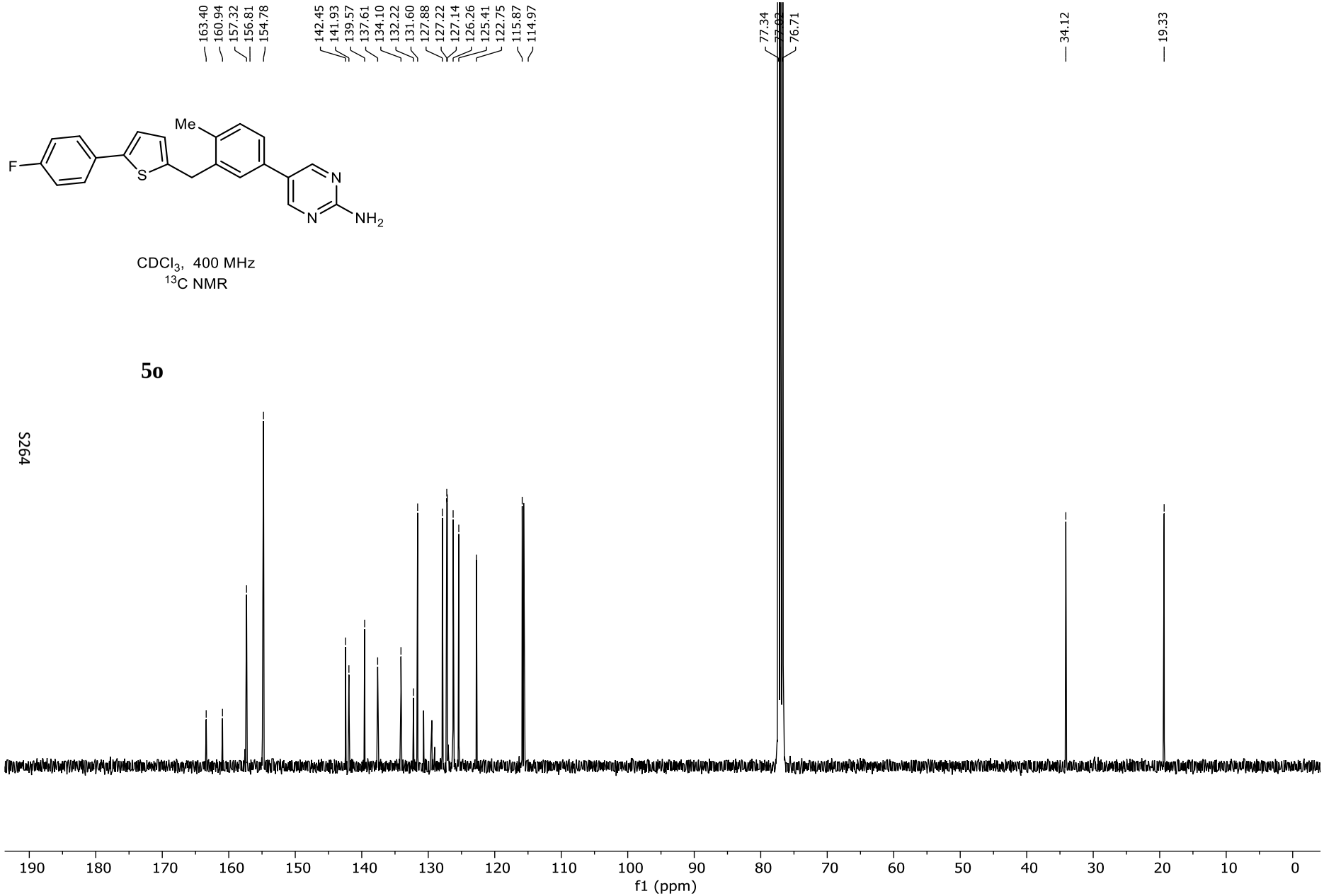

161.70
159.53
158.24
157.87
157.50
157.13
151.29
150.94
150.58
150.23
148.79
136.82
133.67
121.05
121.03
121.00
120.97
120.90
119.96
119.01
118.16
77.16 CDCl3
S259
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
N
N
CF3
F3C
N
CDCl3, 100 MHz
13C NMR
5m

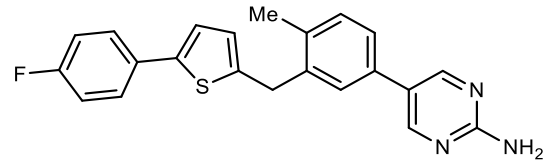

-68.17
-70.61
S260
N
N
CF3
F3C
N
CDCl3, 375 MHz
19F NMR
5m
3.02
3.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)


8.21
7.97
7.96
7.95
7.33
7.32
7.26
7.24
7.22
7.16
7.15
7.12
7.11
5.19
5.14
3.86
3.85
3.85
3.83
3.82
3.81
2.84
2.83
2.81
2.80
2.78
2.77
2.59
2.58
2.57
2.56
2.55
2.54
2.53
2.52
1.88
1.87
1.84
1.83
1.77
1.75
1.73
1.72
1.70
1.69
1.67
1.66
Ph
N
S
O
O
Me
N
N
NH2
CDCl3, 400 MHz
1H NMR
5n
S261
2.00
1.00
2.00
2.00
3.00
2.00
2.00
2.00
1.00
3.00
2.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


162.16
158.23
144.88
138.50
138.01
136.20
134.66
130.19
128.64
126.71
125.93
124.50
77.36
77.04
76.72
45.94
42.12
32.91
17.66
Ph
N
S
O
O
Me
N
N
NH2
CDCl3, 400 MHz
1H NMR
5n
S262
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

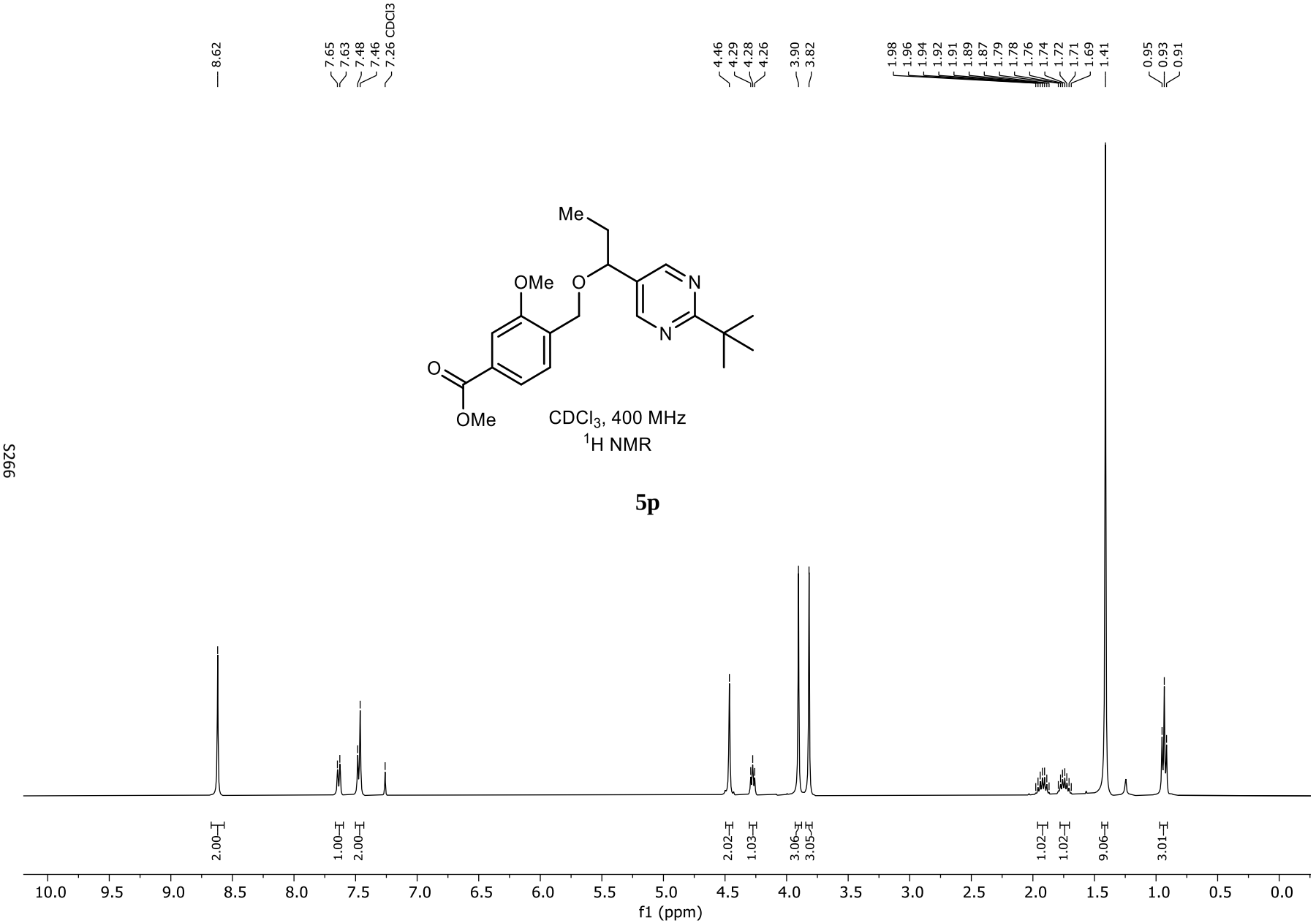

8.48
7.49
7.49
7.48
7.47
7.47
7.46
7.33
7.32
7.27
7.26
7.05
7.04
7.02
7.01
7.00
6.99
6.71
6.70
5.08
4.23
2.37
Me
F
S
N
N
NH2
CDCl3, 400 MHz
1H NMR
5o
S263
2.00
2.00
2.00
4.00
1.00
2.00
2.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


163.40
160.94
157.32
156.81
154.78
142.45
141.93
139.57
137.61
134.10
132.22
131.60
127.88
127.22
127.14
126.26
125.41
122.75
115.87
114.97
77.34
77.03
76.71
34.12
19.33
Me
F
S
N
N
NH2
CDCl3, 400 MHz
13C NMR
5o
S264
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

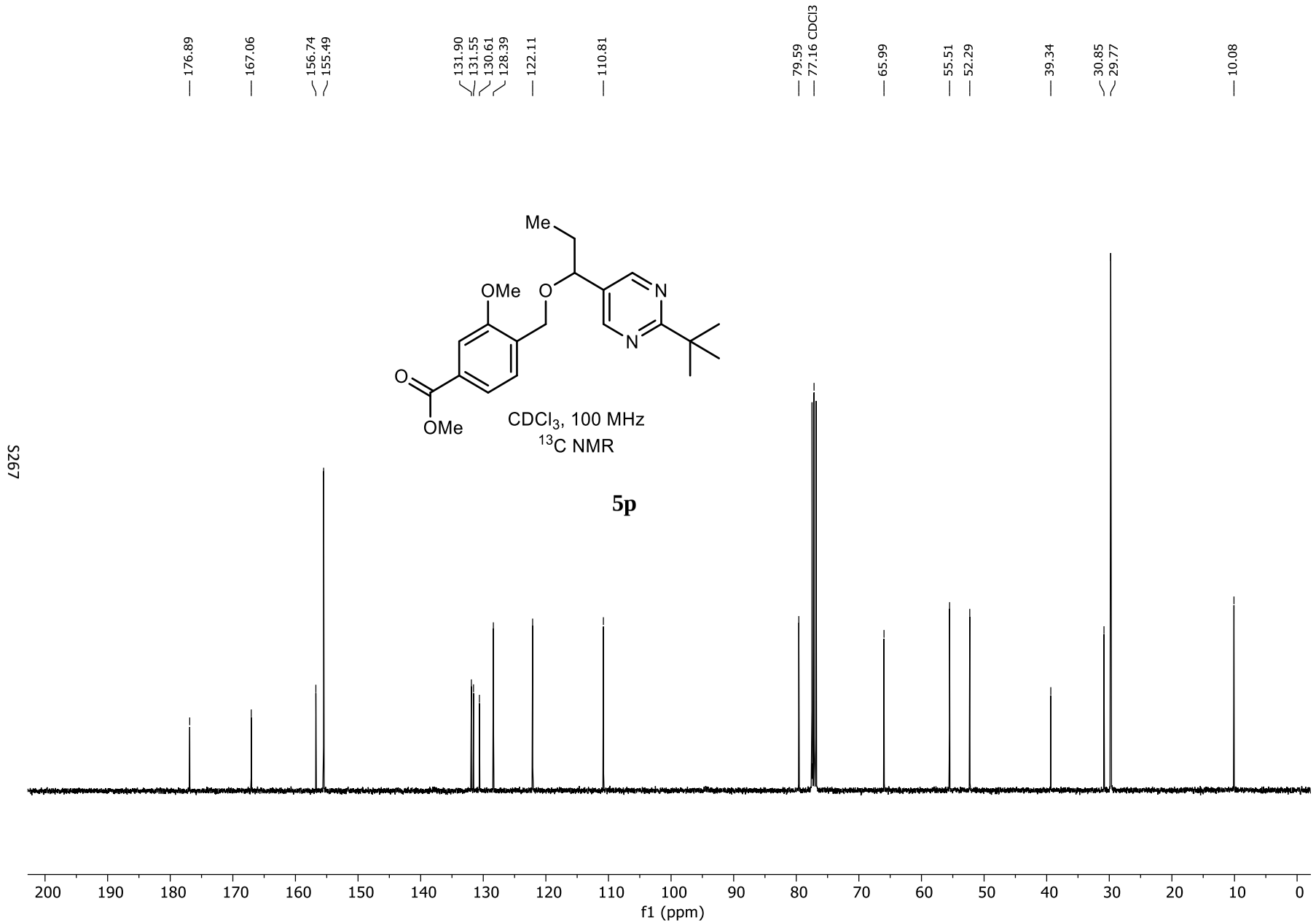


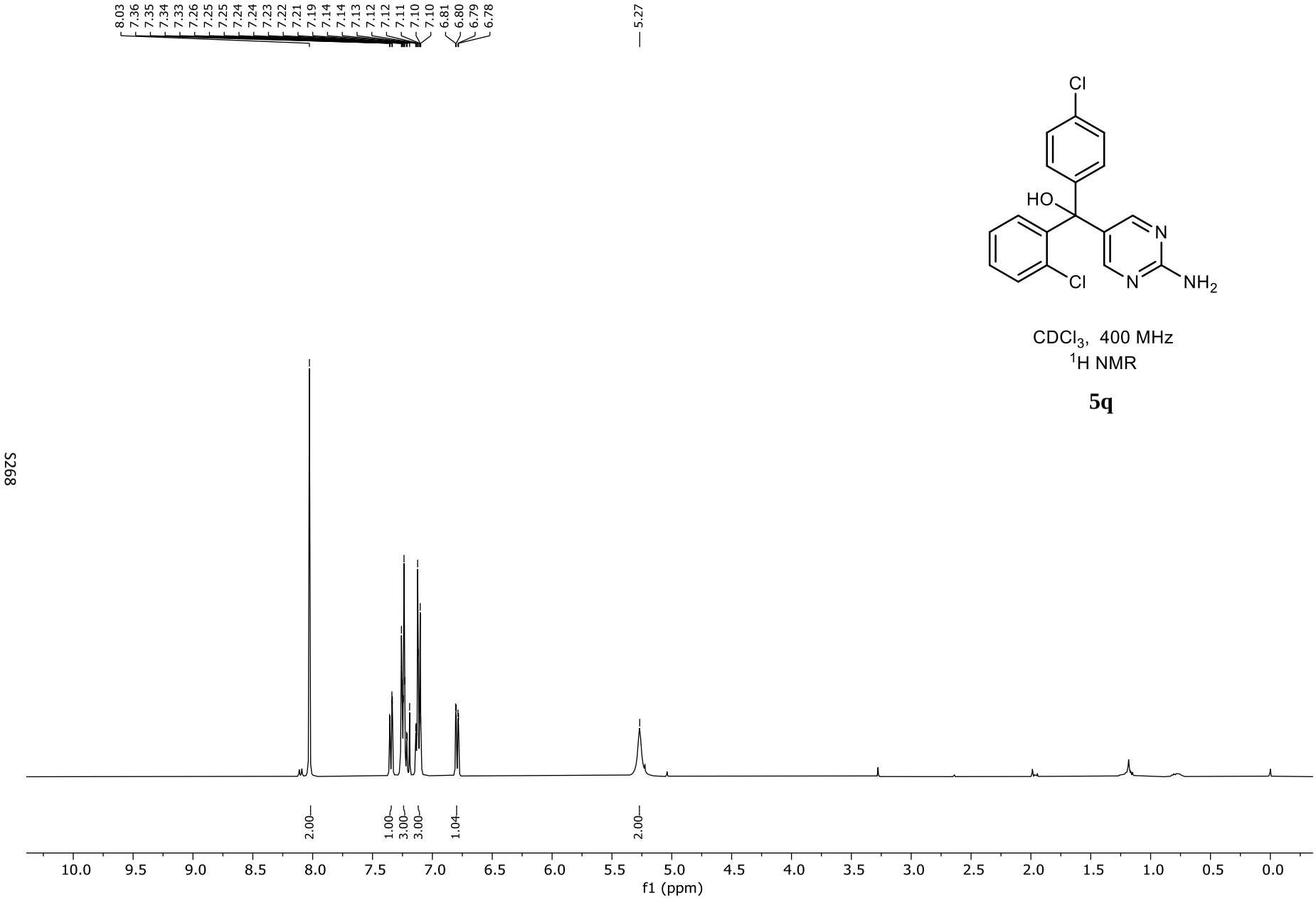
$CDCl_3$, 400 MHz
^{19}F NMR

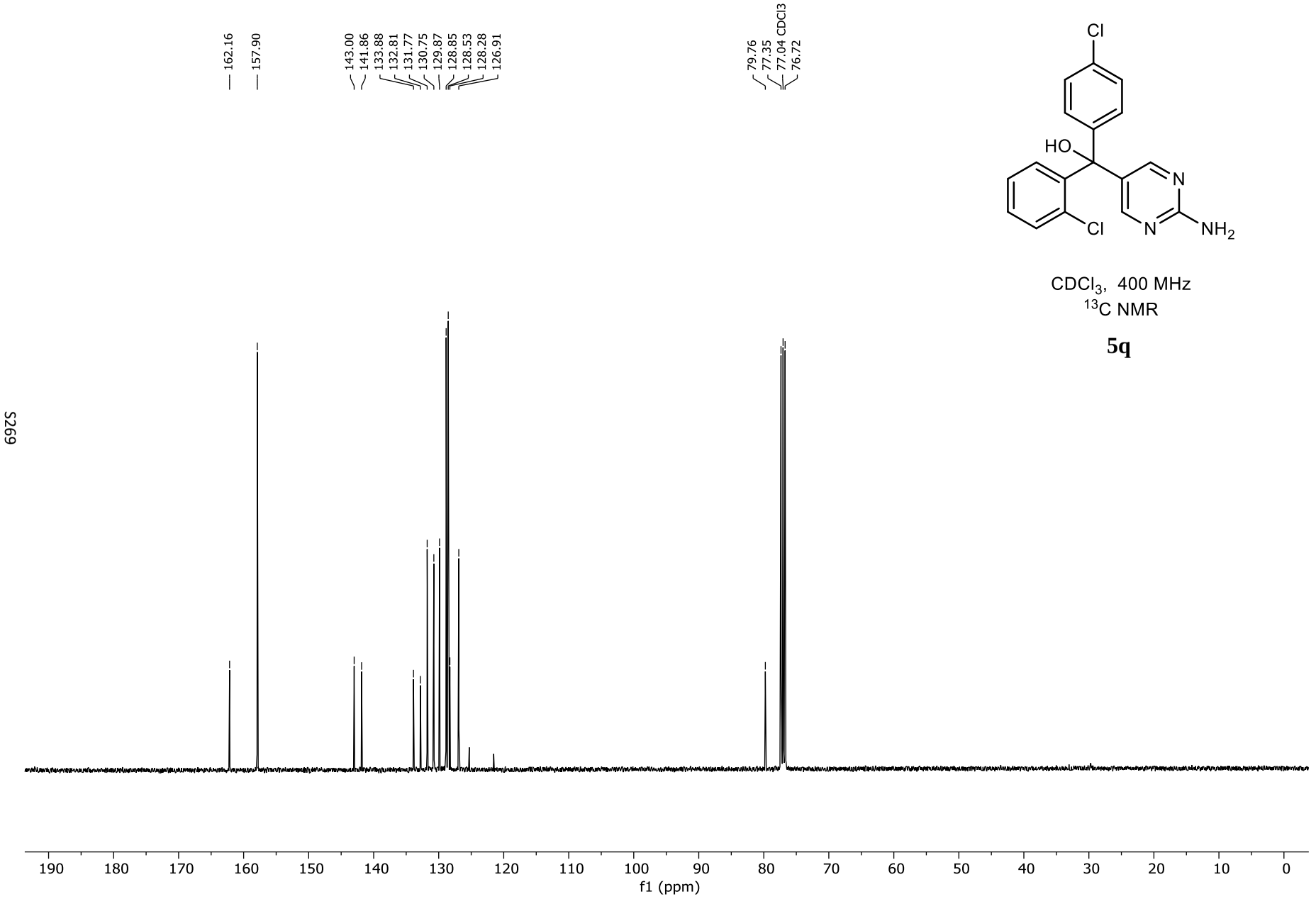
5o


8.62
7.65
7.63
7.48
7.46
7.26 CDCl3
4.46
4.29
4.28
4.26
3.90
3.82
1.98
1.96
1.94
1.92
1.91
1.89
1.87
1.79
1.78
1.76
1.74
1.72
1.71
1.69
1.41
0.95
0.93
0.91
Me
OMe
O
N
N
O
OMe
CDCl3, 400 MHz
1H NMR
2.00
1.00
2.00
2.02
1.03
3.06
3.05
1.02
1.02
9.06
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

5p


176.89
167.06
156.74
155.49
131.90
131.55
130.61
128.39
122.11
110.81
79.59
77.16 CDCl3
65.99
55.51
52.29
39.34
30.85
29.77
10.08
Me
OMe
O
N
N
O
OMe
CDCl3, 100 MHz
13C NMR
5p
S267
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


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
5.27
Cl
HO
N
N
NH2
Cl
CDCl3, 400 MHz
1H NMR
5q
S268
2.00
1.00
3.00
3.00
1.04
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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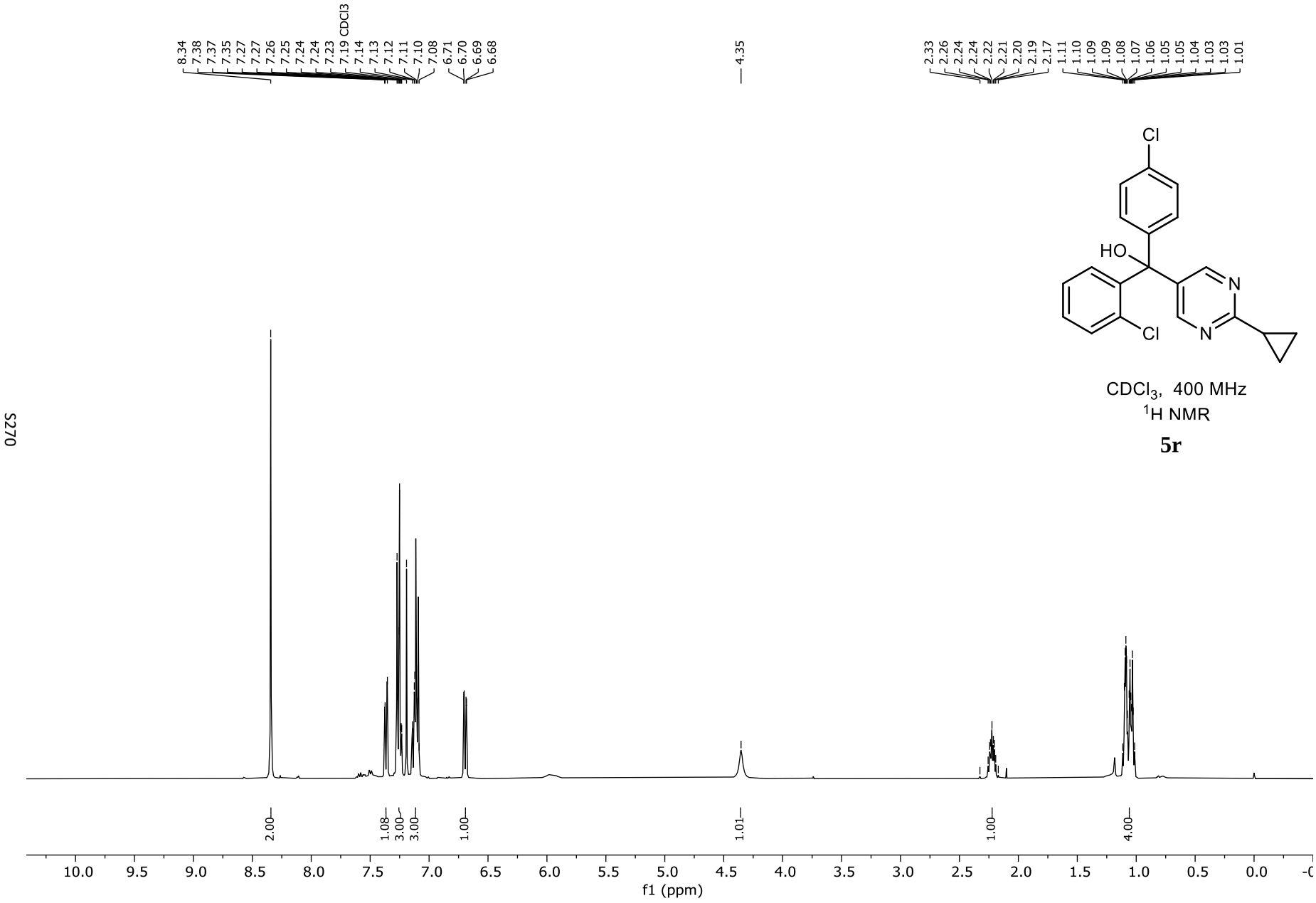
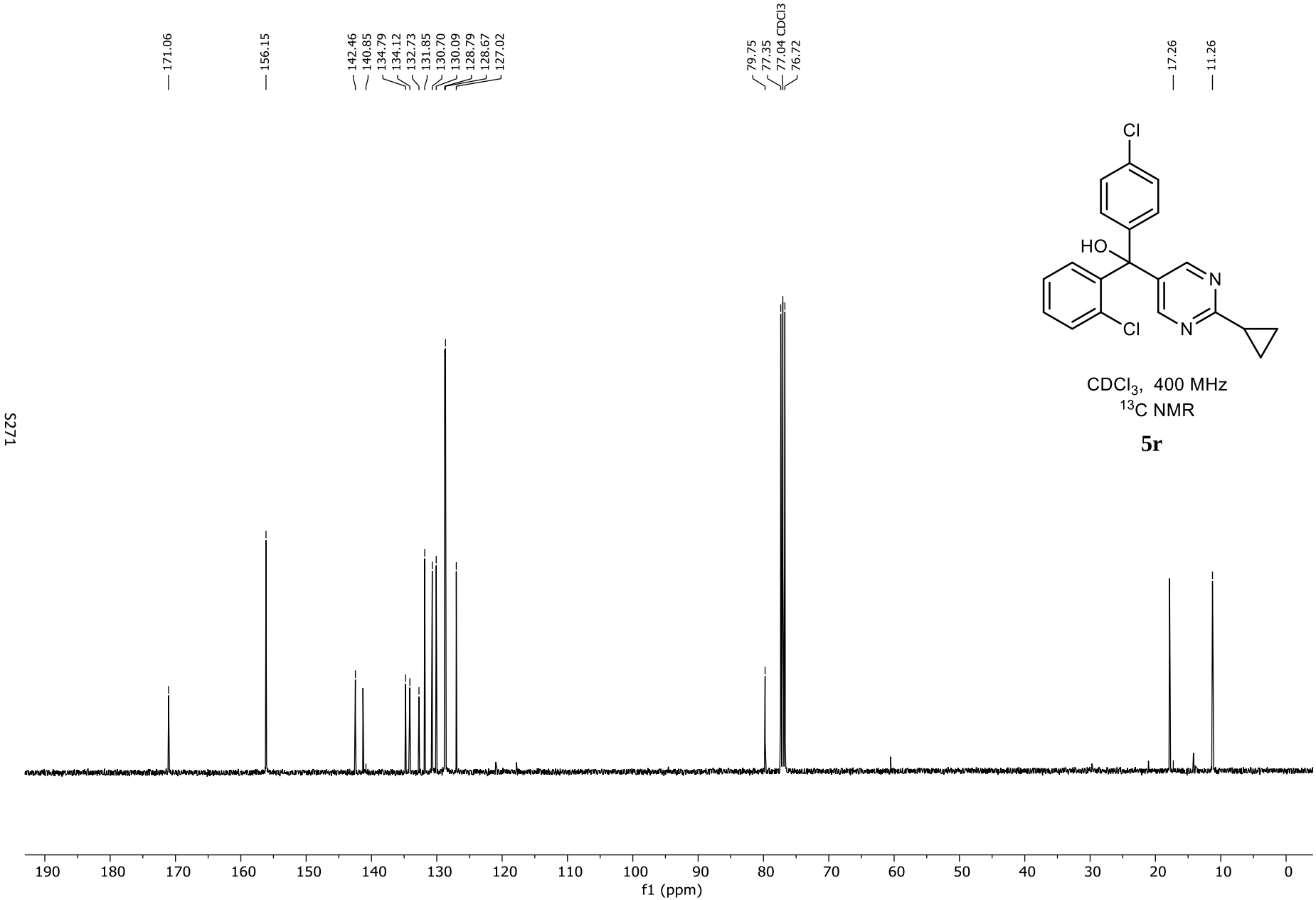
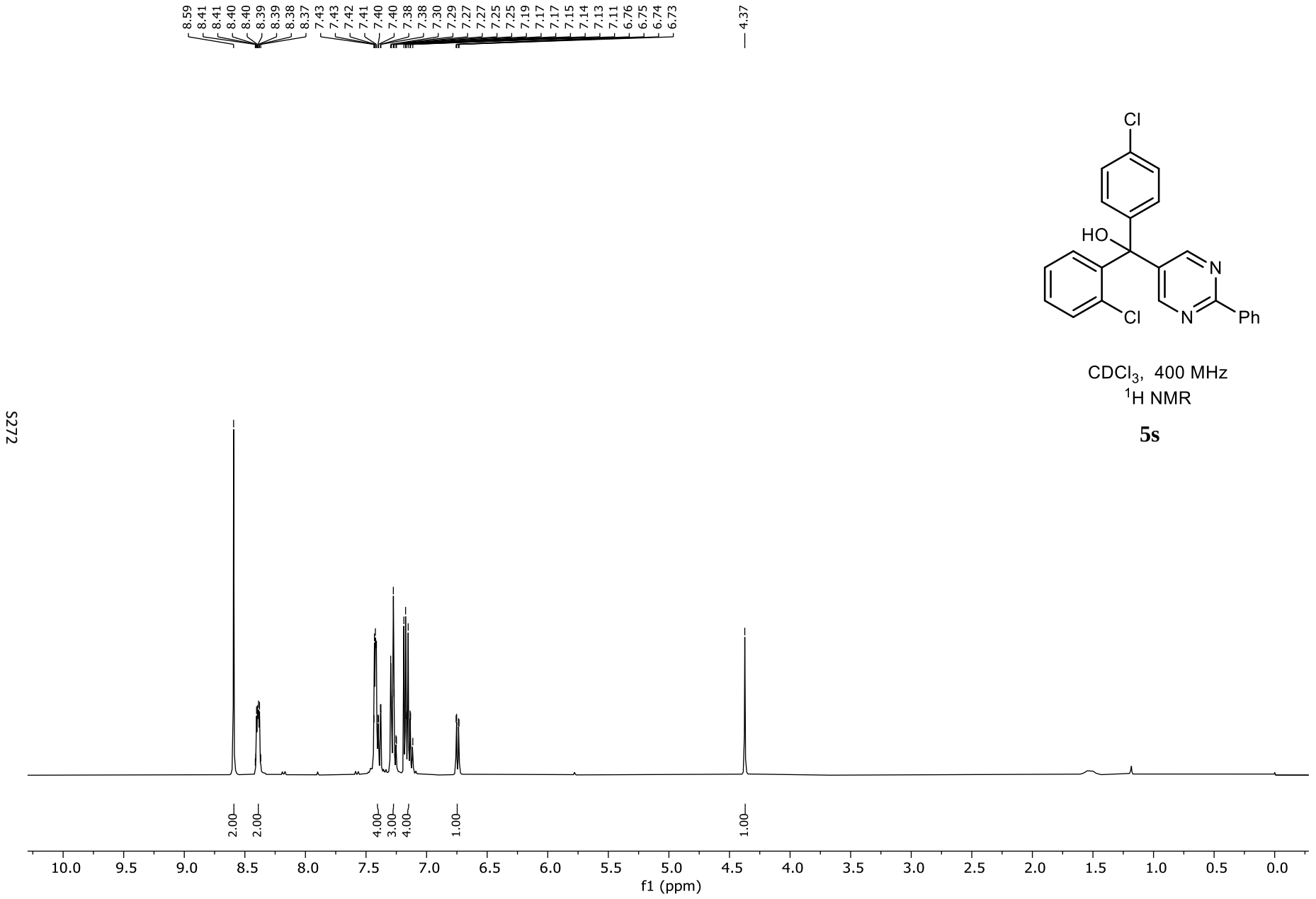
133.88
132.81
131.77
130.75
129.87
128.85
128.53
128.28
126.91
79.76
77.35
77.04 CDCl3
76.72
Cl
HO
N
N
NH2
Cl
CDCl3, 400 MHz
13C NMR
5q
S269
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.34
7.38
7.37
7.35
7.27
7.27
7.26
7.25
7.24
7.24
7.23
7.19 CDCl3
7.14
7.13
7.12
7.11
7.10
7.08
6.71
6.70
6.69
6.68
4.35
2.33
2.26
2.24
2.24
2.22
2.21
2.20
2.19
2.17
1.11
1.10
1.09
1.09
1.08
1.07
1.06
1.05
1.05
1.04
1.03
1.03
1.01
Cl
HO
N
N
Cl
CDCl3, 400 MHz
1H NMR
5r
S270
2.00
1.08
3.00
3.00
1.00
1.01
1.00
4.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


171.06
156.15
142.46
140.85
134.79
134.12
132.73
131.85
130.70
130.09
128.79
128.67
127.02
79.75
77.35
77.04 CDCl3
76.72
17.26
11.26
Cl
HO
N
N
Cl
CDCl3, 400 MHz
13C NMR
5r
S271
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.59
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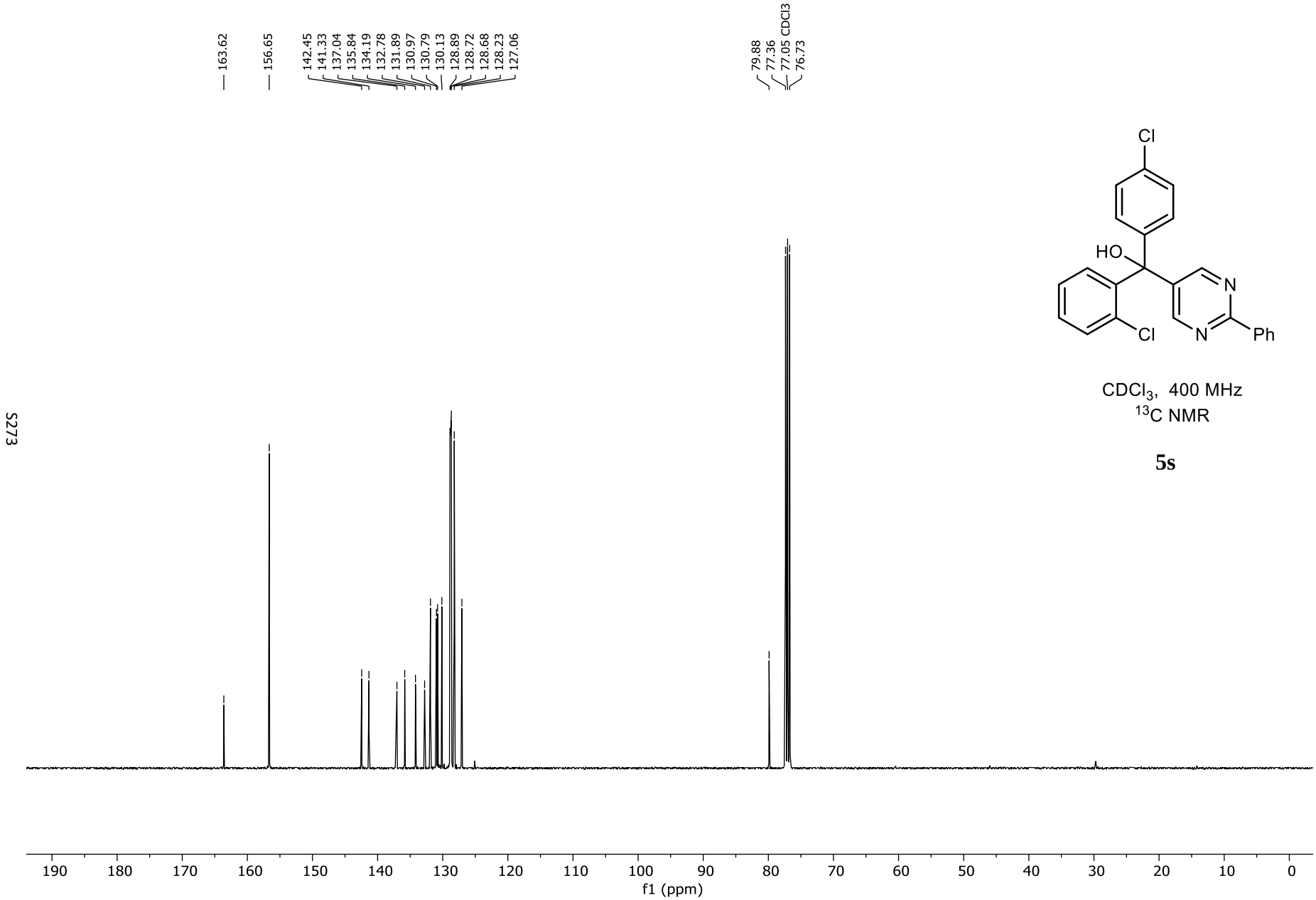
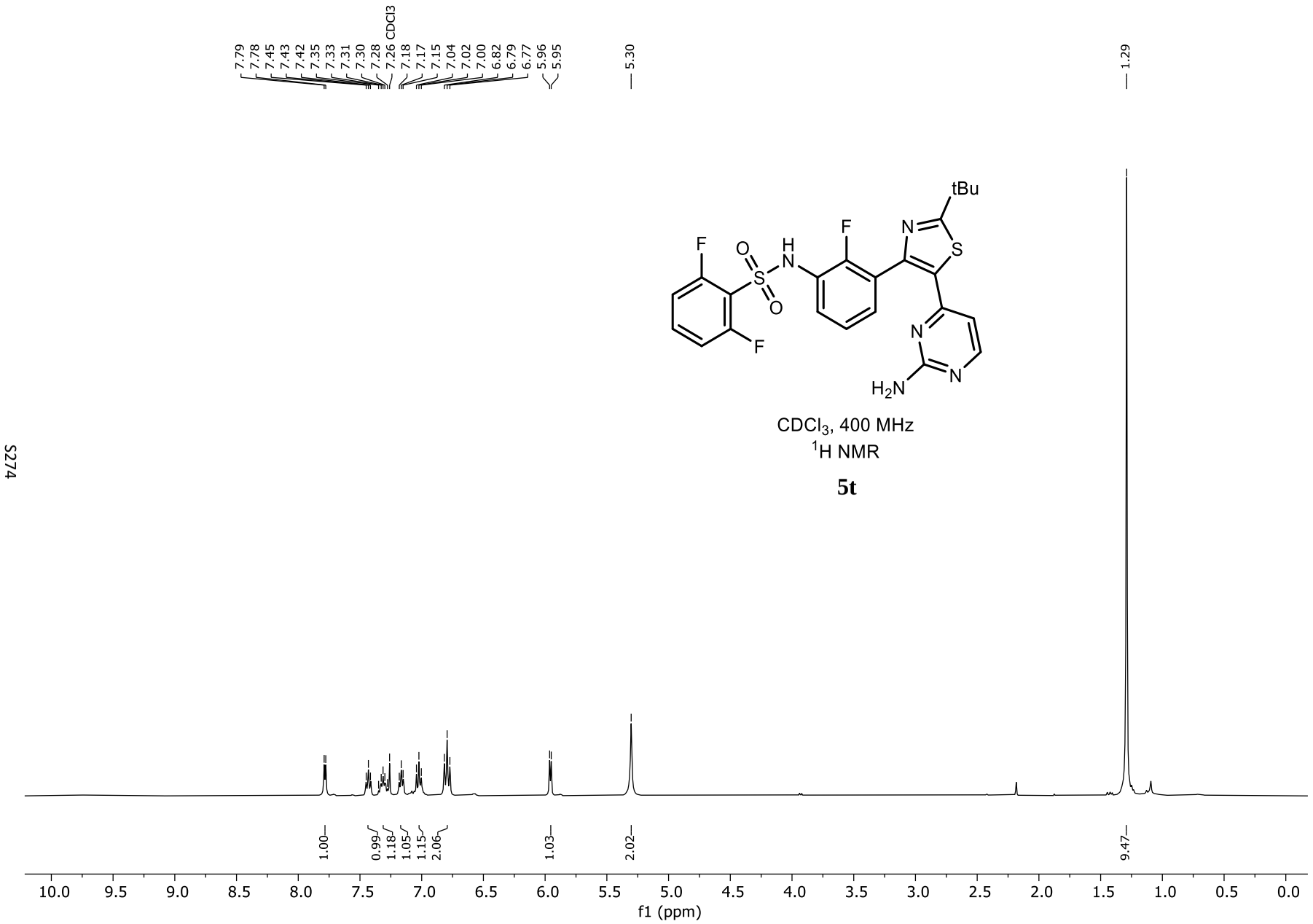
8.41
8.40
8.40
8.39
8.39
8.38
8.37
7.43
7.43
7.42
7.41
7.40
7.40
7.38
7.38
7.30
7.29
7.27
7.27
7.25
7.25
7.19
7.17
7.17
7.15
7.14
7.13
7.11
6.76
6.75
6.74
6.73
4.37
Cl
HO
N
Cl
N
Ph
CDCl3, 400 MHz
1H NMR
5s
S272
2.00
2.00
4.00
3.00
4.00
1.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

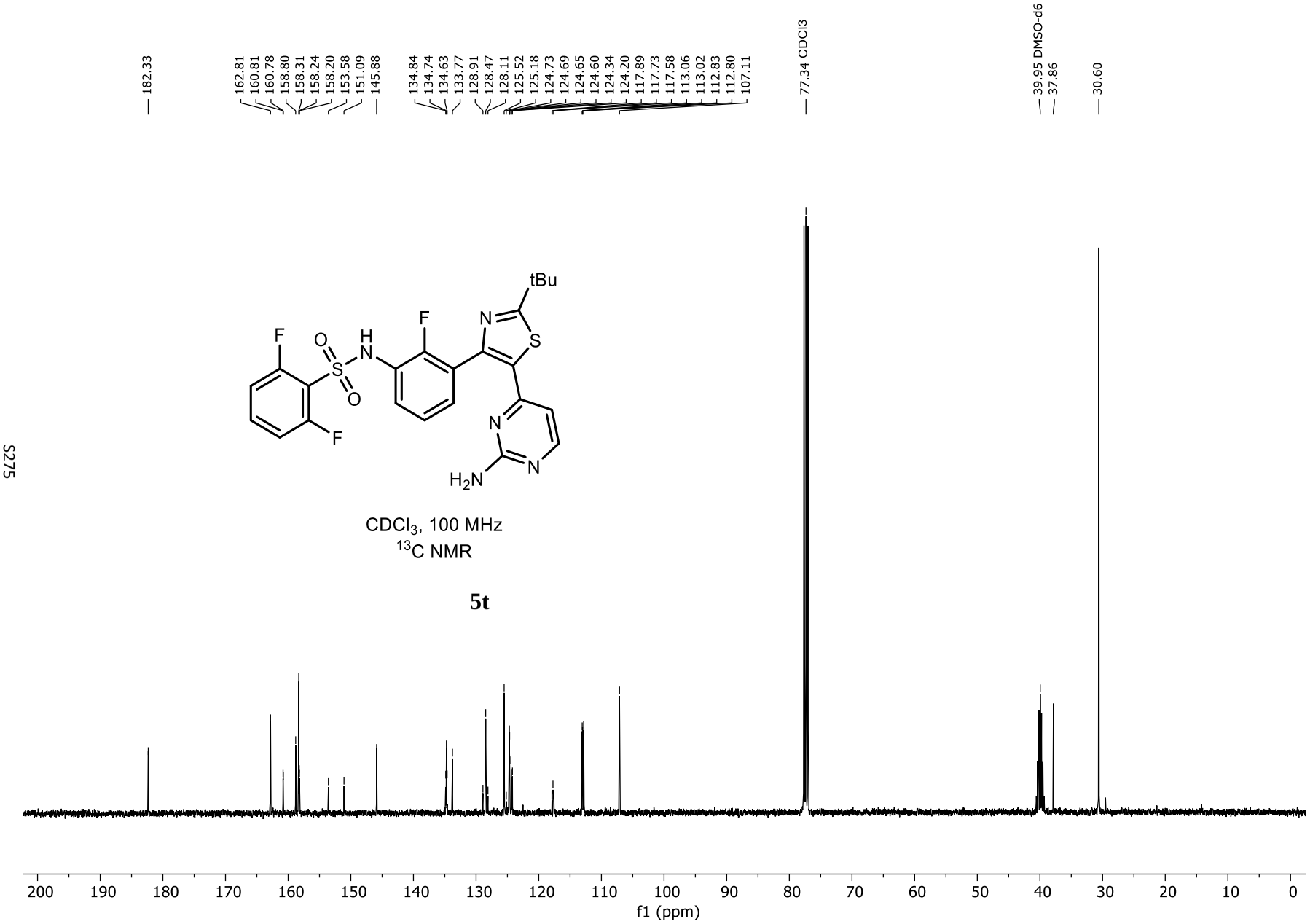

163.62
156.65
142.45
141.33
137.04
135.84
134.19
132.78
131.89
130.97
130.79
130.13
128.89
128.72
128.68
128.23
127.06
79.88
77.36
77.05 CDCl3
76.73
Cl
HO
N
Cl
N
Ph
CDCl3, 400 MHz
13C NMR
5s
S273
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

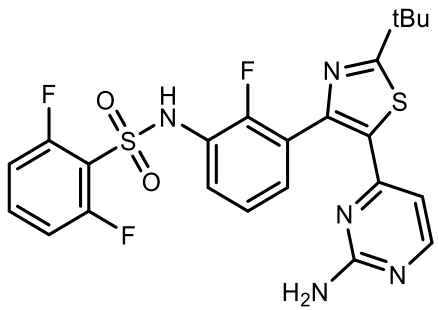


$CDCl_3$, 400 MHz

^1H NMR

5t

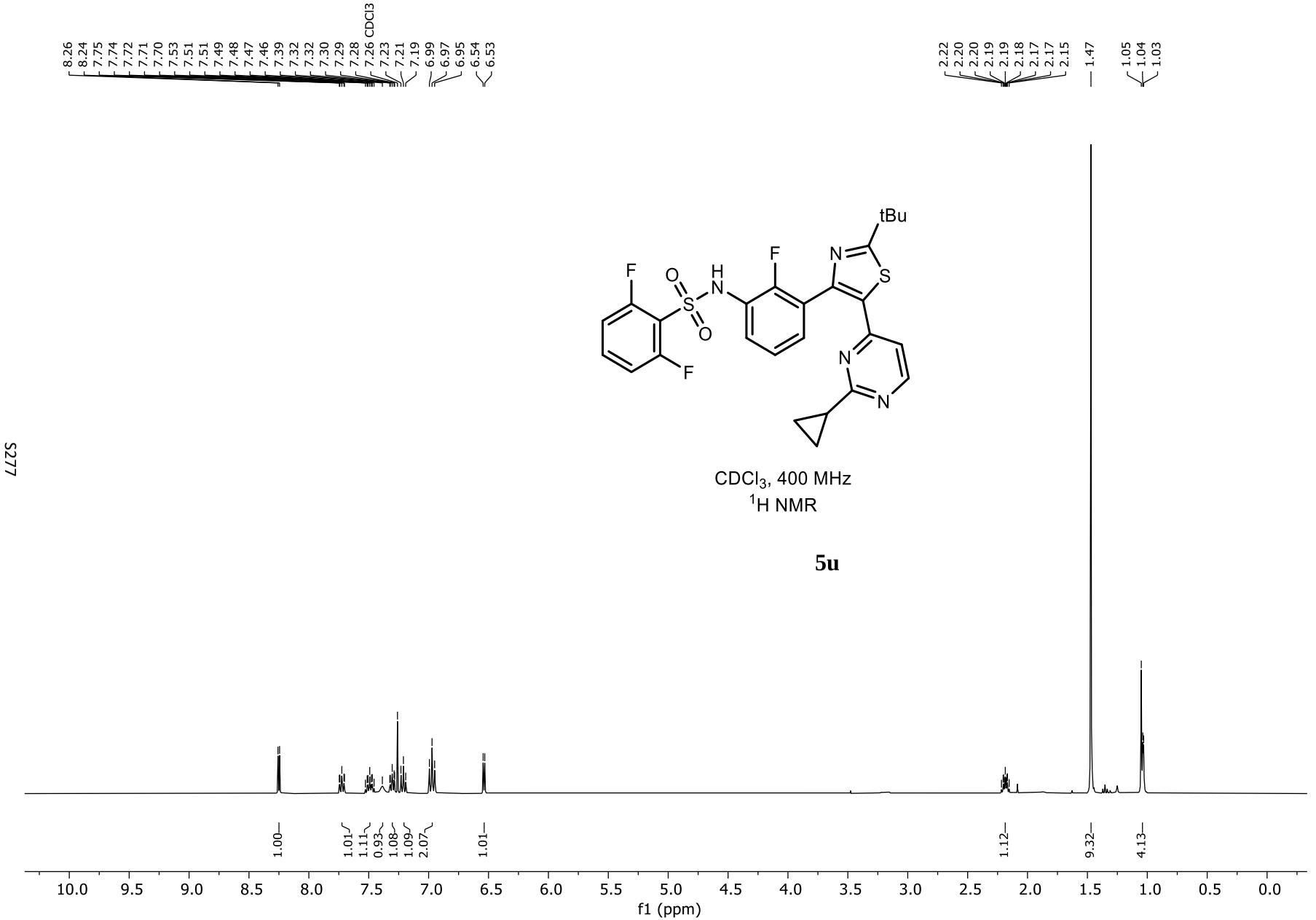

182.33
162.81
160.81
160.78
158.80
158.31
158.24
158.20
153.58
151.09
145.88
134.84
134.74
134.63
133.77
128.91
128.47
128.11
125.52
125.18
124.73
124.69
124.65
124.60
124.34
124.20
117.89
117.73
117.58
113.06
113.02
112.83
112.80
107.11
77.34 CDCl3
39.95 DMSO-d6
37.86
30.60
tBu
F
O
H
N
S
F
N
S
O
F
N
N
H2N
CDCl3, 100 MHz
13C NMR
5t
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

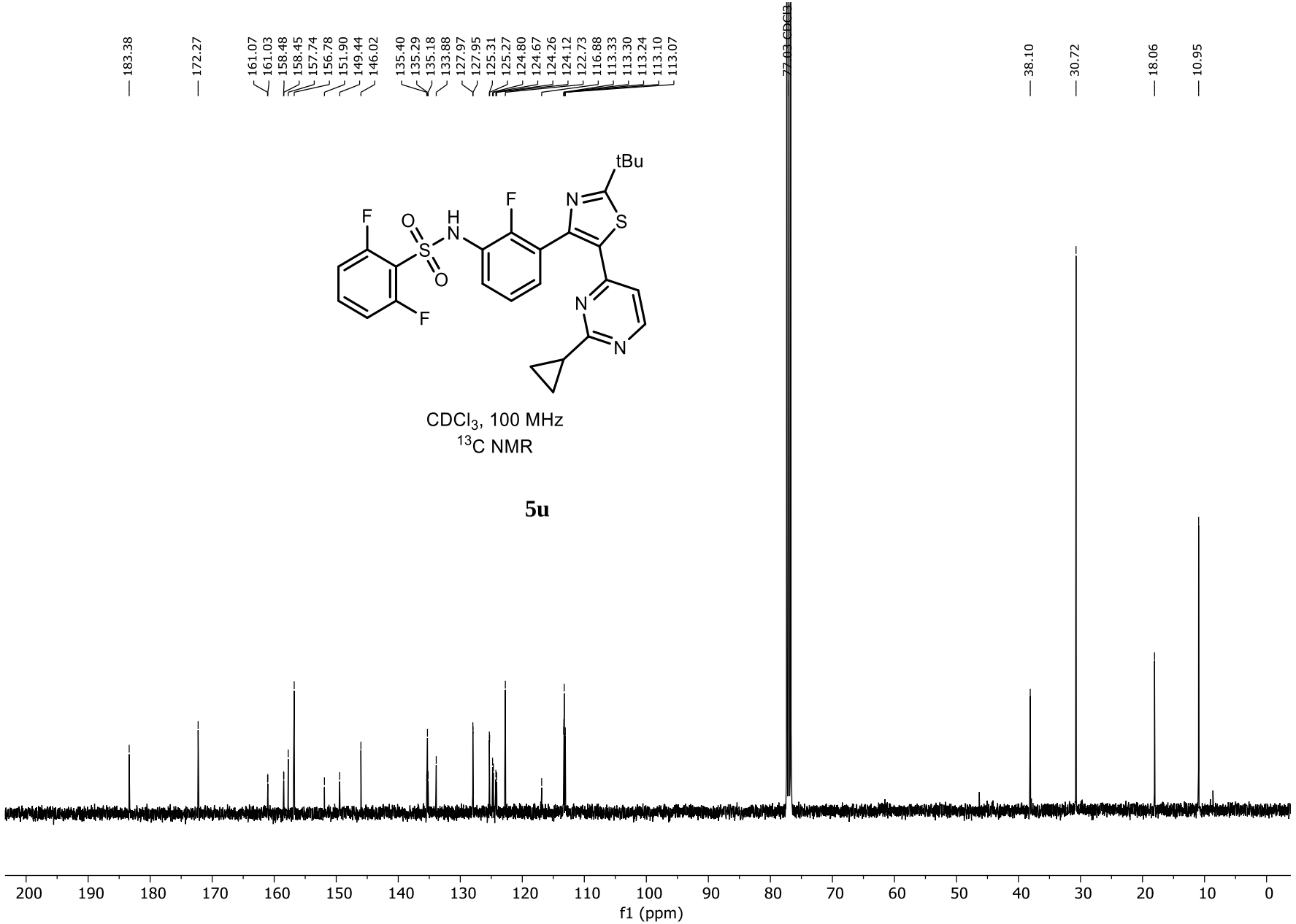


$CDCl_3$, 375 MHz

^{19}F NMR

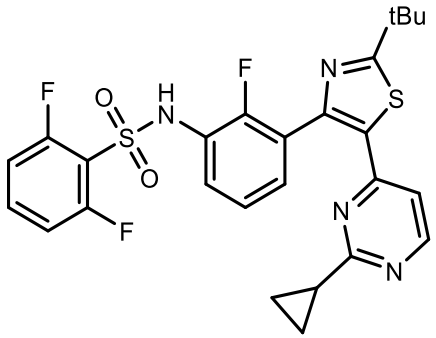
5t


8.26
8.24
7.75
7.74
7.72
7.71
7.70
7.53
7.51
7.51
7.49
7.48
7.47
7.46
7.39
7.32
7.32
7.30
7.29
7.28
7.26 CDCl3
7.23
7.21
7.19
6.99
6.97
6.95
6.54
6.53
2.22
2.20
2.20
2.19
2.19
2.18
2.17
2.17
2.15
1.47
1.05
1.04
1.03
tBu
F
O
H
N
F
N
S
S
O
F
N
N
CDCl3, 400 MHz
1H NMR
5u
1.00
1.01
1.11
0.93
1.08
1.09
2.07
1.01
1.12
9.32
4.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



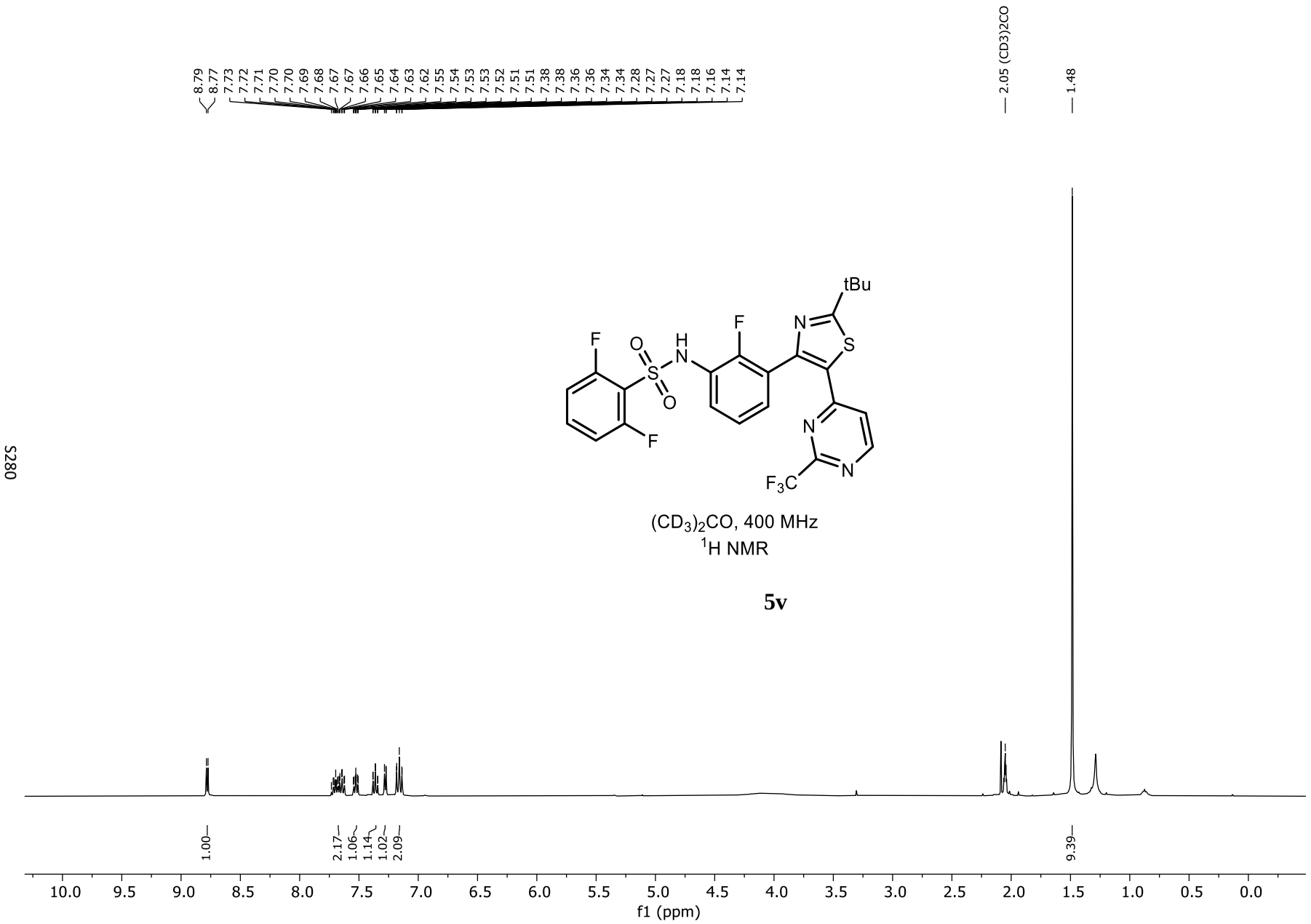
$CDCl_3$, 100 MHz
^{13}C NMR

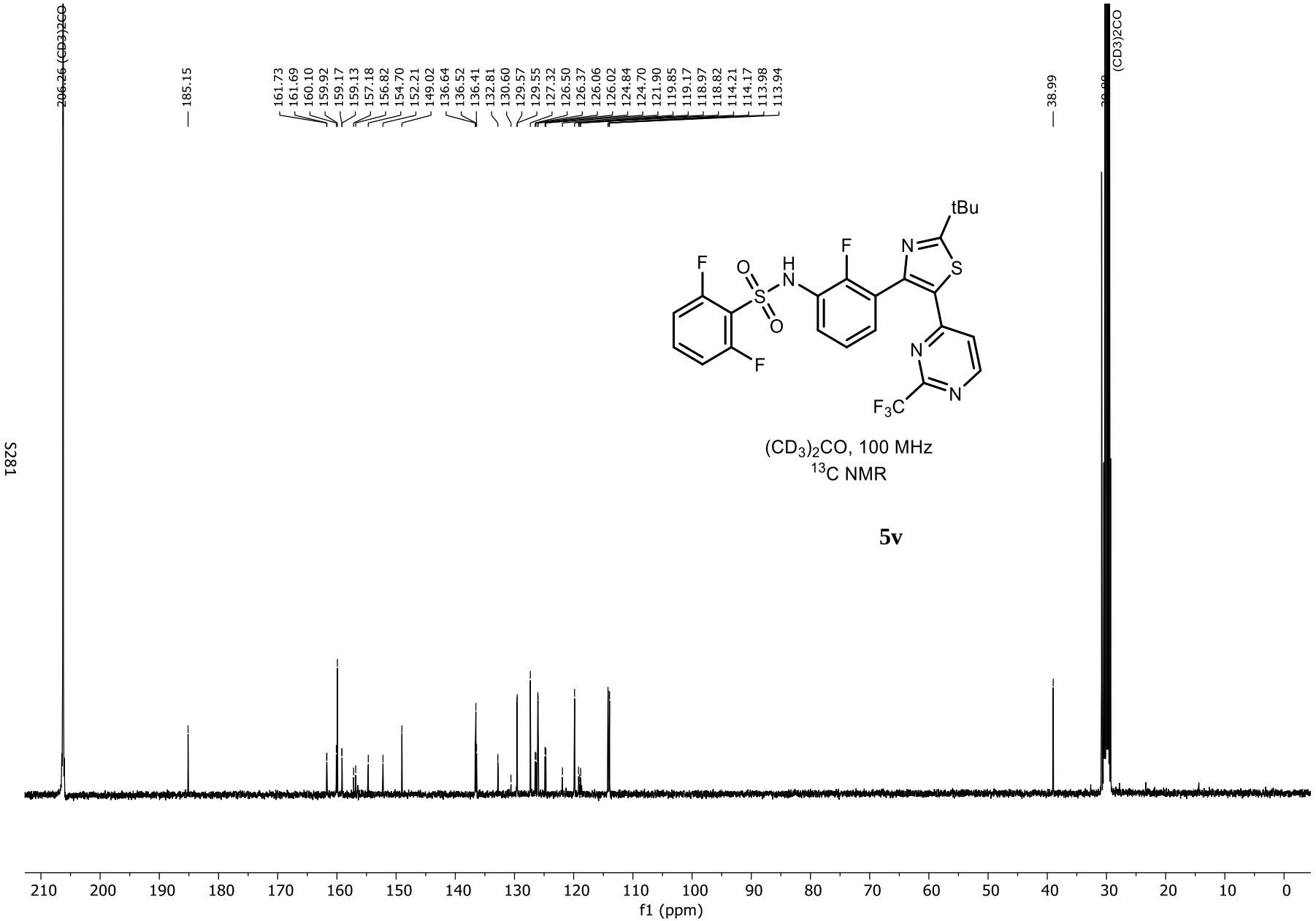
5u

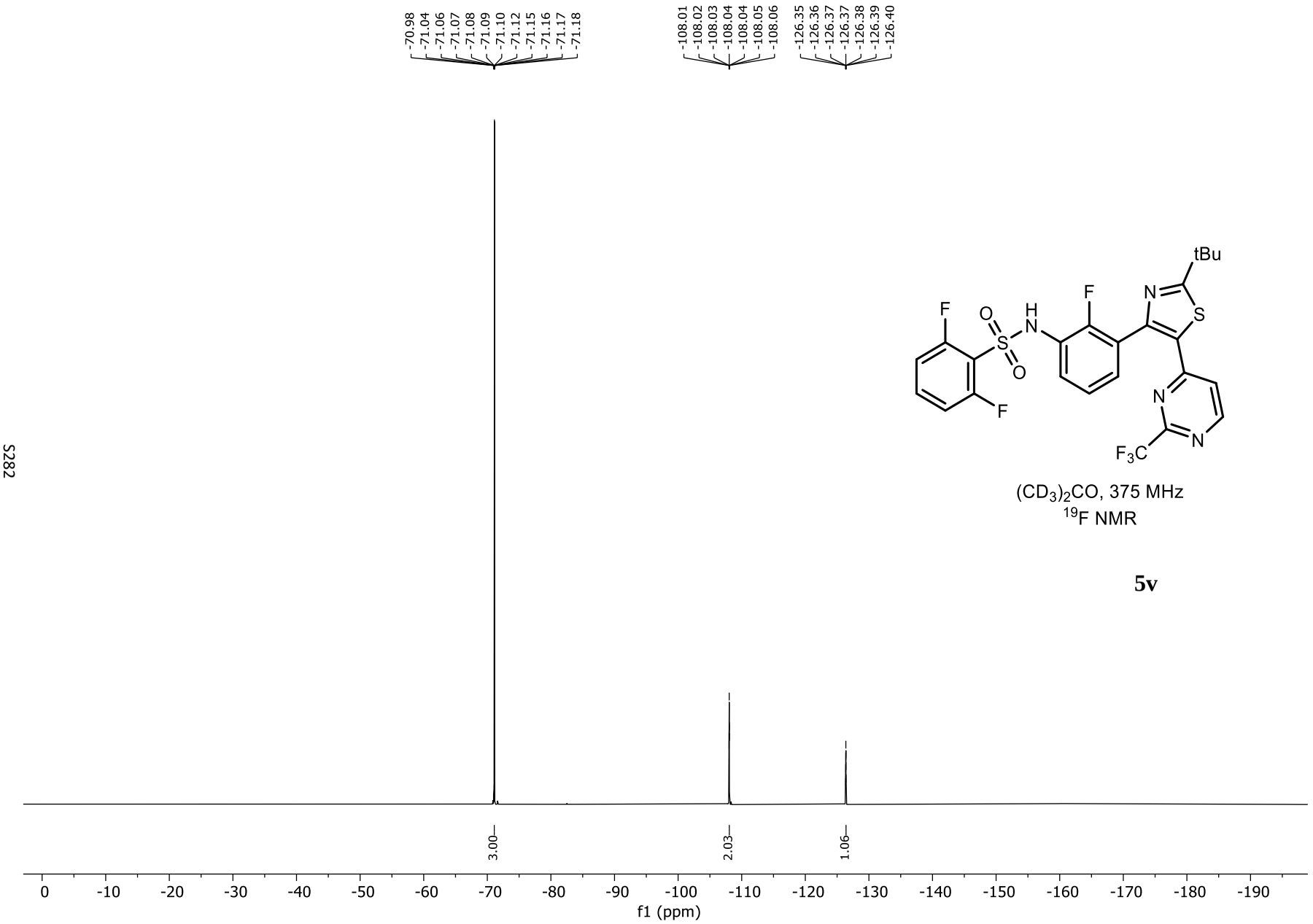


$CDCl_3$, 375 MHz
^{19}F NMR

5u

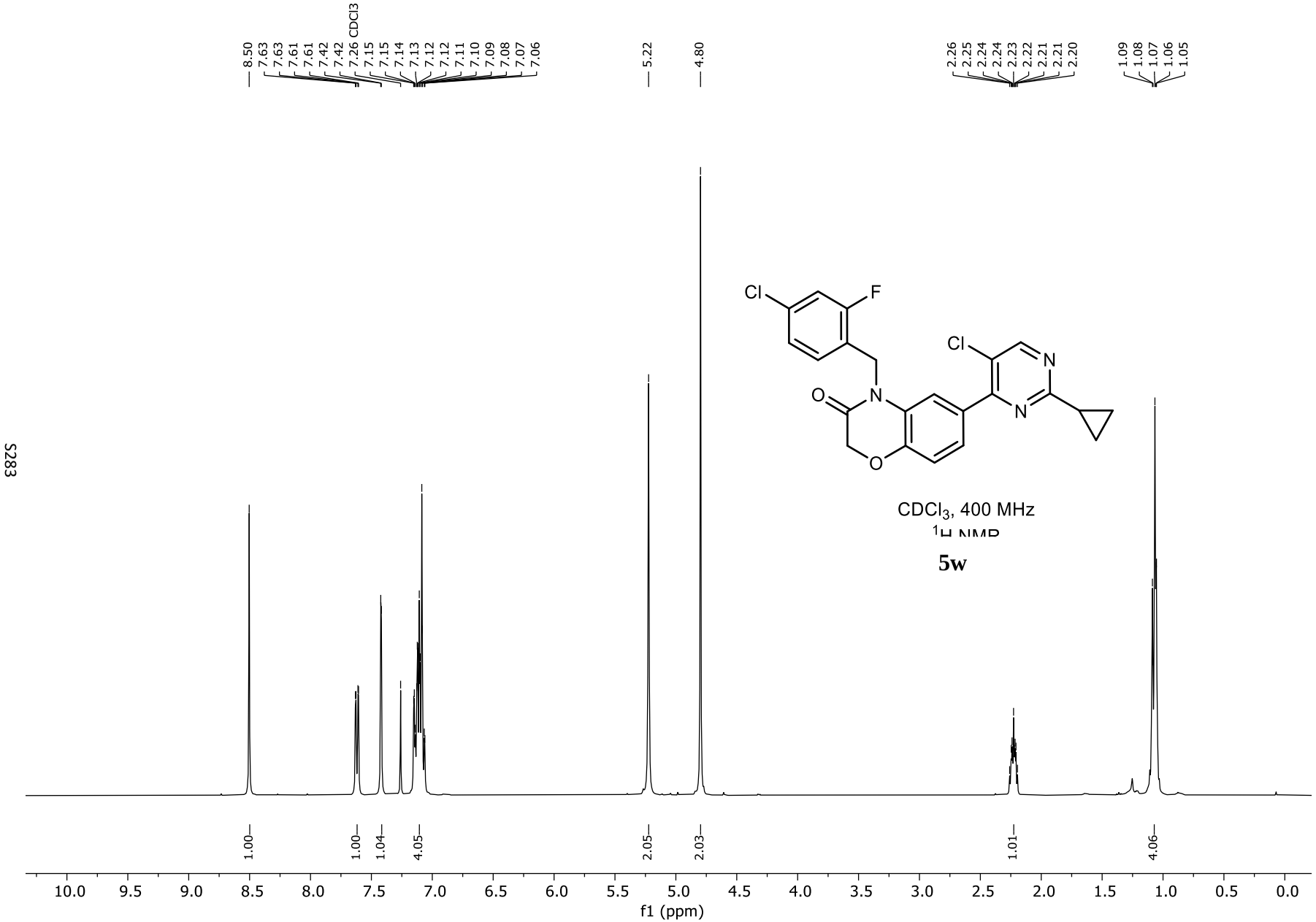

8.79
8.77
7.73
7.72
7.71
7.70
7.70
7.69
7.68
7.67
7.67
7.66
7.65
7.64
7.63
7.62
7.55
7.54
7.53
7.53
7.52
7.51
7.51
7.38
7.38
7.36
7.36
7.34
7.34
7.28
7.27
7.27
7.18
7.18
7.16
7.14
7.14
2.05 (CD3)2CO
1.48
tBu
F
O
H
N
F
N
S
S
O
O
N
F
N
F3C
(CD3)2CO, 400 MHz
1H NMR
5v
S280
1.00
2.17
1.06
1.14
1.02
2.09
9.39
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

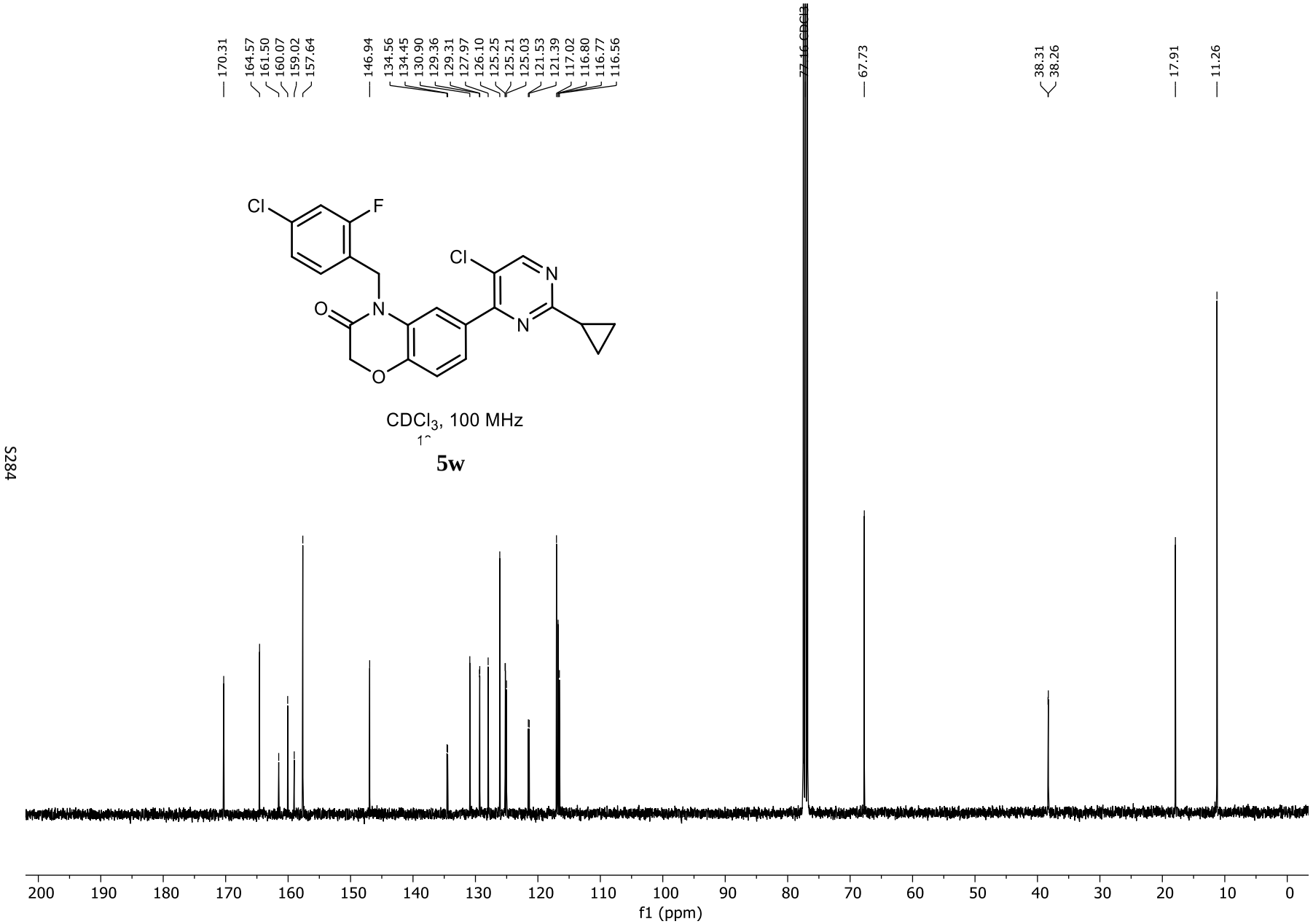

206.26 (CD3)2CO
185.15
161.73
161.69
160.10
159.92
159.17
159.13
157.18
156.82
154.70
152.21
149.02
136.64
136.52
136.41
132.81
130.60
129.57
129.55
127.32
126.50
126.37
126.06
126.02
124.84
124.70
121.90
119.85
119.17
118.97
118.82
114.21
114.17
113.98
113.94
38.99
(CD3)2CO
tBu
F
N
S
H
O
F
F
N
N
F3C
(CD3)2CO, 100 MHz
13C NMR
5v
S281
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

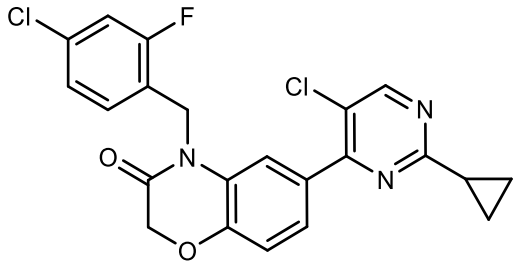


$(CD_3)_2CO$, 375 MHz
^{19}F NMR

5v


8.50
7.63
7.63
7.61
7.61
7.42
7.42
7.26 CDCl3
7.15
7.15
7.14
7.13
7.12
7.12
7.11
7.10
7.09
7.08
7.07
7.06
5.22
4.80
2.26
2.25
2.24
2.24
2.23
2.22
2.21
2.21
2.20
1.09
1.08
1.07
1.06
1.05
Cl
F
Cl
N
N
O
N
O
CDCl3, 400 MHz
1H NMR
5w
1.00
1.00
1.04
4.05
2.05
2.03
1.01
4.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

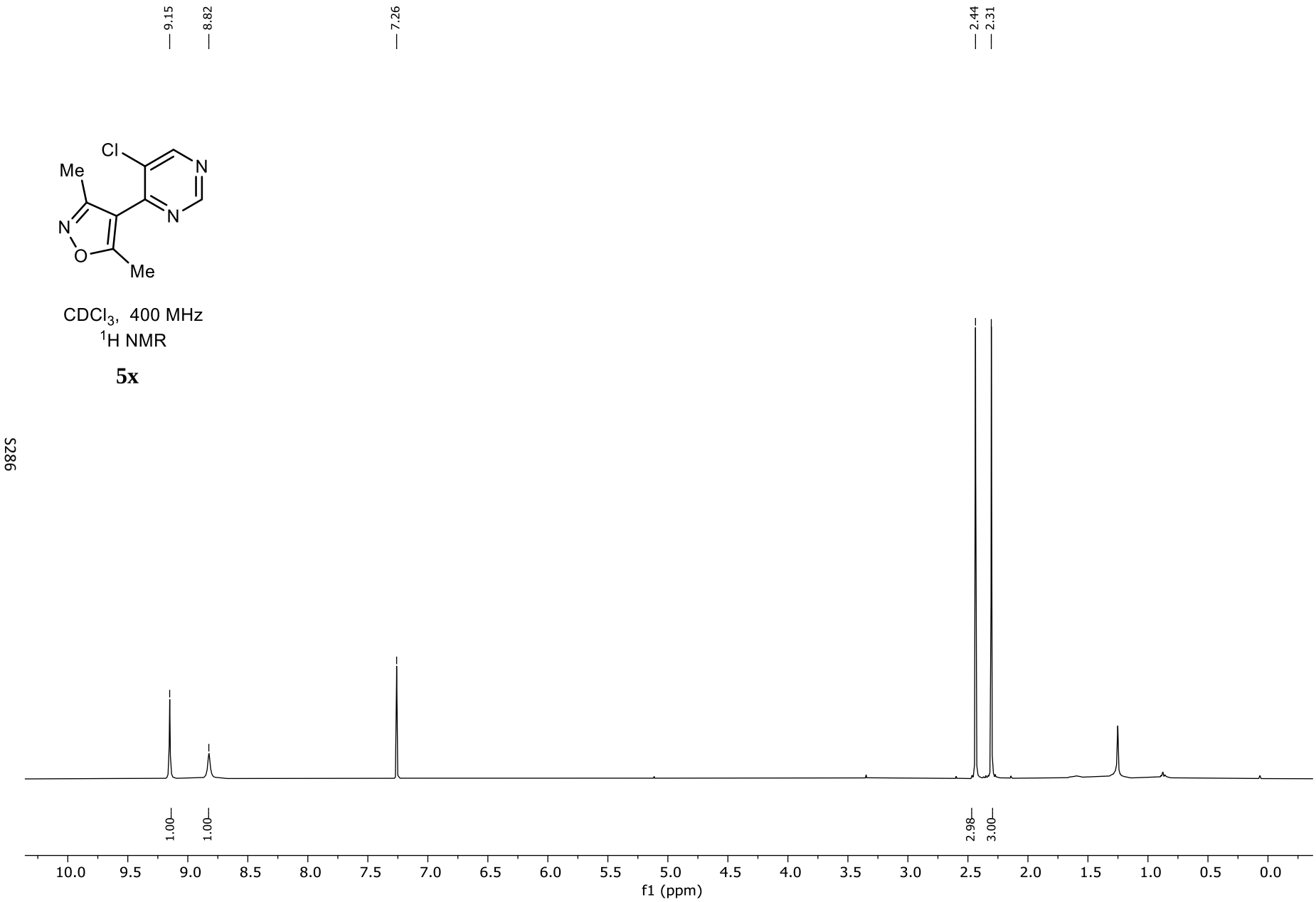

170.31
164.57
161.50
160.07
159.02
157.64
146.94
134.56
134.45
130.90
129.36
129.31
127.97
126.10
125.25
125.21
125.03
121.53
121.39
117.02
116.80
116.77
116.56
77.16 CDCl3
67.73
38.31
38.26
17.91
11.26
Cl
F
Cl
N
O
N
N
O
CDCl3, 100 MHz
1^
5w
S284
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

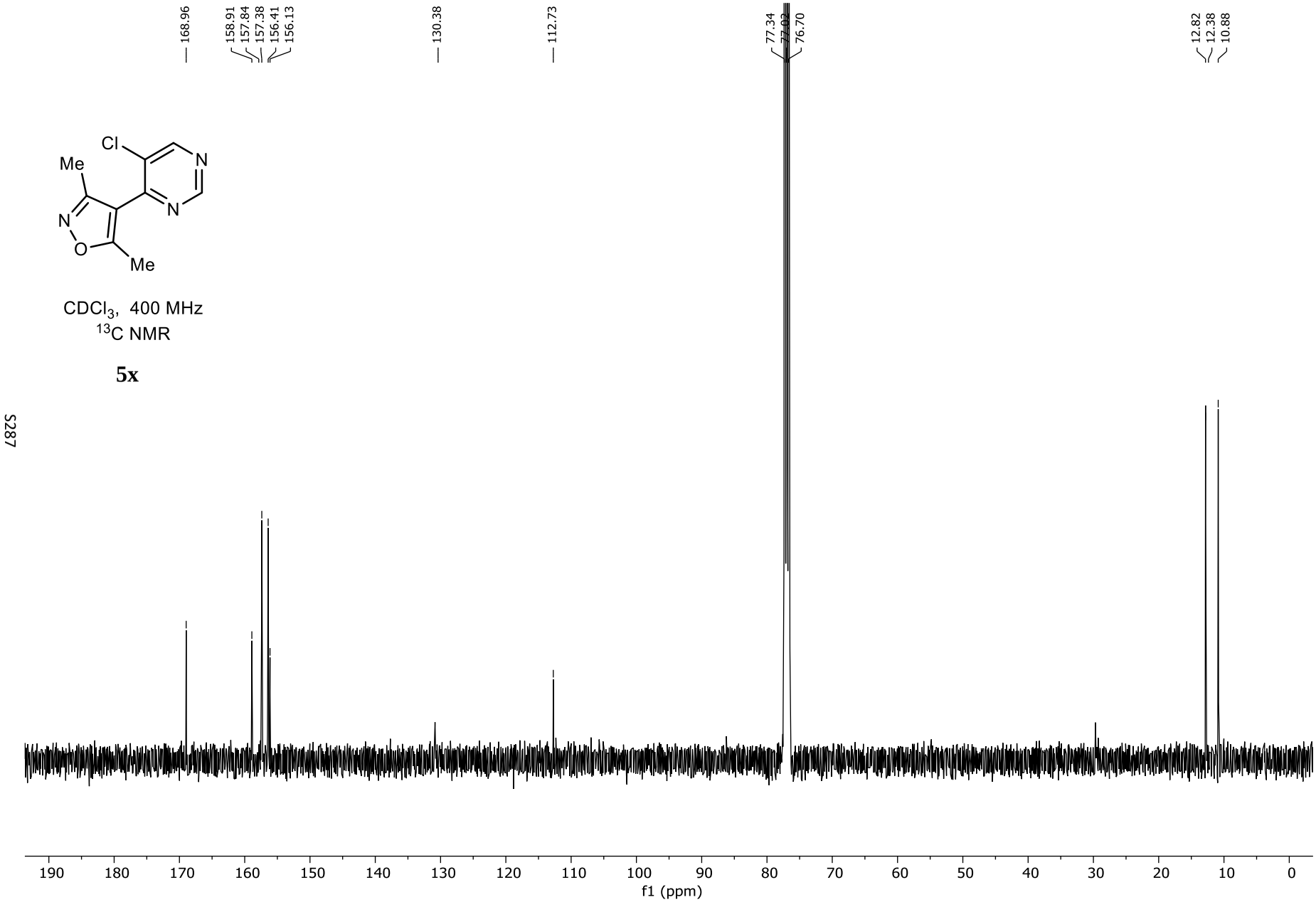


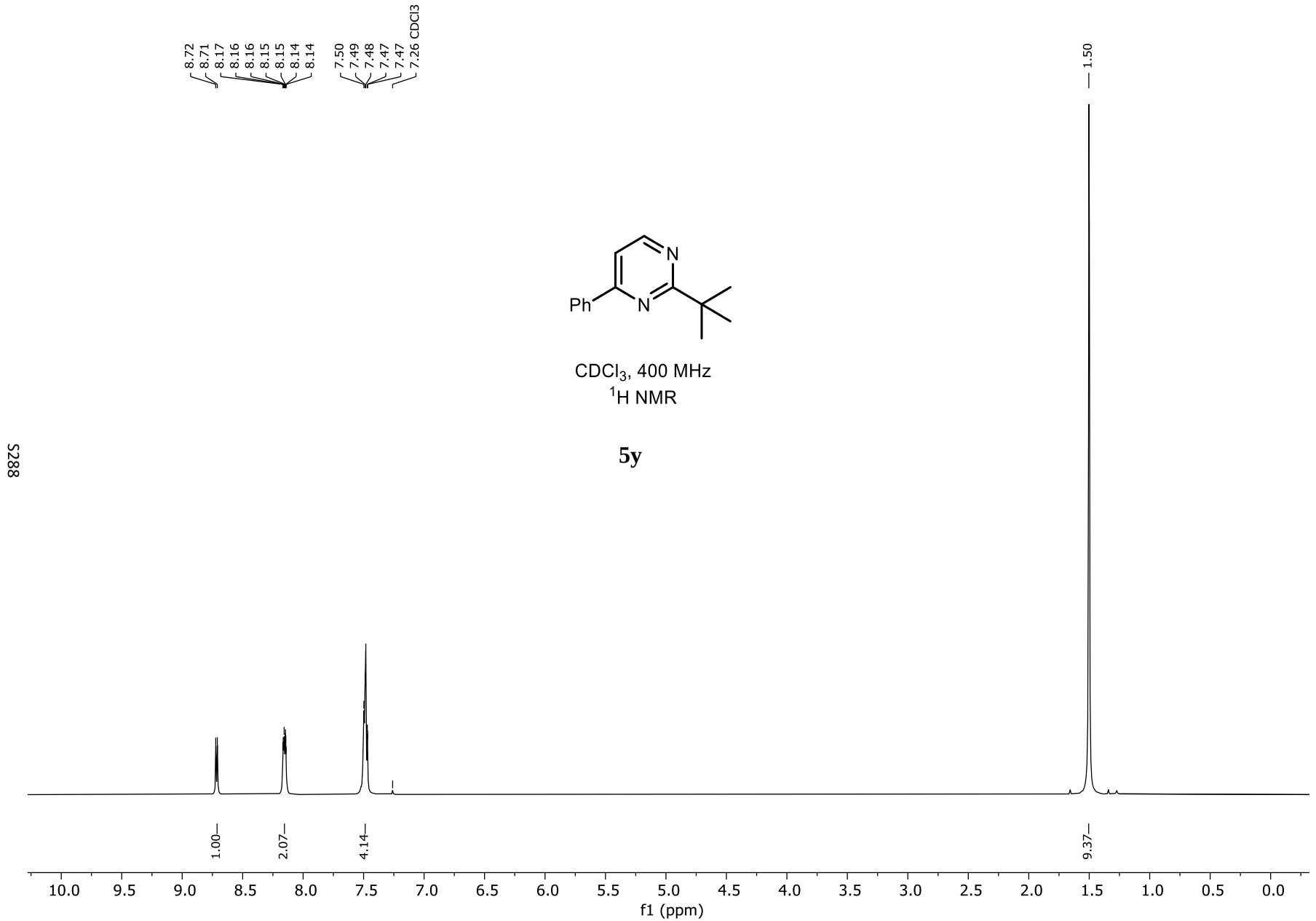
$CDCl_3$, 375 MHz

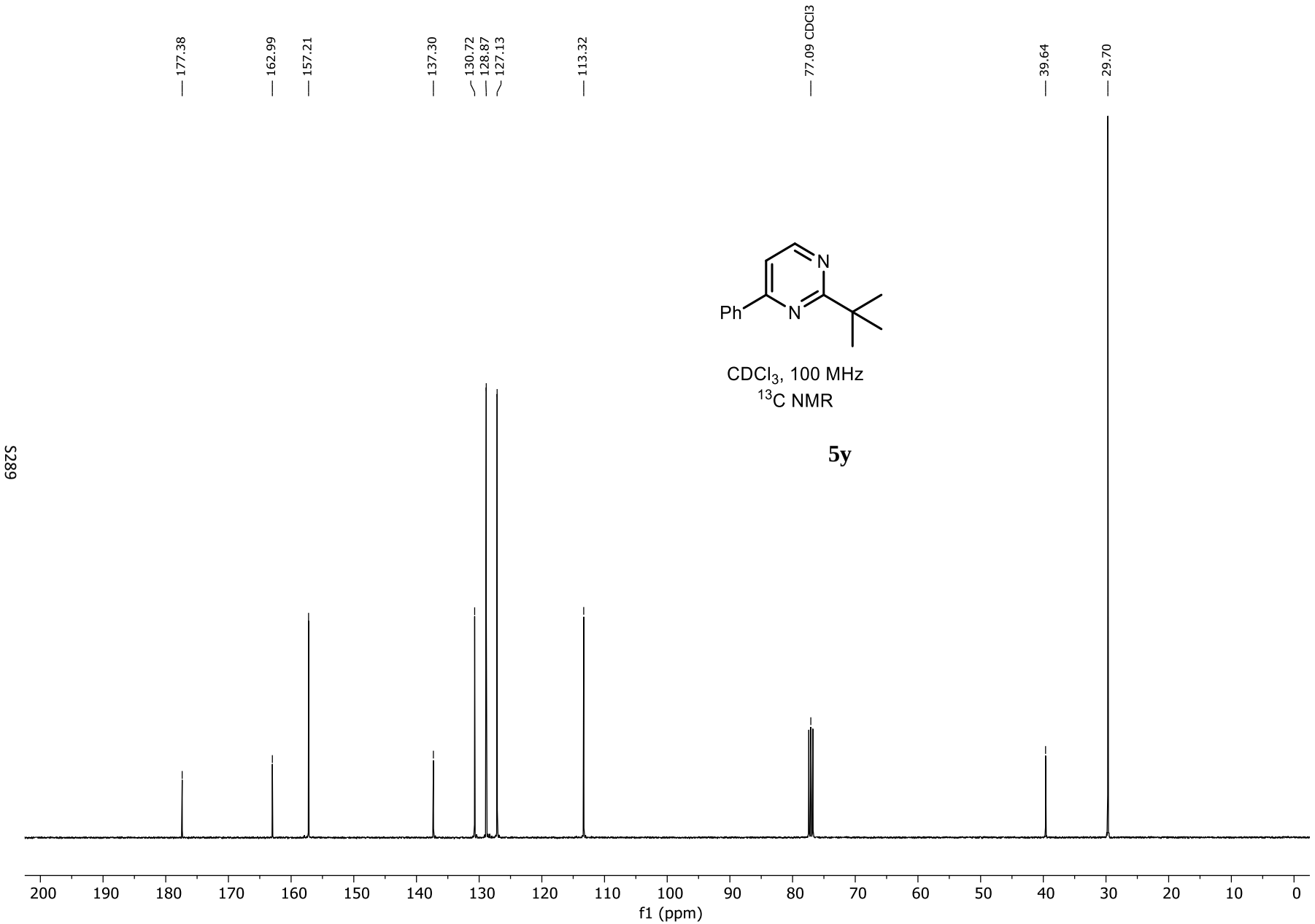
^{19}F NMR

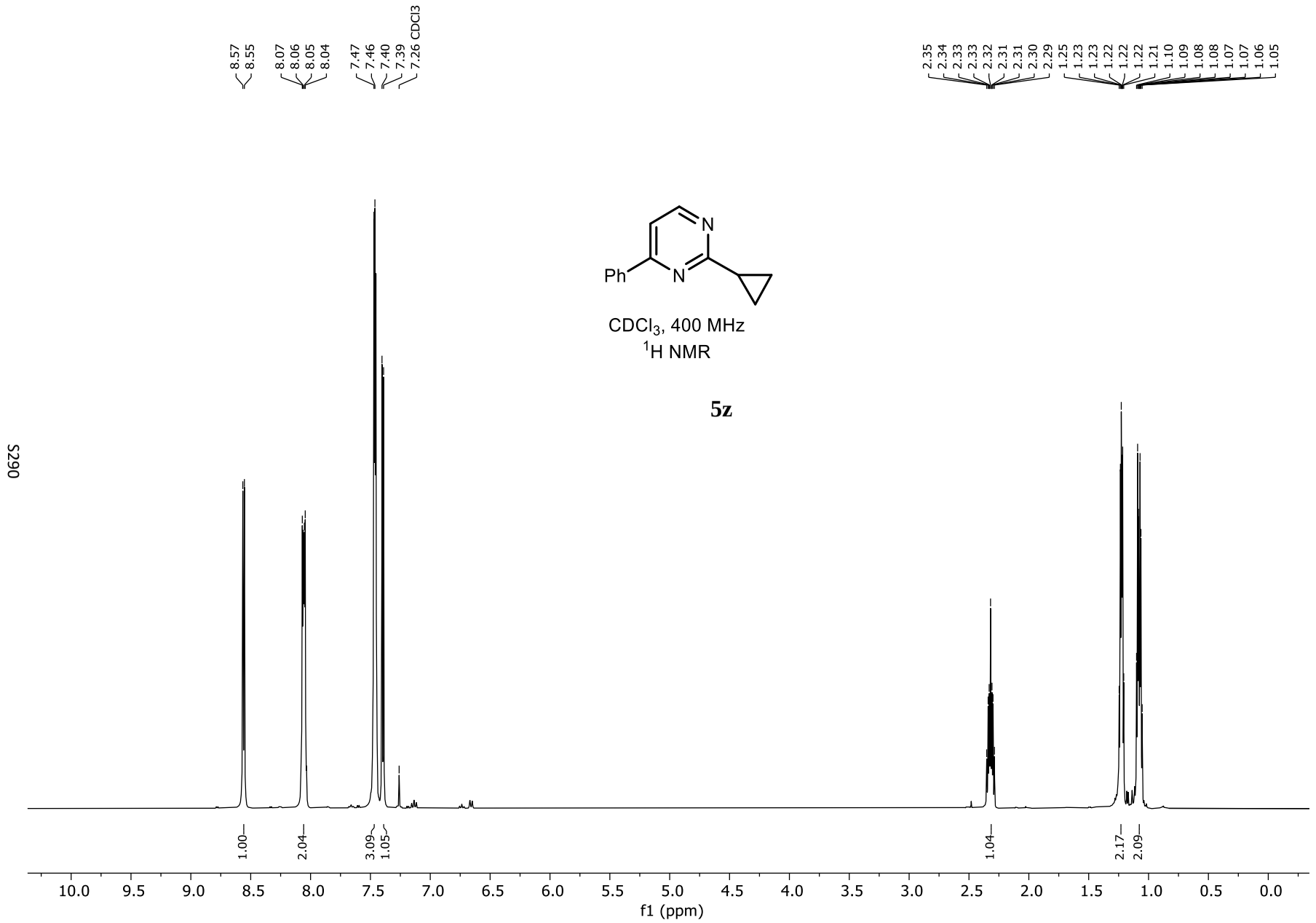
5w

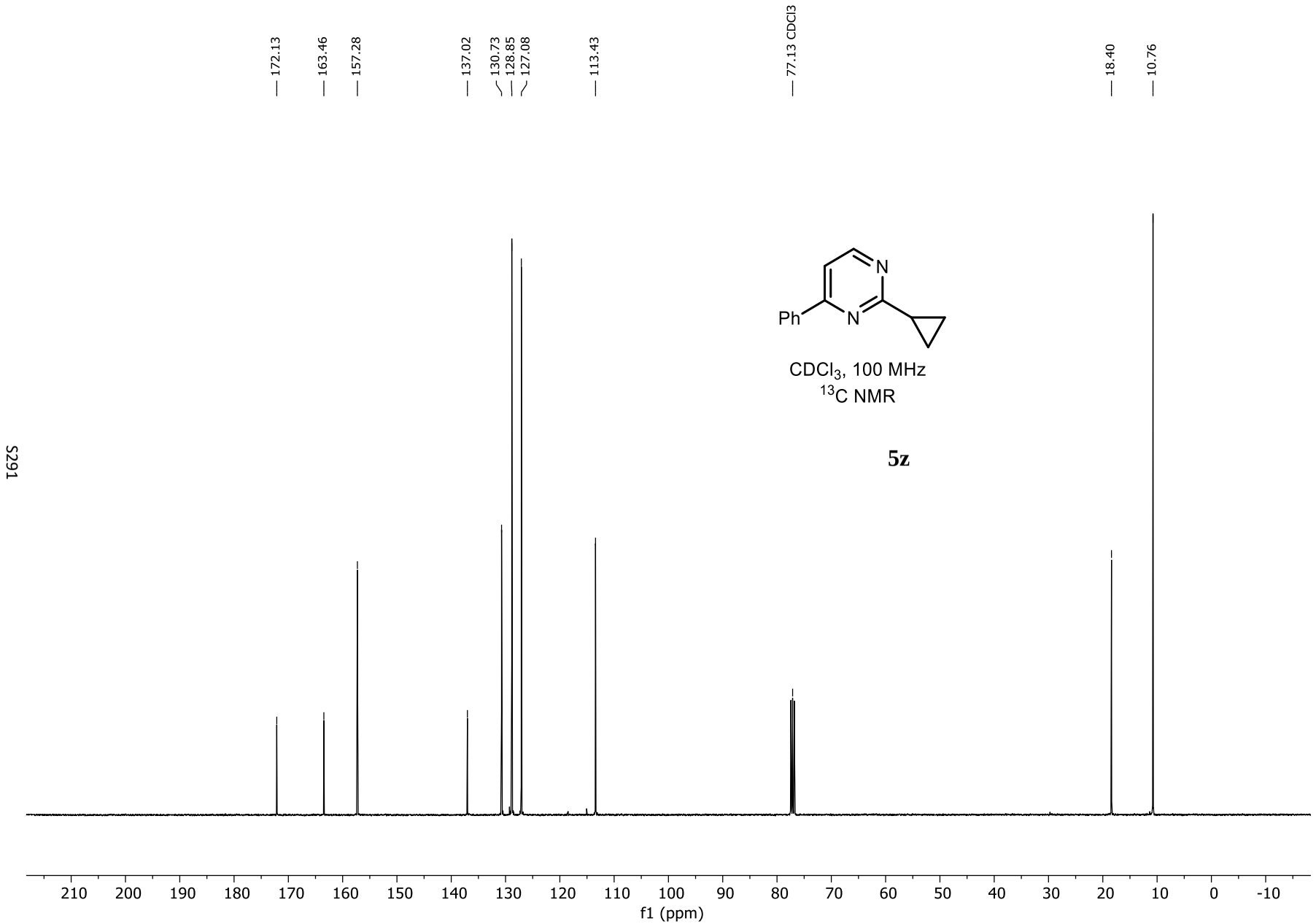

9.15
8.82
7.26
2.44
2.31
Cl
N
Me
N
N
O
Me
CDCl3, 400 MHz
1H NMR
5x
S286
1.00
1.00
2.98
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

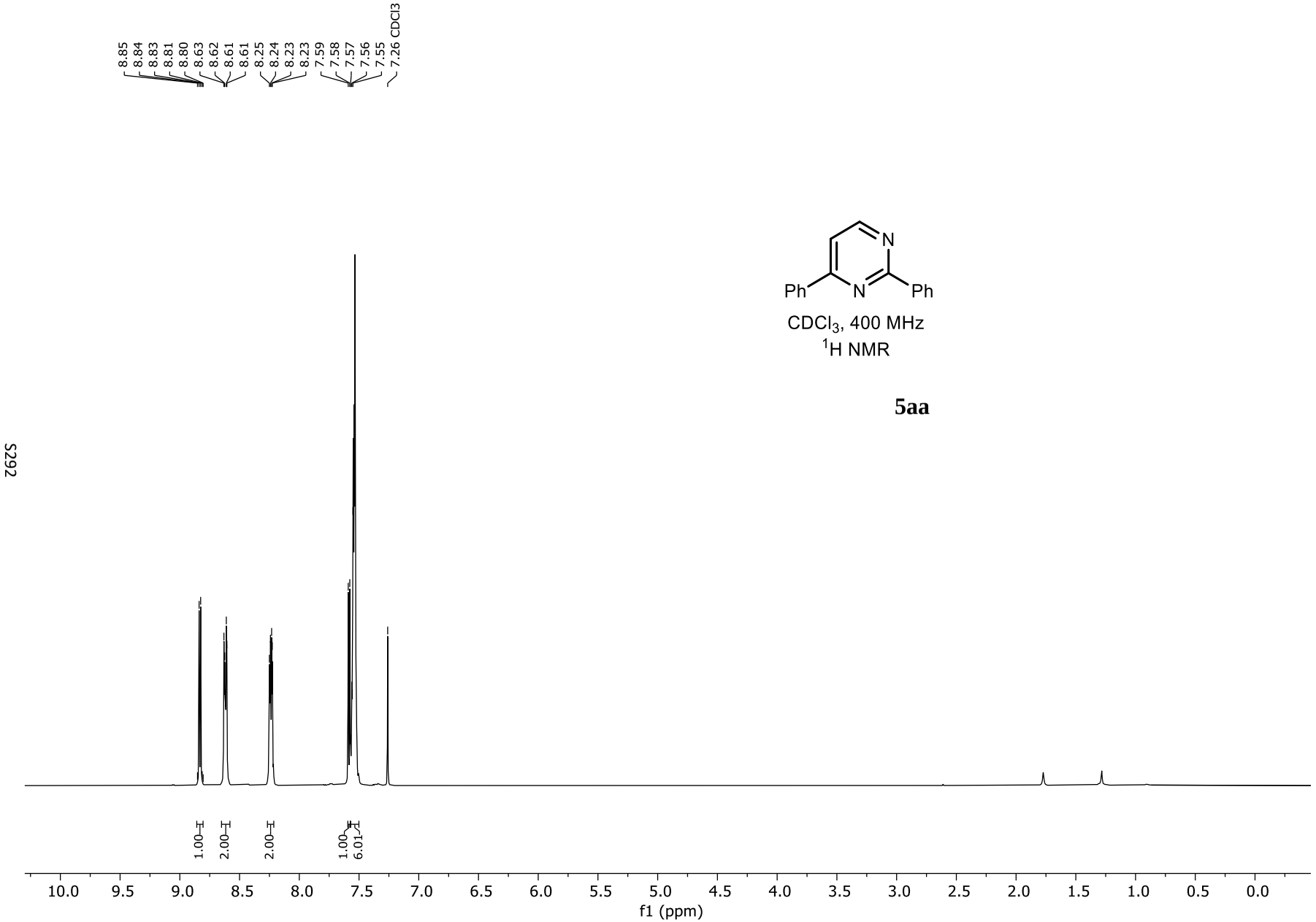

168.96
158.91
157.84
157.38
156.41
156.13
130.38
112.73
77.34
77.02
76.70
12.82
12.38
10.88
Cl
Me
N
N
N
O
Me
CDCl3, 400 MHz
13C NMR
5x
S287
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

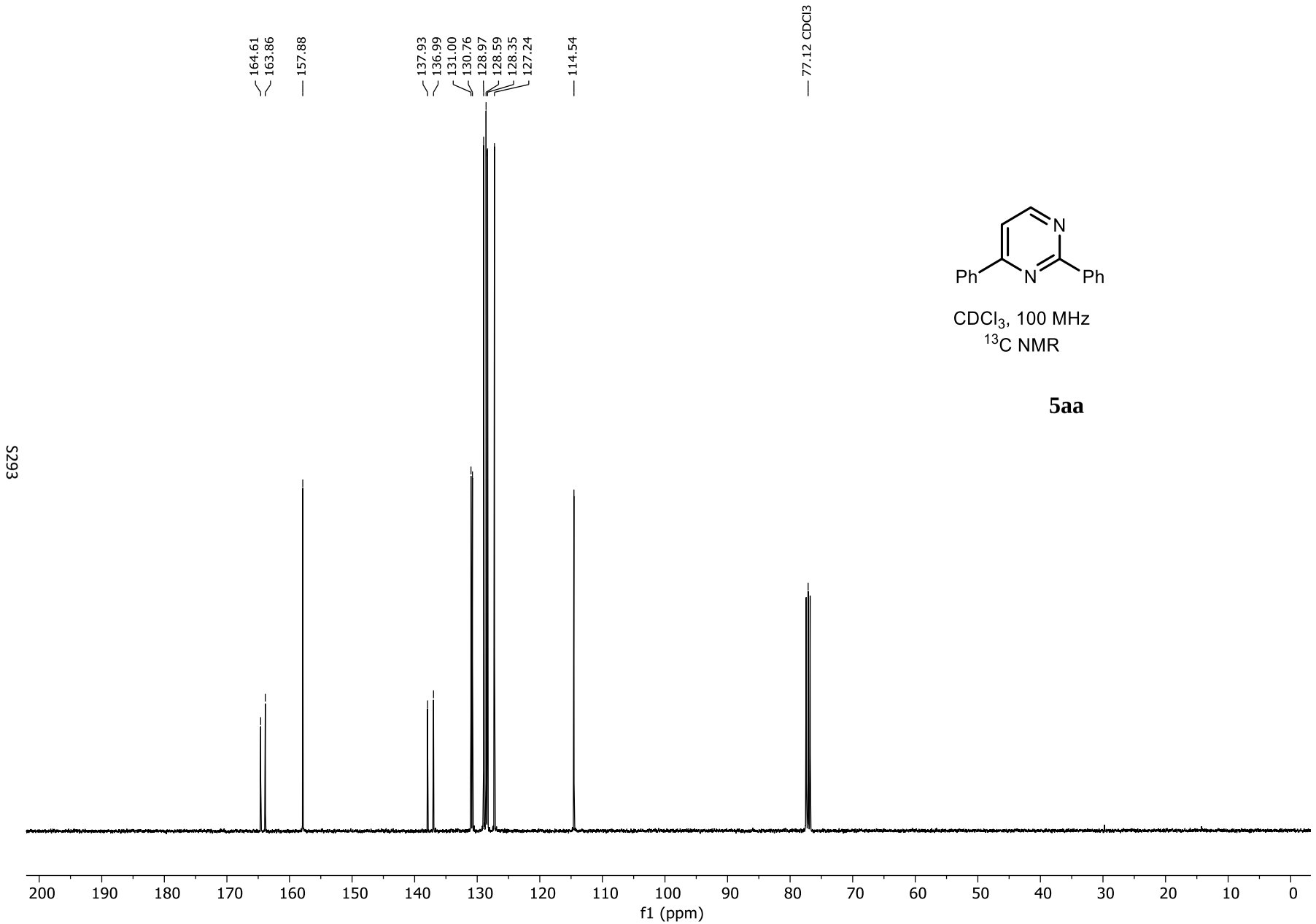

8.72
8.71
8.17
8.16
8.16
8.15
8.15
8.14
8.14
7.50
7.49
7.48
7.47
7.47
7.26 CDCl3
1.50
Ph
N
N
CDCl3, 400 MHz
1H NMR
5y
S288
1.00
2.07
4.14
9.37
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

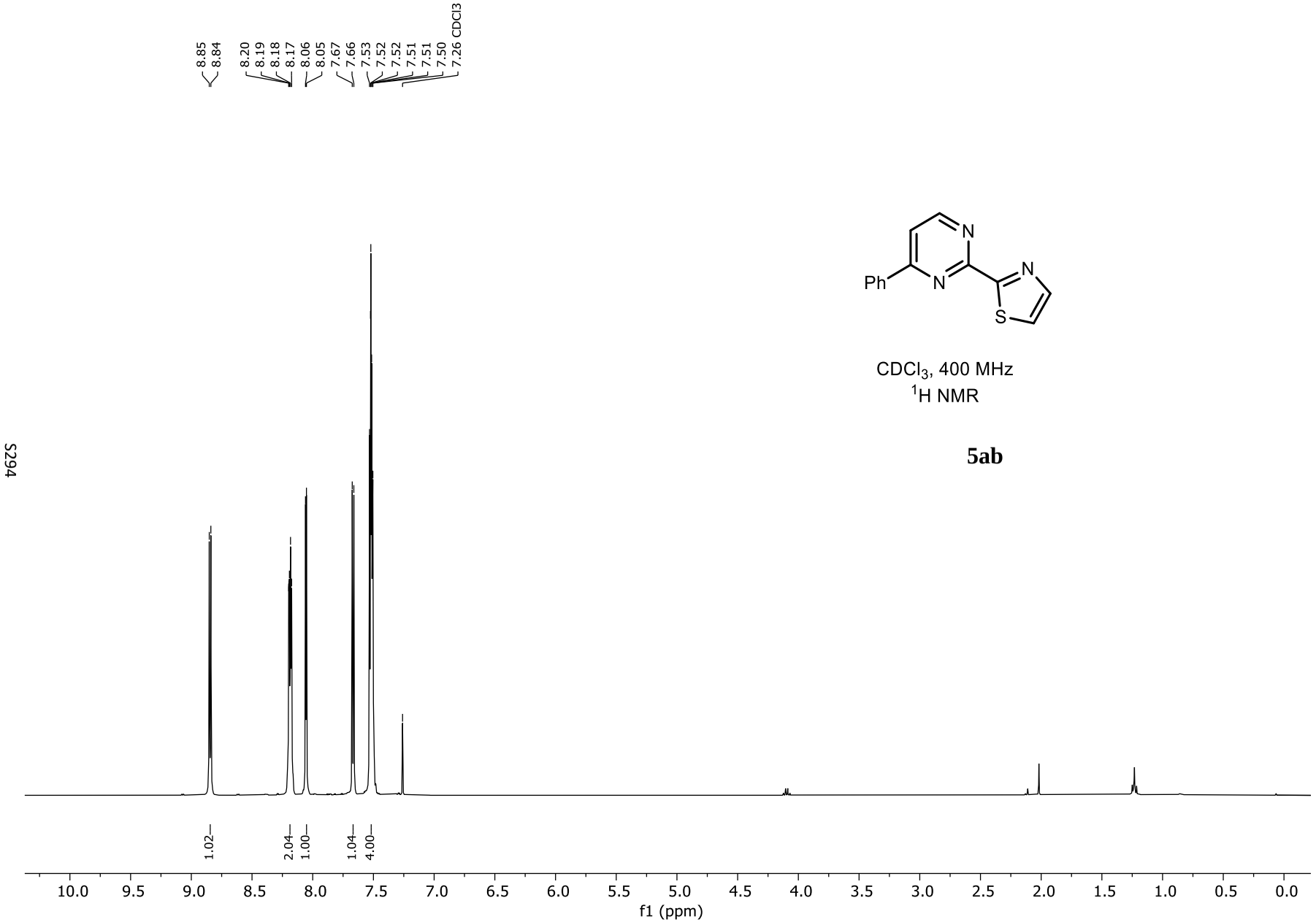

177.38
162.99
157.21
137.30
130.72
128.87
127.13
113.32
77.09 CDCl3
39.64
29.70
N
Ph
N
CDCl3, 100 MHz
13C NMR
5y
S289
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.57
8.55
8.07
8.06
8.05
8.04
7.47
7.46
7.40
7.39
7.26 CDCl3
2.35
2.34
2.33
2.33
2.32
2.31
2.31
2.30
2.29
1.25
1.23
1.23
1.22
1.22
1.22
1.21
1.10
1.09
1.08
1.08
1.07
1.07
1.06
1.05
Ph
N
N
CDCl3, 400 MHz
1H NMR
5z
S290
1.00
2.04
3.09
1.05
1.04
2.17
2.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


172.13
163.46
157.28
137.02
130.73
128.85
127.08
113.43
77.13 CDCl3
18.40
10.76
N
N
Ph
CDCl3, 100 MHz
13C NMR
5z
S291
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

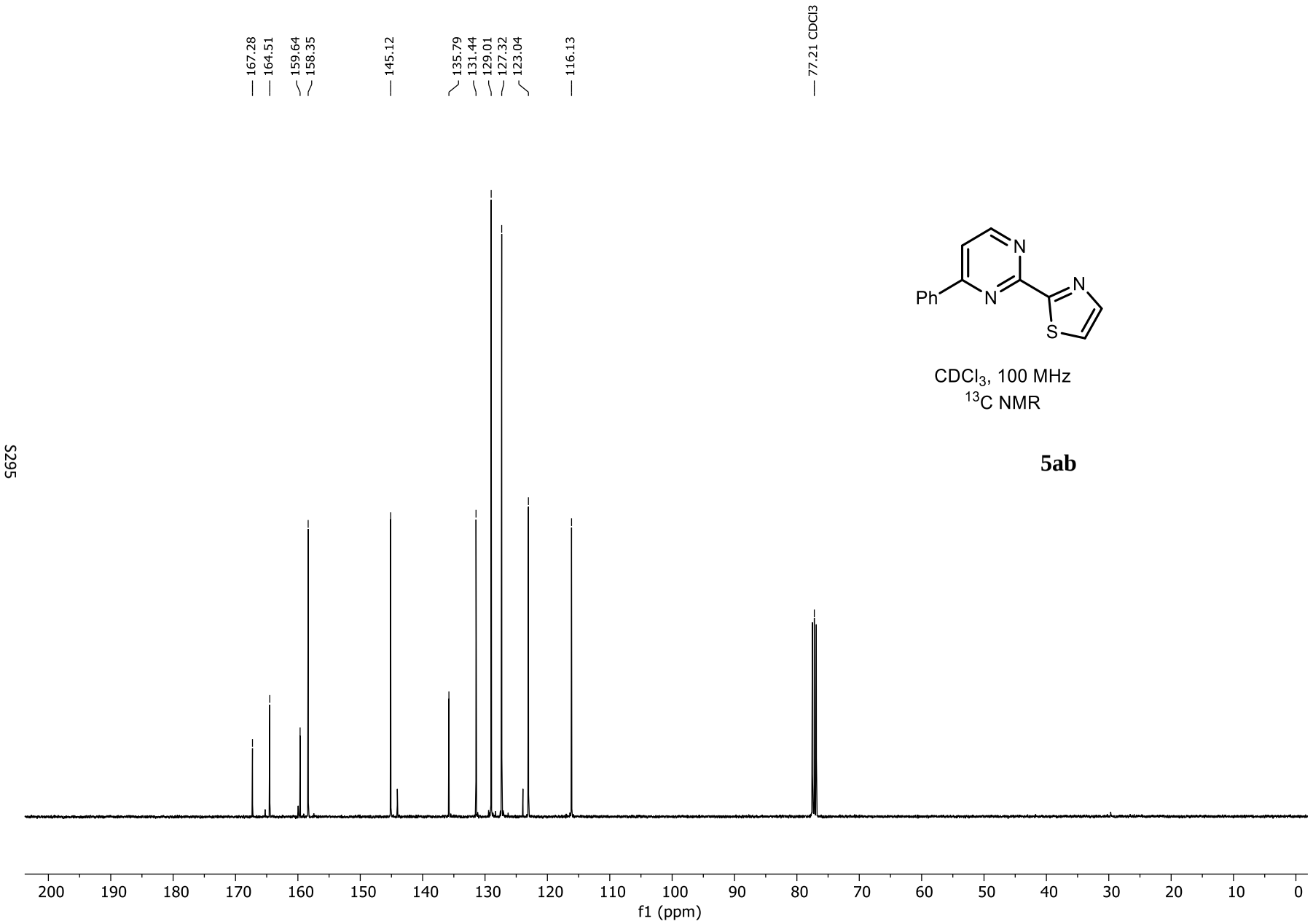

8.85
8.84
8.83
8.81
8.80
8.63
8.62
8.61
8.61
8.25
8.24
8.23
8.23
7.59
7.58
7.57
7.56
7.55
7.26 CDCl3
N
Ph
N
Ph
CDCl3, 400 MHz
1H NMR
5aa
S292
1.00
2.00
2.00
1.00
6.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

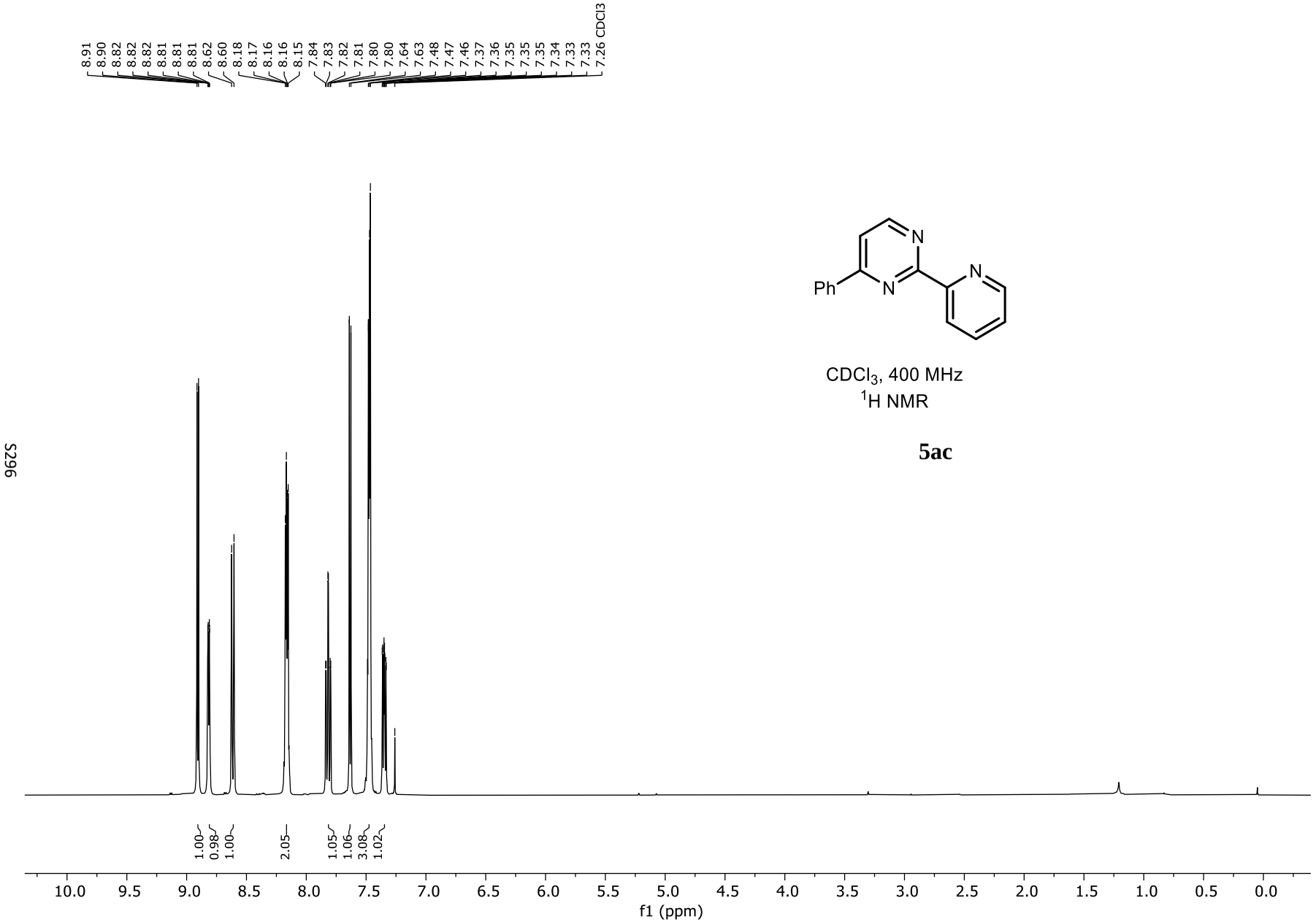

164.61
163.86
157.88
137.93
136.99
131.00
130.76
128.97
128.59
128.35
127.24
114.54
77.12 CDCl3
N
Ph
N
Ph
CDCl3, 100 MHz
13C NMR
5aa
S293
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

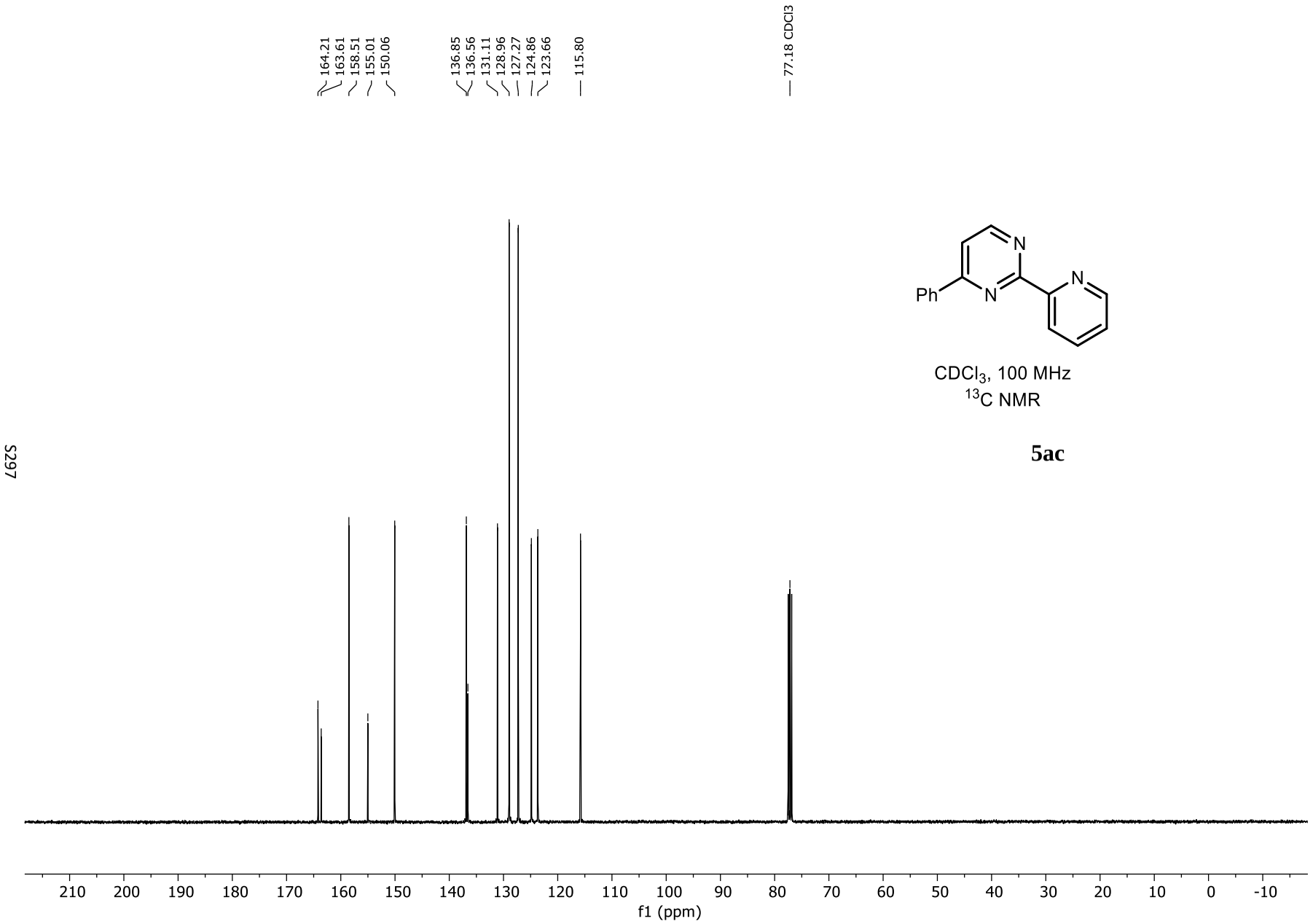


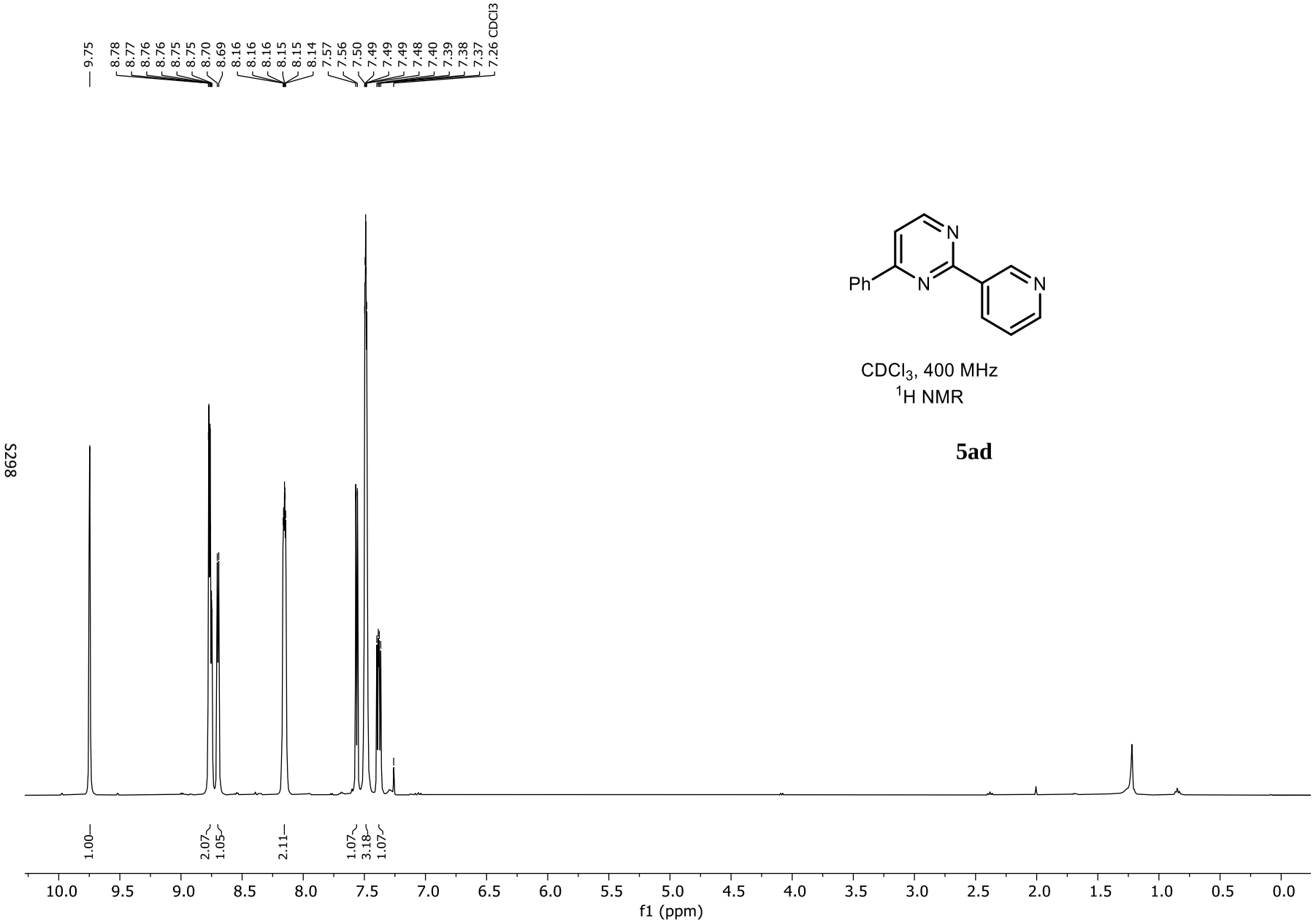
$CDCl_3$, 400 MHz
^1H NMR

5ab


167.28
164.51
159.64
158.35
145.12
135.79
131.44
129.01
127.32
123.04
116.13
77.21 CDCl3
N
N
N
S
Ph
CDCl3, 100 MHz
13C NMR
5ab
S295
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.91
8.90
8.82
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
7.35
7.34
7.33
7.33
7.26 CDCl3
S296
Ph
N
N
N
CDCl3, 400 MHz
1H NMR
5ac
1.00
0.98
1.00
2.05
1.05
1.06
3.08
1.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

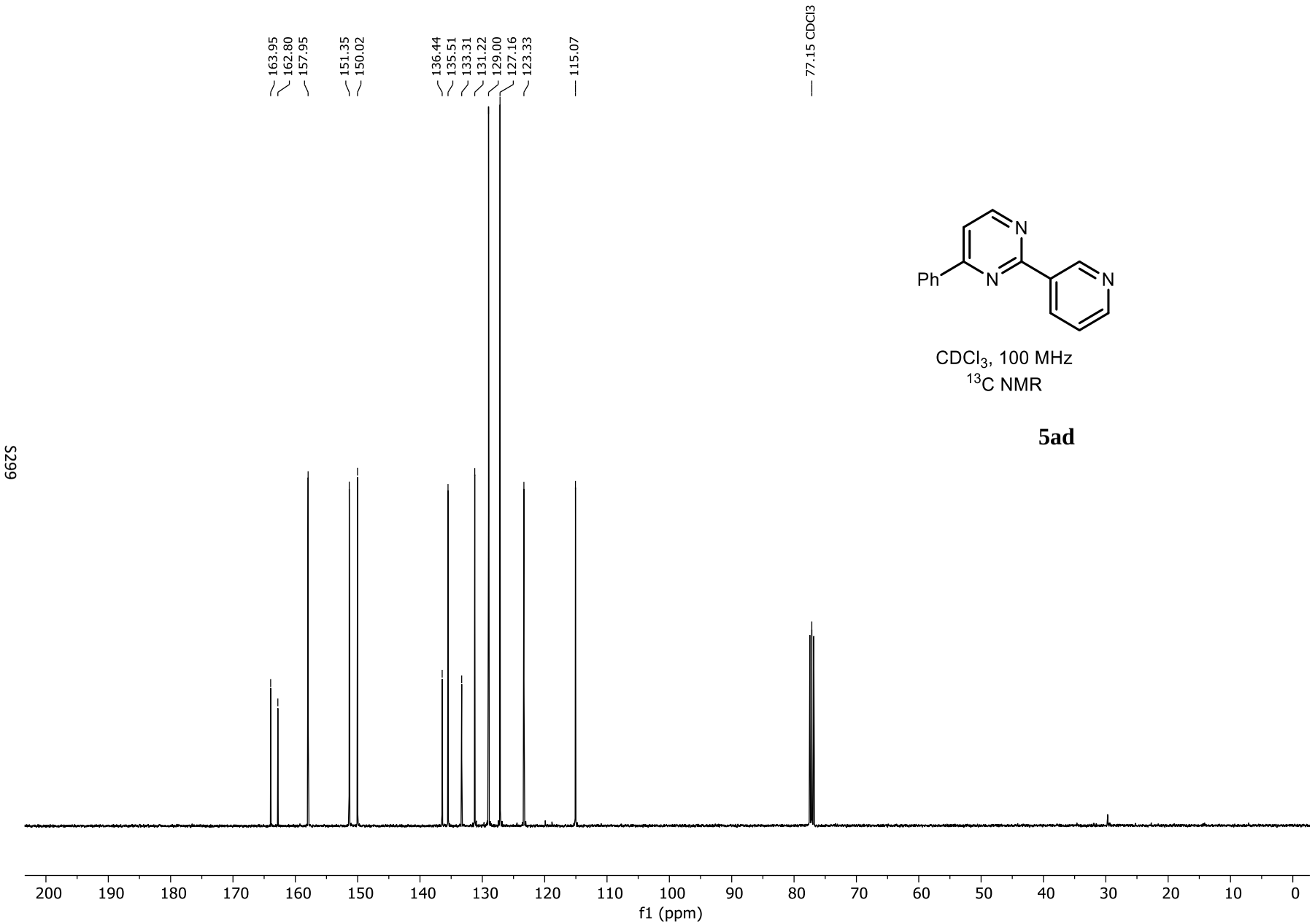

164.21
163.61
158.51
155.01
150.06
136.85
136.56
131.11
128.96
127.27
124.86
123.66
115.80
77.18 CDCl3
Ph
N
N
N
CDCl3, 100 MHz
13C NMR
5ac
S297
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

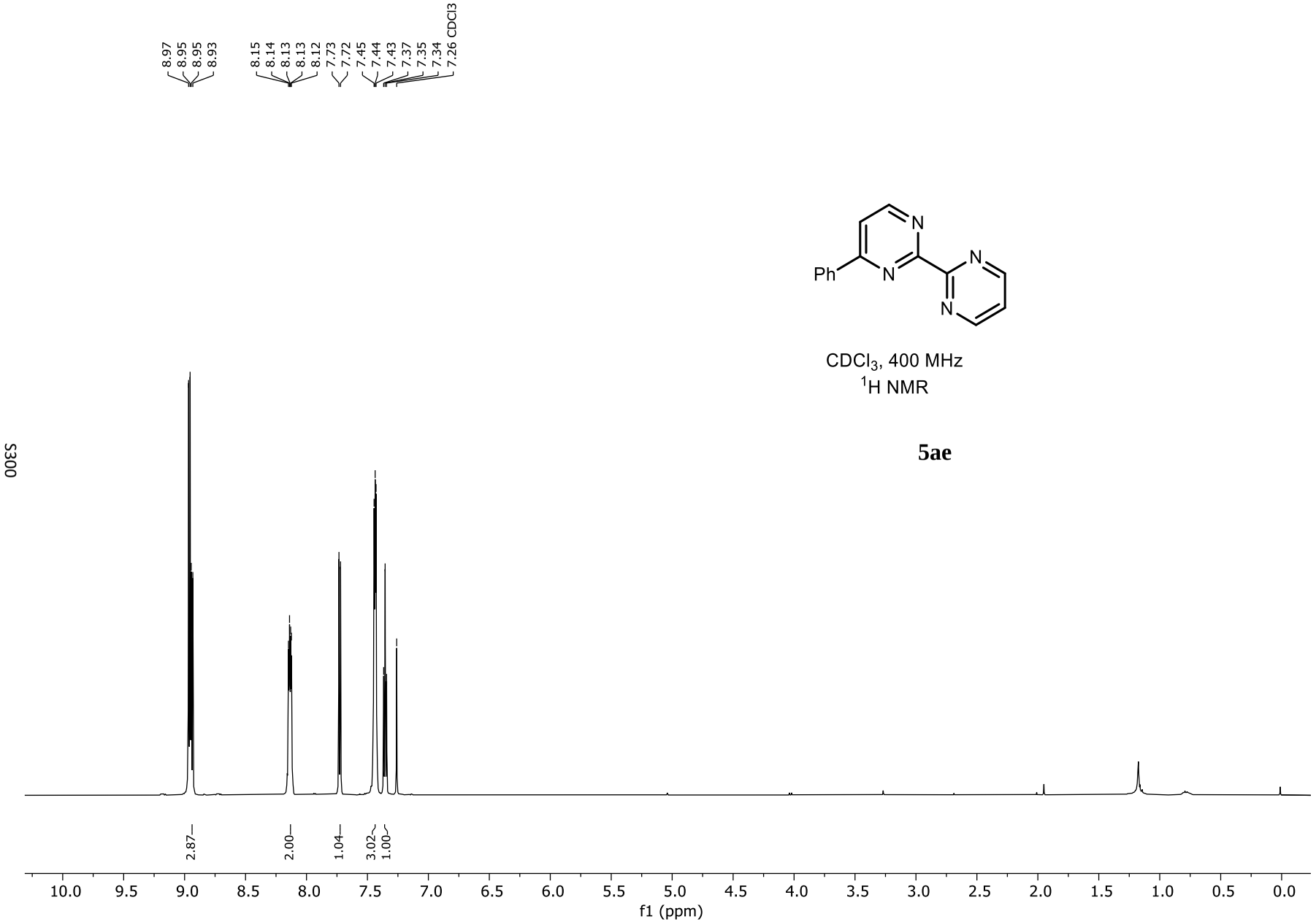


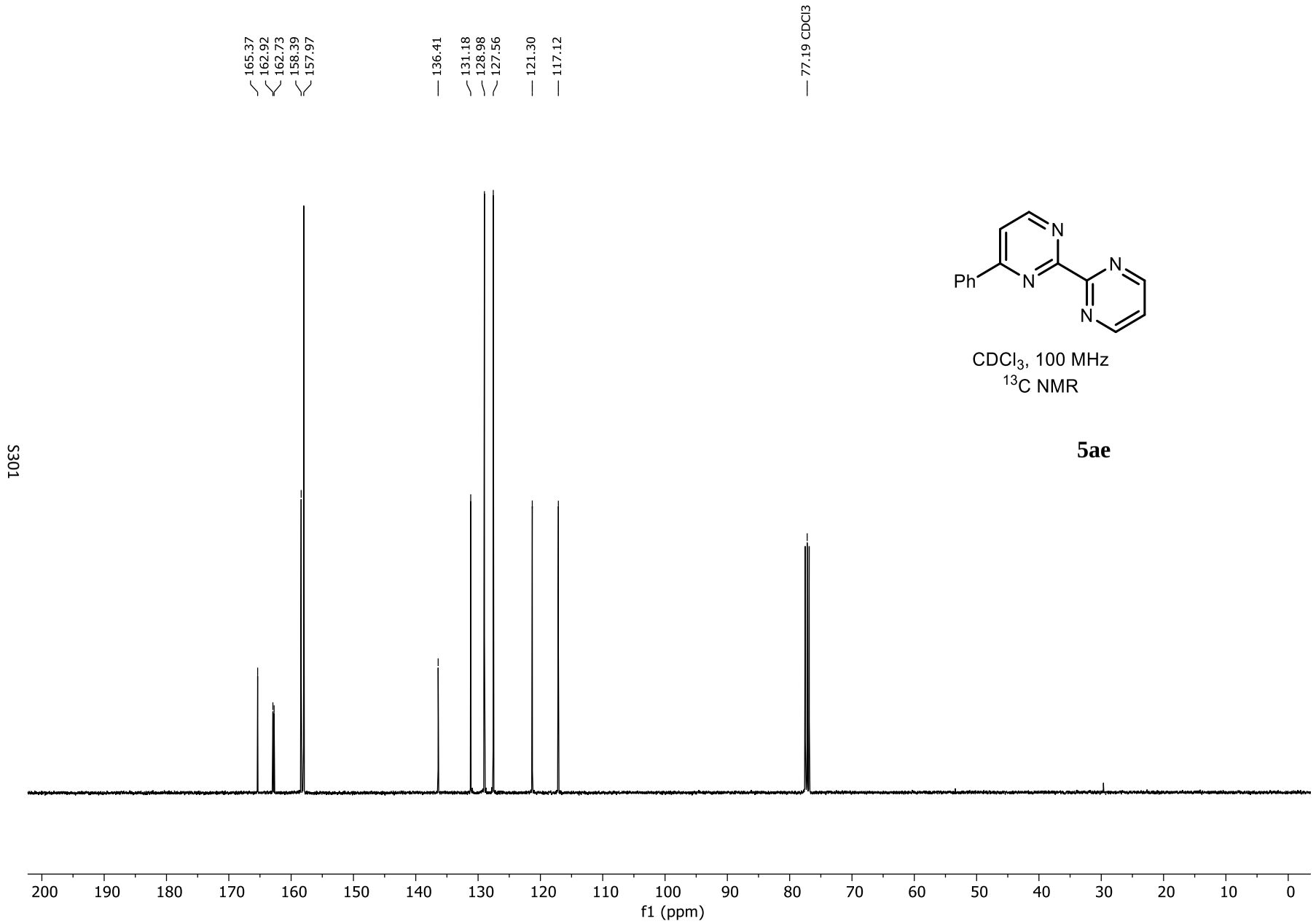
$CDCl_3$, 400 MHz

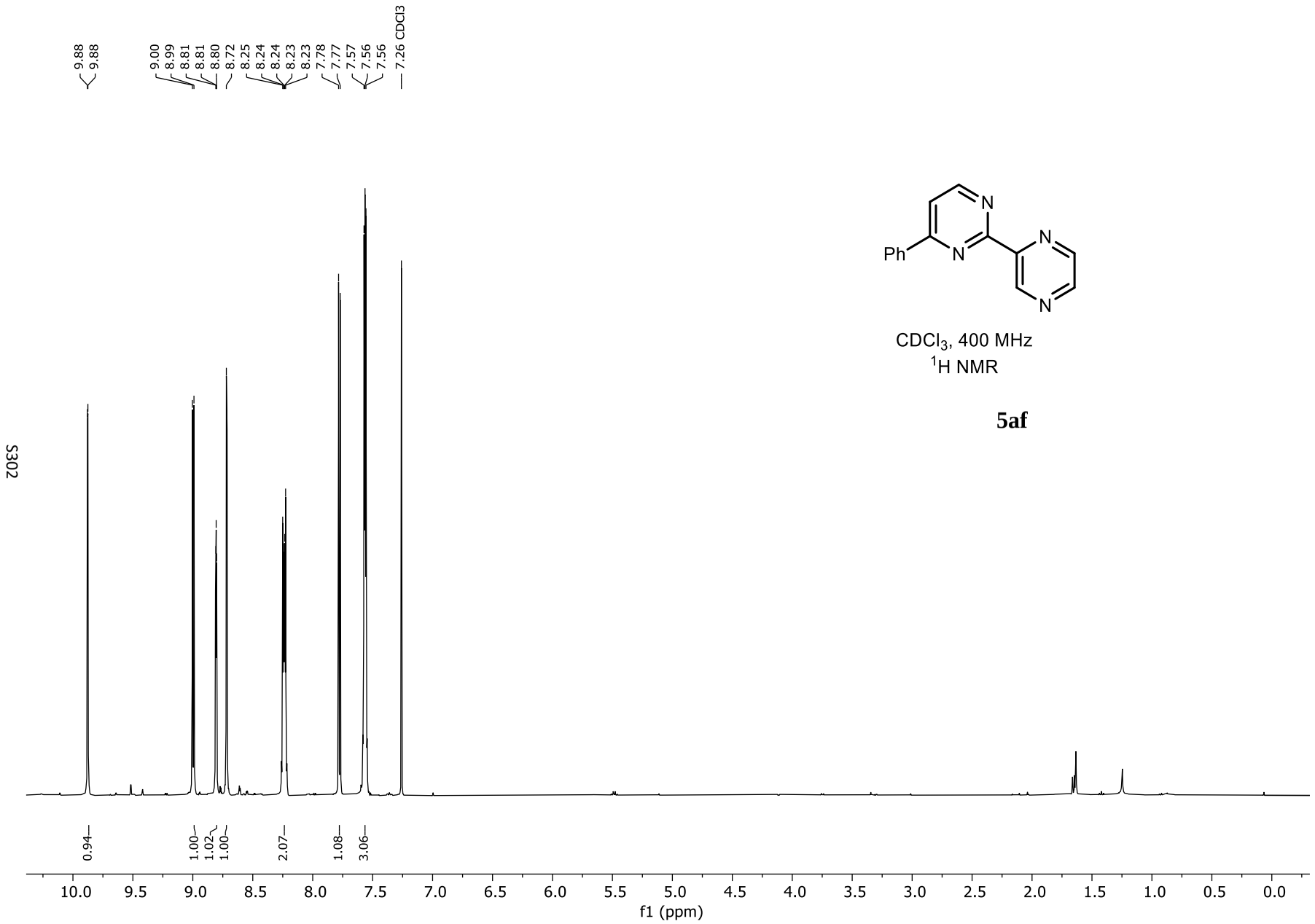
^1H NMR

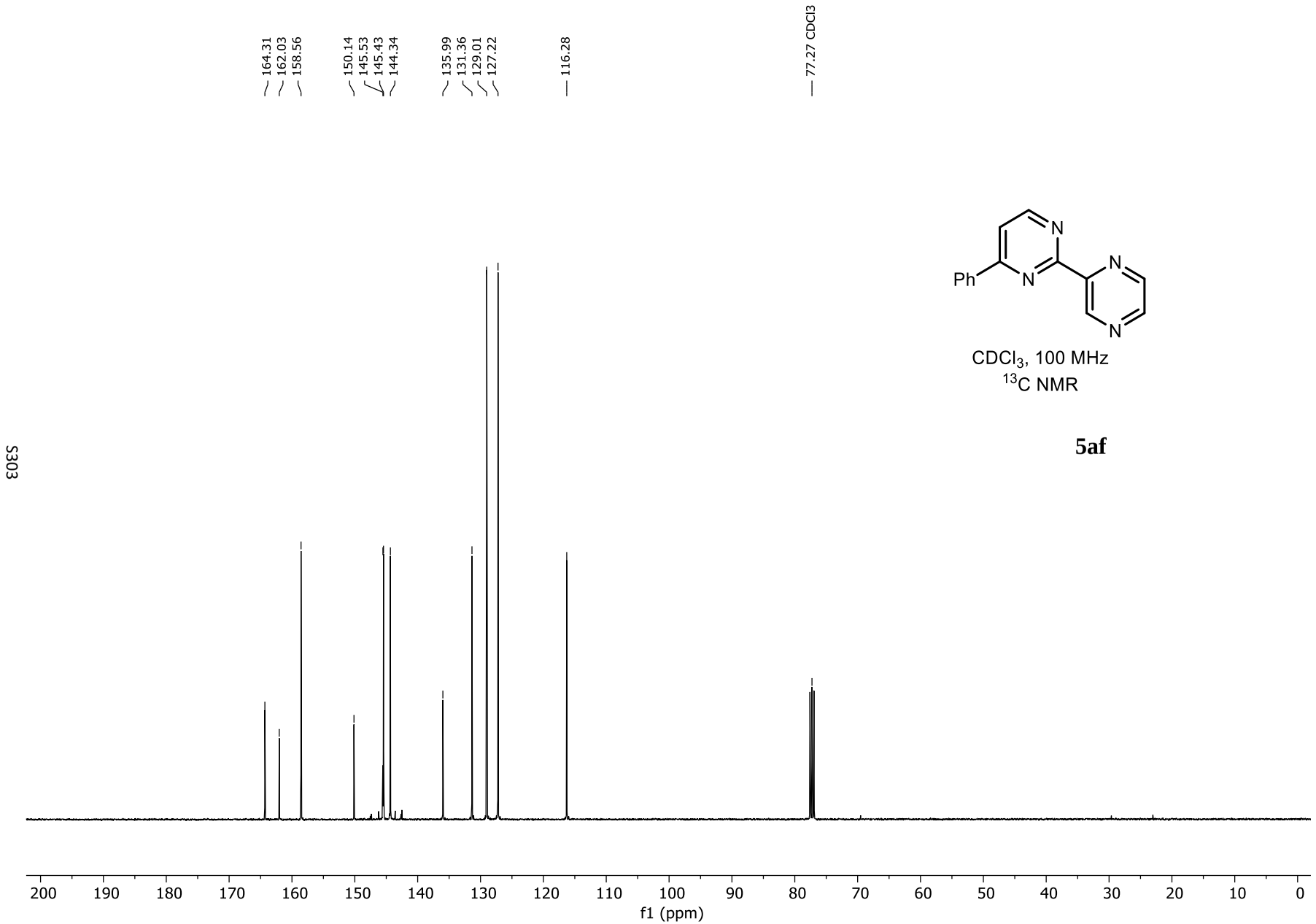
5ad

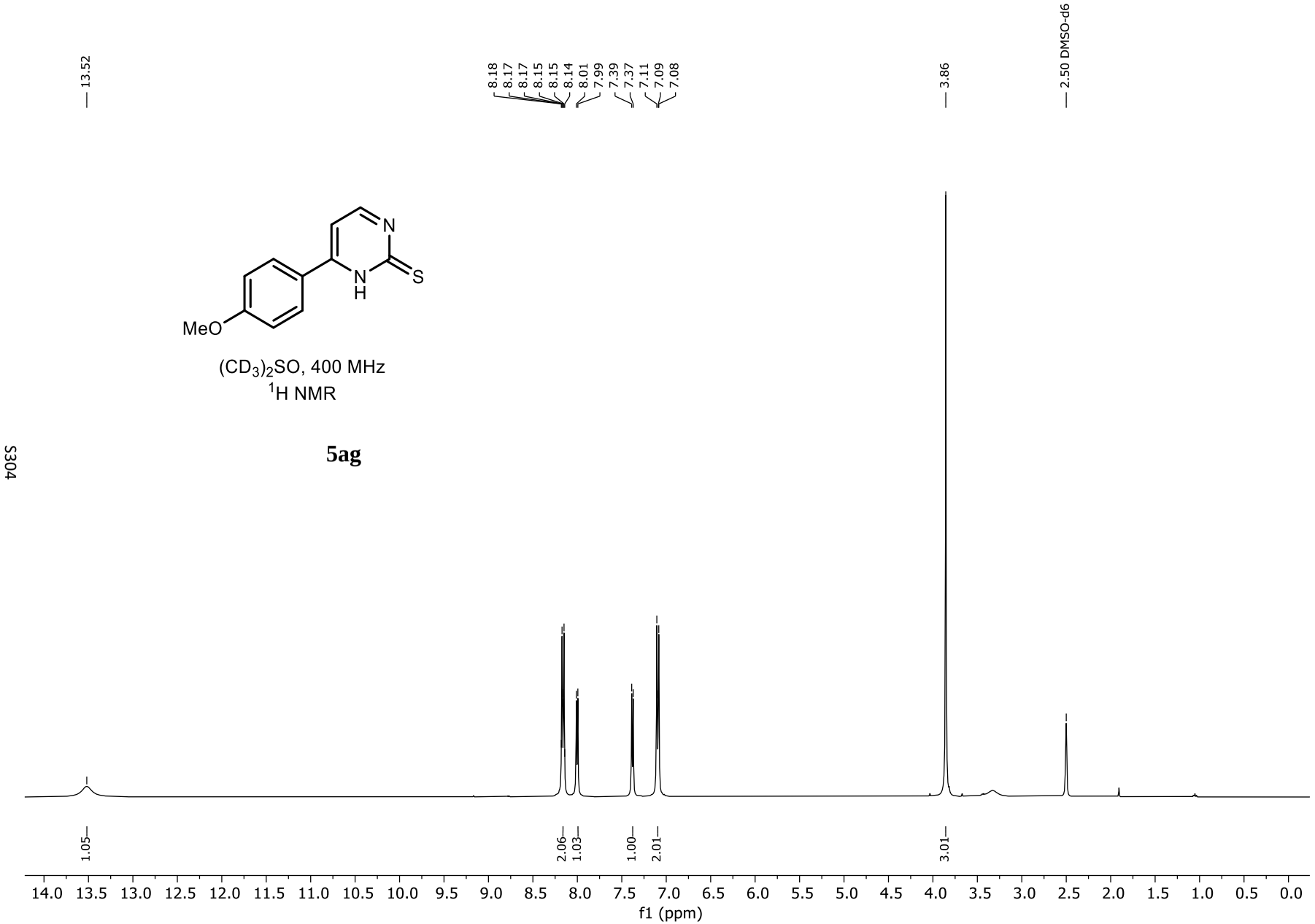

163.95
162.80
157.95
151.35
150.02
136.44
135.51
133.31
131.22
129.00
127.16
123.33
115.07
77.15 CDCl3
S299
Ph
N
N
N
CDCl3, 100 MHz
13C NMR
5ad
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

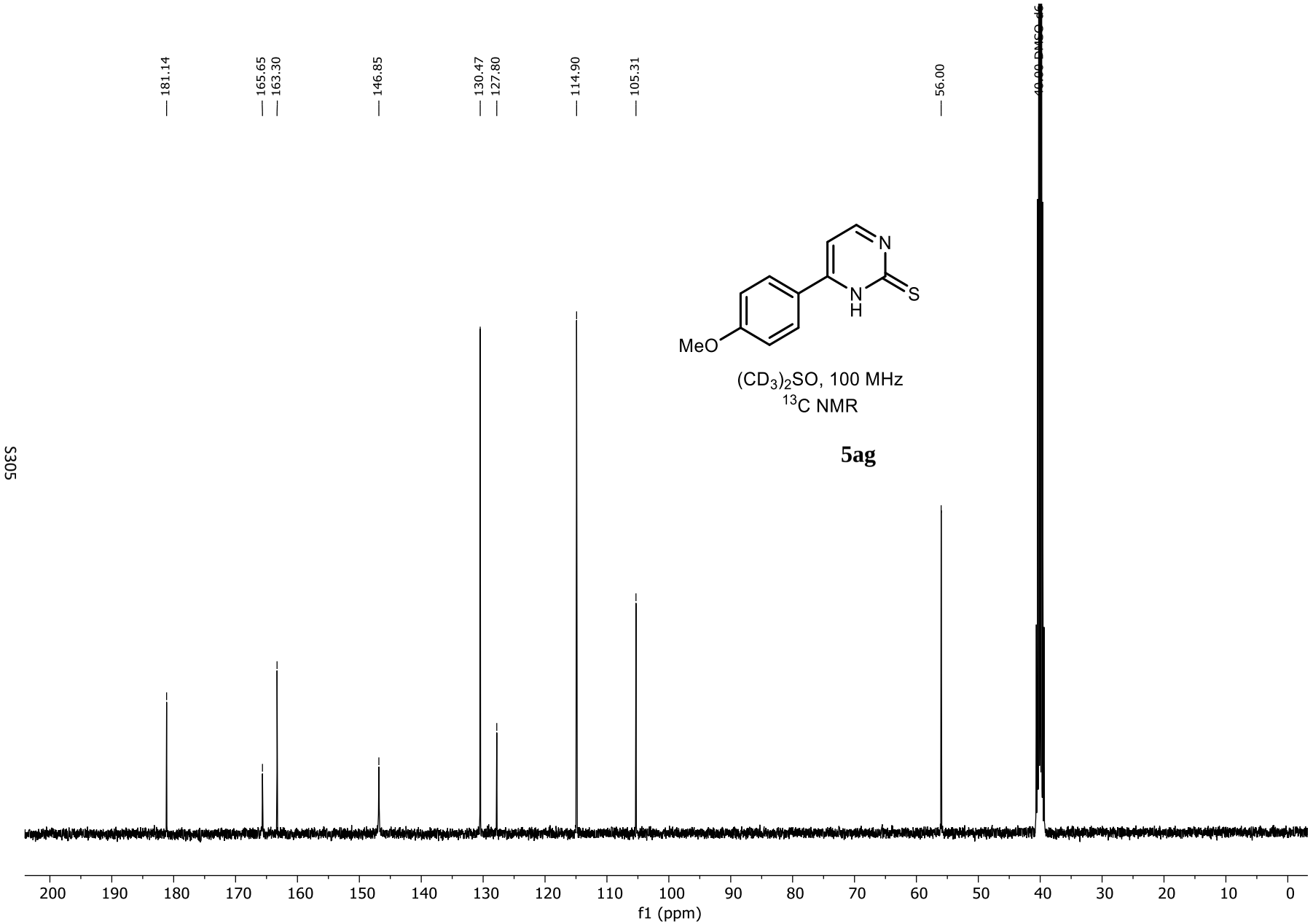

8.97
8.95
8.95
8.93
8.15
8.14
8.13
8.13
8.12
7.73
7.72
7.45
7.44
7.43
7.37
7.35
7.34
7.26 CDCl3
Ph
N
N
N
N
CDCl3, 400 MHz
1H NMR
5ae
S300
2.87
2.00
1.04
3.02
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

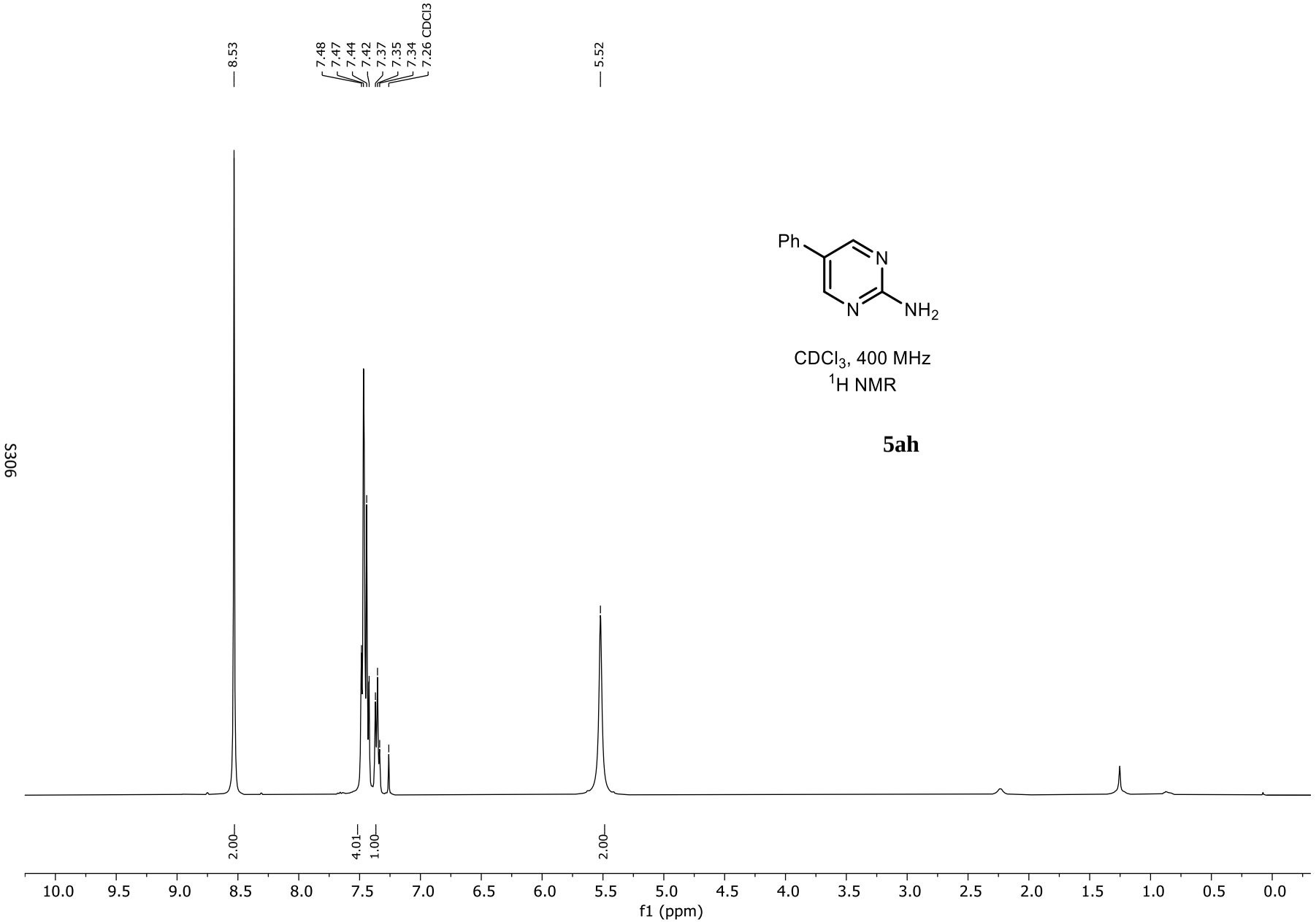

165.37
162.92
162.73
158.39
157.97
136.41
131.18
128.98
127.56
121.30
117.12
77.19 CDCl3
S301
Ph
N
N
N
N
CDCl3, 100 MHz
13C NMR
5ae
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

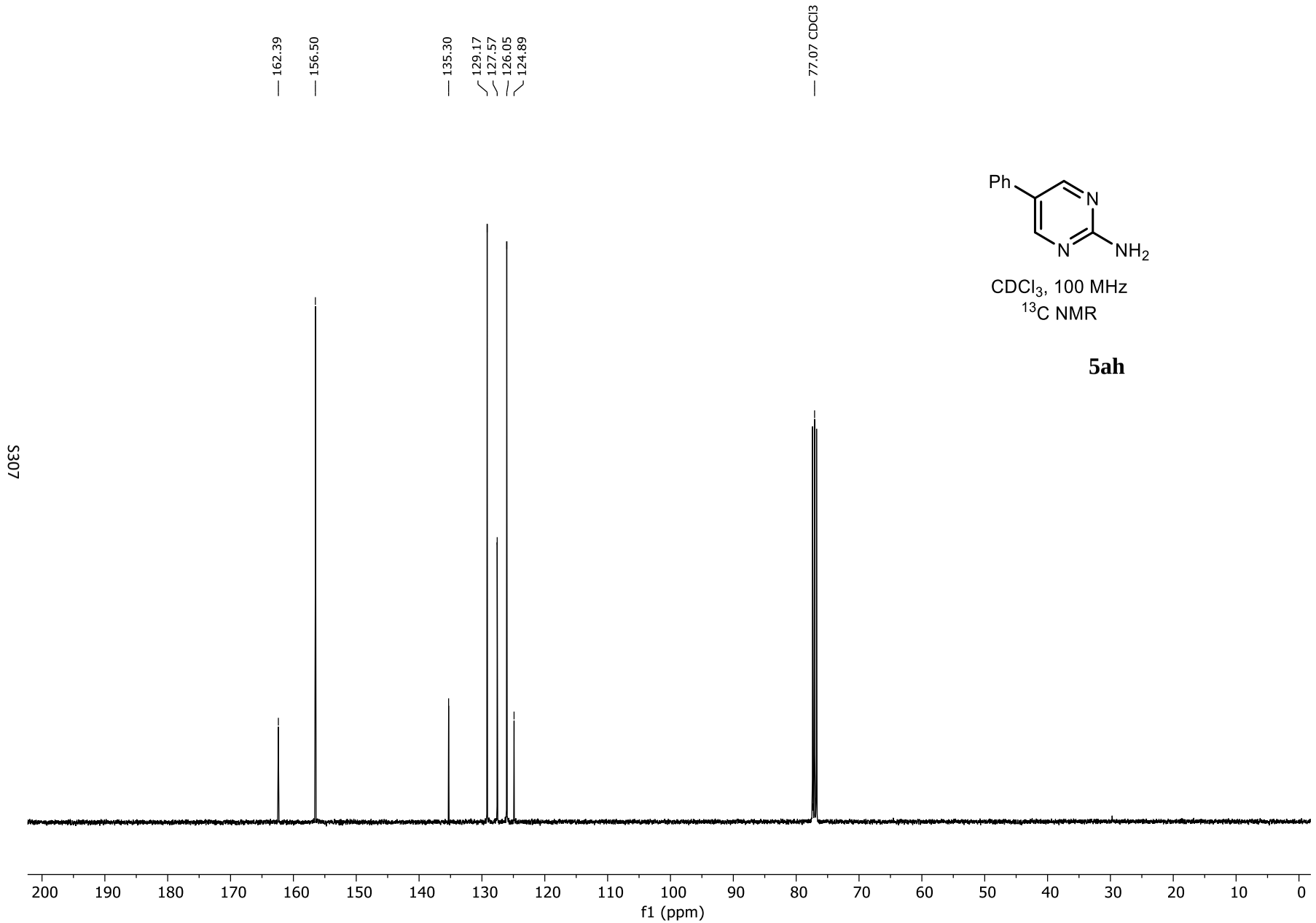

9.88
9.88
9.00
8.99
8.81
8.81
8.80
8.72
8.25
8.24
8.24
8.23
8.23
7.78
7.77
7.57
7.56
7.56
7.26 CDCl3
S302
Ph
N
N
N
N
CDCl3, 400 MHz
1H NMR
5af
0.94
1.00
1.02
1.00
2.07
1.08
3.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

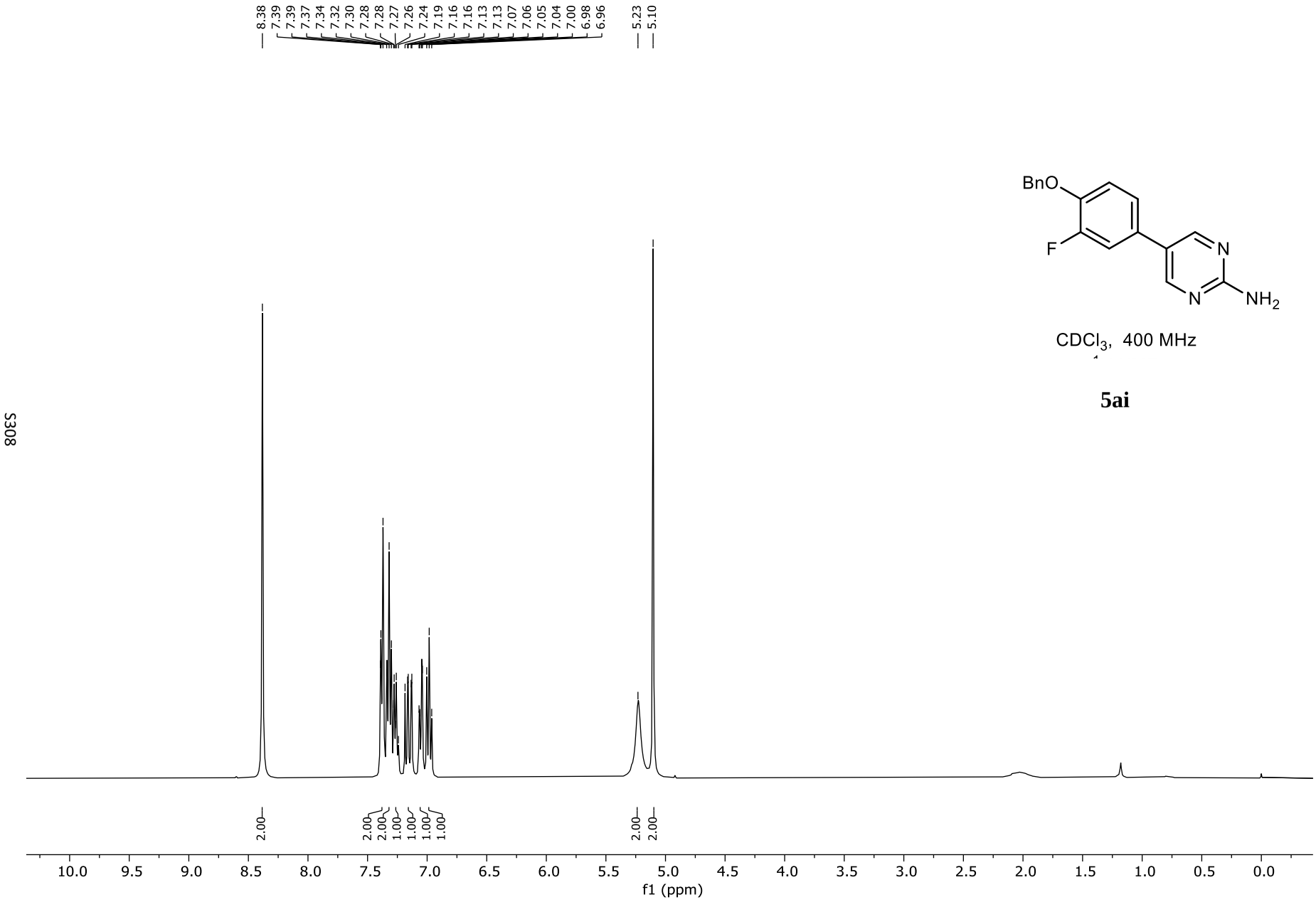

164.31
162.03
158.56
150.14
145.53
145.43
144.34
135.99
131.36
129.01
127.22
116.28
77.27 CDCl3
Ph
N
N
N
N
CDCl3, 100 MHz
13C NMR
5af
S303
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

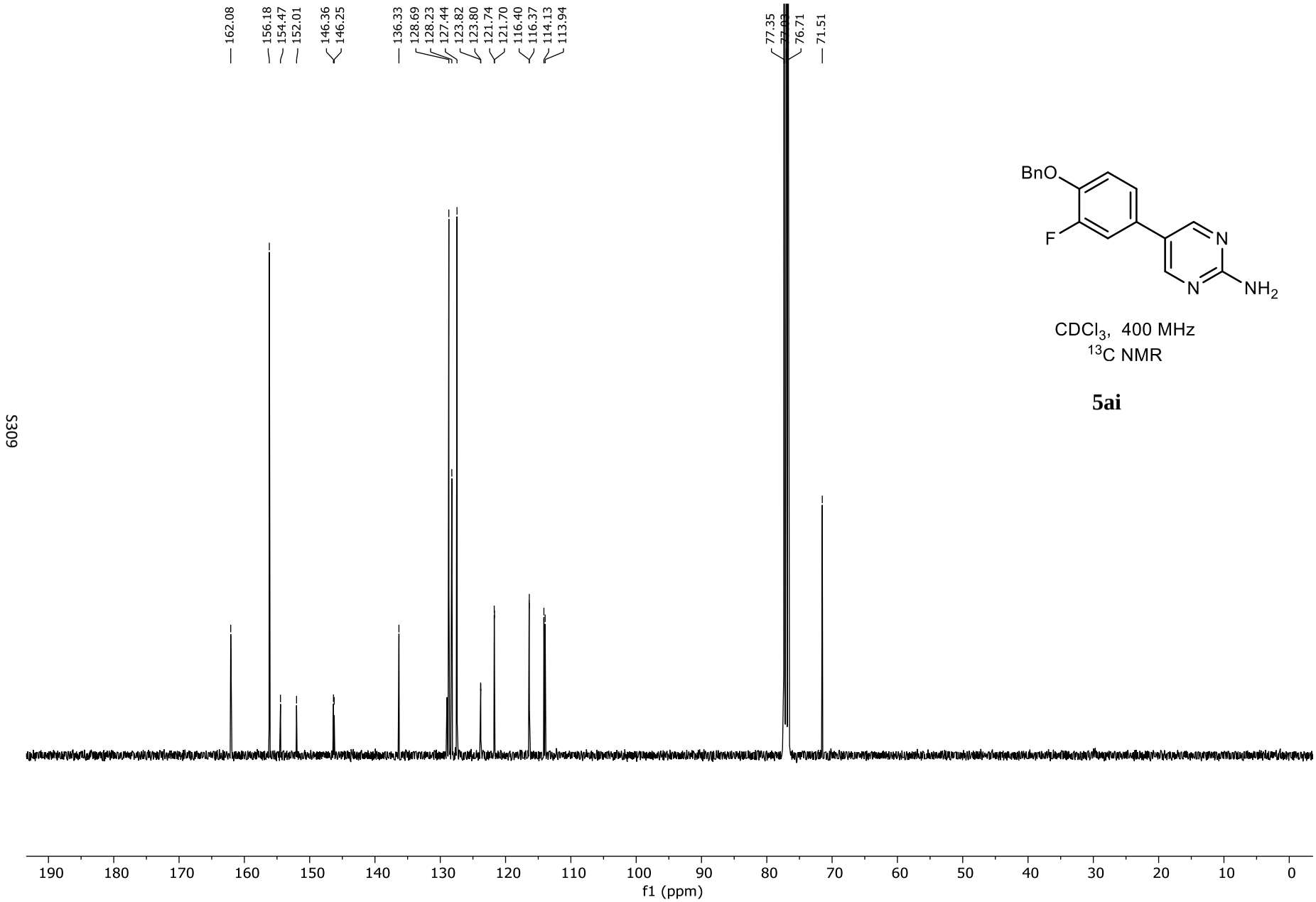

13.52
8.18
8.17
8.17
8.15
8.15
8.14
8.01
7.99
7.39
7.37
7.11
7.09
7.08
3.86
2.50 DMSO-d6
N
N
H
S
MeO
(CD3)2SO, 400 MHz
1H NMR
5ag
1.05
2.06
1.03
1.00
2.01
3.01
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

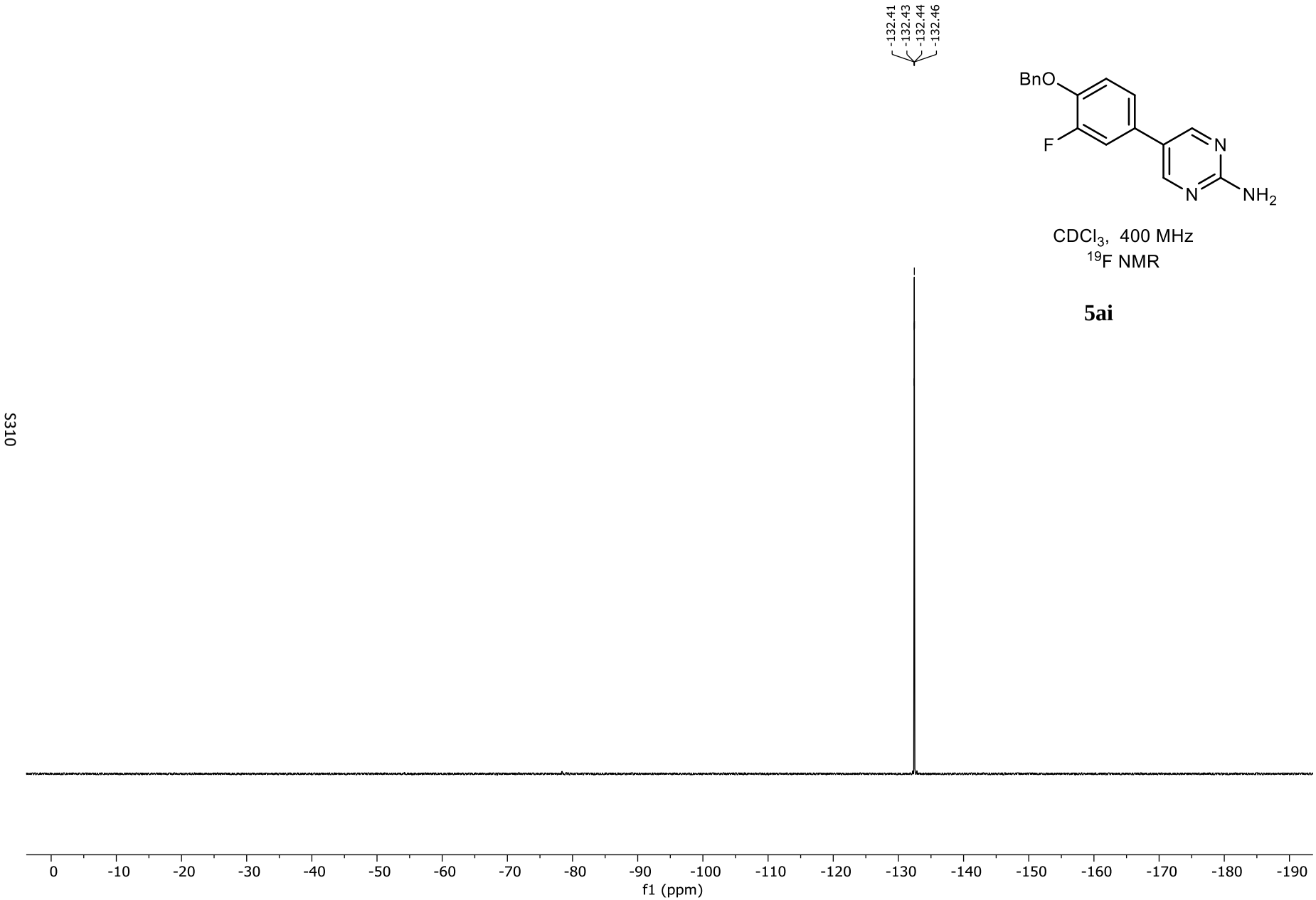

181.14
165.65
163.30
146.85
130.47
127.80
114.90
105.31
56.00
40.00 DMSO-d6
N
N
H
S
MeO
(CD3)2SO, 100 MHz
13C NMR
5ag
S305
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

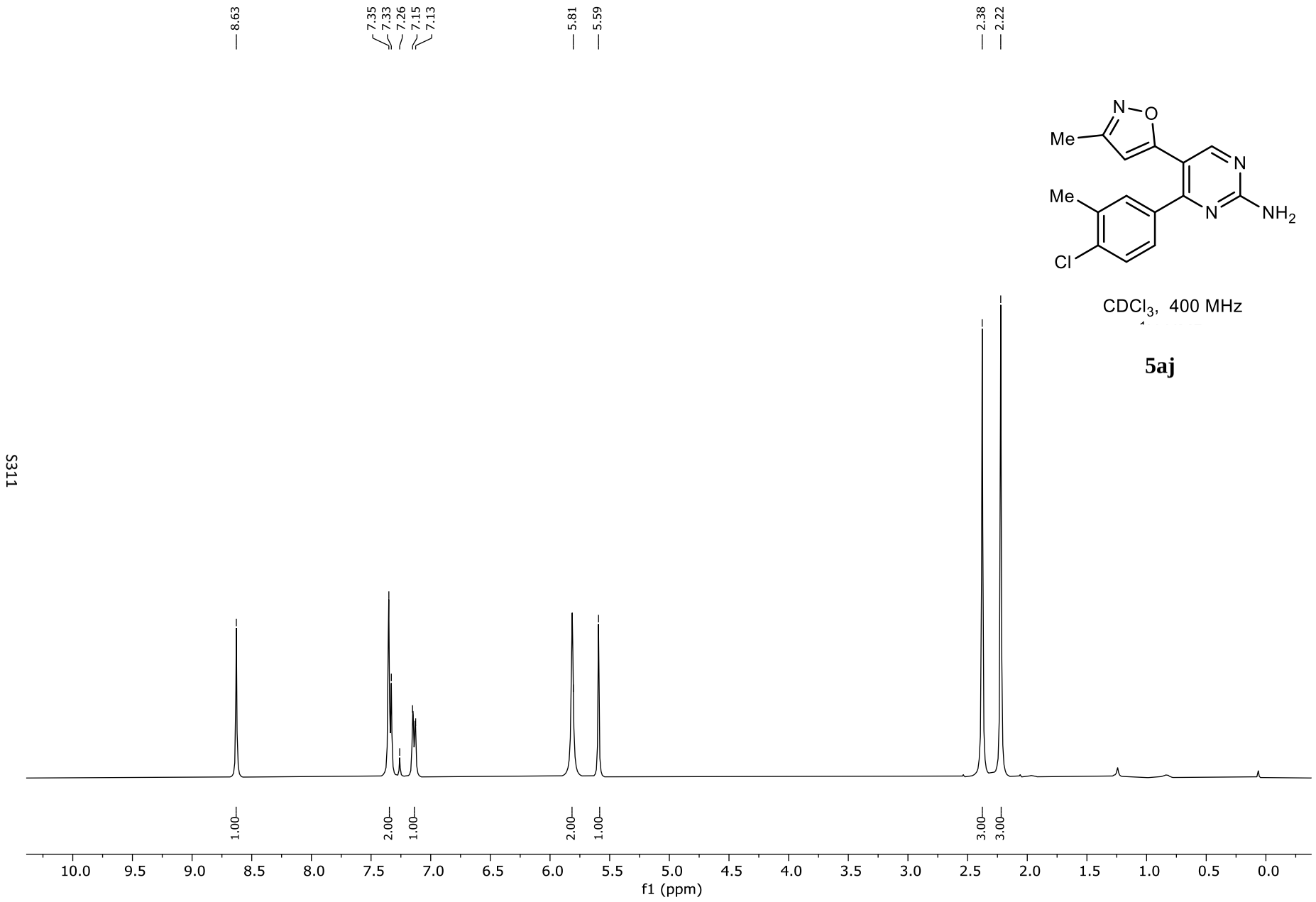

8.53
7.48
7.47
7.44
7.42
7.37
7.35
7.34
7.26 CDCl3
5.52
Ph
N
N
NH2
CDCl3, 400 MHz
1H NMR
5ah
S306
2.00
4.01
1.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

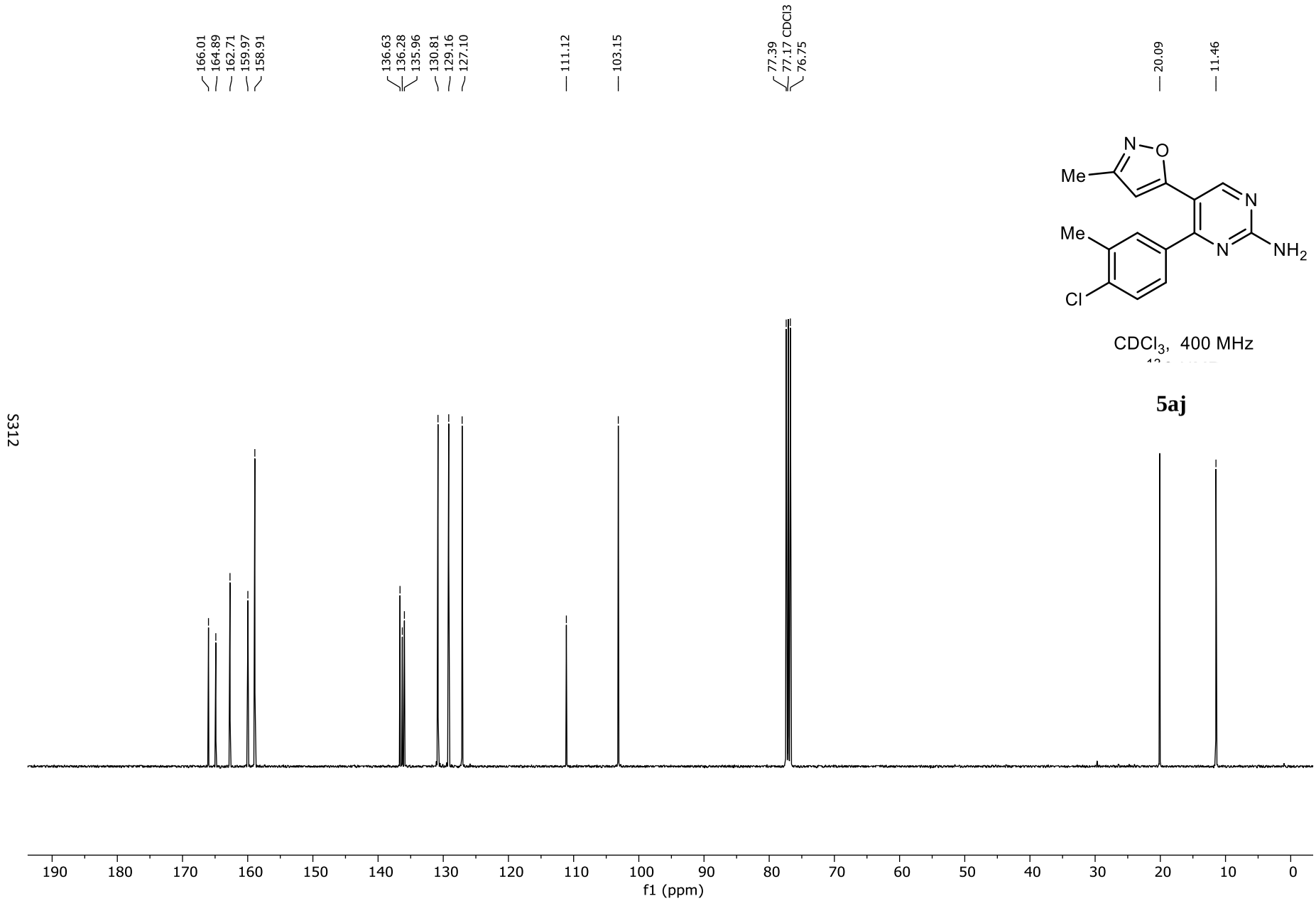

162.39
156.50
135.30
129.17
127.57
126.05
124.89
77.07 CDCl3
Ph
N
N
NH2
CDCl3, 100 MHz
13C NMR
5ah
S307
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

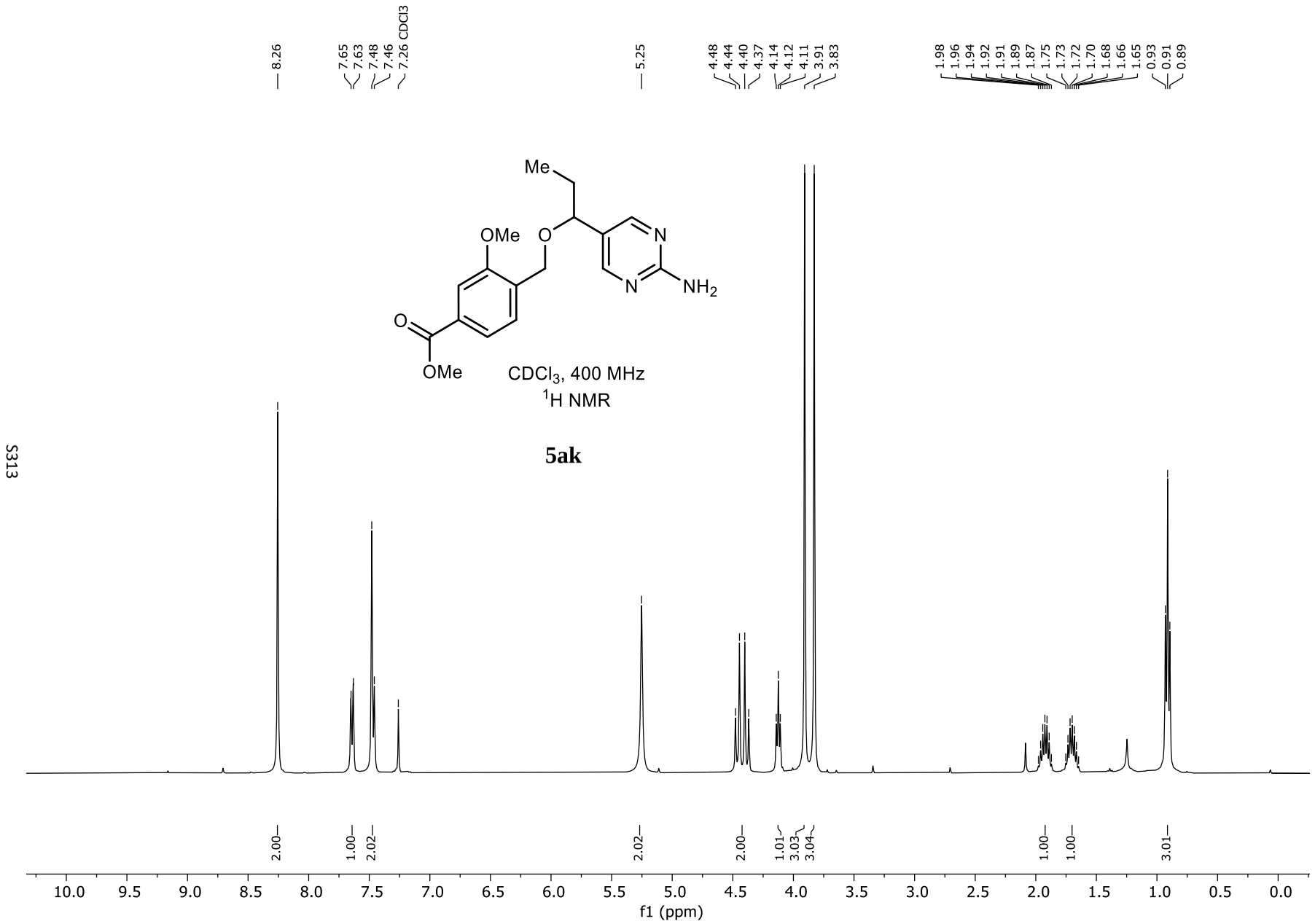

8.38
7.39
7.39
7.37
7.34
7.32
7.30
7.28
7.28
7.27
7.26
7.24
7.19
7.16
7.16
7.13
7.13
7.07
7.06
7.05
7.04
7.00
6.98
6.96
5.23
5.10
BnO
F
N
N
NH2
CDCl3, 400 MHz
5ai
S308
2.00
2.00
2.00
1.00
1.00
1.00
2.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

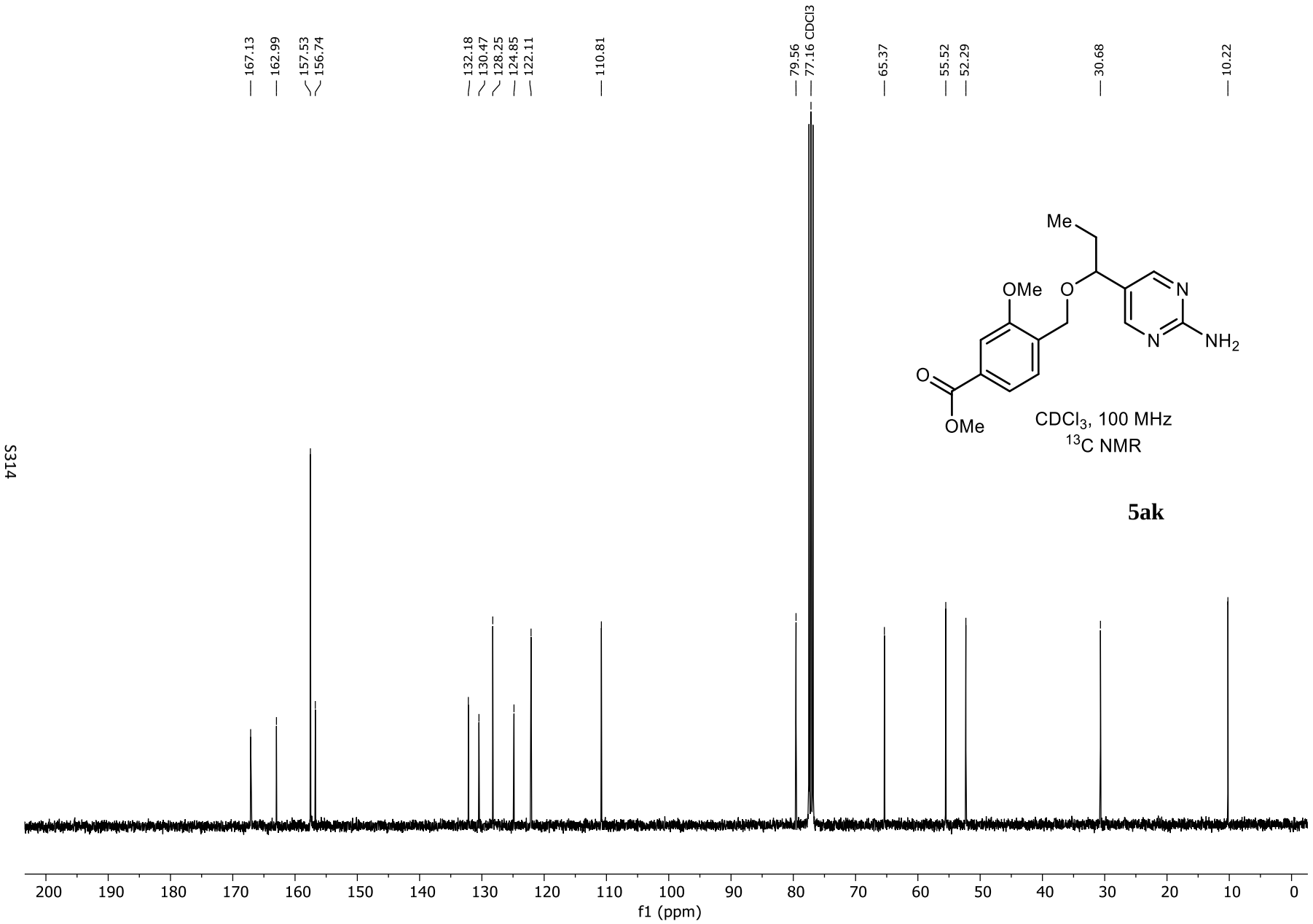

162.08
156.18
154.47
152.01
146.36
146.25
136.33
128.69
128.23
127.44
123.82
123.80
121.74
121.70
116.40
116.37
114.13
113.94
77.35
77.03
76.71
71.51
BnO
F
N
N
NH2
CDCl3, 400 MHz
13C NMR
5ai
S309
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

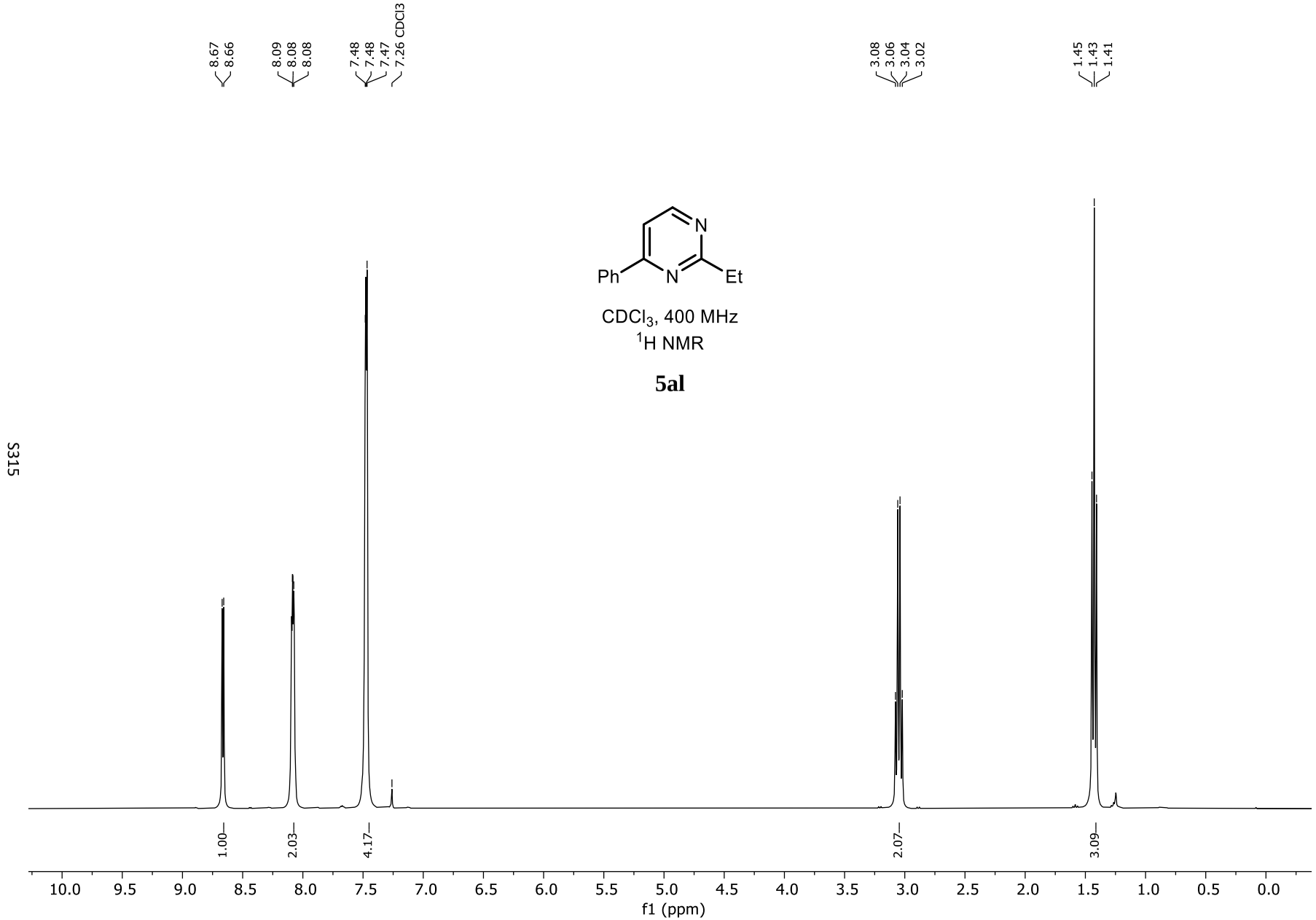

-132.41
-132.43
-132.44
-132.46
BnO
F
N
N
NH2
CDCl3, 400 MHz
19F NMR
5ai
S310
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

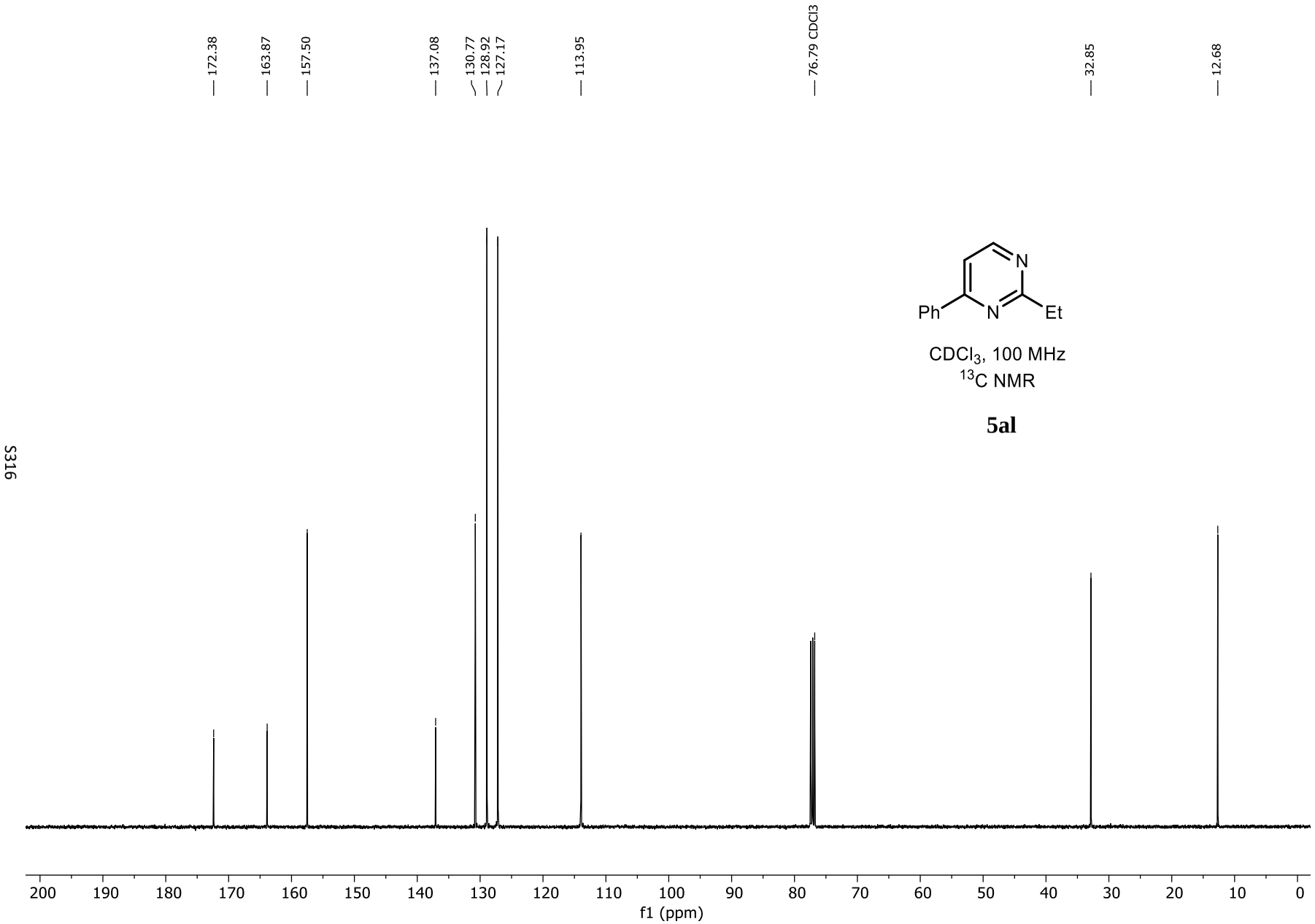

8.63
7.35
7.33
7.26
7.15
7.13
5.81
5.59
2.38
2.22
Me
N
O
N
Me
N
NH2
Cl
CDCl3, 400 MHz
5aj
1.00
2.00
1.00
2.00
1.00
3.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

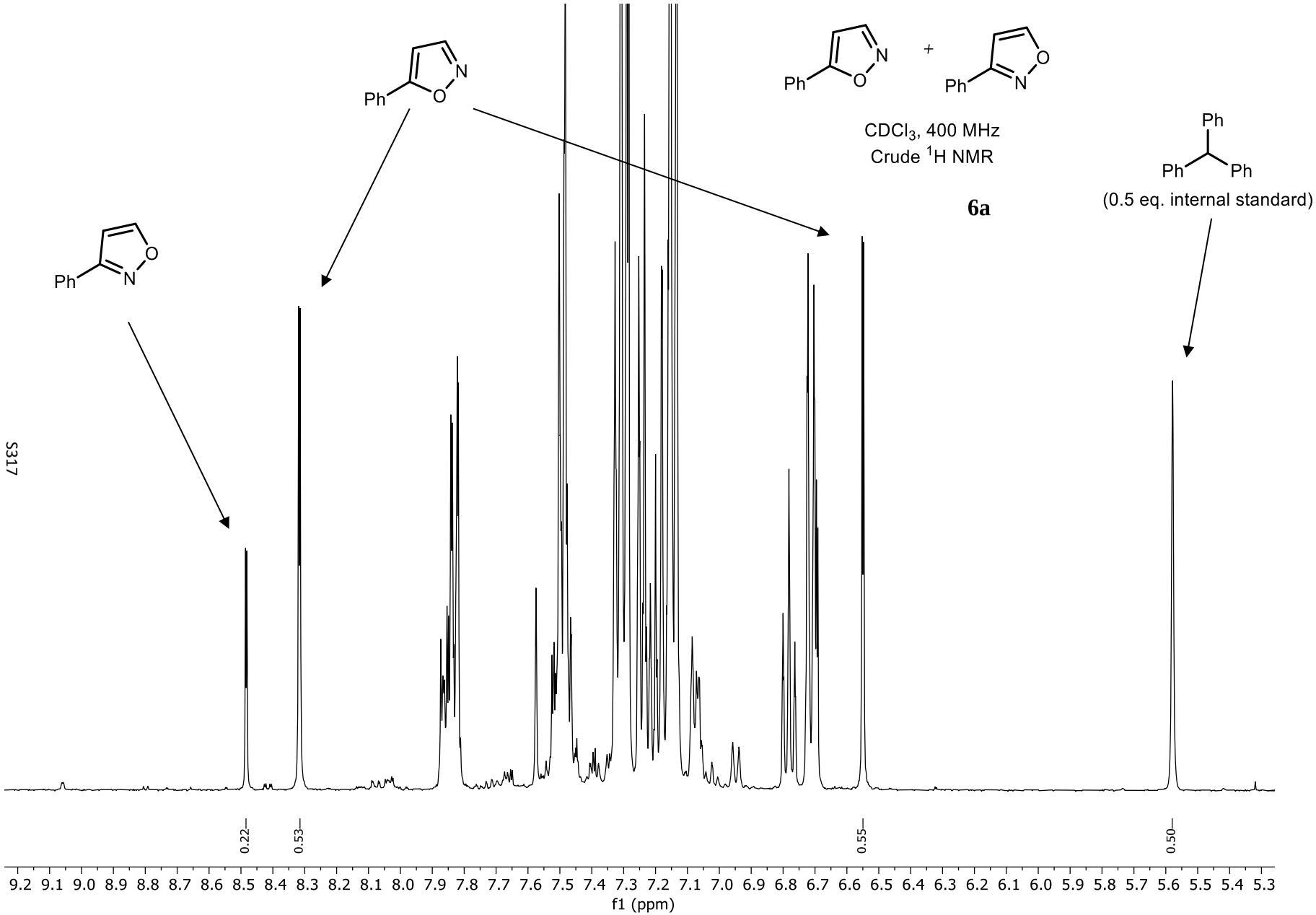

166.01
164.89
162.71
159.97
158.91
136.63
136.28
135.96
130.81
129.16
127.10
111.12
103.15
77.39
77.17 CDCl3
76.75
20.09
11.46
N
O
Me
N
Me
N
NH2
Cl
CDCl3, 400 MHz
5aj
S312
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

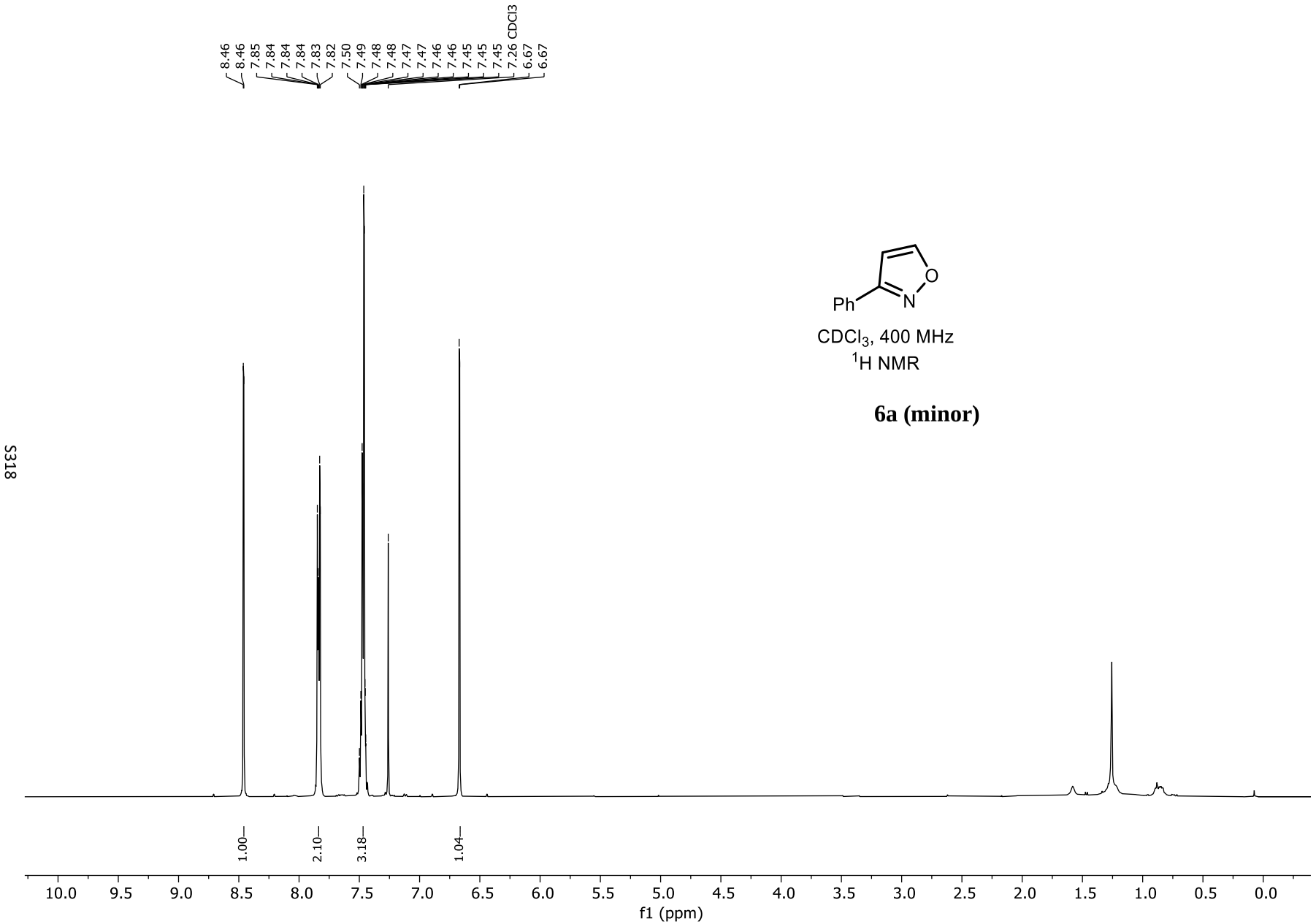

8.26
7.65
7.63
7.48
7.46
7.26 CDCl3
5.25
4.48
4.44
4.40
4.37
4.14
4.12
4.11
3.91
3.83
1.98
1.96
1.94
1.92
1.91
1.89
1.87
1.75
1.73
1.72
1.70
1.68
1.66
1.65
0.93
0.91
0.89
Me
OMe
O
N
N
NH2
O
OMe
CDCl3, 400 MHz
1H NMR
5ak
2.00
1.00
2.02
2.02
2.00
1.01
3.03
3.04
1.00
1.00
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

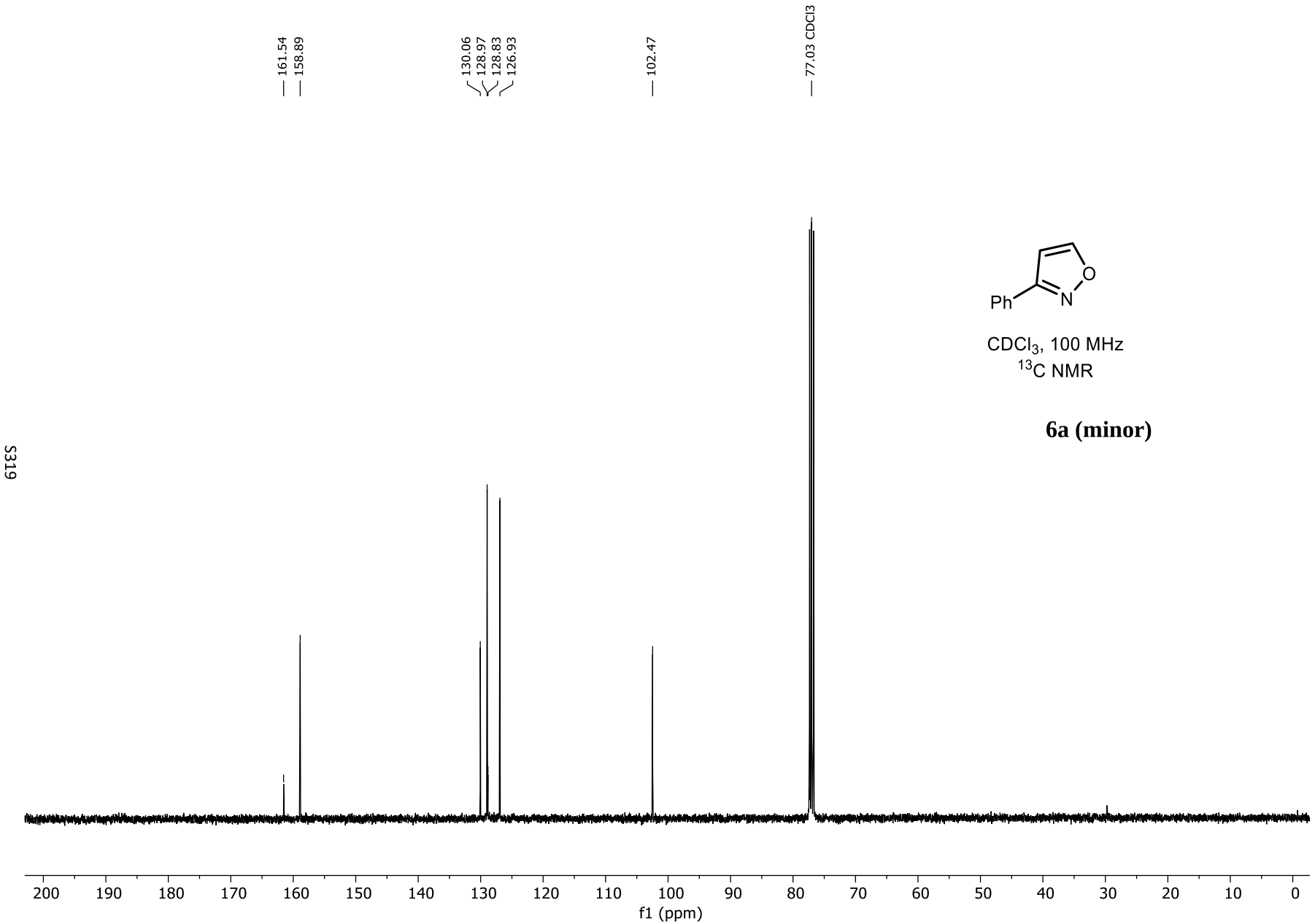

167.13
162.99
157.53
156.74
132.18
130.47
128.25
124.85
122.11
110.81
79.56
77.16 CDCl3
65.37
55.52
52.29
30.68
10.22
Me
OMe
O
N
N
NH2
O
OMe
CDCl3, 100 MHz
13C NMR
5ak
f1 (ppm)

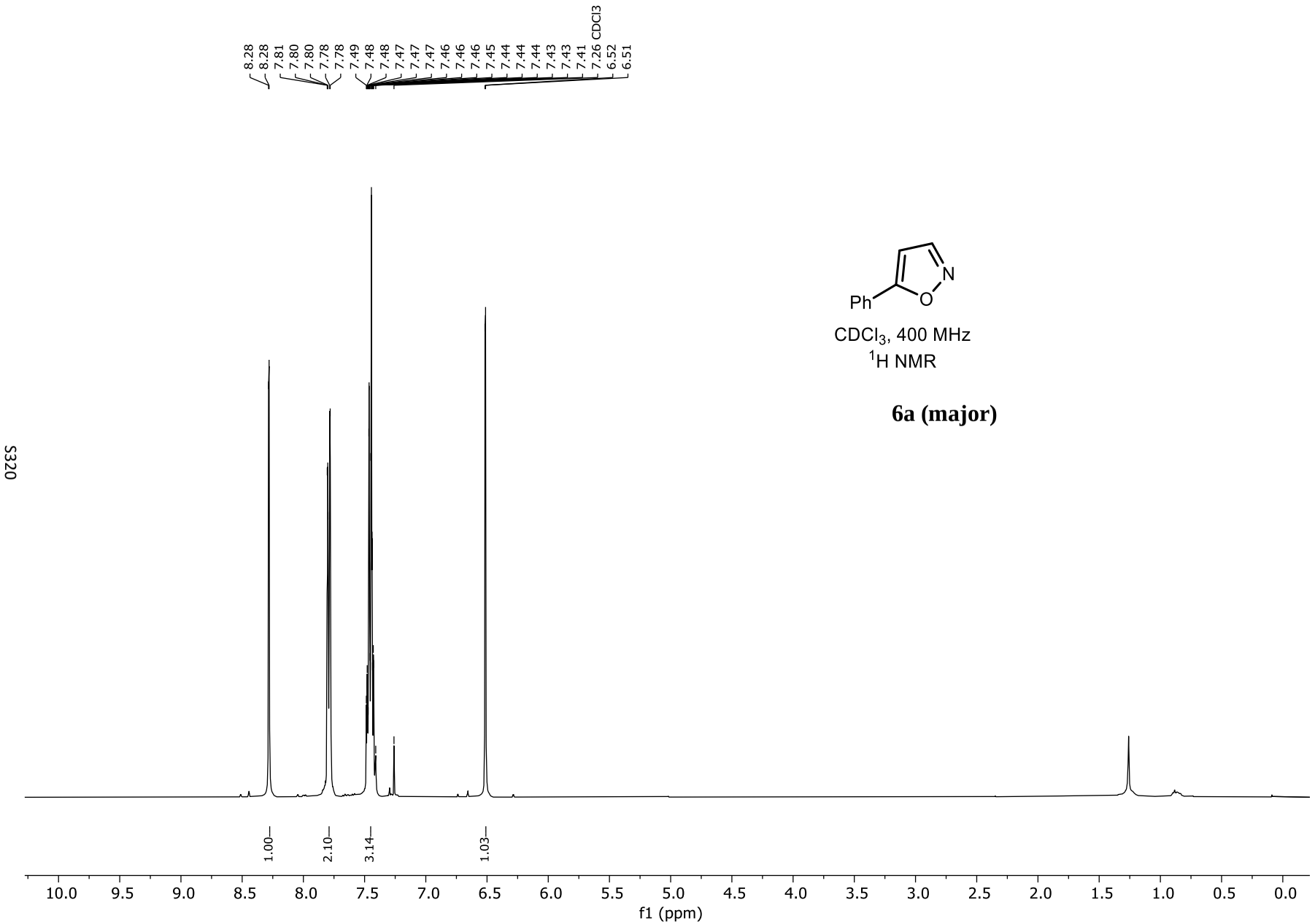

8.67
8.66
8.09
8.08
8.08
7.48
7.48
7.47
7.26 CDCl3
3.08
3.06
3.04
3.02
1.45
1.43
1.41
N
Ph
N
Et
CDCl3, 400 MHz
1H NMR
5al
1.00
2.03
4.17
2.07
3.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

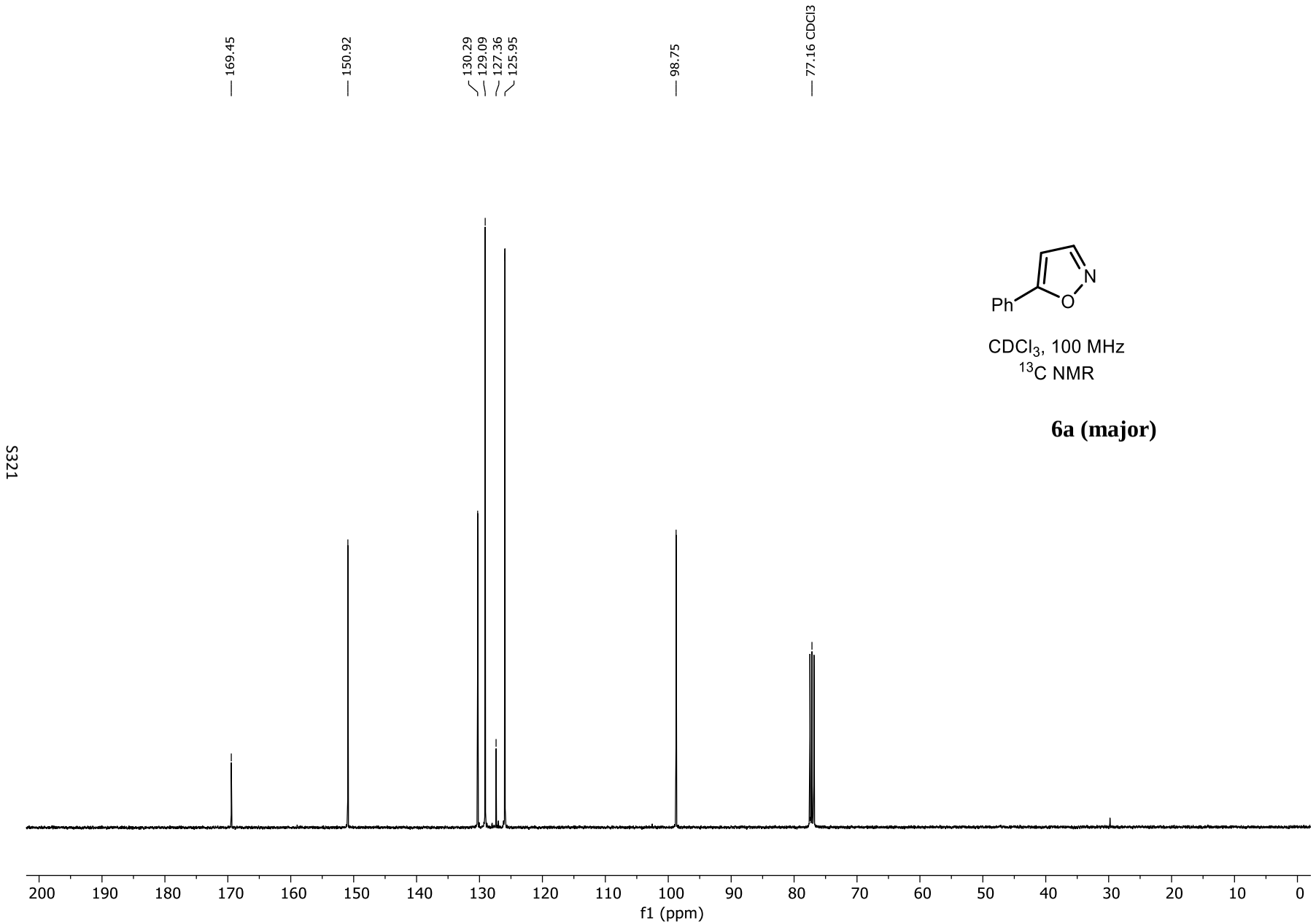

172.38
163.87
157.50
137.08
130.77
128.92
127.17
113.95
76.79 CDCl3
32.85
12.68
N
Ph
N
Et
CDCl3, 100 MHz
13C NMR
5al
S316
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

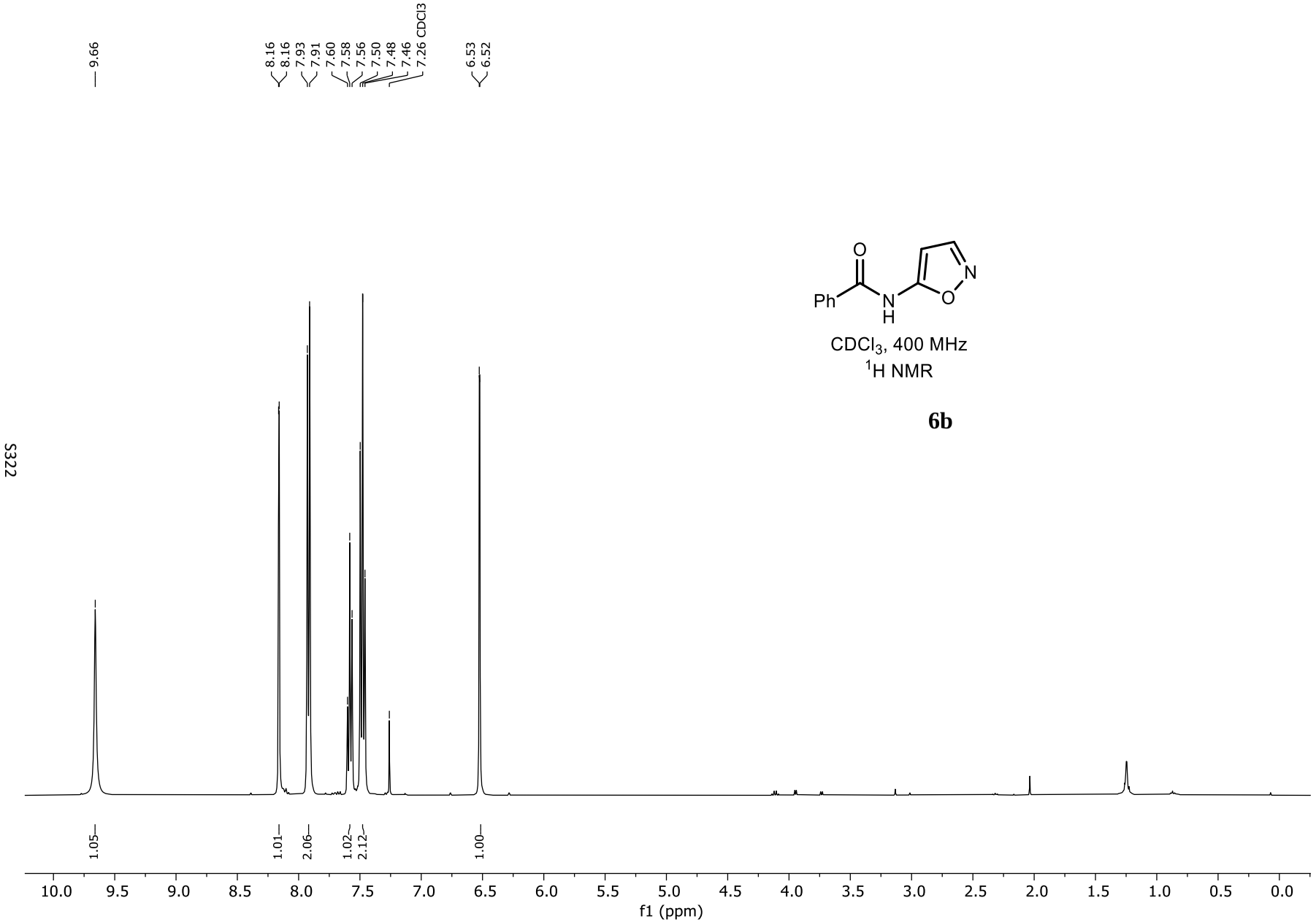

Ph
N
O
+
Ph
O
N
CDCl3, 400 MHz
Crude 1H NMR
6a
Ph
Ph
Ph
(0.5 eq. internal standard)
Ph
N
O
S317
0.22
0.53
0.55
0.50
9.2 9.1 9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3
f1 (ppm)


8.46
8.46
7.85
7.84
7.84
7.84
7.83
7.82
7.50
7.49
7.48
7.48
7.47
7.47
7.46
7.46
7.45
7.45
7.45
7.26 CDCl3
6.67
6.67
S318
Ph
O
N
CDCl3, 400 MHz
1H NMR
6a (minor)
1.00
2.10
3.18
1.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.54
158.89
130.06
128.97
128.83
126.93
102.47
77.03 CDCl3
Ph
O
N
CDCl3, 100 MHz
13C NMR
6a (minor)
f1 (ppm)


8.28
8.28
7.81
7.80
7.80
7.78
7.78
7.49
7.48
7.48
7.47
7.47
7.47
7.46
7.46
7.46
7.45
7.44
7.44
7.44
7.43
7.41
7.26 CDCl3
6.52
6.51
S320
Ph
O
N
CDCl3, 400 MHz
1H NMR
6a (major)
1.00
2.10
3.14
1.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

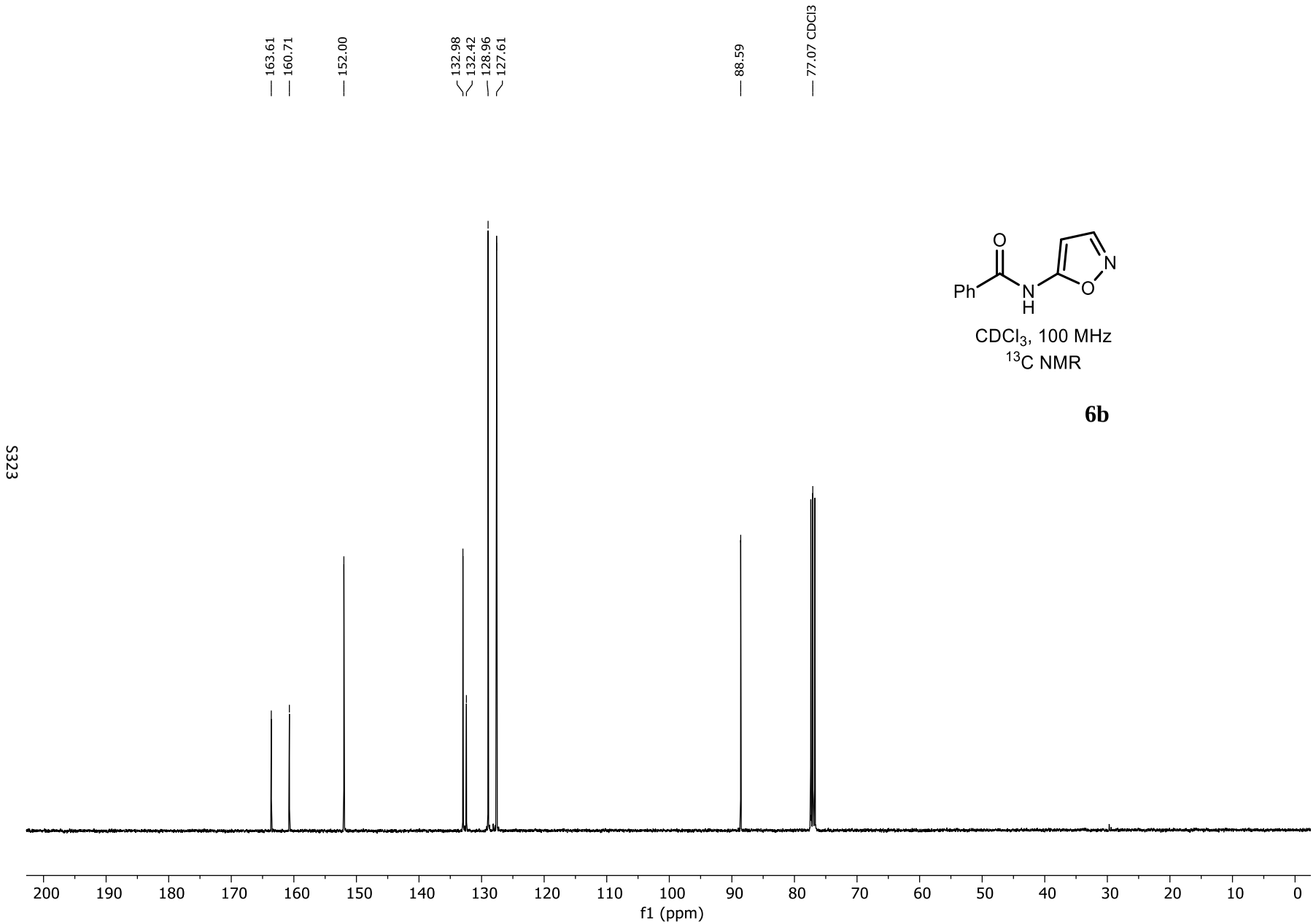

169.45
150.92
130.29
129.09
127.36
125.95
98.75
77.16 CDCl3
Ph
O
N
CDCl3, 100 MHz
13C NMR
6a (major)
S321
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

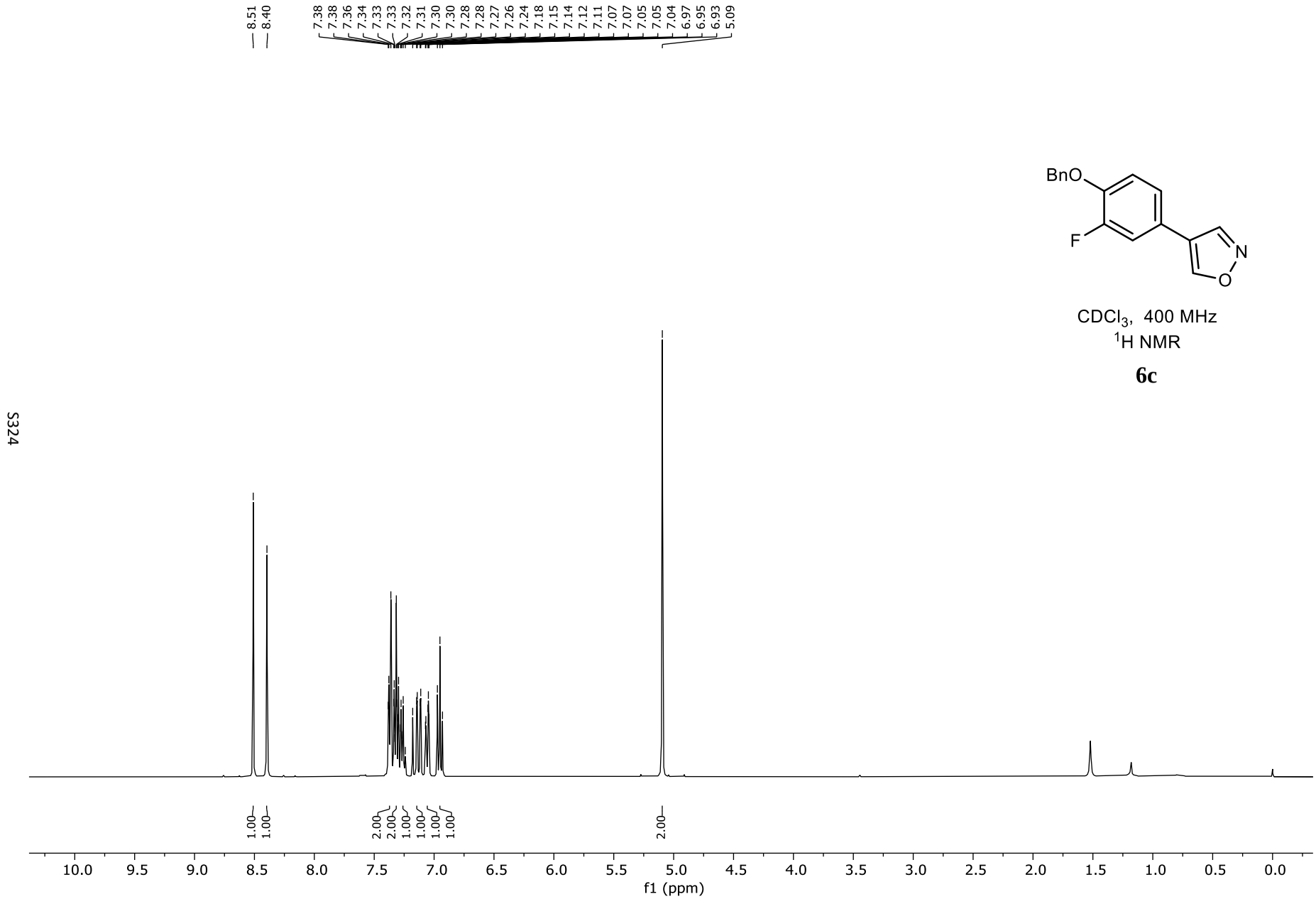


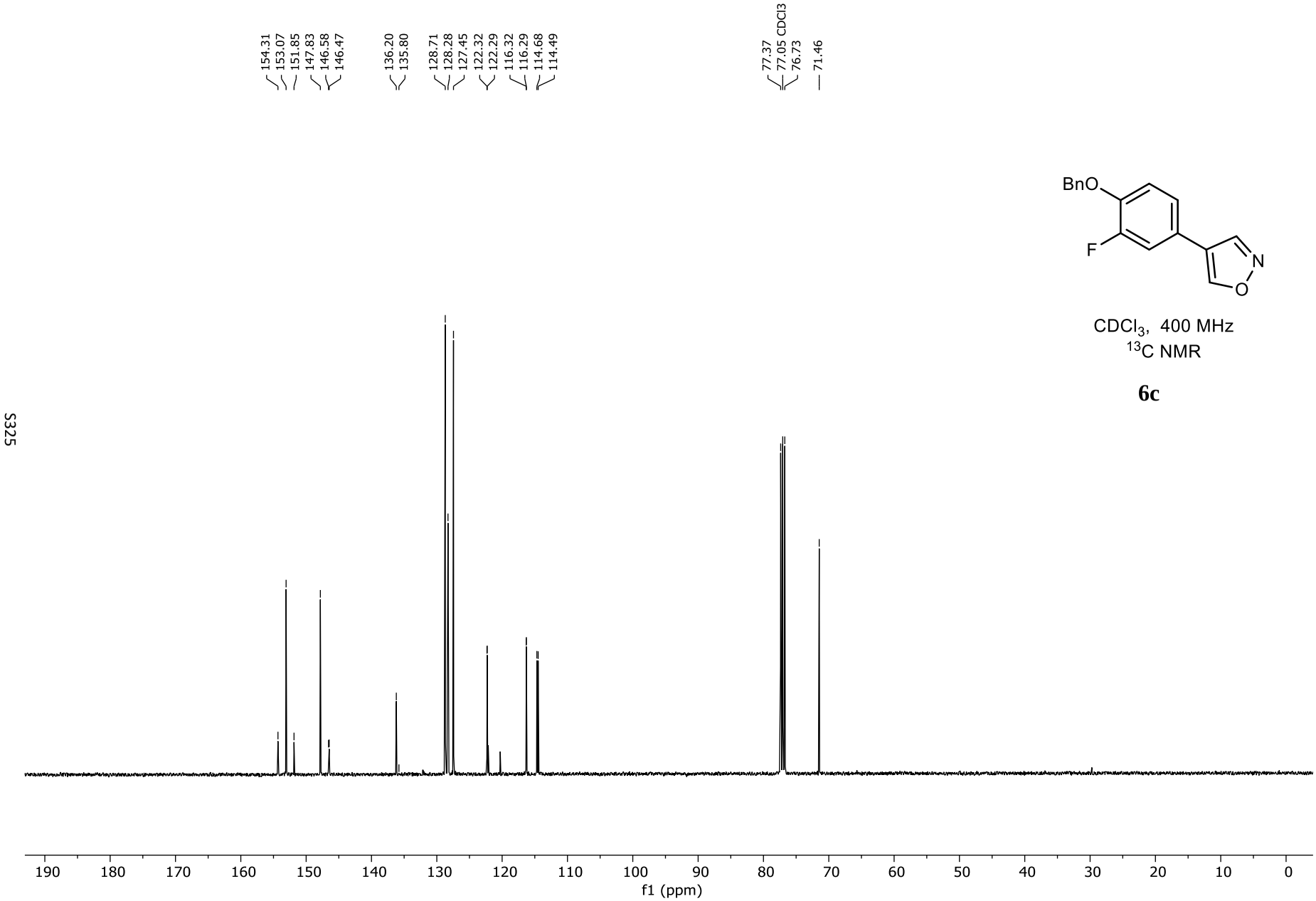
$CDCl_3$, 400 MHz

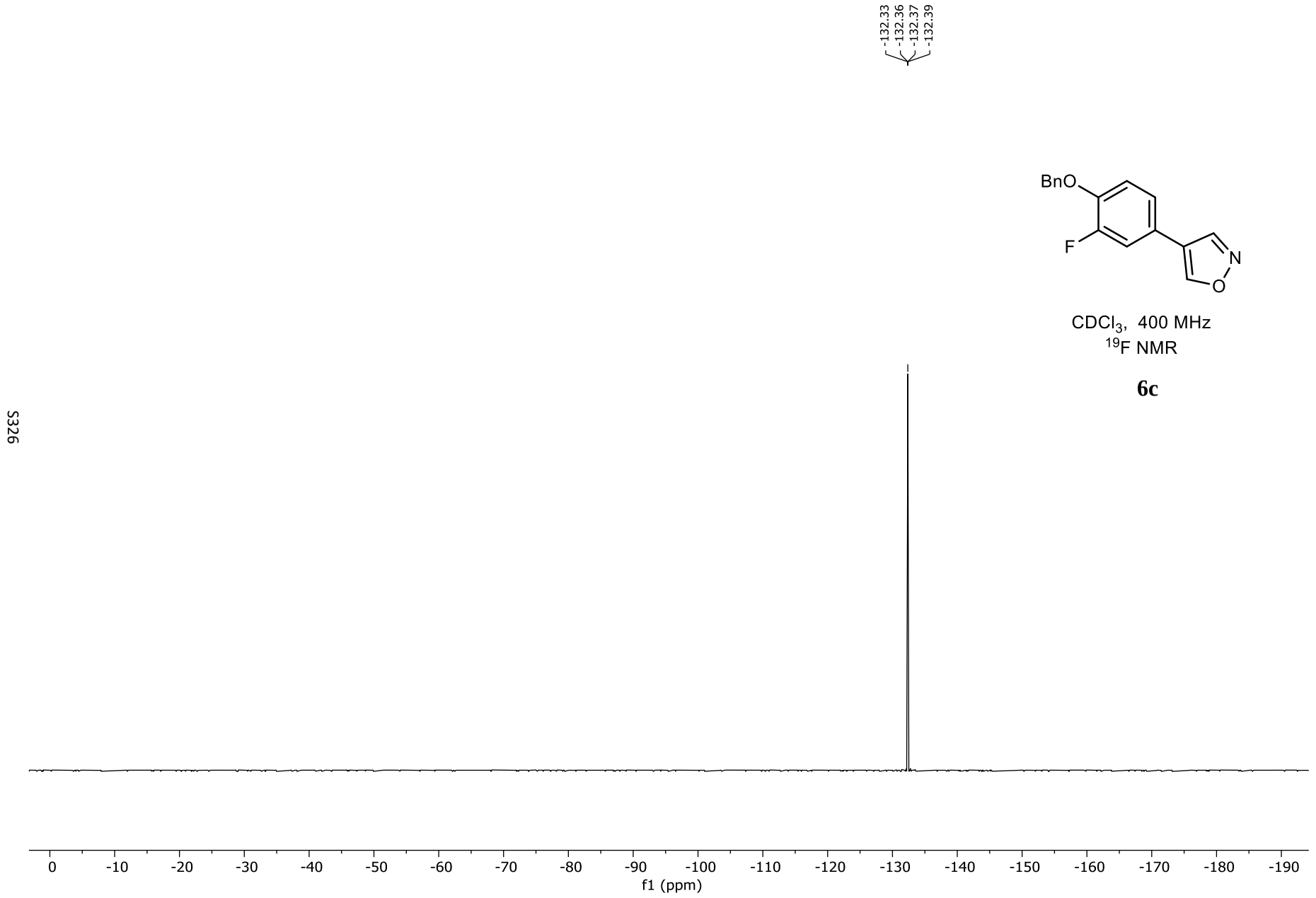
^1H NMR

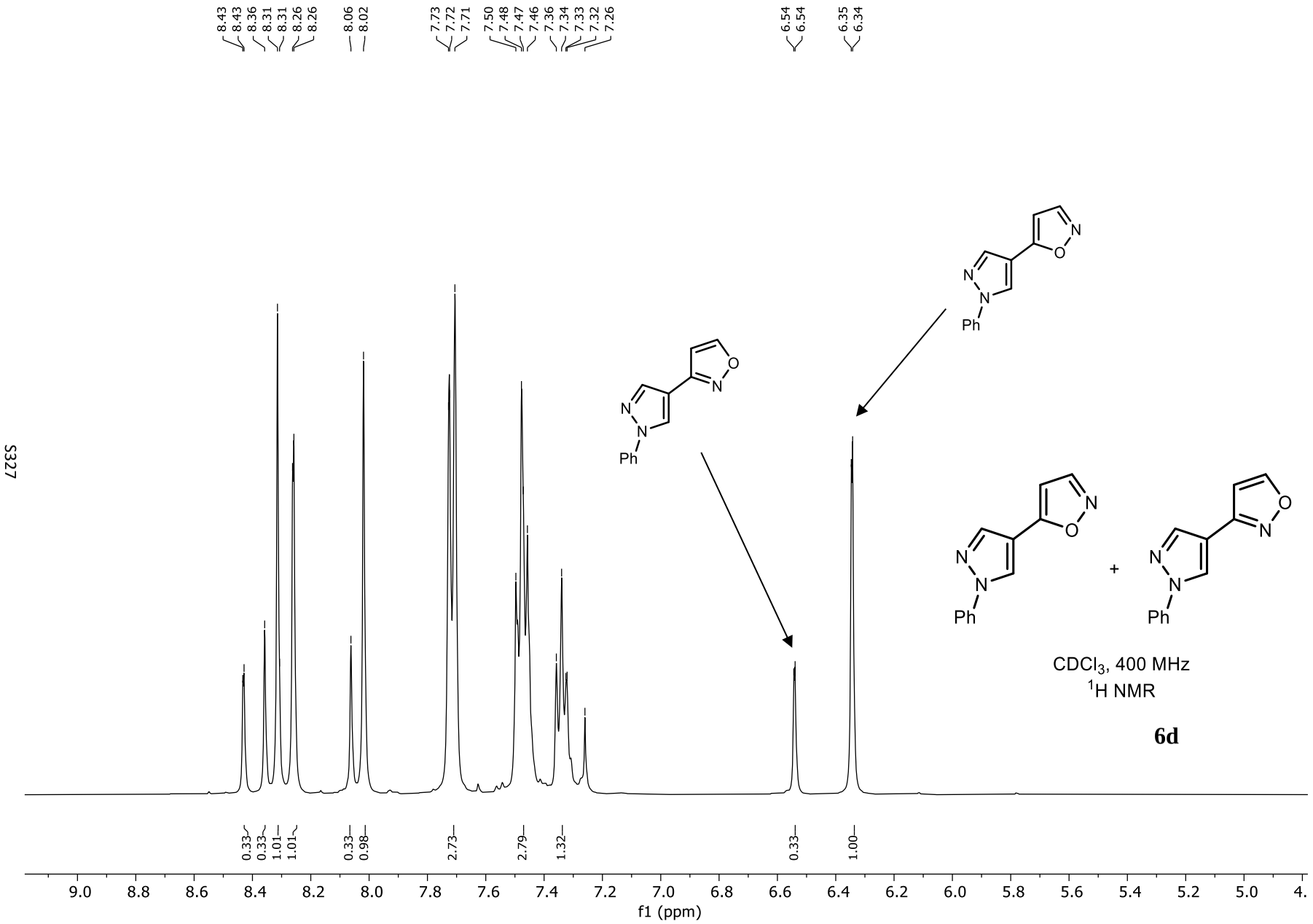
6b

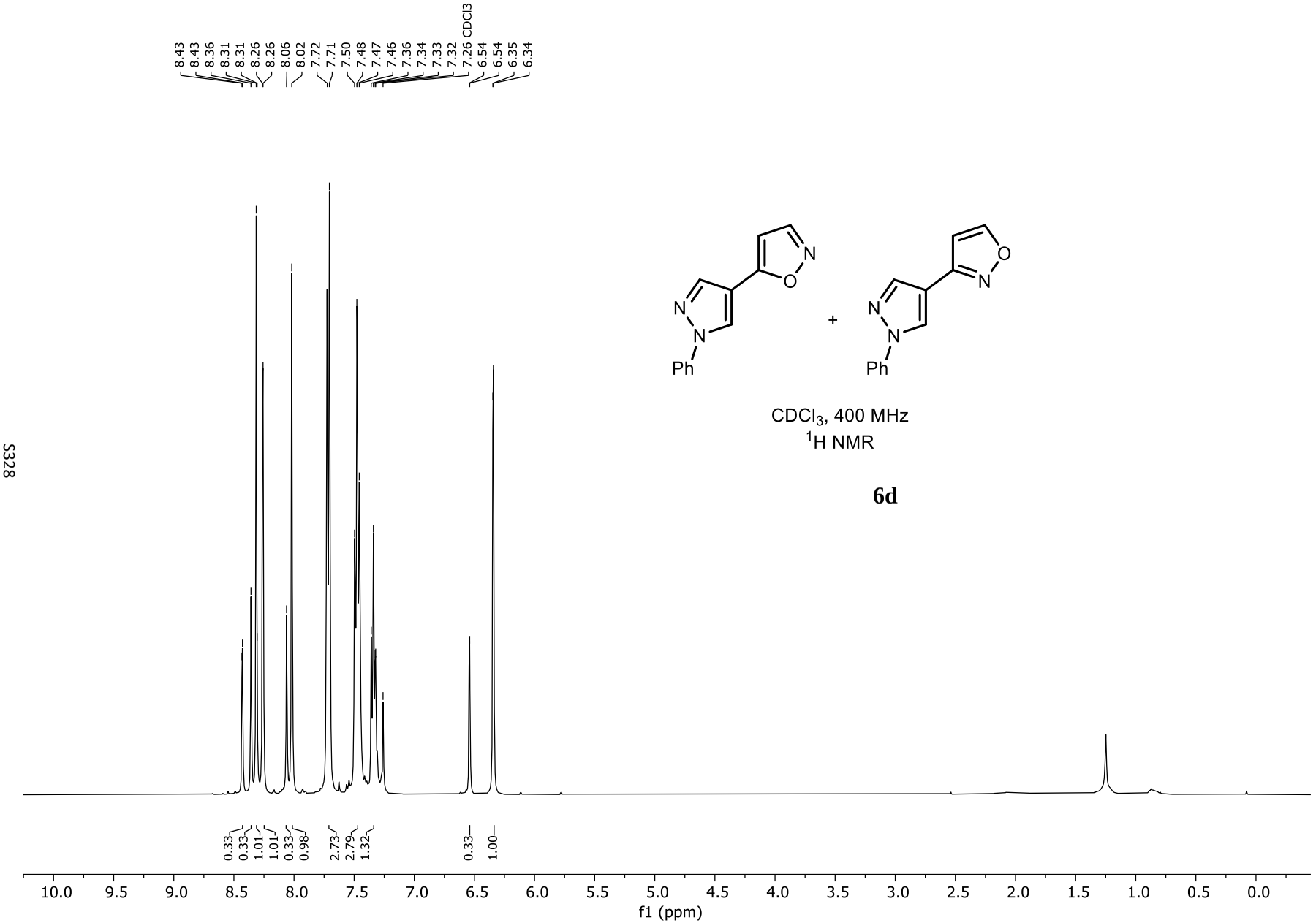

163.61
160.71
152.00
132.98
132.42
128.96
127.61
88.59
77.07 CDCl3
O
N
Ph
N
H
O
CDCl3, 100 MHz
13C NMR
6b
S323
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

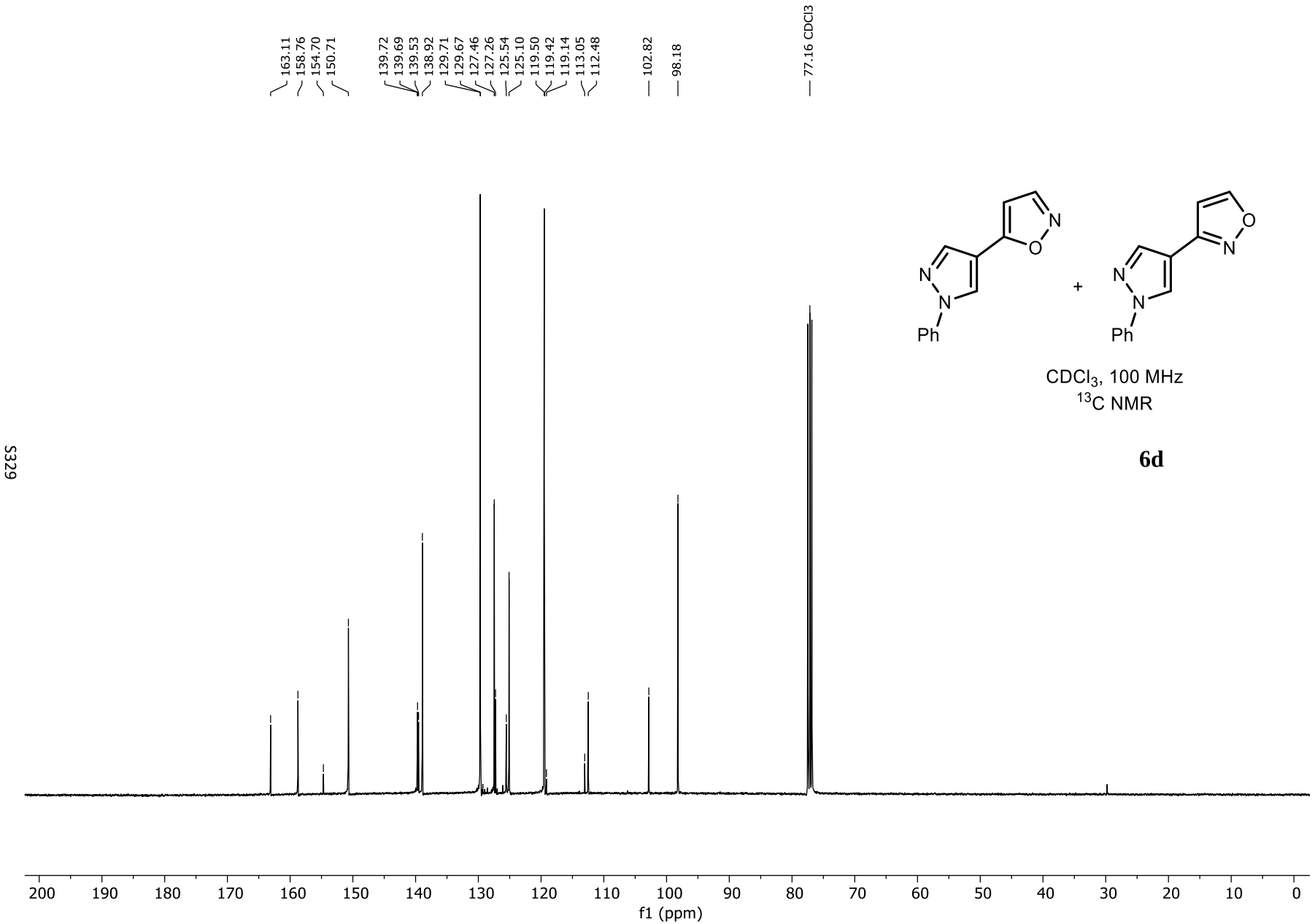

8.51
8.40
7.38
7.38
7.36
7.34
7.33
7.33
7.32
7.31
7.30
7.30
7.28
7.28
7.27
7.26
7.24
7.18
7.15
7.14
7.12
7.11
7.07
7.07
7.05
7.05
7.04
6.97
6.95
6.93
5.09
BnO
F
N
O
CDCl3, 400 MHz
1H NMR
6c
1.00
1.00
2.00
2.00
1.00
1.00
1.00
1.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

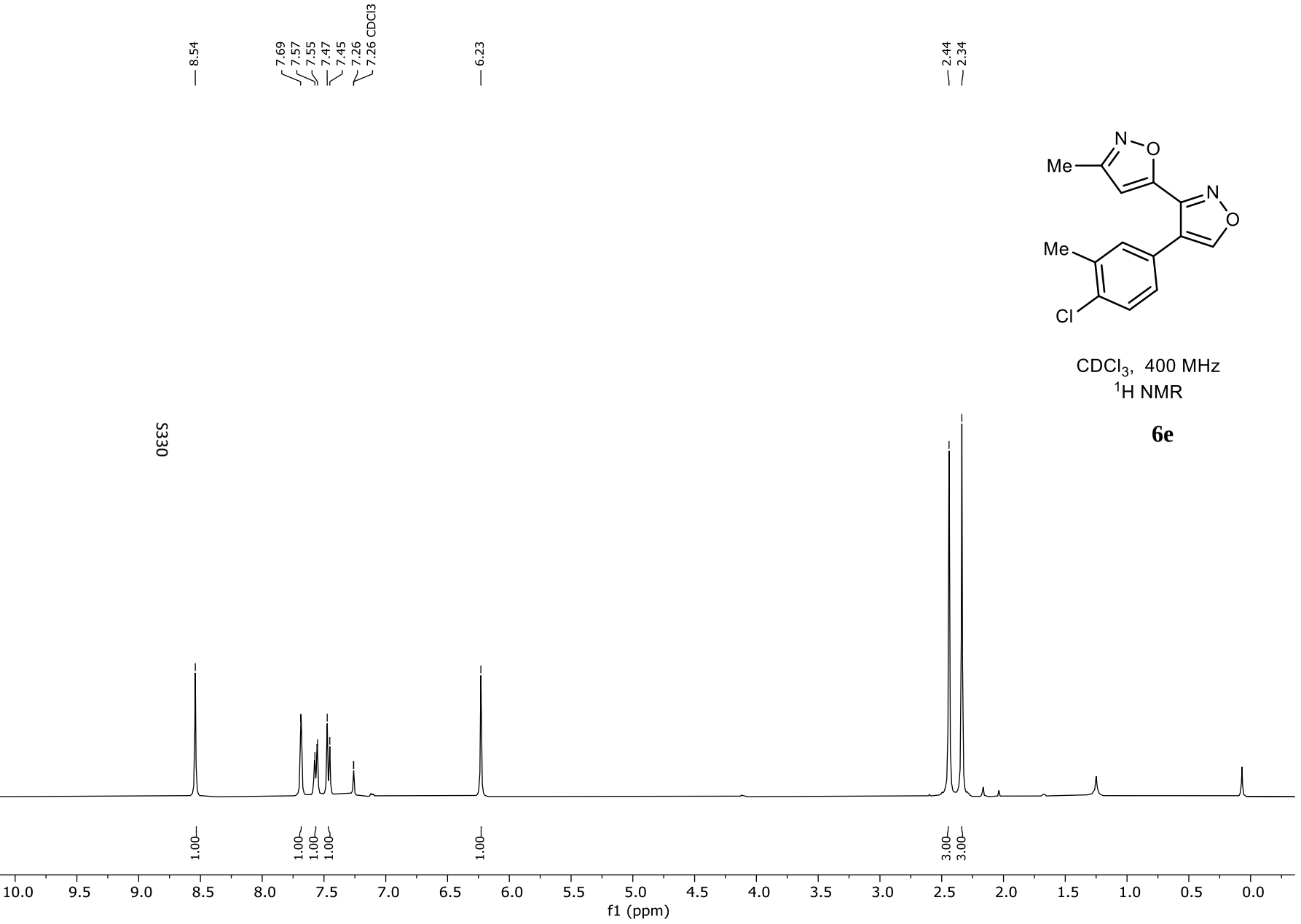

154.31
153.07
151.85
147.83
146.58
146.47
136.20
135.80
128.71
128.28
127.45
122.32
122.29
116.32
116.29
114.68
114.49
77.37
77.05 CDCl3
76.73
71.46
BnO
F
N
O
CDCl3, 400 MHz
13C NMR
6c
S325
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

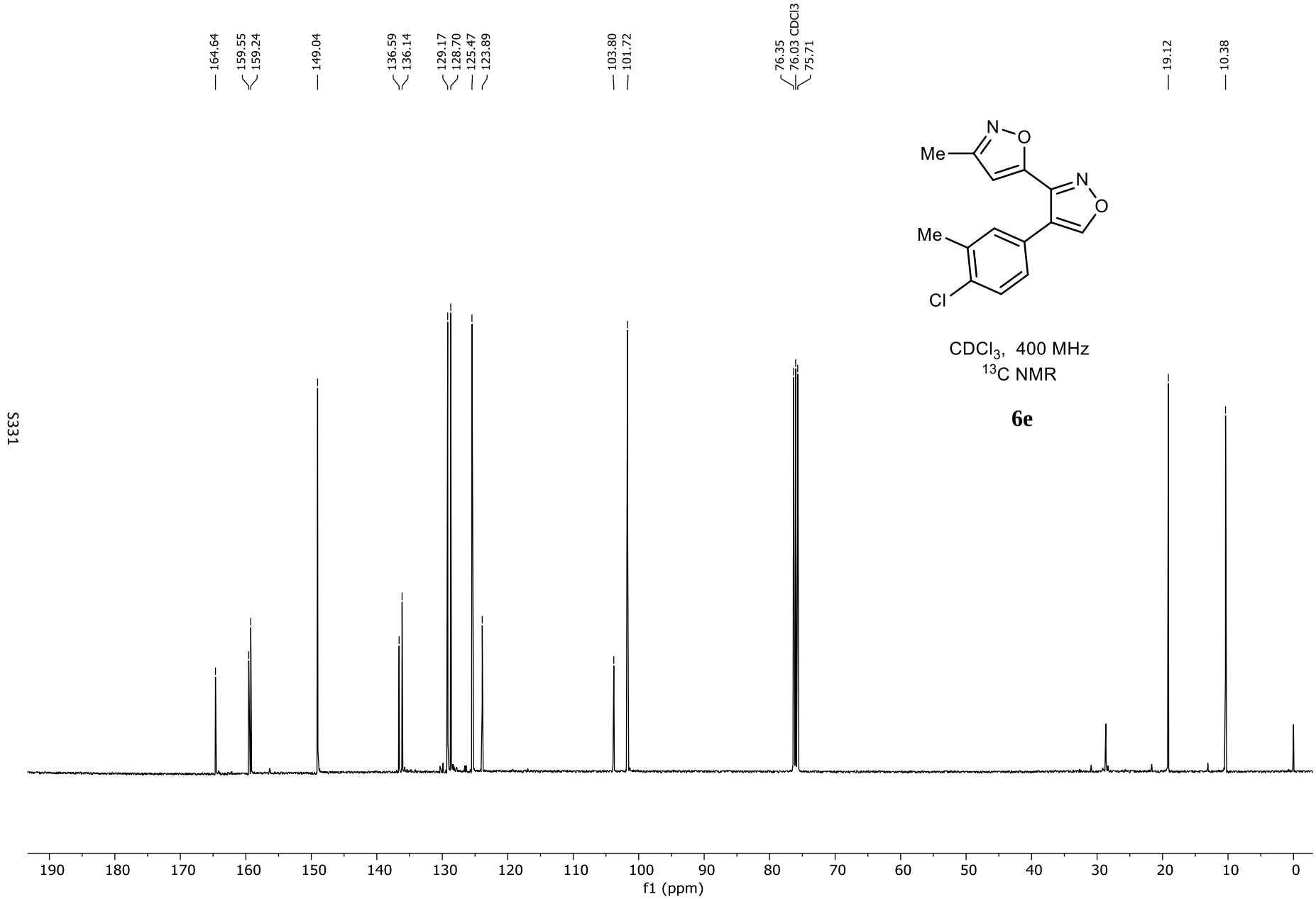

-132.33
-132.36
-132.37
-132.39
BnO
F
N
O
CDCl3, 400 MHz
19F NMR
6c
S326
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

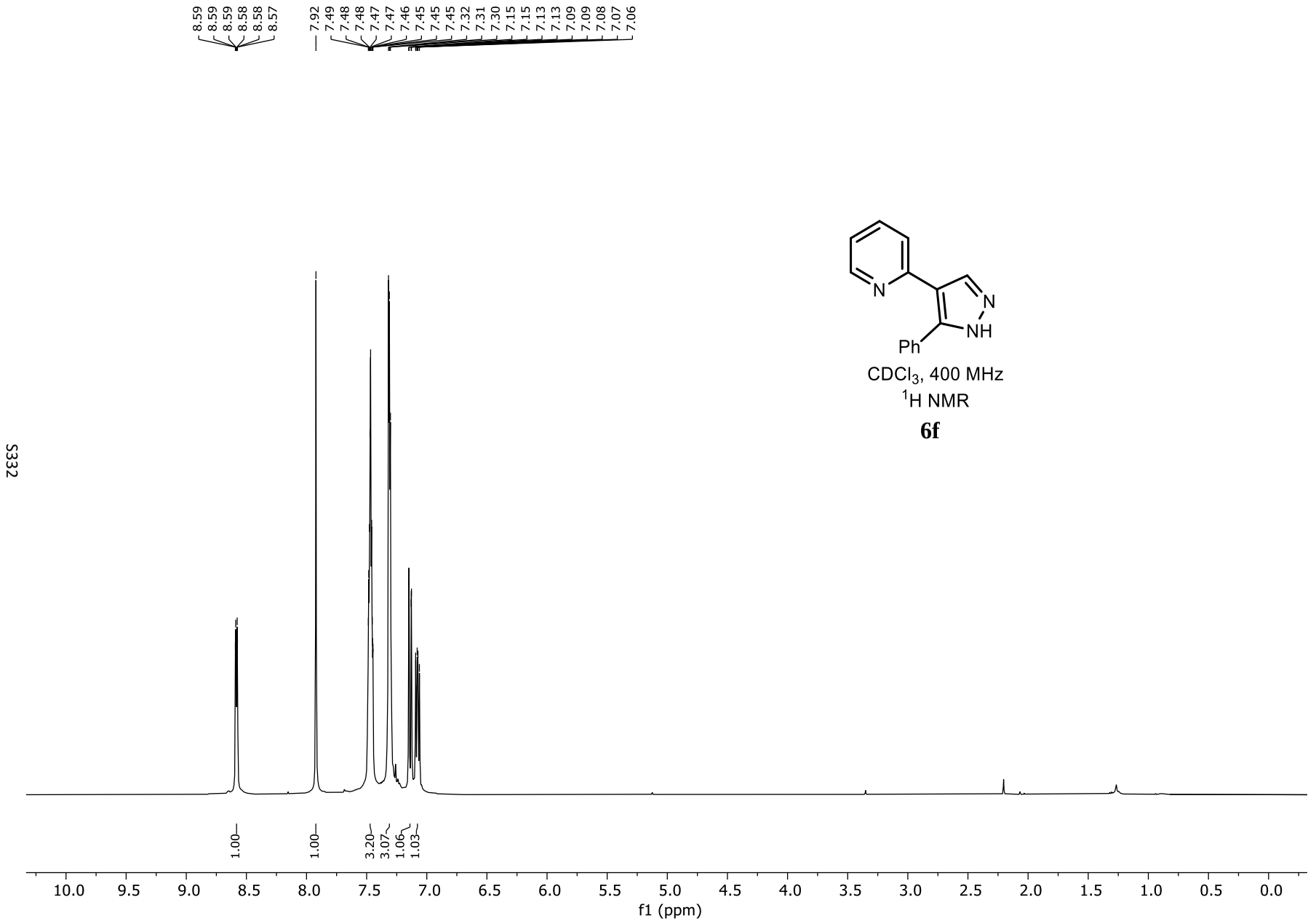

8.43
8.43
8.36
8.31
8.31
8.26
8.26
8.06
8.02
7.73
7.72
7.71
7.50
7.48
7.47
7.46
7.36
7.34
7.33
7.32
7.26
6.54
6.54
6.35
6.34
0.33
0.33
1.01
1.01
0.33
0.98
2.73
2.79
1.32
0.33
1.00
9.0
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.
f1 (ppm)
Ph
Ph
Ph
Ph
+
CDCl3, 400 MHz
1H NMR
6d

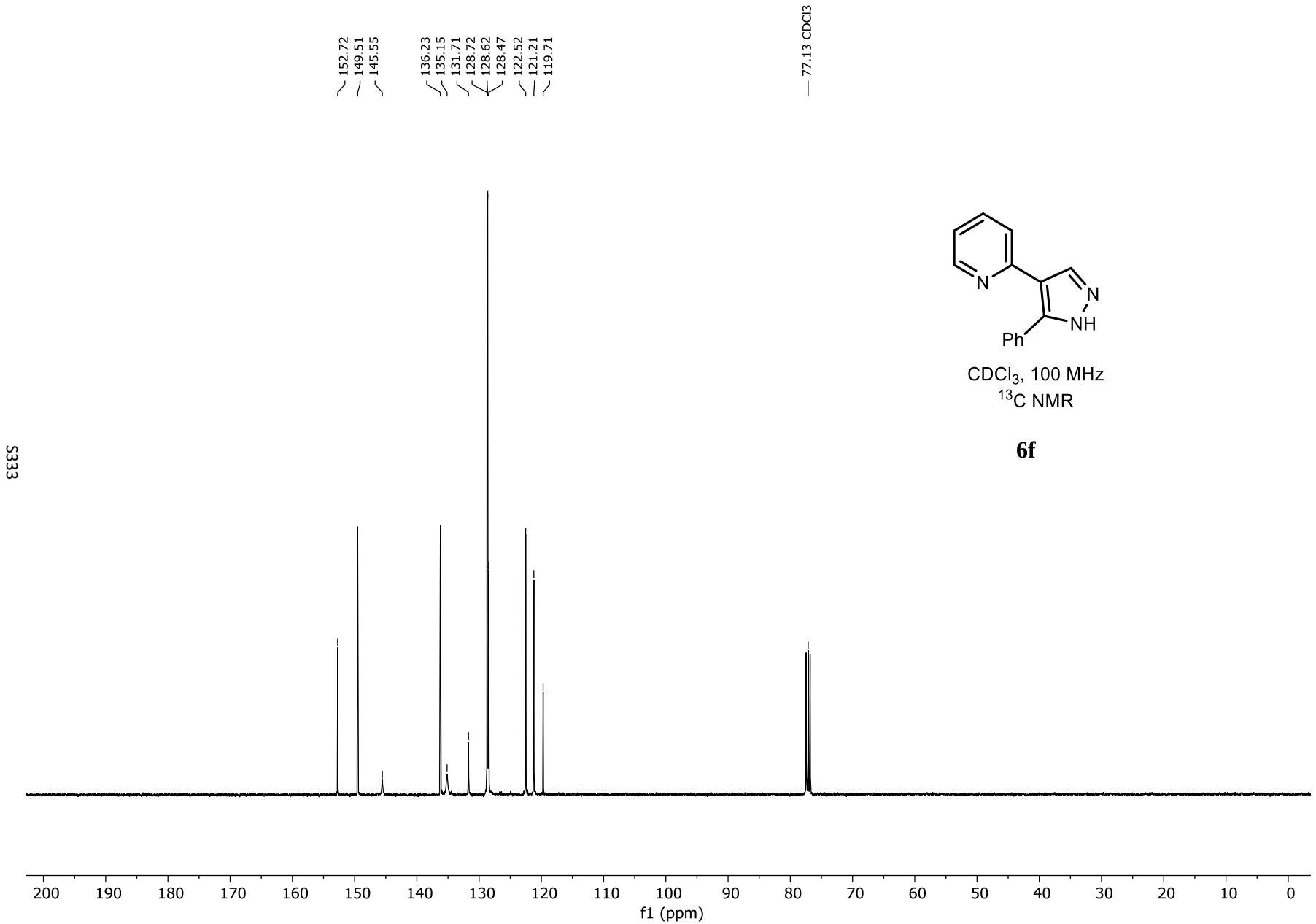

8.43
8.43
8.36
8.31
8.31
8.26
8.26
8.06
8.02
7.72
7.71
7.50
7.48
7.47
7.46
7.36
7.34
7.33
7.32
7.26 CDCl3
6.54
6.54
6.35
6.34
N
O
N
Ph
+
O
N
N
N
Ph
CDCl3, 400 MHz
1H NMR
6d
0.33
0.33
1.01
1.01
0.33
0.98
2.73
2.79
1.32
0.33
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

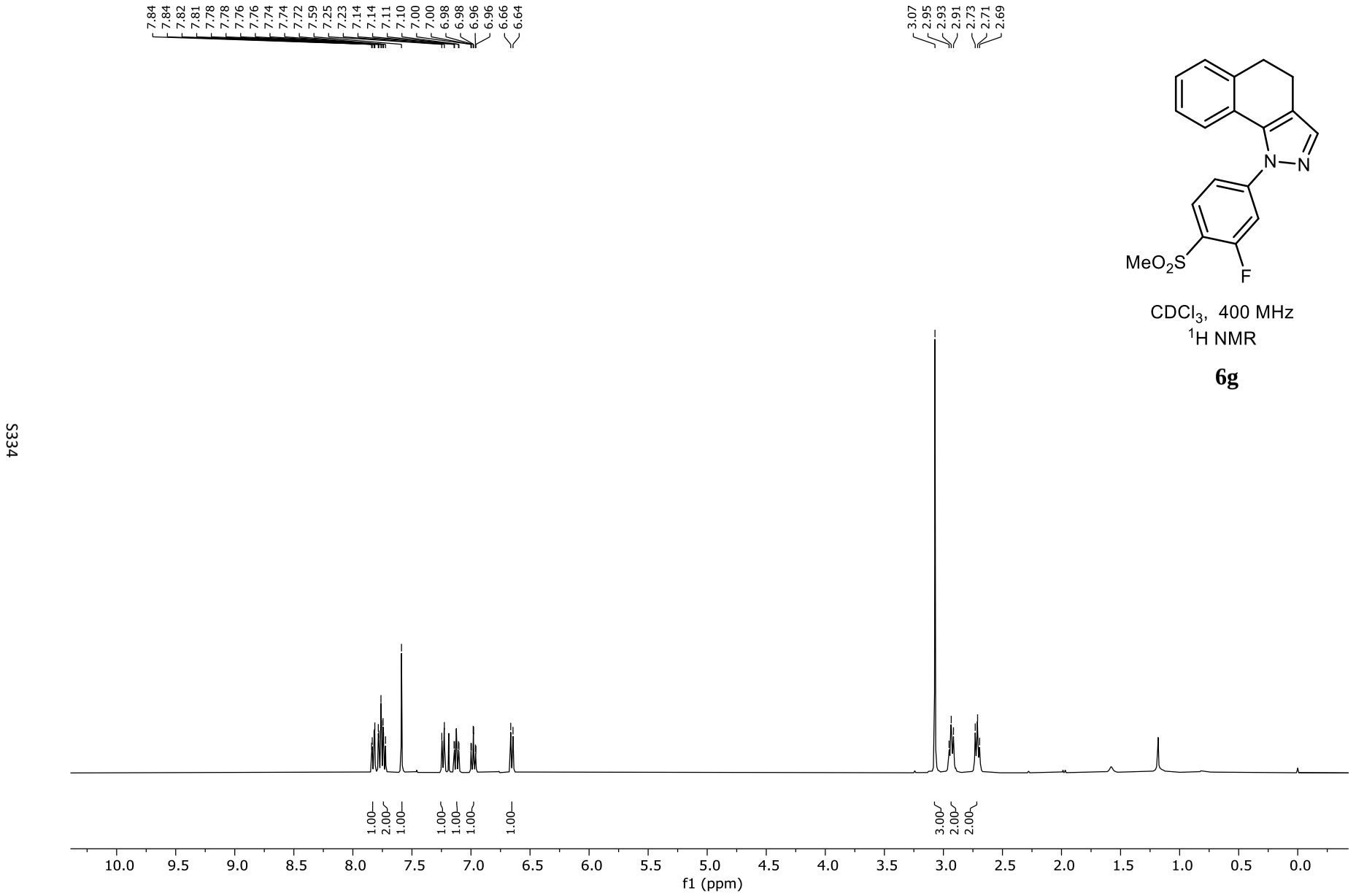

163.11
158.76
154.70
150.71
139.72
139.69
139.53
138.92
129.71
129.67
127.46
127.26
125.54
125.10
119.50
119.42
119.14
113.05
112.48
102.82
98.18
77.16 CDCl3
N
O
N
Ph
+
O
N
N
Ph
CDCl3, 100 MHz
13C NMR
6d
f1 (ppm)

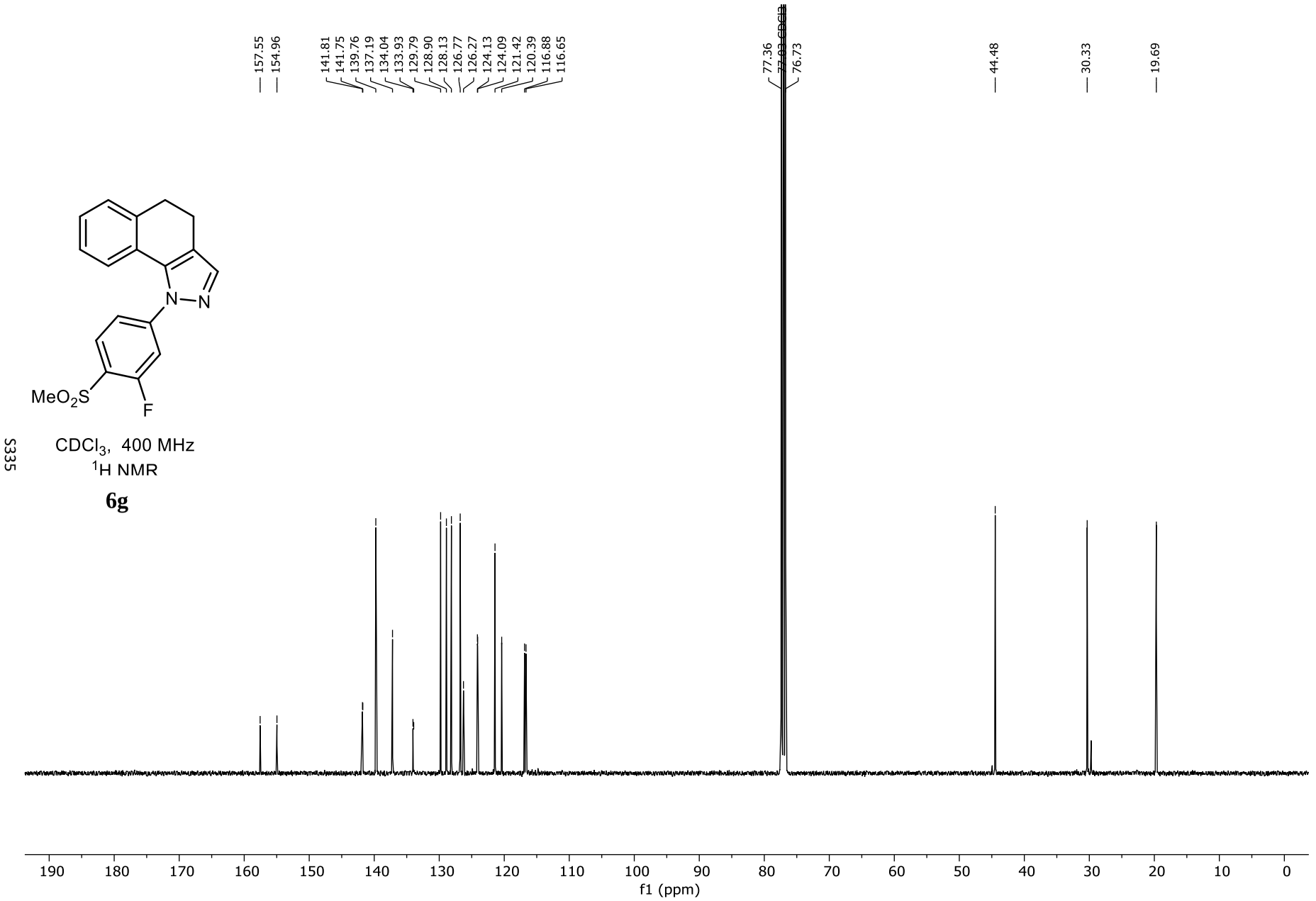

8.54
7.69
7.57
7.55
7.47
7.45
7.26
7.26 CDCl3
6.23
2.44
2.34
S330
Me
N
O
N
O
Me
Cl
CDCl3, 400 MHz
1H NMR
6e
1.00
1.00
1.00
1.00
1.00
3.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

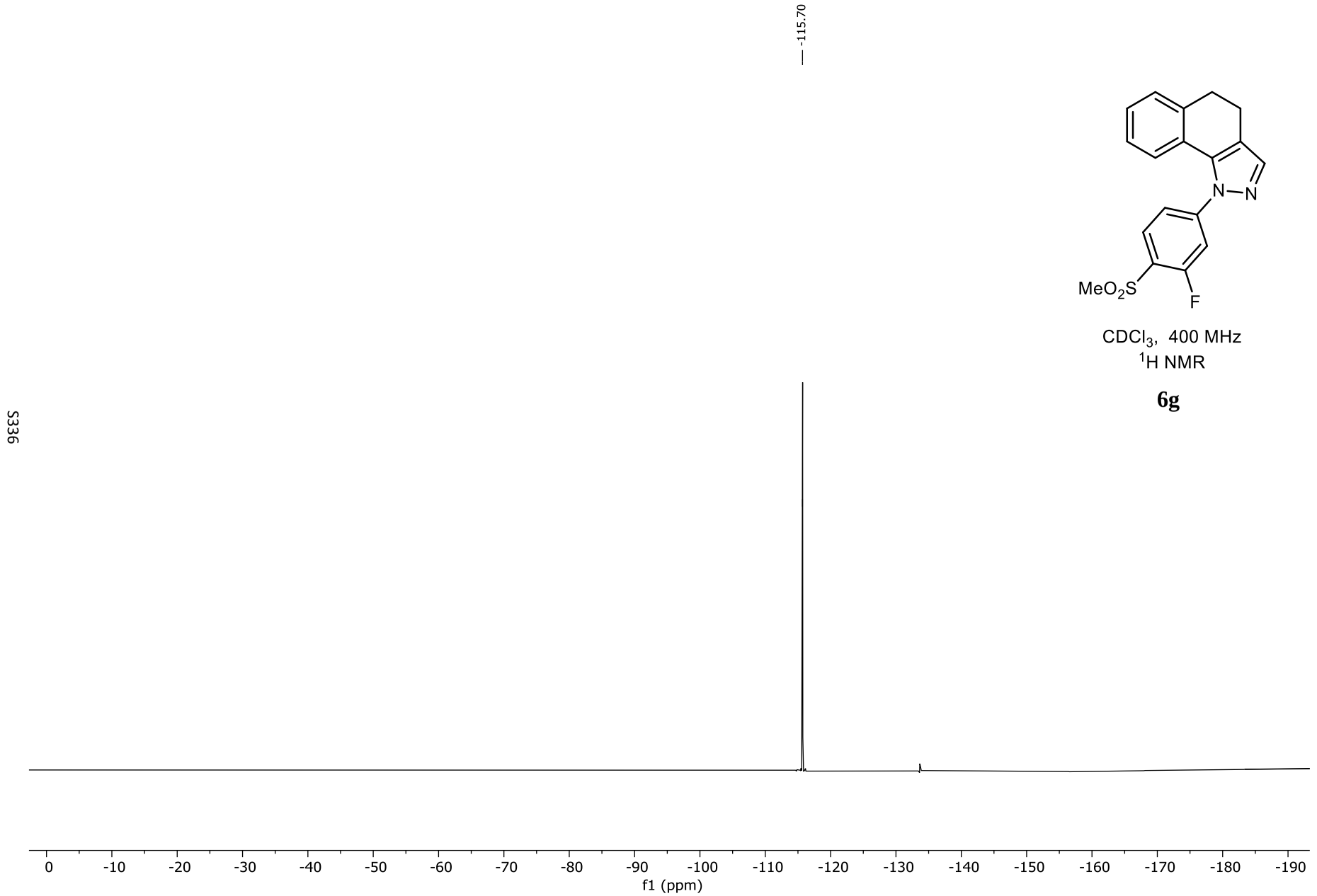

164.64
159.55
159.24
149.04
136.59
136.14
129.17
128.70
125.47
123.89
103.80
101.72
76.35
76.03 CDCl3
75.71
19.12
10.38
N
O
Me
N
O
Me
Cl
CDCl3, 400 MHz
13C NMR
6e
S331
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

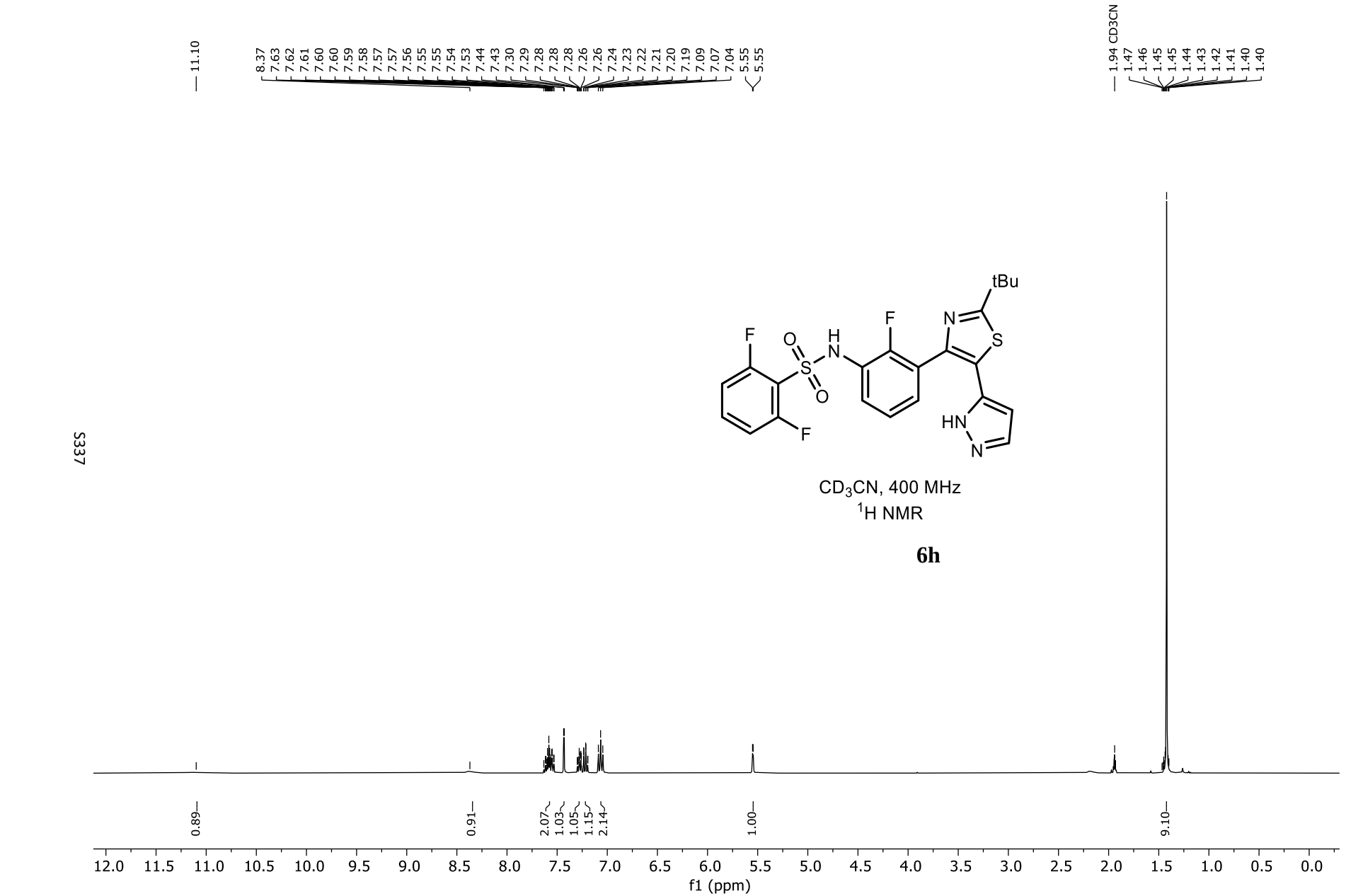

8.59
8.59
8.59
8.58
8.58
8.57
7.92
7.49
7.48
7.48
7.47
7.47
7.46
7.45
7.45
7.45
7.32
7.31
7.30
7.15
7.15
7.13
7.13
7.09
7.09
7.08
7.07
7.06
N
N
NH
Ph
CDCl3, 400 MHz
1H NMR
6f
S332
1.00
1.00
3.20
3.07
1.06
1.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

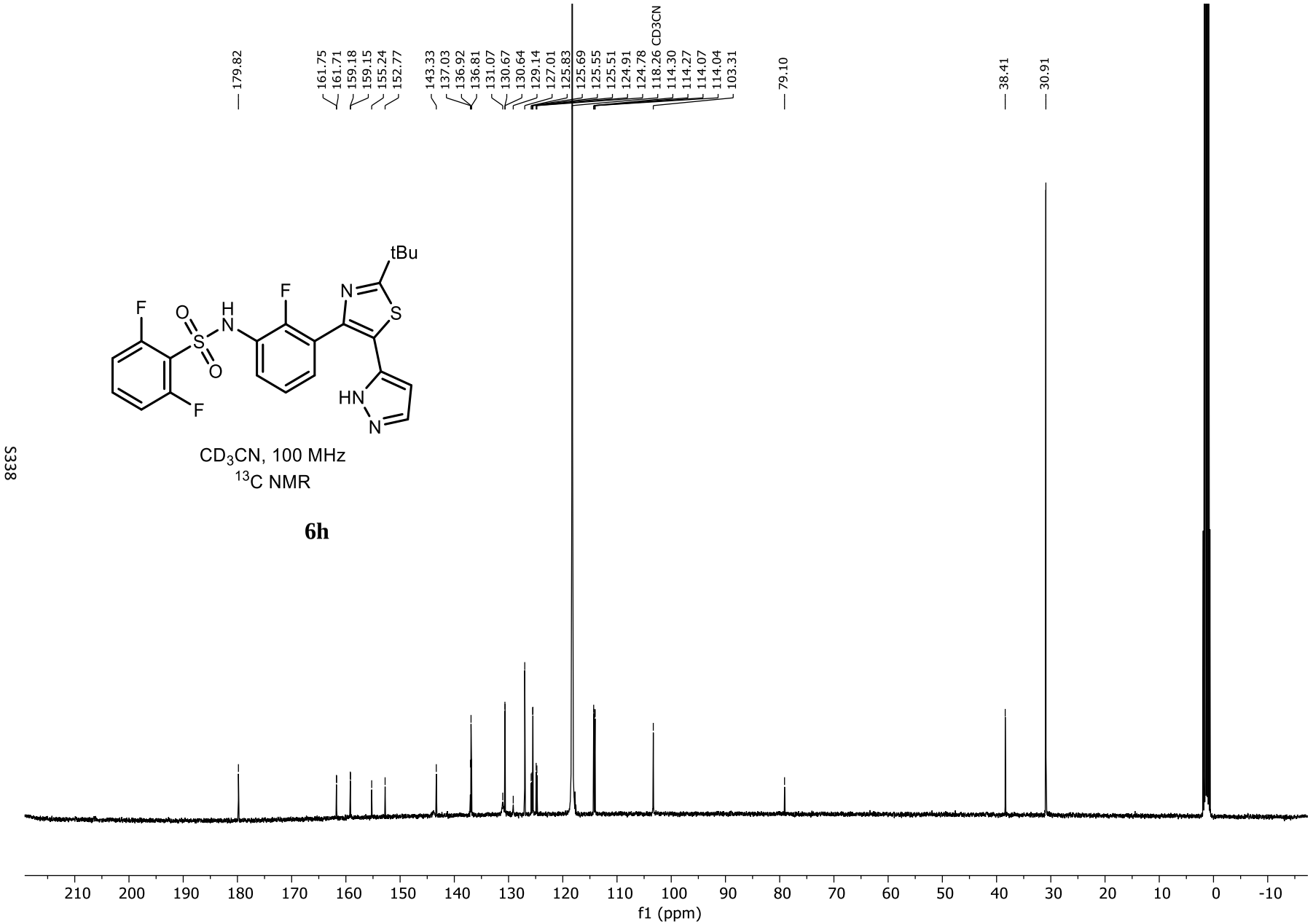

152.72
149.51
145.55
136.23
135.15
131.71
128.72
128.62
128.47
122.52
121.21
119.71
77.13 CDCl3
N
N
NH
Ph
CDCl3, 100 MHz
13C NMR
6f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

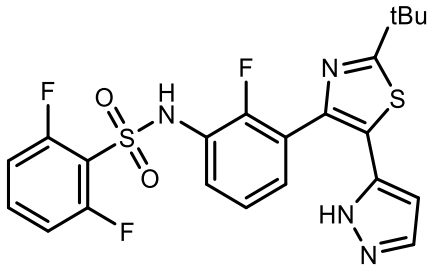

7.84
7.84
7.82
7.81
7.78
7.78
7.76
7.76
7.74
7.74
7.72
7.59
7.25
7.23
7.14
7.14
7.11
7.10
7.00
7.00
6.98
6.98
6.96
6.96
6.66
6.64
3.07
2.95
2.93
2.91
2.73
2.71
2.69
MeO2S
F
CDCl3, 400 MHz
1H NMR
6g
1.00
2.00
1.00
1.00
1.00
1.00
1.00
3.00
2.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


157.55
154.96
141.81
141.75
139.76
137.19
134.04
133.93
129.79
128.90
128.13
126.77
126.27
124.13
124.09
121.42
120.39
116.88
116.65
77.36
76.73
44.48
30.33
19.69
MeO2S
F
CDCl3, 400 MHz
1H NMR
6g
f1 (ppm)


-115.70
S336
MeO2S
F
CDCl3, 400 MHz
1H NMR
6g
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


11.10
8.37
7.63
7.62
7.61
7.60
7.60
7.59
7.58
7.57
7.57
7.56
7.55
7.55
7.54
7.53
7.44
7.43
7.30
7.29
7.28
7.28
7.28
7.26
7.26
7.24
7.23
7.22
7.21
7.20
7.19
7.09
7.07
7.04
5.55
5.55
1.94 CD3CN
1.47
1.46
1.45
1.45
1.44
1.43
1.42
1.41
1.40
1.40
tBu
F
N
S
F
O
H
N
S
O
F
HN
N
CD3CN, 400 MHz
1H NMR
6h
0.89
0.91
2.07
1.03
1.05
1.15
2.14
1.00
9.10
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

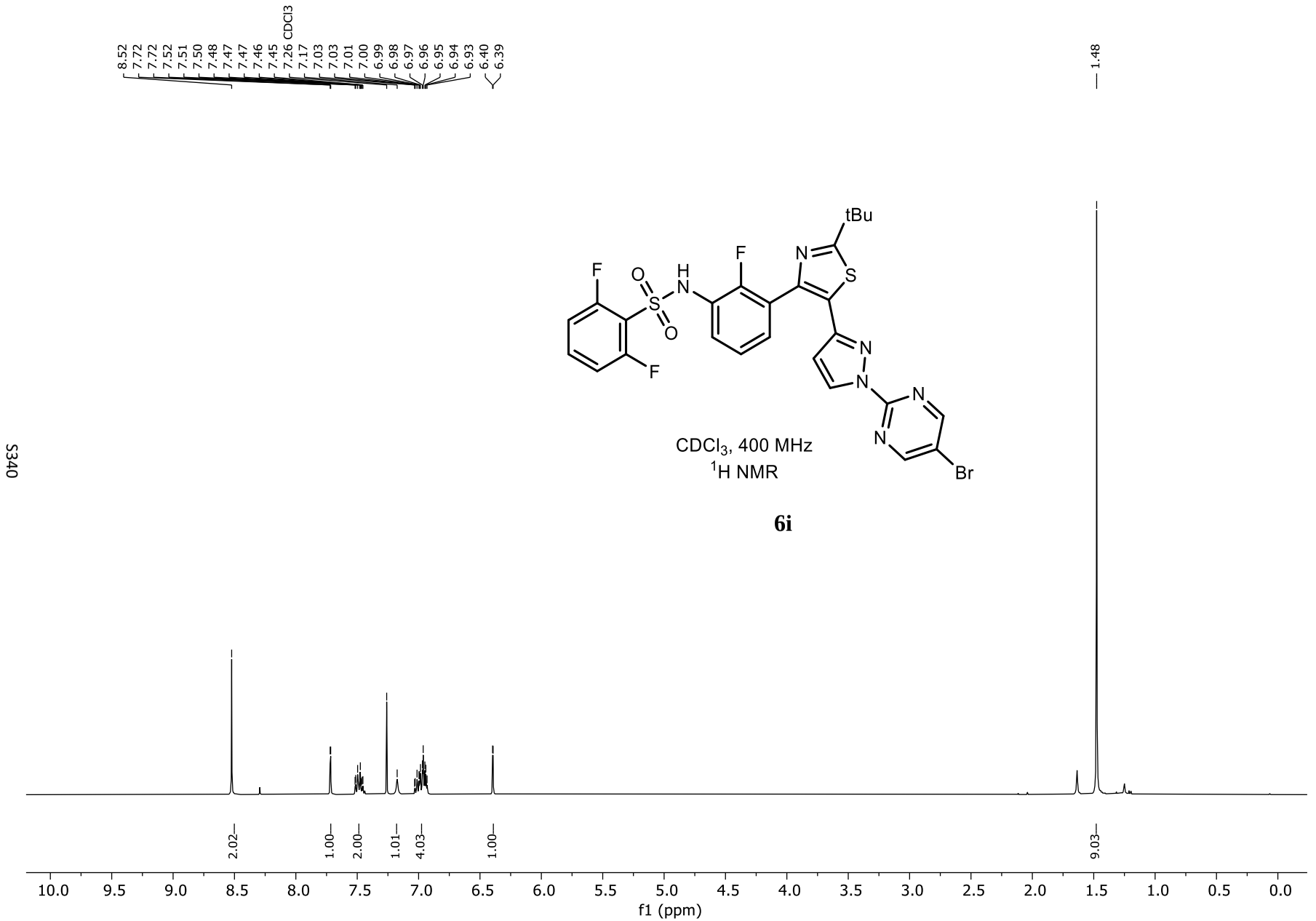

179.82
161.75
161.71
159.18
159.15
155.24
152.77
143.33
137.03
136.92
136.81
131.07
130.67
130.64
129.14
127.01
125.83
125.69
125.55
125.51
124.91
124.78
118.26
CD3CN
114.30
114.27
114.07
114.04
103.31
79.10
38.41
30.91
tBu
F
O
H
N
S
O
F
F
N
S
HN
N
CD3CN, 100 MHz
13C NMR
6h
f1 (ppm)

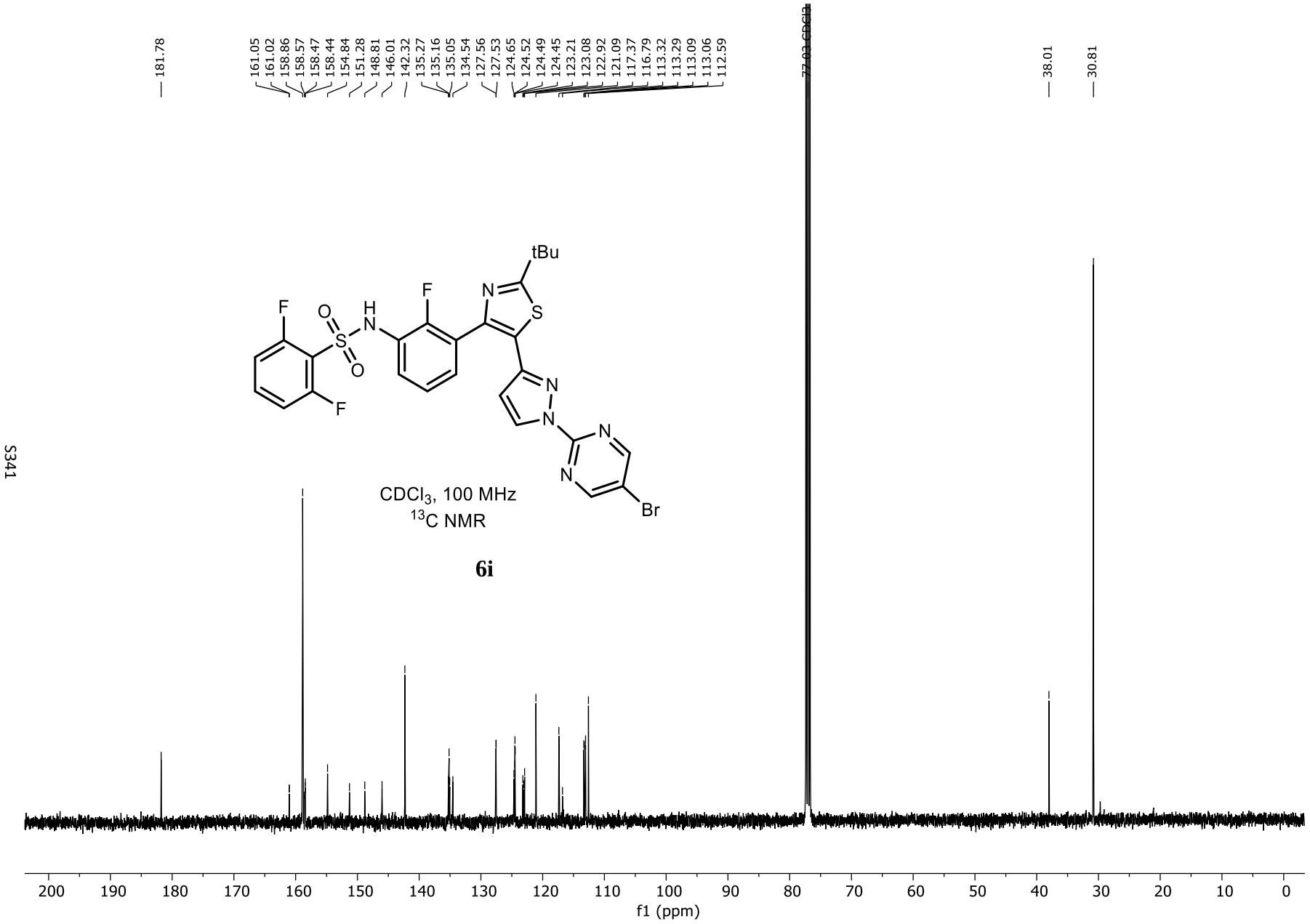


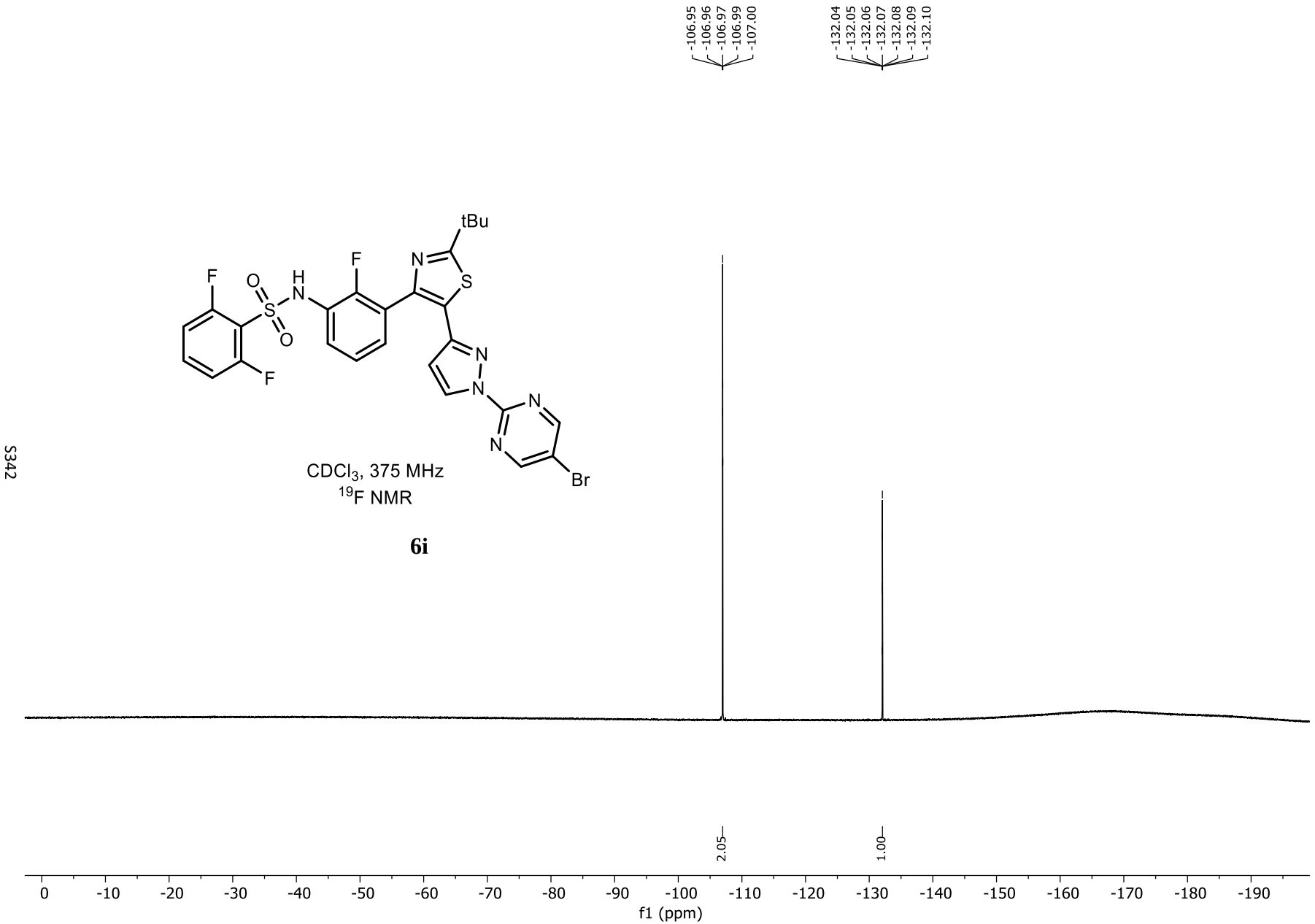
CD_3CN, 375 MHz

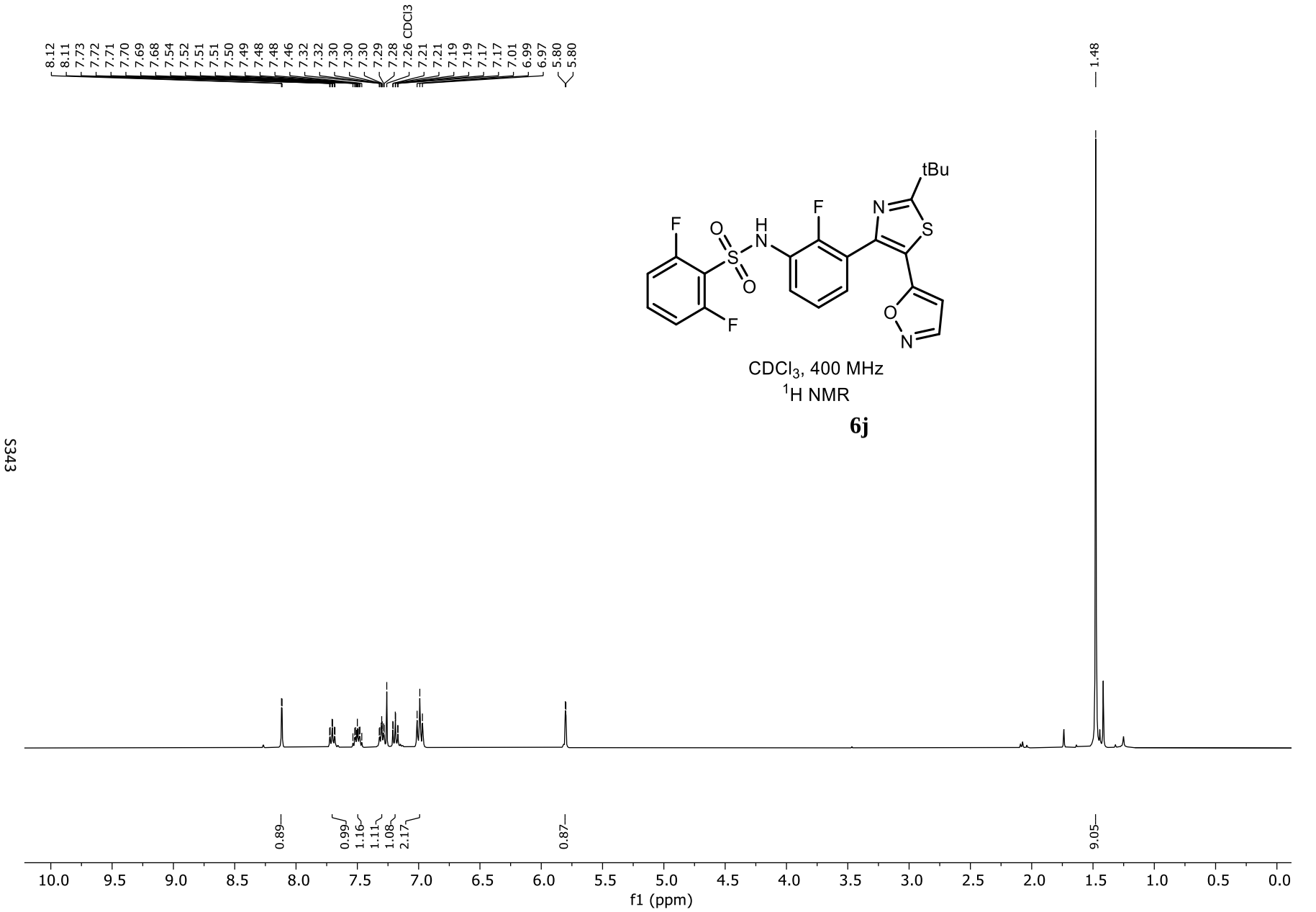
^{19}F NMR

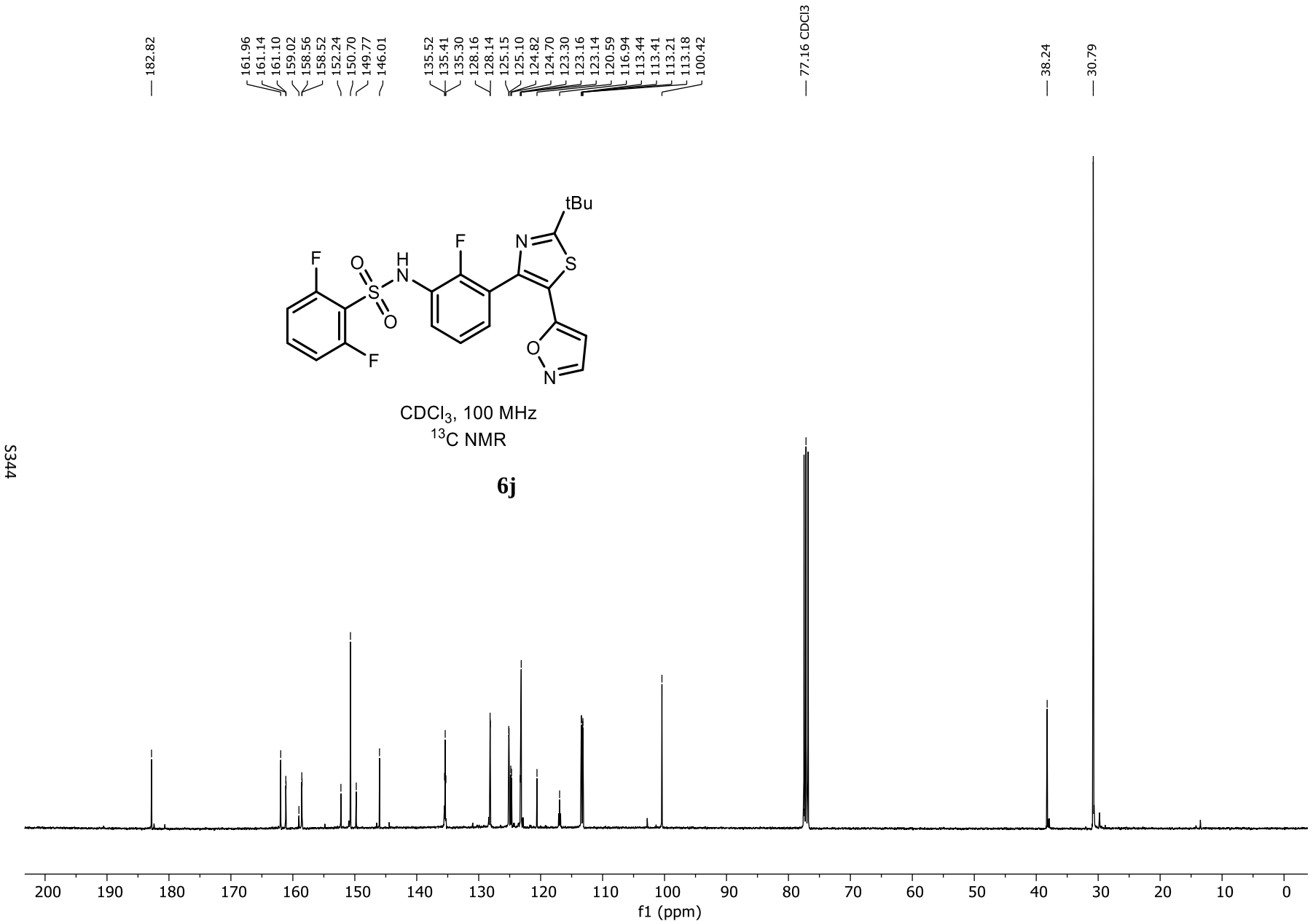
6h

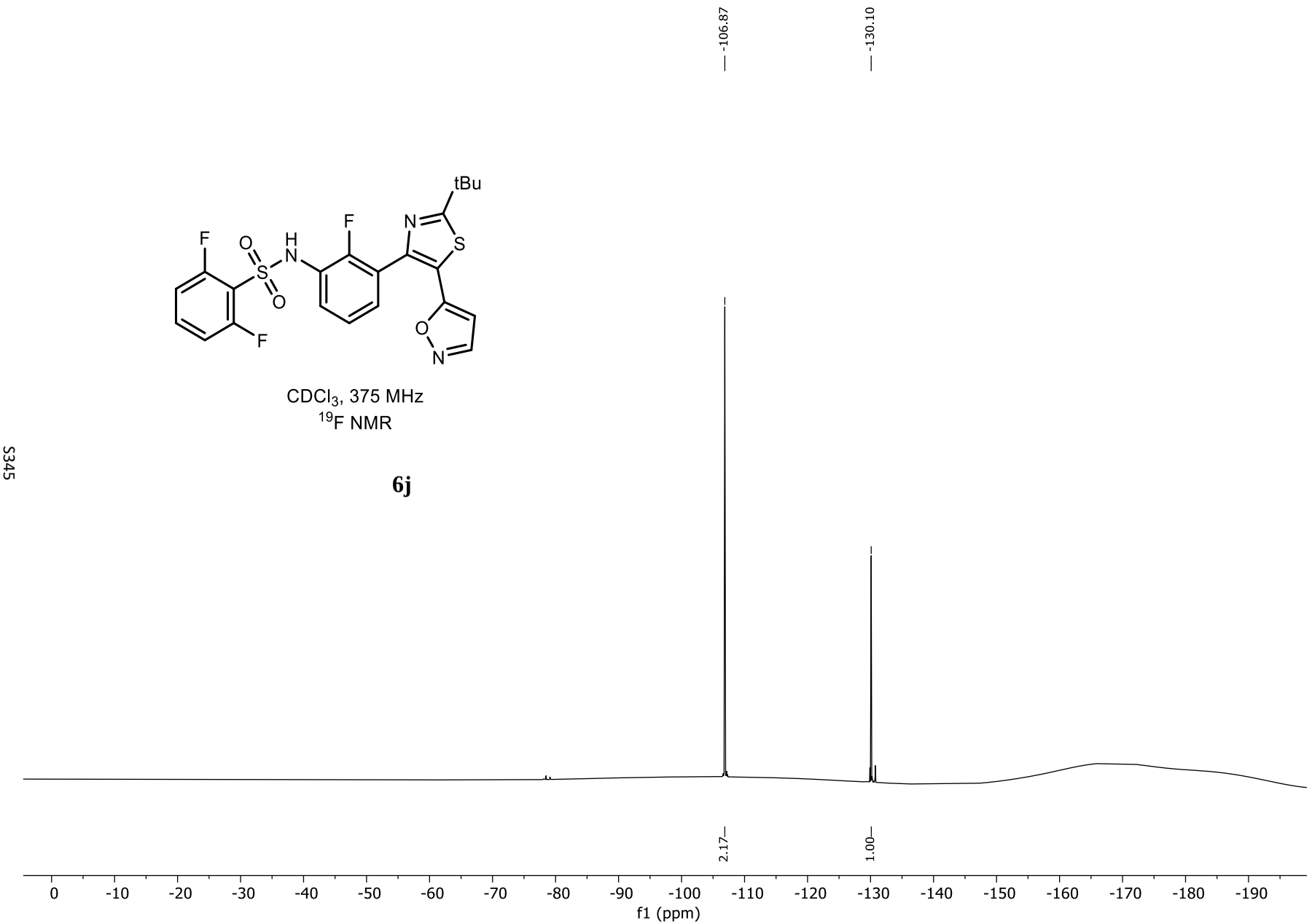

8.52
7.72
7.72
7.52
7.51
7.50
7.48
7.47
7.47
7.46
7.45
7.26 CDCl3
7.17
7.03
7.03
7.01
7.00
6.99
6.98
6.97
6.96
6.95
6.94
6.93
6.40
6.39
1.48
tBu
F
N
S
F
O
H
N
S
O
F
N
N
N
N
Br
CDCl3, 400 MHz
1H NMR
6i
S340
2.02
1.00
2.00
1.01
4.03
1.00
9.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

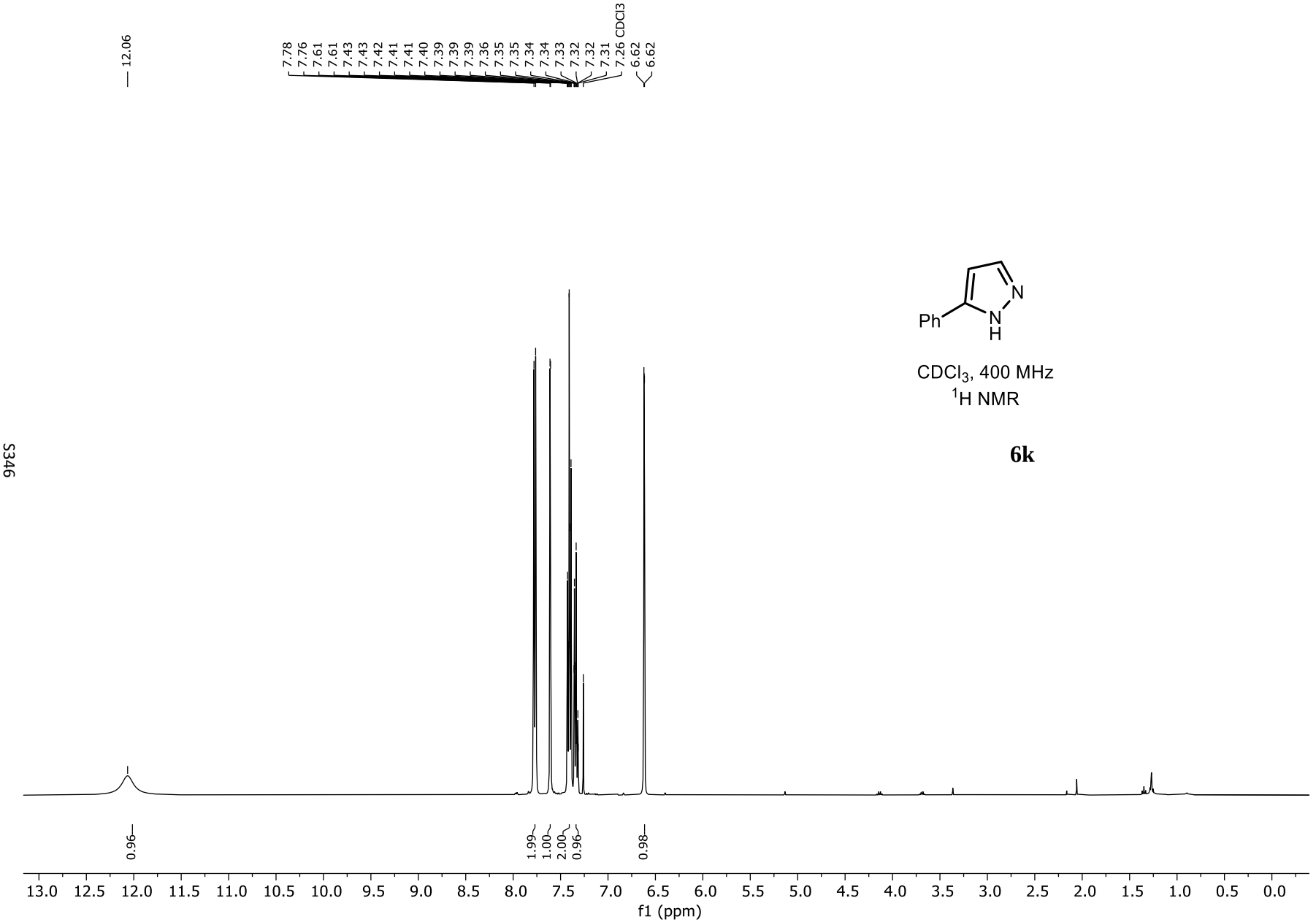

181.78
161.05
161.02
158.86
158.57
158.47
158.44
154.84
151.28
148.81
146.01
142.32
135.27
135.16
135.05
134.54
127.56
127.53
124.65
124.52
124.49
124.45
123.21
123.08
122.92
121.09
117.37
116.79
113.32
113.29
113.09
113.06
112.59
77.03
38.01
30.81
tBu
F
O
H
N
S
F
N
S
O
F
N
N
N
N
Br
CDCl3, 100 MHz
13C NMR
6i
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

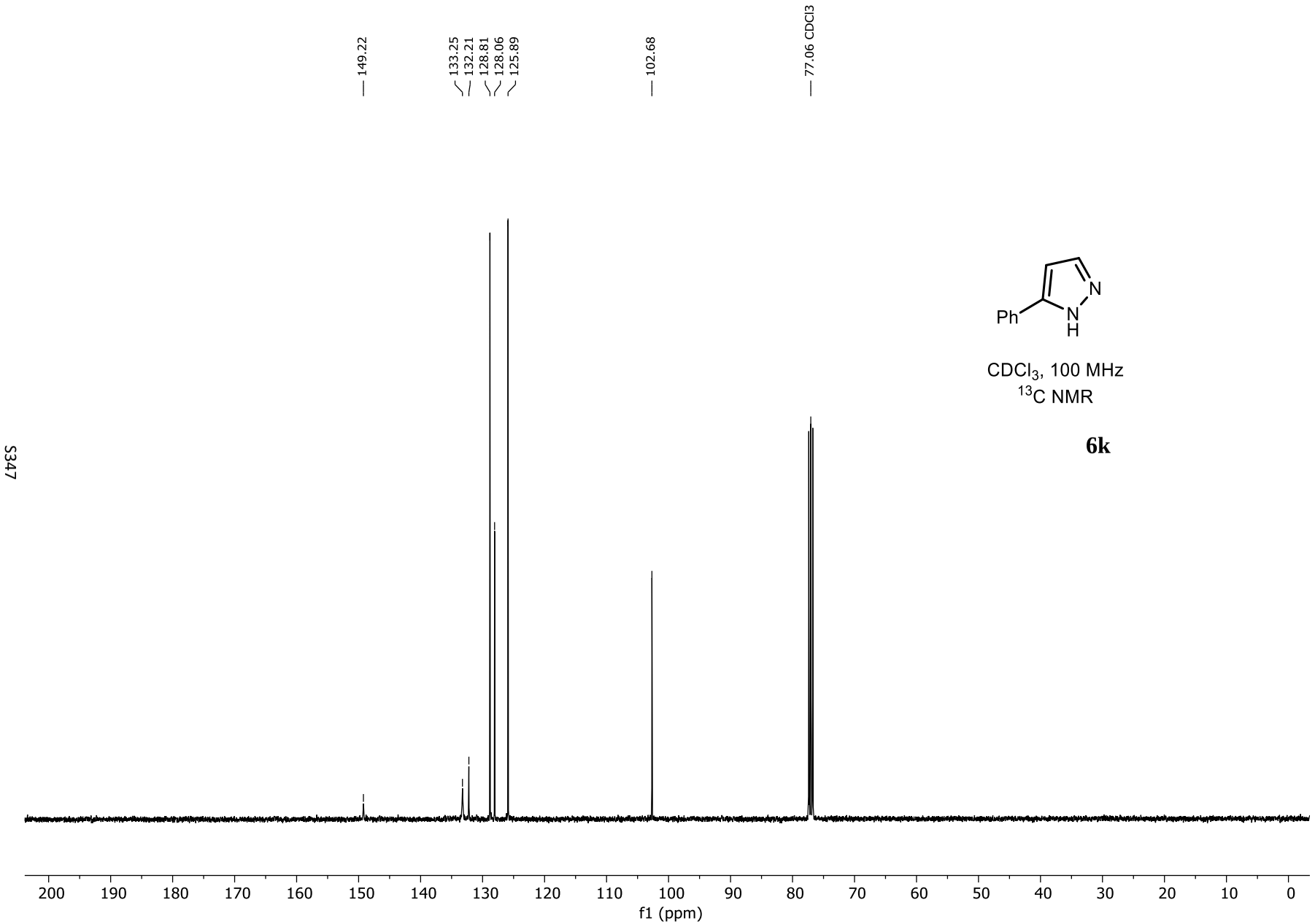

-106.95
-106.96
-106.97
-106.99
-107.00
-132.04
-132.05
-132.06
-132.07
-132.08
-132.09
-132.10
tBu
F
O
S
O
H
N
F
N
S
N
N
N
N
Br
F
CDCl3, 375 MHz
19F NMR
6i
2.05
1.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

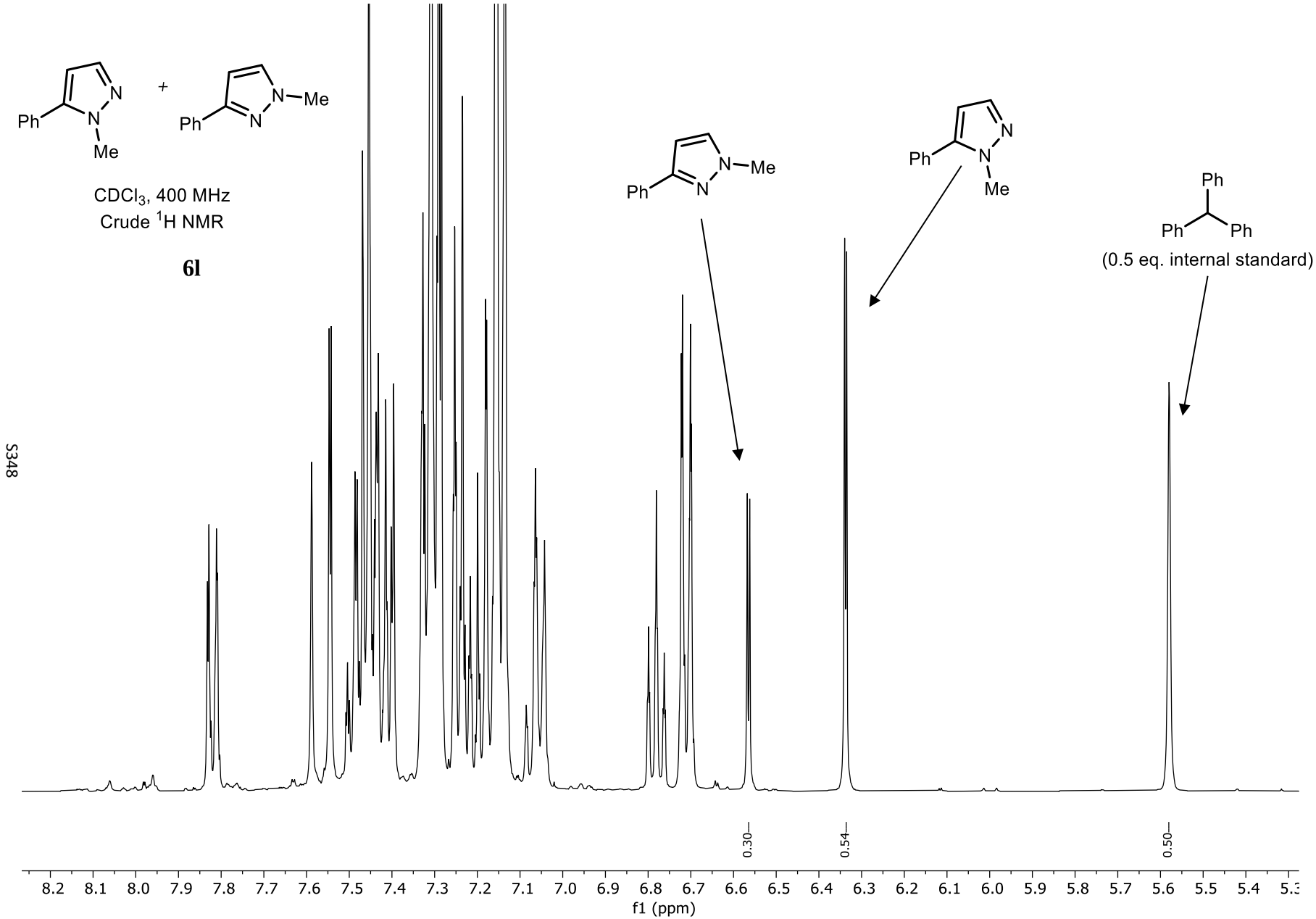

8.12
8.11
7.73
7.72
7.71
7.70
7.69
7.68
7.54
7.52
7.51
7.51
7.50
7.49
7.48
7.48
7.46
7.32
7.32
7.30
7.30
7.30
7.29
7.28
7.26 CDCl3
7.21
7.21
7.19
7.19
7.17
7.17
7.01
6.99
6.97
5.80
5.80
1.48
tBu
F
N
S
H
N
O
S
O
F
F
O
N
CDCl3, 400 MHz
1H NMR
6j
0.89
0.99
1.16
1.11
1.08
2.17
0.87
9.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

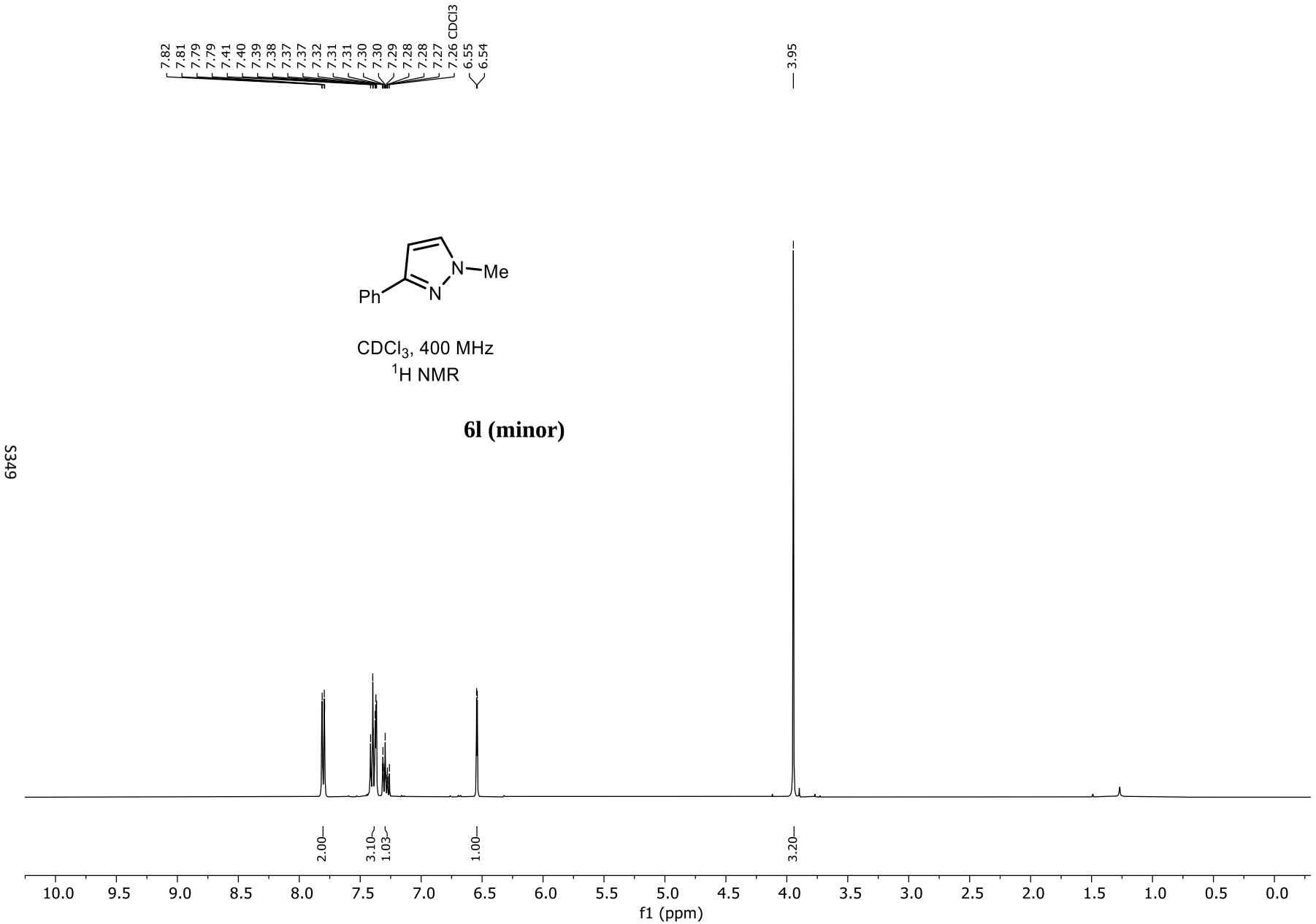

182.82
161.96
161.14
161.10
159.02
158.56
158.52
152.24
150.70
149.77
146.01
135.52
135.41
135.30
128.16
128.14
125.15
125.10
124.82
124.70
123.30
123.16
123.14
120.59
116.94
113.44
113.41
113.21
113.18
100.42
77.16 CDCl3
38.24
30.79
tBu
F
O
H
N
S
F
F
N
S
O
O
N
CDCl3, 100 MHz
13C NMR
6j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

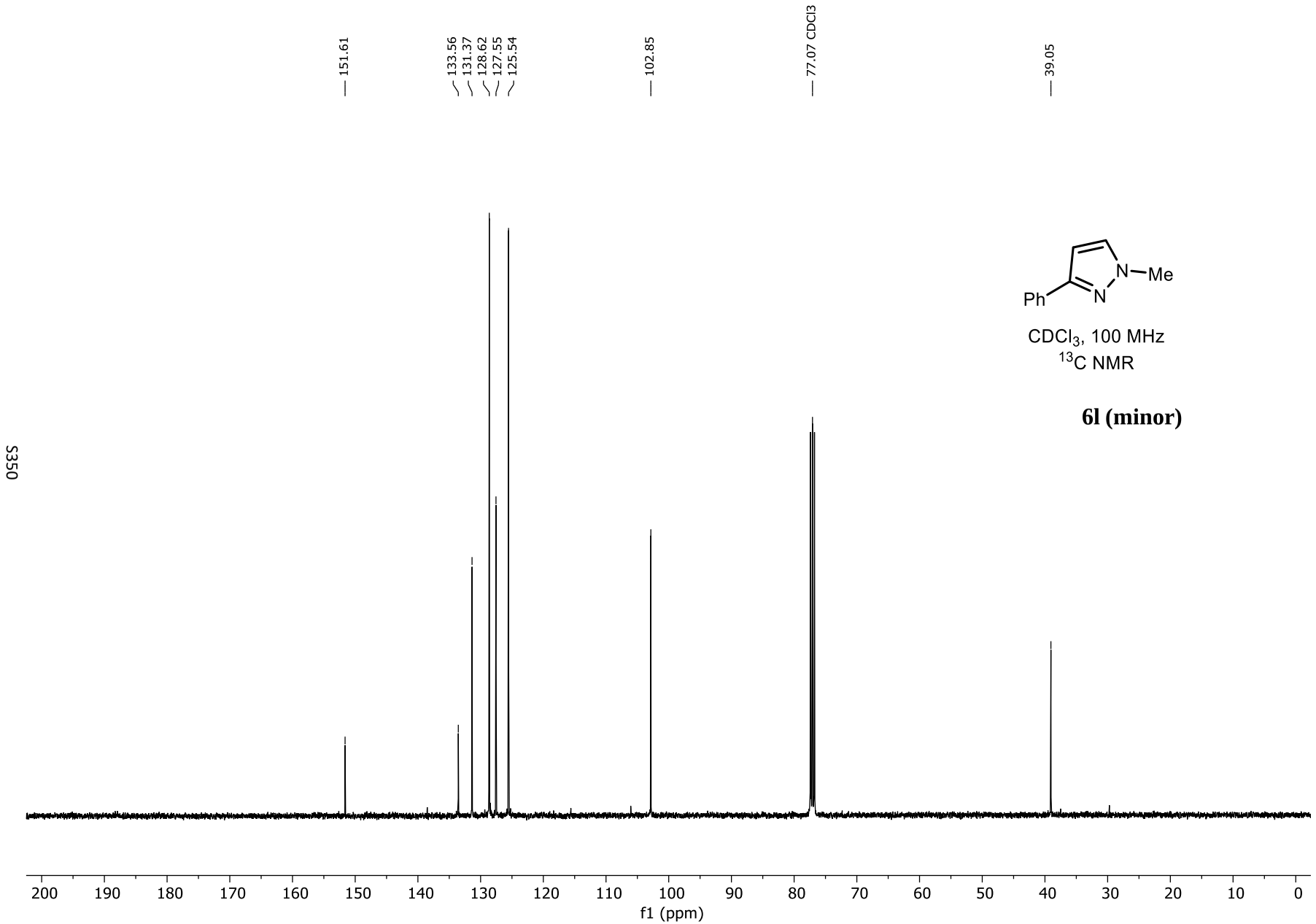

-106.87
-130.10
tBu
F
O
H
N
F
N
S
S
O
F
O
N
CDCl3, 375 MHz
19F NMR
6j
2.17
1.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

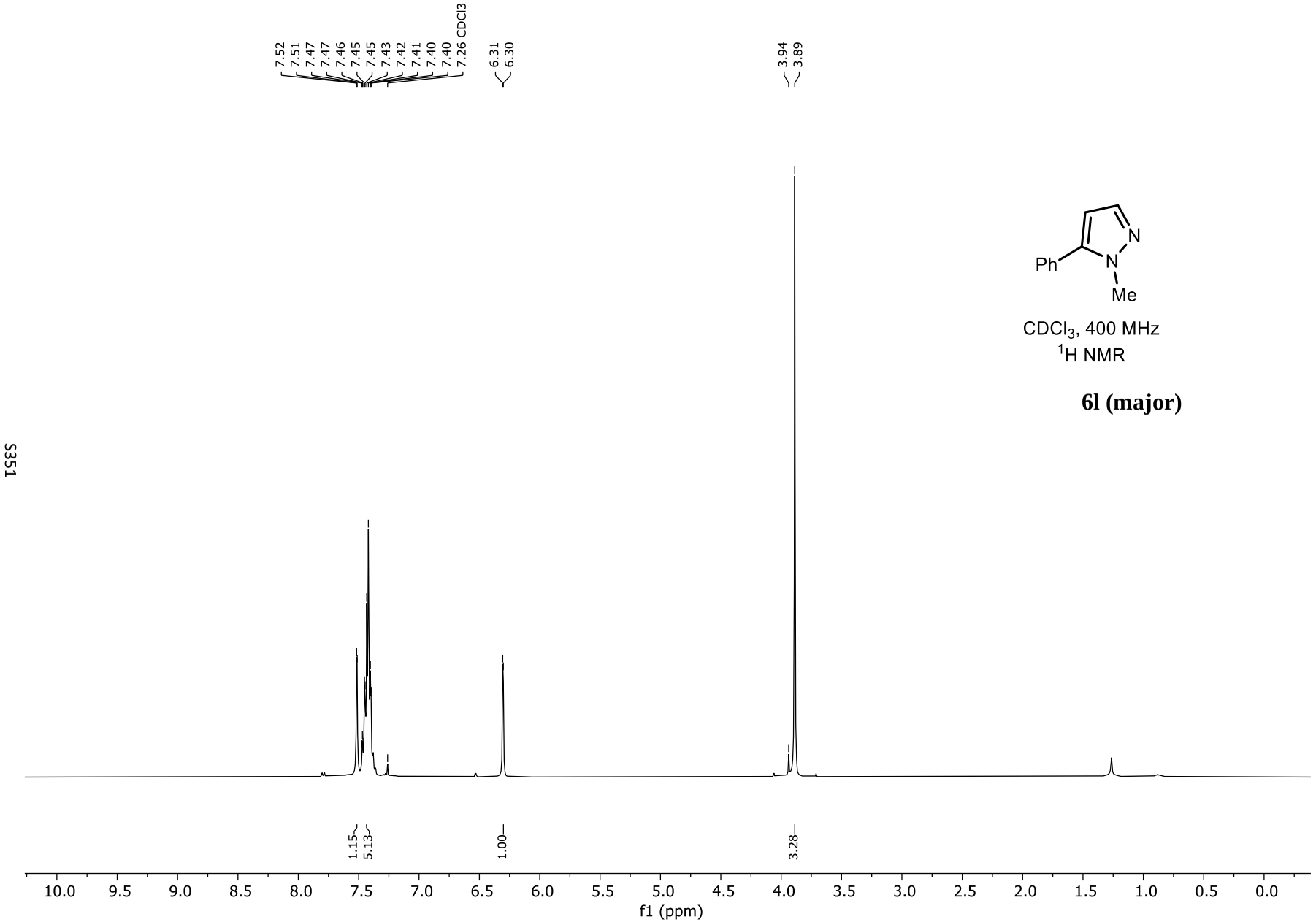

12.06
7.78
7.76
7.61
7.61
7.43
7.43
7.42
7.41
7.41
7.40
7.39
7.39
7.39
7.36
7.35
7.35
7.34
7.34
7.33
7.32
7.32
7.31
7.26 CDCl3
6.62
6.62
Ph
N
N
H
CDCl3, 400 MHz
1H NMR
6k
0.96
1.99
1.00
2.00
0.96
0.98
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

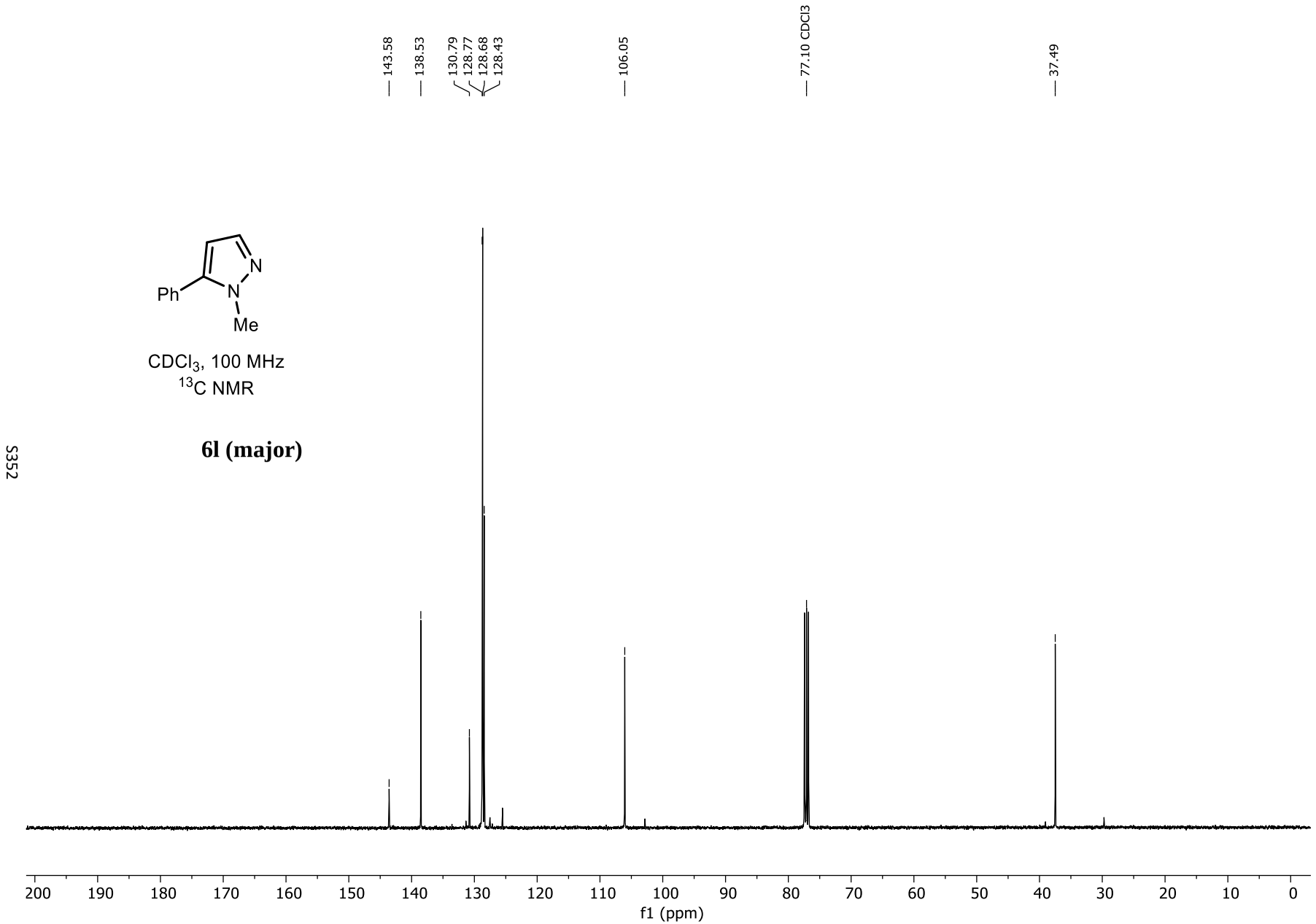

149.22
133.25
132.21
128.81
128.06
125.89
102.68
77.06 CDCl3
Ph
N
N
H
CDCl3, 100 MHz
13C NMR
6k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

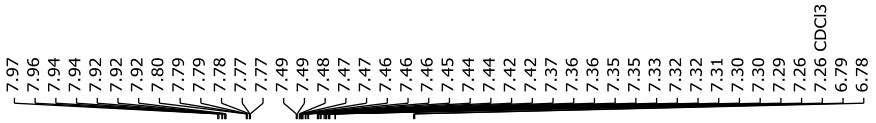

Ph
N
N
Me
+
Ph
N
N
Me
CDCl3, 400 MHz
Crude 1H NMR
6l
Ph
N
N
Me
Ph
N
N
Me
Ph
Ph
Ph
(0.5 eq. internal standard)
0.30
0.54
0.50
8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3
f1 (ppm)

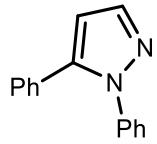

7.82
7.81
7.79
7.79
7.41
7.40
7.39
7.38
7.37
7.37
7.32
7.31
7.31
7.30
7.30
7.29
7.28
7.28
7.27
7.26 CDCl3
6.55
6.54
3.95
N
Me
N
Ph
CDCl3, 400 MHz
1H NMR
6l (minor)
2.00
3.10
1.03
1.00
3.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


151.61
133.56
131.37
128.62
127.55
125.54
102.85
77.07 CDCl3
39.05
S350
Ph
N
N
Me
CDCl3, 100 MHz
13C NMR
6l (minor)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.52
7.51
7.47
7.47
7.46
7.45
7.45
7.43
7.42
7.41
7.40
7.40
7.26 CDCl3
6.31
6.30
3.94
3.89
S351
Ph
N
N
Me
CDCl3, 400 MHz
1H NMR
6l (major)
1.15
5.13
1.00
3.28
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


143.58
138.53
130.79
128.77
128.68
128.43
106.05
77.10 CDCl3
37.49
Ph
N
N
Me
CDCl3, 100 MHz
13C NMR
6l (major)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

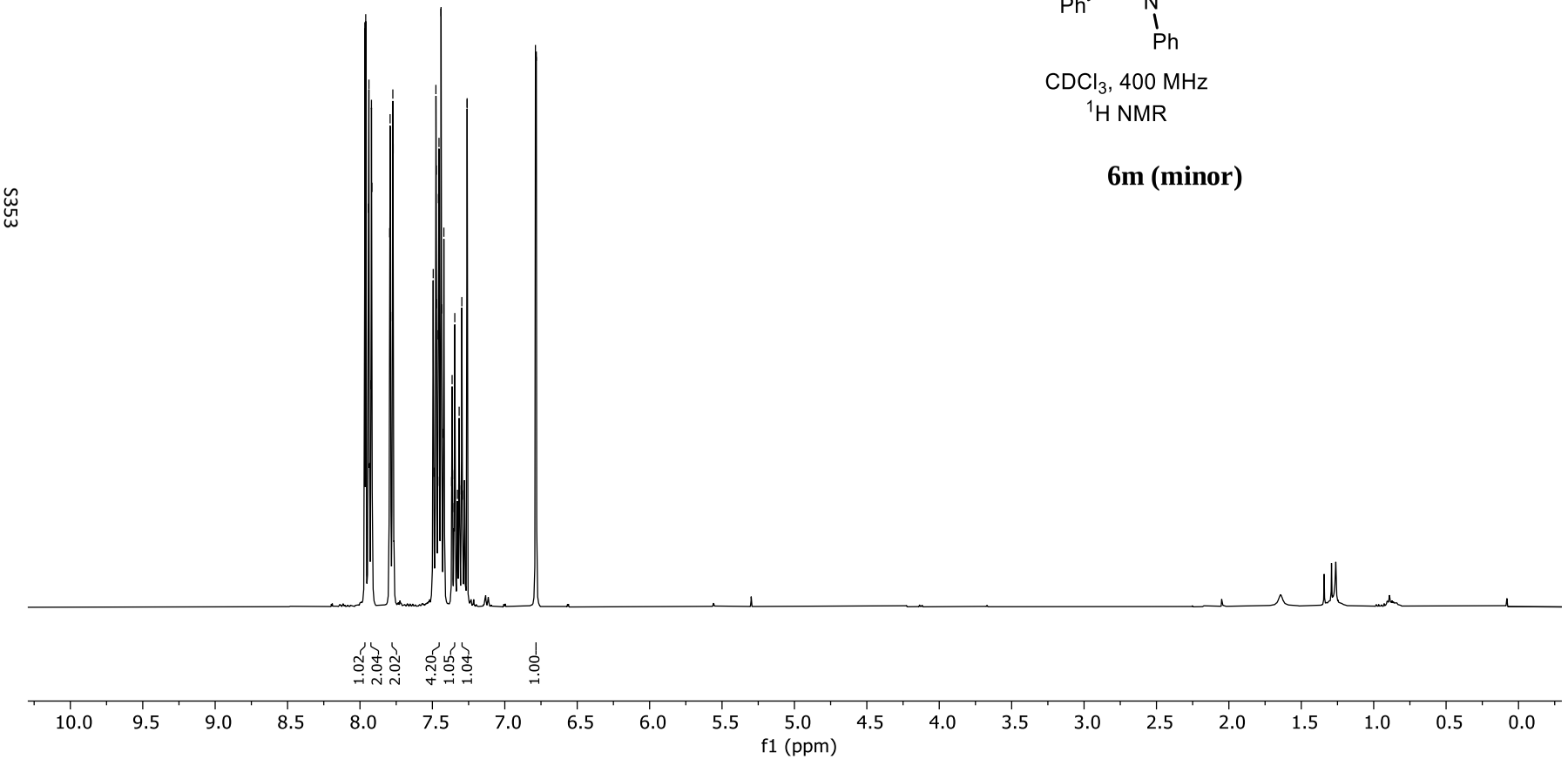


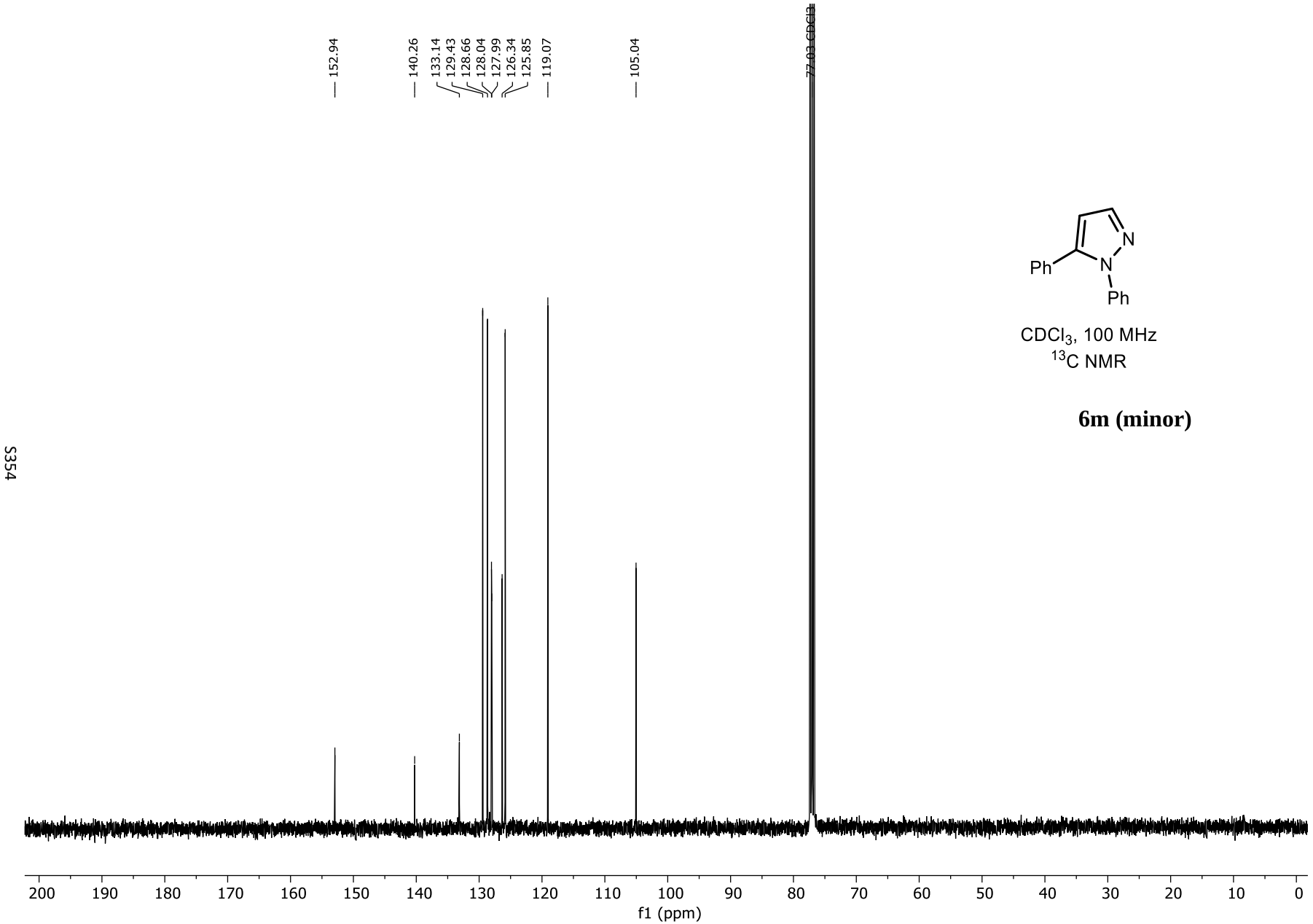


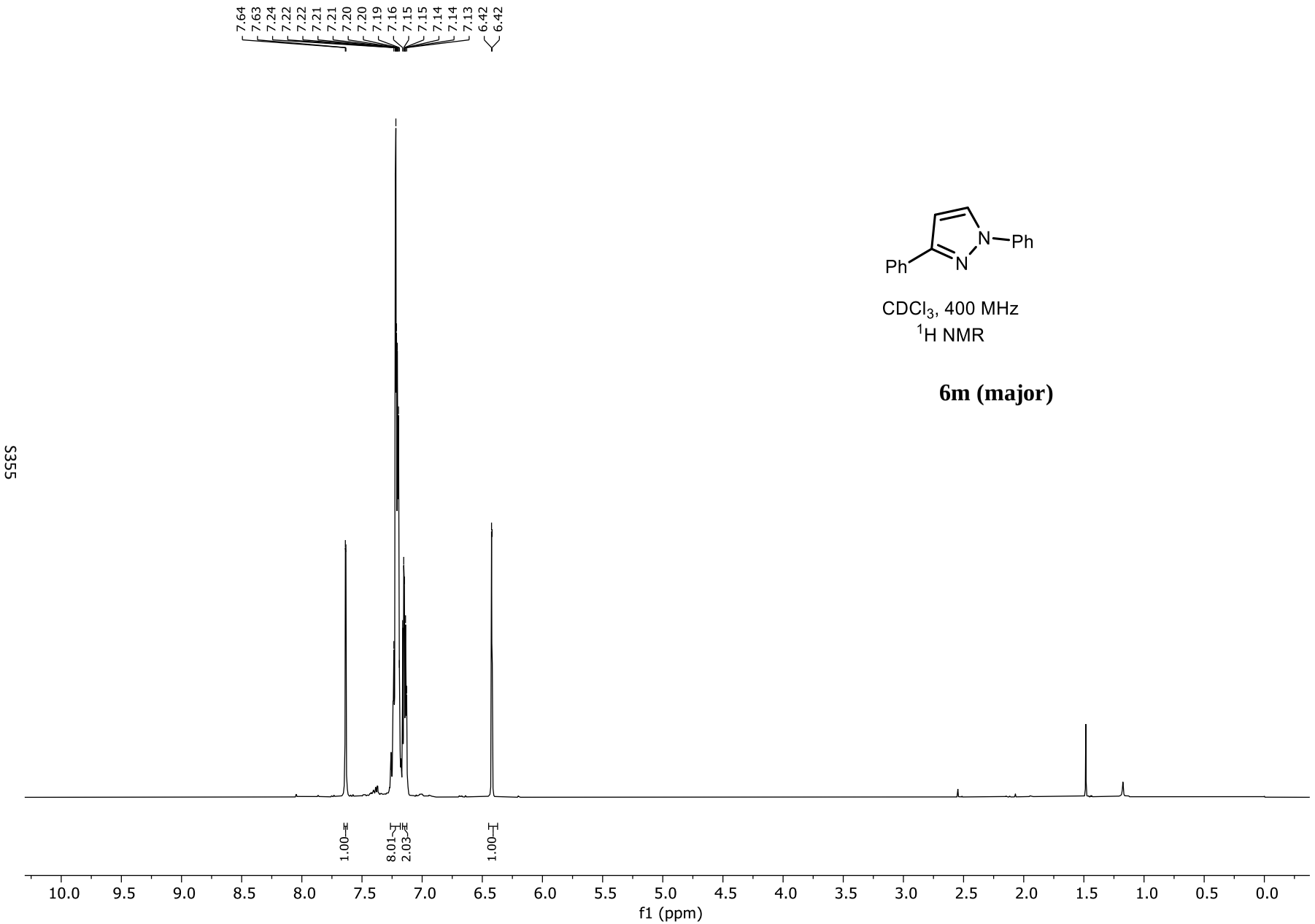
$CDCl_3$, 400 MHz

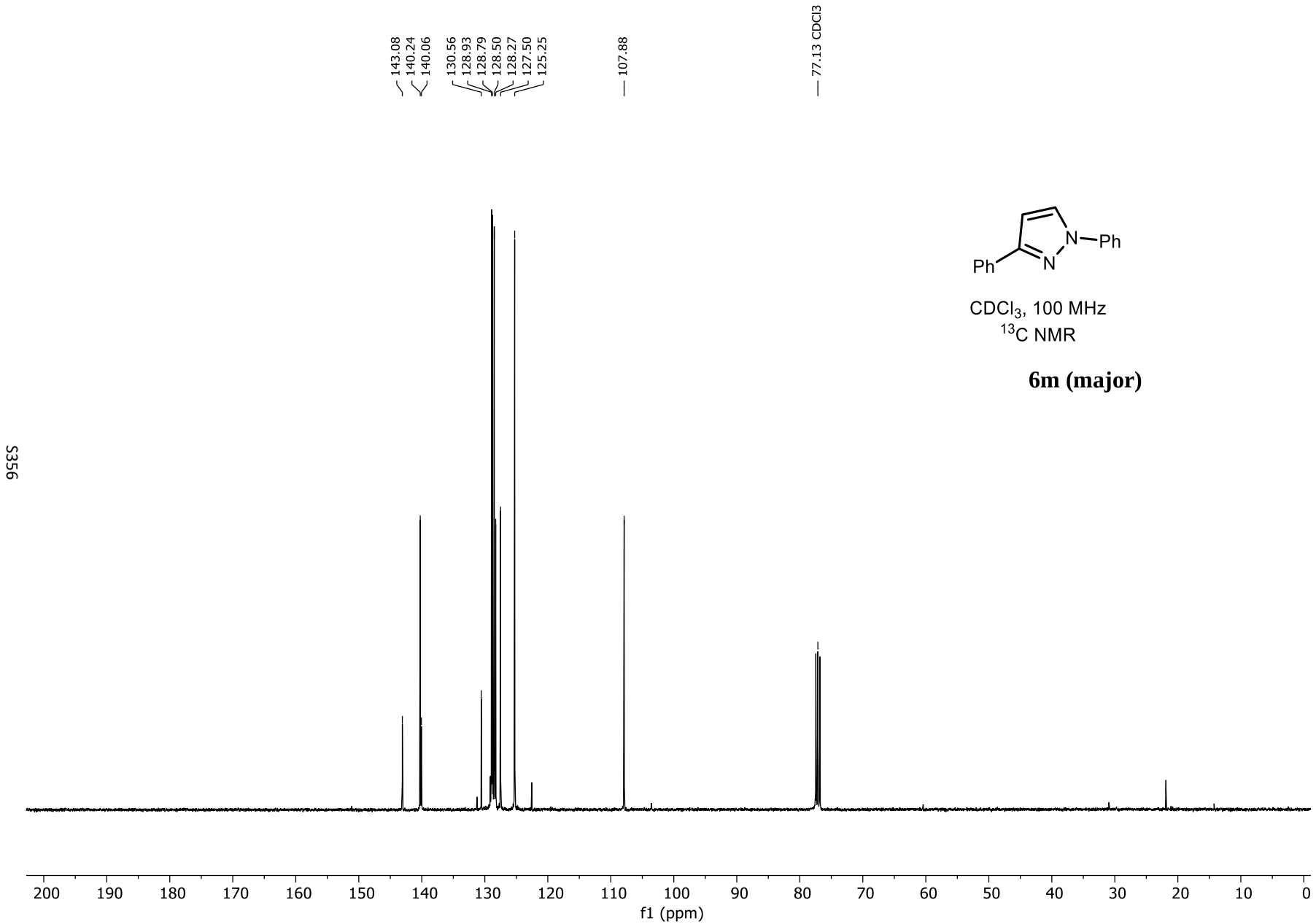
^1H NMR

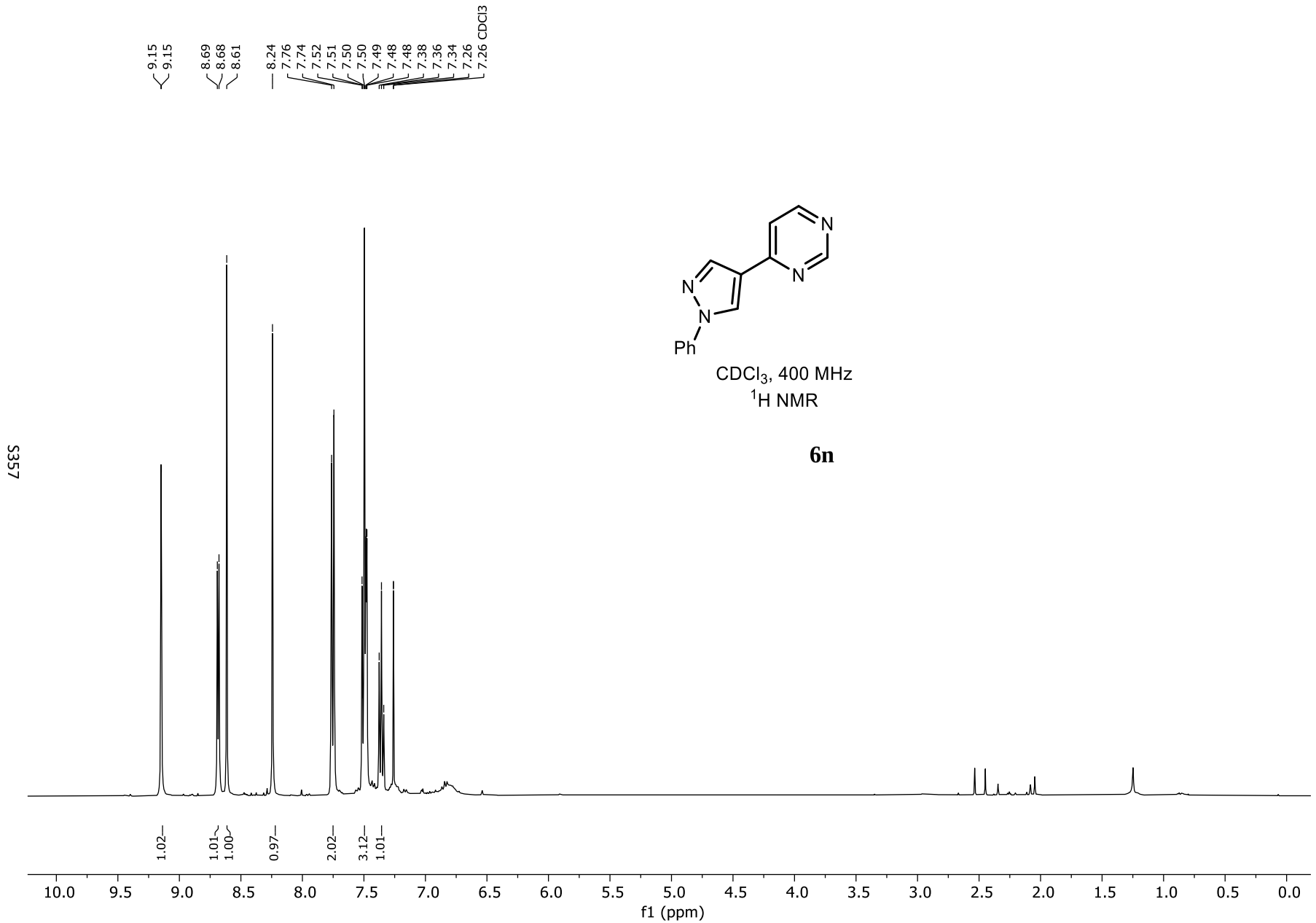
6m (minor)

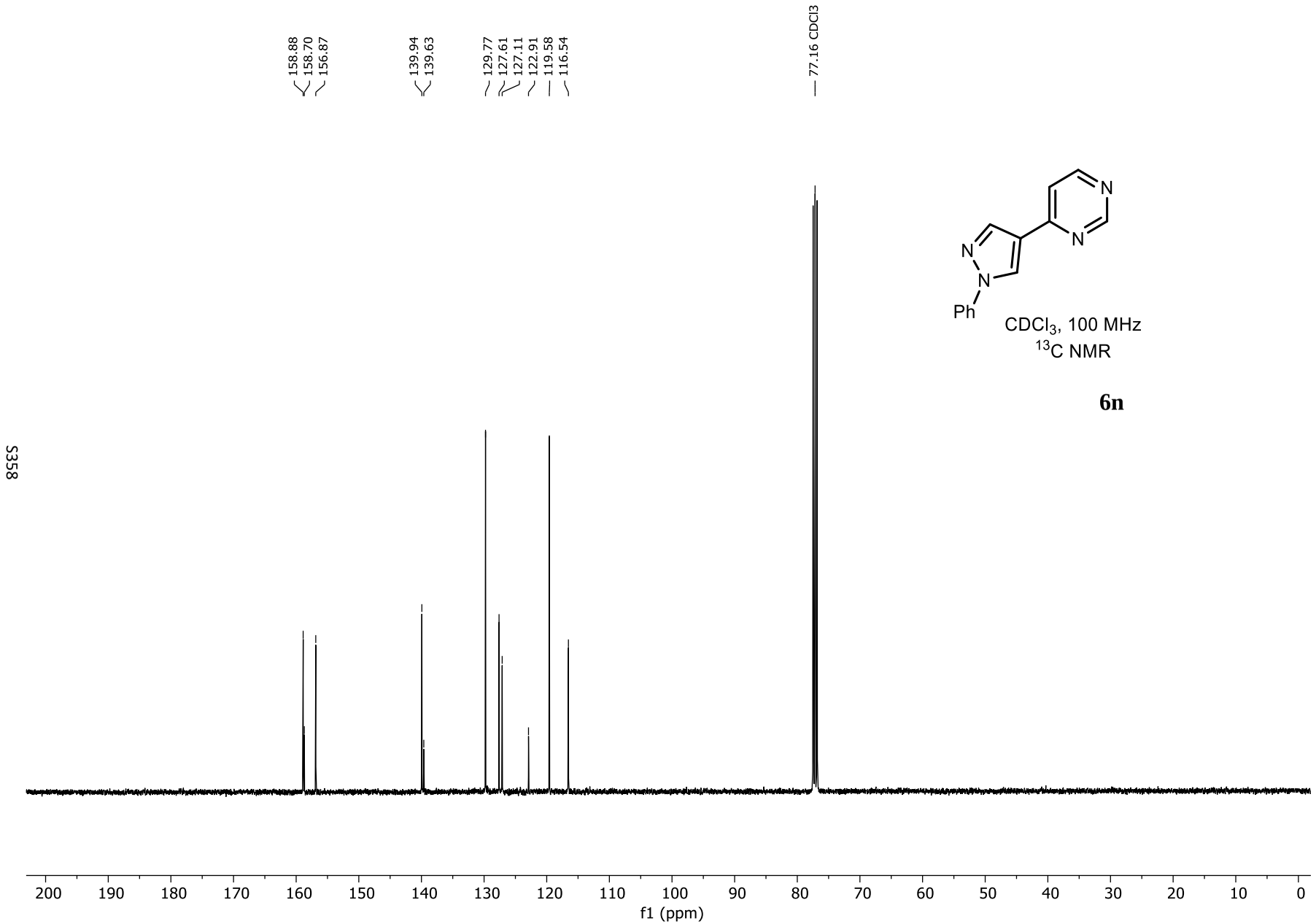


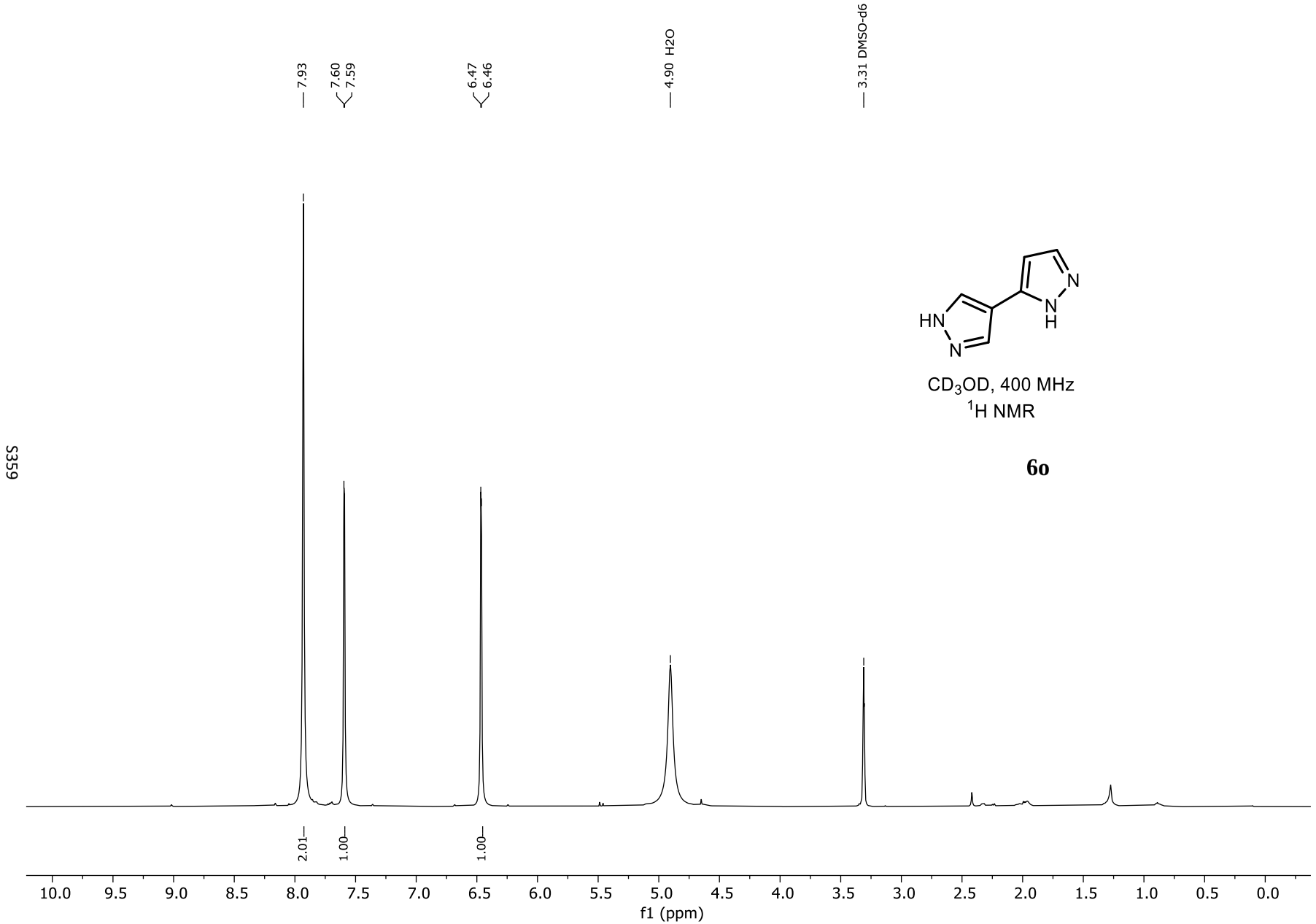

152.94
140.26
133.14
129.43
128.66
128.04
127.99
126.34
125.85
119.07
105.04
77.03 CDCl3
Ph
N
N
Ph
CDCl3, 100 MHz
13C NMR
6m (minor)
S354
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

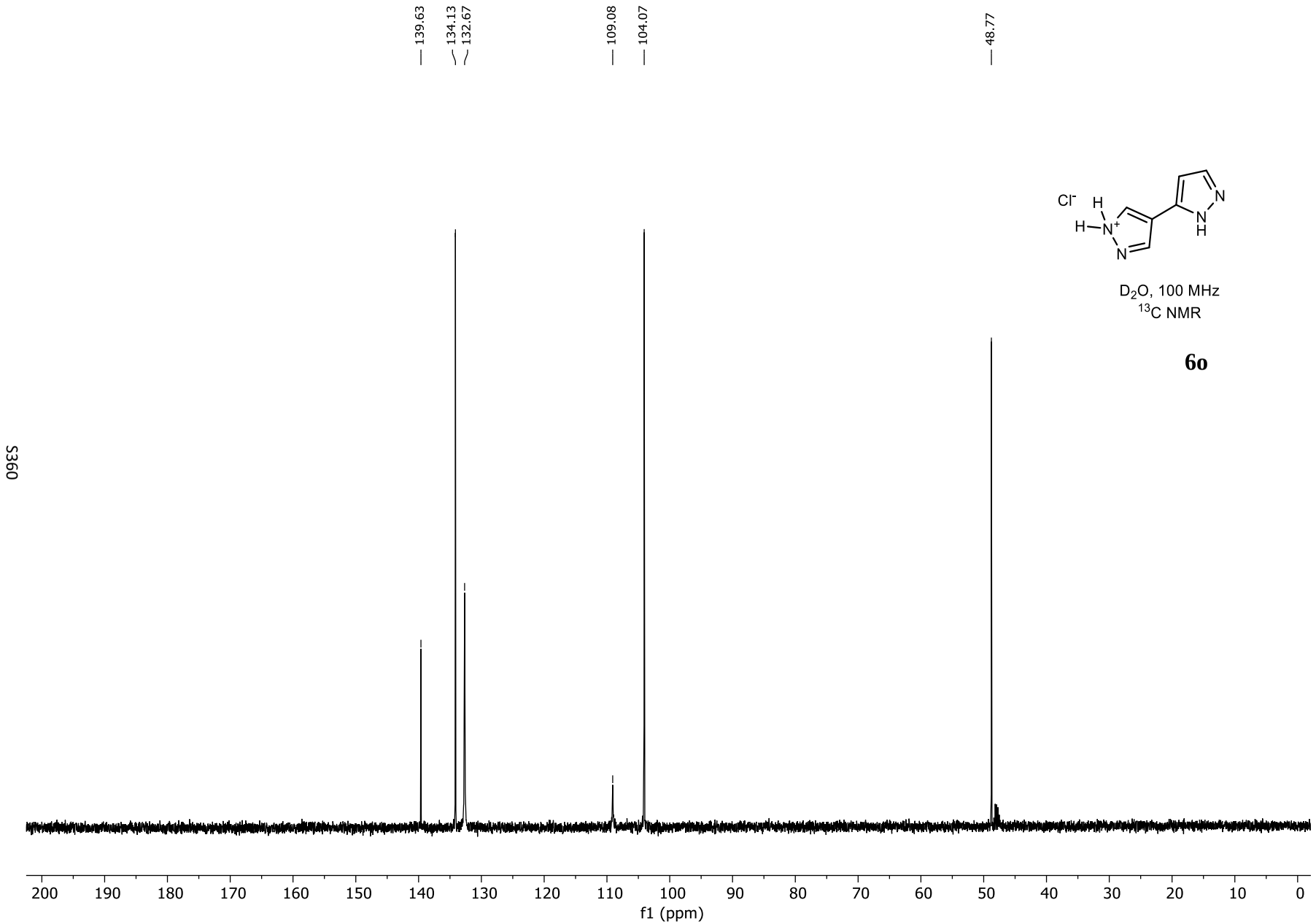

7.64
7.63
7.24
7.22
7.22
7.21
7.21
7.20
7.20
7.19
7.16
7.15
7.15
7.14
7.14
7.13
6.42
6.42
N
Ph
Ph
N
CDCl3, 400 MHz
1H NMR
6m (major)
S355
1.00
8.01
2.03
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

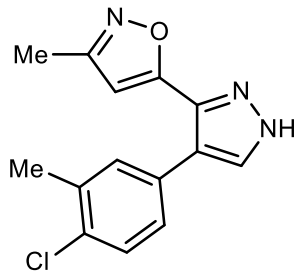

143.08
140.24
140.06
130.56
128.93
128.79
128.50
128.27
127.50
125.25
107.88
77.13 CDCl3
S356
Ph
N
N
Ph
CDCl3, 100 MHz
13C NMR
6m (major)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.15
9.15
8.69
8.68
8.61
8.24
7.76
7.74
7.52
7.51
7.50
7.50
7.49
7.48
7.48
7.38
7.36
7.34
7.26
7.26 CDCl3
N
N
N
N
Ph
CDCl3, 400 MHz
1H NMR
6n
S357
1.02
1.01
1.00
0.97
2.02
3.12
1.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


158.88
158.70
156.87
139.94
139.63
129.77
127.61
127.11
122.91
119.58
116.54
77.16 CDCl3
S358
N
N
N
Ph
CDCl3, 100 MHz
13C NMR
6n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.93
7.60
7.59
6.47
6.46
4.90 H2O
3.31 DMSO-d6
HN
N
N
H
CD3OD, 400 MHz
1H NMR
6o
S359
2.01
1.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

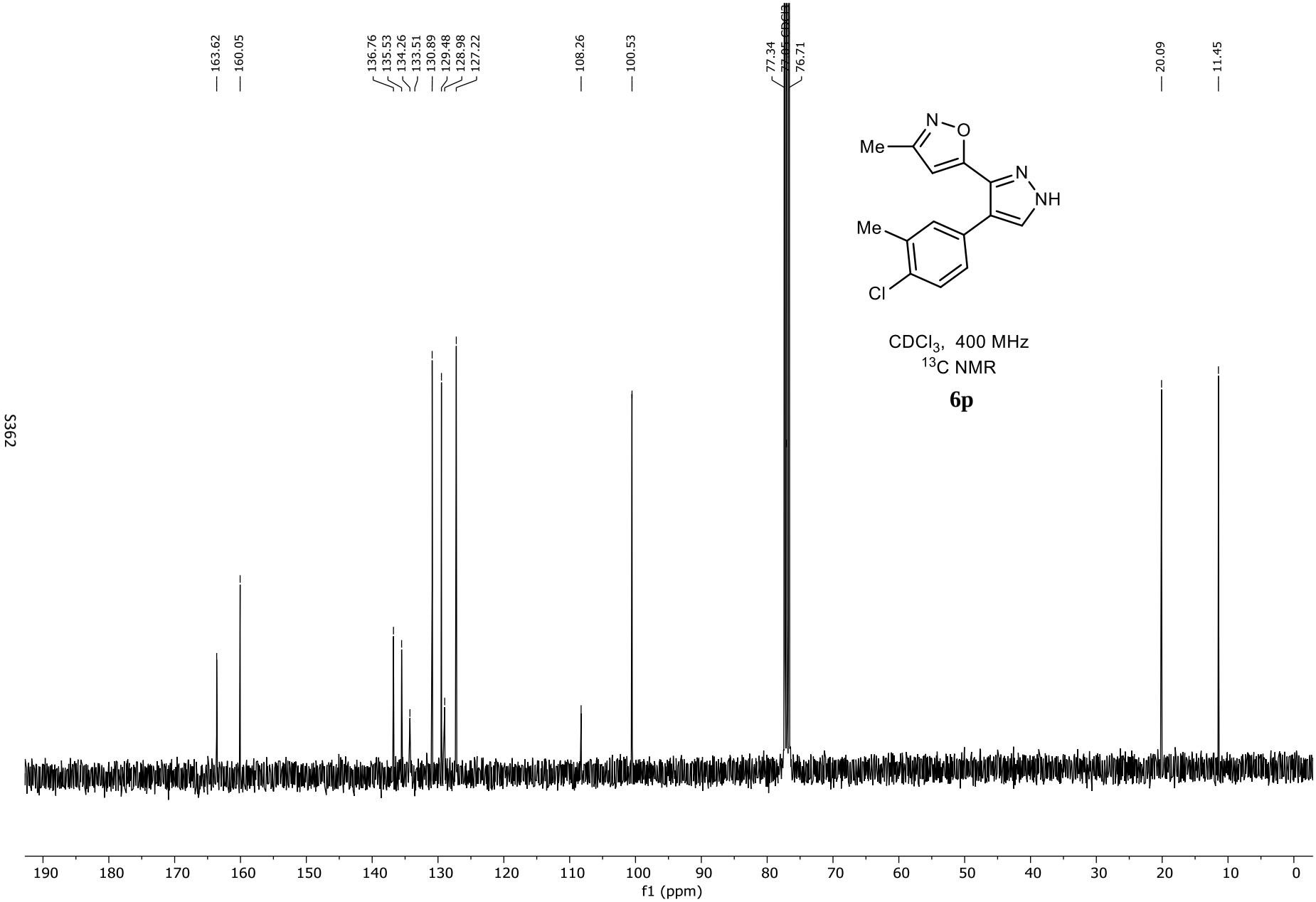

139.63
134.13
132.67
109.08
104.07
48.77
Cl⁻
H
H
N⁺
N
N
H
N
D2O, 100 MHz
13C NMR
6o
S360
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

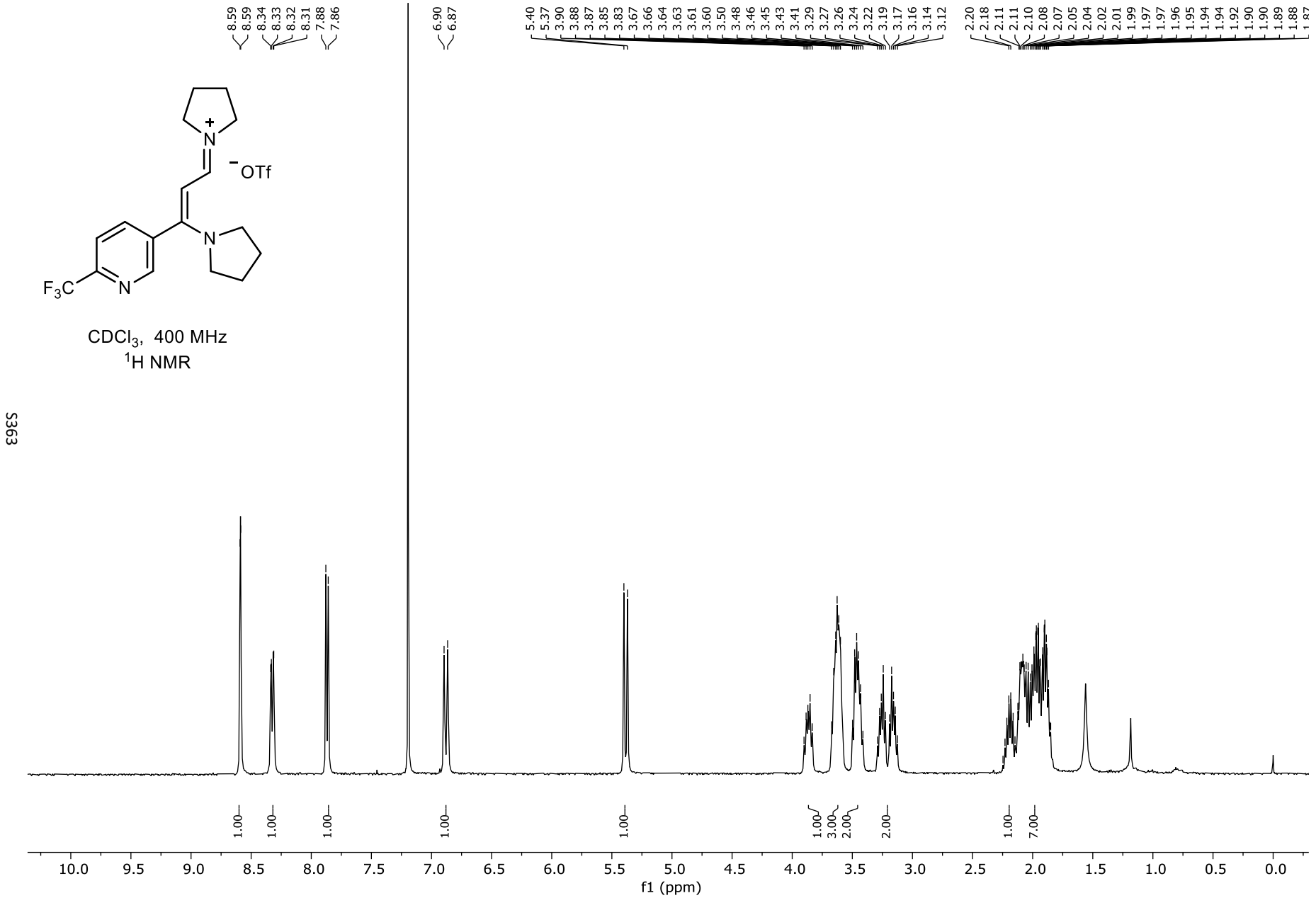


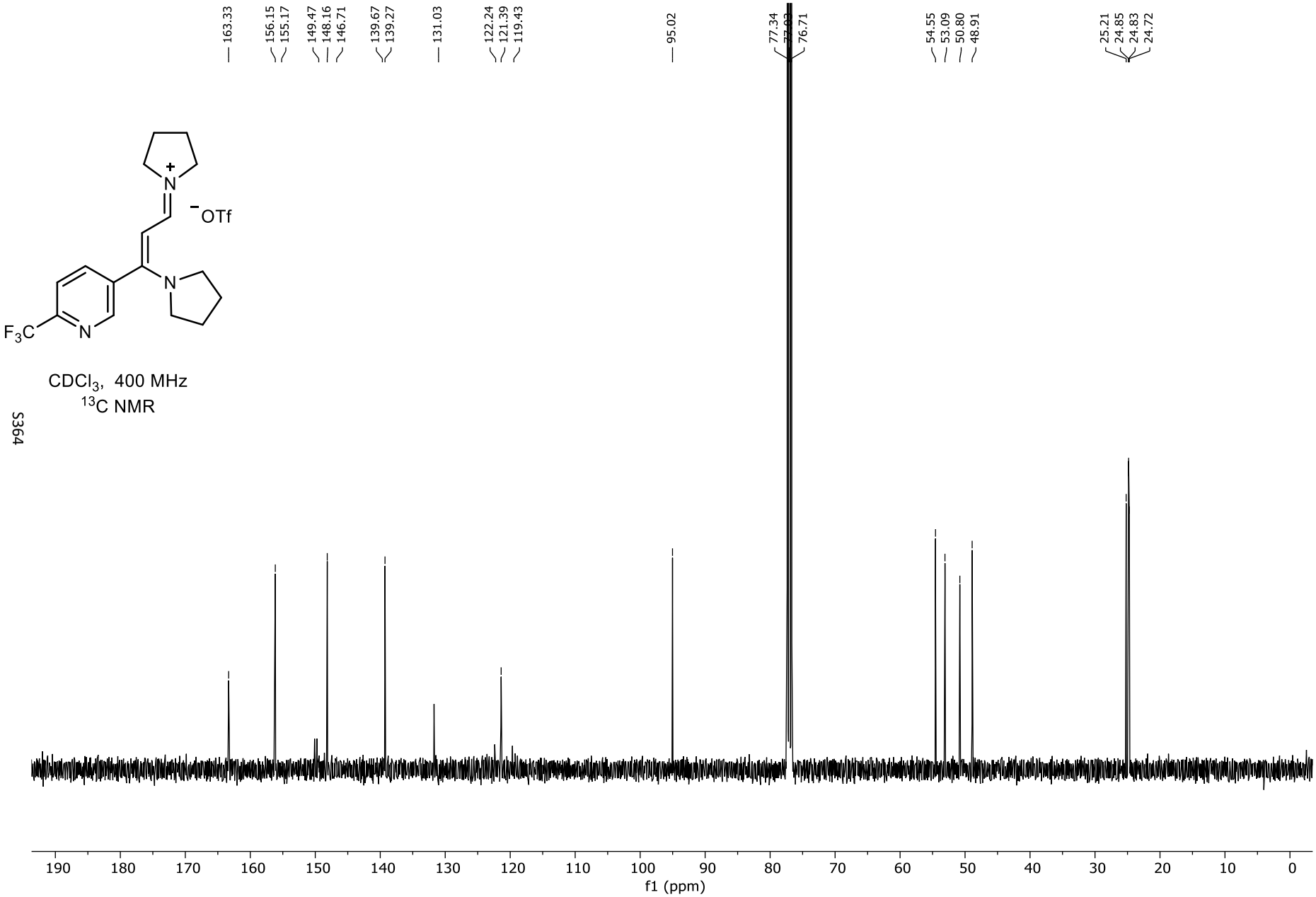
$CDCl_3$, 400 MHz

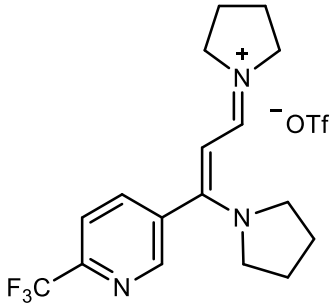
^1H NMR

6p


163.62
160.05
136.76
135.53
134.26
133.51
130.89
129.48
128.98
127.22
108.26
100.53
77.34
76.71
20.09
11.45
N
O
Me
N
NH
Me
Cl
CDCl3, 400 MHz
13C NMR
6p
S362
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.59
8.59
8.34
8.33
8.32
8.31
7.88
7.86
6.90
6.87
5.40
5.37
3.90
3.88
3.87
3.85
3.83
3.67
3.66
3.64
3.63
3.61
3.60
3.50
3.48
3.46
3.45
3.43
3.41
3.29
3.27
3.26
3.24
3.22
3.19
3.17
3.16
3.14
3.12
2.20
2.18
2.11
2.11
2.10
2.08
2.07
2.05
2.04
2.02
2.01
1.99
1.97
1.97
1.96
1.95
1.94
1.94
1.92
1.90
1.90
1.89
1.88
N
OTf
N
N
F3C
CDCl3, 400 MHz
1H NMR
S363
1.00
1.00
1.00
1.00
1.00
1.00
3.00
2.00
2.00
1.00
7.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


163.33
156.15
155.17
149.47
148.16
146.71
139.67
139.27
131.03
122.24
121.39
119.43
95.02
77.34
77.03
76.71
54.55
53.09
50.80
48.91
25.21
24.85
24.83
24.72
OTf
F3C
CDCl3, 400 MHz
13C NMR
S364
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

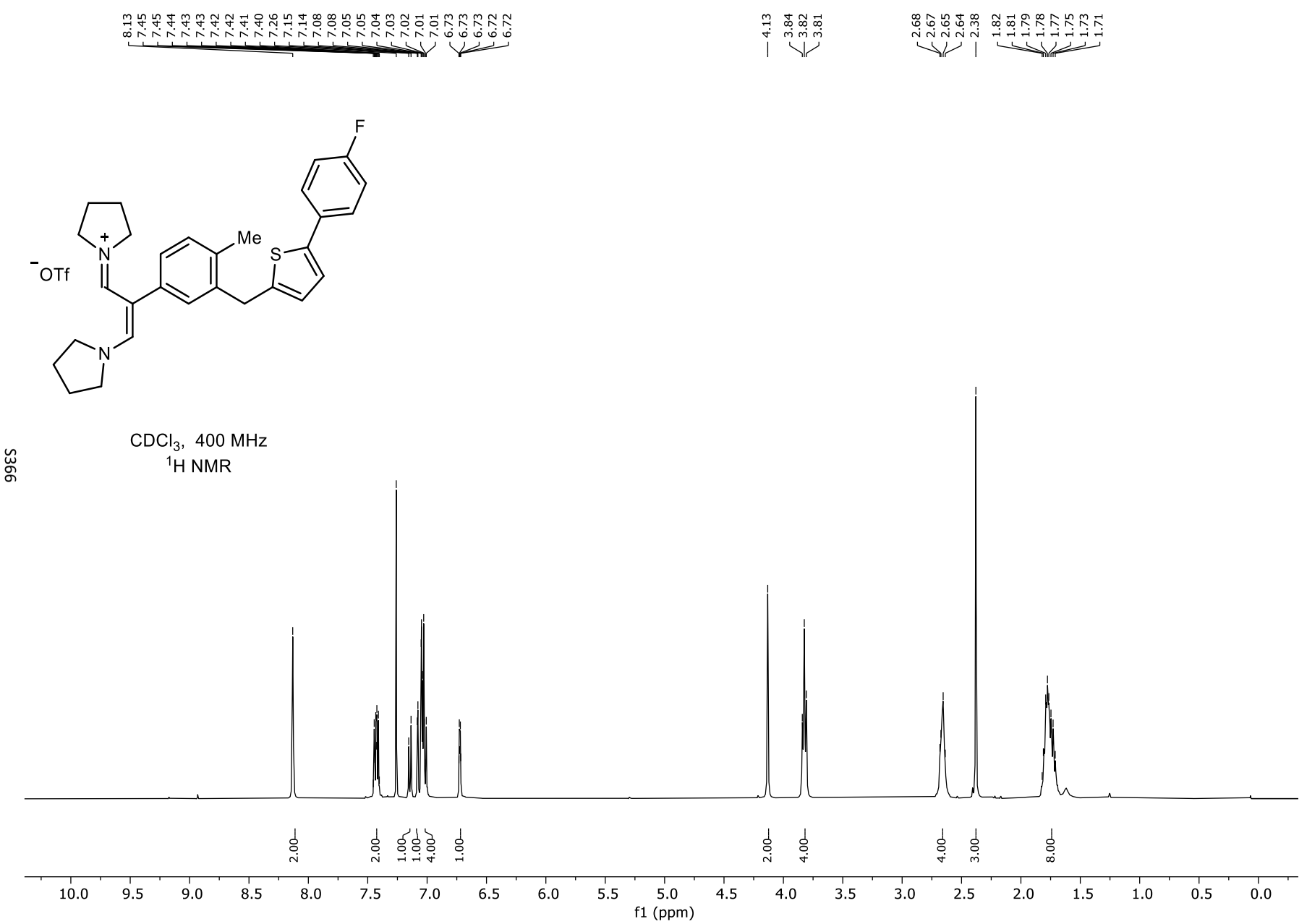


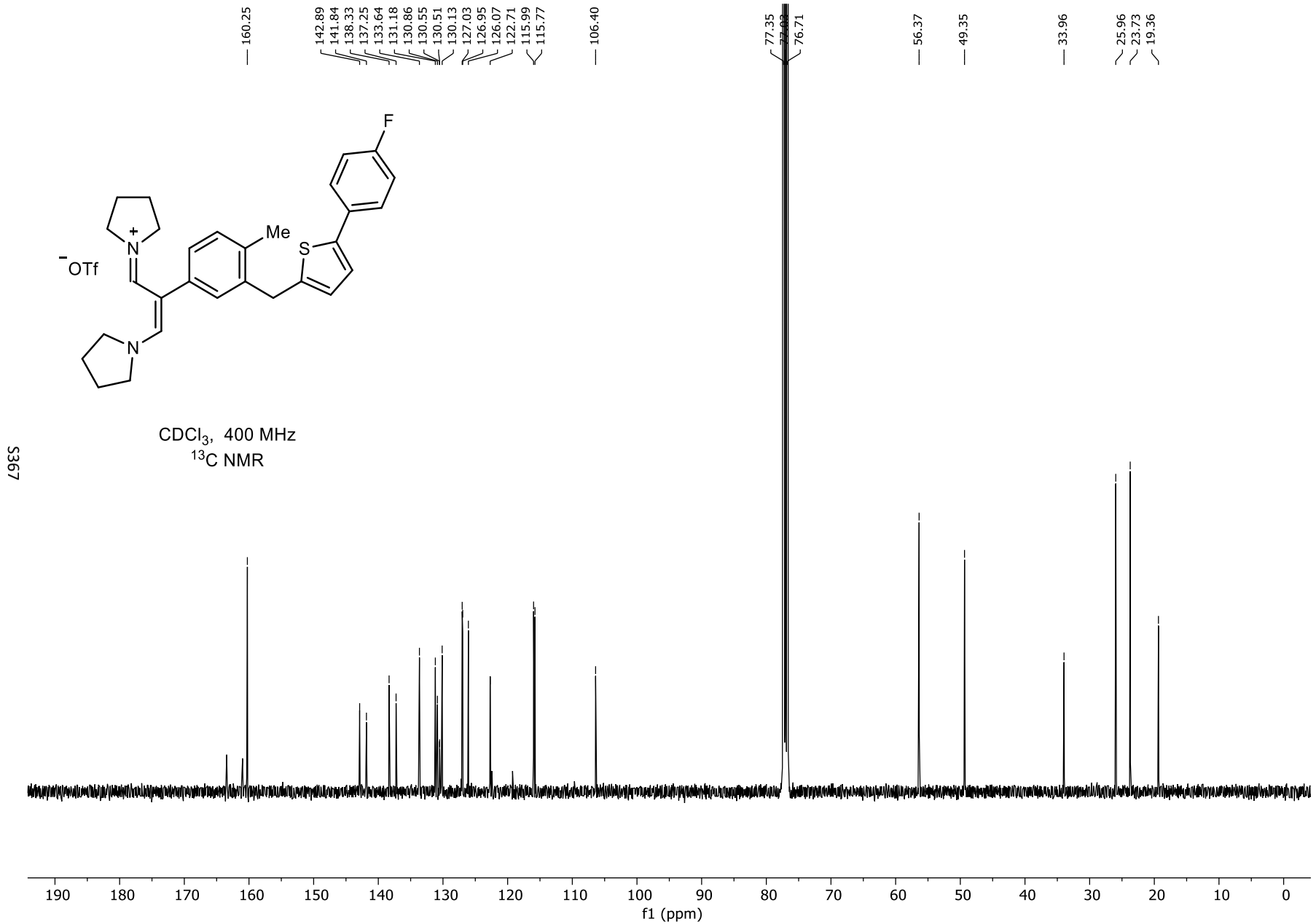
$CDCl_3$, 400 MHz
^{19}F NMR

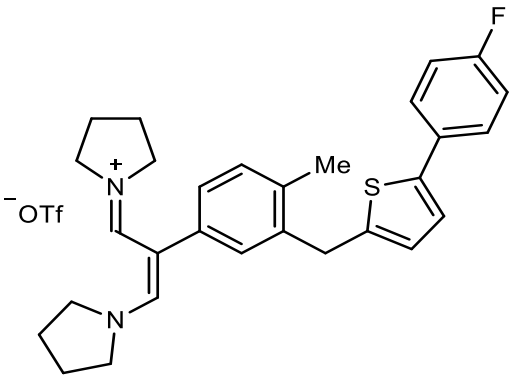
S365

-68.15
-78.32

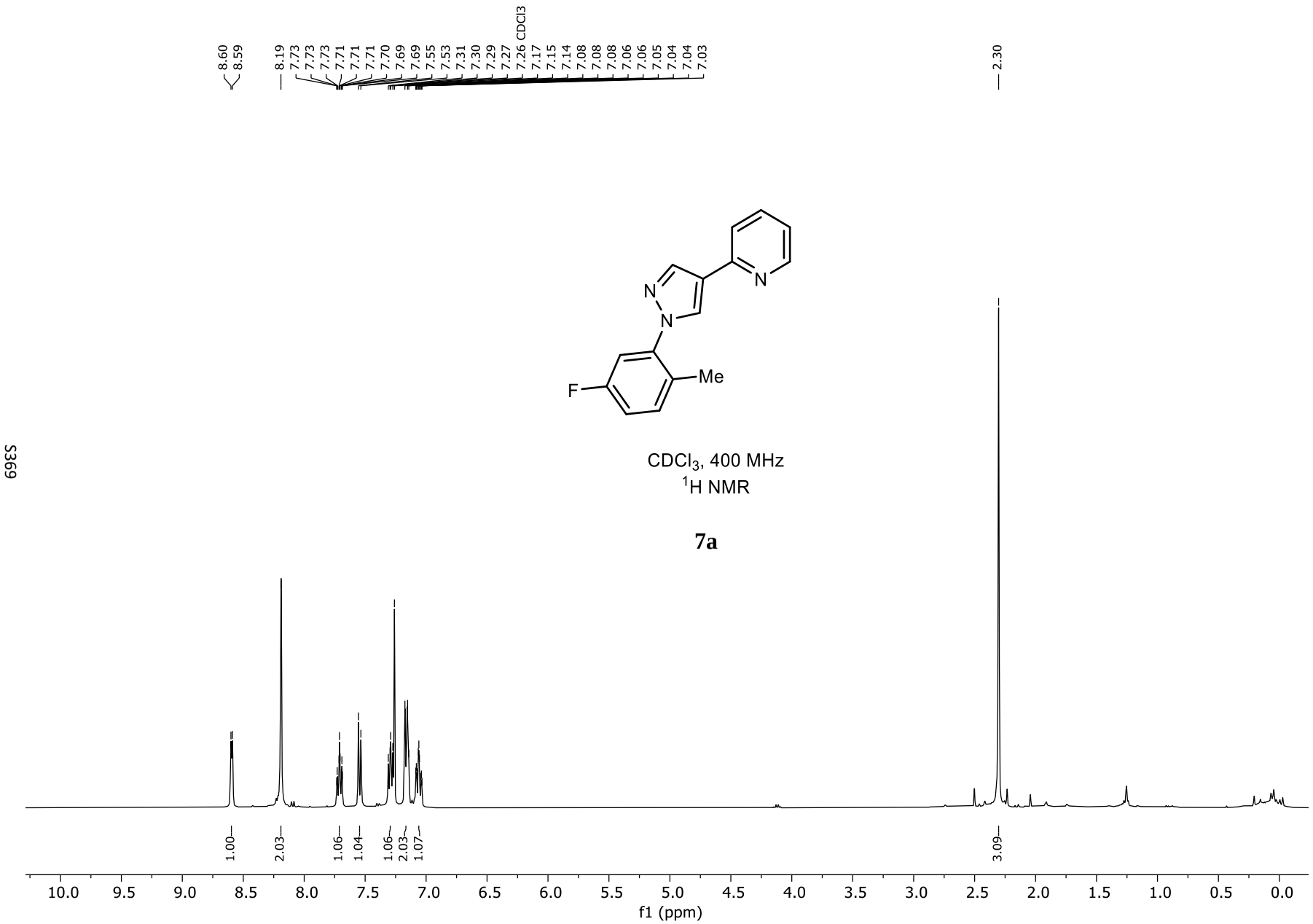
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

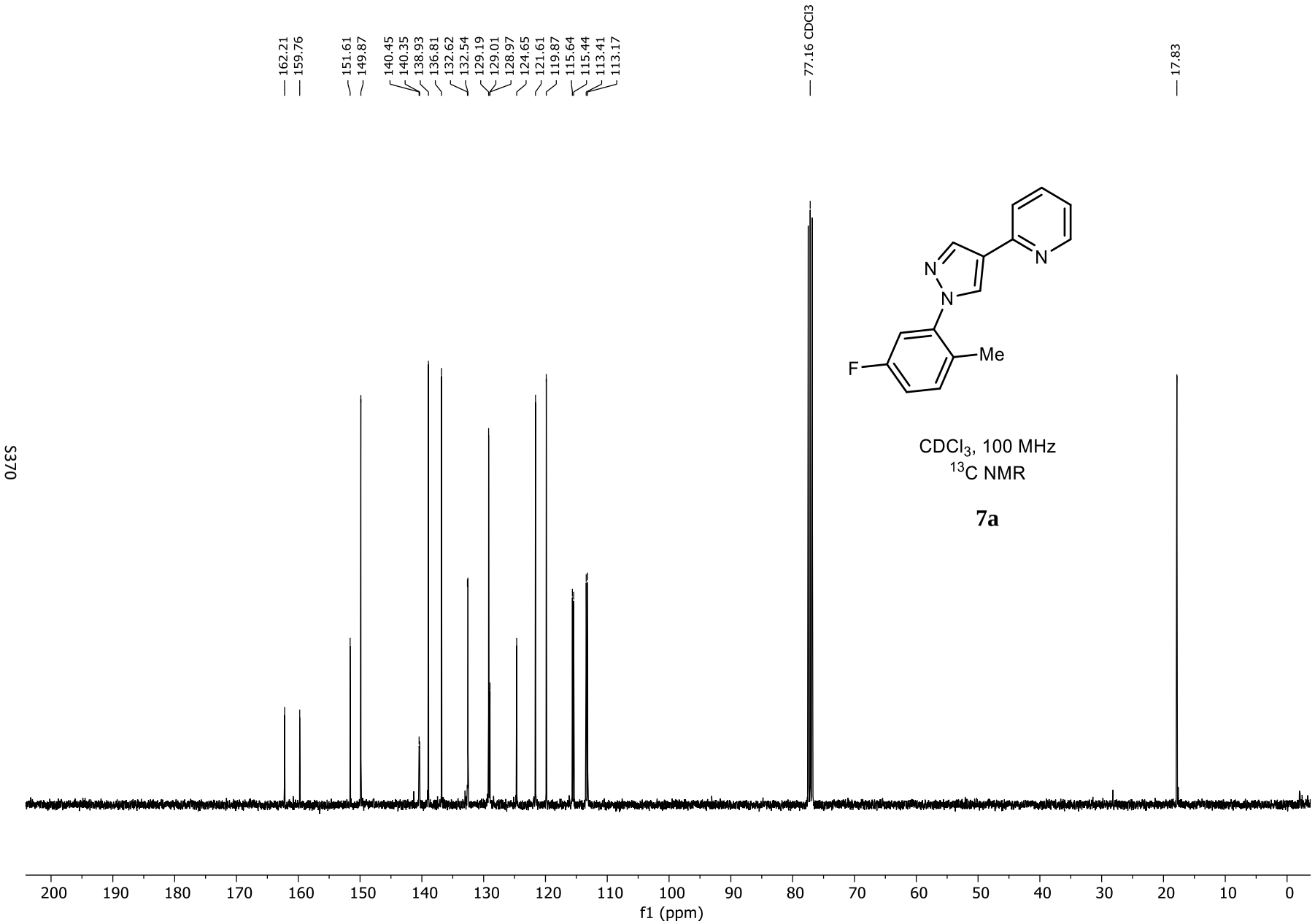

8.13
7.45
7.45
7.44
7.43
7.43
7.42
7.42
7.41
7.40
7.26
7.15
7.14
7.08
7.08
7.05
7.05
7.04
7.03
7.02
7.01
7.01
6.73
6.73
6.73
6.72
6.72
4.13
3.84
3.82
3.81
2.68
2.67
2.65
2.64
2.38
1.82
1.81
1.79
1.78
1.77
1.75
1.73
1.71
F
Me
S
N
N
OTf
CDCl3, 400 MHz
1H NMR
S366
2.00
2.00
1.00
1.00
4.00
1.00
2.00
4.00
4.00
3.00
8.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

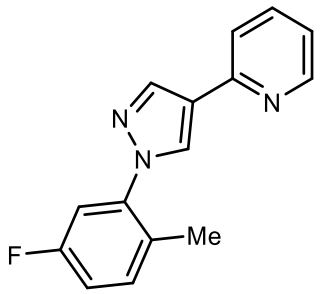

160.25
142.89
141.84
138.33
137.25
133.64
131.18
130.86
130.55
130.51
130.13
127.03
126.95
126.07
122.71
115.99
115.77
106.40
77.35
77.03
76.71
56.37
49.35
33.96
25.96
23.73
19.36
F
Me
S
N
N
OTf
CDCl3, 400 MHz
13C NMR
S367
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



$CDCl_3$, 400 MHz
^{19}F NMR

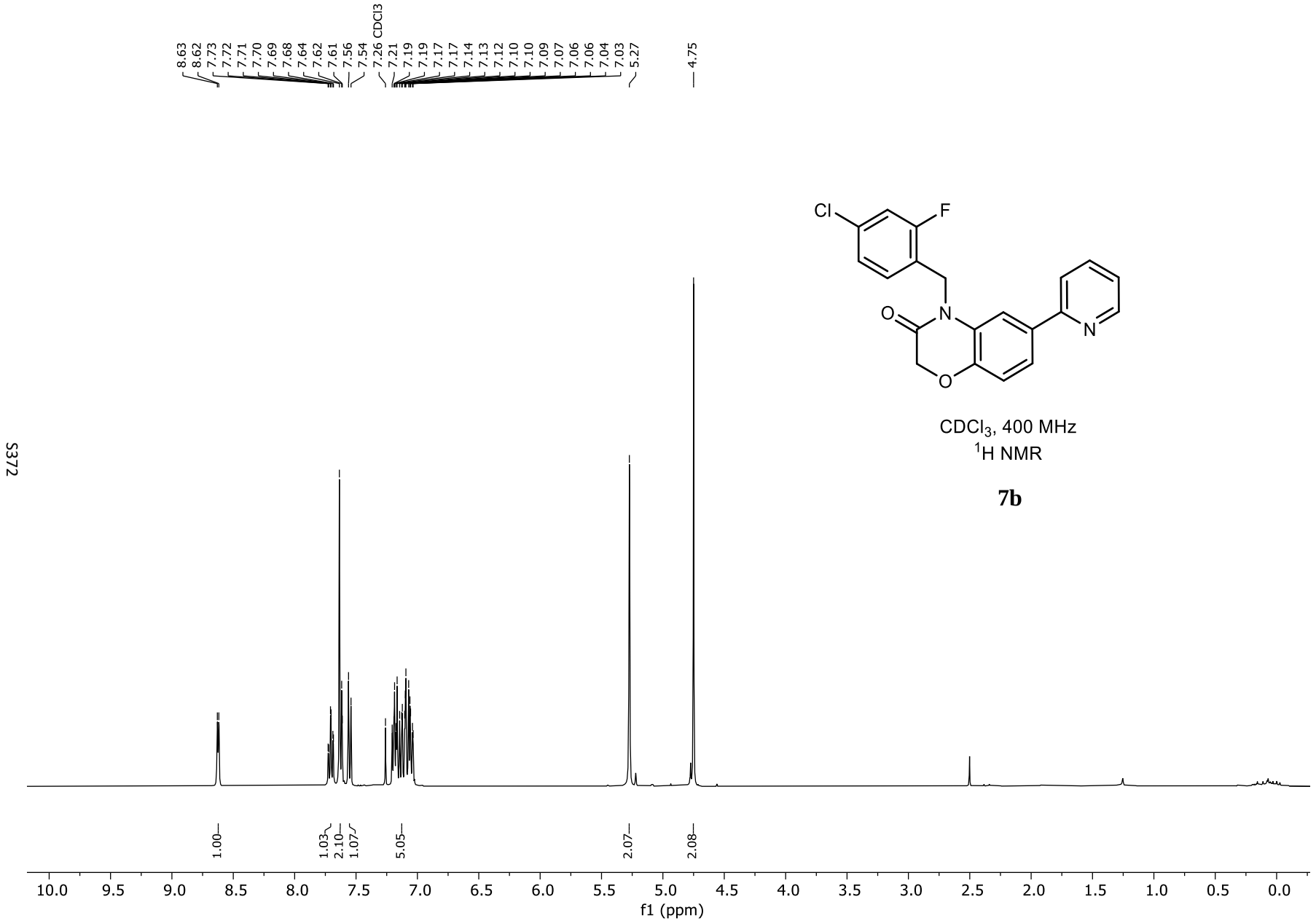

8.60
8.59
8.19
7.73
7.73
7.73
7.71
7.71
7.71
7.70
7.69
7.69
7.55
7.53
7.31
7.30
7.29
7.27
7.26 CDCl3
7.17
7.15
7.14
7.08
7.08
7.08
7.06
7.06
7.05
7.04
7.04
7.03
2.30
N
N
N
F
Me
CDCl3, 400 MHz
1H NMR
7a
S369
1.00
2.03
1.06
1.04
1.06
2.03
1.07
3.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

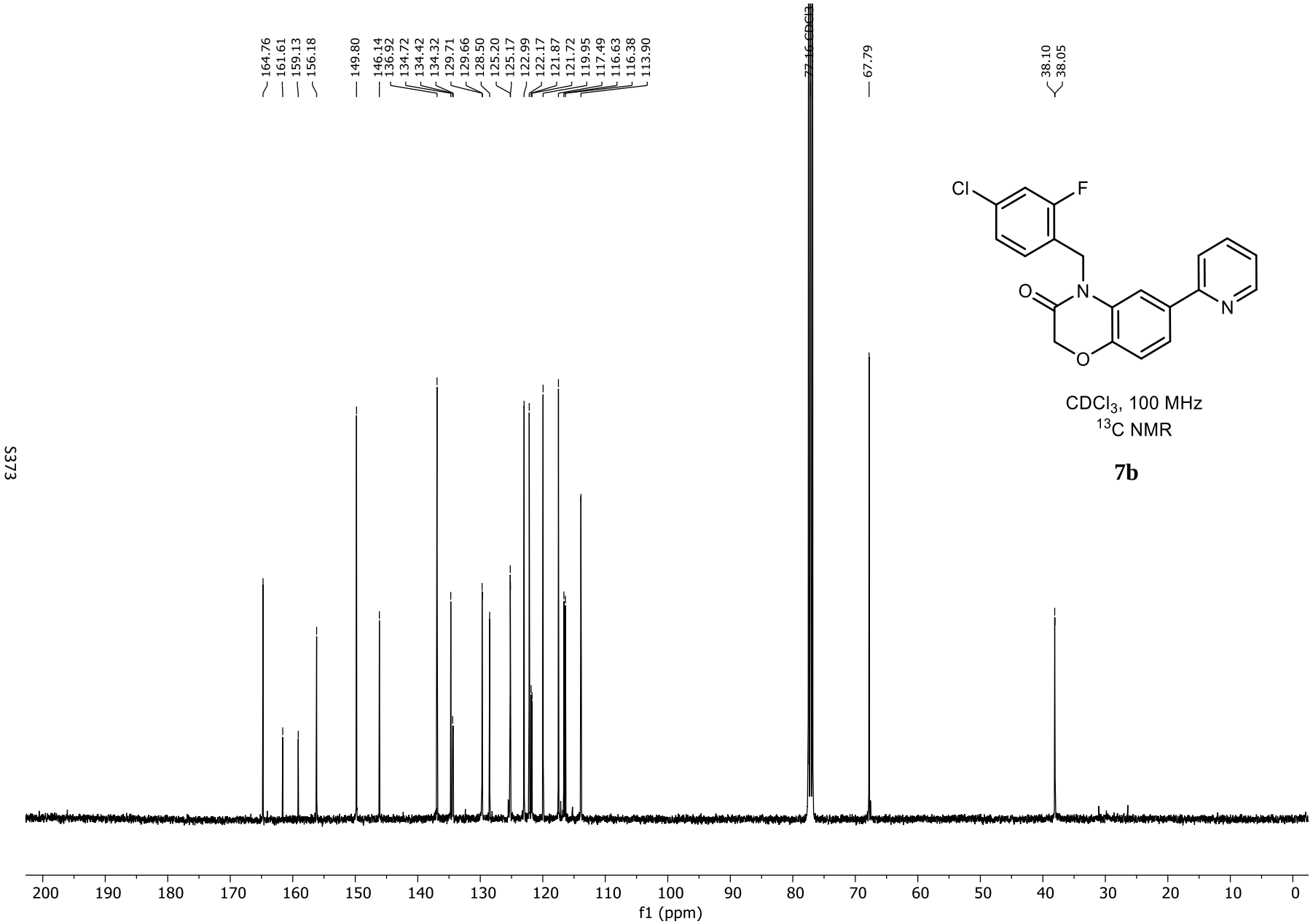

162.21
159.76
151.61
149.87
140.45
140.35
138.93
136.81
132.62
132.54
129.19
129.01
128.97
124.65
121.61
119.87
115.64
115.44
113.41
113.17
77.16 CDCl3
17.83
N
N
N
F
Me
CDCl3, 100 MHz
13C NMR
7a
S370
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

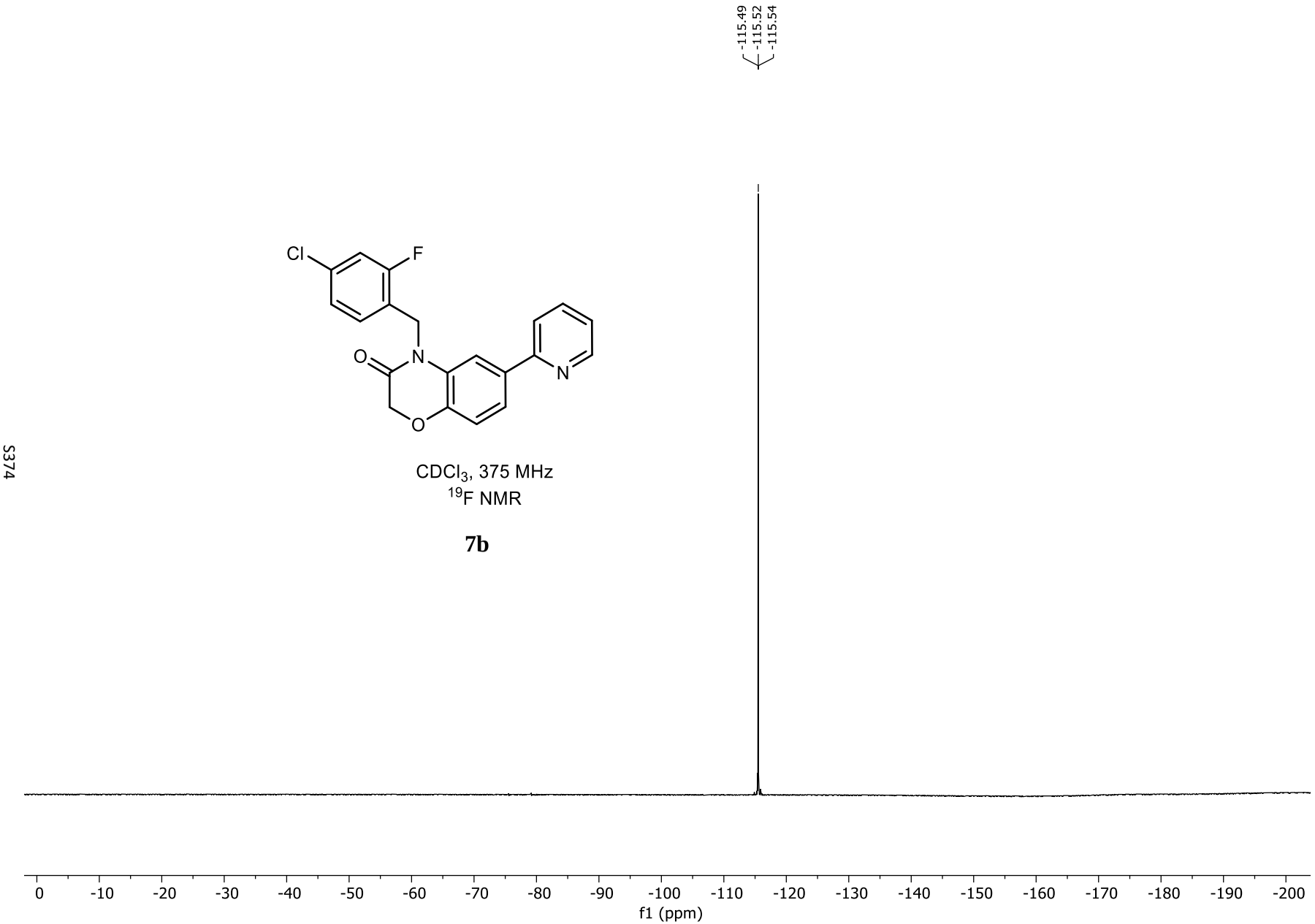


$CDCl_3$, 375 MHz
^{19}F NMR

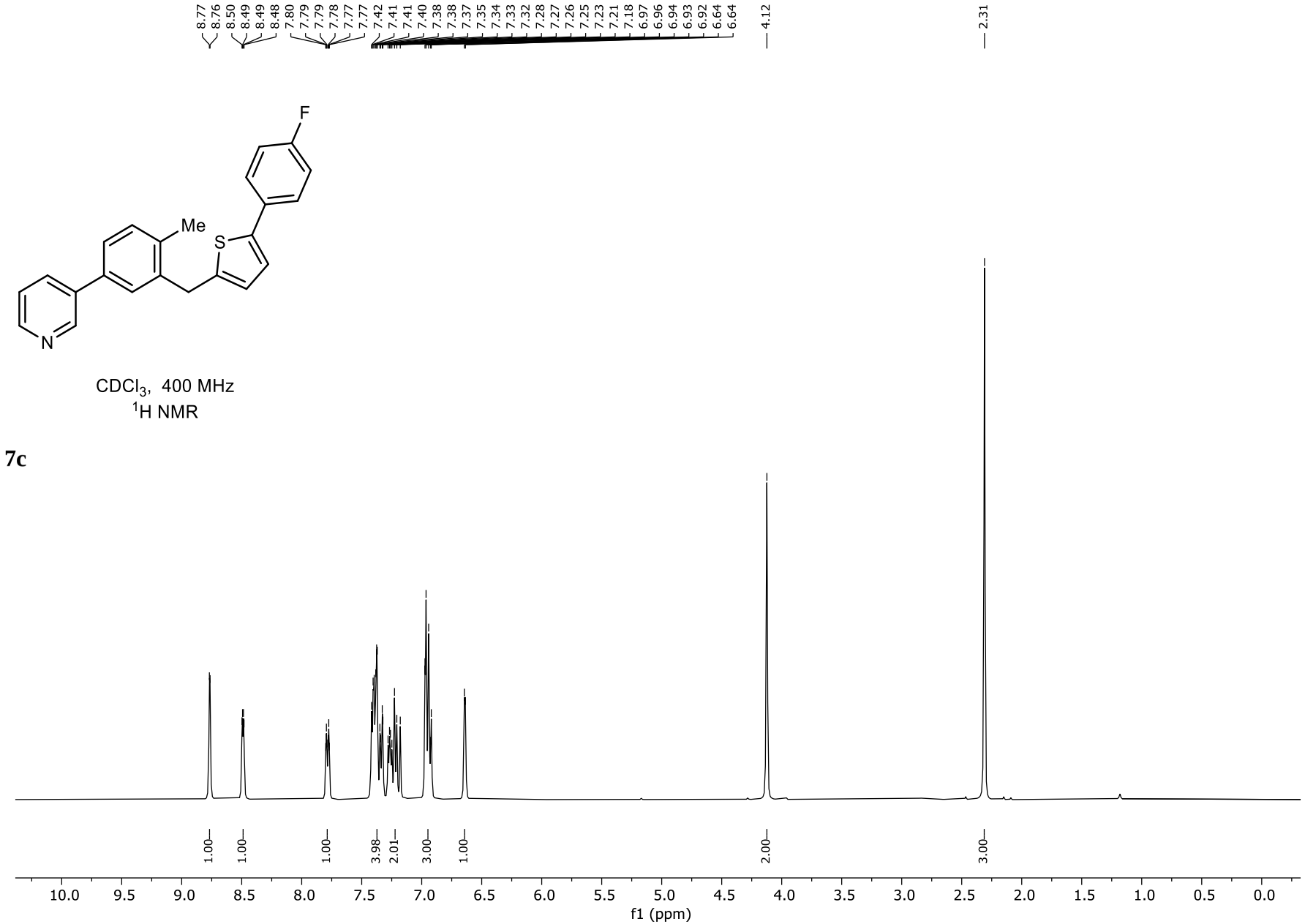
7a

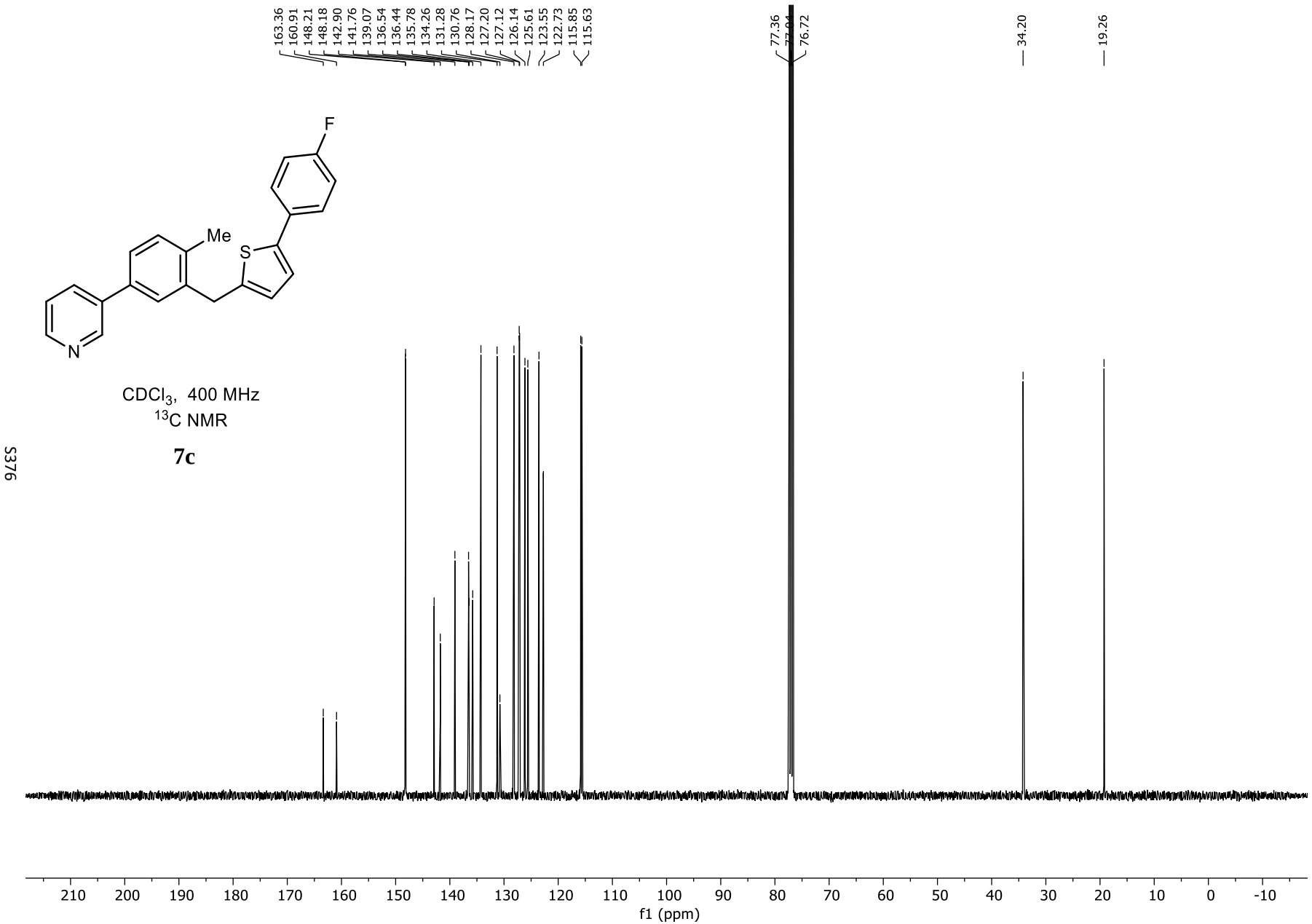

8.63
8.62
7.73
7.72
7.71
7.70
7.69
7.68
7.64
7.62
7.61
7.56
7.54
7.26 CDCl3
7.21
7.19
7.19
7.17
7.17
7.14
7.13
7.12
7.10
7.10
7.09
7.07
7.06
7.06
7.04
7.03
5.27
4.75
Cl
F
O
N
N
O
CDCl3, 400 MHz
1H NMR
7b
S372
1.00
1.03
2.10
1.07
5.05
2.07
2.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

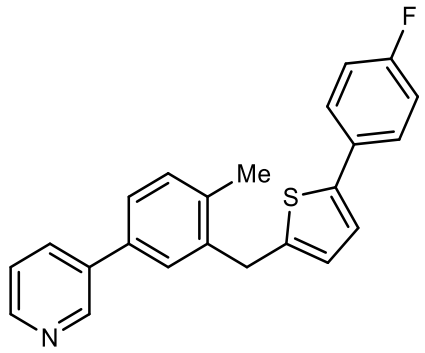

164.76
161.61
159.13
156.18
149.80
146.14
136.92
134.72
134.42
134.32
129.71
129.66
128.50
125.20
125.17
122.99
122.17
121.87
121.72
119.95
117.49
116.63
116.38
113.90
77.16 CDCl3
67.79
38.10
38.05
Cl
F
O
N
N
O
CDCl3, 100 MHz
13C NMR
7b
f1 (ppm)


-115.49
-115.52
-115.54
Cl
F
O
N
N
O
CDCl3, 375 MHz
19F NMR
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

7b


8.77
8.76
8.50
8.49
8.49
8.48
7.80
7.79
7.79
7.78
7.77
7.77
7.42
7.41
7.41
7.40
7.38
7.38
7.37
7.35
7.34
7.33
7.32
7.28
7.27
7.26
7.25
7.23
7.21
7.18
6.97
6.96
6.94
6.93
6.92
6.64
6.64
4.12
2.31
F
Me
S
N
CDCl3, 400 MHz
1H NMR
7c
1.00
1.00
1.00
3.98
2.01
3.00
1.00
2.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

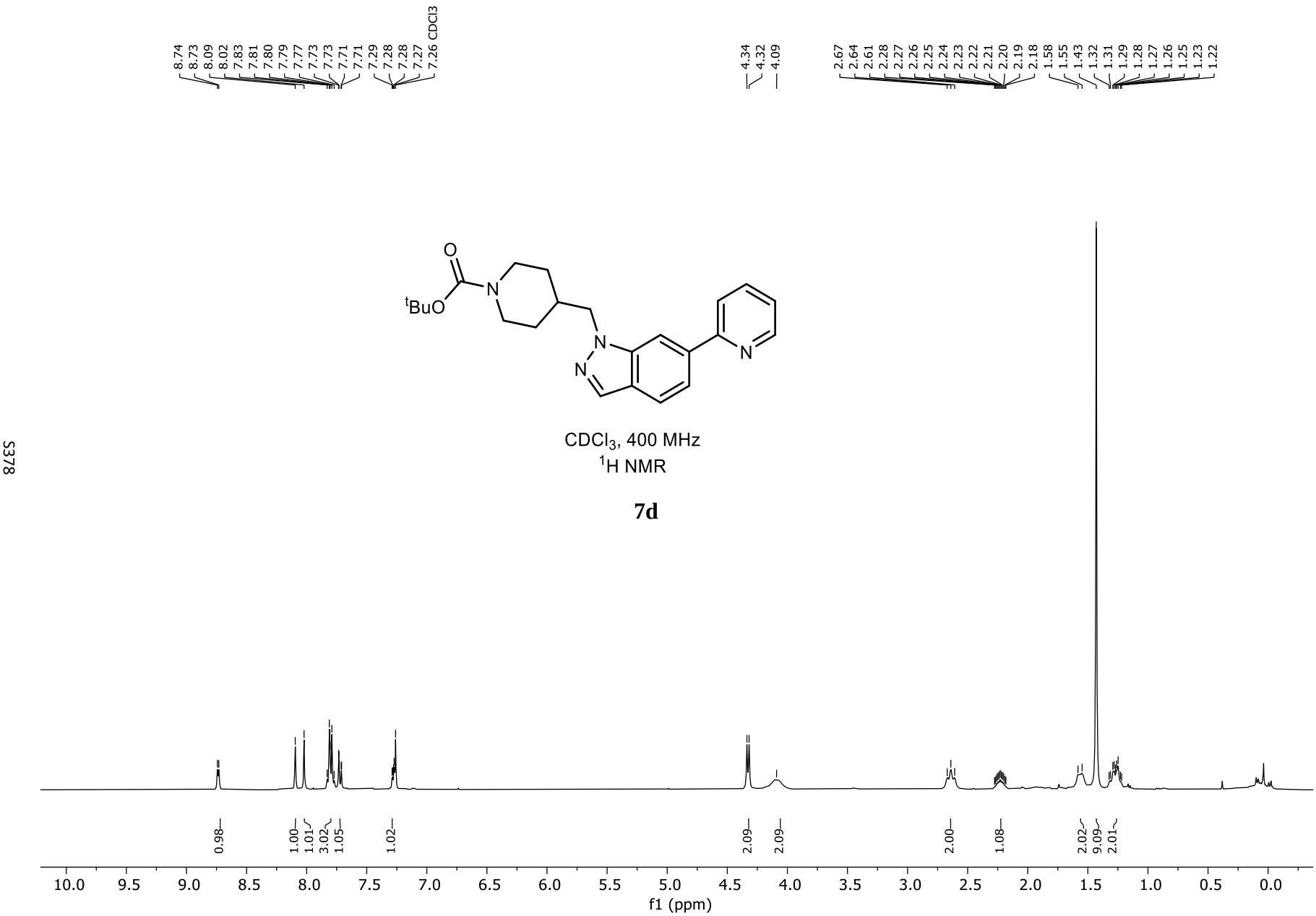

163.36
160.91
148.21
148.18
142.90
141.76
139.07
136.54
136.44
135.78
134.26
131.28
130.76
128.17
127.20
127.12
126.14
125.61
123.55
122.73
115.85
115.63
77.36
76.72
34.20
19.26
F
Me
S
N
CDCl3, 400 MHz
13C NMR
7c
S376
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

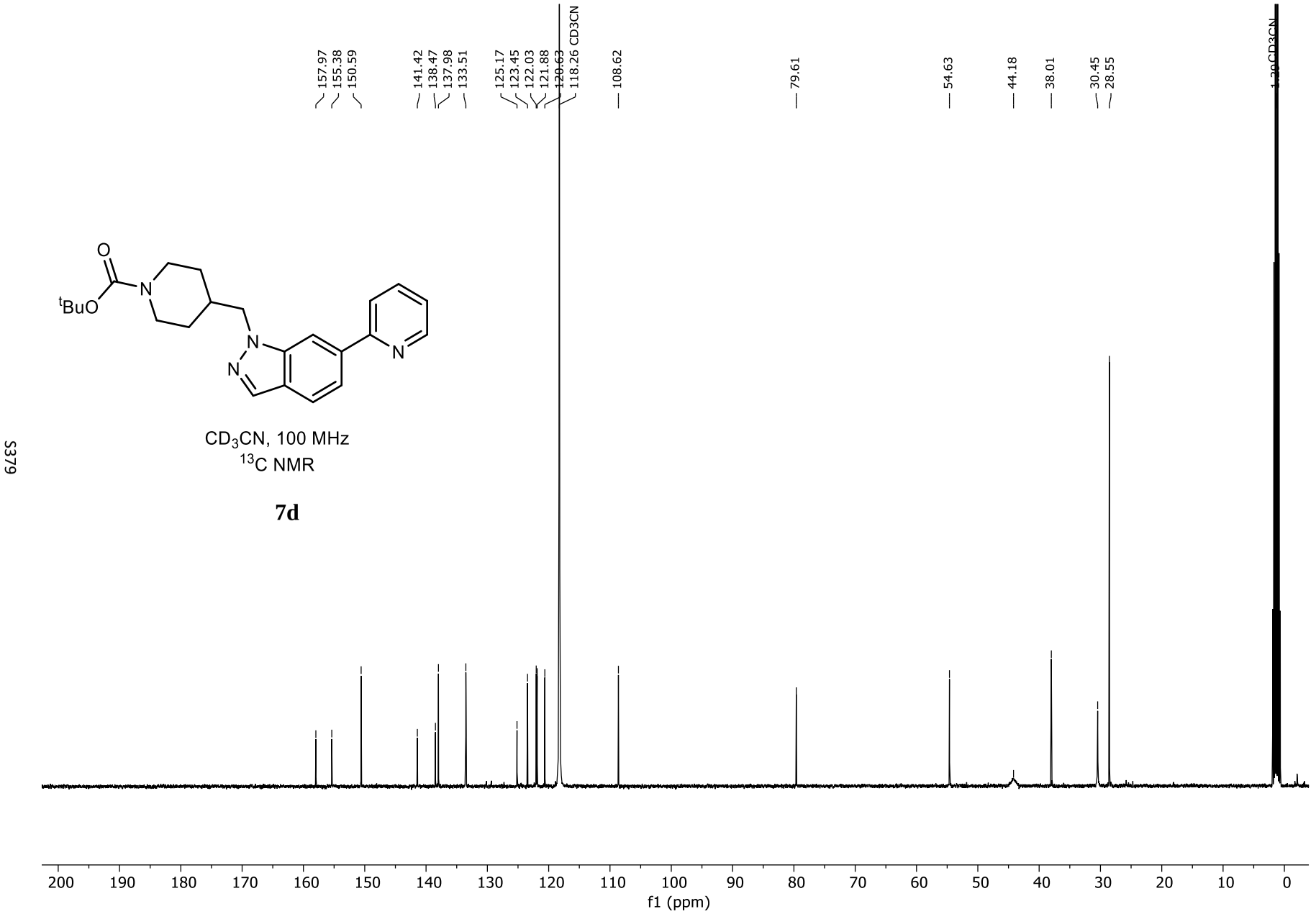


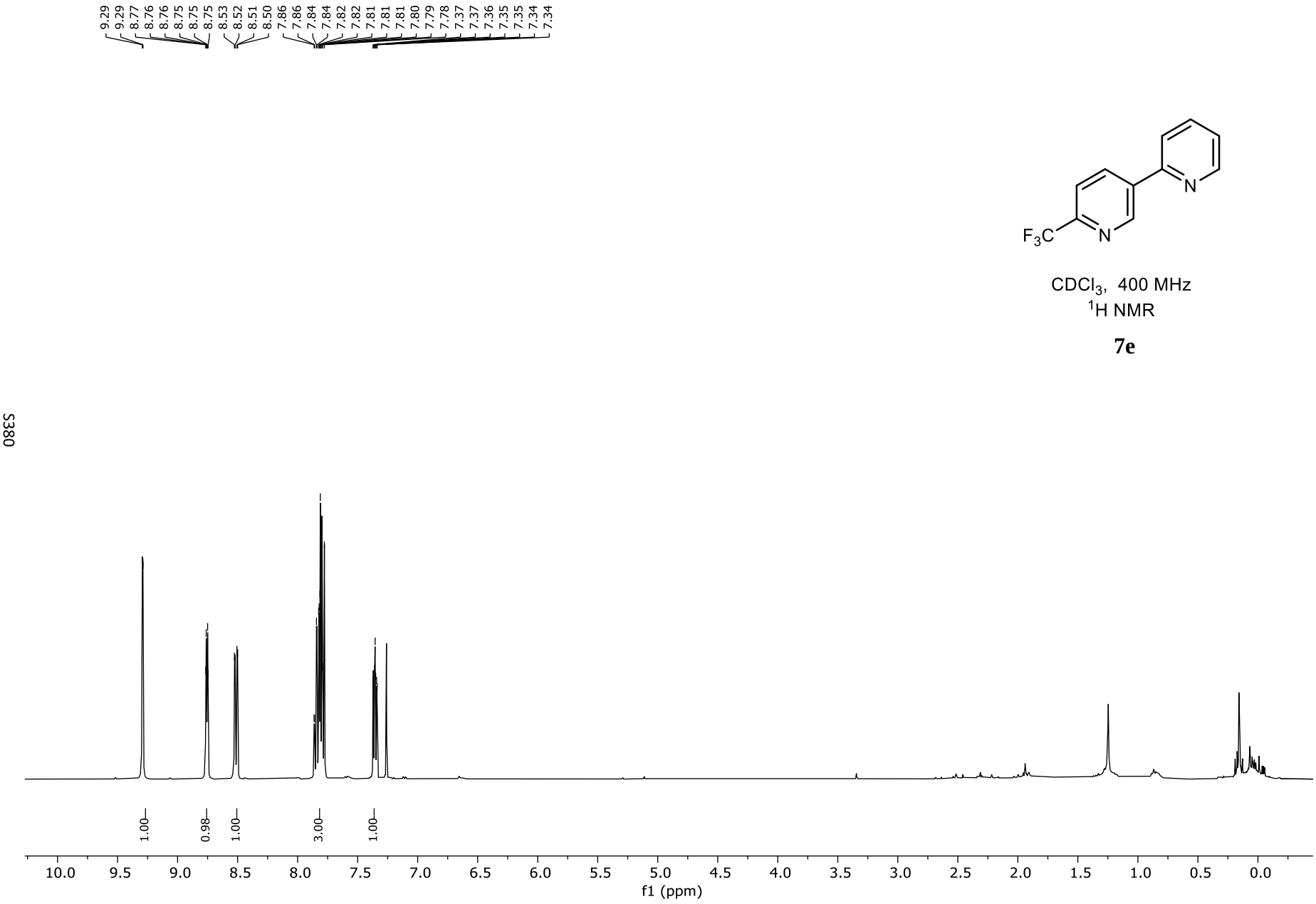
$CDCl_3$, 400 MHz

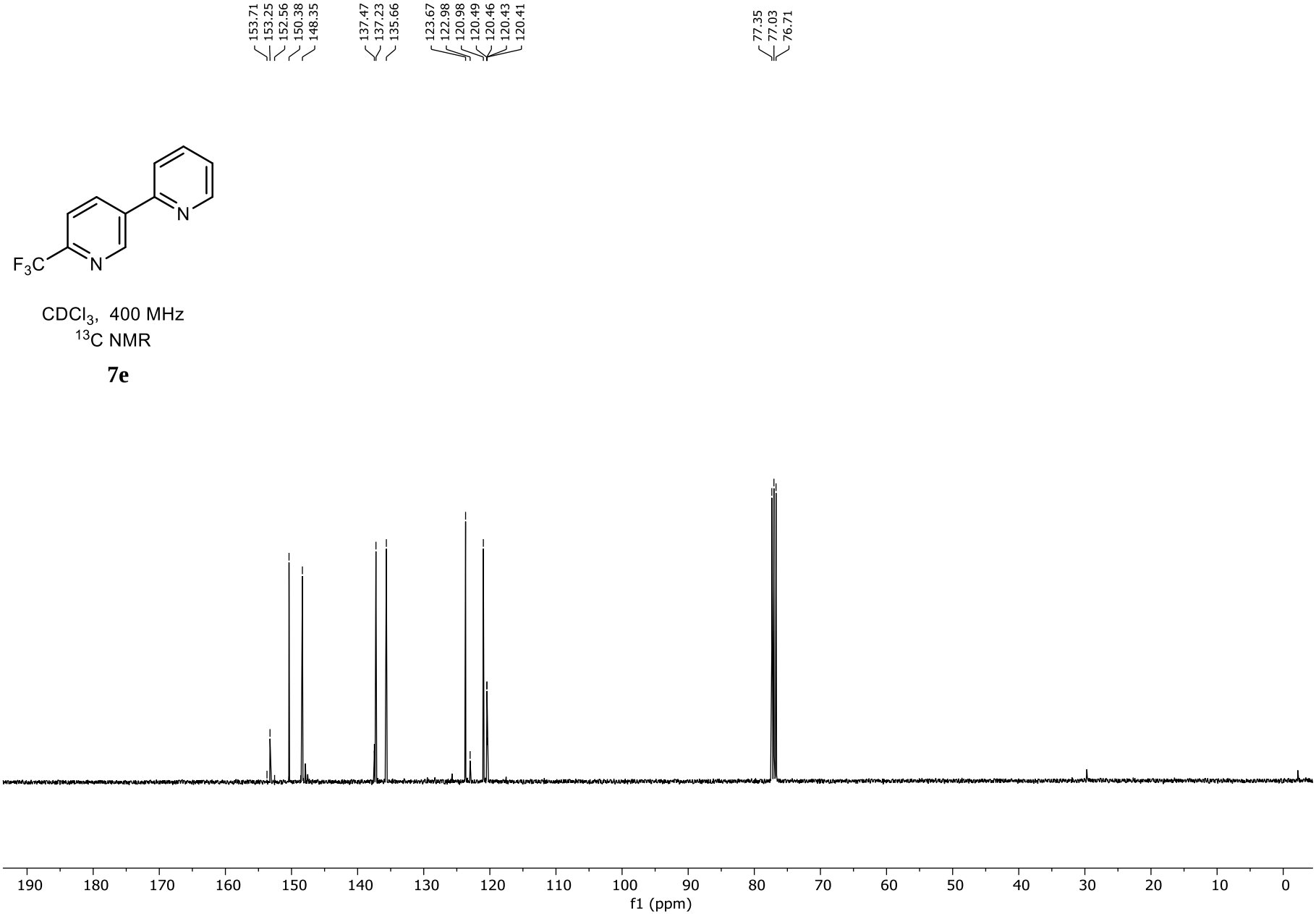
^{19}F NMR

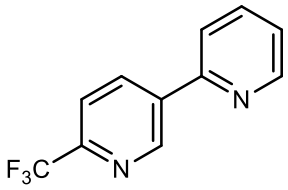
7c


8.74
8.73
8.09
8.02
7.83
7.81
7.80
7.79
7.77
7.73
7.73
7.71
7.71
7.29
7.28
7.28
7.27
7.26 CDCl3
4.34
4.32
4.09
2.67
2.64
2.61
2.28
2.27
2.26
2.25
2.24
2.23
2.22
2.21
2.20
2.19
2.18
1.58
1.55
1.43
1.32
1.31
1.29
1.28
1.27
1.26
1.25
1.23
1.22
O
tBuO
N
N
N
N
CDCl3, 400 MHz
1H NMR
7d
0.98
1.00
1.01
3.02
1.05
1.02
2.09
2.09
2.00
1.08
2.02
9.09
2.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


157.97
155.38
150.59
141.42
138.47
137.98
133.51
125.17
123.45
122.03
121.88
120.63
118.26 CD3CN
108.62
79.61
54.63
44.18
38.01
30.45
28.55
1.39CD3CN
O
tBuO
N
N
N
N
CD3CN, 100 MHz
13C NMR
7d
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

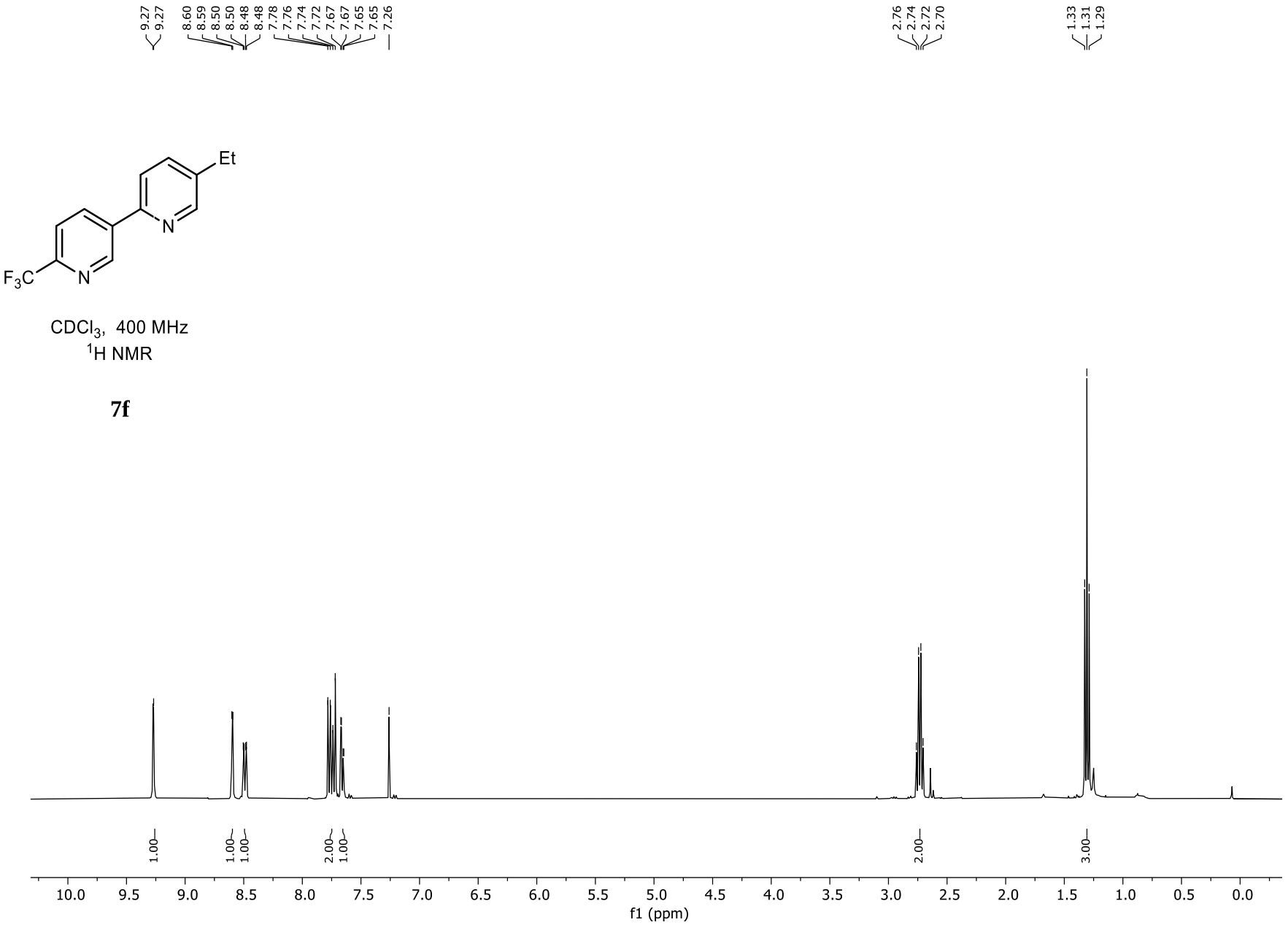

9.29
9.29
8.77
8.76
8.76
8.75
8.75
8.75
8.53
8.52
8.51
8.50
7.86
7.86
7.84
7.84
7.82
7.82
7.81
7.81
7.81
7.80
7.79
7.78
7.37
7.37
7.36
7.35
7.35
7.34
7.34
F3C
N
N
CDCl3, 400 MHz
1H NMR
7e
S380
1.00
0.98
1.00
3.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

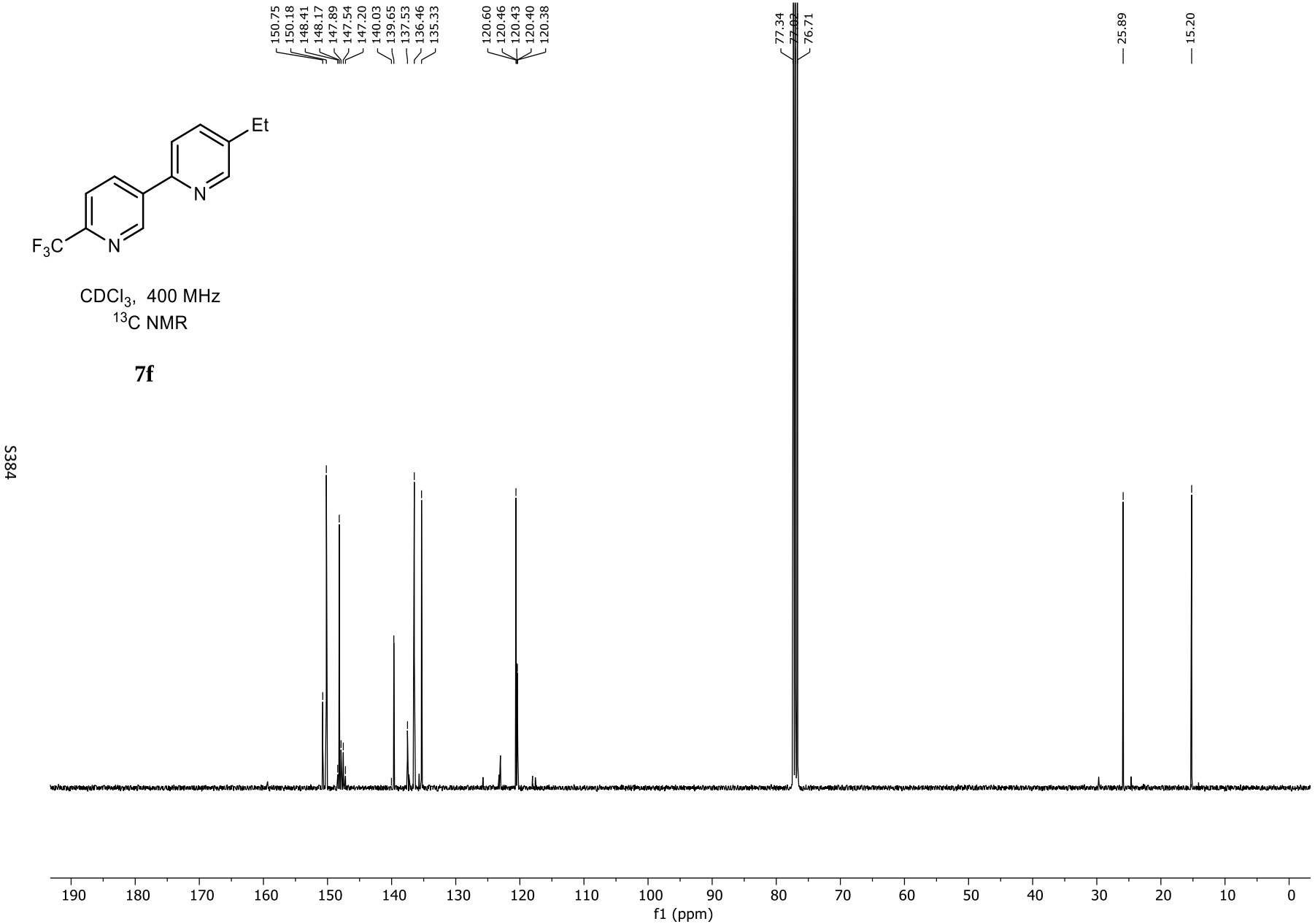

153.71
153.25
152.56
150.38
148.35
137.47
137.23
135.66
123.67
122.98
120.98
120.49
120.46
120.43
120.41
77.35
77.03
76.71
N
N
F3C
CDCl3, 400 MHz
13C NMR
7e
S381
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

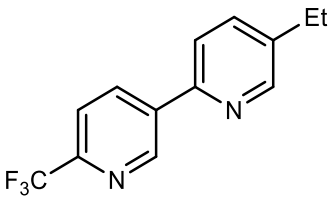


$CDCl_3$, 400 MHz
^{19}F NMR

7e

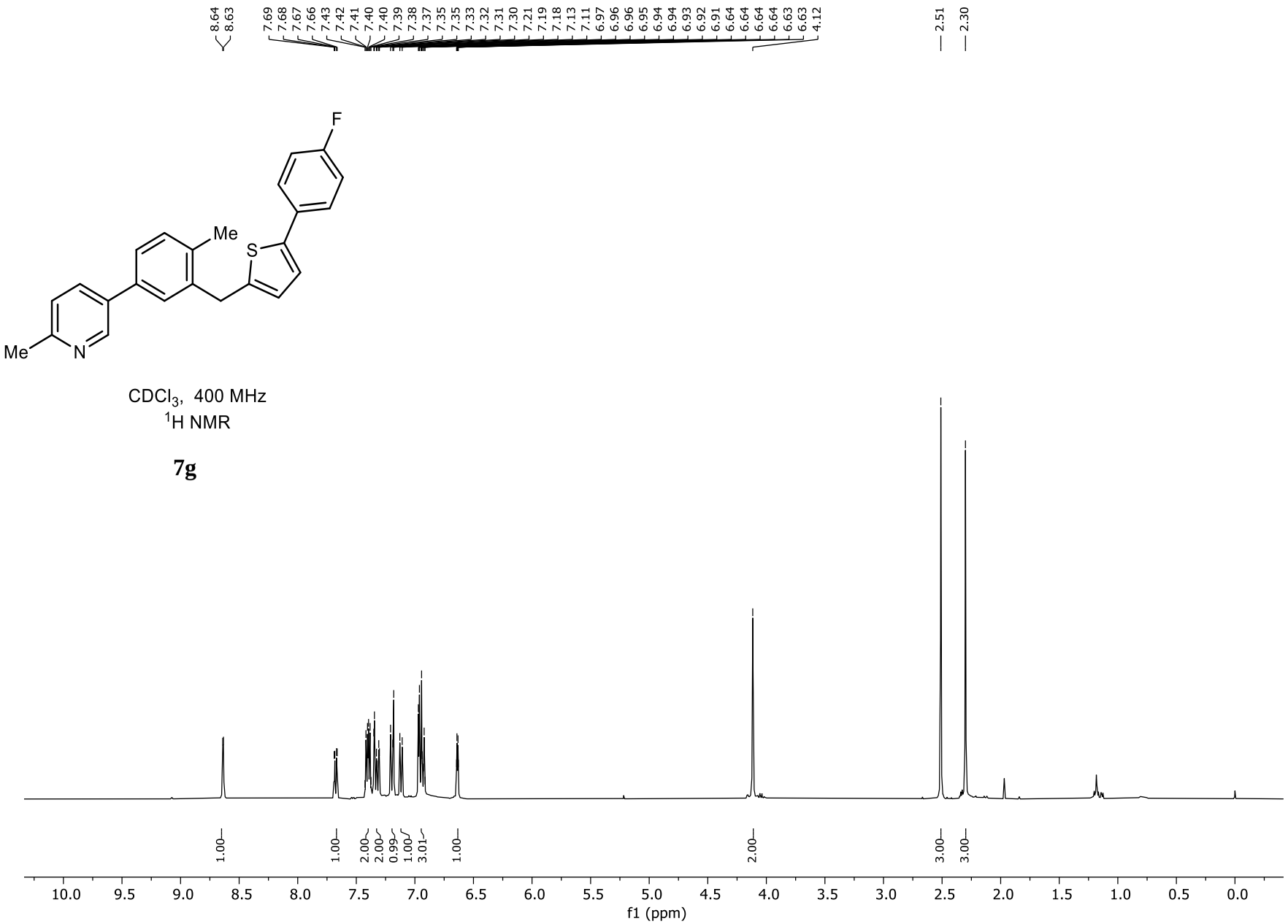

9.27
9.27
8.60
8.59
8.50
8.50
8.48
8.48
7.78
7.76
7.74
7.72
7.67
7.67
7.65
7.65
7.26
2.76
2.74
2.72
2.70
1.33
1.31
1.29
Et
N
F3C
N
CDCl3, 400 MHz
1H NMR
7f
1.00
1.00
1.00
2.00
1.00
2.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


150.75
150.18
148.41
148.17
147.89
147.54
147.20
140.03
139.65
137.53
136.46
135.33
120.60
120.46
120.43
120.40
120.38
77.34
77.02
76.71
25.89
15.20
Et
N
N
F3C
CDCl3, 400 MHz
13C NMR
7f
S384
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



$CDCl_3$, 400 MHz
^{19}F NMR

7f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7.37
7.35
7.35
7.33
7.32
7.31
7.30
7.21
7.19
7.18
7.13
7.11
6.97
6.96
6.96
6.95
6.94
6.94
6.93
6.92
6.91
6.64
6.64
6.64
6.63
6.63
4.12
2.51
2.30
F
Me
S
Me
N
CDCl3, 400 MHz
1H NMR
7g
1.00
1.00
2.00
2.00
0.99
1.00
3.01
1.00
2.00
3.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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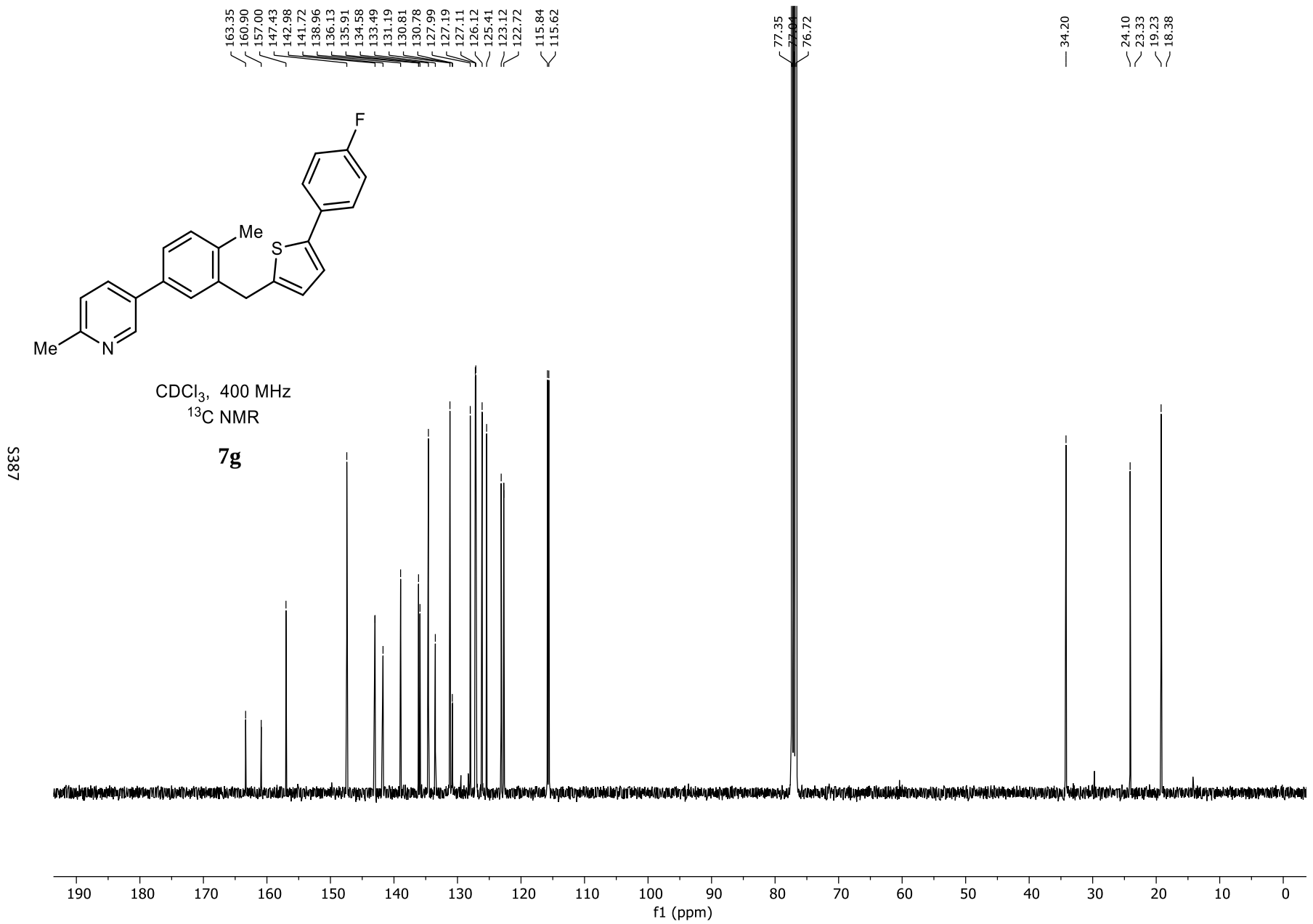
0.0
f1 (ppm)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127.99
127.19
127.11
126.12
125.41
123.12
122.72
115.84
115.62
77.35
77.04
76.72
34.20
24.10
23.33
19.23
18.38
F
Me
S
Me
N
CDCl3, 400 MHz
13C NMR
7g
S387
190
180
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130
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90
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50
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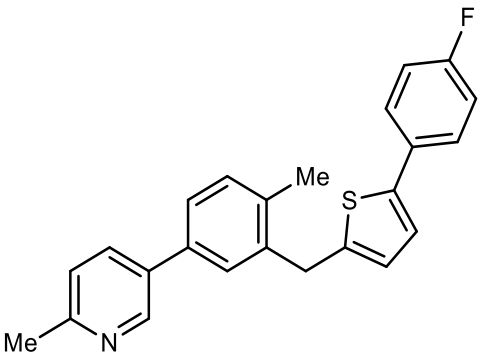
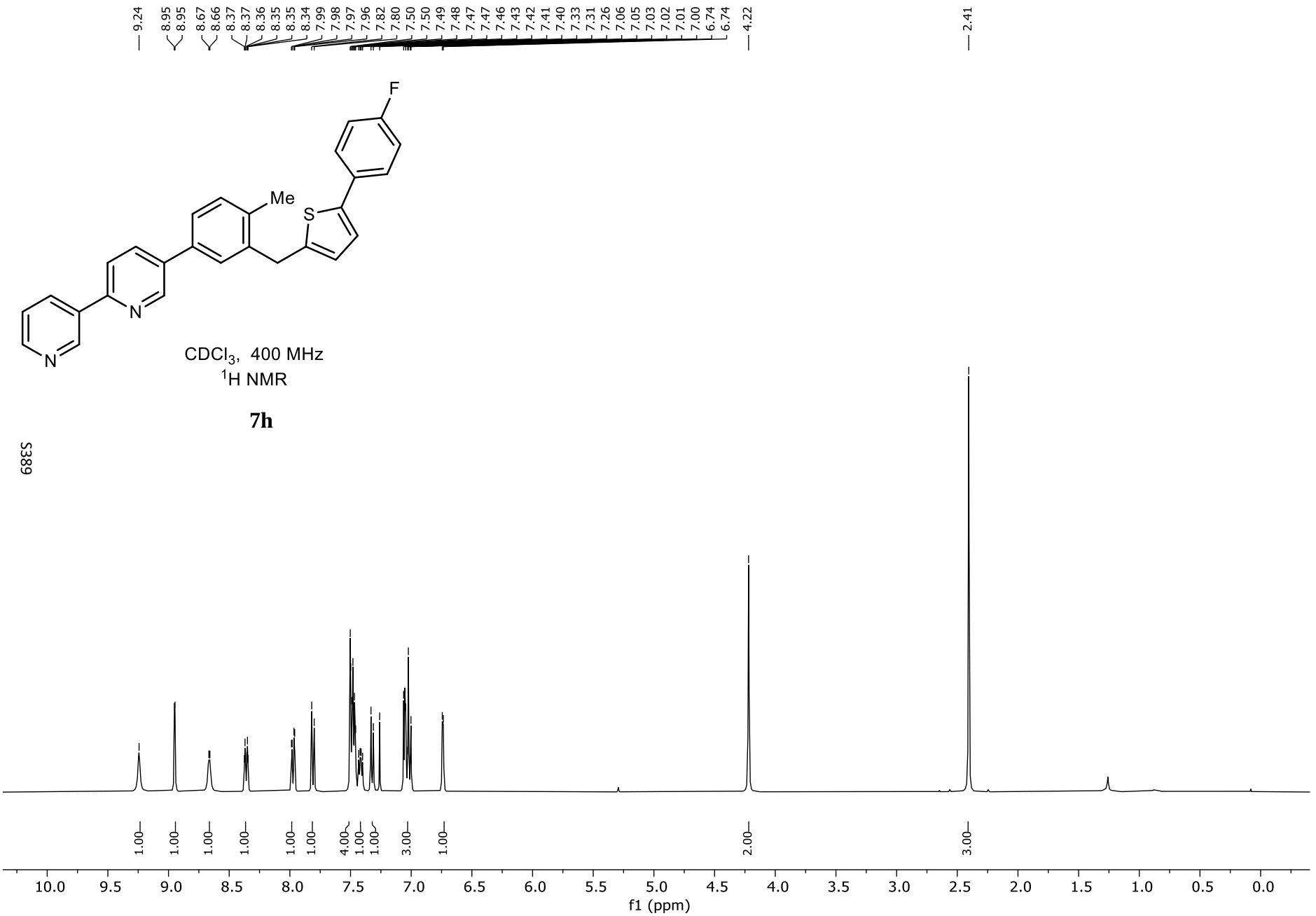
10
0
f1 (ppm)



$CDCl_3$, 400 MHz

^{19}F NMR

7g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7.97
7.96
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7.47
7.46
7.43
7.42
7.41
7.40
7.33
7.31
7.26
7.06
7.05
7.03
7.02
7.01
7.00
6.74
6.74
4.22
2.41
F
Me
S
N
N
CDCl3, 400 MHz
1H NMR
7h
S389
1.00
1.00
1.00
1.00
1.00
1.00
4.00
1.00
1.00
3.00
1.00
2.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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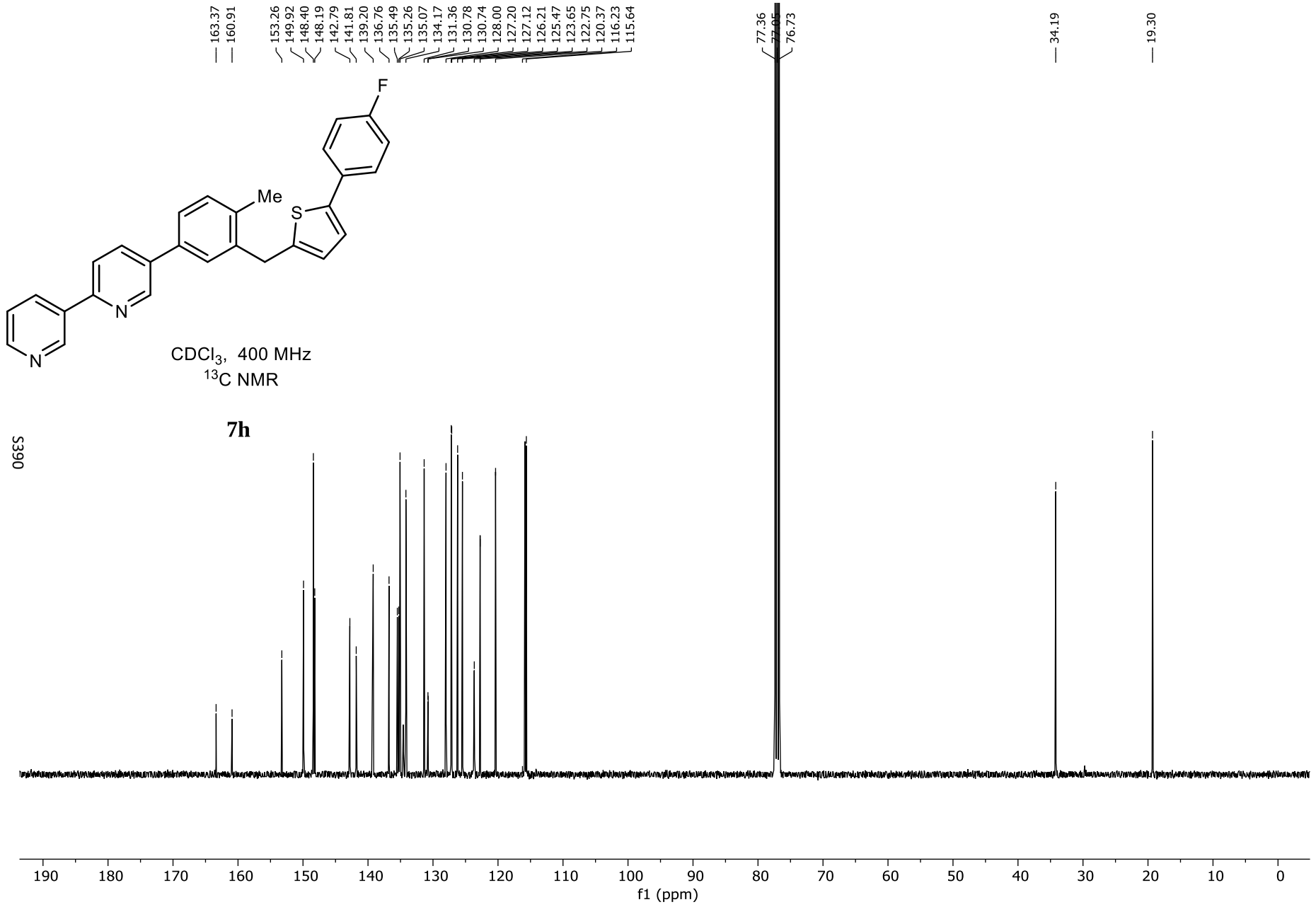
f1 (ppm)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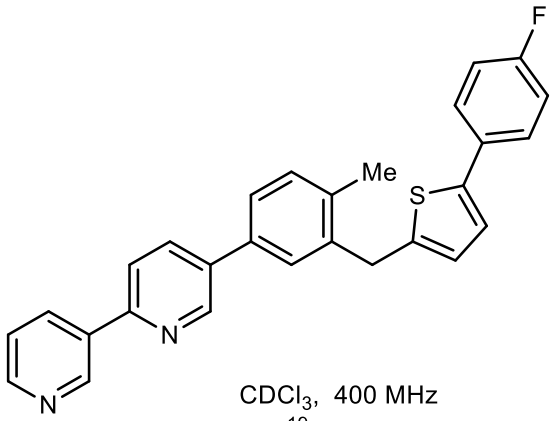
135.07
134.17
131.36
130.78
130.74
128.00
127.20
127.12
126.21
125.47
123.65
122.75
120.37
116.23
115.64
77.36
77.05
76.73
34.19
19.30
F
Me
S
N
N
CDCl3, 400 MHz
13C NMR
7h
S390
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



$CDCl_3$, 400 MHz

^{19}F NMR

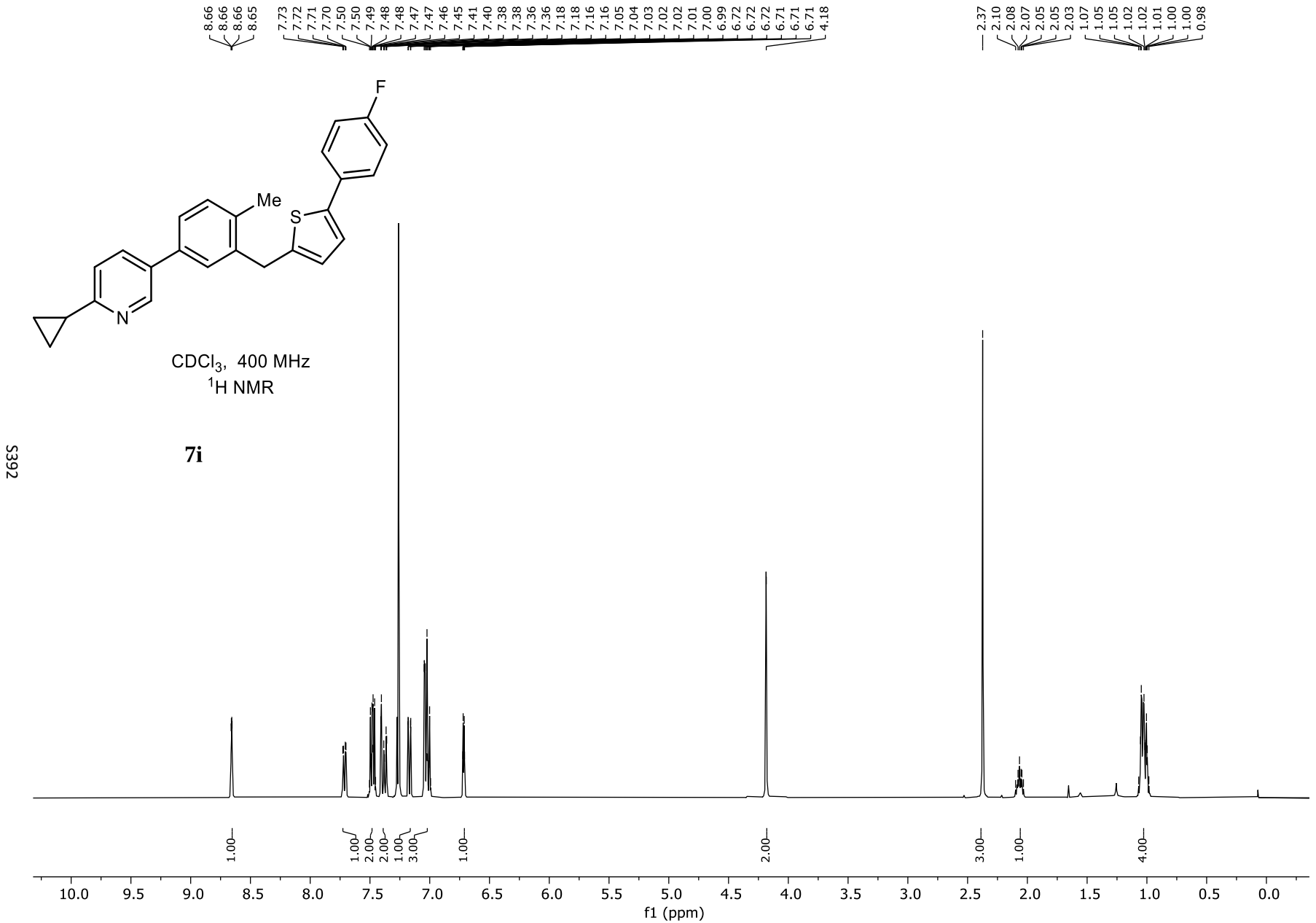
7h

S391

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

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

f1 (ppm)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7.00
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2.08
2.07
2.05
2.05
2.03
1.07
1.05
1.05
1.02
1.02
1.01
1.00
1.00
0.98
F
Me
S
N
CDCl3, 400 MHz
1H NMR
7i
S392
1.00
1.00
2.00
2.00
1.00
3.00
1.00
2.00
3.00
1.00
4.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.5
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2.5
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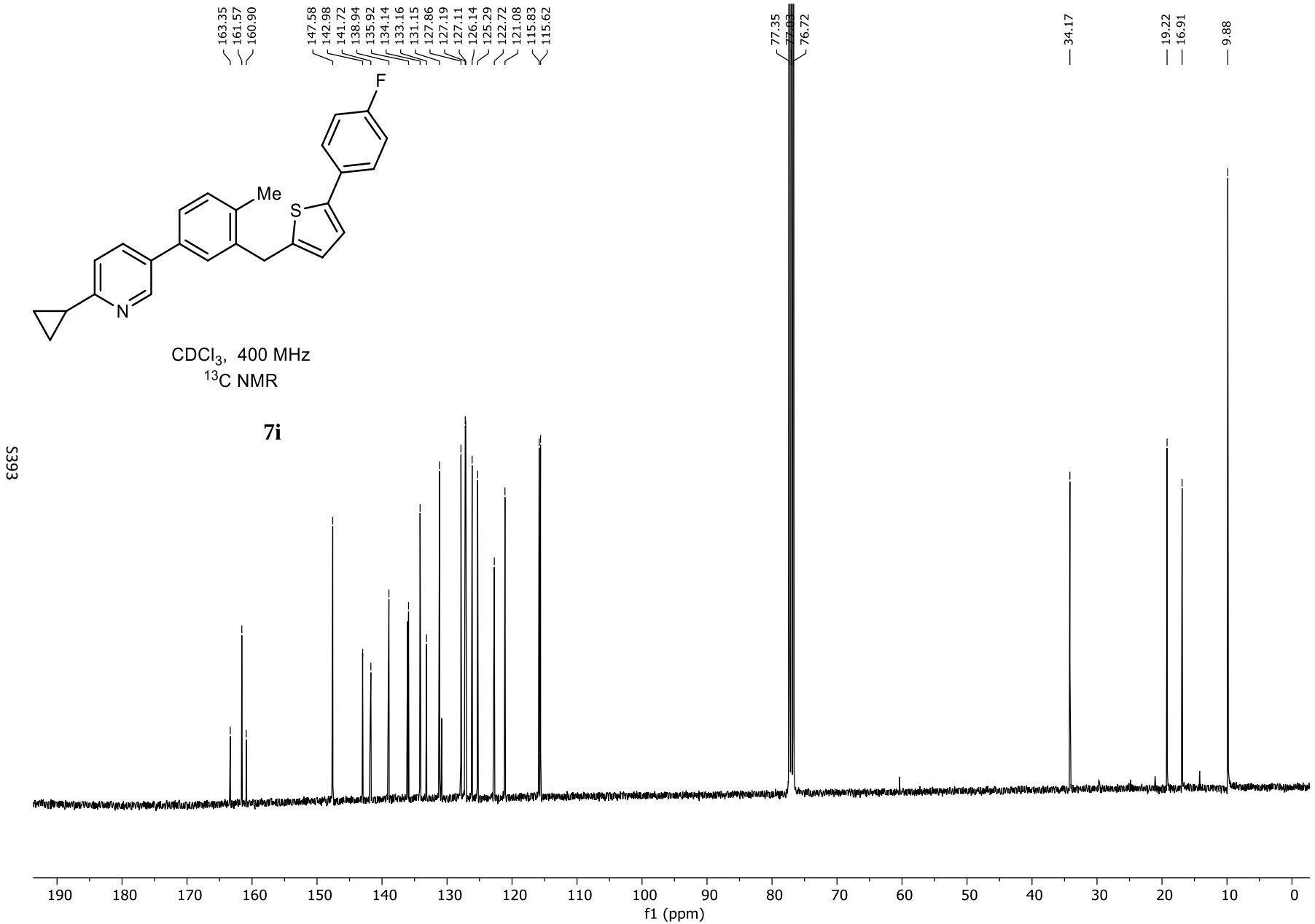
1.0
0.5
0.0
f1 (ppm)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134.14
133.16
131.15
127.86
127.19
127.11
126.14
125.29
122.72
121.08
115.83
115.62
77.35
77.03
76.72
34.17
19.22
16.91
9.88
F
Me
S
N
CDCl3, 400 MHz
13C NMR
7i
S393
190
180
170
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130
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110
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90
80
70
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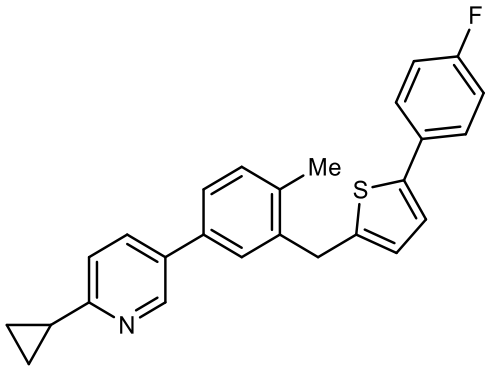
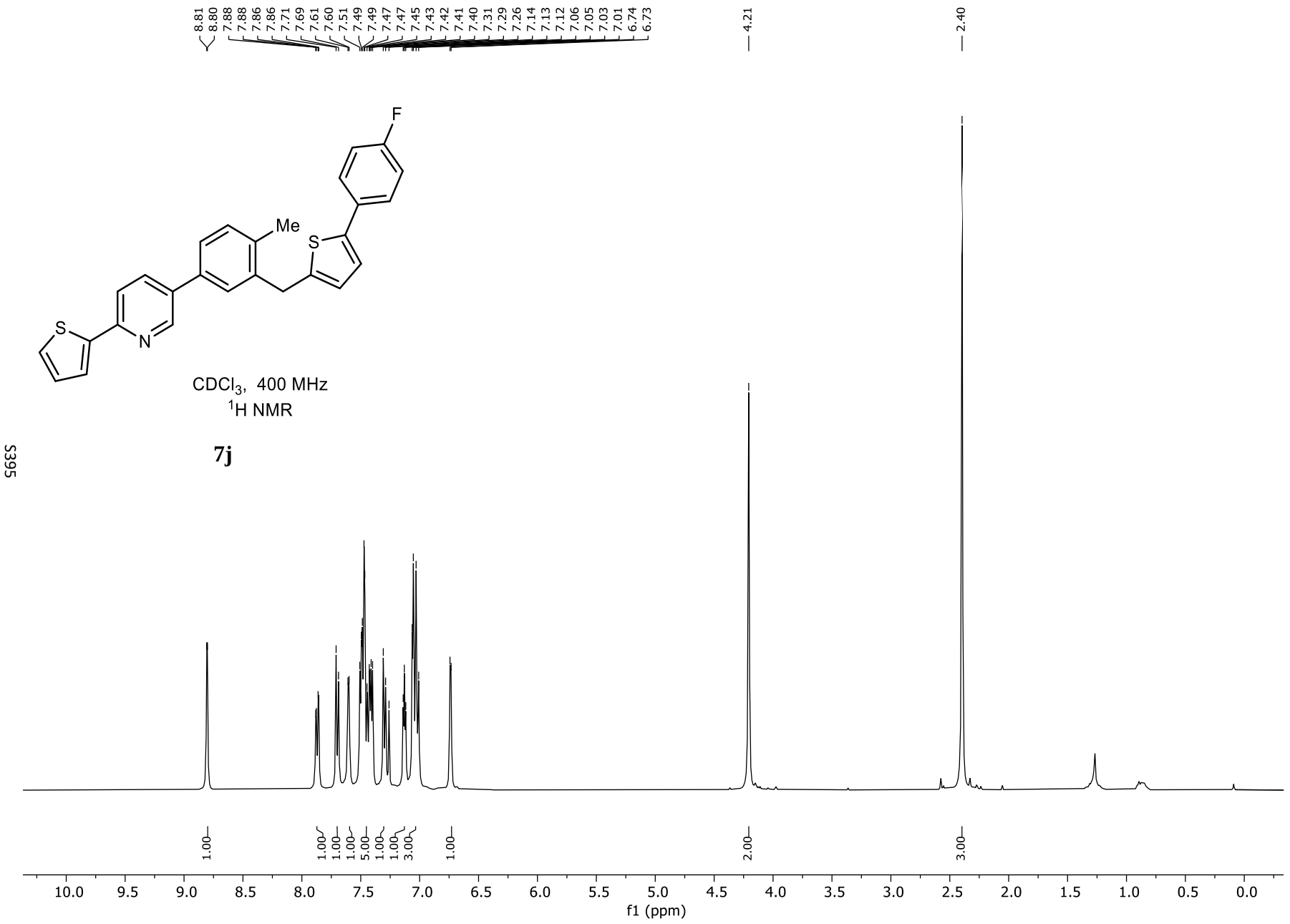
50
40
30
20
10
0
f1 (ppm)



$CDCl_3$, 400 MHz
^{19}F NMR

7i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7.41
7.40
7.31
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7.26
7.14
7.13
7.12
7.06
7.05
7.03
7.01
6.74
6.73
4.21
2.40
F
Me
S
S
N
CDCl3, 400 MHz
1H NMR
7j
S395
1.00
1.00
1.00
5.00
1.00
1.00
3.00
1.00
2.00
3.00
10.0
9.5
9.0
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8.0
7.5
7.0
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6.0
5.5
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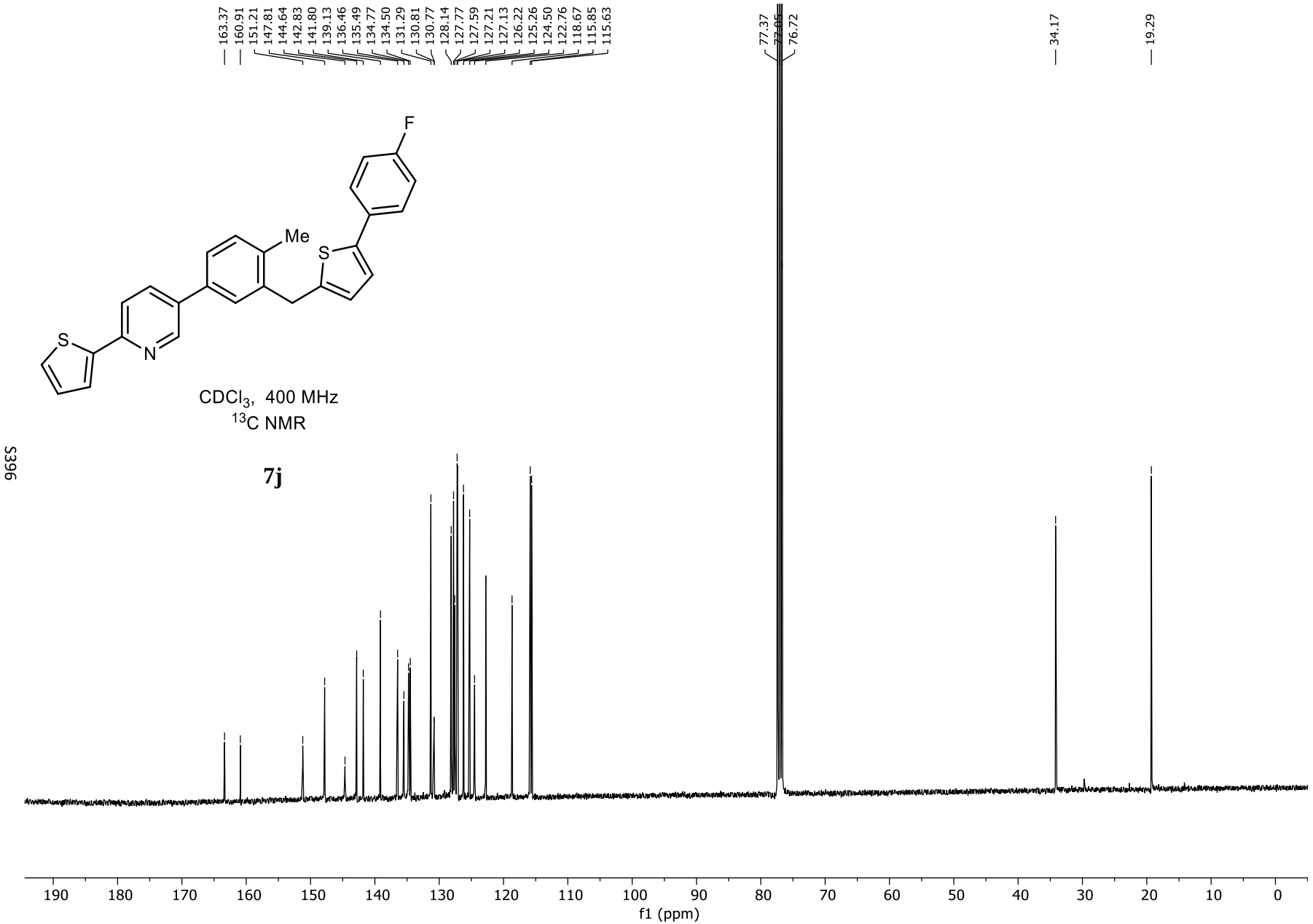
f1 (ppm)


163.37
160.91
151.21
147.81
144.64
142.83
141.80
139.13
136.46
135.49
134.77
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131.29
130.81
130.77
128.14
127.77
127.59
127.21
127.13
126.22
125.26
124.50
122.76
118.67
115.85
115.63
77.37
77.05
76.72
34.17
19.29
F
Me
S
S
N
CDCl3, 400 MHz
13C NMR
7j
S396
190
180
170
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130
120
110
100
90
80
70
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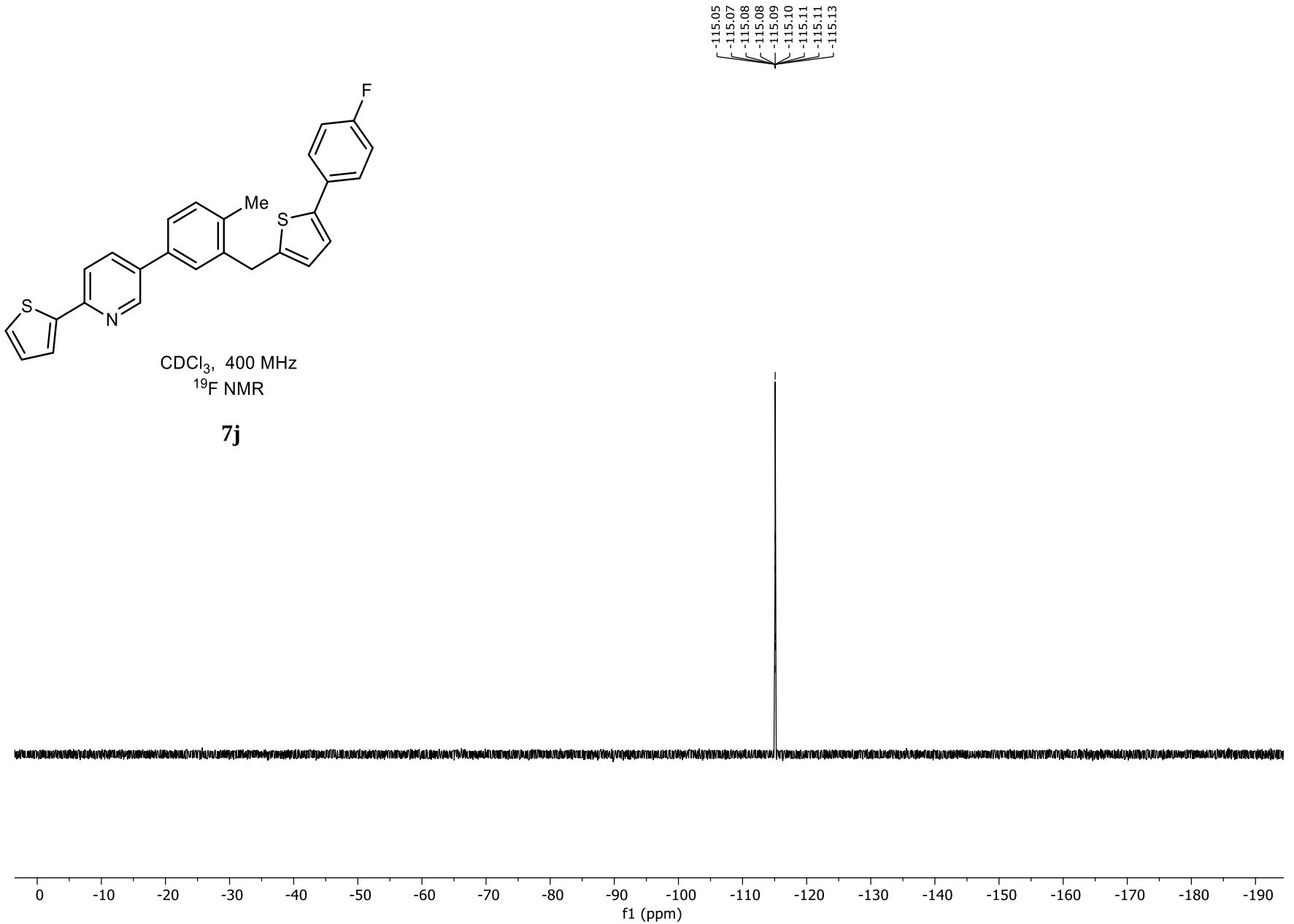
50
40
30
20
10
0
f1 (ppm)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-115.07
-115.08
-115.08
-115.09
-115.10
-115.11
-115.11
-115.13
F
Me
S
S
N
CDCl3, 400 MHz
19F NMR
7j
S397
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

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