Copper-Mediated a-Trifluoromethylation of *N*-phenylcinnamamides Coupled with Dearomatization: Access to Trifluoromethylated 1-Azaspiro[4.5]decanes

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Supporting Information

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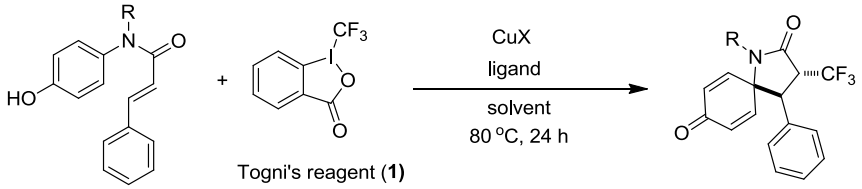
General Information: All reagents were used as received. 1,2-dichloroethane (DCE) was distilled on phosphorus pentoxide. ^{1}H, ^{13}C, and ^{19}F Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker Avance 400 Ultrashield NMR spectrometers. Chemical shifts (δ) were given in parts per million (ppm) and were measured downfield from internal tetramethylsilane. High-resolution mass spectrometry (HRMS) data were obtained on an FTICR-MS instrument (Ionspec 7.0 T). The melting points were determined on an X-4 microscope melting point apparatus and are uncorrected. Conversion was monitored by thin layer chromatography (TLC). Flash column chromatography was performed over silica gel (200-300 mesh). Togni's reagent **1** was synthesized with a described procedure previously.[S1]

Table S1 Optimization of reaction conditions.[a]



2a R= Me
2b R= *i*-Pr

Togni's reagent (**1**)

3a R= Me
3b R= *i*-Pr

entry	CuX (50 mol %)	Ligand	Solvent[b]	Yield%[c]
1	$Cu(CH_3CN)PF_6$	—	$CHCl_3$	20%
2	CuCl	—	$CHCl_3$	36%
3	CuBr	—	$CHCl_3$	56%
4	CuI	—	$CHCl_3$	40%
5	CuTc	—	$CHCl_3$	40%
6	CuCN	—	$CHCl_3$	52%
7	Cu_2O	—	$CHCl_3$	40%
8	CuBr	—	DCE	63%
9	CuBr	—	dioxane	32%
10	CuBr	—	DMF	21%
11	CuBr	—	EtOH	<5%
12	CuBr	—	DMSO	55%
13	CuBr	—	CH_3CN	43%
14	CuBr	2,2'-Bipy	DCE	41%
15	CuBr	1,10-phen	DCE	50%
16	CuBr	2,2'-biquinoline	DCE	40%
17	CuBr	2,2'-Bipy	DMSO	52%
18	CuBr	1,10-phen	DMSO	54%
19	CuBr	2,2'-biquinoline	DMSO	46%
20[d]	CuBr	—	DCE	70%
21[d,e]	CuBr	—	DCE	74%
22[d,e,f]	CuBr	—	DCE	80%(76%)[g]

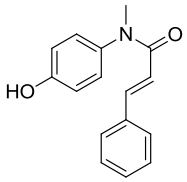
[a]Reaction conditions: **2a** (0.2 mmol), **1** (0.4 mmol), catalyst (0.1 mmol), solvent (3 mL), 80 °C, 24 h, under N_2. (unless otherwise noted) [b]Reaction temperature in $CHCl_3$ was 60 °C. [c]Determined by

[19]F NMR analysis with (trifluoromethyl)benzene as an internal standard. [d]Compound **2b** was used. [e]100 mol% Cu catalyst was used. [f]4Å molecular sieves were added. [g]The value in parentheses was isolated yield.

Characterization of starting materials

All starting materials were prepared according to previously reported procedures. Characterization of non-previously reported compounds is given.

***N*-(4-hydroxyphenyl)-*N*-methylcinnamamide (2a)**



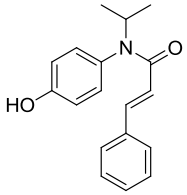
White solid. Mp: 184–188 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.73 (s, 1H), 7.47 (d, J = 15.6 Hz, 1H), 7.34 (s, 5H), 7.12 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 6.36 (d, J = 15.6 Hz, 1H), 3.23 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 156.6, 140.1, 134.8, 134.5, 129.5, 128.9, 128.4, 127.5, 119.1, 116.0, 37.2.

HRMS (ESI) calcd for $C_{16}H_{16}NO_2$ $[M+H]^+$ 254.1176, found 254.1182.

***N*-(4-hydroxyphenyl)-*N*-isopropylcinnamamide (2b)**



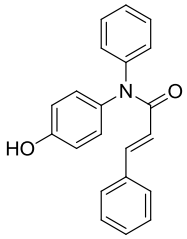
White solid. Mp: 216–218ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 15.6 Hz, 1H), 7.26 (br, 5H), 7.08 – 6.86 (m, 4H), 6.18 (d, J = 15.6 Hz, 1H), 5.18 – 5.04 (m, 1H), 1.12 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO) δ 164.4, 157.2, 140.0, 134.8, 131.5, 129.4, 128.9, 128.6, 127.3, 120.0, 115.7, 45. 3, 20.7.

HRMS (ESI) calcd for $C_{18}H_{20}NO_2$ $[M+H]^+$ 282.1489, found 282.1494.

***N*-(4-hydroxyphenyl)-*N*-phenylcinnamamide (2c)**

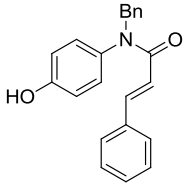


White solid. Mp: 247–249 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.71 (s, 1H), 7.57 (d, J = 15.6 Hz, 1H), 7.46 – 7.24 (m, 10H), 7.16 (d, J = 8.2 Hz, 2H), 6.81 (d, J = 8.2 Hz, 2H), 6.46 (d, J = 15.6 Hz, 1H).

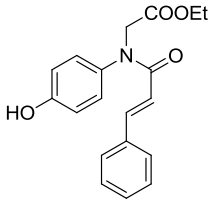
^{13}C NMR (100 MHz, DMSO-d_6) δ 165.5, 157.0, 143.7, 141.6, 135.1, 134.2, 130.3, 129.8, 129.4, 128.1, 127.4, 126.7, 120.4, 116.5.
HRMS (ESI) calcd for $C_{21}H_{18}NO_2$ $[M+H]^+$ 316.1332, found 316.1338.

_N_-benzyl-_N_-(4-hydroxyphenyl)cinnamamide (2d)



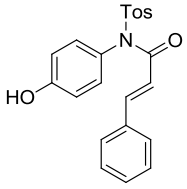
White solid. Mp: 218–221 ºC.
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 7.60 (d, J = 15.6 Hz, 1H), 7.52 – 7.12 (m, 10H), 6.97 (d, J = 7.6 Hz, 2H), 6.78 (d, J = 7.6 Hz, 2H), 6.40 (d, J = 15.6 Hz, 1H), 4.95 (s, 2H).
^{13}C NMR (100 MHz, DMSO-d_6) δ 166.3, 157.9, 142.1, 138.9, 135.9, 133.9, 130.8, 130.4, 130.1, 129.5, 129.2, 128.8, 128.2, 120.3, 117.1, 53.5.
HRMS (ESI) calcd for $C_{22}H_{20}NO_2$ $[M+H]^+$ 330.1489, found 330.1490.

ethyl 2-(_N_-(4-hydroxyphenyl)cinnamamido)acetate (2e)



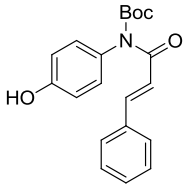
White solid. Mp: 144–145 ºC.
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.83 (s, 1H), 7.54 (d, J = 15.6 Hz, 1H), 7.44 – 7.28 (m, 5H), 7.20 (d, J = 7.6 Hz, 2H), 6.86 (d, J = 7.6 Hz, 2H), 6.40 (d, J = 15.6 Hz, 1H), 4.42 (s, 2H), 4.12 (q, J = 6.4 Hz, 2H), 1.21 (t, J = 5.6 Hz, 3H).
^{13}C NMR (100 MHz, DMSO-d_6) δ 170.3, 166.4, 158.1, 142.4, 135.7, 134.4, 131.0, 130.3, 130.1, 128.8, 119.4, 117.1, 61.8, 52.6, 15.2.
HRMS (ESI) calcd for $C_{19}H_{20}NO_4$ $[M+H]^+$326.1387, found 326.1393.

_N_-(4-hydroxyphenyl)-_N_-tosylcinnamamide (2f)



White solid. Mp: 172–174 ºC.
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (s, 1H), 7.84 – 7.78 (m, 3H), 7.66 (d, J = 8.0 Hz, 2H), 7.47 – 7.43 (m, 3H), 7.36 (d, J = 8.4 Hz, 2H), 7.14 – 7.07 (m, 4H), 6.84 (d, J = 16.0 Hz, 1H), 2.35 (s, 3H).
^{13}C NMR (100 MHz, DMSO-d_6) δ 165.4, 147.2, 146.9, 143.8, 137.0, 135.8, 134.3, 131.4, 130.2, 129.5, 129.1, 127.2, 123.0, 121.5, 117.5, 21.4.
HRMS (ESI) calcd for $C_{22}H_{20}NO_4S$ $[M+H]^+$394.1108, found 394.1108.

(*E*)-tert-butyl cinnamoyl(4-hydroxyphenyl)carbamate (2g)



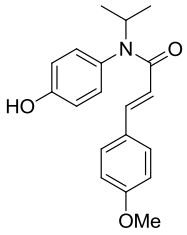
White solid. Mp: 149–151 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.61 (s, 1H), 7.70 – 7.62 (m, 2H), 7.55 (d, J = 15.6 Hz, 1H), 7.50 – 7.40 (m, 3H), 7.30 (d, J = 16.0 Hz, 1H), 6.98 (d, J = 8.0 Hz, 2H), 6.78 (d, J = 7.2 Hz, 2H), 1.38 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 169.1, 157.8, 153.9, 143.1, 135.7, 131.4, 131.2, 130.5, 130.2, 129.2, 123.1, 116.5, 83.8, 28.7.

HRMS (ESI) calcd for $C_{20}H_{22}NNaO_4$ $[M+H]^+$ 362.1363, found 362.1366.

(*E*)-*N*-(4-hydroxyphenyl)-*N*-isopropyl-3-(4-methoxyphenyl)acrylamide (2h)



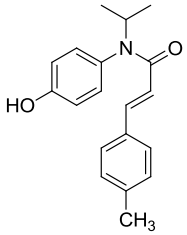
White solid. Mp: 223–224 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 15.6 Hz, 1H), 7.21 (d, J = 8.8 Hz, 2H), 7.03 – 6.98 (m, 2H), 6.97 – 6.89 (m, 2H), 6.78 (d, J = 8.8 Hz, 2H), 6.46 (s, 1H), 6.03 (d, J = 15.6 Hz, 1H), 5.11 (heptet, J = 6.8 Hz, 1H), 3.77 (s, 3H), 1.10 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 169.9, 165.5, 162.3, 145.0, 136.8, 134.2, 134.0, 132.6, 122.8, 120.9, 119.6, 60.4, 50.4, 26.0.

HRMS (ESI) calcd for $C_{19}H_{22}NO_3$ $[M+H]^+$ 312.1594, found 312.1598.

(*E*)-*N*-(4-hydroxyphenyl)-*N*-isopropyl-3-(p-tolyl)acrylamide (2i)



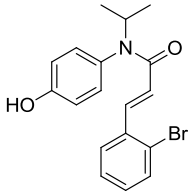
White solid. Mp: 248–251 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.77 (s, 1H), 7.41 (d, J = 15.6 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H)7.01 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 6.05 (d, J = 15.6 Hz, 1H), 4.94 – 4.82 (m, 1H), 2.26 (s, 3H), 1.01 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 165.0, 157.6, 140.5, 139.7, 132.6, 132.0, 130.0, 129.2, 127.8, 119.5, 116.2, 45.8, 21.4, 21.2.

HRMS (ESI) calcd for $C_{19}H_{22}NO_2$ $[M+H]^+$ 296.1645, found 296.1655.

(*E*)-3-(2-bromophenyl)-*N*-(4-hydroxyphenyl)-*N*-isopropylacrylamide (2j)



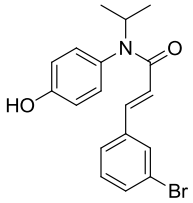
White solid. Mp: 232–235 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 7.71 (d, J = 15.6 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.34 - 7.22 (m, 3H), 7.04 (d, J = 7.9 Hz, 2H), 6.85 (d, J = 7.7 Hz, 2H), 6.13 (d, J = 15.2 Hz, 1H), 4.95 – 4.83 (m, 1H), 1.04 (d, J = 6.4 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 164.4, 157.7, 138.4, 134.9, 133.6, 132.0, 131.6, 128.9, 128.8, 128.0, 124.5, 123.7, 116.2, 46.1, 21.2.

HRMS (ESI) calcd for $C_{18}H_{19}BrNO_2$ $[M+H]^+$ 360.0594, found 360.0594.

(*E*)-3-(3-bromophenyl)-*N*-(4-hydroxyphenyl)-*N*-isopropylacrylamide (2k)



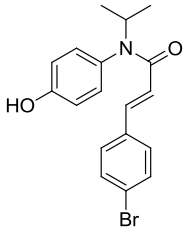
White solid. Mp: 226–227 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.77 (s, 1H), 7.59 – 7.43 (m, 2H), 7.42 (d, J = 15.6 Hz, 1H), 7.28 (m, 2H), 7.01 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 6.14 (d, J = 15.6 Hz, 1H), 4.93 – 4.80 (m, 1H), 1.02 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 164.6, 157.7, 138.8, 137.9, 132.5, 132.0, 131.5, 130.7, 129.0, 126.4, 122.6, 122.3, 116.2, 46.0, 21.2.

HRMS (ESI) calcd for $C_{18}H_{19}BrNO_2$ $[M+H]^+$ 360.0594, found 360.0594.

(*E*)-3-(4-bromophenyl)-*N*-(4-hydroxyphenyl)-*N*-isopropylacrylamide (2l)



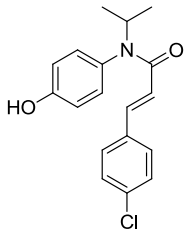
White solid. Mp: 263–265 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.43 (d, J = 15.6 Hz, 1H), 7.26 (d, J = 7.6 Hz, 2H), 7.01 (d, J = 7.6 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 6.13 (d, J = 15.6 Hz, 1H), 4.87 (br, 1H), 1.01 (d, J = 5.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 164.7, 157.6, 139.3, 134.6, 132.4, 132.0, 129.8, 129.0, 123.1, 121.3, 116.2, 45.9, 21.2.

HRMS (ESI) calcd for $C_{18}H_{19}BrNO_2$ $[M+H]^+$ 360.0594, found 360.0594.

(*E*)-3-(4-chlorophenyl)-*N*-(4-hydroxyphenyl)-*N*-isopropylacrylamide (2m)



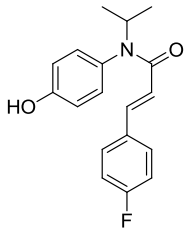
White solid. Mp: 243–244 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 7.44 (d, J = 16.0Hz, 1H), 7.39 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 6.11 (d, J = 15.6 Hz, 1H), 4.95 – 4.82 (m, 1H), 1.01 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 165.4, 158.3, 139.9, 135.1, 134.9, 132.7, 130.3, 130.1, 129.7, 122.0, 116.9, 46.6, 21.9.

HRMS (ESI) calcd for $C_{18}H_{19}ClNO_2$ $[M+H]^+$ 316.1099, found 316.1104.

(*E*)-3-(4-fluorophenyl)-*N*-(4-hydroxyphenyl)-*N*-isopropylacrylamide (2n)



White solid. Mp: 230–233 ºC.

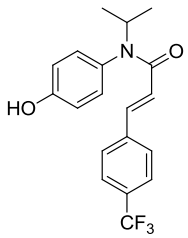
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 7.46 (d, J = 15.6 Hz, 1H), 7.37 (s, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.02 (d, J = 6.8 Hz, 2H), 6.85 (d, J = 7.6 Hz, 2H), 6.07 (d, J = 15.6 Hz, 1H), 4.94 – 4.81 (m, 1H), 1.03 (d, J = 5.6 Hz, 6H).

^{19}F NMR (376 MHz, DMSO) δ -111.41.

^{13}C NMR (100 MHz, DMSO-d_6) δ 164.3, 162.6(d, J = 248.2 Hz), 157.1, 138.8, 131.5, 129.5(d, J = 8.6 Hz), 128.6, 120.0, 115.9(d, J = 22.1 Hz), 115.7, 45.4, 20.7.

HRMS (ESI) calcd for $C_{18}H_{19}FNO_2$ $[M+H]^+$ 300.1394, found 300.1400.

(*E*)-*N*-(4-hydroxyphenyl)-*N*-isopropyl-3-(4-(trifluoromethyl)phenyl)acrylamide (2o)



White solid. Mp: 222–224 ºC.

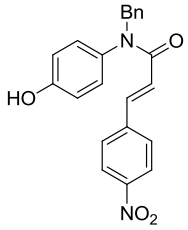
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 7.69 (d, J = 8.4 Hz, 2H), 7.54 – 7.50 (m, 3H), 7.03 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 6.24 (d, J = 15.6 Hz, 1H), 4.92 – 4.84 (m, 1H), 1.02 (d, J = 6.8 Hz, 6H).

^{19}F NMR (376 MHz, DMSO) δ -61.22.

^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 157.2, 138.8, 138.3, 131.4, 129.2 (q, J = 32.1 Hz, 1C), 128.4, 128.0, 125.7 (q, J = 3.8 Hz), 124.0 (q, J = 270.5 Hz) 122.8, 115.8, 45.6, 20.7.

HRMS (ESI) calcd for $C_{19}H_{19}F_3NO_2$ $[M+H]^+$ 350.1362, found 350.1370.

(*E*)-*N*-benzyl-*N*-(4-hydroxyphenyl)-3-(4-nitrophenyl)acrylamide (2p)



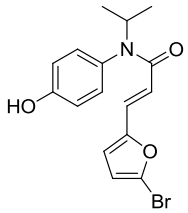
Yellow solid. Mp: 190–191 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.8 Hz, 2H), 7.73 (d, J = 15.6 Hz, 1H), 7.43 (d, J = 8.8 Hz, 2H), 7.30 – 7.20 (m, 5H), 6.93 – 6.83 (m, 4H), 6.55 (s, 1H), 6.48 (d, J = 15.6 Hz, 1H), 5.00 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 156.0, 148.0, 141.3, 139.6, 136.9, 133.7, 129.5, 128.8, 128.5, 128.4, 127.6, 124.0, 122.8, 116.5, 53.7.

HRMS (ESI) calcd for $C_{22}H_{19}N_2O_4$ $[M+H]^+$ 375.1339, found 375.1346.

(*E*)-3-(5-bromofuran-2-yl)-*N*-(4-hydroxyphenyl)-*N*-isopropylacrylamide (2q)



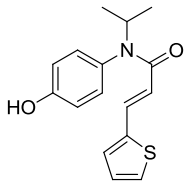
White solid. Mp: 201–202 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 15.6 Hz, 1H), 7.09 – 6.91 (m, 5H), 6.40 (d, J = 3.6 Hz, 1H), 6.29 (d, J = 3.6 Hz, 1H), 6.03 (d, J = 15.6 Hz, 1H), 5.08 (heptet, J = 6.8 Hz, 1H), 1.10 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO) δ 164.5, 157.7, 153.6, 132.0, 129.0, 126.8, 124.4, 117.9, 117.2, 116.3, 115.0, 46.0, 21.2.

HRMS (ESI) calcd for $C_{16}H_{17}BrNO_3$ $[M+H]^+$ 350.0386, found 350.0390.

(*E*)-*N*-(4-hydroxyphenyl)-*N*-isopropyl-3-(thiophen-2-yl)acrylamide (2r)



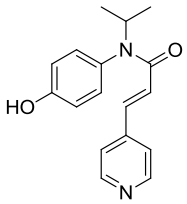
White solid. Mp: 249–253 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 7.59 (d, J = 15.2 Hz, 1H), 7.49 (d, J = 5.2 Hz, 1H), 7.28 (d, J = 3.2 Hz, 1H), 7.09 – 7.02 (m, 1H), 7.00 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 5.83 (d, J = 15.2 Hz, 1H), 4.91 – 4.82 (m, 1H), 1.00 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 157.2, 139.8, 133.1, 131.5, 130.7, 128.5, 128.3, 128.0, 118.7, 115.7, 45.3, 20.7.

HRMS (ESI) calcd for $C_{16}H_{18}NO_2S$ $[M+H]^+$ 288.1053, found 288.1052.

(*E*)-*N*-(4-hydroxyphenyl)-*N*-isopropyl-3-(pyridin-4-yl)acrylamide (2s)



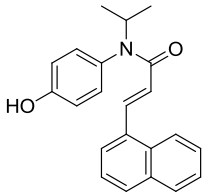
White solid. Mp: 183–185 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.80 (s, 1H), 8.52 (s, 2H), 7.42 (d, J = 15.7 Hz, 1H), 7.26 (d, J = 5.0 Hz, 2H), 7.03 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 6.32 (d, J = 15.7 Hz, 1H), 4.91 – 4.82 (m, 1H), 1.02 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 164.3, 157.7, 150.7, 142.4, 137.8, 131.9, 128.8, 124.9, 121.9, 116.2, 46.1, 21.1.

HRMS (ESI) calcd for $C_{17}H_{19}N_2O_2$ $[M+H]^+$ 283.1441, found 283.1445.

(*E*)-*N*-(4-hydroxyphenyl)-*N*-isopropyl-3-(naphthalen-1-yl)acrylamide (2t)



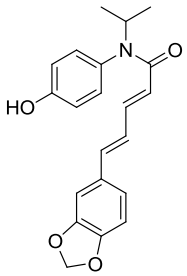
White solid. Mp: 235–238 ºC.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.77 (s, 1H), 8.20 (d, J = 15.6 Hz, 1H), 8.08 (d, J = 7.2 Hz, 1H), 7.95 – 7.90 (m, 2H), 7.60 – 7.54 (m, 2H), 7.44 (t, J = 7.8, Hz, 1H), 7.35 (d, J = 7.2 Hz, 1H), 7.07 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 6.18 (d, J = 15.6 Hz, 1H), 4.99 – 4.89 (m, 1H), 1.06 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 157.7, 137.2, 133.7, 132.7, 132.0, 131.1, 130.0, 129.2, 129.1, 127.3, 126.7, 126.1, 124.9, 123.9, 123.6, 116.2, 46.0, 21.2.

HRMS (ESI) calcd for $C_{22}H_{22}NO_2$ $[M+H]^+$ 332.1645, found 332.1651.

(2*E*,4*E*)-5-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(4-hydroxyphenyl)-*N*-isopropylpenta-2,4-dienamide (2u)



Pale yellow solid. Mp: 235–239 ºC.

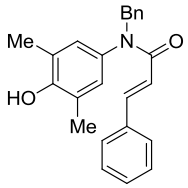
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, J = 14.8, 11.2 Hz, 1H), 7.26 (s, 1H), 6.99 (d, J = 8.8 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 6.88 (s, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.76 – 6.66 (m, 2H), 6.49 (dd, J = 15.6, 11.2 Hz, 1H), 5.94 (s, 2H), 5.68 (d, J = 14.8 Hz, 1H), 5.09 (heptet, J = 6.8 Hz, 1H), 1.10

(d, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, DMSO) δ 164.7, 157.1, 147.9, 147.7, 141.1, 138.3, 131.5, 130.8, 128.7, 125.4, 122.9, 122.2, 115.7, 108.3, 105.5, 101.2, 45.1, 20.8.

HRMS (ESI) calcd for $C_{21}H_{22}NO_4$ $[M+H]^+$ 352.1543, found 352.1550.

ethyl 2-(*N*-(4-hydroxy-3,5-dimethylphenyl)cinnamamido)acetate (2v)



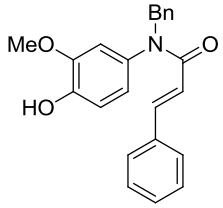
White solid. Mp: 225–226 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 15.6 Hz, 1H), 7.28 (br, 10H), 6.65 (s, 2H), 6.38 (d, *J* = 15.6 Hz, 1H), 5.25 (s, 1H), 4.96 (s, 2H), 2.20 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 151.8, 142.0, 137.7, 135.3, 134.0, 129.4, 128.7, 128.6, 128.3, 127.9, 127.2, 124.2, 118.9, 53.6, 16.0.

HRMS (ESI) calcd for $C_{24}H_{24}NO_2$ $[M+H]^+$ 358.1802, found 358.1808.

ethyl 2-(*N*-(4-hydroxy-3-methoxyphenyl)cinnamamido)acetate (2w)



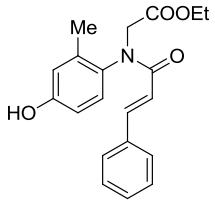
White solid. Mp: 132–133 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 15.6 Hz, 1H), 7.37 – 7.18 (m, 10H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.59 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.41 (d, *J* = 2.0 Hz, 1H), 6.36 (d, *J* = 15.6 Hz, 1H), 5.75 (s, 1H), 4.98 (s, 2H), 3.71 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 146.9, 145.4, 142.3, 137.7, 135.2, 134.0, 129.6, 129.1, 128.7, 128.4, 127.9, 127.4, 121.6, 118.7, 114.8, 111.3, 56.0, 53.4.

HRMS (ESI) calcd for $C_{23}H_{22}NO_3$ $[M+H]^+$ 360.1594, found 360.1600.

ethyl 2-(*N*-(4-hydroxy-2-methylphenyl)cinnamamido)acetate (2x)



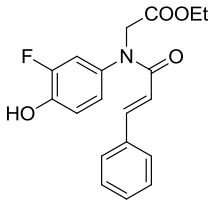
White solid. Mp: 163–164 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 15.6 Hz, 1H), 7.33 – 7.25(m, 6H), 6.87 (s, 1H), 6.84 (d, *J* = 2.8 Hz, 1H), 6.77 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.30 (d, *J* = 15.6 Hz, 1H), 4.89 (d, *J* = 16.8 Hz, 1H), 4.24 – 4.17 (m, 2H), 3.83 (d, *J* = 16.8 Hz, 1H), 2.19 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 167.8, 157.0, 143.6, 137.0, 134.8, 132.9, 130.3, 129.9, 128.7, 128.0, 117.9, 117.0, 114.4, 61.4, 51.4, 17.9, 14.2.

HRMS (ESI) calcd for $C_{20}H_{22}NO_4$ $[M+H]^+$ 340.1543, found 340.1548.

ethyl 2-(*N*-(3-fluoro-4-hydroxyphenyl)cinnamamido)acetate (2y)



White solid. Mp: 155–156 ºC.

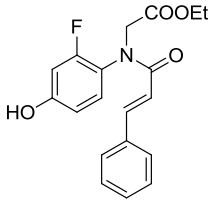
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 15.2 Hz, 1H), 7.39 – 7.28 (m, 5H), 7.23 – 7.16 (m, 1H), 7.10 – 7.00 (m, 2H), 6.37 (d, *J* = 15.6 Hz, 1H), 5.89 (d, *J* = 3.6 Hz, 1H), 4.44 (s, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) *δ* -136.30.

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 167.1, 150.9 (d, *J* = 243.4 Hz), 144.6 (d, *J* = 13.3 Hz), 143.6, 134.7, 134.1 (d, *J* = 8.0 Hz), 130.0, 128.8, 128.1, 124.8 (d, *J* = 3.0 Hz), 118.1 (d, *J* = 3.0 Hz), 117.2, 116.1 (d, *J* = 19.1 Hz), 61.6, 51.9, 14.1.

HRMS (ESI) calcd for $C_{19}H_{19}FNO_4$ $[M+H]^+$ 344.1293, found 344.1295.

ethyl 2-(*N*-(2-fluoro-4-hydroxyphenyl)cinnamamido)acetate (2z)



White solid. Mp: 135–137 ºC.

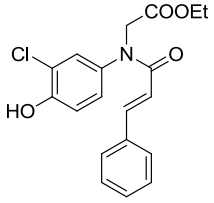
^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.01 (s, 1H), 7.72 (d, *J* = 15.6 Hz, 1H), 7.46 – 7.21 (m, 6H), 6.90 – 6.64 (m, 2H), 6.41 (d, *J* = 15.6 Hz, 1H), 4.95 (d, *J* = 17.2 Hz, 1H), 4.20 (p, *J* = 7.2 Hz, 2H), 3.94 (d, *J* = 17.2 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) *δ* -118.63.

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 169.1, 168.0, 158.7 (d, *J* = 11.1 Hz), 158.2 (d, *J* = 250.7 Hz), 144.1, 134.6, 131.2, 130.1, 128.8, 128.1, 121.0 (d, *J* = 12.9 Hz), 116.72, 112.3 (d, *J* = 2.6 Hz), 104.4 (d, *J* = 22.6 Hz), 61.6, 51.2, 14.1.

HRMS (ESI) calcd for $C_{19}H_{19}FNO_4$ $[M+H]^+$ 344.1293, found 344.1295.

ethyl 2-(*N*-(3-chloro-4-hydroxyphenyl)cinnamamido)acetate (2aa)

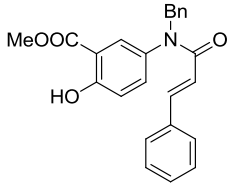


White solid. Mp: 146–148 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.72 (d, *J* = 15.6 Hz, 1H), 7.42 (d, *J* = 2.4 Hz, 1H), 7.38 – 7.28 (m, 5H), 7.22 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 6.37 (d, *J* = 15.6 Hz, 2H), 4.44 (s, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 166.8, 152.0, 143.6, 135.1, 134.89, 130.0, 129.0, 128.8, 128.5, 128.1, 120.6, 117.2, 117.0, 61.5, 51.9, 14.2.
HRMS (ESI) calcd for $C_{19}H_{19}ClNO_4$ $[M+H]^+$ 360.0997, found 360.0997.

methyl 5-(*N*-benzylcinnamamido)-2-hydroxybenzoate (2ab)



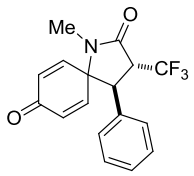
White solid. Mp: 132–134 ºC.
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.57 (s, 1H), 7.61 (d, J = 15.6 Hz, 1H), 7.54 (d, J = 2.4 Hz, 1H), 7.48 – 7.38 (m, 2H), 7.36 – 7.19 (m, 9H), 6.99 (d, J = 8.8 Hz, 1H), 6.37 (d, J = 15.6 Hz, 1H), 4.96 (s, 2H), 3.83 (s, 3H).
^{13}C NMR (100 MHz, DMSO-d_6) δ 168.6, 165.5, 159.3, 142.1, 137.8, 136.0, 135.1, 133.3, 130.3, 129.8, 129.4, 128.9, 128.6, 128.3, 127.7, 119.2, 119.0, 114.4, 53.0, 52.7.
HRMS (ESI) calcd for $C_{24}H_{22}NO_4$ $[M+H]^+$ 388.1543, found 388.1549.

General procedure to synthesize 3a-3ab

An oven dried reaction tube was charged with CuBr (1 equiv), substrates **2** (0.2 mmol, 1.0 equiv), and Togni's reagent (2 equiv). The vial was evacuated and backfilled with nitrogen (this process was repeated three times) and then DCE (3 mL) was added. The reaction mixture was stirred at 80 ^{o}C for 24 h. Upon consumption of the starting material, to the mixture was added H_2O and extracted with DCM. And the organic layer was washed with saturated aqueous solution of $NaHCO_3$, and saturated brine, concentrated under in vacuo to give the crude product, which was purified by flash column chromatography (elution: PE:EA = 5:1) to give the desired compound **3**.

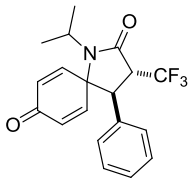
Characterization of products

1-methyl-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3a)



36.0 mg. Yield: 56%. White solid. Mp: 185–187 ºC.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.30 (m, 3H), 7.12 – 7.10 (m, 2H), 6.82 (dd, J = 10.0, 3.2 Hz, 1H), 6.47 (dd, J = 10.0, 3.2 Hz, 1H), 6.46 (dd, J = 10.0, 2.0 Hz, 1H), 6.04 (dd, J = 10.0, 2.0 Hz, 1H), 3.95 (dq, J = 11.6, 8.0 Hz, 1H), 3.75 (d, J = 11.6 Hz, 1H), 2.79 (s, 3H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.60 (d, J = 8.0 Hz, 3F).
^{13}C NMR (100 MHz, $CDCl_3$) δ 183.7, 166.5, 147.4, 145.3, 133.0, 132.5, 132.0, 128.9, 128.9, 127.6, 124.4 (q, J = 280.2 Hz), 64.3, 49.2, 48.4 (q, J = 28.6 Hz), 27.4.
HRMS (ESI) calcd for $C_{17}H_{15}F_3NO_2$ $[M+H]^+$ 322.1049, found 322.1046.

1-isopropyl-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3b)



53.1 mg. Yield: 76%. White solid. Mp: 211–214 °C.

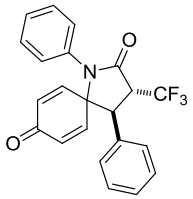
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 3H), 7.10 – 7.05 (m, 2H), 6.87 (dd, *J* = 10.0, 3.2 Hz, 1H), 6.55 (dd, *J* = 10.4, 3.2 Hz, 1H), 6.43 (dd, *J* = 10.0, 2.0 Hz, 1H), 5.98 (dd, *J* = 10.4, 2.0 Hz, 1H), 3.88 (dq, *J* = 11.6, 8.0 Hz, 1H), 3.71 (d, *J* = 11.6 Hz, 1H), 3.34 (heptet, *J* = 6.8 Hz, 1H), 1.41 (d, *J* = 6.8 Hz, 3H), 1.38 (d, *J* = 6.8 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.66 (d, *J* = 8.0 Hz, 3F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 182.8, 164.9, 146.8, 145.4, 131.5, 131.4, 129.9, 127.8, 126.6, 123.4 (q, *J* = 280.2 Hz), 64.40, 48.6, 47.7 (q, *J* = 28.3 Hz), 47.1, 19.7, 19.2.

HRMS (ESI) calcd for $C_{19}H_{19}F_3NO_2$ $[M+H]^+$ 350.1362, found 350.1367.

1,4-diphenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3c)



29.9 mg. Yield: 39%. White solid. Mp: 97–99 °C.

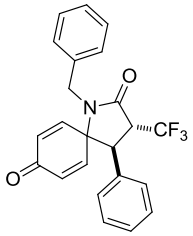
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 6H), 7.20 (d, *J* = 6.8 Hz, 2H), 7.15 – 7.08 (m, 2H), 6.89 (dd, *J* = 10.0, 3.2 Hz, 1H), 6.84 (dd, *J* = 10.0, 3.2 Hz, 1H), 6.24 (dd, *J* = 10.0, 1.6 Hz, 1H), 5.97 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.14 (dq, *J* = 12.0, 8.0 Hz, 1H), 3.91 (d, *J* = 12.0 Hz, 1H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.24 (d, *J* = 8.0 Hz, 3F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.7, 166.0, 147.1, 146.7, 135.4, 132.3, 131.9, 131.1, 129.3, 129.0, 128.8, 128.5, 127.9, 126.3, 124.4 (q, *J* = 280.6 Hz), 66.0, 50.5, 48.3 (q, *J* = 28.6 Hz).

HRMS (ESI) calcd for $C_{22}H_{17}F_3NO_2$ $[M+H]^+$ 384.1206, found 384.1200.

1-benzyl-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3d)



63.6 mg. Yield: 80%.White solid. Mp: 70–72 °C.

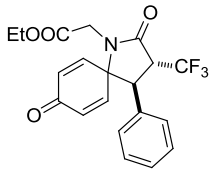
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (br, 6H), 7.22 – 7.14 (m, 2H), 7.08 – 6.96 (m, 2H), 6.59 (dd, *J* = 10.0, 3.2 Hz, 1H), 6.31 (dd, *J* = 10.0, 3.2 Hz, 1H), 6.26 (dd, *J* = 10.0, 2.0 Hz, 1H), 5.82 (dd, *J* = 10.0, 2.0 Hz, 1H), 4.60 (d, *J* = 15.2 Hz, 1H), 4.24 (d, *J* = 14.8 Hz, 1H), 4.04 – 3.86 (m, 1H), 3.73 (d, *J* = 11.6 Hz, 1H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.52 (d, *J* = 8.0 Hz, 3F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.9, 166.7, 147.3, 145.5, 136.7, 132.1, 132.1, 131.1, 128.9,

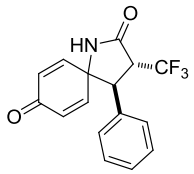
128.8, 128.8, 128.6, 128.1, 127.6, 124.5(q, *J* = 280.2 Hz), 64.6, 49.7, 48.3 (q, *J* = 28.6 Hz), 45.7.
HRMS (ESI) calcd for $C_{23}H_{19}F_3NO_2$ $[M+H]^+$ 398.1362, found 398.1360.

ethyl 2-(2,8-dioxo-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-dien-1-yl)acetate (3e)



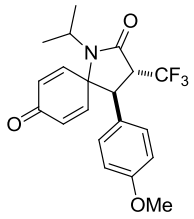
62.9 mg. Yield: 86%. Oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 3H), 7.19 – 7.13 (m, 2H), 6.90 (dd, *J* = 10.0, 3.2 Hz, 1H), 6.68 (dd, *J* = 10.0, 3.2 Hz, 1H), 6.41 (dd, *J* = 10.0, 1.6 Hz, 1H), 5.96 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.21 – 4.16 (m, 2H), 4.14 – 4.07 (m, 1H), 3.94 – 3.86 (m, 3H), 1.26 (t, *J* = 7.2 Hz, 3H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.45 (d, *J* = 8.0 Hz, 3F).
^{13}C NMR (100 MHz, $CDCl_3$) δ 183.8, 167.8, 166.8, 146.6, 145.2, 132.9, 132.4, 131.0, 128.9, 127.6, 124.3 (q, *J* = 280.3 Hz), 64.2, 62.0, 49.7, 48.0 (q, *J* = 28.7 Hz), 42.8, 14.0.
HRMS (ESI) calcd for $C_{20}H_{19}F_3NO_4$ $[M+H]^+$ 394.1261, found 394.1264.

4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3g')



27.7 mg. Yield: 45%. White solid. Mp: 232–234 °C.
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.91 (s, 1H), 7.40 – 7.21 (m, 5H), 7.16 (t, *J* = 9.4 Hz, 2H), 6.22 (d, *J* = 9.2 Hz, 1H), 5.84 (d, *J* = 9.6 Hz, 1H), 4.80 (s, 1H), 4.00 (d, *J* = 12.4 Hz, 1H).
^{19}F NMR (376 MHz, DMSO-d_6) δ -65.58 (d, *J* = 8.3 Hz, 3F).
^{13}C NMR (101 MHz, DMSO-d_6) δ 184.2, 168.2, 149.4, 148.7, 133.5, 130.1, 128.3, 128.1, 128.0, 127.9, 125.2 (q, *J* = 277.8 Hz), 59.1, 50.4, 47.2 (d, *J* = 26.9 Hz).
HRMS (ESI) calcd for $C_{16}H_{13}F_3NO_2$ $[M+H]^+$ 308.0893, found 308.0896.

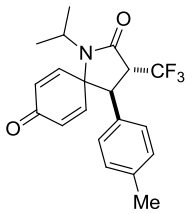
1-isopropyl-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3h)



49.3 mg. Yield: 65%. White solid. Mp: 221–224 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, *J* = 7.6 Hz, 2H), 6.85 (d, *J* = 9.6 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 2H), 6.55 (d, *J* = 10.4 Hz, 1H), 6.42 (d, *J* = 10.0 Hz, 1H), 6.01 (d, *J* = 10.0 Hz, 1H), 3.85 – 3.70 (m, 4H), 3.67 (d, *J* = 12.4 Hz, 1H), 3.35 (br, 1H), 1.41 – 1.37 (m, 6H).

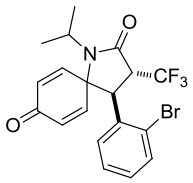
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.66 (d, J = 7.9 Hz, 3F).
^{13}C NMR (100 MHz, $CDCl_3$) δ 183.9, 166.0, 159.7, 148.0, 146.6, 132.4, 130.9, 128.8, 124.5(d, J = 280.5 Hz), 124.4, 114.2, 65.6, 55.2, 49.1, 49.0 (d, J = 28.1 Hz) 48.1, 20.7, 20.2.
HRMS (ESI) calcd for $C_{20}H_{21}F_3NO_3$ $[M+H]^+$ 380.1468, found 380.1468.

1-isopropyl-4-(p-tolyl)-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3i)



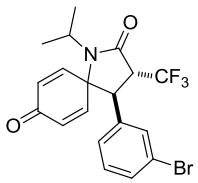
48.7 mg. Yield: 67%. White solid. Mp: 202–205 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 6.85 (dd, J = 10.0, 3.2 Hz, 1H), 6.54 (dd, J = 10.4, 3.2 Hz, 1H), 6.41 (dd, J = 10.0, 2.0 Hz, 1H), 5.99 (dd, J = 10.0, 2.0 Hz, 1H), 3.83 (dq, J = 12.0, 8.0 Hz, 1H), 3.68 (d, J = 11.6 Hz, 1H), 3.33 (heptet, J = 6.8 Hz, 1H), 2.30 (s, 2H), 1.41 (d, J = 6.8 Hz, 3H), 1.38 (d, J = 6.8 Hz, 3H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.68 (d, J = 8.0 Hz, 3F).
^{13}C NMR (100 MHz, $CDCl_3$) δ 184.0, 166.0, 147.9, 146.5, 138.6, 132.4, 130.9, 129.5, 127.5, 124.5 (q, J = 280.4 Hz), 65.49, 49.4, 48.9 (q, J = 27.9 Hz), 48.1, 21.1, 20.7, 20.2.
HRMS (ESI) calcd for $C_{20}H_{21}F_3NO_2$ $[M+H]^+$ 364.1519, found 364.1519.

4-(2-bromophenyl)-1-isopropyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3j)



67.7 mg. Yield: 79%. White solid. Mp: 236–239 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.20 –7.14 (m, 2H), 7.02 (dd, J = 10.0, 3.2 Hz, 1H), 6.59 (dd, J = 10.0, 3.2 Hz, 1H), 6.37 (dd, J = 10.0, 2.0 Hz, 1H), 6.11 (dd, J = 10.0, 2.0 Hz, 1H), 4.54 (d, J = 10.4 Hz, 1H), 3.69 (dq, J = 16.5, 8.0 Hz, 1H), 3.31 (heptet, J = 6.8 Hz, 1H), 1.42 (d, J = 7.2 Hz, 3H), 1.40 (d, J = 6.8 Hz, 3H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.86 (d, J = 7.9 Hz, 3F).
^{13}C NMR (100 MHz, $CDCl_3$) δ 183.8, 165.7, 148.4, 146.0, 134.0, 133.5, 131.8, 131.3, 130.1, 128.7, 127.6, 125.9, 124.3 (q, J = 280.3 Hz), 65.1, 51.1 (q, J = 28.3 Hz), 48.0, 47.7, 20.6, 20.2.
HRMS (ESI) calcd for $C_{19}H_{18}BrF_3NO_2$ $[M+H]^+$ 428.0468, found 428.0458.

4-(3-bromophenyl)-1-isopropyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3k)



65.9 mg. Yield: 77%. White solid. Mp:191–194 °C.

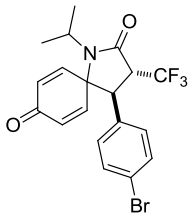
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.0 Hz, 1H), 7.24 (s, 1H), 7.18 (t, J = 8.0 Hz, 1H), 7.02 (d, J = 7.6 Hz, 1H), 6.84 (dd, J = 10.0, 3.2 Hz, 1H), 6.56 (dd, J = 10.0, 3.2 Hz, 1H), 6.46 (dd, J = 10.0, 2.0 Hz, 1H), 6.06 (dd, J = 10.0, 2.0 Hz, 1H), 3.87 – 3.74 (m, 1H), 3.66 (d, J = 11.6 Hz, 1H), 3.34 (heptet, J = 6.8 Hz, 1H), 1.41 (d, J = 6.8 Hz, 3H), 1.38 (d, J = 6.8 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.63 (d, J = 7.8 Hz, 3F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 165.6, 147.4, 145.9, 134.9, 132.7, 132.0, 131.2, 130.7, 130.3, 126.5, 124.3 (q, J = 280.3 Hz), 122.8, 65.2, 49.3, 48.7 (q, J = 28.3 Hz), 48.2, 20.7, 20.2.

HRMS (ESI) calcd for $C_{19}H_{18}BrF_3NO_2$ $[M+H]^+$ 428.0468, found 428.0460.

4-(4-bromophenyl)-1-isopropyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3l)



60.0 mg. Yield 70%. White solid. Mp: 258–263 °C.

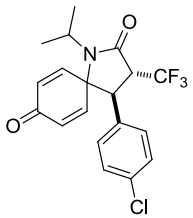
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 6.85 (dd, J = 10.0, 3.2 Hz, 1H), 6.53 (dd, J = 10.4, 3.2 Hz, 1H), 6.44 (dd, J = 10.0, 1.6 Hz, 1H), 6.04 (dd, J = 10.4, 2.0 Hz, 1H), 3.87 – 3.73 (m, 1H), 3.67 (d, J = 12.0 Hz, 1H), 3.34 (heptet, J = 6.8 Hz, 1H), 1.41 (d, J = 6.8 Hz, 3H), 1.38 (d, J = 6.8 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.63 (d, J = 7.9 Hz, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.5, 165.5, 147.5, 145.9, 132.7, 132.1, 131.7, 131.3, 129.3, 124.3 (q, J = 284.3 Hz), 123.0 , 65.2, 49.2, 48.7 (q, J = 28.4 Hz), 48.2, 20.7, 20.2.

HRMS (ESI) calcd for $C_{19}H_{18}BrF_3NO_2$ $[M+H]^+$ 428.0468, found 428.0460.

4-(4-chlorophenyl)-1-isopropyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3m)



67.5 mg. Yield 88%. White solid. Mp: 251–253 °C.

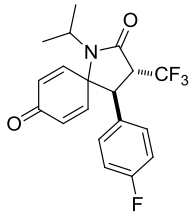
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 8.4 Hz, 3H), 7.02 (d, J = 8.4 Hz, 2H), 6.85 (dd, J = 10.4, 3.2 Hz, 1H), 6.53 (dd, J = 10.0, 3.2 Hz, 1H), 6.44 (dd, J = 10.0, 2.0 Hz, 1H), 6.04 (dd, J = 10.0, 2.0 Hz, 1H), 3.81 (dq, J = 11.6, 7.6 Hz, 1H), 3.68 (d, J = 12.4 Hz, 1H), 3.34 (heptet, J = 6.8 Hz, 1H), 1.41 (d, J = 6.8 Hz, 3H), 1.38 (d, J = 6.8 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.64 (d, J = 7.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 165.6, 147.5, 145.9, 134.8, 132.7, 131.3, 131.1, 129.1, 129.0, 124.3 (q, J = 280.3 Hz), 65.3, 49.2, 48.8 (q, J = 28.3 Hz), 48.2, 20.7, 20.2.

HRMS (ESI) calcd for $C_{19}H_{18}ClF_3NO_2$ $[M+H]^+$ 384.0973, found 384.0973.

4-(4-fluorophenyl)-1-isopropyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3n)



58.8 mg. Yield: 80%. White solid. Mp: 236–240 °C.

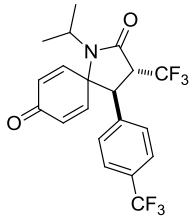
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (dd, J = 8.8, 5.2 Hz, 2H), 7.00 (t, J = 8.4 Hz, 2H), 6.85 (dd, J = 10.0, 3.2 Hz, 1H), 6.54 (dd, J = 10.4, 3.2 Hz, 1H), 6.44 (dd, J = 10.0, 2.0 Hz, 1H), 6.03 (dd, J = 10.0, 2.0 Hz, 1H), 3.81 (dq, J = 12.0, 8.0 Hz, 1H), 3.69 (d, J = 12.0 Hz, 1H), 3.35 (heptet, J = 6.8 Hz, 1H), 1.41 (d, J = 6.8 Hz, 3H), 1.38 (d, J = 6.8 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.65 (d, J = 7.5 Hz, 3F), -112.32 (s, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 165.7, 162.6 (d, J = 250.0 Hz), 147.6, 146.2, 132.6, 131.2, 129.4 (d, J = 8.1 Hz), 128.3 (d, J = 3.2 Hz), 124.4 (q, J = 280.3 Hz), 115.9 (d, J = 21.8 Hz), 65.4, 49.1, 48.9 (q, J = 28.2 Hz), 48.2, 20.7, 20.2.

HRMS (ESI) calcd for $C_{19}H_{18}F_4NO_2$ $[M+H]^+$ 368.1268, found 368.1267.

1-isopropyl-3-(trifluoromethyl)-4-(4-(trifluoromethyl)phenyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3o)



65.1 mg. Yield: 78%. White solid. Mp: 229–230 °C.

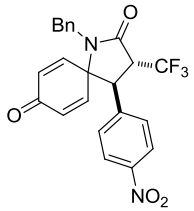
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 6.88 (dd, J = 10.0, 3.2 Hz, 1H), 6.54 (dd, J = 10.0, 3.2 Hz, 1H), 6.46 (dd, J = 10.0, 2.0 Hz, 1H), 6.03 (dd, J = 10.0, 2.0 Hz, 1H), 3.94 – 3.81 (m, 1H), 3.77 (d, J = 12.0 Hz, 1H), 3.34 (heptet, J = 6.8 Hz, 1H), 1.42 (d, J = 6.8 Hz, 3H), 1.39 (d, J = 6.8 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.81 (s, 3F), -67.63 (d, J = 7.5 Hz, 3F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.4, 165.4, 147.3, 145.6, 136.7, 132.8, 31.4, 128.2, 125.9 (q, J = 3.7 Hz), 124.3 (q, J = 280.1 Hz), 123.6 (q, J = 273.6 Hz), 65.1, 49.4, 48.7 (q, J = 28.4 Hz), 48.2, 20.7, 20.2.

HRMS (ESI) calcd for $C_{20}H_{18}F_6NO_2$ $[M+H]^+$ 418.1236, found 418.1230.

1-benzyl-4-(4-nitrophenyl)-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3p)



72.5 mg. Yield: 82%.White solid. Mp:196–198 °C.

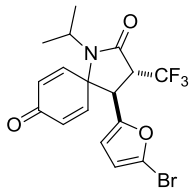
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.8 Hz, 2H), 7.35 – 7.23 (m, 5H), 7.19 (br, 2H), 6.62 (dd, J = 10.0, 3.2 Hz, 1H), 6.31 (dd, J = 10.0, 2.0 Hz, 2H), 5.86 (dd, J = 10.0, 2.0 Hz, 1H), 4.60 (d, J = 15.2 Hz, 1H), 4.29 (d, J = 14.8 Hz, 1H), 4.04 – 3.95 (m, 1H), 3.82 (d, J = 12.0 Hz, 1H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.41 (d, J = 7.7 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.2, 165.7, 148.0, 146.4, 144.3, 139.3, 136.3, 132.6, 131.7, 128.9, 128.8, 128.6, 128.4, 124.0, 64.2, 49.4, 48.2 (d, J = 28.7 Hz), 45.8.

HRMS (ESI) calcd for $C_{23}H_{18}F_3N2O_4$ $[M+H]^+$ 443.1213, found 443.1206.

4-(5-bromofuran-2-yl)-1-isopropyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3q)



51.8 mg. Yield: 62%. Oil.

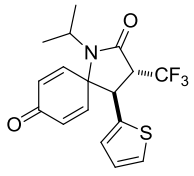
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (dd, J = 10.0, 3.2 Hz, 1H), 6.71 (dd, J = 10.0, 3.2 Hz, 1H), 6.46 (dd, J = 10.0, 2.0 Hz, 1H), 6.20 (d, J = 3.2 Hz, 1H), 6.17 – 6.14 (m, 2H), 3.90 (dq, J = 11.6, 8.0 Hz, 1H), 3.70 (d, J = 11.6 Hz, 1H), 3.40 (heptet, J = 6.8 Hz, 1H), 1.38 (t, J = 6.8 Hz, 6H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.32 (d, J = 8.1 Hz, 3F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.7, 165.0, 148.2, 147.2, 145.8, 132.3, 131.0, 124.1 (q, J = 280.1 Hz), 122.5, 112.6, 112.3, 64.7, 48.1, 47.8 (q, J = 28.8 Hz), 43.6, 20.7, 20.2.

HRMS (ESI) calcd for $C_{17}H_{16}BrF_3NO_3$ $[M+H]^+$ 418.0260, found 418.0260.

1-isopropyl-4-(thiophen-2-yl)-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3r)



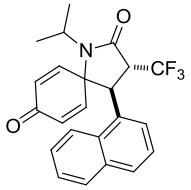
34.8 mg. Yield: 49%. White solid. Mp: 150–153 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, J = 5.2 Hz, 1H), 6.93 (dd, J = 5.2, 3.6 Hz, 1H), 6.84 (d, J = 3.6 Hz, 1H), 6.82 (dd, J = 10.0, 3.2 Hz, 1H), 6.57 (dd, J = 10.0, 3.2 Hz, 1H), 6.49 (dd, J = 10.0, 2.0 Hz, 1H), 6.07 (dd, J = 10.0, 2.0 Hz, 1H), 3.97 (d, J = 12.0 Hz, 1H), 3.77 (dq, J = 12.0, 7.9 Hz, 1H), 3.36 (heptet, J = 6.8 Hz, 1H), 1.40 (d, J = 6.8 Hz, 3H), 1.38 (d, J = 6.8 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.74 (d, J = 7.9 Hz, 3F).

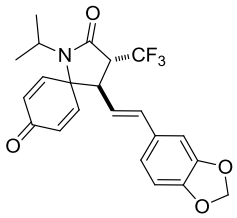
^{13}C NMR (100 MHz, $CDCl_3$) δ 183.9, 165.3, 147.1, 145.9, 135.7, 133.0, 131.1, 127.2, 126.4, 125.5, 124.2 (q, J = 280.2 Hz), 65.3, 50.7 (q, J = 28.4 Hz), 48.3, 45.1, 20.7, 20.2.
HRMS (ESI) calcd for $C_{17}H_{17}F_3NO_2S$ $[M+H]^+$ 356.0927, found 356.0935.

1-isopropyl-4-(naphthalen-1-yl)-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3t)



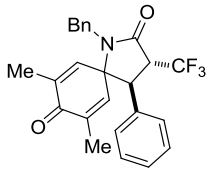
26.4 mg. Yield: 33%. White solid. Mp: 242–244 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.75 (m, 3H), 7.49 – 7.45 (m, 3H), 7.37 (d, J = 7.6 Hz, 1H), 7.09 (dd, J = 10.0, 3.2 Hz, 1H), 6.50 (dd, J = 10.4, 3.2 Hz, 1H), 6.28 (dd, J = 10.0, 2.0 Hz, 1H), 5.83 (dd, J = 10.0, 2.0 Hz, 1H), 4.74 (d, J = 9.2 Hz, 1H), 4.02 – 3.95 (m, 1H), 3.27 (heptet, J = 6.8 Hz, 1H), 1.46 (d, J = 6.8 Hz, 3H), 1.42 (d, J = 6.8 Hz, 3H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.83 (d, J = 8.6 Hz, 3F).
^{13}C NMR (100 MHz, $CDCl_3$) δ 183.5, 166.1, 148.5, 146.8, 134.1, 131.8, 131.7, 131.0, 130.5, 129.4, 129.3, 126.9, 126.3, 124.9, 124.8, 124.6 (q, J = 280.2 Hz), 122.7, 64.9, 51.7 (q, J = 28.1 Hz), 47.9, 42.8, 20.6, 20.2.
HRMS (ESI) calcd for $C_{23}H_{21}F_3NO_2$ $[M+H]^+$ 400.1519, found 400.1508.

4-((*E*)-2-(benzo[d][1,3]dioxol-5-yl)vinyl)-1-isopropyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione (3u)



40.3 mg. Yield: 48%. White solid. Mp 187–189 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 – 6.65 (m, 5H), 6.46 (dd, J = 10.0, 2.0 Hz, 1H), 6.40 (dd, J = 10.0, 2.0 Hz, 1H), 6.33 (d, J = 15.6 Hz, 1H), 5.95 (s, 2H), 5.59 (dd, J = 15.6, 8.8 Hz, 1H), 3.48 – 3.36 (m, 1H), 3.35 – 3.01 (m, 1H), 3.21 – 3.10 (m, 1H), 1.37 (t, J = 6.6 Hz, 6H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.48 (d, J = 8.0 Hz, 3F).
^{13}C NMR (100 MHz, $CDCl_3$) δ 184.0, 165.9, 148.1, 148.0, 147.7, 146.1, 135.5, 132.5, 131.7, 129.8, 124.4 (q, J = 280.2 Hz), 121.7, 119.3, 108.3, 105.7, 101.3, 65.3, 50.3 (q, J = 27.8 Hz), 48.2, 48.0, 20.7, 20.4.
HRMS (ESI) calcd for $C_{22}H_{21}F_3NO_4$ $[M+H]^+$ 420.1417, found 420.1416.

ethyl 2-(7,9-dimethyl-2,8-dioxo-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-dien-1-yl)acetate (3v)



66.4 mg. Yield: 78%. White solid. Mp:154–158 °C.

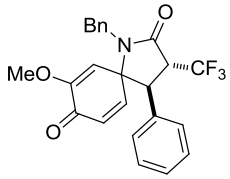
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.20 (m, 6H), 7.17 – 7.14 (m, 2H), 7.01 – 6.98 (m, 2H), 6.28 (dd, *J* = 3.2, 1.6 Hz, 1H), 6.04 (dd, *J* = 3.2, 1.6 Hz, 1H), 4.57 (d, *J* = 14.8 Hz, 1H), 4.18 (d, *J* = 14.8 Hz, 1H), 3.93 (dq, *J* = 12.0, 8.0 Hz, 1H), 3.66 (d, *J* = 12.0 Hz, 1H), 1.80 (d, *J* = 1.6 Hz, 3H), 1.44 (d, *J* = 1.6 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.47 (d, *J* = 8.0 Hz, 3F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 166.6, 142.5, 140.7, 138.9, 137.9, 137.2, 132.7, 128.7, 128.7, 128.6, 128.5, 128.5, 127.9, 127.5, 124.6 (q, *J* = 280.4 Hz), 64.6, 49.9, 48.3 (q, *J* = 28.3 Hz), 45.6, 15.8, 15.4.

HRMS (ESI) calcd for $C_{22}H_{23}F_3NO_4$ $[M+H]^+$ 422.1574, found 422.1578.

ethyl 2-(7-methoxy-2,8-dioxo-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-dien-1-yl)acetate (3w)



Yield: 74%. dr = 1:1.

Isomeride I. 31.6 mg. White solid. Mp: 85–88 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.24 (m, 6H), 7.21 – 7.14 (m, 2H), 7.08 (d, *J* = 4.0 Hz, 2H), 6.44 (dd, *J* = 10.0, 2.0 Hz, 1H), 5.93 (d, *J* = 10.0 Hz, 1H), 5.24 (d, *J* = 2.0 Hz, 1H), 4.89 (d, *J* = 15.2 Hz, 1H), 4.08 – 3.97 (m, 1H), 3.87 (d, *J* = 15.2 Hz, 1H), 3.76 (d, *J* = 12.0 Hz, 1H), 3.33 (s, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.41 (d, *J* = 8.0 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 165.5, 151.1, 144.4, 136.7, 131.2, 129.6, 127.8, 127.8, 127.3, 126.9, 126.4, 123.5 (q, *J* = 280.4 Hz), 113.7, 65.1, 54.0, 49.8, 47.1 (q, *J* = 28.4 Hz), 44.1.

HRMS (ESI) calcd for $C_{24}H_{21}F_3NO_3$ $[M+H]^+$ 428.1468, found 428.1468.

Isomeride II. 31.5 mg. White solid. Mp: 176–178 °C.

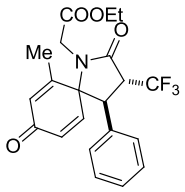
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 6H), 7.21 – 7.15 (m, 2H), 7.09 – 7.00 (m, 2H), 6.66 (dd, *J* = 10.0, 2.8 Hz, 1H), 6.30 (d, *J* = 10.0 Hz, 1H), 5.02 (d, *J* = 2.8 Hz, 1H), 4.49 – 4.36 (m, 2H), 4.00 (dq, *J* = 11.6, 8.0 Hz, 1H), 3.78 (d, *J* = 11.6 Hz, 1H), 3.15 (s, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.38 (d, *J* = 8.1 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 179.4, 166.5, 151.3, 148.0, 137.2, 132.9, 131.2, 128.8, 128.8, 128.7, 128.7, 128.0, 127.6, 124.5 (q, *J* = 280.6 Hz), 112.9, 66.3, 54.6, 49.5, 48.4 (q, *J* = 28.4 Hz), 45.6.

HRMS (ESI) calcd for $C_{24}H_{21}F_3NO_3$ $[M+H]^+$ 428.1468, found 428.1468.

ethyl 2-(6-methyl-2,8-dioxo-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-dien-1-yl) acetate (3x)



Yield:56%. dr = 1.8:1.

Major: 29.3 mg. Oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.25 (m, 3H), 7.10 – 7.02 (m, 2H), 6.73 (d, *J* = 10.0 Hz, 1H), 6.37 (s, 1H), 5.86 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.30 – 4.06 (m, 4H), 3.95 (d, *J* = 12.0 Hz, 1H), 3.29 (d, *J* = 17.2 Hz, 1H), 2.16 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.48 (d, *J* = 7.9 Hz, 3F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.8, 167.1, 153.2, 146.4, 133.2, 132.4, 130.0, 128.9, 128.9, 127.4, 124.4 (q, *J* = 280.3 Hz), 66.9, 62.0, 47.5 (q, *J* = 28.8 Hz), 47.2, 43.1, 17.9, 14.0.

HRMS (ESI) calcd for $C_{21}H_{21}F_3NO_4$ $[M+H]^+$ 408.1417, found 408.1413.

Minor: 16.3 mg. Oil.

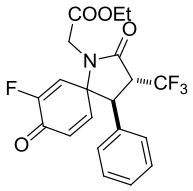
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 3H), 7.19 – 7.12 (m, 2H), 7.08 (d, *J* = 10.0 Hz, 1H), 6.44 (dd, *J* = 10.0, 1.6 Hz, 1H), 5.89 (s, 1H), 4.27 (d, *J* = 17.2 Hz, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.11 – 3.97 (m, 2H), 3.32 (d, *J* = 17.2 Hz, 1H), 1.73 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.91 (d, *J* = 6.8 Hz, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 184.1, 167.4, 166.9, 154.1, 148.8, 132.2, 131.8, 131.4, 128.9, 128.9, 126.7, 67.9, 62.0, 48.3, 47.2(q, *J* = 28.8 Hz), 43.0, 19.9, 14.4.

HRMS (ESI) calcd for $C_{21}H_{21}F_3NO_4$ $[M+H]^+$ 408.1417, found 408.1413.

ethyl 2-(7-fluoro-2,8-dioxo-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-dien-1-yl) acetate (3y)



55.1 mg. Yield: 67%. dr = 1.4:1.

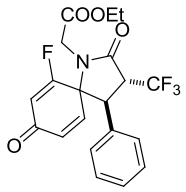
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 7H), 7.20 – 7.11 (m, 5H), 6.96 (dd, *J* = 10.0, 2.8 Hz, 1.4H), 6.74 (dd, *J* = 10.0, 2.8 Hz, 1H), 6.48 (dd, *J* = 11.6, 2.8 Hz, 1H), 6.42 (dd, *J* = 10.0, 6.8 Hz, 1.4H), 6.27 (dd, *J* = 12.4, 2.8 Hz, 1.4H), 5.96 (dd, *J* = 10.0, 7.2 Hz, 1H), 4.22 – 4.11 (m, 5H), 4.14 – 4.03 (m, 2.5H), 3.95 – 3.83 (m, 7H), 1.27 (t, *J* = 7.2 Hz, 7H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.39 (d, *J* = 8.3 Hz, 4.2F), -67.42 (d, *J* = 8.5 Hz, 3F), -121.82 (dd, *J* = 11.6, 7.2 Hz, 1F), -123.45 (dd, *J* = 12.2, 7.1 Hz, 1.4F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.9 (d, *J* = 8.6 Hz), 175.7 (d, *J* = 8.8 Hz), 166.7, 166.7, 165.5, 154.3 (d, *J* = 274.1 Hz), 152.5 (d, *J* = 273.0 Hz), 146.5, 146.5, 145.4, 145.3, 131.0, 130.8, 130.7, 130.7, 128.7, 128.7, 128.2, 128.1, 128.1, 128.0, 126.6, 126.6, 123.1 (q, *J* = 280.4 Hz), 121.5 (d, *J* = 14.2 Hz), 120.5 (d, *J* = 13.7 Hz), 65.31 (d, *J* = 8.1 Hz), 65.03 (d, *J* = 8.5 Hz), 61.1, 49.3, 48.7, 47.0 (q, *J* = 28.9 Hz), 46.9 (q, *J* = 29.1 Hz), 41.8, 41.7, 13.0.

HRMS (ESI) calcd for $C_{20}H_{18}F_4NO_4$ $[M+H]^+$ 412.1166, found 412.1166.

ethyl 2-(6-fluoro-2,8-dioxo-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-dien-1-yl) acetate (3z)



60.9 mg. Yield: 74%. dr = 1:1.

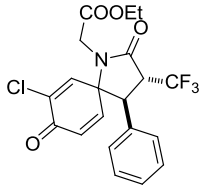
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 6H), 7.22 – 7.11 (m, 4H), 6.91 (t, *J* = 10.4 Hz, 1H), 6.64 (t, *J* = 10.4 Hz, 1H), 6.38 (d, *J* = 10.0 Hz, 1H), 6.21 (dd, *J* = 12.8, 2.0 Hz, 1H), 5.87 (d, *J* = 10.4 Hz, 1H), 5.73 (dd, *J* = 14.0, 1.6 Hz, 1H), 4.35 (d, *J* = 17.6 Hz, 1H), 4.29 (d, *J* = 17.6 Hz, 1H), 4.25 – 4.06 (m, 7H), 3.93 (d, *J* = 12.4 Hz, 1H), 3.53 (d, *J* = 17.6 Hz, 1H), 3.43 (d, *J* = 17.6 Hz, 1H), 1.28 (t, *J* = 5.7 Hz, 3H), 1.25 (t, *J* = 5.7 Hz, 3H)

^{19}F NMR (376 MHz, $CDCl_3$) *δ* -67.47 (d, *J* = 7.5 Hz, 3F), -67.88 (d, *J* = 7.8 Hz, 3F), -92.42 (t, *J* = 12.3 Hz, 1F), -99.83 (t, *J* = 11.8 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 185.1 (d, *J* = 4.6 Hz), 185.0 (d, *J* = 3.8 Hz), 170.8 (d, *J* = 289.0 Hz), 168.8 (d, *J* = 290.0 Hz), 167.5, 167.2, 167.2, 166.6, 142.3 (d, *J* = 4.6 Hz), 142.0 (d, *J* = 2.3 Hz), 132.3, 131.6, 130.6, 129.5, 129.3, 129.2, 129.1, 129.1, 127.6, 127.4, 124.0 (q, *J* = 281.9 Hz), 114.3 (d, *J* = 9.5 Hz), 113.0 (d, *J* = 9.3 Hz), 66.4 (d, *J* = 20.9 Hz), 65.4 (d, *J* = 21.0 Hz), 62.1, 49.7, 47.6 (q, *J* = 28.8 Hz), 47.4 (q, *J* = 29.2 Hz), 46.5, 42.9, 42.7, 14.0,14.0.

HRMS (ESI) calcd for $C_{20}H_{18}F_4NO_4$ $[M+H]^+$ 412.1166, found 412.1169.

ethyl 2-(7-chloro-2,8-dioxo-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-dien-1-yl) acetate (3aa)



62.4 mg. Yield: 73%. dr = 1.6:1.

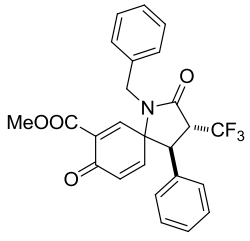
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.32 (m, 8H), 7.18 – 7.11 (m, 5H), 7.10 (d, *J* = 3.2 Hz, 1H), 6.94 (dd, *J* = 10.0, 2.8 Hz, 1.7H), 6.87 (d, *J* = 2.8 Hz, 1.6H), 6.70 (dd, *J* = 10.4, 2.8 Hz, 1H), 6.49 (d, *J* = 10.0 Hz, 1.6H), 6.03 (d, *J* = 10.0 Hz, 1H), 4.22 – 4.17 (m, 5H), 4.09 – 4.03 (m, 3H), 3.97 – 3.82 (m, 8H), 1.30 – 1.23 (m, 8H).

^{19}F NMR (376 MHz, $CDCl_3$) *δ* -67.41 (d, *J* = 8.1 Hz, 3F), -67.44 (d, *J* = 8.0 Hz, 4.8F).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 176.9, 176.9, 167.6, 166.5, 146.7, 145.7, 142.4, 141.7, 136.4, 134.2, 132.0, 131.8, 131.7, 129.8, 129.3, 129.2, 129.1, 129.1, 127.5, 127.5, 124.1 (q, *J* = 280.8 Hz), 66.4, 66.1, 62.2, 62.2, 50.0, 49.9, 48.0 (q, *J* = 28.9 Hz), 48.0 (q, *J* = 29.1Hz), 43.0, 42.9, 14.0.

HRMS (ESI) calcd for $C_{20}H_{18}ClF_3NO_4$ $[M+H]^+$ 428.0871, found 428.0874.

methyl 1-benzyl-2,8-dioxo-4-phenyl-3-(trifluoromethyl)-1-azaspiro[4.5]deca-6,9-diene-7-carboxylate (3ab)



Yield: 40%. dr > 5:1

Major: 36.4 mg. White solid. Mp: 116–118°C.

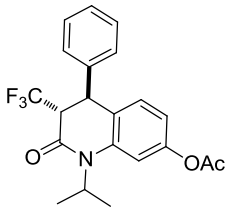
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.90 (s, 1H), 7.38 – 7.11 (m, 9H), 6.98 – 6.78 (m, 3H), 5.42 (d, *J* = 15.2 Hz, 2H), 4.96 (d, *J* = 15.6 Hz, 1H), 3.76 (s, 3H), 3.69 (q, *J* = 9.2 Hz, 1H).

^{19}F NMR (376 MHz, $CDCl_3$) *δ* -66.78 (d, *J* = 9.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 170.2, 161.0, 159.1, 139.1, 135.8, 132.8, 129.1, 128.9, 127.6, 127.5, 127.0, 126.7,124.4 (q, *J* = 284.0 Hz), 123.5, 118.3, 111.8, 53.5 (q, *J* = 26.1 Hz), 52.6, 47.4, 39.9, 39.8.

HRMS (ESI) calcd for $C_{25}H_{21}F_3NO_4$ $[M+H]^+$ 456.1417, found 456.1421.

1-isopropyl-2-oxo-4-phenyl-3-(trifluoromethyl)-1,2,3,4-tetrahydroquinolin-7-yl acetate (4e)



33.3 mg. Yield: 85%. White solid. Mp:107-108 °C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.32 – 7.25 (m, 3H), 7.22 (d, *J* = 9.2 Hz, 1H), 7.11 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 2H), 7.01 (d, *J* = 2.4 Hz, 1H), 4.64 (heptet, *J* = 6.8 Hz, 1H), 4.39 (s, 1H), 3.62 (qd, *J* = 9.6, 1.2 Hz, 1H), 2.27 (s, 3H), 1.51 (d, *J* = 7.2 Hz, 3H), 1.47 (d, *J* = 6.8 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -66.70 (d, *J* = 9.4 Hz, 3F).

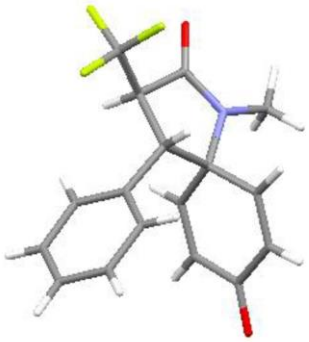
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 169.2, 161.7, 146.7, 138.7, 136.9, 129.1, 127.7, 127.1,124.4 (q, *J* = 283.6 Hz), 122.3, 121.4, 117.4, 54.3 (q, *J* = 26.2 Hz), 50.0, 41.8, 21.1, 20.4, 19.1.

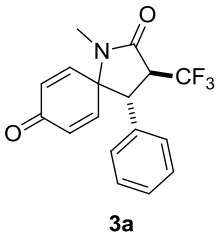
HRMS (ESI) calcd for $C_{21}H_{21}F_3NO_3$ $[M+H]^+$ 392.1468, found 392.1471.

References

S1 Eisenberger, P.; Gischig, S.; Togni, A. *Chem. Eur. J.* **2006**, *12*, 2579.

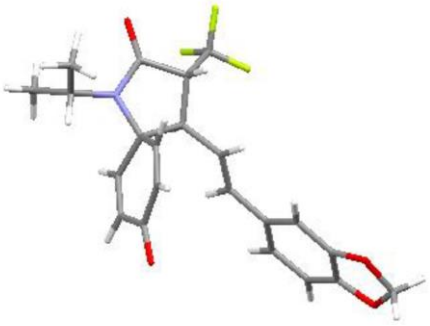
X-Ray structures of product 3a and 3u

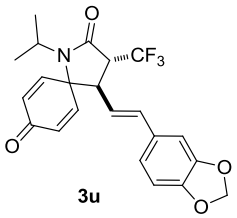




3a

CCDC 1024303 (**3a**)





3u

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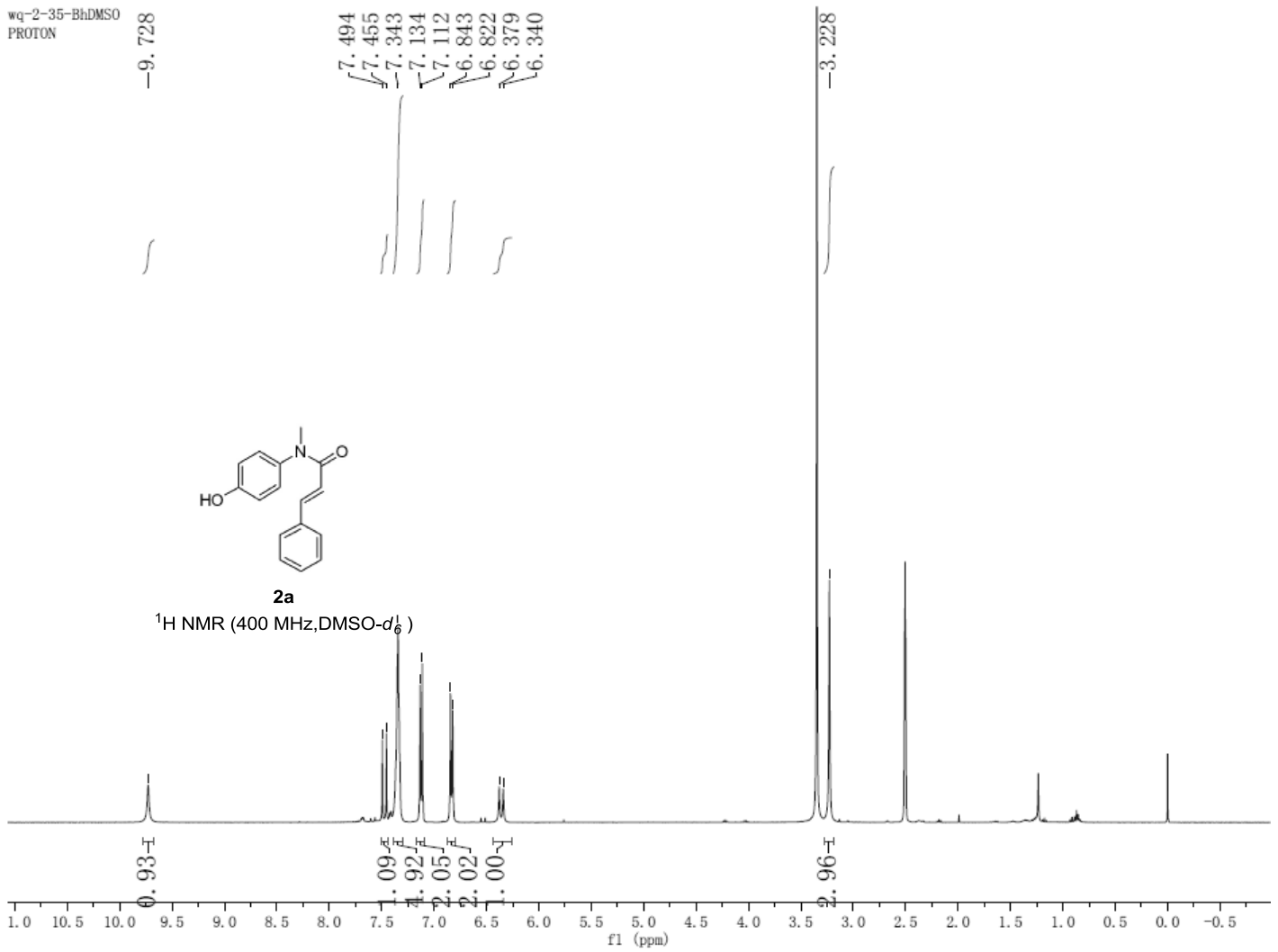
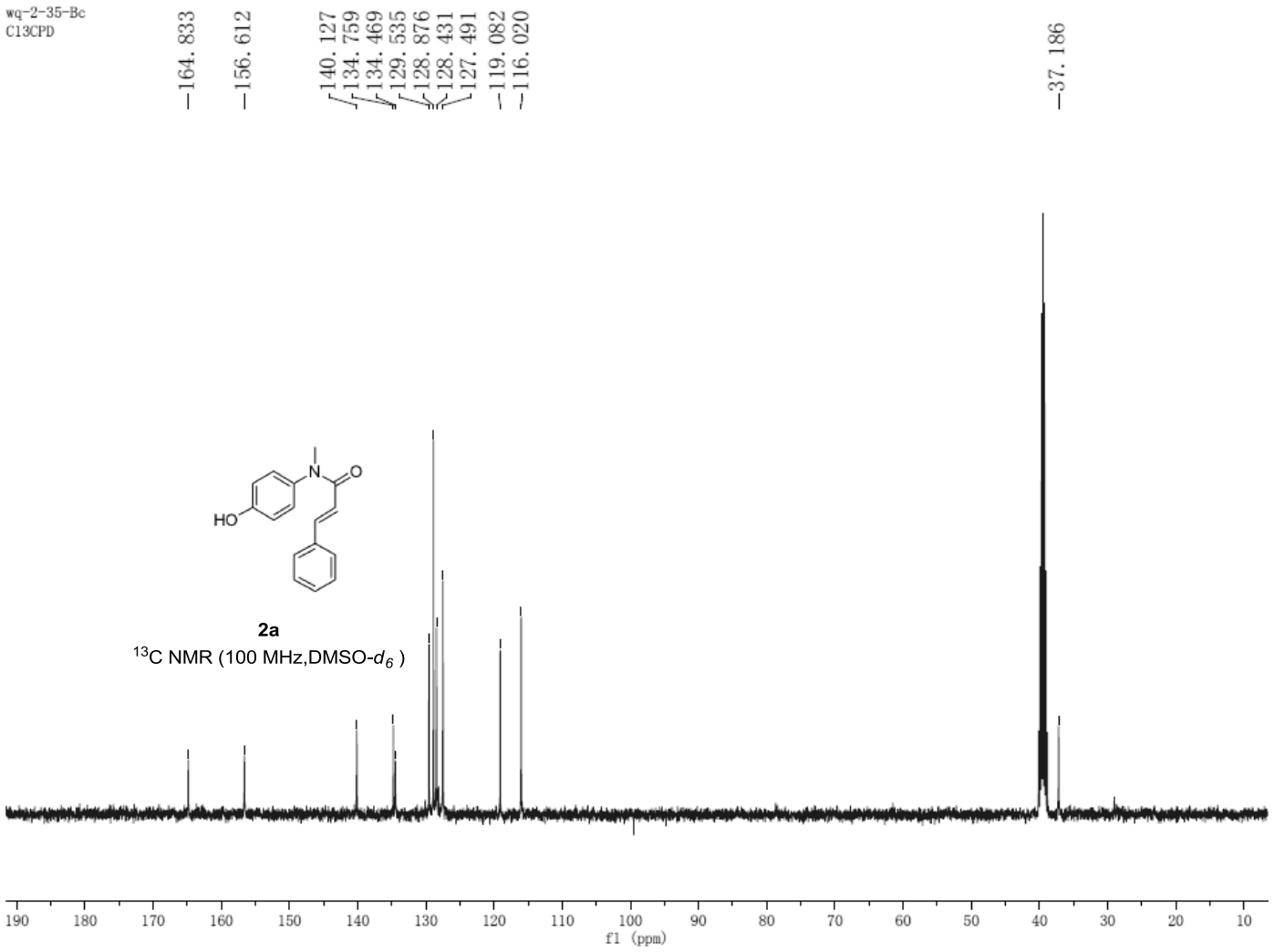


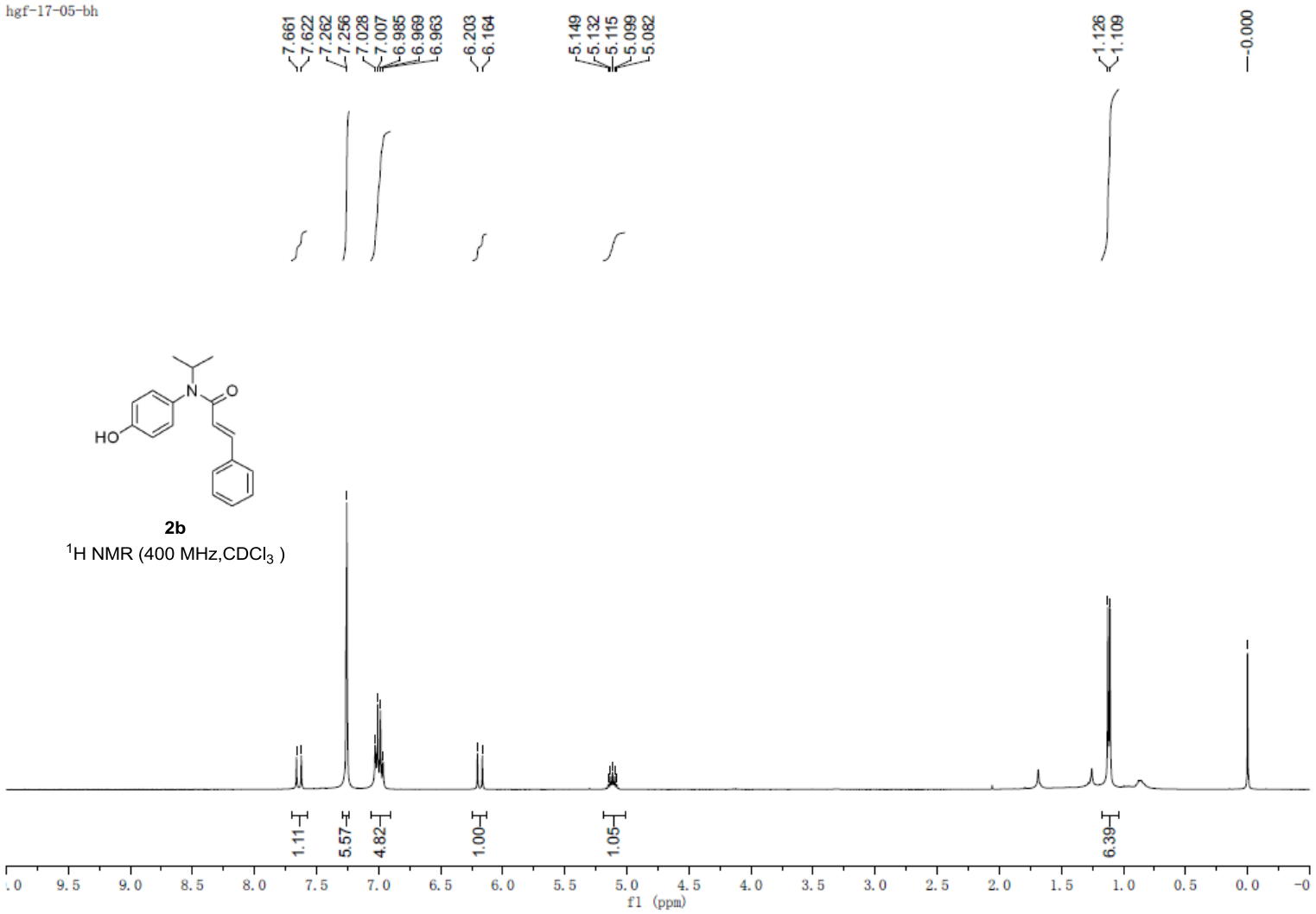
2a

^{1}H NMR (400 MHz,DMSO-d_6)



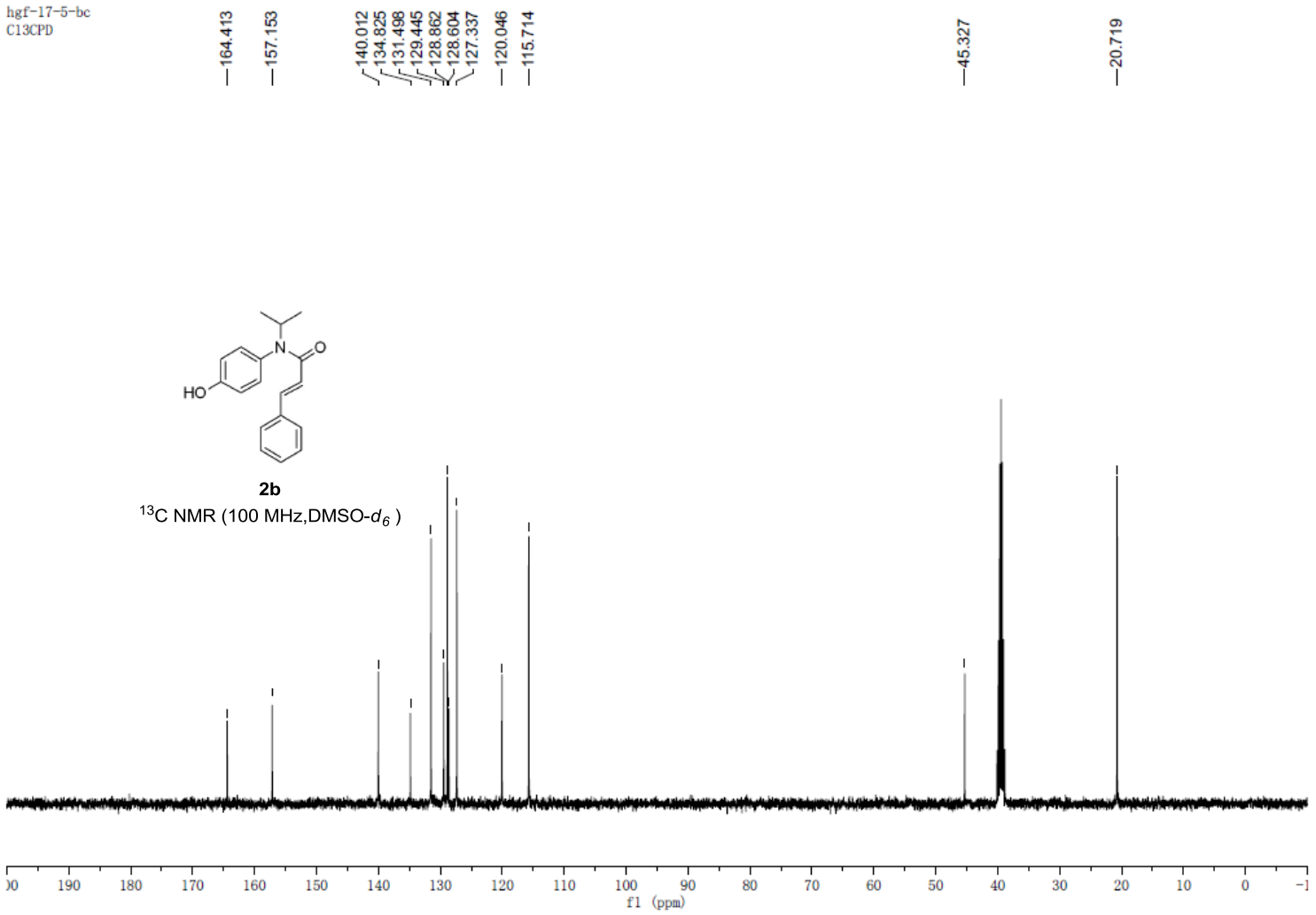
2a

^{13}C NMR (100 MHz,DMSO-d_6)



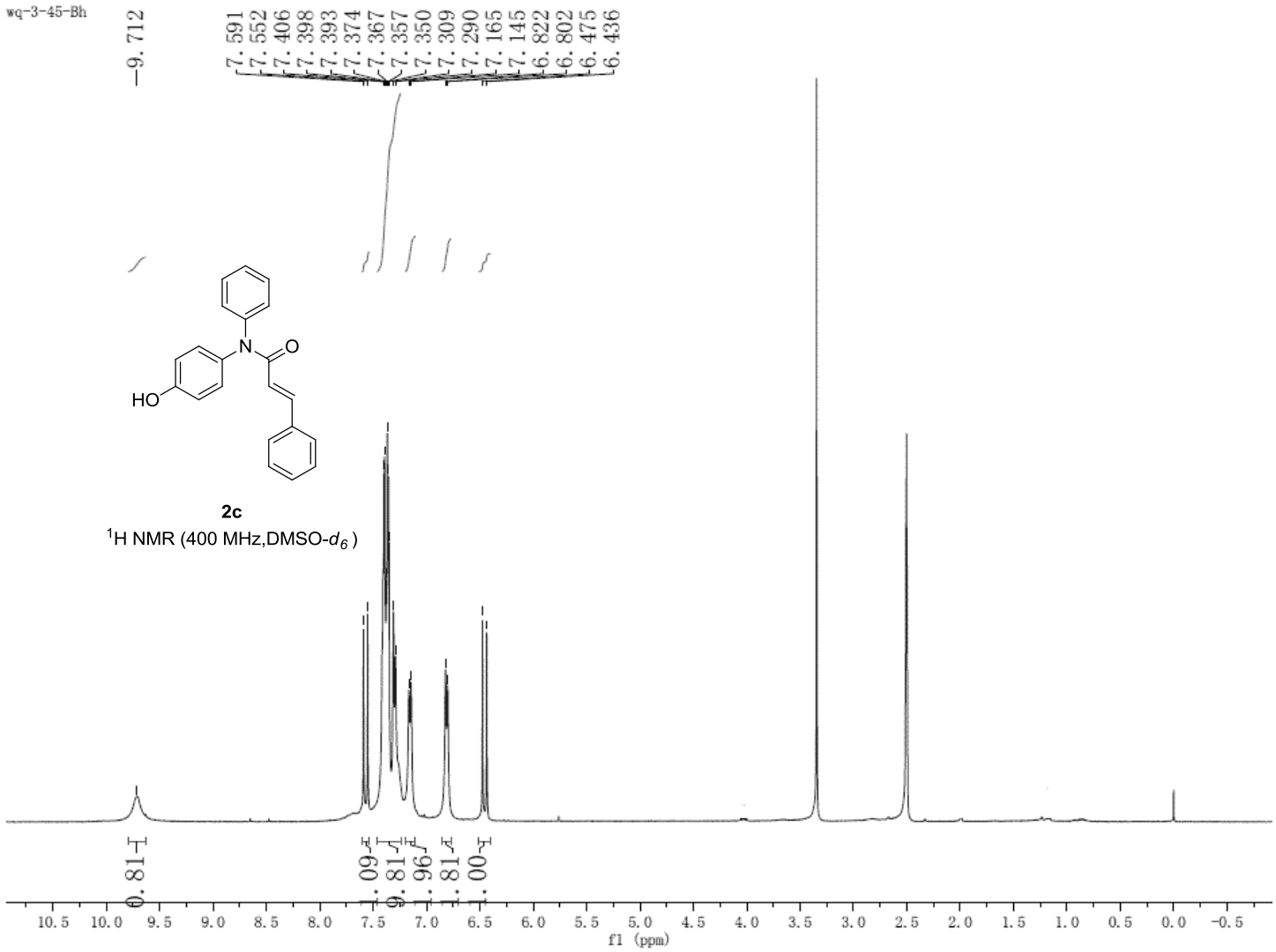
2b

^{1}H NMR (400 MHz,$CDCl_3$)



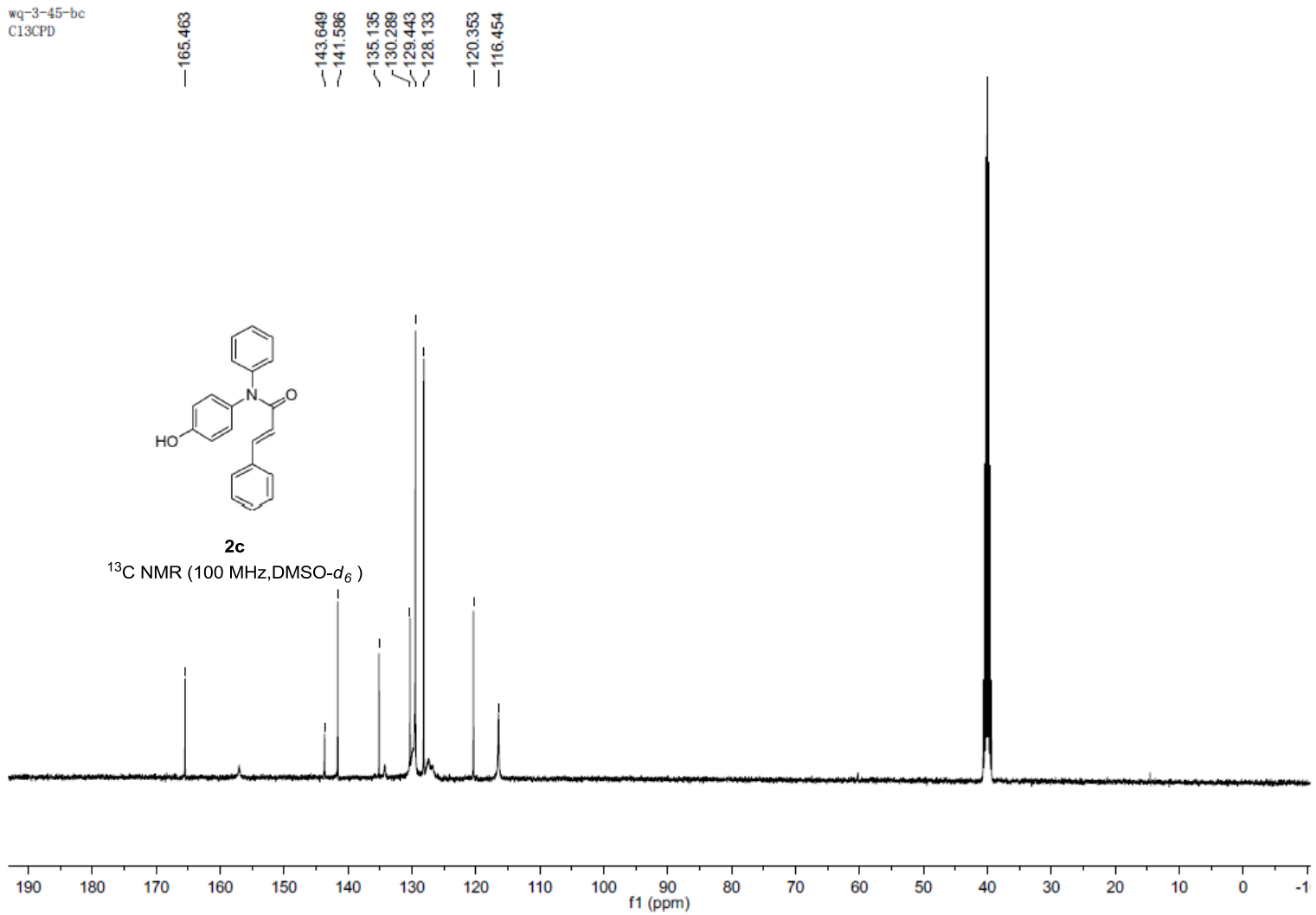
2b

^{13}C NMR (100 MHz,DMSO-d_6)



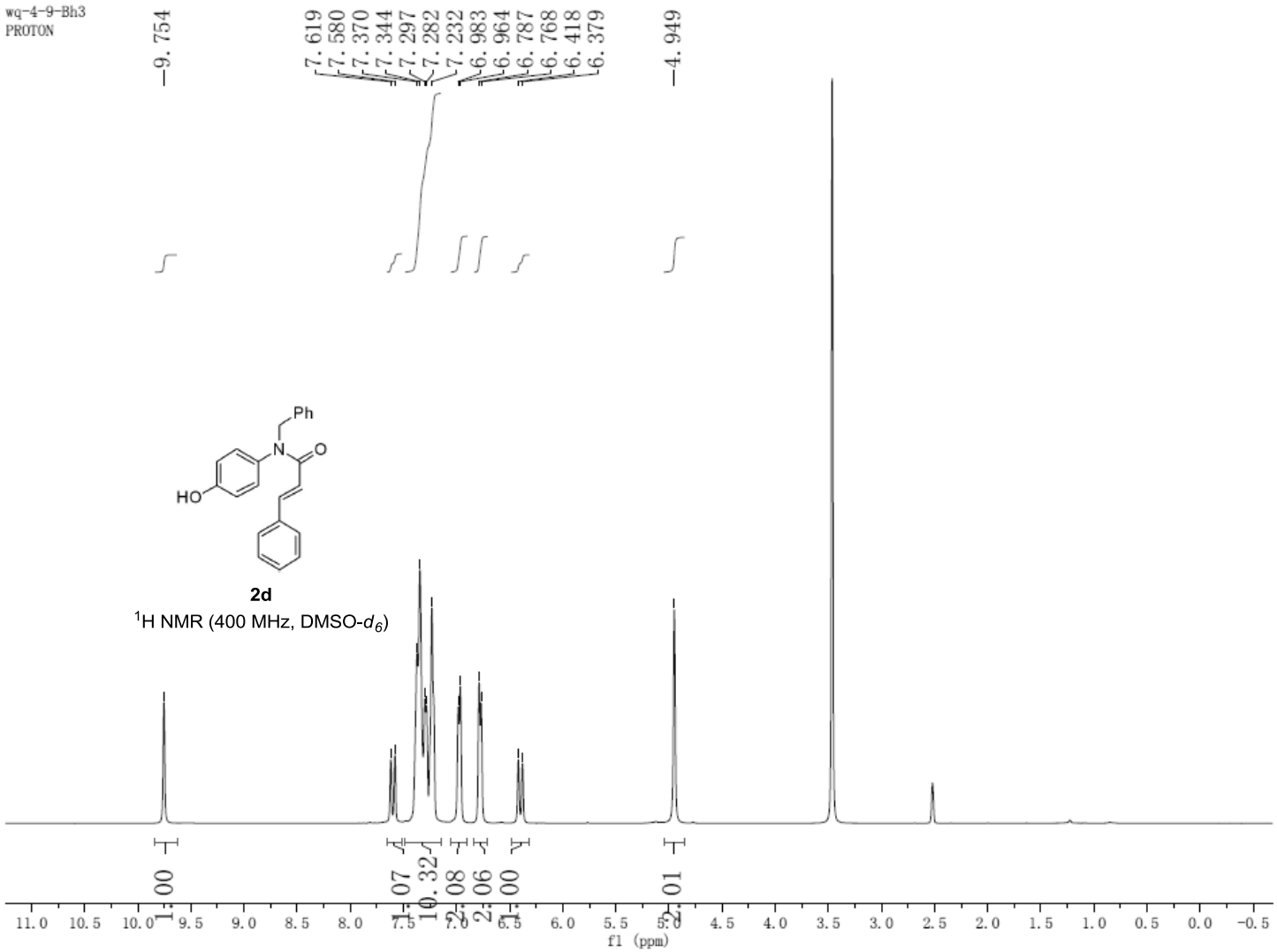
2c

^{1}H NMR (400 MHz,DMSO-d_6)



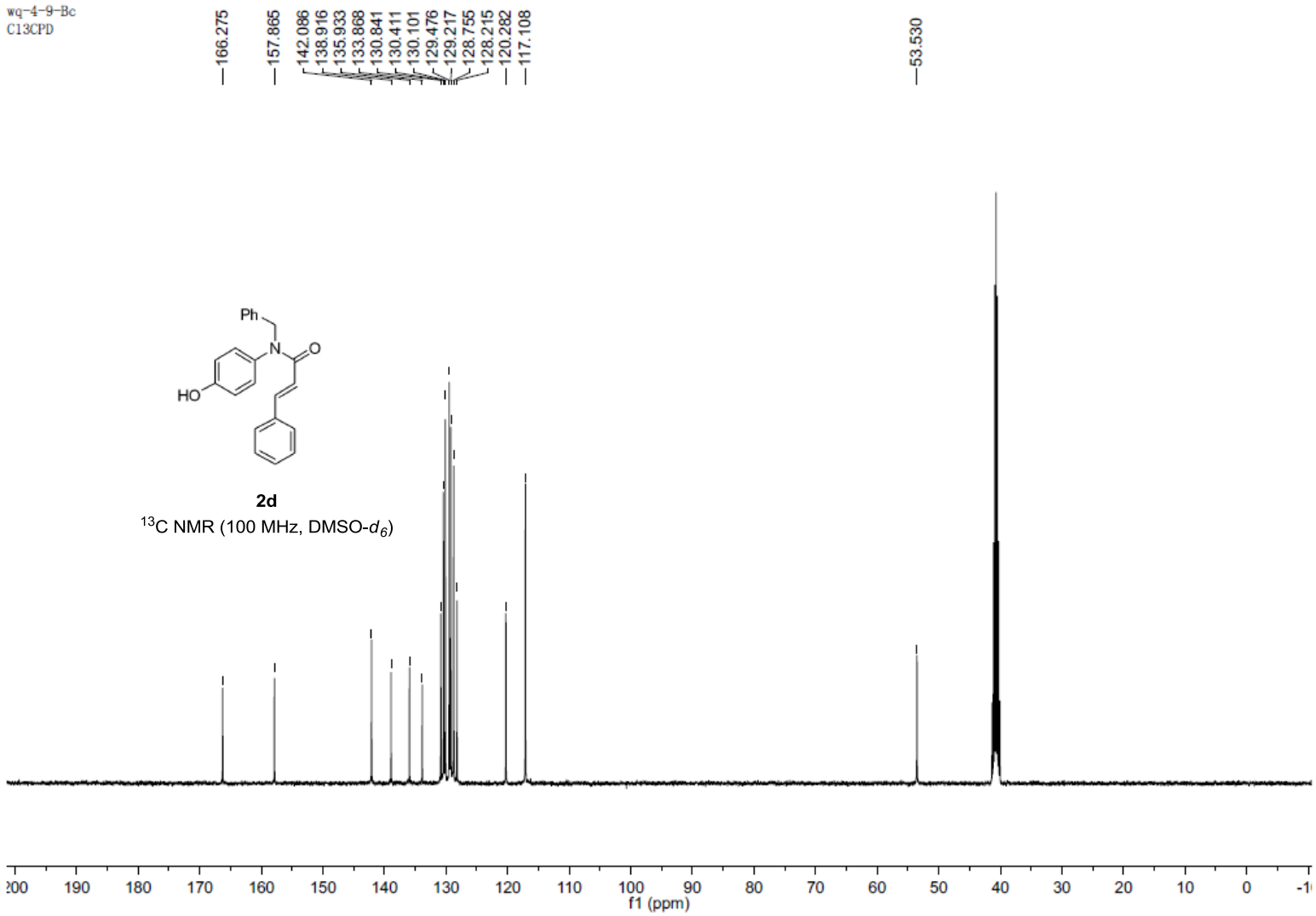
2c

^{13}C NMR (100 MHz,DMSO-d_6)



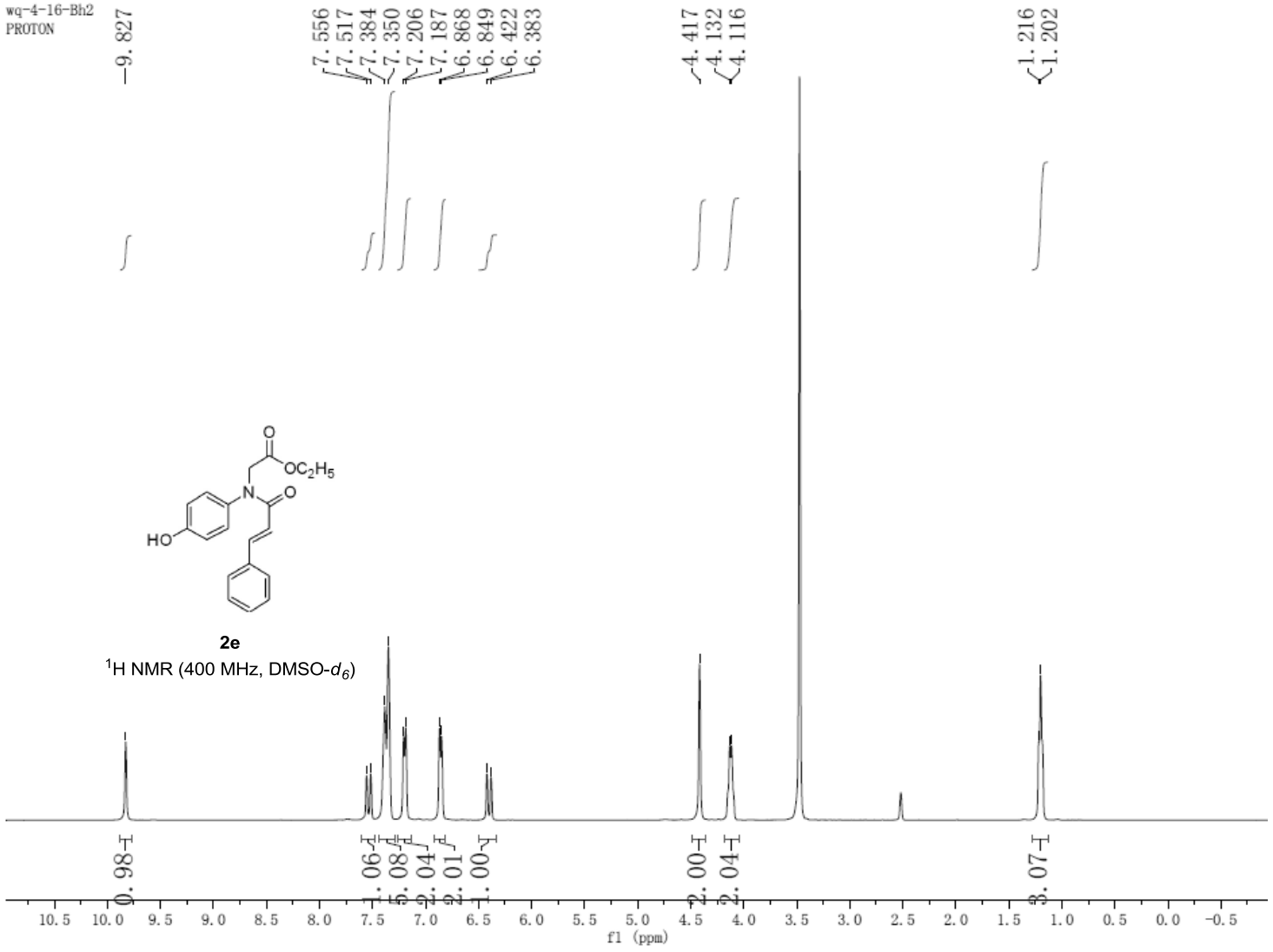
2d

^{1}H NMR (400 MHz, DMSO-d_6)



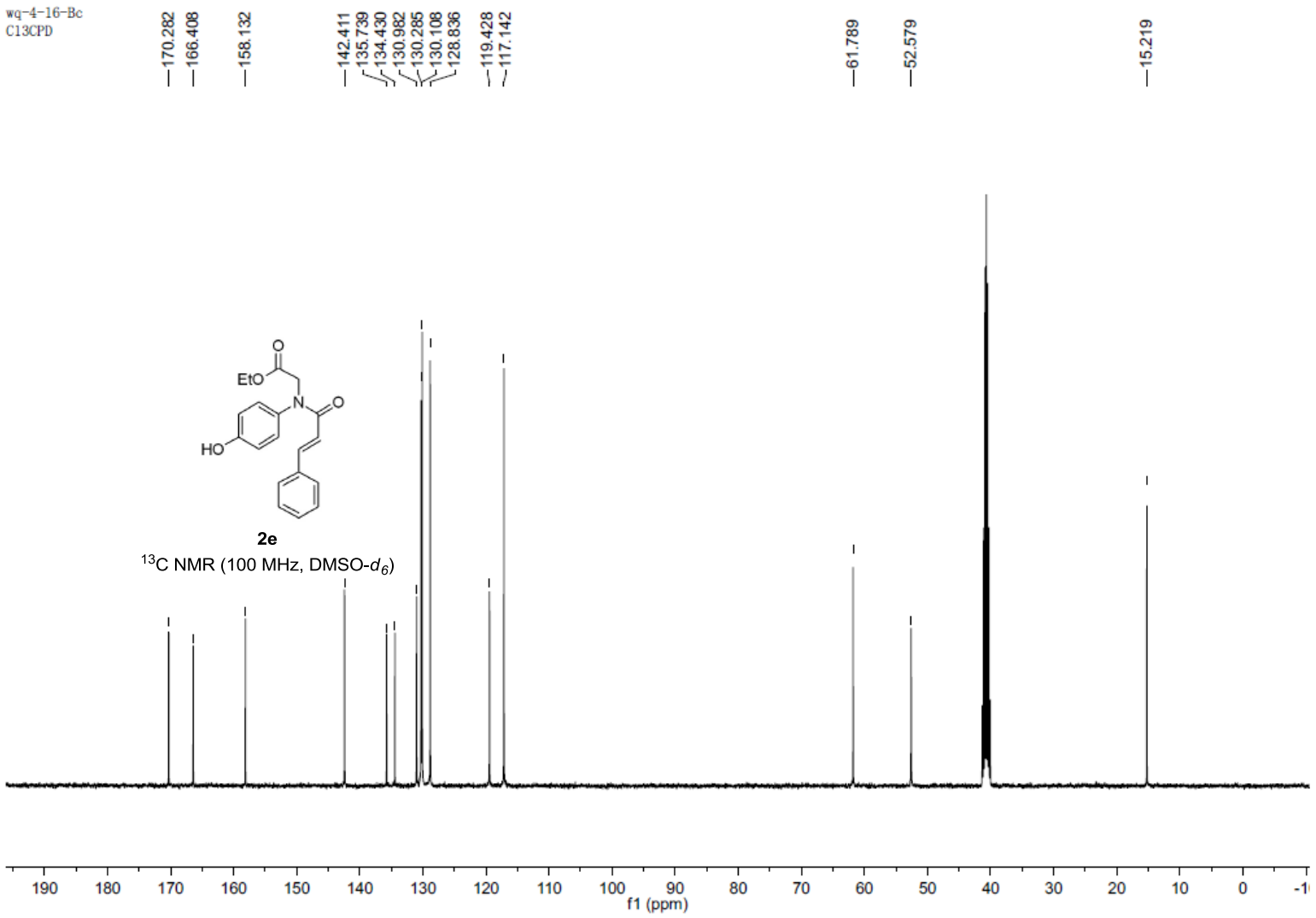
2d

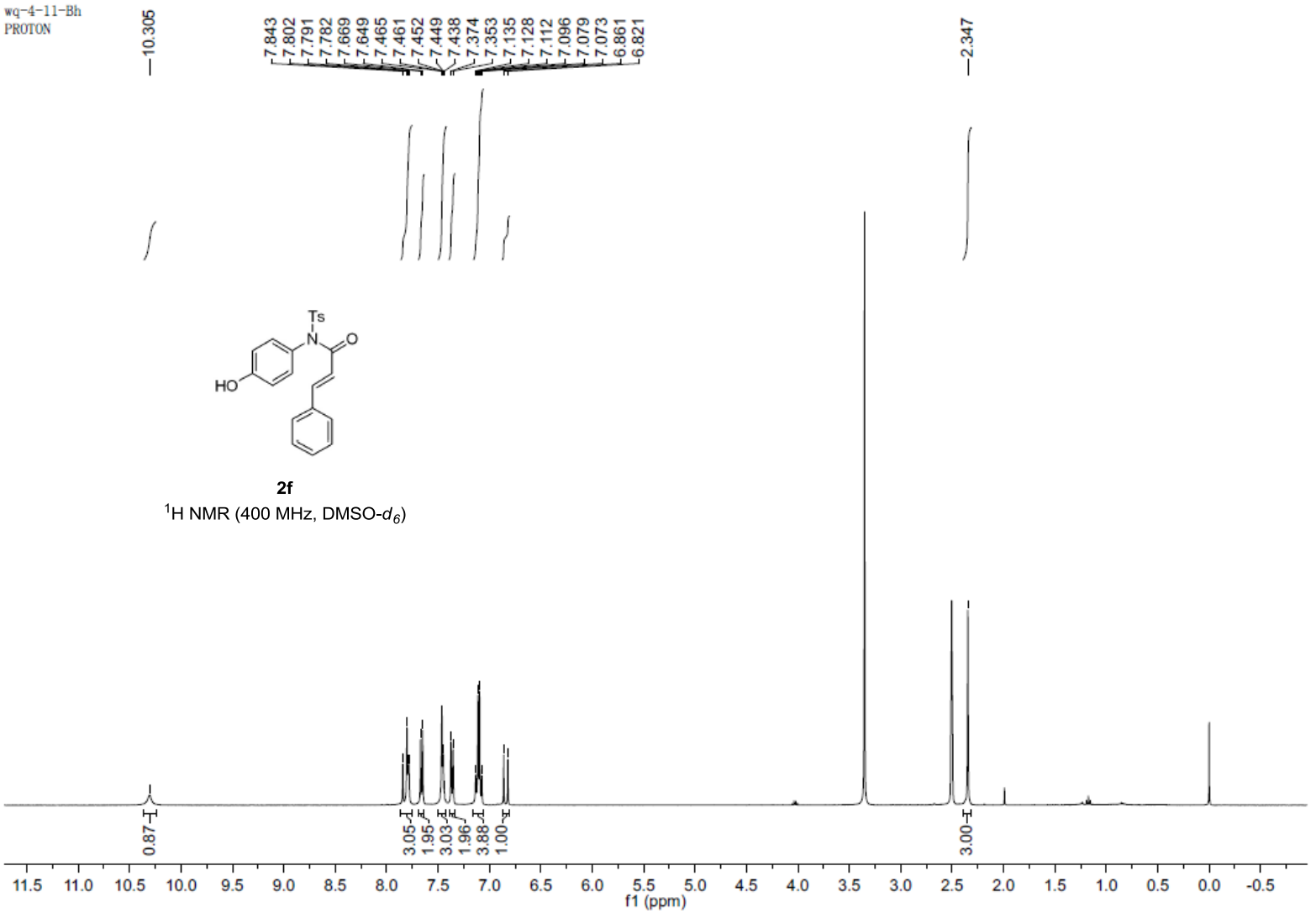
^{13}C NMR (100 MHz, DMSO-d_6)



2e

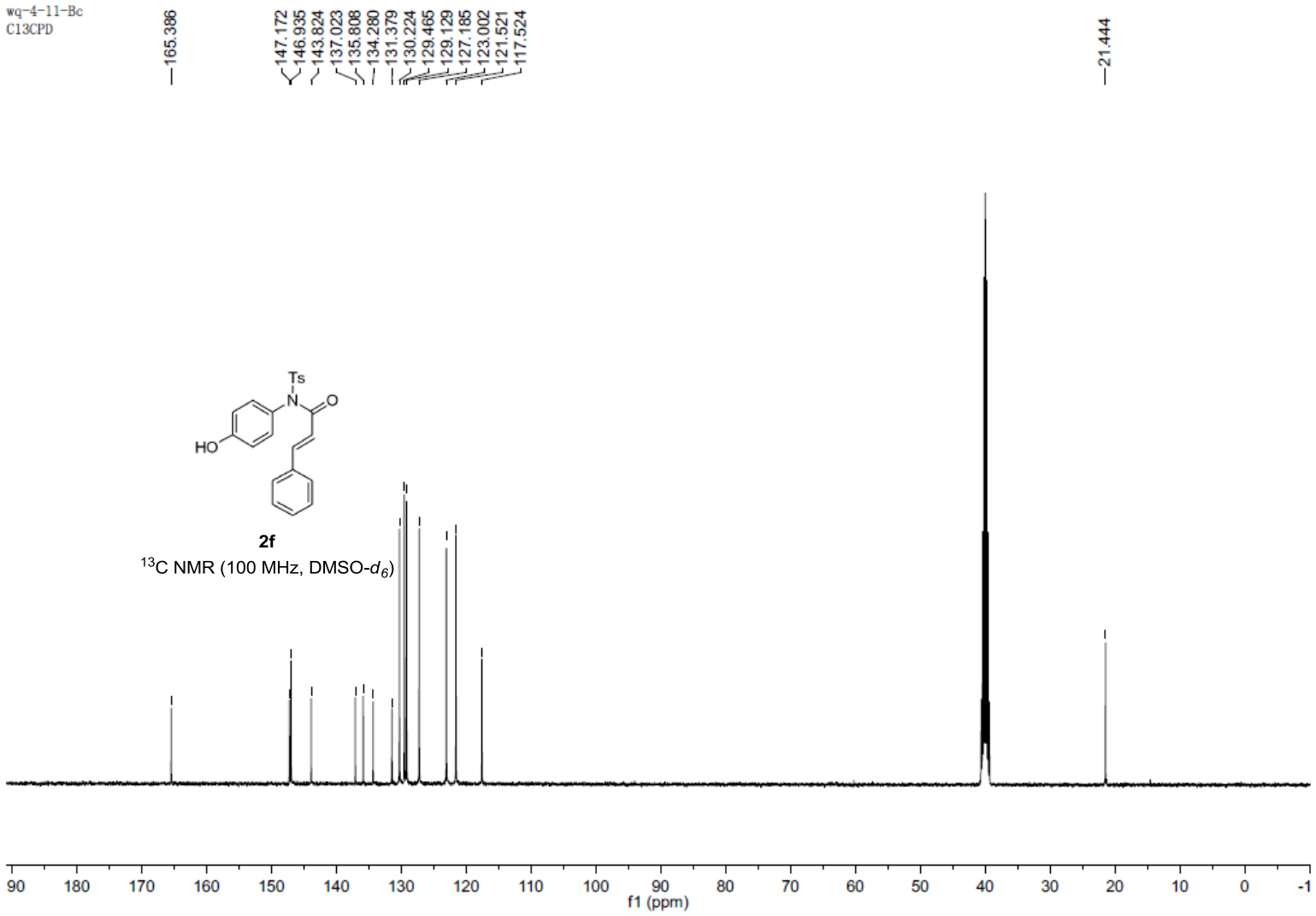
^{1}H NMR (400 MHz, DMSO-d_6)

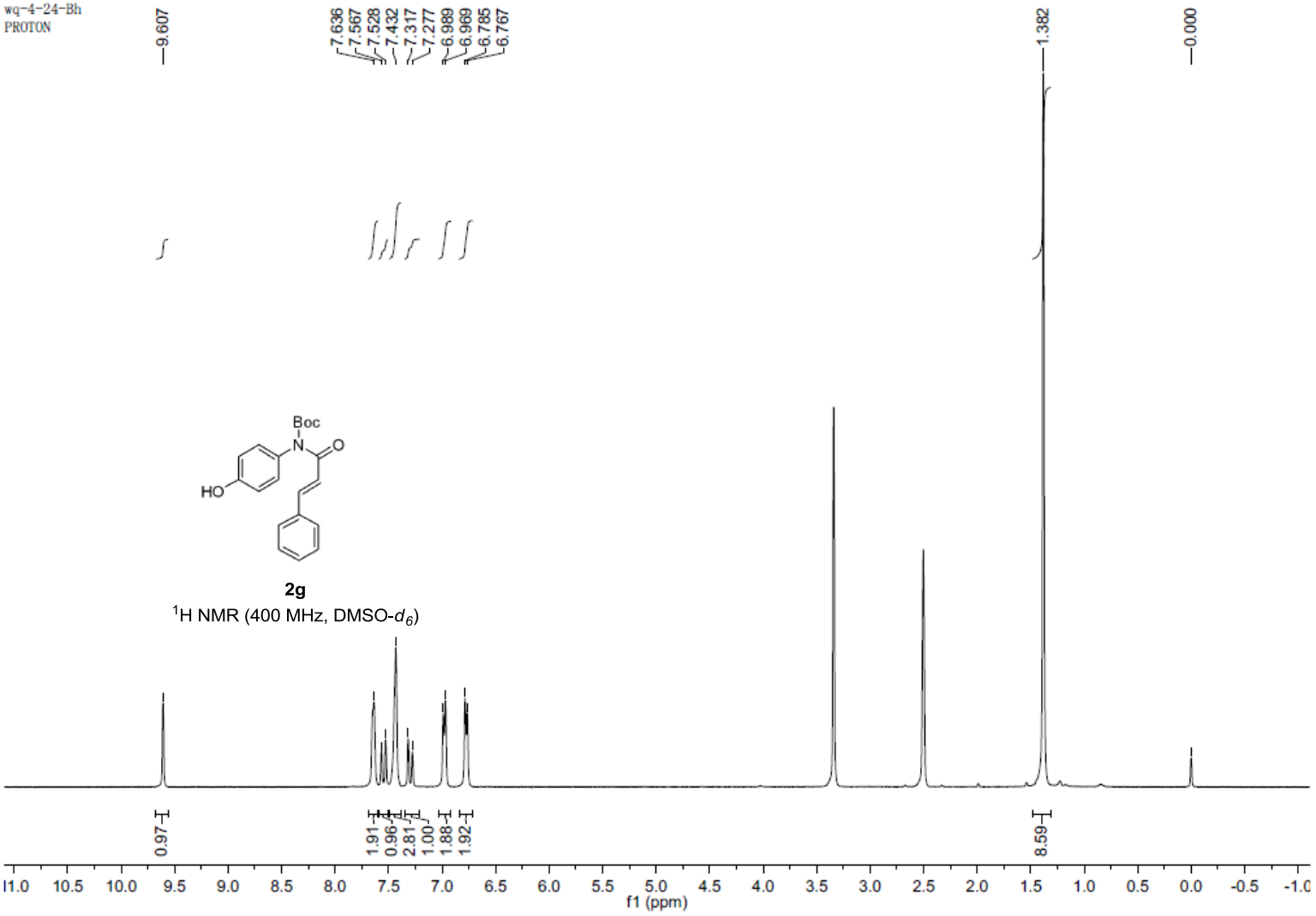

wq-4-16-Bc
C13CPD
170.282
166.408
158.132
142.411
135.739
134.430
130.982
130.285
130.108
128.836
119.428
117.142
61.789
52.579
15.219
EtO
O
N
O
HO
2e
13C NMR (100 MHz, DMSO-d6)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



2f

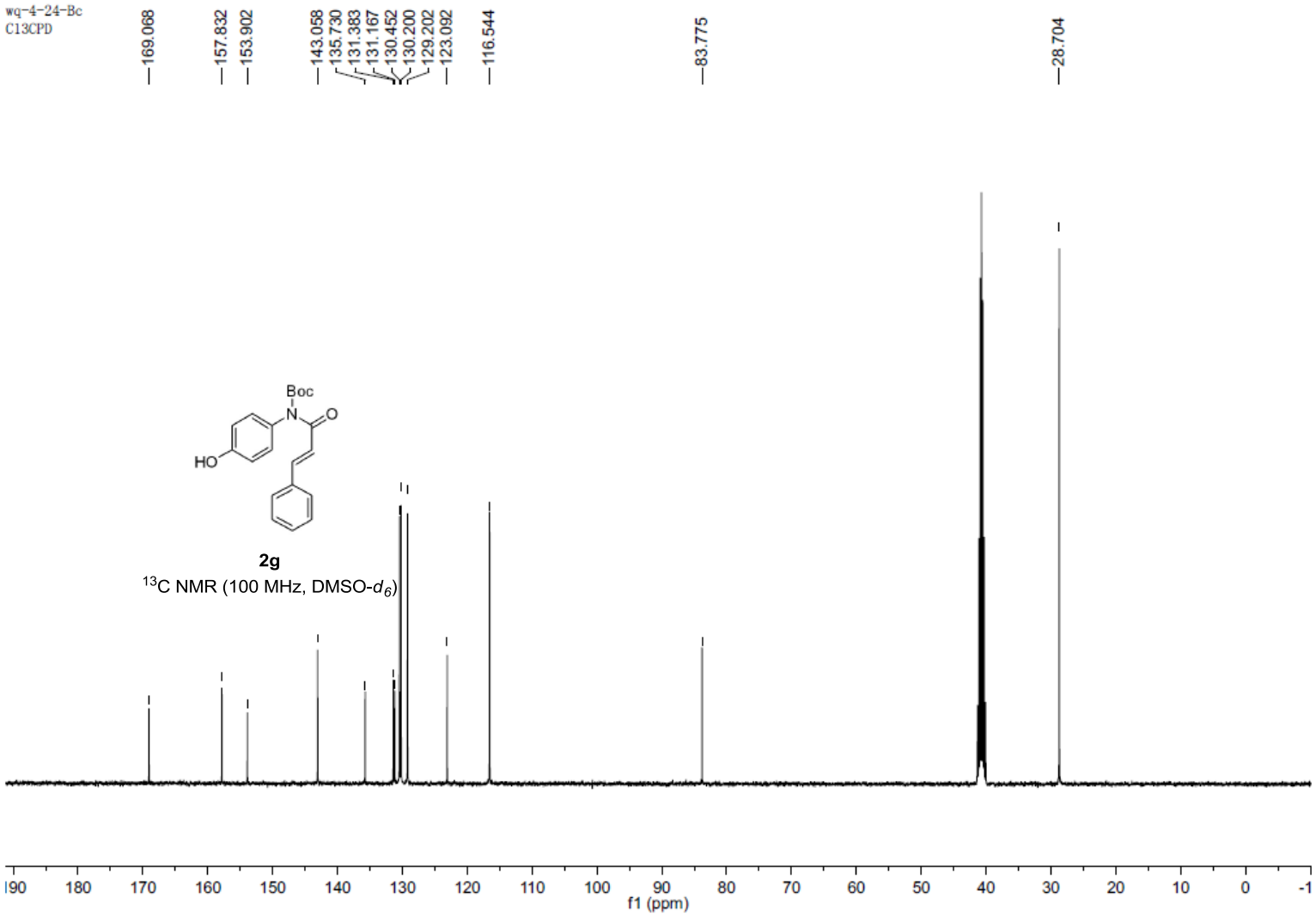
^{1}H NMR (400 MHz, DMSO-d_6)

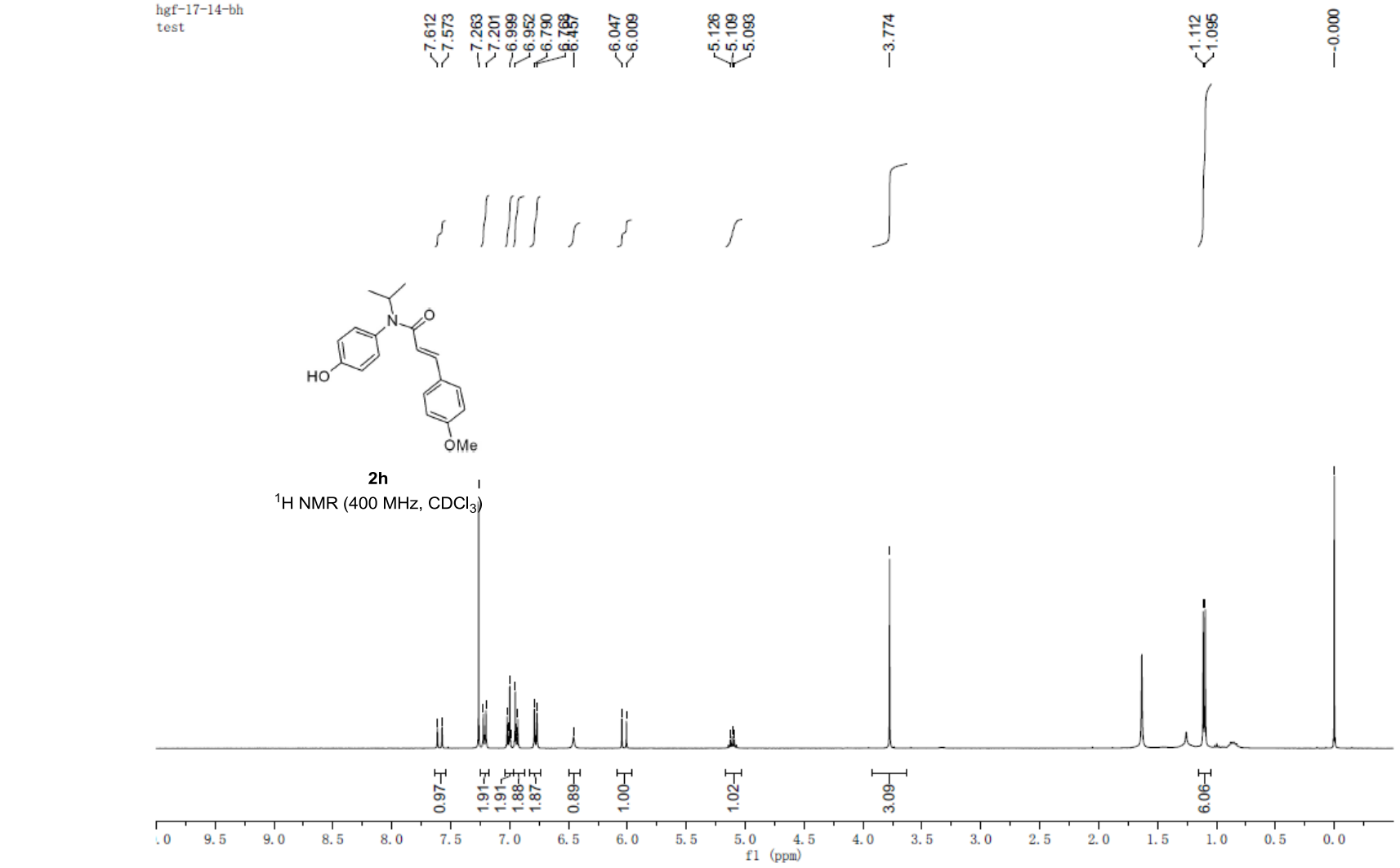

wq-4-11-Bc
C13CPD
165.386
147.172
146.935
143.824
137.023
135.808
134.280
131.379
130.224
129.465
129.129
127.185
123.002
121.521
117.524
21.444
Ts
N
O
HO
2f
13C NMR (100 MHz, DMSO-d6)
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

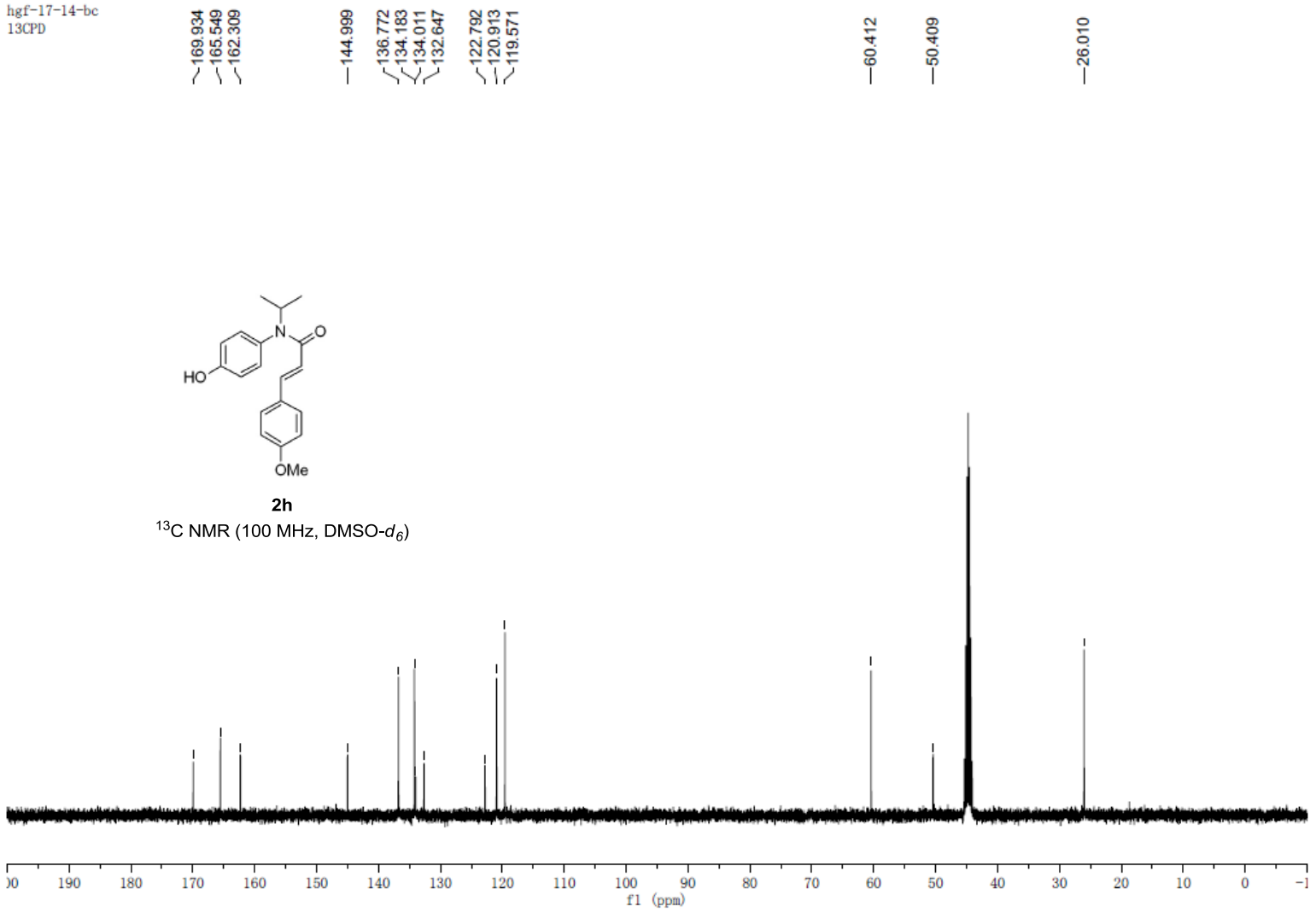


2g

^{1}H NMR (400 MHz, DMSO-d_6)

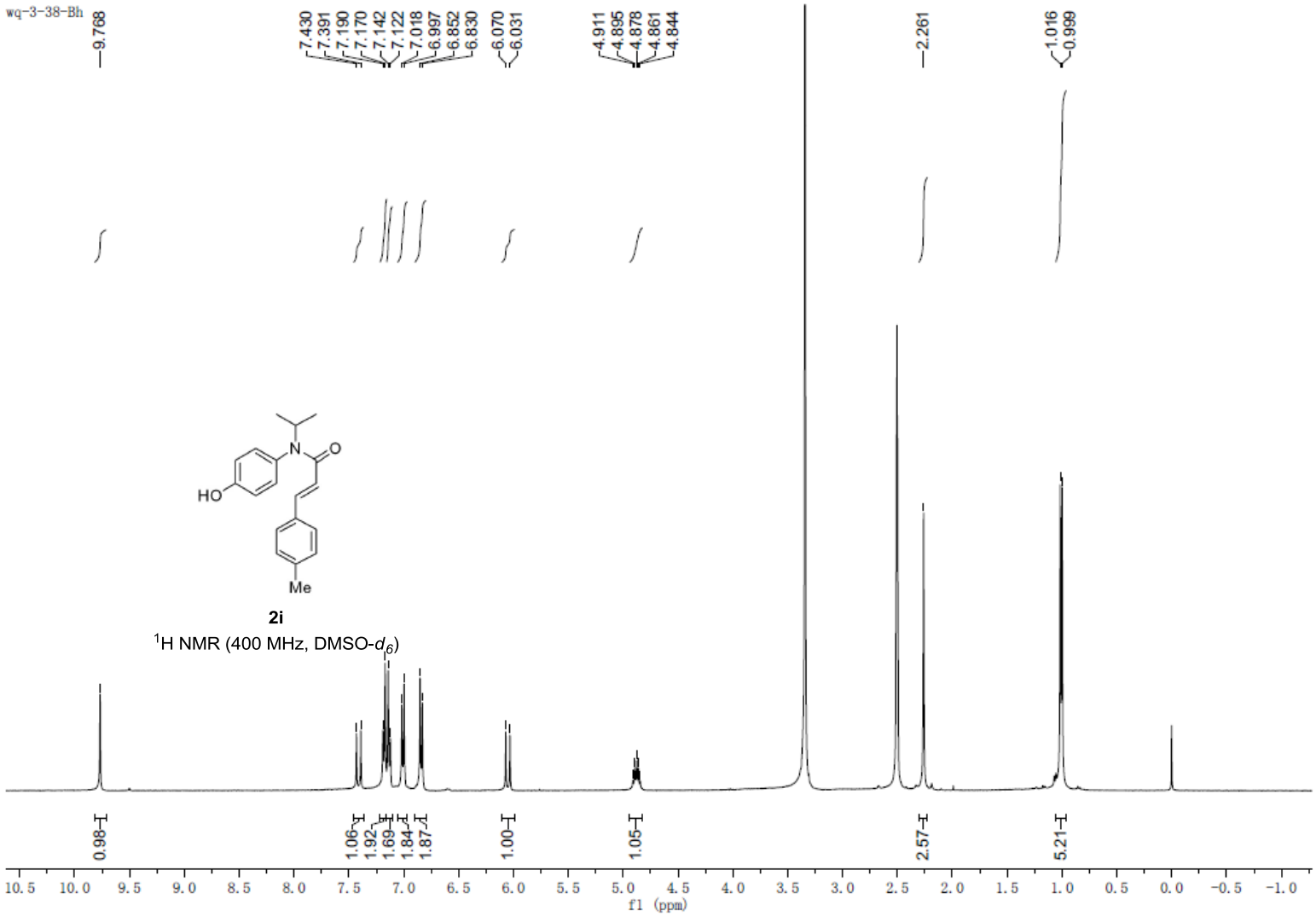

wq-4-24-Bc
C13CPD
169.068
157.832
153.902
143.058
135.730
131.383
131.167
130.452
130.200
129.202
123.092
116.544
83.775
28.704
Boc
N
O
HO
2g
13C NMR (100 MHz, DMSO-d6)
f1 (ppm)


hgf-17-14-bh
test
7.612
7.573
7.263
7.201
6.999
6.952
6.790
6.768
6.457
6.047
6.009
5.126
5.109
5.093
3.774
1.112
1.095
0.000
HO
N
O
OMe
2h
1H NMR (400 MHz, CDCl3)
0.97
1.91
1.91
1.88
1.87
0.89
1.00
1.02
3.09
6.06
f1 (ppm)



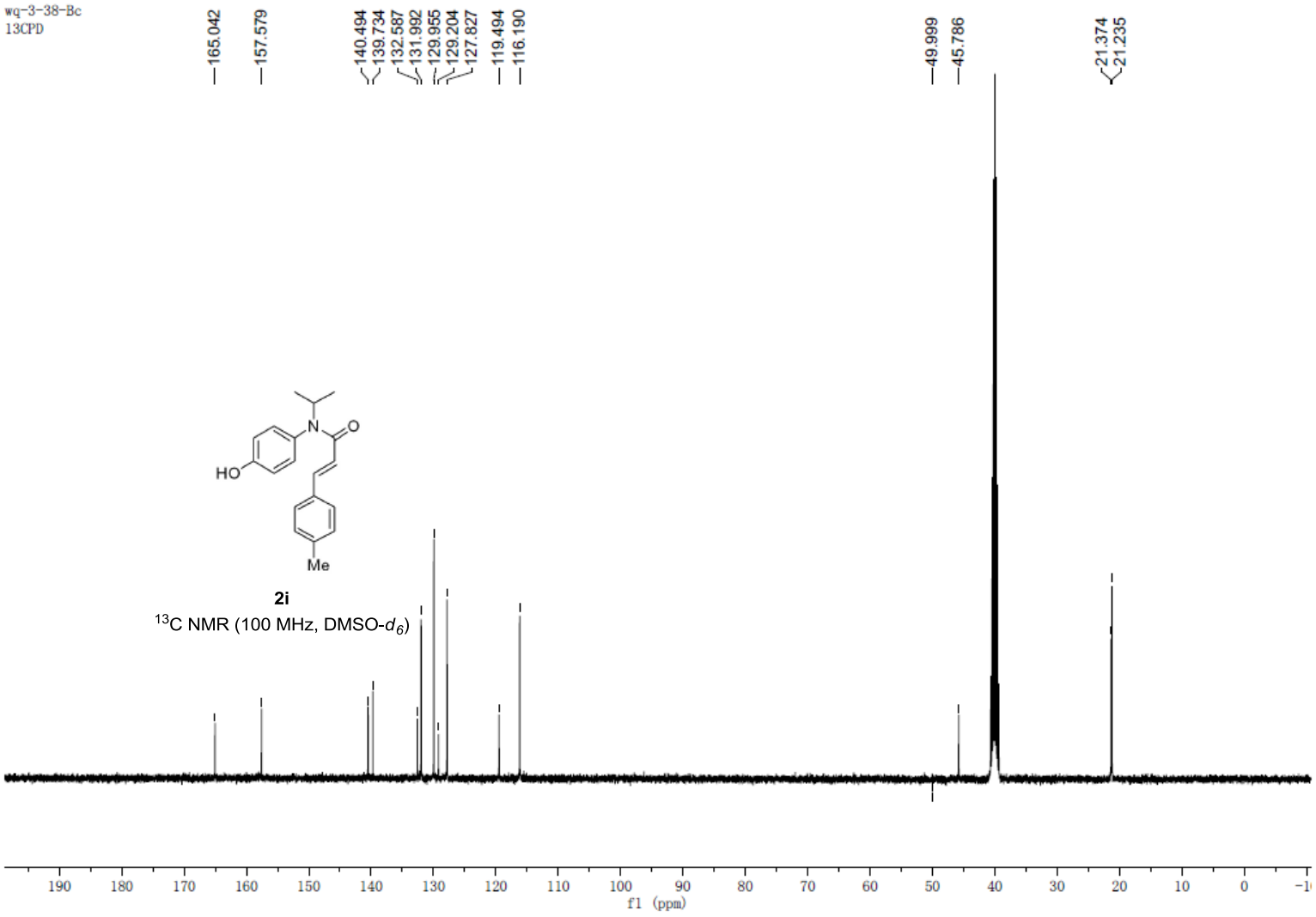
2h

^{13}C NMR (100 MHz, DMSO-d_6)



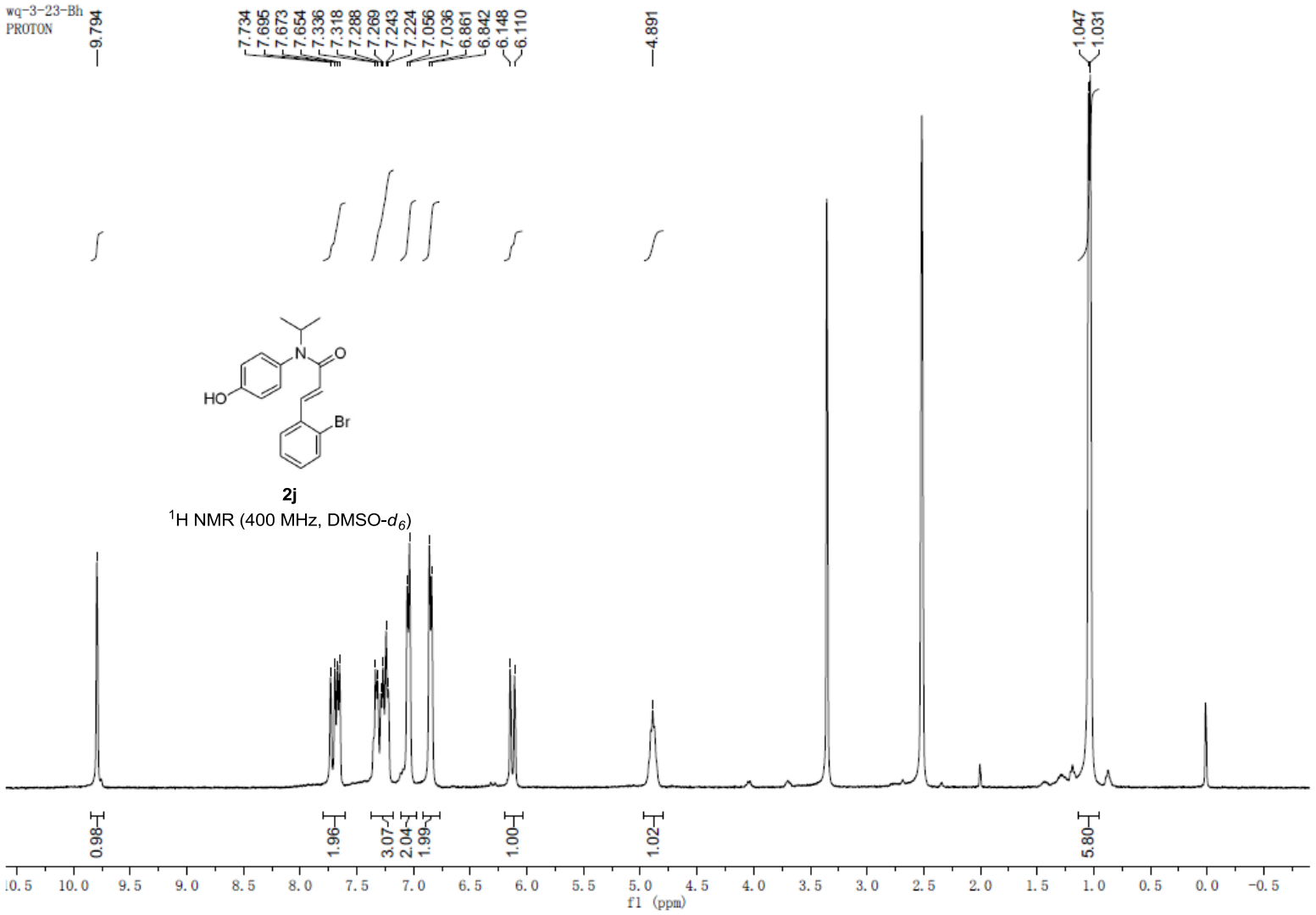
2i

^{1}H NMR (400 MHz, DMSO-d_6)



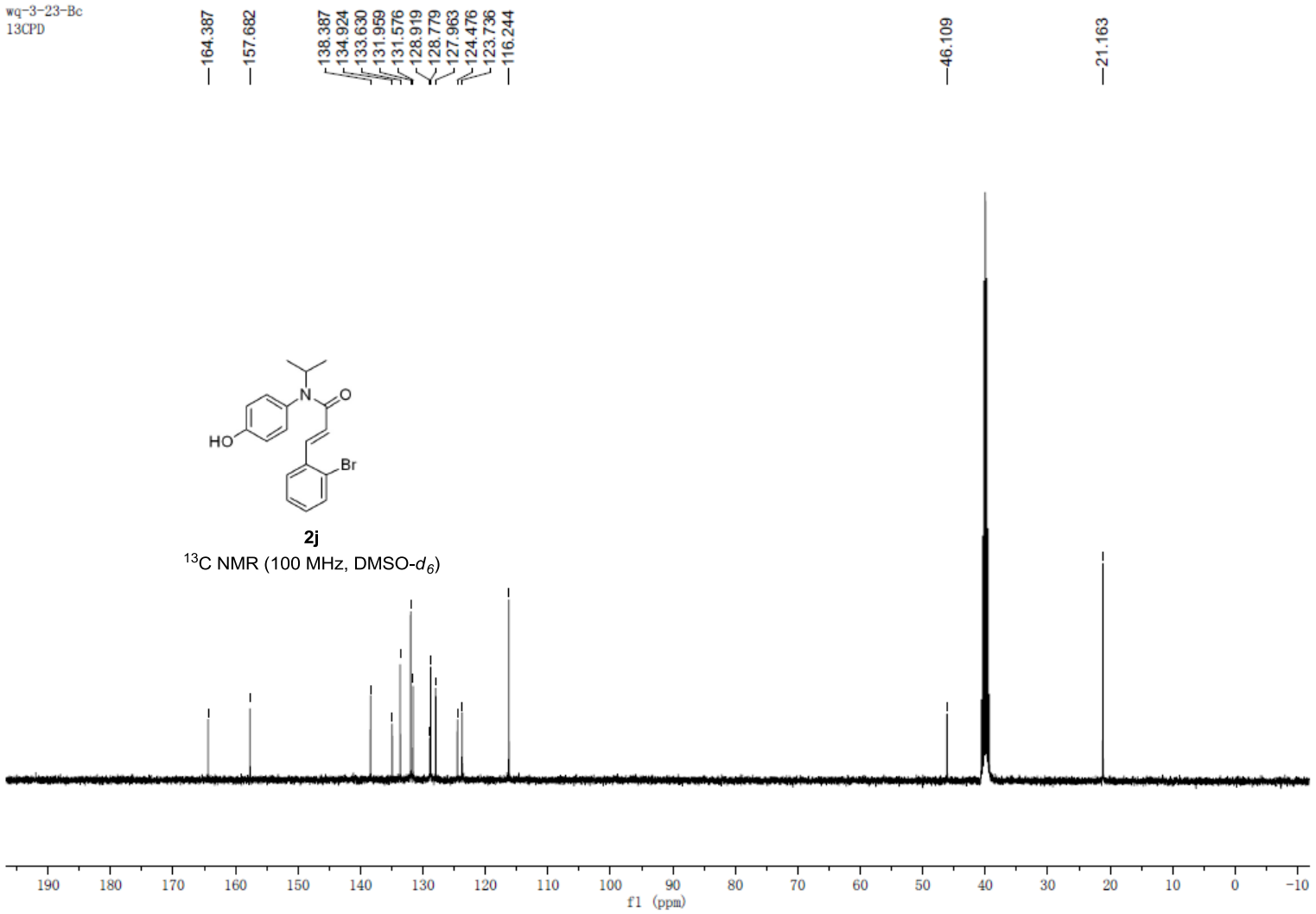
2i

^{13}C NMR (100 MHz, DMSO-d_6)



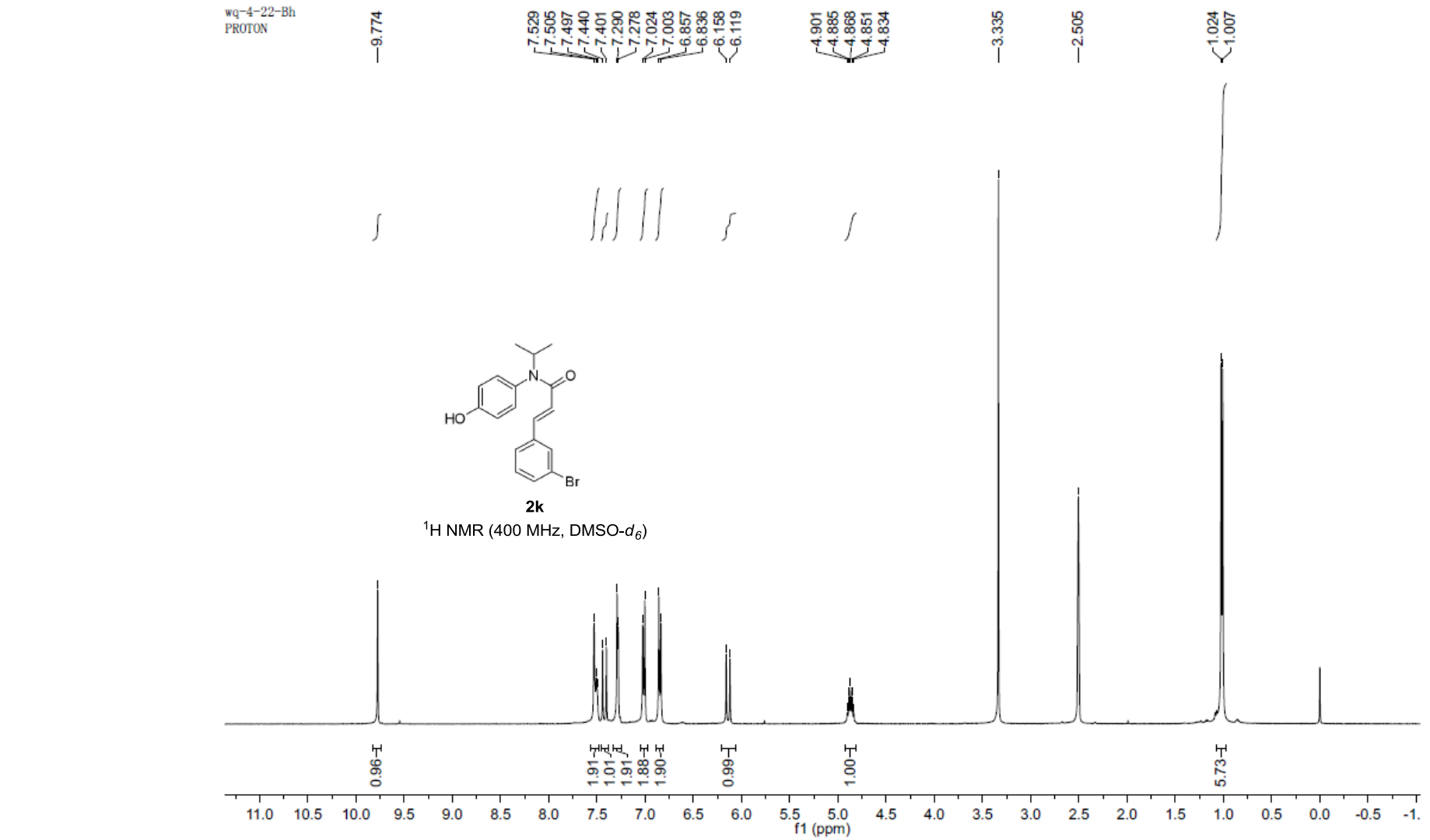
2j

^{1}H NMR (400 MHz, DMSO-d_6)



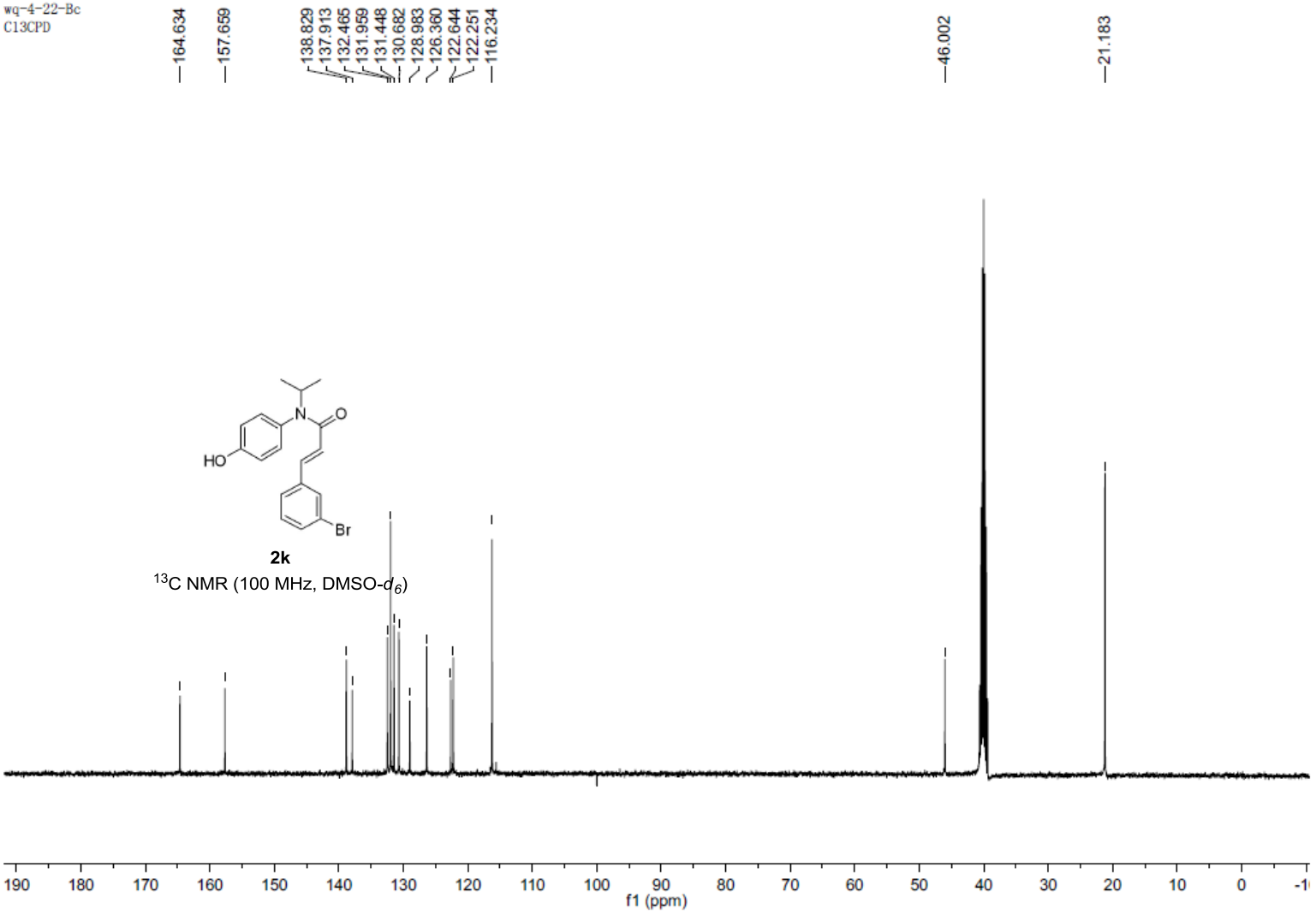
2j

^{13}C NMR (100 MHz, DMSO-d_6)



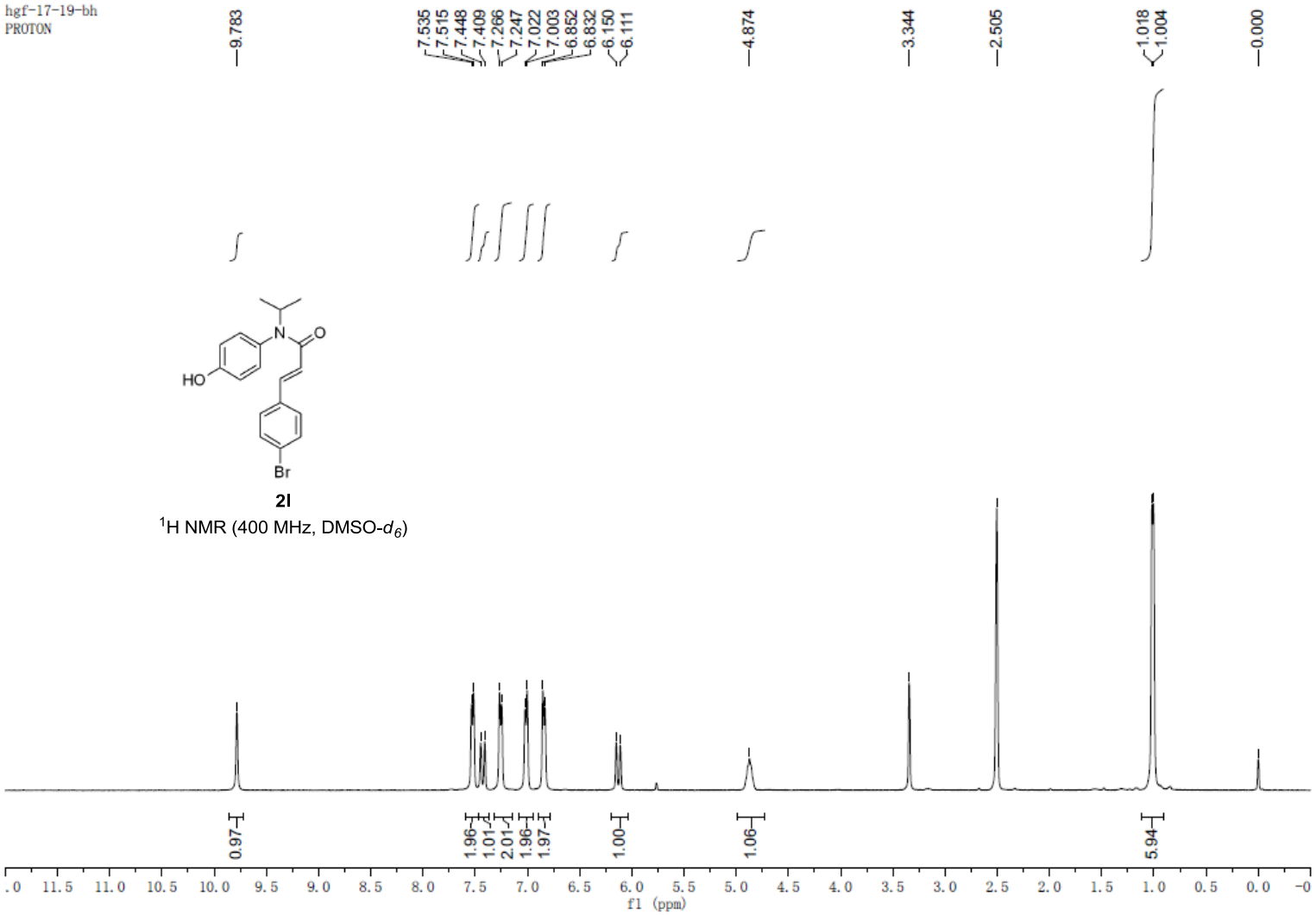
2k

^{1}H NMR (400 MHz, DMSO-d_6)



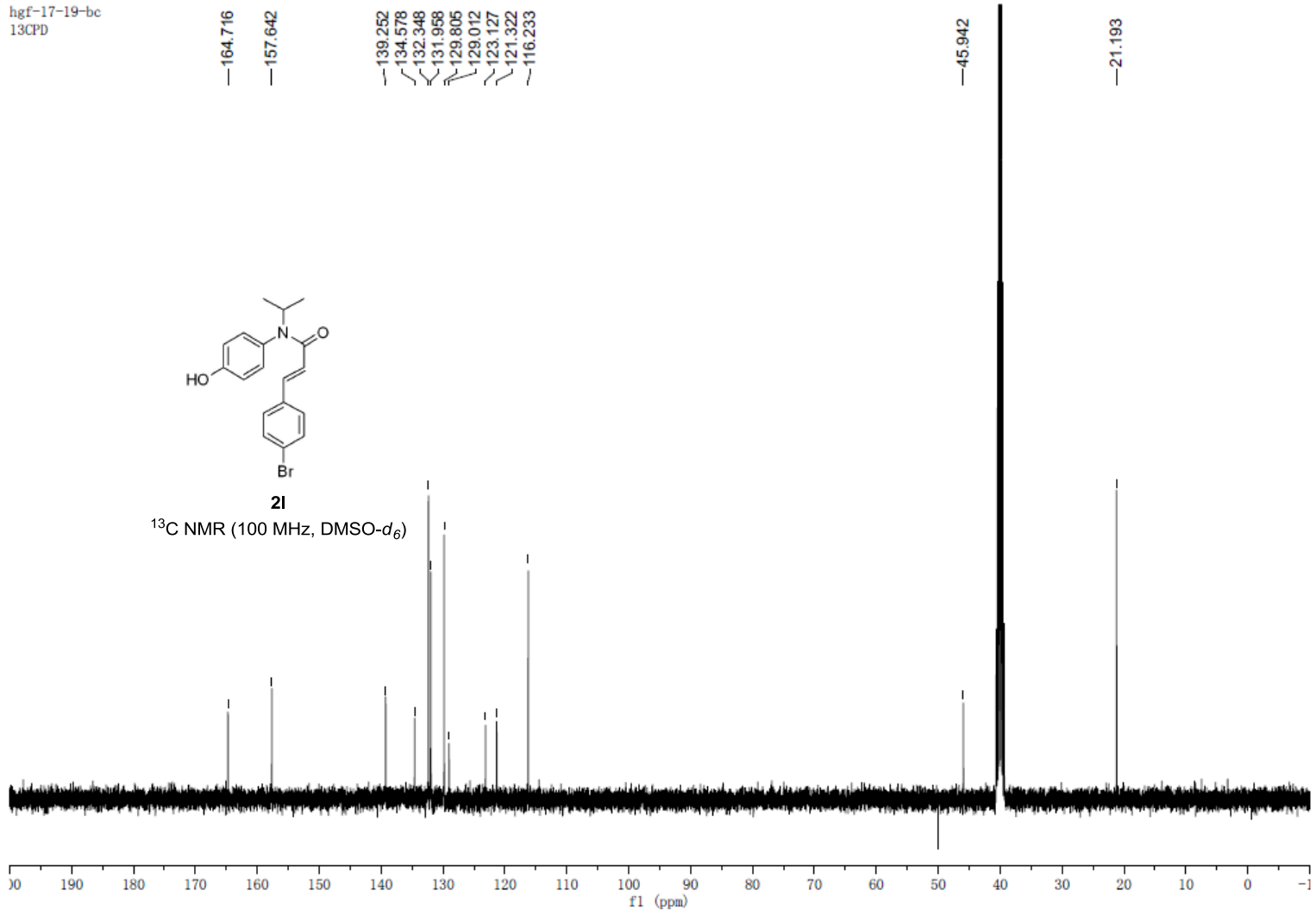
2k

^{13}C NMR (100 MHz, DMSO-d_6)



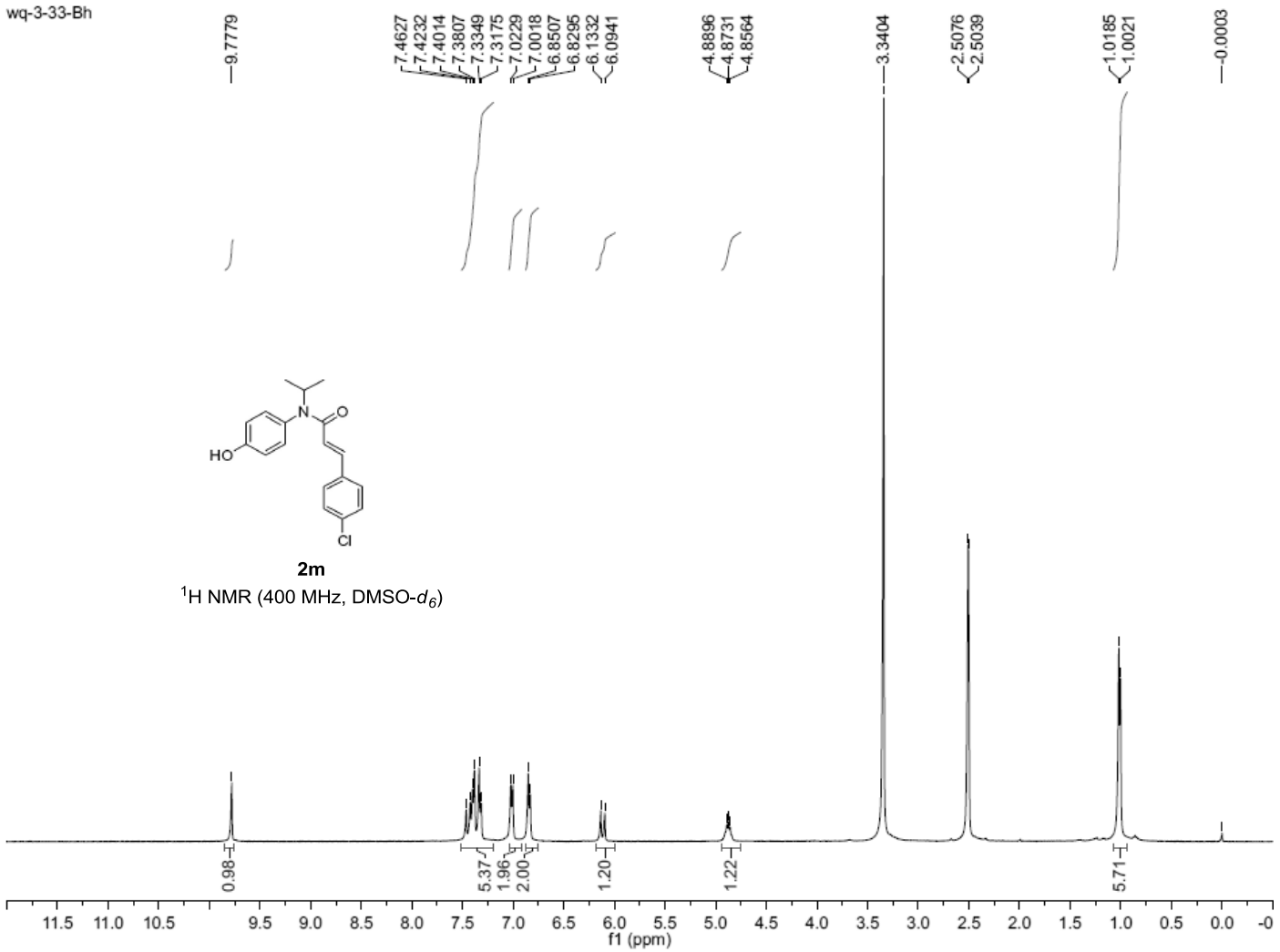
2l

^{1}H NMR (400 MHz, DMSO-d_6)



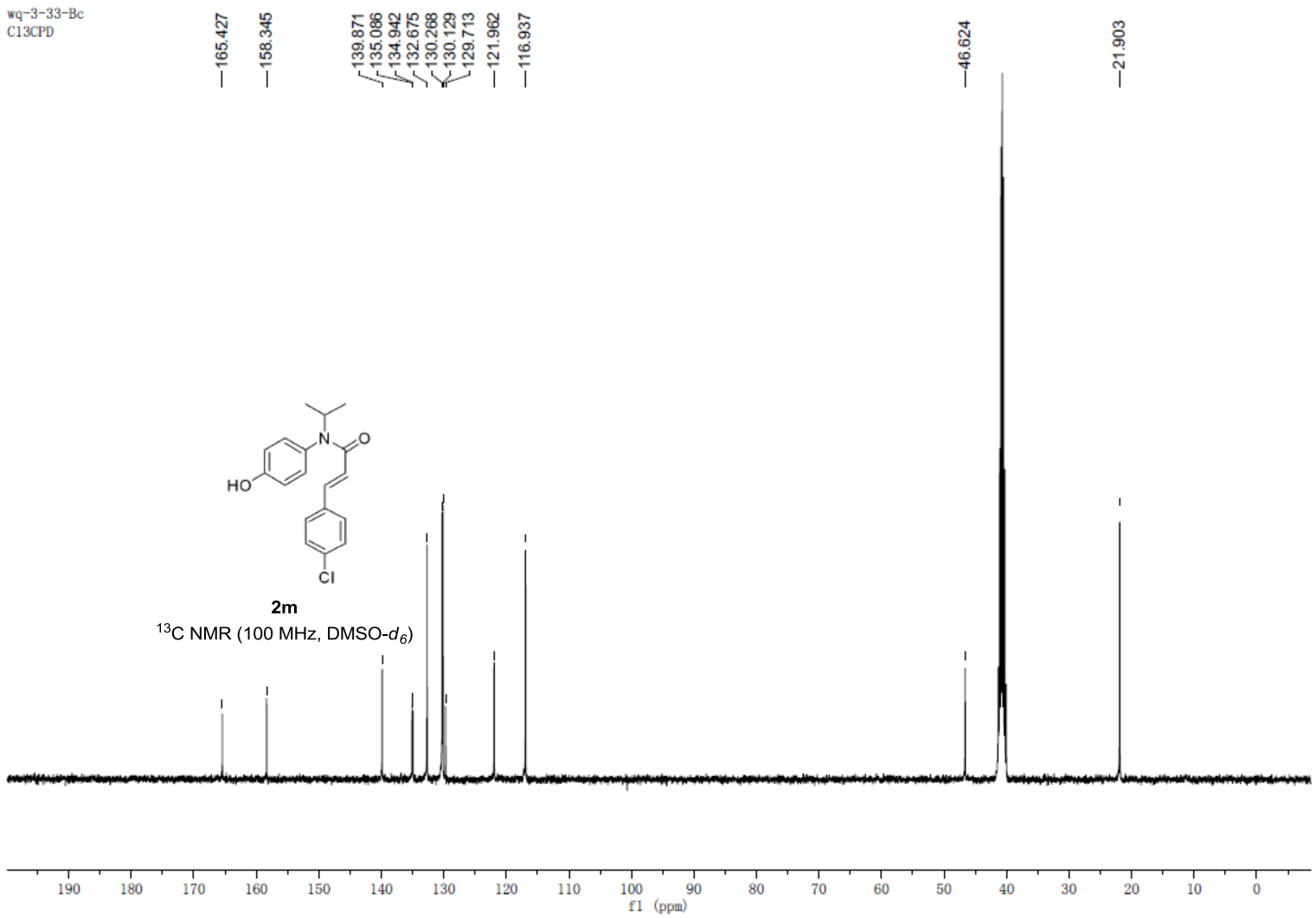
2l

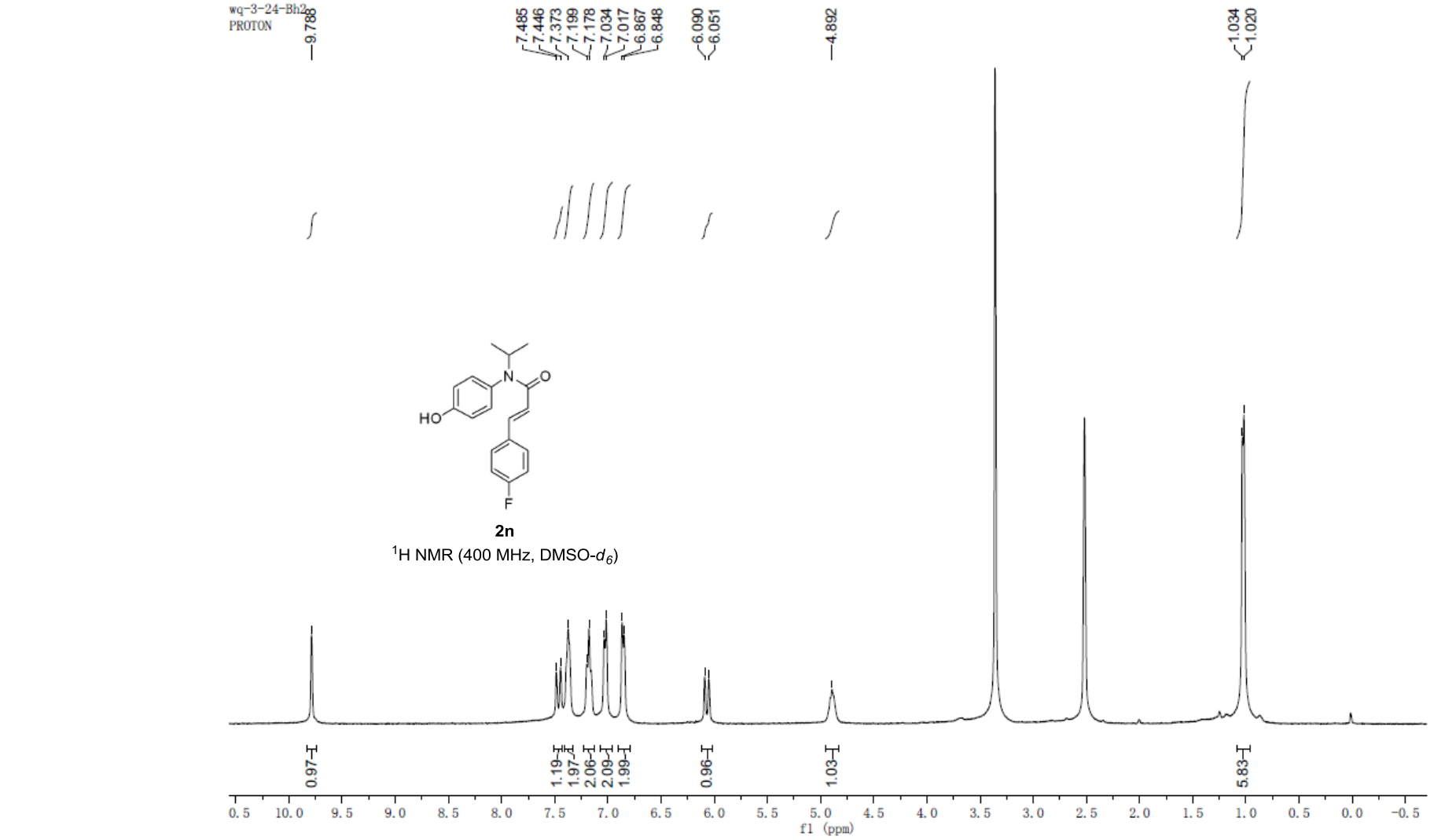
^{13}C NMR (100 MHz, DMSO-d_6)



2m

^{1}H NMR (400 MHz, DMSO-d_6)

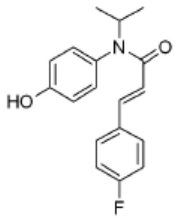

wq-3-33-Bc
C13CPD
165.427
158.345
139.871
135.086
134.942
132.675
130.268
130.129
129.713
121.962
116.937
46.624
21.903
HO
N
O
Cl
2m
13C NMR (100 MHz, DMSO-d6)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



2n

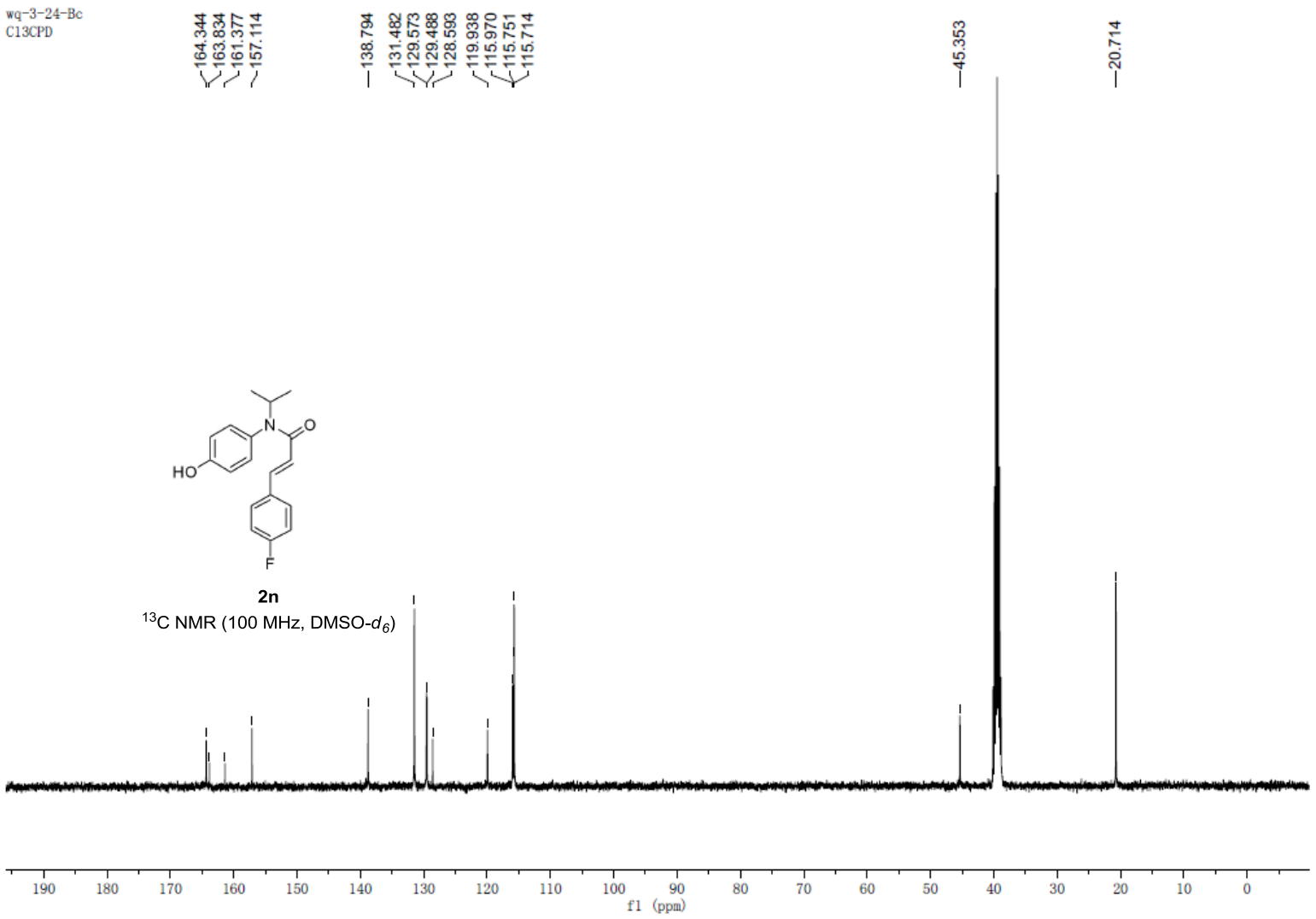
^{1}H NMR (400 MHz, DMSO-d_6)

hgf-2n-f
F19CPD



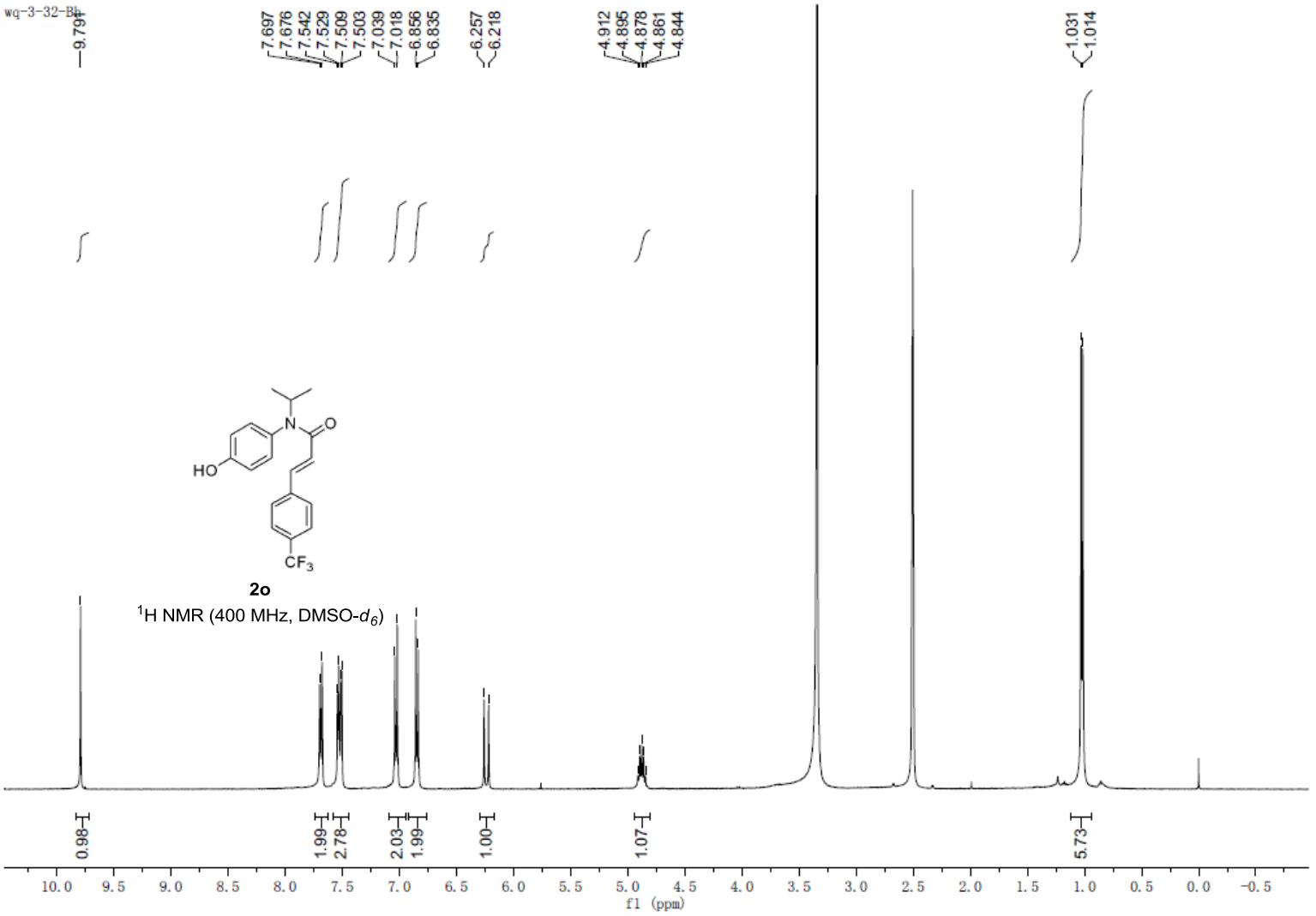
2n

^{19}F NMR (376 MHz, DMSO-d_6)



2n

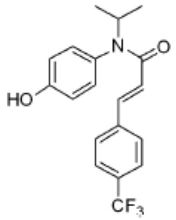
^{13}C NMR (100 MHz, DMSO-d_6)



2o

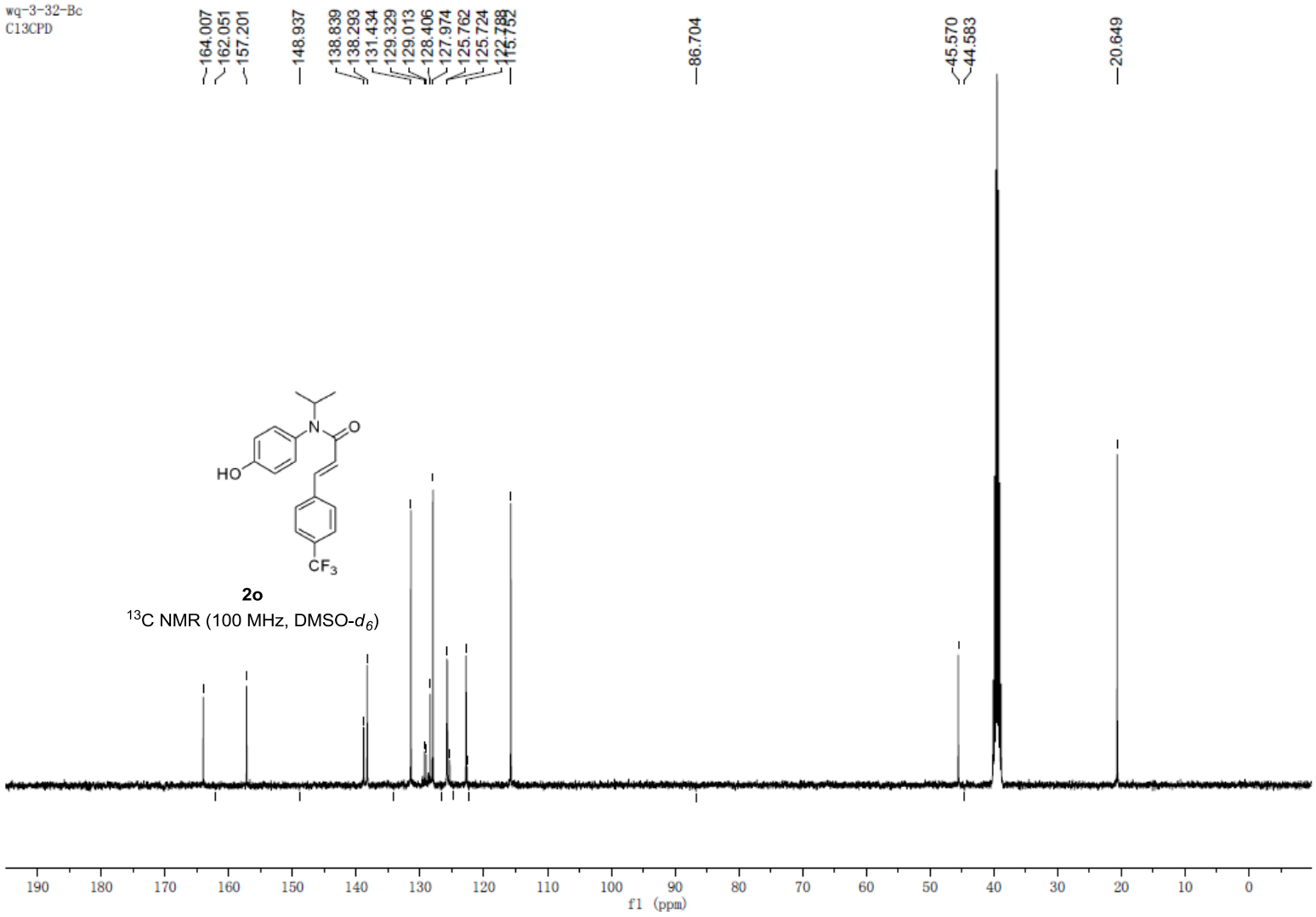
^{1}H NMR (400 MHz, DMSO-d_6)

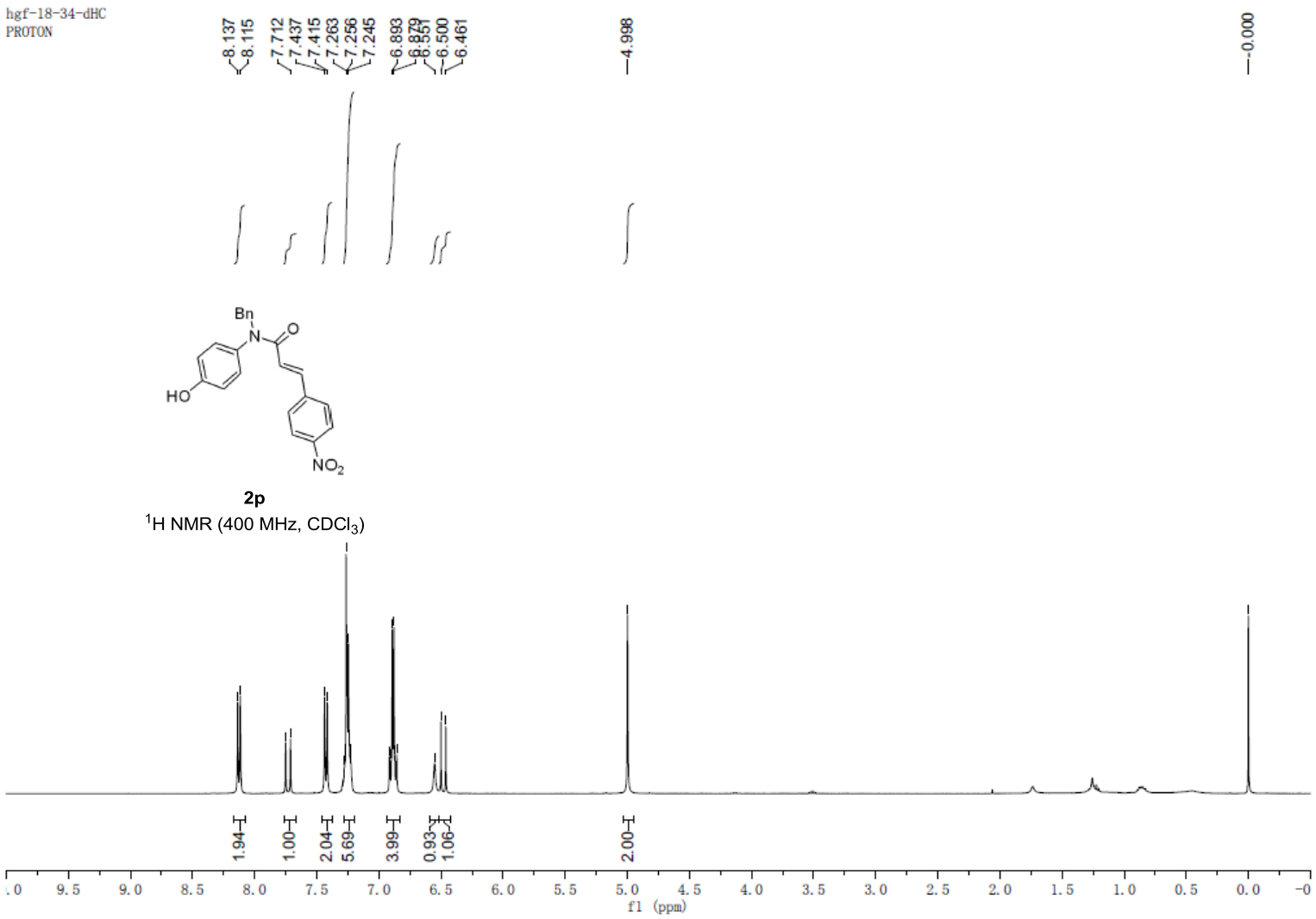
hgf-2o-f
F19CPD



2o

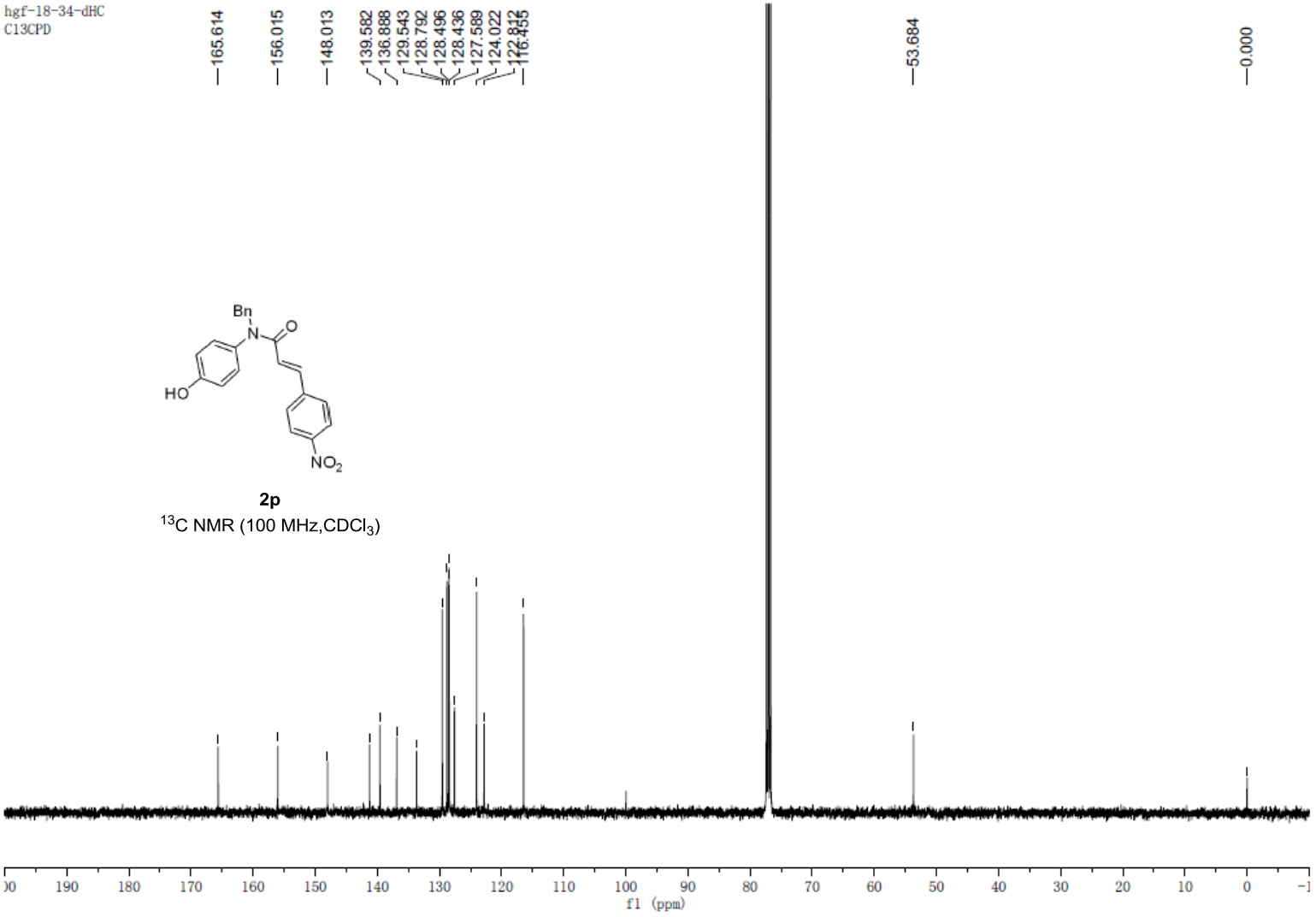
^{19}F NMR (376 MHz, DMSO-d_6)


wq-3-32-Bc
C13CPD
164.007
162.051
157.201
148.937
138.839
138.293
131.434
129.329
129.013
128.406
127.974
125.762
125.724
122.788
115.752
86.704
45.570
44.583
20.649
HO
N
O
CF3
2o
13C NMR (100 MHz, DMSO-d6)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



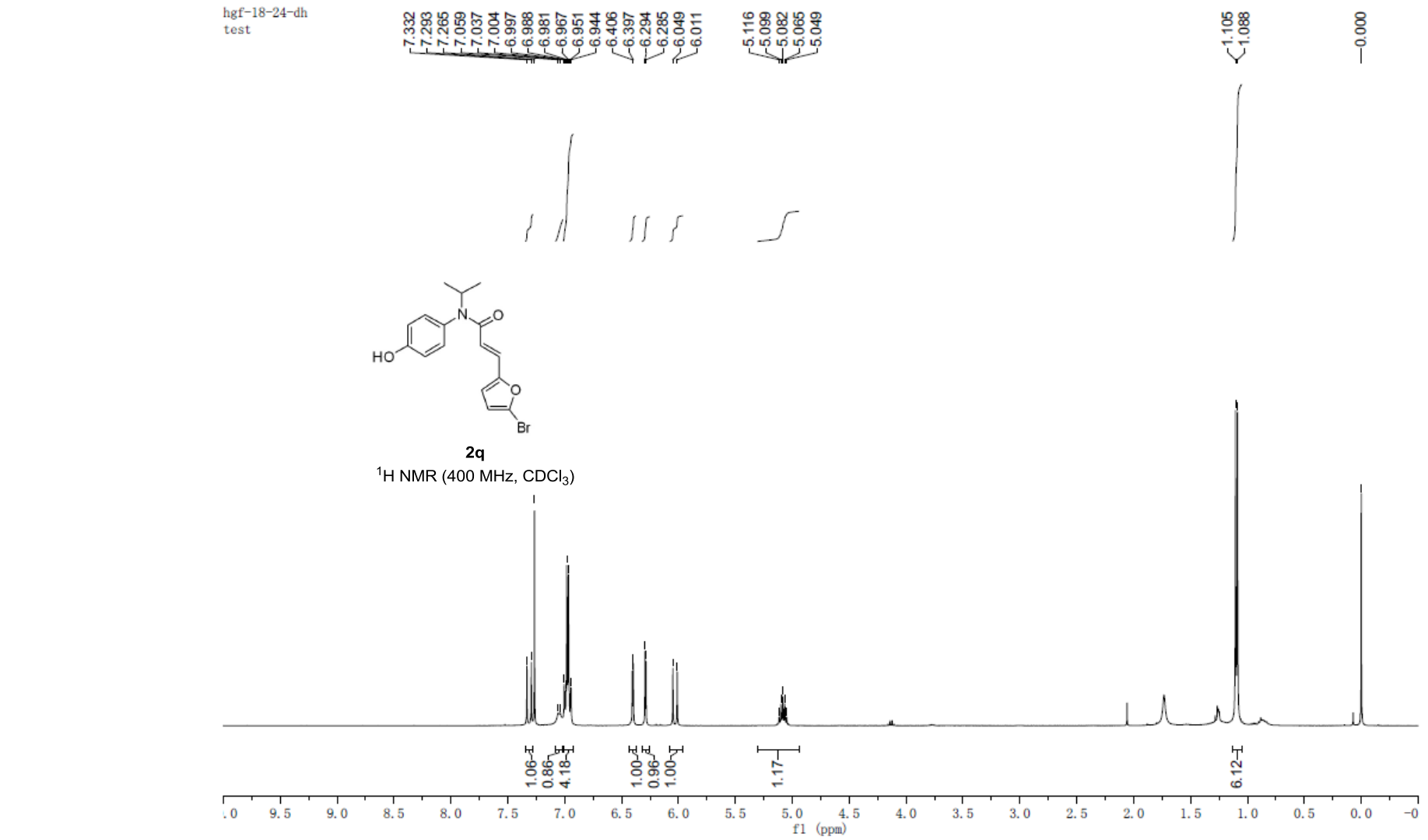
2p

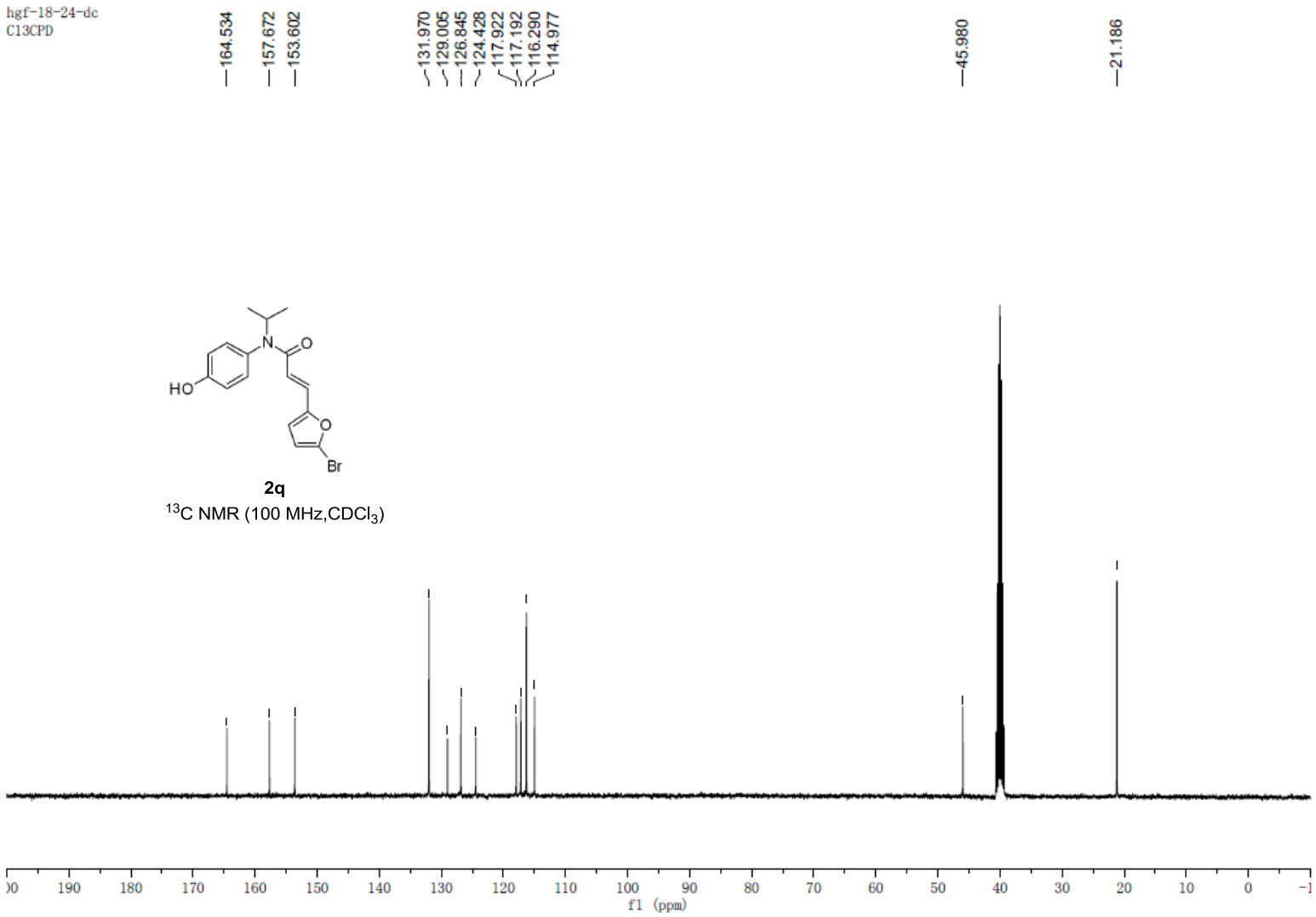
^{1}H NMR (400 MHz, $CDCl_3$)



2p

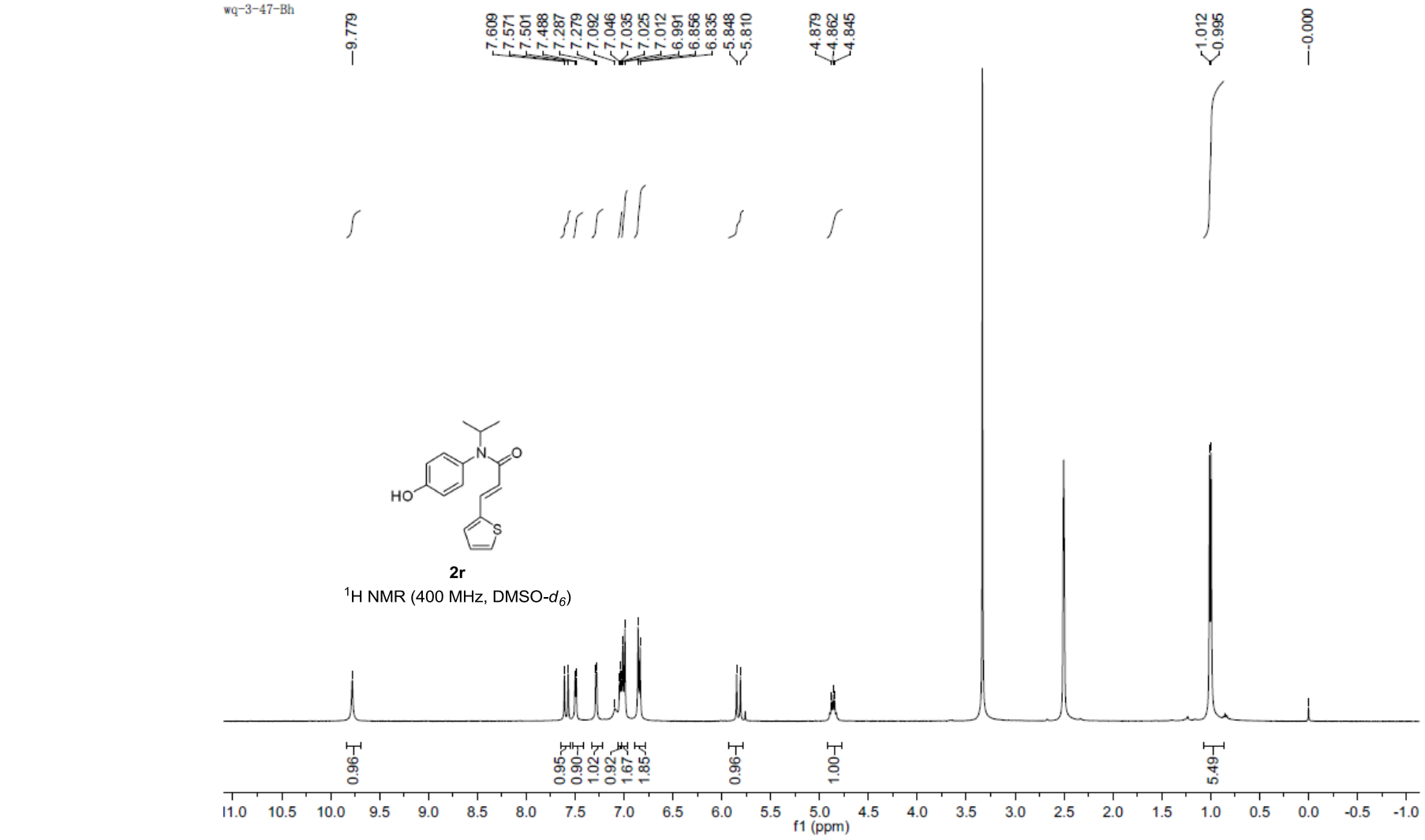
^{13}C NMR (100 MHz,$CDCl_3$)


hgf-18-24-dh
test
7.332
7.293
7.265
7.059
7.037
7.004
6.997
6.988
6.981
6.967
6.951
6.944
6.406
6.397
6.294
6.285
6.049
6.011
5.116
5.099
5.082
5.065
5.049
1.105
1.088
0.000
HO
N
O
O
Br
2q
1H NMR (400 MHz, CDCl3)
1.06
0.86
4.18
1.00
0.96
1.00
1.17
6.12
f1 (ppm)



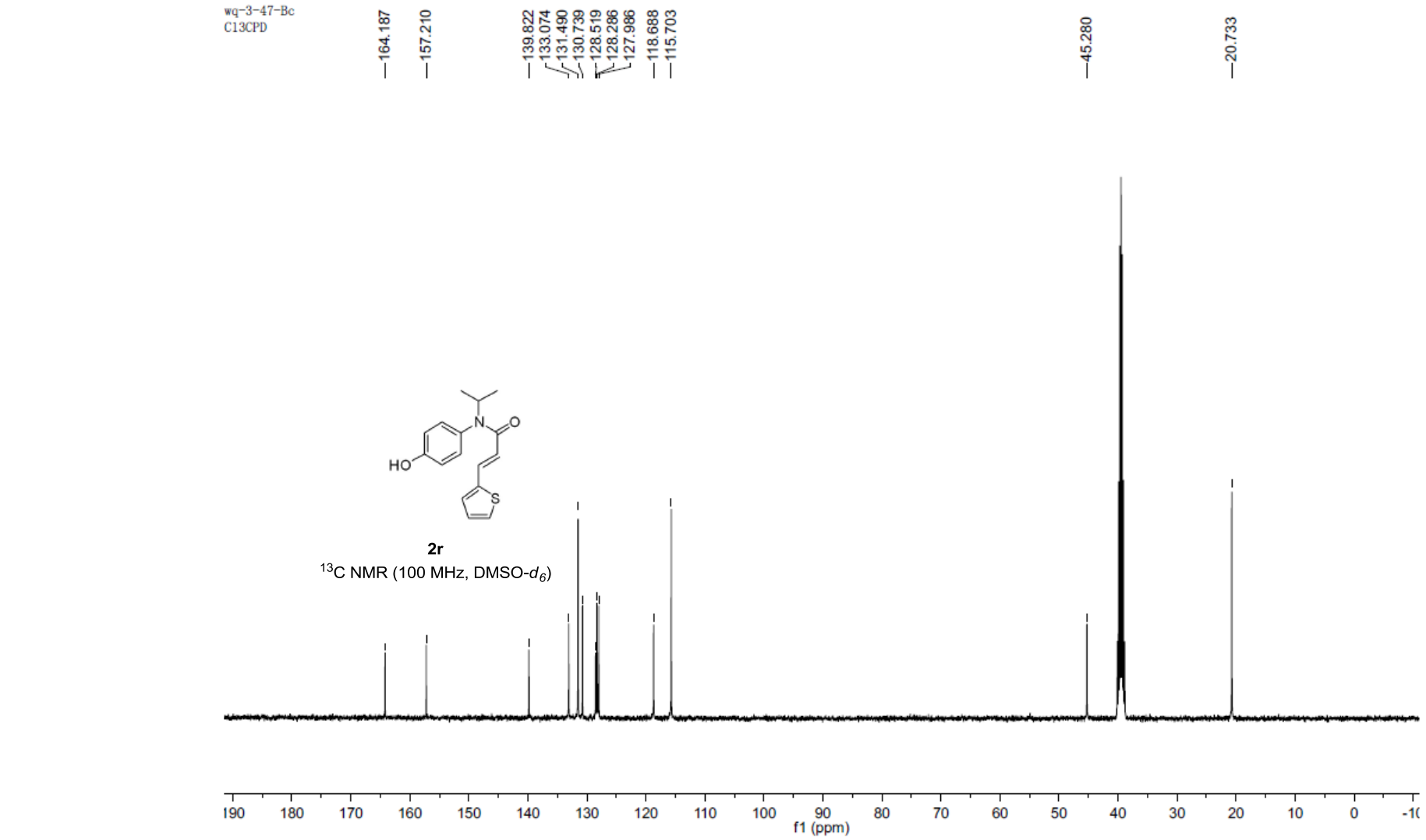
2q

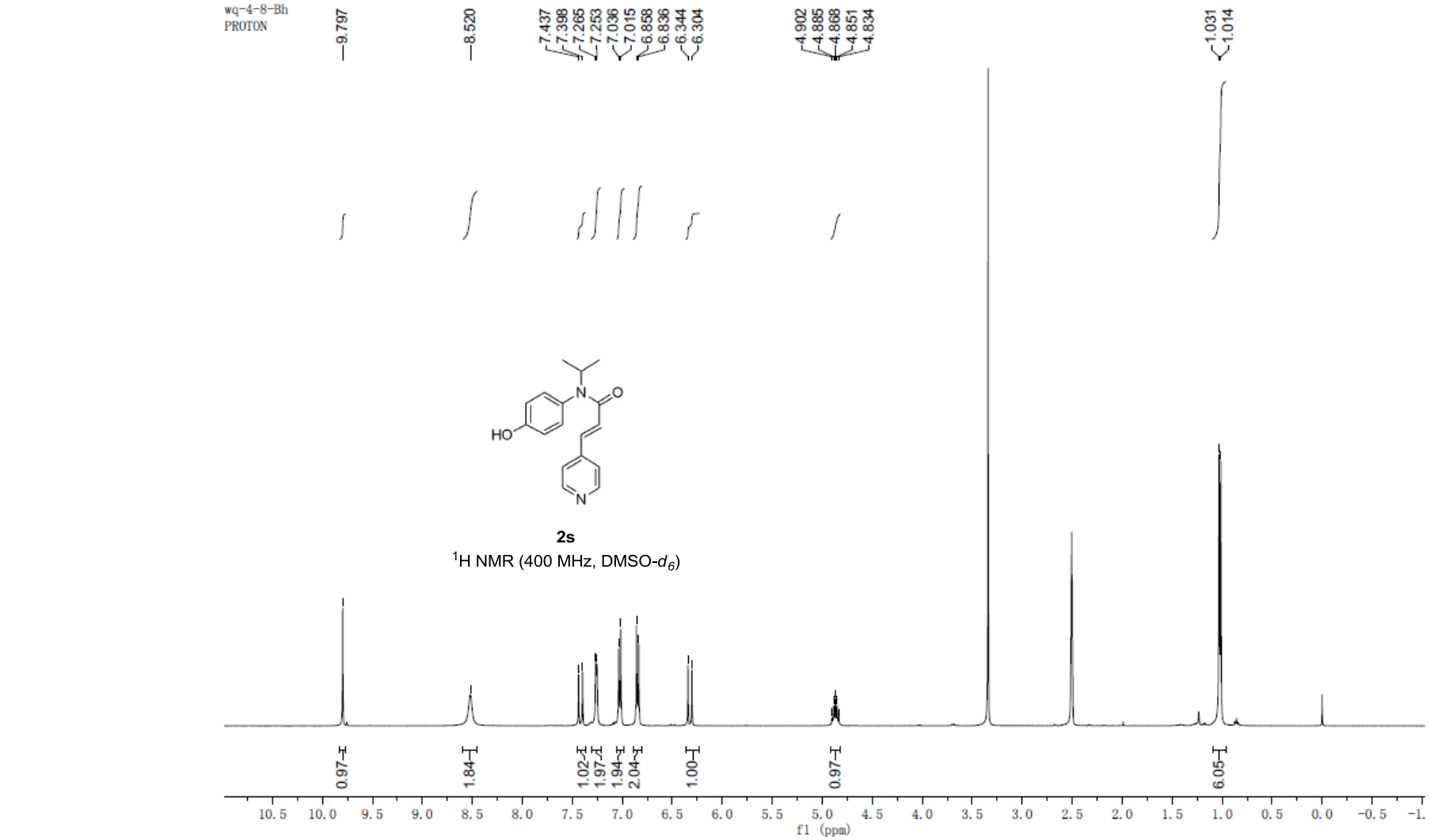
^{13}C NMR (100 MHz,$CDCl_3$)



2r

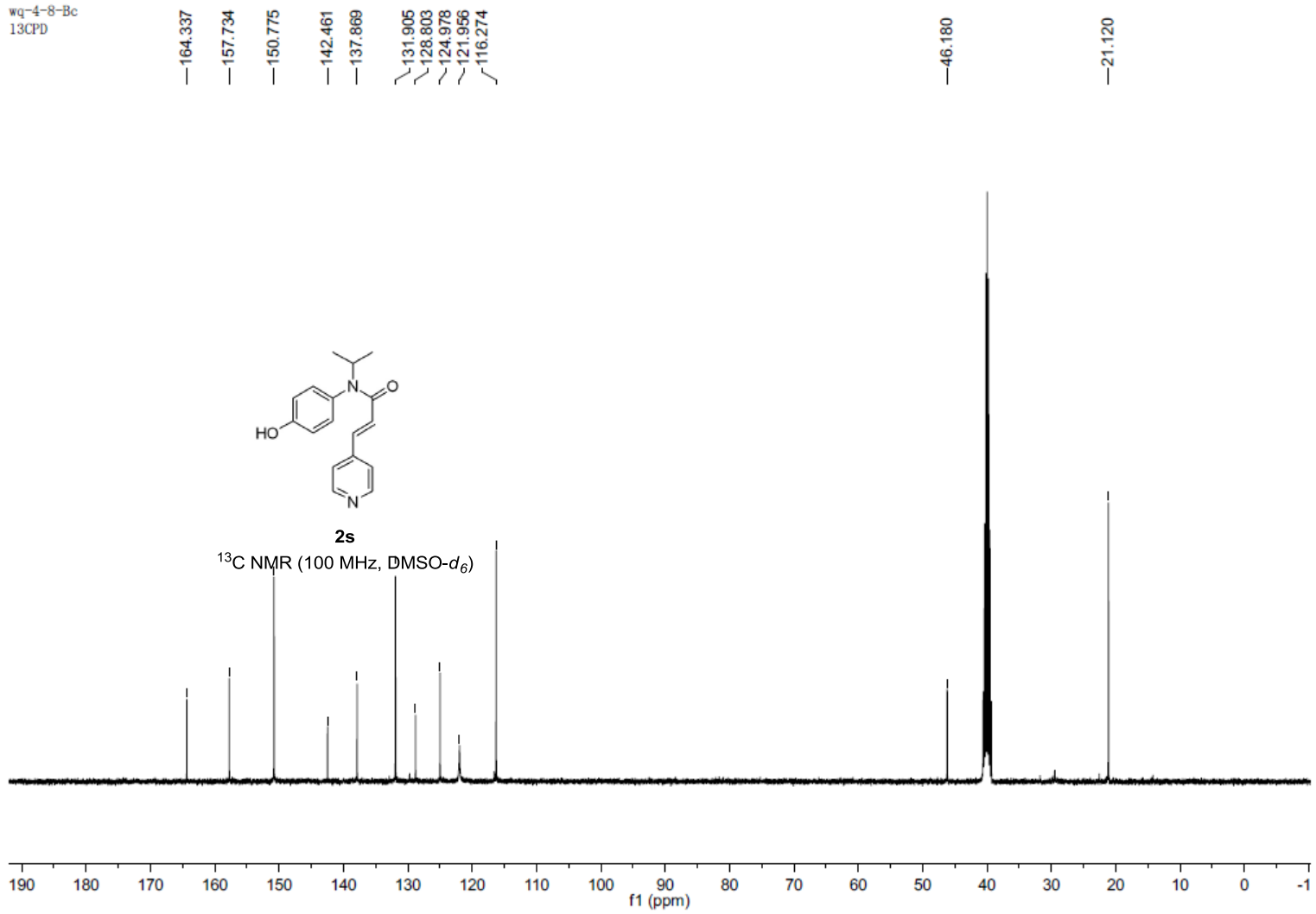
^{1}H NMR (400 MHz, DMSO-d_6)

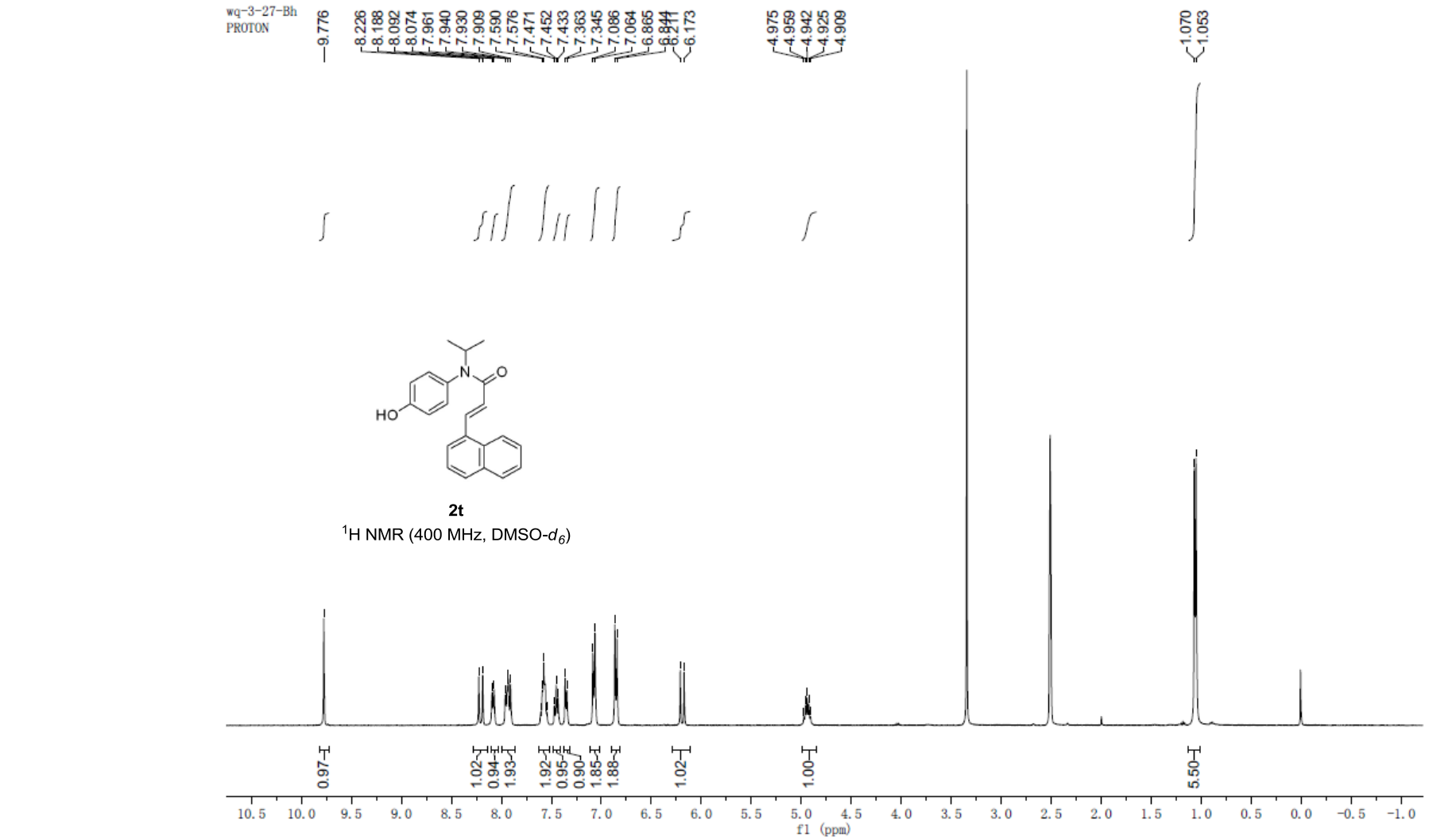

wq-3-47-Bc
C13CPD
164.187
157.210
139.822
133.074
131.490
130.739
128.519
128.286
127.986
118.688
115.703
45.280
20.733
HO
N
O
S
2r
13C NMR (100 MHz, DMSO-d6)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



2s

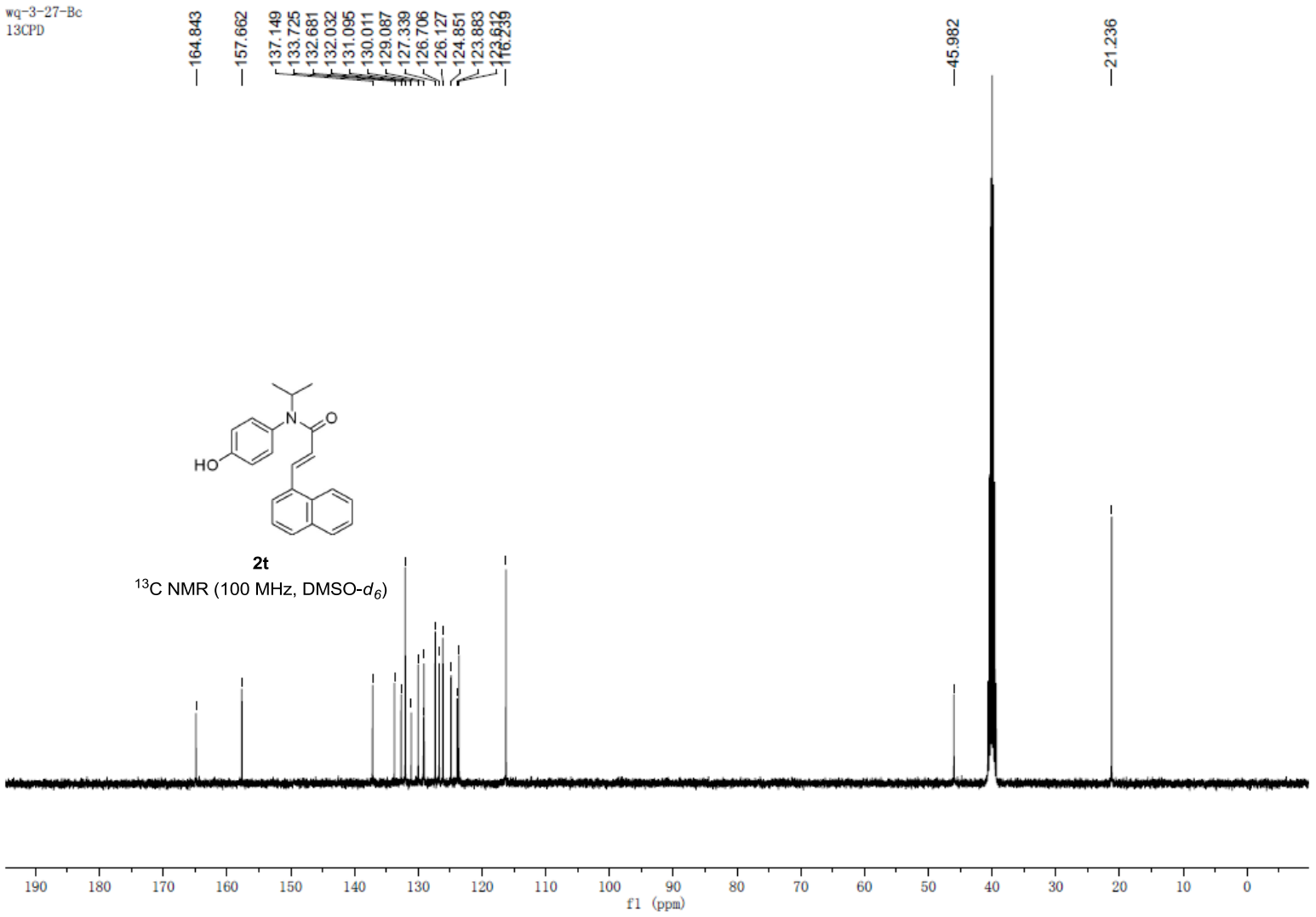
^{1}H NMR (400 MHz, DMSO-d_6)


wq-4-8-Bc
13CPD
164.337
157.734
150.775
142.461
137.869
131.905
128.803
124.978
121.956
116.274
46.180
21.120
HO
N
O
N
2s
13C NMR (100 MHz, DMSO-d6)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



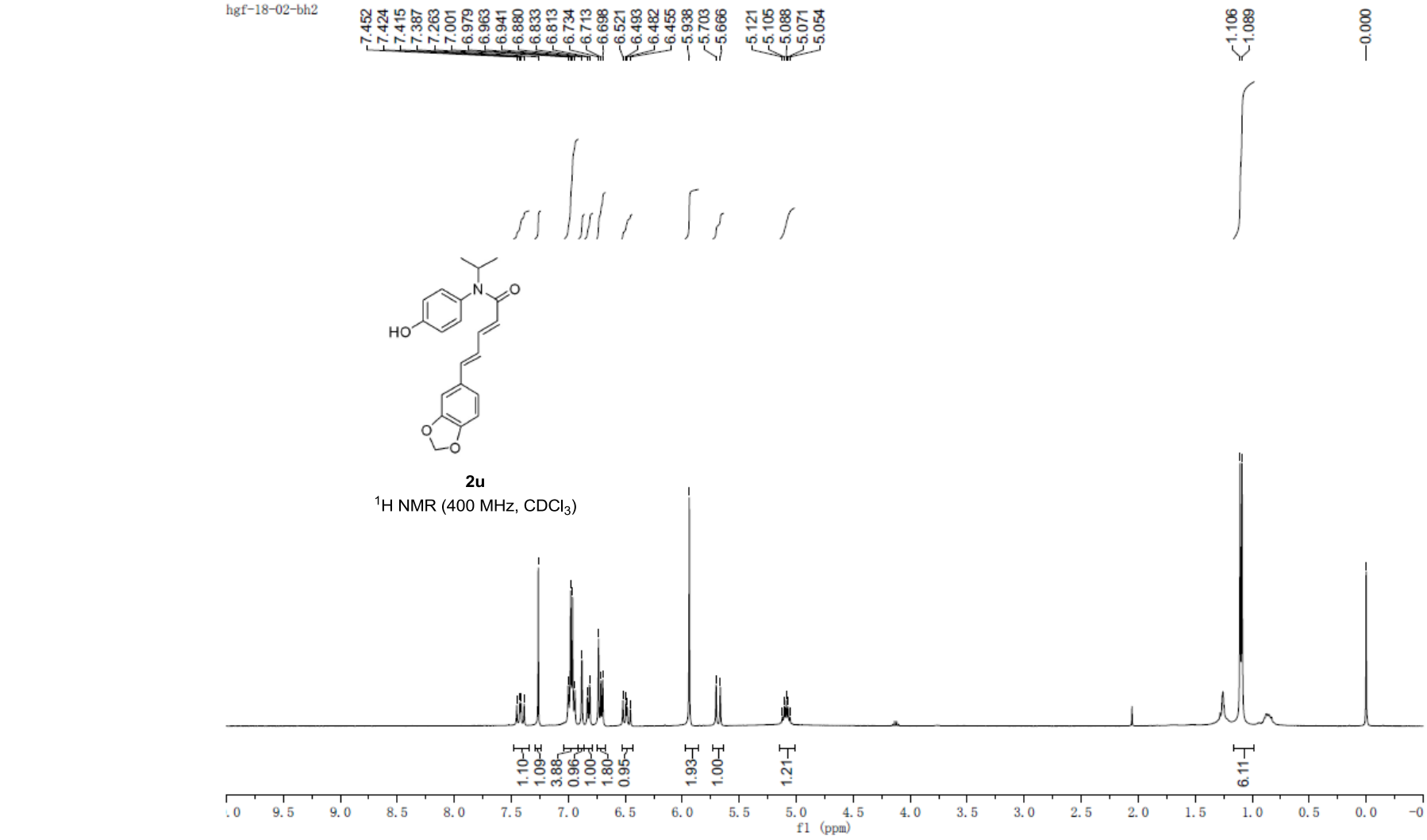
2t

^{1}H NMR (400 MHz, DMSO-d_6)



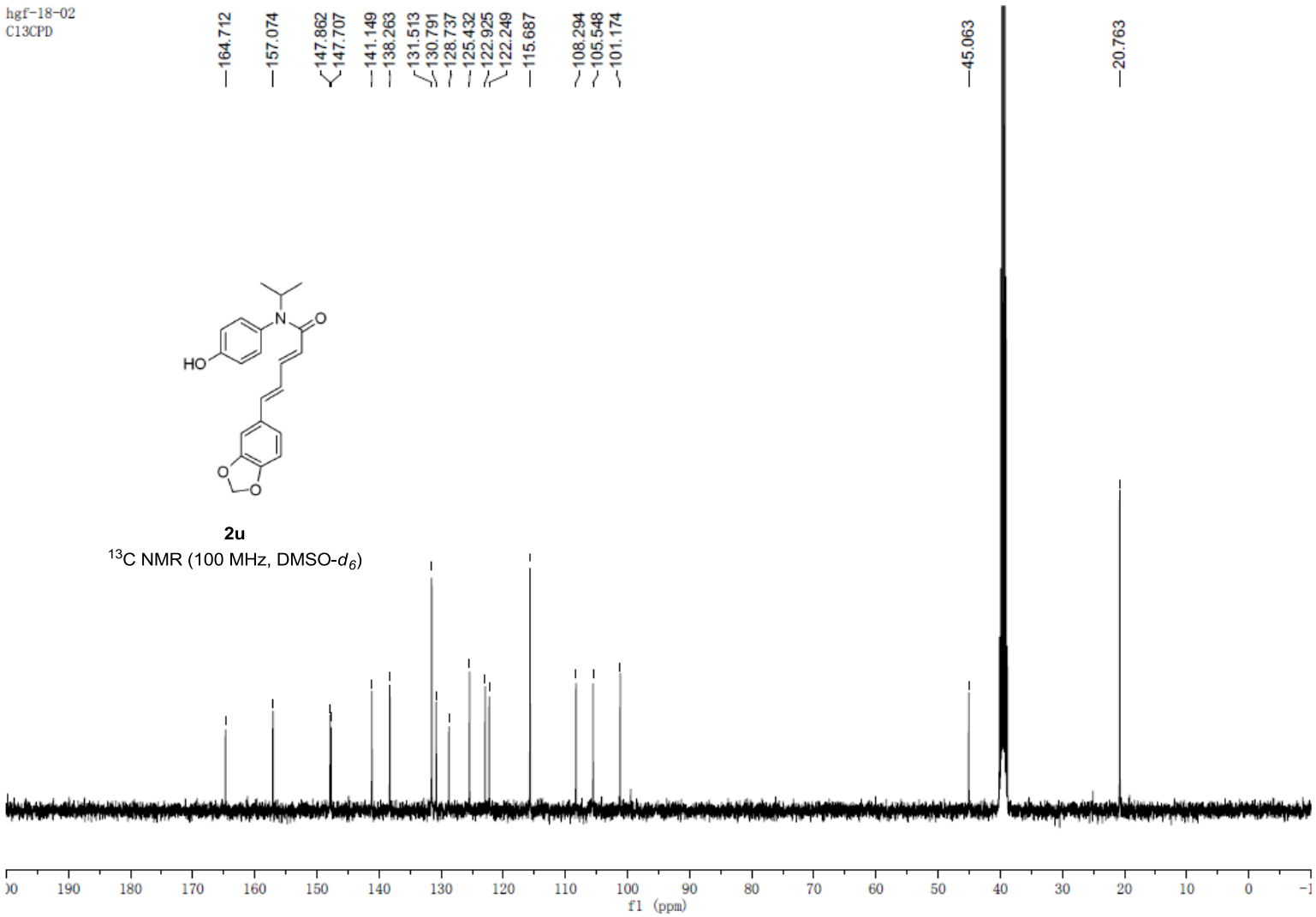
2t

^{13}C NMR (100 MHz, DMSO-d_6)



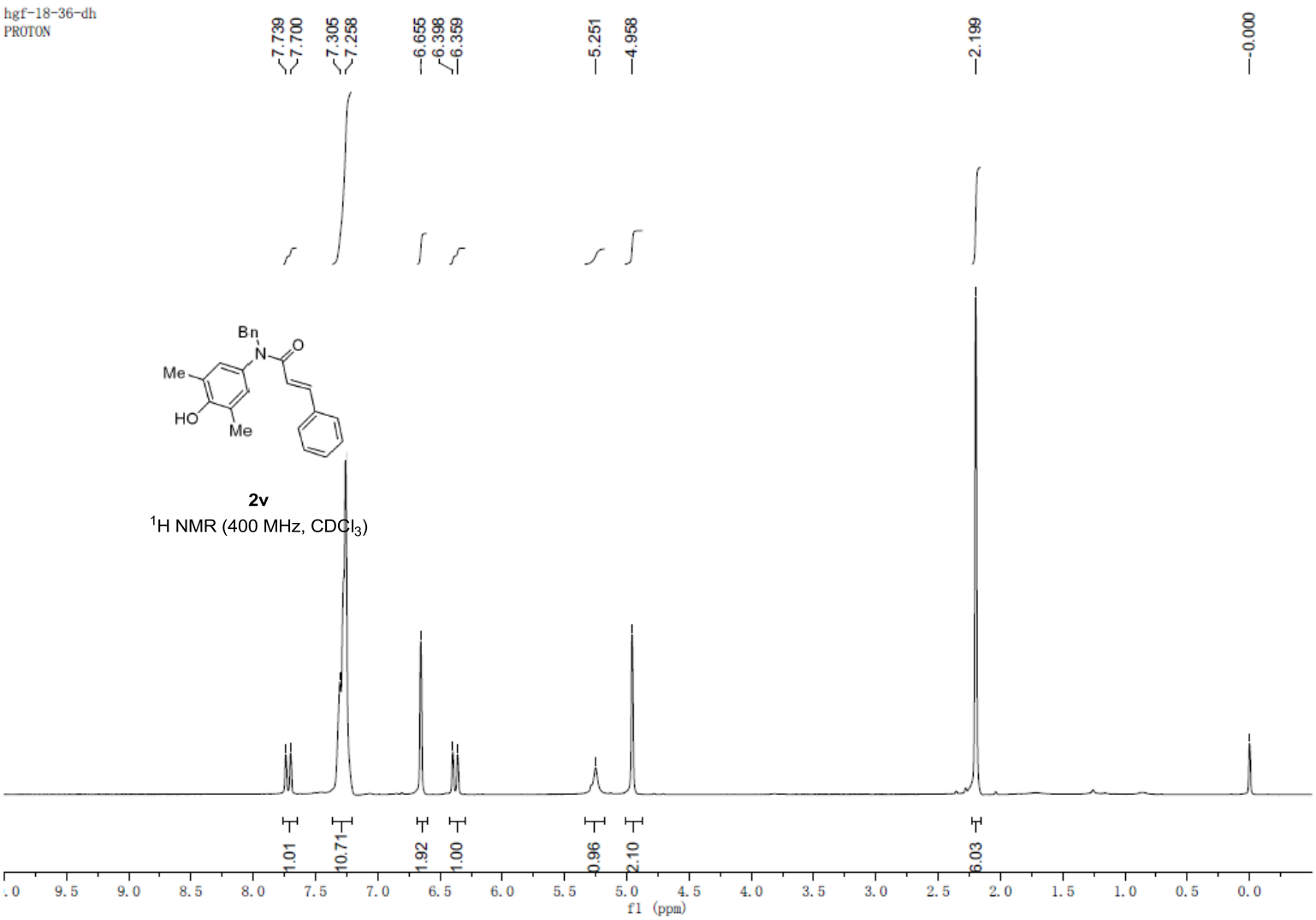
2u

^{1}H NMR (400 MHz, $CDCl_3$)



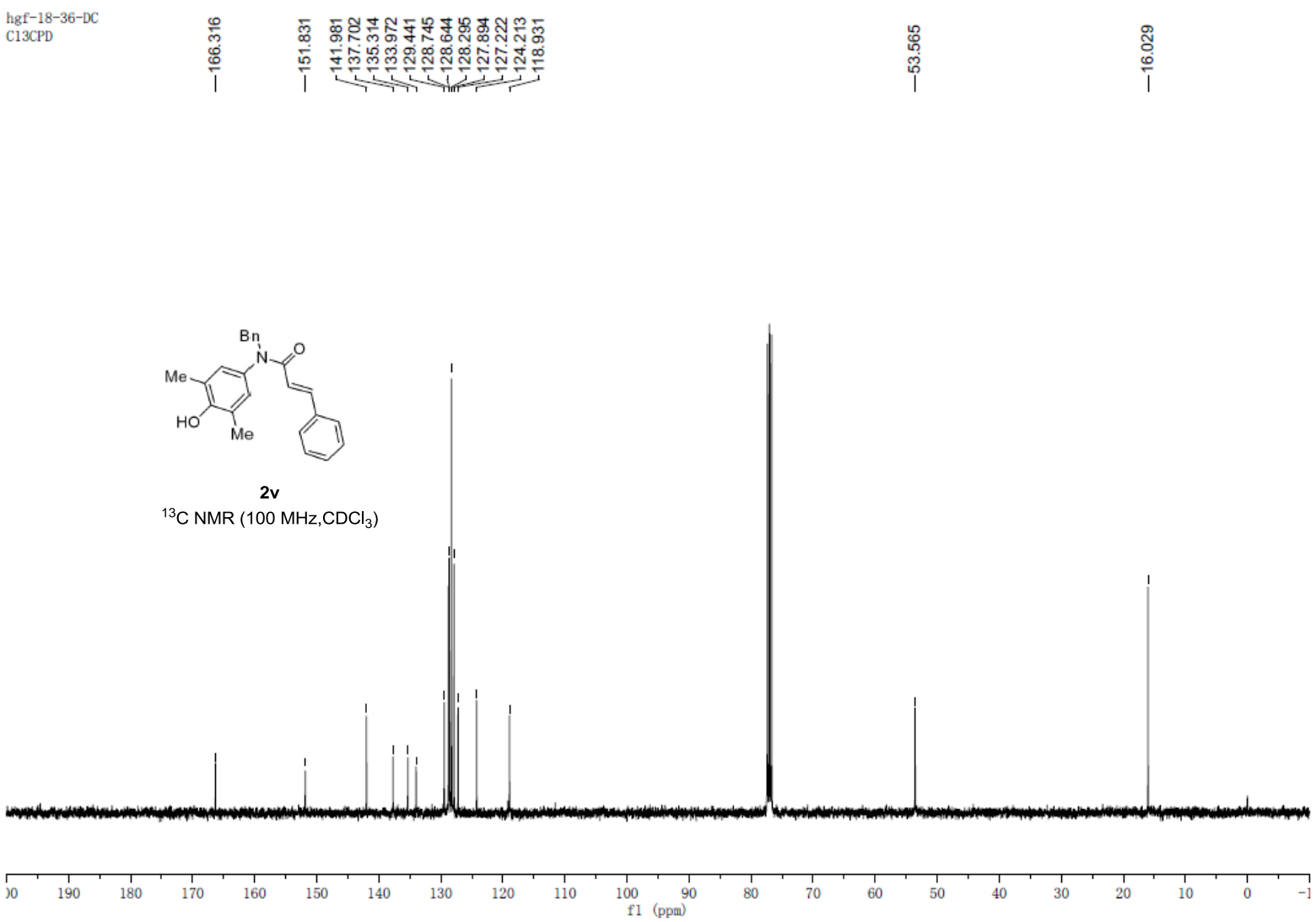
2u

^{13}C NMR (100 MHz, DMSO-d_6)



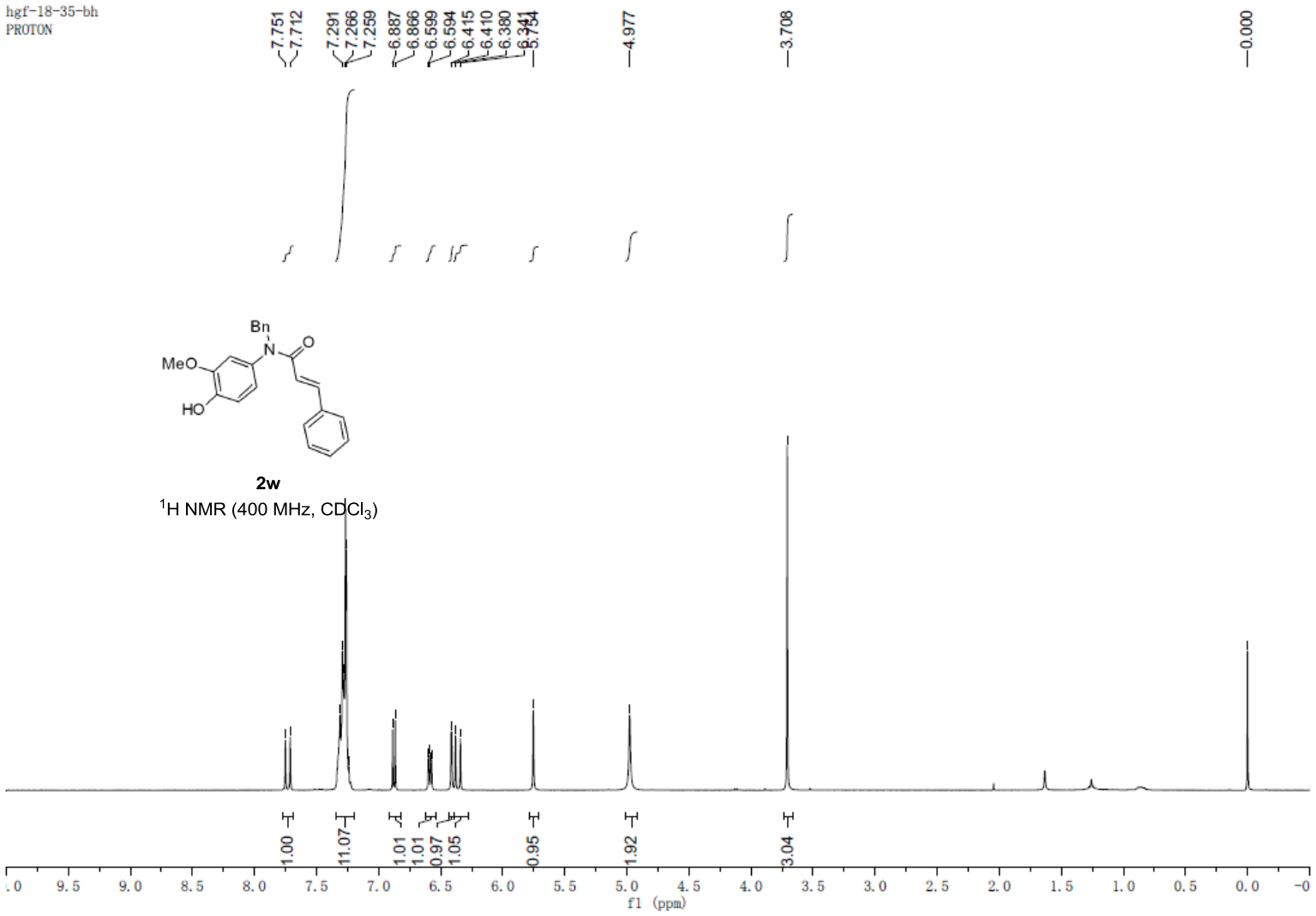
2v

^{1}H NMR (400 MHz, $CDCl_3$)



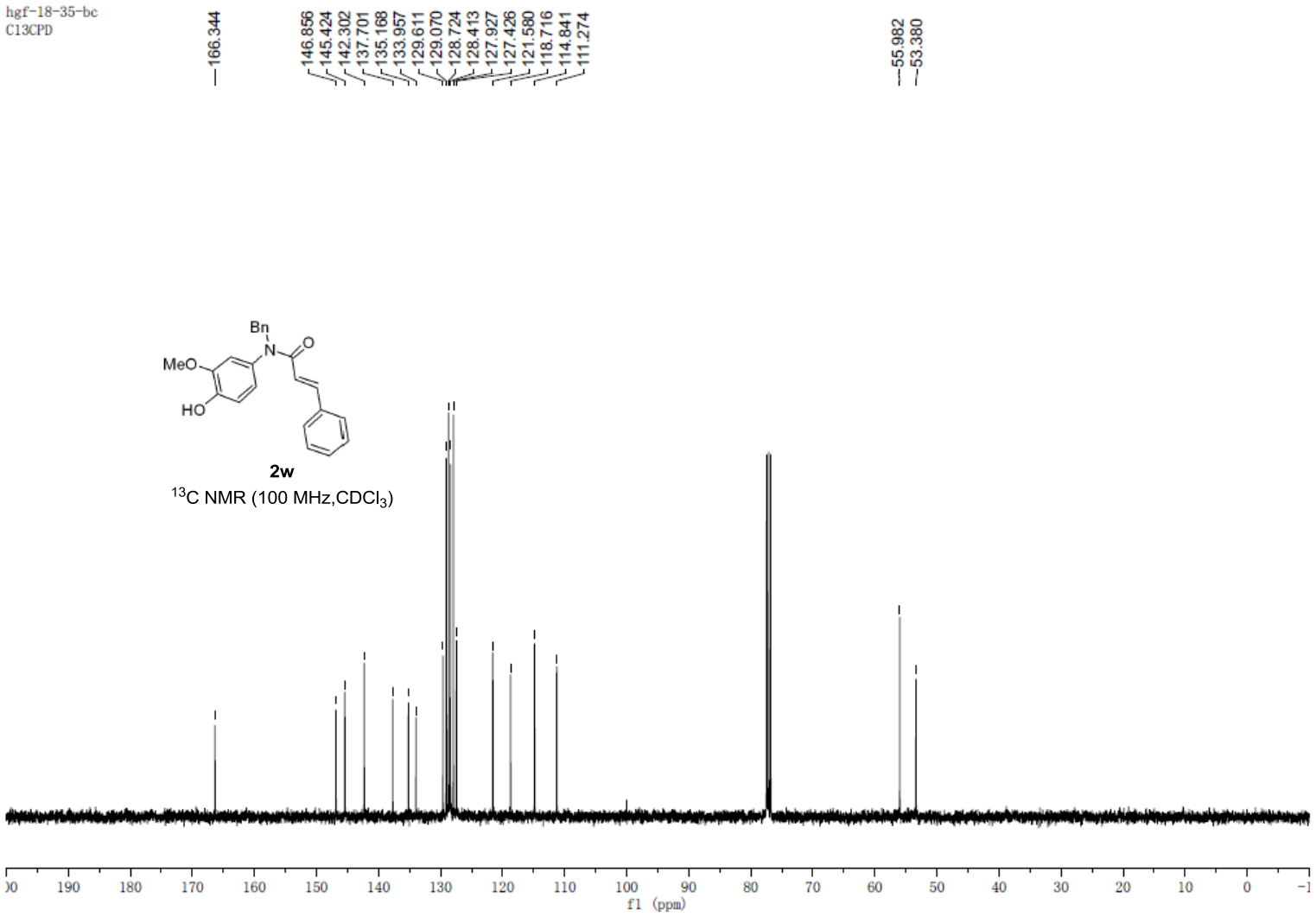
2v

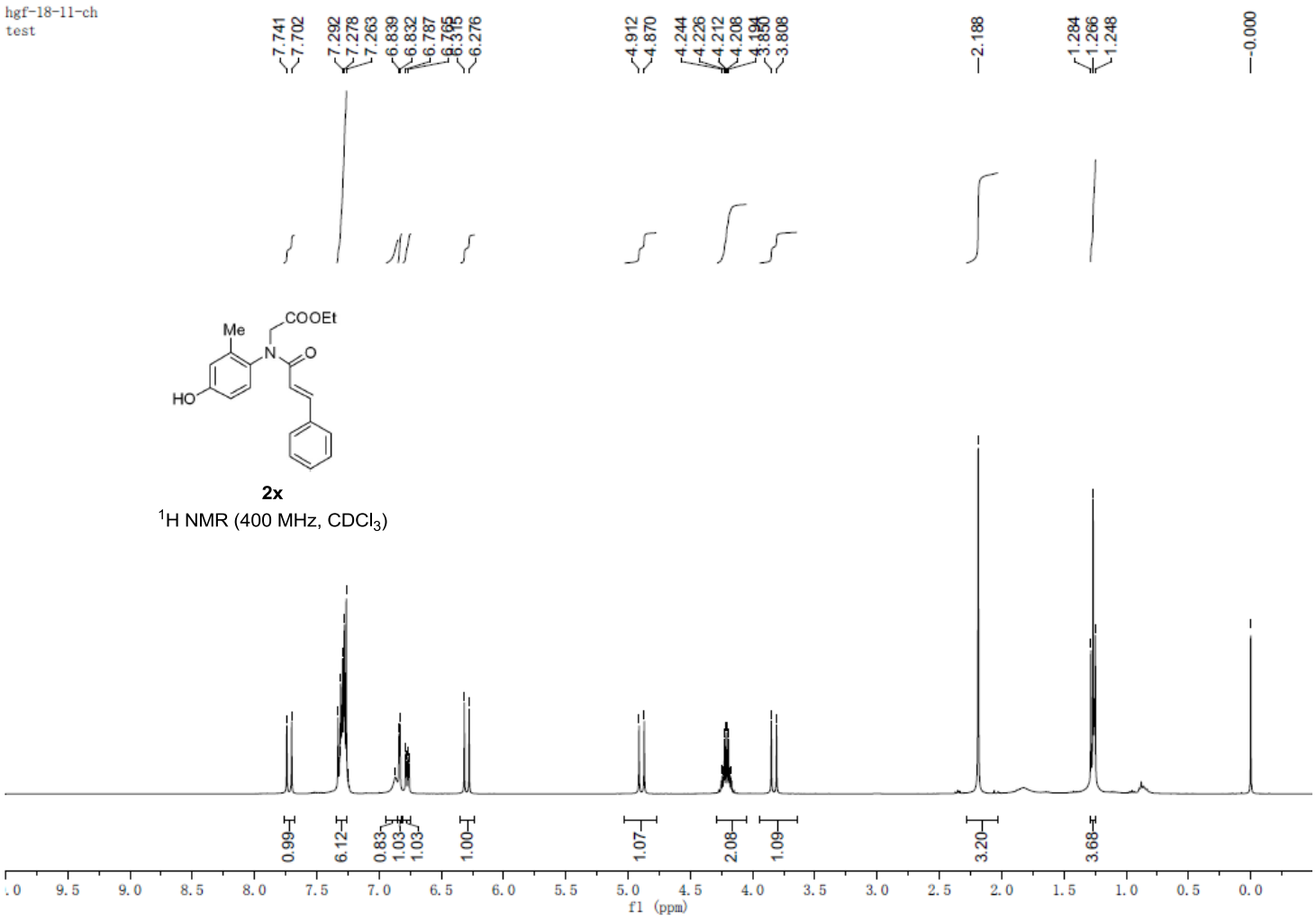
^{13}C NMR (100 MHz,$CDCl_3$)



2w

^{1}H NMR (400 MHz, $CDCl_3$)


hgf-18-35-bc
C13CPD
166.344
146.856
145.424
142.302
137.701
135.168
133.957
129.611
129.070
128.724
128.413
127.927
127.426
121.580
118.716
114.841
111.274
55.982
53.380
Bn
N
O
MeO
HO
2w
13C NMR (100 MHz,CDCl3)
f1 (ppm)

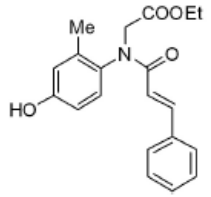


2x

^{1}H NMR (400 MHz, $CDCl_3$)

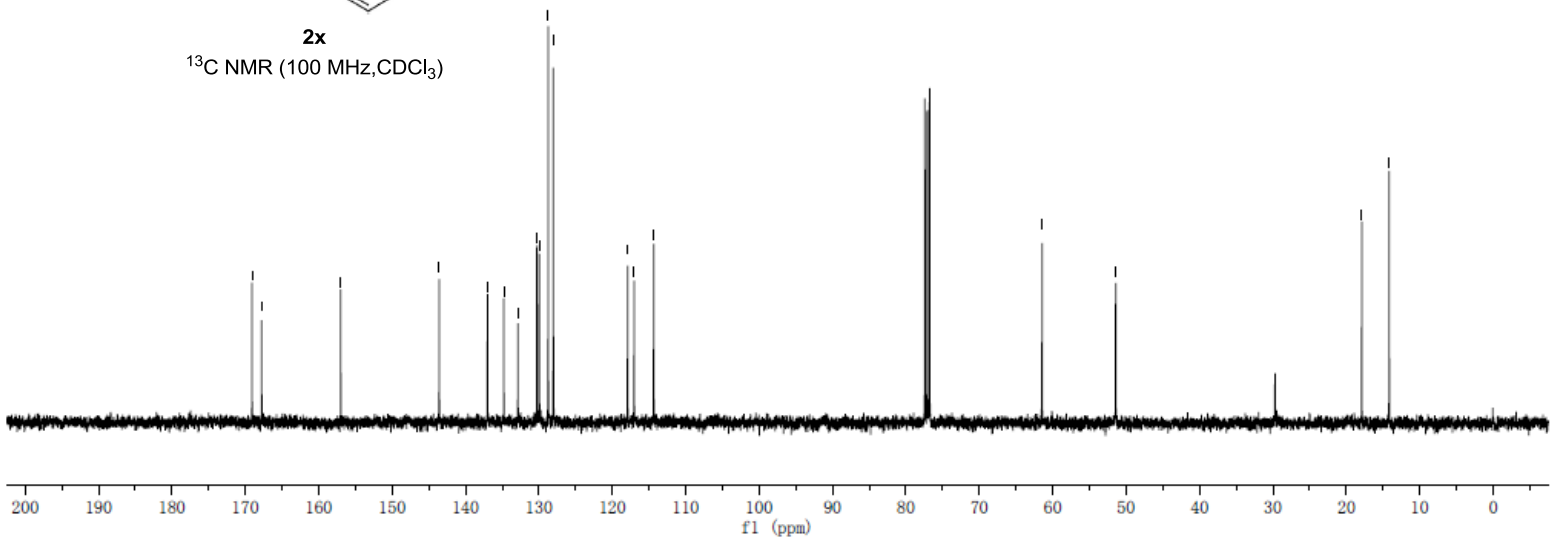
hgf-18-11-cc
C13CPD

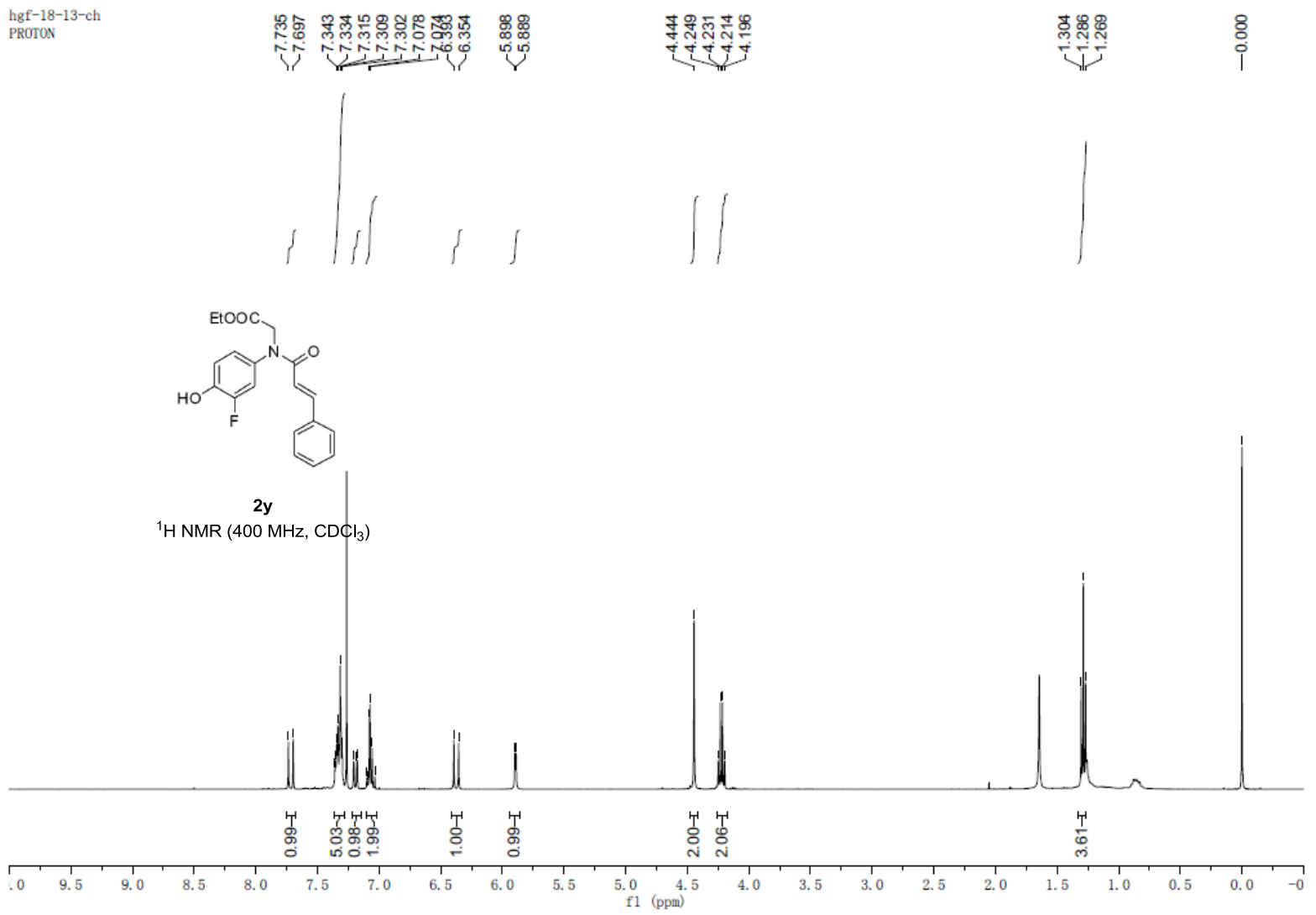
169.092
167.776
157.002
143.578
137.006
134.785
132.860
130.269
129.945
128.731
128.043
117.913
117.022
114.356
61.442
51.409
17.889
14.153



2x

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

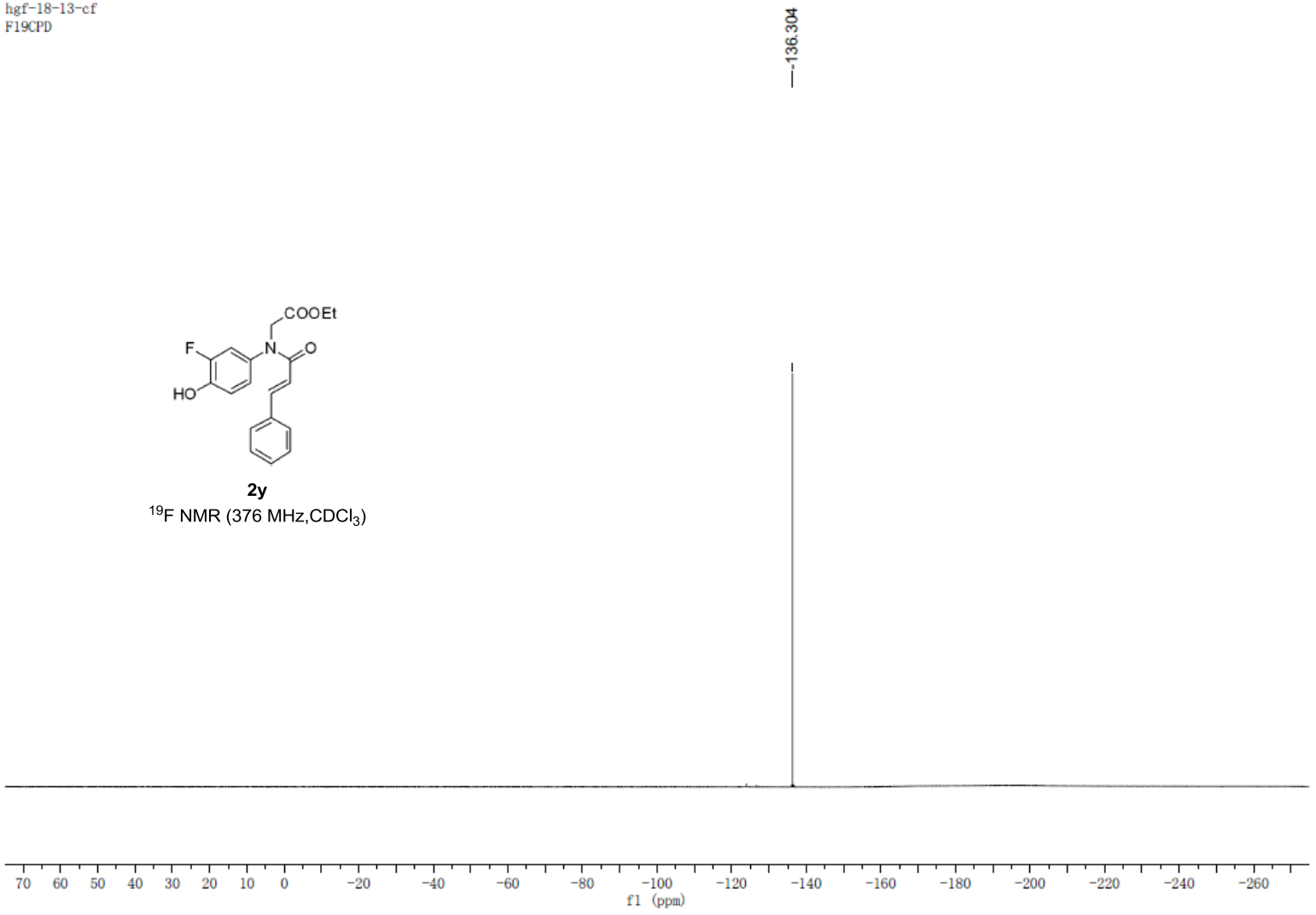




2y

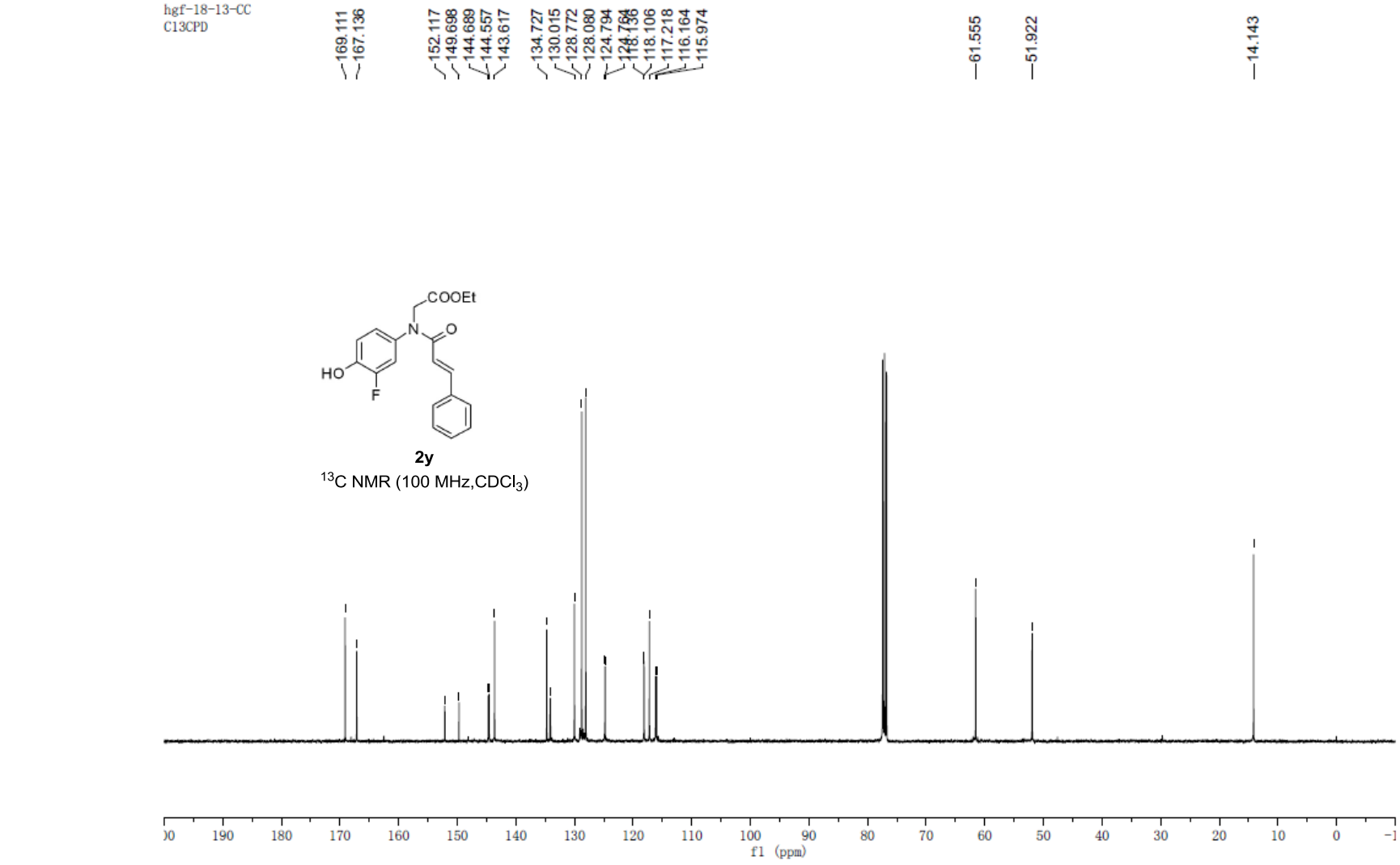
^{1}H NMR (400 MHz, $CDCl_3$)

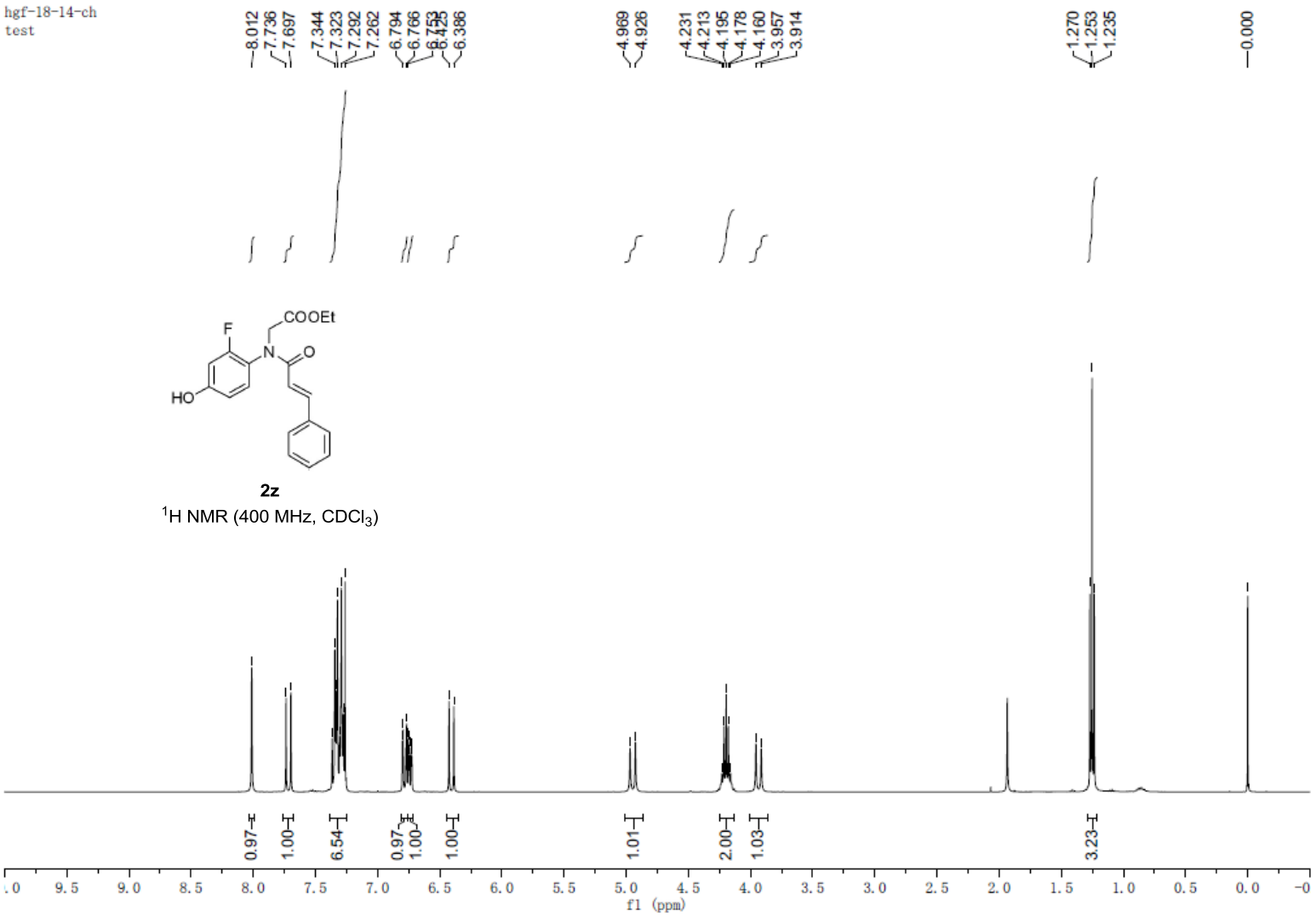
hgf-18-13-cf
F19CPD



2y

^{19}F NMR (376 MHz,$CDCl_3$)

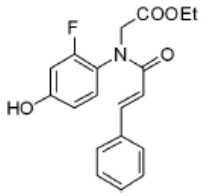

hgf-18-13-CC
C13CPD
169.111
167.136
152.117
149.698
144.689
144.557
143.617
134.727
130.015
128.772
128.080
124.794
124.764
118.136
118.106
117.218
116.164
115.974
61.555
51.922
14.143
COOEt
N
O
HO
F
2y
13C NMR (100 MHz,CDCl3)
f1 (ppm)



2z

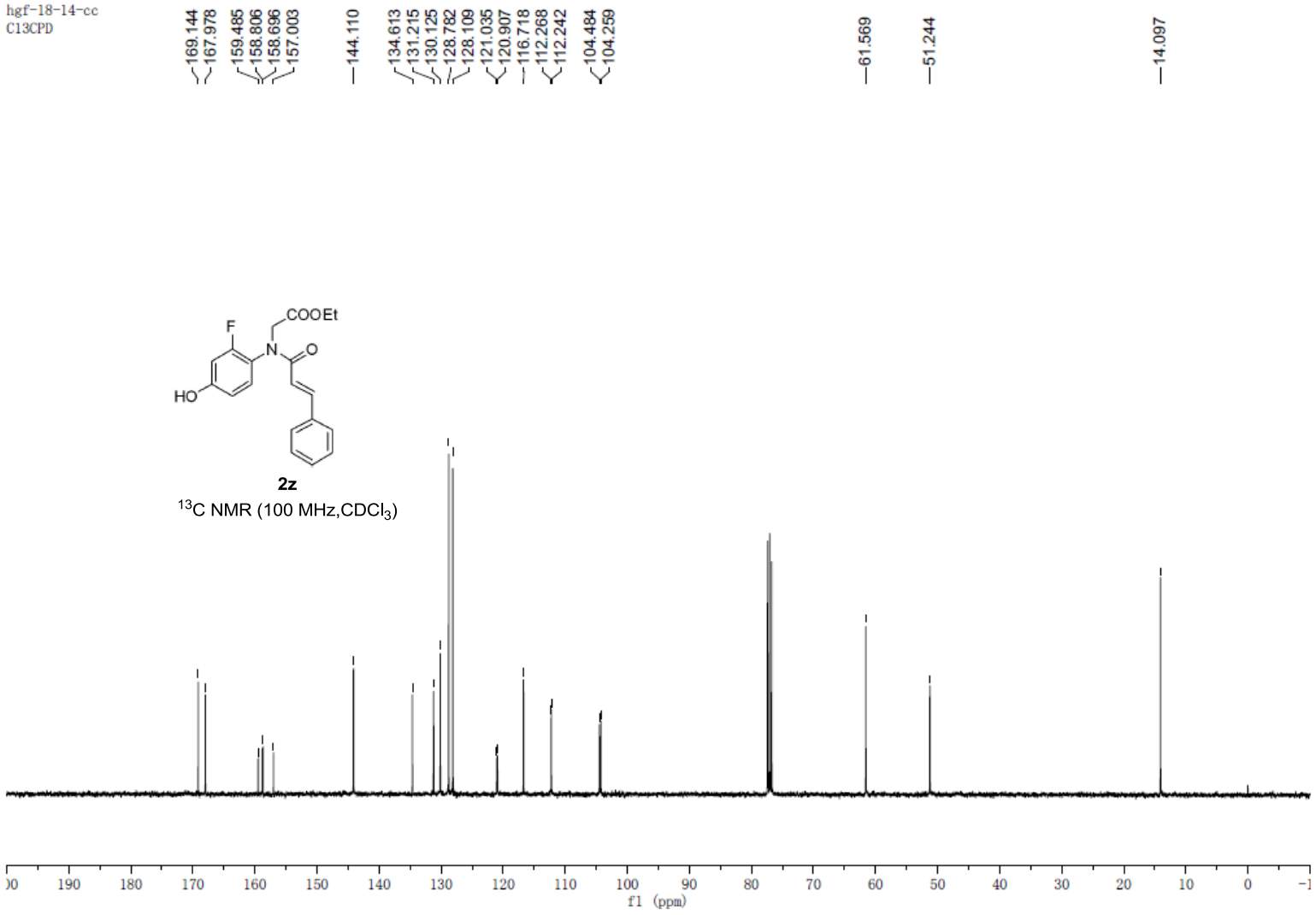
^{1}H NMR (400 MHz, $CDCl_3$)

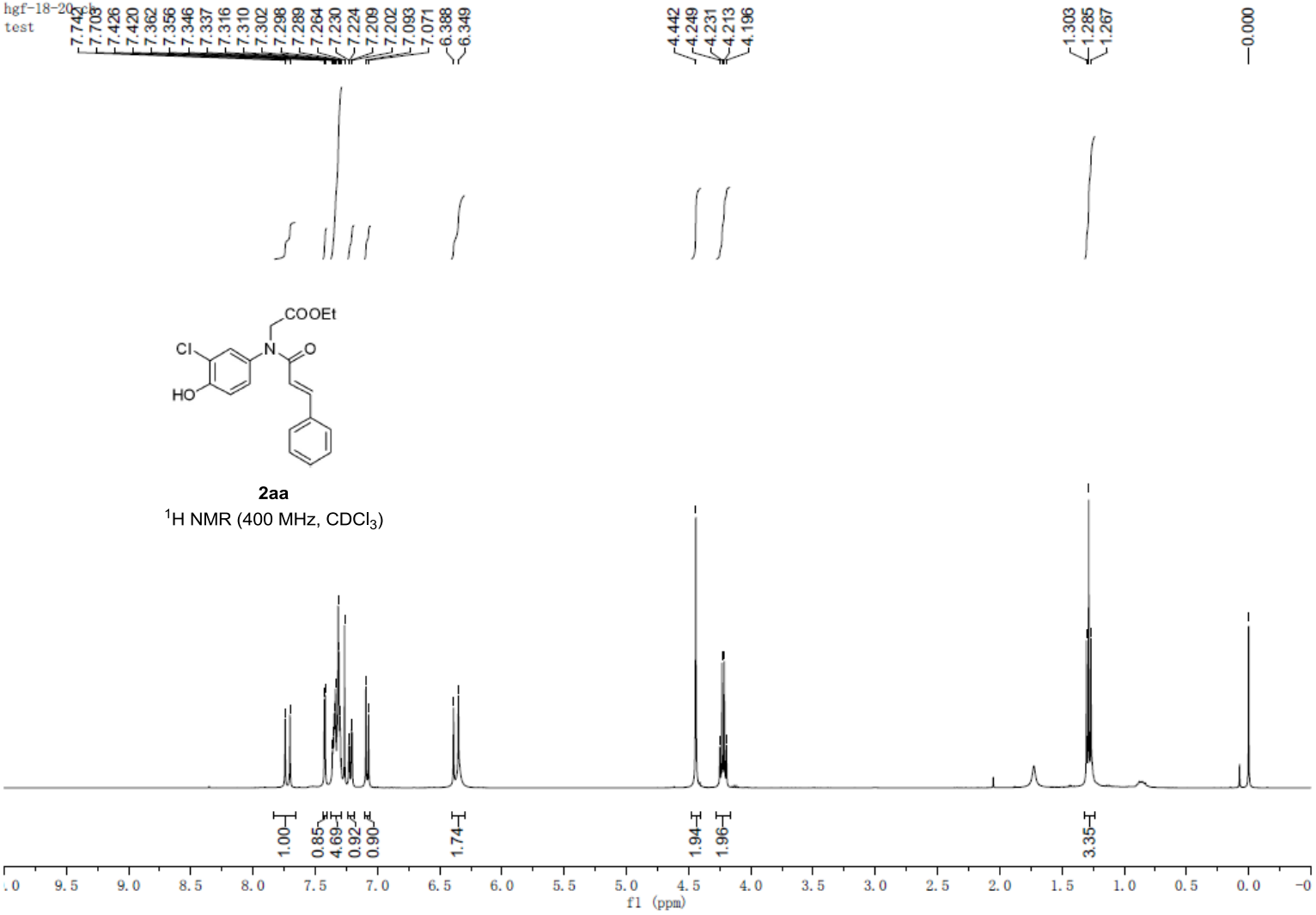
hgf-18-14-cf
F19CPD



2z

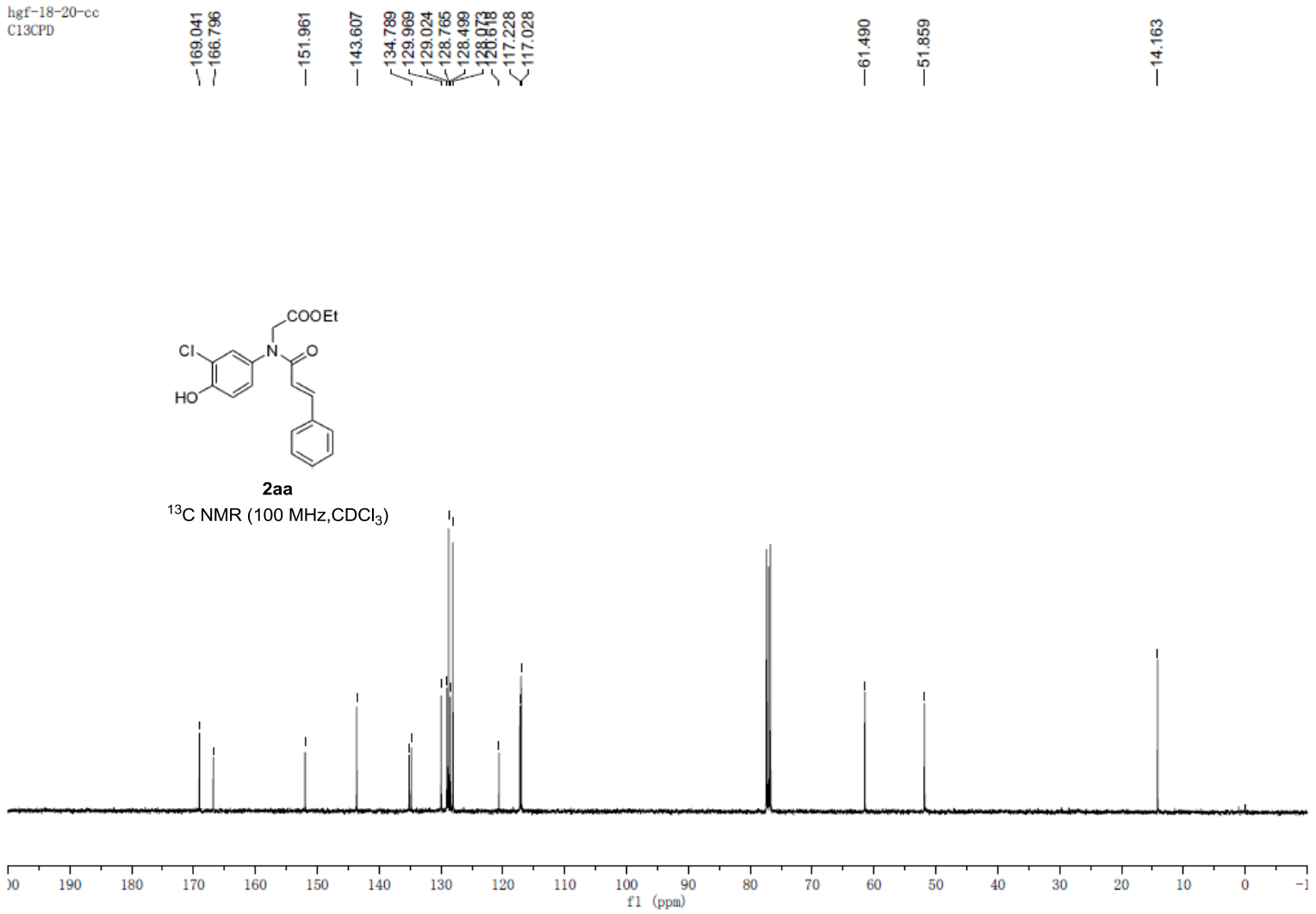
^{19}F NMR (376 MHz, $CDCl_3$)

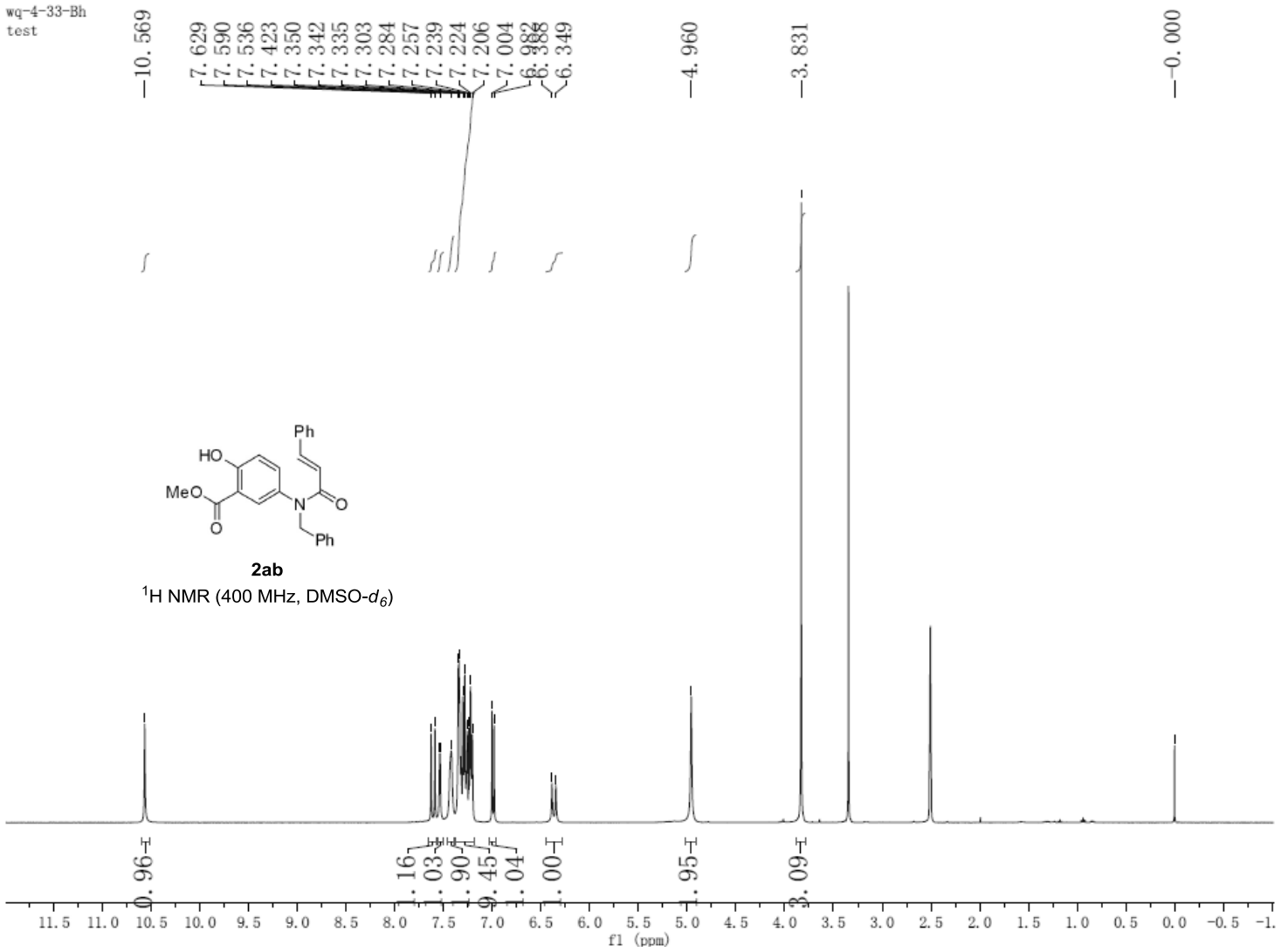

hgf-18-14-cc
C13CPD
169.144
167.978
159.485
158.806
158.696
157.003
144.110
134.613
131.215
130.125
128.782
128.109
121.035
120.907
116.718
112.268
112.242
104.484
104.259
61.569
51.244
14.097
F
COOEt
N
O
HO
2z
13C NMR (100 MHz,CDCl3)
f1 (ppm)



2aa

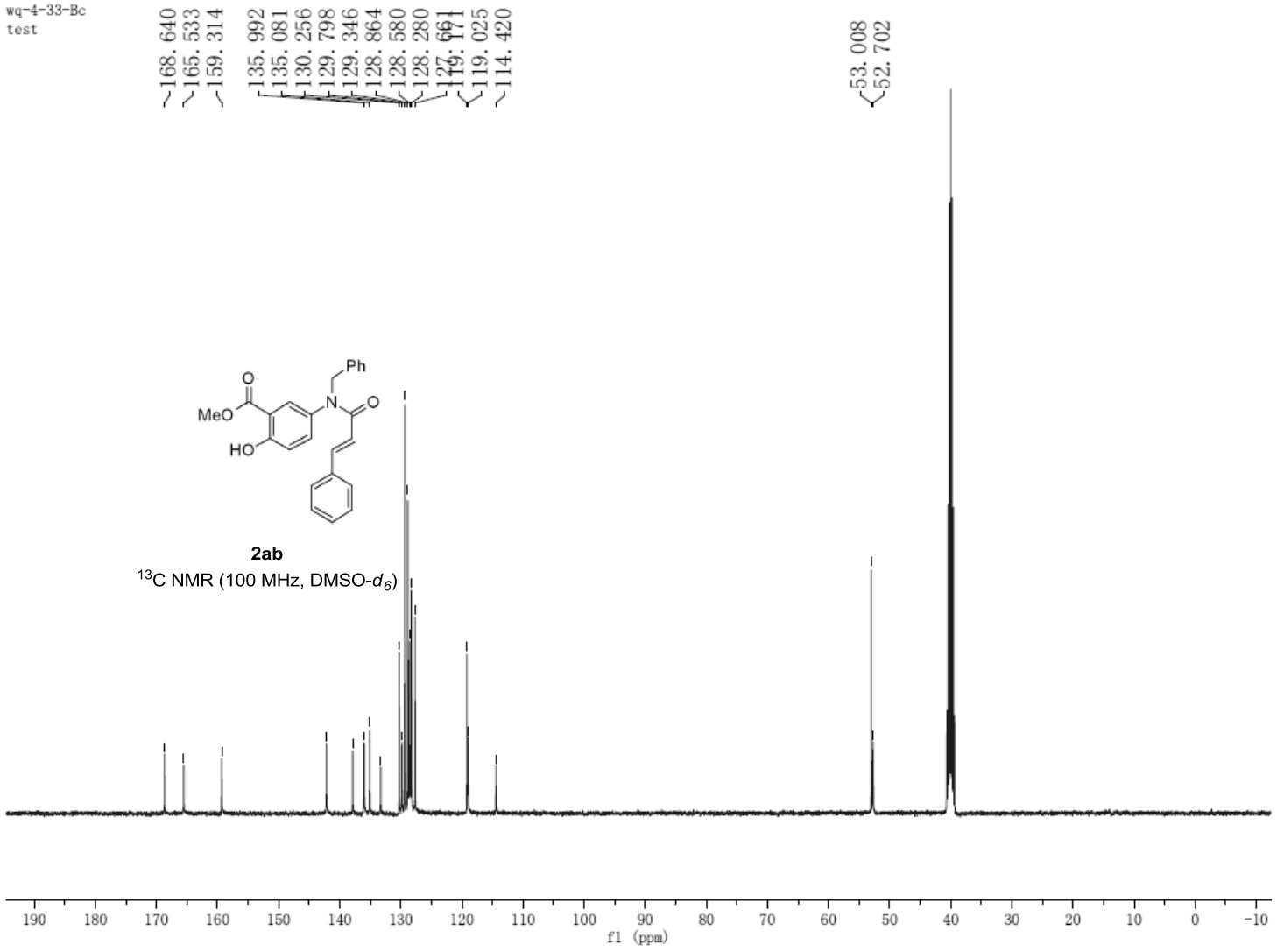
^{1}H NMR (400 MHz, $CDCl_3$)


hgf-18-20-cc
C13CPD
169.041
166.796
151.961
143.607
134.789
129.969
129.024
128.765
128.499
128.073
120.818
117.228
117.028
61.490
51.859
14.163
COOEt
Cl
N
O
HO
2aa
13C NMR (100 MHz,CDCl3)
f1 (ppm)



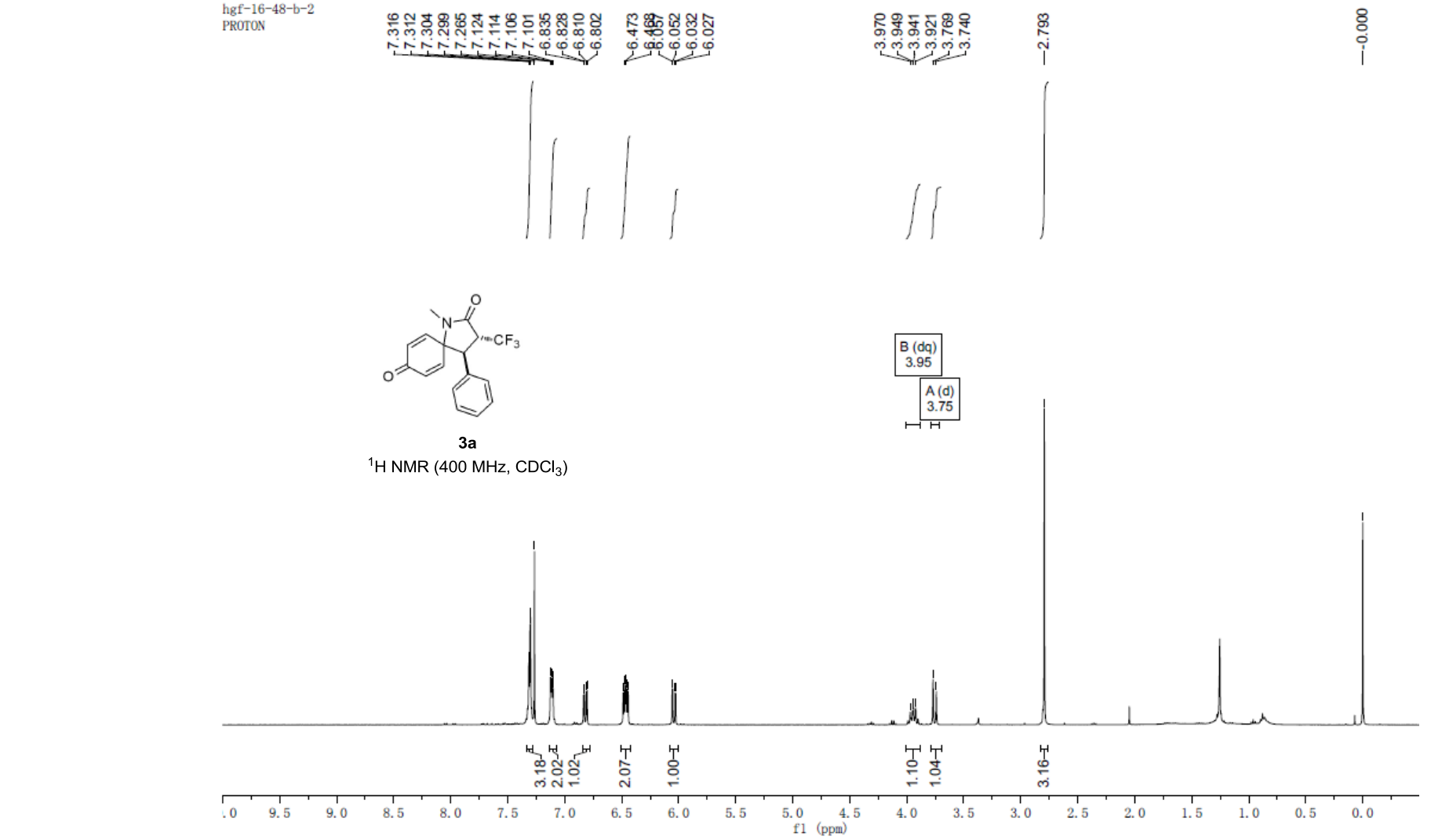
2ab

^{1}H NMR (400 MHz, DMSO-d_6)



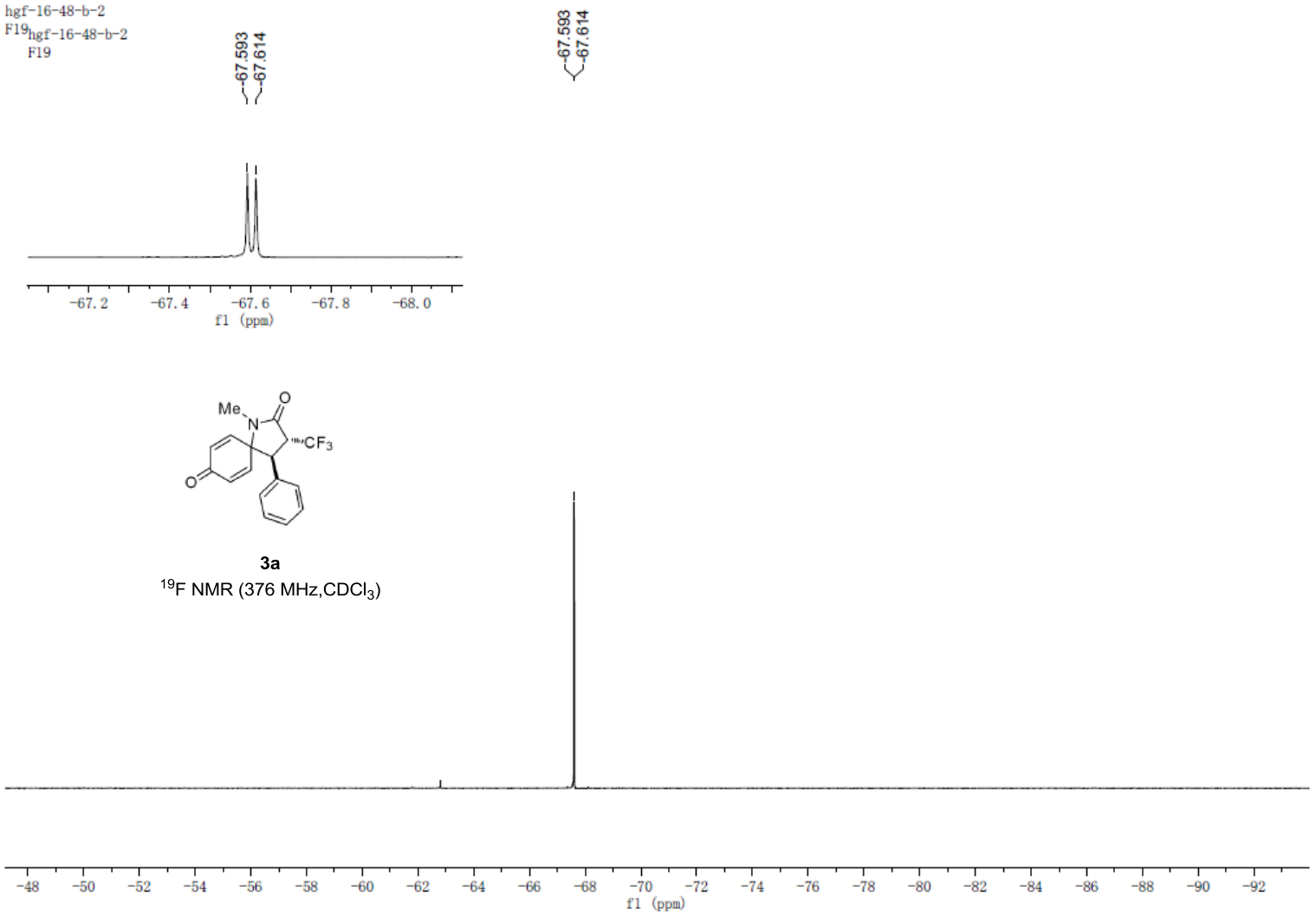
2ab

^{13}C NMR (100 MHz, DMSO-d_6)



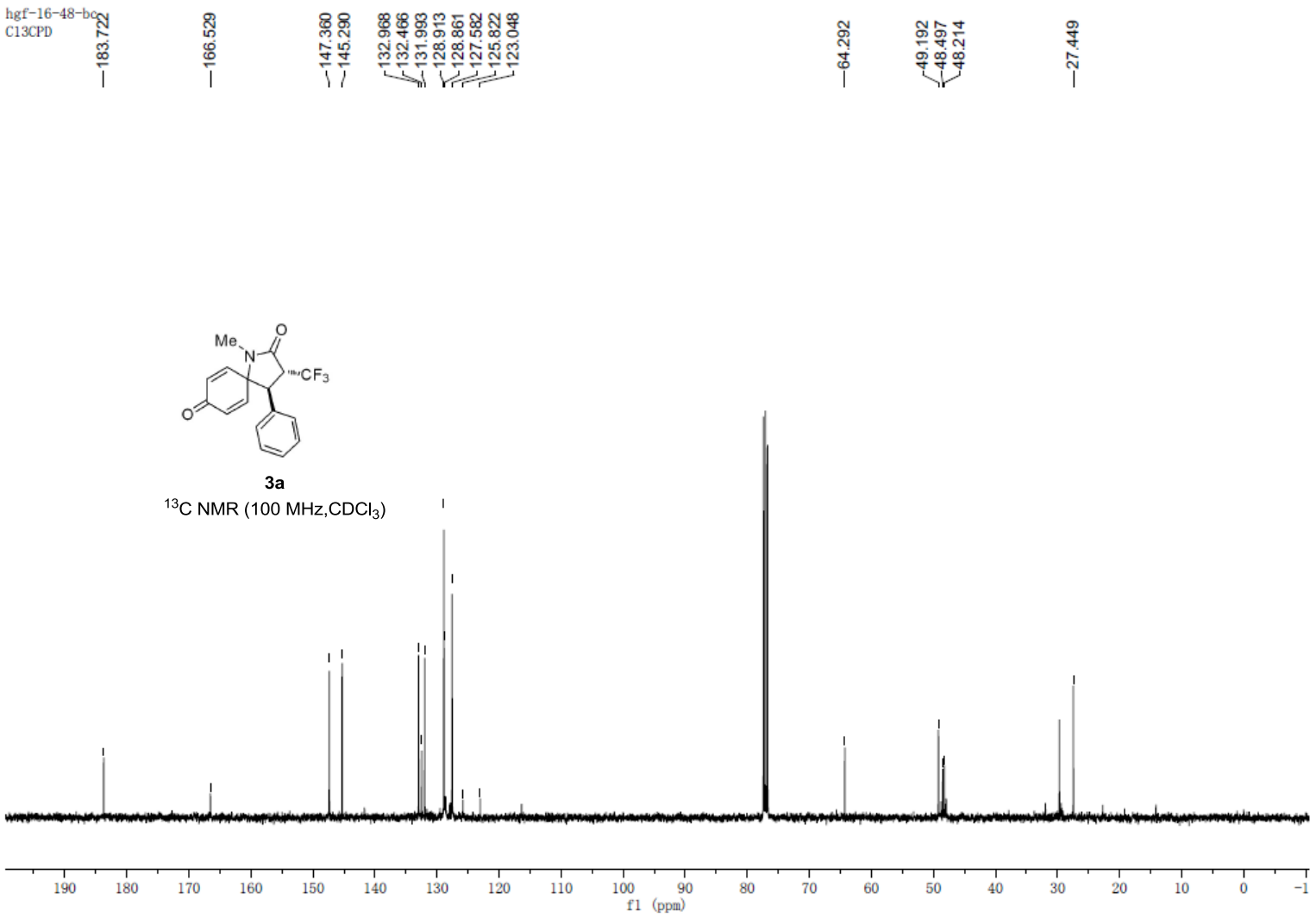
3a

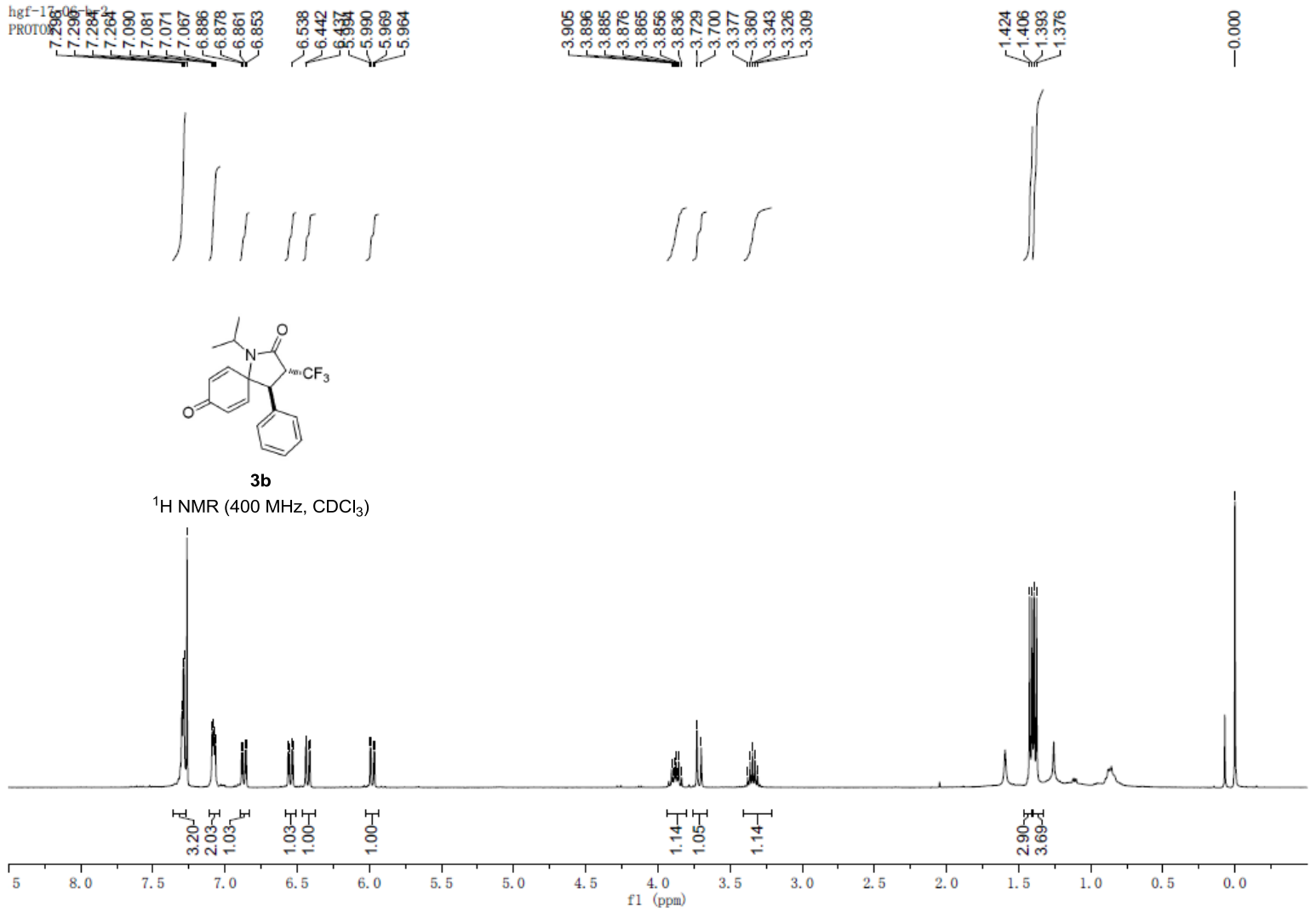
^{1}H NMR (400 MHz, $CDCl_3$)



3a

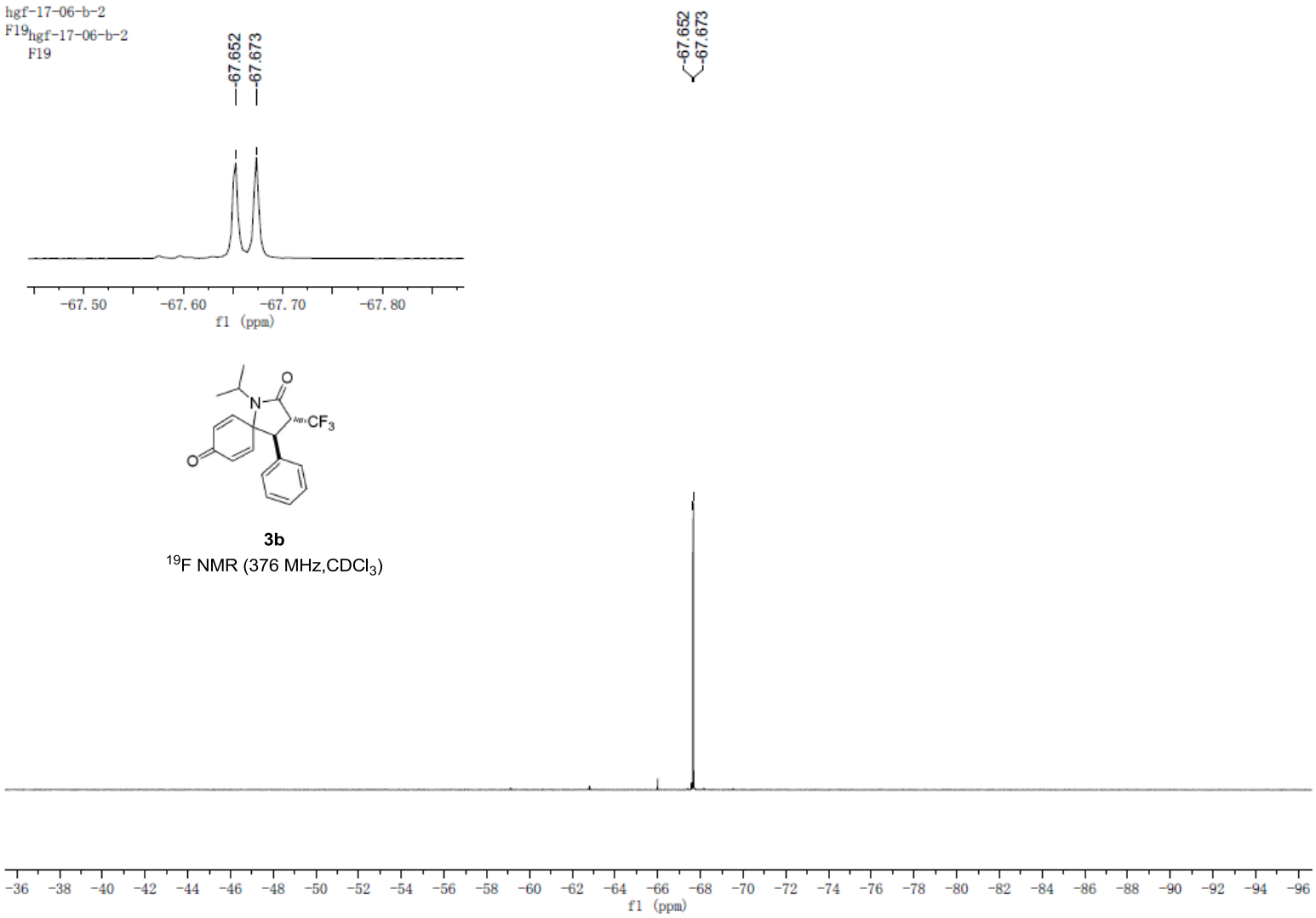
^{19}F NMR (376 MHz,$CDCl_3$)


hgf-16-48-bc
C13CPD
183.722
166.529
147.360
145.290
132.968
132.466
131.993
128.913
128.861
127.582
125.822
123.048
64.292
49.192
48.497
48.214
27.449
Me
N
O
O
CF3
3a
13C NMR (100 MHz,CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)



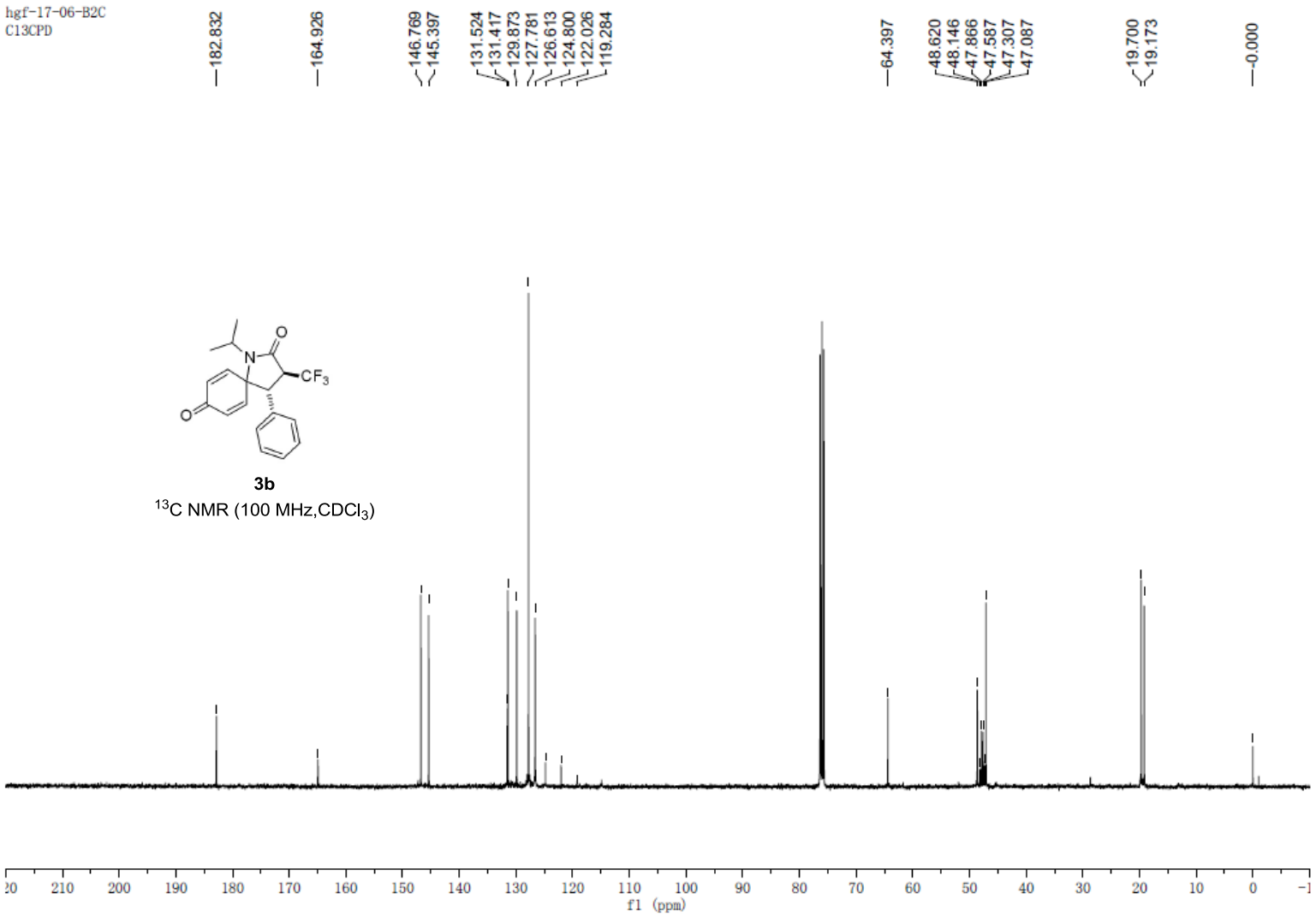
3b

^{1}H NMR (400 MHz, $CDCl_3$)



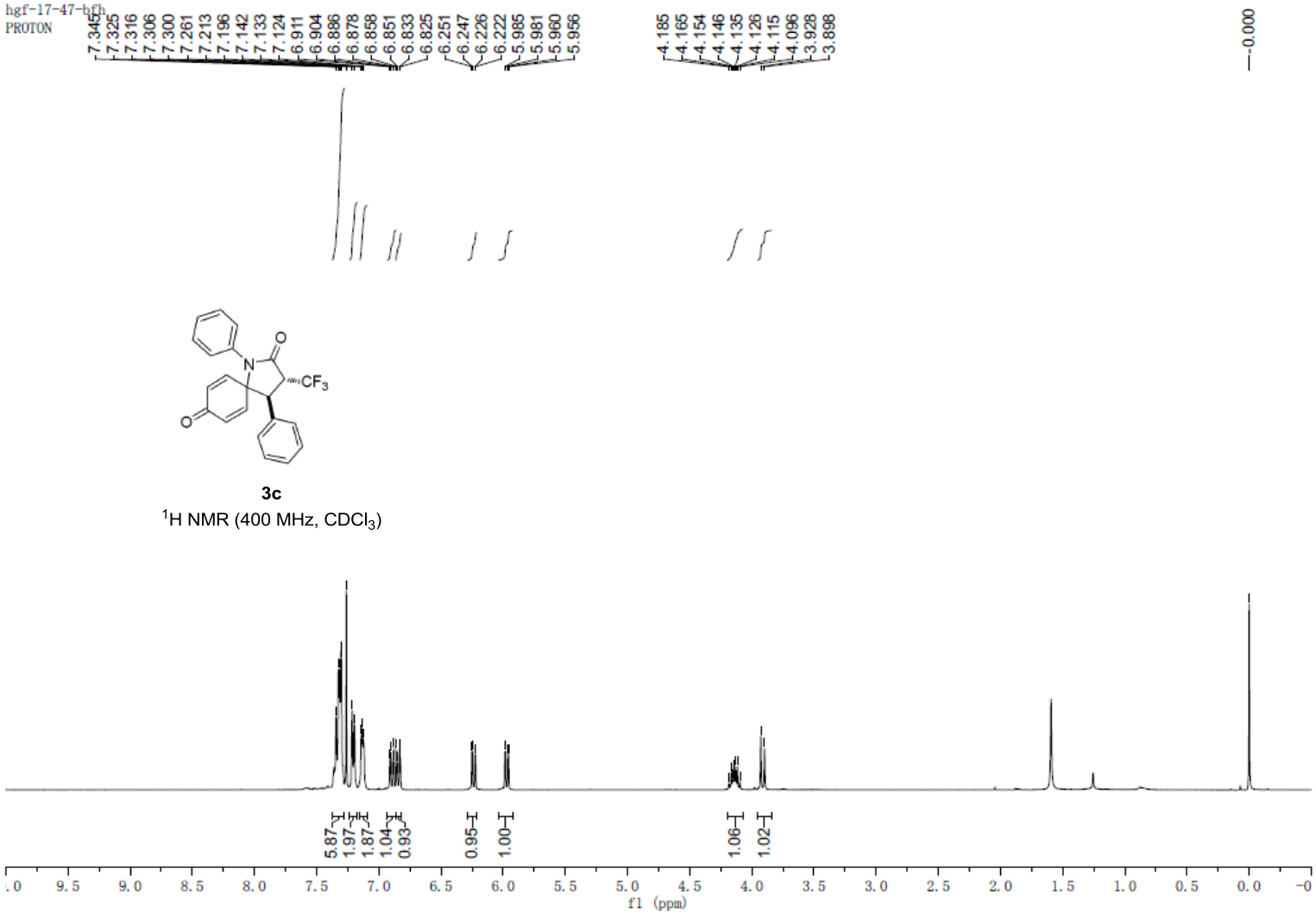
3b

^{19}F NMR (376 MHz,$CDCl_3$)



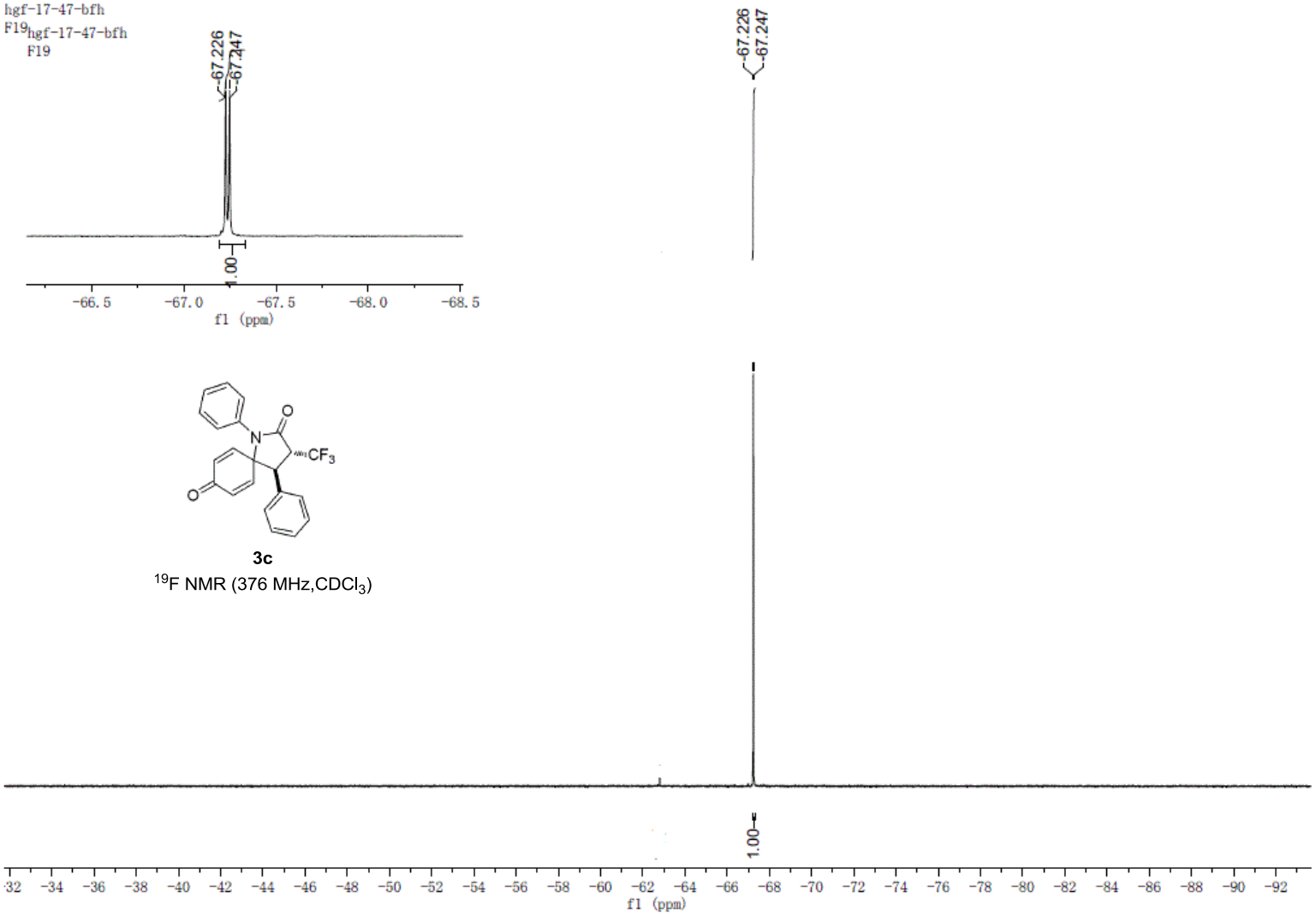
3b

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



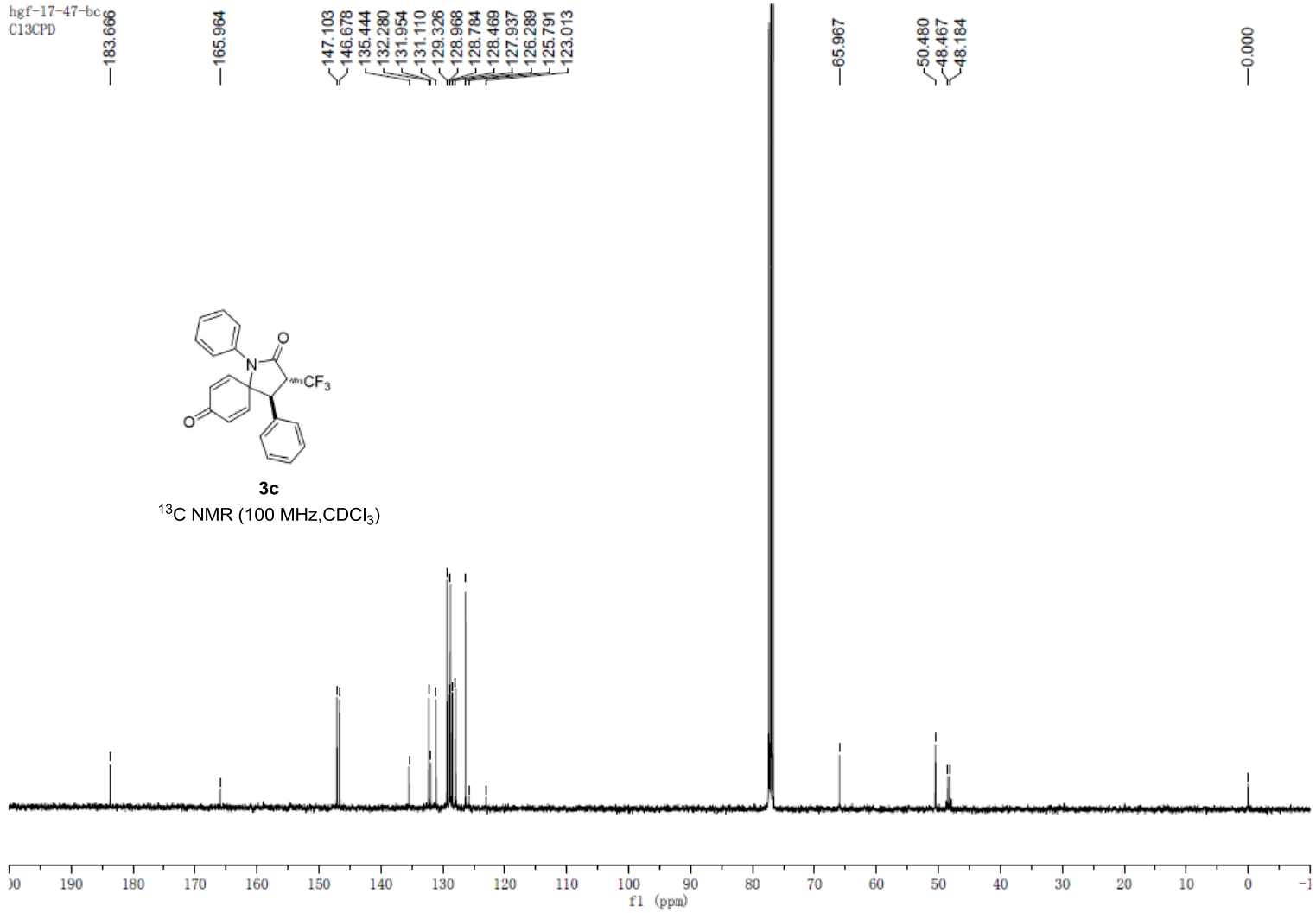
3c

^{1}H NMR (400 MHz, $CDCl_3$)



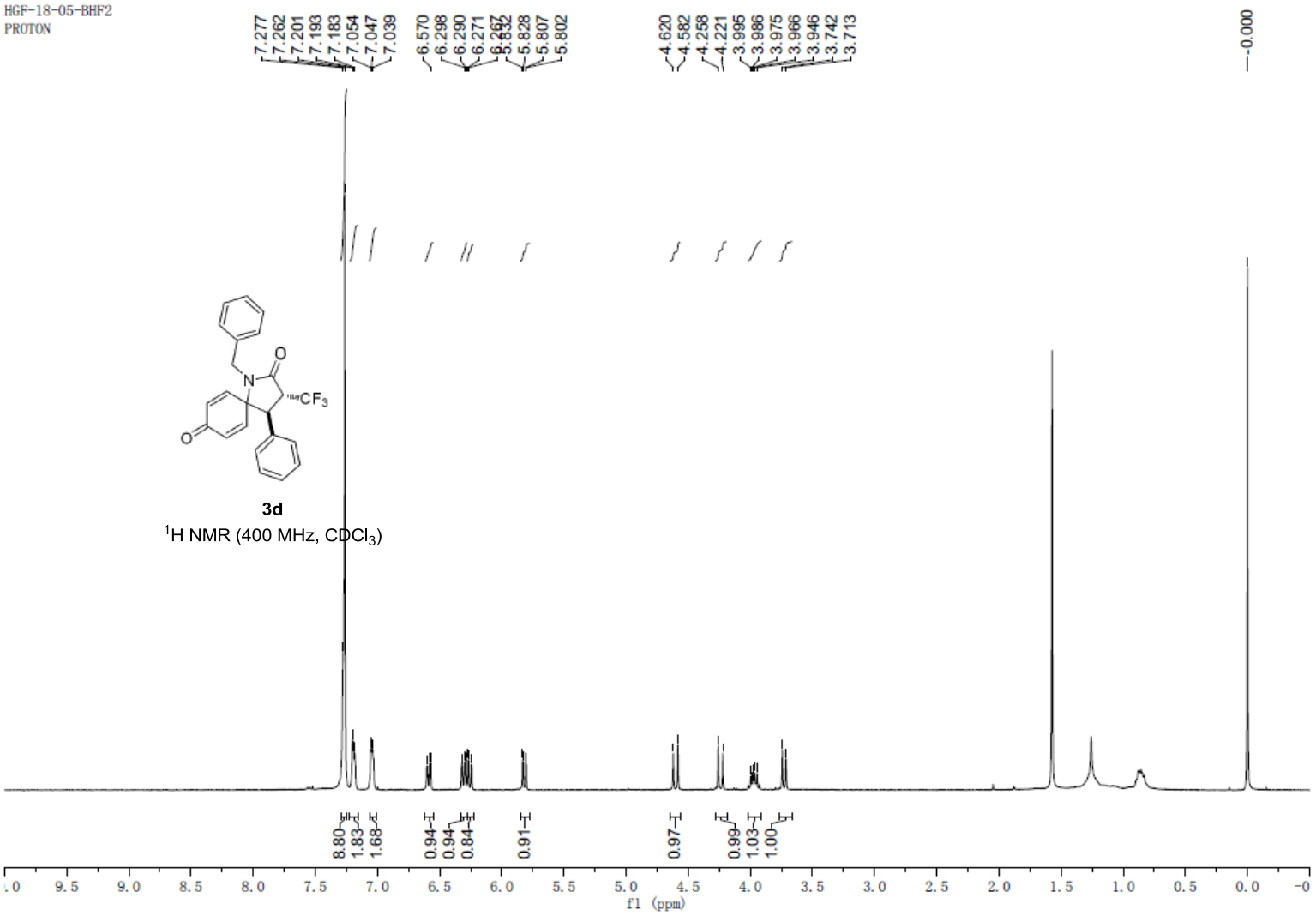
3c

^{19}F NMR (376 MHz,$CDCl_3$)



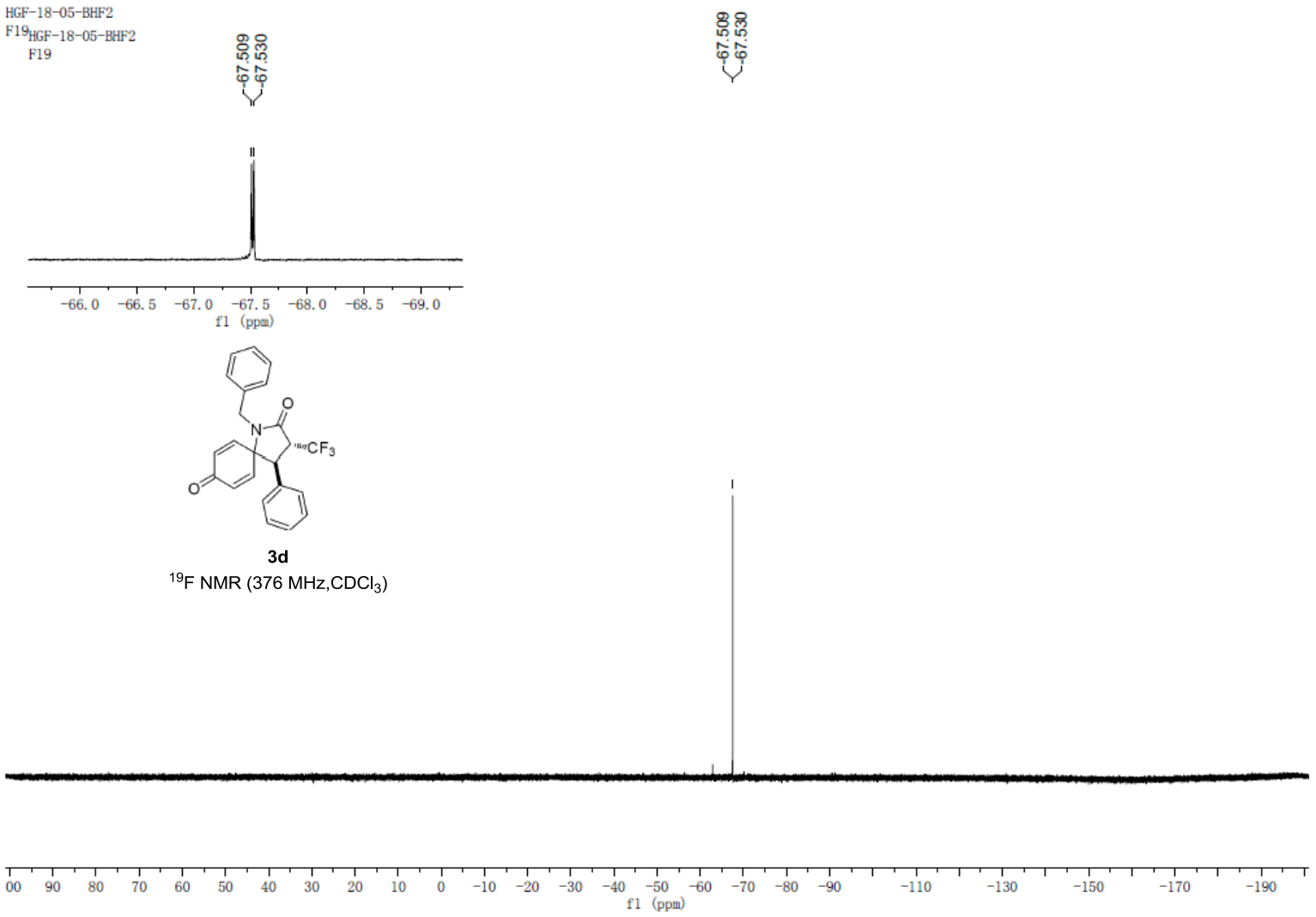
3c

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



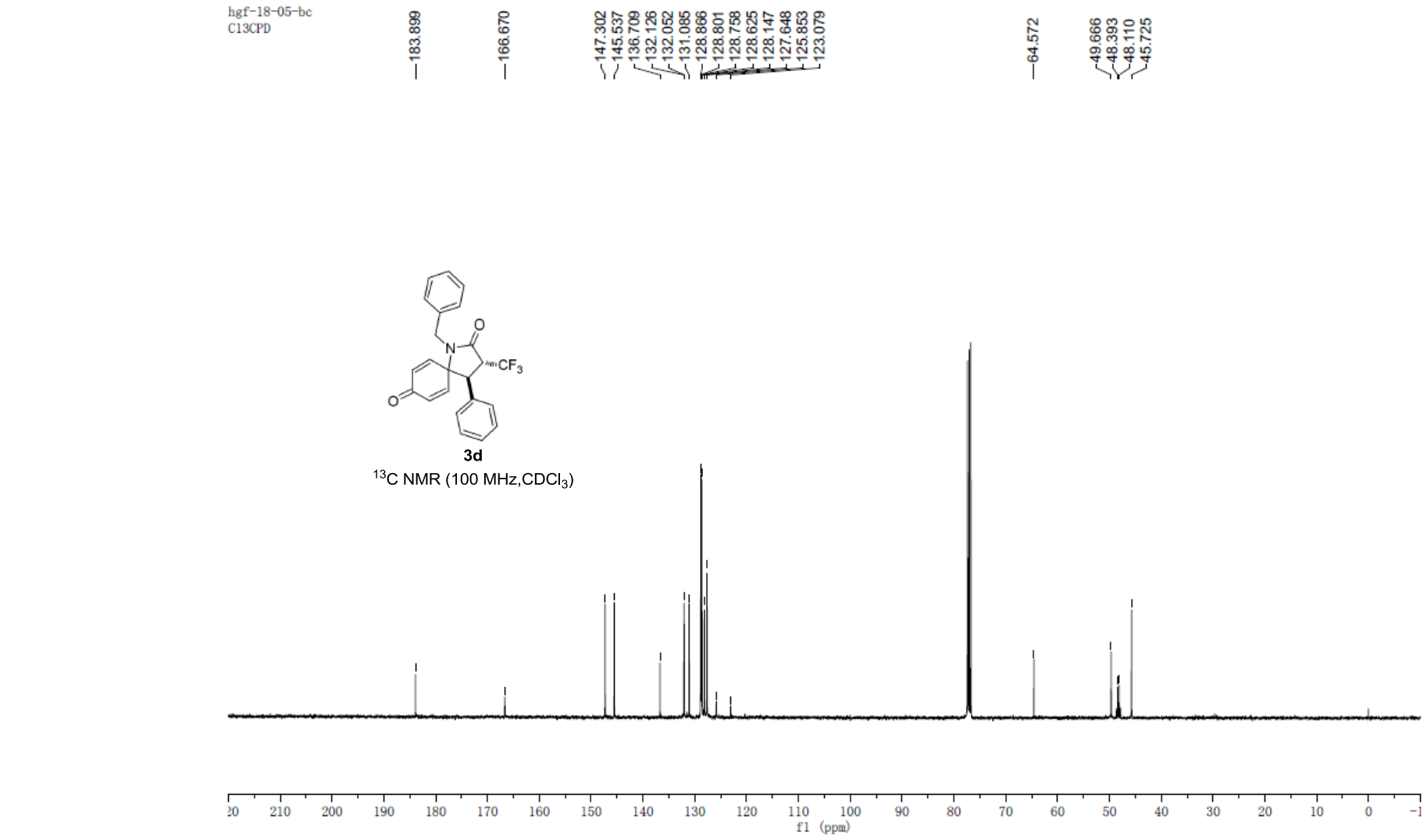
3d

^{1}H NMR (400 MHz, $CDCl_3$)



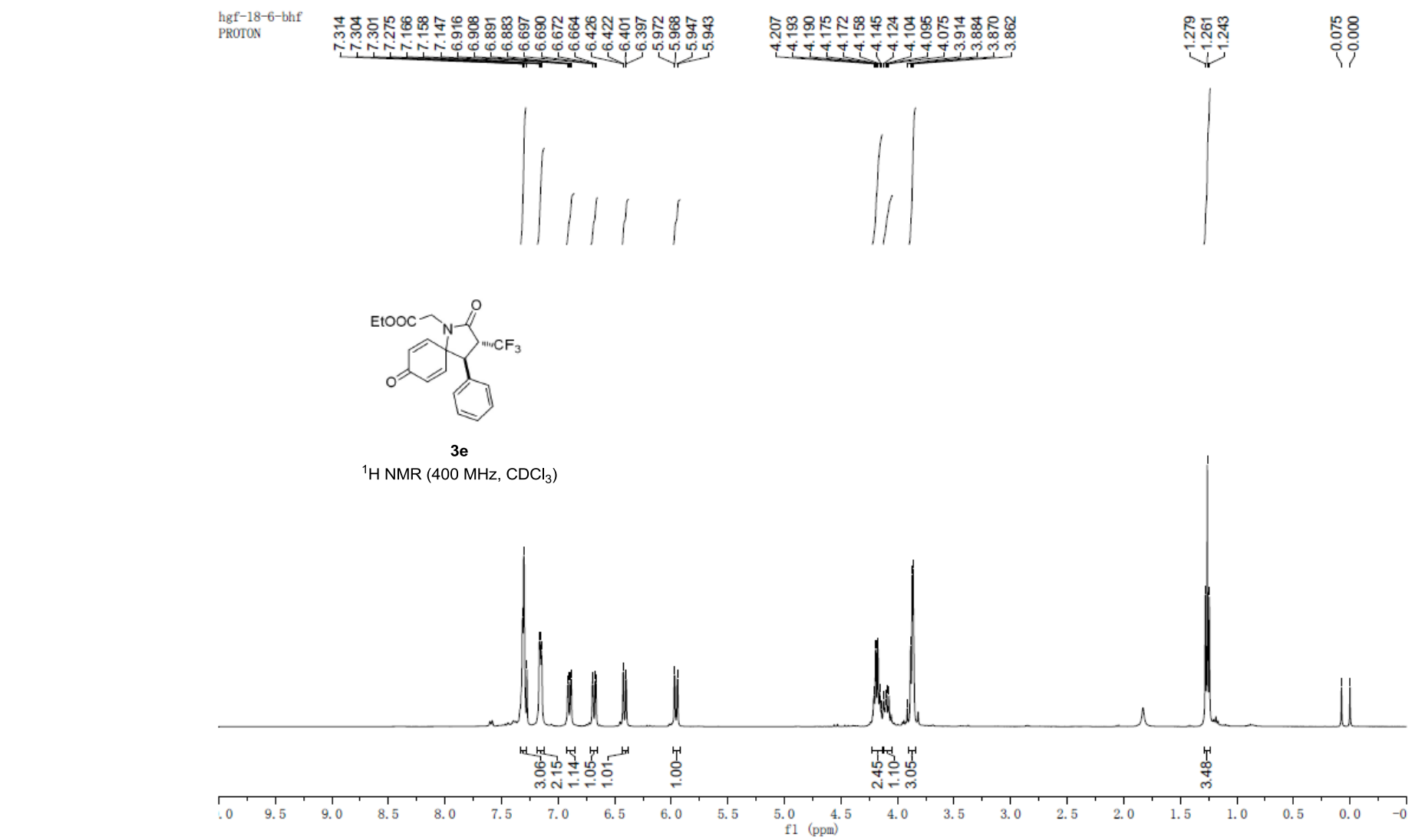
3d

^{19}F NMR (376 MHz,$CDCl_3$)



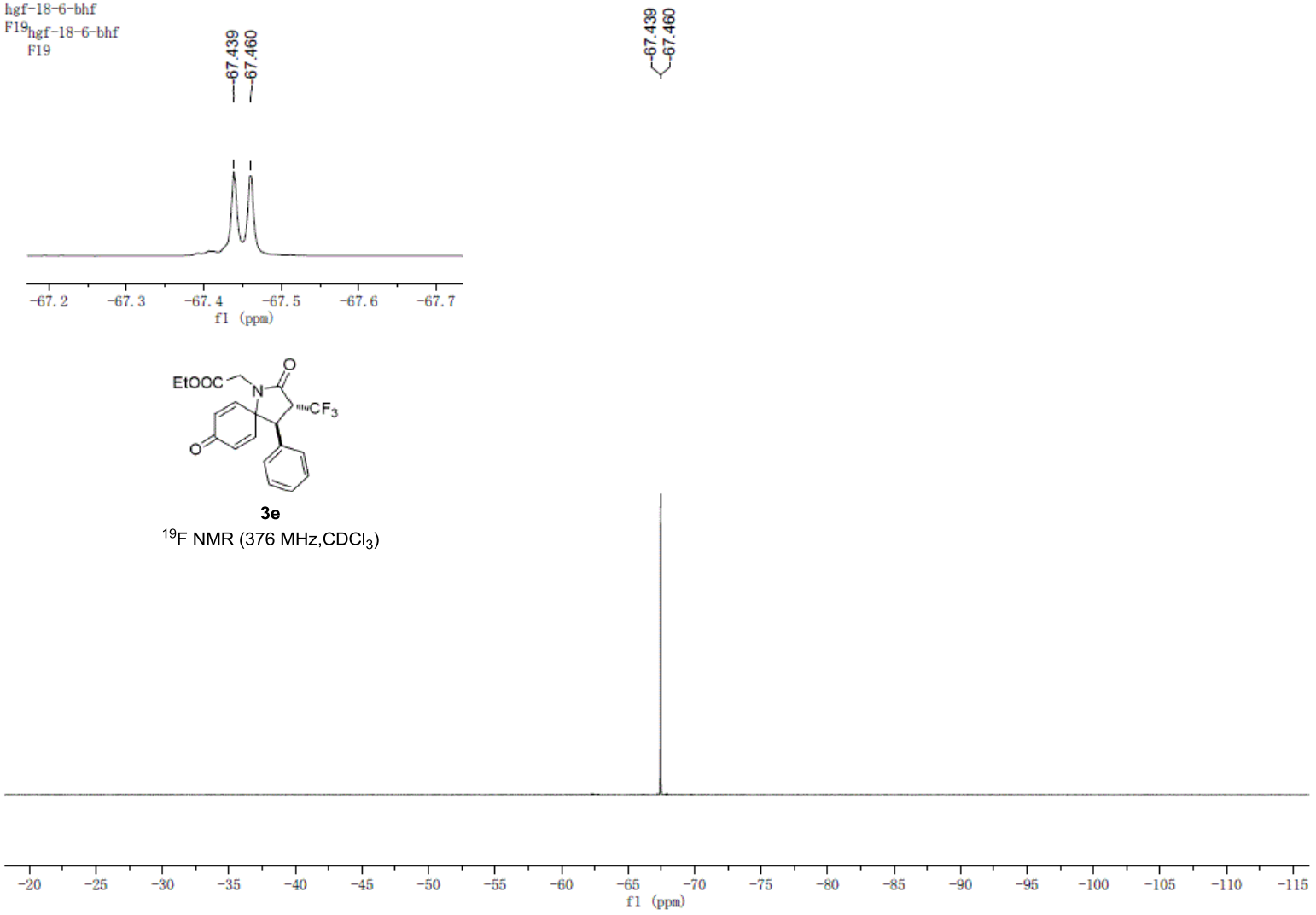
3d

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



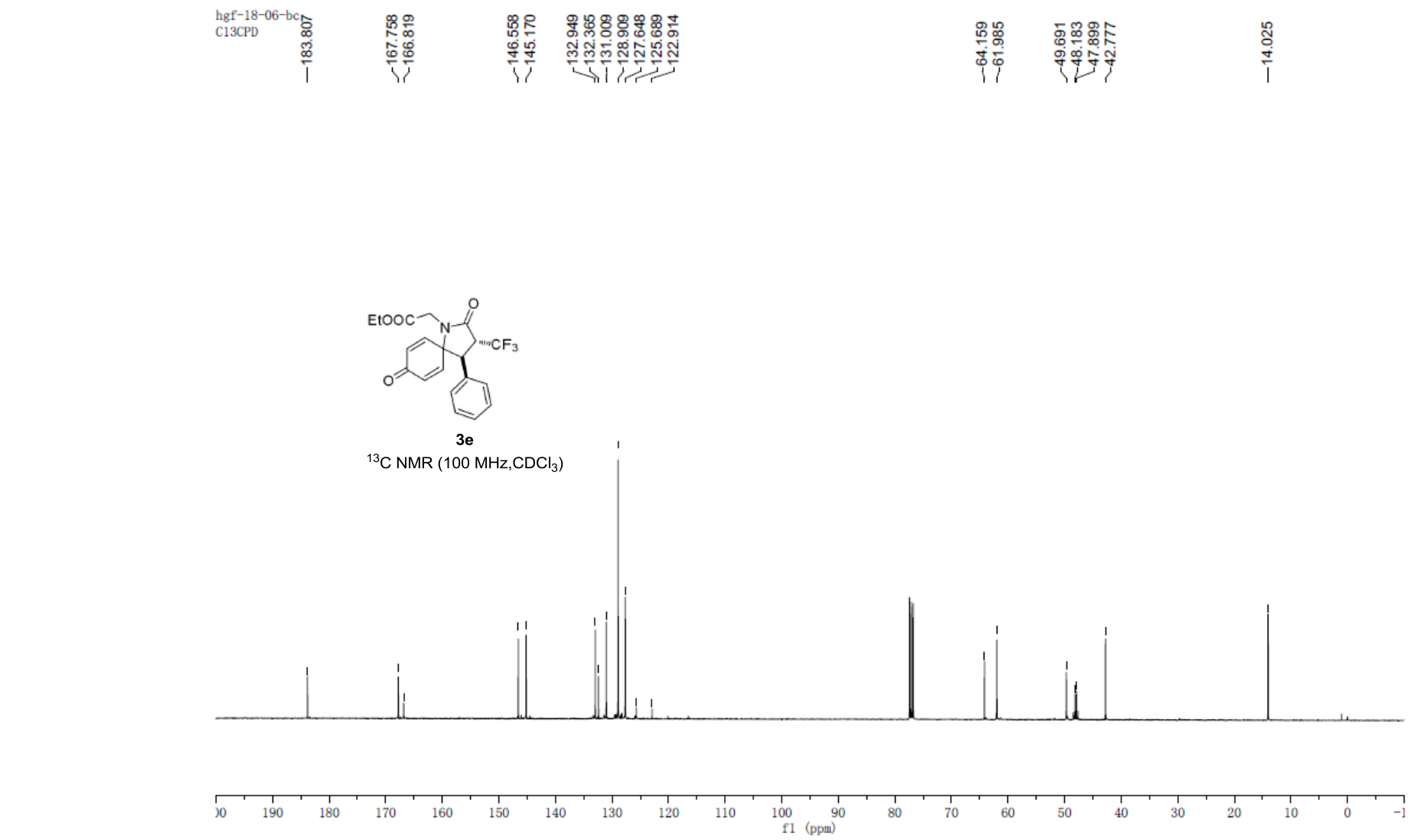
3e

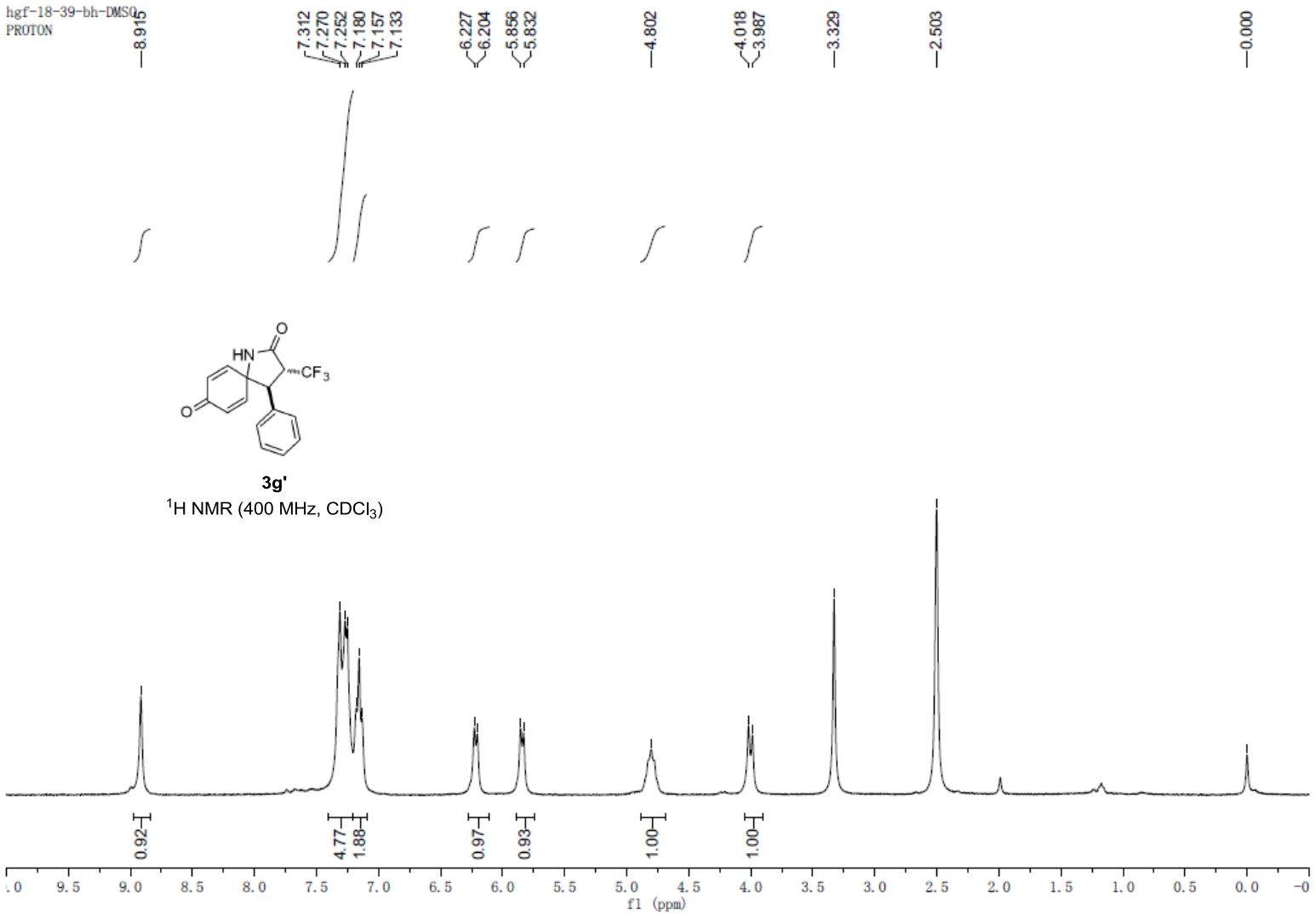
^{1}H NMR (400 MHz, $CDCl_3$)



3e

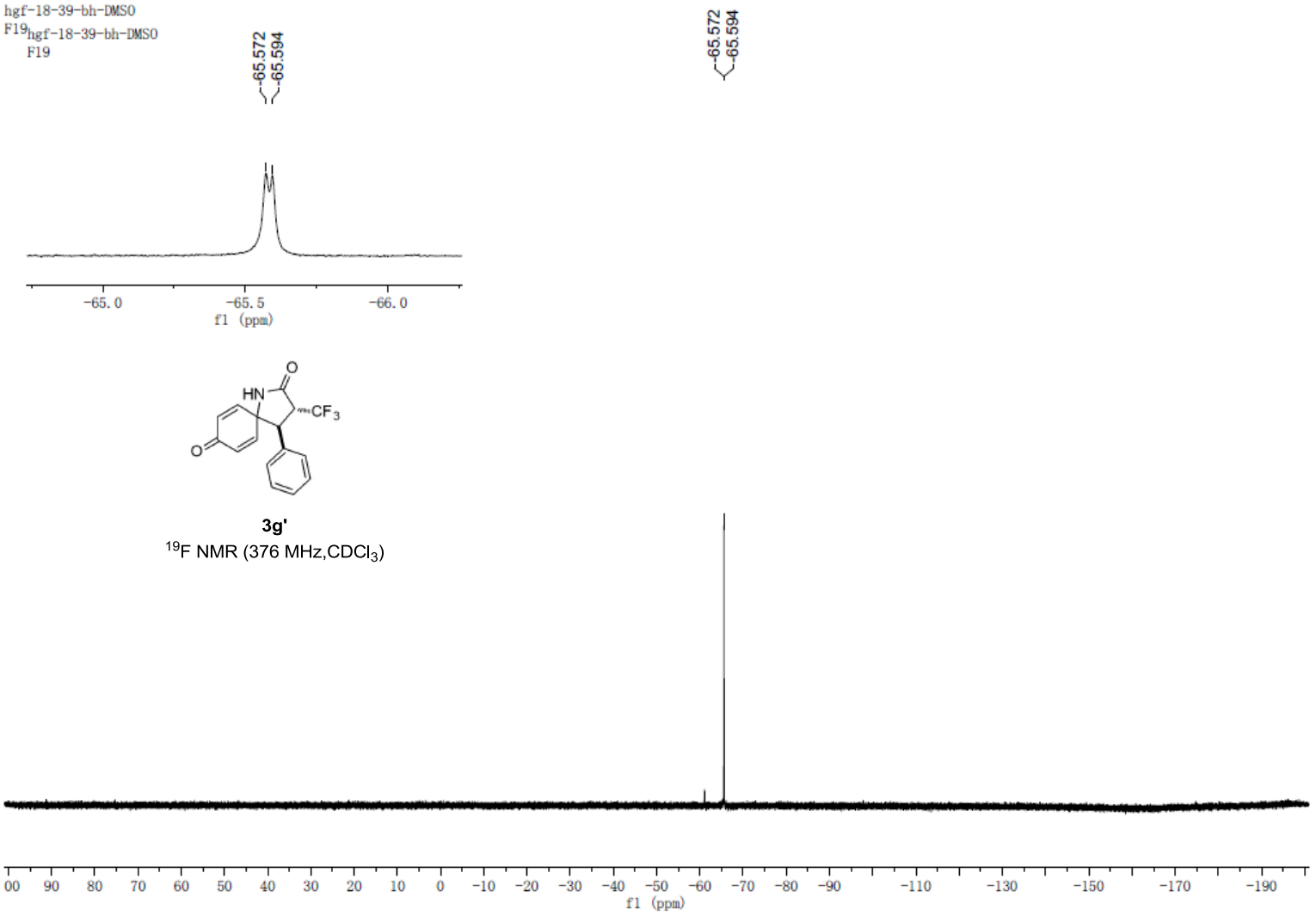
^{19}F NMR (376 MHz,$CDCl_3$)


hgf-18-06-bc
C13CPD
183.807
167.758
166.819
146.558
145.170
132.949
132.365
131.009
128.909
127.648
125.689
122.914
64.159
61.985
49.691
48.183
47.899
42.777
14.025
EtOOC
N
O
O
CF3
3e
13C NMR (100 MHz,CDCl3)
f1 (ppm)



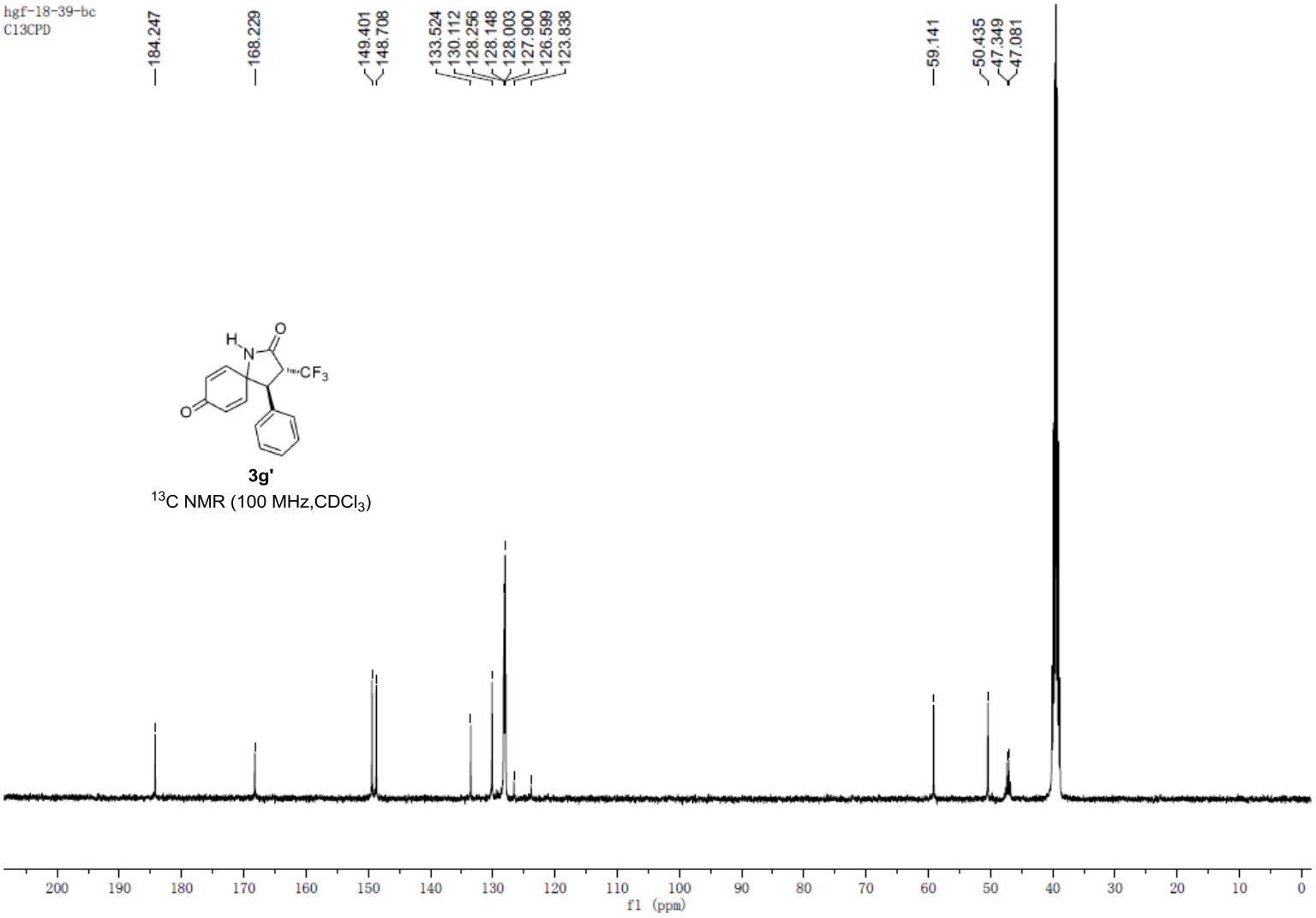
3g'

^{1}H NMR (400 MHz, $CDCl_3$)



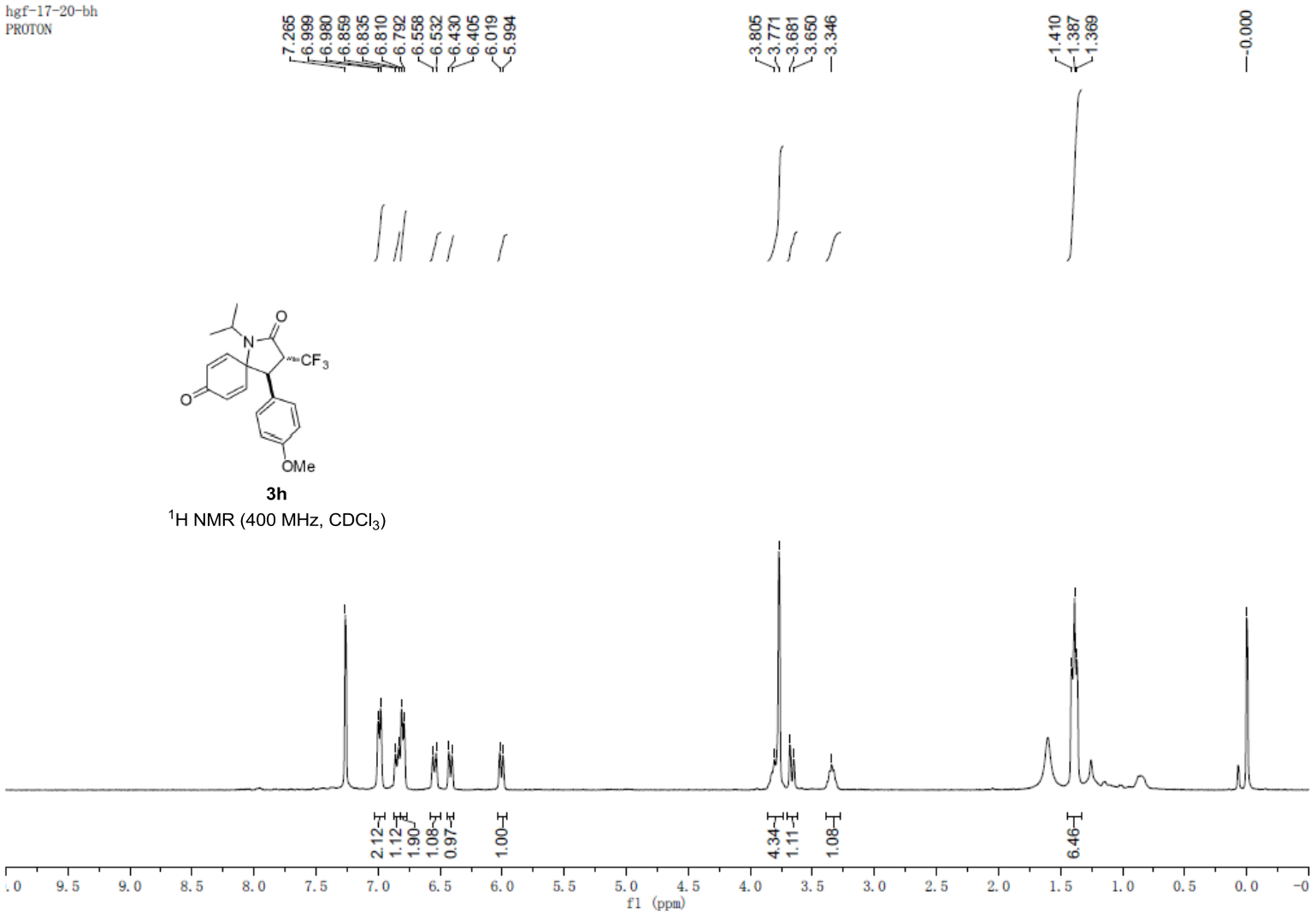
3g'

^{19}F NMR (376 MHz,$CDCl_3$)



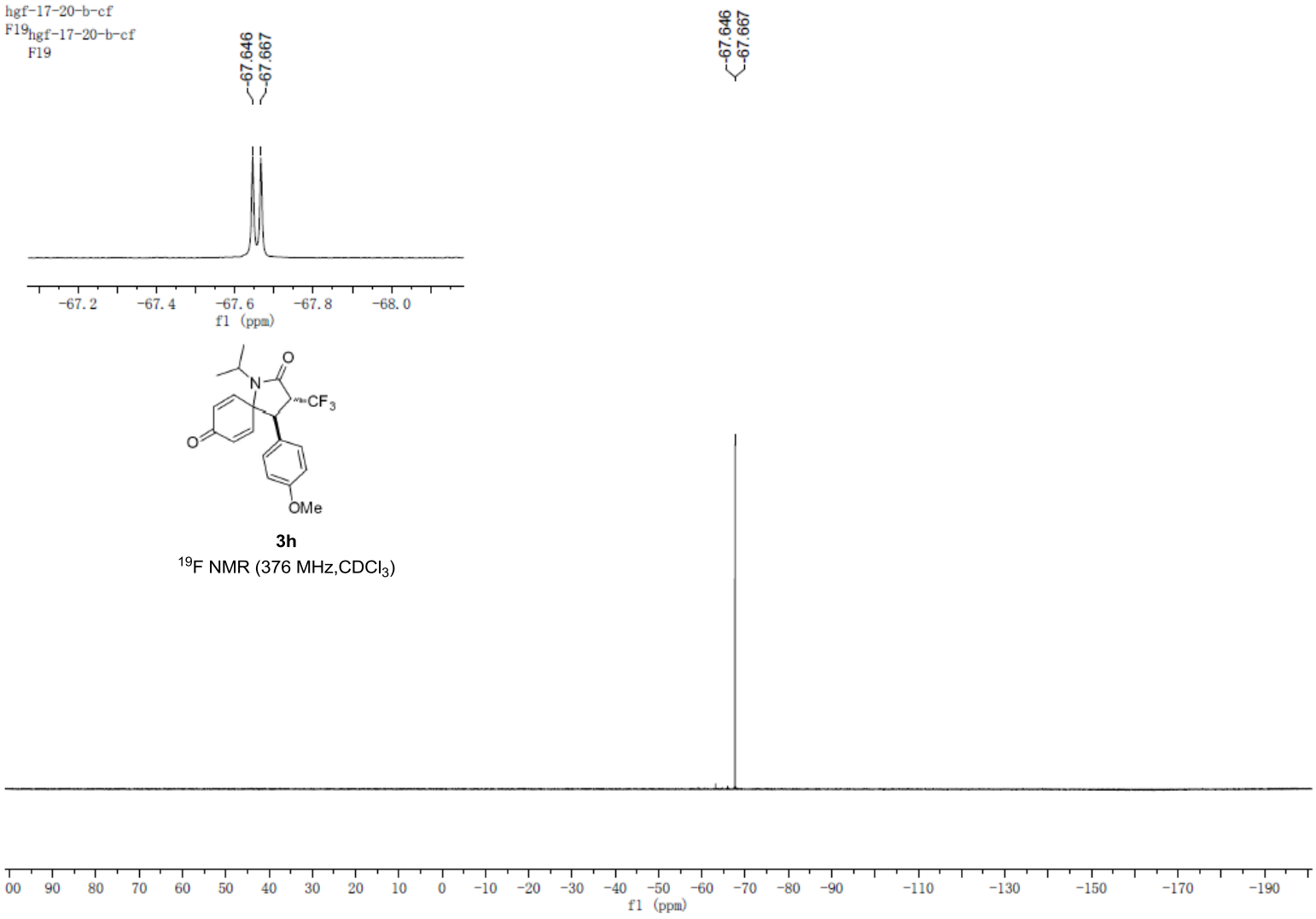
3g'

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



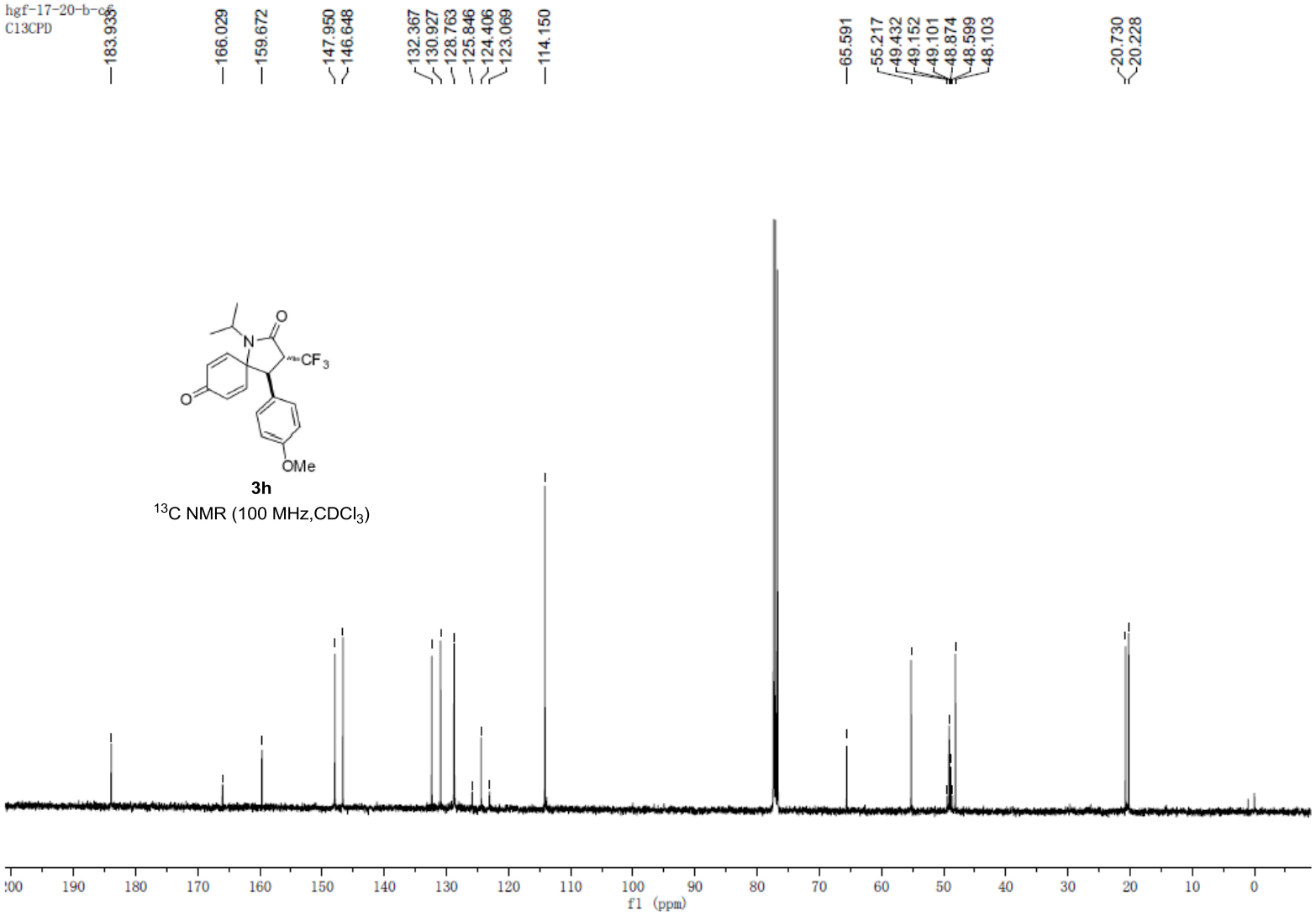
3h

^{1}H NMR (400 MHz, $CDCl_3$)



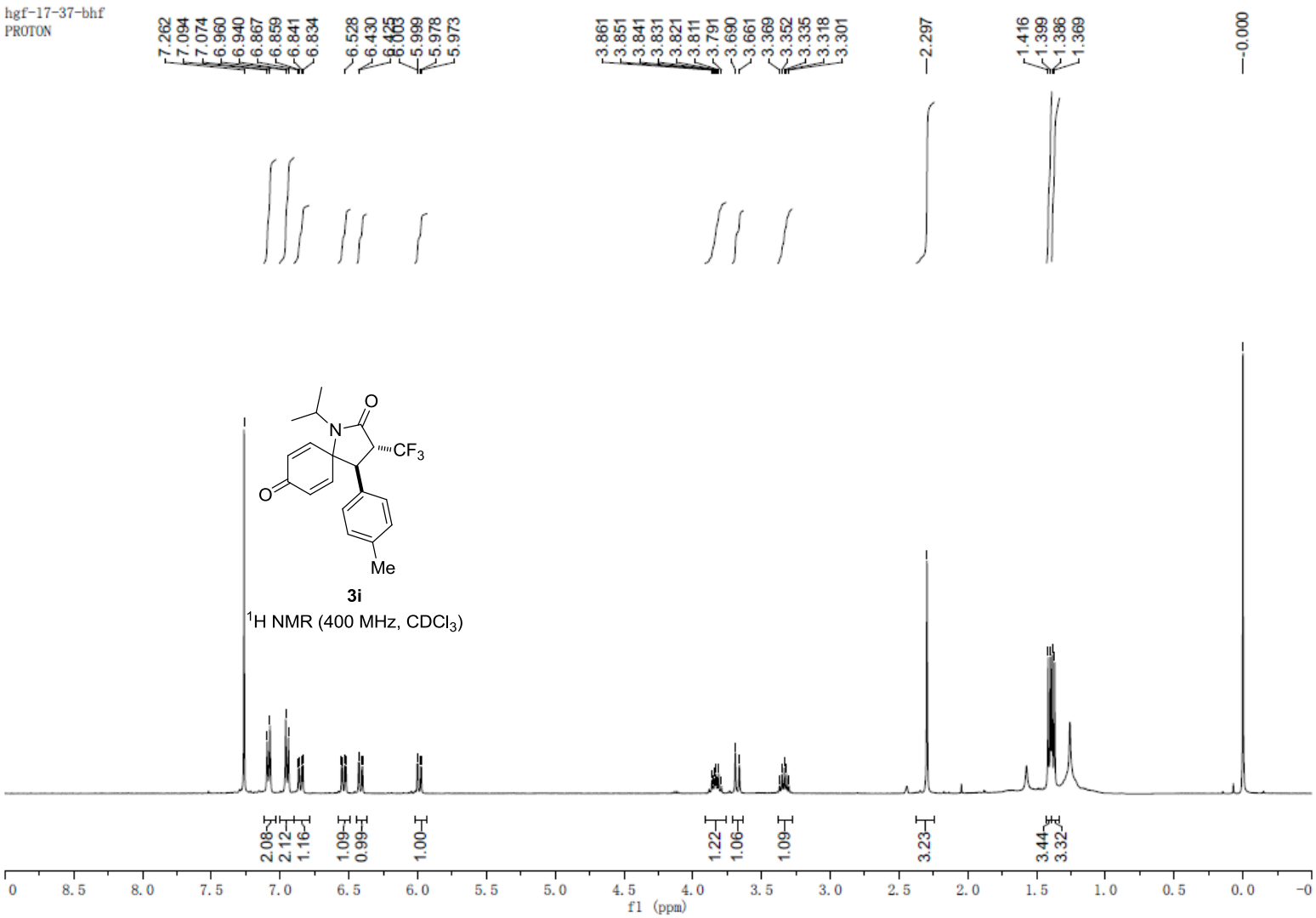
3h

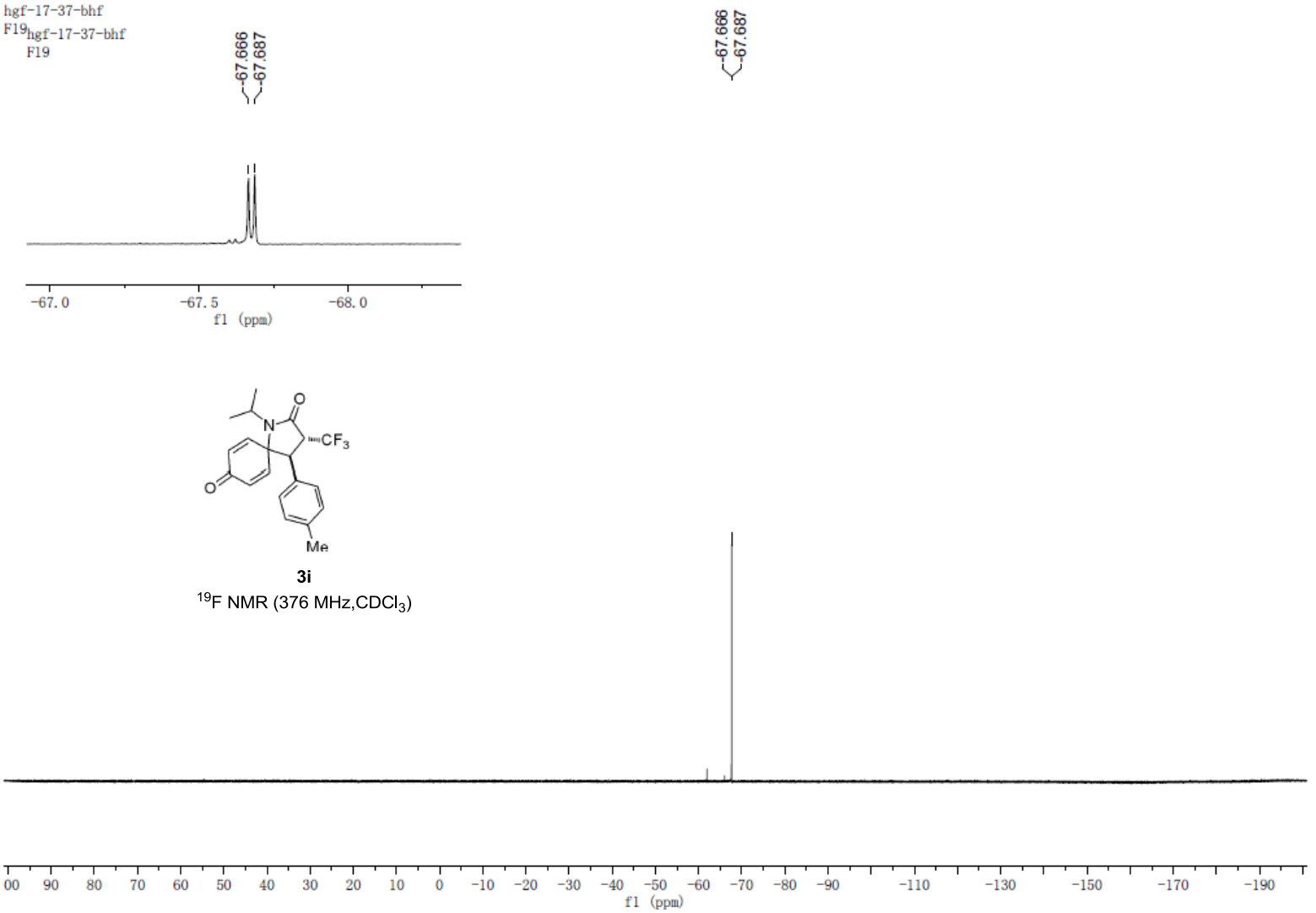
^{19}F NMR (376 MHz,$CDCl_3$)



3h

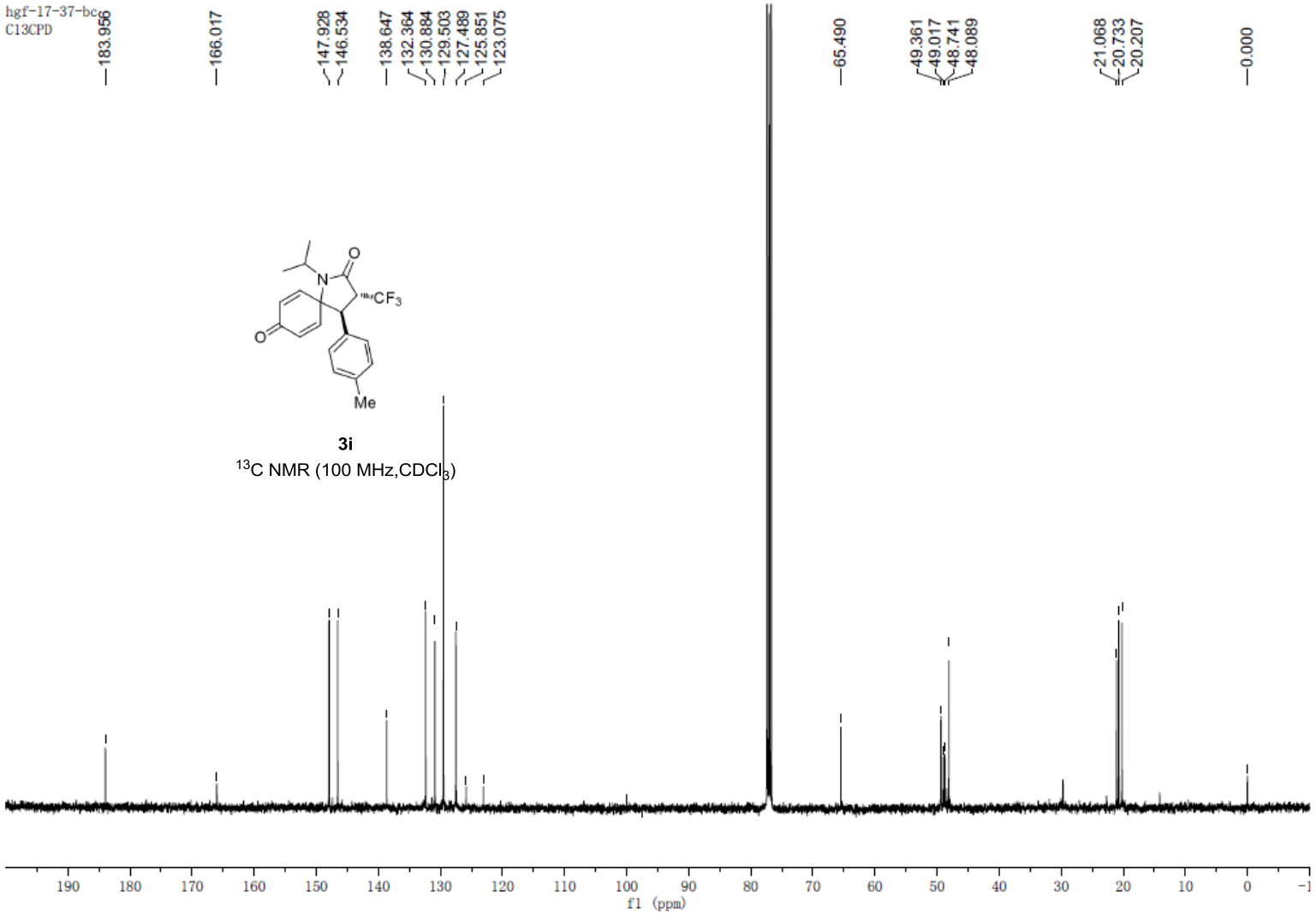
^{13}C NMR (100 MHz,$CDCl_3$)


hgf-17-37-bhf
PROTON
7.262
7.094
7.074
6.960
6.940
6.867
6.859
6.841
6.834
6.528
6.430
6.425
6.003
5.999
5.978
5.973
3.861
3.851
3.841
3.831
3.821
3.811
3.791
3.690
3.661
3.369
3.352
3.335
3.318
3.301
2.297
1.416
1.399
1.386
1.369
0.000
O
N
CF3
O
Me
3i
1H NMR (400 MHz, CDCl3)
2.08
2.12
1.16
1.09
0.99
1.00
1.22
1.06
1.09
3.23
3.44
3.32
f1 (ppm)



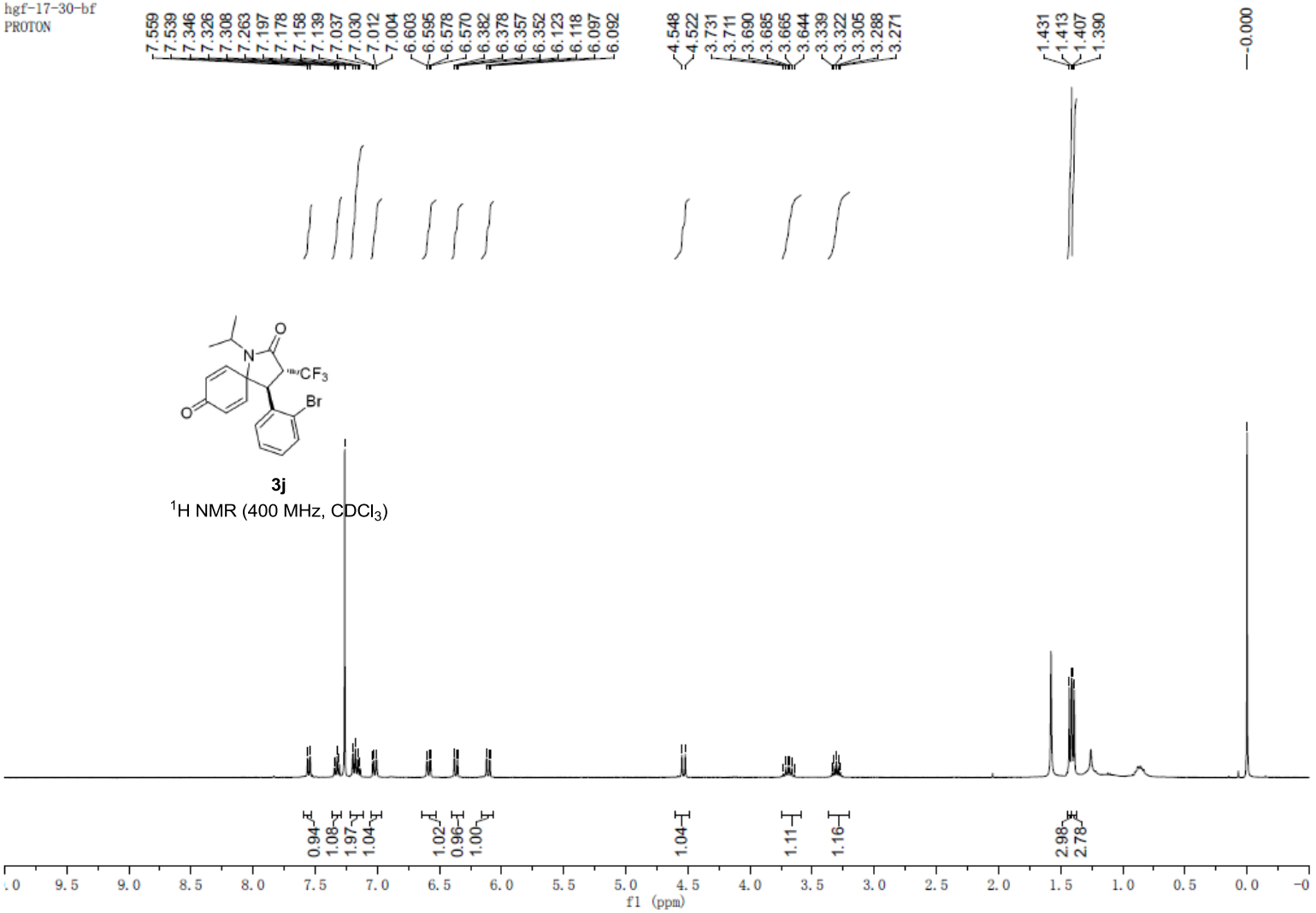
3i

^{19}F NMR (376 MHz,$CDCl_3$)



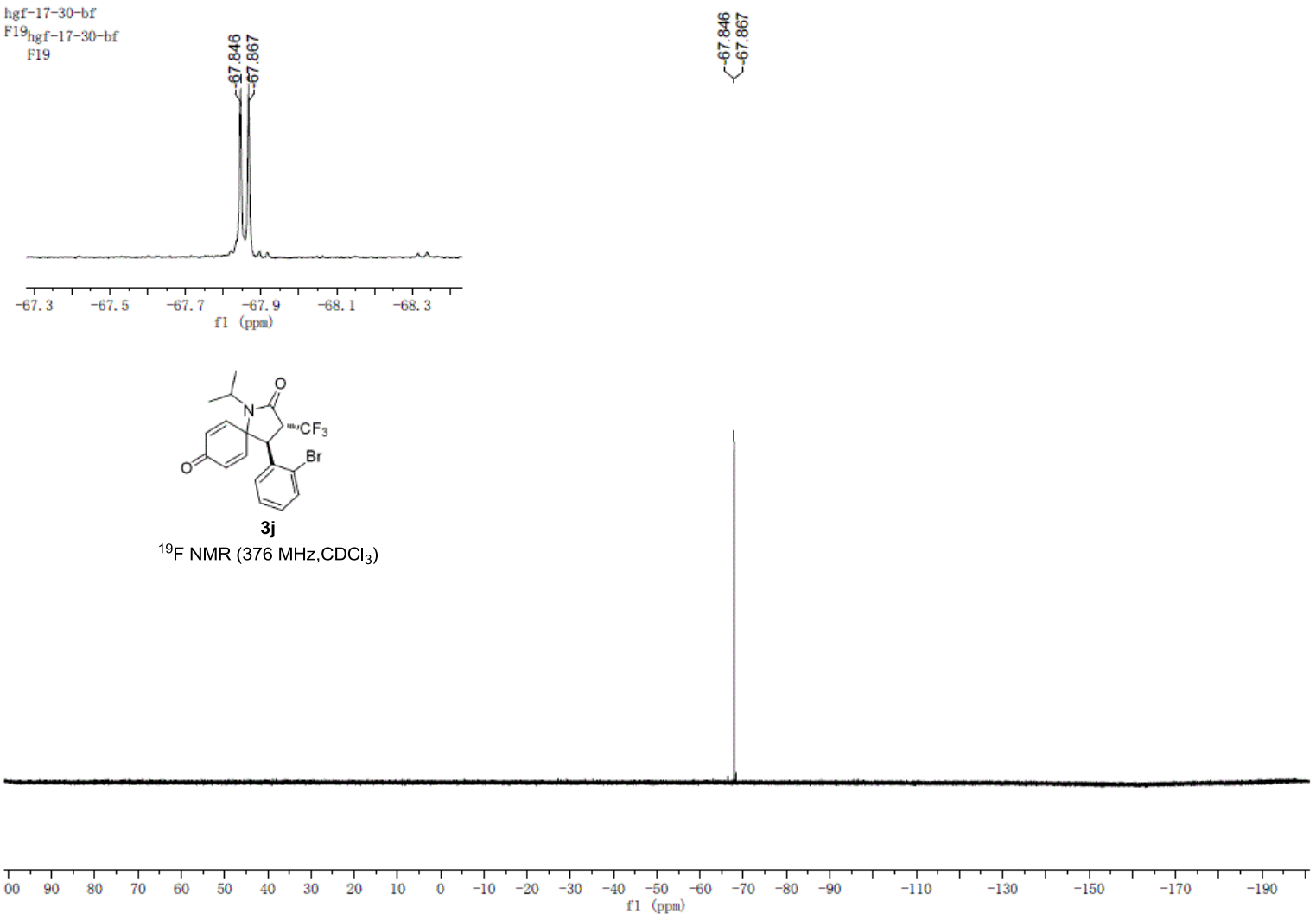
3i

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



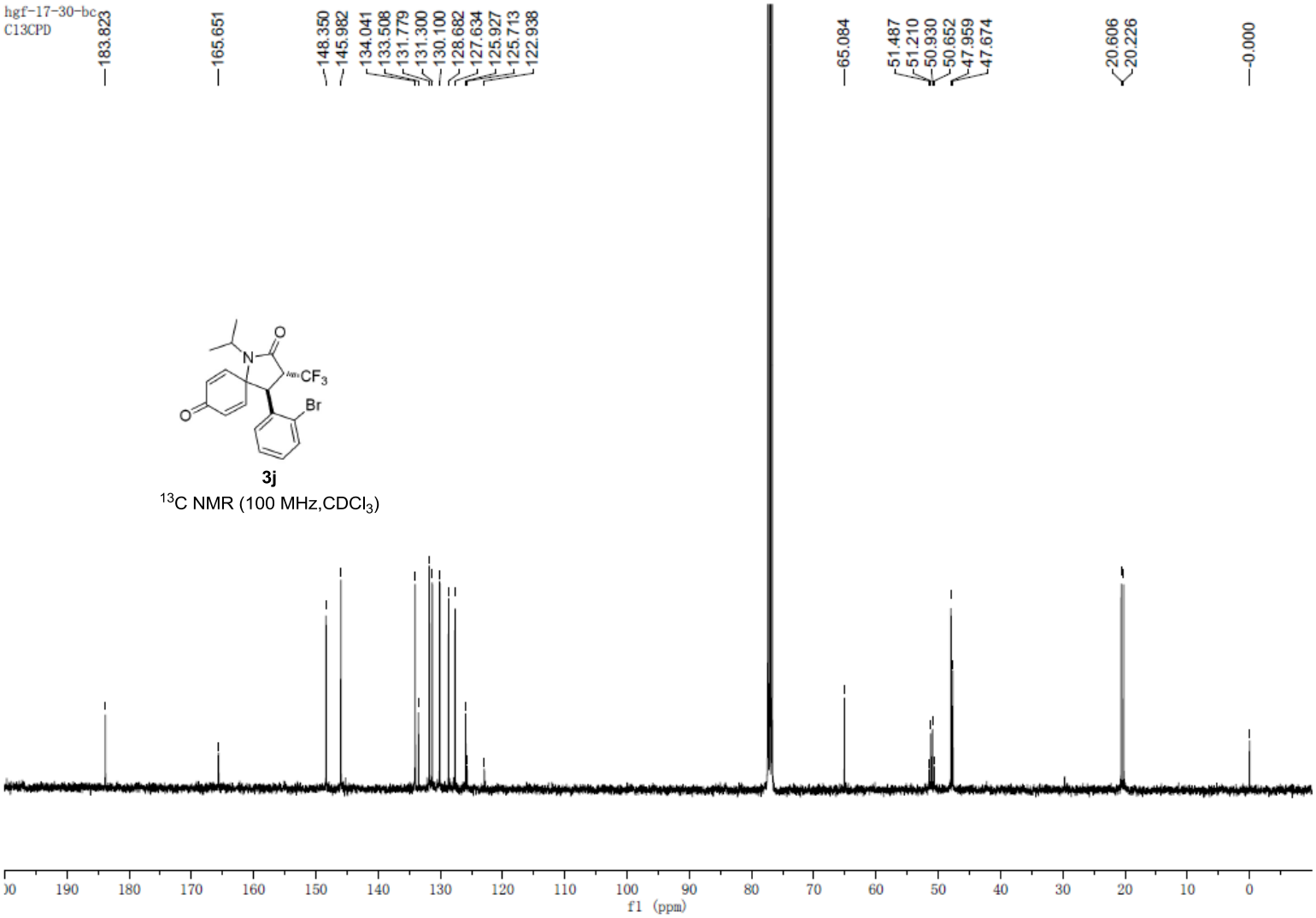
3j

^{1}H NMR (400 MHz, $CDCl_3$)



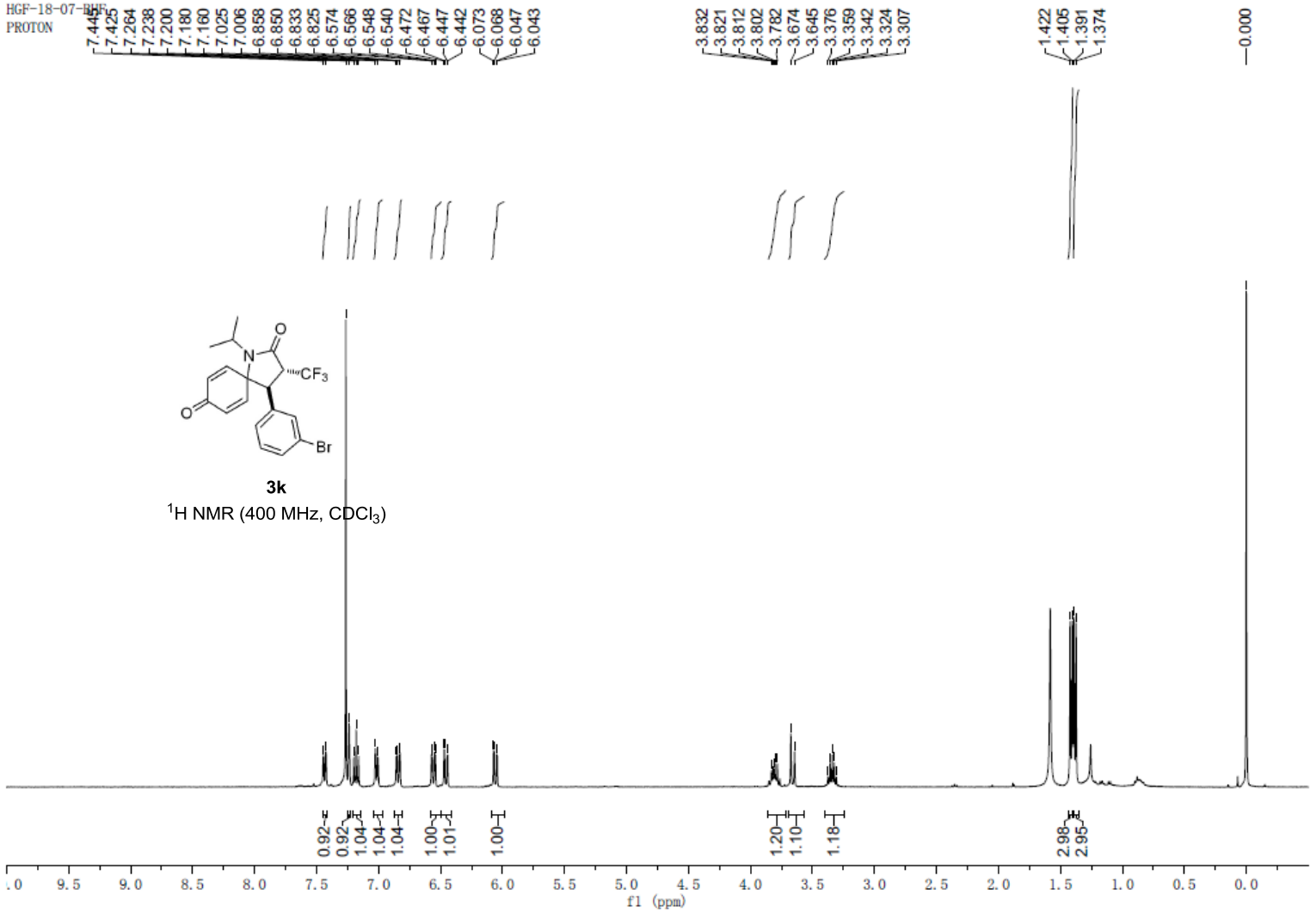
3j

^{19}F NMR (376 MHz,$CDCl_3$)



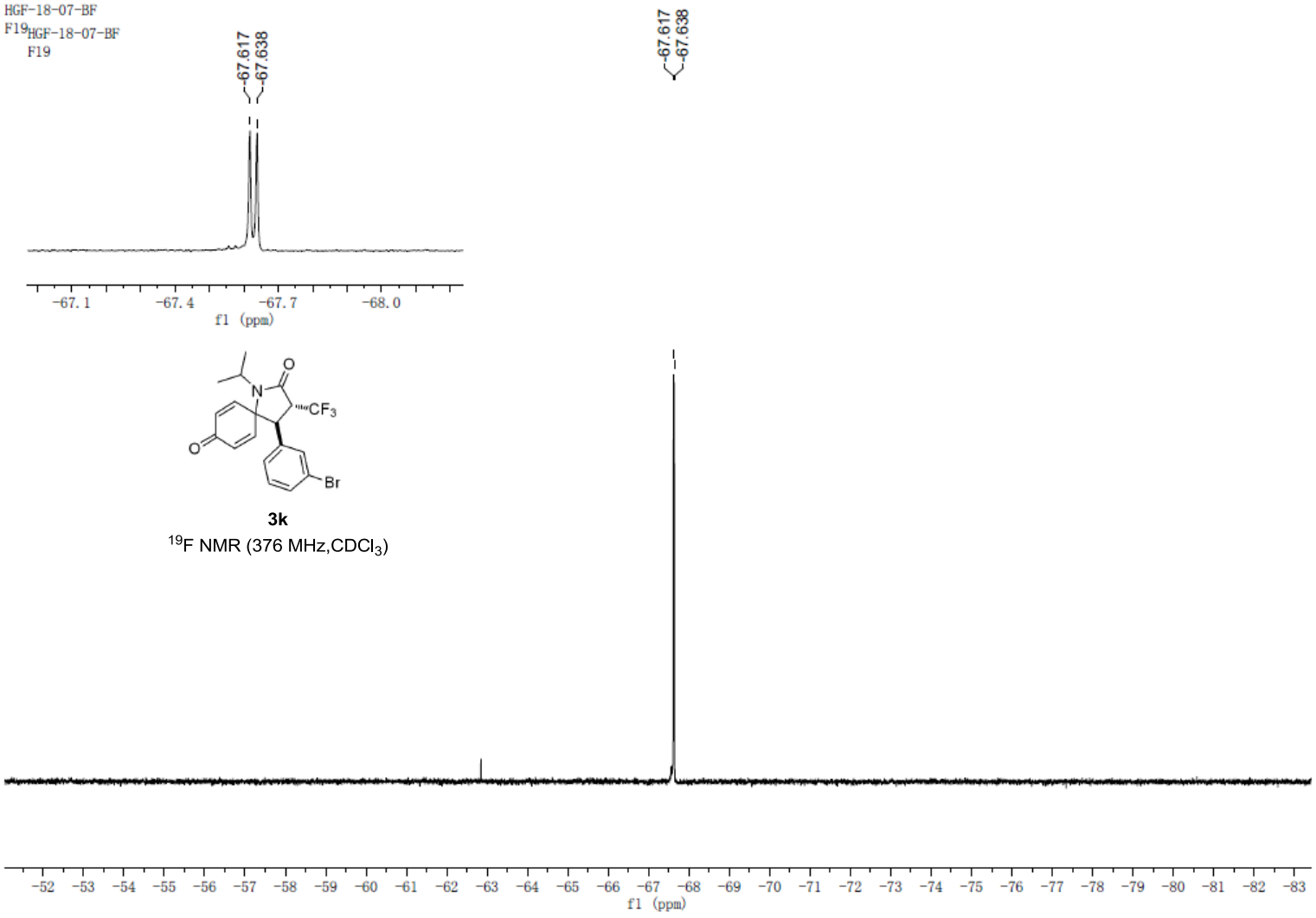
3j

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



3k

^{1}H NMR (400 MHz, $CDCl_3$)

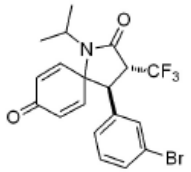


3k

^{19}F NMR (376 MHz,$CDCl_3$)

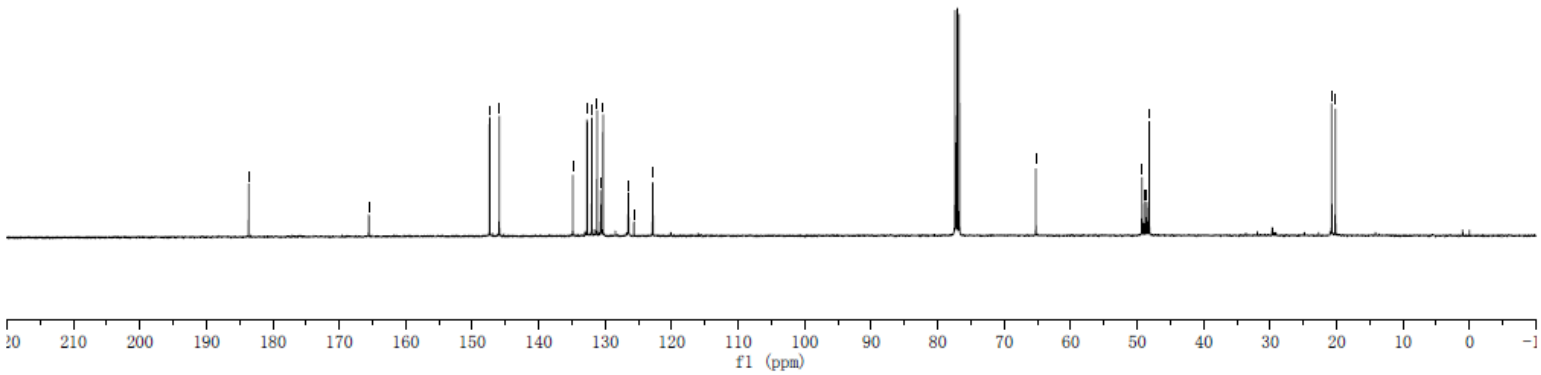
HGF-18-07-BC
test

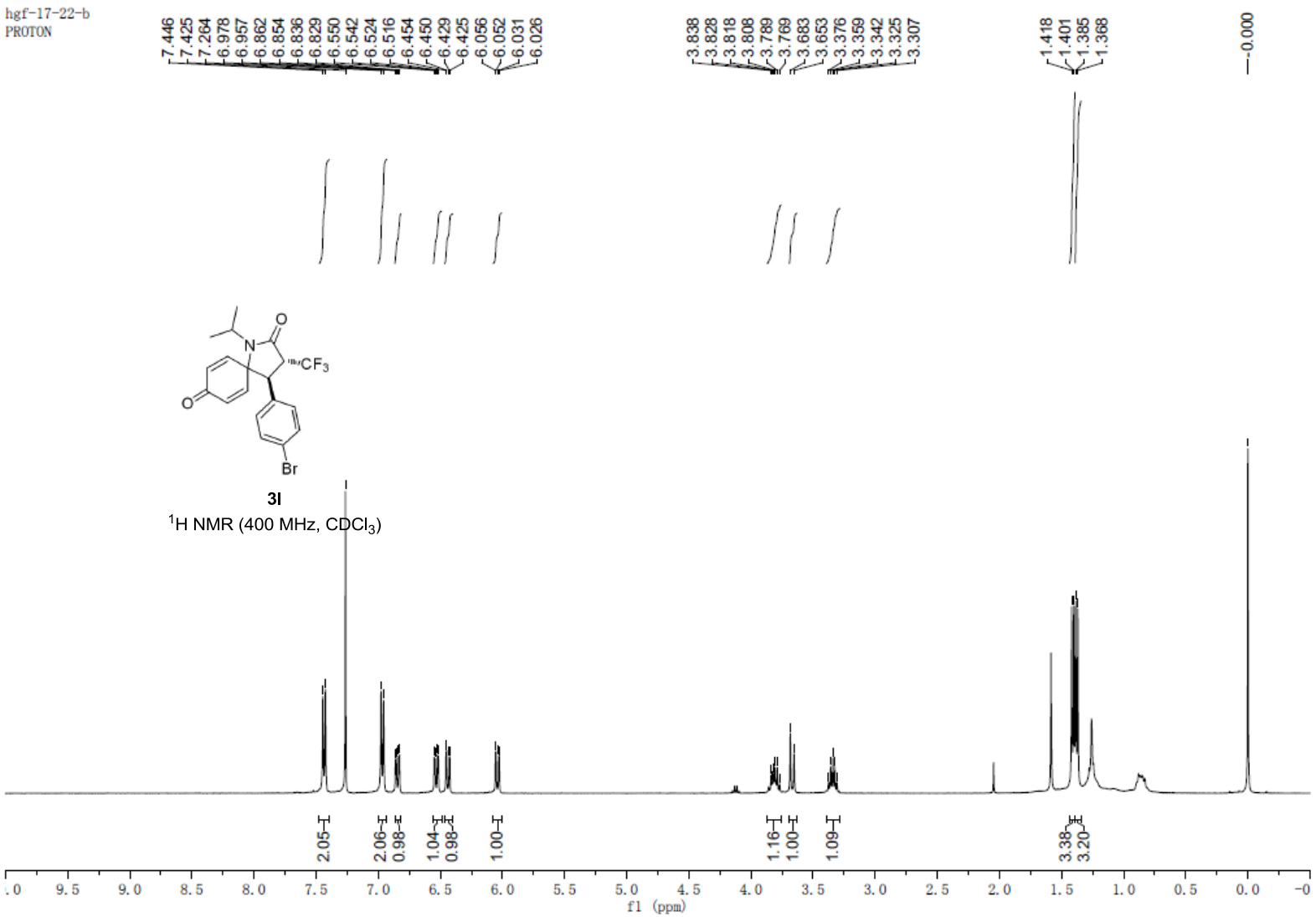
183.630
165.560
147.392
145.934
134.878
132.733
132.029
131.233
130.688
130.325
126.521
125.684
122.909
122.835
65.234
49.253
48.817
48.537
48.187
20.734
20.180



3k

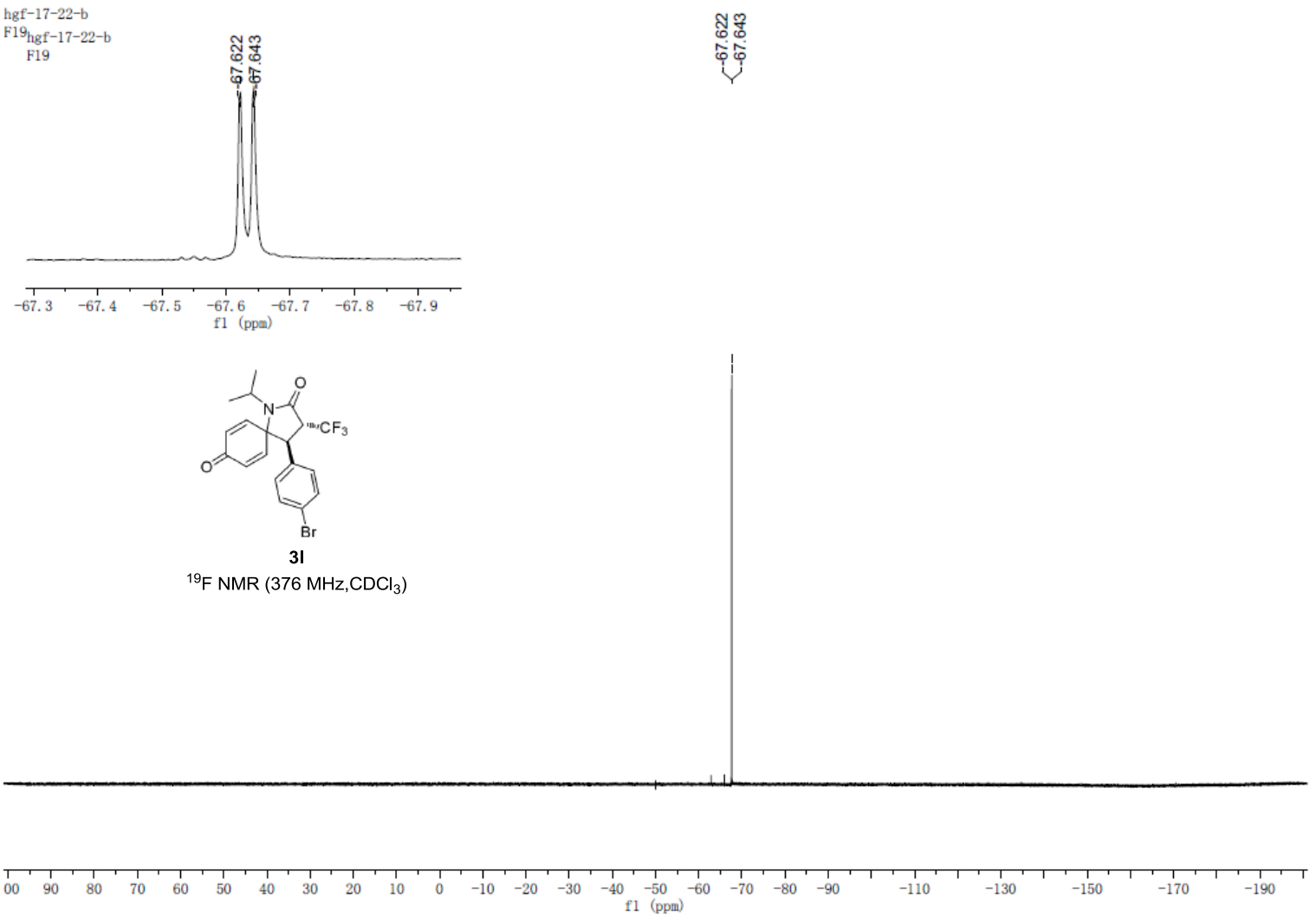
^{13}C NMR (100 MHz,$CDCl_3$)





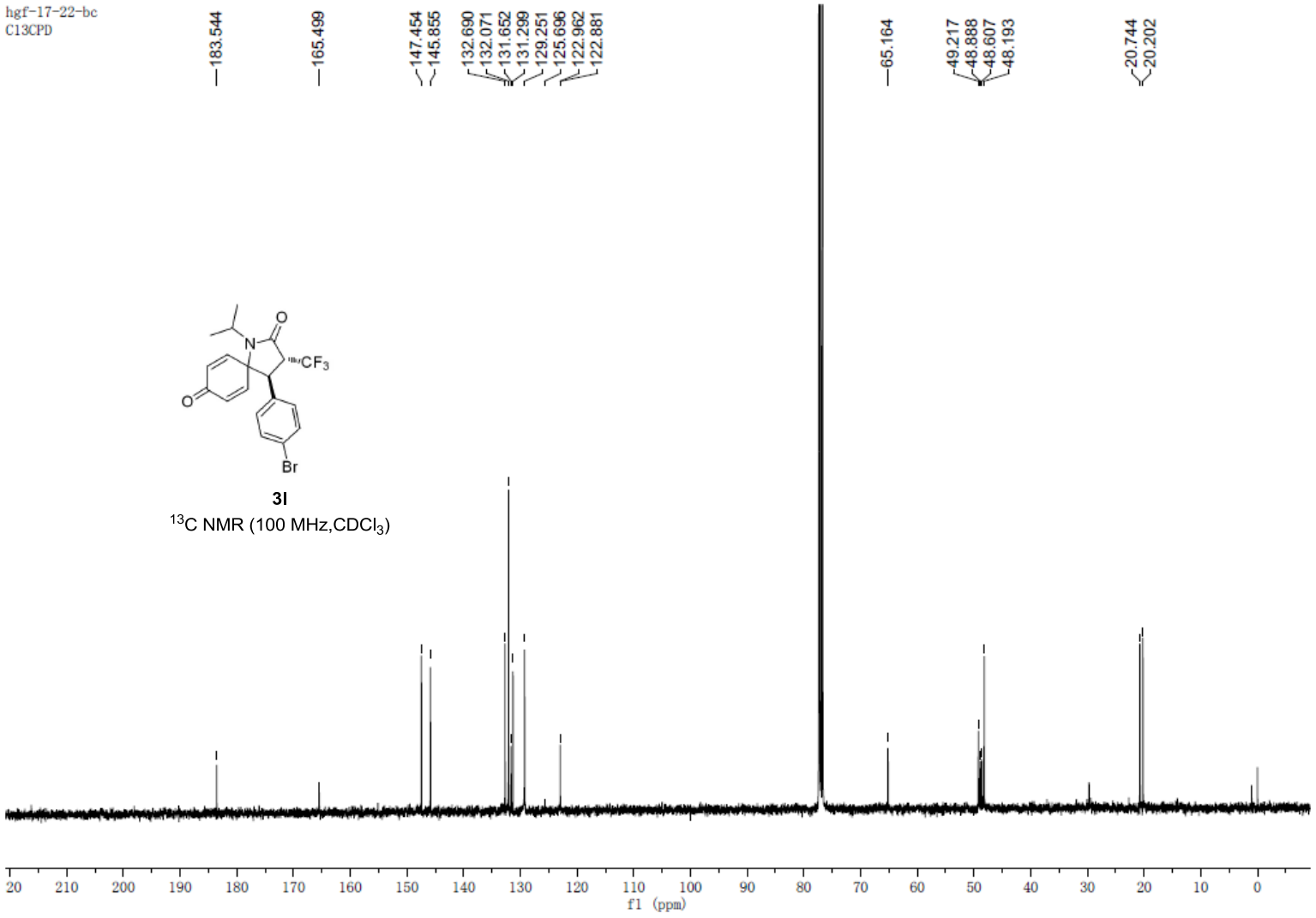
3l

^{1}H NMR (400 MHz, $CDCl_3$)



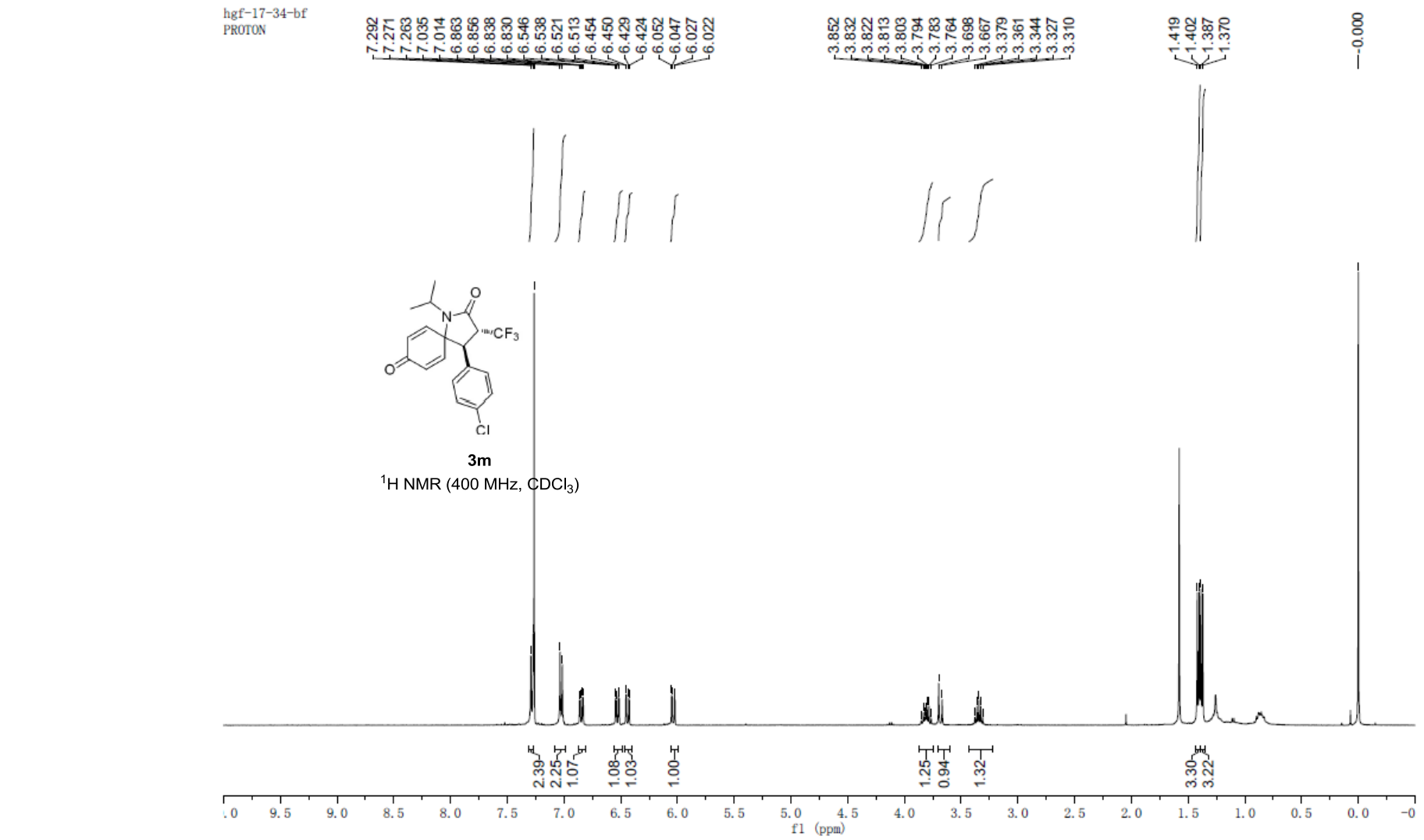
3l

^{19}F NMR (376 MHz,$CDCl_3$)



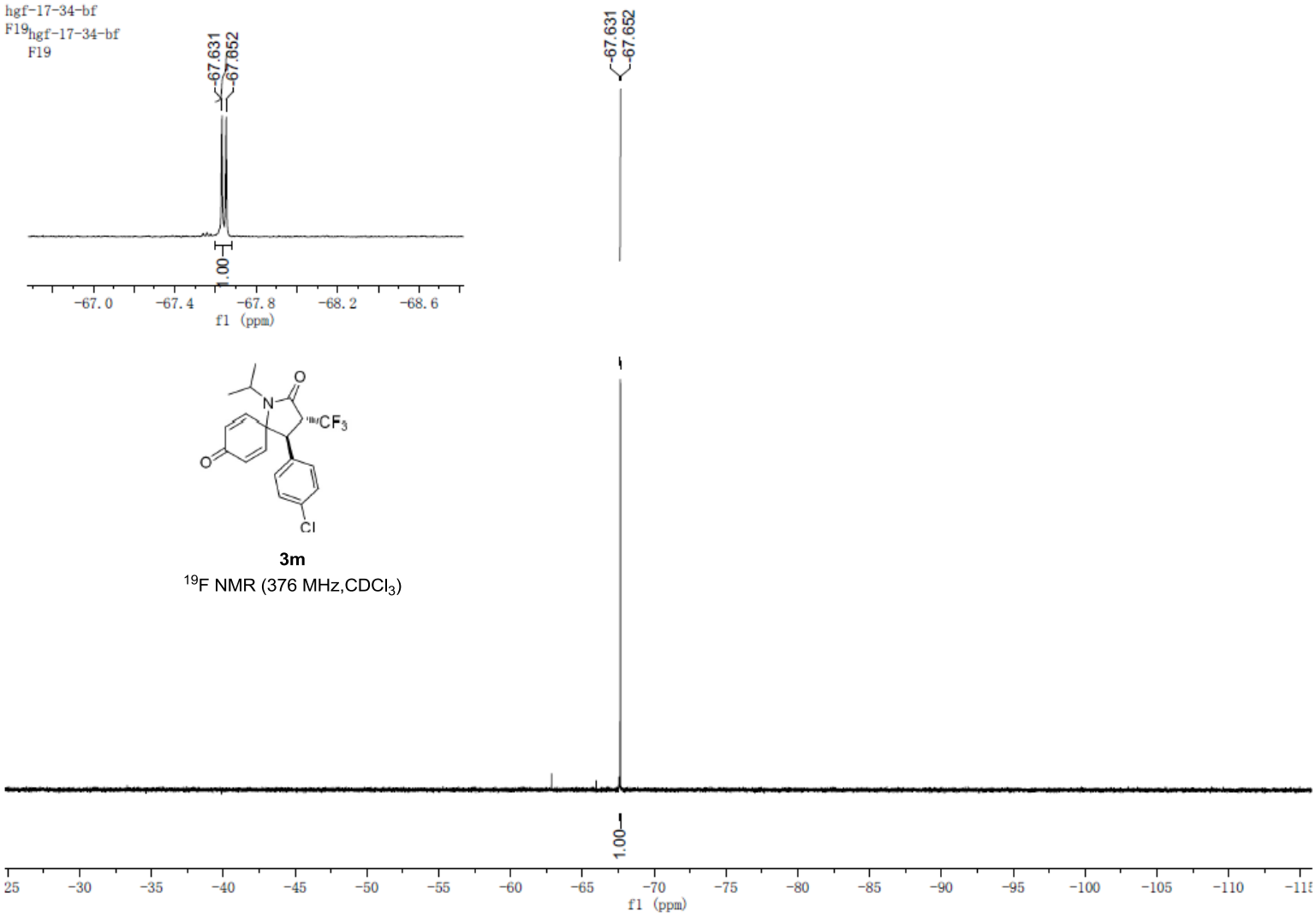
3l

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



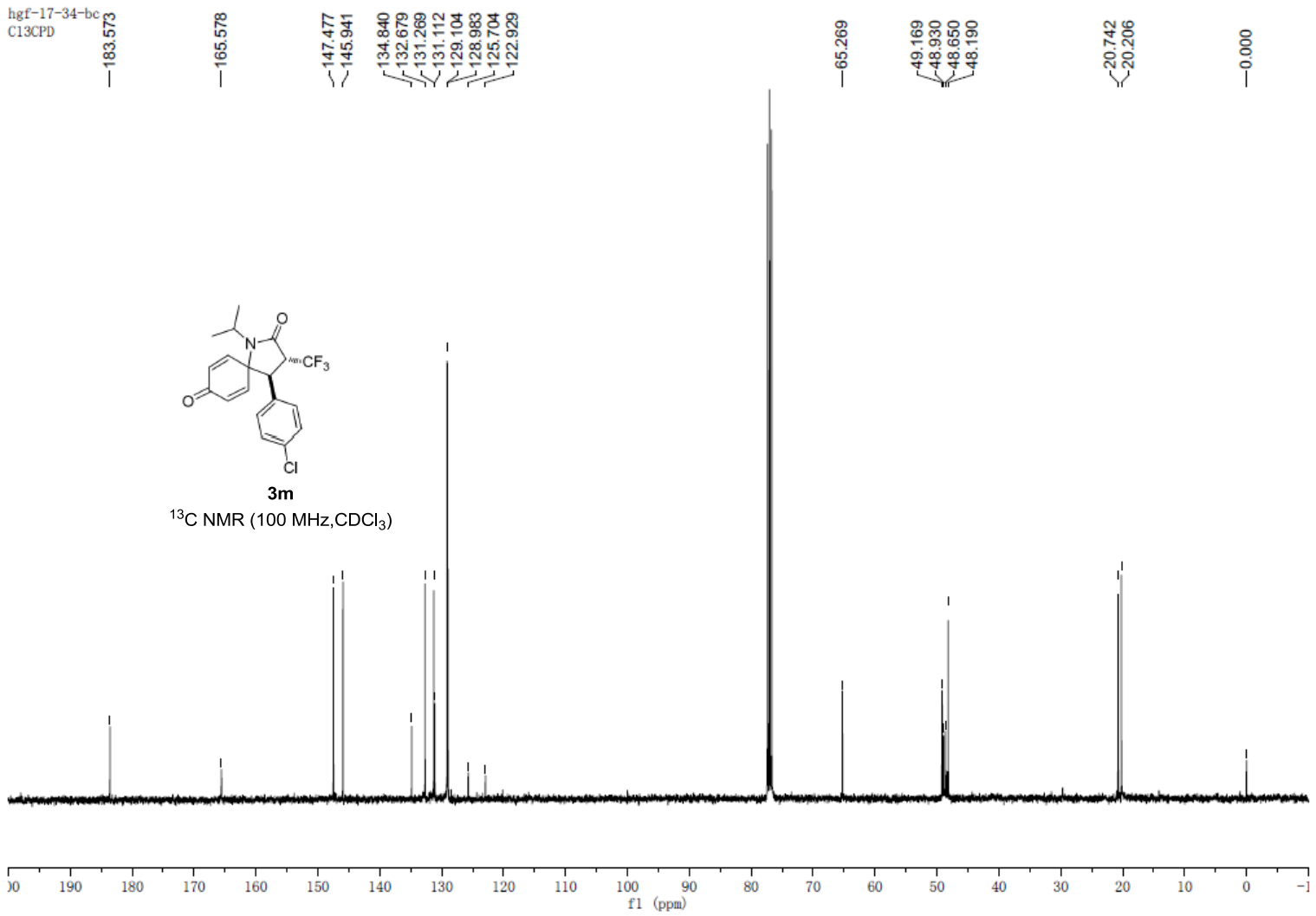
3m

^{1}H NMR (400 MHz, $CDCl_3$)



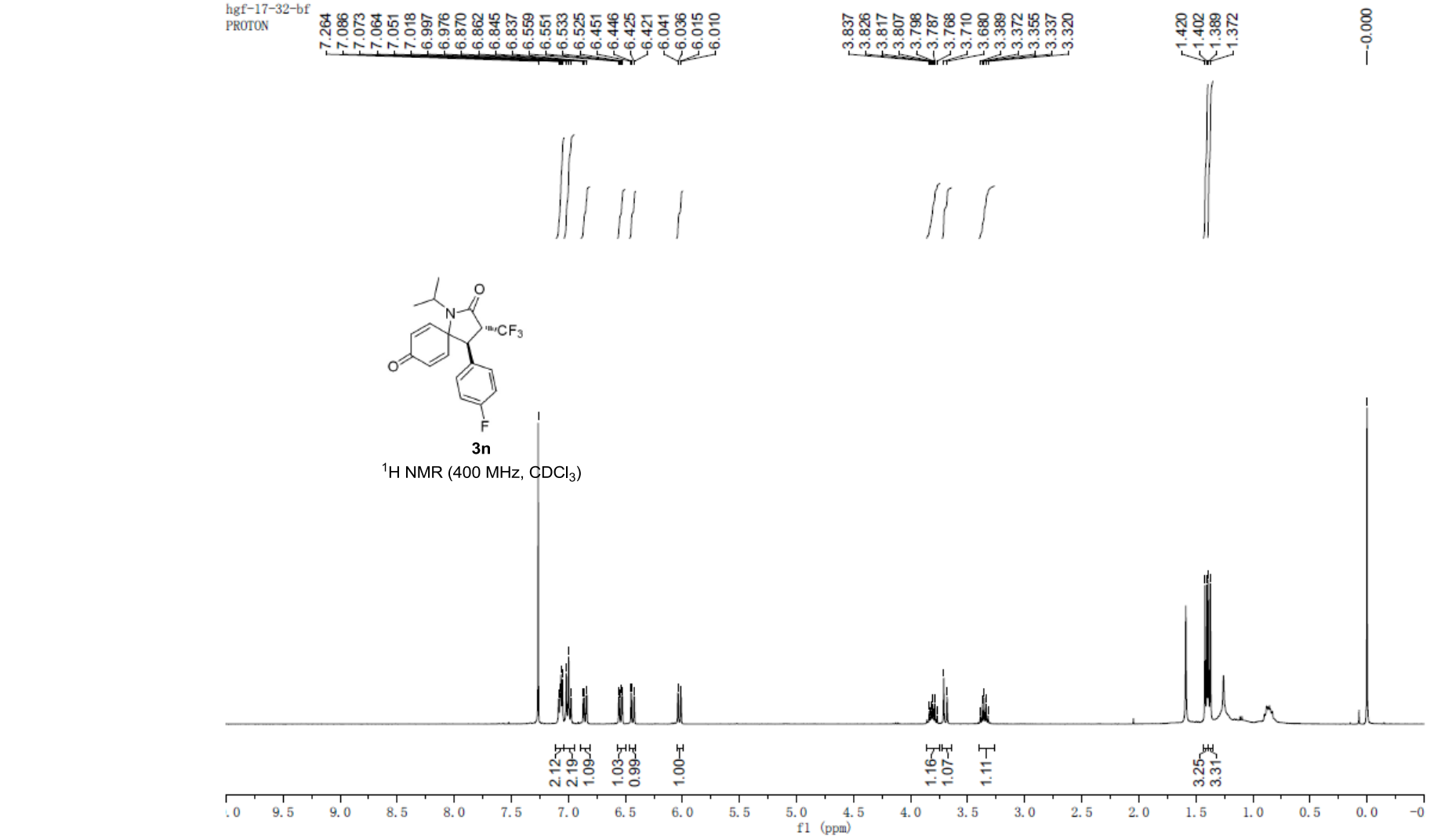
3m

^{19}F NMR (376 MHz,$CDCl_3$)



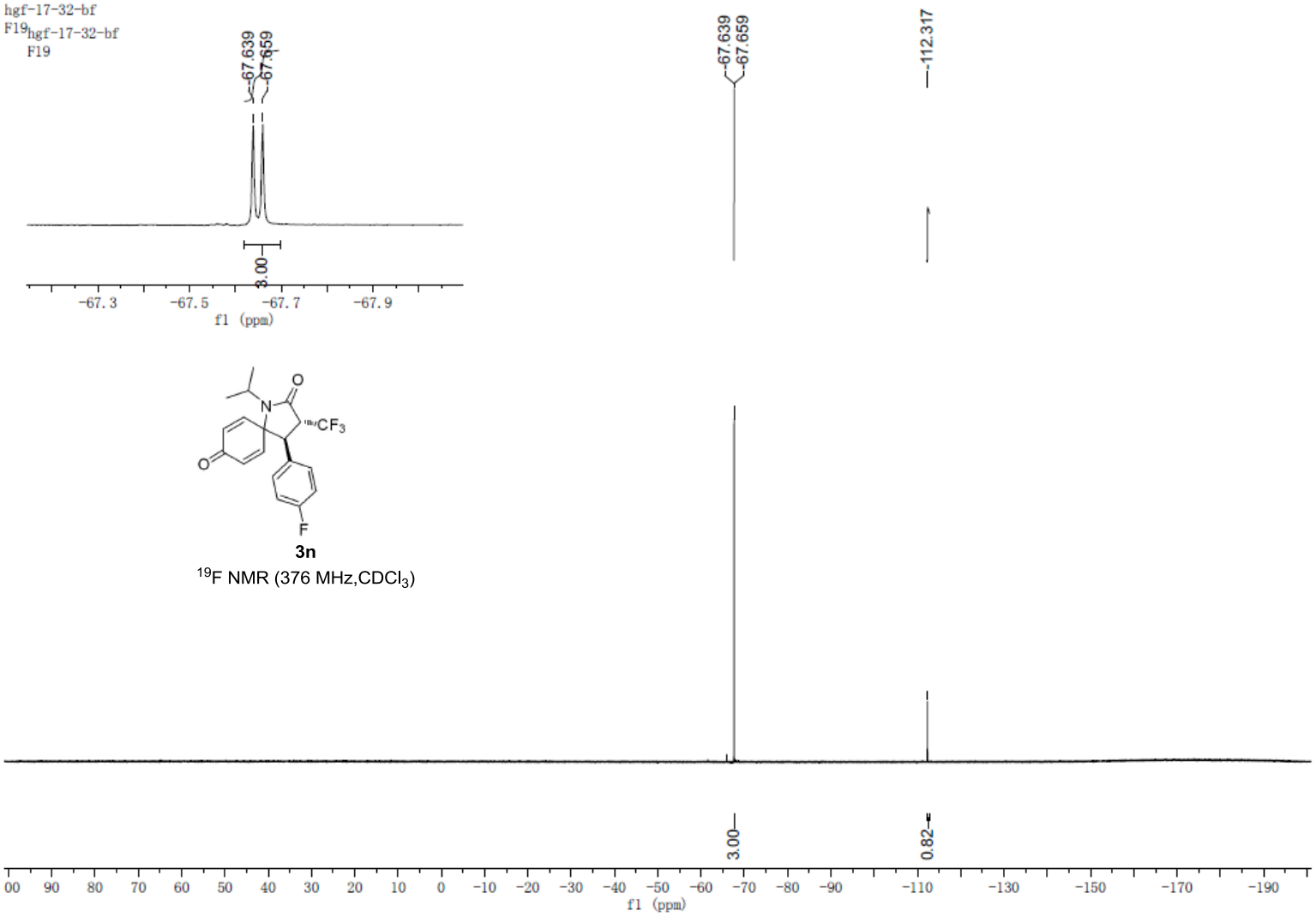
3m

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



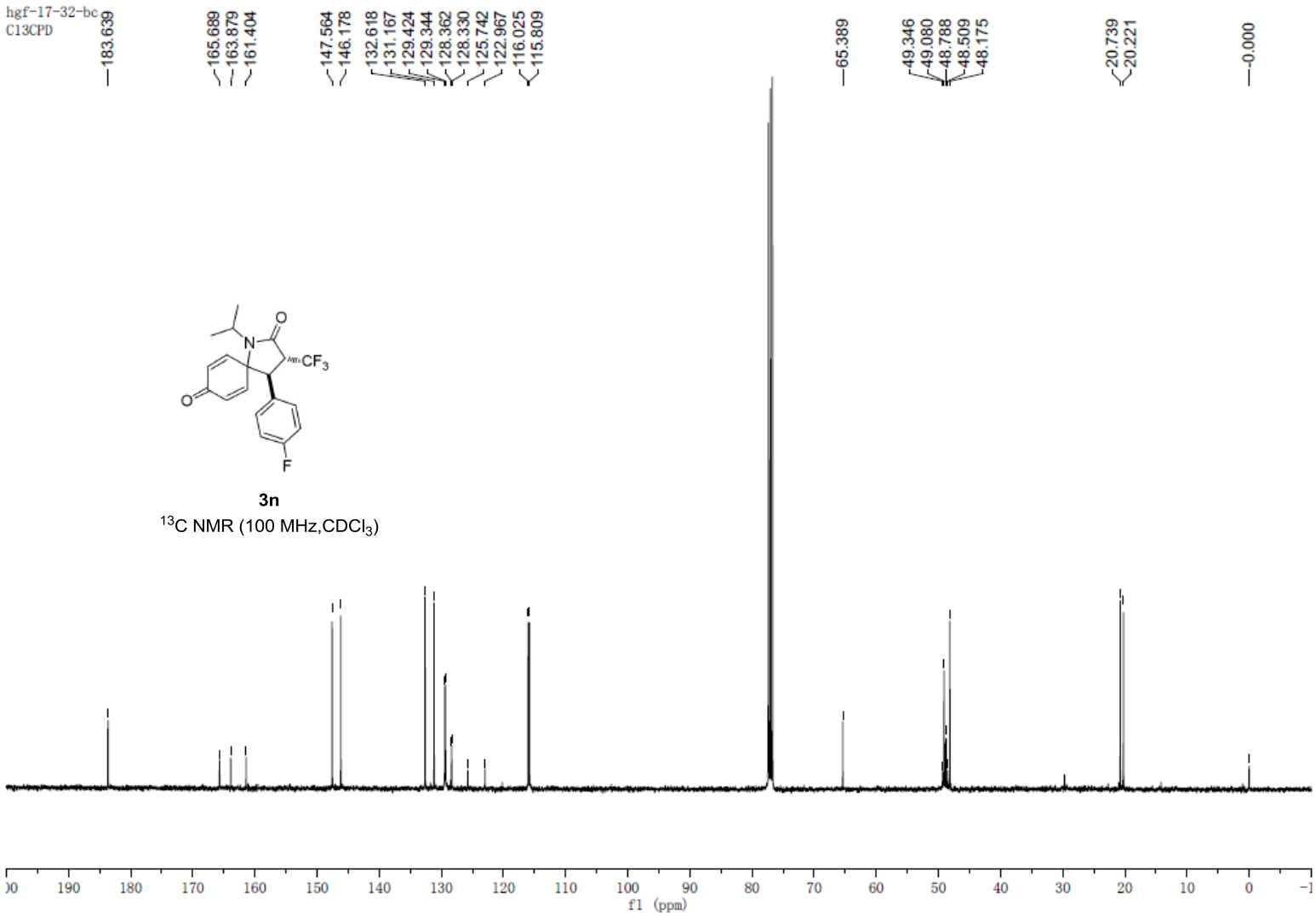
3n

^{1}H NMR (400 MHz, $CDCl_3$)



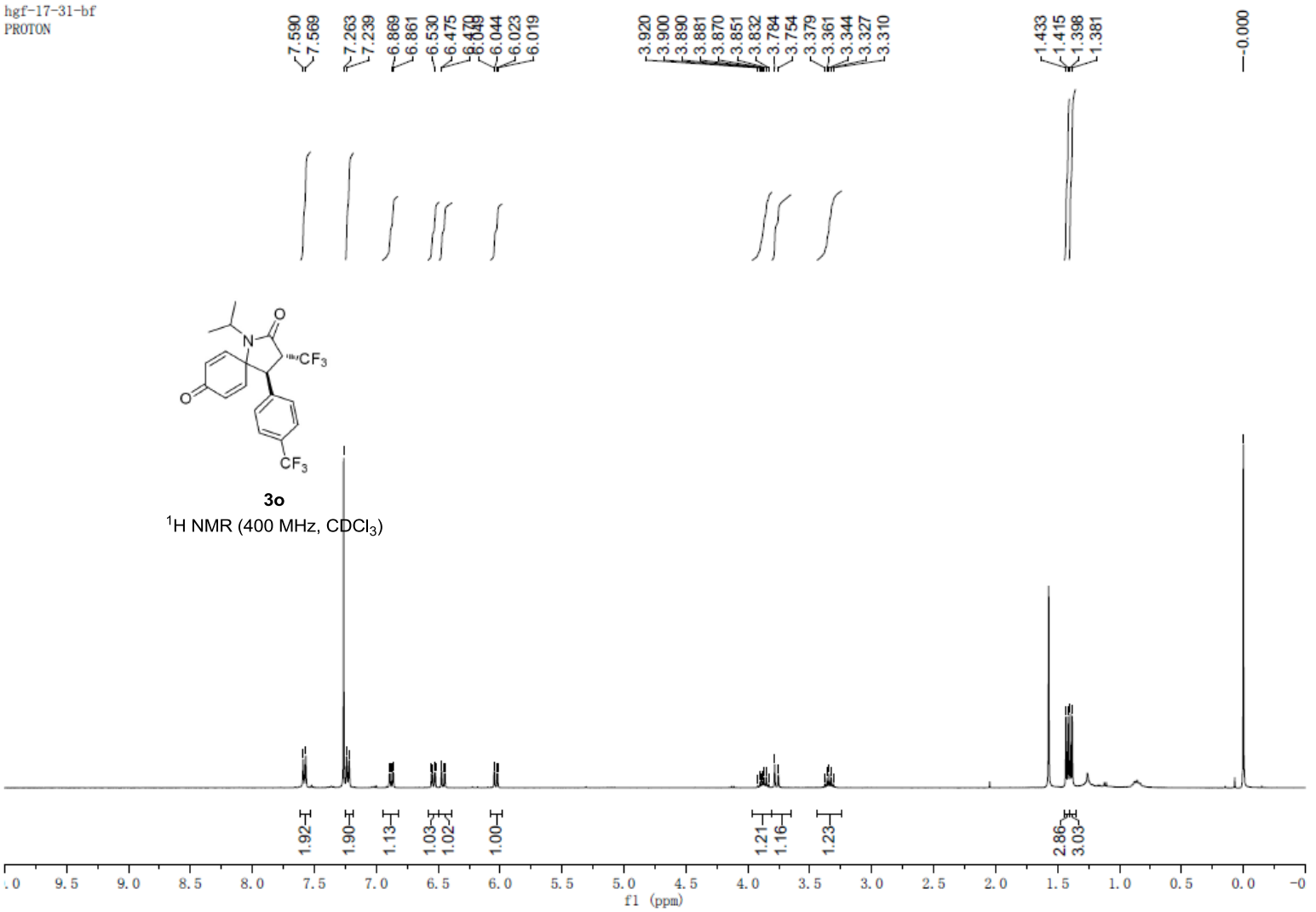
3n

^{19}F NMR (376 MHz,$CDCl_3$)



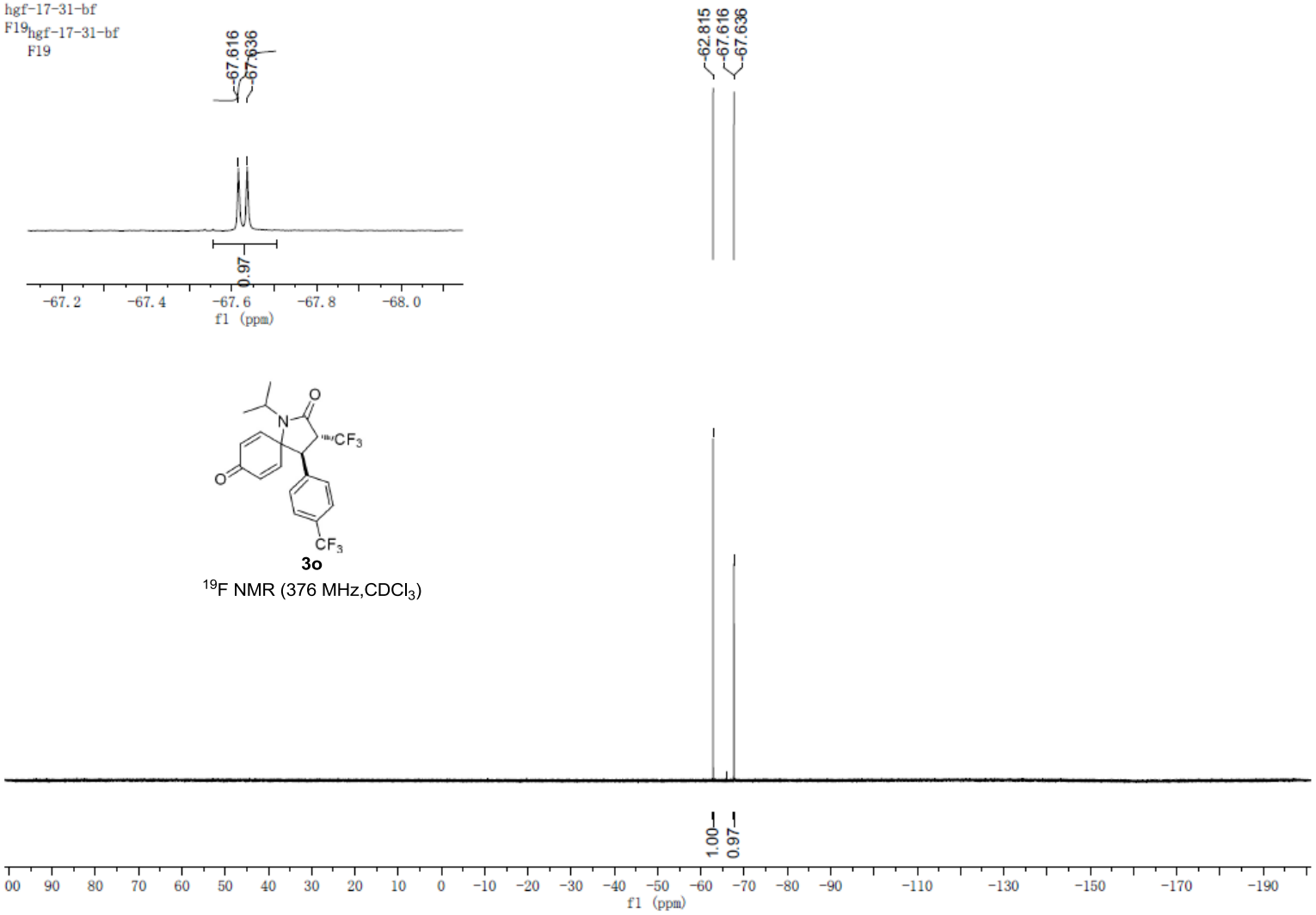
3n

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



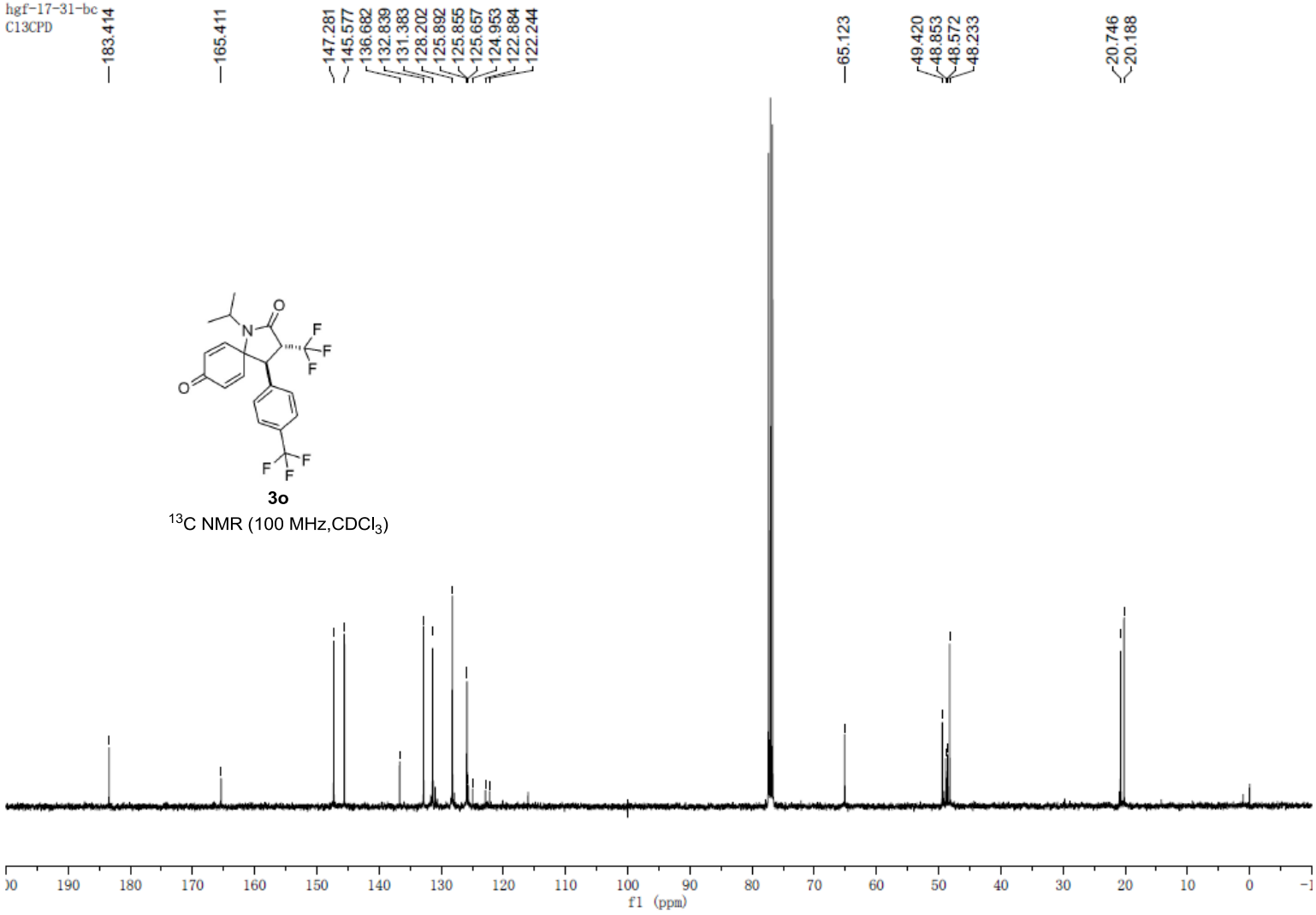
3o

^{1}H NMR (400 MHz, $CDCl_3$)



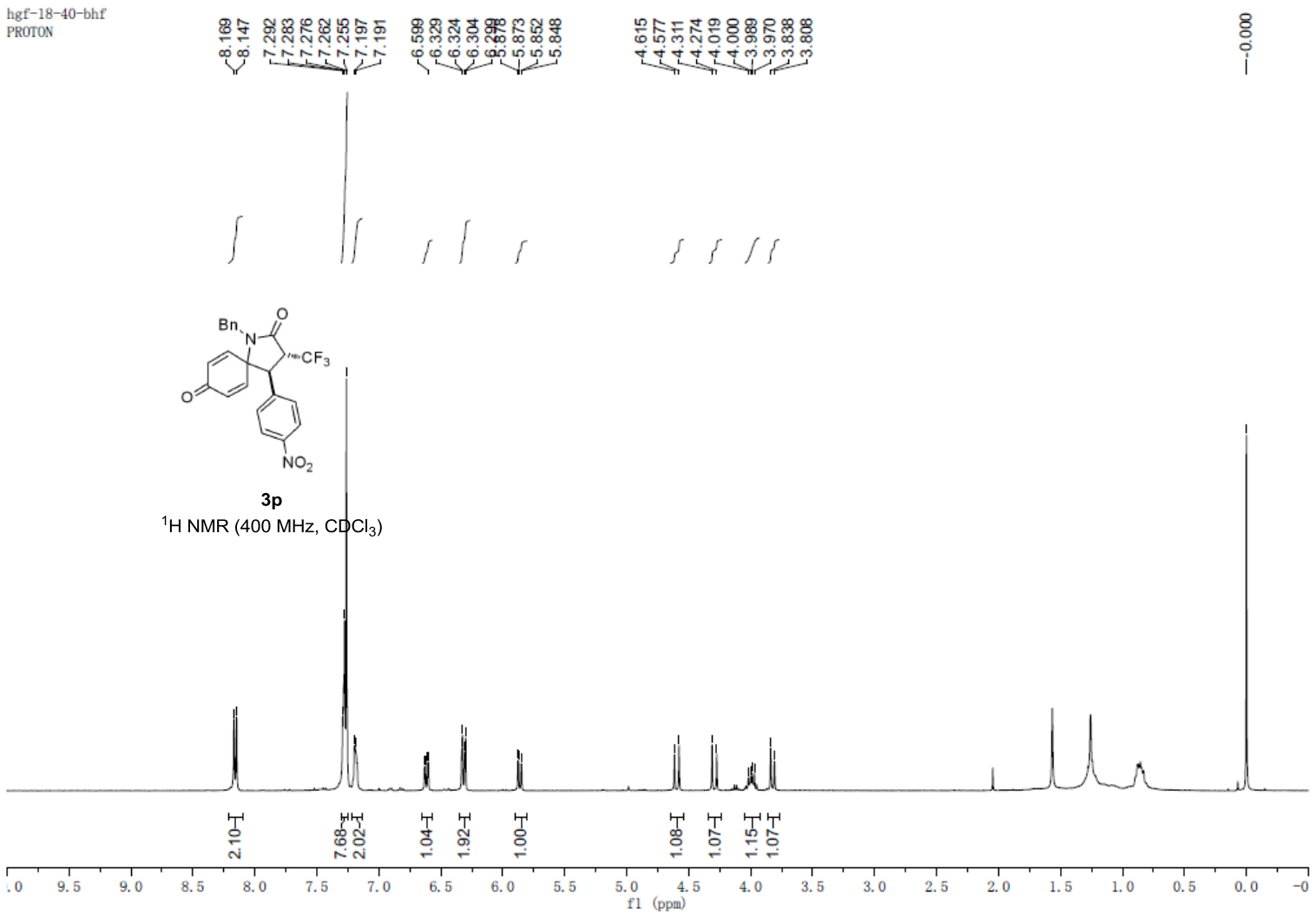
3o

^{19}F NMR (376 MHz,$CDCl_3$)



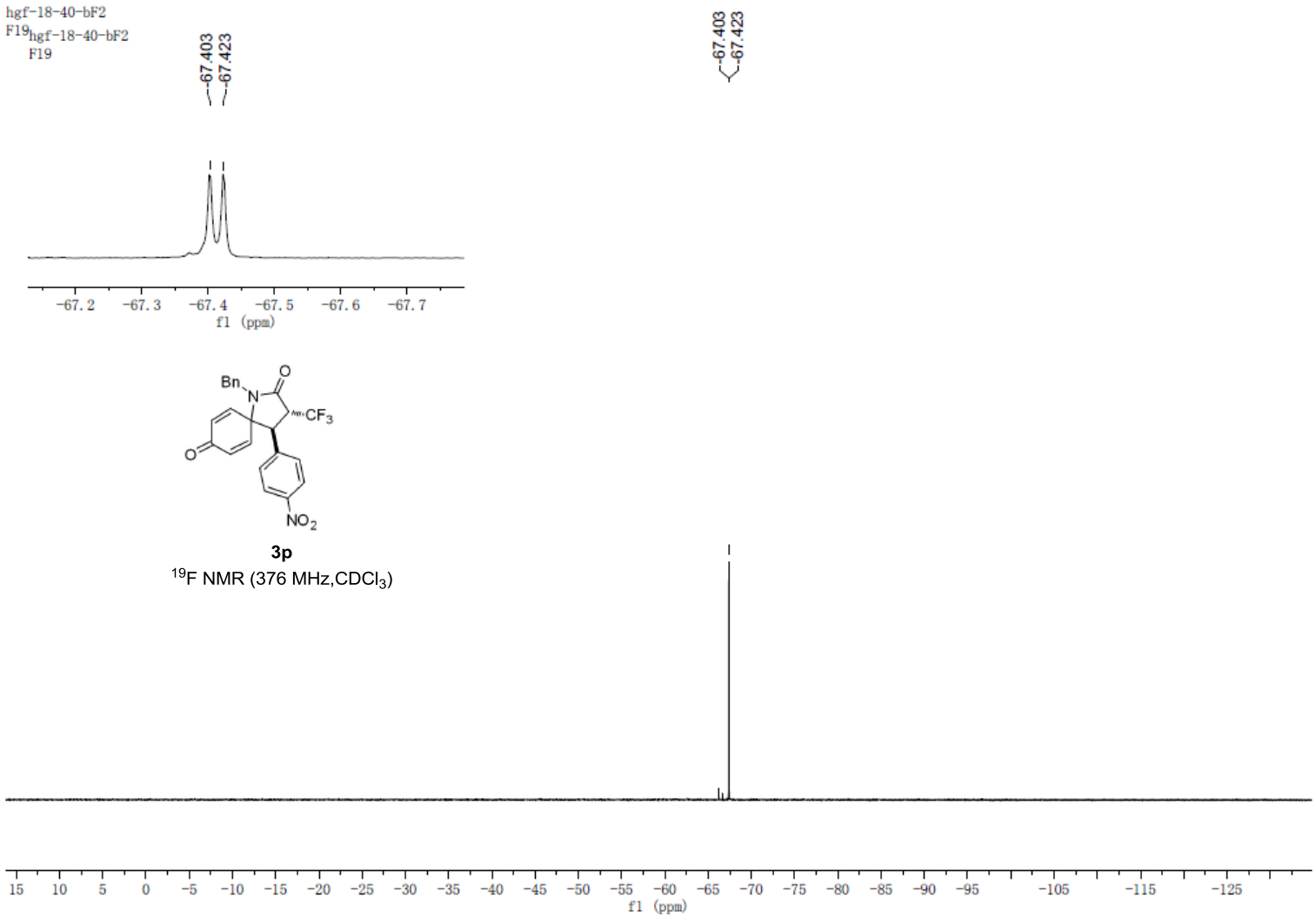
3o

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



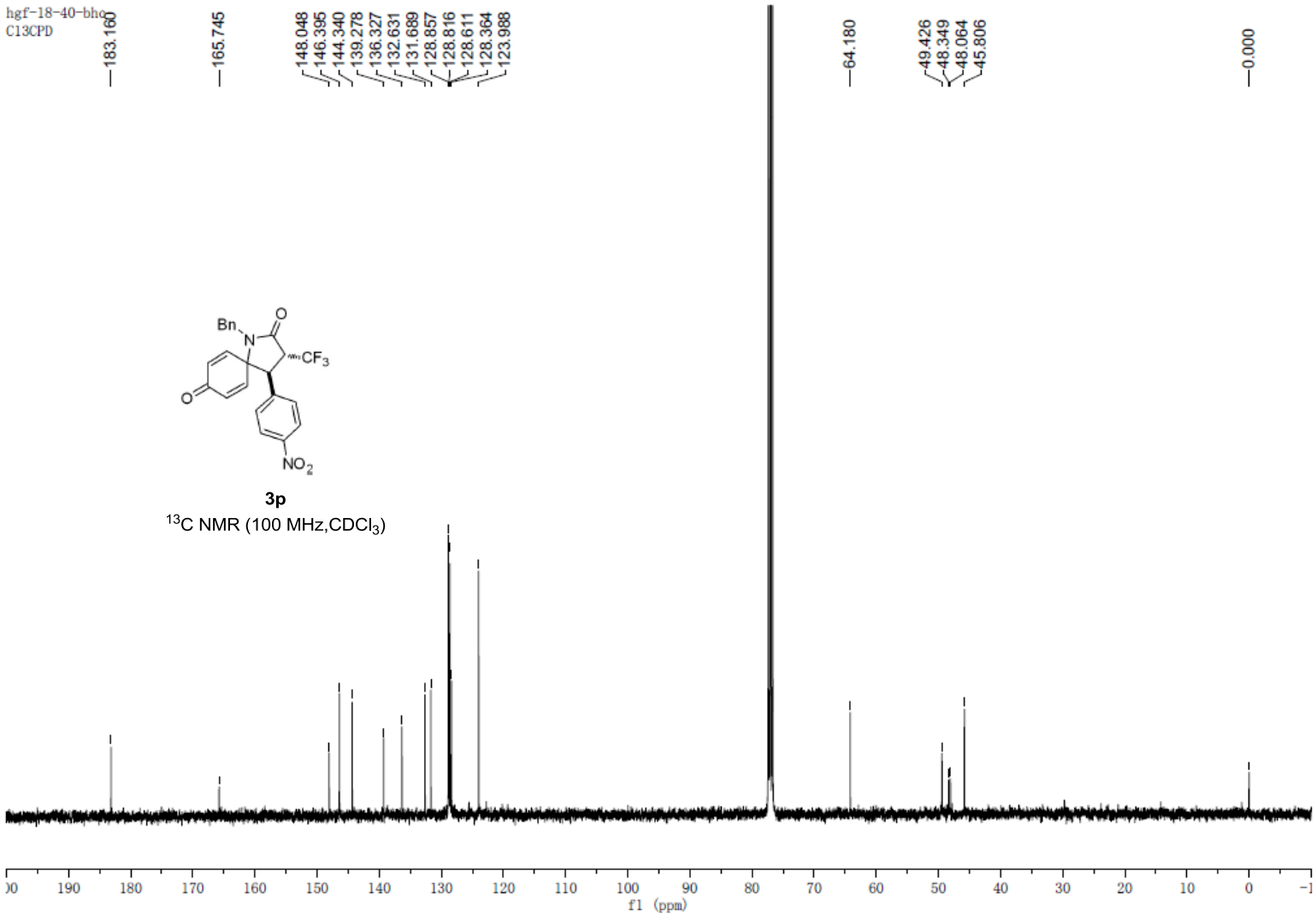
3p

^{1}H NMR (400 MHz, $CDCl_3$)



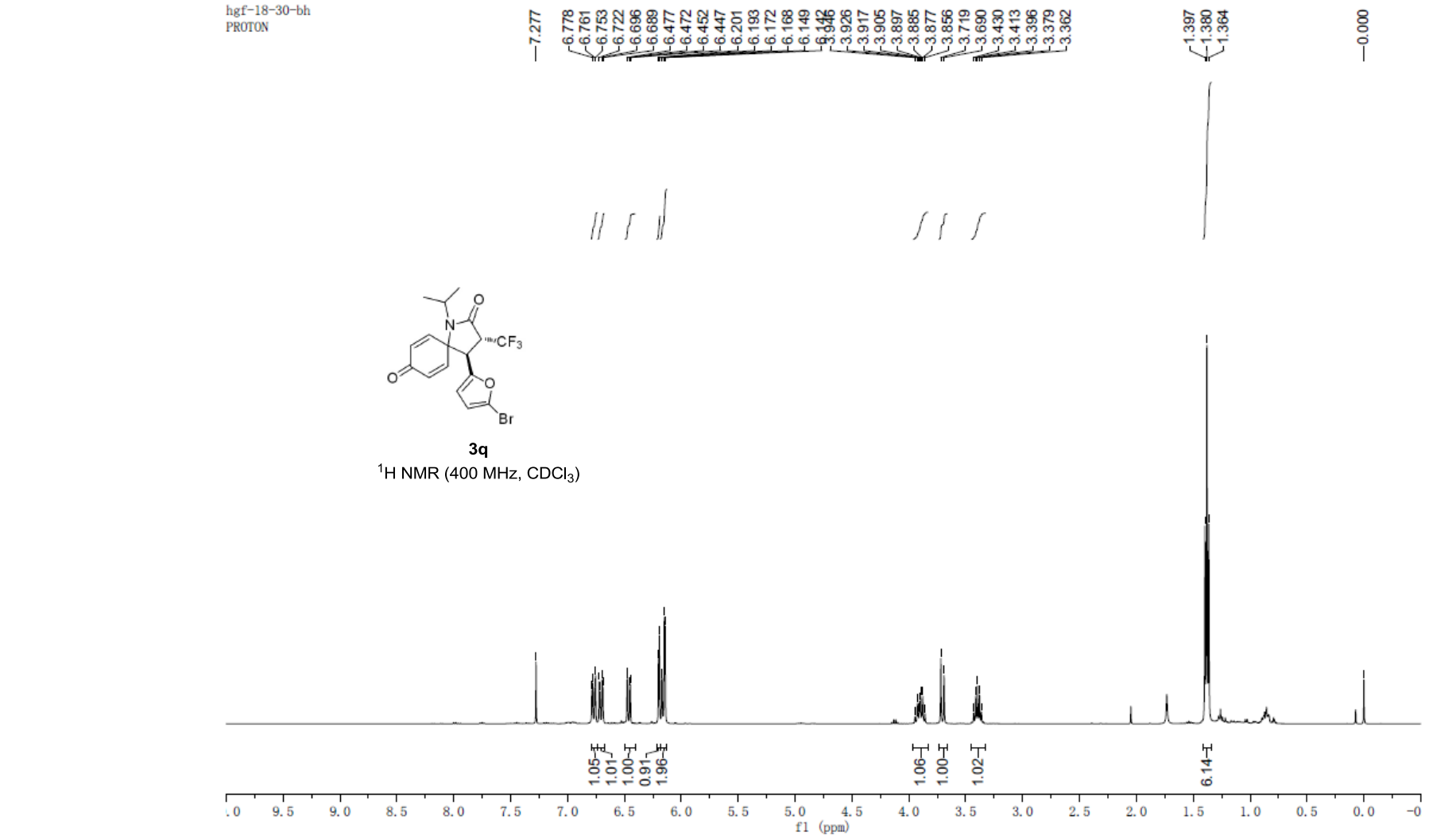
3p

^{19}F NMR (376 MHz,$CDCl_3$)



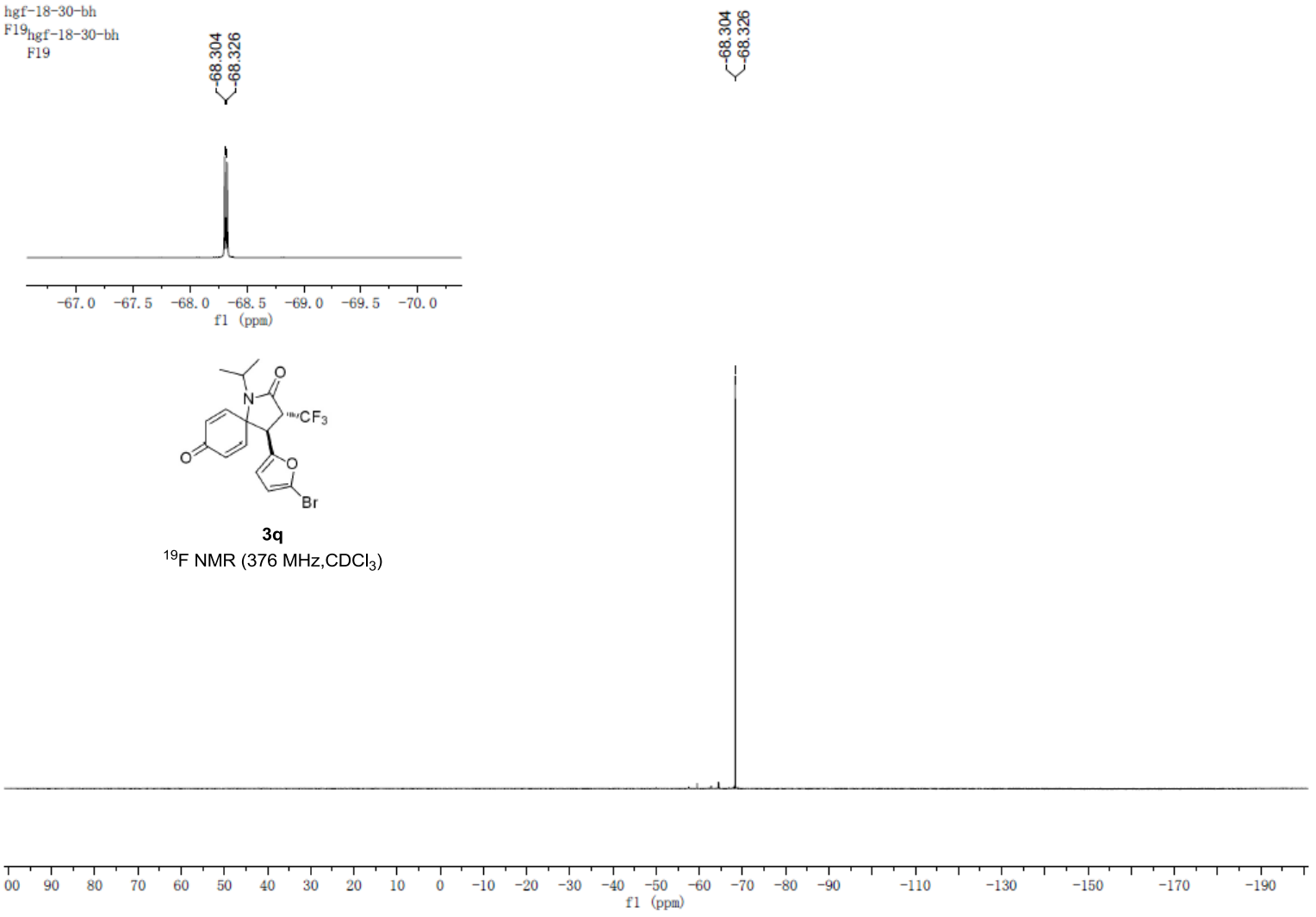
3p

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



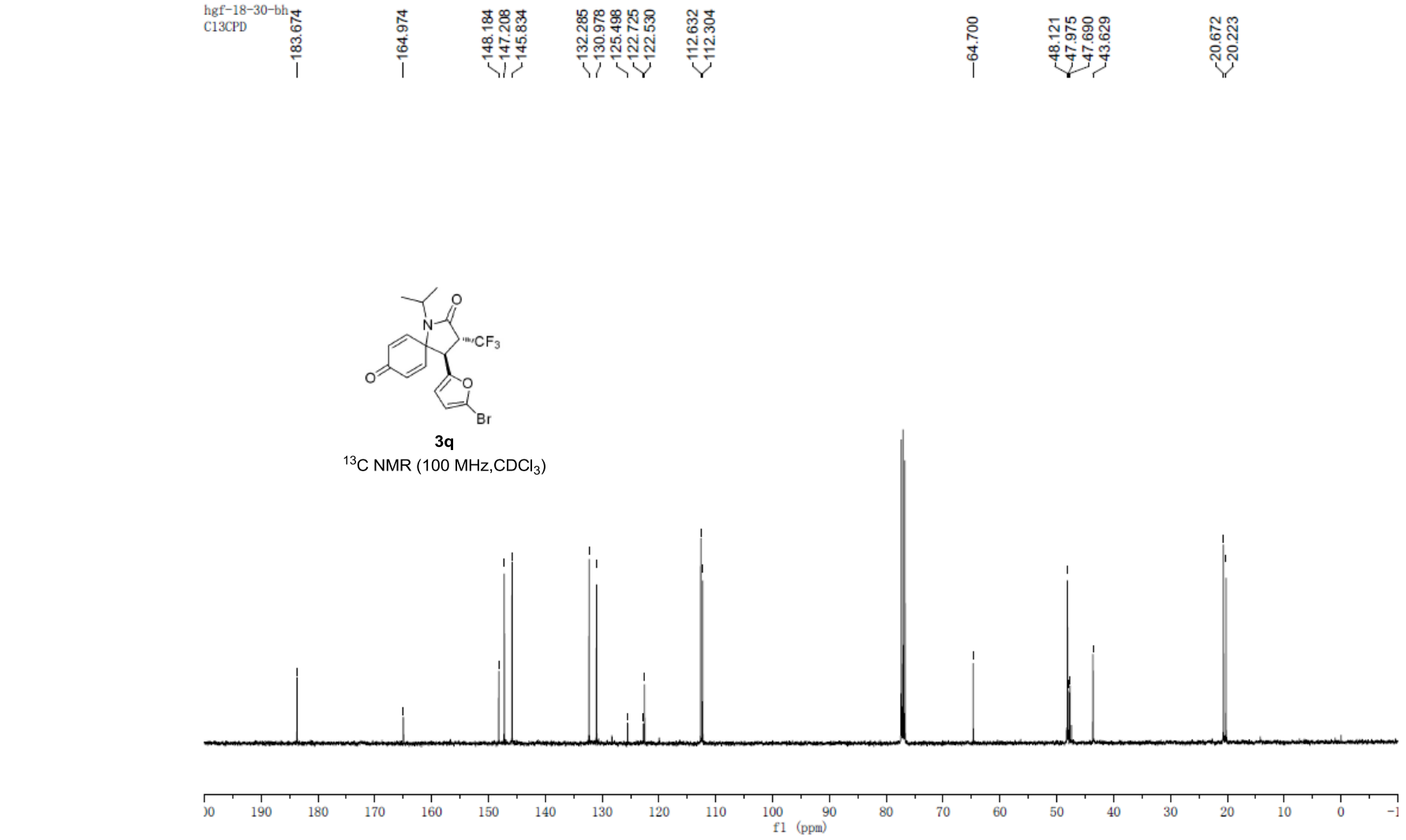
3q

^{1}H NMR (400 MHz, $CDCl_3$)



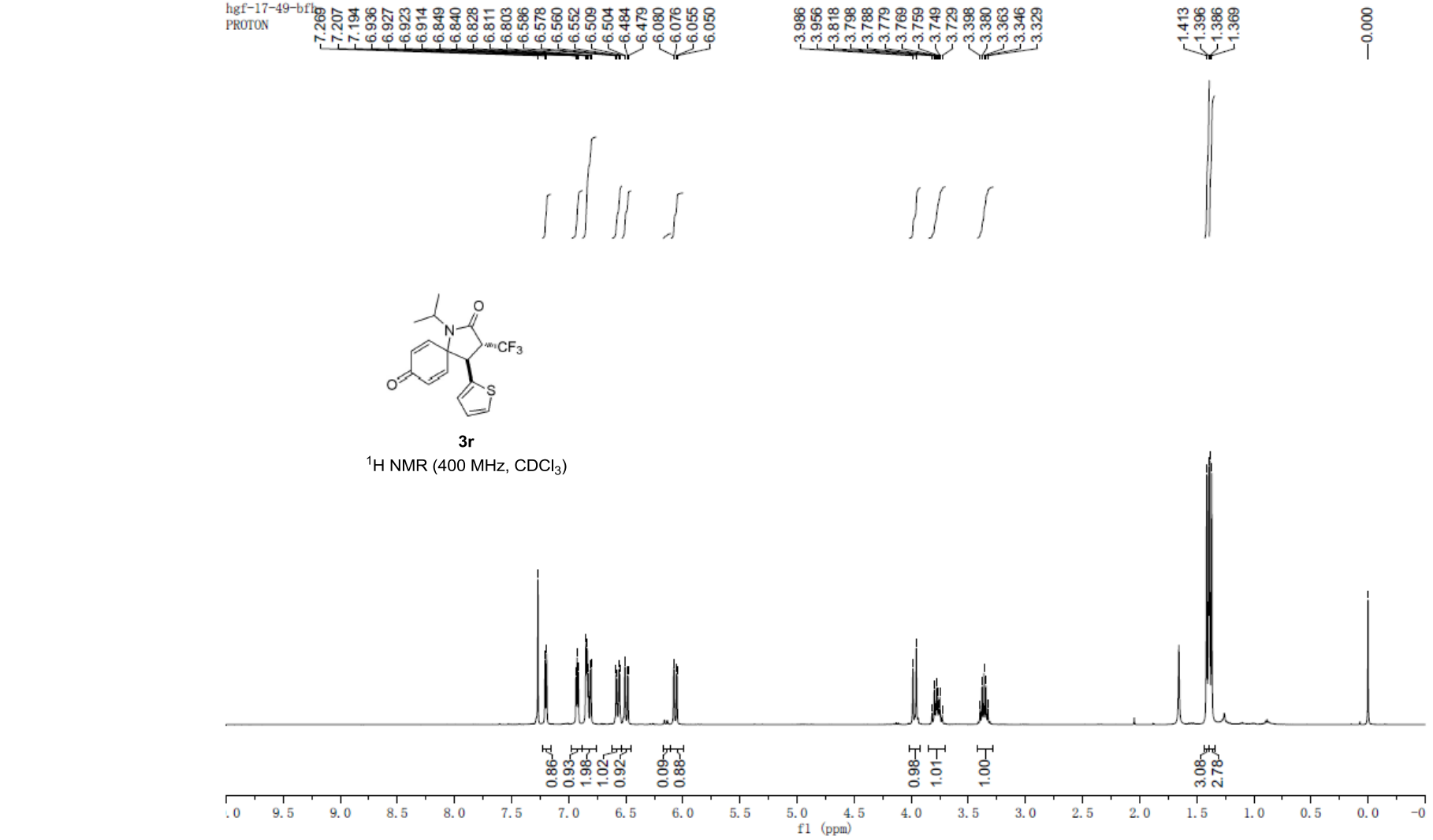
3q

^{19}F NMR (376 MHz,$CDCl_3$)



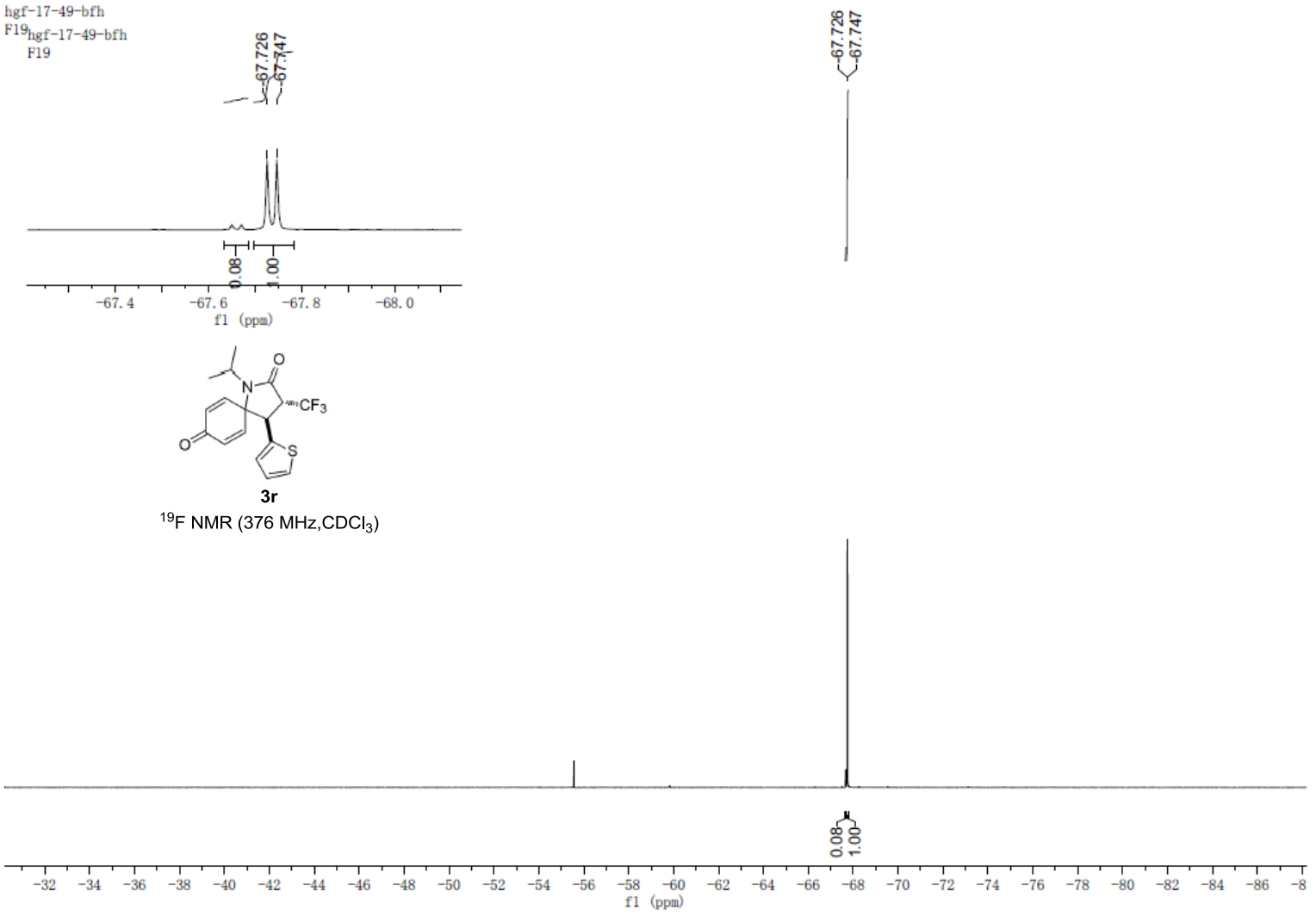
3q

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



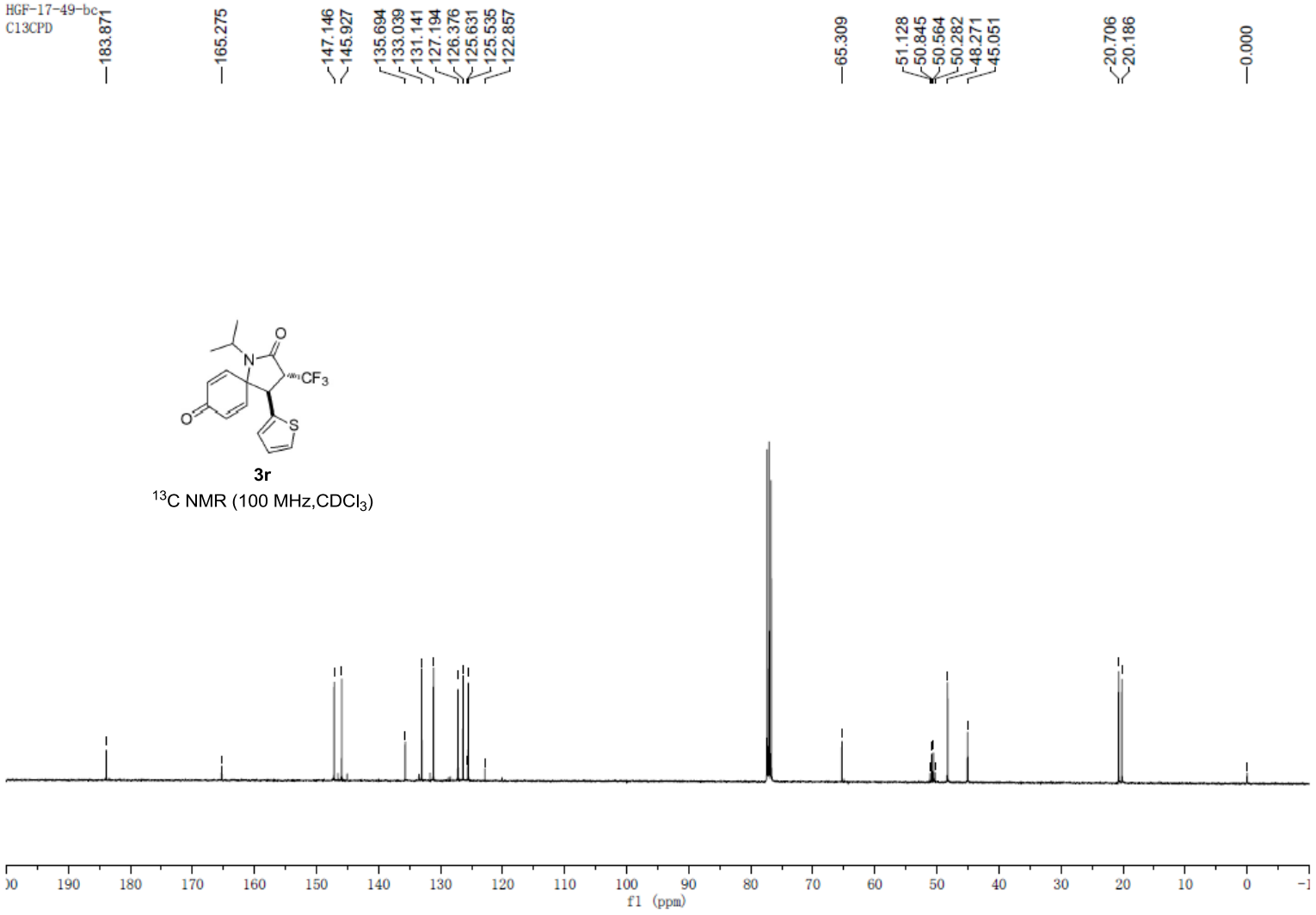
3r

^{1}H NMR (400 MHz, $CDCl_3$)



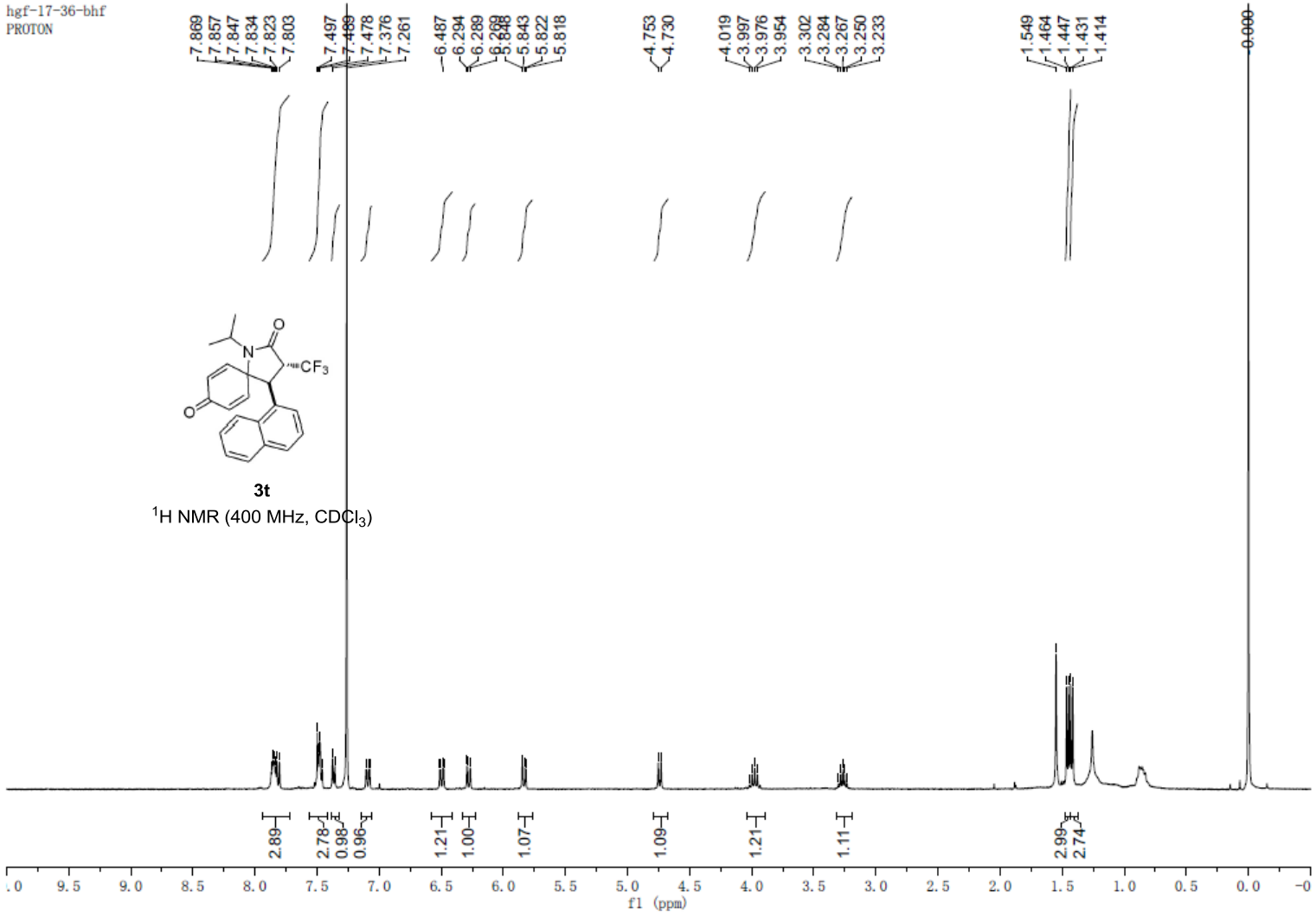
3r

^{19}F NMR (376 MHz,$CDCl_3$)



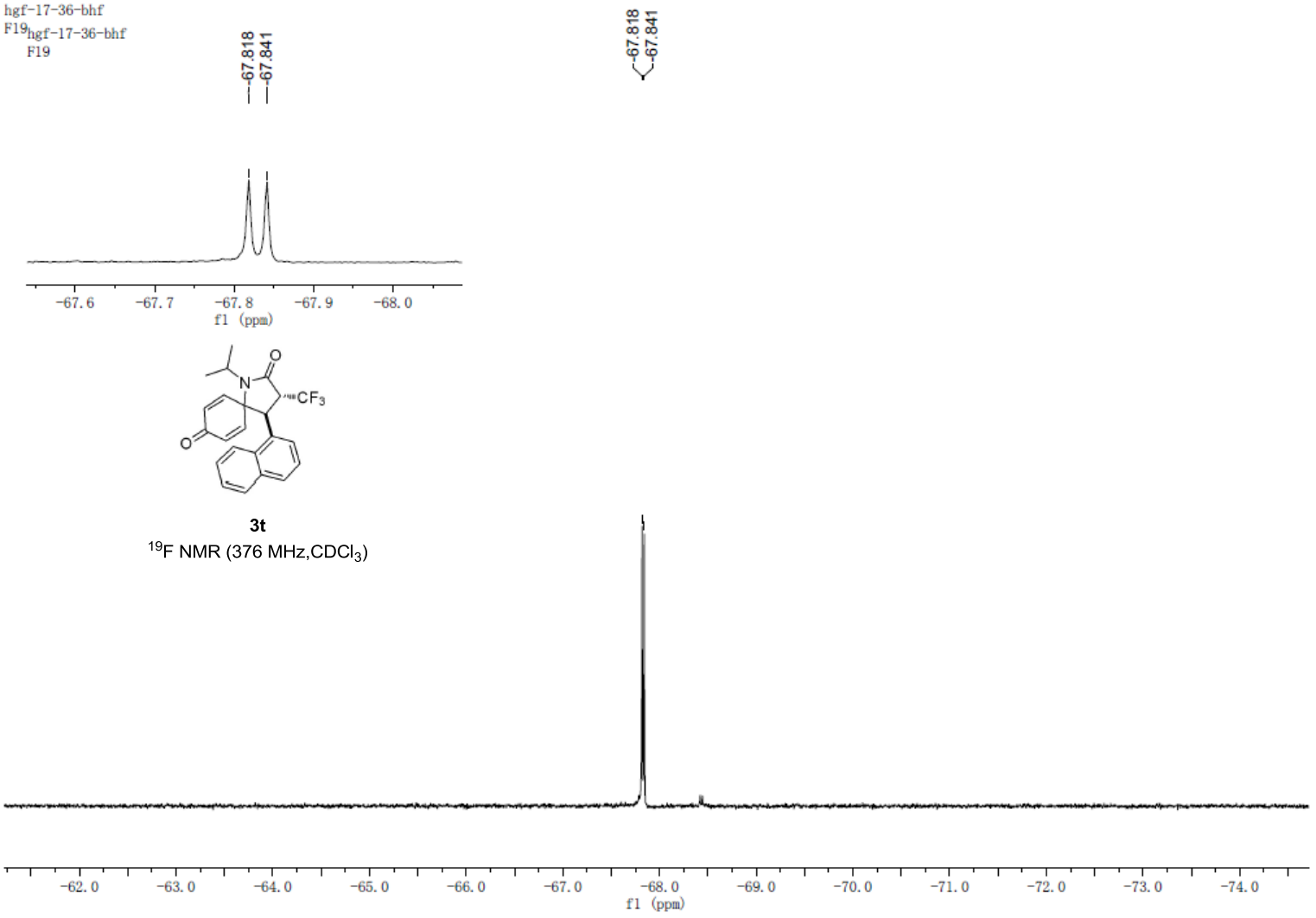
3r

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



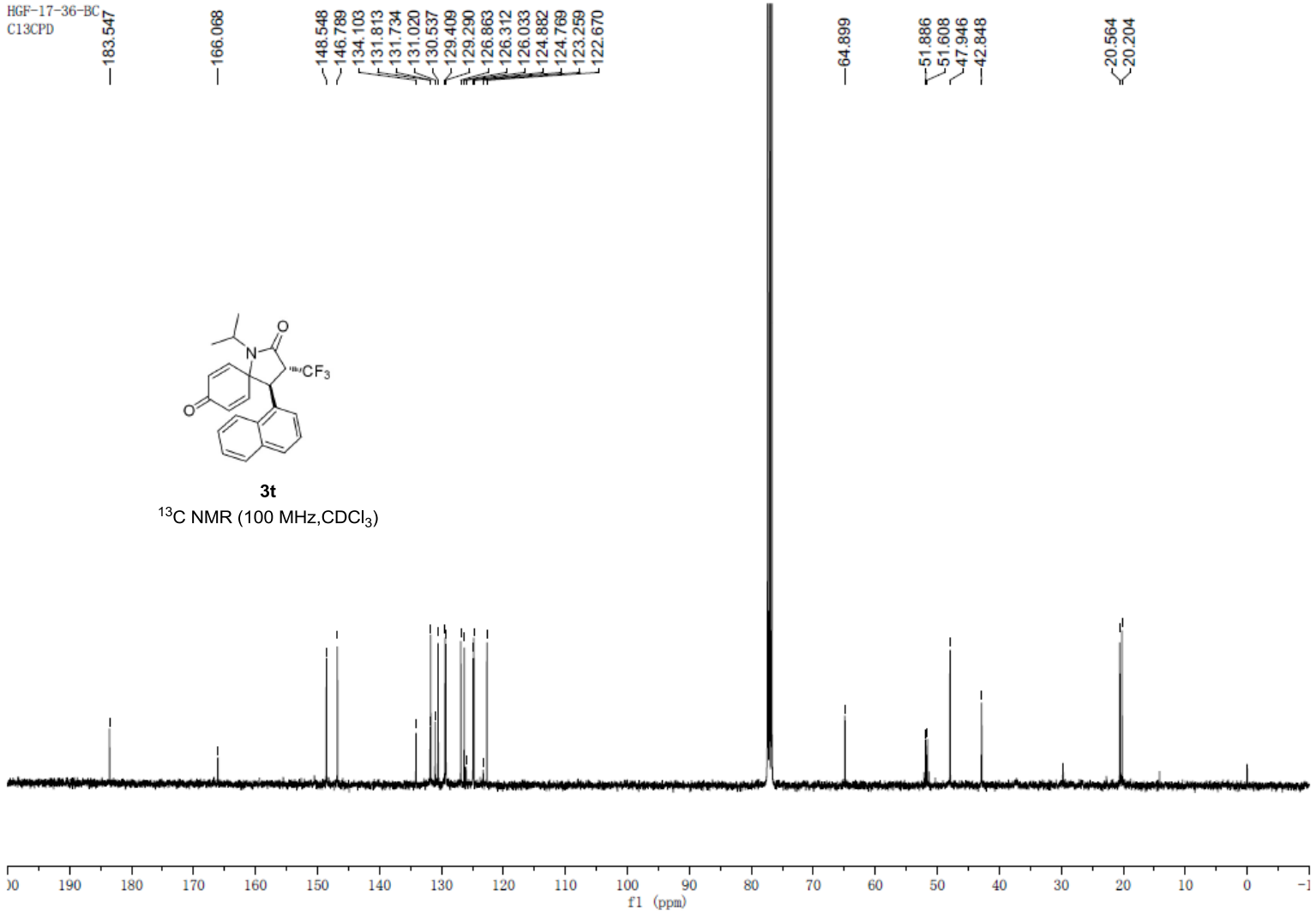
3t

^{1}H NMR (400 MHz, $CDCl_3$)



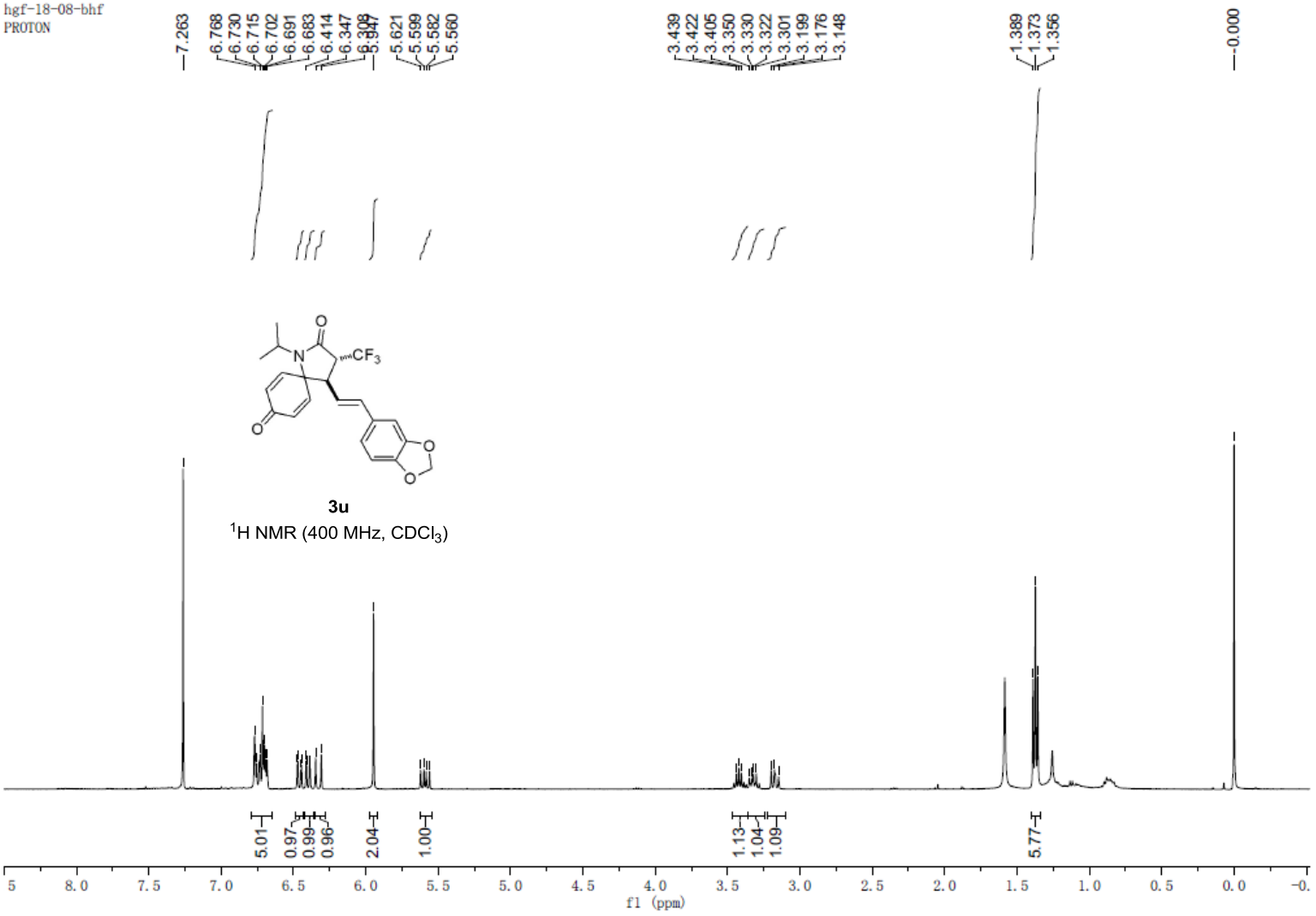
3t

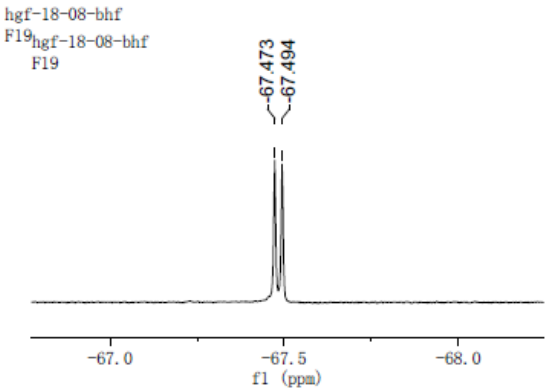
^{19}F NMR (376 MHz,$CDCl_3$)

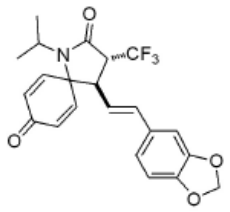


3t

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


hgf-18-08-bhf
PROTON
7.263
6.768
6.730
6.715
6.702
6.691
6.683
6.414
6.347
6.308
5.947
5.621
5.599
5.582
5.560
3.439
3.422
3.405
3.350
3.330
3.322
3.301
3.199
3.176
3.148
1.389
1.373
1.356
0.000
CF3
O
N
O
O
O
3u
1H NMR (400 MHz, CDCl3)
5.01
0.97
0.99
0.96
2.04
1.00
1.13
1.04
1.09
5.77
f1 (ppm)



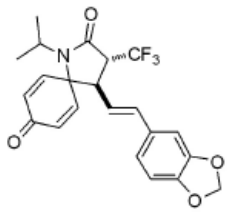


3u

^{19}F NMR (376 MHz,$CDCl_3$)

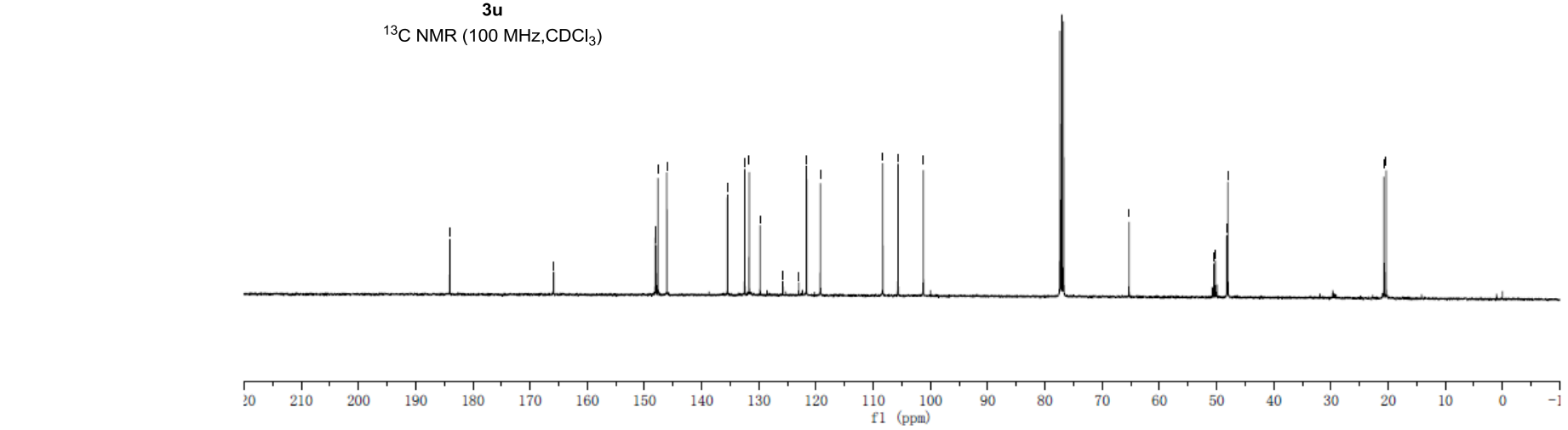
hgf-18-08-bc
test

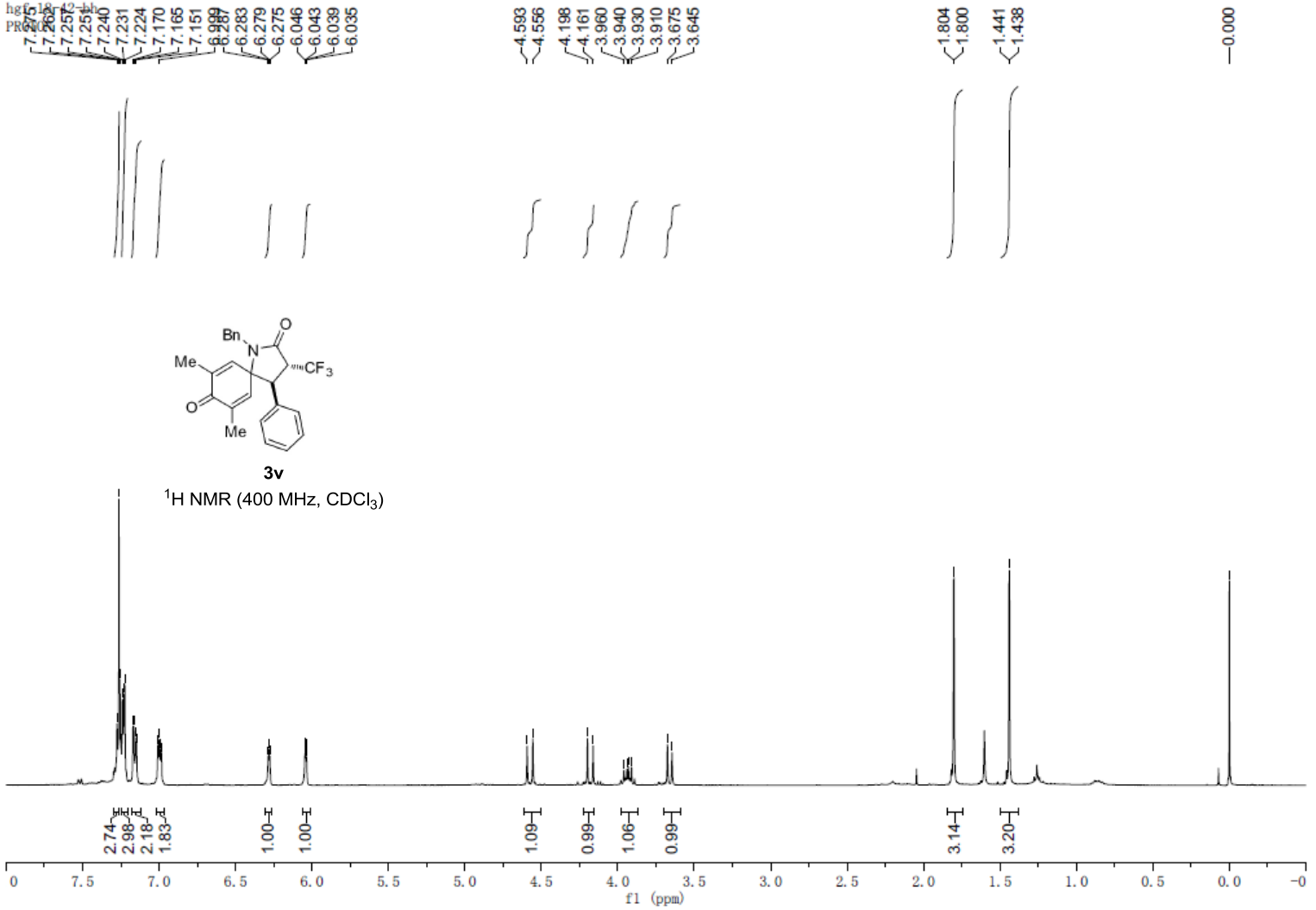
184.033
165.882
148.111
147.981
147.660
146.082
135.481
132.476
131.687
129.786
125.812
123.038
121.682
119.255
108.347
105.678
101.262
65.307
50.455
50.180
48.203
48.003
20.732
20.356



3u

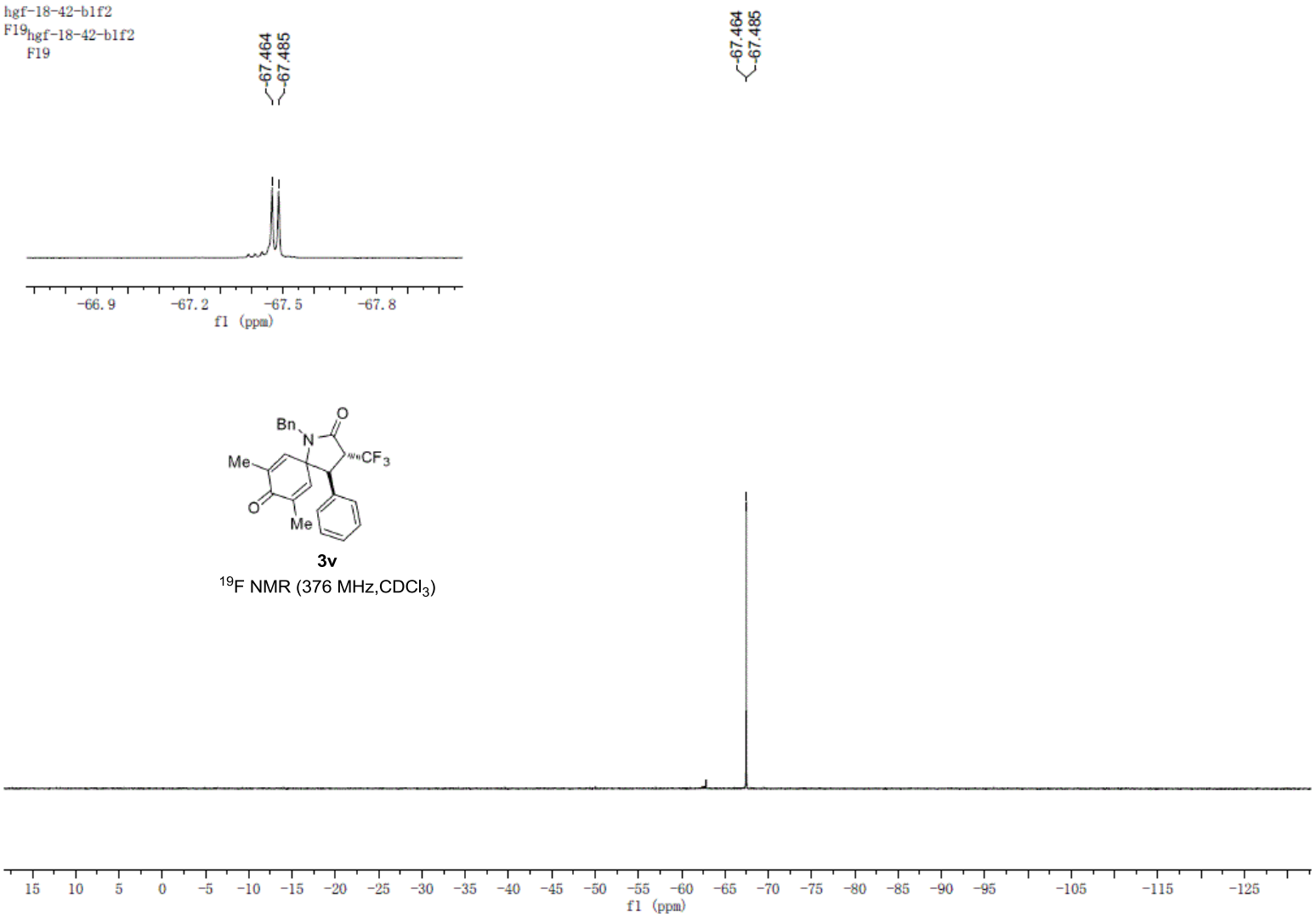
^{13}C NMR (100 MHz,$CDCl_3$)





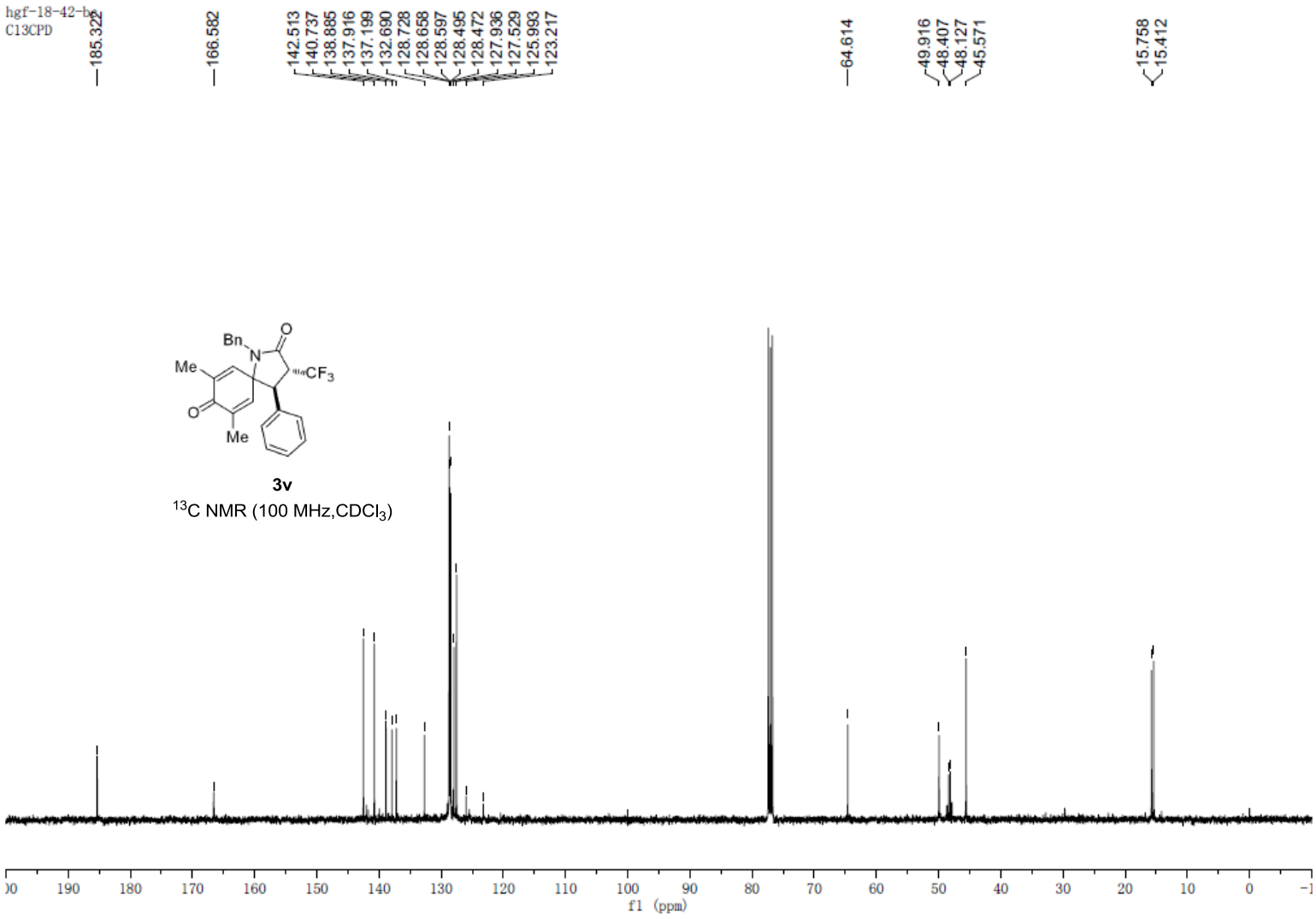
3v

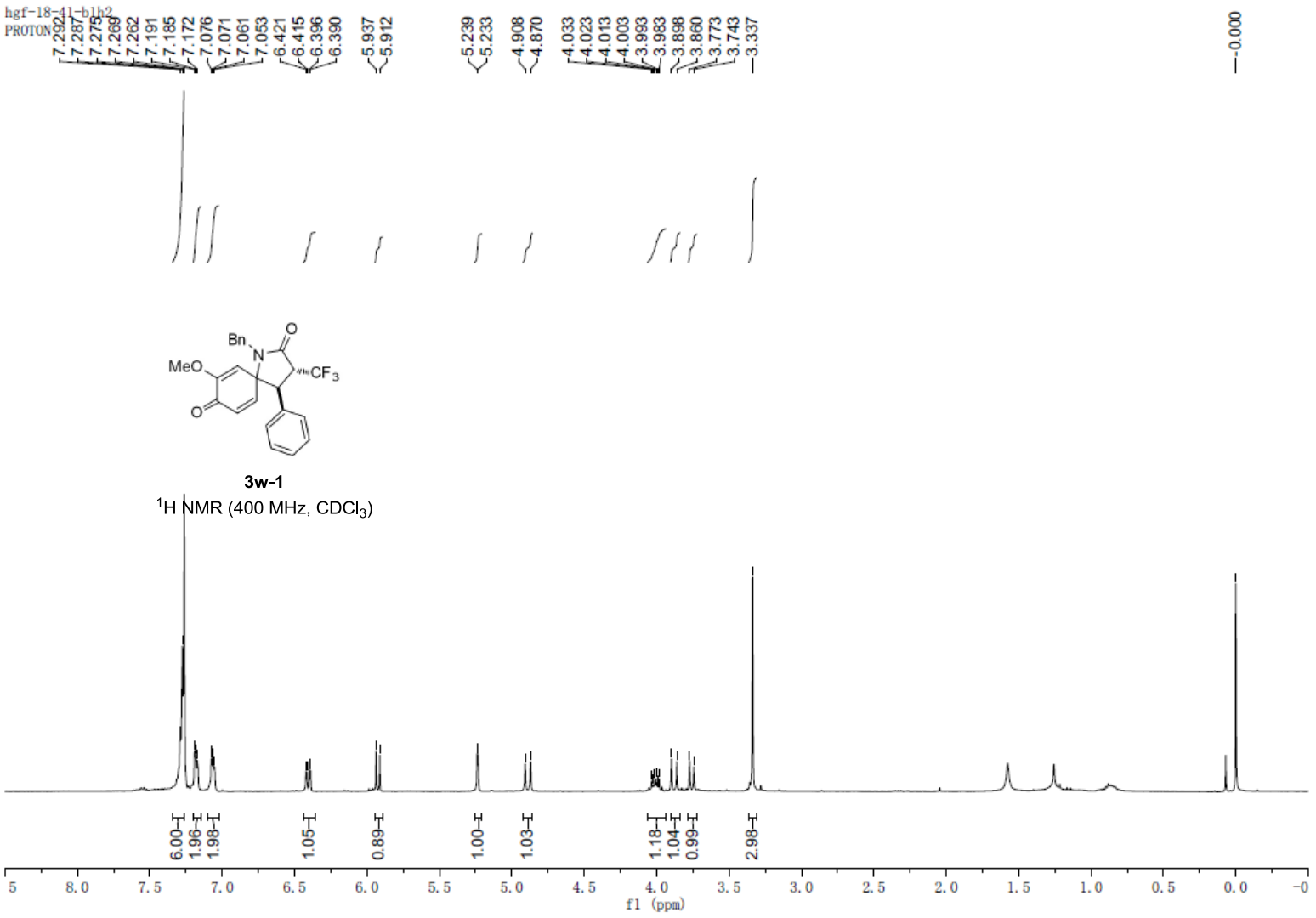
^{1}H NMR (400 MHz, $CDCl_3$)



3v

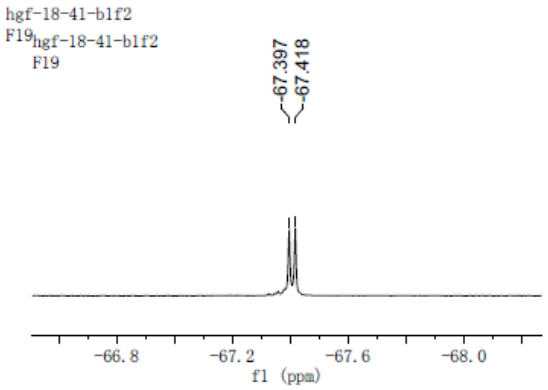
^{19}F NMR (376 MHz,$CDCl_3$)

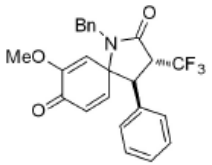

hgf-18-42-bc
C13CPD
185.322
166.582
142.513
140.737
138.885
137.916
137.199
132.690
128.728
128.658
128.597
128.495
128.472
127.936
127.529
125.993
123.217
64.614
49.916
48.407
48.127
45.571
15.758
15.412
Bn
N
O
Me
CF3
O
Me
3v
13C NMR (100 MHz,CDCl3)
f1 (ppm)



3w-1

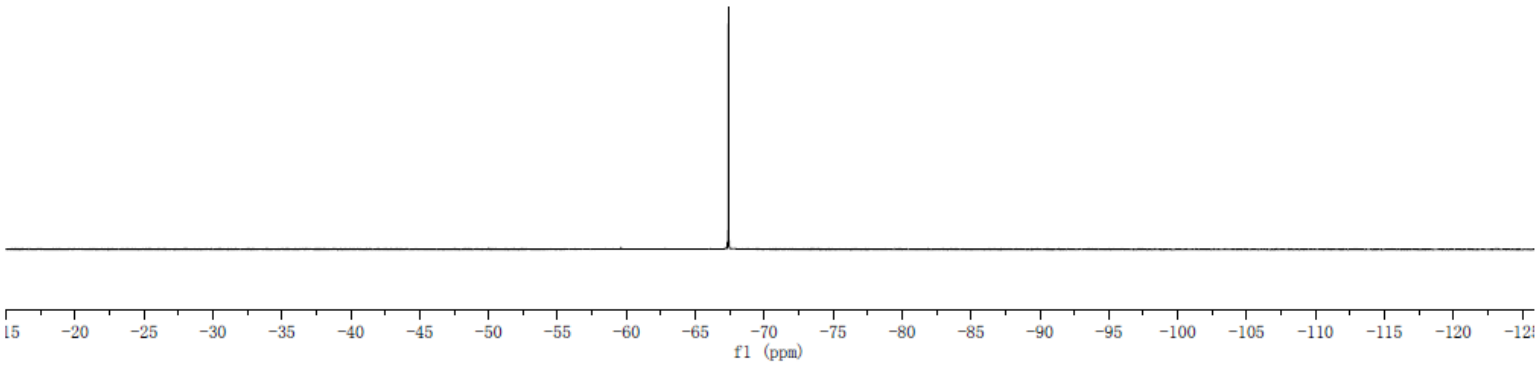
^{1}H NMR (400 MHz, $CDCl_3$)

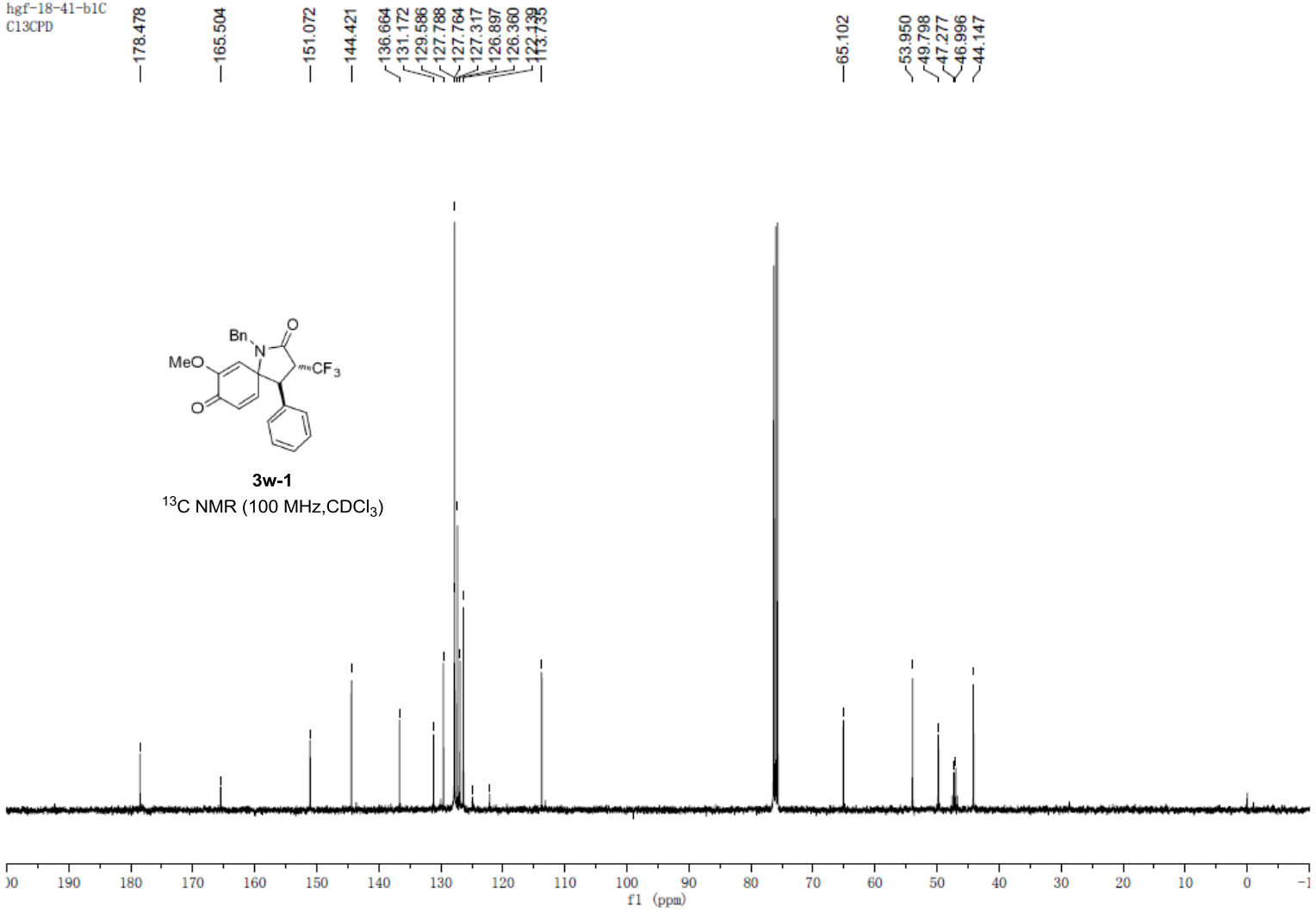




3w-1

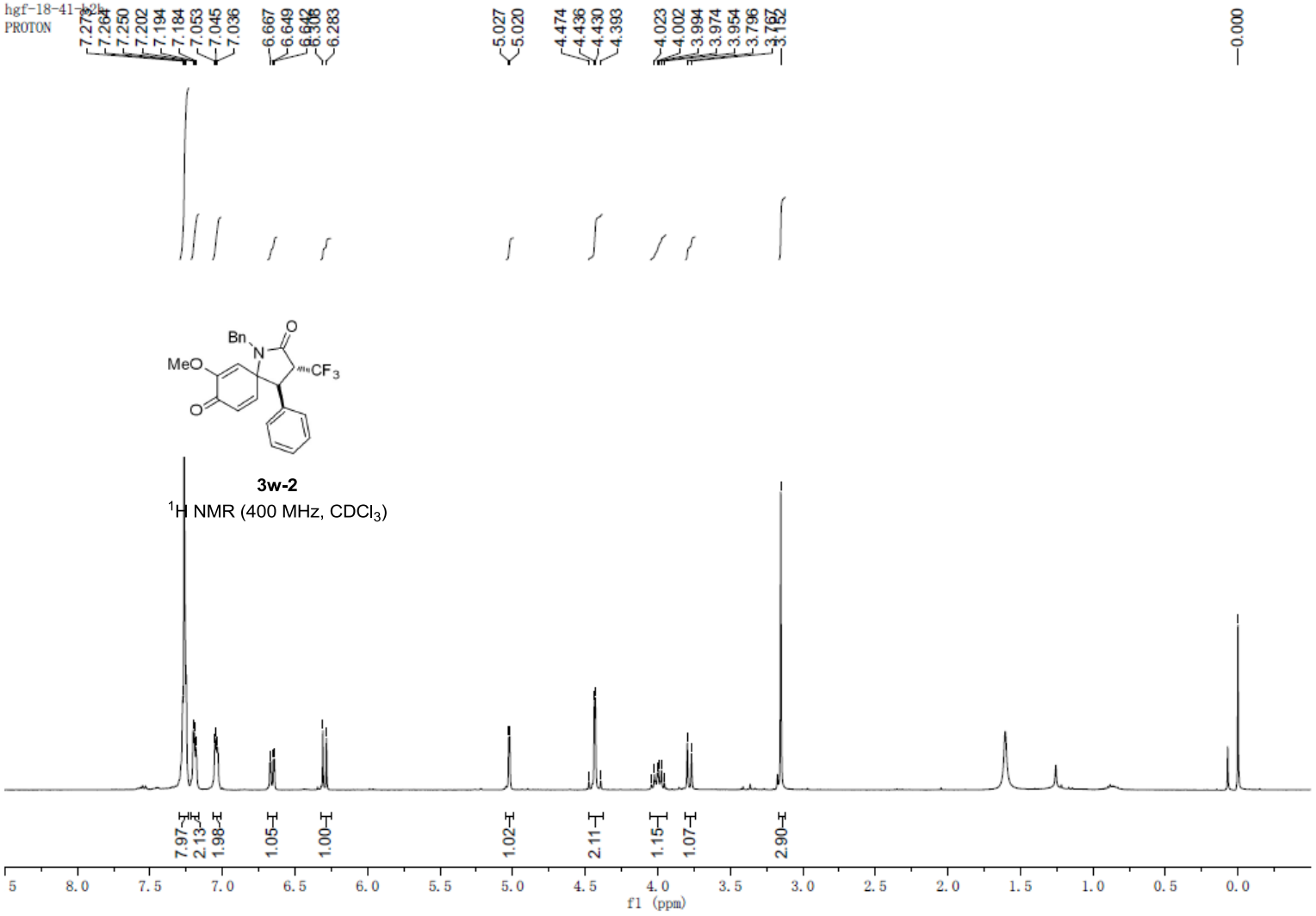
^{19}F NMR (376 MHz,$CDCl_3$)





3w-1

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

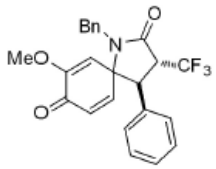


3w-2

^{1}H NMR (400 MHz, $CDCl_3$)

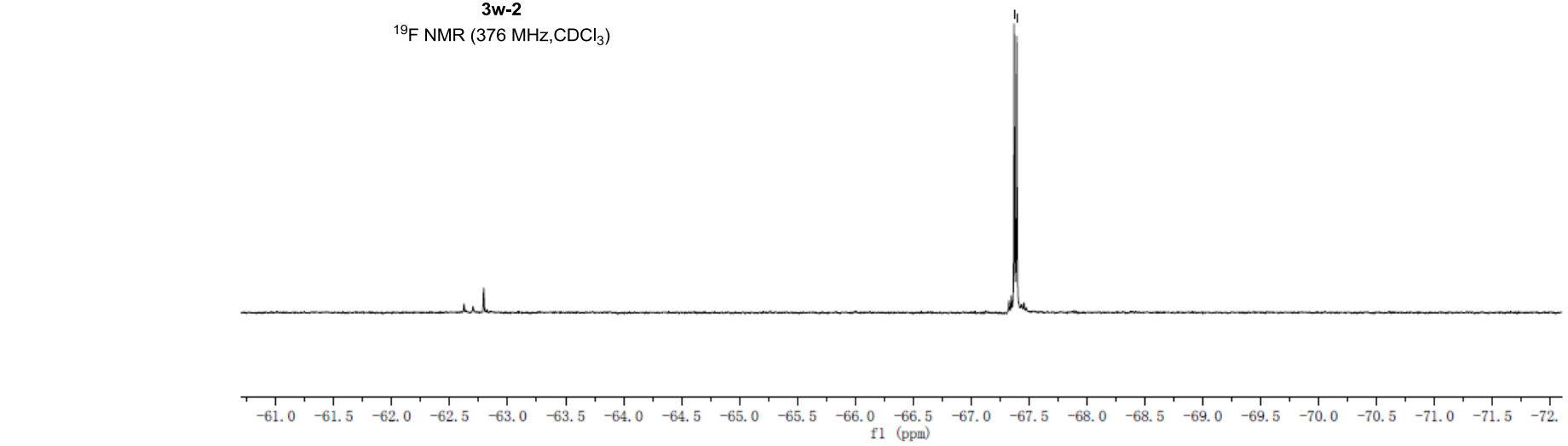
hgf-18-41-b2h
F19

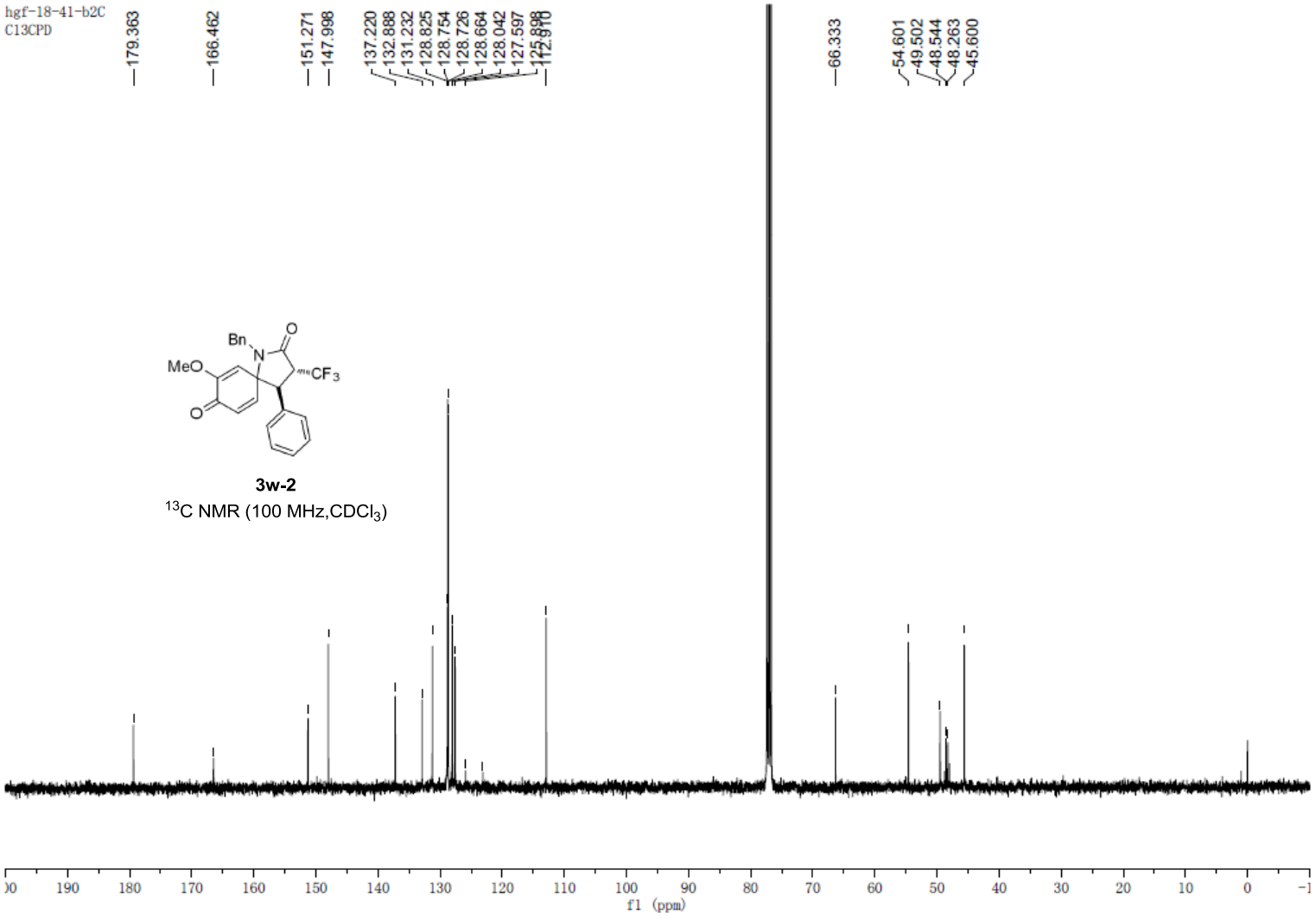
-67.372
-67.394



3w-2

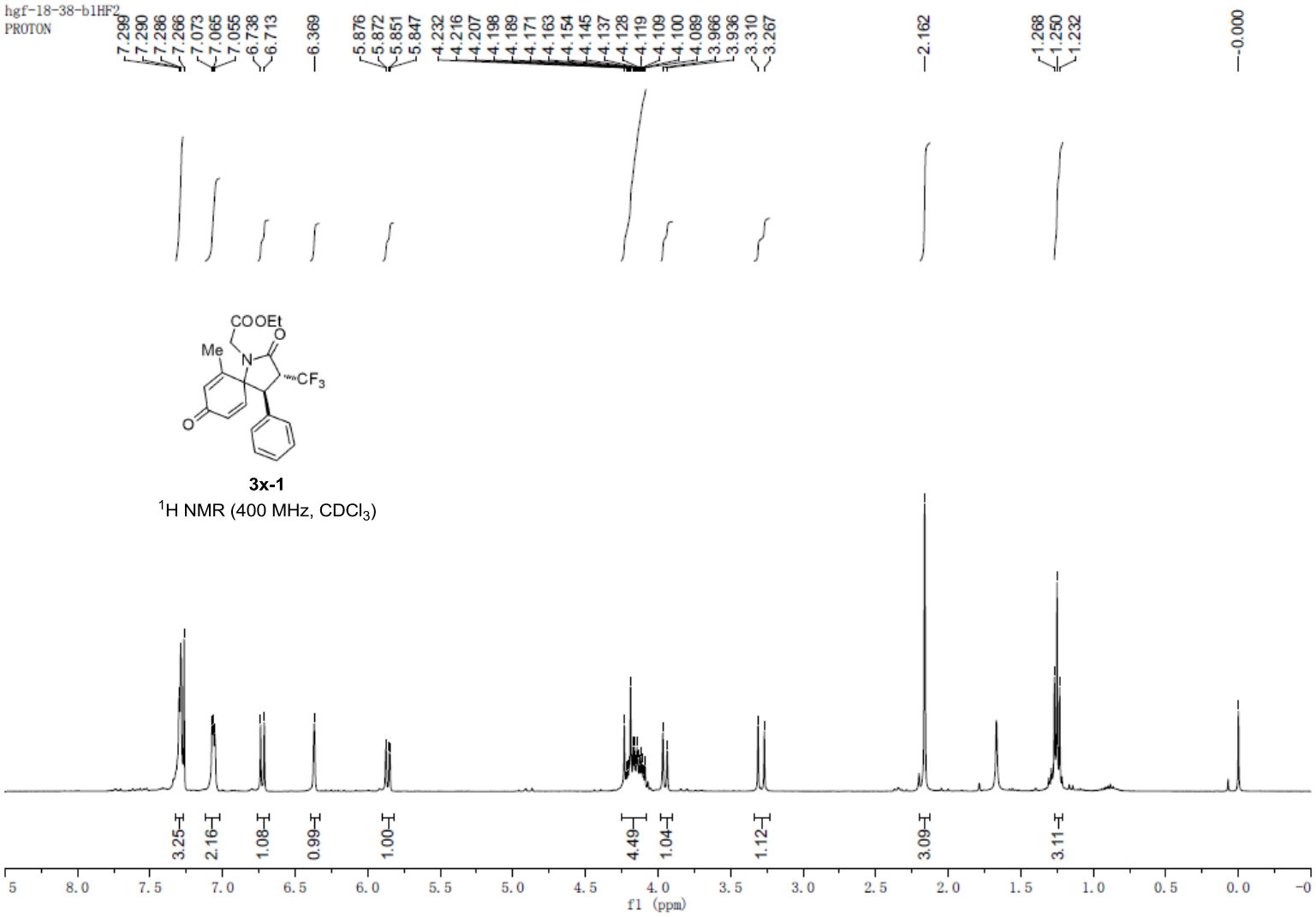
^{19}F NMR (376 MHz,$CDCl_3$)





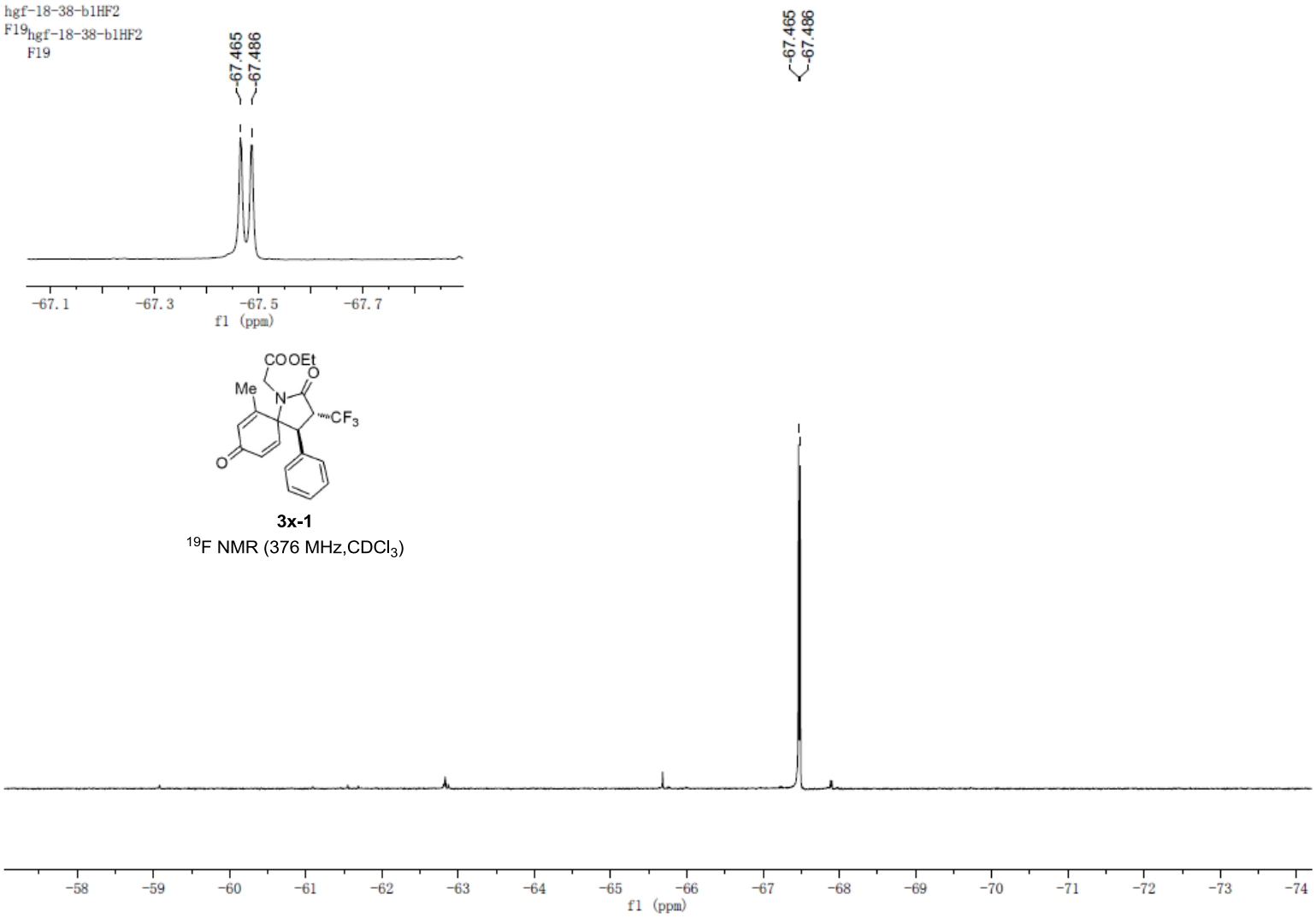
3w-2

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



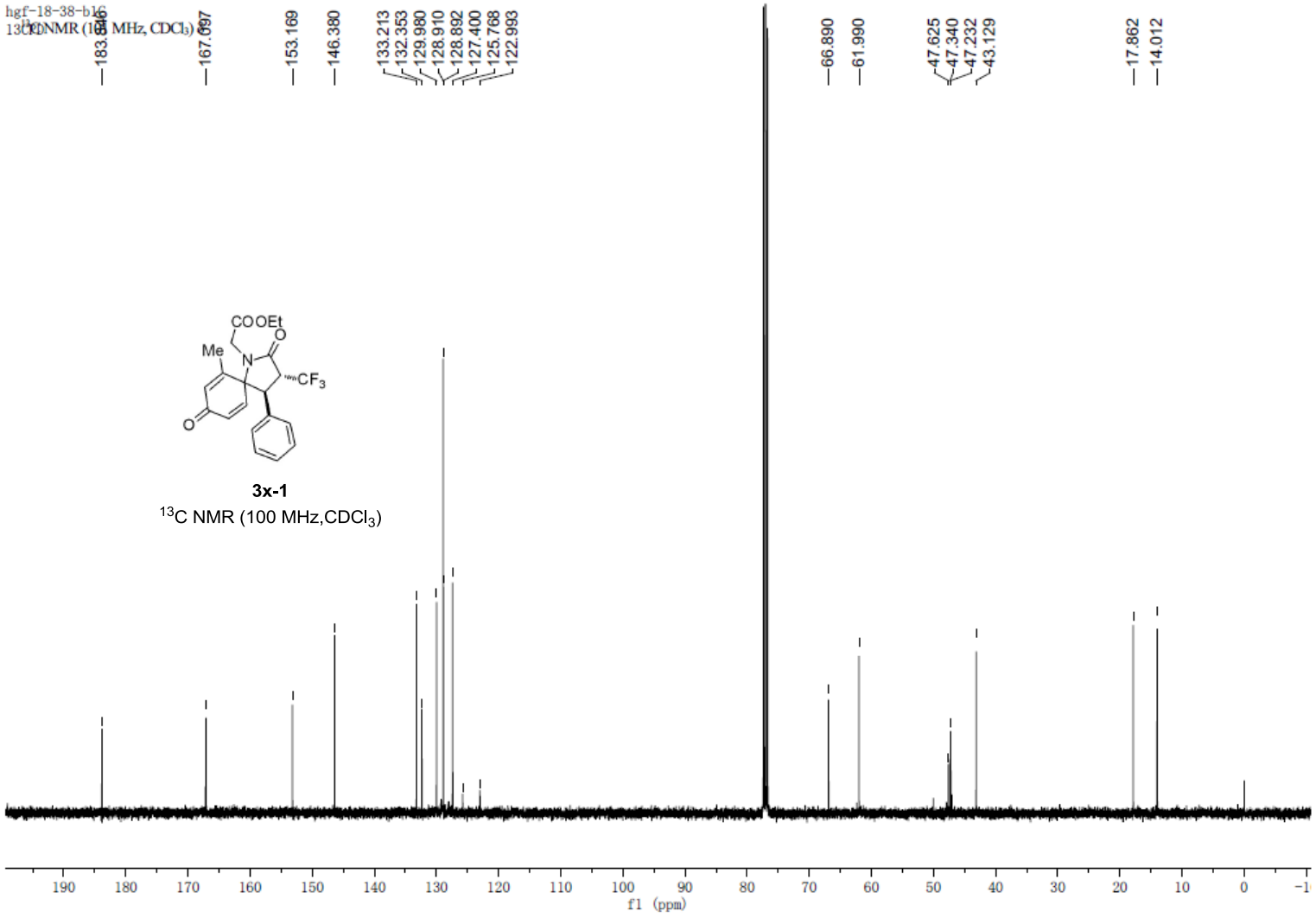
3x-1

^{1}H NMR (400 MHz, $CDCl_3$)



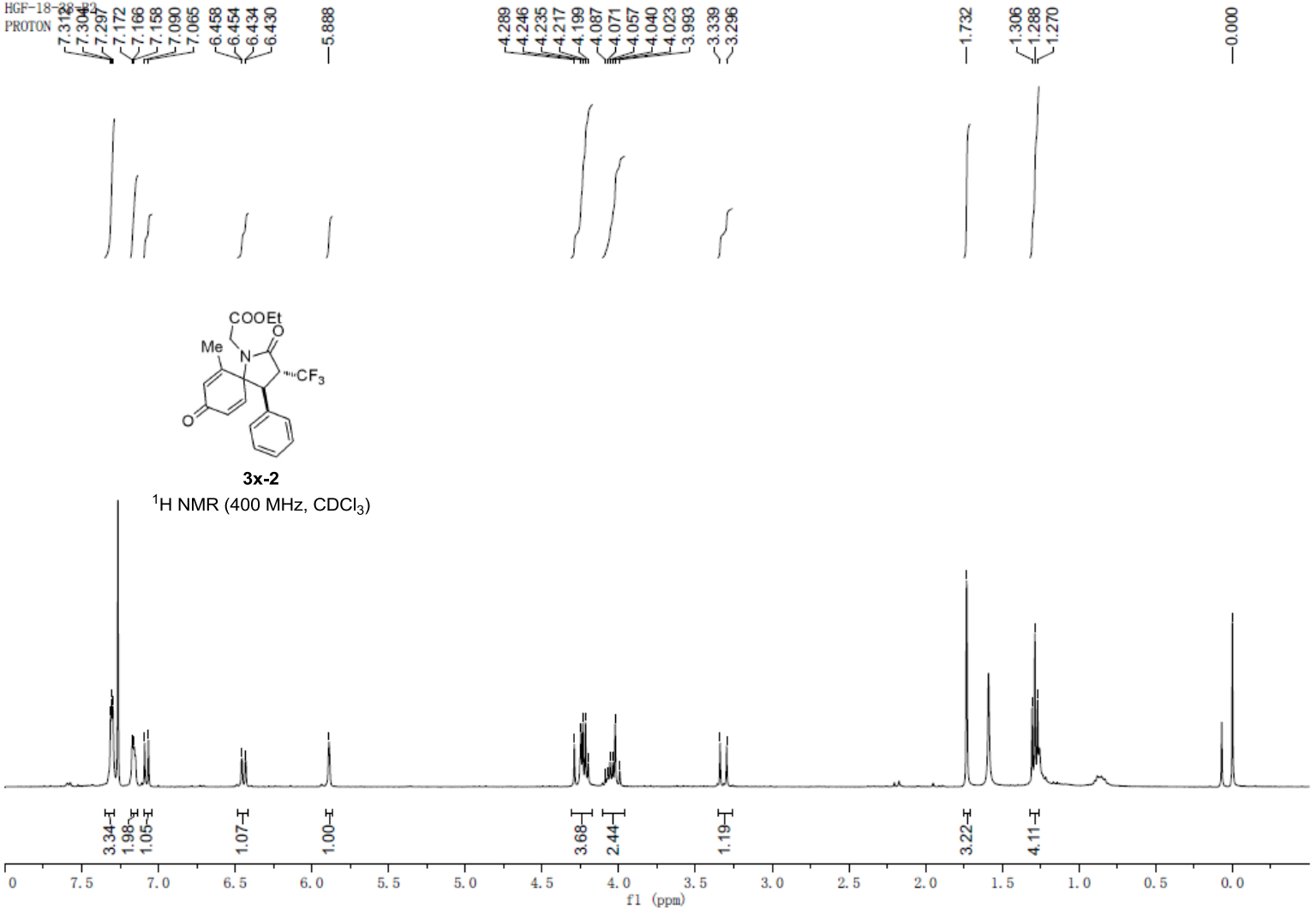
3x-1

^{19}F NMR (376 MHz,$CDCl_3$)



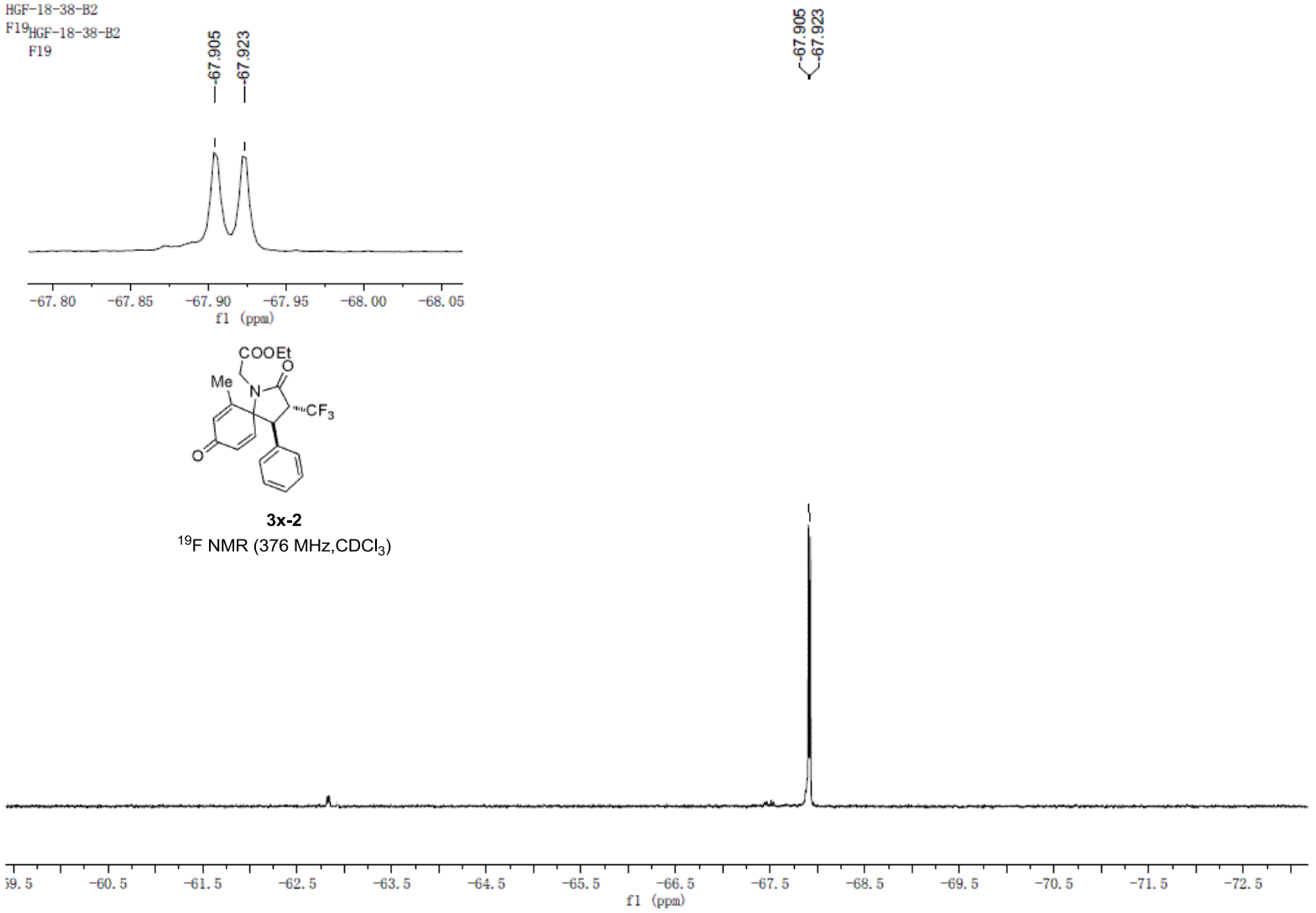
3x-1

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



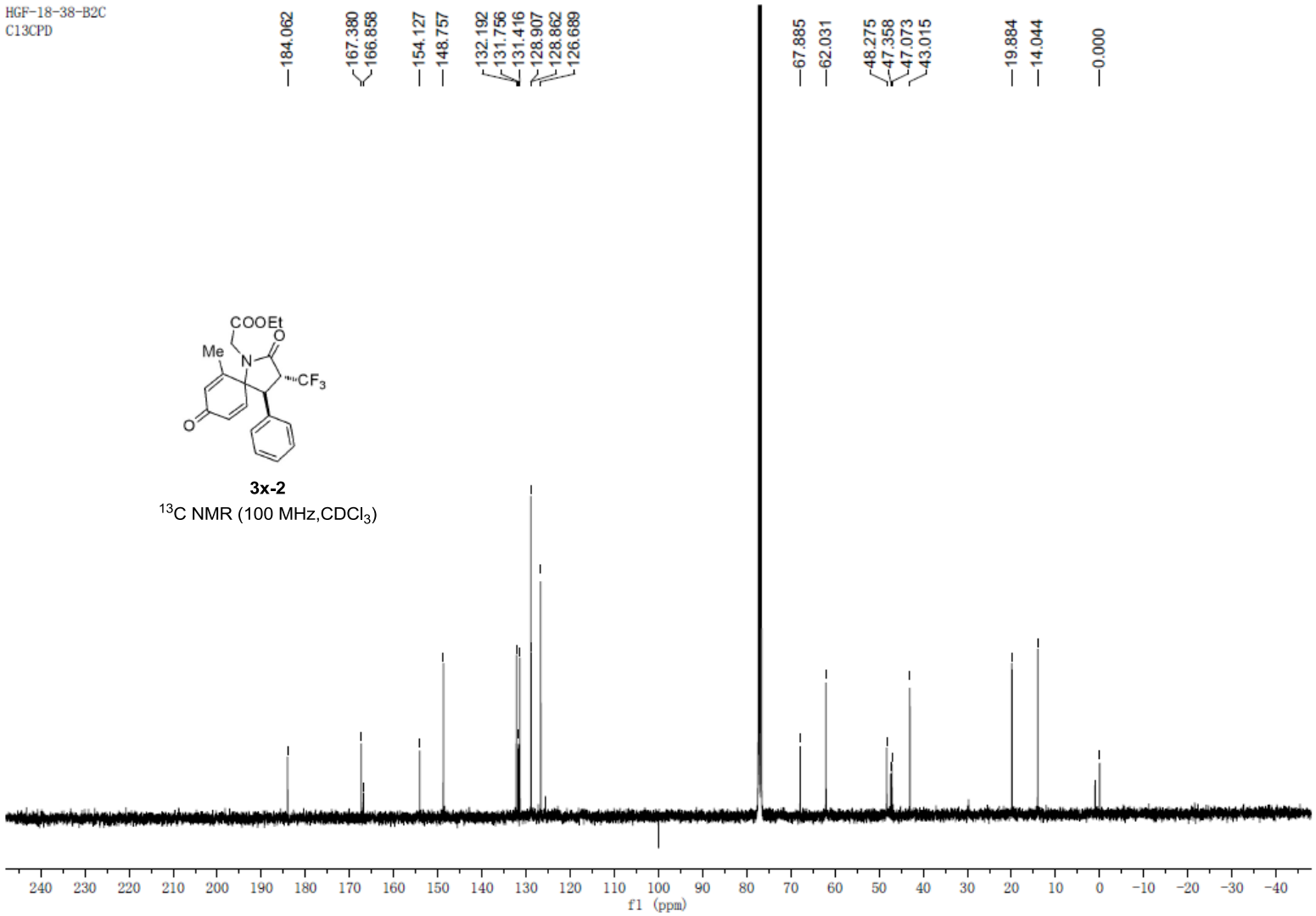
3x-2

^{1}H NMR (400 MHz, $CDCl_3$)



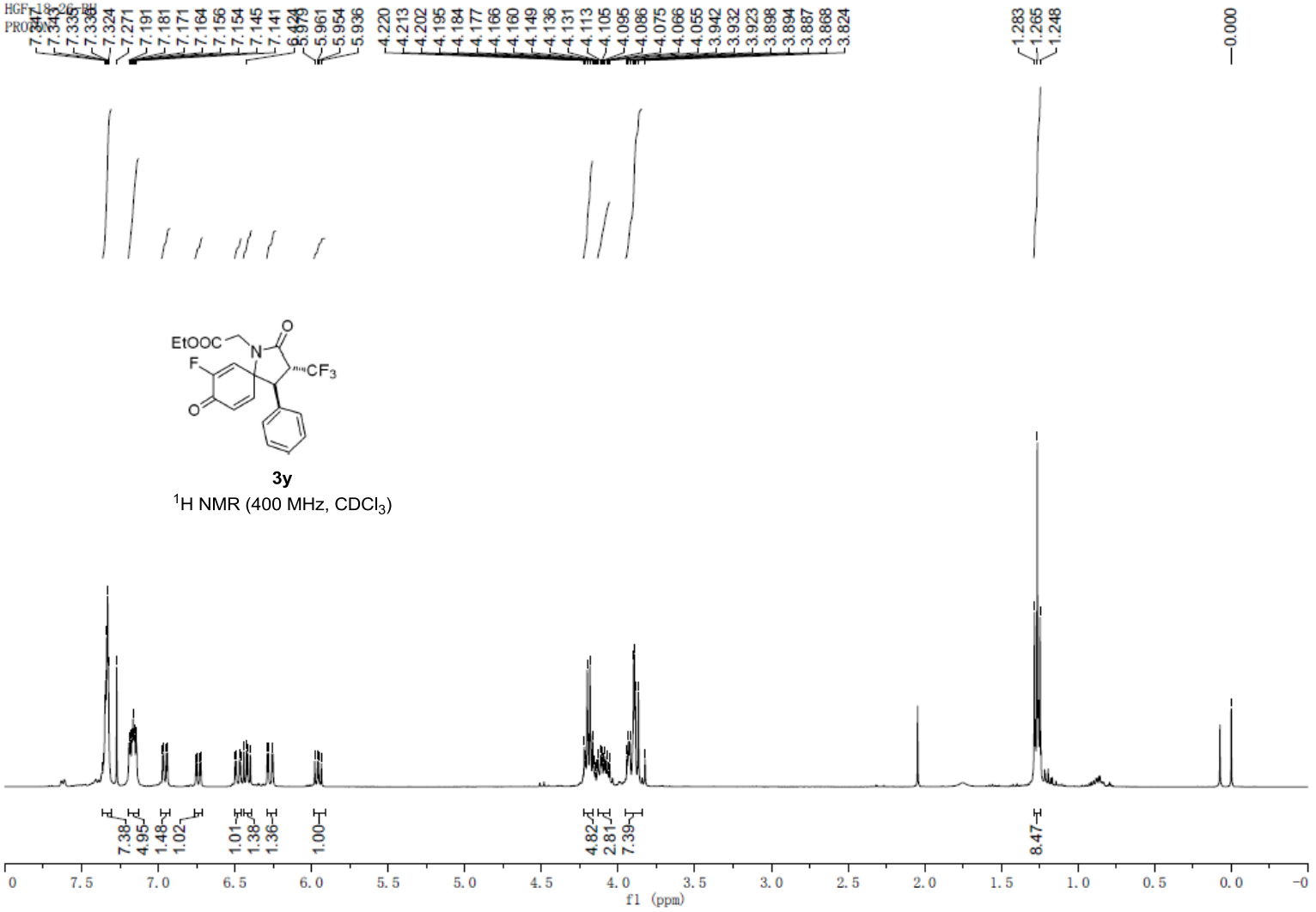
3x-2

^{19}F NMR (376 MHz,$CDCl_3$)



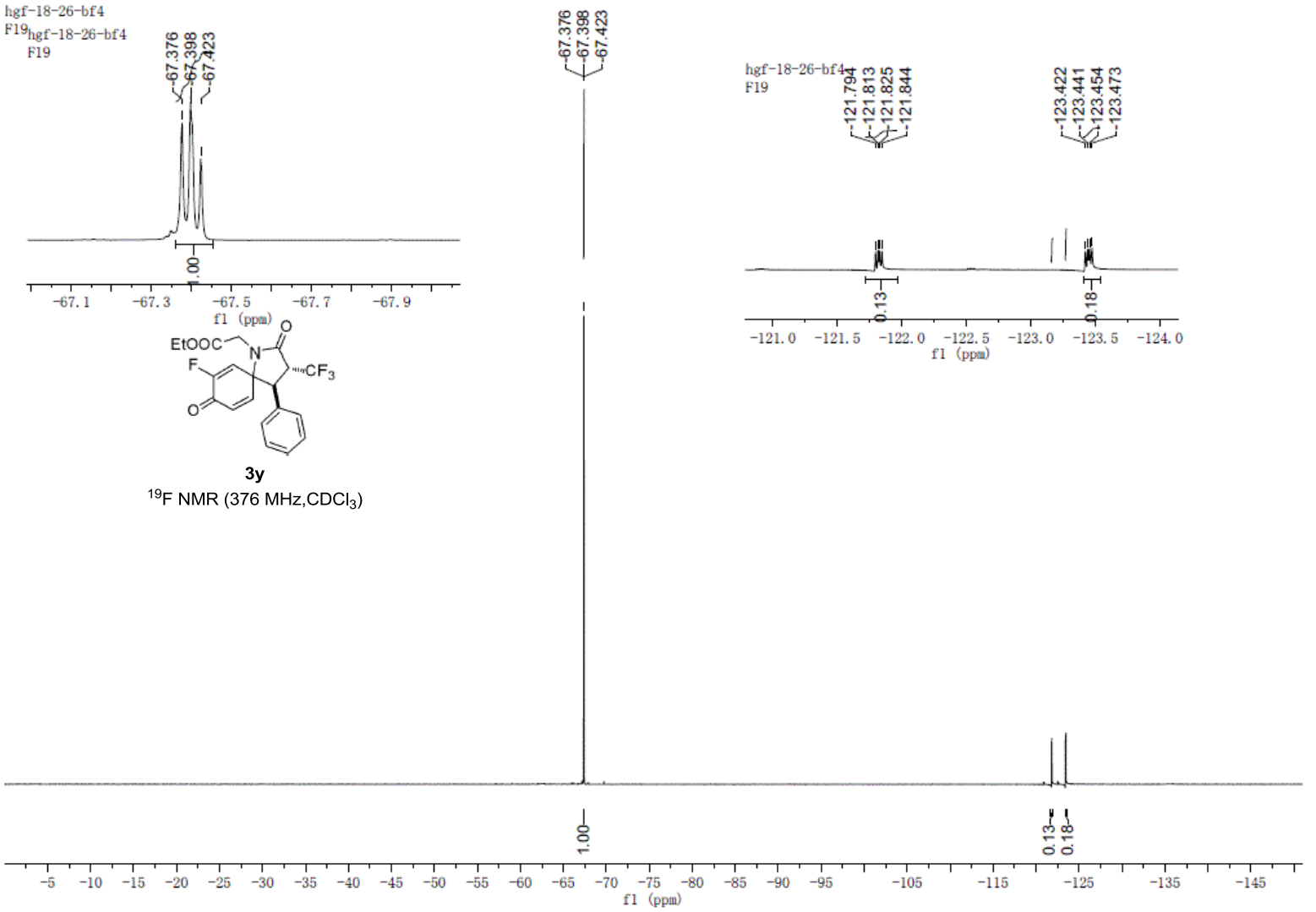
3x-2

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



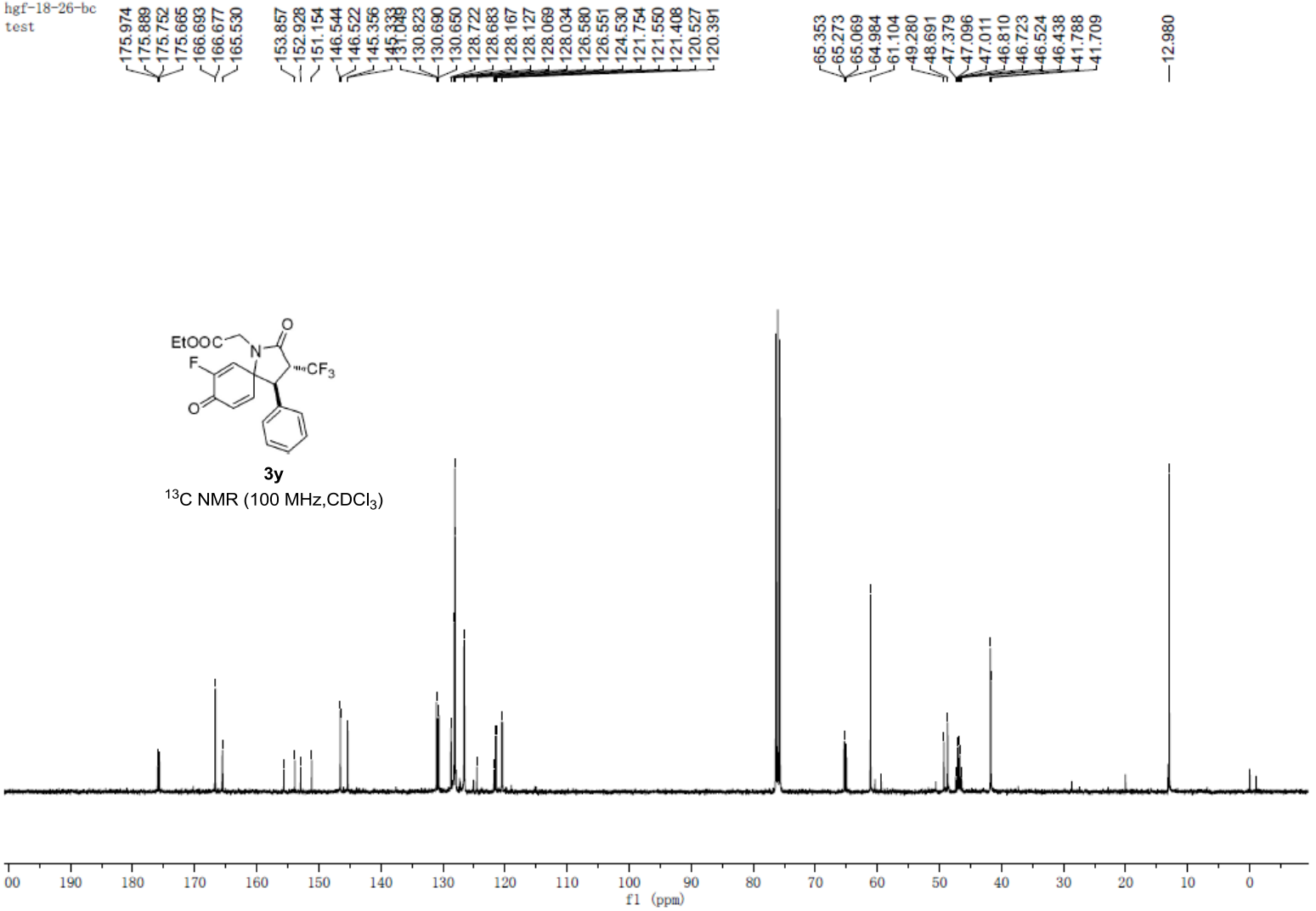
3y

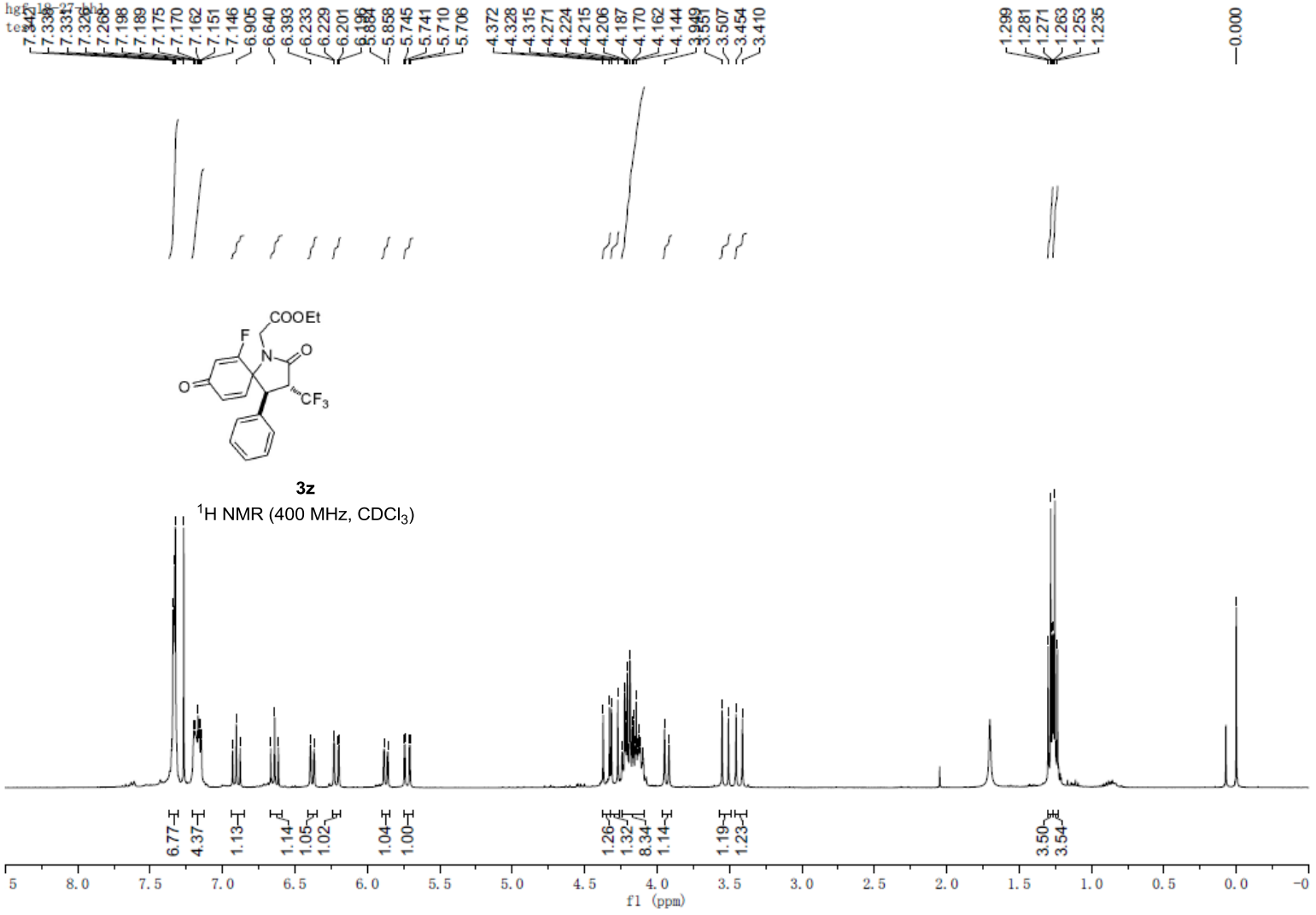
^{1}H NMR (400 MHz, $CDCl_3$)

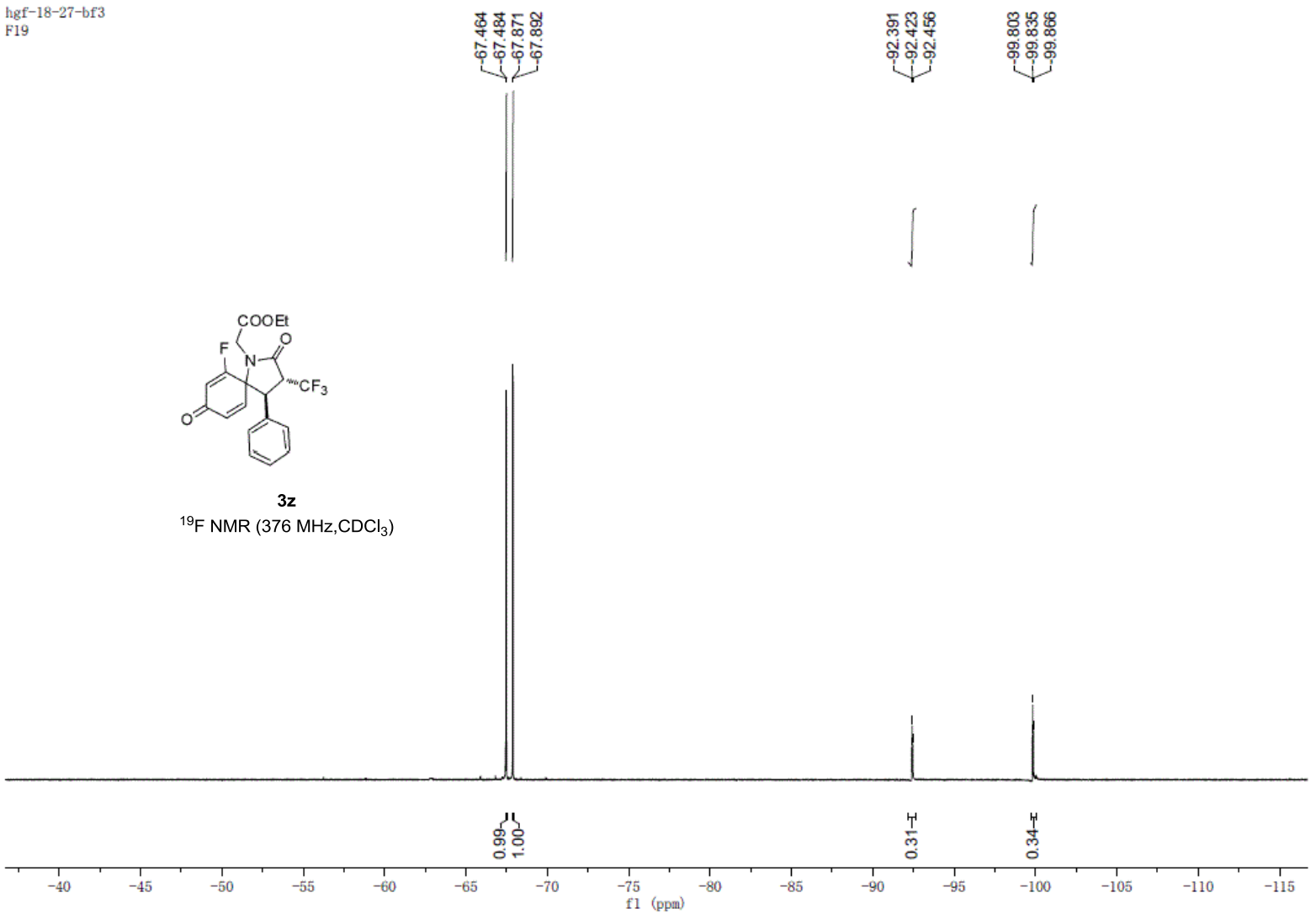


3y

^{19}F NMR (376 MHz,$CDCl_3$)

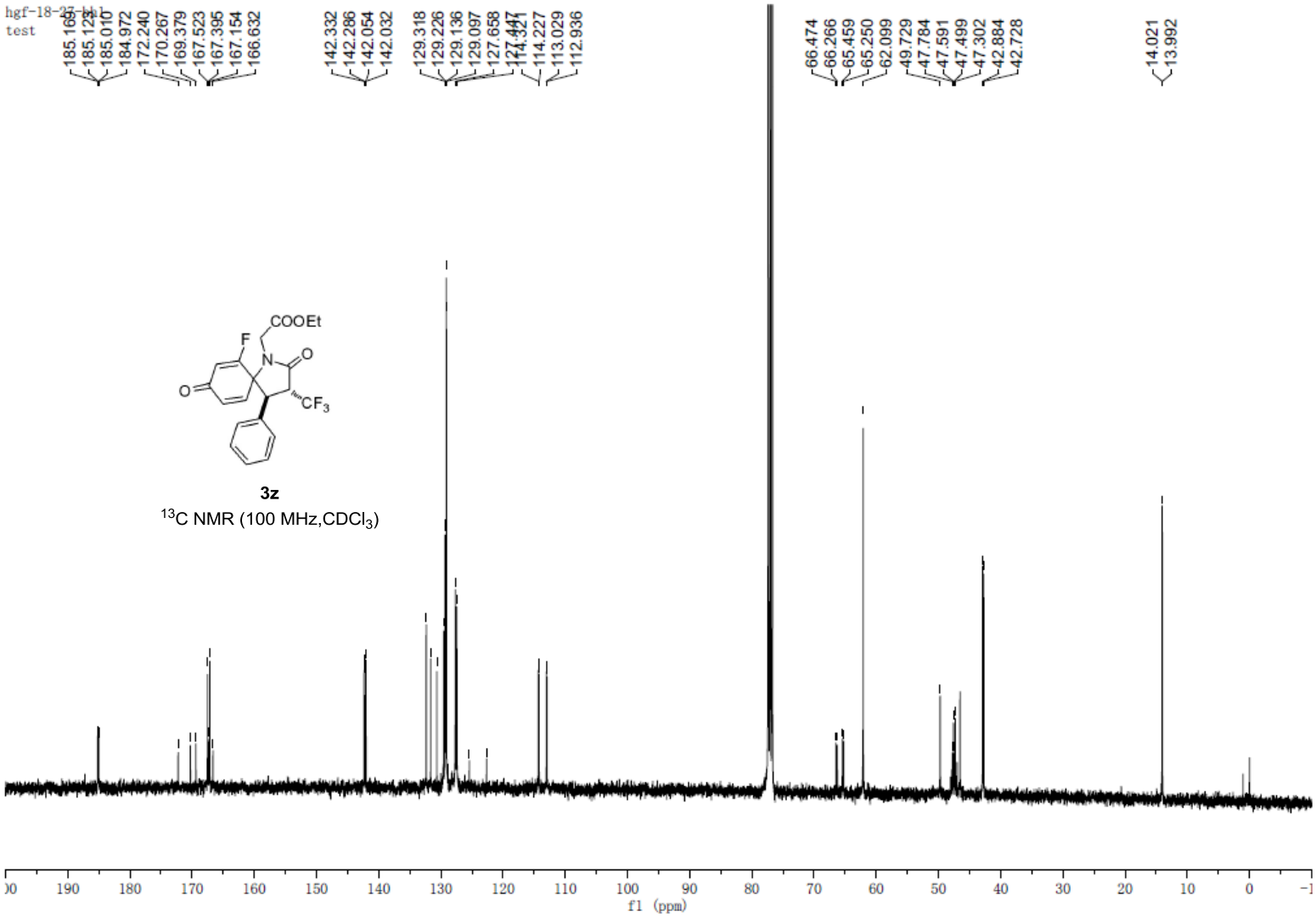

hgf-18-26-bc
test
175.974
175.889
175.752
175.665
166.693
166.677
165.530
153.857
152.928
151.154
146.544
146.522
145.356
145.333
131.049
130.823
130.690
130.650
128.722
128.683
128.167
128.127
128.069
128.034
126.580
126.551
124.530
121.754
121.550
121.408
120.527
120.391
65.353
65.273
65.069
64.984
61.104
49.280
48.691
47.379
47.096
47.011
46.810
46.723
46.524
46.438
41.788
41.709
12.980
EtOOC
N
O
F
O
CF3
3y
13C NMR (100 MHz,CDCl3)
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


COOEt
F
N
O
O
CF3
3z
1H NMR (400 MHz, CDCl3)
f1 (ppm)



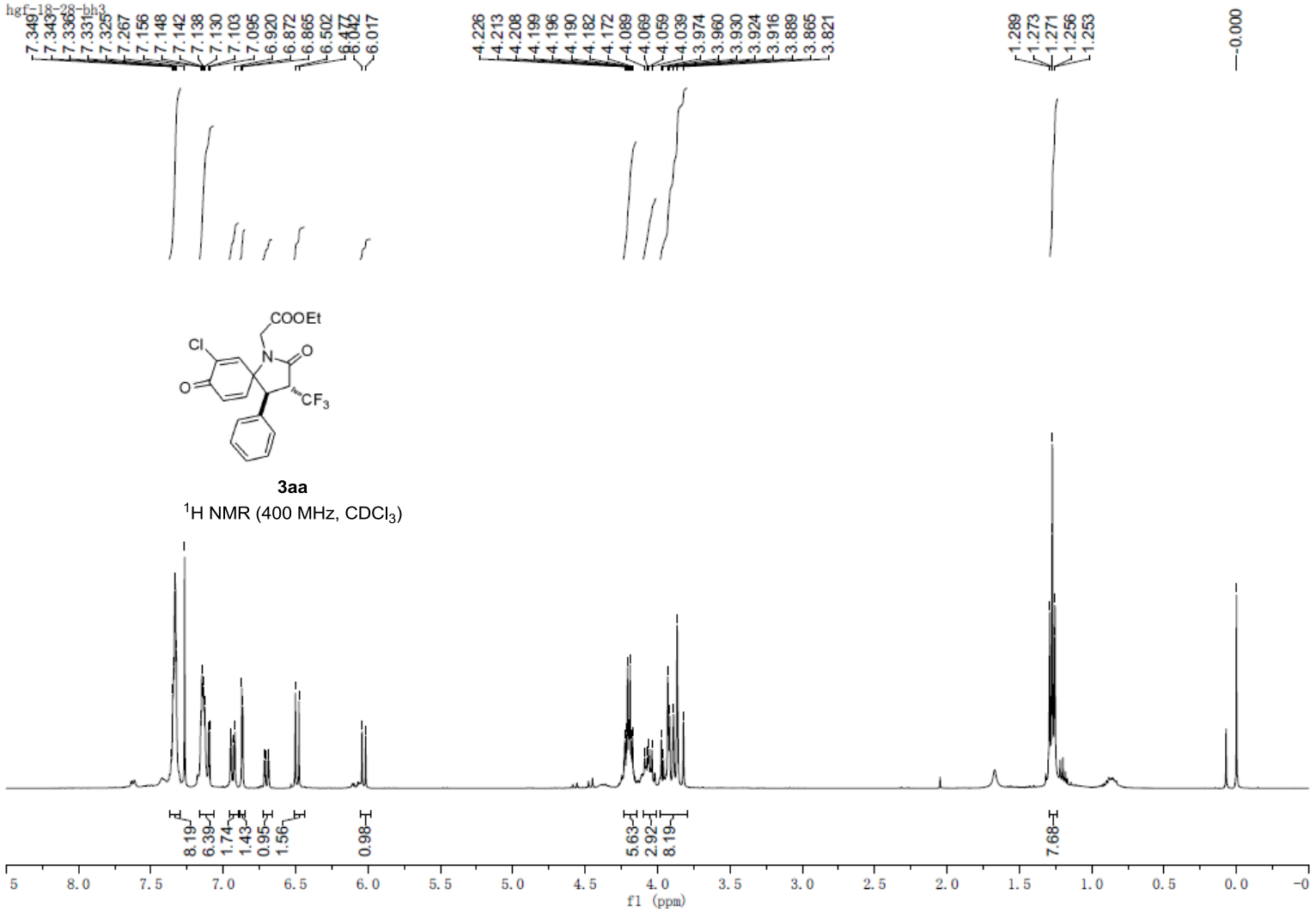
3z

^{19}F NMR (376 MHz,$CDCl_3$)



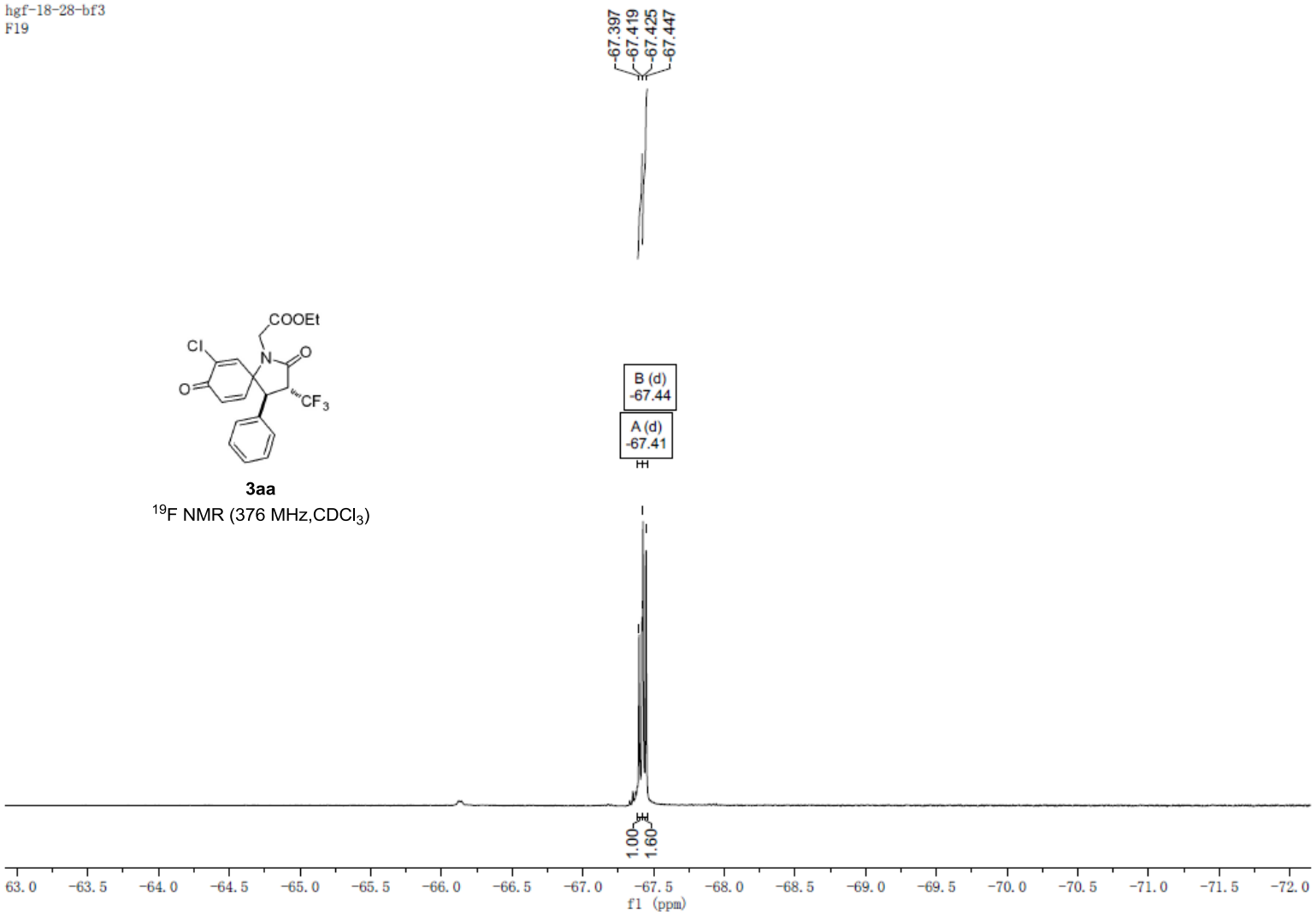
3z

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



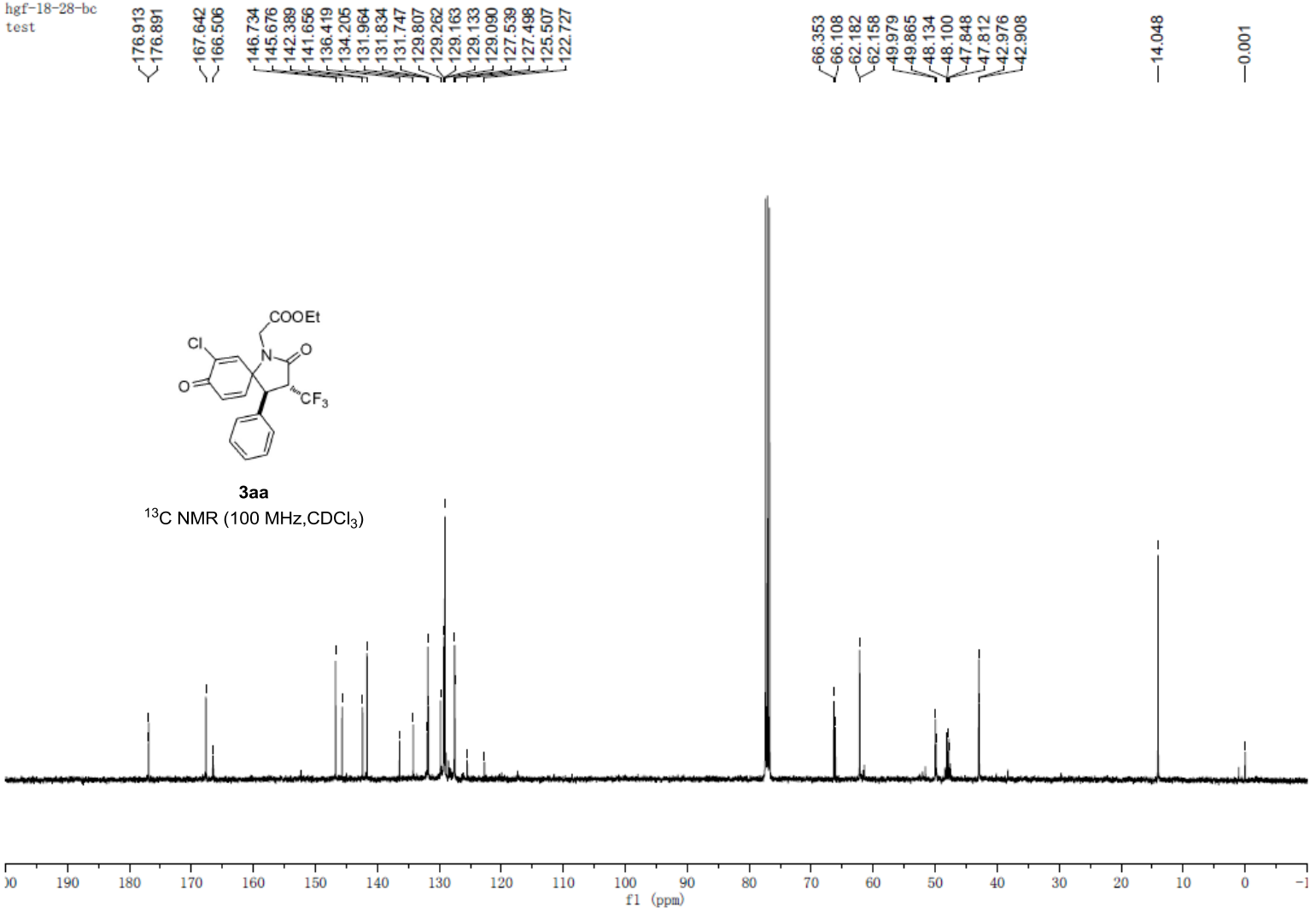
3aa

^{1}H NMR (400 MHz, $CDCl_3$)



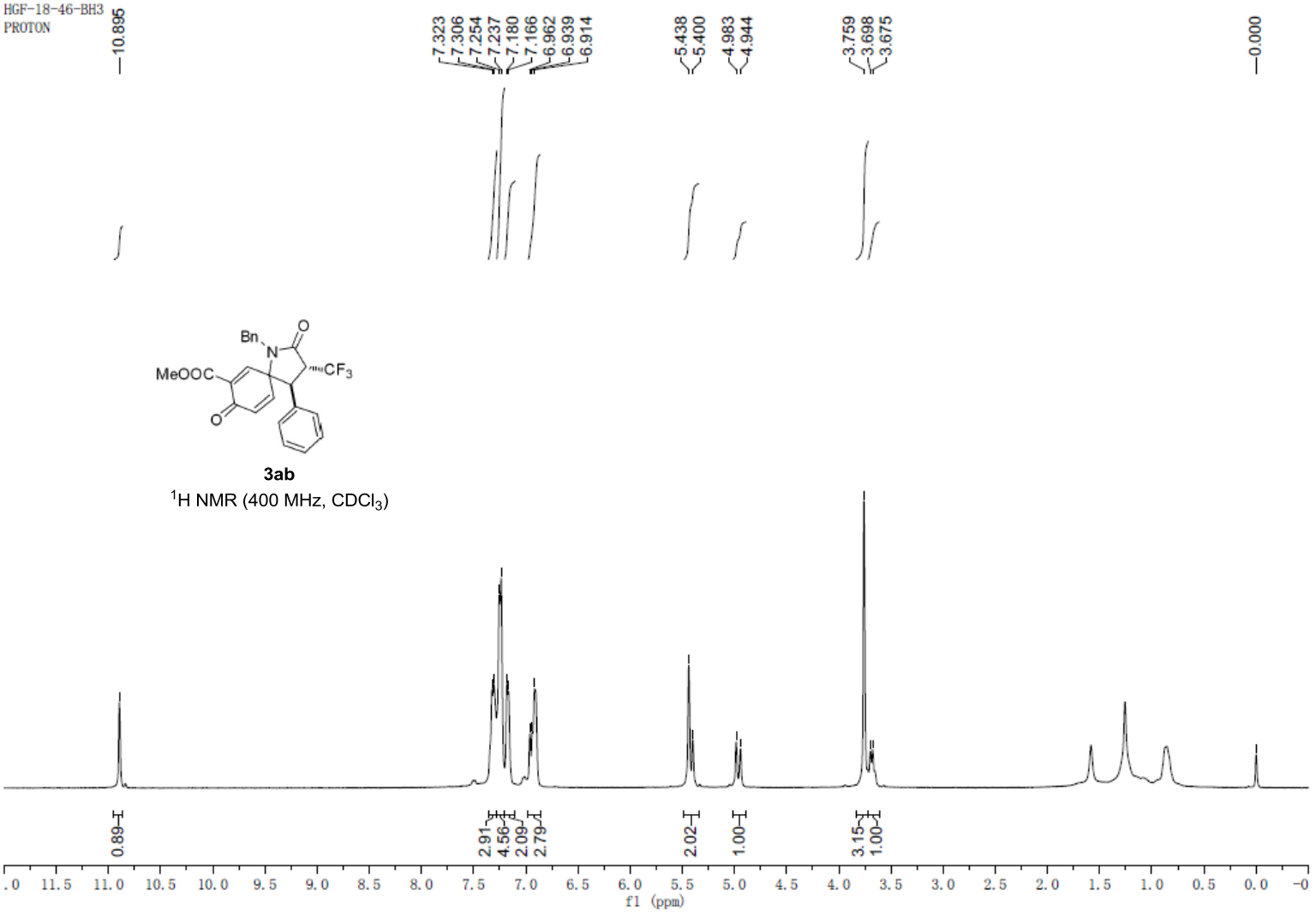
3aa

^{19}F NMR (376 MHz,$CDCl_3$)



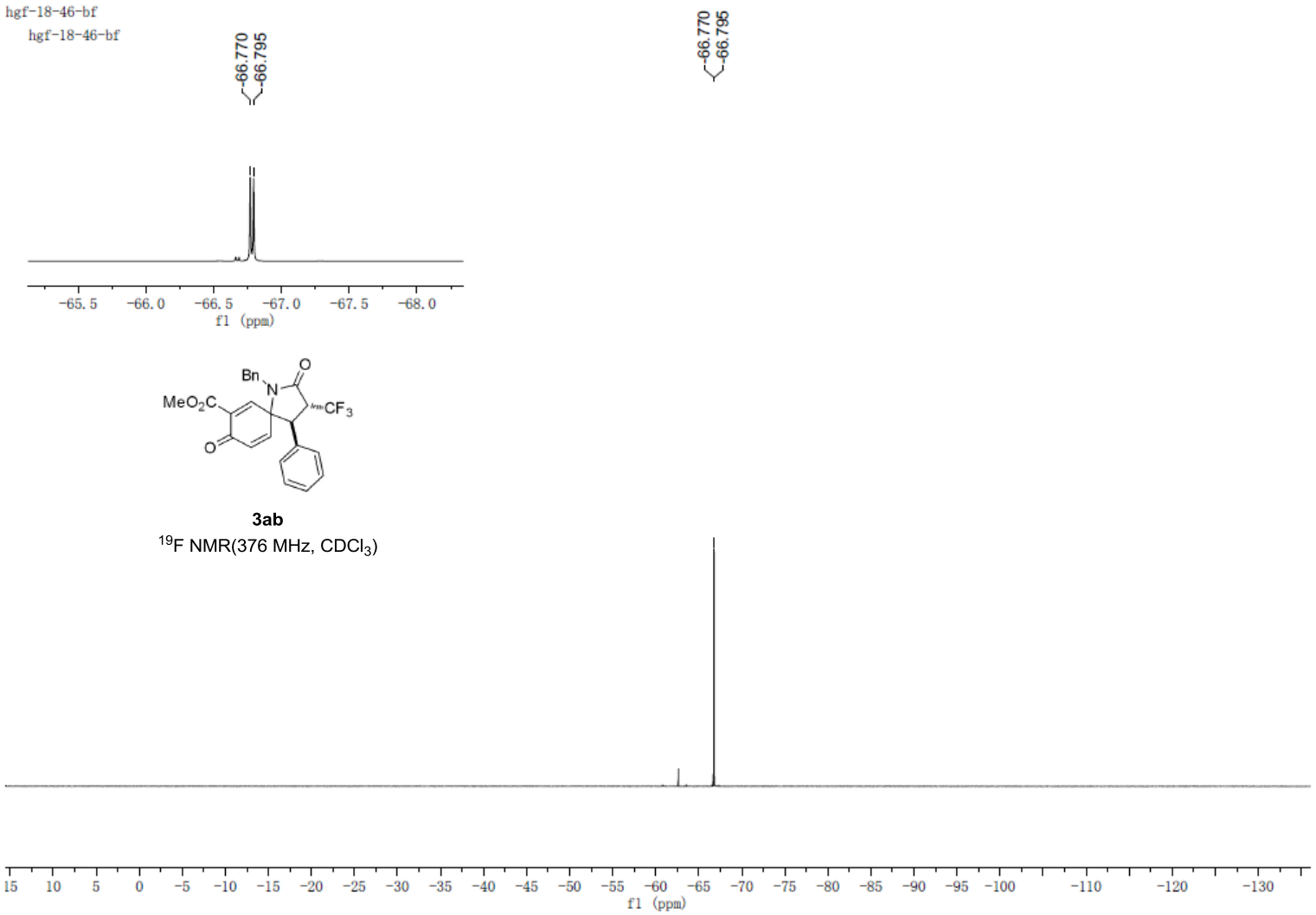
3aa

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



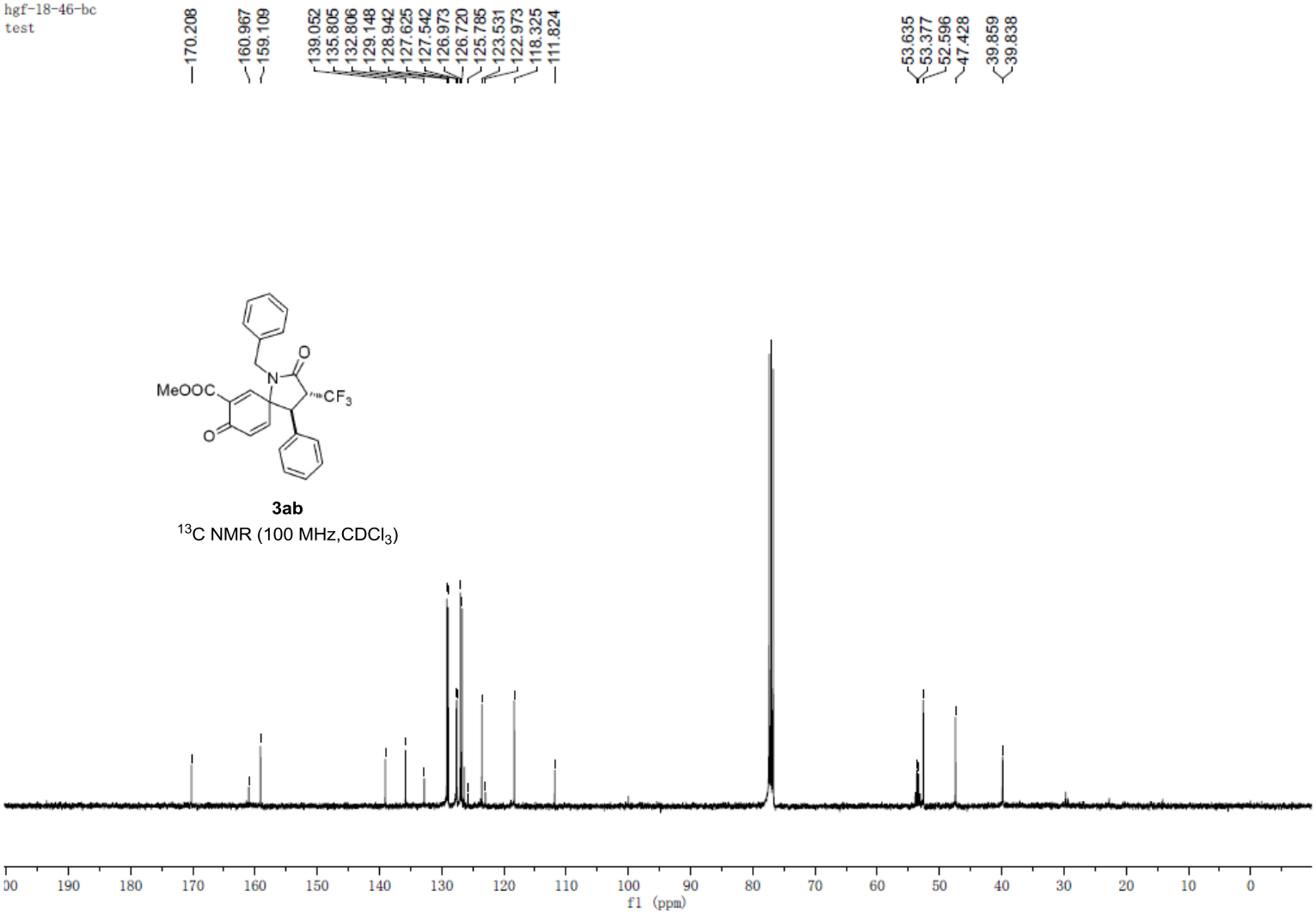
3ab

^{1}H NMR (400 MHz, $CDCl_3$)



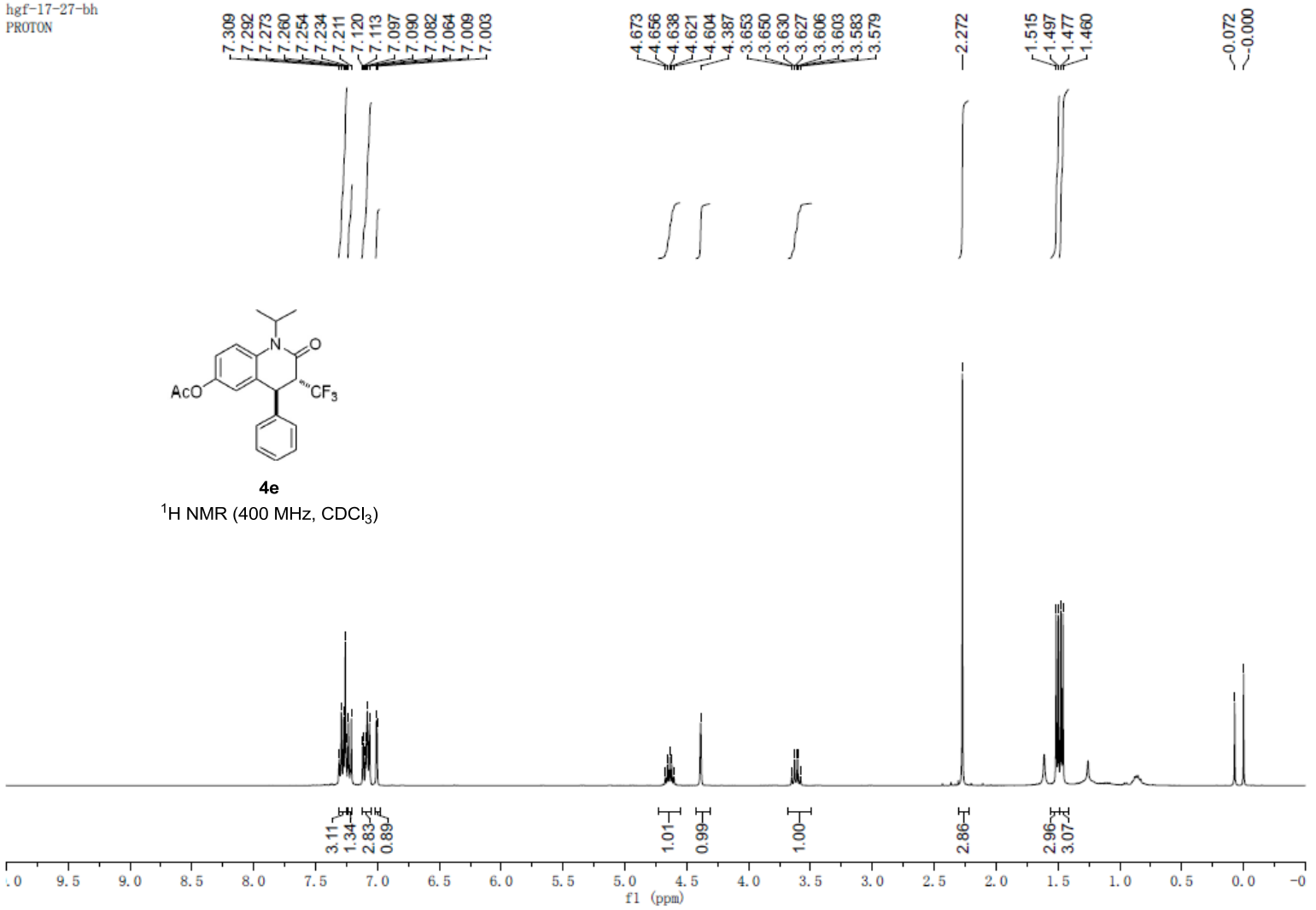
3ab

^{19}F NMR(376 MHz, $CDCl_3$)



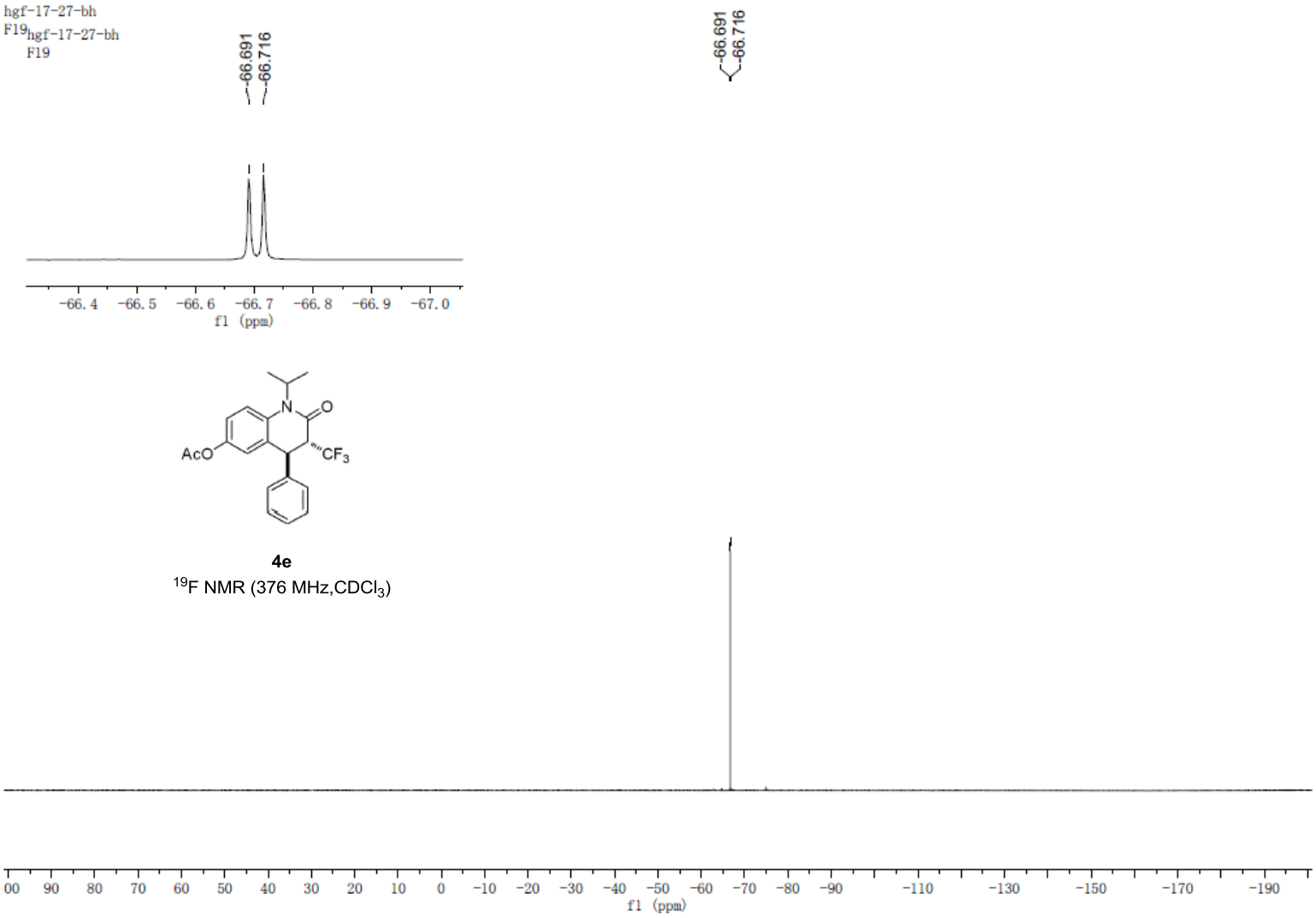
3ab

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



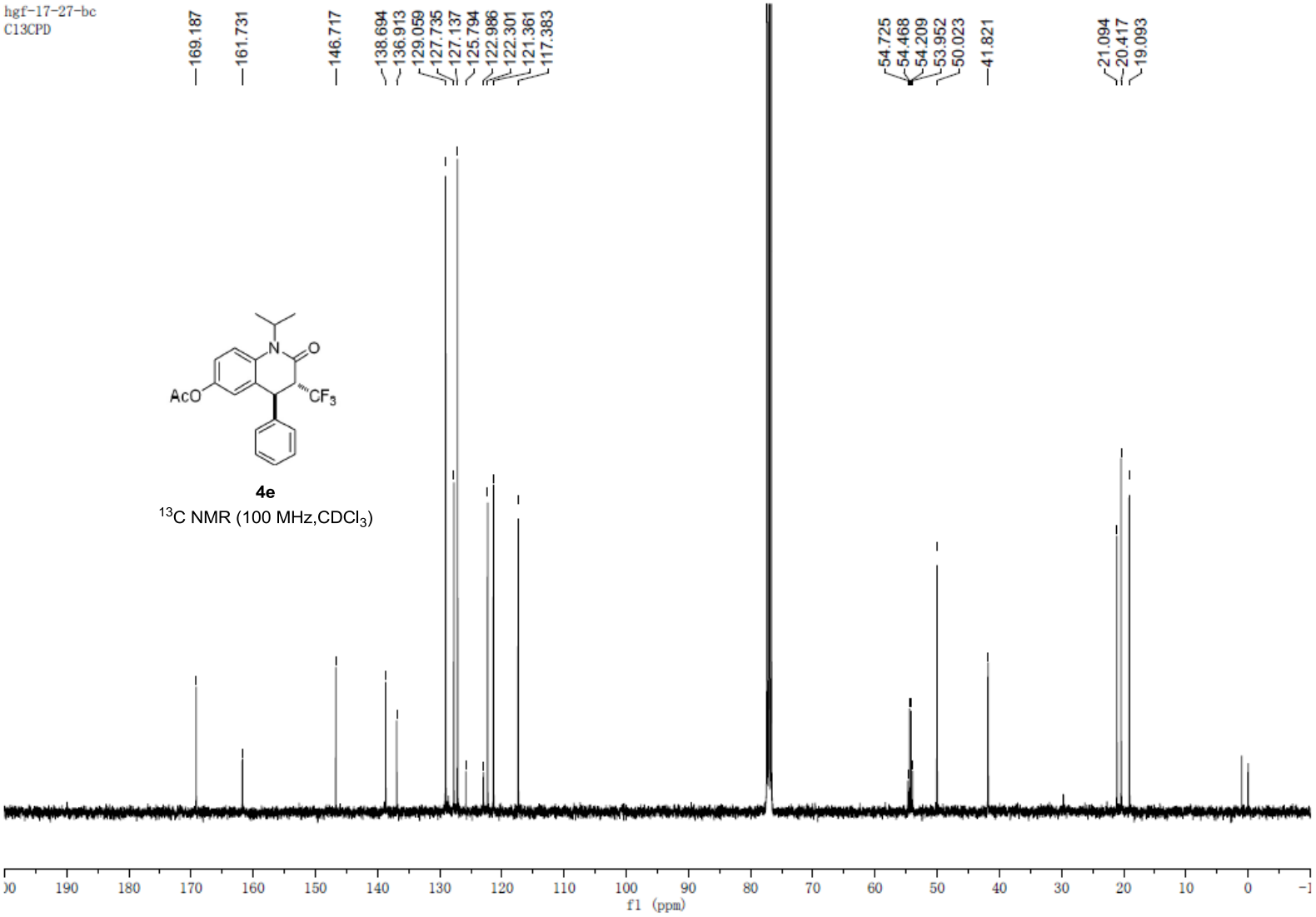
4e

^{1}H NMR (400 MHz, $CDCl_3$)



4e

^{19}F NMR (376 MHz,$CDCl_3$)



4e

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