Supplementary Information

Catalyst-free Electroreductive Carboxylic Acids −Nitroarenes Coupling

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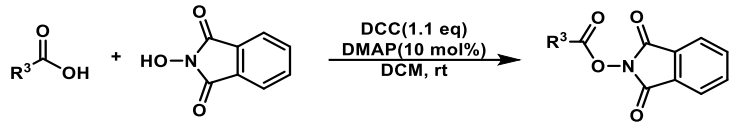
content

Supplementary Methods

General Methods. All reactions were performed in flame-dried glassware with magnetic stirring bar and sealed with a rubber septum. The solvents were distilled by standard methods. Reagents were obtained from commercial suppliers and used without further purification unless otherwise noted. Silica gel column chromatography was carried out using silica Gel 60 (230–400 mesh). Analytical thin layer chromatography (TLC) was done using silica Gel (silica gel 60 F254). TLC was performed on pre-coated silica gel plated, using short-wave UV light as the visualizing agent. NMR experiments were measured on a Bruker AVANCE III-400 spectrometer and carried out indeuterochloroform ($CDCl_3$) ^1H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz spectrometers respectively. ^{19}F NMR spectra were recorded at 377 MHz spectrometers. Chemical shifts are reported as δ valuesrelative to internal TMS (δ 0.00 for ^1H NMR), chloroform (δ 7.26 for ^1H NMR), chloroform (δ 77.00 for ^{13}C NMR). The following abbreviations are used for the multiplicities: s: singlet, d: doublet, dd:doublet of doublet, t: triplet, q: quadruplet, m: multiplet, br: broad signal for proton spectra; Coupling constants (J) are reported in Hertz (Hz). Melting points were uncorrected. HRMS were recorded on a Bruker microTOF-Q111. GC-MS spectra were performed on Shimadzu QP2010 (EI Source). A borosilicate glass tube was used as a reaction tube.

Synthesis of Starting Materials.

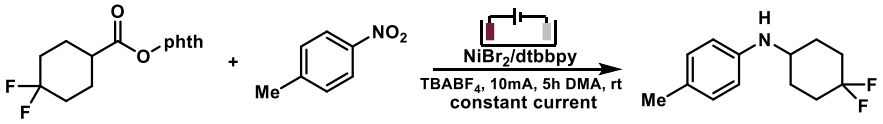
Synthesis of NHPI Redox-Active Esters (Procedure A)



NHPI esters were prepared according to a previously reported procedure.[1] Aroundbottom flask or culture tube was charged with carboxylic acid (1.0 equiv), Nhydroxyphthalimide (1.0-1.1 equiv) and 4-dimethylaminopyridine (0.1 equiv). CH_2Cl_2 was added (0.1-0.2 M), and the mixture was stirred vigorously. [Note: Carboxylic acid was added via syringe (if liquid)]. DCC (1.1 equiv) was then added dropwise via syringe, and the mixture was allowed to stir until the acid was consumed (determined by TLC). Typical reaction times were between 0.5 and 12 hours. The mixture was filtered (through a thin pad of Celite®, SiO_2, or frit funnel) and rinsed with additional CH_2Cl_2/Et_2O. Solvents were removed under reduced pressure, and purification of the crude mixture by column chromatography afforded the desired NHPI redox-active ester. If necessary, the NHPI redox-active ester could be further recrystallized from CH_2Cl_2/MeOH.

Optimization Tables

Supplementary Table 1. Optimization of anode/cathode

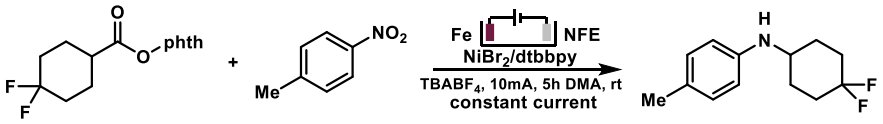


1, 0.3 mmol 2, 0.2 mmol 3

Entry	anode/cathode	yield[b]
1	Zn/NFE	14%
2	Fe/NFE	22%
3	Mg/NFE	n.d
4	SST/NFE	n.d
5	Fe/Zn	21%
6	Fe/Fe	22%
7	NFE/NFE	n.d
8	Zn/Zn	17%

[a] Reaction condition: 1 (0.3 mmol), 2 (0.2 mmol), catalyst (10 mol %), ligand (20% mol), $TBABF_4$(0.1 M), solvent (4 mL), 10 mA, 5h, under argon atmosphere ,rt. [b] detected by GC, Ph-Ph as internal standard.
NFE = nickel foamed electrode

Supplementary Table 2. Optimization of catalyst

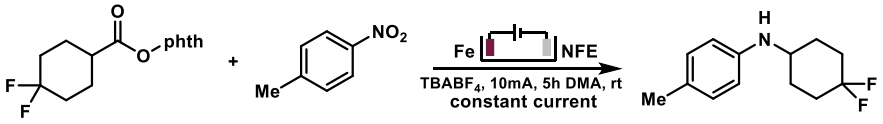


1, 0.3 mmol 2, 0.2 mmol 5

Entry	[M] catalyst	yield[b]
1	$NiBr_2$/dtbbpy	22%
2	$Ni(BF_4)_2$/dtbbpy	11%
3	-	25%
4	$FeCl_2 \bullet 4H_2O$	23%
5	$FeCl_2 \bullet 4H_2O$/TMSCl	20%

[a] Reaction condition: 1 (0.3 mmol), 2 (0.2 mmol), catalyst (10 mol %), ligand (20% mol), $TBABF_4$(0.1 M), solvent (4 mL), 10 mA, 5h, under argon atmosphere ,rt. [b] detected by GC, Ph-Ph as internal standard.
NFE = nickel foamed electrode

Supplementary Table 3. Optimization of solvent

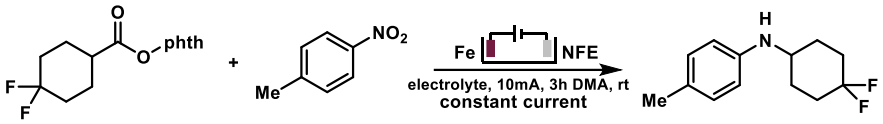


1, 0.3 mmol 2, 0.2 mmol 5

Entry	solvent	yield[b]
1	DMA	25%
2	DMSO	21%
3	NMP	23%
4	MeCN	15%

[a] Reaction condition: 1 (0.3 mmol), 2 (0.2 mmol), catalyst (10 mol %), ligand (20% mol), $TBABF_4$(0.1 M), solvent (4 mL), 10 mA, 5h, under argon atmosphere ,rt. [b] detected by GC, Ph-Ph as internal standard.
NFE = nickel foamed electrode

Supplementary Table 4. Optimization of electrolyte

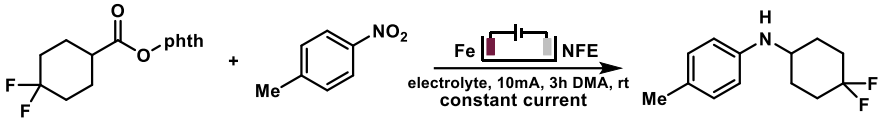


1, 0.3 mmol 2, 0.2 mmol 5

Entry	electrolyte	yield[b]
1	n-Bu_4BF_4	25%
2	n-Bu_4I	52%
3	n-Bu_4ClO_4	trace
4	n-Bu_4Br	77%
5	n-Bu_4PF_6	49%
6	LiBr	n.d
7	n-Bu_4OTs	57%

[a] Reaction condition: 1 (0.3 mmol), 2 (0.2 mmol), electrolyte(0.1 M), solvent(4 mL), 10 mA, 3h, under argon atmosphere ,rt. [b] detected by GC, Ph-Ph as internal standard.
NFE = nickel foamed electrode

Supplementary Table 5. Optimization of additive



1, 0.3 mmol 2, 0.2 mmol 5

Entry	addtive	yield[b]
1	HCl(3eq)	trace
2	AcOH(10eq)	trace
3	HFIP(0.5 mL)	trace
4	H_2O	n.d
5	TMSCl	21%
6	Hu`s condition: $FeCl_2$•$4H_2O$, TMSCl, Zn, NMP, 12h, 90oC/rt	n.d/n.d
7	$NiBr_2$, TMSCl, Zn, DMA, 12h, 90°C/rt	n.d/n.d

[a] Reaction condition: 1 (0.3 mmol), 2 (0.2 mmol), electrolyte(0.1 M), solvent(4 mL), 10 mA, 5h, under argon atmosphere ,rt. [b] detected by GC, Ph-Ph as internal standard.
NFE = nickel foamed electrode

Supplementary Table 6. The yield of the target product corresponding to different time and current

Time/h	1.5	2	3	6	12
Current/mA	20	15	10	5	2.5
Yield/%	65	72	77	43	13

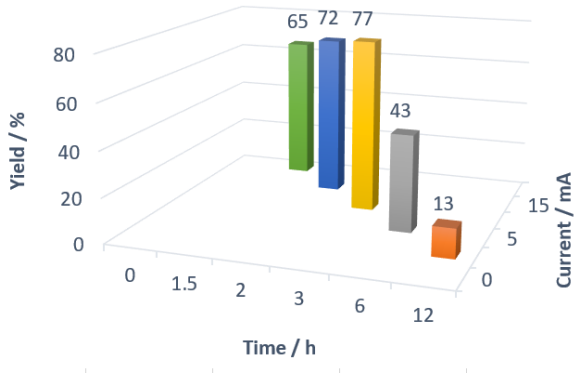


Fig 1. The yield of product 5

Supplementary Table 7. The yield of the byproduct (p-toluidine) corresponding to different time and current

Time/h	1.5	2	3	6	12
Current/mA	20	15	10	5	2.5
Yield/%	4	4	8	21	62

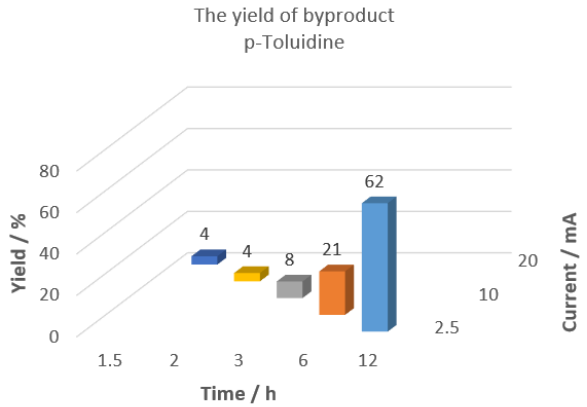
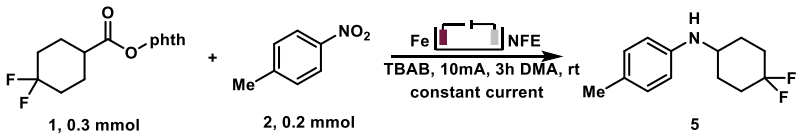


Fig 2. The yield of byproduct (p-toluidine)

General Procedure

Procedure for Decarboxylation ammoniation



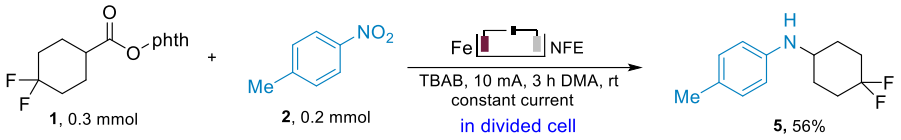
Method A (Procedure B)

In glovebox, an oven-dried undivided reactor (5 mL) equipped with the RAE **1** (0.3 mmol, 1.5 equiv, 92 mg), 1-methyl-4-nitrobenzene **2** (0.2 mmol, 1 equiv, 28 mg), TBAB (0.15 M, 200 mg) and a stir bar before adding DMA (4 mL). The reactor was equipped with Fe electrode (52.5 × 8 × 2 mm) as the anode and foamed nickel electrode (52.5 × 8 × 2 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA (The dual display potentiostat was operating in constant current mode) under room temperature for 3 h. When the reaction was completed, the solution was extract by ethyl acetate (3 × 15 mL), and the combined organic layers were concentrated with a rotary evaporator. The crude product was purified by PTLC to afford the corresponding product (Hexane: ethyl acetate=10:1).

Procedure C

The RAE 1 (0.3 mmol, 1.5 equiv, 92 mg), 1-methyl-4-nitrobenzene 2 (0.2 mmol, 1 equiv, 28 mg) were weighed directly into the cathode compartment divided by an anion-exchange membrane before adding DMA (5 mL). To the anode compartment was added 5.0 mL of DMA. To both the anode and cathode was added TBAB (0.15 M, 200 mg). Stir bars were added to both compartments and the reaction was stirred for 2 min before electrodes were inserted. The reactor was equipped with Fe electrode (10 × 8 × 2 mm) as the anode and foamed nickel electrode (10 × 8 × 2 mm) as the cathode. The electrodes were then connected to the potentiostat and controlled current electrolysis set at 10 mA for 3 h was initiated. When the reaction was completed, the solution was extract by ethyl acetate (3 × 15 mL), and the combined organic layers were concentrated with a rotary evaporator. The crude product was purified by PTLC to afford the corresponding product (Hexane: ethyl acetate=10:1)

In divided cell and catalyst-free:



In divided cell, 10 mol% $FeBr_2$ was added into the cathode tank:

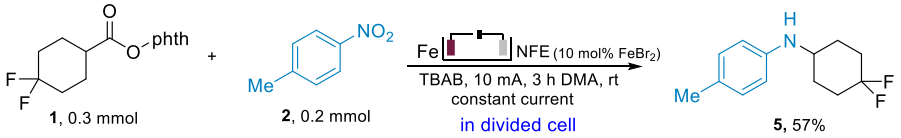
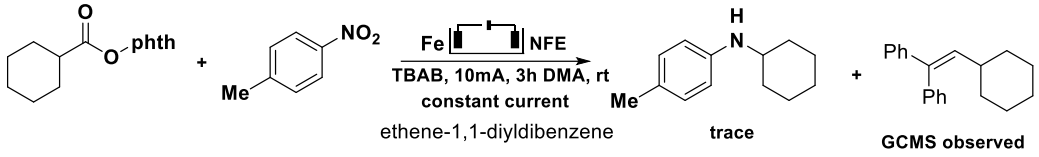


Fig. 3 During reaction. Fig. 4 After reaction. Fig. 5 anion-exchange membrane

we employed a divided electrolysis cell to avoid interference from sacrificial anode metal cations during the reaction process. Interestingly, we discovered that even with the use of an anion-exchange membrane to separate the anodic and cathodic electrolytic compartments, the cathodic electrolysis chamber still enabled give a 56% yield of the desired product. Subsequently, we introduced 10% mol FeBr2 into the cathode compartment of the same divided cell reactor, leading to a 57% yield of the desired product. This outcome closely aligns with the result obtained without the addition of the catalyst. This observation could potentially negate the hypothesis that the iron-catalyzed reaction leads to an increase in the target product yield.

Mechanistic Investigations

Radical trap experiments:



An oven-dried undivided reactor (5 mL) equipped with the RAE **1** (0.3 mmol, 1.5 equiv, 92 mg), 1-methyl-4-nitrobenzene **2** (0.2 mmol, 1 equiv, 28 mg), TBAB (0.15 M, 200 mg) and a stir bar before adding DMA (4 mL). The reactor was equipped with Fe electrode (52.5 × 8 × 2 mm) as the anode and foamed nickel electrode (52.5 × 8 × 2 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA (The dual display potentiostat was operating in constant current mode) under room temperature for 3 h. After the reaction was completed, 5 mL of saturated aqueous sodium bicarbonate solution and 10 ml x 3 of ethyl acetate were added and the combined organic layers was dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was monitored by GCMS.

Structural Stability of Metal Electrodes

For the anode:

We have investigated the correlation between electrode usage frequency and yield (see below). From the graph, it is evident that the anode material can be reused multiple times (10 times) with minimal impact on product yield. However, the electrode material does experience gradual corrosion over time. It is essential to emphasize that this phenomenon is inherent to the nature of electrochemistry. We are also exploring alternative methods to replace sacrificial anodes. For instance, the use of inert electrodes (carbon, platinum) as anodes, employing strategies such as external addition of reducing agents (triethylamine, etc.) to the reaction system. This is also an objective we plan to investigate in our future research.

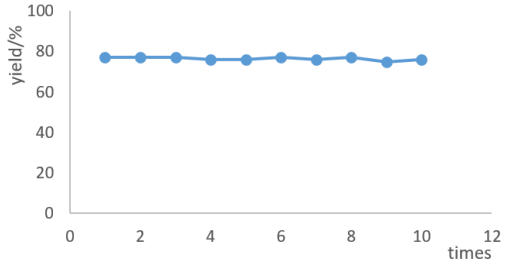


Fig. 6. The yield of product 5

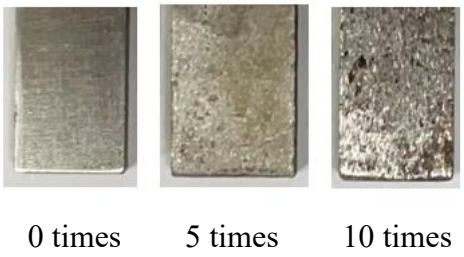


Fig. 7. Front photo of anode material (Fe)

For the cathode:

In fact, we consistently reuse the cathode material (nickel foam) throughout our experiments. This practice is supported by the absence of precipitated substances observed on the cathode surface following reactions. Upon completion of the reaction, the cathode can be directly reused after a cleaning process.

Furthermore, considering material stability, we investigated the impact of nickel foam with varying pore sizes on the reaction outcomes. The results indicate that nickel foam with different pore sizes has minimal influence on the reaction yield.

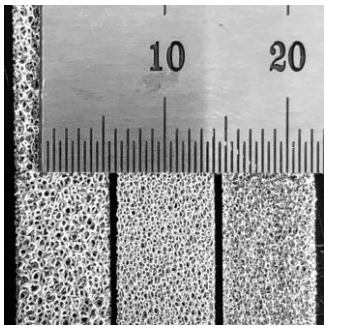


Fig. 8. Nickel foam with different pore sizes (left)

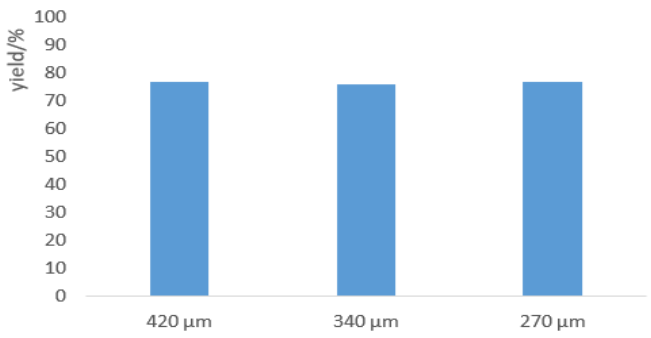
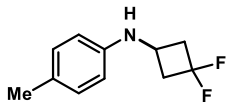


Fig. 9. The yield of product 5 under different NFE (right)

Characterization Data for Products

Compound 3

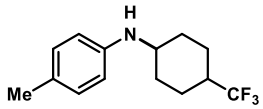


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 22.9 mg (58%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01 (d, J = 8.1 Hz, 2H), 6.48 (d, J = 8.4 Hz, 2H), 3.84 (dt, J = 11.1, 7.2 Hz, 1H), 3.72 (s, 1H), 3.13 – 2.79 (m, 2H), 2.48 – 2.30 (m, 2H), 2.25 (s, 3H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$)** δ 144.1, 129.9, 127.8, 122.7 (t, J = 121.74 Hz), 113.4, 43.4 (t, J = 21.5 Hz), 38.5 (t, J = 5.6 Hz), 20.4 (s) ppm. **^{19}F NMR (377 MHz, $CDCl_3$)** δ -75.78 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{11}H_{14}F_2N$ $[M+H]^+$: 198.1094, found: 198.1095.

Compound 4

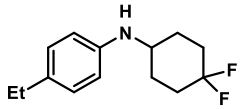


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 27.3 mg (53%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 8.0 Hz, 2H), 6.60 – 6.33 (m, 2H), 3.20 (ddd, *J* = 15.0, 7.5, 3.8 Hz, 1H), 2.94 (s, 1H), 2.24 (d, *J* = 8.5 Hz, 5H), 2.09 – 1.91 (m, 3H), 1.45 (qd, *J* = 13.5, 3.2 Hz, 2H), 1.20 – 0.95 (m, 2H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 144.6, 129.8, 127.6 (q, *J* = 278.5 Hz), 126.7, 113.5, 51.7, 41.5 (q, *J* = 26.6 Hz), 32.0, 24.1 (q, *J* = 2.5 Hz), 20.3 (s) ppm. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -73.52 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{14}H_{19}F_3N$ $[M+H]^+$: 258.1470, found: 258.1470.

Compound 5

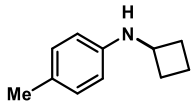


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 30.7 mg (64%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.02 (d, *J* = 8.2 Hz, 2H), 6.62 – 6.46 (m, 2H), 3.40 (t, *J* = 9.8 Hz, 2H), 2.55 (q, *J* = 7.6 Hz, 2H), 2.21 – 2.03 (m, 4H), 1.99 – 1.71 (m, 2H), 1.66 – 1.44 (m, 2H), 1.20 (t, *J* = 7.6 Hz, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 144.7, 133.6, 128.7, 122.9 (t, *J* = 242.4 Hz), 113.5, 49.8, 32.0 (t, *J* = 24.7 Hz), 28.9 (d, *J* = 10.0 Hz), 27.9, 15.9 (s) ppm. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -95.53 (d, *J* = 238.7 Hz), -99.85 (d, *J* = 230.3 Hz) ppm. **HRMS (ESI-TOF):** calculated for $C_{14}H_{20}F_2N$ $[M+H]^+$: 240.1564, found: 240.1564.

Compound 6

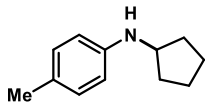


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 20.1 mg (62%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 8.0 Hz, 2H), 6.57 – 6.37 (m, 2H), 3.91 (ddt, *J* = 12.1, 8.6, 4.2 Hz, 1H), 3.67 (s, 1H), 2.51 – 2.34 (m, 2H), 2.24 (s, 3H), 1.95 – 1.66 (m, 4H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 144.9, 129.7, 126.5, 113.2, 49.3, 31.3, 20.4, 15.2 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{11}H_{16}N$ $[M+H]^+$: 162.1283, found: 162.1284.

Compound 7

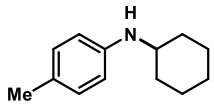


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 27.1 mg (77%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99 (d, *J* = 8.0 Hz, 2H), 6.62 – 6.46 (m, 2H), 3.88 – 3.68 (m, 1H), 3.39 (s, 1H), 2.25 (s, 3H), 2.12 – 1.92 (m, 2H), 1.80 – 1.67 (m, 2H), 1.67 – 1.53 (m, 2H), 1.53 – 1.35 (m, 2H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.8, 129.7, 126.1, 113.4, 54.9, 33.6, 24.1, 20.4 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{12}H_{18}N$ $[M+H]^+$: 176.1439, found: 176.1439.

Compound 8

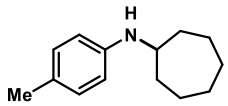


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 30.4 mg (80%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (d, *J* = 8.0 Hz, 2H), 6.63 – 6.40 (m, 2H), 3.22 (tt, *J* = 10.1, 3.7 Hz, 2H), 2.23 (s, 3H), 2.13 – 1.98 (m, 2H), 1.81 – 1.71 (m, 2H), 1.70 – 1.60 (m, 1H), 1.47 – 1.30 (m, 2H), 1.28 – 1.19 (m, 1H), 1.13 (ddd, *J* = 15.0, 12.7, 3.2 Hz, 2H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.1, 129.7, 126.1, 113.5, 52.1, 33.5, 26.0, 25.0, 20.3 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{13}H_{20}N$ $[M+H]^+$: 190.1596, found: 190.1597.

Compound 9



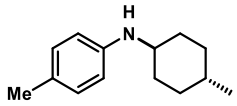
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 30.6 mg (75%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 8.3 Hz, 2H), 6.49 (d, *J* = 8.3 Hz, 2H), 3.43 (tt, *J* = 7.9, 3.9 Hz, 2H), 2.24 (s, 3H), 2.08 – 1.91 (m, 2H), 1.77 – 1.36 (m, 10H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.1, 129.7, 126.0, 113.5, 53.9, 34.8, 28.3, 24.4,

20.37 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{14}H_{21}N$ $[M+H]^+$: 204.1752, found: 204.1752.

Compound 10

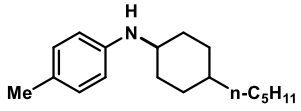


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 27.3 mg (67%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (d, *J* = 8.2 Hz, 3H), 6.61 – 6.34 (m, 3H), 3.33 – 2.96 (m, 3H), 2.23 (s, 3H), 2.17 – 2.03 (m, 2H), 1.84 – 1.63 (m, 2H), 1.42 – 1.34 (m, 1H), 1.16 – 1.00 (m, 4H), 0.92 (d, *J* = 6.5 Hz, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.2, 129.7, 126.1, 113.5, 52.4, 34.1, 33.6, 32.3, 22.2, 20.3 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{14}H_{21}N$ $[M+H]^+$: 204.1752, found: 204.1752.

Compound 11

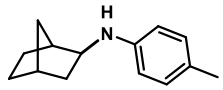


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 29.1 mg (56%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (d, *J* = 8.4 Hz, 2H), 6.53 (t, *J* = 5.5 Hz, 2H), 3.27 – 3.05 (m, 1H), 2.86 (s, 1H), 2.23 (s, 3H), 2.19 – 2.01 (m, 2H), 1.81 (d, *J* = 12.2 Hz, 2H), 1.37 – 1.16 (m, 10H), 1.15 – 0.95 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.2, 129.7, 126.1, 113.5, 52.8, 37.3, 36.9, 33.6, 32.2, 3.1, 26.80, 22.7, 20.3, 14.1 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{18}H_{30}N$ $[M+H]^+$: 260.2378, found: 260.2378.

Compound 12

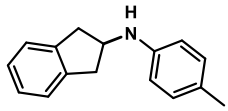


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 25.8 mg (64%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 8.1 Hz, 2H), 6.60 – 6.34 (m, 2H), 3.39 (d, *J* = 7.5 Hz, 1H), 3.29 – 3.09 (m, 1H), 2.28 (dd, *J* = 3.1, 1.4 Hz, 2H), 2.20 (s, 3H), 1.81 (ddd, *J* = 12.8, 7.6, 2.4 Hz, 1H), 1.65 – 1.49 (m, 2H), 1.46 – 1.38 (m, 1H), 1.34 – 1.03 (m, 4H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.4, 129.6, 126.0, 113.3, 56.9, 41.1 (d, *J* = 2.1 Hz), 35.6, 35.2, 28.4, 26.4, 20.3 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{14}H_{20}N$ $[M+H]^+$: 202.1596, found: 202.1541.

Compound 13

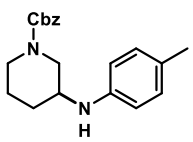


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 27.8 mg (62%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (ddd, *J* = 21.7, 5.3, 3.4 Hz, 4H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.55 (d, *J* = 8.4 Hz, 2H), 4.32 (ddd, *J* = 6.8, 4.4, 2.4 Hz, 1H), 3.72 (s, 1H), 3.33 (dd, *J* = 16.0, 6.8 Hz, 2H), 2.86 (dd, *J* = 15.9, 4.4 Hz, 2H), 2.24 (s, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.1, 141.5, 129.8, 126.7, 126.6, 125.0, 113.7, 54.3, 40.2, 20.4 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{16}H_{17}N$ $[M+H]^+$: 224.1439, found: 224.1438.

Compound 14



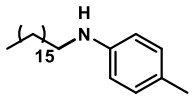
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded

53 mg (82%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.21 (m, 5H), 6.94 (s, 2H), 6.51 (s, 2H), 5.13 (q, *J* = 12.0 Hz, 2H), 4.10 (d, *J* = 6.8 Hz, 1H), 3.91 – 3.61 (m, 1H), 3.35 (s, 1H), 3.10 (s, 1H), 2.99 – 2.71 (m, 1H), 2.22 (s, 3H), 2.07 – 1.89 (m, 1H), 1.74 (dd, *J* = 9.0, 4.2 Hz, 1H), 1.51 (dd, *J* = 27.7, 18.3 Hz, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 155.4, 144.2, 136.7, 129.9, 128.5, 128.0, 127.9, 126.8, 113.3, 67.2, 49.2, 44.4, 30.8, 20.4 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{20}H_{25}N_2O_2$ $[M+H]^+$: 325.1916, found: 325.1916.

Compound 15

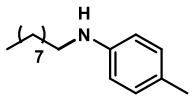


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 39.5 mg (61%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 8.2 Hz, 2H), 6.53 (d, *J* = 8.4 Hz, 2H), 3.41 (s, 1H), 3.07 (t, *J* = 7.1 Hz, 1H), 2.23 (s, 3H), 1.60 (dt, *J* = 14.5, 7.1 Hz, 2H), 1.26 (s, 28H), 0.88 (t, *J* = 6.8 Hz, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 146.3, 129.7, 126.2, 112.9, 44.4, 31.9, 29.72, 29.71, 29.70, 29.6, 29.65, 29.62, 29.4, 29.3, 27.2, 22.71, 20.3, 14.1 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{24}H_{44}N$ $[M+H]^+$: 325.1916, found: 325.1916.

Compound 16

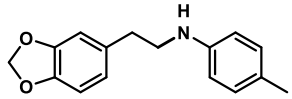


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 29.3 mg (63%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 8.1 Hz, 2H), 6.63 – 6.45 (m, 2H), 3.08 (t, *J* = 7.1 Hz, 3H), 2.24 (s, 3H), 1.69 – 1.51 (m, 2H), 1.42 – 1.14 (m, 14H), 0.89 (t, *J* = 6.9 Hz, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 146.3, 129.7, 126.3, 112.9, 44.4, 31.8, 29.6, 29.5, 29.4, 29.29, 27.20, 22.6, 20.3, 14.1 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{16}H_{28}N$ $[M+H]^+$: 234.2222, found: 234.2222.

Compound 17

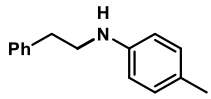


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 21.9 mg (43%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (d, *J* = 8.2 Hz, 2H), 6.74 (dd, *J* = 17.9, 4.7 Hz, 2H), 6.67 (dd, *J* = 7.9, 1.6 Hz, 1H), 6.59 – 6.50 (m, 2H), 5.94 (s, 2H), 3.34 (t, *J* = 6.9 Hz, 3H), 2.83 (t, *J* = 6.9 Hz, 2H), 2.25 (s, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 147.8, 146.1, 145.6, 133.1, 129.7, 126.8, 121.6, 113.2, 109.1, 108.3, 100.8, 45.6, 35.2, 20.4 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{16}H_{18}NO_2$ $[M+H]^+$: 256.1338, found: 256.1337.

Compound 18

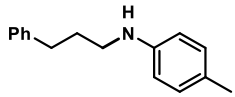


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 19.8 mg (47%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (t, *J* = 7.4 Hz, 2H), 7.23 (dd, *J* = 12.0, 5.0 Hz, 3H), 6.99 (d, *J* = 8.2 Hz, 2H), 6.55 (d, *J* = 8.4 Hz, 2H), 3.38 (t, *J* = 7.0 Hz, 3H), 2.91 (t, *J* = 7.0 Hz, 2H), 2.24 (s, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.7, 139.4, 129.7, 128.8, 128.5, 126.7, 126.3, 113.2, 45.4, 35.5, 20.4 (s). ppm**. HRMS (ESI-TOF):** calculated for $C_{15}H_{18}N$ $[M+H]^+$: 212.1439, found: 212.1437.

Compound 19

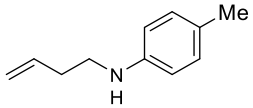


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 23.3 mg (51%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (dd, *J* = 14.1, 6.9 Hz, 2H), 7.19 (dd, *J* = 5.3, 2.5 Hz, 3H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.60 – 6.33 (m, 2H), 3.13 (t, *J* = 7.0 Hz, 3H), 2.81 – 2.53 (m, 2H), 2.23 (s, 3H), 1.94 (td, *J* = 14.1, 7.1 Hz, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 146.0, 141.7, 129.7, 128.4, 126.5, 125.9, 113.0, 43.8, 33.4, 31.1, 20.3 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{16}H_{20}N$ $[M+H]^+$: 226.1596, found: 226.1596.

Compound 20

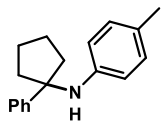


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 13.2 mg (41%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.03 – 6.94 (m, 2H), 6.58 – 6.50 (m, 2H), 5.82 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H), 5.19 – 5.06 (m, 2H), 3.16 (t, J = 6.7 Hz, 2H), 2.37 (qt, J = 6.8, 1.4 Hz, 2H), 2.23 (s, 3H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 146.0, 135.8, 126.6, 117.0, 113.1, 43.2, 33.6, 20.3. ppm. **HRMS (ESI-TOF):** calculated for $C_{11}H_{16}N$ $[M+H]^+$: 162.1283, found: 162.1285.

Compound 21



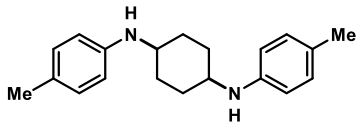
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded

22.3 mg (45%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (dt, *J* = 8.3, 1.7 Hz, 2H), 7.36 – 7.26 (m, 2H), 7.22 – 7.13 (m, 1H), 6.83 (d, *J* = 8.1 Hz, 2H), 6.40 – 6.09 (m, 2H), 3.96 (s, 1H), 2.16 (s, 3H), 2.10 (dd, *J* = 11.3, 6.1 Hz, 4H), 1.92 – 1.70 (m, 4H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 146.7, 143.5, 129.2, 128.3, 126.1, 125.9, 122.1, 115.3, 67.0, 40.7, 24.1, 20.3 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{18}H_{22}N$ $[M+H]^+$: 252.1752, found: 252.1753.

Compound 22

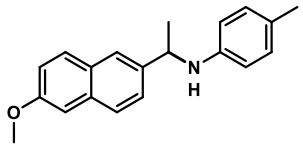


0.20 mmol scale. Purification by column chromatography (petroleum ether/ethyl acetate = 5:1) afforded 27.1 mg (46%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (d, *J* = 8.2 Hz, 4H), 6.53 (d, *J* = 8.4 Hz, 4H), 3.71 – 2.75 (m, 4H), 2.23 (s, 6H), 2.18 (d, *J* = 6.6 Hz, 4H), 1.33 – 0.99 (m, 4H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.0, 129.8, 126.4, 113.5, 52.1, 32.3, 20.3 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{20}H_{26}N_2$ $[M+H]^+$: 295.2174, found: 295.2172.

Compound 23



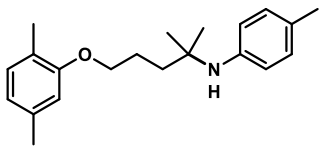
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 5:1) afforded 39.6 mg (68%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 – 7.61 (m, 3H), 7.45 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.15 – 7.04 (m, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.53 – 6.30 (m, 2H), 4.56 (q, *J* = 6.7 Hz,

1H), 3.96 (s, 1H), 3.88 (s, 3H), 2.16 (s, 3H), 1.55 (d, *J* = 6.7 Hz, 3H). ppm. **^{13}C NMR (100 MHz, CDCl$_3$):** δ 157.4, 145.1, 140.7, 133.8, 129.6, 129.3, 129.0, 127.2, 126.4, 125.0, 124.1, 118.7, 113.5, 105.7, 55.3, 53.8, 25.0, 20.3 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{20}H_{22}NO$ $[M+H]^+$: 292.1701, found: 292.1702.

Compound 24

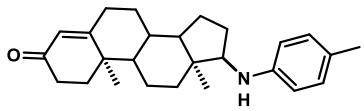


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 5:1) afforded 32.9 mg (53%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ 6.97 (dd, *J* = 15.2, 7.7 Hz, 3H), 6.76 – 6.62 (m, 3H), 6.58 (s, 1H), 3.91 (t, *J* = 6.0 Hz, 2H), 3.09 (s, 1H), 2.29 (s, 3H), 2.23 (s, 3H), 2.17 (s, 3H), 1.93 – 1.82 (m, 2H), 1.80 – 1.67 (m, 2H), 1.29 (s, 6H). ppm. **^{13}C NMR (100 MHz, CDCl$_3$):** δ 157.0, 144.1, 136.4, 130.3, 129.5, 128.0, 123.5, 120.6, 118.1, 111.9, 68.0, 53.7, 38.0, 28.5, 24.4, 21.4, 20.4, 15.8 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{21}H_{30}NO$ $[M+H]^+$: 312.2327, found: 312.2327.

Compound 25



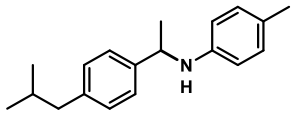
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 2:1) afforded 36.9 mg (49%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ 6.94 (d, *J* = 8.2 Hz, 2H), 6.47 (d, *J* = 8.4 Hz, 2H), 5.72 (s, 1H), 3.51 (s, 1H), 3.44 (dd, *J* = 7.4, 1.2 Hz, 1H), 2.46 – 2.27 (m, 6H), 2.21 (s, 3H), 1.99 (ddd, *J* = 13.4, 4.9, 3.3 Hz, 1H), 1.94 – 1.83 (m, 1H), 1.84 – 1.72 (m, 1H), 1.65 – 1.52 (m, 4H), 1.48 – 1.35 (m, 3H), 1.31 – 1.21 (m, 3H), 1.17 (s, 3H), 0.89 (s, 3H). ppm. **^{13}C NMR (100 MHz, CDCl$_3$):** δ 199.5, 171.2, 145.9, 129.6, 123.8, 115.2, 112.7, 61.8,

53.5, 49.9, 45.4, 38.6, 36.0, 35.6, 33.9, 33.0, 32.8, 32.3, 31.6, 24.7, 20.7, 20.3, 18.5, 17.4 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{26}H_{36}NO$ $[M+H]^+$: 378.2797, found: 378.2796.

Compound 26

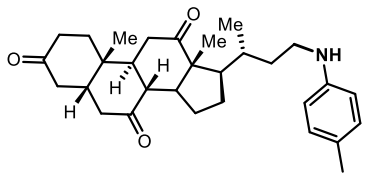


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 32.5 mg (61%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.2 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 6.44 (d, *J* = 8.4 Hz, 2H), 4.43 (q, *J* = 6.7 Hz, 1H), 3.85 (s, 1H), 2.43 (d, *J* = 7.2 Hz, 2H), 2.18 (s, 3H), 1.83 (dp, *J* = 13.5, 6.7 Hz, 1H), 1.48 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 6H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.1, 142.6, 140.1, 129.6, 129.3, 126.2, 125.6, 113.4, 53.4, 45.1, 30.2, 24.8, 22.4 (d, *J* = 1.2 Hz), 20.3 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{19}H_{25}N$ $[M+H]^+$: 268.2065, found: 268.2065.

Compound 27



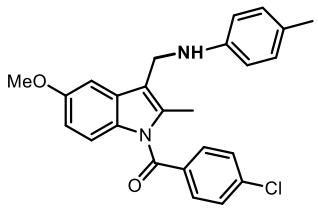
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 2:1) afforded 43.5 mg (47%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 8.1 Hz, 2H), 6.53 (d, *J* = 8.4 Hz, 2H), 2.99 – 2.79 (m, 3H), 2.36 – 2.28 (m, 4H), 2.23 (s, 3H), 2.21 – 2.11 (m, 4H), 2.10 – 1.92 (m, 6H), 1.89 – 1.72 (m, 3H), 1.62 (dt, *J* = 14.3, 7.2 Hz, 1H), 1.40 (s, 3H), 1.29 (ddd, *J* = 23.5, 12.6, 4.6 Hz, 3H), 1.09 (s, 3H), 0.92 (d, *J* = 6.1 Hz, 3H). ppm. **^{13}C NMR (100**

MHz, $CDCl_3$): δ 211.9, 209.0, 208.7, 146.2, 129.7, 126.3, 112.9, 56.9, 51.7, 49.0, 46.8, 45.9, 45.5, 45.0, 42.8, 42.1, 38.6, 36.5, 36.0, 35.4, 35.2, 34.3, 27.8, 25.1, 21.9, 20.3, 19.2, 11.8 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{30}H_{42}NO_3$ $[M+H]^+$: 464.3165, found: 464.3166.

Compound 28

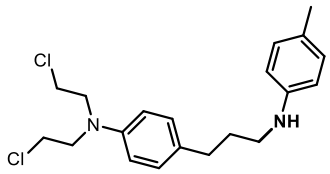


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 1:1) afforded 51.8 mg (62%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (dt, *J* = 7.0, 3.5 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.70 – 7.64 (m, 2H), 7.50 – 7.44 (m, 2H), 6.90 (dd, *J* = 9.3, 6.3 Hz, 1H), 6.79 (d, *J* = 2.7 Hz, 1H), 6.68 – 6.59 (m, 1H), 3.85 (s, 2H), 3.82 (s, 1H), 3.71 (s, 3H), 2.34 (s, 3H), 2.18 (s, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 167.9, 155.8, 141.9, 139.1, 135.1, 134.3, 132.6, 131.1, 129.9, 129.1, 127.8, 123.6, 116.5, 116.0, 114.9, 111.6, 101.6, 55.5, 26.3, 20.6, 13.4 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{25}H_{24}ClN_2O_3$ $[M+H]^+$: 419.1526, found: 419.1525.

Compound 29

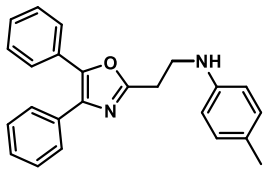


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 5:1) afforded 47 mg (65%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (d, *J* = 8.7 Hz, 2H), 6.85 (dd, *J* = 11.4, 3.4 Hz, 2H), 6.63 (ddd, *J* = 15.2, 8.5, 5.4 Hz, 3H), 3.76 – 3.67 (m, 4H), 3.67 – 3.53 (m, 4H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.55 – 2.43 (m, 2H), 2.24 (s, 3H), 1.98 – 1.74 (m, 2H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 144.2, 141.3, 131.4, 130.0, 129.6, 127.3, 115.8, 112.2, 53.6, 40.5, 34.5, 30.6, 30.5, 20.5 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{20}H_{28}Cl_2N_2$ $[M+H]^+$: 365.1551, found: 365.1528.

Compound 30

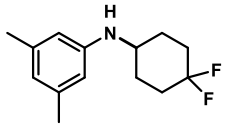


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 5:1) afforded 34.6 mg (49%).

Physical State: white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.60 (m, 2H), 7.55 (ddd, *J* = 7.2, 3.9, 1.5 Hz, 2H), 7.40 – 7.26 (m, 6H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.64 – 6.57 (m, 2H), 4.05 (s, 1H), 3.65 (t, *J* = 6.6 Hz, 2H), 3.14 (t, *J* = 6.6 Hz, 2H), 2.24 (s, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 161.5, 145.3, 135.1, 132.4, 129.8, 128.9, 128.6, 128.5, 128.5, 128.1, 127.9, 127.0, 126.5, 126.4, 113.4, 41.6, 28.1, 20.4 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{24}H_{23}N_2O$ $[M+H]^+$: 355.1810, found: 355.1762.

Compound 31



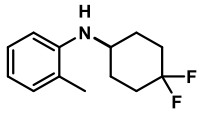
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 33 mg (71%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.39 (s, 1H), 6.25 (s, 2H), 3.42 (t, *J* = 9.3 Hz, 2H), 2.25 (s, 6H), 2.11 (dd, *J* = 11.3, 4.2 Hz, 4H), 2.01 – 1.74 (m, 2H), 1.67 – 1.42 (m, 2H). ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9, 139.1, 122.9 (t, *J* = 241.2 Hz), 119.6, 111.2, 49.4, 32.0 (t, *J* = 24.7 Hz), 28.9 (d, *J* = 10.0 Hz), 21.5 (s). ppm. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -95.50 (d, *J* = 237.7 Hz), -99.88 (d, *J* = 237.4 Hz). ppm. **HRMS (ESI-TOF):** calculated for $C_{14}H_{20}F_2N$ $[M+H]^+$: 240.1564, found: 240.1564.

Compound 32

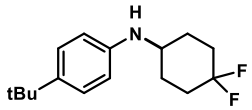


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 33.3 mg (74%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 – 7.08 (m, 1H), 7.06 (d, *J* = 7.3 Hz, 1H), 6.70 – 6.57 (m, 2H), 3.49 (dd, *J* = 13.3, 5.9 Hz, 1H), 3.36 (s, 1H), 2.22 – 2.04 (m, 7H), 2.01 – 1.79 (m, 2H), 1.59 (dt, *J* = 15.0, 6.6 Hz, 2H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 144.7, 130.4, 127.1, 122.9 (t, *J* = 241.2 Hz), 122.0, 117.1, 110.2, 49.3, 32.1 (t, *J* = 24.7 Hz), 28.9 (d, *J* = 10.0 Hz), 17.5 (s). ppm. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -91.87 (d, *J* = 237.0 Hz), -95.56 (d, *J* = 238.3 Hz), -99.86 (d, *J* = 239.4 Hz), -102.60 (d, *J* = 237.1 Hz). ppm. **HRMS (ESI-TOF):** calculated for $C_{13}H_{18}F_2N$ $[M+H]^+$: 226.1407, found: 26.1406.

Compound 33



0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 38.5 mg (72%).

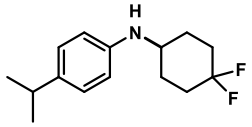
Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 – 7.10 (m, 2H), 6.62 – 6.42 (m, 2H), 3.40 (t, *J* = 9.7 Hz, 2H), 2.20 – 2.01 (m, 4H), 1.87 (dtd, *J* = 21.5, 14.9, 5.3 Hz, 2H), 1.64 – 1.44 (m, 2H), 1.27 (s, 9H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 144.4, 140.4, 126.1, 122.9 (t, *J* = 241.2 Hz), 113.0, 49.7, 32.0 (t, *J* = 24.6 Hz), 31.5, 28.9 (d, *J* = 10.0 Hz). ppm. **^{19}F**

NMR (377 MHz, $CDCl_3$): δ -95.60 (d, *J* = 237.3 Hz), -99.73 (d, *J* = 237.2 Hz). ppm.

HRMS (ESI-TOF): calculated for $C_{16}H_{24}F_2N$ $[M+H]^+$: 268.1877, found: 268.1877.

Compound 34



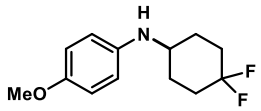
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 30.8 mg (61%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 – 6.94 (m, 2H), 6.66 – 6.38 (m, 2H), 3.39 (t, *J* = 9.7 Hz, 2H), 2.80 (dt, *J* = 13.8, 6.9 Hz, 1H), 2.24 – 2.00 (m, 4H), 1.98 – 1.73 (m, 2H), 1.64 – 1.40 (m, 2H), 1.20 (d, *J* = 6.9 Hz, 6H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 144.8, 138.2, 127.2, 122.9 (t, *J* = 241.4 Hz), 113.3, 49.8, 33.1, 32.0 (t, *J* = 24.7 Hz), 28.9 (d, *J* = 10.0 Hz), 24.2. ppm. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -91.32 (d, *J* = 236.0 Hz), -95.54 (d, *J* = 238.2 Hz), -99.76 (d, *J* = 236.2 Hz), -101.99 (d, *J* = 236.1 Hz). ppm.

HRMS (ESI-TOF): calculated for $C_{15}H_{21}F_2N$ $[M+H]^+$: 254.1720, found: 254.1718.

Compound 35



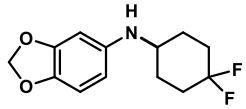
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 31.8 mg (66%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.85 – 6.69 (m, 2H), 6.71 – 6.42 (m, 2H), 3.75 (s, 3H), 3.47 – 3.18 (m, 1H), 2.94 (s, 1H), 2.21 – 1.99 (m, 4H), 1.98 – 1.67 (m, 2H), 1.62 – 1.41 (m, 2H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.4, 140.9, 122.9 (t, *J* = 242.4 Hz), 115.1, 115.0, 55.8, 50.7, 32.0 (t, *J* = 24.7 Hz), 28.9 (d, *J* = 9.9 Hz). ppm. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -91.45 (d, *J* = 236.3 Hz), -95.45 (d, *J* = 237.4 Hz), -99.93 (d, *J* = 238.7

Hz), -102.13 (d, J = 236.3 Hz). ppm. **HRMS (ESI-TOF):** calculated for $C_{13}H_{18}F_2NO$ $[M+H]^+$: 242.1356, found: 242.1357.

Compound 36

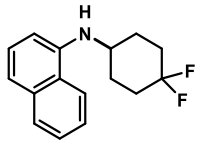


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 5:1) afforded 26 mg (51%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.65 (d, J = 8.3 Hz, 1H), 6.24 (d, J = 2.3 Hz, 1H), 6.05 (dd, J = 8.3, 2.3 Hz, 1H), 5.86 (s, 2H), 3.41 – 3.16 (m, 1H), 2.96 (br, 1H), 2.20 – 2.00 (m, 4H), 1.97 – 1.66 (m, 2H), 1.62 – 1.38 (m, 2H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 148.4, 142.4, 139.9, 122.8 (t, J = 242.4Hz), 108.7, 105.5, 100.6, 96.7, 50.7, 32.0 (t, J = 24.7 Hz), 28.8 (d, J = 10.0 Hz). ppm. **HRMS (ESI-TOF):** calculated for $C_{13}H_{16}F_2NO_2$ $[M+H]^+$: 256.1149, found: 256.1149.

Compound 37

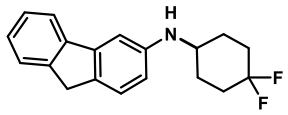


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 20:1) afforded 28.2 mg (54%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 – 7.64 (m, 2H), 7.54 – 7.38 (m, 2H), 7.32 (q, J = 8.6 Hz, 2H), 4.19 (s, 2H), 2.99 – 2.68 (m, 1H), 2.29 (ddd, J = 12.6, 9.0, 2.5 Hz, 2H), 2.05 – 1.75 (m, 6H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 137.8, 132.9, 128.4, 125.3, 125.2, 124.0, 123.7, 123.1 (t, J = 243.4Hz), 123.0, 120.6, 119.0, 36.9, 34.4 (dd, J = 25.7, 22.6 Hz), 28.7 (d, J = 10.1 Hz). ppm. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -91.21 (d, J = 236.3 Hz), -102.14 (d, J = 235.8 Hz). ppm. **HRMS (ESI-TOF):** calculated for $C_{16}H_{18}F_2N$ $[M+H]^+$: 262.1407, found: 262.1406.

Compound 38

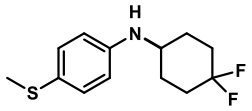


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 30.5 mg (51%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$):δ 7.61 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.45 (d, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.17 (td, *J* = 7.4, 1.0 Hz, 1H), 6.79 (s, 1H), 6.62 (dd, *J* = 8.2, 2.2 Hz, 1H), 3.81 (s, 3H), 3.63 – 3.34 (m, 1H), 2.39 – 2.04 (m, 4H), 2.11 – 1.80 (m, 2H), 1.59 (dt, *J* = 13.4, 6.7 Hz, 2H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 146.3, 145.3, 142.1, 142.1, 132.2, 126.6, 124.9, 124.7, 122.8 (t, *J* = 242.4 Hz), 120.7, 118.4, 112.5, 109.7, 49.9, 36.9, 32.1 (t, *J* = 24.7 Hz), 28.9 (d, *J* = 9.9 Hz). ppm. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -95.44 (d, *J* = 236.0 Hz), -100.02 (d, *J* = 232.9 Hz). ppm. **HRMS (ESI-TOF):** calculated for $C_{19}H_{20}F_2N$ $[M+H]^+$: 3001564, found: 300.1563.

Compound 39



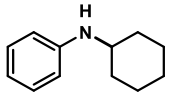
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 35.9 mg (70%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 – 7.16 (m, 2H), 6.60 – 6.42 (m, 2H), 3.54 (br, 1H), 3.46 – 3.23 (m, 1H), 2.41 (s, 3H), 2.10 (t, *J* = 7.6 Hz, 4H), 1.95 – 1.70 (m, 2H), 1.54 (dt, *J* = 13.5, 6.5 Hz, 2H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.6, 131.5, 124.6, 122.7 (t, *J* = 242.4 Hz), 113.9, 49.6, 32.0 (t, *J* = 24.7 Hz), 28.7 (d, *J* = 10.0 Hz), 19.0 (s). ppm. **^{19}F NMR (377 MHz, $CDCl_3$):** ^{19}F NMR (377 MHz, $CDCl_3$) δ -91.52 (d, *J* = 236.8 Hz), -95.51 (d, *J* = 236.7 Hz), -100.00 (d, *J* = 235.8 Hz), -102.03 (d, *J* = 236.2

Hz). ppm. **HRMS (ESI-TOF):** calculated for $C_{13}H_{18}F_2NS$ $[M+H]^+$: 258.1128, found: 258.1125.

Compound 40

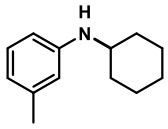


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 27.6 mg (79%).

Physical State: colorless oil.

The NMR data of **40** were consistent with previous literature[2].

Compound 41

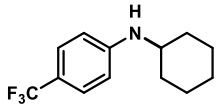


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 34.2 mg (76%).

Physical State: colorless oil.

The NMR data of **41** were consistent with previous literature[3].

Compound 42

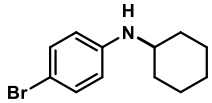


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 29.2 mg (60%).

Physical State: colorless oil.

The NMR data of **42** were consistent with previous literature[4].

Compound 43



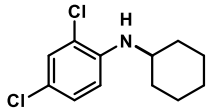
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 20:1) afforded

36.4 mg (63%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.16 (m, 2H), 6.46 – 6.33 (m, 2H), 3.62 (s, 1H), 3.40 (td, *J* = 8.4, 4.1 Hz, 1H), 2.08 – 1.88 (m, 2H), 1.65 (ddd, *J* = 13.7, 13.1, 5.0 Hz, 3H), 1.56 – 1.29 (m, 5H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 146.3, 131.9, 114.7, 108.1, 53.7, 34.6, 28.2, 24.3 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{12}H_{17}BrN$ $[M+H]^+$: 254.0544, found: 254.0544.

Compound 44

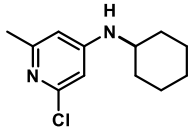


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 30.1 mg (62%).

Physical State: colorless oil.

The NMR data of **44** were consistent with previous literature[5].

Compound 45

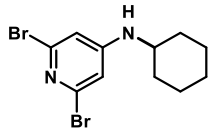


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 1:1) afforded 20.6 mg (46%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.28 (d, J = 1.6 Hz, 1H), 6.21 – 6.16 (m, 1H), 4.33 (s, 1H), 3.26 (dp, J = 11.1, 5.5, 3.6 Hz, 1H), 2.36 (s, 3H), 2.11 – 1.95 (m, 2H), 1.77 (dt, J = 12.8, 3.5 Hz, 2H), 1.67 (dt, J = 12.5, 3.5 Hz, 1H), 1.47 – 1.31 (m, 2H), 1.28 – 1.14 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 158.3, 154.8, 150.9, 106.1, 103.7, 51.0, 32.8, 25.5, 24.7, 23.9. (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{12}H_{18}ClN_2$ $[M+H]^+$: 225.1159, found: 225.1155.

Compound 46

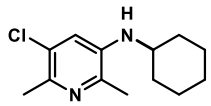


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 1:1) afforded 28.5 mg (43%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.55 (s, 2H), 4.48 (s, 1H), 3.25 (td, J = 10.2, 5.1 Hz, 1H), 2.03 – 1.95 (m, 2H), 1.82 – 1.77 (m, 2H), 1.67 (dt, J = 12.8, 3.7 Hz, 1H), 1.44 – 1.31 (m, 2H), 1.25 (d, J = 3.5 Hz, 3H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 155.1, 140.4, 109.9, 51.3, 32.6, 25.4, 24.6. (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{11}H_{15}Br_2N_2$ $[M+H]^+$: 332.9602, found: 332.9598.

Compound 47

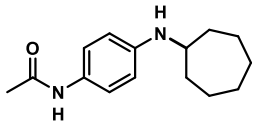


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 1:1) afforded 24.7 mg (52%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (s, 1H), 3.36 (s, 1H), 3.13 – 2.94 (m, 1H), 2.51 (s, 3H), 2.42 (s, 3H), 1.91 (d, *J* = 12.0 Hz, 2H), 1.82 – 1.67 (m, 3H), 1.66 – 1.52 (m, 1H), 1.32 – 1.07 (m, 4H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.6, 150.4, 137.0, 135.83, 121.4, 56.2, 34.4, 25.7, 25.2, 23.3, 22.2 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{13}H_{20}ClN_2$ $[M+H]^+$: 239.1315, found: 239.1316.

Compound 48



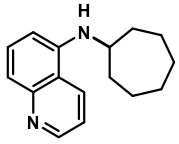
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 2:1) afforded

27.5 mg (56%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (bs, 1H), 7.24 – 7.19 (m, 2H), 6.53 – 6.42 (m, 2H), 3.71 (bs, 1H), 3.41 (td, *J* = 8.5, 4.1 Hz, 1H), 2.10 (s, 3H), 1.98 (ddd, *J* = 13.8, 8.1, 5.4 Hz, 2H), 1.71 – 1.39 (m, 10H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 168.3, 144.6, 127.6, 122.5, 113.4, 54.0, 34.7, 28.3, 24.4, 24.1 (s). ppm. **HRMS (ESI-TOF):** calculated for $C_{15}H_{23}N_2O$ $[M+H]^+$: 247.1810, found: 247.1810.

Compound 49

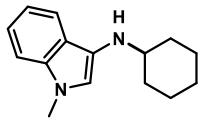


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 2:1) afforded 22.1 mg (46%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.18 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.87 (dt, *J* = 6.9, 3.5 Hz, 1H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 6.81 (d, *J* = 7.8 Hz, 1H), 4.04 (d, *J* = 3.5 Hz, 2H), 2.01 (t, *J* = 10.7 Hz, 2H), 1.80 (dd, *J* = 15.0, 8.0 Hz, 3H), 1.68 (dd, *J* = 17.6, 8.0 Hz, 7H).ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 167.9, 148.9, 134.3, 132.6, 129.6, 126.2, 123.6, 119.2, 110.5, 38.7, 36.5, 28.2, 27.3 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{16}H_{21}N_2$ $[M+H]^+$: 241.1705, found: 241.1704.

Compound 50

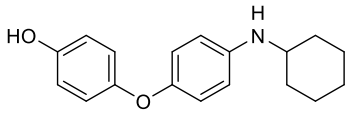


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 2:1) afforded 18.7 mg (41%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (dd, *J* = 7.7, 0.9 Hz, 1H), 8.08 (dd, *J* = 7.7, 0.9 Hz, 1H), 7.80 (td, *J* = 7.6, 1.4 Hz, 1H), 7.72 (td, *J* = 7.6, 1.4 Hz, 1H), 6.97 (s, 1H), 2.06 – 1.92 (m, 2H), 1.79 (ddd, *J* = 9.2, 5.6, 2.8 Hz, 5H), 1.71 – 1.49 (m, 3H), 1.46 – 1.28 (m, 3H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 196.0, 162.0, 134.8, 133.1, 131.2, 130.6, 128.2, 126.8, 63.6, 35.3, 24.5, 20.5 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{15}H_{21}N_2$ $[M+H]^+$: 229.1705, found: 229.1703.

Compound 52

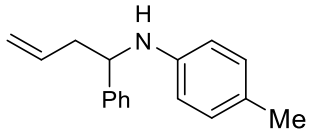


0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 2:1) afforded 41.5 mg (73%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.91 – 6.75 (m, 4H), 6.71 – 6.61 (m, 4H), 4.21 – 3.63 (s, 2H), 2.47 (ddd, J = 11.4, 8.5, 2.9 Hz, 1H), 1.92 – 1.81 (m, 4H), 1.50 – 1.16 (m, 6H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.2, 150.8, 138.3, 134.3, 118.8, 117.5, 117.1, 116.1, 38.6, 32.8, 27.0, 26.2. ppm. **HRMS (ESI-TOF):** calculated for $C_{18}H_{22}NO_2$ $[M+H]^+$: 284.1651, found: 284.1650.

Compound 54



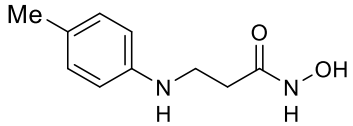
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 37.1 mg (78%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.25 (m, 4H), 7.25 – 7.17 (m, 1H), 6.92 – 6.84 (m, 2H), 6.45 – 6.37 (m, 2H), 5.75 (dddd, J = 16.7, 10.1, 7.7, 6.4 Hz, 1H), 5.22 – 5.12 (m, 2H), 4.34 (dd, J = 8.1, 5.1 Hz, 1H), 4.03 (s, 1H), 2.59 (dddt, J = 14.4, 6.5, 5.0, 1.4 Hz, 1H), 2.47 (dtt, J = 14.3, 7.9, 1.2 Hz, 1H), 2.17 (s, 3H) ppm. **^{13}C NMR (100 MHz,**

CDCl$_3$): δ 145.1, 143.7, 134.7, 129.5, 128.5, 126.9, 126.5, 126.3, 118.2, 113.5, 57.4, 43.3, 20.3. ppm. **HRMS (ESI-TOF):** calculated for $C_{17}H_{20}N$ $[M+H]^+$: 238.1596, found: 238.1596.

Compound 55

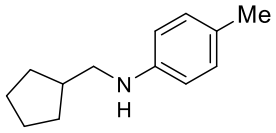


0.20 mmol scale. Purification by PTLC (DCM/MeOH = 20:1) afforded 24.2 mg (62%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): 1H NMR (400 MHz, Chloroform-d) δ 7.22 – 7.13 (m, 2H), 6.72 (tt, J = 7.3, 1.1 Hz, 1H), 6.66 – 6.58 (m, 2H), 3.69 (s, 3H), 3.45 (t, J = 6.4 Hz, 2H), 2.62 (t, J = 6.4 Hz, 2H) ppm. **^{13}C NMR (100 MHz, CDCl$_3$):** δ 172.8, 147.5, 129.3, 117.8, 113.0, 51.7, 39.4, 33.7 (s) ppm. **HRMS (ESI-TOF):** calculated for $C_{10}H_{15}N_2O_2$ $[M+H]^+$: 195.1134, found: 195.1136.

Compound 58



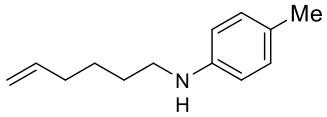
0.20 mmol scale. Purification by PTLC (petroleum ether/ethyl acetate = 10:1) afforded 11.8 mg (31%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ 6.98 (d, J = 8.2 Hz, 2H), 6.54 (d, J = 8.4 Hz, 2H), 3.00 (d, J = 7.2 Hz, 2H), 2.23 (s, 3H), 2.14 (dq, J = 14.9, 7.5 Hz, 1H), 1.88 – 1.75 (m, 2H), 1.67 – 1.48 (m, 6H). ppm.

The NMR data of **58** were consistent with previous literature[6].

Compound 59



0.20 mmol scale. Purification by PTLC (DCM/MeOH = 20:1) afforded 32.5 mg (43%).

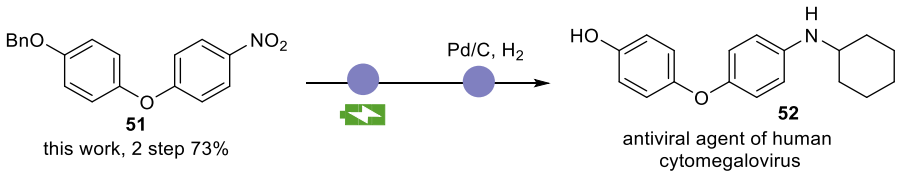
Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, J = 8.0 Hz, 2H), 6.57 – 6.49 (m, 2H), 5.81 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.07 – 4.92 (m, 2H), 3.09 (t, J = 7.0 Hz, 3H), 2.23 (s, 3H), 2.17 – 2.04 (m, 2H), 1.63 (dq, J = 8.8, 6.4 Hz, 2H), 1.56 – 1.44 (m, 2H). ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 138.6, 129.7, 126.3, 114.6, 112.9, 44.2, 33.5, 29.0, 26.4, 20.3. ppm. **HRMS (ESI-TOF):** calculated for $C_{13}H_{20}N$ $[M+H]^+$: 190.1596, found: 190.1598.

Synthetic applications

Procedure for 52

Synthesis of 52 (Procedure C)

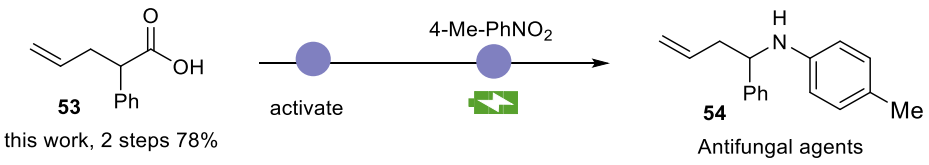


In glovebox, An oven-dried undivided reactor (5 mL) equipped with the RAE 1a (0.3 mmol, 1.5 equiv, 81 mg), 1-(benzyloxy)-4-(4-nitrophenoxy)benzene 51 (0.2 mmol, 1 equiv, 64 mg), TBAB (0.15 M, 200 mg) and a stir bar before adding DMA (4 mL). The reactor was equipped with Fe electrode (52.5 × 8 × 2 mm) as the anode and foamed nickel electrode (52.5 × 8 × 2 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA (The dual display potentiostat was operating in constant current mode) under room temperature for 3 h. When the reaction was completed, the solution was extract by ethyl acetate (3 × 15 mL), and the combined organic layers were concentrated with a rotary evaporator. The crude product was directly put into the next step without purification.

To a solution of above crude product in methanol (25 mL) was added Pd/C (20 mg) portion wise and the resulting mixture. Then pump three times to make the system full of H2. The reaction mixture was stirred at room temperature for 8 hours. After reaction completion, the solution was concentrated in vacuo. The product was purified by reversed phase flash chromatography eluting a gradient of petroleum ether/ethyl acetate = 2:1 to obtain the 52 as an oil (41.5 mg, 73%).

Procedure for 54

Synthesis of 54 (Procedure D)

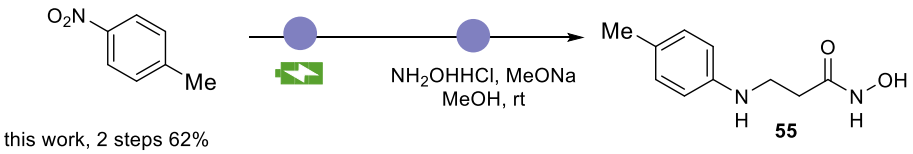


Around bottom flask or culture tube was charged with carboxylic acid **53** (0.3

mmol), N-hydroxyphthalimide (1.0-1.1 equiv) and 4-dimethylaminopyridine (0.1 equiv). CH_2Cl_2 was added (0.1-0.2 M), and the mixture was stirred vigorously. [Note: Carboxylic acid was added via syringe (if liquid)]. DCC (1.1 equiv) was then added dropwise via syringe, and the mixture was allowed to stir until the acid was consumed (determined by TLC). Typical reaction times were between 0.5. The mixture was filtered (through a thin pad of Celite®, SiO_2, or frit funnel) and rinsed with additional CH_2Cl_2/Et_2O. Solvents were removed under reduced pressure and the white solid obtained. Then, in glovebox, an oven-dried undivided reactor (5 mL) equipped with the RAE obtained above, 1-methyl-4-nitrobenzene 2 (0.2 mmol, 1 equiv, 28 mg), TBAB (0.15 M, 200 mg) and a stir bar before adding DMA (4 mL). The reactor was equipped with Fe electrode (52.5 × 8 × 2 mm) as the anode and foamed nickel electrode (52.5 × 8 × 2 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA (The dual display potentiostat was operating in constant current mode) under room temperature for 3 h. When the reaction was completed, the solution was extract by ethyl acetate (3 × 15 mL), and the combined organic layers were concentrated with a rotary evaporator. The crude product was purified by PTLC to afford the corresponding product (Hexane: ethyl acetate=10:1, 37.1 mg, 78%).

Procedure for 55

Synthesis of 55 (Procedure E)



this work, 2 steps 62%

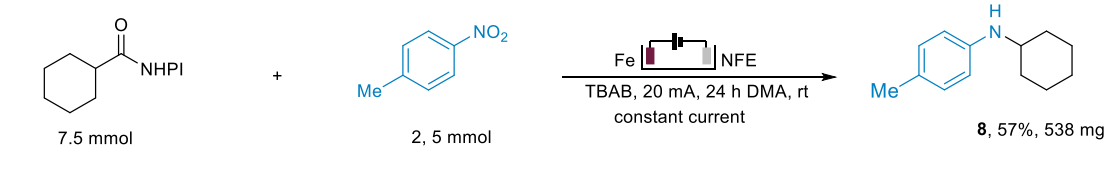
In glovebox, An oven-dried undivided reactor (5 mL) equipped with the RAE 1,3-dioxoisoindolin-2-yl methyl succinate (0.3 mmol, 1.5 equiv, 83.1 mg), 1-methyl-4-nitrobenzene **2** (0.2 mmol, 1 equiv, 28 mg), TBAB (0.15 M, 200 mg) and a stir bar before adding DMA (4 mL). The reactor was equipped with Fe electrode (52.5 × 8 × 2 mm) as the anode and foamed nickel electrode (52.5 × 8 × 2 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA (The dual display potentiostat was operating in constant current mode) under room temperature

for 3 h. When the reaction was completed, the solution was extract by ethyl acetate (3 × 15 mL), and the combined organic layers were concentrated with a rotary evaporator. The crude product was purified by PTLC to afford the corresponding product (Hexane: ethyl acetate=10:1).

To an ice-cooled solution of hydroxylamine hydrochloride (20 eq) in methanol (25 mL) was added powdered KOH (25 eq) portion wise and the resulting mixture was stirred at room temperature for 1 hour after the addition of KOH was completed. The precipitate was filtered off and the filtrate was added dropwise to an ice-cooled solution of methyl ester (0.6 mmol, compounds obtained in the previous step) in methanol (5 mL). An additional amount of KOH (10 eq) was added to the reaction solution and the reaction was monitored by TLC using methanol: dichloromethane (1:9) solvent system. After reaction completion, the solution was concentrated in vacuo and water was added. The pH of the solution was adjusted to pH 8.0 by dropwise addition of 1 M HCl and the product was extracted with dichloromethane (3 × 25 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The product was purified by reversed phase flash chromatography eluting a gradient of methanol: water (10:90 to 90:10) to obtain 55 as an oil (24.2 mg, 62%).

Procedure for gram scale synthesis

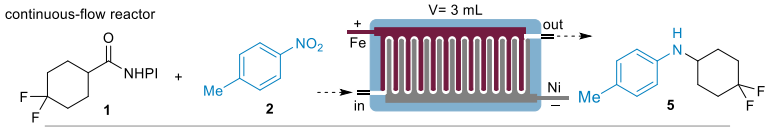
D. gram scale synthesis



In glovebox, An oven-dried undivided reactor (80 mL) equipped with the RAE **1a** (7.5 mmol, 1.5 equiv, 2.05 g), 1-methyl-4-nitrobenzene **2** (5 mmol, 1 equiv, 685 mg), TBAB (2.5g mg) and a stir bar before adding DMA (50 mL). The reactor was equipped

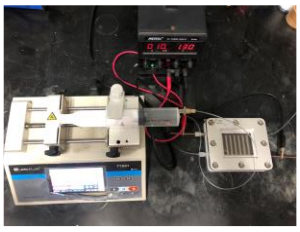
with Fe electrode (6 × 4 × 0.2 cm) as the anode and foamed nickel electrode (6 × 4 × 0.2 cm) as the anode. The reaction mixture was stirred and electrolyzed at a constant current of 20 mA (The dual display potentiostat was operating in constant current mode) under room temperature for 24 h. When the reaction was completed, the solution was extract by ethyl acetate (3 × 150 mL), and the combined organic layers were concentrated with a rotary evaporator. The crude product was purified by PTLC to afford the corresponding product (Hexane: ethyl acetate=10:1, 538 mg, 57%).

Procedure for continuous-flow reactor



Entry	Flow rate	Current	Residence time	Coversion	Yield
1	0.1 mL/min	10 mA	30 min	7%	<5%
2	0.1 mL/min	20 mA	30 min	20%	13%
3	0.1 mL/min	30 mA	30 min	70%	47%
4	0.05 mL/min	10 mA	60 min	67%	41%
5	0.05 mL/min	20 mA	60 min	86%	62%

reaction condition:1 (0.075M), 2 (0.05M), TBAB (0.05M), DMF, rt. GC yield



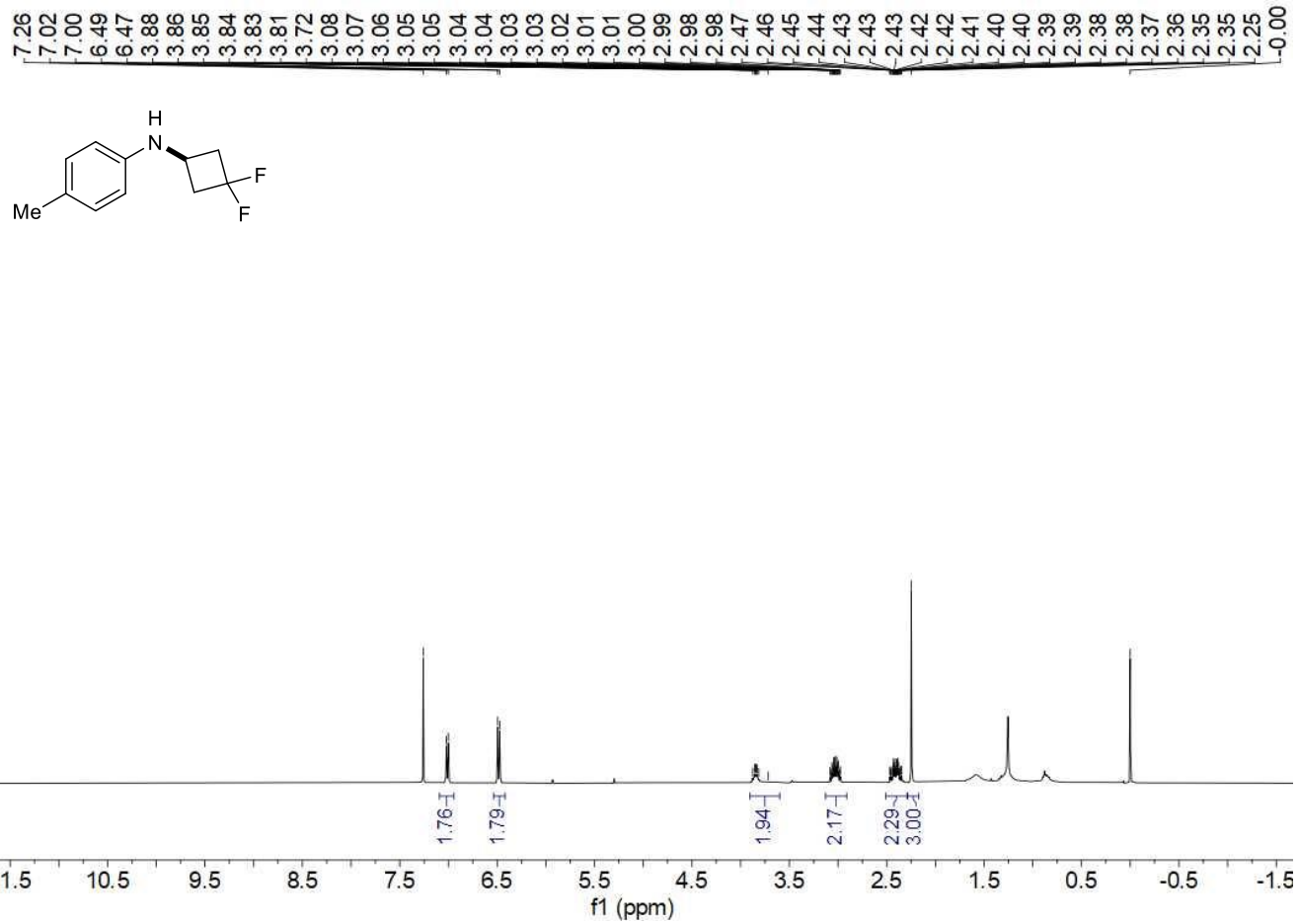
First, assembled and installed the flow electrochemistry device, the anode as Fe electrode, cathode as nickel electrode and the cell volume was 3 mL. Second, **1** (0.075 M), **2** (0.05 M), n-Bu_4Br (0.05 M) were dissolved in DMA (30 mL). n-dodecane as internal standard. The reaction mixture was pumped into the flow cell via a syringe and electrolyzed at a constant current of 20 mA at room temperature. The flow rate was 0.05 mL/min and residence time was 1 h. The out flow of the reaction mixture was collected and monitored by GCMS.

References

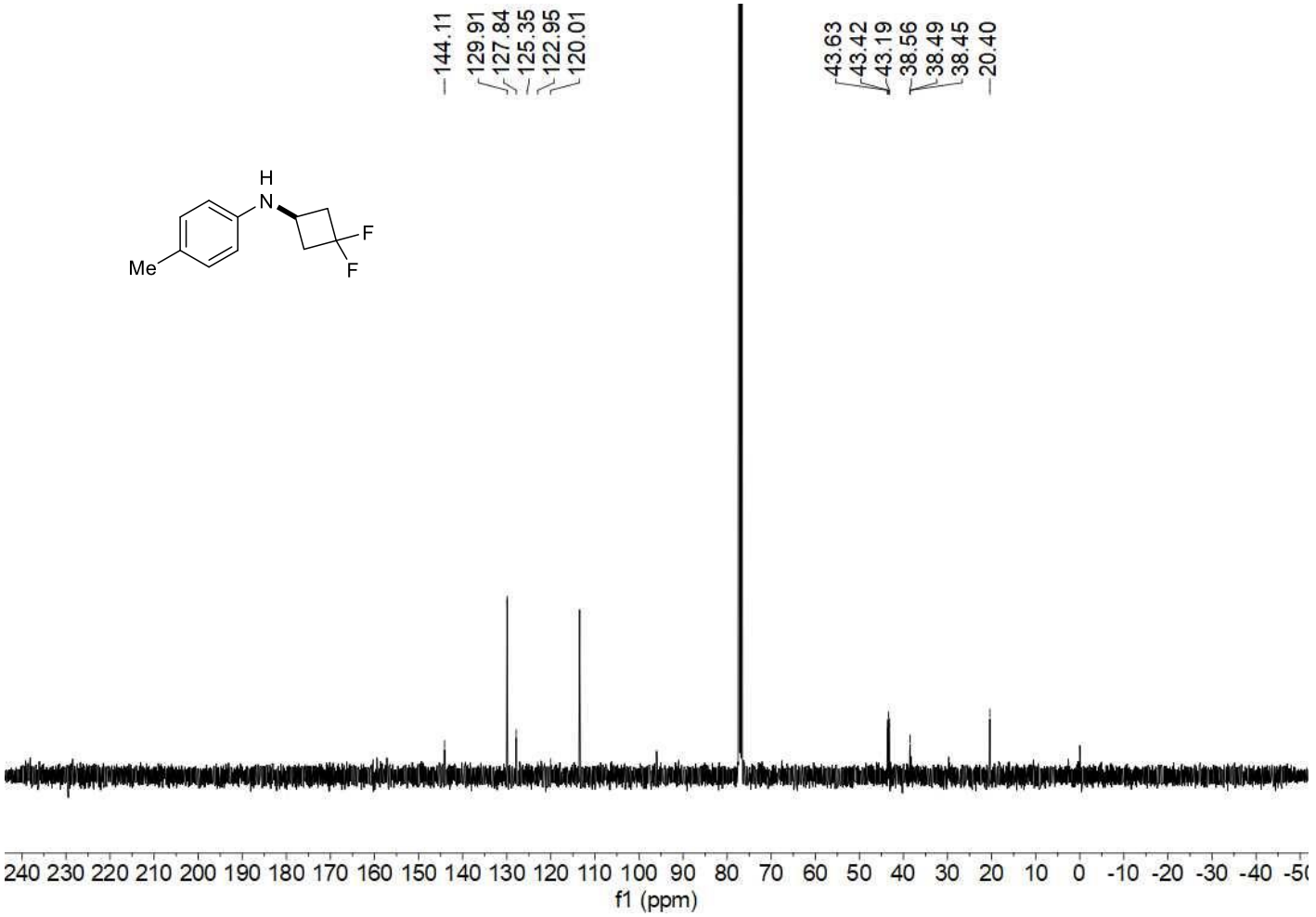
1. S. Ni, N. M. Padial, C. Kingston, J. C. Vantourout, D. C. Schmitt, J. T. Edwards, M. M. Kruszyk, R. R. Merchant, P. K. Mykhailiuk, B. B. Sanchez, S. Yang, M. A. Perry, G. M. Gallego, J. J. Mousseau, M. R. Collins, R. J. Cherney, P. S. Lebed, J. S. Chen, T. Qin and P. S. Baran, *J. Am. Chem. Soc.*, 2019, 141, 6726-6739.
2. Q. Shen, T. Ogata and J. F. Hartwig, *J. Am. Chem. Soc.*, 2008, **130**, 6586-6596.
3. R. Mao, A. Frey, J. Balon and X. Hu, *Nat. Catal.*, 2018, **1**, 120-126.
4. A. Jati, K. Dey, M. Nurhuda, M. A. Addicoat, R. Banerjee and B. Maji, *J. Am. Chem. Soc.*, 2022, **144**, 7822-7833.
5. A. F. Abdel-Magid, K. G. Carson, B. D. Harris, C. A. Maryanoff and R. D. Shah, *J. Org. Chem.*, 1996, **61**, 3849-3862.
6. V. T. Nguyen, V. D. Nguyen, G. C. Haug, N. T. H. Vuong, H. T. Dang, H. D. Arman and O. V. Larionov, *Angew. Chem. Int. Ed.*, 2020, **59**, 7921-7927.

NMR Spectra

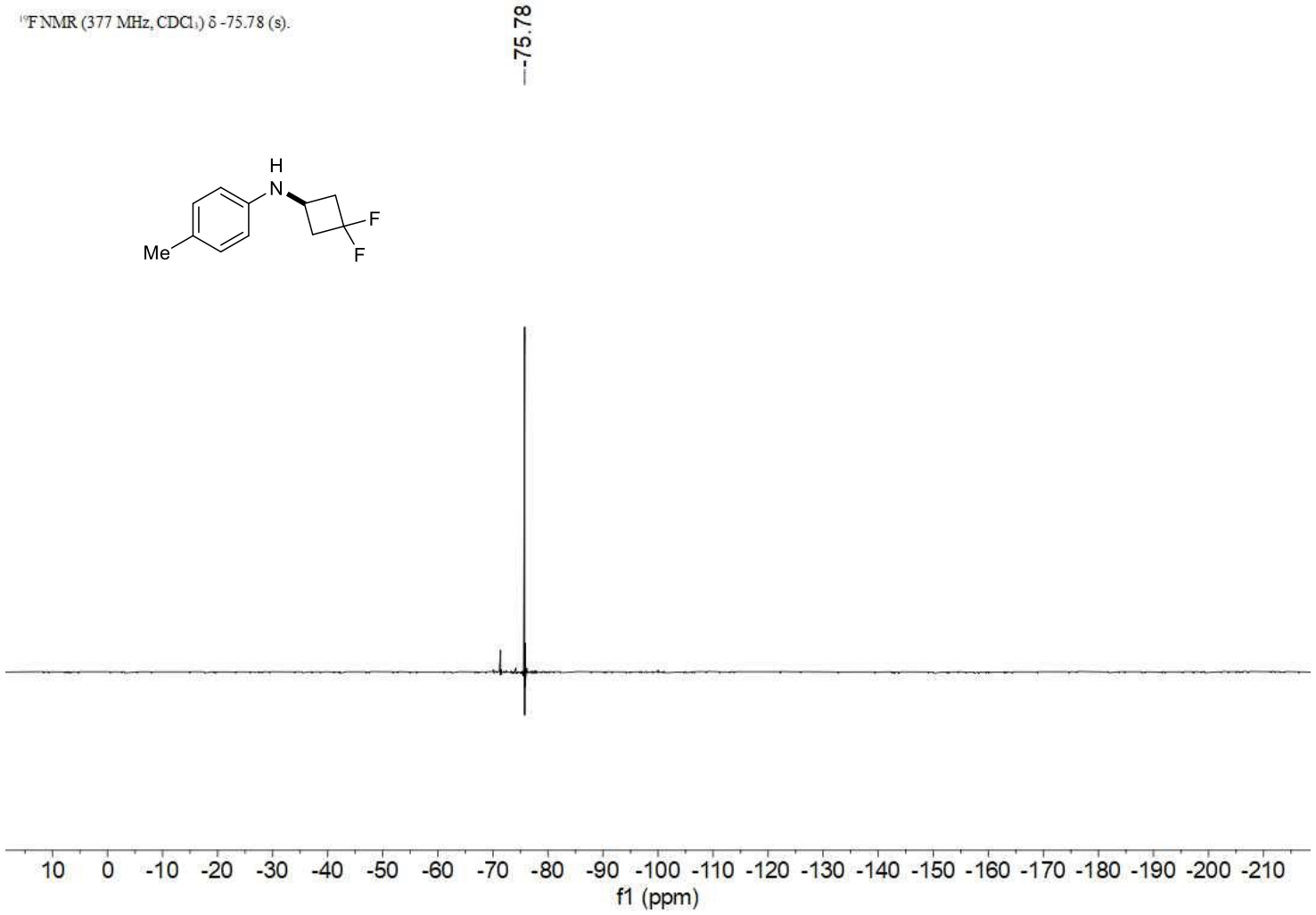
Compound **3** ^{1}H NMR



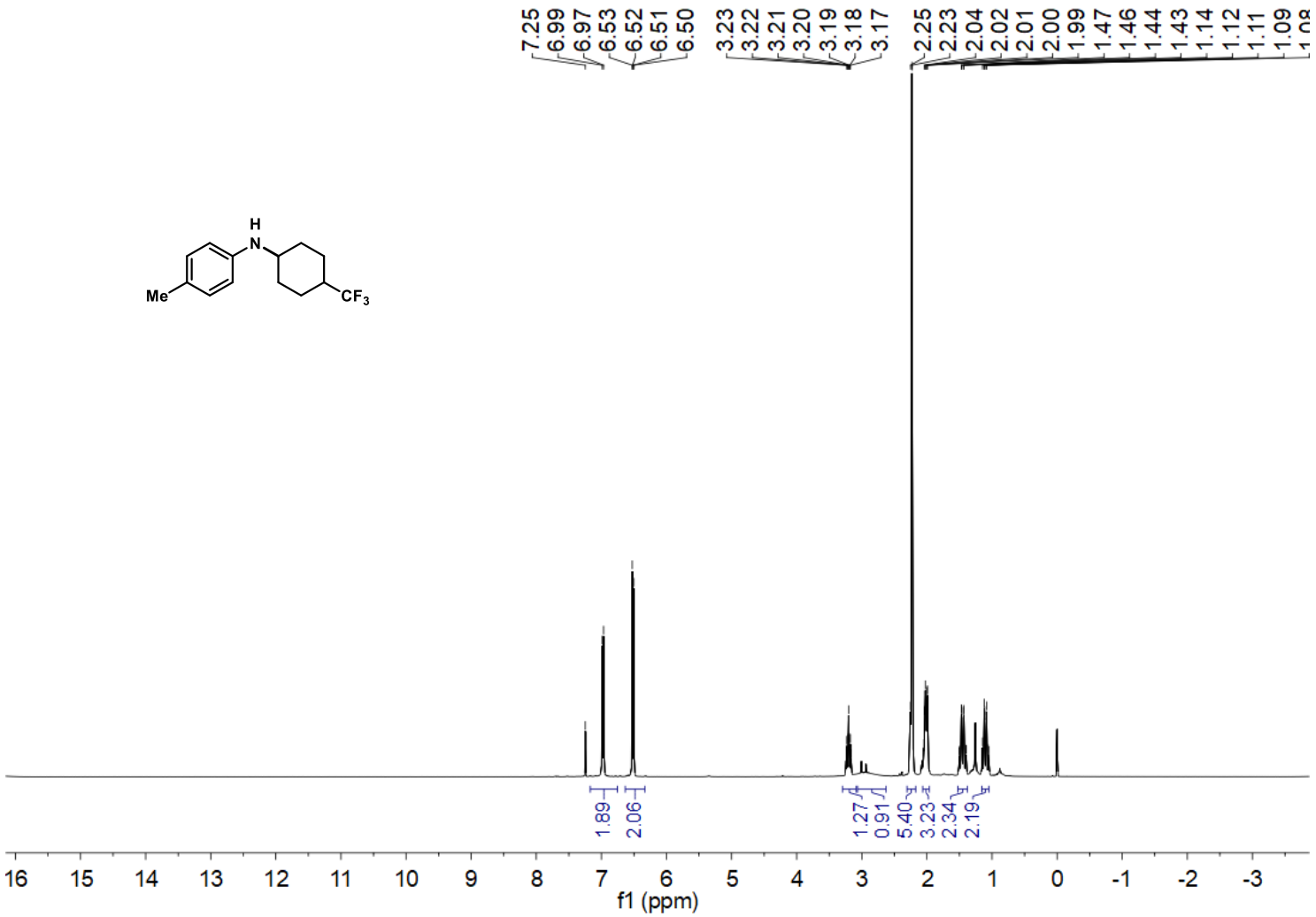
Compound **3** ^{13}C NMR



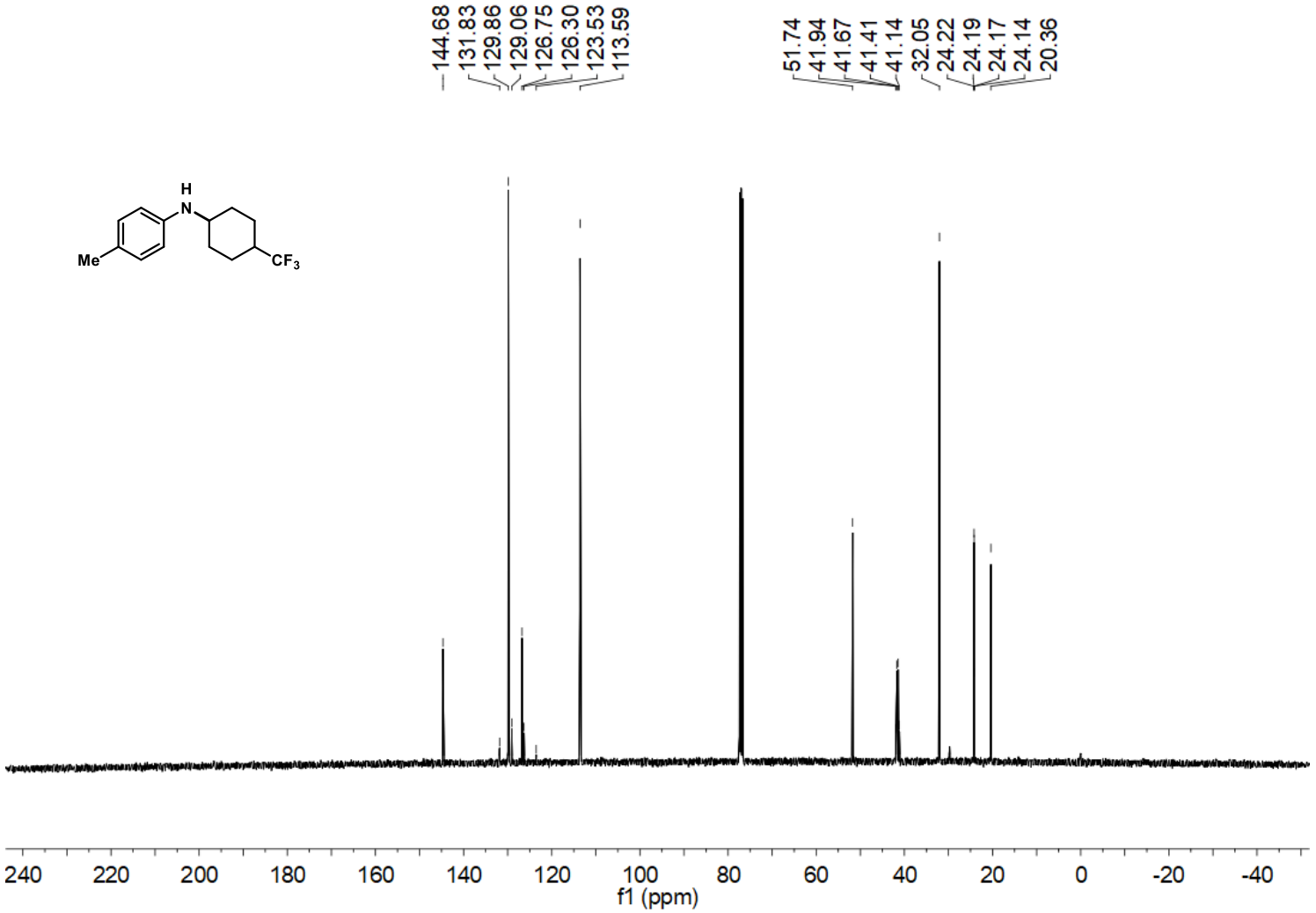
Compound **3** ^{19}F NMR



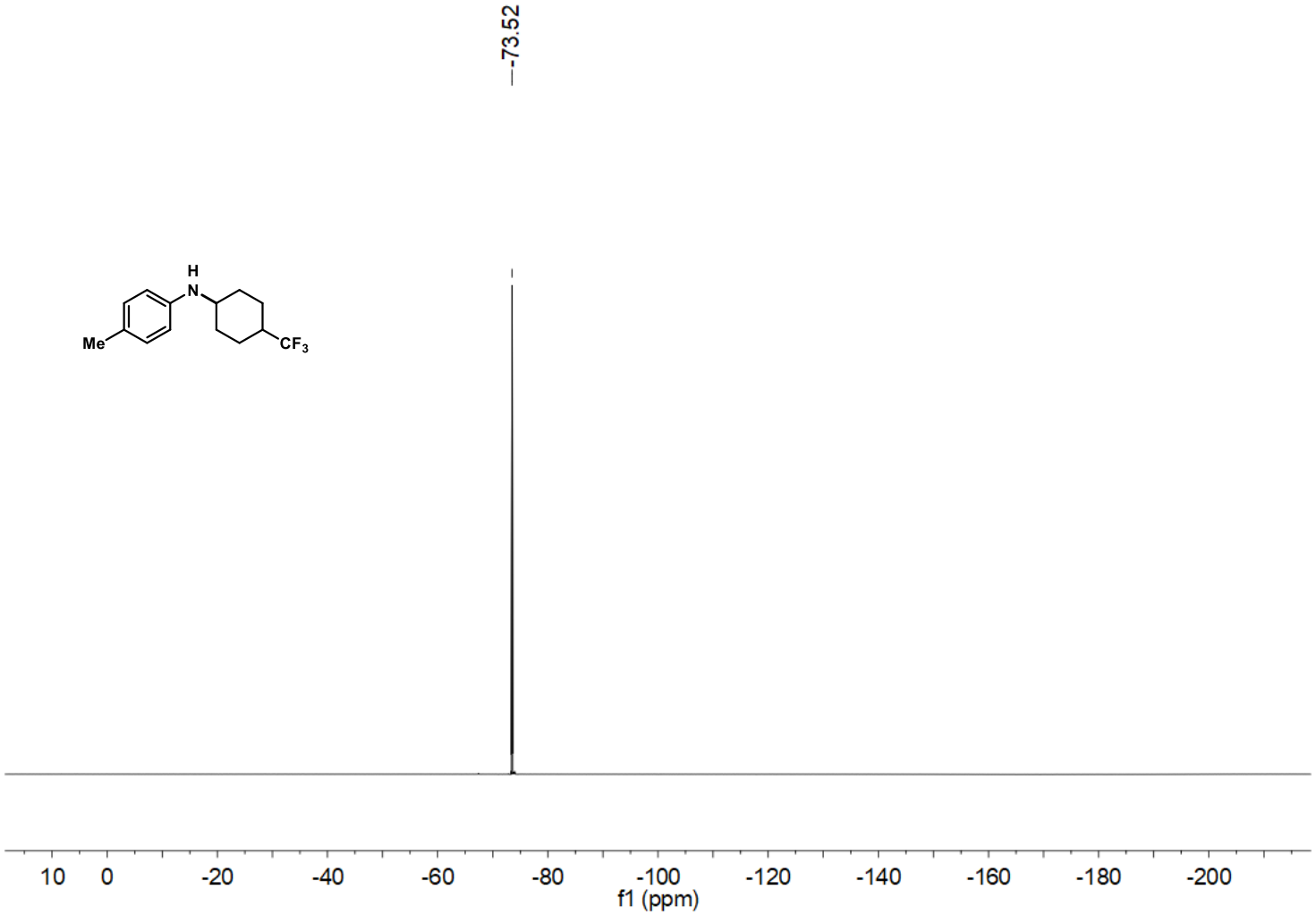
Compound **4** ^{1}H NMR



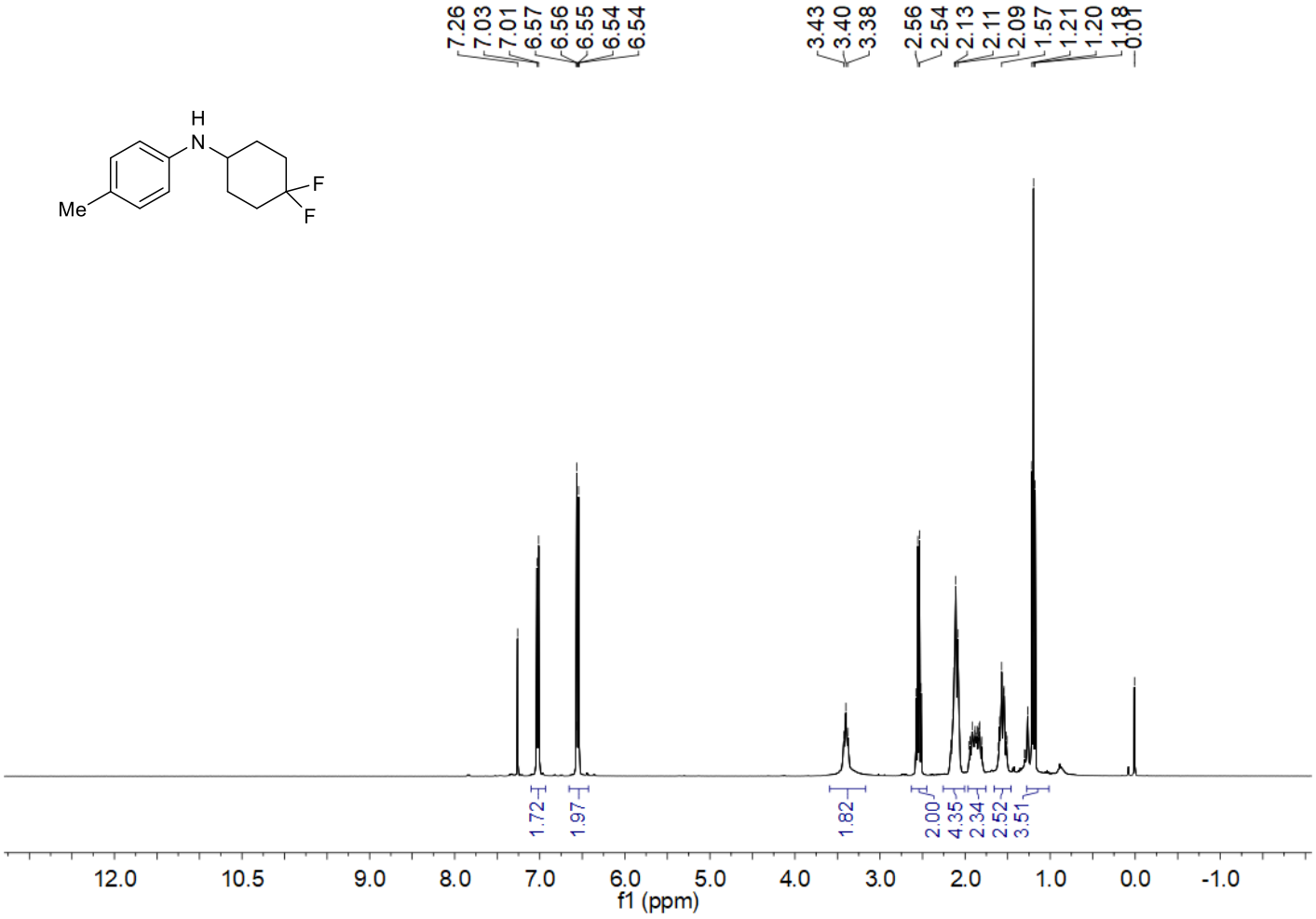
Compound **4** ^{13}C NMR



Compound **4** ^{19}F NMR



Compound **5** ^{1}H NMR



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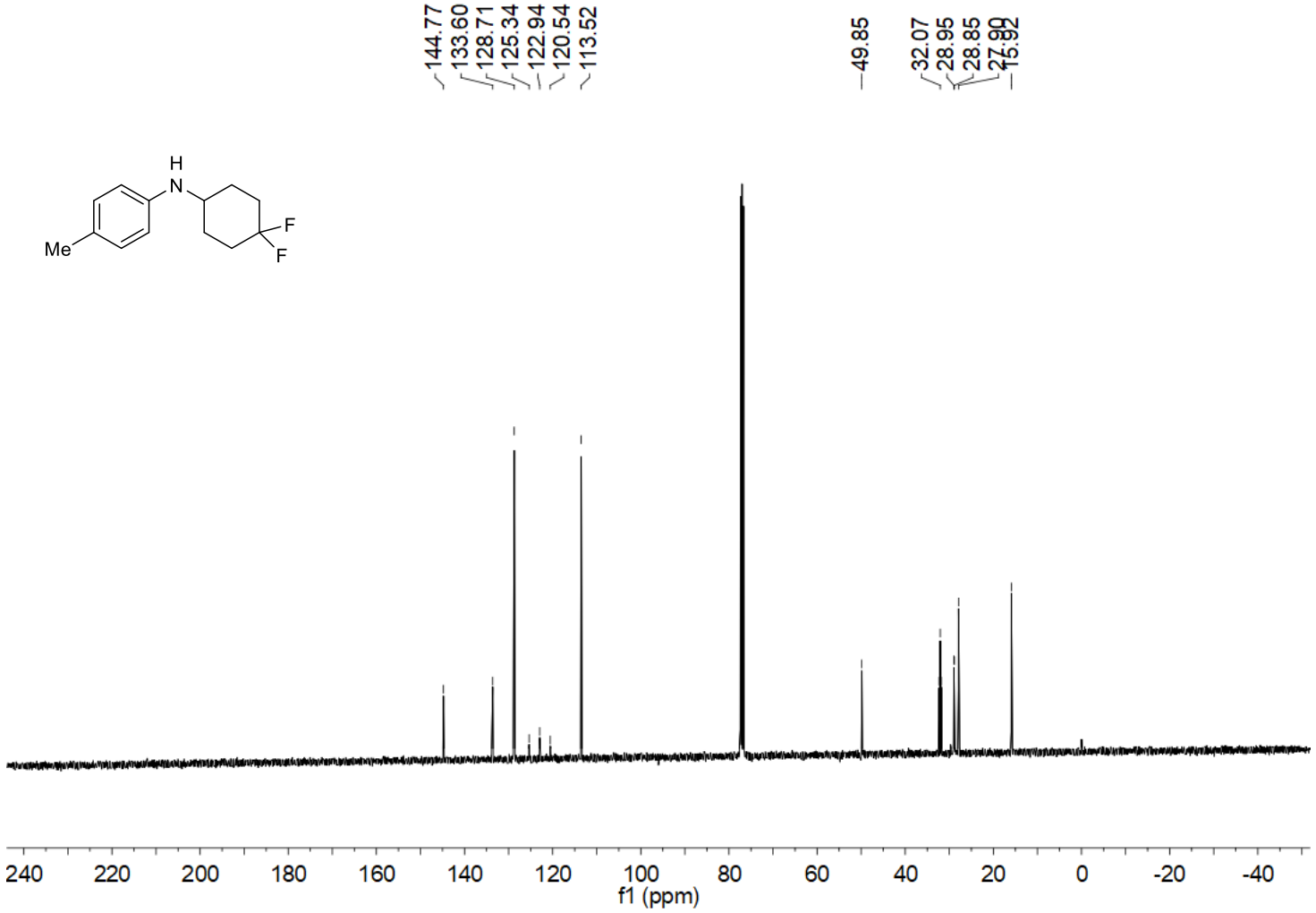

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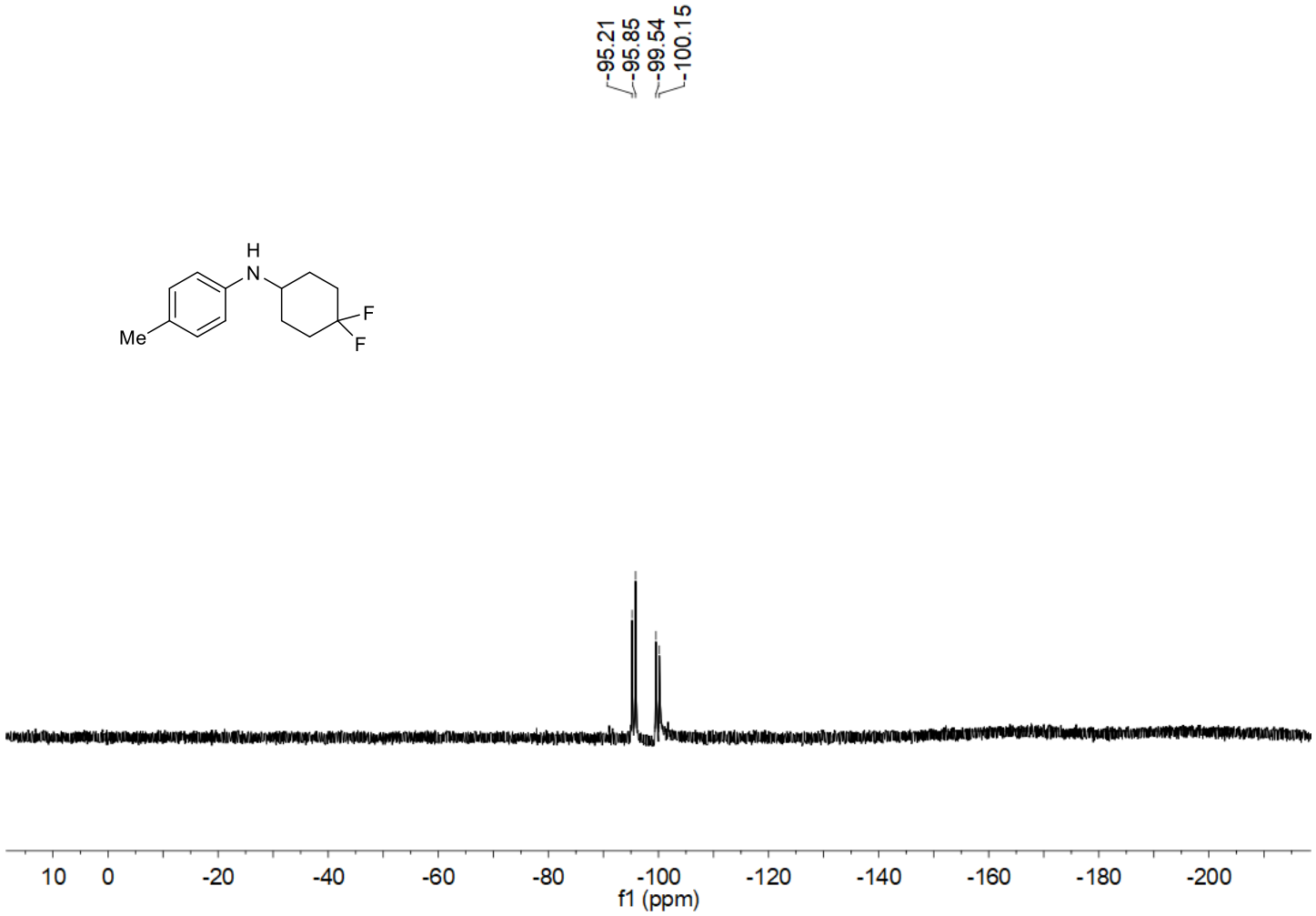
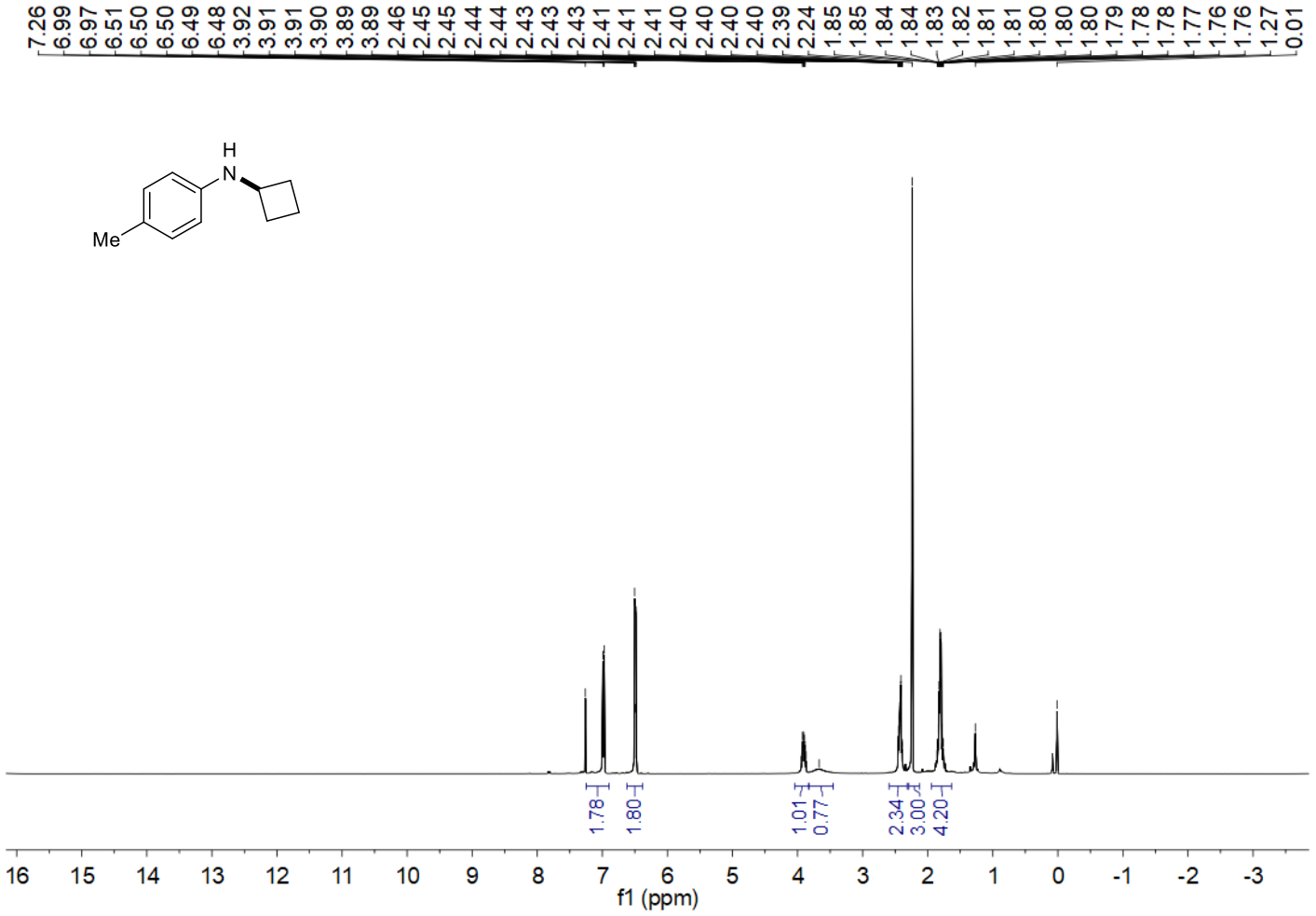
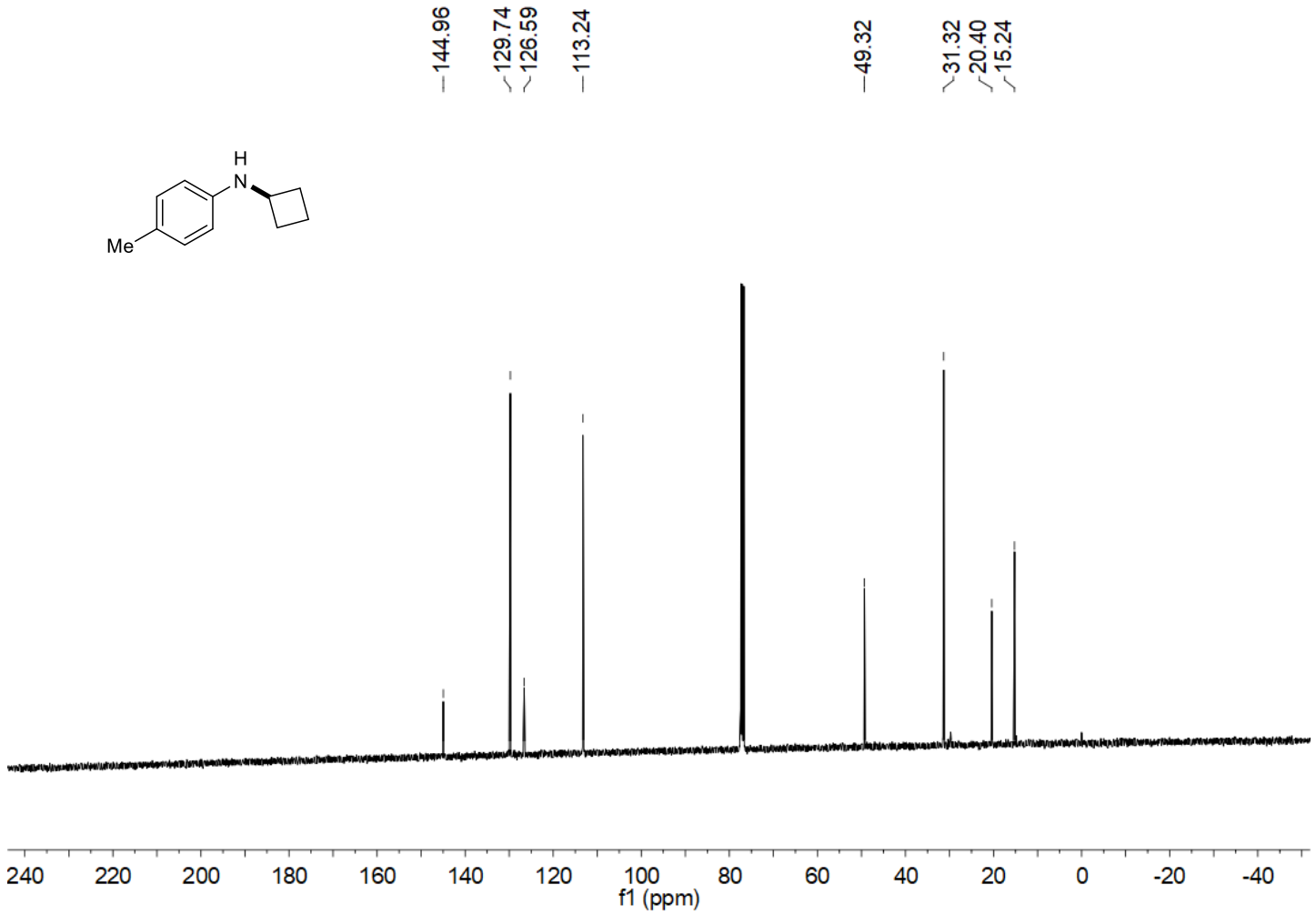


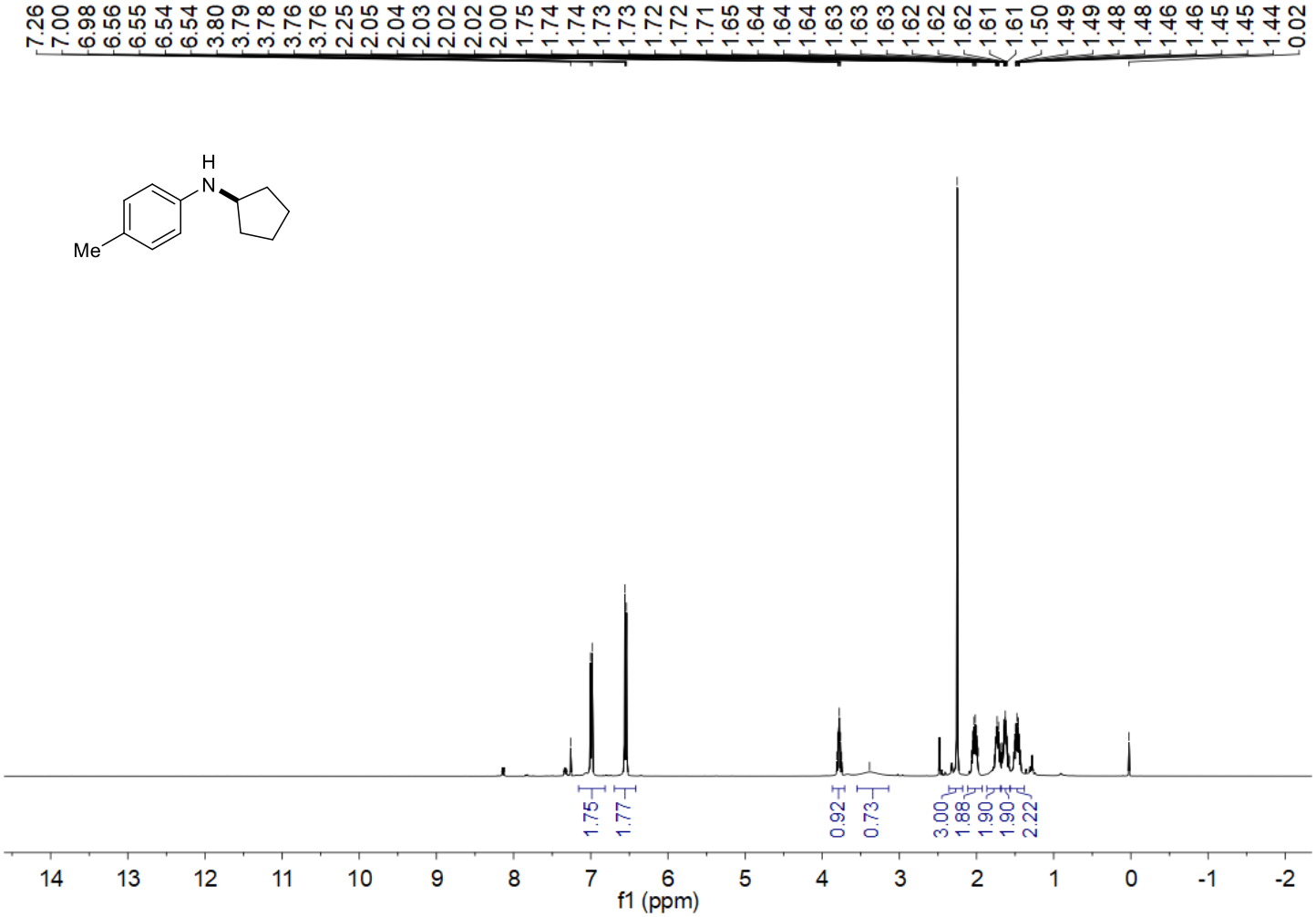
Compound **6** ^{1}H NMR



Compound **6** ^{13}C NMR



Compound **7** ^{1}H NMR



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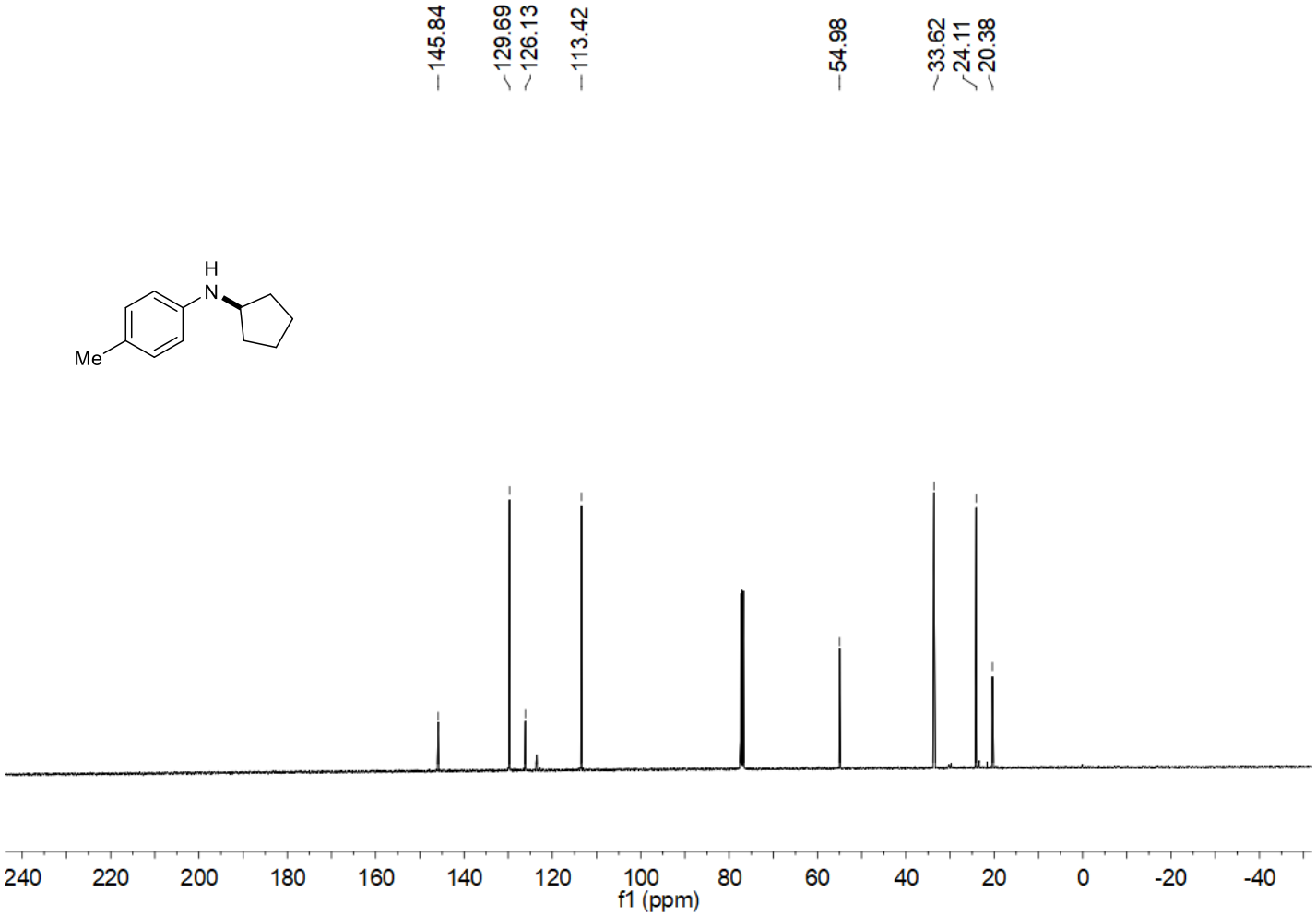
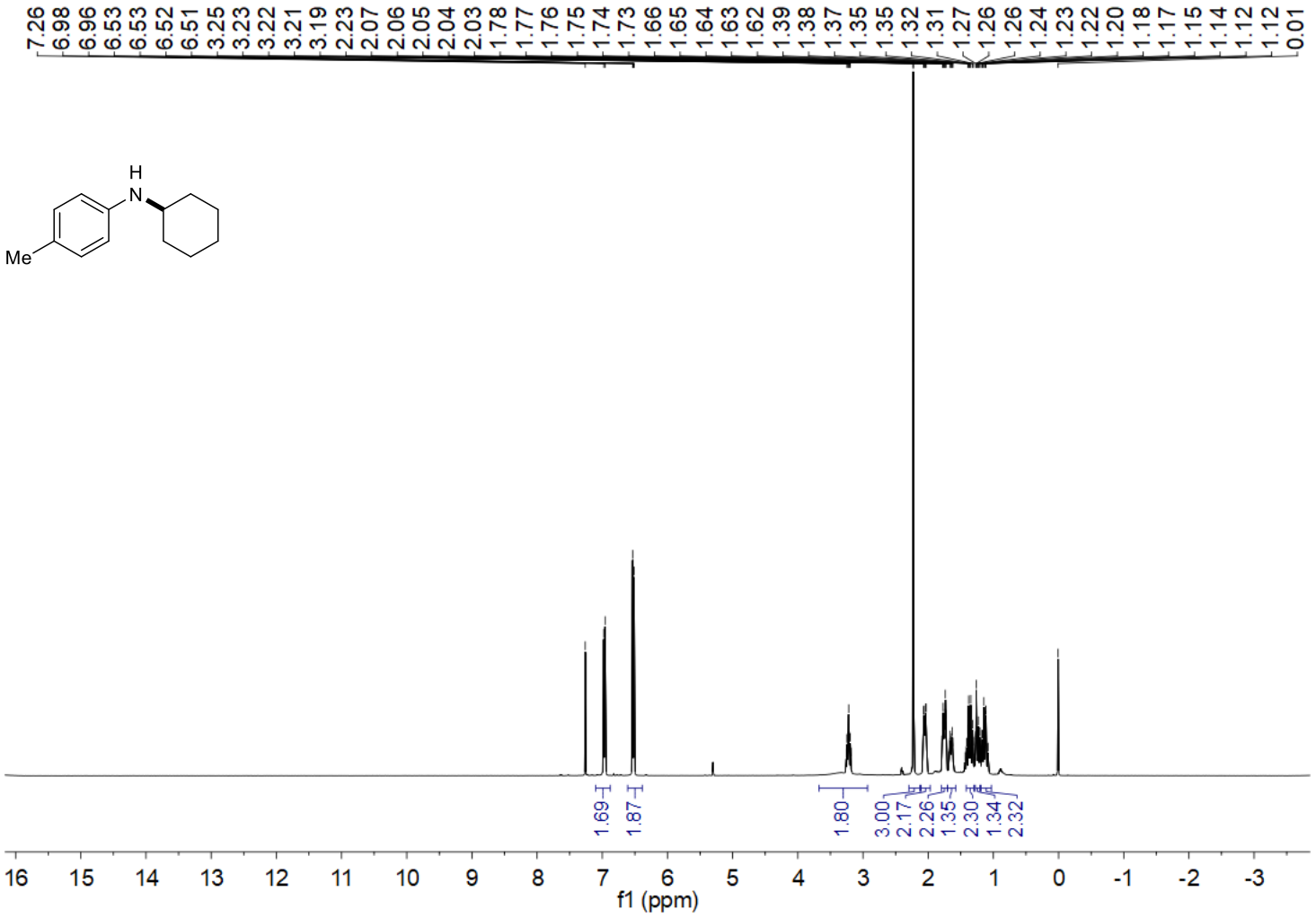


Compound **8** ^{1}H NMR



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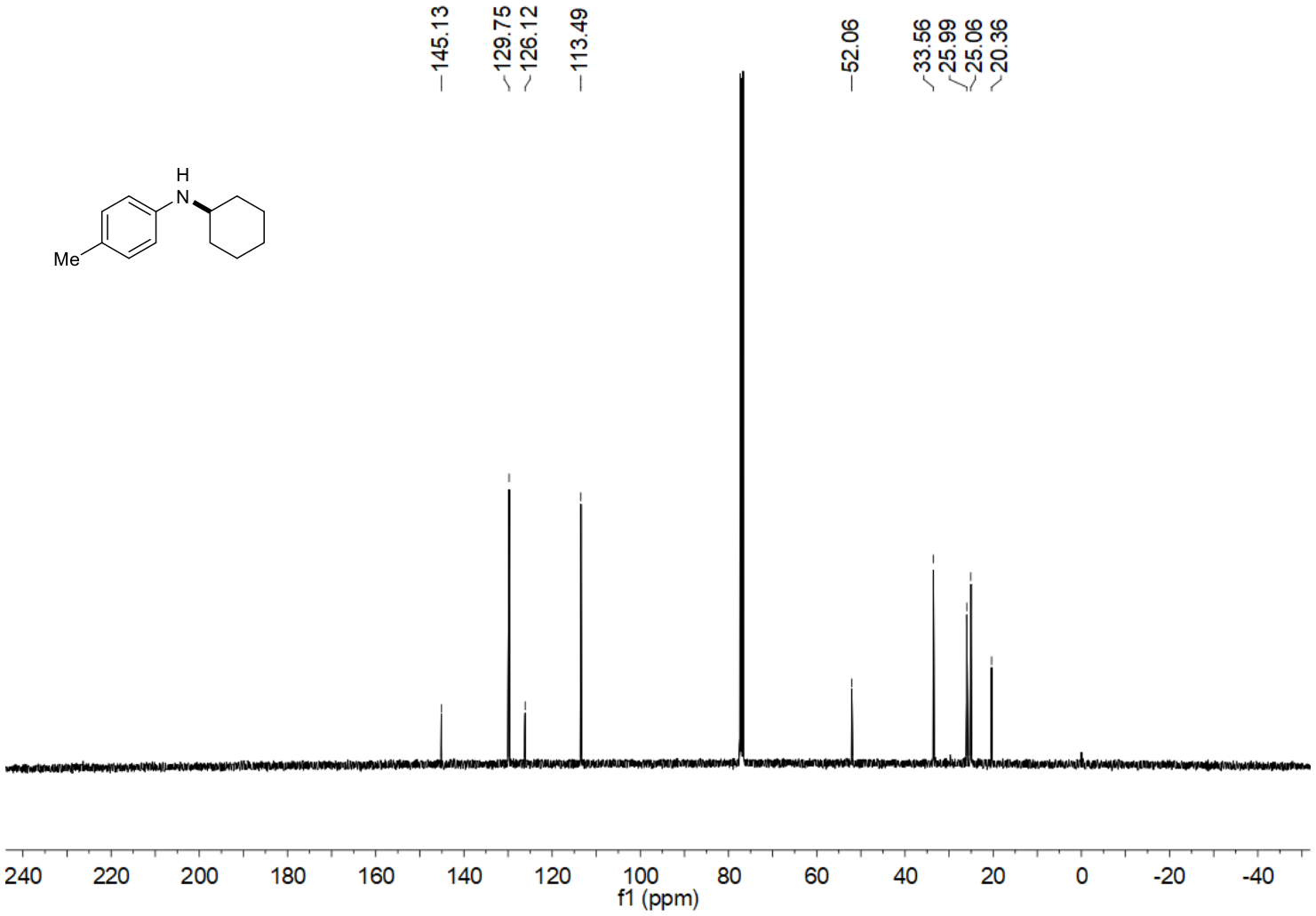
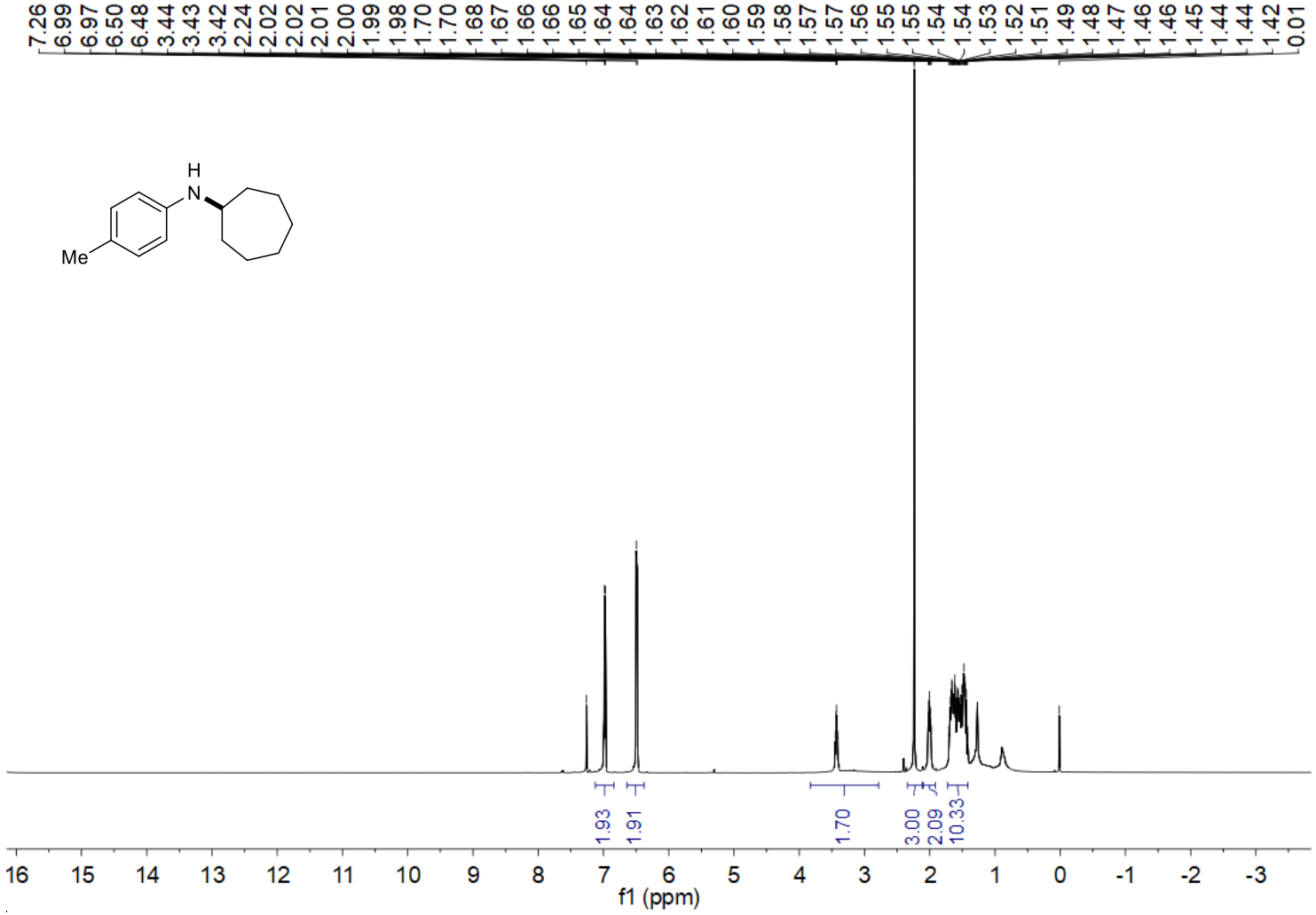
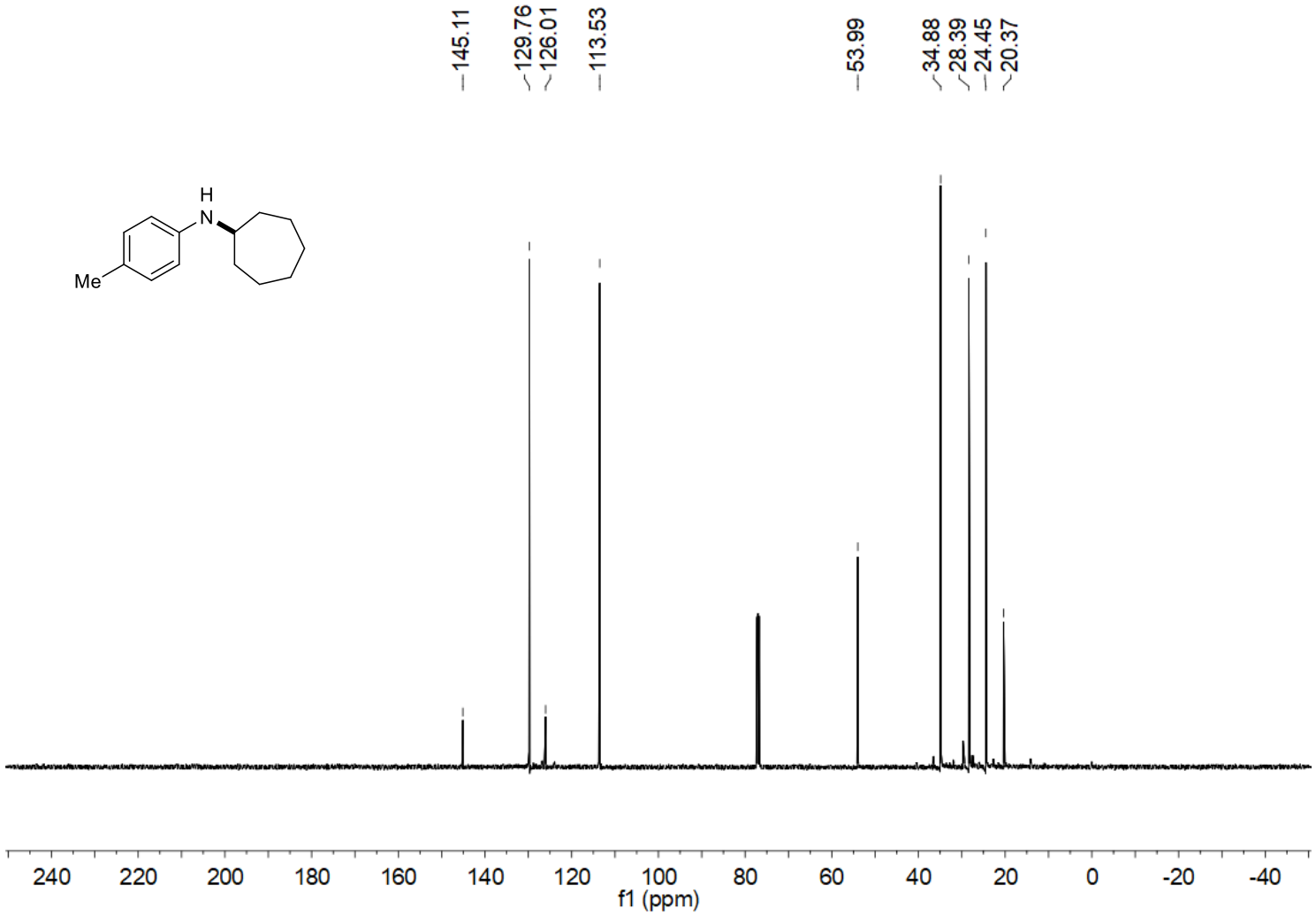


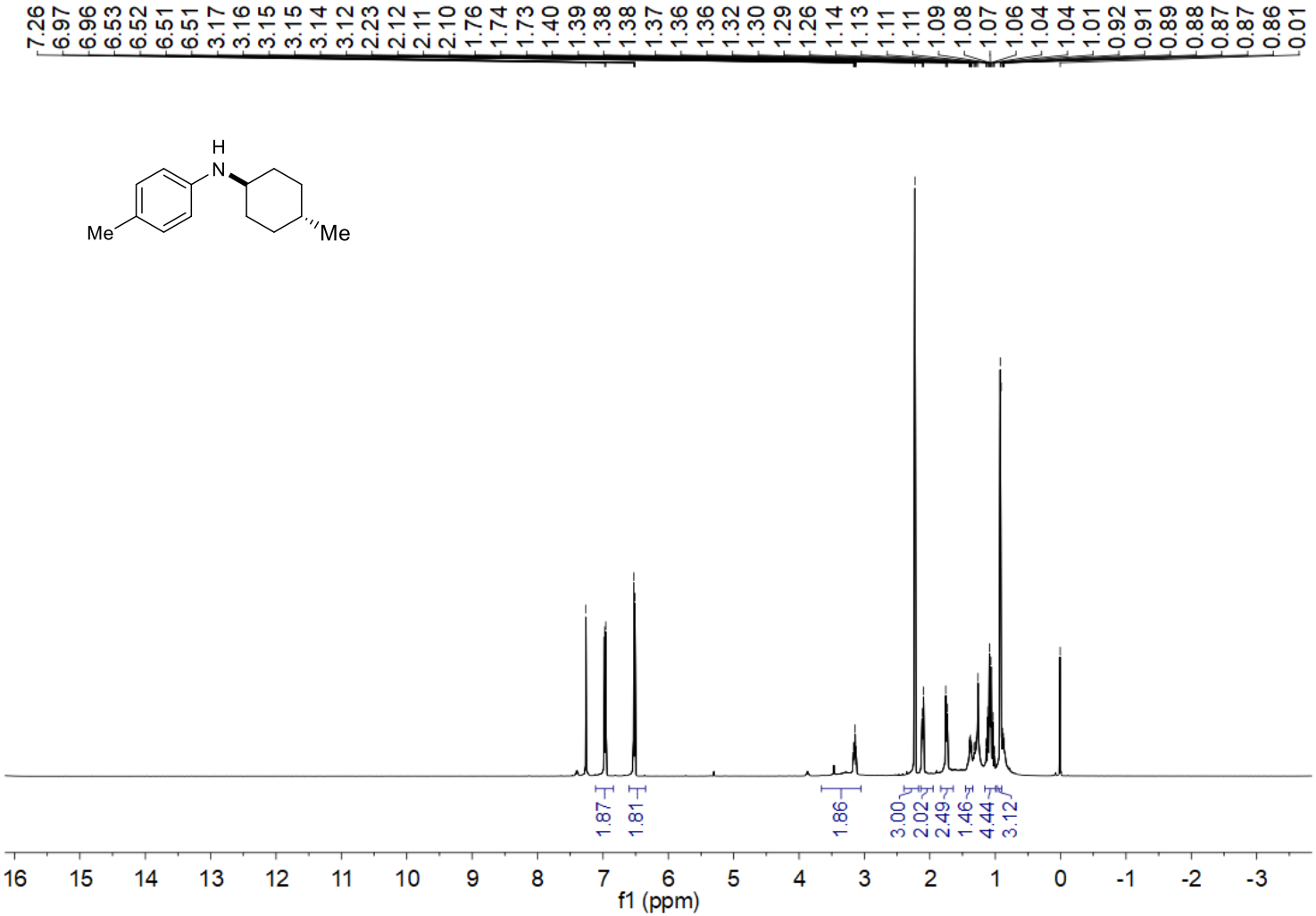
Compound **9** ^{1}H NMR



Compound **9** ^{13}C NMR



Compound **10** ^{1}H NMR



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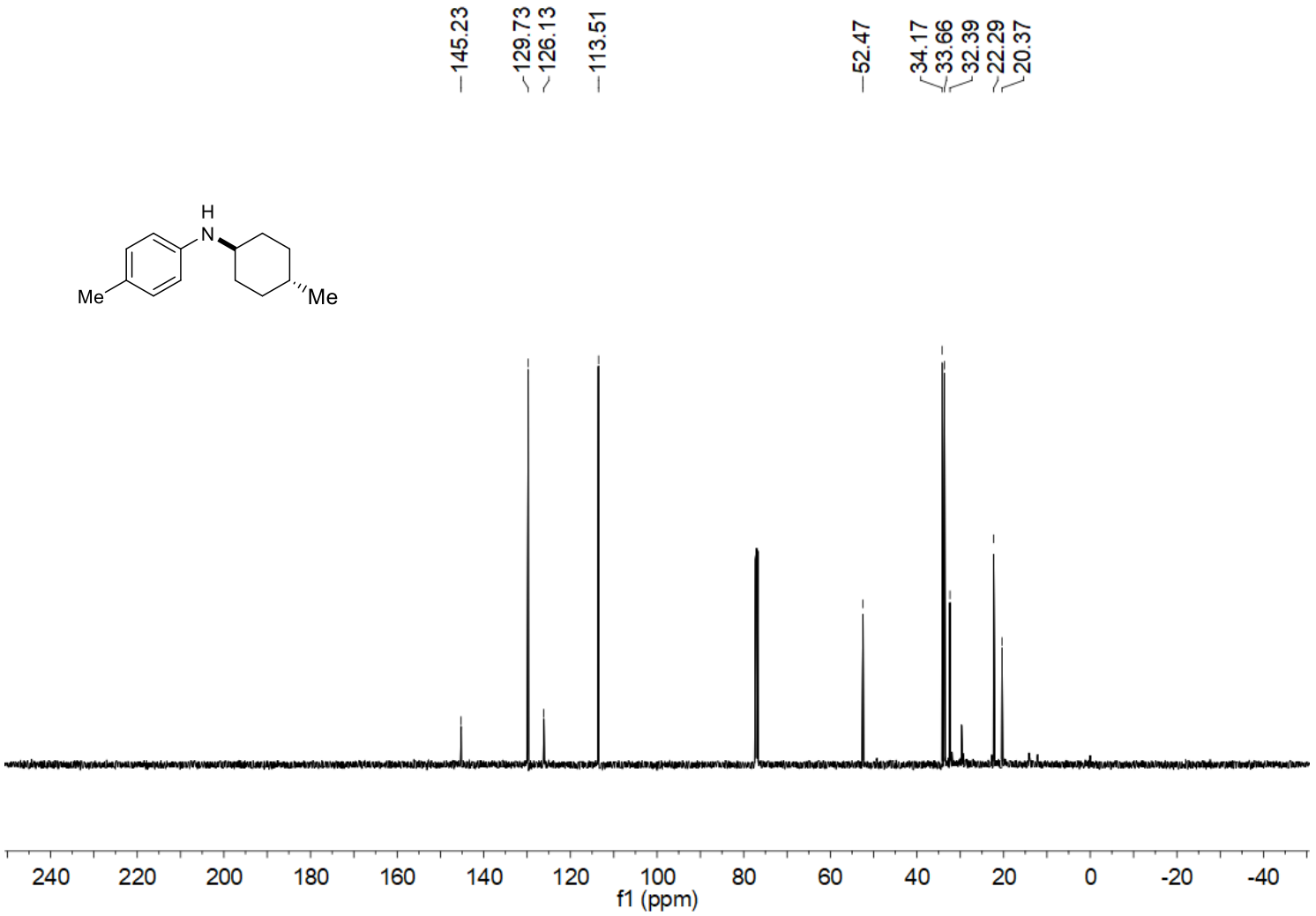
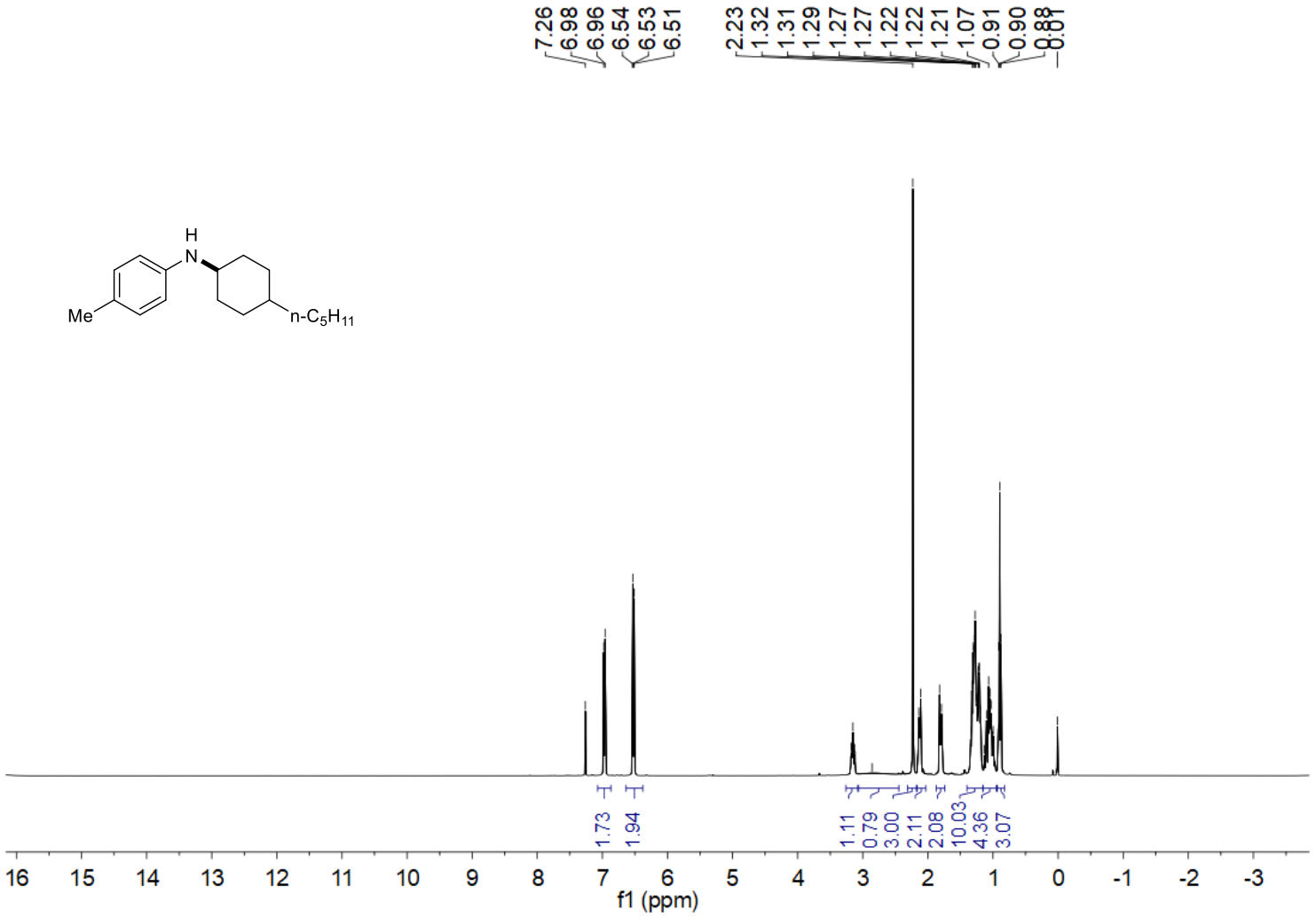
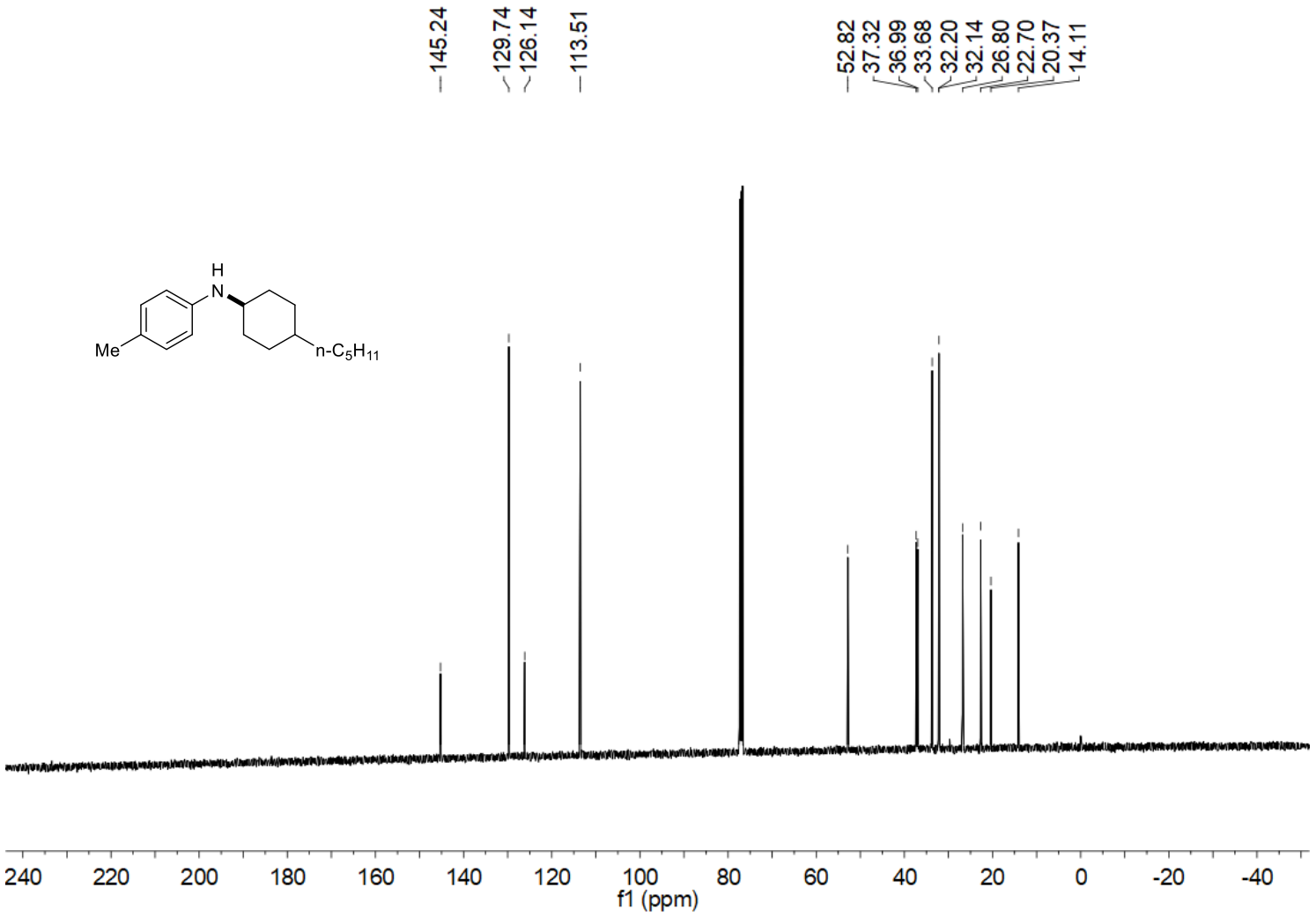


Compound **11** ^{1}H NMR



Compound **11** ^{13}C NMR



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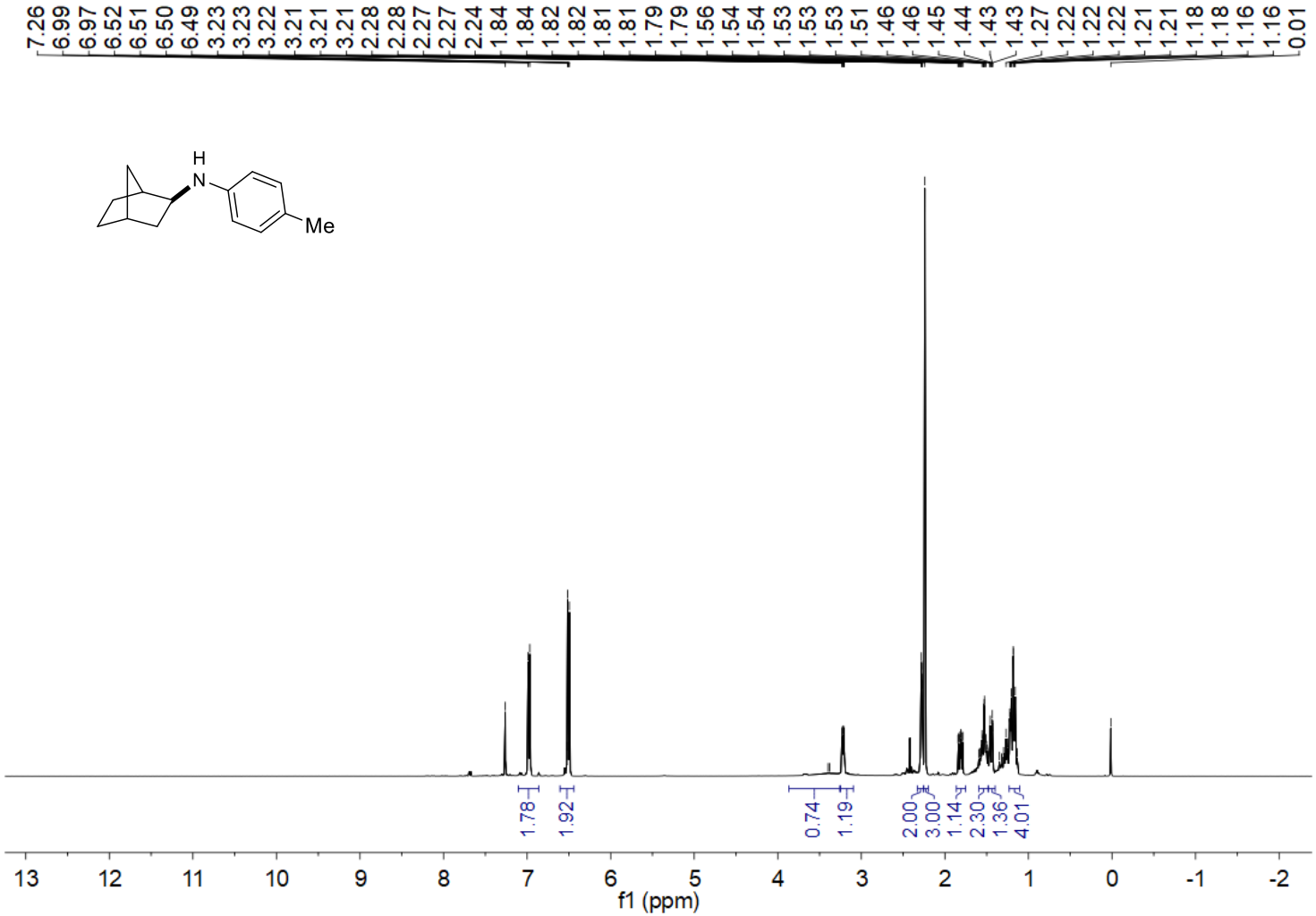

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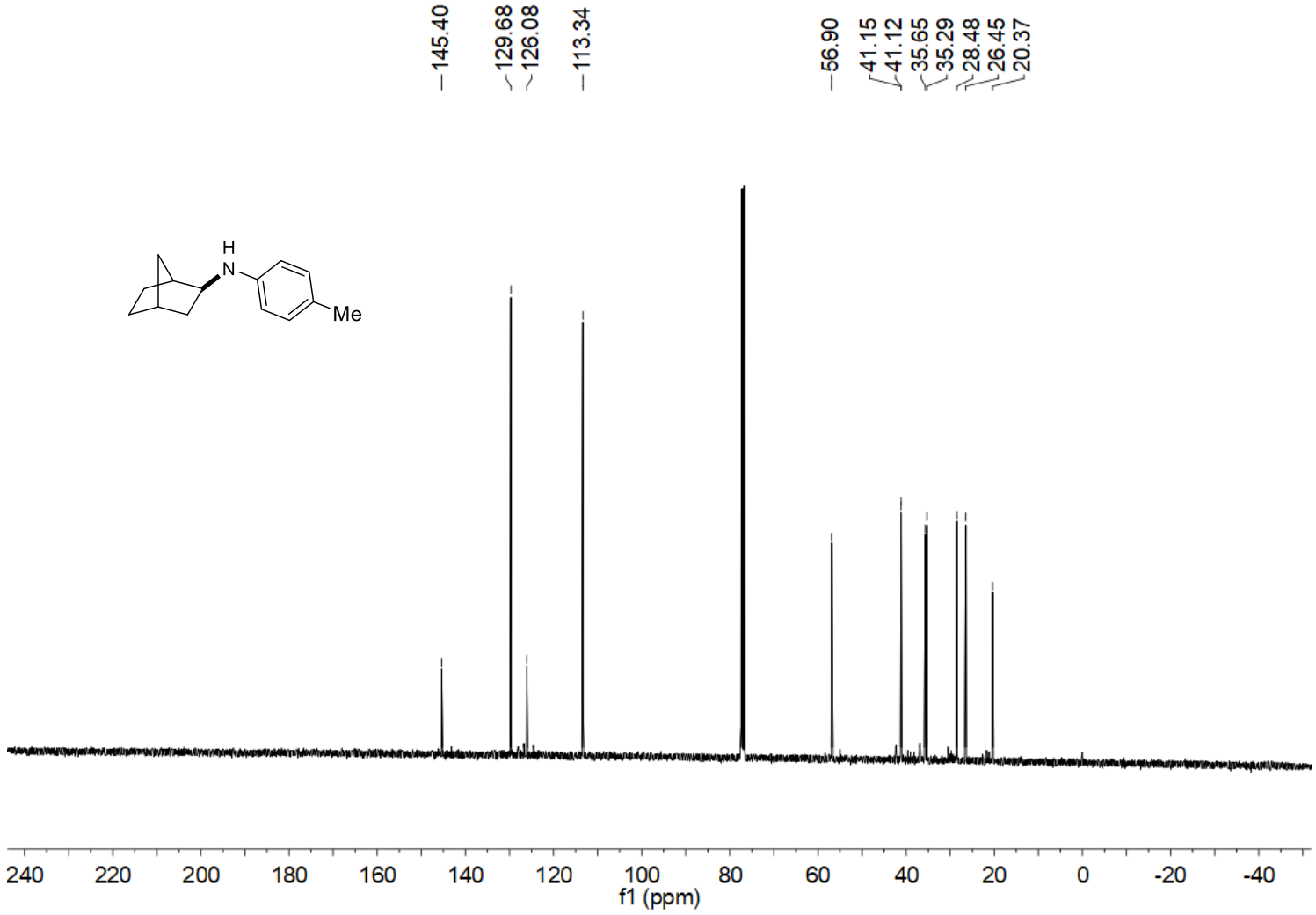
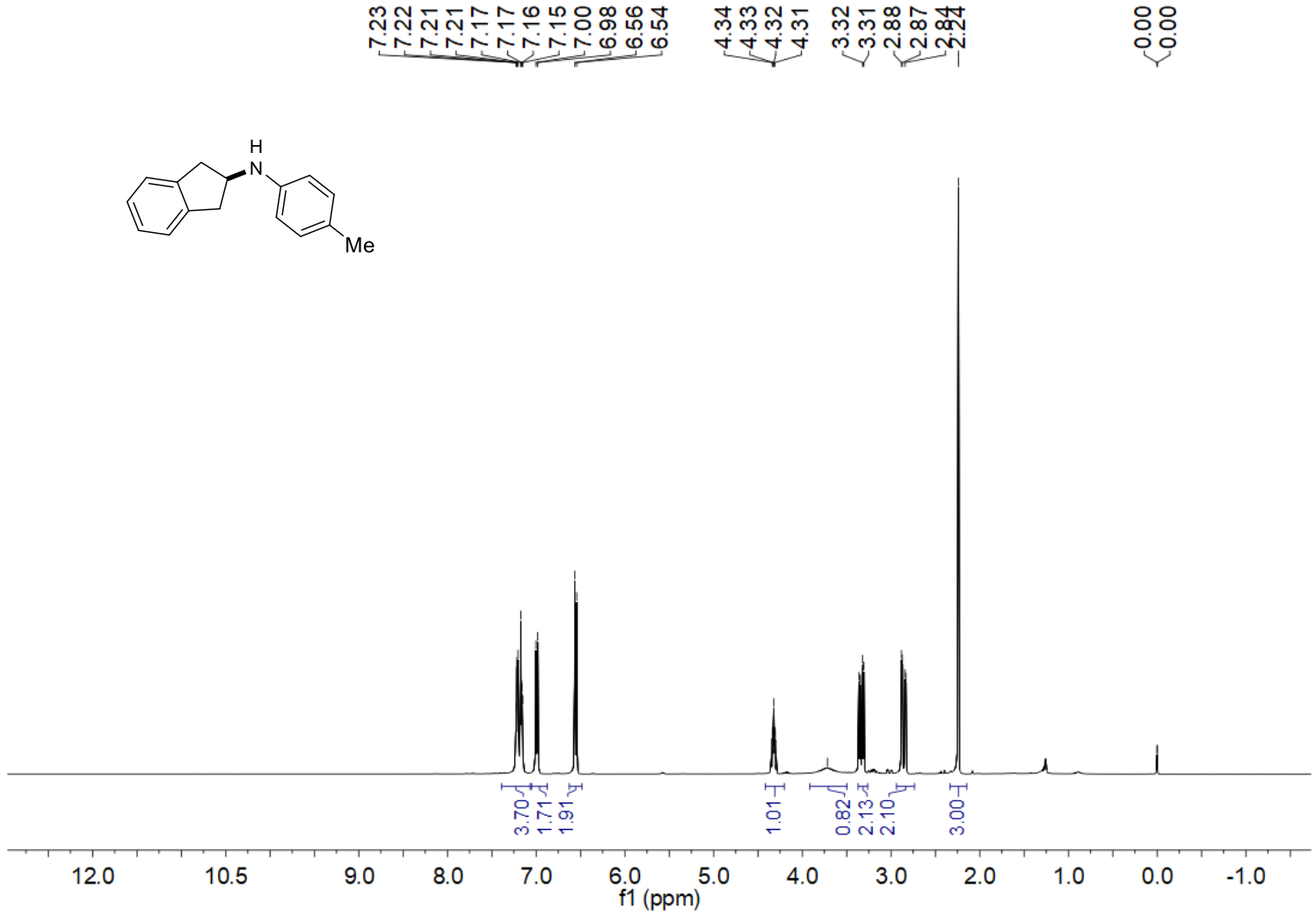


Compound **13** ^{1}H NMR



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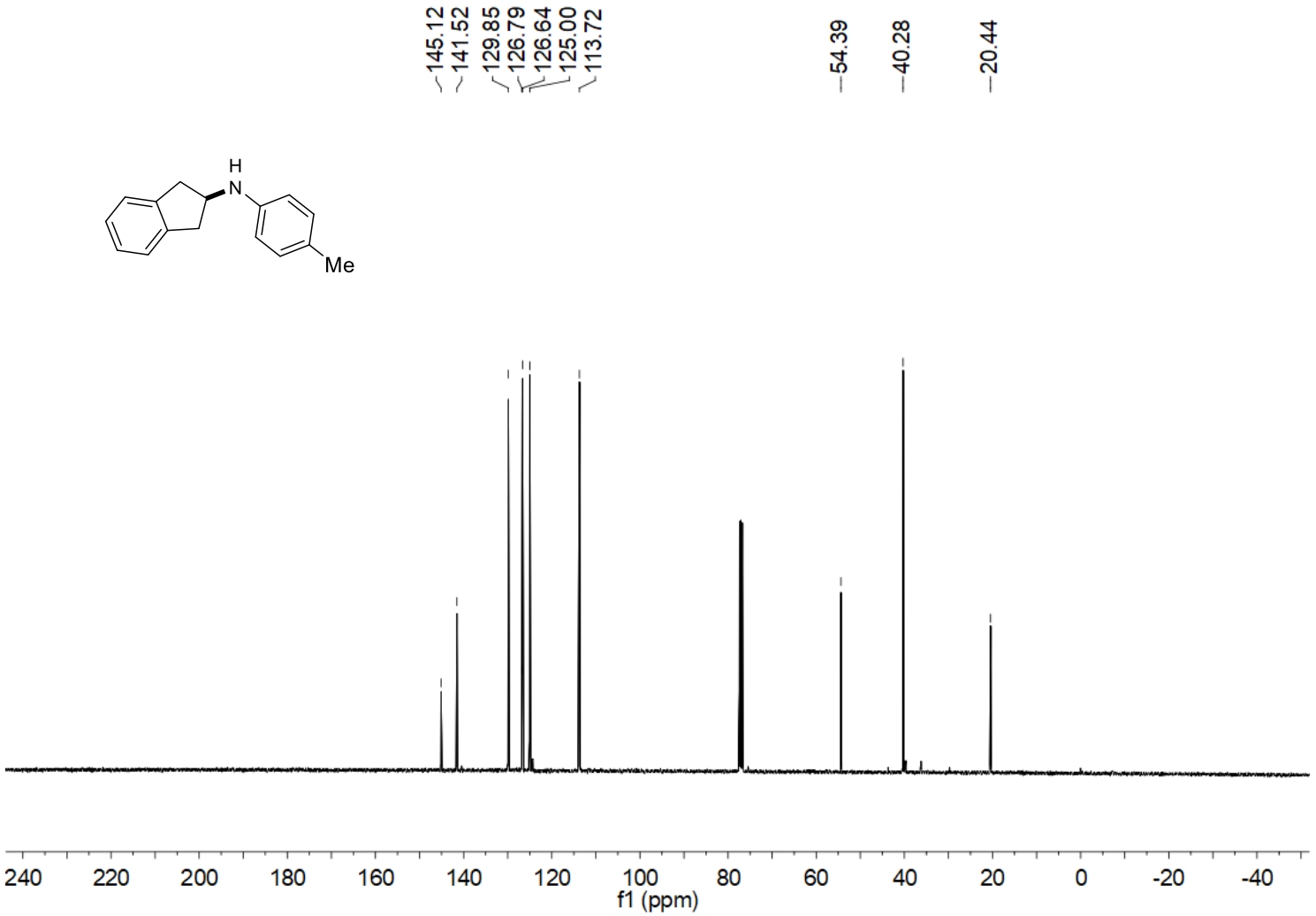
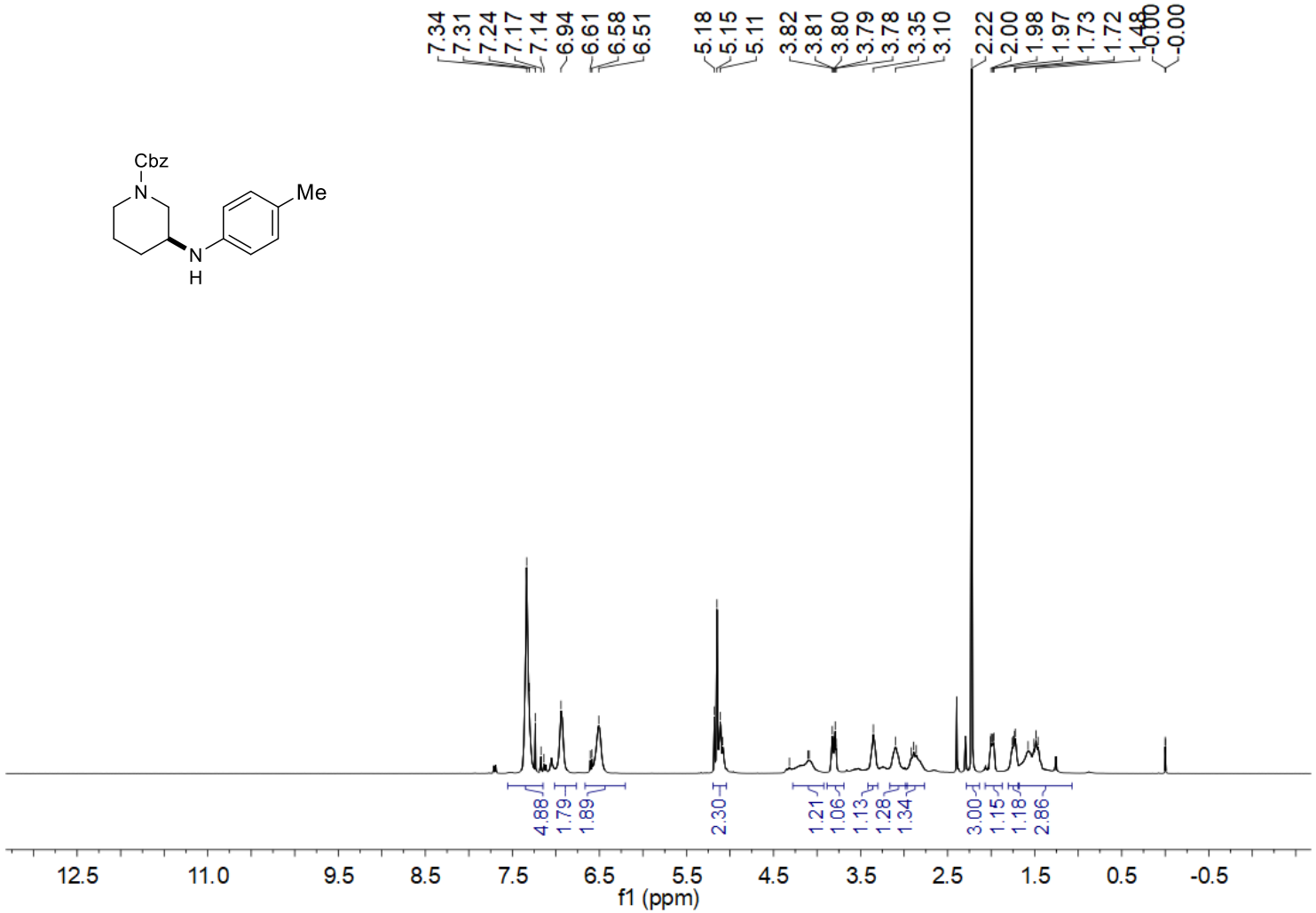
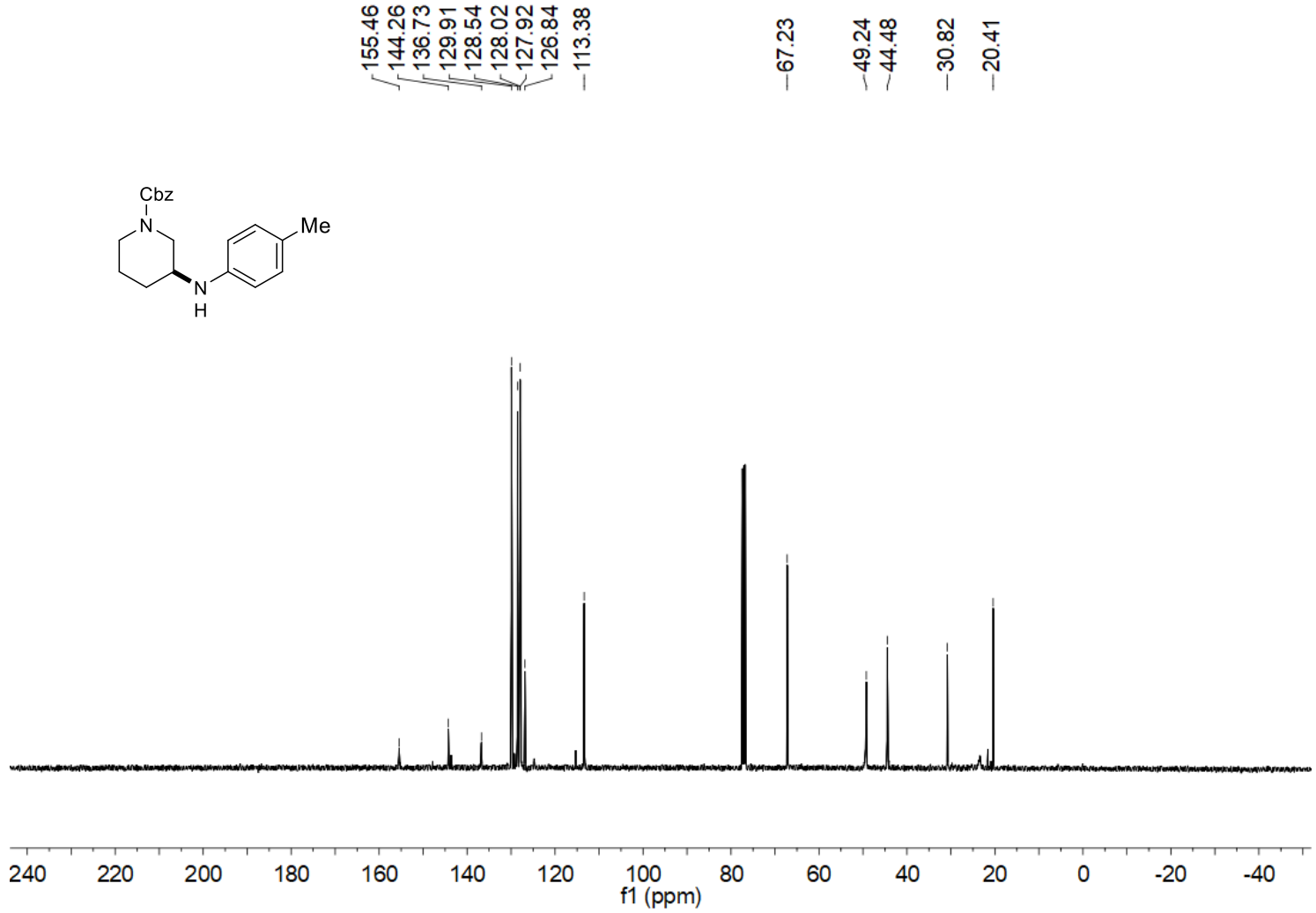


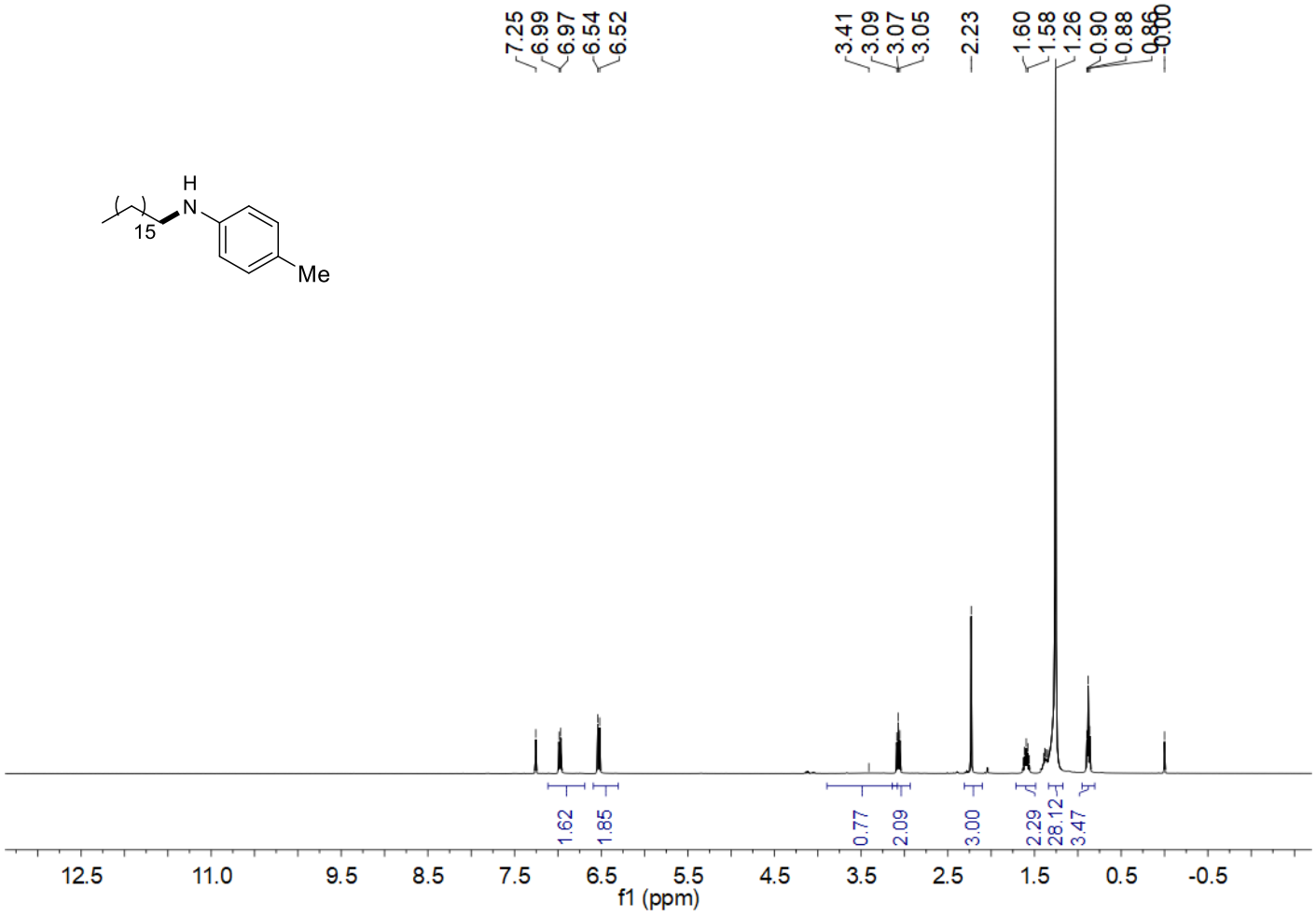
Compound **14** ^{1}H NMR



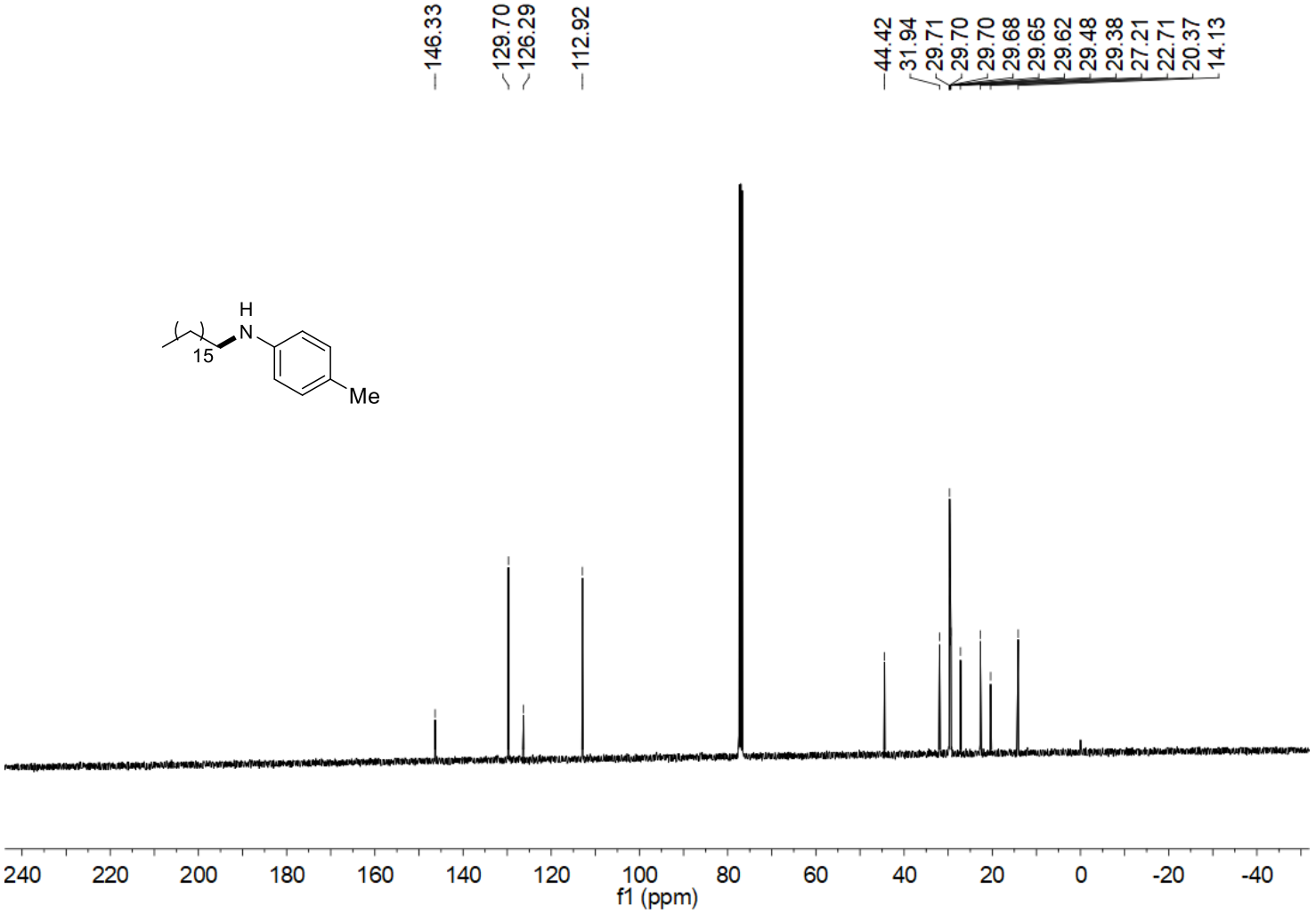
Compound **14** ^{13}C NMR



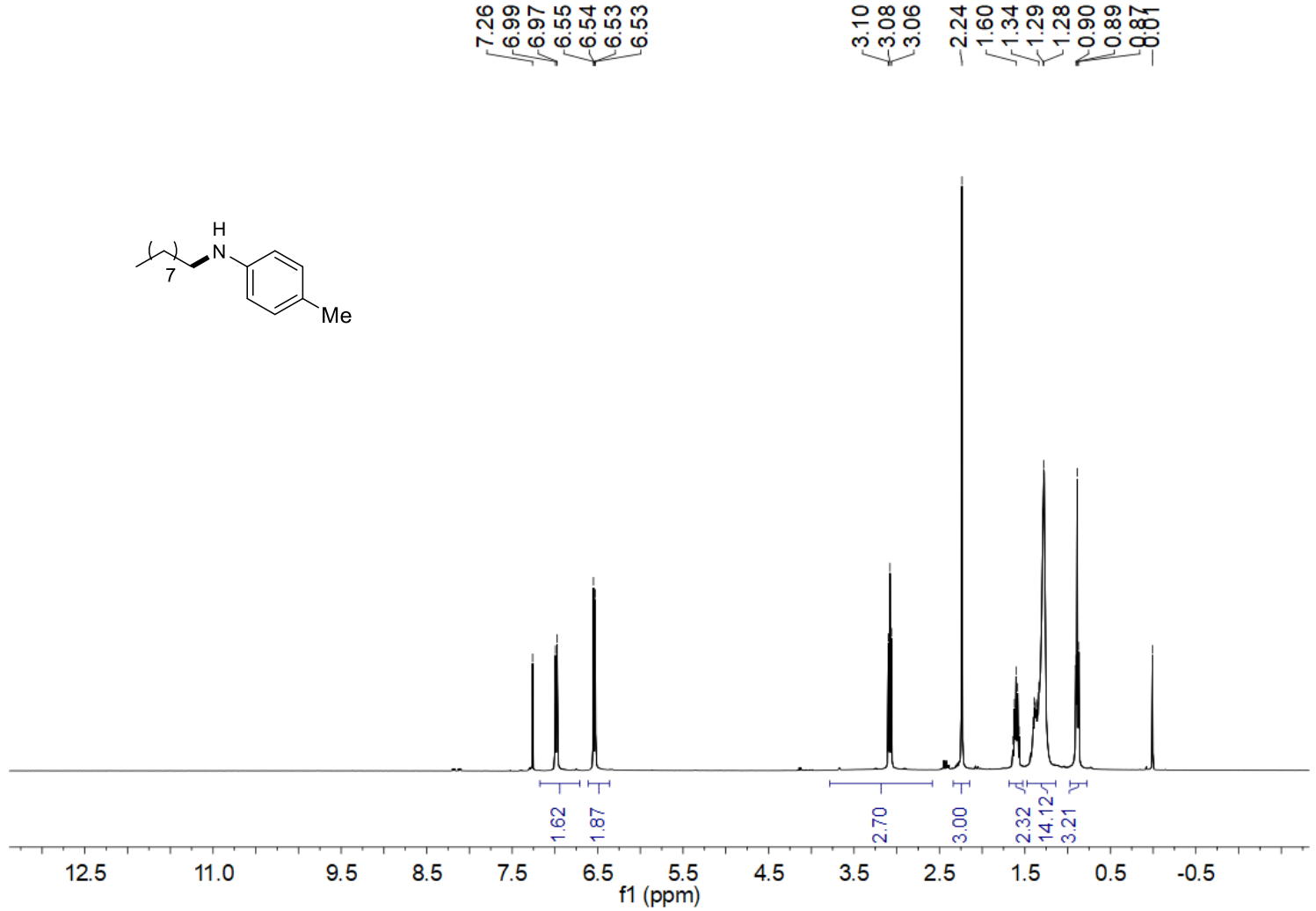
Compound **15** ^{1}H NMR



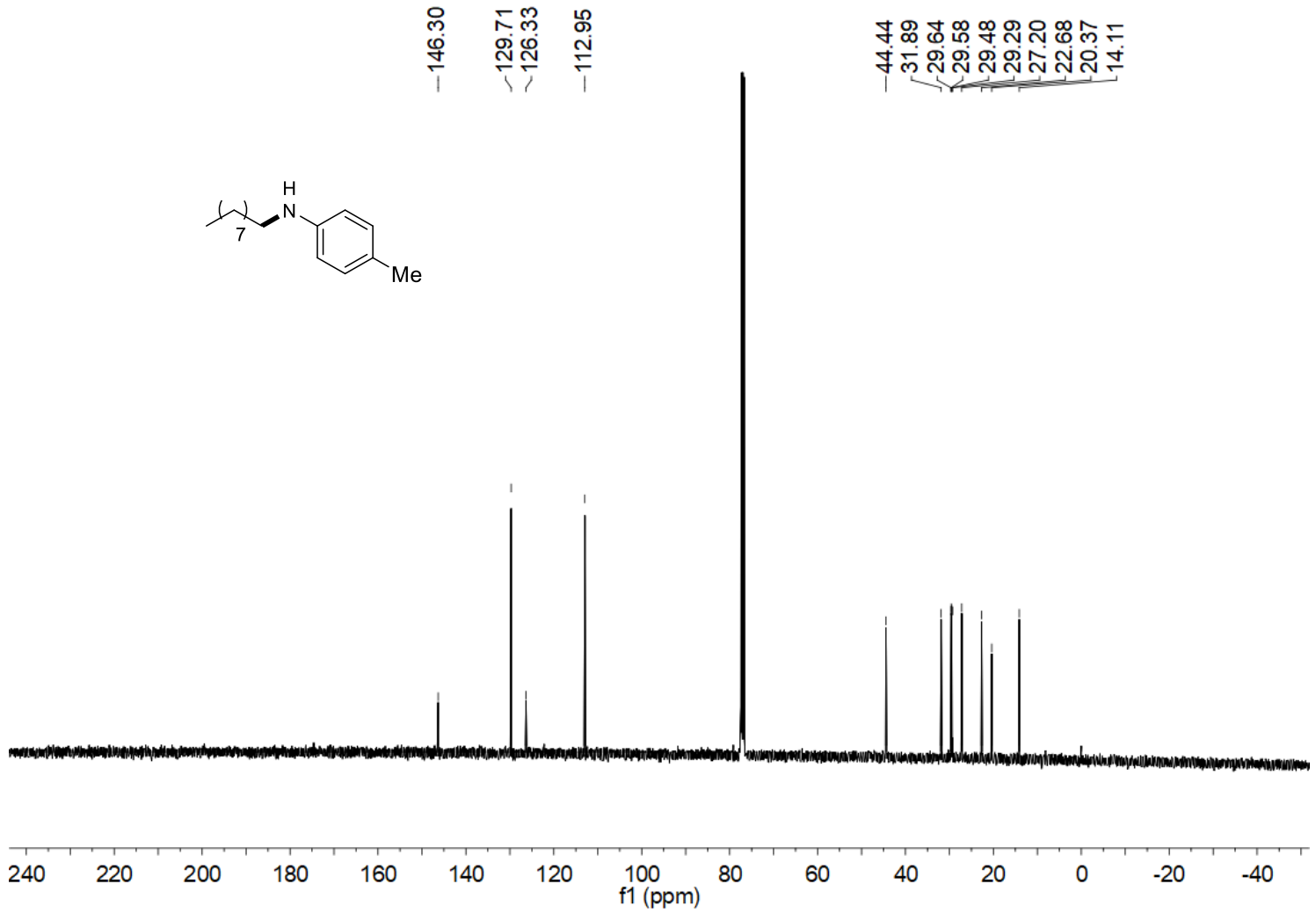
Compound **15** ^{13}C NMR



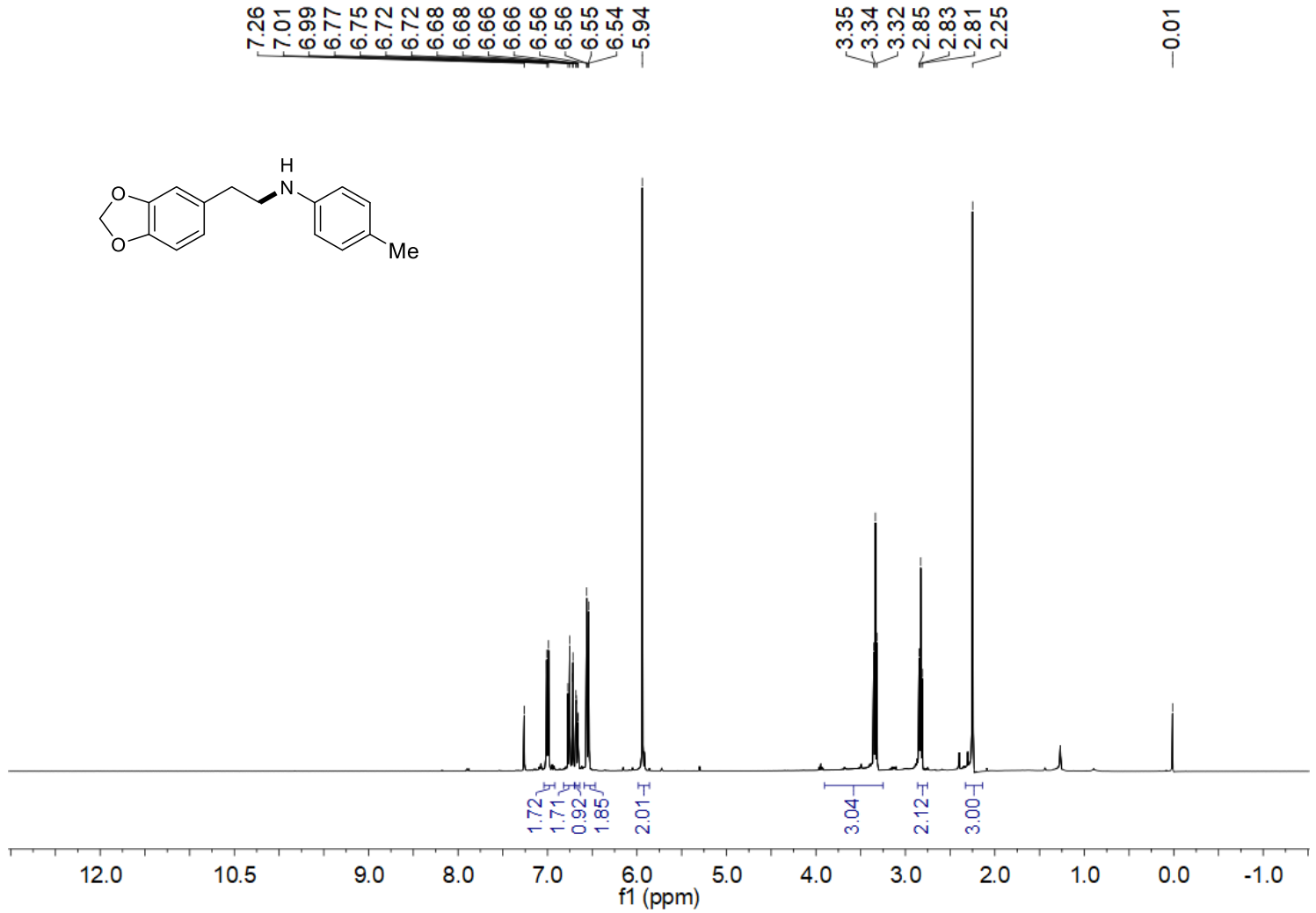
Compound **16** ^{1}H NMR



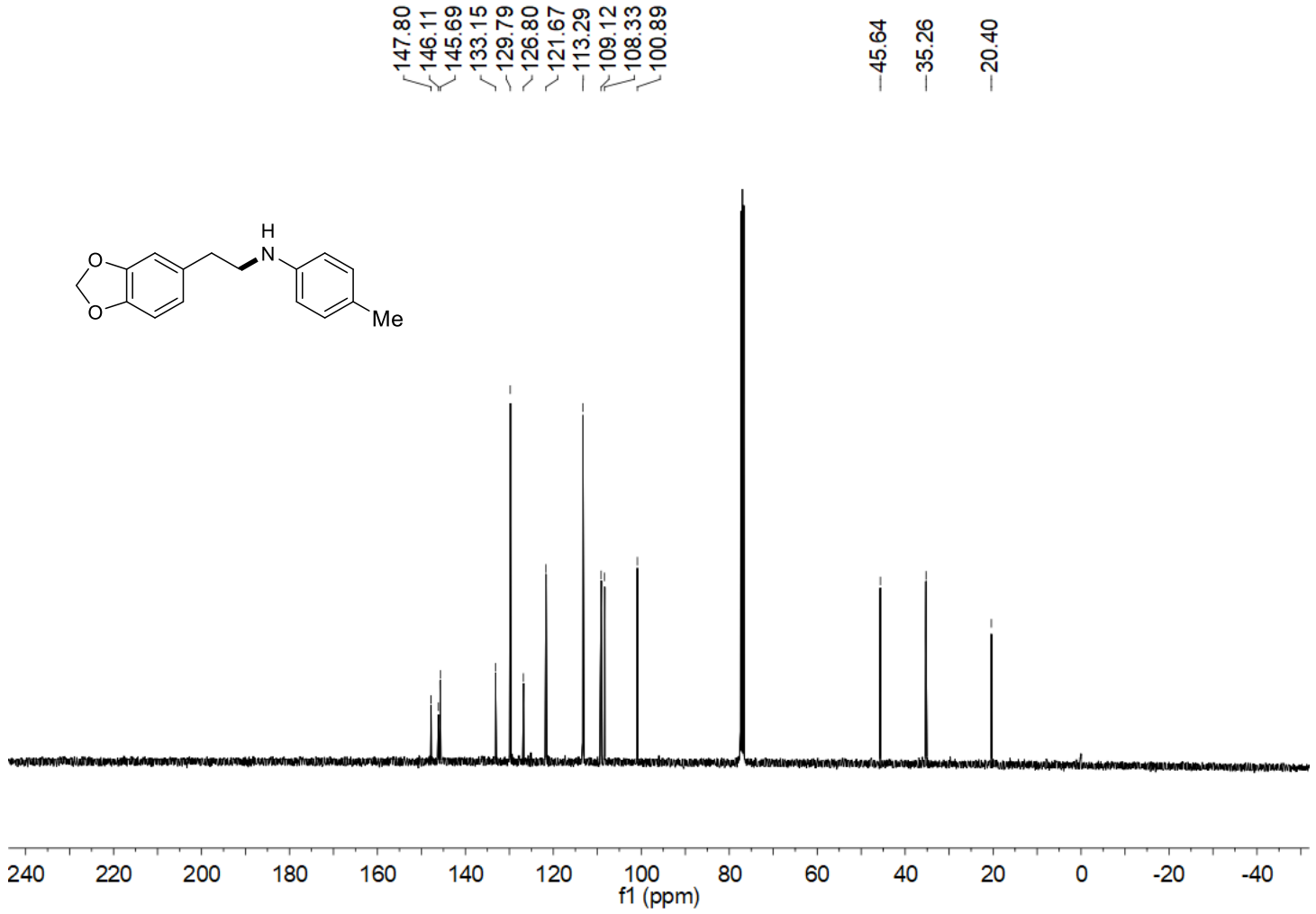
Compound **16** ^{13}C NMR



Compound **17** ^{1}H NMR



Compound **17** ^{13}C NMR



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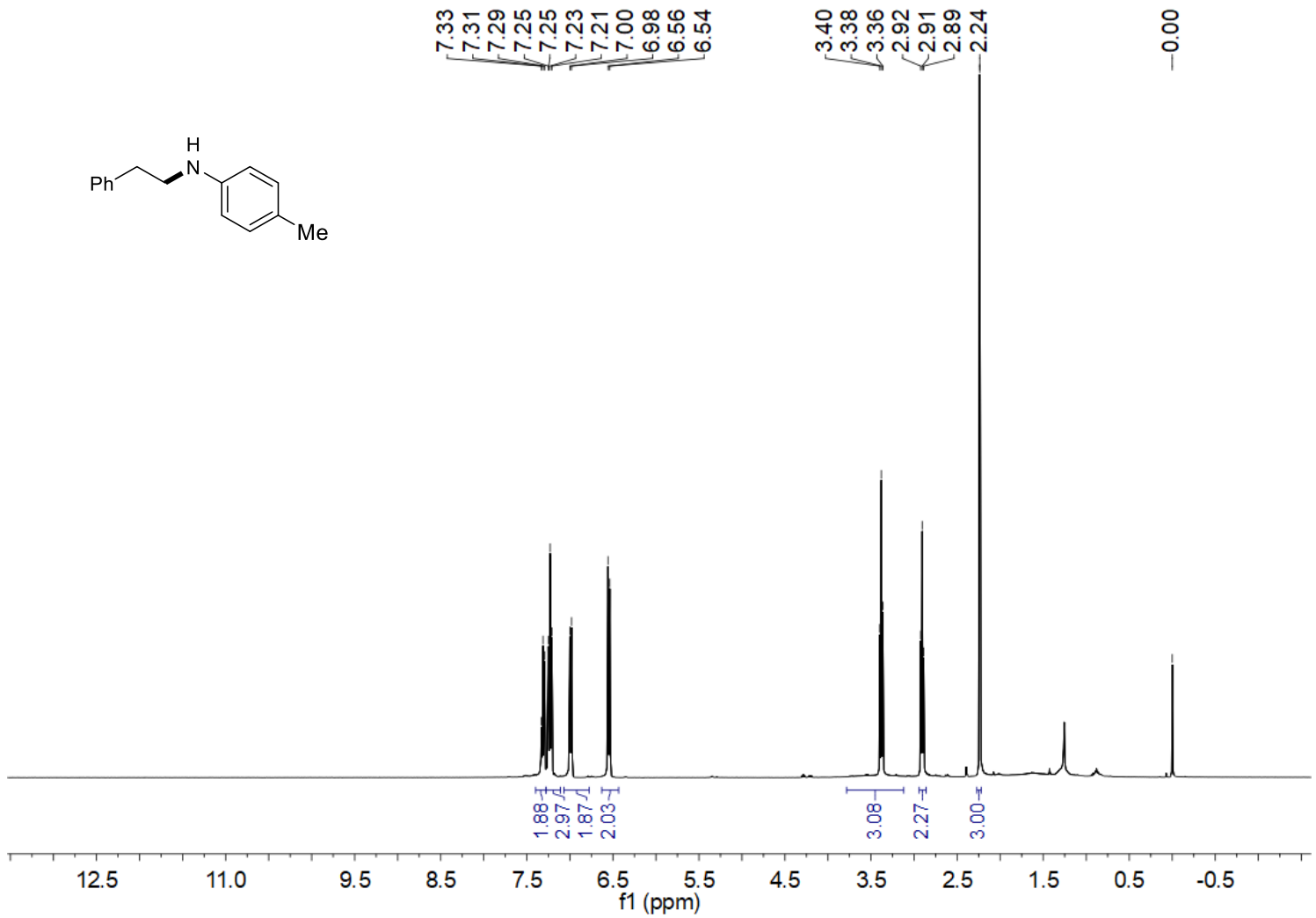
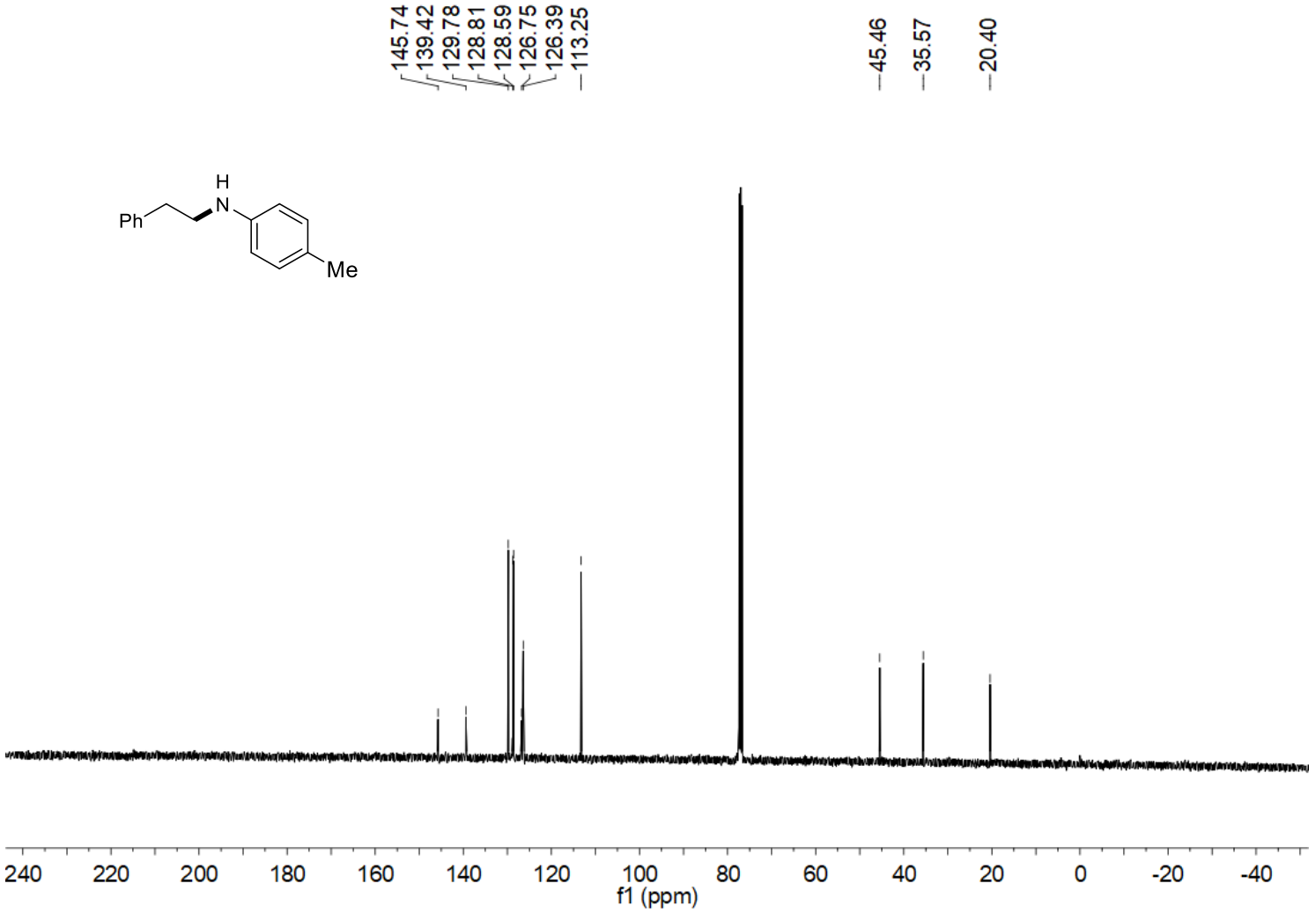
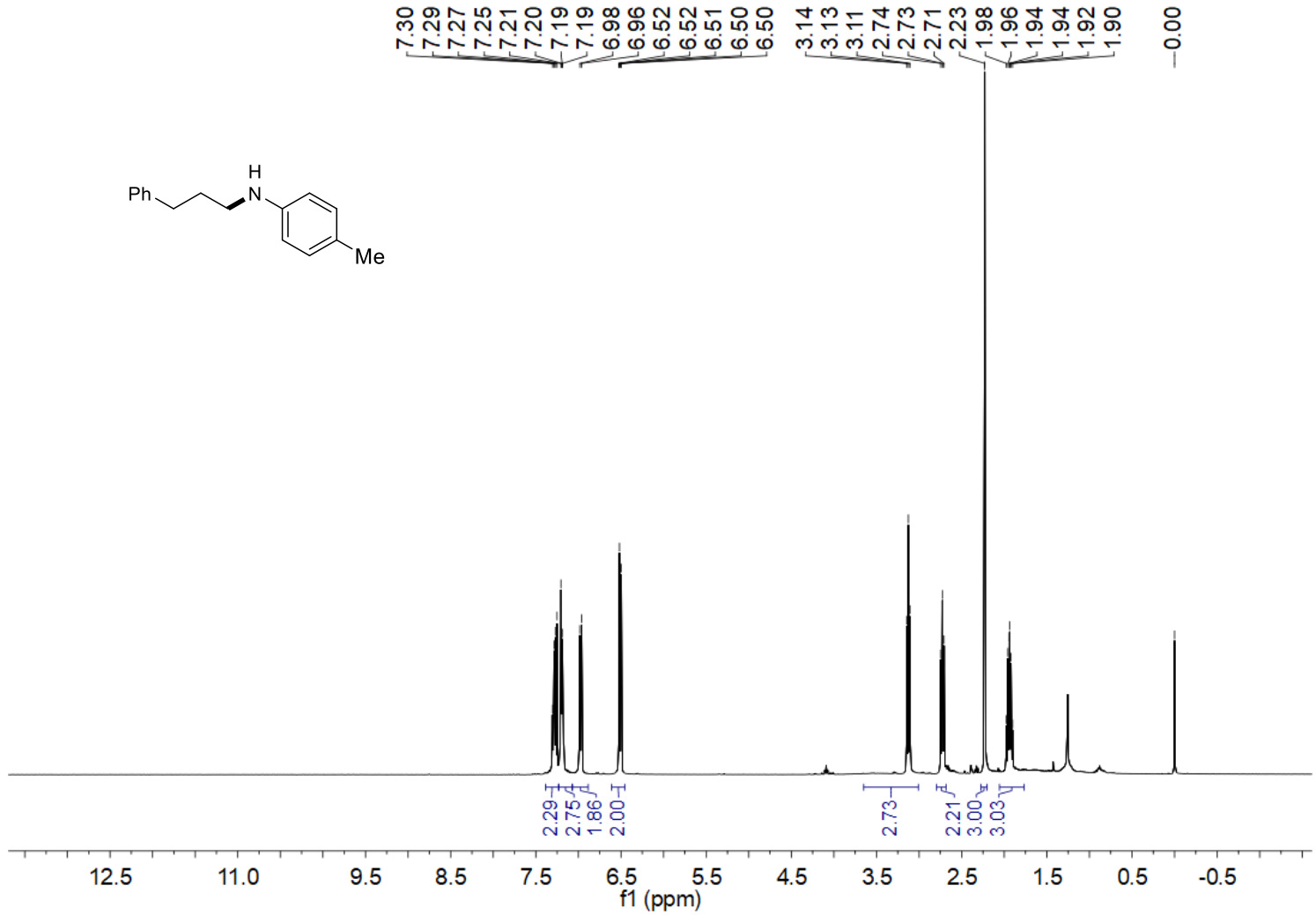


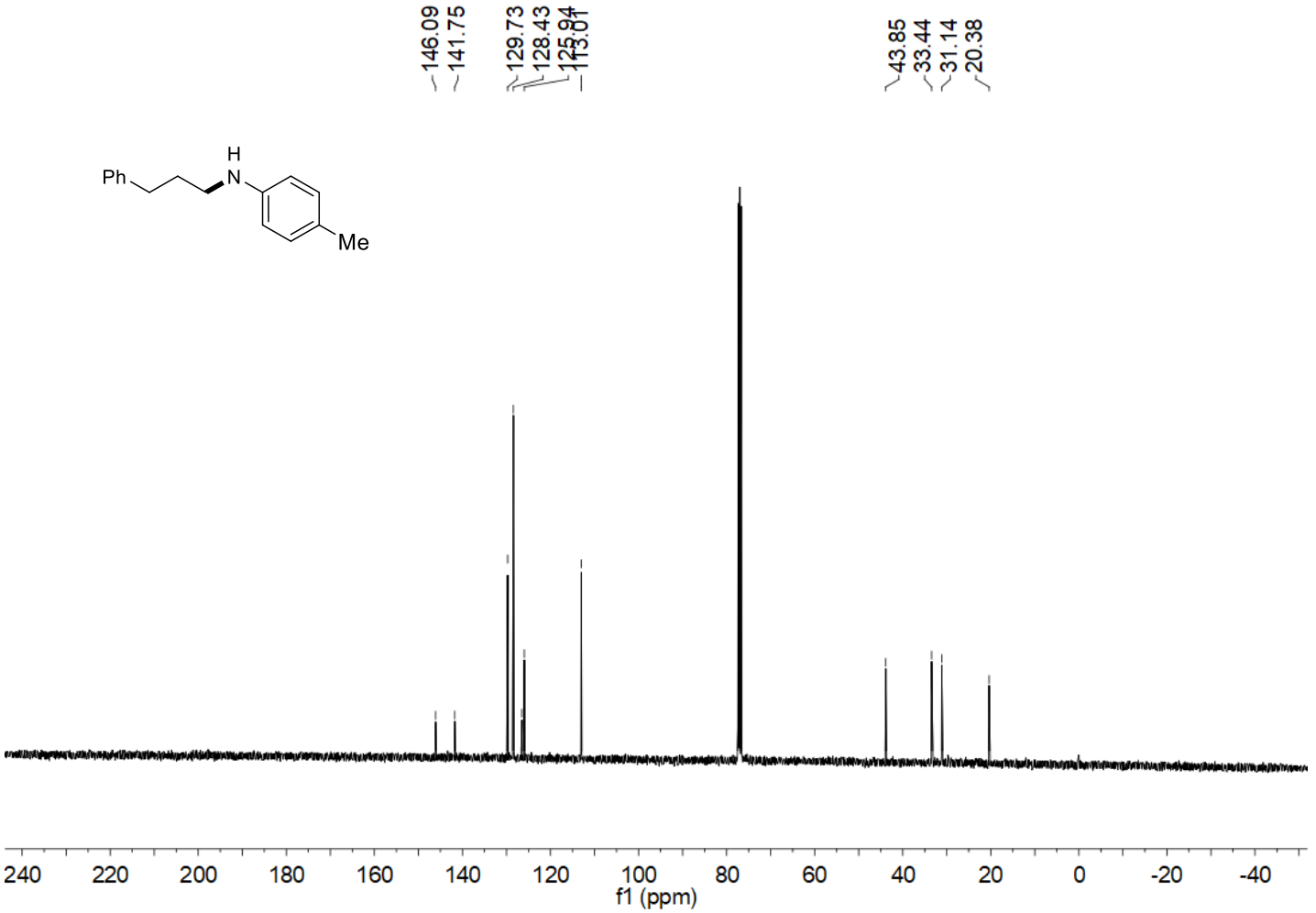
Compound **18** ^{13}C NMR



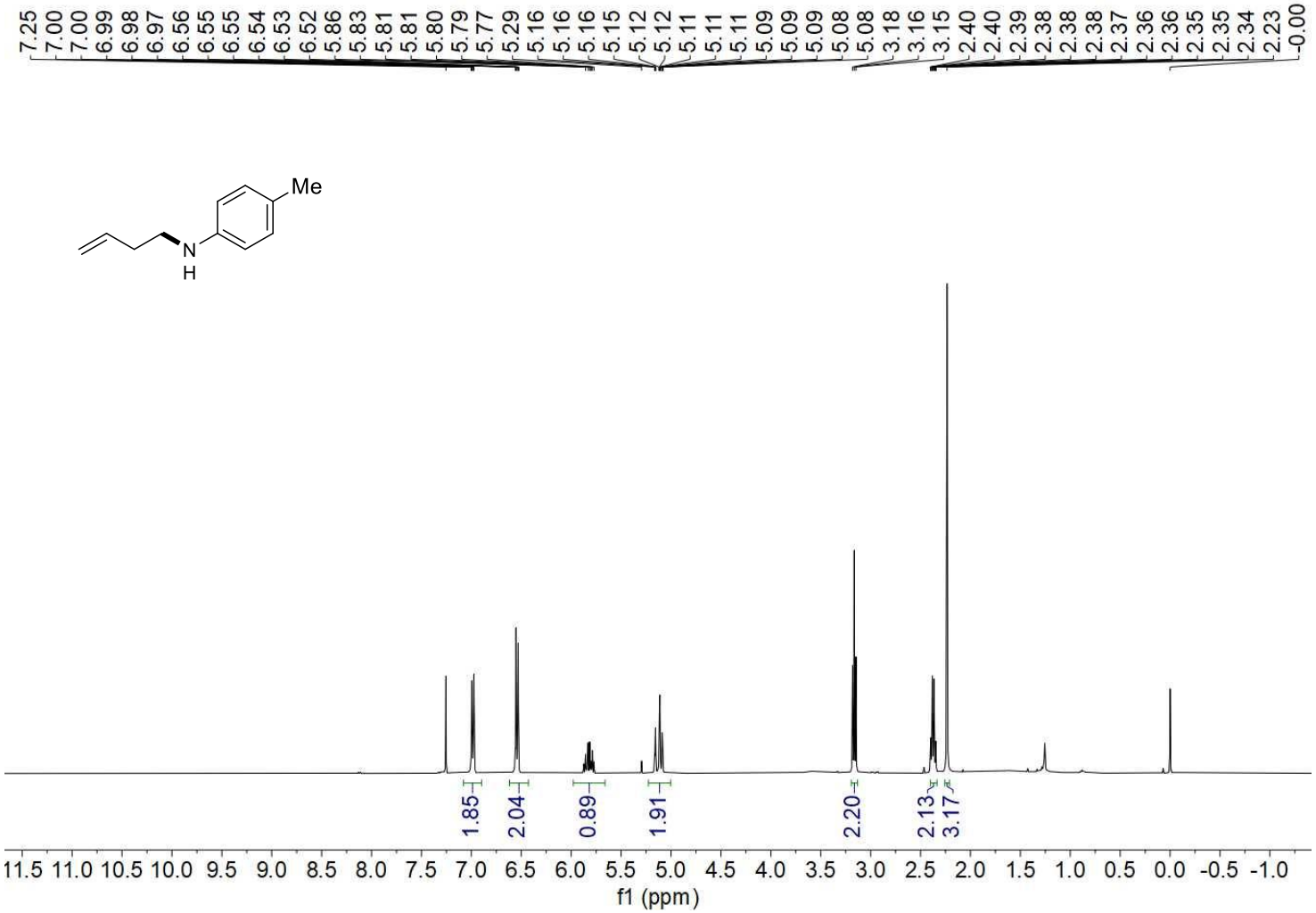
Compound **19** ^{1}H NMR



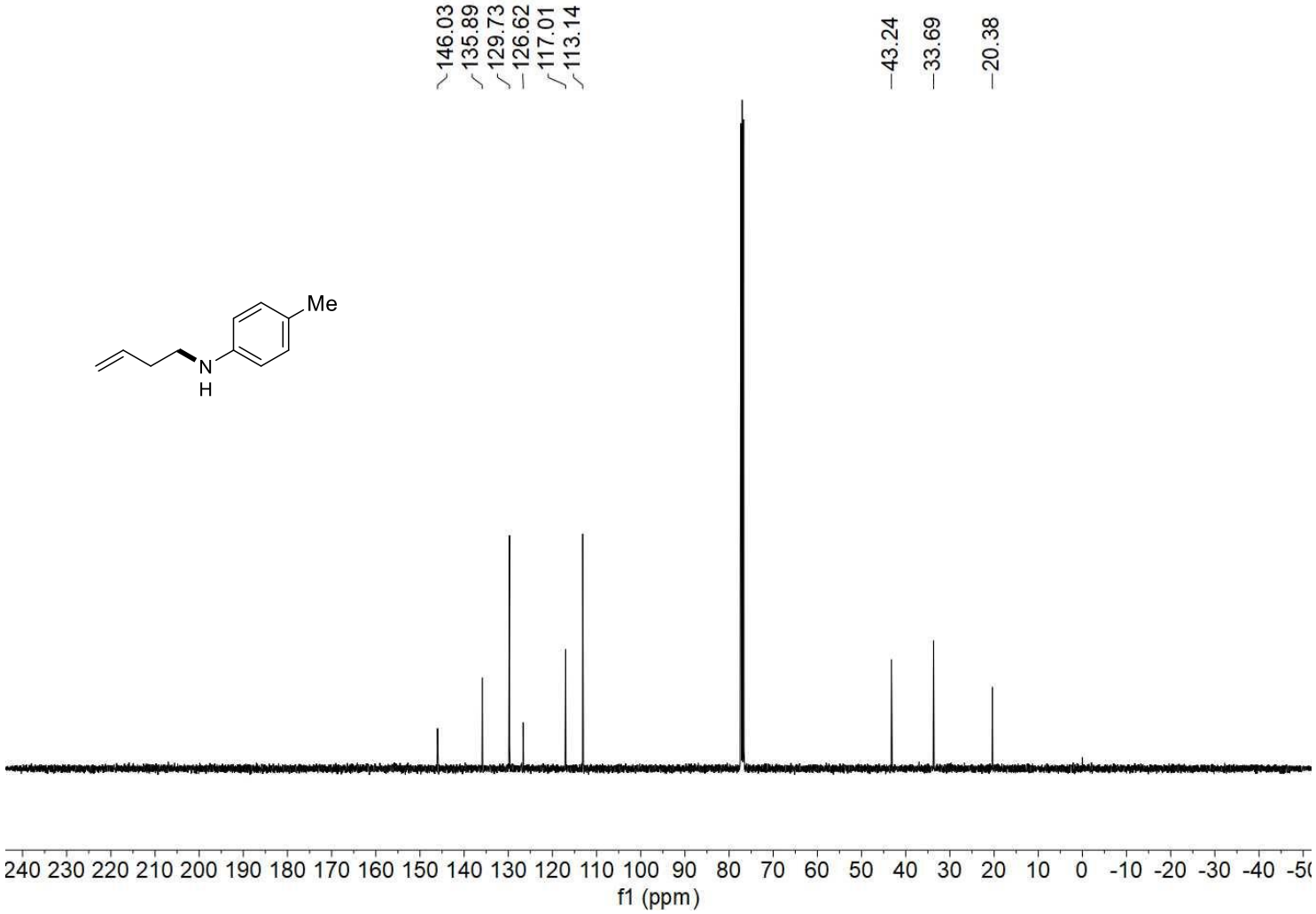
Compound **19** ^{13}C NMR



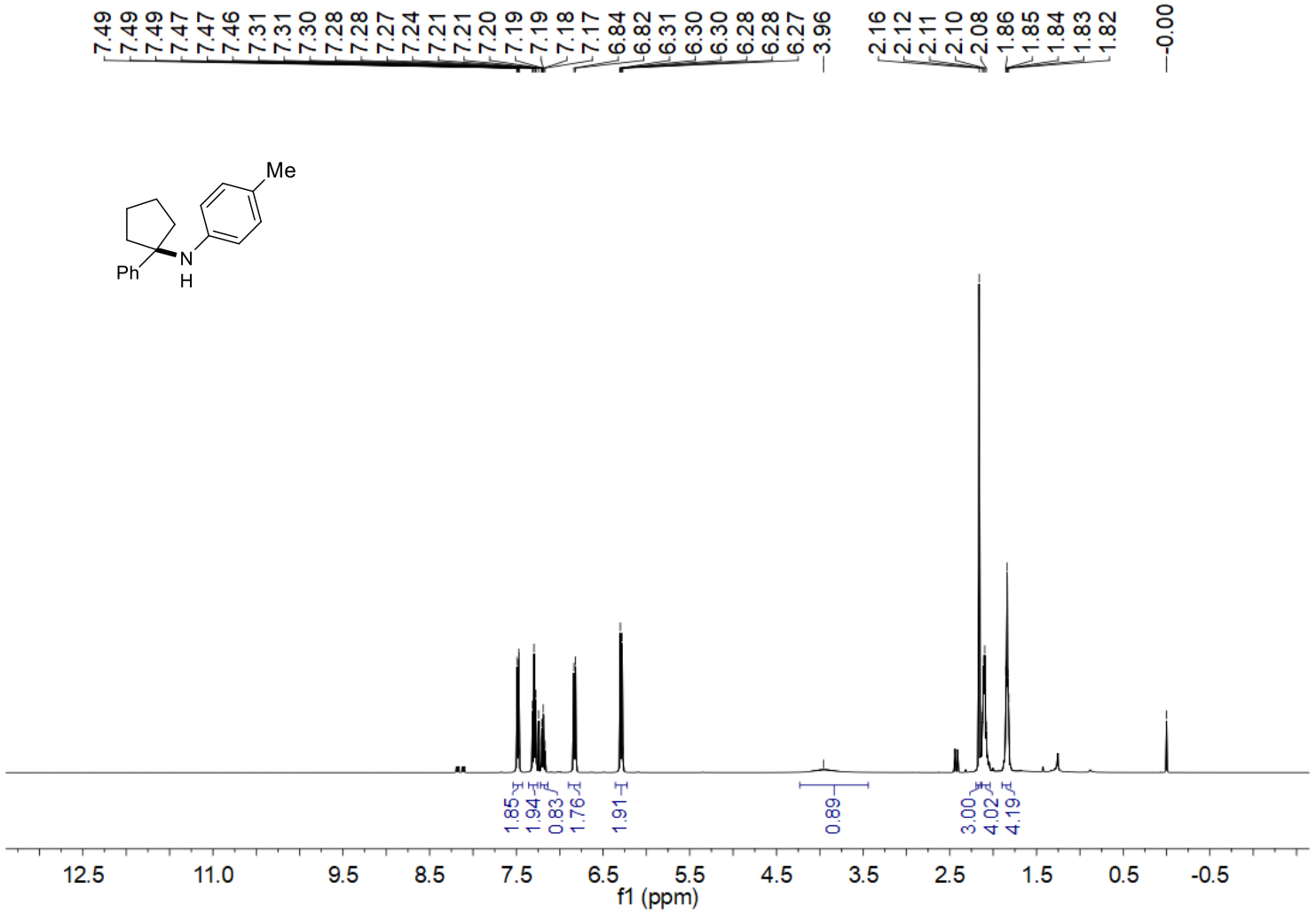
Compound **20** ^{1}H NMR



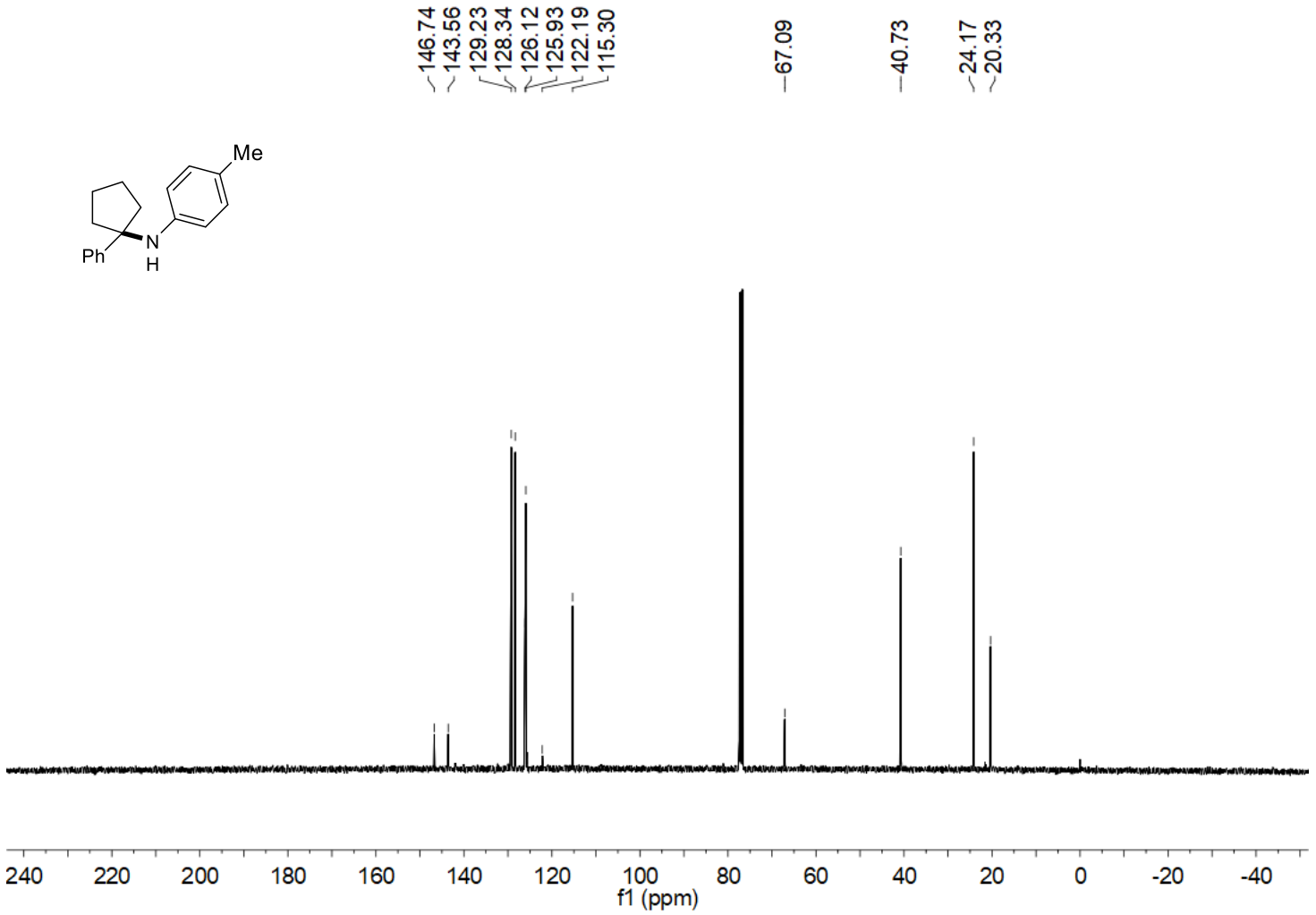
Compound **20** ^{13}C NMR



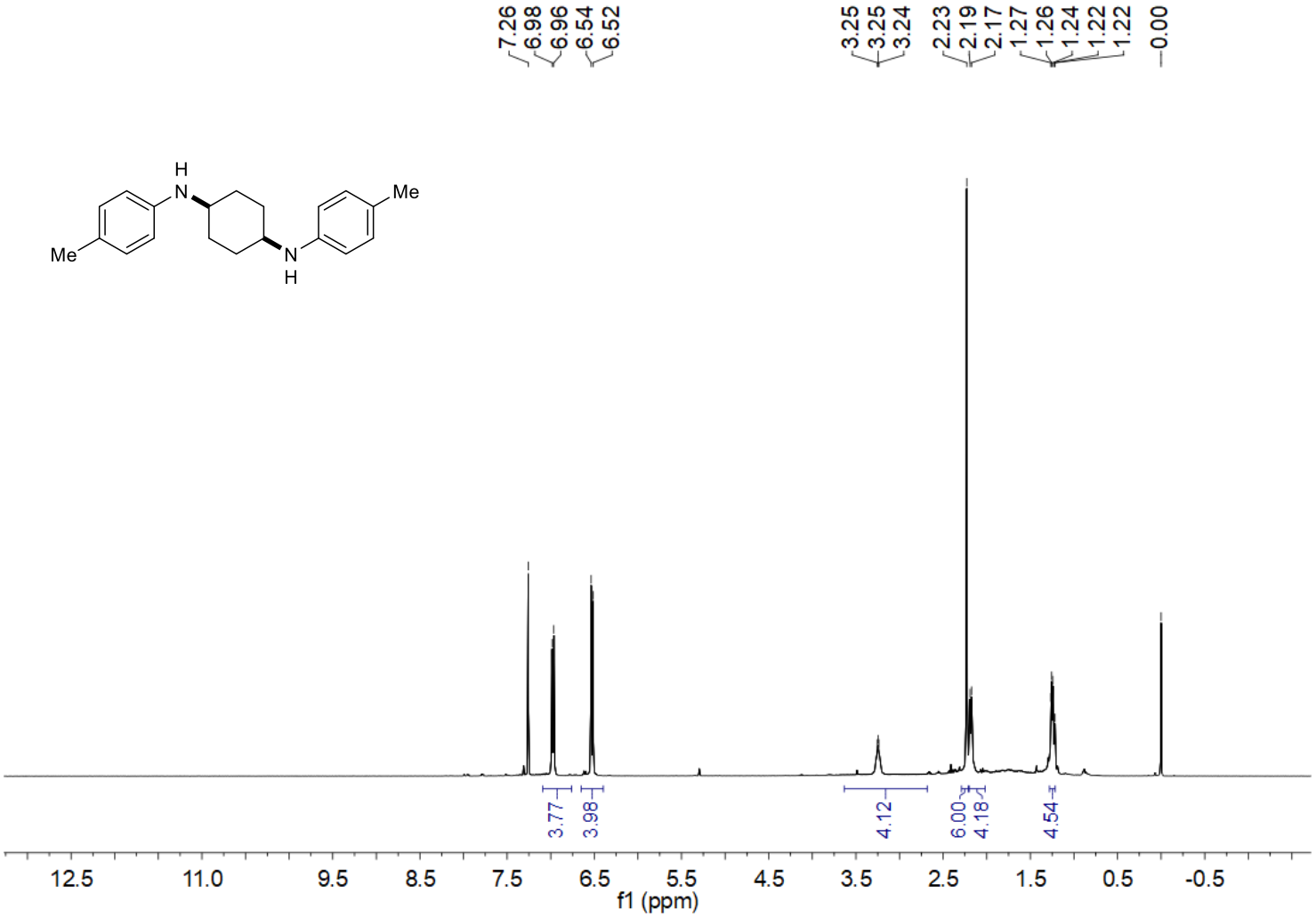
Compound **21** ^{1}H NMR



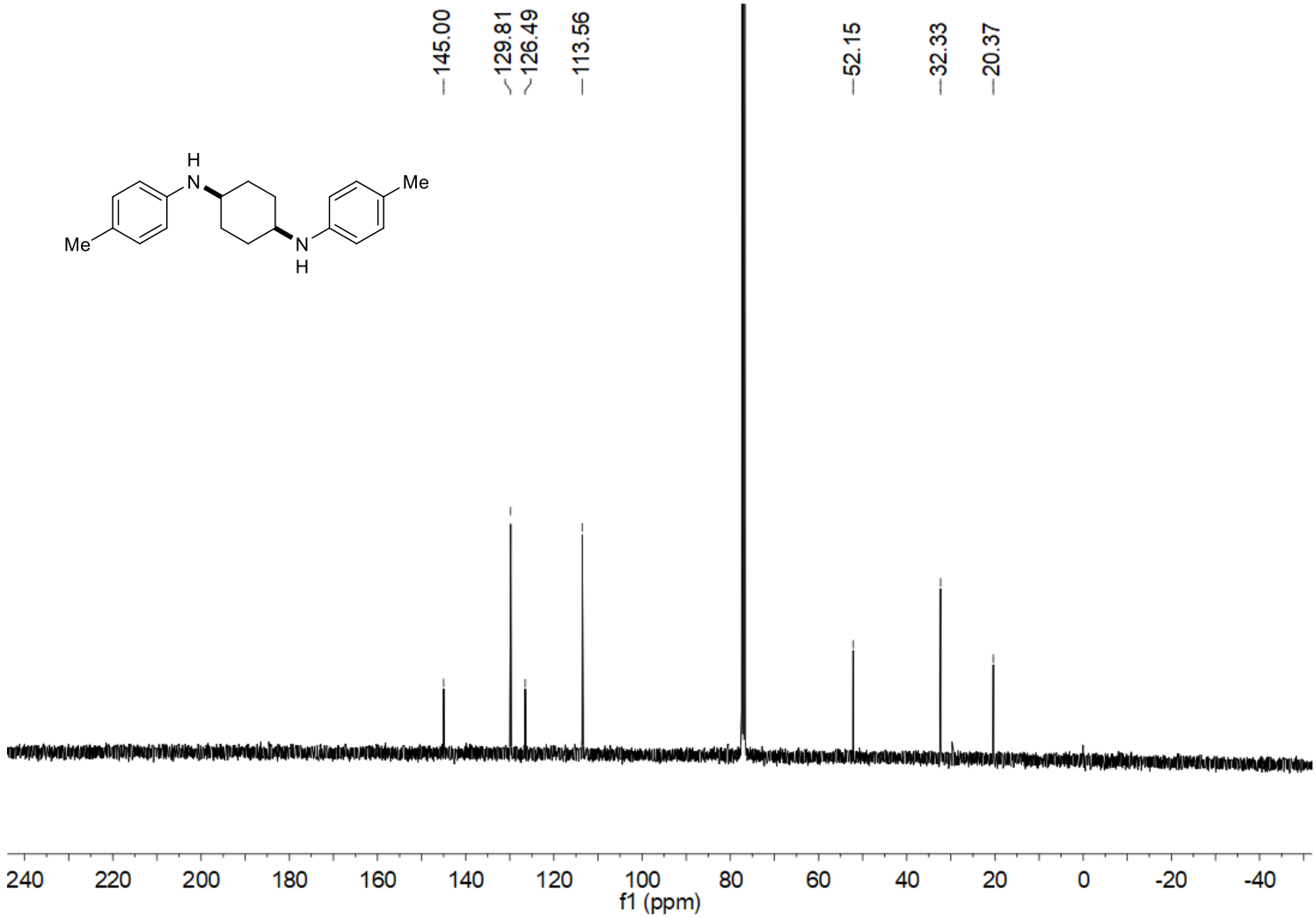
Compound **21** ^{13}C NMR



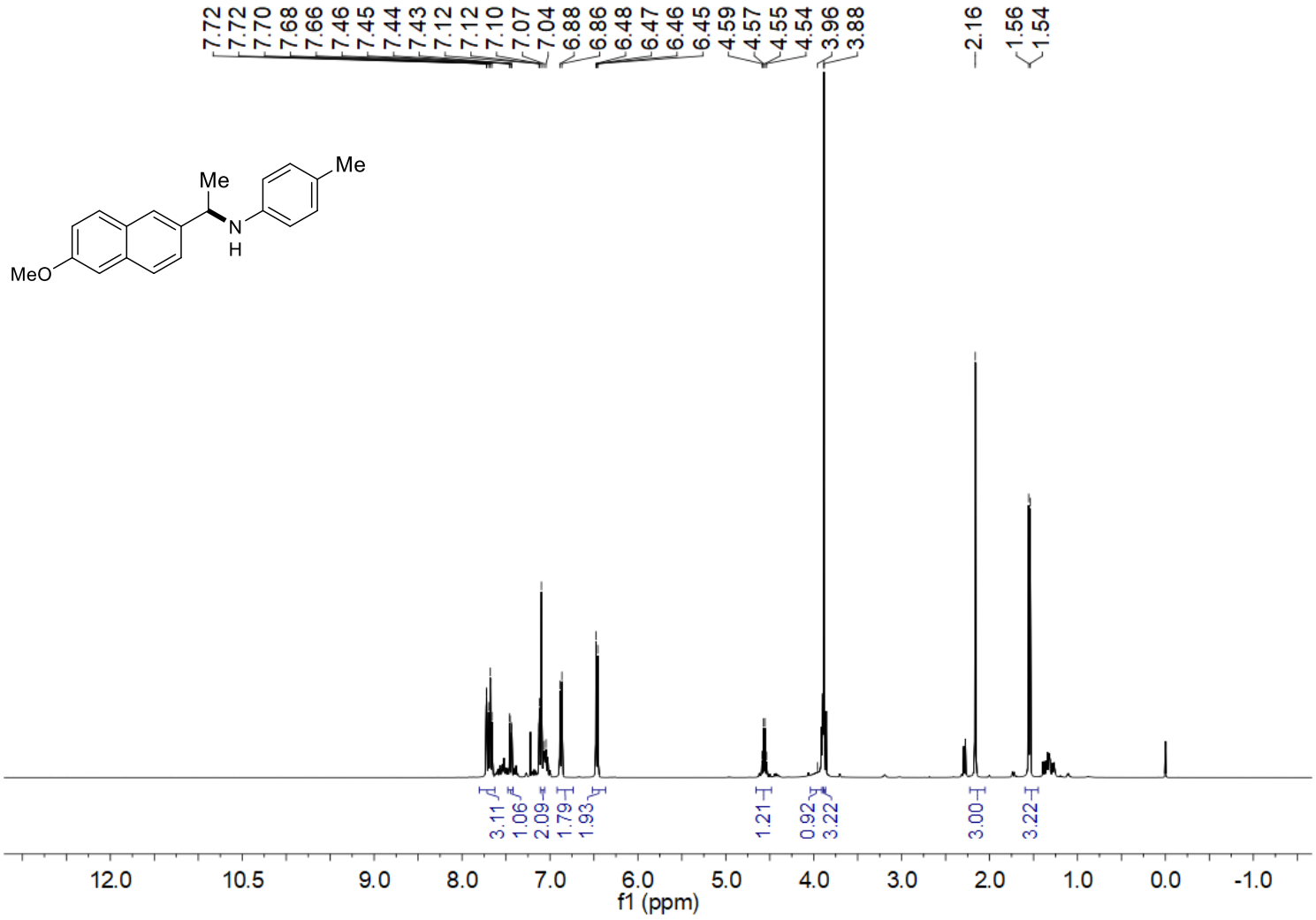
Compound **22** ^{1}H NMR



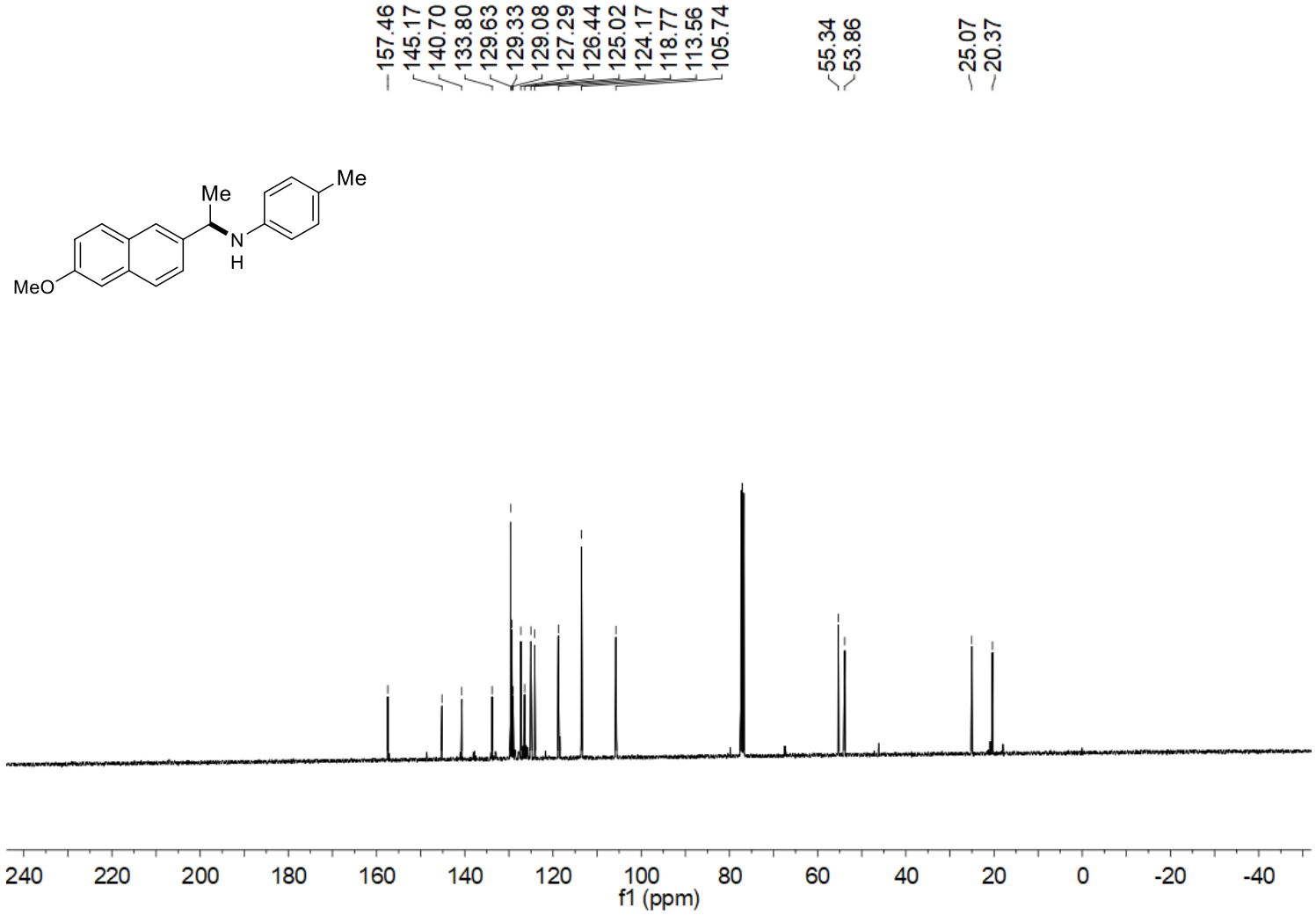
Compound **22** ^{13}C NMR



Compound **23** ^{1}H NMR



Compound **23** ^{13}C NMR



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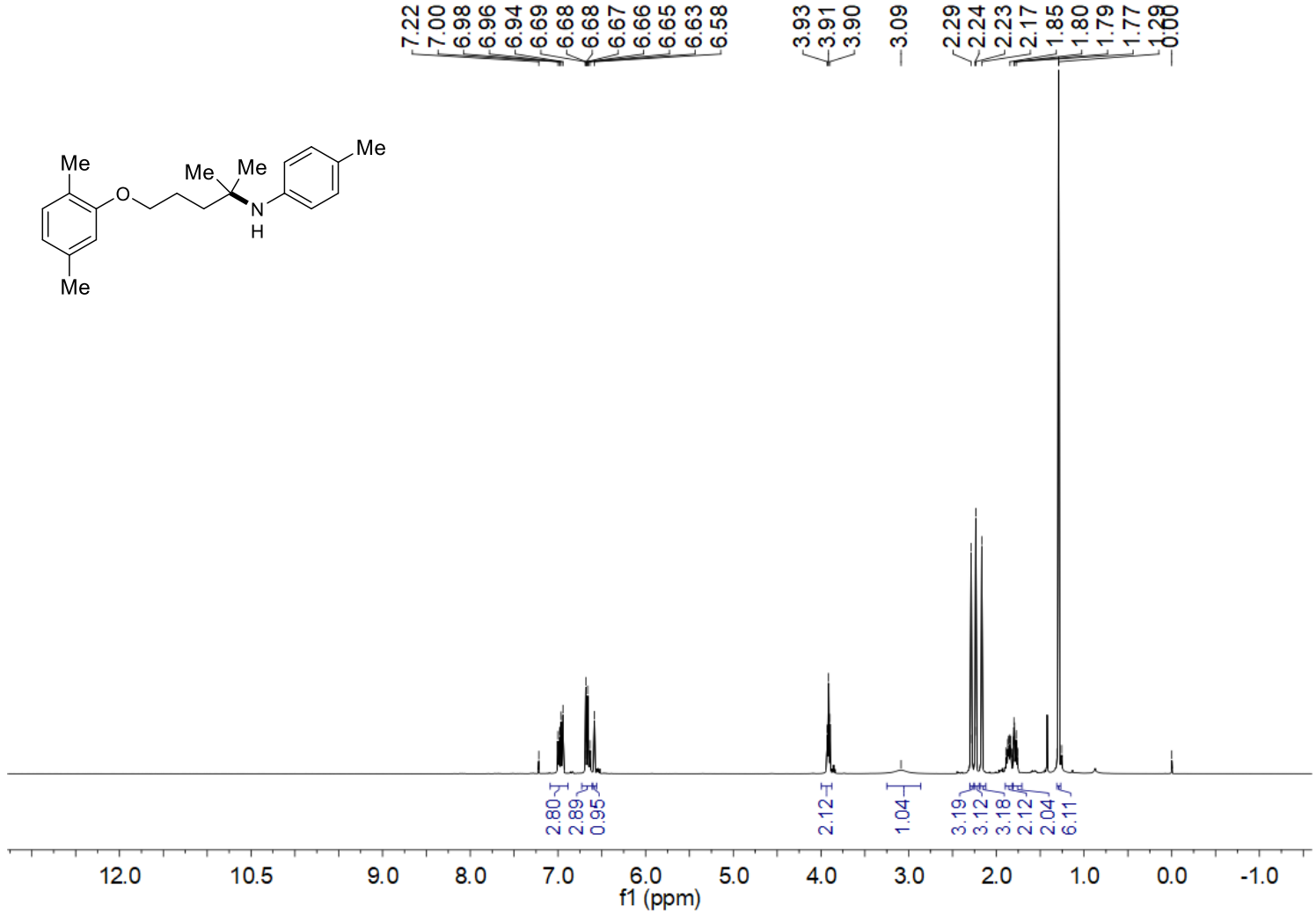
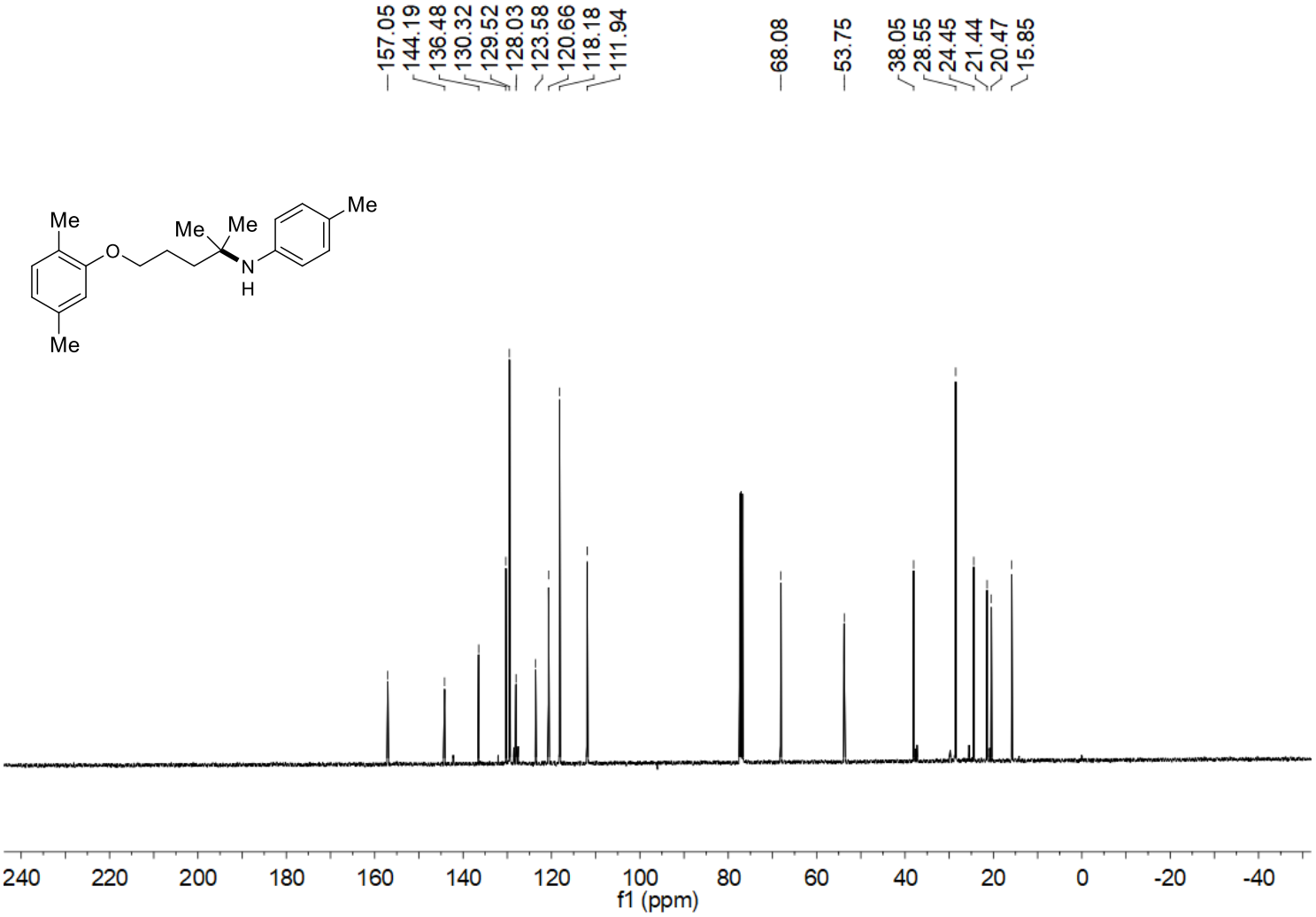


Compound **24** ^{13}C NMR



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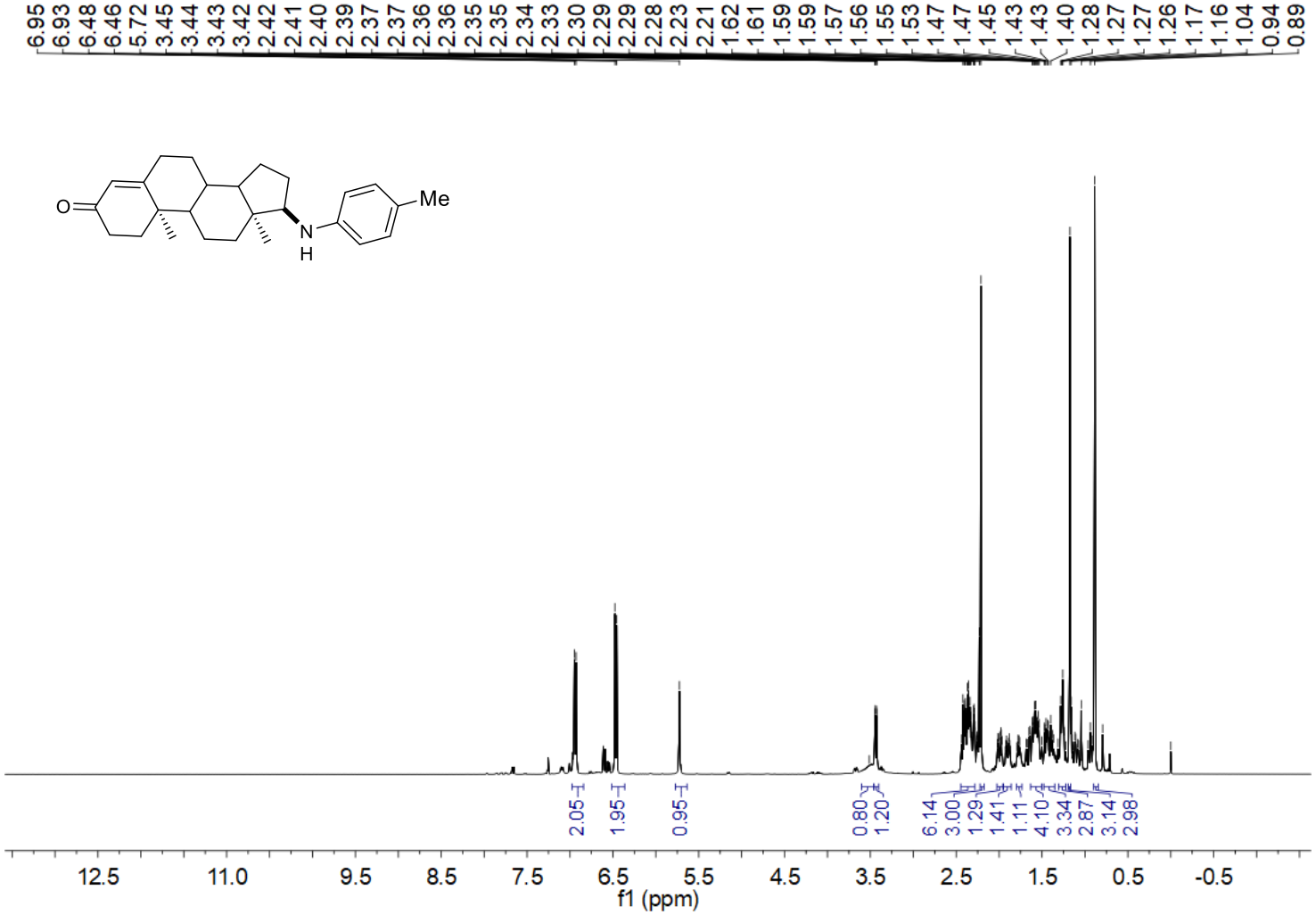
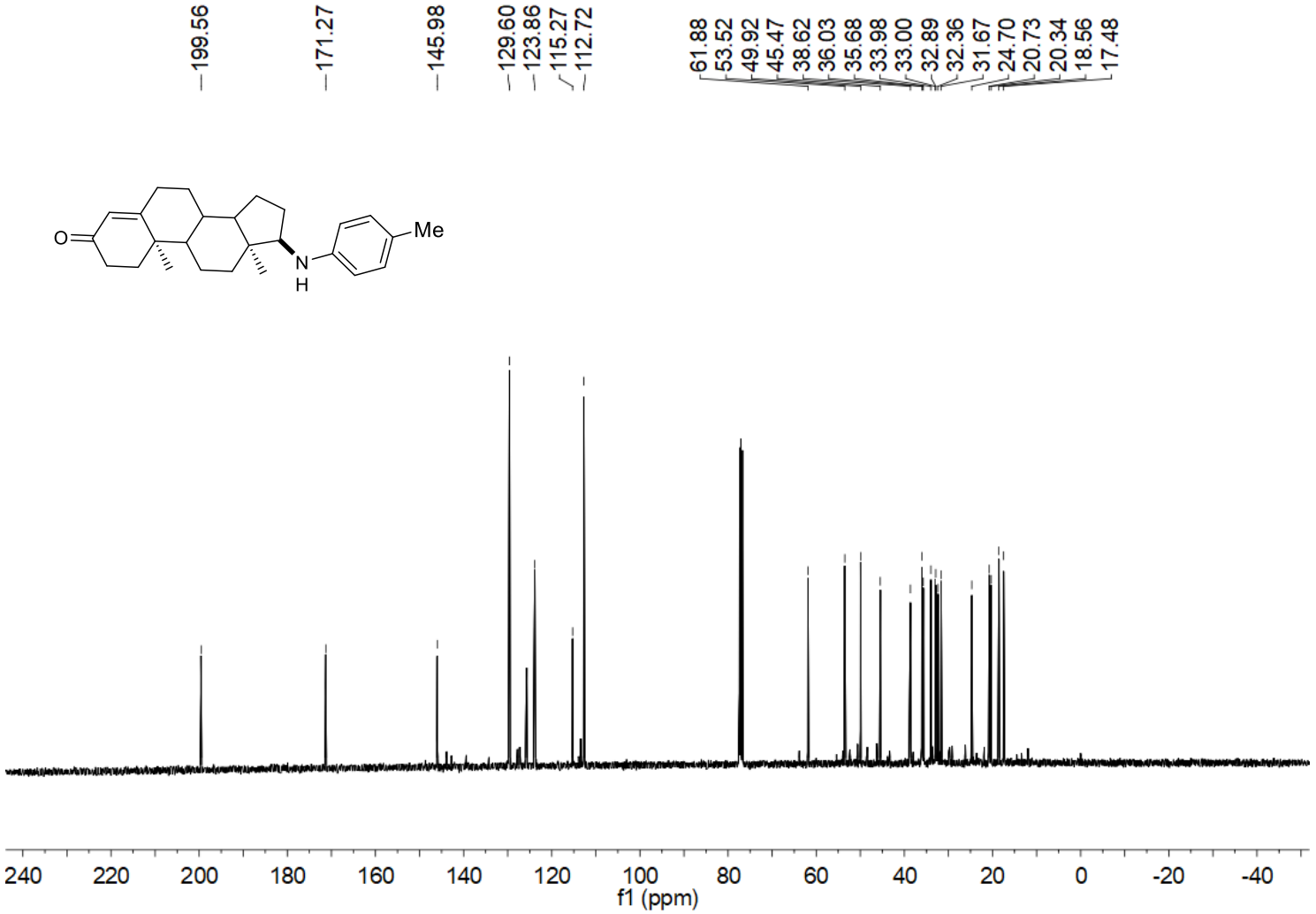
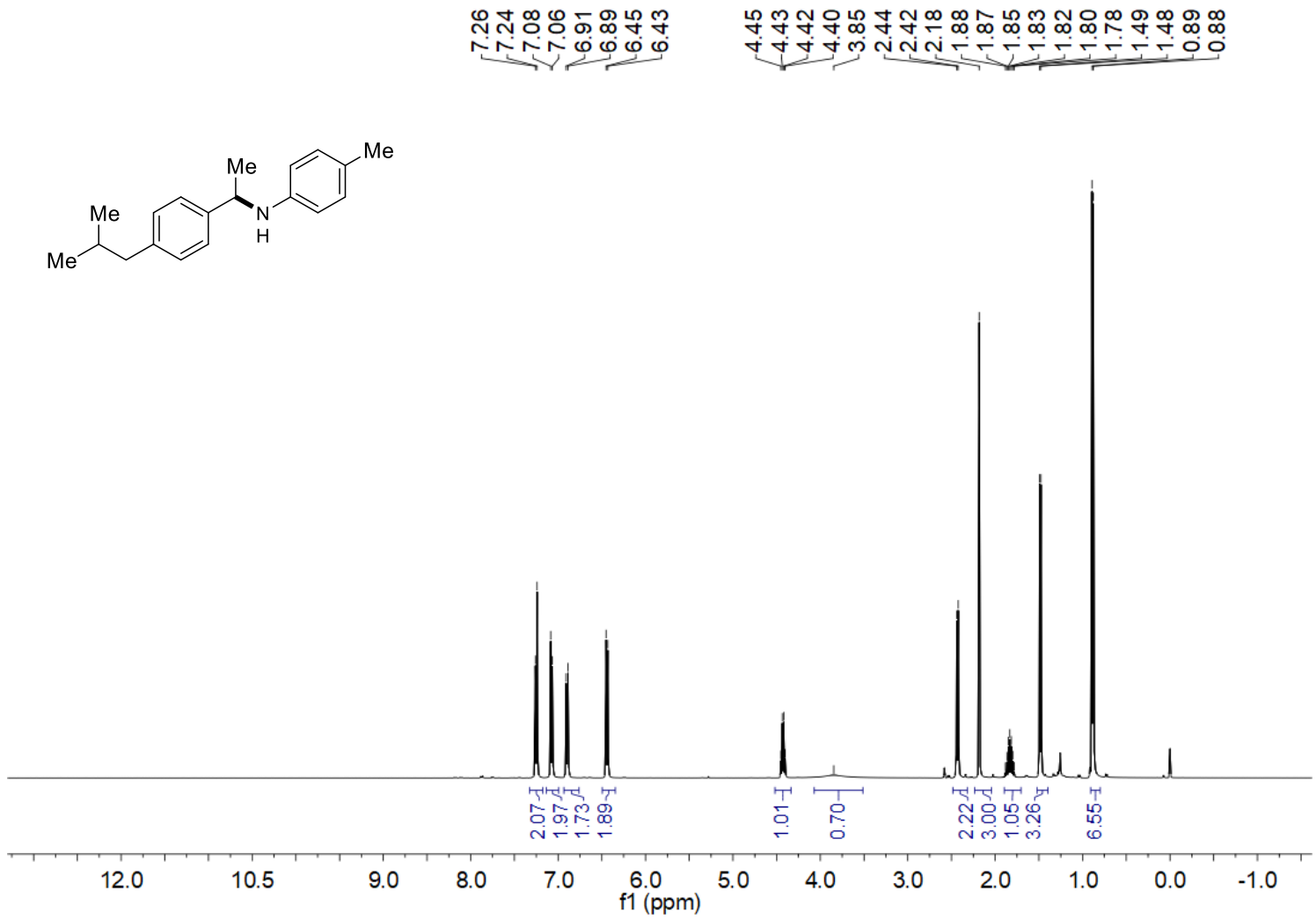


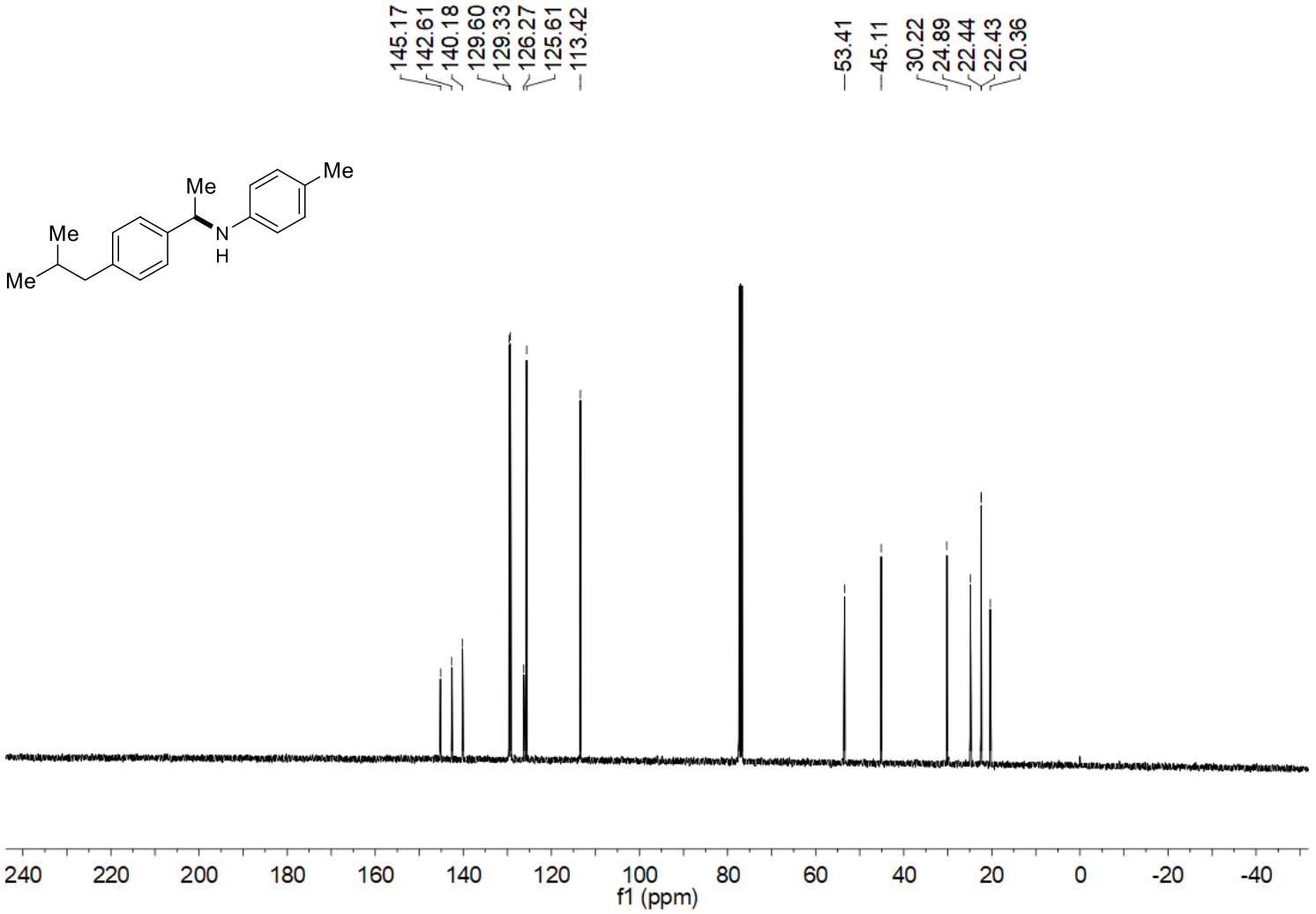
Compound **25** ^{13}C NMR



Compound **26** ^{1}H NMR



Compound **26** ^{13}C NMR



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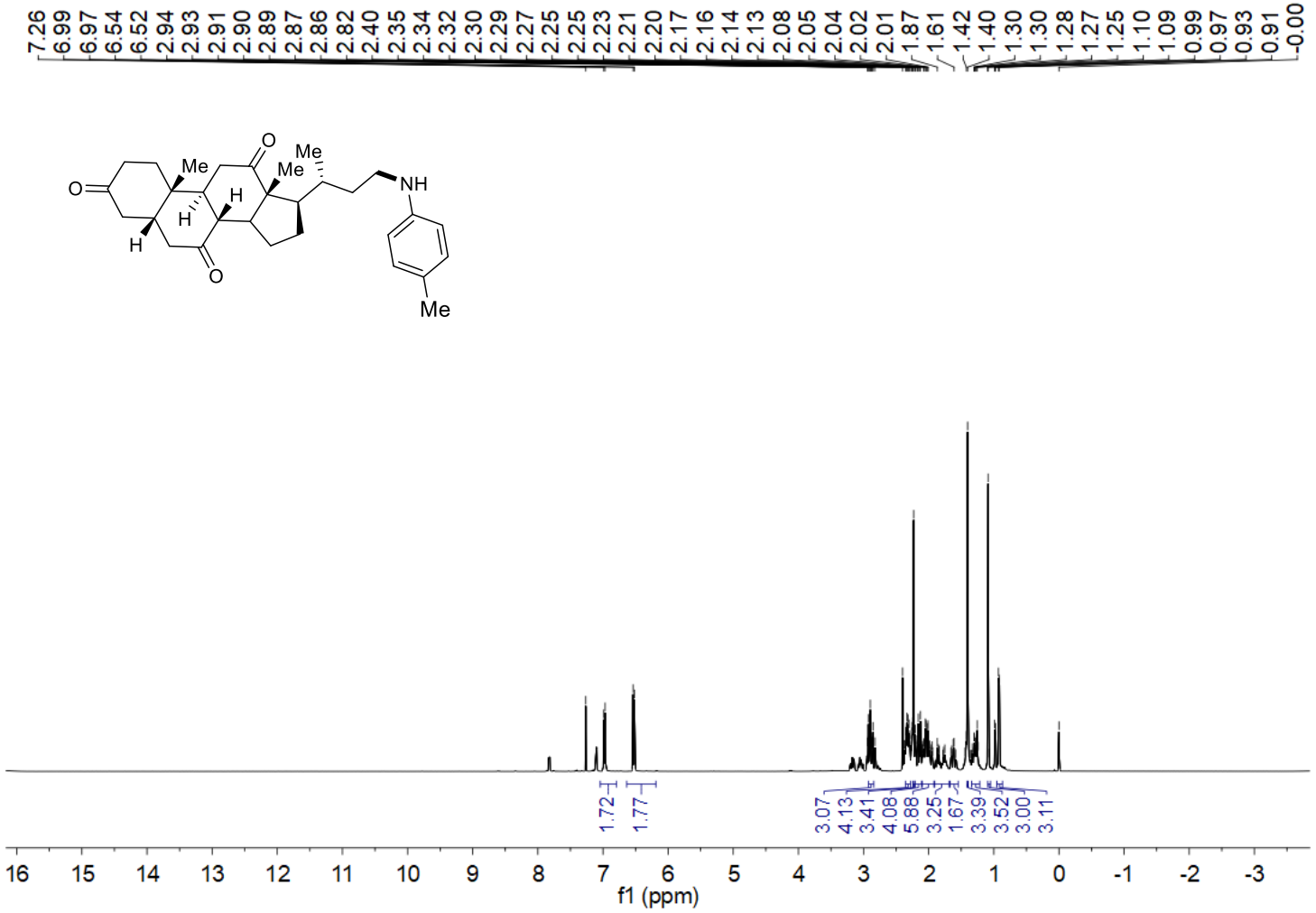
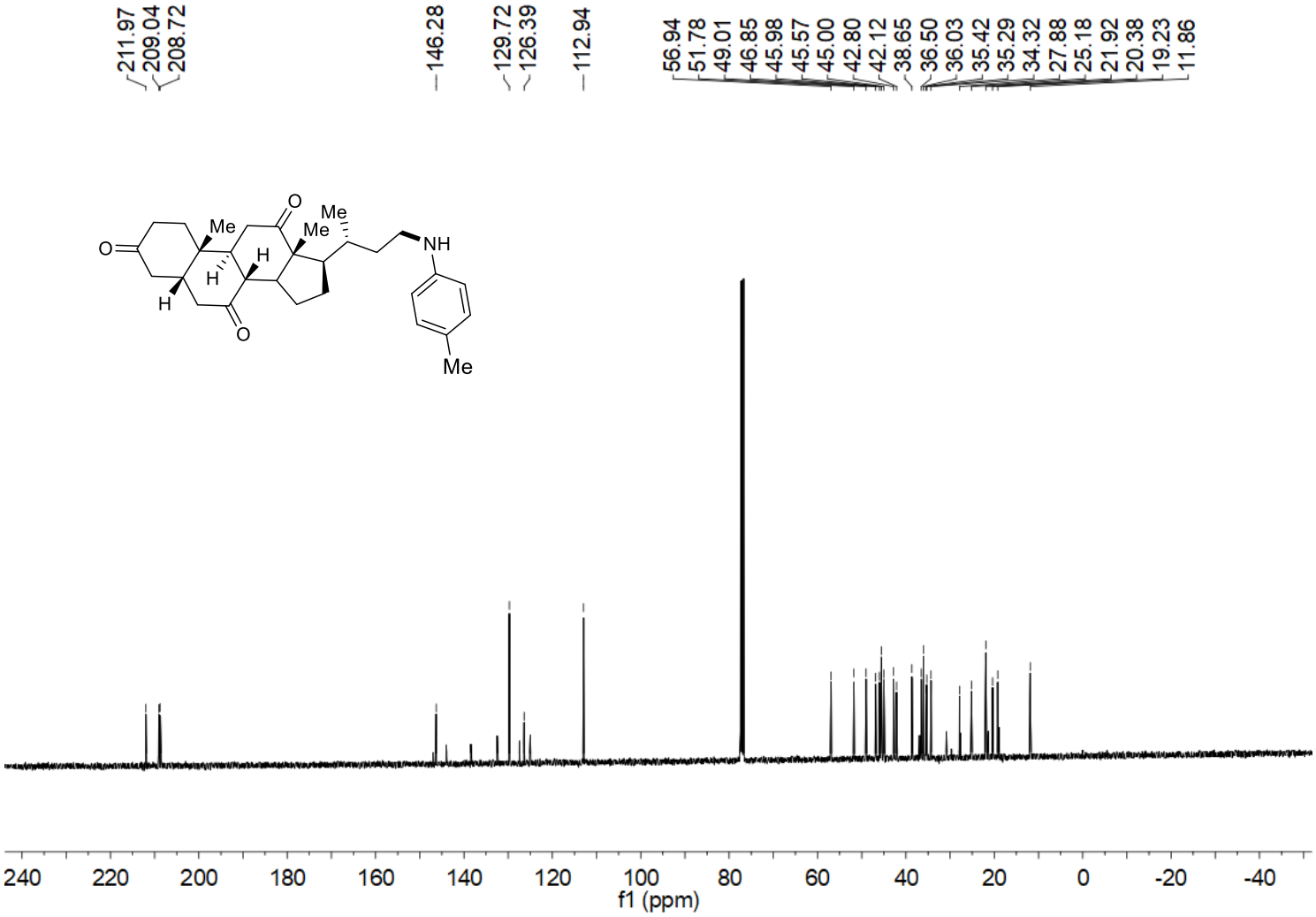
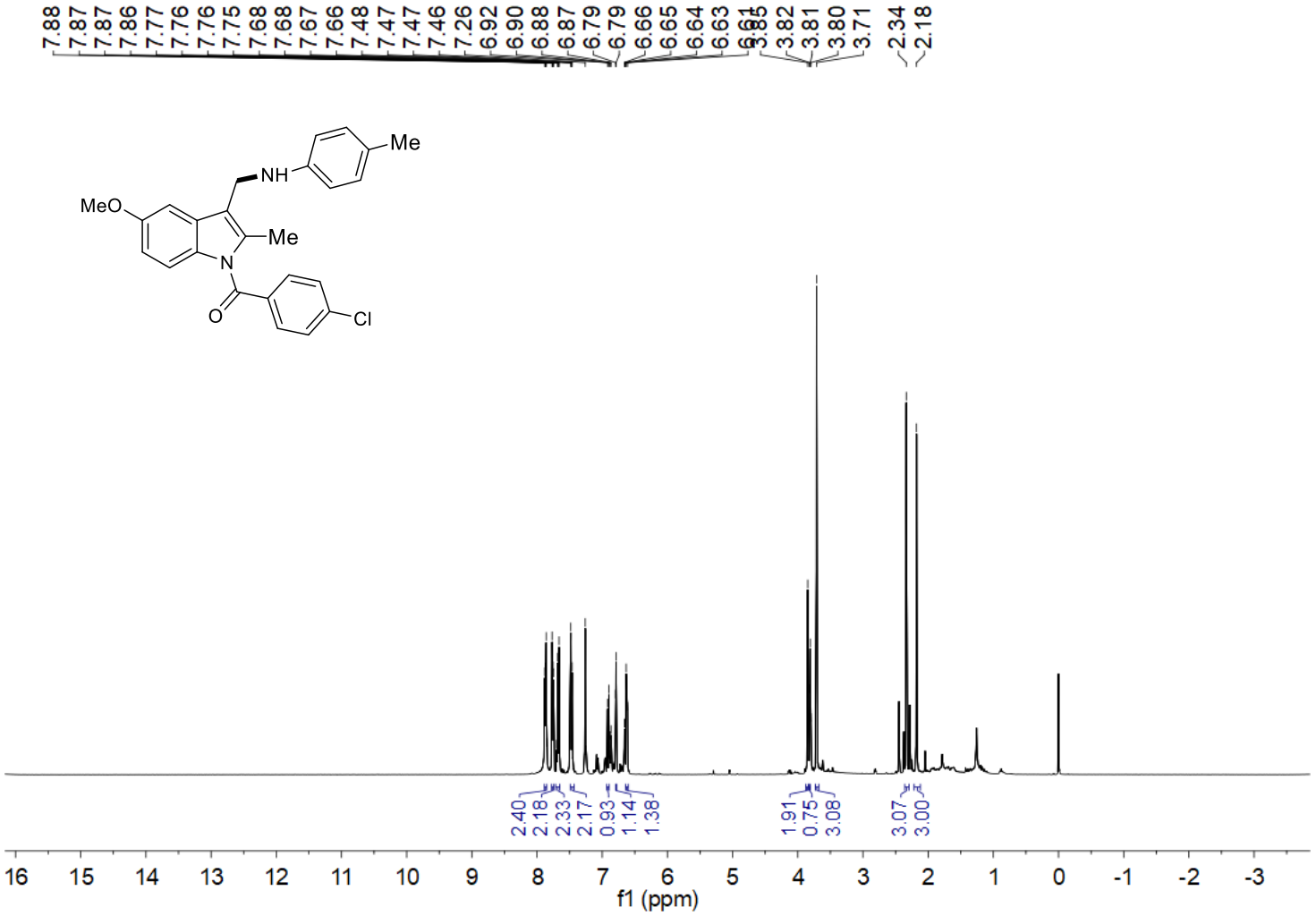


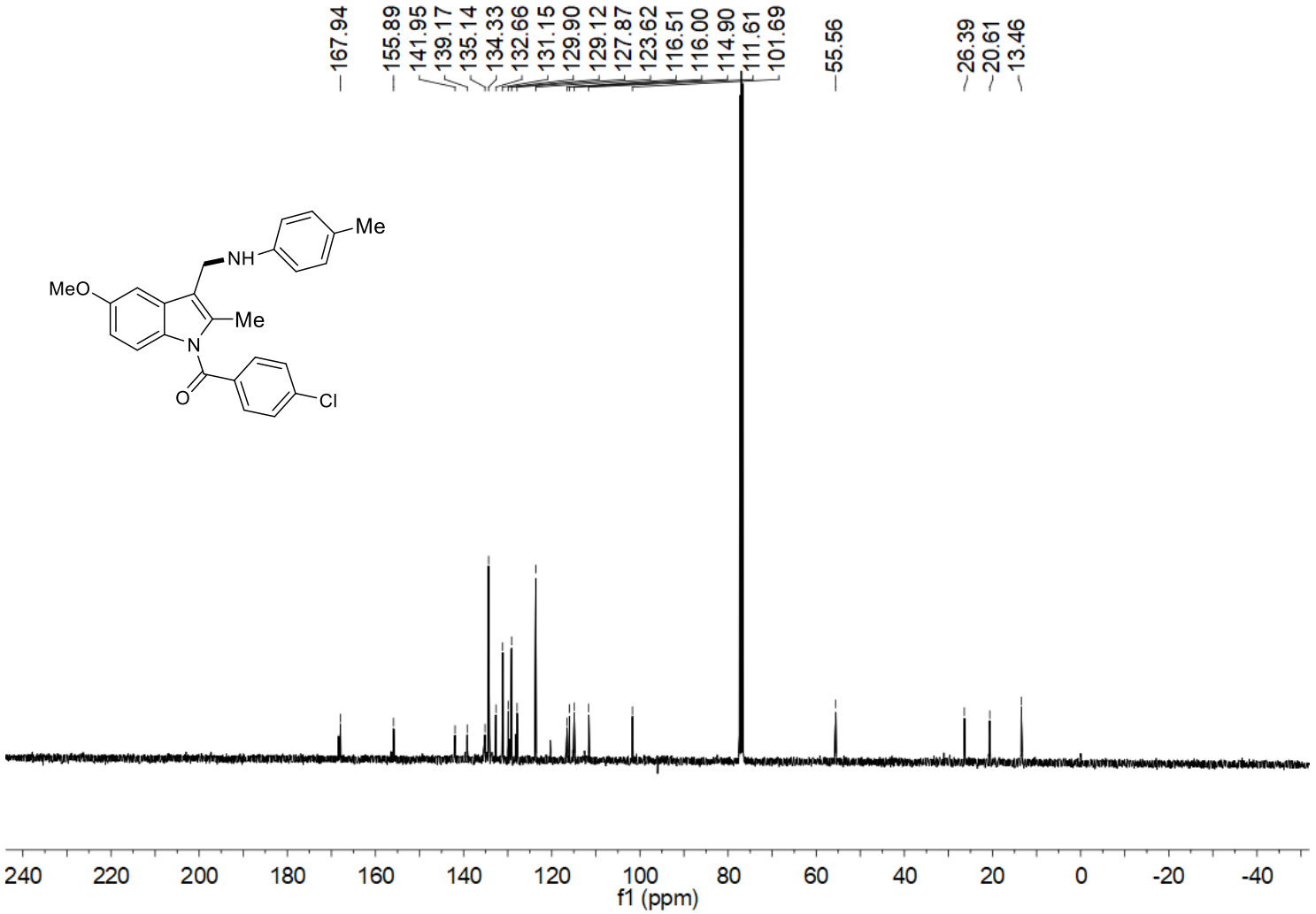
Compound **27** ^{13}C NMR



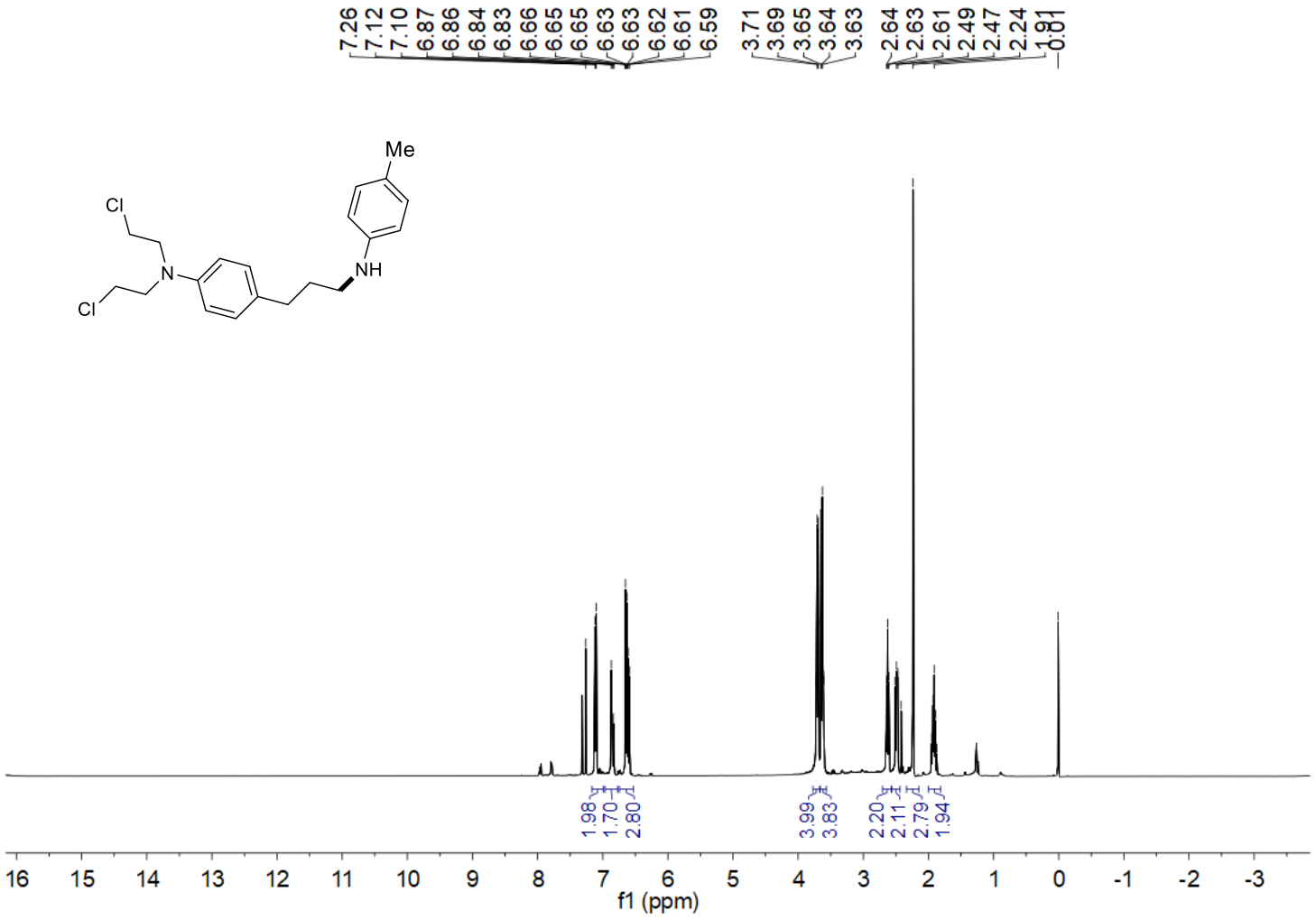
Compound **28** ^{1}H NMR



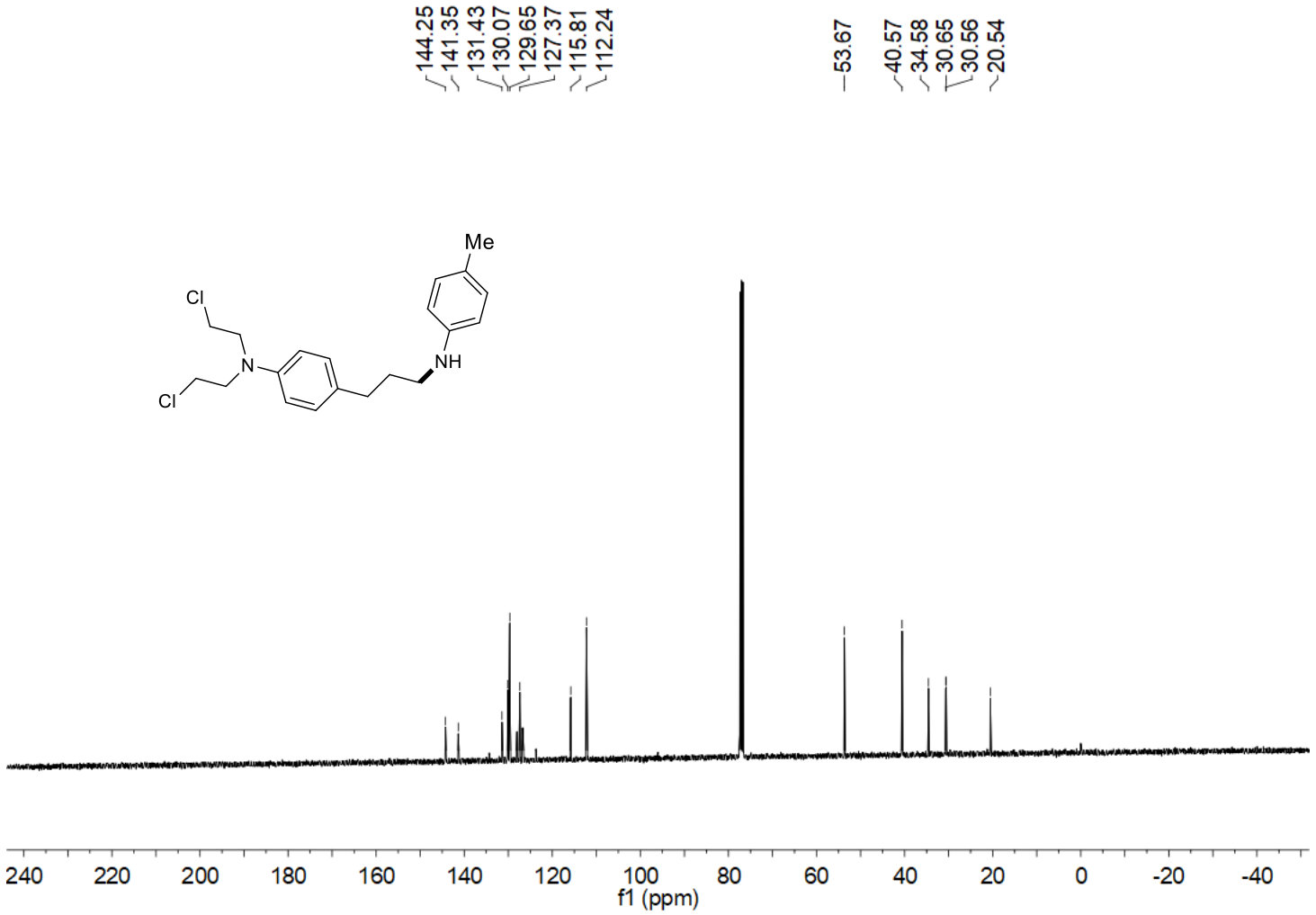
Compound **28** ^{13}C NMR



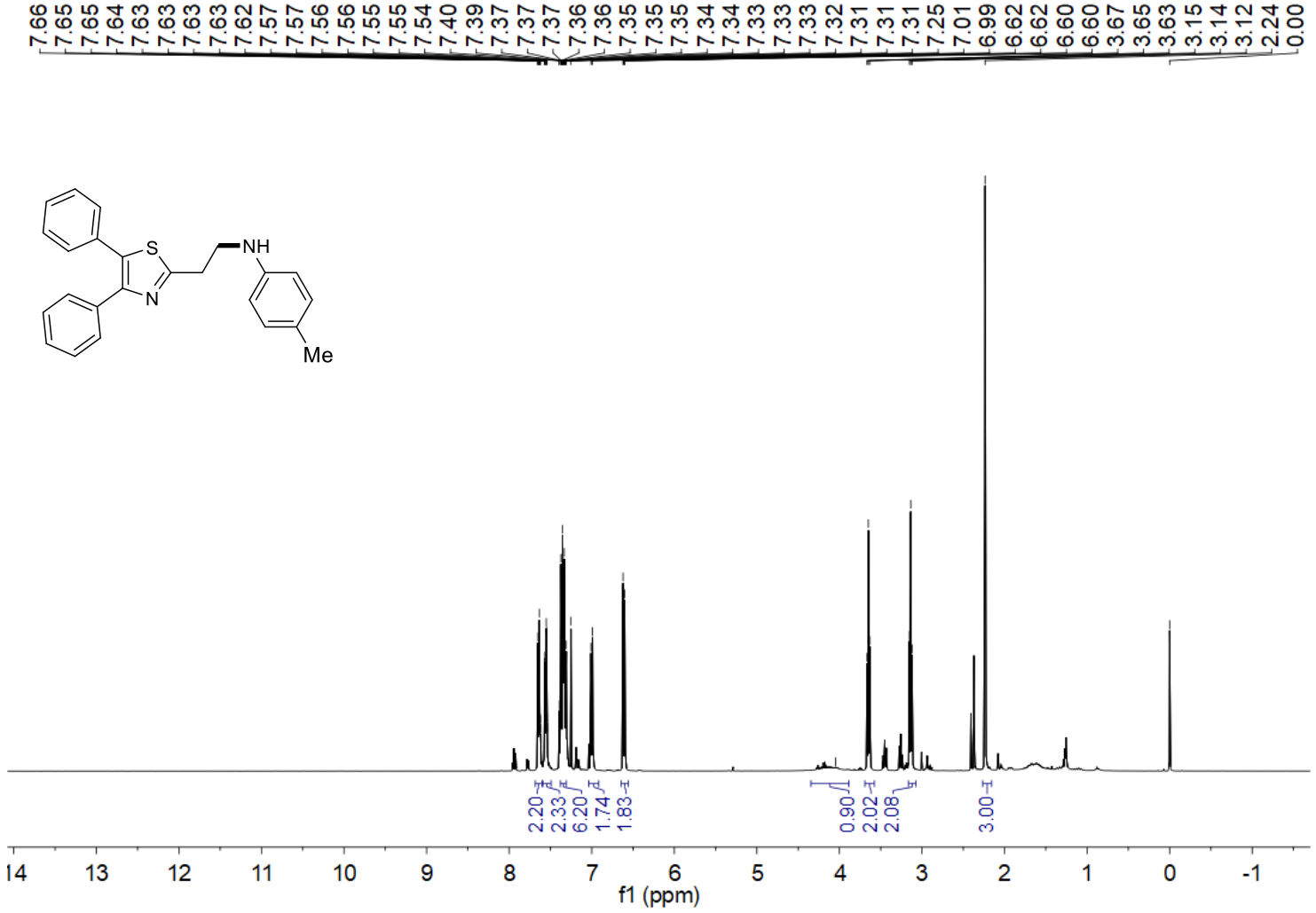
Compound **29** ^{1}H NMR



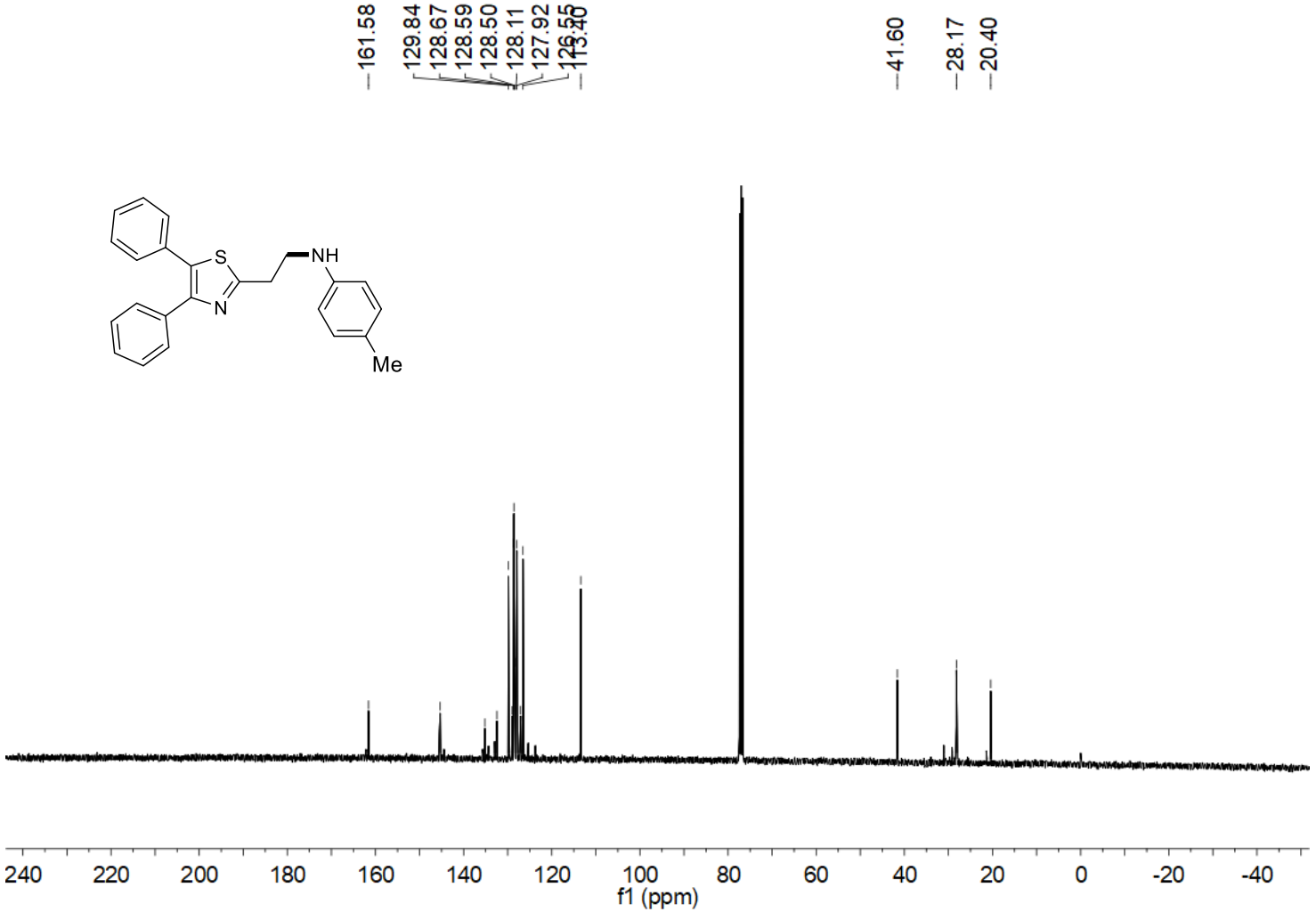
Compound **29** ^{13}C NMR



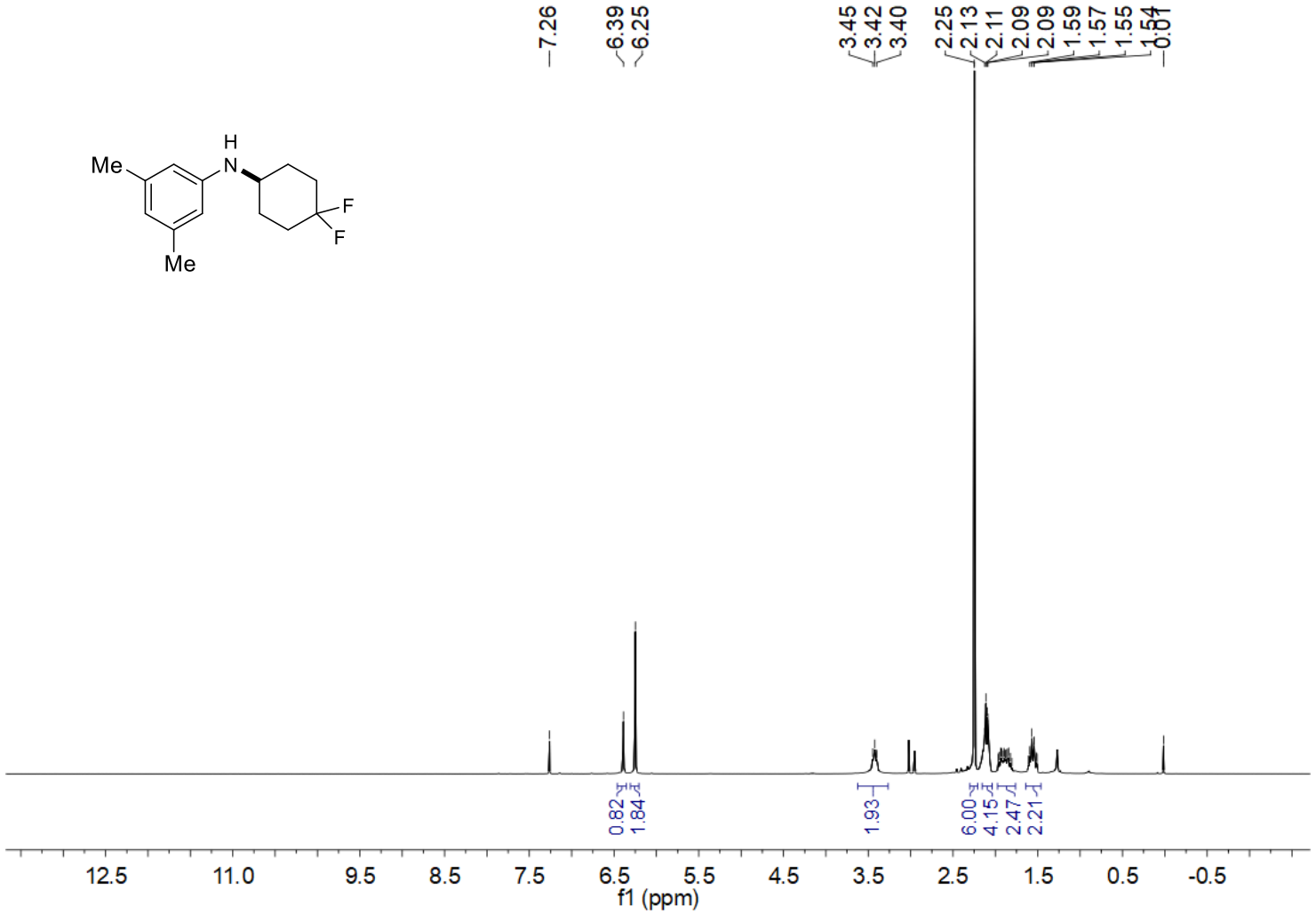
Compound **30** ^{1}H NMR



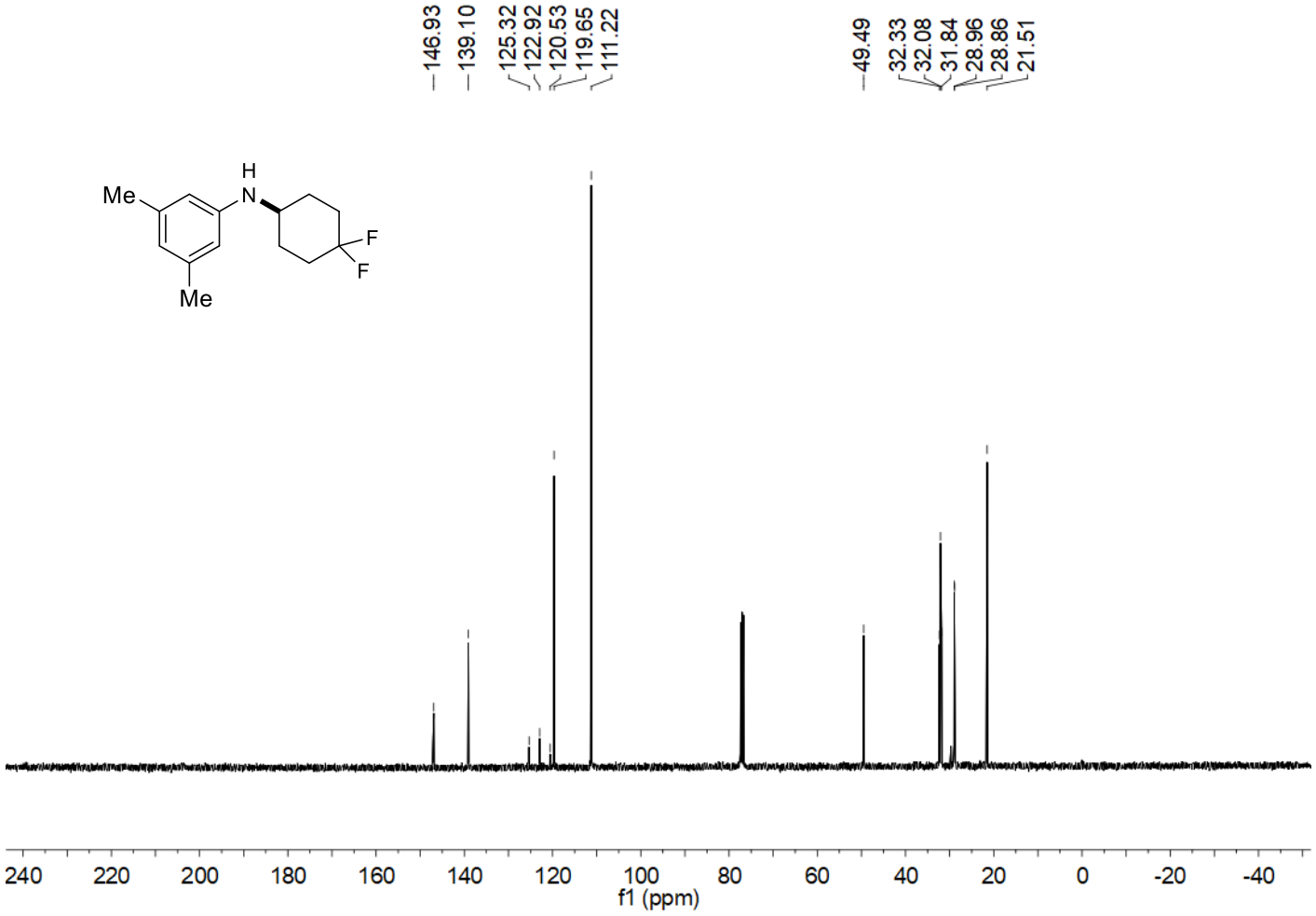
Compound **30** ^{13}C NMR



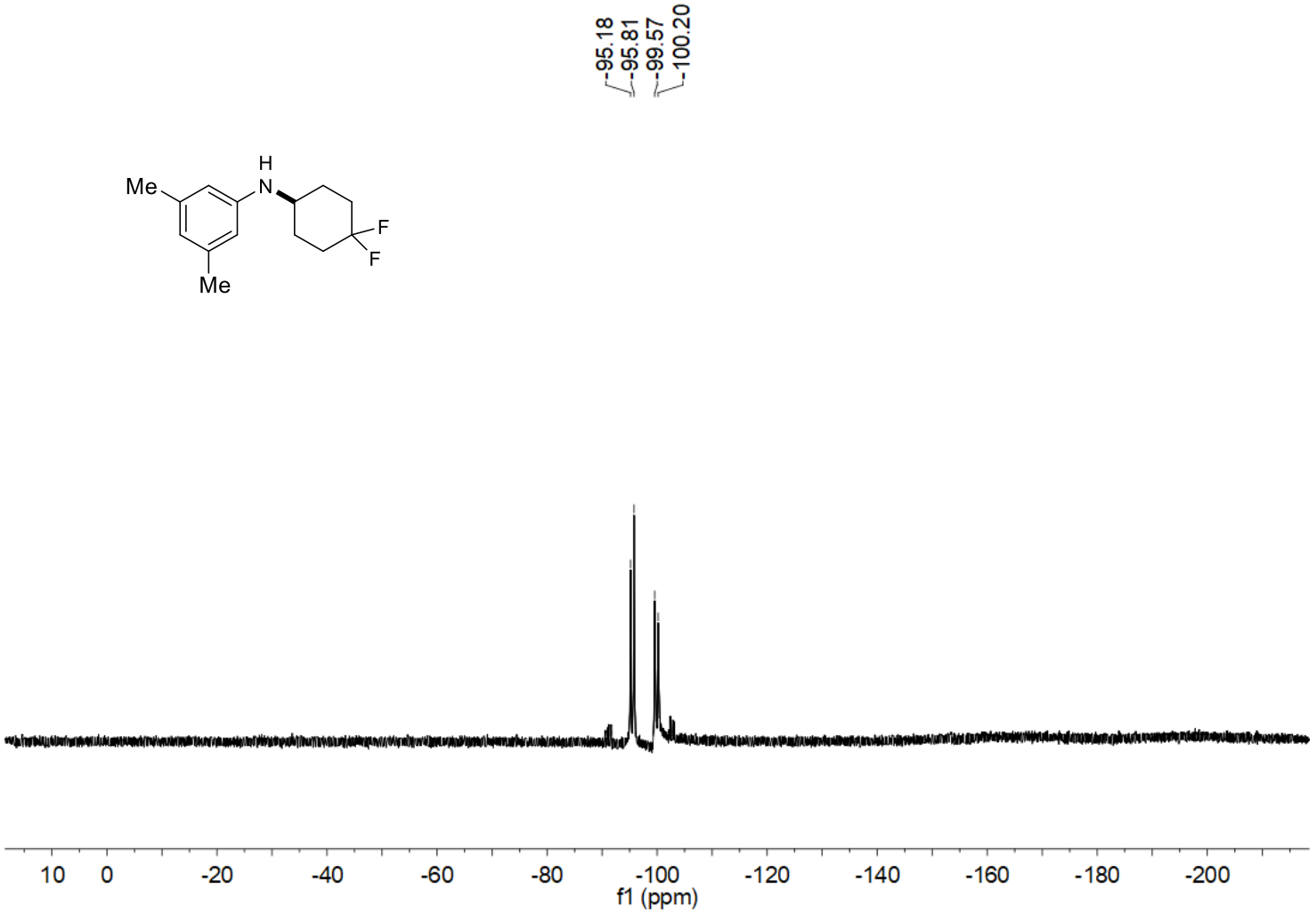
Compound **31** ^{1}H NMR



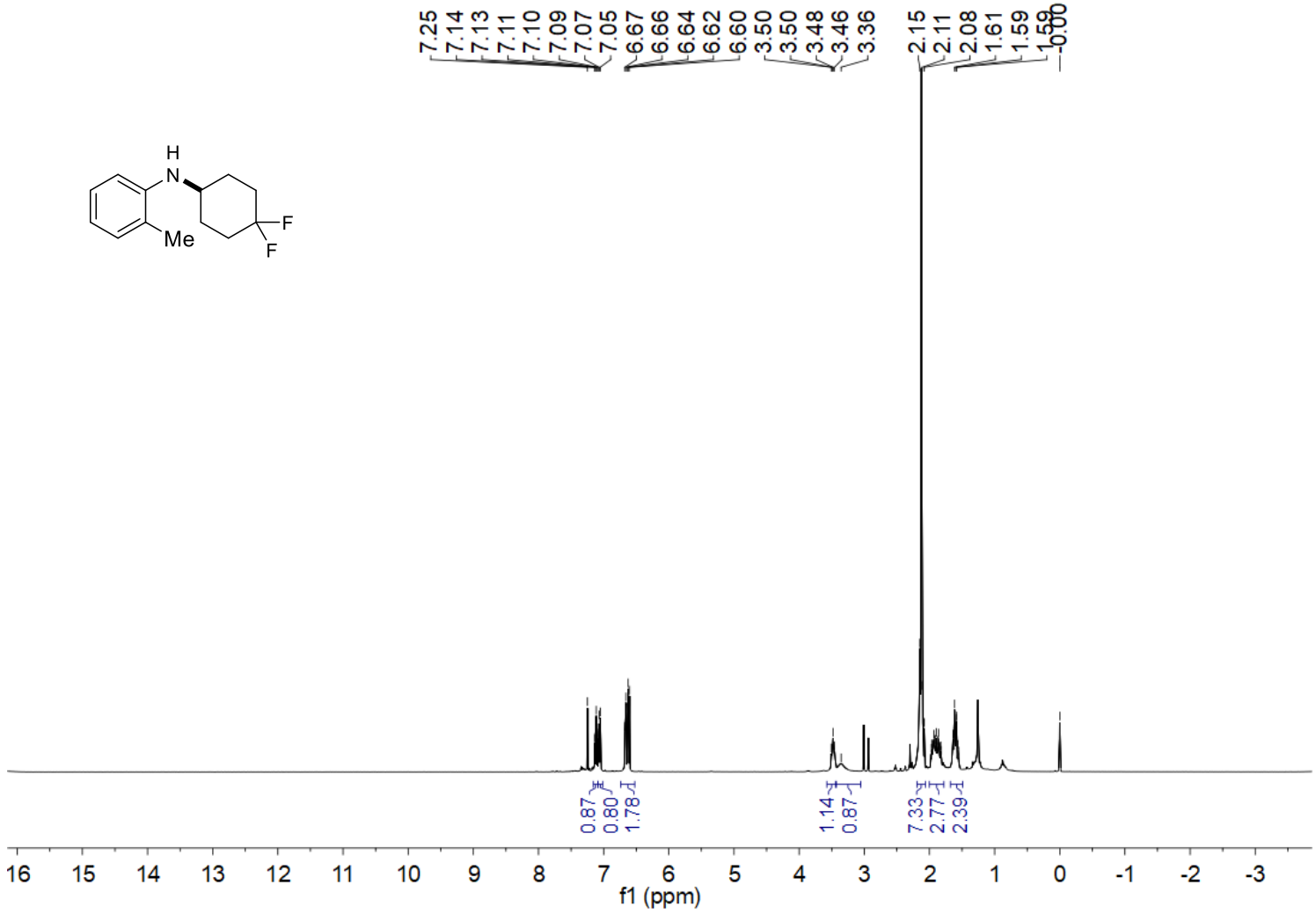
Compound **31** ^{13}C NMR



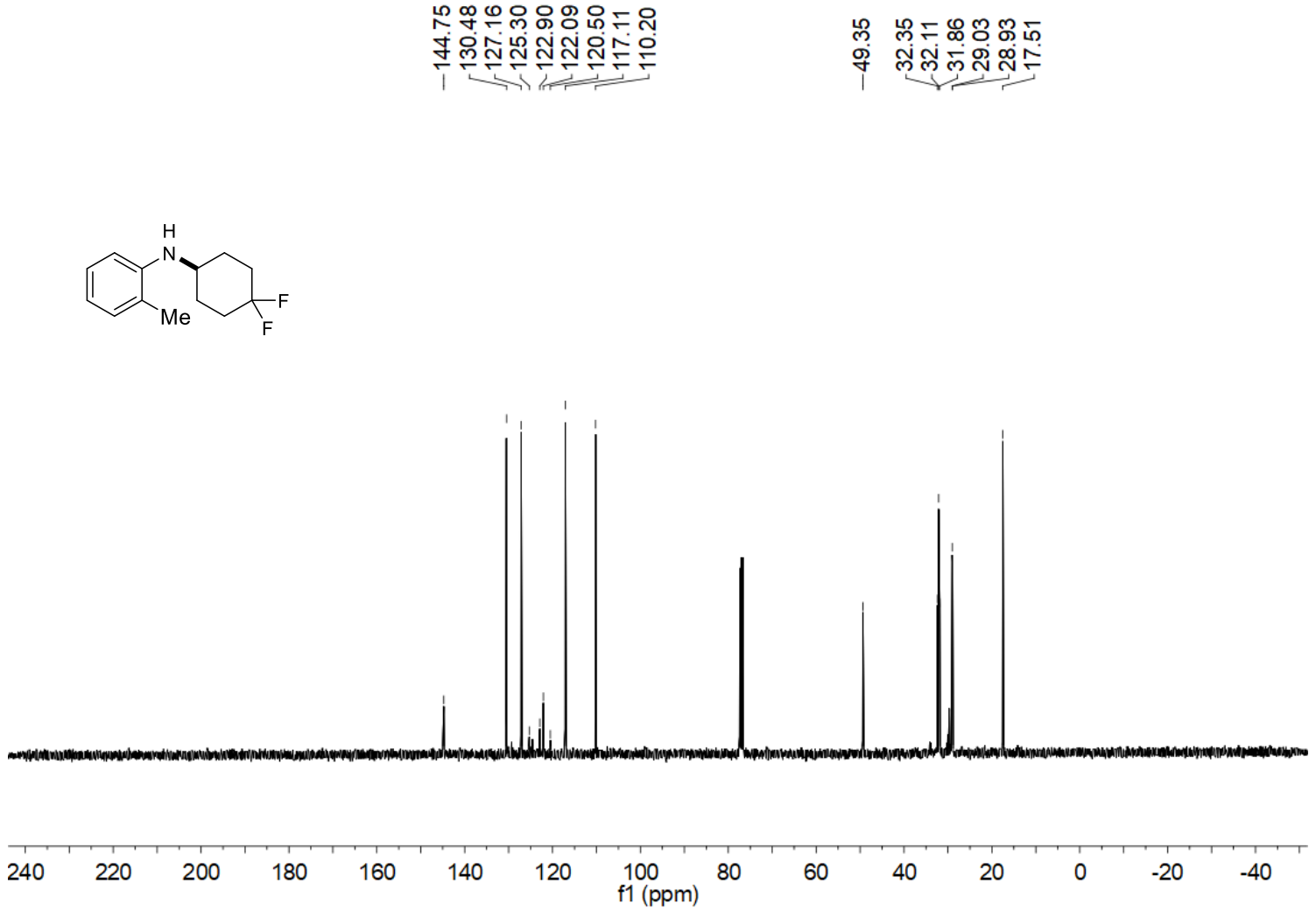
Compound **31** ^{19}F NMR



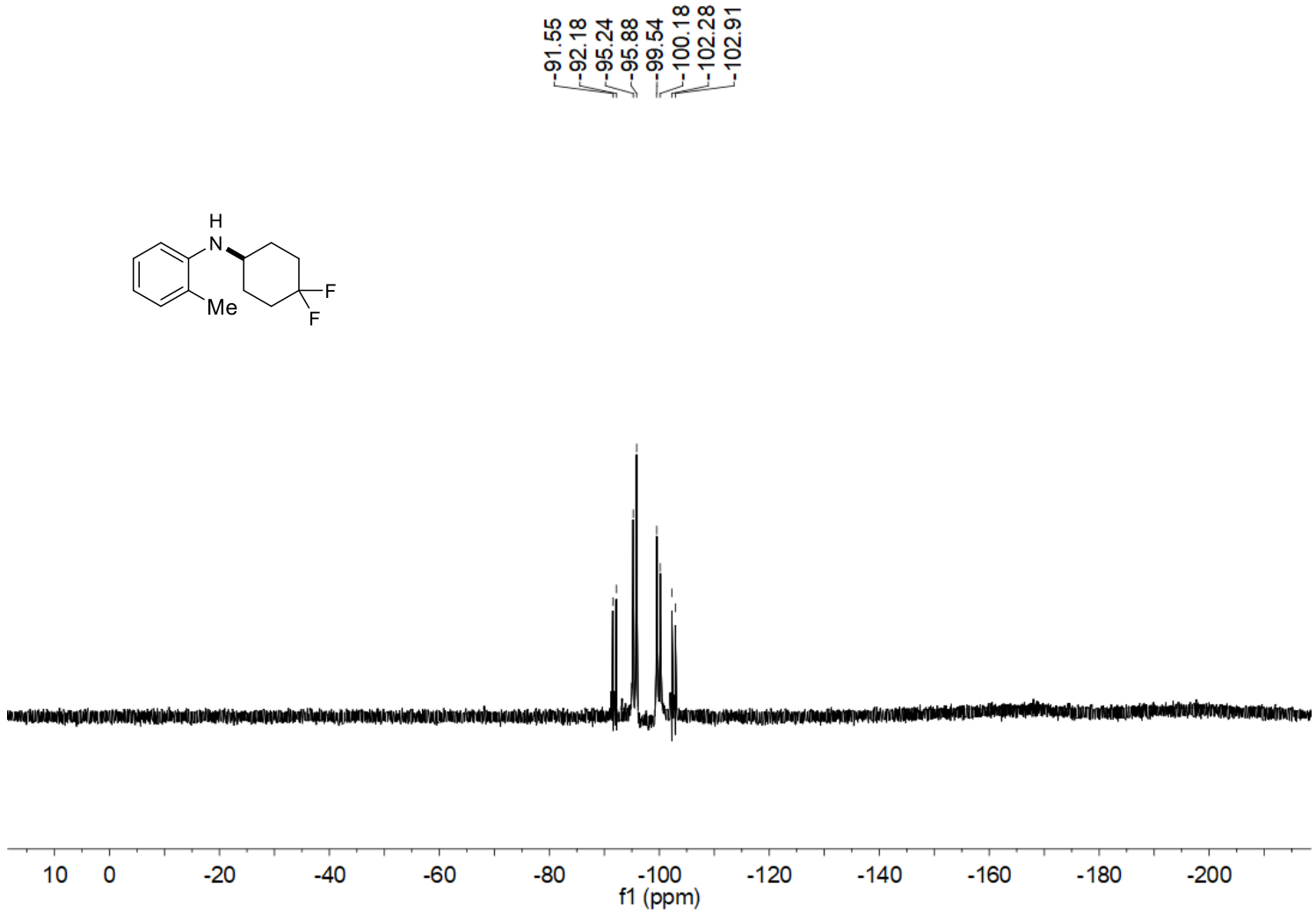
Compound **32** ^{1}H NMR



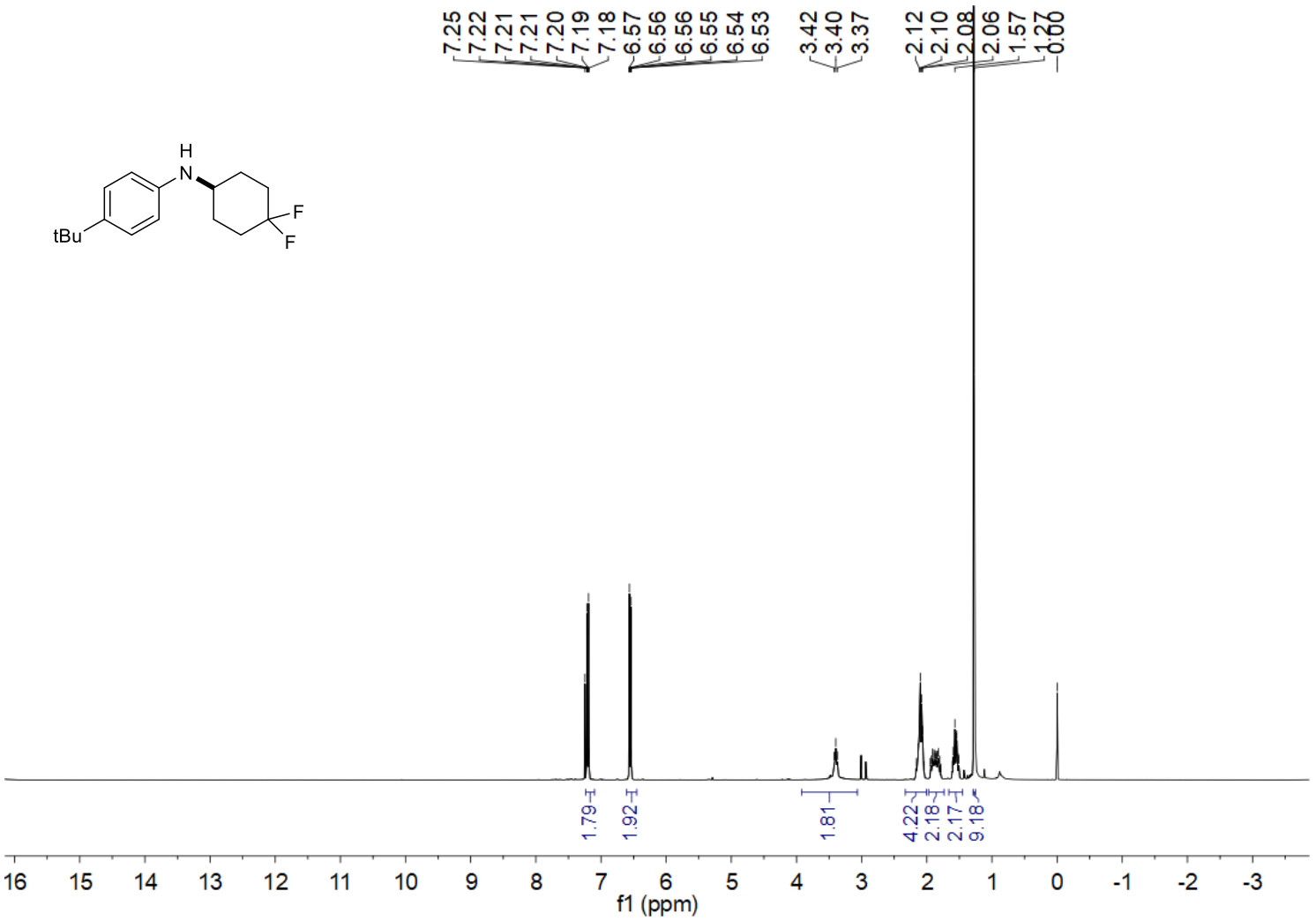
Compound **32** ^{13}C NMR



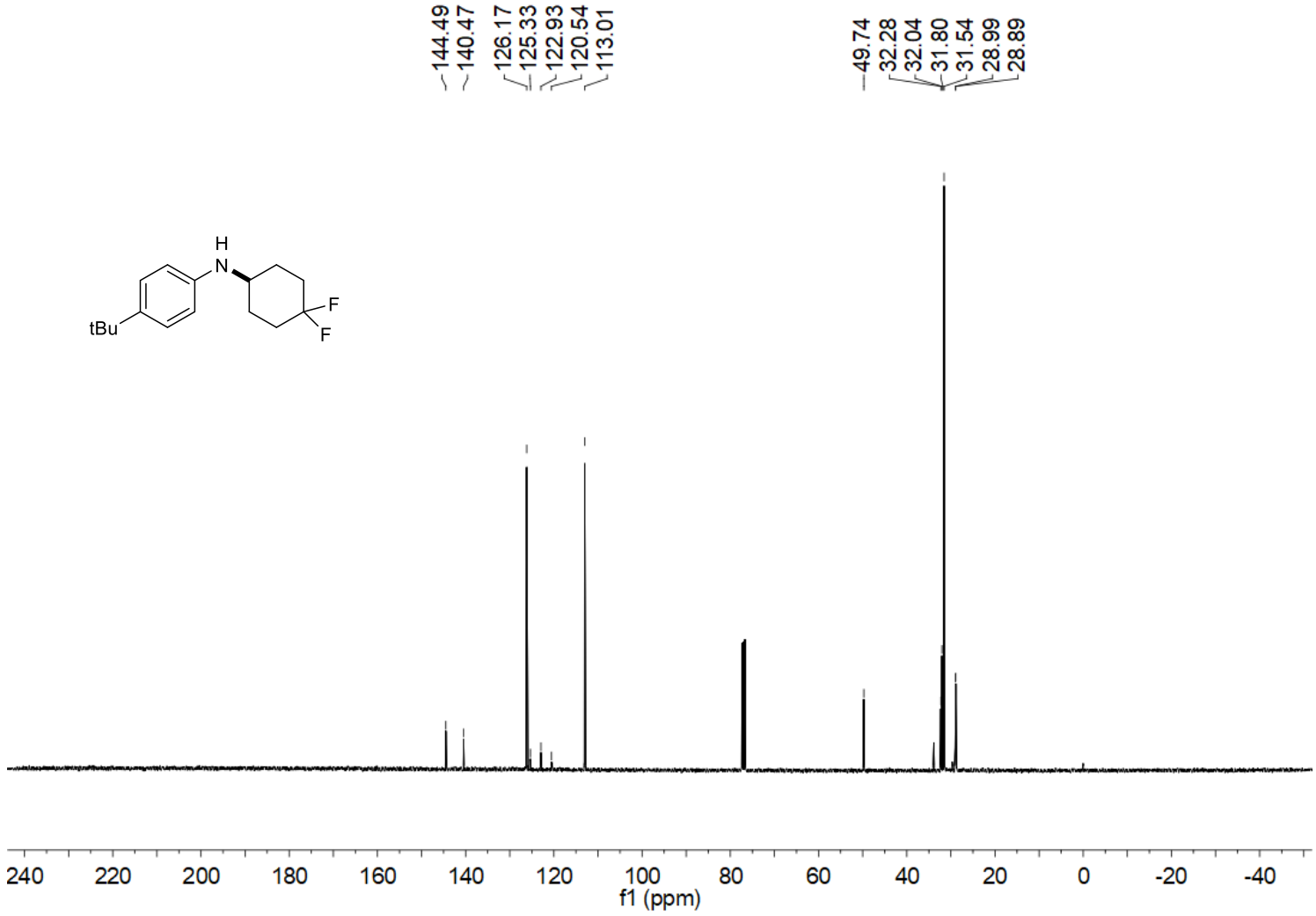
Compound **32** ^{19}F NMR



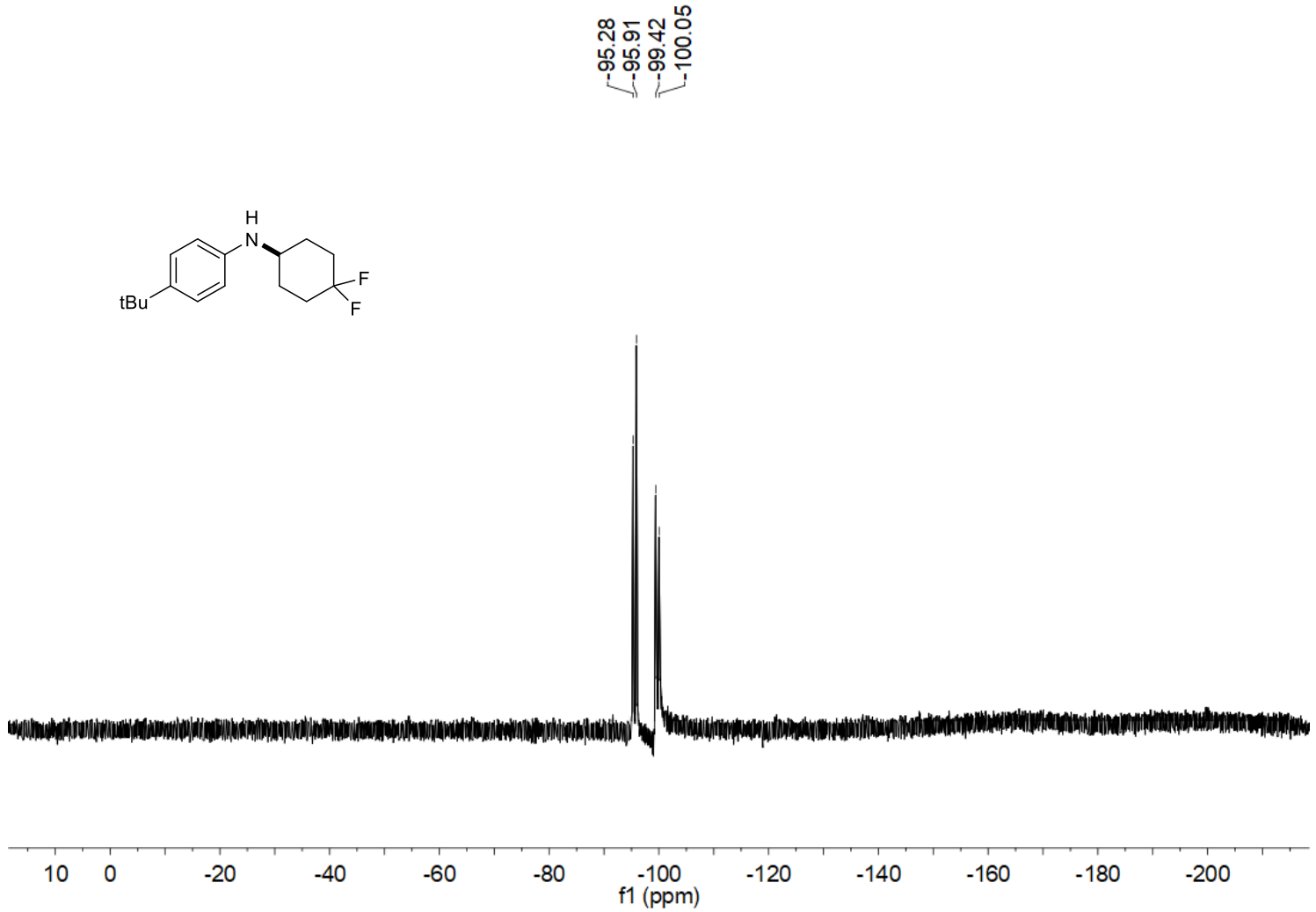
Compound **33** ^{1}H NMR



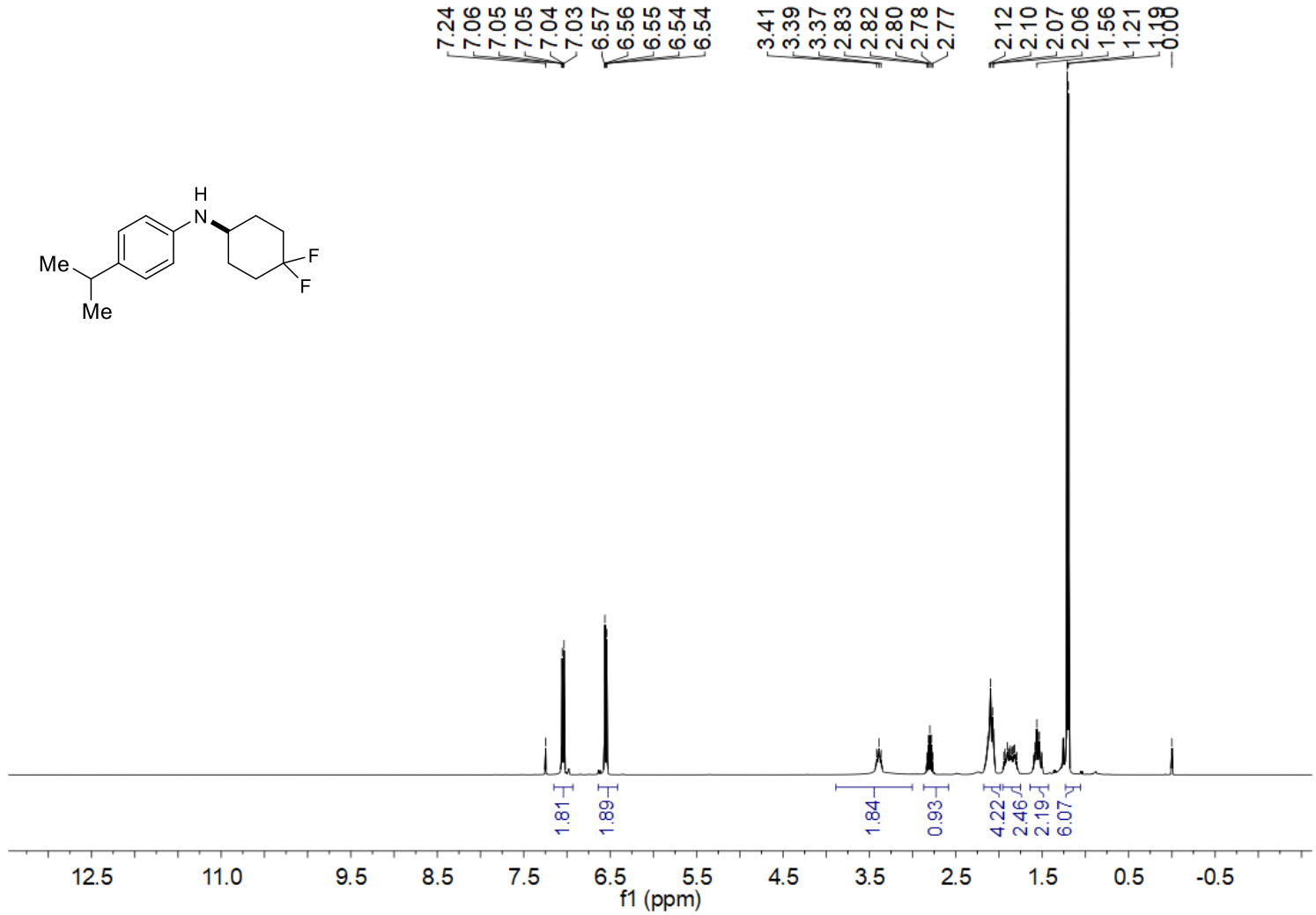
Compound **33** ^{13}C NMR



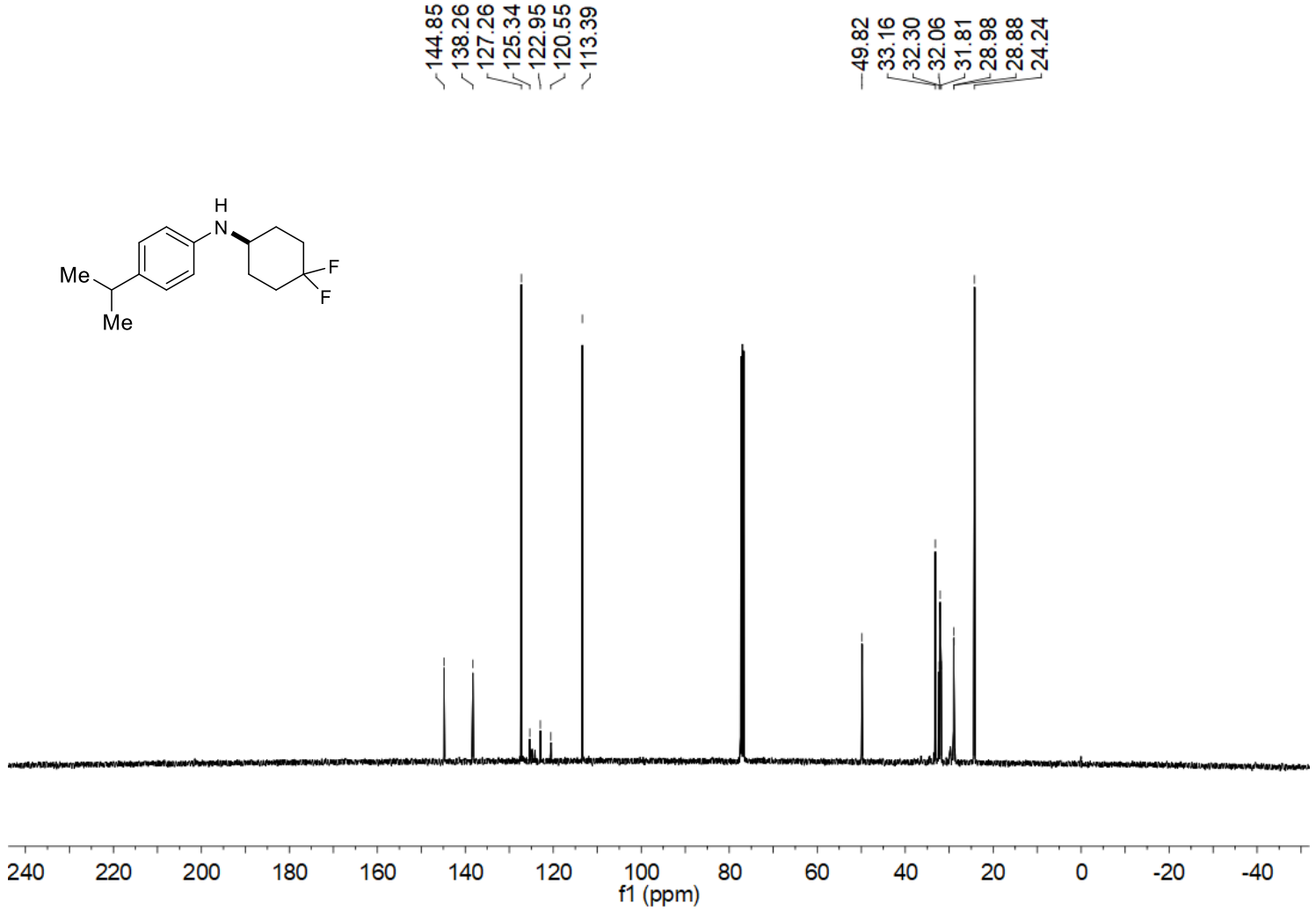
Compound **33** ^{19}F NMR



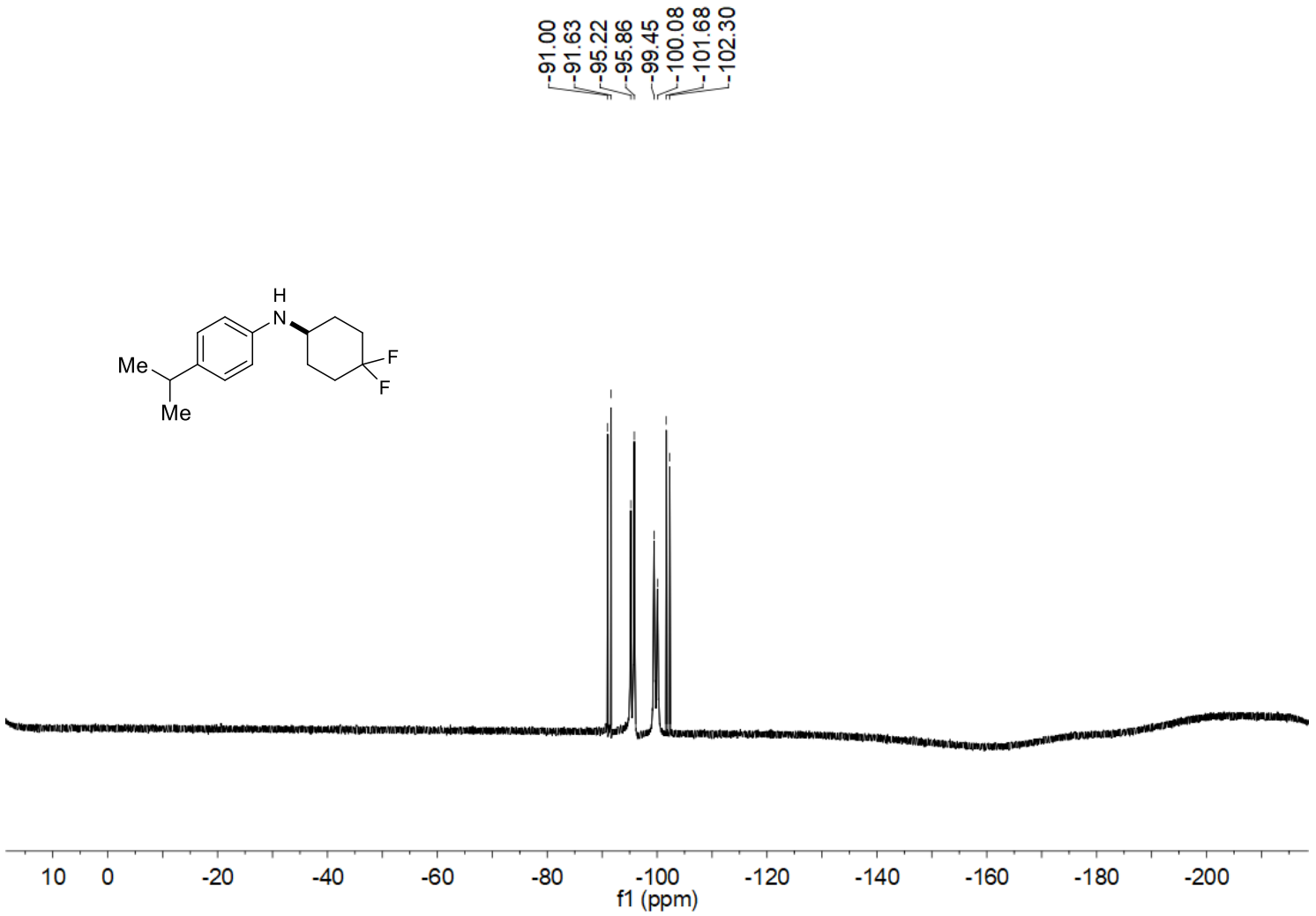
Compound **34** ^{1}H NMR



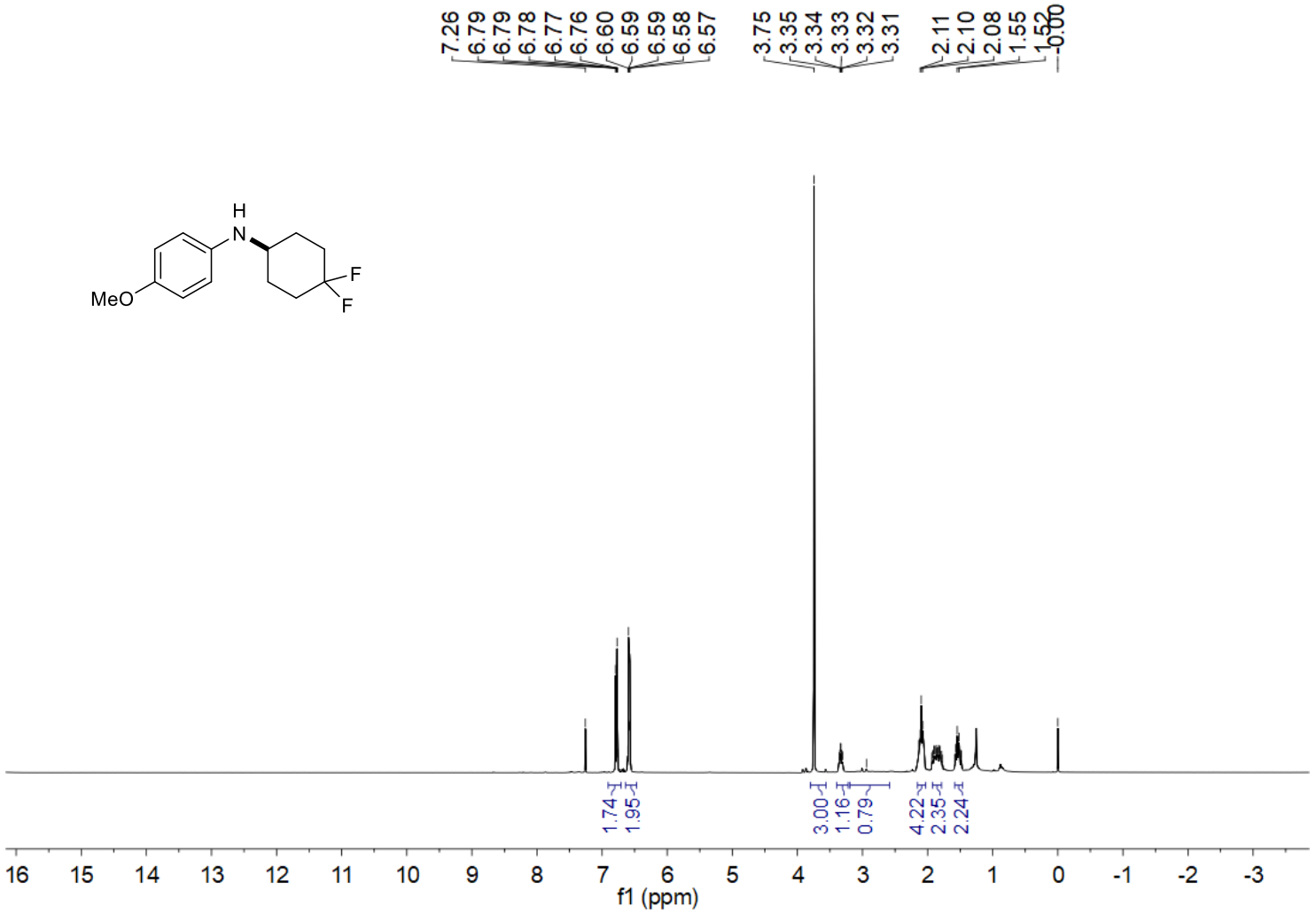
Compound **34** ^{13}C NMR



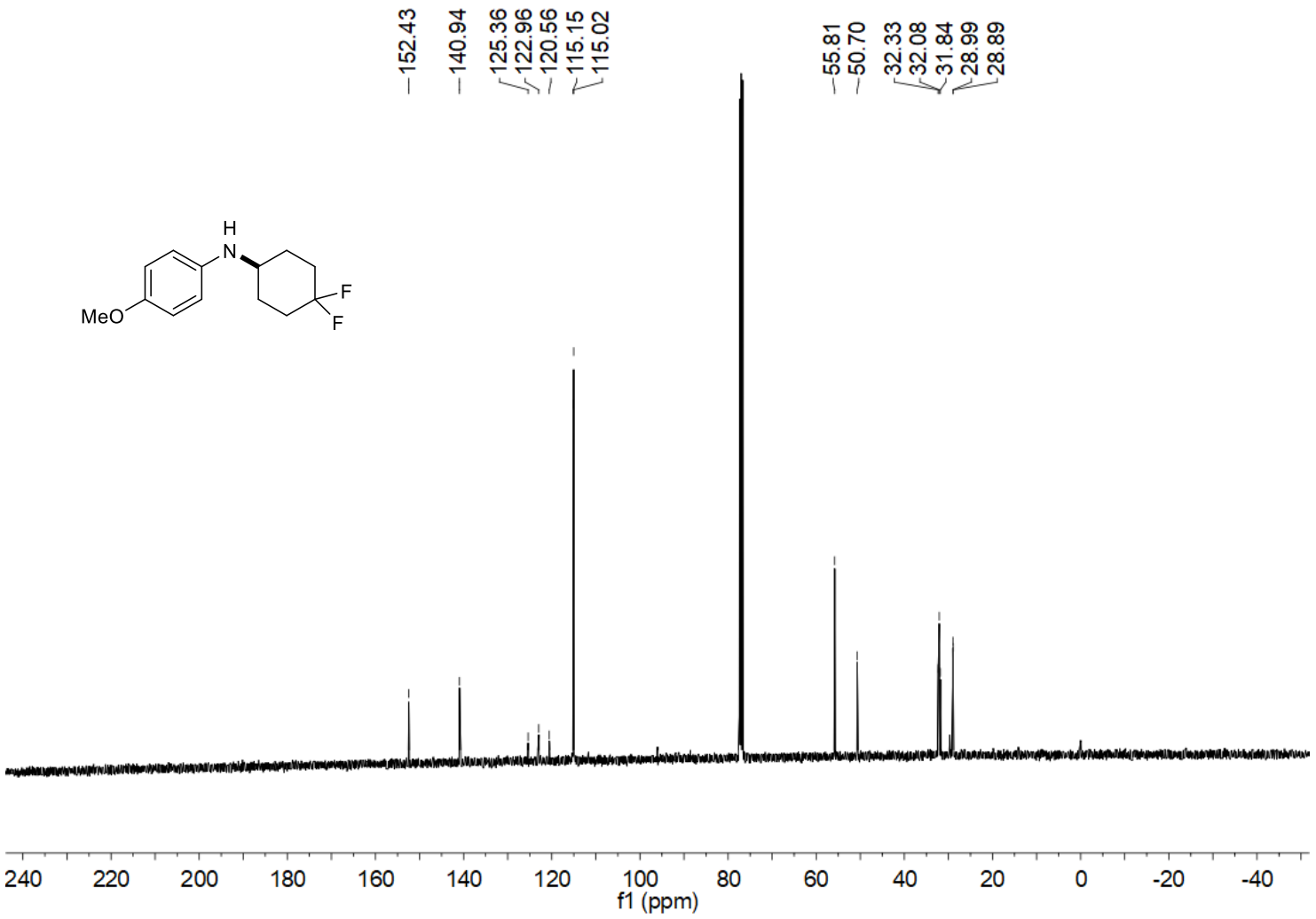
Compound **34** ^{19}F NMR



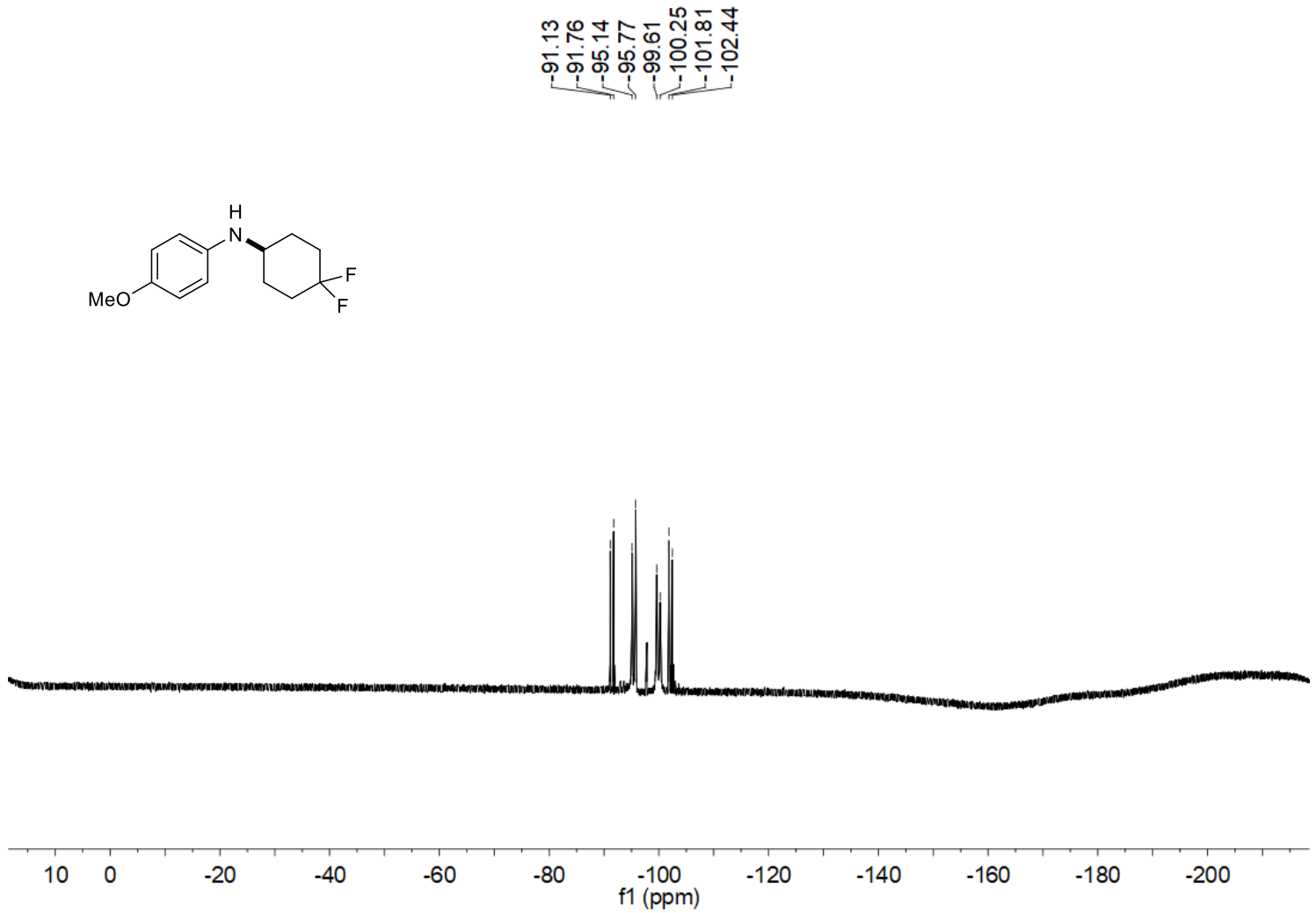
Compound **35** ^{1}H NMR



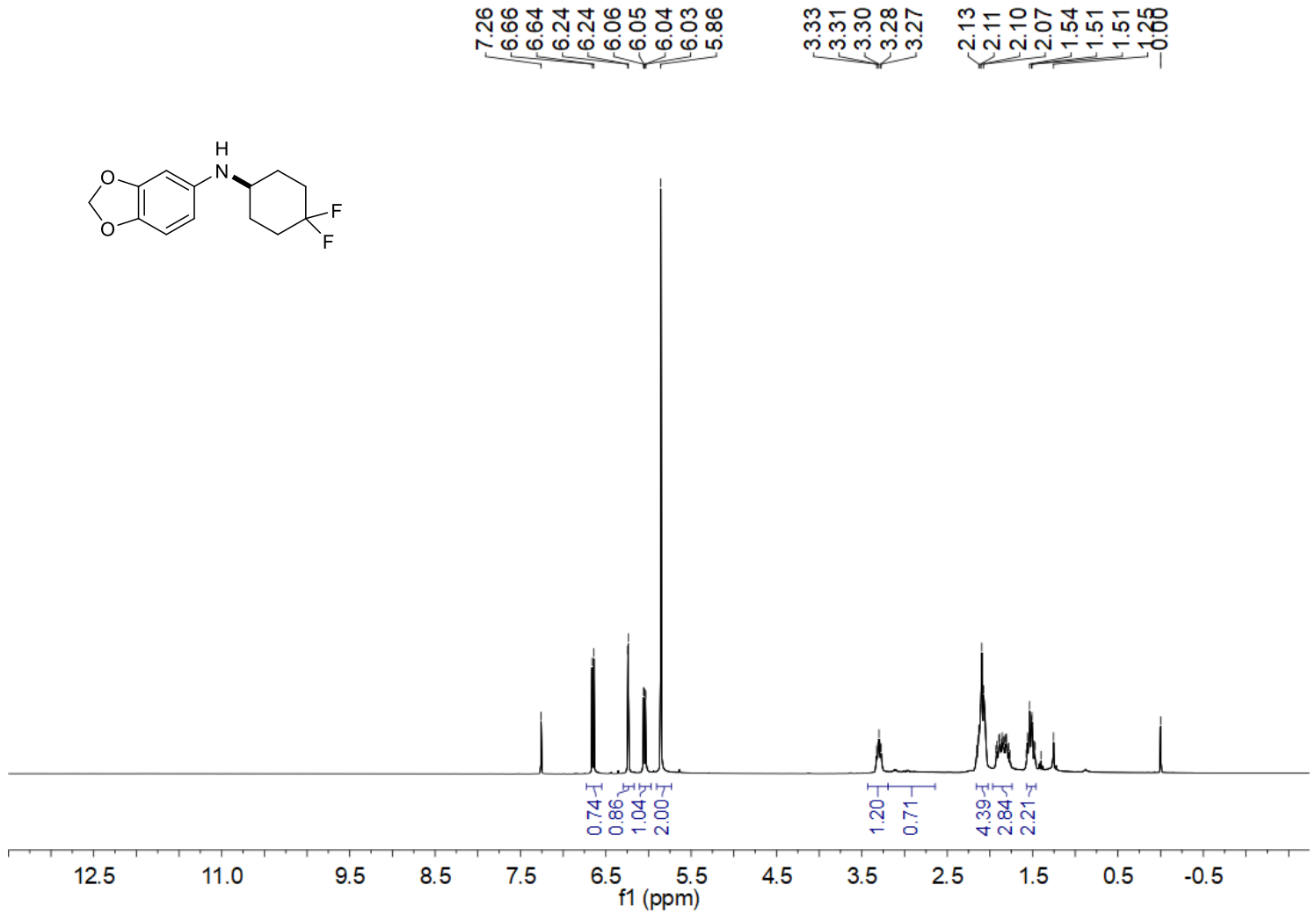
Compound **35** ^{13}C NMR



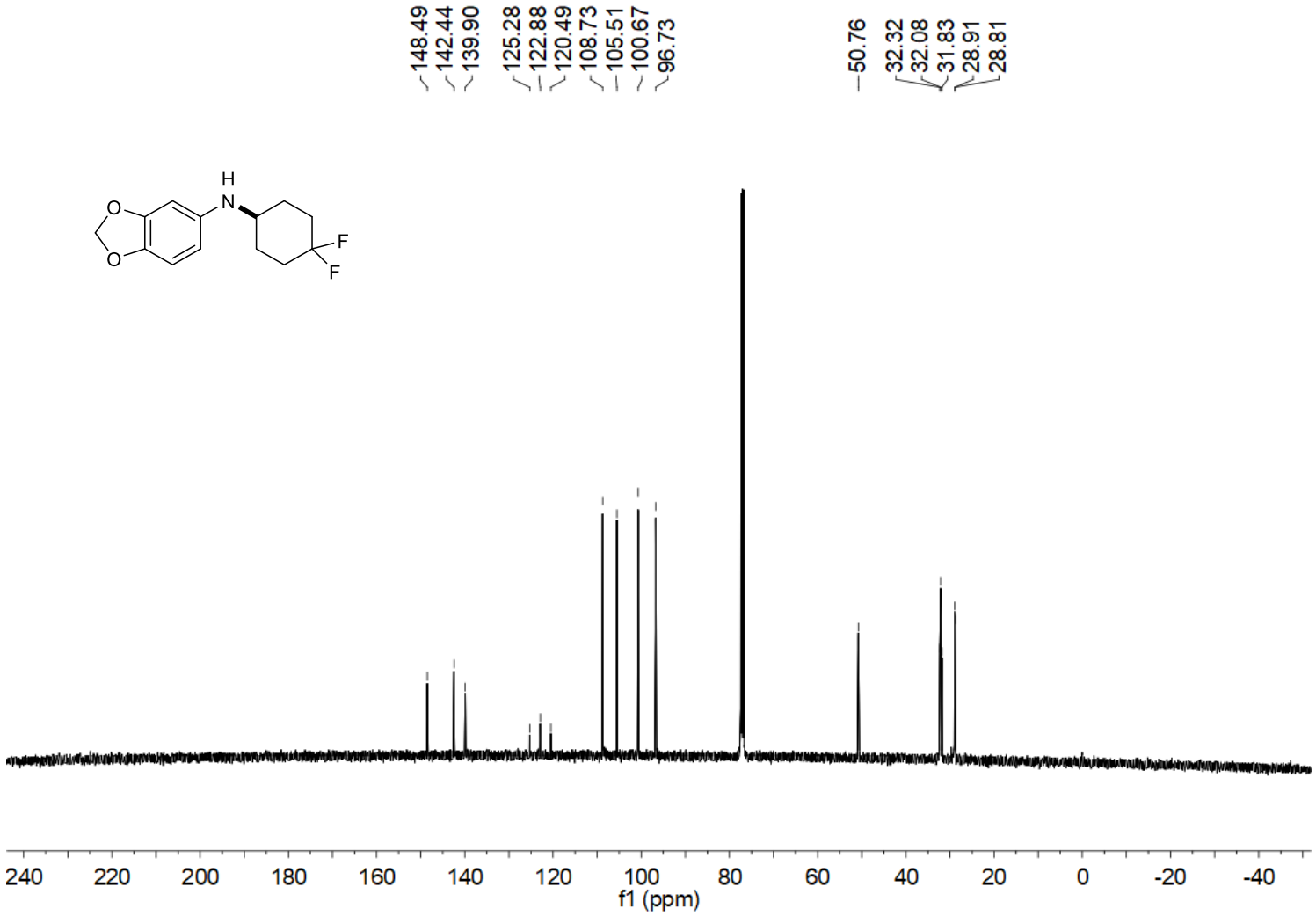
Compound **35** ^{19}F NMR



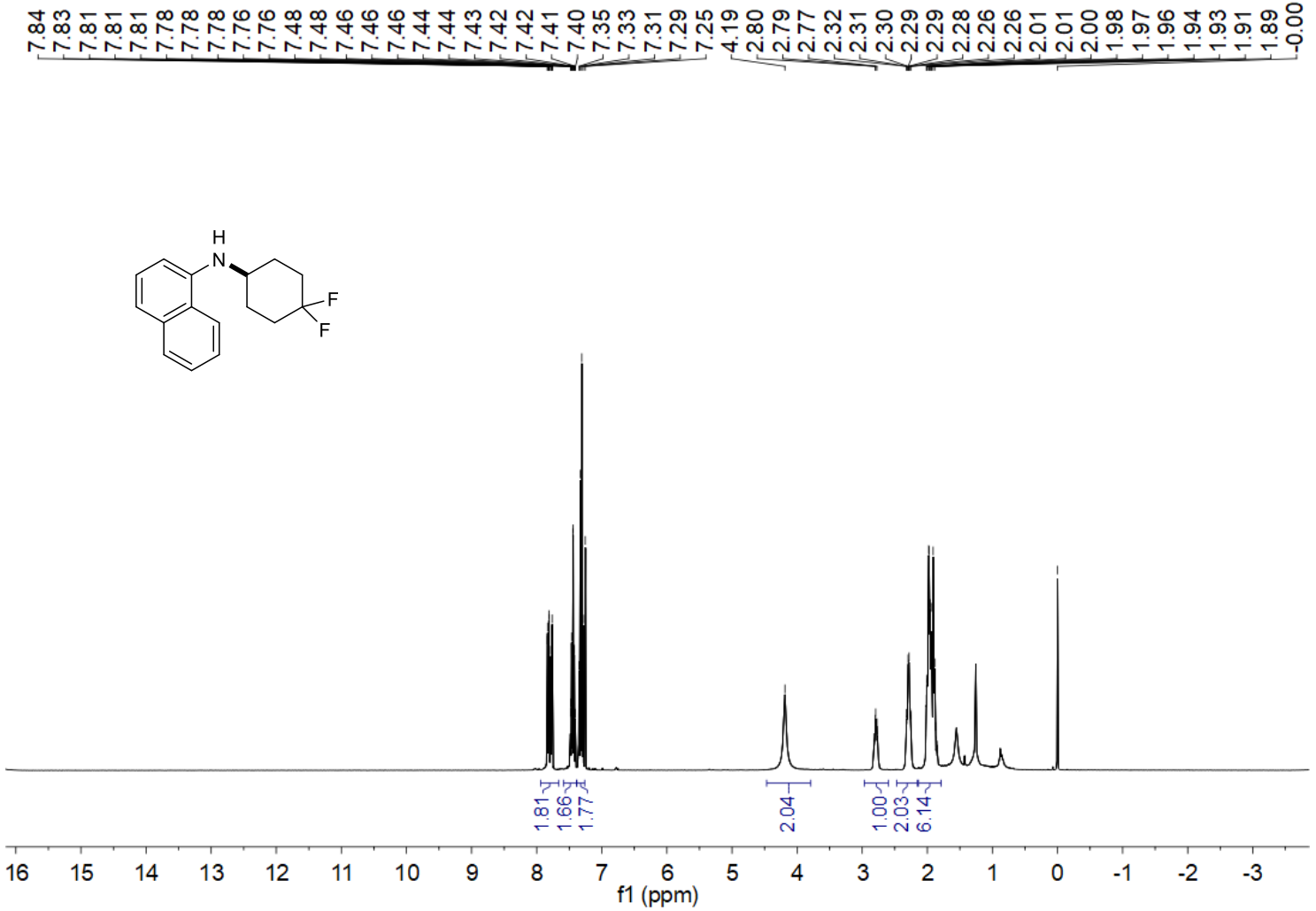
Compound **36** ^{1}H NMR



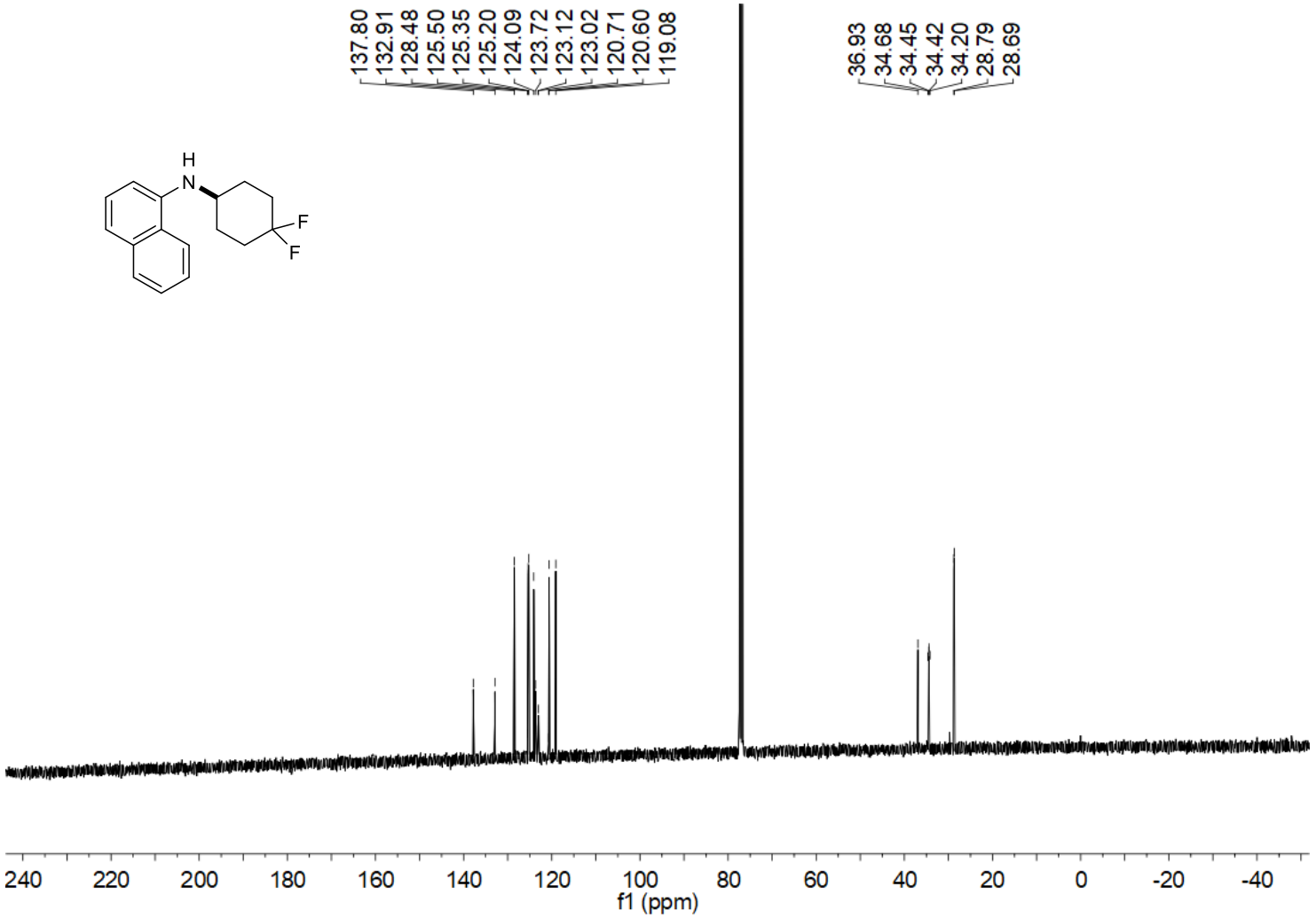
Compound **36** ^{13}C NMR



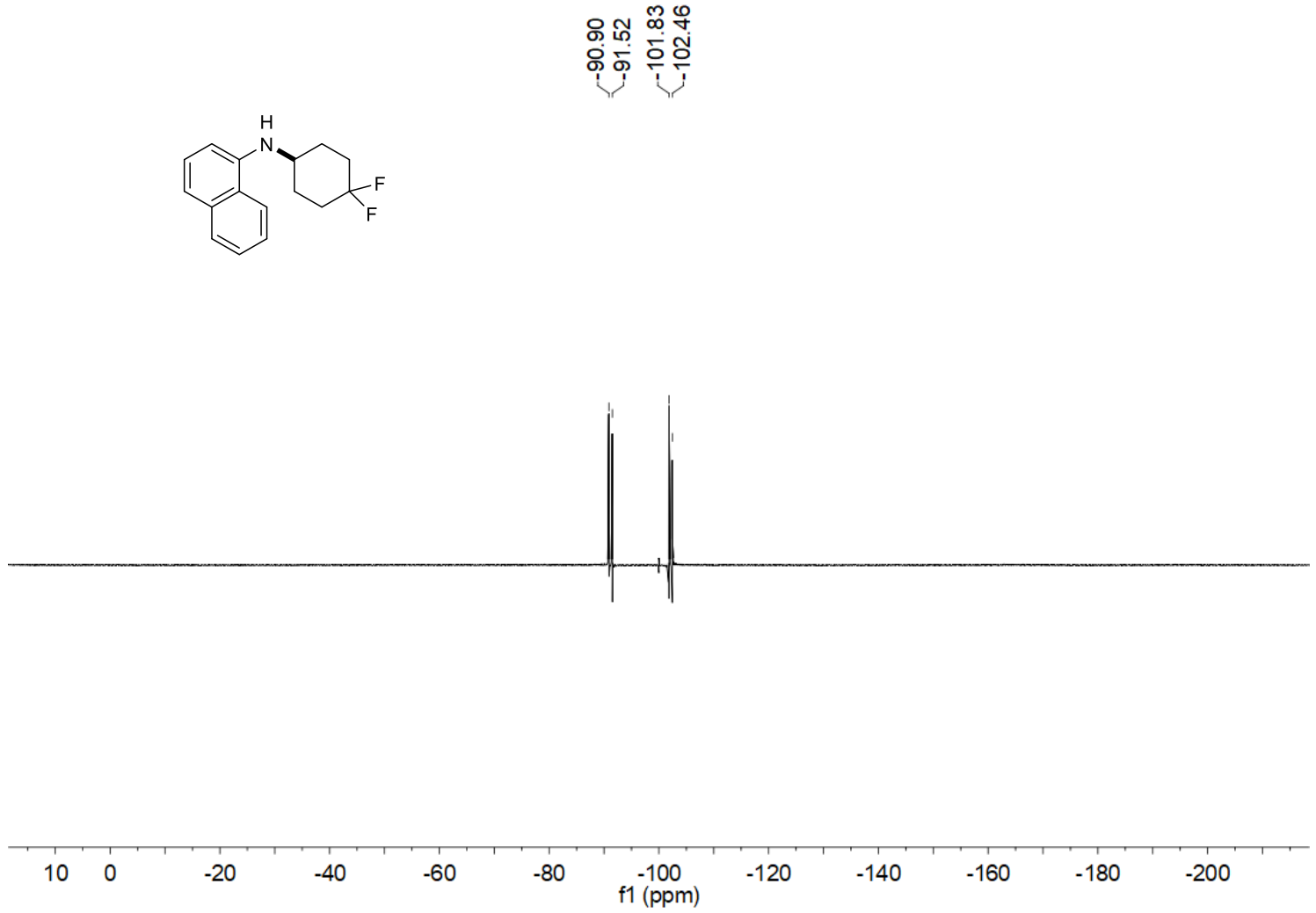
Compound **37** ^{1}H NMR



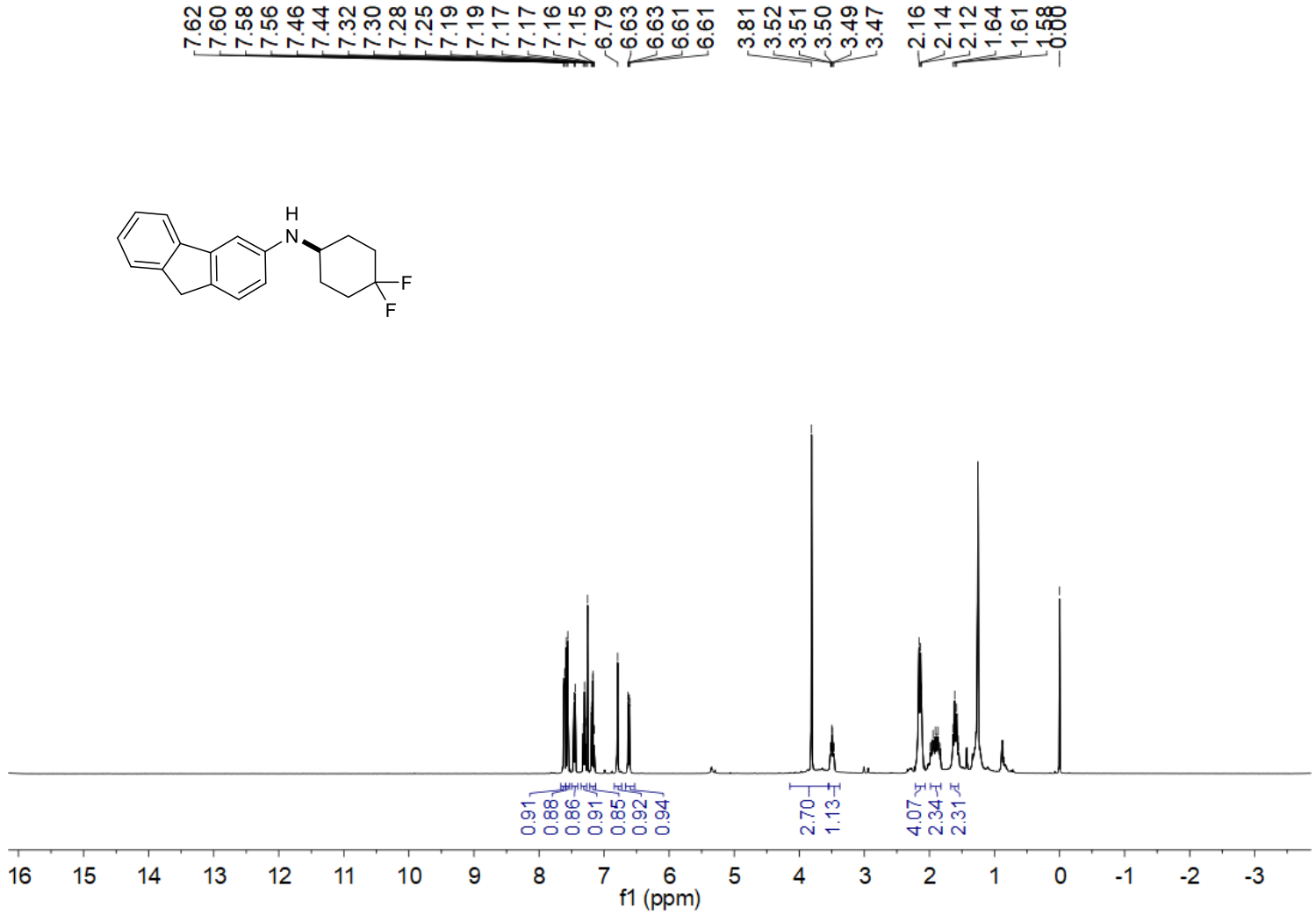
Compound **37** ^{13}C NMR



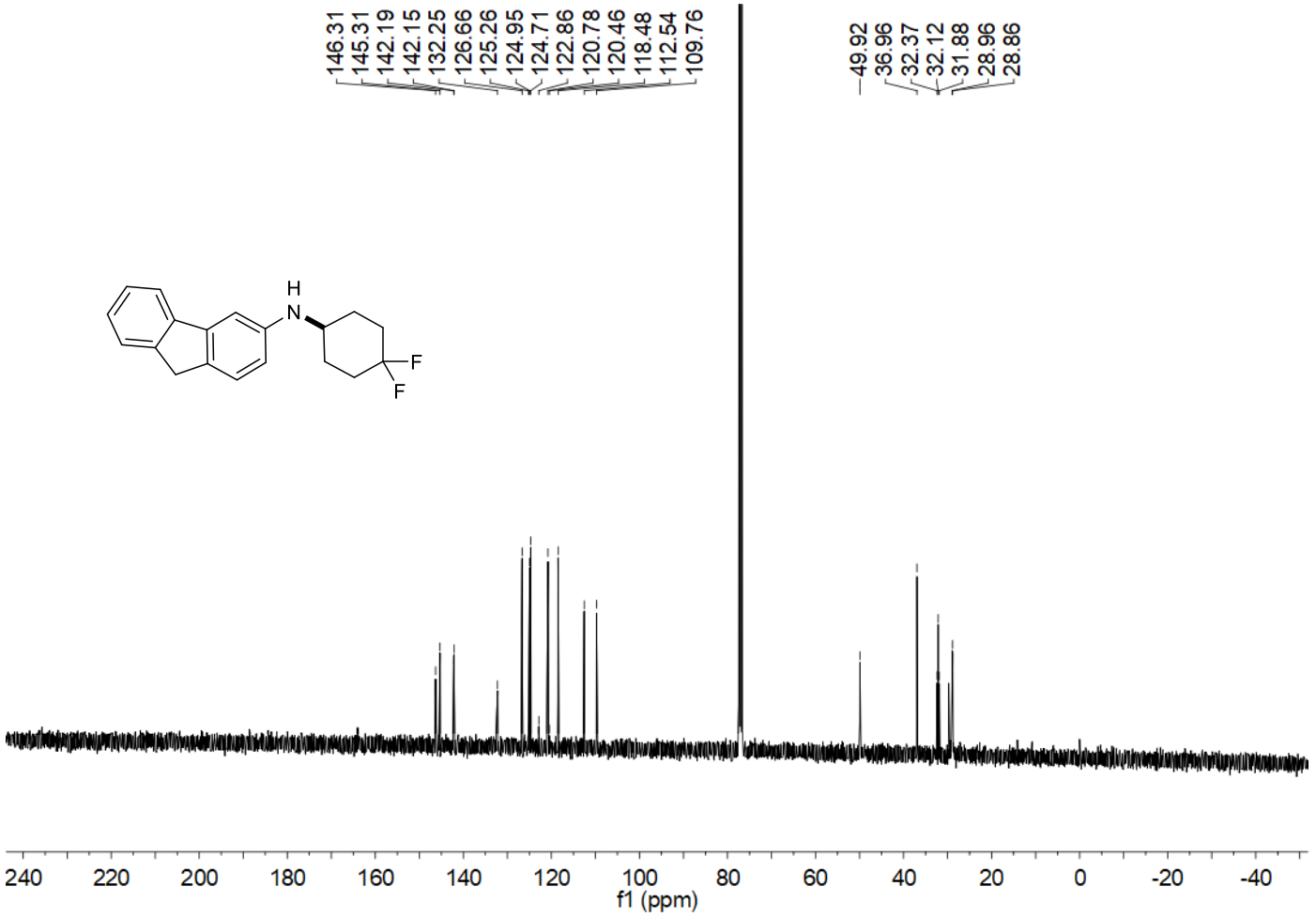
Compound **37** ^{19}F NMR



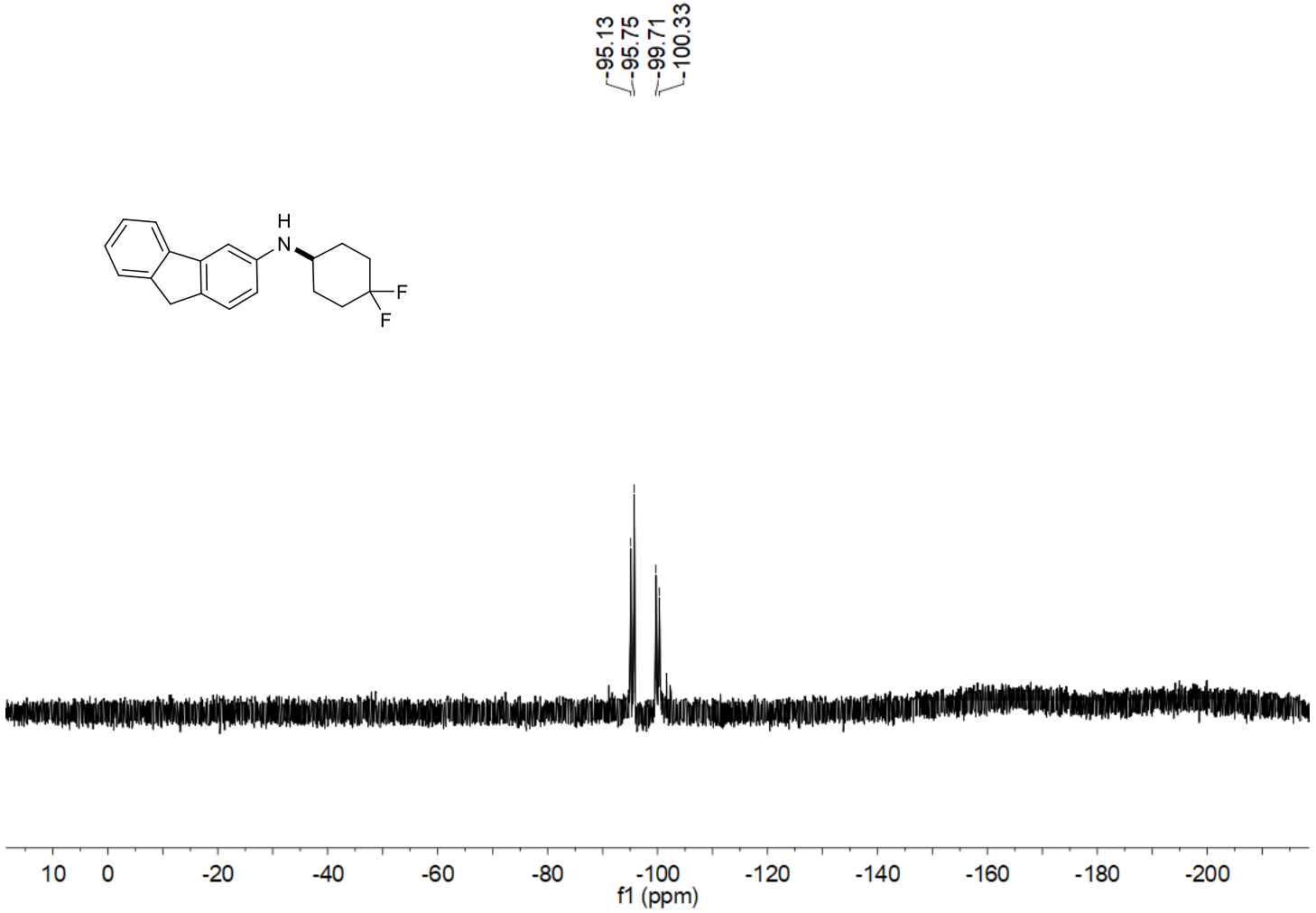
Compound **38** ^{1}H NMR



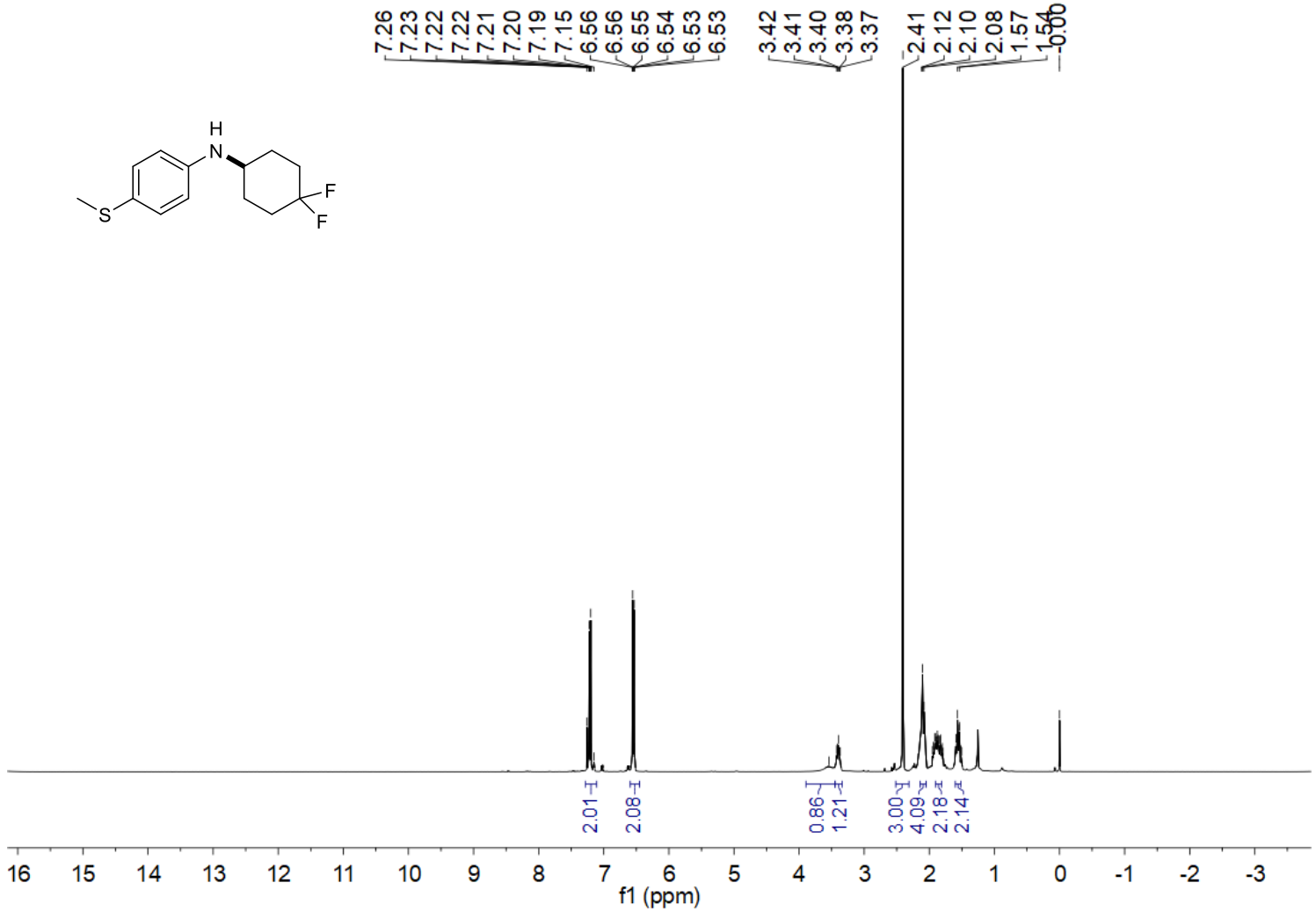
Compound **38** ^{13}C NMR



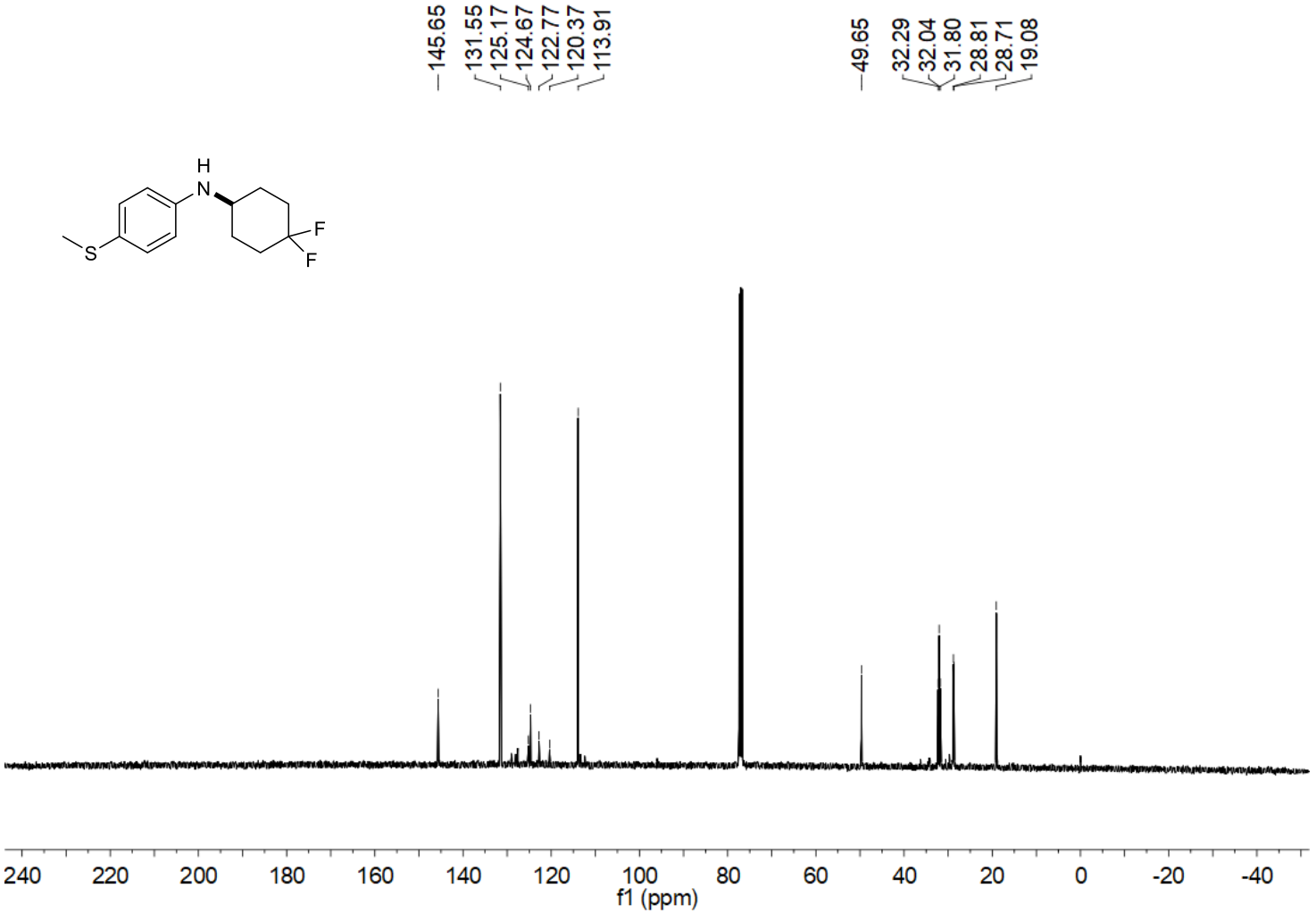
Compound **38** ^{19}F NMR



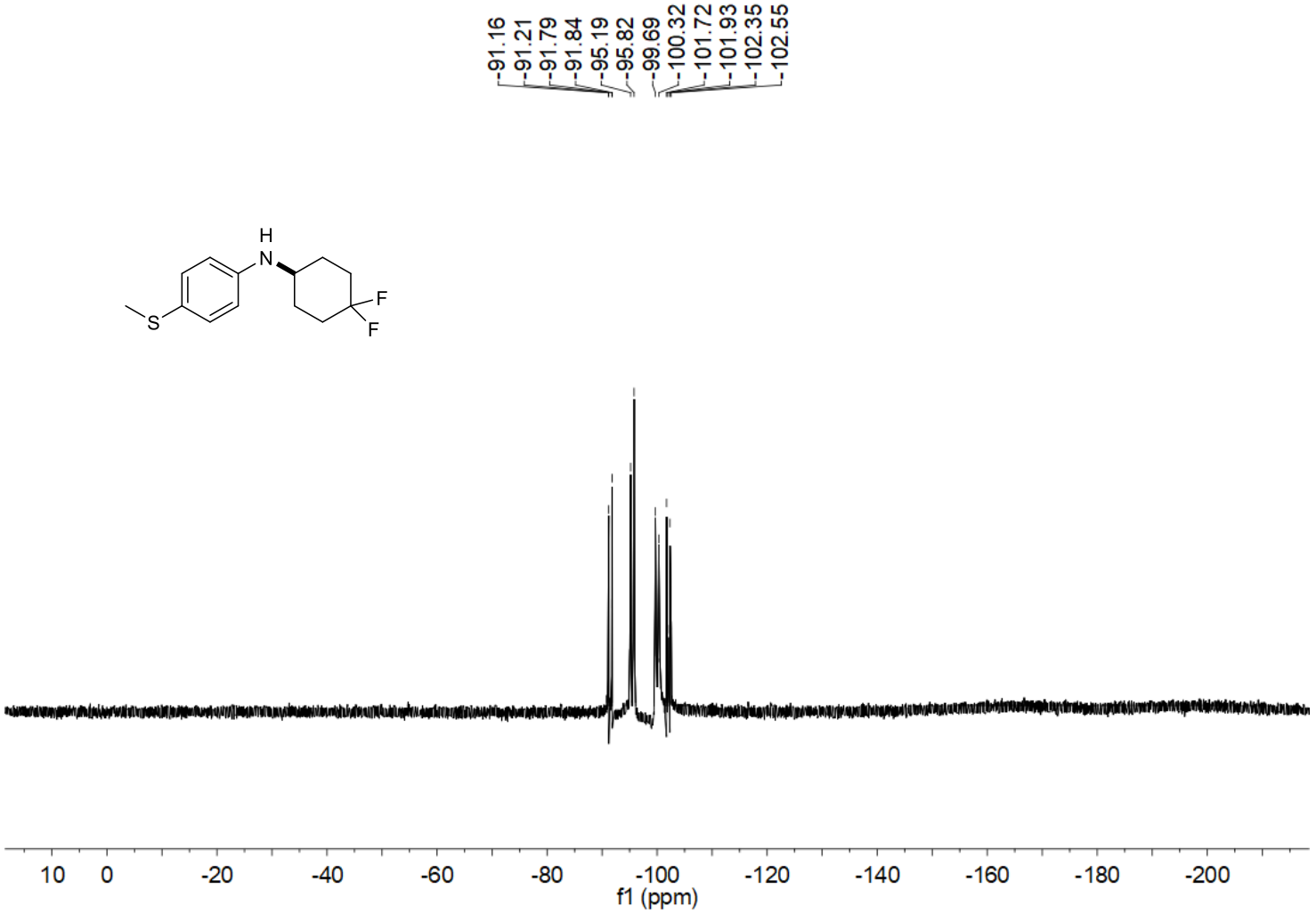
Compound **39** ^{1}H NMR



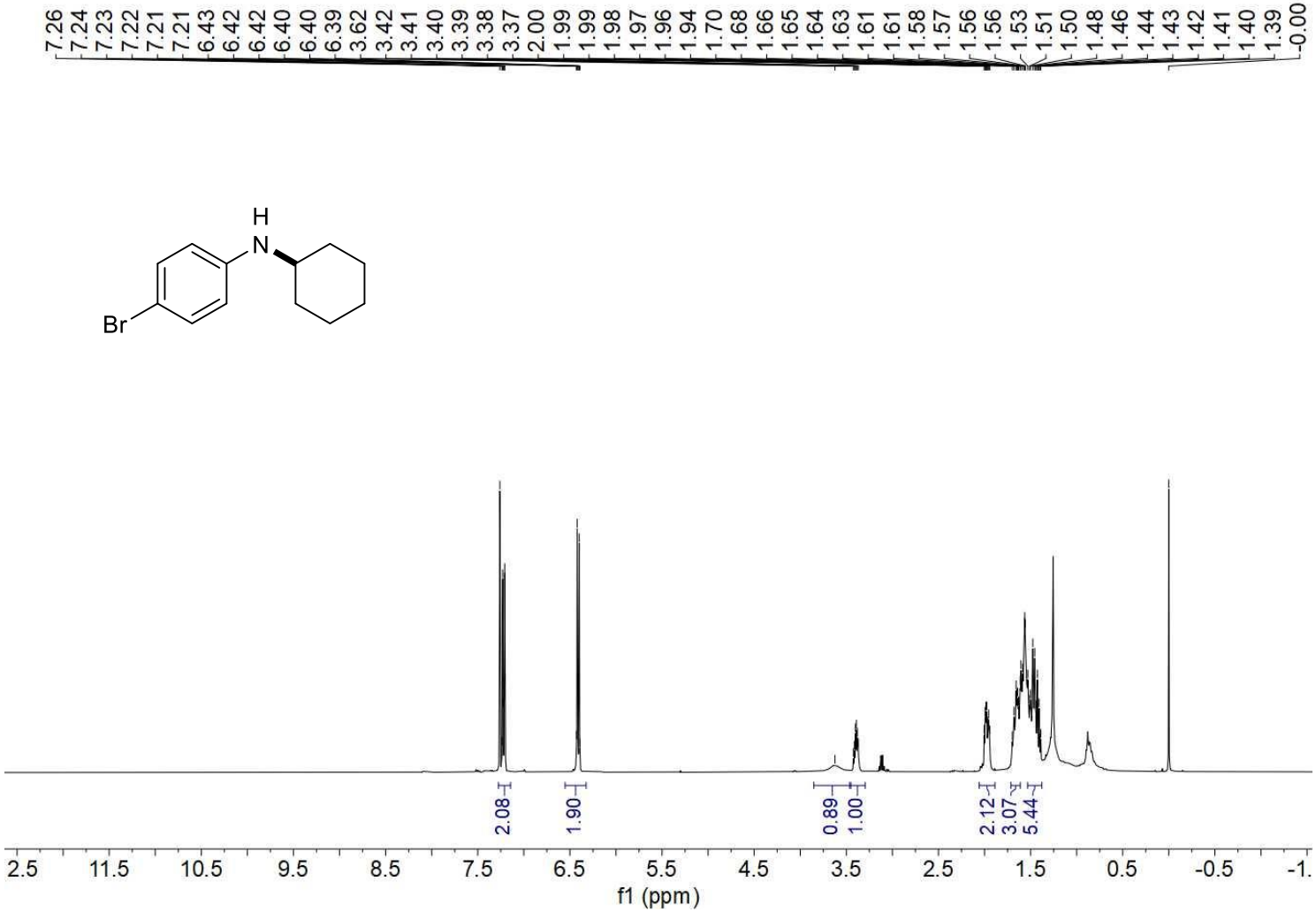
Compound **39** ^{13}C NMR



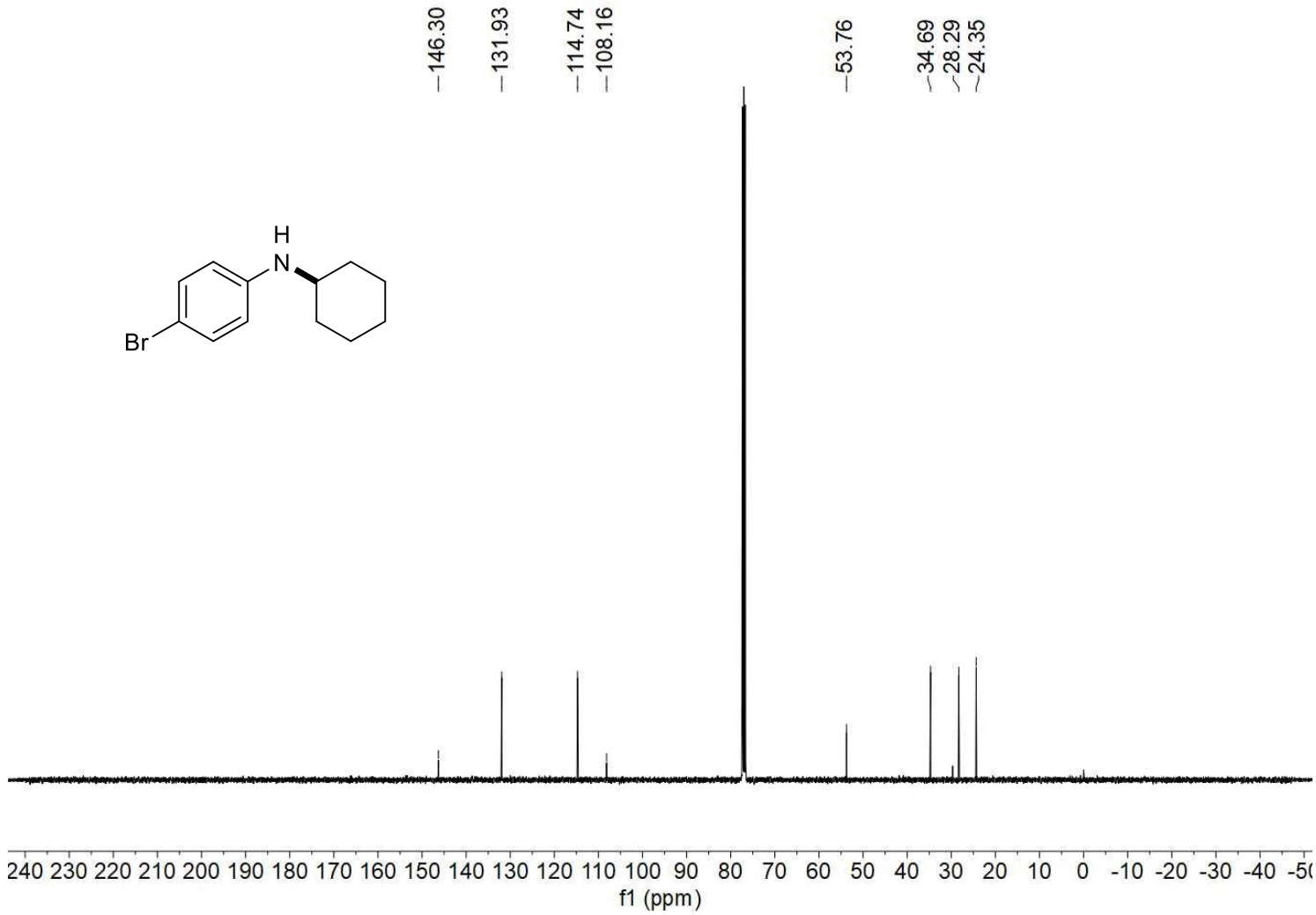
Compound **39** ^{19}F NMR



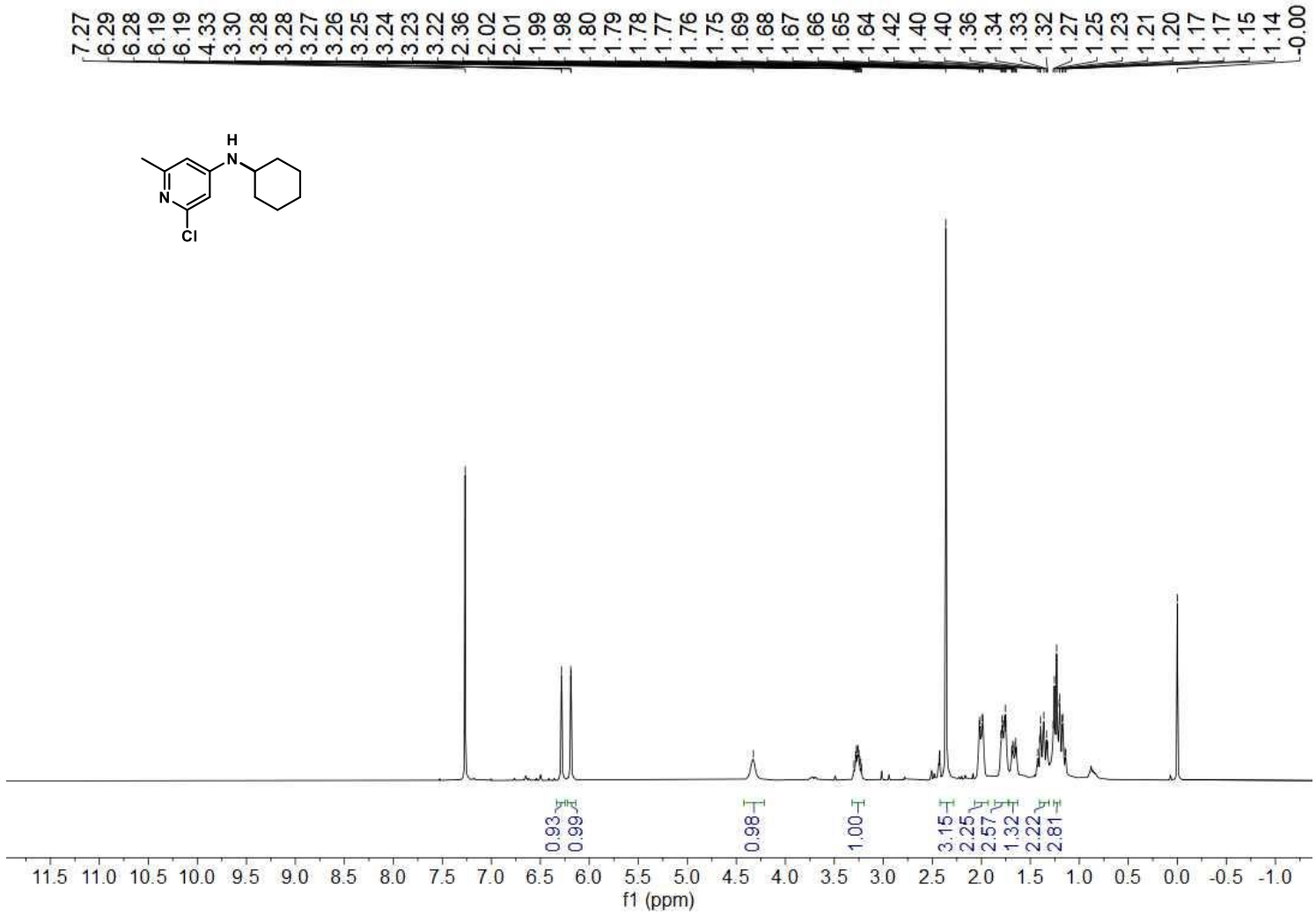
Compound **43** ^{1}H NMR



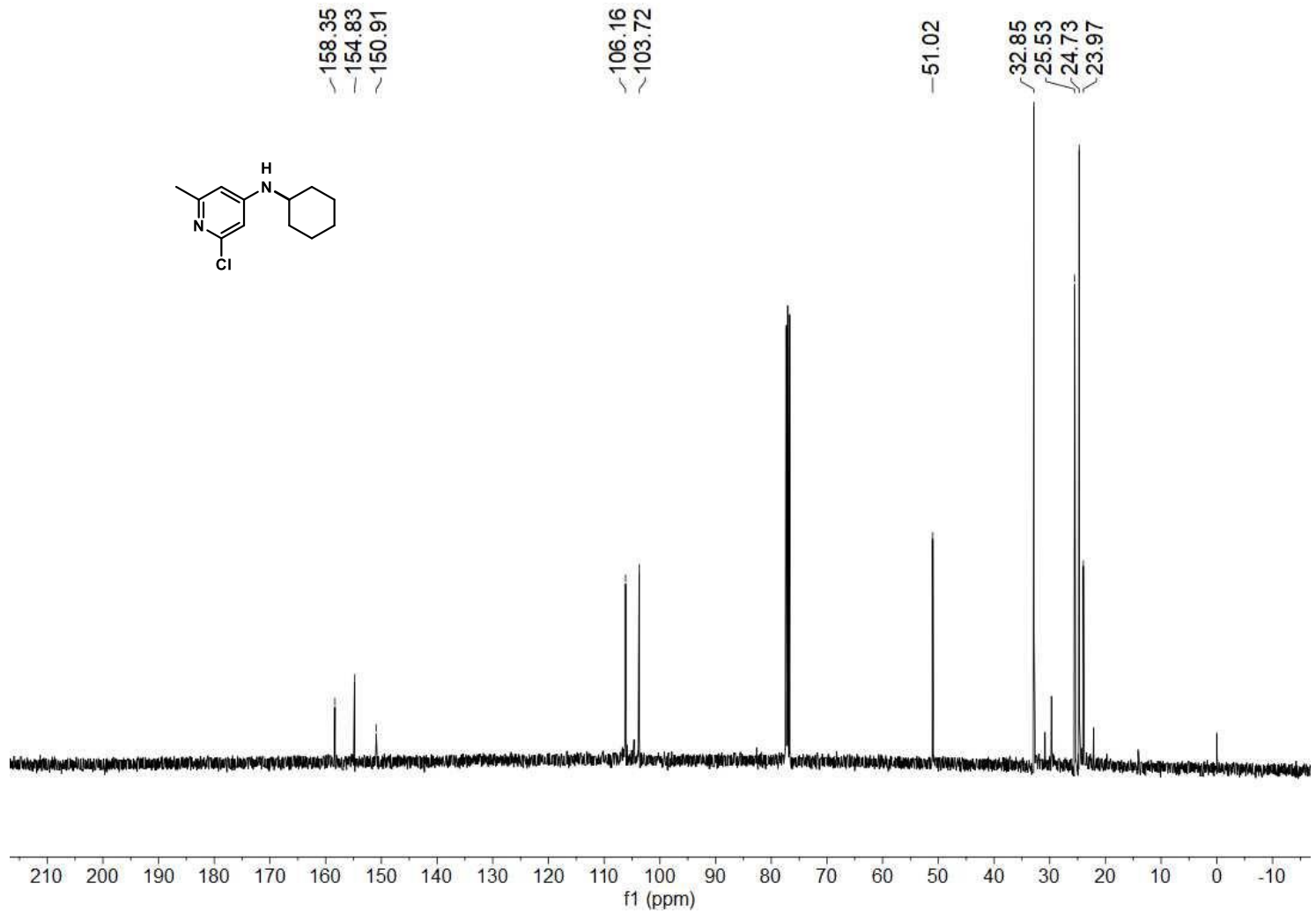
Compound **43** ^{13}C NMR



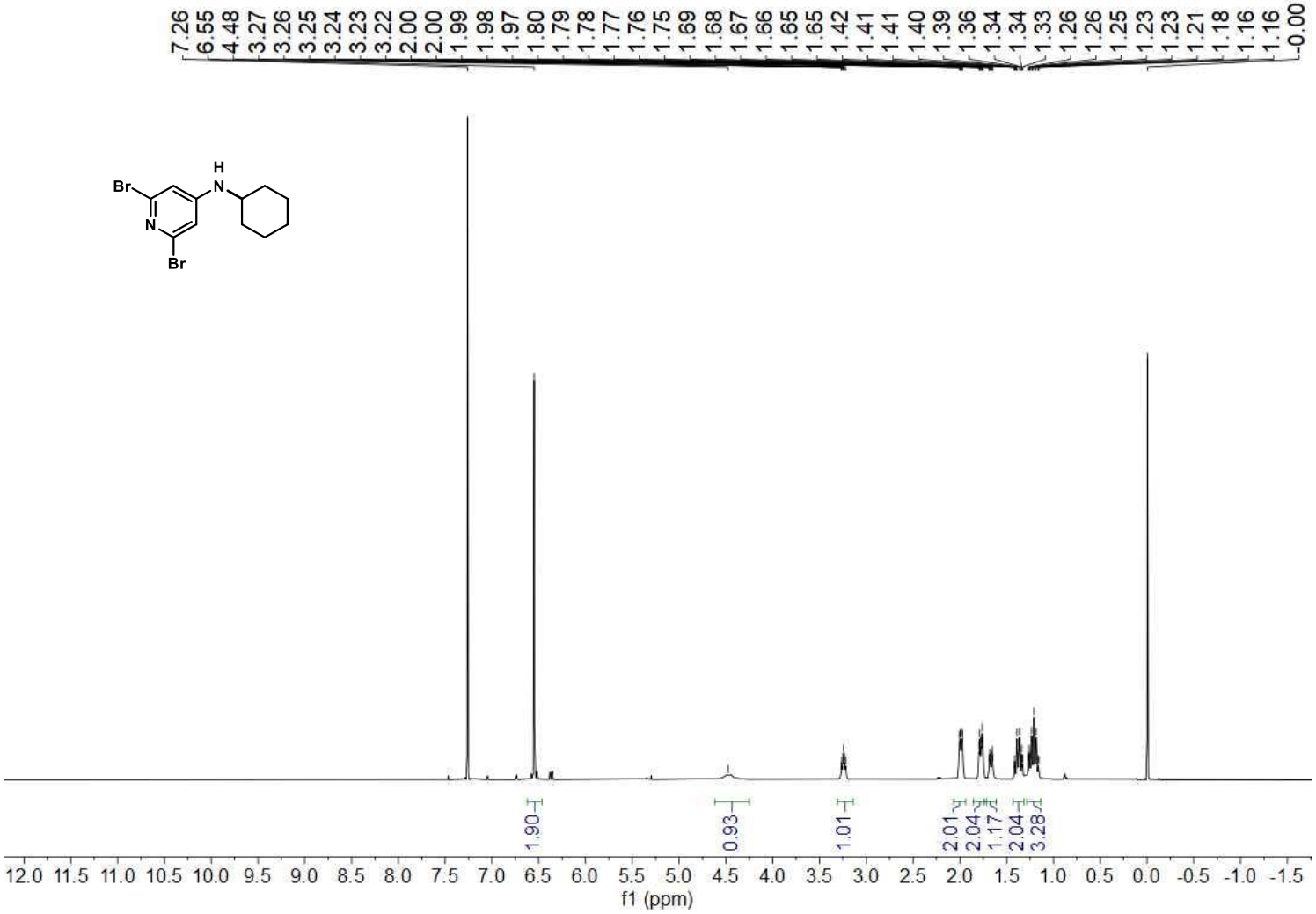
Compound **45** ^{1}H NMR



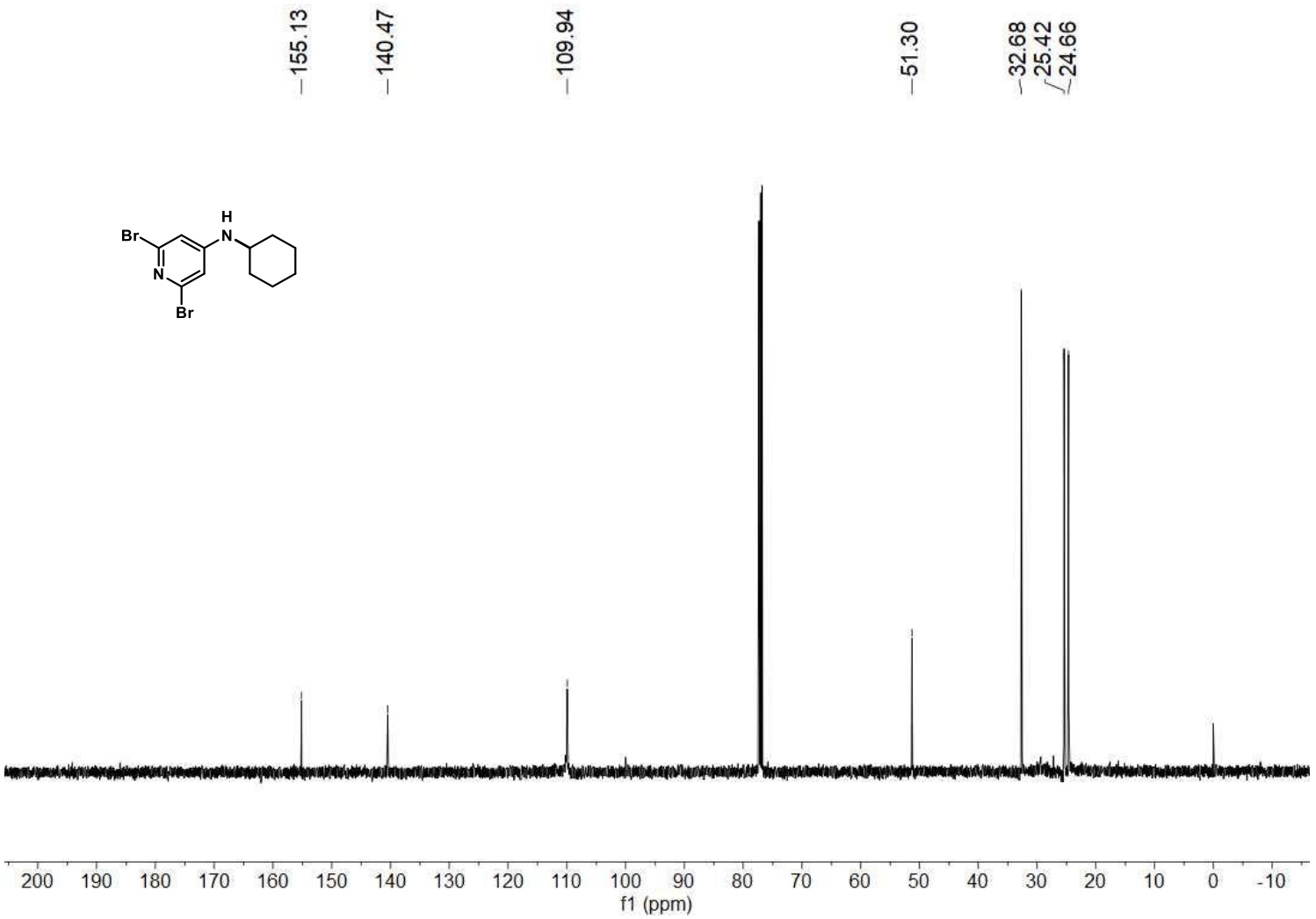
Compound **45** ^{13}C NMR



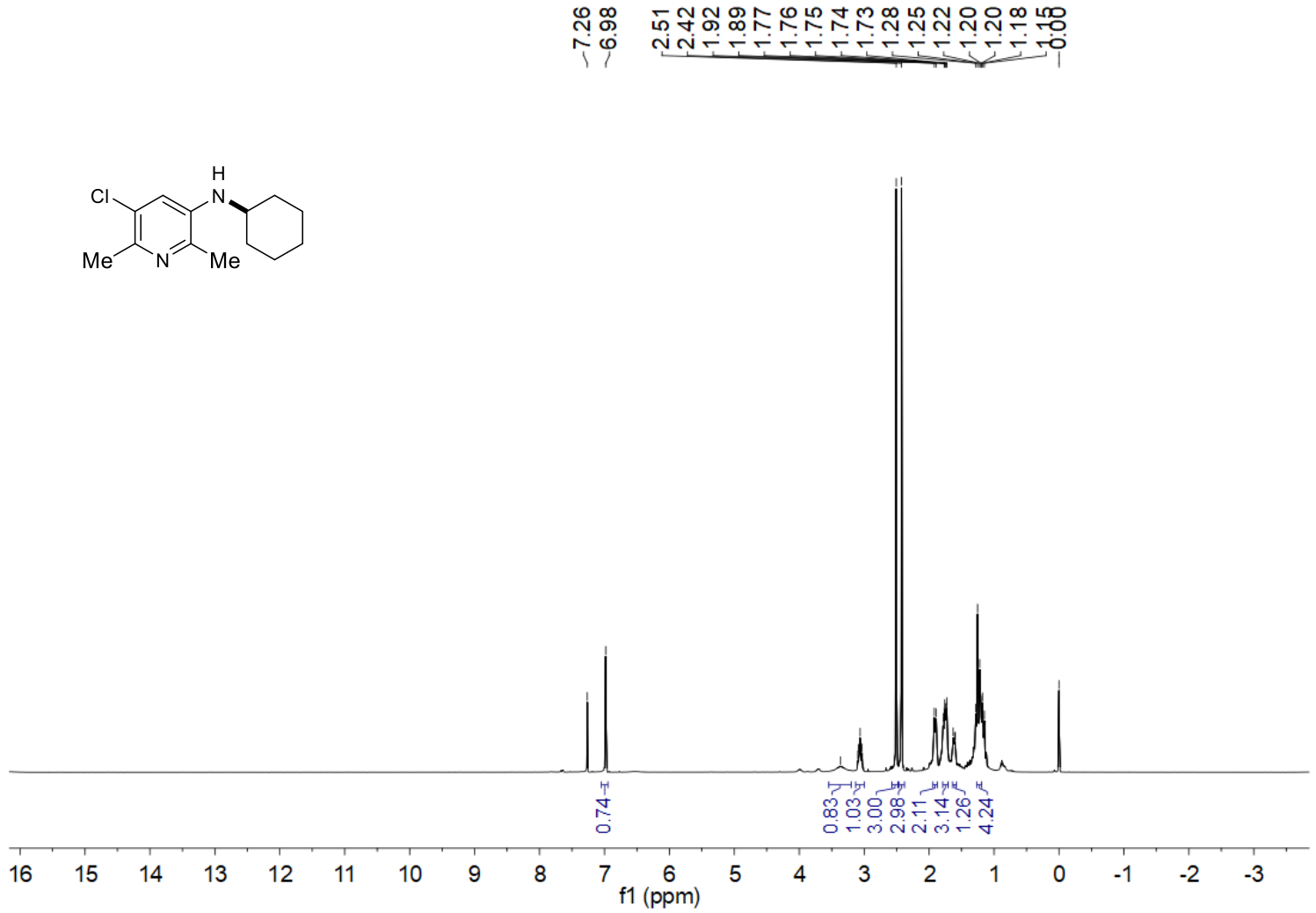
Compound **46** ^{1}H NMR



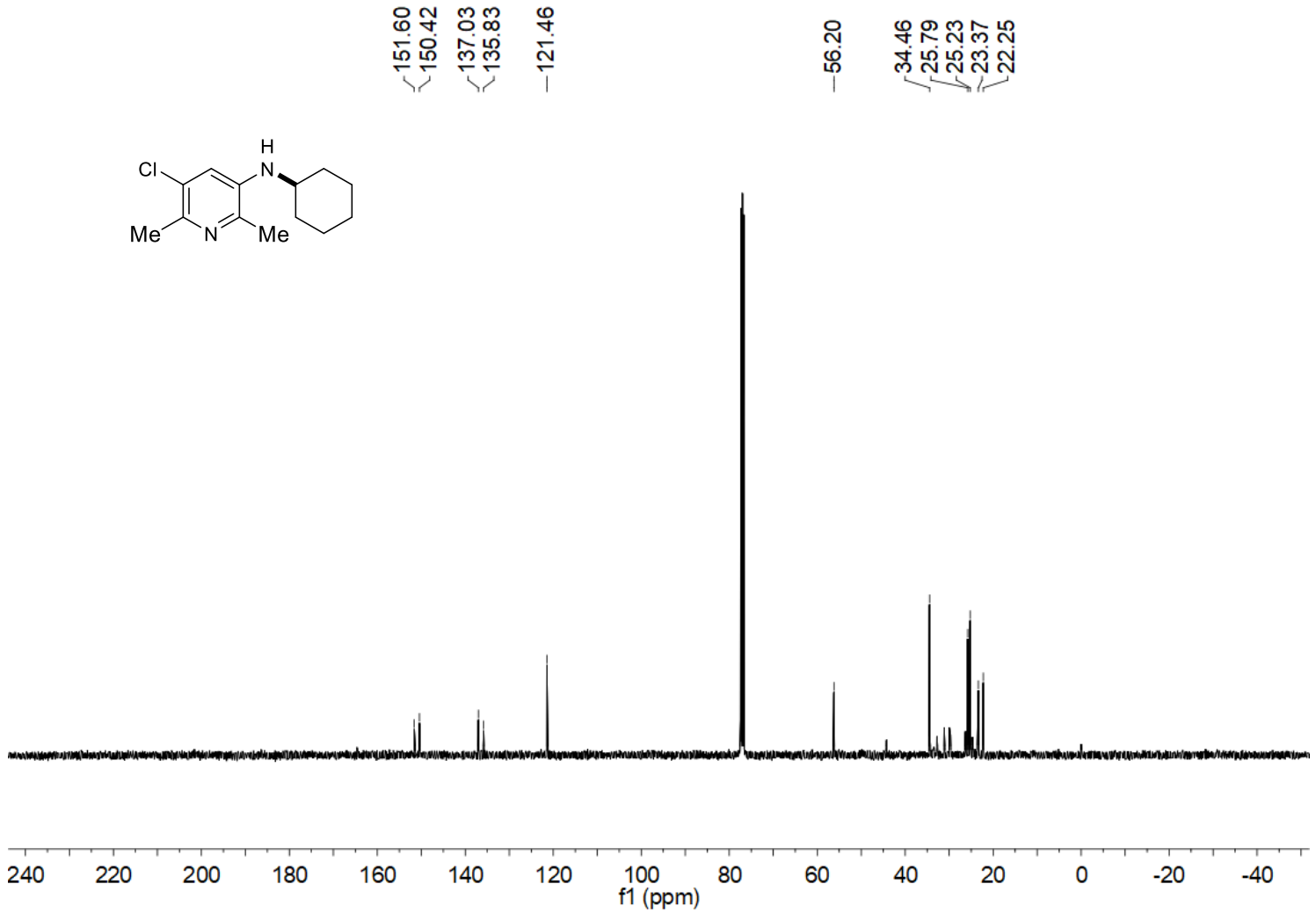
Compound **46** ^{13}C NMR



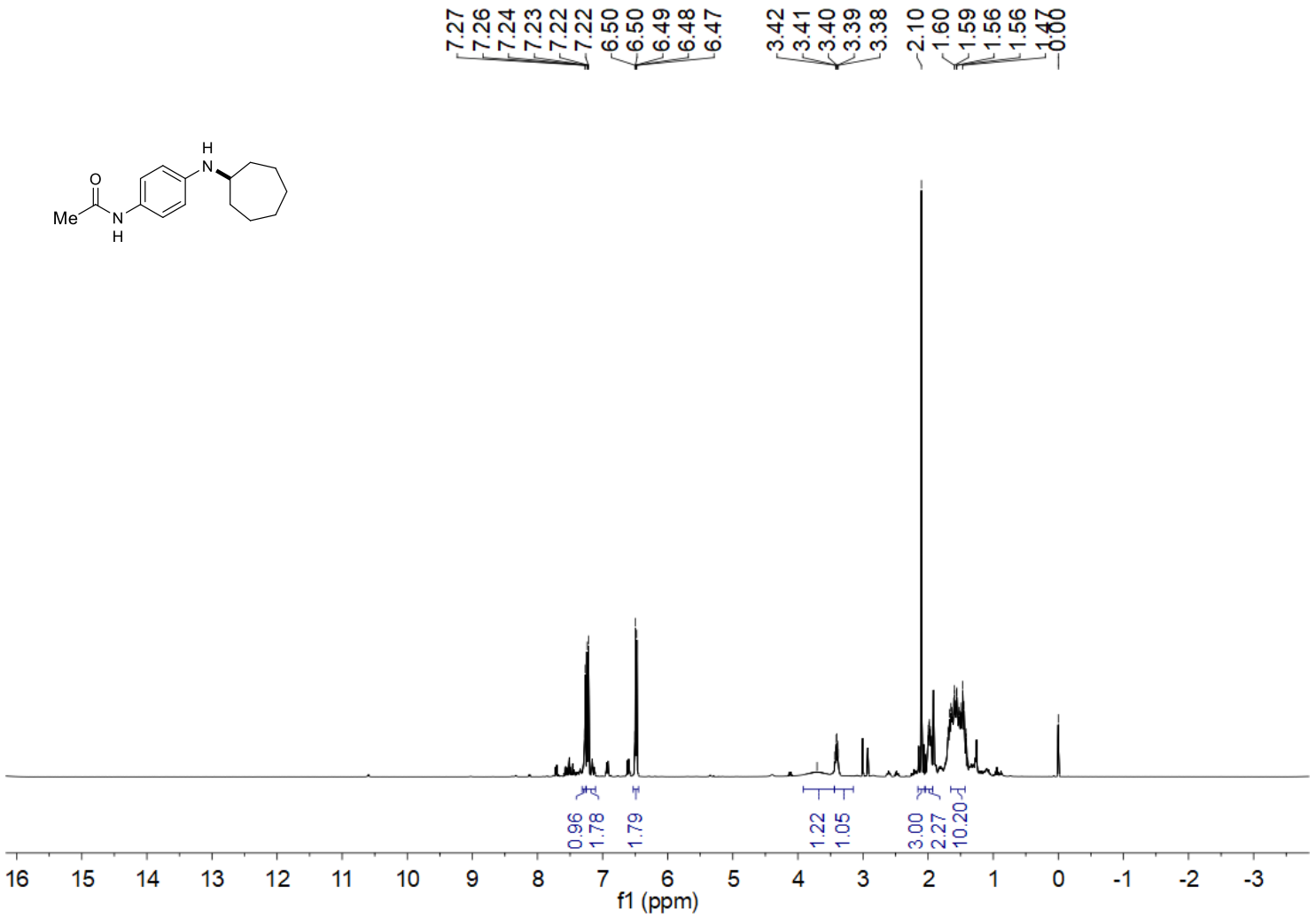
Compound **47** ^{1}H NMR



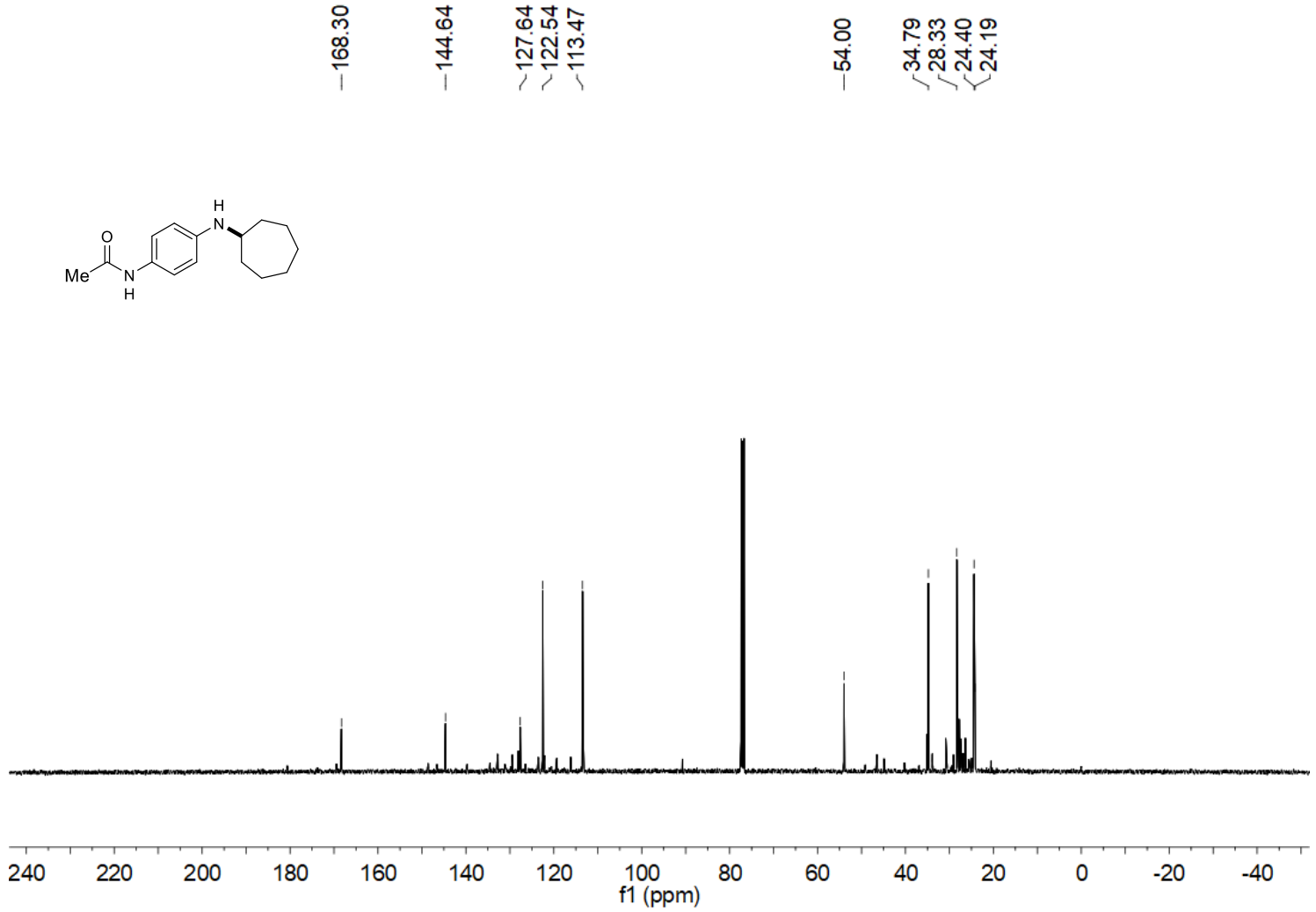
Compound **47** ^{13}C NMR



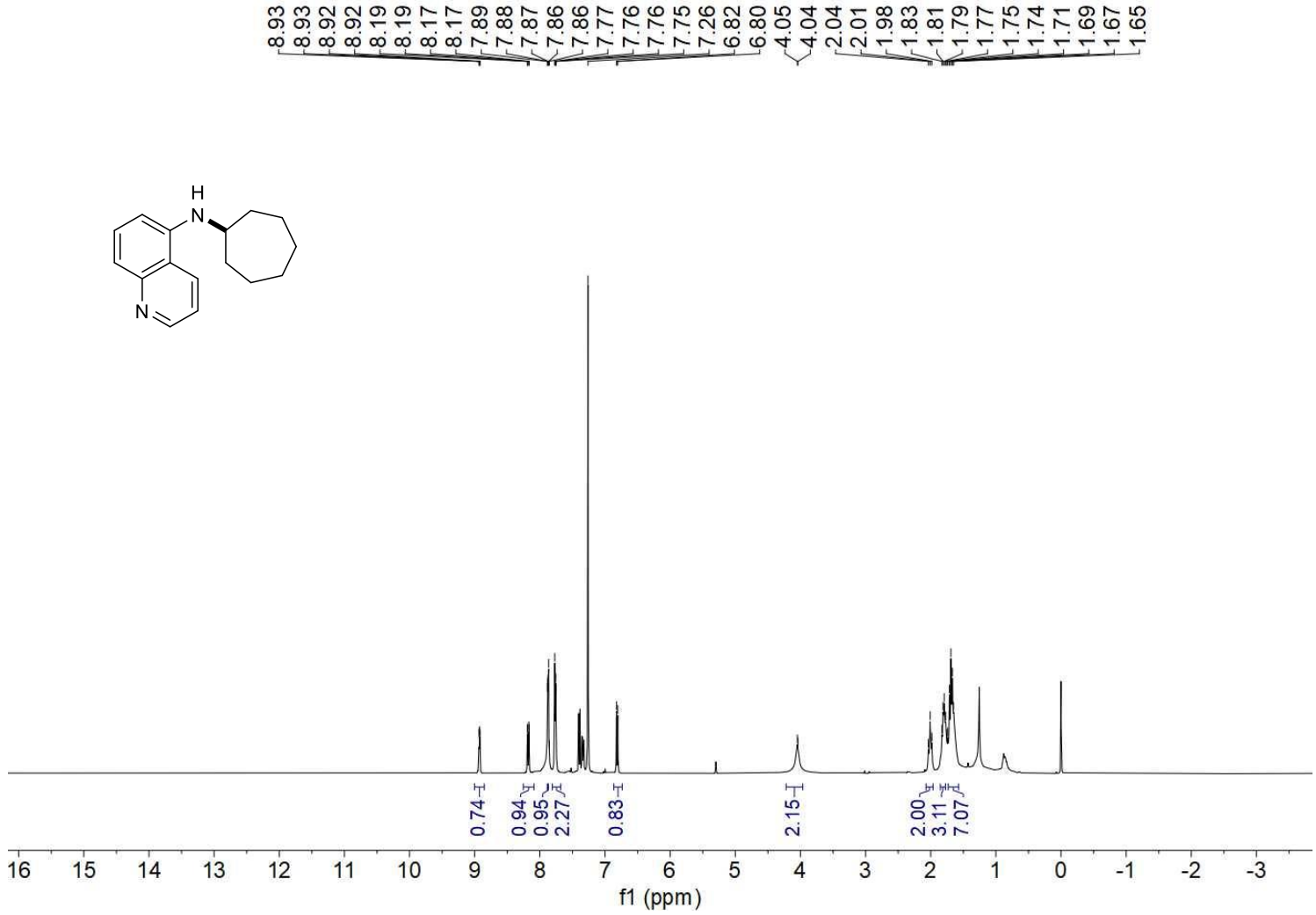
Compound **48** ^{1}H NMR



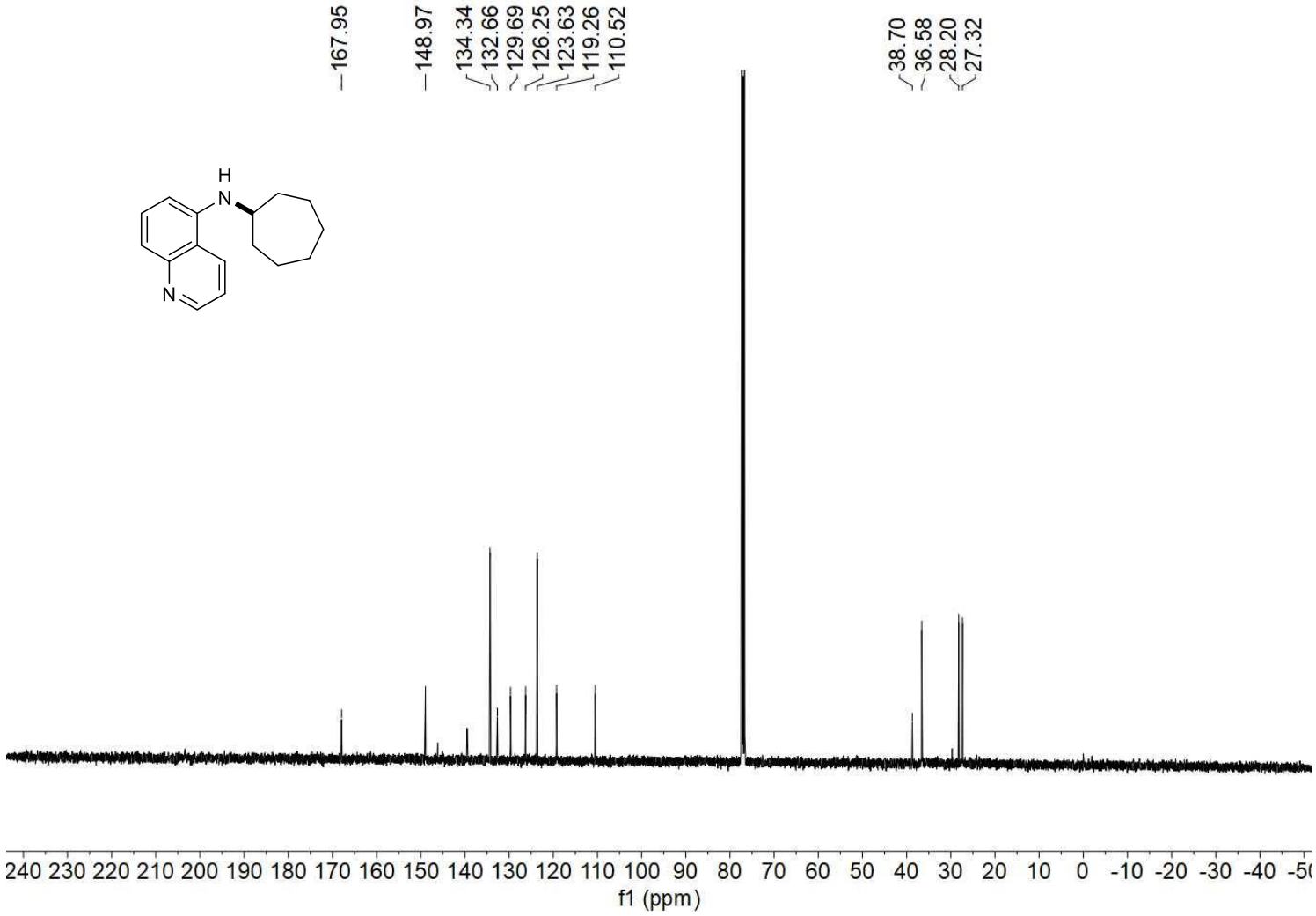
Compound **48** ^{13}C NMR



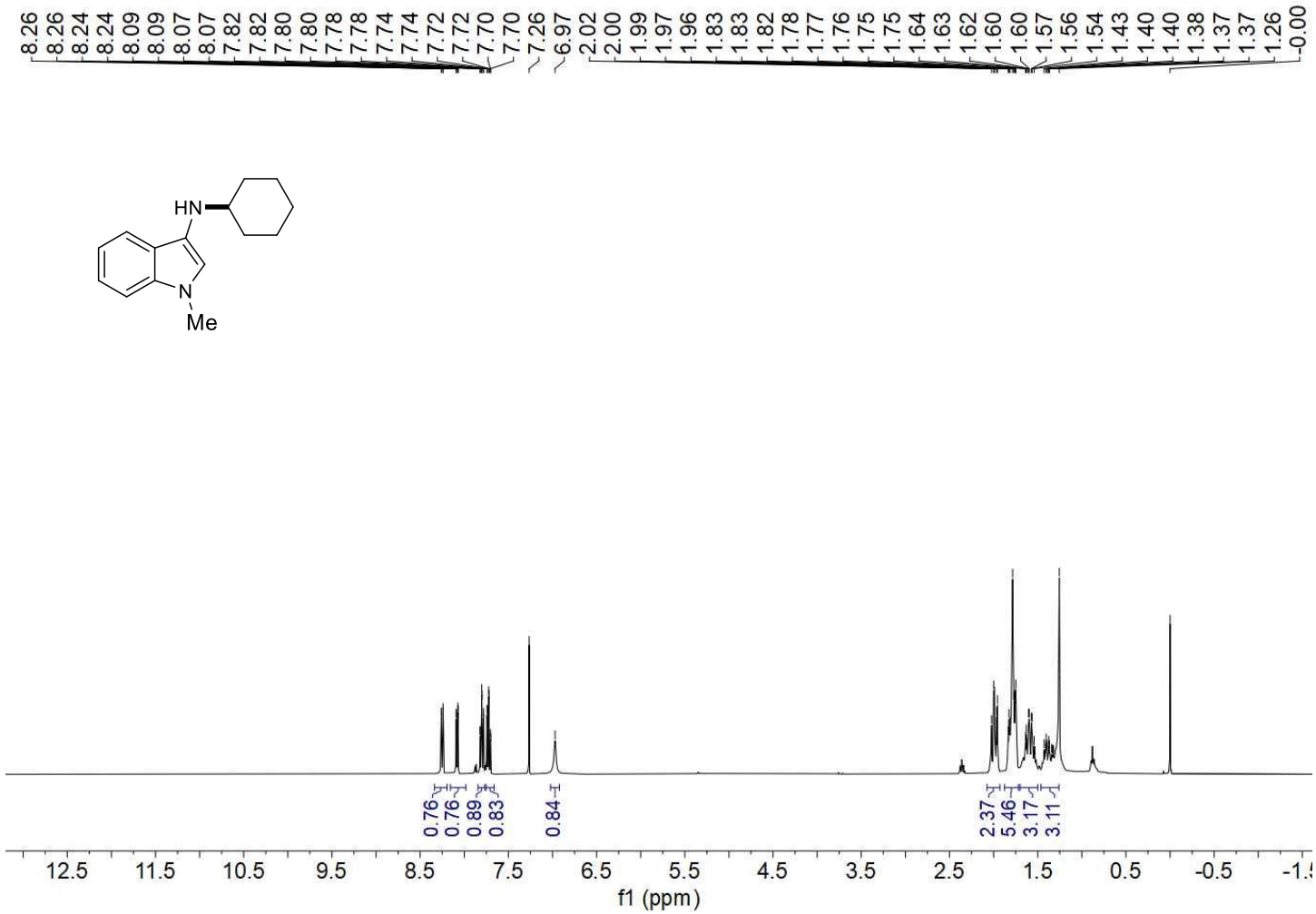
Compound **49** ^{1}H NMR



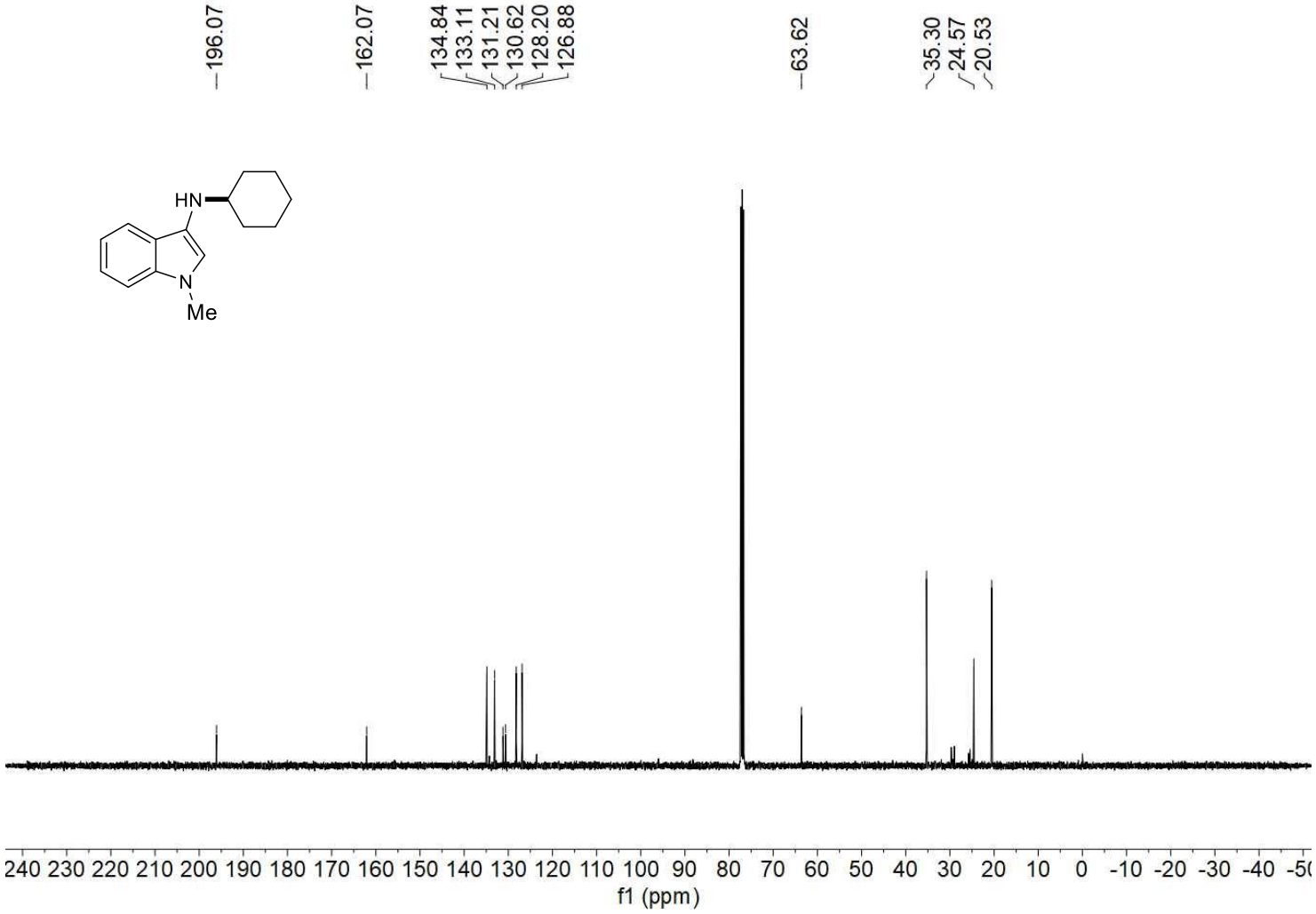
Compound **49** ^{13}C NMR



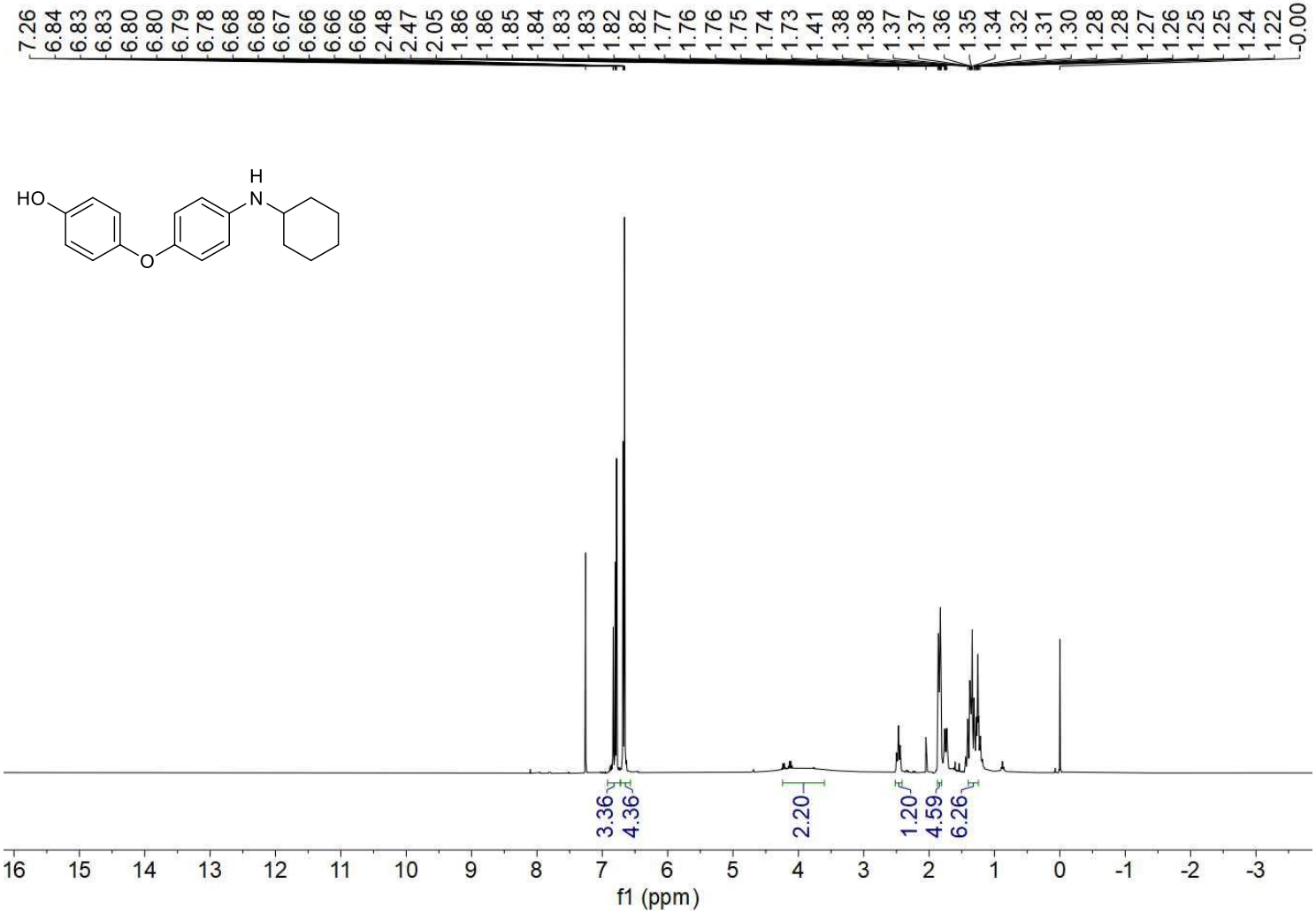
Compound **50** ^{1}H NMR



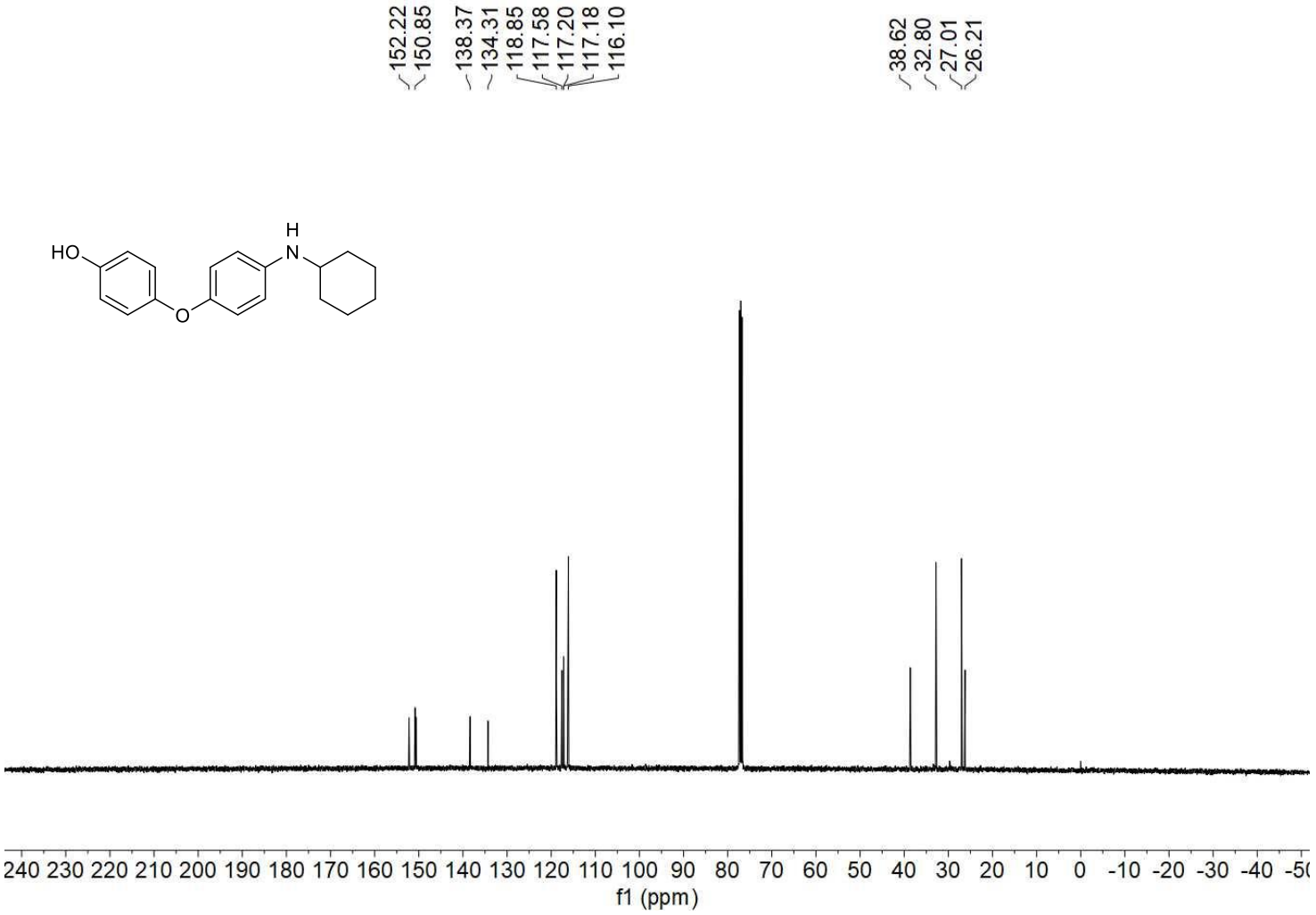
Compound **50** ^{13}C NMR



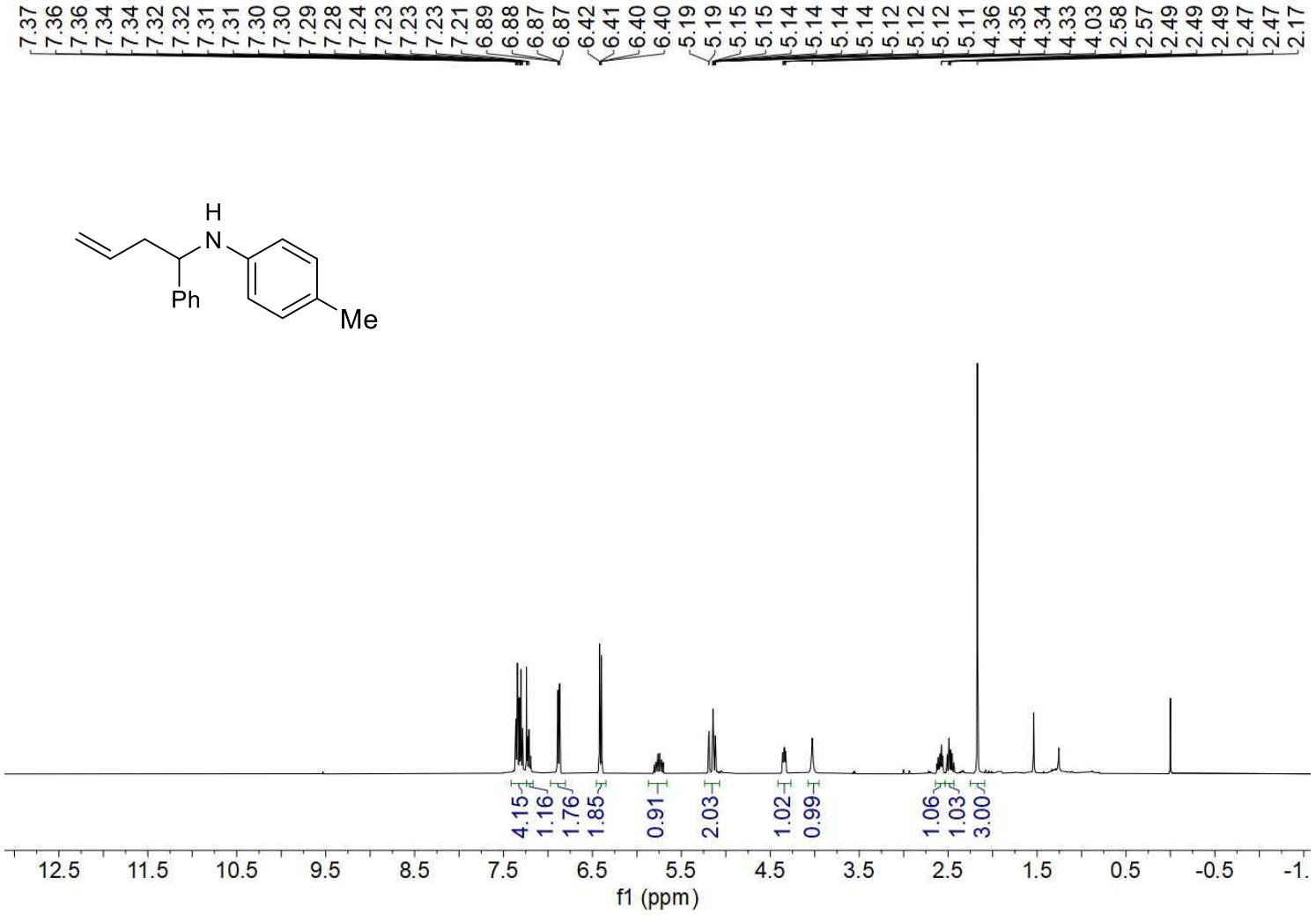
Compound **52** ^{1}H NMR



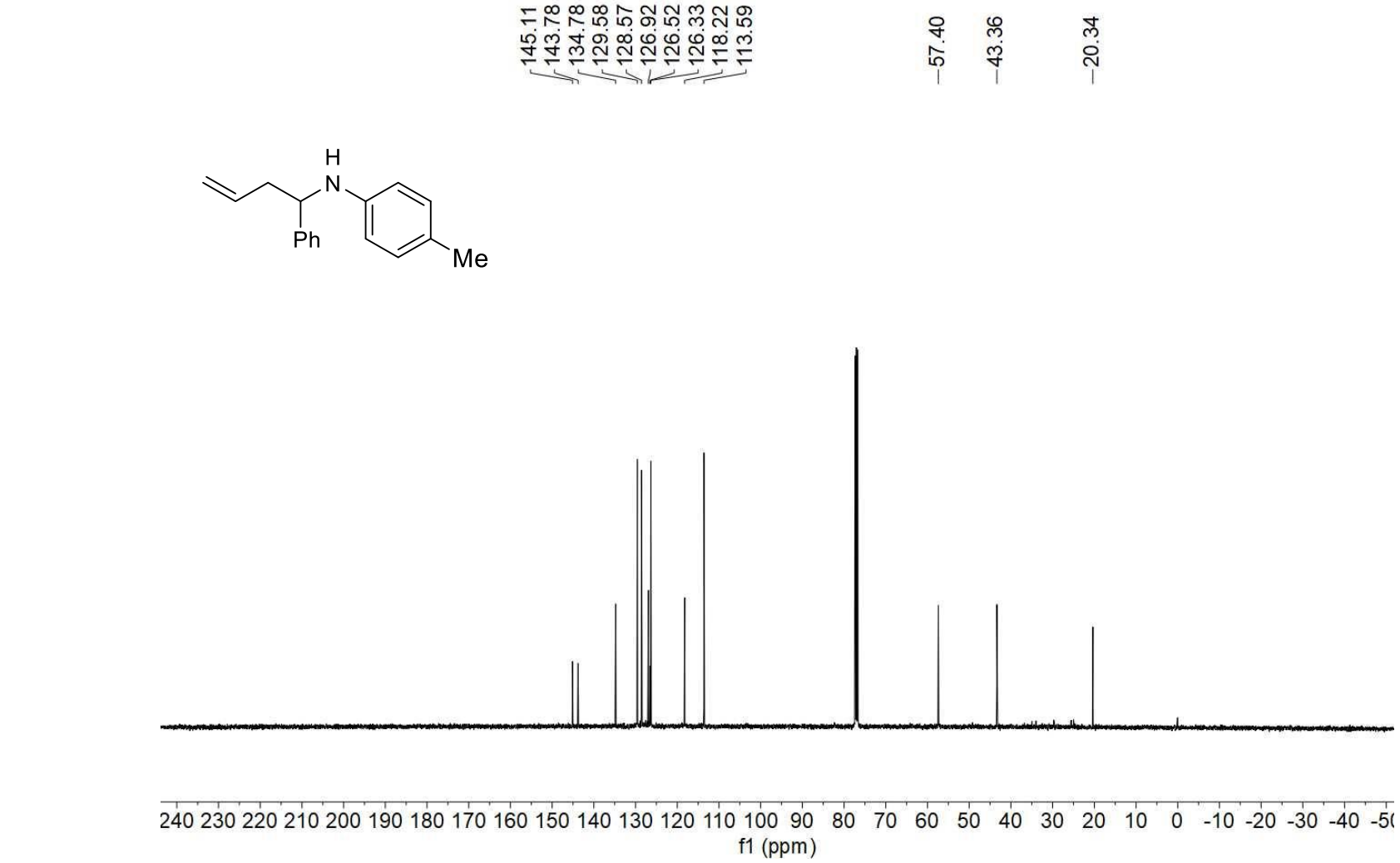
Compound **52** ^{13}C NMR



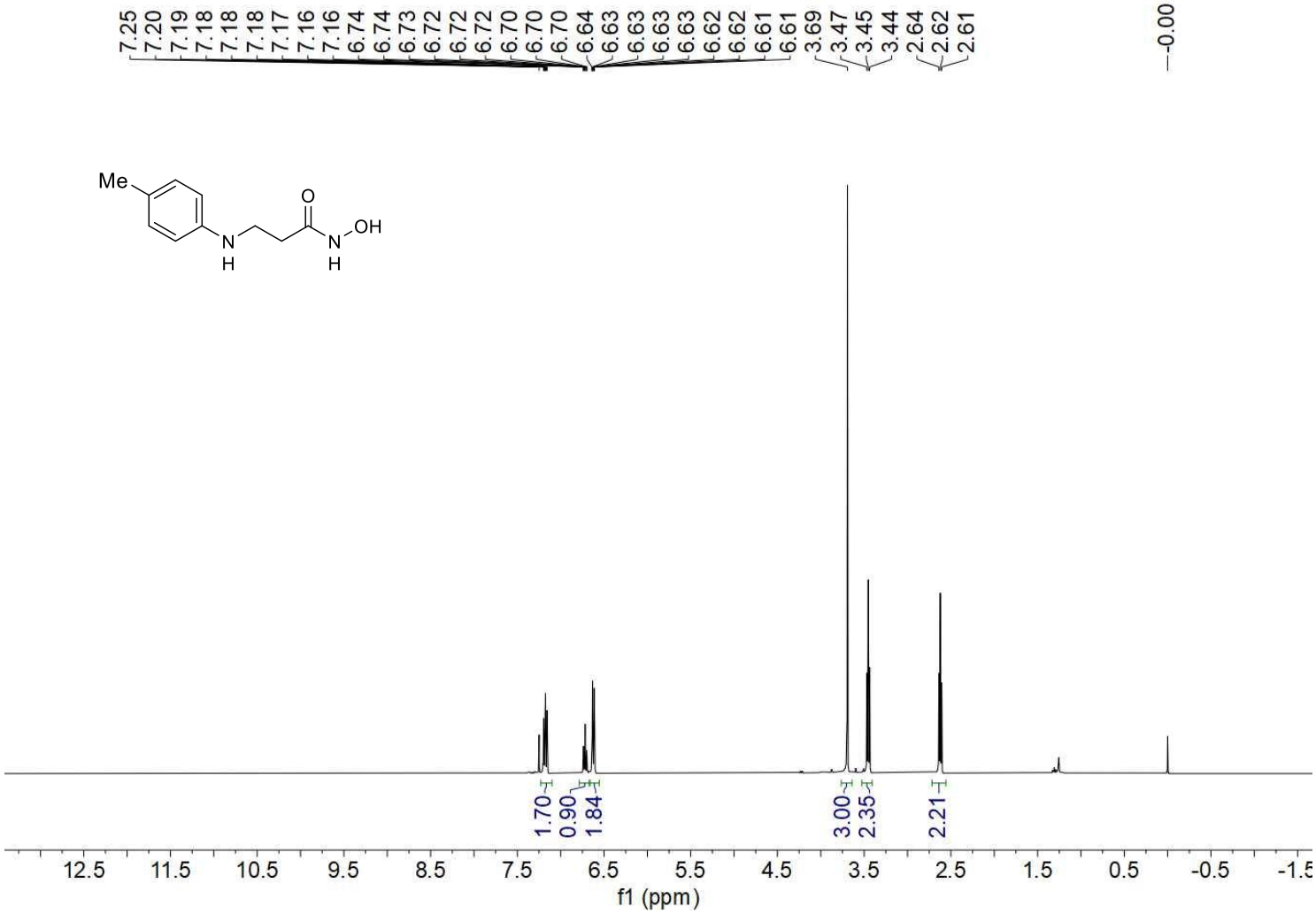
Compound **54** ^{1}H NMR



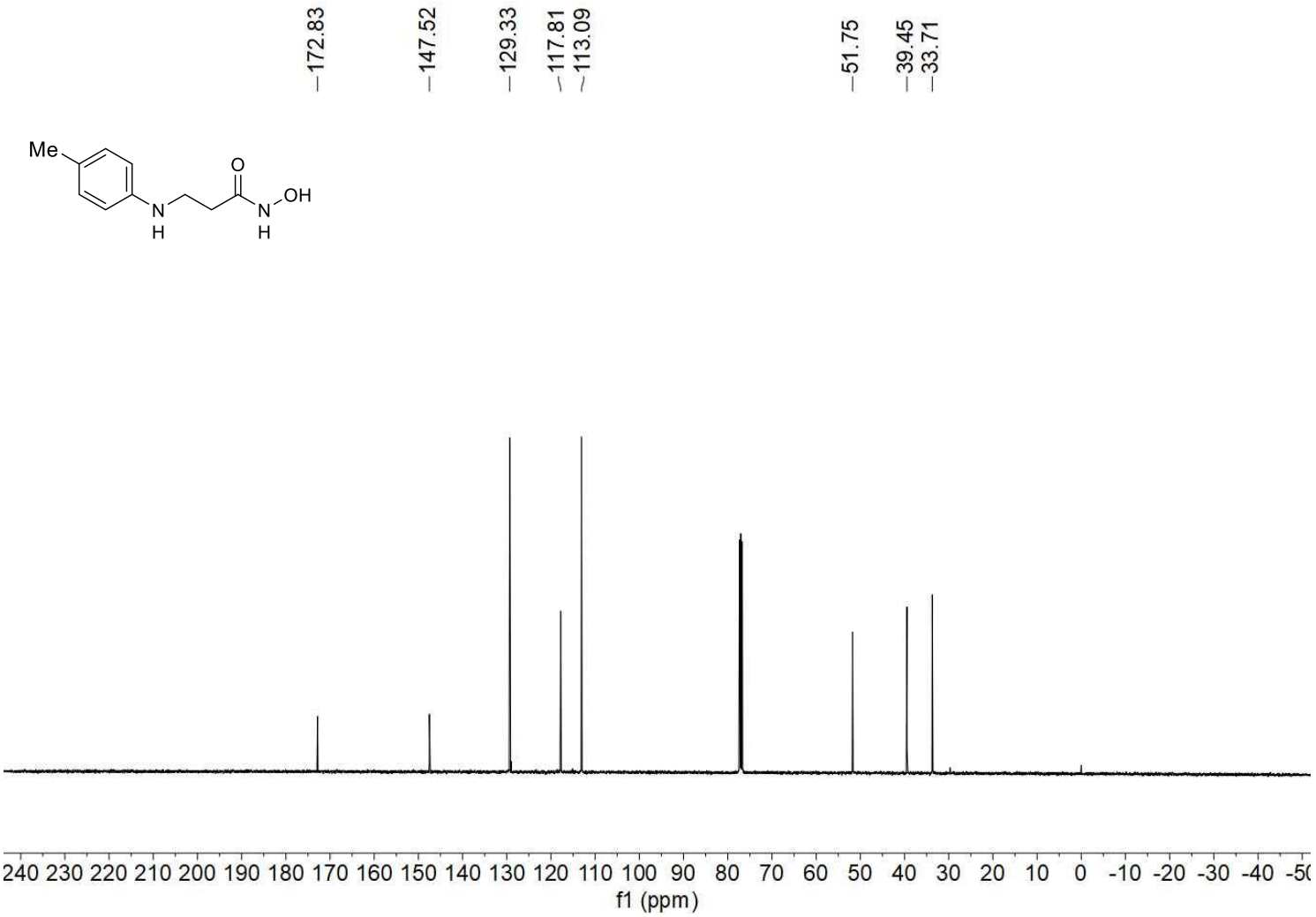
Compound **54** ^{13}C NMR



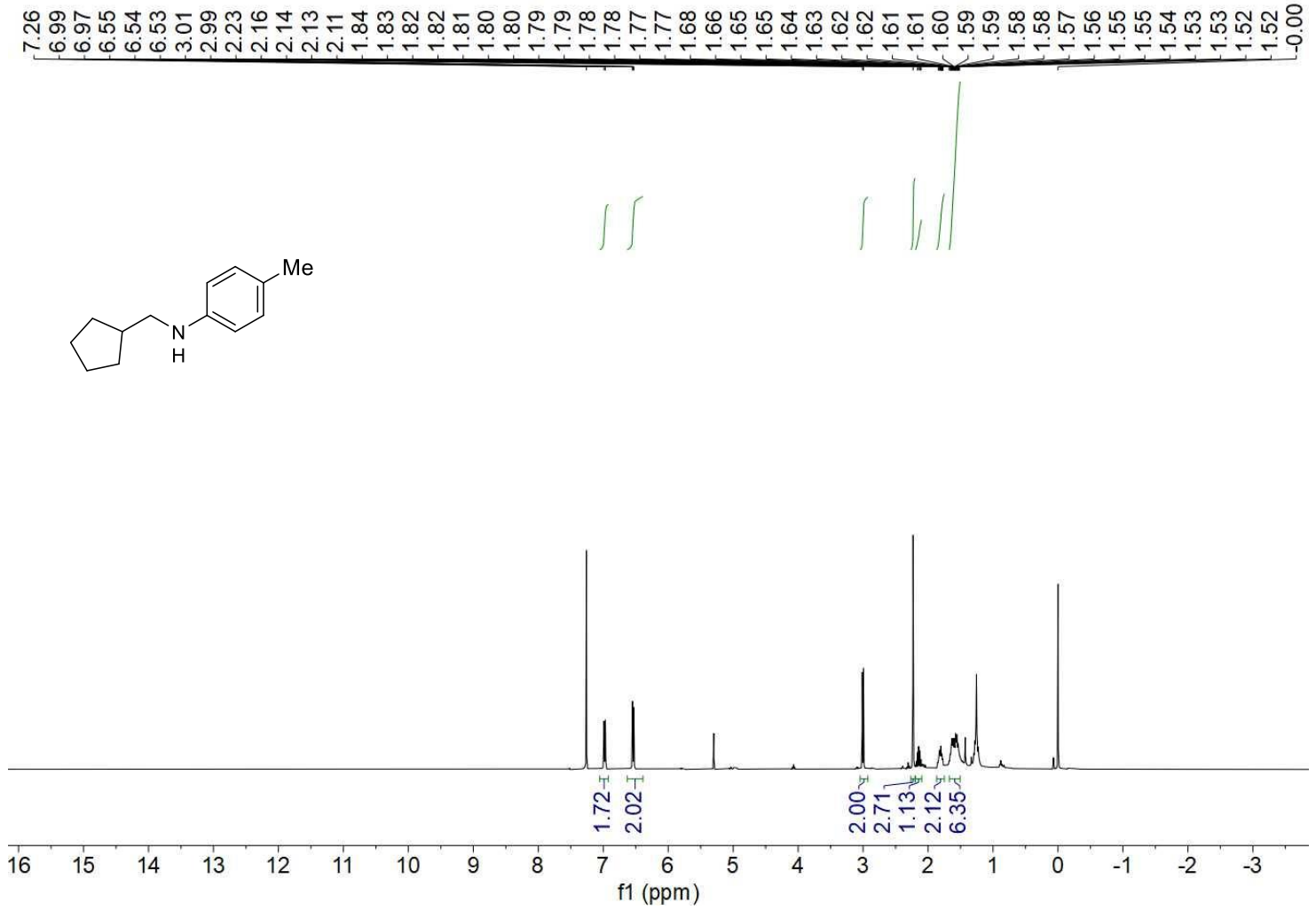
Compound **55** ^{1}H NMR



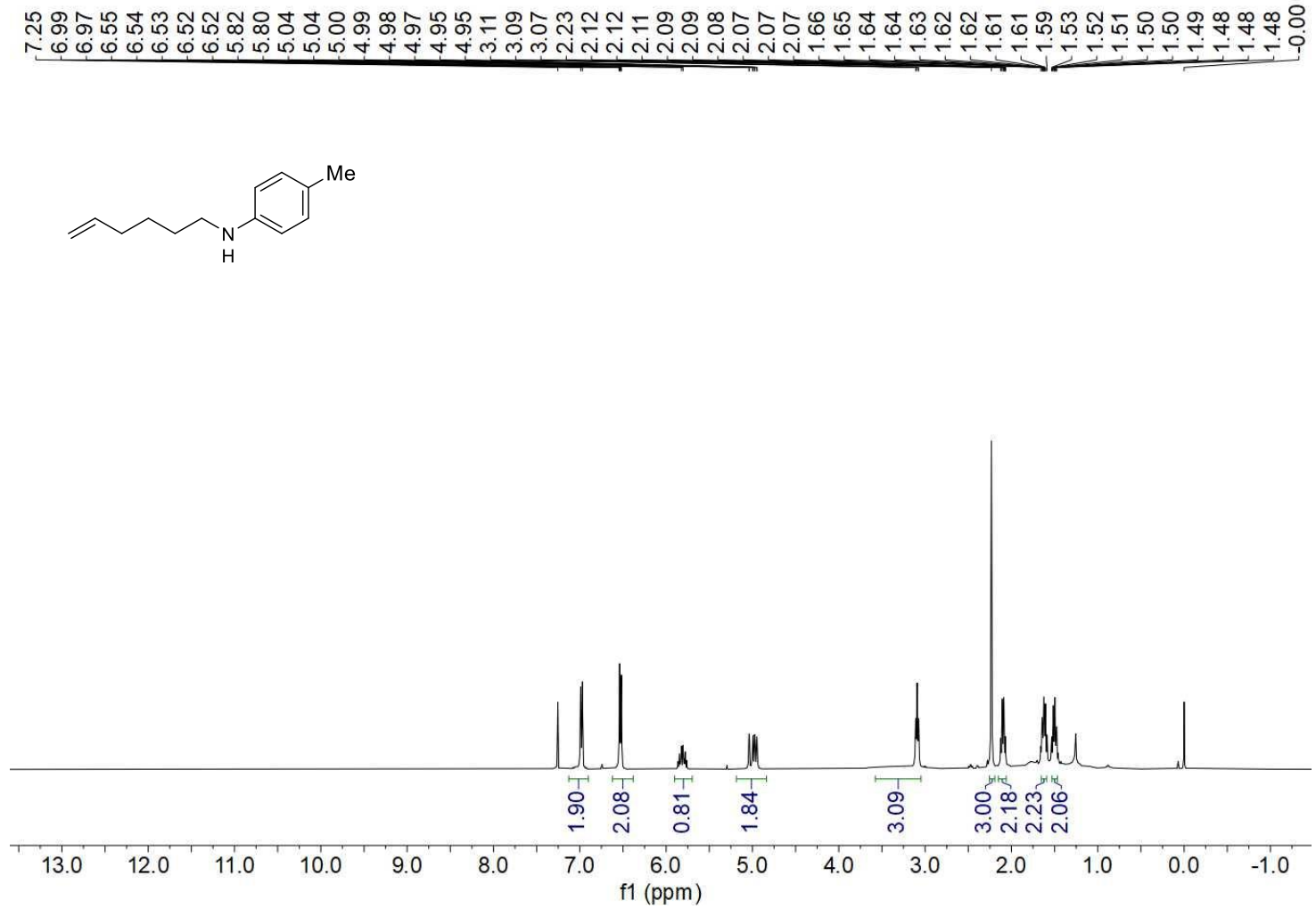
Compound **55** ^{13}C NMR



Compound **58** ^{1}H NMR



Compound **59** ^{1}H NMR



Compound **59** ^{13}C NMR