Catalytic asymmetric 1,6-type Friedel–Crafts (hetero)arylations of δ-Cyano substituted para-quinone methides with 5-aminopyrazoles

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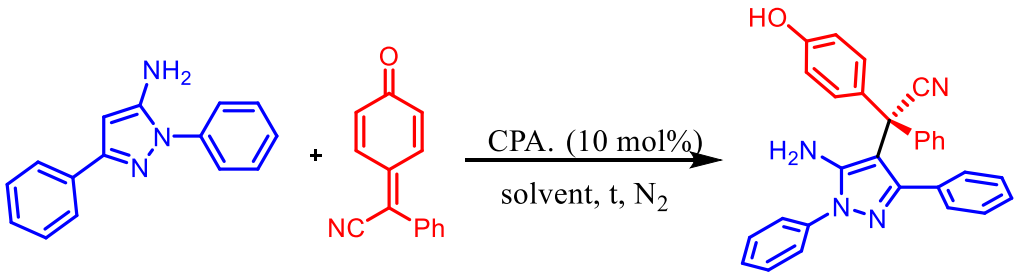
1. General information

All reactions were performed using oven-dried or flame-dried glassware equipped with a magnetic stir bar before used.

All reagents were purchased from commercial suppliers and used without further purification. All solvents were purified by standard operating method.

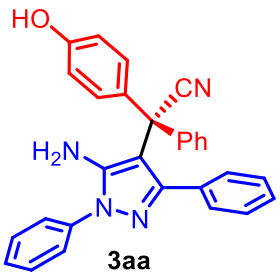
Thin-layer chromatography was performed with EMD silica gel 60 F_{254} plates eluting with solvents indicated, visualized by a 254 nm UV lamp and stained with phosphomolybdic acid (PMA). **^{1}H NMR**, **^{13}C NMR** and **^{19}F NMR** spectra were obtained on Bruker AM-400, Chemical shifts (δ) were quoted in ppm relative to tetramethylsilane or residual protio solvent as internal standard $CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.0 ppm for ^{13}C NMR； solvent d_6-DMSO (2.50 ppm), tetramethylsilane (0.00 ppm) asinternal reference for ^{1}H NMR and the deuterated solvent DMSO-d_6 (39.50 ppm) tetramethylsilane (0.00 ppm) as internal standard for ^{13}C NMR. multiplicities are as indicated: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. **High-resolution mass spectral analysis (HRMS) data** was measured on a Bruker impact II (Q-TOF) mass spectrum by means of the ESI technique. The **enantiomeric excesses** (ee) of the products were determined by high performance liquid chromatography (HPLC) analysis employing Daicel Chiralpak AD-H, OD-H columns.The 1,3-diphenyl-1H-pyrazol-5-amine **1** were prepared according to the reported procedures. [1] The δ-aryl-δ-cyano-disubstituted para-quinones **2** were prepared according to the reported procedures.[2]

2. General procedure for the synthesis of products



1 2 3

General procedure for the preparation of **3** and **5**: Unless otherwise noted, reactions were performed: 1,3-diphenyl-1H-pyrazol-5-amine (0.025 mmol), 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile (0.05 mmol), Cat.**C1** (10 mol%), in DCM (0.25 mL) at -40 °C using Low temperature reactor under N_2. Then stirred for 1-2 d. The resulting yellow mixture was concentrated under vacuum, the crude product was purified by flash column chromatography using petroleum ether/ EtOAc to give the title compound **3** and **5**.



3aa

(*S*)-2-(5-amino-1,3-diphenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3aa)

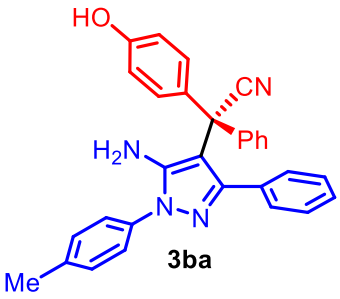
According to the general procedure, **3aa** was obtained using 1,3-diphenyl-1H-pyrazol-5-amine **1a** (5.9 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 87% yield (9.6 mg) and 91%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.50 (t, J = 8.0 Hz, 2H), 7.46 - 7.40 (m, 2H), 7.40 - 7.31 (m, 4H), 7.23 - 7.07 (m, 7H), 6.84 (d, J = 8.0 Hz, 2H), 3.97 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.4, 150.2, 144.6, 139.8, 138.4, 134.0, 129.3, 129.2, 129.1, 129.0, 128.3, 127.8, 127.5, 127.4, 127.2, 124.0, 122.2, 115.9, 98.5, 49.3.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{23}N_4O$ $(M+H)^+$: 443.1866, found 443.1858.

Enantiomeric excess is 91% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.12 min; minor isomer: tr = 8.30 min. $[\alpha]^{20}_D$ = -55.17(c = 0.2, $CHCl_3$).



3ba

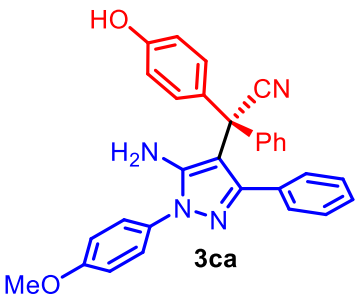
(*S*)-2-(5-amino-3-phenyl-1-(p-tolyl)-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile(3ba) According to the general procedure, **3ba** was obtained using 3-phenyl-1-(p-tolyl)-1H-pyrazol-5-amine **1b** (6.2 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 90% yield (10.3 mg) and 86%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 8.0 Hz, 4H), 7.18 (d, J = 4.0 Hz, 1H), 7.14 (t, J = 8.0 Hz, 2H), 7.08 (dd, J = 8.0, 12.0 Hz, 4H), 6.81 (d, J = 8.0 Hz, 2H), 3.89 (s, 2H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.4, 149.9, 144.5, 139.8, 136.7, 135.9, 134.1, 129.8, 129.2, 129.2, 29.1, 128.3, 127.8, 127.4, 127.4, 124.0, 122.2, 115.9, 98.2, 49.2, 20.6.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O$ $(M+H)^+$: 457.2023, found 457.2014.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.48 min; minor isomer: tr = 9.59 min $[\alpha]^{20}_D$ = 34.50(c = 0.2, $CHCl_3$).



3ca

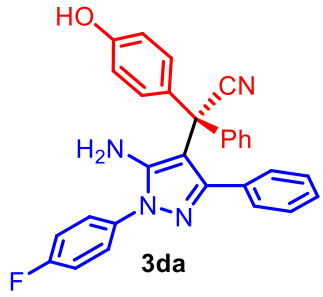
(*S*)-2-(5-amino-1-(4-methoxyphenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3ca) According to the general procedure, **3ca** was obtained using 1-(4-methoxyphenyl)-3-phenyl-1H-pyrazol-5-amine **1c** (6.2 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 71% yield (8.4 mg) and 92%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.45 - 7.39 (m, 2H), 7.37-7.33 (m, 3H), 7.22 - 7.17 (m, 1H), 7.16 - 7.12 (m, 3H), 7.10 - 7.06 (m, 4H), 7.04 (s, 1H), 6.83 (d, J = 12.0 Hz, 2H), 3.84 (s, 2H), 3.79 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 158.4, 157.4, 149.7, 144.6, 139.9, 134.1, 131.2, 129.3, 129.2, 129.1, 128.9, 128.3, 127.8, 127.4, 127.4, 126.0, 122.3, 115.9, 114.4, 97.9, 55.4, 49.3.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O_2$ $(M+H)^+$: 473.1972, found 473.1968.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 15.72 min; minor isomer: tr = 13.62 min. $[\alpha]^{20}_D$ = 7.50(c = 0.1, $CHCl_3$).



3da

(S)-2-(5-amino-1-(4-fluorophenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3da) According to the general procedure, **3da** was obtained using 1-(4-fluorophenyl)-3-phenyl-1H-pyrazol-5-amine **1d** (6.3 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 97% yield (11.2 mg) and 83%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1).

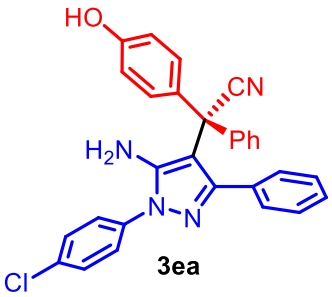
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.65 (dd, J = 8.9, 4.9 Hz, 2H), 7.43 (t, J = 7.3 Hz, 2H), 7.38-7.31 (m, 5H), 7.22 – 7.18 (m, 1H), 7.14 (t, J = 7.4 Hz, 2H), 7.11 – 7.07 (m, 4H), 6.82 (d, J = 8.7 Hz, 2H), 3.95 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 160.9 (d, J = 250.0 Hz), 157.4, 150.2, 144.8, 139.8, 134.7 (d, J = 3.0 Hz), 133.9, 129.2, 129.15, 125.13, 128.9, 128.4, 127.8, 127.6, 127.4, 126.5 (d, J = 8.0 Hz), 122.2, 116.2, 115.9, 98.4, 49.2.

^{19}F NMR (375 MHz, DMSO) δ -114.7.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}FN_4ONa$ $(M+Na)^+$: 483.1592, found 483.1596.

Enantiomeric excess is 83% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.74 min; minor isomer: tr = 10.39 min.



3ea

(*S*)-2-(5-amino-1-(4-chlorophenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3ea) According to the general procedure, **3ea** was obtained using 1-(4-chlorophenyl)-3-phenyl-1H-pyrazol-5-amine **1e** (6.7 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 87% yield (10.4 mg) and 88%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1).

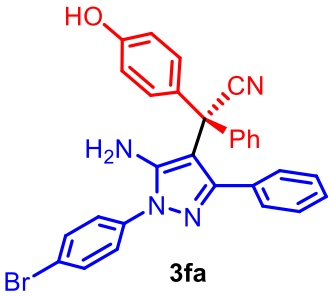
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 7.66 -7.62 (m, 2H), 7.56 - 7.52 (m, 2H), 7.44 - 7.40 (m, 2H), 7.38 - 7.33 (m, 1H), 7.33 - 7.30 (m, 2H), 7.22 - 7.17 (m, 1H), 7.15 - 7.11 (m, 2H), 7.09 (d, *J* = 1.9 Hz, 1H), 7.07 - 7.04 (m, 3H), 6.80 (d, *J* = 8.8 Hz, 2H), 4.00 (s, 2H).

^{13}C NMR (100 MHz, DMSO) δ 157.4, 150.5, 144.8, 139.7, 137.3, 133.8, 131.4, 129.16, 129.11, 129.0, 128.9, 128.3,127.8, 127.6, 127.4, 125.6, 122.1, 115.9, 98.8, 49.2.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{35}ClN_4ONa(M+Na)^+$: 499.1296, found 499.1291.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{37}ClN_4ONa(M+Na)^+$: 501.1296 found 501.1296.

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 14.45 min; minor isomer: tr = 11.75 min. $[\alpha]^{20}_D$ = 27.00(c = 0.2, $CHCl_3$).



3fa

(*S*)-2-(5-amino-1-(4-bromophenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3fa) According to the general procedure, **3fa** was obtained using 1-(4-bromophenyl)-3-phenyl-1H-pyrazol-5-aminee **1f** (7.9 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 75% yield (9.8 mg) and 86%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

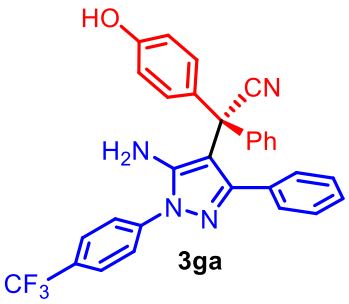
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 7.70 - 7.66 (m, 2H), 7.61 - 7.57 (m, 2H), 7.44 - 7.41 (t, J = 7.2 Hz, 2H), 7.37 (d, J = 8.0 Hz, 1H), 7.34 - 7.32 (m, 2H), 7.23 - 7.18 (m, 1H), 7.16 - 7.12 (m, 2H), 7.11 - 7.05 (m, 4H), 6.82 (d, J = 8.0 Hz, 2H), 4.03 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.4, 150.6, 144.8, 139.7, 137.7, 133.8, 132.1, 129.2, 129.1, 129.0, 128.9, 128.3, 127.8, 127.6, 127.4, 125.9, 122.1, 119.8, 115.9, 98.8, 49.2.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}{}^{79}BrN_4O$ $(M+H)^+$: 520.0972, found 520.0985.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}{}^{81}BrN_4O$ $(M+H)^+$: 522.0972, found 522.0973.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 16.19 min; minor isomer: tr = 12.83 min. $[\alpha]^{20}_D$ = 13.83(c = 0.2, $CHCl_3$).



3ga

(*S*)-2-(5-amino-3-phenyl-1-(4-(trifluoromethyl)phenyl)-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3ga) According to the general procedure, **3ga** was obtained using 3-phenyl-1-(4-(trifluoromethyl)phenyl)-1H-pyrazol-5-amine **1g** (7.6 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 94% yield (12.0 mg) and 91%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

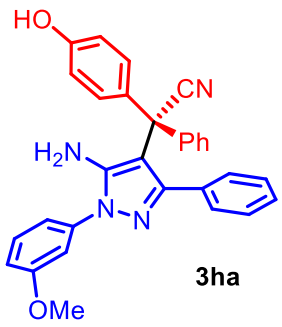
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.65 (q, J = 4.0 Hz, 2H), 7.45 - 7.41 (m, 2H), 7.38 - 7.31 (m, 5H), 7.22 - 7.18 (m, 1H), 7.16 - 7.13 (m, 2H), 7.13 - 7.08 (m, 4H), 6.83 (d, J = 12.0 Hz, 2H), 3.95 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.5, 151.2, 145.2, 141.8, 139.6, 133.7, 132.6, 129.2, 128.9, 128.4, 127.8, 127.7, 127.5, 126.9 (d, J = 32.0 Hz), 126.4 (d, J=4.0 Hz), 124.1 (d, J=270.0 Hz), 123.9, 122.1, 116.0, 115.3, 99.4, 49.2.

^{19}F NMR (376 MHz, DMSO) δ -114.7.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{22}F_3N_4O$ $(M+H)^+$:511.1740 found 511.1740.

Enantiomeric excess is 91% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 14.20 min; minor isomer: tr = 10.55 min. $[\alpha]^{20}_D$ = 22.50(c = 0.2, $CHCl_3$).



3ha

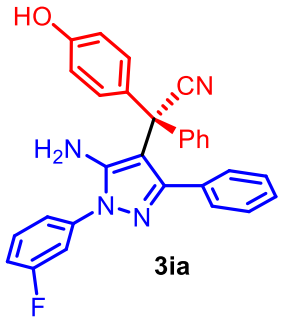
(*S*)-2-(5-amino-1-(3-methoxyphenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3ha) According to the general procedure, **3ha** was obtained using 1-(3-methoxyphenyl)-3-phenyl-1H-pyrazol-5-amine **1h** (6.6 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 85% yield (10.0 mg) and 88%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.45 - 7.41 (m, 2H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.35 - 7.33 (m, 2H), 7.22 - 7.18 (m, 3H), 7.17 - 7.12 (m, 3H), 7.10 - 7.07 (m, 3H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 2H), 3.99 (s, 2H), 3.80 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 159.8, 157.4, 150.2, 144.7, 139.8, 139.4, 134.0, 130.1, 129.2, 129.13, 129.11, 129.0, 128.3, 127.8, 127.5, 127.4, 122.2, 116.1, 115.9, 113.3, 109.3, 98.4, 55.4, 49.3 .

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O_2$ $(M+H)^+$: 473.1972, found 473.1968.

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.37 min; minor isomer: tr = 8.01 min. $[\alpha]^{20}_D$ = 36.83(c = 0.2, $CHCl_3$).



3ia

(*S*)-2-(5-amino-1-(3-fluorophenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3ia) According to the general procedure, **3ia** was obtained using 1-(3-fluorophenyl)-3-phenyl-1H-pyrazol-5-amine **1i** (6.3 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 98% yield (11.3 mg) and 84%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

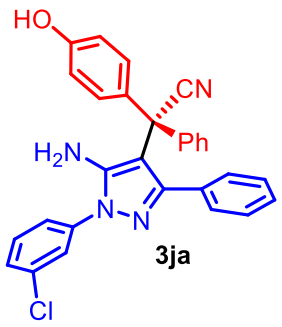
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.83 (s, 1H), 7.54 - 7.49 (m, 3H), 7.43 (t, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.23 - 7.19 (m, 2H), 7.15 (t, J = 8.0 Hz, 2H), 7.09 (t, J = 8.0 Hz, 4H), 6.83 (d, J = 8.0 Hz, 2H), 4.08 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 162.1 (d, J = 240.0 Hz), 157.5, 150.7, 144.9, 139.9 (d, J = 10.0 Hz), 139.7, 133.8, 130.9 (d, J = 9.1 Hz), 129.23, 129.18, 129.0, 128.9, 128.4, 127.8, 127.7, 127.5, 122.1, 119.7 (d, J = 2.8 Hz), 115.9, 113.9 (d, J = 21 Hz), 111.0 (d, J = 25 Hz), 99.0, 49.2.

^{19}F NMR (376 MHz, DMSO-d_6) δ -111.5.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}FN_4ONa$ $(M+Na)^+$: 483.1592, found 483.1609.

Enantiomeric excess is 84% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.43 min; minor isomer: tr = 7.37 min. $[\alpha]^{20}_D$ = (c = 0.2, $CHCl_3$).



3ja

(*S*)-2-(5-amino-1-(3-chlorophenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3ja) According to the general procedure, **3ja** was obtained using 1-(3-chlorophenyl)-3-phenyl-1H-pyrazol-5-amine **1j** (6.7 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 93% yield (11.1 mg) and 82%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

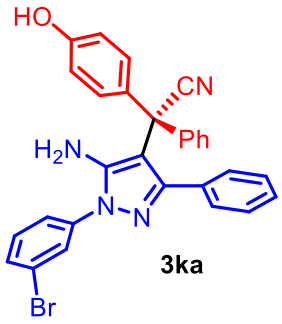
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.83 (s, 1H), 7.71 (t, *J* = 4.0 Hz, 1H), 7.63 - 7.61 (m, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.45 - 7.41 (m, 3H), 7.39 - 7.35 (m, 1H), 7.34 - 7.32 (m, 2H), 7.23 - 7.19 (m, 1H), 7.15 (t, *J* = 8.0 Hz, 2H), 7.11 - 7.06 (m, 4H), 6.82 (d, *J* = 8.0 Hz, 2H), 4.07 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.5, 150.8, 145.0, 139.7 (d, J = 4.0 Hz), 133.7, 133.5, 130.9, 129.21, 129.15, 129.0, 128.9, 128.4, 127.8, 127.7, 127.4, 127.0, 123.6, 122.4, 122.1, 115.9, 99.0, 49.2.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{35}ClN_4ONa$ $(M+Na)^+$: 499.1296, found 499.1291.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{37}ClN_4ONa$ $(M+Na)^+$: 501.1296, found 501.1296.

Enantiomeric excess is 82% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.15 min; minor isomer: tr = 7.41 min. $[\alpha]^{20}_D$ = 29.17(c = 0.2, $CHCl_3$).



3ka

(*S*)-2-(5-amino-1-(3-bromophenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3ka) According to the general procedure, **3ka** was obtained using 1-(3-bromophenyl)-3-phenyl-1H-pyrazol-5-amine **1k** (7.9 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 99% yield (12.9 mg) and 83%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

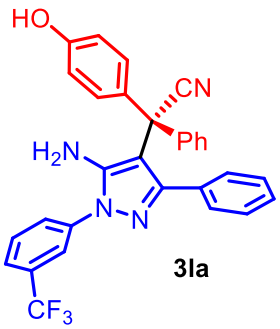
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 7.83 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.44 (q, *J* = 7.6, 7.2 Hz, 3H), 7.38 (d, *J* = 6.7 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 2H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 2H), 7.07 (t, *J* = 10.1 Hz, 4H), 6.81 (d, *J* = 7.7 Hz, 2H), 4.05 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.4, 150.7, 144.9, 139.8, 139.6, 133.7, 131.1, 129.8, 129.2, 129.1, 129.0, 128.9, 128.3, 127.8, 127.6, 127.4, 126.4, 122.7, 122.1, 121.7, 115.9, 99.0, 49.2.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}{}^{79}BrN_4O$ $(M+H)^+$: 520.0972, found 520.0985.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}{}^{81}BrN_4O$ $(M+H)^+$: 522.0972, found 522.0969.

Enantiomeric excess is 83% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.33 min; minor isomer: tr = 7.70 min. $[\alpha]^{20}_D$ = 27.33(c = 0.2, $CHCl_3$).



3la

(*S*)-2-(5-amino-3-phenyl-1-(3-(trifluoromethyl)phenyl)-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3la) According to the general procedure, **3la** was obtained using 3-phenyl-1-(3-(trifluoromethyl)phenyl)-1H-pyrazol-5-amine **1l** (7.6 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 87% yield (11.1 mg) and 74%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

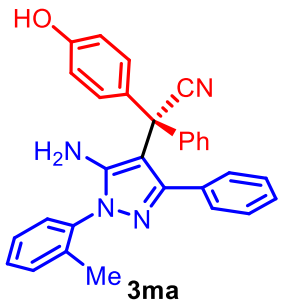
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.98 - 7.95 (m, 2H), 7.73 (d, J = 8.0 Hz, 2H), 7.45 - 7.42 (m, 2H), 7.39 - 7.36 (m, 1H), 7.34 - 7.32 (m, 2H), 7.24 - 7.20 (m, 1H), 7.17 - 7.14 (m, 2H), 7.11 - 7.06 (m, 4H), 6.82 (d, J = 8.0 Hz, 2H), 4.11 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.5, 151.2, 145.2, 141.8, 139.6, 133.7, 132.6, 129.2, 129.2, 128.9, 128.1 (d, J =67.0 Hz), 127.8, 127.5, 126.9 (d, J = 32.0 Hz), 126.4 (d, J = 4.0 Hz), 124.1 (d, J = 270.0 Hz), 123.9, 122.1, 116.0, 115.3, 99.4, 49.2.

^{19}F NMR (376 MHz, DMSO-d_6) δ -61.1.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{22}F_3N_4O$ $(M+H)^+$: 511.1740, found 511.1738.

Enantiomeric excess is 74% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.55 min; minor isomer: tr = 5.83 min. $[\alpha]^{20}_D$ = (c = 0.2, $CHCl_3$).



3ma

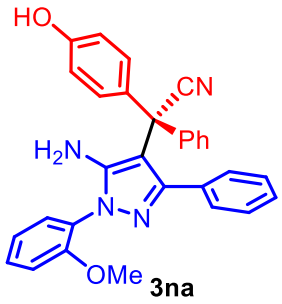
(*S*)-2-(5-amino-3-phenyl-1-(o-tolyl)-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3ma) According to the general procedure, **3ma** was obtained using 3-phenyl-1-(o-tolyl)-1H-pyrazol-5-amine **1m** (6.2 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 94% yield (10.7 mg) and 92%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 7.44 (t, J = 8.0 Hz, 2H), 7.40 - 7.37 (m, 4H), 7.36 - 7.32 (m, 3H), 7.21 - 7.17 (m, 1H), 7.15 - 7.12 (m, 2H), 7.10 - 7.06 (m, 4H), 6.82 (d, J = 8.0 Hz, 2H), 3.62 (s, 2H), 2.11 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.3, 149.6, 145.5, 140.1, 136.7, 136.1, 134.2, 131.0, 129.5, 129.3, 129.11, 129.08, 128.9, 128.3, 128.2, 127.7, 127.3, 126.8, 122.3, 115.8, 96.6, 49.2, 17.2.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_2O$ $(M+H)^+$: 429.1961, found 429.1968.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.28 min; minor isomer: tr = 6.78 min. $[\alpha]^{20}_D$ = 39.67(c = 0.2, $CHCl_3$).



3na

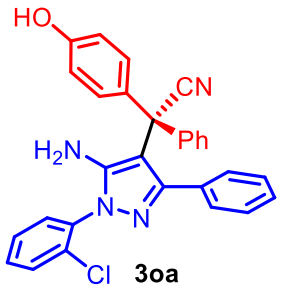
(*S*)-2-(5-amino-1-(2-methoxyphenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3na) According to the general procedure, **3na** was obtained using 1-(2-methoxyphenyl)-3-phenyl-1H-pyrazol-5-amine **1n** (6.2 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 92% yield (10.9 mg) and 92% ee as a yellow solid (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.45 - 7.41 (m, 2H), 7.38 (t, J = 8.0 Hz, 2H), 7.35 - 7.33 (m, 2H), 7.22 - 7.18 (m, 3H), 7.17 - 7.12 (m, 3H), 7.10 - 7.07 (m, 3H), 6.95 (d, J = 8.0 Hz, 1H), 6.83 (d, J = 8.0 Hz, 2H), 3.99 (s, 2H), 3.80 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 159.8, 157.4, 150.2, 144.7, 139.8, 139.4, 134.0, 130.1, 129.2, 129.13, 129.11, 129.0, 128.3, 127.8, 127.5, 127.4, 122.2, 116.1, 115.9, 113.3, 109.3, 98.4, 55.4, 49.3.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_2O_2$ $(M+H)^+$: 445.1911, found 445.1920.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.75 min; minor isomer: tr = 10.30 min. $[\alpha]^{20}_D$ = 41.50(c = 0.2, $CHCl_3$).



3oa

(*S*)-2-(5-amino-1-(2-chlorophenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3oa) According to the general procedure, **3oa** was obtained using 1-(2-chlorophenyl)-3-phenyl-1H-pyrazol-5-amine **1o** (6.7 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 89% yield (10.6 mg) and 92%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

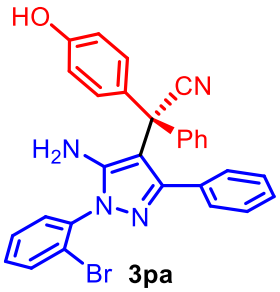
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.85 (s, 1H), 7.68 - 7.62 (m, 2H), 7.56 - 7.49 (m, 2H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 2H), 7.07 (t, *J* = 8.0 Hz, 4H), 6.83 (d, *J* = 8.0 Hz, 2H), 3.73 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.4, 150.2, 146.1, 140.0, 135.3, 134.0, 132.1, 131.1, 130.6, 130.3, 129.3, 129.2, 129.1, 128.9, 128.3 (d, *J* = 12.0 Hz), 127.8, 127.5, 127.4, 122.3, 115.9, 96.5, 49.1.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{35}ClN_4ONa$ $(M+Na)^+$: 499.1296, found 499.1291.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{37}ClN_4ONa$ $(M+Na)^+$: 501.1296, found 501.1291.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 14.10 min; minor isomer: tr = 8.32 min. $[\alpha]^{20}_D$ = 31.83(c = 0.2, $CHCl_3$).



3pa

(*S*)-2-(5-amino-1-(2-bromophenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3pa) According to the general procedure, **3pa** was obtained using 1-(2-bromophenyl)-3-phenyl-1H-pyrazol-5-aminee **1p** (7.9 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 95% yield (12.4 mg) and 86% ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

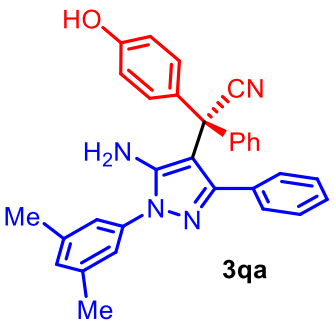
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.85 (s, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.47 - 7.43 (m, 3H), 7.40 - 7.36 (m, 3H), 7.22 - 7.11 (m, 7H), 6.87 (d, *J* = 8.4 Hz, 2H), 3.73 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.4, 150.1, 145.9, 140.0, 136.9, 134.0, 133.4, 131.4, 130.8, 129.5, 129.26, 129.1, 128.9, 128.8, 127.93 (d, *J* = 81.0 Hz), 127.87, 127.4, 122.7, 122.3, 115.9, 96.7, 49.1.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}{}^{79}BrN_4O$ $(M+H)^+$: 520.0972, found 520.0985.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}{}^{81}BrN_4O$ $(M+H)^+$: 522.0972, found 522.0969.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 18.08 min; minor isomer: tr = 9.09 min. $[\alpha]^{20}_D$ = (c = 0.2, $CHCl_3$).



3qa

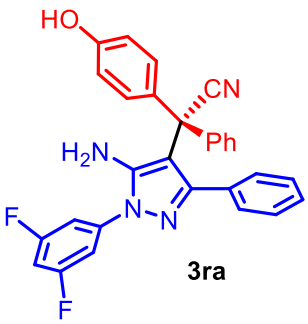
(*S*)-2-(5-amino-1-(3,5-dimethylphenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3qa) According to the general procedure, **3qa** was obtained using 1-(3,5-dimethylphenyl)-3-phenyl-1H-pyrazol-5-amine **1q** (6.6 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 90% yield (10.6 mg) and 91%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (600 MHz, DMSO-d_6) δ 9.77 (s, 1H), 7.42 (dd, J = 8.2, 6.8 Hz, 2H), 7.38 - 7.35 (m, 1H), 7.31 - 7.29 (m, 2H), 7.20 - 7.18 (m, 3H), 7.13 (t, J = 7.4 Hz, 2H), 7.07 - 7.06 (m, 2H), 7.04 - 7.03 (m, 2H), 7.01 (s, 1H), 6.81 - 6.79 (m, 2H), 3.88 (s, 2H), 2.31 (s, 6H).

^{13}C NMR (150 MHz, DMSO-d_6) δ 157.3, 149.9, 144.4, 139.8, 138.5, 138.1, 134.0, 129.2, 129.1, 129.1, 128.9, 128.3, 127.8, 127.4, 127.3, 122.2, 121.7, 115.8, 98.0, 49.2, 20.8.

HRMS (ESI) *m/z* calcd. for $C_{31}H_{27}N_4O$ $(M+H)^+$: 471.2179, found 471.2173.

Enantiomeric excess is 91% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.50 min; minor isomer: tr = 5.12 min. [α]20D = 17.33(c = 0.2, CHCl3).



3ra

(*S*)-2-(5-amino-1-(3,5-difluorophenyl)-3-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3ra) According to the general procedure, **3ra** was obtained using 1-(3,5-difluorophenyl)-3-phenyl-1H-pyrazol-5-amine **1r** (6.8 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 84% yield (10.0 mg) and 90%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

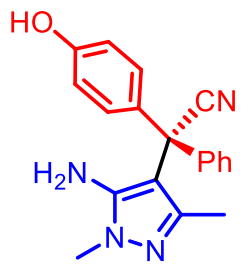
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.88 (s, 1H), 7.46 - 7.41 (m, 4H), 7.38 - 7.35 (m, 3H), 7.27 - 7.20 (m, 2H), 7.18 - 7.15 (m, 3H), 7.12 - 7.10 (m, 3H), 6.86 (d, *J* = 8.8 Hz, 2H), 4.22 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 162.5 (dd, *J* = 15.0Hz, 244 Hz), 157.6, 151.2, 145.3, 140.7 (t, *J* = 13.0 Hz), 139.6, 133.6, 129.3, 129.2, 129.0, 128.9, 128.5, 127.9, 127.8, 127.5, 122.1, 116.0, 107.1 (d, *J* = 29.0 Hz), 102.3 (t, *J* = 26.0 Hz), 99.6, 49.3.

^{19}F NMR (376 MHz, DMSO-d_6) δ -108.3.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}F_2N_4O$ $(M+H)^+$: 479.1678, found 479.1686.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.09 min; minor isomer: tr = 5.61 min. $[\alpha]^{20}_D$ = (c = 0.2, $CHCl_3$).



3sa

(S)-2-(5-amino-1,3-dimethyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (3sa)

According to the general procedure, **3sa** was obtained using 1,3-dimethyl-1H-pyrazol-5-amine **1s** (2.8 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 91% yield (7.2 mg) and 93%ee as a white solid (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

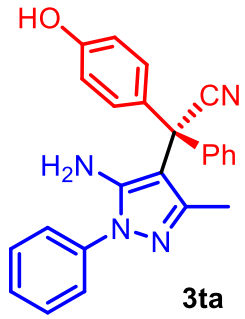
^{1}H NMR (600 MHz, DMSO-d_6) δ 9.77 (s, 1H), 7.47 – 7.43 (m, 2H), 7.39 (t, J = 7.3 Hz, 1H), 7.25 (d, J = 7.3 Hz, 2H), 7.02 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.5 Hz, 2H), 3.71 (s, 2H), 3.42 (s, 3H), 1.58 (s, 3H).

^{13}C NMR (150 MHz, DMSO-d_6) δ 157.4, 144.0, 143.5, 139.6, 129.04, 129.02, 128.9, 128.3, 127.7, 122.7, 115.8, 96.8, 49.0, 34.2, 13.5.

HRMS (ESI) *m/z* calcd. for $C_{19}H_{18}N_4O$ $(M+H)^+$: 319.1553, found 319.1550.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AS-H, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 40.2 min; minor isomer: tr = 35.1min.

$[\alpha]^{20}_D$ =18.36 (c = 0.2, $CHCl_3$).



3ta

(S)-2-(5-amino-3-methyl-1-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile(3ta) According to the general procedure, **3sa** was obtained using 3-methyl-1-phenyl-1H-pyrazol-5-amine **1s** (2.8 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 93% yield (8.8 mg) and 84%ee as a white solid (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

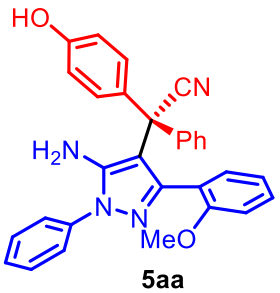
^{1}H NMR (600 MHz, DMSO-d_6) δ 9.81 (s, 1H), 7.52 – 7.41 (m, 7H), 7.35 – 7.31 (m, 3H), 7.13 – 7.07 (m, 2H), 6.88 – 6.83 (m, 2H), 3.83 (s, 2H), 1.68 (s, 3H).

^{13}C NMR (150 MHz, DMSO-d_6) δ 157.5, 146.4, 144.0, 139.3, 138.5, 129.17, 129.15, 129.1, 128.5, 128.4, 127.7, 126.8, 123.7, 122.5, 115.9, 98.0, 49.1, 13.7.

HRMS (ESI) *m/z* calcd. for $C_{19}H_{18}N_4O$ $(M+H)^+$: 381.1710, found 381.1711.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AS-H, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 54.02 min; minor isomer: tr = 42.5 min.

$[\alpha]^{20}_D$ = 32.54(c = 0.2, $CHCl_3$).



5aa

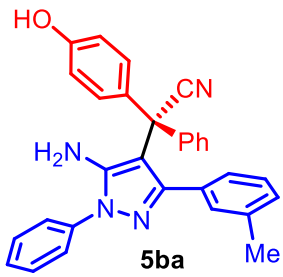
(*S*)-2-(5-amino-3-(2-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (5aa) According to the general procedure, **5aa** was obtained using 3-(2-methoxyphenyl)-1-phenyl-1H-pyrazol-5-amine **4a** (6.2 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 87% yield (10.3 mg) and 74%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 7.45 (dd, *J* = 14.6, 7.2 Hz, 4H), 7.39 - 7.37 (m, 1H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 9.2 Hz, 2H), 7.14 - 7.11 (m, 2H), 7.06 (t, *J* = 7.3 Hz, 5H), 6.84 - 6.79 (m, 2H), 3.82 (s, 3H), 3.54 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.0, 156.7, 147.8, 143.9, 138.9, 138.6, 130.8, 129.2, 129.1, 128.9, 128.2, 127.7, 127.5, 126.9, 123.4, 123.1, 121.9, 119.2, 115.2, 109.7, 99.8, 53.8, 49.6.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O_2$ $(M+H)^+$: 473.1972, found 473.1968.

Enantiomeric excess is 74% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.35 min; minor isomer: tr = 10.09 min. $[\alpha]^{20}_D$ = 23.67(c = 0.2, $CHCl_3$).



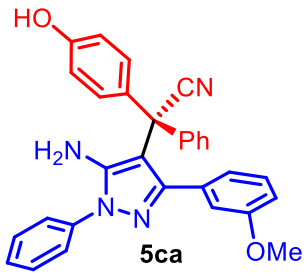
5ba

(*S*)-2-(5-amino-1-phenyl-3-(m-tolyl)-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (5ba) According to the general procedure, **5ba** was obtained using 1-phenyl-3-(m-tolyl)-1H-pyrazol-5-amine **4b** (6.2 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 92% yield (10.5 mg) and 91%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.4, 150.2, 144.5, 139.9, 138.4, 136.2, 133.8, 129.8, 129.3, 129.2, 129.1, 128.3, 128.1, 127.8, 127.3, 127.2, 125.9, 124.0, 122.1, 115.8, 98.5, 49.3, 20.9.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O$ $(M+H)^+$: 457.2023, found 457.2014.

Enantiomeric excess is 91% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.26 min; minor isomer: tr = 7.46 min. $[\alpha]^{20}_D$ = (c = 0.2, $CHCl_3$).



5ca

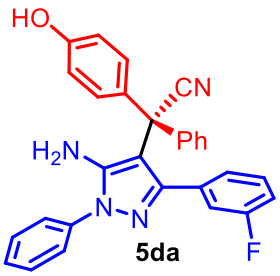
(*S*)-2-(5-amino-3-(3-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (5ca) According to the general procedure, **5ca** was obtained using 3-(3-methoxyphenyl)-1-phenyl-1H-pyrazol-5-amine **4c** (6.2 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 88% yield (10.4 mg) and 90%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.77 (s, 1H), 7.59 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.43 (d, *J* = 7.4 Hz, 2H), 7.38 (d, *J* = 7.0 Hz, 2H), 7.32 (d, *J* = 7.7 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 3H), 6.81 (d, *J* = 8.8 Hz, 2H), 6.76 - 6.74 (m, 2H), 6.55 (s, 1H), 3.88 (s, 2H), 3.50 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 158.2, 157.5, 150.0, 144.7, 139.9, 138.4, 135.3, 129.3, 129.2, 128.6, 128.4, 127.9, 127.3, 124.1, 122.2, 121.4, 115.9, 114.0, 113.9, 98.2, 54.9, 54.6, 49.3.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O_2$ $(M+H)^+$: 473.1972, found 473.1968.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 44.32 min; minor isomer: tr = 39.01 min. $[\alpha]^{20}_D$ = 39.00(c = 0.2, $CHCl_3$).



5da

(*S*)-2-(5-amino-3-(3-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (5da) According to the general procedure, **5da** was obtained using 3-(3-fluorophenyl)-1-phenyl-1H-pyrazol-5-amine **4d** (6.3 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 90% yield (10.4 mg) and 86%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

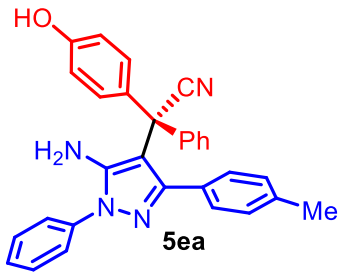
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 8.0 Hz, 2H), 7.45 - 7.42 (m, 2H), 7.40 - 7.37 (m, 2H), 7.34 (d, *J* = 6.9 Hz, 2H), 7.22 - 7.17 (m, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.04 (td, *J* = 8.6, 8.1, 2.4 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.78 - 6.75 (m, 1H), 4.03 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3 (d, *J* = 241.0 Hz), 157.5, 148.9, 144.8, 139.6, 138.2, 136.3 (d, *J* = 8.0 Hz), 129.5, 129.4, 129.3, 129.2, 128.9, 128.5, 127.9,127.4, 125.1, 124.1, 122.2, 116.0, 115.6 (d, *J* = 22.0 Hz), 114.3 (d, *J* = 21.0 Hz), 98.5, 49.2.

^{19}F NMR (376 MHz, DMSO-d_6) δ -114.1.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}FNaN_4ONa$ $(M+Na)^+$: 483.1592, found 483.1609.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.04 min; minor isomer: tr = 8.71 min. $[\alpha]^{20}_D$ = 27.83(c = 0.2, $CHCl_3$).



5ea

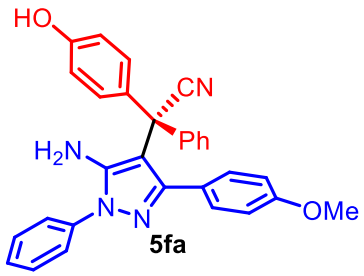
(*S*)-2-(5-amino-1-phenyl-3-(p-tolyl)-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (5ea) According to the general procedure, **5ea** was obtained using 1-phenyl-3-(p-tolyl)-1H-pyrazol-5-amine **4e** (6.2 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 97% yield (11.1 mg) and 90%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 7.60 (d, *J* = 7.5 Hz, 2H), 7.47 (dt, *J* = 15.9, 7.6 Hz, 4H), 7.41 - 7.36 (m, 2H), 7.34 - 7.2 (m, 2H), 7.08 (d, *J* = 8.7 Hz, 2H), 6.96 (s, 4H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 2H), 2.24 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.4, 150.1, 144.6, 139.9, 138.4, 136.7, 131.1, 129.3, 129.2, 128.8, 128.37, 128.1, 127.9, 127.2, 124.0, 122.2, 115.9, 98.4, 49.3, 20.8.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O$ $(M+H)^+$: 457.2023, found 457.2024.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.10 min; minor isomer: tr = 7.80 min. $[\alpha]^{20}_D$ = 37.50(c = 0.2, $CHCl_3$).



5fa

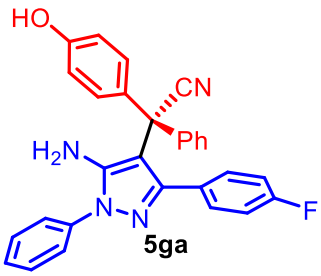
(*S*)-2-(5-amino-3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (5fa) According to the general procedure, **5fa** was obtained using 3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-5-amine **4f** (6.3 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 92% yield (10.9 mg) and 90% ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.47 (dt, *J* = 14.2, 7.6 Hz, 4H), 7.41 - 7.36 (m, 2H), 7.33 (d, *J* = 7.3 Hz, 2H), 7.09 (d, *J* = 8.7 Hz, 2H), 7.00 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 2H), 3.70 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 158.7, 157.4, 149.9, 144.6, 139.9, 138.5, 130.2, 129.3, 129.2, 128.4, 127.87, 127.1, 126.3, 124.0, 122.3, 115.9, 112.9, 98.3, 55.0, 49.3.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O_2$ $(M+H)^+$: 473.1972, found 473.1972.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.82 min; minor isomer: tr = 9.62 min. $[\alpha]^{20}_D$ = 27.17(c = 0.2, $CHCl_3$).



5ga

(S)-2-(5-amino-3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (5ga) According to the general procedure, **5ga** was obtained using 3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-5-amine **4g** (6.3 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 87% yield (10.9 mg) and 84% ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1).

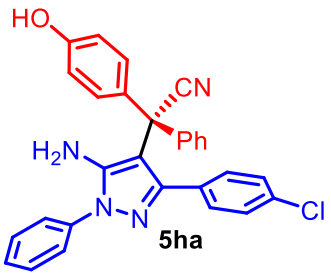
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.65 (dd, J = 8.8, 4.9 Hz, 2H), 7.45 - 7.31 (m, 7H), 7.22 - 7.07 (m, 7H), 6.82 (d, J = 8.7 Hz, 2H), 3.95 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3 (d, J=240.0 Hz), 157.5, 148.9 (d, J=3.0 Hz), 144.8, 139.6, 138.2, 136.3 (d, J=8.0 Hz), 129.5, 129.3, 129.2, 128.9, 128.5, 127.8, 127.4, 125.1 (d, J=3.0 Hz,), 124.1, 122.2, 116.0, 115.0 (dd, J=132.0, 22.0 Hz), 98.5, 49.3.

^{19}F NMR (376 MHz, DMSO-d_6) δ -114.1.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}FN_4O$ $(M+H)^+$: 461.1772, found 467.1767.

Enantiomeric excess is 84% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.38 min; minor isomer: tr = 7.18 min. $[\alpha]^{20}_D$ = 30.06(c = 0.2, $CHCl_3$).



(*S*)-2-(5-amino-3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (5ha) According to the general procedure, **5ha** was obtained using 3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-5-amine **4h** (6.4 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 93% yield (11.1 mg) and 88%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

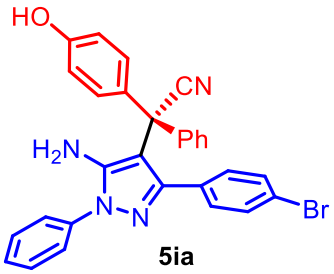
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 7.63 - 7.60 (m, 2H), 7.50 (t, *J* = 7.9 Hz, 2H), 7.43 - 7.37 (m, 4H), 7.33 (d, *J* = 6.9 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 7.08 (dd, *J* = 16.5, 8.6 Hz, 4H), 6.83 (t, *J* = 12.0 Hz, 2H), 4.03 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.5, 149.0, 144.8, 139.6, 138.3, 132.9, 132.4, 130.6, 129.3, 129.2, 128.9, 128.4, 127.8, 127.5, 127.4, 124.1, 122.2, 116.0, 98.5, 49.2.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{35}ClN_4ONa$ $(M+Na)^+$: 499.1296, found 499.1291.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{37}ClN_4ONa$ $(M+Na)^+$: 501.1296, found 501.1291.

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.41. min; minor isomer: tr = 7.67 min. $[\alpha]^{20}_D$ = 76.58(c = 0.2, $CHCl_3$).



5ia

(*S*)-2-(5-amino-3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-phenylacetonitrile (5ia) According to the general procedure, **5ia** was obtained using 3-(4-bromophenyl)-1-phenyl-1H-pyrazol-5-amine **4i** (6.7 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-phenylacetonitrile **2a** (10.4 mg, 0.05 mmol) in 95% yield (12.4 mg) and 86%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

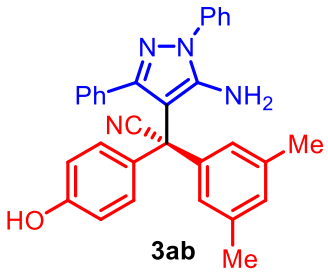
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 7.61 (d, *J* = 7.1 Hz, 2H), 7.50 (t, *J* = 7.9 Hz, 2H), 7.42 (d, *J* = 7.7 Hz, 2H), 7.37 (d, *J* = 9.7 Hz, 3H), 7.32 (d, *J* = 7.2 Hz, 3H), 7.10 (d, *J* = 8.7 Hz, 2H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 4.02 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.5, 149.1, 144.8, 139.6, 138.3, 133.3, 130.9, 130.4, 129.3, 129.2, 128.9, 128.4, 127.8, 127.4, 124.1, 122.2, 121.0, 116.0, 98.5, 49.2.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}{}^{79}BrN_4O$ $(M+H)^+$: 520.0972, found 520.0985.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}{}^{81}BrN_4O$ $(M+H)^+$: 522.0972, found 522.0973.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.92. min; minor isomer: tr = 8.25 min. $[\alpha]^{20}_D$ = 42.32(c = 0.2, $CHCl_3$).



3ab

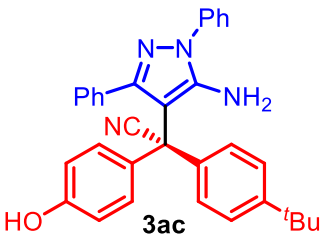
(S)-2-(5-amino-1,3-diphenyl-1H-pyrazol-4-yl)-2-(3,5-dimethylphenyl)-2-(4-hydroxyphenyl)acetonitrile (3ab) According to the general procedure, **3ab** was obtained using 1,3-diphenyl-1H-pyrazol-5-amine **1a** (5.9 mg, 0.025 mmol) and 2-(3,5-dimethylphenyl)-2-(4-oxocyclohexa-2,5-dien-1-ylidene)acetonitrile **2b** (11.8 mg, 0.05 mmol) in 75% yield (8.8 mg) and 86%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 7.64 (d, *J* = 7.7 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.19 – 7.09 (m, 7H), 6.92 (d, *J* = 9.2 Hz, 3H), 6.84 (d, *J* = 8.7 Hz, 2H), 4.02 (s, 2H), 2.21 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.3, 150.3, 144.6, 139.5, 138.4, 138.1, 134.1, 129.6, 129.2, 129.1, 128.8, 127.3, 127.2, 127.1, 125.5, 123.9, 122.3, 115.8, 98.6, 49.1, 21.0.

HRMS (ESI) *m/z* calcd. for $C_{31}H_{27}N_4O$ $(M+H)^+$: 471.2179, found 471.2173.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.04. min; minor isomer: tr = 7.40 min. $[\alpha]^{20}_D$ = 12.83(c = 0.2, $CHCl_3$).



3ac

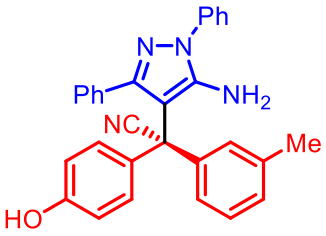
(*R*)-2-(5-amino-1,3-diphenyl-1H-pyrazol-4-yl)-2-(4-(tert-butyl)phenyl)-2-(4-hydroxyphenyl)acetonitrile (3ac) According to the general procedure, **3ac** was obtained using 1,3-diphenyl-1H-pyrazol-5-amine **1a** (5.9 mg, 0.025 mmol) and 2-(4-(tert-butyl)phenyl)-2-(4-oxocyclohexa-2,5-dien-1-ylidene)acetonitrile **2c** (13.2 mg, 0.05 mmol) in 85% yield (10.6 mg) and 88%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.76 (s, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.39 - 7.34 (m, 3H), 7.19 (s, 1H), 7.17 (s, 1H), 7.15 (d, *J* = 2.7 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.05 - 7.03 (m, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 4.03 (s, 2H), 1.25 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.3, 150.6, 150.3, 144.5, 138.4, 136.6, 134.0, 129.20, 129.17, 128.95, 128.93, 127.6, 127.24, 127.18, 125.6, 123.9, 122.2, 115.8, 98.6, 48.9, 34.2, 31.0.

HRMS (ESI) *m/z* calcd. for $C_{33}H_{31}N_4O$ $(M+H)^+$: 499.2492, found 499.2483.

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 4.33min; minor isomer: tr = 6.34 min. $[\alpha]^{20}_D$ = -34.67(c = 0.2, $CHCl_3$).



3ad

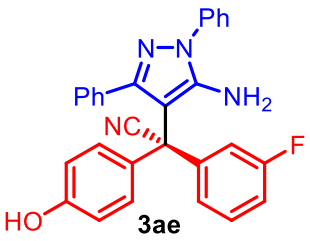
(*S*)-2-(5-amino-1,3-diphenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-(m-tolyl)acetonitrile (3ad) According to the general procedure, **3ad** was obtained using 1,3-diphenyl-1H-pyrazol-5-amine **1a** (5.9 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-(m-tolyl)acetonitrile **2d** (11.1 mg, 0.05 mmol) in 92% yield (10.5 mg) and 75%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 7.61 (d, *J* = 7.1 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.45 - 7.36 (m, 4H), 7.33 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 7.08 (dd, *J* = 16.5, 8.6 Hz, 4H), 6.82 (d, *J* = 8.8 Hz, 2H), 4.03 (s, 2H), 3.43 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.5, 149.0, 144.8, 139.6, 138.3, 132.9, 132.4, 130.6, 129.3, 129.2, 128.9, 128.4, 127.8, 127.5, 127.4, 124.1, 122.2, 116.0, 98.5, 49.2.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O$ $(M+H)^+$: 457.2023, found 457.2014.

Enantiomeric excess is 75% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 5.84. min; minor isomer: tr = 7.91 min. $[\alpha]^{20}_D$ = 48.83(c = 0.2, $CHCl_3$).



3ae

(*S*)-2-(5-amino-1,3-diphenyl-1H-pyrazol-4-yl)-2-(3-fluorophenyl)-2-(4-hydroxyphenyl)acetonitrile (3ae) According to the general procedure, **3ae** was obtained using 1,3-diphenyl-1H-pyrazol-5-amine **1a** (5.9 mg, 0.025 mmol) and 2-(3-fluorophenyl)-2-(4-oxocyclohexa-2,5-dien-1-ylidene)acetonitrile **2e** (11.3 mg, 0.05 mmol) in 89% yield (10.2 mg) and 86%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

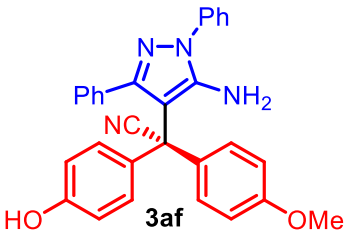
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.88 (s, 1H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 7.9 Hz, 2H), 7.46 – 7.36 (m, 2H), 7.22 – 7.13 (m, 7H), 7.08 – 7.06 (m, 2H), 7.02 (dt, *J* = 10.2, 2.2 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.13 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2 (d, *J* = 244.0 Hz), 157.6, 150.2, 144.7, 142.5 (d, *J* = 7.0 Hz), 138.4, 134.0, 131.2 (d, *J* = 8.0 Hz), 129.3, 129.1, 128.9, 128.4, 127.4 (t, *J* = 10.0 Hz), 124.1, 123.9 (d, *J* = 3.0 Hz), 121.8, 116.1, 115.4, 115.2, 115.0, 114.7, 98.0, 49.1.

^{19}F NMR (376 MHz, DMSO-d_6) δ -111.6.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}FN_4O$ $(M+H)^+$: 461.1772, found 461.1762.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 5.88 min; minor isomer: tr = 9.01 min. $[\alpha]^{20}_D$ = -9.83(c = 0.2, $CHCl_3$).



3af

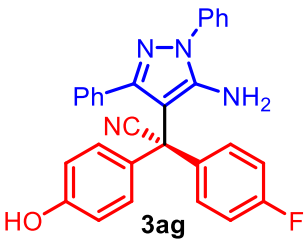
(*S*)-2-(5-amino-1,3-diphenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-(4-methoxyphenyl)acetonitrile (3af) According to the general procedure, **3af** was obtained using 1,3-diphenyl-1H-pyrazol-5-amine **1a** (5.9 mg, 0.025 mmol) and 2-(4-methoxyphenyl)-2-(4-oxocyclohexa-2,5-dien-1-ylidene)acetonitrile **2f** (11.9 mg, 0.05 mmol) in 93% yield (11.0 mg) and 90%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 7.61 (d, *J* = 7.9 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.21 – 7.14 (m, 5H), 7.08 (d, *J* = 5.9 Hz, 4H), 6.98 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 3.97 (s, 2H), 3.75 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 129.3, 129.2, 129.0, 127.4, 124.0, 115.9, 114.5, 55.3, 40.1, 39.9, 39.7, 39.5, 39.3, 39.1, 38.9.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O_2$ $(M+H)^+$: 473.1972, found 473.1968.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.21 min; minor isomer: tr = 28.56 min. $[\alpha]^{20}_D$ = 41.50(c = 0.2, $CHCl_3$).



3ag

(*S*)-2-(5-amino-1,3-diphenyl-1H-pyrazol-4-yl)-2-(4-fluorophenyl)-2-(4-hydroxyphenyl)acetonitrile (3ag) According to the general procedure, **3ag** was obtained using 1,3-diphenyl-1H-pyrazol-5-amine **1a** (5.9 mg, 0.025 mmol) and 2-(4-fluorophenyl)-2-(4-oxocyclohexa-2,5-dien-1-ylidene)acetonitrile **2g** (11.3 mg, 0.05 mmol) in 95% yield (10.9 mg) and 83%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

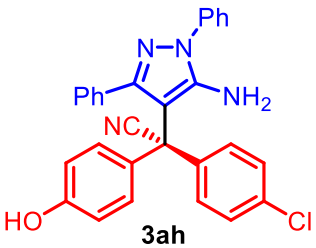
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 7.63 (d, *J* = 7.9 Hz, 2H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.33 (dd, *J* = 8.6, 5.2 Hz, 2H), 7.21 (t, *J* = 8.0 Hz, 3H), 7.15 (t, *J* = 8.9 Hz, 4H), 7.07 (d, *J* = 7.4 Hz, 2H), 6.85 (d, *J* = 8.3 Hz, 2H), 4.09 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 161.6 (d, *J* = 244.0 Hz), 157.6, 150.3, 144.6, 138.4, 136.0 (d, *J* = 3.0 Hz), 134.0, 130.09, 130.01, 129.3, 129.2, 129.0, 128.9, 127.5, 127.43, 127.39, 124.0, 122.1, 116.0, 115.9, 115.8, 98.4, 48.8.

^{19}F NMR (376 MHz, DMSO-d_6) δ -114.0.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{22}FN_4O$ $(M+H)^+$: 477.1721, found 477.1727.

Enantiomeric excess is 83% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 6.09 min; minor isomer: tr = 6.68 min. $[\alpha]^{20}_D$ =39.64 (c = 0.2, $CHCl_3$).



3ah

(*S*)-2-(5-amino-1,3-diphenyl-1H-pyrazol-4-yl)-2-(4-chlorophenyl)-2-(4-hydroxyphenyl)acetonitrile (3ah) According to the general procedure, **3ah** was obtained using 1,3-diphenyl-1H-pyrazol-5-amine **1a** (5.9 mg, 0.025 mmol) and 2-(4-chlorophenyl)-2-(4-oxocyclohexa-2,5-dien-1-ylidene)acetonitrile **2h** (12.1 mg, 0.05 mmol) in 87% yield (10.4 mg) and 91%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

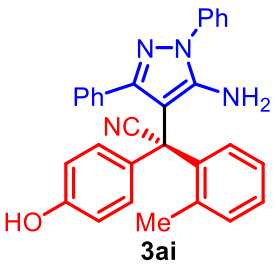
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.85 (s, 1H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 7.0 Hz, 1H), 7.14 (t, *J* = 7.3 Hz, 2H), 7.10 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 7.0 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 4.10 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.6, 150.2, 144.6, 138.8, 138.3, 133.9, 133.0, 129.7, 129.3, 129.1, 129.0, 128.6, 127.4, 127.3, 125.1, 124.0, 122.9, 121.9, 116.1, 98.1, 48.9.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{35}ClN_4ONa$ $(M+Na)^+$: 499.1296, found 499.1291.

HRMS (ESI) *m/z* calcd. for $C_{29}H_{21}{}^{37}ClN_4ONa$ $(M+Na)^+$: 501.1296, found 501.1296.

Enantiomeric excess is 91% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 3.88 min; minor isomer: tr = 5.47 min. $[\alpha]^{20}_D$ = 54.32(c = 0.2, $CHCl_3$).



3ai

(*S*)-2-(5-amino-1,3-diphenyl-1H-pyrazol-4-yl)-2-(4-hydroxyphenyl)-2-(o-tolyl)acetonitrile

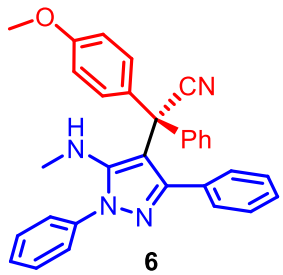
(3ai) According to the general procedure, **3ai** was obtained using 1,3-diphenyl-1H-pyrazol-5-amine **1a** (5.9 mg, 0.025 mmol) and 2-(4-oxocyclohexa-2,5-dien-1-ylidene)-2-(o-tolyl)acetonitrile **2i** (11.1 mg, 0.05 mmol) in 90% yield (10.3 mg) and 87%ee as a yellow oily (silica gel flash chromatography: petroleum ether/EtOAc = 3:1). R_f = 0.30 (petroleum ether/EtOAc = 2:1)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.85 (s, 1H), 7.59 (d, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.9 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 7.1 Hz, 2H), 7.25 - 7.21 (m, 1H), 7.20 - 7.19 (m, 1H), 7.15 (t, *J* = 7.9 Hz, 4H), 7.04 (d, *J* = 6.8 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.65 (d, *J* = 8.0 Hz, 1H), 3.93 (s, 2H), 2.27 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 157.5, 150.0, 144.2, 138.4, 137.4, 137.4, 133.8, 132.7, 129.3, 128.9, 128.8, 128.7, 128.5, 127.6, 127.4, 127.2, 126.3, 124.0, 120.8, 116.1, 97.1, 47.8, 20.7.

HRMS (ESI) *m/z* calcd. for $C_{30}H_{25}N_4O$ $(M+H)^+$: 457.2023, found 457.2014.

Enantiomeric excess is 87% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.02 min; minor isomer: tr = 17.72 min. $[\alpha]^{20}_D$ = 48.83(c = 0.2, $CHCl_3$).



6

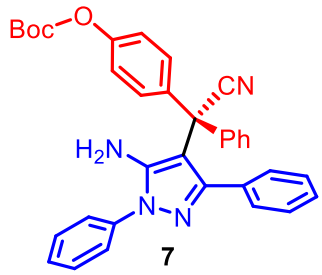
(*S*)-2-(4-methoxyphenyl)-2-(5-(methylamino)-1,3-diphenyl-1H-pyrazol-4-yl)-2-phenylacetonitrile (6)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 7.62 (d, J = 7.5 Hz, 2H), 7.50 (t, J = 7.8 Hz, 2H), 7.37 (q, J = 7.9, 7.3 Hz, 2H), 7.21 - 7.08 (m, 7H), 6.96 - 6.92 (m, 2H), 6.84 - 6.81 (m, 2H), 6.77 (t, J = 2.2 Hz, 1H), 4.02 (s, 2H), 3.71 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 159.9, 157.9, 150.6, 145.1, 141.7, 138.8, 134.4, 130.8, 129.7, 129.6, 129.5, 129.3, 127.9, 127.8, 127.7, 124.4, 122.5, 120.5, 116.3, 114.6, 113.6, 98.8, 55.6, 49.63.

HRMS (ESI) *m/z* calcd. for $C_{31}H_{27}N_4O$ $(M+H)^+$: 471.2179, found 471.2178.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.04. min; minor isomer: tr = 8.12 min. $[\alpha]^{20}_{D}$ = -67.1(c = 0.2, $CHCl_3$).



7

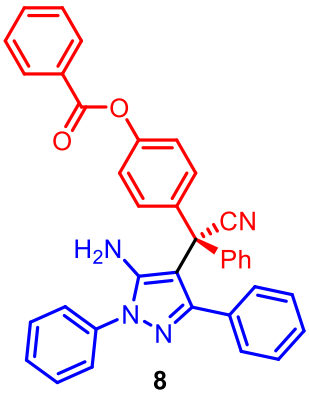
(*S*)-4-((5-amino-1,3-diphenyl-1H-pyrazol-4-yl)(cyano)(phenyl)methyl)phenyl tert-butyl carbonate (7)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 8.5, 1.3 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.43 - 7.31 (m, 8H), 7.20 - 7.09 (m, 7H), 3.28 (s, 2H), 1.56 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0, 158.8, 148.6, 147.1, 141.9, 138.1, 133.7, 132.7, 129.7, 129.2, 128.5, 128.5, 128.5, 1285, 127.94, 127.5, 127., 125.61, 113.8, 109.5, 62.4, 55.2, 30.4.

HRMS (ESI) *m/z* calcd. for $C_{34}H_{31}N_4O_3$ $(M+H)^+$: 543.2391, found 543.2383.

Enantiomeric excess is 89% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.77. min; minor isomer: tr = 11.67 min. $[\alpha]^{20}_D$ = 65.83(c = 0.2, $CHCl_3$).



8

(*S*)-4-((5-amino-1,3-diphenyl-1H-pyrazol-4-yl)(cyano)(phenyl)methyl)phenyl benzoate (8)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.8 Hz, 2H), 7.68 - 7.61 (m, 3H), 7.55 - 7.44 (m, 9H), 7.40 –-7.33 (m, 4H), 7.21 (d, *J* = 8.4 Hz, 3H), 7.16 (d, *J* = 3.3 Hz, 3H), 3.30 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 151.5, 150., 7.31, 139.0, 137.7, 136.7, 133.8, 133.3, 130.1, 129.6, 129.5, 129.3, 129.1, 129.0, 128.6, 128.5, 128.3, 128.0, 127.8, 127.6, 124.6, 122.1, 121.8, 98.8, 49.9.

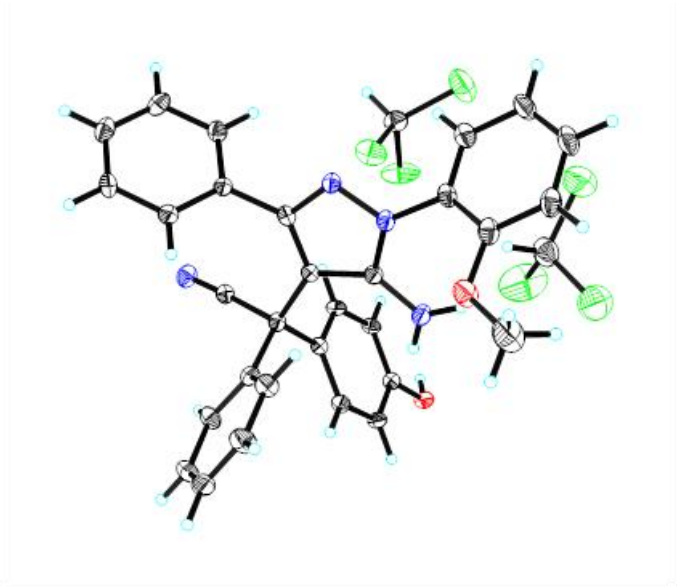
HRMS (ESI) *m/z* calcd. for $C_{36}H_{27}N_4O_2$ $(M+H)^+$: 547.2129, found 547.2125.

Enantiomeric excess is 92% determined by HPLC (Chiralpak OD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.33 min; minor isomer: tr = 23.65 min. $[\alpha]^{20}_D$ = 49.72(c = 0.2, $CHCl_3$).

3. Crystal of 3na

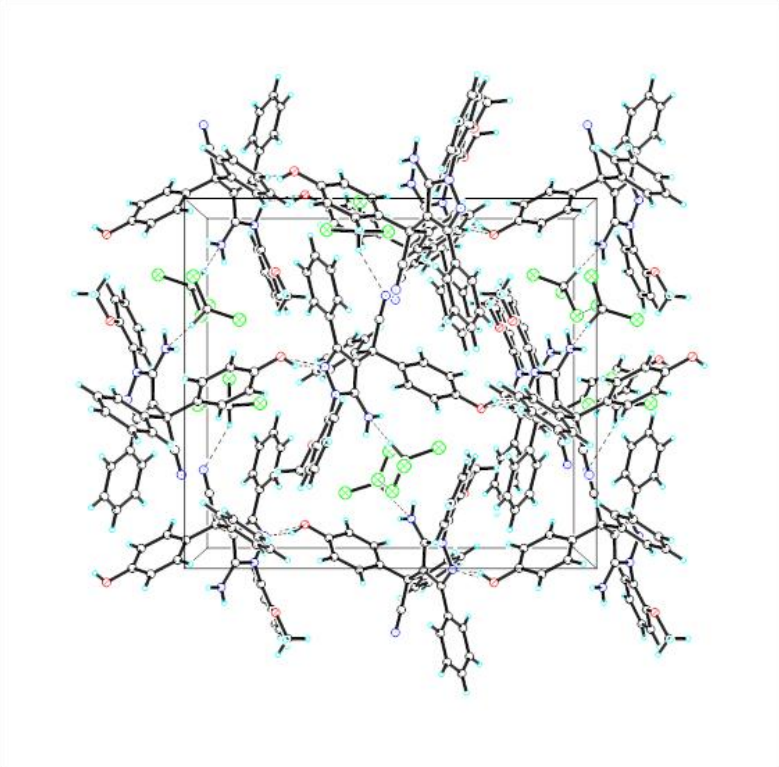
The crystal of **3na** suitable for crystallographic analysis was grown from dichloromethane by slow crystallization in 2 mL flat bottom bottle.

Crystal data for **3na**: $C_{30}H_{24}N_4O_2$•2($CHCl_3$), M = 711.27, a = 11.5859(2) Å, b = 16.1437(4) Å, c = 17.9952(4) Å, α = 90°, β = 90°, γ = 90°, V = 3365.81(13) Å^3, T = 150.(2) K, space group $P212121$, Z = 4, μ(Cu Kα) = 4.948 mm^{-1}, 20259 reflections measured, 6006 independent reflections (R_{int} = 0.0632). The final R_1 values were 0.0646 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1801 ($I > 2\sigma(I)$). The final R_1 values were 0.0668 (all data). The final $wR(F^2)$ values were 0.1825 (all data). The goodness of fit on F^2 was 1.044. Flack parameter = 0.123(7).



View of the molecules in an asymmetric unit.

Displacement ellipsoids are drawn at the 30% probability level



View of the pack drawing of **3na.**

Table 1. Crystal data and structure refinement for 3ad.

Identification code	global	
Empirical formula	C32 H26 Cl6 N4 O2	
Formula weight	711.27	
Temperature	150(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 11.5859(2) Å	a= 90°.
	b = 16.1437(4) Å	b= 90°.
	c = 17.9952(4) Å	g = 90°.
Volume	3365.81(13) $Å^3$	
Z	4	
Density (calculated)	1.404 Mg/m^3	
Absorption coefficient	4.948 mm^{-1}	

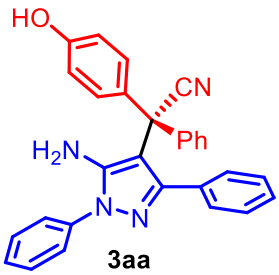
F(000)	1456	
Crystal size	0.350 x 0.180 x 0.170 mm^3	
Theta range for data collection	3.68 to 68.23°.	
Index ranges	-13<=h<=13, -15<=k<=19, -21<=l<=21	
Reflections collected	20259	
Independent reflections	6006 [R(int) = 0.0632]	
Completeness to theta = 68.23°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.49 and 0.18	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6006 / 0 / 399	
Goodness-of-fit on F^2	1.044	
Final R indices [I>2sigma(I)]	R1 = 0.0646, wR2 = 0.1801	
R indices (all data)	R1 = 0.0668, wR2 = 0.1825	
Absolute structure parameter	0.123(7)	
Largest diff. peak and hole	0.933 and -0.908 $e.Å^{-3}$	

4. References.

[1] Shi-Na Zhao, Qian Li, Xiu-Xiu Qiao, Yonghui He, Ganpeng Li, and Xiao-Jing Zhao; Asymmetric Synthesis of Axially Chiral N, N-1,2-Pentatomic Heterobiaryl Diamines by an Organocatalytic Arylation Reactions. [J] *Chem. Eur. J.* **2024**, e202402843.

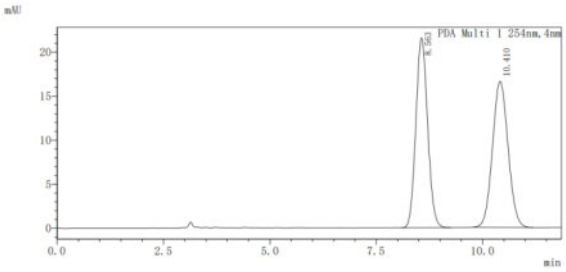
[2] Qi Y, Zhang F, Wang L, et al. δ-Cyano substituted para-quinone methides enable access to unsymmetric tri- and tetraarylmethanes containing all-carbon quaternary stereocenters [J]. Organic & Biomolecular Chemistry, 2020, 18, 3522-3526.

5. Copies of HPLC.



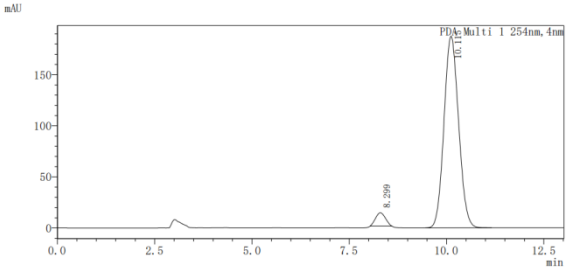
3aa

Enantiomeric excess is 91% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.12 min; minor isomer: tr = 8.30 min.



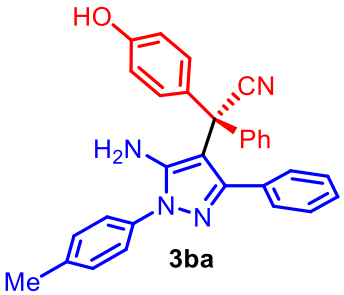
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.563	414183	21563	49.542
2	10.410	421834	16589	50.458
Totals		836017	38153	100.000



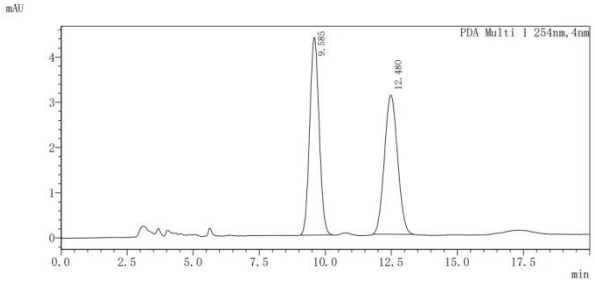
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.299	232553	13159	4.537
2	10.115	4893589	187533	95.463
Totals		5126141	200692	100.000



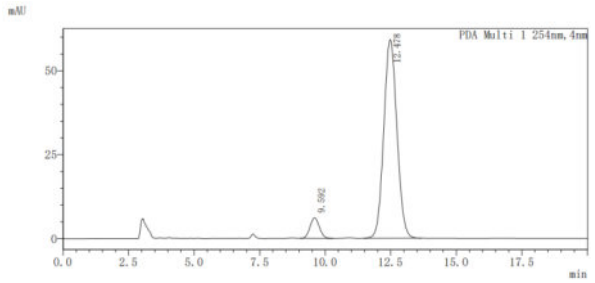
3ba

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.48 min; minor isomer: tr = 9.59 min.



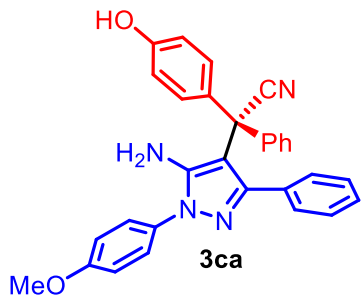
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	9.585	108662	4369	50.484
2	12.480	106576	3074	49.516
Totals		215238	7444	100.000



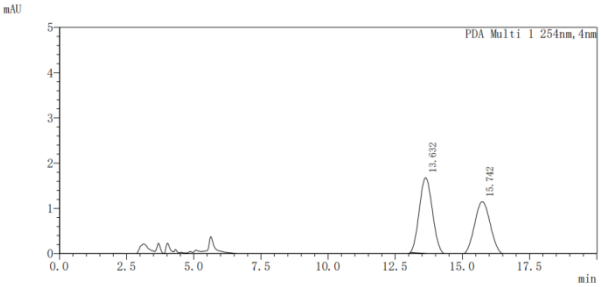
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	9.592	152118	6111	6.865
2	12.478	2063708	59169	93.135
Totals		2215826	65281	100.000



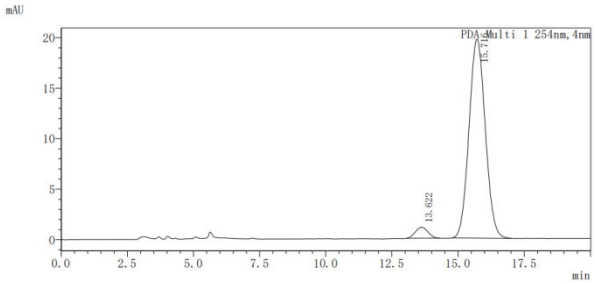
3ca

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 15.72 min; minor isomer: tr = 13.62 min.



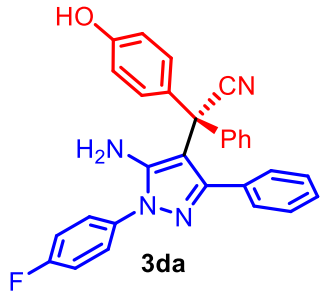
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	13.632	57276	1676	52.848
2	15.742	51104	1204	47.152
Totals		108380	2880	100.000



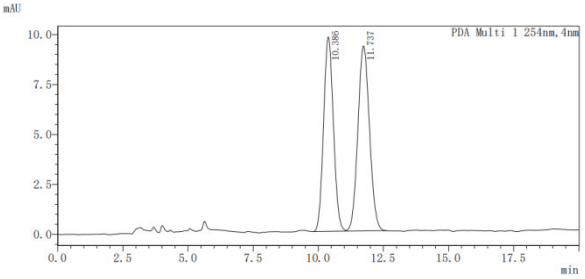
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	13.622	35903	1091	4.091
2	15.716	841691	19701	95.909
Totals		877594	20792	100.000



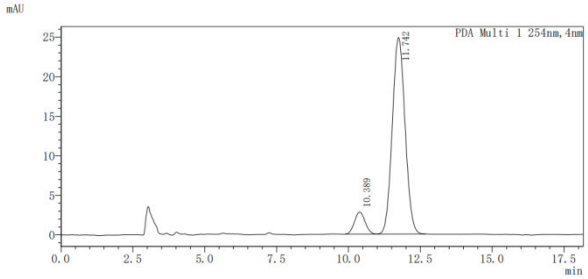
3da

Enantiomeric excess is 83% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.74 min; minor isomer: tr = 10.39 min.



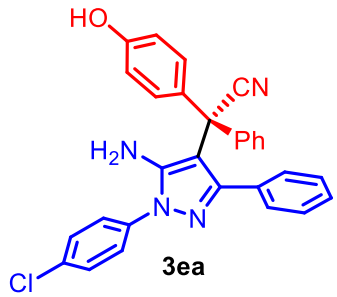
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.386	255163	9724	47.054
2	11.737	287112	9255	52.946
Totals		542276	18979	100.000



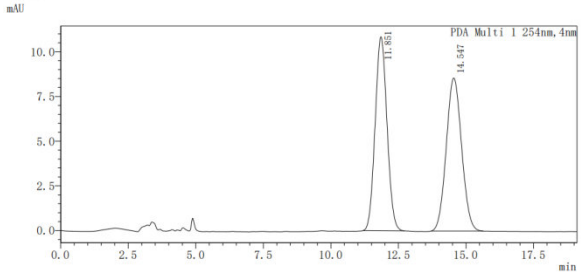
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.389	72088	2789	8.584
2	11.742	767708	24835	91.416
Totals		839796	27624	100.000



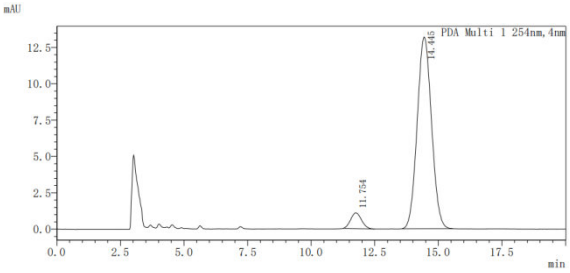
3ea

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 14.45 min; minor isomer: tr = 11.75 min.



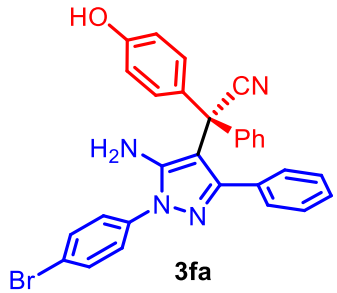
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	11.851	331168	10840	49.423
2	14.547	338904	8560	50.577
Totals		670072	19401	100.000



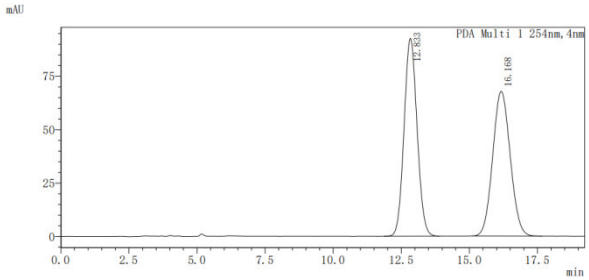
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	11.754	32203	1085	5.858
2	14.445	517477	13188	94.142
Totals		549679	14273	100.000



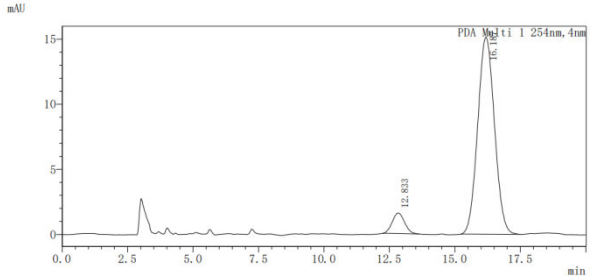
3fa

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 16.19 min; minor isomer: tr = 12.83 min.



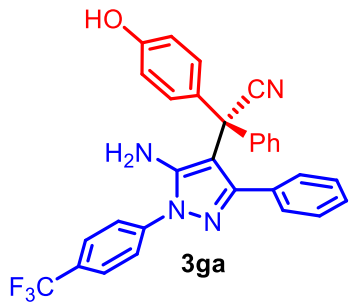
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	12.833	3074220	92591	50.348
2	16.168	3031779	67747	49.652
Totals		6105999	160338	100.000



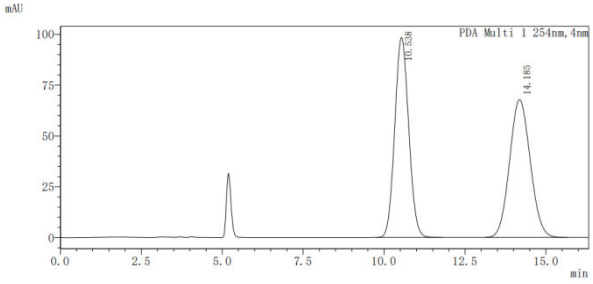
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	12.833	51704	1583	7.121
2	16.187	674353	15126	92.879
Totals		726057	16709	100.000



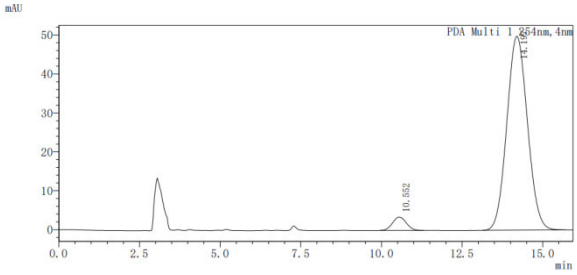
3ga

Enantiomeric excess is 91% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 14.20 min; minor isomer: tr = 10.55 min.



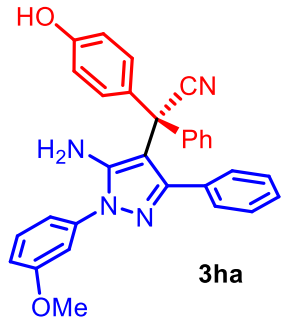
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.538	2952170	98358	49.490
2	14.185	3013061	67794	50.510
Totals		5965230	166152	100.000



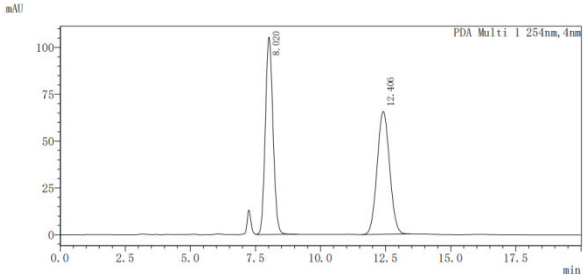
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.552	102978	3464	4.437
2	14.197	2218143	49821	95.563
Totals		2321120	53285	100.000



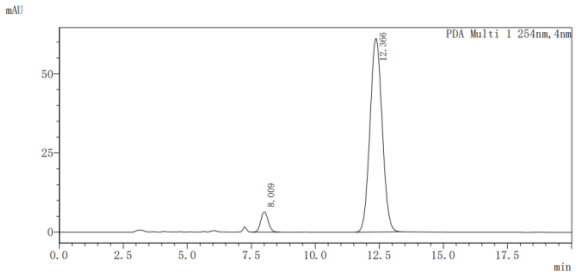
3ha

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.37 min; minor isomer: tr = 8.01 min.



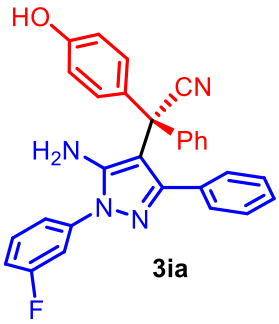
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.020	2159704	105337	49.616
2	12.406	2193121	65683	50.384
Totals		4352825	171020	100.000



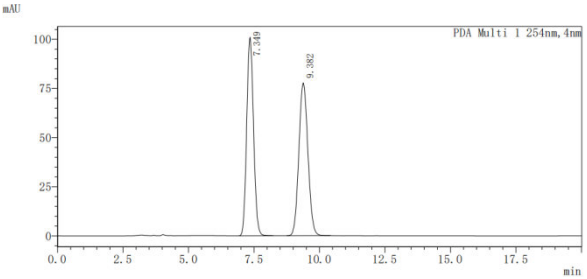
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.009	130085	6412	6.041
2	12.366	2023432	61086	93.959
Totals		2153518	67499	100.000



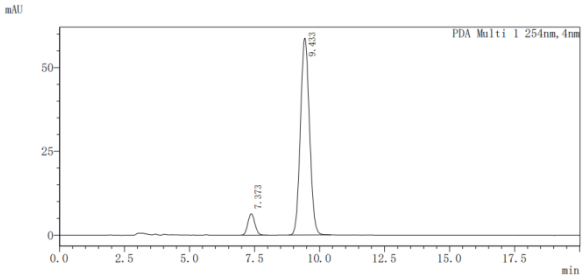
3ia

Enantiomeric excess is 84% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.43 min; minor isomer: tr = 7.37 min.



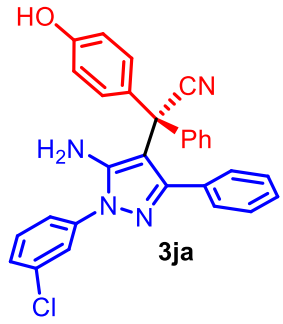
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.349	1828879	100812	49.462
2	9.382	1868689	77622	50.538
Totals		3697568	178434	100.000



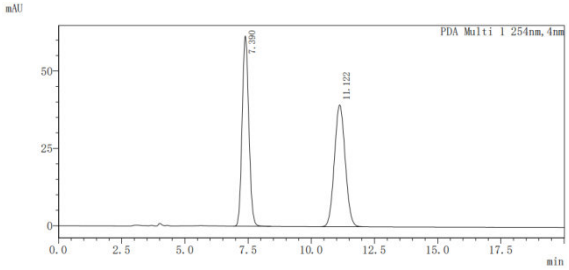
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.373	118949	6369	7.698
2	9.433	1426168	58724	92.302
Totals		1545117	65094	100.000



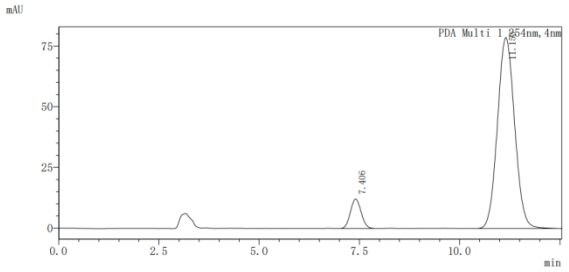
3ja

Enantiomeric excess is 82% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.15 min; minor isomer: tr = 7.41 min.



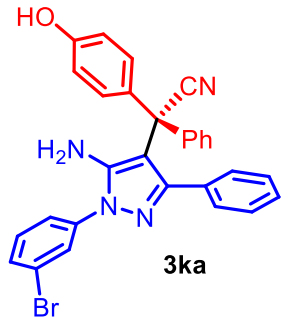
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.390	1131199	61439	49.163
2	11.122	1169710	39341	50.837
Totals		2300909	100780	100.000



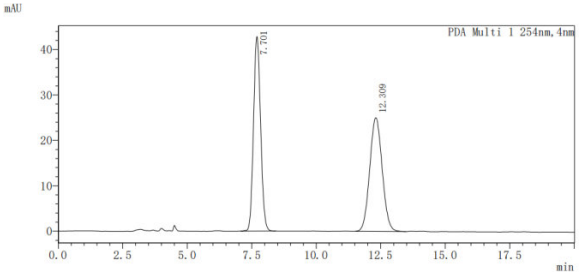
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.406	227163	12177	8.819
2	11.153	2348651	78697	91.181
Totals		2575814	90874	100.000



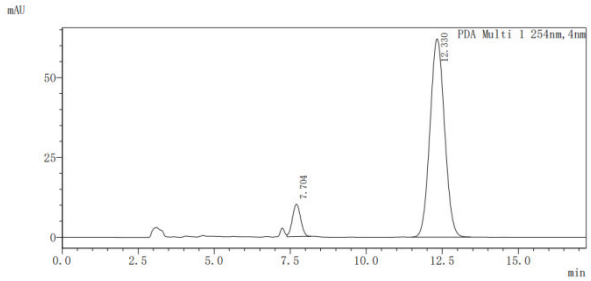
3ka

Enantiomeric excess is 83% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.33 min; minor isomer: tr = 7.70 min.



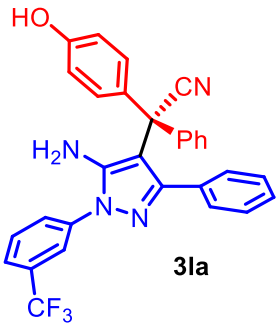
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.701	820382	42834	49.350
2	12.309	842001	25051	50.650
Totals		1662383	67885	100.000



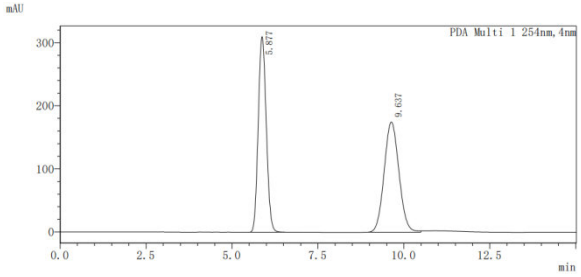
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.704	191142	10132	8.451
2	12.330	2070542	62099	91.549
Totals		2261684	72231	100.000



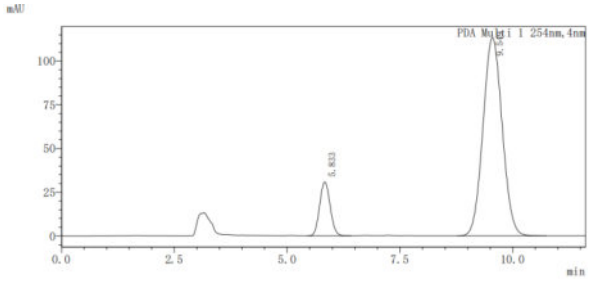
3la

Enantiomeric excess is 74% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.55 min; minor isomer: tr = 5.83 min.



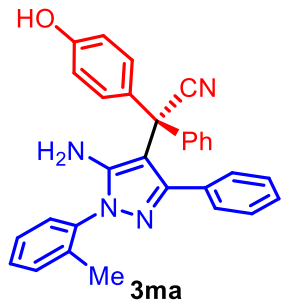
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.877	5037433	309623	49.024
2	9.637	5237975	174677	50.976
Totals		10275407	484300	100.000



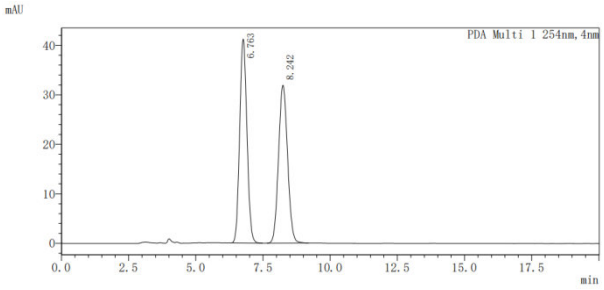
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.833	497824	30777	12.924
2	9.549	3354180	113350	87.076
Totals		3852004	144127	100.000



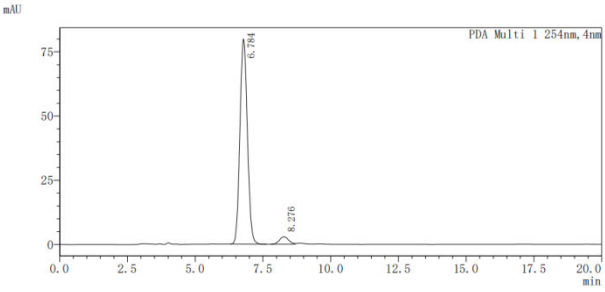
3ma

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.28 min; minor isomer: tr = 6.78 min.



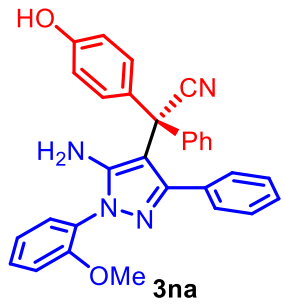
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	6.763	775447	41128	50.997
2	8.242	745117	31878	49.003
Totals		1520563	73006	100.000



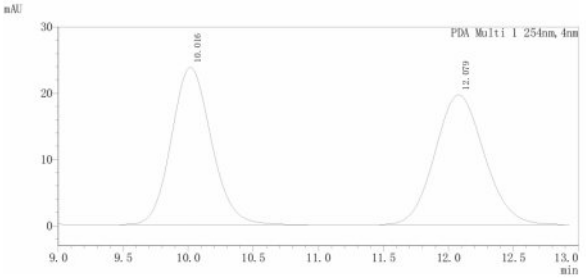
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	6.784	1526697	79738	95.775
2	8.276	67347	2883	4.225
Totals		1594044	82621	100.000



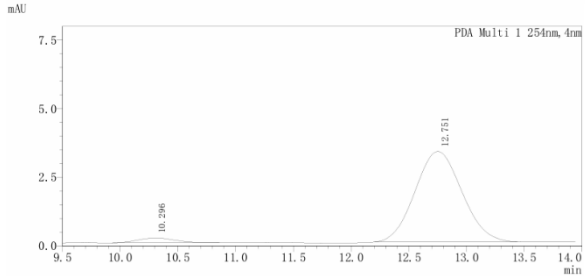
3na

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.75 min; minor isomer: tr = 10.30 min.



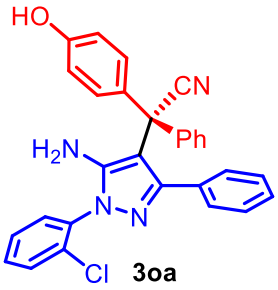
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.016	506896	23719	49.597
2	12.079	515124	19545	50.403
Totals		1022021	43264	100.000



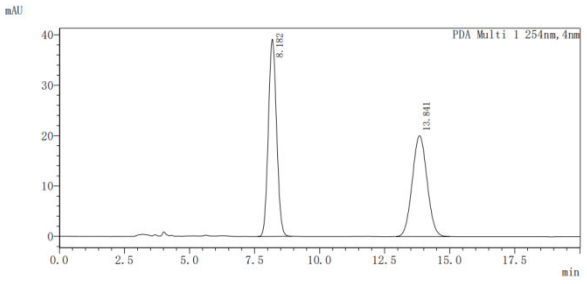
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.296	3804	174	3.922
2	12.751	93196	3299	96.078
Totals		97000	3473	100.000



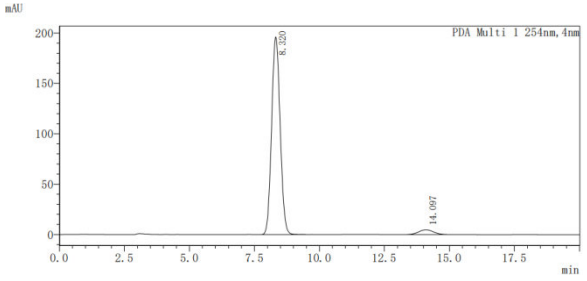
3oa

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 14.10 min; minor isomer: tr = 8.32 min.



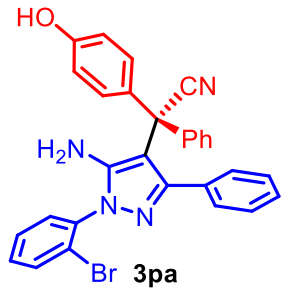
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.182	864143	39148	52.100
2	13.841	794480	20020	47.900
Totals		1658624	59168	100.000



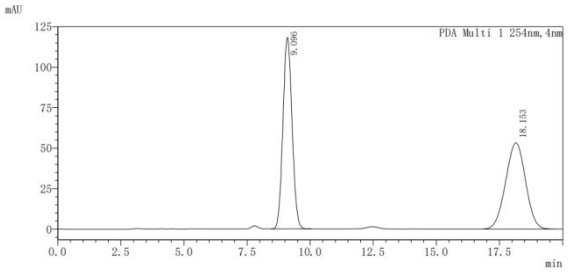
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.320	4484893	196106	95.951
2	14.097	189245	4755	4.049
Totals		4674138	200862	100.000



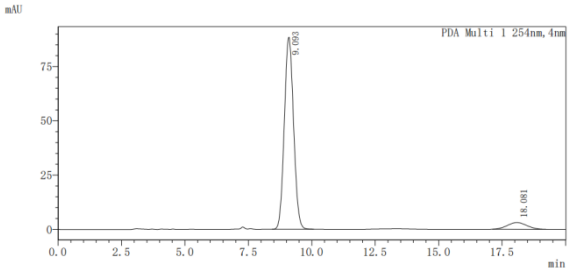
3pa

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 18.08 min; minor isomer: tr = 9.09 min.



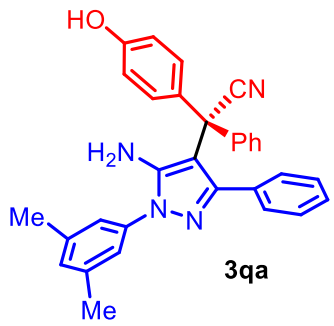
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	9.096	2980509	118189	50.501
2	18.153	2921314	53225	49.499
Totals		5901823	171414	100.000



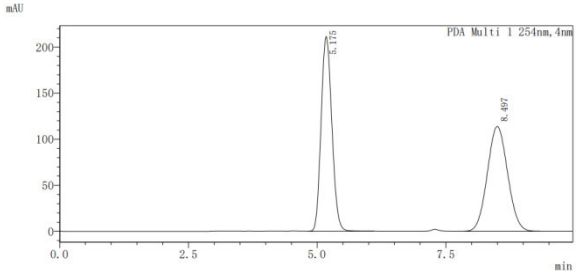
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	9.093	2239666	88390	93.217
2	18.081	162973	3066	6.783
Totals		2402640	91455	100.000



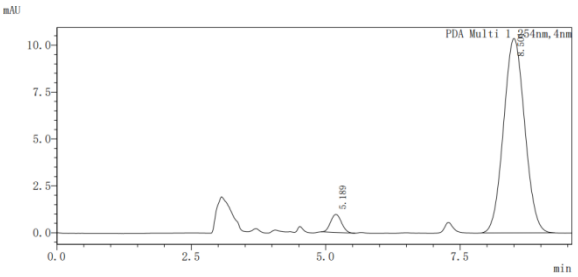
3qa

Enantiomeric excess is 91% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.50 min; minor isomer: tr = 5.12 min.



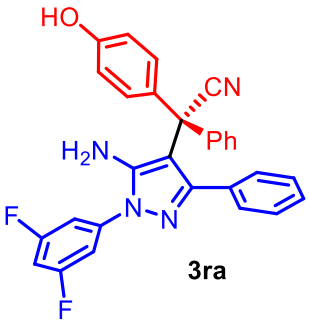
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.175	3073857	211281	49.639
2	8.497	3118613	113778	50.361
Totals		6192470	325059	100.000



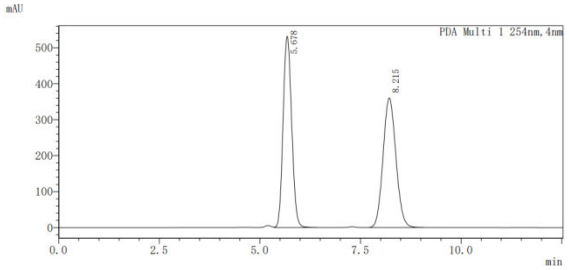
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.189	13450	963	4.520
2	8.501	284095	10370	95.480
Totals		297545	11333	100.000



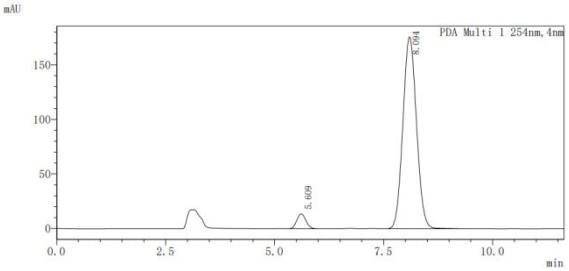
3ra

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.09 min; minor isomer: tr = 5.61 min.



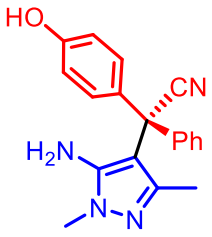
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.678	7874066	531332	49.507
2	8.215	8031013	360467	50.493
Totals		15905079	891799	100.000



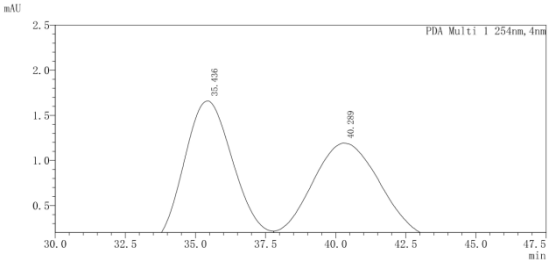
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.609	198236	13573	4.942
2	8.094	3812768	175821	95.058
Totals		4011004	189394	100.000



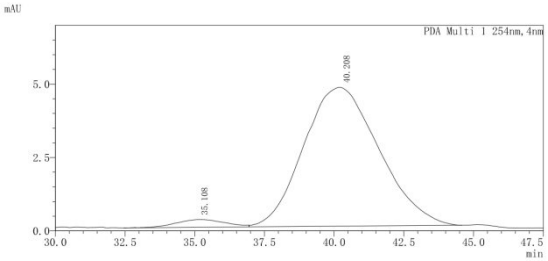
3sa

Enantiomeric excess is 90% determined by HPLC (Chiralpak AS-H, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm): major isomer: tr =40.21min; minor isomer: tr = 35.11 min.



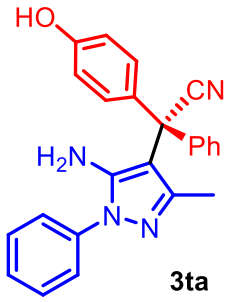
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	35.436	208971	1628	49.098
2	40.289	216647	1161	50.902
Totals		425618	2789	100.000



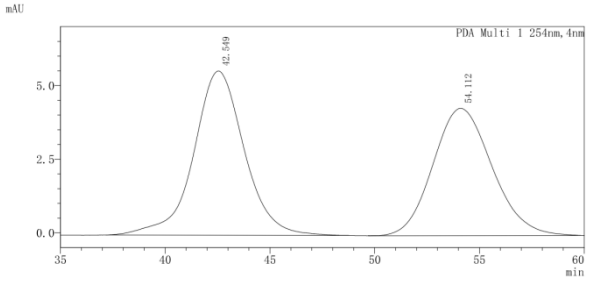
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	35.108	31898	263	3.458
2	40.208	890492	4724	96.542
Totals		922390	4987	100.000



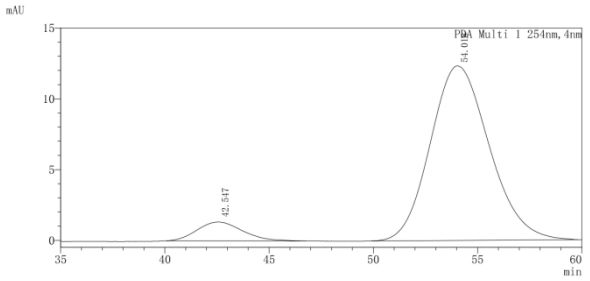
3ta

Enantiomeric excess is 90% determined by HPLC (Chiralpak AS-H, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm): major isomer: tr =54.02min; minor isomer: tr = 42.55 min.



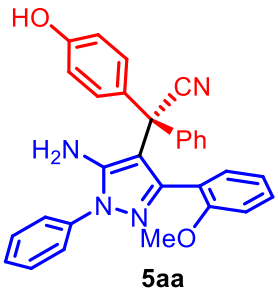
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	42.549	936867	5572	52.463
2	54.112	848885	4322	47.537
Totals		1785752	9894	100.000



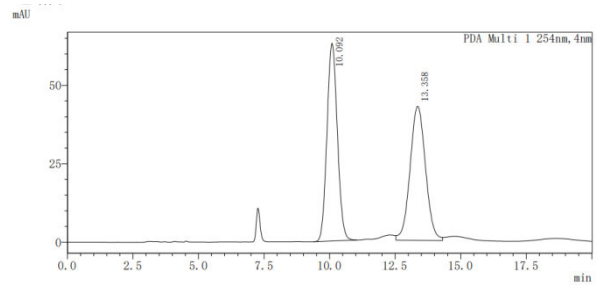
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	42.547	204267	1340	7.761
2	54.018	2427642	12324	92.239
Totals		2631908	13664	100.000



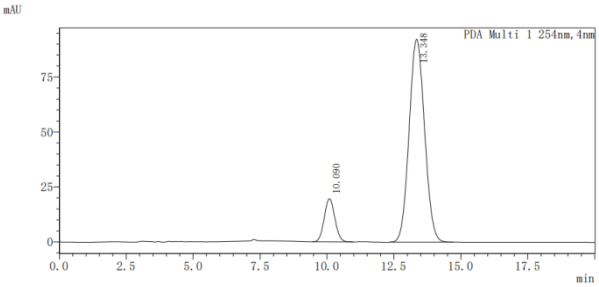
5aa

Enantiomeric excess is 74% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.35 min; minor isomer: tr = 10.09 min.



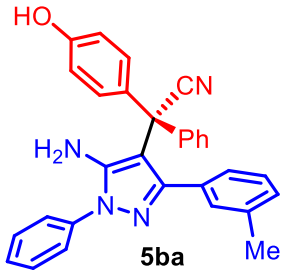
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.092	1737451	63055	49.751
2	13.358	1754851	42797	50.249
Totals		3492301	105852	100.000



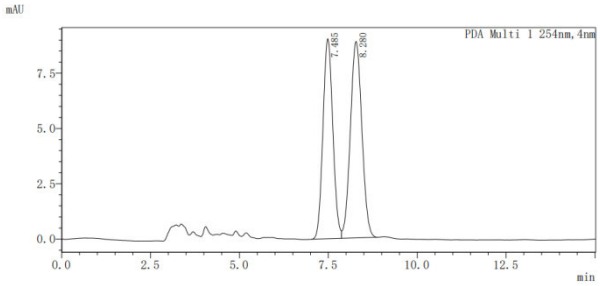
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.090	539998	19608	12.685
2	13.348	3716955	92266	87.315
Totals		4256953	111874	100.000



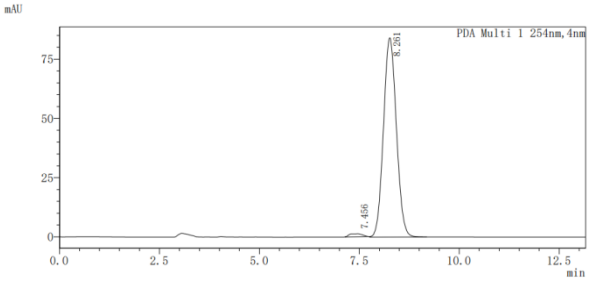
5ba

Enantiomeric excess is 97% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.26 min; minor isomer: tr = 7.46 min.



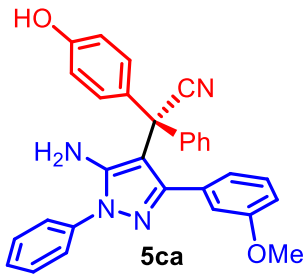
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.485	174744	9042	46.582
2	8.280	200384	8883	53.418
Totals		375129	17925	100.000



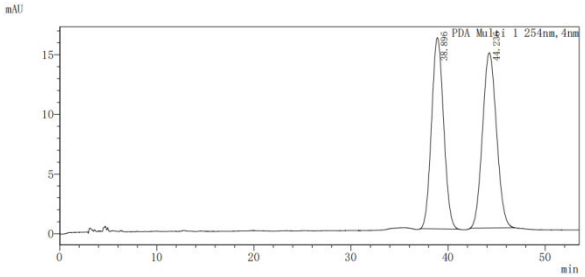
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.456	29173	1249	1.521
2	8.261	1889219	84017	98.479
Totals		1918393	85266	100.000



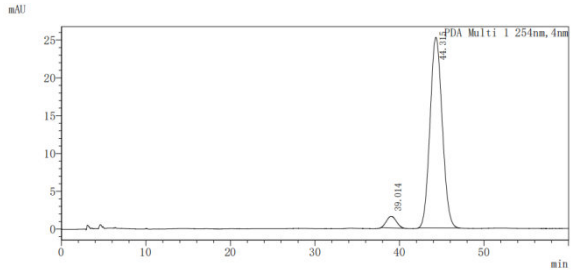
5ca

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 44.32 min; minor isomer: tr = 39.01 min.



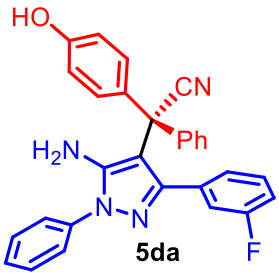
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	38.896	1388123	16026	48.493
2	44.236	1474383	14690	51.507
Totals		2862506	30716	100.000

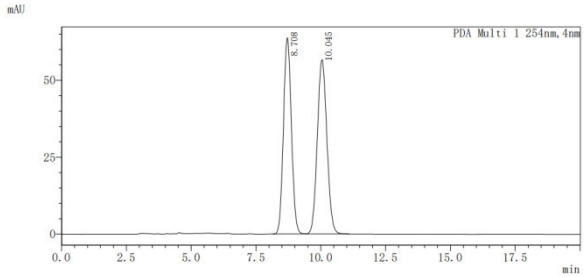


<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	39.014	123765	1535	4.657
2	44.315	2533982	25189	95.343
Totals		2657747	26724	100.000

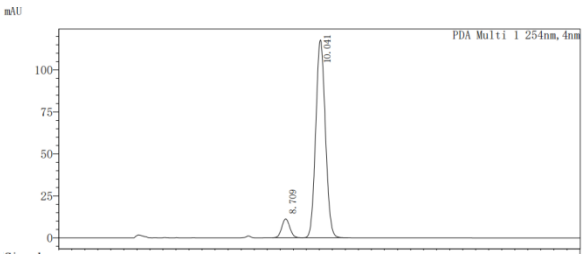


Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.04 min; minor isomer: tr = 8.71 min.



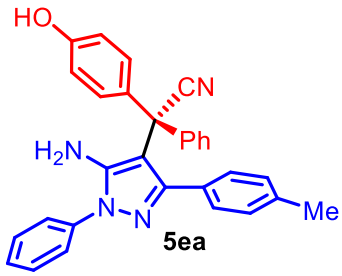
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.708	1359798	63738	48.243
2	10.045	1458859	56631	51.757
Totals		2818658	120369	100.000



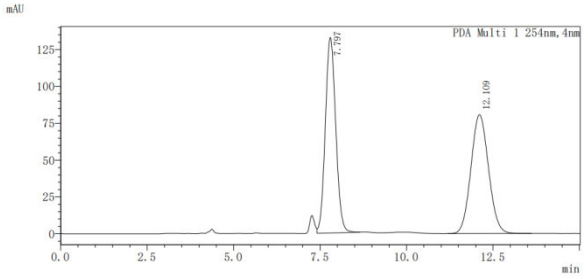
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.709	238876	11180	7.330
2	10.041	3019867	117713	92.670
Totals		3258743	128893	100.000



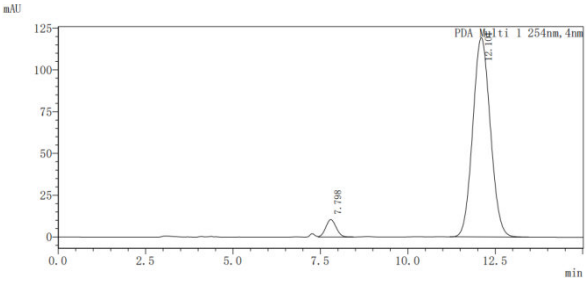
5ea

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.10 min; minor isomer: tr = 7.80 min.



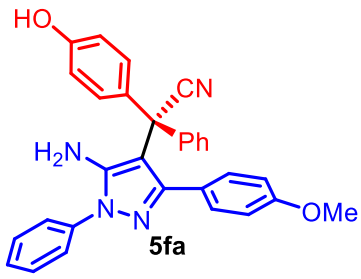
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.797	2776080	132637	49.251
2	12.109	2860547	80695	50.749
Totals		5636627	213332	100.000



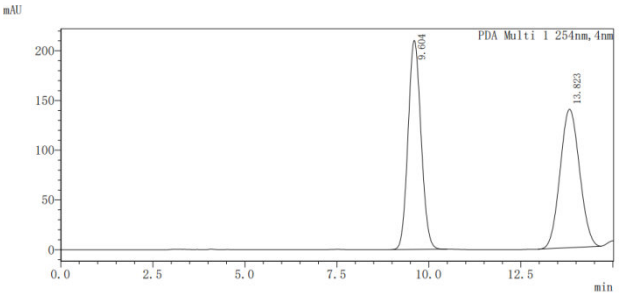
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.798	216722	10419	4.928
2	12.101	4181244	119212	95.072
Totals		4397966	129631	100.000



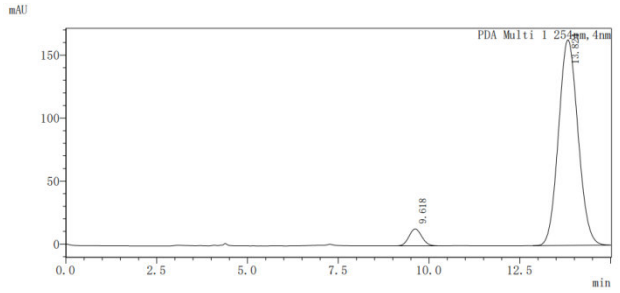
5fa

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.82 min; minor isomer: tr = 9.62 min.



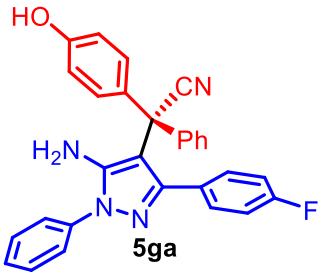
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	9.604	5161853	210221	50.184
2	13.823	5124063	139229	49.816
Totals		10285916	349450	100.000



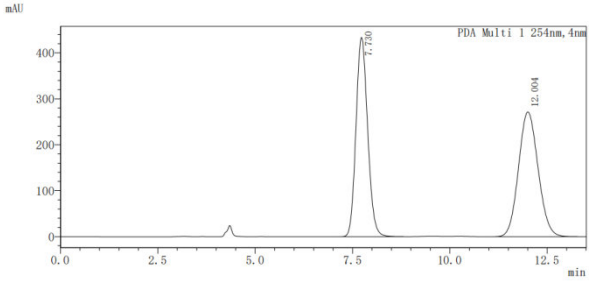
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	9.618	332459	13477	5.172
2	13.824	6095806	163256	94.828
Totals		6428265	176733	100.000



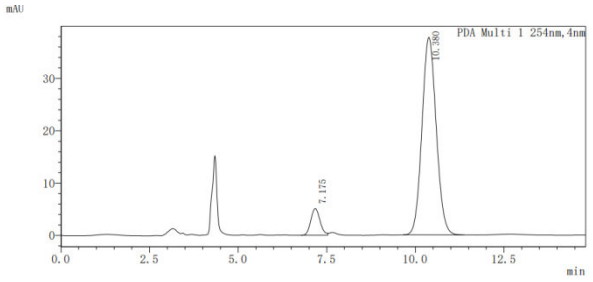
5ga

Enantiomeric excess is 84% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.38 min; minor isomer: tr = 7.18 min.



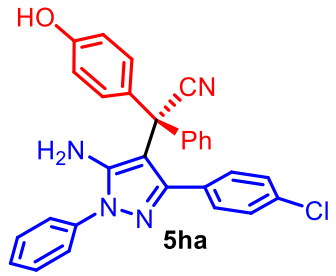
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.730	9033203	433814	48.746
2	12.004	9498014	271488	51.254
Totals		18531217	705301	100.000



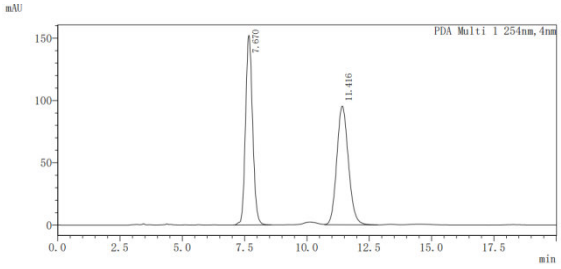
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.175	92326	5108	8.048
2	10.380	1054831	37741	91.952
Totals		1147157	42849	100.000



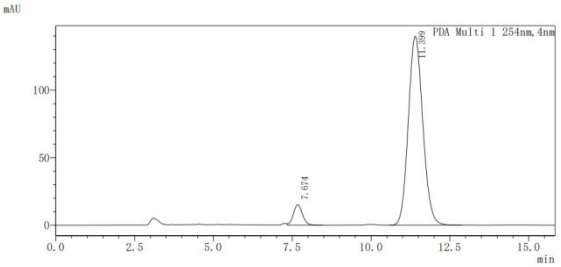
5ha

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.41. min; minor isomer: tr = 7.67 min.



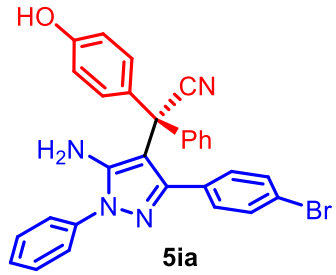
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.670	3004531	152098	49.242
2	11.416	3097062	95375	50.758
Totals		6101594	247474	100.000



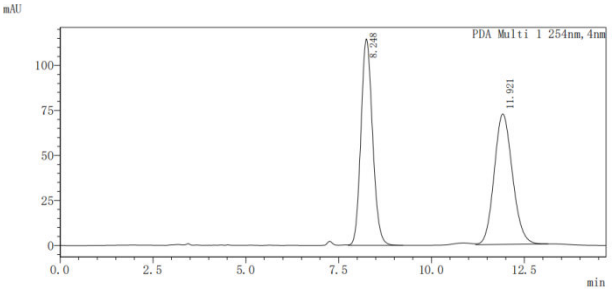
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.674	298443	15047	6.259
2	11.399	4469621	139816	93.741
Totals		4768064	154863	100.000



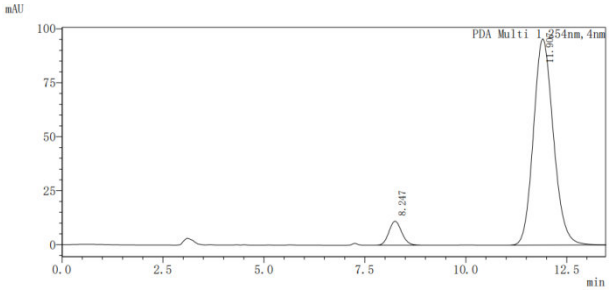
5ia

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.92. min; minor isomer: tr = 8.25 min.



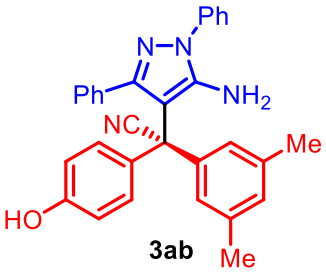
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.248	2501297	114626	50.194
2	11.921	2481999	72420	49.806
Totals		4983296	187046	100.000



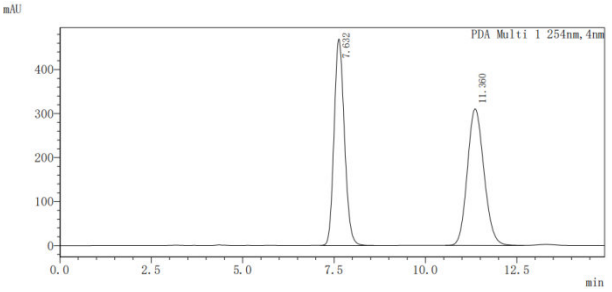
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.247	245113	11094	6.941
2	11.907	3286250	95500	93.059
Totals		3531364	106594	100.000



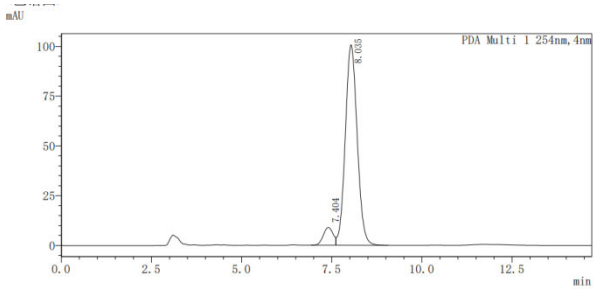
3ab

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.04. min; minor isomer: tr = 7.40 min.



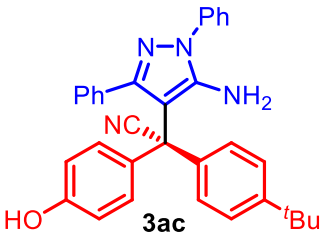
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.632	9246837	468846	48.486
2	11.360	9824256	310375	51.514
Totals		19071093	779221	100.000



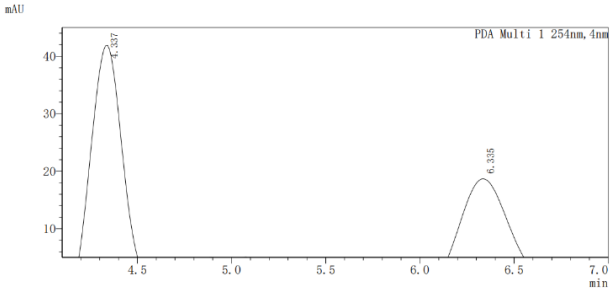
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.404	170520	8954	6.881
2	8.035	2307468	100656	93.119
Totals		2477988	109610	100.000



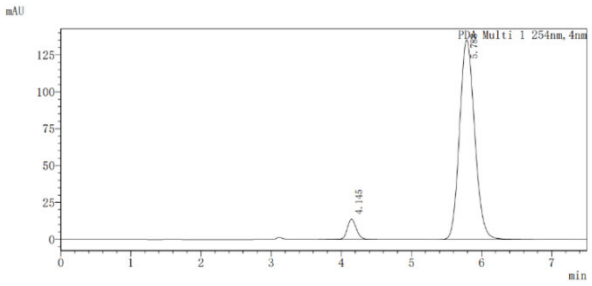
3ac

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 4.33min; minor isomer: tr = 6.34 min.



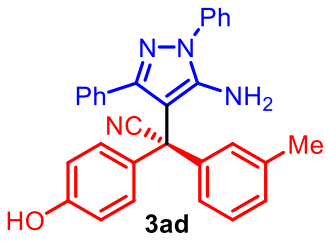
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	4.337	505994	42498	57.113
2	6.335	379956	19344	42.887
总计		885950	61842	100.000



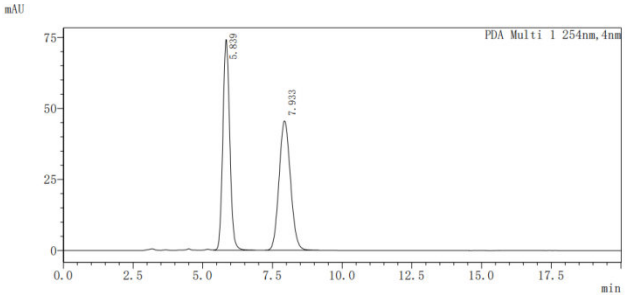
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	4.145	125275	13777	5.815
2	5.788	2029043	135293	94.185
总计		2154318	149069	100.000



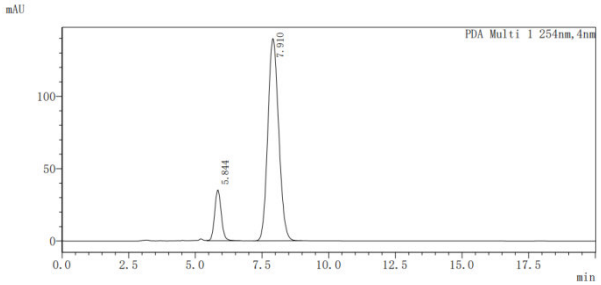
3ad

Enantiomeric excess is 75% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 5.84. min; minor isomer: tr = 7.91 min.



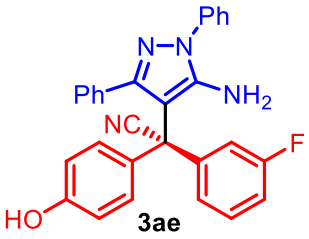
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.839	1280080	74105	49.607
2	7.933	1300361	45541	50.393
Totals		2580441	119645	100.000



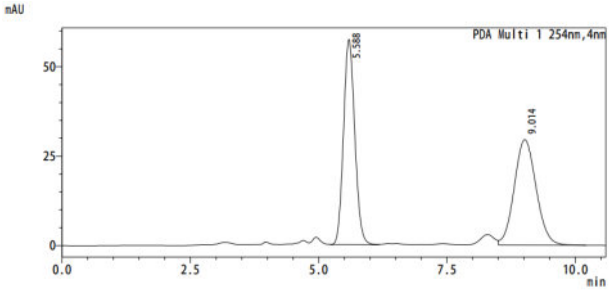
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.844	604519	35095	13.243
2	7.910	3960414	139715	86.757
Totals		4564933	174810	100.000



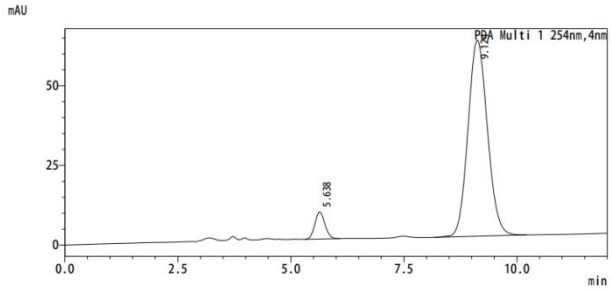
3ae

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 5.88 min; minor isomer: tr = 9.01 min.



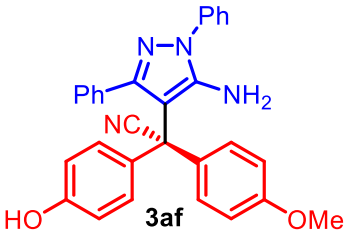
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.588	878515	57401	50.148
2	9.014	873324	29499	49.852
总计		1751838	86901	100.000



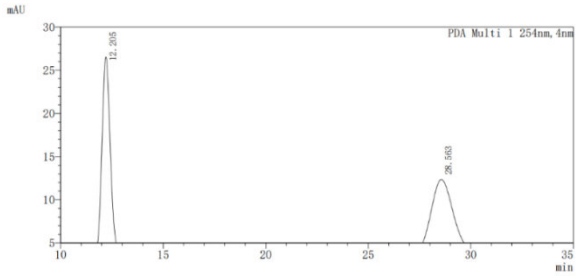
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.638	132456	8483	6.703
2	9.124	1843701	61567	93.297
总计		1976157	70051	100.000



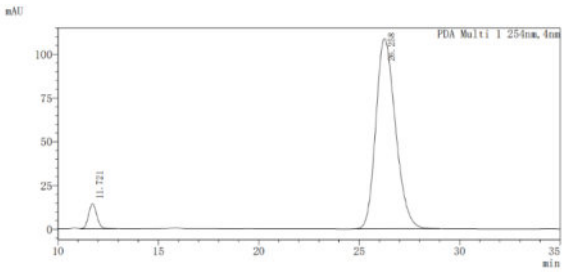
3af

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.21 min; minor isomer: tr = 28.56 min.



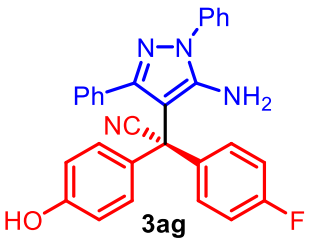
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	12.205	657042	23045	50.539
2	28.563	643021	8522	49.461
总计		1300063	31567	100.000



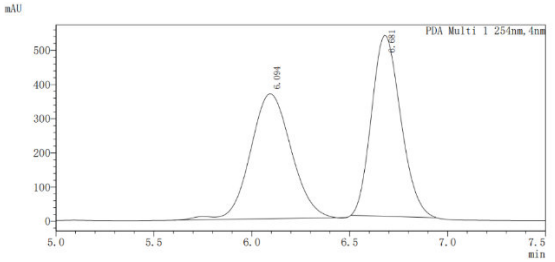
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	11.721	414836	14377	5.284
2	26.258	7435379	108781	94.716
总计		7850216	123158	100.000



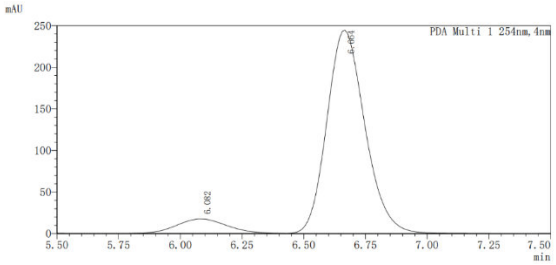
3ag

Enantiomeric excess is 83% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 6.09 min; minor isomer: tr = 6.68 min.



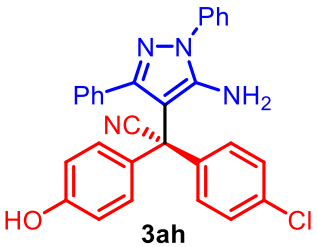
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	6.094	5307377	365194	49.113
2	6.681	5499064	529237	50.887
总计		10806441	894431	100.000



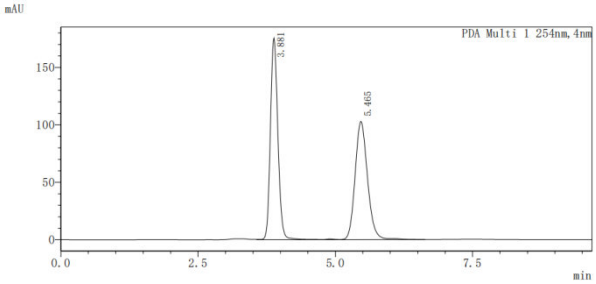
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	6.082	243199	17276	8.494
2	6.664	2620084	244528	91.506
总计		2863283	261804	100.000



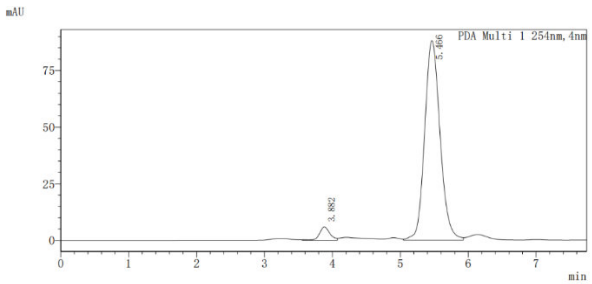
3ah

Enantiomeric excess is 91% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 3.88 min; minor isomer: tr = 5.47 min.



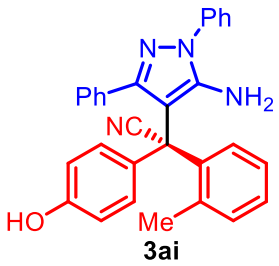
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	3.881	1662163	175353	50.498
2	5.465	1629410	102940	49.502
总计		3291572	278293	100.000



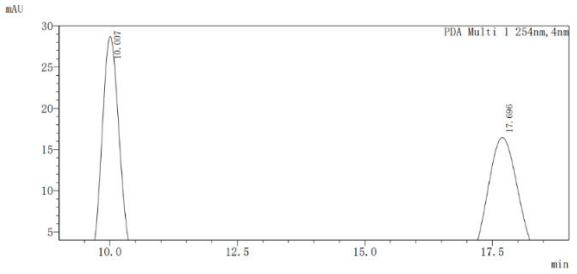
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	3.882	62801	5922	4.318
2	5.466	1391567	88039	95.682
总计		1454368	93962	100.000



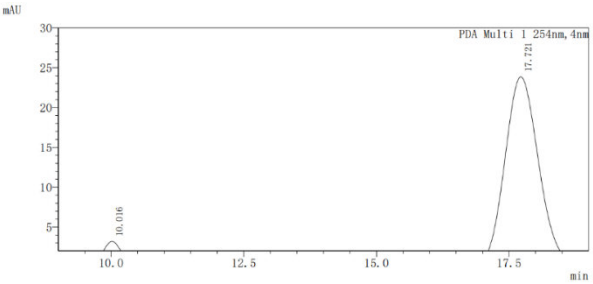
3ai

Enantiomeric excess is 87% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.02 min; minor isomer: tr = 17.72 min.



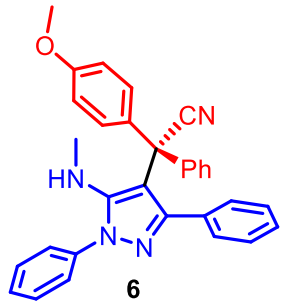
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Heiht	Area%
1	10.007	697823	28494	49.653
2	17.696	707585	16044	50.347
总计		1405408	44538	100.000



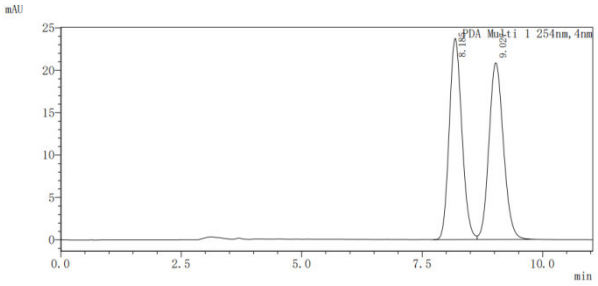
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.016	69918	2924	6.241
2	17.721	1050438	23681	93.759
总计		1120357	26605	100.000



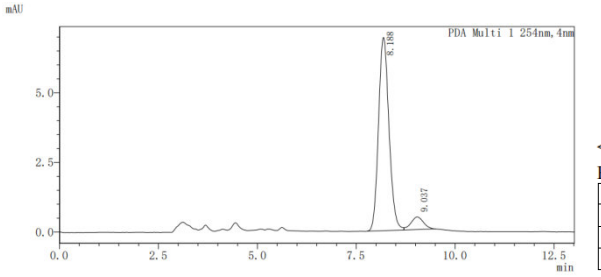
6

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.04. min; minor isomer: tr = 8.12 min.



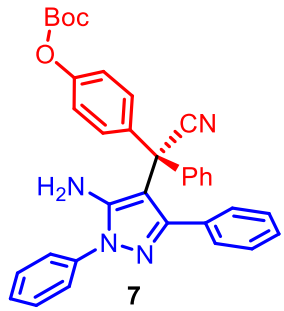
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.185	433868	23707	49.887
2	9.027	435831	20832	50.113
Totals		869699	44539	100.000



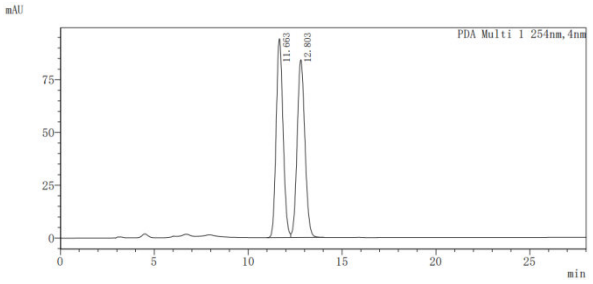
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.188	127660	6936	92.748
2	9.037	9982	450	7.252
Totals		137643	7386	100.000



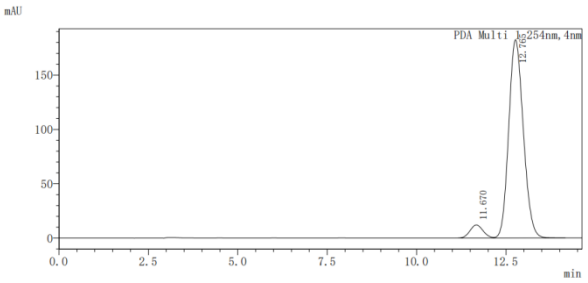
7

Enantiomeric excess is 89% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.77. min; minor isomer: tr = 11.67 min.



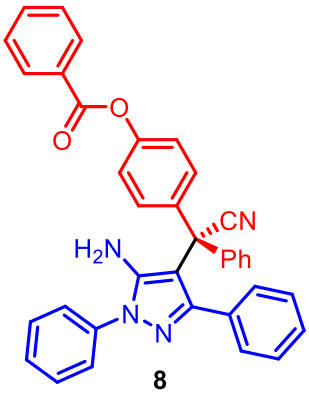
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	11.663	2408707	94104	49.943
2	12.803	2414237	84089	50.057
Totals		4822943	178193	100.000



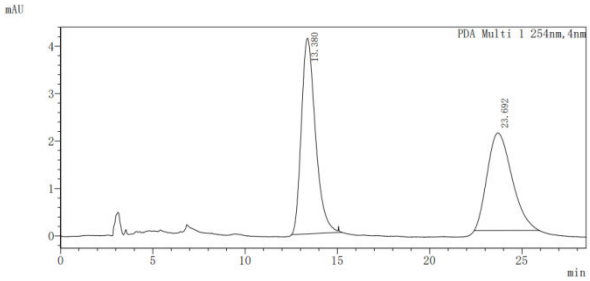
<Singal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	11.670	307952	12038	5.608
2	12.765	5183446	182439	94.392
Totals		5491399	194477	100.000



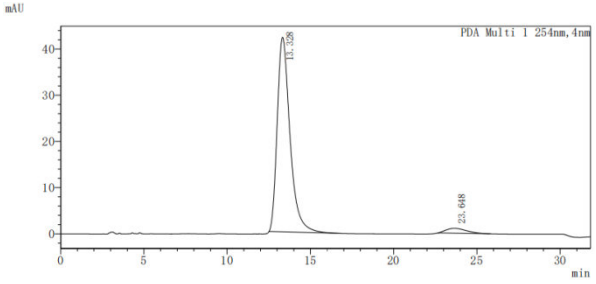
8

Enantiomeric excess is 92% determined by HPLC (Chiralpak OD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.33 min; minor isomer: tr = 23.65 min.



<Singal>
PDA Ch1 254nm

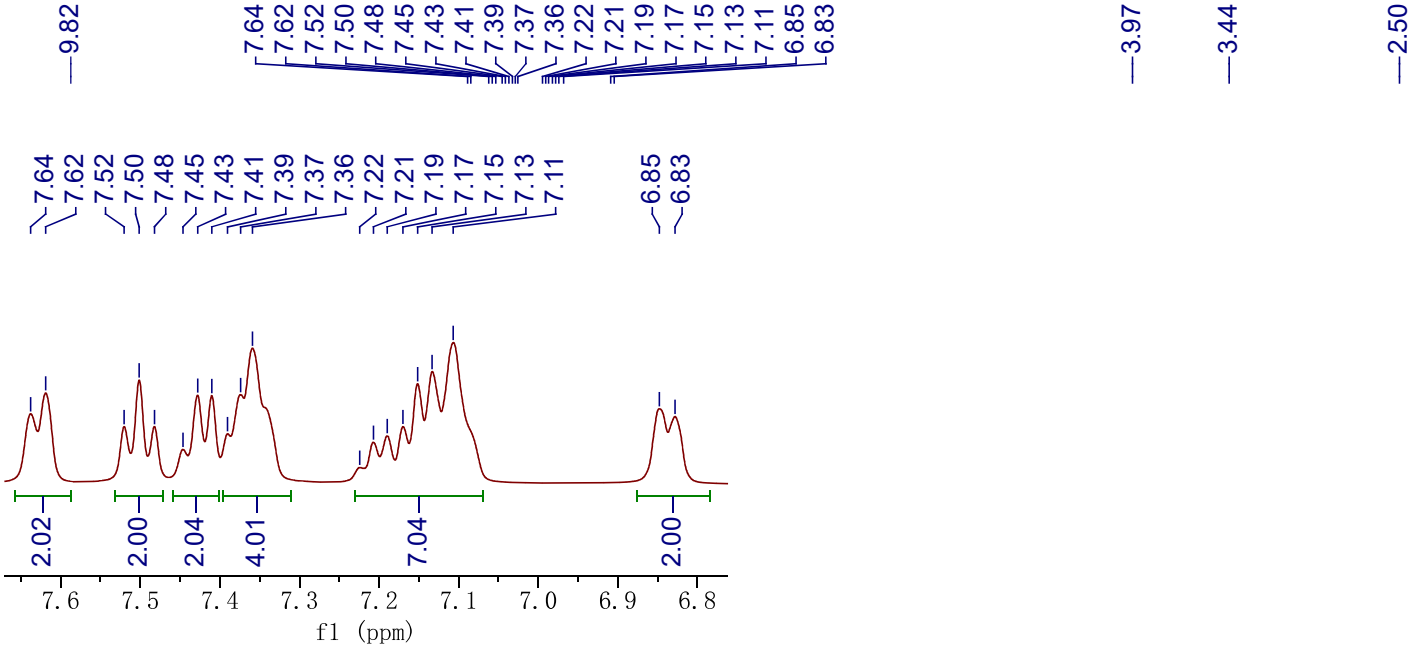
Peak	RetTime	Area	Height	Area%
1	13.380	218926	4124	53.370
2	23.692	191281	2056	46.630
Totals		410207	6180	100.000



PDA Ch1 254nm

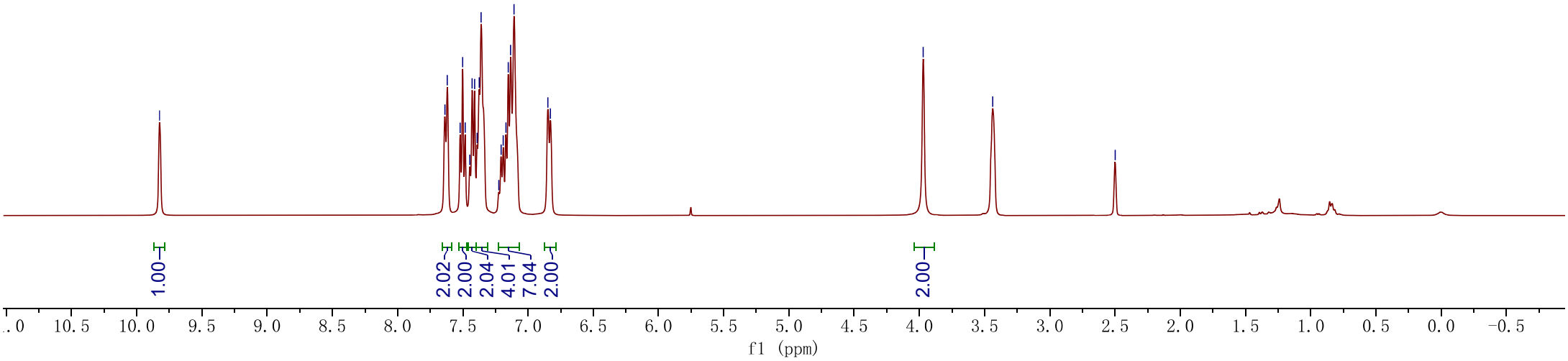
Peak	RetTime	Area	Height	Area%
1	13.328	2249817	42097	96.112
2	23.648	91019	1058	3.888
Totals		2340836	43155	100.000

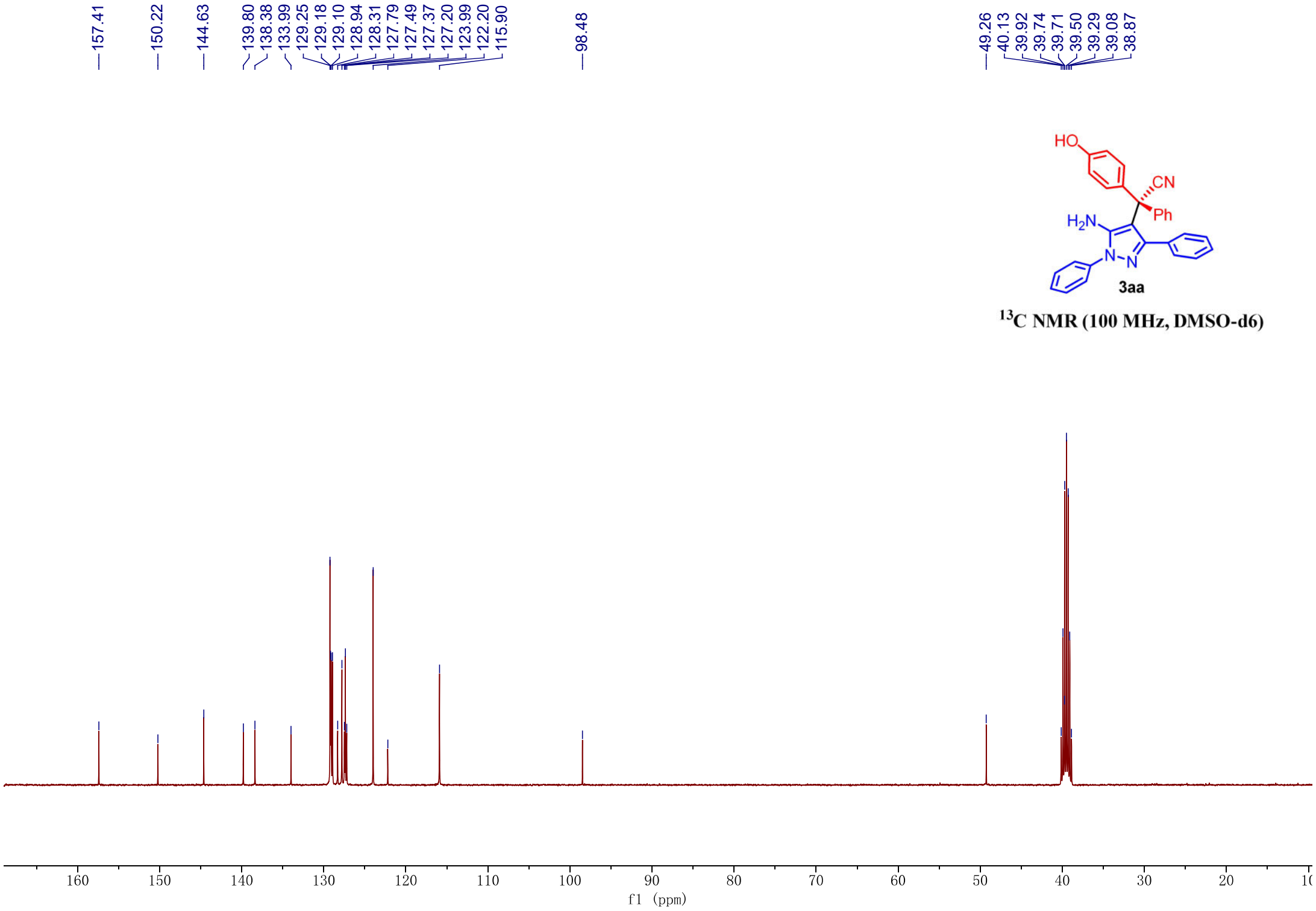
6. Copies of NMR spectra



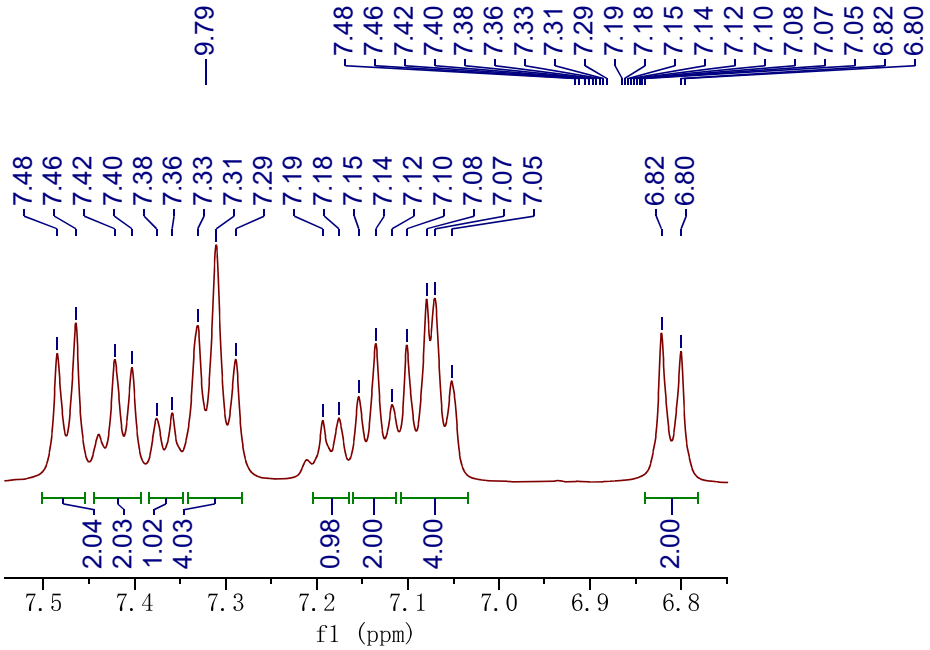
3aa

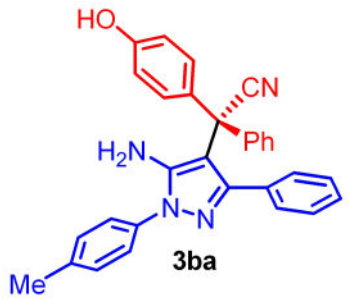
^{1}H NMR (400 MHz, DMSO-d6)



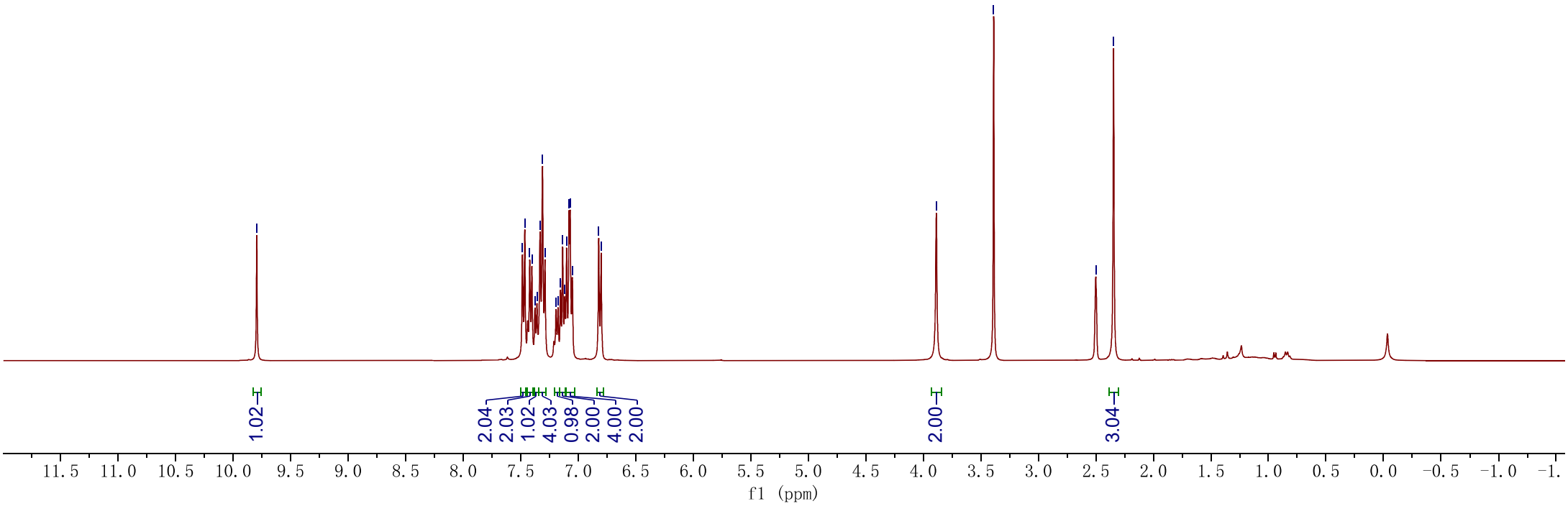


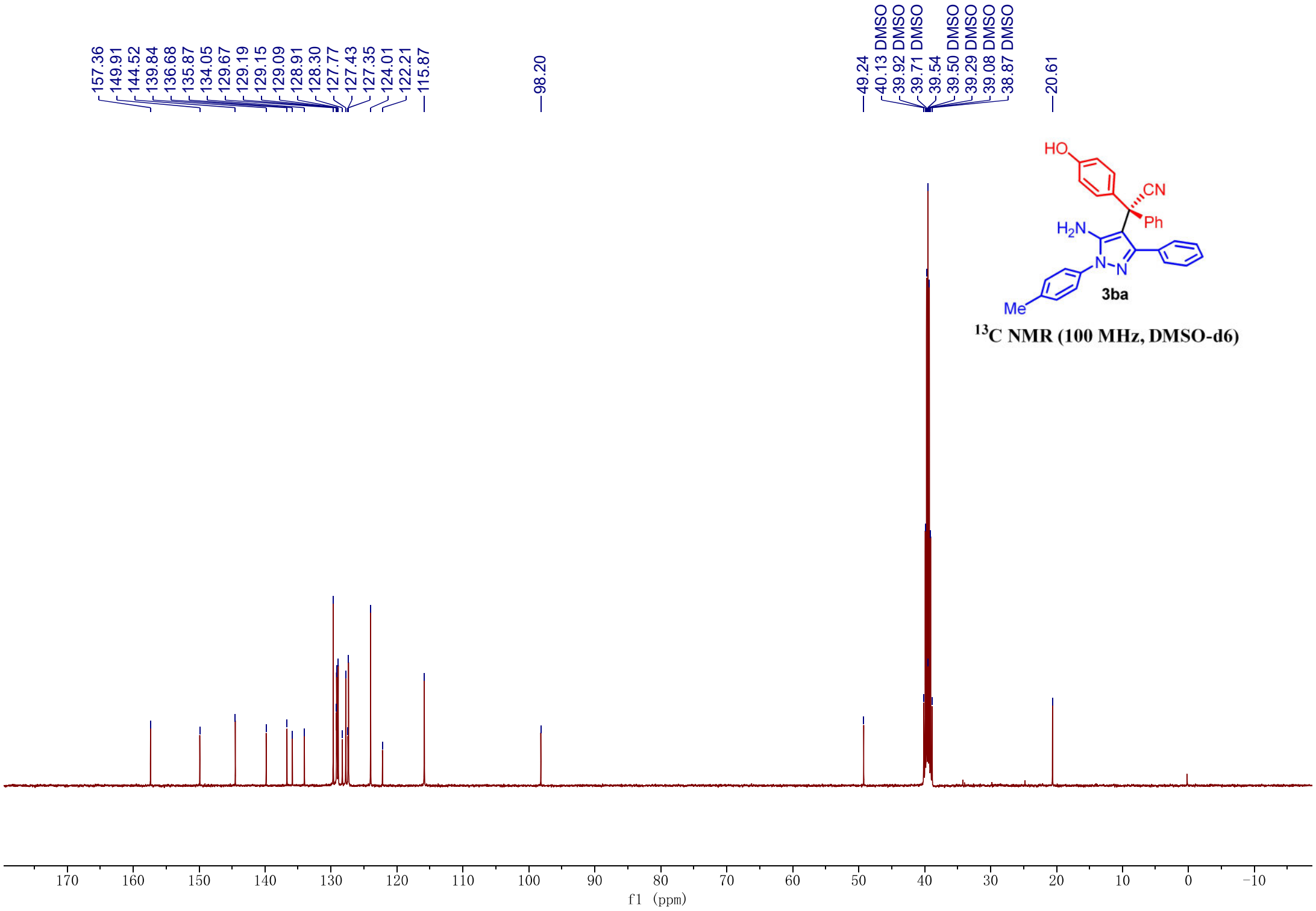
^{13}C NMR (100 MHz, DMSO-d6)

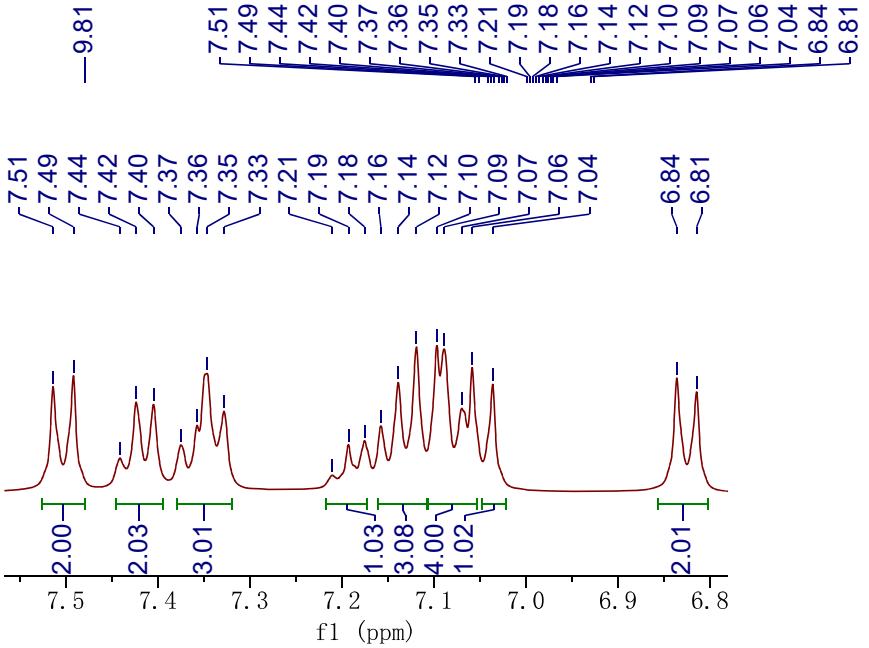


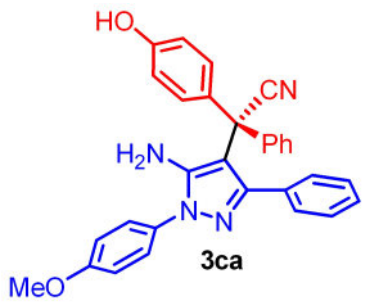


^{1}H NMR (400 MHz, DMSO-d6)

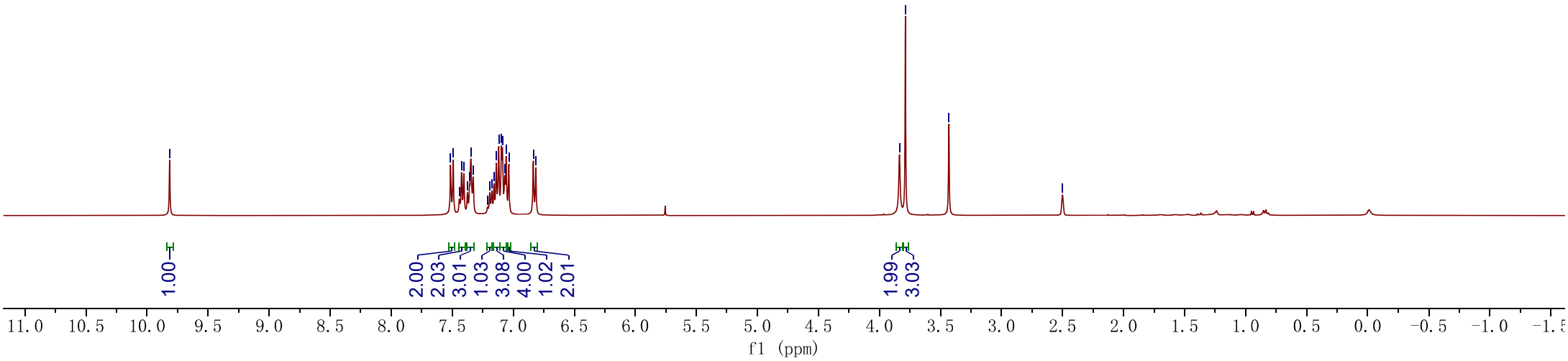


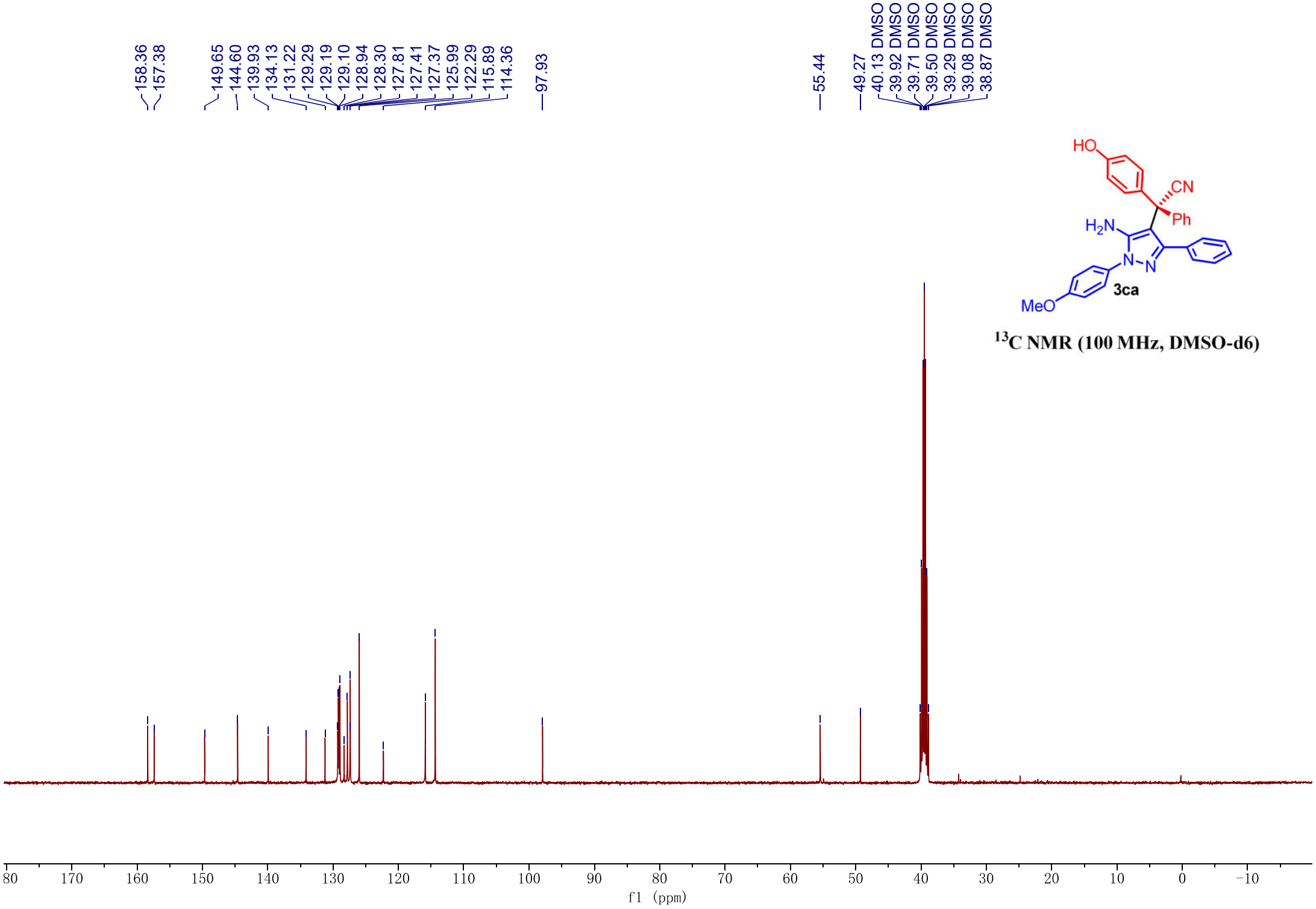

157.36
149.91
144.52
139.84
136.68
135.87
134.05
129.67
129.19
129.15
129.09
128.91
128.30
127.77
127.43
127.35
124.01
122.21
115.87
98.20
49.24
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.54
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
20.61
HO
CN
Ph
H2N
N
N
Me
3ba
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)



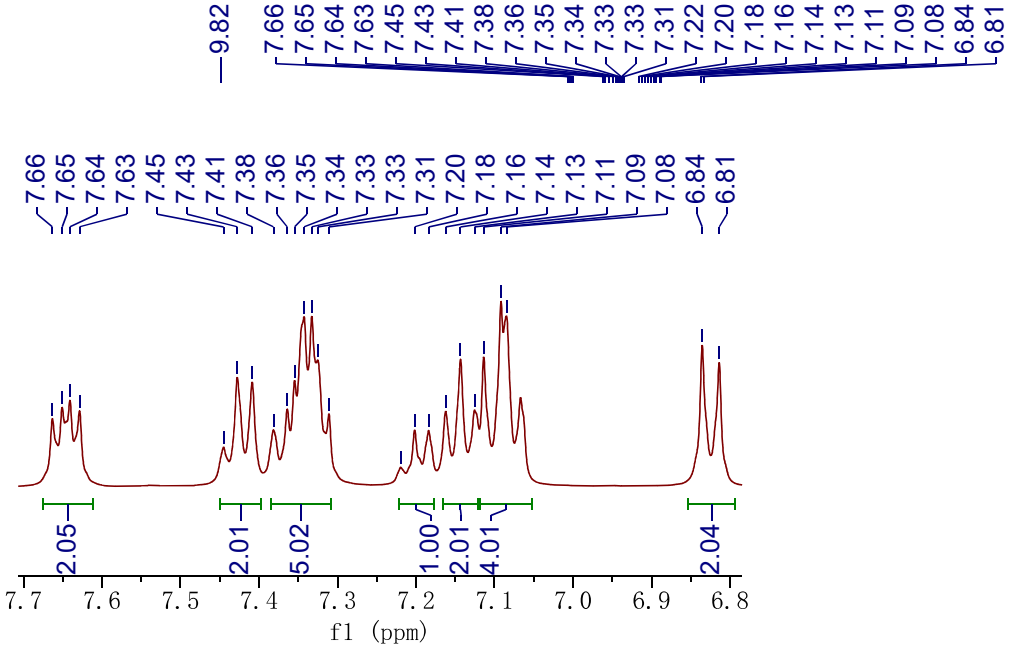


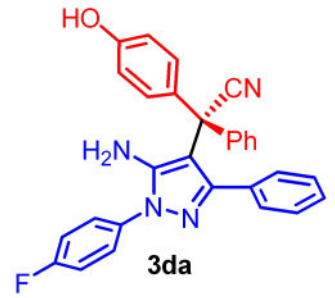
^{1}H NMR (400 MHz, DMSO-d6)



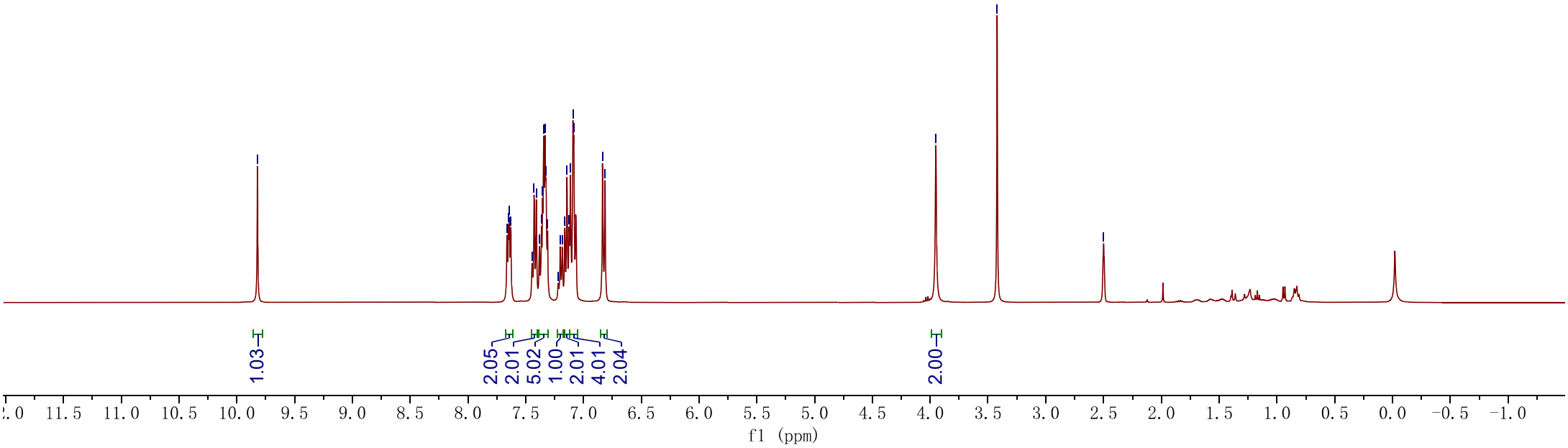


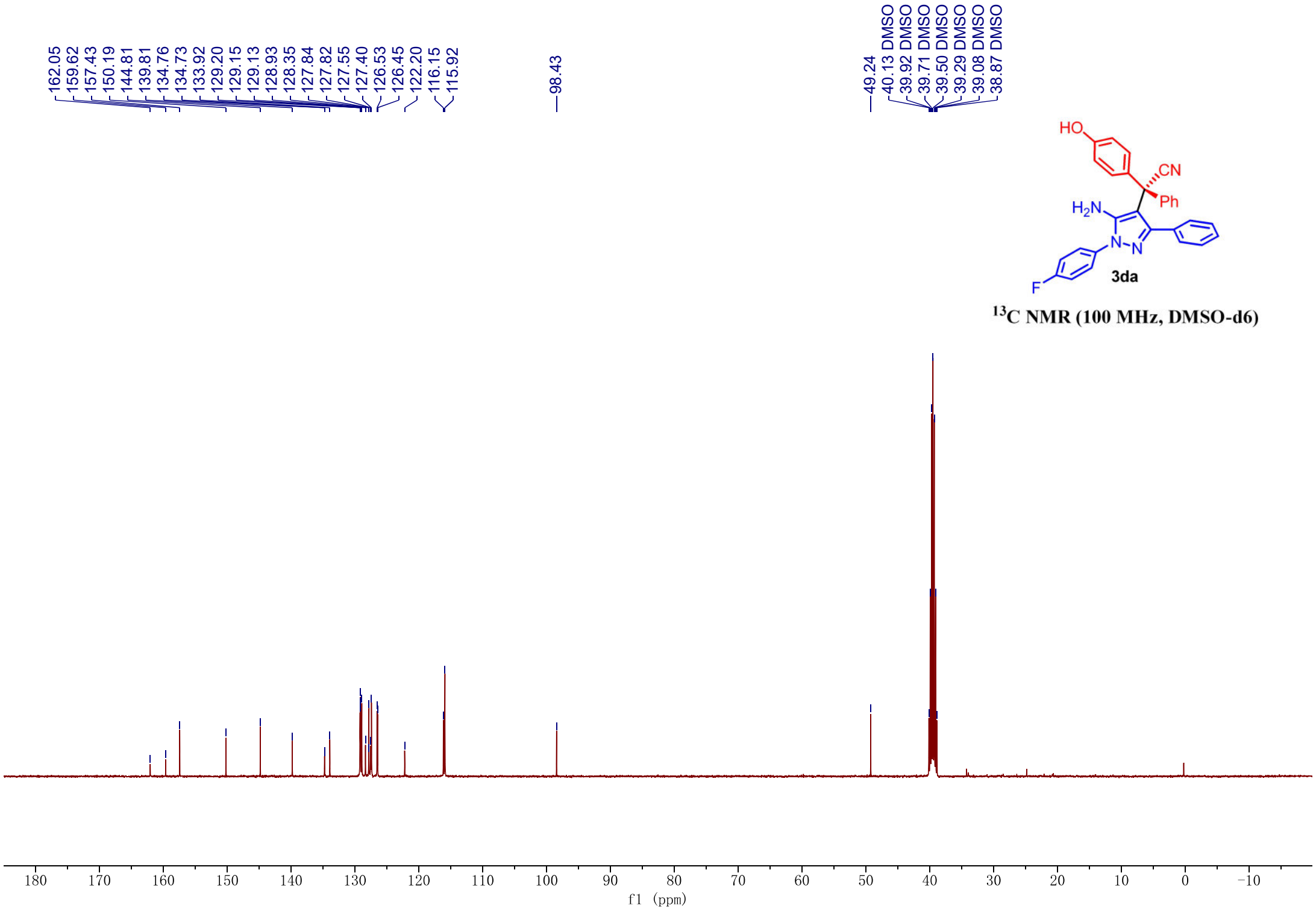
^{13}C NMR (100 MHz, DMSO-d6)

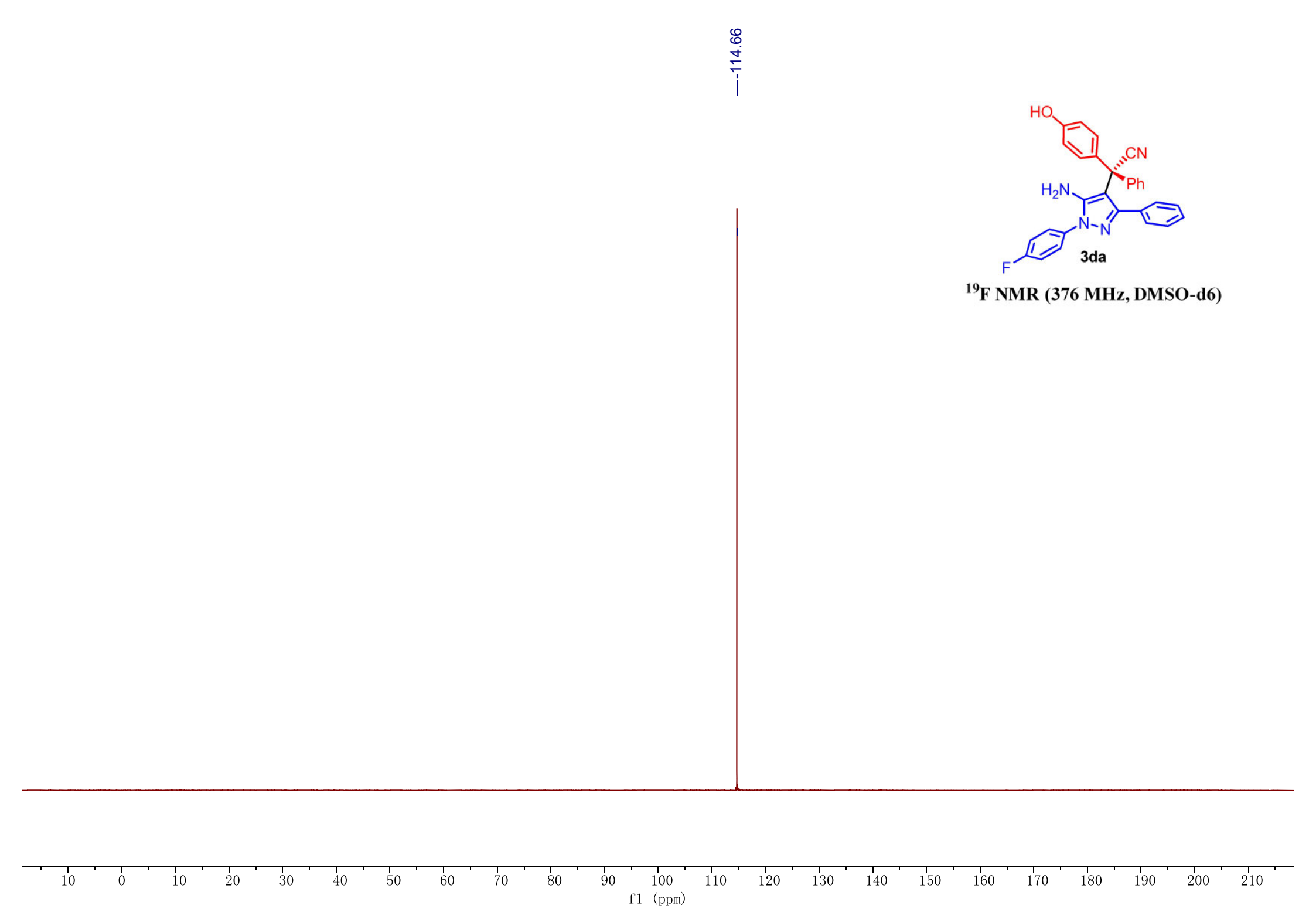




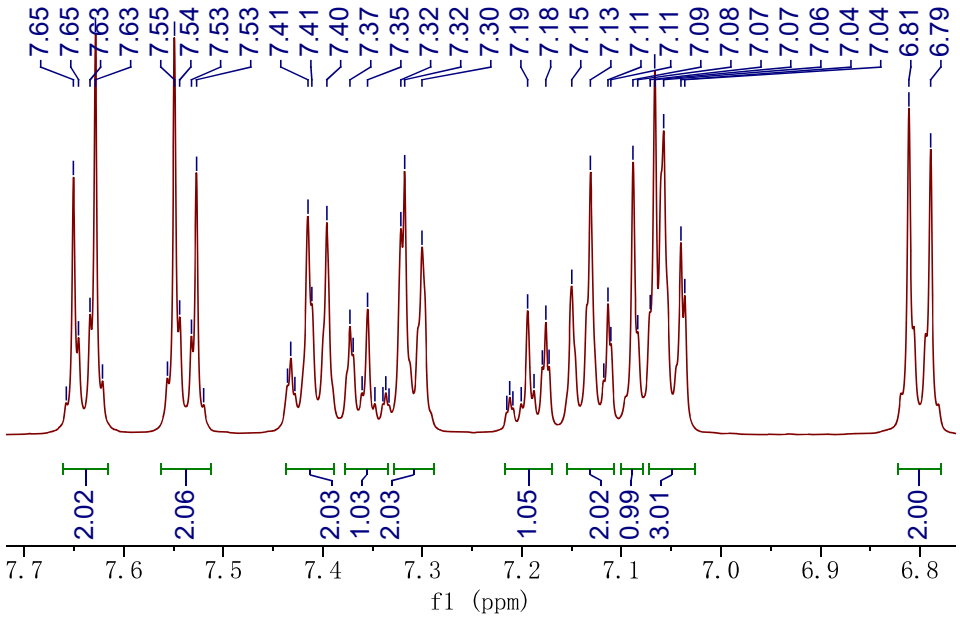
^{1}H NMR (400 MHz, DMSO-d6)

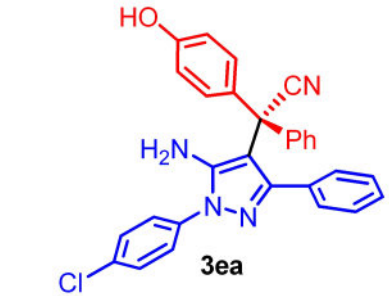



162.05
159.62
157.43
150.19
144.81
139.81
134.76
134.73
133.92
129.20
129.15
129.13
128.93
128.35
127.84
127.82
127.55
127.40
126.53
126.45
122.20
116.15
115.92
98.43
49.24
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
F
3da
13C NMR (100 MHz, DMSO-d6)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)



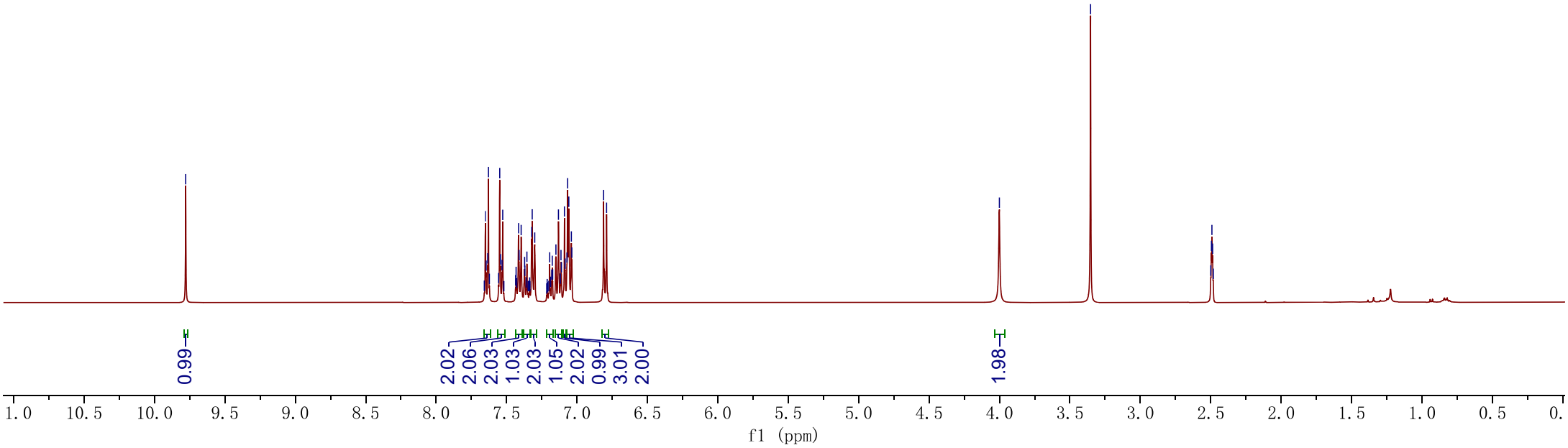
^{19}F NMR (376 MHz, DMSO-d6)

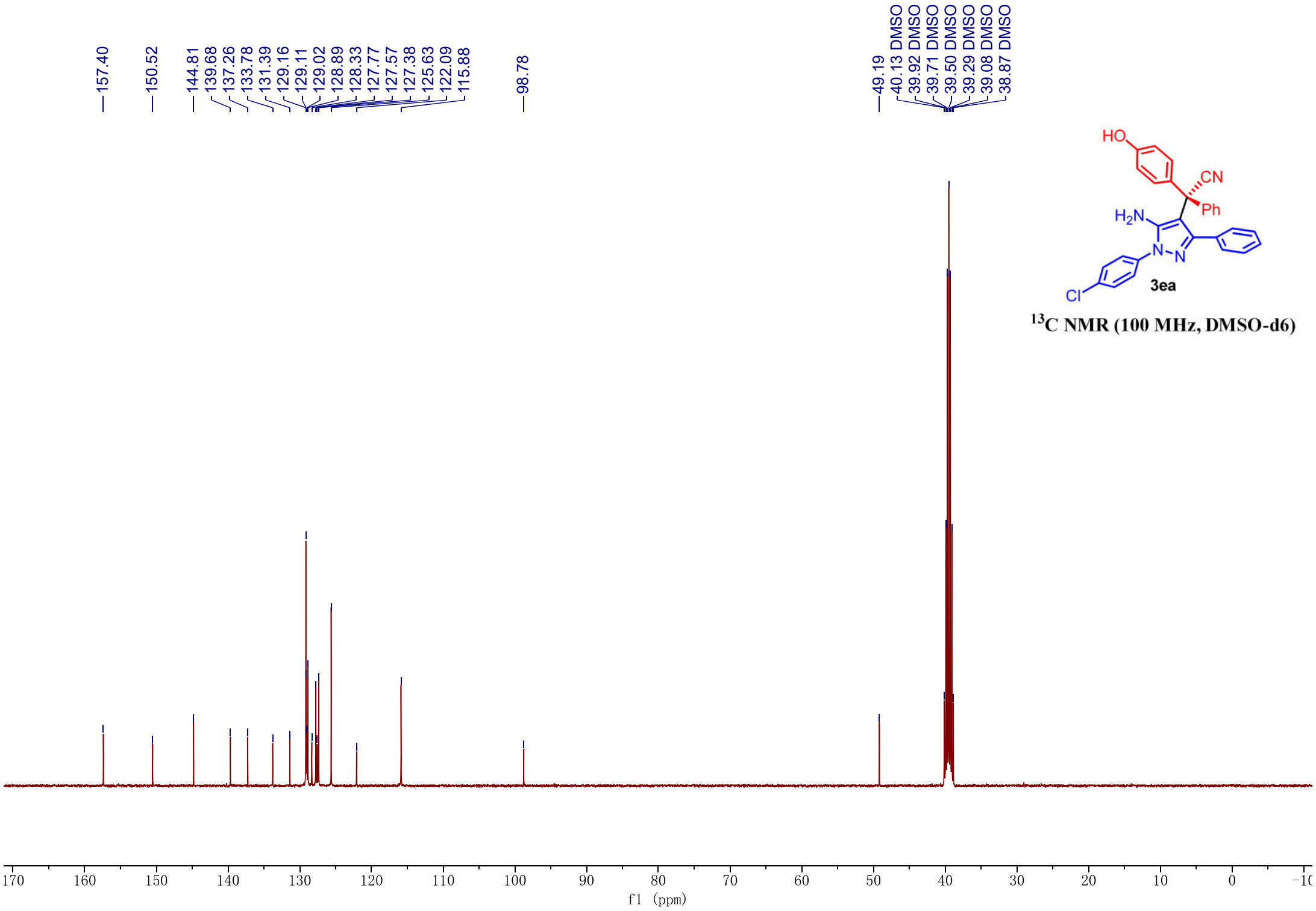


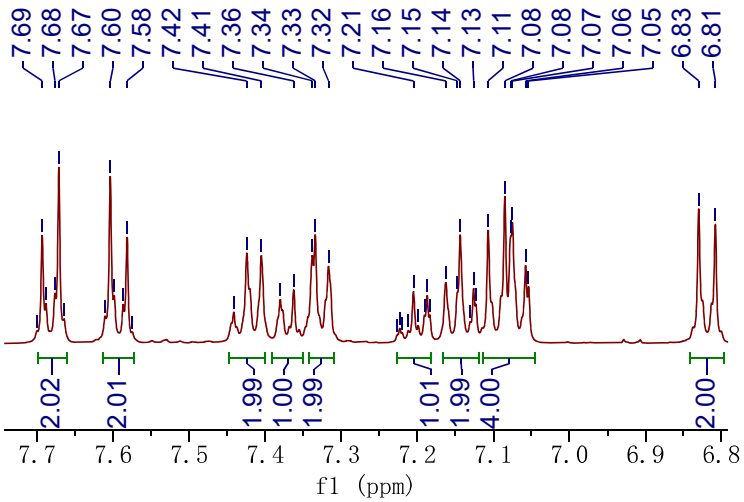


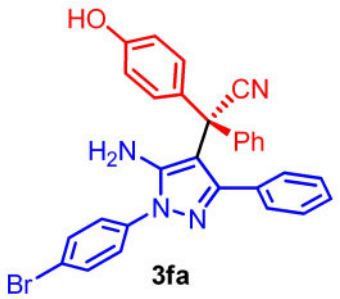
3ea

^{1}H NMR (400 MHz, DMSO-d6)



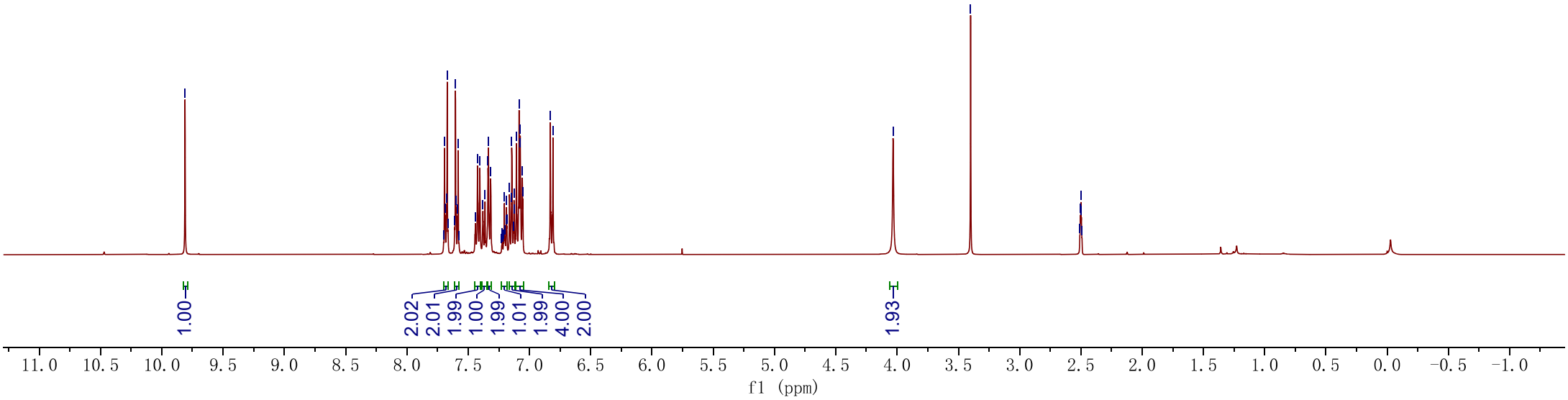

157.40
150.52
144.81
139.68
137.26
133.78
131.39
129.16
129.11
129.02
128.89
128.33
127.77
127.57
127.38
125.63
122.09
115.88
98.78
49.19
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
Cl
3ea
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

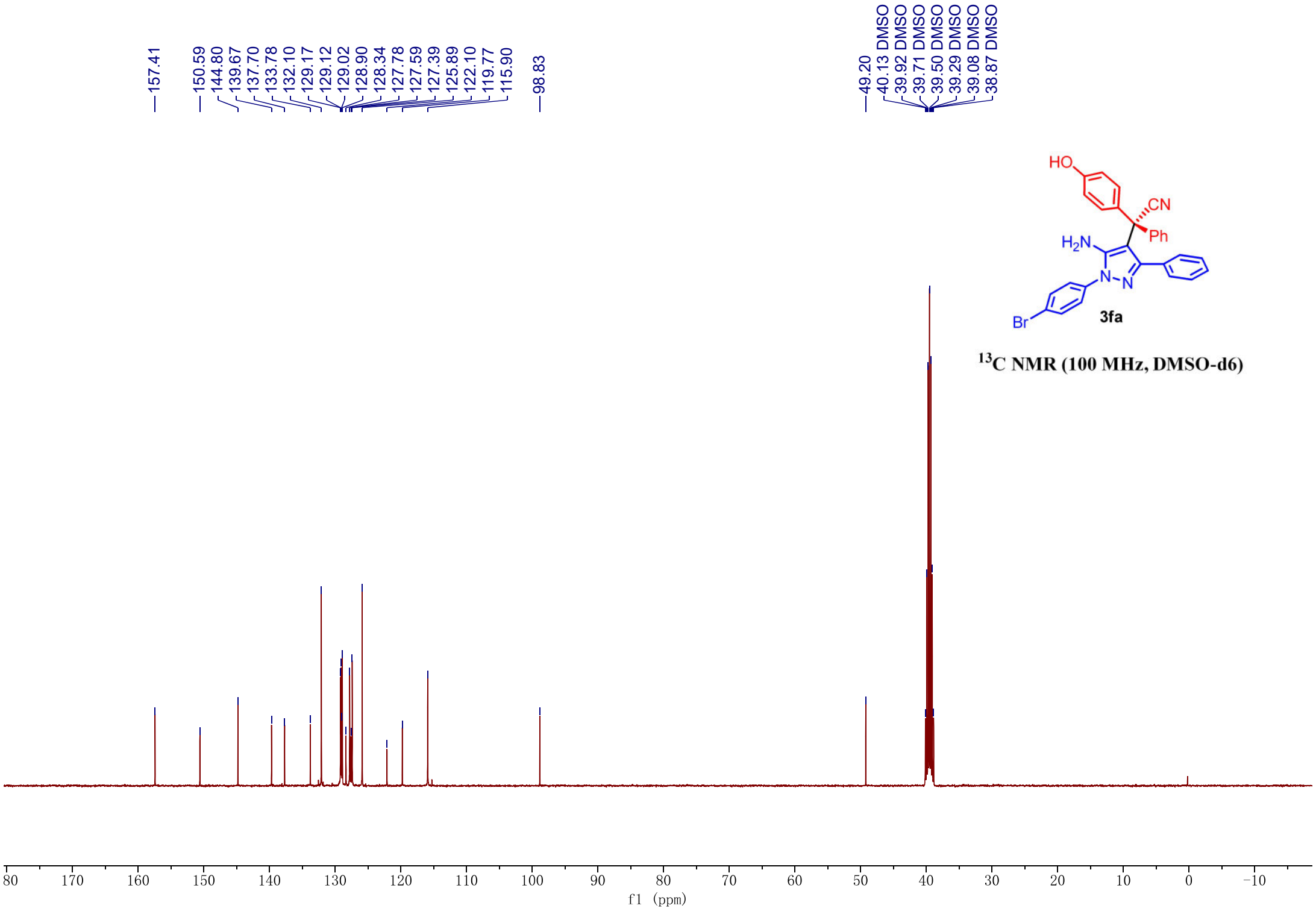


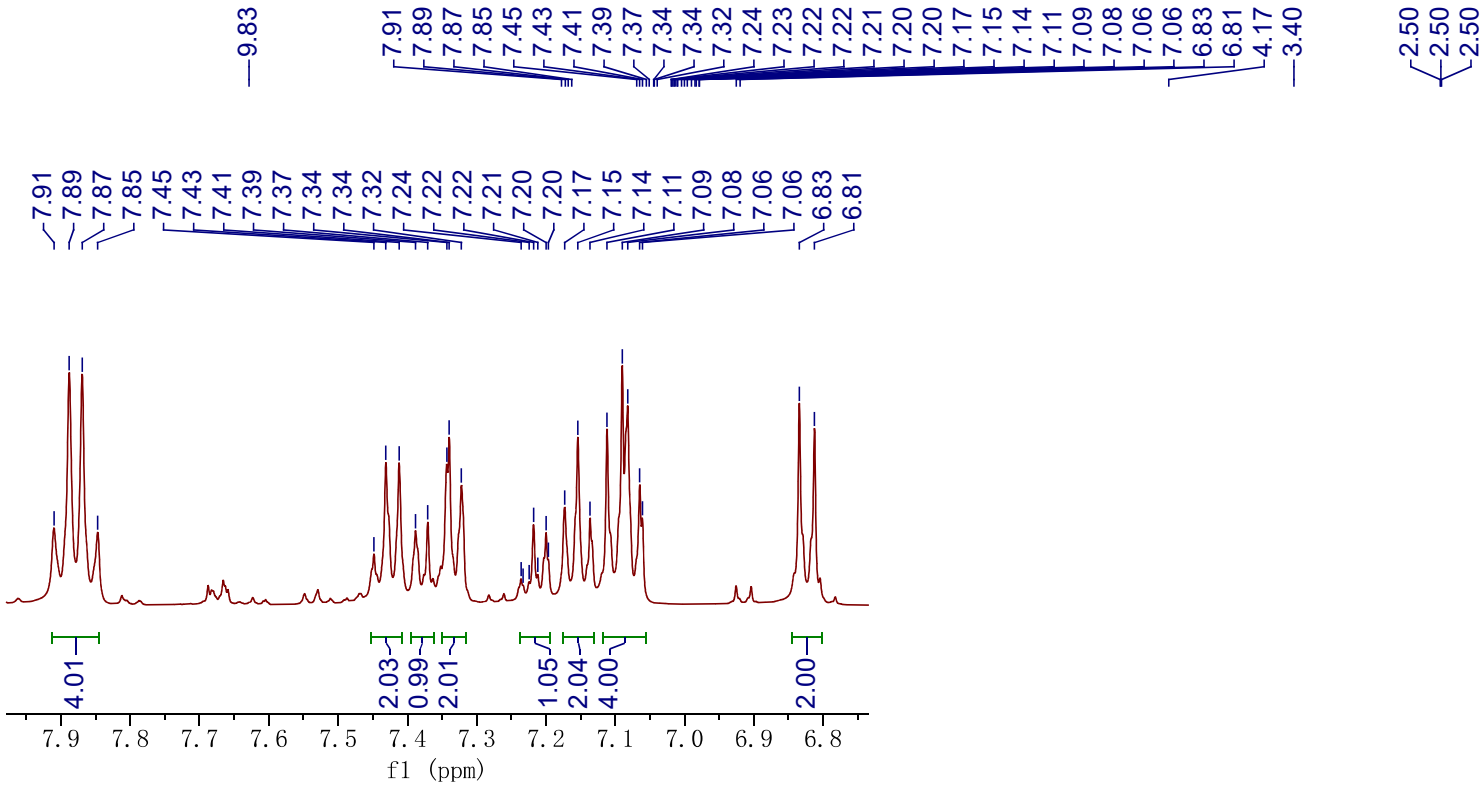


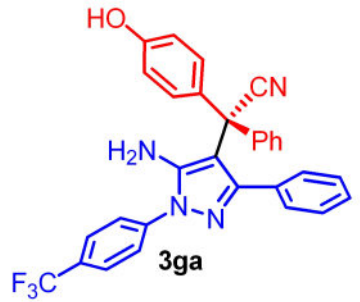
3fa

^{1}H NMR (400 MHz, DMSO-d6)

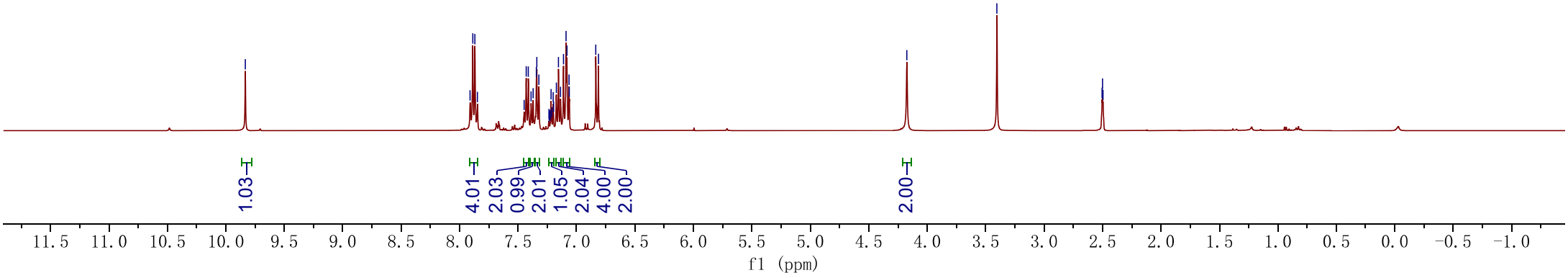


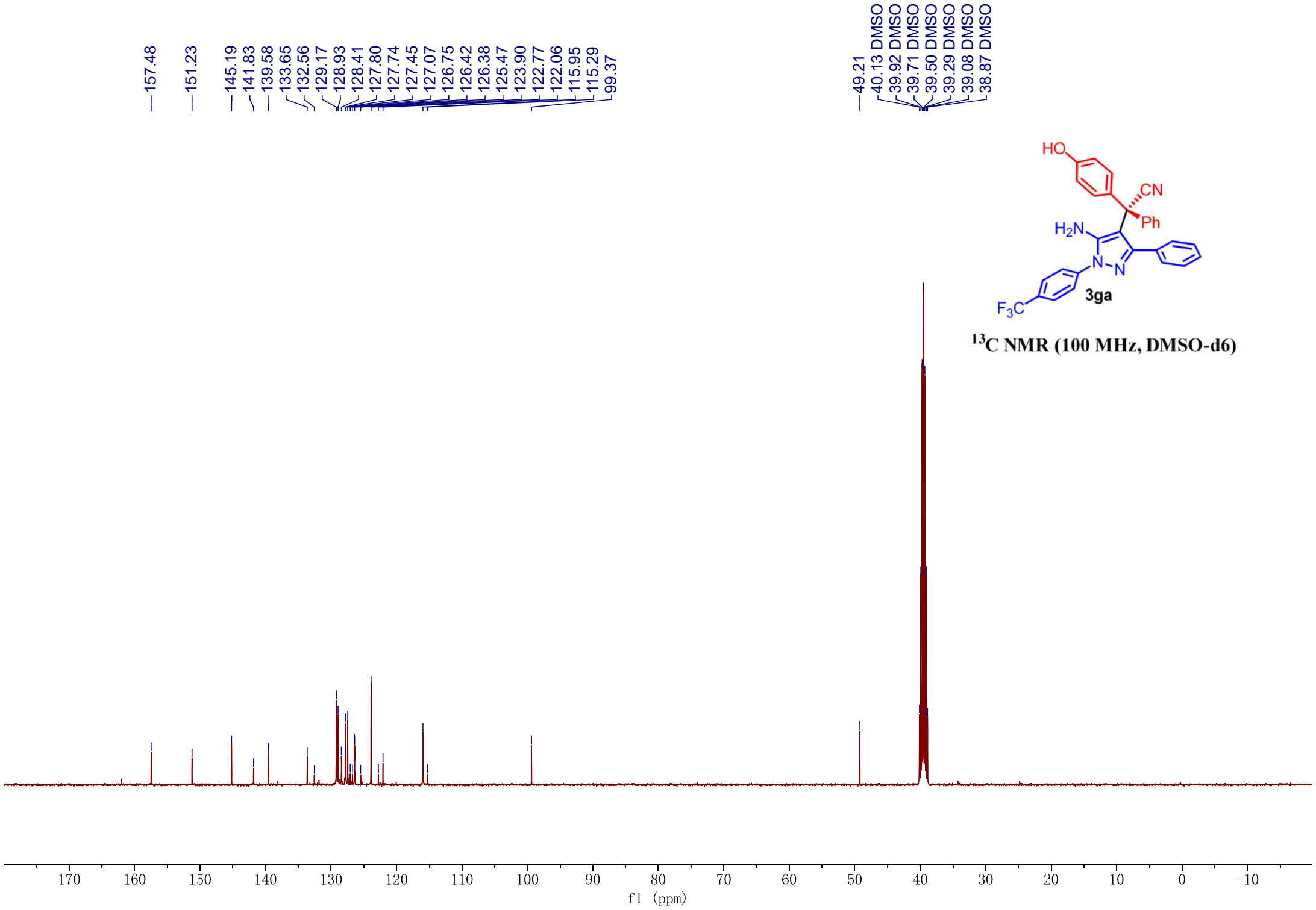

157.41
150.59
144.80
139.67
137.70
133.78
132.10
129.17
129.12
129.02
128.90
128.34
127.78
127.59
127.39
125.89
122.10
119.77
115.90
98.83
49.20
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
Br
3fa
13C NMR (100 MHz, DMSO-d6)
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

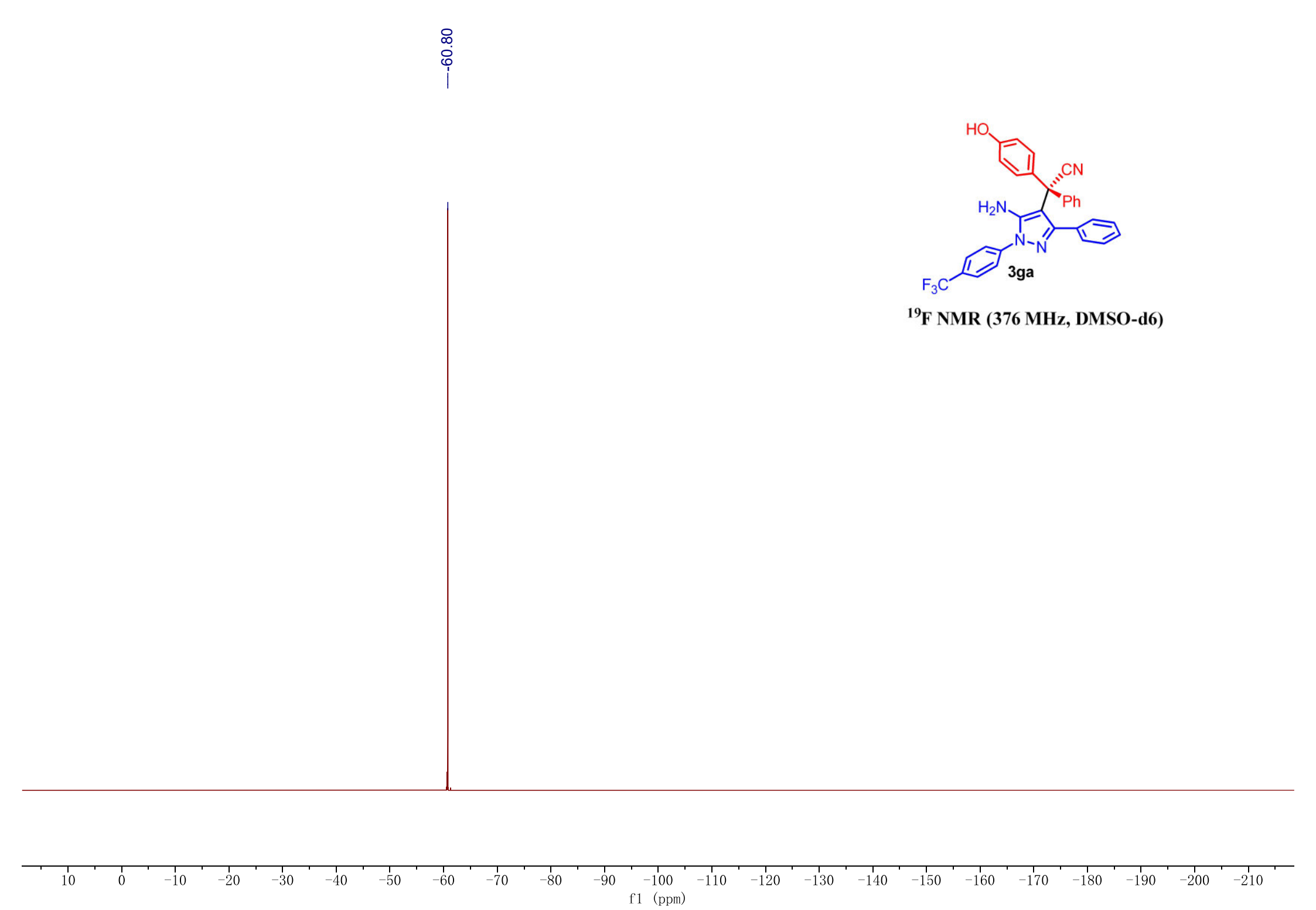




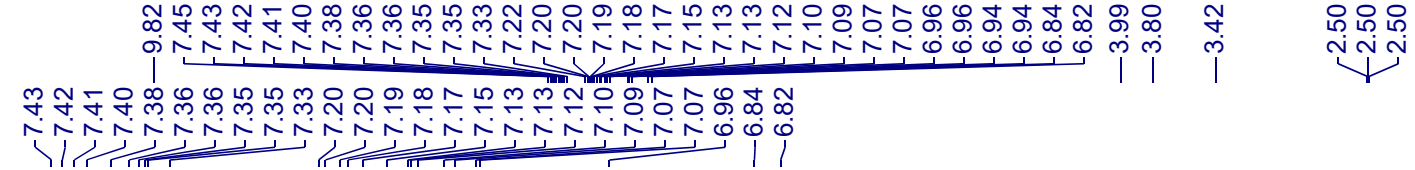
^{1}H NMR (400 MHz, DMSO-d6)

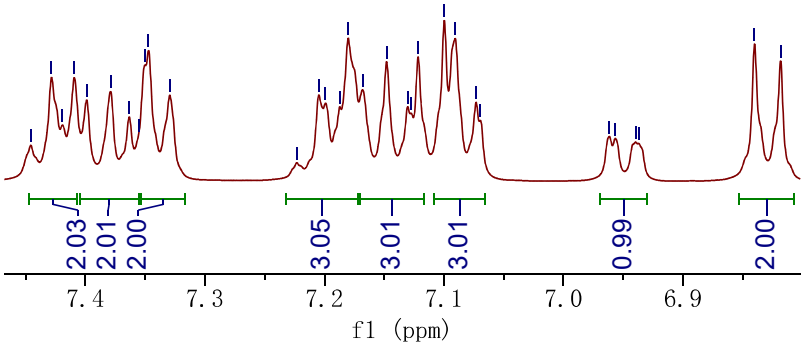


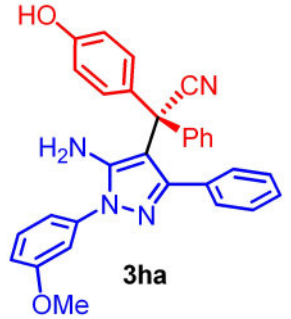

157.48
151.23
145.19
141.83
139.58
133.65
132.56
129.17
128.93
128.41
127.80
127.74
127.45
127.07
126.75
126.42
126.38
125.47
123.90
122.77
122.06
115.95
115.29
99.37
49.21
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
F3C
3ga
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



^{19}F NMR (376 MHz, DMSO-d6)

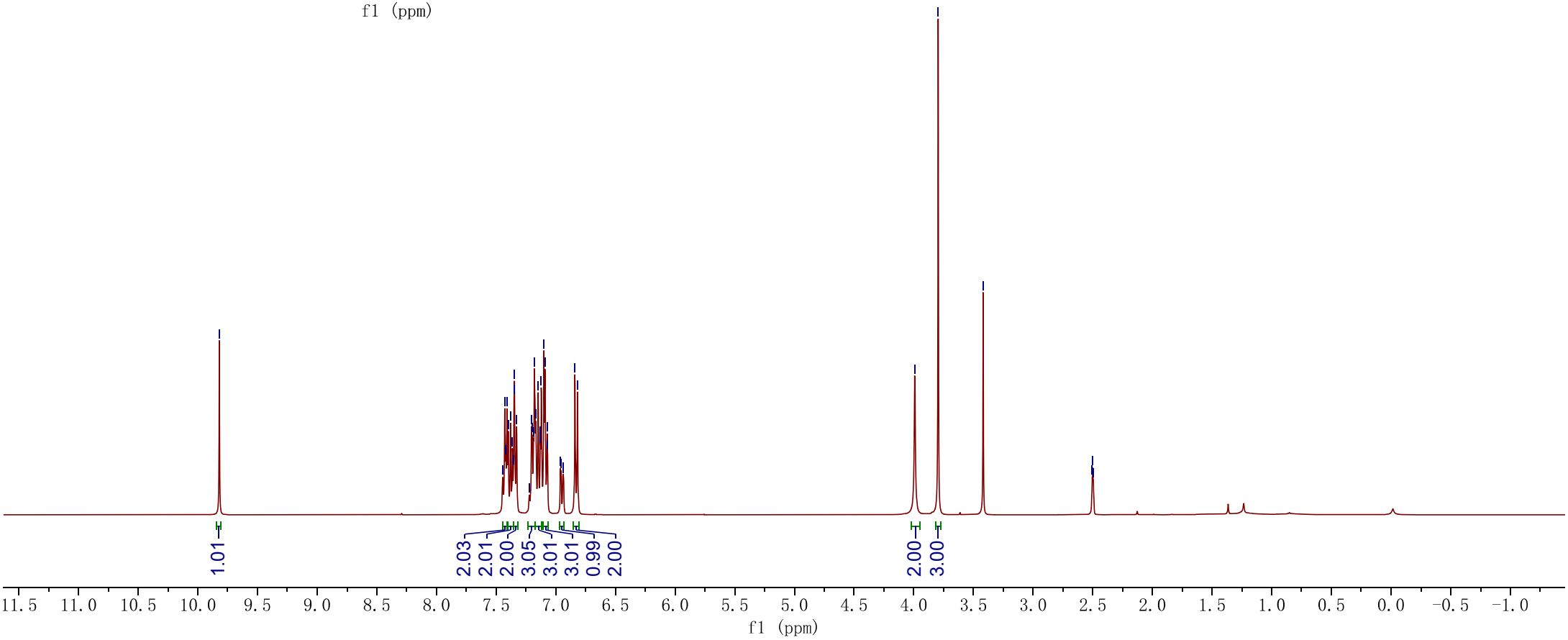


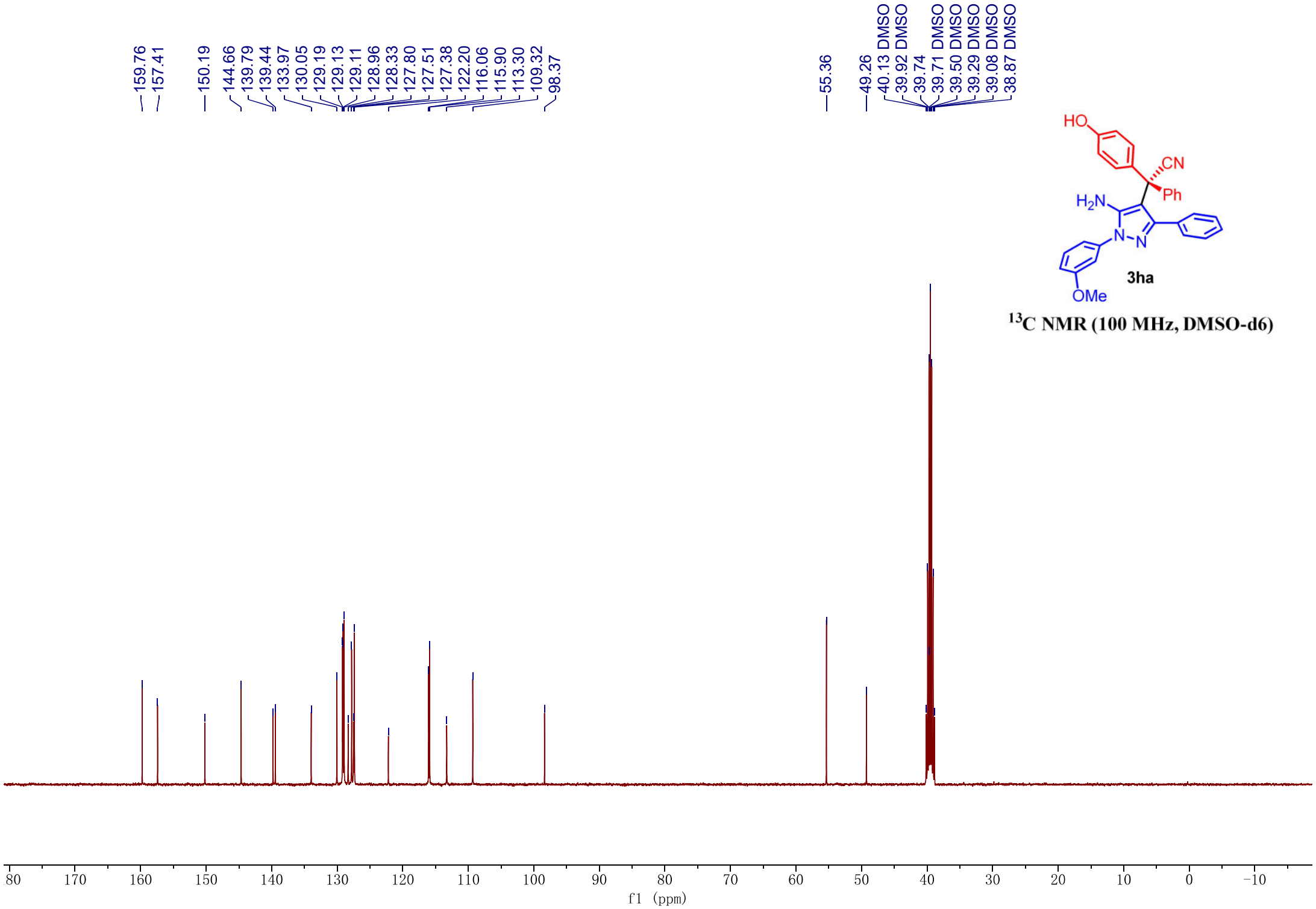


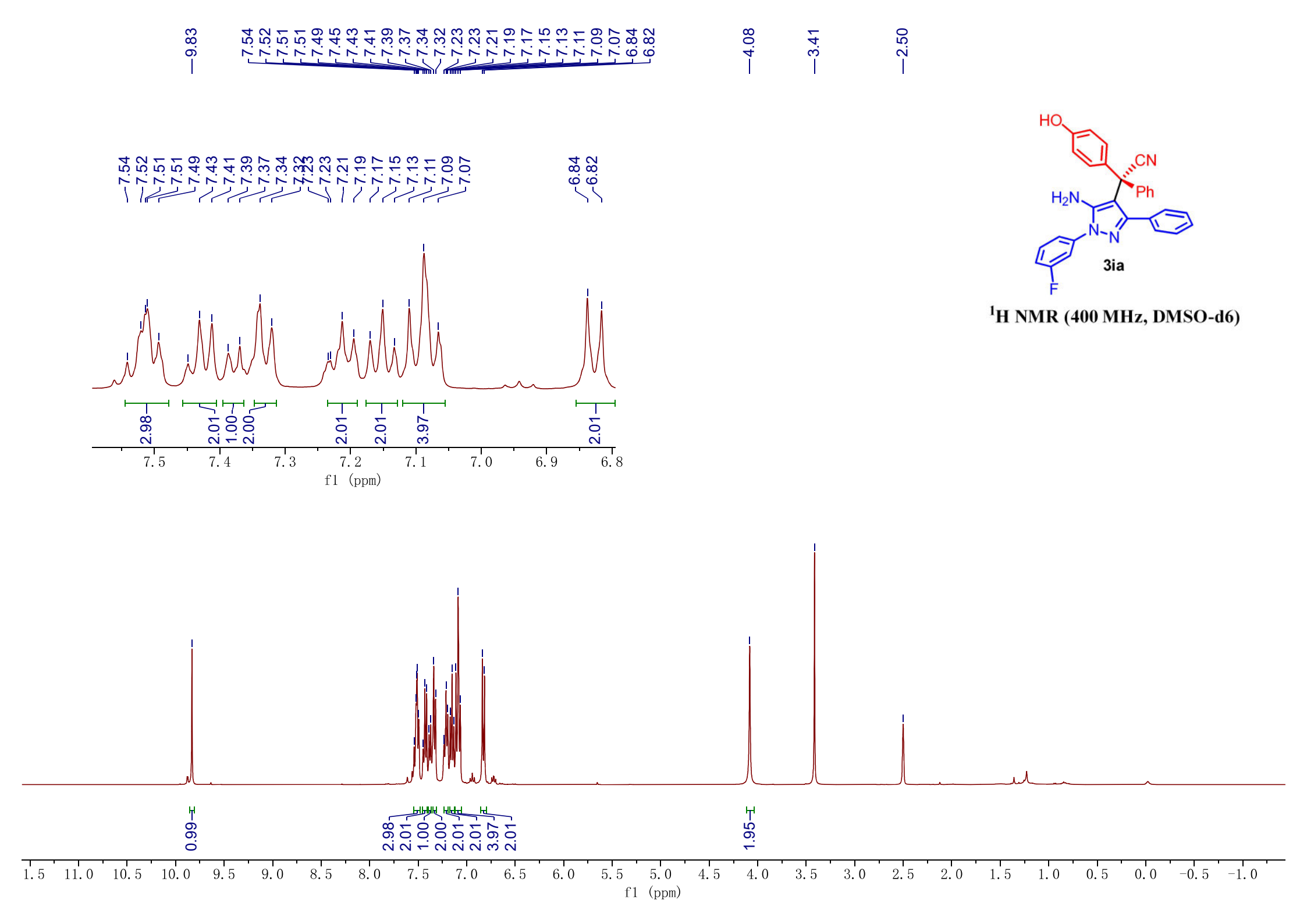


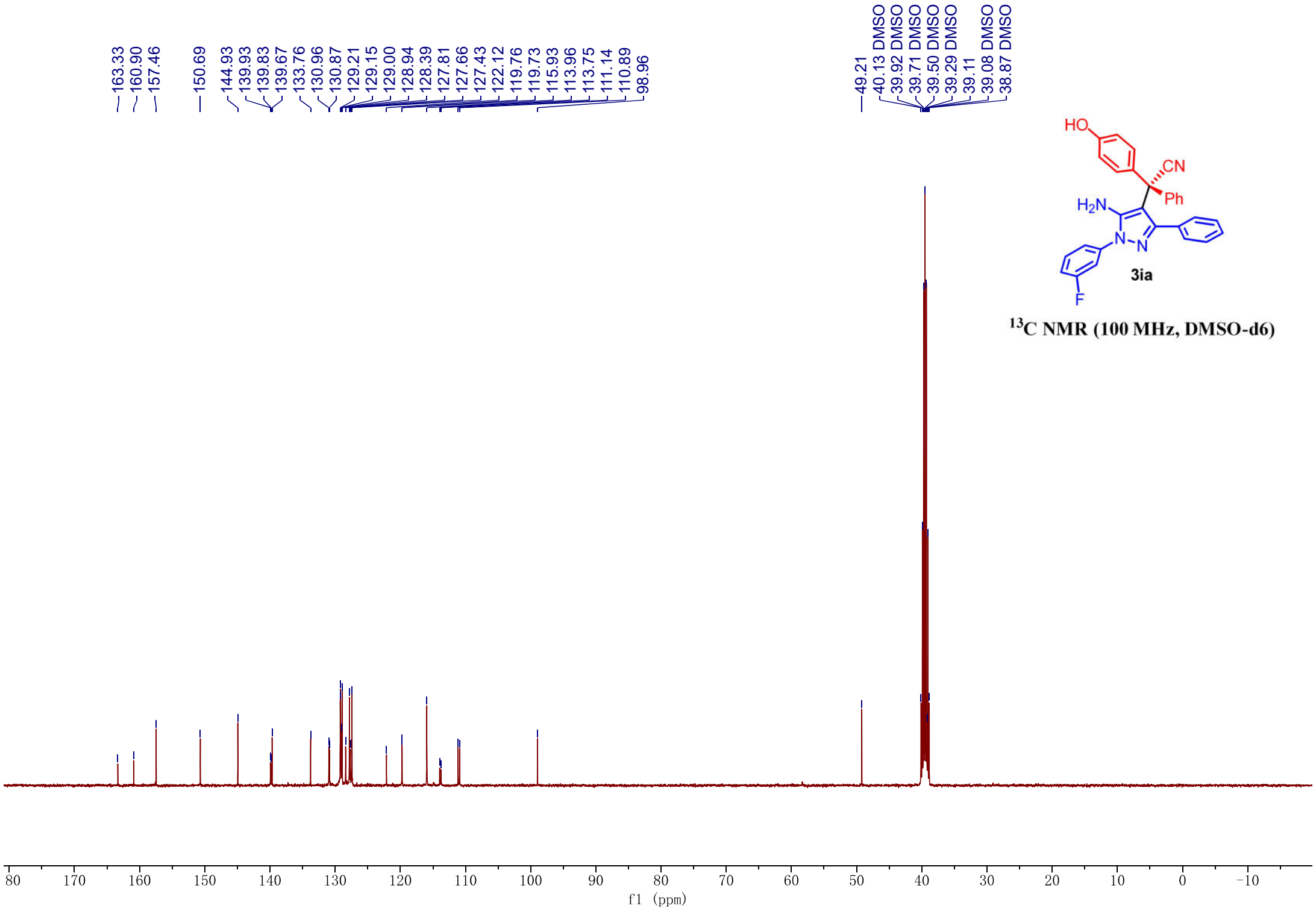
3ha

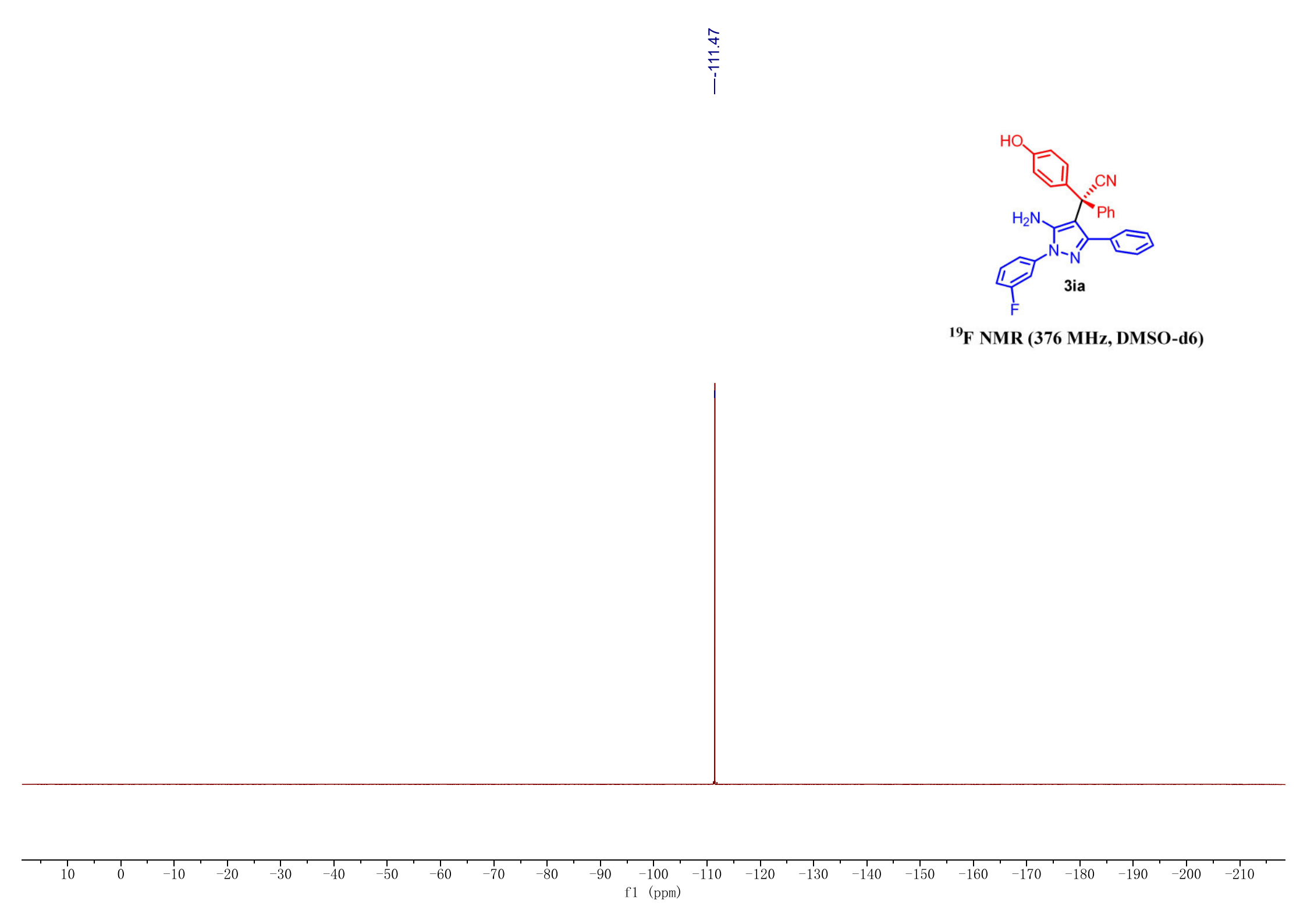
^{1}H NMR (400 MHz, DMSO-d6)

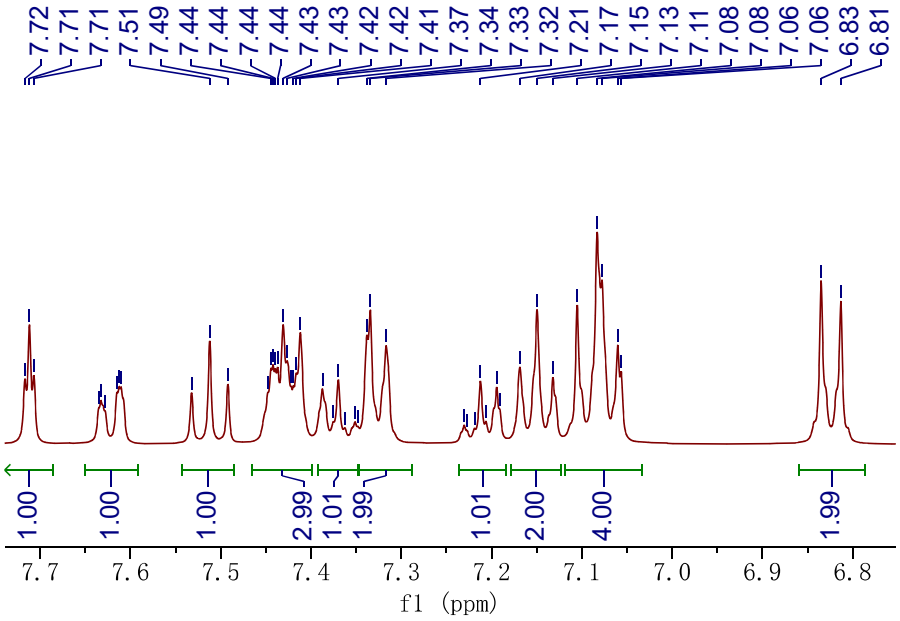


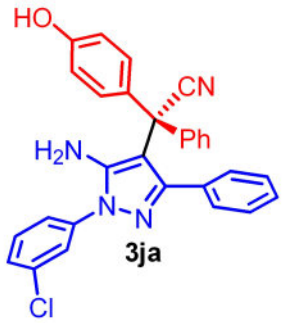

159.76
157.41
150.19
144.66
139.79
139.44
133.97
130.05
129.19
129.13
129.11
128.96
128.33
127.80
127.51
127.38
122.20
116.06
115.90
113.30
109.32
98.37
55.36
49.26
40.13 DMSO
39.92 DMSO
39.74
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
OMe
3ha
13C NMR (100 MHz, DMSO-d6)
f1 (ppm)


9.83
7.54
7.52
7.51
7.51
7.49
7.45
7.43
7.41
7.39
7.37
7.34
7.32
7.23
7.23
7.21
7.19
7.17
7.15
7.13
7.11
7.09
7.07
6.84
6.82
4.08
3.41
2.50
HO
CN
Ph
H2N
N
N
F
3ia
1H NMR (400 MHz, DMSO-d6)
2.98
2.01
1.00
2.00
2.01
2.01
3.97
2.01
f1 (ppm)
0.99
2.98
2.01
1.00
2.00
2.01
2.01
3.97
2.01
1.95
f1 (ppm)


163.33
160.90
157.46
150.69
144.93
139.93
139.83
139.67
133.76
130.96
130.87
129.21
129.15
129.00
128.94
128.39
127.81
127.66
127.43
122.12
119.76
119.73
115.93
113.96
113.75
111.14
110.89
98.96
49.21
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.11
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
F
3ia
13C NMR (100 MHz, DMSO-d6)
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

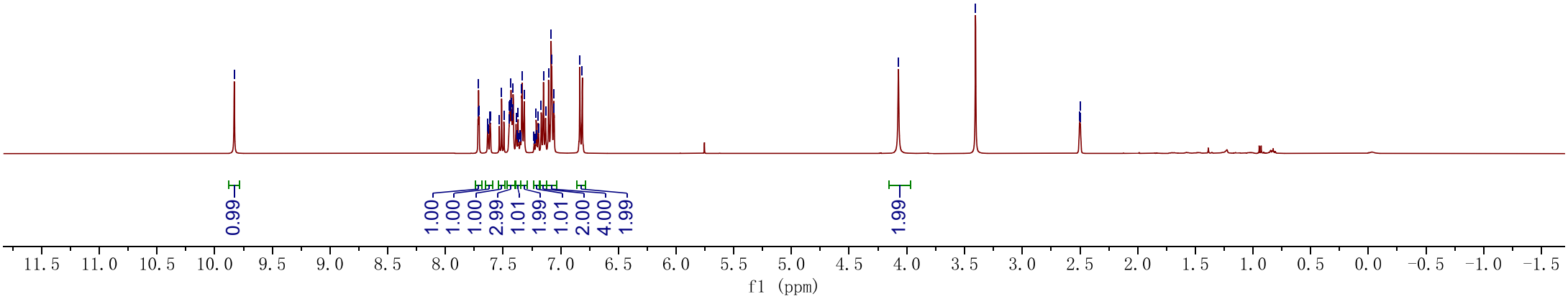

-111.47
HO
CN
Ph
H2N
N
N
F
3ia
19F NMR (376 MHz, DMSO-d6)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

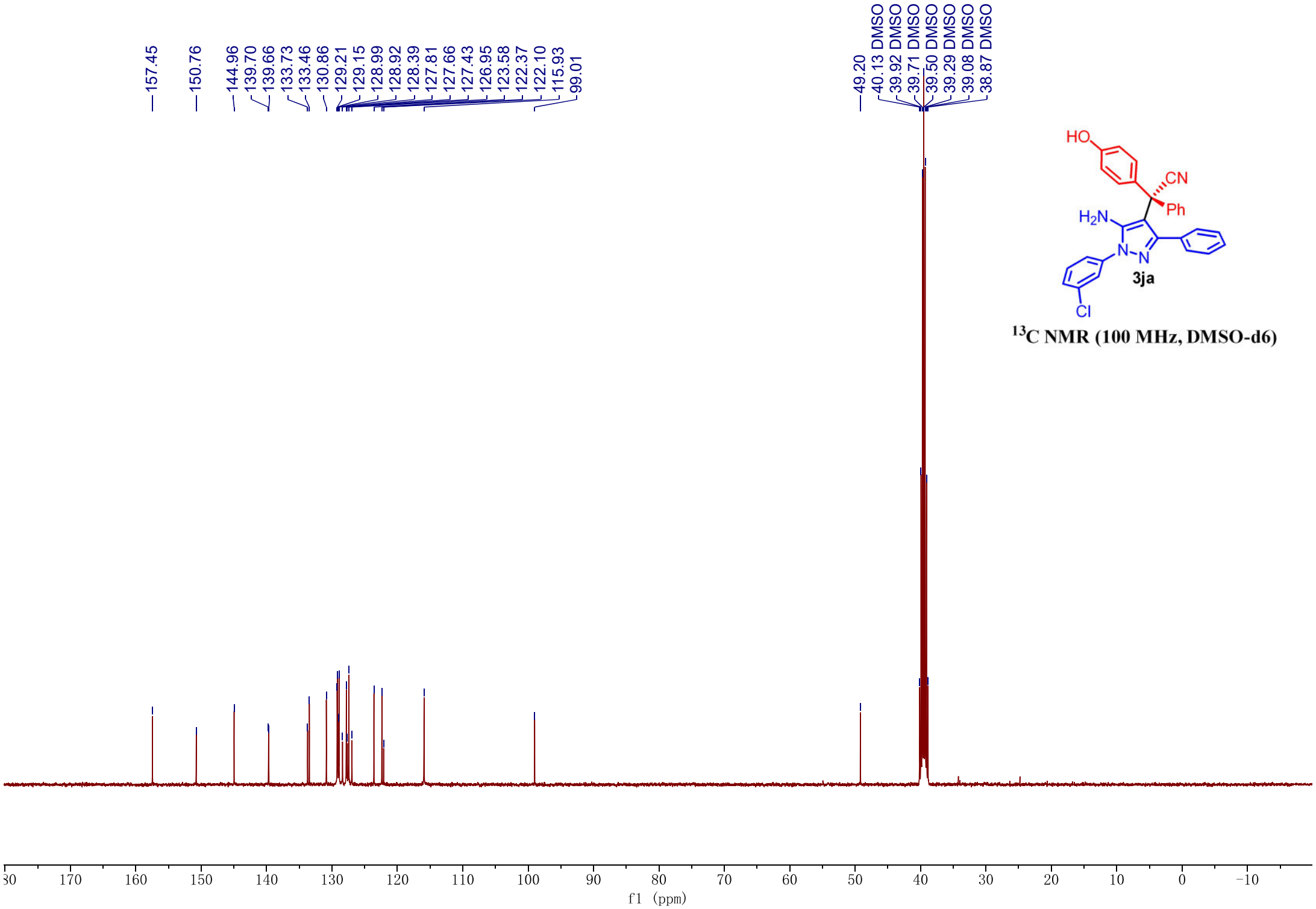


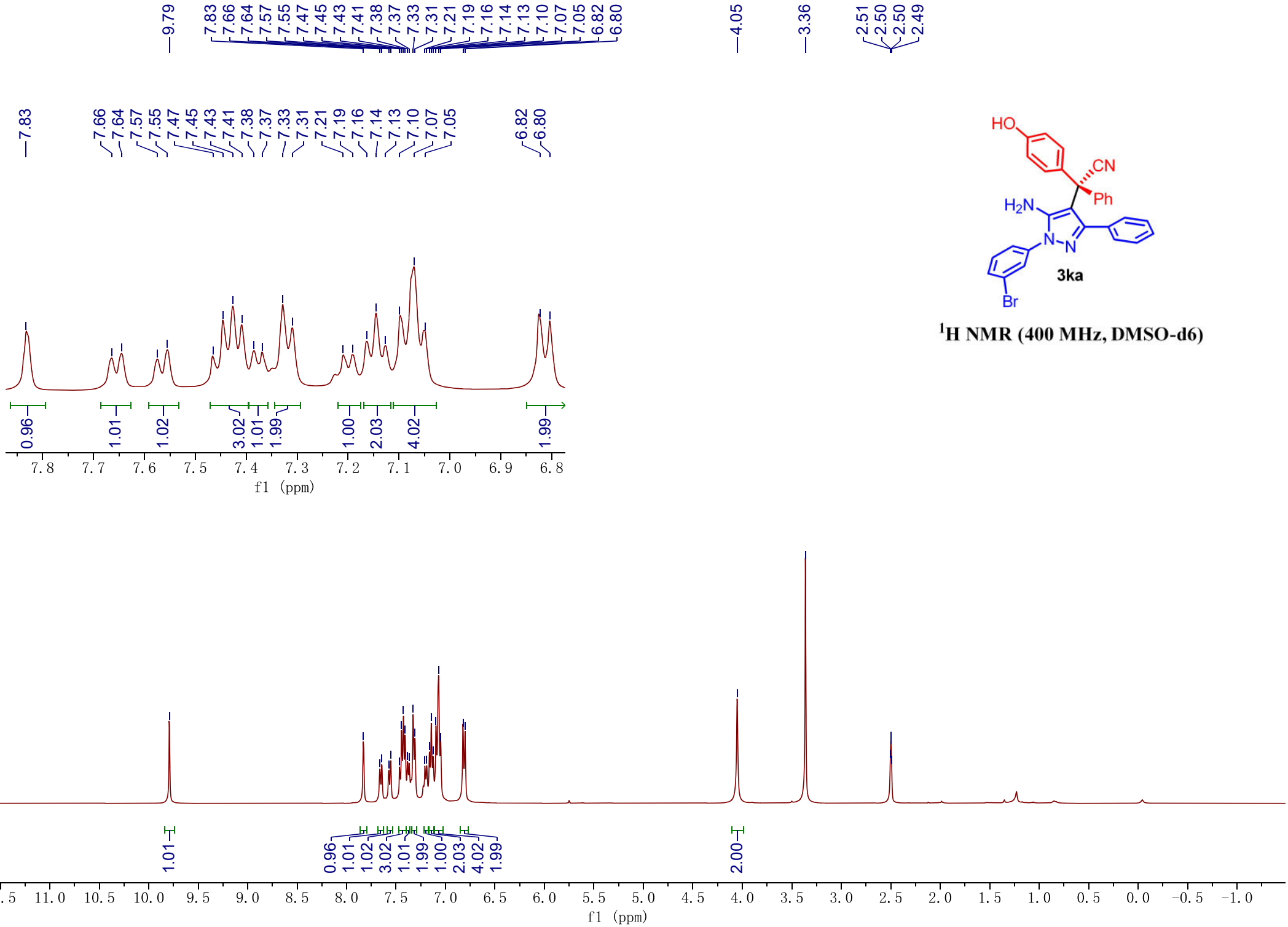


3ja

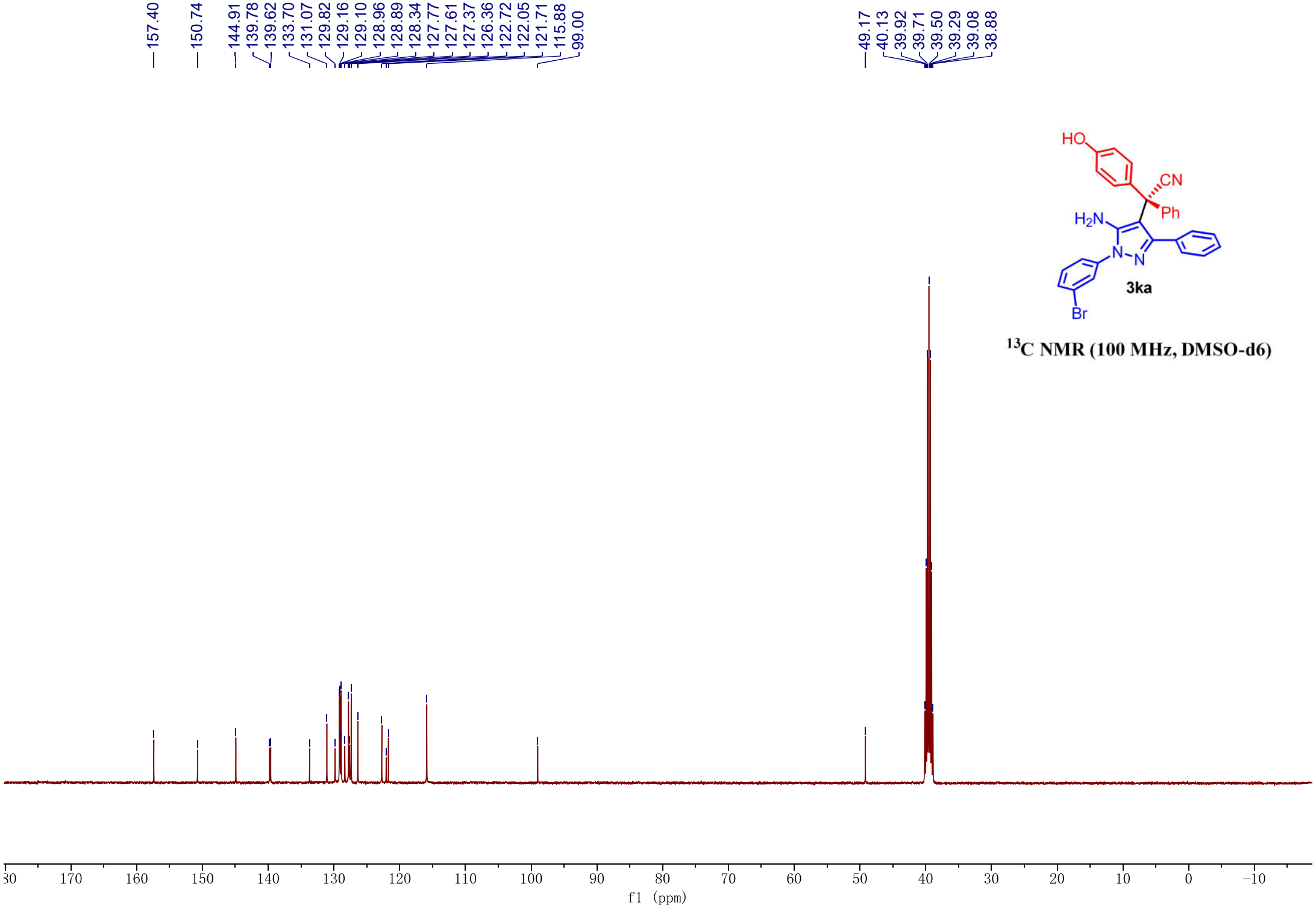
^{1}H NMR (400 MHz, DMSO-d6)

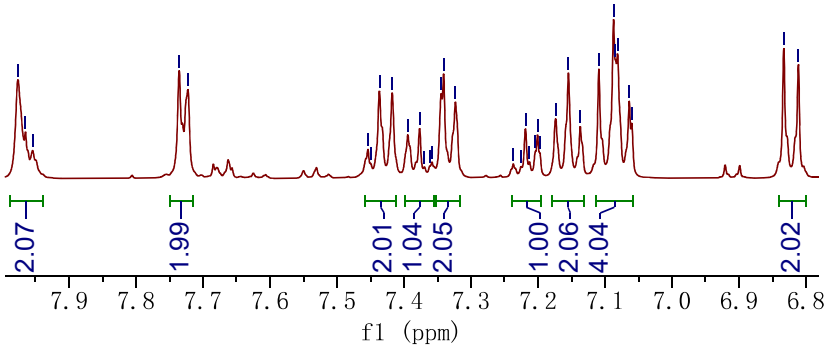


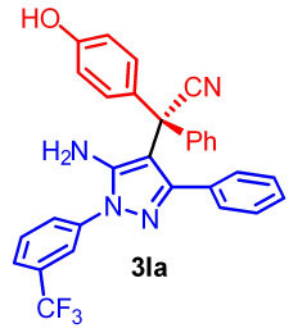

157.45
150.76
144.96
139.70
139.66
133.73
133.46
130.86
129.21
129.15
128.99
128.92
128.39
127.81
127.66
127.43
126.95
123.58
122.37
122.10
115.93
99.01
49.20
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
Cl
3ja
13C NMR (100 MHz, DMSO-d6)
f1 (ppm)



^{1}H NMR (400 MHz, DMSO-d6)

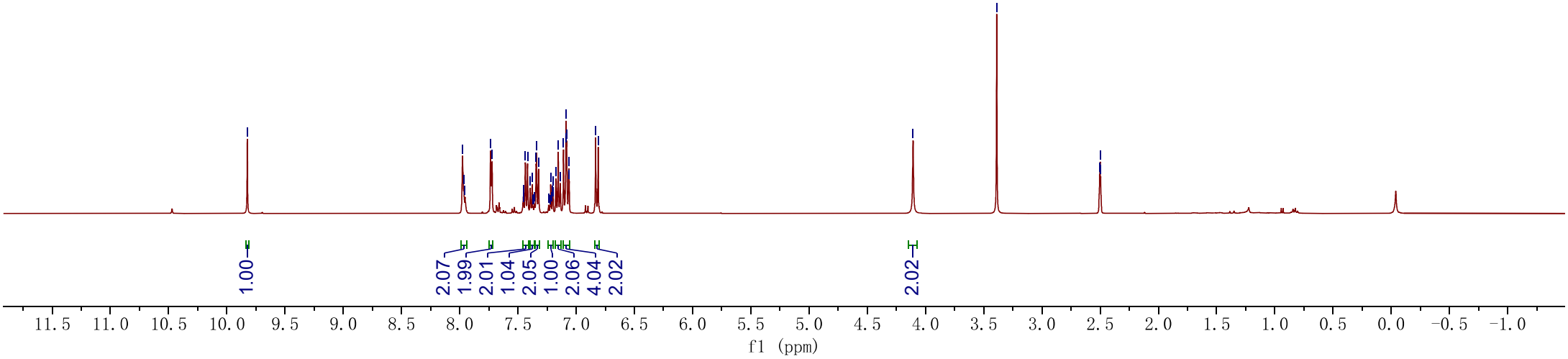

157.40
150.74
144.91
139.78
139.62
133.70
131.07
129.82
129.16
129.10
128.96
128.89
128.34
127.77
127.61
127.37
126.36
122.72
122.05
121.71
115.88
99.00
49.17
40.13
39.92
39.71
39.50
39.29
39.08
38.88
HO
CN
Ph
H2N
N
N
Br
3ka
13C NMR (100 MHz, DMSO-d6)
f1 (ppm)

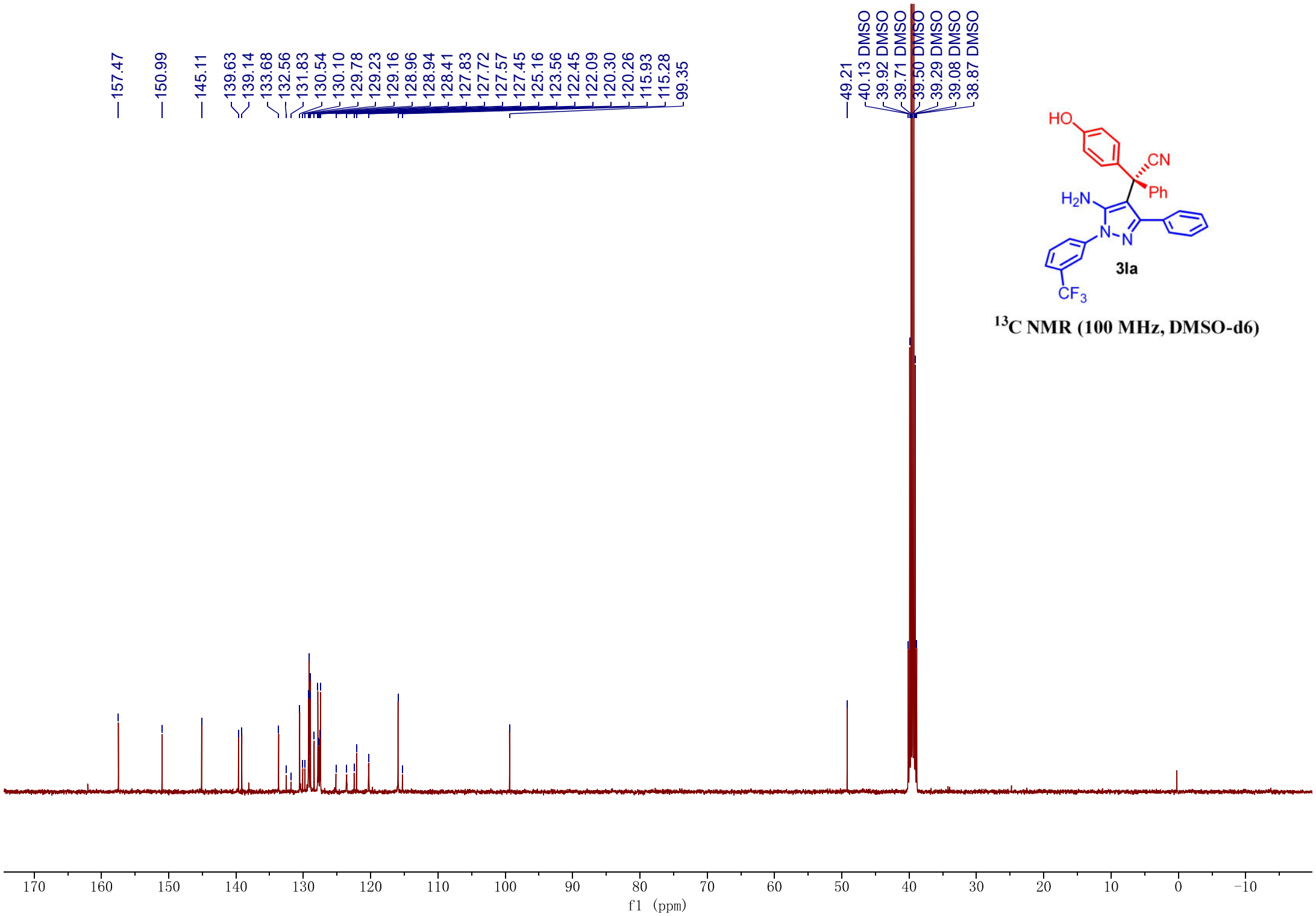


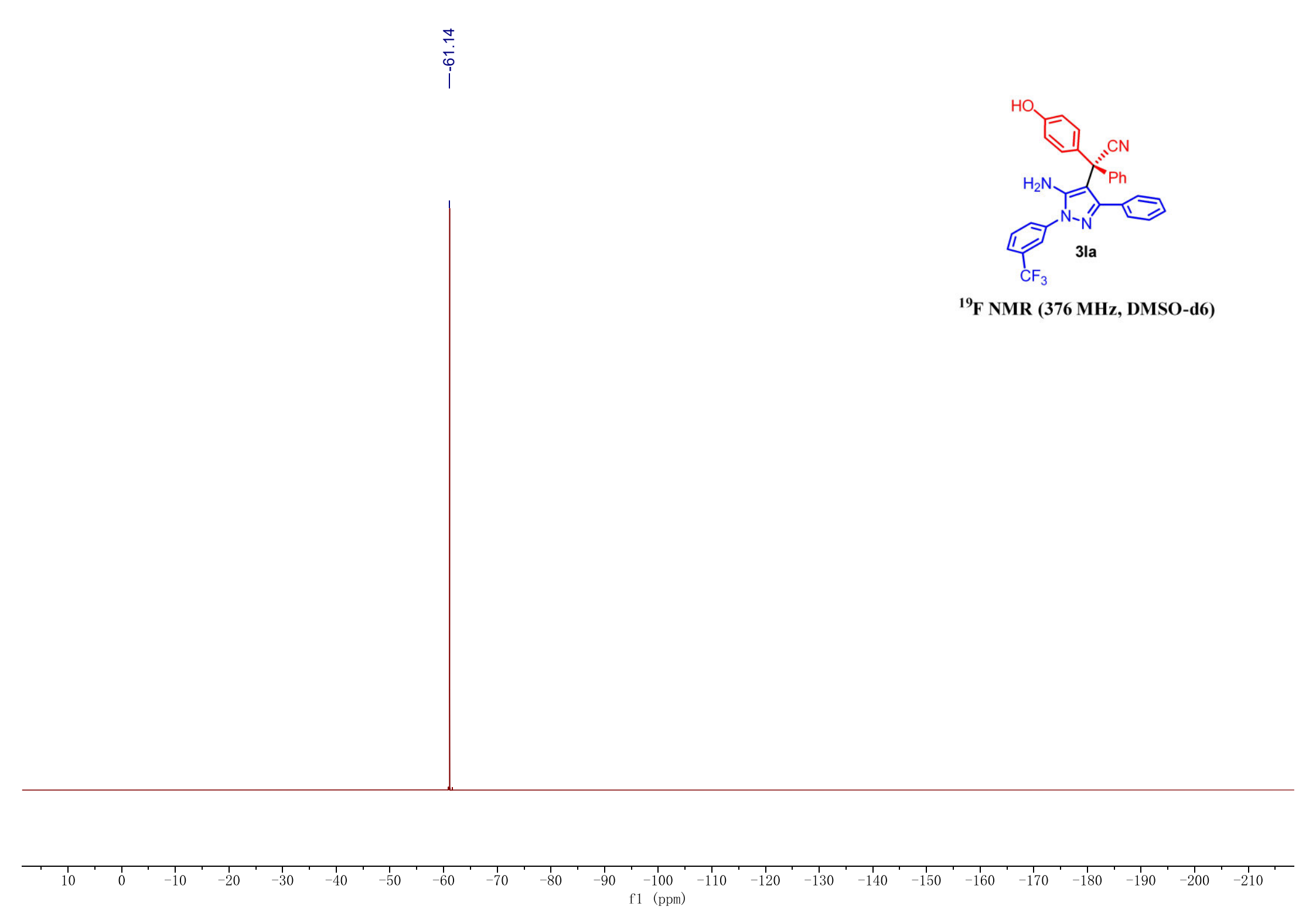


3la

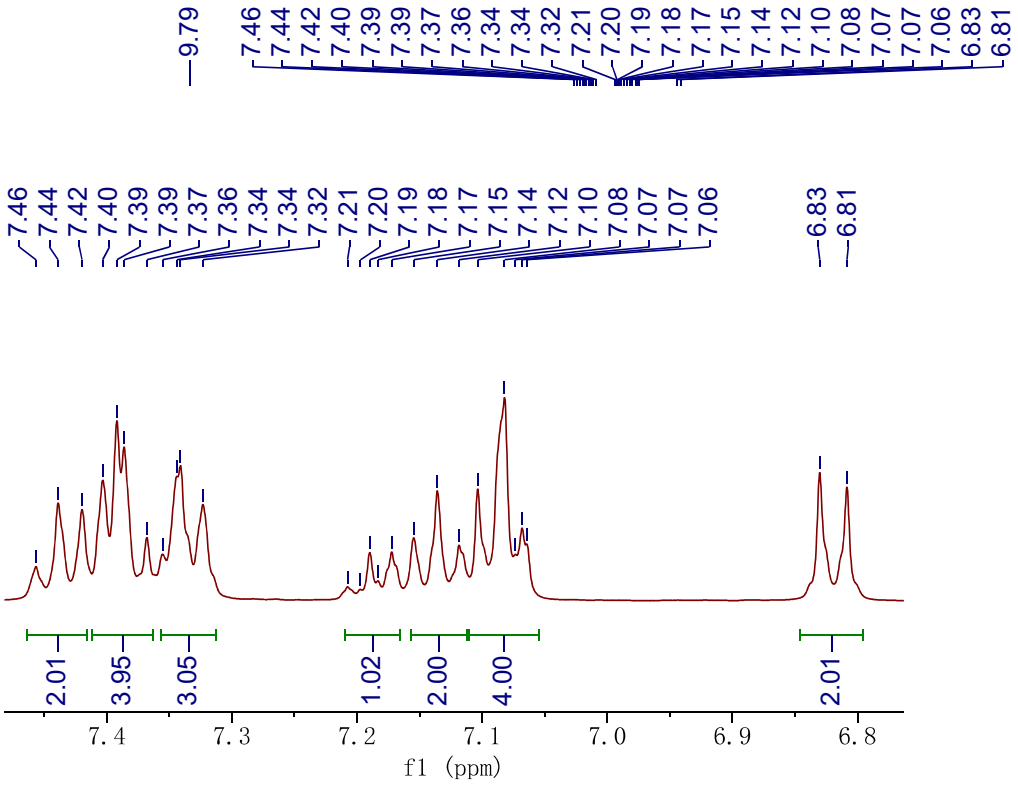
^{1}H NMR (400 MHz, DMSO-d6)

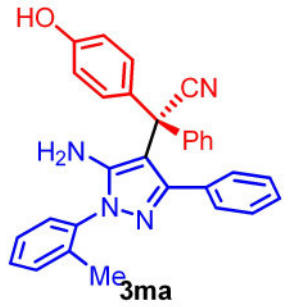



157.47
150.99
145.11
139.63
139.14
133.68
132.56
131.83
130.54
130.10
129.78
129.23
129.16
128.96
128.94
128.41
127.83
127.72
127.57
127.45
125.16
123.56
122.45
122.09
120.30
120.26
115.93
115.28
99.35
49.21
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
CF3
3la
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

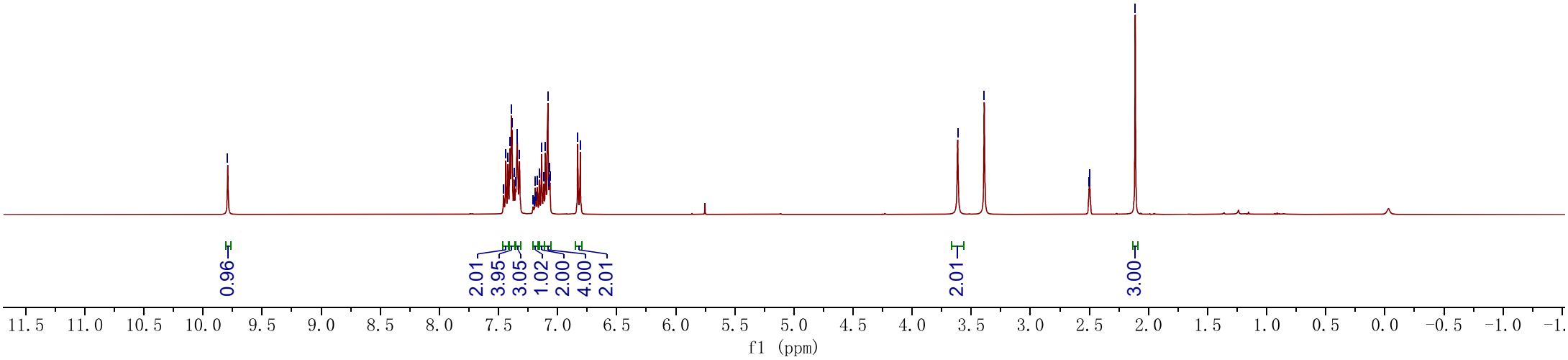


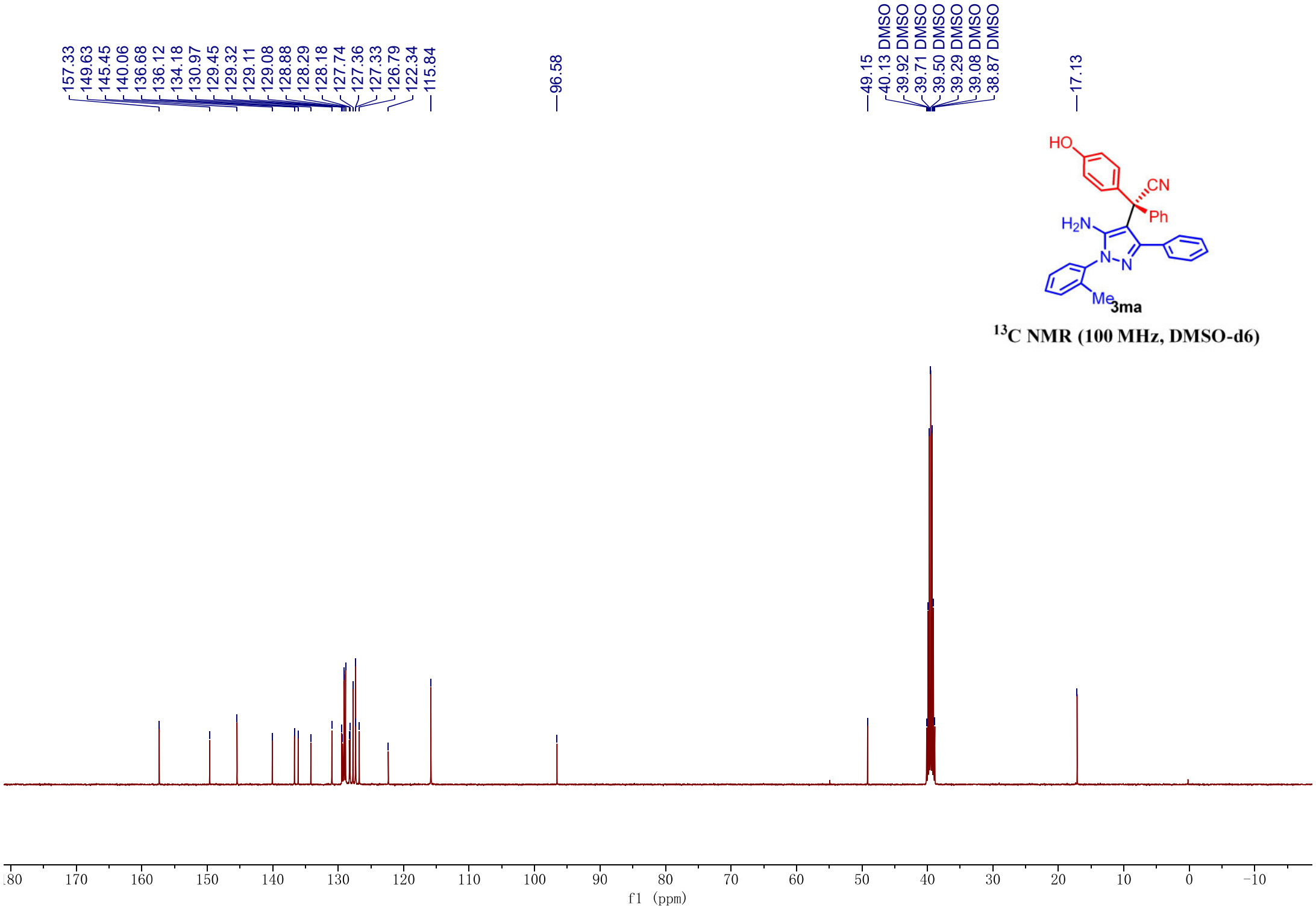
^{19}F NMR (376 MHz, DMSO-d6)



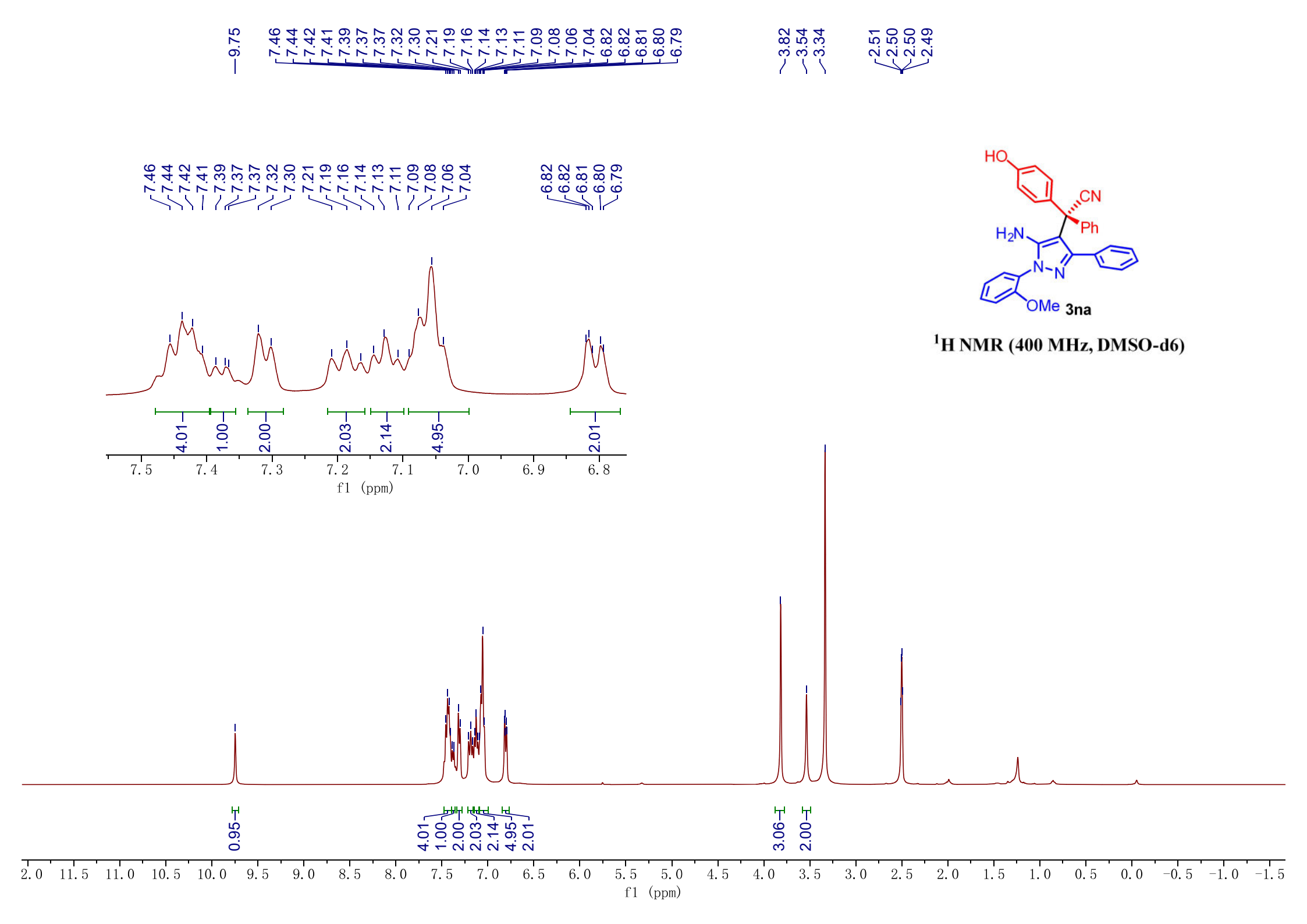


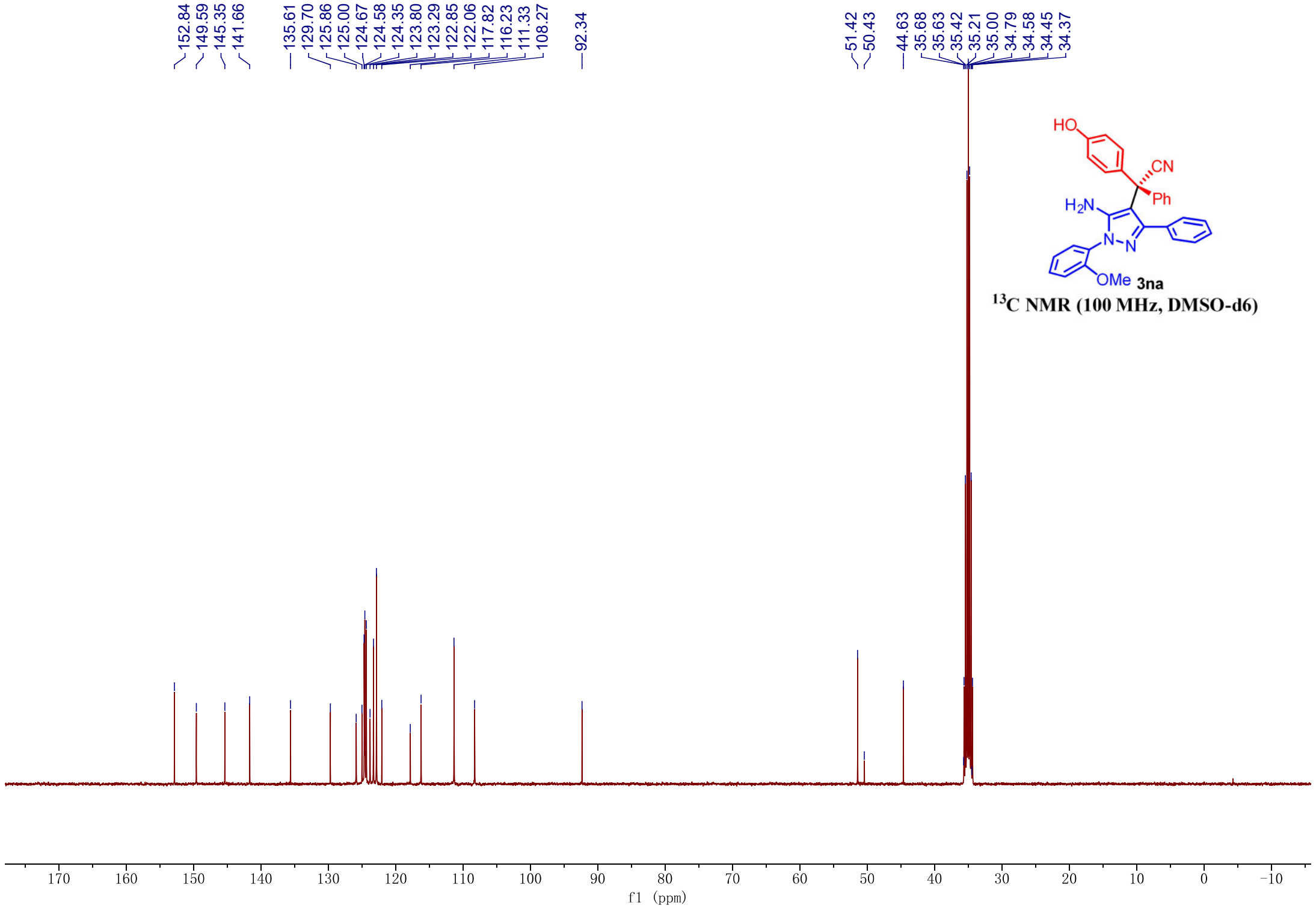
^{1}H NMR (400 MHz, DMSO-d6)

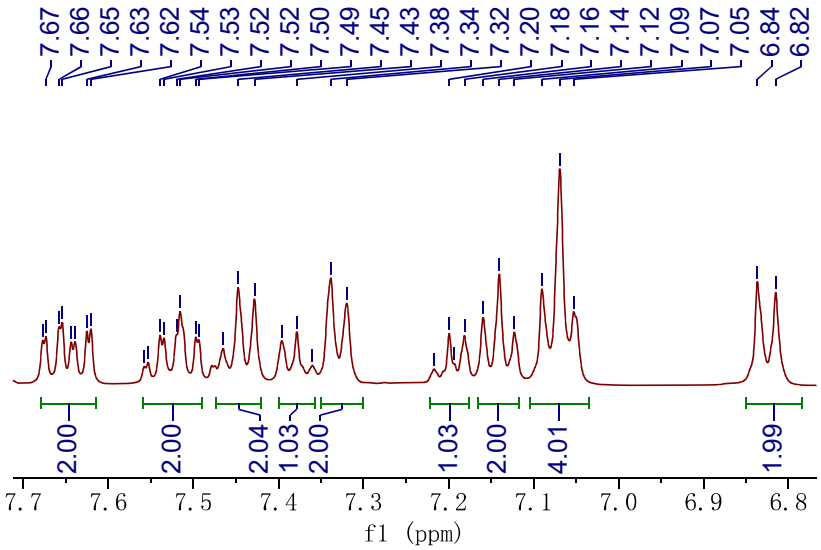




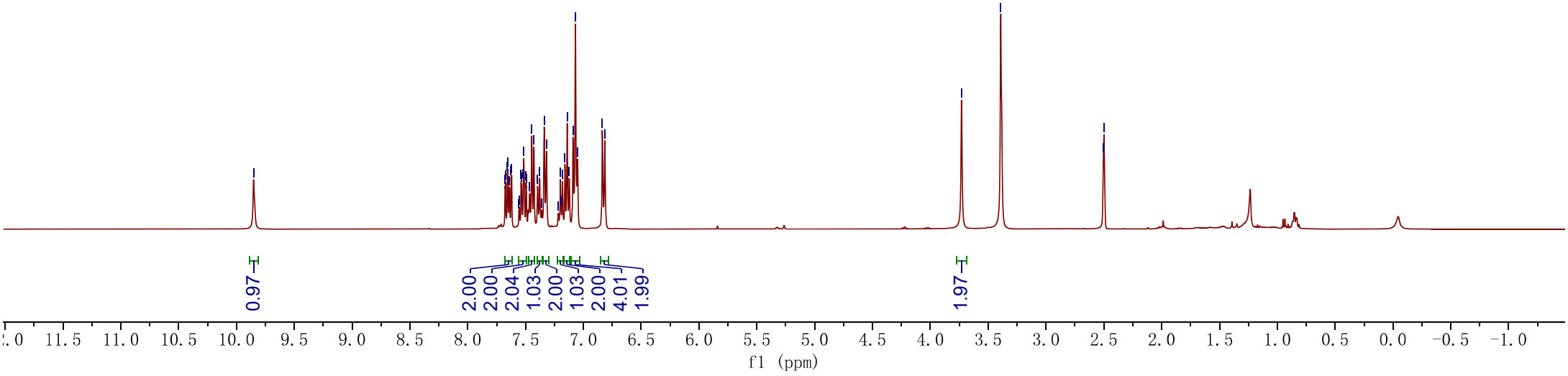
^{13}C NMR (100 MHz, DMSO-d6)

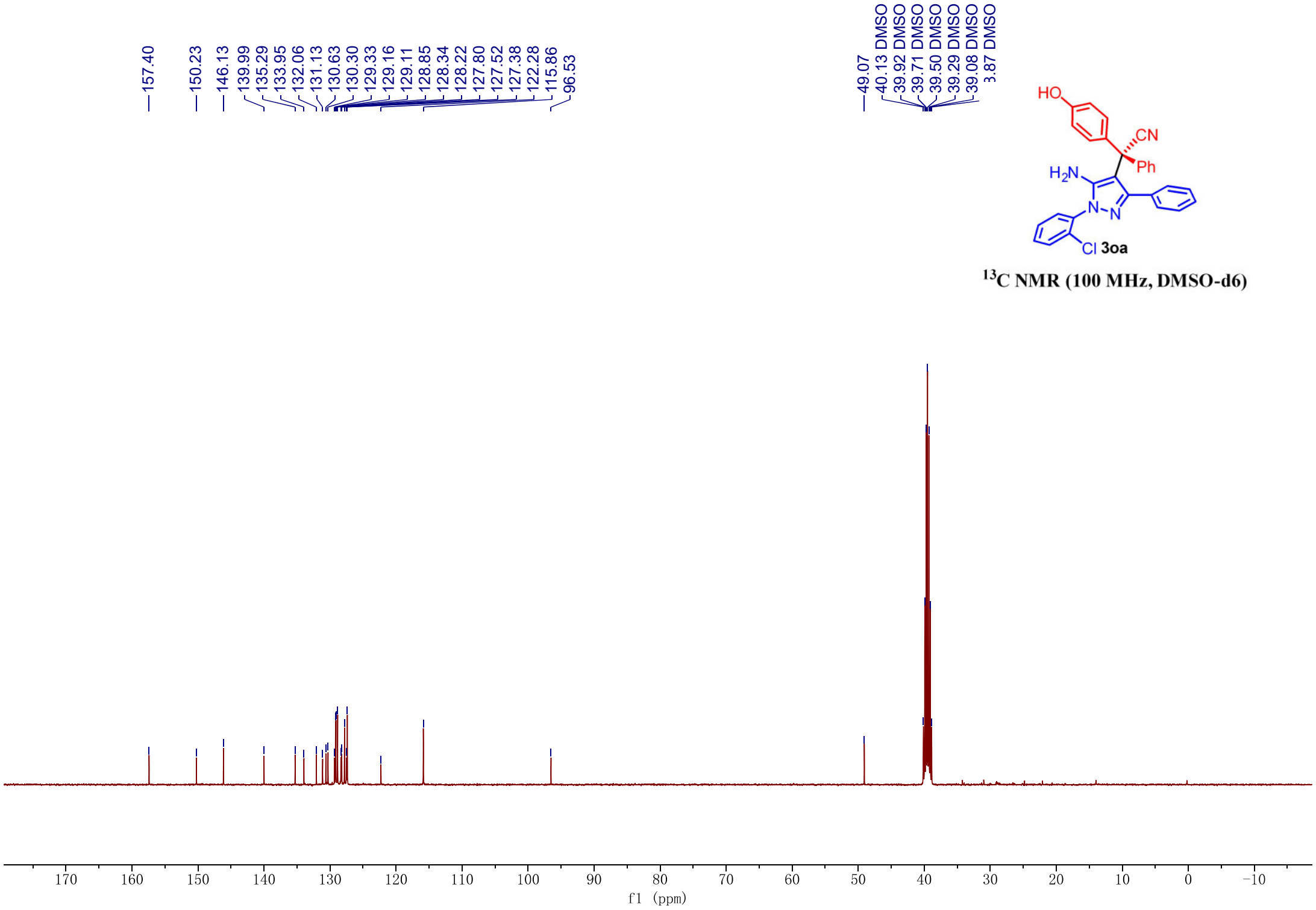

9.75
7.46
7.44
7.42
7.41
7.39
7.37
7.37
7.32
7.30
7.21
7.19
7.16
7.14
7.13
7.11
7.09
7.08
7.06
7.04
6.82
6.82
6.81
6.80
6.79
3.82
3.54
3.34
2.51
2.50
2.50
2.49
4.01
1.00
2.00
2.03
2.14
4.95
2.01
f1 (ppm)
HO
CN
Ph
H2N
N
N
OMe
3na
1H NMR (400 MHz, DMSO-d6)
0.95
3.06
2.00
f1 (ppm)

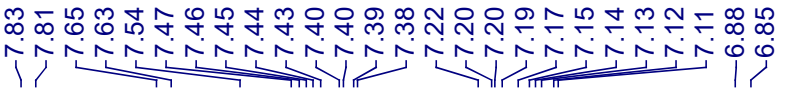

152.84
149.59
145.35
141.66
135.61
129.70
125.86
125.00
124.67
124.58
124.35
123.80
123.29
122.85
122.06
117.82
116.23
111.33
108.27
92.34
51.42
50.43
44.63
35.68
35.63
35.42
35.21
35.00
34.79
34.58
34.45
34.37
HO
CN
Ph
H2N
N
N
OMe
3na
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

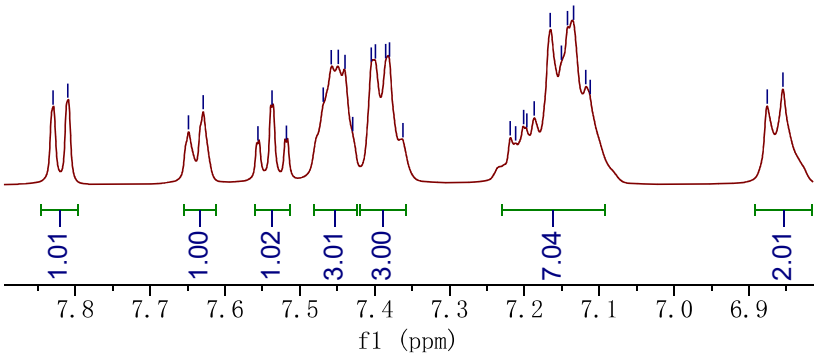


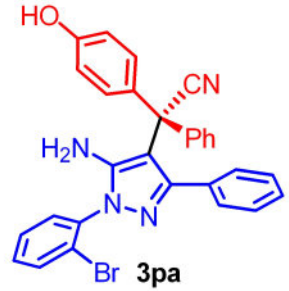
^{1}H NMR (400 MHz, DMSO-d6)




157.40
150.23
146.13
139.99
135.29
133.95
132.06
131.13
130.63
130.30
129.33
129.16
129.11
128.85
128.34
128.22
127.80
127.52
127.38
122.28
115.86
96.53
49.07
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
3.87 DMSO
HO
CN
Ph
H2N
N
N
Cl
3oa
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

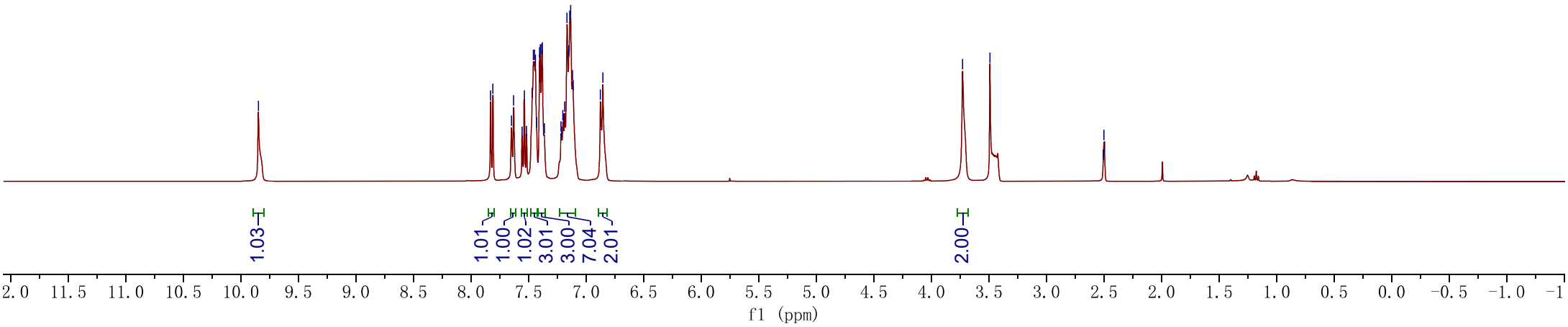


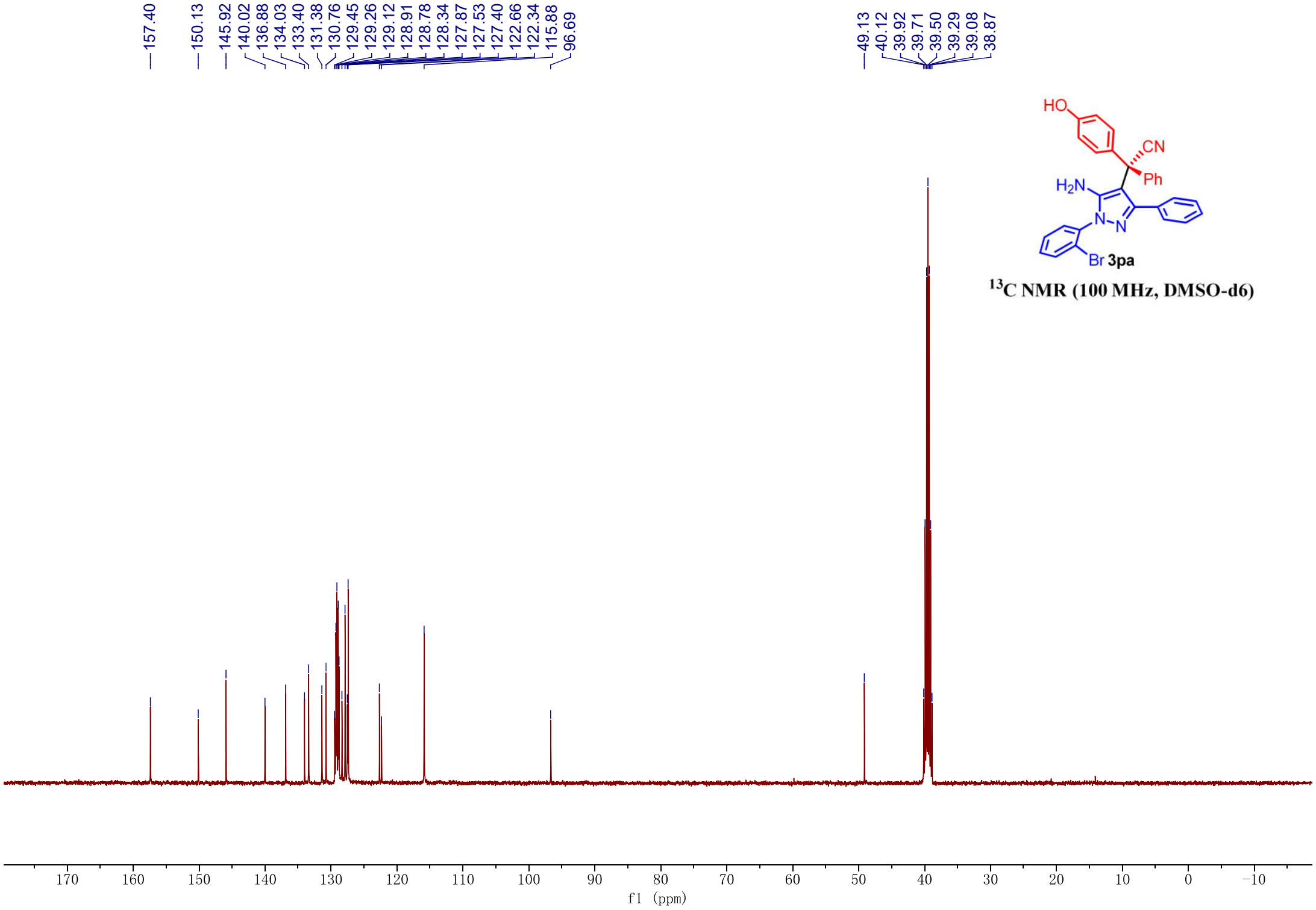


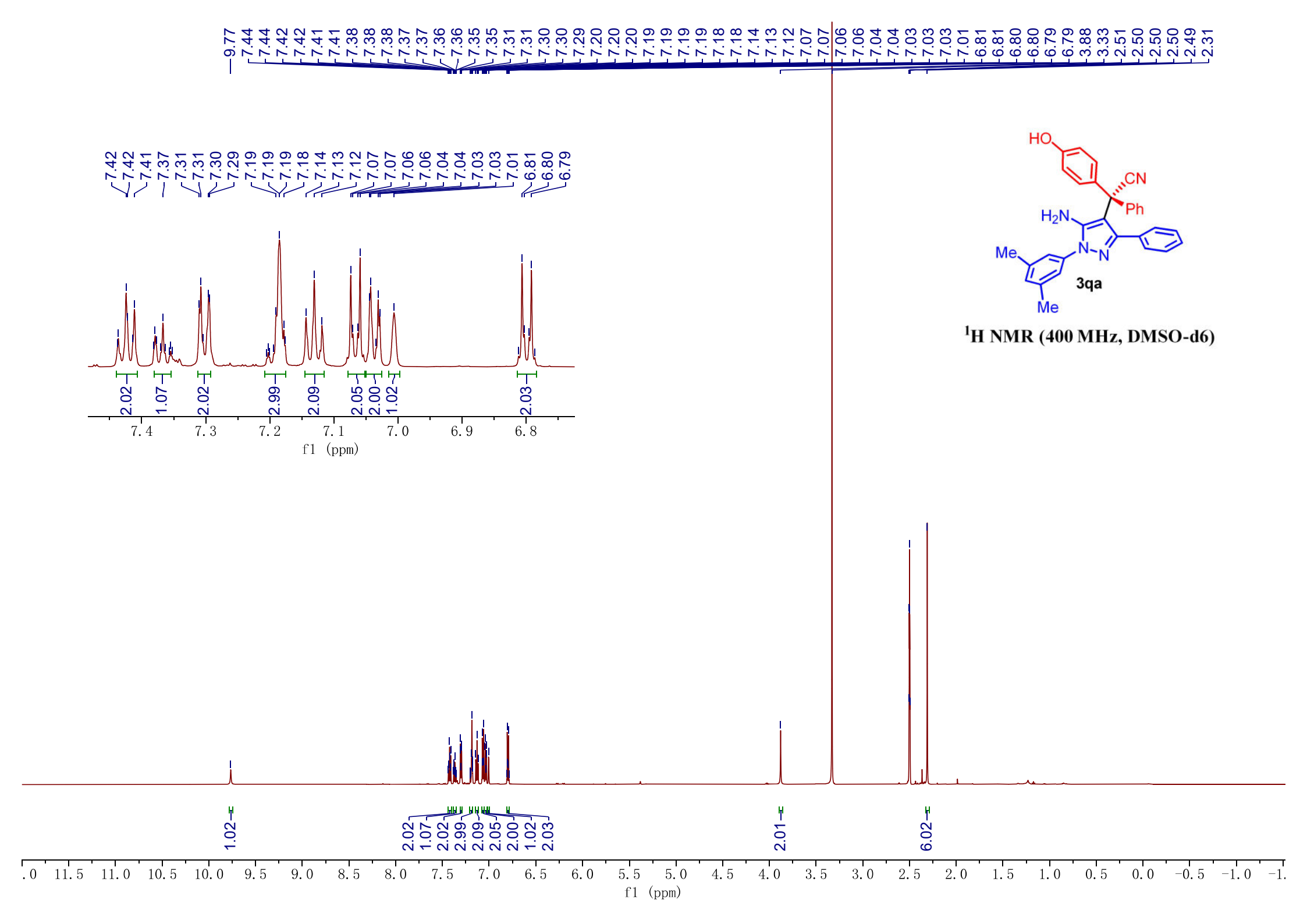


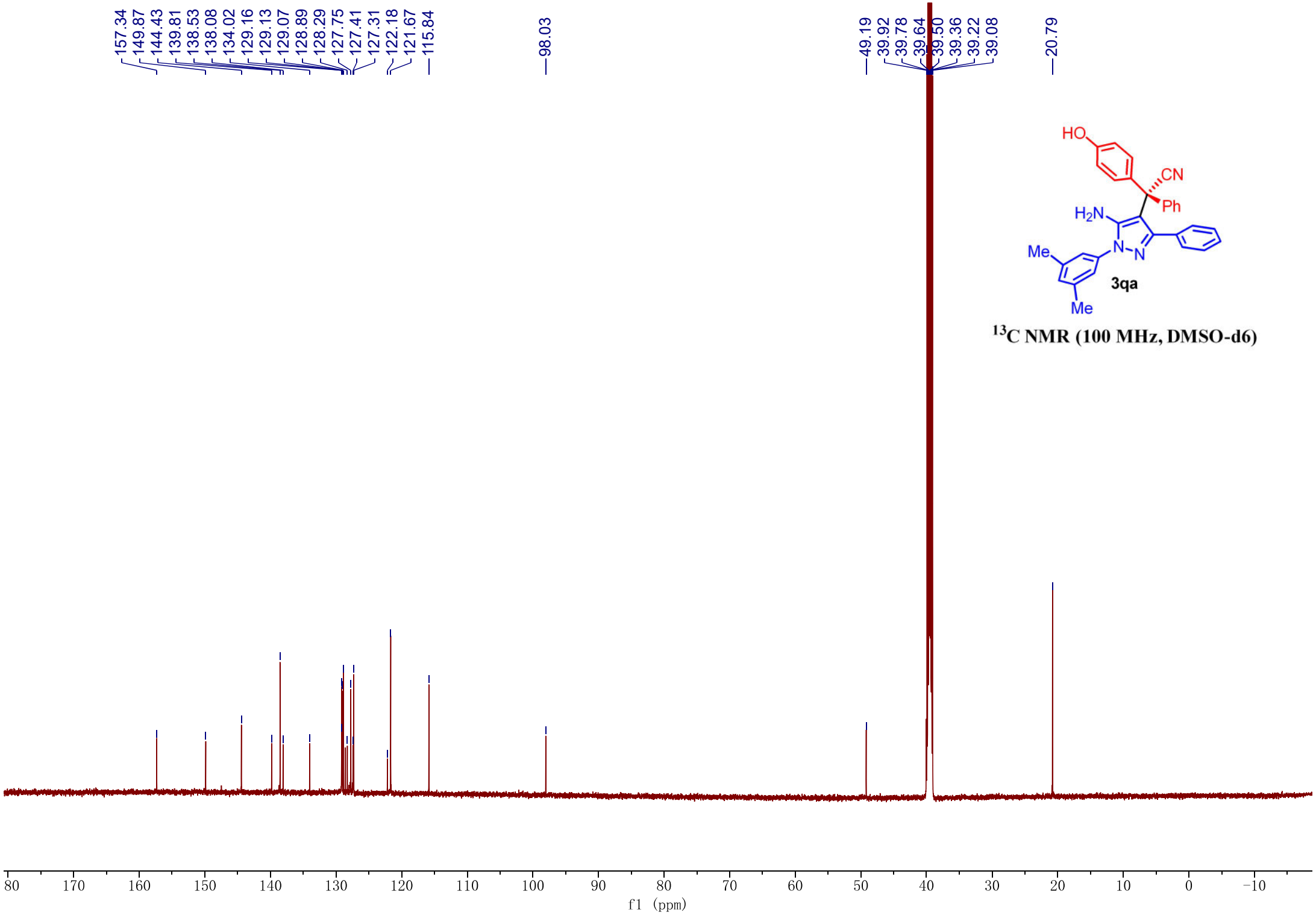
3pa

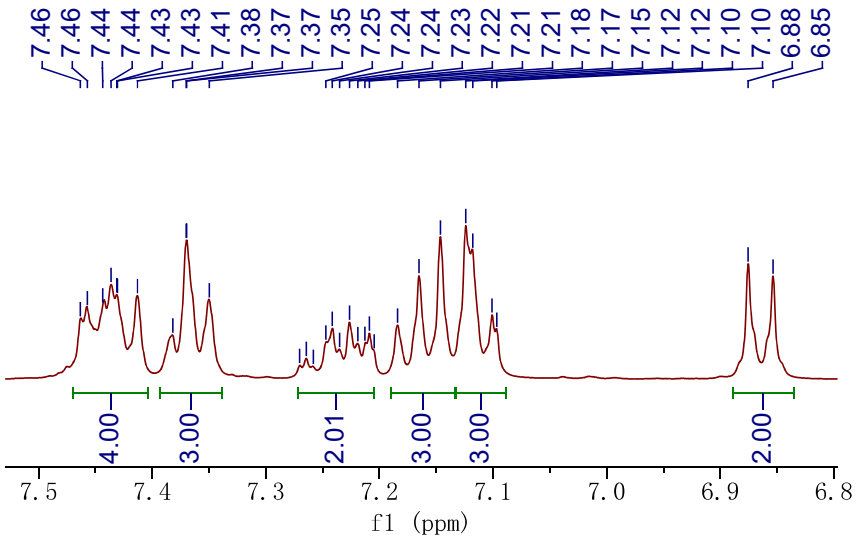
^{1}H NMR (400 MHz, DMSO-d6)

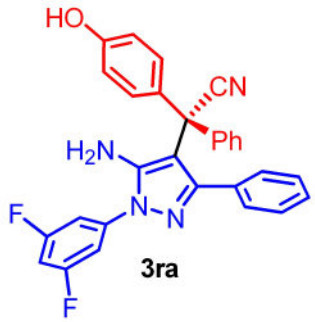



157.40
150.13
145.92
140.02
136.88
134.03
133.40
131.38
130.76
129.45
129.26
129.12
128.91
128.78
128.34
127.87
127.53
127.40
122.66
122.34
115.88
96.69
49.13
40.12
39.92
39.71
39.50
39.29
39.08
38.87
HO
CN
Ph
H2N
N
N
Br
3pa
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

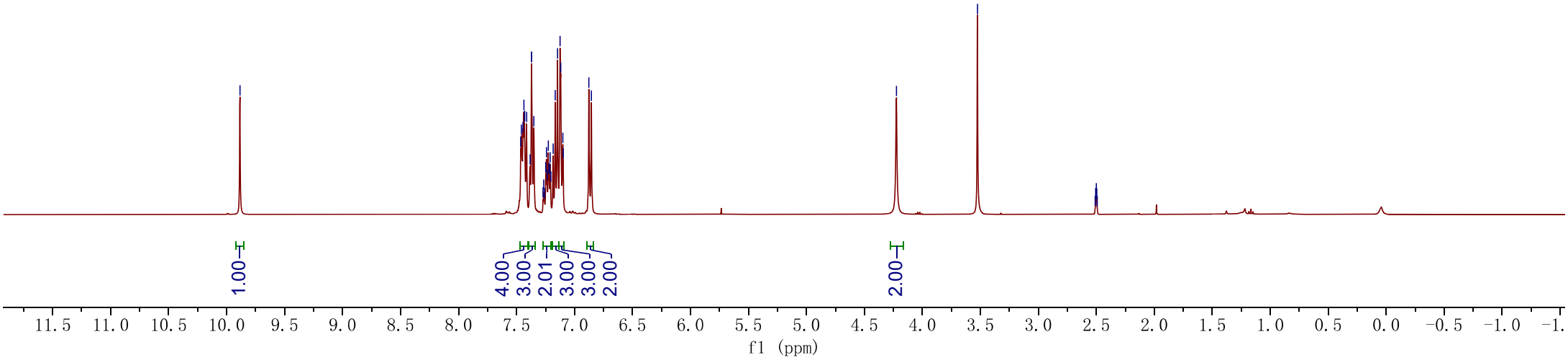

HO
CN
Ph
H2N
N
N
Me
Me
3qa
1H NMR (400 MHz, DMSO-d6)
f1 (ppm)

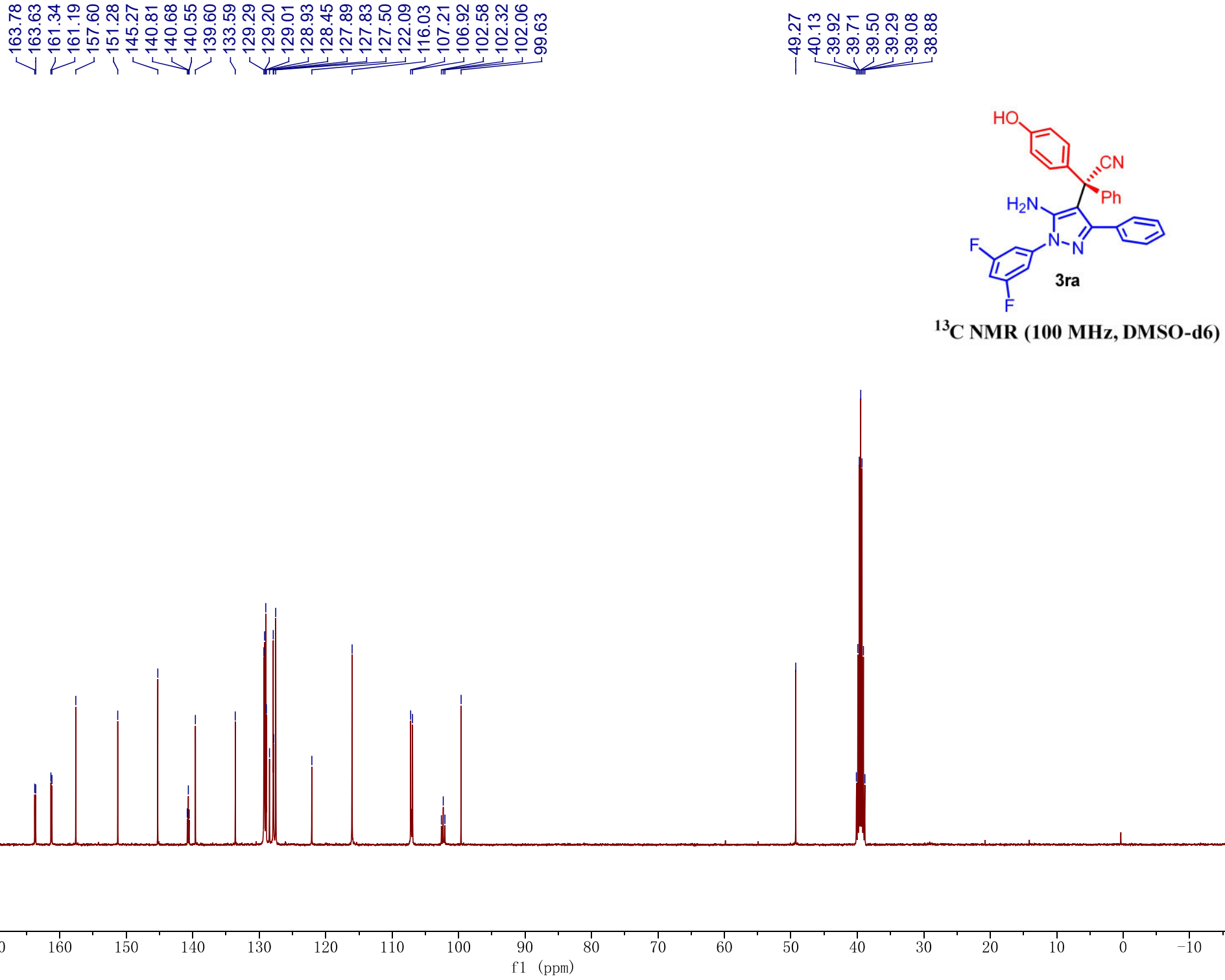

157.34
149.87
144.43
139.81
138.53
138.08
134.02
129.16
129.13
129.07
128.89
128.29
127.75
127.41
127.31
122.18
121.67
115.84
98.03
49.19
39.92
39.78
39.64
39.50
39.36
39.22
39.08
20.79
HO
CN
Ph
H2N
N
N
Me
Me
3qa
13C NMR (100 MHz, DMSO-d6)
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)



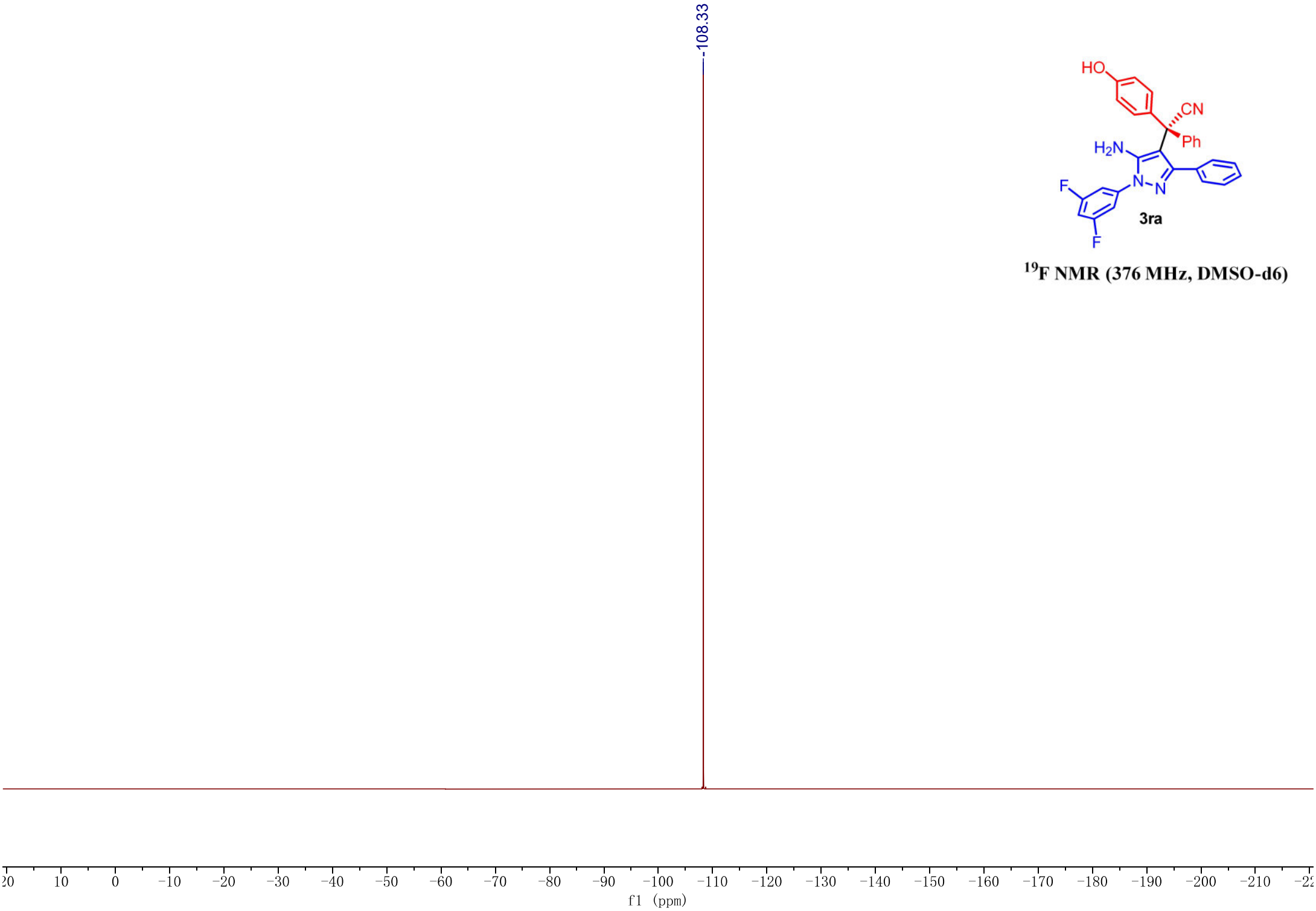


^{1}H NMR (400 MHz, DMSO-d6)

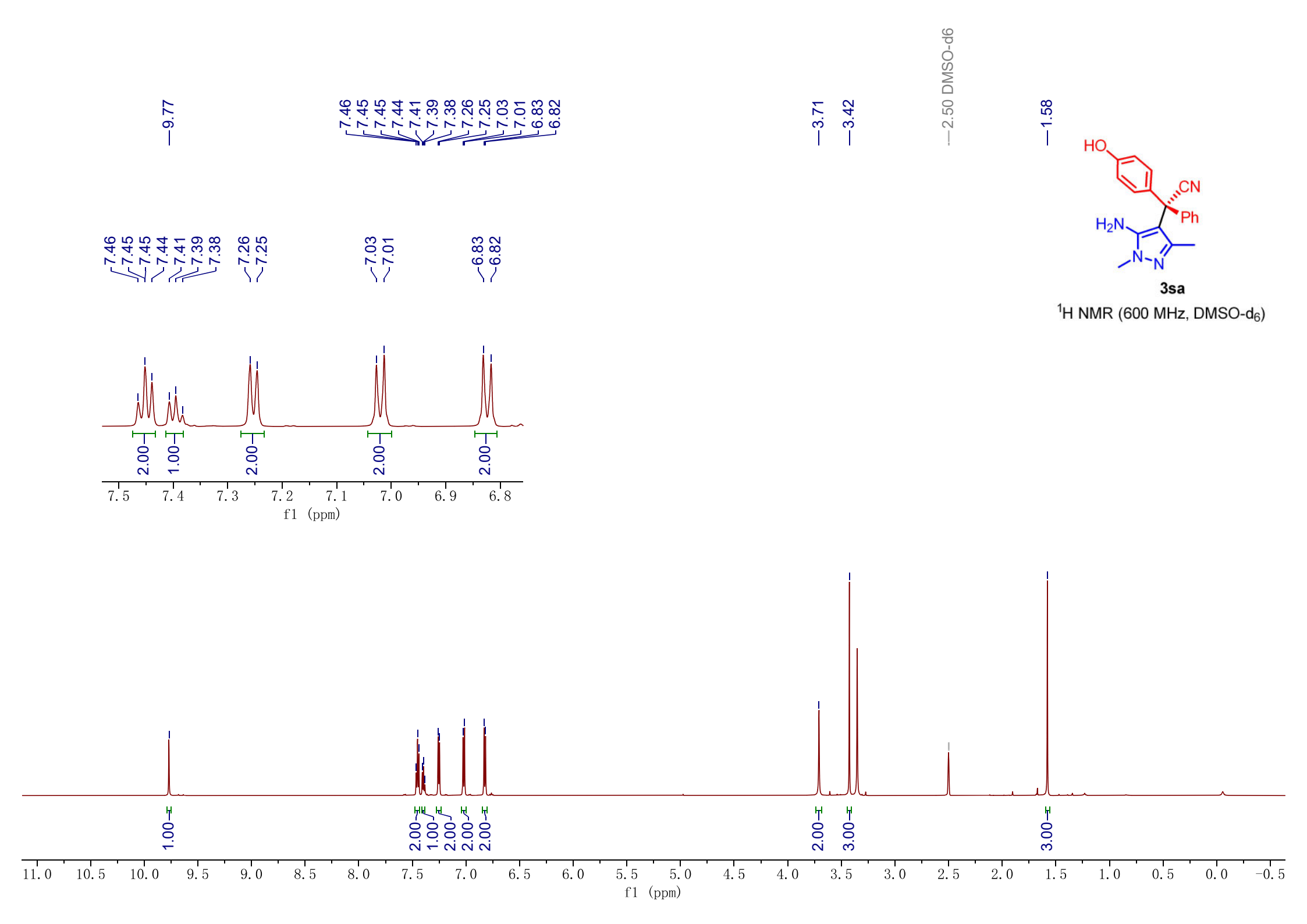


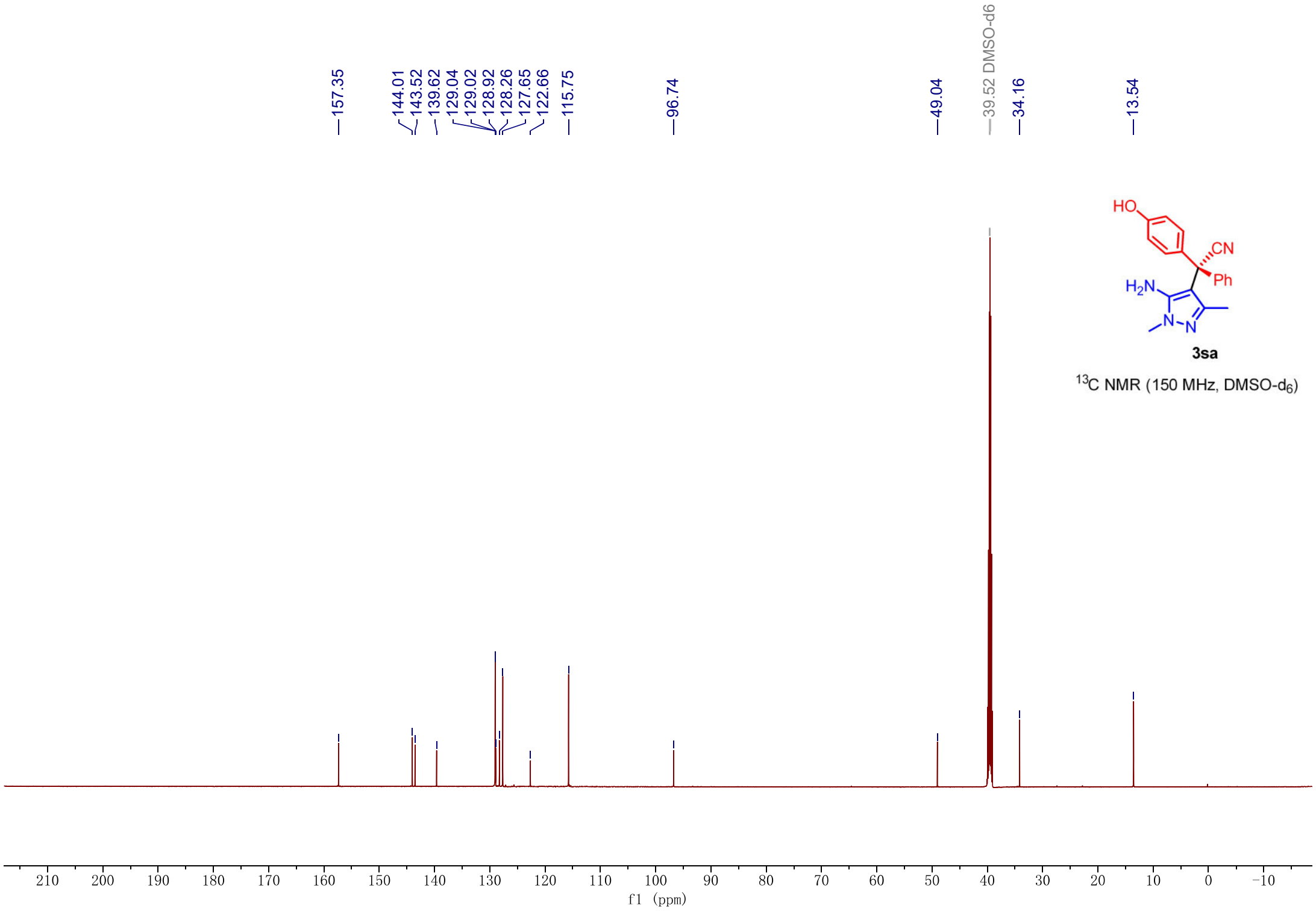


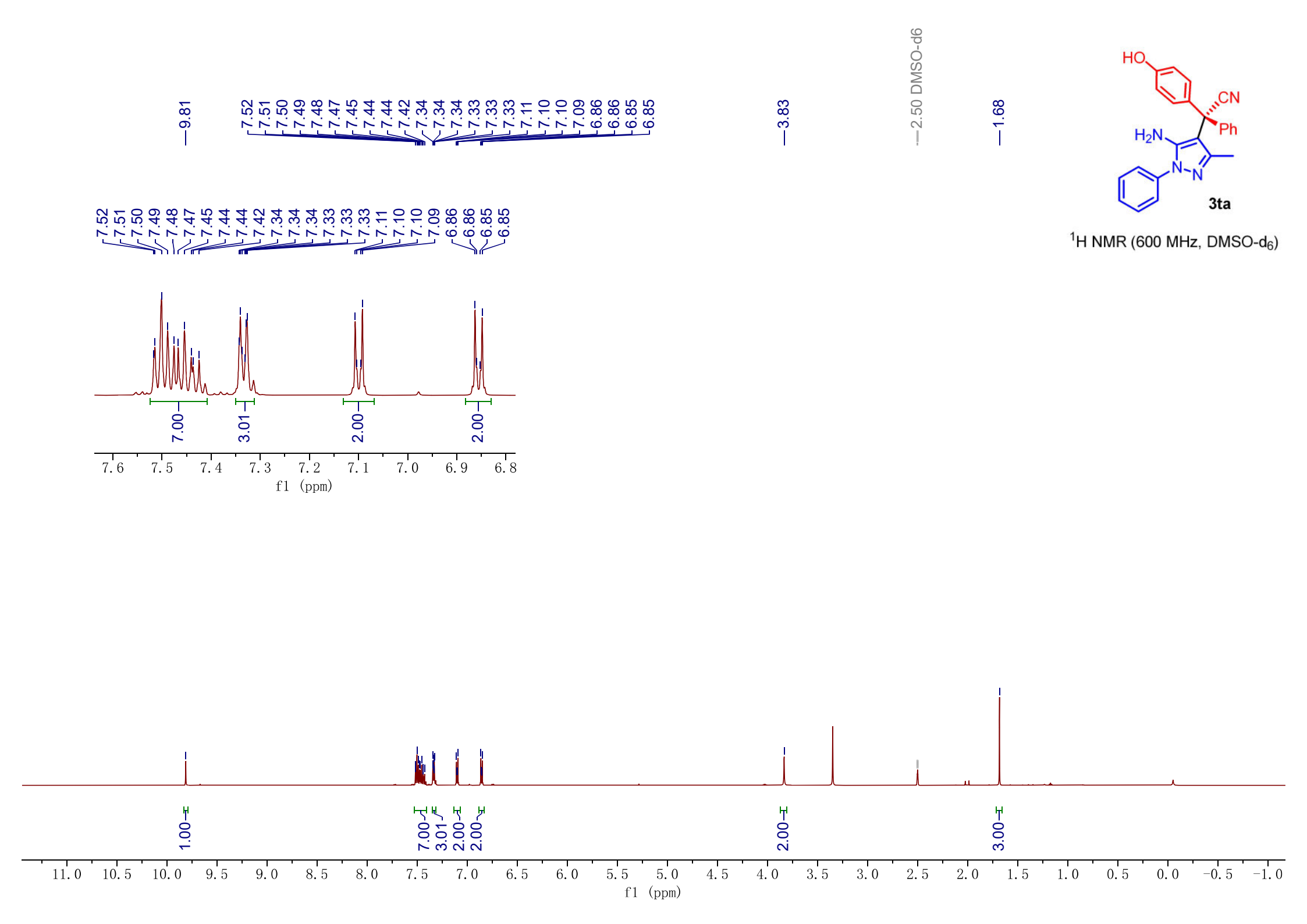
^{13}C NMR (100 MHz, DMSO-d6)

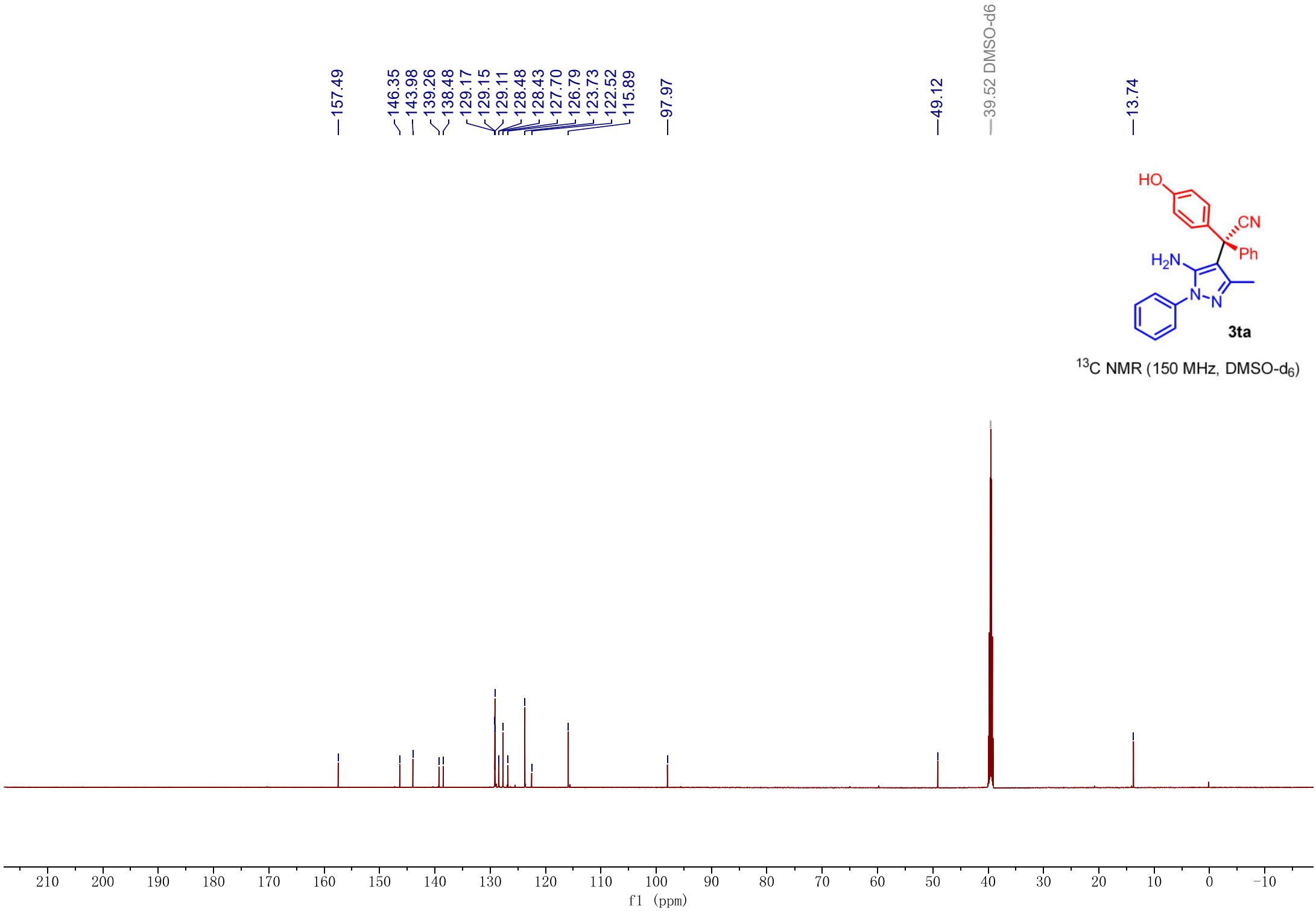


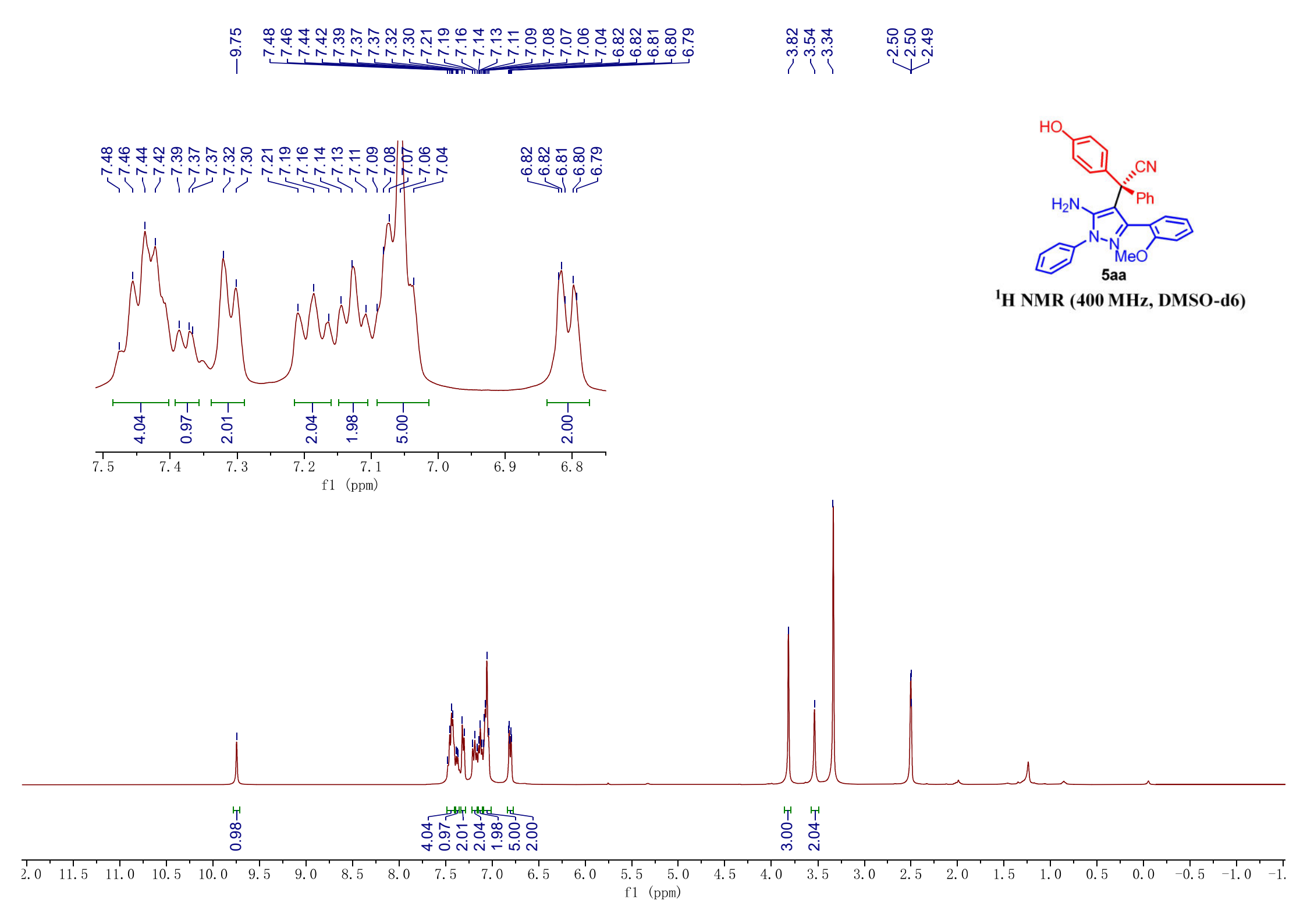
^{19}F NMR (376 MHz, DMSO-d6)

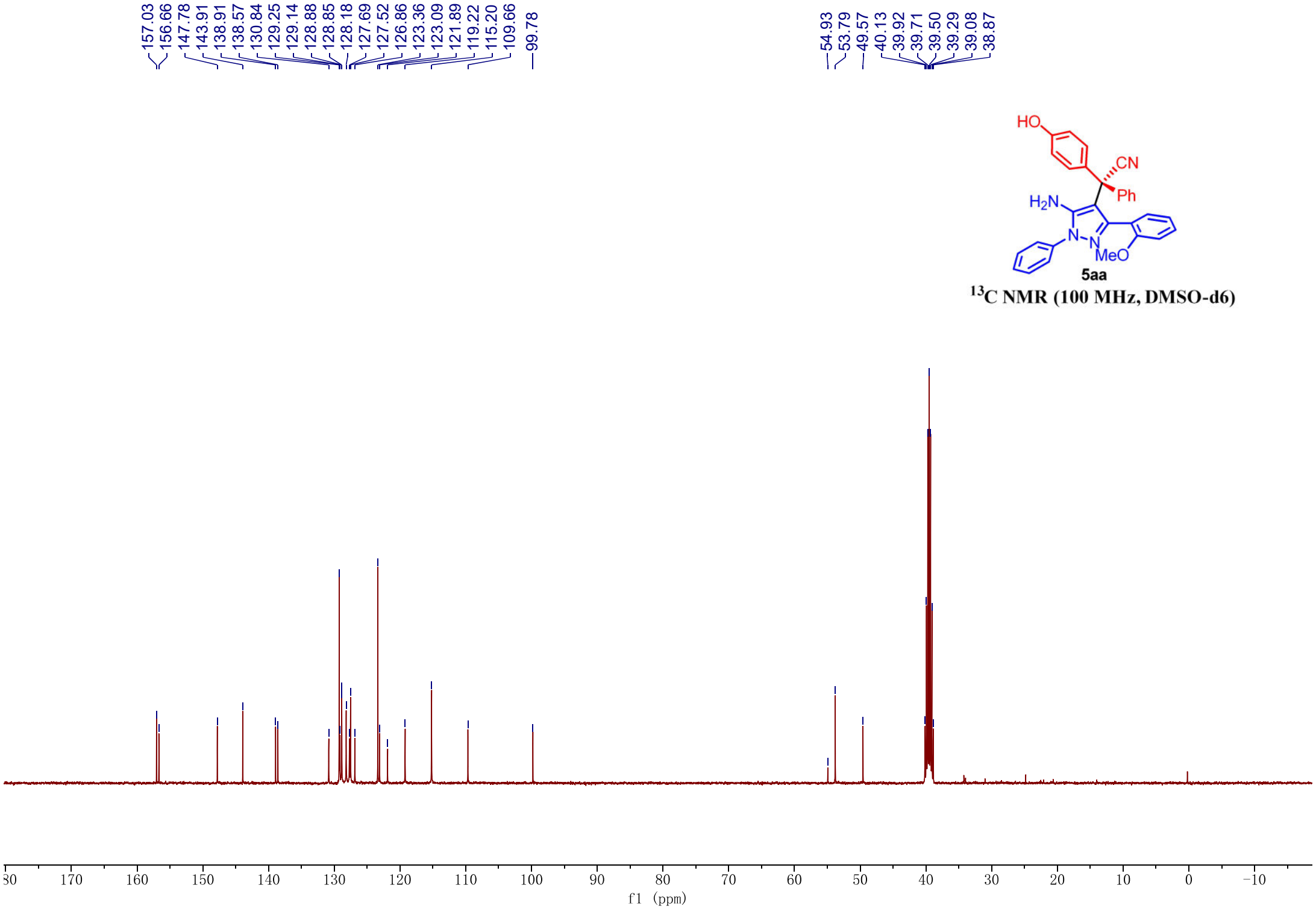

9.77
7.46
7.45
7.45
7.44
7.41
7.39
7.38
7.26
7.25
7.03
7.01
6.83
6.82
3.71
3.42
2.50 DMSO-d6
1.58
HO
CN
Ph
H2N
N
N
3sa
1H NMR (600 MHz, DMSO-d6)
2.00
1.00
2.00
2.00
2.00
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
f1 (ppm)
1.00
2.00
1.00
2.00
2.00
2.00
2.00
3.00
3.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

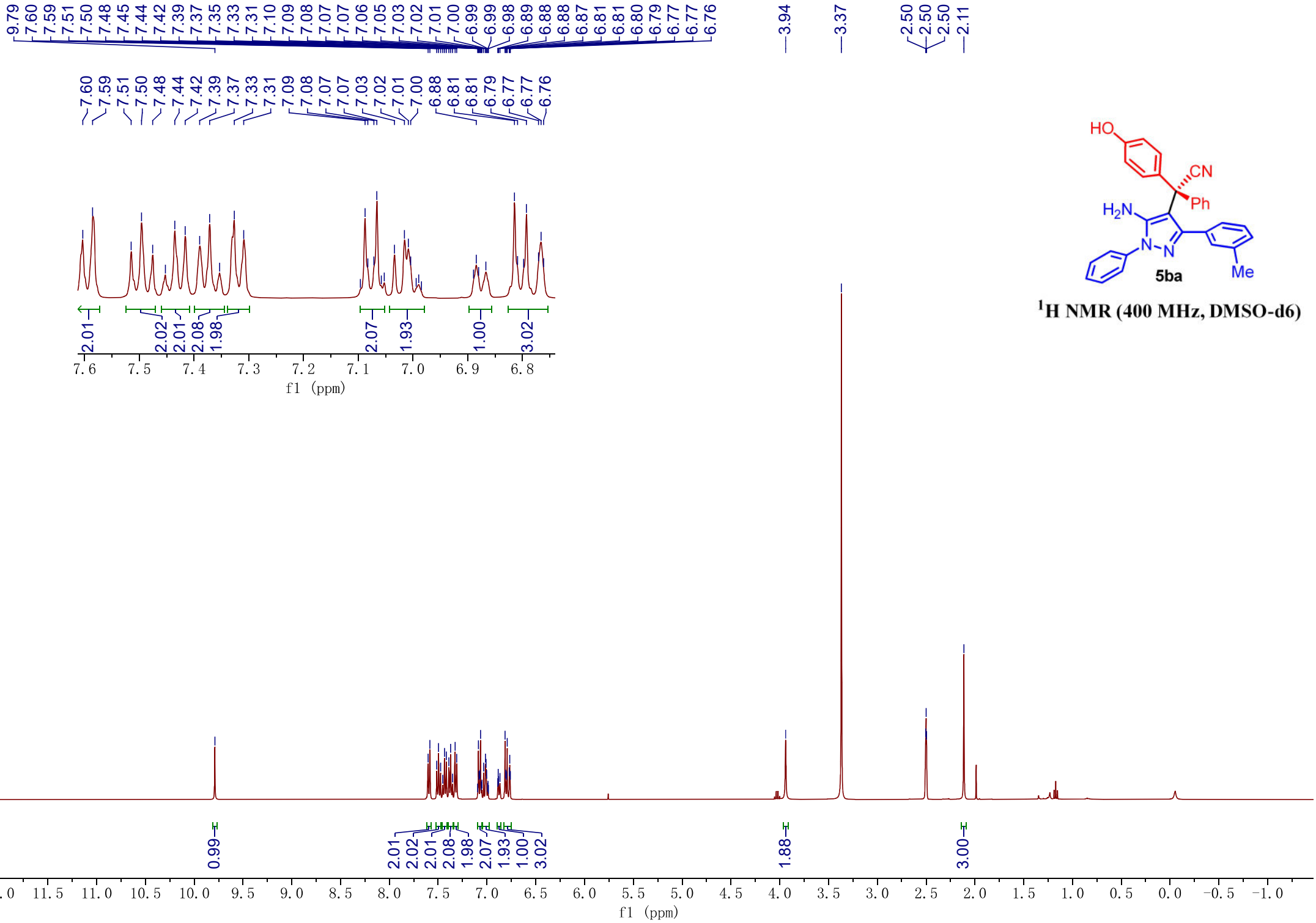

157.35
144.01
143.52
139.62
129.04
129.02
128.92
128.26
127.65
122.66
115.75
96.74
49.04
39.52 DMSO-d6
34.16
13.54
HO
CN
Ph
H2N
N
N
3sa
13C NMR (150 MHz, DMSO-d6)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

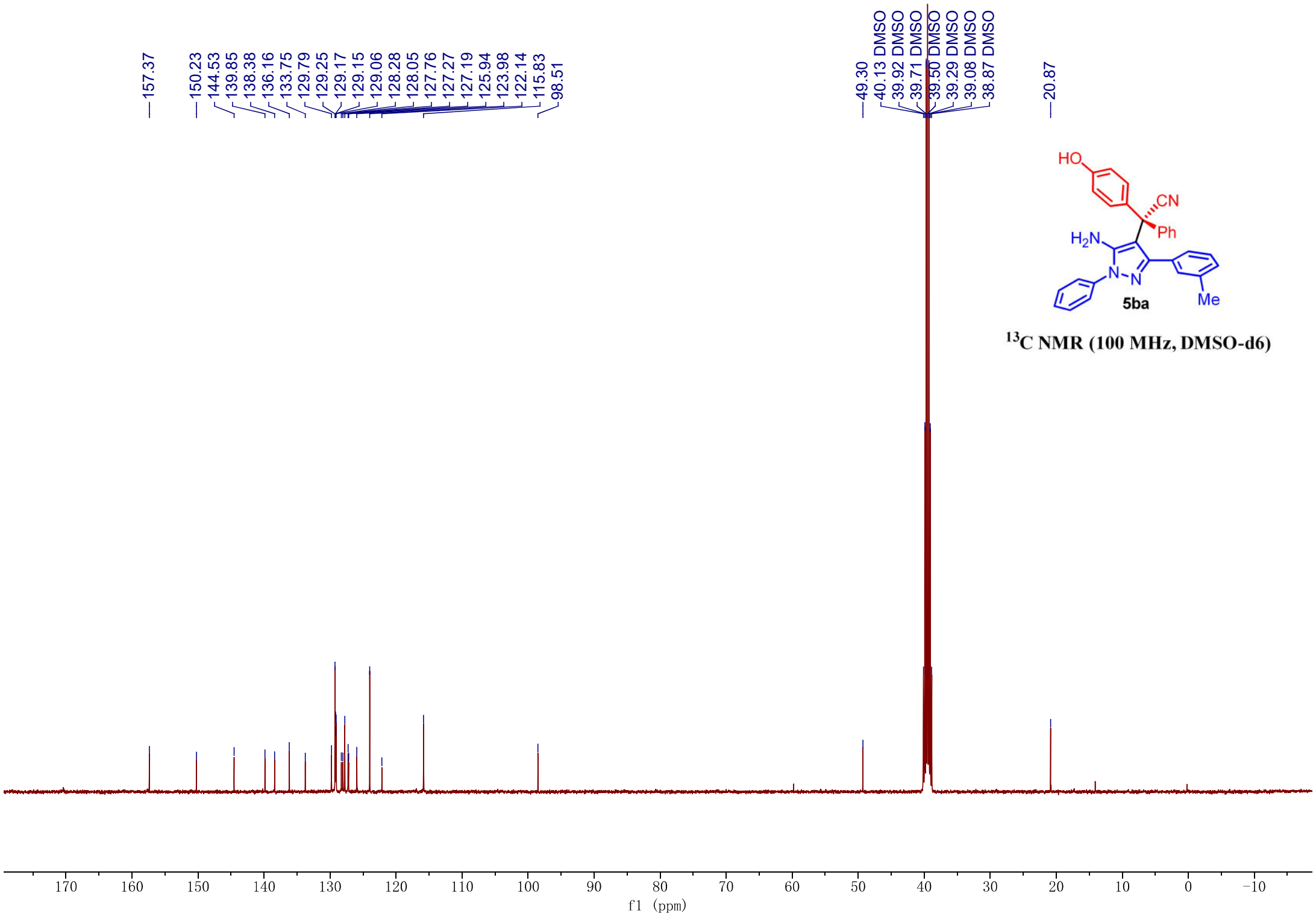

9.81
7.52
7.51
7.50
7.49
7.48
7.47
7.45
7.44
7.44
7.42
7.34
7.34
7.34
7.33
7.33
7.33
7.11
7.10
7.10
7.09
6.86
6.86
6.85
6.85
3.83
2.50 DMSO-d6
1.68
HO
CN
Ph
H2N
N
N
3ta
1H NMR (600 MHz, DMSO-d6)
7.00
3.01
2.00
2.00
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
f1 (ppm)
1.00
7.00
3.01
2.00
2.00
2.00
3.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

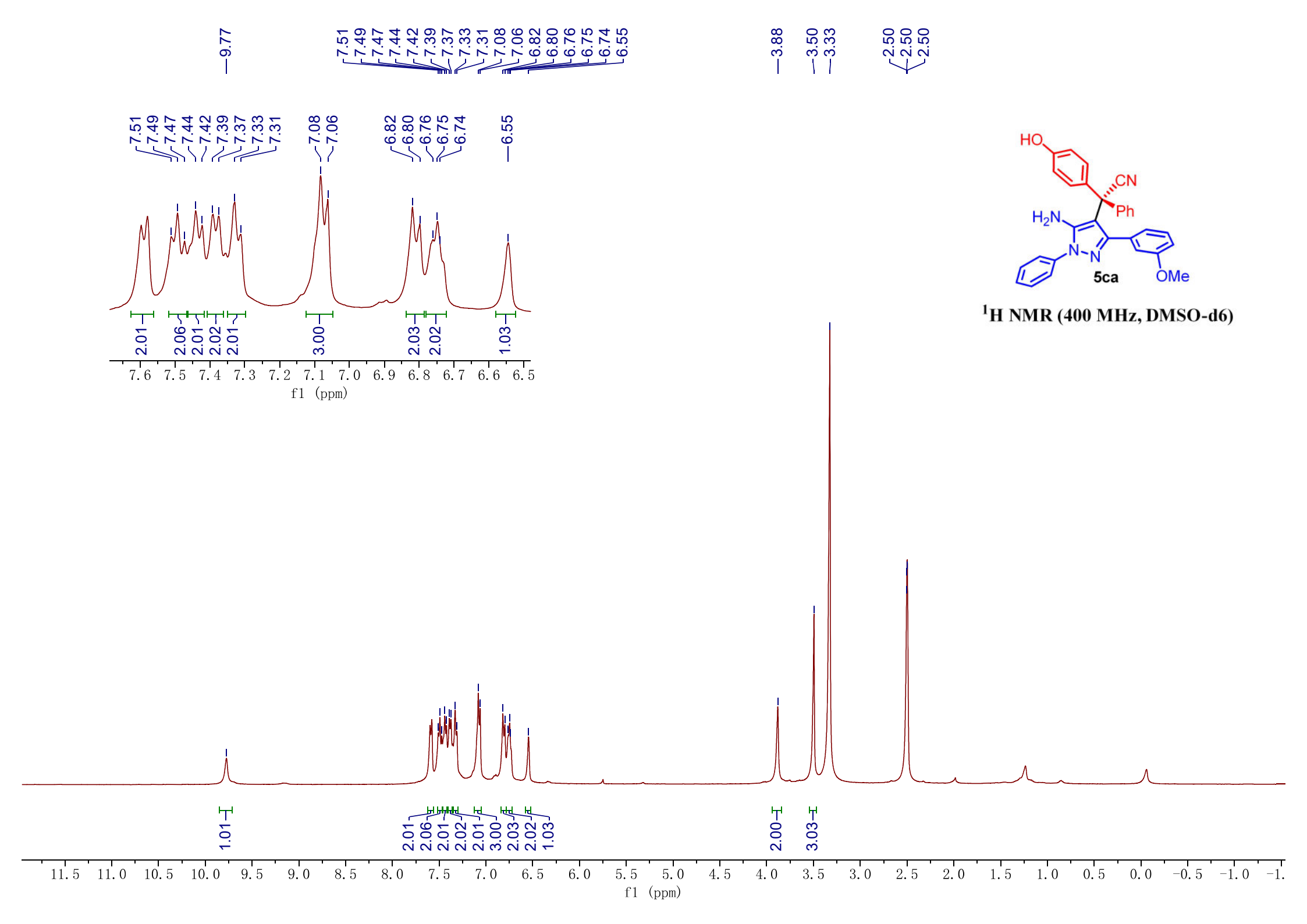

157.49
146.35
143.98
139.26
138.48
129.17
129.15
129.11
128.48
128.43
127.70
126.79
123.73
122.52
115.89
97.97
49.12
39.52 DMSO-d6
13.74
HO
CN
Ph
H2N
N
N
3ta
13C NMR (150 MHz, DMSO-d6)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

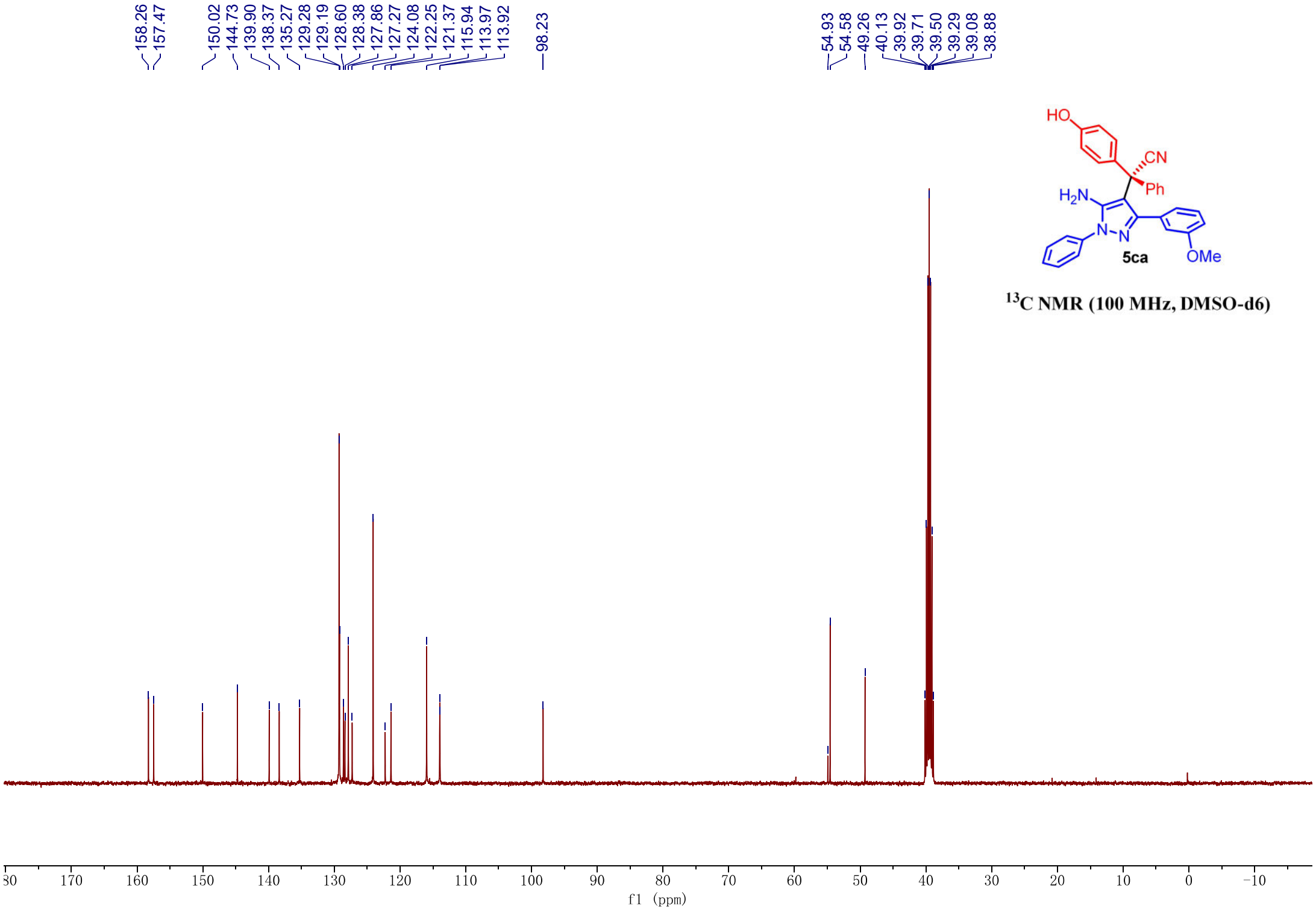

9.75
7.48 7.46 7.44 7.42 7.39 7.37 7.37 7.32 7.30 7.21 7.19 7.16 7.14 7.13 7.11 7.09 7.08 7.07 7.06 7.04 6.82 6.82 6.81 6.80 6.79
3.82 3.54 3.34
2.50 2.50 2.49
4.04 0.97 2.01 2.04 1.98 5.00 2.00
f1 (ppm)
HO
CN
Ph
H2N
N
N
MeO
5aa
1H NMR (400 MHz, DMSO-d6)
0.98 4.04 0.97 2.01 2.04 1.98 5.00 2.00 3.00 2.04
f1 (ppm)

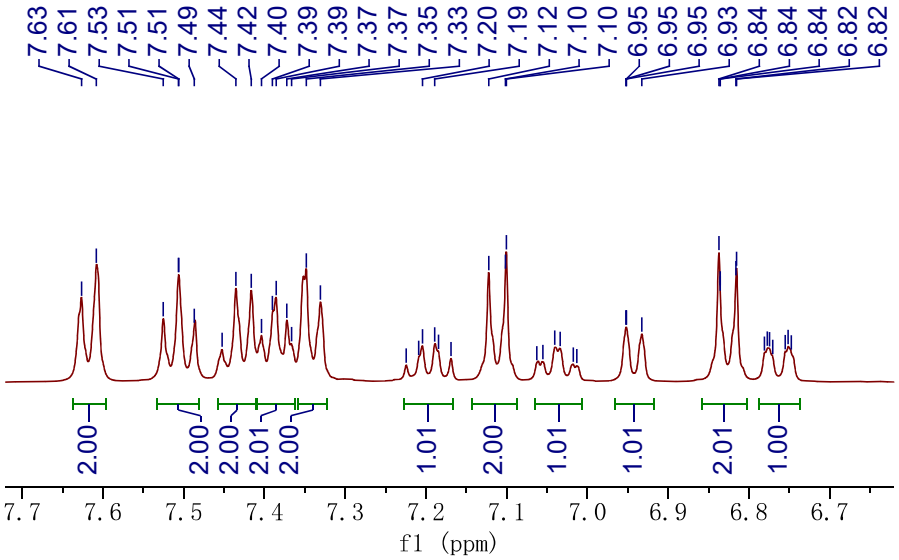

157.03
156.66
147.78
143.91
138.91
138.57
130.84
129.25
129.14
128.88
128.85
128.18
127.69
127.52
126.86
123.36
123.09
121.89
119.22
115.20
109.66
99.78
54.93
53.79
49.57
40.13
39.92
39.71
39.50
39.29
39.08
38.87
HO
CN
Ph
H2N
N
N
MeO
5aa
13C NMR (100 MHz, DMSO-d6)
f1 (ppm)

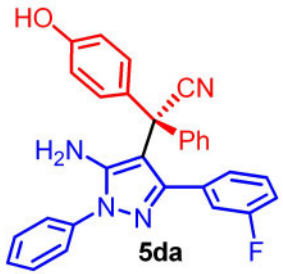

9.79 7.60 7.59 7.51 7.50 7.48 7.45 7.44 7.42 7.39 7.37 7.35 7.33 7.31 7.10 7.09 7.08 7.07 7.07 7.06 7.05 7.03 7.02 7.01 7.00 6.99 6.99 6.98 6.89 6.88 6.88 6.87 6.81 6.81 6.80 6.79 6.77 6.77 6.76
3.94
3.37
2.50 2.50 2.50
2.11
7.60 7.59 7.51 7.50 7.48 7.44 7.42 7.39 7.37 7.33 7.31 7.09 7.08 7.07 7.07 7.03 7.02 7.01 7.00 6.88 6.81 6.81 6.79 6.77 6.77 6.76
2.01 2.02 2.01 2.08 1.98 2.07 1.93 1.00 3.02
7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
f1 (ppm)
HO
CN
Ph
H2N
N
N
Me
5ba
1H NMR (400 MHz, DMSO-d6)
0.99 2.01 2.02 2.01 2.08 1.98 2.07 1.93 1.00 3.02 1.88 3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


157.37
150.23
144.53
139.85
138.38
136.16
133.75
129.79
129.25
129.17
129.15
129.06
128.28
128.05
127.76
127.27
127.19
125.94
123.98
122.14
115.83
98.51
49.30
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
20.87
HO
CN
Ph
H2N
N
N
Me
5ba
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

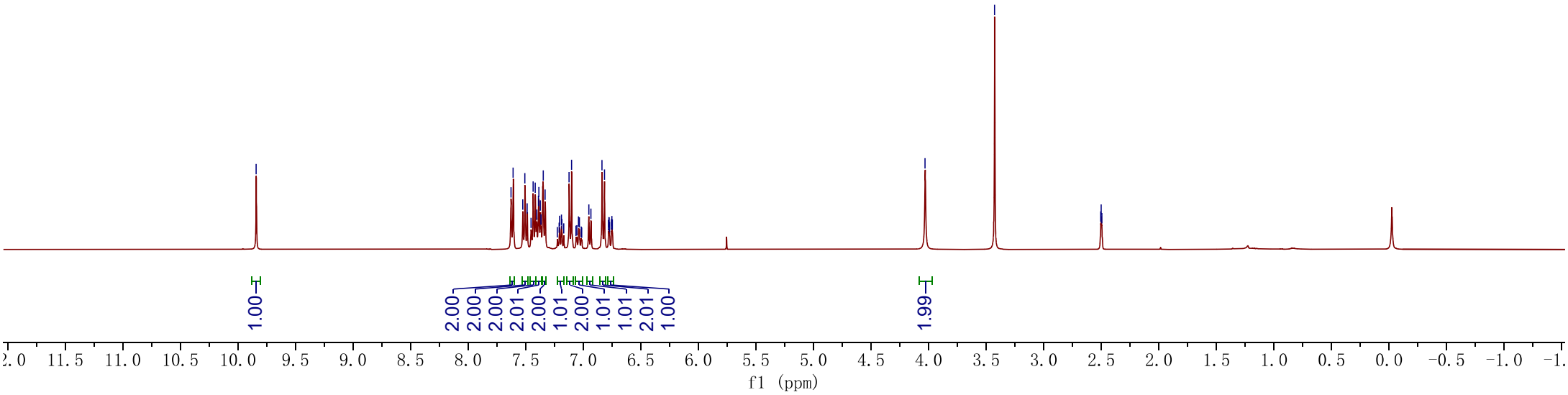

9.77
7.51
7.49
7.47
7.44
7.42
7.39
7.37
7.33
7.31
7.08
7.06
6.82
6.80
6.76
6.75
6.74
6.55
3.88
3.50
3.33
2.50
2.50
2.50
2.01
2.06
2.01
2.02
2.01
3.00
2.03
2.02
1.03
f1 (ppm)
HO
CN
Ph
H2N
N
N
OMe
5ca
1H NMR (400 MHz, DMSO-d6)
1.01
2.00
3.03
f1 (ppm)

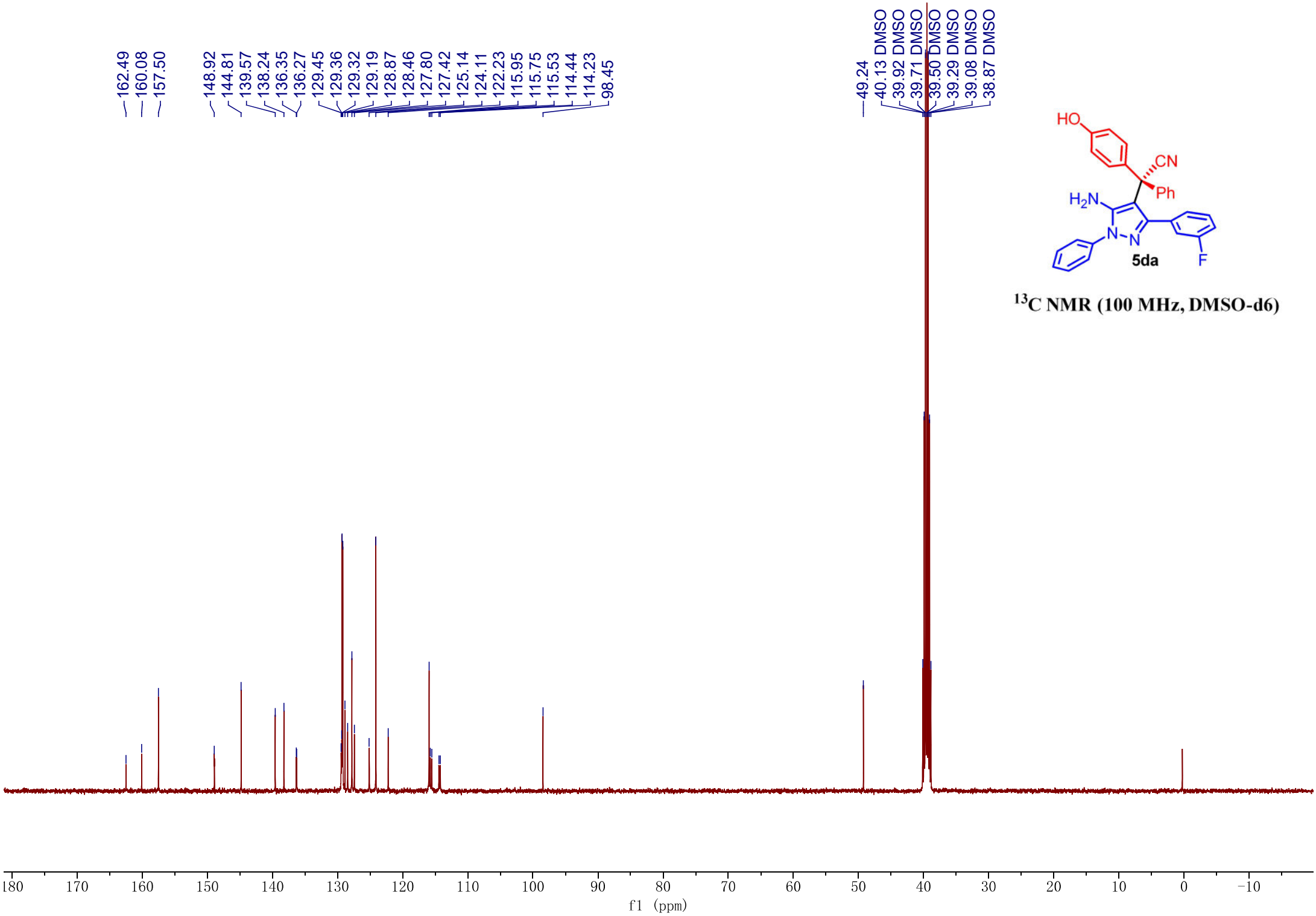

158.26
157.47
150.02
144.73
139.90
138.37
135.27
129.28
129.19
128.60
128.38
127.86
127.27
124.08
122.25
121.37
115.94
113.97
113.92
98.23
54.93
54.58
49.26
40.13
39.92
39.71
39.50
39.29
39.08
38.88
HO
CN
Ph
H2N
N
N
OMe
5ca
13C NMR (100 MHz, DMSO-d6)
f1 (ppm)

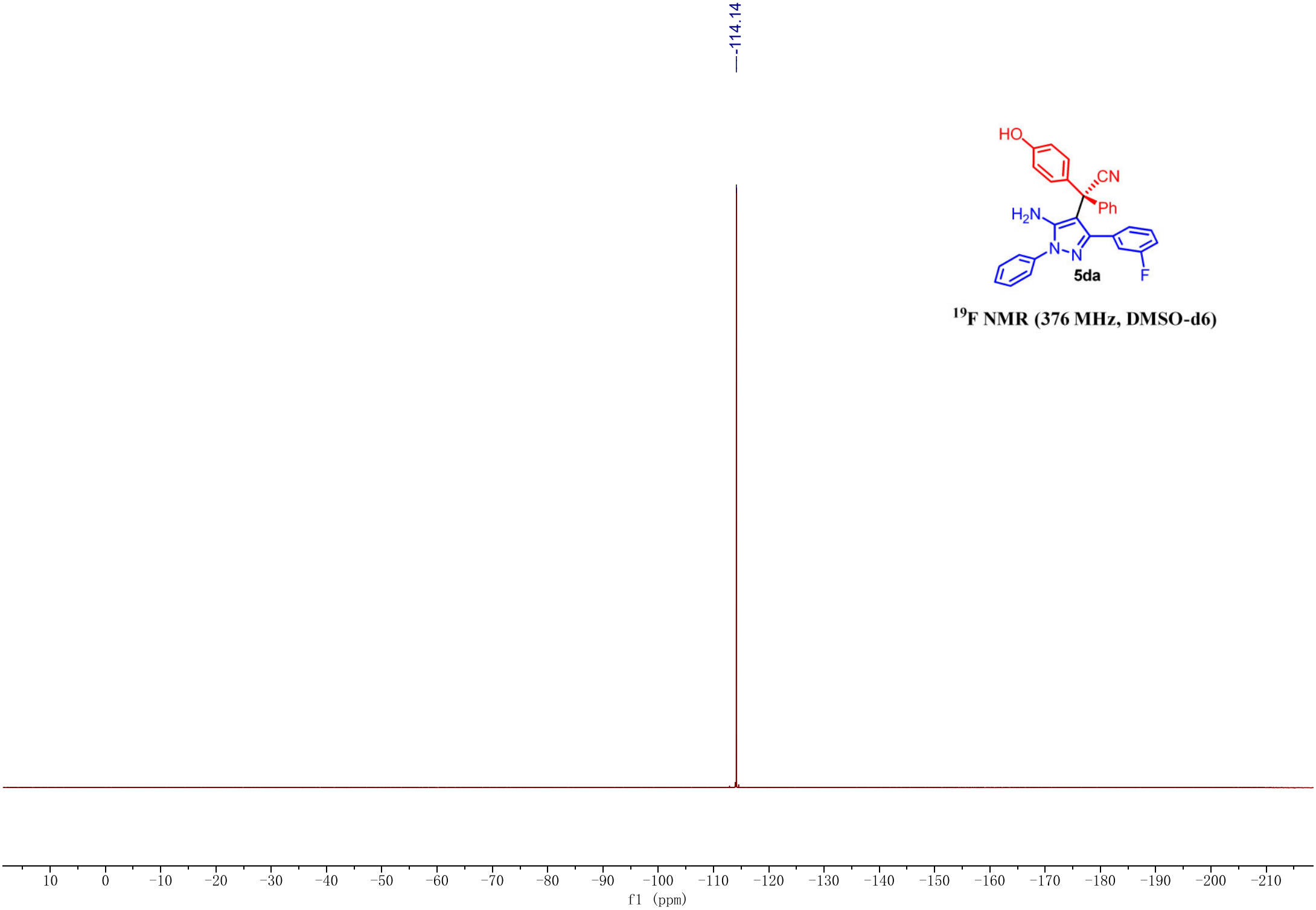




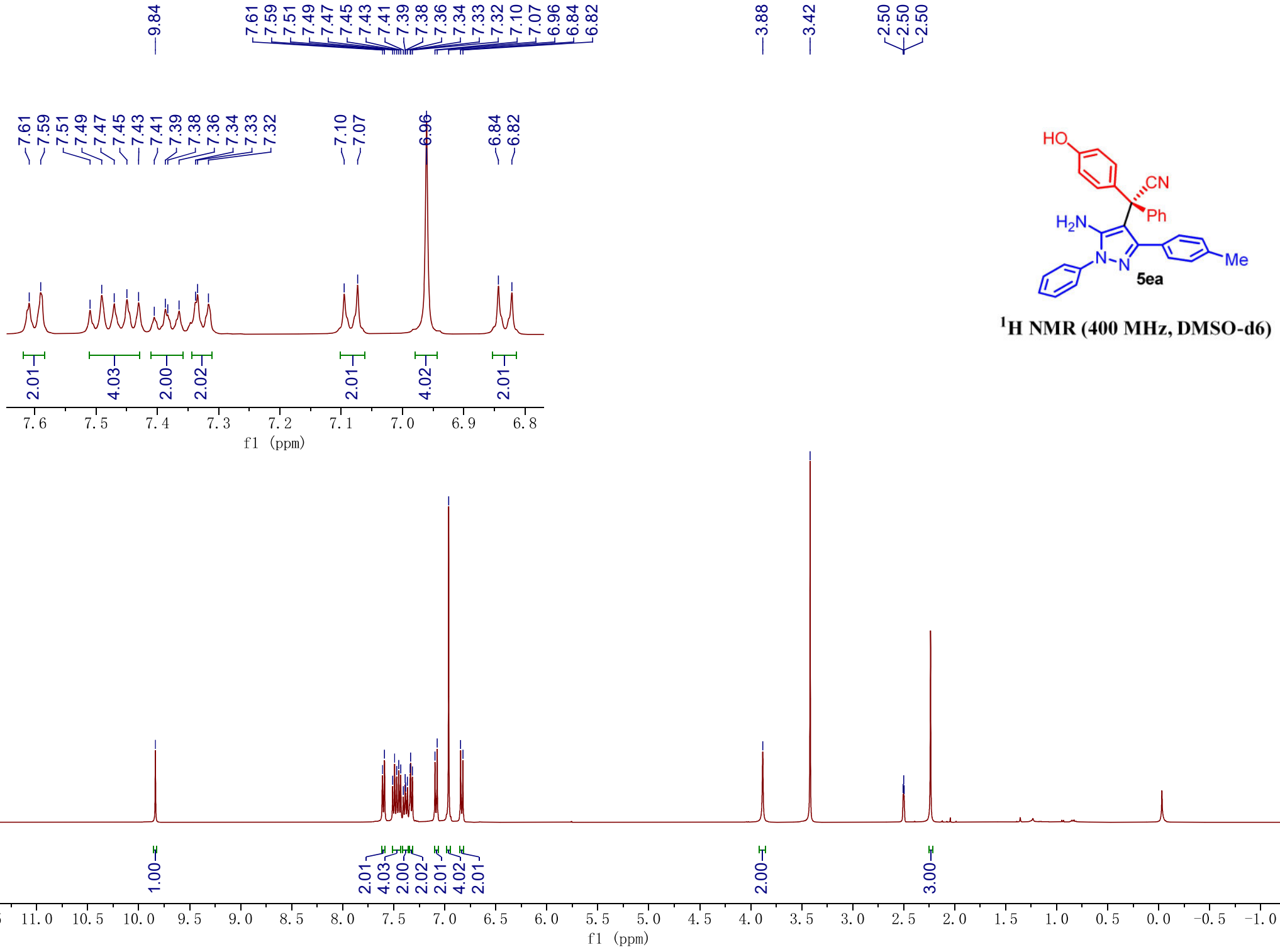
^{1}H NMR (400 MHz, DMSO-d6)

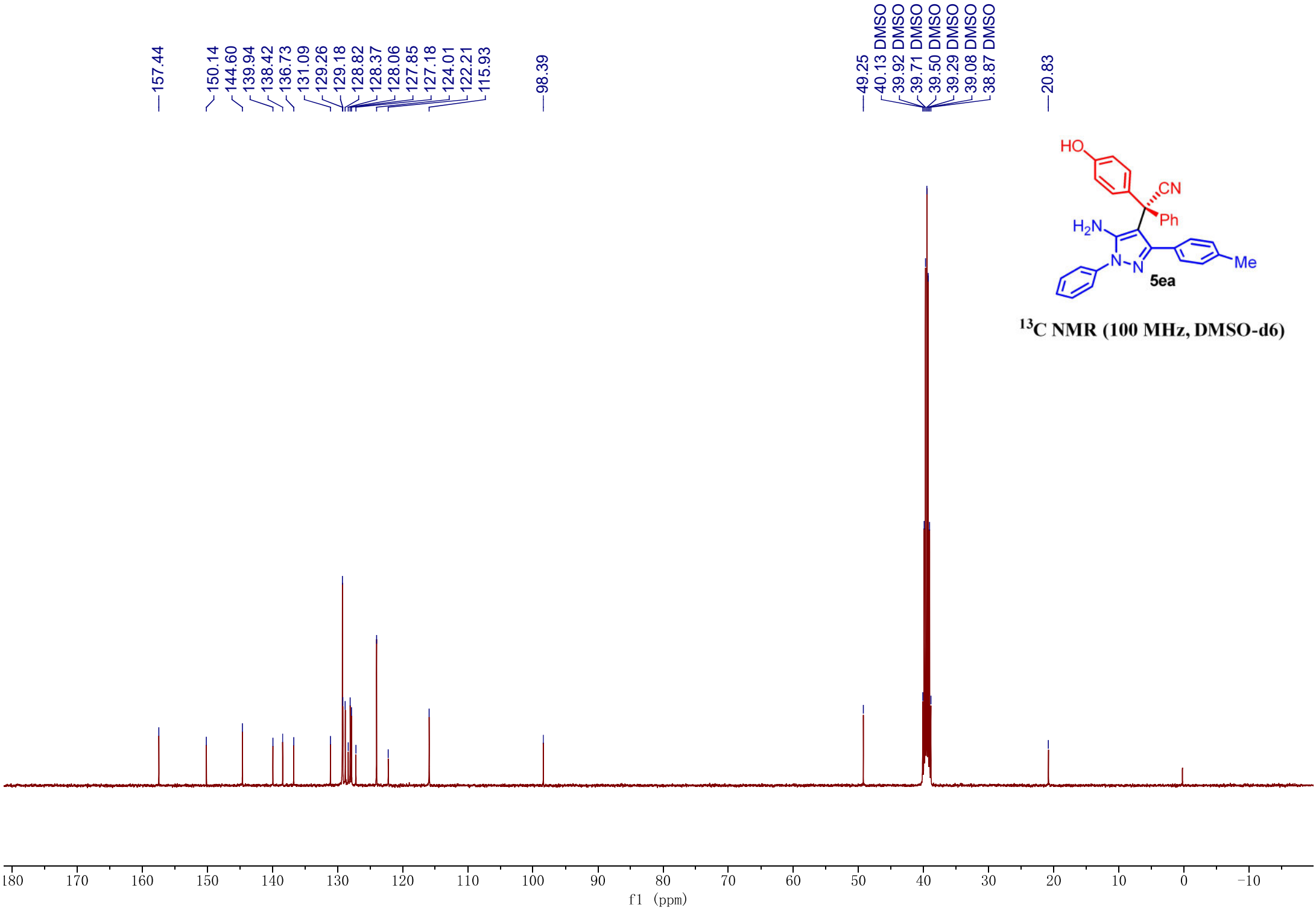


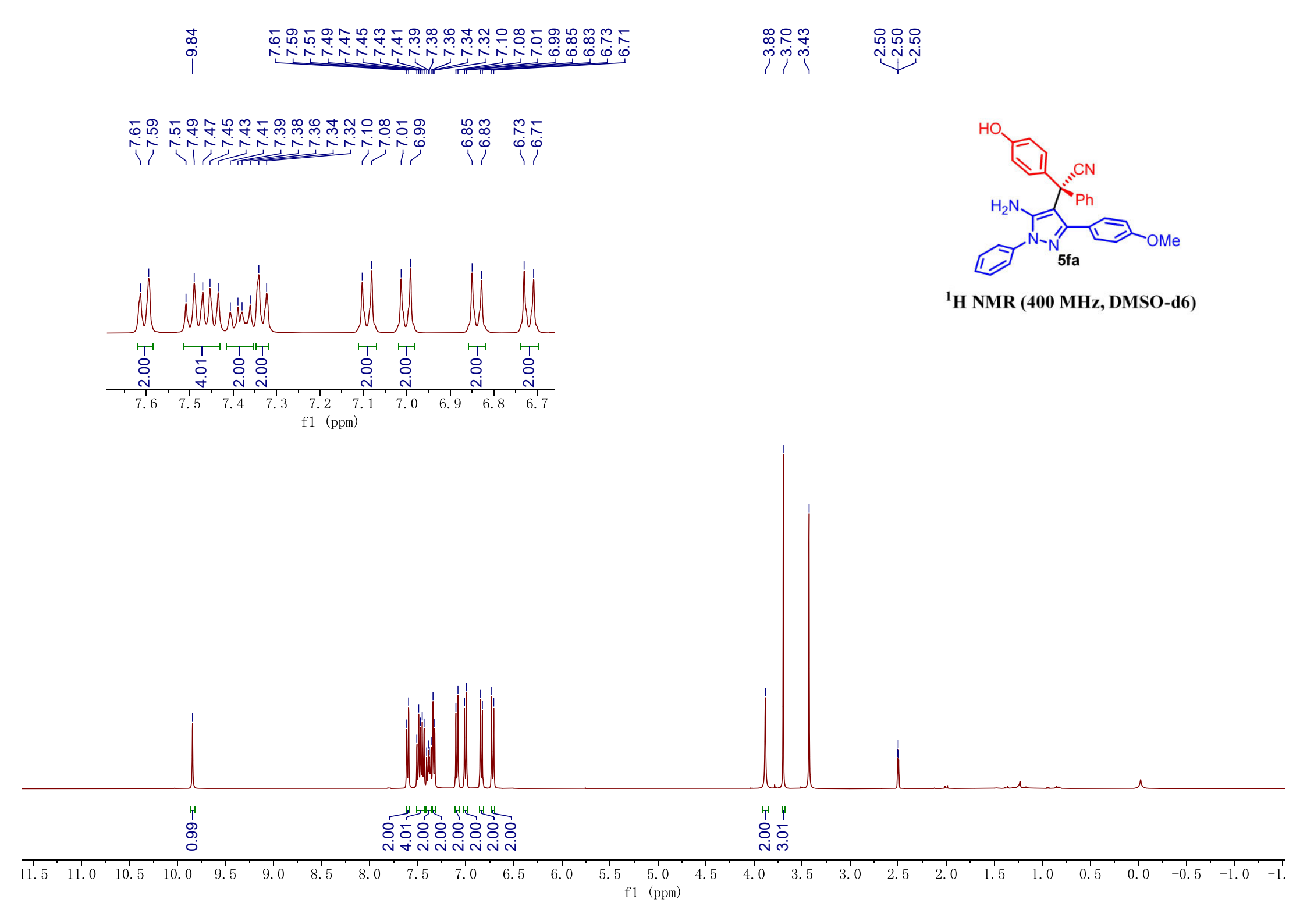

162.49
160.08
157.50
148.92
144.81
139.57
138.24
136.35
136.27
129.45
129.36
129.32
129.19
128.87
128.46
127.80
127.42
125.14
124.11
122.23
115.95
115.75
115.53
114.44
114.23
98.45
49.24
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
F
5da
13C NMR (100 MHz, DMSO-d6)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

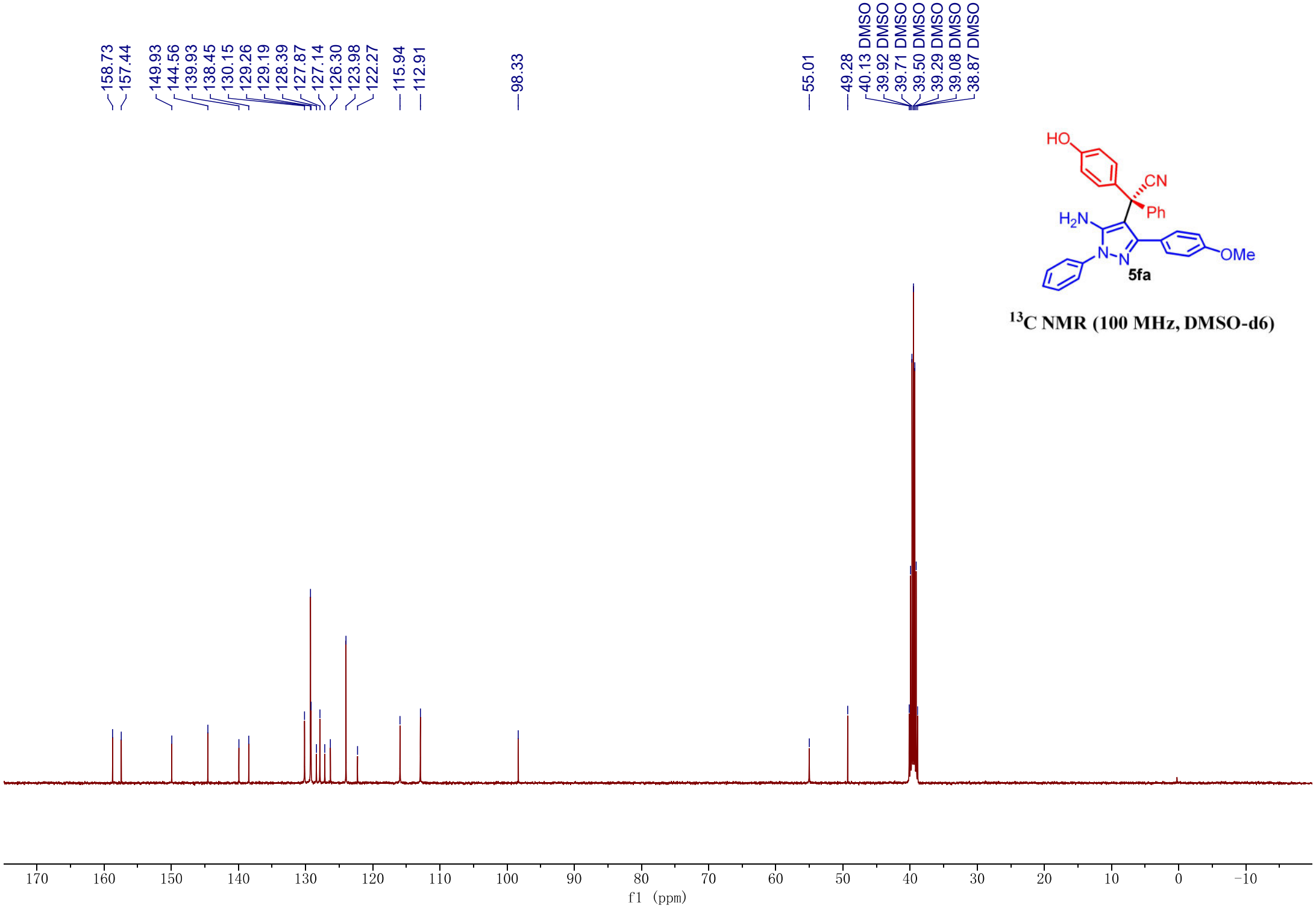


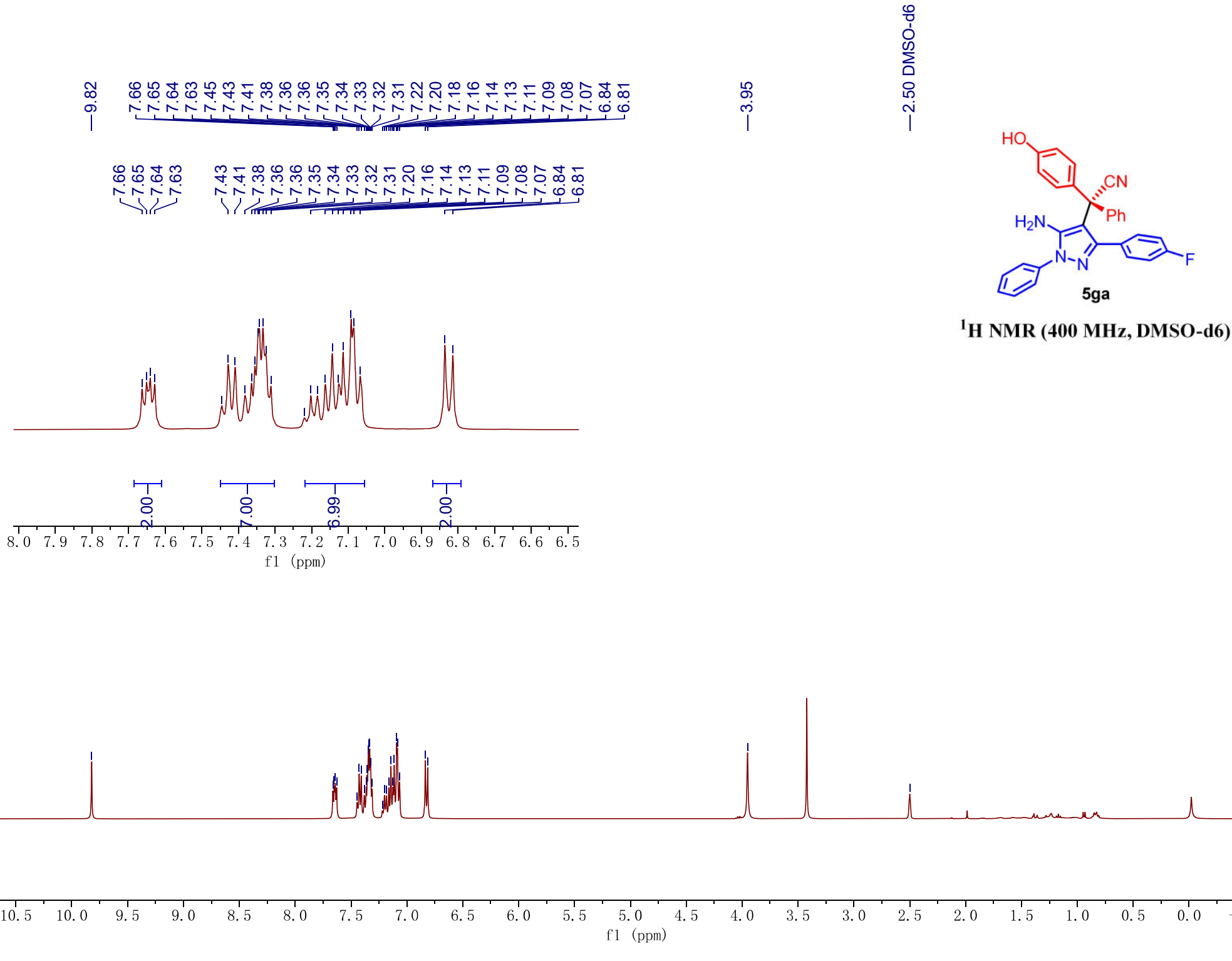
^{19}F NMR (376 MHz, DMSO-d6)

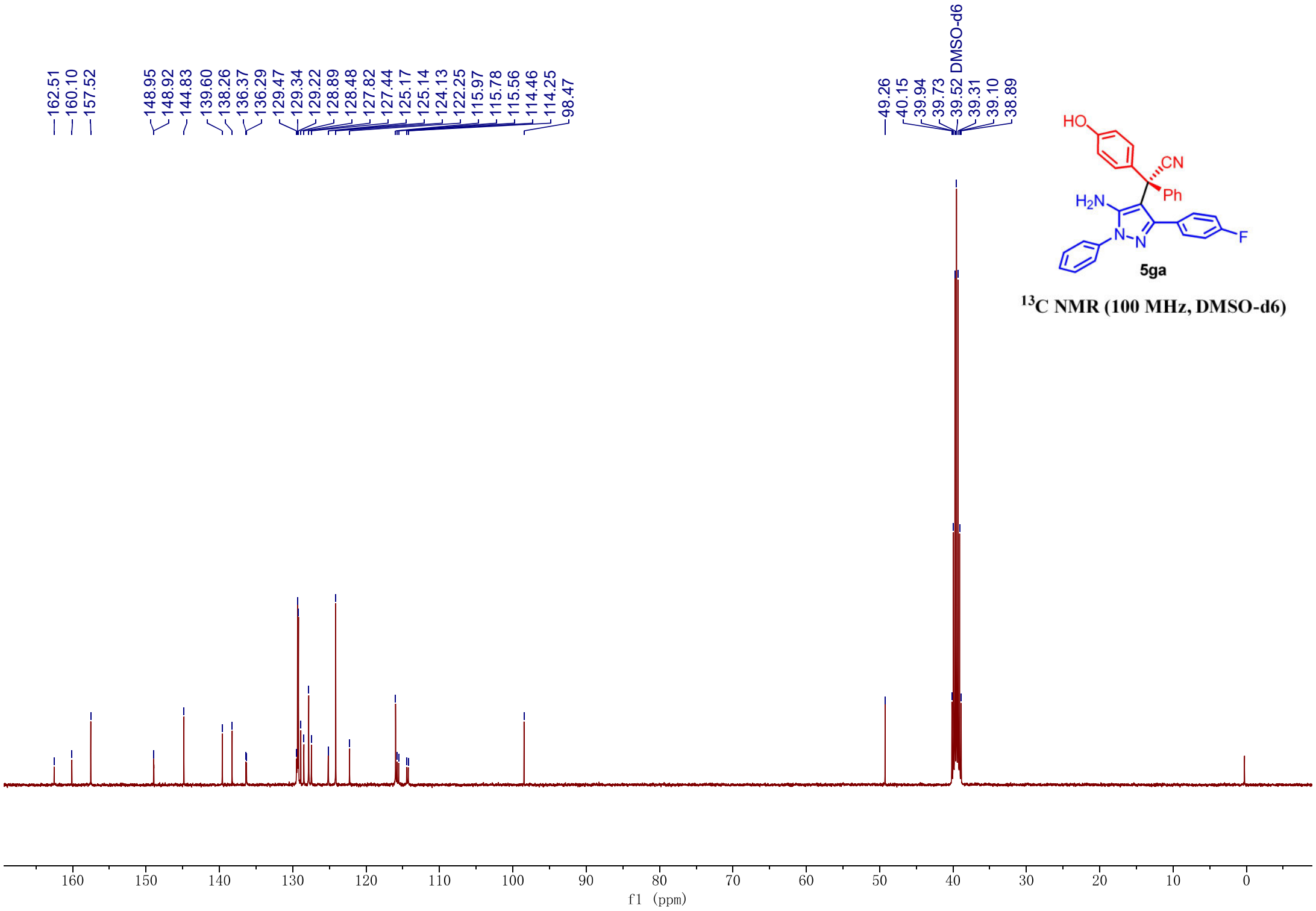

9.84
7.61
7.59
7.51
7.49
7.47
7.45
7.43
7.41
7.39
7.38
7.36
7.34
7.33
7.32
7.10
7.07
6.96
6.84
6.82
3.88
3.42
2.50
2.50
2.50
2.01
4.03
2.00
2.02
2.01
4.02
2.01
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
f1 (ppm)
HO
CN
Ph
H2N
N
N
Me
5ea
1H NMR (400 MHz, DMSO-d6)
1.00
2.01
4.03
2.00
2.02
2.01
4.02
2.01
2.00
3.00
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

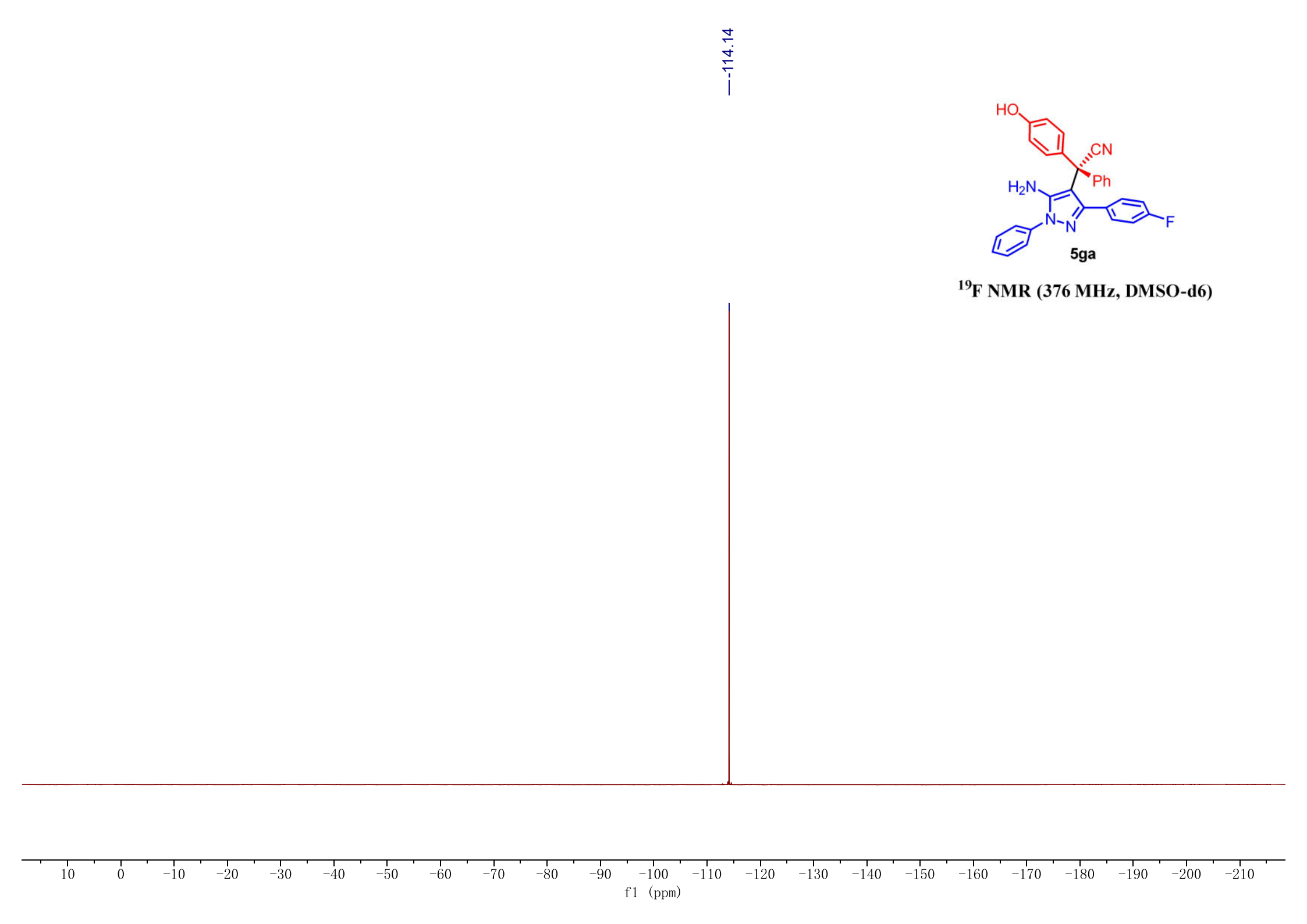

157.44
150.14
144.60
139.94
138.42
136.73
131.09
129.26
129.18
128.82
128.37
128.06
127.85
127.18
124.01
122.21
115.93
98.39
49.25
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
20.83
HO
CN
Ph
H2N
N
N
Me
5ea
13C NMR (100 MHz, DMSO-d6)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

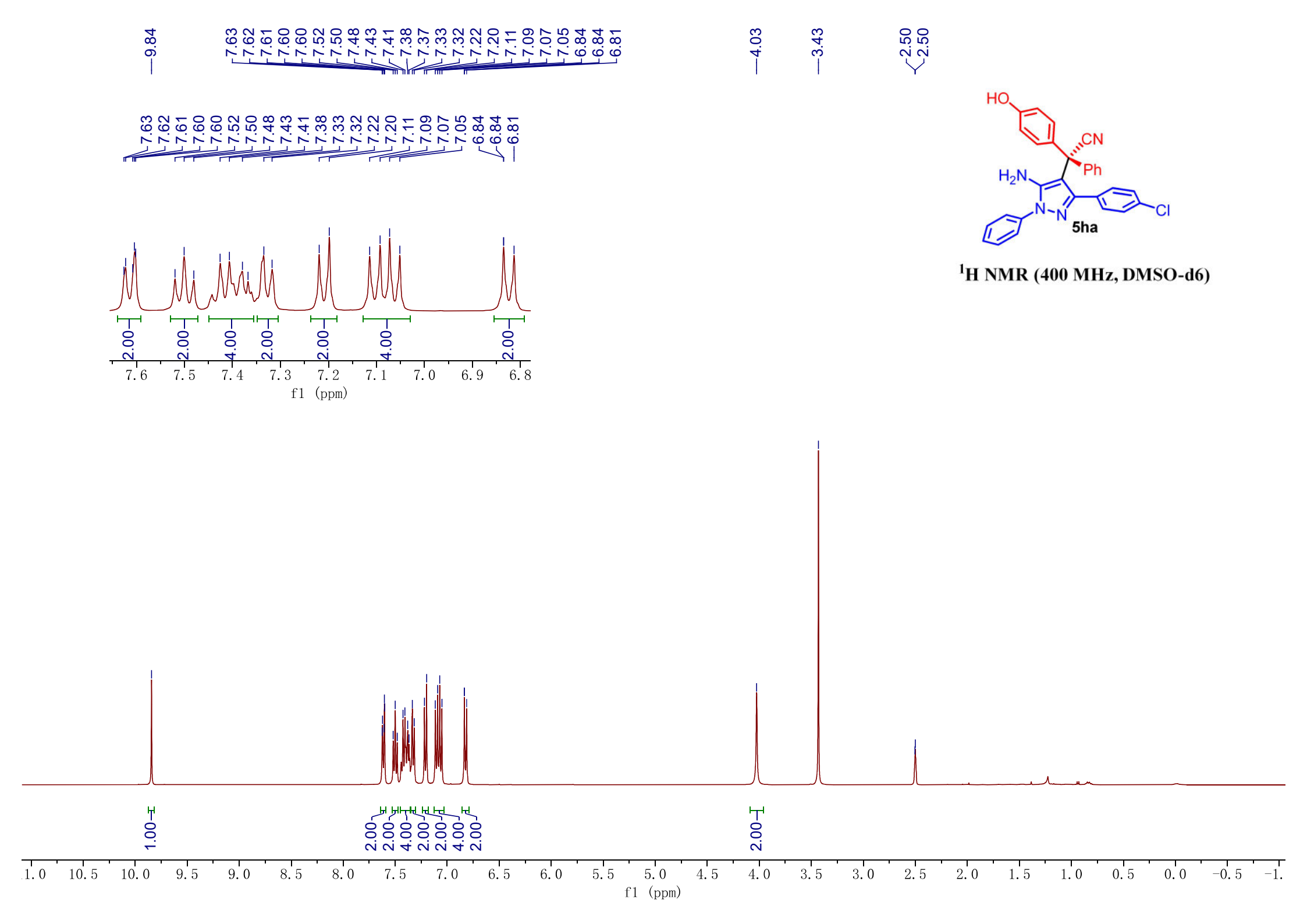

9.84
7.61
7.59
7.51
7.49
7.47
7.45
7.43
7.41
7.39
7.38
7.36
7.34
7.32
7.10
7.08
7.01
6.99
6.85
6.83
6.73
6.71
3.88
3.70
3.43
2.50
2.50
2.50
2.00
4.01
2.00
2.00
2.00
2.00
2.00
2.00
f1 (ppm)
HO
CN
Ph
H2N
N
N
OMe
5fa
1H NMR (400 MHz, DMSO-d6)
0.99
2.00
4.01
2.00
2.00
2.00
2.00
2.00
2.00
3.01
f1 (ppm)


158.73
157.44
149.93
144.56
139.93
138.45
130.15
129.26
129.19
128.39
127.87
127.14
126.30
123.98
122.27
115.94
112.91
98.33
55.01
49.28
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
OMe
5fa
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

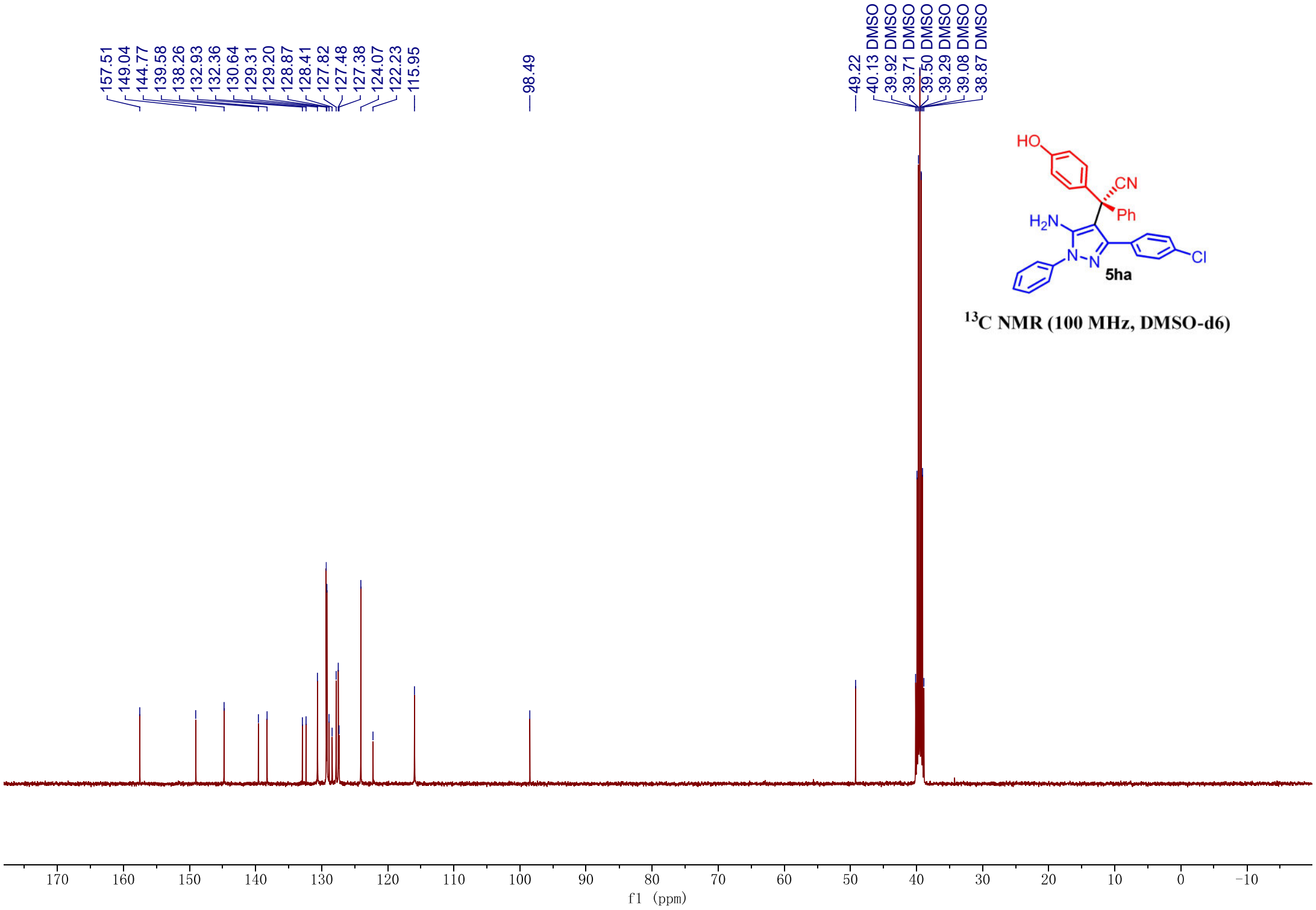

9.82
7.66
7.65
7.64
7.63
7.45
7.43
7.41
7.38
7.36
7.36
7.35
7.34
7.33
7.32
7.31
7.22
7.20
7.18
7.16
7.14
7.13
7.11
7.09
7.08
7.07
6.84
6.81
3.95
2.50 DMSO-d6
HO
CN
Ph
H2N
N
N
F
5ga
1H NMR (400 MHz, DMSO-d6)
2.00
7.00
6.99
2.00
f1 (ppm)
f1 (ppm)

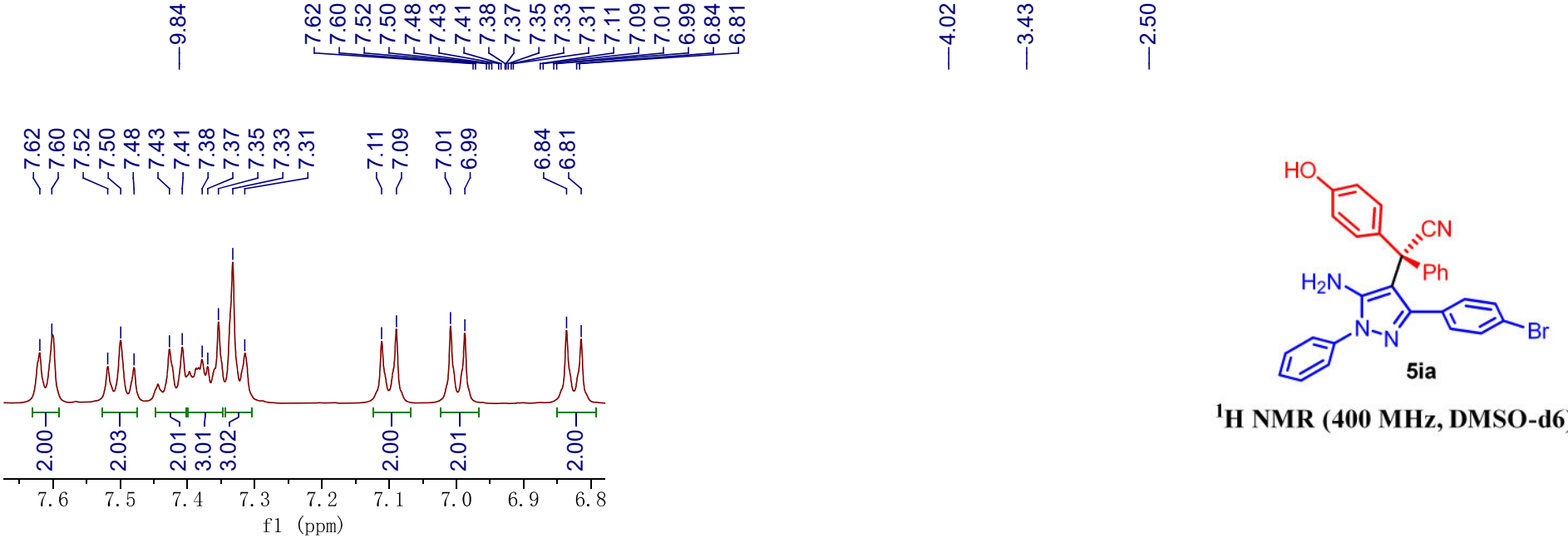

162.51
160.10
157.52
148.95
148.92
144.83
139.60
138.26
136.37
136.29
129.47
129.34
129.22
128.89
128.48
127.82
127.44
125.17
125.14
124.13
122.25
115.97
115.78
115.56
114.46
114.25
98.47
49.26
40.15
39.94
39.73
39.52 DMSO-d6
39.31
39.10
38.89
HO
CN
Ph
H2N
N
N
F
5ga
13C NMR (100 MHz, DMSO-d6)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-114.14
HO
CN
Ph
H2N
N
N
F
5ga
19F NMR (376 MHz, DMSO-d6)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



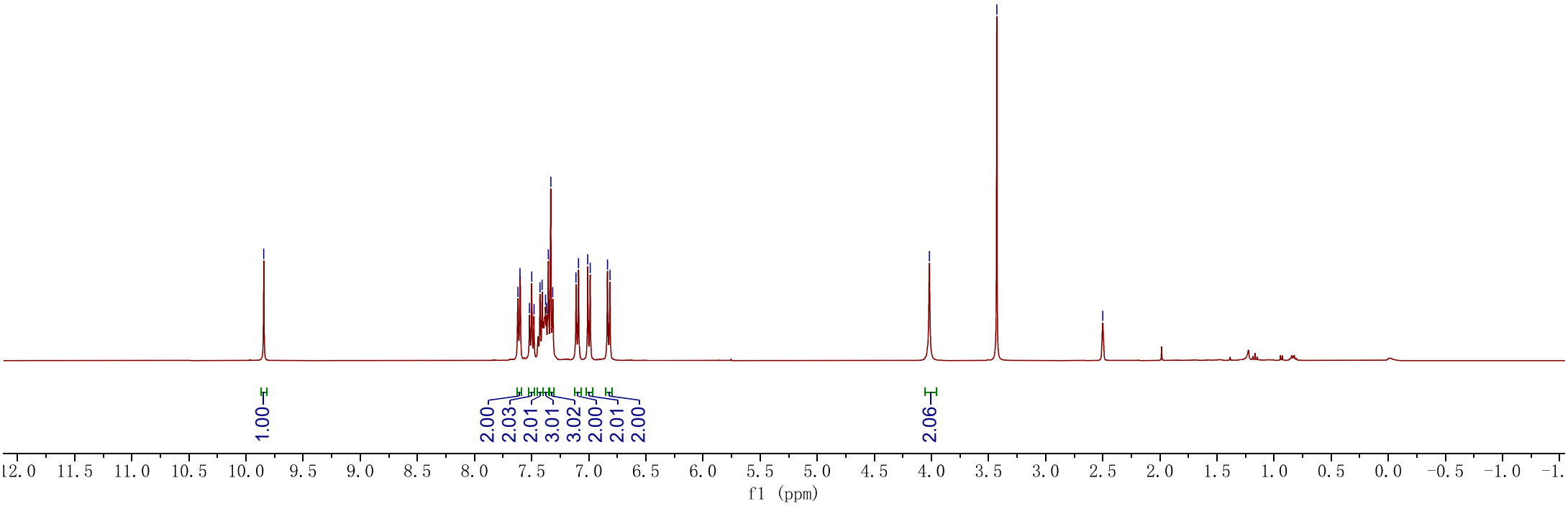
^{1}H NMR (400 MHz, DMSO-d6)

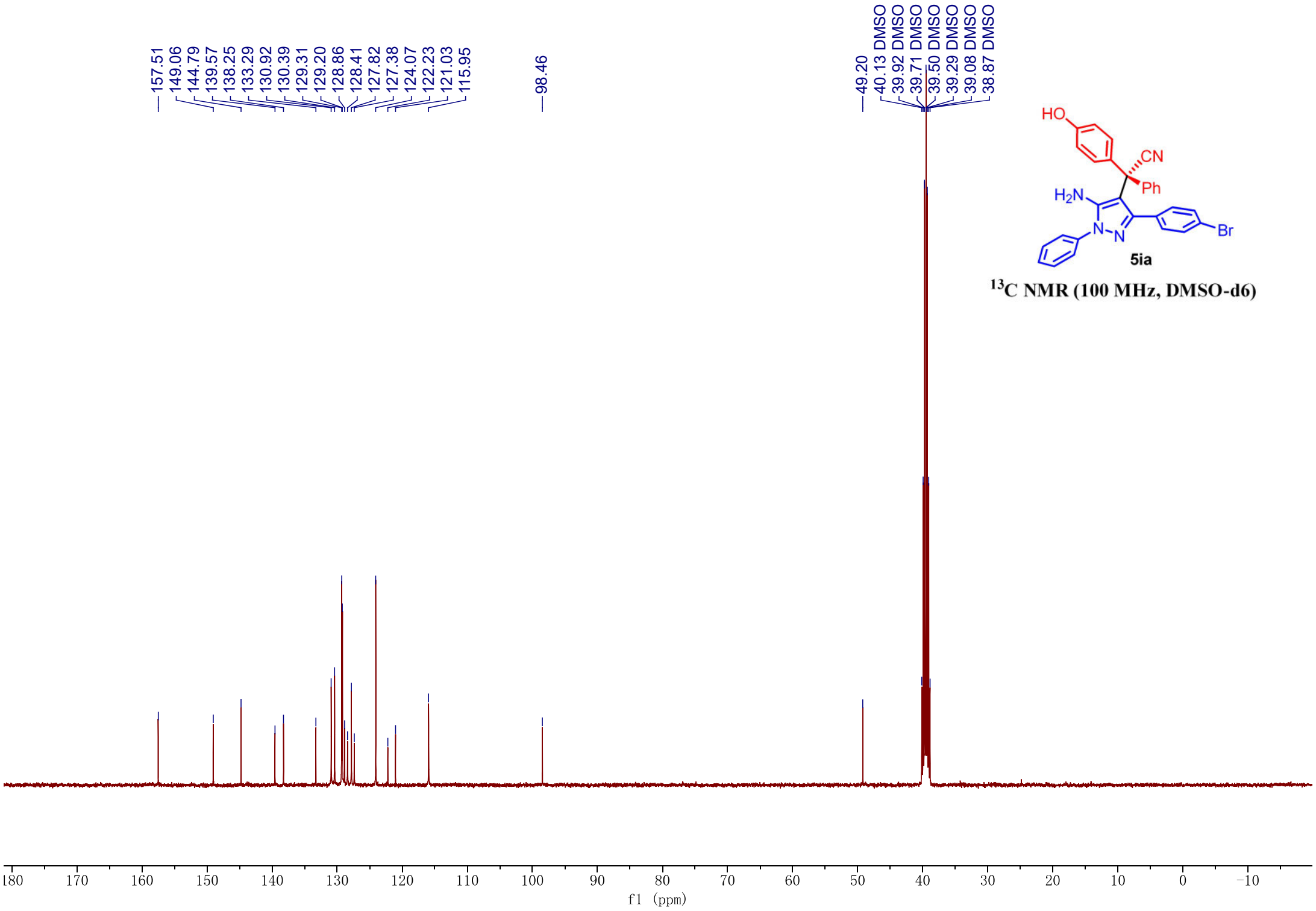

157.51
149.04
144.77
139.58
138.26
132.93
132.36
130.64
129.31
129.20
128.87
128.41
127.82
127.48
127.38
124.07
122.23
115.95
98.49
49.22
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
Cl
5ha
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

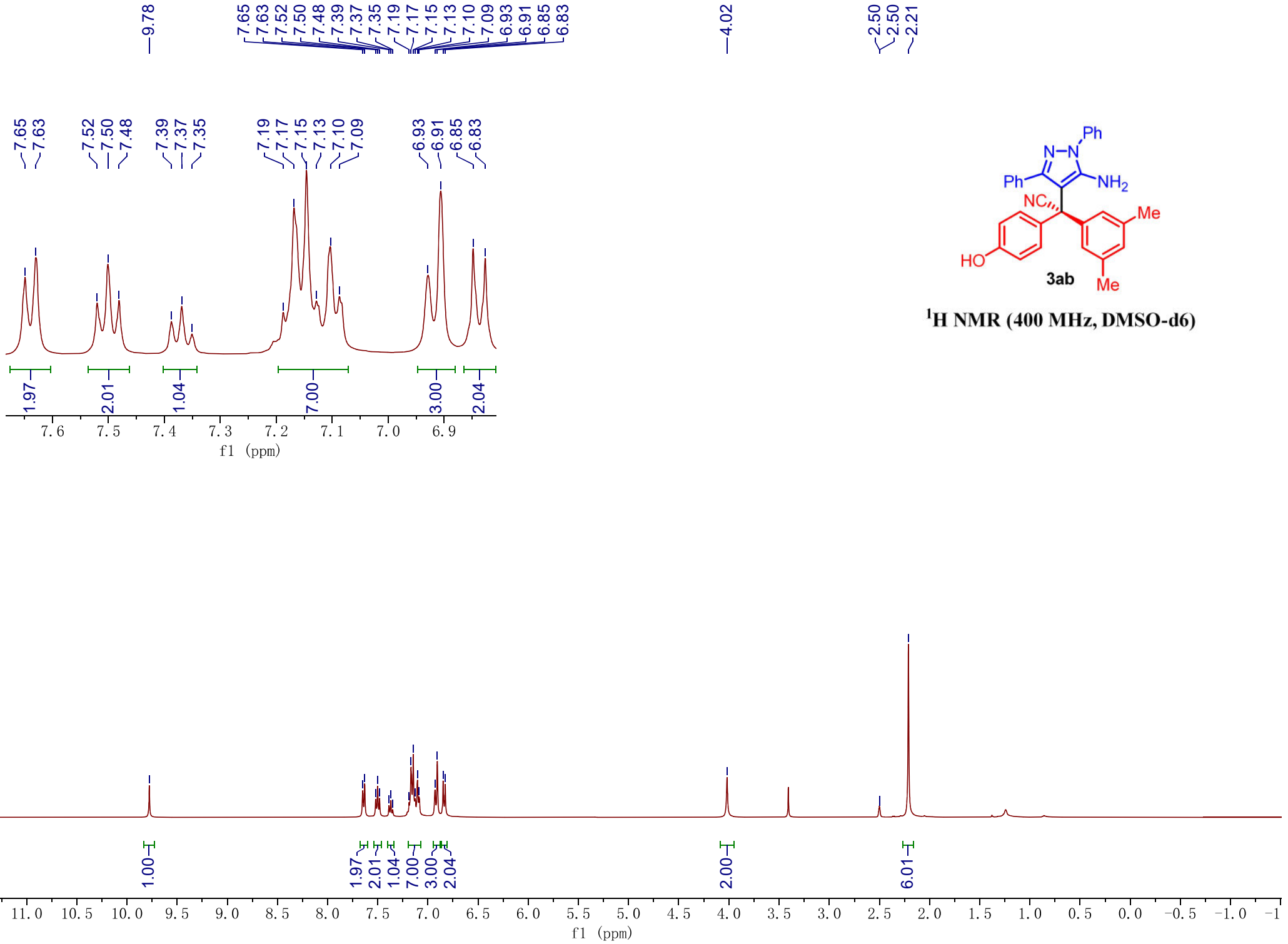


5ia

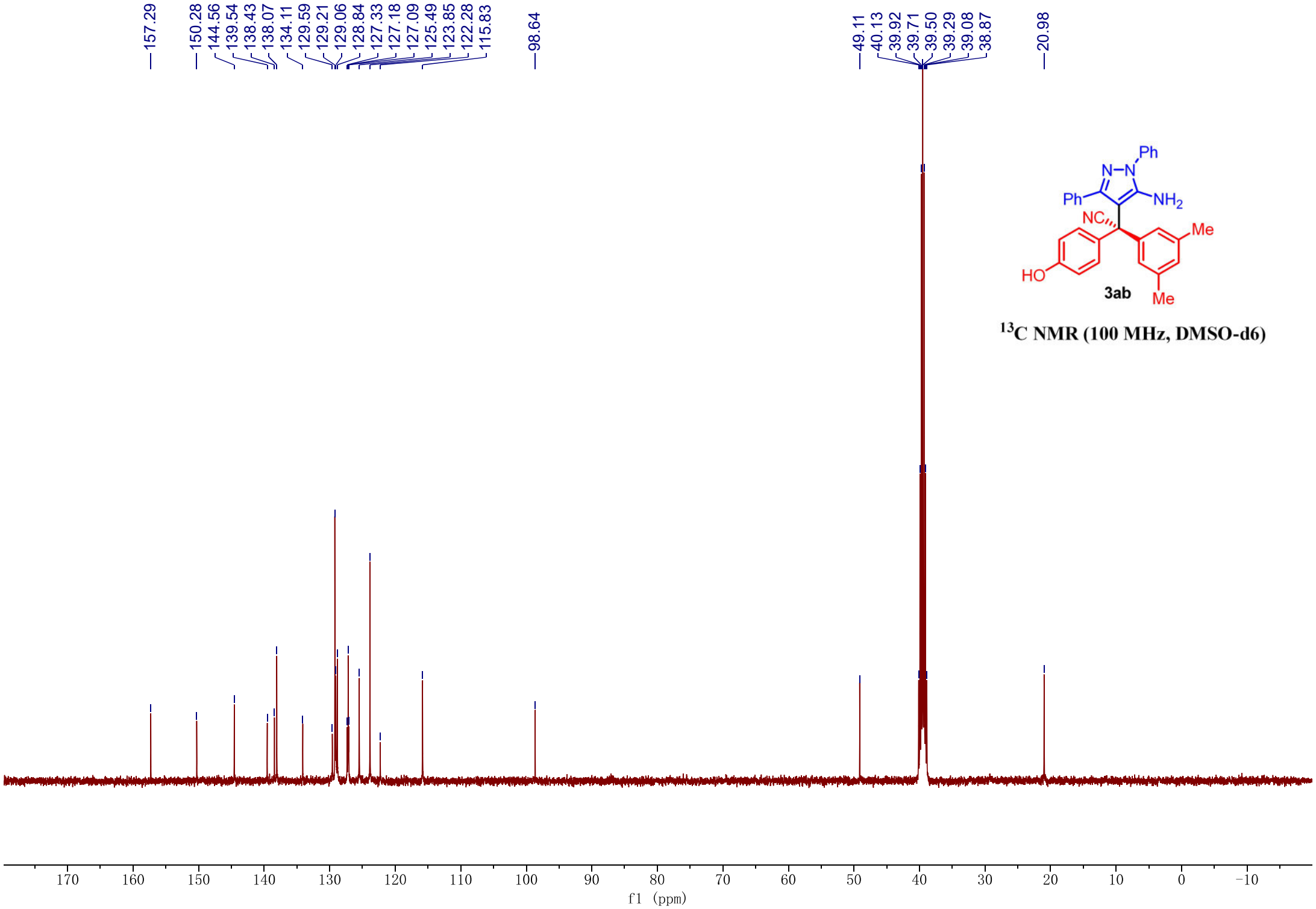
^{1}H NMR (400 MHz, DMSO-d6)



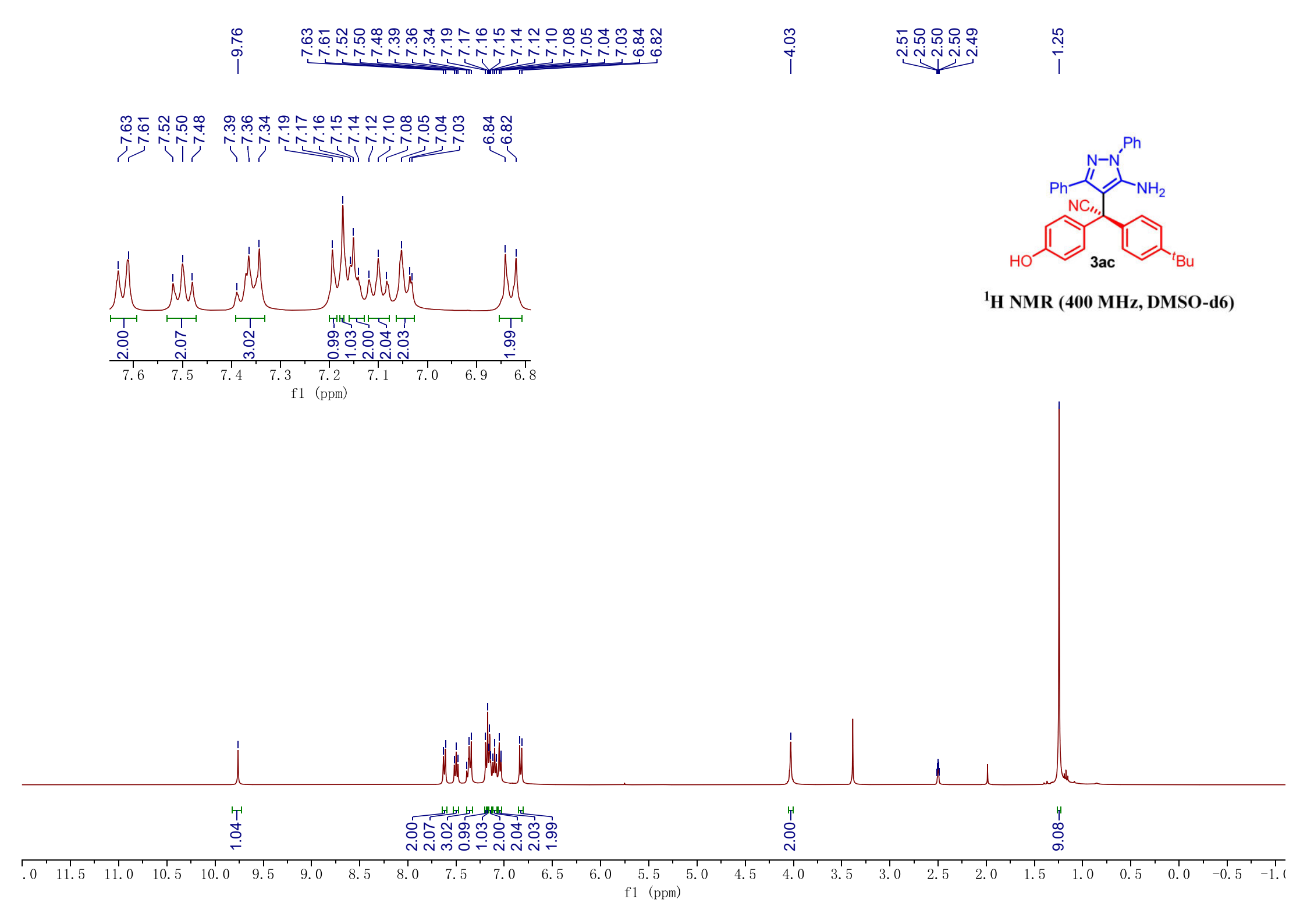

157.51
149.06
144.79
139.57
138.25
133.29
130.92
130.39
129.31
129.20
128.86
128.41
127.82
127.38
124.07
122.23
121.03
115.95
98.46
49.20
40.13 DMSO
39.92 DMSO
39.71 DMSO
39.50 DMSO
39.29 DMSO
39.08 DMSO
38.87 DMSO
HO
CN
Ph
H2N
N
N
Br
5ia
13C NMR (100 MHz, DMSO-d6)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



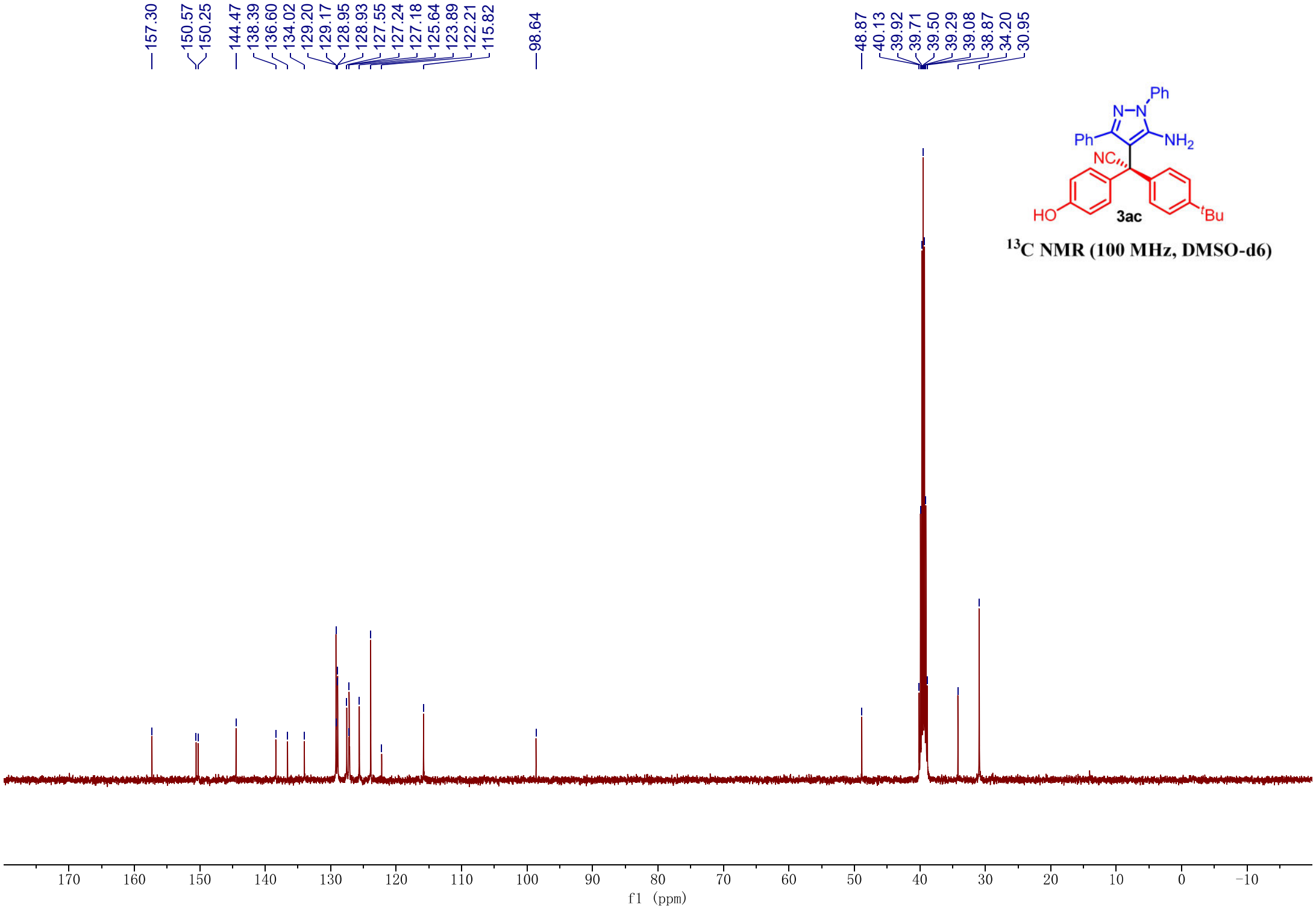
^{1}H NMR (400 MHz, DMSO-d6)

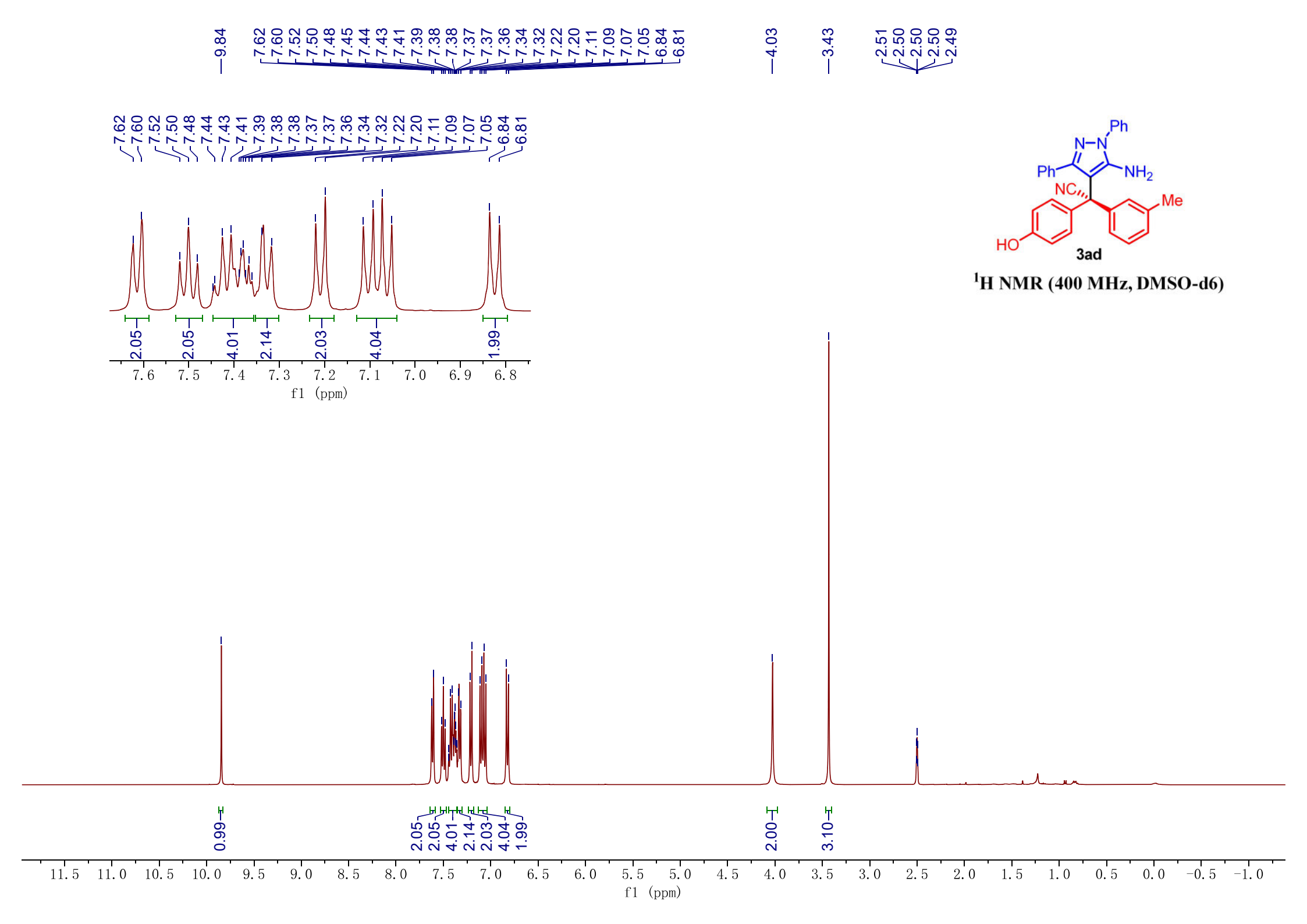


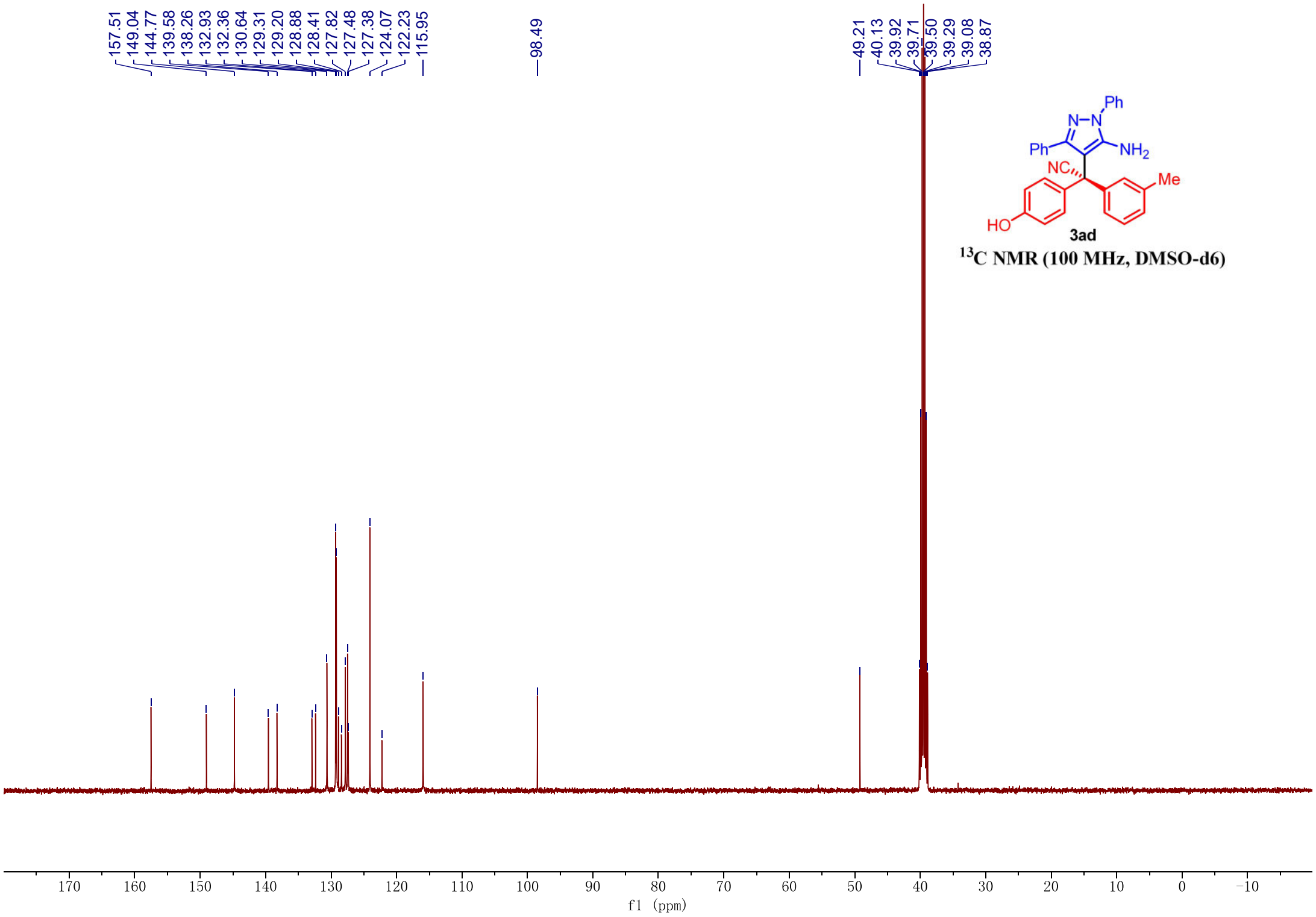
^{13}C NMR (100 MHz, DMSO-d6)

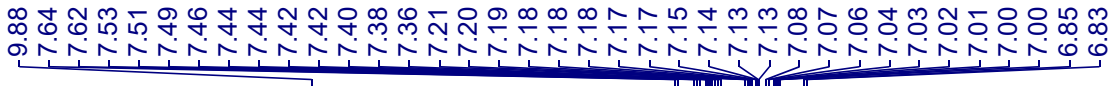


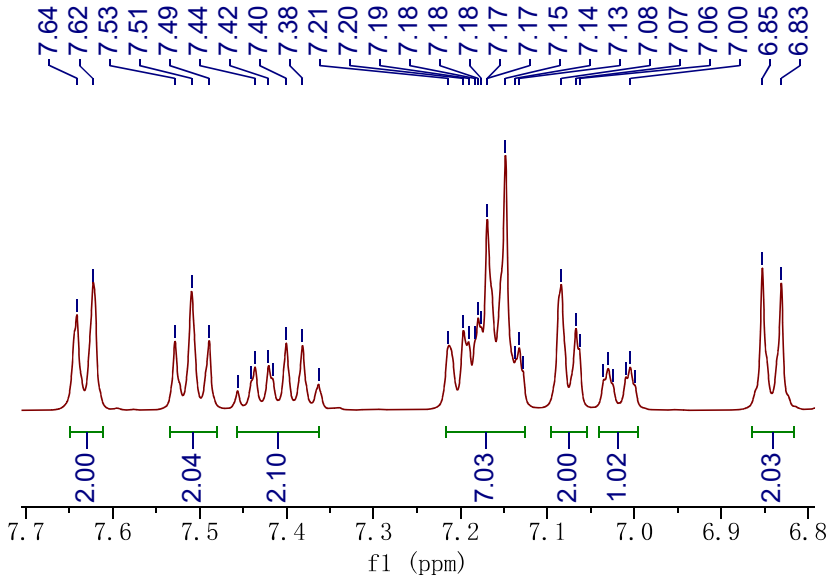
^{1}H NMR (400 MHz, DMSO-d6)

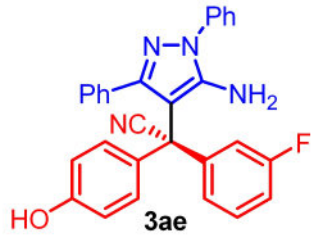

157.30
150.57
150.25
144.47
138.39
136.60
134.02
129.20
129.17
128.95
128.93
127.55
127.24
127.18
125.64
123.89
122.21
115.82
98.64
48.87
40.13
39.92
39.71
39.50
39.29
39.08
38.87
34.20
30.95
Ph
N–N
Ph
NH2
NC
HO
tBu
3ac
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)


9.84
7.62
7.60
7.52
7.50
7.48
7.45
7.44
7.43
7.41
7.39
7.38
7.38
7.37
7.37
7.36
7.34
7.32
7.22
7.20
7.11
7.09
7.07
7.05
6.84
6.81
4.03
3.43
2.51
2.50
2.50
2.50
2.49
2.05
2.05
4.01
2.14
2.03
4.04
1.99
f1 (ppm)
Ph
N–N
Ph
NH2
NC
Me
HO
3ad
1H NMR (400 MHz, DMSO-d6)
0.99
2.00
3.10
f1 (ppm)

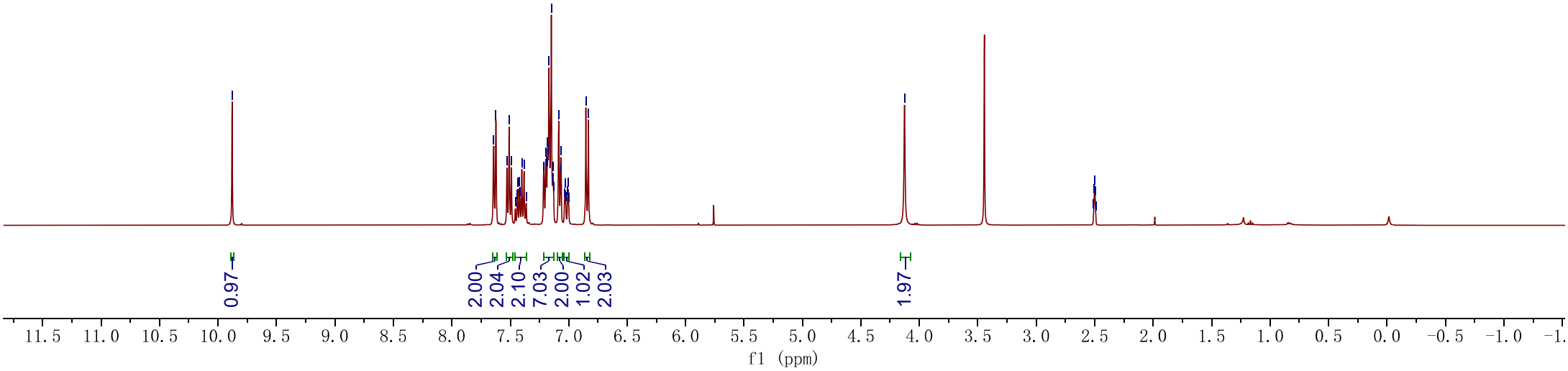

157.51
149.04
144.77
139.58
138.26
132.93
132.36
130.64
129.31
129.20
128.88
128.41
127.82
127.48
127.38
124.07
122.23
115.95
98.49
49.21
40.13
39.92
39.71
39.50
39.29
39.08
38.87
Ph
N–N
Ph
NH2
NC
Me
HO
3ad
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

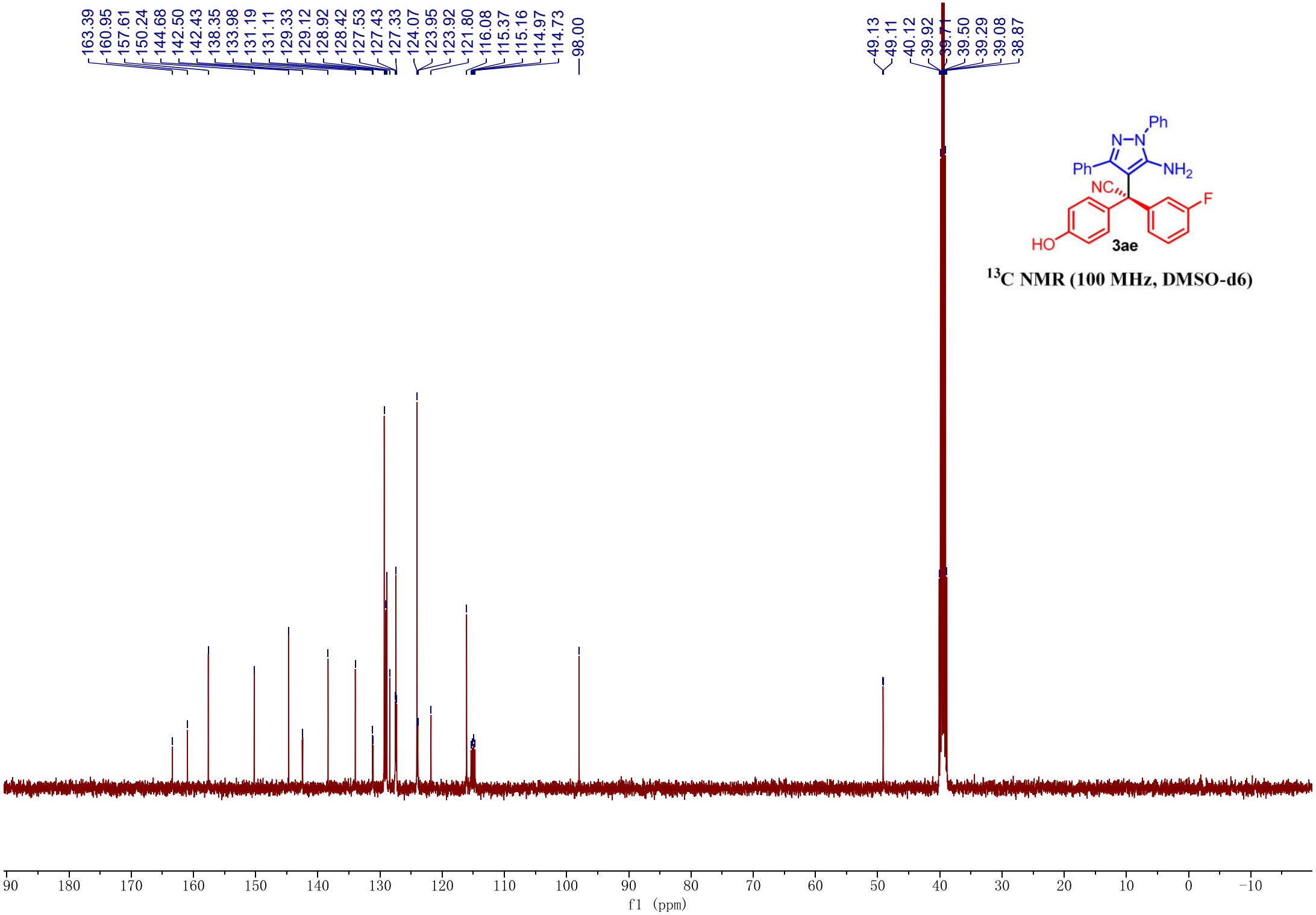


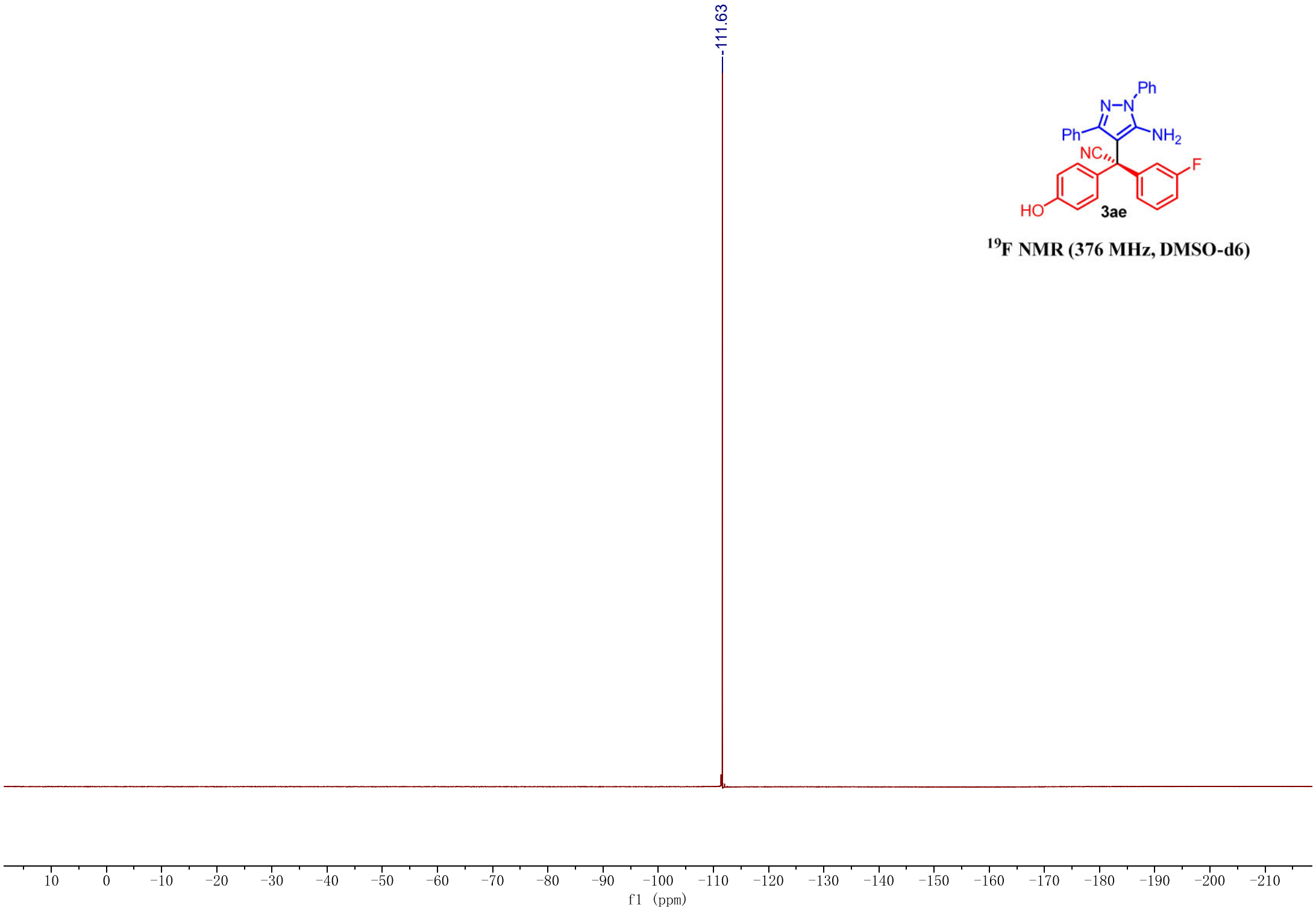




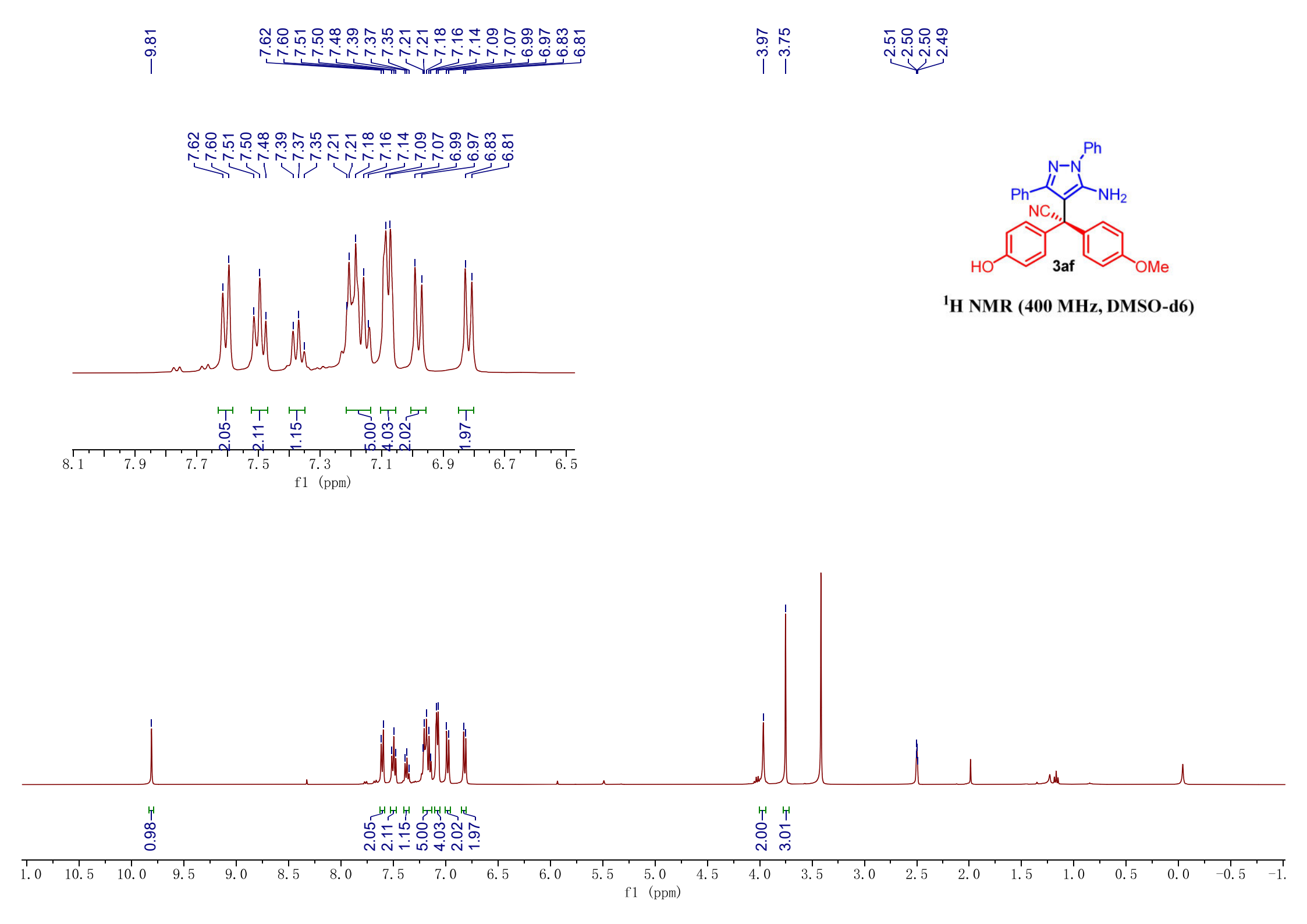
^{1}H NMR (400 MHz, DMSO-d6)



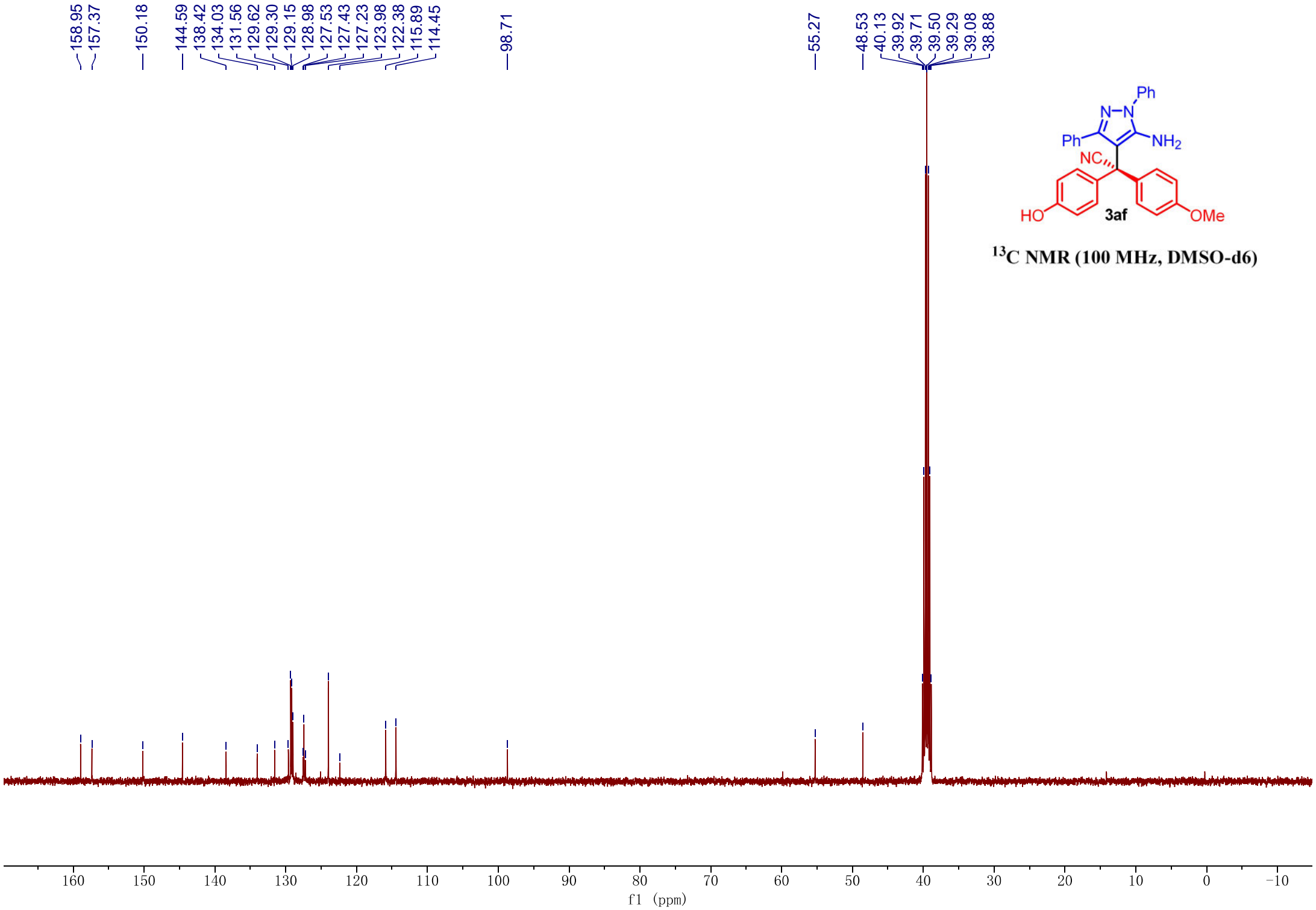

163.39
160.95
157.61
150.24
144.68
142.50
142.43
138.35
133.98
131.19
131.11
129.33
129.12
128.92
128.42
127.53
127.43
127.33
124.07
123.95
123.92
121.80
116.08
115.37
115.16
114.97
114.73
98.00
49.13
49.11
40.12
39.92
39.71
39.50
39.29
39.08
38.87
Ph
N–N
Ph
NH2
NC
F
HO
3ae
13C NMR (100 MHz, DMSO-d6)
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)



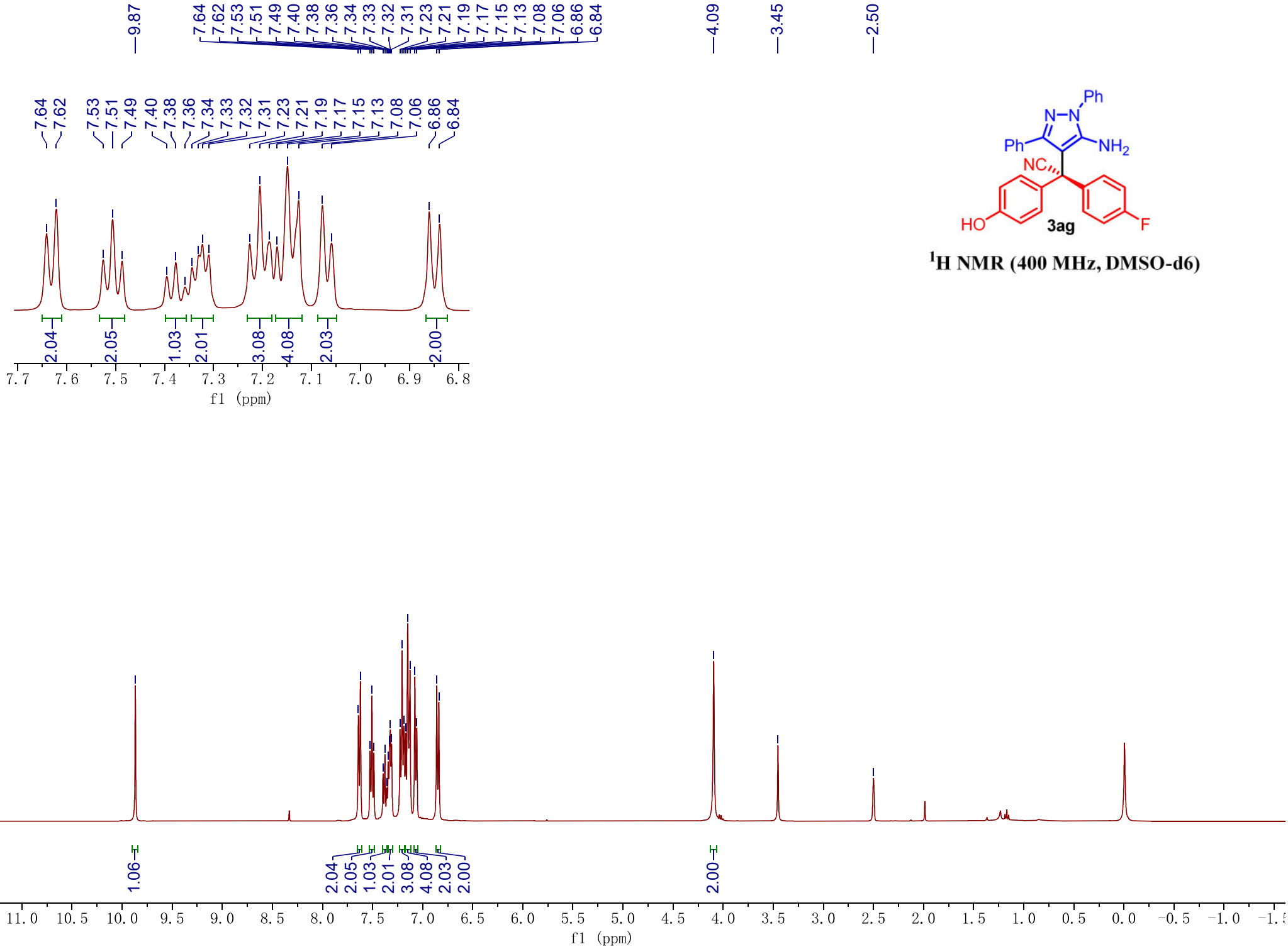
^{19}F NMR (376 MHz, DMSO-d6)



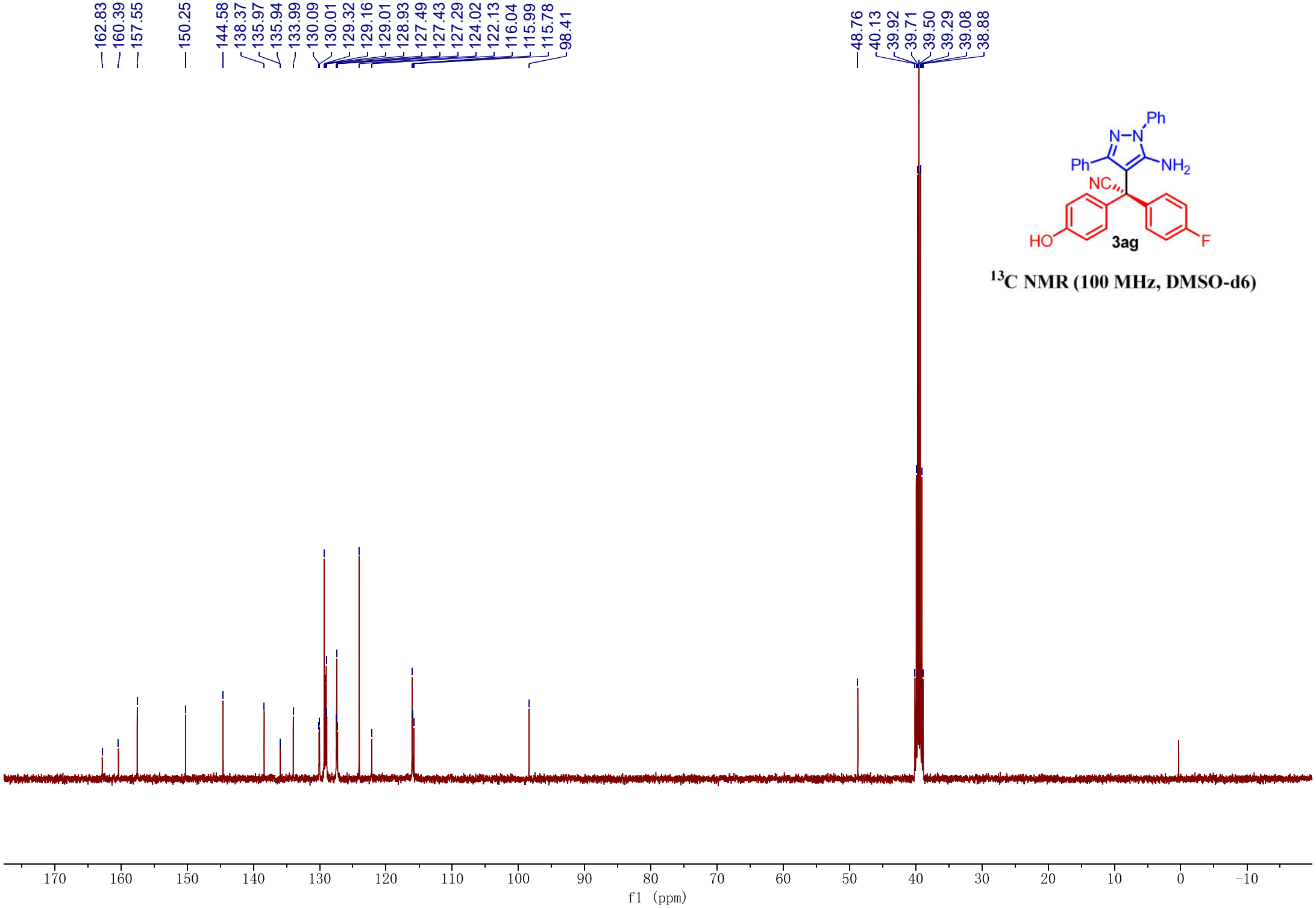
^{1}H NMR (400 MHz, DMSO-d6)

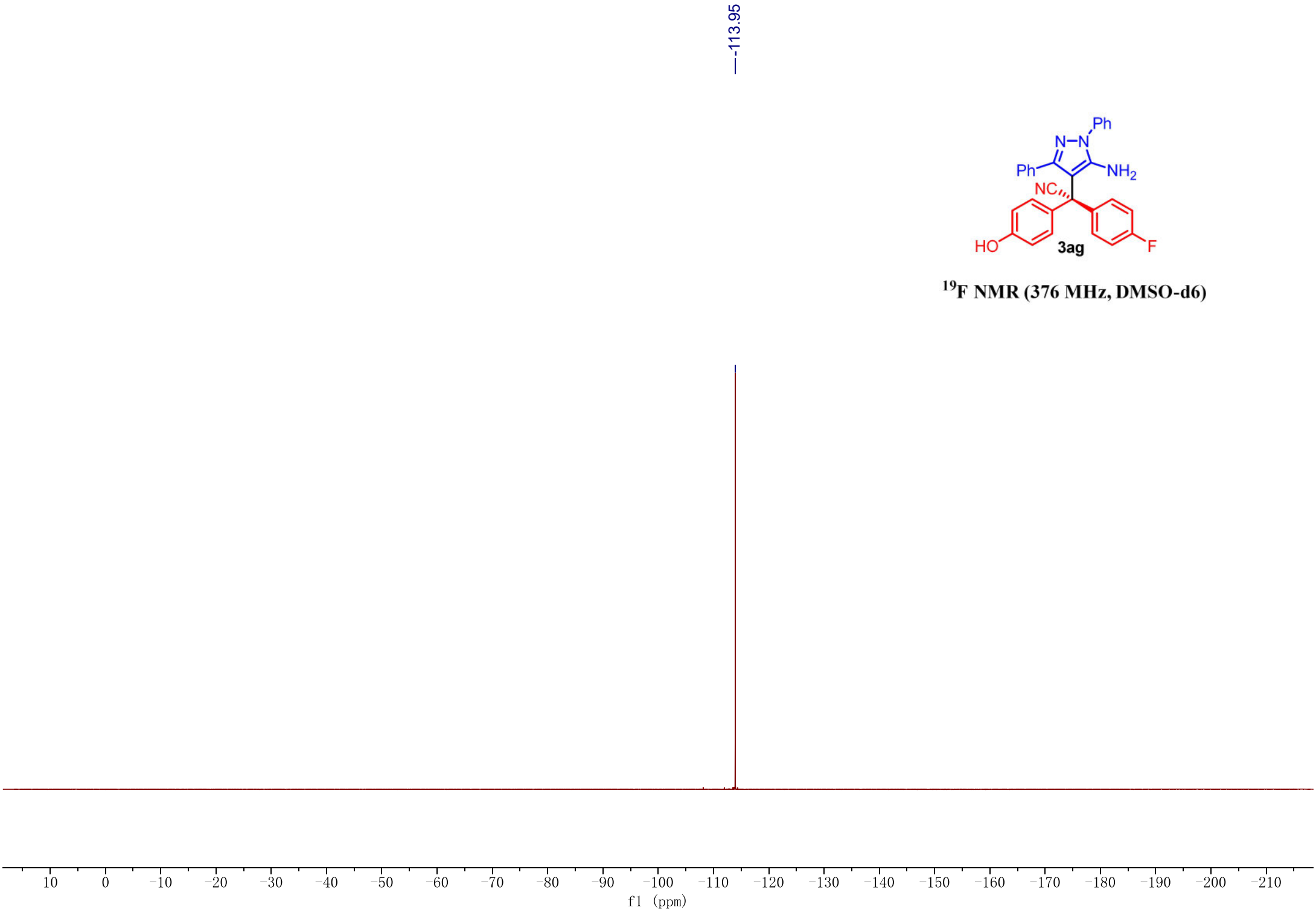


^{13}C NMR (100 MHz, DMSO-d6)

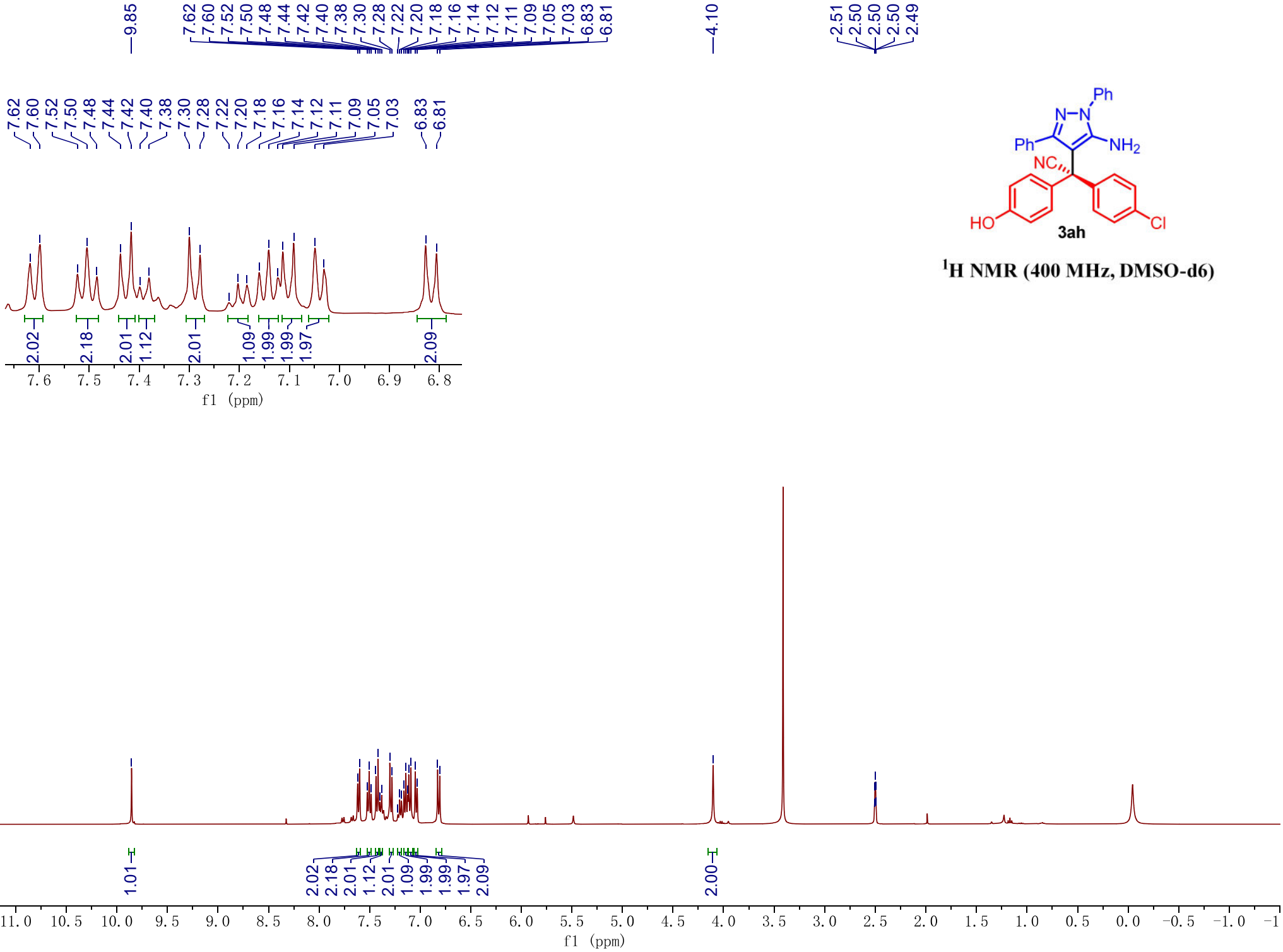


^{1}H NMR (400 MHz, DMSO-d6)

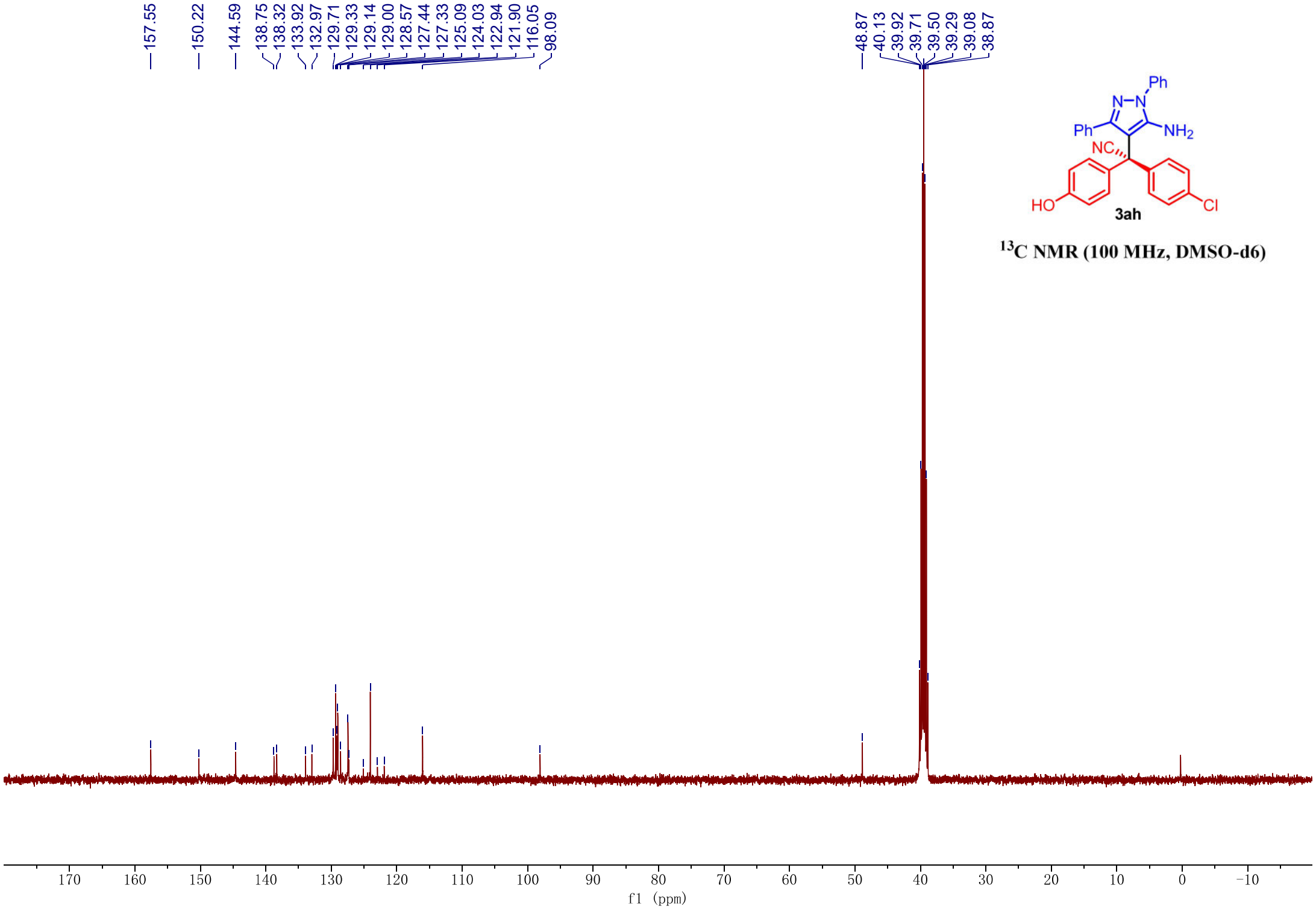

162.83
160.39
157.55
150.25
144.58
138.37
135.97
135.94
133.99
130.09
130.01
129.32
129.16
129.01
128.93
127.49
127.43
127.29
124.02
122.13
116.04
115.99
115.78
98.41
48.76
40.13
39.92
39.71
39.50
39.29
39.08
38.88
Ph
N–N
Ph
NH2
NC
HO
F
3ag
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

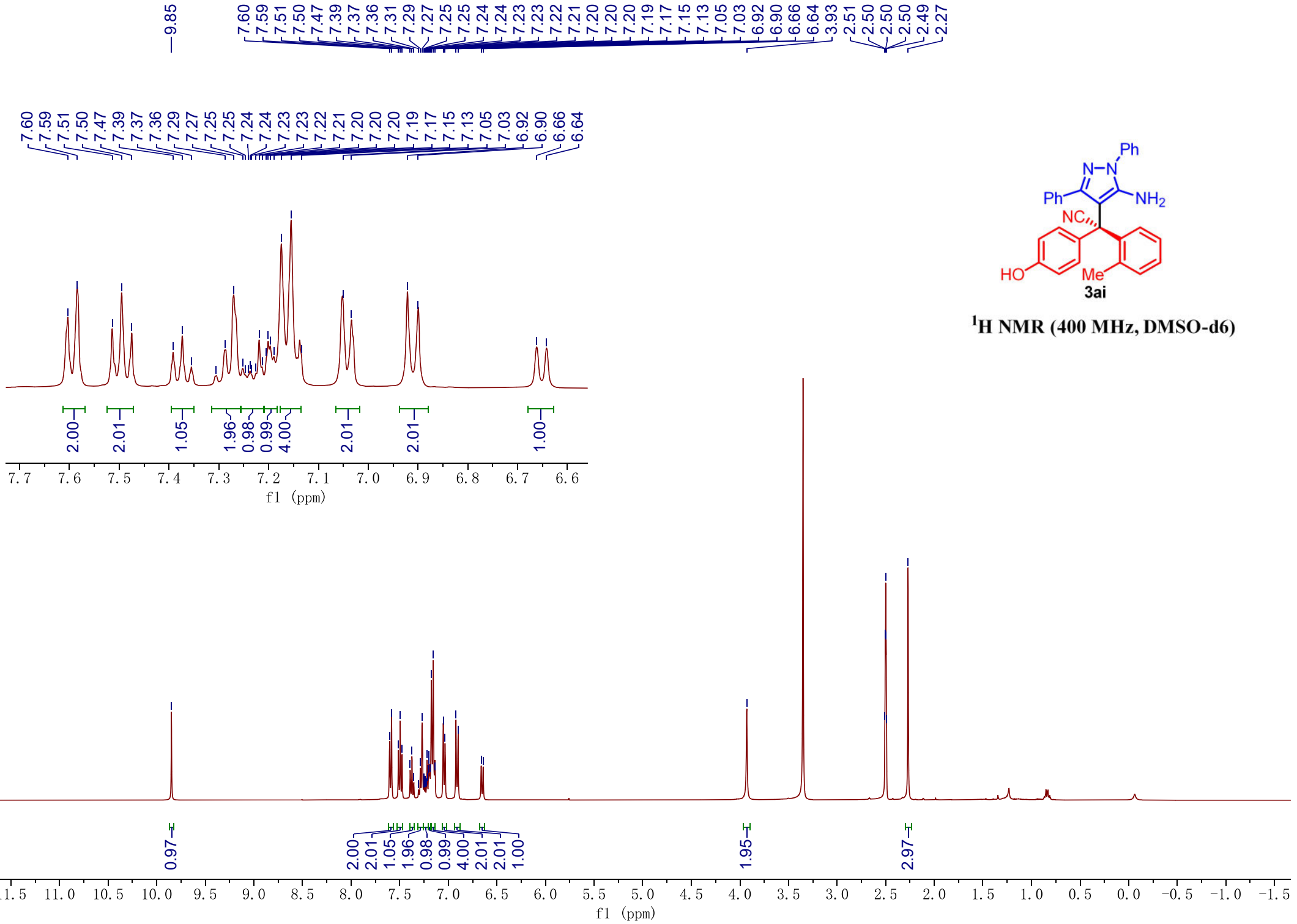


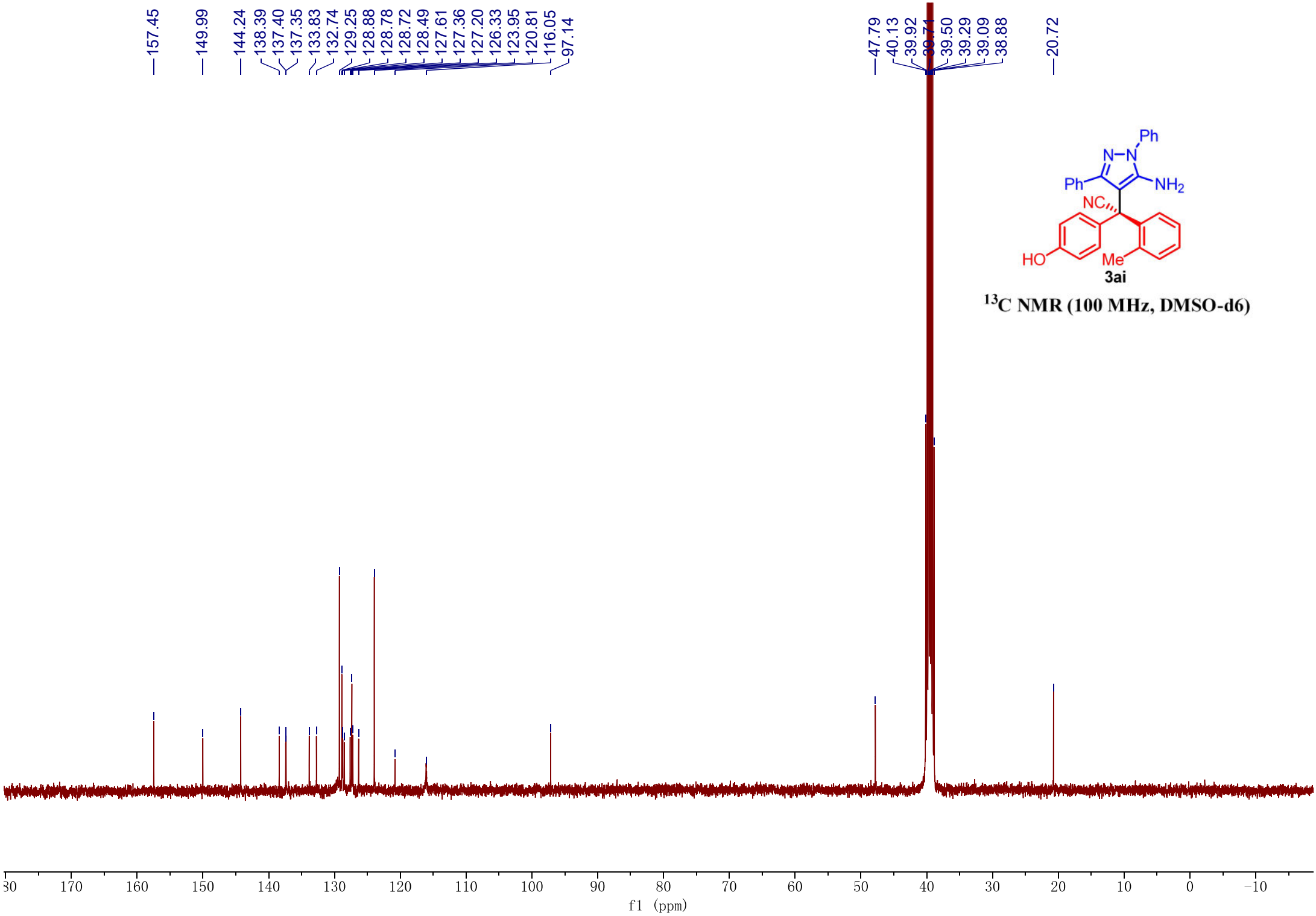
^{19}F NMR (376 MHz, DMSO-d6)

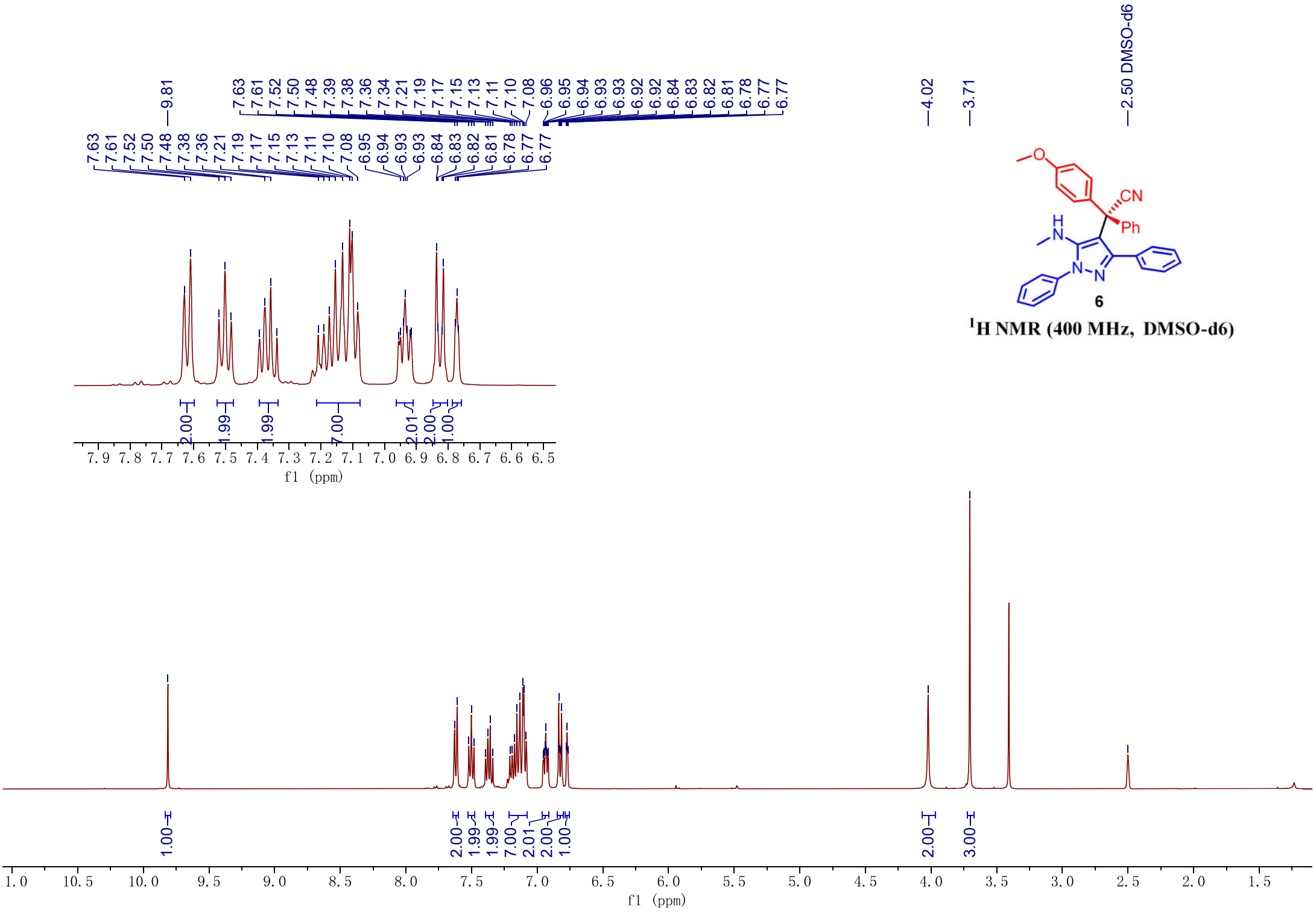


^{1}H NMR (400 MHz, DMSO-d6)

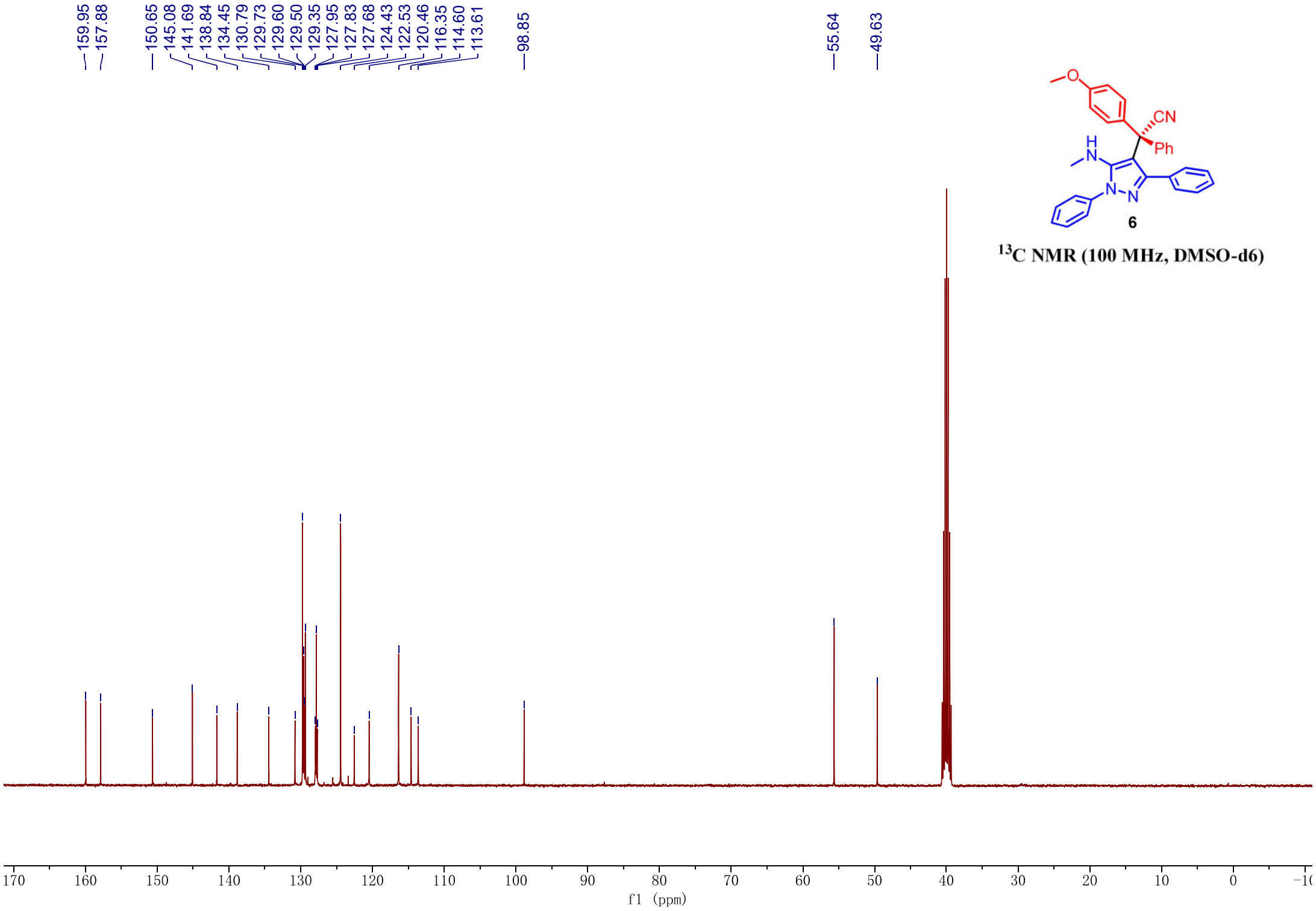

157.55
150.22
144.59
138.75
138.32
133.92
132.97
129.71
129.33
129.14
129.00
128.57
127.44
127.33
125.09
124.03
122.94
121.90
116.05
98.09
48.87
40.13
39.92
39.71
39.50
39.29
39.08
38.87
Ph
N–N
Ph
NH2
NC
HO
Cl
3ah
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

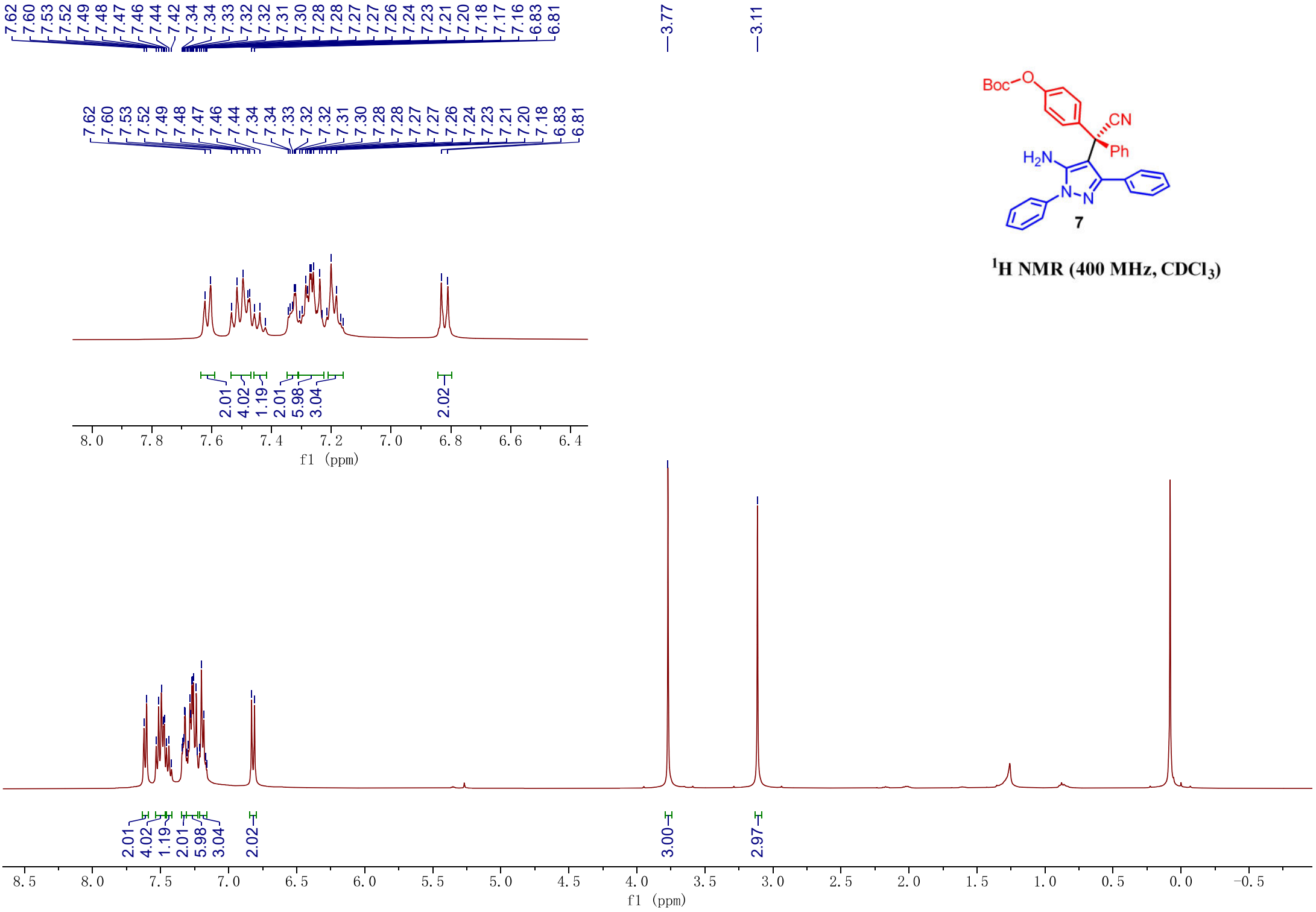

9.85
7.60 7.59 7.51 7.50 7.47 7.39 7.37 7.36 7.31 7.29 7.27 7.25 7.25 7.24 7.24 7.23 7.23 7.22 7.21 7.20 7.20 7.20 7.19 7.17 7.15 7.13 7.05 7.03 6.92 6.90 6.66 6.64 3.93 2.51 2.50 2.50 2.50 2.49 2.27
2.00 2.01 1.05 1.96 0.98 0.99 4.00 2.01 2.01 1.00
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6
f1 (ppm)
Ph
N–N
Ph
NH2
NC
HO
Me
3ai
1H NMR (400 MHz, DMSO-d6)
0.97 2.00 2.01 1.05 1.96 0.98 0.99 4.00 2.01 2.01 1.00 1.95 2.97
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0 −1.5
f1 (ppm)

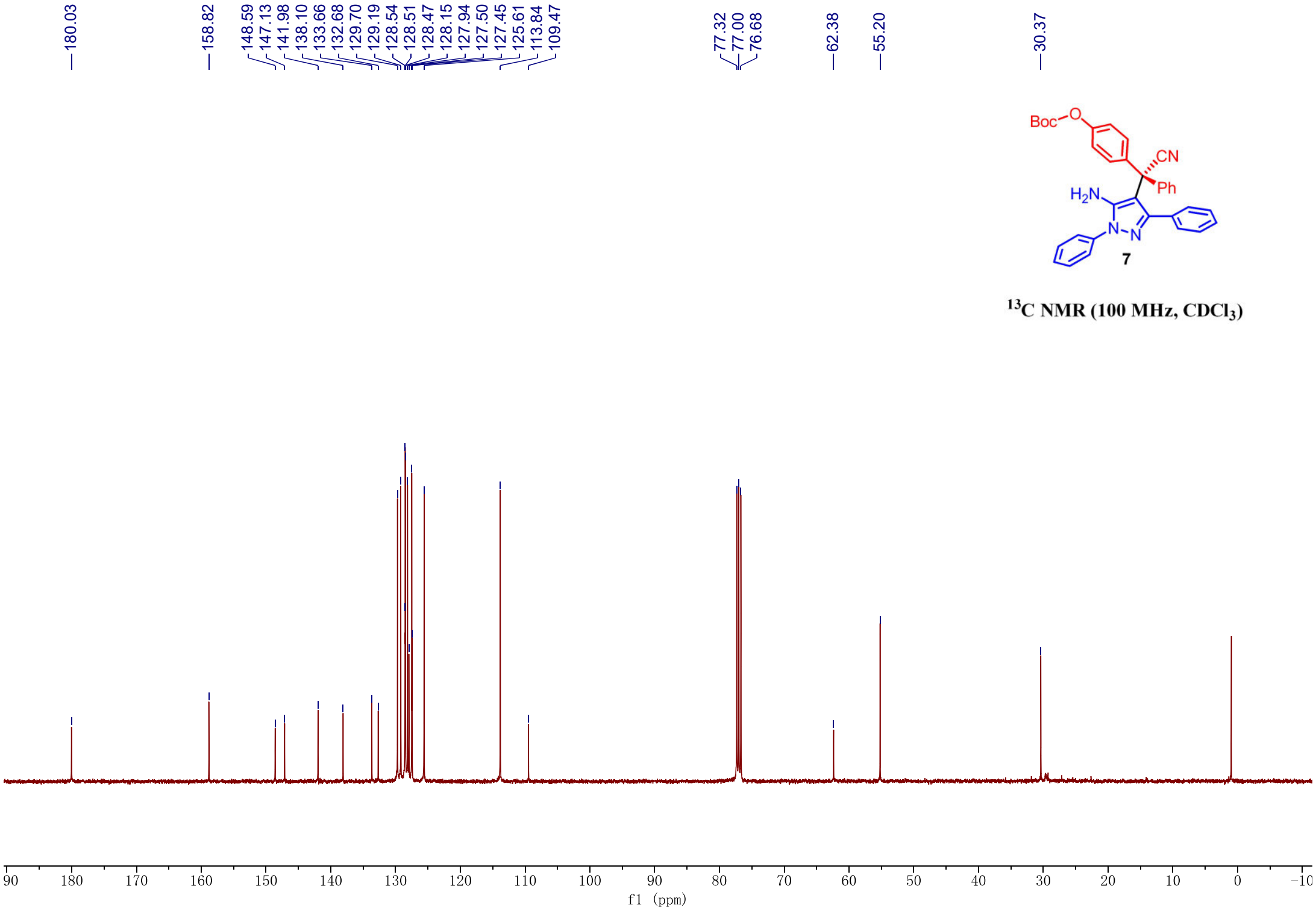

157.45
149.99
144.24
138.39
137.40
137.35
133.83
132.74
129.25
128.88
128.78
128.72
128.49
127.61
127.36
127.20
126.33
123.95
120.81
116.05
97.14
47.79
40.13
39.92
39.71
39.50
39.29
39.09
38.88
20.72
Ph
N–N
Ph
NH2
NC
HO
Me
3ai
13C NMR (100 MHz, DMSO-d6)
f1 (ppm)



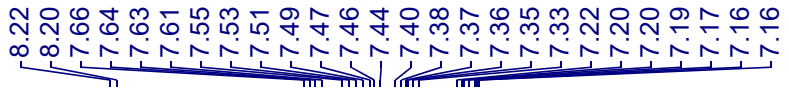
^{1}H NMR (400 MHz, DMSO-d6)

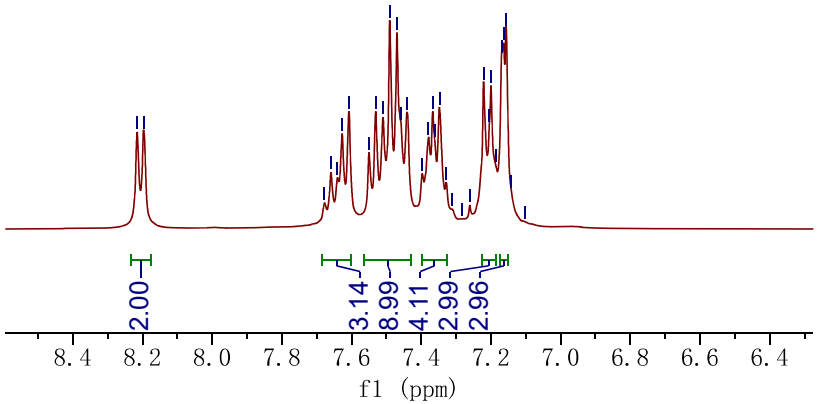

159.95
157.88
150.65
145.08
141.69
138.84
134.45
130.79
129.73
129.60
129.50
129.35
127.95
127.83
127.68
124.43
122.53
120.46
116.35
114.60
113.61
98.85
55.64
49.63
O
CN
Ph
H
N
N
N
6
13C NMR (100 MHz, DMSO-d6)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

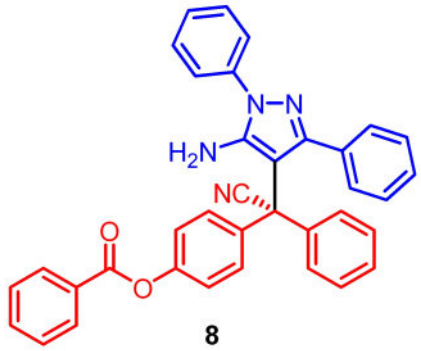

7.62
7.60
7.53
7.52
7.49
7.48
7.47
7.46
7.44
7.42
7.34
7.34
7.33
7.32
7.32
7.31
7.30
7.28
7.28
7.27
7.27
7.26
7.24
7.23
7.21
7.20
7.18
7.17
7.16
6.83
6.81
3.77
3.11
Boc
O
CN
Ph
H2N
N
N
7
1H NMR (400 MHz, CDCl3)
2.01
4.02
1.19
2.01
5.98
3.04
2.02
3.00
2.97
f1 (ppm)



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

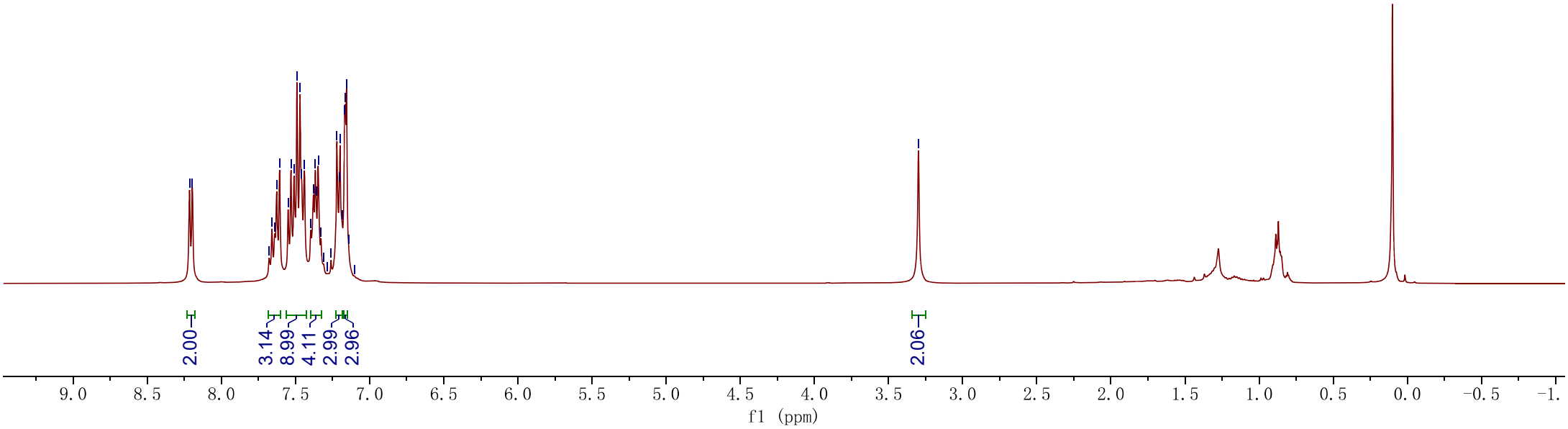


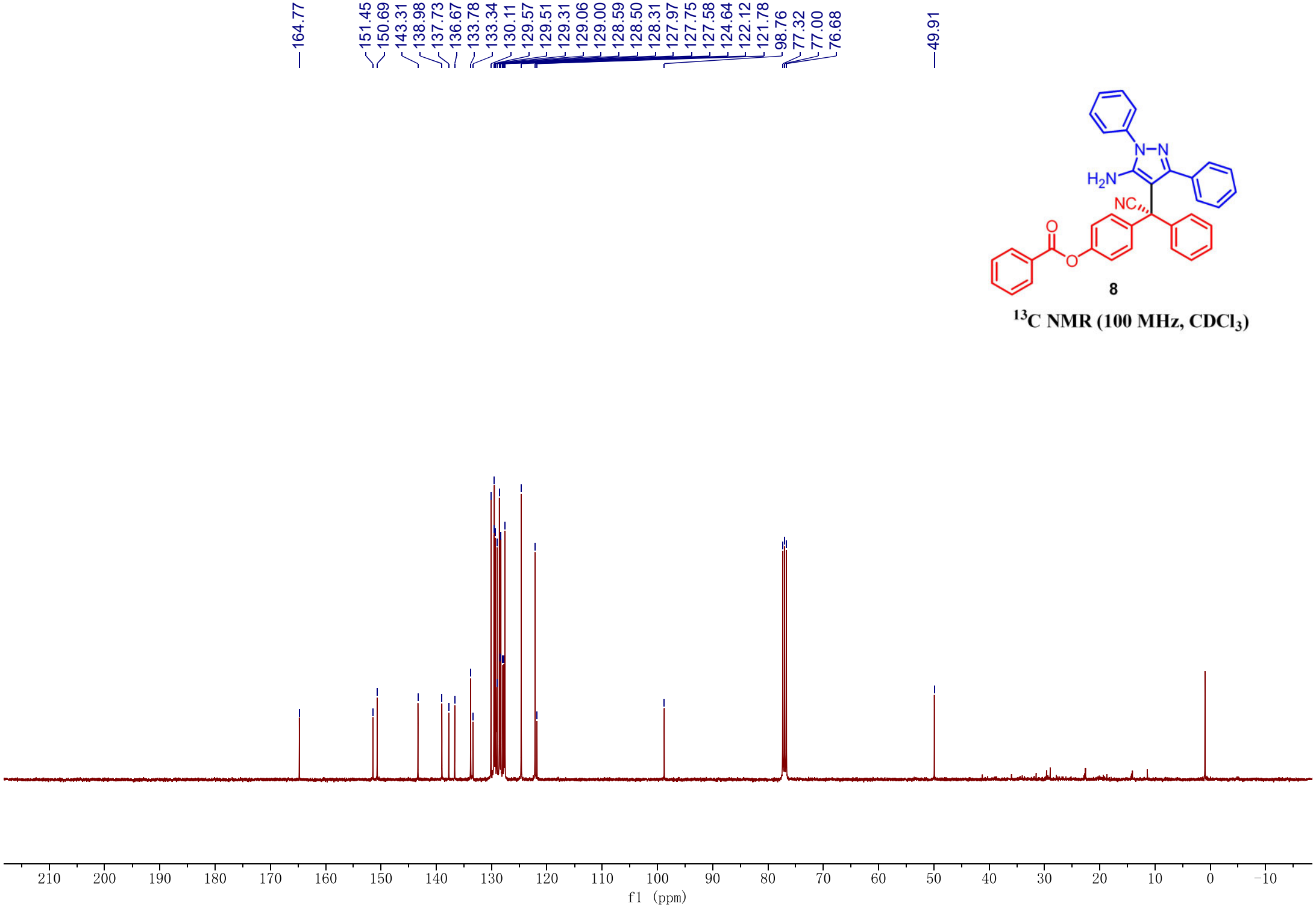




8

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




164.77
151.45
150.69
143.31
138.98
137.73
136.67
133.78
133.34
130.11
129.57
129.51
129.31
129.06
129.00
128.59
128.50
128.31
127.97
127.75
127.58
124.64
122.12
121.78
98.76
77.32
77.00
76.68
49.91
N–N
H2N
NC
O
O
8
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)