

Silver-Catalyzed Minisci Reactions Using Selectfluor as a Mild Oxidant

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Supporting Information

Experimental procedures, characterization data for new compounds, and copies of NMR spectra

Table of Contents

General Considerations and Reaction Procedures	S2
ReactIR Reaction Progress Data	S3
Experimental Procedures and Characterization Data	S7
References	S27
Spectroscopic Data for New Compounds	S28

General Considerations

Reagents and solvents were purchased at the highest commercial quality and used without purification. Yields refer to chromatographically and spectroscopically (^1H NMR, ^{13}C NMR, ^{19}F NMR) homogenous material, unless otherwise noted. Reactions were monitored by GCMS (Agilent Technologies 5975 Series MSD GCMS) and thin-layer chromatography using 0.25 mm E. Merck silica gel plates (60F-254) using UV light. NMR spectra were recorded on a Varian-INOVA 400 MHz or 500 MHz spectrometer and calibrated using residual undeuterated solvent as an internal reference (CDCl_3 – ^1H NMR 7.26 ppm, ^{13}C NMR 77.16 ppm). The following abbreviations were used to explain multiplicities (s – singlet, d – doublet, t – triplet, q – quartet, m – multiplet).

General Reaction Procedures

(A) General Procedure for the Functionalization of Heterocycles

The threads of a 3 mL borosilicate scintillation vial were thoroughly taped with Teflon tape. To this vial containing a stir bar was added heterocycle (0.2 mmol, 1 equiv), radical precursor (0.4 mmol, 2 equiv), Selectfluor (142 mg, 0.4 mmol, 2 equiv) and trifluoroacetic acid (16 μL , 0.2 mmol, 1 equiv). Dichloroethane (1 mL) and H_2O (0.9 mL) were then added and stirred for approximately 1 minute at room temperature. A solution of AgNO_3 (0.1 mL of a 0.4M solution in H_2O , 0.04 mmol) was added in one portion. The reaction was capped with a teflon screw cap and rubber septum (24/40). The reaction was heated to 50 $^\circ\text{C}$ until reaction was completed as judged by GCMS (up to 24 hours).

Upon completion, the reaction was diluted with ethyl acetate (1 mL) and transferred to a test tube containing 2M NaOH (3 mL). The aqueous phase was extracted with ethyl acetate (3 x 3 mL) and the combined organic layers were dried over MgSO_4 , filtered and carefully concentrated *in vacuo*. The crude material was purified by silica gel chromatography to yield the desired product.

(B) General Procedure for the Functionalization of Quinones

The threads of a 3 mL borosilicate scintillation vial were thoroughly taped with Teflon tape. To this vial containing a stir bar was added quinone (0.2 mmol, 1 equiv), radical precursor (0.4 mmol, 2 equiv) and Selectfluor (142 mg, 0.4 mmol, 2 equiv). Dichloroethane (1 mL) and H_2O (0.9 mL) were then added and stirred for approximately 1 minute at room temperature. A solution of AgNO_3 (0.1 mL of a 0.4M solution in H_2O , 0.04 mmol) was added in one portion. The reaction was capped and stirred overnight at room temperature (up to 24 hours).

Upon completion, the reaction was diluted with ethyl acetate (1 mL) and transferred to a test tube containing saturated NaHCO_3 (3 mL). The aqueous phase was extracted with ethyl acetate (3 x 3 mL) and the combined organic layers were dried over MgSO_4 , filtered and carefully concentrated *in vacuo*. The crude material was purified by silica gel chromatography to yield the desired product.

ReactIR Reaction Progress Data

Experimental Procedure–Manuscript Scheme 2 (experiment with no pyridine additive)

In a 3 mL borosilicate scintillation vial containing a stir bar, Selectfluor (354 mg, 1.0 mmol), and *p*-tolyl acetate (29 μ L, 0.2 mmol) were combined with CH₃CN (1 mL) and H₂O (1 mL). The resulting mixture was stirred for approximately 1 minute at room temperature. A bored-through 14/20 rubber septum was fitted firmly over the opening of the vial. The ReactIR probe was inserted through the opening of the septum. The reaction was heated to 35 °C and stirred at 600 rpm. Data acquisition was initiated. After approximately 5 minutes, isobutyric acid (91 μ L, 1.0 mmol) was added via gas-tight syringe and allowed to thermally equilibrate while stirring. After an additional 5 minutes, AgNO₃ was added as an aqueous solution (100 μ L of a 0.4 M solution, 0.04 mmol). Data were collected for more than 3 hours, during which time no appreciable reaction was observed. Data were acquired using a Mettler Toledo ReactIR 15 instrument, and analyzed with the Mettler Toledo iC IR 7.0 software package. Graphical analysis was performed using Excel.

ReactIR Parameters

Detector: MCT

Apodization: HappGenzel

Probe: DiComp (Diamond)

Interface: AgX 6 mm x 1.5 m fiber
(Silver Halide)

Sampling: 3000 to 650 cm⁻¹

Resolution: 8

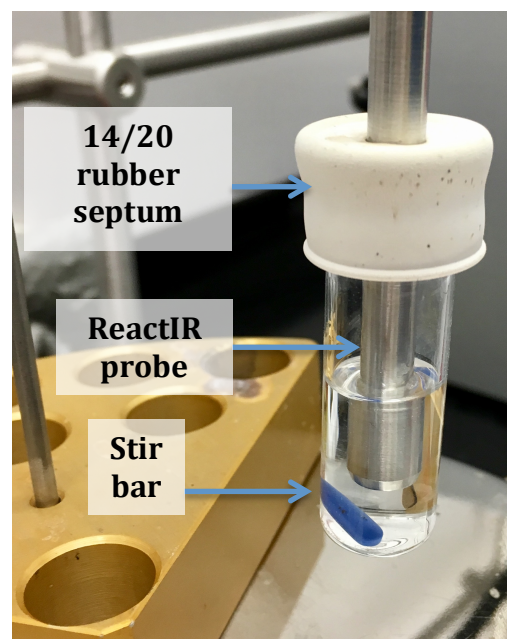
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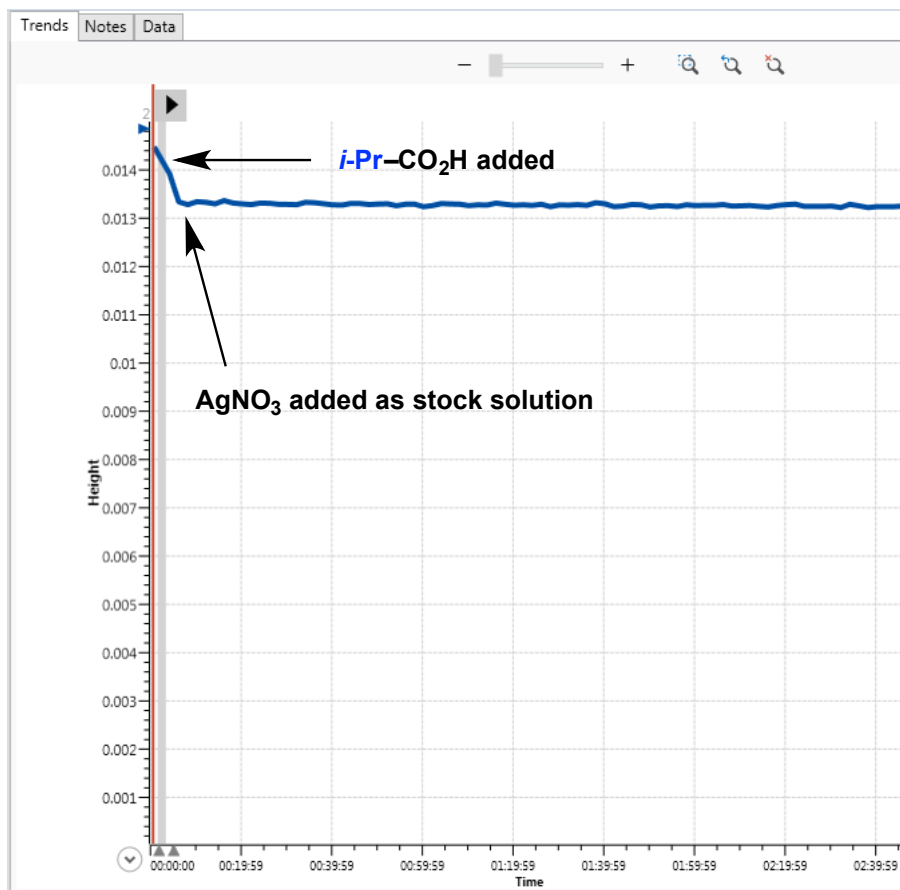
Time Interval: Data collected every
2 minutes

Spectrum Math: Second Derivative

Baseline: Two-point baseline



ReactIR Trend Plot for Peak at $\sim 1010\text{ cm}^{-1}$ (Selectfluor)



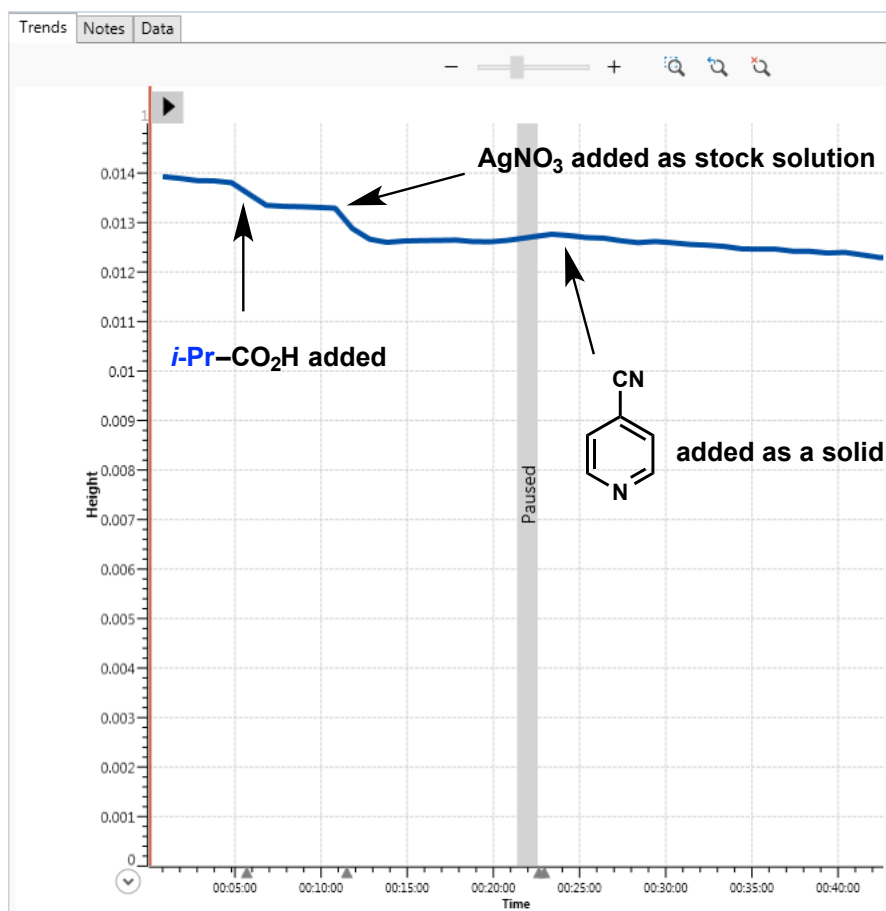
Experimental Procedure–Manuscript Scheme 2 (experiment with 4-cyanopyridine additive)

In a 3 mL borosilicate scintillation vial containing a stir bar, Selectfluor (354 mg, 1.0 mmol), and *p*-tolyl acetate (29 μL , 0.2 mmol) were combined with CH_3CN (1 mL) and H_2O (1 mL). The resulting mixture was stirred for approximately 1 minute at room temperature. A bored-through 14/20 rubber septum was fitted firmly over the opening of the vial. The ReactIR probe was inserted through the opening of the septum. The reaction was heated to $35\text{ }^\circ\text{C}$ and stirred at 600 rpm. Data acquisition was initiated. After approximately 5 minutes, isobutyric acid (91 μL , 1.0 mmol) was added via gas-tight syringe and allowed to thermally equilibrate while stirring. After an additional 5 minutes, AgNO_3 was added as an aqueous solution (100 μL of a 0.4 M solution, 0.04 mmol). Data were acquired for 10 minutes, during which time no appreciable reaction was observed. Data acquisition was paused, and 4-cyanopyridine (21 mg, 0.2 mmol) was added as a solid. Data acquisition was resumed and the consumption of Selectfluor was monitored over the course of an additional 3 hours.

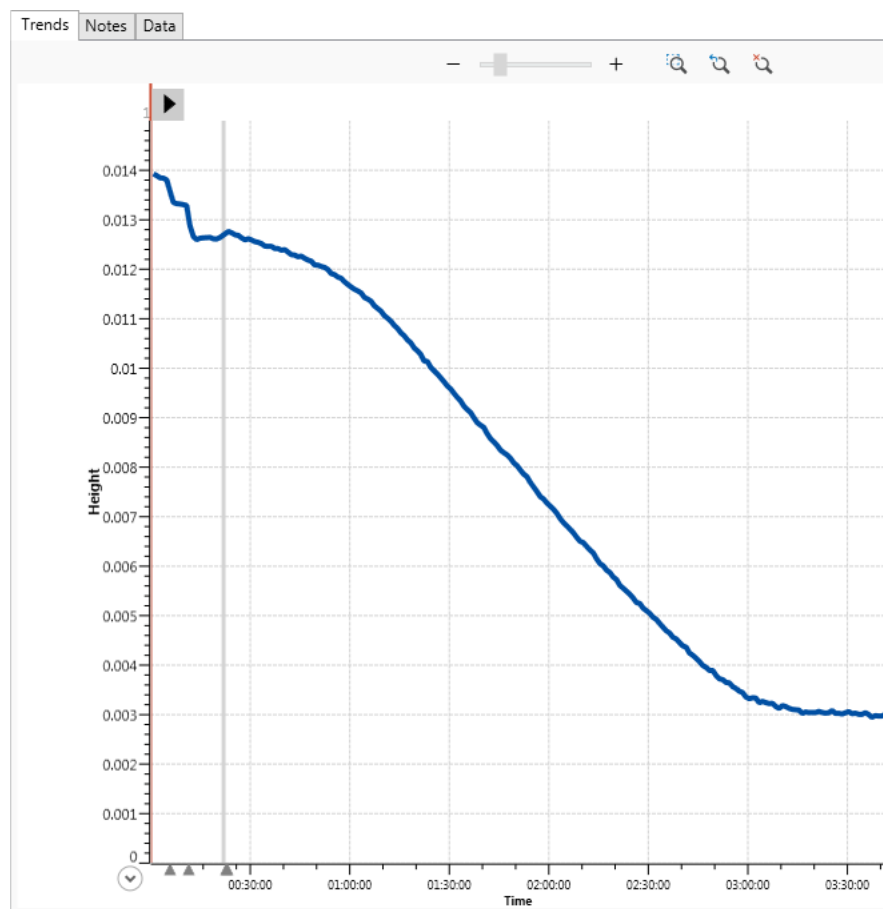
Upon completion, the reaction was diluted with ethyl acetate (1 mL) and transferred to a test tube containing 2 M NaOH (3 mL). 1, 3, 5-Trimethoxybenzene (16.8 mg, 0.1 mmol) was added to the crude mixture for ^1H NMR analysis. The aqueous phase was extracted with ethyl acetate (3 x 3 mL) and the combined organic layers were dried over MgSO_4 ,

filtered and carefully concentrated *in vacuo*. The crude material was dissolved in CDCl_3 and analyzed by ^1H NMR yielding 70% conversion to fluorinated *p*-tolyl acetate, and 37% conversion to 2-isopropylisonicotinitrile.

ReactIR Trend Plot for Peak at $\sim 1010\text{ cm}^{-1}$ (Selectfluor, Early Reaction)

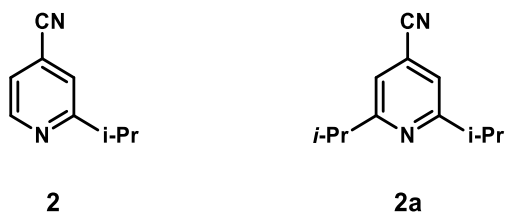


ReactIR Trend Plot for Peak at $\sim 1010\text{ cm}^{-1}$ (Selectfluor, Full Reaction)

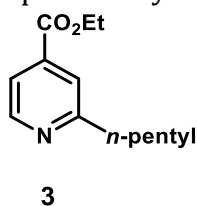


Experimental Procedures and Characterization Data

Scheme 3 Compounds (2–17)



2-isopropylisonicotinotrile (2) and 2,6-diisopropylisonicotinonitrile (2a). General procedure **A** was employed using 4-cyanopyridine (21 mg, 0.2 mmol) and isobutyric acid (37 μ L, 0.4 mmol). The reaction afforded **2** (13.5 mg, 53% yield) and **2a** (1.6 mg, 4% yield) as pale yellow oils separated by silica gel (5 to 20% EtOAc in hexanes). The data matches those previously reported.¹ For 1 mmol scale, General Procedure **A** was followed on 4-cyanopyridine (104 mg, 1.0 mmol), with isobutyric acid (182 μ L, 2.0 mmol), selectfluor (709 mg, 2.0 mmol), trifluoroacetic acid (77 μ L, 1.0 mmol), and silver(I)nitrate (34.0 mg, 0.2 mmol) in DCE:H₂O (5 mL: 5mL). The reaction afforded **2** (67.9 mg, 46% yield) and **2a** (9.8 mg, 5% yield) as pale yellow oils separated by silica gel (20% EtOAc in hexanes).

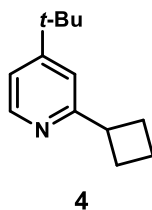


ethyl 2-pentylisonicotinate (3). General procedure **A** was modified using ethyl isonicotinate (30 μ L, 0.2 mmol) and hexanoic acid (125 μ L, 1.0 mmol, 5 equiv). The reaction afforded **3** (18.0 mg, 41% yield) as a pale yellow oil separated by silica gel (20% EtOAc in hexanes).

¹H NMR (500 MHz, CDCl₃): 8.66 (d, *J* = 5.0 Hz, 1H), 7.70 (s, 1H), 7.64 (dd, *J* = 5.1, 1.6 Hz, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 2.85 (t, *J* = 7.8 Hz, 2H), 1.79–1.70 (m, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.38–1.32 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H)

¹³C NMR (125 MHz, CDCl₃): 165.7, 163.8, 150.1, 138.1, 122.0, 120.2, 61.8, 38.5, 31.7, 29.7, 22.7, 14.4, 14.2

HRMS (ESI-TOF): calcd for C₁₃H₁₉NO₂ [M+H]⁺ 221.1494 found 222.1485

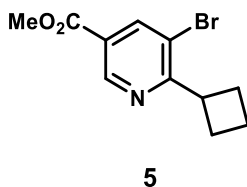


4-(*tert*-butyl)-2-cyclobutylpyridine (4). General procedure **A** was employed using 4-*tert*-butylpyridine (30 μ L, 0.2 mmol) and cyclobutane carboxylic acid (39 μ L, 0.4 mmol). The reaction afforded **4** (20.0 mg, 53% yield) as a pale yellow oil separated by silica gel (10 to 20% EtOAc in hexanes).

^1H NMR (500 MHz, CDCl_3): 8.46 (d, J = 5.3 Hz, 1H), 7.11 (s, 1H), 7.08 (dd, J = 5.3, 1.8 Hz, 1H), 3.70–3.61 (m, 1H), 2.35 (td, J = 8.9, 5.9 Hz, 4H), 2.11–2.00 (m, 1H), 1.94–1.85 (m, 1H), 1.30 (s, 9H)

^{13}C NMR (125 MHz, CDCl_3): 164.5, 160.2, 149.2, 118.3, 118.0, 42.4, 34.8, 30.7, 28.7, 18.4

HRMS (ESI-TOF): calcd for $\text{C}_{13}\text{H}_{19}\text{N}$ $[\text{M}+\text{H}]^+$ 190.1590 found 190.1574

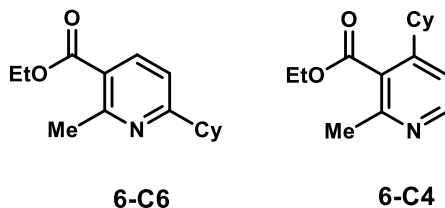


methyl 5-bromo-6-cyclobutylnicotinate (5). General procedure **A** was employed using methyl 5-bromonicotinate (43.2 mg, 0.2 mmol) and cyclobutanecarboxylic acid (39 μ L, 0.4 mmol). The reaction afforded **5** (14.7 mg, 27% yield) as a colorless oil separated by silica gel (10% EtOAc in hexanes).

^1H NMR (500 MHz, CDCl_3): δ 9.09 (d, J = 1.8 Hz, 1H), 8.37 (d, J = 1.9 Hz, 1H), 4.08–4.00 (m, 1H), 3.94 (s, 3H), 2.49–2.37 (m, 4H), 2.14–2.00 (m, 1H), 1.94–1.85 (m, 1H)

^{13}C NMR (125 MHz, CDCl_3): 166.5, 165.0, 148.7, 140.7, 125.0, 120.5, 52.7, 41.5, 27.3, 18.0

HRMS (ESI-TOF): calcd for $\text{C}_{11}\text{H}_{12}\text{BrNO}_2$ $[\text{M}+\text{H}]^+$ 270.0124 found 270.0117



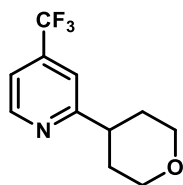
ethyl 6-cyclohexyl-2-methylnicotinate (6-C6) and ethyl 4-cyclohexyl-2-methylnicotinate (6-C4). General procedure **A** was employed using ethyl 2-methylnicotinate (31 μ L, 0.2 mmol) and cyclohexanecarboxylic acid (51 mg, 0.4 mmol). The regioisomeric ratio of C6:C4 was determined to be 1.3:1 by crude ^1H NMR. The reaction afforded **6-C6** (14.5 mg, 29% yield) and **6-C4** (4.5 mg, 9% yield) as a pale yellow oils separated by silica gel (20 to 50% EtOAc in hexanes). The data for **6-C6** matches those previously reported.¹

Data for 6-C4

^1H NMR (500 MHz, CDCl_3): 8.43 (d, J = 5.3 Hz, 1H), 7.06 (d, J = 5.3 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 2.55 – 2.48 (m, 4H), 1.88–1.81 (m, 4H), 1.45–1.28 (m, 9H).

^{13}C NMR (125 MHz, CDCl_3): 169.2, 154.6, 153.6, 149.7, 129.31, 118.7, 61.6, 41.8, 33.6, 26.7, 26.0, 22.9, 14.4.

HRMS (ESI-TOF): calcd for $\text{C}_{15}\text{H}_{21}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 248.1645 found 248.1622



7

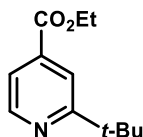
2-(tetrahydro-2H-pyran-4-yl)-4-(trifluoromethyl)pyridine (7). General procedure **A** was employed using 4-(trifluoromethyl)pyridine (23 μL , 0.2 mmol) and tetrahydropyran-4-yl-carboxylic acid (52 mg, 0.4 mmol). The reaction afforded **7** (19.0 mg, 41% yield) as a yellow oil separated by silica gel (20% EtOAc in hexanes).

^1H NMR (500 MHz, CDCl_3): 8.73 (d, J = 5.0 Hz, 1H), 7.40–7.35 (m, 2H), 4.15–4.08 (m, 2H), 3.56 (td, J = 11.4, 3.0 Hz, 2H), 3.09–3.01 (m, 1H), 1.98–1.85 (m, 4H)

^{13}C NMR (125 MHz, CDCl_3): 166.1, 150.4, 139.0 (q, J = 33.7 Hz), 123.1 (q, J = 273.1 Hz), 117.3 (q, J = 3.4 Hz), 116.7 (q, J = 3.5 Hz), 68.1, 43.6, 37.3

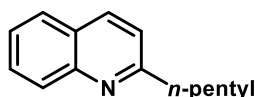
^{19}F NMR (470 MHz, CDCl_3): -64.79

HRMS (ESI-TOF): calcd for $\text{C}_{11}\text{H}_{12}\text{F}_3\text{NO}$ $[\text{M}+\text{H}]^+$ 232.0944 found 232.0924

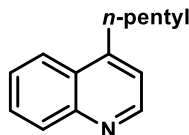


8

ethyl 2-(tert-butyl)isonicotinate (8). General procedure **A** was employed using ethyl isonicotinate (30 μL , 0.2 mmol) and pivalic acid (41 mg, 0.4 mmol). The reaction afforded **8** (11.2 mg, 27% yield) as a pale yellow oil separated by silica gel (10 to 20% EtOAc in hexanes). The data matches those previously reported.¹

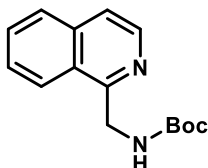


9-C2

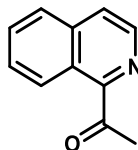


9-C4

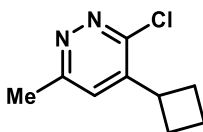
2-pentylquinoline (9-C2) and 4-pentylquinoline (9-C4). General procedure **A** was modified using quinoline (24 μ L, 0.2 mmol) and hexanoic acid (125 μ L, 1.0 mmol, 5 equiv). The regioisomeric ratio of C2:C4 was determined to be 1.3:1 by crude ^1H NMR. The reaction afforded **9-C2** (12.1 mg, 30% yield) and **9-C4** (9.7 mg, 24% yield) as colorless oils separated by silica gel (10 to 30% EtOAc in hexanes). The data matches those previously reported.^{2a-b}

**10**

tert-butyl (isoquinolin-1-ylmethyl)carbamate (10). General procedure **A** was modified using isoquinoline (24 μ L, 0.2 mmol) and *N*-Boc glycine (70 mg, 0.4 mmol) with acetone (1 mL) substituted for dichloroethane (1 mL). The reaction afforded **10** (22 mg, 43% yield) as a yellow oil separated by silica gel (40% EtOAc in hexanes). The data matches those previously reported.³

**11**

1-(isoquinolin-1-yl)ethan-1-one (11). General procedure **A** was employed using isoquinoline (24 μ L, 0.2 mmol) and pyruvic acid (28 μ L, 0.4 mmol). The reaction afforded **11** (30.2 mg, 88% yield) as a colorless oil separated by silica gel (10% EtOAc in hexanes). The data matches those previously reported.⁴

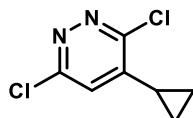
**12**

3-chloro-4-cyclobutyl-6-methylpyridazine (12). General procedure **A** was employed using 3-chloro-6-methylpyridazine (26 mg, 0.2 mmol) and cyclobutanecarboxylic acid (39 μ L, 0.4 mmol). The reaction afforded **12** (21.0 mg, 57% yield) as a pale yellow oil separated by silica gel (20% EtOAc in hexanes).

^1H NMR (500 MHz, CDCl_3): 7.19 (s, 1H), 3.72–3.63 (m, 1H), 2.68 (s, 3H), 2.49–2.40 (m, 2H), 2.18–2.06 (m, 3H), 1.93–1.84 (m, 1H)

^{13}C NMR (125 MHz, CDCl_3): 159.7, 155.3, 143.9, 126.1, 36.8, 27.5, 21.8, 18.3

HRMS (ESI-TOF): calcd for $\text{C}_9\text{H}_{11}\text{ClN}_2$ $[\text{M}+\text{H}]^+$ 183.0684 found 183.0665

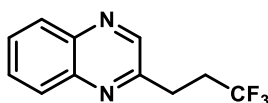
**13**

3,6-dichloro-4-cyclopropylpyridazine (13). General procedure **A** was employed using 3,6-dichloropyridazine (30 mg, 0.2 mmol) and cyclopropanecarboxylic acid (32 μ L, 0.4 mmol). The reaction afforded **13** (8.7 mg, 23% yield) as a colorless oil separated by silica gel (10% EtOAc in hexanes).

^1H NMR (500 MHz, CDCl_3): 6.93 (s, 1H), 2.24–2.16 (m, 1H), 1.33–1.23 (m, 2H), 0.90–0.83 (m, 2H)

^{13}C NMR (125 MHz, CDCl_3): 157.5, 155.9, 146.9, 124.3, 12.6, 10.8

HRMS (ESI-TOF): calcd for $\text{C}_7\text{H}_6\text{Cl}_2\text{N}_2$ $[\text{M}+\text{H}]^+$ 188.9981 found 188.9962

**14**

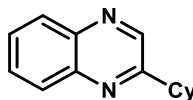
2-(3,3,3-trifluoropropyl)quinoxaline (14). General procedure **A** was modified using quinoxaline (26 mg, 0.2 mmol) and 4,4,4-trifluorobutyric acid (109 μ L, 1.0 mmol). The reaction afforded **14** (16.4 mg, 36% yield) as a yellow oil separated by silica gel (30% EtOAc in hexanes).

^1H NMR (500 MHz, CDCl_3): 8.76 (s, 1H), 8.12–8.08 (m, 1H), 8.06–8.03 (m, 1H), 7.80–7.72 (m, 2H), 3.32–3.27 (m, 2H), 2.84–2.73 (m, 2H)

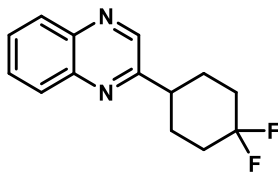
^{13}C NMR (125 MHz, CDCl_3): 153.7, 145.5, 142.2, 141.7, 130.4, 129.7, 129.4, 129.1, 32.3 (q, J = 29.3 Hz), 30.5, 28.4 (q, J = 3.1 Hz)

^{19}F NMR (470 MHz, CDCl_3): -66.40 (t, J = 10.7 Hz)

HRMS (ESI-TOF): calcd for $\text{C}_{11}\text{H}_9\text{F}_3\text{N}_2$ $[\text{M}+\text{H}]^+$ 227.0791 found 227.0767

**15**

2-cyclohexylquinoxaline (15). General procedure **A** was employed using quinoxaline (26 mg, 0.2 mmol) and cyclohexanecarboxylic acid (51 mg, 0.4 mmol). The reaction afforded **15** (27.7 mg, 65% yield) as a colorless oil separated by silica gel (10 to 20% EtOAc in hexanes). The data matches those previously reported.⁵

**16**

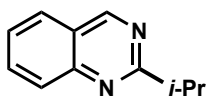
2-(4,4-difluorocyclohexyl)quinoxaline (16). General procedure **A** was employed using quinoxaline (26 mg, 0.2 mmol) and 4,4-difluorocyclohexanecarboxylic acid (66 mg, 0.4 mmol). The reaction afforded **16** (33.2 mg, 67% yield) as a pale yellow oil separated by silica gel (10% EtOAc in hexanes).

¹H NMR (500 MHz, CDCl₃): 8.80 (s, 1H), 8.11–8.04 (m, 2H), 7.79–7.71 (m, 2H), 3.12–3.04 (m, 1H), 2.36–2.26 (m, 2H), 2.17–2.10 (m, 4H), 2.02–1.87 (m, 2H).

¹³C NMR (125 MHz, CDCl₃): 158.8, 158.8, 144.6, 142.2, 141.7, 130.2, 129.5, 129.3 (d, *J* = 7.3 Hz), 123.0 (dd, *J* = 242.3, 240.0 Hz), 42.6 (d, *J* = 0.6 Hz), 33.7 (dd, *J* = 25.5, 23.3 Hz), 28.4 (d, *J* = 9.7 Hz).

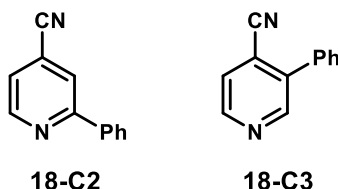
¹⁹F NMR (470 MHz, CDCl₃): -92.29 (d, *J* = 237.1 Hz), -101.36 (d, *J* = 233.2 Hz)

HRMS (ESI-TOF): calcd for C₁₄H₁₄F₂N₂ [M+H]⁺ 249.1198 found 249.1176

**17**

2-isopropylquinazoline (17). General procedure **A** was employed using quinazoline (26 mg, 0.2 mmol) and isobutyric acid (37 μL, 0.4 mmol). The reaction afforded **17** (11.5 mg, 33% yield) as a white solid separated by silica gel (30% EtOAc in hexanes). The data matches those previously reported.⁶

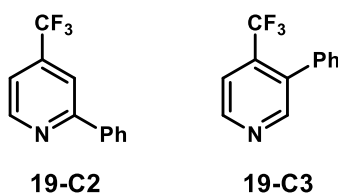
Scheme 4 Compounds (18–39)



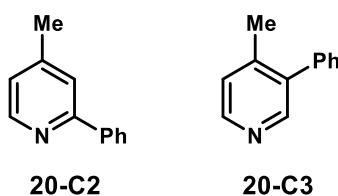
2-phenylisonicotinonitrile (18-C2) and 3-phenylisonicotinonitrile (18-C3). General procedure **A** was employed using 4-cyanopyridine (21 mg, 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The regioisomeric ratio of C2:C3 was determined to be 2:1 by crude ^1H NMR. The reaction afforded **18-C2** (18.6 mg, 52% yield) and **18-C3** (12.4 mg, 34% yield) as yellow solids separated by silica gel (10 to 20% EtOAc in hexanes).

With phenylboronic acid pinacol ester (82 mg, 0.4 mmol), the regioisomeric ratio of C2:C3 was determined to be 1.5:1 by crude ^1H NMR. The reaction afforded **18-C2** (12.5 mg, 30% yield) and **18-C3** (8.3 mg, 20% yield).

With potassium phenyltrifluoroborate (74 mg, 0.4 mmol), the regioisomeric ratio of C2:C3 was determined to be 2.5:1 by crude ^1H NMR. The reaction afforded **18-C2** (15.7 mg, 37% yield) and **18-C3** (7.1 mg, 17% yield). The data matches those previously reported.⁷

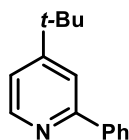


2-phenyl-4-(trifluoromethyl)pyridine (19-C2) and 3-phenyl-4-(trifluoromethyl)pyridine (19-C3). General procedure **A** was employed using 4-(trifluoromethyl)pyridine (23 μL , 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The regioisomeric ratio of C2:C3 was determined to be 4:1 by crude ^1H NMR. The reaction afforded **19-C2** (24.0 mg, 54% yield) and **19-C3** (2.0 mg, 4% yield) as pale yellow oils separated by silica gel (5% EtOAc in hexanes). The data matches those previously reported.⁷

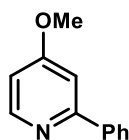


4-methyl-2-phenylpyridine (20-C2) and 4-methyl-3-phenylpyridine (20-C3). General procedure **A** was employed using 4-methylpyridine (20 μL , 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The regioisomeric ratio of C2:C3 was determined to be 3.5:1 by

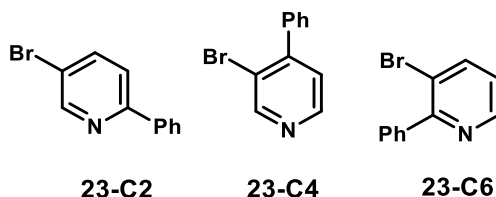
crude ^1H NMR. The reaction afforded **20-C2** (17.1 mg, 50% yield) and **20-C3** (4.8 mg, 14% yield) as pale yellow oils separated by silica gel (5 to 10% EtOAc in hexanes). The data matches those previously reported.⁸

**21**

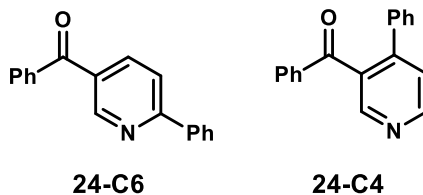
4-(tert-butyl)-2-phenylpyridine (21). General procedure **A** was employed using 4-tert-pyridine (21 μL , 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The reaction afforded **21** (21.9 mg, 52% yield) as a pale yellow oil separated by silica gel (5% EtOAc in hexanes). The data matches those previously reported.⁷

**22**

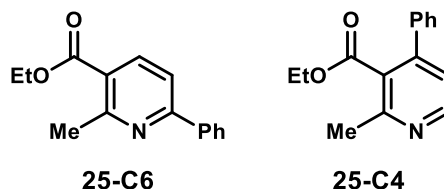
2-phenyl-4-(methoxy)pyridine (22). General procedure **A** was employed using 4-(methoxy)pyridine (22 μL , 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The reaction afforded **22** (14.4 mg, 39% yield) as a pale yellow oil separated by silica gel (5 to 20% EtOAc in hexanes). The data matches those previously reported.⁹

**23-C2****23-C4****23-C6**

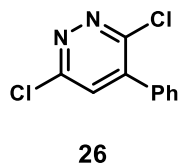
3-bromo-2-phenylpyridine (23-C2) and 3-bromo-4-phenylpyridine (23-C4), 5-bromo-2-phenylpyridine (23). General procedure **A** was employed using 3-bromopyridine (19.3 μL , 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The regioisomeric ratio of C2:C4:C6 was determined to be 1:1:1 by crude ^1H NMR. The reaction afforded **23** (12.8 mg, 27% yield) as a pale yellow oil. **23-C2** and **23-C4** were isolated as a 1:1 mixture (31.6 mg, 68% yield) as pale yellow oils. The mixtures were separated by silica gel (5 to 20% EtOAc in hexanes). The data matches those previously reported.⁷



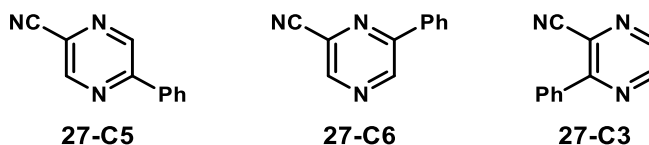
phenyl(6-phenylpyridin-3-yl)methanone (24-C6) and phenyl(4-phenylpyridin-3-yl)methanone (24-C4). General procedure **A** was employed using 3-benzoylpyridine (37 mg, 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The regioisomeric ratio of C2:C4 was determined to be 3.5:1 by crude ^1H NMR. The reaction afforded **24-C6** (14.0 mg, 27% yield) and **24-C4** (14.5 mg, 28% yield) as pale yellow oils separated by silica gel (20% EtOAc in hexanes). The data matches those previously reported.^{10a-b}



ethyl 2-methyl-6-phenylnicotinate (25-C6) and ethyl 2-methyl-4-phenylnicotinate (25-C4). General procedure **A** was employed using ethyl-2-methylnicotinate (31 μL , 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The regioisomeric ratio of C6:C4 was determined to be 1.3:1 by crude ^1H NMR. The reaction afforded **25-C6** (21.6 mg, 45% yield) and **25-C4** (16.5 mg, 34% yield) as pale yellow oils separated by silica gel (5 to 20% EtOAc in hexanes). The data matches those previously reported.^{11a-b}

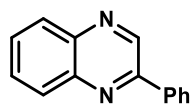


3,6-dichloro-4-phenylpyridazine (26). General procedure **A** was employed using 1,3-dichloropyrazine (30 mg, 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The reaction afforded **26** (15.5 mg, 34% yield) as a colorless solid separated by silica gel (10% EtOAc in hexanes). The data matches those previously reported.⁷

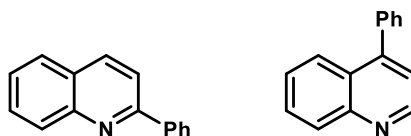


5-phenylpyrazine-2-carbonitrile (27-C5), 6-phenylpyrazine-2-carbonitrile (27-C6), and 3-phenylpyrazine-2-carbonitrile (27-C3). General procedure **A** was employed using 2-cyanopyrazine (18 μL , 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The regioisomeric ratio of C5:C6:C3 was determined to be 1:1.5:1.5 by crude ^1H NMR. The

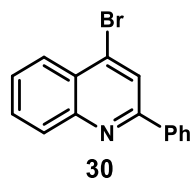
reaction afforded **27-C5** (6.0 mg, 17%), **27-C6** (9.6 mg, 26%), and **27-C3** (8.7 mg, 24% yield) as pale yellow solids separated by silica gel (5 to 15% EtOAc in hexanes). The data matches those previously reported.¹²

**28**

2-phenylquinazoline (28). General procedure **A** was employed using quinoxaline (26 mg, 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The reaction afforded **28** (26.3 mg, 64% yield) as a yellow solid separated by silica gel (20% EtOAc in hexanes). The data matches those previously reported.⁷

**29-C2****29-C4**

2-phenylquinoline (29-C2) and 4-phenylquinoline (29-C4). General procedure **A** was employed using quinoline (24 μ L, 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The regioisomeric ratio of C2:C4 was determined to be 1:1 by crude ¹H NMR. The reaction afforded **29-C2** (15 mg, 37% yield) as an off-white solid and **29-C4** (15 mg, 37% yield) as a pale yellow oil separated by silica gel (20% EtOAc in hexanes). The data matches those previously reported.⁷

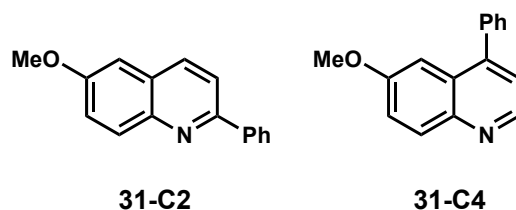
**30**

4-bromo-2-phenylquinoline (30). General procedure **A** was employed using 4-bromoquinoline (41.6 mg, 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The reaction afforded **30** (19.3 mg, 34% yield) as a white solid separated by silica gel (2.5 to 10% EtOAc in hexanes).

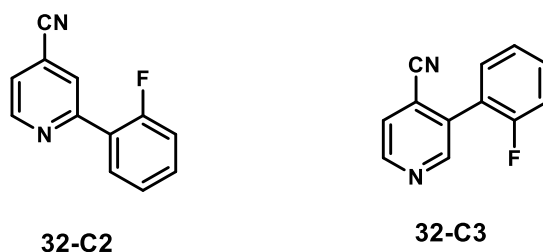
¹H NMR (400 MHz, CDCl₃): 8.21–8.12 (m, 5H), 7.80–7.74 (m, 1H), 7.66–7.59 (m, 1H), 7.57–7.46 (m, 3H)

¹³C NMR (100 MHz, CDCl₃): 157.4, 148.9, 138.5, 134.8, 130.7, 130.3, 129.9, 129.1, 127.7, 127.6, 126.8, 126.7, 123.1

HRMS (ESI-TOF): calcd for C₁₅H₁₀BrN [M+H]⁺ 284.0069 found 284.0054



6-methoxy-2-phenylquinoline (31-C2) and 6-methoxy-3-phenylquinoline (31-C4). General procedure A was employed using 6-methoxyquinoline (26 mg, 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The regioisomeric ratio of C2:C4 was determined to be 1:1.5 by crude ^1H NMR. The reaction afforded **31-C2** (16.8 mg, 36% yield) as a yellow solid and **31-C4** (23.9 mg, 51% yield) as a dark yellow oil separated by silica gel (5 to 30% EtOAc in hexanes). The data matches those previously reported.¹³



2-(2-fluorophenyl)isonicotinonitrile (32-C2) and 3-(2-fluorophenyl)isonicotinonitrile (32-C3). General procedure A was employed using 4-cyanopyridine (21 mg, 0.2 mmol) and 2-fluorophenylboronic acid (56 mg, 0.4 mmol). The regioisomeric ratio of C2:C3 was determined to be 2:1 by crude ^1H NMR. The reaction afforded **32-C2** (10.4 mg, 26%) and **32-C3** (11.6 mg, 29%) as pale yellow oils separated by silica gel (10 to 20% EtOAc in hexanes).

Data for 32-C2

^1H NMR (500 MHz, CDCl_3): 8.90 (dd, $J = 4.9, 0.6$ Hz, 1H), 8.07–8.01 (m, 2H), 7.49–7.43 (m, 2H), 7.30 (td, $J = 7.7, 1.0$ Hz, 1H), 7.23–7.17 (m, 1H)

^{13}C NMR (125 MHz, CDCl_3): 160.7 (d, $J = 250.9$ Hz), 154.8 (d, $J = 2.3$ Hz), 150.7, 131.9 (d, $J = 8.8$ Hz), 131.0 (d, $J = 2.4$ Hz), 126.1 (d, $J = 11.0$ Hz), 125.6 (d, $J = 10.9$ Hz), 125.0 (d, $J = 3.6$ Hz), 123.7, 121.1, 116.8, 116.6 (d, $J = 22.9$ Hz)

^{19}F NMR (470 MHz, CDCl_3): -116.76 (m)

HRMS (ESI-TOF): calcd for $\text{C}_{12}\text{H}_7\text{FN}_2$ $[\text{M}+\text{H}]^+$ 199.0666 found 199.0648

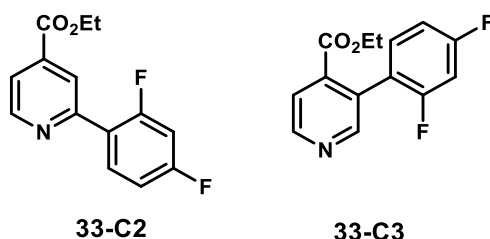
Data for 32-C3

^1H NMR (500 MHz, CDCl_3): 8.85 (s, 1H), 8.80 (d, $J = 4.7$ Hz, 1H), 7.65 (d, $J = 5.0$ Hz, 1H), 7.54–7.49 (m, 1H), 7.47–7.42 (m, 1H), 7.33 (td, $J = 7.6, 1.0$ Hz, 1H), 7.30–7.26 (m, 1H).

^{13}C NMR (125 MHz, CDCl_3): 159.7 (d, $J = 249.6$ Hz), 151.8 (d, $J = 2.2$ Hz), 149.5, 132.0 (d, $J = 8.2$ Hz), 131.3 (d, $J = 2.3$ Hz), 125.9, 125.0 (d, $J = 3.8$ Hz), 122.5, 122.4, 120.7, 116.6 (d, $J = 21.7$ Hz), 115.9.

^{19}F NMR (470 MHz, CDCl_3): -114.84 (m).

HRMS (ESI-TOF): calcd for $\text{C}_{12}\text{H}_7\text{FN}_2$ $[\text{M}+\text{H}]^+$ 199.0666 found 199.0650



ethyl 2-(2,4-difluorophenyl)isonicotinate (33-C2) and ethyl 3-(2,4-difluorophenyl)isonicotinate (33-C3). General procedure A was employed using ethyl isonicotinate (30 μ L, 0.2 mmol) and 2,4-difluorophenylboronic acid (64 mg, 0.4 mmol). The regioisomeric ratio of C2:C3 was determined to be 1.2:1 by crude ^1H NMR. The reaction afforded **33-C2** (8.0 mg, 15%) and **33-C3** (7.3 mg, 14%) as a white solid and pale yellow oil separated by silica gel (10 to 20% EtOAc in hexanes).

Data for 33-C2

^1H NMR (500 MHz, CDCl_3): 8.85 (d, $J = 4.9$ Hz, 1H), 8.30 (s, 1H), 8.01 (td, $J = 8.8, 6.6$ Hz, 1H), 7.82 (dd, $J = 5.0, 1.4$ Hz, 1H), 7.05–6.99 (m, 1H), 6.97–6.92 (m, 1H), 4.44 (q, $J = 7.1$ Hz, 2H), 1.43 (t, $J = 7.1$ Hz, 3H)

^{13}C NMR (125 MHz, CDCl_3): 165.2, 163.6 (dd, $J = 251.7, 12.0$ Hz), 160.8 (dd, $J = 253.3, 12.0$ Hz), 153.8 (d, $J = 2.4$ Hz), 150.6, 138.6, 132.3 (dd, $J = 9.7, 4.3$ Hz), 123.5 (d, $J = 9.6$ Hz), 121.7, 112.3 (d, $J = 3.7$ Hz), 112.1 (d, $J = 3.7$ Hz), 104.7 (dd, $J = 26.7, 25.5$ Hz), 62.1, 14.4

^{19}F NMR (470 MHz, CDCl_3): -108.40 (m), -112.48 (m)

HRMS (ESI-TOF): calcd for $\text{C}_{14}\text{H}_{11}\text{F}_2\text{NO}_2$ $[\text{M}+\text{H}]^+$ 264.0831 found 264.0805

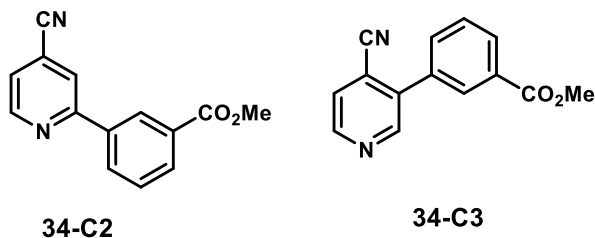
Data for 33-C3

^1H NMR (500 MHz, CDCl_3): 8.77 (d, $J = 5.0$ Hz, 1H), 8.63 (s, 1H), 7.81–7.78 (m, 1H), 7.34–7.27 (m, 1H), 7.02–6.97 (m, 1H), 6.90 (ddd, $J = 10.0, 8.9, 2.5$ Hz, 1H), 4.23 (q, $J = 7.1$ Hz, 2H), 1.17 (t, $J = 7.1$ Hz, 3H)

^{13}C NMR (125 MHz, CDCl_3): 165.9, 163.2 (dd, $J = 250.3, 11.9$ Hz), 160.1 (dd, $J = 249.4, 12.0$ Hz), 152.6, 150.1, 138.2, 131.3 (dd, $J = 9.6, 4.6$ Hz), 129.8, 123.2, 111.7, (d, $J = 3.8$ Hz), 111.5 (d, $J = 3.8$ Hz), 104.0 (t, $J = 25.7$ Hz), 61.9, 13.9

^{19}F NMR (470 MHz, CDCl_3): -109.50 (m), -111.30 (m)

HRMS (ESI-TOF): calcd for $\text{C}_{14}\text{H}_{11}\text{F}_2\text{NO}_2$ $[\text{M}+\text{H}]^+$ 264.0805 found 264.0805



methyl 3-(4-cyanopyridin-2-yl)benzoate (34-C2) and methyl 3-(4-cyanopyridin-3-yl)benzoate (34-C3). General procedure A was employed using 4-cyanopyridine (21 mg,

0.2 mmol and 3-methoxycarbonylphenyl boronic acid (76 mg, 0.4 mmol). The regioisomeric ratio of C2:C3 was determined to be 2:1 by crude ^1H NMR. The reaction afforded **34-C2** (16 mg, 34%) and **34-C3** (8.0 mg, 17%) as off-white solids separated by silica gel (10 to 45% EtOAc in hexanes).

Data for 34-C2

^1H NMR (500 MHz, CDCl_3): 8.89 (d, $J = 4.9$ Hz, 0.8 Hz, 1H), 8.66–8.64 (m, 1H), 8.26–8.22 (m, 1H), 8.18–8.14 (m, 1H), 8.02–8.00 (m, 1H), 7.61 (t, $J = 7.8$ Hz, 1H), 7.49 (dd, $J = 4.9$, 1.4 Hz, 1H), 3.97 (s, 3H)

^{13}C NMR (125 MHz, CDCl_3): 166.7, 157.8, 150.9, 137.8, 131.4, 131.3, 131.2, 129.4, 128.2, 123.8, 122.2, 121.6, 116.7, 52.5

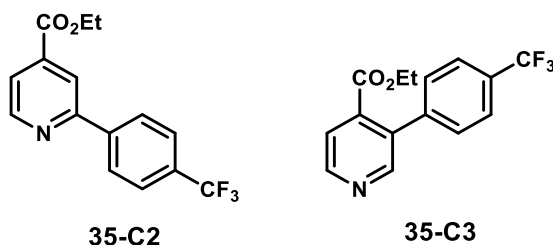
HRMS (ESI-TOF): calcd for $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 239.0815 found 239.0790

Data for 34-C3

^1H NMR (400 MHz, CDCl_3): 8.89 (s, 1H), 8.80 (d, $J = 4.8$ Hz, 1H), 8.25 (s, 1H), 8.20 (d, $J = 7.8$ Hz, 1H), 7.80 (d, $J = 7.7$ Hz, 1H), 7.68–7.61 (m, 2H), 3.96 (s, 3H)

^{13}C NMR (100 MHz, CDCl_3): 166.4, 151.0, 149.4, 137.9, 134.9, 133.2, 131.4, 130.8, 130.1, 129.5, 126.2, 119.2, 116.1, 52.5

HRMS (ESI-TOF): calcd for $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 239.0815 found 239.0791



ethyl 2-[4-(trifluoromethyl)phenyl]isonicotinate (35-C2) and ethyl 3-[4-(trifluoromethyl)phenyl]isonicotinate (35-C3). General procedure A was employed using ethyl isonicotinate (30 μL , 0.2 mmol) and 4-trifluoromethylphenylboronic acid (76 mg, 0.4 mmol). The regioisomeric ratio of C2:C3 was determined to be 4:1 by crude ^1H NMR. The reaction afforded **35-C2** (13.9 mg, 24%) and **35-C3** (4.9 mg, 8%) as off-white solids separated by silica gel (10 to 40% EtOAc in hexanes).

Data for 35-C2

^1H NMR (500 MHz, CDCl_3): 8.87 (d, $J = 5.0$ Hz, 1H), 8.33 (s, 1H), 8.18 (d, $J = 8.1$ Hz, 2H), 7.85 (dd, $J = 5.0$, 1.4 Hz, 1H), 7.76 (d, $J = 8.2$ Hz, 2H), 4.47 (q, $J = 7.1$ Hz, 2H), 1.45 (t, $J = 7.1$ Hz, 3H)

^{13}C NMR (125 MHz, CDCl_3): 165.2, 157.0, 150.8, 142.0, 139.0, 131.4 (q, $J = 32.5$ Hz), 127.5, 126.0, 124.2 (q, $J = 272.1$ Hz), 122.2, 120.2, 62.2, 14.4

^{19}F NMR (470 MHz, CDCl_3): -62.66

HRMS (ESI-TOF): calcd for $\text{C}_{15}\text{H}_{12}\text{F}_3\text{NO}_2$ $[\text{M}+\text{H}]^+$ 296.0898 found 296.0860

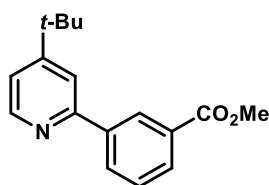
Data for 35-C3

¹H NMR (400 MHz, CDCl₃): 8.77 (d, *J* = 5.0 Hz, 1H), 8.66 (s, 1H), 7.73–7.68 (m, 3H), 7.45 (d, *J* = 8.0 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 1.06 (t, *J* = 7.1 Hz, 3H)

¹³C NMR (100 MHz, CDCl₃): 166.4, 151.3, 149.9, 141.4, 138.0, 135.1, 130.4 (q, *J* = 32.6 Hz), 129.3, 125.6 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 272.1 Hz), 123.0, 62.0, 13.8

¹⁹F NMR (376 MHz, CDCl₃): -62.59

HRMS (ESI-TOF): calcd for C₁₅H₁₂F₃NO₂ [M+H]⁺ 296.0898 found 296.0866



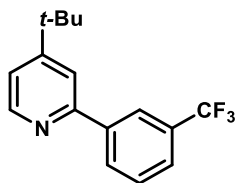
36

methyl 3-[4-(*tert*-butyl)pyridin-2-yl]benzoate (36). General procedure **A** was employed using 4-*tert*-butylpyridine (30 μL, 0.2 mmol) and 3-methoxycarbonylphenyl boronic acid (72 mg, 0.4 mmol). The reaction afforded **36** (25.4 mg, 47%) as a colorless oil separated by silica gel (10% EtOAc in hexanes).

¹H NMR (400 MHz, CDCl₃): 8.60 (d, *J* = 4.2 Hz, 2H), 8.20 (d, *J* = 7.7 Hz, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.73 (s, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.24 (s, 1H), 3.94 (s, 3H), 1.36 (s, 9H)

¹³C NMR (100 MHz, CDCl₃): 167.2, 161.1, 156.6, 149.8, 140.5, 131.7, 130.8, 129.9, 129.0, 128.2, 119.9, 117.9, 52.3, 35.1, 30.8

HRMS (ESI-TOF): calcd for C₁₇H₁₉NO₂ [M+H]⁺ 270.1489 found 270.1460



37

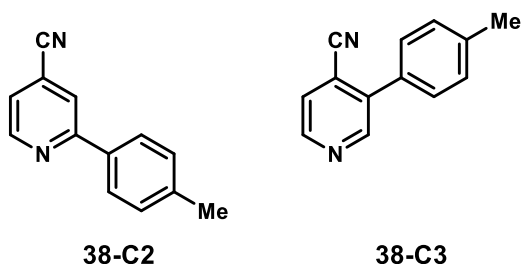
4-(*tert*-butyl)-2-[3-(trifluoromethyl)phenyl]pyridine (37): General procedure **A** was employed using 4-*tert*-butylpyridine (30 μL, 0.2 mmol) and 3-trifluoromethylphenylboronic acid (76 mg, 0.4 mmol). The reaction afforded **37** (13.8 mg, 25%) as a colorless oil separated by silica gel (20% EtOAc in hexanes).

¹H NMR (500 MHz, CDCl₃): 8.62 (d, *J* = 5.2 Hz, 1H), 8.25 (s, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 1.2 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.30 (dd, *J* = 5.3, 1.8 Hz, 1H), 1.39 (s, 9H)

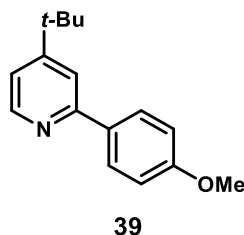
¹³C NMR (125 MHz, CDCl₃): 161.3, 156.1, 149.9, 140.9, 131.3 (q, *J* = 32.2 Hz), 131.0, 130.4, 129.3, 125.5 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 3.9 Hz), 120.2, 117.9, 35.1, 30.8

¹⁹F NMR (470 MHz, CDCl₃): -62.55

HRMS (ESI-TOF): calcd for C₁₆H₁₆F₃N [M+H]⁺ 280.1308 found 280.1283

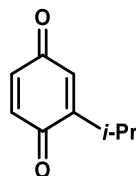


2-(*p*-tolyl)isonicotinonitrile (38-C2**) and 3-(*p*-tolyl)isonicotinonitrile (**38-C3**)**. General procedure **A** was employed using 4-cyanopyridine (21 mg, 0.2 mmol) and *p*-tolylboronic acid (54 mg, 0.4 mmol). The regioisomeric ratio of C2:C3 was determined to be 2:1 by crude ¹H NMR. The reaction afforded **38-C2** (14.4 mg, 37%) and **38-C3** (8.5 mg, 22%) as yellow and white solids separated by silica gel (5 to 15% EtOAc in hexanes). The data matches those previously reported.⁶



4-(*tert*-butyl)-2-(4-methoxyphenyl)pyridine (39**)**. General procedure **A** was employed using 4-*tert*-butylpyridine (30 μ L, 0.2 mmol) and 4-methoxyphenylboronic acid (61 mg, 0.4 mmol). The reaction afforded **39** (7.1 mg, 15%) as a yellow oil separated by silica gel (20% EtOAc in hexanes). The data matches those previously reported.¹⁴

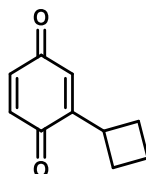
Scheme 5 Compounds (44–55)



44

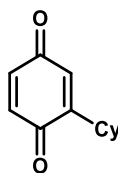
2-isopropylcyclohexa-2,5-diene-1,4-dione (44). General procedure **B** was employed using 1,4-benzoquinone (22 mg, 0.2 mmol) and isobutyric acid (37 μ L, 0.4 mmol). The reaction afforded **44** (16.1 mg, 54%) as a yellow oil separated by silica gel (5% EtOAc in hexanes). The data matches those previously reported.¹⁵

When ammonium persulfate (91 mg, 0.4 mmol) was used, the reaction afforded **44** (9.9 mg, 33%) as a yellow oil.



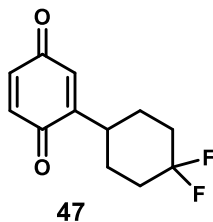
45

2-cyclobutylcyclohexa-2,5-diene-1,4-dione (45). General procedure **B** was employed using 1,4-benzoquinone (22 mg, 0.2 mmol) and cyclobutane carboxylic acid (39 μ L, 0.4 mmol). The reaction afforded **45** (15.7 mg, 48%) as a yellow oil separated by silica gel (5% EtOAc in hexanes). The data matches those previously reported.¹⁶



46

[1,1'-bi(cyclohexane)]-3,6-diene-2,5-dione (46). General procedure **B** was employed using 1,4-benzoquinone (22 mg, 0.2 mmol) and cyclohexanoic acid (51 mg, 0.4 mmol). The reaction afforded **46** (17.9 mg, 47%) as a yellow oil separated by silica gel (5% EtOAc in hexanes). The data matches those previously reported.¹⁶



47

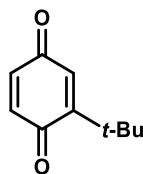
4',4'-difluoro-[1,1'-bi(cyclohexane)]-3,6-diene-2,5-dione (47). General procedure **B** was employed using 1,4-benzoquinone (22 mg, 0.2 mmol) and 4,4-difluorocyclohexane carboxylic acid (66 mg, 0.4 mmol). The reaction afforded **47** (20.2 mg, 45%) as a yellow solid separated by silica gel (10% EtOAc in hexanes).

¹H NMR (500 MHz, CDCl₃): 6.81–6.72 (m, 2H), 6.55 (dd, *J* = 2.3, 1.0 Hz, 1H), 2.79 (t, *J* = 12.6 Hz, 1H), 2.26–2.15 (m, 2H), 1.95–1.78 (m, 4H), 1.62–1.50 (m, 2H)

¹³C NMR (125 MHz, CDCl₃): 187.7, 186.8, 151.7 (d, *J* = 2.3 Hz), 137.1, 136.3, 131.3, 122.7 (dd, *J* = 239.3, 234.1 Hz), 34.5 (d, *J* = 1.6 Hz), 33.8 (dd, *J* = 32.3, 25.7 Hz), 28.0 (d, *J* = 10.3 Hz)

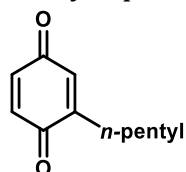
¹⁹F NMR (470 MHz, CDCl₃): -92.02 (d, *J* = 237.5 Hz), -102.3 (m), -102.8 (m)

HRMS (ESI-TOF): calcd for C₁₂H₁₂F₂O₂ [M+H]⁺ 227.0884 found 227.0903



48

2-(tert-butyl)cyclohexa-2,5-diene-1,4-dione (48). General procedure **B** was employed using 1,4-benzoquinone (22 mg, 0.2 mmol) and pivalic acid (41 mg, 0.4 mmol). The reaction afforded **48** (8.8 mg, 27%) as a yellow oil separated by silica gel (10% EtOAc in hexanes). The data matches those previously reported.¹⁷

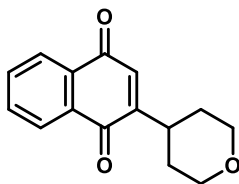


49

2-pentylcyclohexa-2,5-diene-1,4-dione (49). General procedure **B** was employed using 1,4-benzoquinone (22 mg, 0.2 mmol) and hexanoic acid (50 μL, 0.4 mmol). The reaction afforded **49** (4.5 mg, 13%) as a yellow oil separated by silica gel (5% EtOAc in hexanes). **¹H NMR** (400 MHz, CDCl₃): 6.75 (d, *J* = 10.1 Hz, 1H), 6.71 (dd, *J* = 10.1, 2.4 Hz, 1H), 6.58–6.55 (m, 1H), 2.45–2.36 (m, 2H), 1.55–1.46 (m, 2H), 1.38–1.30 (m, 4H), 0.93–0.86 (m, 3H).

¹³C NMR (125 MHz, CDCl₃): 188.0, 187.7, 149.9, 137.0, 136.4, 132.5, 31.6, 29.1, 27.6, 22.5, 14.1.

HRMS (ESI-TOF): calcd for C₁₁H₁₄O₂ [M+H]⁺ 179.1067 found 179.1068

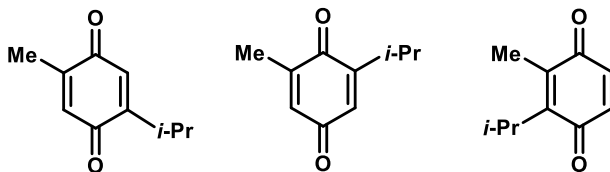
**50**

2-(tetrahydro-2H-pyran-4-yl)naphthalene-1,4-dione (50). General procedure **B** was employed using 1,4-naphthoquinone (32 mg, 0.2 mmol) and tetrahydropyran-4-yl-carboxylic acid (52 mg, 0.4 mmol). The reaction afforded **50** (14.5 mg, 30%) as a yellow oil separated by silica gel (20% EtOAc in hexanes).

¹H NMR (500 MHz, CDCl₃): 8.13–8.03 (m, 2H), 7.77–7.71 (m, 2H), 6.75 (s, 1H), 4.08 (dd, *J* = 11.5, 4.2 Hz, 2H), 3.58 (td, *J* = 11.8, 1.7 Hz, 2H), 3.17 (tt, *J* = 11.7, 3.0 Hz, 1H), 1.79–1.73 (m, 2H), 1.63 (qd, *J* = 12.4, 4.3 Hz, 2H)

¹³C NMR (125 MHz, CDCl₃): 185.4, 184.7, 154.2, 133.9, 133.9, 133.6, 132.5, 132.0, 126.9, 126.2, 68.0, 34.4, 31.8.

HRMS (ESI-TOF): calcd for C₁₅H₁₄O₃ [*M*+*H*]⁺ 243.1016 found 243.1014

**51-C5****51-C6****51-C3**

2-isopropyl-5-methylcyclohexa-2,5-diene-1,4-dione (51-C5), 2-isopropyl-6-methylcyclohexa-2,5-diene-1,4-dione (51-C6), 2-isopropyl-3-methylcyclohexa-2,5-diene-1,4-dione (51-C3). General procedure **B** was employed using 2-methyl-1,4-benzoquinone (29 mg, 0.4 mmol) and isobutyric acid (37 μL, 0.4 mmol). The reaction afforded **51-C5**,^{18a} **51-C6**,^{18b} and **51-C3** (28.6 mg, 81%) as a mixture (1.1:1.5:1) of yellow oils. The data is for the mixture separated by silica gel (50% DCM in hexanes).

Data for 51-C5^{18a}

¹H NMR (400 MHz, CDCl₃): 6.58 (q, *J* = 1.6 Hz, 1H), 3.09–2.97 (m, 1H), 2.03 (d, *J* = 1.6 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 6H)

¹³C NMR (100 MHz, CDCl₃): 188.8, 187.6, 155.1, 145.3, 134.0, 130.4, 26.7, 21.6, 15.5

Data for 51-C6^{18b}

¹H NMR (400 MHz, CDCl₃): 6.55 (dq, *J* = 2.6, 1.6 Hz, 1H), 6.47 (dd, *J* = 2.6, 1.2 Hz, 1H), 3.09–2.97 (m, 1H), 2.06 (d, *J* = 1.6 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 6H).

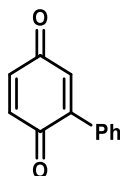
¹³C NMR (100 MHz, CDCl₃): 188.4, 187.7, 152.2, 146.3, 133.0, 130.5, 27.0, 21.6, 16.3

Data for 51-C3

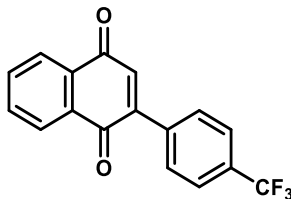
¹H NMR (400 MHz, CDCl₃): 6.68 (d, *J* = 10.0 Hz, 1H), 6.62 (d, *J* = 10.0 Hz, 1H), 3.22–3.10 (m, 1H), 2.06 (s, 3H), 1.27 (d, *J* = 7.1 Hz, 6H)

¹³C NMR (100 MHz, CDCl₃): 188.2, 187.7, 149.0, 140.3, 137.4, 135.6, 28.9, 20.1, 11.9

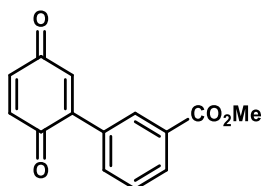
HRMS (ESI-TOF): calcd for C₁₀H₁₂O₂ [M+H]⁺ 165.0916 found 165.0909

**52**

[1,1'-biphenyl]-2,5-dione (52). General procedure **B** was employed using 1,4-benzoquinone (22 mg, 0.2 mmol) and phenylboronic acid (49 mg, 0.4 mmol). The reaction afforded **52** (24.8 mg, 67%) as a yellow solid separated by silica gel (10% EtOAc in hexanes). With potassium phenyltrifluoroborate (74 mg, 0.4 mmol), the reaction afforded **52** (22.6 mg, 61%) as a yellow solid. With phenylboronic acid pinacol ester (82 mg, 0.4 mmol), the reaction afforded **52** (23.1 mg, 63%) as a yellow solid. The data matches those previously reported.¹⁹

**53**

2-[4-(trifluoromethyl)phenyl]naphthalene-1,4-dione (53). General procedure was employed using 1,4-naphthoquinone (41 mg, 0.4 mmol) and 4-trifluoromethylphenylboronic acid (76 mg, 0.4 mmol). The reaction afforded **53** (24.0 mg, 40%) as a yellow solid separated by silica gel (10% DCM in hexanes). The data matches those previously reported.²⁰

**54**

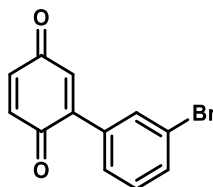
methyl 2',5'-dioxo-2',5'-dihydro-[1,1'-biphenyl]-3-carboxylate (54). General procedure **B** was employed using 1,4-benzoquinone (22 mg, 0.2 mmol) and 3-

methoxycarbonylphenyl boronic acid (72 mg, 0.4 mmol). The reaction afforded **54** (27.5 mg, 51%) as a yellow solid separated by silica gel (5 to 10% EtOAc in hexanes).

¹H NMR (400 MHz, CDCl₃): 8.15–8.10 (m, 2H), 7.70–7.65 (m, 1H), 7.56–7.50 (m, 1H), 6.91 (t, *J* = 2.0 Hz, 1H), 6.87 (d, *J* = 3.2 Hz, 1H), 6.86 (d, *J* = 2.4 Hz, 0.8H), 6.83 (d, *J* = 2.4 Hz, 0.2H), 3.93 (s, .3H).

¹³C NMR (100 MHz, CDCl₃): 187.4, 186.3, 166.5, 145.2, 137.1, 136.5, 133.7, 133.3, 133.0, 131.2, 130.8, 130.4, 128.8, 52.5.

HRMS (ESI-TOF): calcd for C₁₄H₁₀O₄ [M+H]⁺ 243.0652 found 243.0656

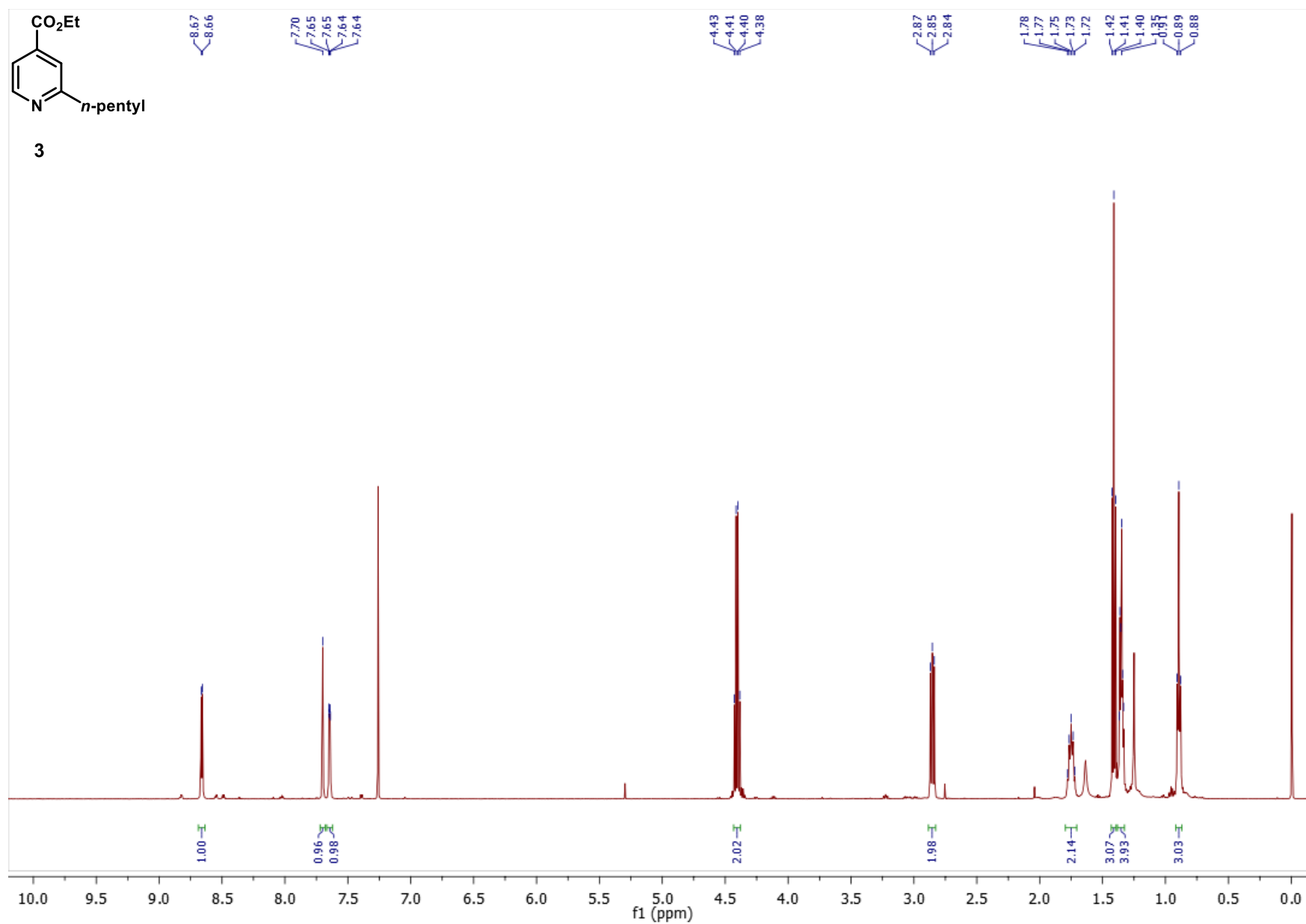


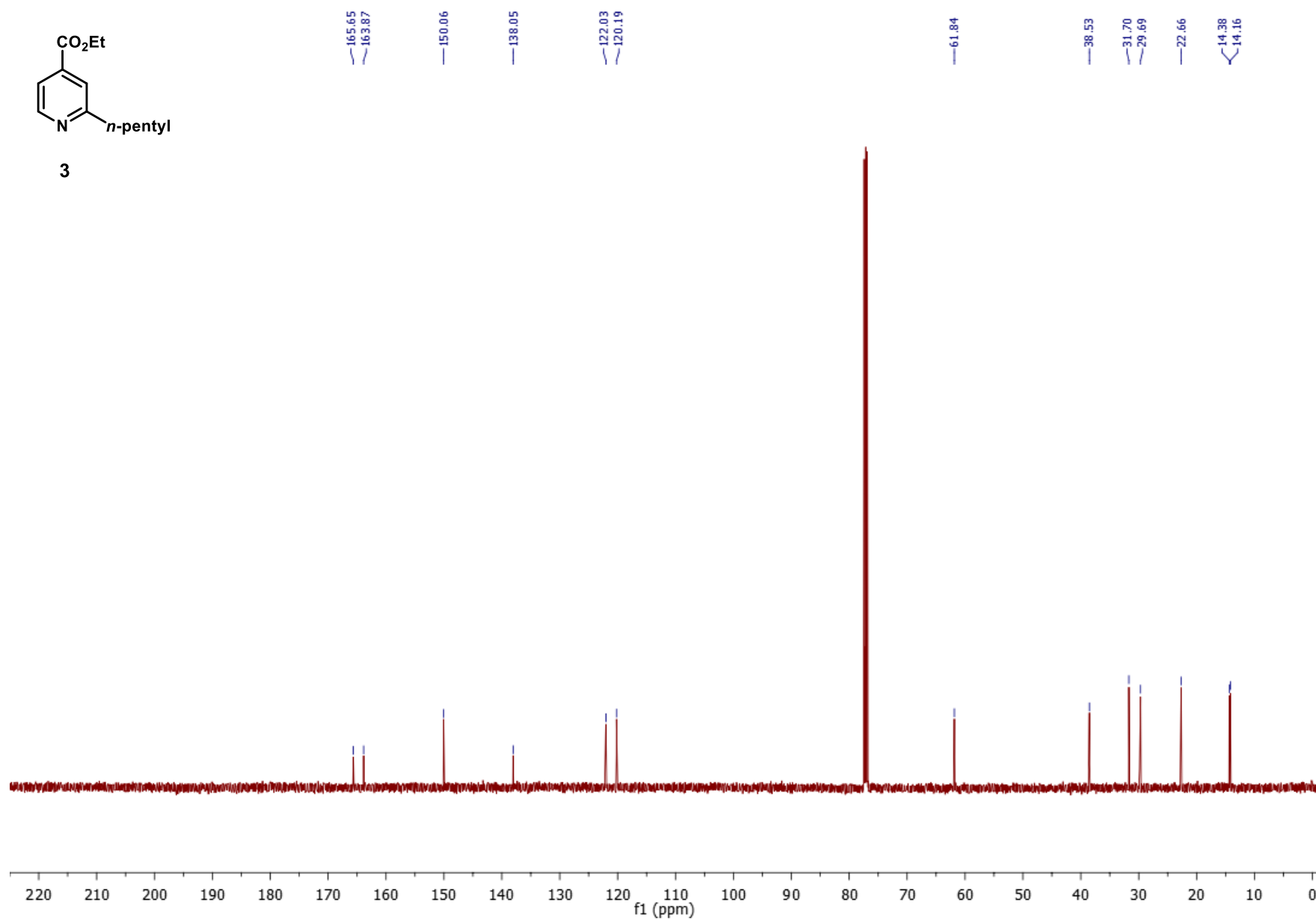
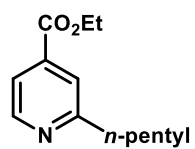
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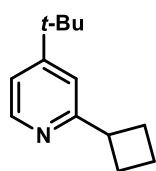
3'-bromo-[1,1'-biphenyl]-2,5-dione (55). General procedure **B** was employed using 1,4-benzoquinone (22 mg, 0.2 mmol) and 3-bromophenyl boronic acid (56 mg, 0.4 mmol). The reaction afforded **55** (18.8 mg, 36% yield) as a yellow solid separated by silica gel (40% DCM in hexanes). The data matches those previously reported.¹⁹

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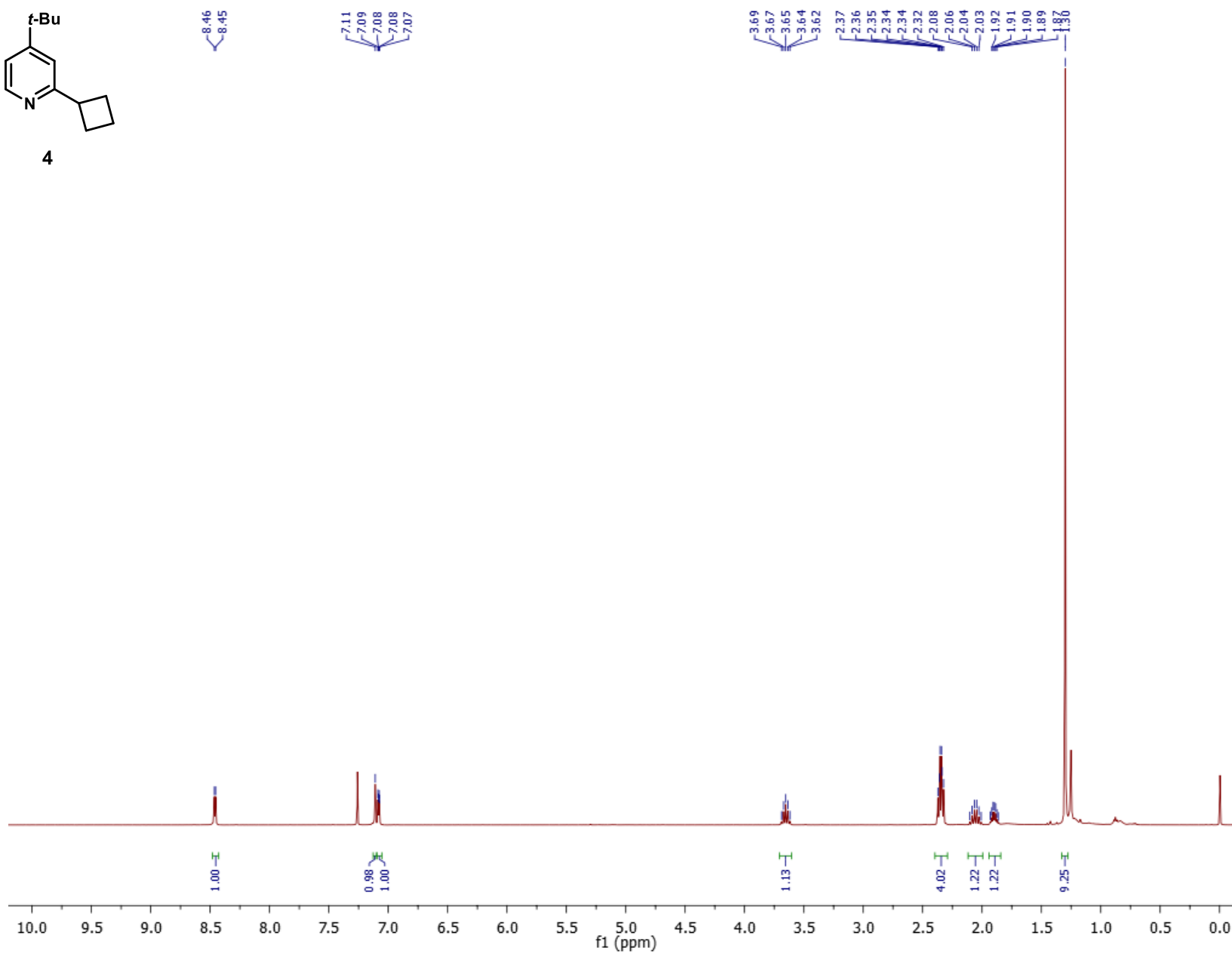
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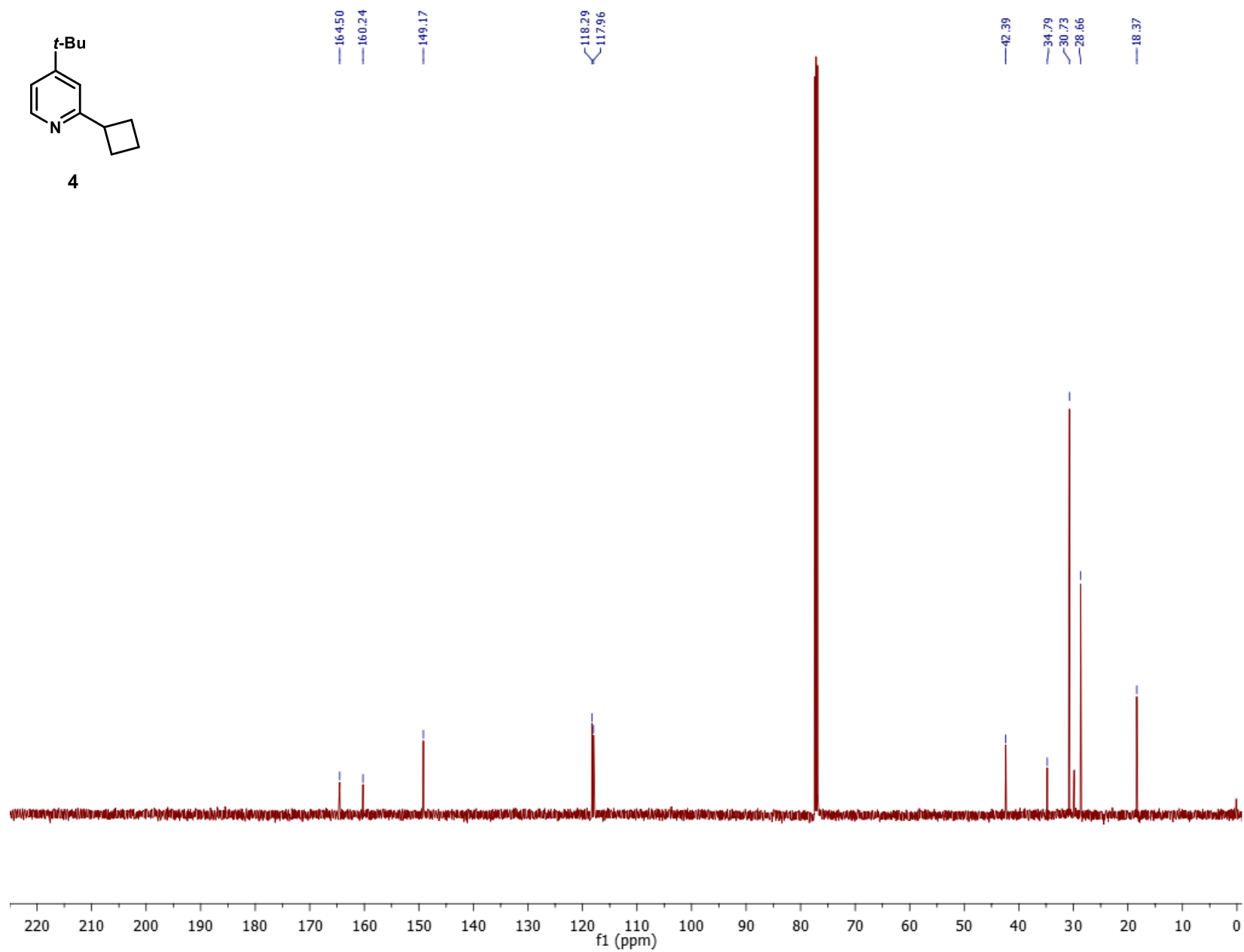


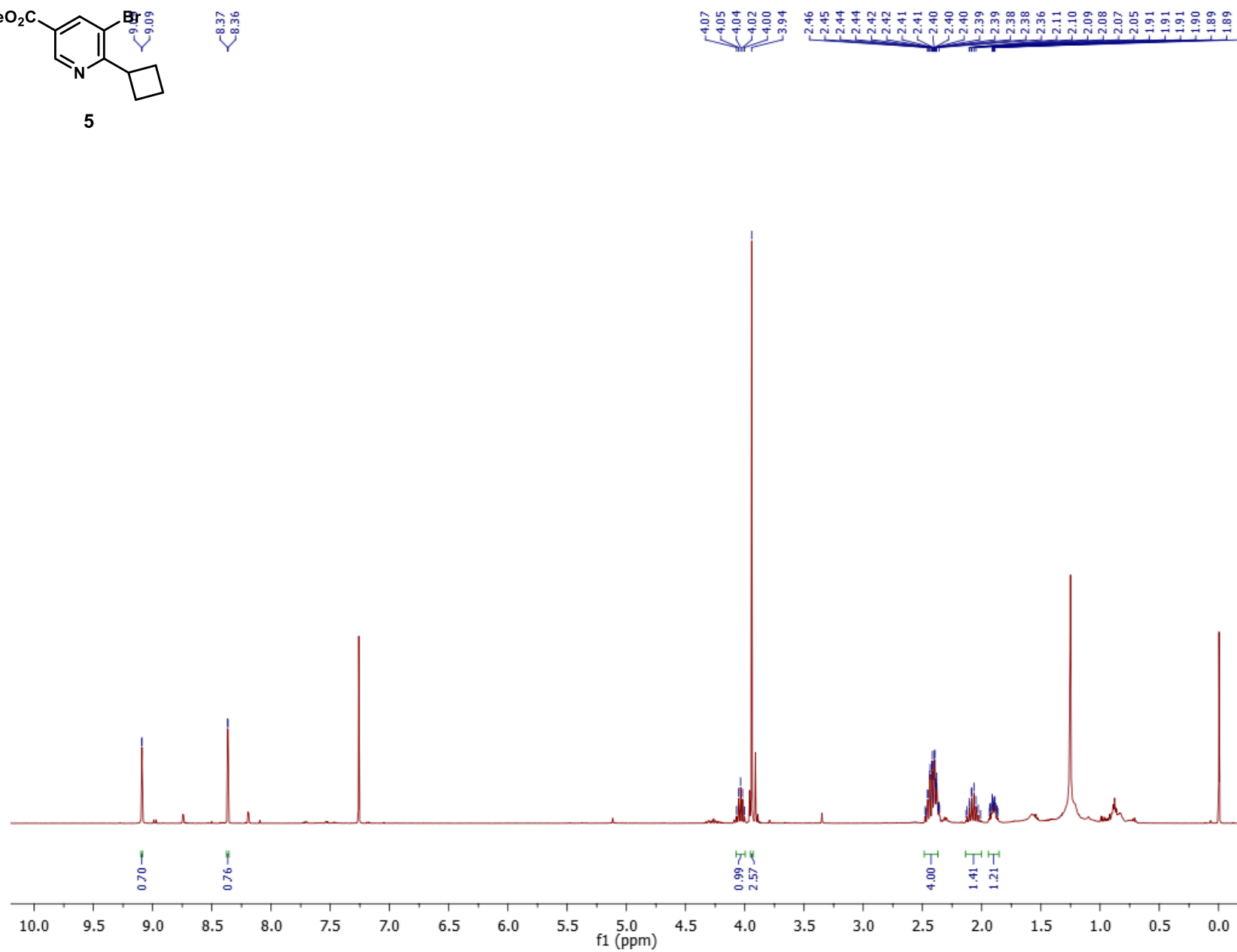
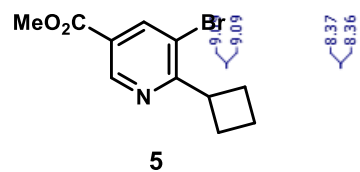


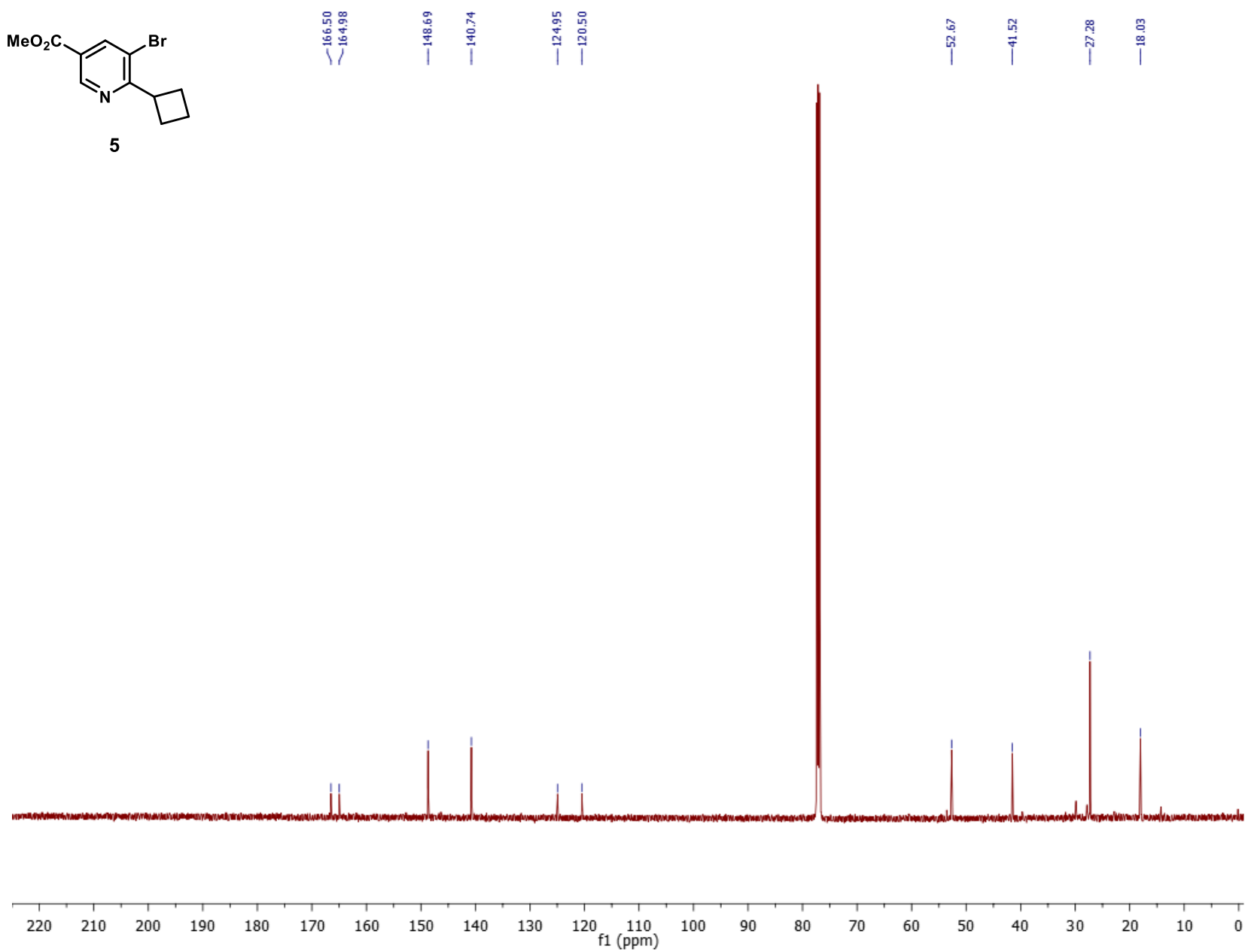
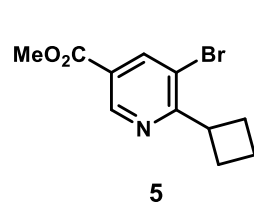


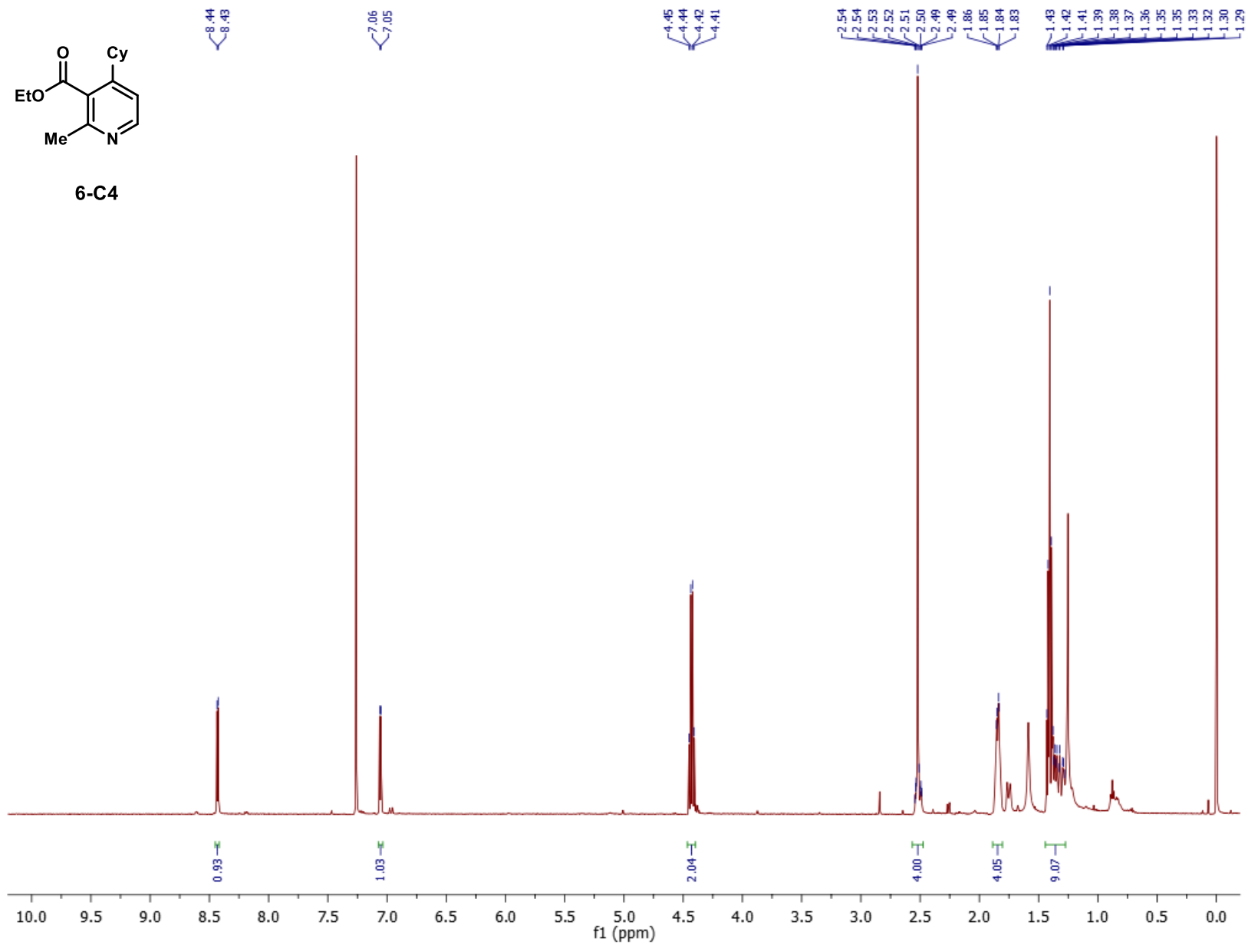
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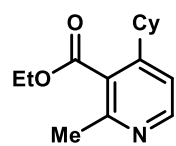




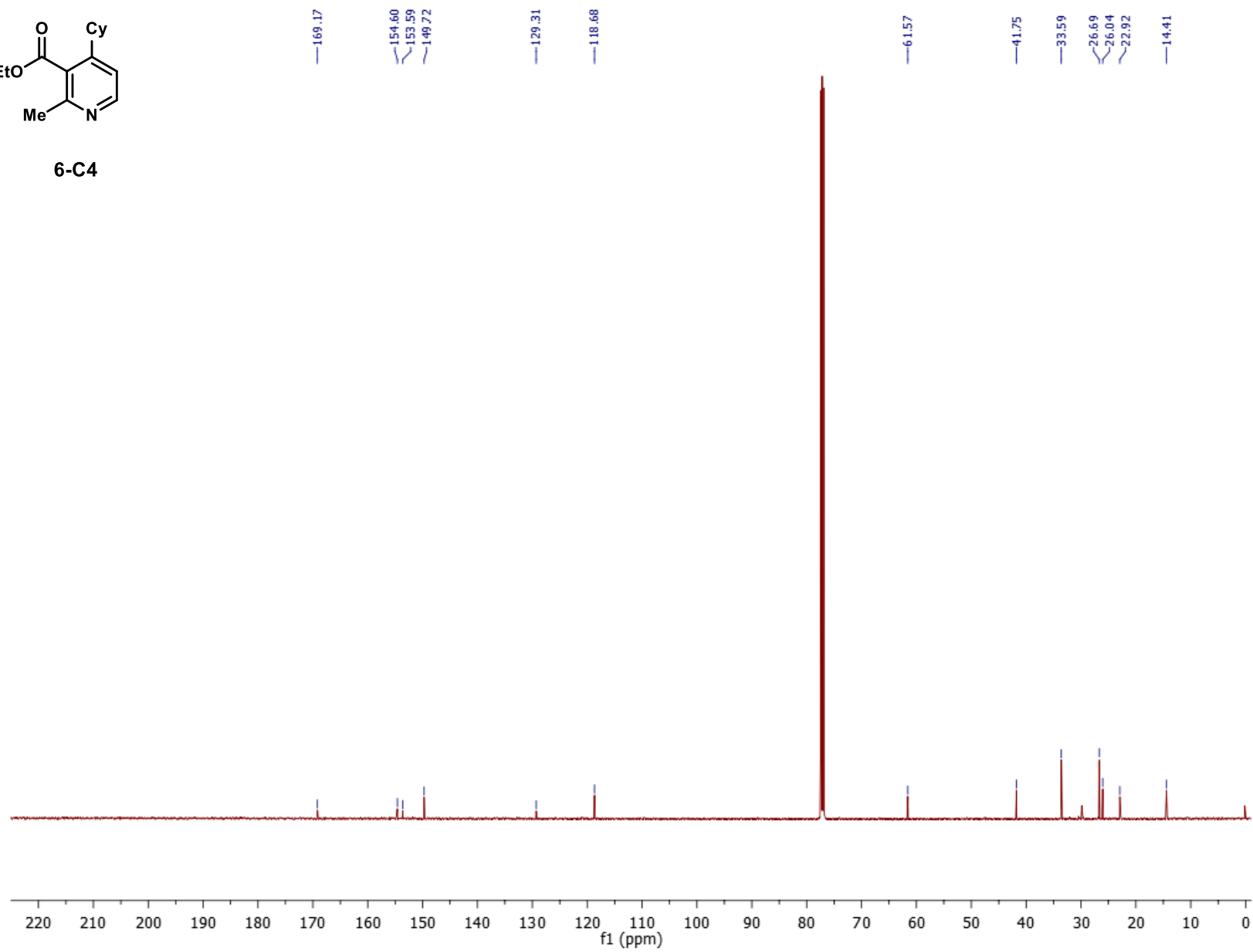


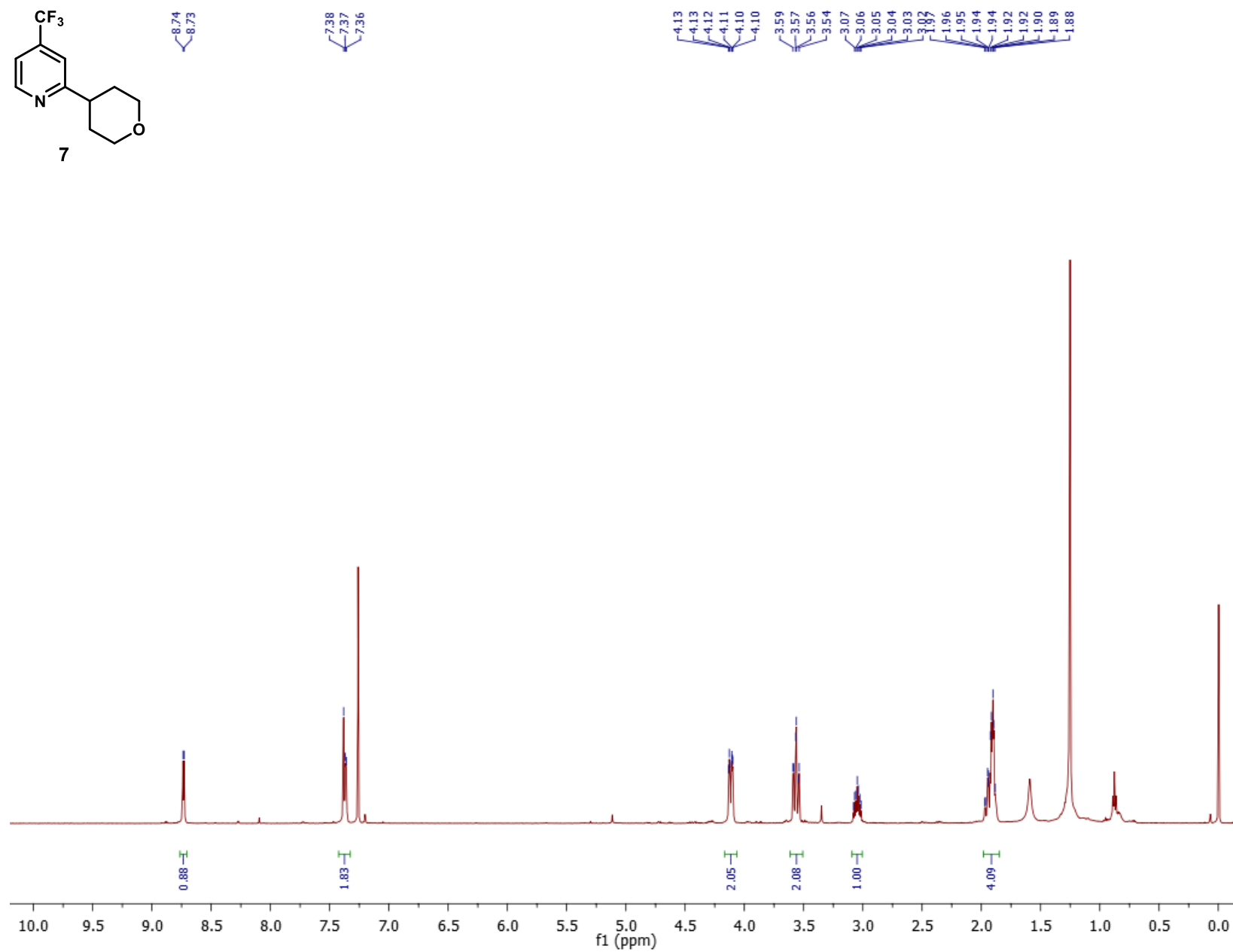
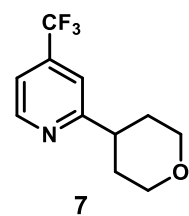


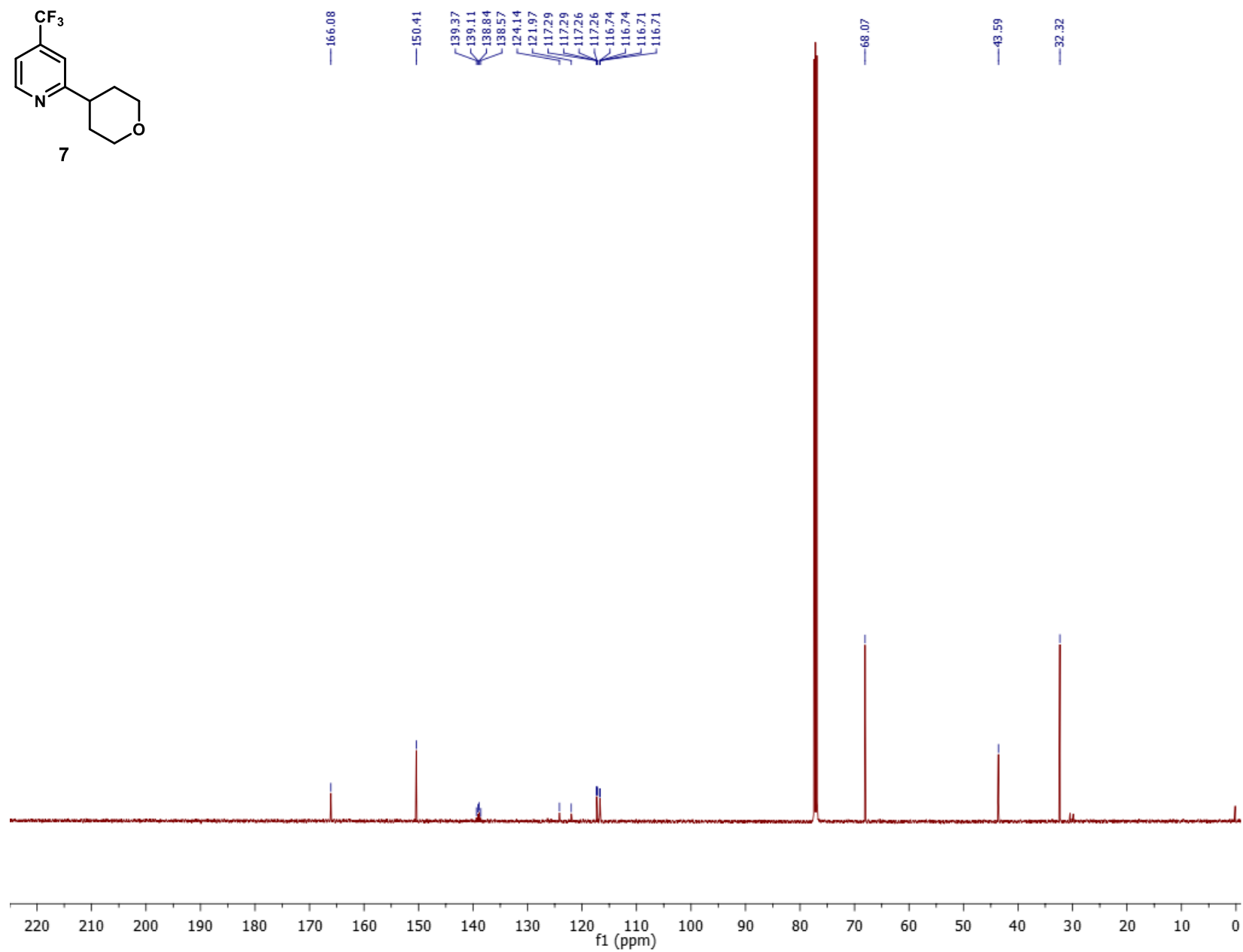
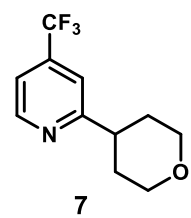


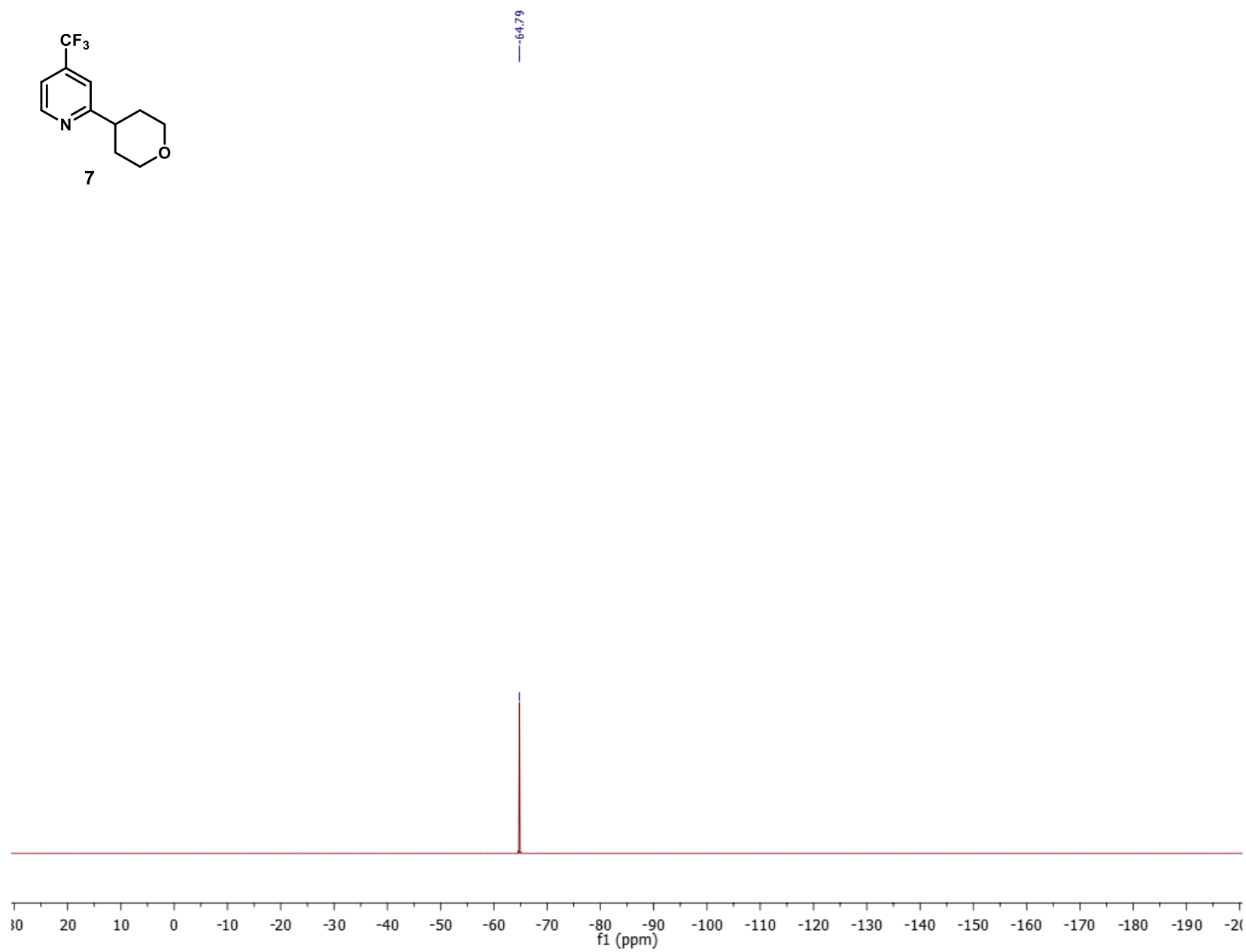
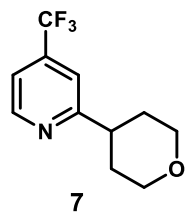


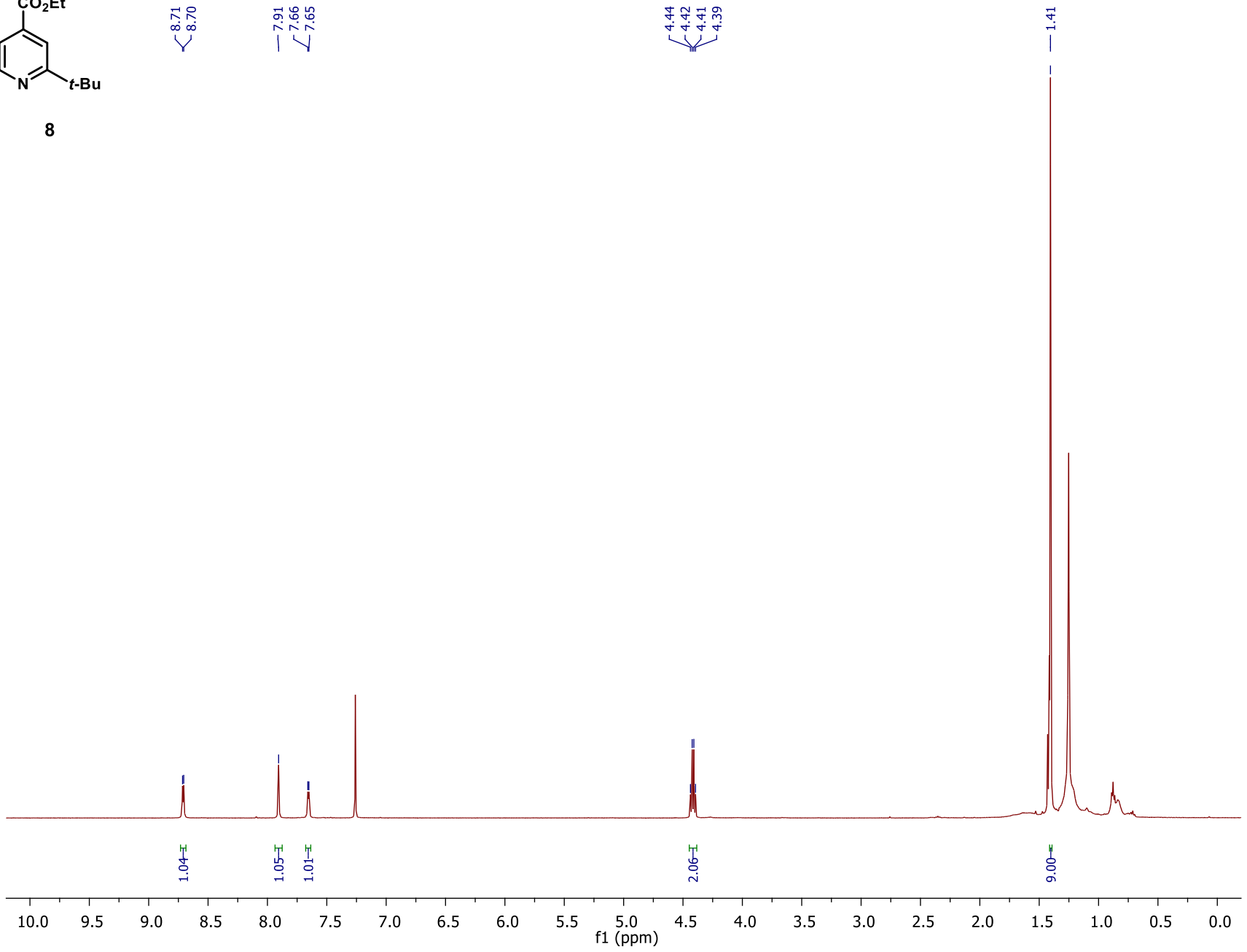
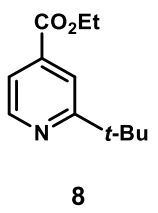
6-C4

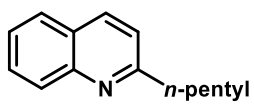




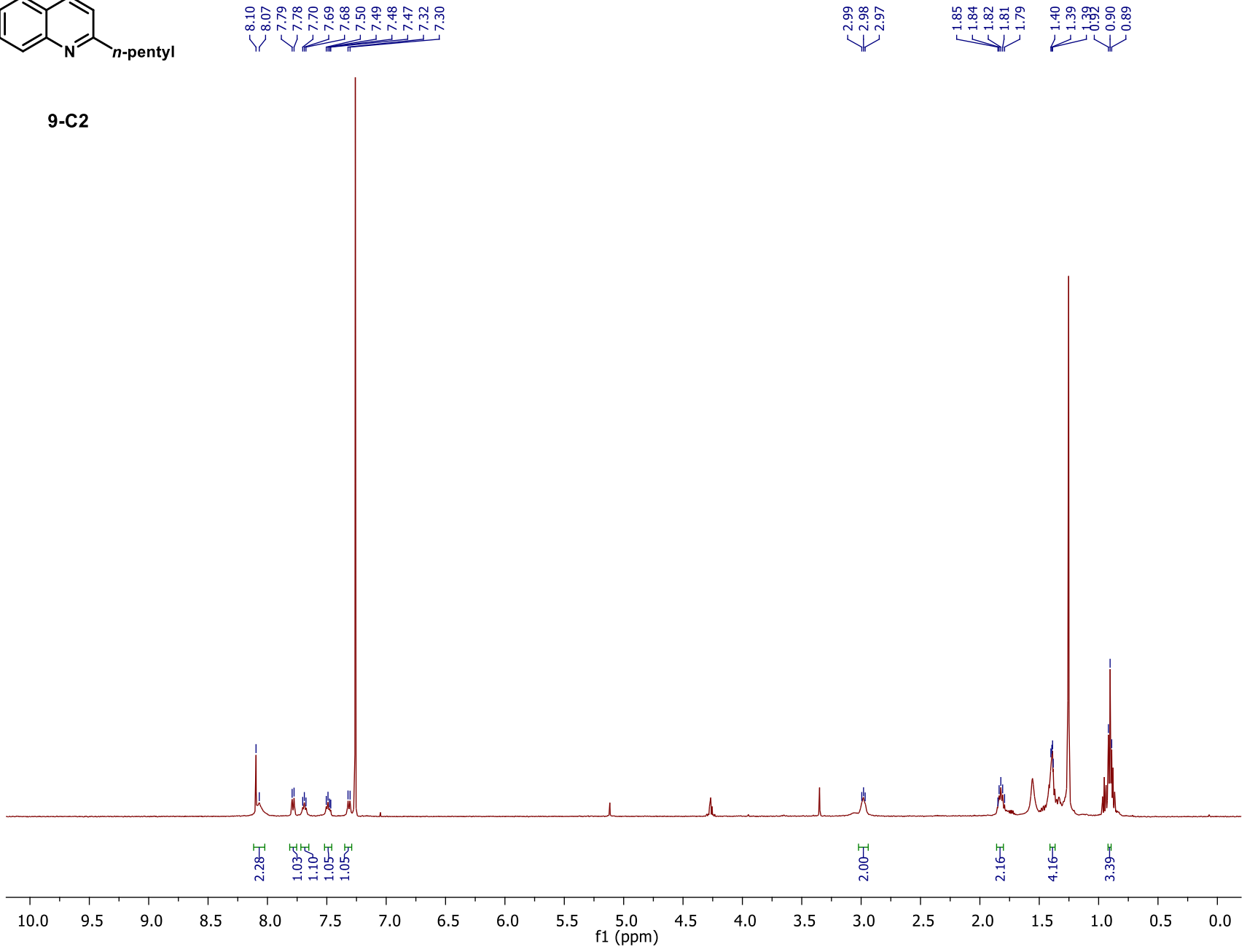


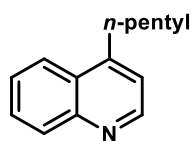




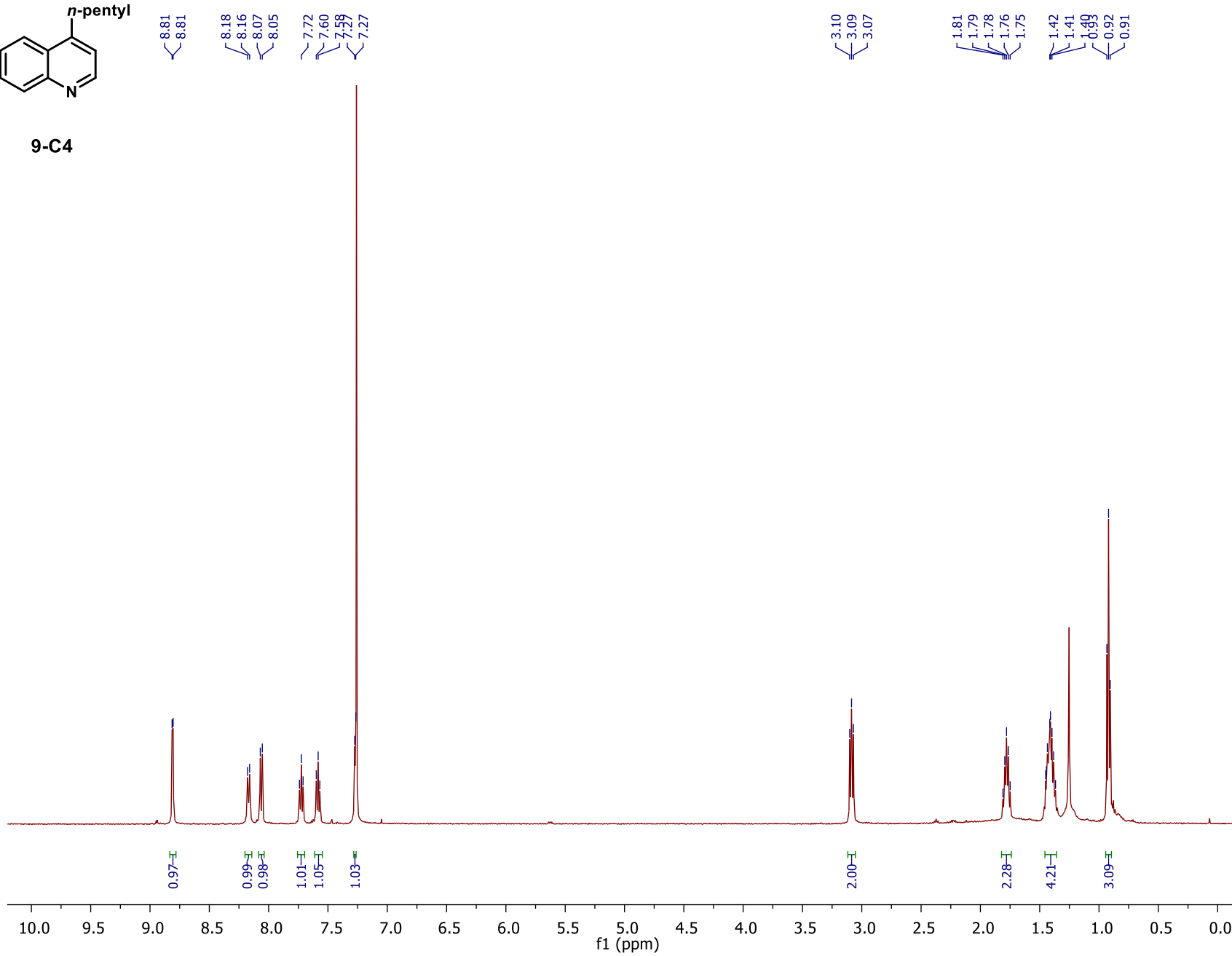


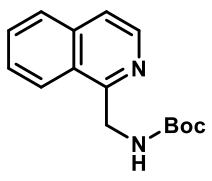
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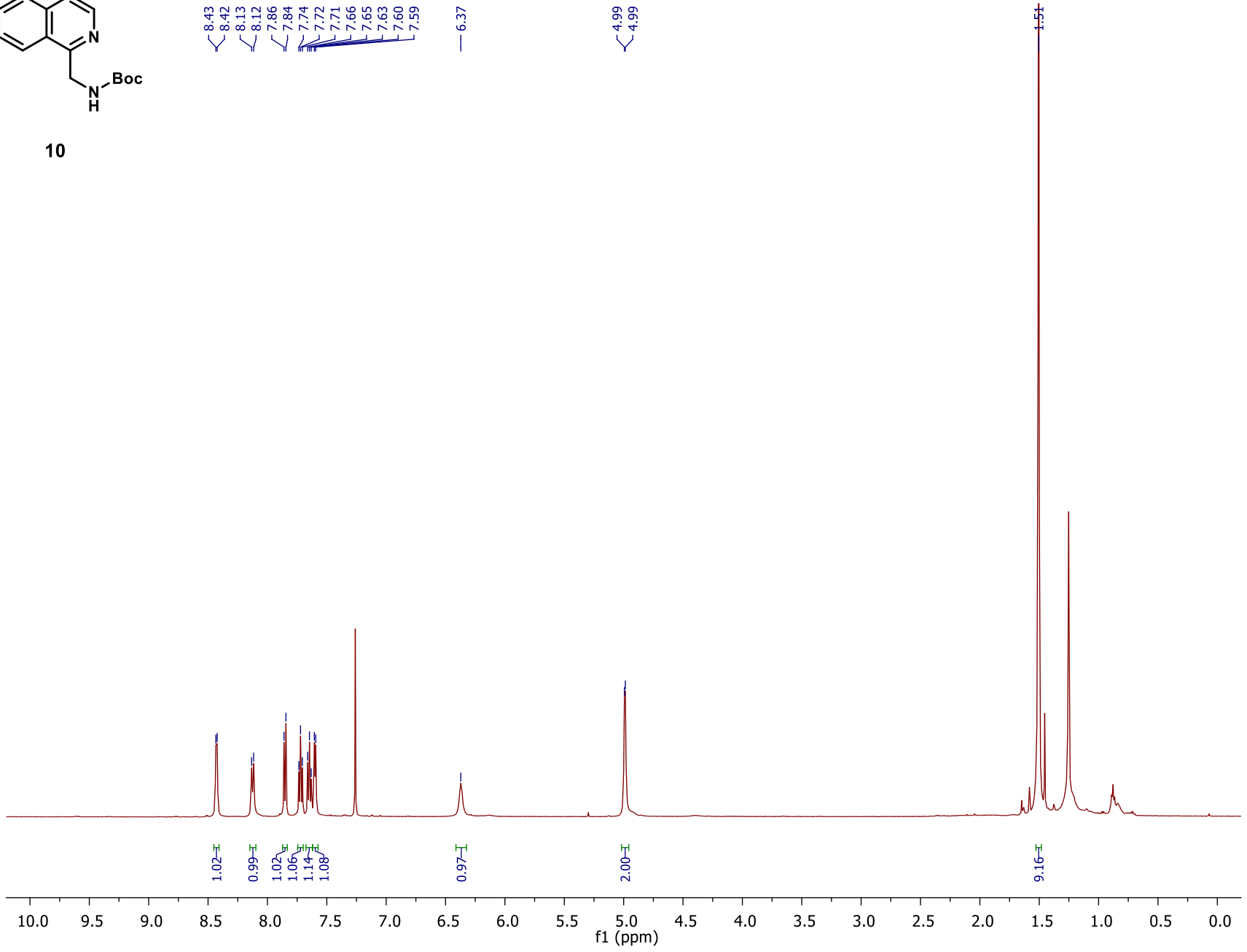


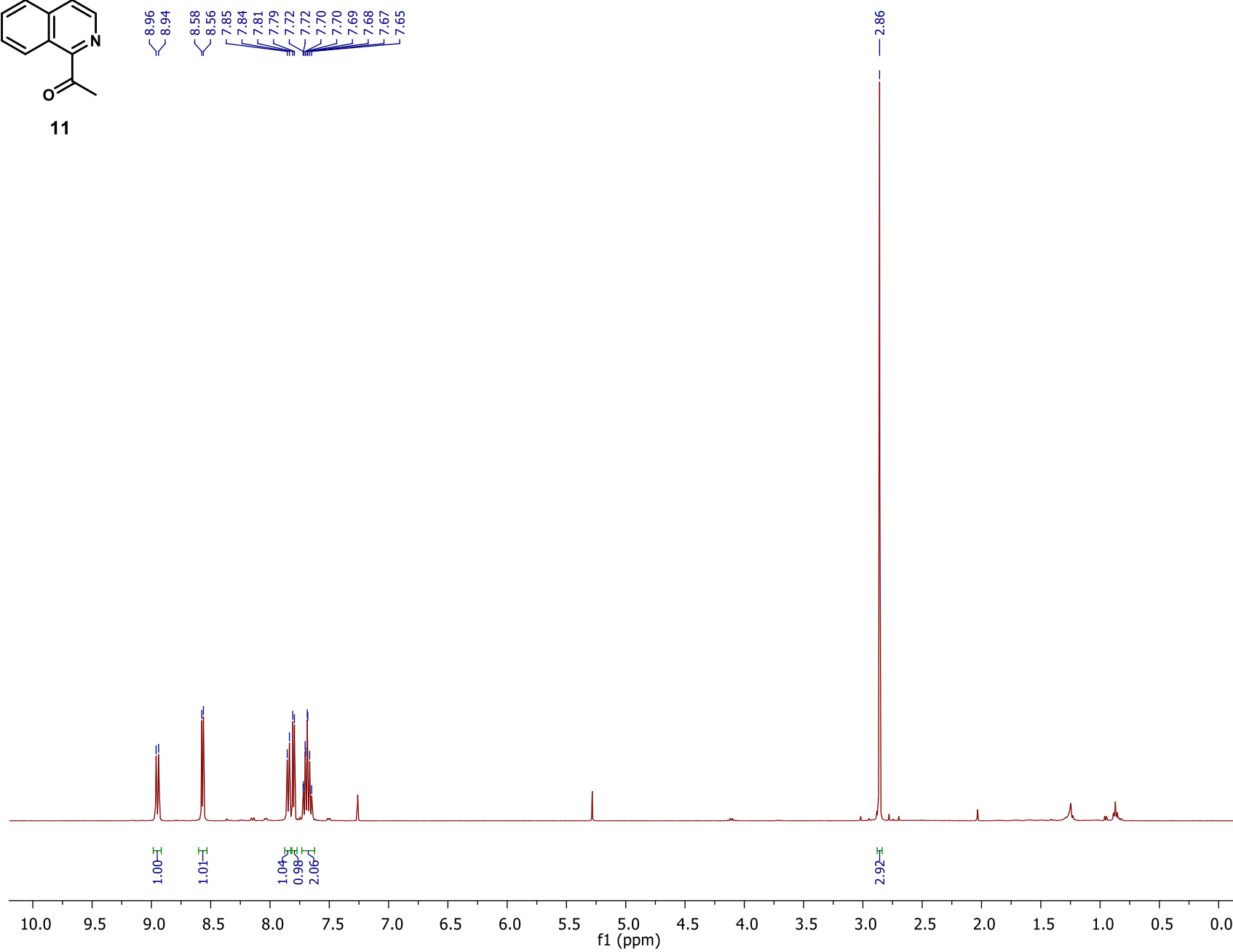
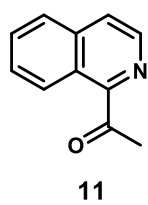
9-C4

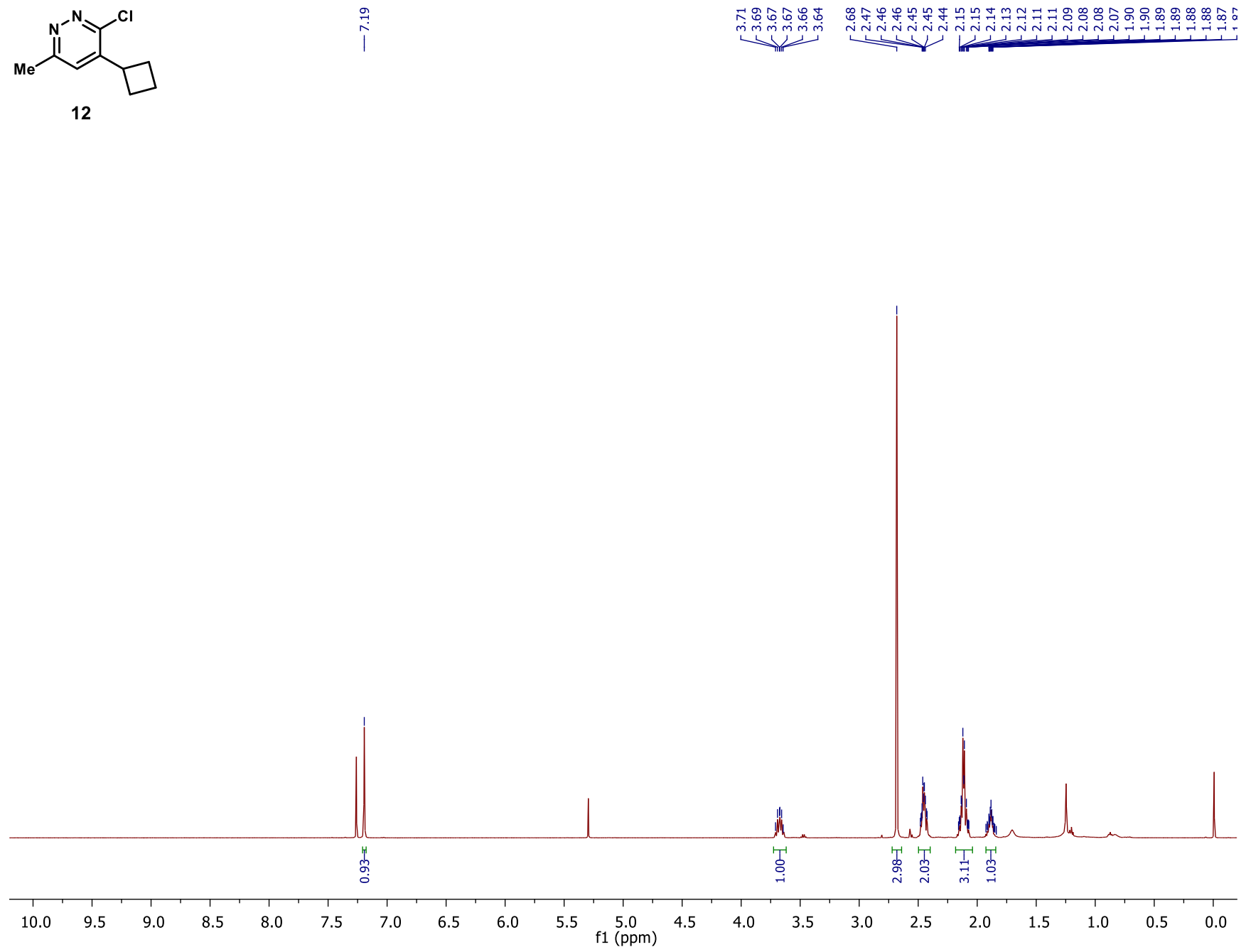
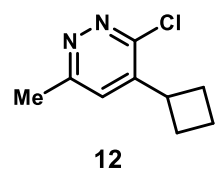


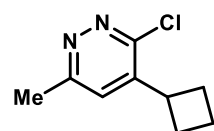


10

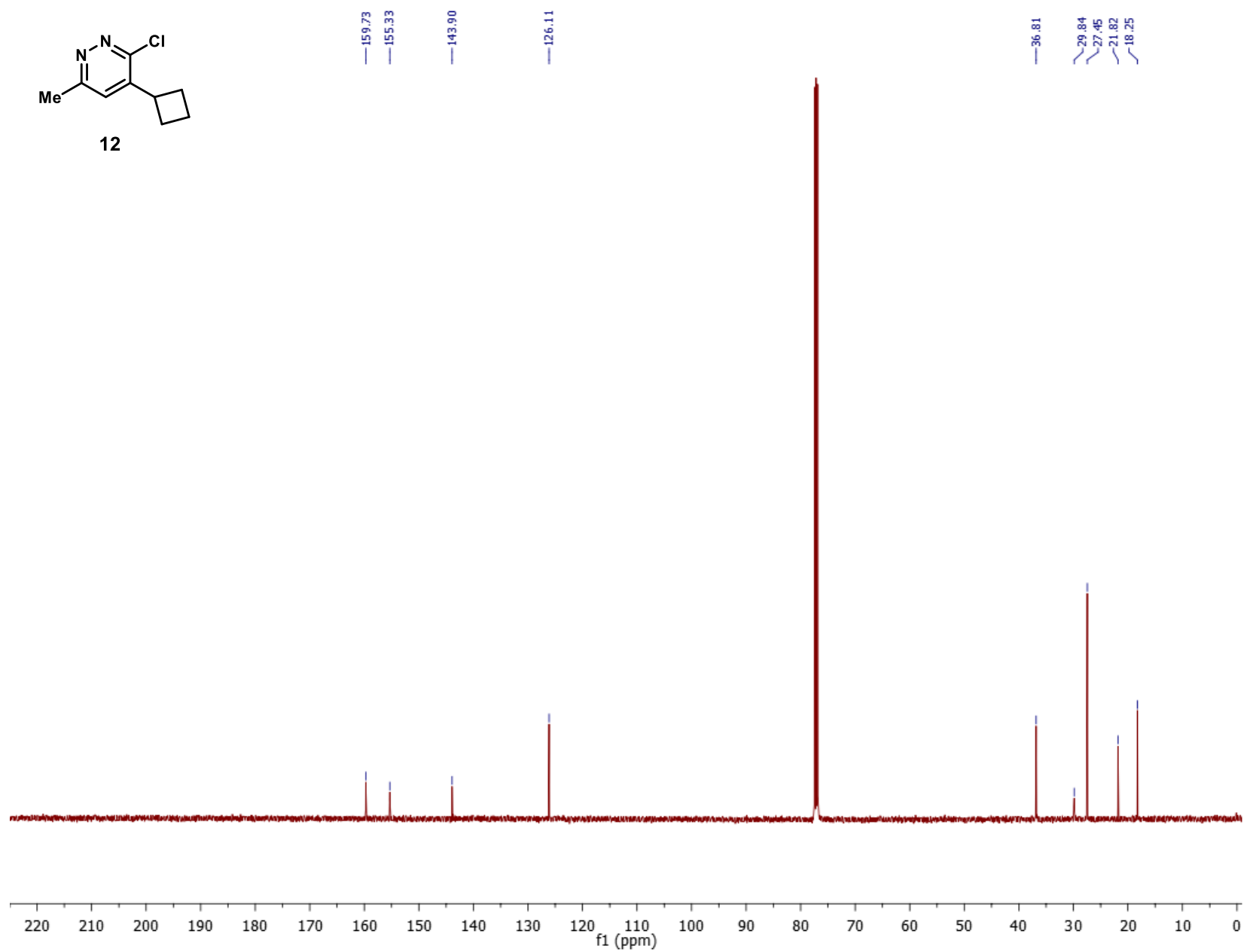


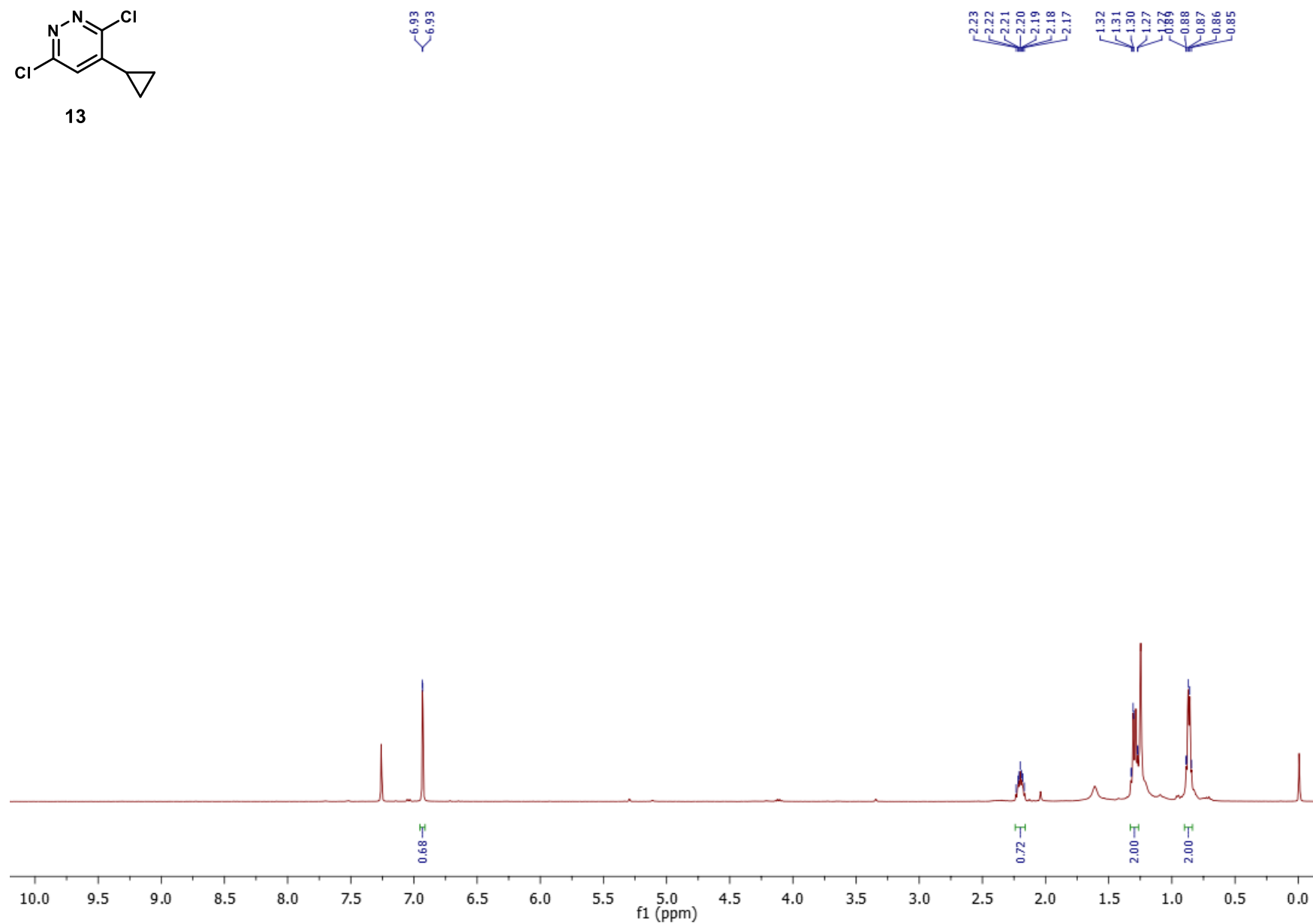
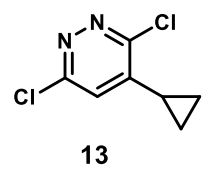


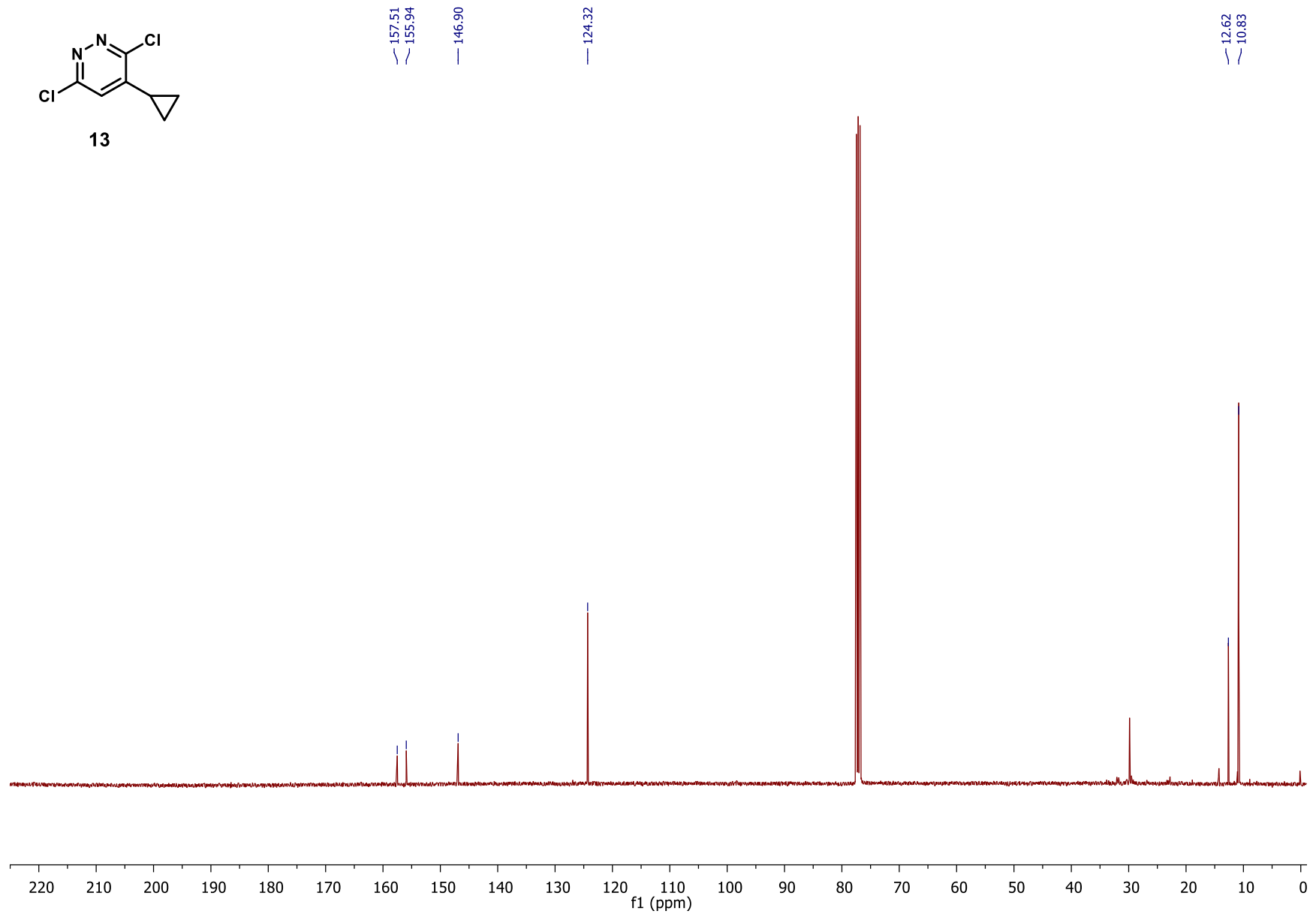
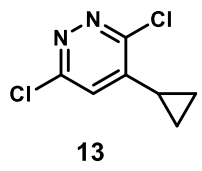


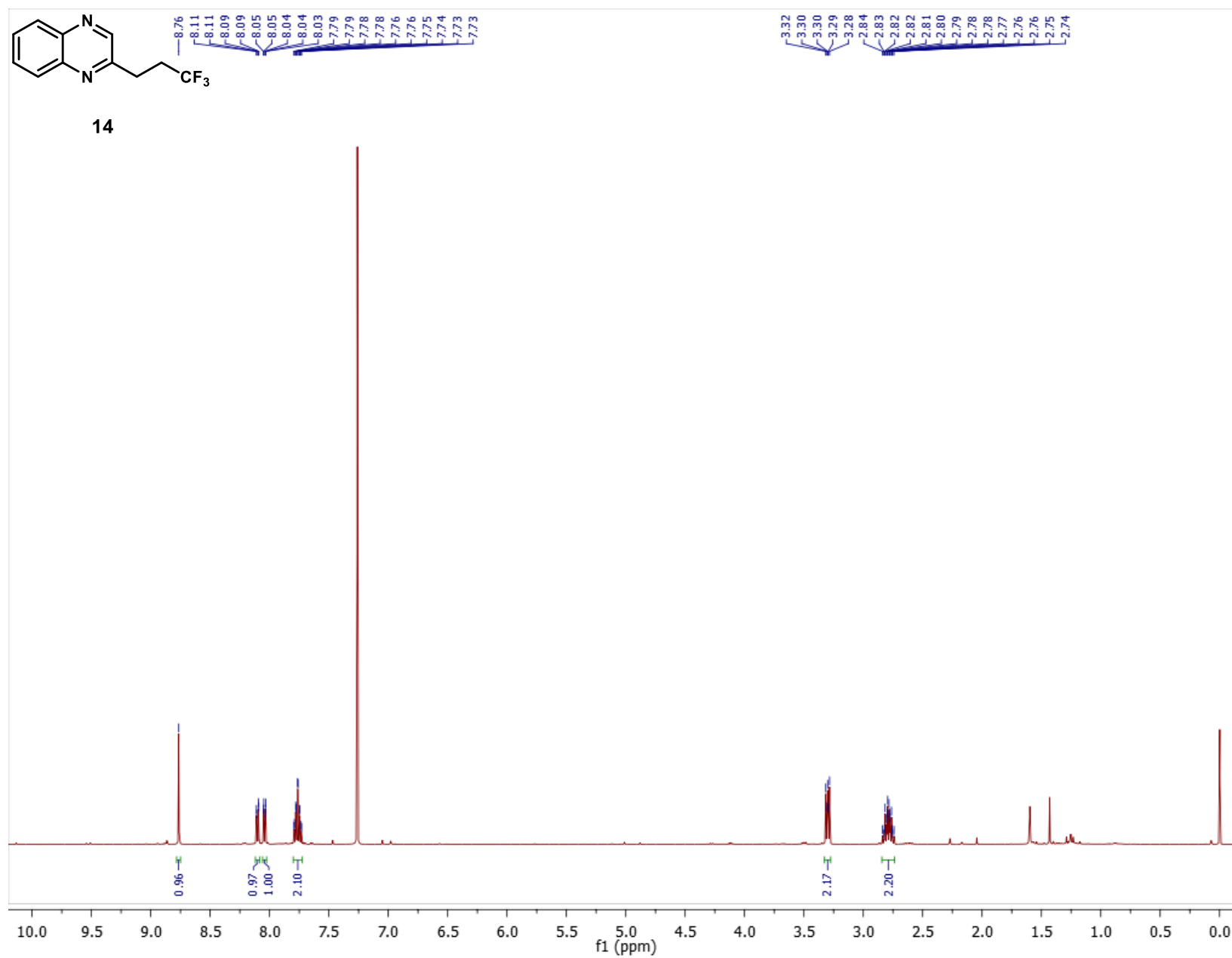


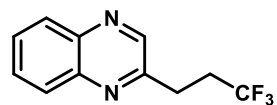
12



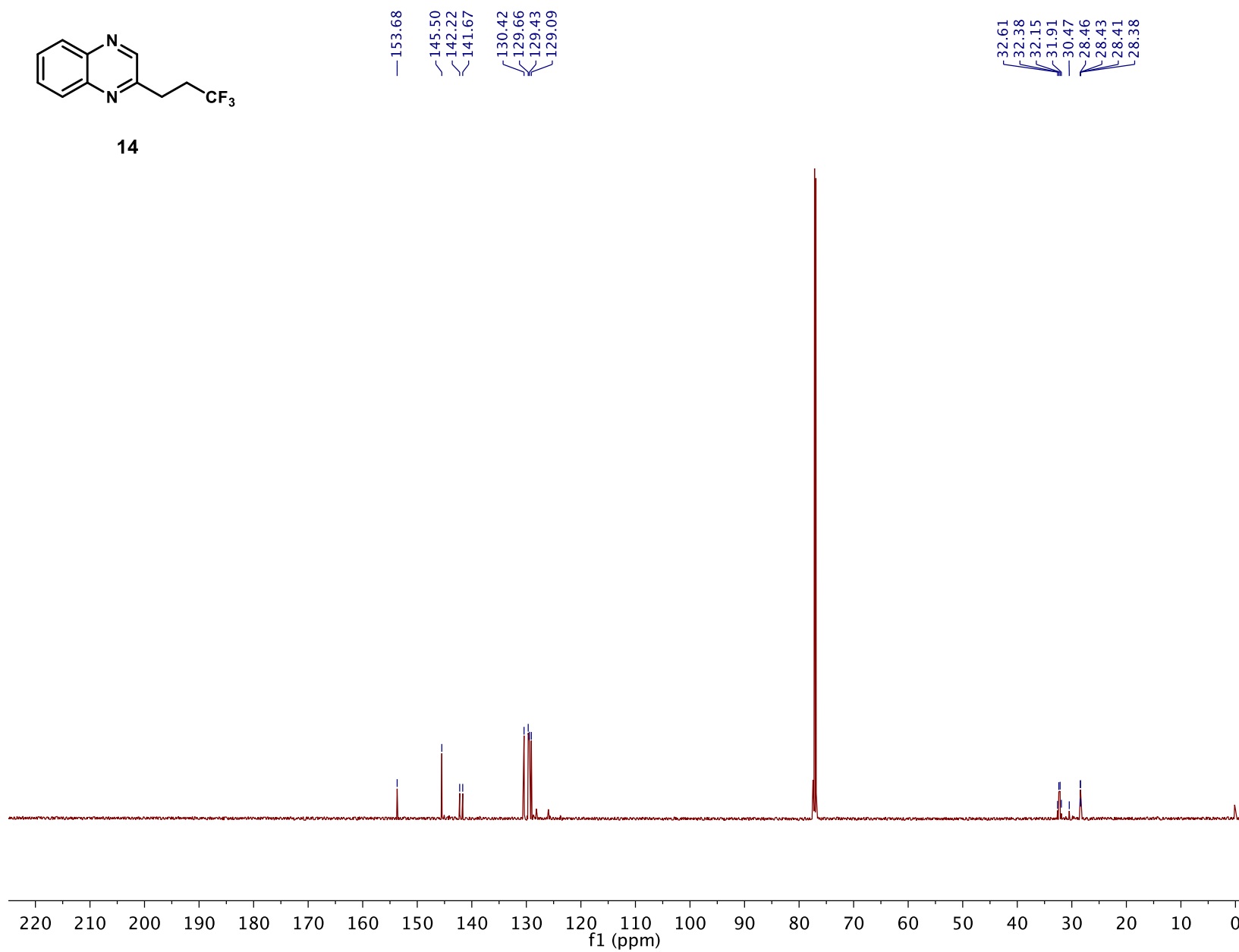


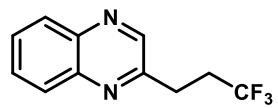






14





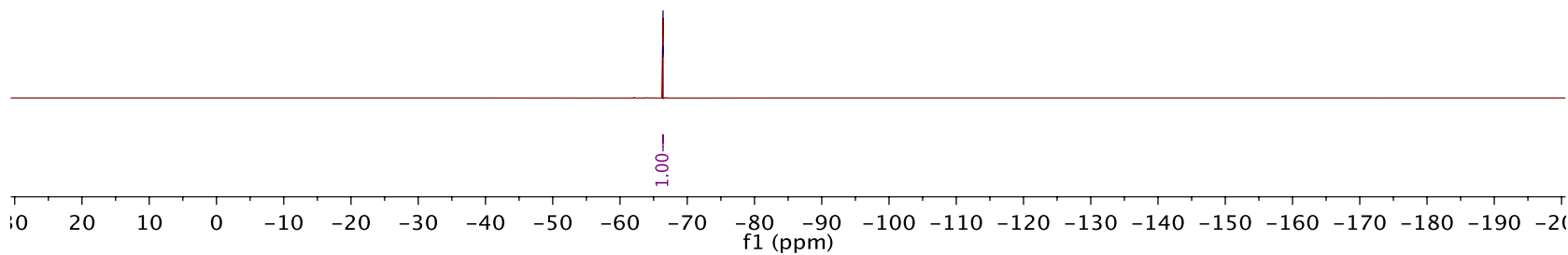
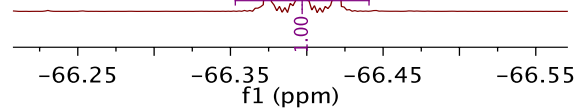
14

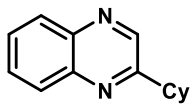


A (t)
-66.40

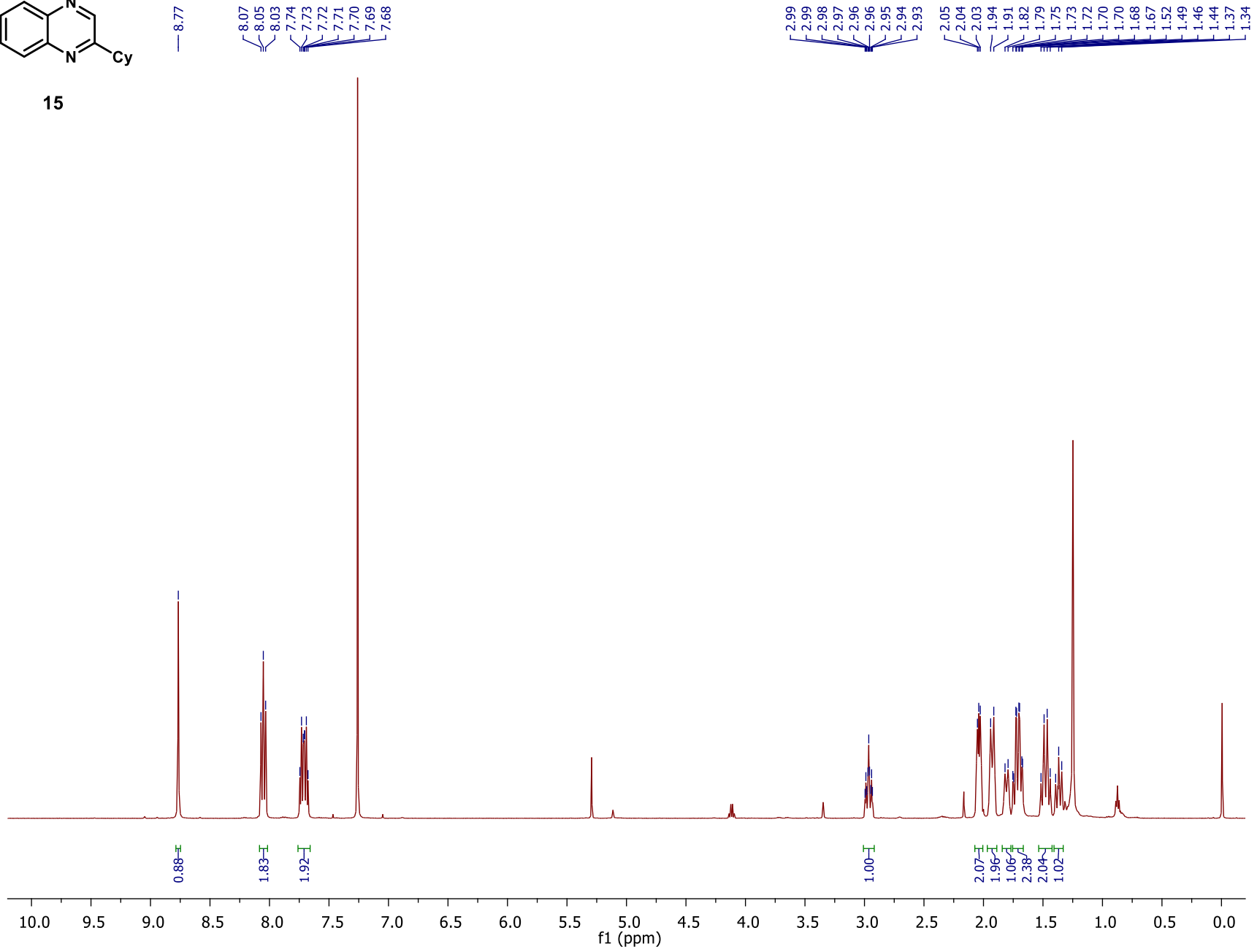


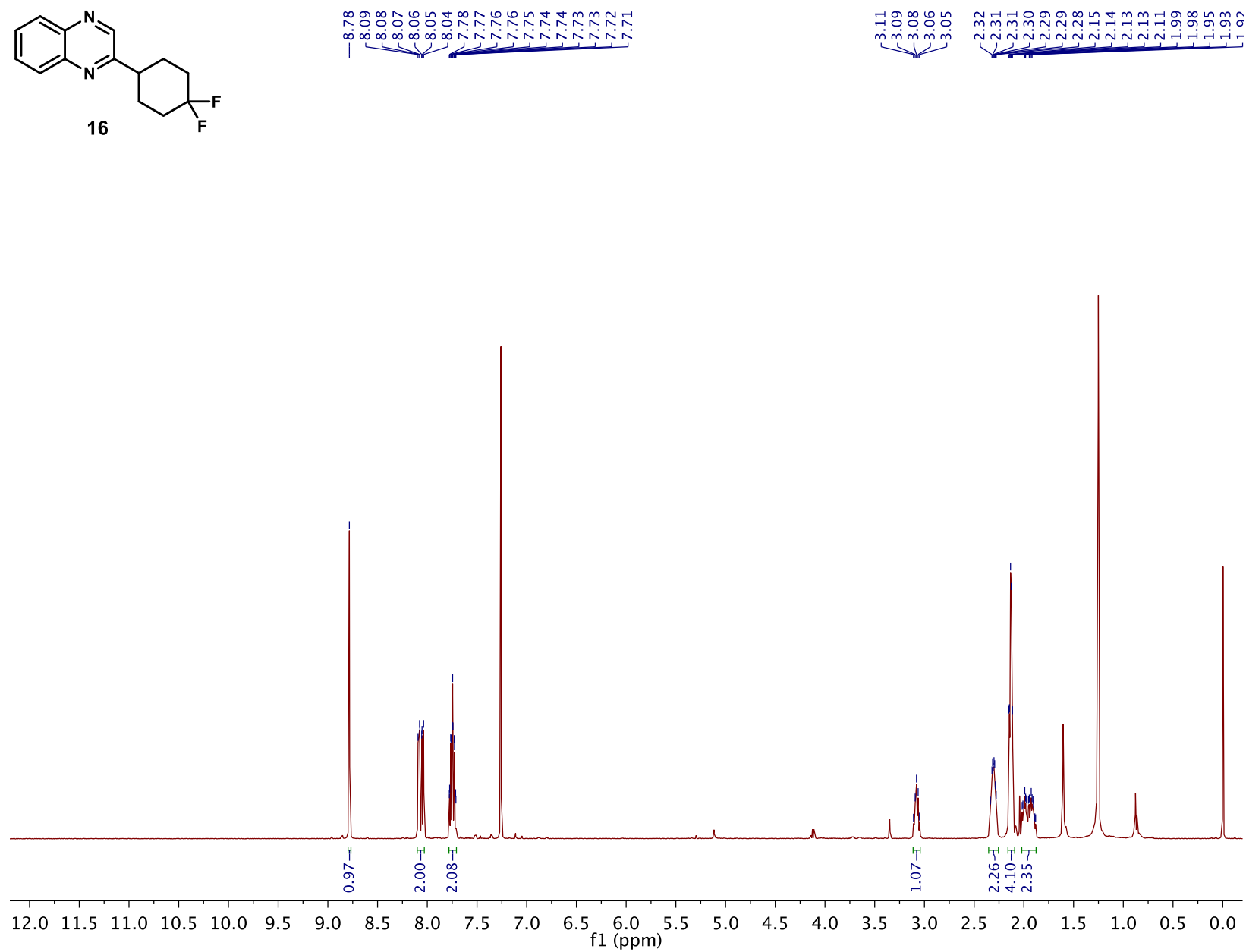
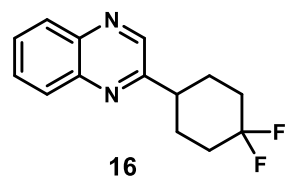
A (t)
-66.40

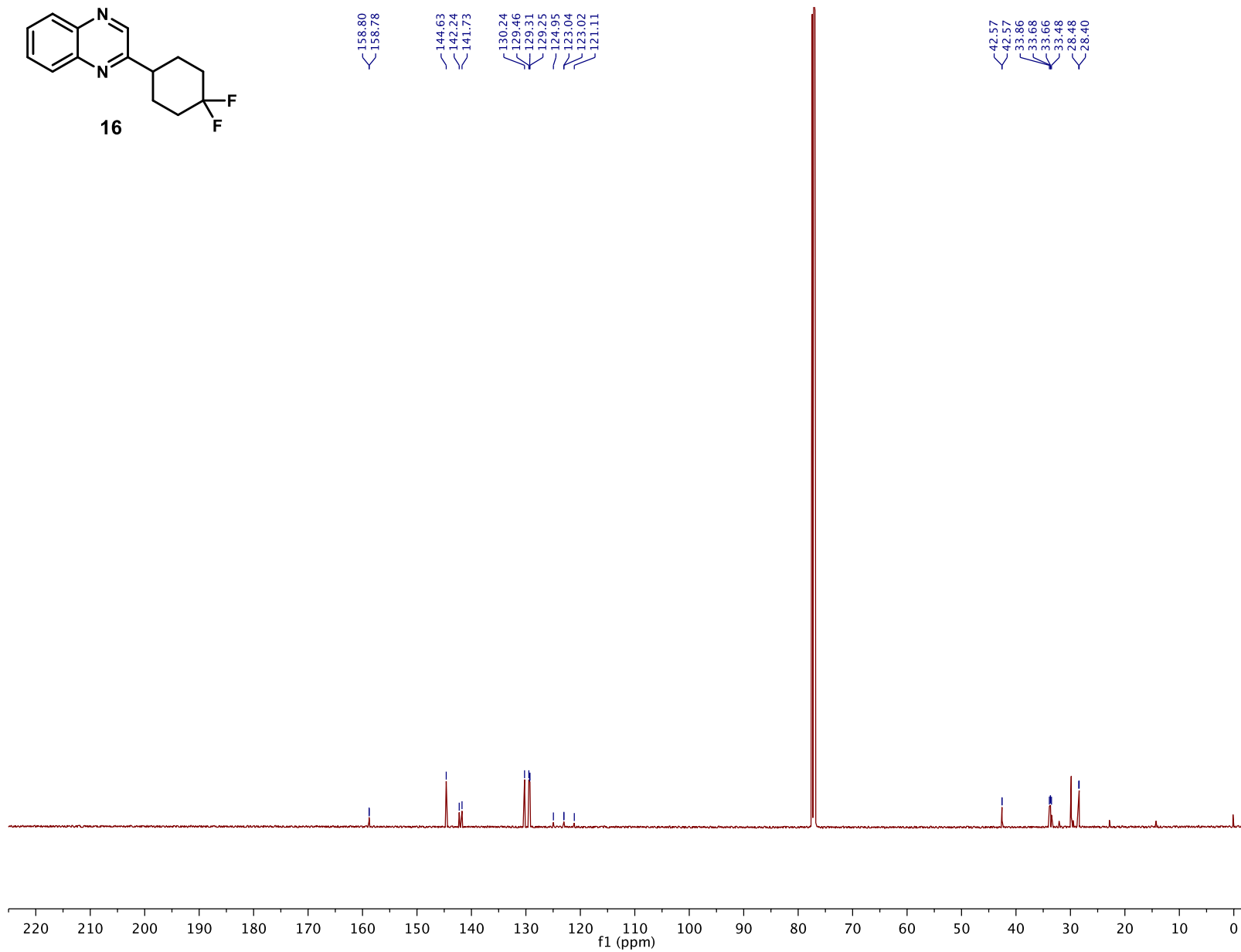
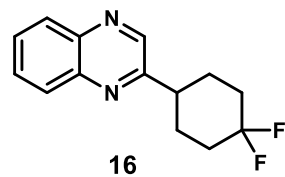


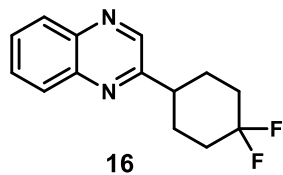


15

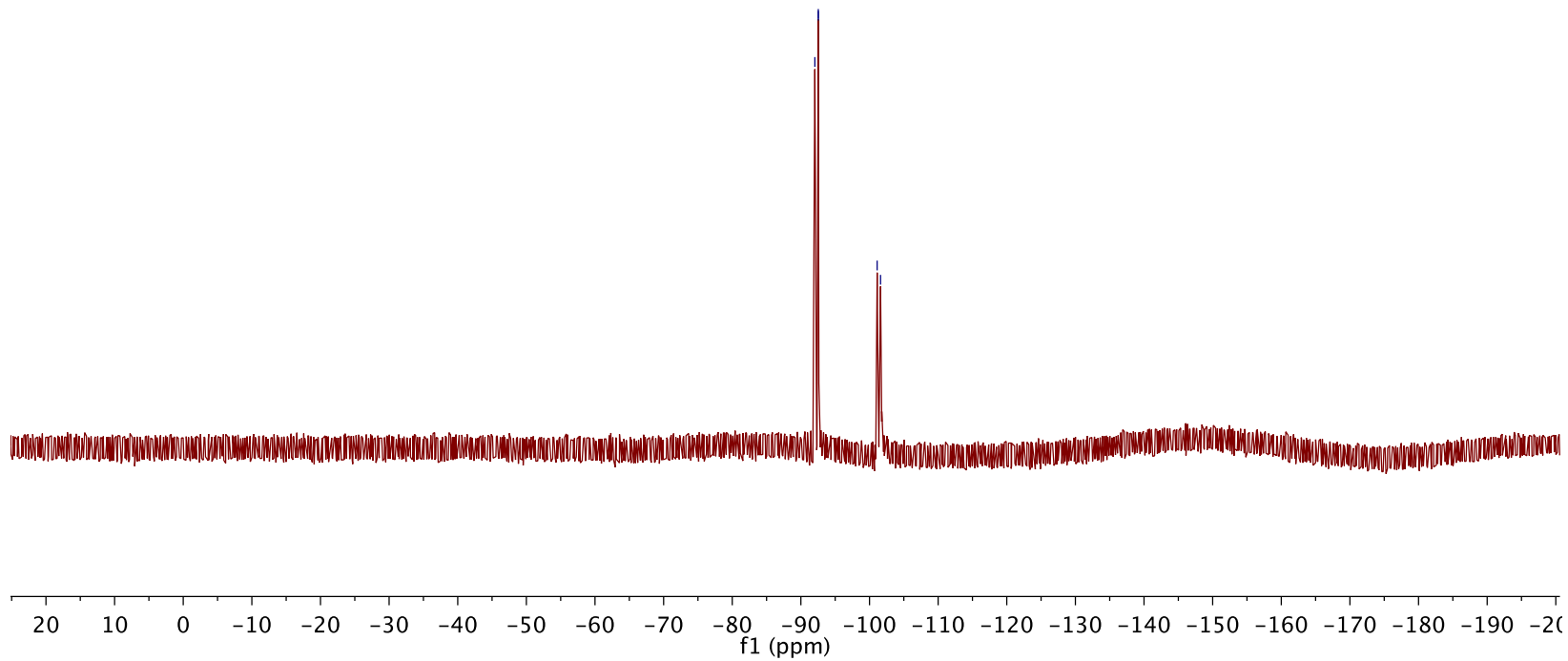


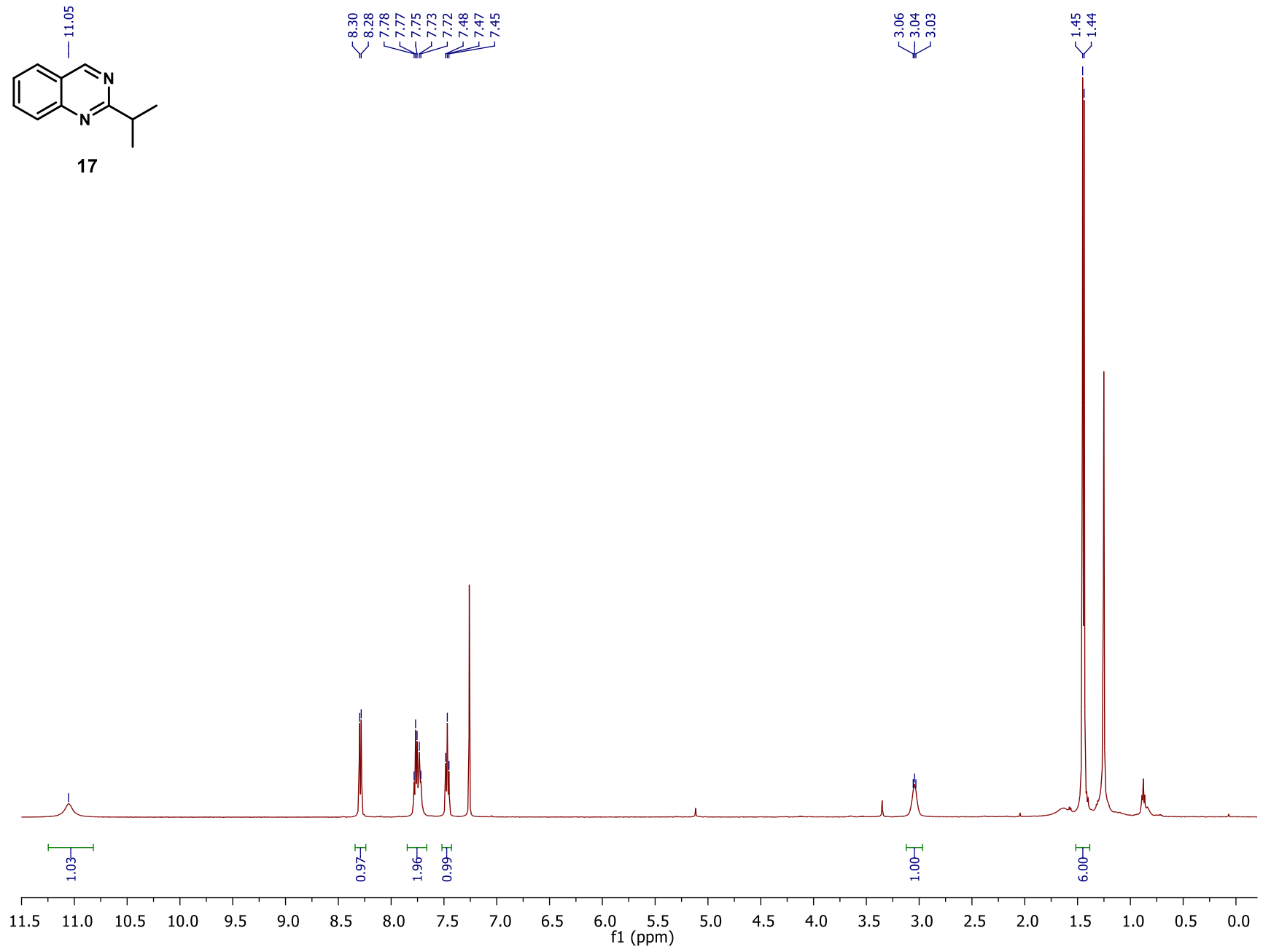


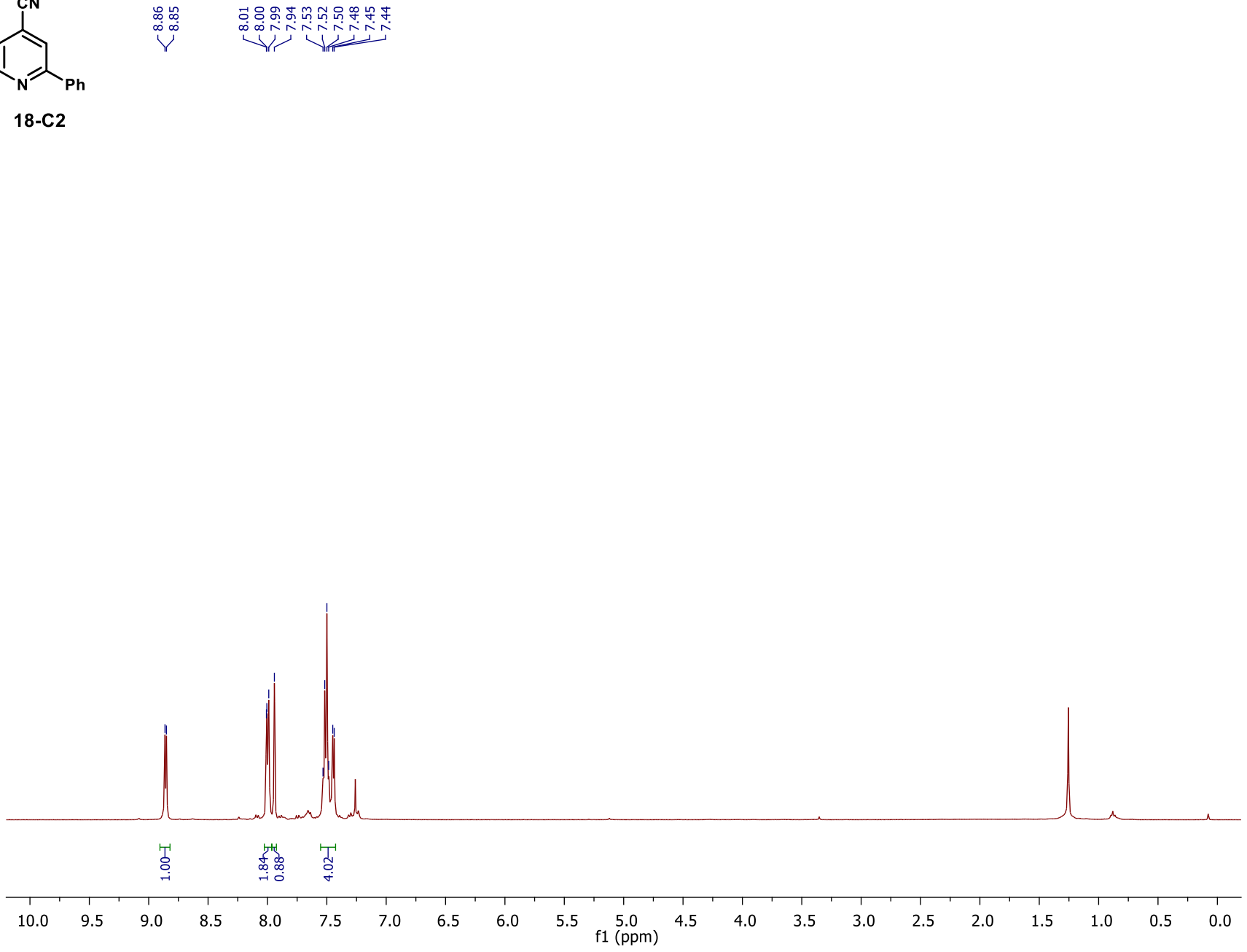
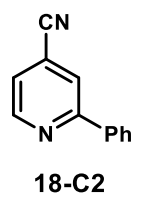


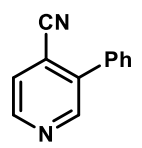


-92.04
-92.54
-92.54
-101.11
-101.61





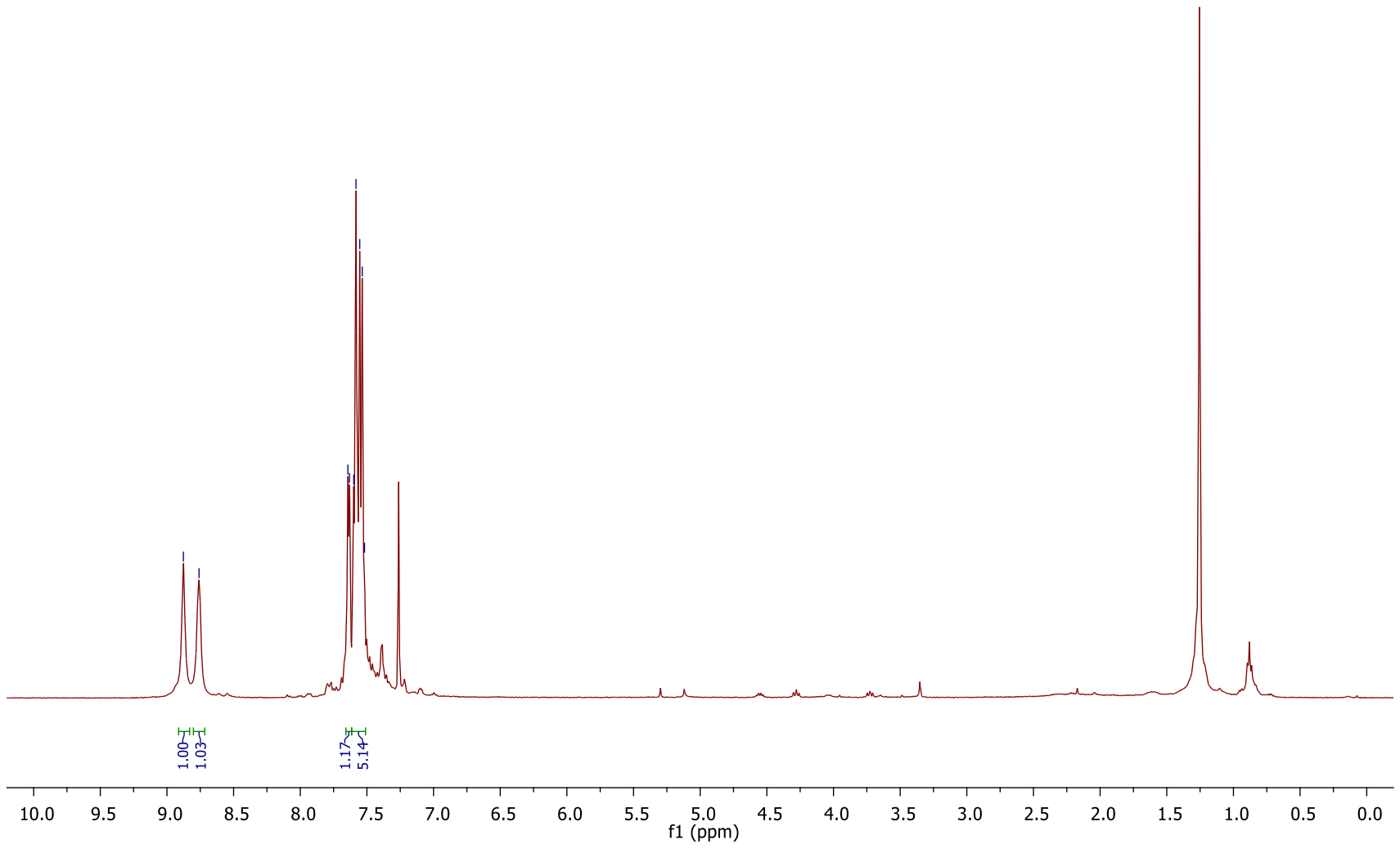


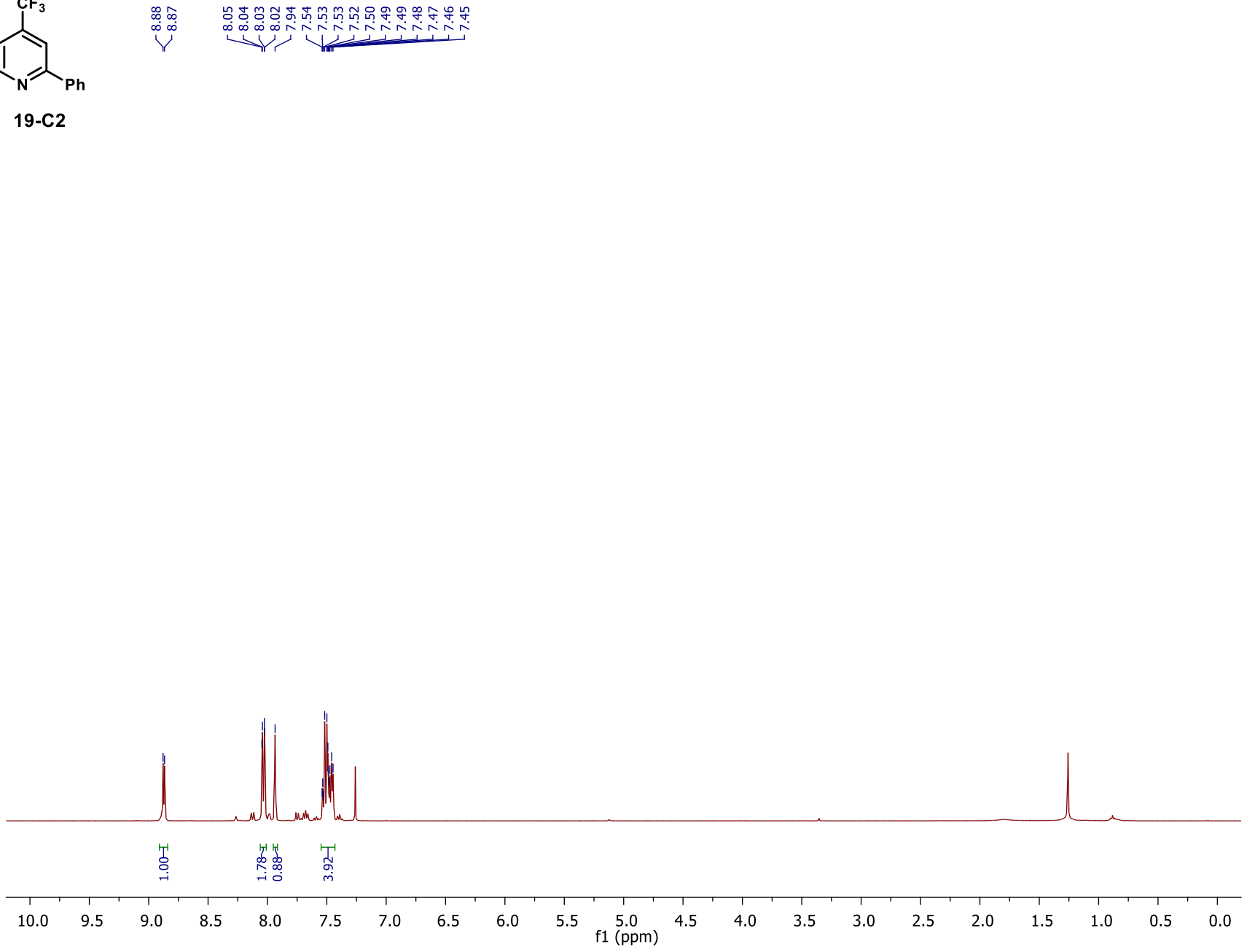
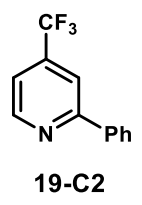


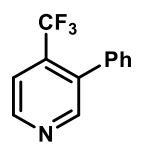
18-C3

8.88
8.76

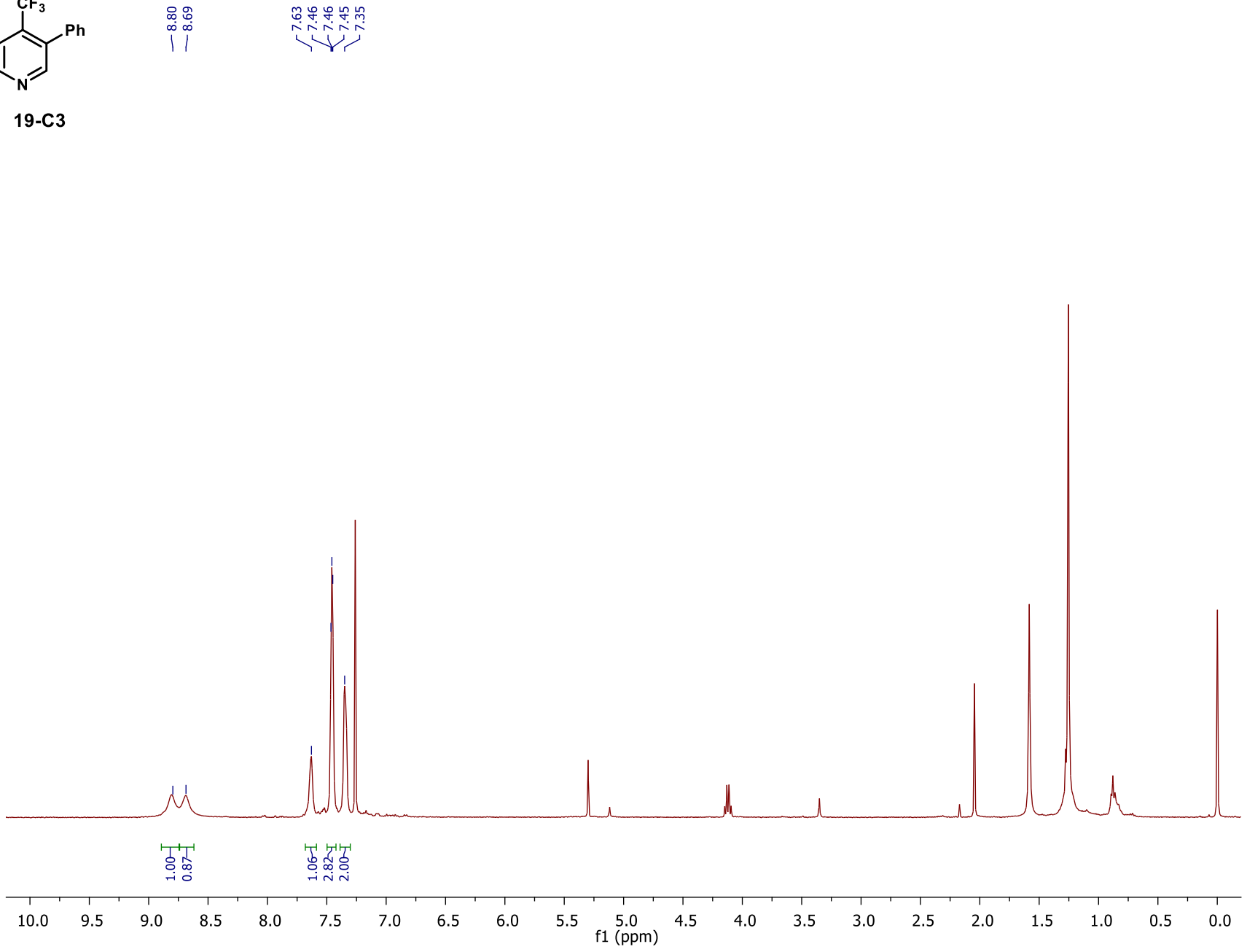
7.64
7.63
7.60
7.58
7.55
7.54
7.52

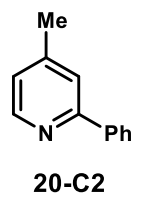






19-C3

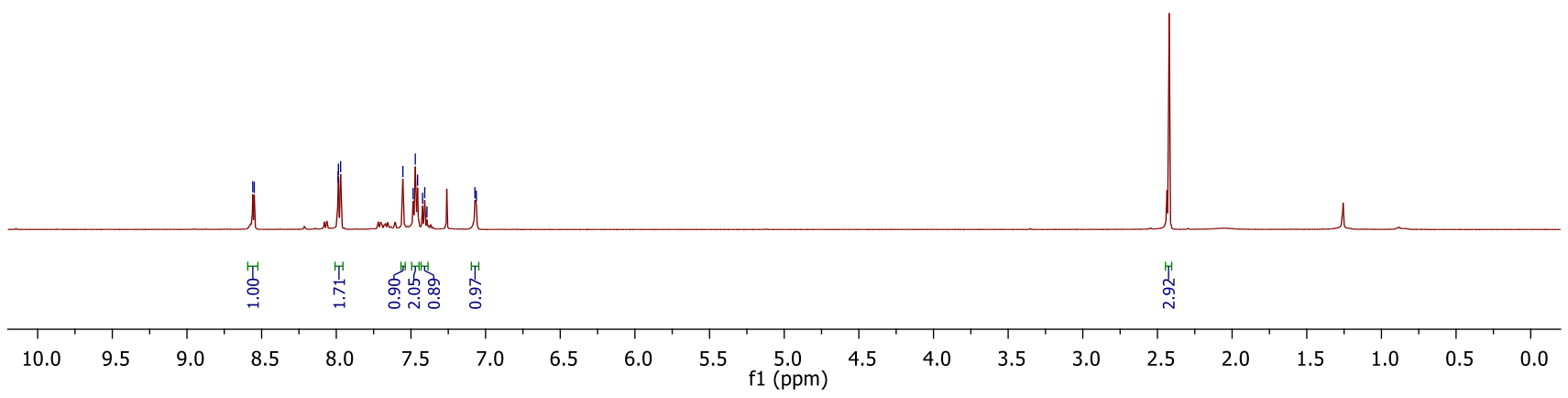


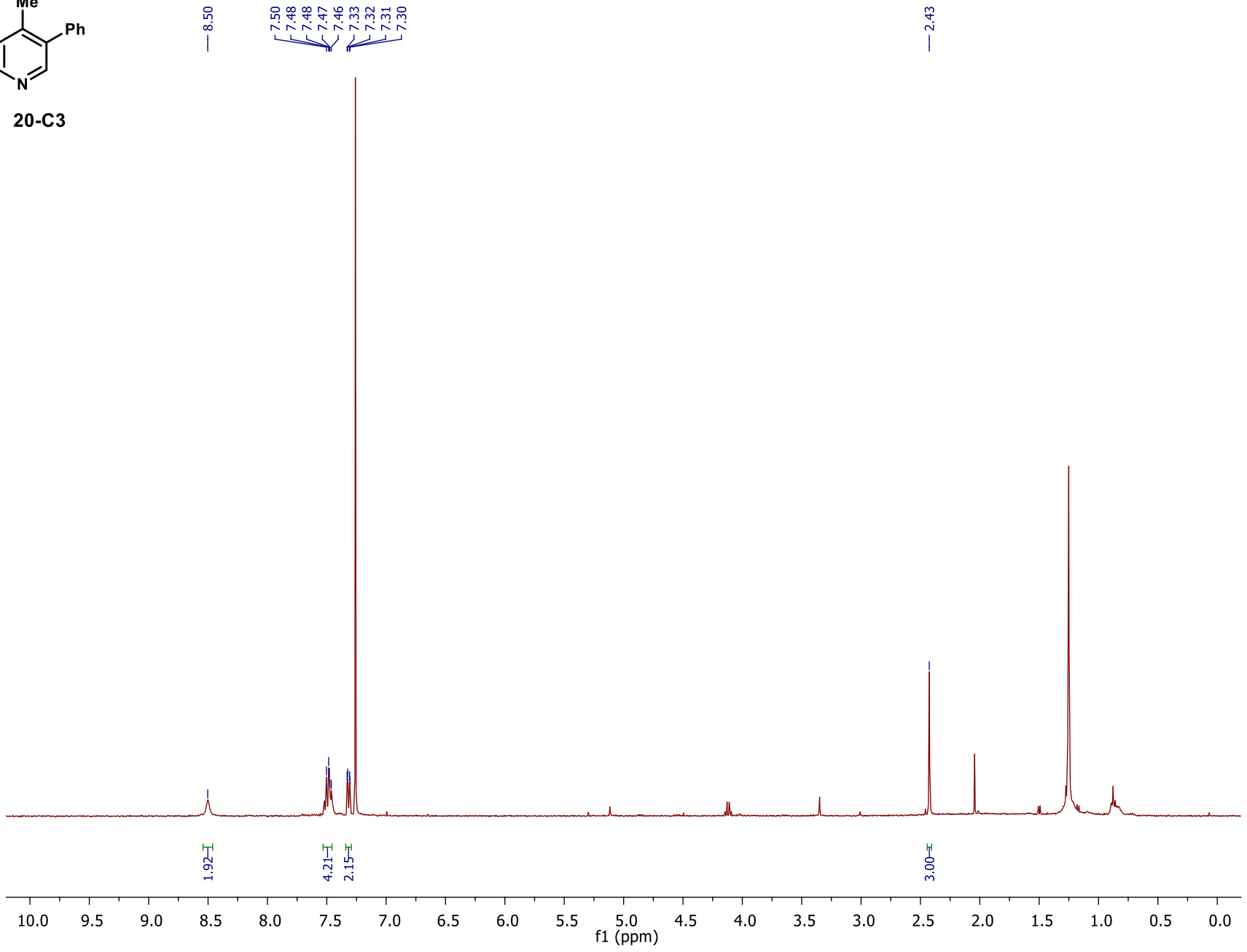
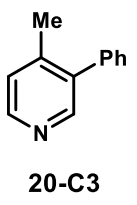


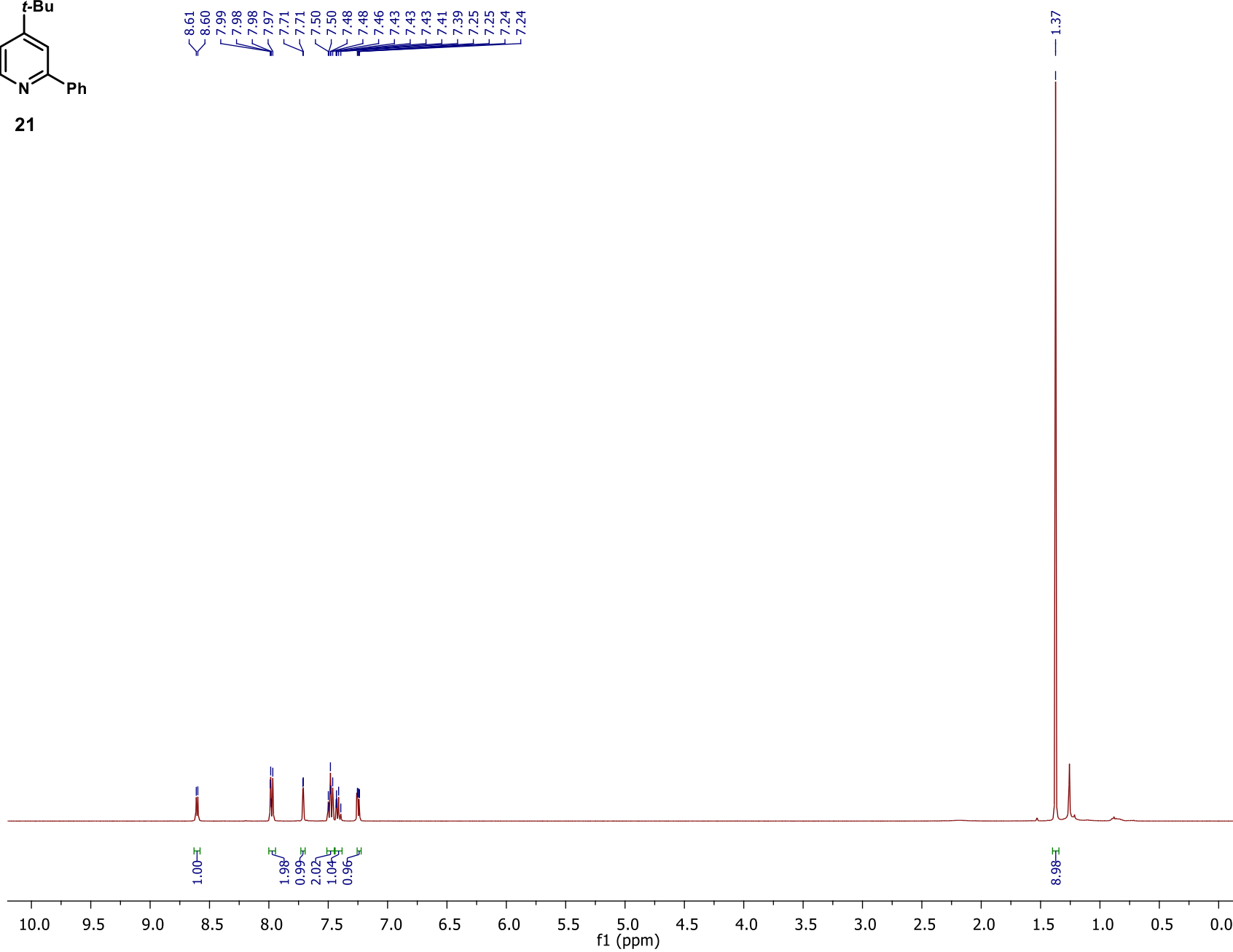
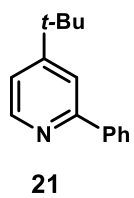
8.56
8.55

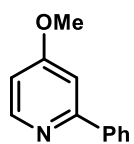
7.99
7.99
7.97

7.55
7.47
7.46
7.41
7.06

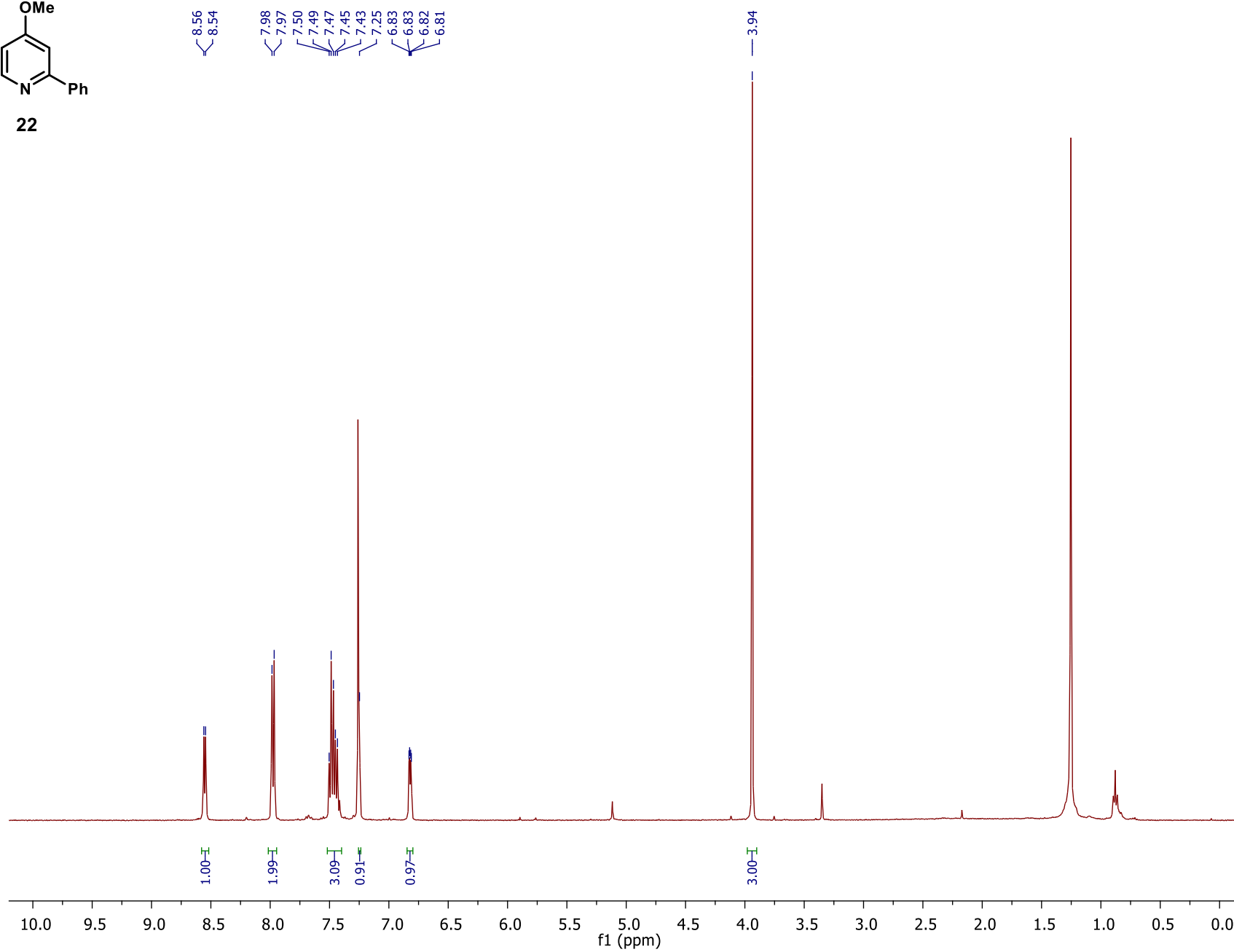


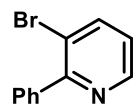




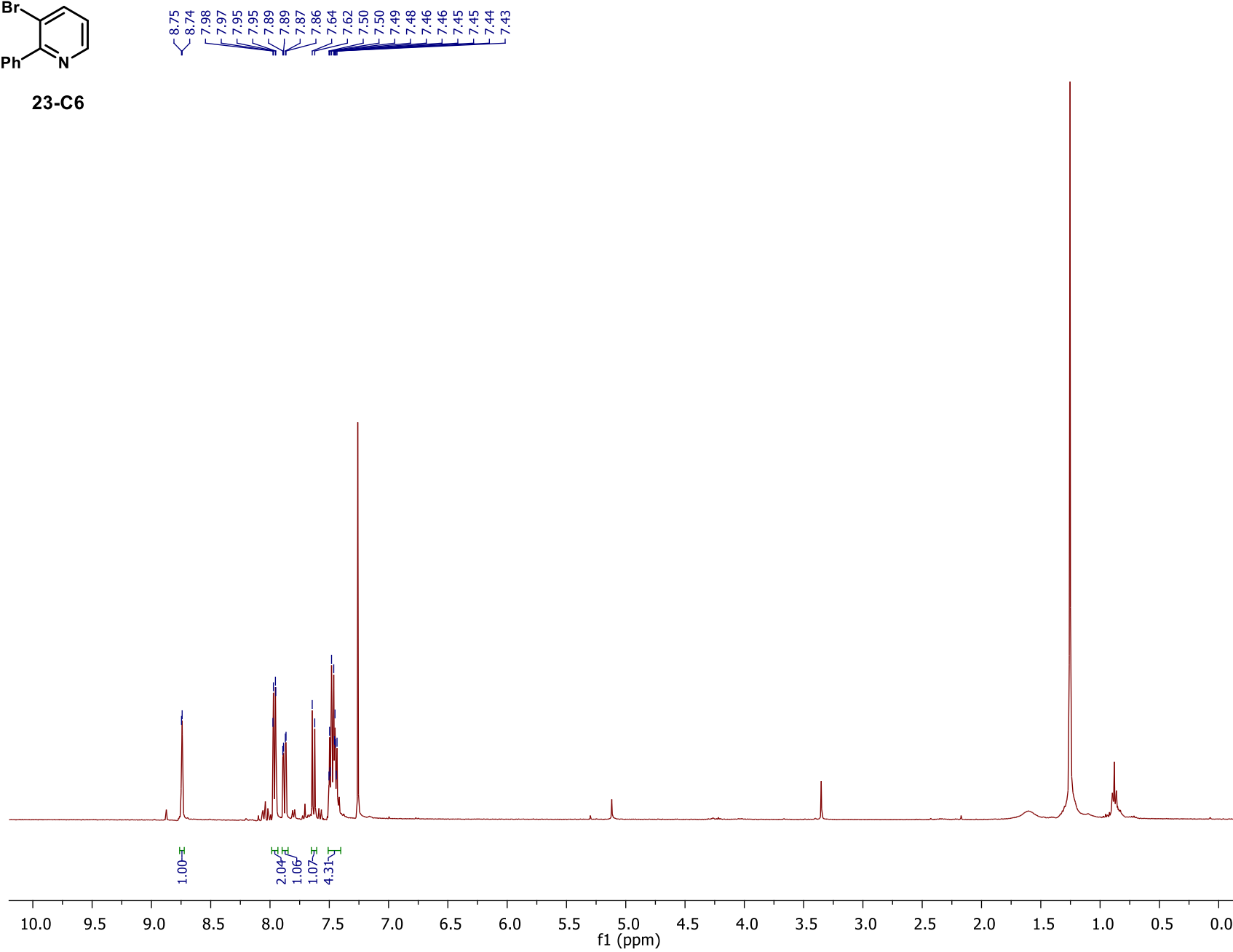


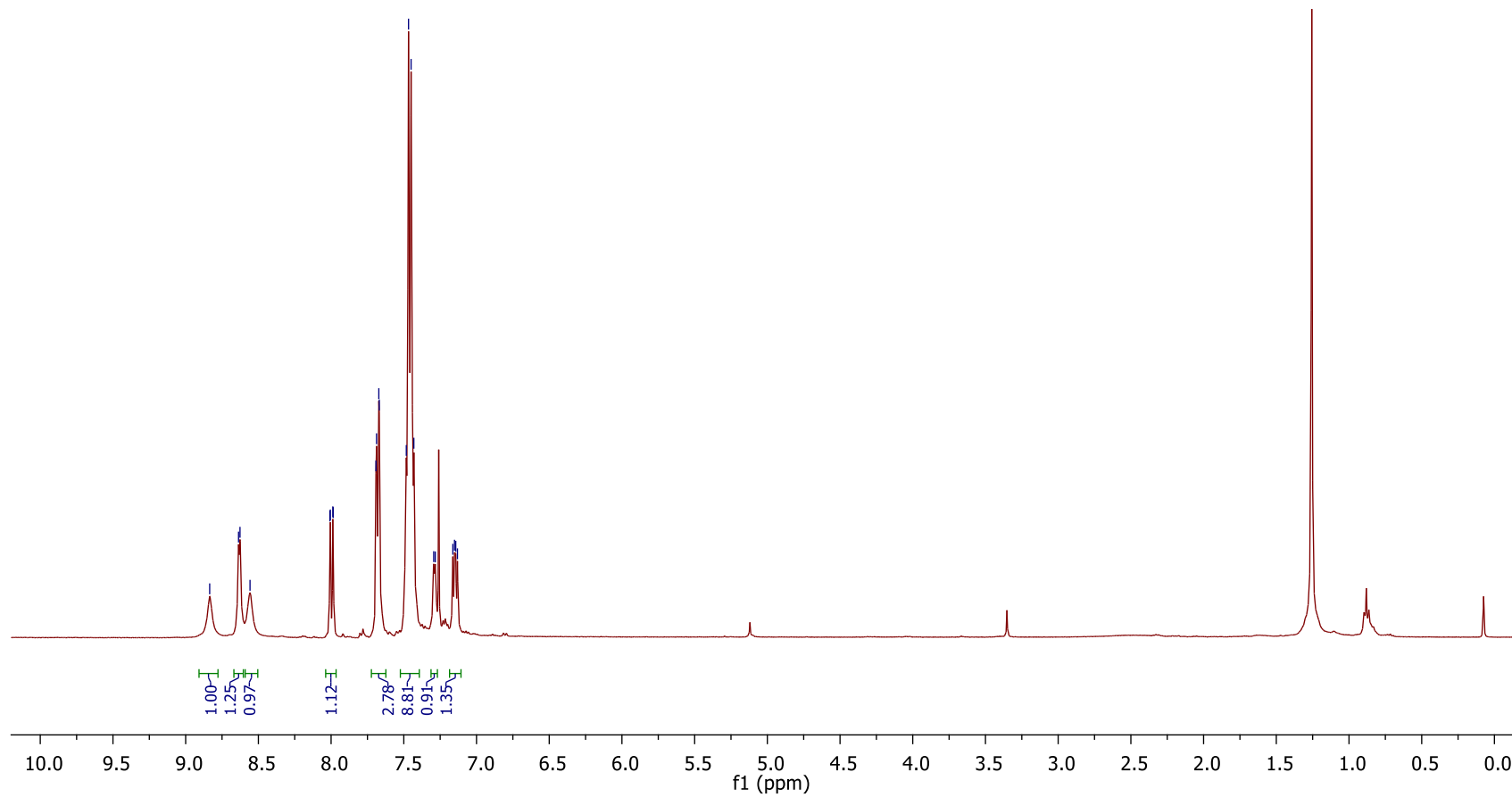
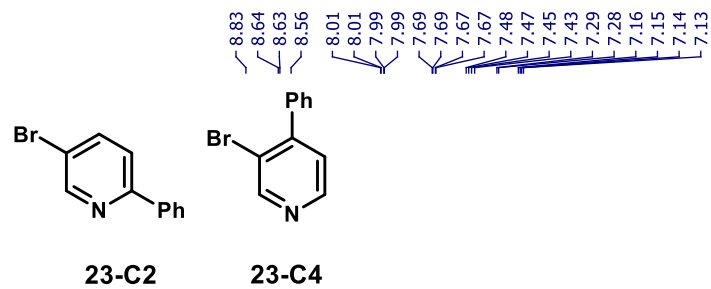
22

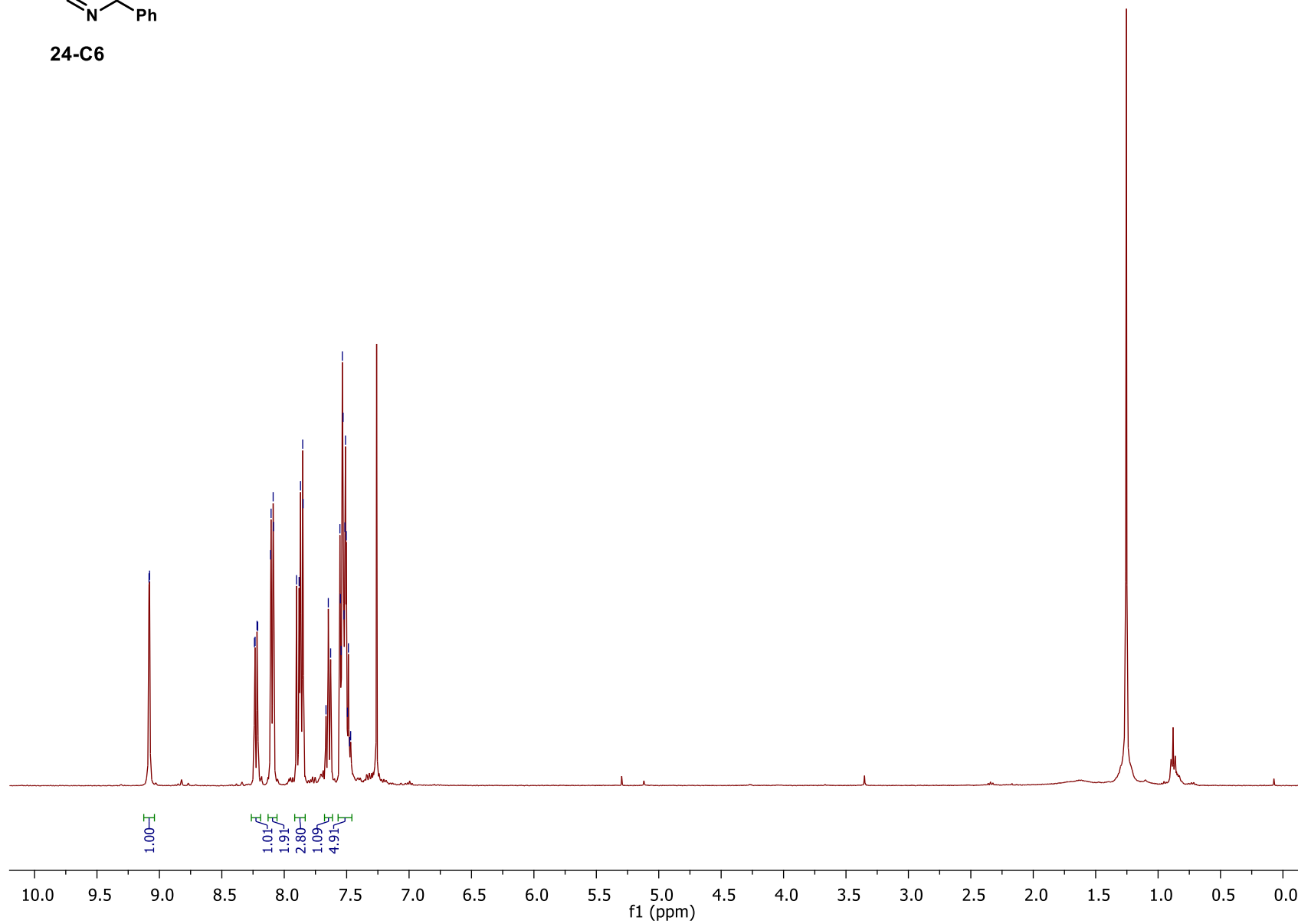
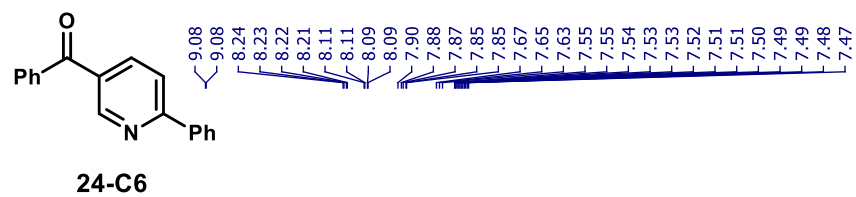


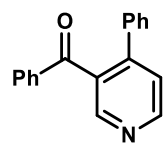


23-C6

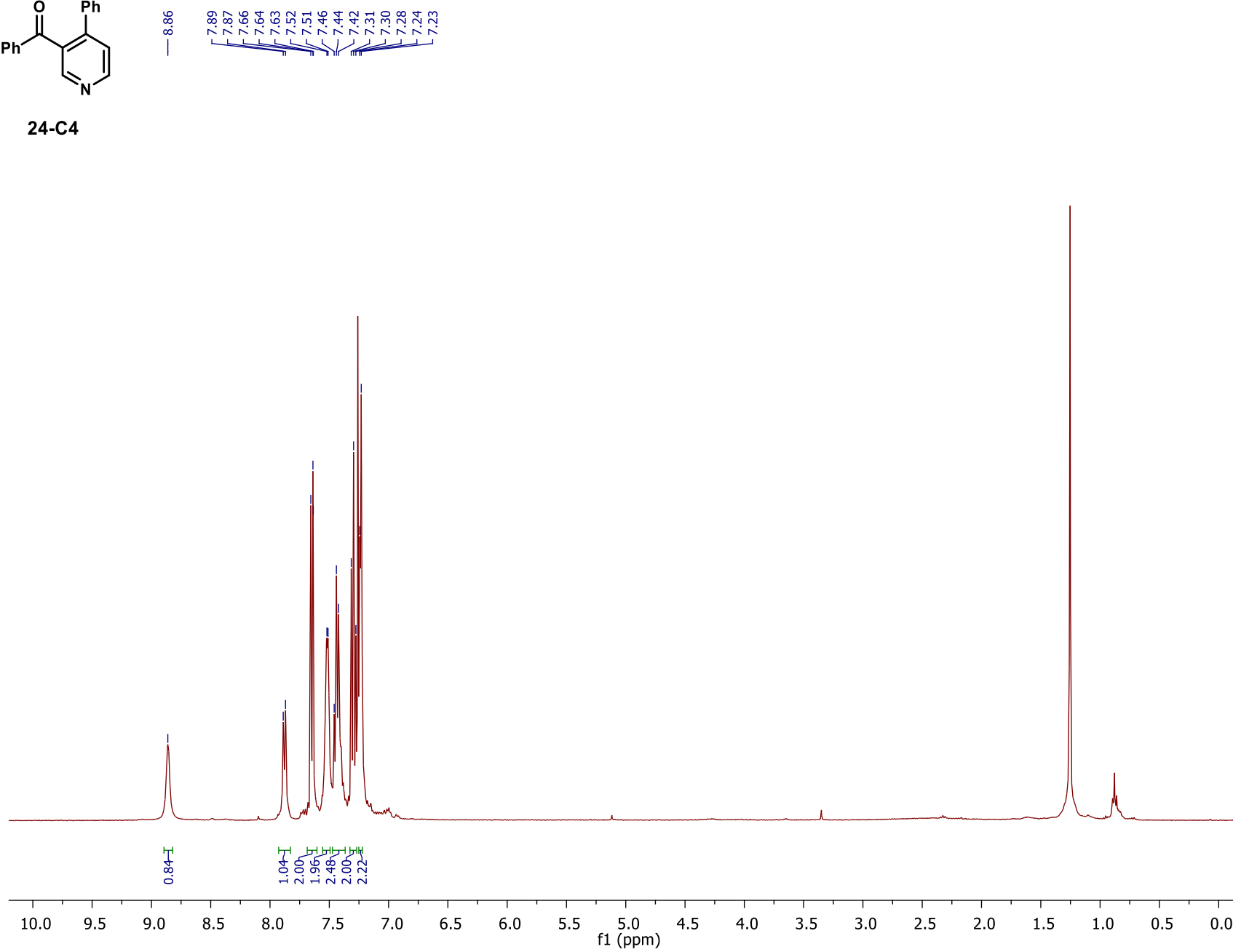


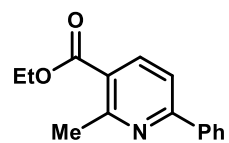




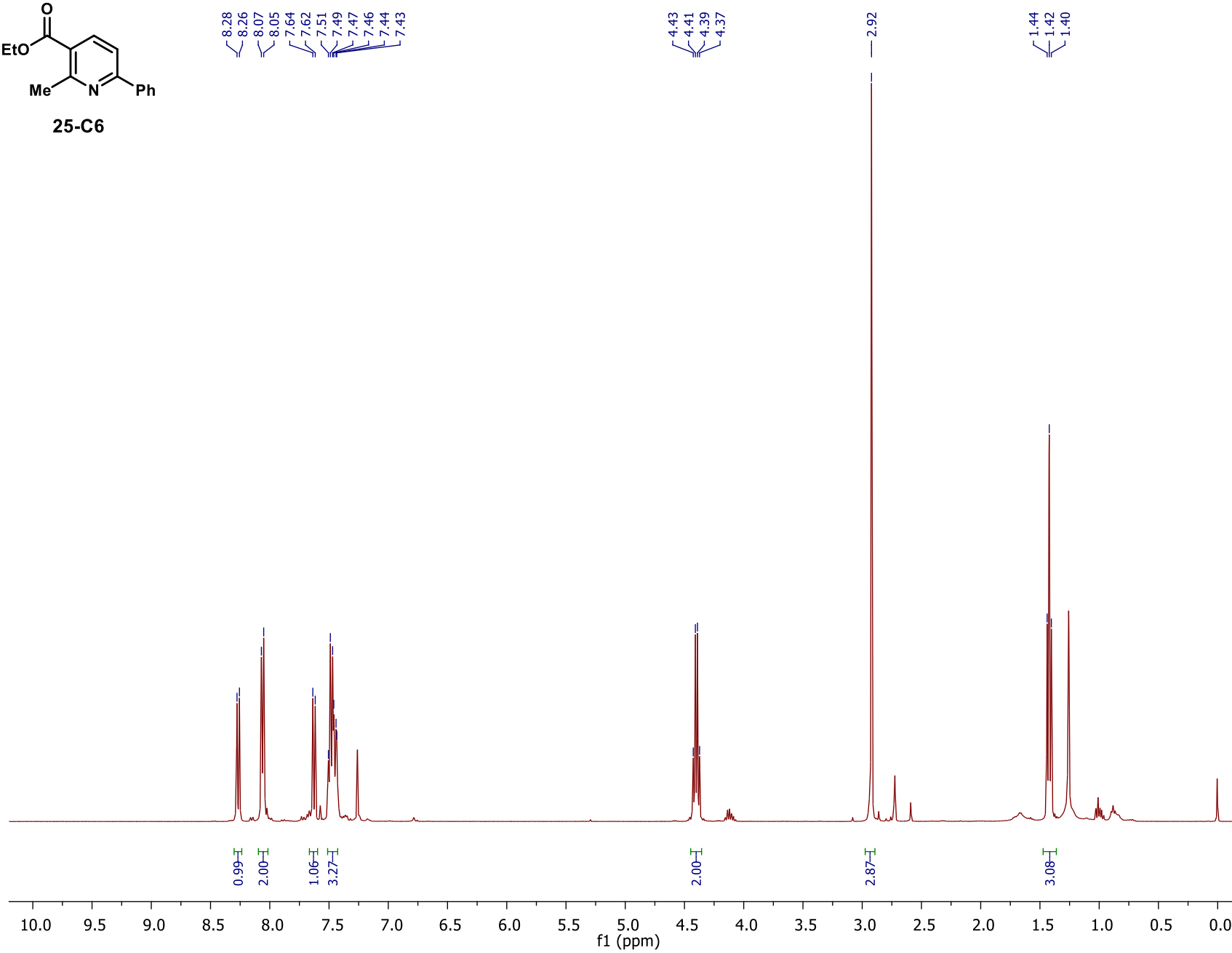


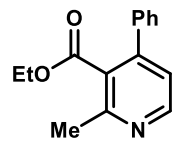
24-C4



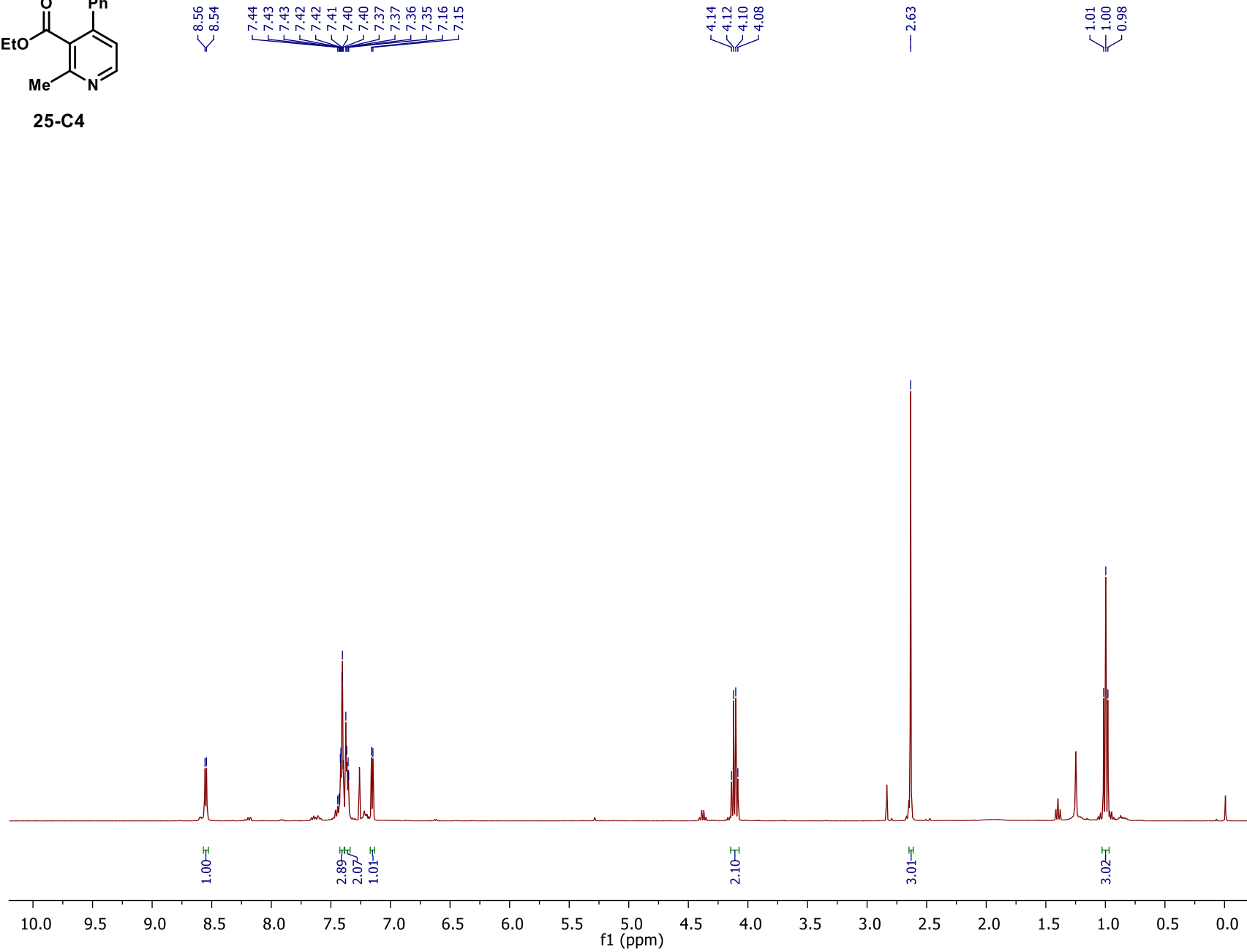


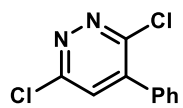
25-C6





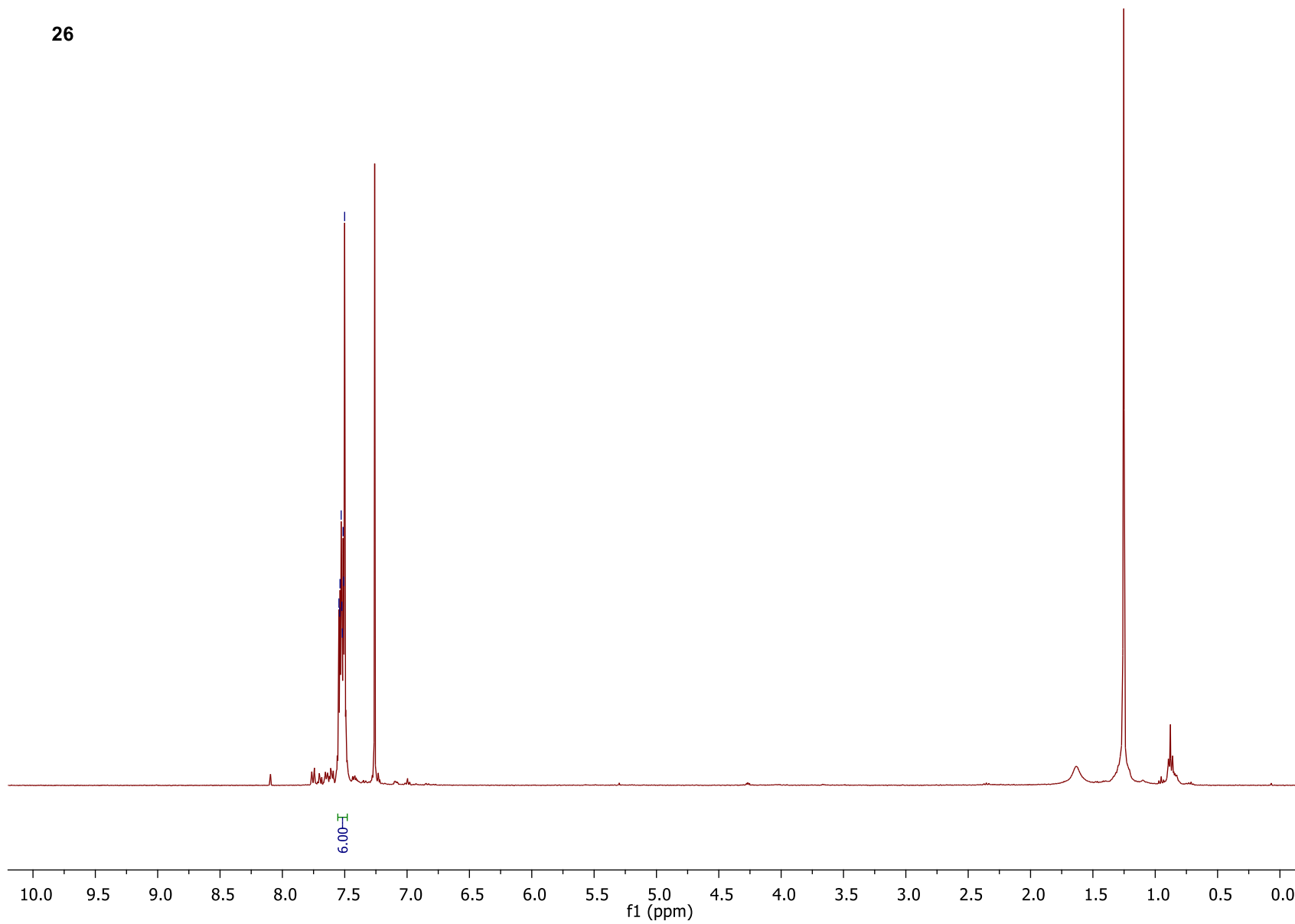
25-C4

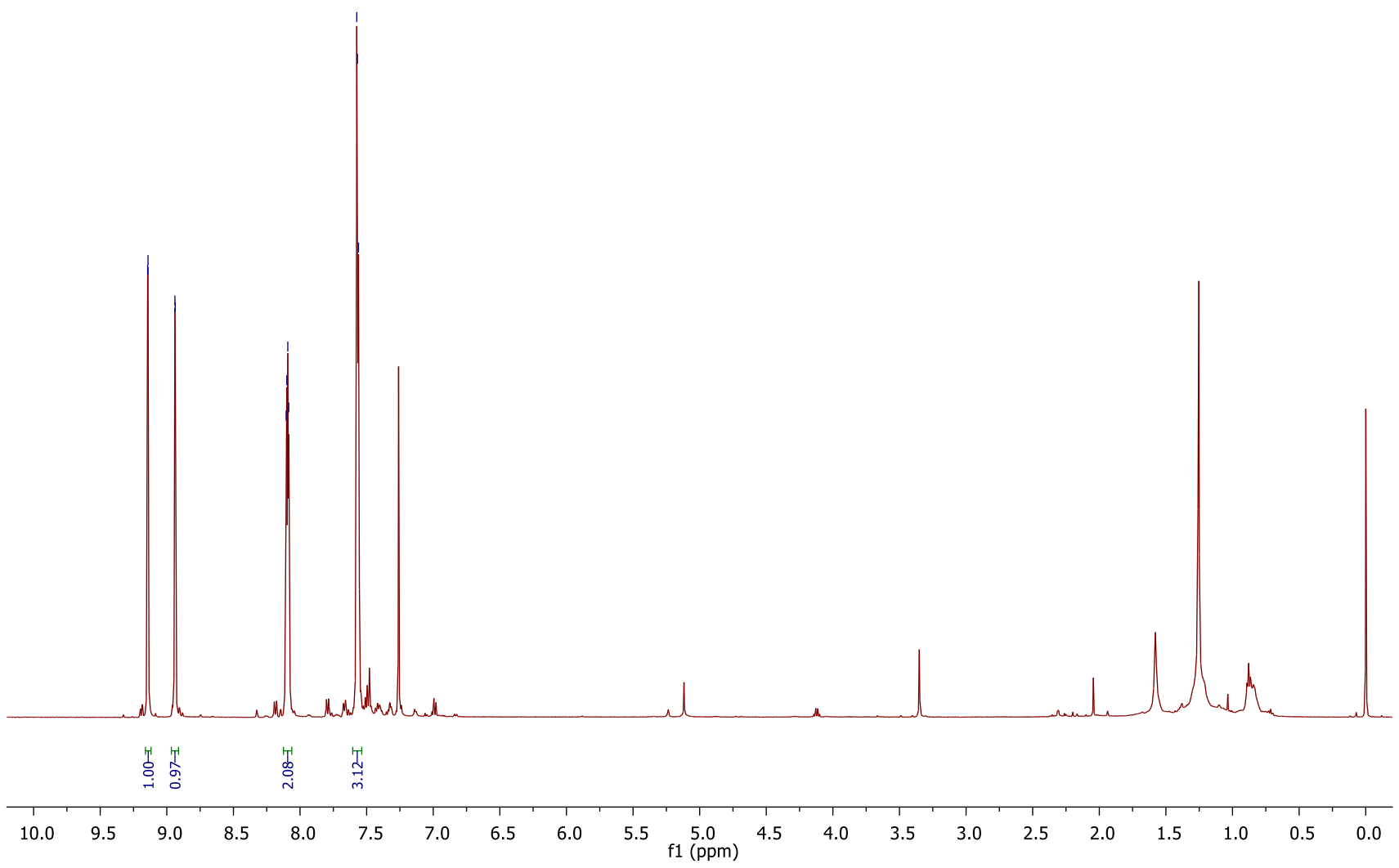
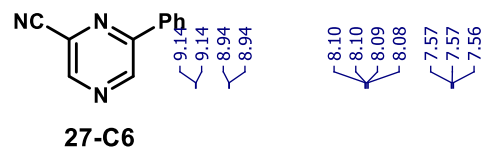


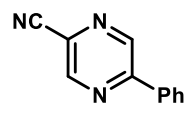


26

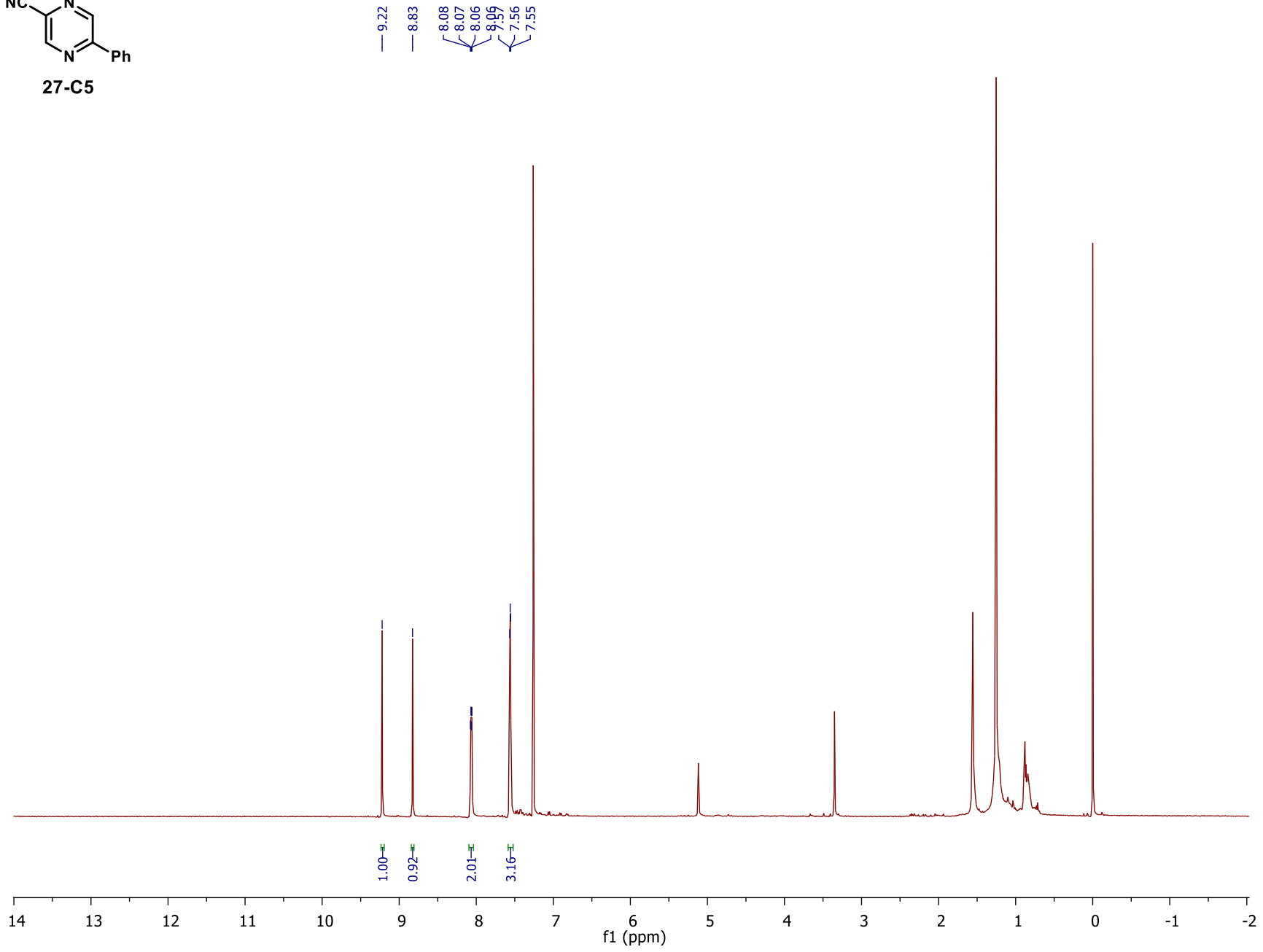
7.55
7.54
7.54
7.53
7.52
7.52
7.51
7.51
7.50

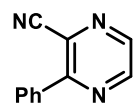




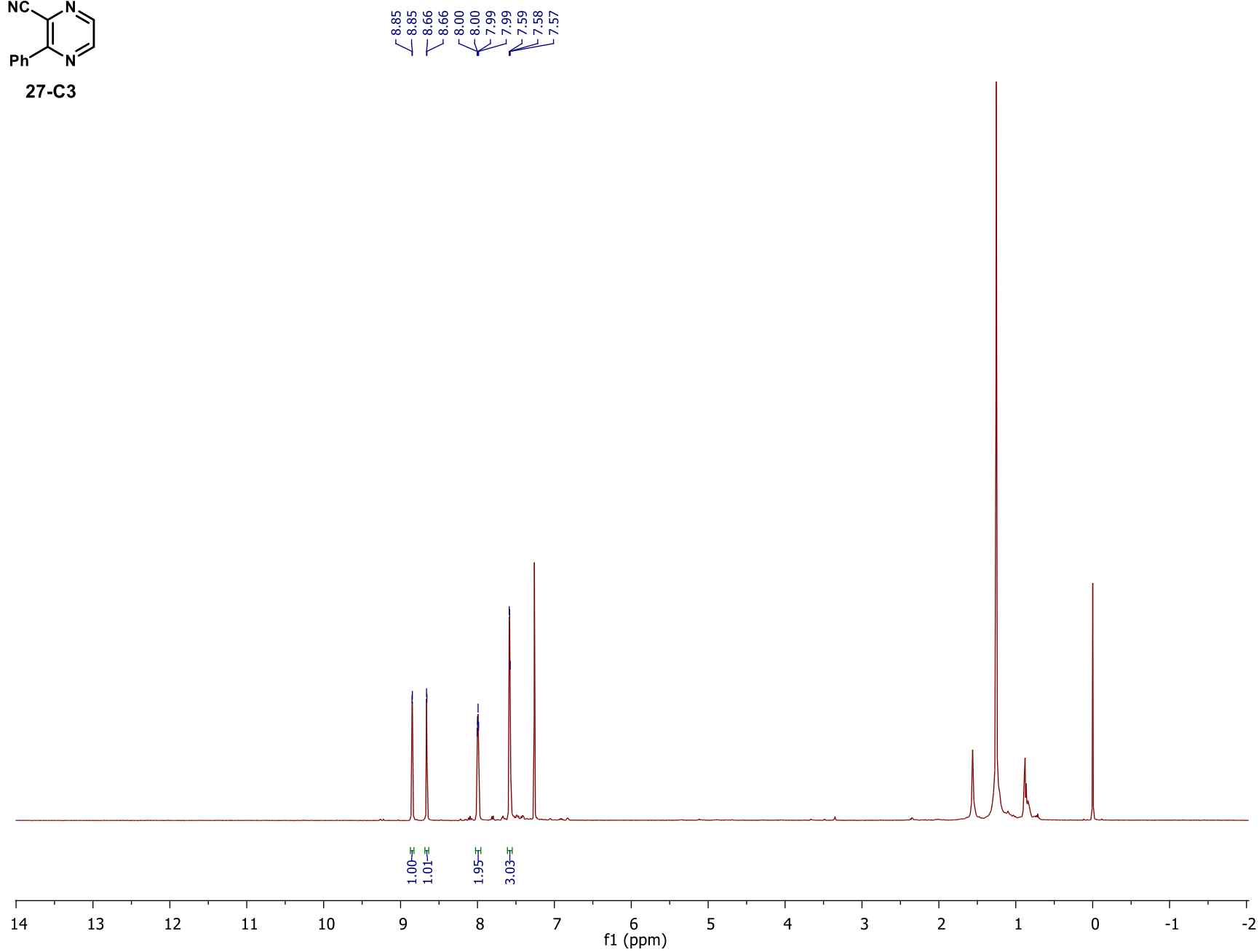


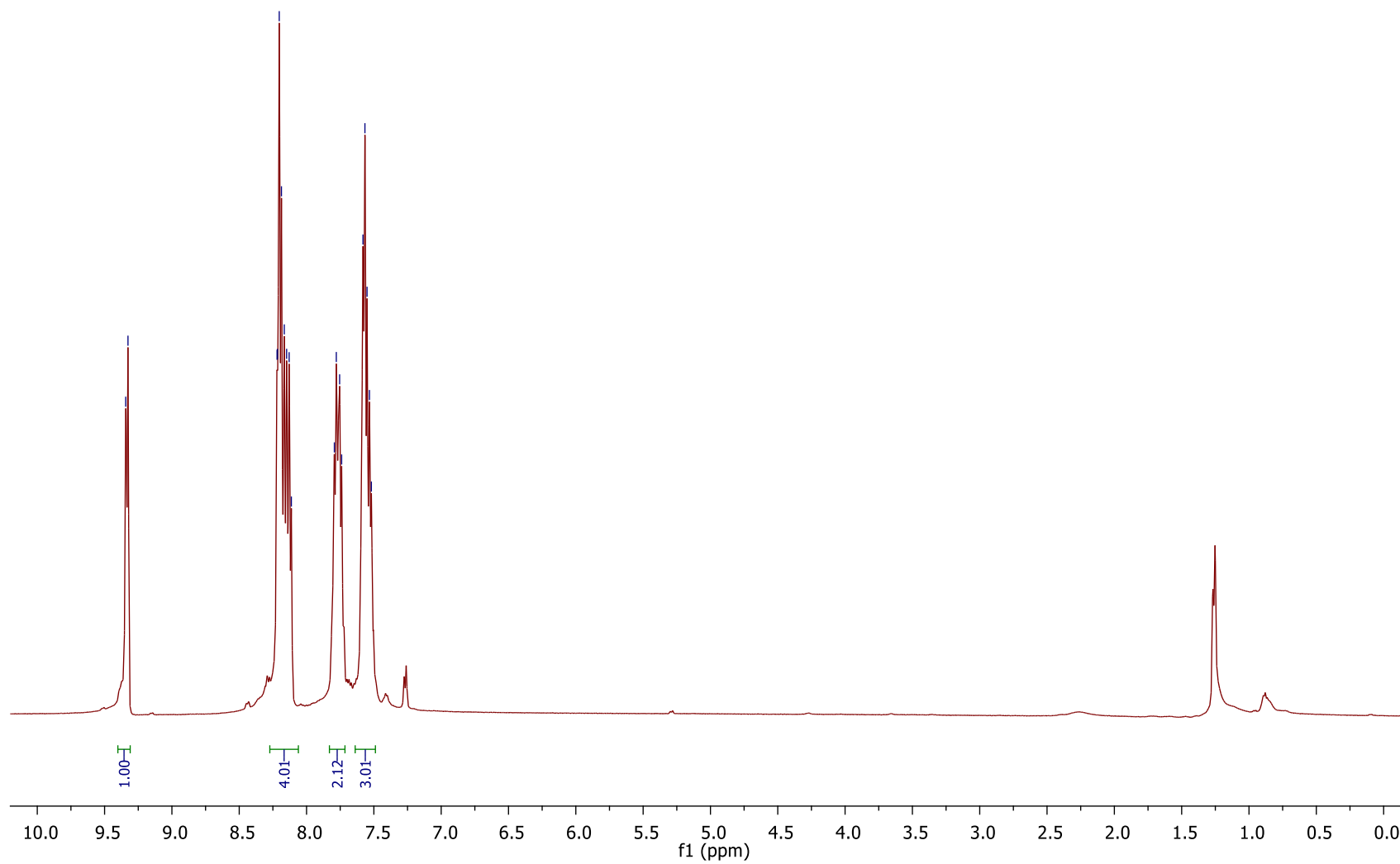
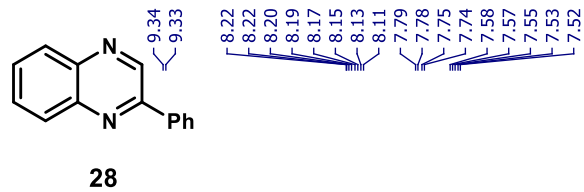
27-C5

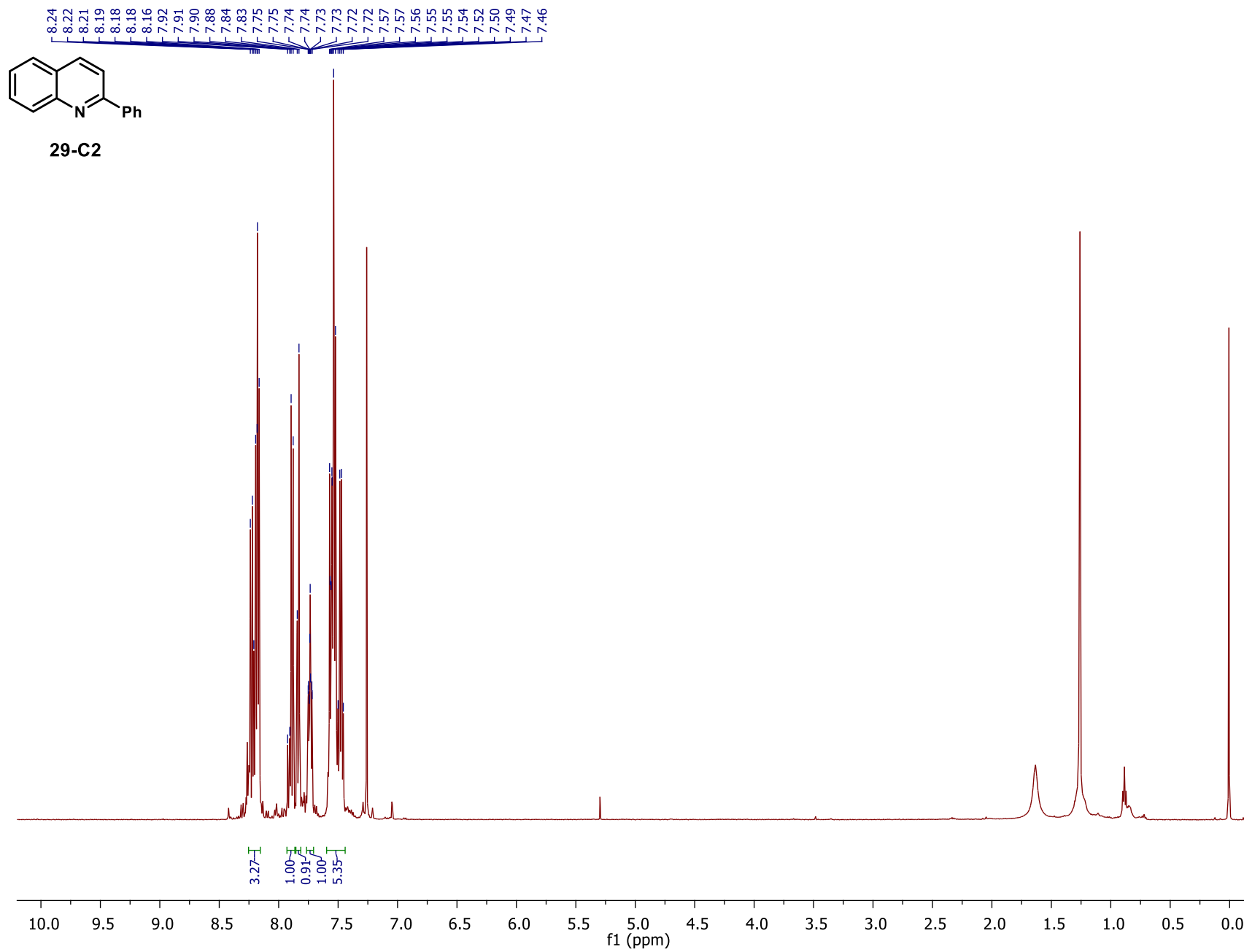


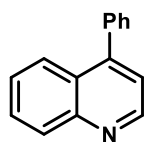


27-C3

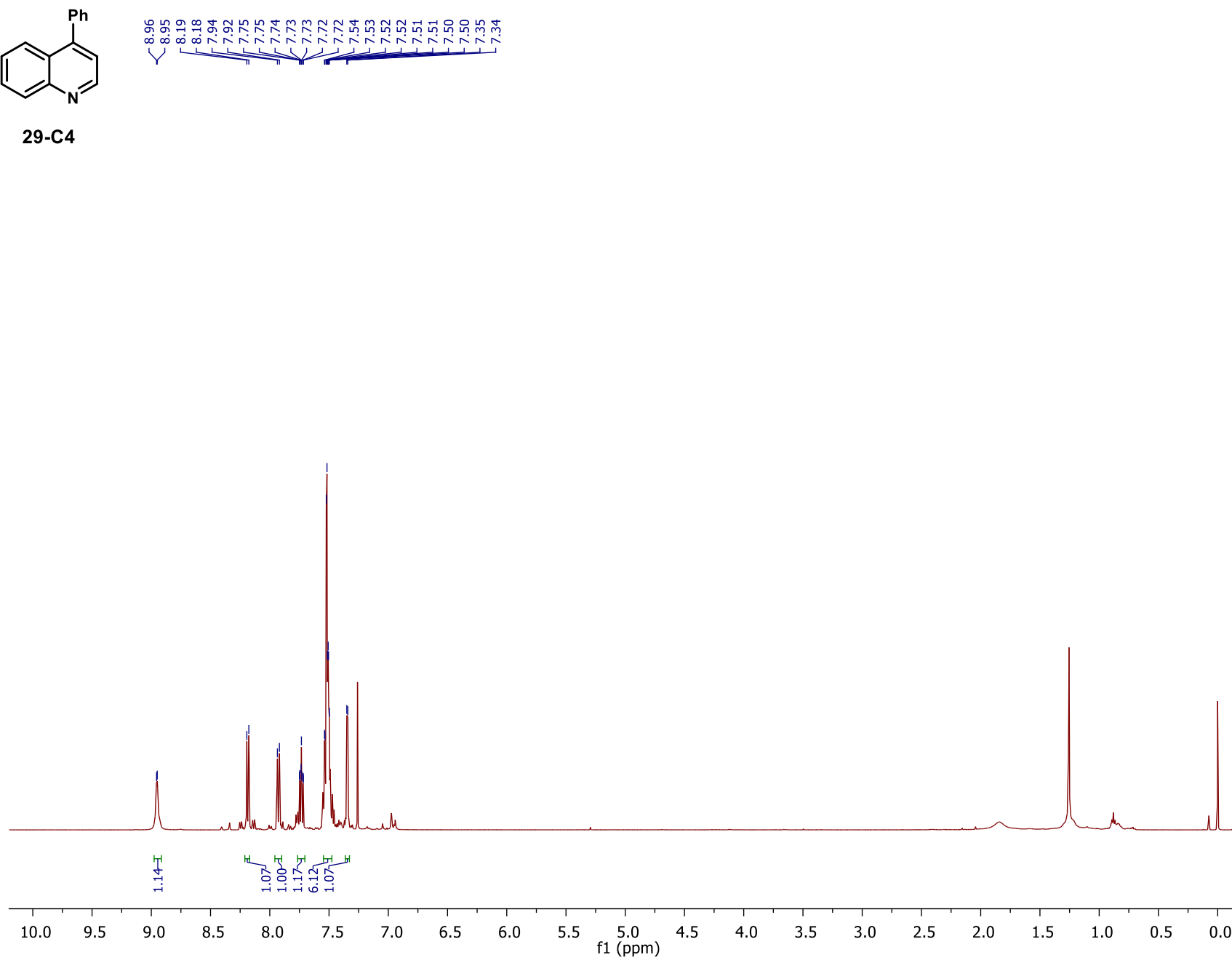


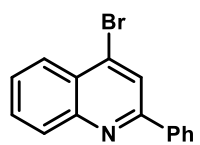






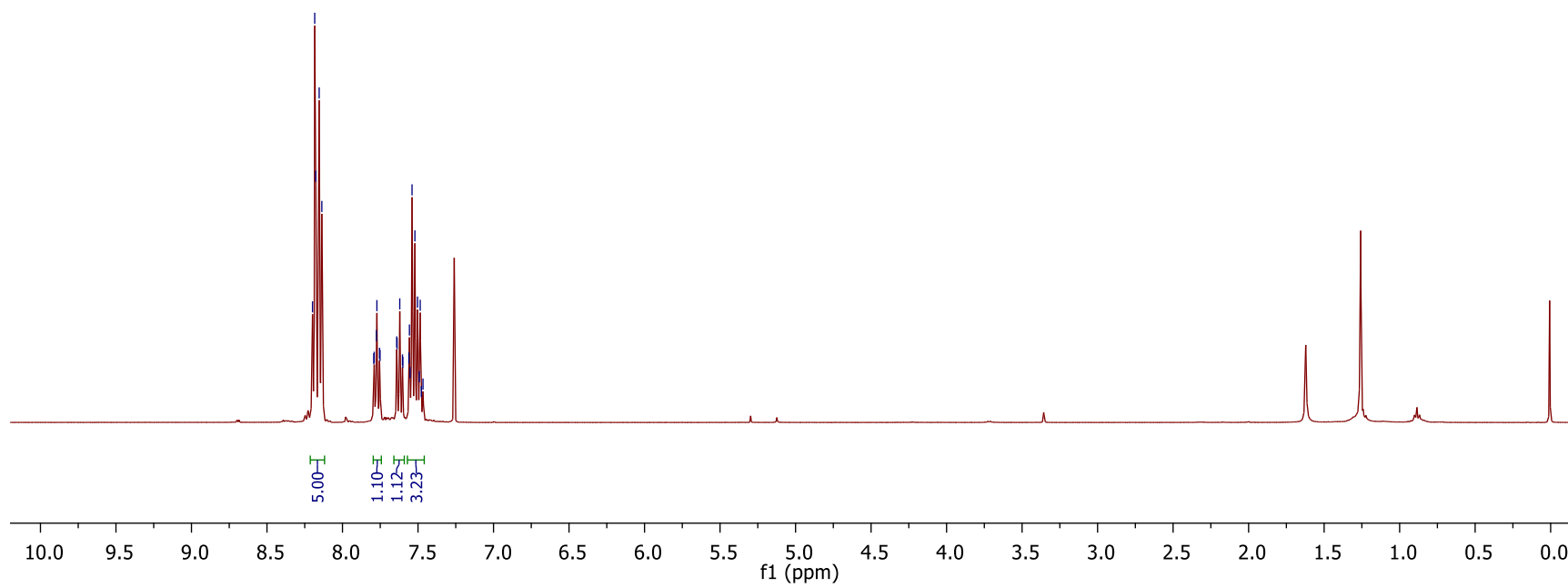
29-C4

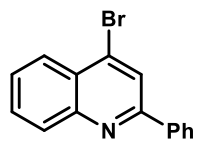




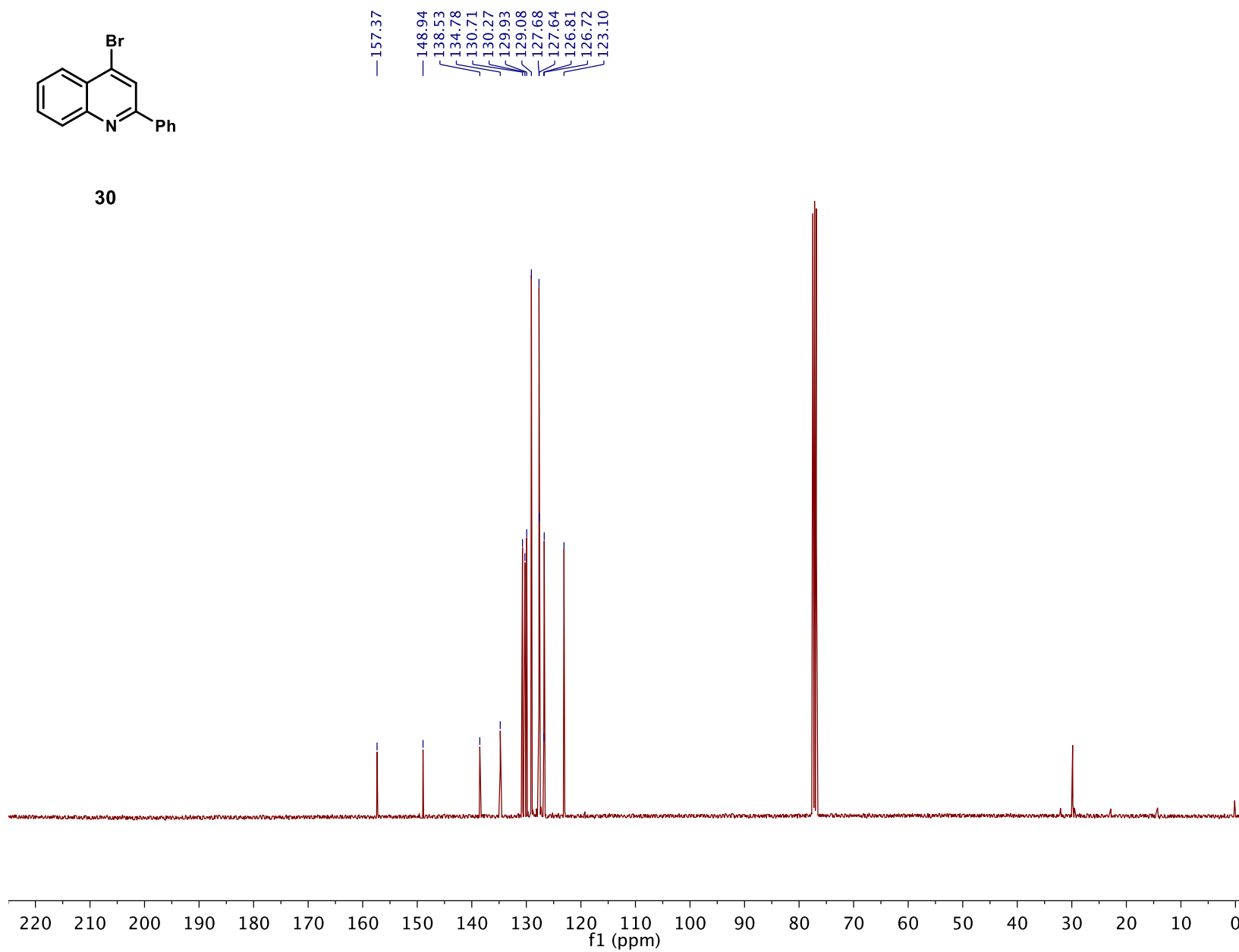
30

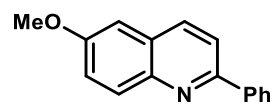
8.20
8.18
8.18
8.15
8.14
7.79
7.79
7.78
7.77
7.75
7.75
7.64
7.64
7.62
7.60
7.60
7.56
7.56
7.55
7.54
7.52
7.50
7.49
7.49
7.48
7.47





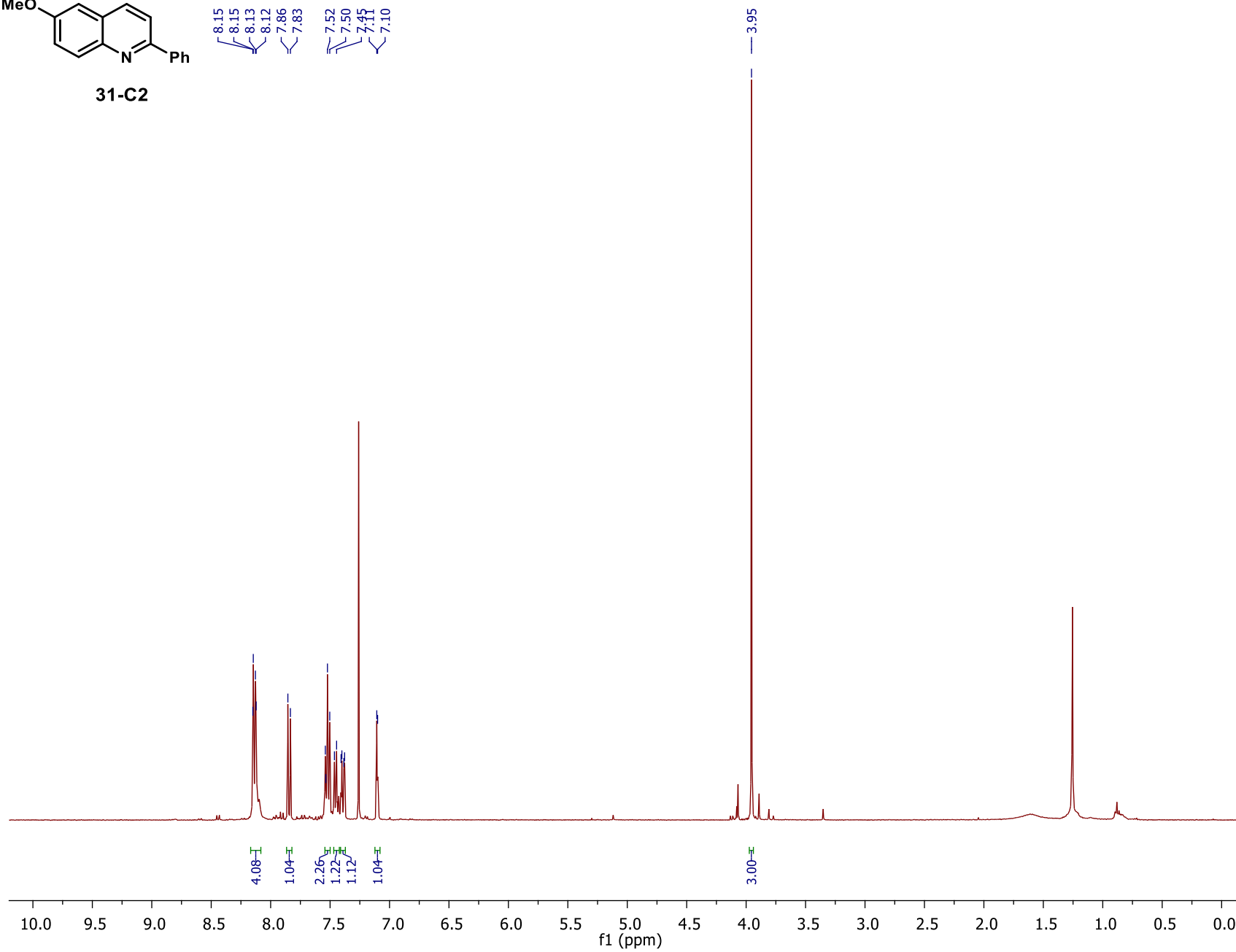
30

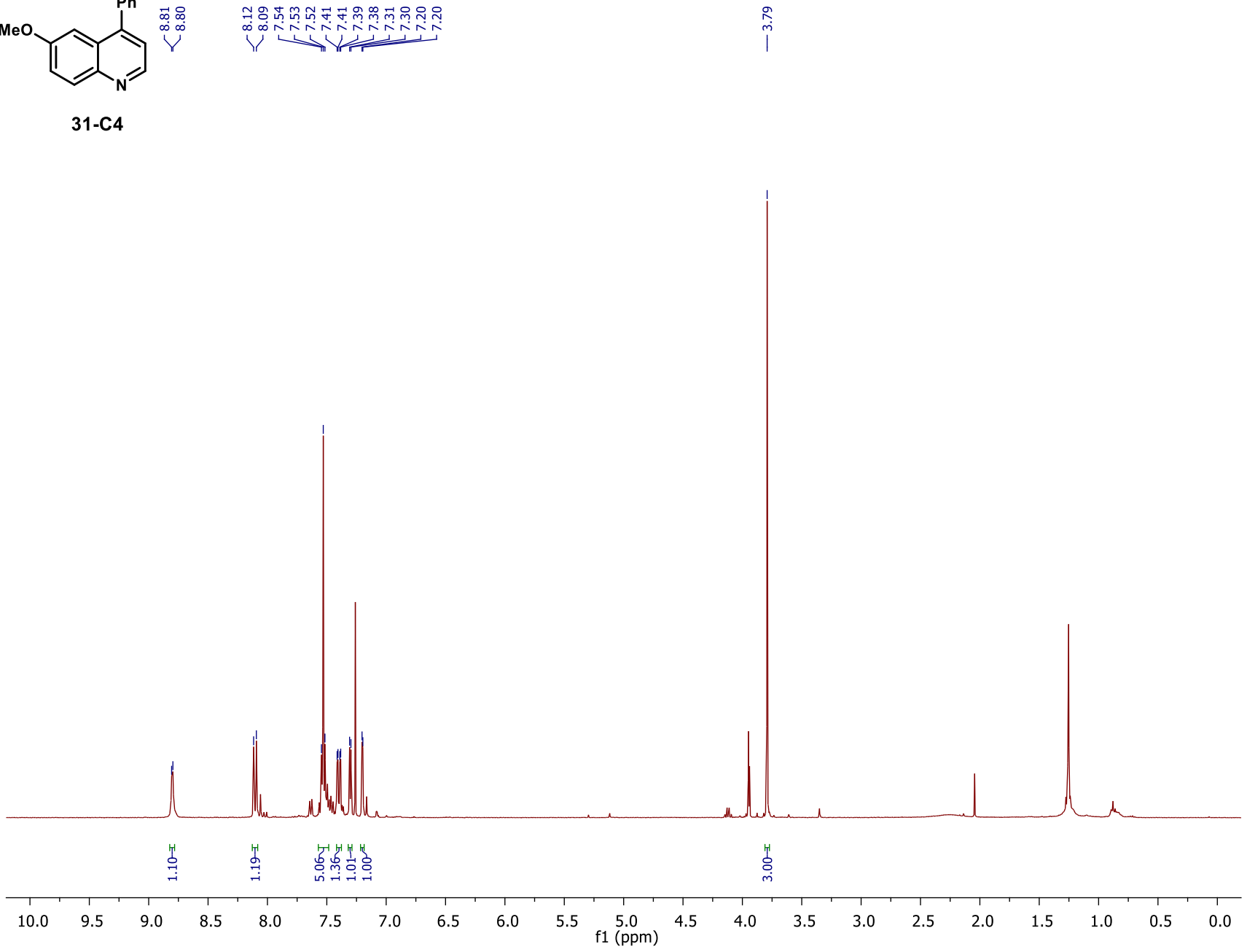
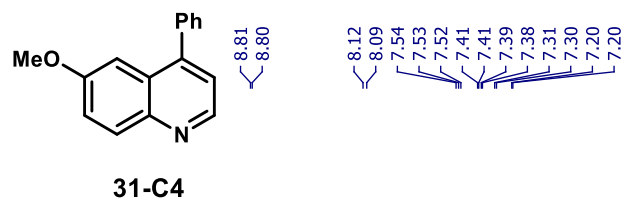


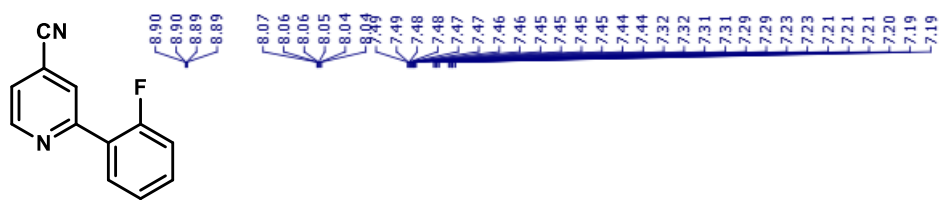


31-C2

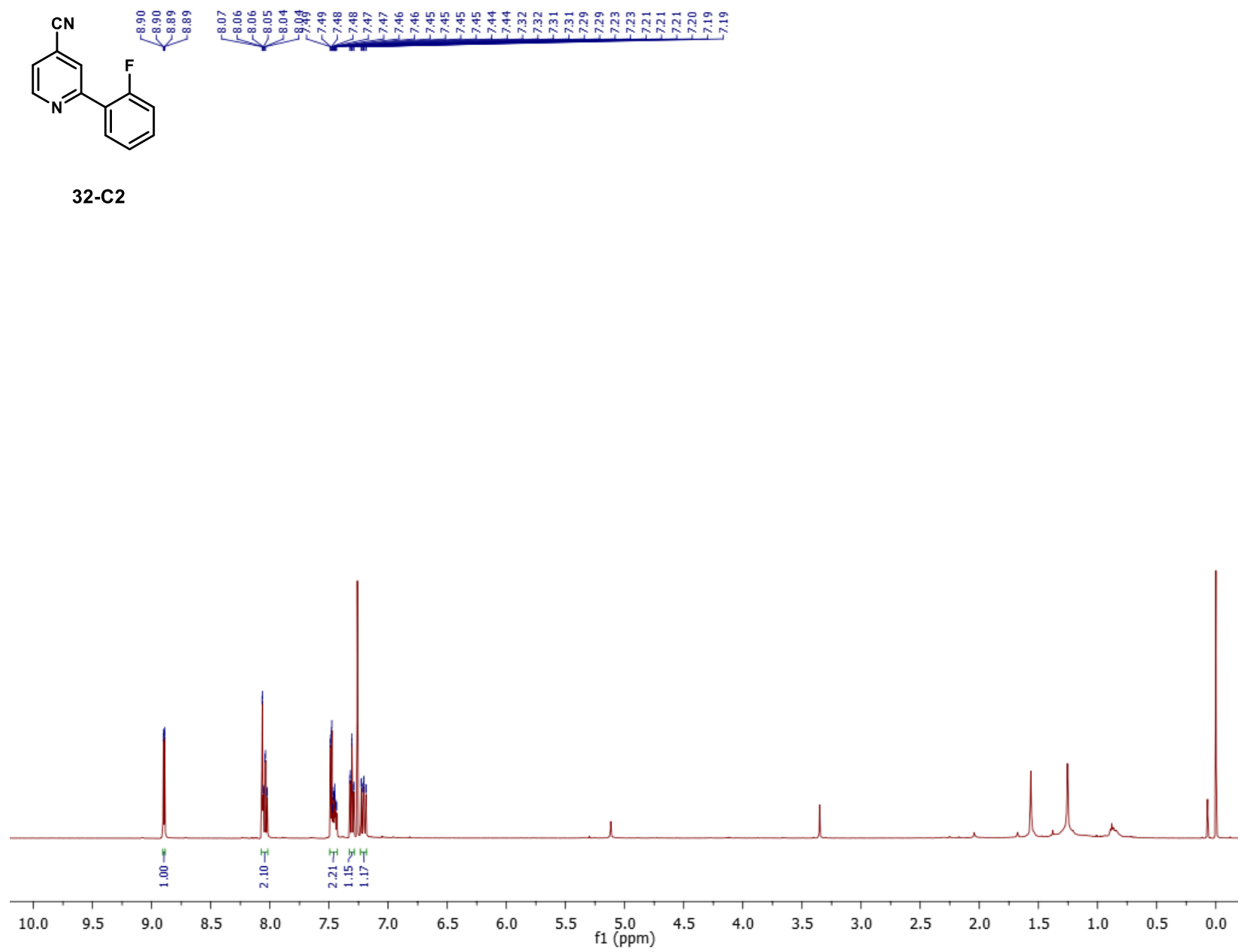
8.15
8.15
8.13
8.12
7.86
7.83
7.52
7.50
7.45
7.41
7.10

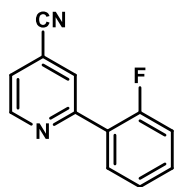




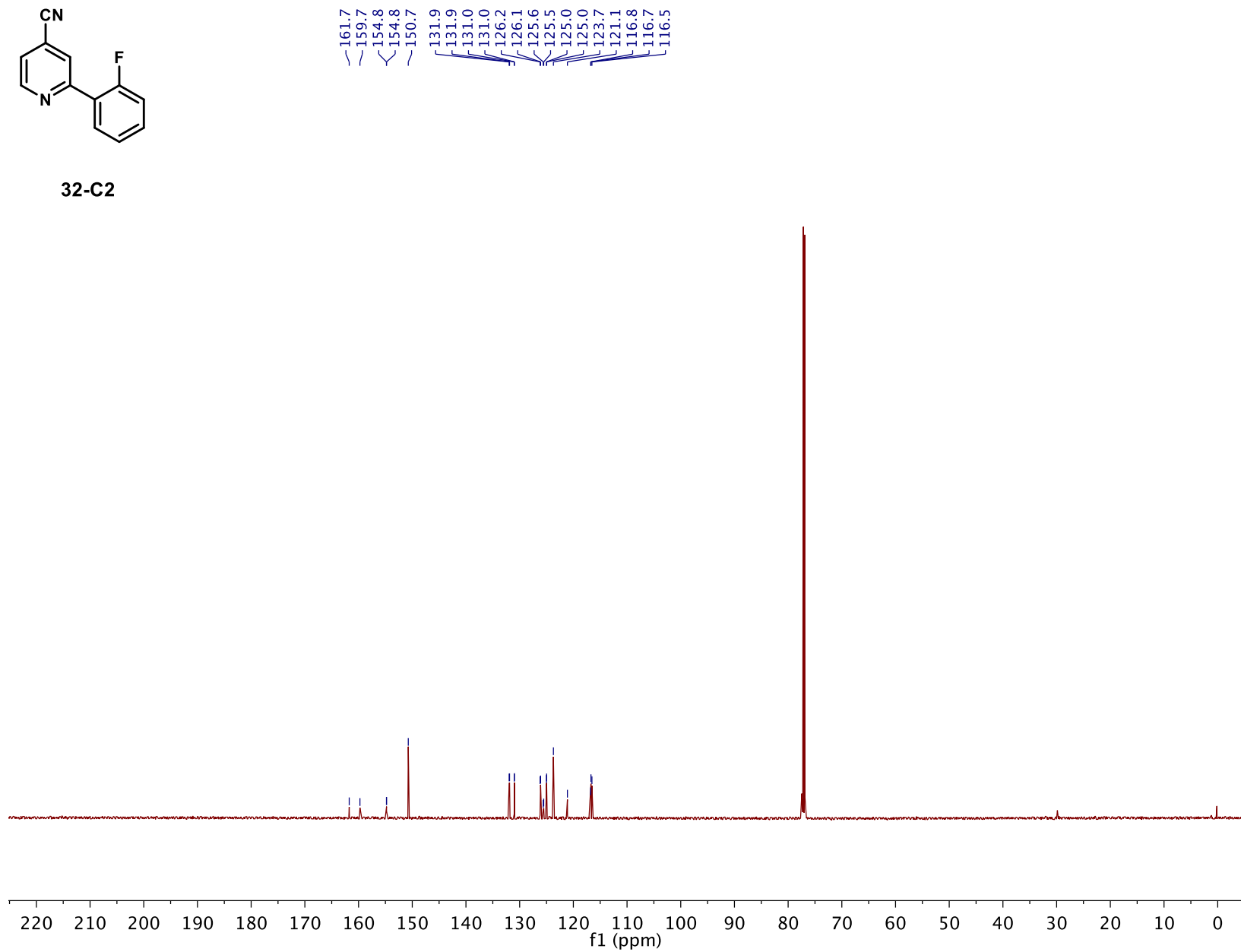


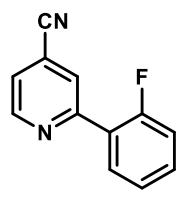
32-C2



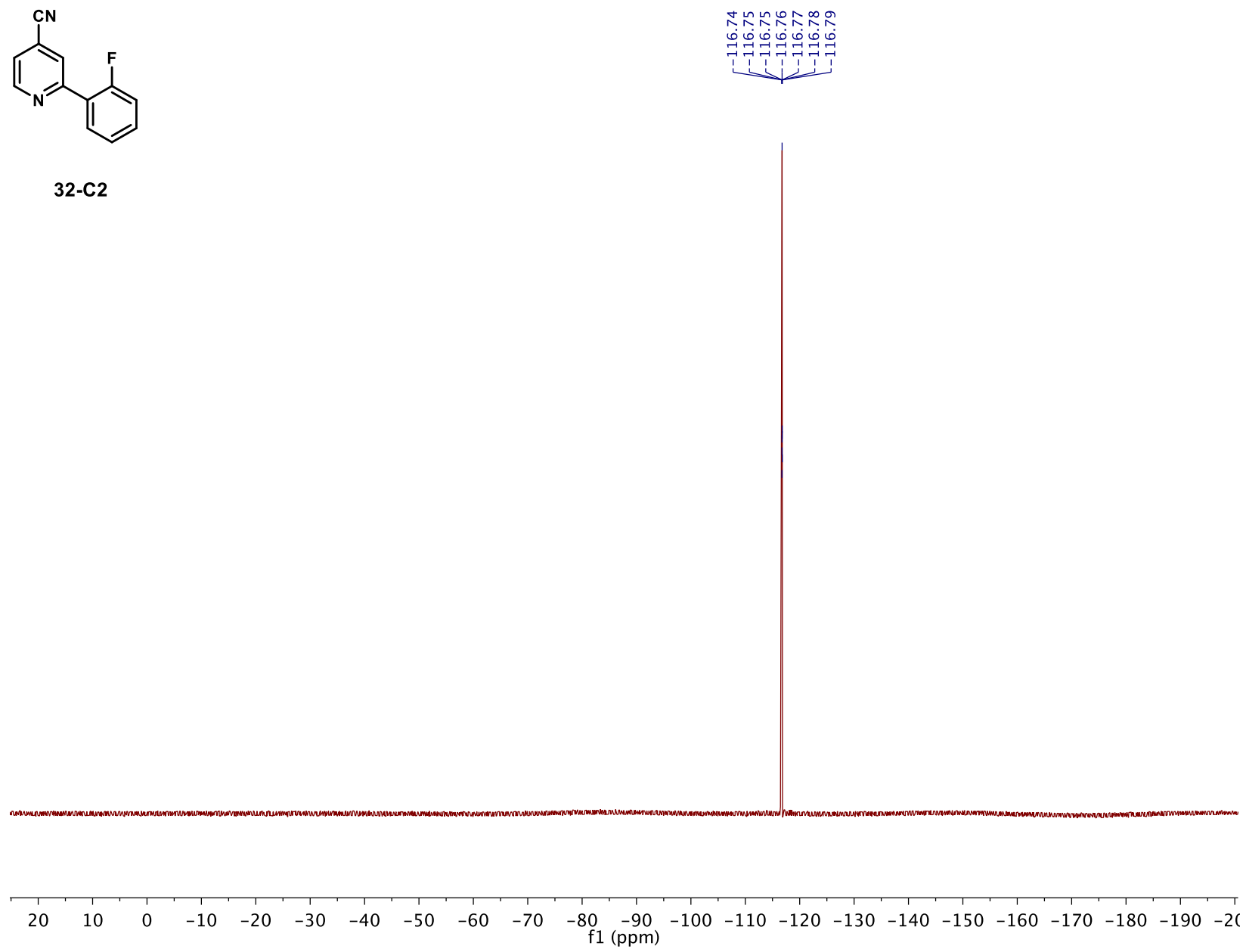


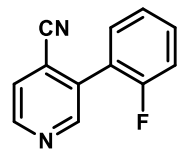
32-C2



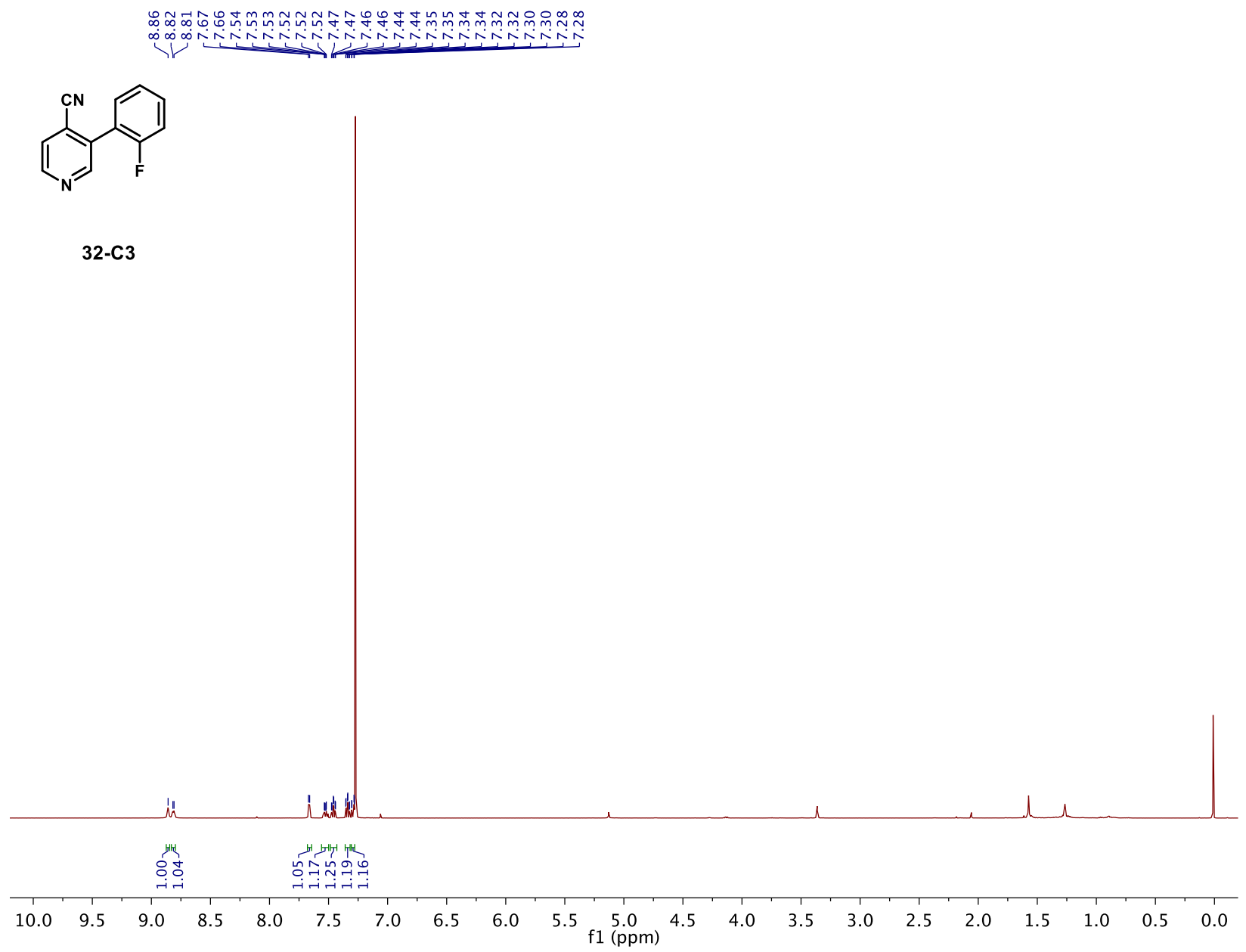


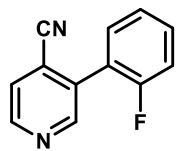
32-C2



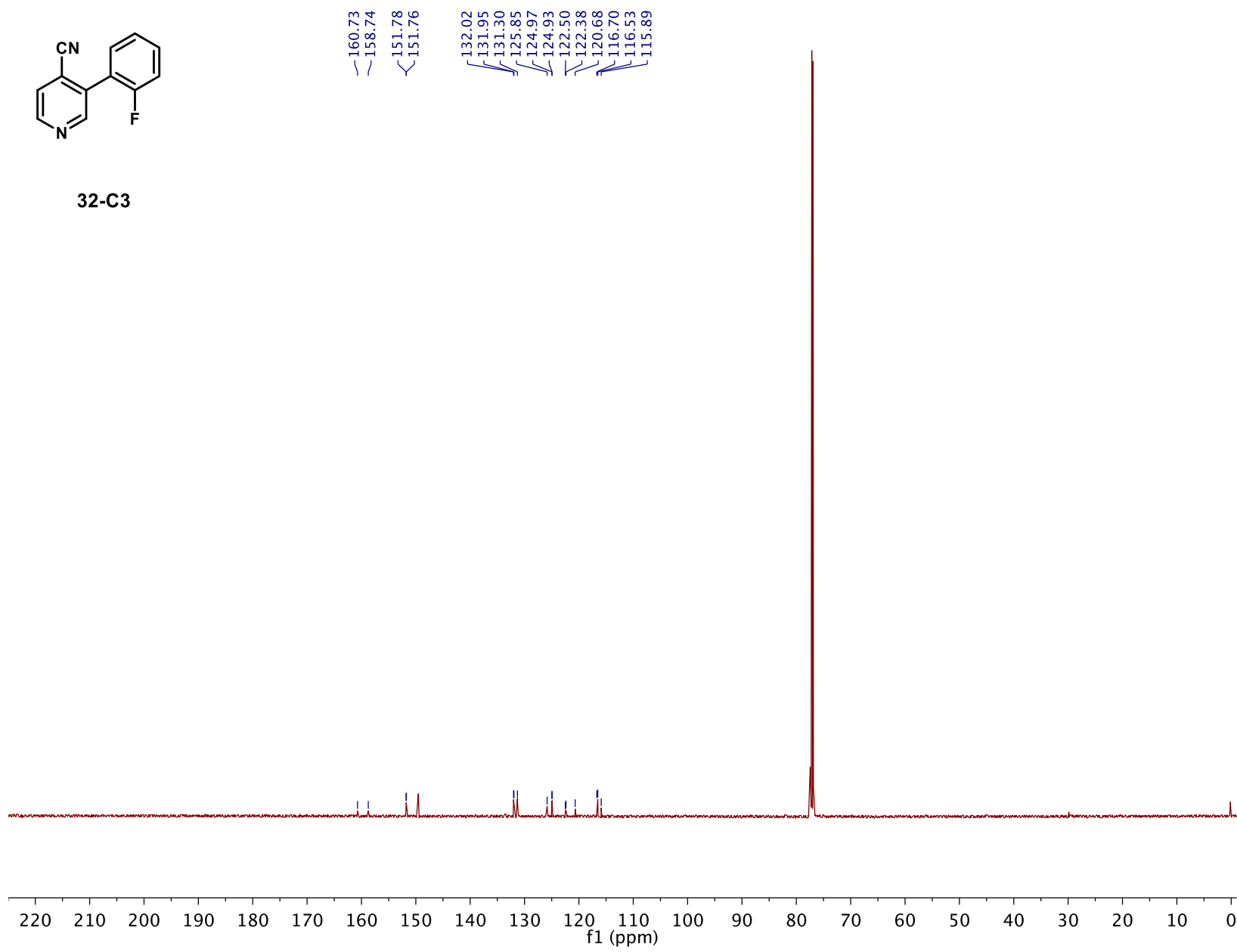


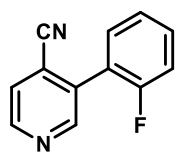
32-C3



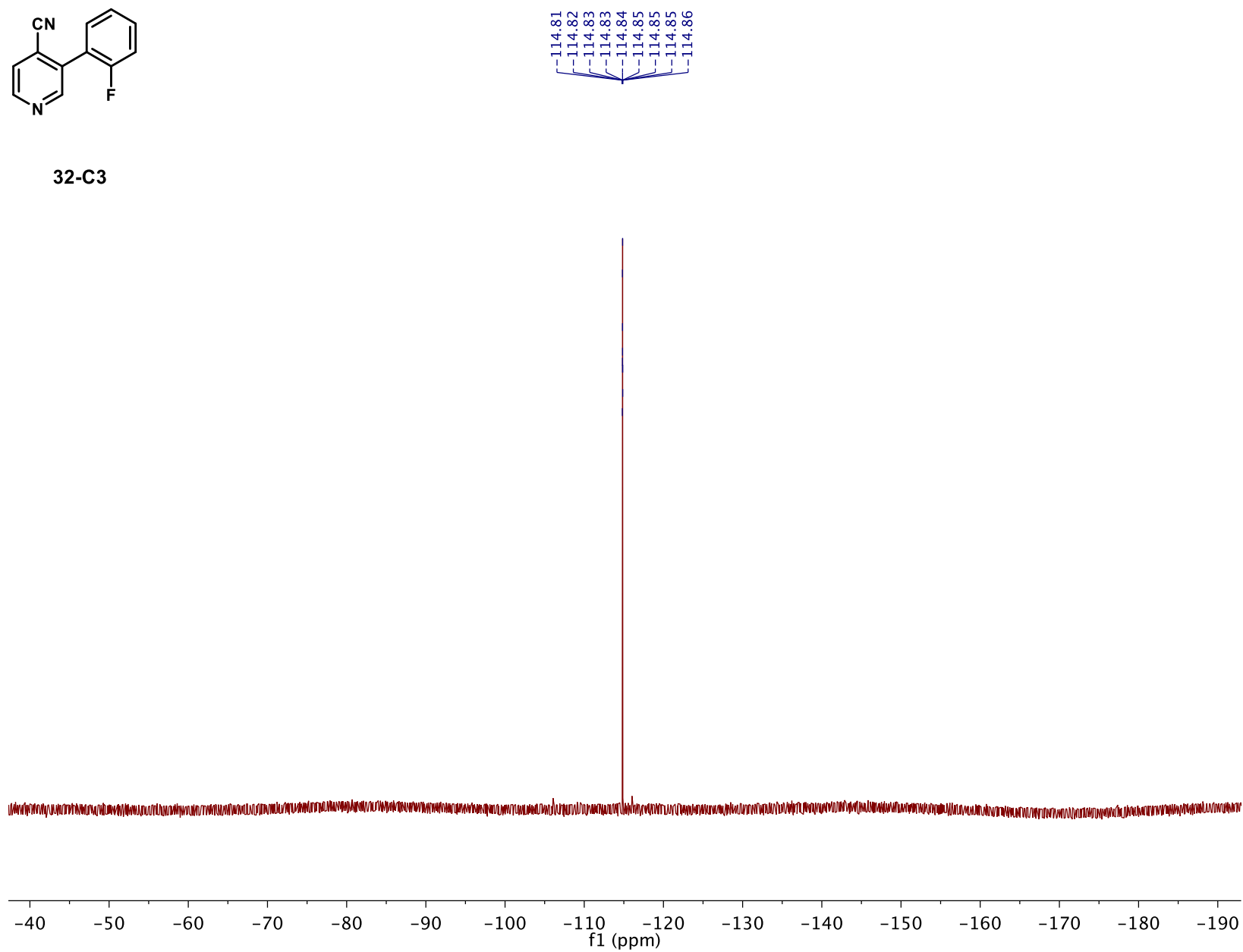


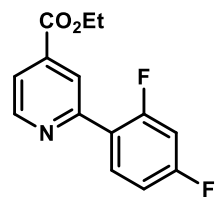
32-C3



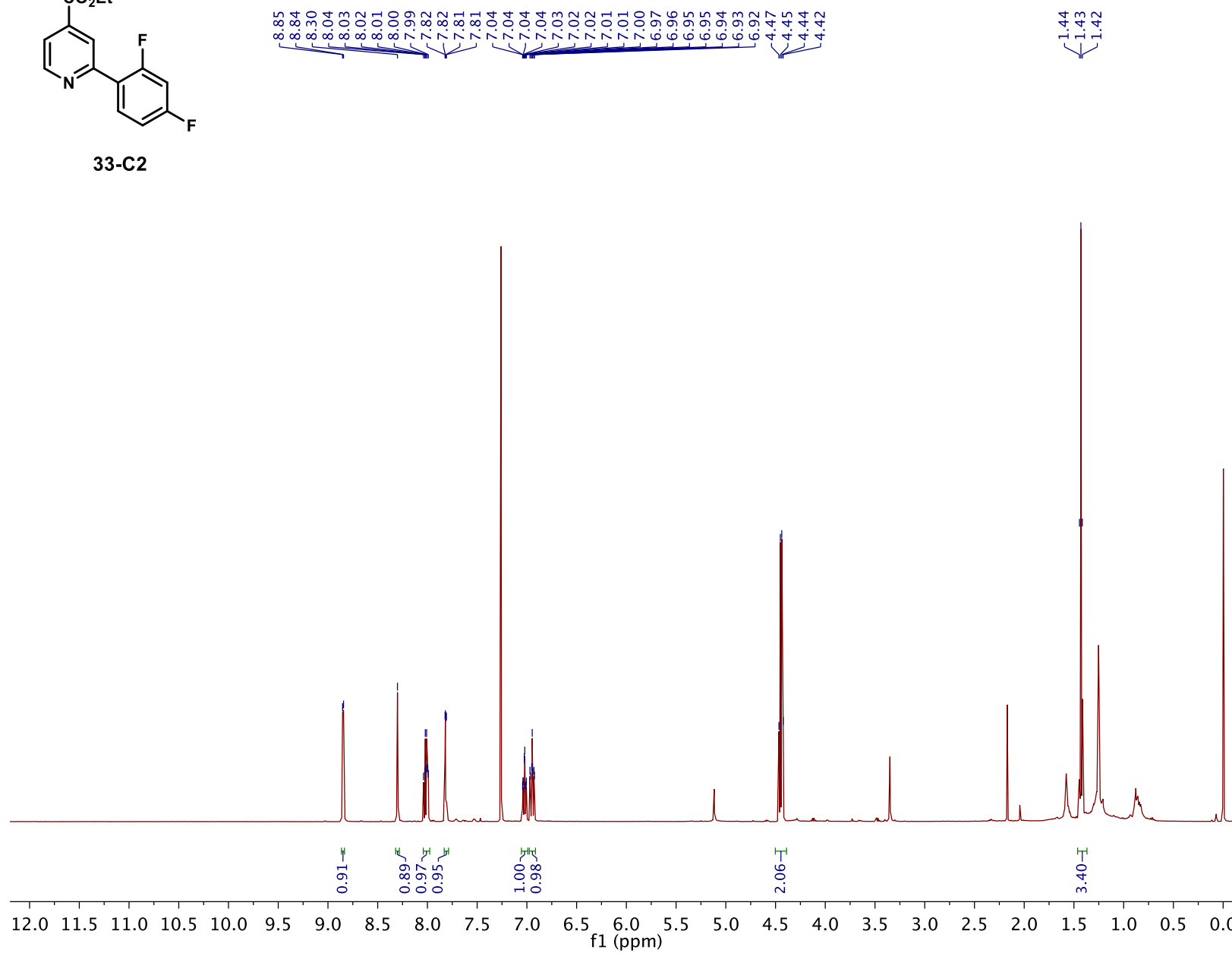


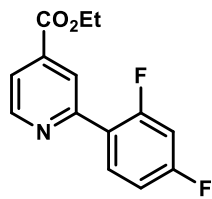
32-C3



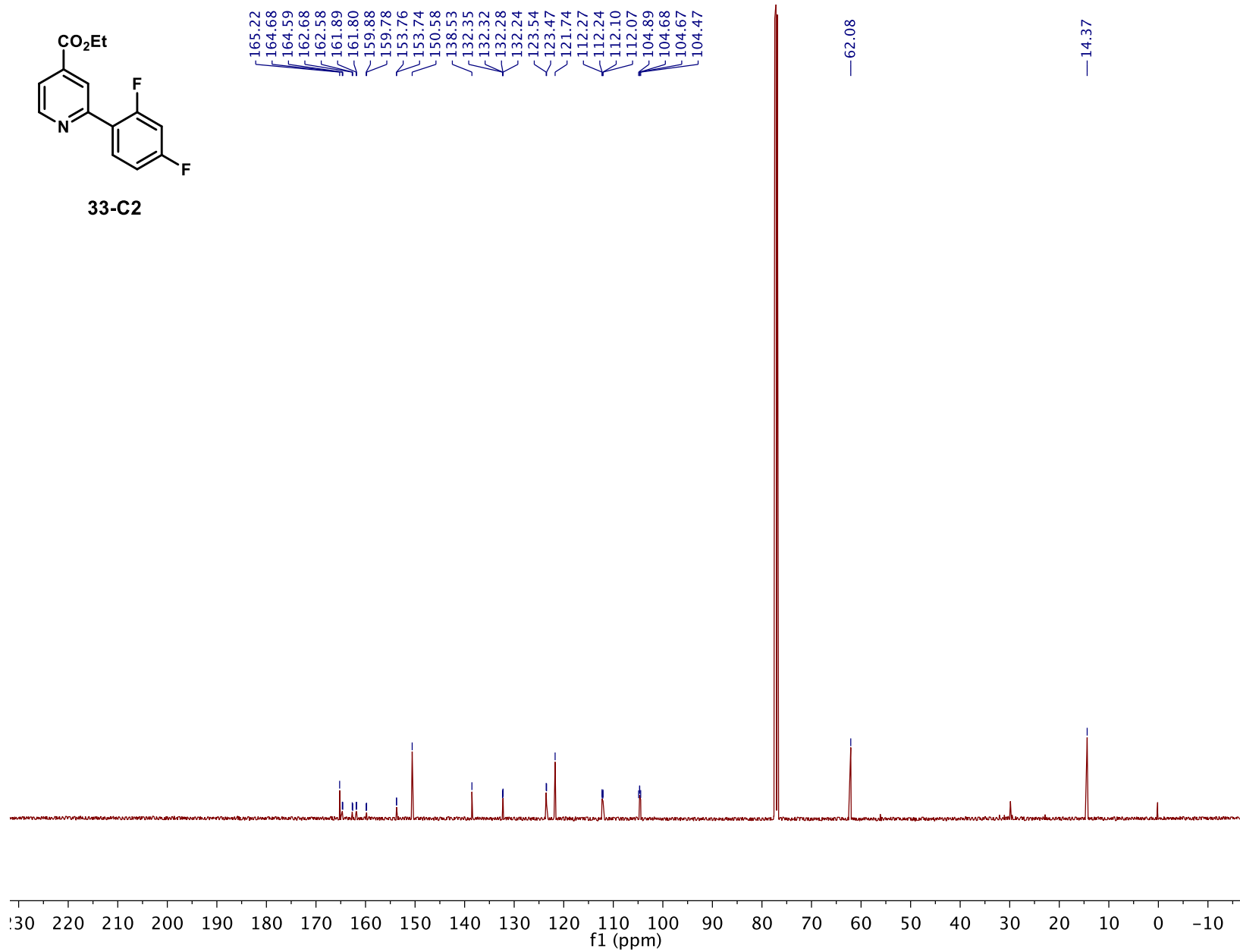


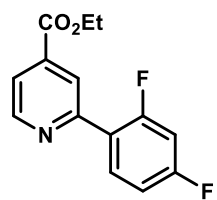
33-C2





33-C2

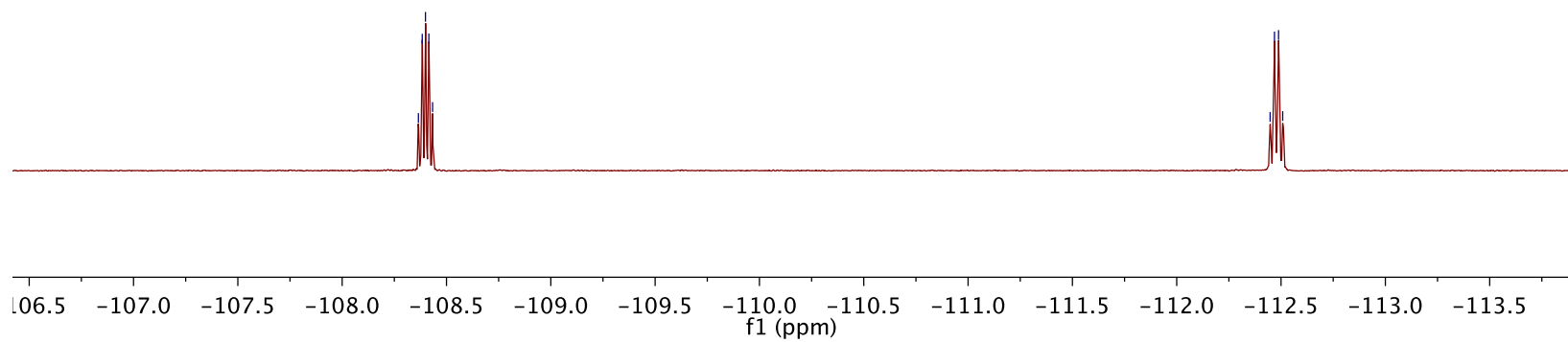


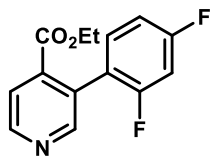


33-C2

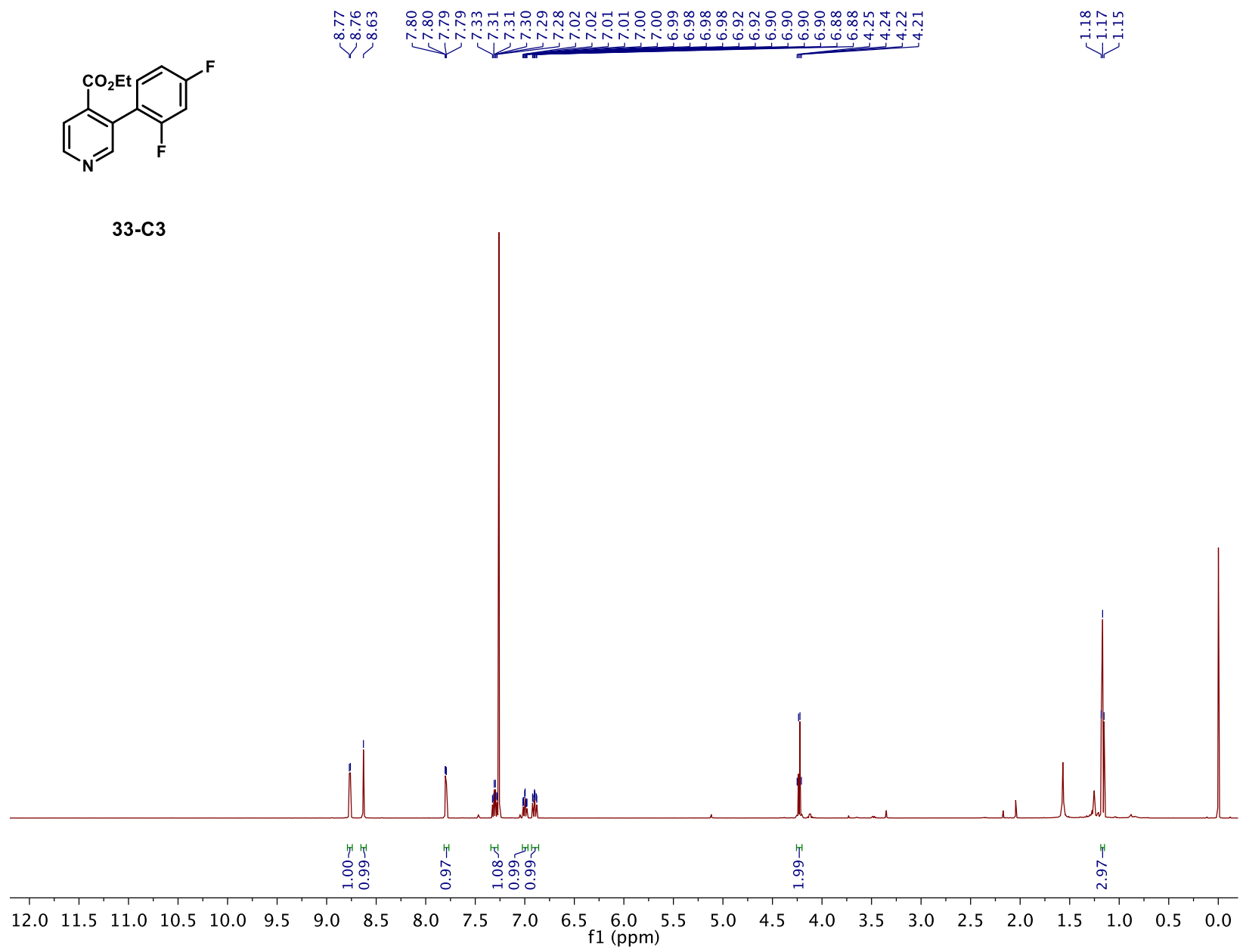
108.37
108.38
108.40
108.42
108.43

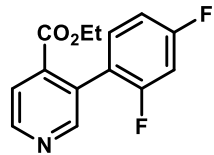
112.45
112.47
112.49
112.51



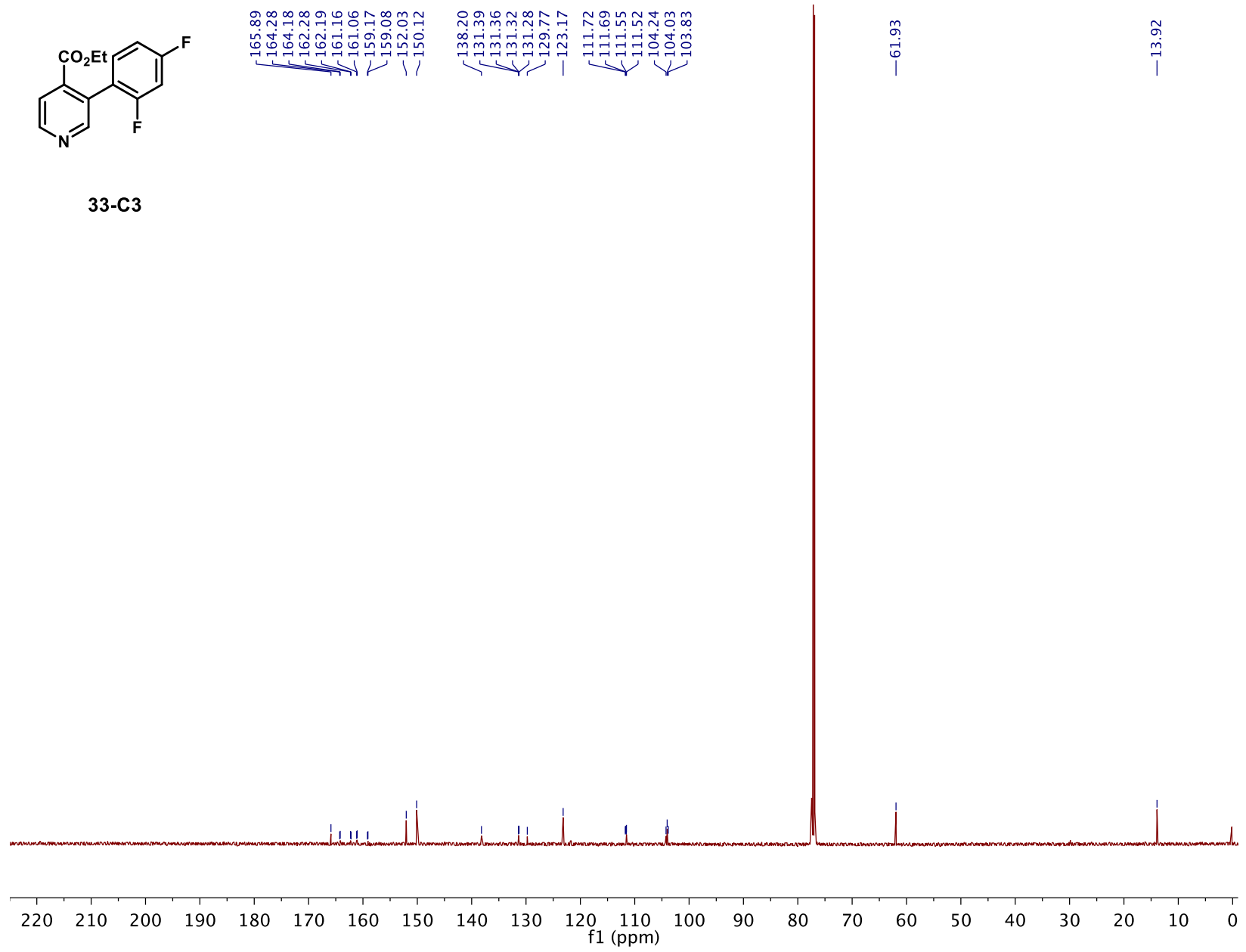


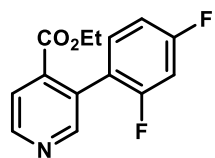
33-C3



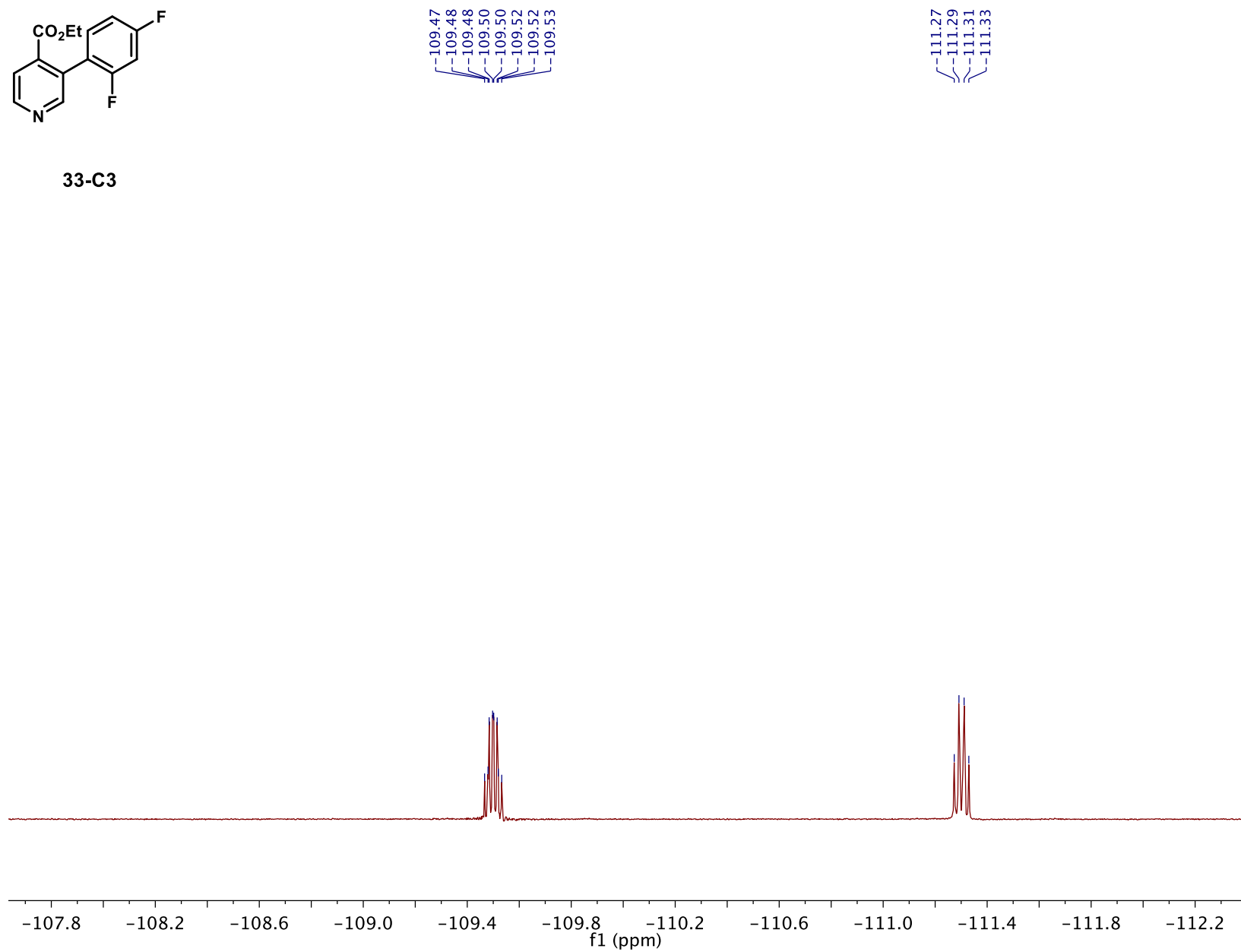


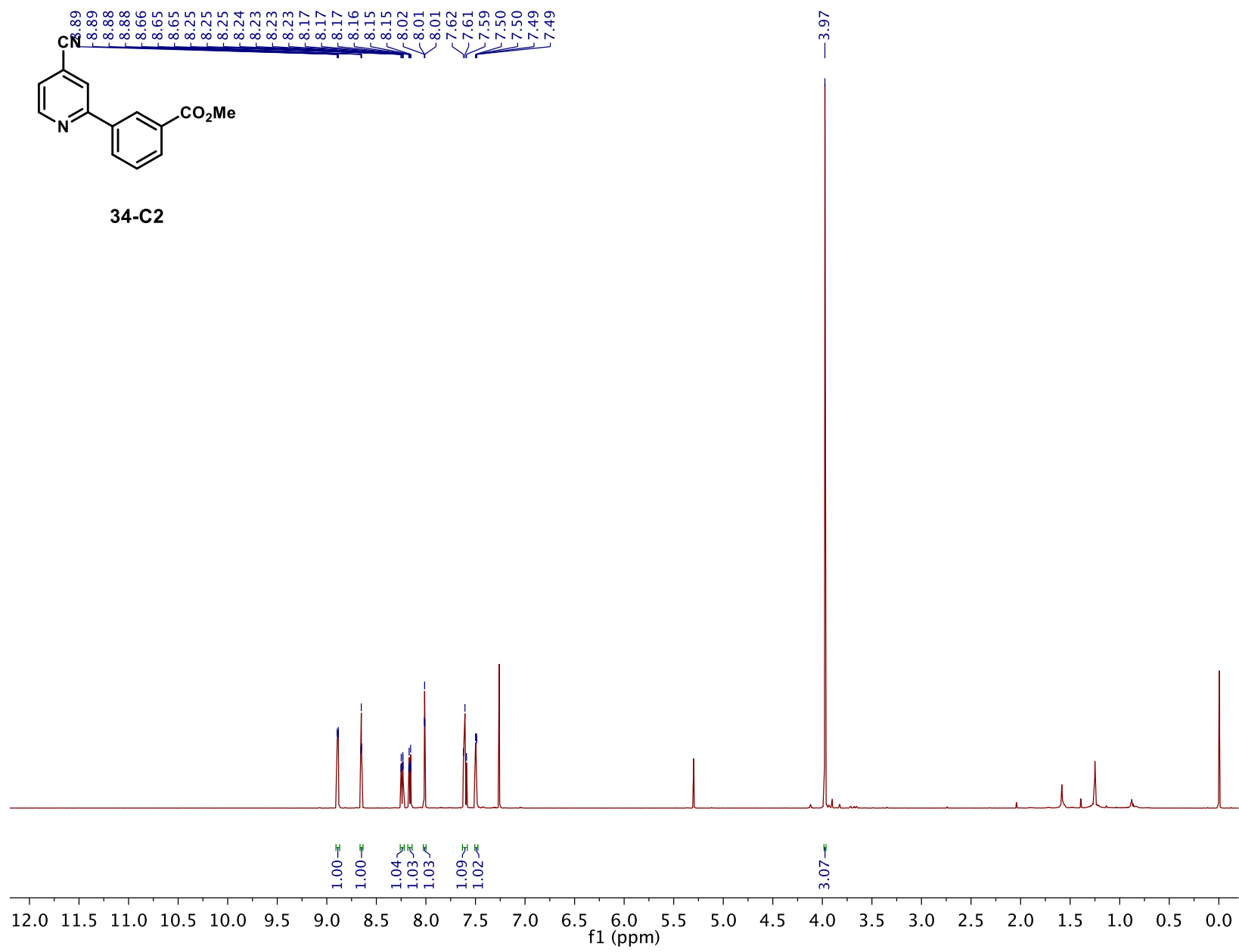
33-C3

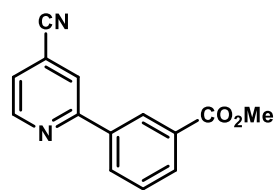




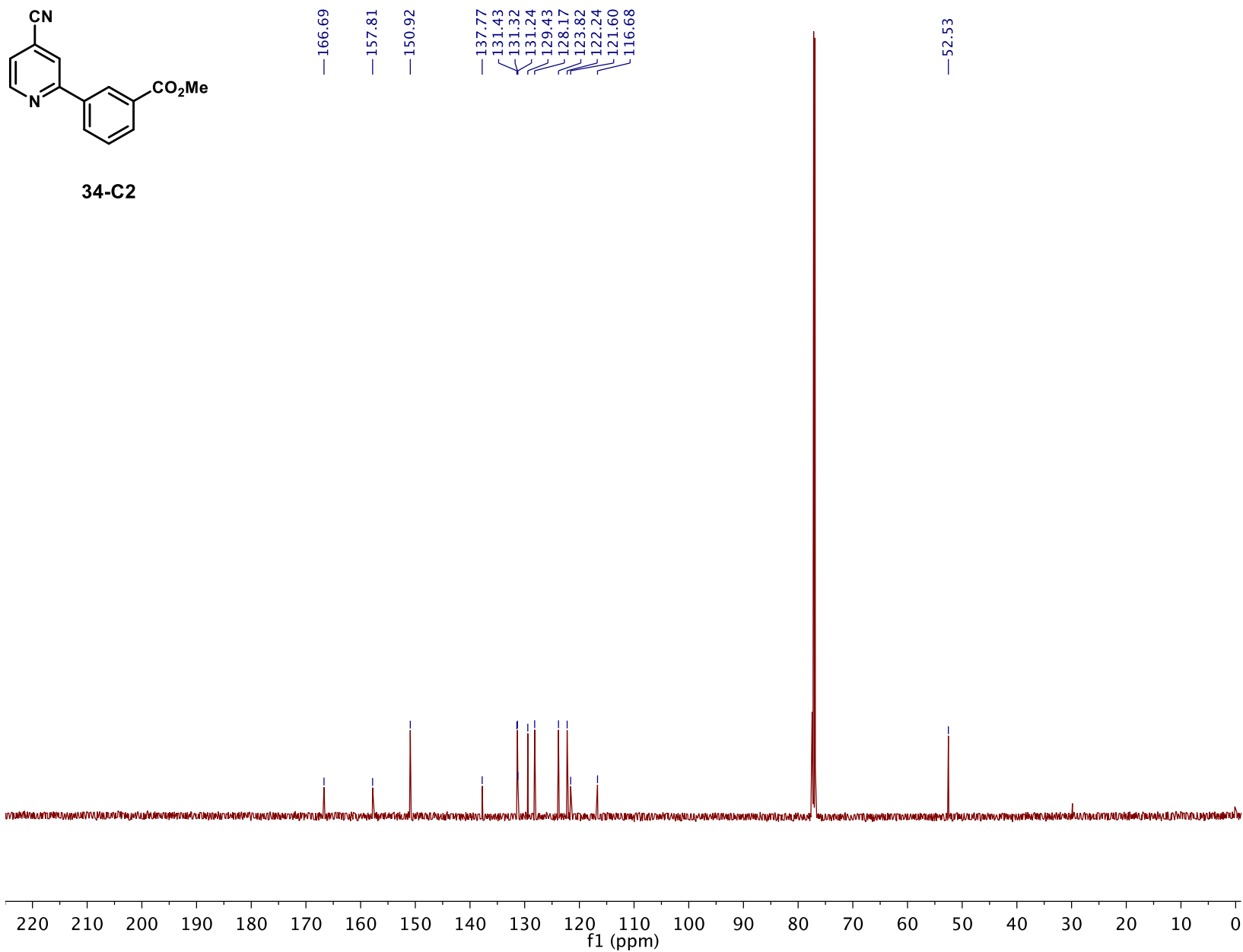
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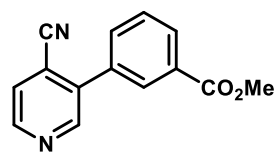




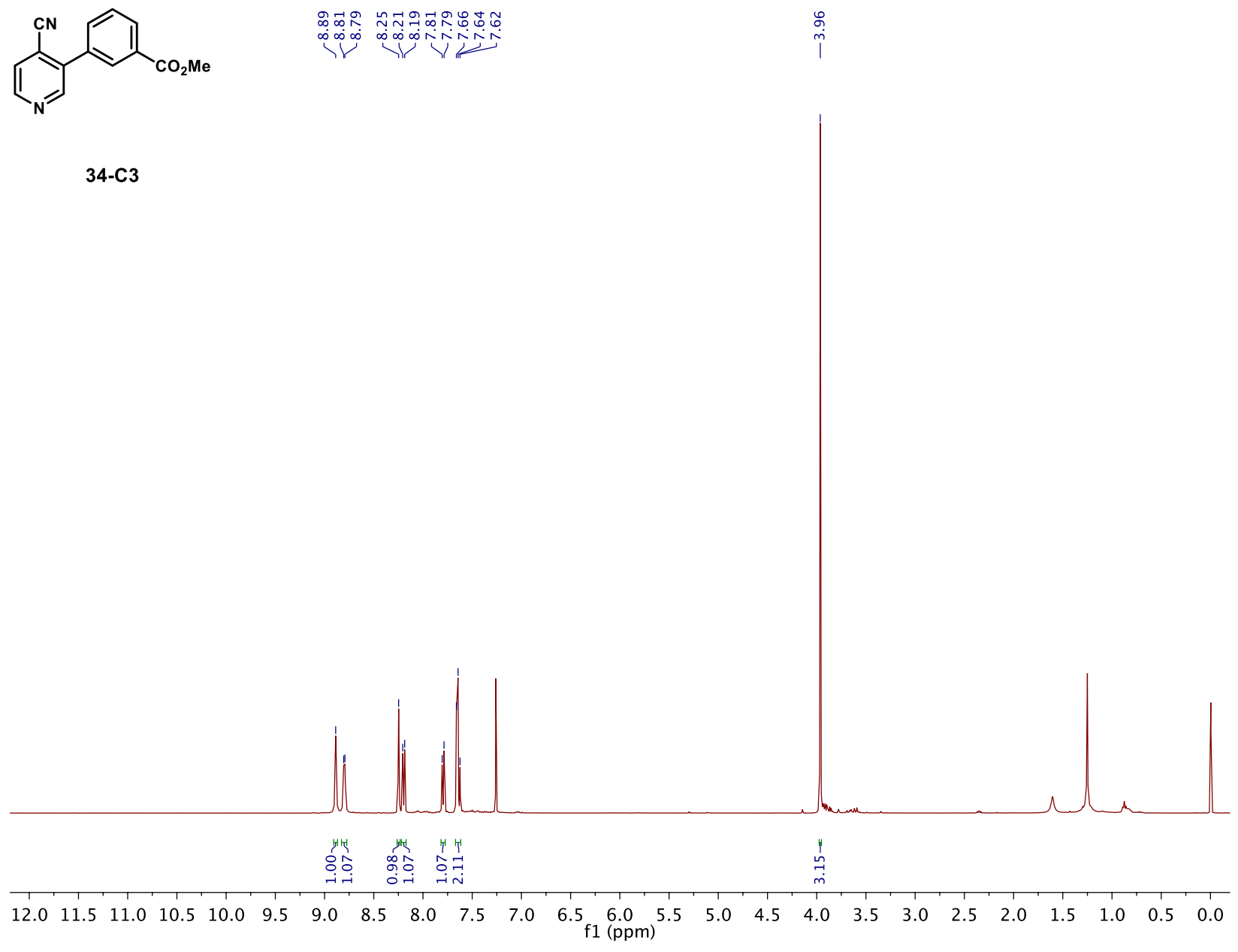


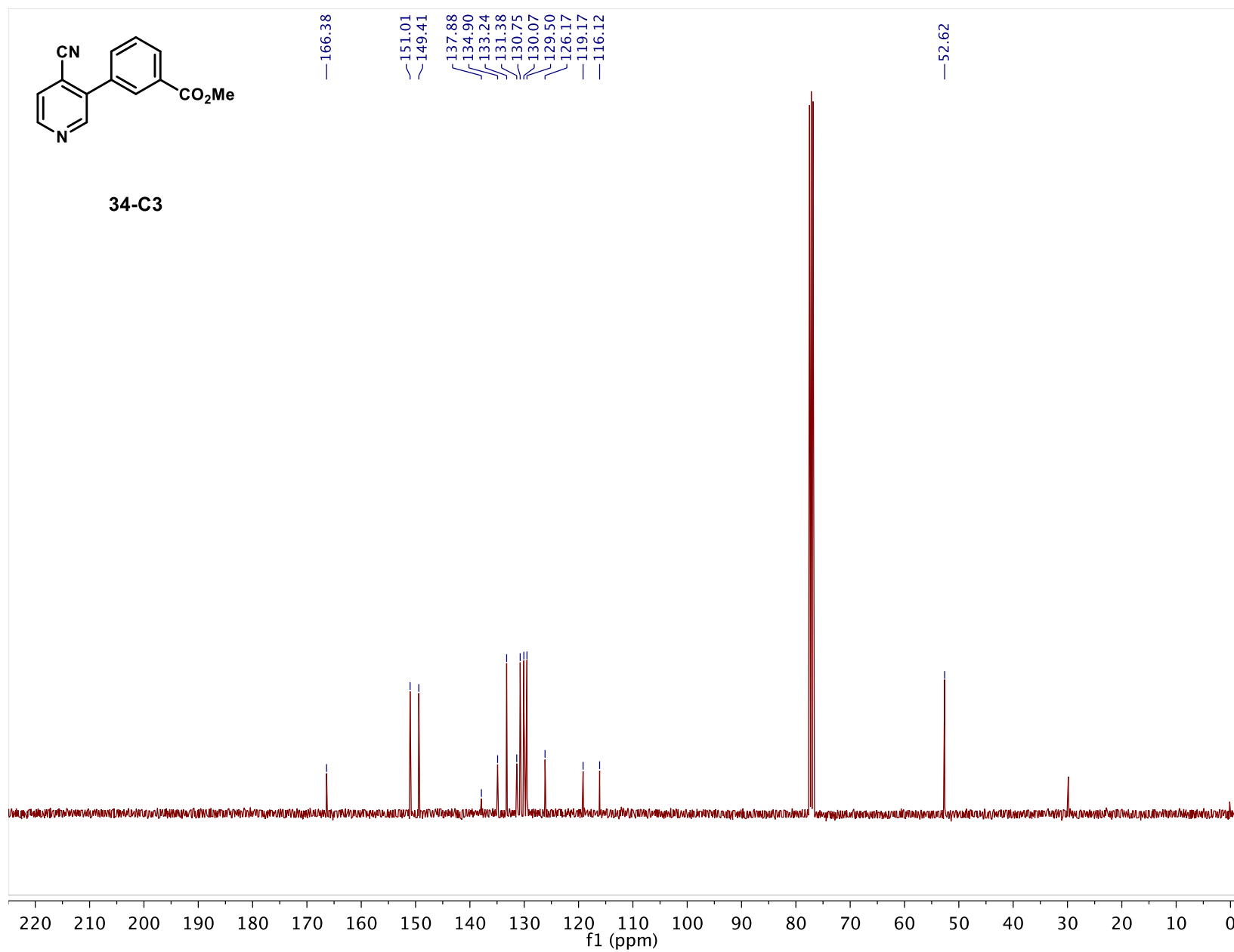
34-C2

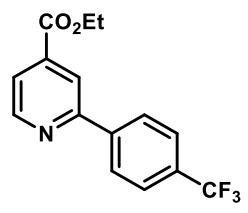




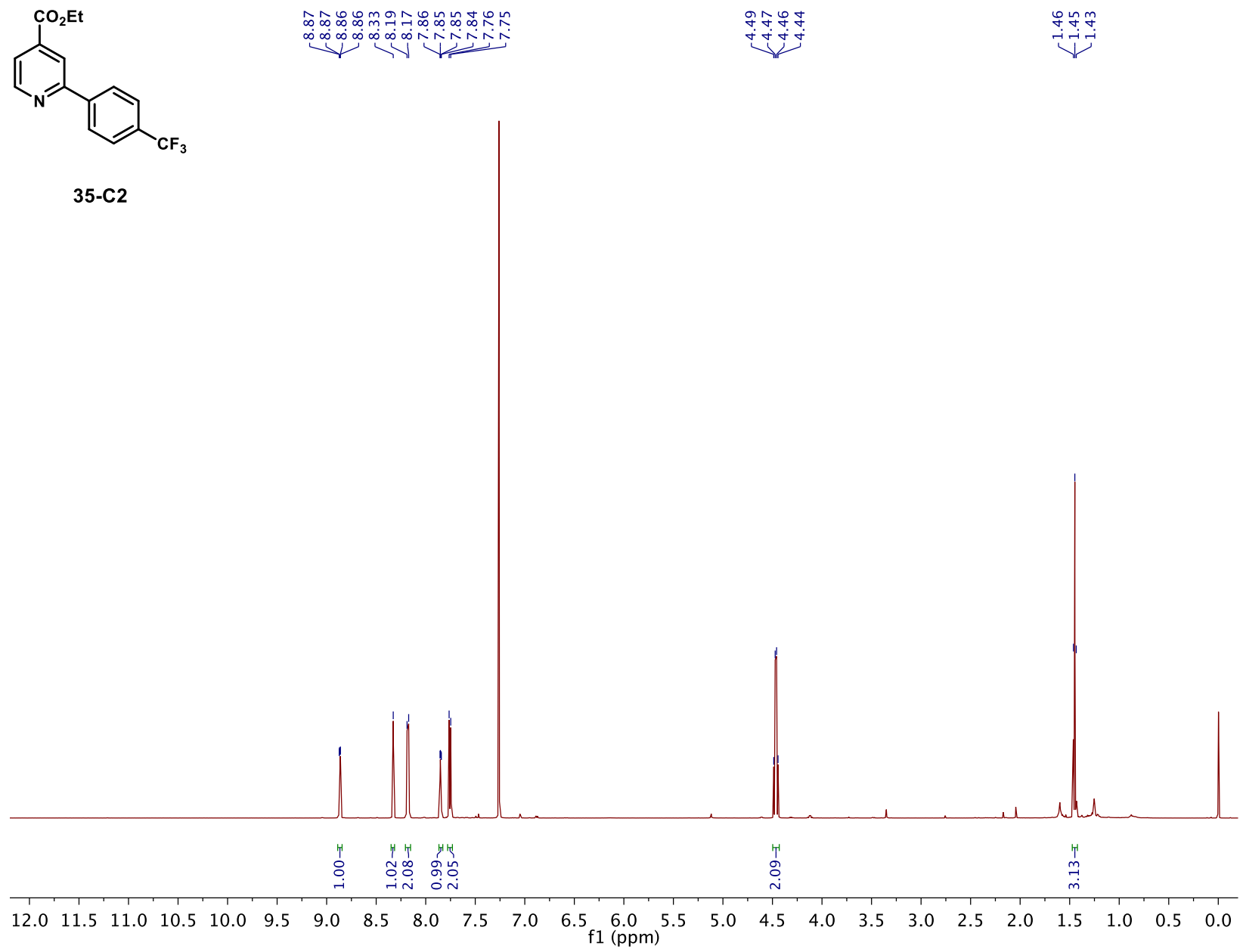
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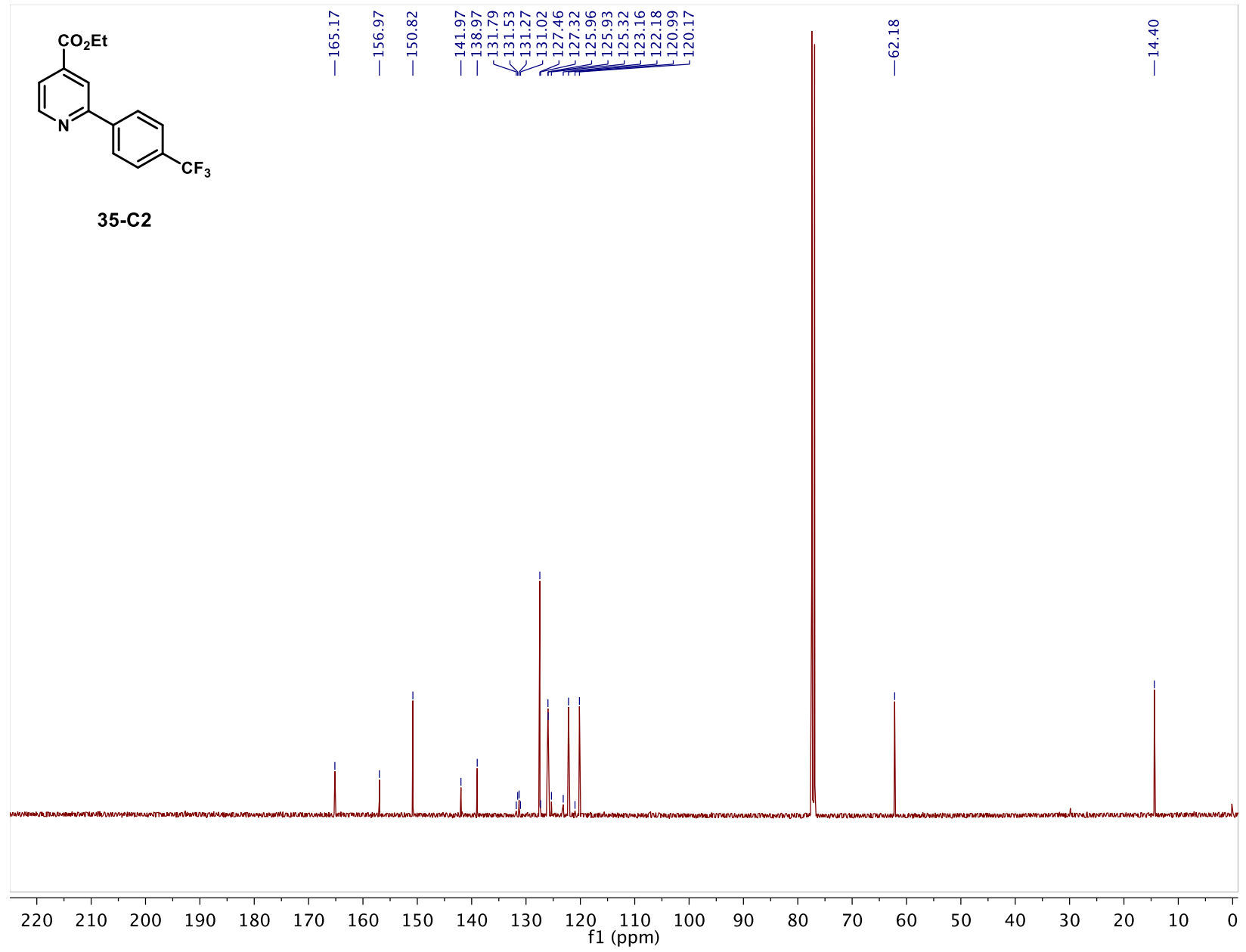


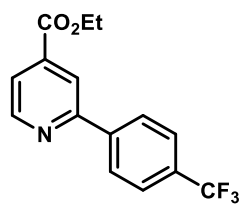




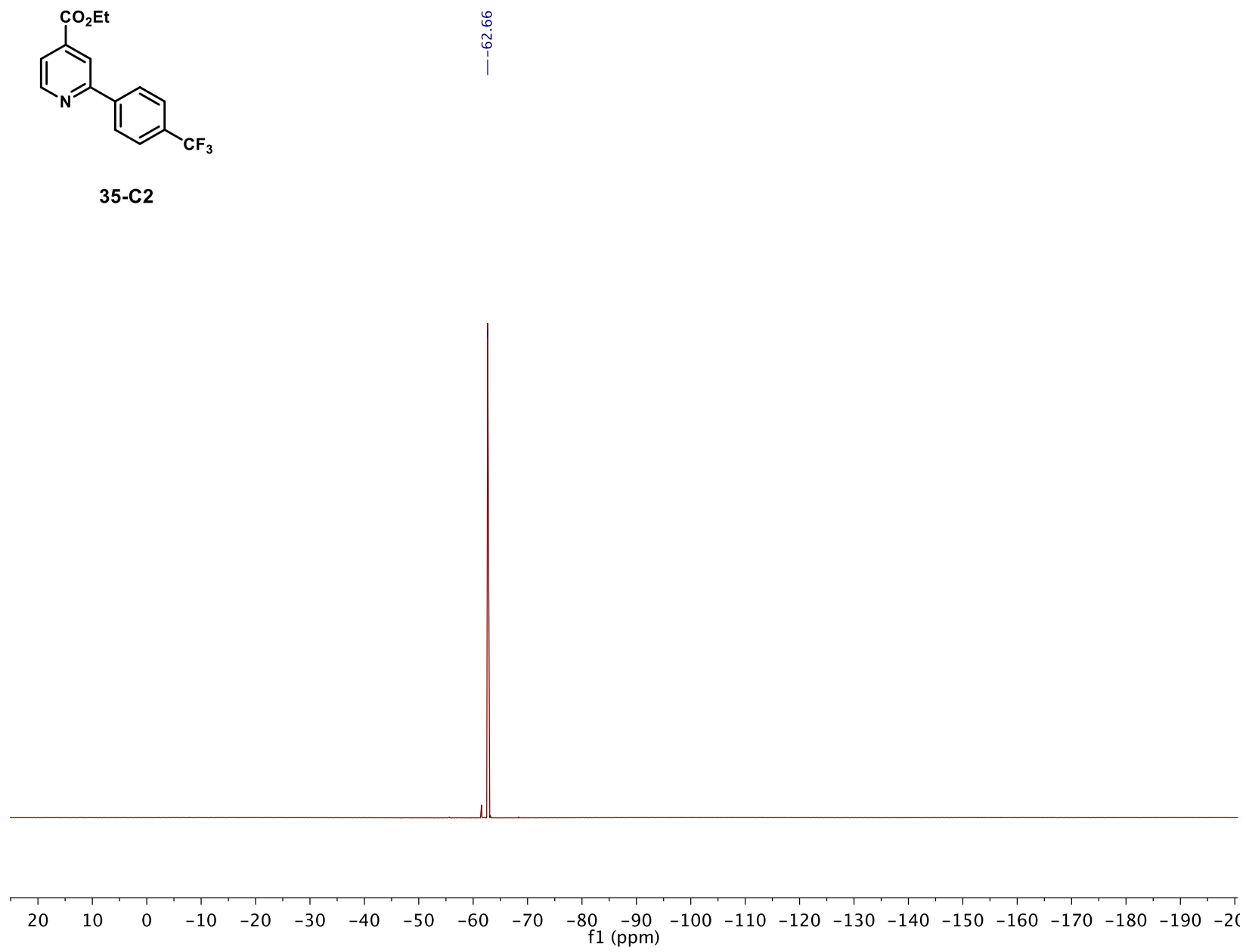
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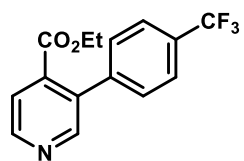




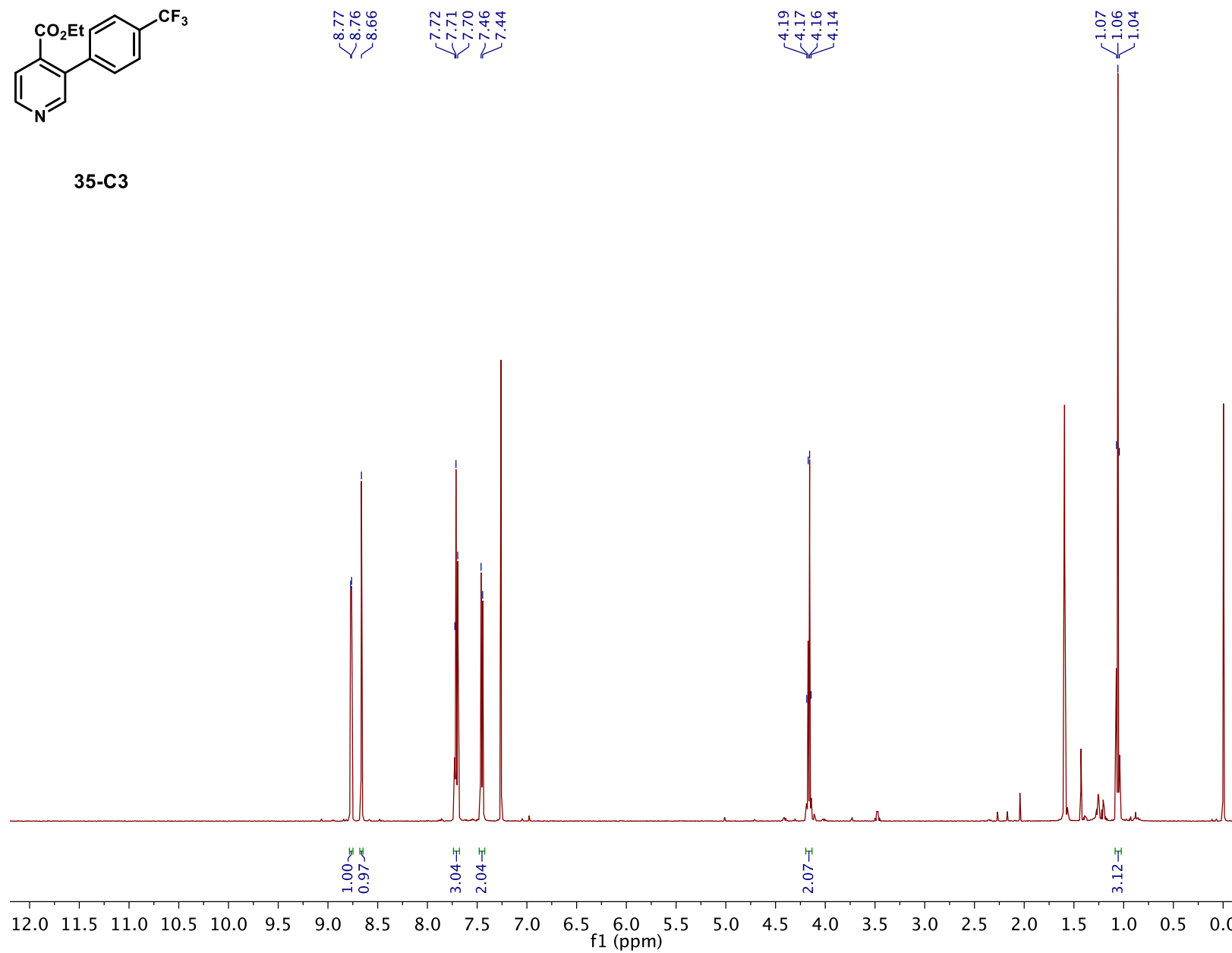


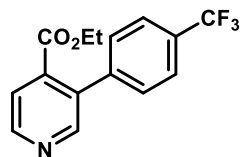
35-C2



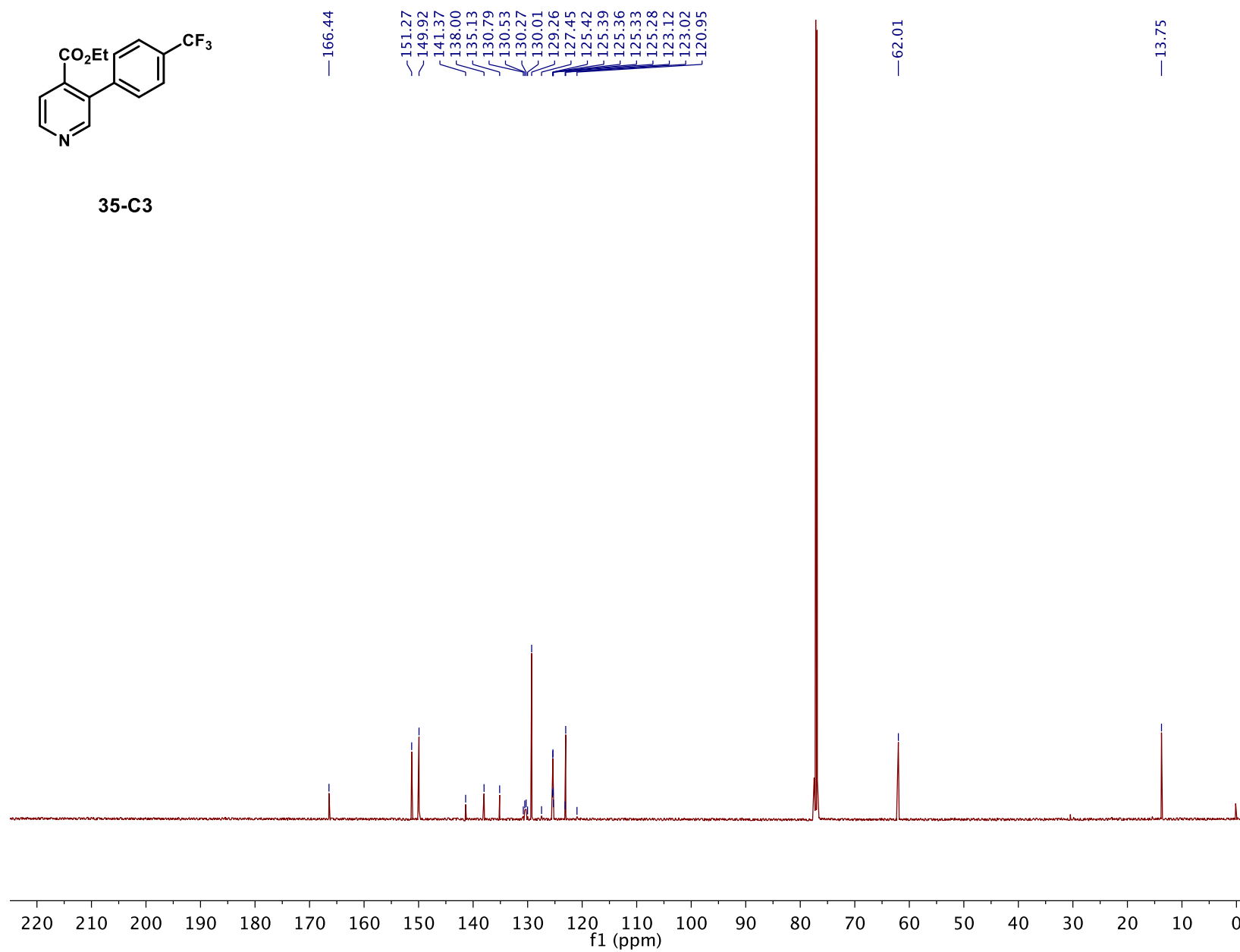


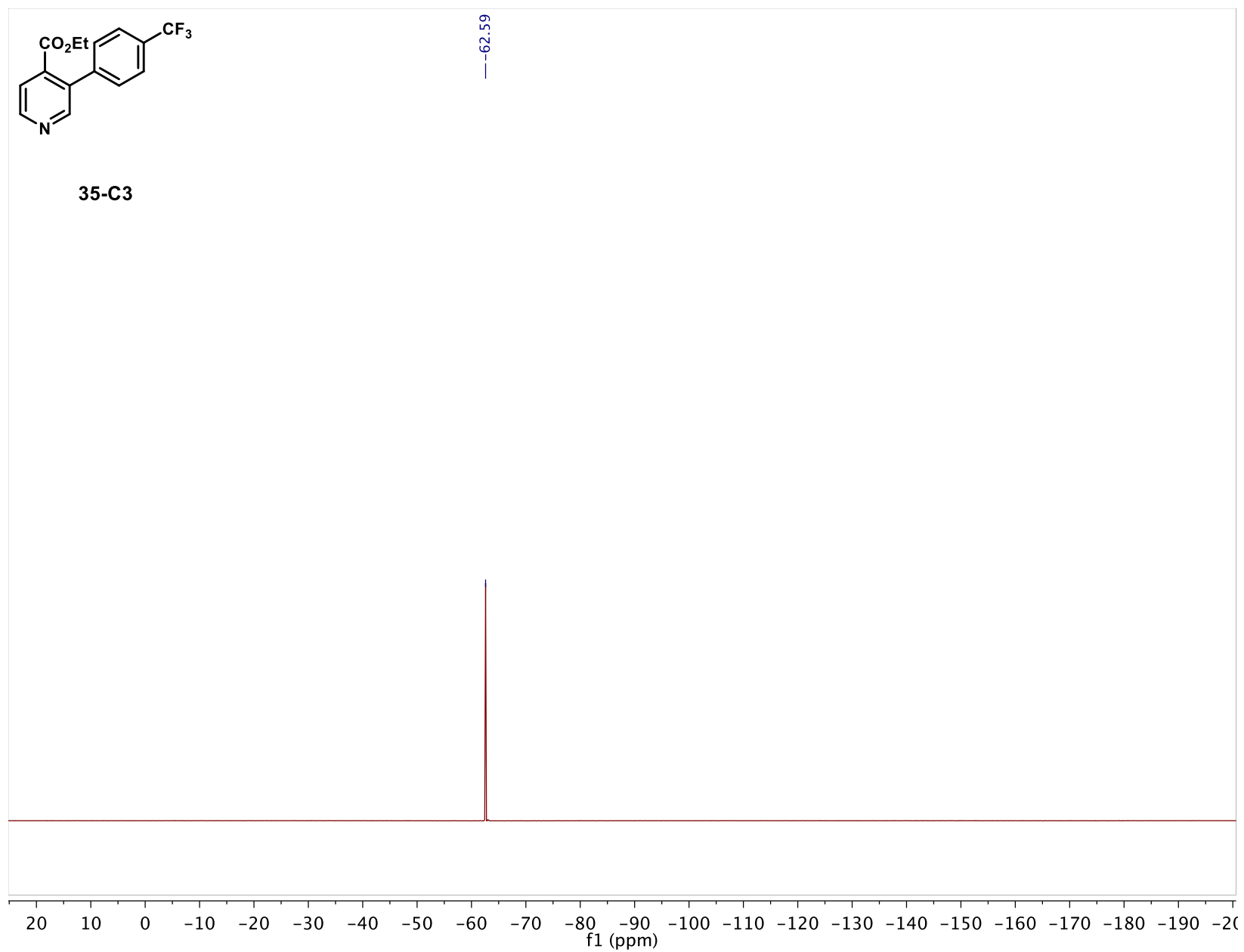
35-C3

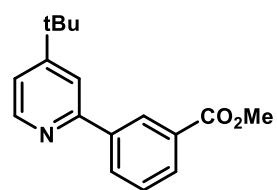




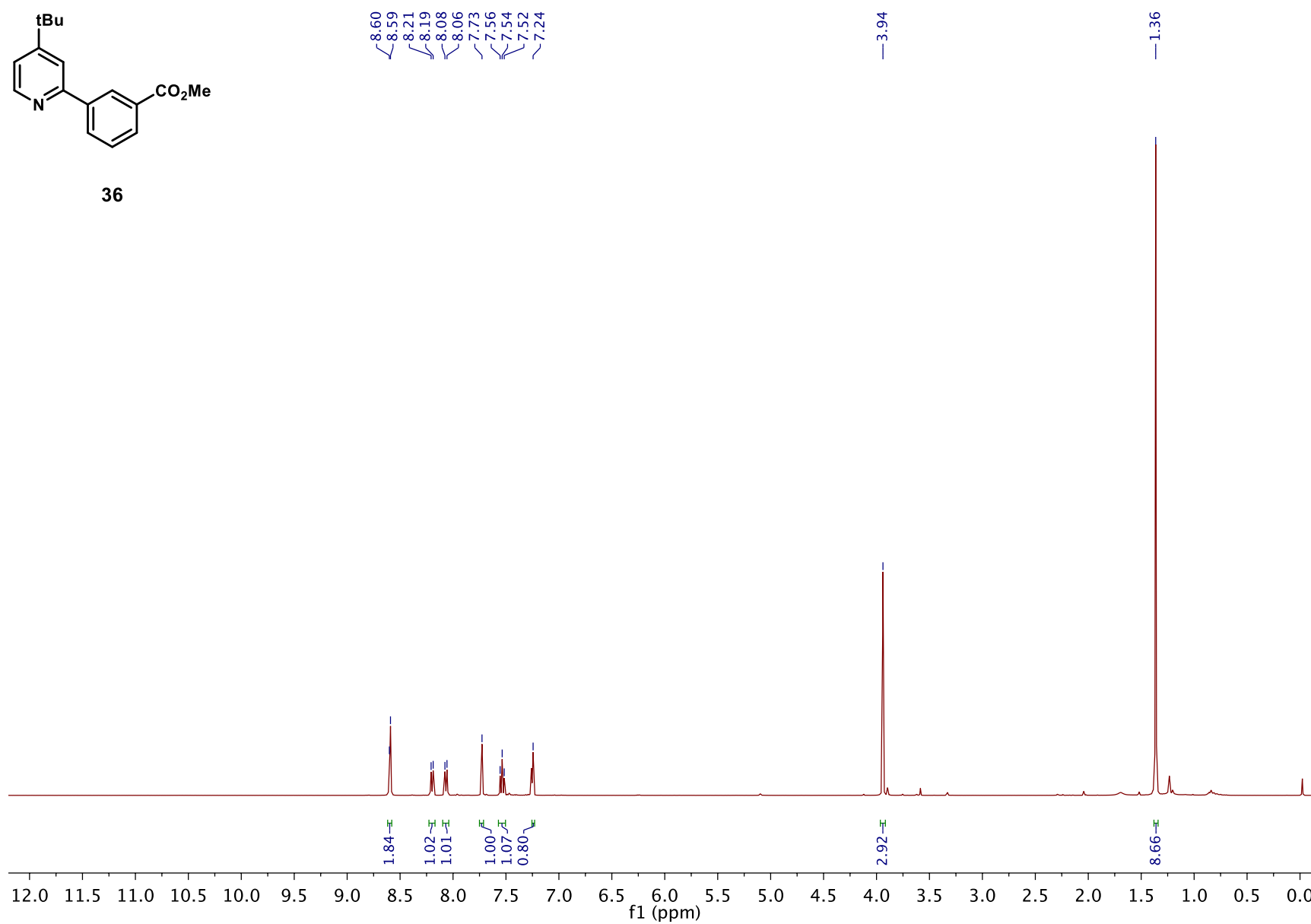
35-C3

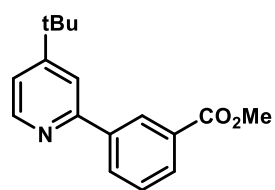
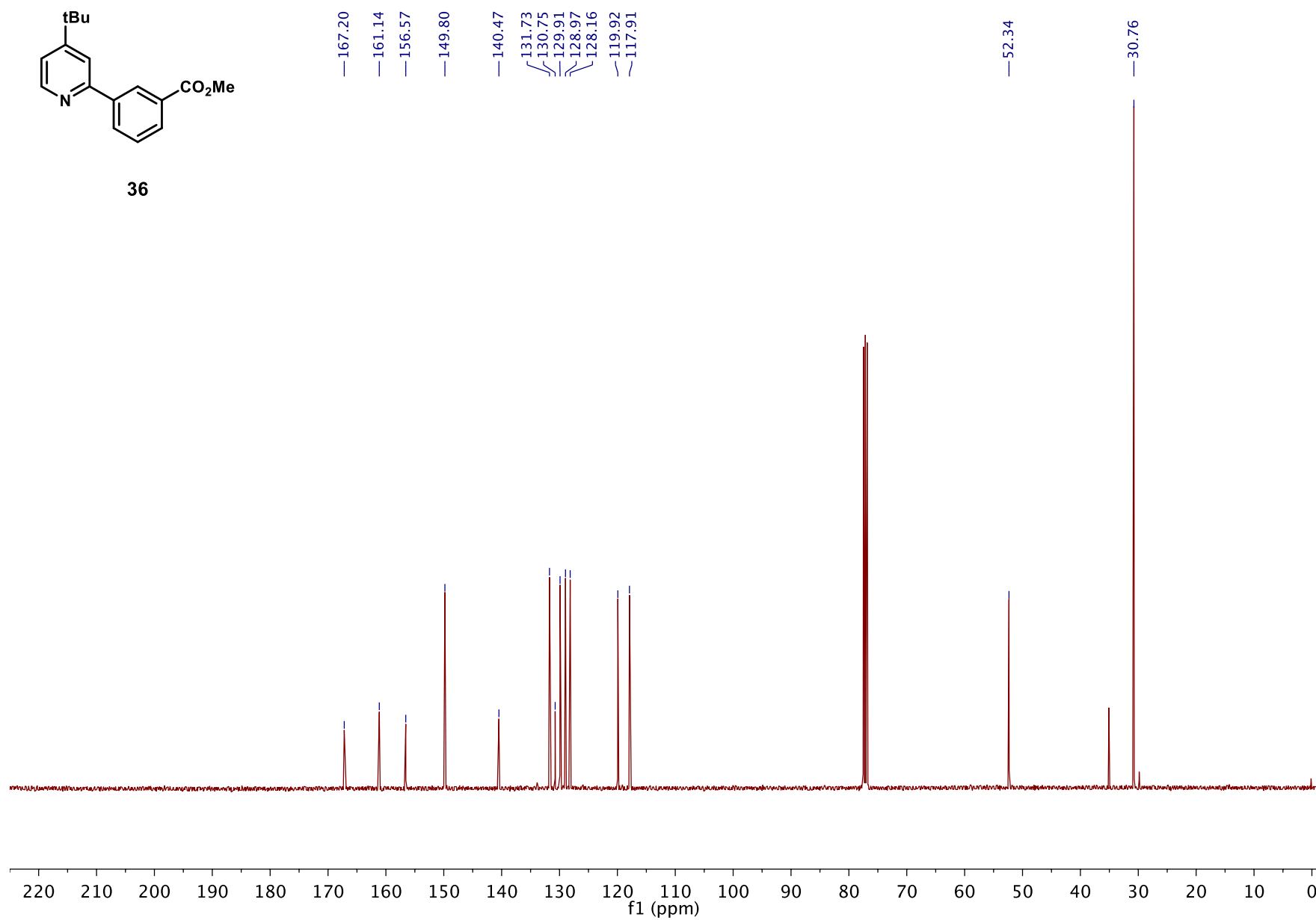


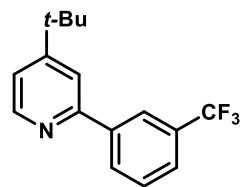




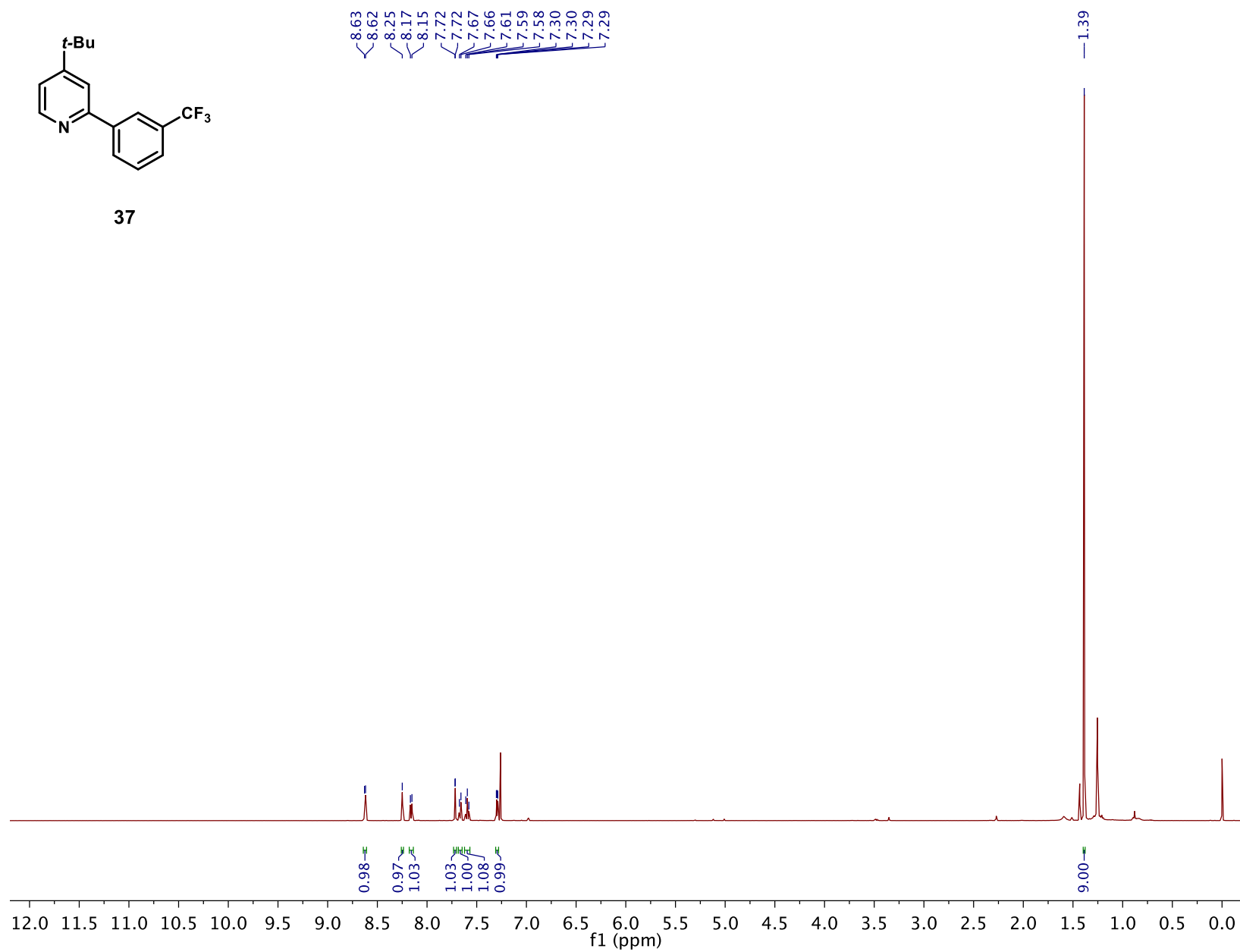
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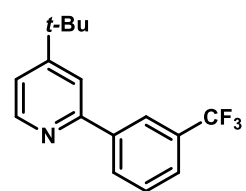


**36**

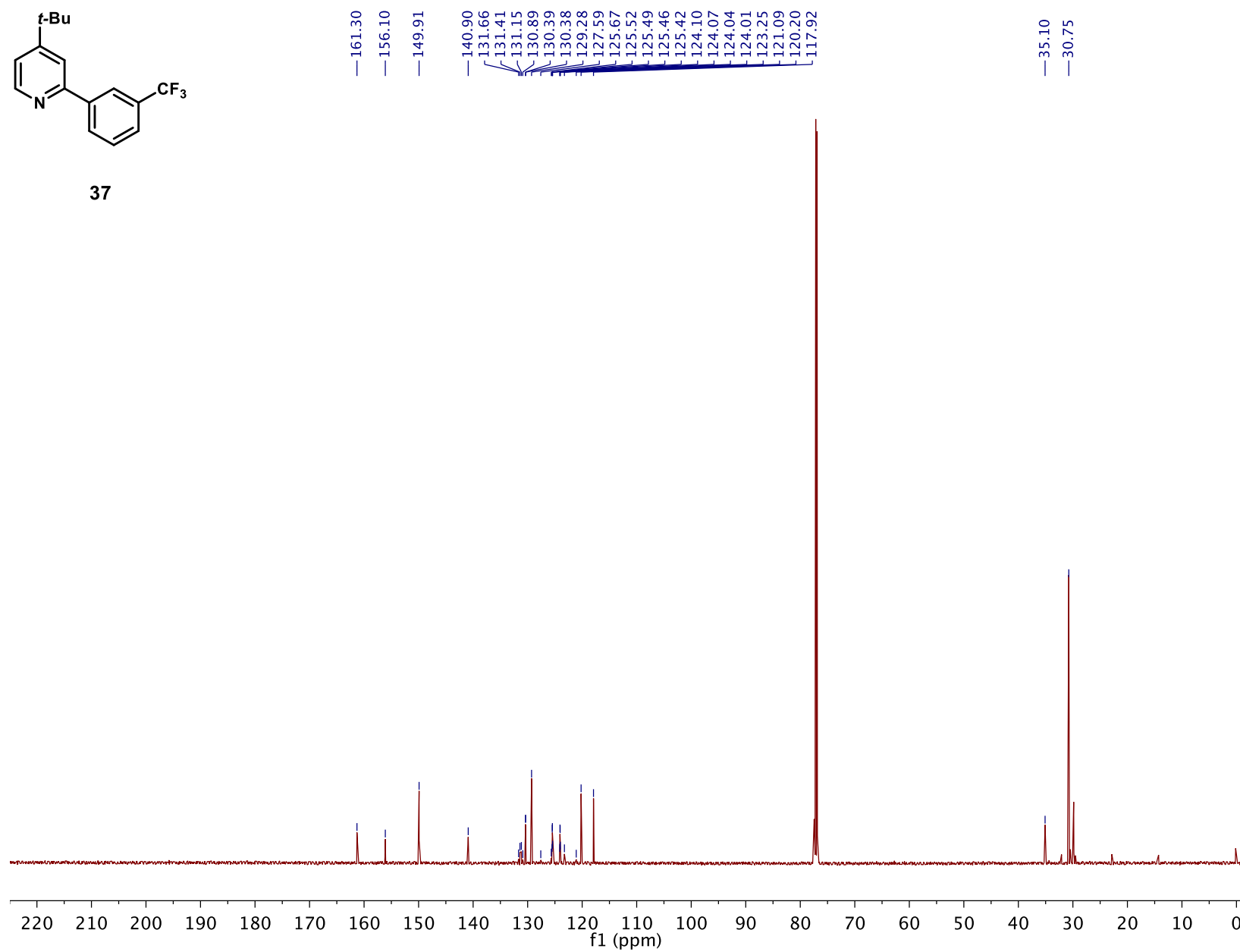


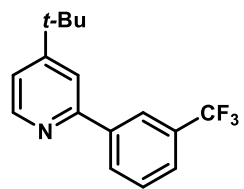
37



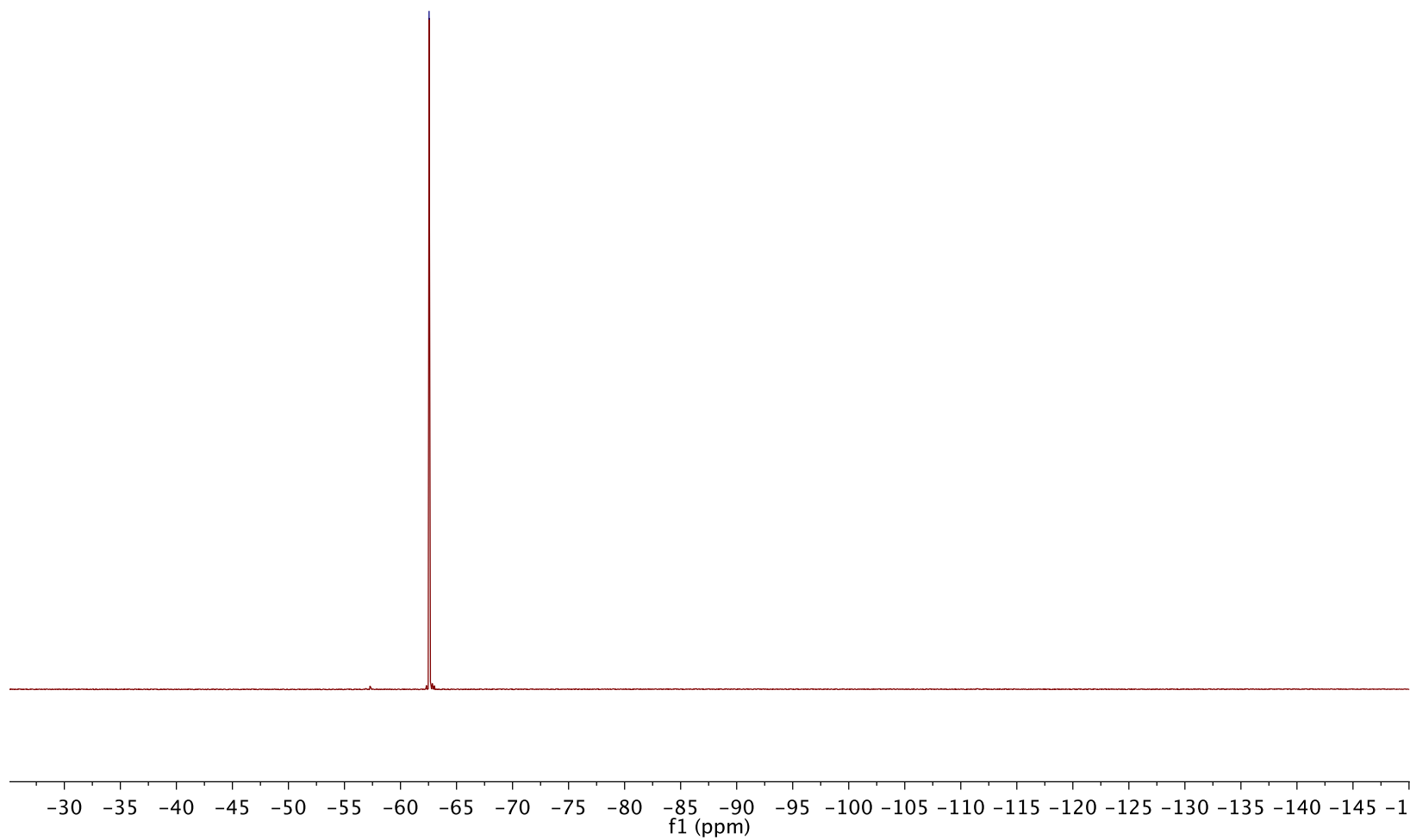


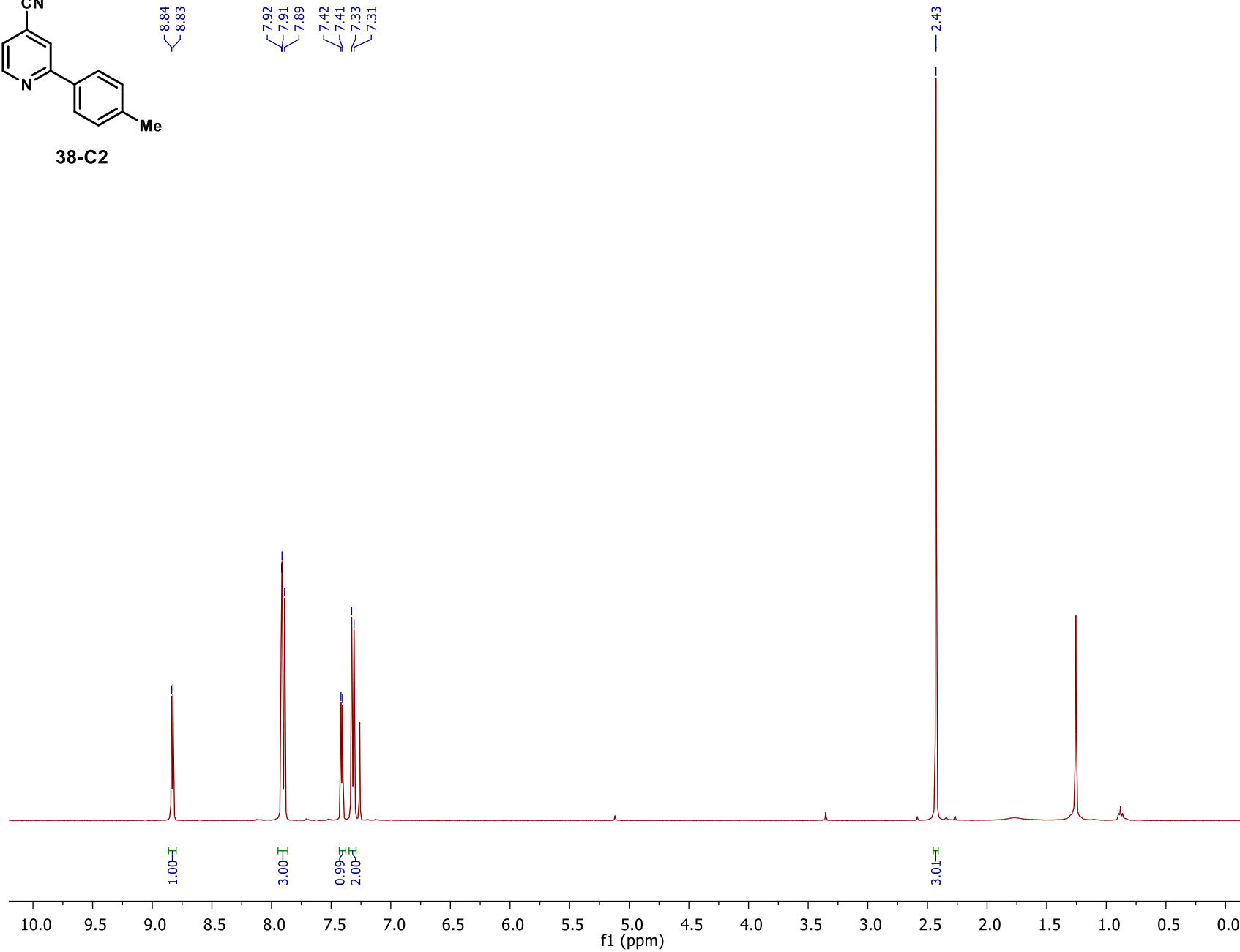
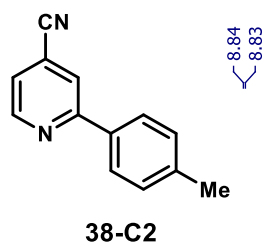
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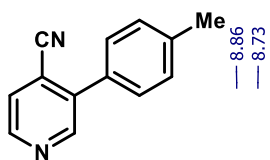


**37**

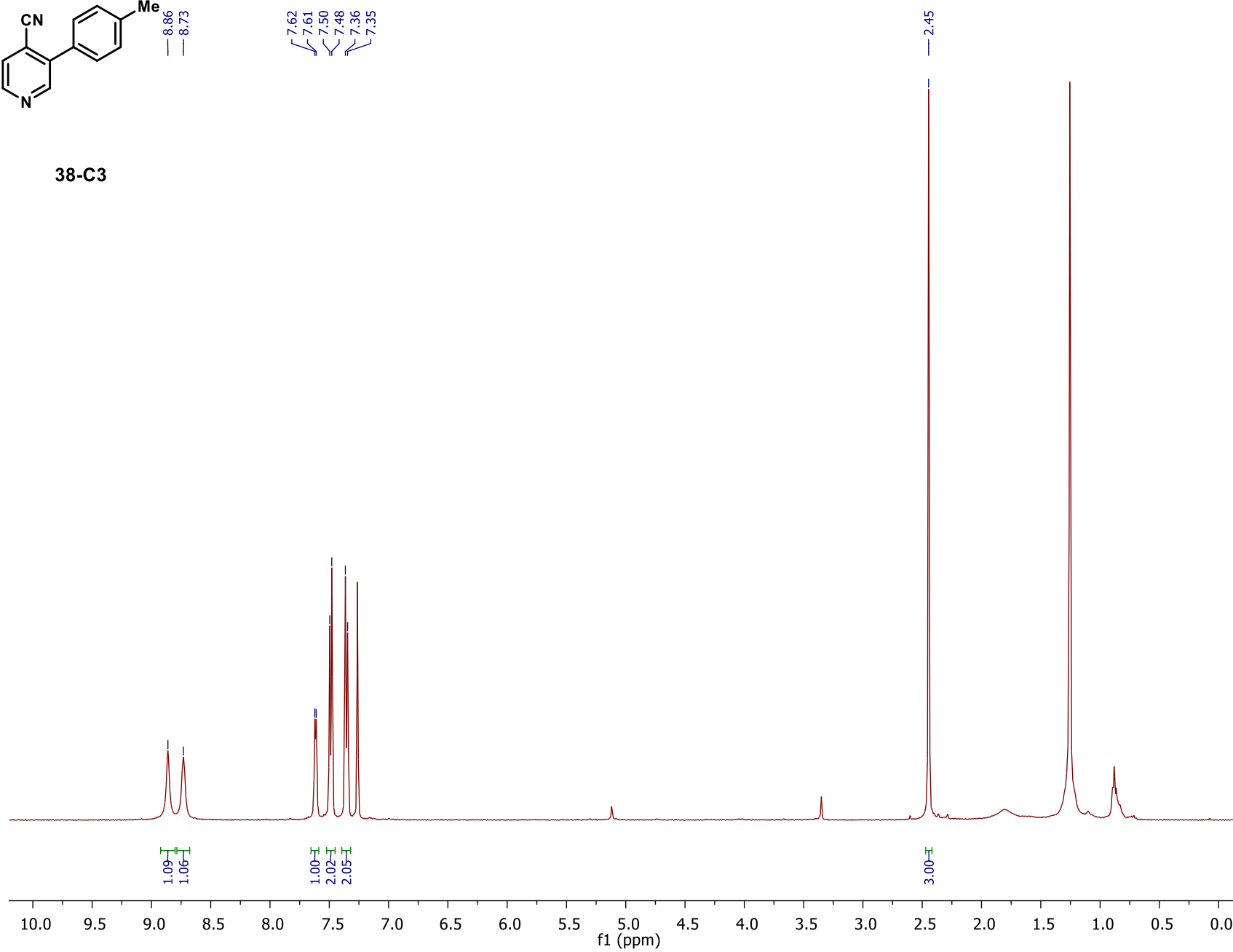
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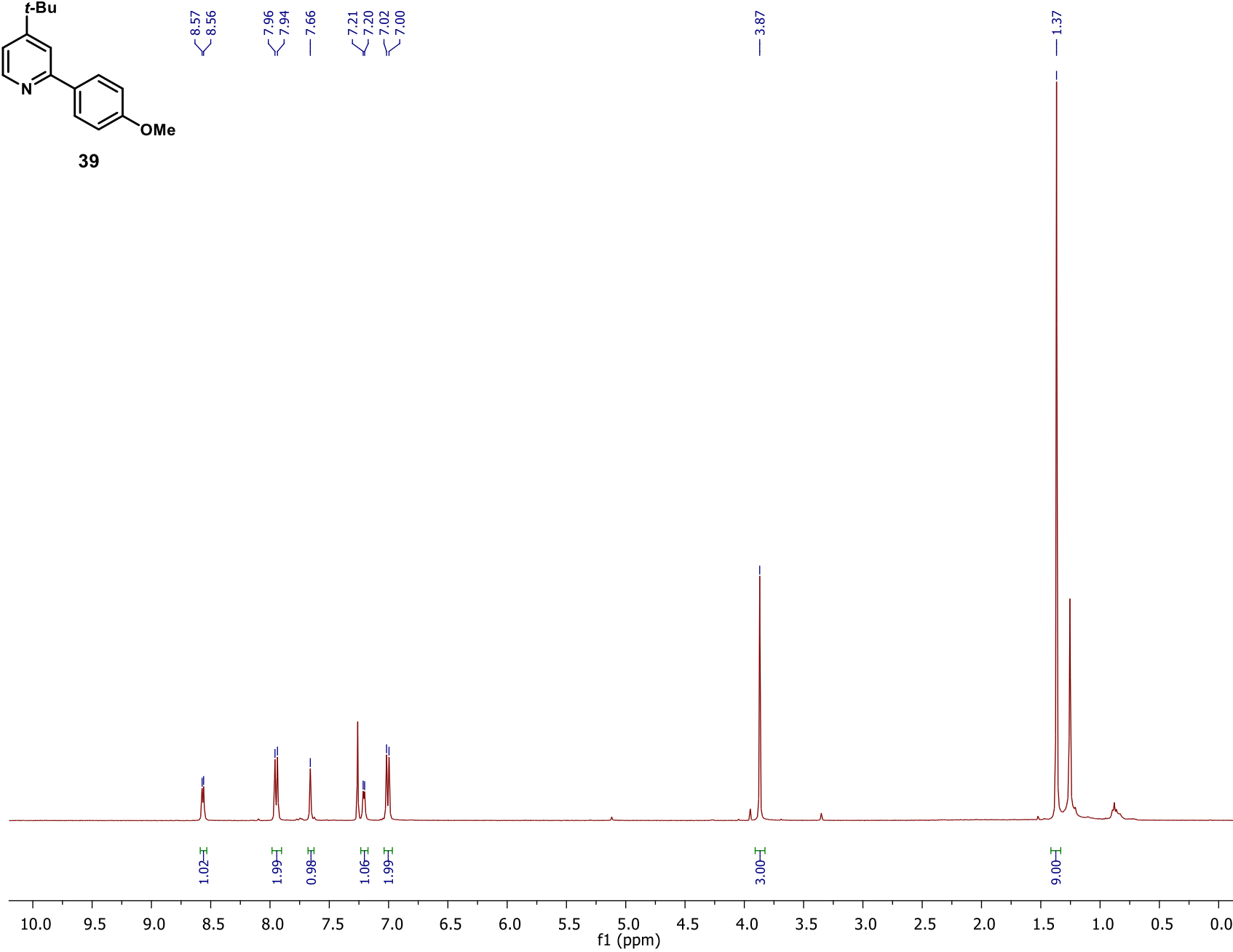
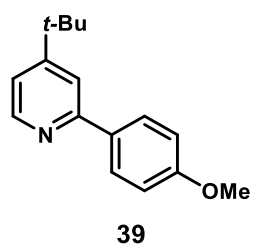


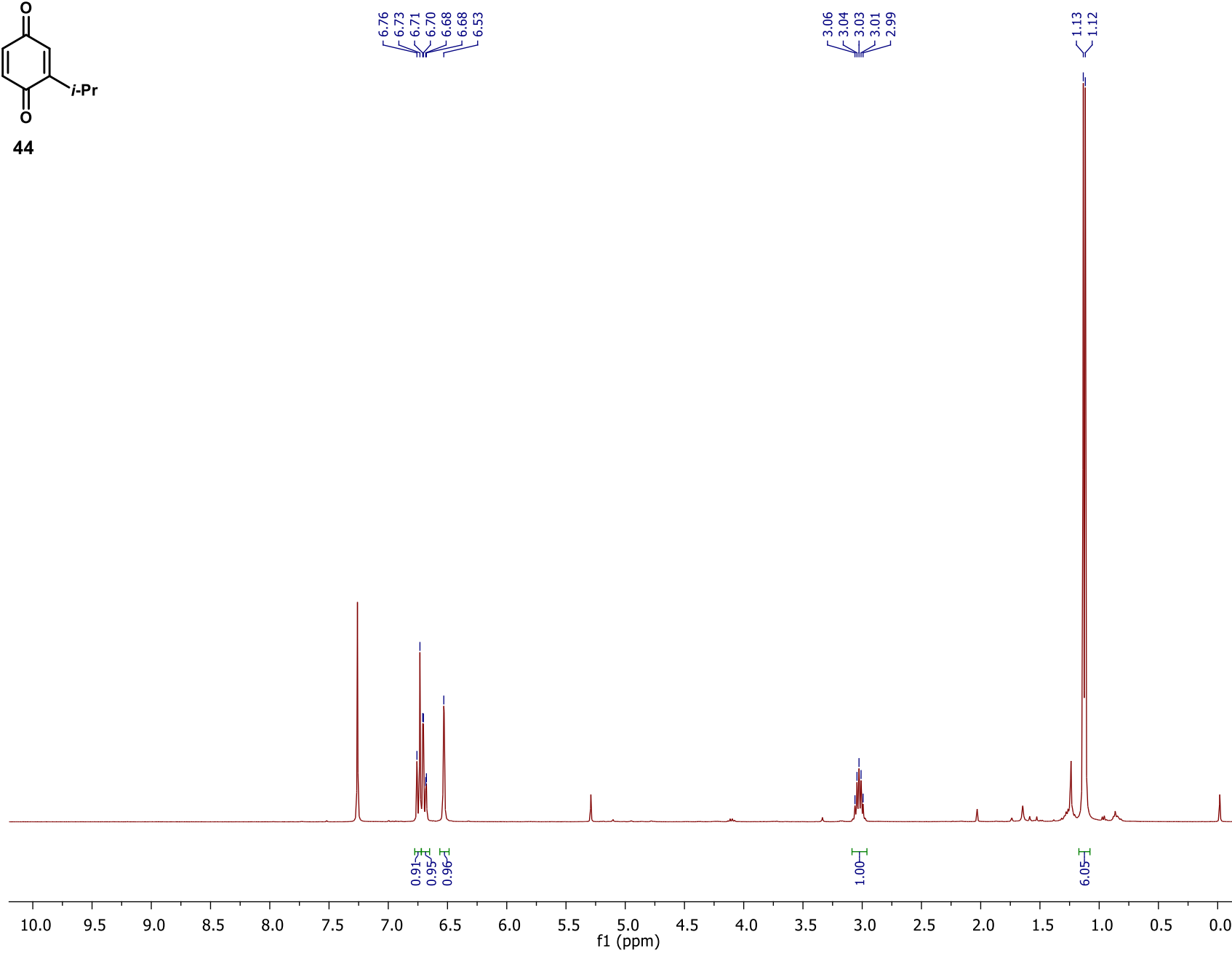
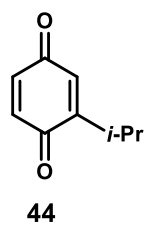


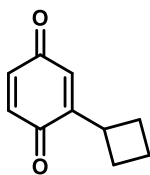


38-C3

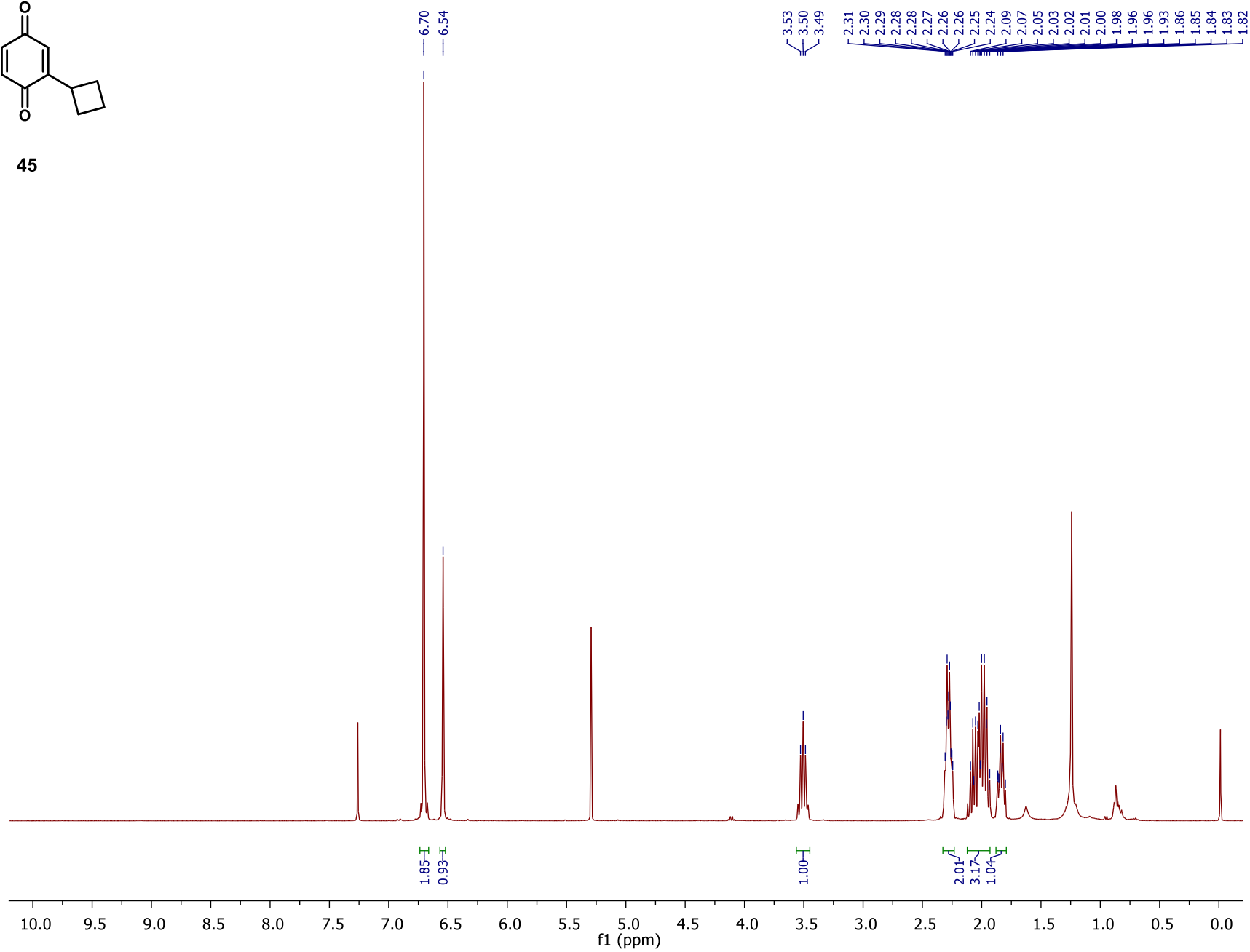


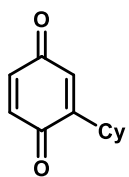




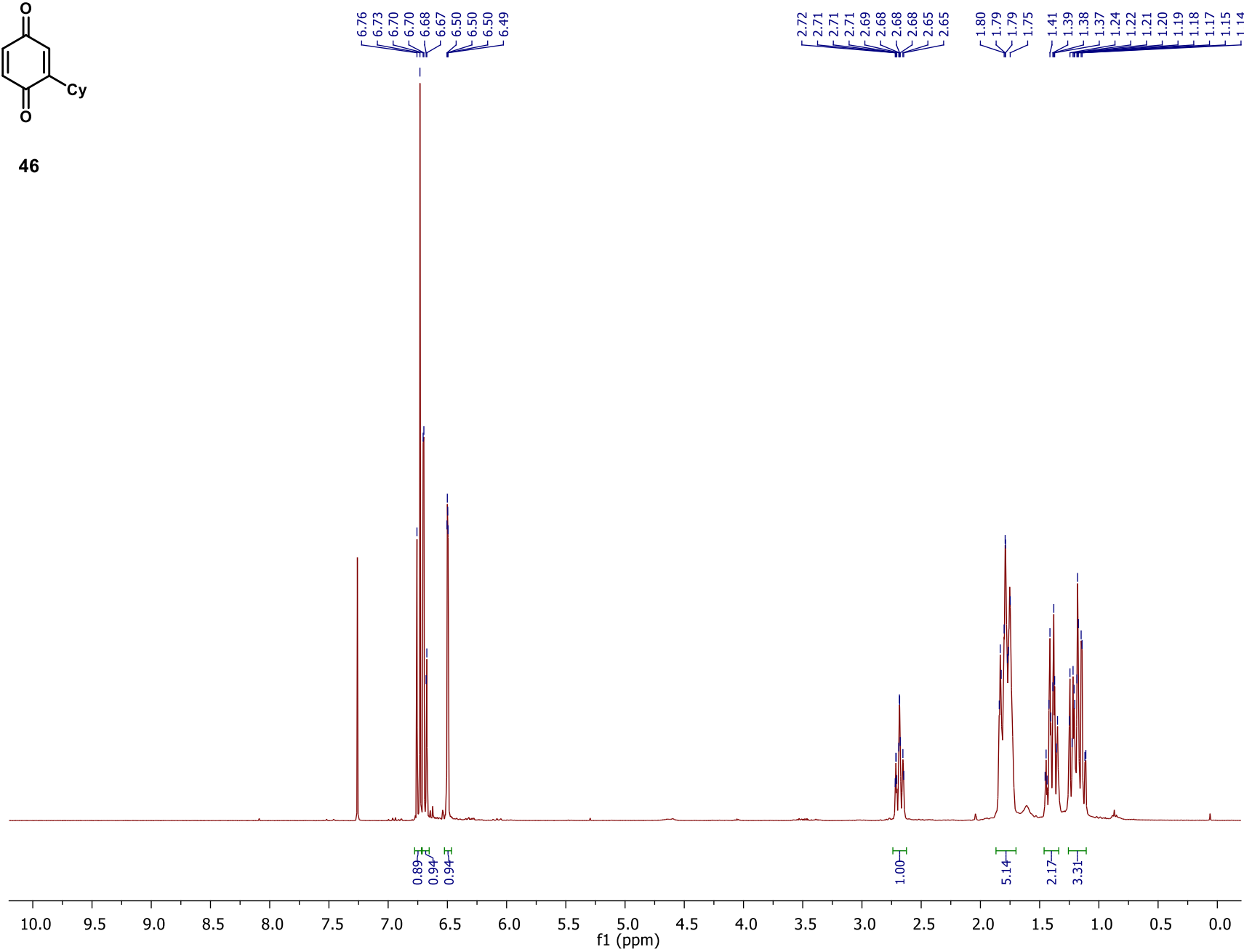


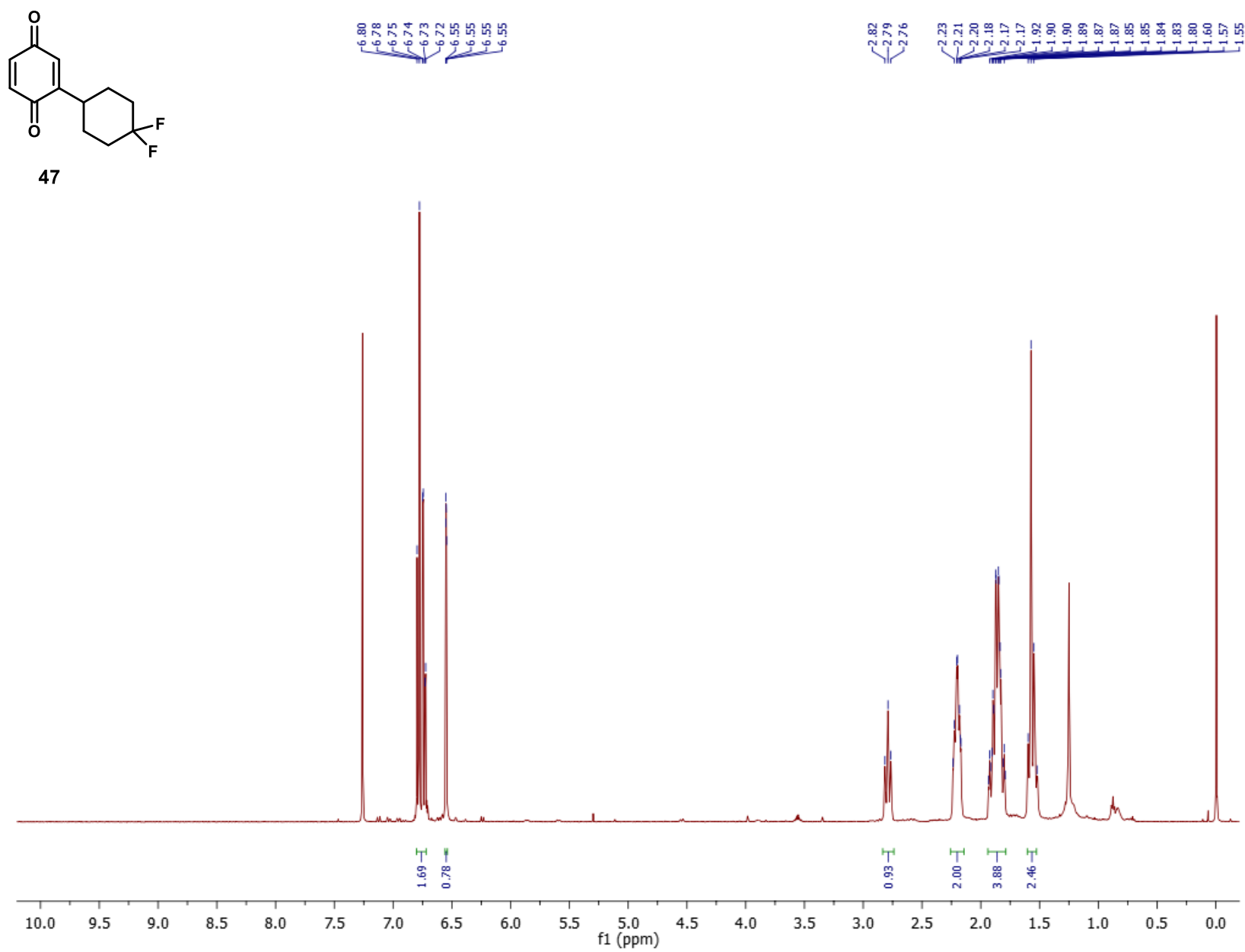
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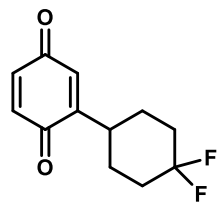




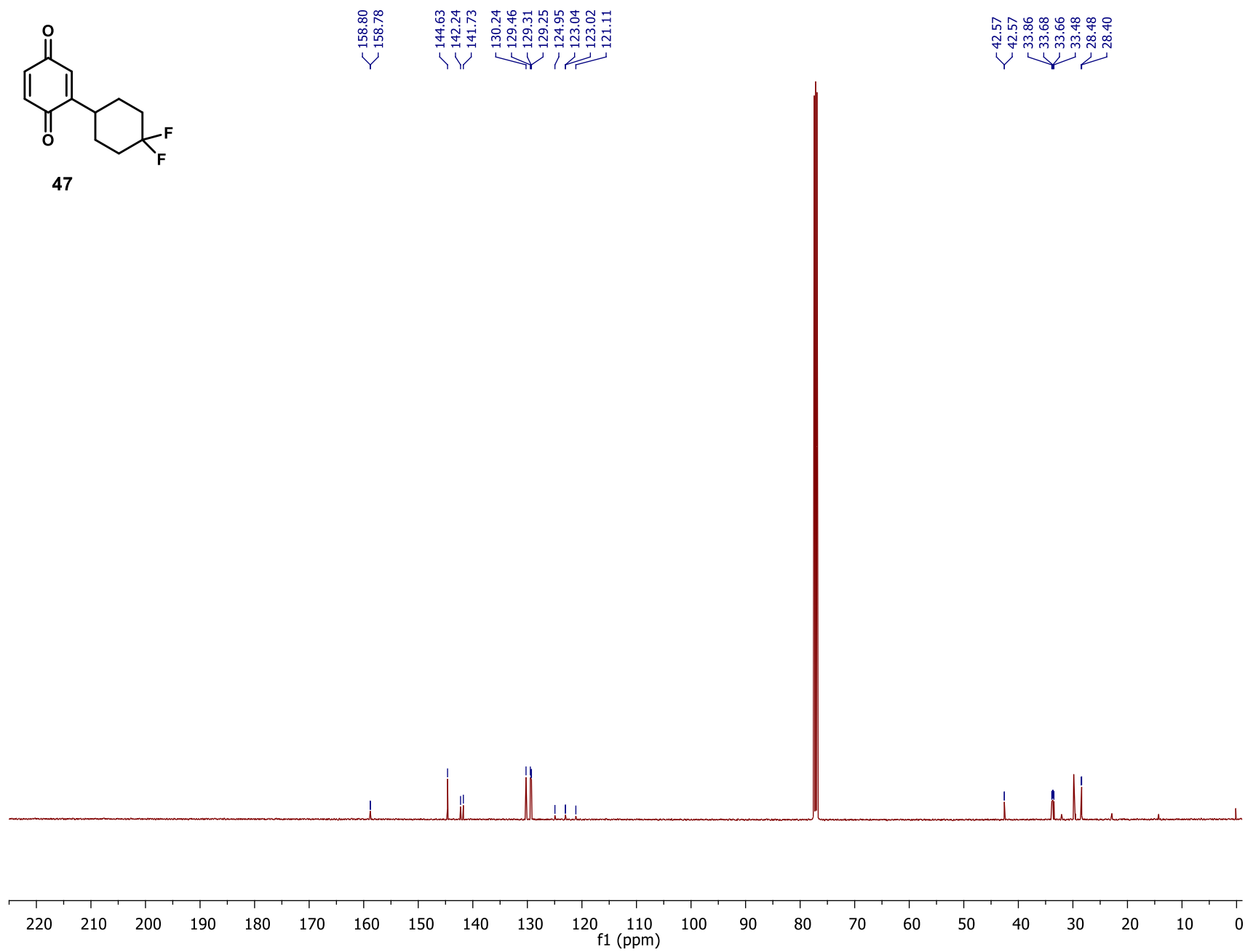
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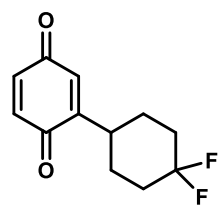




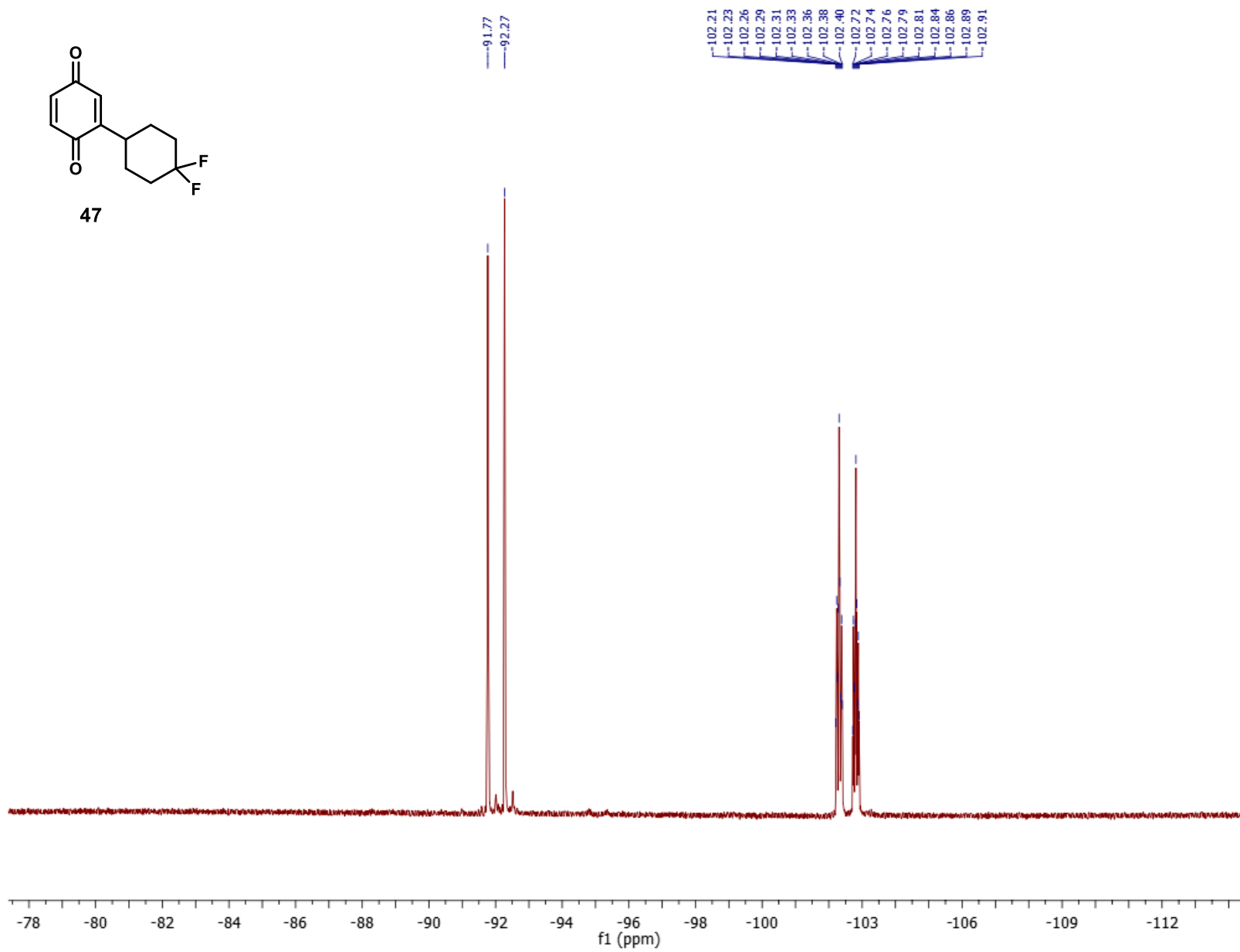


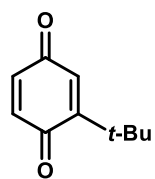
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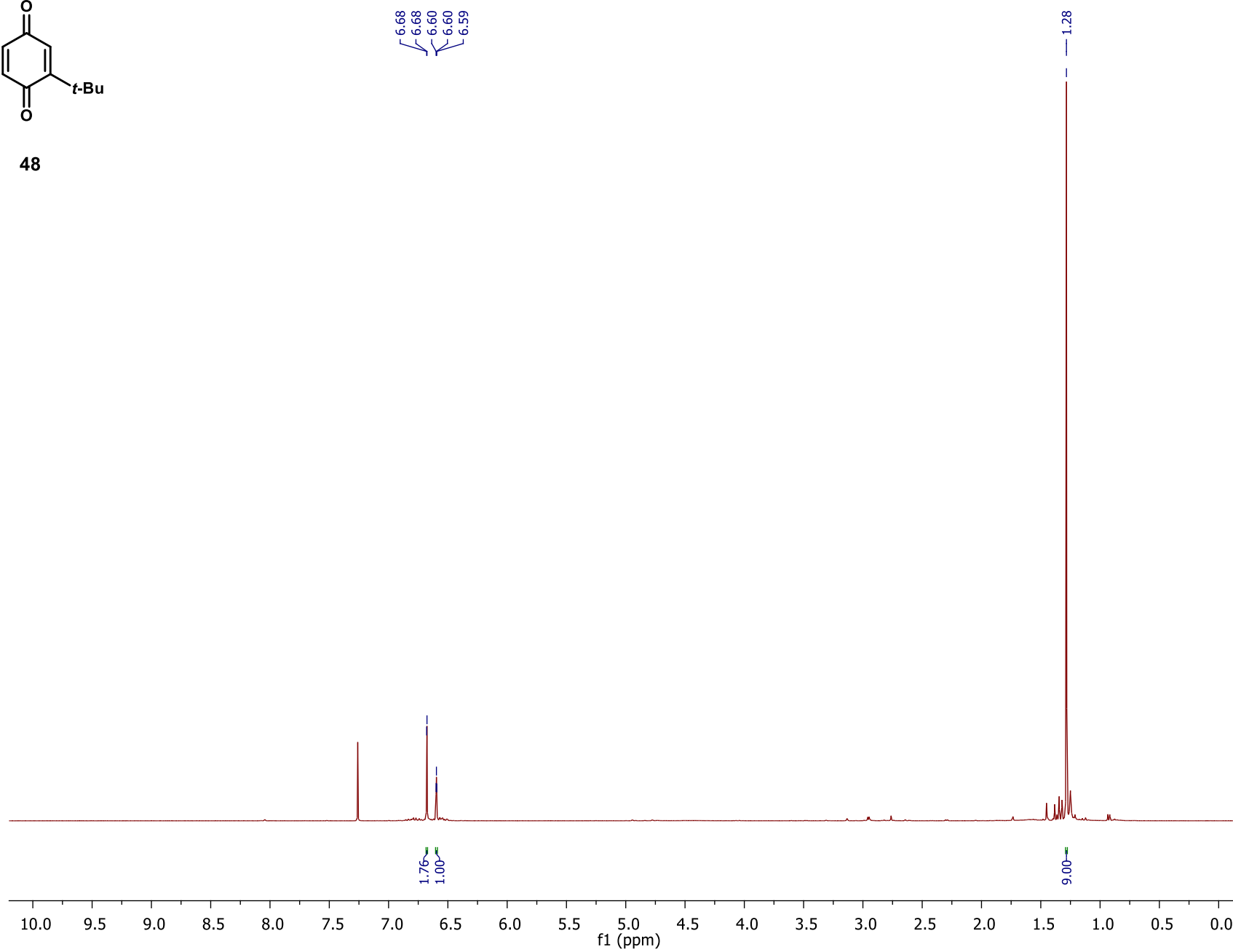


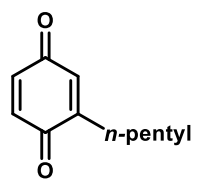
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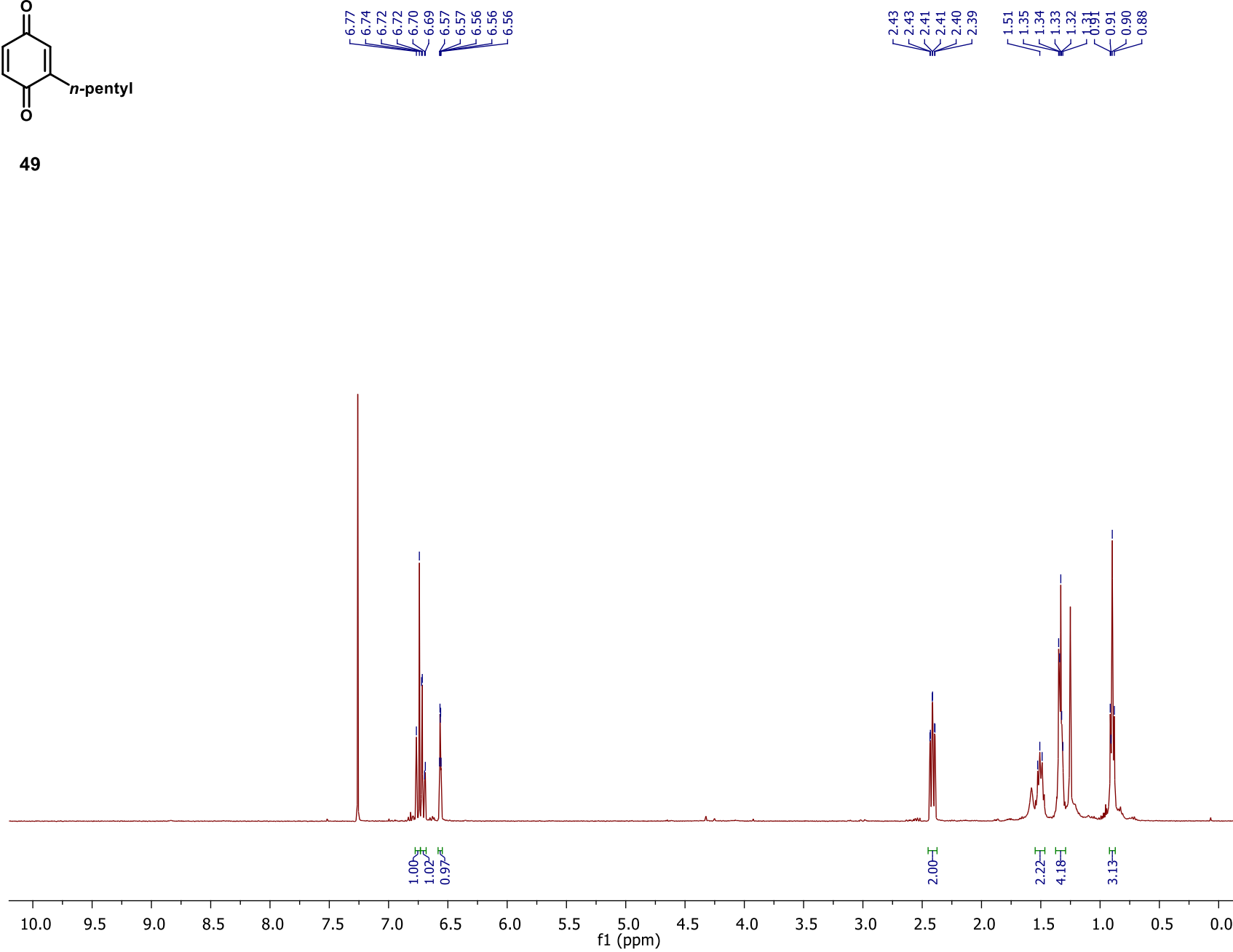


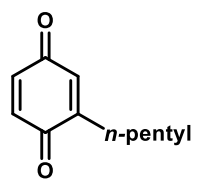
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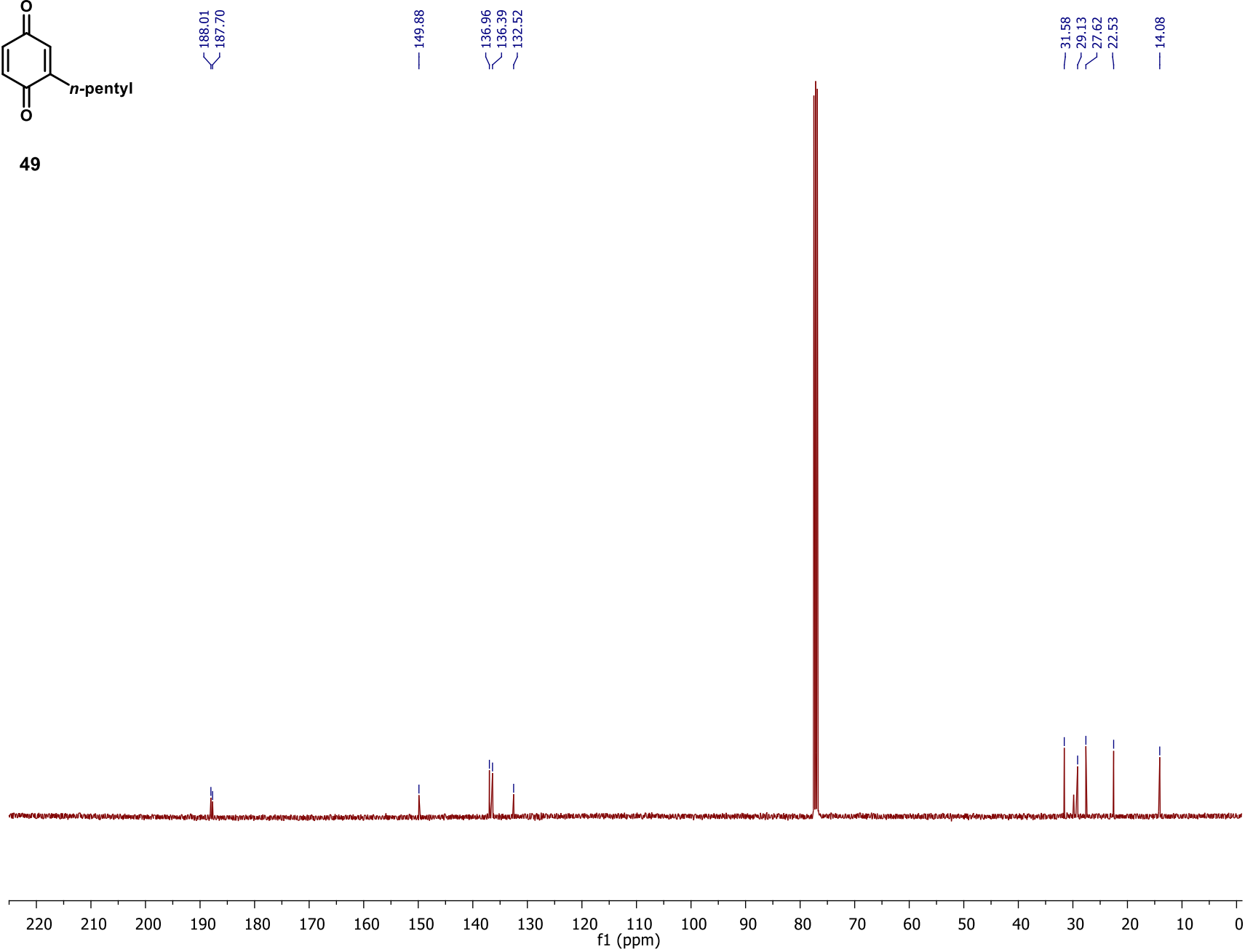


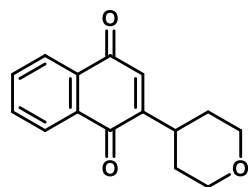
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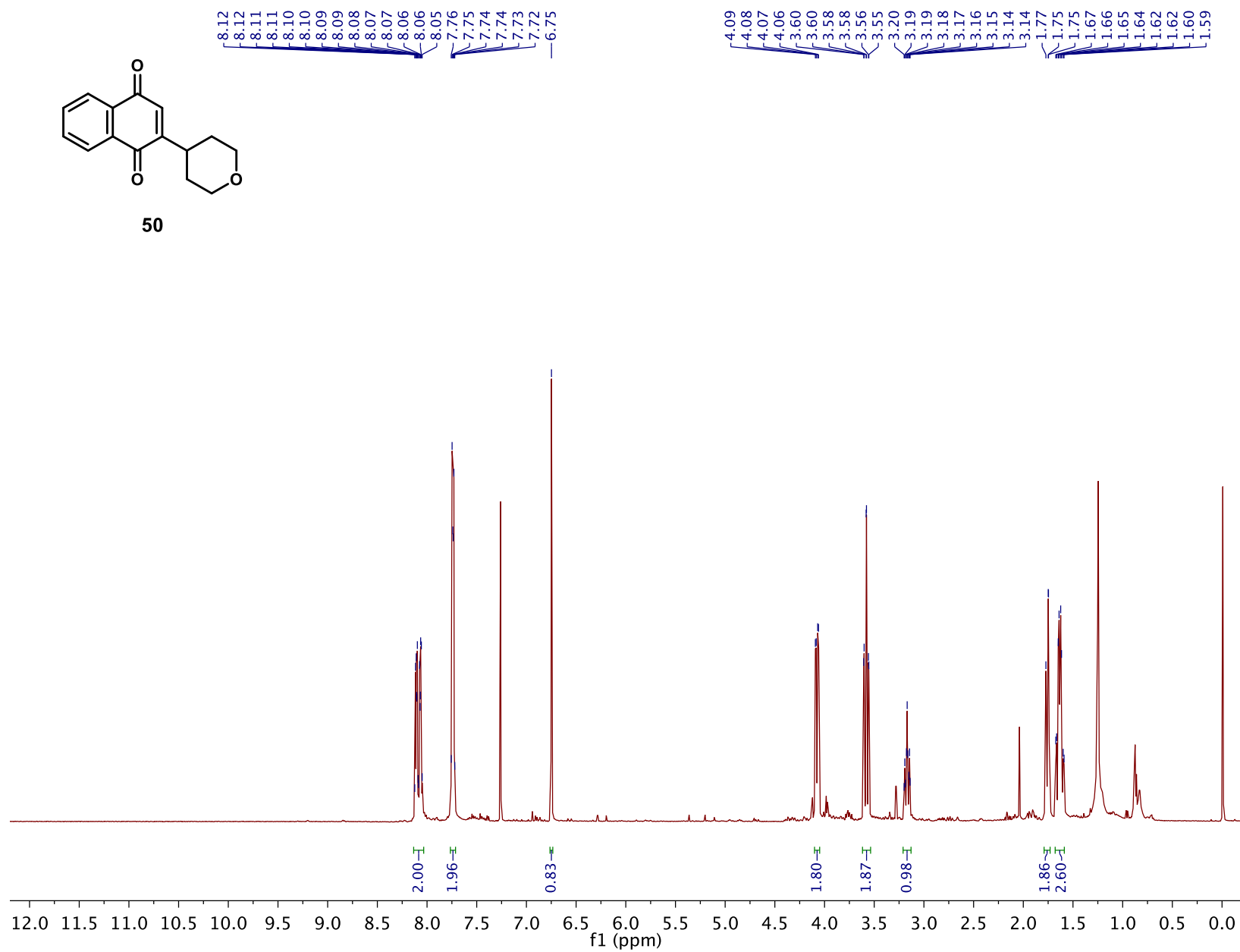


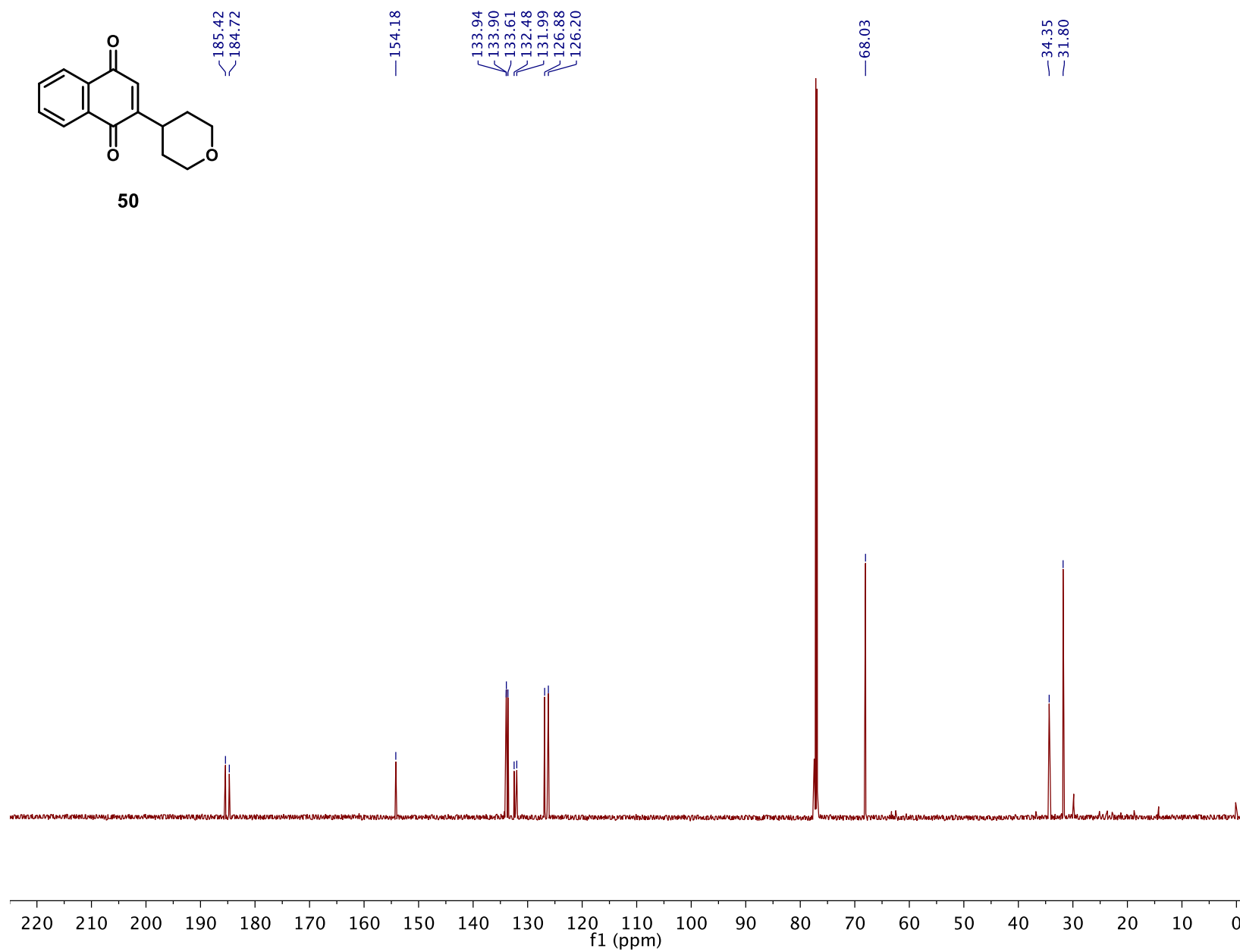
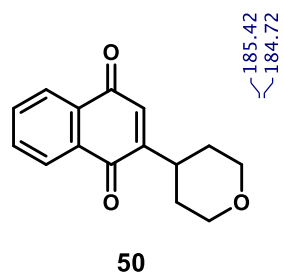
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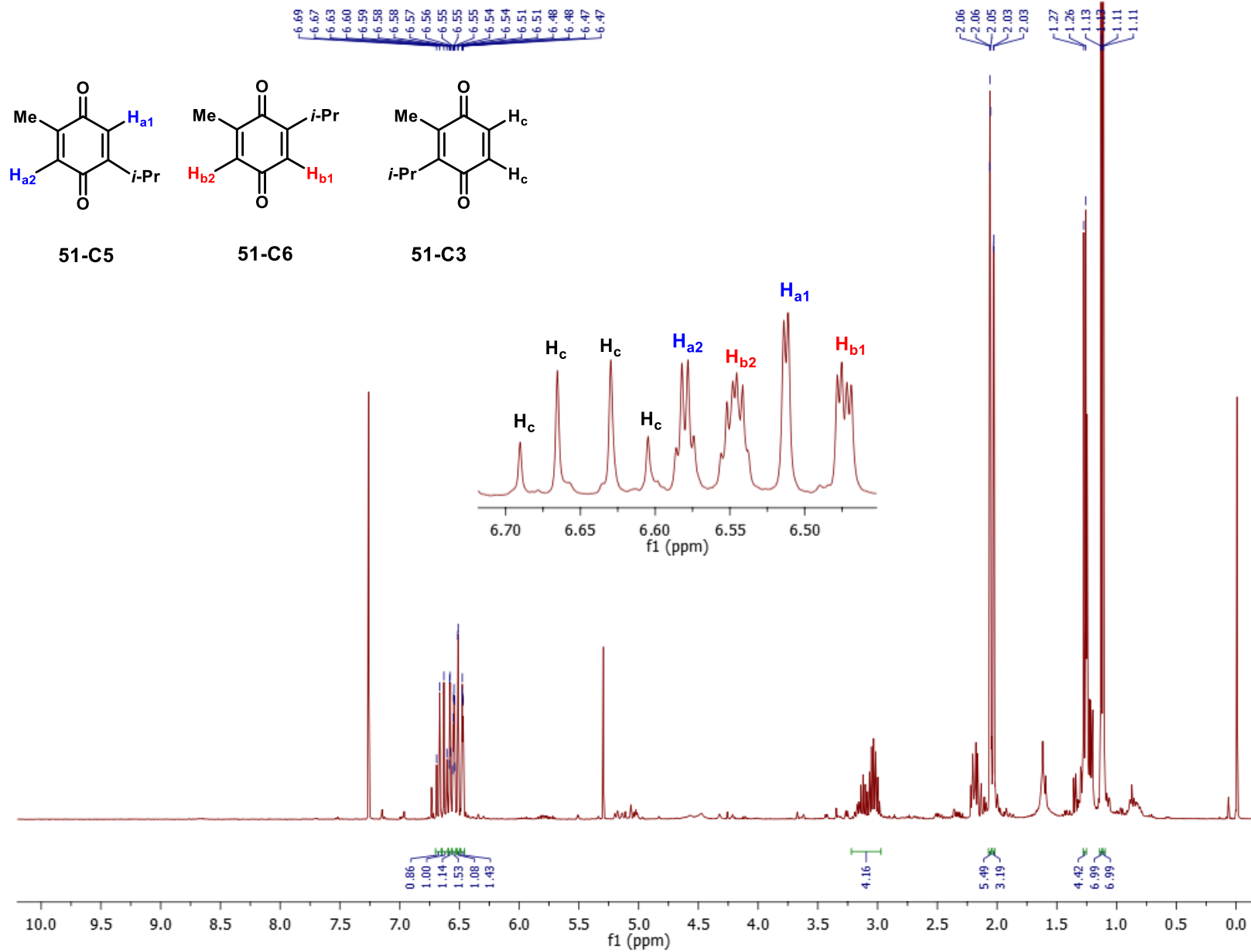


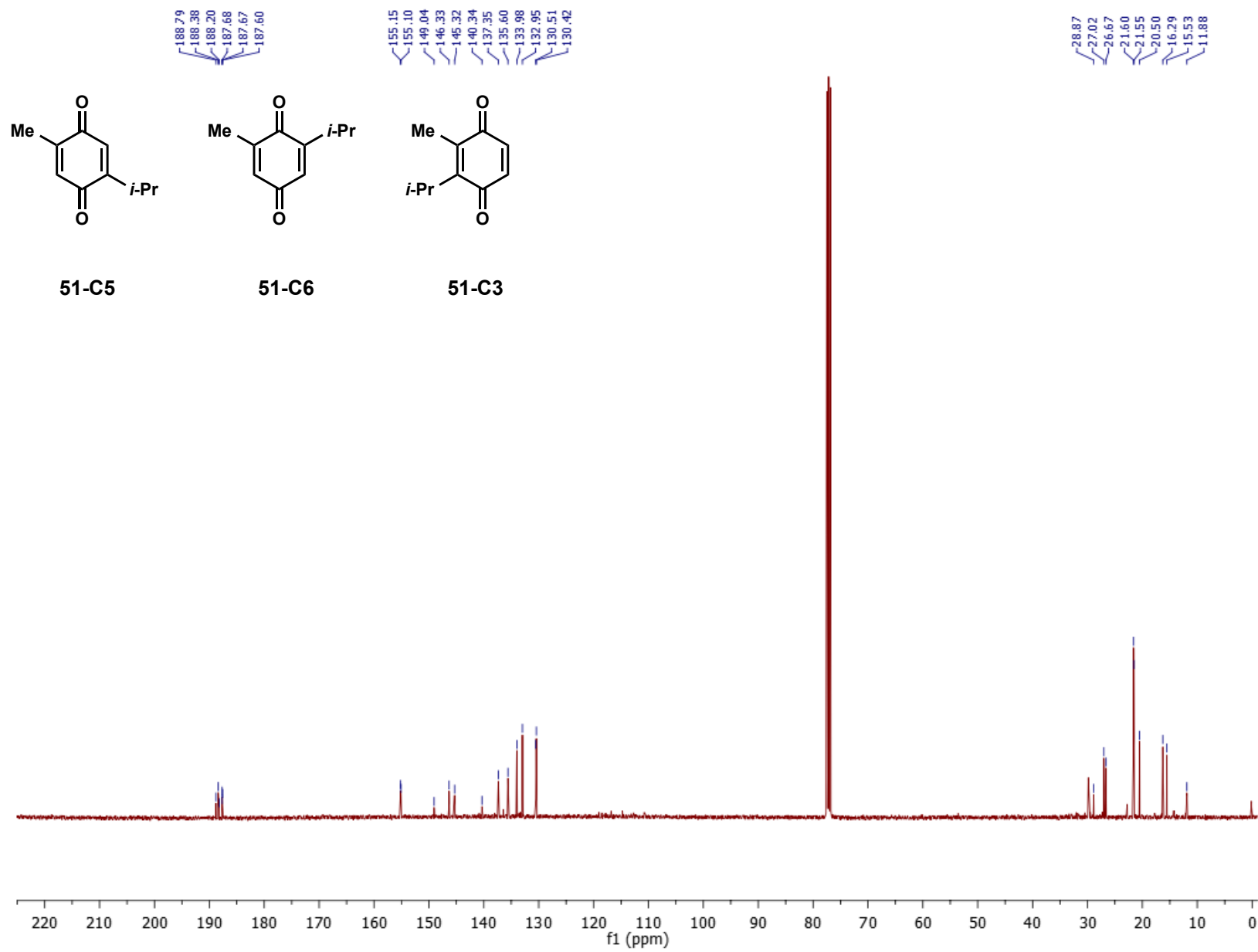


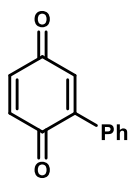
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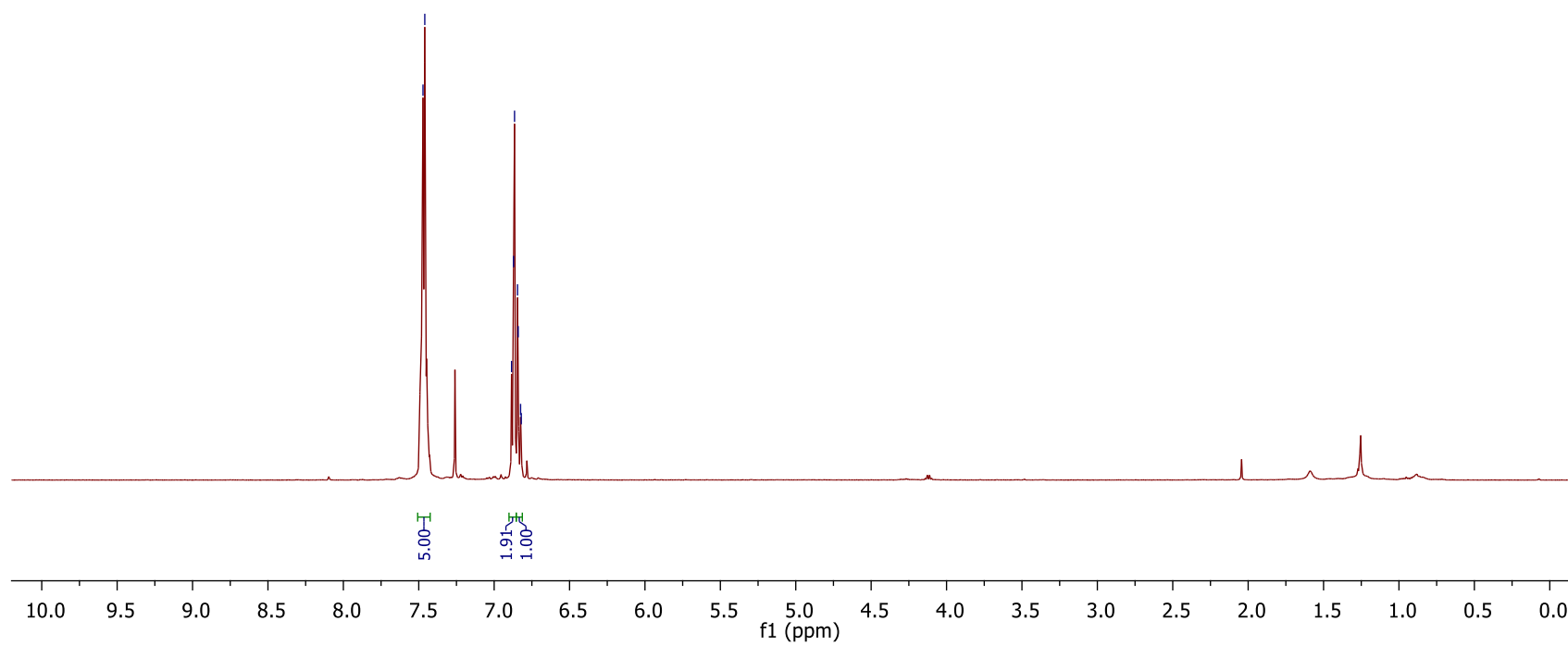


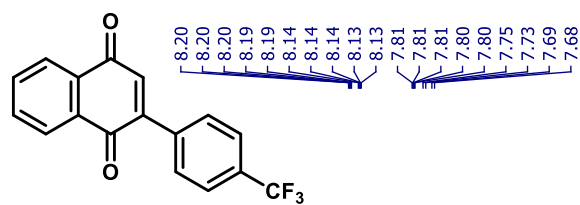




52

7.47
7.46
6.88
6.87
6.86
6.84
6.84
6.82
6.82





53

