Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information

Access to 2-pyridinones comprising enaminonitriles via AgOAc promoted cascade reactions of thioesters with aminomethylene malononitriles

Chen Zhu,[a,b] Jubao Zhou,[b] Tianxing Li,[b] Jiaxin Yang,[b] Hui Jin,*[,b] and Lixin Zhang*[,a,b]

[a] School of Chemical Engineering, University of Science and Technology Liaoning, Anshan 110031, People's Republic of China

[b] National-Local Joint Engineering Laboratory for Development of Boron and Magnesium Resources and Fine Chemical Technology, Liaoning Province Key Laboratory of Green Functional Molecular Design and Development, Institute of Functional Molecules, Shenyang University of Chemical Technology, Shenyang 110142, People's Republic of China

E-mail: hjin@syuct.edu.cn; zhanglixin@syuct.edu.cn

Contents

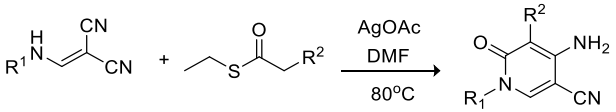
1.General information

Unless stated otherwise, reagents were used directly as obtained commercially. Reactions were monitored by TLC using silica gel GF254 plates. Flash column chromatography was performed using silica gel. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were recorded on Bruker AV III 400MHz NMR spectrometers. Chemical shifts are reported in ppm using tetramethylsilane or the residual solvent peak as a reference. Infrared spectra were recorded on a Bruker Tensor 27 FT-IR. HRMS were recorded on a Waters Xevo G2-XS TOF mass spectrometer. MS were recorded on a Waters Acquity Qda. UV-vis absorption spectroscopy was recorded on Agilent Cary 5000 UV-Vis-NIR. Fluorescence emission spectroscopy was recorded on Edinburgh FS5 Fluorescence Spectrometer.

Thioesters [1] aminomethylene malononitriles, [2] and *N*-phenylcarbonohydrazonoyl dicyanide[3] were prepared according to previously reported procedures.

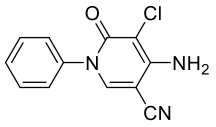
2. Preparation and characterization of 2-pyridinones

General procedure



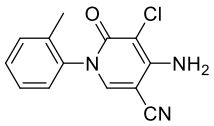
To a stirred solution of **1** (0.2 mmol, 1 equiv.) and thioester **4** (0.4 mmol, 2 equiv.) in *N,N*-dimethylformamide (2 mL) were added AgOAc (0.8 mmol, 4 equiv.). The reaction mixture was stirred for 4h at 80 °C and then extracted with ethyl acetate. The combined organic layer was washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo to give the crude product which was purified by column chromatography (petroleum ether:ethyl acetate = 2:1) to afford the desired product **5** and **6**.

4-amino-5-chloro-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (**5a**)



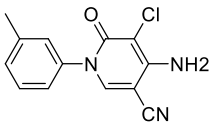
Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol) , **5a** was obtained as a faint yellow solid (44.1 mg, 90% yield). **Gram scale**: Following the general procedure with **1a** (1.44 g, 8.5 mmol) and **4c** (2.35 g, 17.0 mmol), **5a** was obtained as a faint yellow solid (1.90 g, 91% yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.74 (s, 1H), 7.52 - 7.45 (m, 3H), 7.35 - 7.30 (m, 2H), 5.22 (s, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 157.5, 148.4, 142.8, 139.3, 129.6, 129.4, 126.5, 114.0, 101.6, 84.4 ppm; **IR** (KBr) 3472, 3180, 2922, 2220, 1678, 1630, 1507, 1491, 1460, 1451, 1268, 1248, 903, 846, 772, 737, 700, 662, 612 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{12}H_8N_3OClNa$ 268.0254, found 268.0257.

4-amino-5-chloro-6-oxo-1-(*o*-tolyl)-1,6-dihydropyridine-3-carbonitrile (**5b**)



Following the general procedure with 2-((*o*-tolylamino)methylene)malononitrile (36.6 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol) , **5b** was obtained as a faint yellow solid (40.9 mg, 79% yield). R_f = 0.5 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.35 (s, 1H), 7.54 – 7.15 (m, 4H), 6.93 (s, 2H), 2.04 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.2, 150.5, 146.1, 139.4, 135.5, 131.1, 129.7, 128.3, 127.4, 115.2, 98.6, 83.8, 17.5 ppm;**IR** (KBr) 3331, 3201, 2927, 2224, 1626, 1507, 1466, 1385, 1354, 1255, 1095, 1011, 842, 736, 661, 622 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{13}H_{10}N_3OClNa$ 282.0410, found 282.0414.

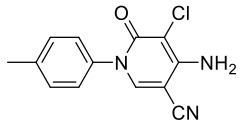
4-amino-5-chloro-6-oxo-1-(*m*-tolyl)-1,6-dihydropyridine-3-carbonitrile (**5c**)



Following the general procedure with 2-((*m*-tolylamino)methylene)malononitrile (36.6 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol) , **5c** was obtained as a faint yellow solid (44.0 mg, 85% yield). R_f = 0.5 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.72 (s, 1H), 7.39 - 7.34 (m, 1H), 7.29 - 7.24 (m, 1H), 7.16 - 7.08 (m, 2H), 5.19 (s, 2H), 2.40 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 157.6, 148.3, 142.9, 139.8, 139.2, 130.2, 129.4, 127.1, 123.4, 114.1,

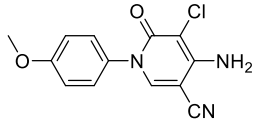
101.7, 84.3, 21.3 ppm; **IR** (KBr) 3382, 3324, 3211, 2920, 2850, 2233, 1638, 1607, 1505, 1473, 1318, 1250, 1037, 845, 773, 556 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{13}H_{10}N_3OClNa$ 282.0410, found 282.0411.

4-amino-5-chloro-6-oxo-1-(*p*-tolyl)-1,6-dihydropyridine-3-carbonitrile (**5d**)



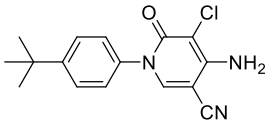
Following the general procedure with 2-((*p*-tolylamino)methylene)malononitrile (36.6 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol) , **5d** was obtained as a faint yellow solid (44.0 mg, 85% yield). R_f = 0.4 (petroleum ether:ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.38 (s, 1H), 7.28 (s, 4H), 6.89 (s, 2H), 2.36 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.4, 150.3, 146.1, 138.7, 137.5, 129.8, 127.2, 115.2, 98.6, 83.6, 21.1 ppm; **IR** (KBr) 3384, 3324, 3215, 2290, 2851, 2234, 1640, 1606, 1504, 1246, 1019, 850, 813, 745, 576 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{13}H_{10}N_3OClNa$ 282.0410, found 282.0414.

4-amino-5-chloro-1-(4-methoxyphenyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5e**)



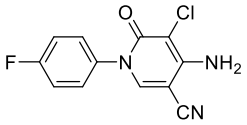
Following the general procedure with 2-(((4-methoxyphenyl)amino)methylene)malononitrile (39.8 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5e** was obtained as a faint yellow solid (41.8 mg, 76% yield). R_f = 0.3 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (600 MHz, $CDCl_3$) *δ* 7.72 (s, 1H), 7.24 (d, *J* = 8.9 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 5.15 (s, 2H), 3.85 (s, 3H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) *δ* 160.1, 157.8, 148.2, 143.1, 132.0, 127.6, 114.7, 114.1, 101.7, 84.1, 55.6 ppm; **IR** (KBr) 3388, 3326, 3215, 2921, 2233, 1638, 1507, 1472, 1245, 1177, 1030, 823, 742, 565 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{13}H_{10}N_3O2ClNa$ 298.0359, found 298.0363.

4-amino-1-(4-(*tert*-butyl)phenyl)-5-chloro-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5f**)



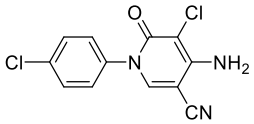
Following the general procedure with 2-(((4-(*tert*-butyl)phenyl)amino)methylene)malononitrile (45.0 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5f** was obtained as a faint yellow solid (55.4 mg, 92% yield). R_f = 0.6 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.74 (s, 1H), 7.52 - 7.47 (m, 2H), 7.29 - 7.19 (m, 2H), 5.17 (s, 2H), 1.34 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 157.6, 152.7, 148.3, 143.0, 136.7, 126.6, 125.9, 114.1, 101.7, 84.2, 34.8, 31.3 ppm; **IR** (KBr) 3461, 3184, 2957, 2218, 1670, 1636, 1609, 1510, 1474, 1357, 1265, 1027, 834, 682, 663 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{16}H_{16}N_3OClNa$ 324.0880, found 324.0885.

4-amino-5-chloro-1-(4-fluorophenyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5g**)



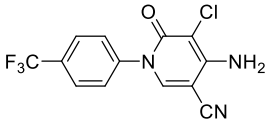
Following the general procedure with 2-(((4-fluorophenyl)amino)methylene)malononitrile (37.4 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5g** was obtained as a faint yellow solid (43.7 mg, 83% yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.43 (s, 1H), 7.51 - 7.43 (m, 2H), 7.37 - 7.30 (m, 2H), 6.94 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.2 (d, J = 245.6 Hz), 136.2 (d, J = 3.0 Hz), 129.9 (d, J = 8.9 Hz), 116.2 (d, J = 23.1 Hz) δ 157.4, 150.4, 146.2, 115.2, 98.5, 83.8 ppm; **IR** (KBr) 3416, 3179, 3921, 2225, 1629, 1501, 1465, 1250, 1217, 1018, 927, 838, 747, 613 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{12}H_7N_3OClFNa$ 286.0159, found 286.0164.

4-amino-5-chloro-1-(4-chlorophenyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5h**)



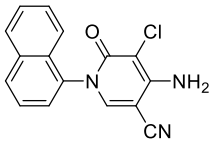
Following the general procedure with 2-(((4-chlorophenyl)amino)methylene)malononitrile (40.6 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5h** was obtained as a faint yellow solid (53.0 mg, 95% yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1);**^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.43 (s, 1H), 7.61 - 7.29 (m, 4H), 6.96 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.3, 150.4, 146.0, 138.7, 133.7, 129.5, 129.4, 115.2, 98.4, 83.9 ppm; **IR** (KBr) 2922, 2853, 2219, 1653, 1590, 1493, 1463, 1370, 1340, 1091, 823, 750, 578 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{12}H_7N_3OCl_2Na$ 301.9864, found 301.9861.

4-amino-5-chloro-6-oxo-1-(4-(trifluoromethyl)phenyl)-1,6-dihydropyridine-3-carbonitrile (**5i**)



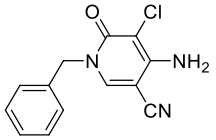
Following the general procedure with 2-(((4-(trifluoromethyl)phenyl)amino)methylene) malononitrile (47.4 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5i** was obtained as a faint yellow solid (55.1 mg, 88% yield). R_f = 0.6 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (600 MHz, $CDCl_3$) *δ* 7.78 (d, *J* = 8.3 Hz, 2H), 7.74 (s, 1H), 7.50 (d, *J* = 8.3 Hz, 2H), 5.23 (s, 2H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 131.66 (q, J = 33.3, 32.9 Hz), 126.83 (q, J = 4.3, 3.9 Hz), 126.32 – 120.49 (m).δ 157.11, 148.35, 142.07, 127.09, 113.63, 101.66, 85.27 ppm; **IR** (KBr) 3490, 3365, 2922, 2233, 1643, 1607, 1510, 1476, 1415, 1317, 1255, 1165, 1111, 1064, 1015, 918, 833, 746, 682, 596 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{13}H_7N_3OClF_3Na$ 336.0127, found 336.0128.

4-amino-5-chloro-1-(naphthalen-1-yl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5j**)



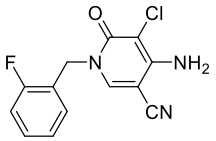
Following the general procedure with 2-((naphthalen-1-ylamino)methylene)malononitrile (43.8 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5j** was obtained as a faint yellow solid (38.9 mg, 66% yield). R_f = 0.5 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.51 (s, 1H), 8.14 - 7.99 (m, 2H), 7.68 - 7.52 (m, 4H), 7.46 - 7.40 (m,, 1H), 7.01 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.8, 150.7, 146.8, 136.81, 134.1, 130.0, 129.7, 128.7, 127.9, 127.2, 126.3, 126.1, 122.8, 115.2, 98.5, 84.1 ppm; **IR** (KBr) 3331, 2925, 2855, 2225, 1746, 1641, 1505, 1392, 1268, 1152, 846, 774 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* [M+Na]$^+$ Calcd for $C_{16}H_{10}N_3OClNa$ 318.0410, found 318.0414.

4-amino-1-benzyl-5-chloro-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5k**)



Following the general procedure with 2-((benzylamino)methylene)malononitrile (36.6 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol) **5k** was obtained as a faint yellow solid (46.6 mg, 90% yield). **Gram scale**: Following the general procedure A with 2-((benzylamino)methylene)malononitrile (1.56 g, 8.5 mmol) and **4c** (2.35 g, 17.0 mmol), **5k** was obtained as a faint yellow solid (2.03 g, 92% yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz,$CDCl_3$) *δ* 7.60 (s, 1H), 7.43 - 7.28 (m, 5H), 5.12 (s, 4H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 164.2, 161.7, 157.8, 148.2, 141.8, 130.7, 130.6, 116.4, 116.2, 114.0, 101.8, 84.2, 52.4 ppm; **IR** (KBr) 3460, 3176, 2921, 2223, 1633, 1603, 1515, 967, 843, 734, 674 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* [M+Na]$^+$ Calcd for $C_{13}H_{10}N_3OClNa$ 282.0410, found 282.0414.

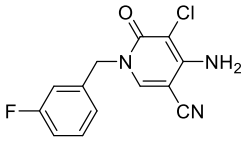
4-amino-5-chloro-1-(2-fluorobenzyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5l**)



Following the general procedure with 2-(((2-fluorobenzyl)amino)methylene)malononitrile (40.2 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5l** was obtained as a faint yellow solid (47.7 mg, 86% yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.61 (s, 1H), 7.43 - 7.36 (m, 2H), 7.22

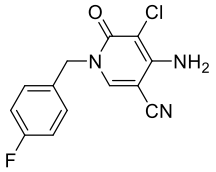
- 7.13 (m, 2H), 6.82 (s, 2H), 5.02 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.2 (d, J = 243.9 Hz), 133.3 (d, J = 3.1 Hz), 130.6 (d, J = 8.4 Hz), 115.8 (d, J = 21.4 Hz). δ 157.4, 150.3, 145.9, 115.3, 98.8, 83.1, 51.9 ppm; **IR** (KBr): v = 3480, 3309, 3194, 2920, 2221, 1634, 1594, 1504, 1212, 894, 846, 821, 768, 742, 644, 591 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* [M+Na]+ Calcd for $C_{13}H_9N_3OClFNa$ 300.0316, found 300.0320.

4-amino-5-chloro-1-(3-fluorobenzyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5m**)



Following the general procedure with 2-(((3-fluorobenzyl)amino)methylene)malononitrile (40.2 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5m** was obtained as a faint yellow solid (47.1 mg, 85 % yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.61 (s, 1H), 7.48 - 6.71 (m, 6H), 5.05 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.6 (d, J = 243.8 Hz), 139.8 (d, J = 7.4 Hz), 131.1 (d, J = 8.3 Hz), 124.3 (d, J = 2.8 Hz), 115.2 (d, J = 21.9 Hz), 115.0 (d, J = 20.9 Hz). 157.4, 150.4, 146.1, 115.3, 98.7 ppm; **IR** (KBr) 3460, 3180, 2224, 1633, 1593, 1514, 1482, 1450, 1138, 949, 900, 839, 794, 755, 670 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* [M+Na]$^+$ Calcd for $C_{13}H_9N_3OFClNa$ 300.0316, found 300.0320.

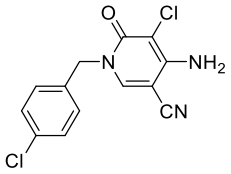
4-amino-5-chloro-1-(4-fluorobenzyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5n**)



Following the general procedure with 2-(((4-fluorobenzyl)amino)methylene)malononitrile (40.2 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5n** was obtained as a faint yellow solid (51.0 mg, 92% yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.61 (s, 1H), 7.36 - 7.29 (m, 2H), 7.10 - 7.01 (m, 2H), 5.10 (s, 2H), 5.09 (s, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.0 (d, J = 248.2 Hz),130.6 (d, J = 8.5 Hz), 116.3 (d, J = 22.1 Hz), δ 157.8, 148.3,

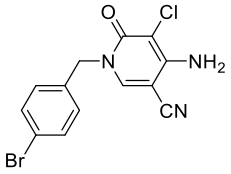
141.8, 130.7, 114.0, 101.7, 84.2, 52.4 ppm; **IR** (KBr) 3480, 3306, 3195, 2921, 2221, 1634, 1594, 1504, 1212, 846, 822, 769, 742, 645, 591 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ Calcd for $C_{13}H_{10}N_3OFCl$ 278.0496, found 278.0501.

4-amino-5-chloro-1-(4-chlorobenzyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5o**)



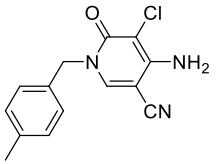
Following the general procedure with 2-(((4-chlorobenzyl)amino)methylene)malononitrile (43.4 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5o** was obtained as a faint yellow solid (54.5 mg, 93% yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.60 (s, 1H), 7.37 - 7.33 (m, 2H), 7.27 (s, 1H), 7.25 (s, 1H), 5.08 (s, 4H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 157.6, 148.3, 141.8, 135.0, 133.3, 130.0, 129.5, 113.9, 112.3, 84.3, 52.4 ppm; **IR** (KBr) 3470, 3340, 2921, 2851, 2227, 1642, 1512, 1490, 1471, 1385, 1090, 890, 840, 801, 758, 742, 578 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{13}H_9N_3OFCl_2Na$ 316.0020, found 316.0025.

4-amino-1-(4-bromobenzyl)-5-chloro-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5p**)



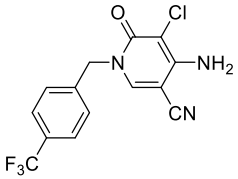
Following the general procedure with 2-(((4-bromobenzyl)amino)methylene)malononitrile (52.2 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5p** was obtained as a faint yellow solid (55.3 mg, 82% yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.60 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.84 (s, 2H), 5.01 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.4, 150.3, 146.0, 136.5, 131.9, 130.6, 121.4, 115.3, 98.8, 83.2, 52.0 ppm; **IR** (KBr) 3541, 3433, 3334, 2222, 1652, 1513, 1485, 1386, 1070, 1009, 889, 837, 796, 758, 740, 628 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{13}H_9BrClN_3ONa$ 359.9515, found 359.9513.

4-amino-5-chloro-1-(4-methylbenzyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5q**)



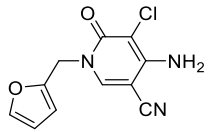
Following the general procedure with 2-(((4-methylbenzyl)amino)methylene)malononitrile (39.4 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5q** was obtained as a faint yellow solid (47 mg, 86% yield). R_f = 0.4 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.20 (s, 4H), 5.07 (s, 4H), 2.35 (s, 3H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.8, 148.2, 141.8, 133.8, 132.5, 130.3, 123.1, 113.9, 101.7, 84.3, 52.5 ppm; **IR** (KBr) 3460, 3179, 2224, 1633, 1593, 1514, 1482, 1450, 1138, 965, 949, 900, 839, 794, 755, 670, 622 cm^{-1}； **HRMS** (ESI-QTOF) *m/z* [M+Na]+ Calcd for $C_{14}H_{12}N_3OCl$296.0567, found 296.0570.

4-amino-5-chloro-6-oxo-1-(4-(trifluoromethyl)benzyl)-1,6-dihydropyridine-3-carbonitrile (**5r**)



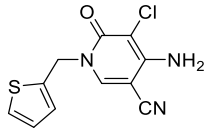
Following the general procedure with 2-(((4-(trifluoromethyl)benzyl)amino)methylene)malononitrile (50.2 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5r** was obtained as a faint yellow solid (53.6 mg, 82% yield). R_f = 0.3 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.63 (d, *J* = 8.1 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 5.17 (s, 2H), 5.15 (s, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 131.1 (q, J = 33.0 Hz), 126.2 (q, J = 3.8 Hz), 123.8 (q, J = 272.2 Hz)δ 157.7, 148.4, 141.9, 138.8, 128.7, 113.8, 101.7, 84.5, 52.7 ppm; **IR** (KBr): v = 3547, 3436, 3343, 2921, 2225, 1647, 1514, 1320, 1168, 1122, 1064, 840, 815, 634, 592 ppm cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{14}H_9N_3OClF_3Na$ 350.0284, found 350.0288.

4-amino-5-chloro-1-(furan-2-ylmethyl)-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5s**)



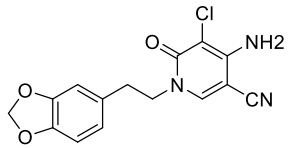
Following the general procedure with 2-(((furan-2-ylmethyl)amino)methylene)malononitrile (34.6 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5s** was obtained as a faint yellow solid (37.4 mg, 75% yield). R_f = 0.3 (petroleum ether:ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.48 (s, 1H), 7.64 - 7.59 (m, 1H), 6.83 (s, 2H), 6.42 (s, 2H), 5.07 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.1, 150.2, 149.7, 145.6, 143.7, 115.2, 111.2, 109.7, 98.6, 83.2, 45.2 ppm **IR** (KBr) 3340, 3333, 3194, 3134, 2920, 2218, 1637, 1598, 1513, 1476, 1151, 1009, 896, 767, 741 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* [M+Na]$^+$ Calcd for $C_{11}H_8N_3O_2ClNa$ 272.0203, found 272.0207.

4-amino-5-chloro-6-oxo-1-(thiophen-2-ylmethyl)-1,6-dihydropyridine-3-carbonitrile (**5t**)



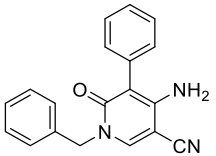
Following the general procedure with 2-(((thiophen-2-ylmethyl)amino)methylene)malononitrile (37.8 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5t** was obtained as a faint yellow solid (41.3 mg, 78% yield). R_f = 0.4 (petroleum ether:ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.64 (s, 1H), 7.36 - 7.33(m, 1H), 7.17 - 7.13 (m, 1H), 7.04 - 6.99 (m, 1H), 5.28 (s, 2H), 5.09 (s, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 157.6, 148.3, 141.4, 135.9, 129.0, 127.6, 127.5, 114.1, 101.6, 84.2, 47.4 ppm; **IR** (KBr) 3451, 3350, 2921, 2219, 1651, 1600, 1513, 1332, 1196, 1077, 1037, 893, 839, 754, 718 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* [M+Na]$^+$ Calcd for $C_{11}H_8N_3OSClNa$ 287.9974, found 287.9976.

4-amino-1-(2-(benzo[*d*][1,3]dioxol-5-yl)ethyl)-5-chloro-6-oxo-1,6-dihydropyridine-3-carbonitrile (**5u**)



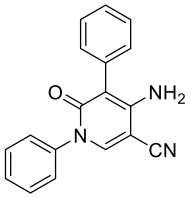
Following the general procedure with 2-(((2-(benzo[*d*][1,3]dioxol-5-yl)ethyl)amino)methylene)malononitrile (48.2 mg, 0.2 mmol) and **4c** (55.2 mg, 0.4 mmol), **5u** was obtained as a faint yellow solid (52.6 mg, 83% yield). R_f = 0.42 (petroleum ether:ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.21 (s, 1H), 6.85 - 6.73 (m, 4H), 6.62 - 6.57 (m, 1H), 5.98 (s, 2H), 4.06 - 3.97 (m, 2H), 2.87 - 2.79 (m, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.4, 150.1, 147.8, 146.3, 145.8, 131.9, 122.3, 115.4, 109.6, 108.7, 101.3, 98.7, 82.2, 51.1, 34.6 ppm; **IR** (KBr 3441, 3353, 2924, 2222, 1661, 1485, 1376, 1242, 1189, 1041, 906, 845, 754 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{15}H_{12}ClN_3O_3Na$ 340.0465, found 340.0460.

4-amino-1-benzyl-6-oxo-5-phenyl-1,6-dihydropyridine-3-carbonitrile (**6a**)



Following the general procedure with 2-((benzylamino)methylene)malononitrile (36.6 mg, 0.2 mmol) and S-ethyl 2-phenylethanethioate (72.0 mg, 0.4 mmol) **6a** was obtained as a faint yellow solid (57.2 mg, 95% yield). **Gram scale**: Following the general procedure A with 2-((benzylamino)methylene)malononitrile (1.56 g, 8.5 mmol) and S-ethyl 2-phenylethanethioate (3.06 g, 17.0 mmol), **6a** was obtained as a faint yellow solid (2.43 g, 95% yield). R_f = 0.48 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.66 (s, 1H), 7.50 - 7.43 (m, 2H), 7.41 - 7.33 (m, 8H), 5.11 (s, 2H), 4.59 (s, 2H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) *δ* 160.7, 148.9, 143.3, 135.3, 132.6, 130.3, 129.3, 129.2, 128.8, 128.6, 128.2, 115.1, 108.1, 84.5, 52.4 ppm; **IR** (KBr) 3470, 3443, 3369, 3343, 2923, 2220, 1647, 1599, 1531, 1469, 1435, 1401, 1122, 781, 702 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{19}H_{15}N_3ONa$ 324.1113, found 324.1109.

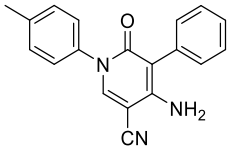
4-amino-6-oxo-1,5-diphenyl-1,6-dihydropyridine-3-carbonitrile (**6b**)



Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-phenylethanethioate (72.0 mg, 0.4 mmol), **6b** was obtained as a faint yellow solid (54.6 mg, 95% yield). **Gram scale**: Following the general procedure A with **1a** (1.44 g, 8.5 mmol) and S-ethyl 2-phenylethanethioate (3.06 g, 17.0 mmol), **6b**

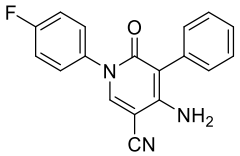
was obtained as a faint yellow solid (2.29 g, 93% yield). R_f = 0.48 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.51-7.32 (m, 10H), 4.72 (s, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.4, 149.0, 144.0, 139.8, 132.4, 130.3, 129.3, 129.2, 129.0, 128.2, 126.6, 115.0, 108.1, 85.1 ppm; **IR** (KBr) 3493, 3458, 3393, 3342, 3042, 2922, 2852, 2221, 1653, 1599, 1525, 1465, 1364, 1308, 1244, 780, 742, 694 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{13}N_3ONa$ 310.0956, found 310.0957.

4-amino-6-oxo-5-phenyl-1-(p-tolyl)-1,6-dihydropyridine-3-carbonitrile (**6c**)



Following the general procedure with 2-((*p*-tolylamino)methylene)malononitrile (36.6 mg, 0.2 mmol) and S-ethyl 2-phenylethanethioate (72.0 mg, 0.4 mmol), **6c** was obtained as a faint yellow solid (55.4 mg, 92% yield). R_f = 0.42 (petroleum ether:ethyl acetate = 1:2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.38 (s, 1H), 7.46 - 7.24 (m, 9H), 5.78 (s, 2H), 2.35 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 160.2, 150.5, 146.9, 138.2, 138.0, 134.1, 131.2, 129.7, 129.1, 127.7, 127.2, 116.0, 106.0, 84.2, 21.1 ppm; **IR** (KBr) 3461, 3341, 3202, 2218, 1650, 1510, 1363, 819, 701 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 302.21

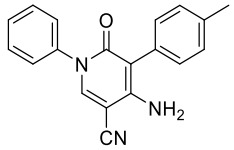
4-amino-1-(4-fluorophenyl)-6-oxo-5-phenyl-1,6-dihydropyridine-3-carbonitrile (**6d**)



Following the general procedure with 2-(((4-fluorophenyl)amino)methylene)malononitrile (37.4 mg, 0.2 mmol) and S-ethyl 2-phenylethanethioate (72.0 mg, 0.4 mmol), **6d** was obtained as a faint yellow solid (58.0mg, 95% yield). R_f = 0.43 (petroleum ether:ethyl acetate = 1:2); The product **6d** was shown to exist as a mixture of tautomers in NMR spectrum recorded in DMSO-d_6. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.46 (s, 0.32H), 8.44 (s, 0.63H), 7.59 – 7.22 (m, 9H), 5.87 (s,

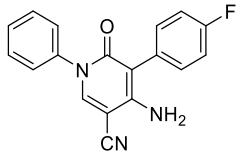
0.68H), 5.83 (s, 1.28H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) (major) δ 162.0 (d, J = 245.1 Hz),136.7 (d, J = 3.0 Hz), 129.8(d, J = 8.9 Hz), 116.1 (d, J = 22.5 Hz),160.1, 150.6, 147.0, 134.0, 131.2, 129.1，127.7, 1234.0 (d, J = 3.0 Hz), 115.9, 105.9, 84.4 ppm;**^{13}C NMR** (101 MHz, DMSO-d_6) (minor) δ 162.1 (d, J = 244.1 Hz),141.7 (d, J = 10.5 Hz), 130.8 (d, J = 9.1 Hz)，123.9 (d, J = 3.0 Hz)，115.5 (d, J = 21.8 Hz), 159.9, 150.6, 146.8, ,133.9, 131.1, 129.1, 127.7, 115.9, 115.2, 105.9, 84.7 ppm; **IR** (KBr) 3452, 3337, 3042, 2218, 1646, 1508, 1465, 1237, 832, 760 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 306.18.

4-amino-6-oxo-1-phenyl-5-(p-tolyl)-1,6-dihydropyridine-3-carbonitrile (**6e**)



Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(p-tolyl)ethanethioate (77.6 mg, 0.4 mmol) **6e** was obtained as a faint yellow solid (56.6 mg, 94% yield). R_f = 0.51 (petroleum ether: ethyl acetate = 1:1); **1H NMR** (400 MHz, $CDCl_3$) *δ* 7.81 (s, 1H), 7.50 - 7.24 (m, 9H), 4.71 (s, 2H), 2.37 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 160.5, 149.0, 143.9, 139.8, 138.0, 130.1, 129.9, 129.3, 129.2, 128.9, 126.6, 115.1, 108.1, 85.0, 21.31 ppm; **IR** (KBr) 3464, 3345, 2923, 2218, 1651, 1580, 1460, 1363, 1306, 1243, 1030, 809, 776, 697 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ Calcd for $C_{19}H_{16}N_3O$ 302.1293, found 302.1292.

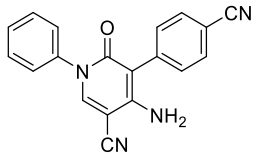
4-amino-5-(4-fluorophenyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (**6f**)



Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(4-fluorophenyl)ethanethioate (79.2 mg, 0.4 mmol), **6f** was obtained as a faint yellow solid (58.0 mg, 95% yield). R_f = 0.51 (petroleum ether:ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.82 (s, 1H), 7.51 - 7.33 (m, 7H), 7.18 - 7.11 (m, 2H), 4.71 (s, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.40 (d, J = 247.7 Hz), 132.29 (d, J = 8.2 Hz), 128.15 (d, J = 3.5 Hz), 116.29 (d, J = 21.5

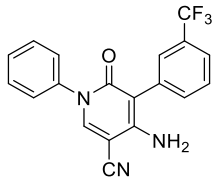
Hz),160.4, 149.2, 144.1, 139.6, 129.3, 129.1, 126.6, 114.9, 107.0, 85.1 ppm; **IR** (KBr) 3455, 3317, 3212, 3063, 2217, 1656, 1535, 1456, 1406, 1241, 1214, 906, 846, 725, 622 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ Calcd for $C_{18}H_{13}FN_3O$ 306.1043, found 306.1046.

4-amino-5-(4-cyanophenyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (**6g**)



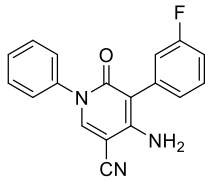
Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(4-cyanophenyl)ethanethioate (82.0 mg, 0.4 mmol), **6g** was obtained as a faint yellow solid (58.1 mg, 93% yield). R_f = 0.46 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.46 (s, 1H), 7.90 - 7.81 (m, 2H), 7.55 - 7.37 (m, 7H), 6.22 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.8, 151.1, 147.5, 140.3, 139.8, 132.8, 132.5, 129.3, 128.8, 127.5, 119.6, 115.8, 110.0, 104.2, 84.6 ppm; **IR** (KBr) 3356, 3059, 2923, 2223, 1652, 1607, 1530, 1465, 1365, 1245, 778, 698 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ Calcd for $C_{19}H_{13}N_4O$ 313.1089, found 313.1093.

4-amino-6-oxo-1-phenyl-5-(3-(trifluoromethyl)phenyl)-1,6-dihydropyridine-3-carbonitrile (**6h**)



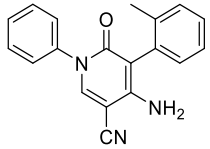
Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(3-(trifluoromethyl)phenyl)ethanethioate (99.2 mg, 0.4 mmol), **6h** was obtained as a faint yellow solid (66.8 mg, 94% yield). R_f = 0.51 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.46 (s, 1H), 7.82 - 7.09 (m, 9H), 6.16 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 129.7 (q, J = 31.3 Hz), 127.9-128.1 (q), 125.2 (q, J = 189.9 Hz),124.2-124.4 (q), 160.1, 151.1, 147.3, 140.3, 135.5, 135.3, 130.1, 129.3, 128.8, 115.9, 104.3, 84.6 ppm; **IR** (KBr) 3340, 3061, 2926, 2221, 1649, 1529, 1490, 1366, 1123, 778, 711, 670 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ Calcd for $C_{19}H_{13}F_3N_3O$ 356.1011, found 356.1008.

4-amino-5-(3-fluorophenyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (**6i**)



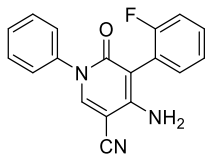
Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(3-fluorophenyl)ethanethioate (79.2 mg, 0.4 mmol), **6i** was obtained as a faint yellow solid (41.5 mg, 96% yield). R_f = 0.55 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.44 (s, 1H), 7.53 - 7.36 (m, 6H), 7.17 - 7.01 (m, 3H), 6.05 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.8 (d, J = 242.9 Hz), 136.5 (d, J = 8.4 Hz), 130.8 (d, J = 8.6 Hz), 127.4 (d, J = 2.7 Hz), 118.1 (d, J = 21.0 Hz), 114.5 (d, J = 20.8 Hz), 104.6 (d, J = 2.0 Hz), 159.9, 150.9, 147.2, 140.4, 129.3, 128.8, 127.5, 115.9, 84.5 ppm; **IR** (KBr) 3341, 3197, 2220, 1648, 1578, 1490, 1366, 1123, 778, 711, 670 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 306.17.

4-amino-6-oxo-1-phenyl-5-(o-tolyl)-1,6-dihydropyridine-3-carbonitrile (**6j**)



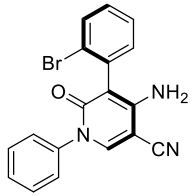
Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(*o*-tolyl)ethanethioate (77.6 mg, 0.4 mmol), **6j** was obtained as a faint yellow solid (56.6 mg, 94% yield). R_f = 0.53 (petroleum ether: ethyl acetate = 1:1);**^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.45 (s, 1H), 7.52 - 7.36 (m, 5H), 7.32 - 7.19 (m, 3H), 7.13 - 7.08 (m, 1H), 5.64 (s, 2H), 2.11 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.6, 150.7, 146.9, 140.4, 138.3, 133.3, 131.5, 130.7, 129.3, 128.7, 128.2, 127.4, 126.6, 116.0, 105.6, 84.2, 19.5 ppm; **IR** (KBr) 3459, 3335, 2219, 1634, 1576, 1466, 1364, 1252, 740 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 302.20；**HPLC** COSMOSIL CHiRAL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ = 254 nm, t_R = 6.53 min and 7.31 min.

4-amino-5-(2-fluorophenyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (**6k**)



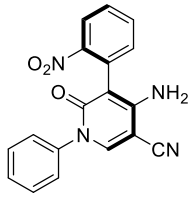
Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(2-fluorophenyl)ethanethioate (79.2 mg, 0.4 mmol), **6k** was obtained as a faint yellow solid (58.0 mg, 95% yield). R_f = 0.52 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.44 (s, 1H), 7.55 – 7.28 (m, 6H), 7.17 – 6.97 (m, 3H), 6.04 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.8 (d, J = 242.8 Hz), 136.5 (d, J = 8.4 Hz), 130.8 (d, J = 8.5 Hz), 128.8, 127.4 (d, J = 2.7 Hz), 118.1 (d, J = 20.9 Hz), 114.5 (d, J = 20.7 Hz), 104.6 (d, J = 2.0 Hz), 159.9, 150.9, 147.2, 140.4, 129.3, 128.8, 127.5, 115.9, 84.5 ppm; **IR** (KBr) 3460, 3338, 2220, 1648, 1579, 1525, 1467, 1188, 792, 711 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 306.18.

4-amino-5-(2-bromophenyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (**6l**)



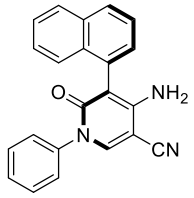
Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(2-bromophenyl)ethanethioate (103.2 mg, 0.4 mmol), **6l** was obtained as a faint yellow solid (62.1 mg, 85% yield). R_f = 0.42 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.88 (s, 1H), 7.74 - 7.69 (m, 1H), 7.52 - 7.27 (m, 8H), 4.54 (s, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 159.6, 149.3, 144.7, 139.6, 133.6, 133.3, 132.7, 130.2, 129.3, 129.0, 128.4, 126.6, 125.5, 114.8, 108.0, 84.8 ppm; **IR** (KBr) 3454, 3345, 3204, 2923, 2219, 1638, 1529, 1363, 1312, 1245, 1025, 775, 595 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ Calcd for $C_{18}H_{13}BrN_3O$ 366.0242, found 366.0240; **HPLC** CHIRALCEL OD-H column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ = 254 nm, t_R = 19.44 min and 23.25 min.

4-amino-5-(2-nitrophenyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (**6m**)



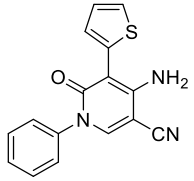
Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(2-nitrophenyl)ethanethioate (90.0 mg, 0.4 mmol), **6m** was obtained as a faint yellow solid (46.5 mg, 70% yield). R_f = 0.48 (petroleum ether: ethyl acetate = 1:2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.46 (s, 1H), 8.08 - 8 (m, *J* = 8.2, 1.3 Hz, 1H), 7.8 - 7.71 (m, 1H), 7.64 – 7.55 (m, 1H), 7.51 – 7.33 (m, 6H), 6.34 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.3, 150.92, 150.3, 147.1, 140.0, 134.3, 133.9, 129.3, 129.3, 129.1, 128.8, 127.3, 125.0, 115.8, 102.7, 84.9 ppm; **IR** (KBr) 3450, 2923, 2853, 2219, 1649, 1524, 1461, 1368, 1248, 781 $cm^{-1.}$; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{12}N_4O_3Na$ 355.0807, found 355.0807; **HPLC** COSMOSIL CHiRAL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ = 254 nm, t_R = 12.05 min and 13.62 min.

4-amino-5-(naphthalen-1-yl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (**6n**)



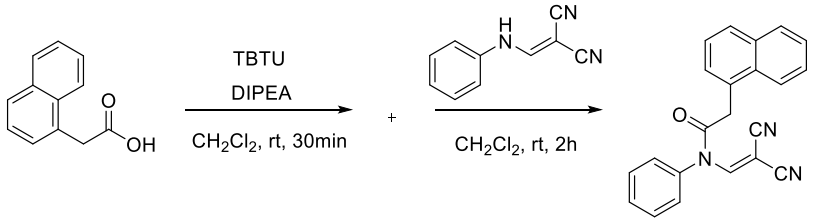
Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(naphthalen-2-yl)ethanethioate (92.0 mg, 0.4 mmol) **6n** was obtained as a faint yellow solid (62.0 mg, 92% yield). R_f = 0.51 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.95 (s, 1H), 7.92 - 7.86 (m, 2H), 7.75 - 7.69 (m, 1H), 7.60 - 7.39 (m, 9H), 4.51 (s, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 160.4, 149.8, 144.5, 139.7, 134.3, 131.4, 129.6, 129.3, 129.1, 129.1, 128.9, 128.7, 126.7, 126.6, 126.2, 126.1, 124.8, 115.0, 106.2, 84.9 ppm; **IR** (KBr) 3340, 3055, 2218, 1652, 1520, 1462, 1248, 1156, 1038, 801, 729, 703, 644 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ Calcd for $C_{22}H_{16}N_3O$ 338.1293, found 338.1294; **HPLC** COSMOSIL CHiRAL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ = 254 nm, t_R = 34.54 min and 53.25 min.

4-amino-6-oxo-1-phenyl-5-(thiophen-2-yl)-1,6-dihydropyridine-3-carbonitrile (**6o**)



Following the general procedure with **1a** (33.8 mg, 0.2 mmol) and S-ethyl 2-(thiophen-2-yl)ethanethioate (74.4 mg, 0.4 mmol) **6o** was obtained as a faint yellow solid (46.9 mg, 80% yield). R_f = 0.76 (petroleum ether: ethyl acetate = 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.44 (s, 1H), 7.61 - 7.38 (m, 6H), 7.21 - 7.04 (m, 2H), 6.29 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.8, 151.4, 146.9, 140.3, 134.8, 129.4, 128.9, 127.9, 127.6, 126.9, 126.8, 115.8, 98.9, 84.4 ppm; **IR** (KBr): v = 3427, 3175, 2219, 1655, 1543, 1505, 1469, 1254, 1089, 777, 730, 701 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* [M+Na]$^+$ Calcd for $C_{16}H_{11}N_3OSNa$ 316.0521, found 316.0525.

3. Synthesis of N-(2,2-dicyanovinyl)-2-(naphthalen-1-yl)-N-phenylacetamide 7



7

To a solution of 2-(naphthalen-1-yl)acetic acid (0.2 mmol, 1 equiv.) in dichloromethane (5 mL) were added TBTU (0.22 mmol, 1.1 equiv), DIPEA (0.3 mmol, 1.5 equiv) successively and the reaction mixture was stirred for 30min at room temperature. added 2-((phenylamino)methylene)malononitrile **1a** (0.22 mmol, 1.1 equiv.) the reaction mixture was stirred for 2h at room temperature and then extracted with ethyl acetate. The combined organic layer was washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo to give the crude product which was purified by column chromatography (petroleum ether:ethyl acetate = 3:1) to afford the desired product **7** as a faint yellow solid (52.6 mg, 78% yield). R_f = 0.58 (petroleum ether: ethyl acetate = 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.60 (s, 1H), 7.88 - 7.78 (m, 2H), 7.65 - 7.27 (m, 9H), 7.12 - 7.07 (m, 1H), 4.03 (s, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 170.2, 150.7, 134.9, 133.9, 132.0,

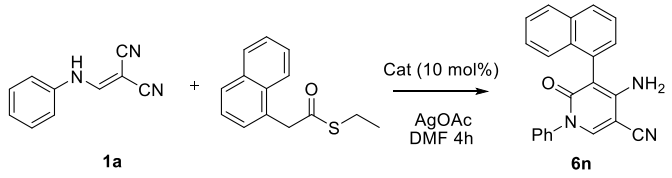
131.6, 130.8, 130.2, 129.1, 129.0, 128.8, 128.3, 128.0, 126.7, 126.1, 125.4, 122.8, 117.5, 114.1, 109.0, 66.3, 39.1 ppm; **IR** (KBr) 3214, 3058, 2917, 2220, 1733, 1603, 1490, 1339, 1203, 1154, 1098, 791, 693, cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ Calcd for $C_{22}H_{15}N_3ONa$ 360.1113, found 360.1112.

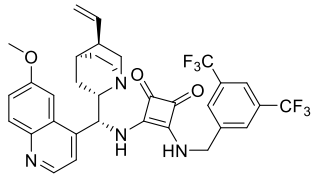
4. Investigation for the asymmetric version of the reactions

General procedure

The reactions were carried out with 10 mol% of indicated chiral catalyst, the crude products were purified by column chromatography and ee values were determined by chiral HPLC system.

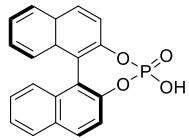
Table S1: Reactions from **1a**.





QD-SQA

Cat 1



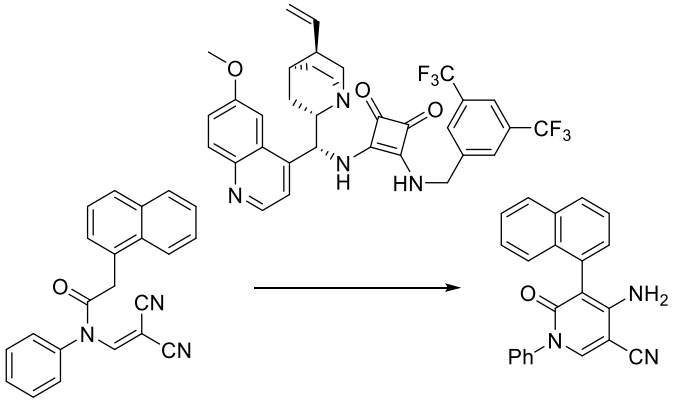
CBA

Cat 2

entry	Reaction conditions[a]	yield (%)[b]	ee (%)
1	Cat 1, rt	48	0
2	Cat 2 , 80 °C	90	0

[a] The reactions were carried out with **1a** (0.2 mmol), acylation reagent (0.4 mmol) and catalyst (10 mmol %) in 2 mL of solvent. [b] Isolated yields based on **1a**.

Table S2: Reactions from **7.**



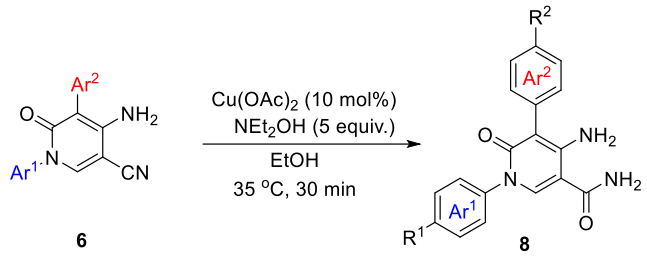
entry	Reaction conditions[a]	yield (%)[b]	ee (%)
1	DMF, 80 °C, 4h	0	0
2	AgOAc, DMF, rt, 1h	87	0
3	AgOAc, toluene, 80 °C, 4h	0	0
4	DMF,rt, 12	35	0

[a] The reactions were carried out with **7** (0.2 mmol) and catalyst (10 mmol %) in 2 mL of solvent. [b] Isolated yields based on **7a**.

5. Synthesis of 6,8-diphenylpyrido[4,3-d]pyrimidine-4,7(3H, 6H)-diones 9

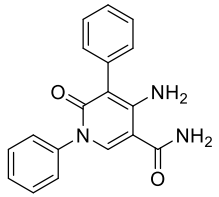
5.1 Synthesis of 4-amino-6-oxo-1,5-diphenyl-1,6-dihydropyridine-3-carboxamides 8[3]

General procedure



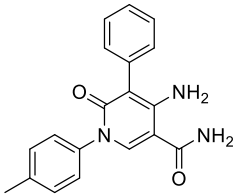
To a stirred solution of **6** (0.2 mmol, 1 equiv.) in EtOH (2 mL) were added NEt_2OH (1 mmol, 5 equiv), $Cu(OAc)_2$ (0.02 mmol, 0.1 equiv) successively and the reaction mixture was stirred for 30min at 35 °C and then extracted with ethyl acetate. The combined organic layer was washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo to give the crude product which was purified by column chromatography (petroleum ether:ethyl acetate = 1:2) to afford the desired product **8**.

4-amino-6-oxo-1,5-diphenyl-1,6-dihydropyridine-3-carboxamide (**8a**)



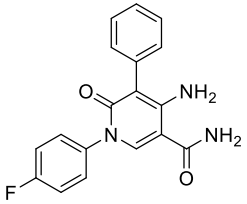
Following the general procedure with 4-amino-6-oxo-1,5-diphenyl-1,6-dihydropyridine-3-carbonitrile (0.2 mmol, 1 equiv.) in alcohol (2 mL) were added NEt_2OH (1 mmol, 5 equiv), $Cu(OAc)_2$ (0.02 mmol, 0.1 equiv), product **8a** was obtained as a faint yellow solid (58.0 mg, 95% yield). R_f = 0.52 (petroleum ether:ethyl acetate = 1:3); **^{1}H NMR** 1H NMR (400 MHz, DMSO-d_6) δ 8.18 (s, 1H), 7.88 (s, 1H), 7.51 - 7.19 (m, 11H), 6.68 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO) δ 169.4, 160.1, 152.9, 141.4, 141.3, 135.1, 131.5, 129.2, 129.0, 128.3, 127.7, 127.2, 105.5, 102.6 ppm; **IR** (KBr) 3478, 3307, 3189, 1667, 1643, 1599, 1528, 1400, 700 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ Calcd for $C_{18}H_{16}N_3O_2$ 306.1243, found 306.1248.

4-amino-6-oxo-5-phenyl-1-(p-tolyl)-1,6-dihydropyridine-3-carboxamide (**8b**)



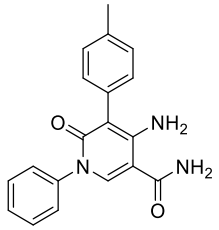
Following the general procedure with 4-amino-6-oxo-5-phenyl-1-(p-tolyl)-1,6-dihydropyridine-3-carbonitrile (0.2 mmol, 1 equiv.) in alcohol (2 mL) were added NEt_2OH (1 mmol, 5 equiv), $Cu(OAc)_2$ (0.02 mmol, 0.1 equiv), product **8b** was obtained as a faint yellow solid (61.3 mg, 96% yield). R_f = 0.53 (petroleum ether:ethyl acetate = 1:3); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.16 (s, 1H), 7.95 (s, 1H), 7.45 - 7.21 (m, 11H), 6.63 (s, 1H), 2.36 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 169.4, 160.2, 152.8, 141.4, 138.9, 137.7, 135.1, 131.5, 129.6, 129.0, 127.4, 127.2, 105.5, 102.5, 21.1 ppm; **IR** (KBr) 3463, 3306, 3192, 1667, 1528, 1396, 1113, 792 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 320.25.

4-amino-1-(4-fluorophenyl)-6-oxo-5-phenyl-1,6-dihydropyridine-3-carboxamide (**8c**)



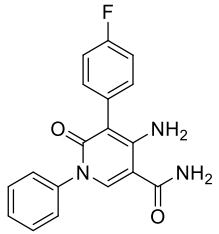
Following the general procedure with 4-amino-1-(4-fluorophenyl)-6-oxo-5-phenyl-1,6-dihydropyridine-3-carbonitrile (0.2 mmol, 1 equiv.) in alcohol (2 mL) were added NEt_2OH (1 mmol, 5 equiv), $Cu(OAc)_2$ (0.02 mmol, 0.1 equiv), product **8c** was obtained as a faint yellow solid (63.0 mg, 97% yield). R_f = 0.52 (petroleum ether:ethyl acetate = 1:3); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.16 (s, 1H), 7.86 (s, 1H), 7.57 – 7.19 (m, 11H), 6.67 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 161.7 (d, J = 244.7 Hz), 129.8 (d, J = 8.8 Hz), 115.9 (d, J = 22.8 Hz). 169.3, 160.1, 153.0, 141.3, 137.6 (d, J = 2.9 Hz), 135.0, 131.5, 129.0, 127.3, 105.4, 102.7 ppm;**IR** (KBr) 3490, 3341, 3174, 1644, 1569, 1508, 1396, 795 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 324.22.

4-amino-6-oxo-1-phenyl-5-(p-tolyl)-1,6-dihydropyridine-3-carboxamide (**8d**)



Following the general procedure with 4-amino-6-oxo-1-phenyl-5-(p-tolyl)-1,6-dihydropyridine-3-carbonitrile (0.2 mmol, 1 equiv.) in alcohol (2 mL) were added NEt_2OH (1 mmol, 5 equiv), $Cu(OAc)_2$ (0.02 mmol, 0.1 equiv), product **8d** was obtained as a faint yellow solid (57.8.0 mg, 96% yield)R_f = 0.55 (petroleum ether:ethyl acetate = 1:3); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.16 (s, 1H), 7.86 (s, 1H), 7.59 - 7.35 (m, 5H), 7.30 - 7.08 (m, 5H), 6.63 (s, 2H), 2.33 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 169.4, 160.1, 152.9, 141.4, 141.1, 136.2, 132.0, 131.3, 129.6, 129.1, 128.2, 127.7, 105.3, 102.6, 21.3 ppm; **IR** (KBr) 3472, 3312, 3183, 1673, 1527, 1400, 1255, 1131, 790, 704 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 320.25.

4-amino-5-(4-fluorophenyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carboxamide (**8e**)

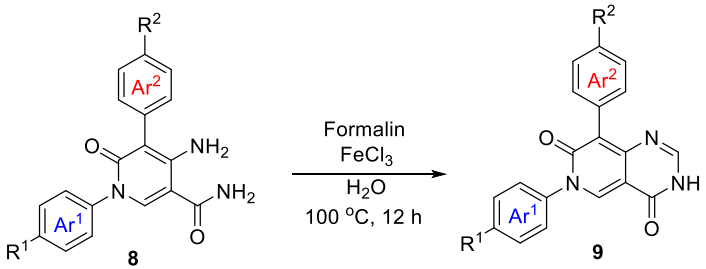


Following the general procedure with 4-amino-5-(4-fluorophenyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (0.2 mmol, 1 equiv.) in alcohol (2 mL) were added NEt_2OH (1 mmol, 5 equiv), $Cu(OAc)_2$ (0.02 mmol, 0.1 equiv), product **8e** was obtained as a faint yellow solid (60.7 mg, 94% yield). R_f = 0.55

(petroleum ether:ethyl acetate = 1:3); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.18 (s, 1H), 7.90 (s, 1H), 7.55 – 7.12 (m, 10H), 6.75 (s, 2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 161.5 (d, J = 242.5 Hz), 141.3 (d, J = 5.9 Hz), 133.5 (d, J = 8.1 Hz), 131.3 (d, J = 3.3 Hz) 169.4, 160.1, 153.1, 129.2, 128.3, 127.7, 115.9, 115.7, 104.5, 102.6 ppm; **IR** (KBr) 3474, 3313, 3185, 1673, 1528, 1400, 1220, 847, 703 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 324.18.

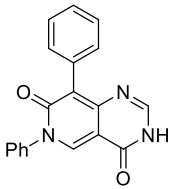
5.2 Synthesis of 6,8-diphenylpyrido[4,3-*d*]pyrimidine-4,7(3*H*,6*H*)-diones 9[4]

General procedure



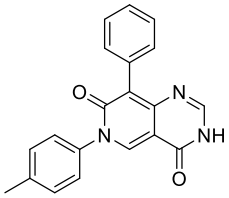
To a solution of **8** (0.2 mmol, 1 equiv.) in H_2O (2 mL) were added formalin (0.4 mmol, 2 equiv.), $FeCl_3$ (1.2 mmol, 6 equiv.) successively and the reaction mixture was stirred at 100 °C for 12h and then extracted with ethyl acetate. The combined organic layer was washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo to give the crude product which was purified by column chromatography (petroleum ether:ethyl acetate = 1:2) to afford the desired product **9**.

6,8-diphenylpyrido[4,3-*d*]pyrimidine-4,7(3*H*,6*H*)-dione (**9a**)



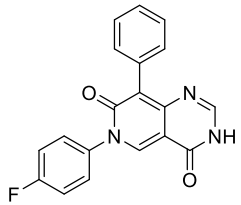
Following the general procedure with **8a** (0.2 mmol, 1 equiv.) in H_2O (2 mL) were added CH_2O (0.4 mmol, 2 equiv.), $FeCl_3$ (1.2 mmol, 6 equiv.), **9a** was obtained as a faint yellow solid (58.0 mg, 92% yield). R_f = 0.52 (petroleum ether:ethyl acetate = 1:2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.90 (s, 1H), 8.48 (s, 1H), 7.92 (s, 1H), 7.55 - 7.26 (m, 10H) ppm; **^{13}C NMR** (151 MHz, DMSO-d_6) δ 162.0, 160.4, 151.0, 149.9, 141.8, 141.0, 134.4, 131.9, 129.6, 129.4, 127.5, 127.4, 127.4, 122.2, 106.3 ppm; **IR** (KBr) 3448, 3057, 2923, 2853, 1717, 1631, 1570, 1383, 798, 695 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ Calcd for $C_{19}H_{14}N_3O_2$ 316.1086, found 316.1087.

8-phenyl-6-(p-tolyl)pyrido[4,3-*d*]pyrimidine-4,7(3*H*,6*H*)-dione (**9b**)



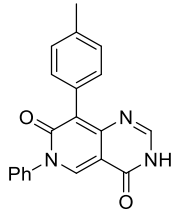
Following the general procedure with 4-amino-6-oxo-5-phenyl-1-(p-tolyl)-1,6-dihydropyridine-3-carboxamide (0.2 mmol, 1 equiv.) in H_2O (2 mL) were added CH_2O (0.4 mmol, 2 equiv.), $FeCl_3$ (1.2 mmol, 6 equiv.), **9b** was obtained as a faint yellow solid (34.9 mg, 53% yield). R_f = 0.50 (petroleum ether:ethyl acetate = 1:2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.89 (s, 1H), 8.45 (s, 1H), 7.91 (s, 1H), 7.55 - 7.11 (m, 9H), 2.39 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.0, 160.4, 150.9, 149.8, 141.8, 138.9, 138.5, 134.5, 131.8, 130.0, 127.5, 127.3, 127.0, 122.1, 106.2, 21.2 ppm; **IR** (KBr) 3509, 3042, 2890, 2763, 1619, 1631, 1575, 1430, 1236, 819 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 330.23.

6-(4-fluorophenyl)-8-phenylpyrido[4,3-d]pyrimidine-4,7(3H,6H)-dione (**9c**)



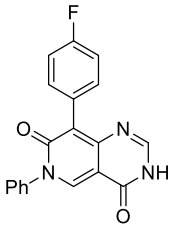
Following the general procedure with 4-amino-1-(4-fluorophenyl)-6-oxo-5-phenyl-1,6-dihydropyridine-3-carboxamide (0.2 mmol, 1 equiv.) in H_2O (2 mL) were added CH_2O (0.4 mmol, 2 equiv.), $FeCl_3$ (1.2 mmol, 6 equiv.), **9c** was obtained as a faint yellow solid (40 mg, 60% yield). R_f = 0.50 (petroleum ether:ethyl acetate = 1:2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.91 (s, 1H), 8.51 (s, 1H), 7.92 (s, 1H), 7.64 - 7.58 (m, 2H), 7.45 – 7.24 (m, 7H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.3 (d, J = 245.8 Hz), 137.2 (d, J = 3.0 Hz), 129.7 (d, J = 9.1 Hz), 116.4 (d, J = 23.0 Hz).δ 162.0, 160.4, 151.0, 149.9, 142.0, 134.4, 131.8, 127.5, 127.3, 122.1, 106.3 ppm; **IR** (KBr) 3124, 2924, 1716, 1578, 1505, 1384, 1221, 800 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 334.23.

6-phenyl-8-(p-tolyl)pyrido[4,3-*d*]pyrimidine-4,7(3*H*,6*H*)-dione (**9d**)



Following the general procedure with 4-amino-6-oxo-1-phenyl-5-(p-tolyl)-1,6-dihydropyridine-3-carboxamide (0.2 mmol, 1 equiv.) in H_2O (2 mL) were added CH_2O (0.4 mmol, 2 equiv.), $FeCl_3$ (1.2 mmol, 6 equiv.), **9d** was obtained as a faint yellow solid (39.6 mg, 62% yield). R_f = 0.51 (petroleum ether:ethyl acetate = 1:2);**^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.87 (s, 1H), 8.45 (s, 1H), 7.90 (s, 1H), 7.59 - 7.46 (m, 5H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 2.33 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.0, 160.4, 150.8, 149.7, 141.4, 141.0, 136.5, 131.7, 131.4, 129.6, 129.3, 128.1, 127.4, 122.2, 106.3, 21.4 ppm; **IR** (KBr) 3117, 2917, 1715, 1590, 1574, 1403, 1230 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 330.24

8-(4-fluorophenyl)-6-phenylpyrido[4,3-*d*]pyrimidine-4,7(3*H*,6*H*)-dione (**9e**)



Following the general procedure with 4-amino-5-(4-fluorophenyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitrile (0.2 mmol, 1 equiv.) in H_2O (2 mL) were added CH_2O (0.4 mmol, 2 equiv.), $FeCl_3$ (1.2 mmol, 6 equiv.), **9e** was obtained as a faint yellow solid (35.5 mg, 55% yield). R_f = 0.51 (petroleum ether:ethyl acetate = 1:2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.93 (s, 1H), 8.49 (s, 1H), 7.94 (s, 1H), 7.60 - 7.38 (m, 7H), 7.23 - 7.14 (m,2H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 161.9 (d, J = 240.1 Hz), 130.5 (d, J = 0.1 Hz), 114.4 (d, J = 21.5 Hz), 106.33. 161.9, 160.4, 151.0, 150.1, 141.8, 140.9, 133.9, 133.8, 129.6, 129.4, 127.4, 121.0, 106.3 ppm; **IR** (KBr) 3119, 2920, 1714, 1591, 1572, 1384, 1223, 841 cm^{-1}; **MS** (ESI) m/z $[M+H]^+$ found 334.22.

6. UV-Vis Absorption Spectroscopy and Fluorescence Emission Spectroscopy of 9

Sample preparation for fluorescence emission spectroscopy (10^{-4} g/mL): To a 20 mL of volumetric flask was added **9** (2.0 mg, 0.006 mmol) and diluted with DMSO to 20 mL. The flask with solution was shaken several times for using. The product was excited at 346 nm.

Sample preparation for UV-Vis absorption spectroscopy (10^{-5} g/mL): 2 mL of above mother liquor (10^{-4} g/mL) was added to a 20 mL volumetric flask and diluted with DMSO to a final volume of 20 mL. The resulting solution was shaken thoroughly before use.

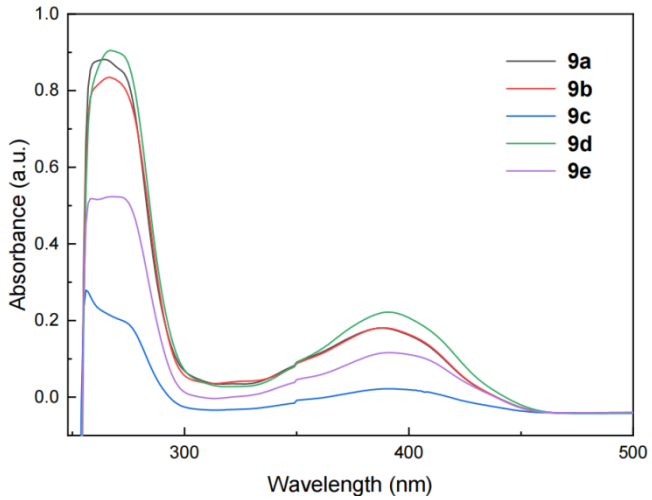


Figure S1. UV-Vis absorption spectrum of **9**.

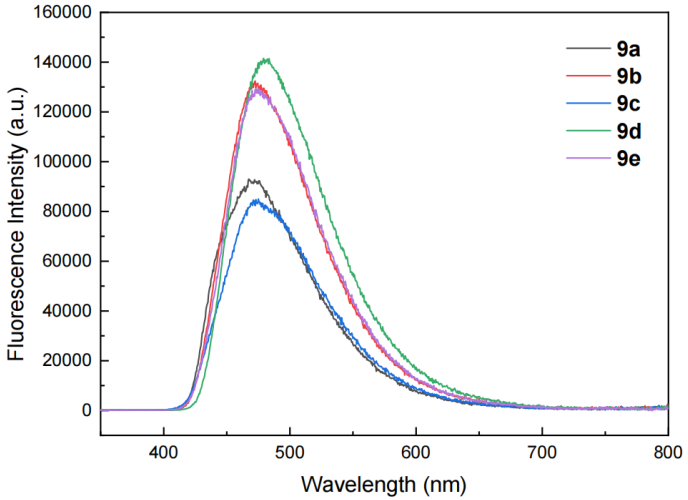


Figure S2. Fluorescence emission spectrum of **9**.

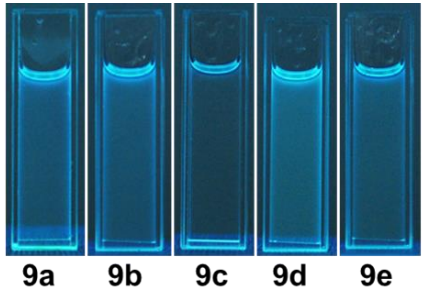


Figure S3. Fluorescence emission under UV light.

7. X-ray crystal structure of 5a (CDCC 2266553)

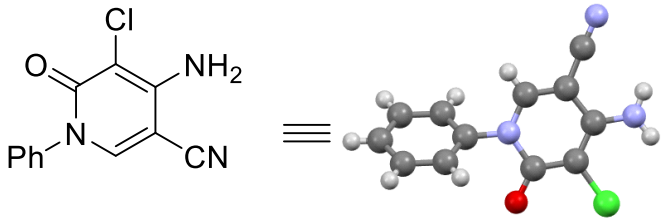
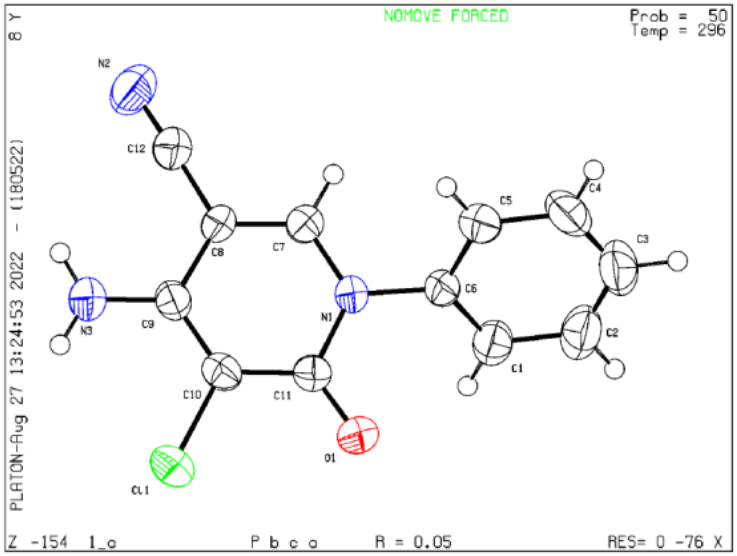


Figure S4. X-ray crystal structure of **5a**.



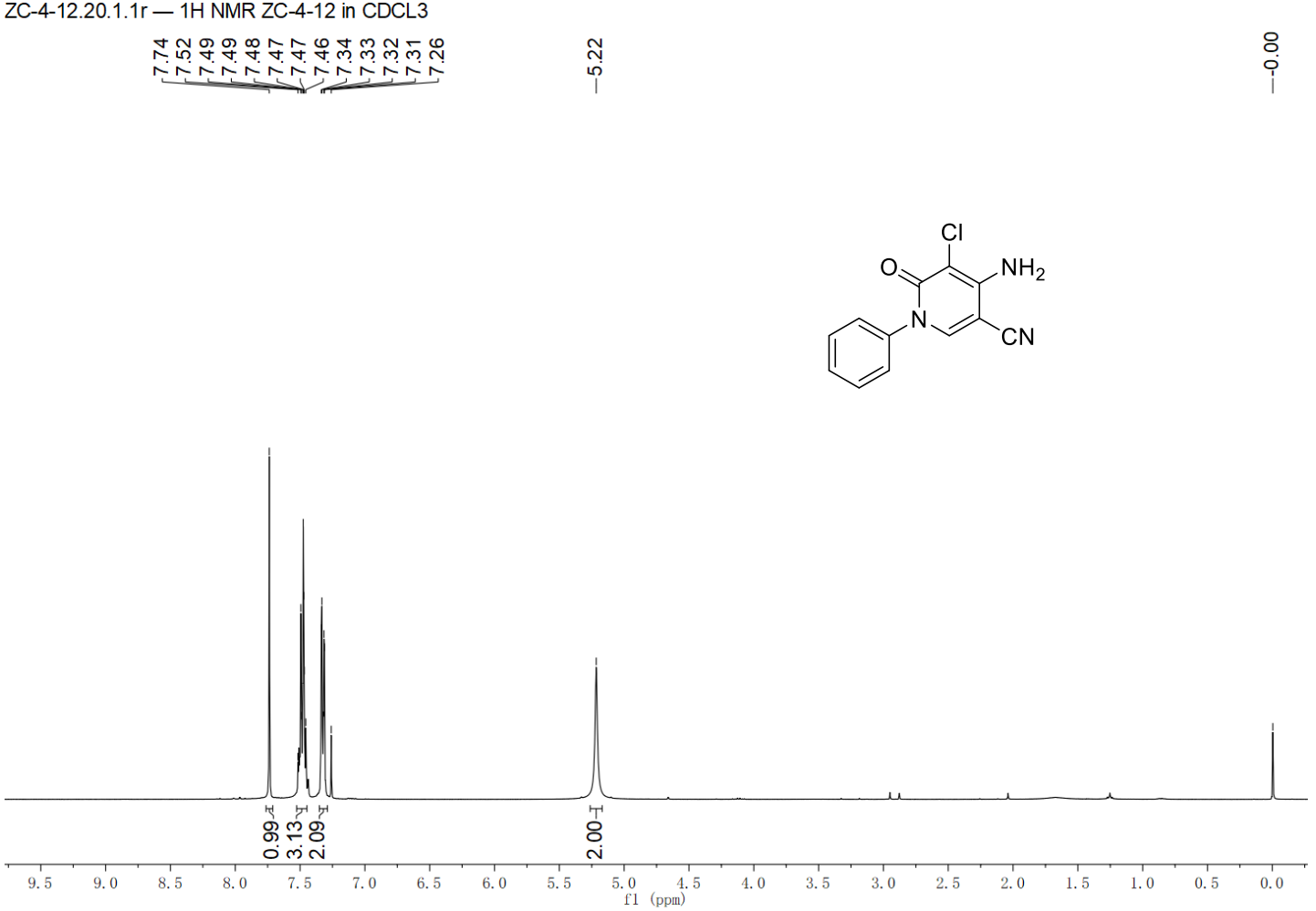
Bond precision:	C-C = 0.0042 A	Wavelength=0.71073	
Cell:	a=11.1261(7)	b=7.8636(5)	c=25.4825(16)
	alpha=90	beta=90	gamma=90
Temperature:	296 K		
Calculated	Reported		
Volume	2229.5(2)	2229.5(2)	
Space group	P b c a	P b c a	
Hall group	-P 2ac 2ab	-P 2ac 2ab	
Moiety formula	C_{12} H_8 Cl N_3 O	?	
Sum formula	C_{12} H_8 Cl N_3 O	C_{12} H_8 Cl N_3 O	
Mr	245.66	245.66	
Dx,g cm-3	1.464	1.464	
Z	8	8	
Mu (mm-1)	0.327	0.327	
F000	1008.0	1008.0	
F000’	1009.53		
h,k,lmax	13,9,30	13,9,30	
N ref	1960	1957	
Tmin,Tmax	0.937,0.937	0.864,0.864	
Tmin’	0.937		

Correction method= # Reported T Limits: Tmin=0.864 Tmax=0.864

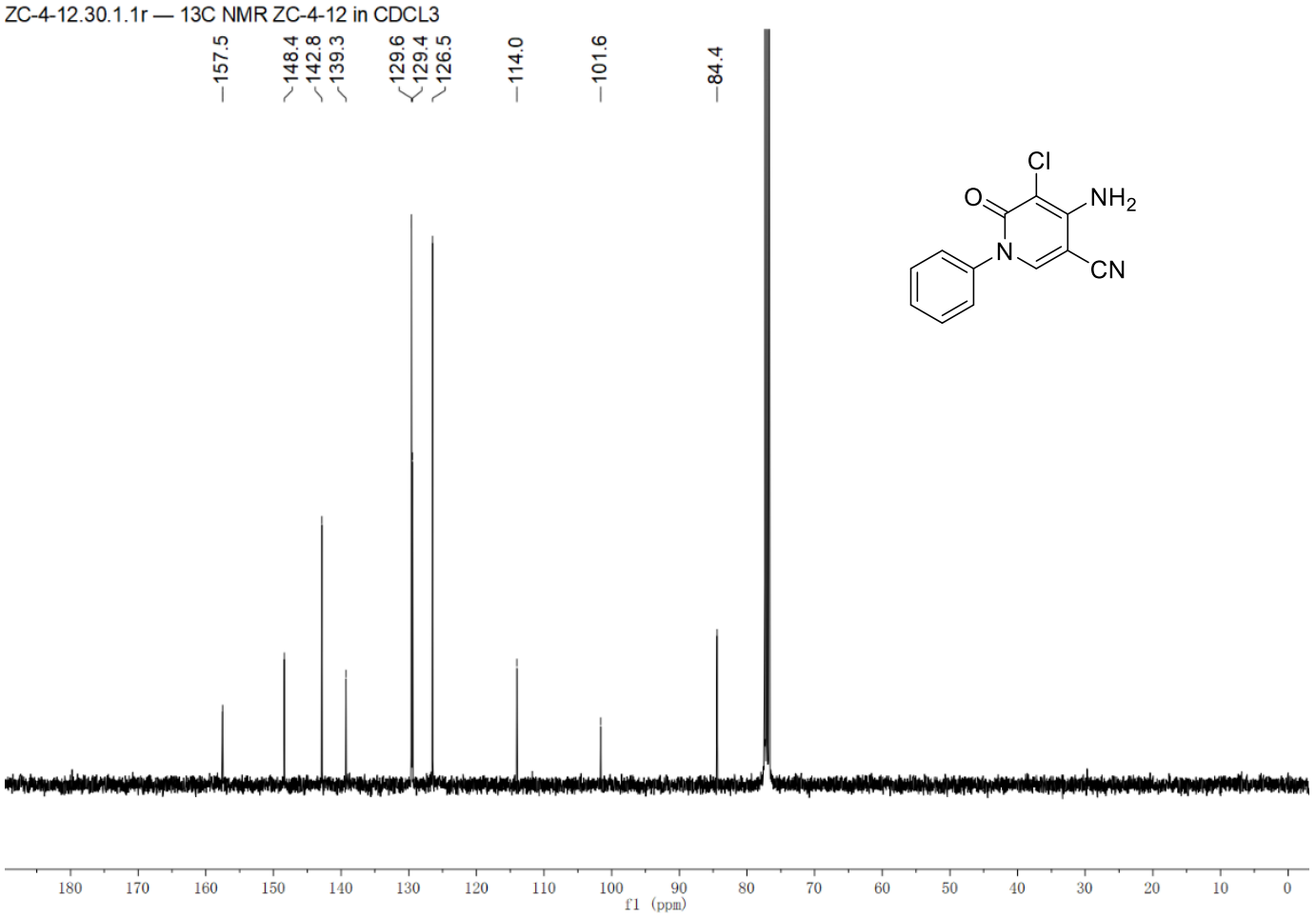
AbsCorr = MULTI-SCAN

Data completeness= 0.998	Theta(max)= 25.003
R(reflections)= 0.0533(1166)	wR2(reflections)= 0.1385(1957)
S = 1.049	Npar= 142

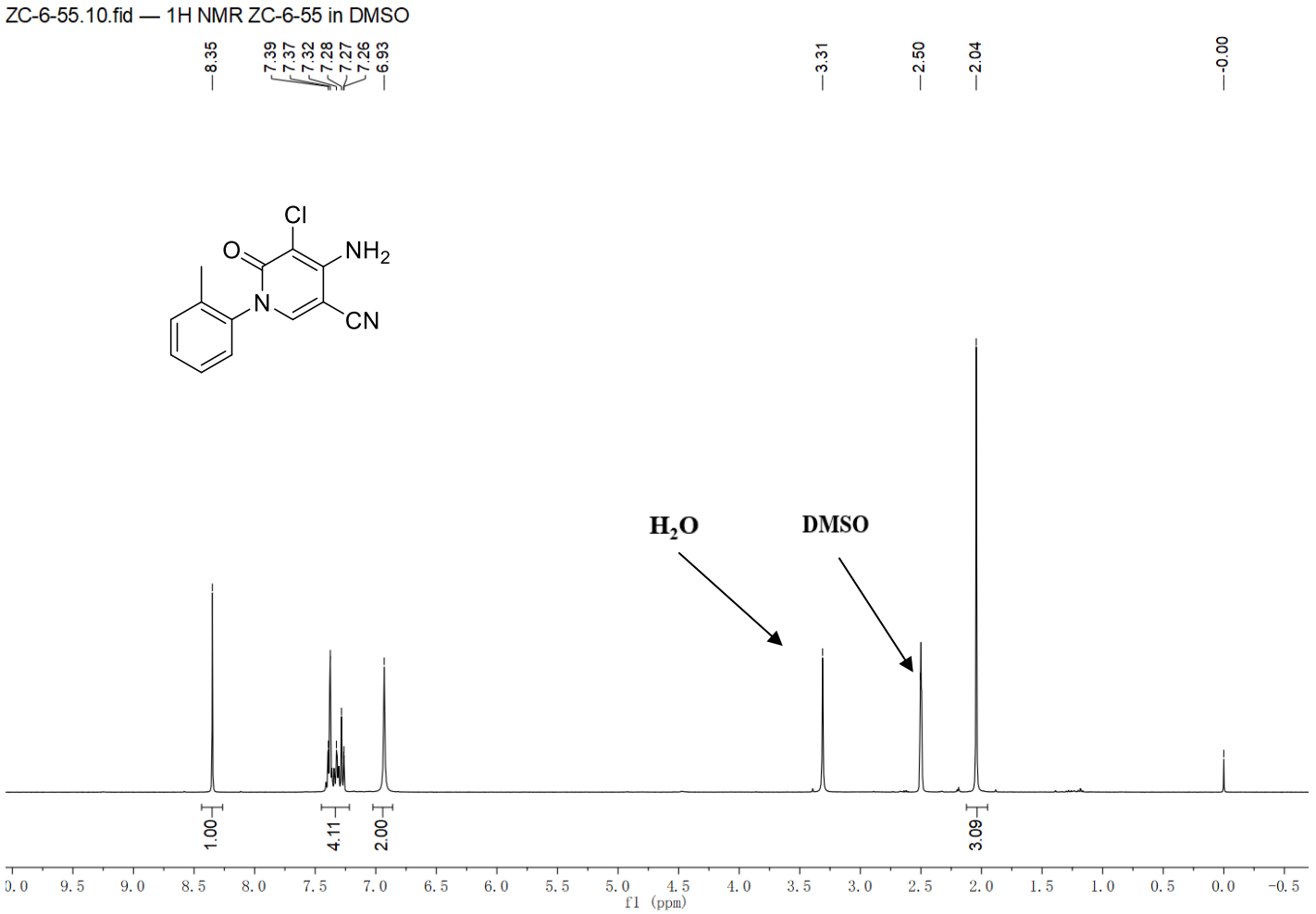
8.Copies of ^{1}H and ^{13}C NMR spectra



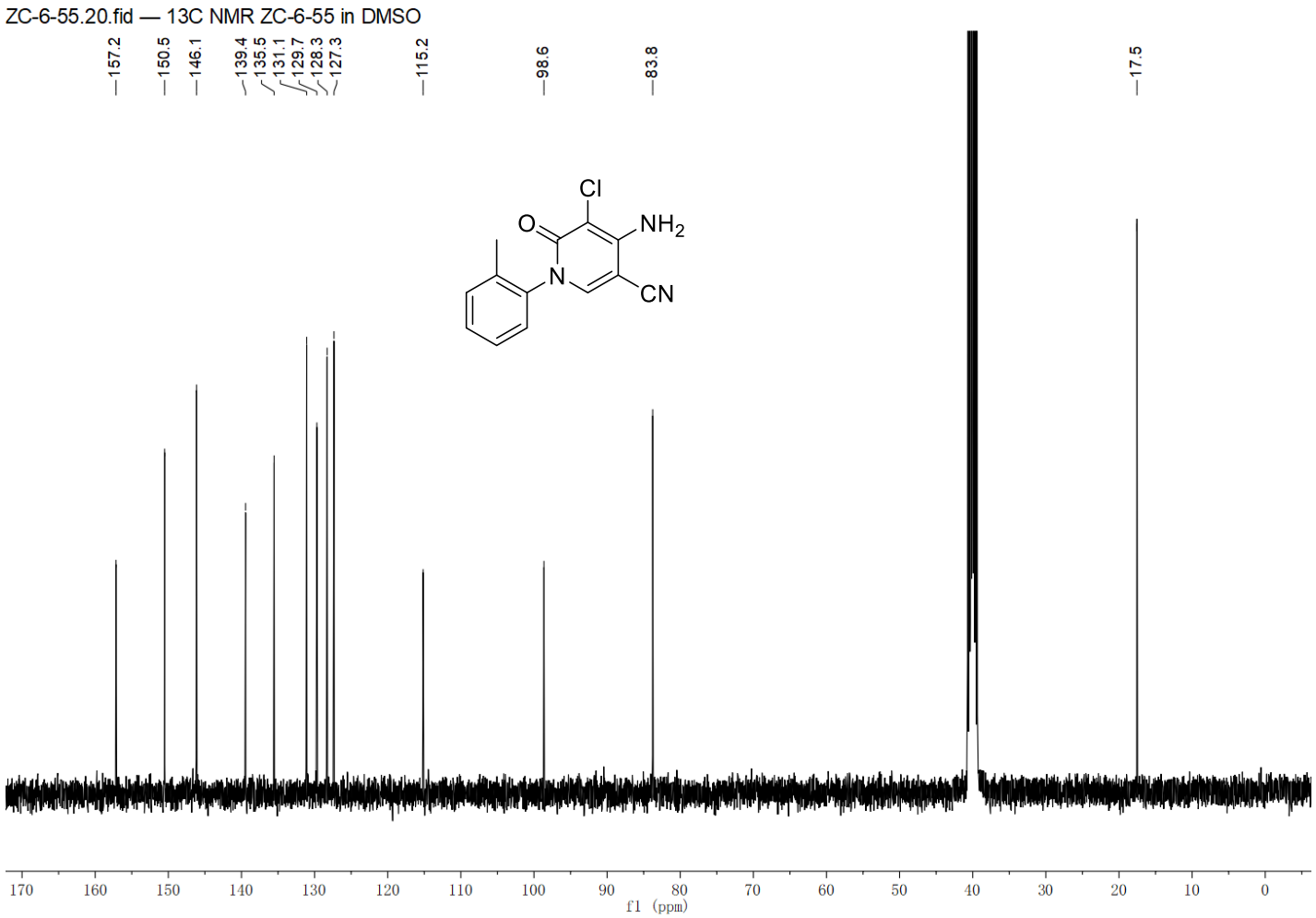
^{1}H NMR spectrum of compound **5a** (400 MHz, $CDCl_3$)



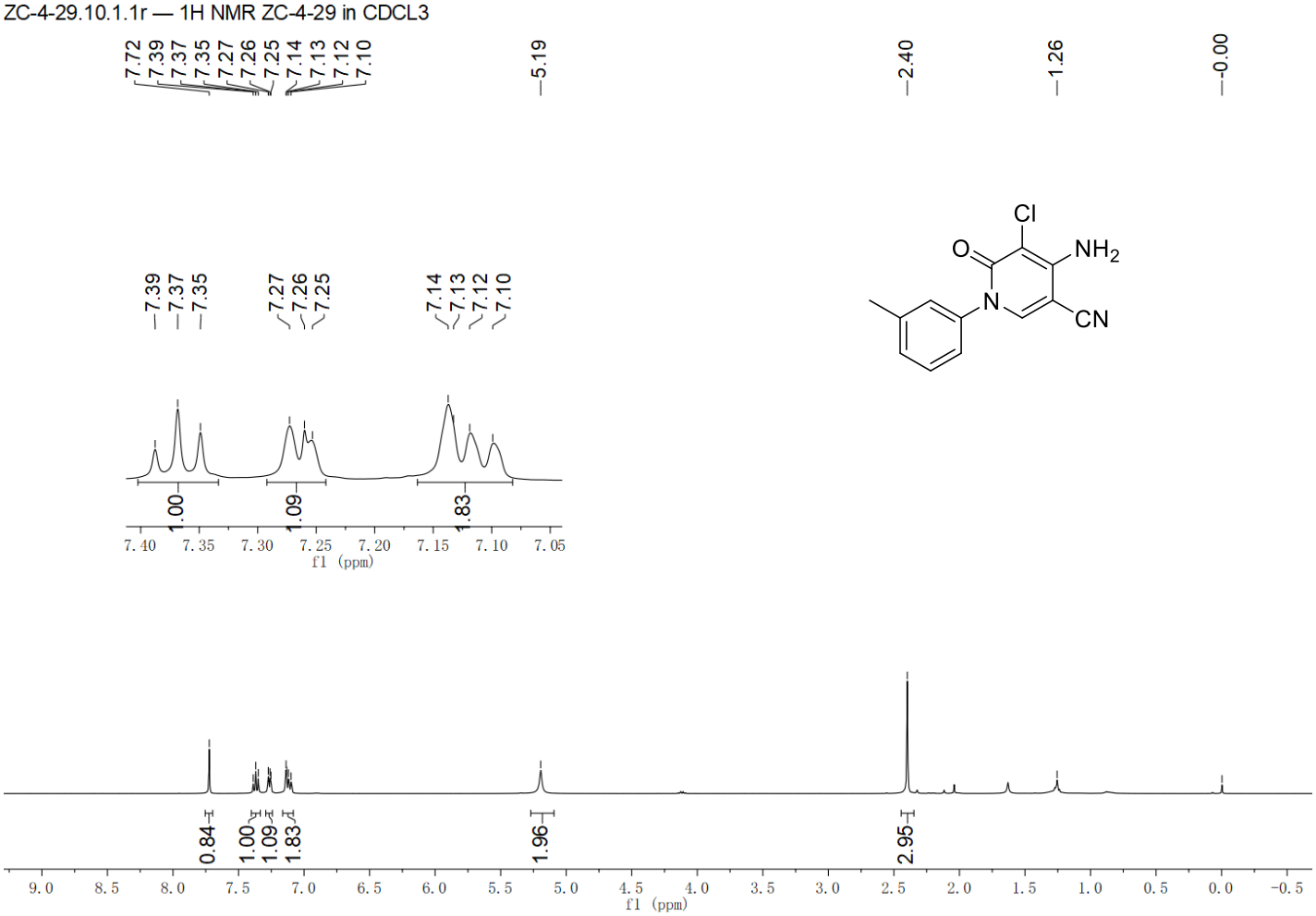
^{13}C NMR spectrum of compound **5a** (101 MHz, $CDCl_3$)



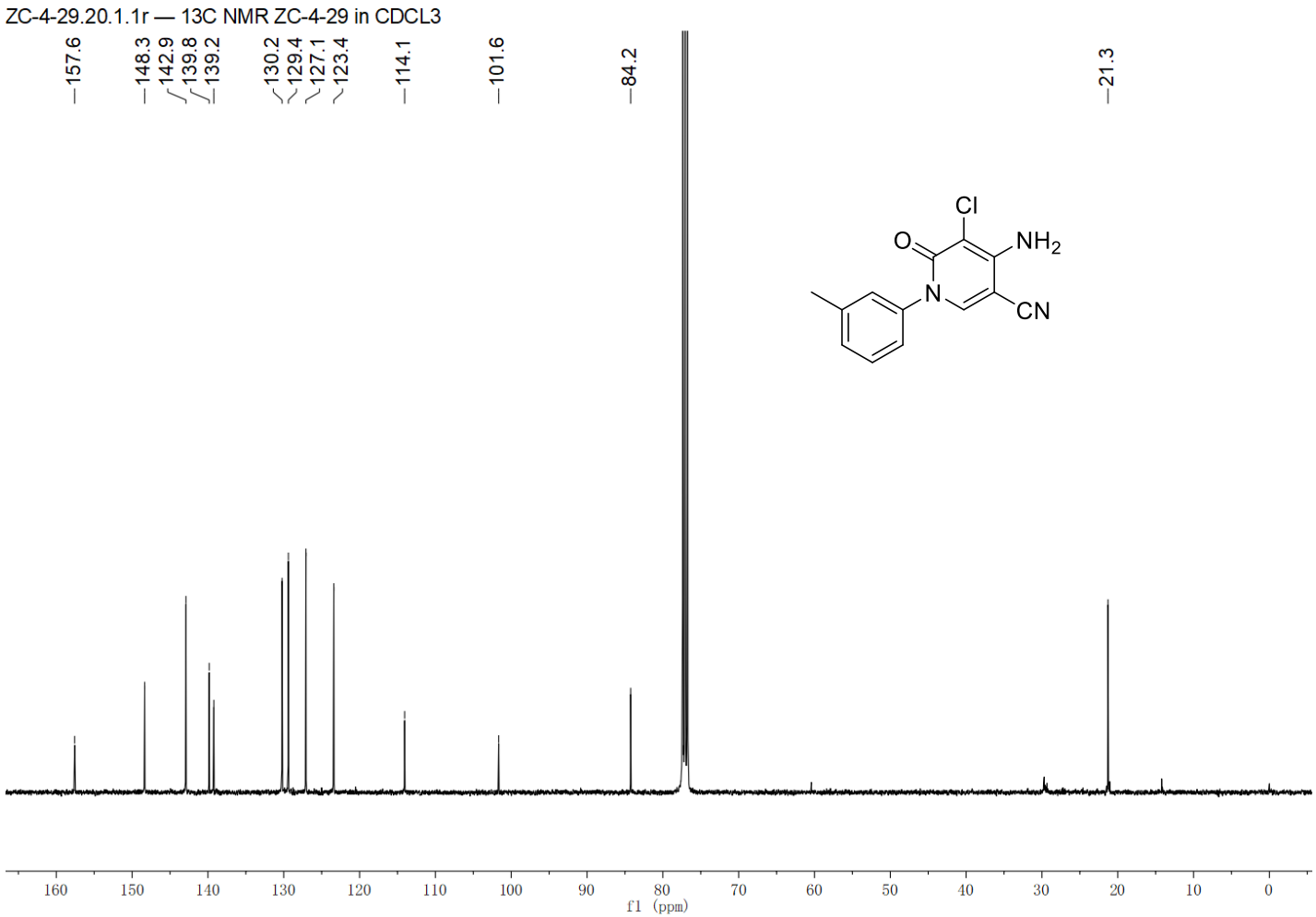
^{1}H NMR spectrum of compound **5b** (400 MHz, DMSO)



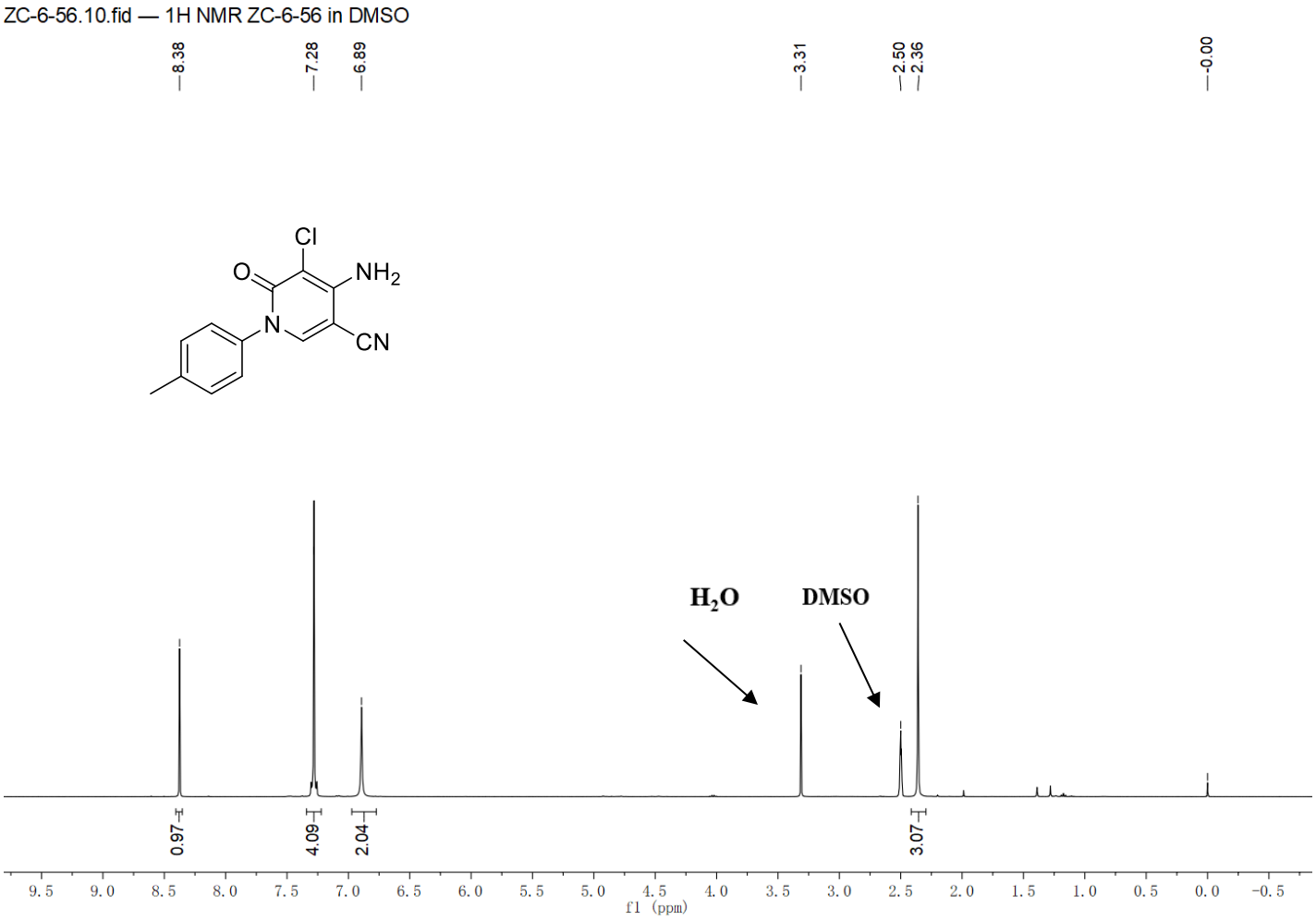
^{13}C NMR spectrum of compound **5b** (101 MHz, DMSO)



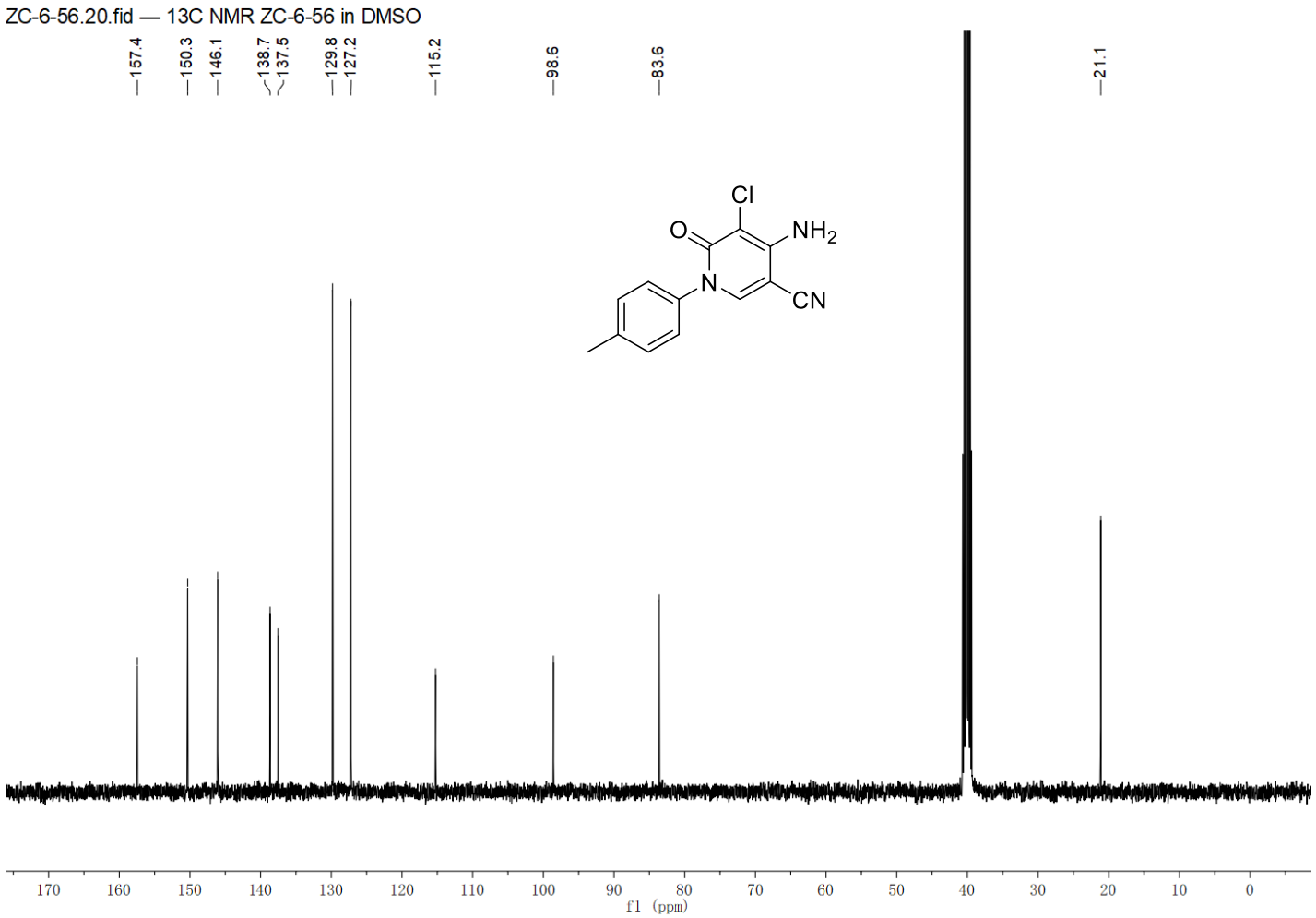
^{1}H NMR spectrum of compound **5c** (400 MHz, $CDCl_3$)



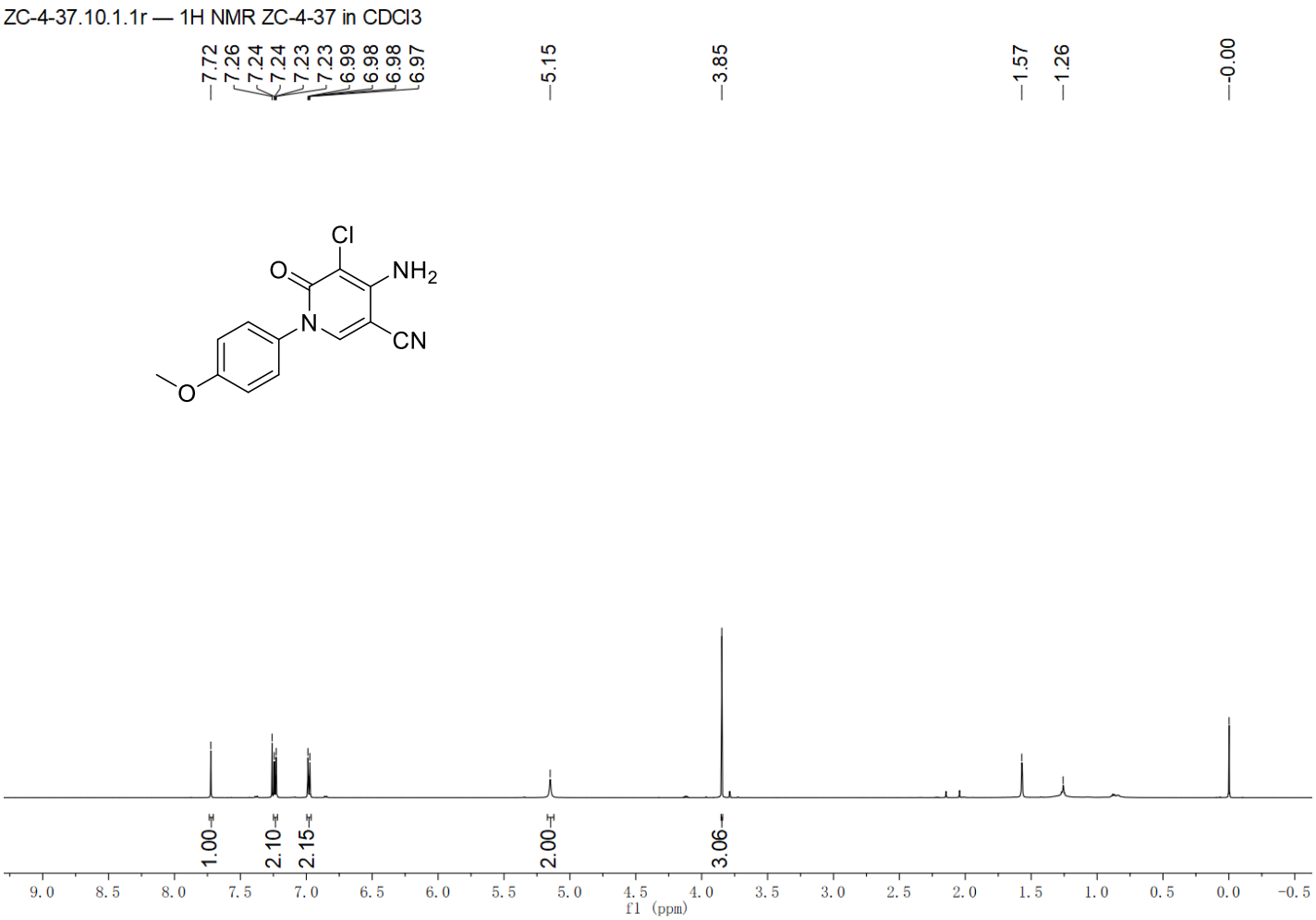
^{13}C NMR spectrum of compound **5c** (101 MHz, $CDCl_3$)



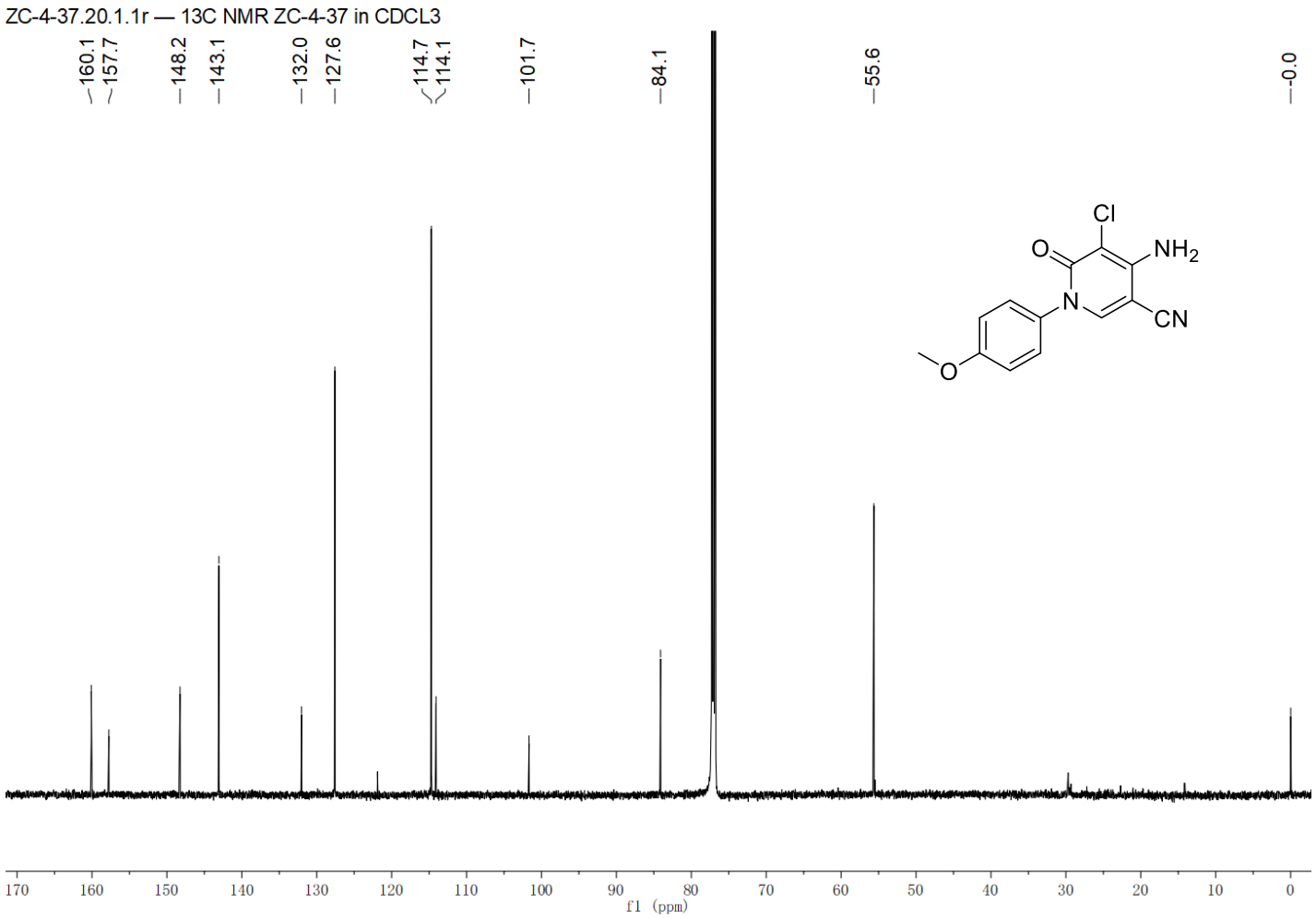
^{1}H NMR spectrum of compound **5d** (400 MHz, DMSO)



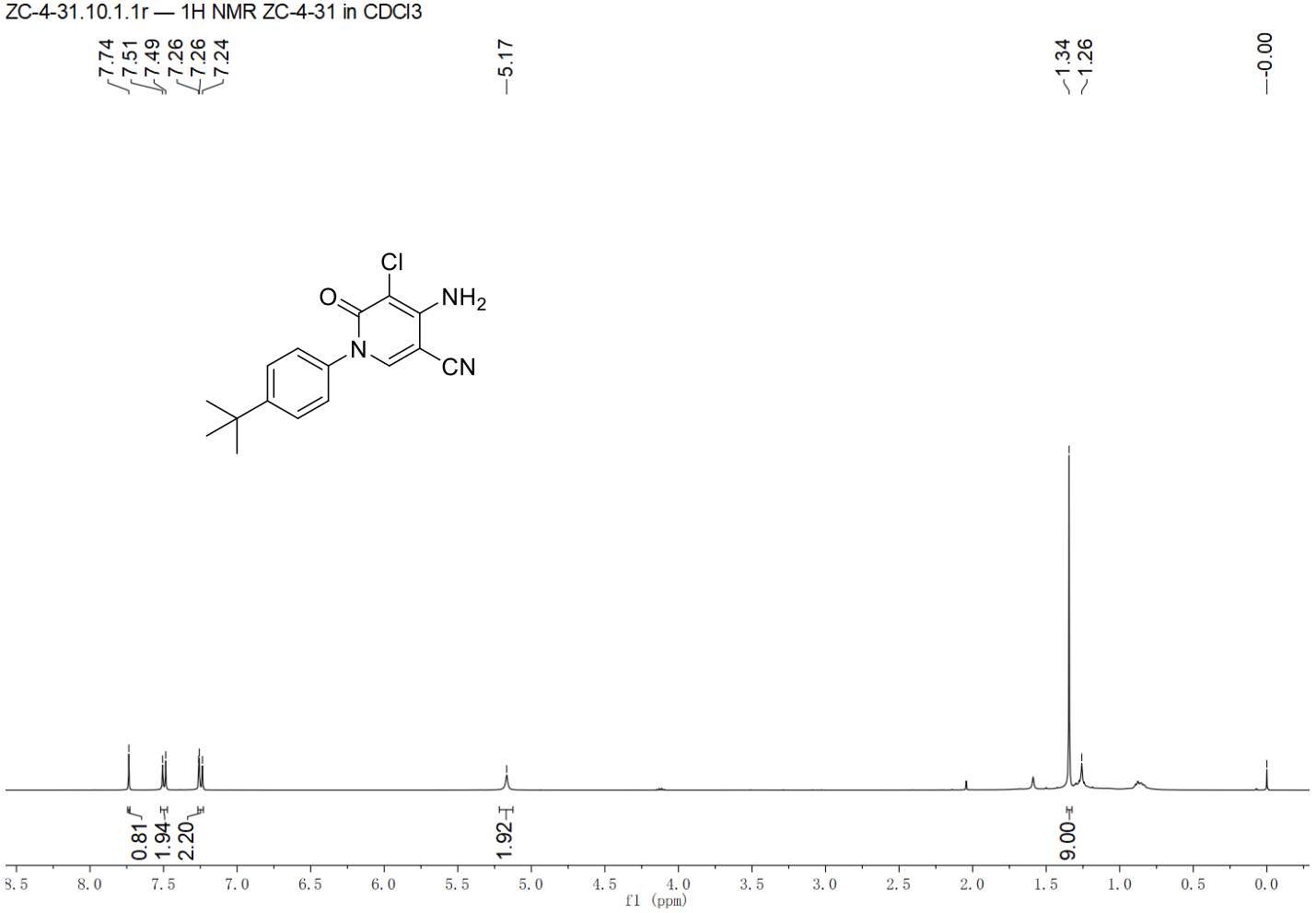
^{13}C NMR spectrum of compound **5d** (101 MHz, DMSO)



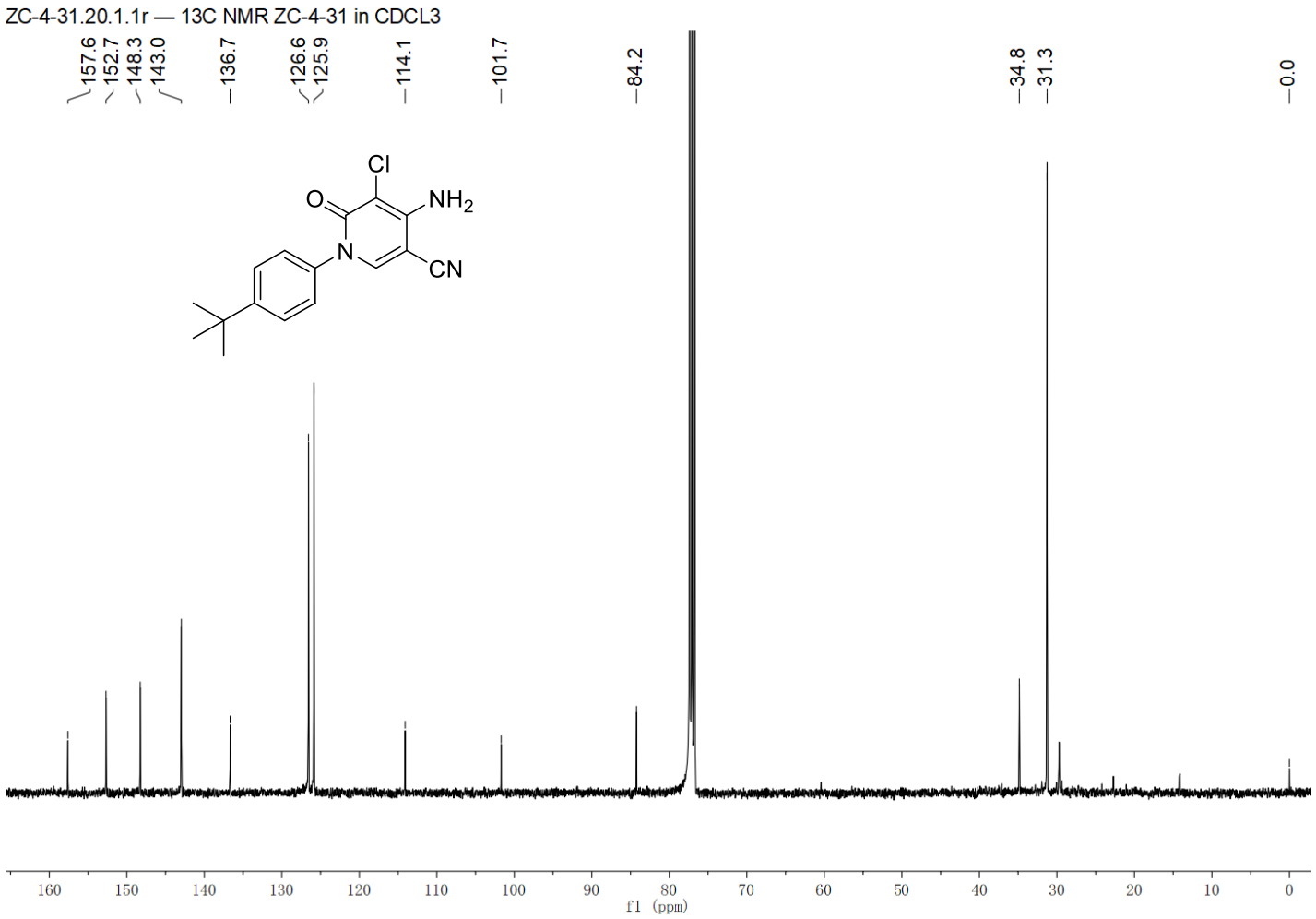
^{1}H NMR spectrum of compound **5e** (400 MHz, $CDCl_3$)



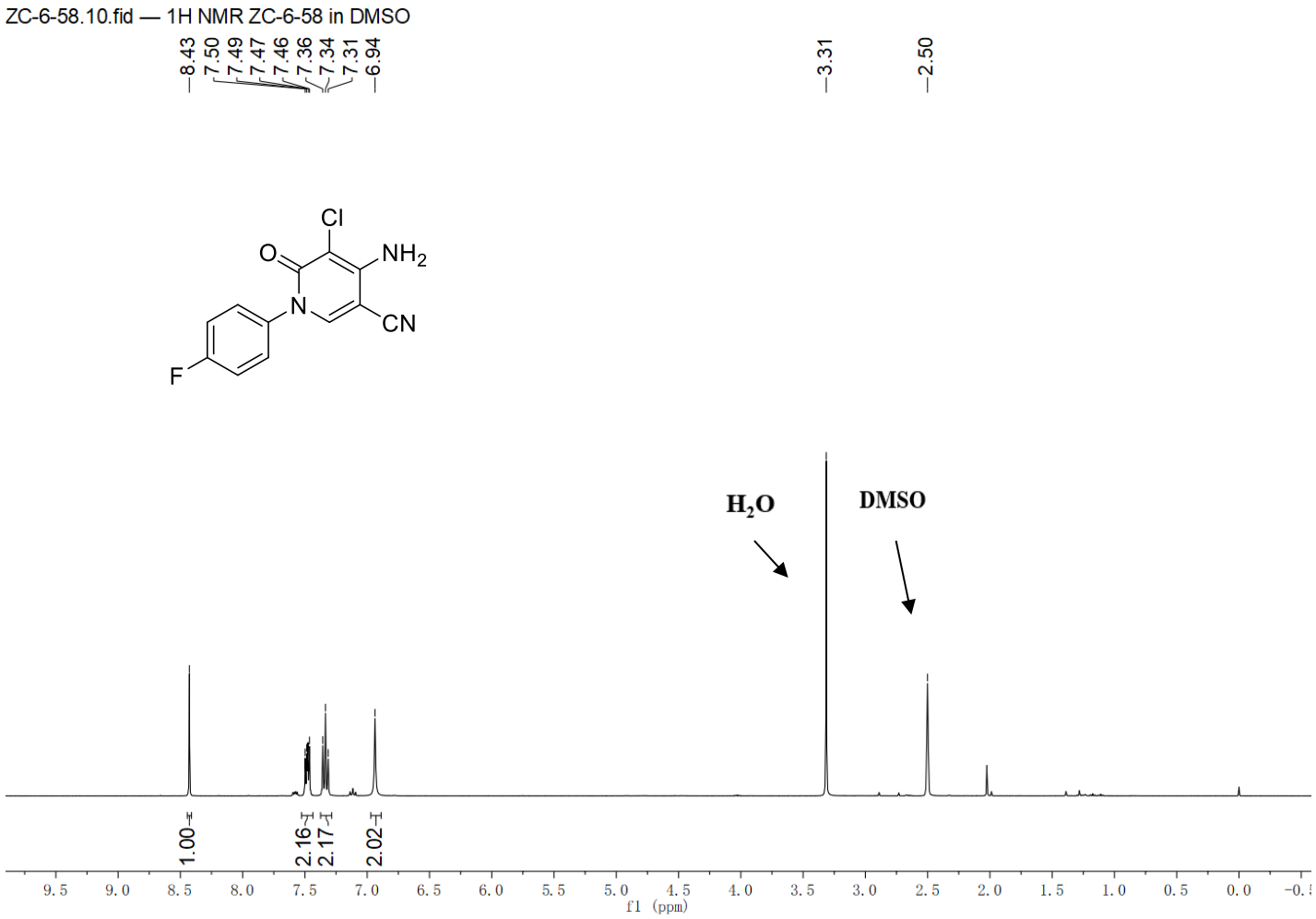
^{13}C NMR spectrum of compound **5e** (151 MHz, $CDCl_3$)



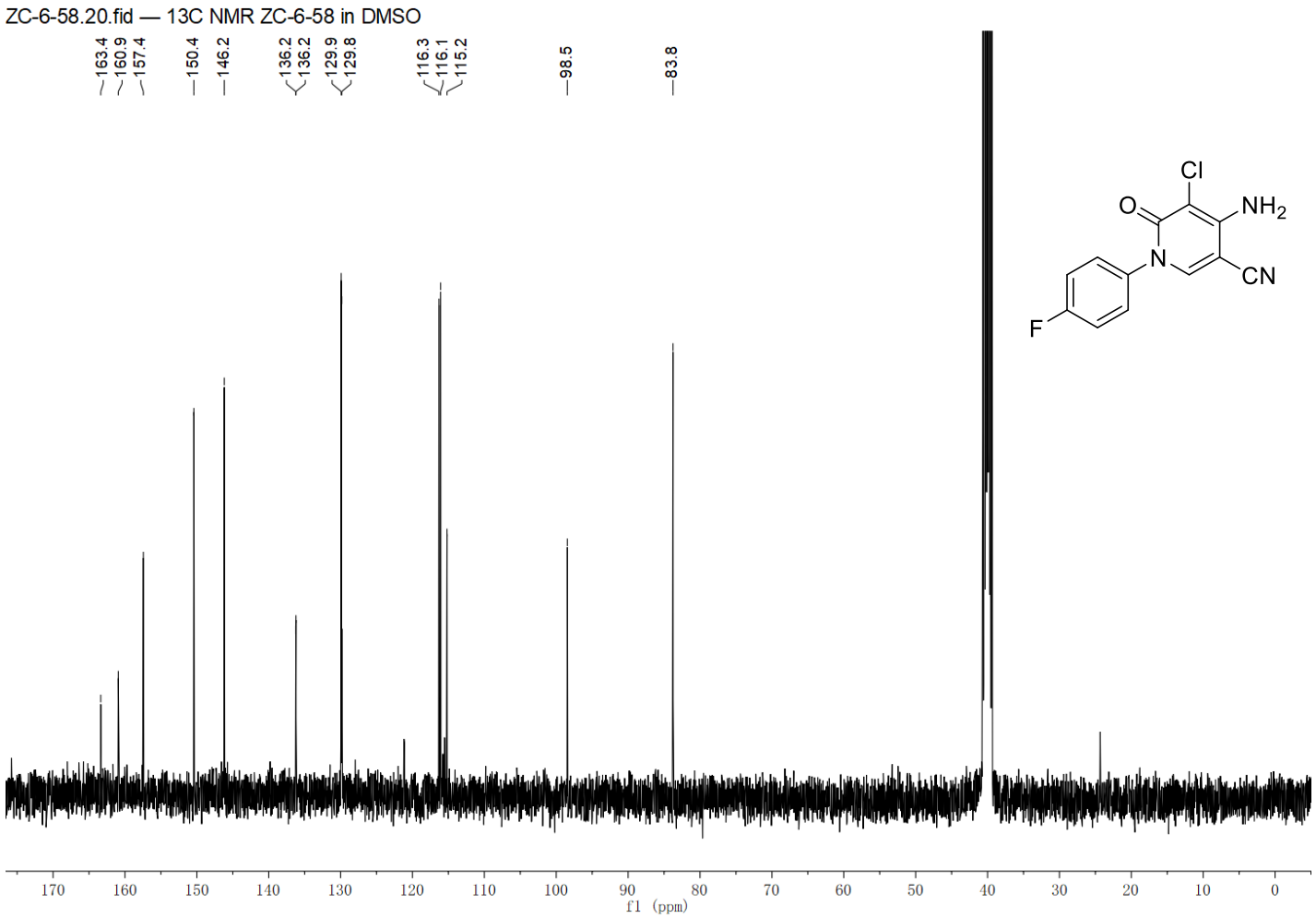
^{1}H NMR spectrum of compound **5f** (400 MHz, $CDCl_3$)



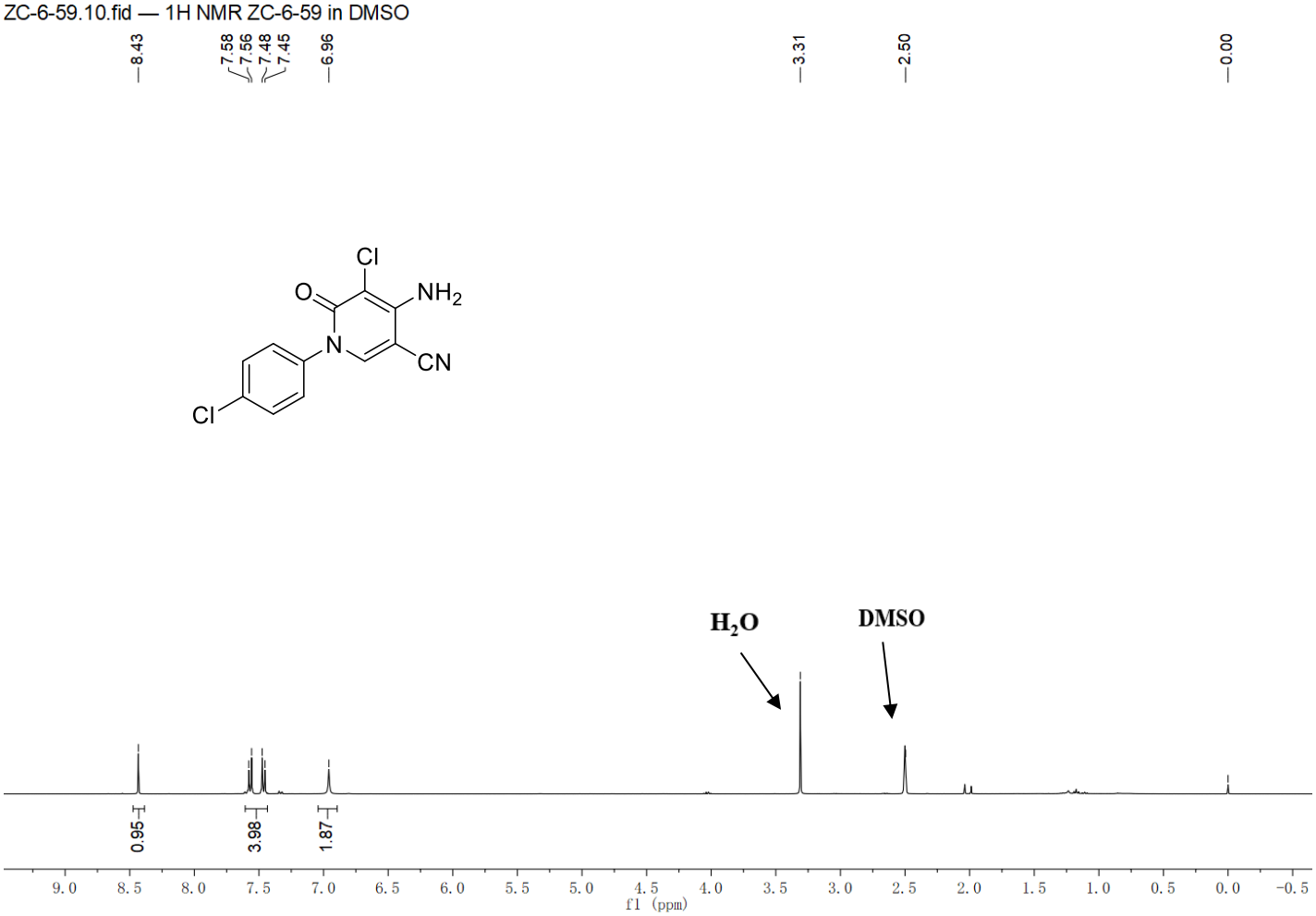
^{13}C NMR spectrum of compound **5f** (101 MHz, $CDCl_3$)



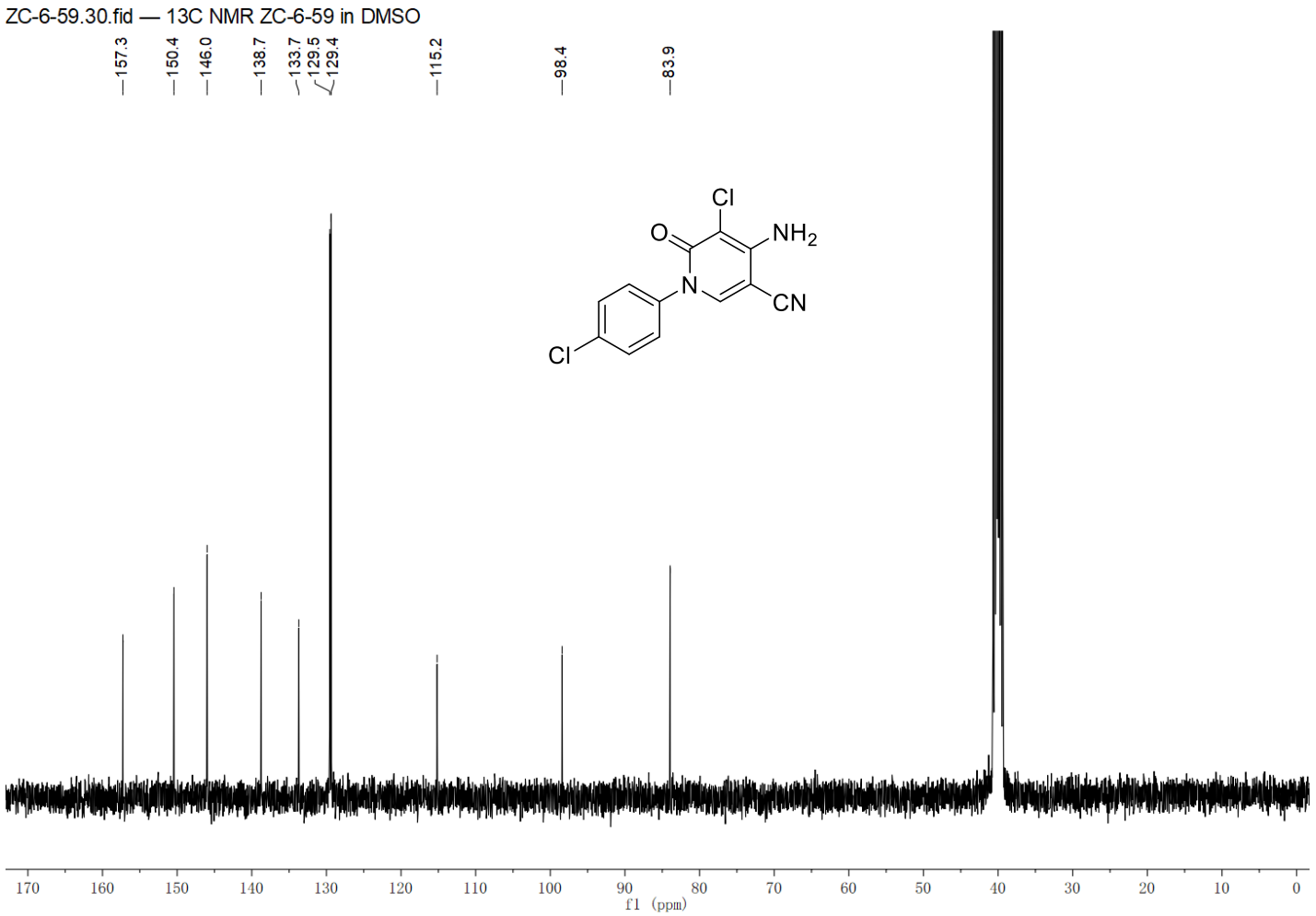
^{1}H NMR spectrum of compound **5g** (400 MHz, DMSO)



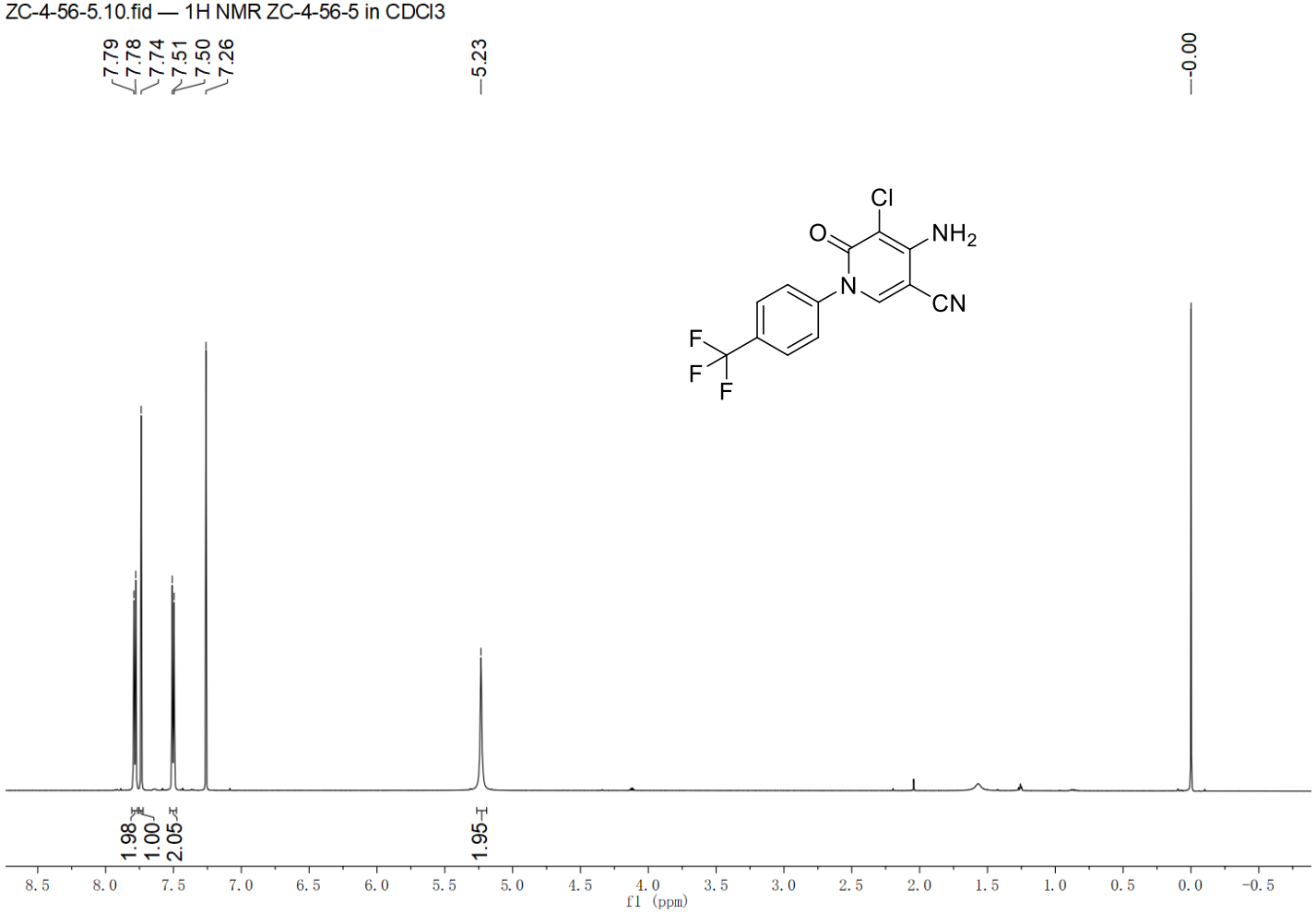
^{13}C NMR spectrum of compound **5g** (101 MHz, DMSO)



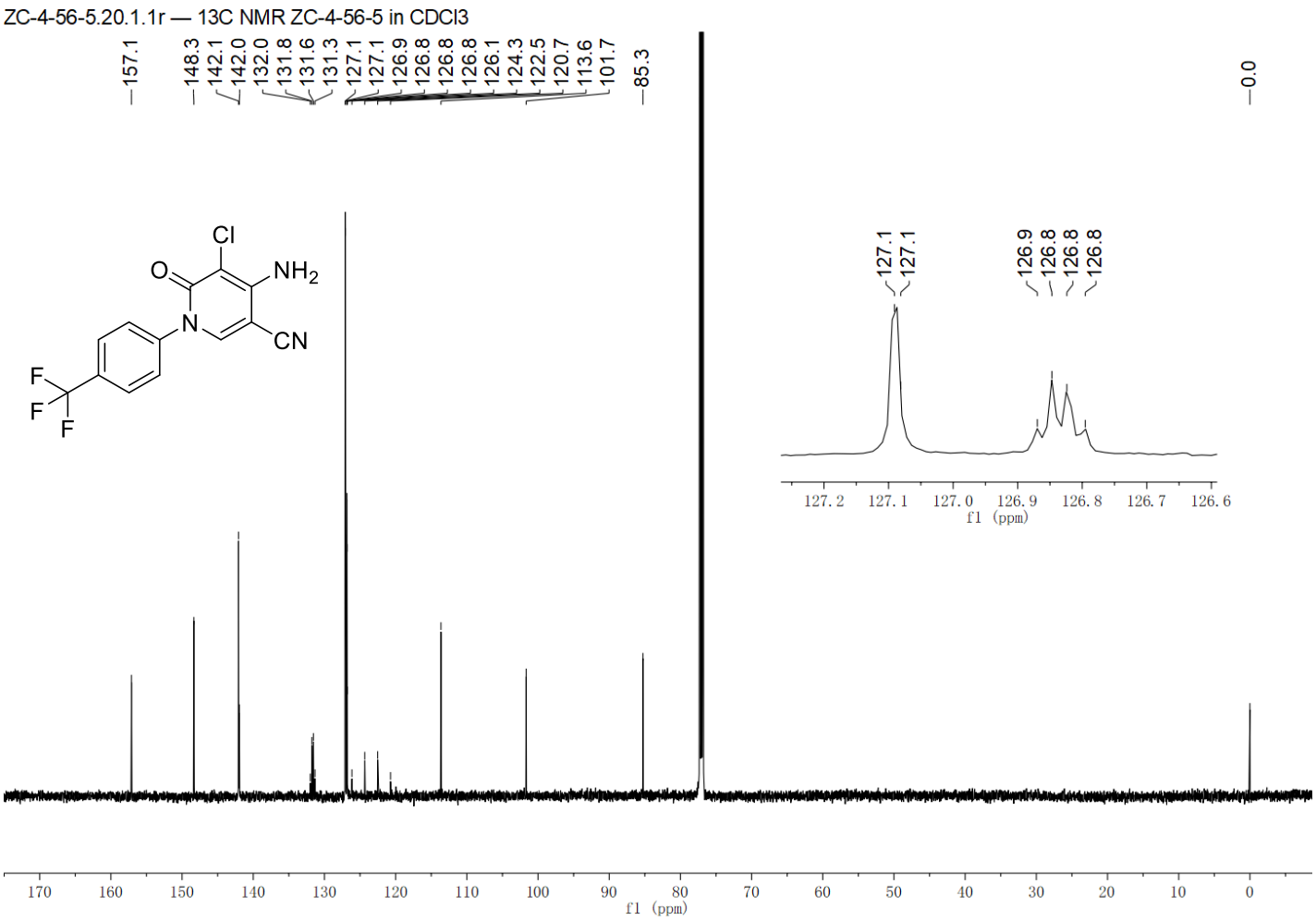
^{1}H NMR spectrum of compound **5h** (400 MHz, DMSO)



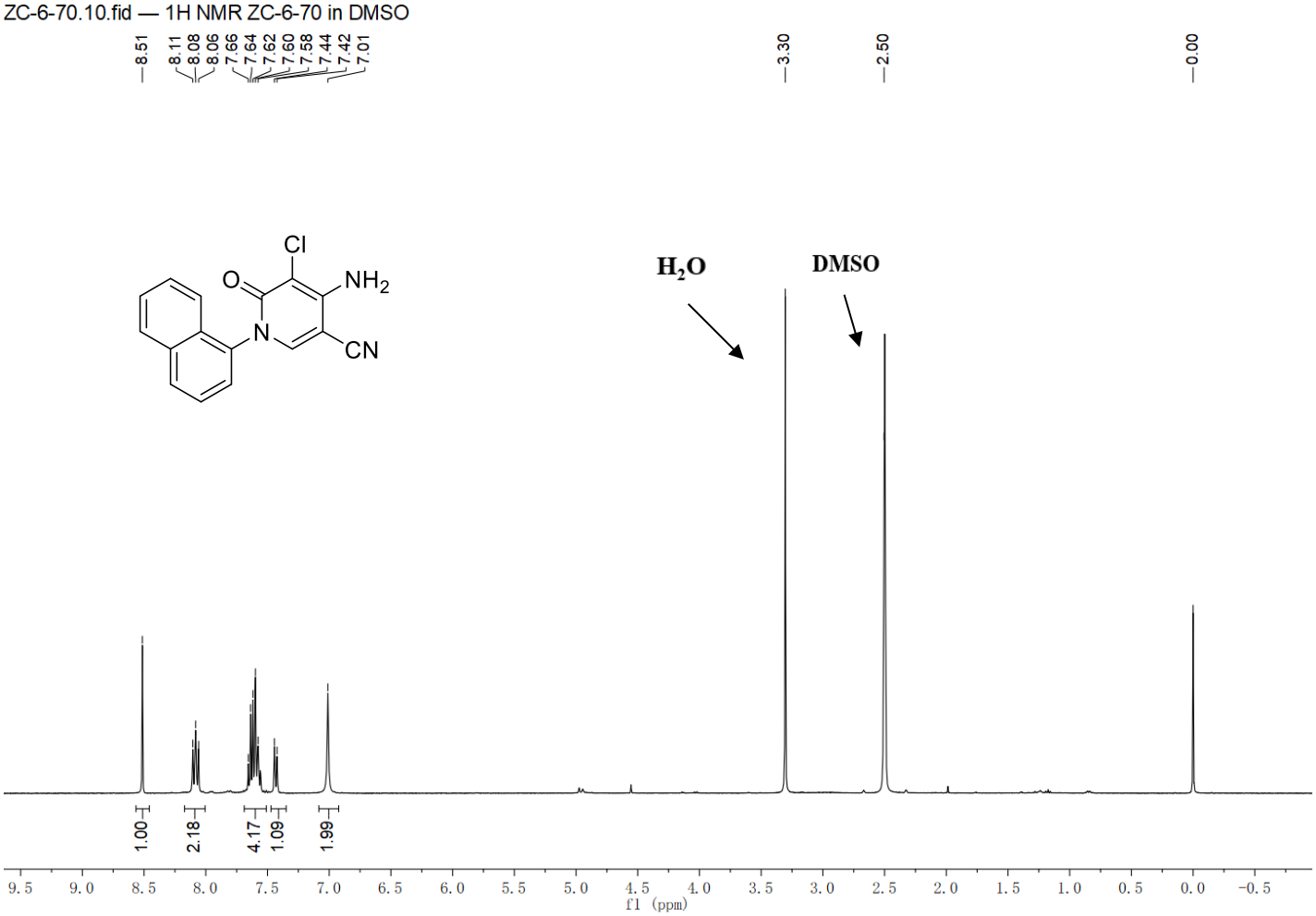
^{13}C NMR spectrum of compound **5h** (101 MHz, DMSO)



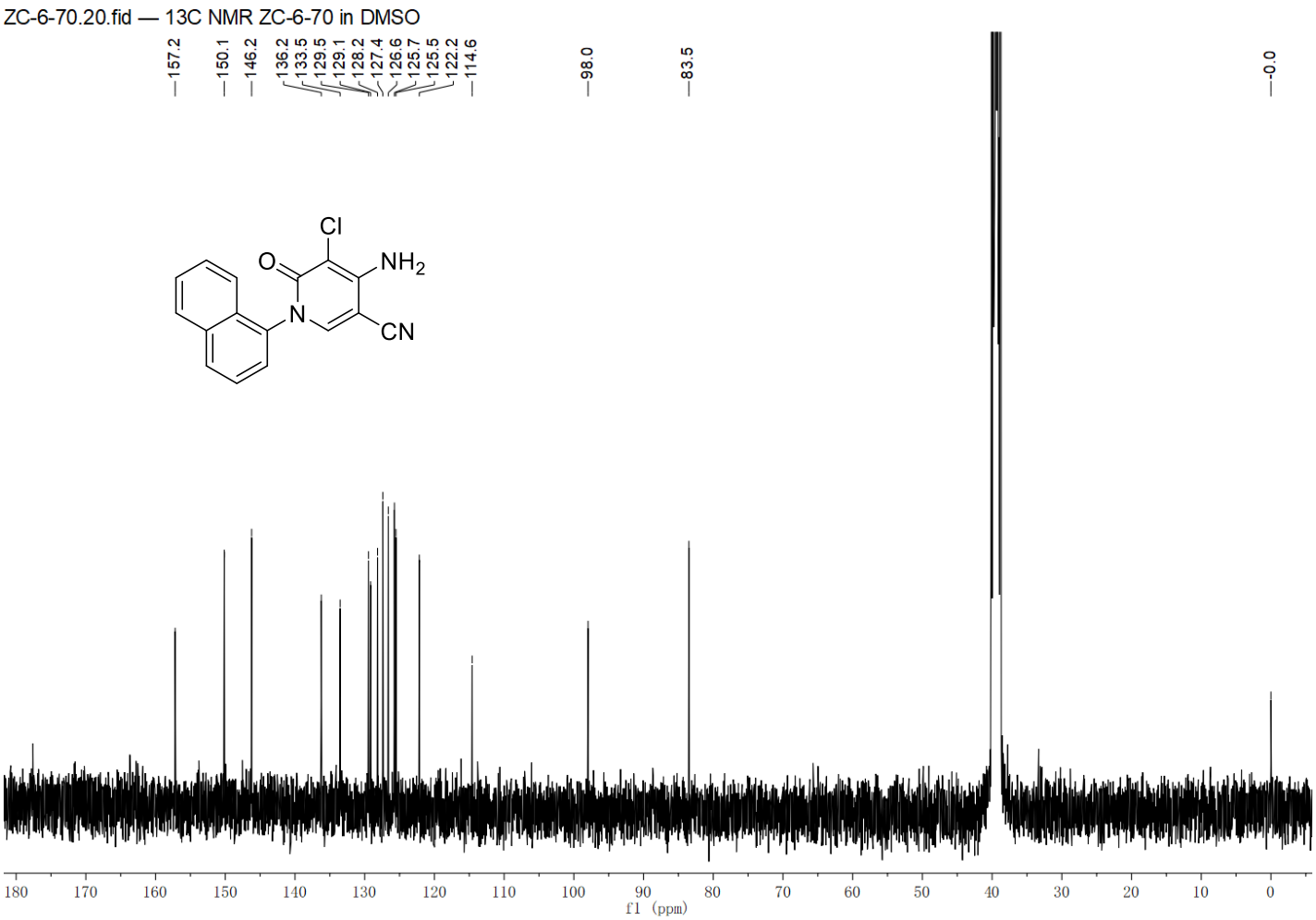
^{1}H NMR spectrum of compound **5i** (600 MHz, $CDCl_3$)



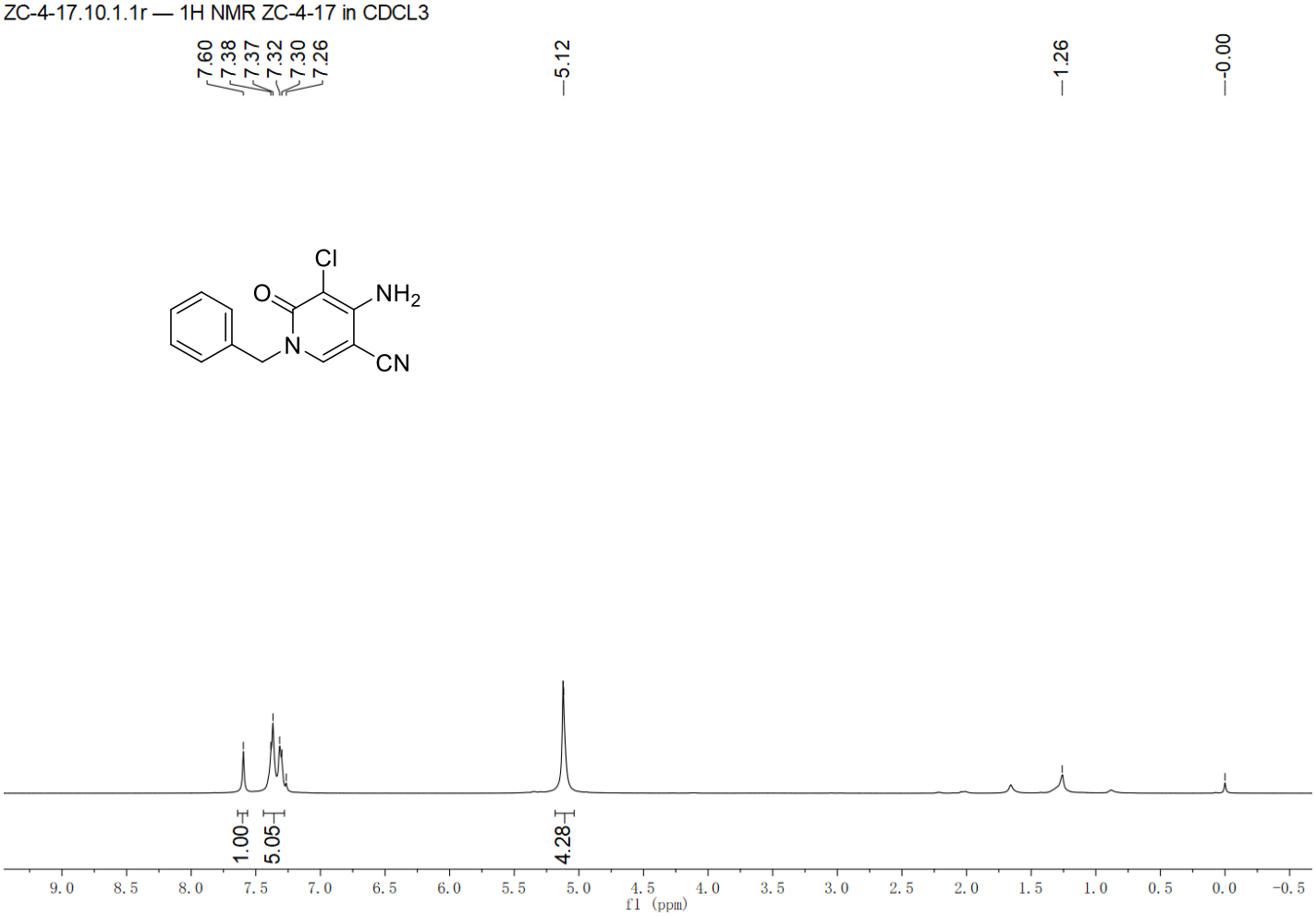
^{13}C NMR spectrum of compound **5i** (151 MHz, $CDCl_3$)



^{1}H NMR spectrum of compound **5j** (400 MHz, DMSO)

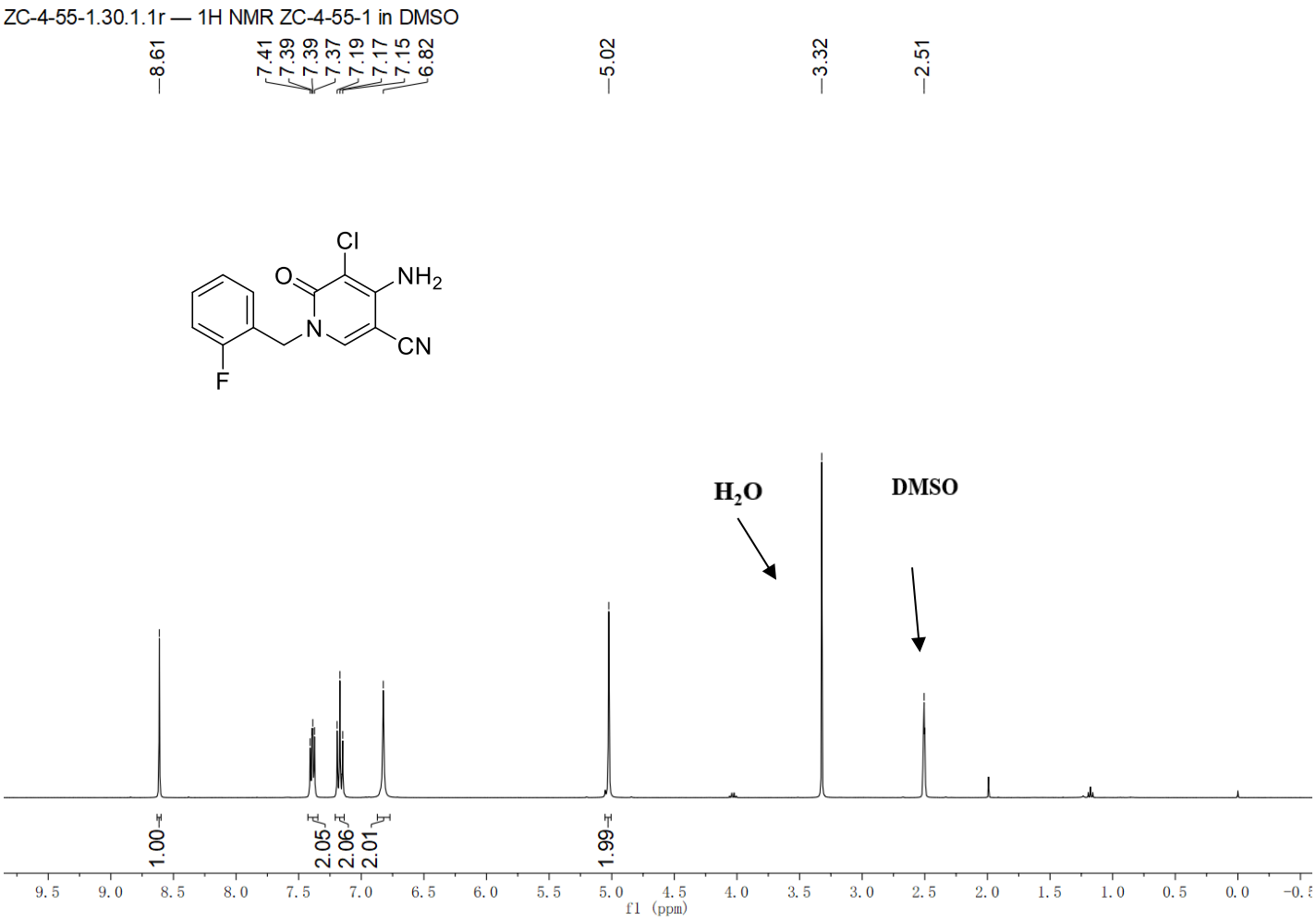


^{13}C NMR spectrum of compound **5j** (101 MHz, DMSO)



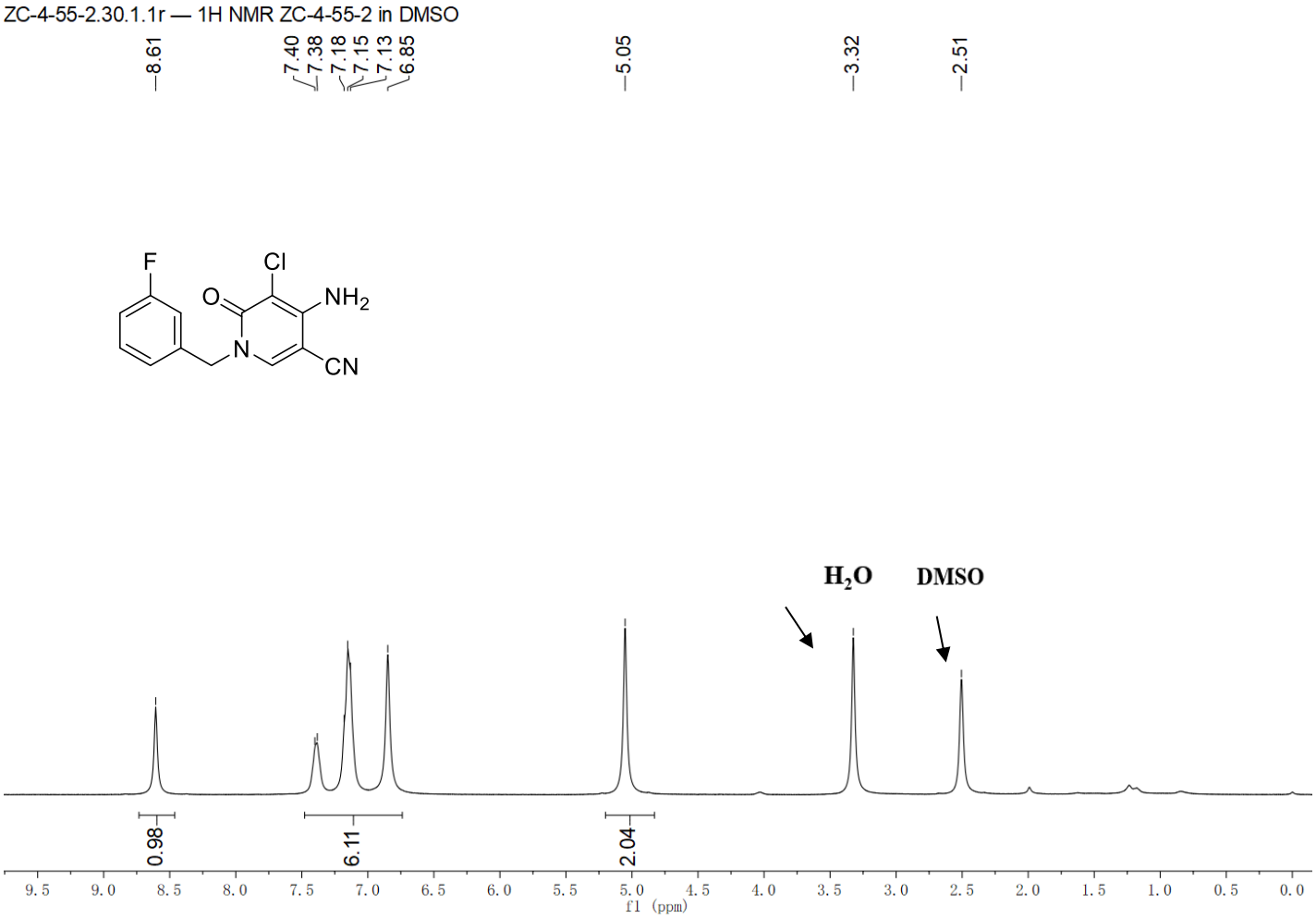
^{1}H NMR spectrum of compound **5k** (400 MHz, $CDCl_3$)

^{13}C NMR spectrum of compound **5k** (101 MHz, $CDCl_3$)

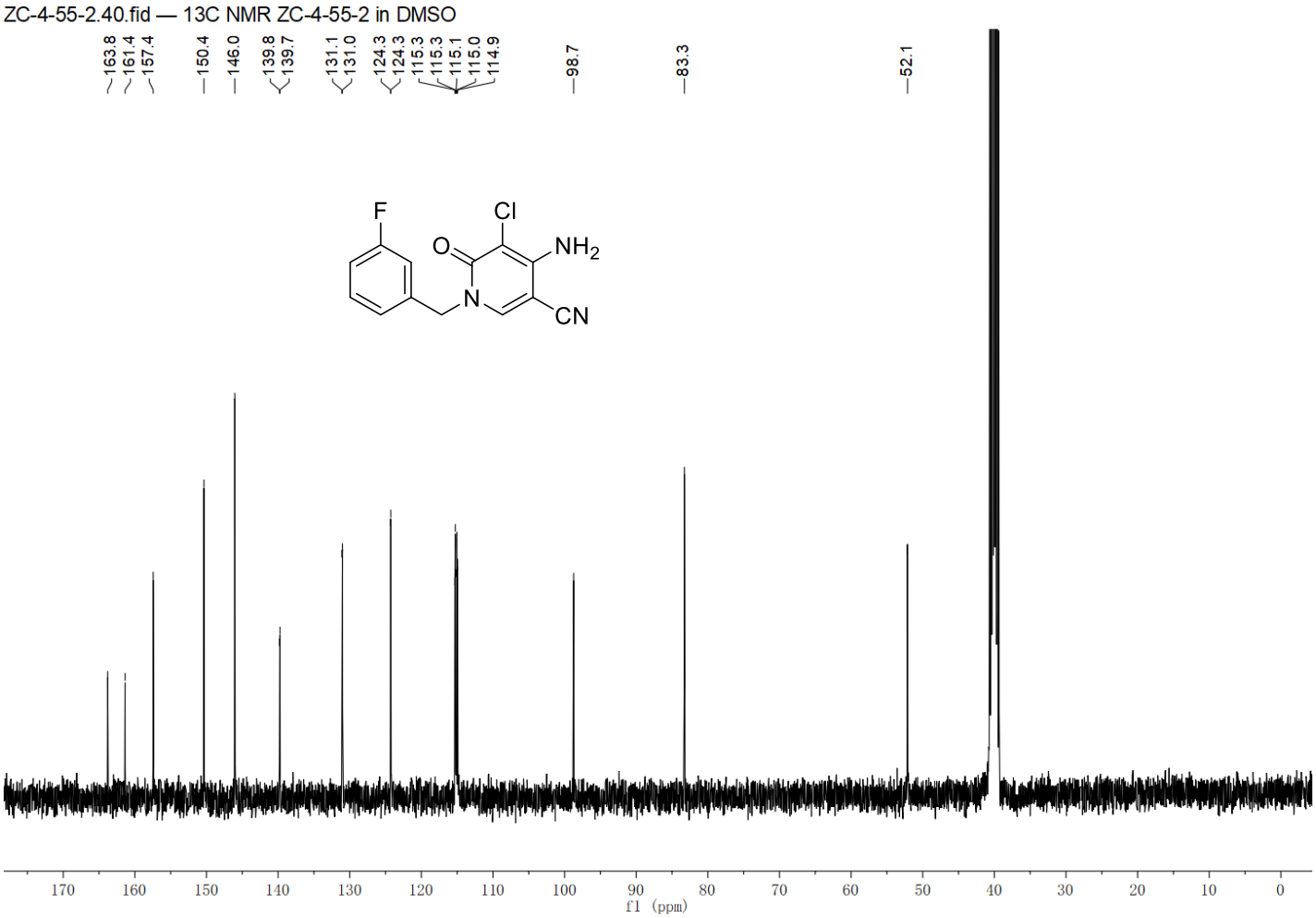


^{1}H NMR spectrum of compound **5l** (400 MHz, DMSO)

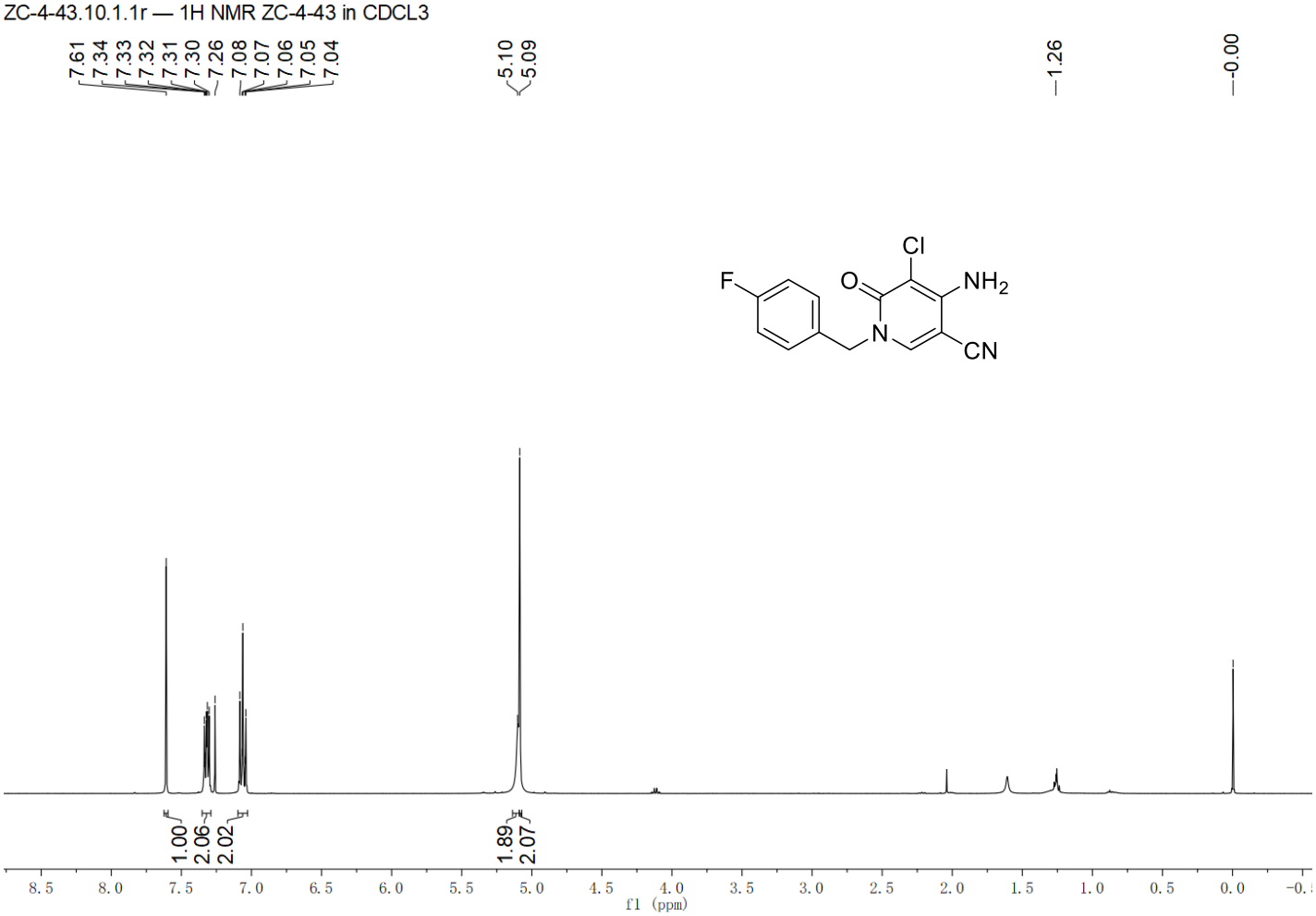
^{13}C NMR spectrum of compound **5l** (101 MHz, DMSO)



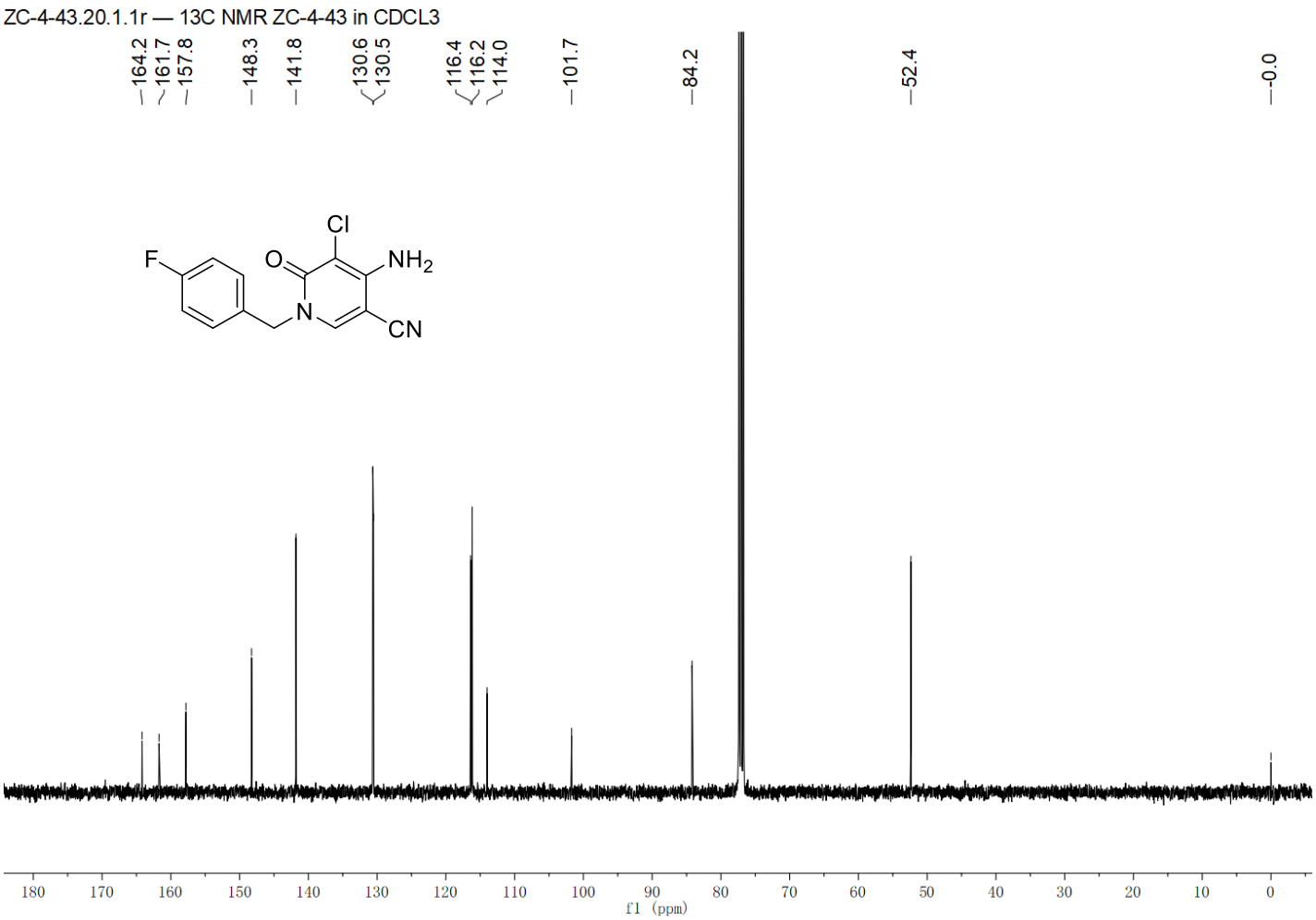
^{1}H NMR spectrum of compound **5m** (400 MHz, DMSO)



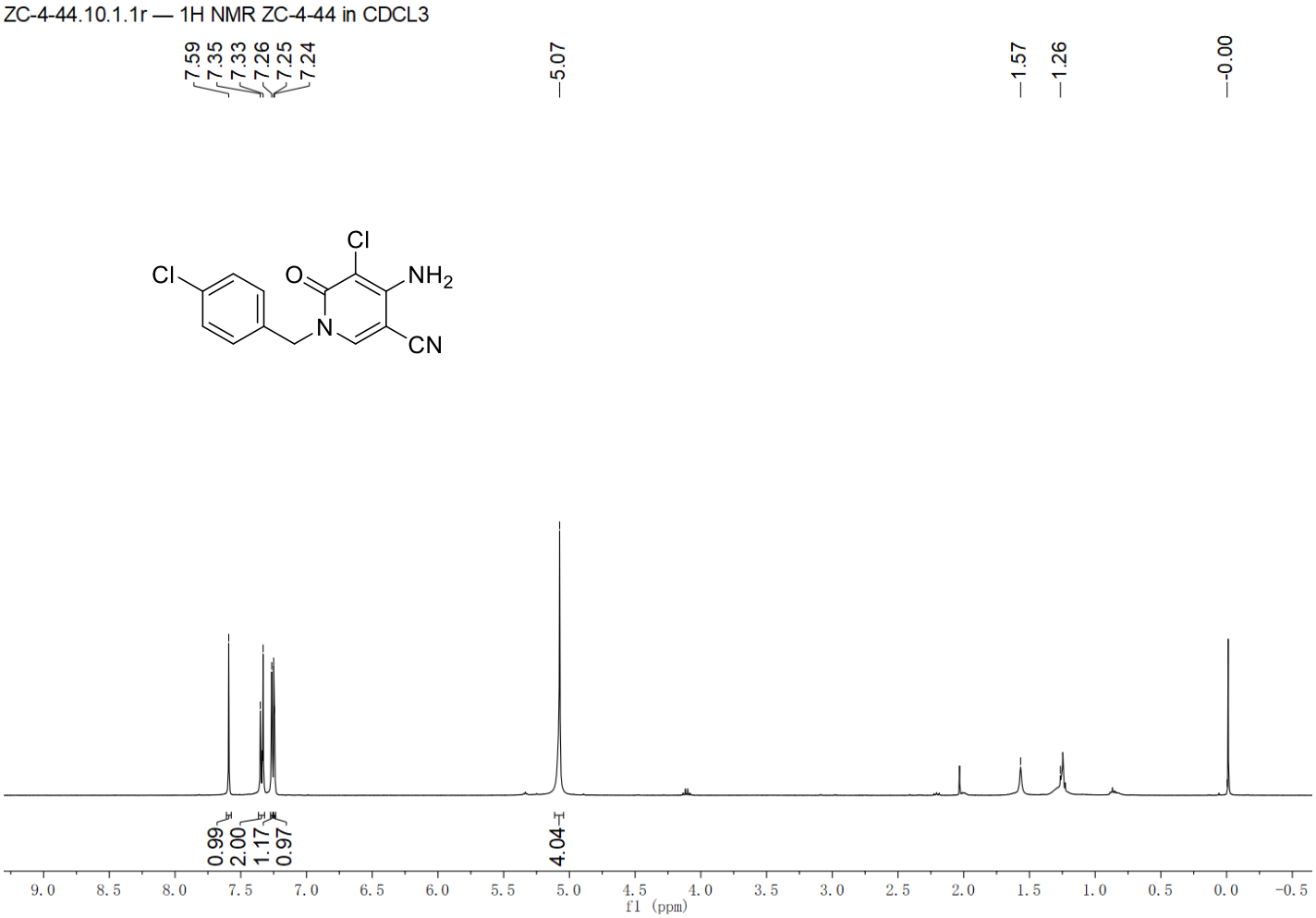
^{13}C NMR spectrum of compound **5m** (101 MHz, DMSO)



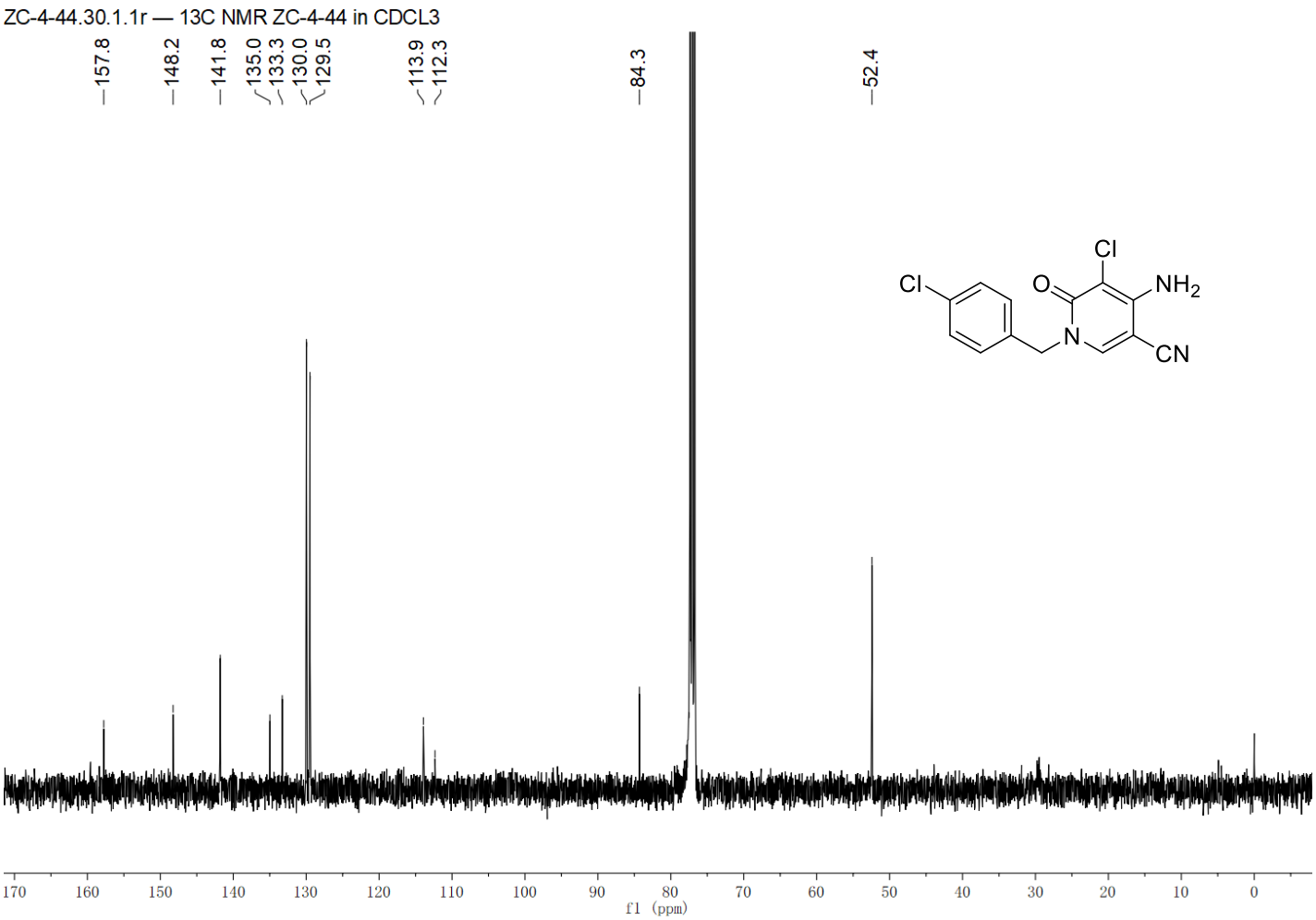
^{1}H NMR spectrum of compound **5n** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of compound **5n** (101 MHz, $CDCl_3$)

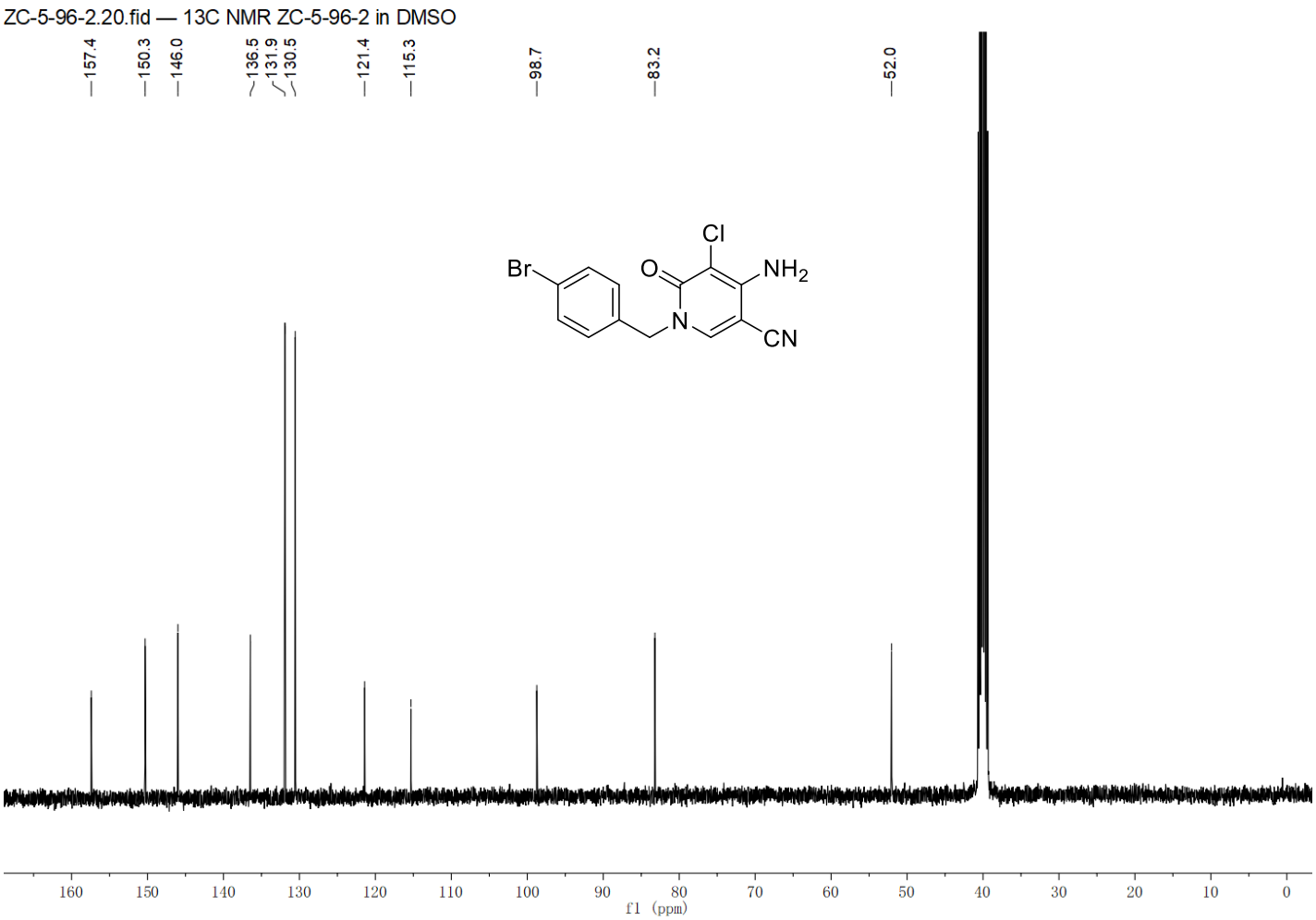


^{1}H NMR spectrum of compound **5o** (400 MHz, $CDCl_3$)

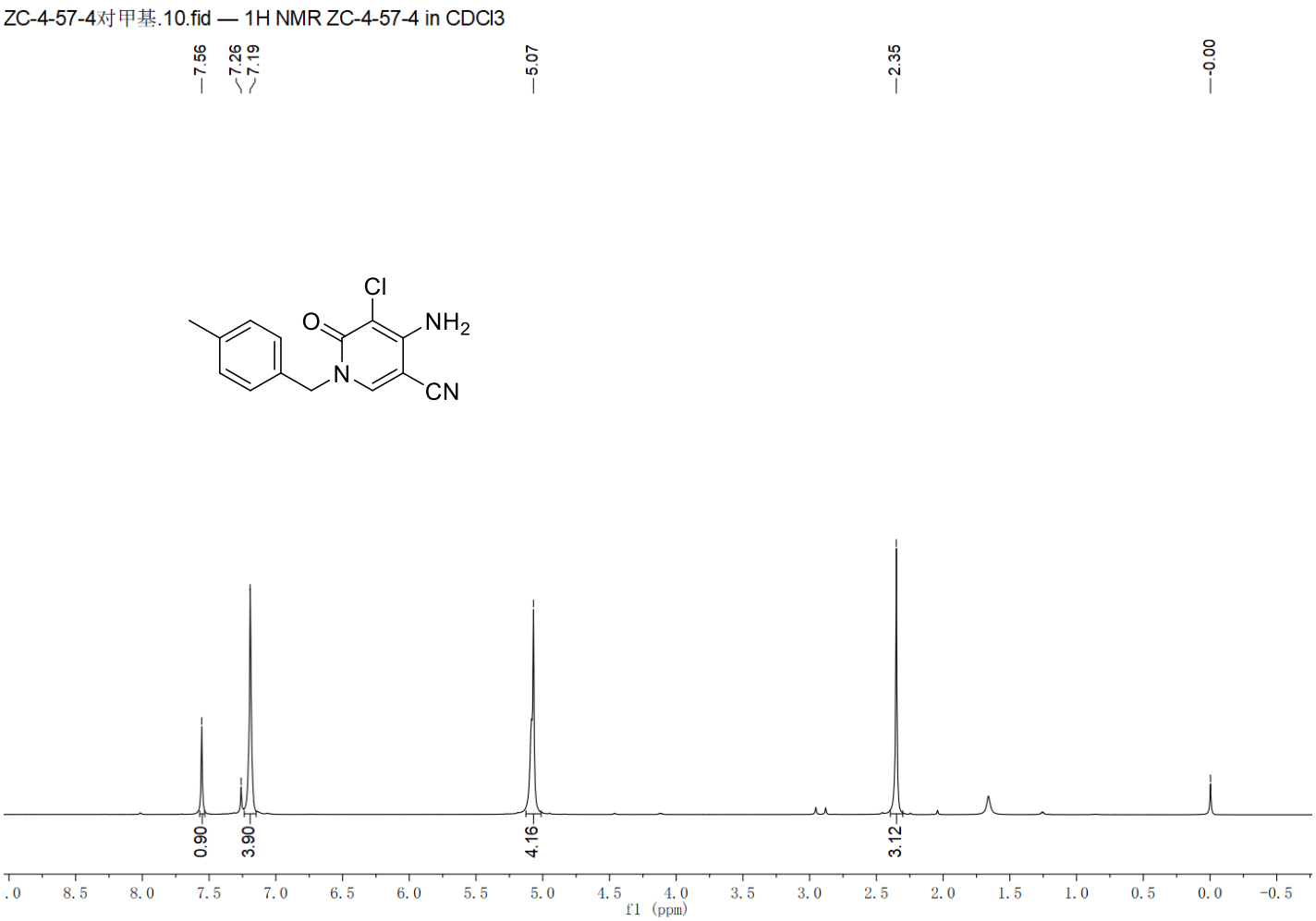


^{13}C NMR spectrum of compound **5o** (101 MHz, $CDCl_3$)

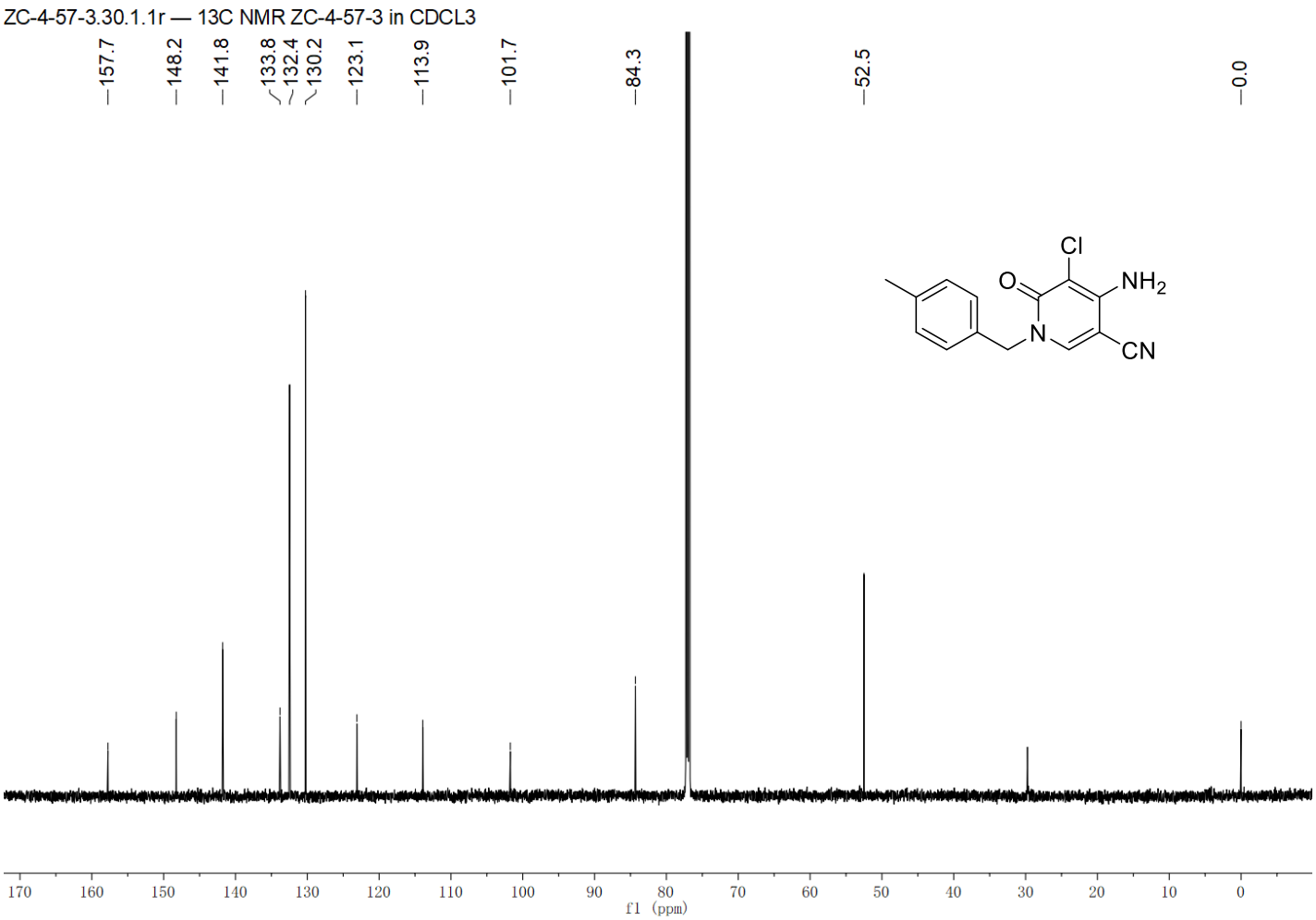
^{1}H NMR spectrum of compound **5p** (400 MHz, DMSO)



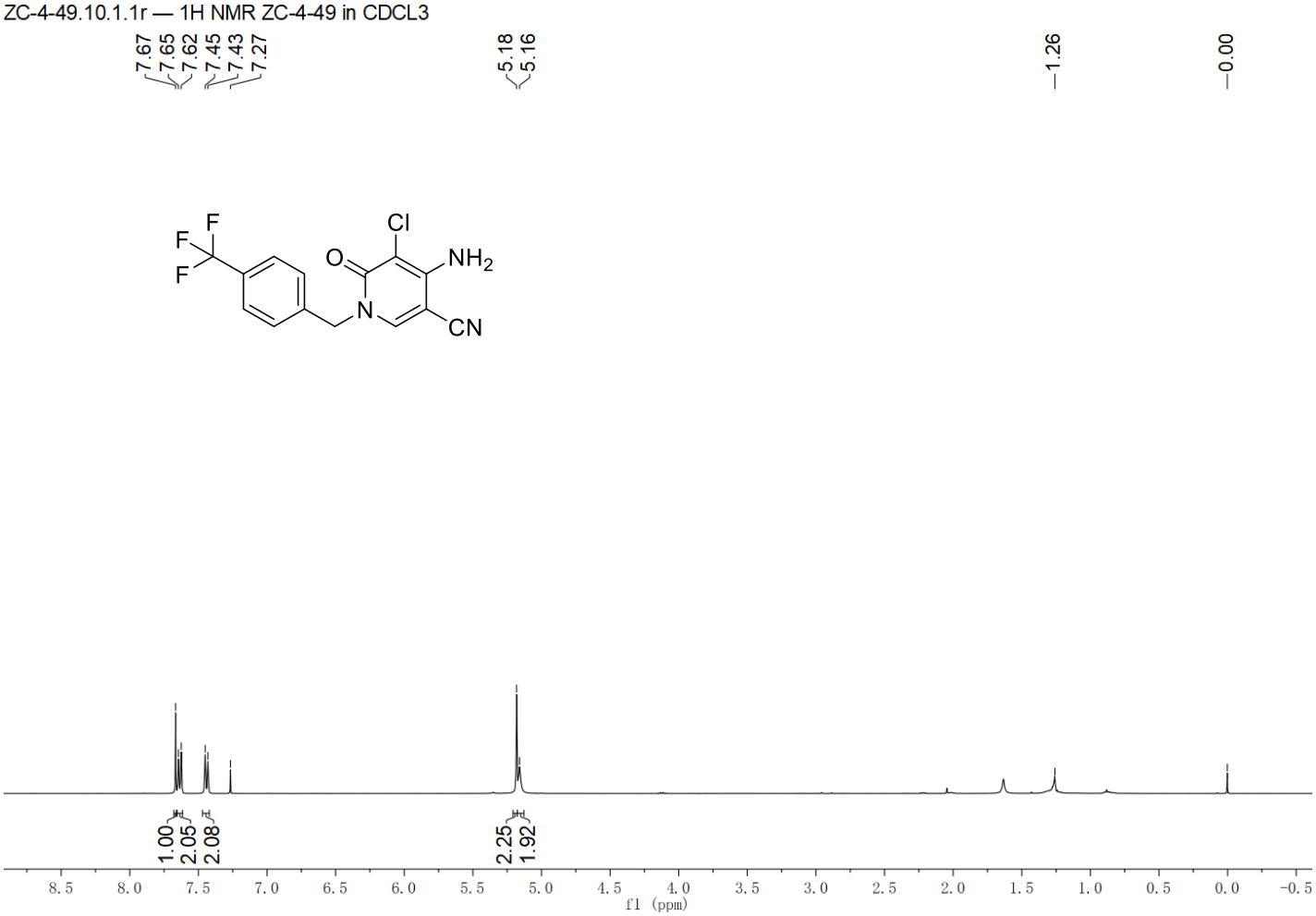
^{13}C NMR spectrum of compound **5p** (101 MHz, DMSO)



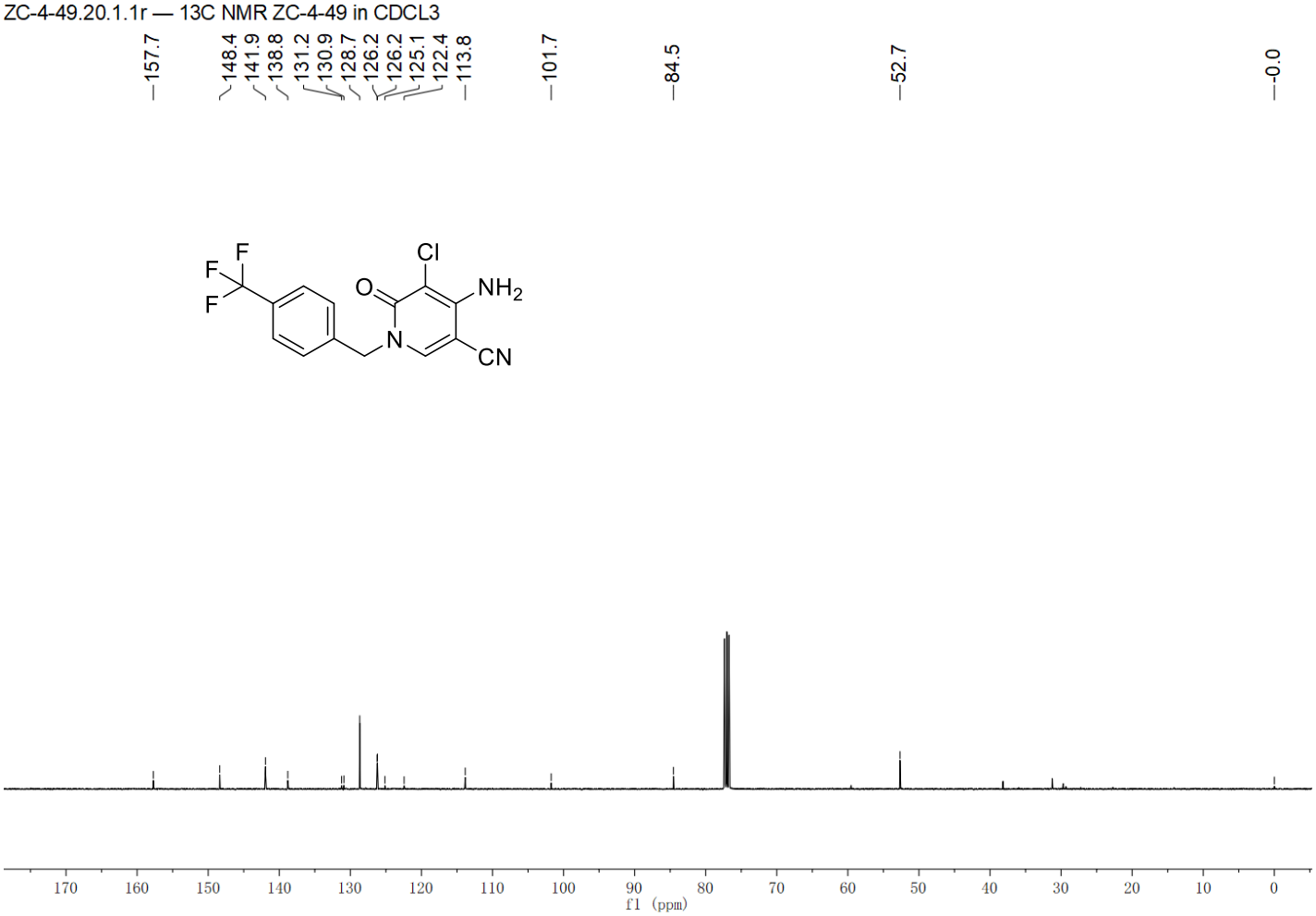
^{1}H NMR spectrum of compound **5q** (600 MHz, $CDCl_3$)



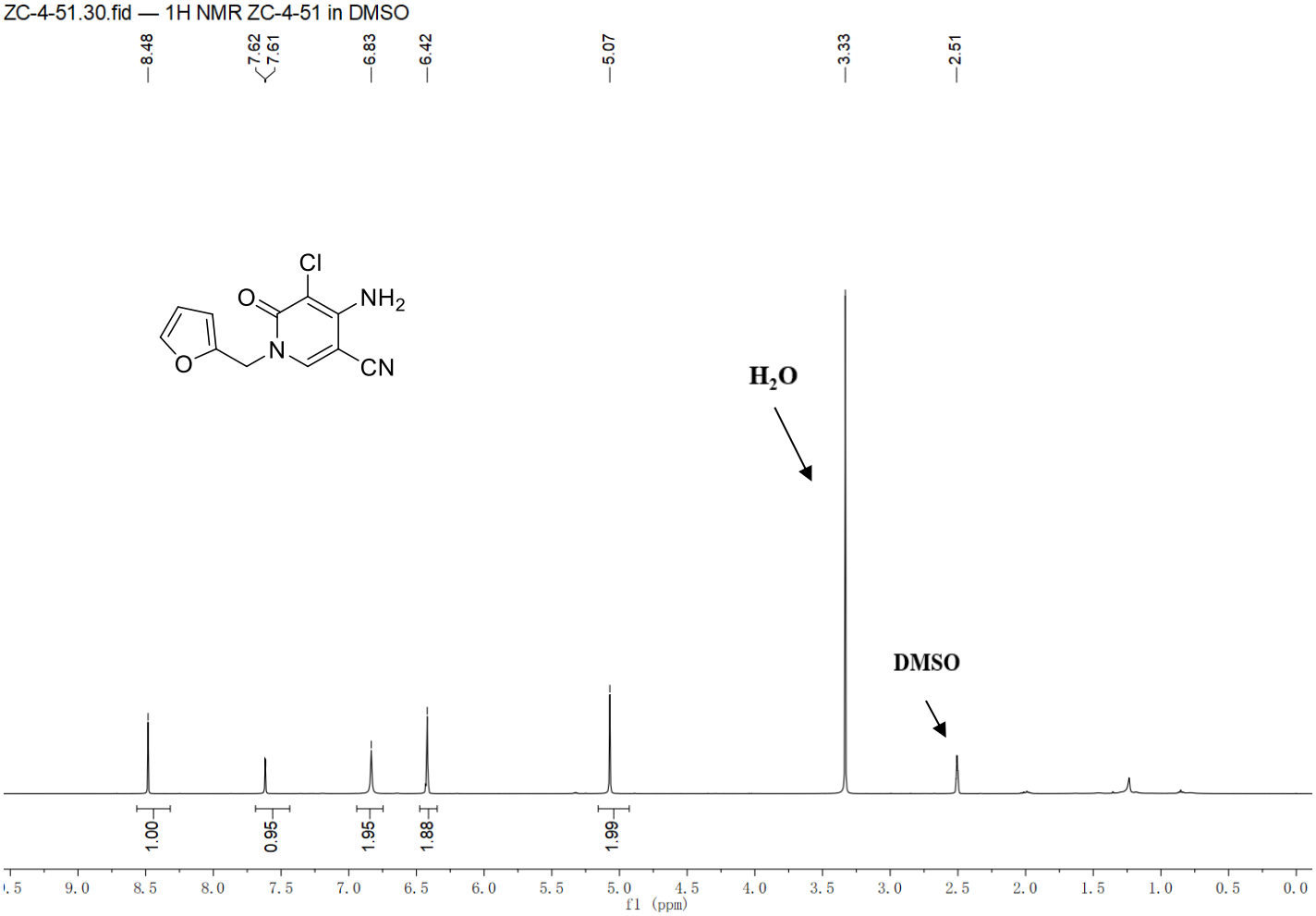
^{13}C NMR spectrum of compound **5q** (151 MHz, $CDCl_3$)



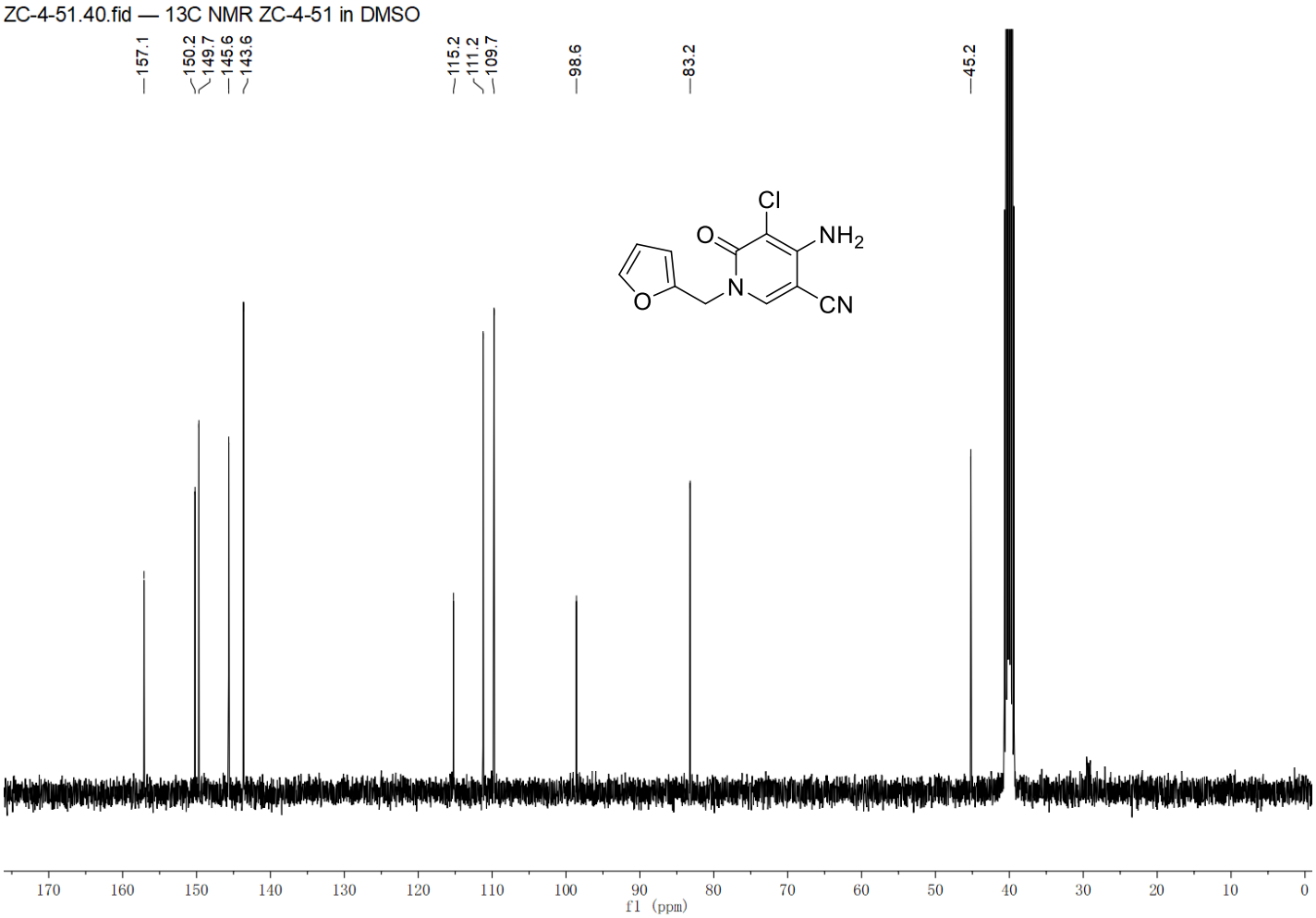
^{1}H NMR spectrum of compound **5r** (400 MHz, $CDCl_3$)



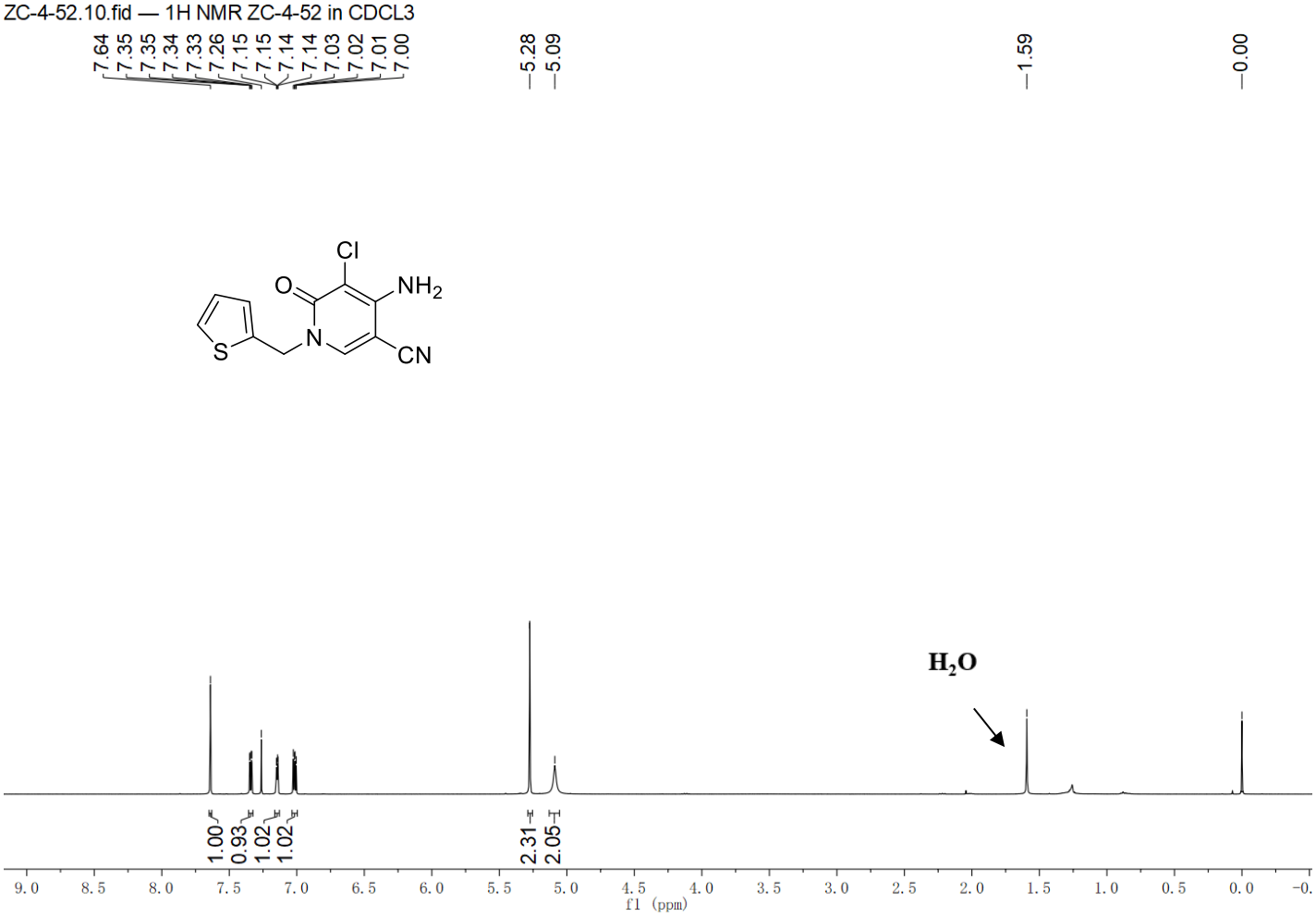
^{13}C NMR spectrum of compound **5r** (101 MHz, $CDCl_3$)



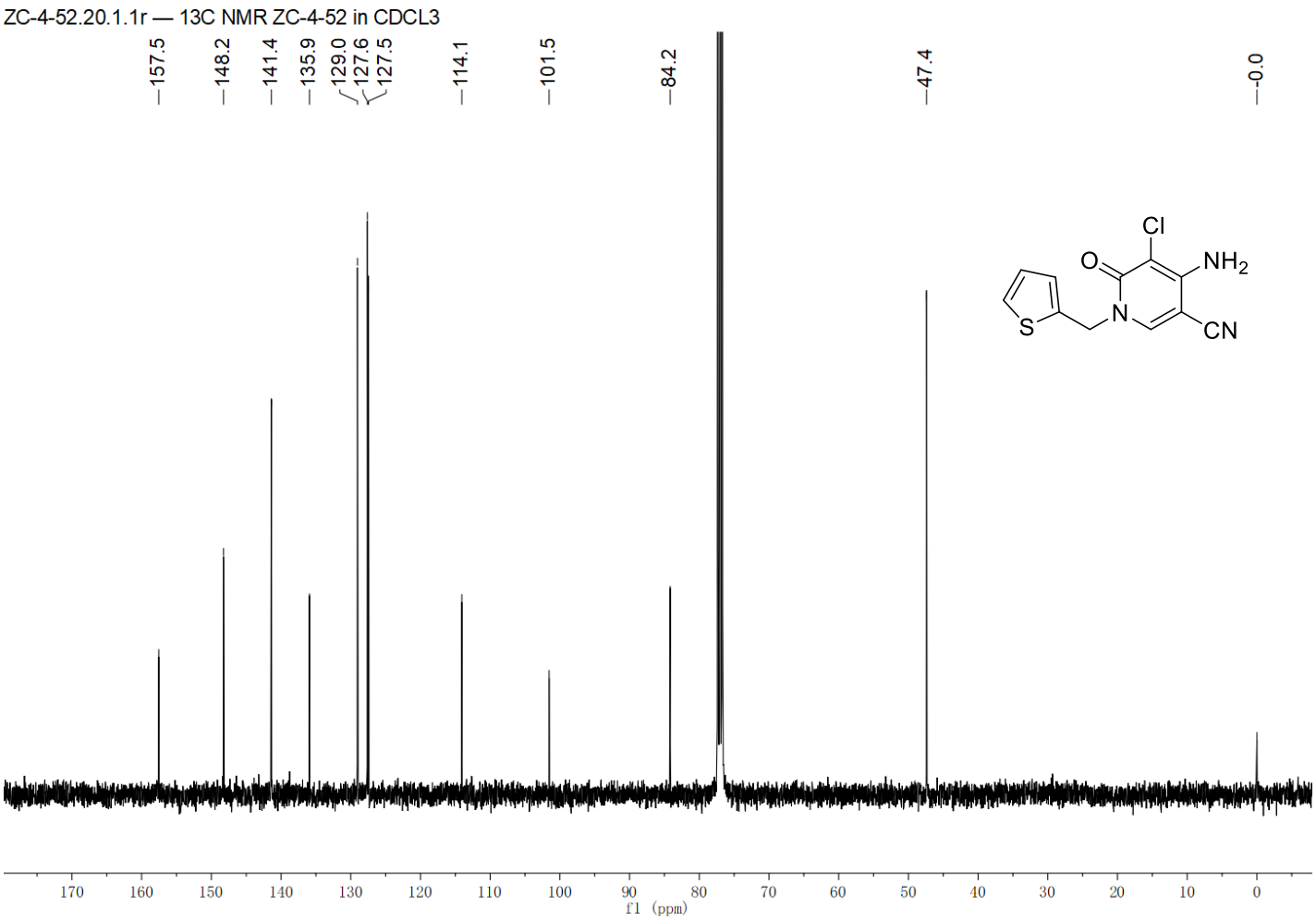
^{1}H NMR spectrum of compound **5s** (400 MHz, DMSO)



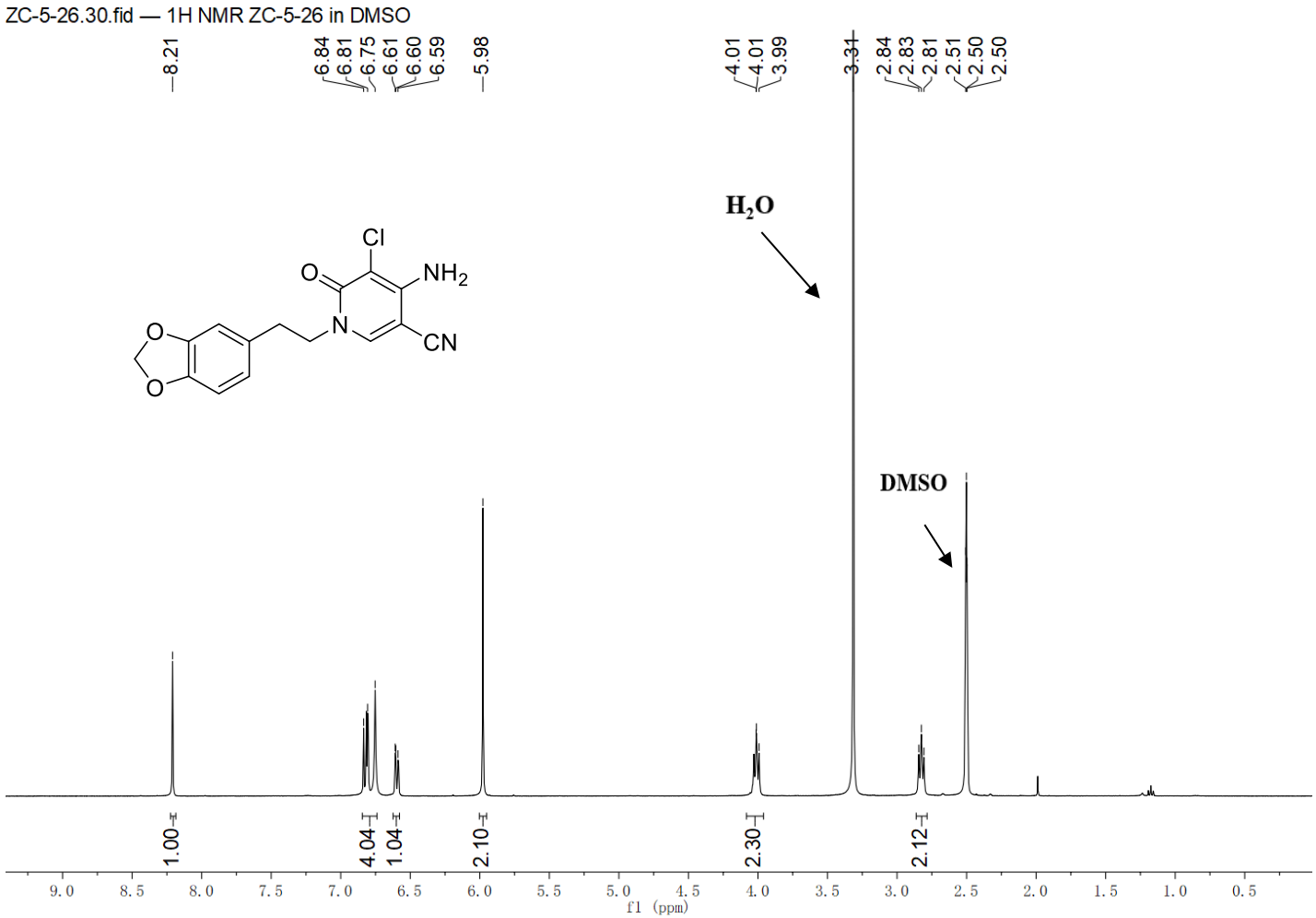
^{13}C NMR spectrum of compound **5s** (101 MHz, DMSO)



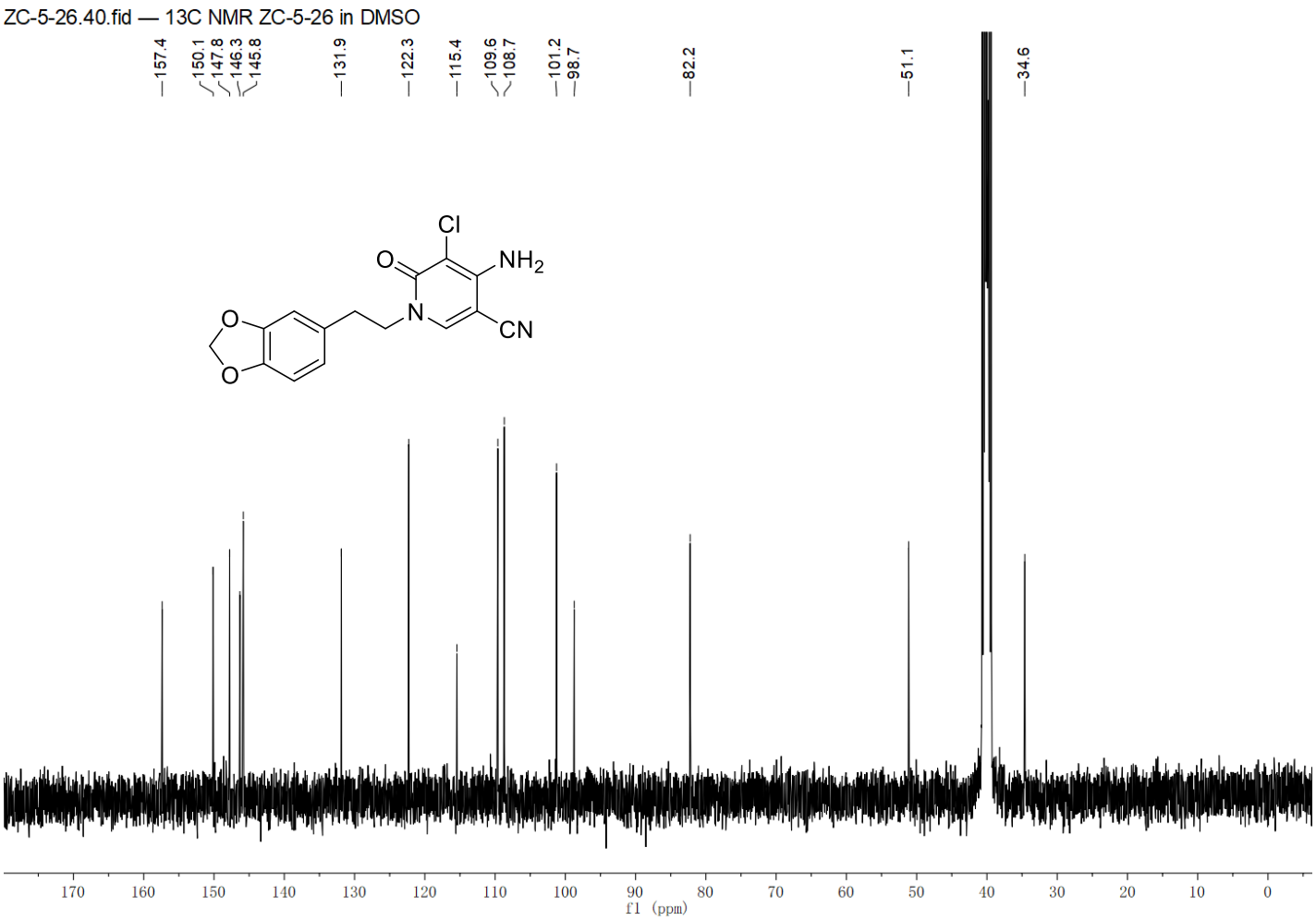
^{1}H NMR spectrum of compound **5t** (400 MHz, $CDCl_3$)



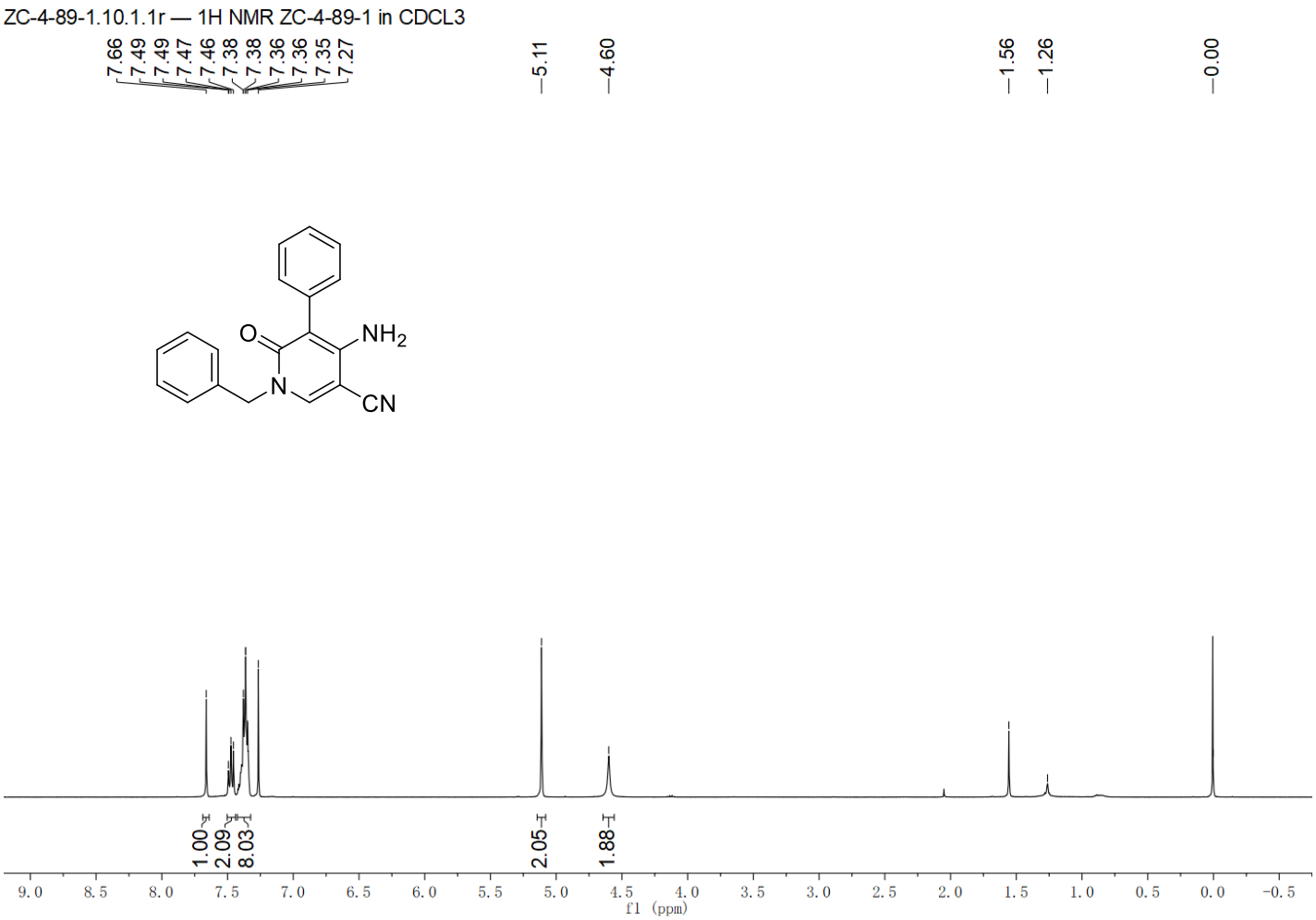
^{13}C NMR spectrum of compound **5t** (101 MHz, $CDCl_3$)



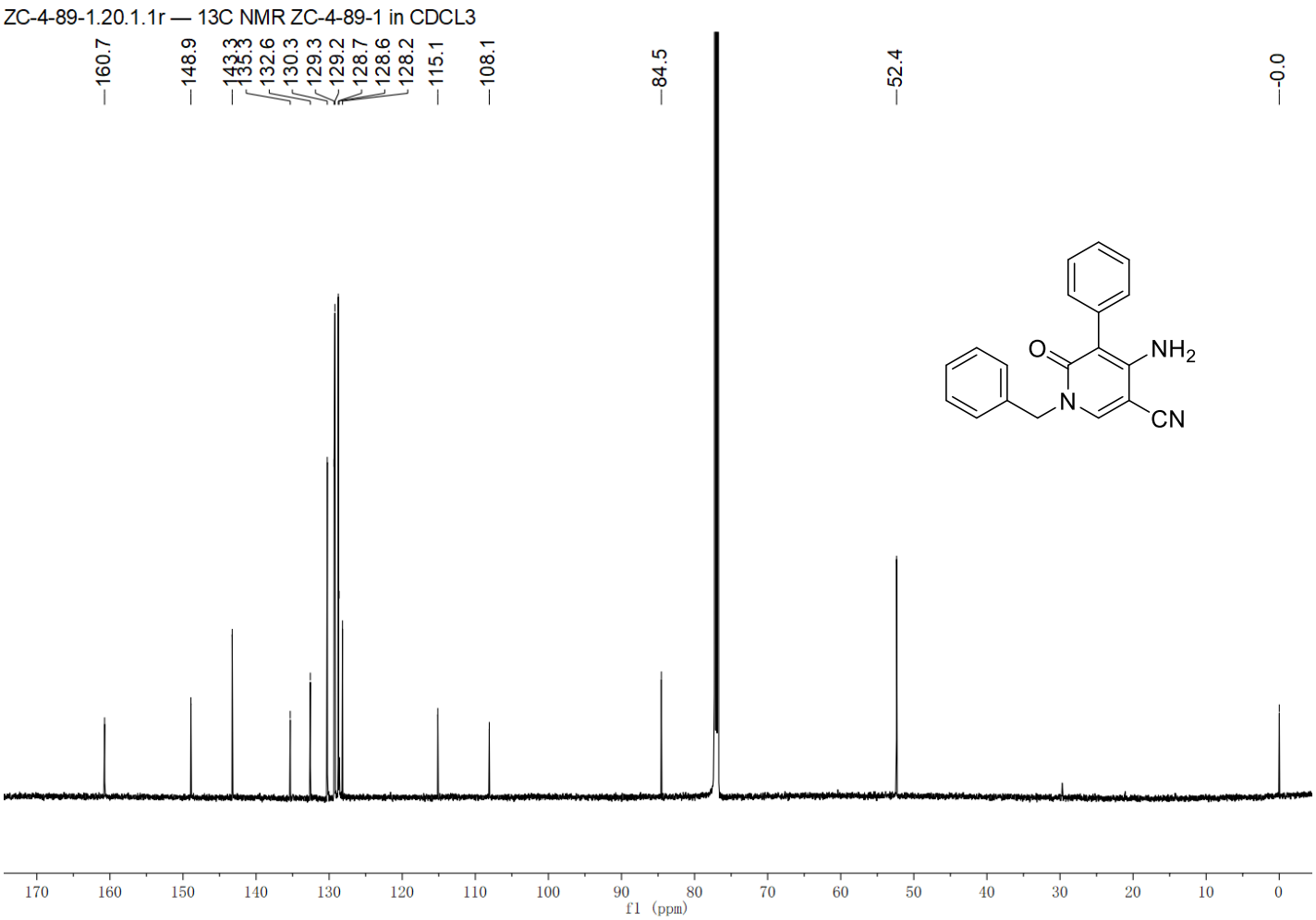
^{1}H NMR spectrum of compound **5u** (400 MHz, DMSO)



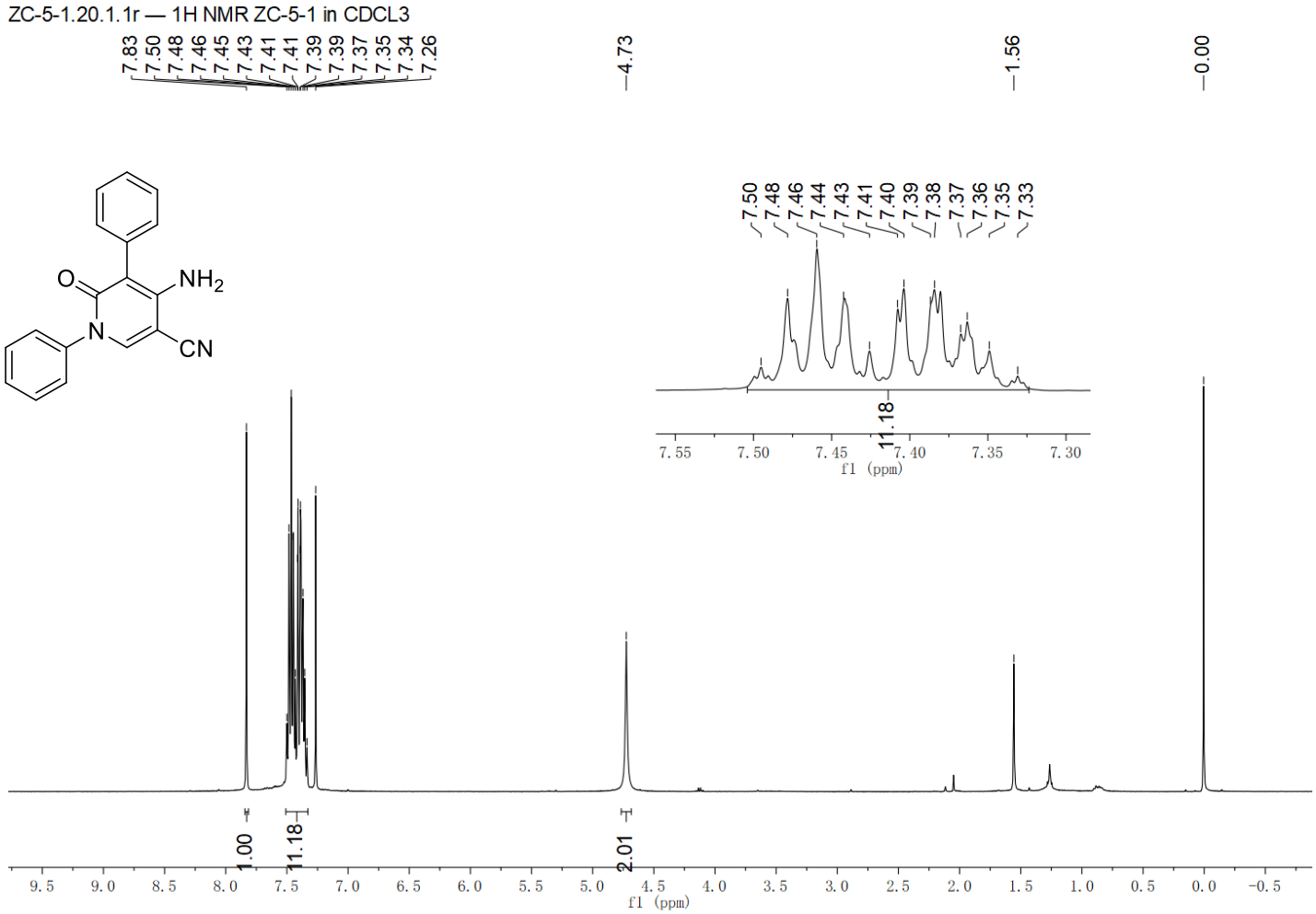
^{13}C NMR spectrum of compound **5u** (101 MHz, DMSO)



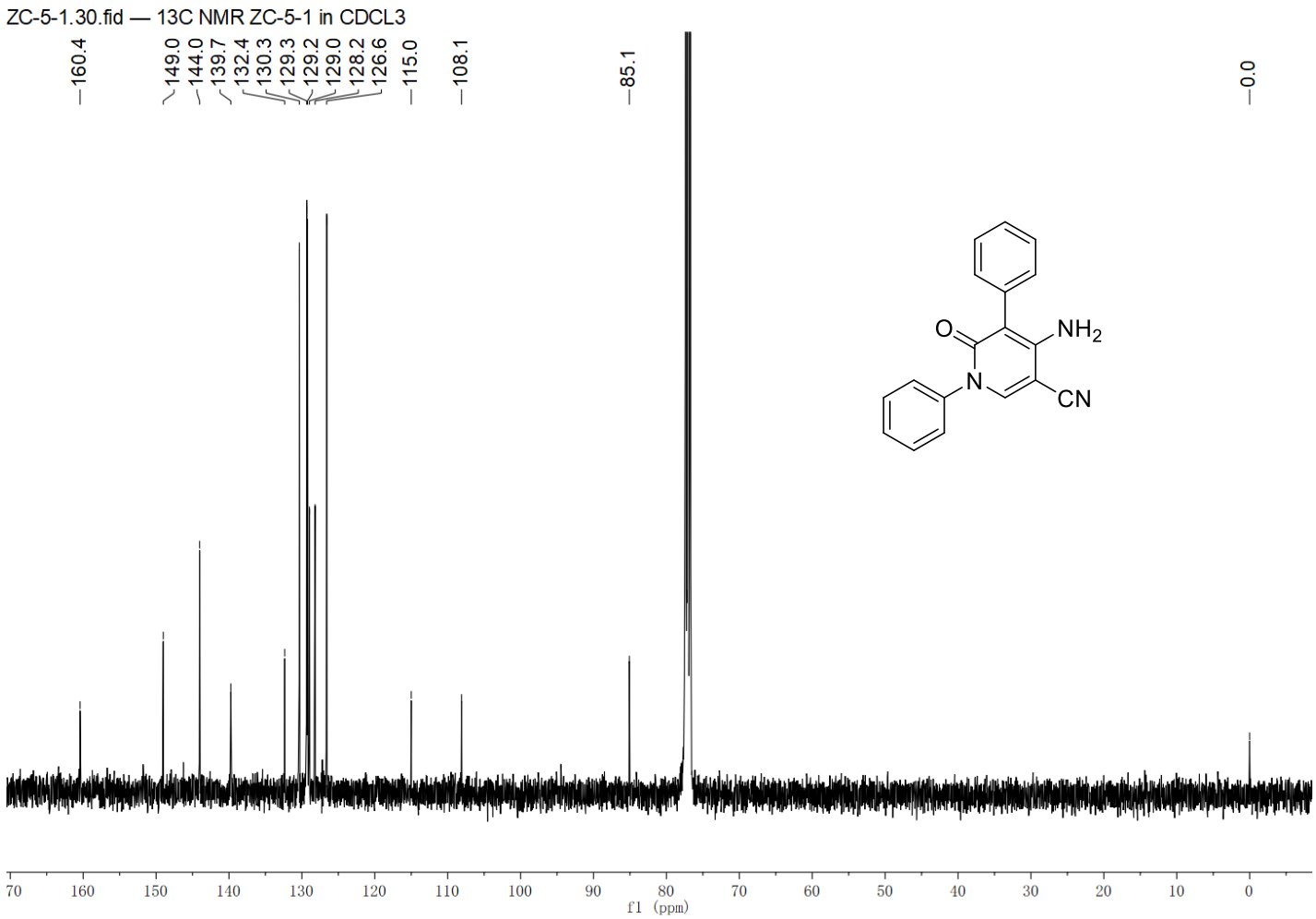
^{1}H NMR spectrum of compound **6a** (400 MHz, $CDCl_3$)



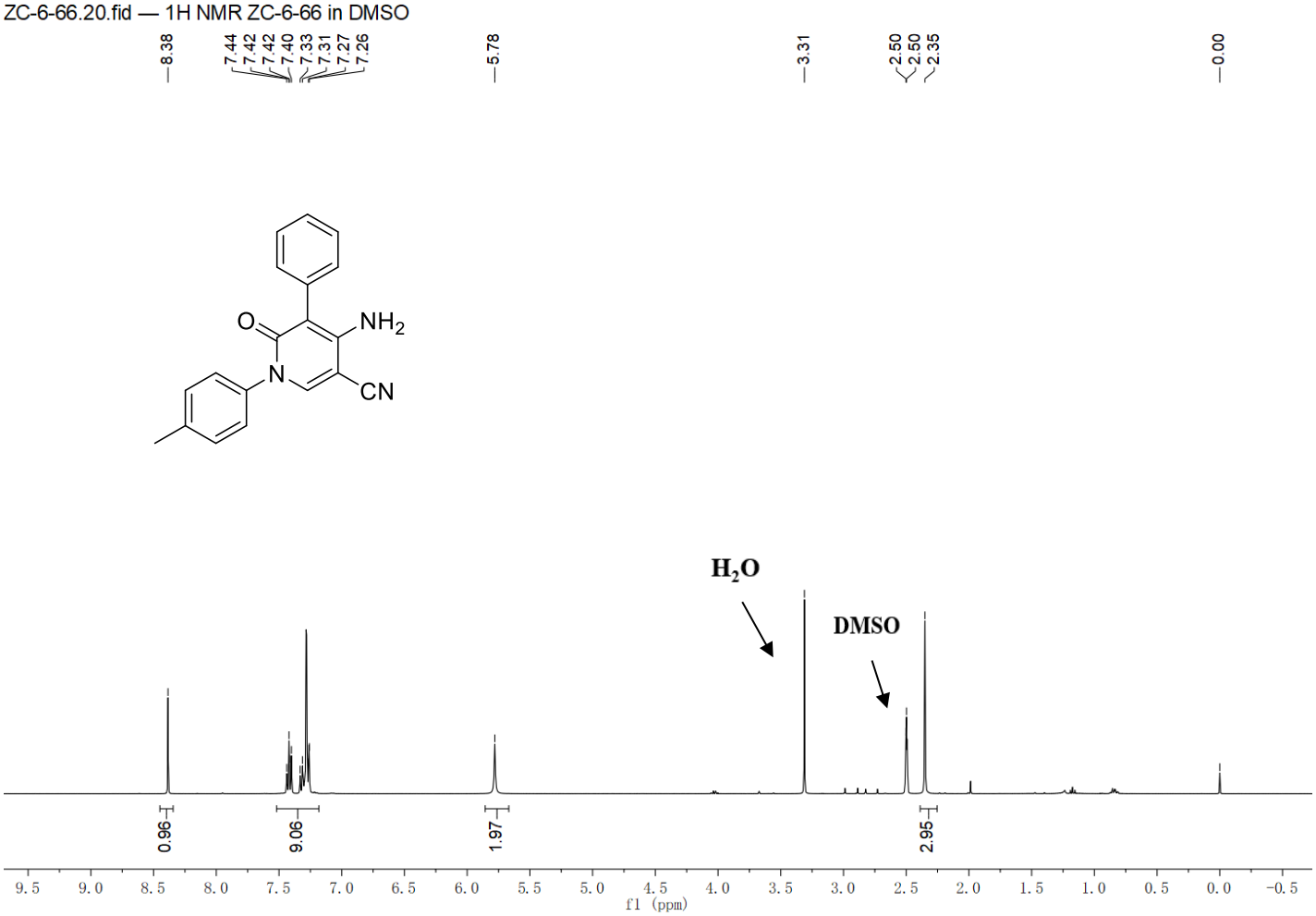
^{13}C NMR spectrum of compound **6a** (101 MHz, $CDCl_3$)



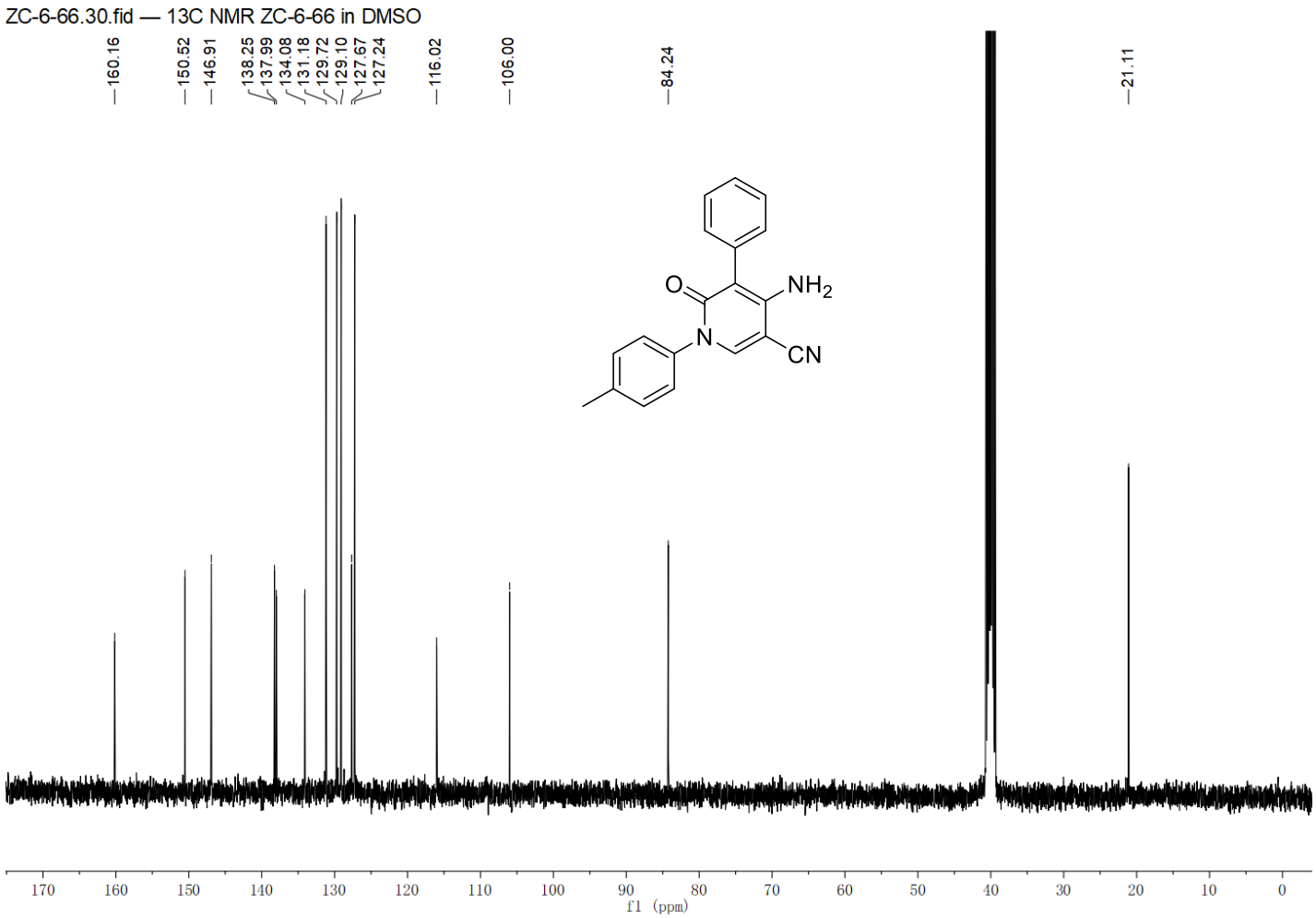
^{1}H NMR spectrum of compound **6b** (400 MHz, $CDCl_3$)



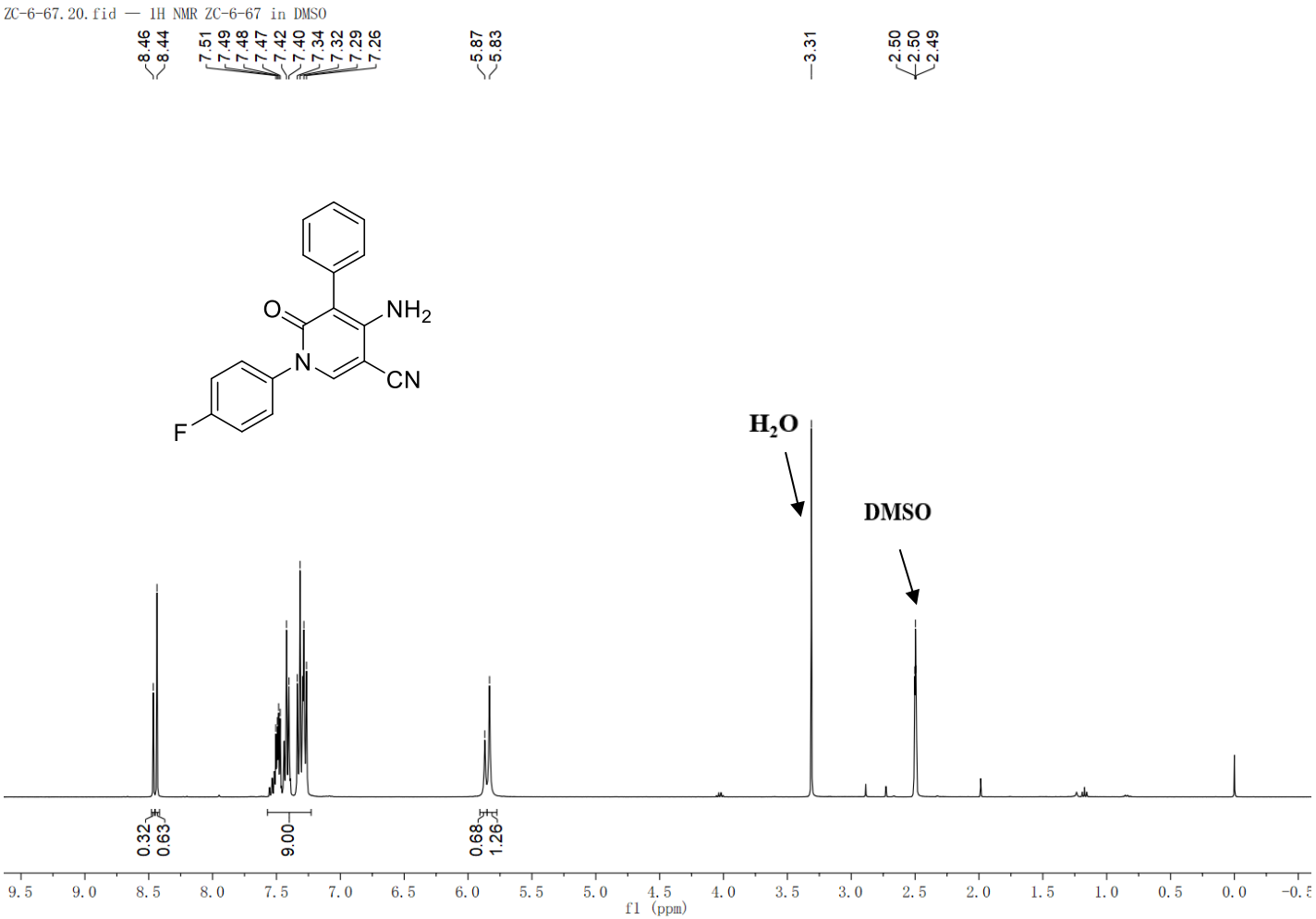
^{13}C NMR spectrum of compound **6b** (101 MHz, $CDCl_3$)



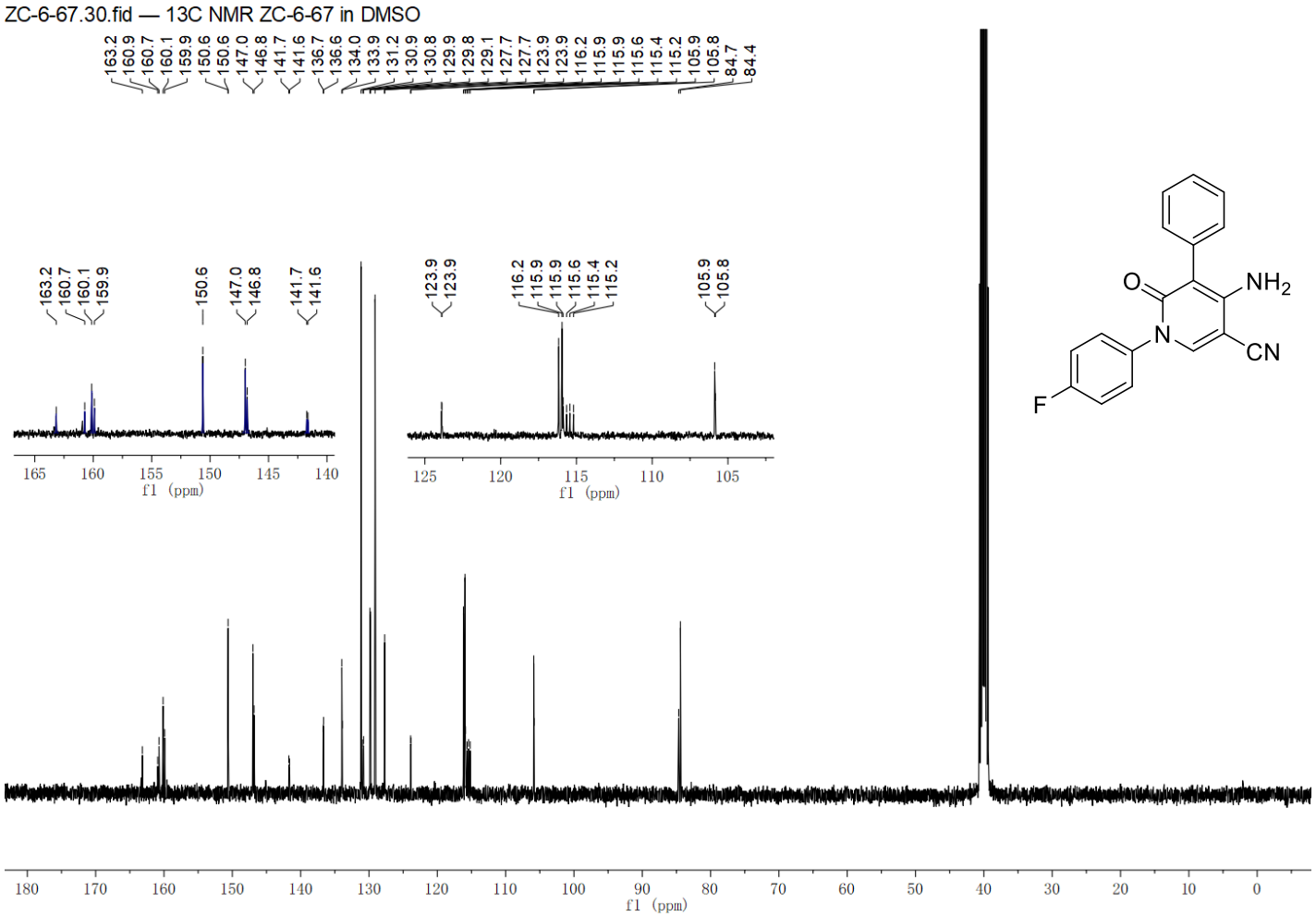
^{1}H NMR spectrum of compound **6c** (400 MHz, DMSO)



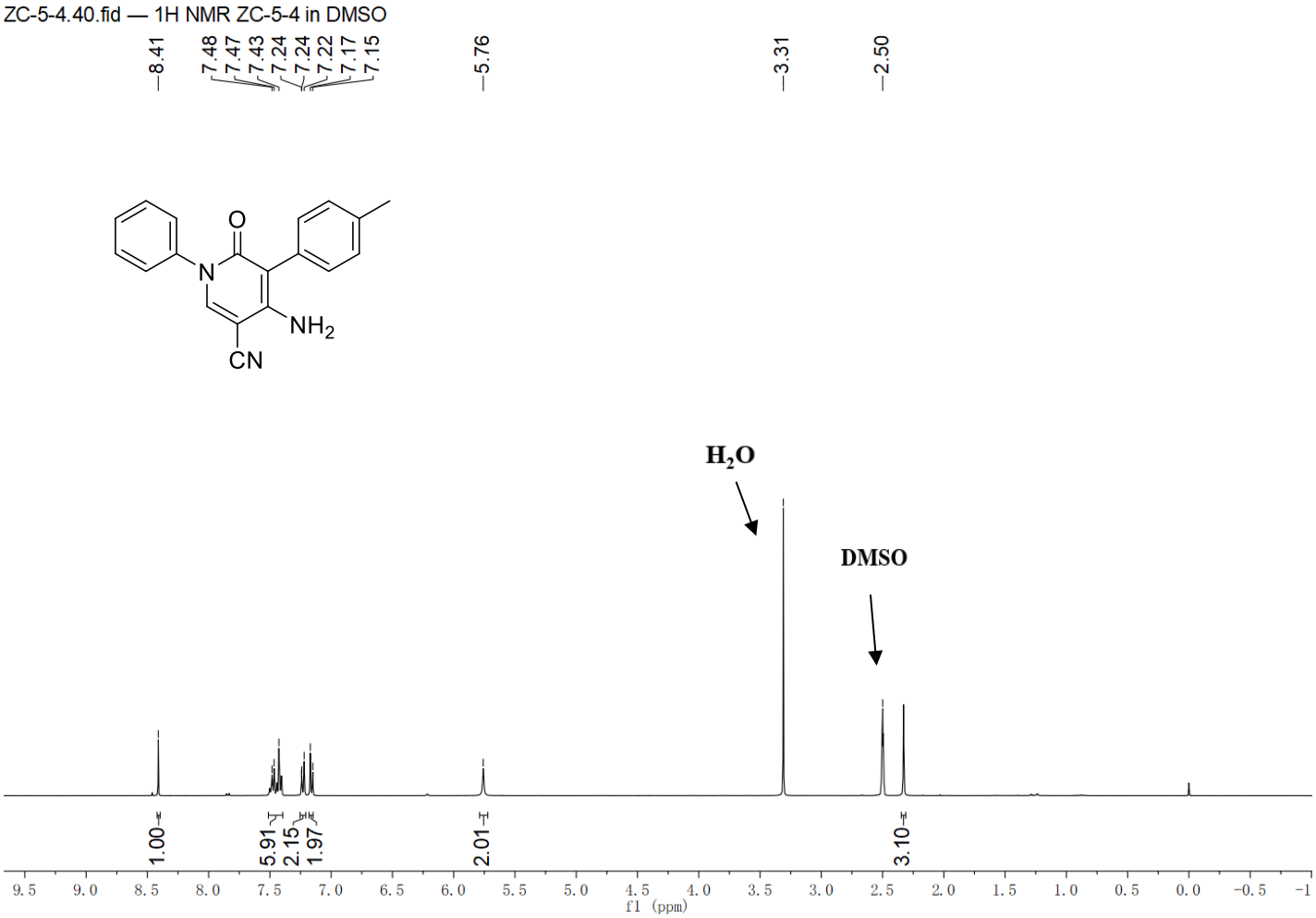
^{1}H NMR spectrum of compound **6c** (400 MHz, DMSO)



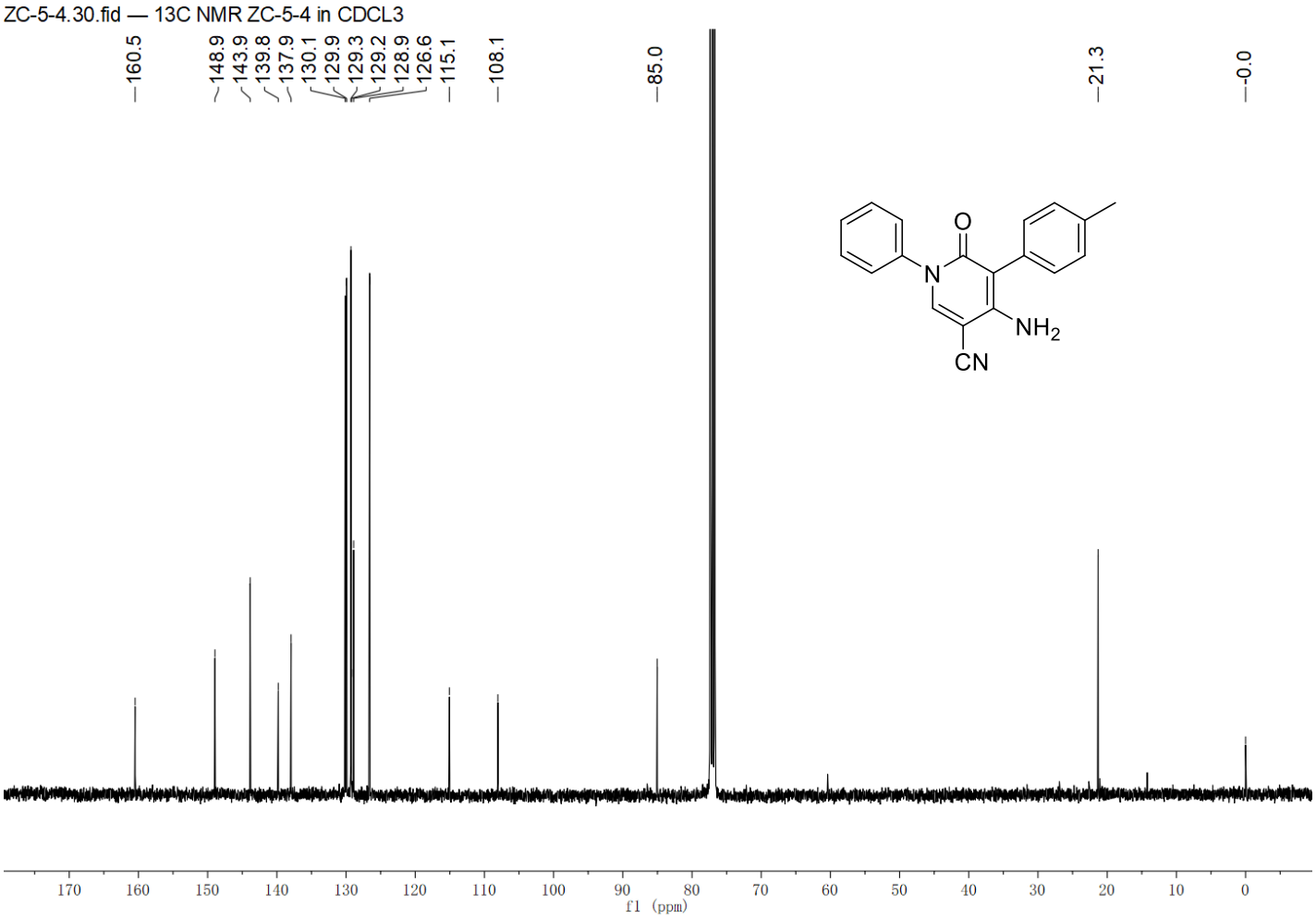
^{1}H NMR spectrum of compound **6d** (400 MHz, DMSO)



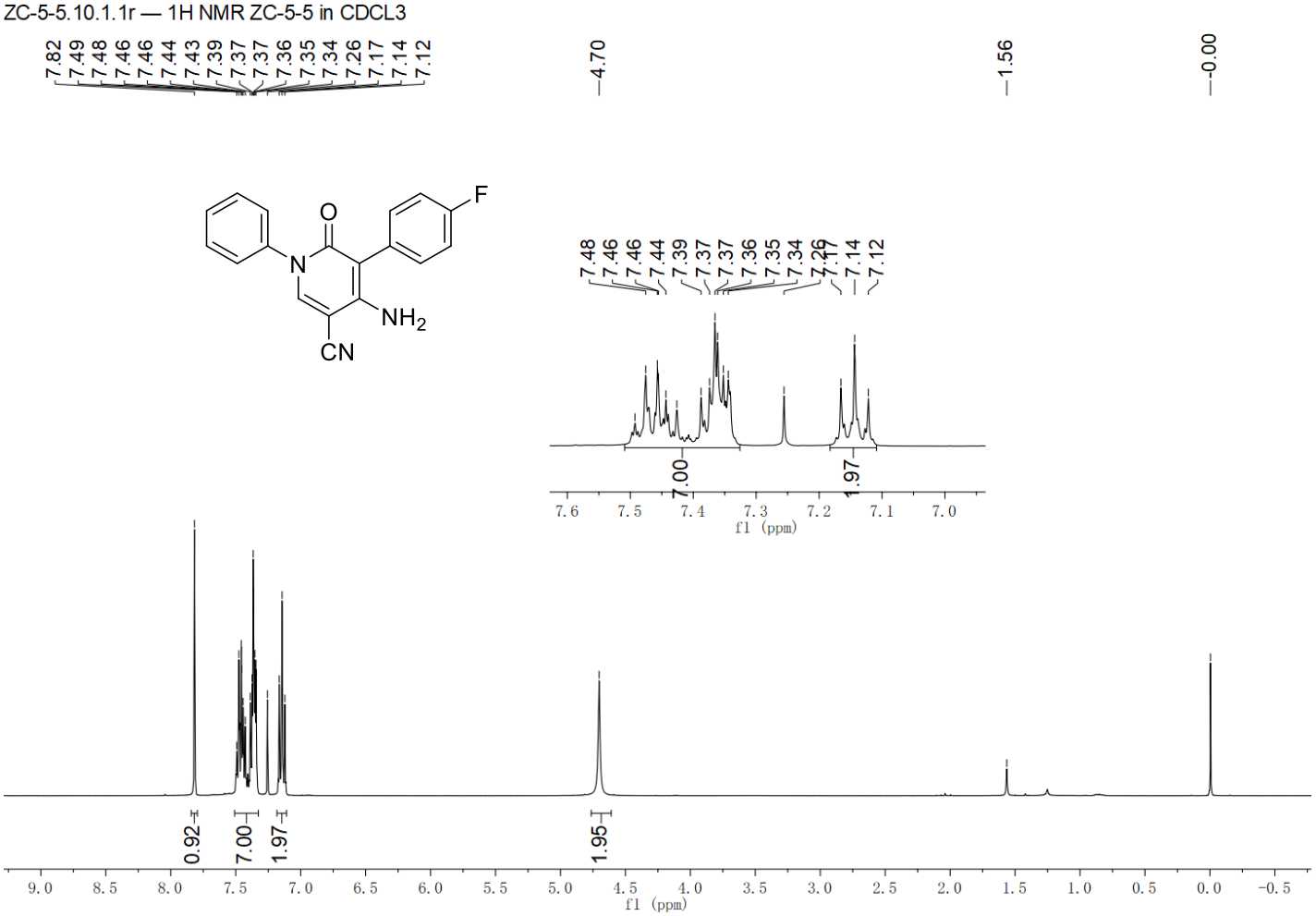
^{13}C NMR spectrum of compound **6d** (101 MHz, DMSO)



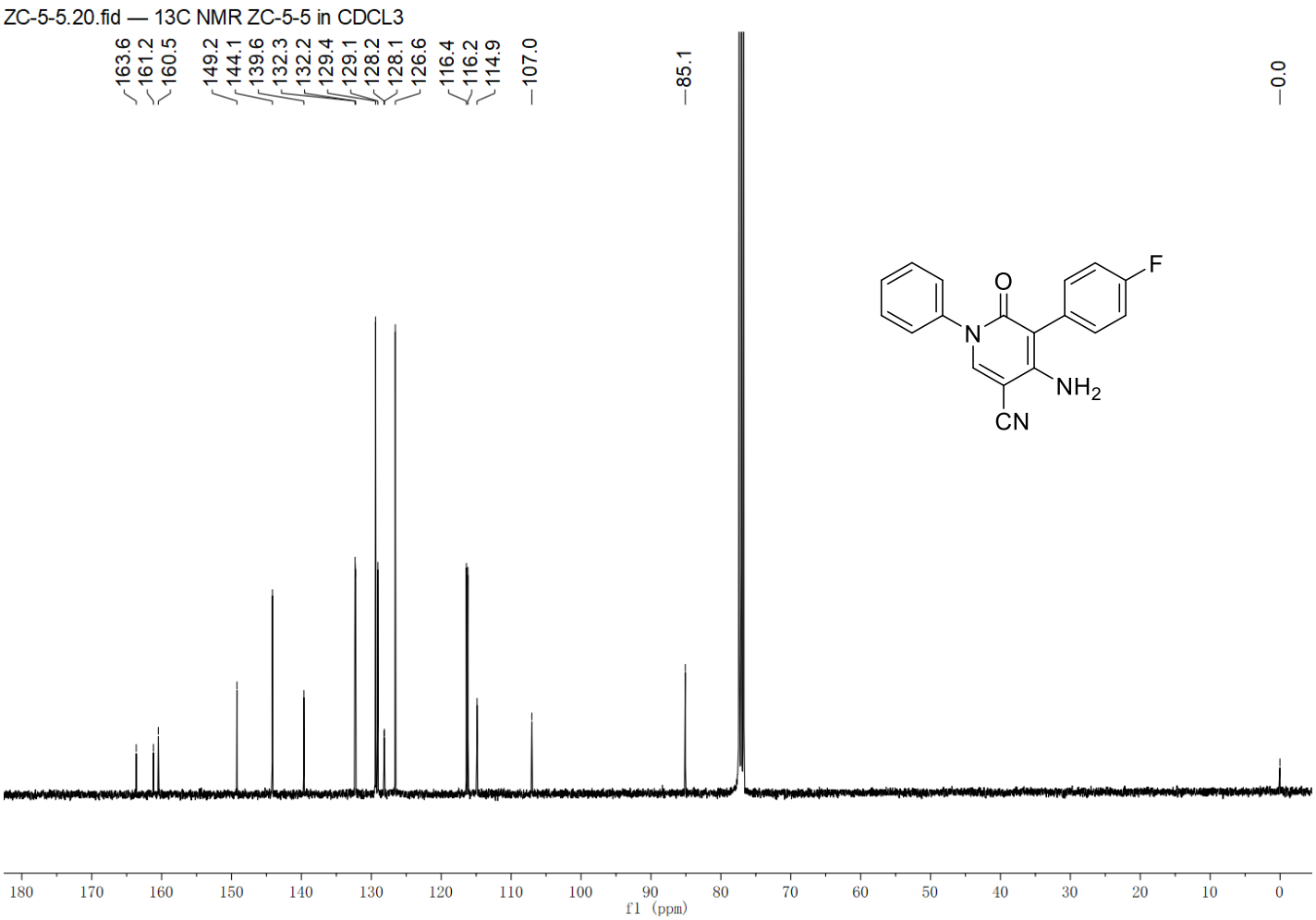
^{1}H NMR spectrum of compound **6e** (400 MHz, DMSO)



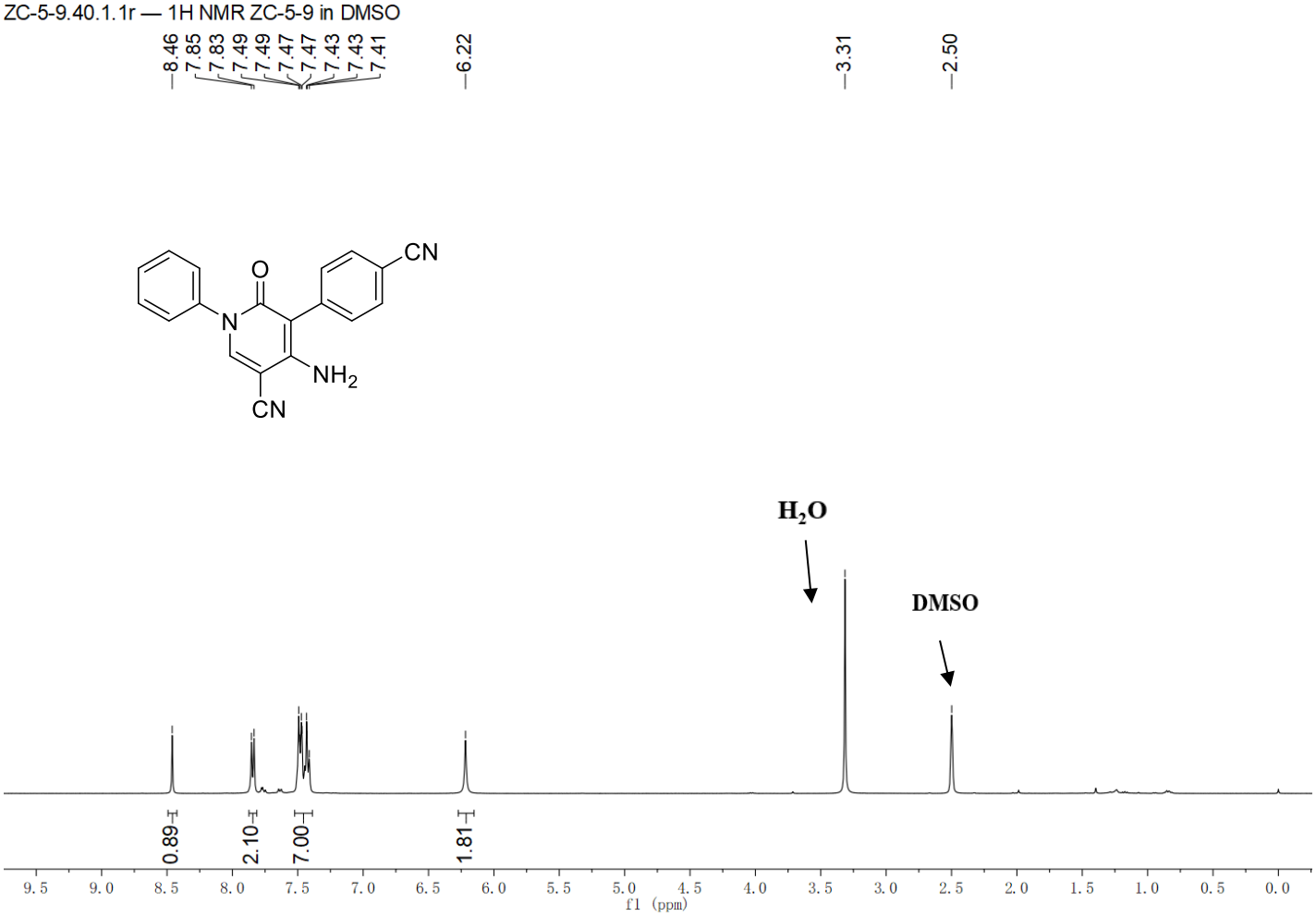
^{13}C NMR spectrum of compound **6e** (101 MHz, DMSO)



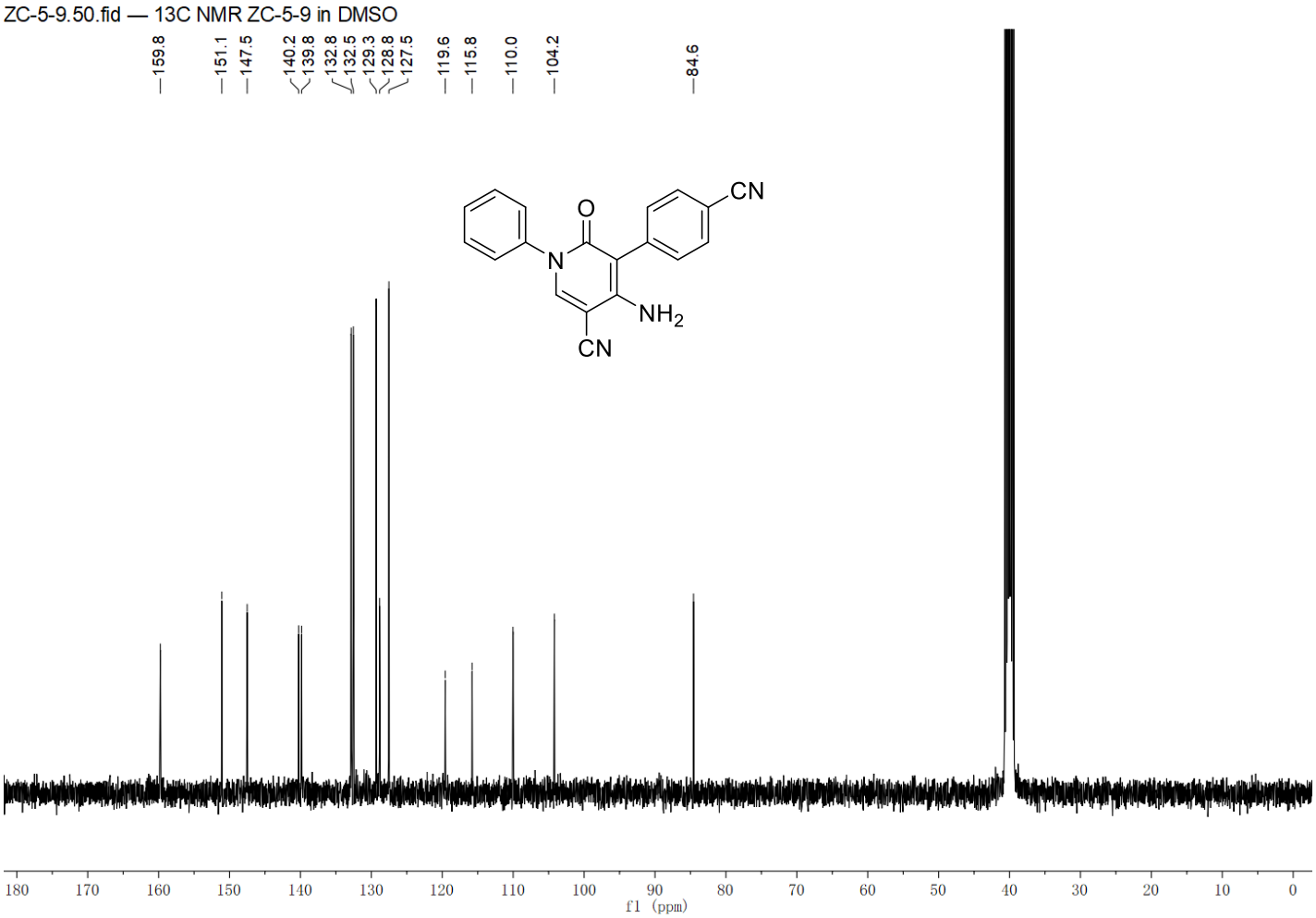
^{1}H NMR spectrum of compound **6f** (400 MHz, $CDCl_3$)



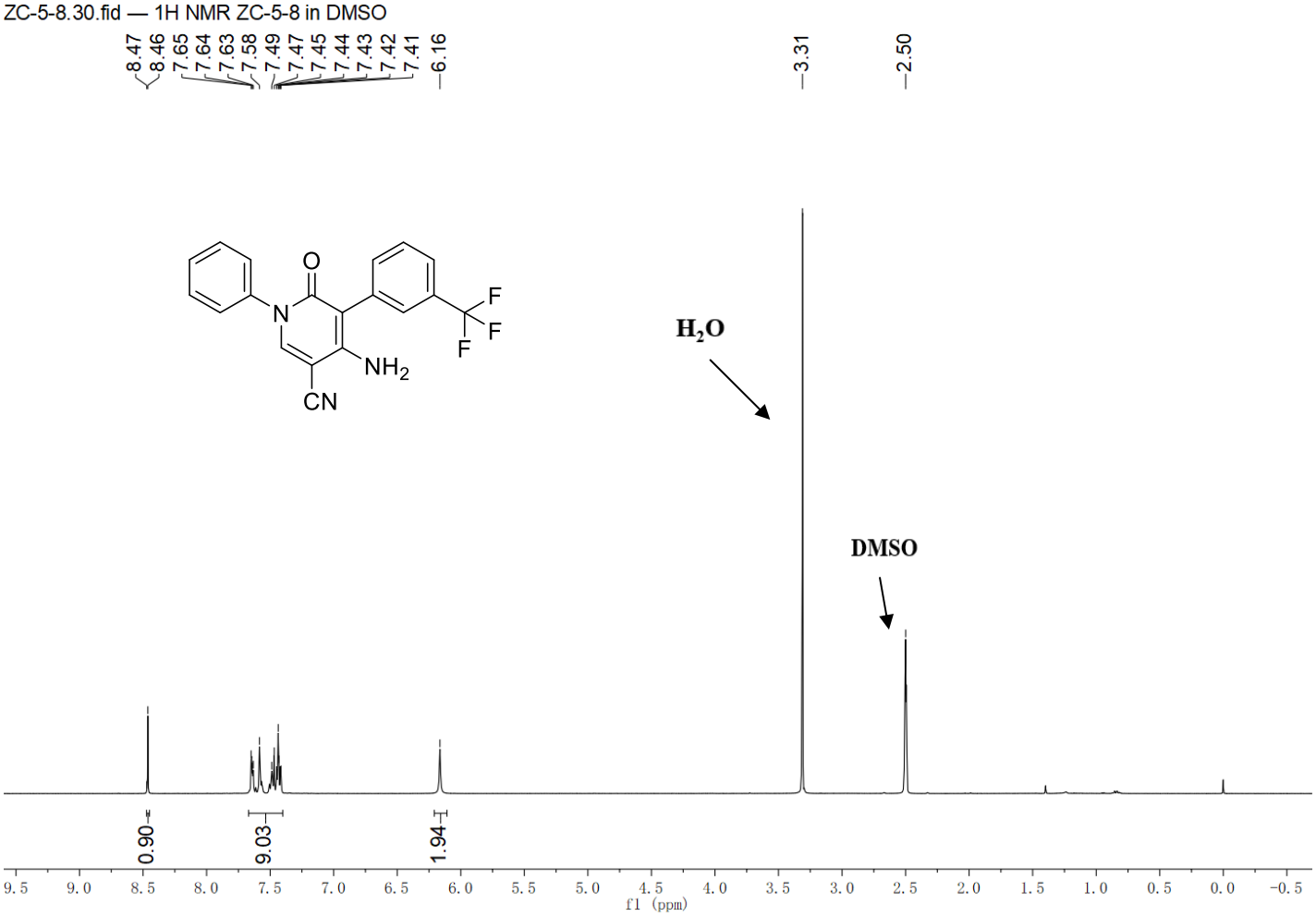
^{13}C NMR spectrum of compound **6f** (101 MHz, $CDCl_3$)



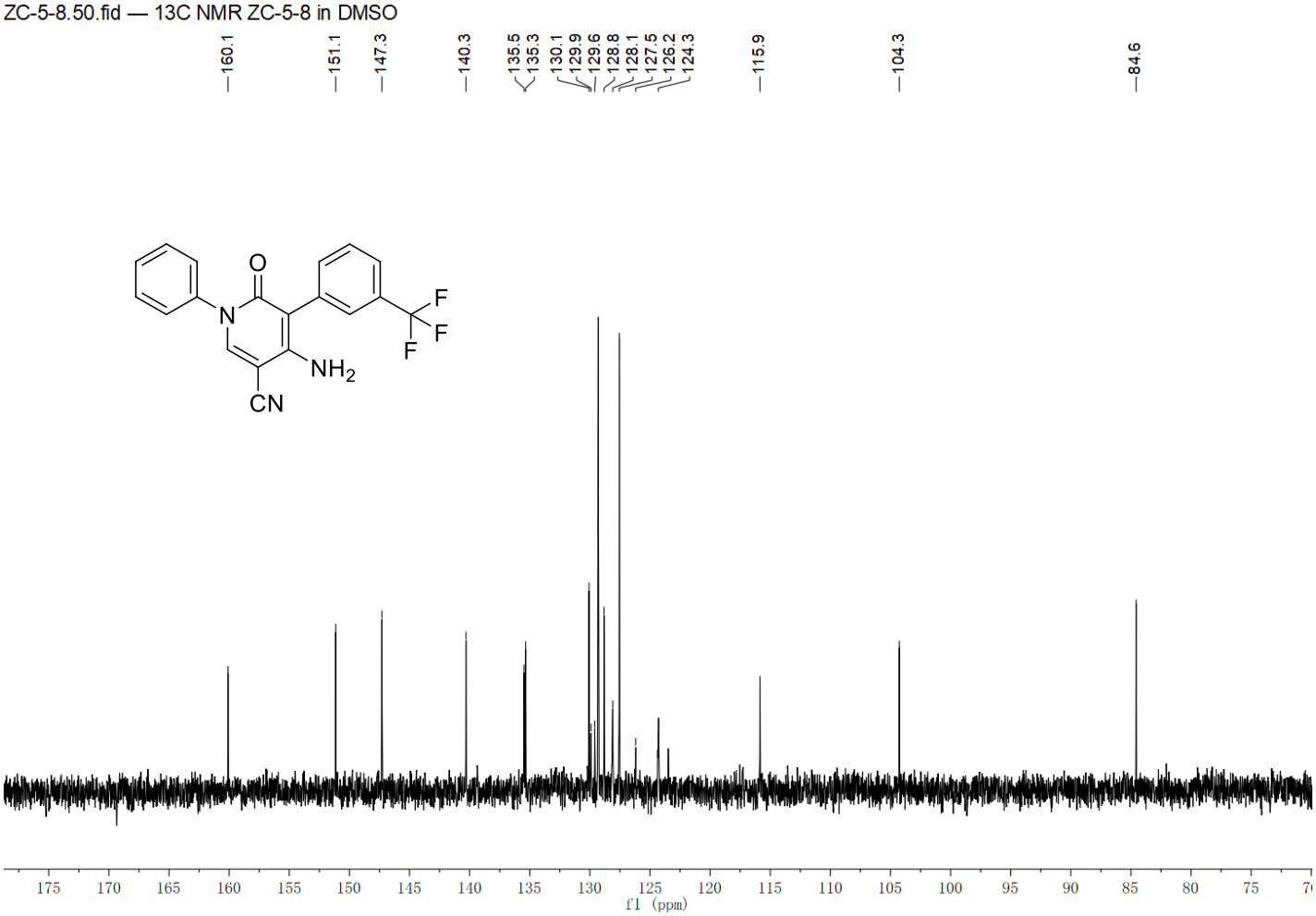
^{1}H NMR spectrum of compound **6g** (400 MHz, DMSO)



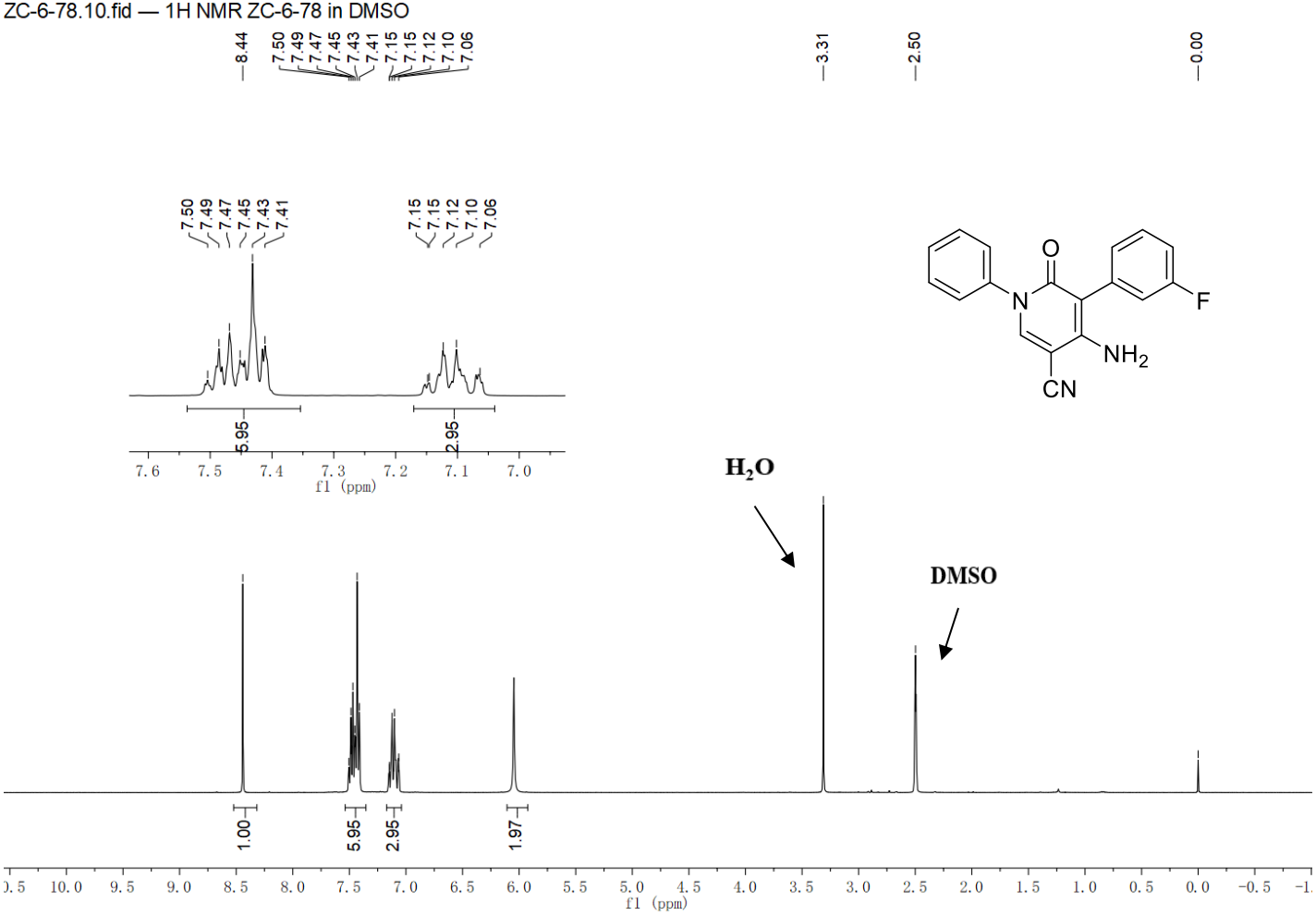
^{13}C NMR spectrum of compound **6g** (101 MHz, DMSO)



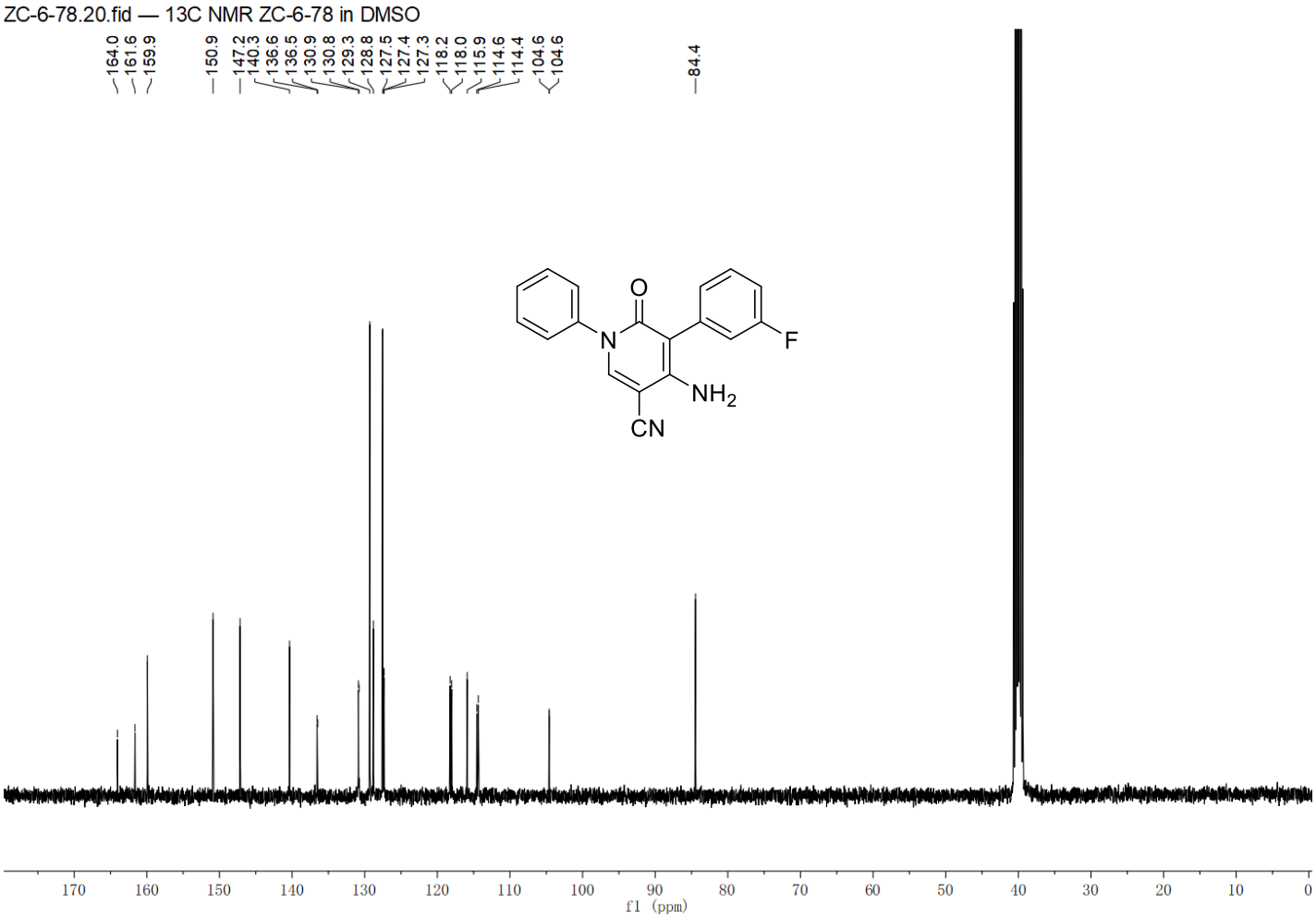
^{1}H NMR spectrum of compound **6h** (400 MHz, DMSO)



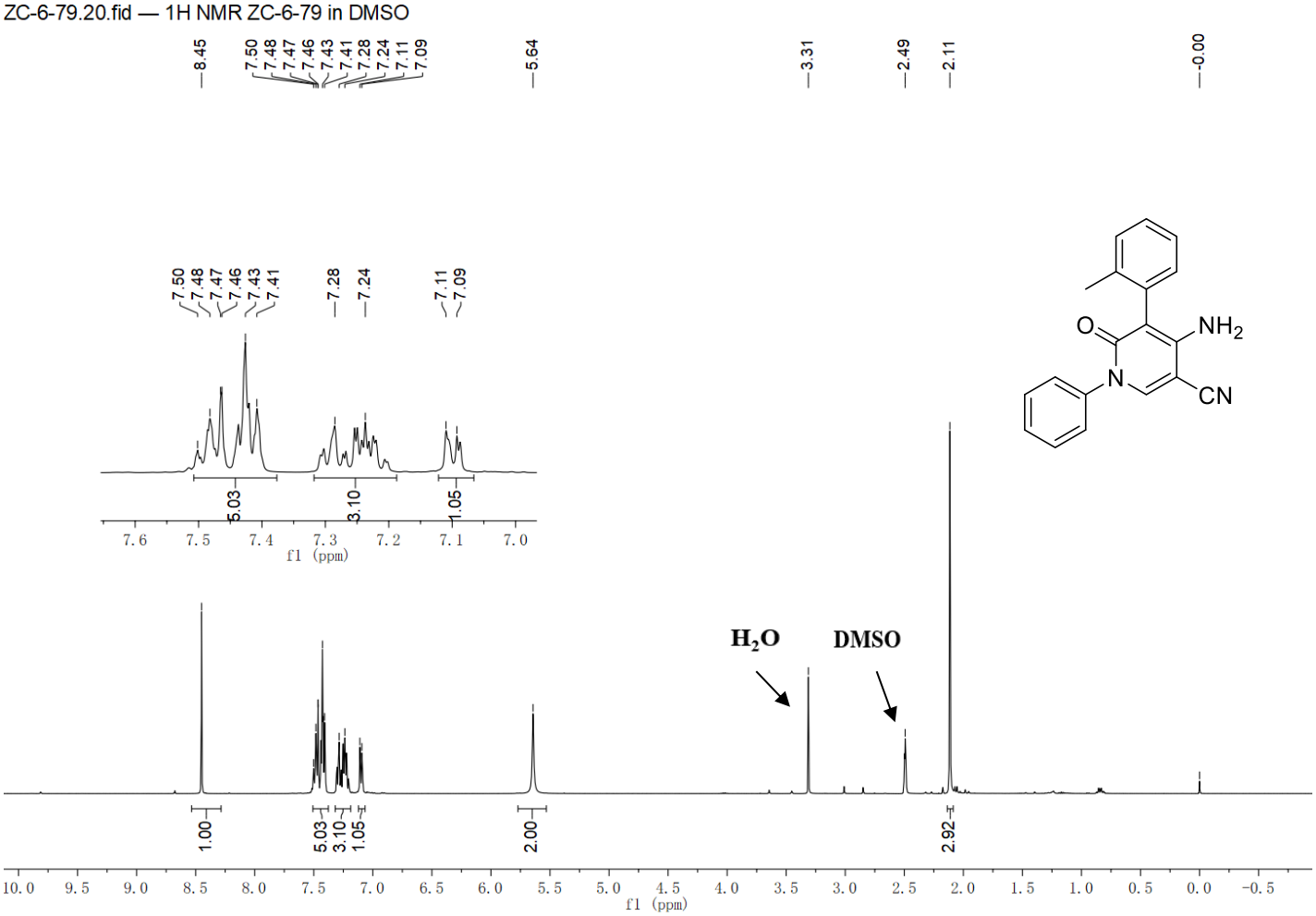
^{13}C NMR spectrum of compound **6h** (101 MHz, DMSO)



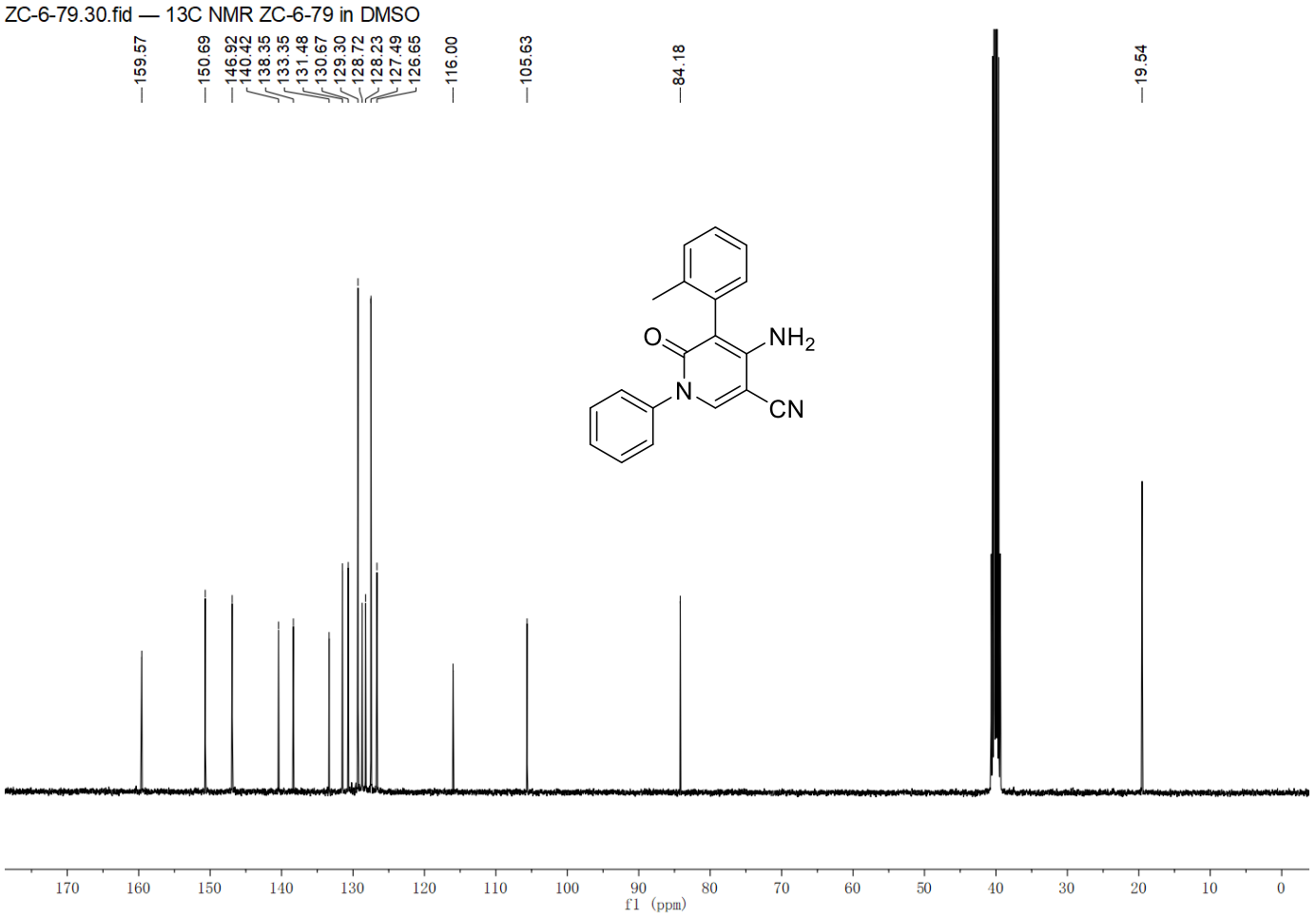
^{1}H NMR spectrum of compound **6i** (400 MHz, DMSO)



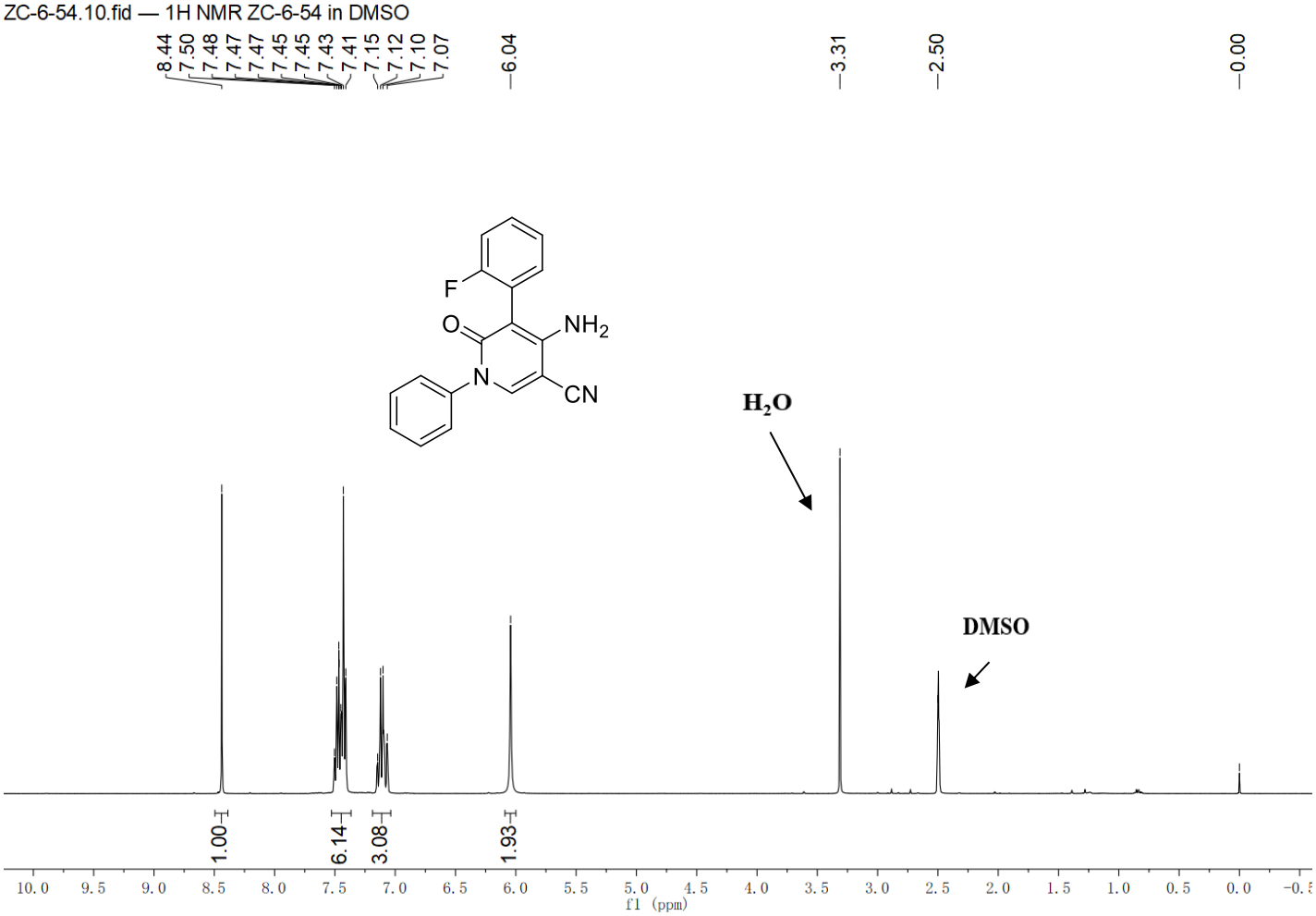
^{13}C NMR spectrum of compound **6i** (101 MHz, DMSO)



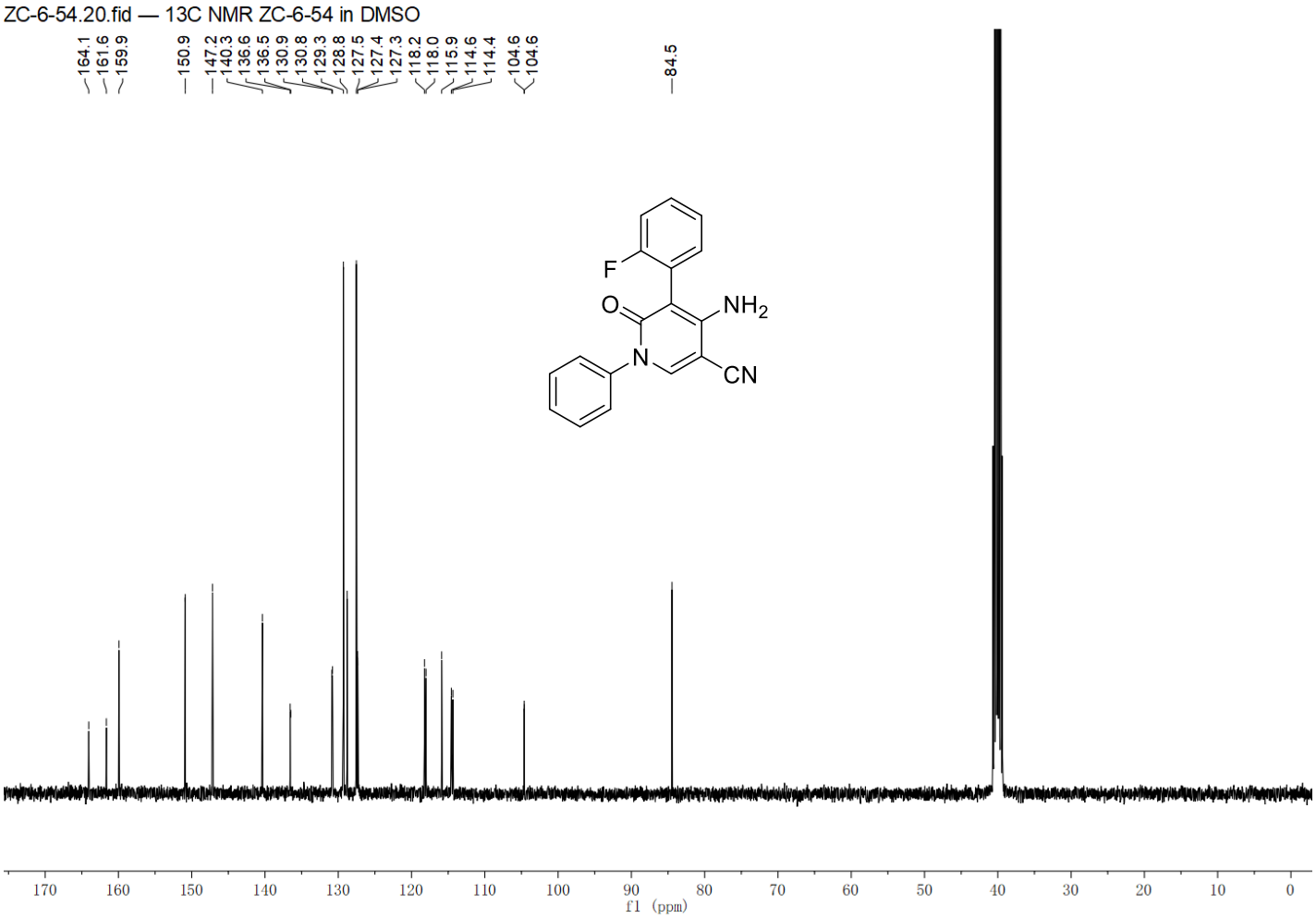
^{1}H NMR spectrum of compound **6j** (400 MHz, DMSO)



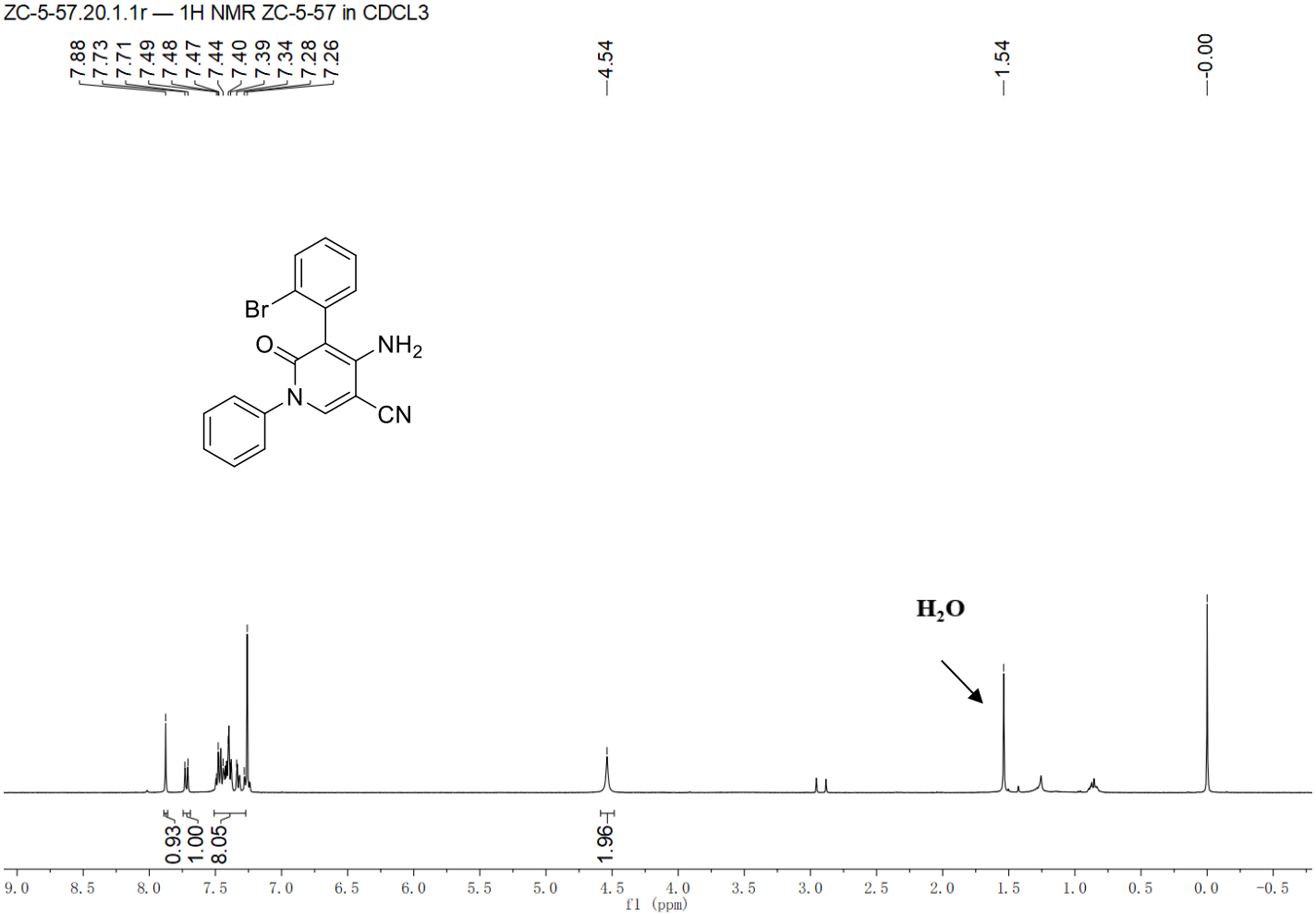
^{13}C NMR spectrum of compound **6j** (101 MHz, DMSO)



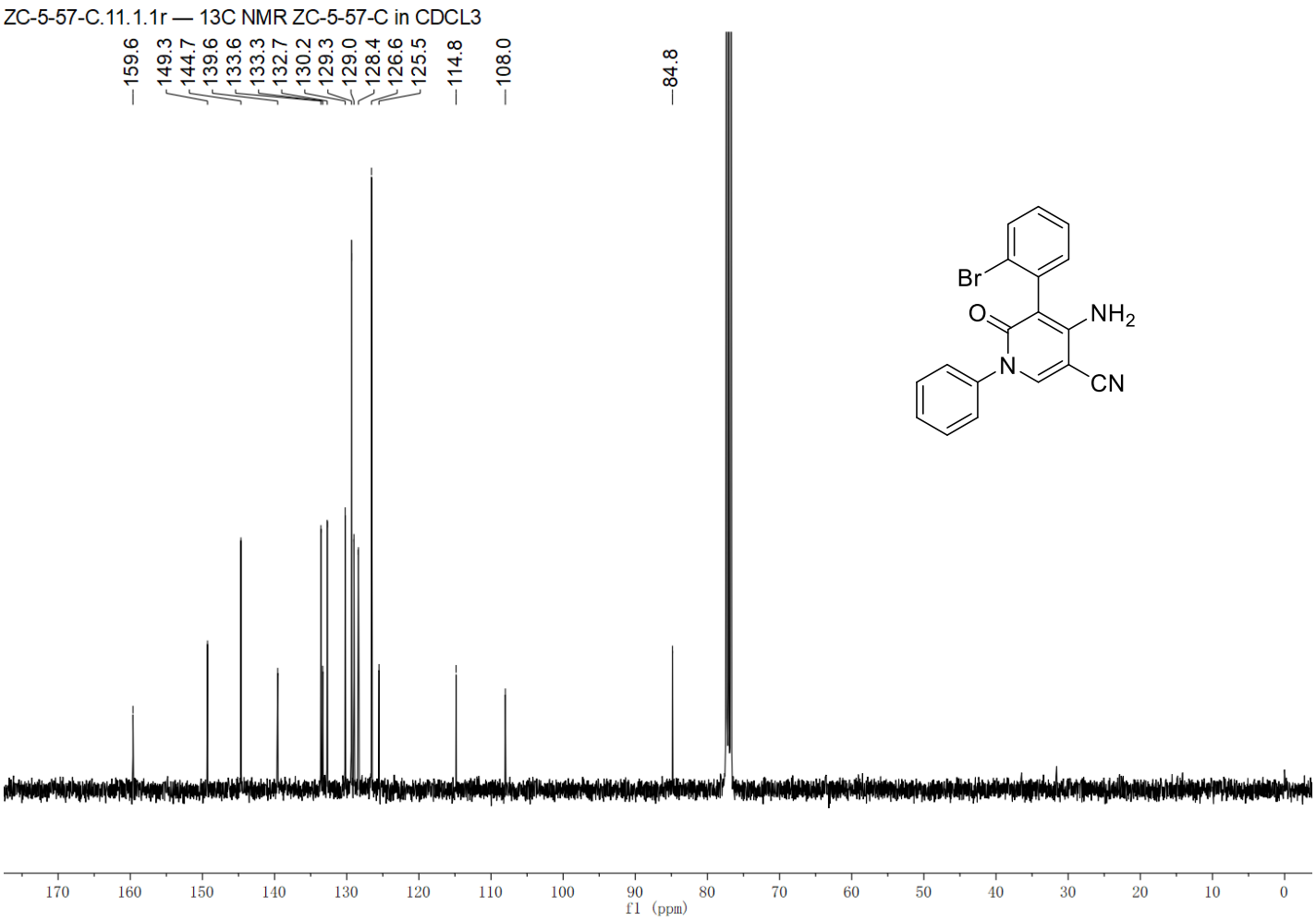
^{1}H NMR spectrum of compound **6k** (400 MHz, DMSO)



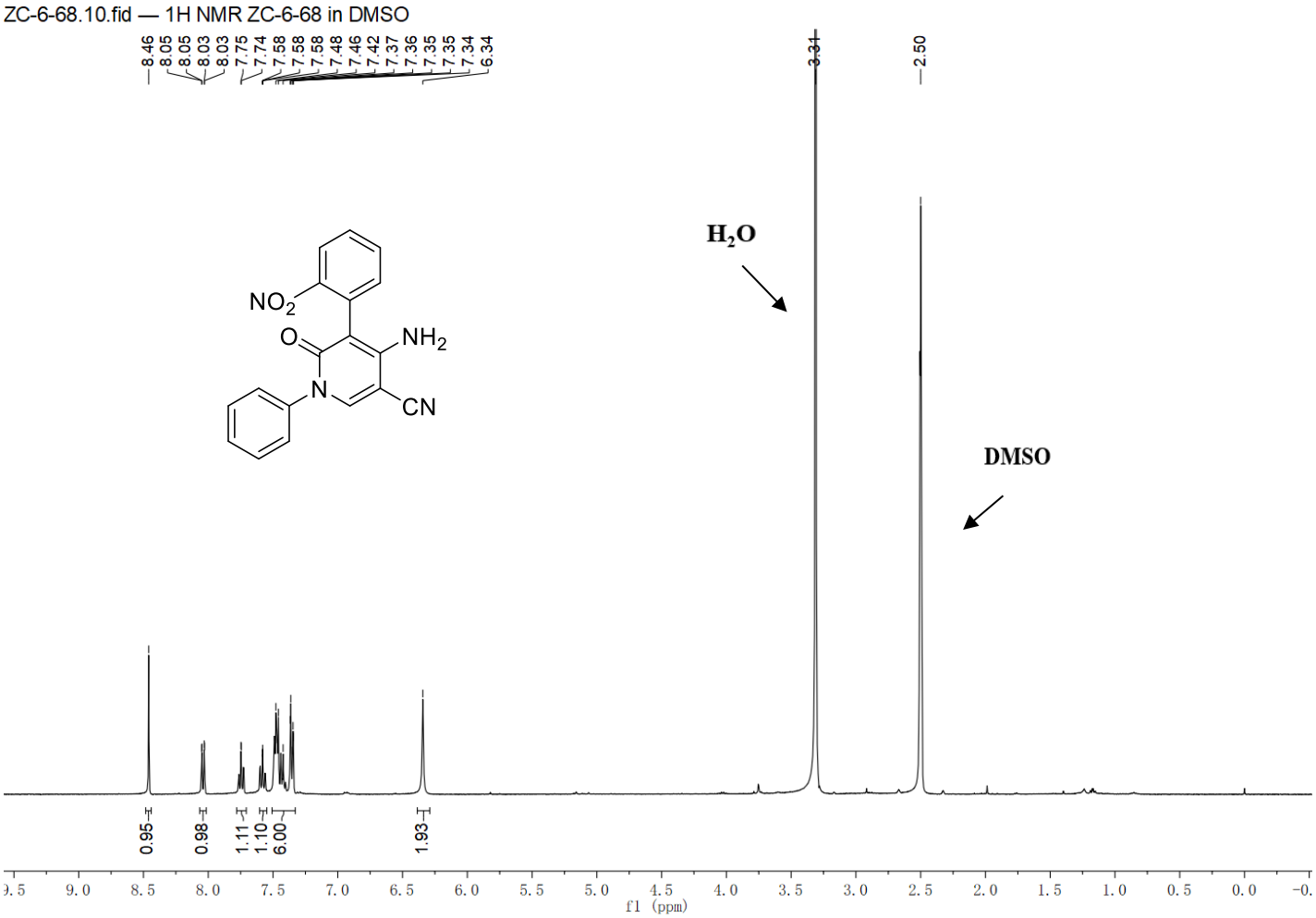
^{13}C NMR spectrum of compound **6k** (101 MHz, DMSO)



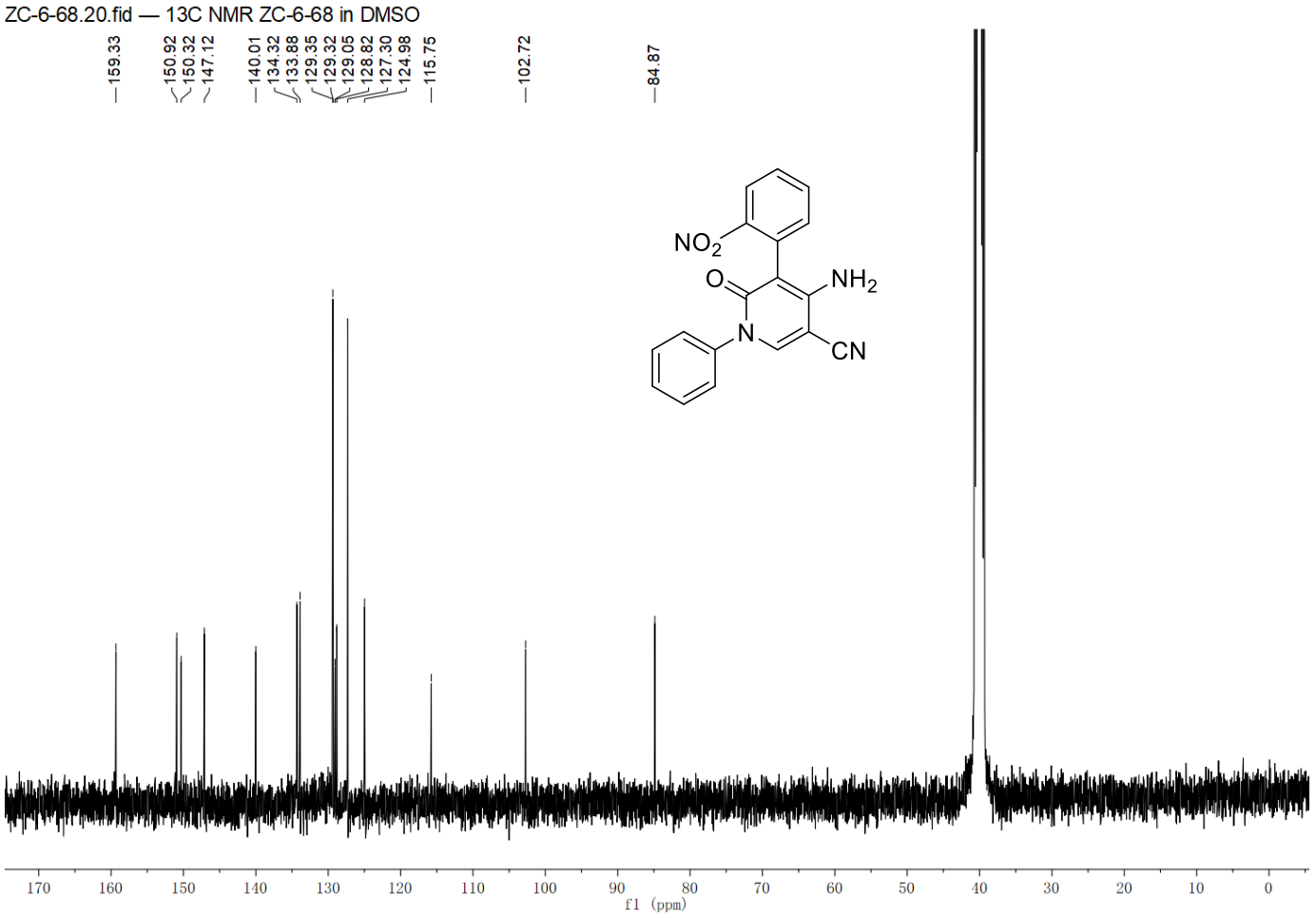
^{1}H NMR spectrum of compound **6l** (400 MHz, $CDCl_3$)



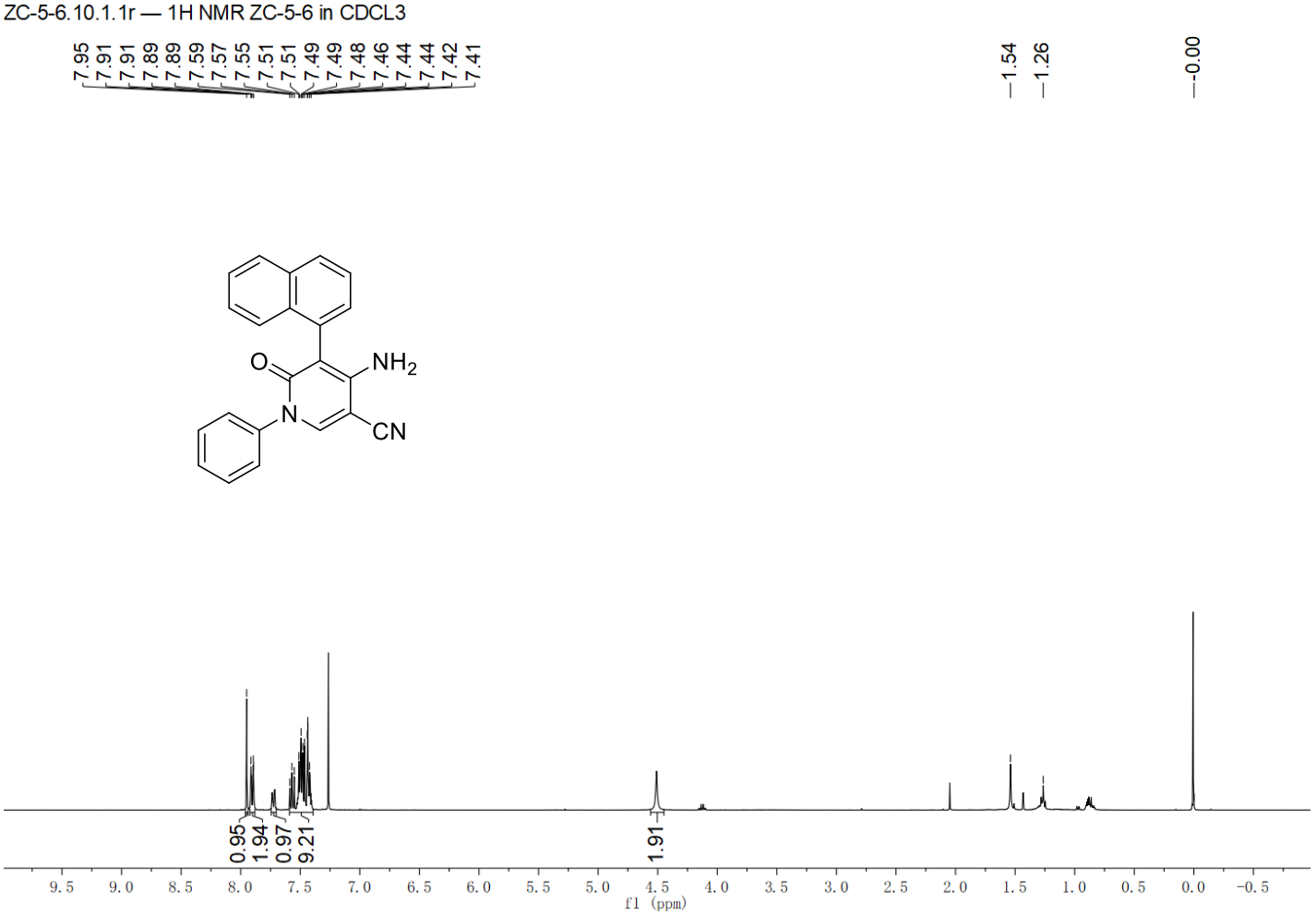
^{13}C NMR spectrum of compound **6l** (101 MHz, $CDCl_3$)



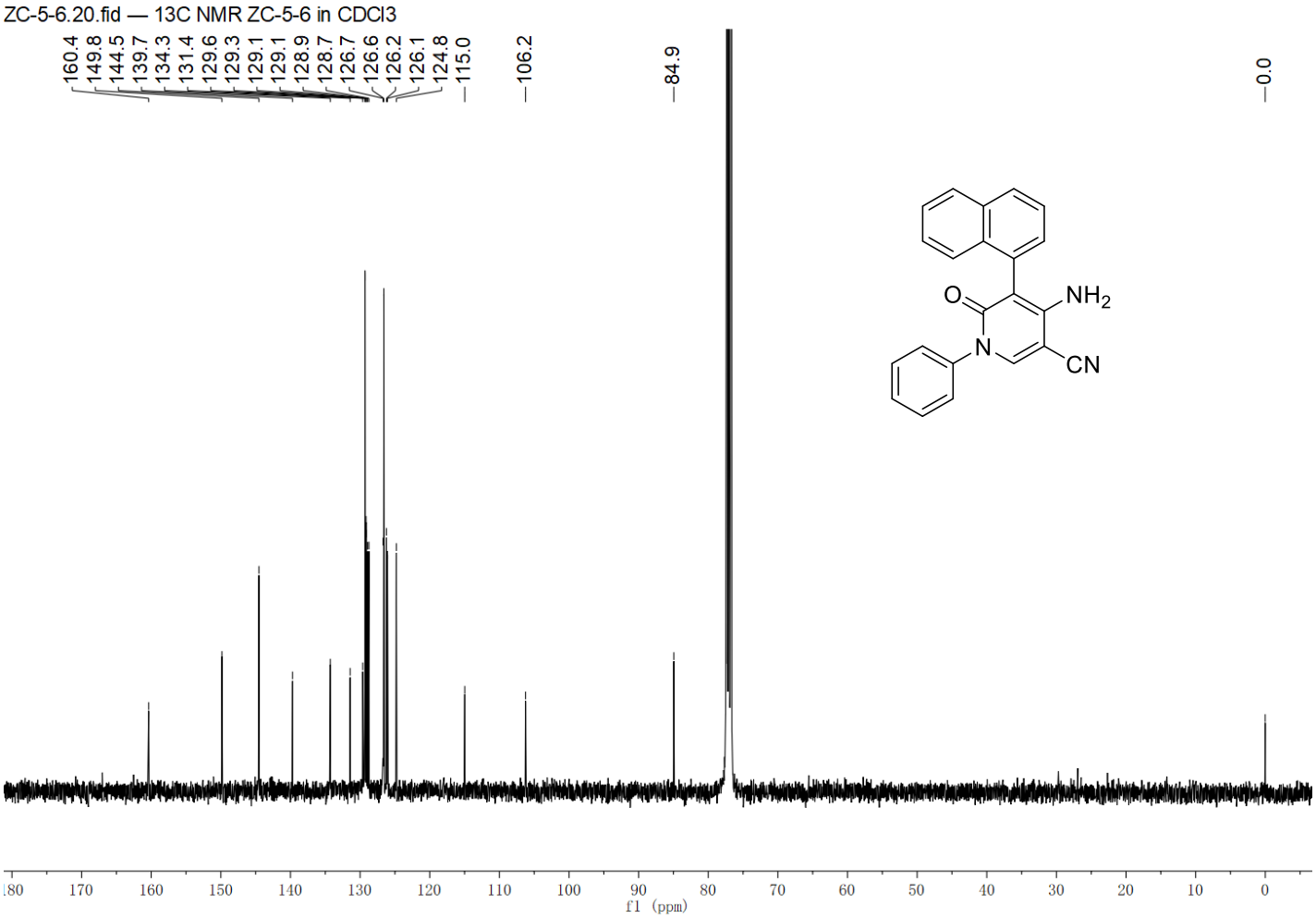
^{1}H NMR spectrum of compound **6m** (400 MHz, DMSO)



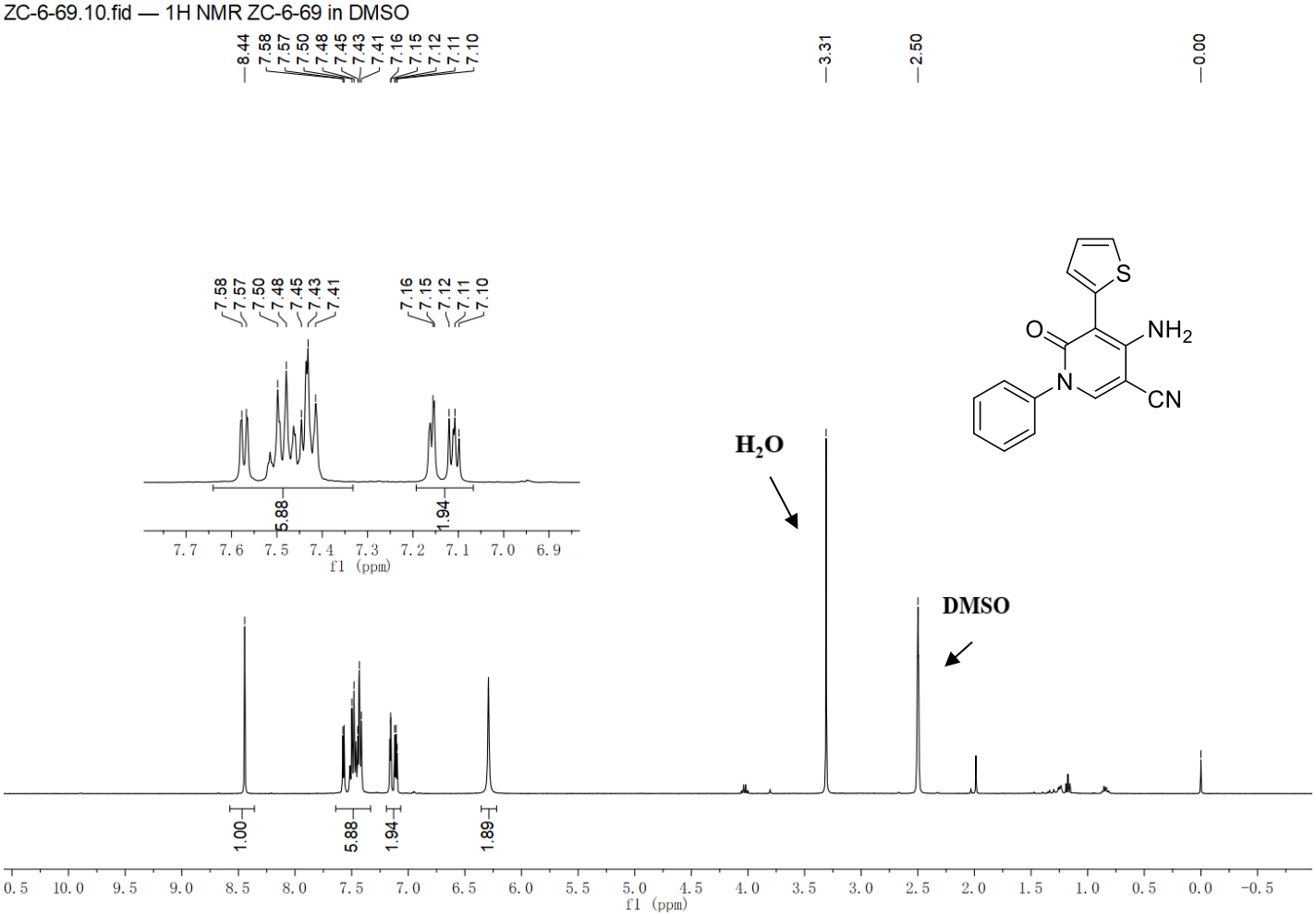
^{13}C NMR spectrum of compound **6m** (101 MHz, DMSO)



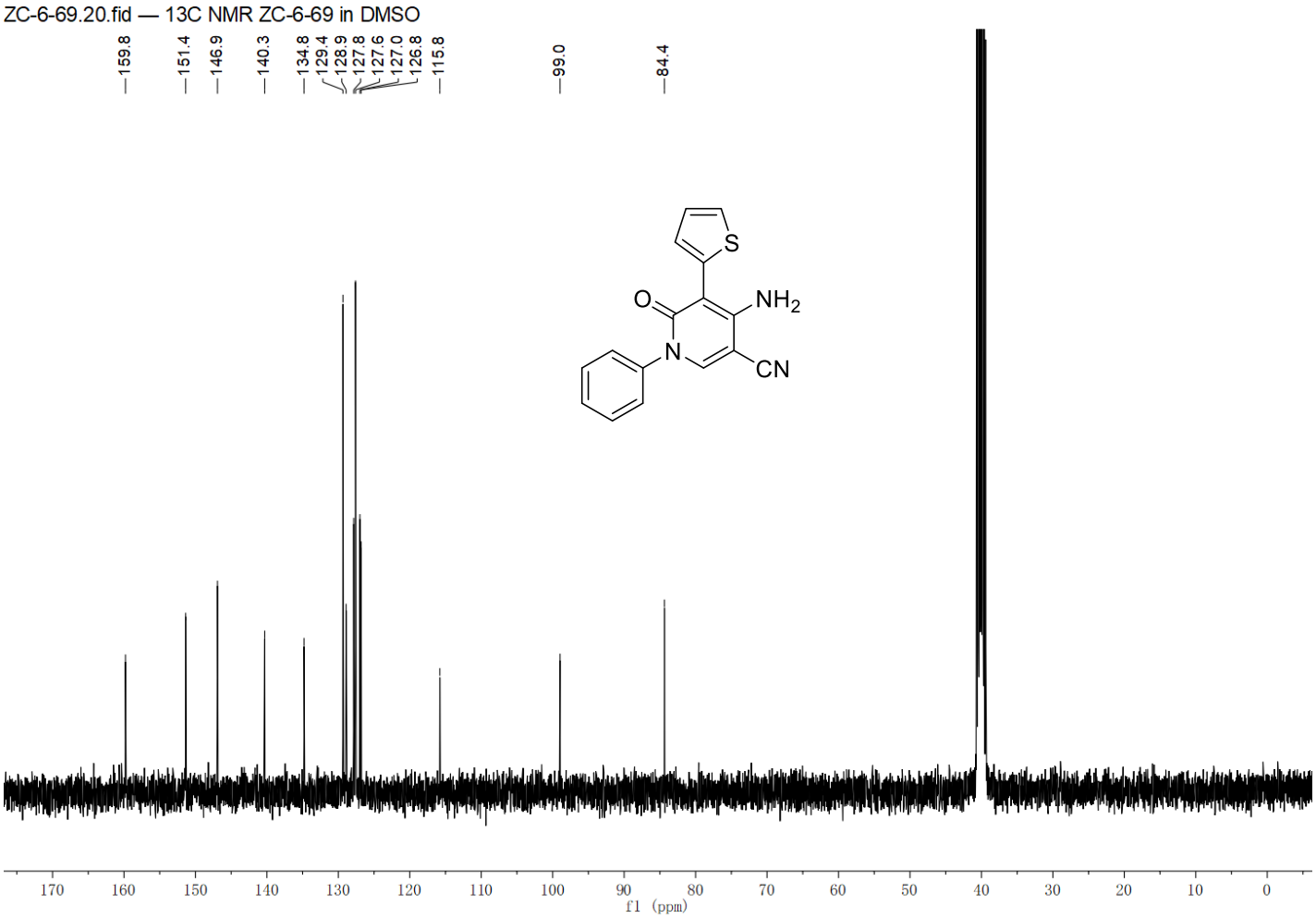
^{1}H NMR spectrum of compound **6n** (400 MHz, $CDCl_3$)



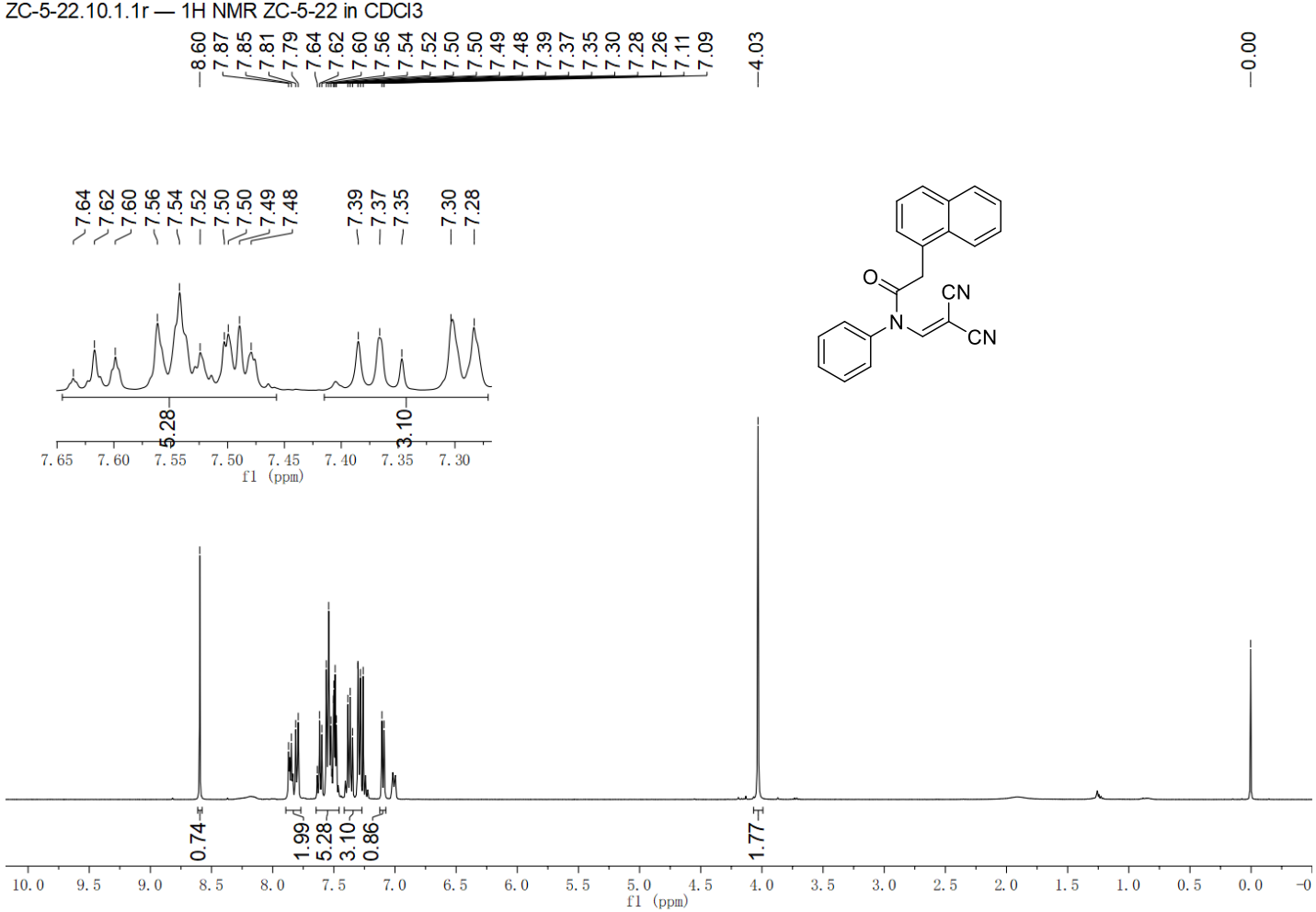
^{13}C NMR spectrum of compound **6n** (101 MHz, $CDCl_3$)



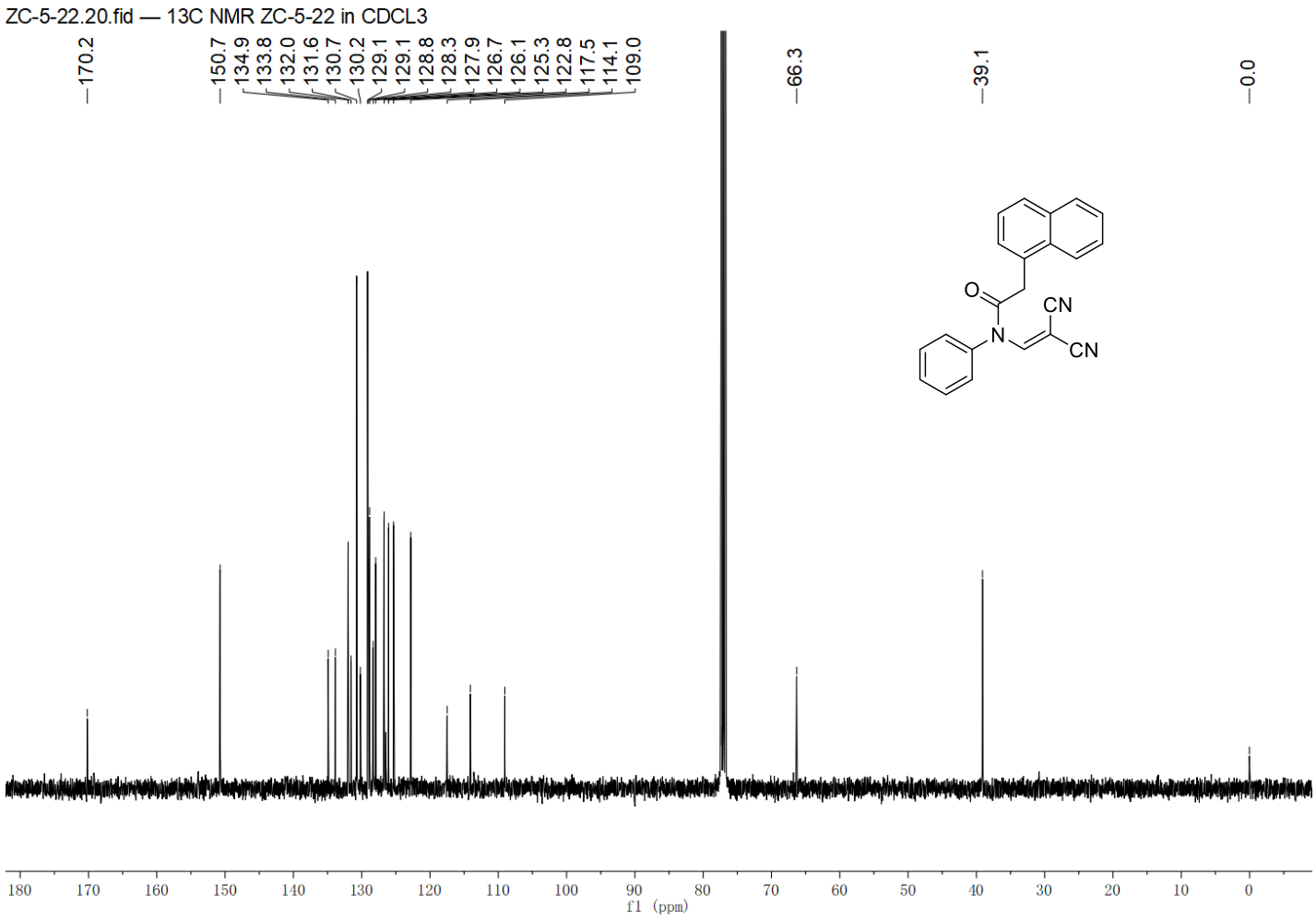
^{1}H NMR spectrum of compound **6o** (400 MHz, DMSO)



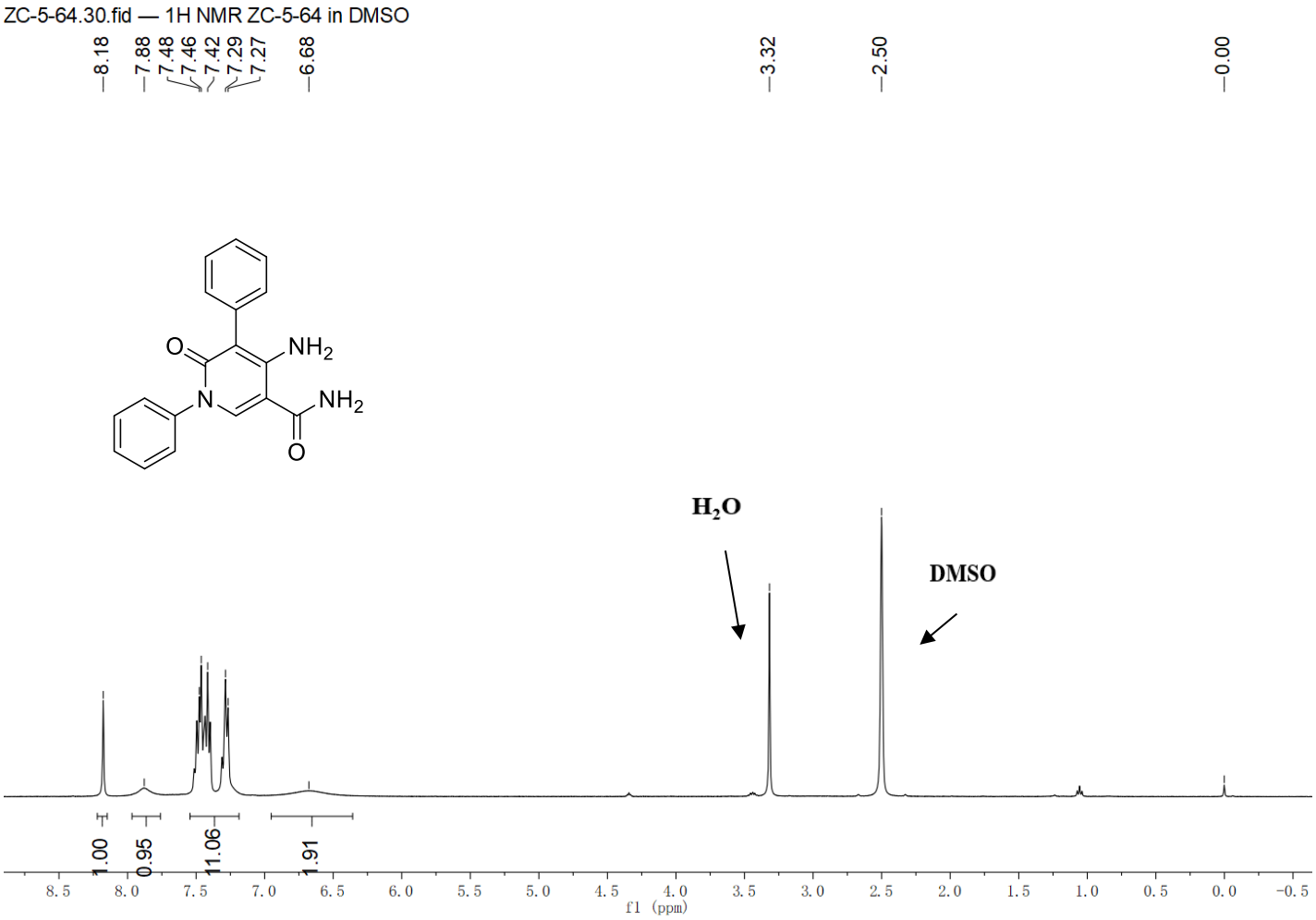
^{13}C NMR spectrum of compound **6o** (101 MHz, DMSO)



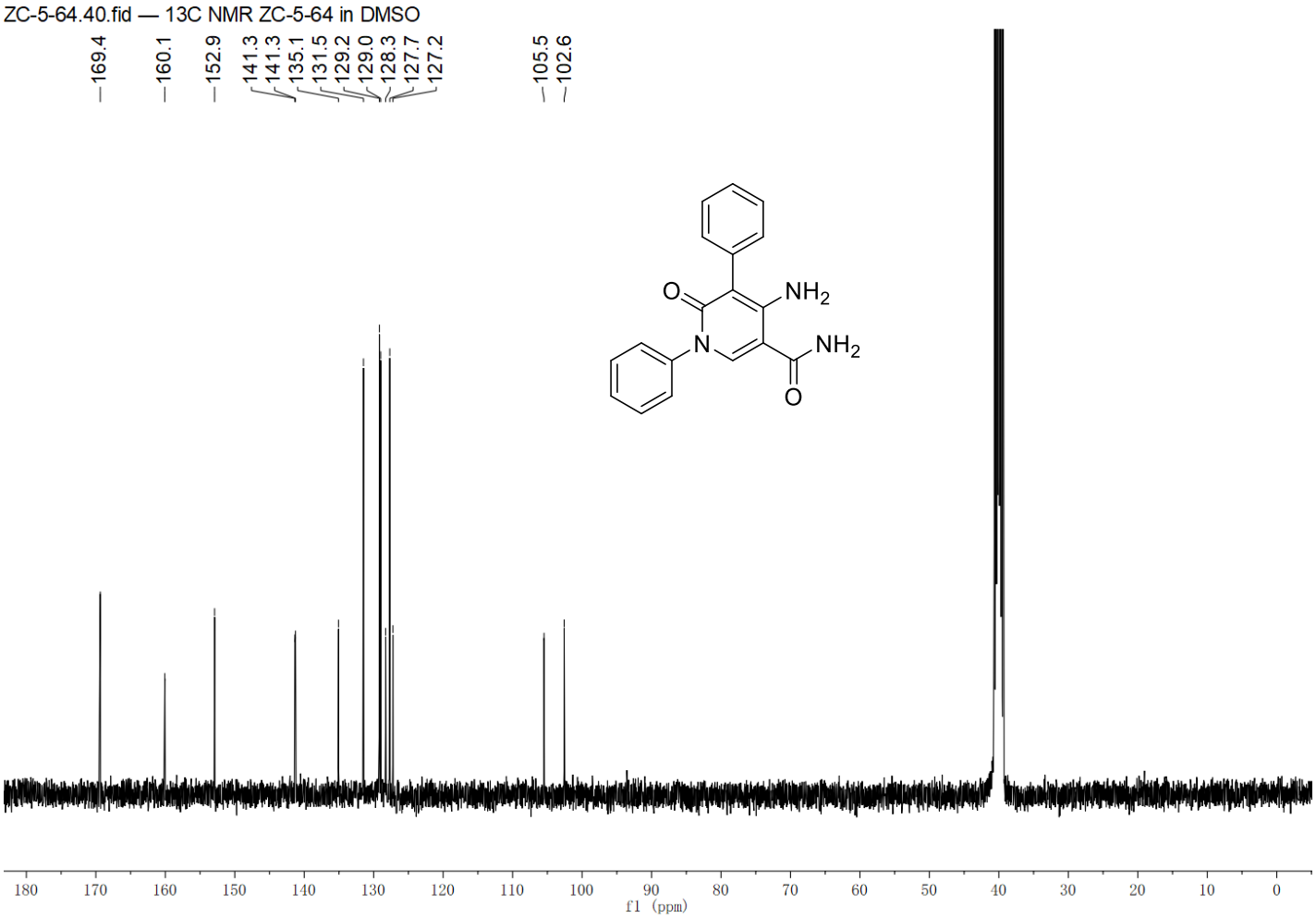
^{1}H NMR spectrum of compound **7** (400 MHz, $CDCl_3$)



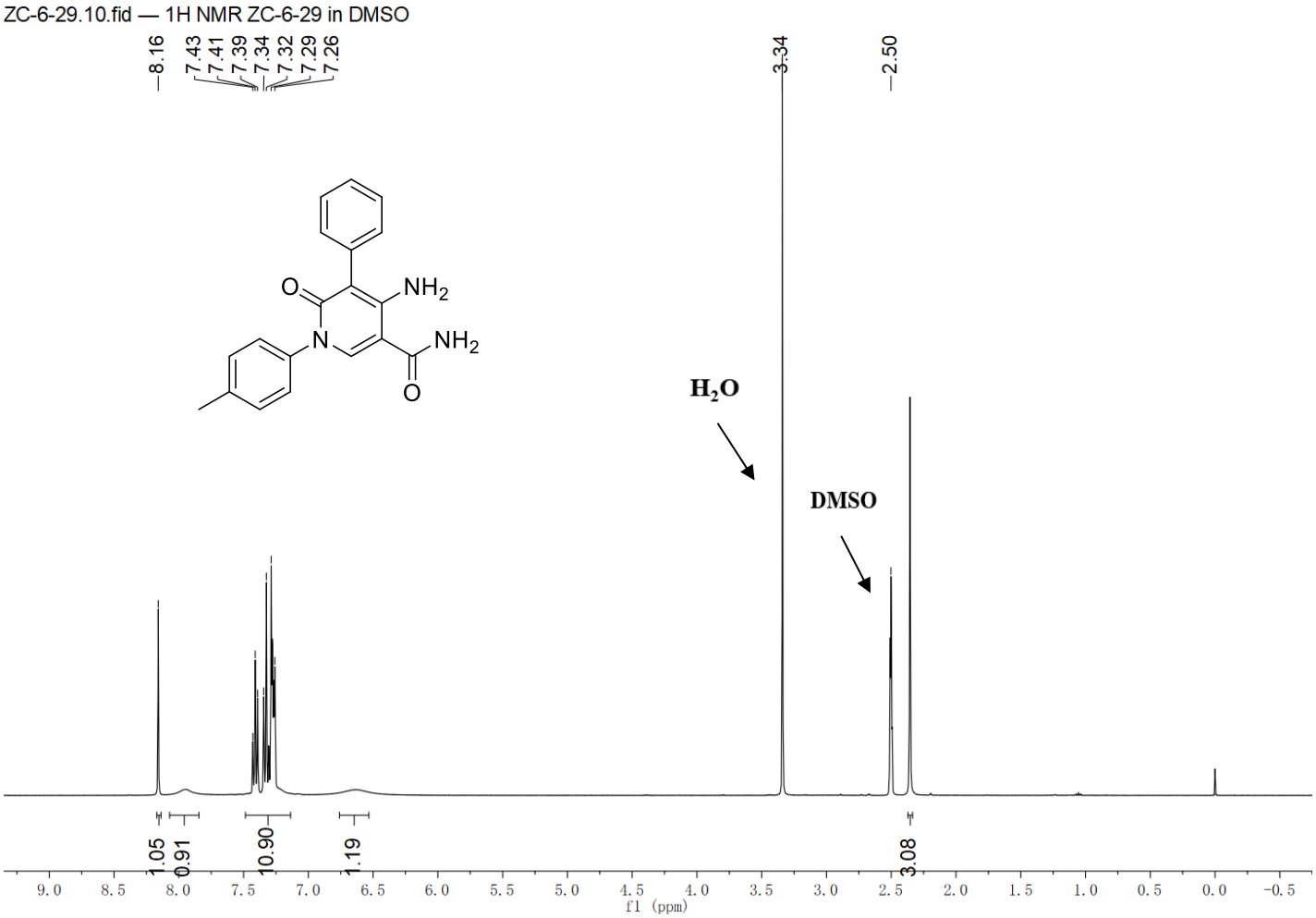
^{13}C NMR spectrum of compound **7** (101 MHz, $CDCl_3$)



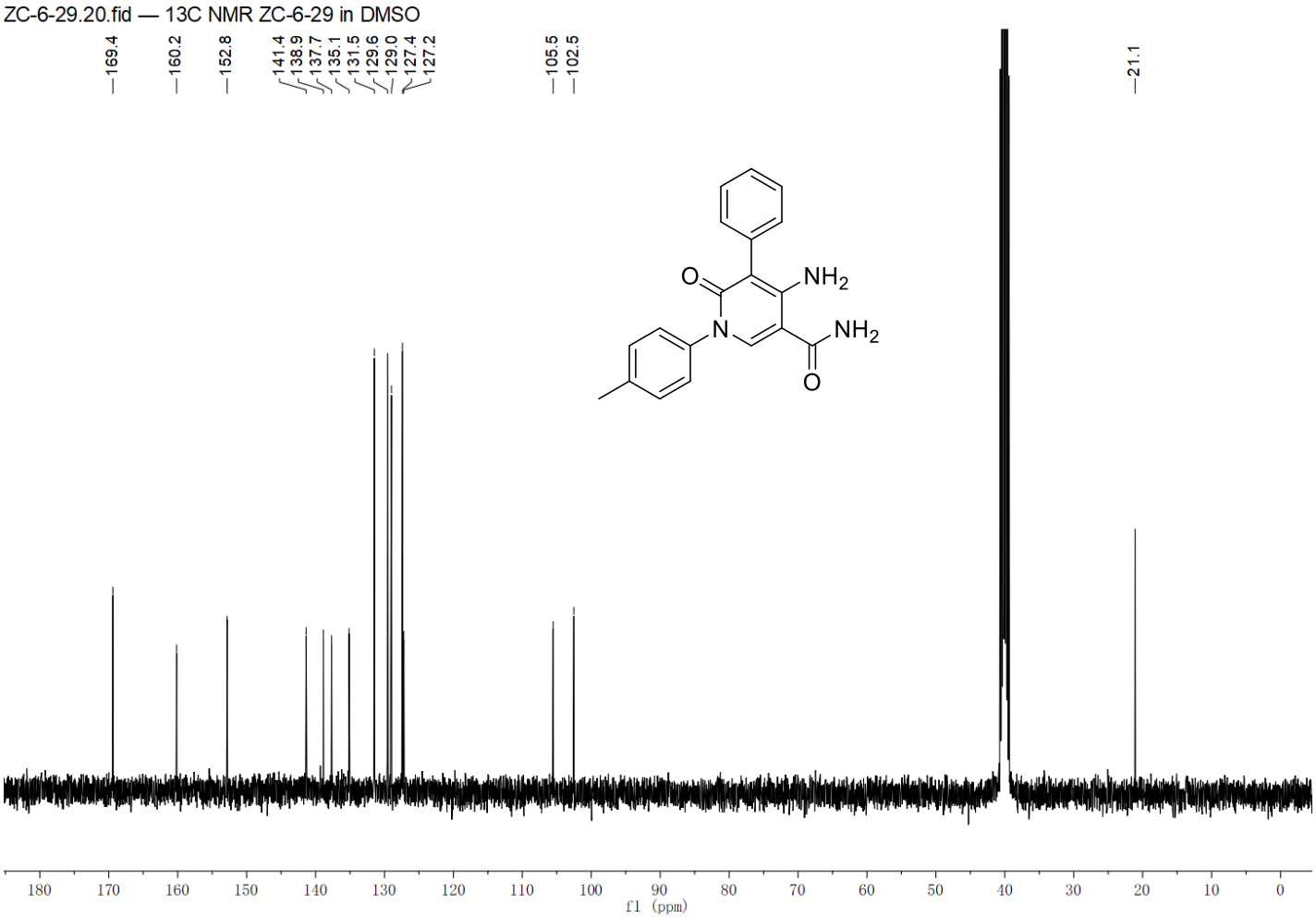
^{1}H NMR spectrum of compound **8a** (400 MHz, DMSO)



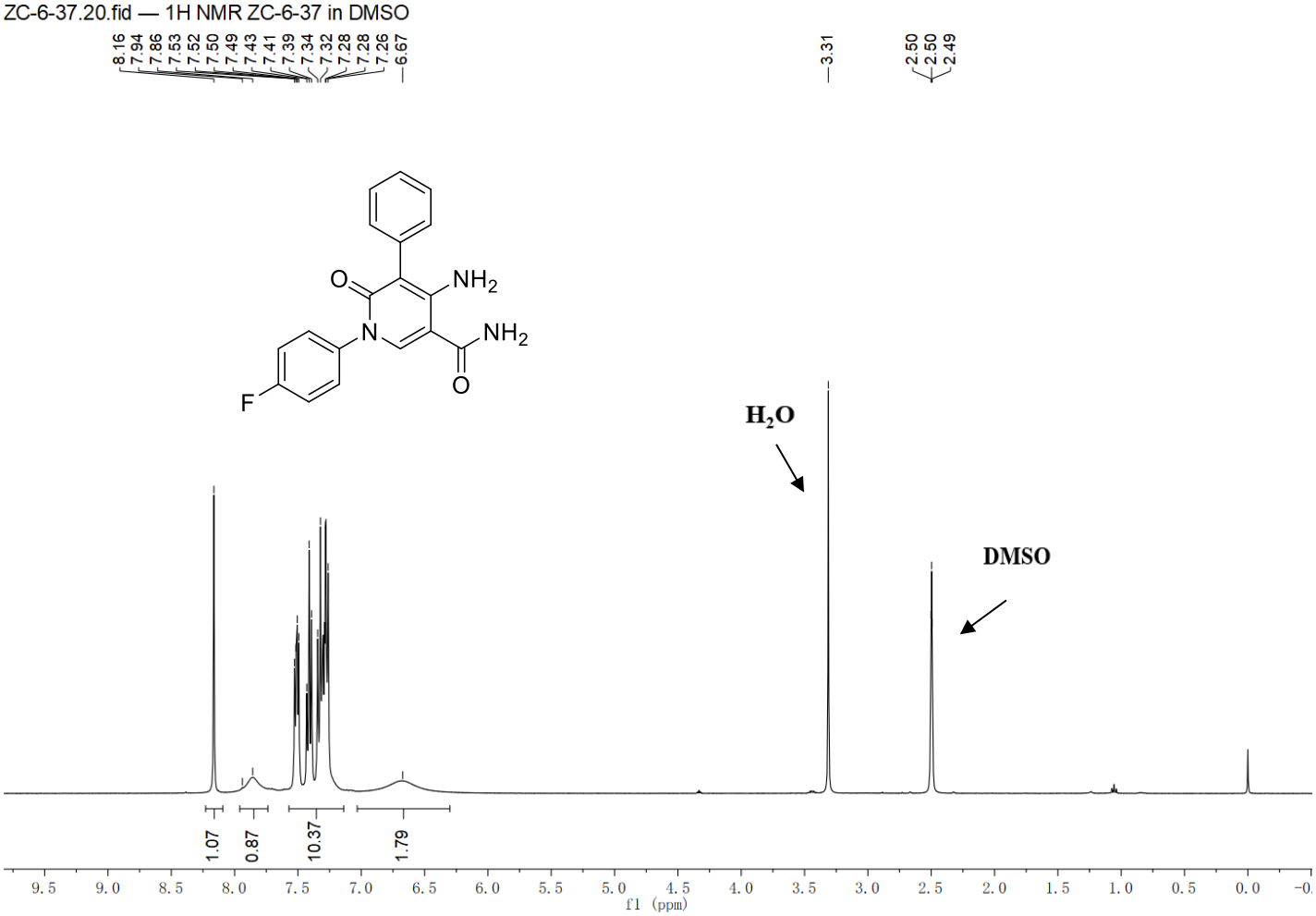
^{13}C NMR spectrum of compound **8a** (101 MHz, DMSO)



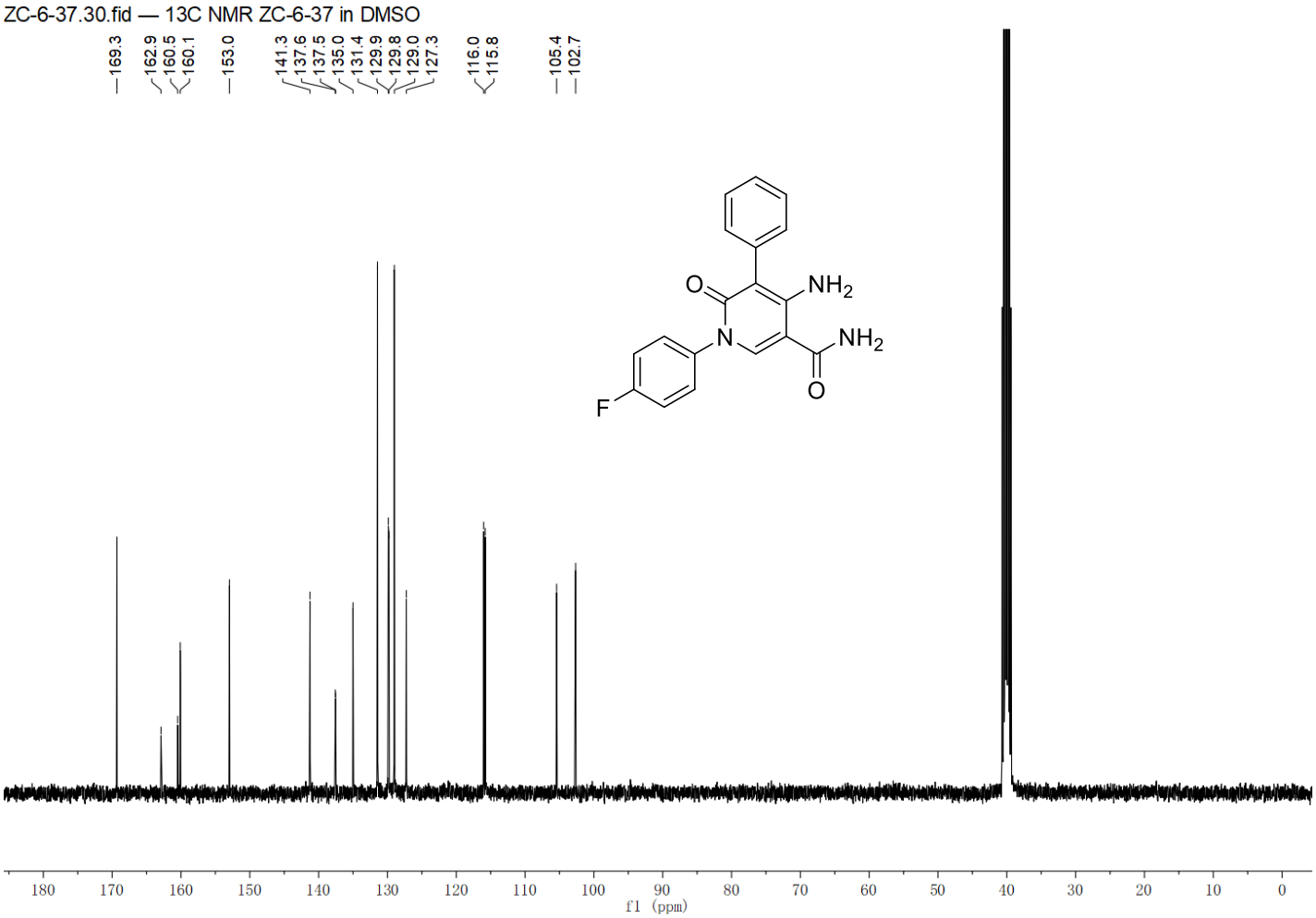
^{1}H NMR spectrum of compound **8b** (400 MHz, DMSO)



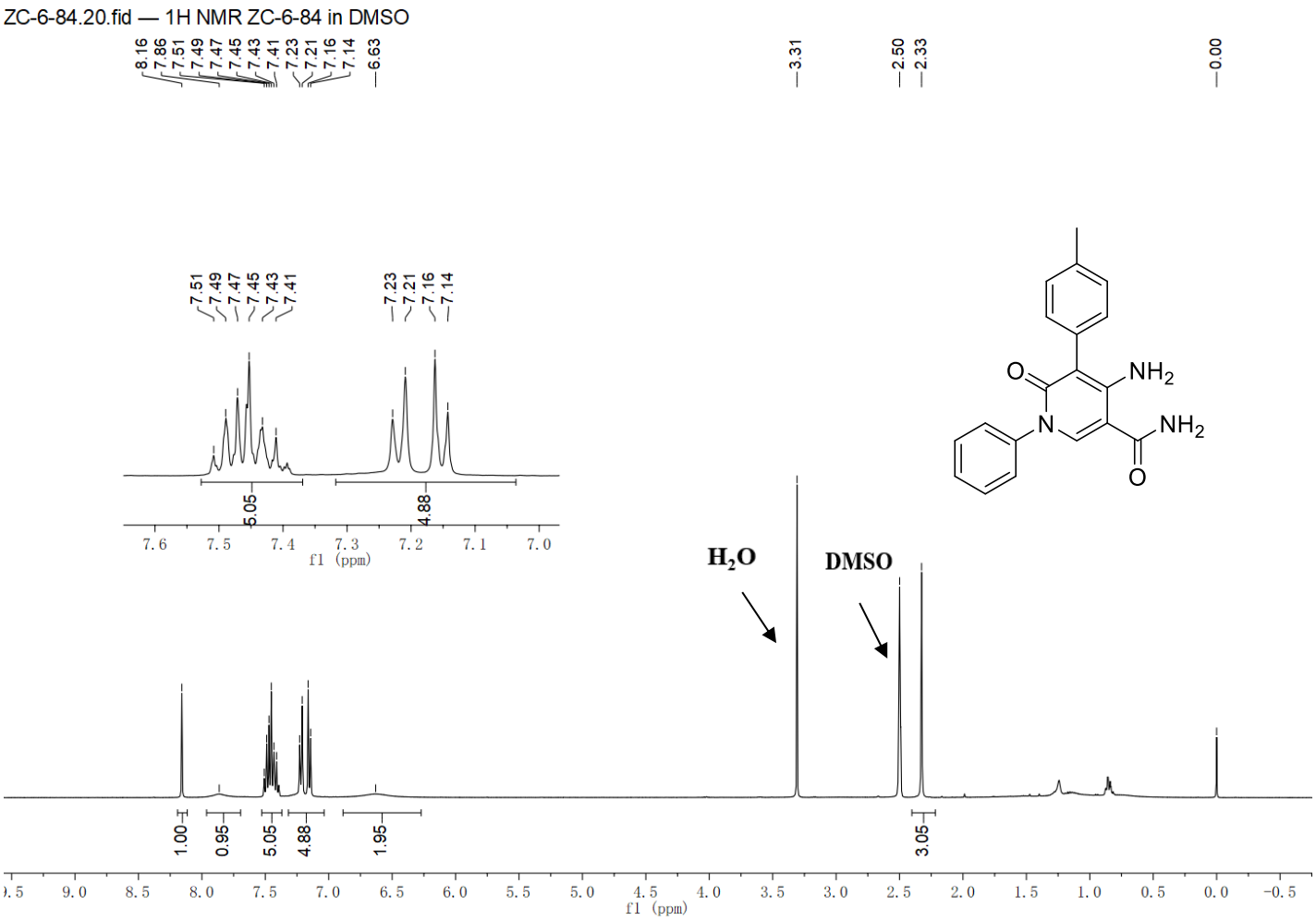
^{13}C NMR spectrum of compound **8b** (101 MHz, DMSO)



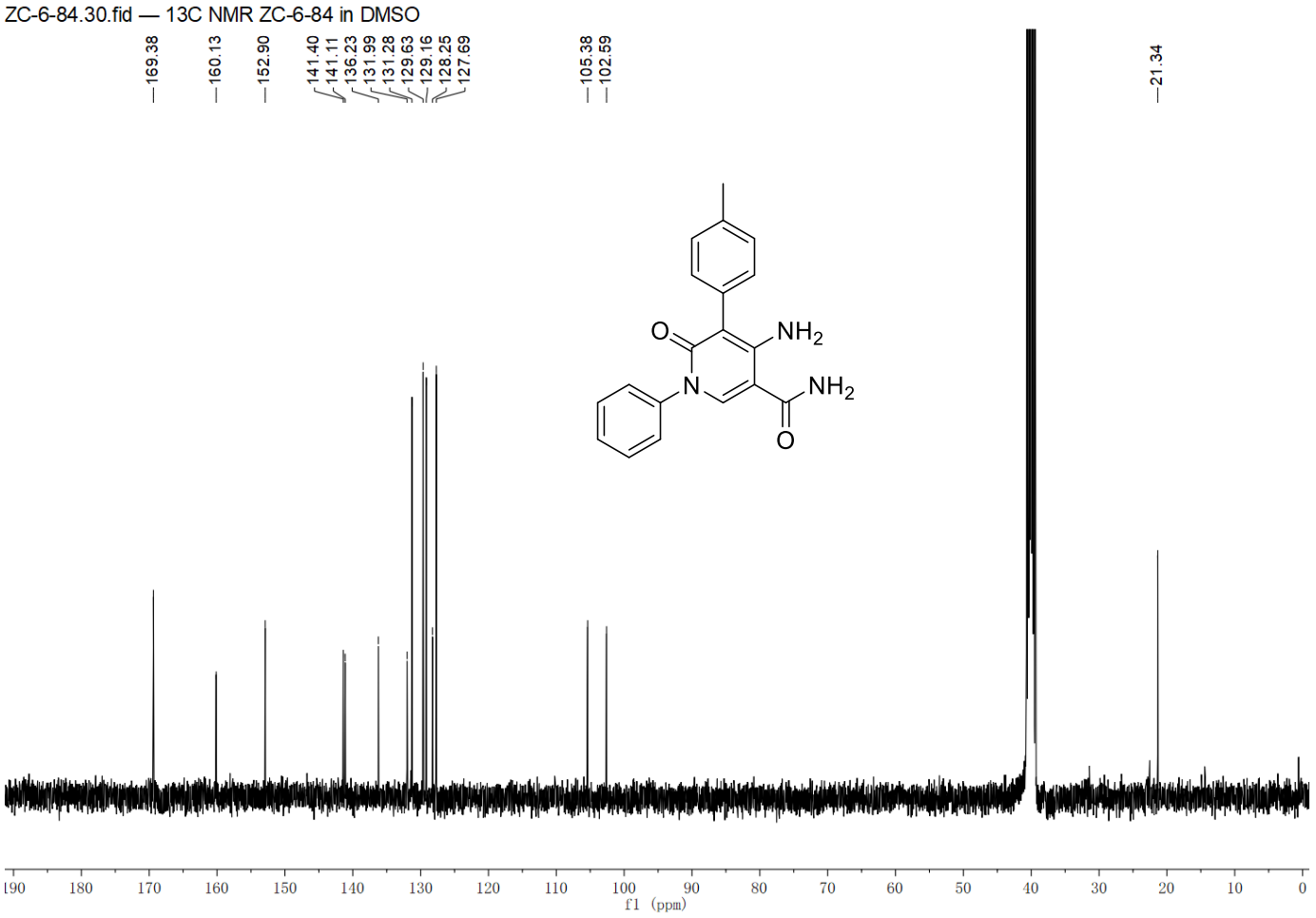
^{1}H NMR spectrum of compound **8c** (400 MHz, DMSO)



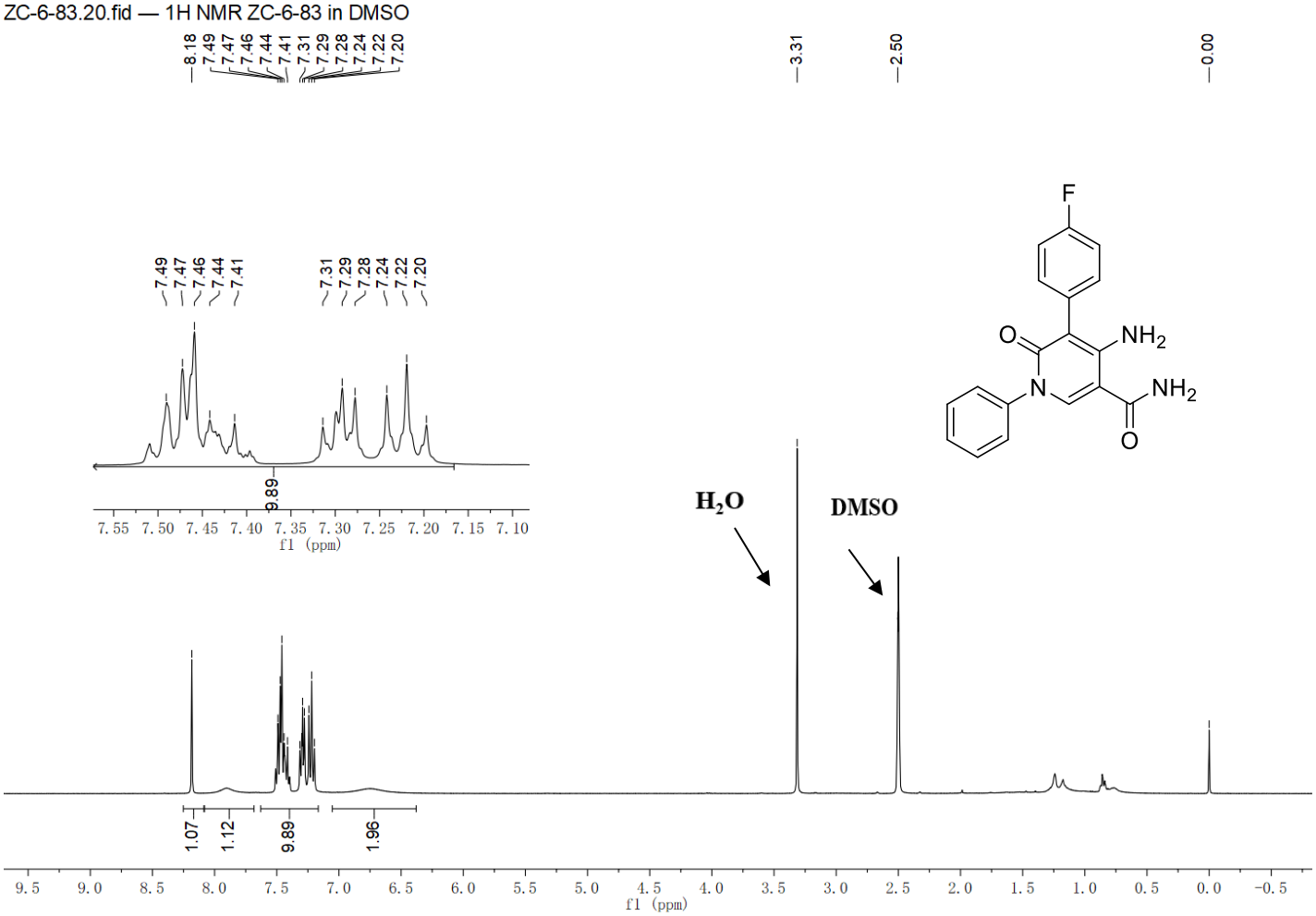
^{13}C NMR spectrum of compound **8c** (101 MHz, DMSO)



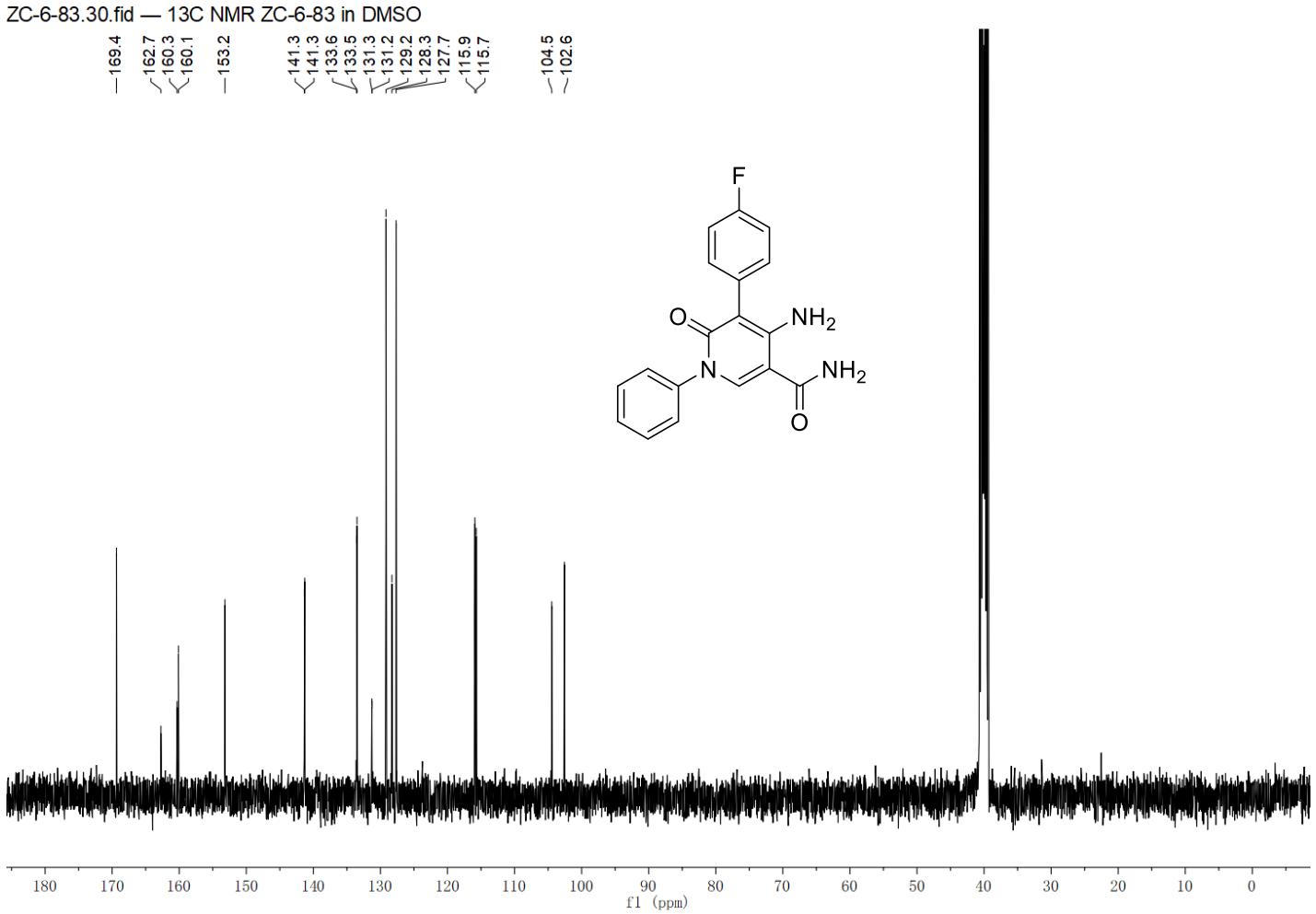
^{1}H NMR spectrum of compound **8d** (400 MHz, DMSO)



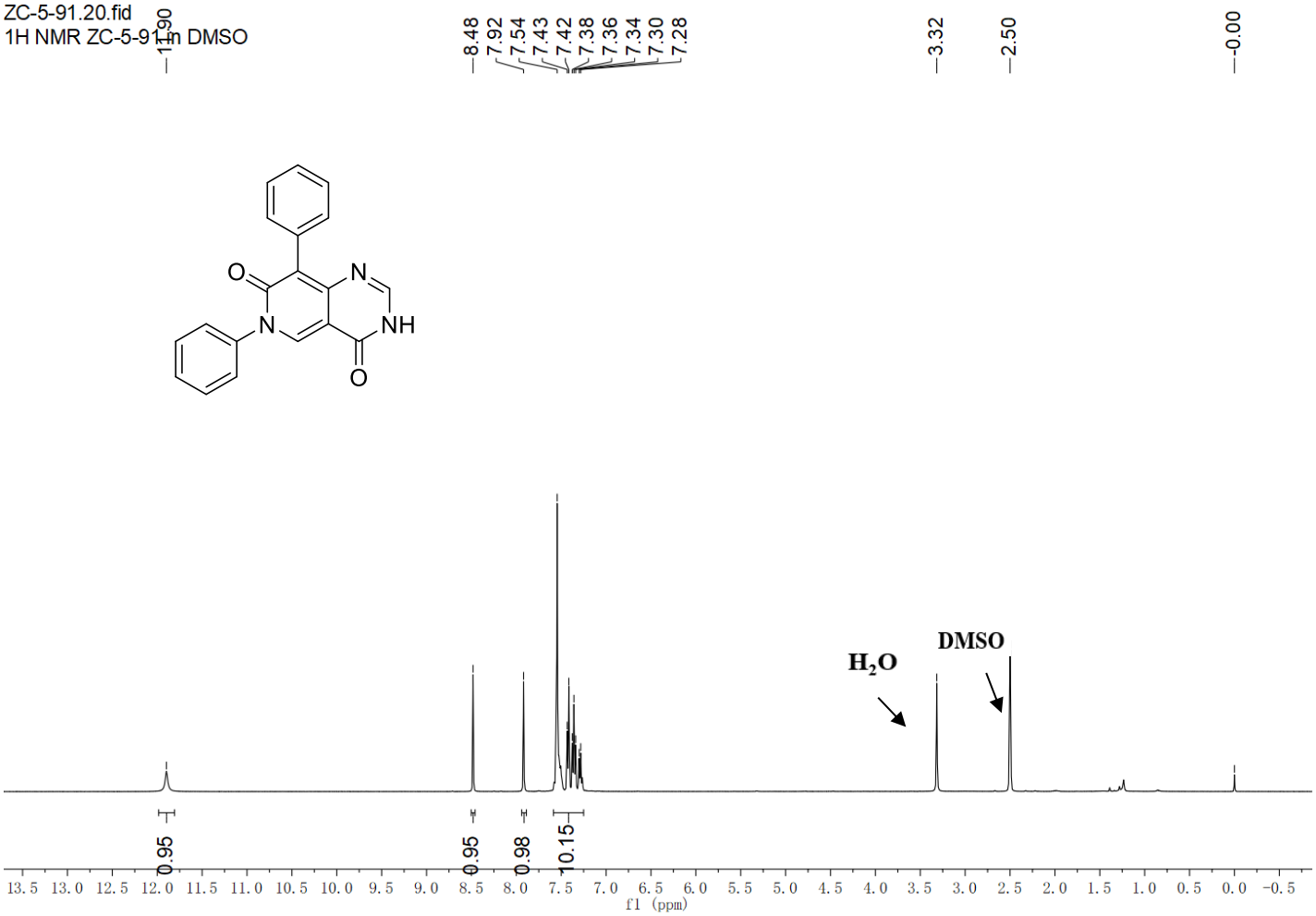
^{13}C NMR spectrum of compound **8d** (101 MHz, DMSO)



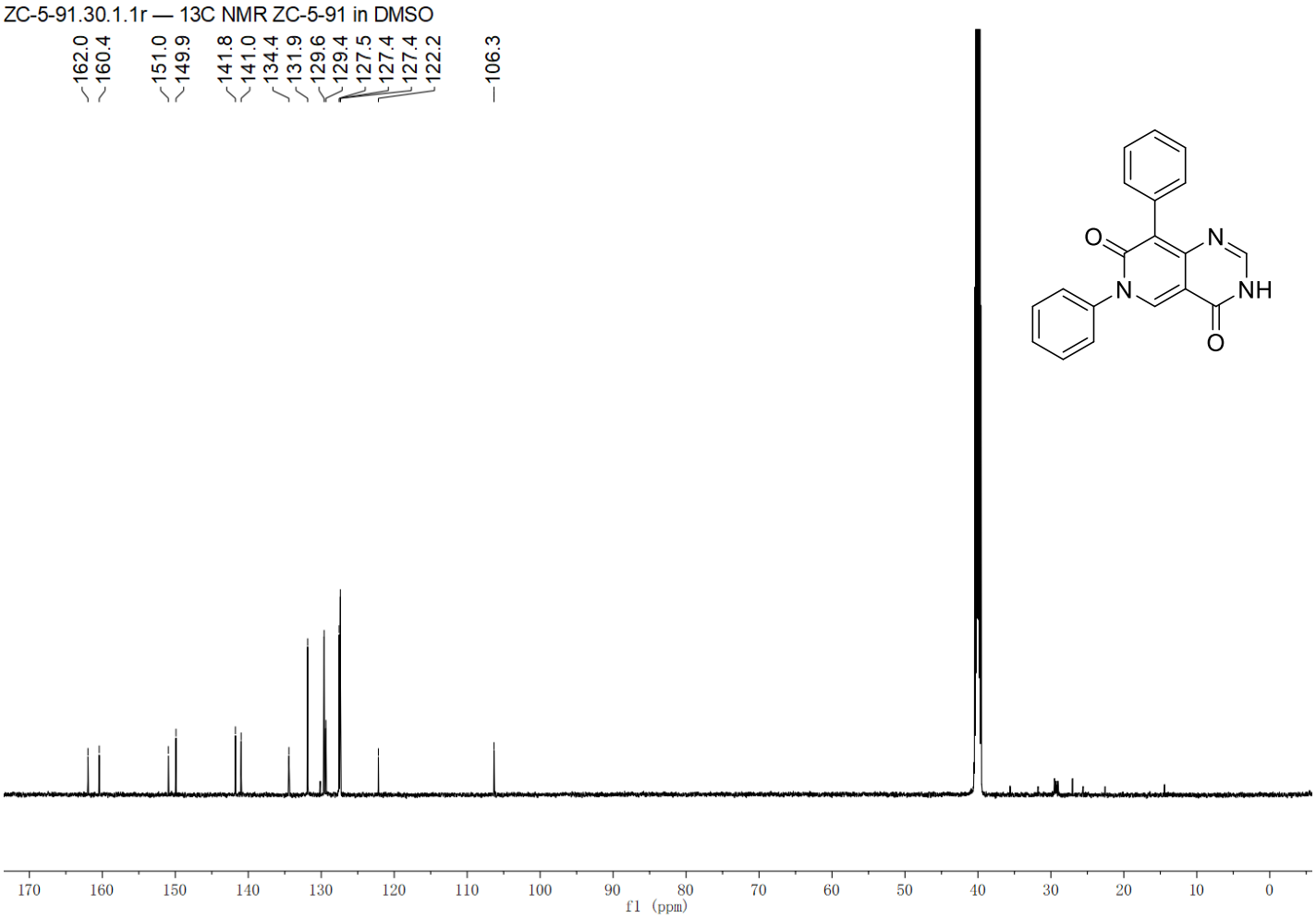
^{1}H NMR spectrum of compound **8e** (400 MHz, DMSO)



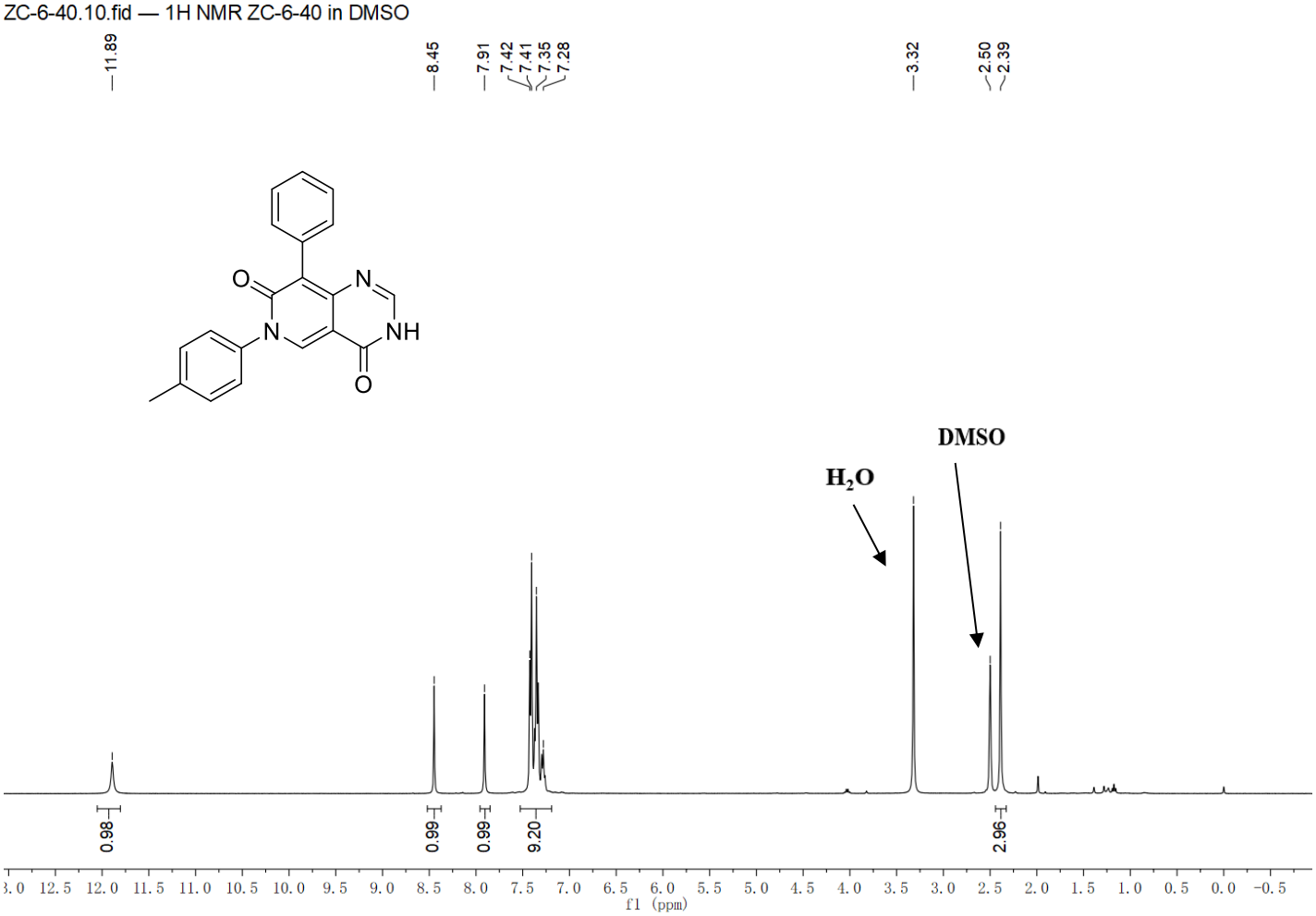
^{13}C NMR spectrum of compound **8e** (101 MHz, DMSO)



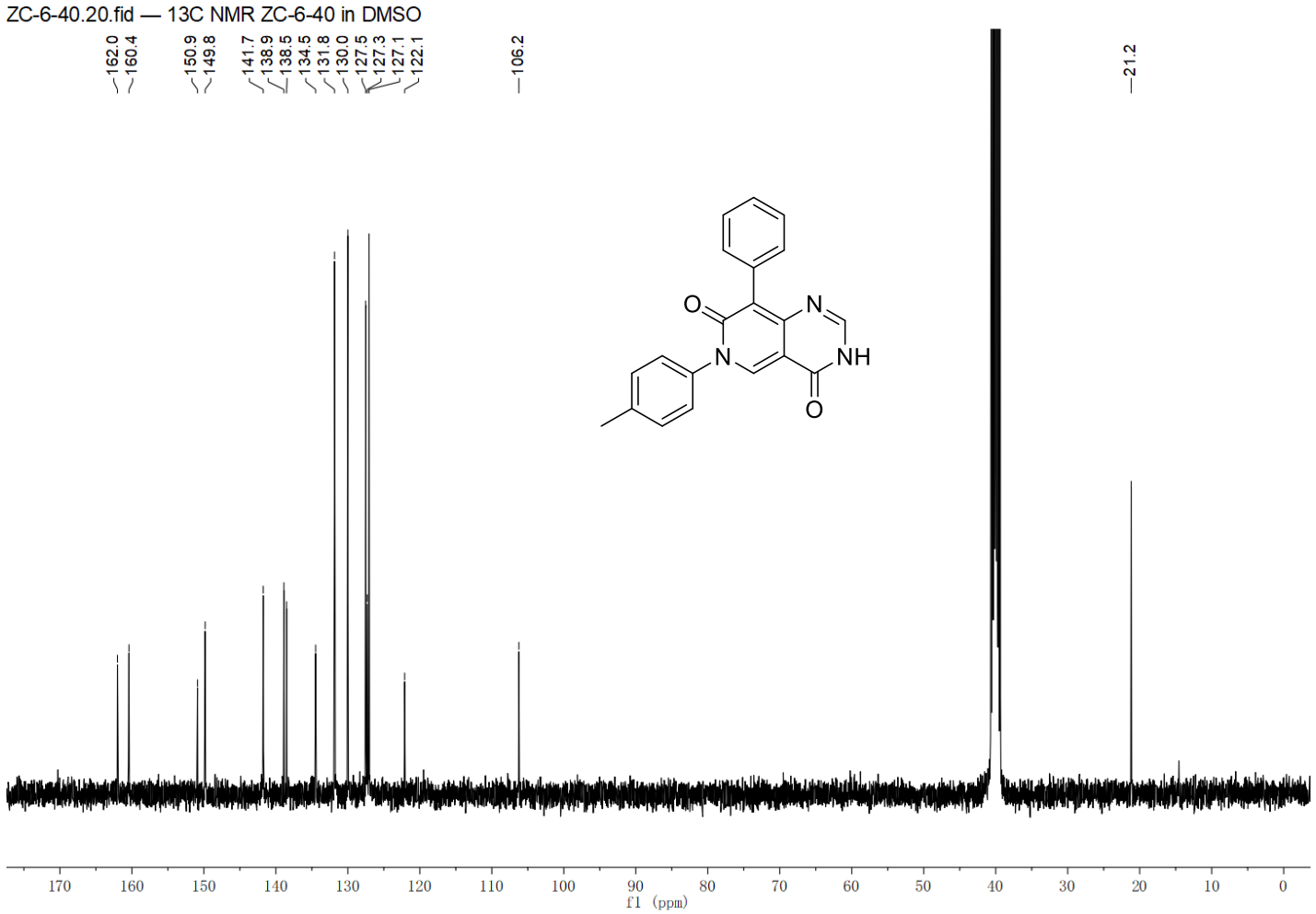
^{1}H NMR spectrum of compound **9a** (400 MHz, DMSO)



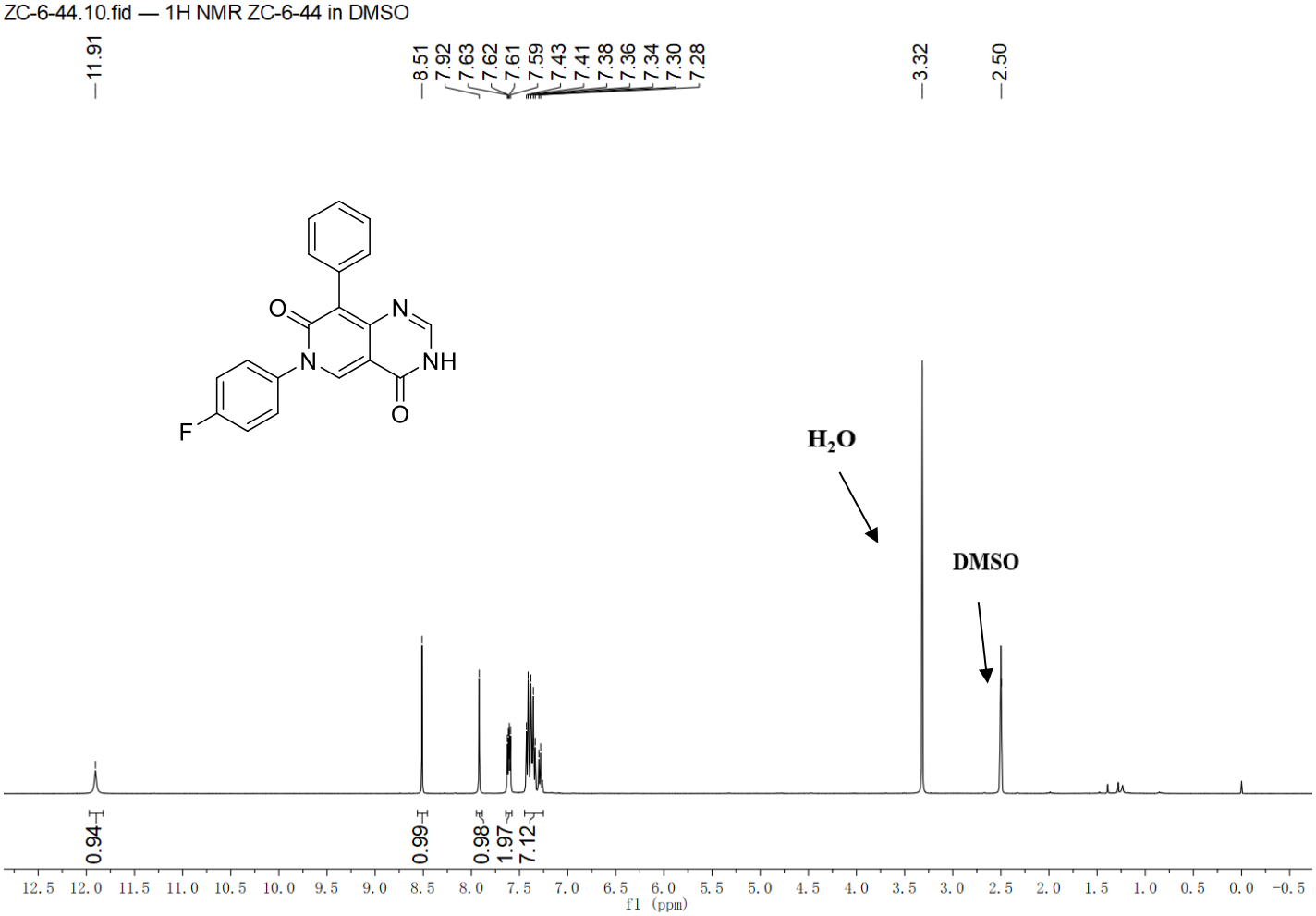
^{13}C NMR spectrum of compound **9a** (151 MHz, DMSO)



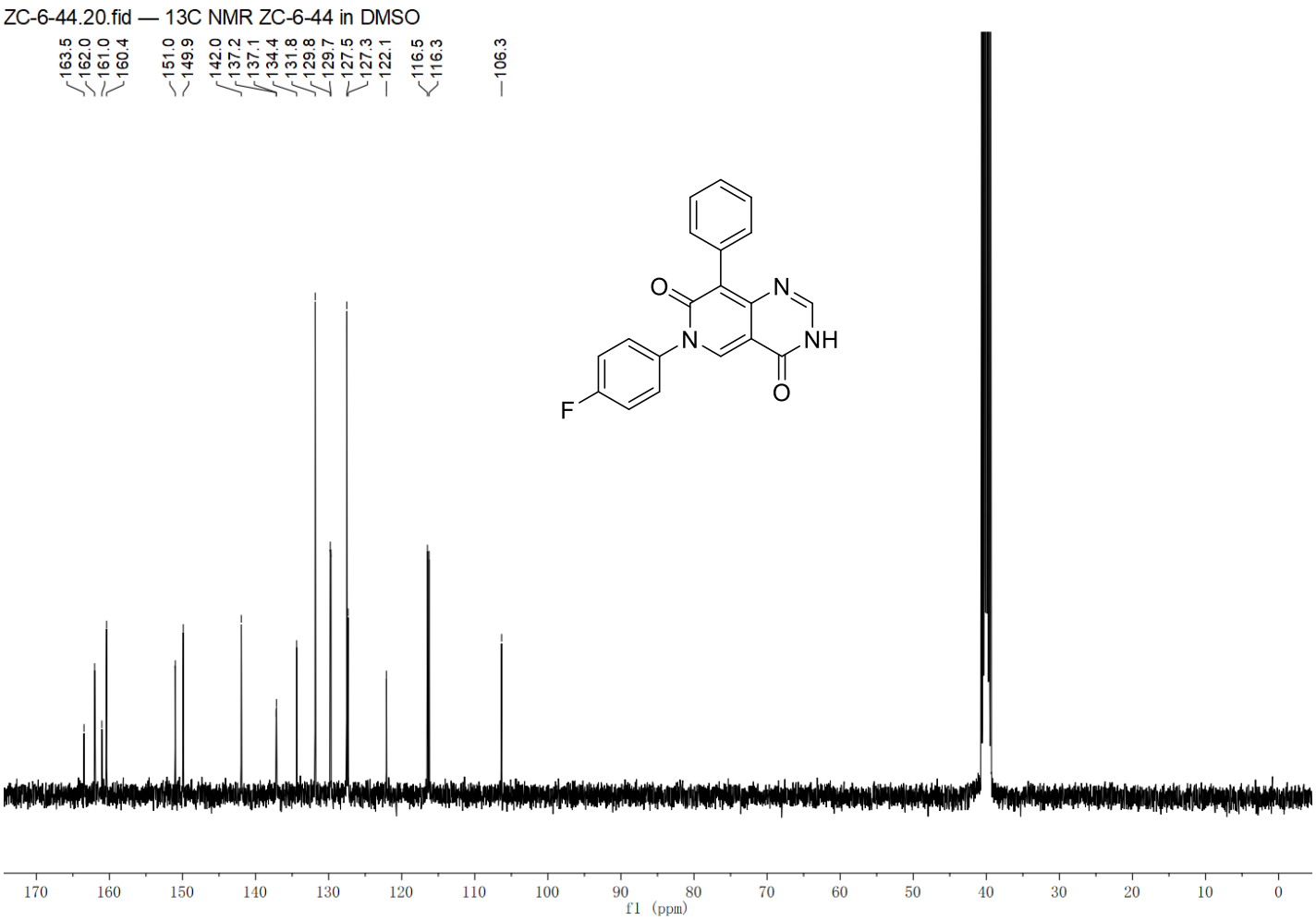
^{1}H NMR spectrum of compound **9b** (400 MHz, DMSO)



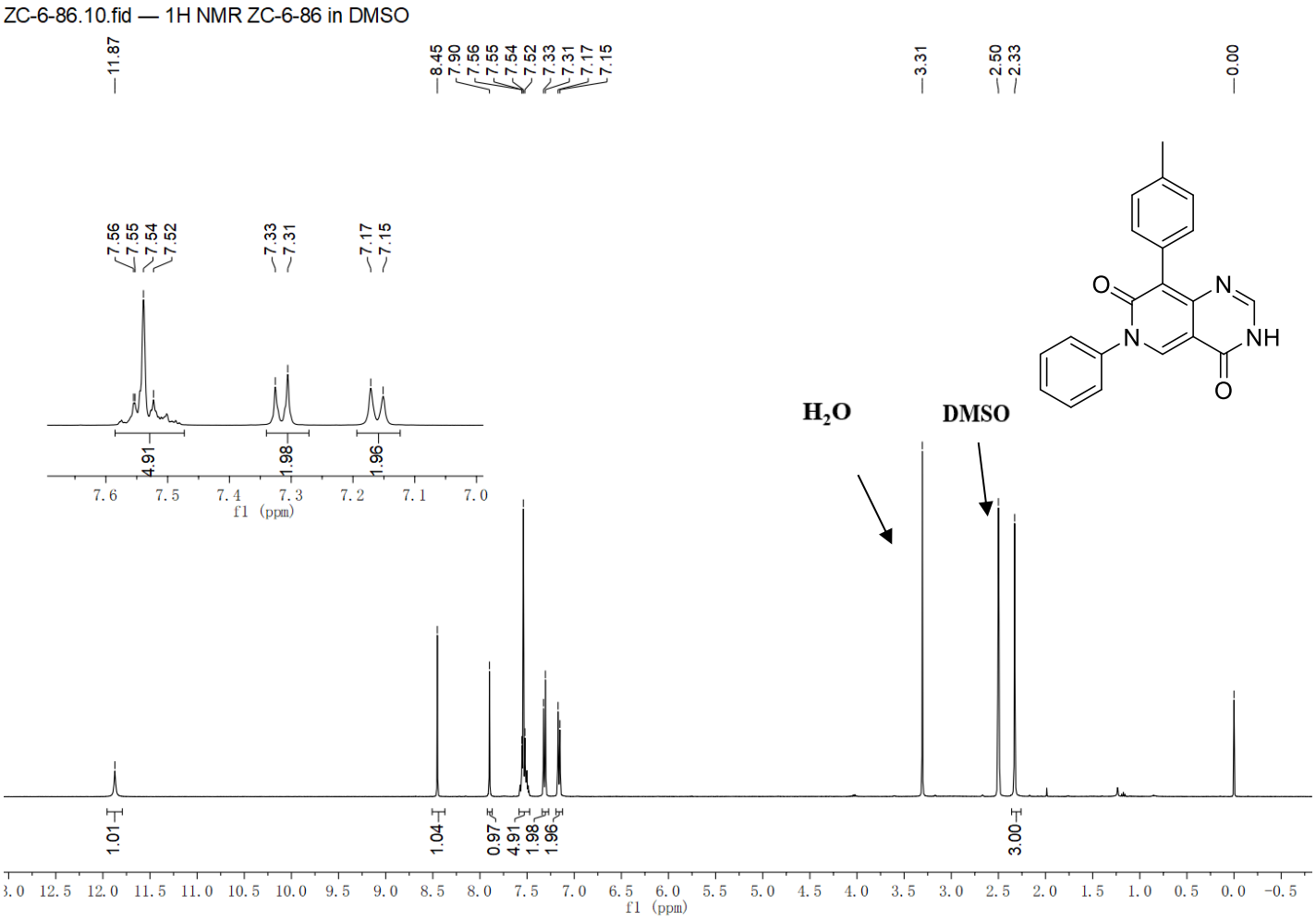
^{13}C NMR spectrum of compound **9b** (101 MHz, DMSO)



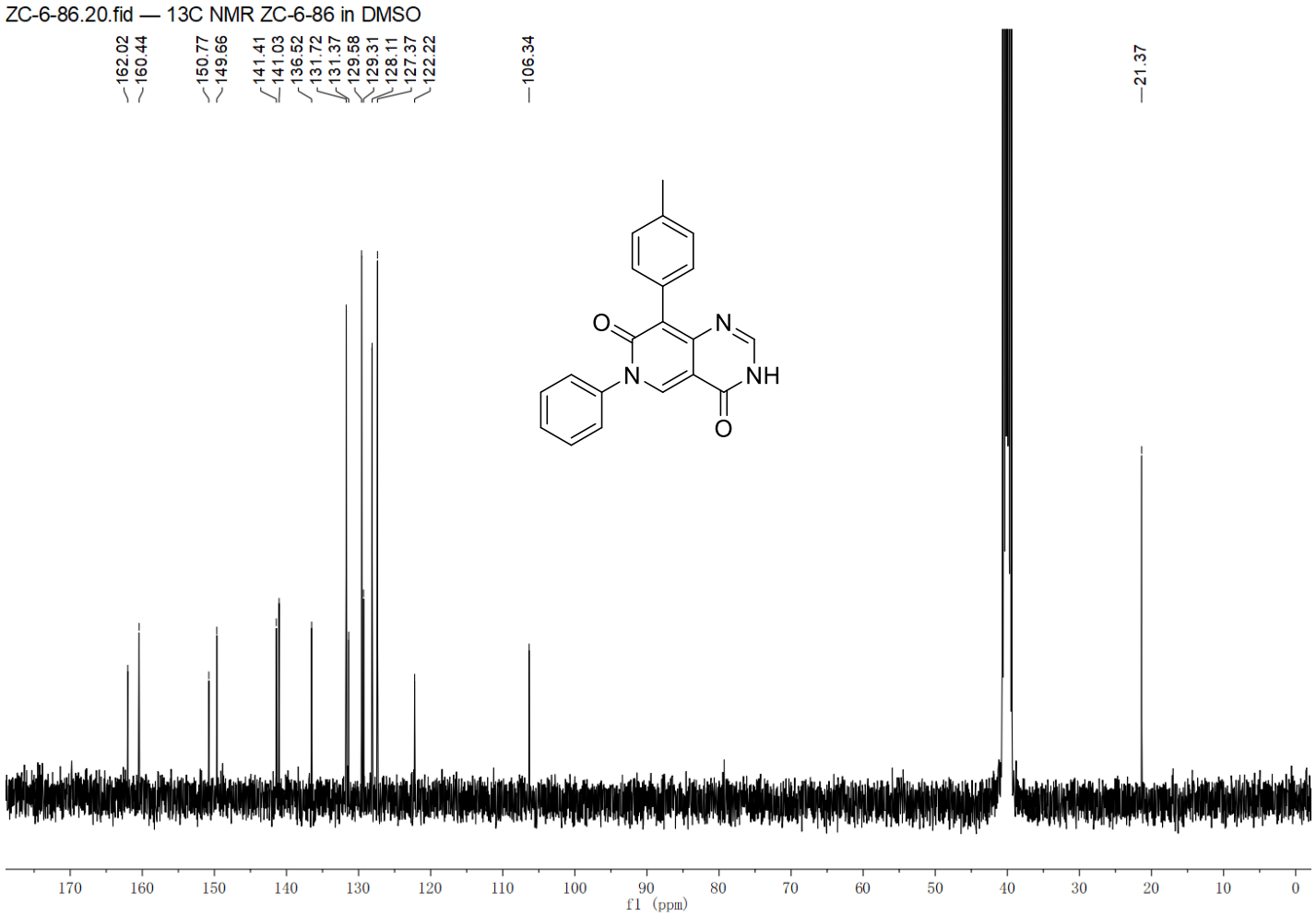
^{1}H NMR spectrum of compound **9c** (400 MHz, DMSO)



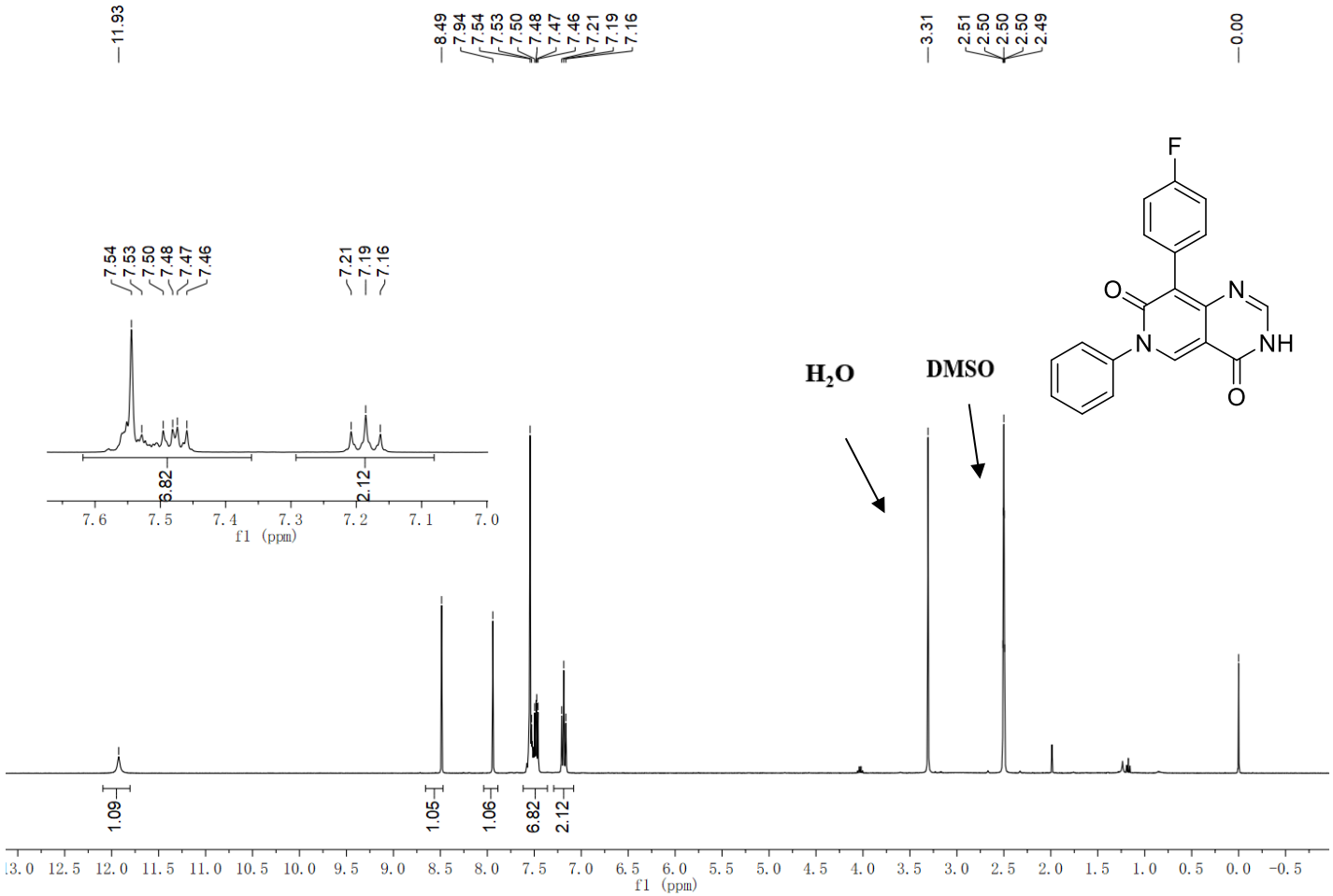
^{13}C NMR spectrum of compound **9c** (101 MHz, DMSO)



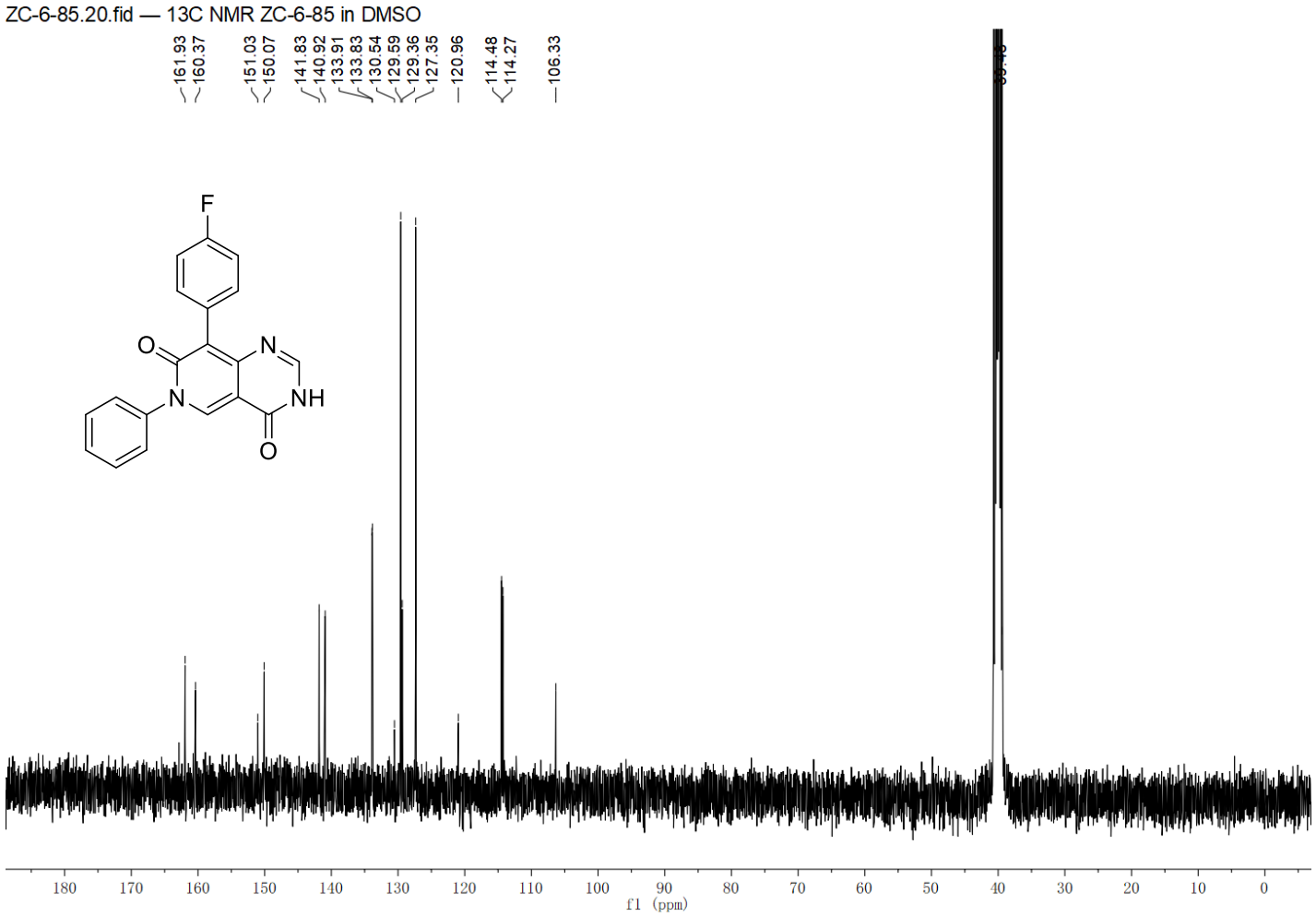
^{1}H NMR spectrum of compound **9d** (400 MHz, DMSO)



^{13}C NMR spectrum of compound **9d** (101 MHz, DMSO)

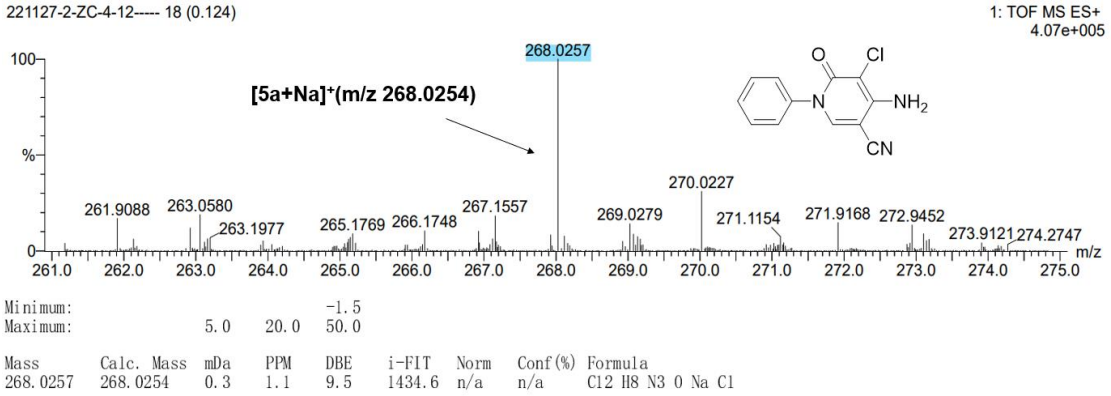


^{1}H NMR spectrum of compound **9e** (400 MHz, DMSO)

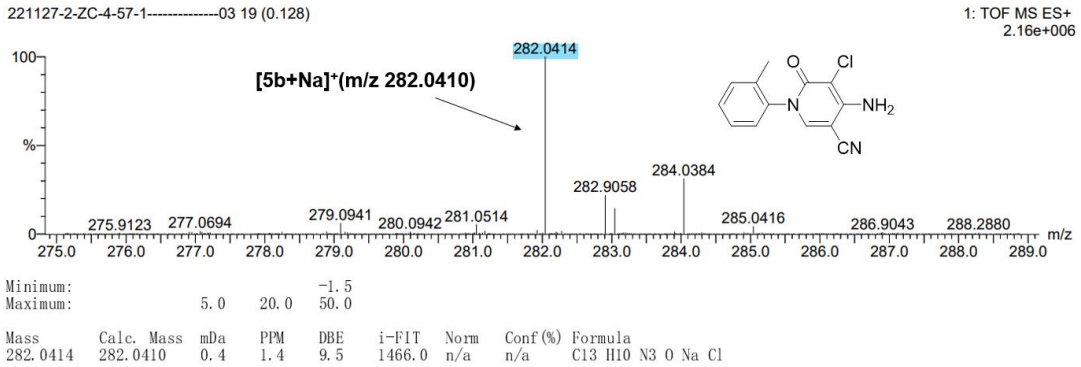


^{13}C NMR spectrum of compound **9e** (101 MHz, DMSO)

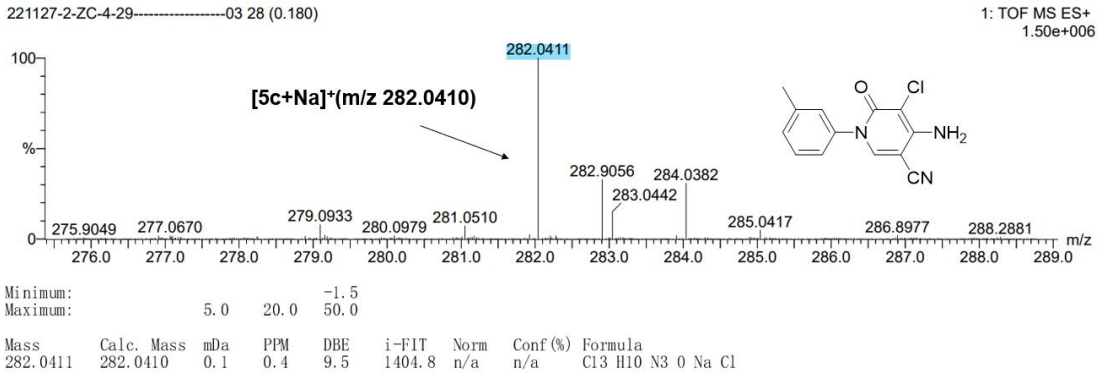
9. Copies of MS spectra



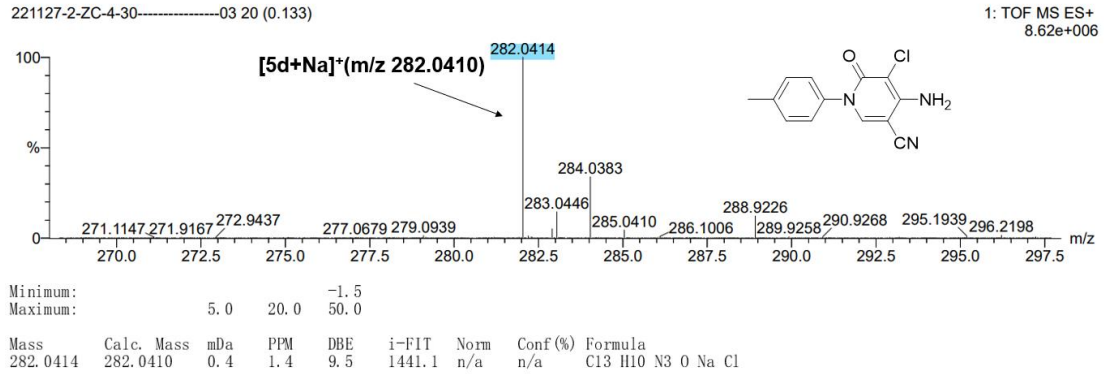
HRMS spectrum of **5a**



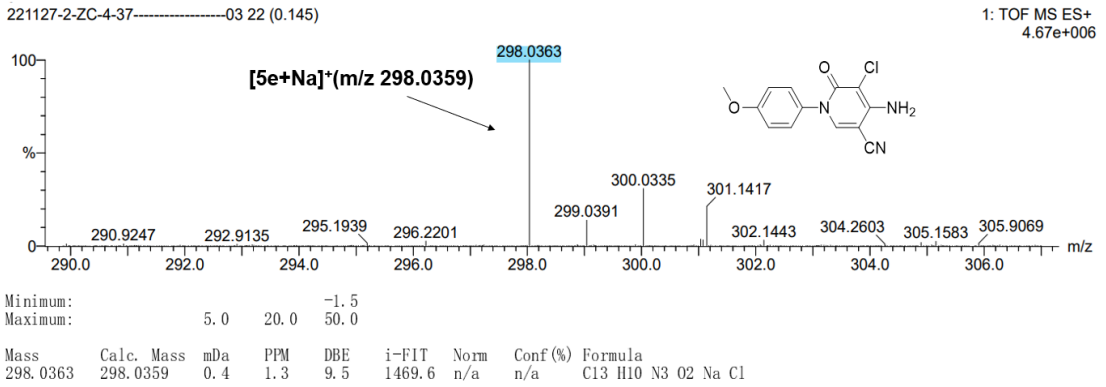
HRMS spectrum of **5b**



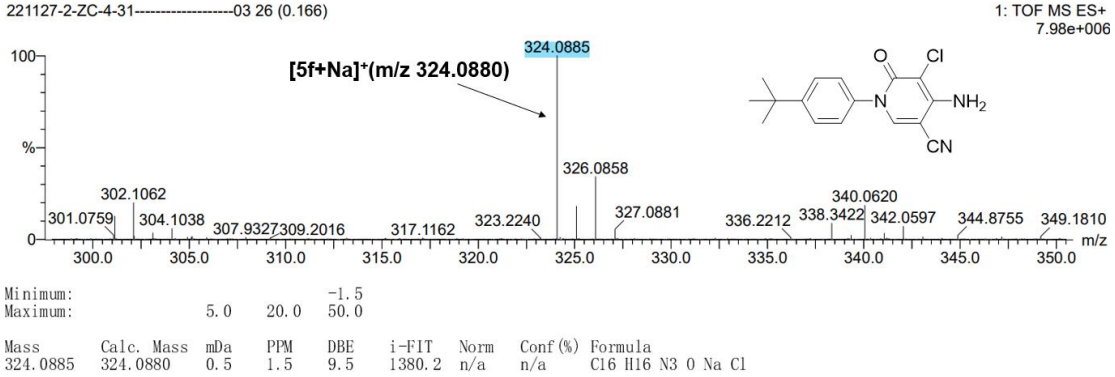
HRMS spectrum of **5c**



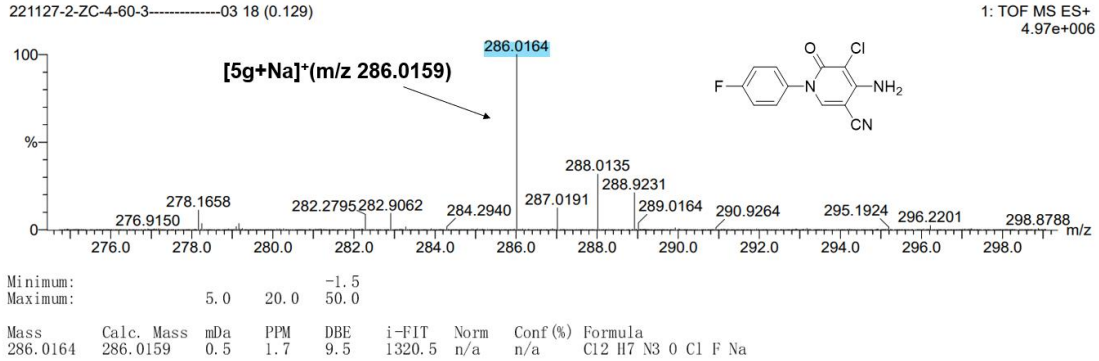
HRMS spectrum of **5d**



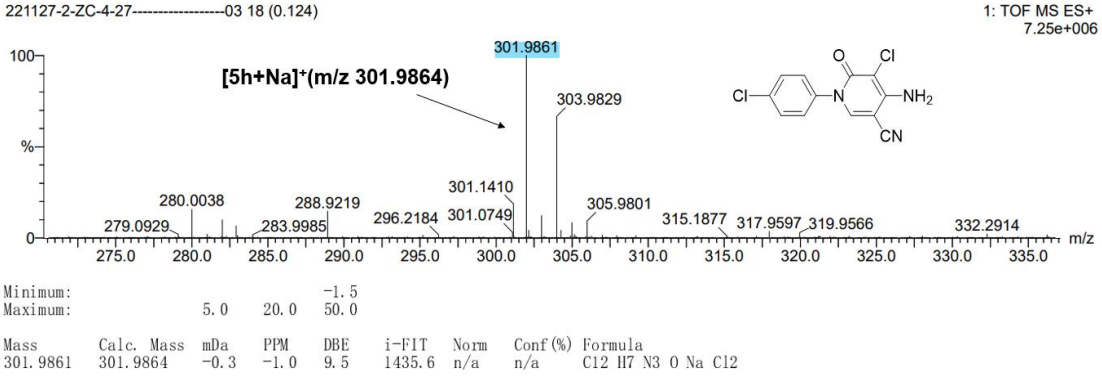
HRMS spectrum of **5e**



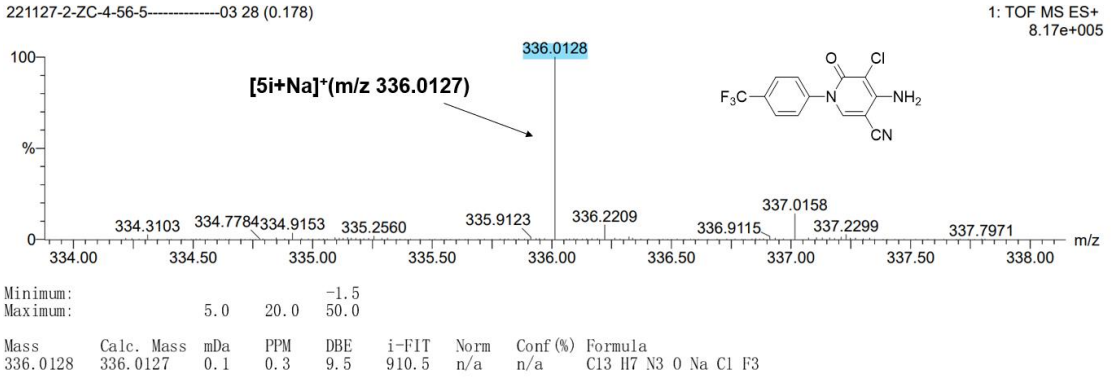
HRMS spectrum of **5f**



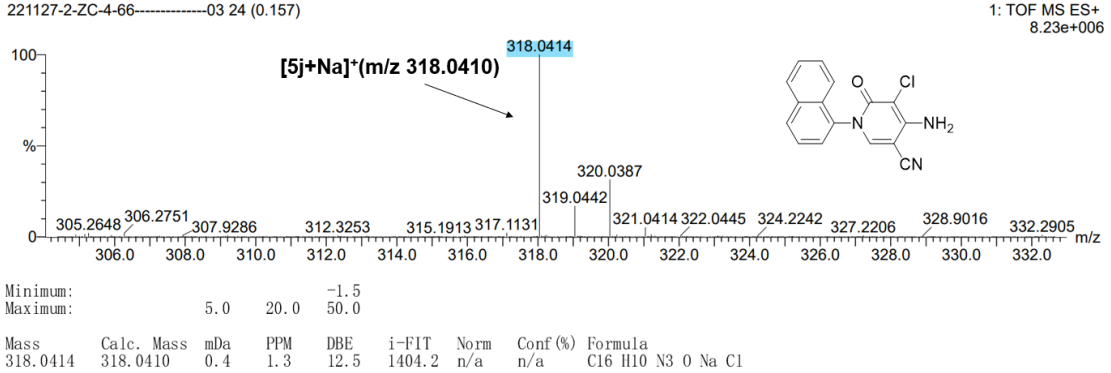
HRMS spectrum of **5g**



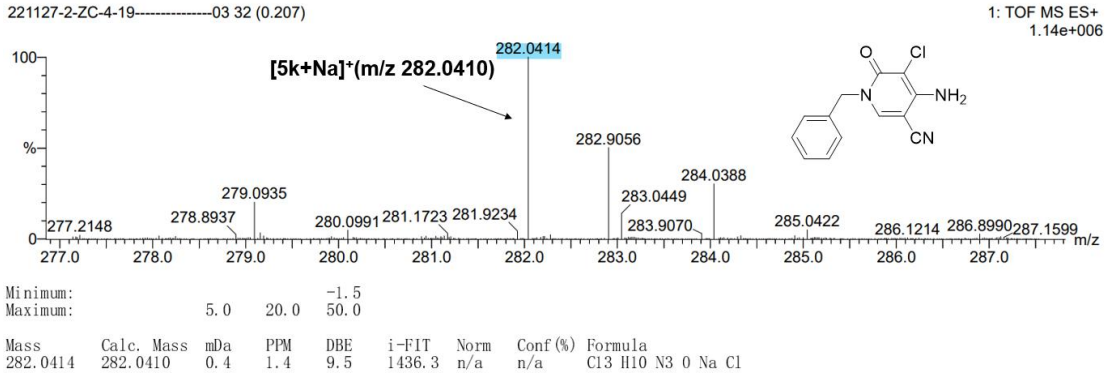
HRMS spectrum of **5h**



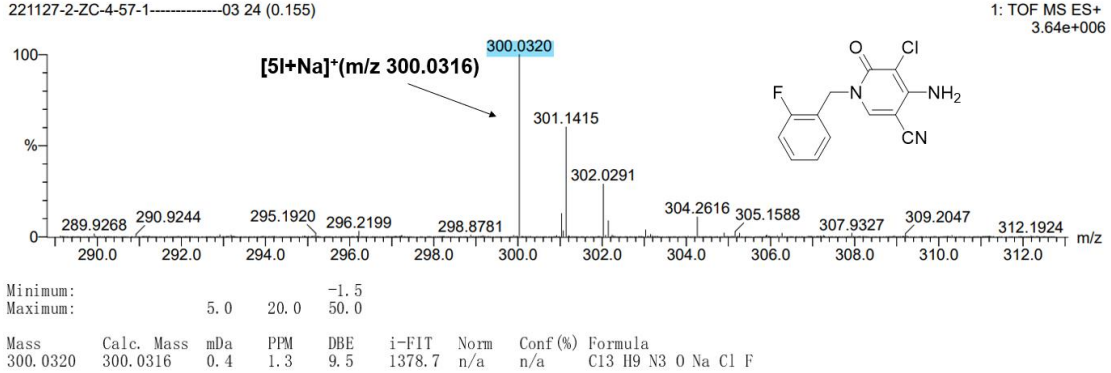
HRMS spectrum of **5i**



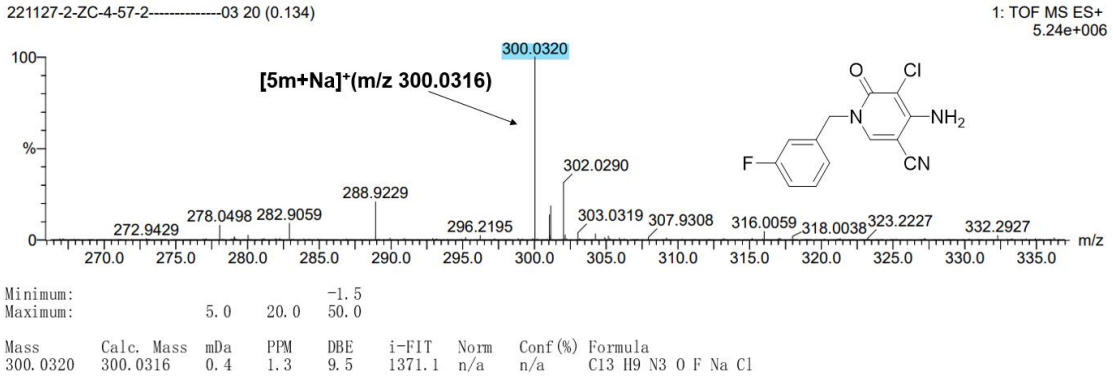
HRMS spectrum of **5j**



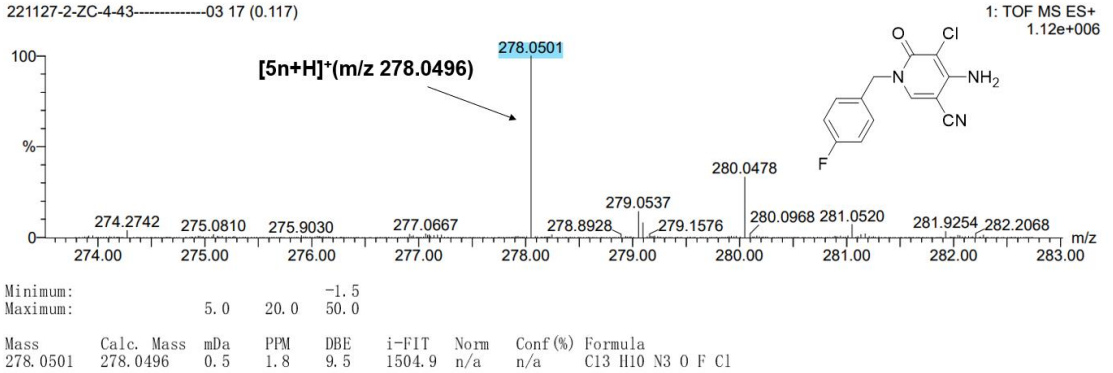
HRMS spectrum of **5k**



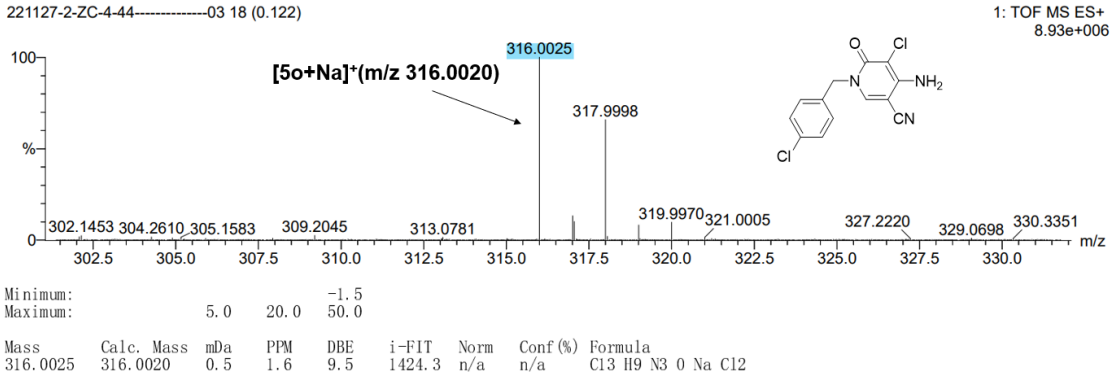
HRMS spectrum of **5l**



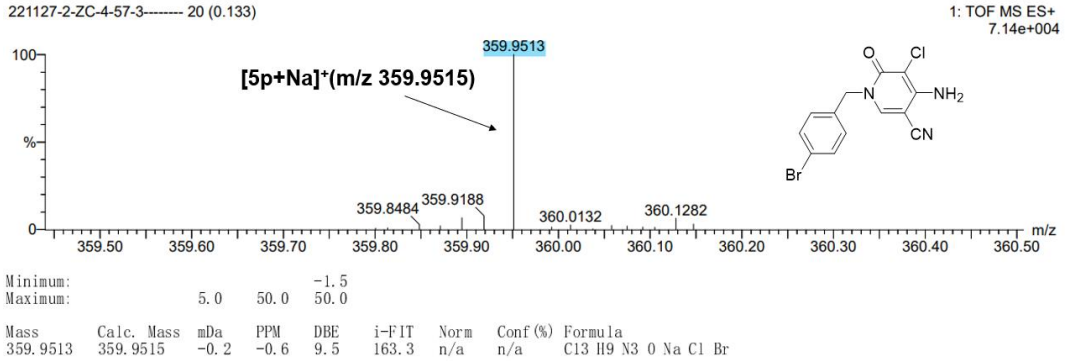
HRMS spectrum of **5m**



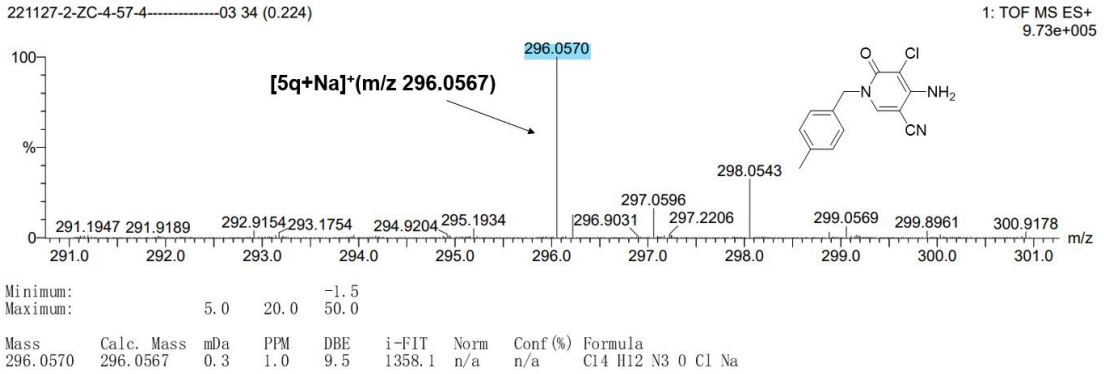
HRMS spectrum of **5n**



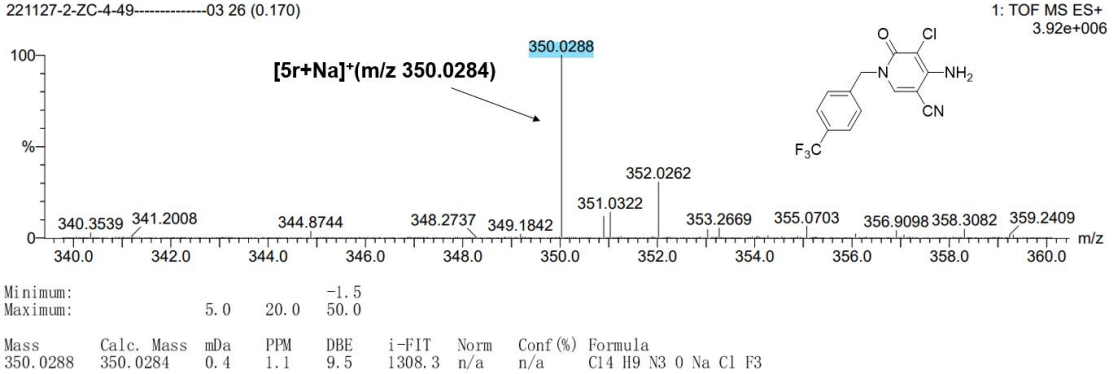
HRMS spectrum of **5o**



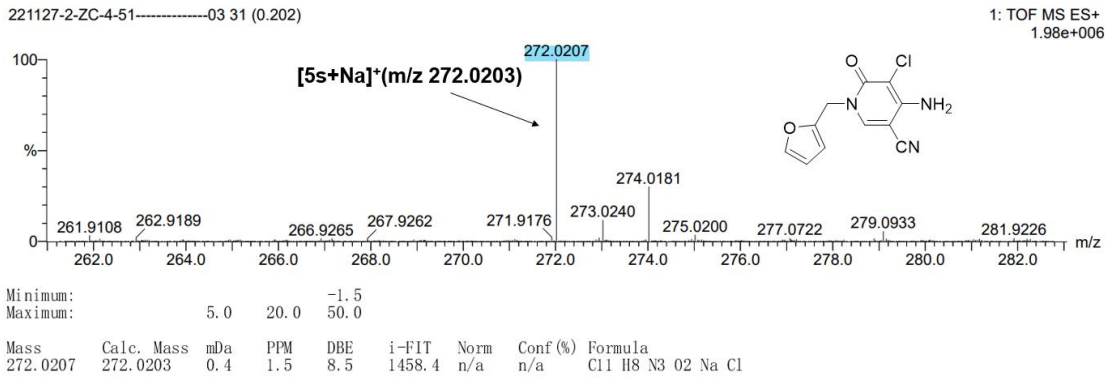
HRMS spectrum of **5p**



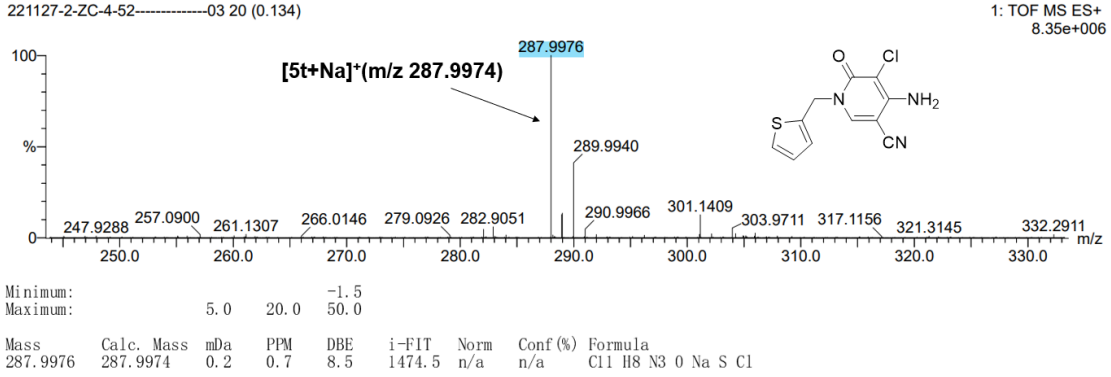
HRMS spectrum of **5q**



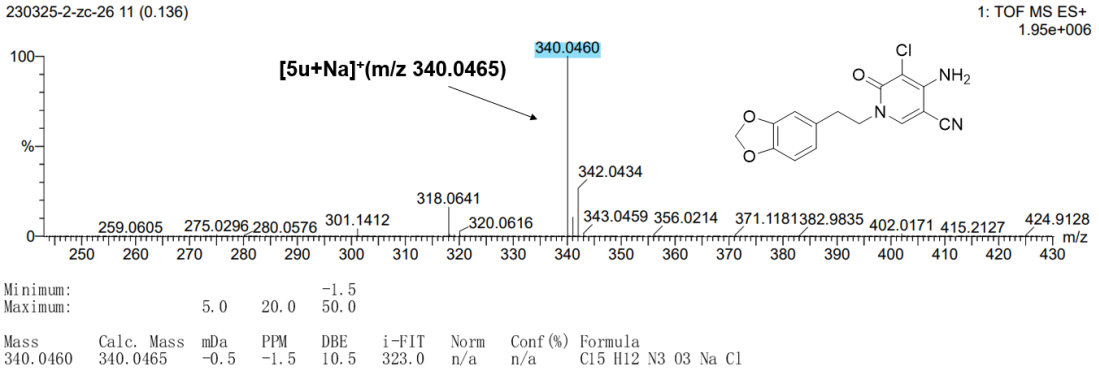
HRMS spectrum of **5r**



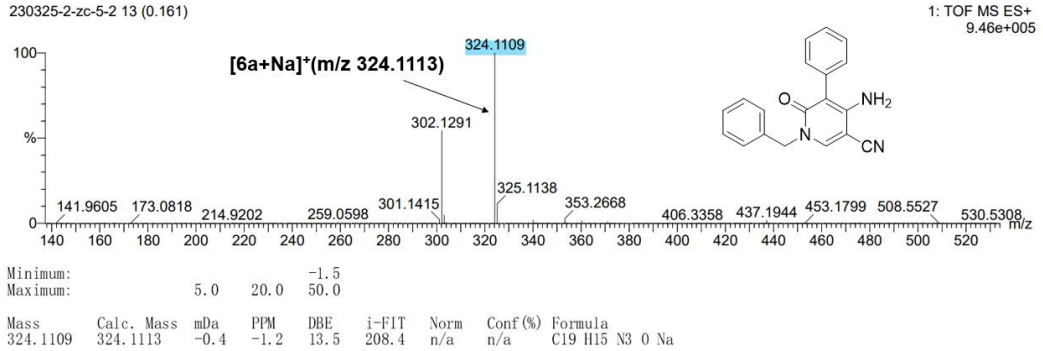
HRMS spectrum of **5s**



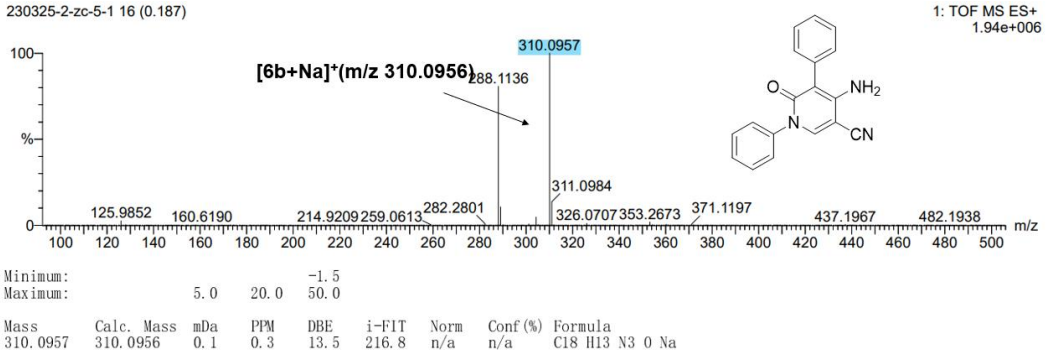
HRMS spectrum of **5t**



HRMS spectrum of **5u**

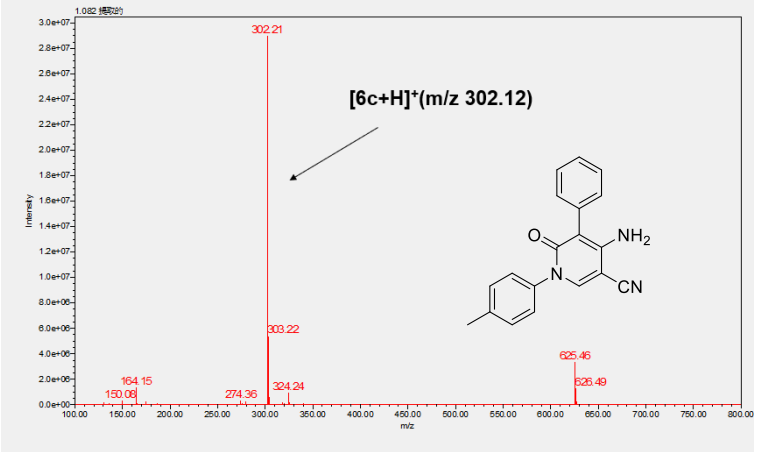


HRMS spectrum of **6a**

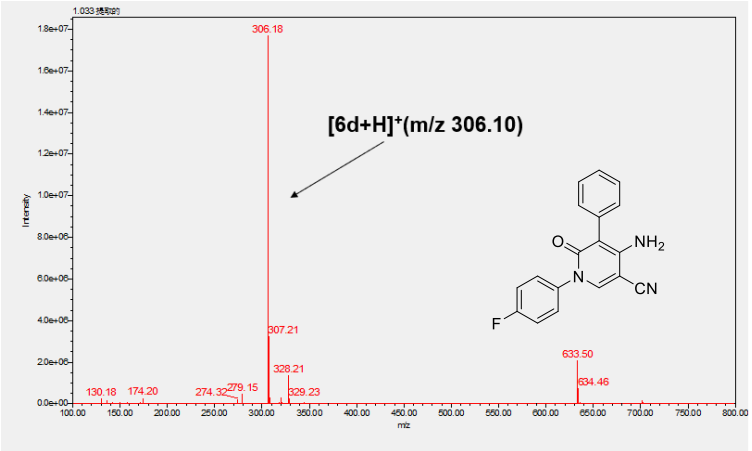


Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
310.0957	310.0956	0.1	0.3	13.5	216.8	n/a	n/a	C18 H13 N3 O Na

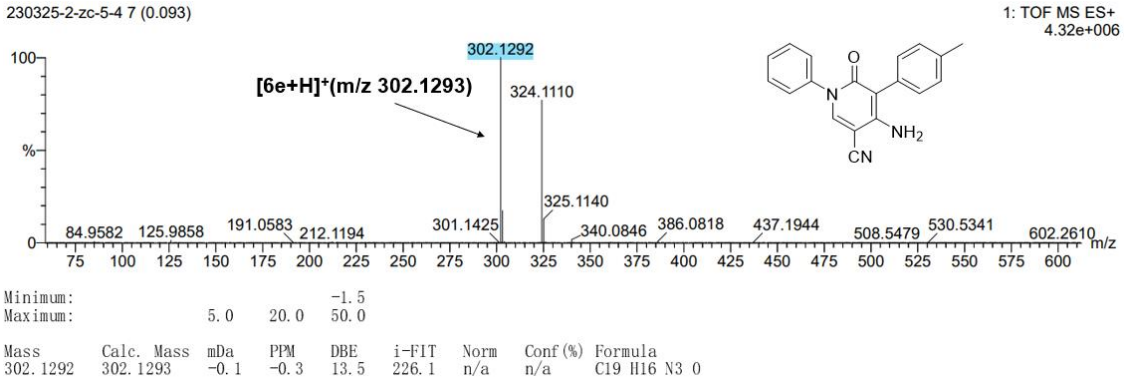
HRMS spectrum of **6b**



MS spectrum of **6c**

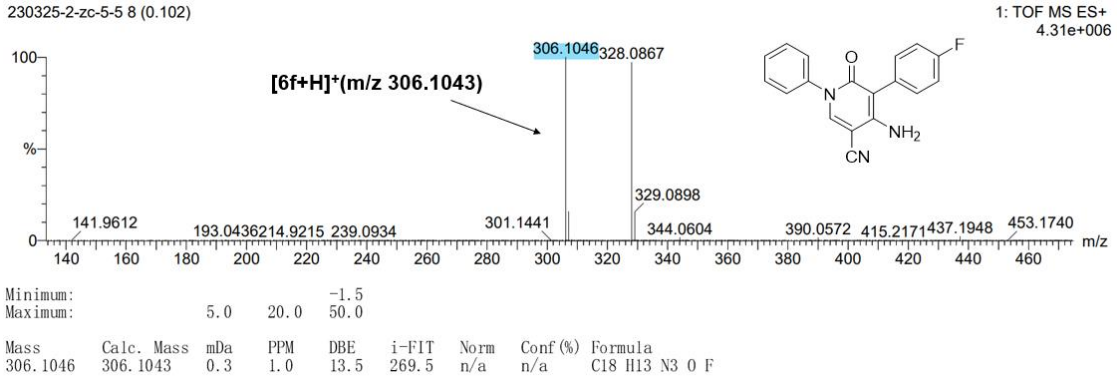


MS spectrum of **6d**



Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
302.1292	302.1293	-0.1	-0.3	13.5	226.1	n/a	n/a	C19 H16 N3 0

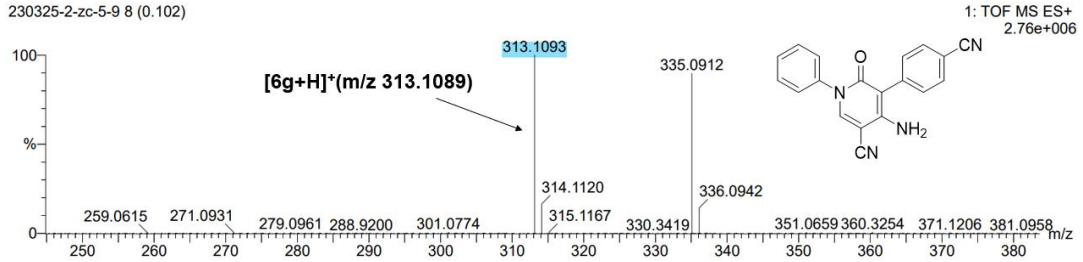
HRMS spectrum of **6e**



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
306.1046	306.1043	0.3	1.0	13.5	269.5	n/a	n/a	C18 H13 N3 O F

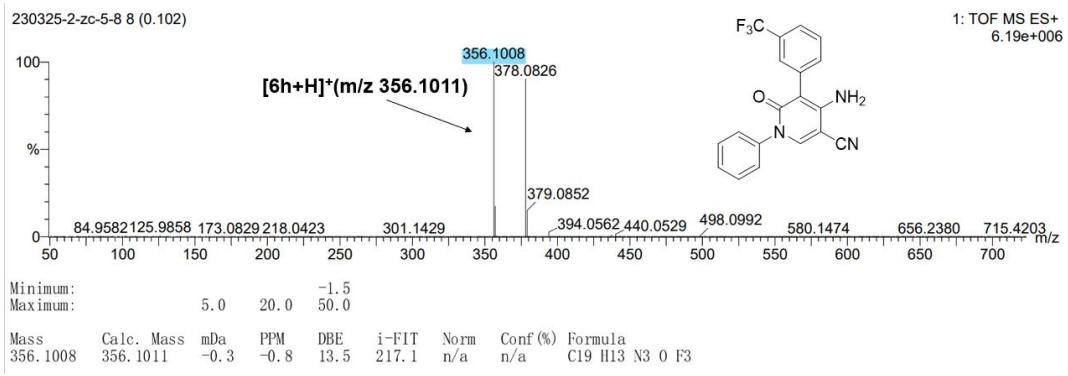
HRMS spectrum of **6f**



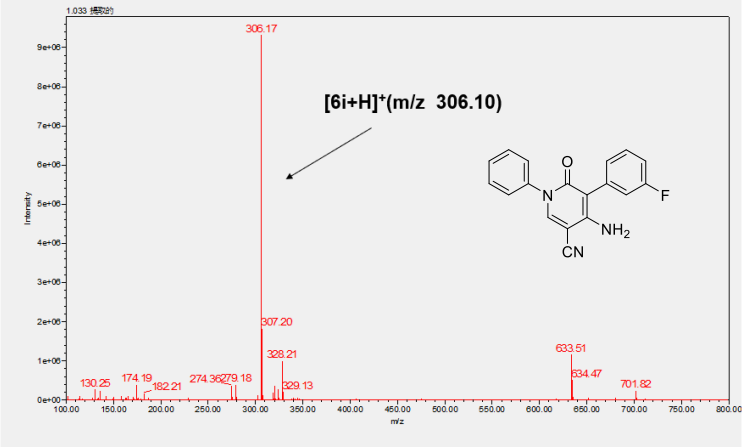
Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
313.1093	313.1089	0.4	1.3	15.5	204.8	n/a	n/a	C19 H13 N4 O

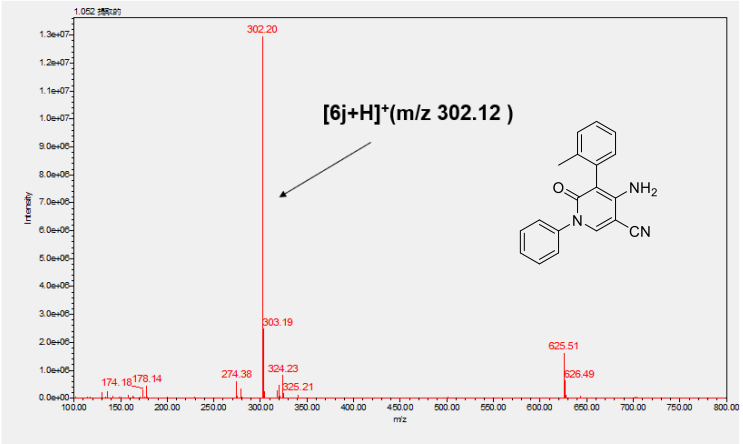
HRMS spectrum of **6g**



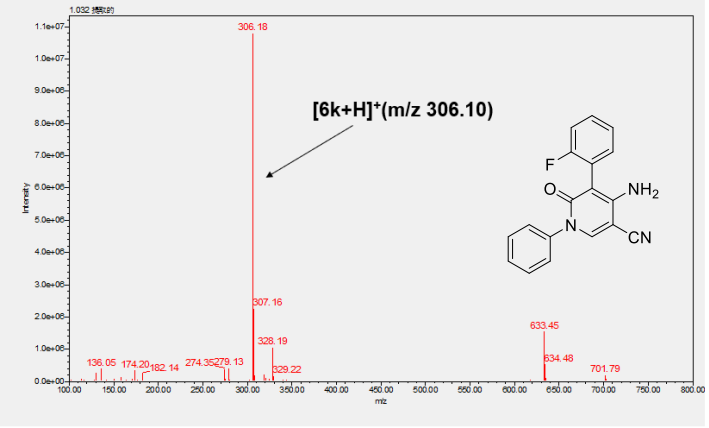
HRMS spectrum of **6h**



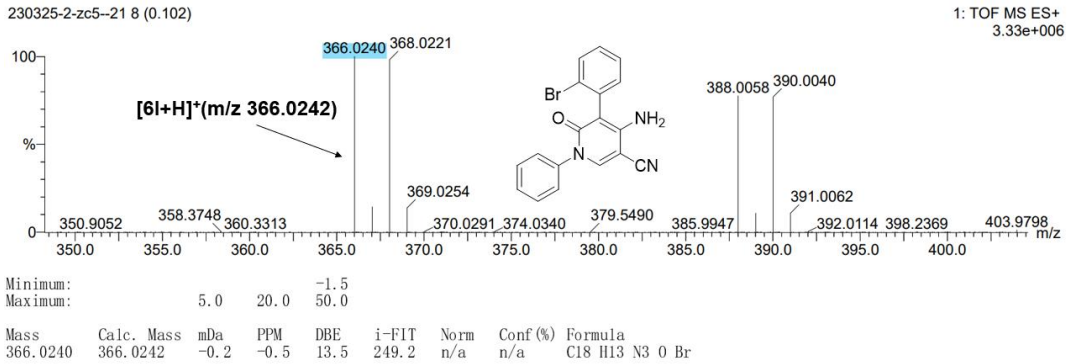
MS spectrum of **6i**



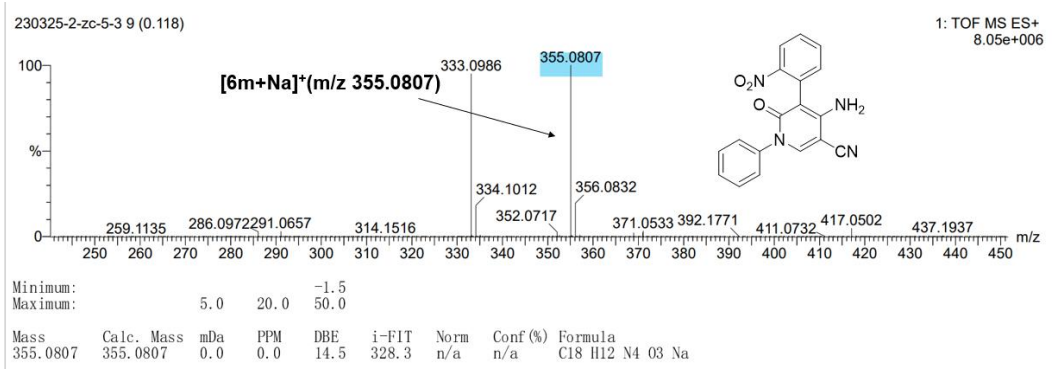
MS spectrum of **6j**



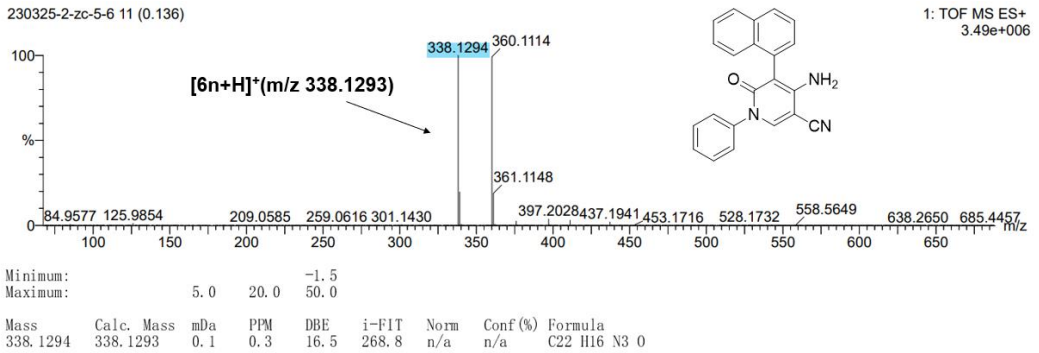
MS spectrum of **6k**



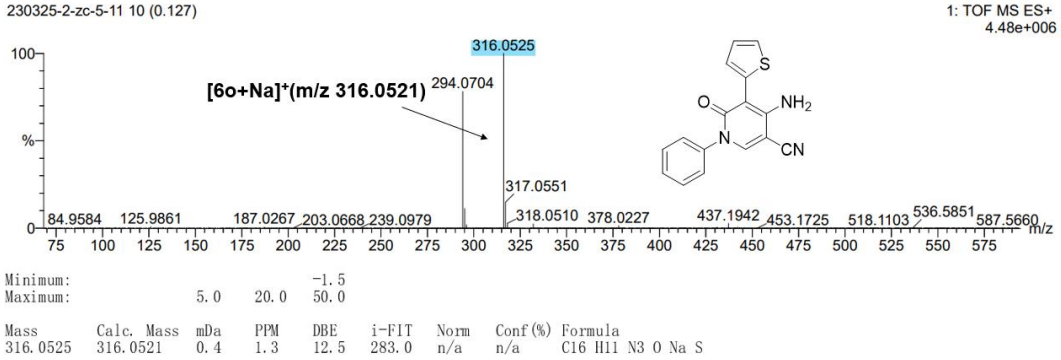
HRMS spectrum of **6l**



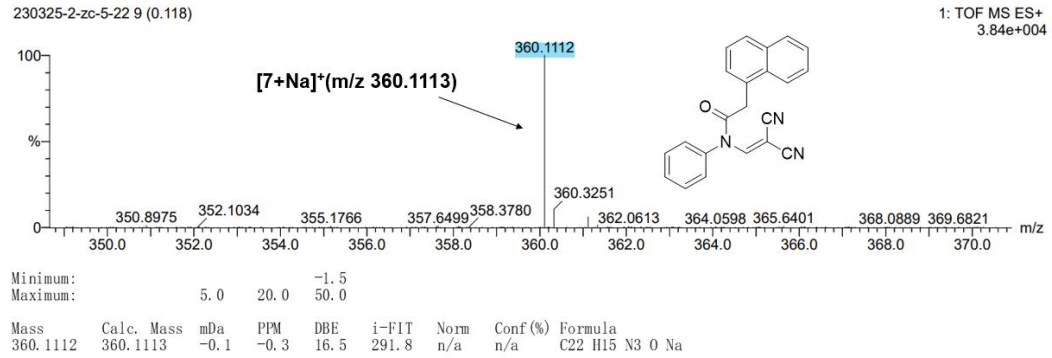
HRMS spectrum of **6m**



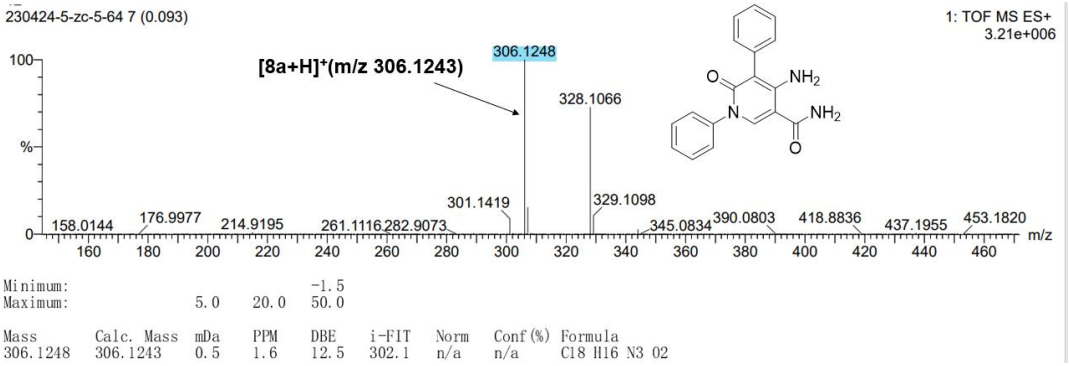
HRMS spectrum of **6n**



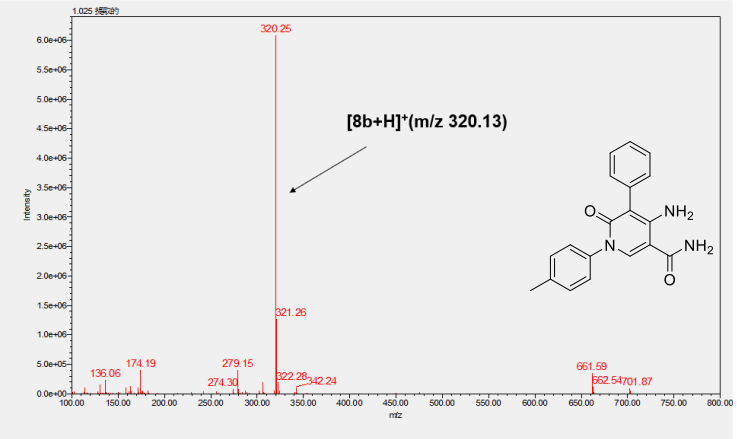
HRMS spectrum of **6o**



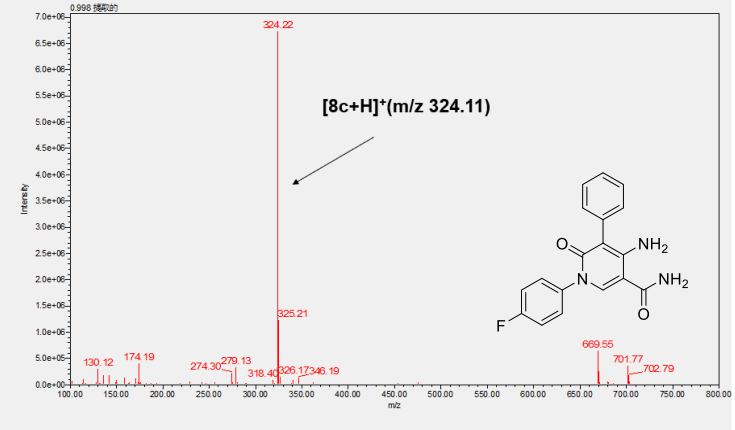
HRMS spectrum of **7**



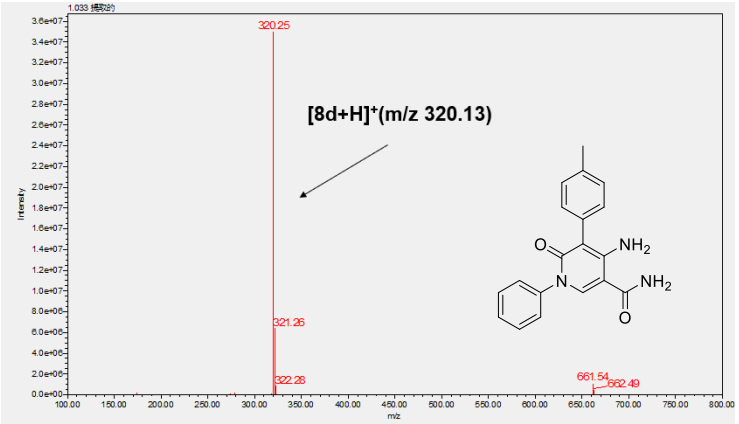
HRMS spectrum of **8a**



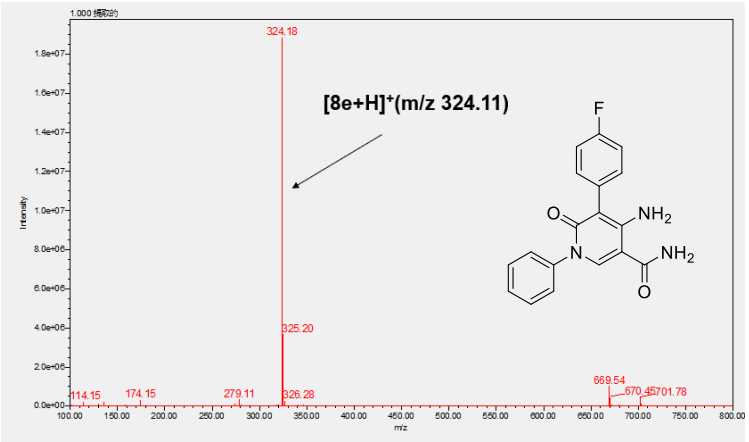
MS spectrum of **8b**



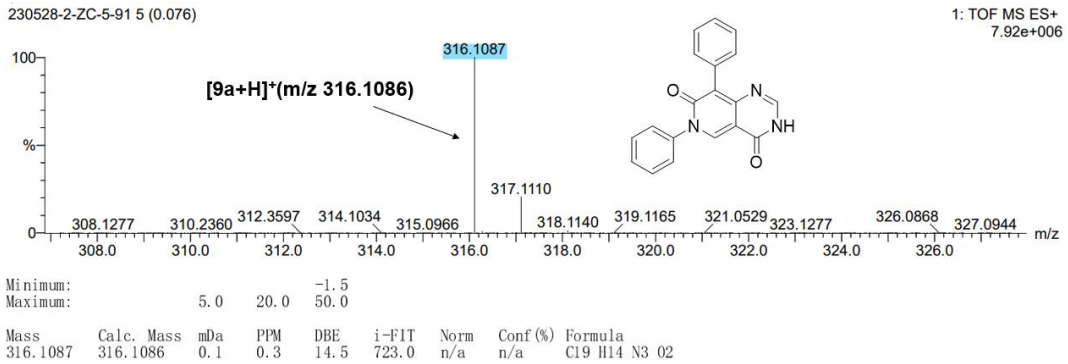
MS spectrum of **8c**



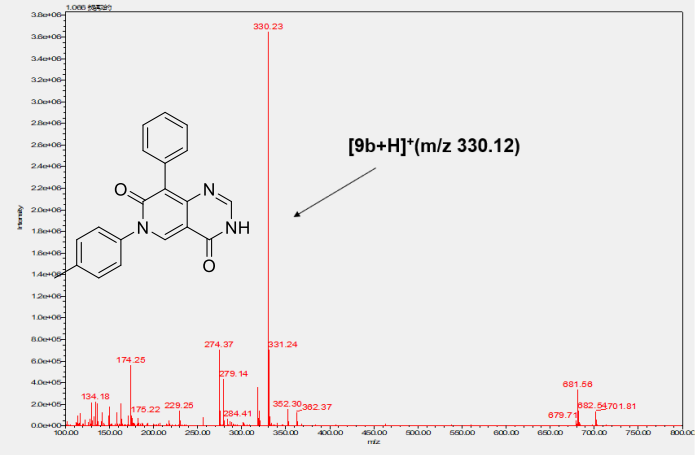
MS spectrum of **8d**



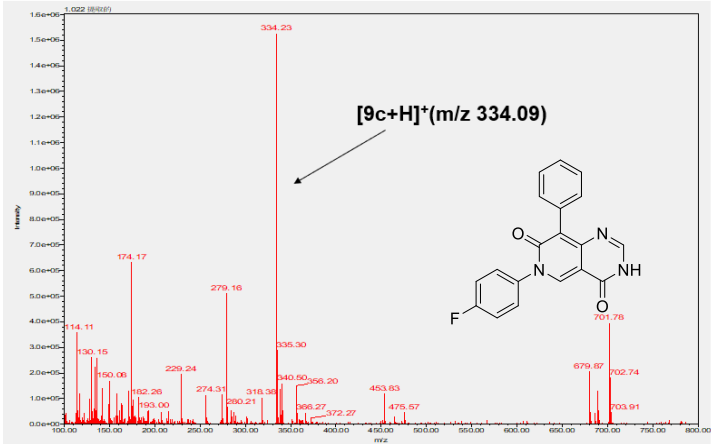
MS spectrum of **8e**



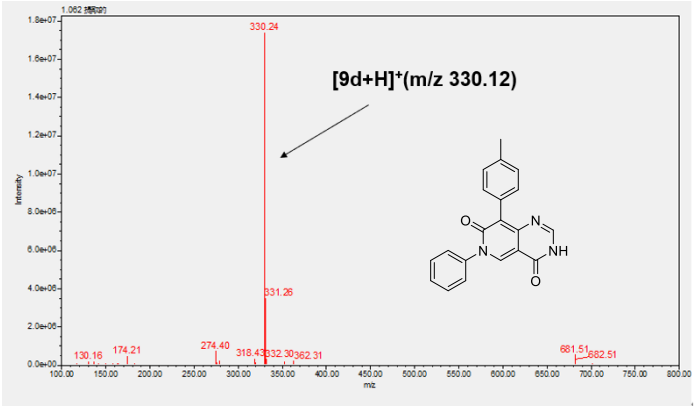
HRMS spectrum of **9a**



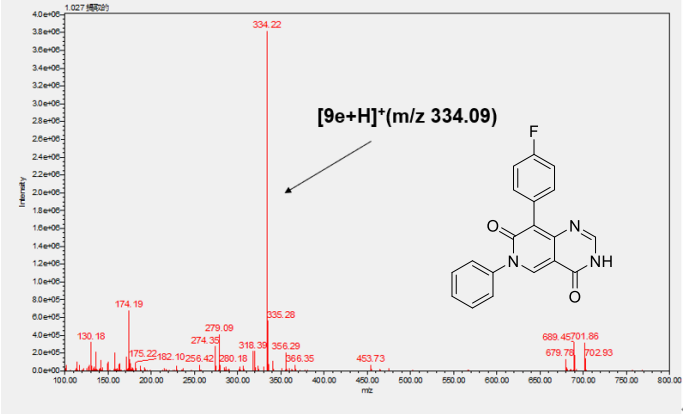
MS spectrum of **9b**



MS spectrum of **9c**

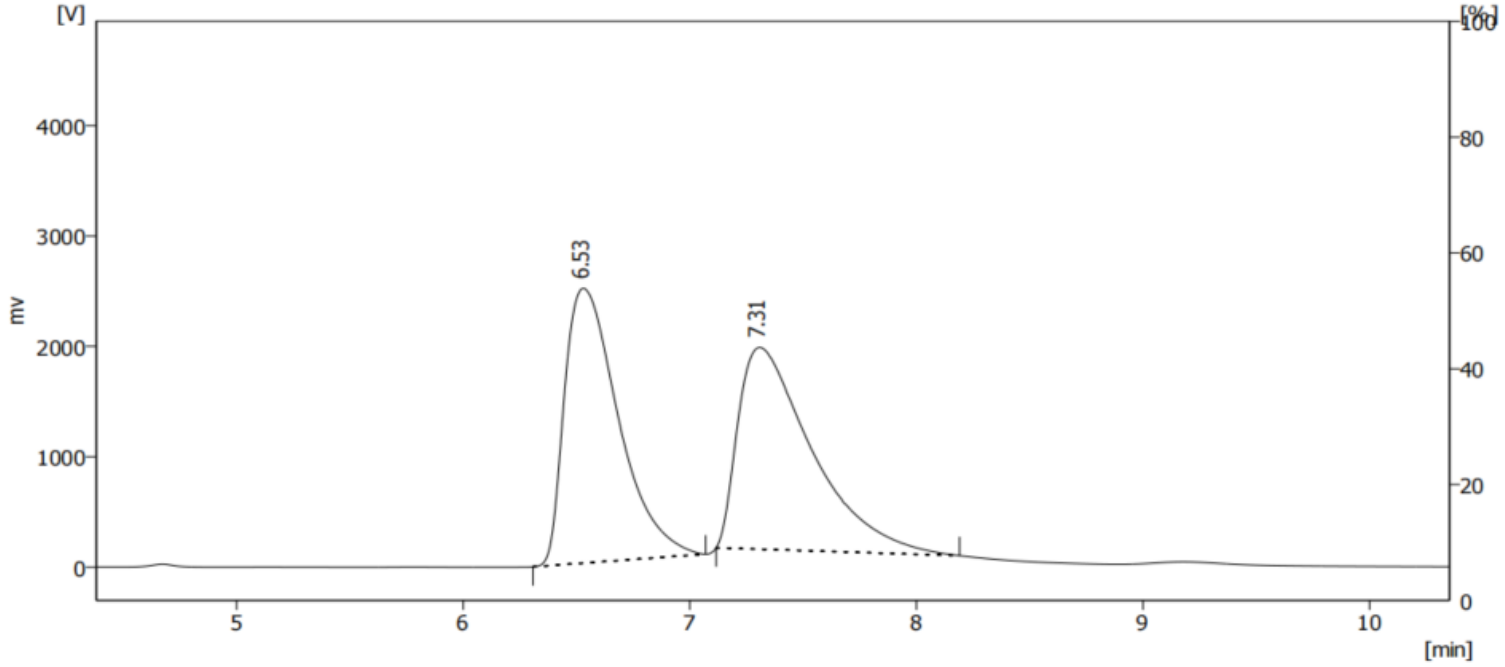


MS spectrum of **9d**



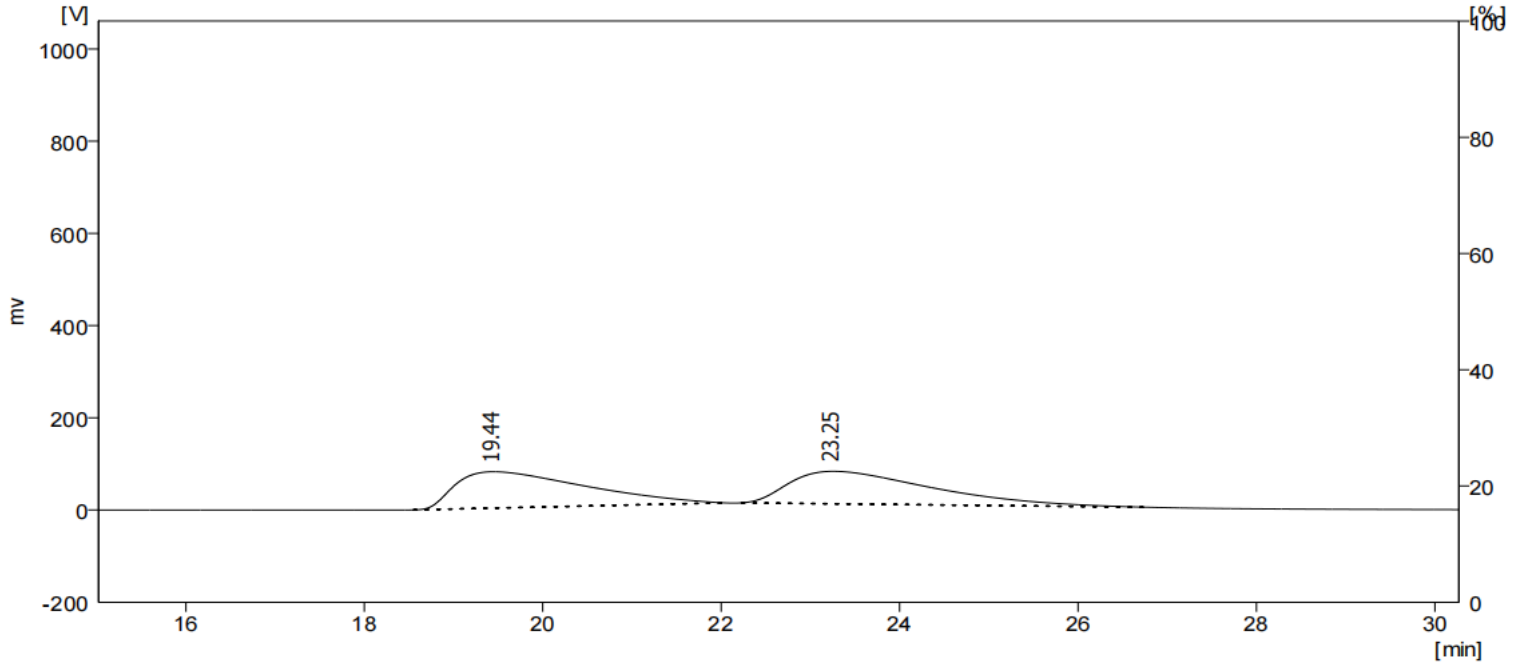
MS spectrum of **9e**

10. Copies of HPLC spectra



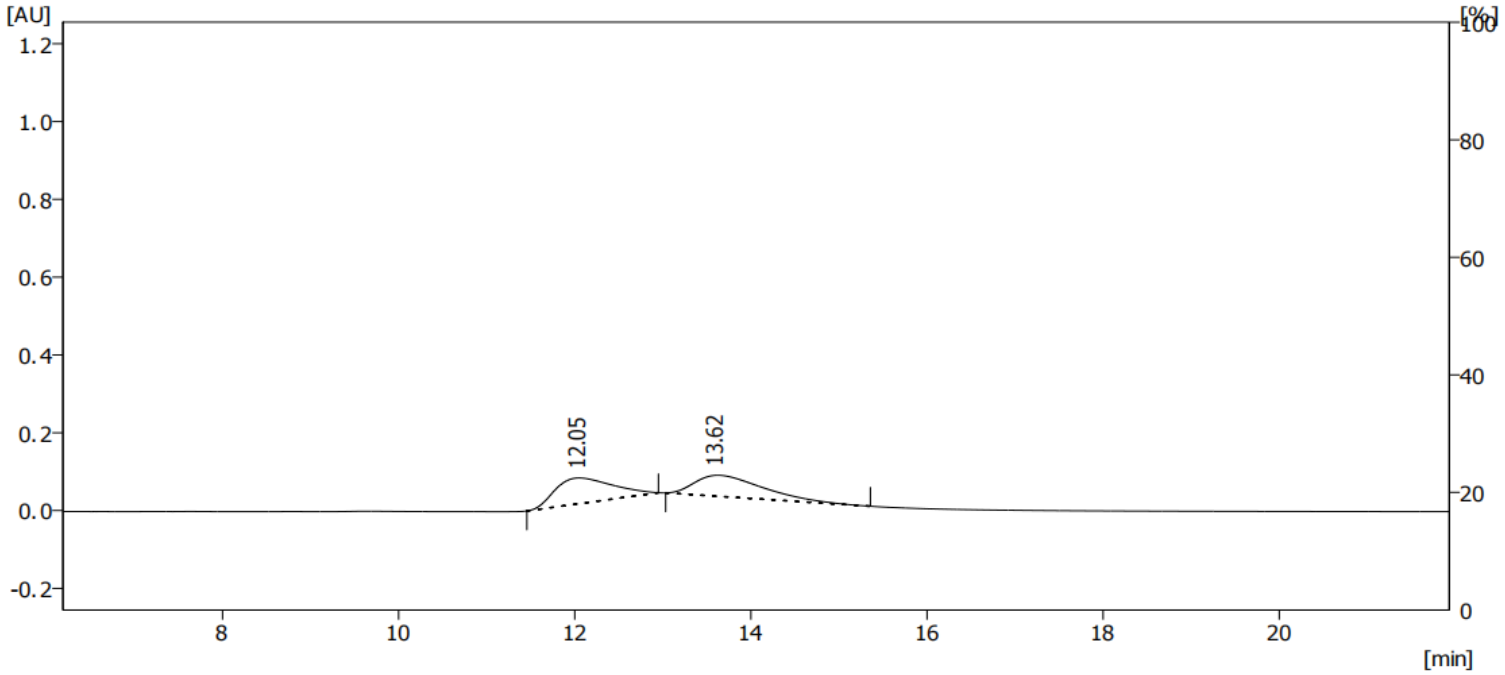
	Peak	Time	Area	Area%
1	1	6.53	49.81	49.8
2	2	7.31	50.19	50.2
	3	13.84	100.00	100.0

HPLC spectrum of compound **6j** (COSMOSIL CHiRAL 5A, i-PrOH/n-hexane = 3:7, 1 mL/min, 254 nm)



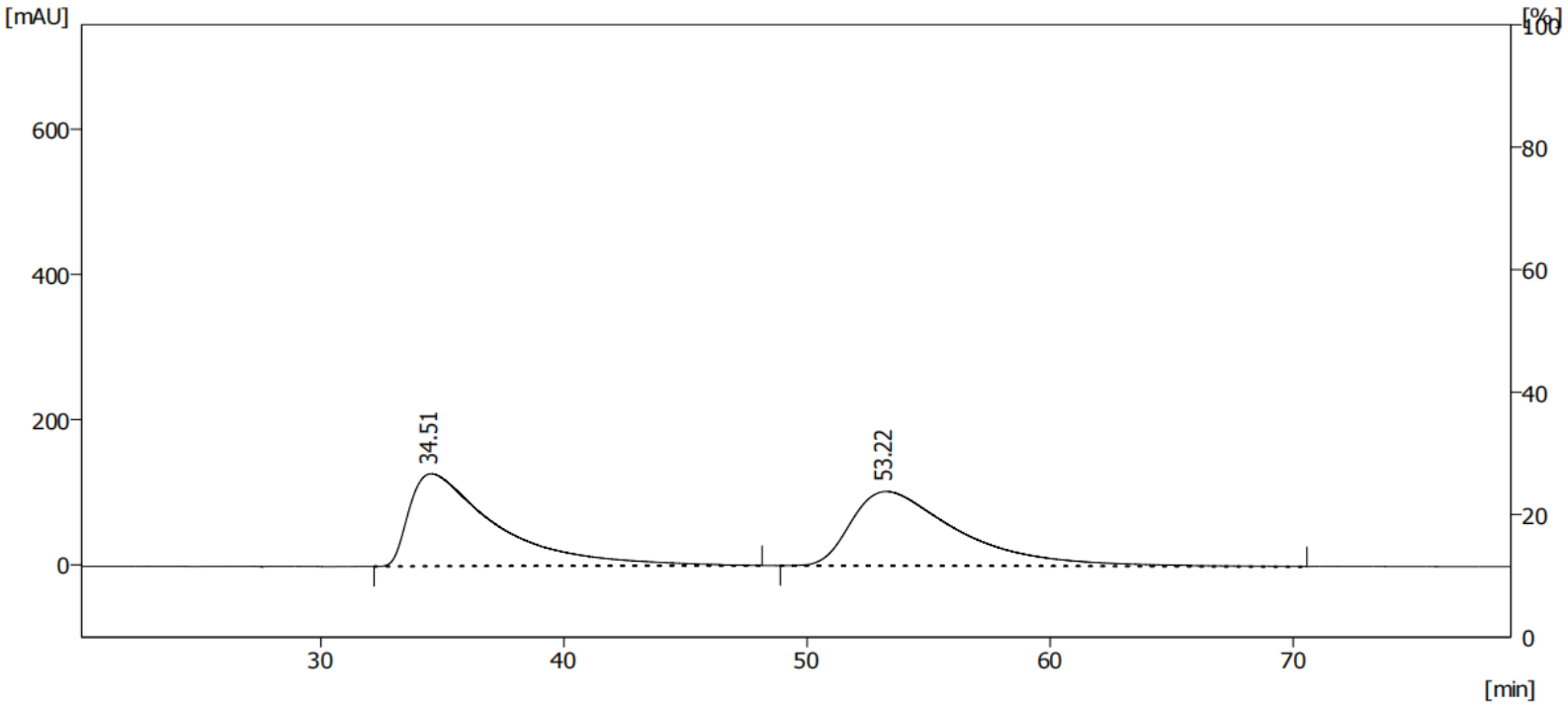
	Peak	Time	Area	Area%
1	1.000	19.44	7958.35	50.4
2	2.000	23.25	7840.49	49.6
	3.000	42.69	15798.84	100.0

HPLC spectrum of compound **6l** (CHIRALCEL OD-H, i-PrOH/n-hexane = 3:7, 1 mL/min, 254 nm)



	Peak	Time [min]	Area	Area%
1	1	12.05	2982.46	50.23
2	2	13.62	2955.25	49.77
	3	25.67	5937.72	100.00

HPLC spectrum of compound **6m** (COSMOSIL CHiRAL 5A, i-PrOH/n-hexane = 3:7, 1 mL/min, 254 nm)



	Peak	Time [min]	Area	Area%
1	1	34.54	31599.61	50.06
2	2	53.25	31528.07	49.94
	3	87.78	63127.68	100.00

HPLC spectrum of compound **6n** (COSMOSIL CHiRAL 5A, i-PrOH/n-hexane = 3:7, 1 mL/min, 254 nm)

11. References

[1] (a) X. Yang , Y. Ma , H. Di , X. Wang, H. Jin, D. H. Ryu and L. Zhang, *Adv. Synth. Catal.*, 2021, **363** , 3201; (b) L. Chen, H. Di, J. Liu, J. Zhang, B. Wang, H. Jin and L. Zhang, *Org. Biomol. Chem.,* 2023, **21**, 3705.

[2] S. M. Schmitt, K. Stefan, and M. Wiese, *J. Med. Chem.,* 2016, **59**, 3018.

[3] L. L. Corre, L. Tak-Tak, A. Guillard, G. Prestat, C. Gravier-Pelletier and P. Busca, *Org. Biomol. Chem.,* 2015, **13**, 409.

[4] G. W. Wang, C. B. Miao and H. Kang, *Bull. Chem. Soc. Jpn.*, 2006, **79**, 1426.