Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Photo-induced Synthesis of Fluoroalkylated Quinolinone during Iron-Catalyzed LMCT Decarboxylation Process

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Table Content

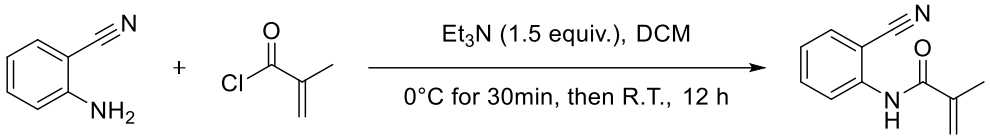
1 General Information

Unless otherwise mentioned, all reagents were purchased from commercial sources and used as received. The visible-light mediated reactions were performed on WPTEC-1020L instruments which are purchased from WATTCAS, China. All yields of products refer to the isolated yields after chromatography. ^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra were recorded on a Bruker AV-400 spectrometer or a Quantum-I Plus 400 in $CDCl_3$. For ^{1}H NMR, $CDCl_3$ (δ = 7.26 ppm) or tetramethylsilane (TMS, δ = 0 ppm) serves as the internal standard; for ^{13}C NMR, $CDCl_3$ (δ = 77.16 ppm) serves as the internal standard. Data are reported as follows: chemical shift (in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, hept = heptet, m = multiplet, br = broad), coupling constant (in Hz), and integration. GC analysis was performed on a 7890B/Agilent, while GC-MS analysis was performed on a 7890A-5975C/Agilent. HRMS spectra were recorded on a Waters Xevo G2QTOF/UPLC mass spectrometer using electrospray ionization. NMR yields of the screening part were calculated using 1,3,5-trimethoxybenzene as the internal standard. All yields of products refer to the isolated yields after chromatography.

2 General Synthetic Procedure

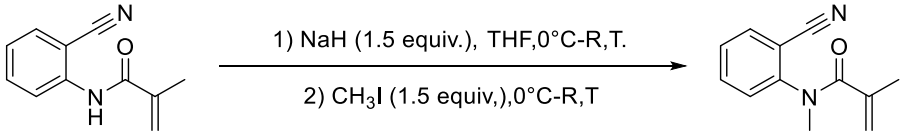
2.1 General procedure for synthesis of N-(2-cyanophenyl)-N-acrylamide

N-(2-cyanophenyl)-N-acrylamides were prepared on gram-scale in 1 or 2 steps according to the procedure disclosed by Feng et al. from inexpensive commercial reagent 2-aminobenzonitriles.[1] We here took synthetic pathway of **1a** for example.



Scheme S1. Synthesis of N-(2-cyanophenyl)methacrylamide

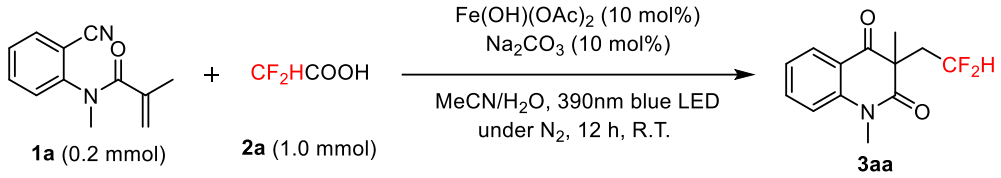
To a 100 mL round bottom flask equipped with a magnetic stirring bar were added with 2-aminobenzonitrile (1.18g, 10 mmol, 1.0 equiv.), dry triethylamine (1,52g, 15 mmol, 1.5 equiv.), DCM (40 mL), then cooled to 0 ℃ in the ice water bath. Methacryloyl chloride (1.14 g, 11 mmol, 1.1 equiv.) was slowly added to the solution at 0 ℃ and then the mixture was stirred at room temperature for 12 h. The solution was concentrated under reduced pressure, and the mixture was purified by flash column chromatography over silica gel (1:20 to 1:5 EtOAc:PE) to afford the N-(2-cyanophenyl)methacrylamide (1.67 g, 9 mmol, 90% yield) as a white solid.



Scheme S2. Synthesis of N-(2-cyanophenyl)-N-methylmethacrylamide

To a solution of N-(2-cyanophenyl)methacrylamide (1.67 g, 9 mmol) in THF (30.0 mL) was added a magnetic stirring bar and 60% NaH (540 mg, 13.5 mmol, 1.5 equiv.) at 0 ℃ and stirred for 30 min. Then methyl iodide (1.92 g, 13.5 mmol, 1.5 equiv.) was added and the reaction was warmed to room temperature. After stirring for 8 h, the reaction was quenched by water and the aqueous layer was extracted with EtOAc (10 mL x 3). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography over silica gel (1:10 to 1:3 EtOAc:PE) to afford **1a** N-(2-cyanophenyl)-N-methylmethacrylamide (1.40 g, 7 mmoL, 78% yield) as a yellow solid. Most substrates followed the reaction pathway of **1a**.

2.2 General procedure for preparation of fluoroalkylated quinoline-2,4-dione



Scheme S3. Procedure for preparation of 3-(2,2-difluoroethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione

To an oven-dried 10 mL quartz reaction tube equipped with a magnetic stir bar were sequentially added the corresponding N-(2-cyanophenyl)-N-acrylamide **1a** (40mg, 0.2 mmol, 1.0 equiv.), $Fe(OH)(OAc)_2$ (3.8 mg, 10 mol%), Na_2CO_3 (2.2 mg, 10 mol%). The tube was degassed three times and was added the solvent $MeCN/H_2O$ (2.0mL), then the reactant difluoroacetic acid **2a** (96mg, 1.0 mmol, 5.0 equiv.). The tube was then put into the reactor and was irradiated under 10 W 390 nm blue LED chip irradiation and stirred for 12 h at room temperature. After the reaction was complete, all reactants were filtered through a short silica gel column, washed with EtOAc, and the crude product was concentrated under reduced pressure, then purified by column chromatography (1:10 to 1:3 EtOAc : petroleum ether). Combined organic layers were washed with brine twice, dried with Na_2SO_4, concentrated and purified by column chromatography.

Figure S1. Photo reactor device and 390nm 10W blue LED chip

2.3 General procedure for gram-scale flow reaction

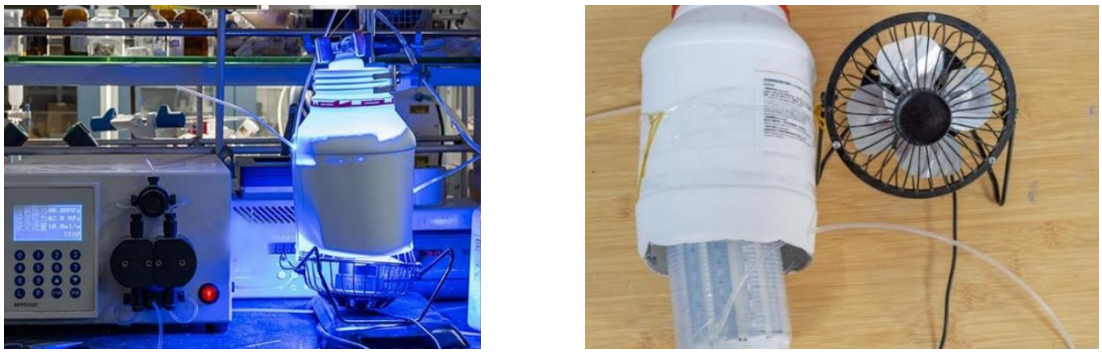
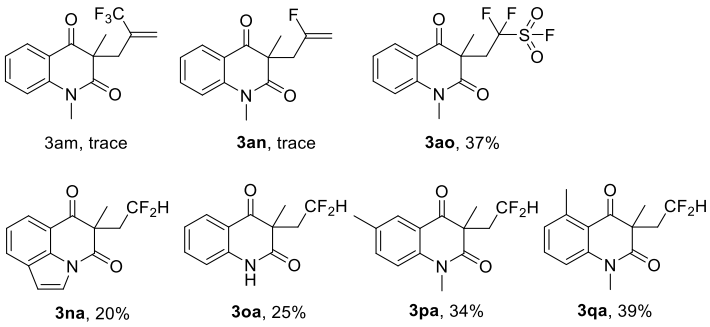


Figure S2. Example figure of gram scale flow reactor of photoreactions

The construction of the photoreaction device followed Qi, et al[2]. An oven dried 200 mL round bottom flask was charged with a stir bar. Substrate **1a** (1.0 g, 5 mmol, 1.0 equiv.), **2a** (2.4 g, 25 mmol, 5.0 equiv.), $Fe(OH)(OAc)_2$ (76mg, 10 mol%) and Na_2CO_3 (55mg, 10 mol%) was added with 40 mL MeCN and 10 mL water. The reaction mixture was pumped into PTFE transparent coil and irradiated with commercially available 390 nm blue light bulbs and flow pump for 12 hours. After the reaction was complete, all reactants were filtered through a short silica gel column, washed with EtOAc, and the crude product was concentrated under reduced pressure, then purified by column chromatography (1:10 to 1:3 EtOAc : petroleum ether). Affording product γ-lactam **3aa** (0.834g, 66% yield) as a yellow oil.

2.4 Typical unsuccessful reaction samples



Scheme S4. Typical unsuccessful reaction samples

3 Optimization of Reaction Conditions

Table 1S. Optimization of solvent.[a]

Entry	Solvent	Yield (%)
1	dry MeCN	N.R.
2	MeCN	28
3	MeCN:Water=2:1	45
4	THF:Water=2:1	trace
5	DMSO:Water=2:1	25
6	MeCN:Water=4:1	50
7	MeCN:Water=9:1	36
8	DMSO	trace
9	DMSO:MeCN=1:1	trace

[a] Reaction conditions: substrate **1a** (0.2mmol), difluoroacetic acid (**2a**) (10 equiv.), $Fe(acac)_3$ (10 mol%), DBU (0.5 equiv.), 10 W 390 nm LEDs at room temperature for 12 hours under N_2 atmosphere.

Table 2S. Optimization of Oxidant.[a]

Entry	Possible Oxidant	Atmosphere	Yield (%)
1	None	N_2	50
2	Open to air	Air	40
3	$Na_2S_2O_8$	N_2	<30
4	$K_2S_2O_8$	N_2	<30
5	$(NH_4)_2S_2O_8$	N_2	<30

[a] Reaction conditions: substrate **1a** (0.2mmol), difluoroacetic acid (**2a**) (10 equiv.), $Fe(acac)_3$ (10 mol%), DBU (0.5 equiv.), MeCN:Water=4:1 (2mL, 0.1M), 10 W 390 nm LEDs at room temperature for 12 hours.

Table 3S. Optimization of photo catalyst.[a]

Entry	Photocatalyst	Yield (%)
1	$Fe(acac)_3$	50
2	$Fe(OH)(OAc)_2$	72
3	$Fe(OH)(OAc)_2$+LiCl	70
4	$FeCl_3$	63
5	$Fe(NO_3)_3$	56
6	$FeCl_2$	41
7	$FeBr_3$	36
8	Mes-$Acr^+ClO_4^-$	n.d.

[a] Reaction conditions: substrate **1a** (0.2mmol), difluoroacetic acid (**2a**) (10 equiv.), DBU (0.5 equiv.), MeCN:Water=4:1 (2mL, 0.1M), 10 W 390 nm LEDs at room temperature for 12 hours under N_2 atmosphere.

Table 4S. Optimization of reactant dosage.[a]

Entry	Acid（equiv.）	Yield (%)
1	3	54
2	5	72
3	10	72

[a] Reaction conditions: substrate **1a** (0.2mmol), difluoroacetic acid (**2a**) (5 equiv.), $Fe(OH)(OAc)_2$ (10 mol%), DBU (0.5 equiv.), MeCN:Water=4:1 (2mL, 0.1M), 10 W 390 nm LEDs at room temperature for 12 hours under N_2 atmosphere.

Table 5S. Optimization of base.[a]

Entry	Base	Yield (%)
1	None	N.R.
2	DBU	72
3	DABCO	48
4	Quinuclidine	34
5	Et_3N	trace
6	LDA	trace
7	Na_2CO_3	87
8	Cs_2CO_3	80
9	K_2HPO_4	45

[a] Reaction conditions: substrate **1a** (0.2mmol), difluoroacetic acid (**2a**) (5 equiv.), $Fe(OH)(OAc)_2$ (10 mol%), MeCN:Water=4:1 (2mL, 0.1M), 10 W 390 nm LEDs at room temperature for 12 hours under N_2 atmosphere.

Table 7S. Optimization of base dosage.[a]

Entry	Na_2CO_3（equiv.）	Yield (%)
1	0.1	87
2	0.2	86
3	0.5	87

[a] Reaction conditions: substrate **1a** (0.2mmol), difluoroacetic acid (**2a**) (5 equiv.), $Fe(OH)(OAc)_2$ (10 mol%), MeCN:Water=4:1 (2mL, 0.1M), 10 W 390 nm LEDs at room temperature for 12 hours under N_2 atmosphere.

Table 6S. Optimization of light resourse.[a]

Entry	Light Source	Yield (%)
1	380nm	71
2	390nm	87
3	400nm	64
4	405nm	56
5	410nm	58
6	460nm	n.d.

[a] Reaction conditions: substrate **1a** (0.2mmol), difluoroacetic acid (**2a**) (5 equiv.), $Fe(OH)(OAc)_2$ (10 mol%), Na_2CO_3 (10 mol%), MeCN:Water=4:1 (2mL, 0.1M), 10 W 390 nm LEDs at room temperature for 12 hours under N_2 atmosphere.

Table 7S. Optimization of react time and additives.[a]

Entry	Other changes	Yield (%)
1	8h react time	66
2	12h react time	87
3	16h react time	80
4	20h react time	59
5	24h react time	33
6	Add 5% HCl	70
7	60°C temp	60
8	5W radiation strength	54

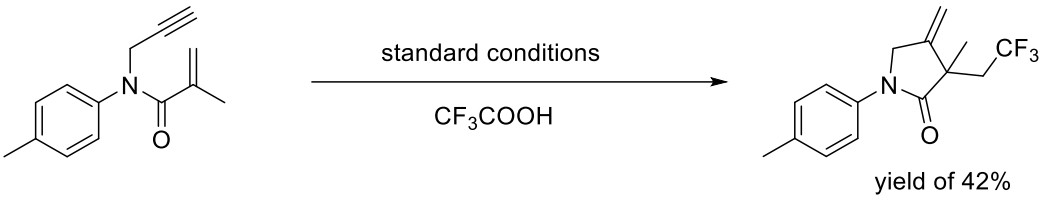
[a)] Standard reaction conditions: substrate **1a** (0.2mmol), difluoroacetic acid (**2a**) (5 equiv.), $Fe(OH)(OAc)_2$ (10 mol%), Na_2CO_3 (10 mol%), MeCN:Water=4:1 (2mL, 0.1M), 10 W 390 nm LEDs at room temperature for 12 hours under N_2 atmosphere. Each entry only changed the conditions represented.

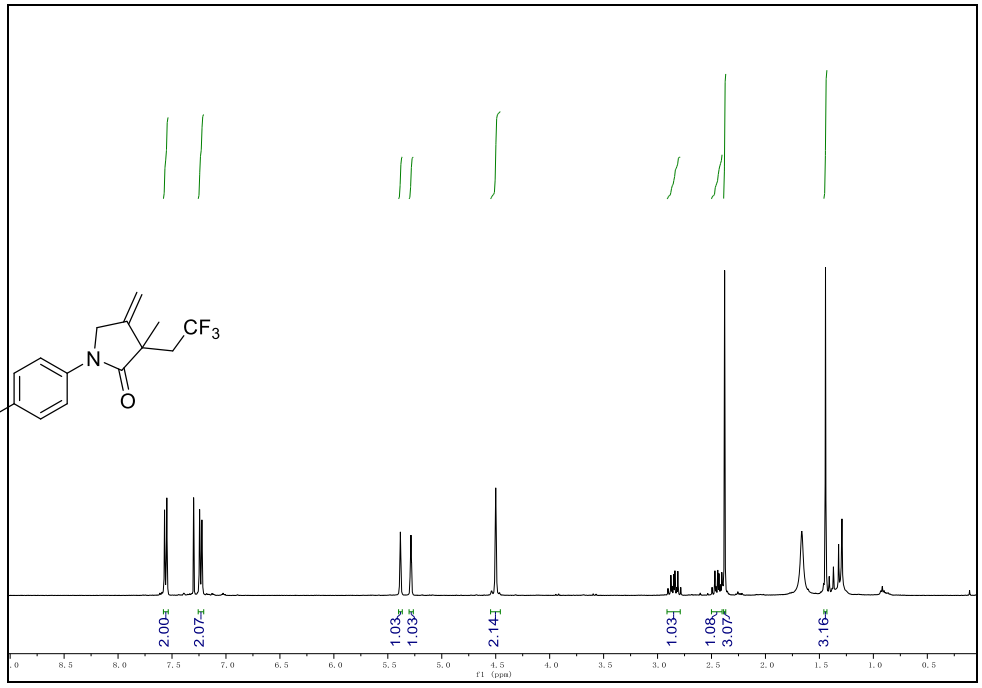
Table 8S. Verifying of optimalized conditions.[a]

Entry	Variation from standard conditions[a]	Yield (%)
1	None	87
2	$FeCl_3$ as photo catalyst	68
3	$FeCl_2$ as photo catalyst	52
4	$Fe(acac)_3$ as photo catalyst	70
5	380 nm LED	71
6	405 nm LED	56
7	$DMSO/H_2O$ as solvent	40
8	Dry MeCN	trace
9	DBU as base	35
10	Cs_2CO_3 as base	80
11	3 equiv. **2a**	54[d]
12	10 equiv. **2a**	86
13	Open to air	63
14	No Photo Catalyst	N.R.
15	React in dark	N.R.

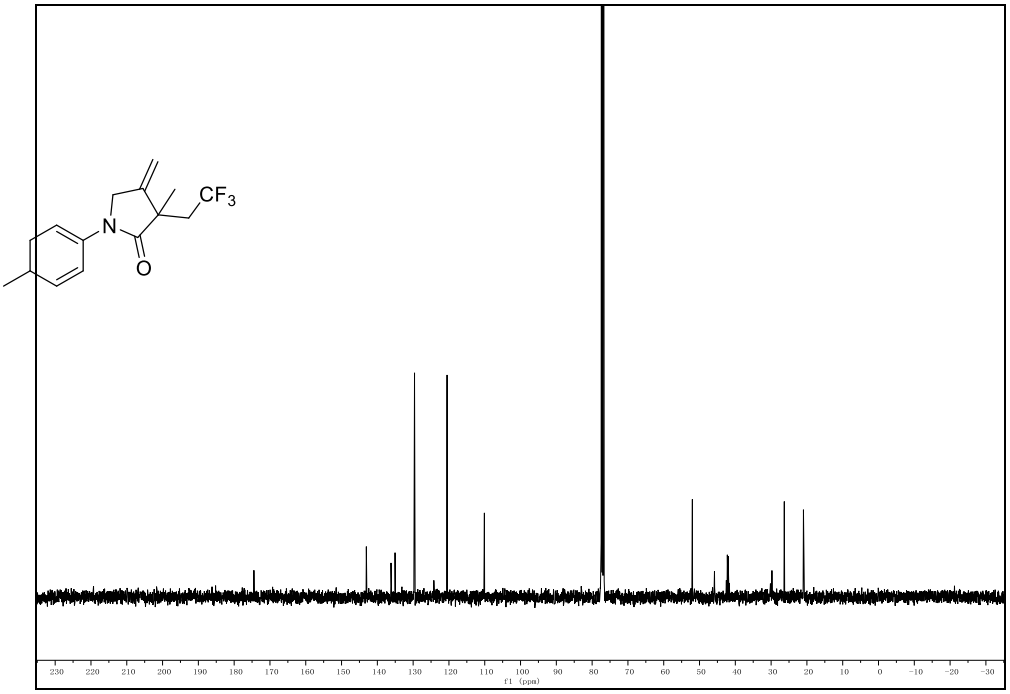
[a)] Standard reaction conditions: substrate **1a** (0.2mmol), difluoroacetic acid (**2a**) (5 equiv.), $Fe(OH)(OAc)_2$ (10 mol%), Na_2CO_3 (10 mol%), MeCN:Water=4:1 (2mL, 0.1M), 10 W 390 nm LEDs at room temperature for 12 hours under N_2 atmosphere. Each entry only changed the conditions represented.

4 Reaction of Other Radical Acceptors

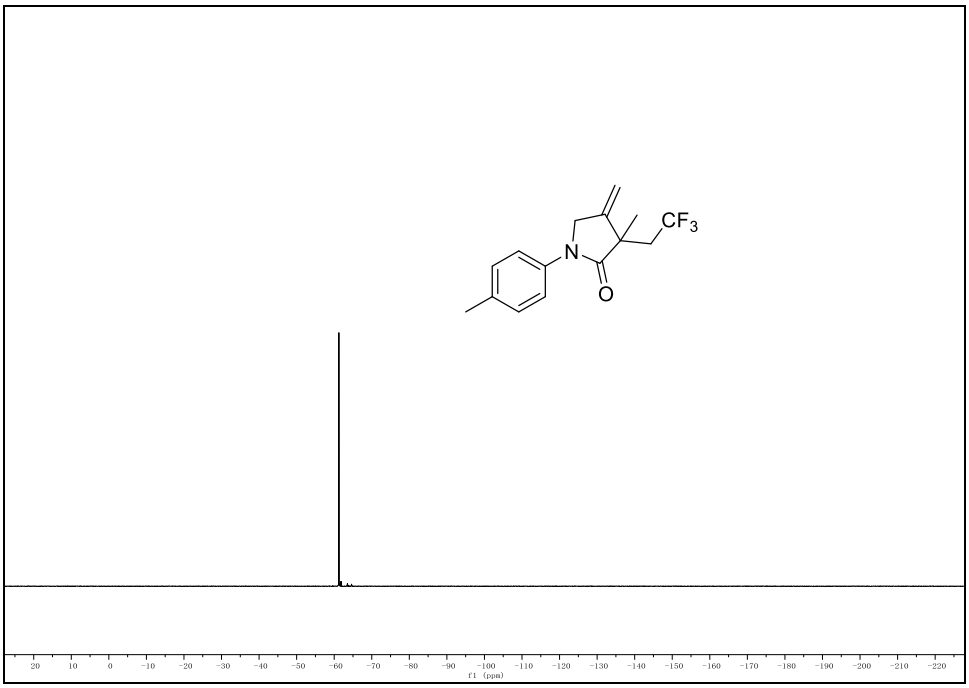




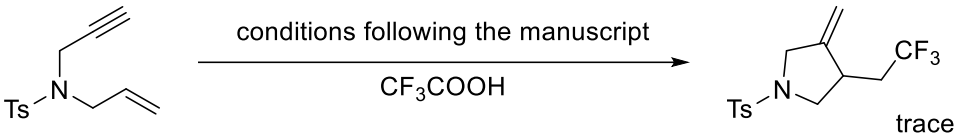
^{1}H NMR Spectrum



^{13}C NMR Spectrum

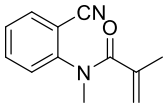


^{19}F NMR Spectrum



5 Substrate Characterization

N-(2-cyanophenyl)-N-methylmethacrylamide (**1a**)

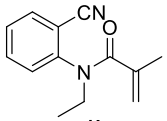


1a

1a was prepared following the above mentioned procedure. The spectroscopic data of **1a** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.35 (m, 2H), 7.21 – 7.08 (m, 2H), 4.74 (d, *J* = 48.5 Hz, 2H), 3.07 (s, 3H), 1.58 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.19, 147.10, 139.78, 134.23, 133.52, 128.65, 128.02, 116.24, 111.54, 19.86. calcd for $[M+H]^+$ 201.1022, found 201.1024.

N-(2-cyanophenyl)-N-ethylmethacrylamide (**1b**)

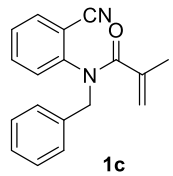


1b

1b was prepared following the above mentioned procedure. The spectroscopic data of **1b** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.65 (dd, *J* = 8.8, 6.7 Hz, 1H), 7.44 (td, *J* = 7.7, 2.1 Hz, 1H), 7.29 (dd, *J* = 5.7, 3.7 Hz, 1H), 5.06 (d, *J* = 40.2 Hz, 2H), 3.91 (s, 2H), 1.90 (s, 3H), 1.19 (td, *J* = 7.1, 2.8 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.25, 145.73, 140.30, 133.84, 132.21, 129.71, 128.01, 116.55, 113.07, 45.20, 20.20, 12.96. calcd for $[M+H]^+$ 215.1179, found 215.1180.

N-benzyl-N-(2-cyanophenyl)methacrylamide (**1c**)

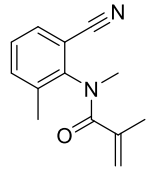


1c

1c was prepared following the above mentioned procedure. The spectroscopic data of **1c** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 7.7 Hz, 1H), 7.46 (td, *J* = 7.8, 1.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.26 (d, *J* = 3.9 Hz, 3H), 7.20 (dd, *J* = 6.9, 2.9 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 1H), 5.06 (d, *J* = 40.5 Hz, 2H), 1.91 (s, 3H).^{13}C NMR (101 MHz, Chloroform-*d*) δ 145.40, 140.09, 136.19, 133.79, 133.51, 129.91, 129.09, 128.62, 127.97, 127.91, 116.43, 112.83, 53.07, 20.30. HRMS (ESI, m/z): calcd for $[M+H]^+$ 277.1335, found 277.1335.

N-(2-cyano-6-methylphenyl)-N-methylmethacrylamide (**1d**)

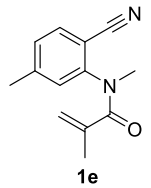


1d

1d was prepared following the above mentioned procedure. The spectroscopic data of **1d** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.16 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 5.00 (dd, *J* = 3.5, 1.8 Hz, 2H), 4.45 (d, *J* = 2.5 Hz, 2H), 2.86 (p, *J* = 6.9 Hz, 1H), 2.16 (t, *J* = 2.5 Hz, 1H), 1.70 (s, 3H), 1.20 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.37, 148.25, 140.05, 139.97, 127.13, 127.10, 119.82, 79.12, 72.00, 39.10, 33.58, 23.82, 20.12. HRMS (ESI, m/z): calcd for $[M+H]^+$ 242.1539, found 242.1542.

N-(2-cyano-5-methylphenyl)-N-methylmethacrylamide (**1e**)

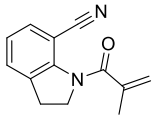


1e

1e was prepared following the above mentioned procedure. The spectroscopic data of **1e** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.16 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 5.00 (dd, *J* = 3.5, 1.8 Hz, 2H), 4.45 (d, *J* = 2.5 Hz, 2H), 2.86 (p, *J* = 6.9 Hz, 1H), 2.16 (t, *J* = 2.5 Hz, 1H), 1.70 (s, 3H), 1.20 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.37, 148.25, 140.05, 139.97, 127.13, 127.10, 119.82, 79.12, 72.00, 39.10, 33.58, 23.82, 20.12. HRMS (ESI, m/z): calcd for $[M+H]^+$ 242.1539, found 242.1540.

1-methacryloylindoline-7-carbonitrile (**1f**)

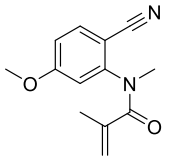


1f

1f was prepared following the above mentioned procedure. The spectroscopic data of **1f** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.17 – 7.08 (m, 1H), 6.75 – 6.63 (m, 3H), 4.93 (td, *J* = 3.6, 1.8 Hz, 2H), 4.37 (d, *J* = 2.6 Hz, 2H), 3.64 (d, *J* = 2.8 Hz, 3H), 2.15 (t, *J* = 2.4 Hz, 1H), 1.65 (q, *J* = 1.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.69, 139.94, 139.87, 130.68, 129.90, 129.77, 129.36, 129.31, 120.61, 120.55, 118.17, 111.67, 79.23, 71.96, 55.42, 55.37, 37.25, 19.80, 19.72. HRMS (ESI, m/z): calcd for $[M+H]^+$ 230.1176, found 230.1173.

N-(2-cyano-5-methoxyphenyl)-N-methylmethacrylamide (**1g**)

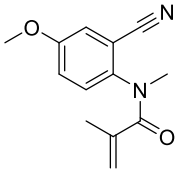


1g

1g was prepared following the above mentioned procedure. The spectroscopic data of **1g** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (dd, *J* = 8.7, 2.2 Hz, 1H), 6.88 (dt, *J* = 8.7, 2.4 Hz, 1H), 6.72 (d, *J* = 2.5 Hz, 1H), 5.08 (d, *J* = 24.6 Hz, 2H), 3.85 (d, *J* = 2.2 Hz, 3H), 3.36 (d, *J* = 2.2 Hz, 3H), 1.89 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.73, 163.69, 149.29, 140.02, 135.11, 116.65, 114.76, 113.50, 103.49, 55.95, 20.18. HRMS (ESI, m/z): calcd for $[M+H]^+$ 231.1128, found 231.1132.

N-(2-cyano-4-methoxyphenyl)-N-methylmethacrylamide (**1h**)

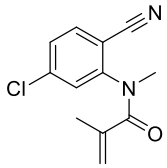


1h

1h was prepared following the above mentioned procedure. The spectroscopic data of **1h** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.18 – 7.09 (m, 3H), 5.04 (d, *J* = 34.4 Hz, 2H), 3.85 (d, *J* = 1.0 Hz, 3H), 3.35 (s, 3H), 1.97 – 1.76 (m, 3H). HRMS (ESI, m/z): calcd for $[M+H]^+$ 231.1128, found 231.1126.

N-(5-chloro-2-cyanophenyl)-N-methylmethacrylamide (**1i**)

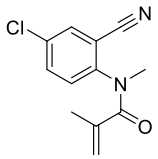


1i

1i was prepared following the above mentioned procedure. The spectroscopic data of **1i** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.43 (dt, *J* = 8.3, 2.0 Hz, 1H), 7.32 (t, *J* = 1.9 Hz, 1H), 5.16 (d, *J* = 62.7 Hz, 2H), 3.45 – 3.40 (m, 3H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.55, 148.63, 140.18, 139.71, 134.53, 129.15, 128.40, 115.59, 110.45, 37.90, 20.08. HRMS (ESI, m/z): calcd for $[M+H]^+$ 235.0633, found 235.0633.

N-(4-chloro-2-cyanophenyl)-N-methylmethacrylamide (**1j**)

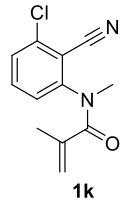


1j

1j was prepared following the above mentioned procedure. The spectroscopic data of **1j** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.69 (t, *J* = 2.4 Hz, 1H), 7.61 (dt, *J* = 8.6, 2.4 Hz, 1H), 7.24 (dd, *J* = 8.6, 2.3 Hz, 1H), 5.13 (d, *J* = 61.3 Hz, 2H), 3.40 (d, *J* = 2.3 Hz, 3H), 1.94 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.58, 146.59, 139.75, 137.26, 136.27, 130.11, 121.13, 114.92, 113.70, 37.83, 20.10. HRMS (ESI, m/z): calcd for $[M+H]^+$ 235.0633, found 235.0630.

N-(3-chloro-2-cyanophenyl)-N-methylmethacrylamide (**1k**)

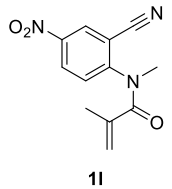


1k

1k was prepared following the above mentioned procedure. The spectroscopic data of **1k** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (td, *J* = 8.1, 1.3 Hz, 1H), 7.46 (dt, *J* = 8.2, 1.2 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 1H), 5.11 (d, *J* = 52.8 Hz, 2H), 3.39 (d, *J* = 1.3 Hz, 3H), 1.92 (s, 3H). HRMS (ESI, m/z): calcd for $[M+H]^+$ 235.0633, found 235.0635.

N-(2-cyano-4-nitrophenyl)-N-methylmethacrylamide (**1l**)

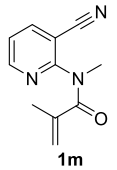


1l

1l was prepared following the above mentioned procedure. The spectroscopic data of **1l** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.55 (d, *J* = 2.6 Hz, 1H), 8.45 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.47 (d, *J* = 8.8 Hz, 1H), 5.27 (d, *J* = 2.1 Hz, 1H), 5.03 (s, 1H), 3.46 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.37, 152.97, 145.87, 139.50, 129.27, 129.17, 128.72, 121.44, 114.48, 112.91, 38.13, 19.88. HRMS (ESI, m/z): calcd for $[M+H]^+$ 246.0873, found 246.0871.

N-(3-cyanopyridin-2-yl)-N-methylmethacrylamide (**1m**)



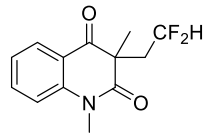
1m

1m was prepared following the above mentioned procedure. The spectroscopic data of **1m** matched well those reported in literature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 (d, *J* = 2.6 Hz, 1H), δ 8.43 (d, *J* = 2.6 Hz, 1H), 7.58 – 7.38 (m, 1H), 5.27 (d, *J* = 2.1 Hz, 1H), 5.03 (s, 1H), 3.46 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.21, 143.81, 139.69, 130.79, 130.56, 130.41, 126.21, 122.53, 120.64, 78.66, 72.76, 39.15, 20.23. HRMS (ESI, m/z): calcd for $[M+H]^+$ 202.0275, found 202.0271.

6 Substrate Characterization

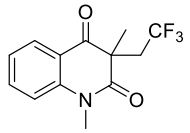
3-(2,2-difluoroethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3aa**)



3aa

Colorless solid, 44.0mg (87% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (dt, *J* = 7.7, 1.6 Hz, 1H), 7.66 (ddt, *J* = 8.6, 7.4, 1.5 Hz, 1H), 7.24 – 7.16 (m, 2H), 5.91 (ttd, *J* = 57.0, 5.1, 1.2 Hz, 1H), 3.49 (s, 3H), 2.78 – 2.67 (m, 2H), 1.49 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.60, 172.53, 143.11, 136.53, 128.61, 123.44, 119.40, 117.77, 115.39, 115.02, 113.00, 53.20, 39.79, 39.57, 39.34, 29.99, 26.90. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.15 (dq, *J* = 57.0, 14.8 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 254.0987, found 254.0986.

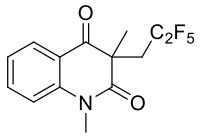
1,3-dimethyl-3-(2,2,2-trifluoroethyl)quinoline-2,4(1H,3H)-dione (**3ab**)



3ab

Colorless solid, 29.8mg (55% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 2H), 3.51 (s, 3H), 3.07 (q, *J* = 10.2 Hz, 2H), 1.50 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.49, 171.70, 143.18, 136.78, 128.73, 126.75, 123.51, 119.15, 115.11, 52.41, 41.07, 40.78, 40.50, 30.00, 29.77, 27.06. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -60.64 (t, *J* = 10.3 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 271.0785, found 271.0785.

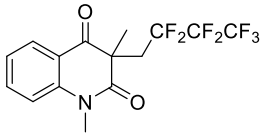
1,3-dimethyl-3-(2,2,3,3,3-pentafluoropropyl)quinoline-2,4(1H,3H)-dione (**3ac**)



3ac

Colorless solid, 45.2mg (71% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 9.5 Hz, 1H), 7.68 (ddd, *J* = 8.6, 7.3, 1.7 Hz, 1H), 7.25 – 7.19 (m, 2H), 3.51 (s, 3H), 3.09 – 2.97 (m, 2H), 1.53 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.42, 171.74, 143.18, 136.80, 128.77, 123.50, 118.98, 115.13, 51.78, 37.53, 37.32, 37.12, 30.01, 27.51. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -86.27, -110.23 – -113.93 (m). HRMS (ESI, m/z): calcd for $[M+H]^+$ 322.0861, found 322.0864.

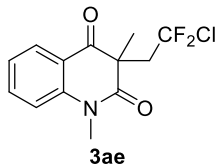
3-(2,2,3,3,4,4,4-heptafluorobutyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ad**)



3ad

Colorless solid, 43.9mg (59% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.70 – 7.65 (m, 1H), 7.21 (dt, *J* = 7.5, 3.2 Hz, 2H), 3.50 (s, 3H), 3.13 – 3.00 (m, 2H), 1.53 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.37, 171.73, 143.19, 136.78, 128.77, 123.48, 118.95, 115.12, 51.64, 37.62, 37.42, 37.22, 29.97, 27.54. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.33 (t, *J* = 9.8 Hz), -107.21 – -110.63 (m), -128.05. HRMS (ESI, m/z): calcd for $[M+H]^+$ 372.0829, found 372.0830.

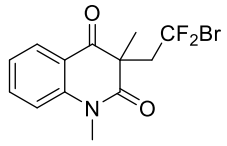
3-(2-chloro-2,2-difluoroethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ae**)



3ae

Colorless solid, 42.9mg (75% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (dt, *J* = 8.0, 1.3 Hz, 1H), 7.67 (ddt, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.24 – 7.18 (m, 2H), 3.50 (s, 3H), 3.38 – 3.27 (m, 2H), 1.50 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.50, 171.71, 143.19, 136.76, 128.70, 127.59, 123.47, 119.28, 115.11, 53.00, 49.21, 48.98, 48.74, 29.98, 27.14. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -45.19 – -45.34 (m), -45.69 (dd, *J* = 16.6, 11.1 Hz), -46.61 (dd, *J* = 16.4, 11.2 Hz), -47.04 (t, *J* = 13.9 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 288.0597, found 288.0593.

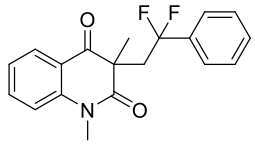
3-(2-bromo-2,2-difluoroethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3af**)



3af

Colorless solid, 57.2mg (82% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.70 – 7.64 (m, 1H), 7.24 – 7.18 (m, 2H), 3.50 (s, 3H), 3.49 – 3.39 (m, 2H), 1.49 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.41, 171.65, 143.18, 136.76, 128.72, 123.47, 122.61, 119.55, 119.28, 116.50, 115.11, 53.38, 51.79, 51.58, 51.37, 29.99, 27.06. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -39.08 – -39.24 (m), -39.58 (dd, *J* = 20.3, 9.7 Hz), -40.93 (dd, *J* = 20.4, 10.1 Hz), -41.26 – -41.42 (m). HRMS (ESI, m/z): calcd for $[M+H]^+$ 332.0092, found 332.0092.

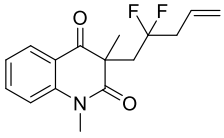
3-(2,2-difluoro-2-phenylethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ag**)



3ag

Colorless solid, 44.1mg (67% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (ddd, *J* = 7.8, 6.2, 1.7 Hz, 1H), 7.64 (ddt, *J* = 9.5, 7.6, 3.8 Hz, 1H), 7.39 – 7.28 (m, 5H), 7.18 (ddd, *J* = 13.0, 7.7, 1.9 Hz, 2H), 3.44 (s, 3H), 3.14 – 3.00 (m, 2H), 1.50 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.72, 172.75, 143.37, 136.45, 133.74, 130.23, 129.96, 128.55, 128.35, 124.99, 124.93, 124.87, 123.20, 119.55, 114.99, 52.21, 48.09, 47.83, 47.57, 29.86, 27.19. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -88.56 – -88.73 (m), -89.29 (dd, *J* = 24.1, 9.4 Hz), -92.64 (dd, *J* = 24.2, 10.8 Hz), -93.21 – -93.38 (m). HRMS (ESI, m/z): calcd for $[M+H]^+$ 330.1300, found 330.1301.

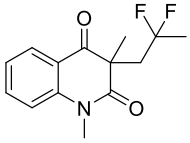
3-(2,2-difluoropent-4-en-1-yl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ah**)



3ah

Colorless solid, 38.1mg (65% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.64 (ddd, *J* = 8.7, 7.3, 1.7 Hz, 1H), 7.19 (dt, *J* = 7.5, 3.2 Hz, 2H), 5.73 (ddt, *J* = 16.0, 10.9, 7.2 Hz, 1H), 5.25 – 5.15 (m, 2H), 3.49 (s, 3H), 2.92 – 2.72 (m, 2H), 2.55 (ddd, *J* = 17.7, 15.6, 7.1 Hz, 2H), 1.47 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.87, 172.98, 143.36, 136.38, 129.06, 129.01, 128.55, 123.16, 122.91, 120.86, 119.41, 114.98, 52.13, 44.46, 44.23, 44.00, 42.92, 42.67, 42.41, 29.88, 26.95. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -90.29 (dt, *J* = 33.7, 16.5 Hz), -90.80 – -91.07 (m), -93.01 (ddd, *J* = 27.2, 22.0, 14.0 Hz), -93.65 (dt, *J* = 32.7, 16.2 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 294.1300, found 294.1296.

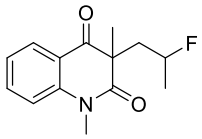
3-(2,2-difluoropropyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ai**)



3ai

Colorless solid, 29.9mg (56% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.64 (ddd, *J* = 8.6, 7.3, 1.7 Hz, 1H), 7.22 – 7.15 (m, 2H), 3.49 (s, 3H), 2.89 – 2.77 (m, 2H), 1.55 (t, *J* = 18.7 Hz, 3H), 1.46 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.86, 172.97, 143.33, 136.39, 128.53, 123.18, 122.98, 119.45, 114.98, 52.34, 46.13, 45.89, 45.65, 29.87, 26.95, 25.40, 25.13, 24.86. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -83.66 – -83.87 (m), -84.41 (td, *J* = 19.2, 12.3 Hz), -86.32 (td, *J* = 19.1, 12.0 Hz), -86.96 (dd, *J* = 34.2, 17.4 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 268.1144, found 268.1144.

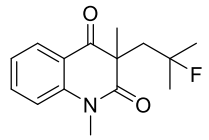
3-(2-fluoropropyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3aj**)



3aj

Colorless oil, 28.4mg (57% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.64 (ddd, *J* = 8.8, 7.3, 1.7 Hz, 1H), 7.21 – 7.15 (m, 2H), 4.74 – 4.52 (m, 1H), 3.47 (s, 3H), 2.64 (ddd, *J* = 14.1, 10.6, 7.9 Hz, 1H), 2.22 (ddd, *J* = 38.3, 14.1, 2.9 Hz, 1H), 1.48 (s, 3H), 1.27 (dd, *J* = 24.3, 6.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.37, 173.76, 143.76, 136.46, 128.23, 122.97, 119.80, 114.94, 89.18, 87.54, 54.17, 45.27, 45.08, 29.88, 26.21, 21.55, 21.33. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -175.33 (ddtd, *J* = 62.7, 48.2, 23.9, 7.7 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 250.1238, found 250.1242.

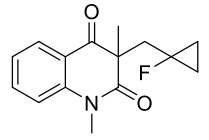
3-(2-fluoro-2-methylpropyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ak**)



3ak

Colorless oil, 42.6mg (81% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.62 (ddd, *J* = 8.6, 7.4, 1.7 Hz, 1H), 7.17 (dt, *J* = 7.4, 3.1 Hz, 2H), 3.48 (s, 3H), 2.64 (dd, *J* = 15.4, 2.1 Hz, 2H), 1.43 (s, 3H), 1.28 (dd, *J* = 22.0, 14.0 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 196.82, 173.85, 143.29, 136.15, 128.47, 123.04, 119.65, 114.87, 95.89, 94.22, 53.82, 53.76, 48.71, 48.51, 29.79, 29.66, 29.41, 29.09, 28.84, 27.61. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -134.85 (ddd, *J* = 22.0, 15.6, 6.9 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 264.1394, found 264.1391.

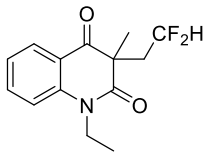
3-((1-fluorocyclopropyl)methyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3al**)



3al

Colorless oil, 43.8mg (84% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.63 (ddd, *J* = 8.7, 7.4, 1.7 Hz, 1H), 7.20 – 7.14 (m, 2H), 3.48 (s, 3H), 2.56 (d, *J* = 21.2 Hz, 2H), 1.53 (s, 3H), 0.87 – 0.67 (m, 2H), 0.58 – 0.41 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.19, 173.59, 143.48, 136.19, 128.21, 123.02, 120.06, 114.82, 76.20, 54.17, 45.57, 45.38, 29.76, 25.31, 11.27, 11.15, 10.94, 10.82. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -177.99 (tt, *J* = 19.8, 9.7 Hz).HRMS (ESI, m/z): calcd for $[M+H]^+$ 262.1238, found 262.1239.

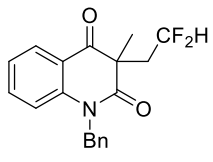
3-(2,2-difluoroethyl)-1-ethyl-3-methylquinoline-2,4(1H,3H)-dione (**3ba**)



3ba

Colorless solid, 46.4mg (87% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.65 (ddd, *J* = 8.7, 7.4, 1.7 Hz, 1H), 7.18 (dt, *J* = 7.4, 3.2 Hz, 2H), 5.91 (tt, *J* = 57.0, 5.1 Hz, 1H), 4.12 (ddt, *J* = 16.8, 14.4, 7.2 Hz, 2H), 2.79 – 2.67 (m, 2H), 1.48 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.77, 172.11, 142.03, 136.56, 128.92, 123.22, 119.62, 117.81, 115.42, 114.90, 113.03, 53.02, 39.80, 39.58, 39.36, 37.55, 26.75, 12.22. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.11 (dq, *J* = 57.1, 14.8 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 268.1144, found 268.1145.

1-benzyl-3-(2,2-difluoroethyl)-3-methylquinoline-2,4(1H,3H)-dione (**3ca**)

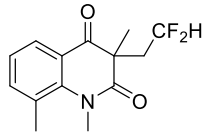


3ca

Colorless solid, 59.9mg (91% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.49 (td, *J* = 8.0, 7.5, 1.7 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 7.0 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.00 (tt, *J* = 57.1, 5.1 Hz, 1H), 5.32 (d, *J* = 5.0 Hz, 2H), 2.83 (td, *J* = 15.9, 5.1 Hz, 2H),

1.59 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.46, 172.95, 142.35, 136.45, 135.80, 129.09, 128.71, 127.59, 126.26, 123.53, 119.58, 116.02, 115.49, 46.27, 39.48, 39.26, 39.04, 27.30. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.16 (dq, *J* = 57.2, 15.3 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 330.1300, found 330.1301.

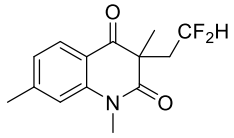
3-(2,2-difluoroethyl)-1,3,8-trimethylquinoline-2,4(1H,3H)-dione (**3da**)



3da

Colorless solid, 44.2mg (83% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.44 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.09 (tt, *J* = 57.2, 5.0 Hz, 1H), 3.44 (s, 3H), 2.57 (td, *J* = 16.0, 5.0 Hz, 2H), 2.50 (s, 3H), 1.44 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 196.93, 173.36, 143.74, 139.68, 127.18, 125.87, 124.59, 123.13, 118.02, 115.64, 113.25, 54.01, 38.90, 38.67, 38.44, 37.48, 24.29, 21.97. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.69 (t, *J* = 16.1 Hz), -113.84 (t, *J* = 16.1 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 268.1144, found 268.1140.

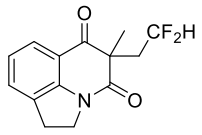
3-(2,2-difluoroethyl)-1,3,7-trimethylquinoline-2,4(1H,3H)-dione (**3ea**)



3ea

Colorless solid, 43.6mg (82% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97 – 7.90 (m, 1H), 7.04 – 6.96 (m, 2H), 5.88 (ttd, *J* = 57.0, 5.1, 1.2 Hz, 1H), 3.47 (s, 3H), 2.77 – 2.64 (m, 2H), 2.46 (s, 3H), 1.46 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.20, 172.82, 148.12, 143.17, 128.64, 124.50, 117.83, 117.19, 115.52, 115.44, 113.06, 52.96, 52.90, 39.86, 39.63, 39.41, 29.93, 27.06, 22.52. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.03 – -115.44 (m). HRMS (ESI, m/z): calcd for $[M+H]^+$ 268.1144, found 268.1143.

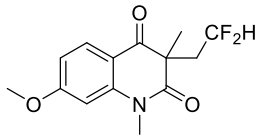
5-(2,2-difluoroethyl)-5-methyl-1,2-dihydro-4H-pyrrolo[3,2,1-ij]quinoline-4,6(5H)-dione (**3fa**)



3fa

Colorless solid, 28.9mg (55% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 7.3 Hz, 1H), 7.09 (td, *J* = 7.7, 1.7 Hz, 1H), 6.01 – 5.68 (m, 1H), 4.25 – 4.13 (m, 2H), 3.32 (t, *J* = 8.5 Hz, 2H), 2.79 – 2.65 (m, 2H), 1.49 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.91, 170.75, 145.84, 132.04, 130.97, 124.77, 124.05, 116.09, 115.36, 45.99, 40.04, 39.82, 39.60, 26.99, 26.81. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.35 (dtd, *J* = 56.7, 16.1, 7.8 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 266.0987, found 266.0983.

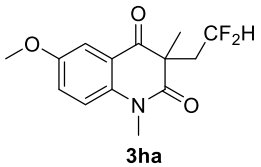
3-(2,2-difluoroethyl)-7-methoxy-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ga**)



3ga

Colorless solid, 44.3mg (79% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 8.7 Hz, 1H), 6.72 (dd, *J* = 8.8, 2.2 Hz, 1H), 6.62 (d, *J* = 2.2 Hz, 1H), 5.87 (tt, *J* = 57.0, 5.1 Hz, 1H), 3.92 (s, 3H), 3.46 (s, 3H), 2.76 – 2.65 (m, 2H), 1.47 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.02, 173.10, 166.34, 145.12, 131.12, 117.83, 115.45, 113.21, 113.06, 108.63, 101.04, 55.89, 52.59, 40.06, 39.84, 39.62, 29.93, 27.18. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.05 – -115.52 (m).HRMS (ESI, m/z): calcd for $[M+H]^+$ 284.1093, found 284.1097.

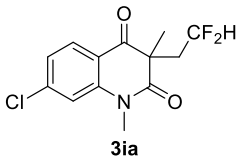
3-(2,2-difluoroethyl)-6-methoxy-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ha**)



3ha

Colorless solid, 36.6mg (65% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 3.1 Hz, 1H), 7.27 (dd, *J* = 9.0, 3.1 Hz, 1H), 7.17 (d, *J* = 9.0 Hz, 1H), 5.93 (tt, *J* = 57.0, 5.1 Hz, 1H), 3.89 (s, 3H), 3.50 (s, 3H), 2.82 – 2.70 (m, 2H), 1.52 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.68, 172.07, 155.68, 137.24, 124.54, 119.99, 117.81, 116.62, 115.43, 113.04, 110.07, 55.86, 52.93, 39.87, 39.65, 39.43, 30.05, 27.06. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.13 (t, *J* = 16.1 Hz), -115.29 (t, *J* = 16.1 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 284.1093, found 284.1088.

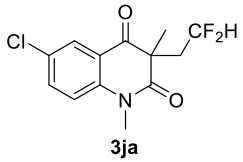
7-chloro-3-(2,2-difluoroethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ia**)



3ia

Yellow solid, 51.0mg (88% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 8.3 Hz, 1H), 7.21 – 7.12 (m, 2H), 5.86 (tt, *J* = 56.9, 5.0 Hz, 1H), 3.48 – 3.43 (m, 3H), 2.70 (tt, *J* = 16.2, 4.5 Hz, 2H), 1.46 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.45, 172.53, 144.04, 142.90, 129.98, 123.70, 117.70, 117.64, 115.39, 115.25, 112.86, 53.17, 39.81, 39.59, 39.37, 30.09, 26.91. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.15 (dt, *J* = 57.0, 16.1 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 288.0597, found 288.0593.

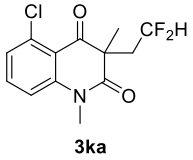
6-chloro-3-(2,2-difluoroethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ja**)



3ja

Yellow solid, 46.4mg (81% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (d, *J* = 2.6 Hz, 1H), 7.60 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.14 (d, *J* = 8.9 Hz, 1H), 5.89 (tt, *J* = 56.9, 5.0 Hz, 1H), 3.47 (s, 3H), 2.73 (tt, *J* = 16.3, 3.9 Hz, 2H), 1.48 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.54, 172.19, 141.61, 136.13, 129.30, 128.04, 120.37, 117.62, 116.69, 115.23, 112.84, 53.21, 39.78, 39.56, 39.34, 30.17, 26.87. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.11 (t, *J* = 16.1 Hz), -115.26 (t, *J* = 16.1 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 288.0597, found 288.0601.

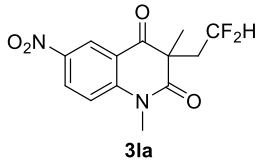
5-chloro-3-(2,2-difluoroethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3ka**)



3ka

Yellow solid, 43.3mg (76% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.45 (m, 1H), 7.23 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.23 – 5.89 (m, 1H), 3.46 (s, 3H), 2.63 (dddd, *J* = 18.7, 9.5, 4.9, 2.3 Hz, 2H), 1.48 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.89, 171.37, 144.40, 135.70, 134.69, 126.76, 118.06, 117.72, 115.34, 113.87, 112.95, 54.76, 38.81, 38.58, 38.35, 30.96, 24.38. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.09 (dt, *J* = 57.0, 15.2 Hz), -113.86 (ddd, *J* = 57.0, 19.5, 10.8 Hz), -114.60 (ddd, *J* = 57.1, 21.6, 11.7 Hz), -115.21 – -115.54 (m). HRMS (ESI, m/z): calcd for $[M+H]^+$ 288.0597, found 288.0597.

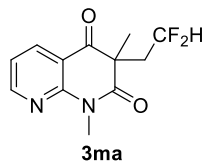
3-(2,2-difluoroethyl)-1,3-dimethyl-6-nitroquinoline-2,4(1H,3H)-dione (**3la**)



3la

Yellow solid, 46.5mg (78% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.88 (d, *J* = 2.7 Hz, 1H), 8.49 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.34 (d, *J* = 9.2 Hz, 1H), 5.91 (tt, *J* = 56.8, 4.9 Hz, 1H), 3.57 (s, 3H), 2.78 (tt, *J* = 16.3, 4.7 Hz, 2H), 1.52 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.64, 172.48, 147.34, 143.26, 130.81, 124.61, 119.24, 117.39, 115.99, 115.00, 112.61, 53.49, 39.91, 39.69, 39.47, 30.67, 26.79. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -114.99 (t, *J* = 15.9 Hz), -115.14 (t, *J* = 16.1 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 299.0838, found 299.0838.

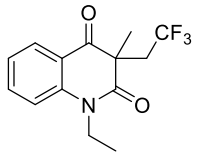
3-(2,2-difluoroethyl)-1,3-dimethyl-1,8-naphthyridine-2,4(1H,3H)-dione (**3ma**)



3ma

Colorless solid, 32.4mg (64% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.67 – 8.57 (m, 1H), 8.29 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.19 – 7.13 (m, 1H), 5.90 (tt, *J* = 56.8, 5.0 Hz, 1H), 3.61 (s, 3H), 2.85 – 2.67 (m, 2H), 1.51 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.07, 173.14, 154.67, 154.09, 137.14, 119.17, 117.60, 115.21, 114.59, 112.82, 53.31, 39.91, 39.69, 39.46, 28.87, 26.99. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -114.99 – -115.41 (m). HRMS (ESI, m/z): calcd for $[M+H]^+$ 255.0490, found 255.0487.

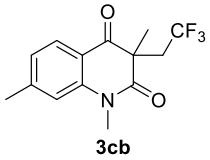
1-ethyl-3-methyl-3-(2,2,2-trifluoroethyl)quinoline-2,4(1H,3H)-dione (**3bb**)



3bb

Colorless solid, 34.0mg (60% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.66 (td, *J* = 7.8, 7.4, 1.8 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 2H), 4.13 (ddq, *J* = 76.4, 14.3, 7.1 Hz, 2H), 3.06 (qd, *J* = 10.3, 1.7 Hz, 2H), 1.49 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.62, 171.27, 142.10, 136.82, 129.04, 123.29, 119.38, 115.02, 52.16, 52.14, 41.12, 40.83, 40.54, 40.26, 37.54, 26.96, 12.05. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -60.60 (t, *J* = 10.3 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 286.1049, found 286.1053.

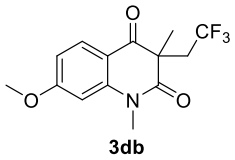
1,3,7-trimethyl-3-(2,2,2-trifluoroethyl)quinoline-2,4(1H,3H)-dione (**3cb**)



3cb

Colorless solid, 41.5g (73% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 7.9 Hz, 1H), 7.04 – 6.99 (m, 2H), 3.49 (s, 3H), 3.05 (q, *J* = 10.3 Hz, 2H), 2.47 (s, 3H), 1.48 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.03, 171.98, 148.37, 143.22, 128.76, 124.57, 124.00, 116.99, 115.58, 52.15, 41.09, 40.81, 40.52, 40.23, 29.93, 27.14, 22.53. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -60.75 (t, *J* = 10.3 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 286.1049, found 286.1049.

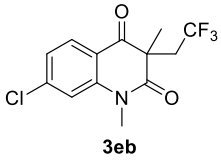
7-methoxy-1,3-dimethyl-3-(2,2,2-trifluoroethyl)quinoline-2,4(1H,3H)-dione (**3db**)



3db

Colorless solid, 20.9mg (80% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 – 8.01 (m, 1H), 6.73 (dq, *J* = 8.8, 2.0 Hz, 1H), 6.64 (q, *J* = 2.1 Hz, 1H), 3.92 (s, 3H), 3.47 (s, 3H), 3.08 – 2.95 (m, 2H), 1.48 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.82, 172.24, 166.50, 145.14, 131.26, 113.02, 108.74, 101.12, 55.90, 51.79, 40.86, 40.57, 40.29, 29.94, 27.27. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -60.93 (t, *J* = 10.3 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 302.0999, found 302.1001.

7-chloro-1,3-dimethyl-3-(2,2,2-trifluoroethyl)quinoline-2,4(1H,3H)-dione (**3eb**)



3eb

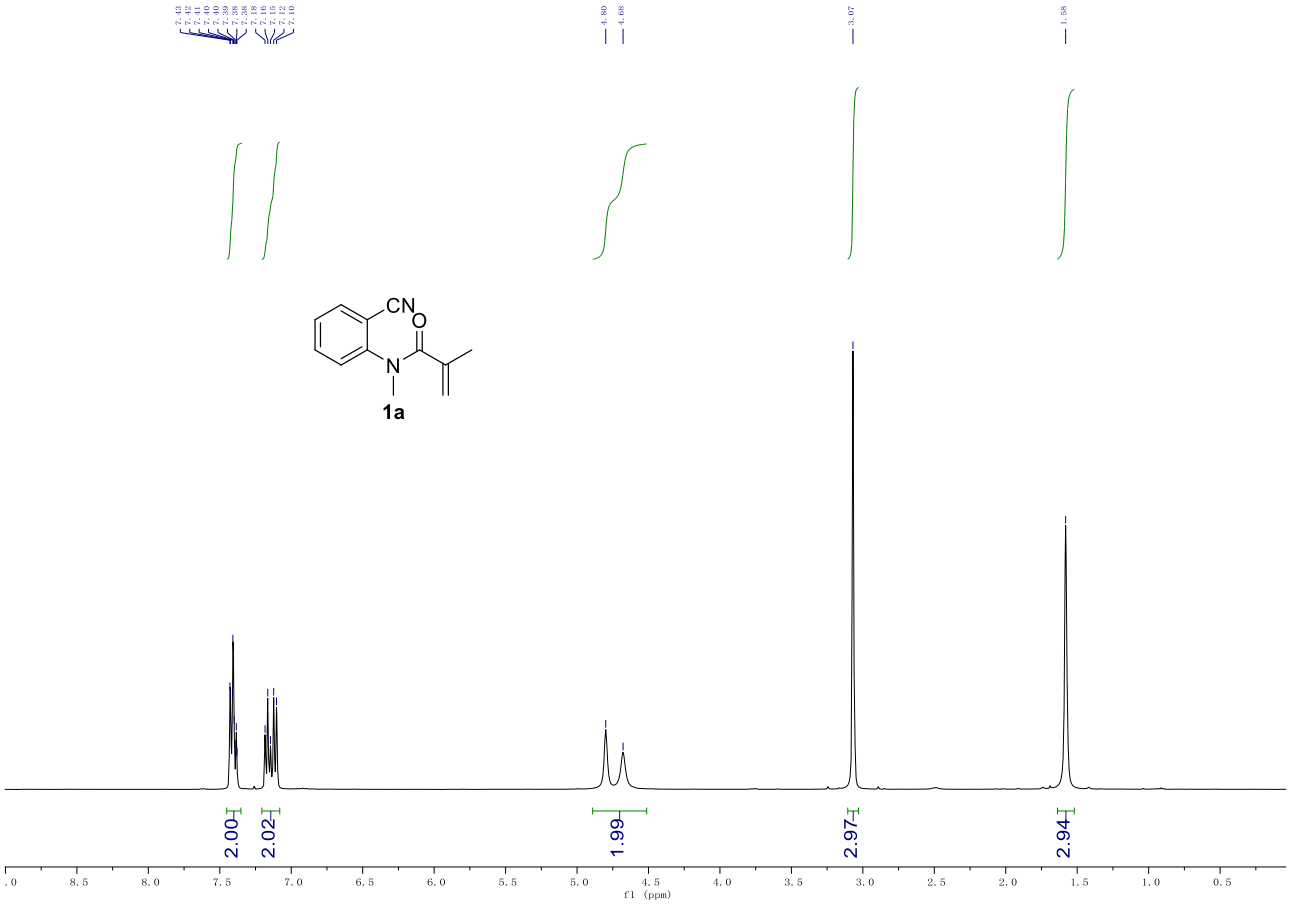
Yellow solid, 45.5mg (75% yield), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.22 – 7.16 (m, 2H), 3.48 (s, 3H), 3.06 (qd, *J* = 10.3, 1.7 Hz, 2H), 1.49 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.40, 171.70, 144.09, 143.24, 130.11, 126.65, 123.83, 117.48, 115.50, 52.38, 41.16, 40.87, 40.59, 40.30, 30.13, 27.05. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -60.71 (t, *J* = 10.2 Hz). HRMS (ESI, m/z): calcd for $[M+H]^+$ 306.0503, found 306.0505.

7 References

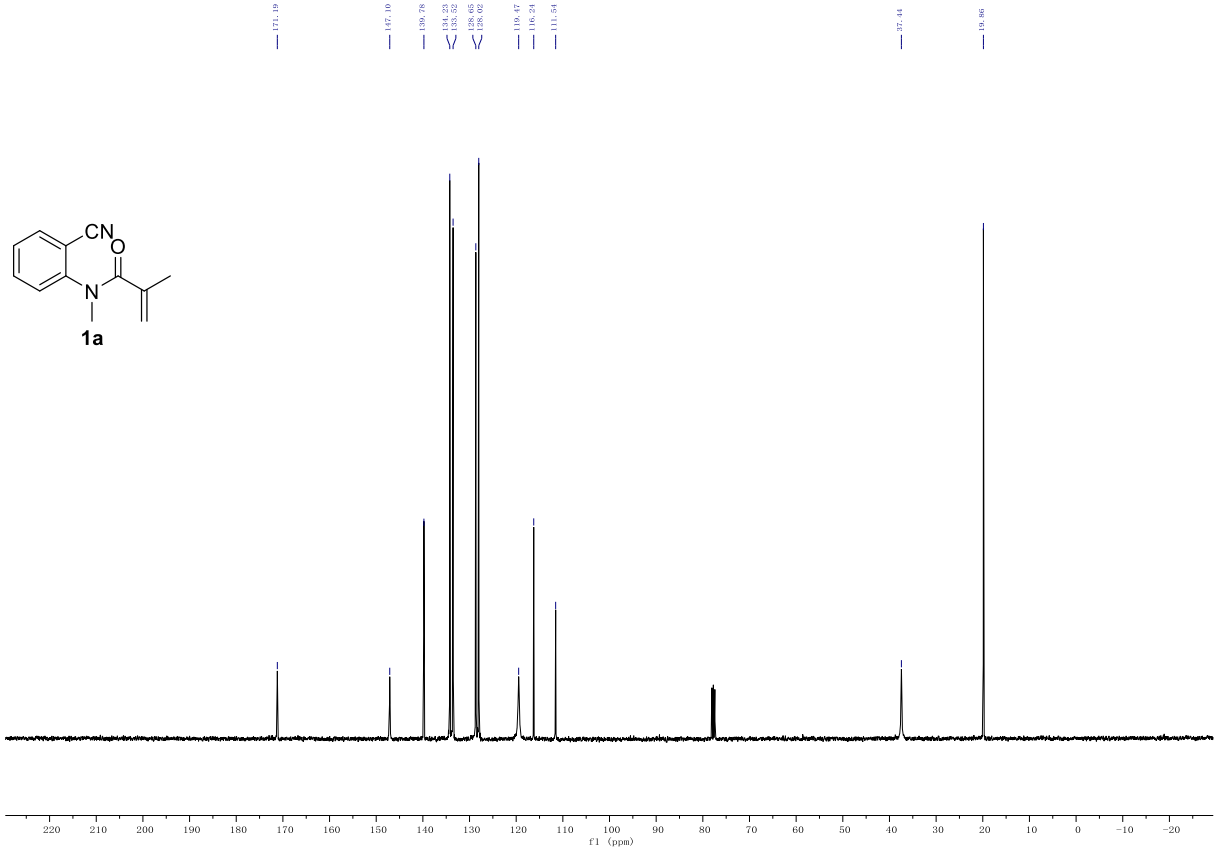
[1] S. Arai, Y. Koike, A. Nishida, *Advanced Synthesis & Catalysis* **2010**, *352*, 893-900.

[2] D. Qi, J. Bai, H. Zhang, B. Li, Z. Song, N. Ma, L. Guo, L. Song, W. Xia, *Green Chemistry* **2022**, *24*, 5046-5051.

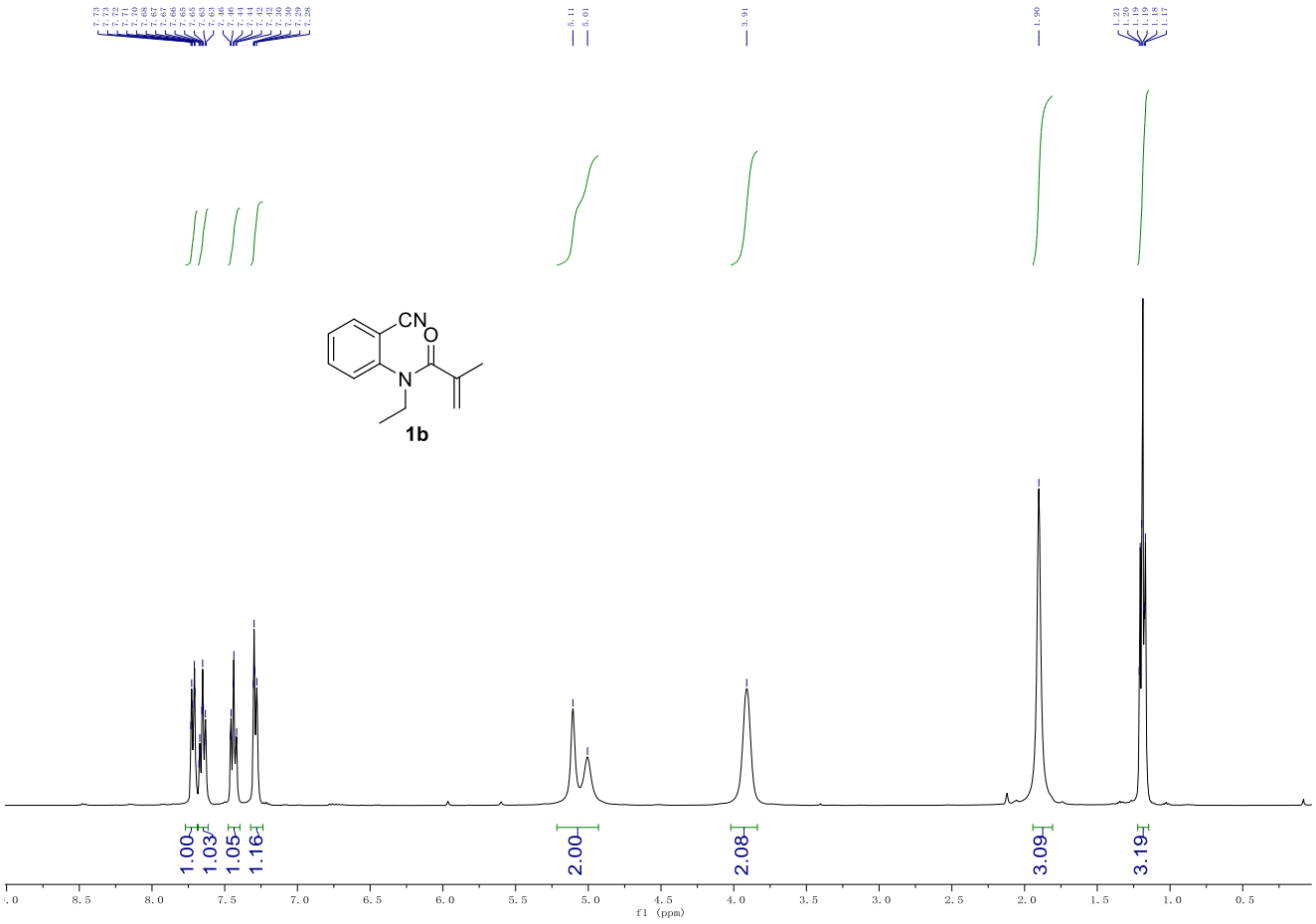
8 Copies of ^{1}H, ^{13}C and ^{19}F NMR Spectra for Substrates



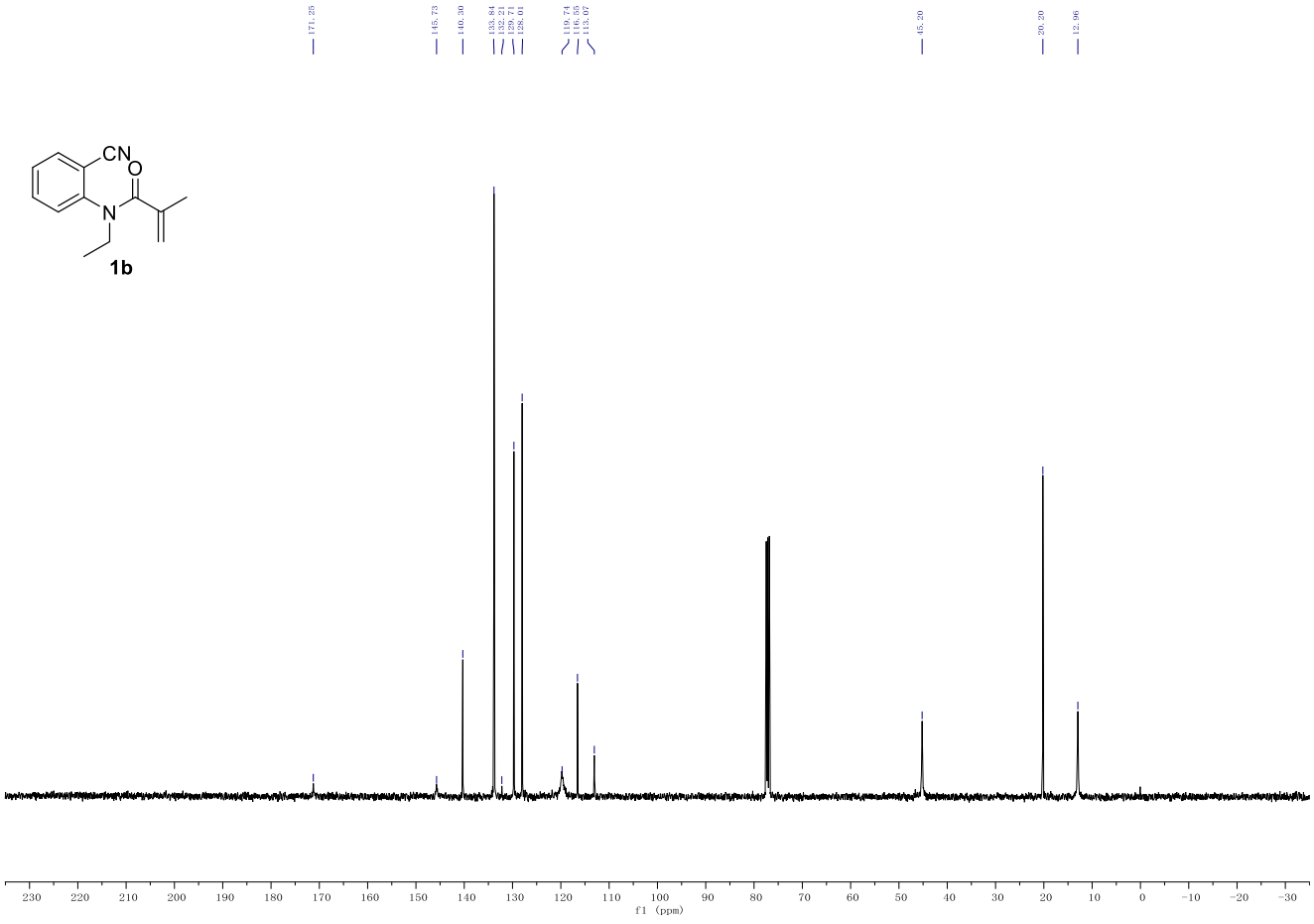
^{1}H NMR Spectrum of Compound 1a



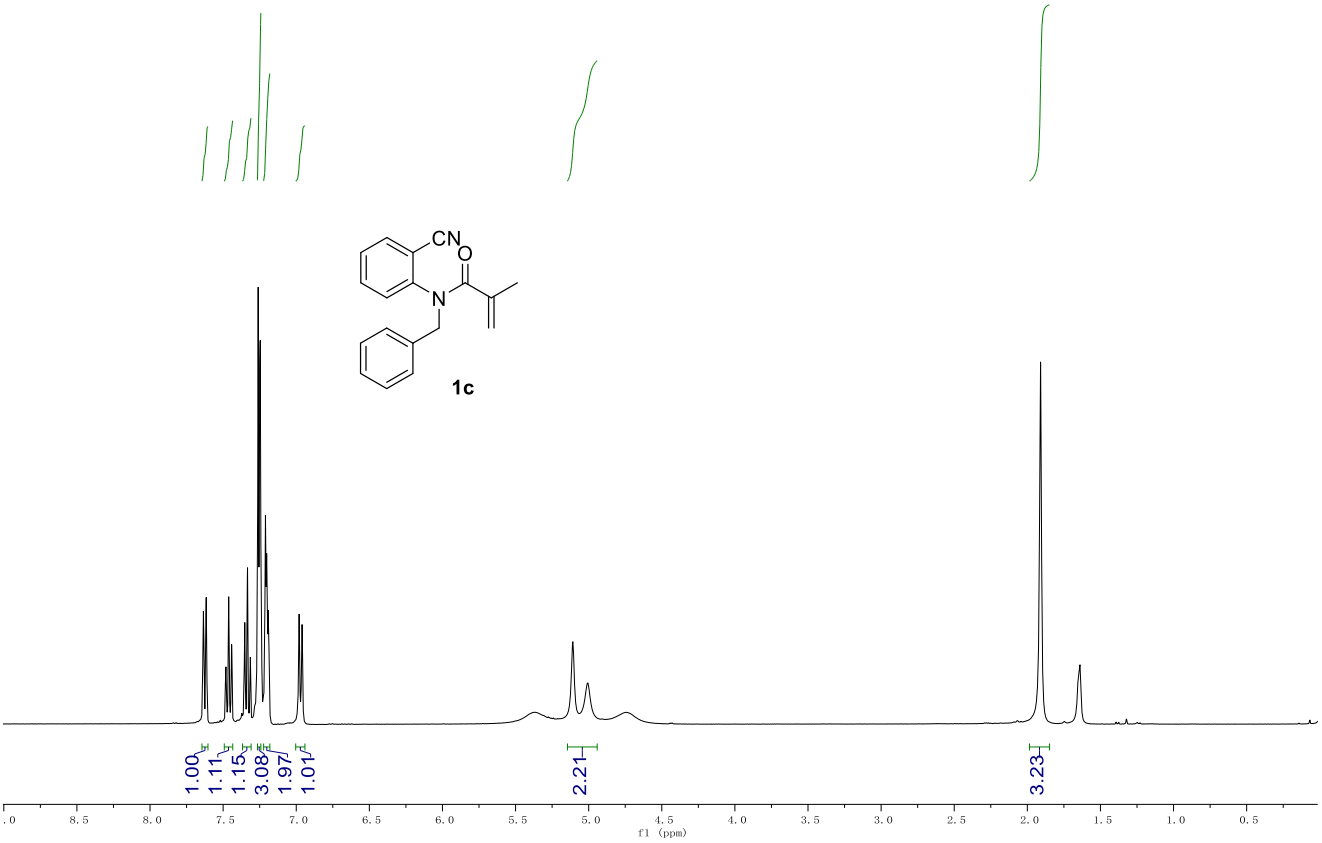
^{13}C NMR Spectrum of Compound 1a



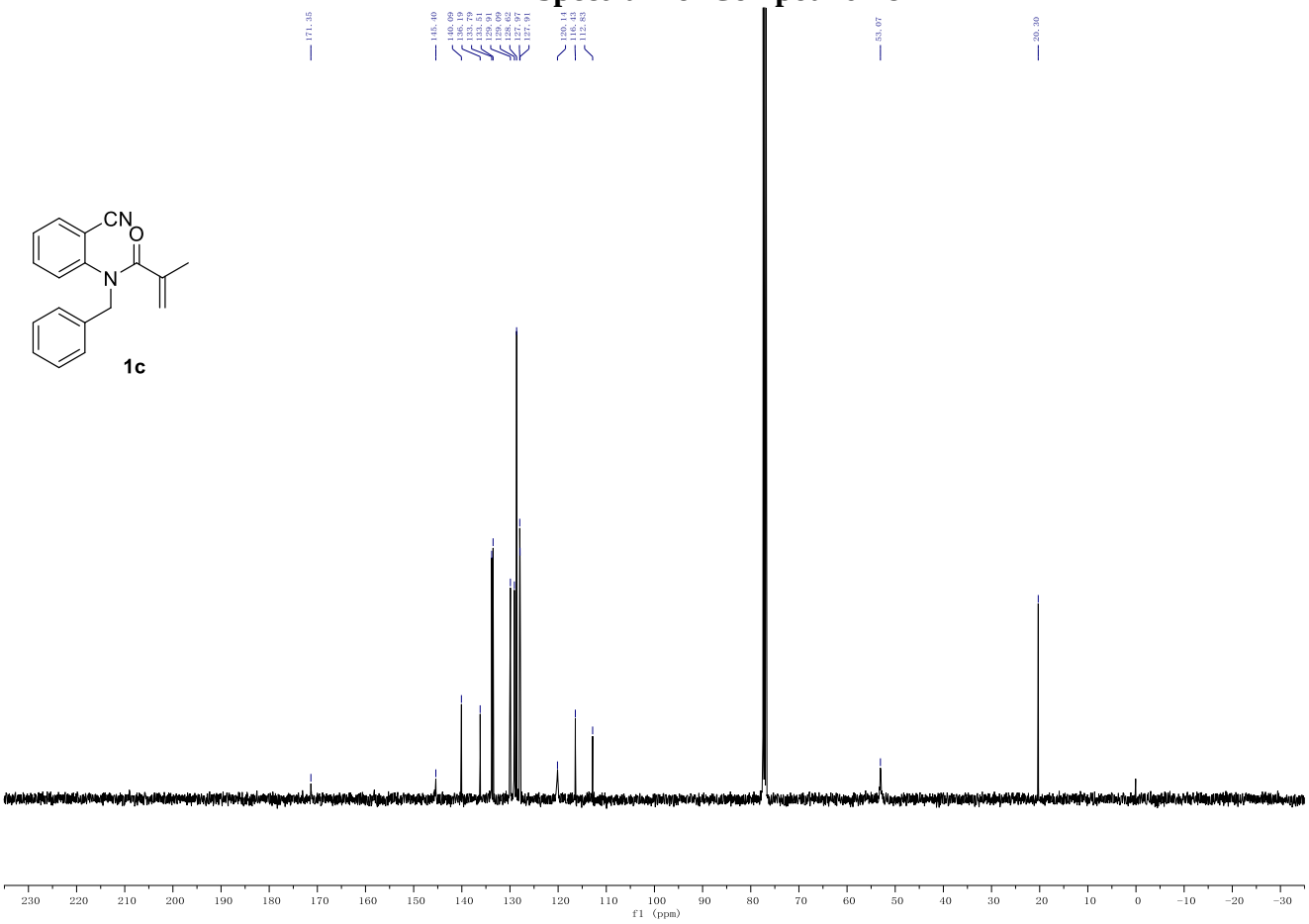
^{1}H NMR Spectrum of Compound 1b



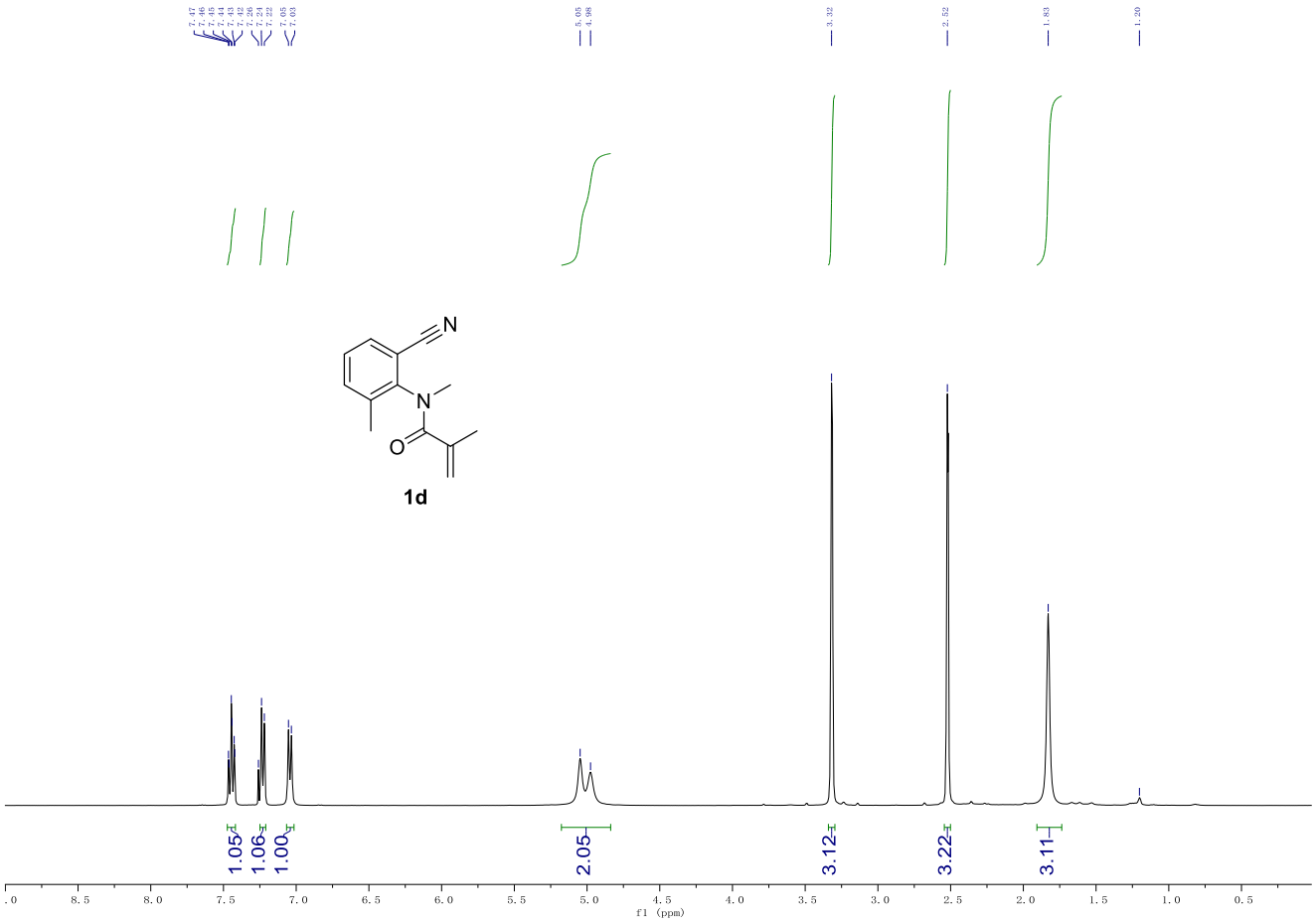
^{13}C NMR Spectrum of Compound 1b



^{1}H NMR Spectrum of Compound 1c



^{13}C NMR Spectrum of Compound 1c



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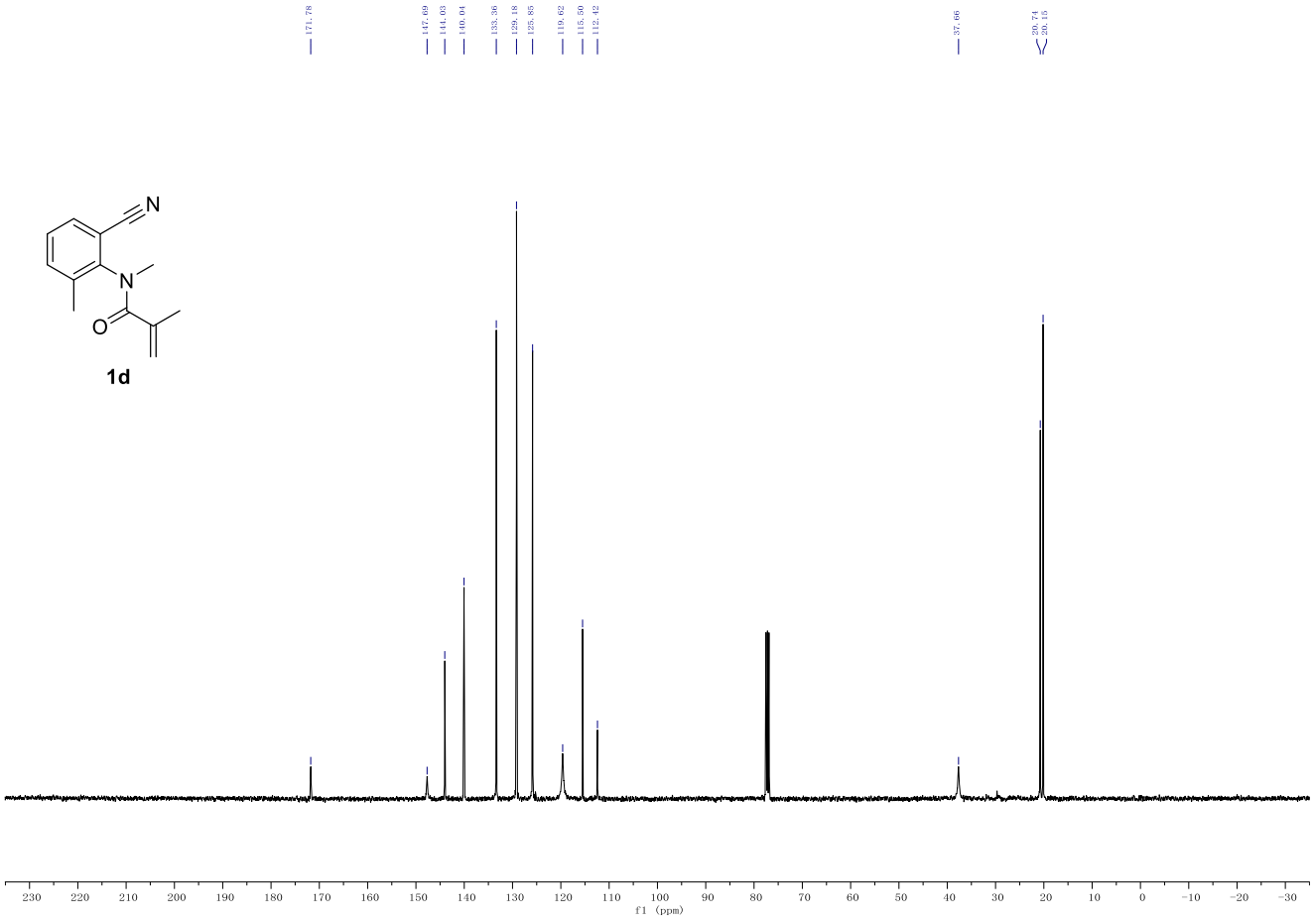
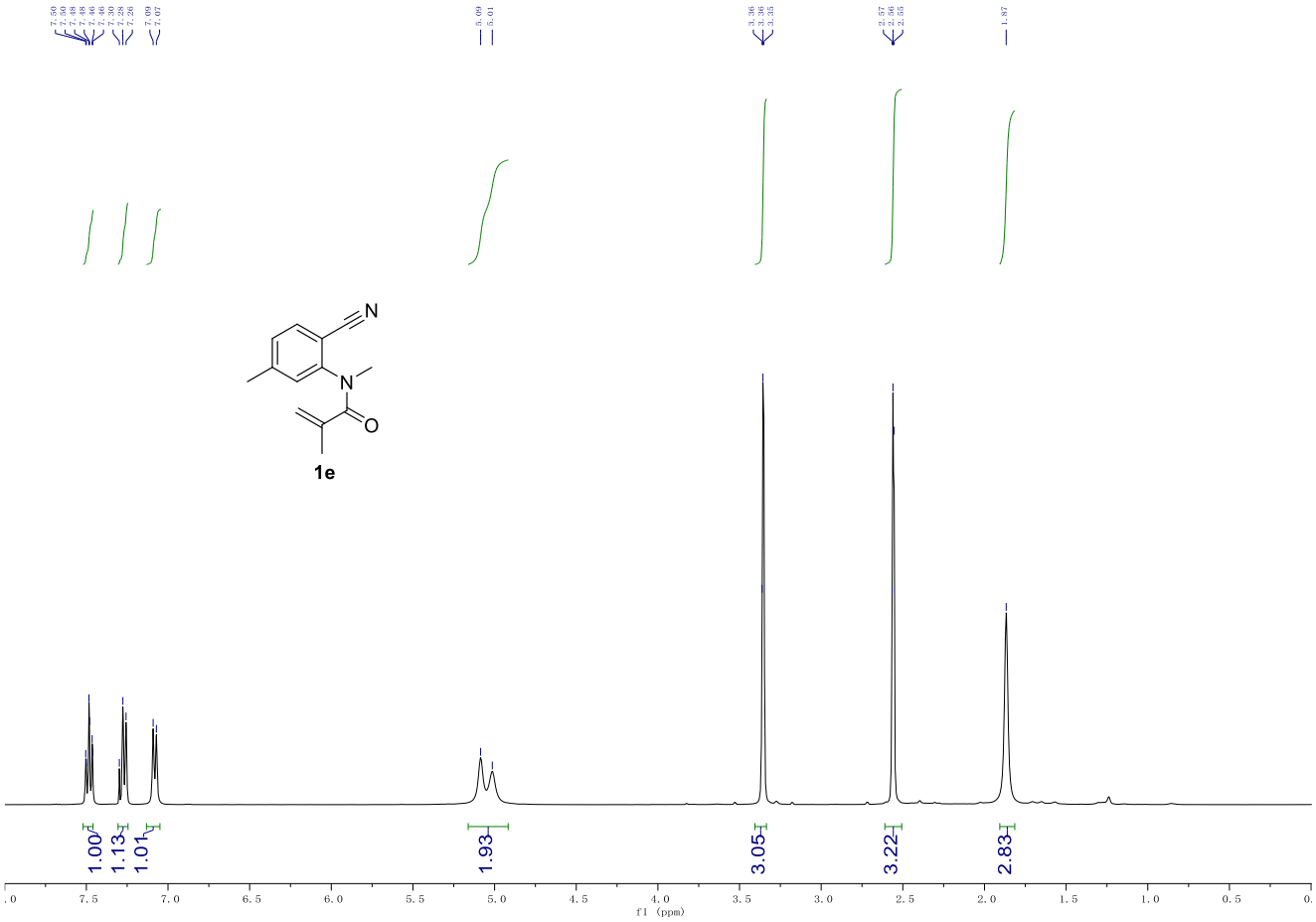


^{13}C NMR Spectrum of Compound 1d



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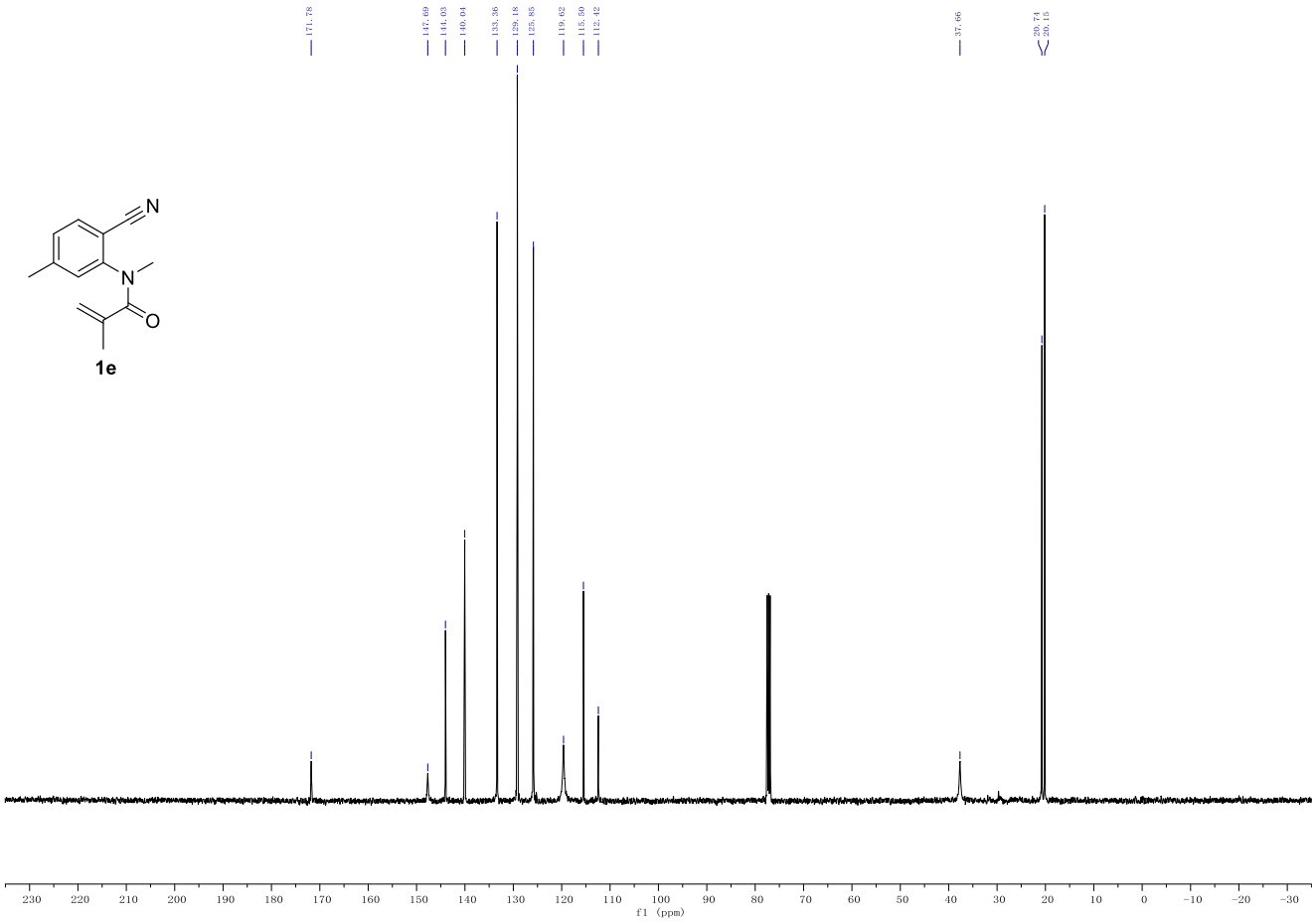
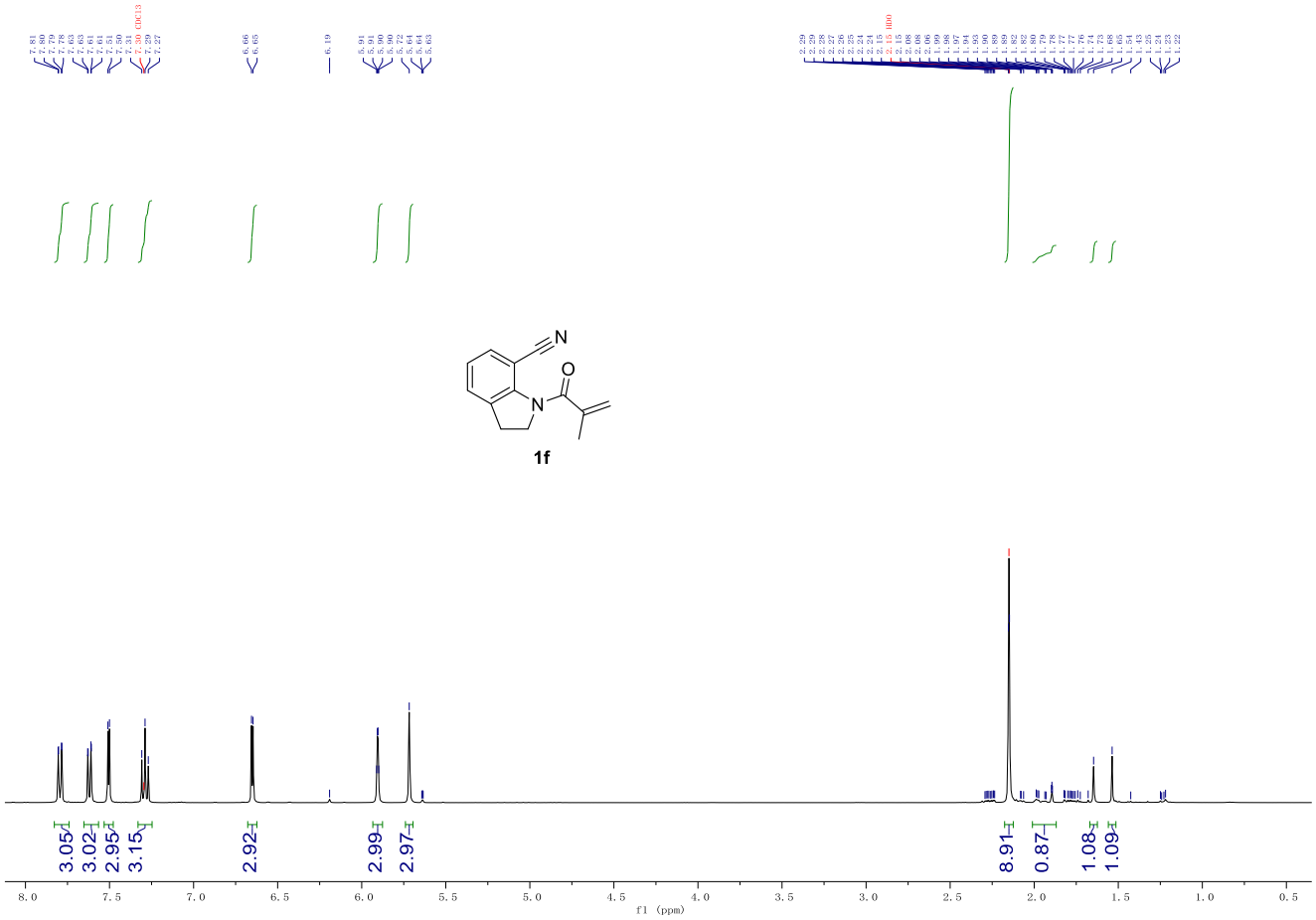


^{13}C NMR Spectrum of Compound 1e



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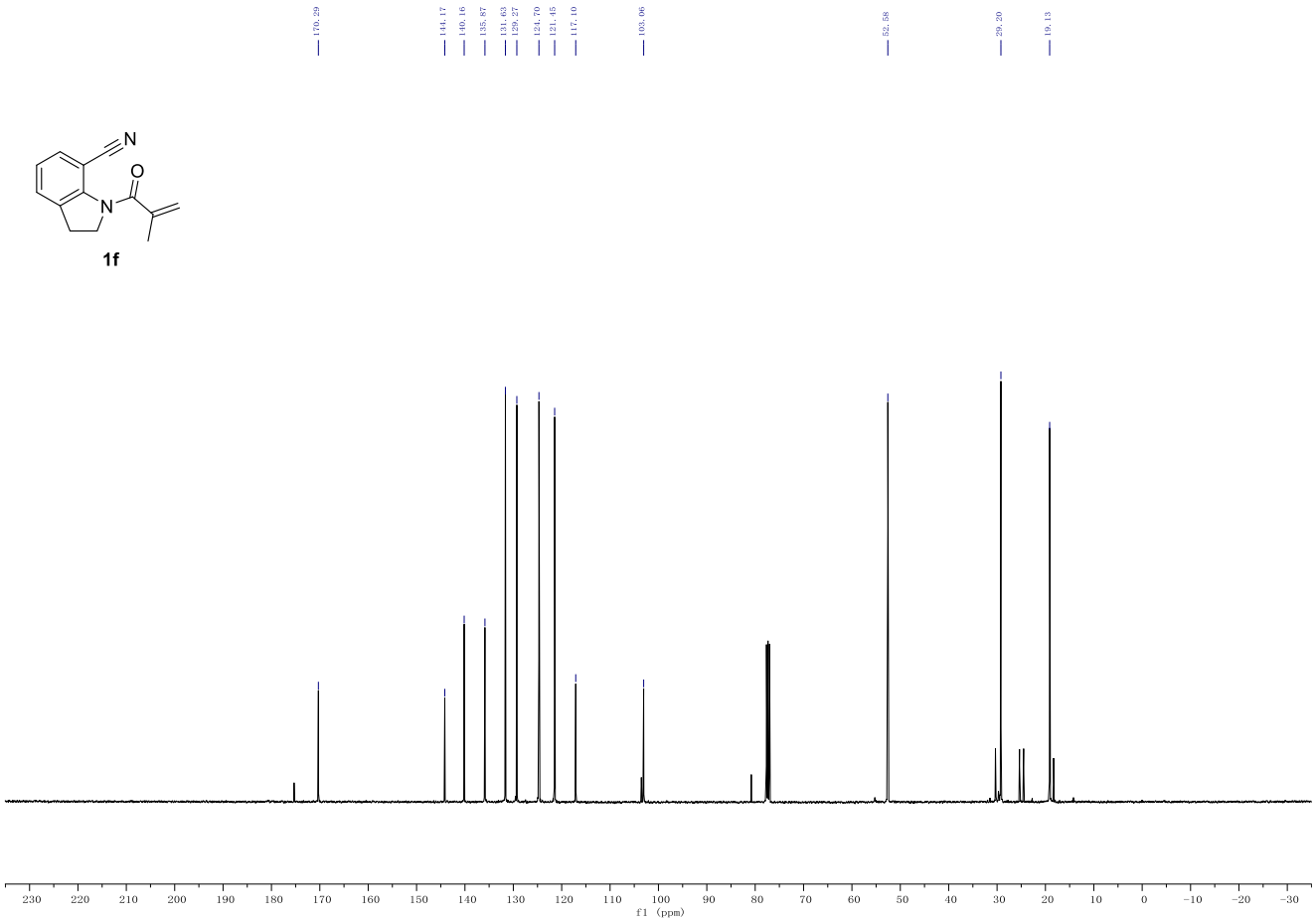
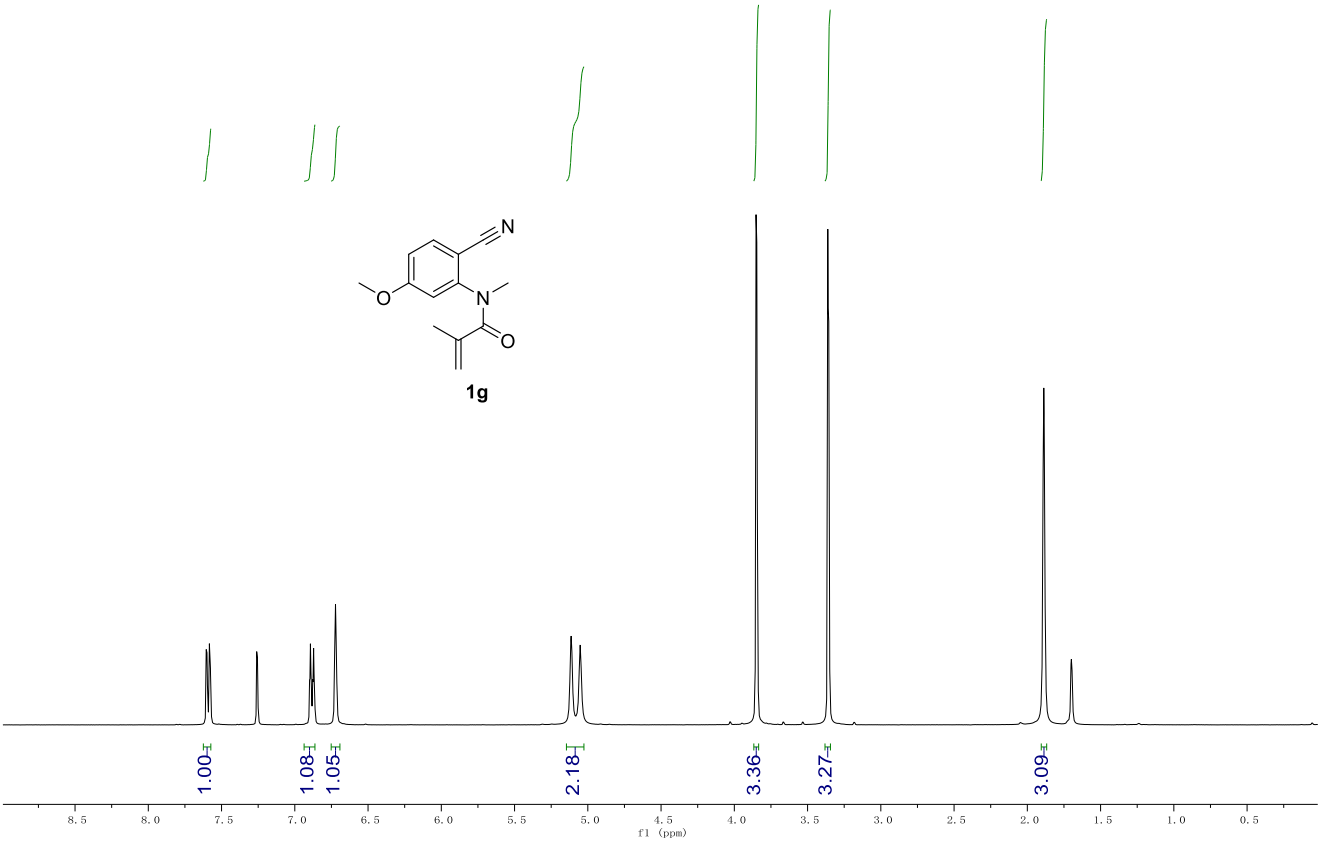
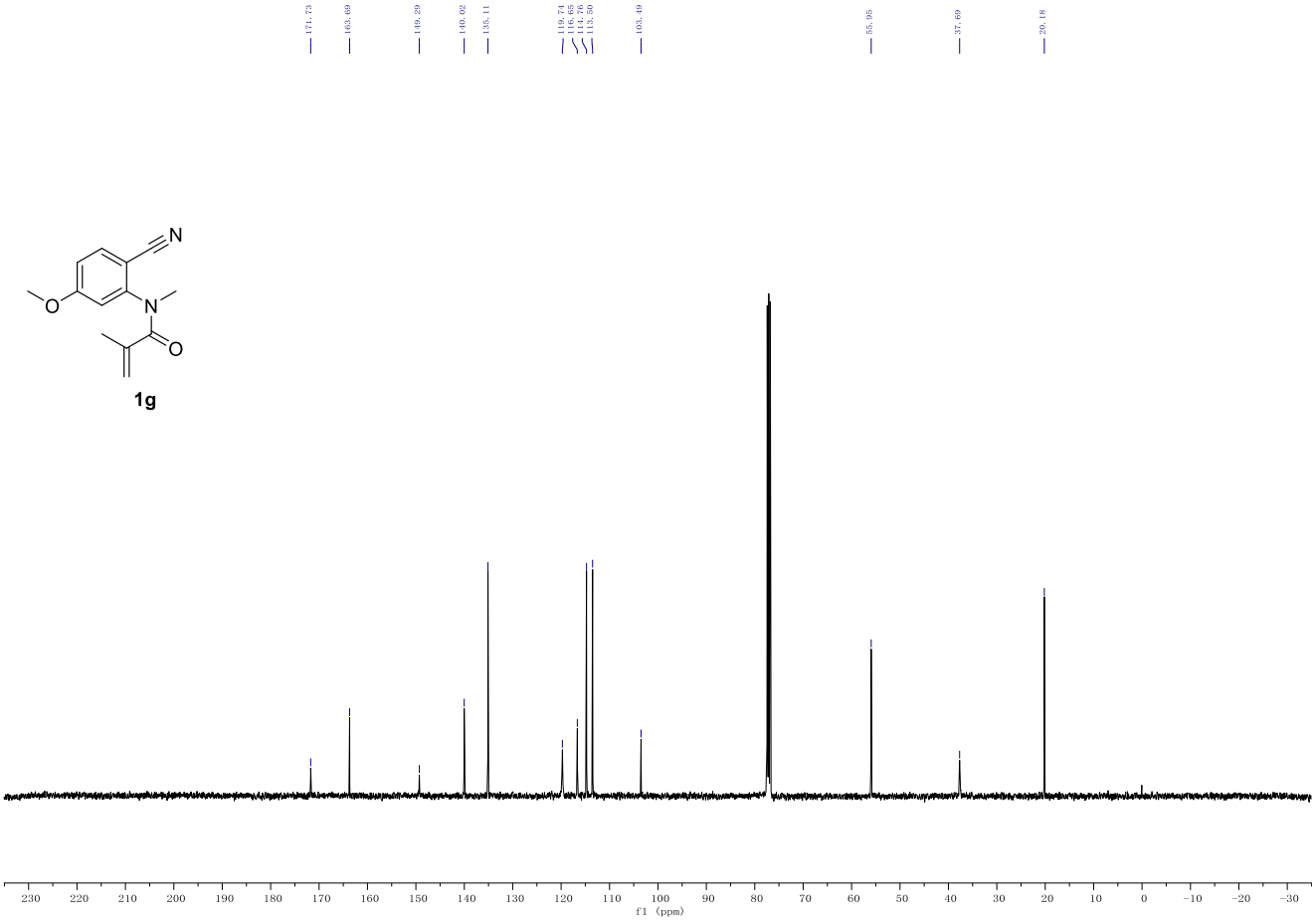


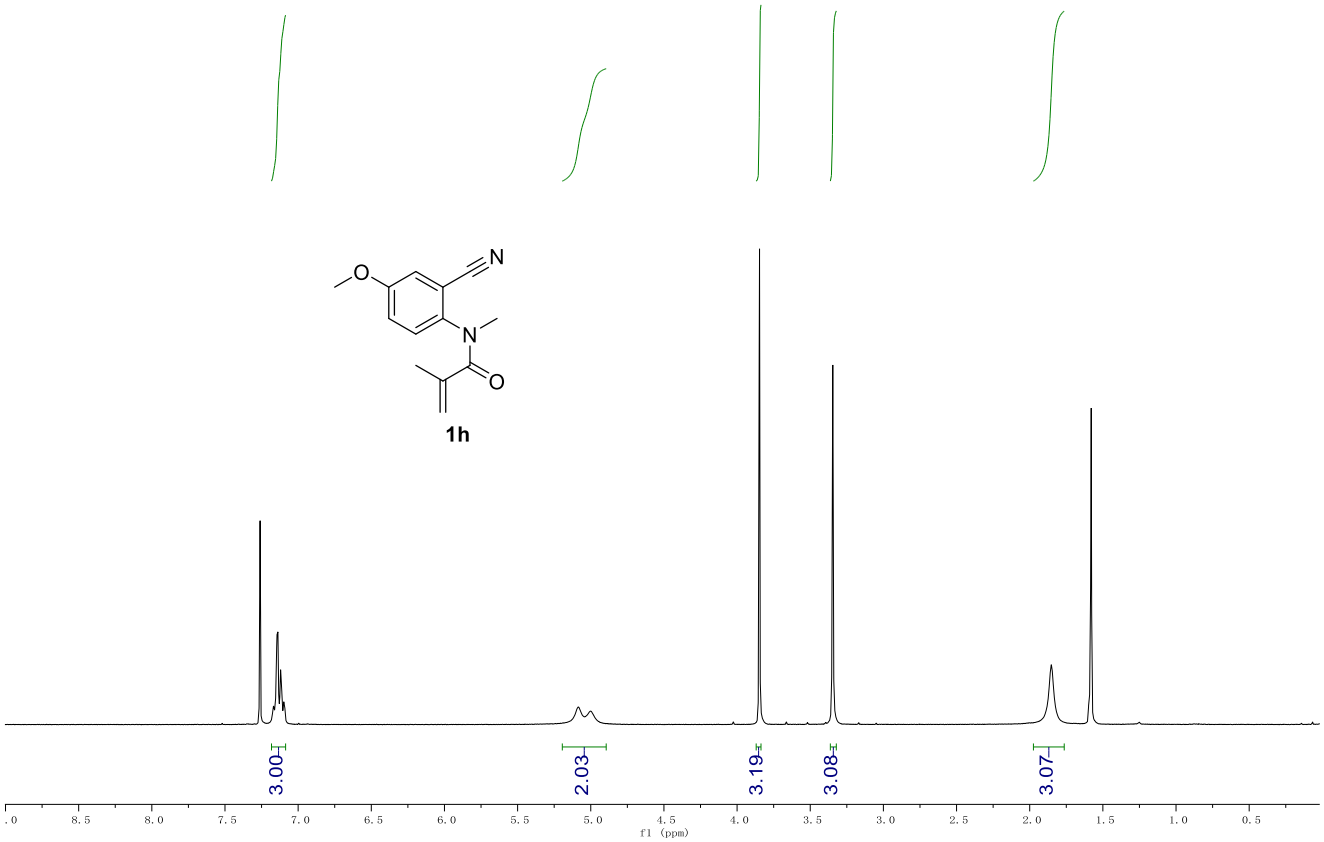
^{13}C NMR Spectrum of Compound 1f



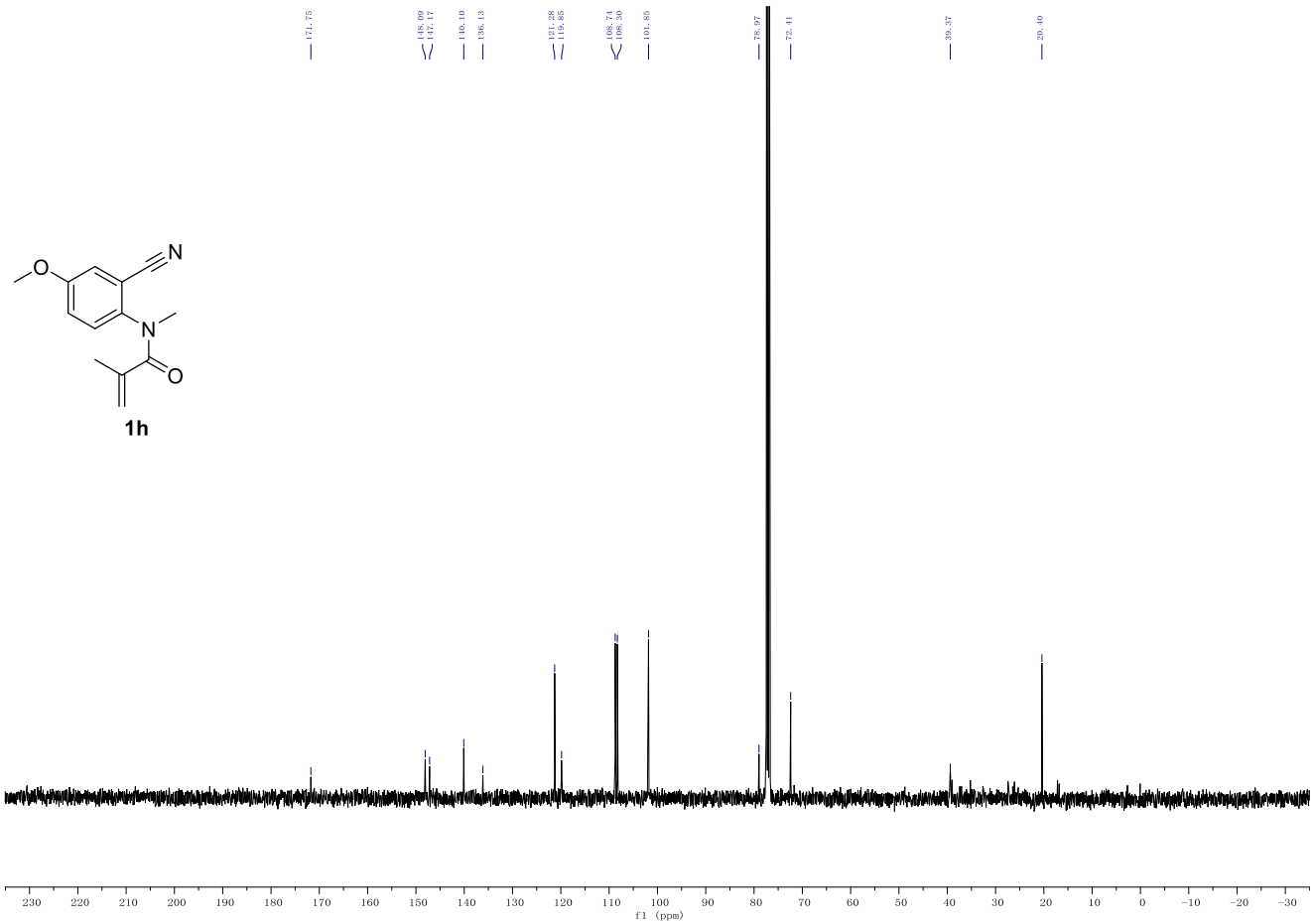
^{1}H NMR Spectrum of Compound 1g



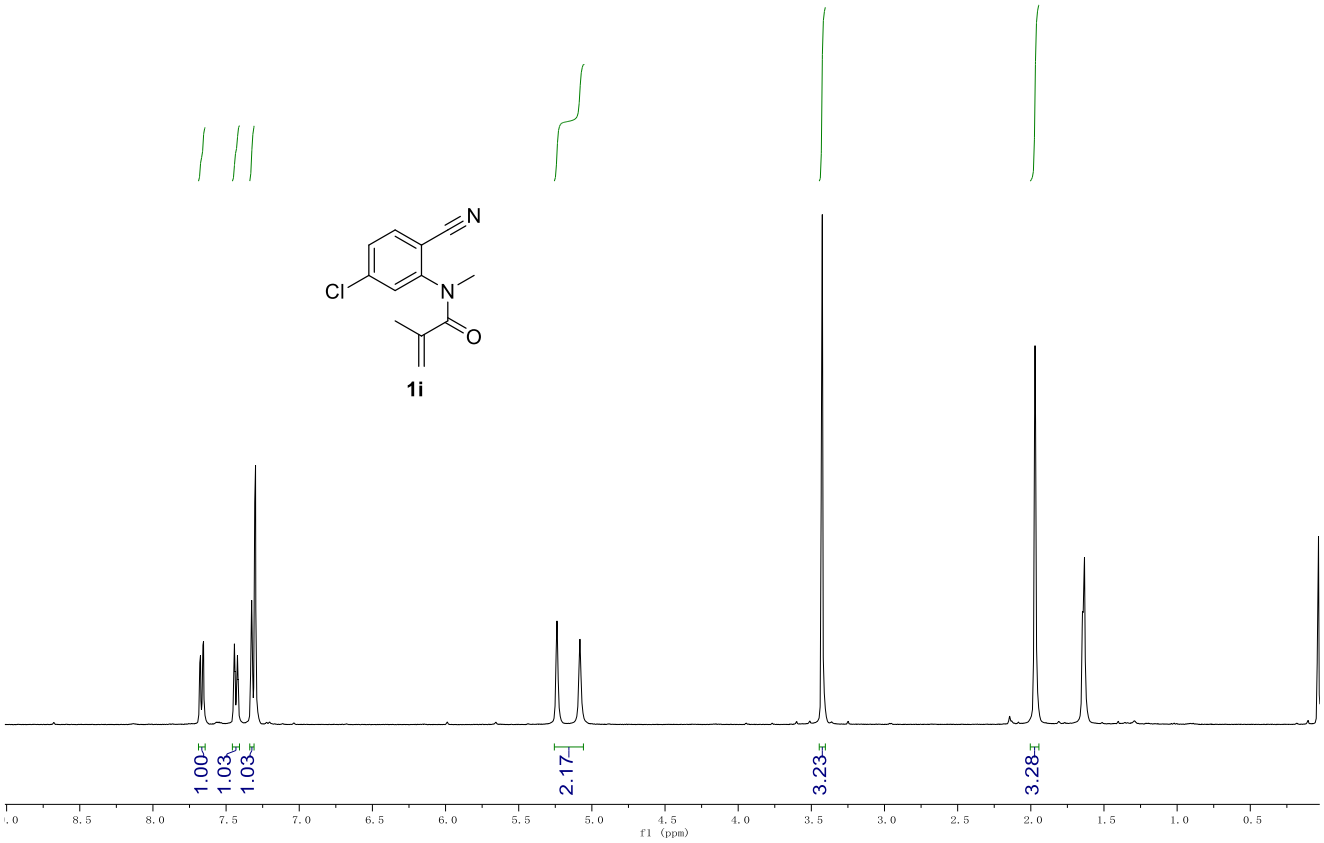
^{13}C NMR Spectrum of Compound 1g



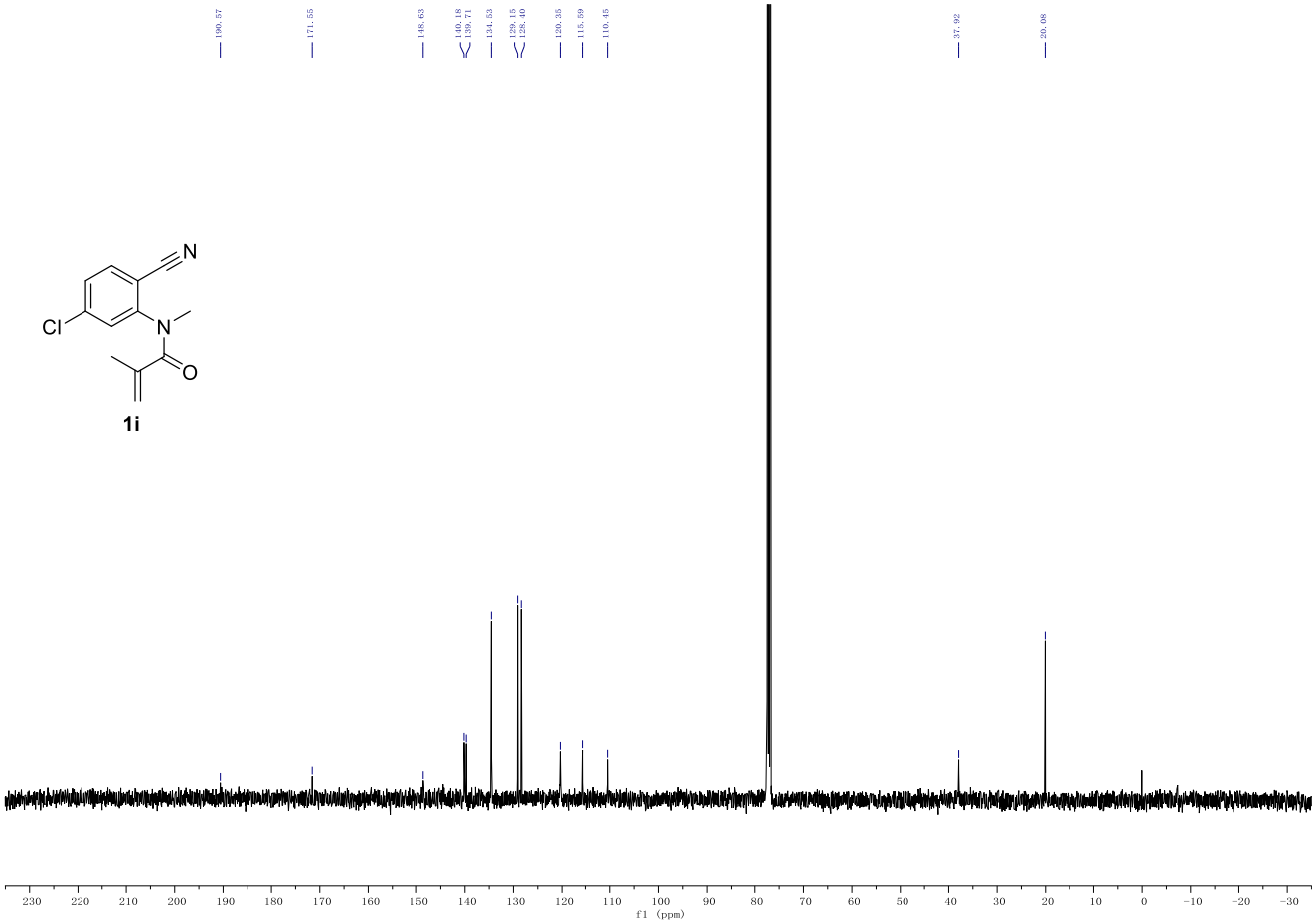
^{1}H NMR Spectrum of Compound 1h



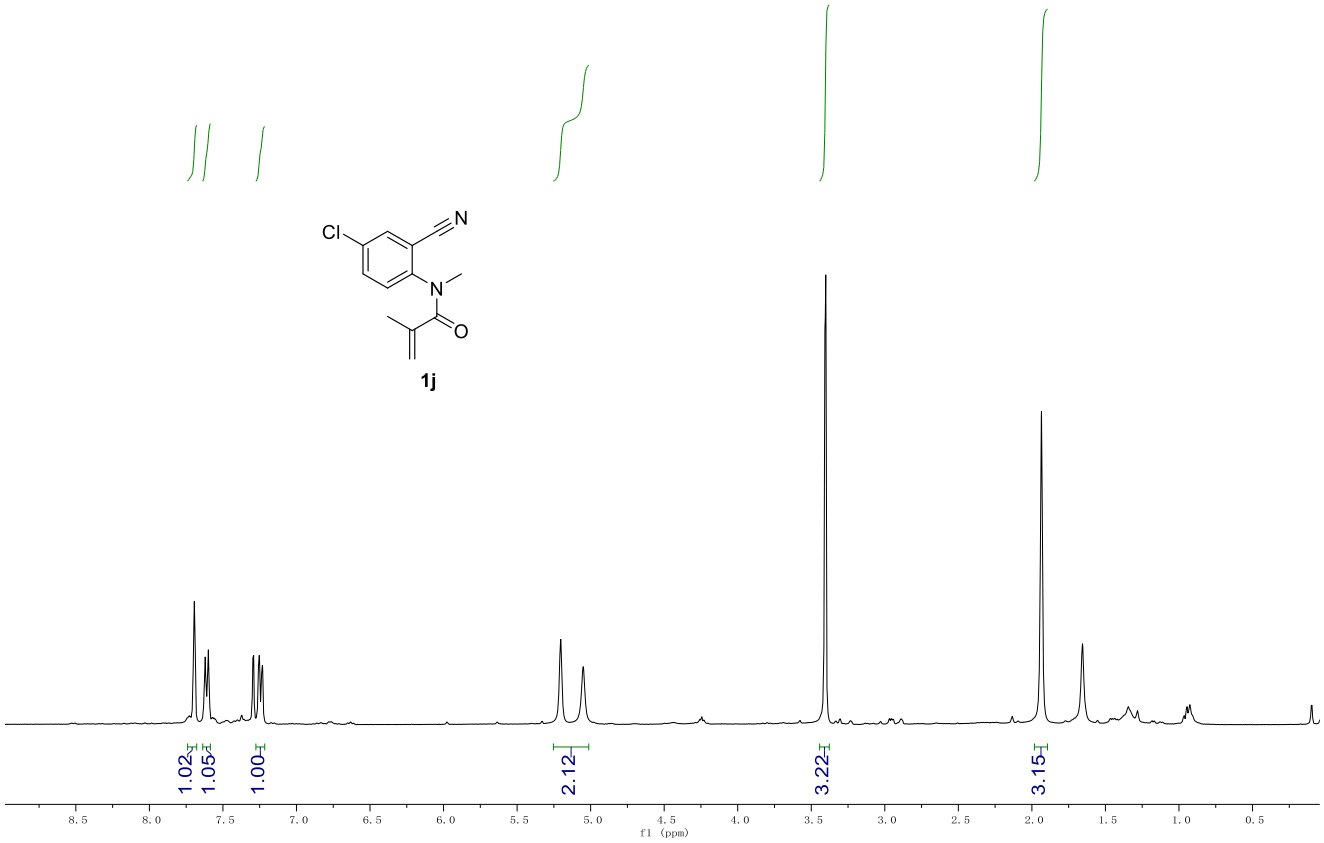
^{13}C NMR Spectrum of Compound 1h



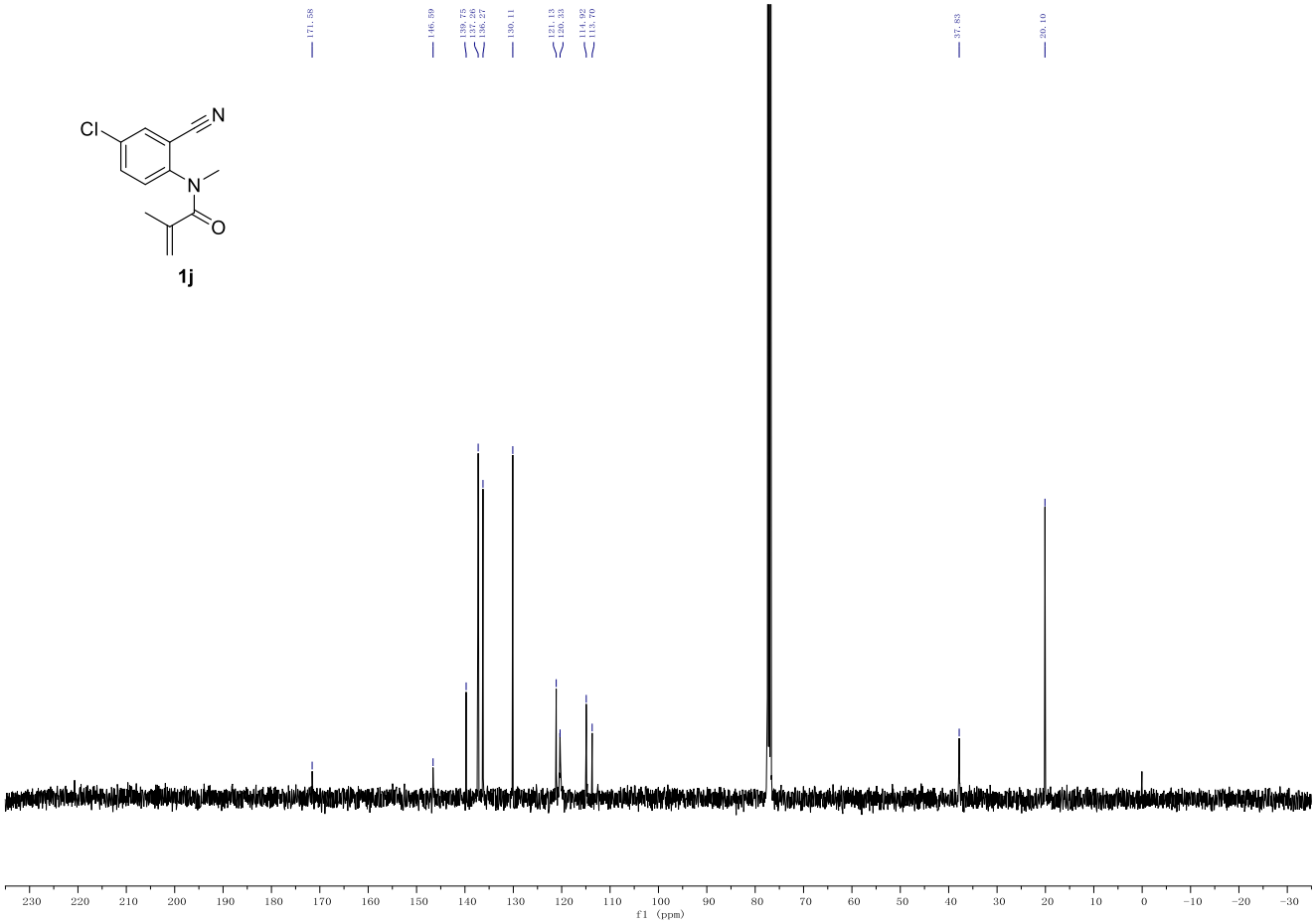
^{1}H NMR Spectrum of Compound 1i



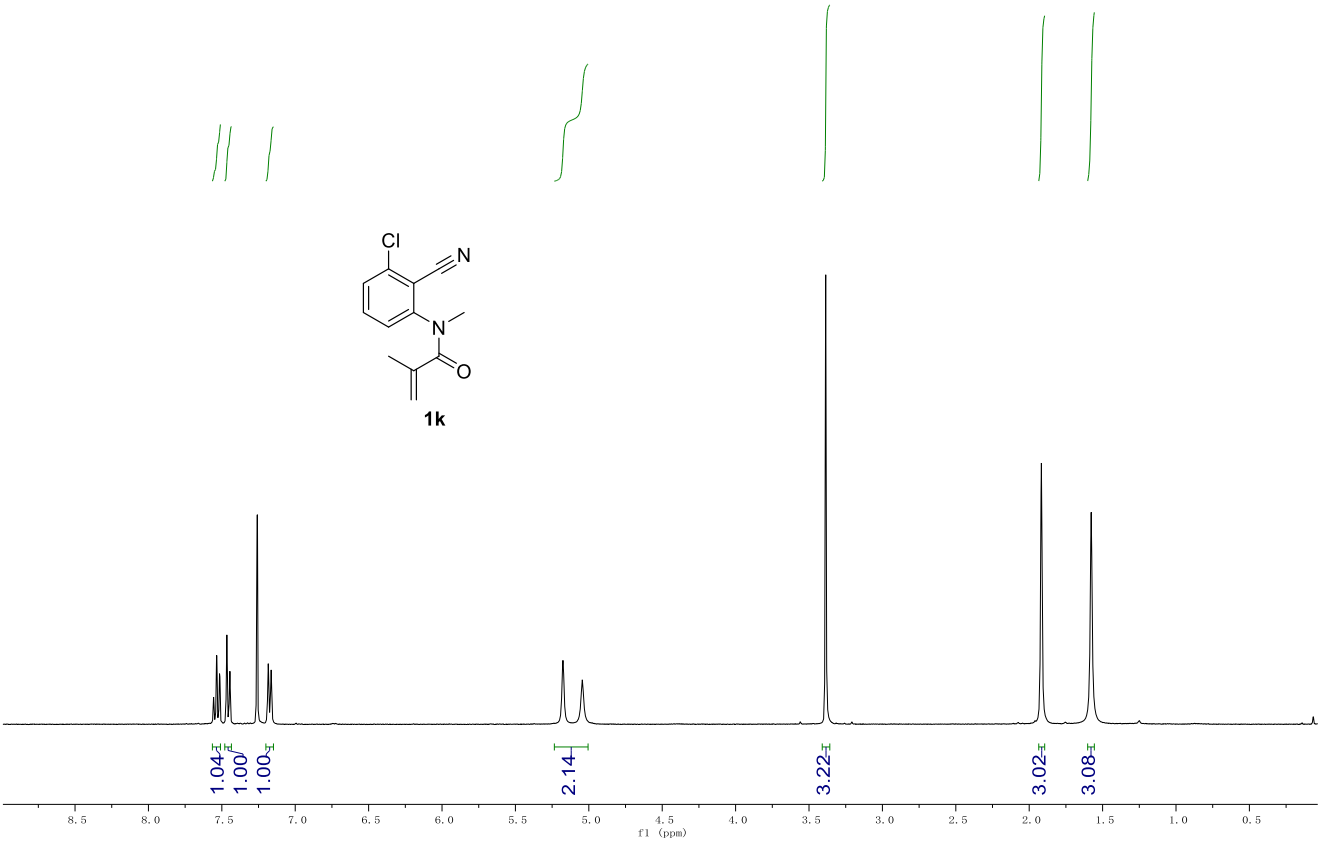
^{13}C NMR Spectrum of Compound 1i



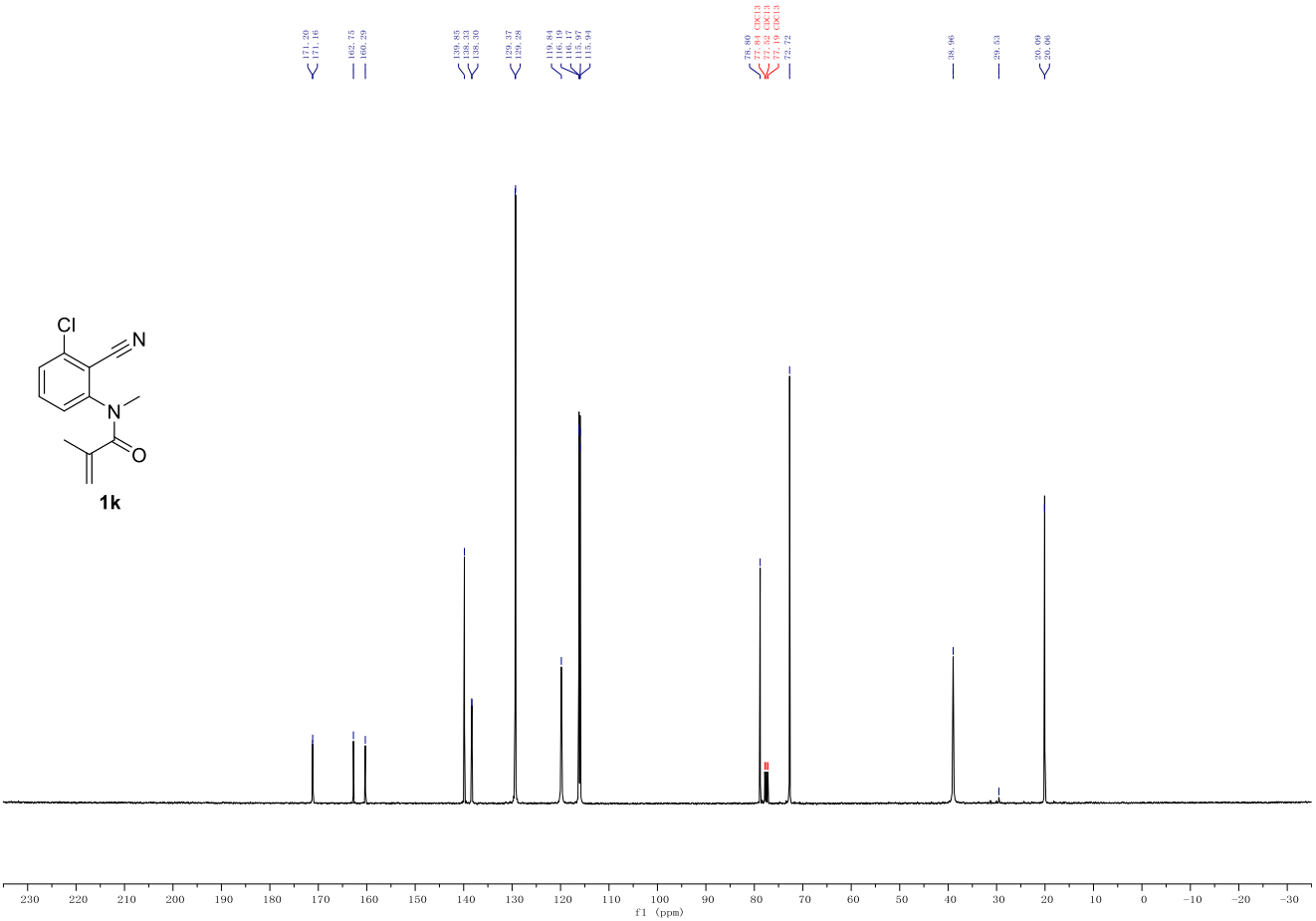
^{1}H NMR Spectrum of Compound 1j



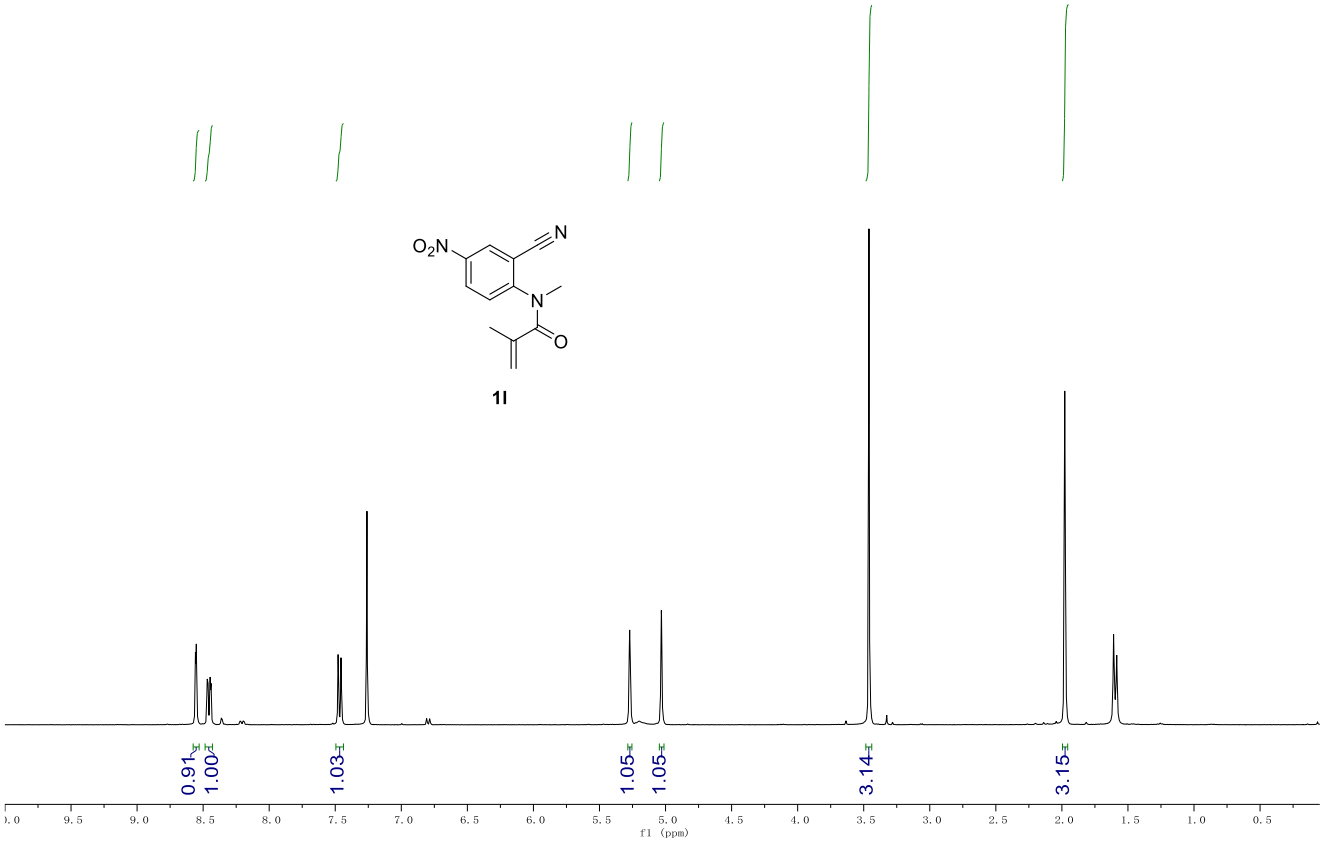
^{13}C NMR Spectrum of Compound 1j



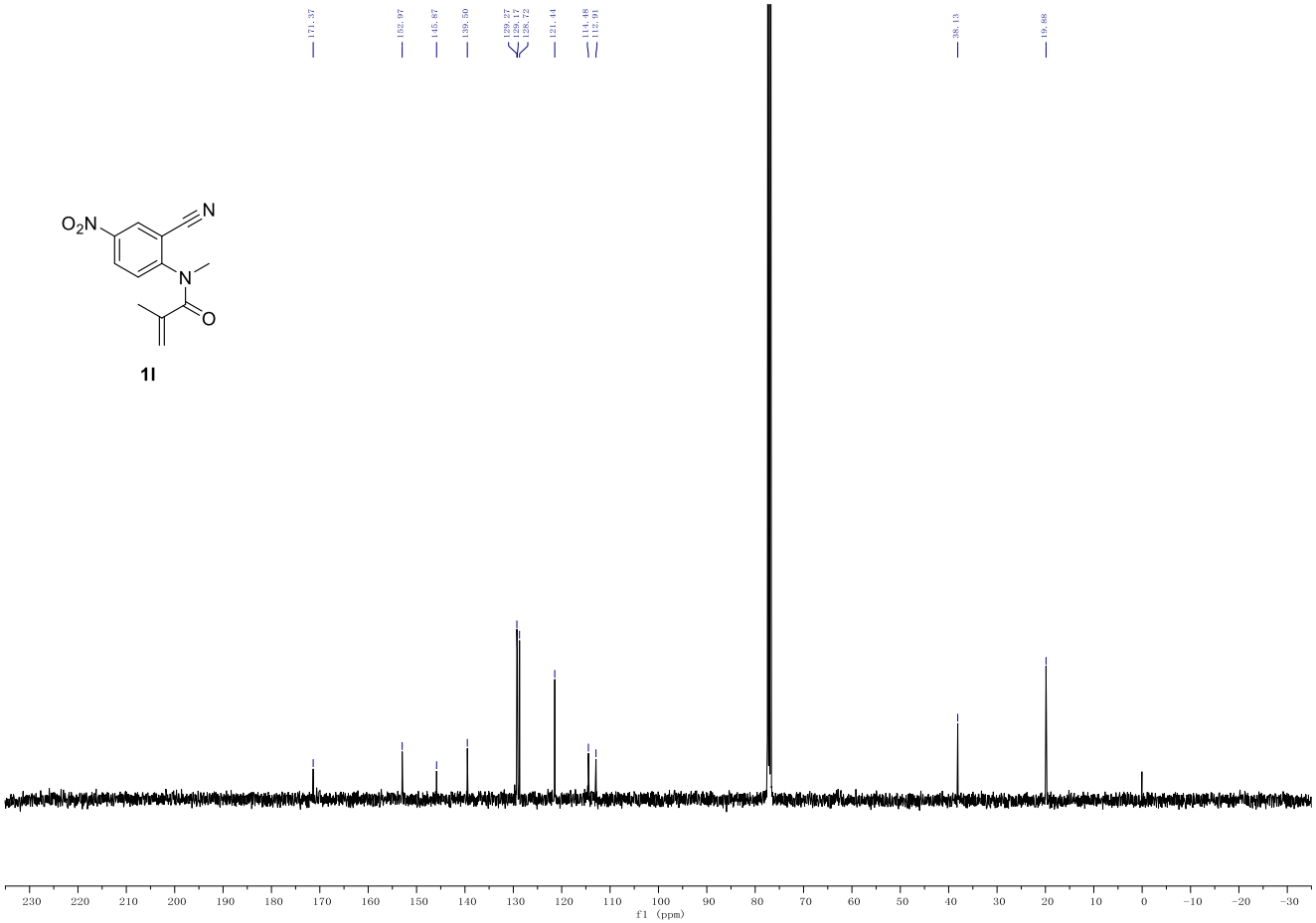
^{1}H NMR Spectrum of Compound 1k



^{13}C NMR Spectrum of Compound 1k

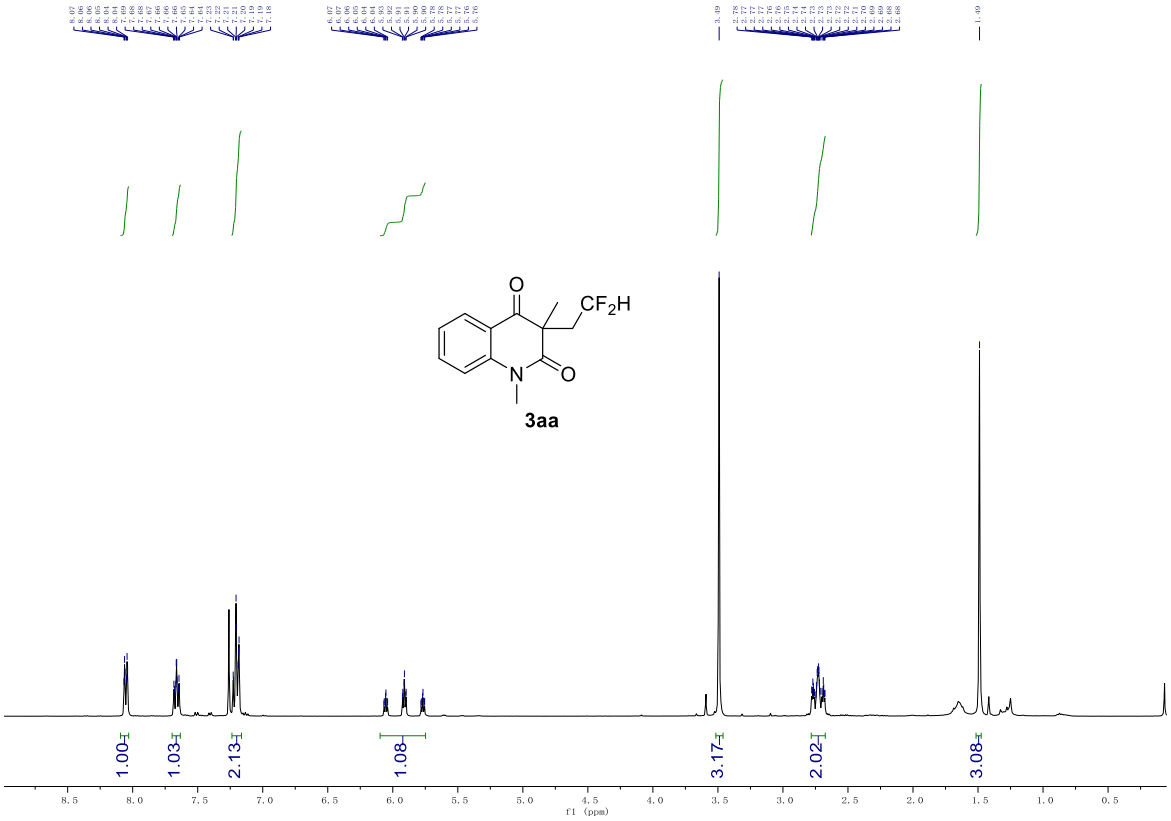


^{1}H NMR Spectrum of Compound 1l

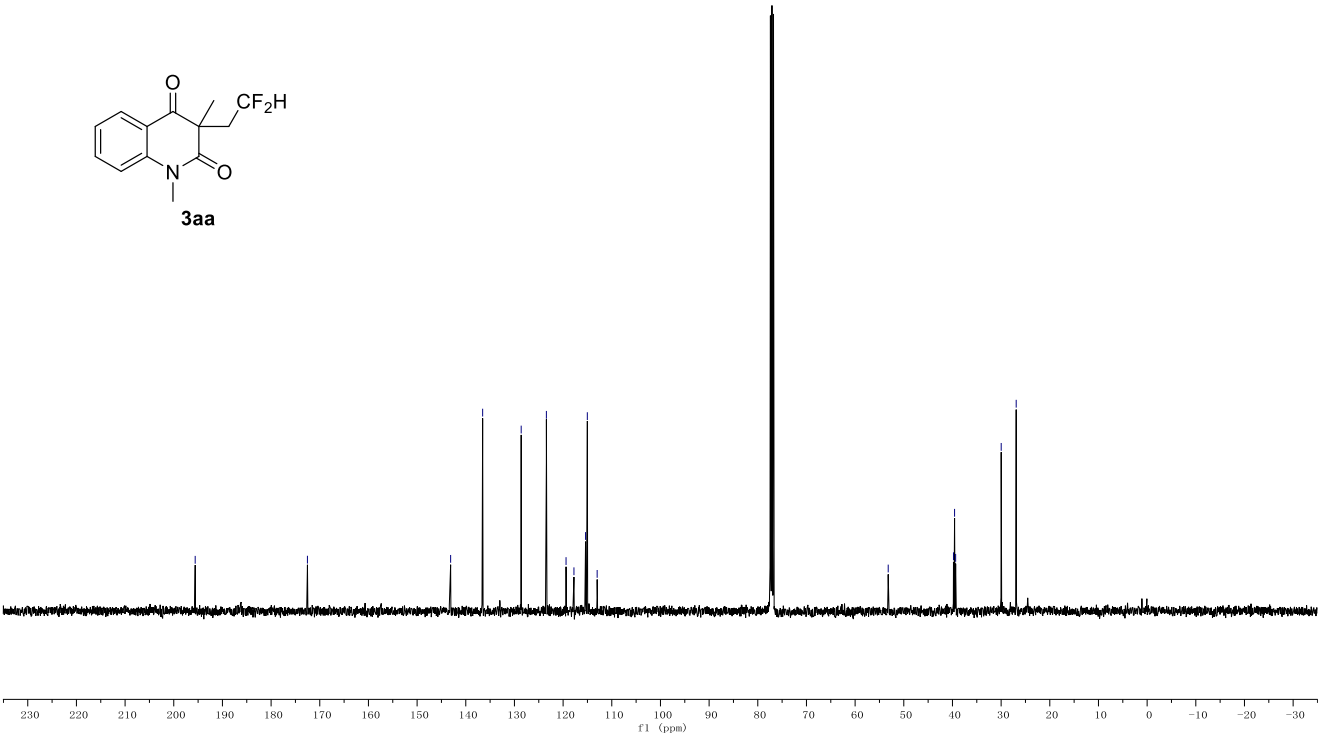


^{13}C NMR Spectrum of Compound 1l

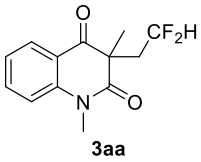
9 Copies of ^{1}H, ^{13}C and ^{19}F NMR Spectra for Products



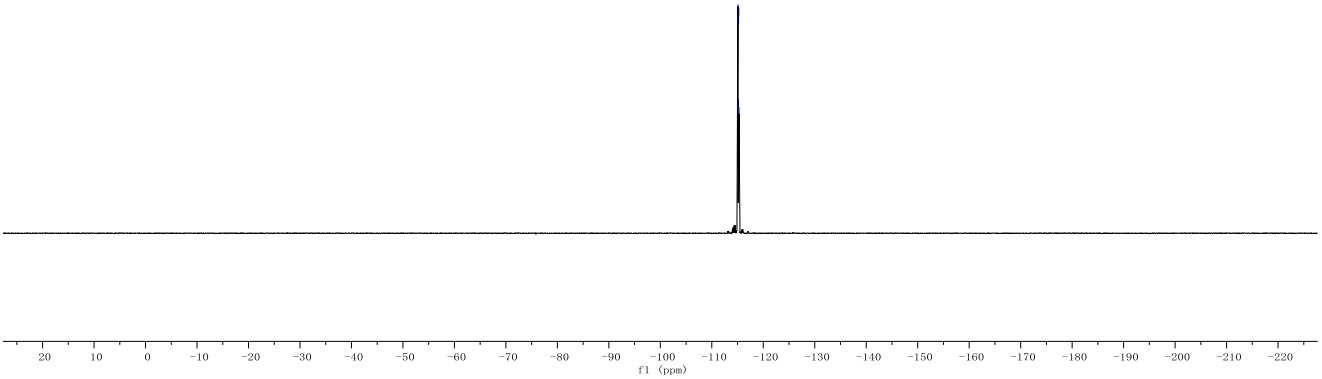
^{1}H NMR Spectrum of Compound 3aa



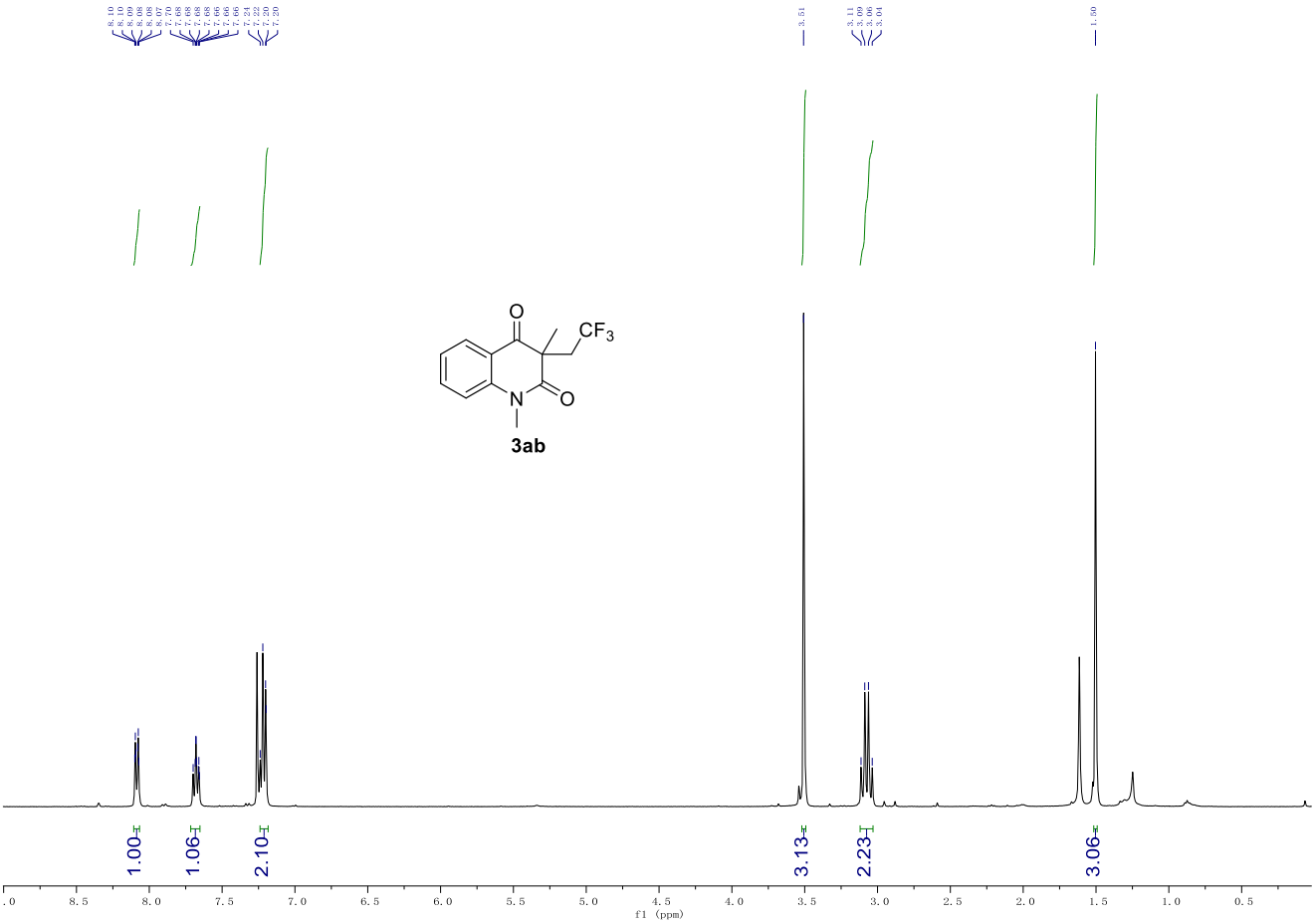
^{13}C NMR Spectrum of Compound 3aa



3aa

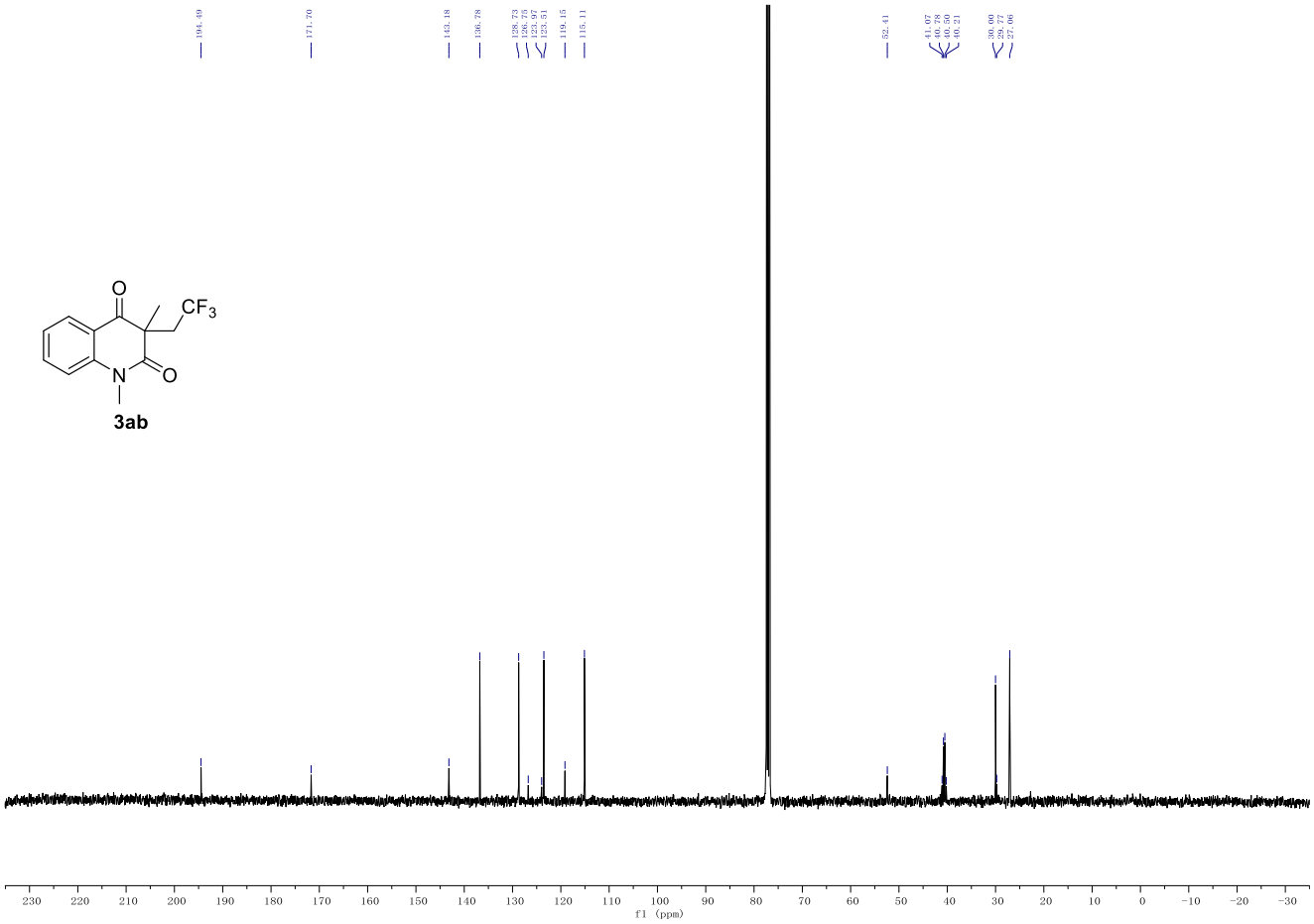


^{19}F NMR Spectrum of Compound 3aa

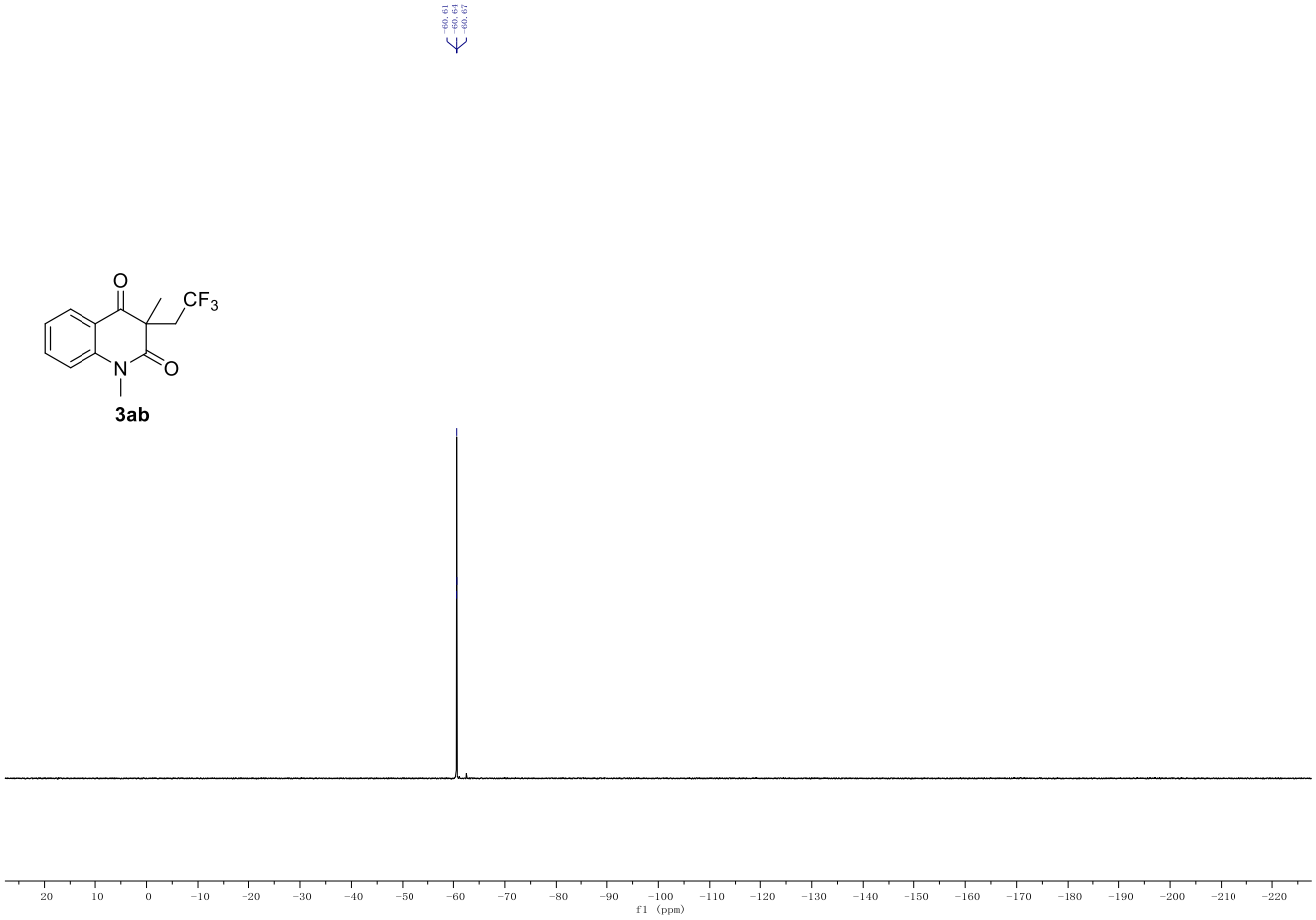


3ab

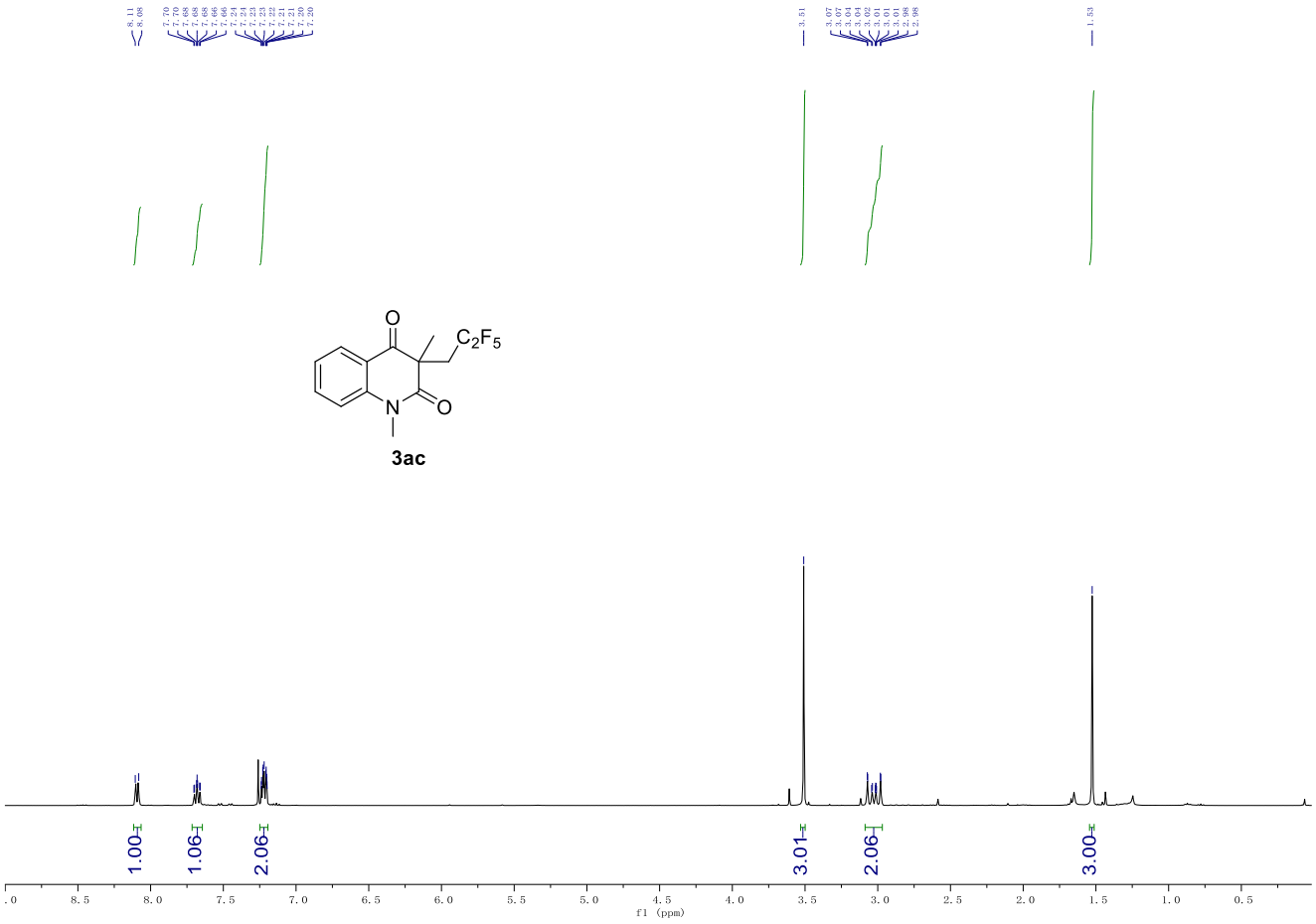
^{1}H NMR Spectrum of Compound 3ab



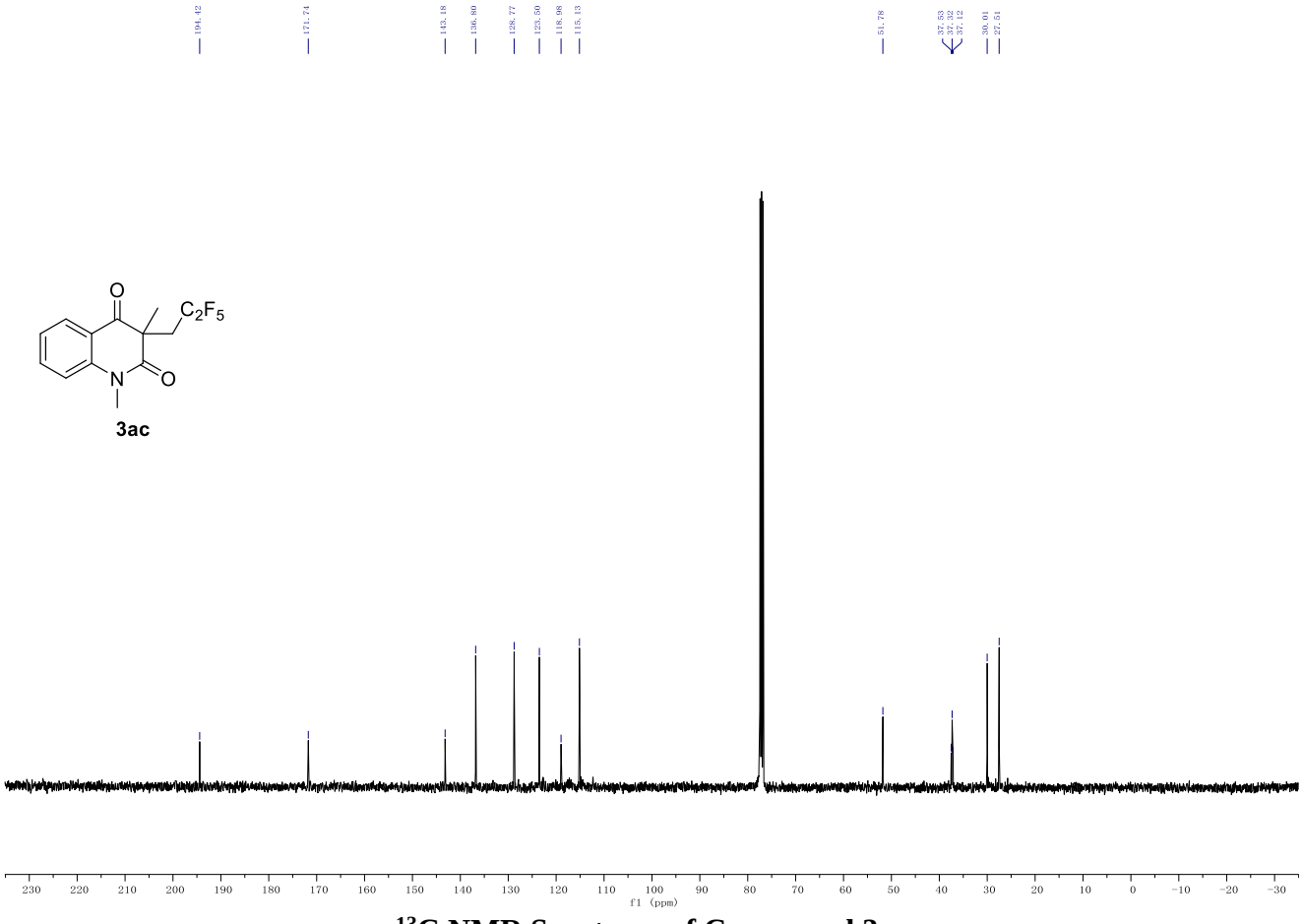
^{13}C NMR Spectrum of Compound 3ab



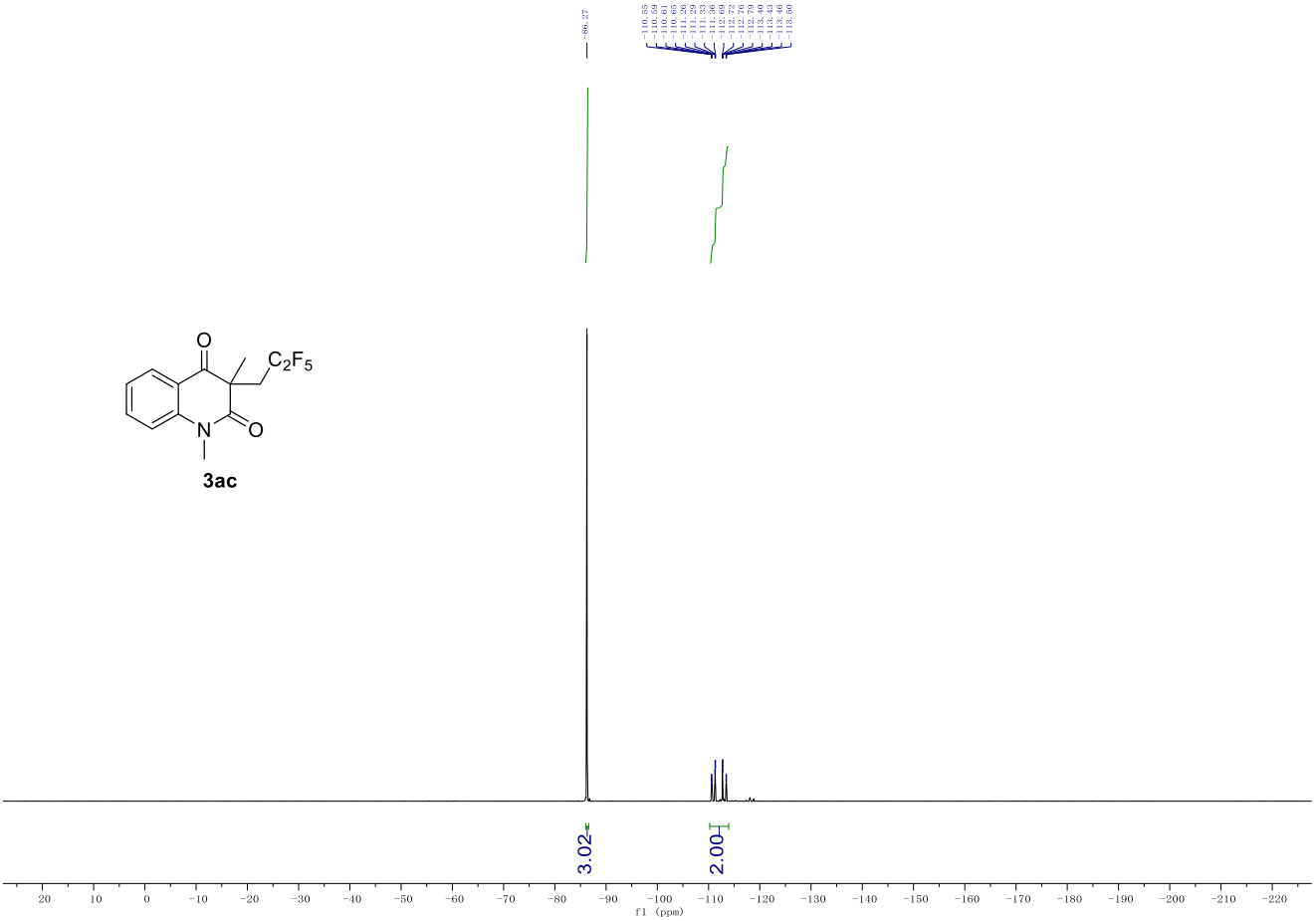
^{19}F NMR Spectrum of Compound 3ab



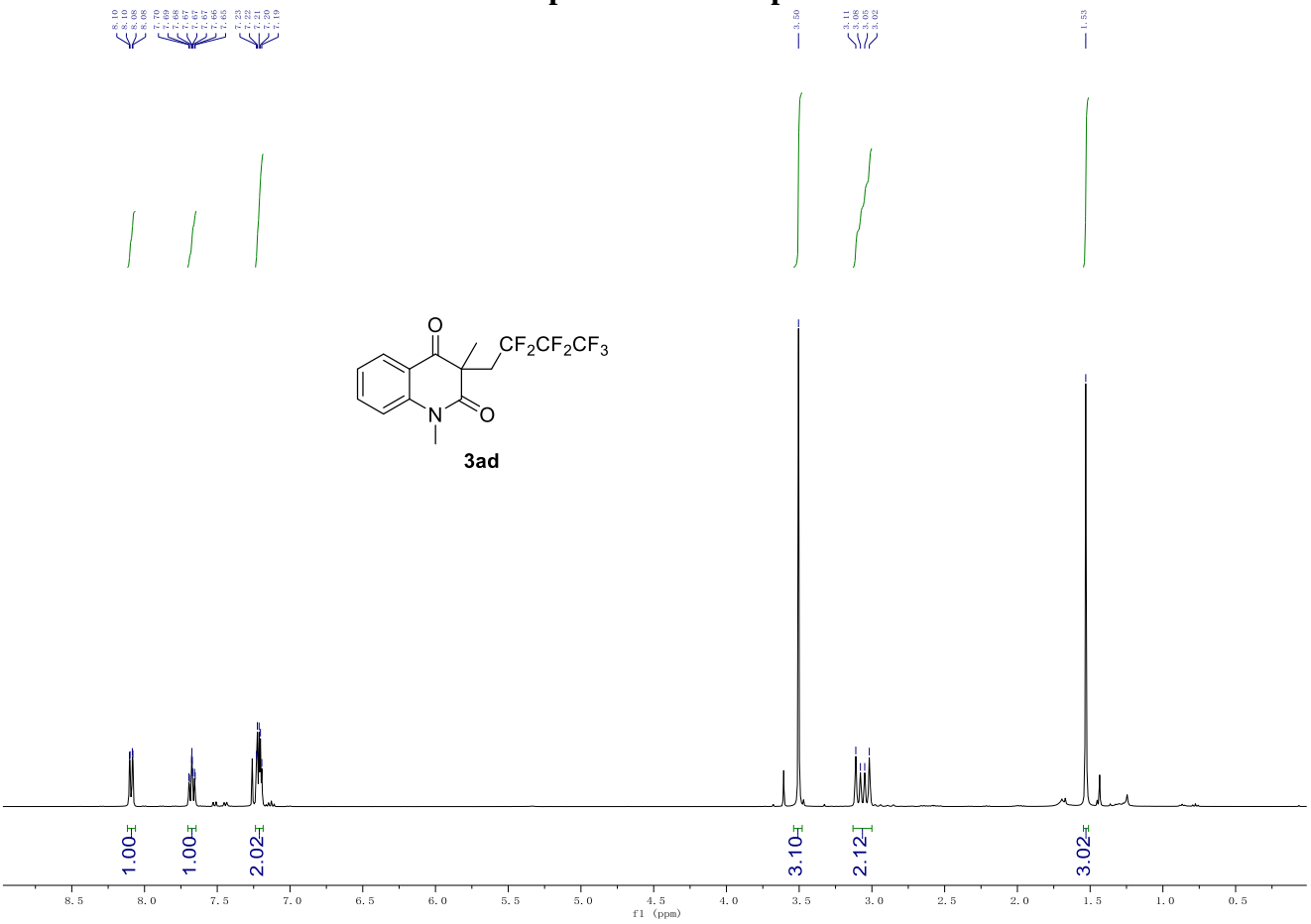
^{1}H NMR Spectrum of Compound 3ac



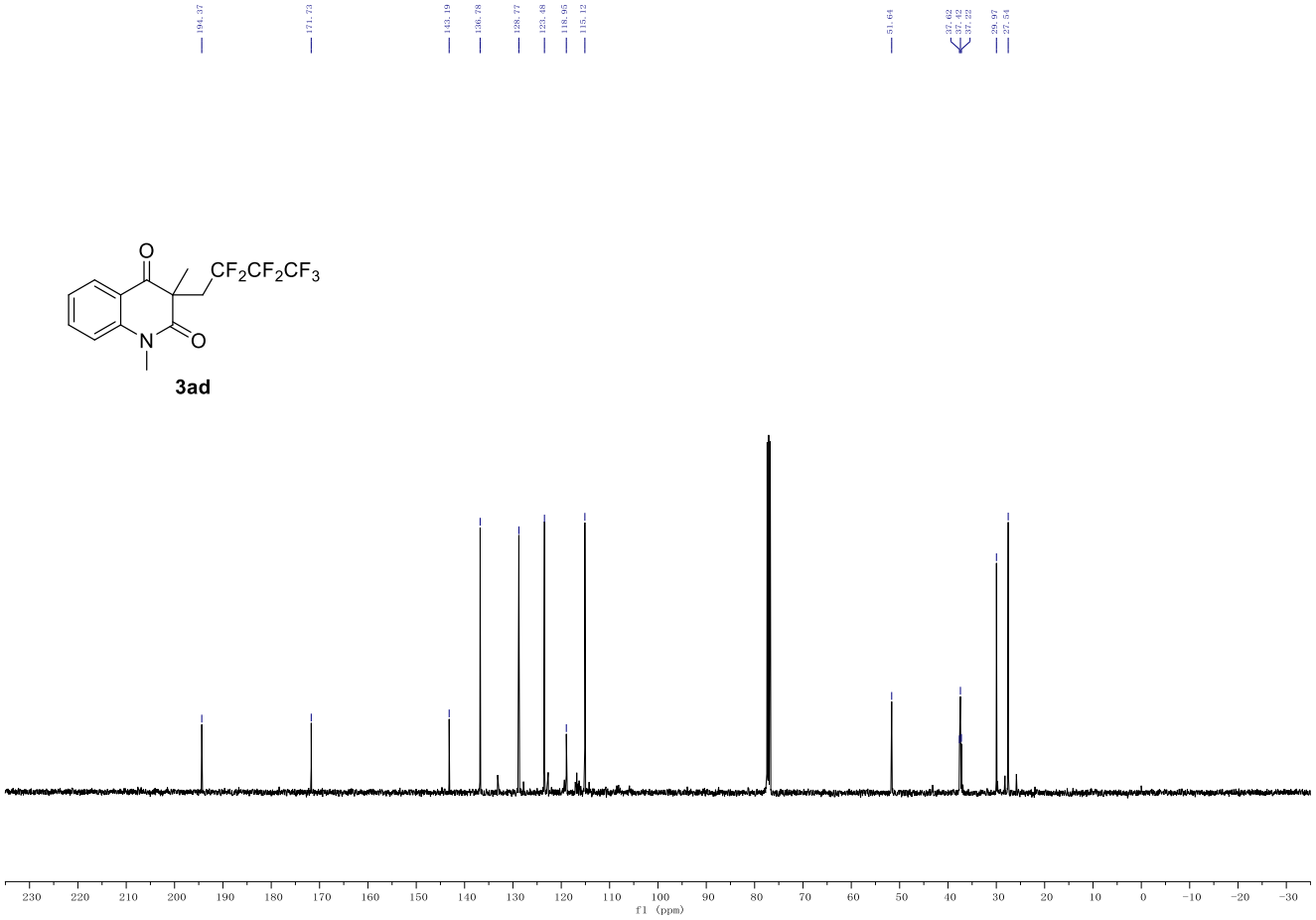
^{13}C NMR Spectrum of Compound 3ac



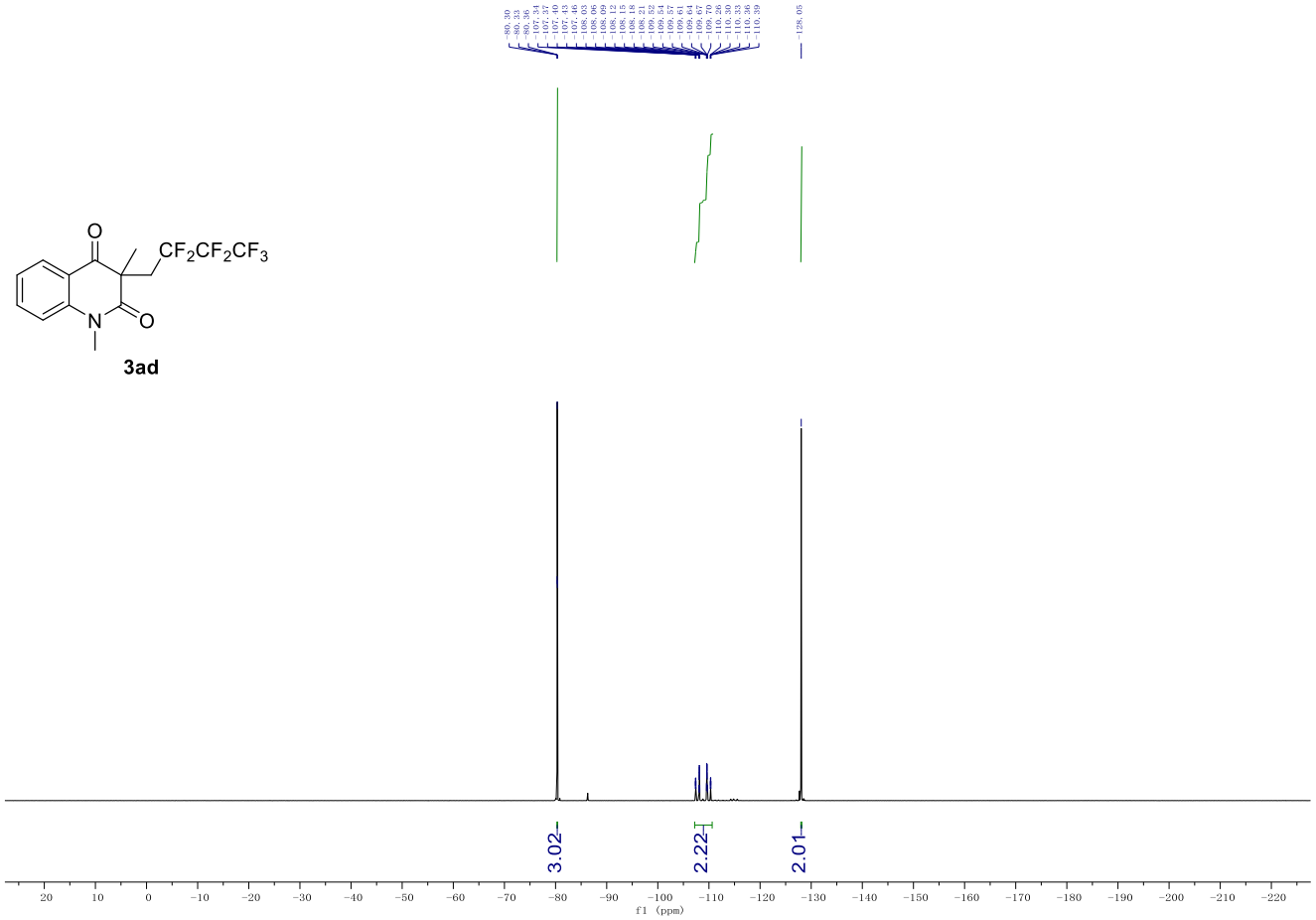
^{19}F NMR Spectrum of Compound 3ac



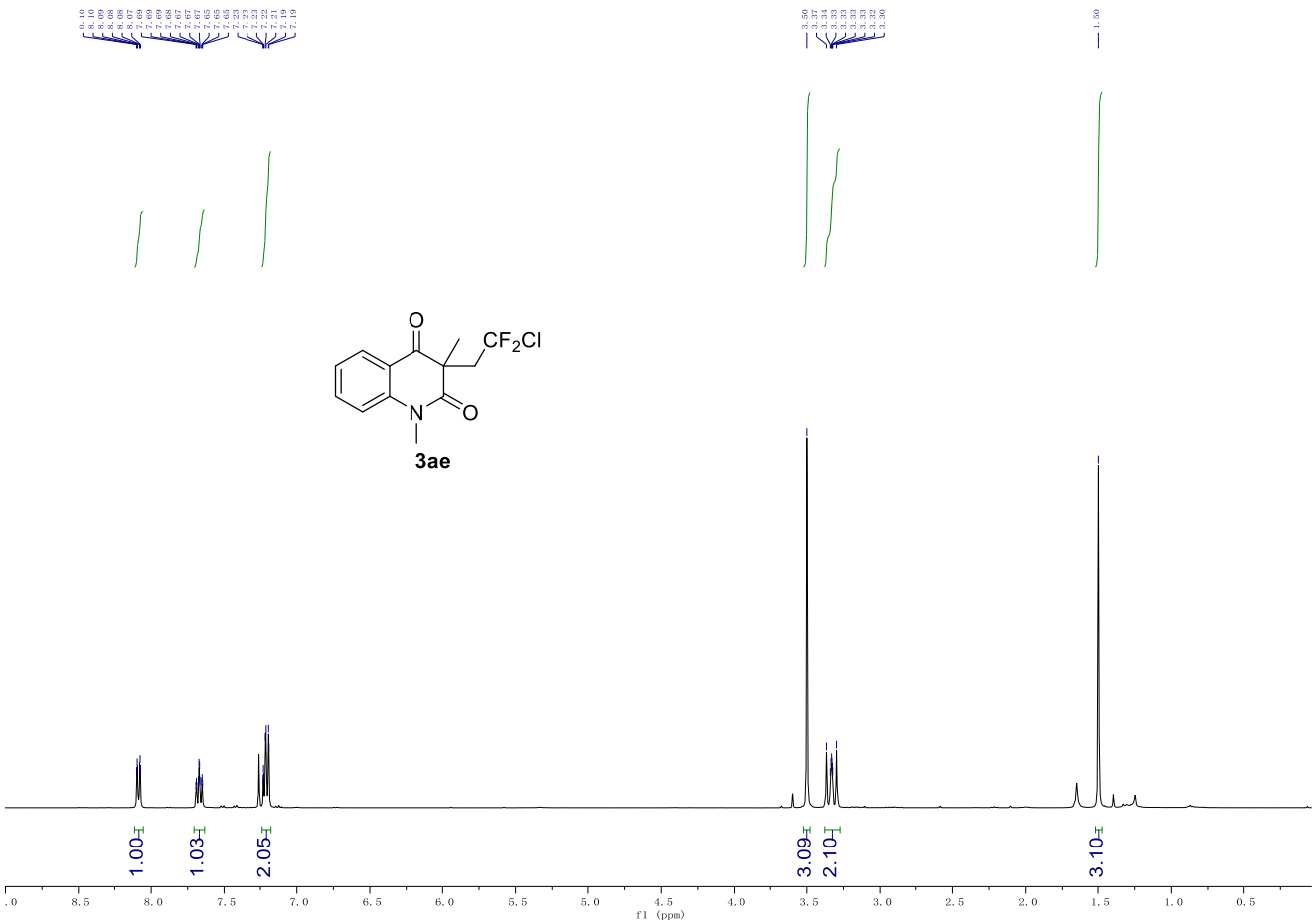
^{1}H NMR Spectrum of Compound 3ad



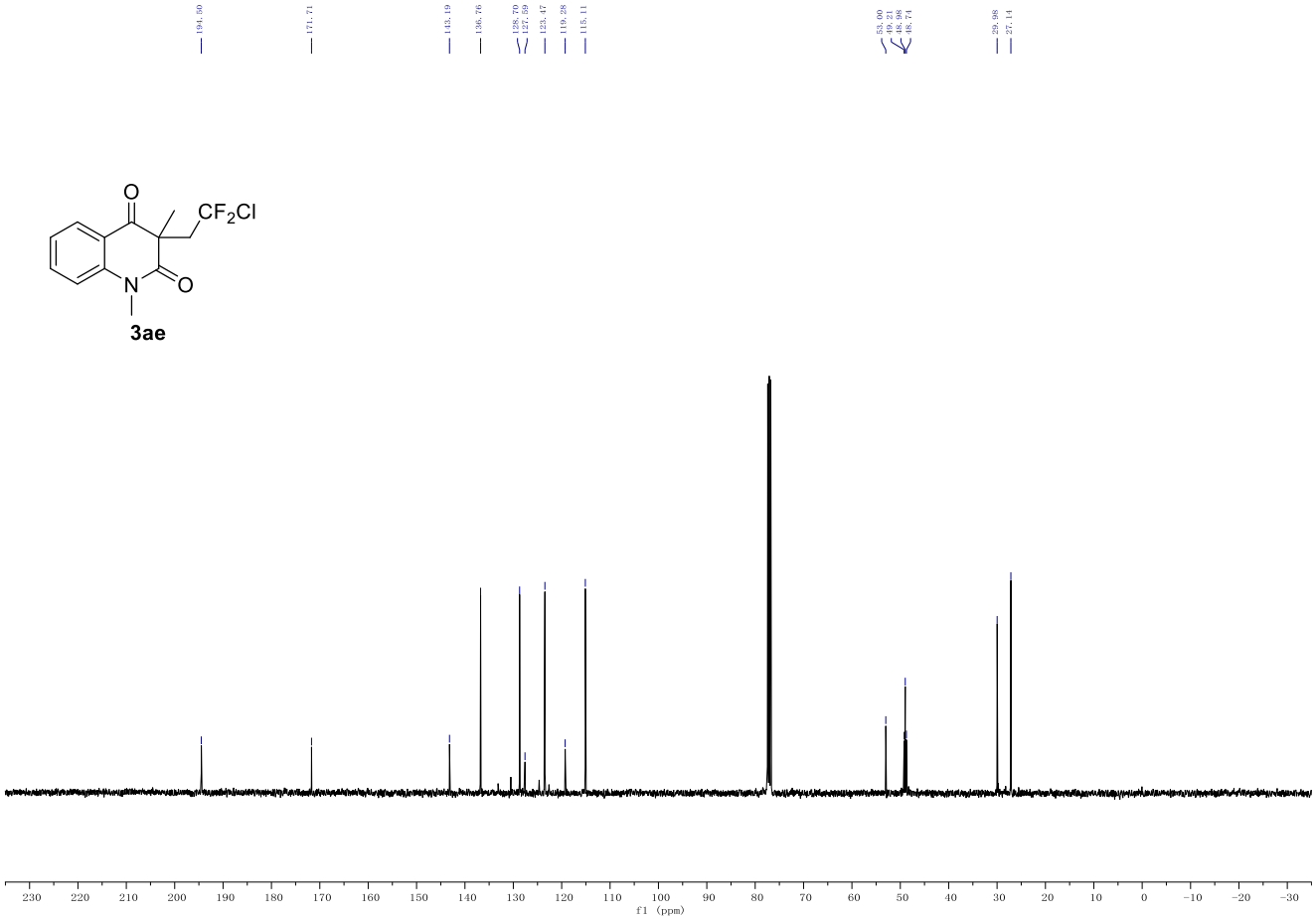
^{13}C NMR Spectrum of Compound 3ad



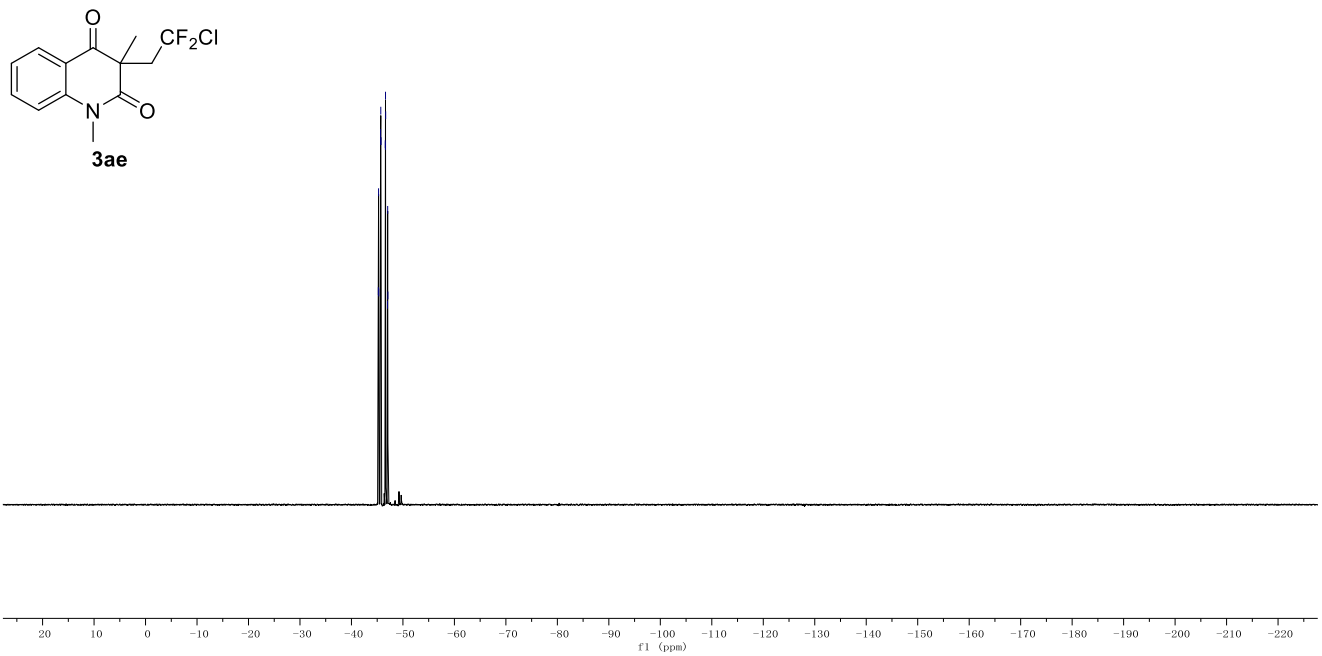
^{19}F NMR Spectrum of Compound 3ad



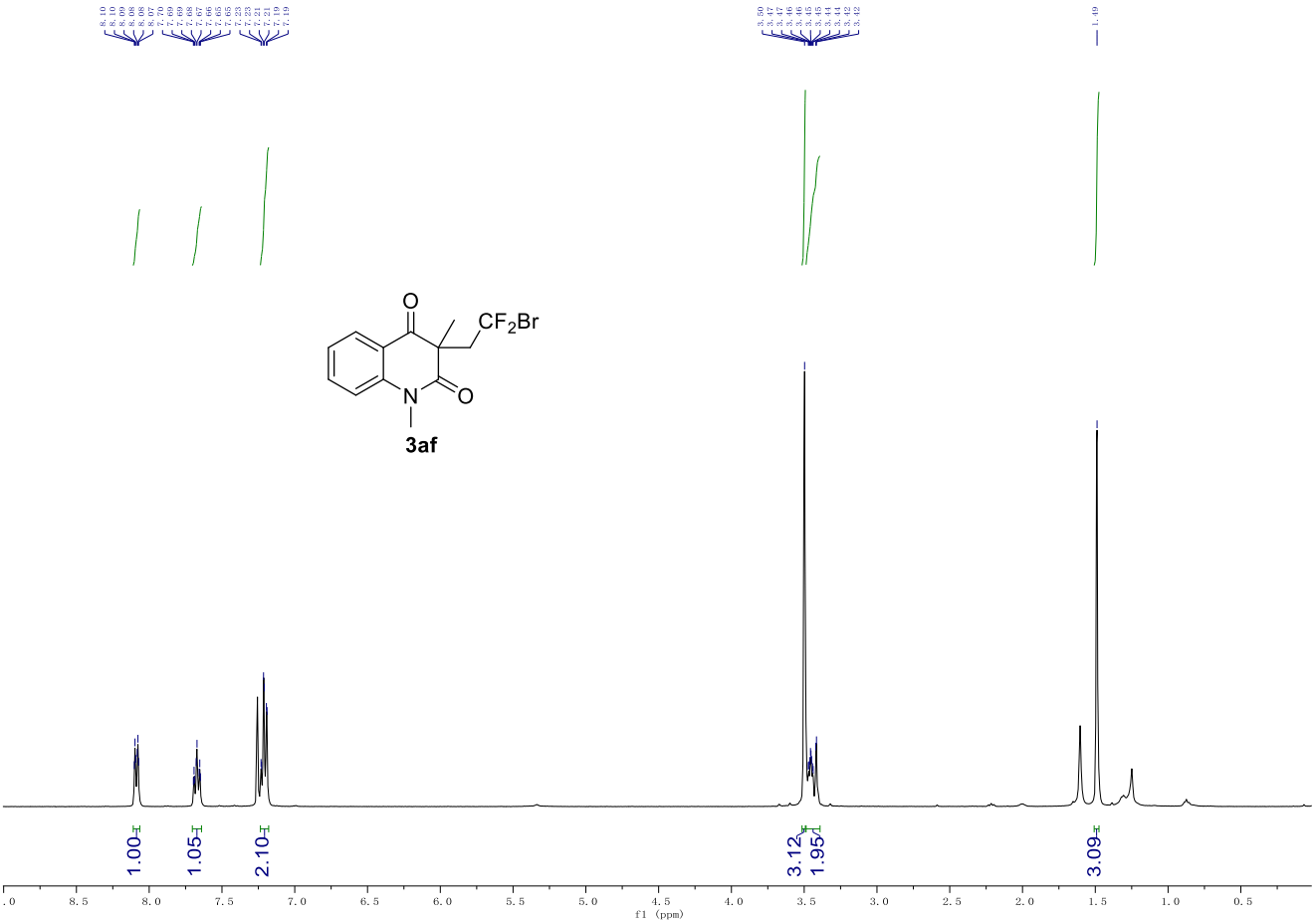
^{1}H NMR Spectrum of Compound 3ae



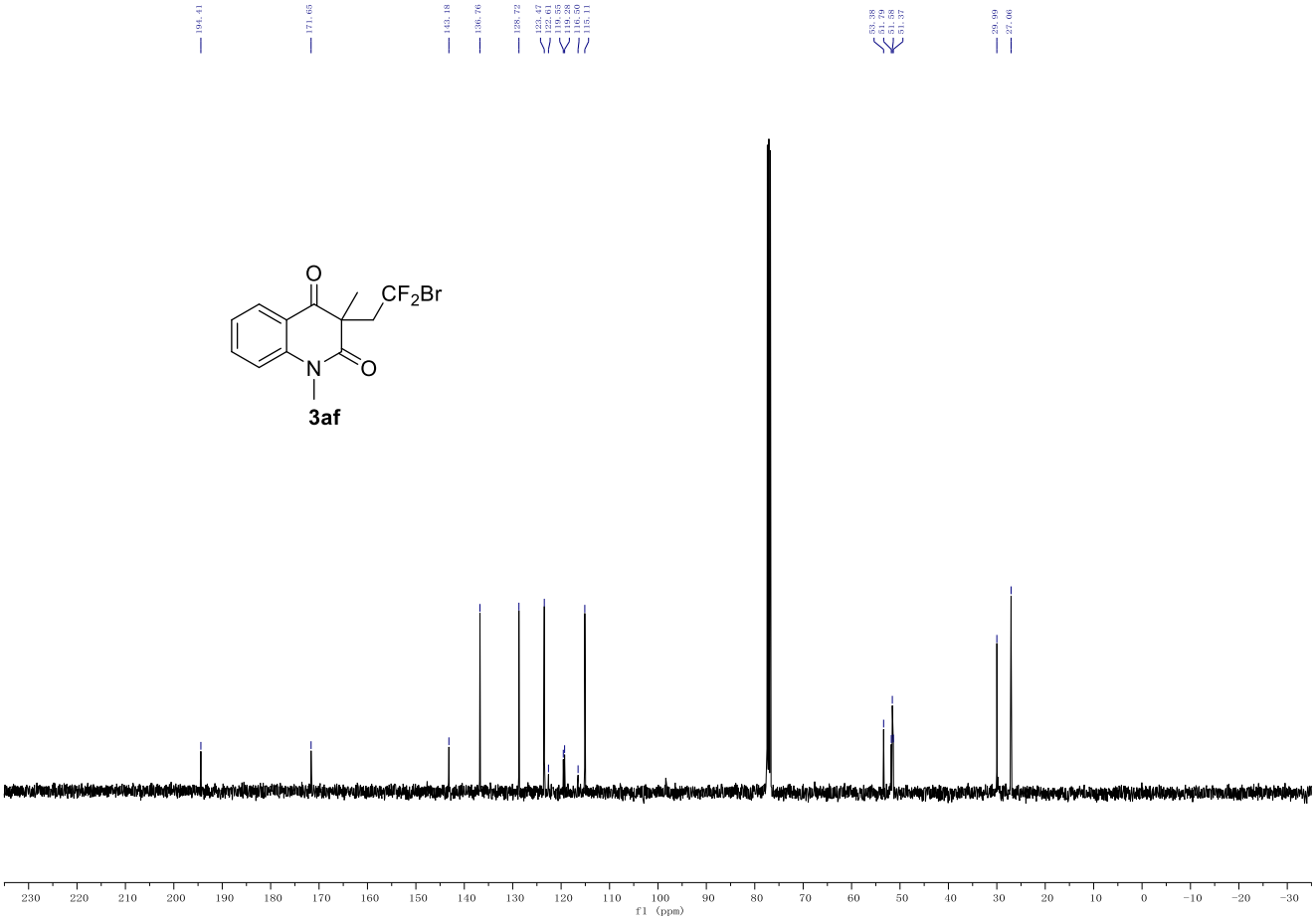
^{13}C NMR Spectrum of Compound 3ae



^{19}F NMR Spectrum of Compound 3ae



^{1}H NMR Spectrum of Compound 3af



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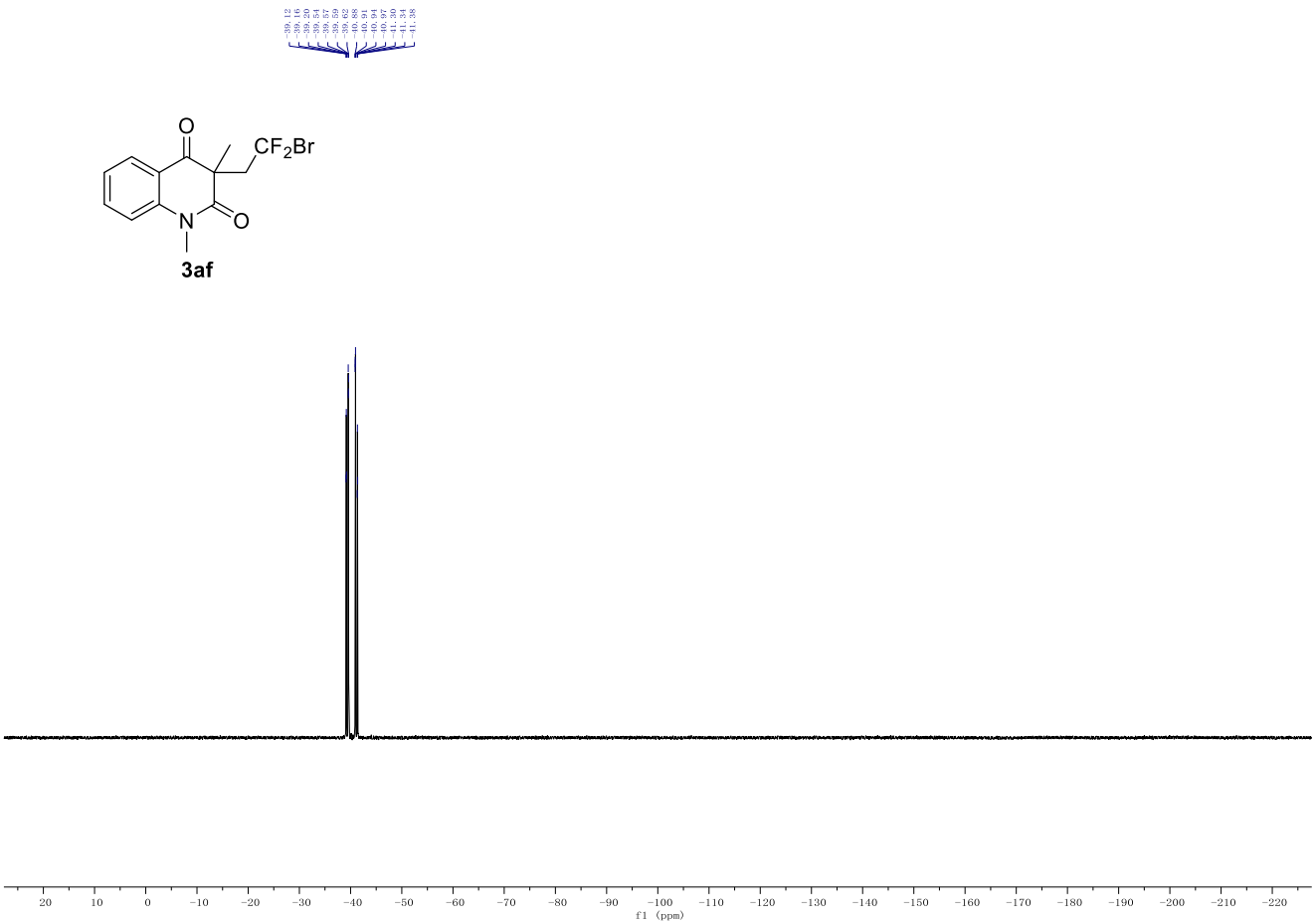
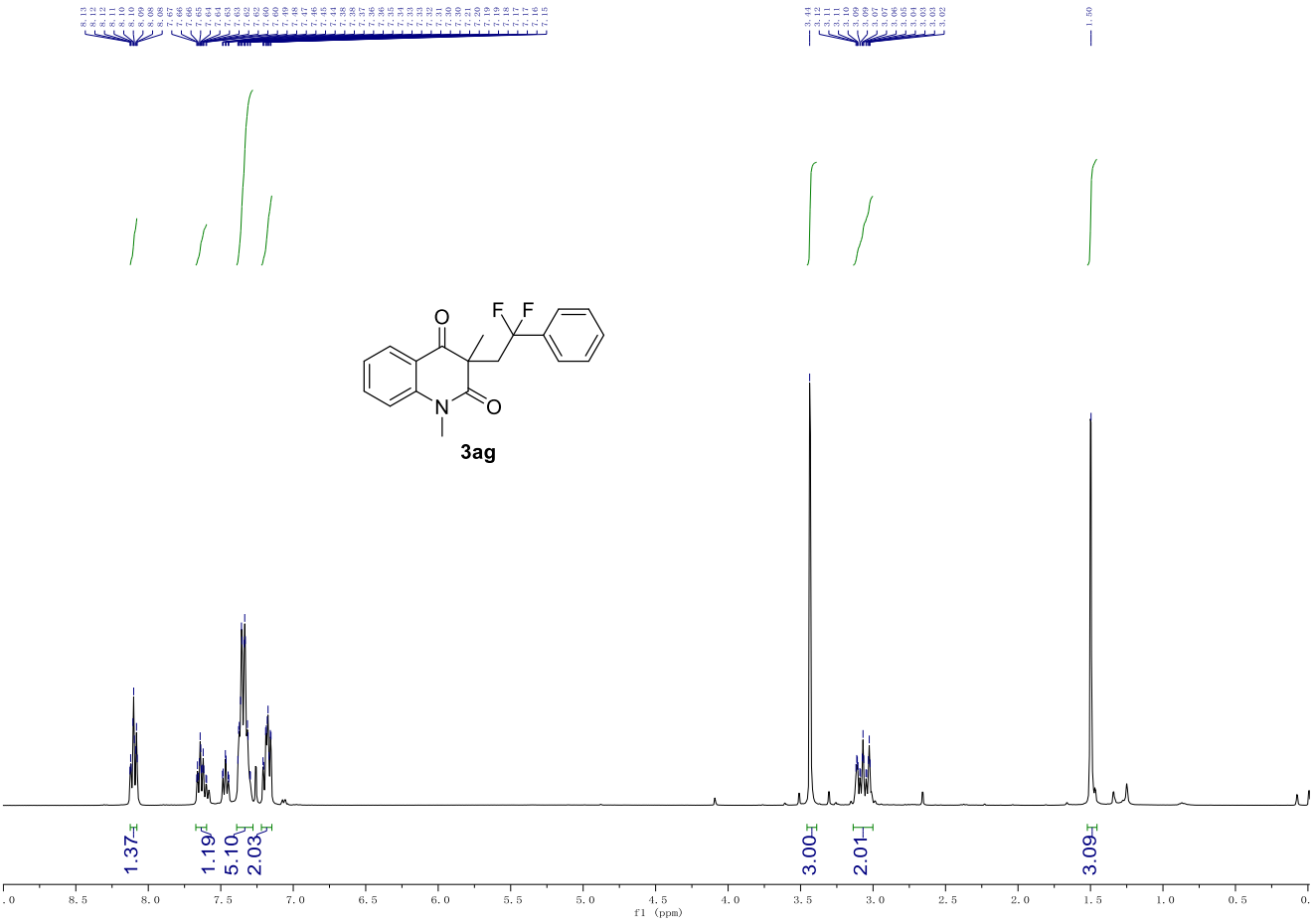


^{19}F NMR Spectrum of Compound 3af



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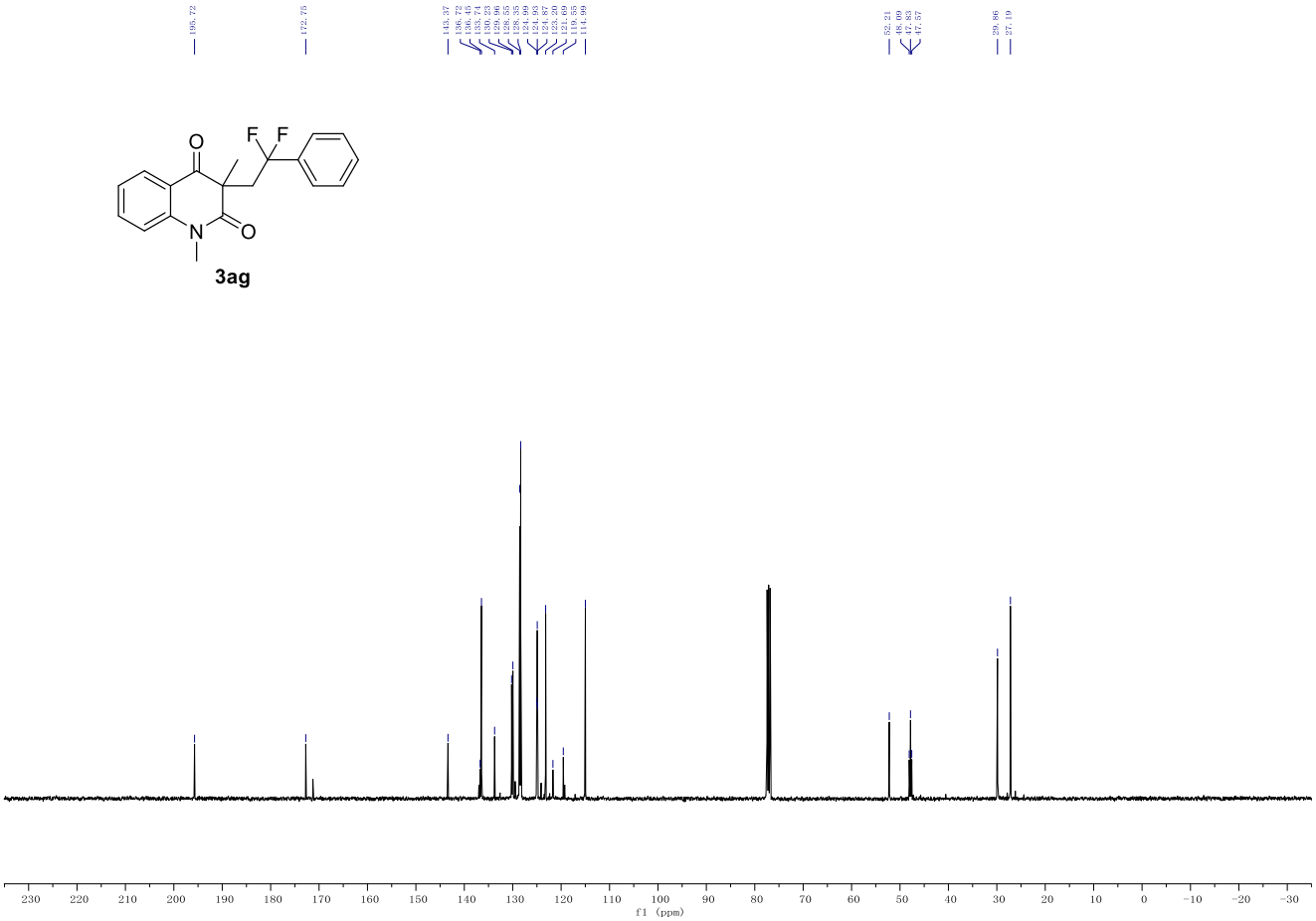
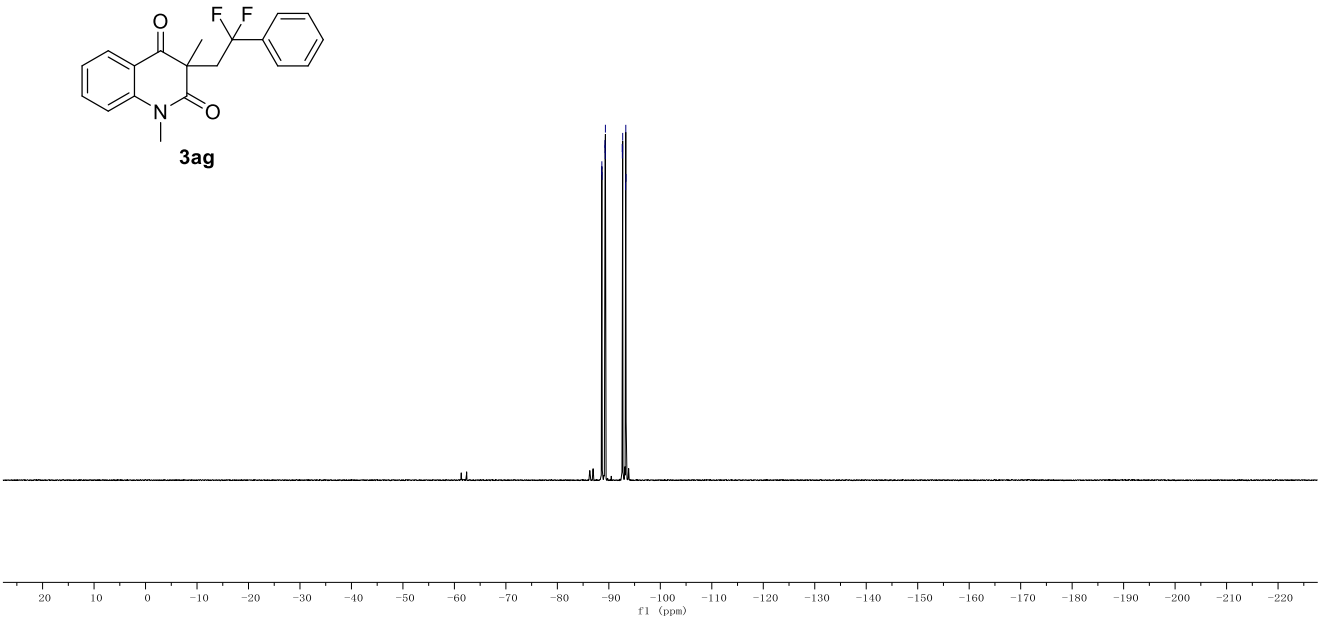
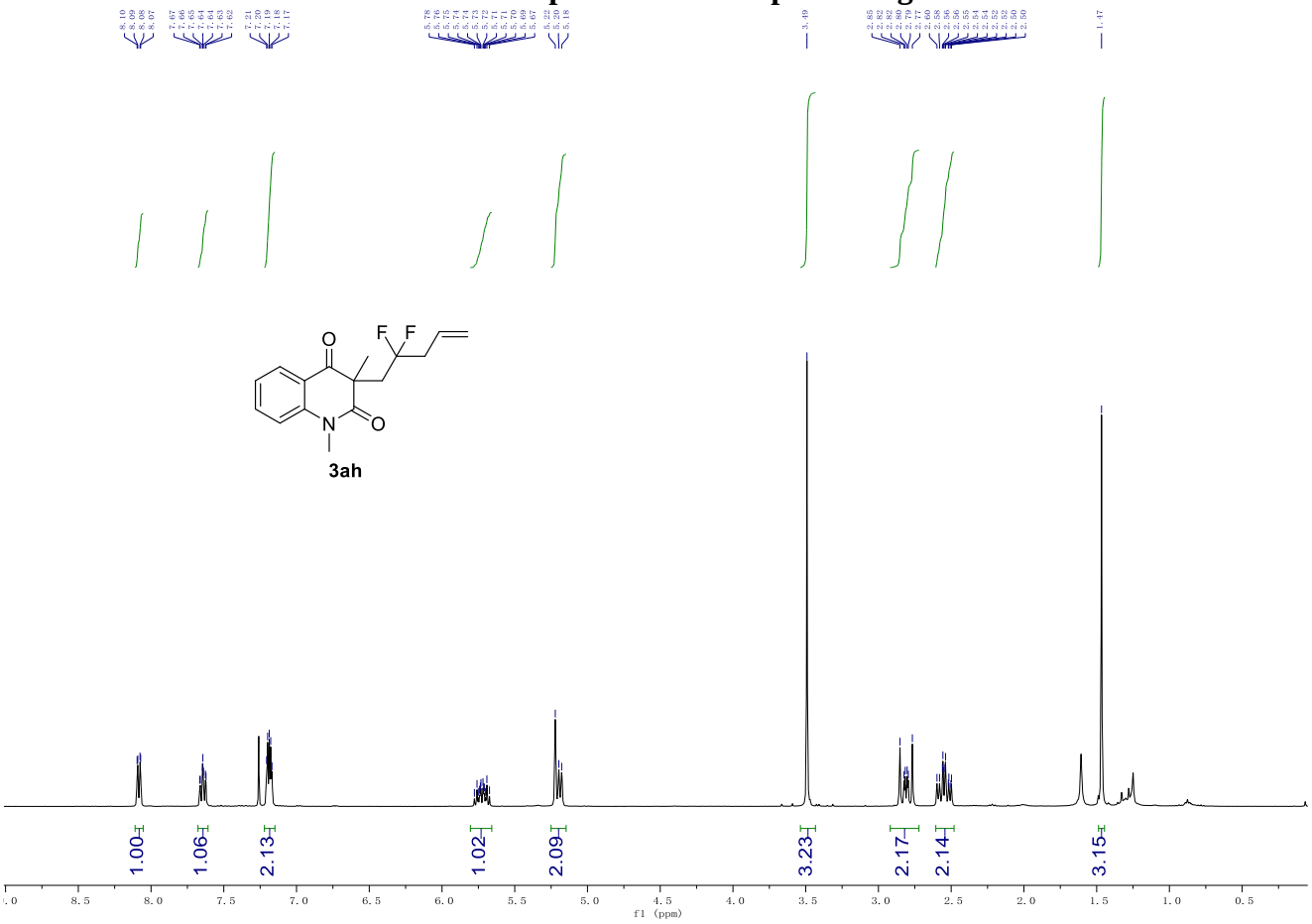


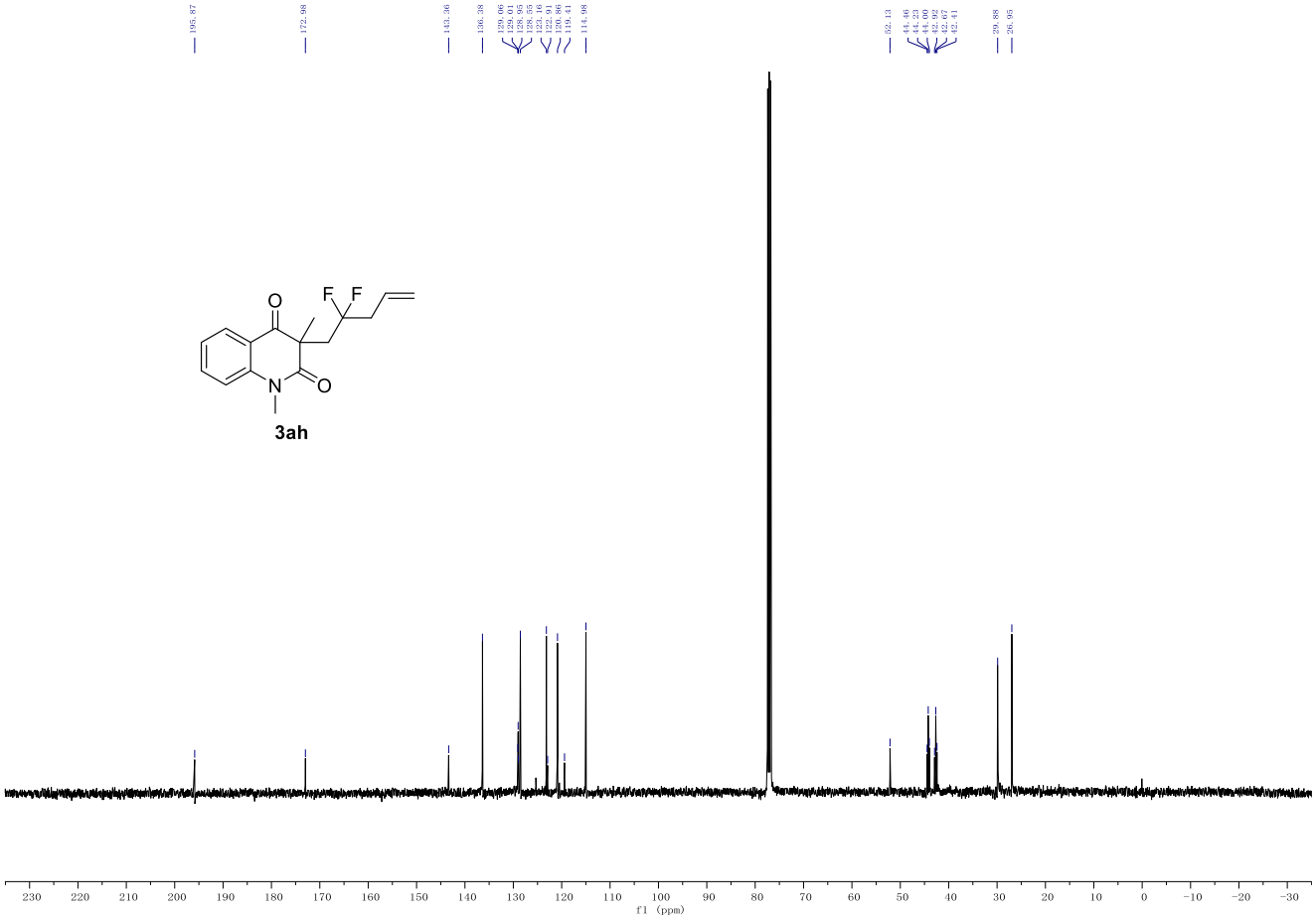
^{13}C NMR Spectrum of Compound 3ag



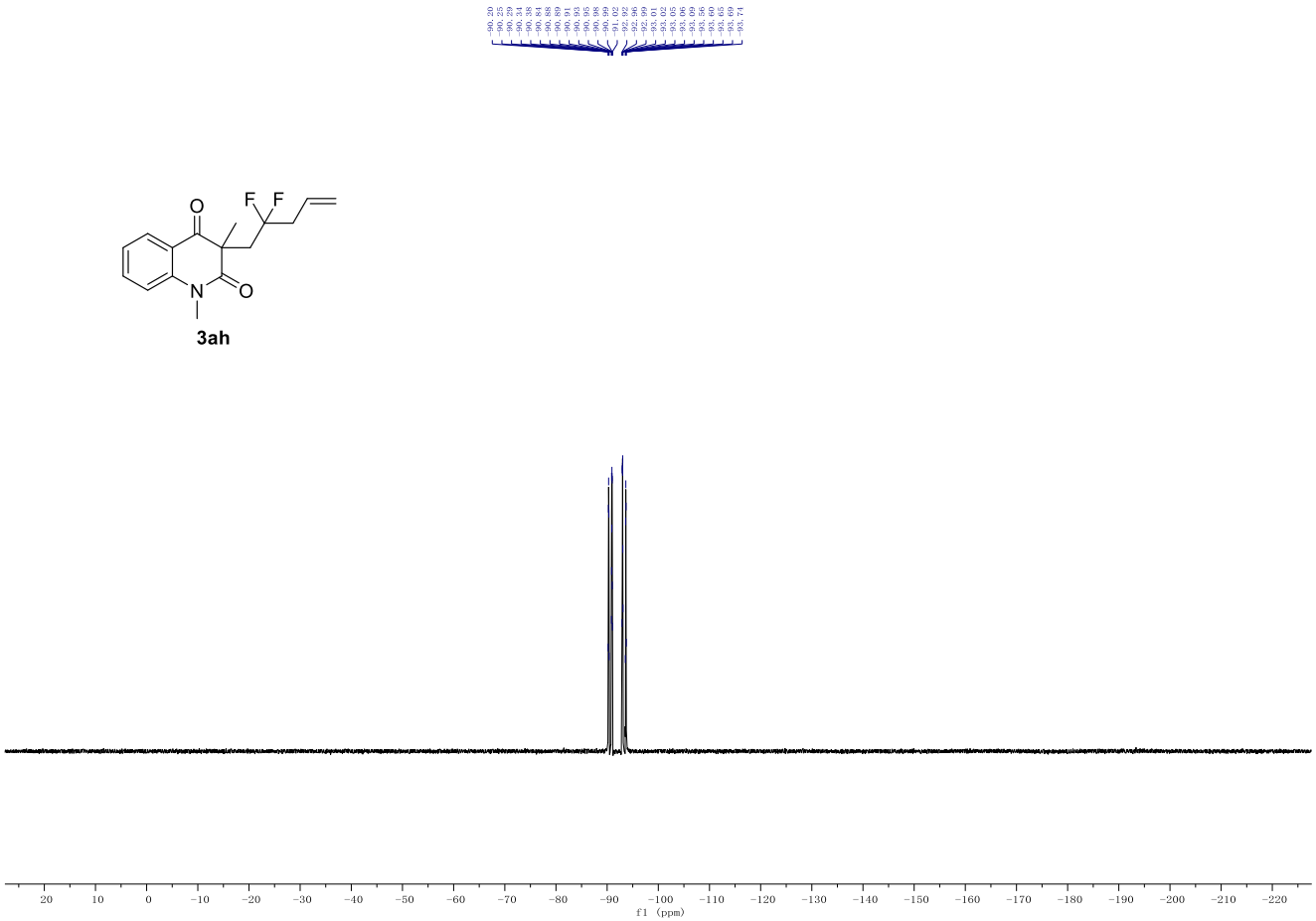
^{19}F NMR Spectrum of Compound 3ag



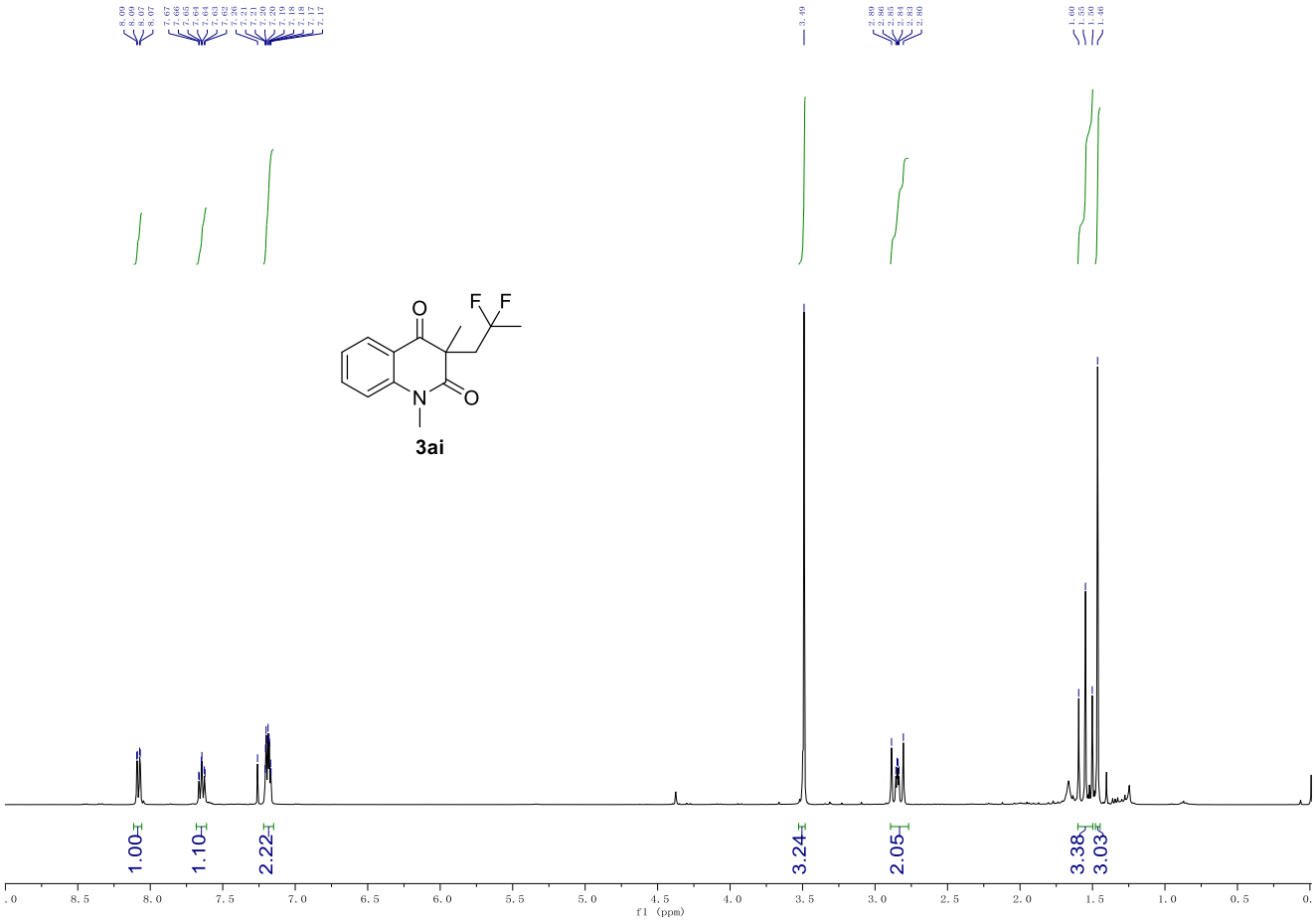
^{1}H NMR Spectrum of Compound 3ah



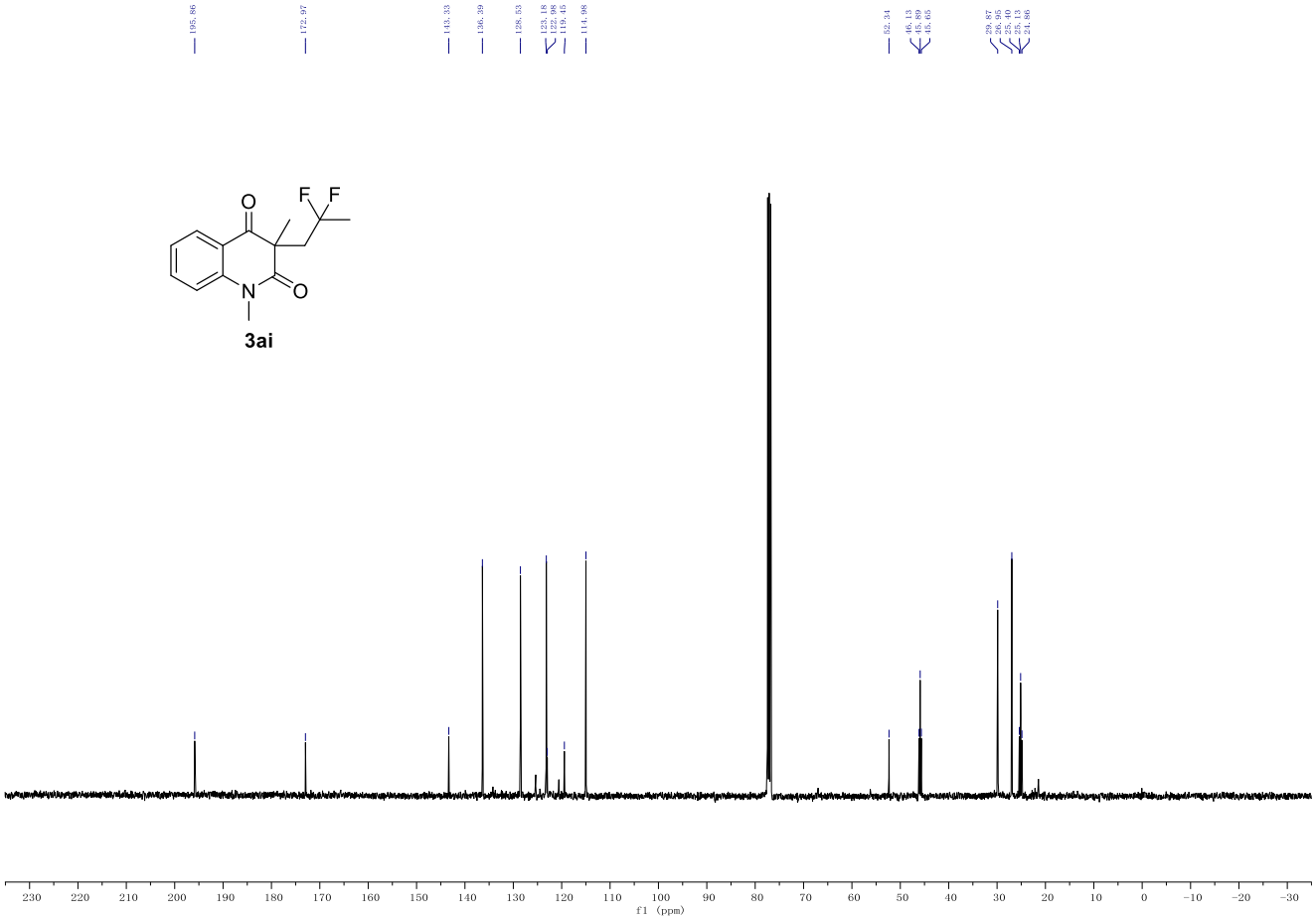
^{13}C NMR Spectrum of Compound 3ah



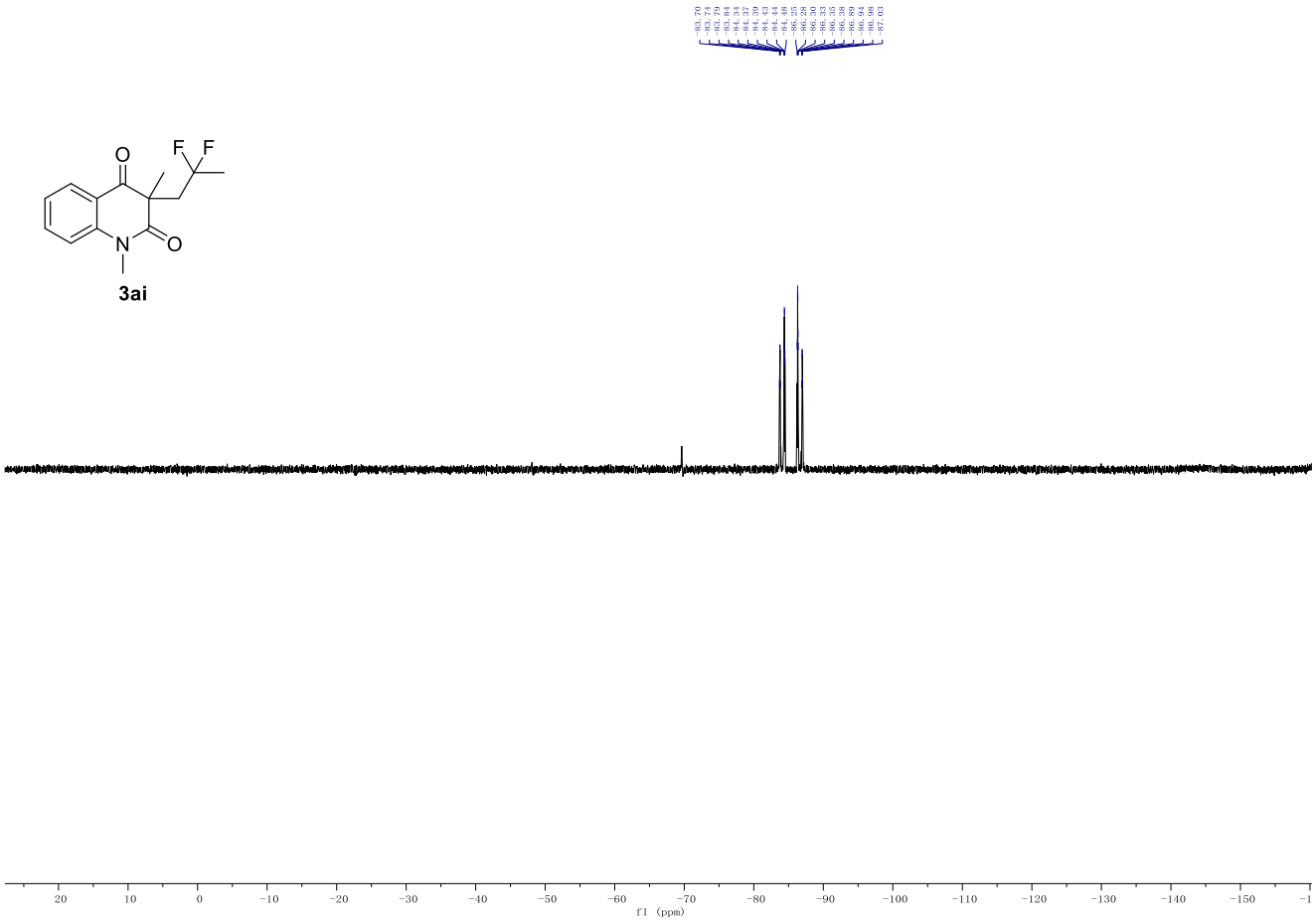
^{19}F NMR Spectrum of Compound 3ah



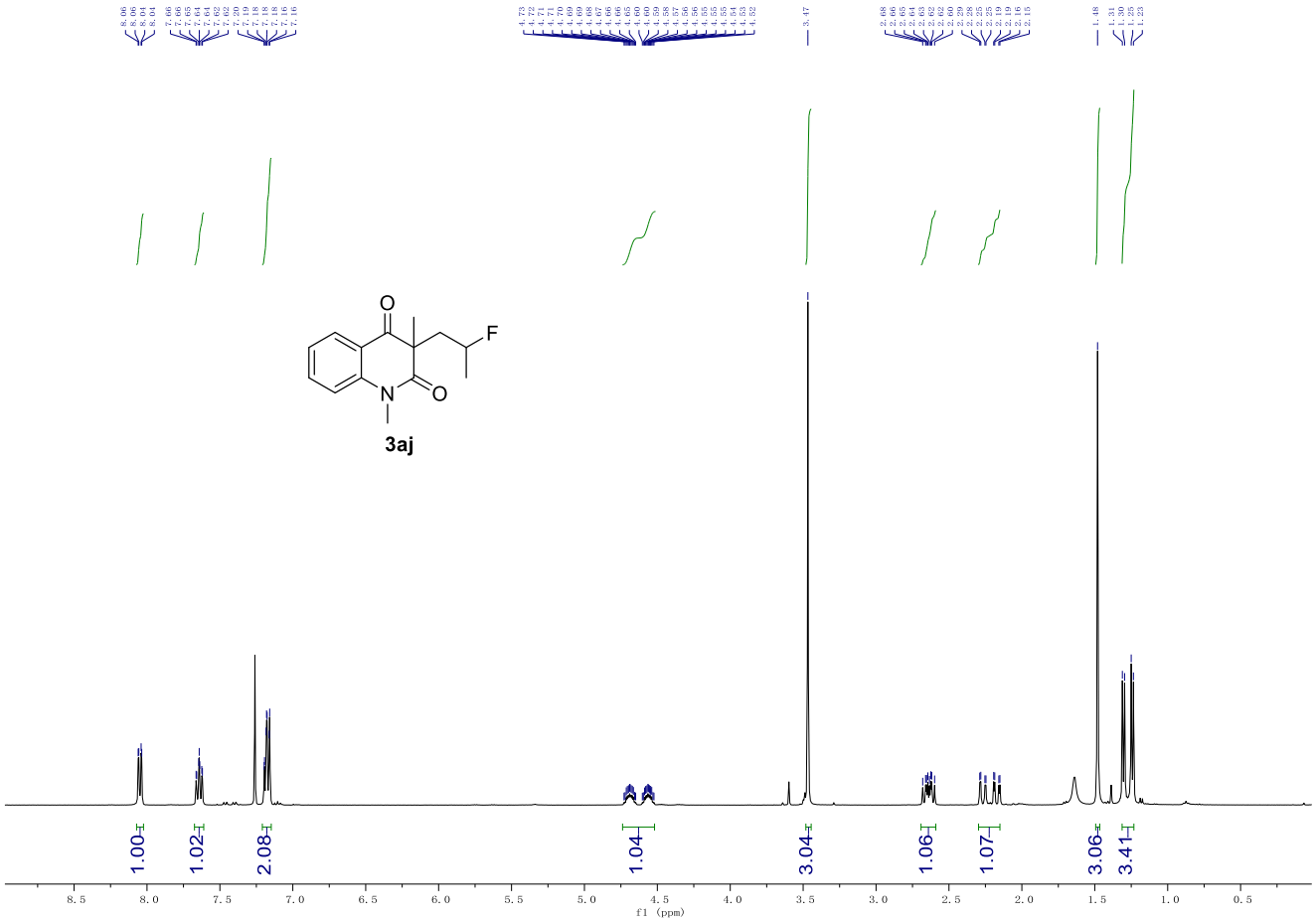
^{1}H NMR Spectrum of Compound 3ai



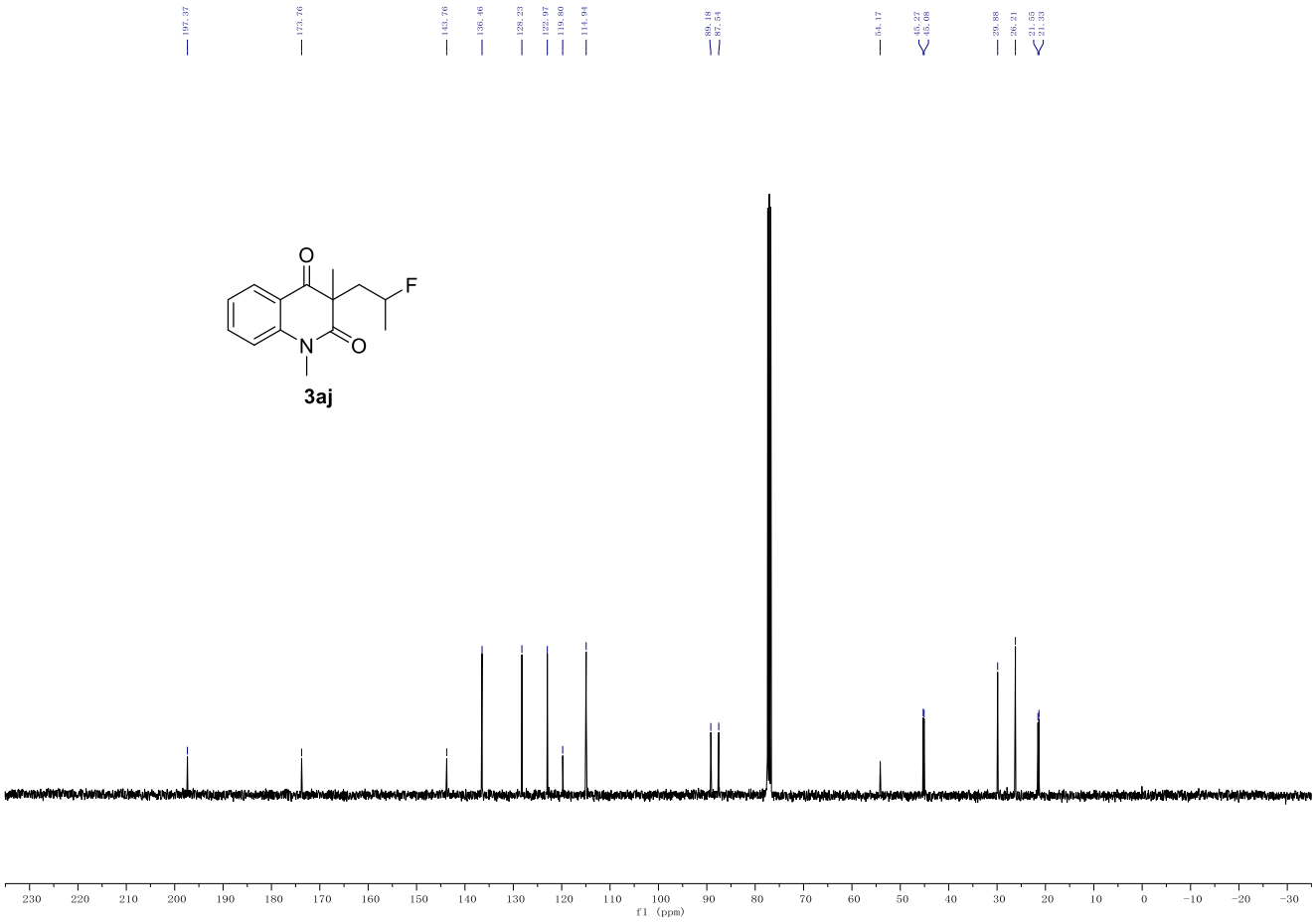
^{13}C NMR Spectrum of Compound 3ai



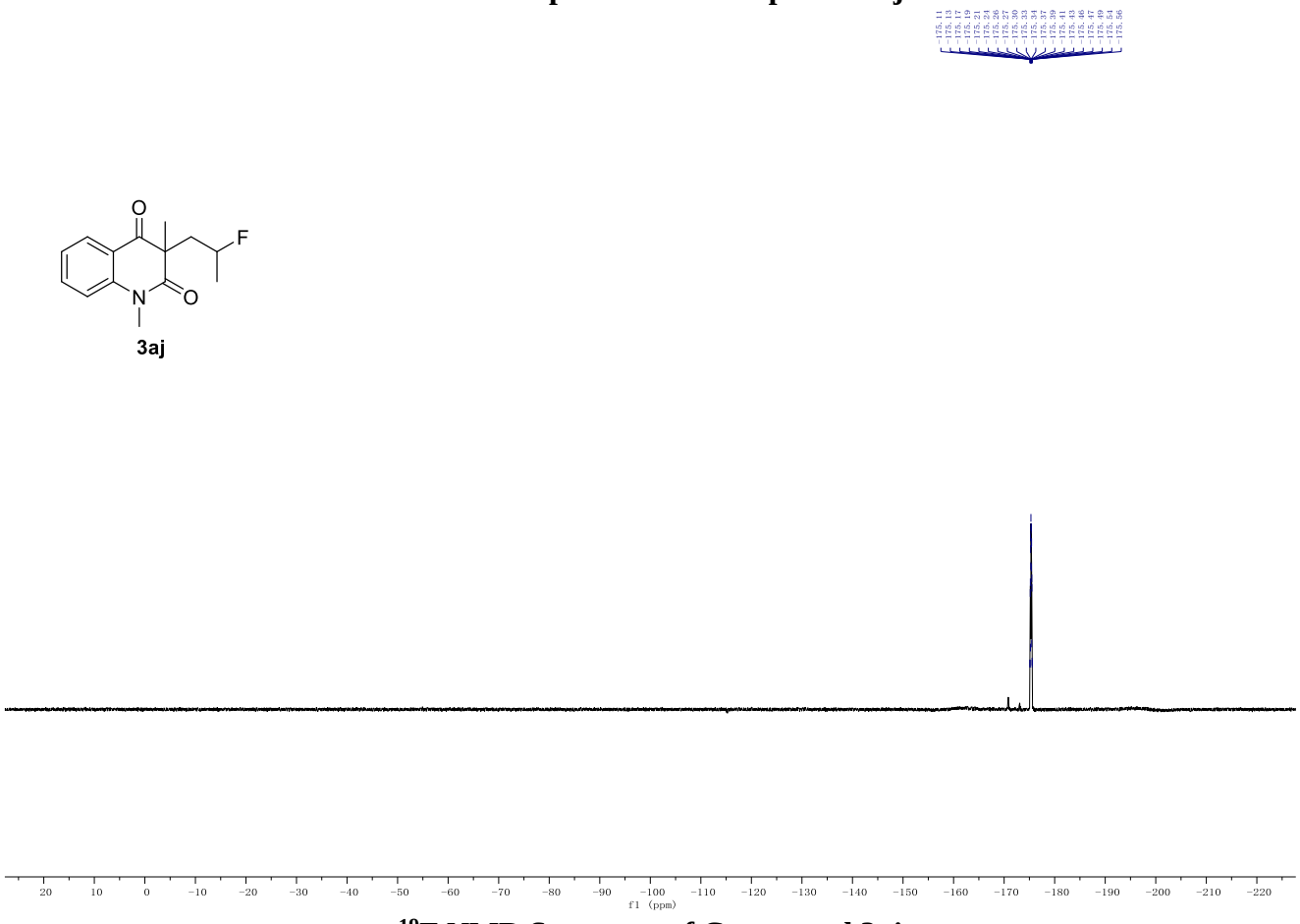
^{19}F NMR Spectrum of Compound 3ai



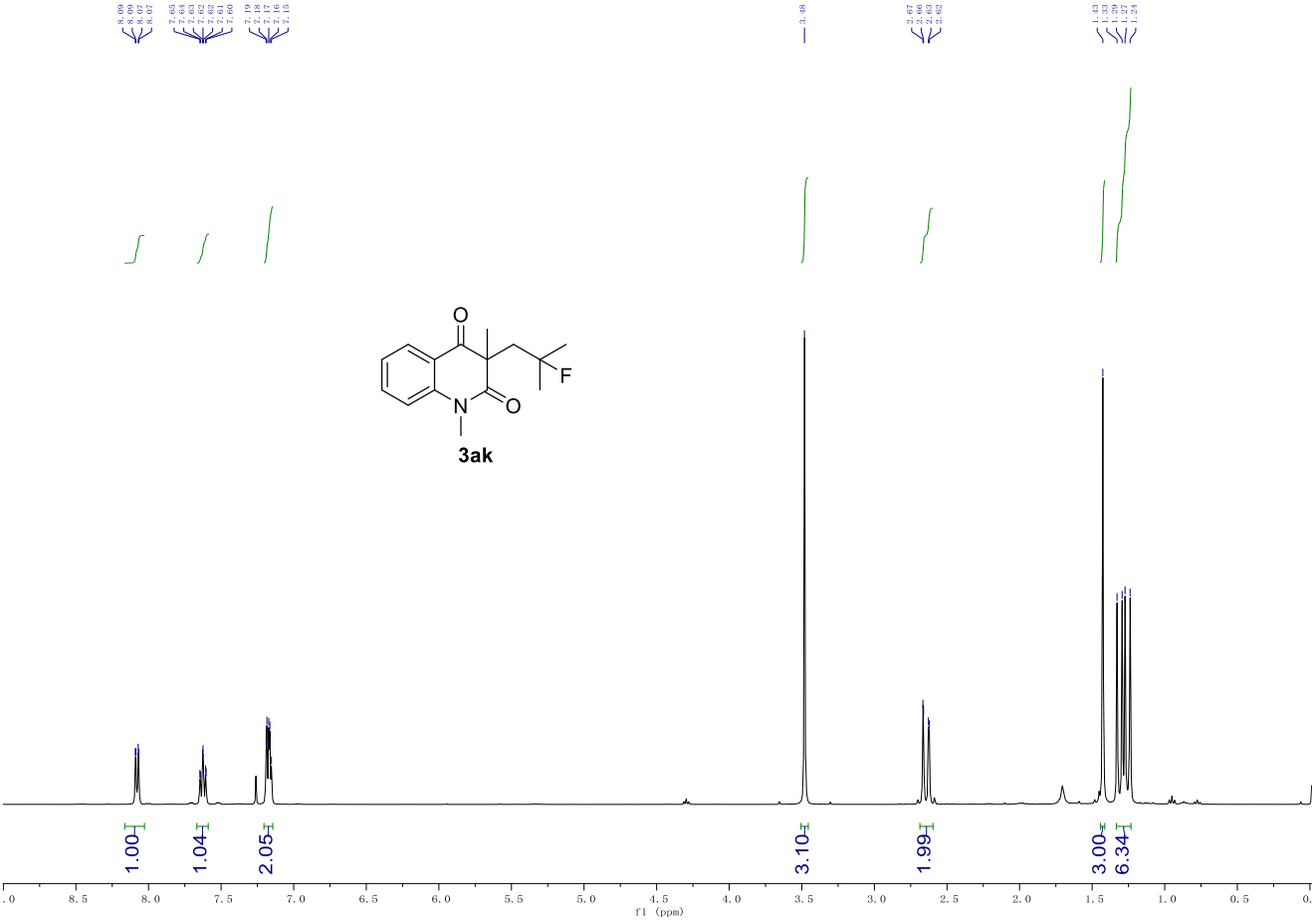
^{1}H NMR Spectrum of Compound 3aj



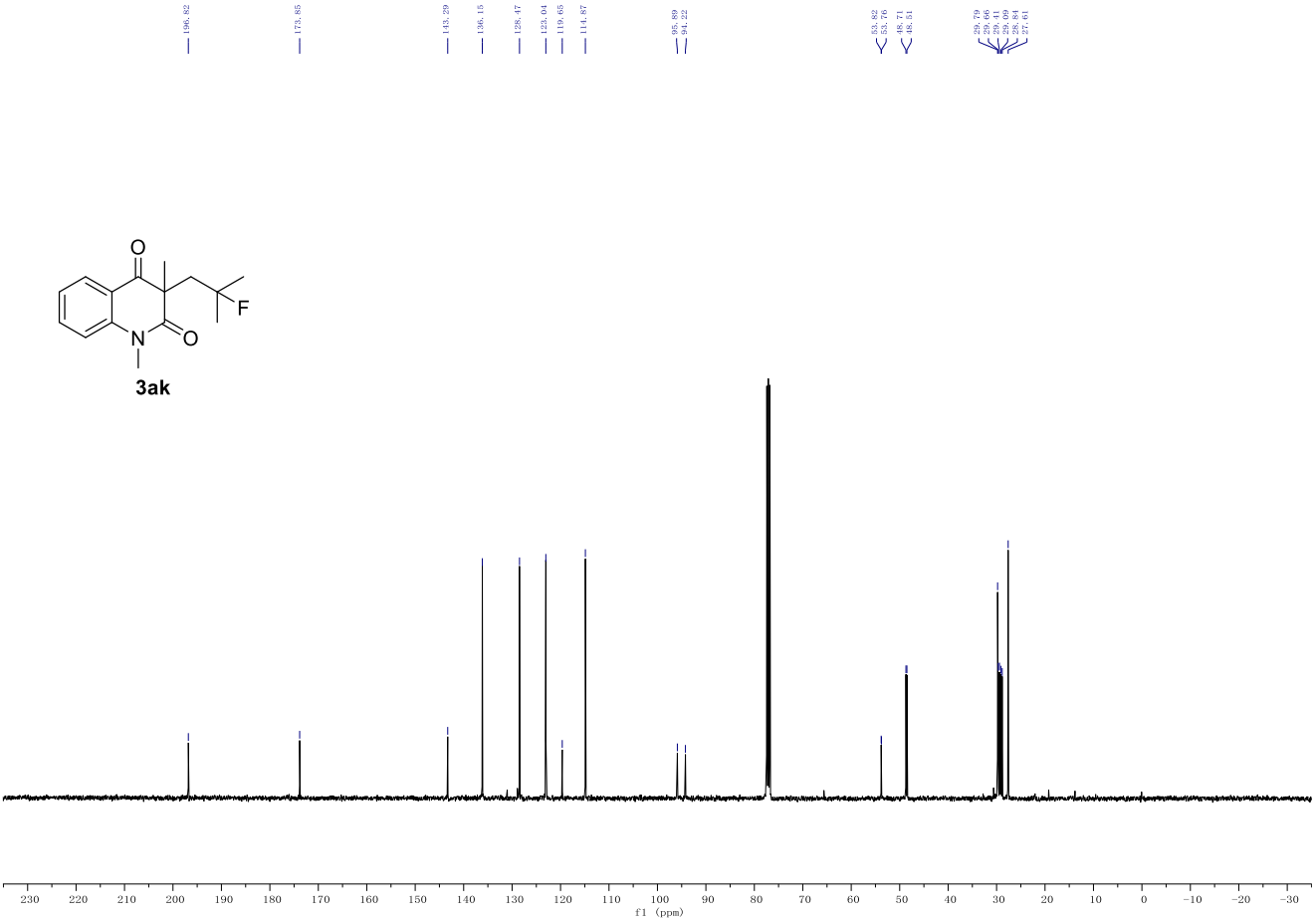
^{13}C NMR Spectrum of Compound 3aj



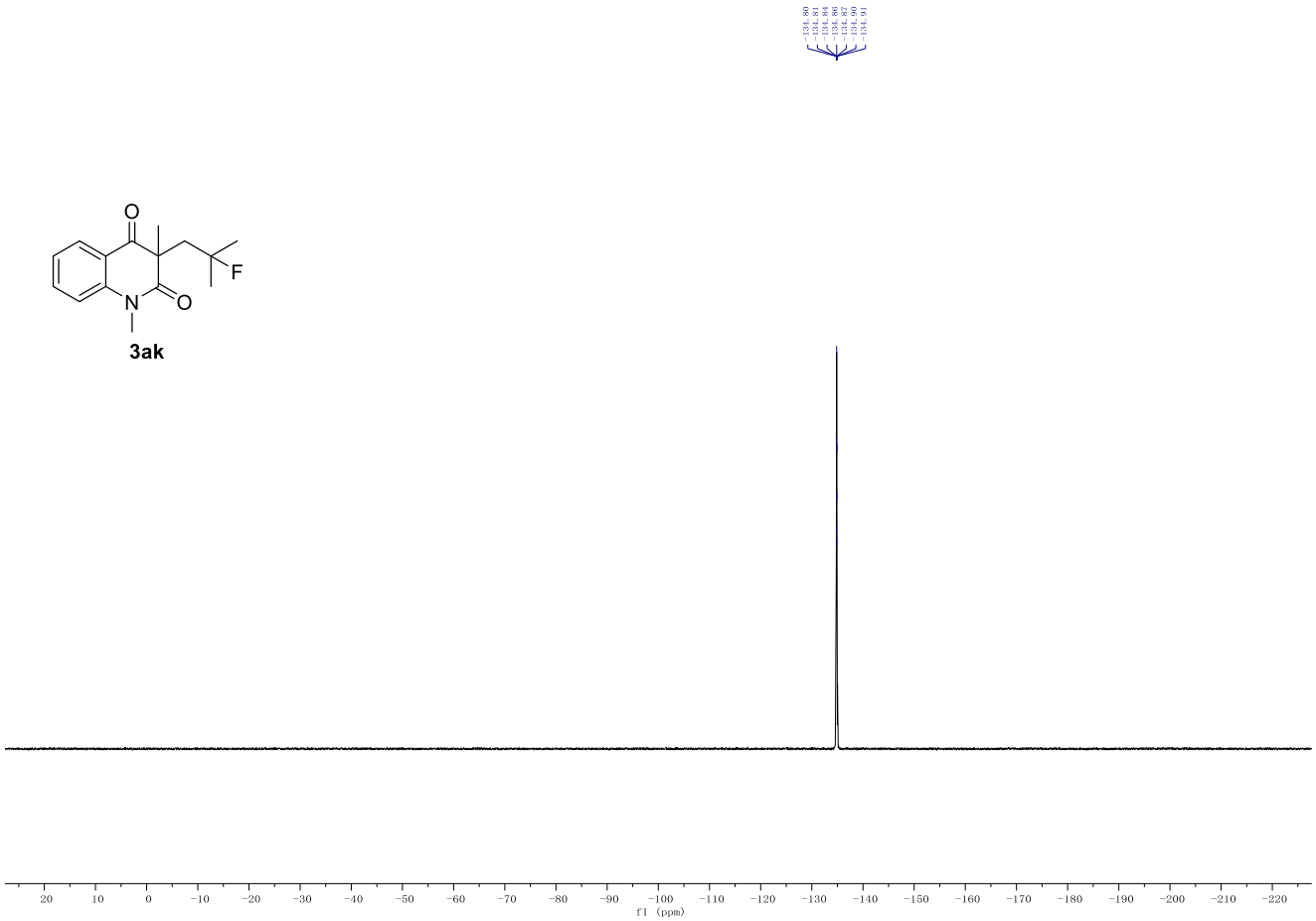
^{19}F NMR Spectrum of Compound 3aj



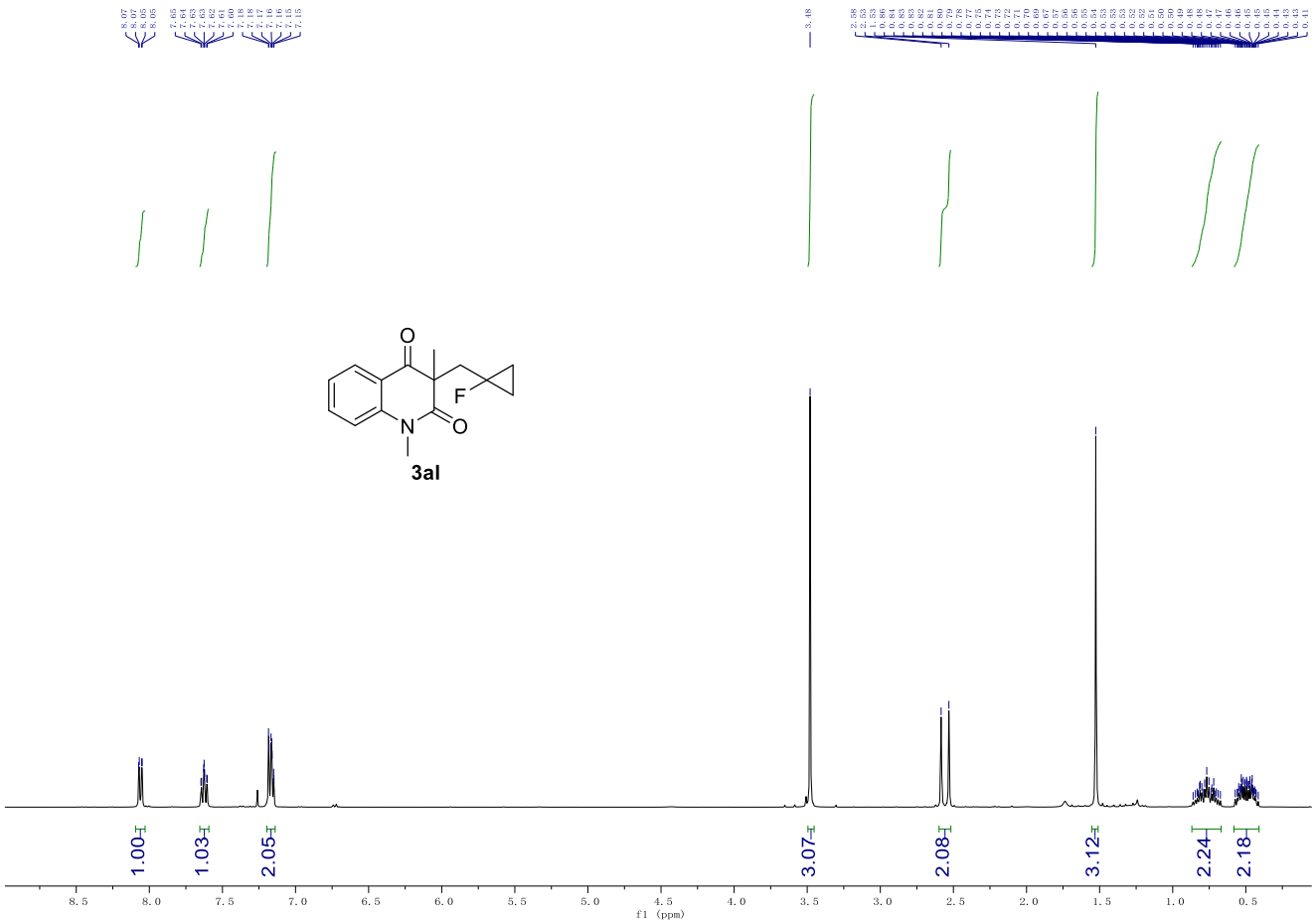
^{1}H NMR Spectrum of Compound 3ak



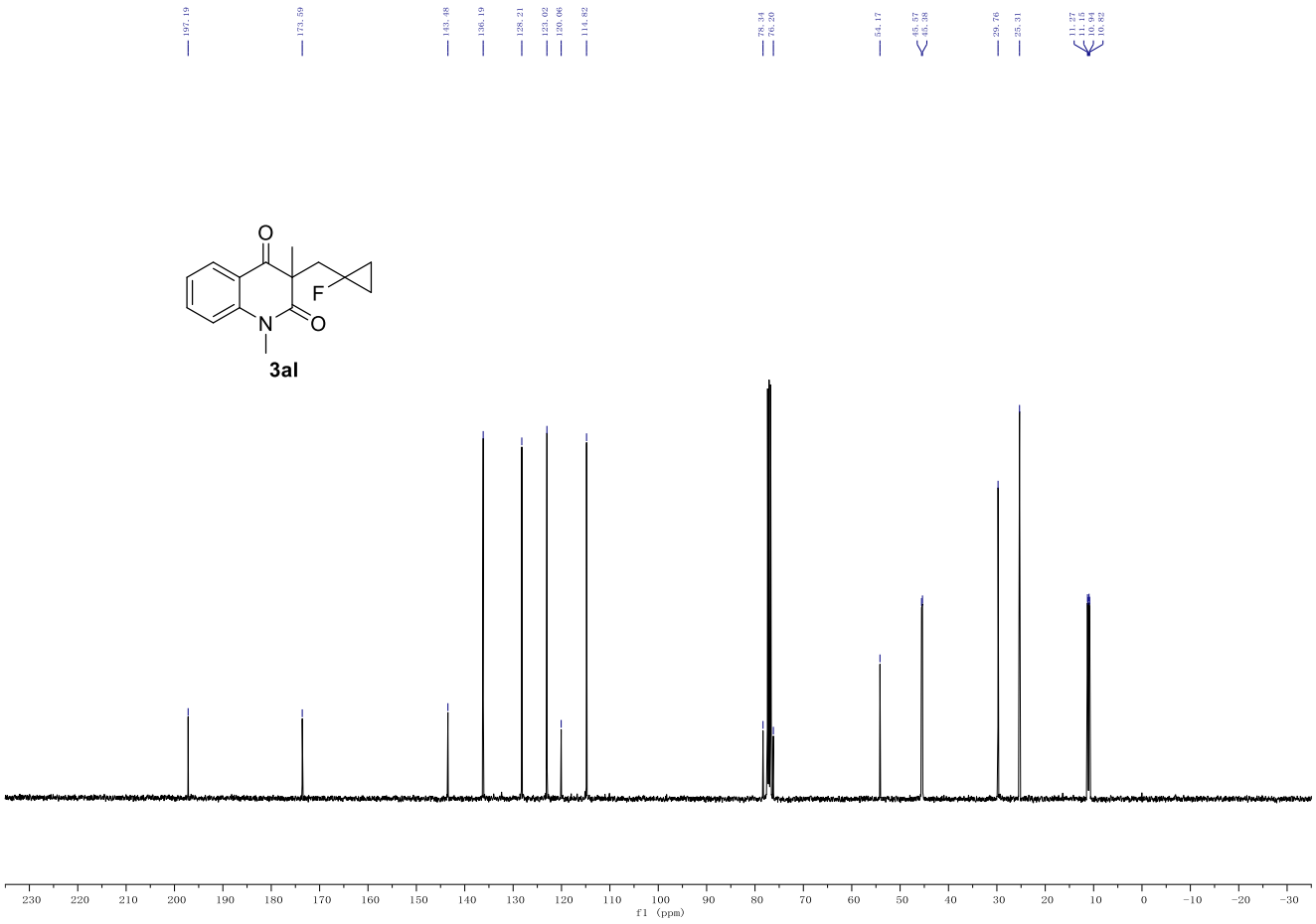
^{13}C NMR Spectrum of Compound 3ak



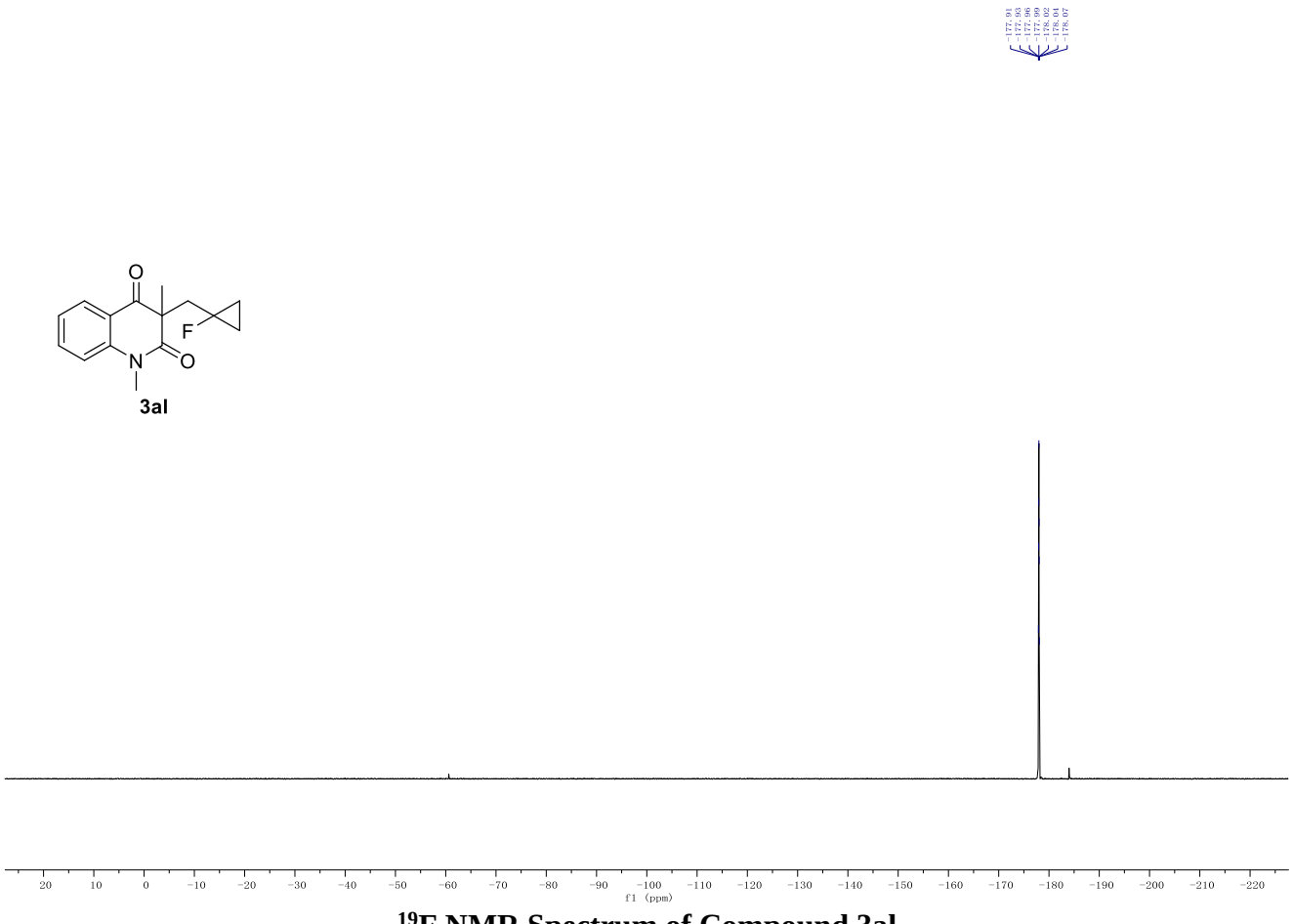
^{19}F NMR Spectrum of Compound 3ak



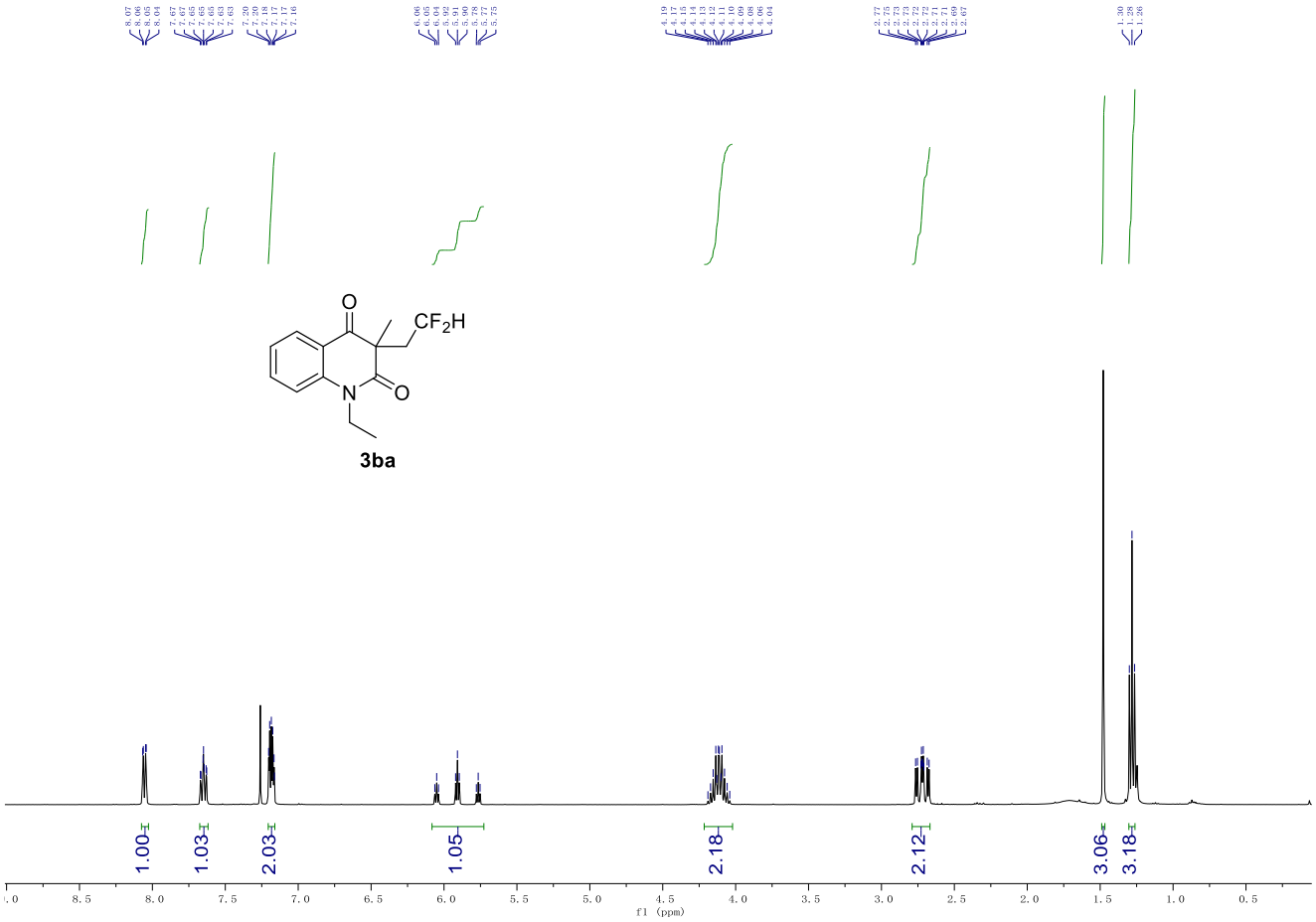
^{1}H NMR Spectrum of Compound 3al



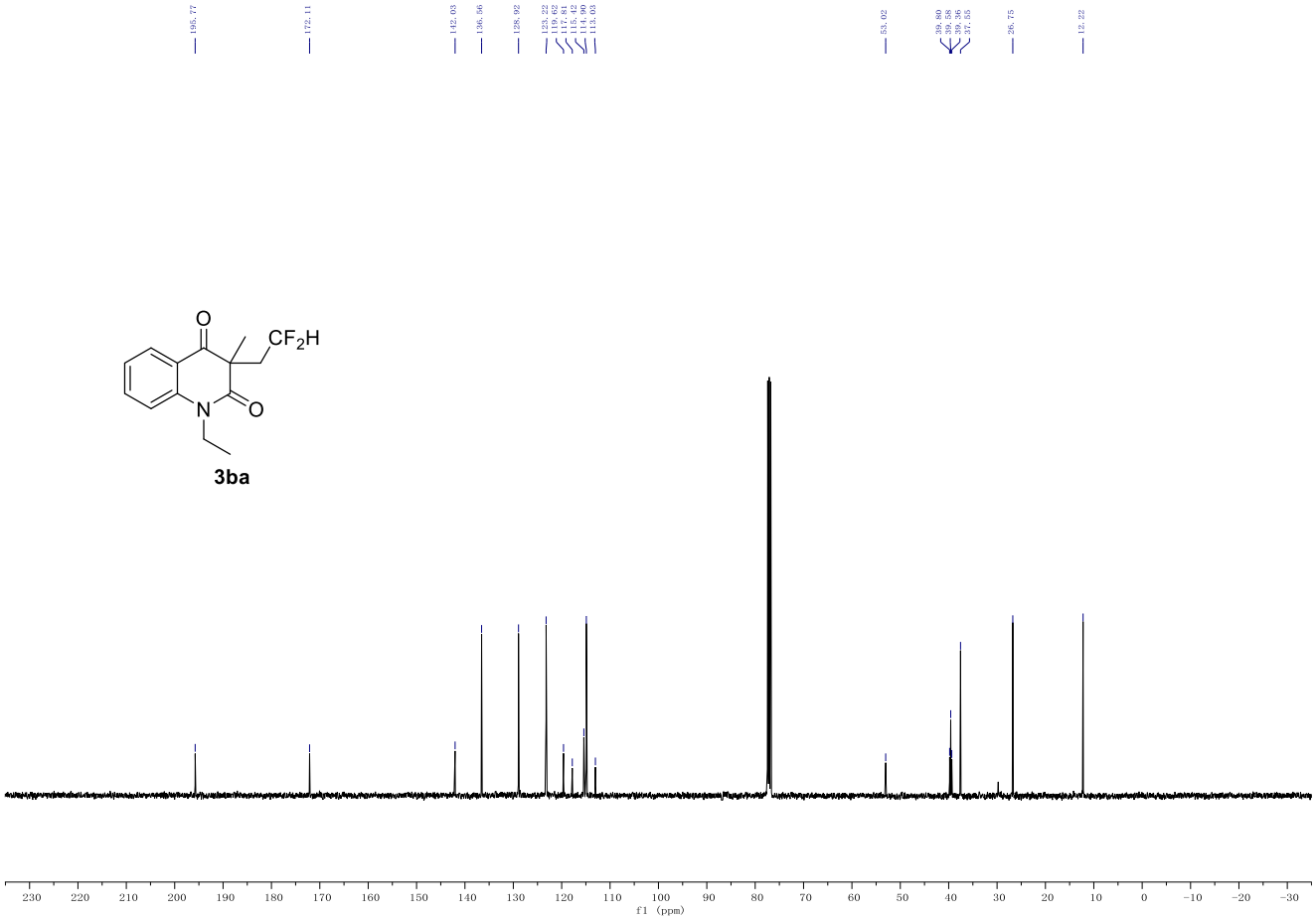
^{13}C NMR Spectrum of Compound 3al



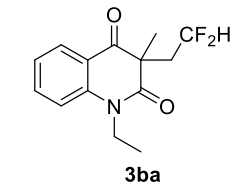
^{19}F NMR Spectrum of Compound 3al



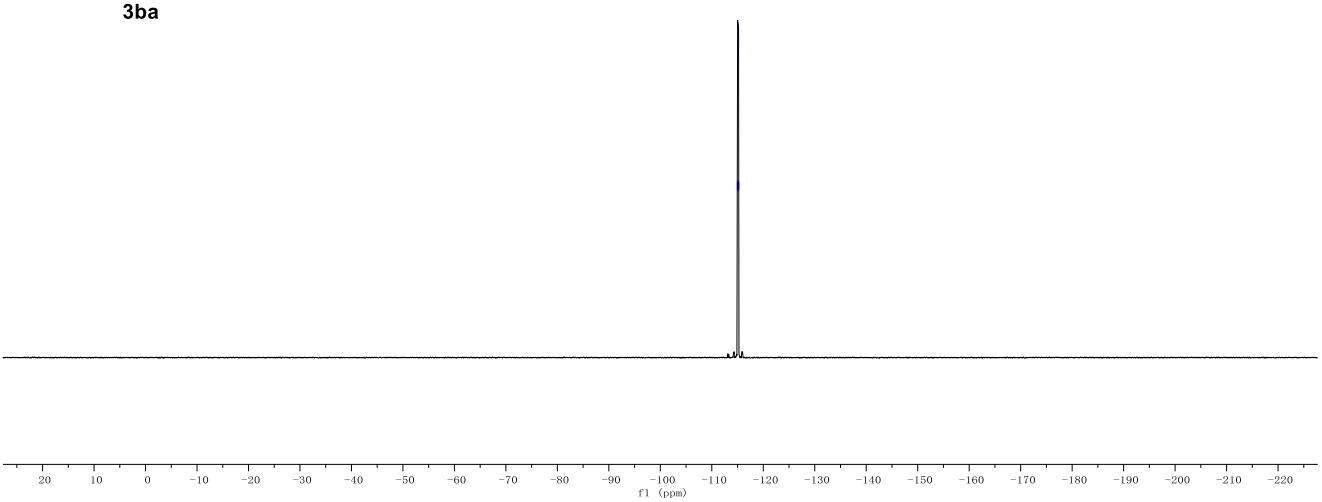
^{1}H NMR Spectrum of Compound 3ba



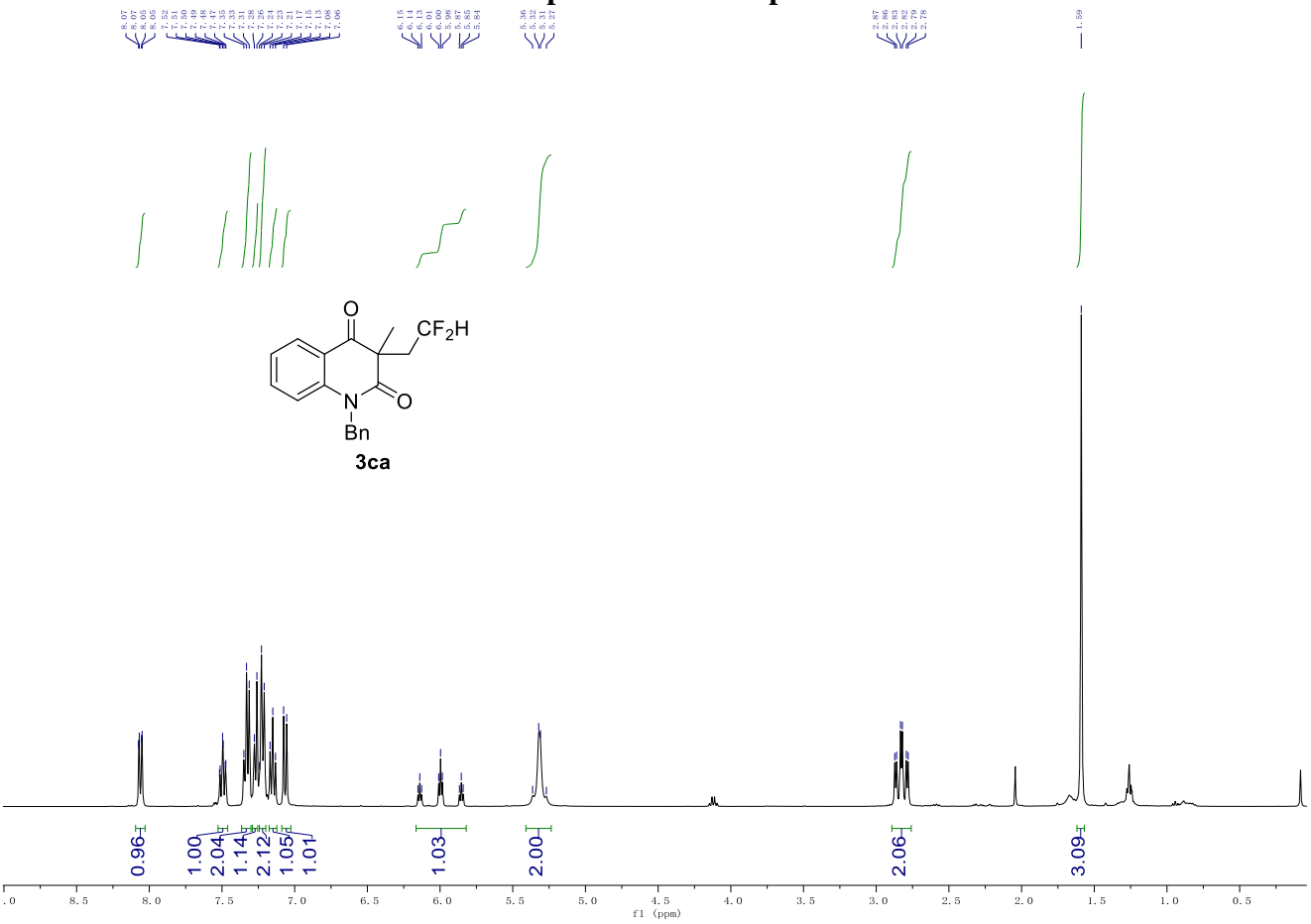
^{13}C NMR Spectrum of Compound 3ba



3ba

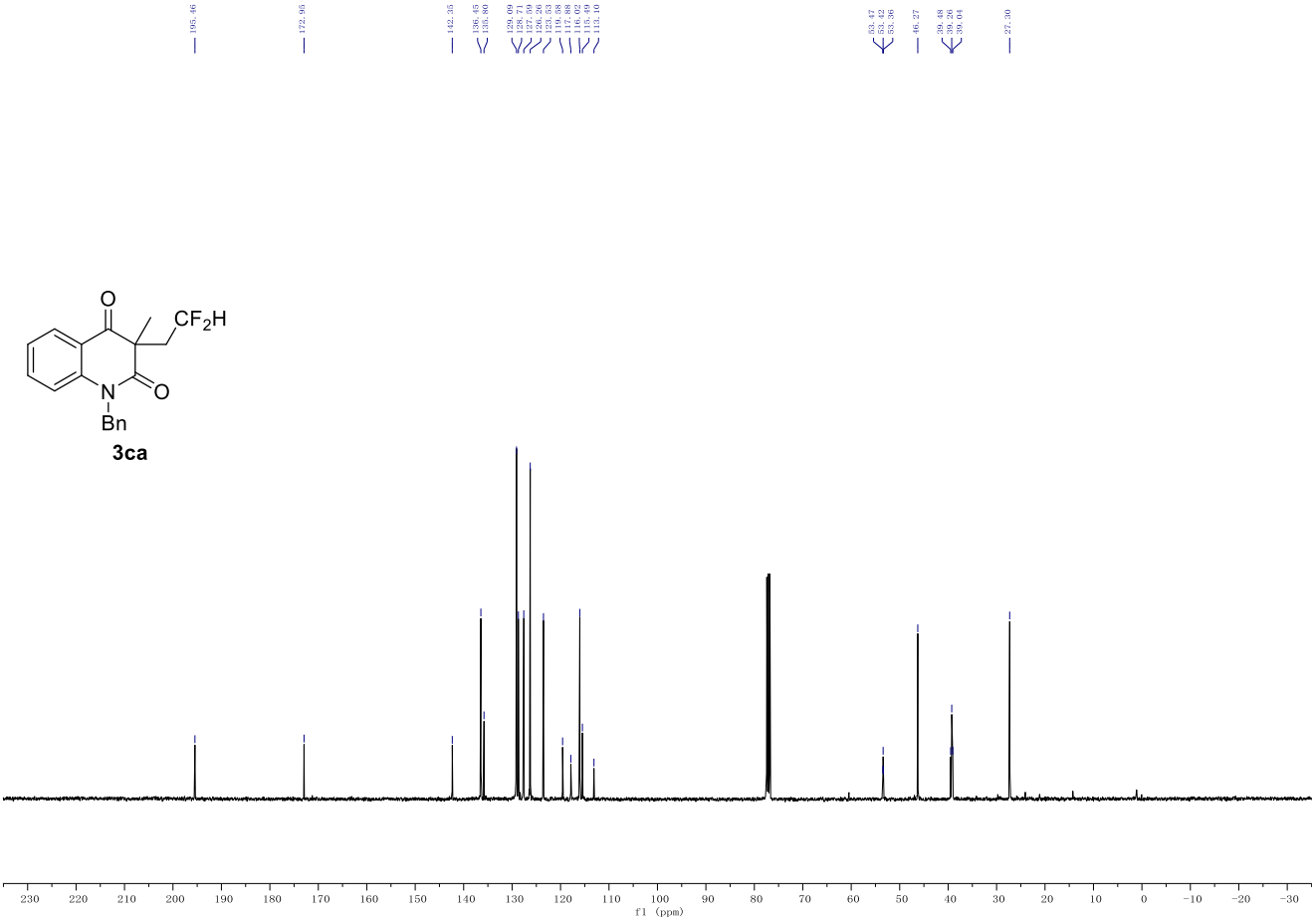


^{19}F NMR Spectrum of Compound 3ba

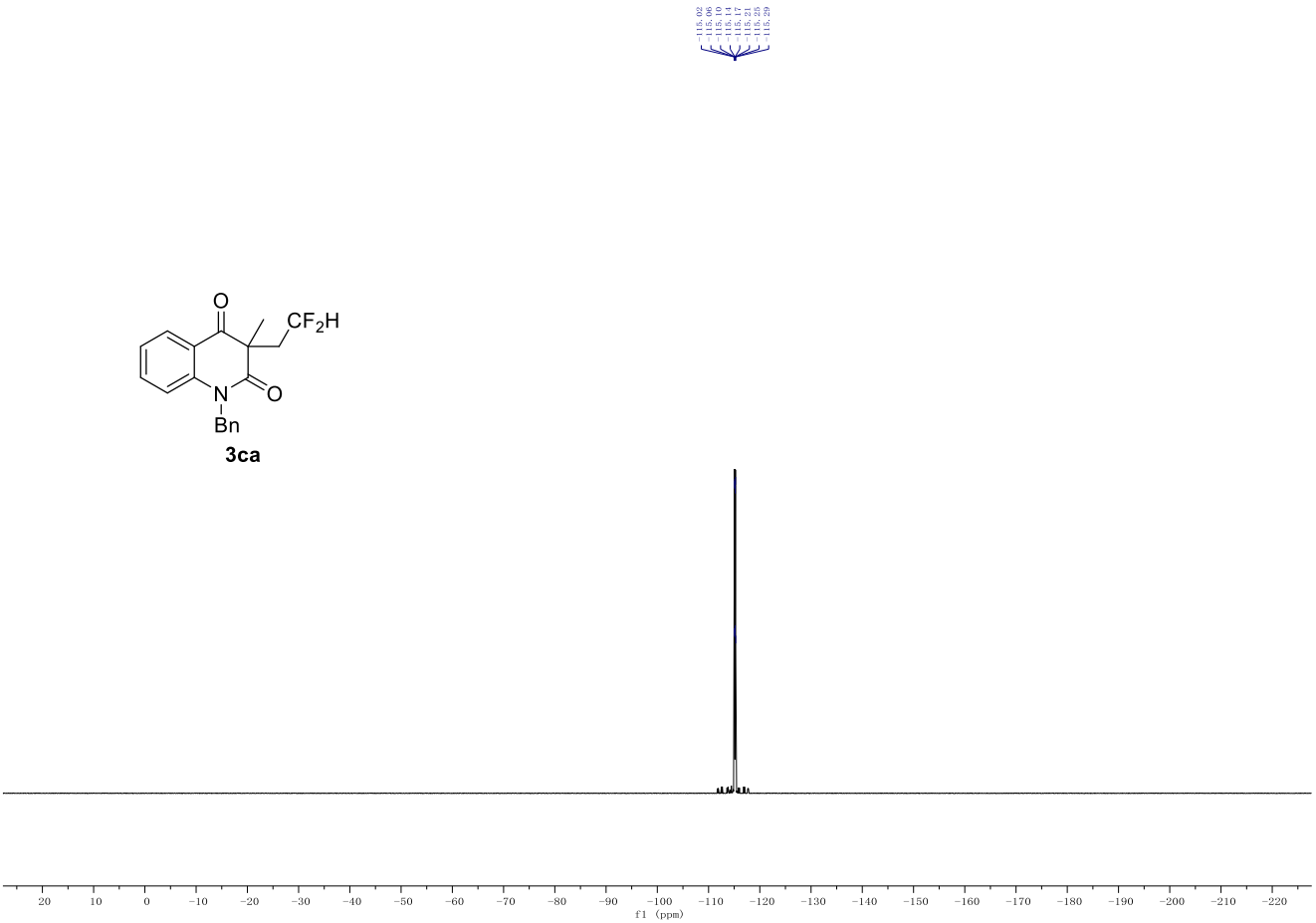


3ca

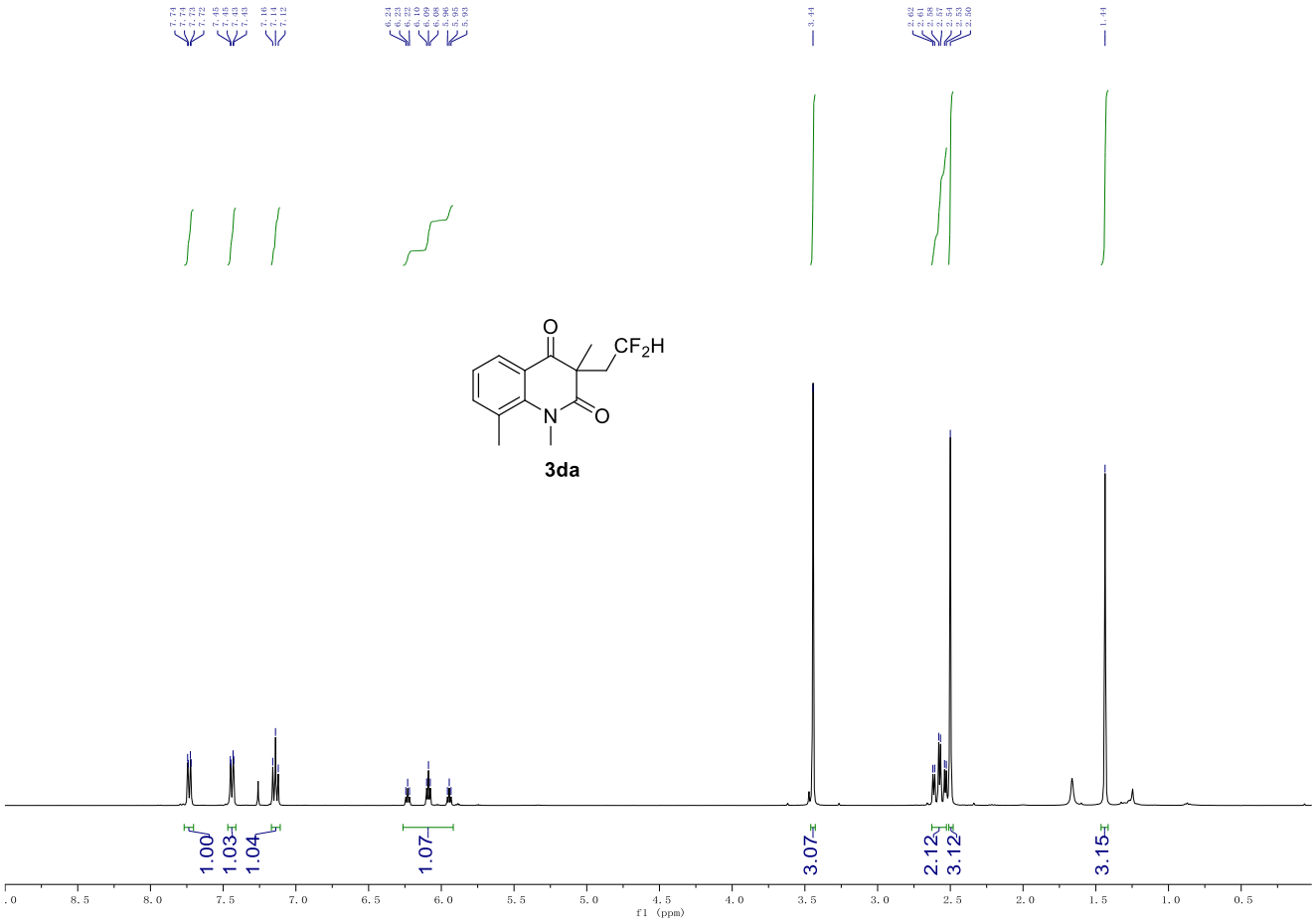
^{1}H NMR Spectrum of Compound 3ca



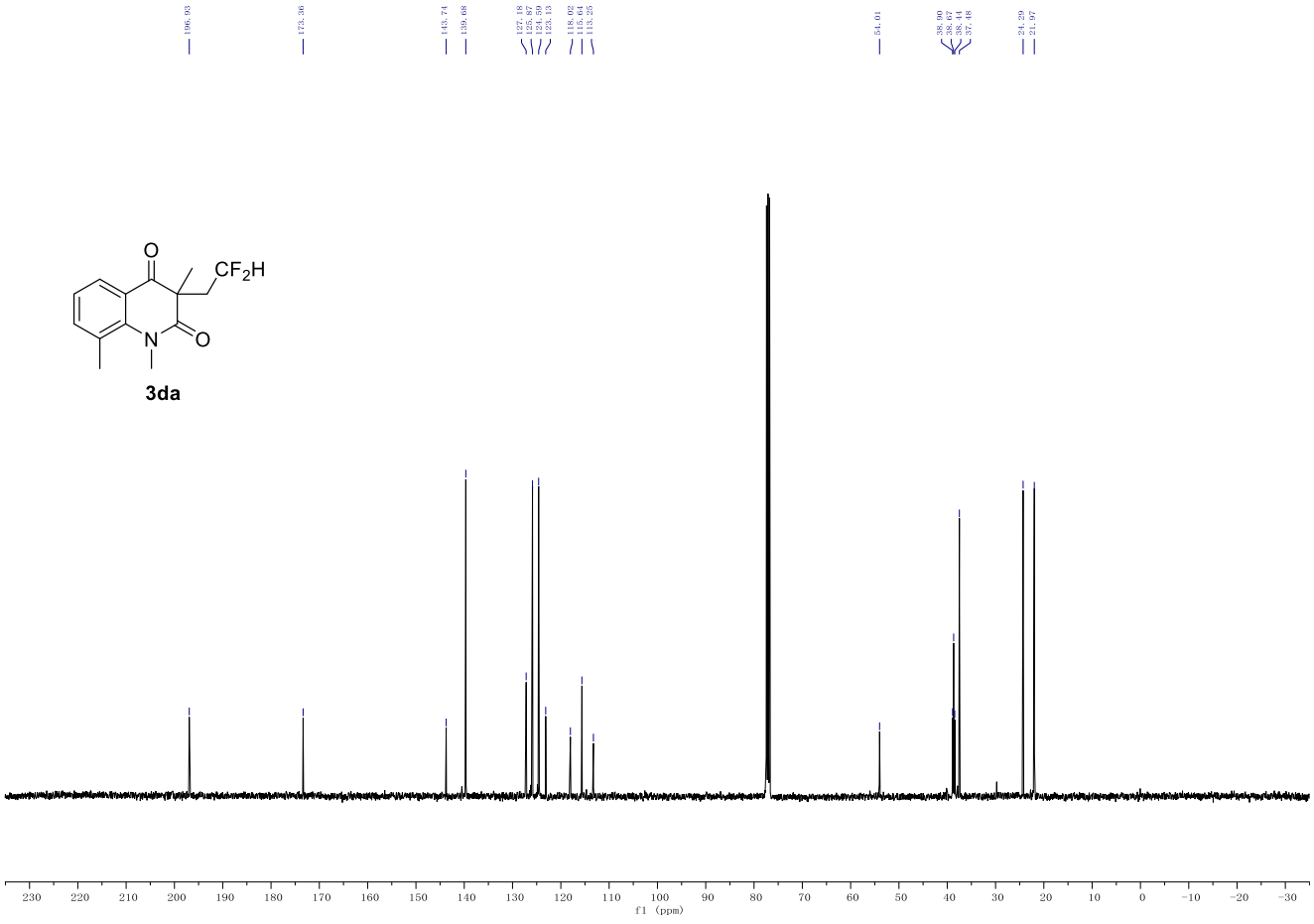
^{13}C NMR Spectrum of Compound 3ca



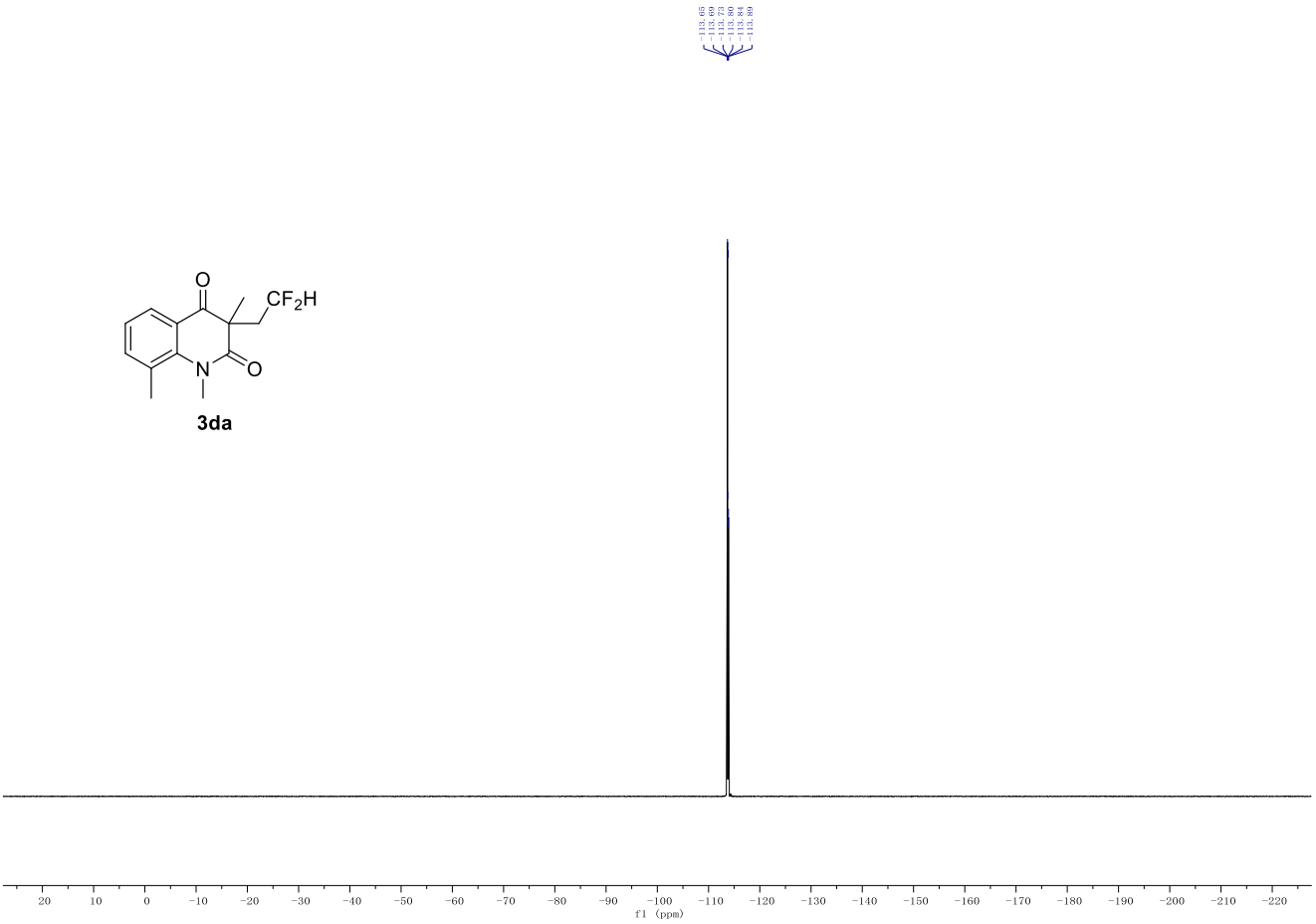
^{19}F NMR Spectrum of Compound 3ca



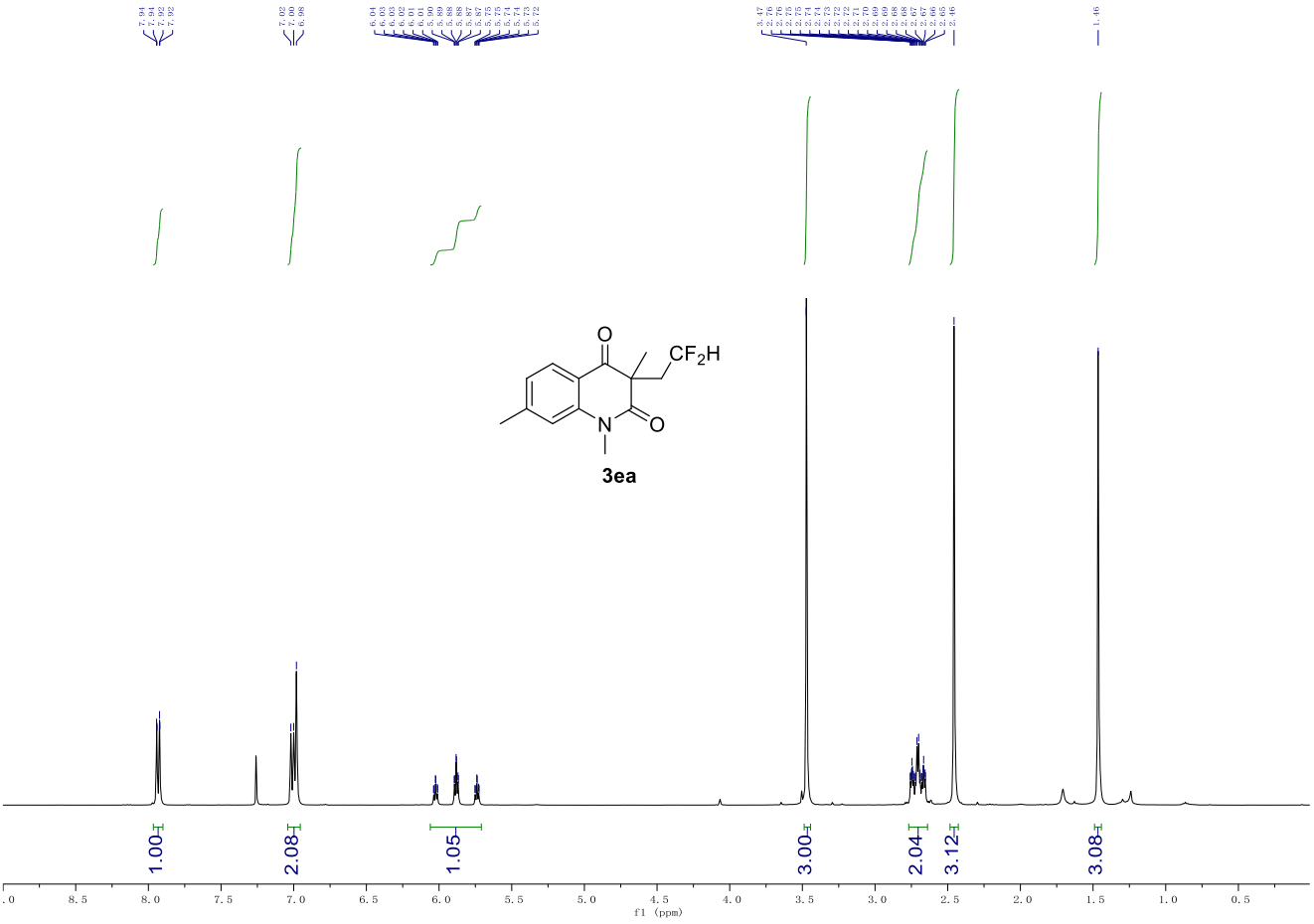
^{1}H NMR Spectrum of Compound 3da



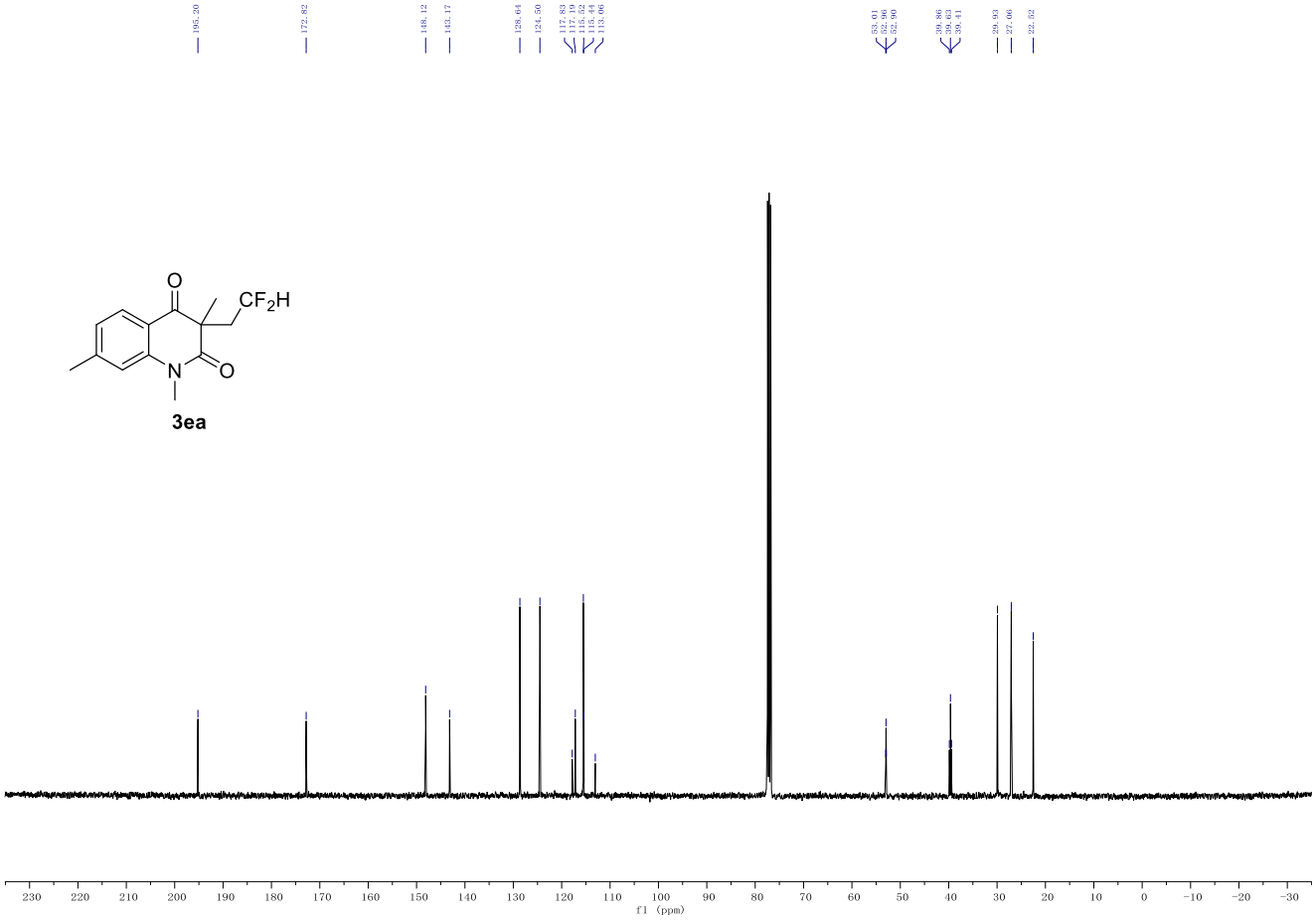
^{13}C NMR Spectrum of Compound 3da



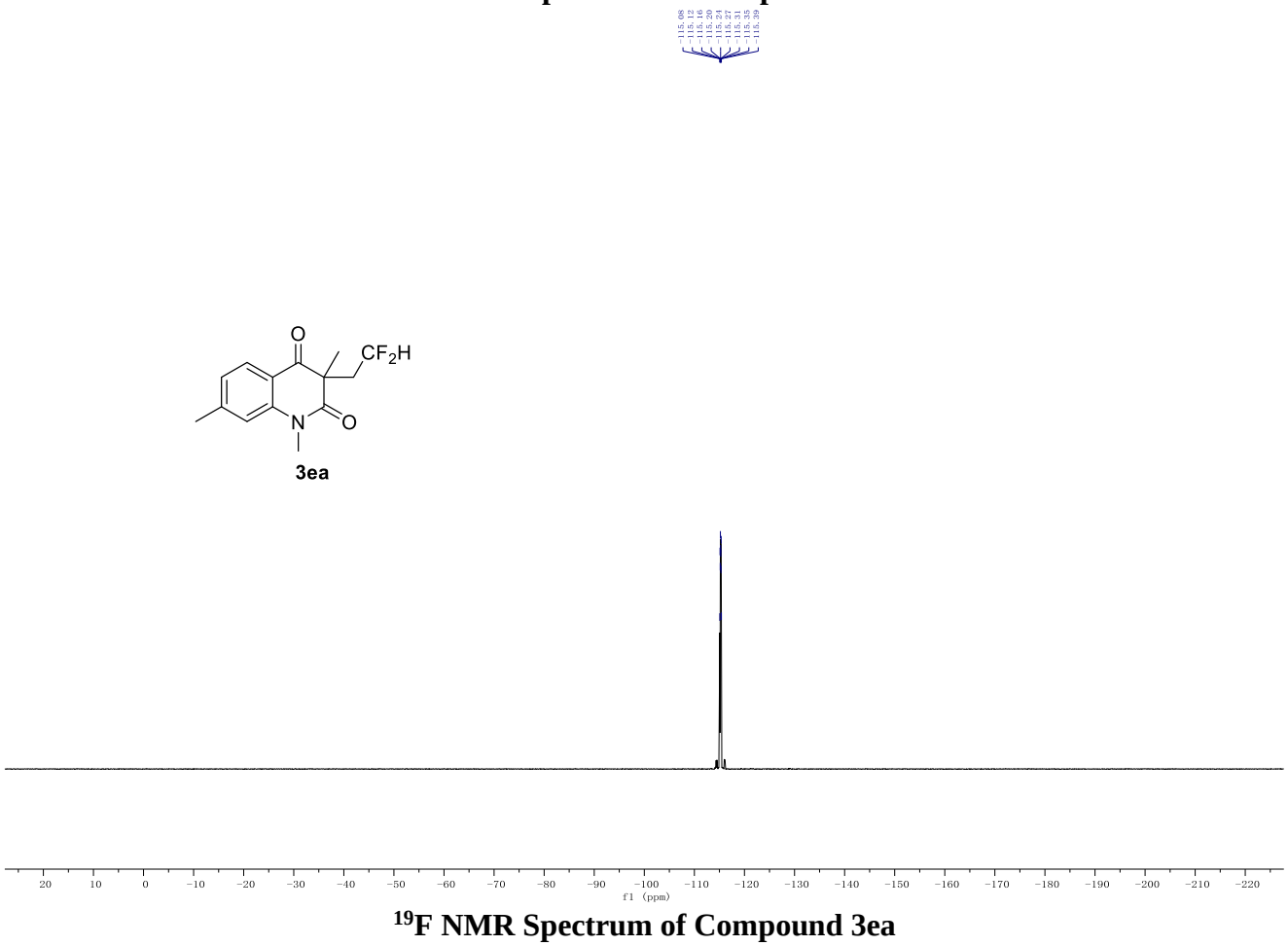
^{19}F NMR Spectrum of Compound 3da



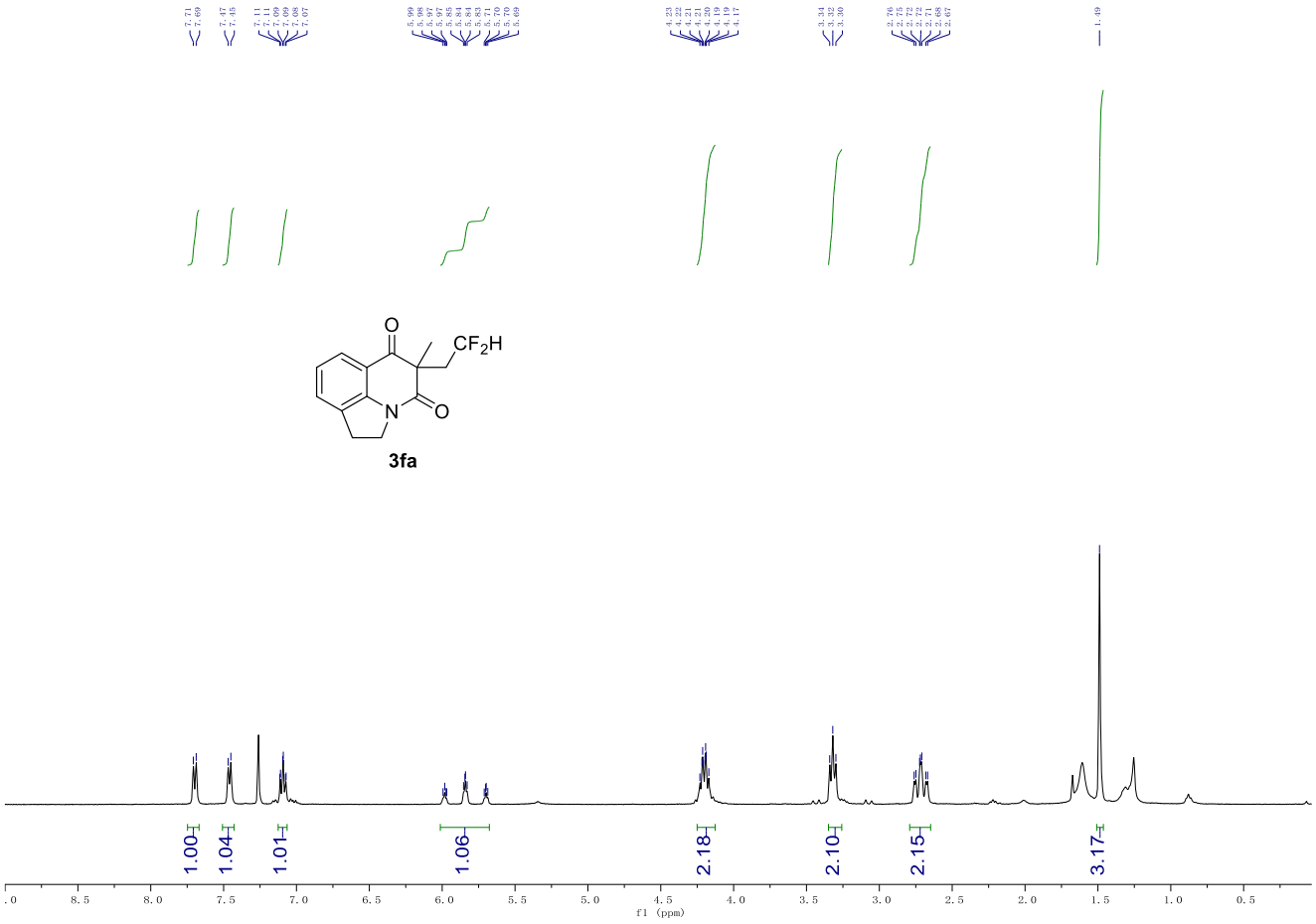
^{1}H NMR Spectrum of Compound 3ea



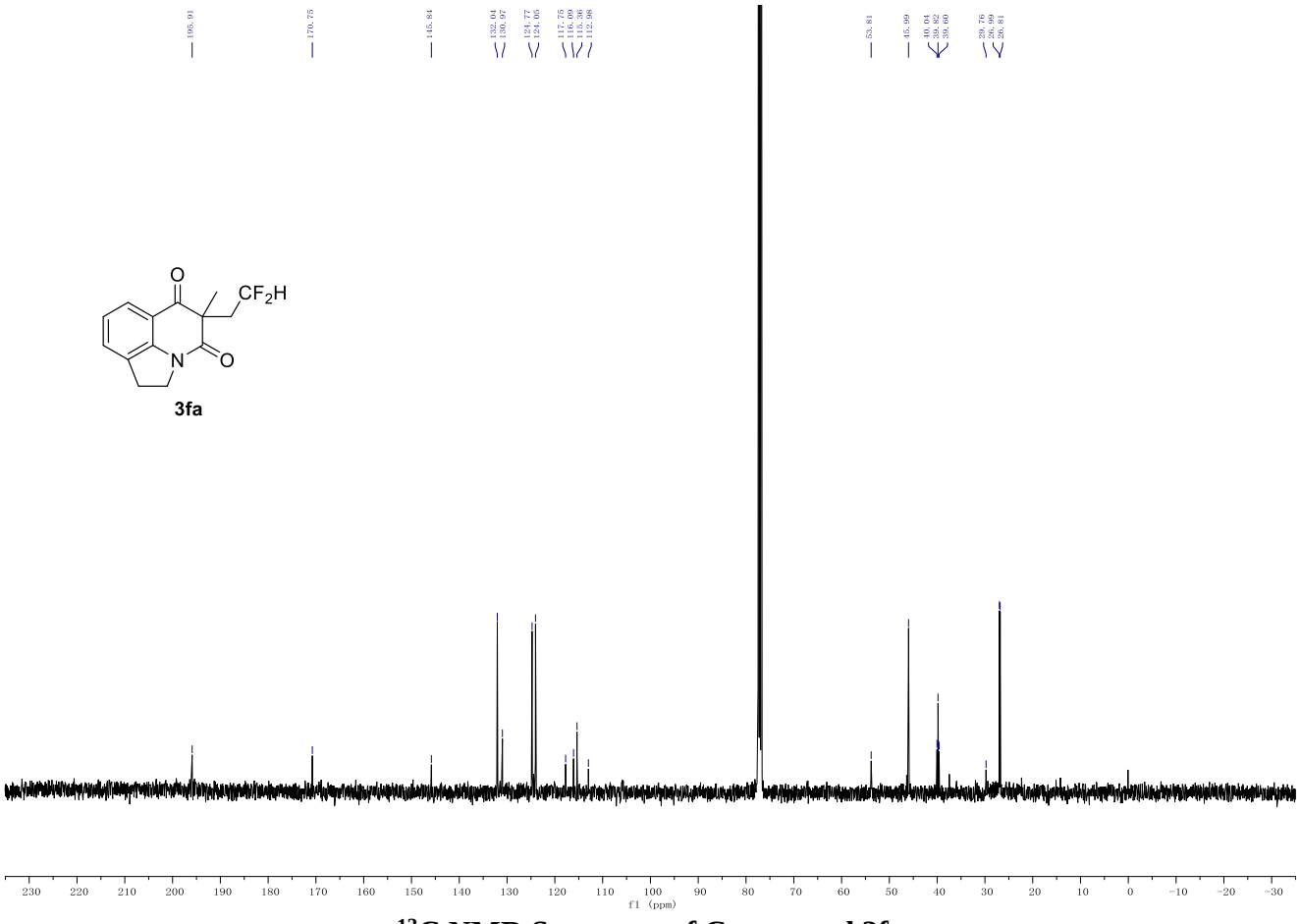
^{13}C NMR Spectrum of Compound 3ea



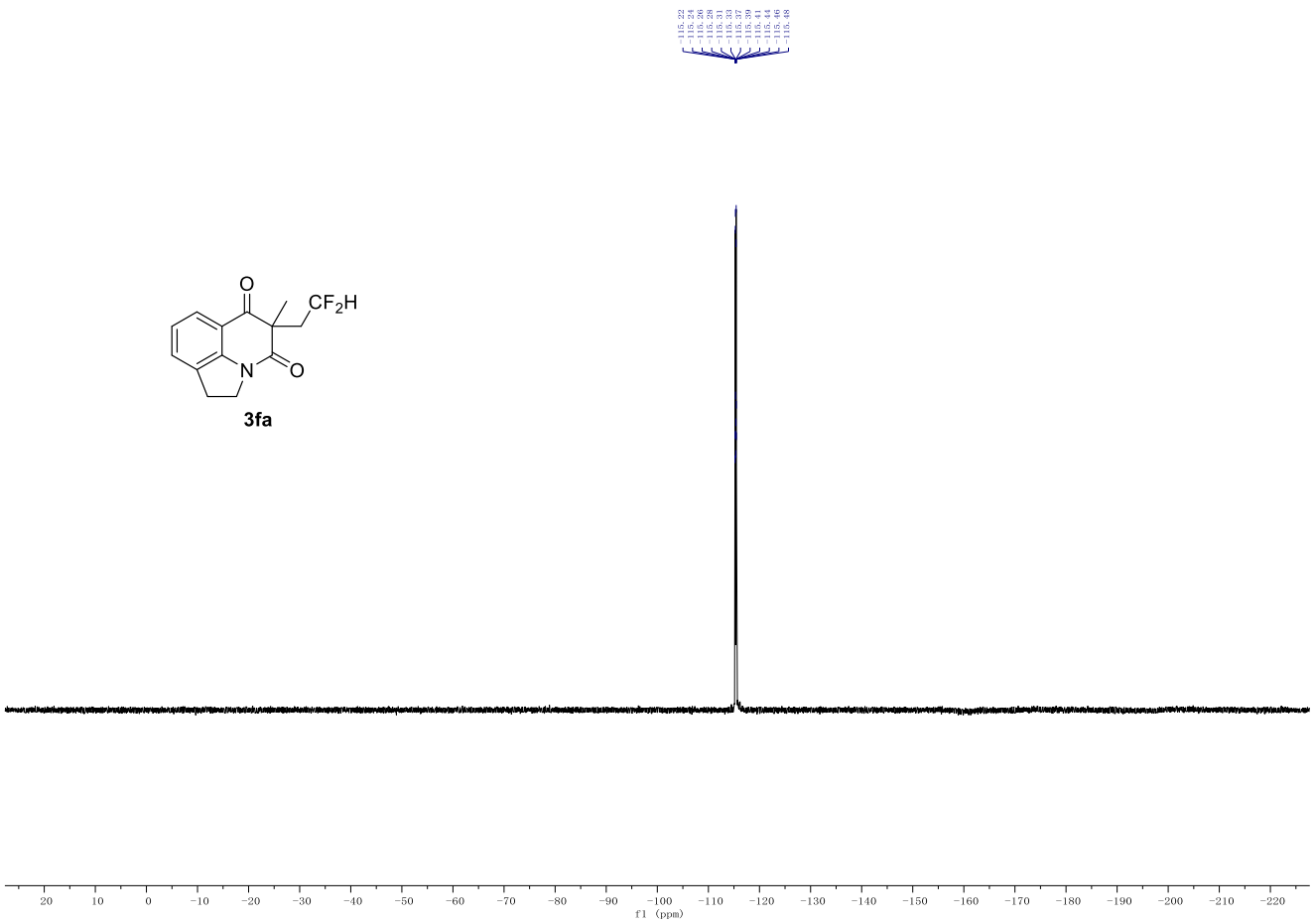
^{19}F NMR Spectrum of Compound 3ea



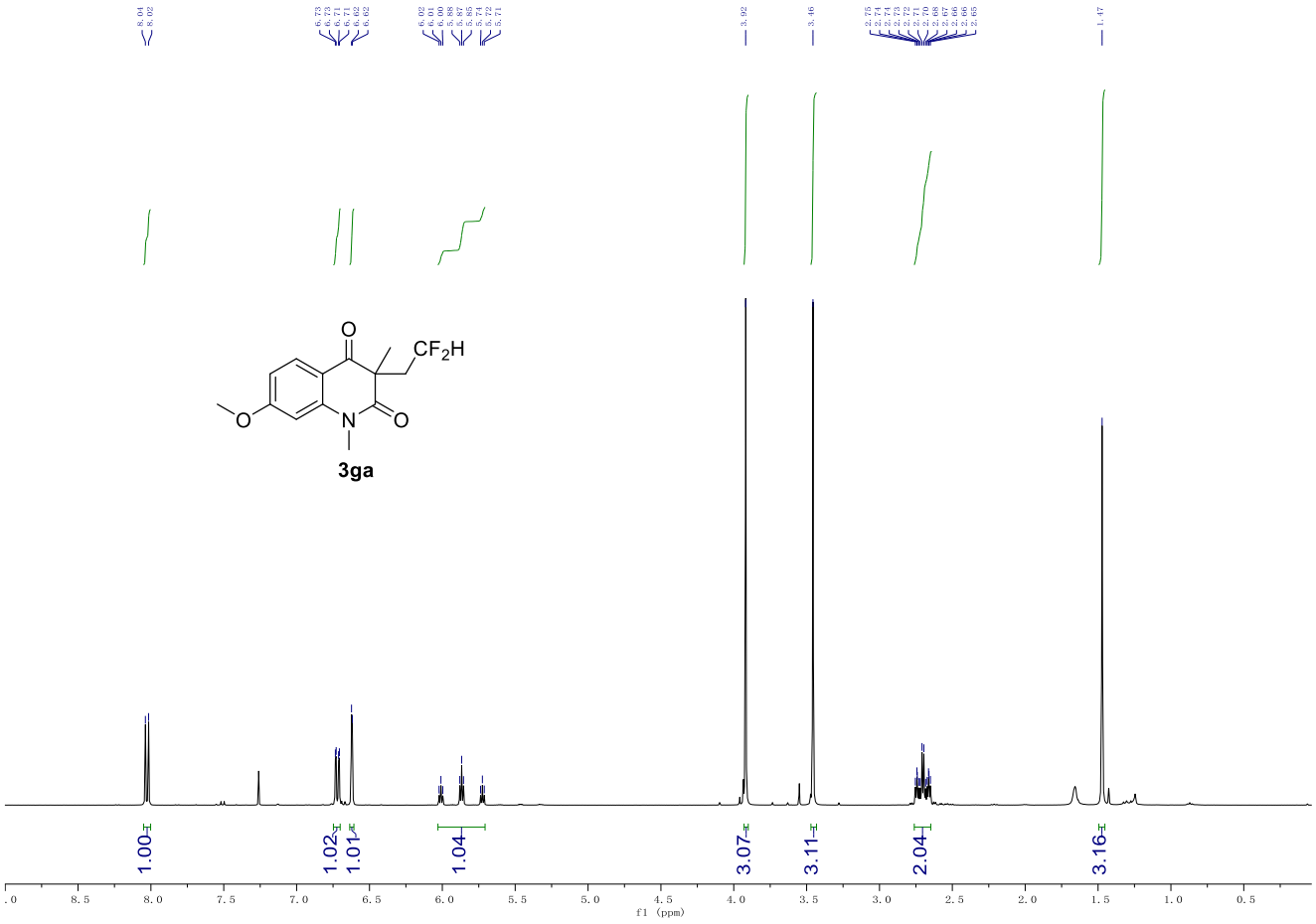
^{1}H NMR Spectrum of Compound 3fa



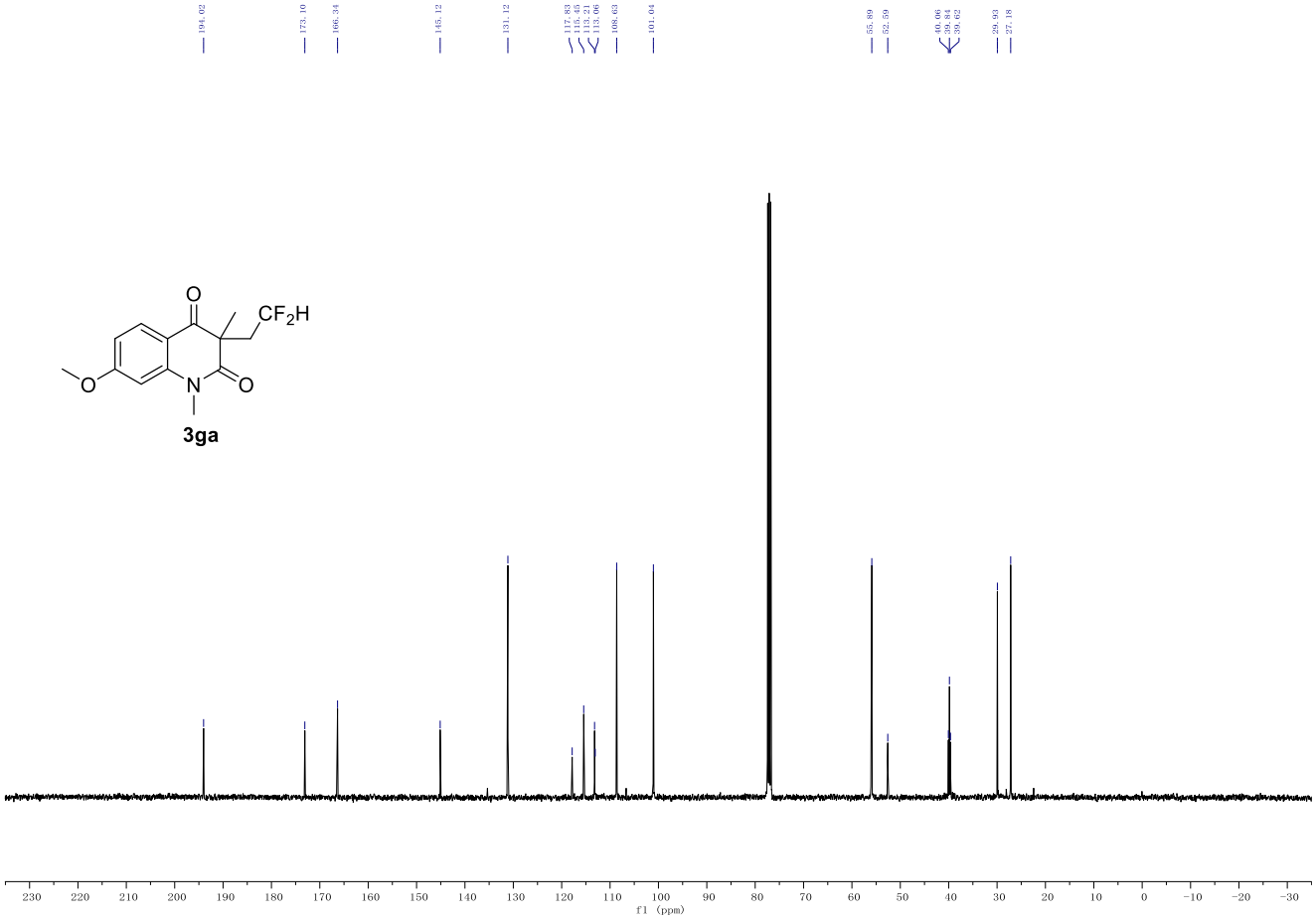
^{13}C NMR Spectrum of Compound 3fa



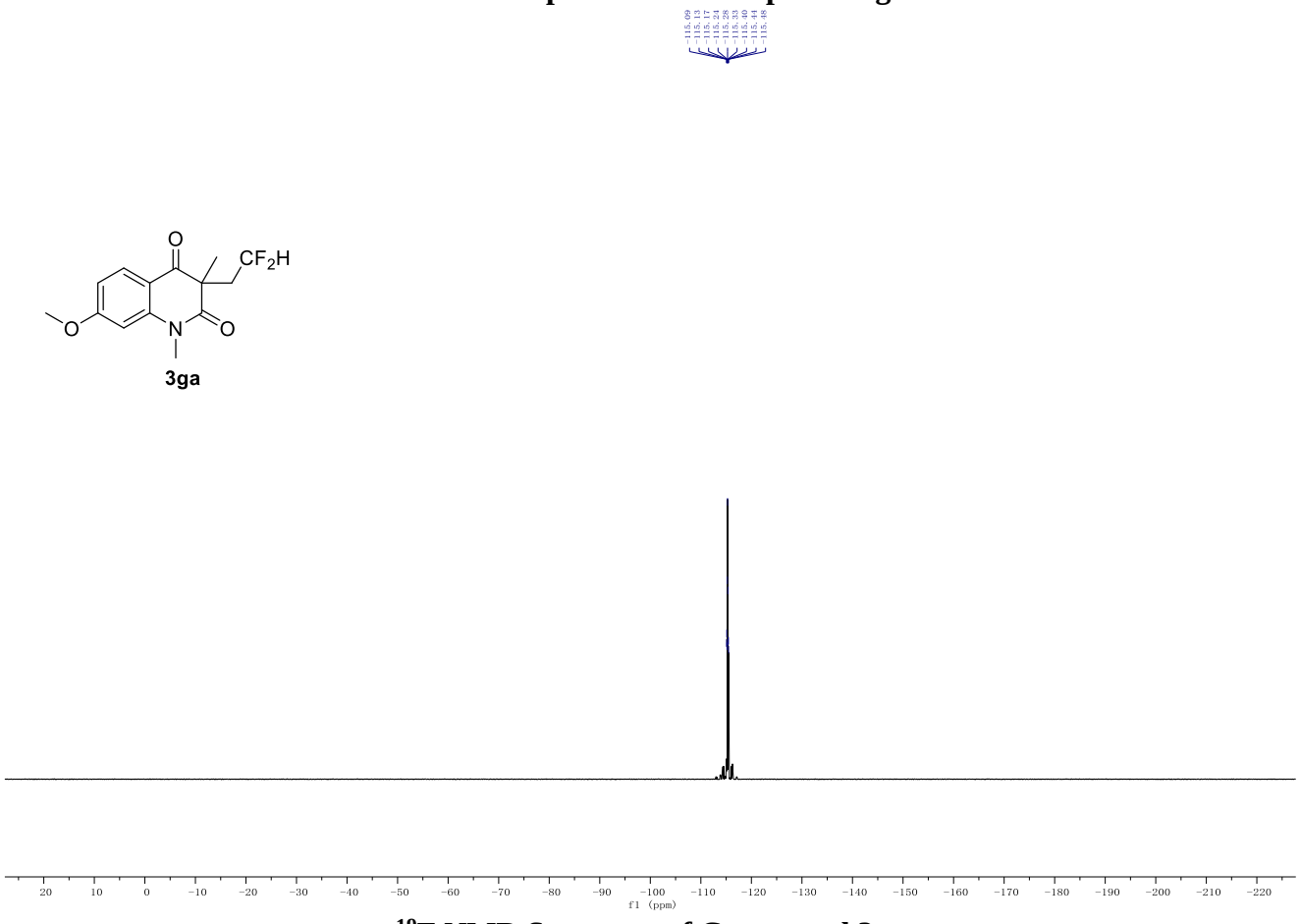
^{19}F NMR Spectrum of Compound 3fa



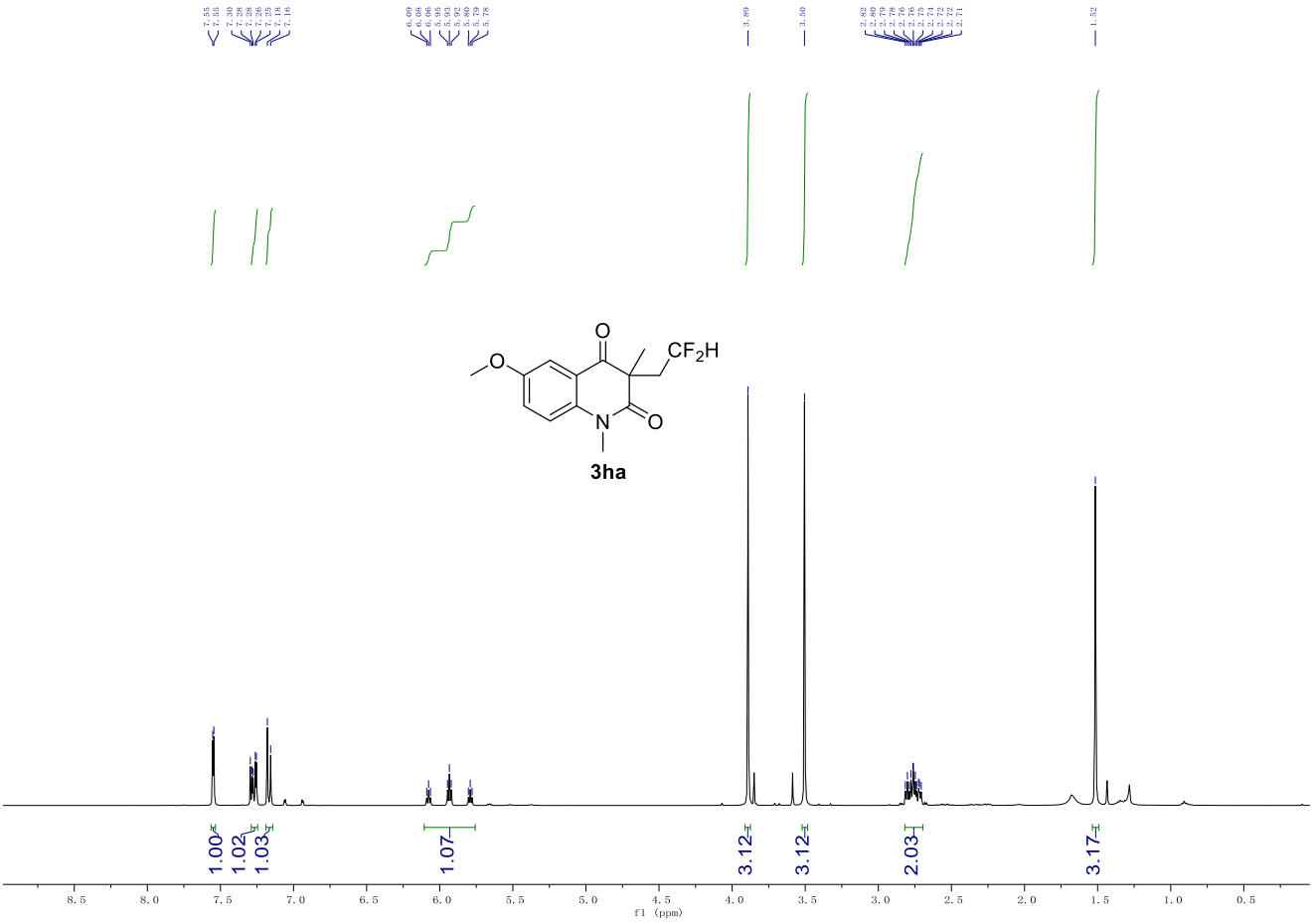
^{1}H NMR Spectrum of Compound 3ga



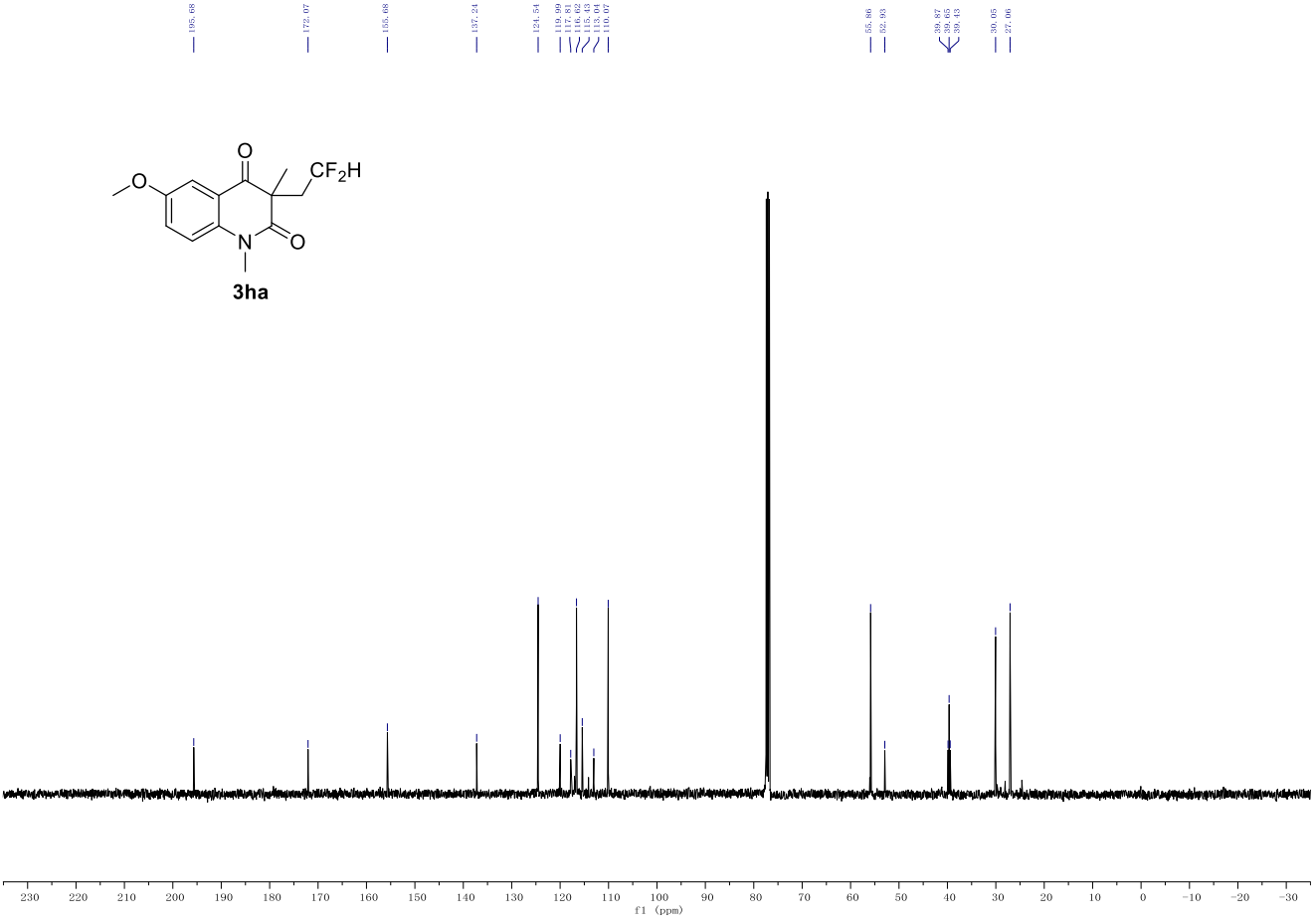
^{13}C NMR Spectrum of Compound 3ga



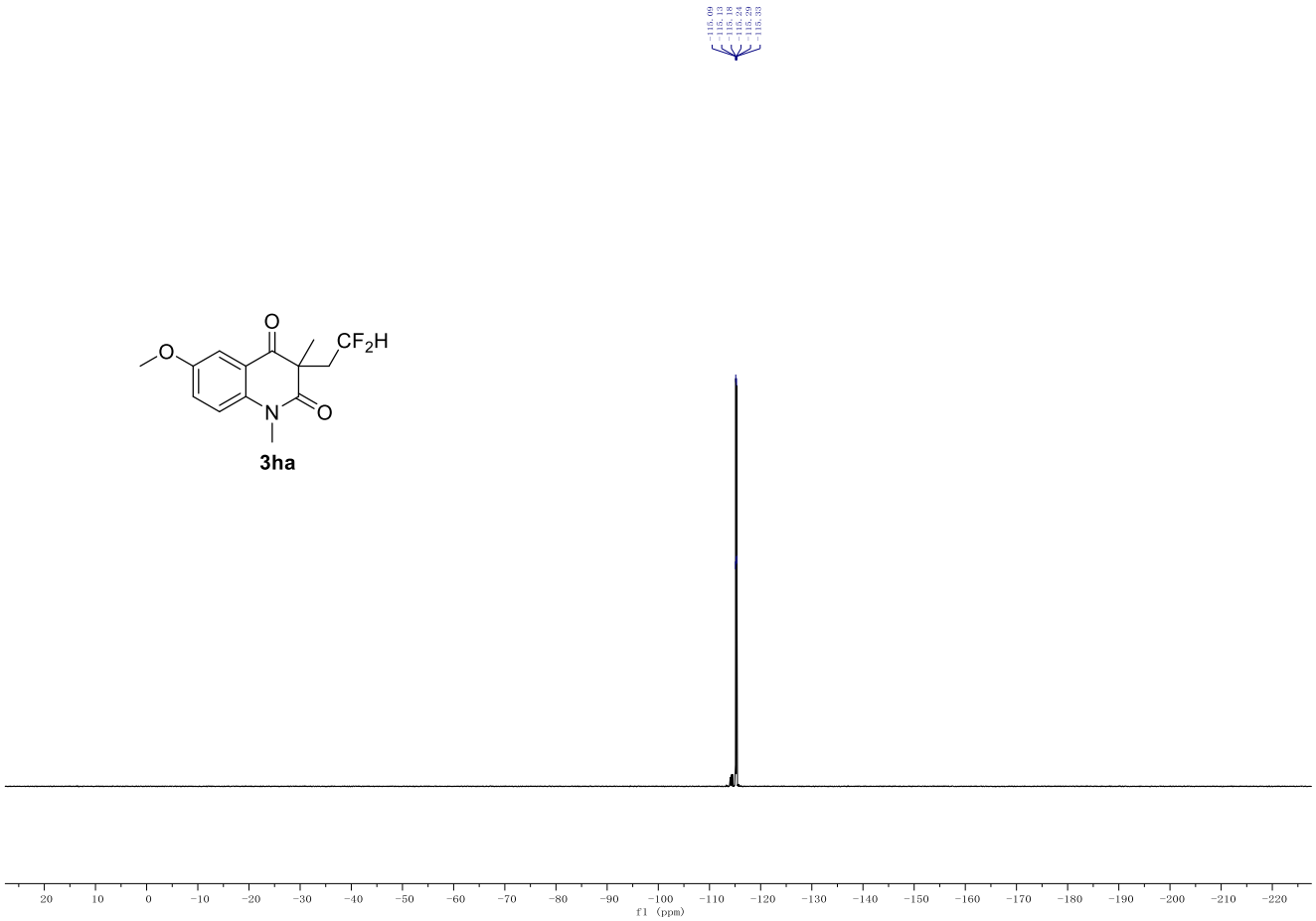
^{19}F NMR Spectrum of Compound 3ga



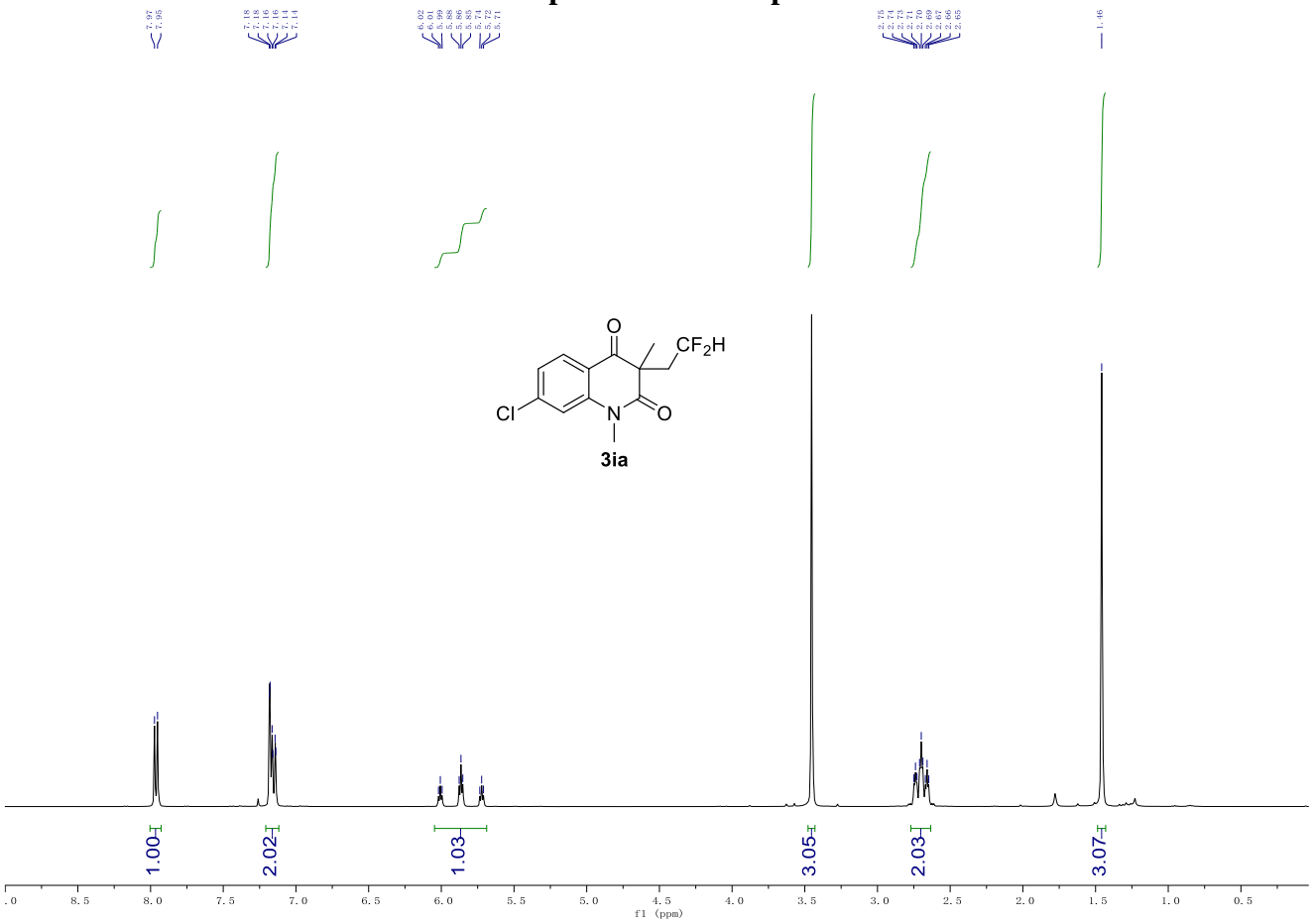
^{1}H NMR Spectrum of Compound 3ha



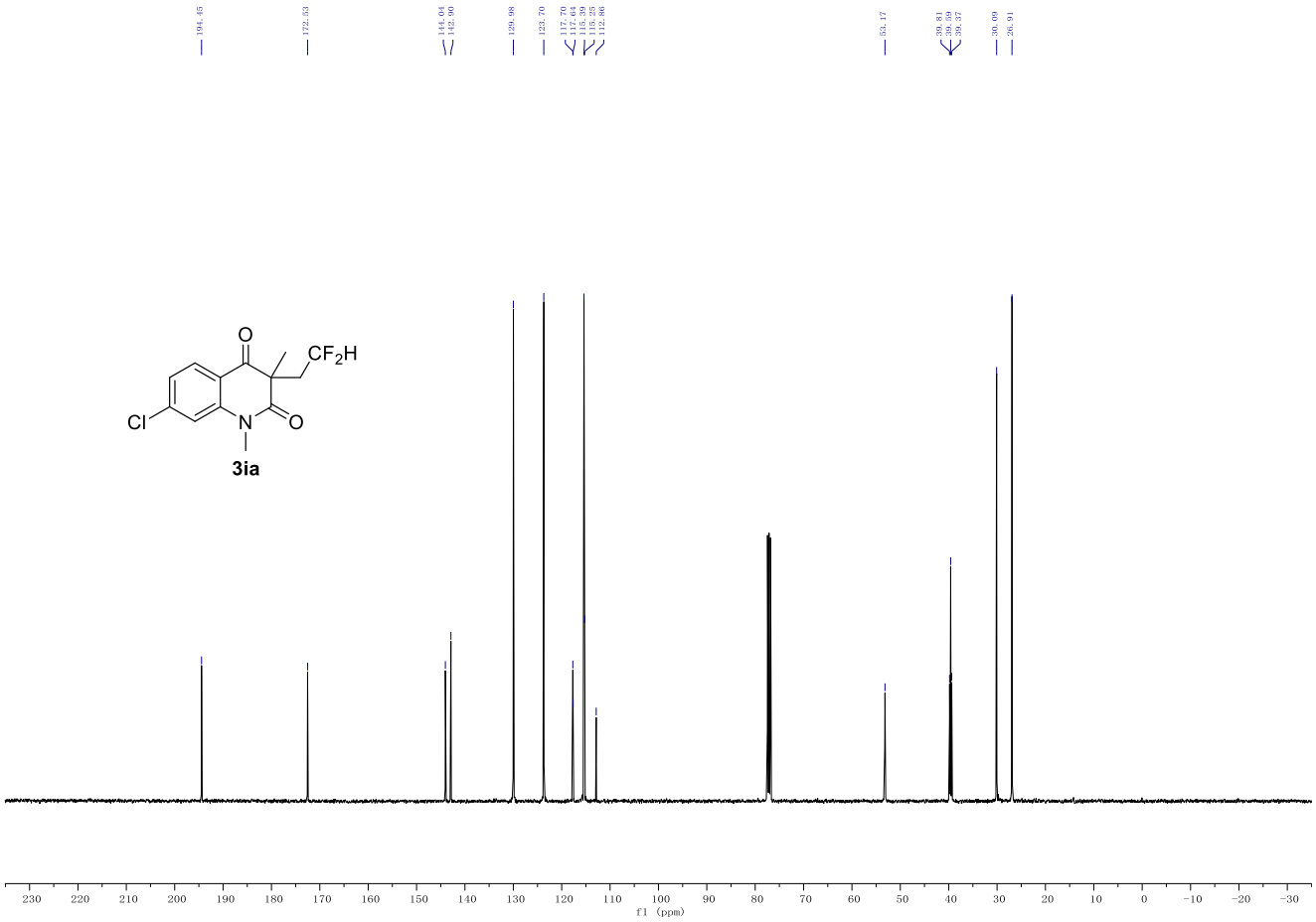
^{13}C NMR Spectrum of Compound 3ha



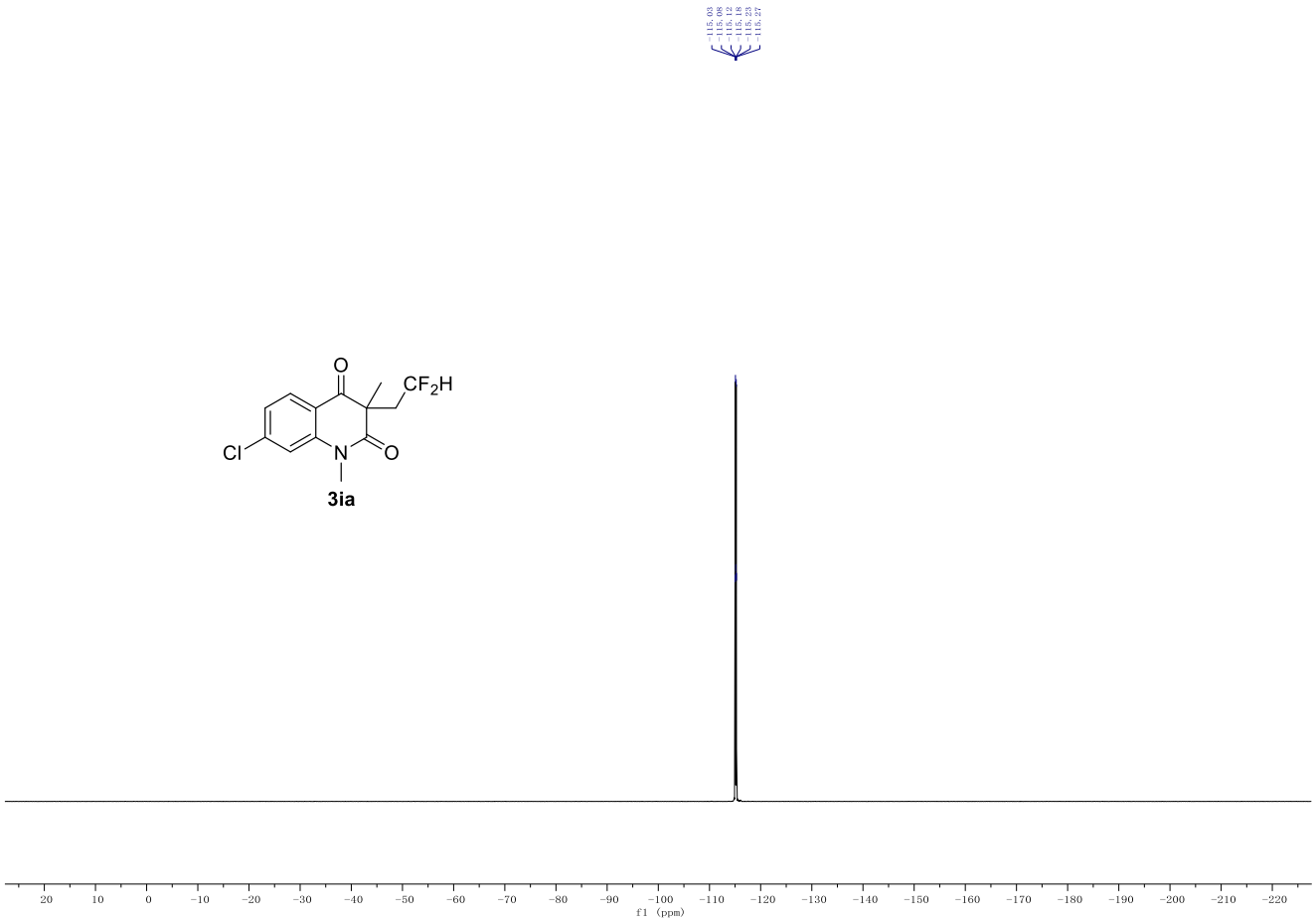
^{19}F NMR Spectrum of Compound 3ha



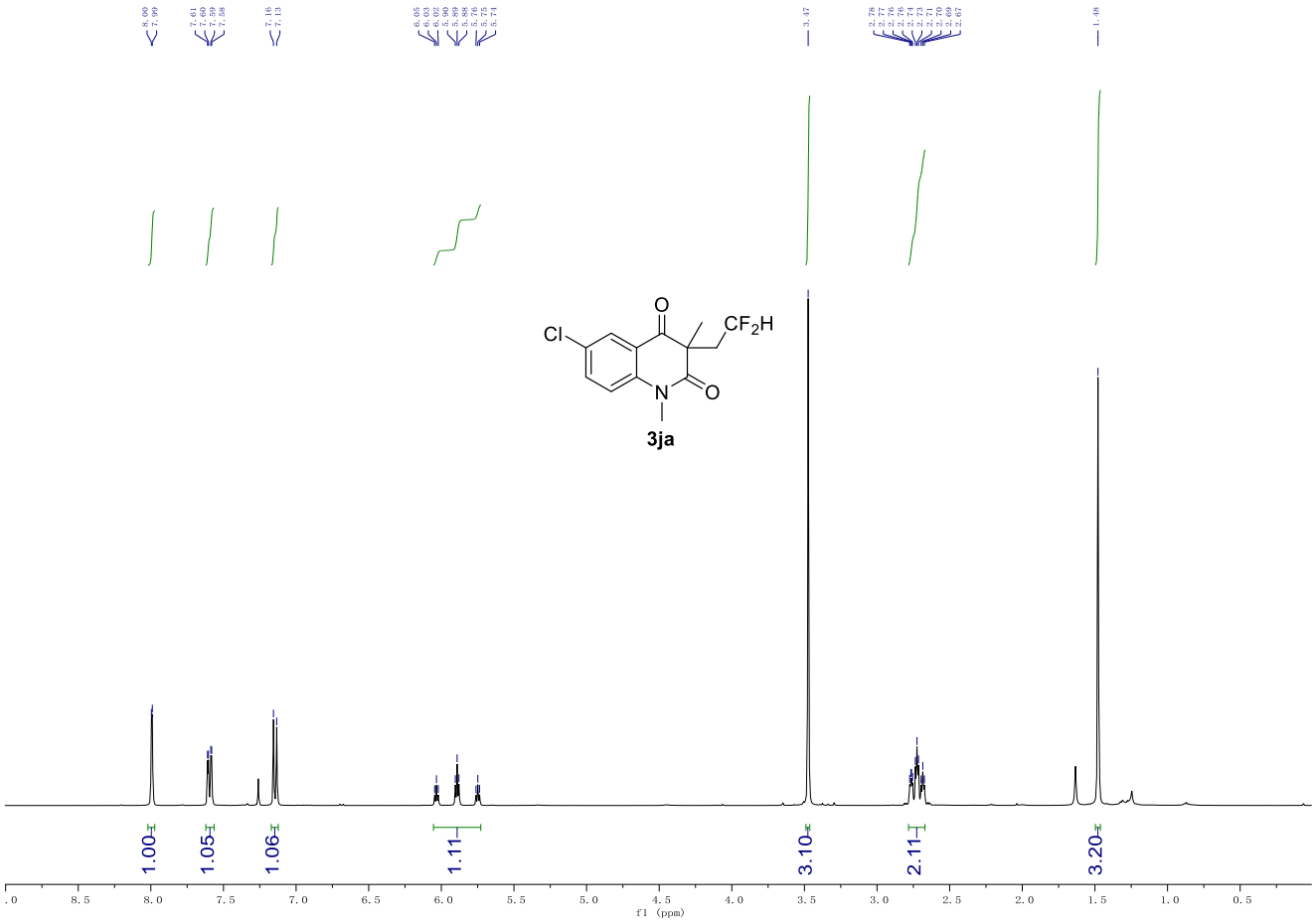
^{1}H NMR Spectrum of Compound 3ia



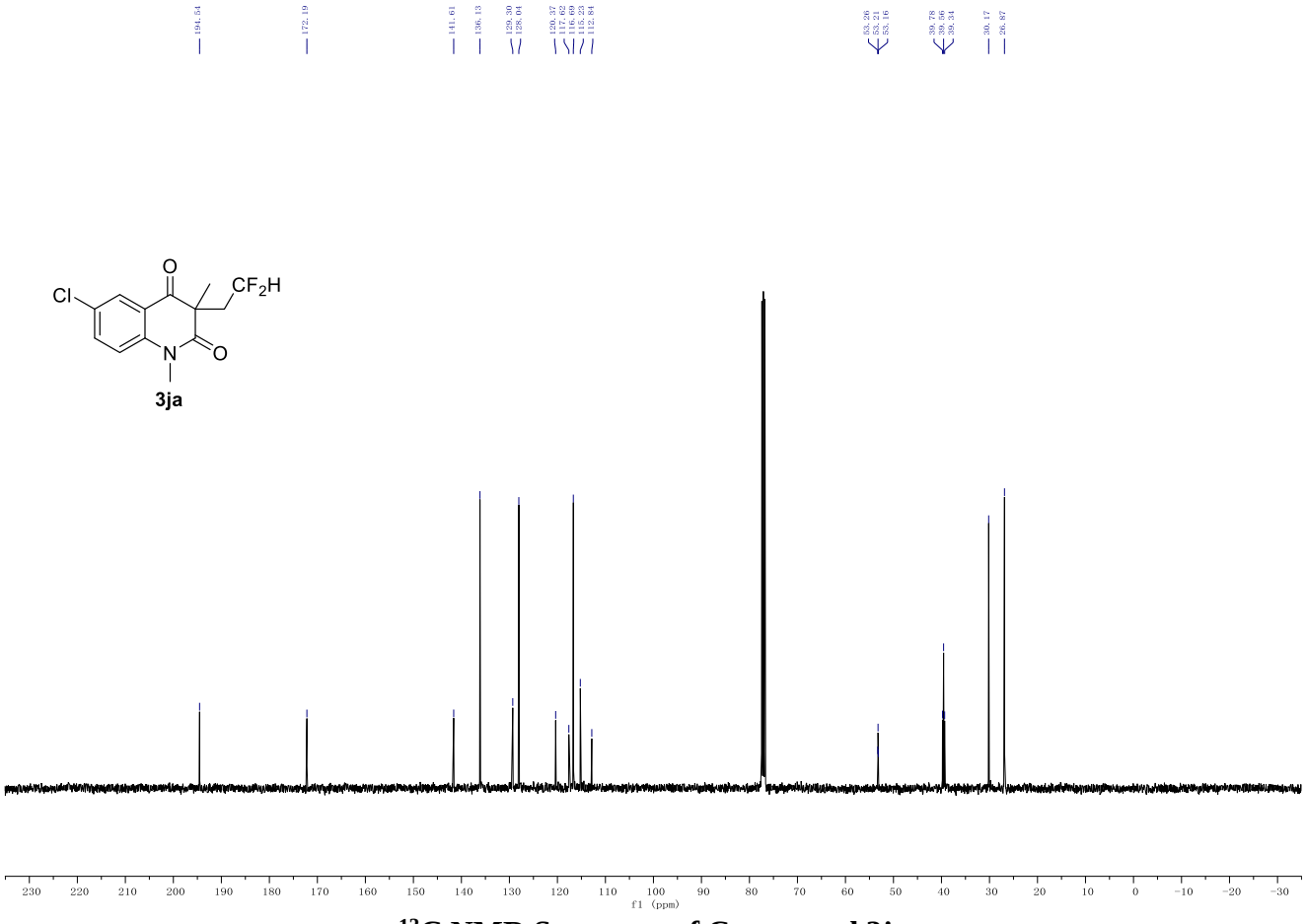
^{13}C NMR Spectrum of Compound 3ia



^{19}F NMR Spectrum of Compound 3ia

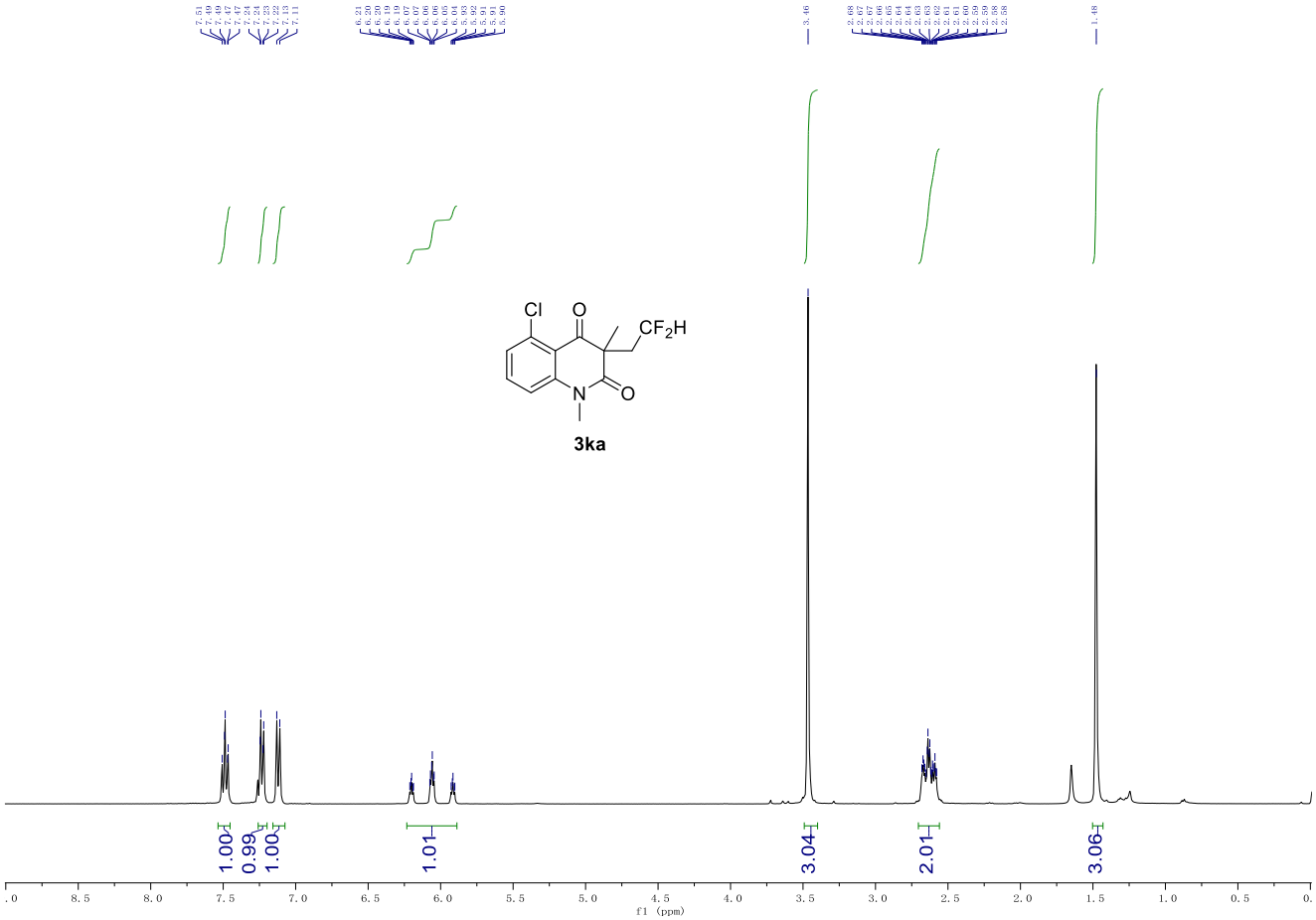


^{1}H NMR Spectrum of Compound 3ja

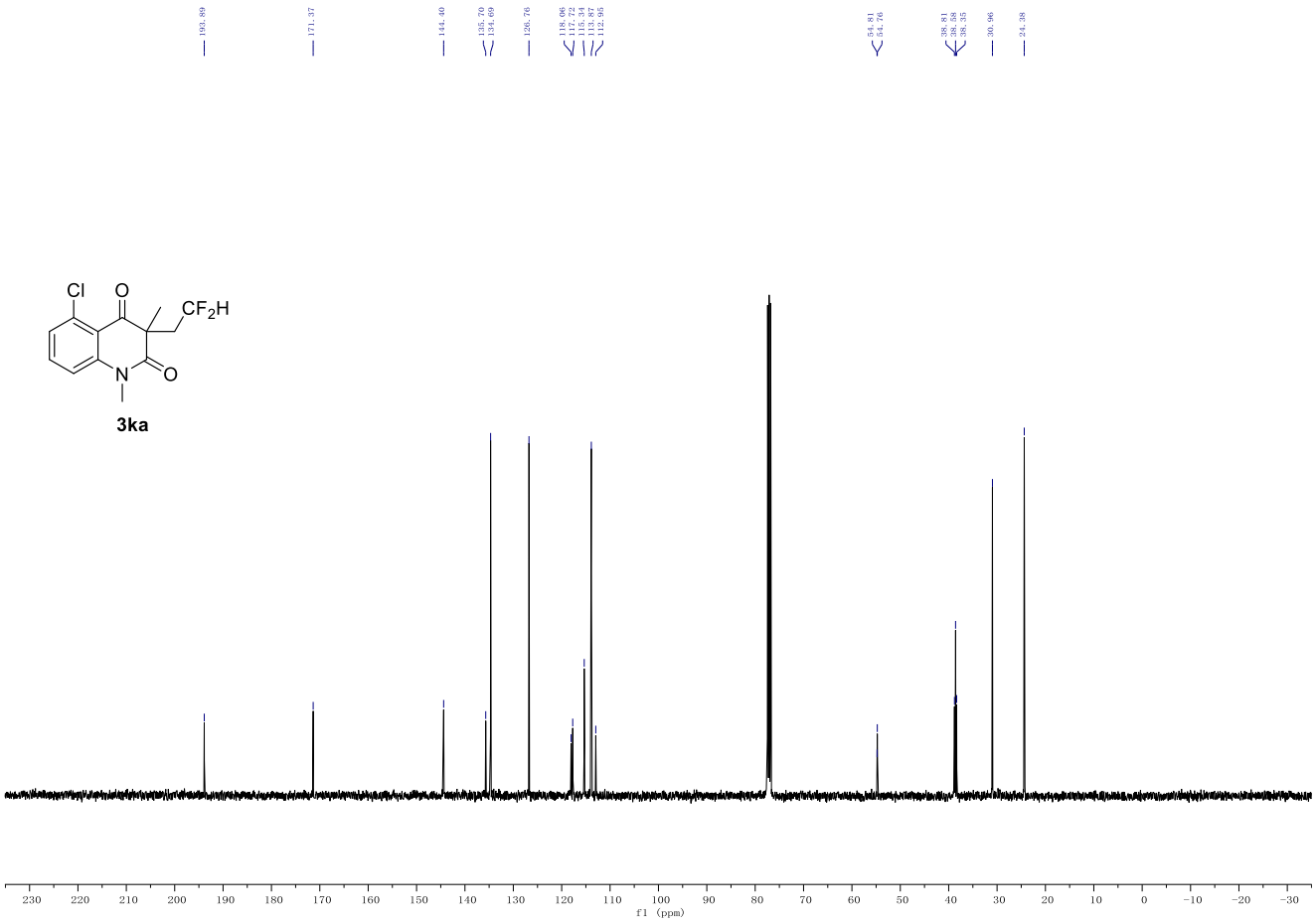


^{13}C NMR Spectrum of Compound 3ja

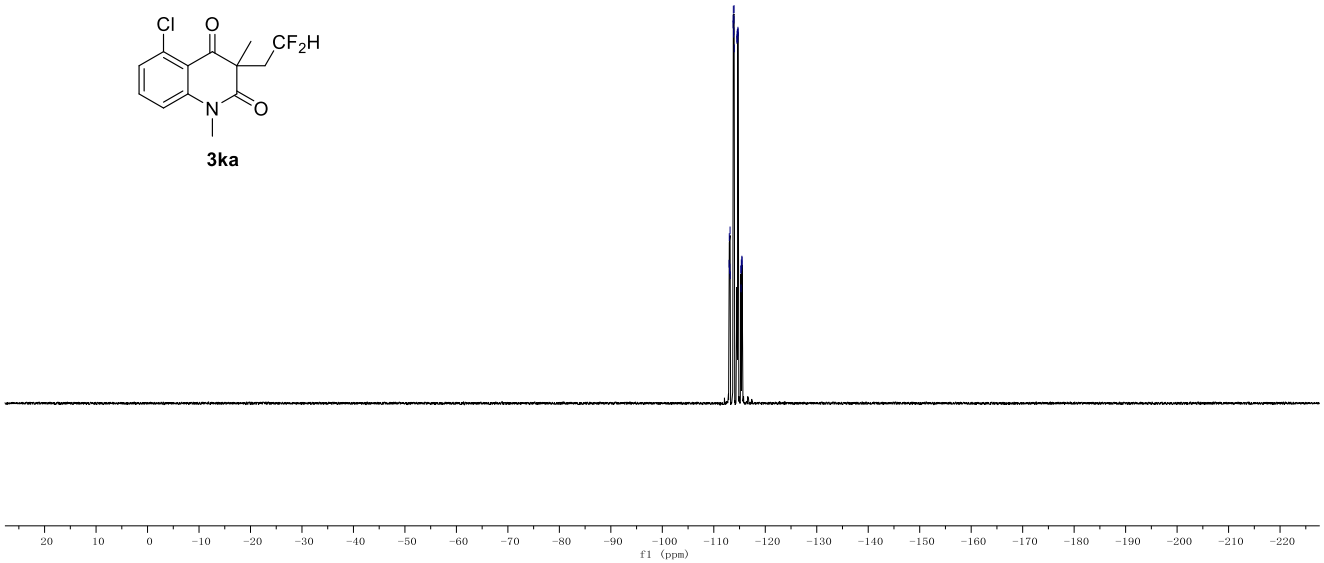
^{19}F NMR Spectrum of Compound 3ja



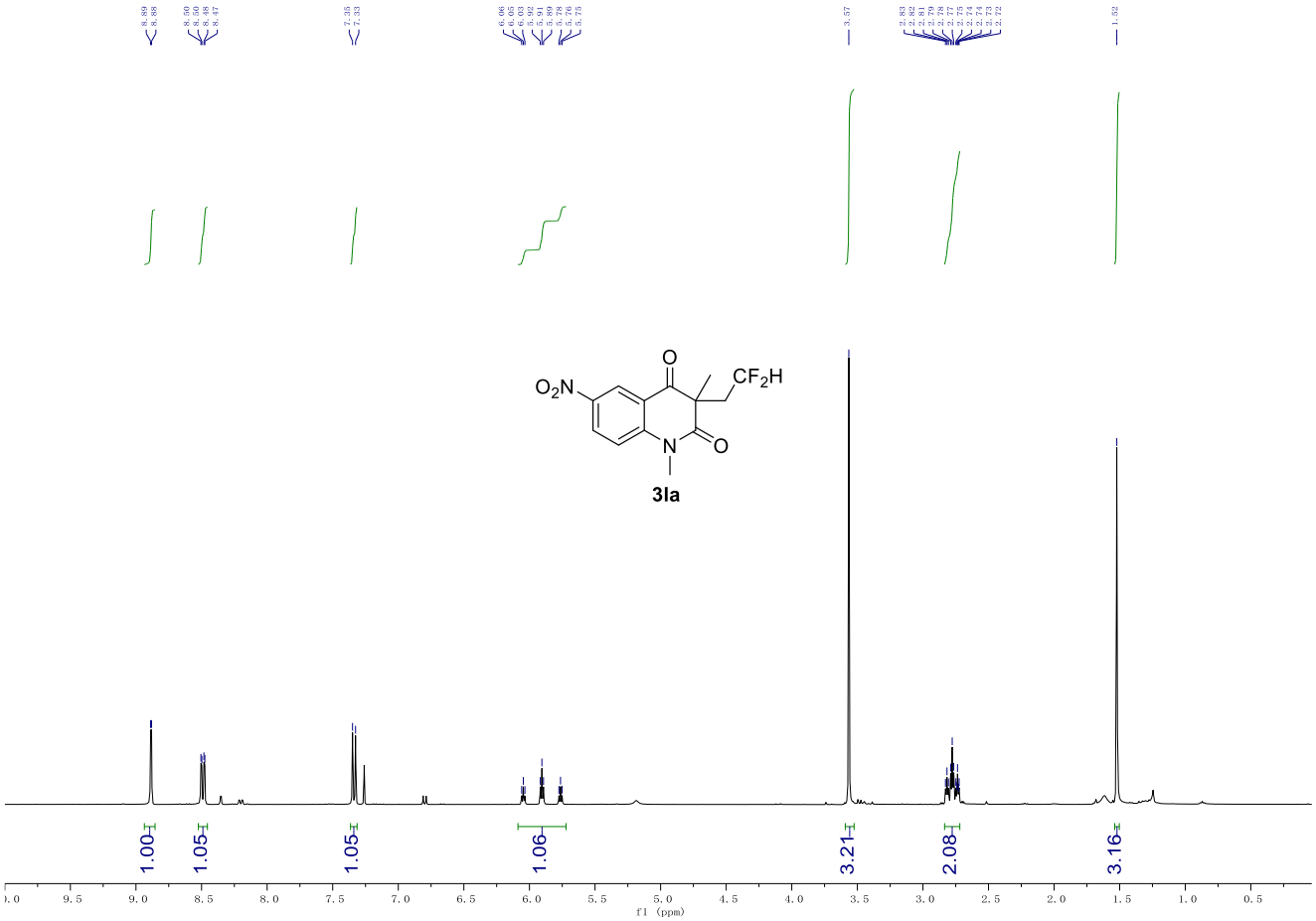
^{1}H NMR Spectrum of Compound 3ka



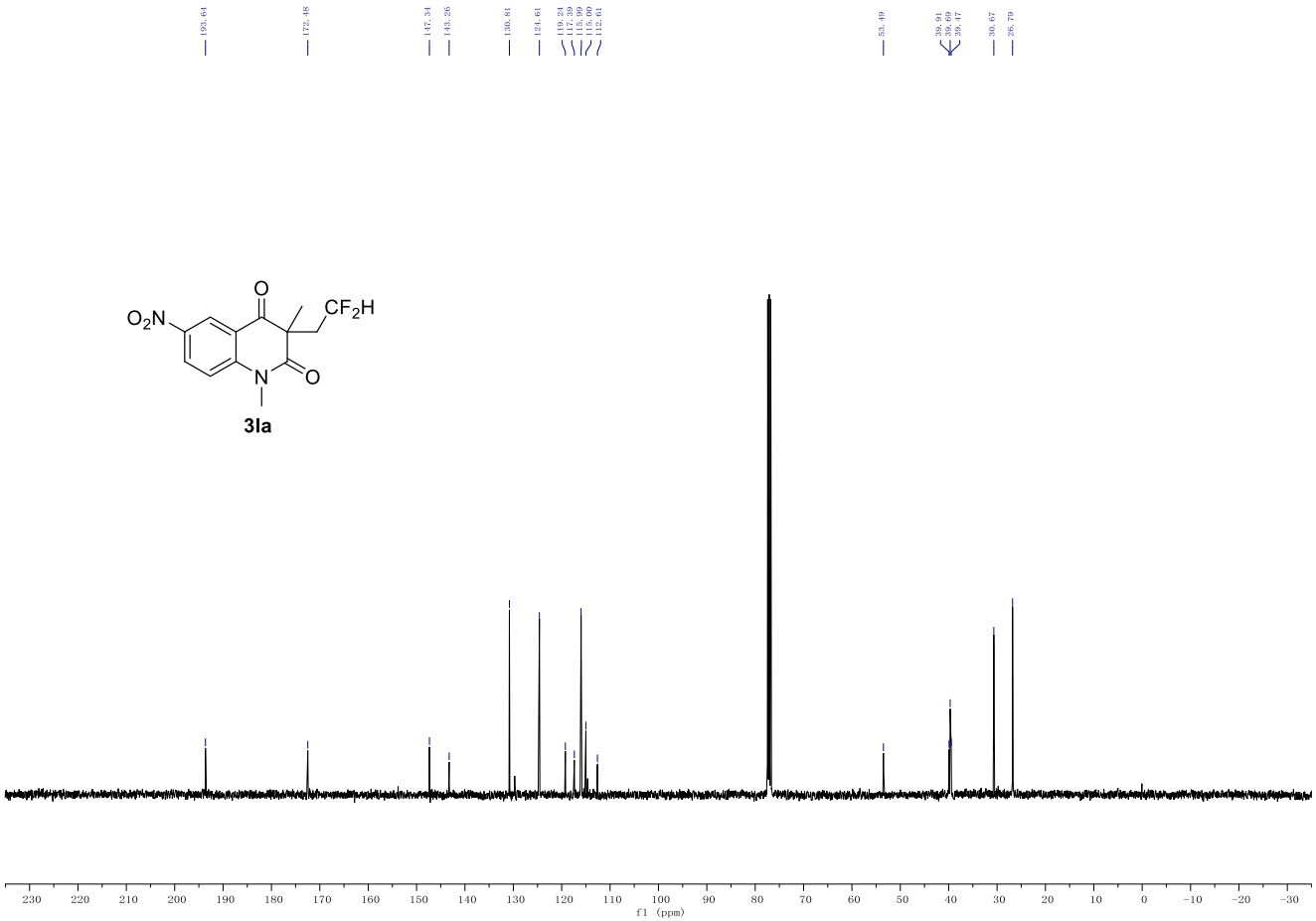
^{13}C NMR Spectrum of Compound 3ka



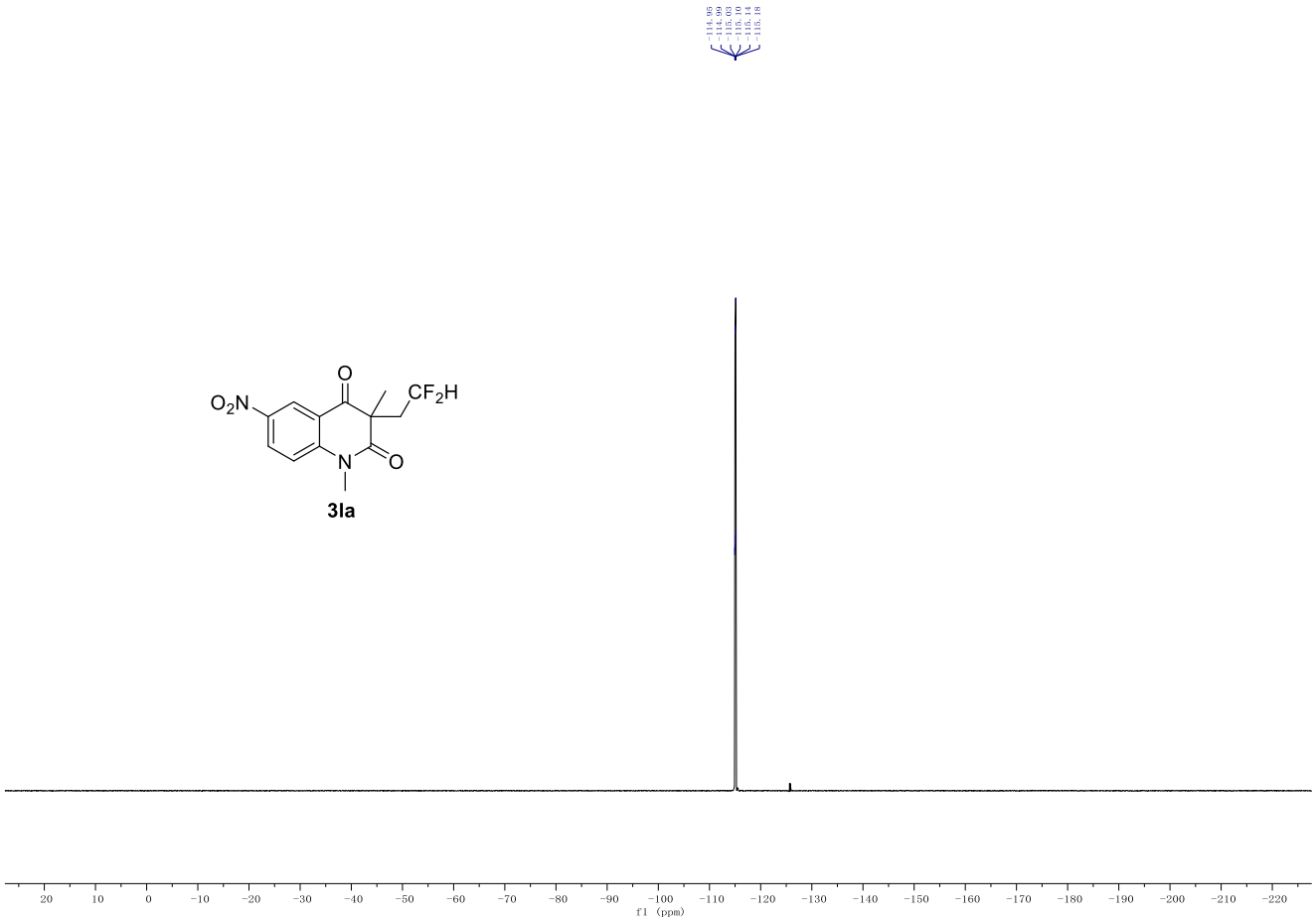
^{19}F NMR Spectrum of Compound 3ka



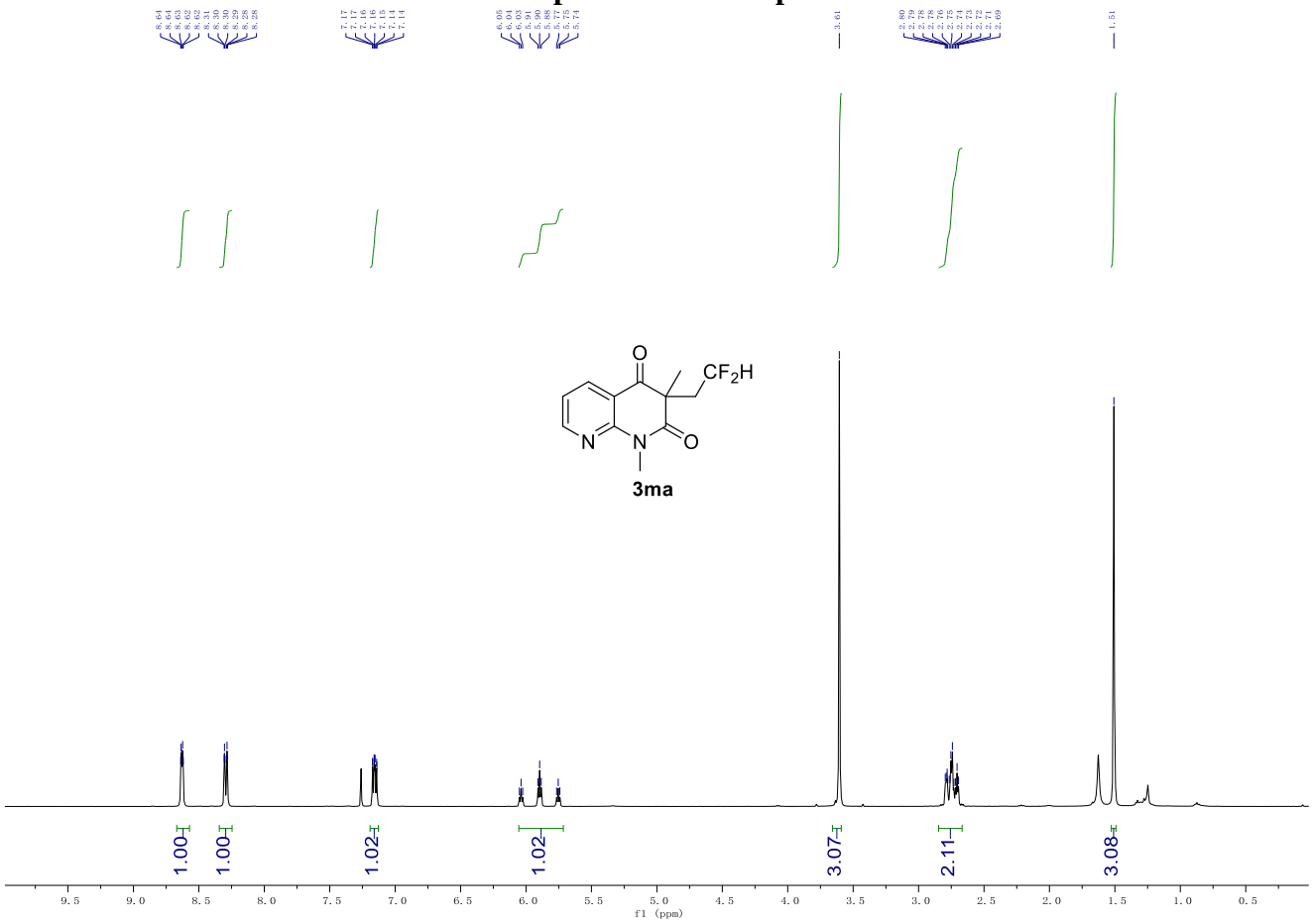
^{1}H NMR Spectrum of Compound 3la



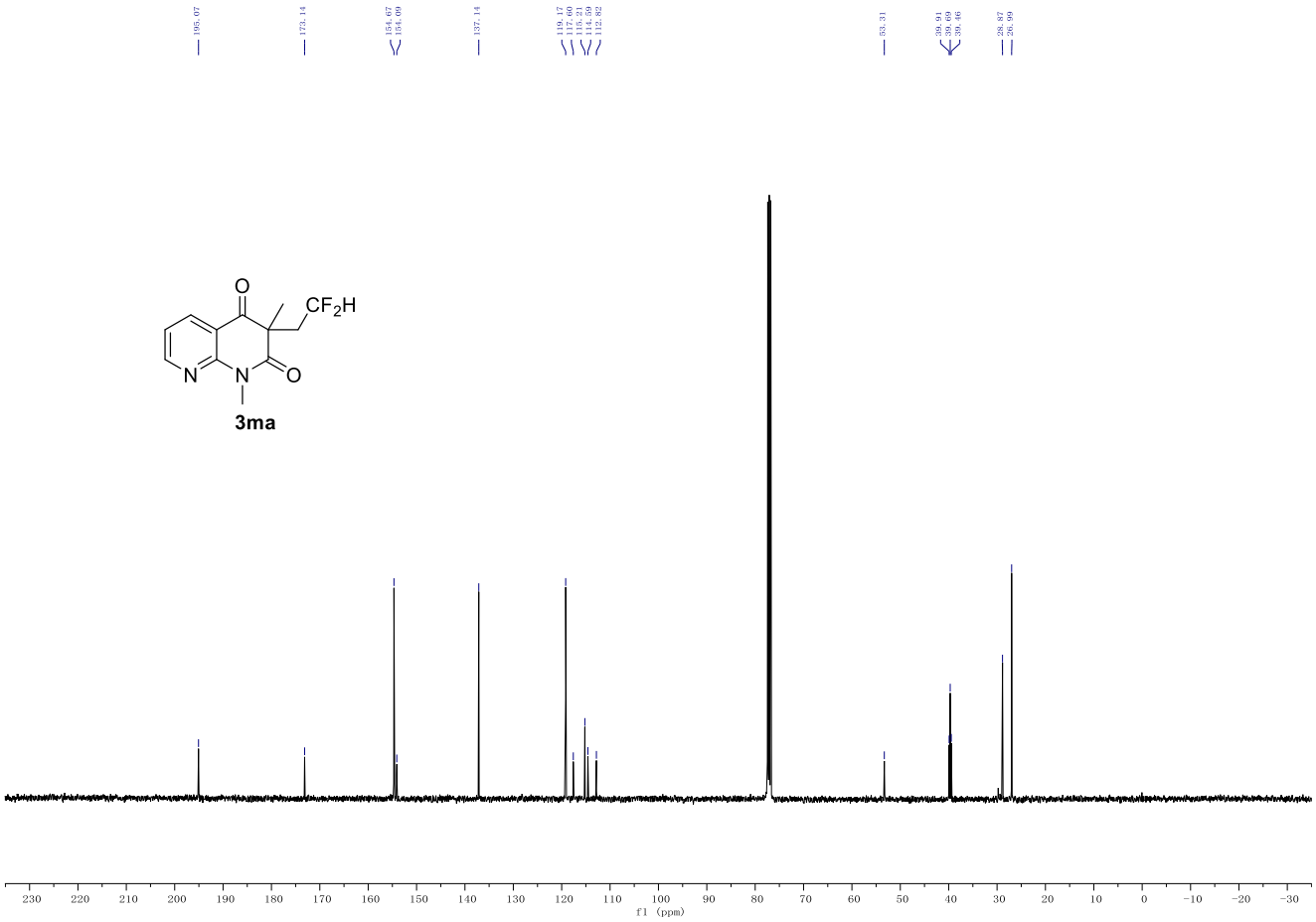
^{13}C NMR Spectrum of Compound 3la



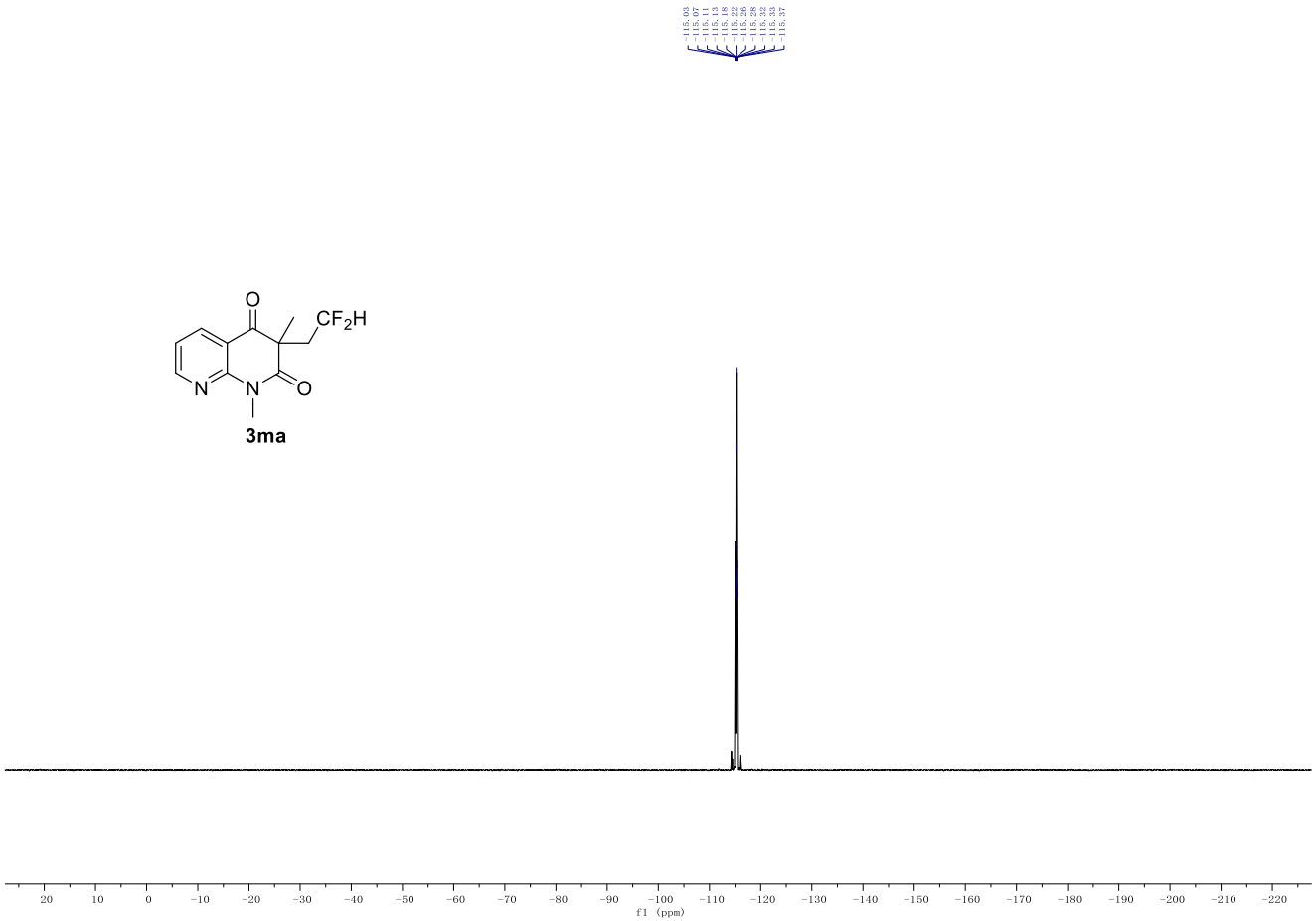
^{19}F NMR Spectrum of Compound 3la



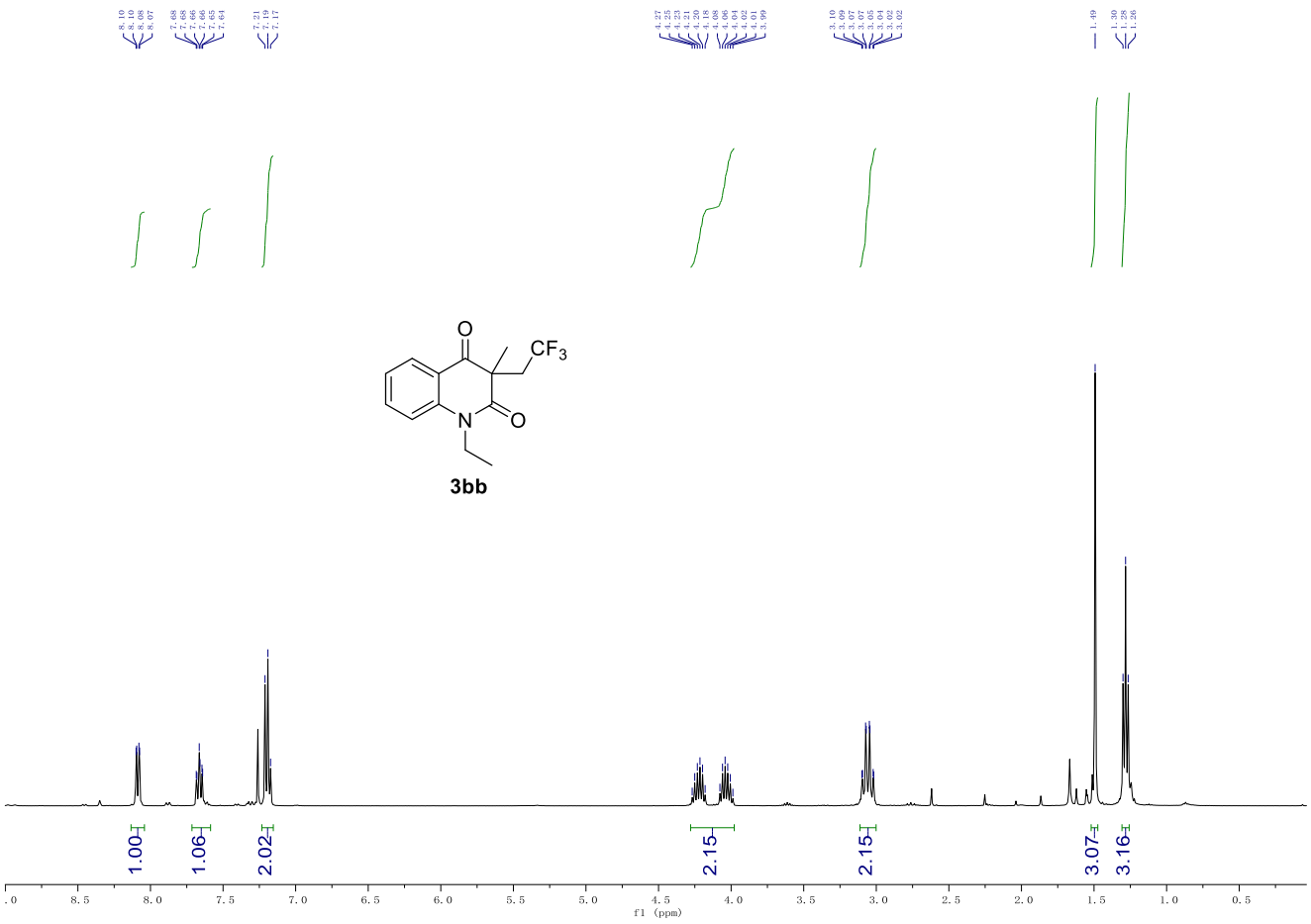
^{1}H NMR Spectrum of Compound 3ma



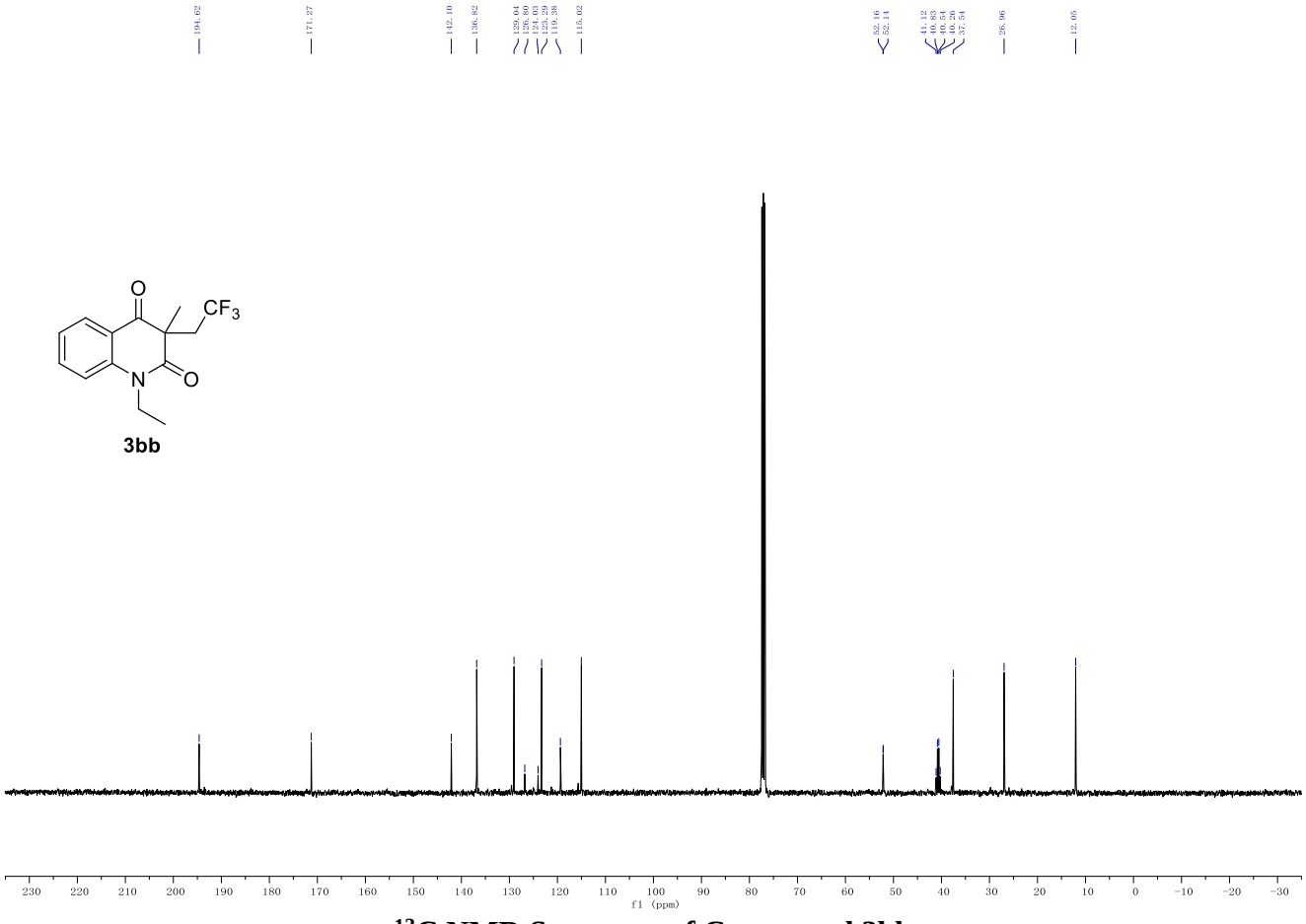
^{13}C NMR Spectrum of Compound 3ma



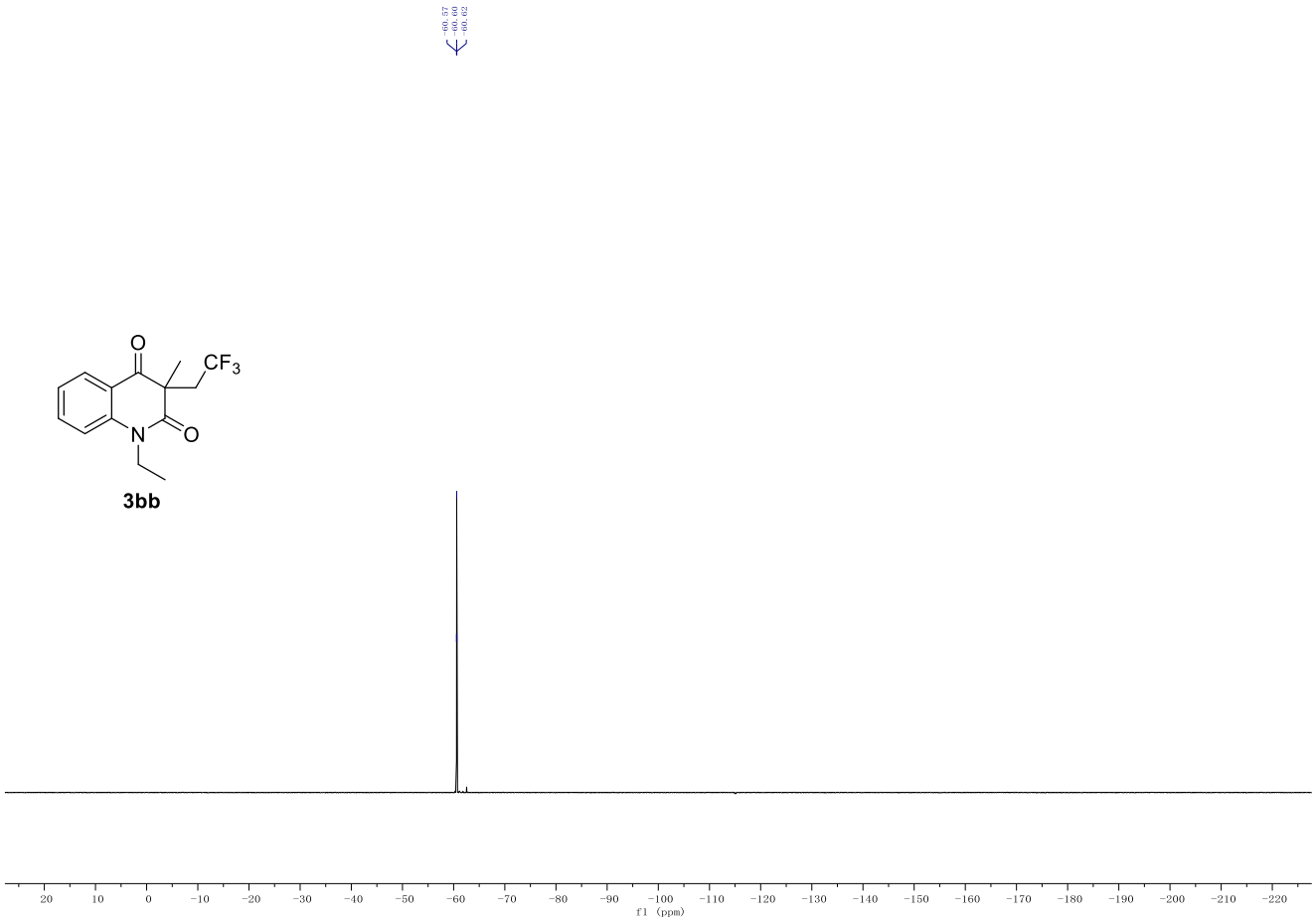
^{19}F NMR Spectrum of Compound 3ma



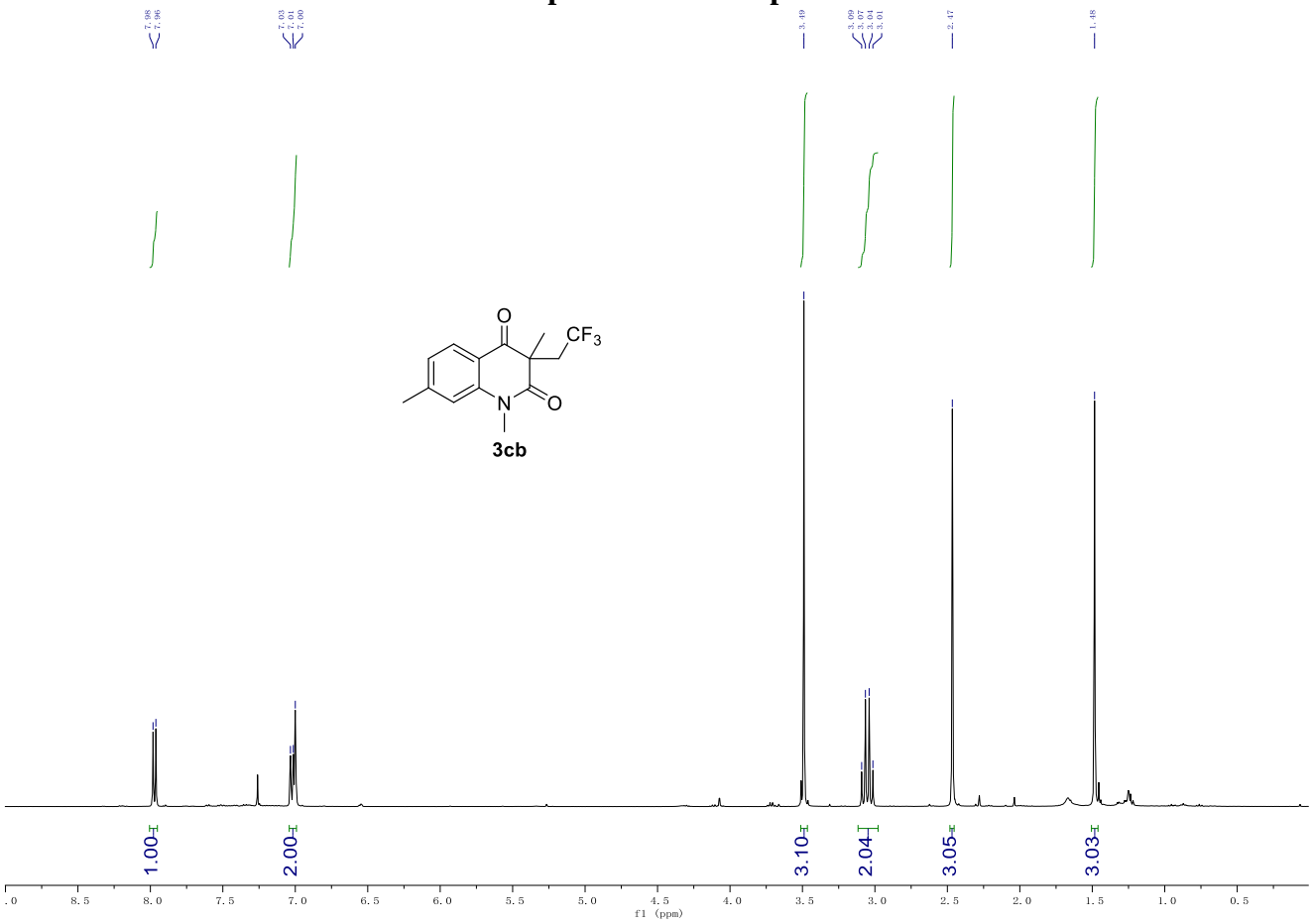
^{1}H NMR Spectrum of Compound 3bb



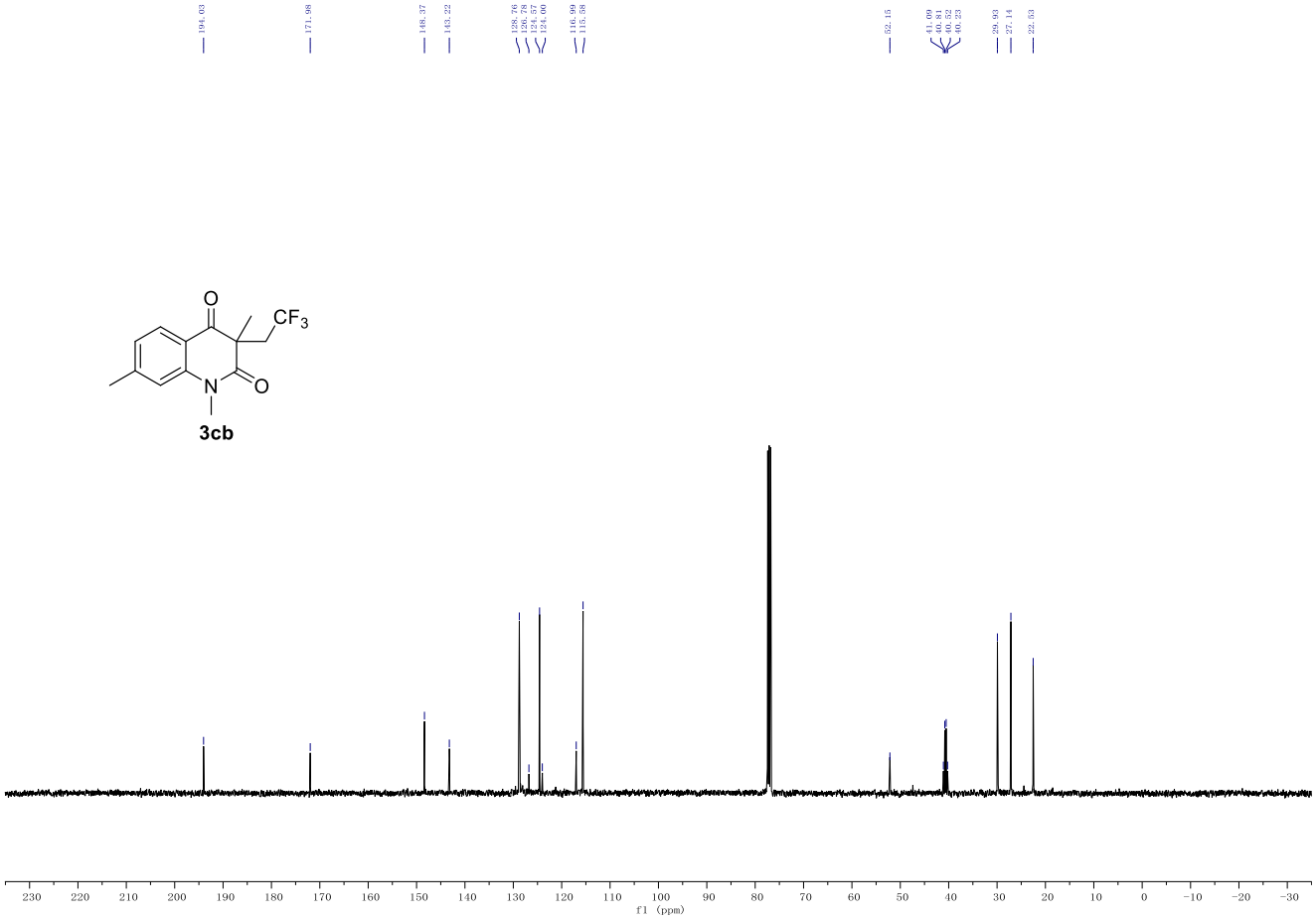
^{13}C NMR Spectrum of Compound 3bb



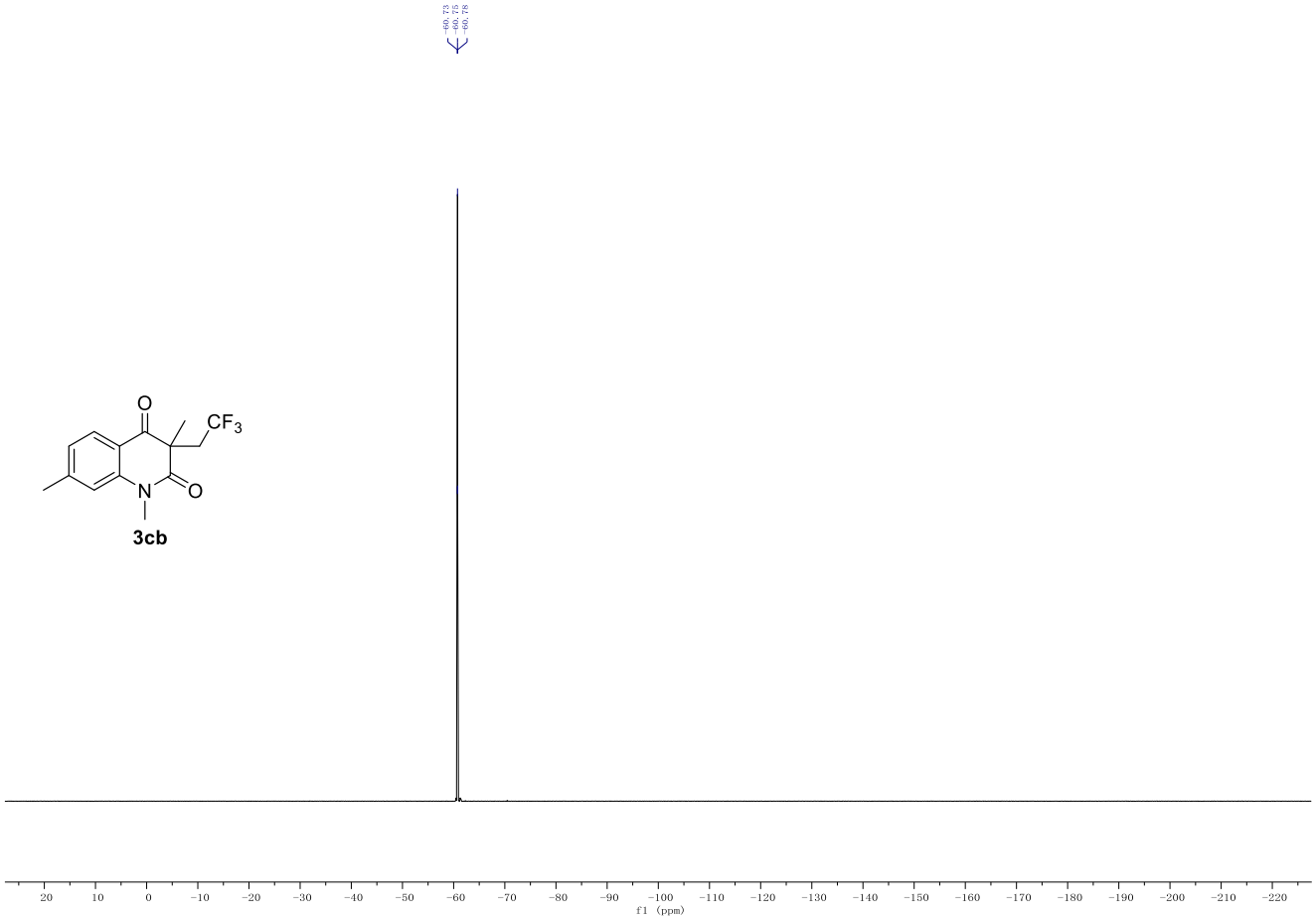
^{19}F NMR Spectrum of Compound 3bb



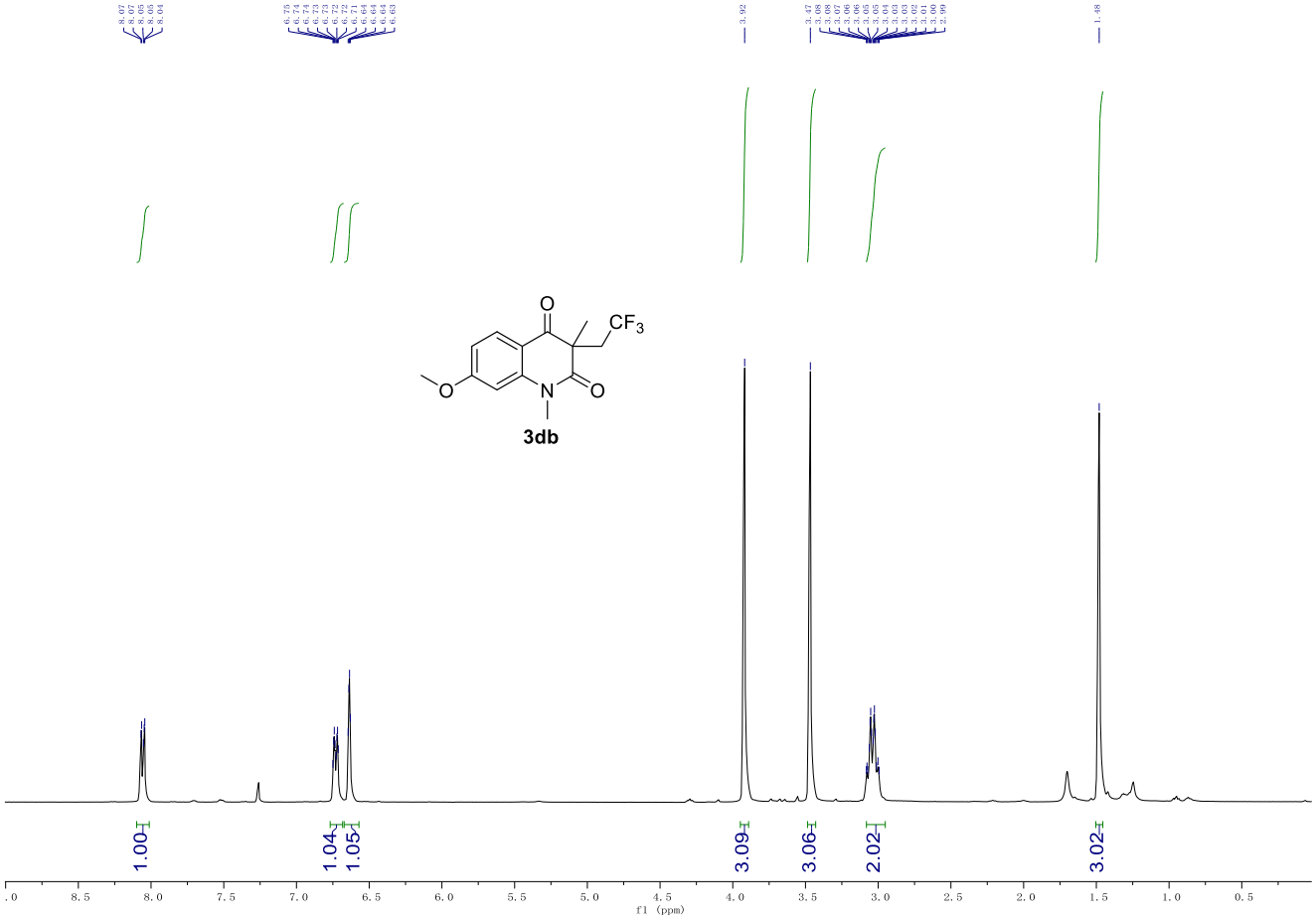
^{1}H NMR Spectrum of Compound 3cb



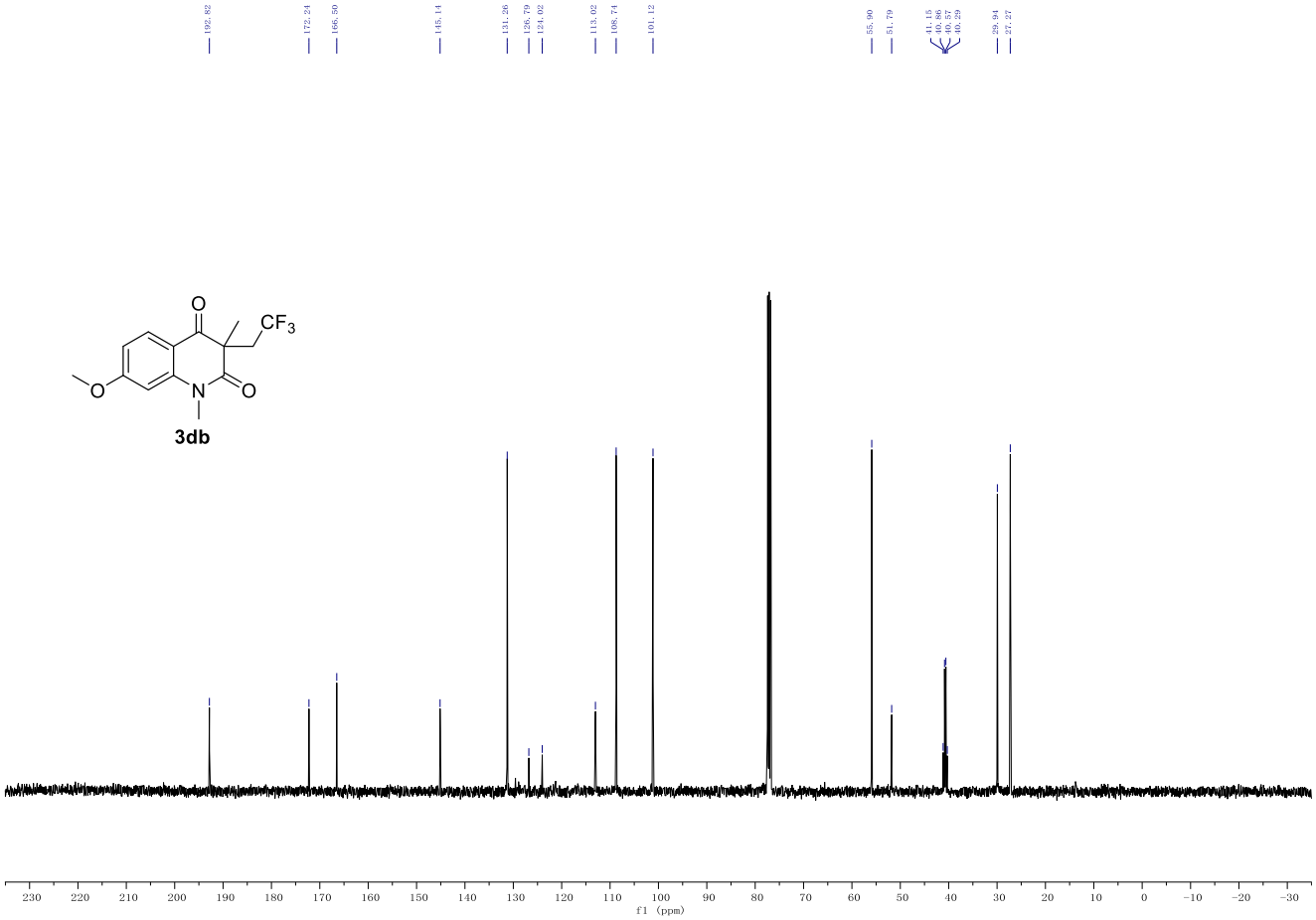
^{13}C NMR Spectrum of Compound 3cb



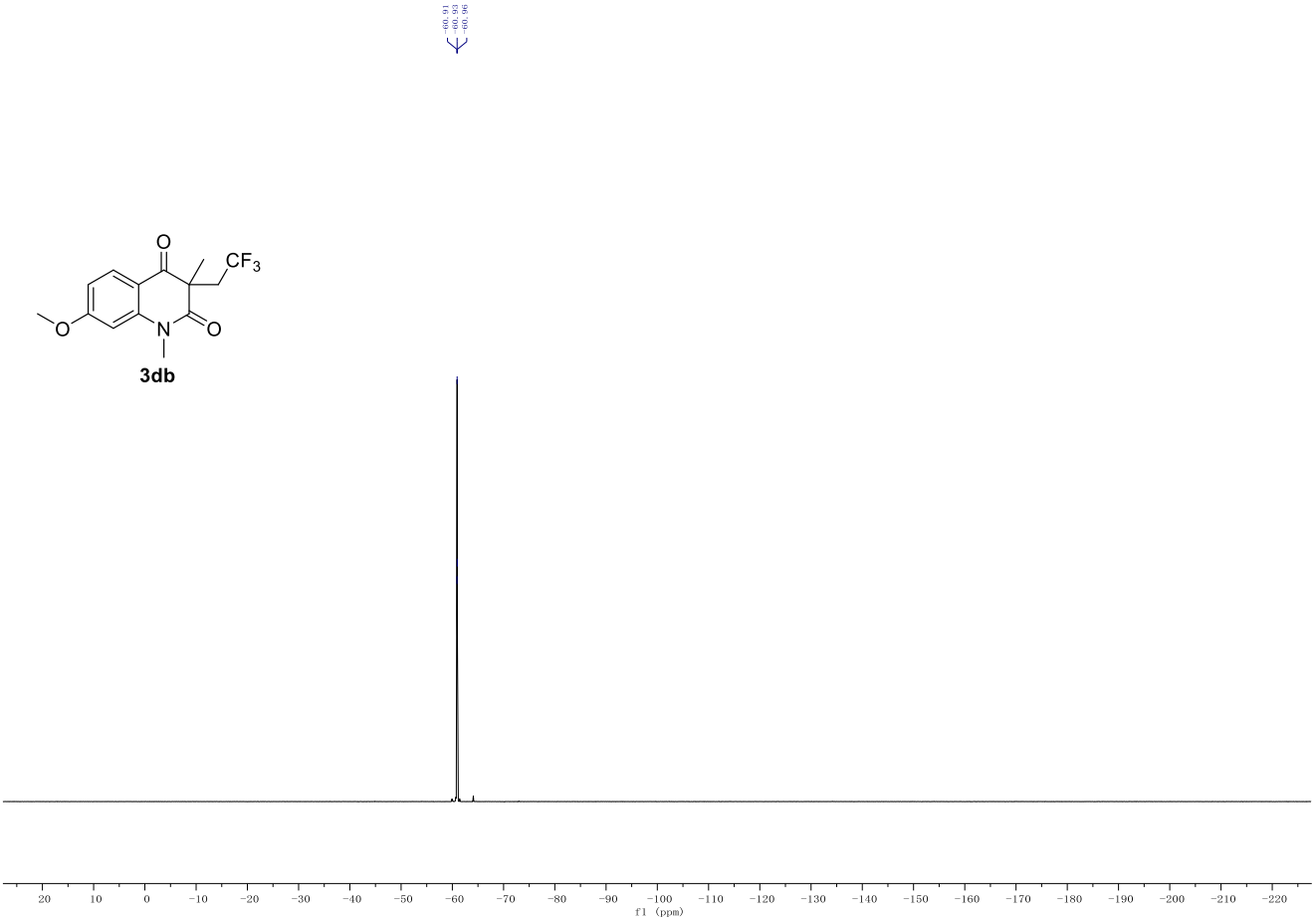
^{19}F NMR Spectrum of Compound 3cb



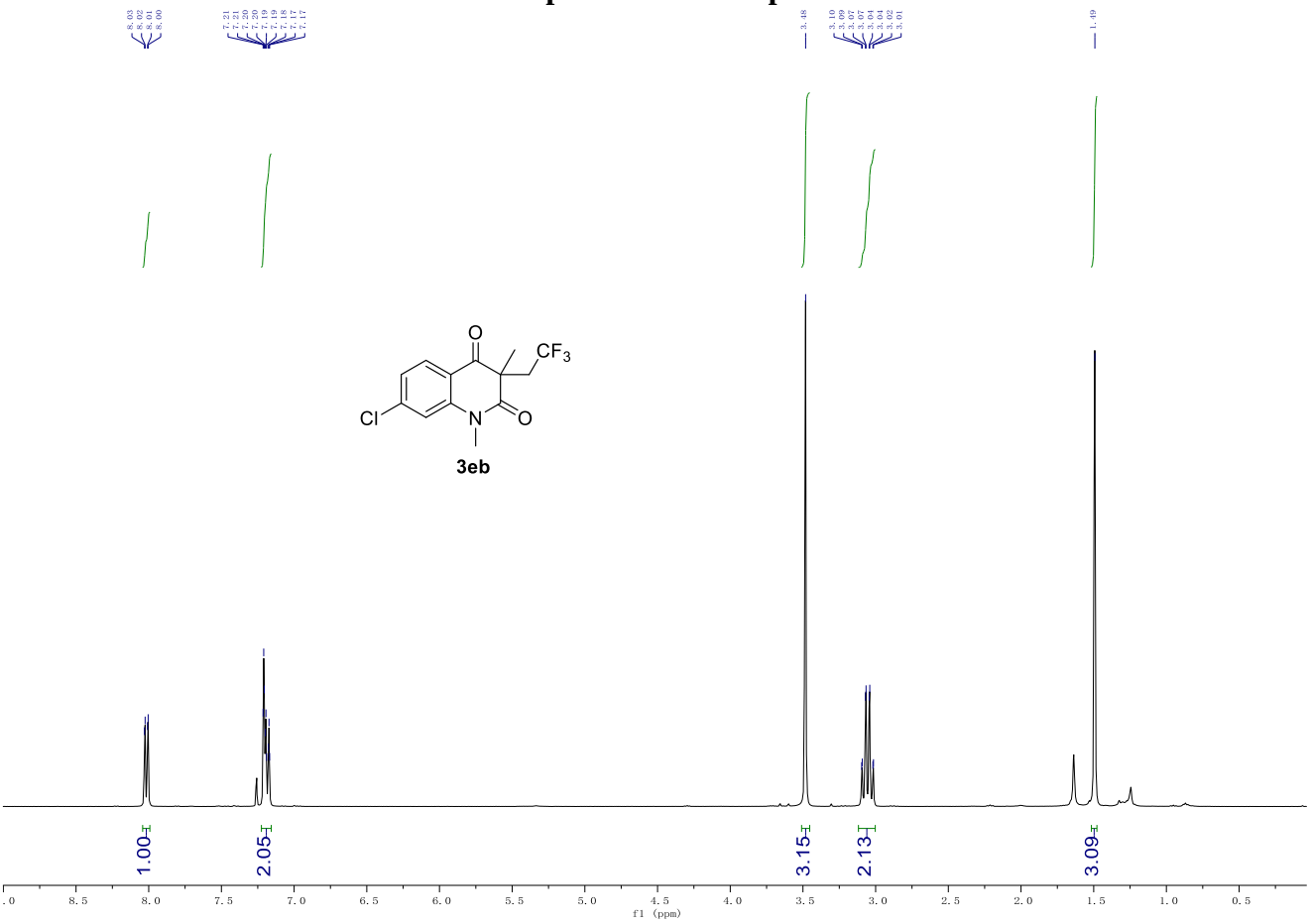
^{1}H NMR Spectrum of Compound 3db



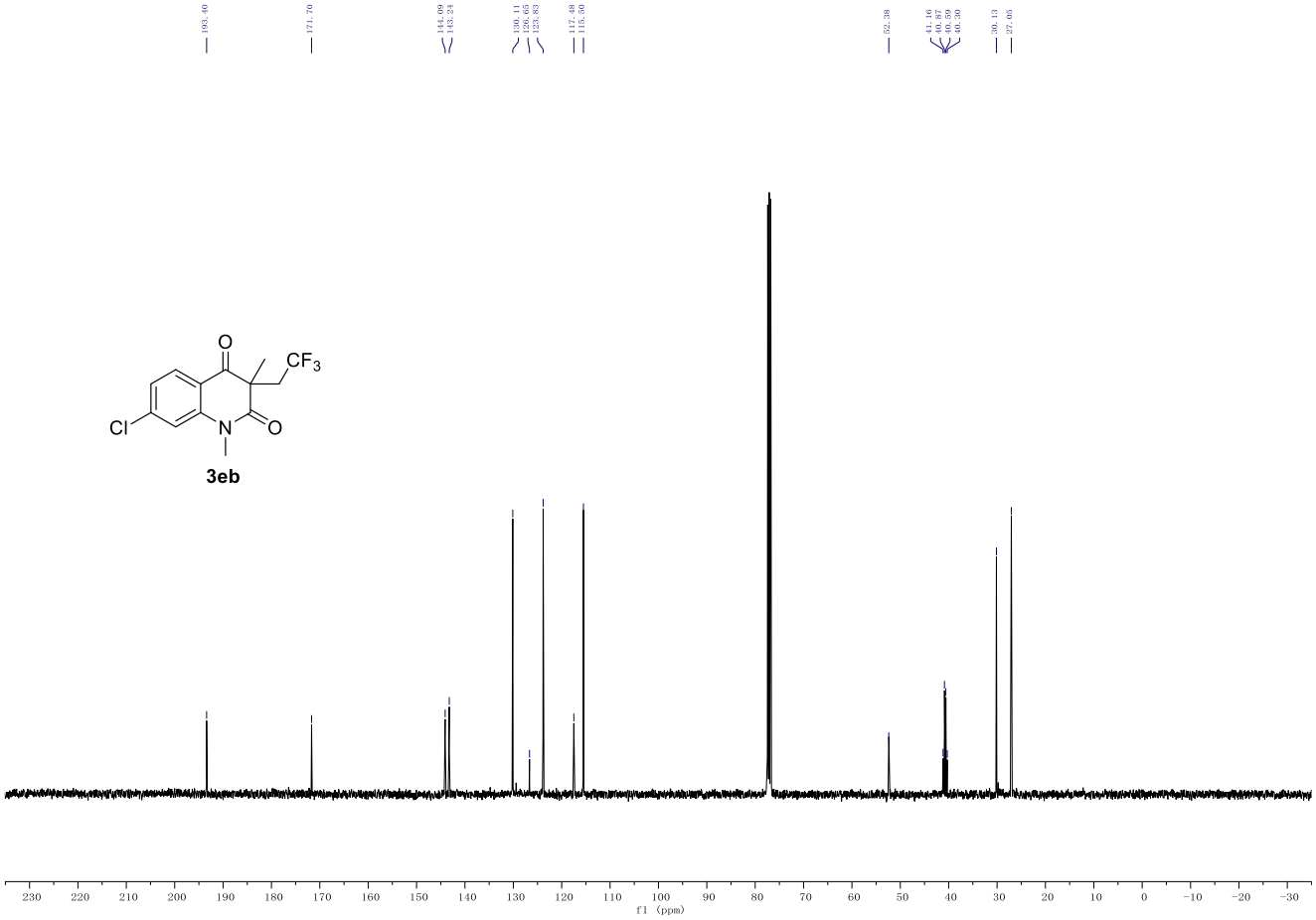
^{13}C NMR Spectrum of Compound 3db



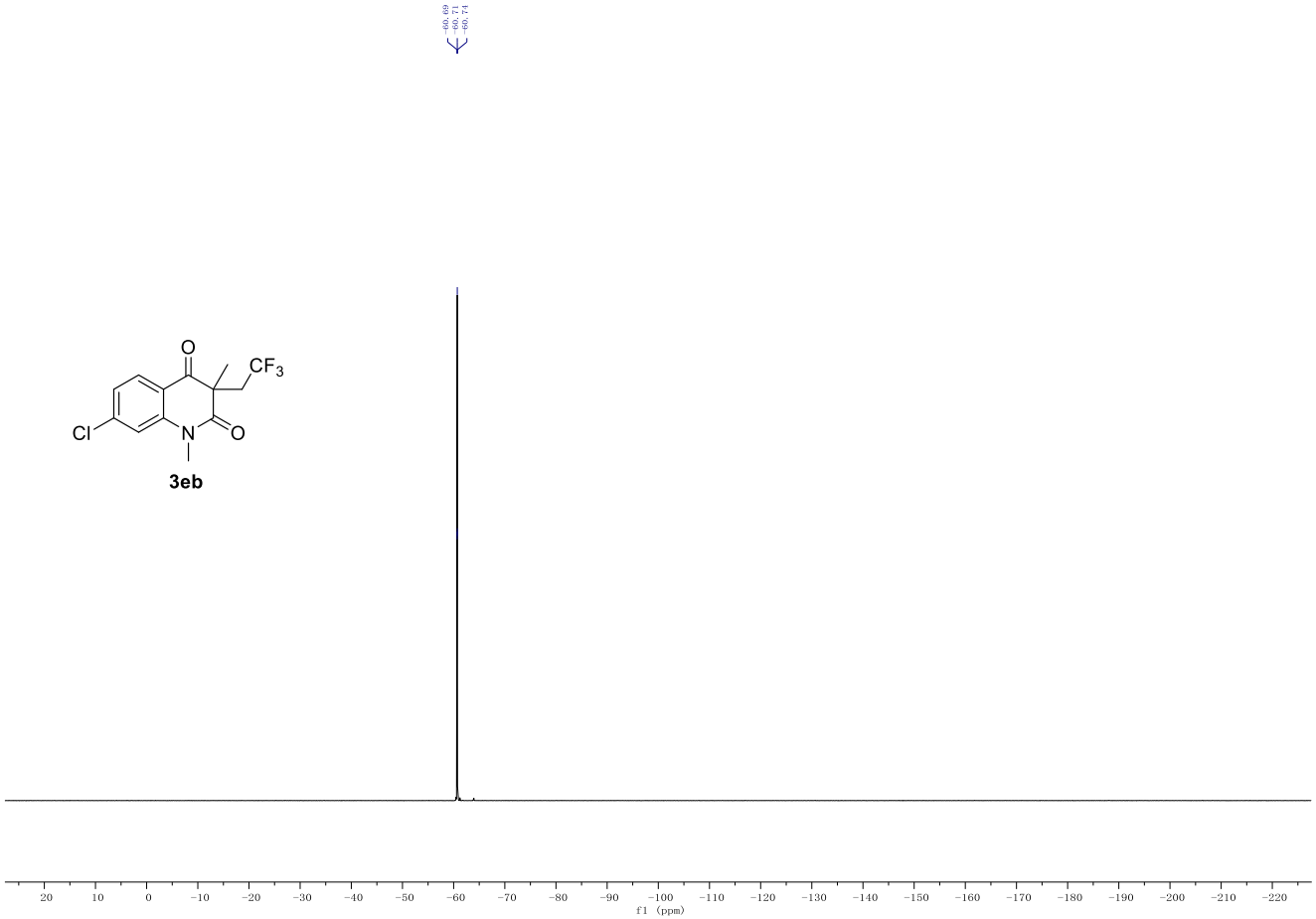
^{19}F NMR Spectrum of Compound 3db



^{1}H NMR Spectrum of Compound 3eb



^{13}C NMR Spectrum of Compound 3eb



^{19}F NMR Spectrum of Compound 3eb