Multi-component solvent-free cascade reaction of 2-cyanoacetamides with ketones and acetone: highly regioselective synthesis of functionalized pyridin-2-ones bearing quaternary centers

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Supporting Information

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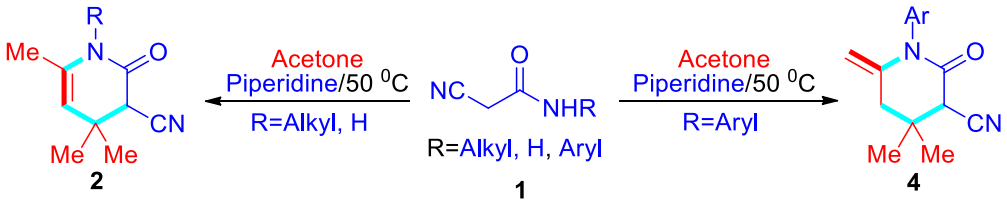
General Information

All compounds were fully characterised by spectroscopic data. The NMR spectra were recorded on a Bruker DRX500 & DRX600. Chemical shifts (δ) are expressed in ppm, *J* values are given in Hz, and deuterated $CDCl_3$ were used as solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on a XT-4A melting point apparatus and are uncorrected. HRMs were performed on an Agilent LC/Msd TOF instrument. Materials used were purchased from Adamas-beta Corporation Limited.

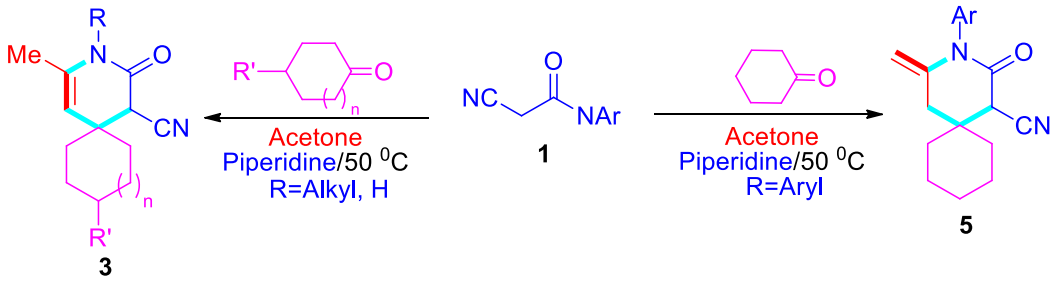
The materials were purchased from Adamas-beta Corporation Limited. All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (200–300 mesh). The 2-cyanoacetamide **1a**–**1c** were commercially available reagents, and 2-cyanoacetamide **1d**–**1g** were prepared according to the literature.[1]

General Procedure for the Preparation of 2 and 4



First, cyanoacetamide **1** (1.0 mmol) and acetone (5 ml) were charged into a round-bottom flask. Then, piperidine (0.5 mmol) was added to the mixture. The mixture was stirred at 50 ℃ for about 8 hours and monitored by TLC until the The intermediate was completely consumed.. The reaction mixture was poured into 20 mL of water and 10 mL of ethyl acetate for extraction and separation. The crude product was purified by column chromatography (petroleum ether/EtOAc =6:1), and a series of compounds **2** or **4** were obtained with 71–95% yield.

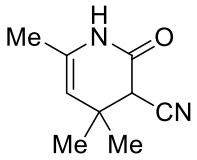
General Procedure for the Preparation of 3 and 5



First, cyanoacetamide **1** (1.0 mmol) and cyclic ketone (0.5 mL) were charged into a round-bottom flask. Then, piperidine (0.5 mmol) was added to the mixture. The mixture was stirred at 50 ℃ for about 2 hours. Next, acetone (1.0 mL) was charged into the reaction mixture. The mixture was continually stirred at 50 ℃ for 6 hours and monitored by TLC until the intermediate of the condensation reaction substrate was completely consumed. The reaction mixture was poured into 20 mL of water and 10 mL of ethyl acetate for extraction and separation. The crude product was purified by column chromatography (petroleum ether/EtOAc =10:1), and a series of compounds **3** or **5** were obtained with 68–90% yield.

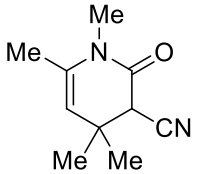
Spectroscopic Data of 2–6

4,4,6-Trimethyl-2-oxo-1,2,3,4-tetrahydropyridine-3-carbonitrile (2a)



White solid; Mp: 138.8–139.4 °C; IR (KBr): 3438, 2969, 1670, 1630, 1497, 1399, 1325, 1167, 1079, 762, 702, 664, 584, 527, 437 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 1.20 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.85 (s, 3H, CH_3), 3.46 (s, 1H, CH), 4.77 (s, 1H, CH), 8.42 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.6, 23.2, 27.6, 35.1, 47.5, 111.4, 115.0, 131.2, 164.0. HRMS (TOF ES^+): *m/z* calcd for $C_9H_{13}N_2O$ [$(M+H)^+$], 165.1022; found, 165.1025.

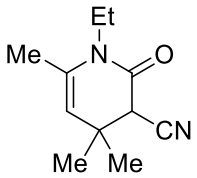
1,4,4,6-Tetramethyl-2-oxo-1,2,3,4-tetrahydropyridine-3-carbonitrile (2b)



White solid; Mp: 148.8–149.6 °C; IR (KBr): 3430, 1626, 1368, 1114, 760, 695,

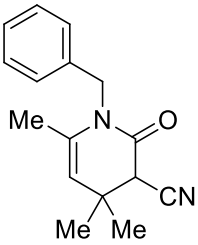
607, 564 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.15 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 3.15 (s, 3H, CH_3), 3.46 (s, 1H, CH), 4.92 (s, 1H, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 19.0, 23.0, 27.2, 29.5, 33.7, 48.1, 114.5, 115.3, 134.6, 162.5. HRMS (TOF ES^+): *m/z* calcd for $C_{10}H_{15}N_2O$ [$(M+H)^+$], 179.1179; found, 179.1180.

1-Ethyl-4,4,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyridine-3-carbonitrile (2c)



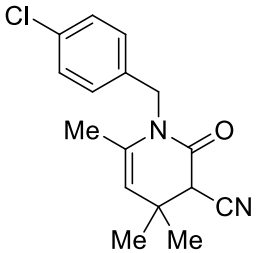
White solid; Mp: 83.7–84.5 °C; IR (KBr): 2974, 1668, 1625, 1390, 1262, 1119, 689, 610, 543 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 6.4 Hz, 6H, CH_3), 1.23 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 3.45 (s, 1H, CH), 3.52–3.86 (m, 2H, CH_2), 4.95 (s, 1H, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.6, 18.6, 22.8, 27.1, 33.7, 37.4, 48.2, 115.4, 115.8, 133.9, 162.0. HRMS (TOF ES^+): *m/z* calcd for $C_{11}H_{17}N_2O$ [$(M+H)^+$], 193.1335; found, 193.1334.

1-Benzyl-4,4,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyridine-3-carbonitrile (2d)



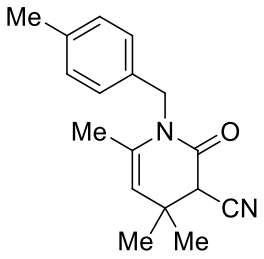
White solid; Mp: 117.1–117.6 °C; IR (KBr): 3442, 2966, 2883, 2837, 1676, 1623, 1498, 1445, 1384, 1238, 1118, 750, 705, 660, 612, 564, 441 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.16 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 3.55 (s, 1H, CH), 4.63–5.11 (m, 2H, CH_2), 4.92 (d, *J* = 1.0 Hz, 1H, CH), 7.21–7.33 (m, 5H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 19.1, 23.0, 27.4, 33.9, 45.8, 48.3, 115.4, 126.8, 127.0, 127.5, 128.8, 134.4, 137.3, 163.0. HRMS (TOF ES^+): *m/z* calcd for $C_{16}H_{19}N_2O$ [$(M+H)^+$], 255.1492; found, 255.1496.

1-(4-Chlorobenzyl)-4,4,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyridine-3-carbonitrile (2e)



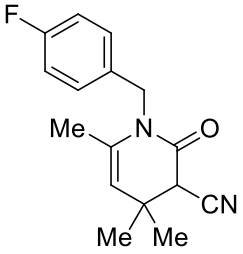
White solid; Mp: 114.5–115.0 °C; IR (KBr): 3440, 2967, 1672, 1629, 1492, 1392, 1237, 1100, 1016, 832, 787, 714, 669, 605, 566, 516 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.15 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 3.55 (s, 1H, CH), 4.59–5.06 (m, 2H, CH_2), 4.92 (s, 1H, CH), 7.17 (d, J = 8.3 Hz, 2H, ArH), 7.29 (d, J = 6.4 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 19.1, 23.0, 27.3, 33.9, 45.2, 48.2, 115.2, 115.7, 128.3, 128.5, 128.9, 129.0, 133.4, 134.0, 135.8, 163.0. HRMS (TOF ES^+): *m/z* calcd for $C_{16}H_{18}ClN_2O$ [$(M+H)^+$], 289.1102; found, 289.1100.

4,4,6-Trimethyl-1-(4-methylbenzyl)-2-oxo-1,2,3,4-tetrahydropyridine-3-carbonitrile (2f)



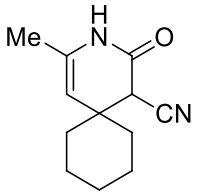
White solid; Mp: 100.7–101.3 °C; IR (KBr): 3443, 2966, 1668, 1627, 1388, 1234, 1116, 789, 673, 596, 539, 443 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.15 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.54 (s, 1H, CH), 4.58–5.08 (m, 2H, CH_2), 4.90 (s, 1H, CH), 7.17 (d, J = 8.3 Hz, 2H, ArH), 7.29 (d, J = 6.4 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 19.1, 21.1, 23.0, 27.4, 33.9, 45.6, 48.3, 115.3, 126.8, 127.0, 129.4, 134.3, 134.4, 137.2, 162.9. HRMS (TOF ES^+): *m/z* calcd for $C_{17}H_{21}N_2O$ [$(M+H)^+$], 269.1648; found, 269.1651.

1-(4-Fluorobenzyl)-4,4,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyridine-3-carbonitrile (2g)



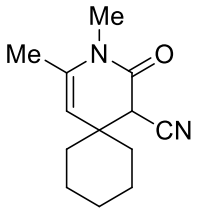
White solid; Mp: 88.9–89.3 °C; IR (KBr): 3432, 2972, 1683, 1619, 1512, 1435, 1388, 1227, 1152, 1101, 842, 808, 675, 611, 545, 485 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.13 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.92 (s, 3H, CH_3), 3.55 (s, 1H, CH), 4.59–5.07(m, 2H, CH_2), 4.94 (s, 1H, CH), 6.99–7.28 (m, 4H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 19.0, 23.0, 27.3, 33.9, 45.2, 48.2, 115.2, 115.7 (t, J = 10.5 Hz), 115.2, 128.9 (d, J = 9.0 Hz), 133.1, 134.1, 161.3, 162.9. HRMS (TOF ES^+): *m/z* calcd for $C_{16}H_{18}FN_2O$ [$(M+H)^+$], 273.1398; found, 273.1395.

4-Methyl-2-oxo-3-azaspiro[5.5]undec-4-ene-1-carbonitrile (3a)



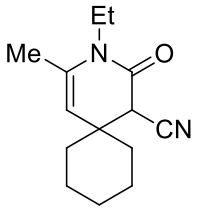
White solid; Mp: 87.4–88.3 °C; IR (KBr): 3434, 2974, 1664, 1625, 1374, 1196, 1118, 770, 670, 610, 441 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.18–1.34 (m, 2H, CH_2), 1.43–1.67 (m, 8H, CH_2), 1.82 (d, J = 9.0 Hz, 3H, CH_3), 3.35 (s, 1H, CH), 4.97 (s, 1H, CH), 8.23 (s, 1H, NH); ^{13}C NMR (150 MHz, $CDCl_3$): δ =19.2, 21.5, 21.8, 25.2, 29.4, 32.1, 34.3, 36.4, 48.5, 111.3, 115.4, 134.8, 162.5 HRMS (TOF ES^+): *m/z* calcd for $C_{12}H_{17}N_2O$ [$(M+H)^+$], 205.1335; found, 205.1331.

3,4-Dimethyl-2-oxo-3-azaspiro[5.5]undec-4-ene-1-carbonitrile (3b)



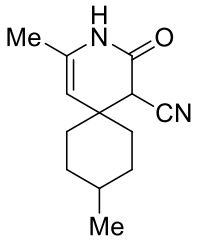
White solid; Mp: 100.9–101.4 °C; IR (KBr): 3422, 2923, 1618, 1384, 1331, 1115, 784, 654, 615 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.14–1.35 (m, 2H, CH_2), 1.39–1.45 (m, 4H, CH_2), 1.51–1.57 (m, 4H, CH_2), 1.92 (s, 3H, CH_3), 3.07 (s, 3H, CH_3), 3.38 (s, 1H, CH), 5.09 (s, 1H, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ =19.2, 21.5, 21.8, 25.2, 29.4, 32.1, 34.3, 36.4, 47.8, 111.3, 115.4, 134.8, 162.5. HRMS (TOF ES^+): *m/z* calcd for $C_{13}H_{19}N_2O$ [$(M+H)^+$], 219.1492; found, 219.1490.

3-Ethyl-4-methyl-2-oxo-3-azaspiro[5.5]undec-4-ene-1-carbonitrile (3c)



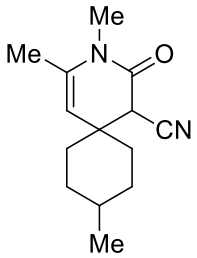
White solid; Mp: 99.7–100.3 °C; IR (KBr): 3435, 2934, 2855, 1675, 1622, 1451, 1392, 1260, 1119, 770, 677, 605, 554 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.13 (t, J =7.1 Hz, 3H, CH_3), 1.25–1.42 (m, 2H, CH_2), 1.47–1.52 (m, 4H, CH_2), 1.58–1.72 (m, 4H, CH_2), 1.98 (s, 3H, CH_3), 3.42 (s, 3H, CH_3), 3.60–3.76 (m, 2H, CH_2), 5.16 (s, 1H, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ =13.6, 18.9, 21.6, 21.8, 25.2, 32.3, 34.3, 36.5, 37.4, 47.8, 112.7, 115.4, 134.1, 162.0. HRMS (TOF ES^+): *m/z* calcd for $C_{14}H_{21}N_2O$ [$(M+H)^+$], 233.1648; found, 233.1649.

4,9-Dimethyl-2-oxo-3-azaspiro[5.5]undec-4-ene-1-carbonitrile (3d)



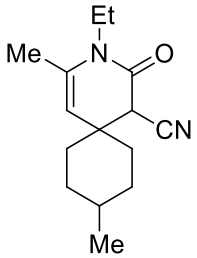
White solid; Mp: 107.7–108.1 °C; IR (KBr): 3429, 3229, 3170, 3113, 2931, 2867, 1708, 1684, 1620, 1452, 1376, 1119, 829, 679, 504 cm^{-1}; ^1H NMR (600 MHz, $CDCl_{36}$): δ = 0.94 (d, J = 1.8 Hz, 3H, CH_3), 0.95–1.17 (m, 2H, CH_2), 1.34–1.50 (m, 2H, CH_2), 1.56–1.72 (m, 4H, CH_2), 1.88 (s, 3H, CH_3), 2.00–2.02 (m, 1H, CH), 3.61 (s, 1H, CH), 4.78 (s, 1H, CH), 8.50 (s, 1H, NH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 18.7, 20.7, 28.8, 29.0, 30.2, 31.0, 32.3, 37.5, 42.1, 110.4, 115.3, 131.6, 163.8. HRMS (TOF ES^+): *m/z* calcd for $C_{13}H_{19}ClN_2O$ [$(M+H)^+$], 219.1492; found, 219.1490.

3,4,9-Trimethyl-2-oxo-3-azaspiro[5.5]undec-4-ene-1-carbonitrile (3e)



White solid; Mp: 109.3–109.9 °C; IR (KBr): 3436, 2935, 1669, 1624, 1441, 1371, 1111, 778, 657, 607, 557 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 0.93 (q, J =3.2 Hz, 3H, CH_3), 1.08–1.14 (m, 2H, CH_2), 1.31–1.45 (m, 2H, CH_2), 1.58–1.72 (m, 4H, CH_2), 1.99 (s, 4H, CH_3, CH), 3.13 (s, 3H, CH_3), 3.68 (s, 1H, CH), 4.90 (s, 1H, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 19.1, 20.9, 28.0, 29.1, 29.5, 30.3, 31.0, 32.5, 36.1, 42.4, 113.9, 115.6, 135.0, 162.2. HRMS (TOF ES^+): *m/z* calcd for $C_{14}H_{21}N_2O$ [$(M+H)^+$], 233.1648; found, 233.1650.

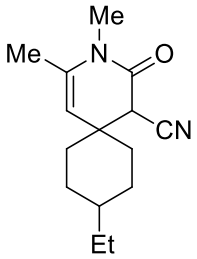
3-Ethyl-4,9-dimethyl-2-oxo-3-azaspiro[5.5]undec-4-ene-1-carbonitrile (3f)



White solid; Mp: 110.0–110.5 °C; IR (KBr): 3437, 2936, 2893, 1675, 1624, 1459, 1391, 1265, 1215, 1119, 780, 664, 604 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 0.93 (d, J =6.7 Hz, 3H, CH_3), 1.08–1.15 (m, 5H, CH_2, CH_3), 1.31–1.44 (m, 2H, CH_2), 1.57–1.65 (m, 4H, CH_2), 1.99 (s, 3H, CH_3), 2.00(s, 1H, CH), 3.50 (q, J =

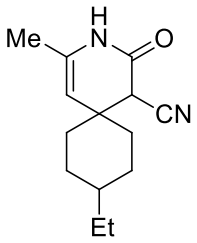
7.0 Hz, 1H, CH_2), 3.65 (s, 1H, CH), 3.84 (q, J = 7.1 Hz, 1H, CH_2), 4.92 (s, 1H, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.4, 18.7, 20.9, 28.8, 29.1, 29.7, 30.6, 30.9, 32.6, 36.2, 37.3, 42.5, 115.0, 115.7, 134.2, 161.7. HRMS (TOF ES^+): *m/z* calcd for $C_{15}H_{23}N_2O$ [$(M+H)^+$], 247.1805; found, 247.1803.

9-Ethyl-3,4-dimethyl-2-oxo-3-azaspiro[5.5]undec-4-ene-1-carbonitrile (3g)



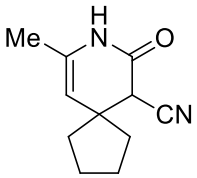
White solid; Mp: 131.7–132.0 °C; IR (KBr): 3422, 3231, 2923, 2899, 1618, 1384, 1331, 1115, 615 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 0.89 (t, J =7.4 Hz, 3H, CH_3), 1.00–1.27 (m, 4H, CH_2), 1.43–1.58 (m, 6H, CH_2), 1.66–1.72 (m, 1H, CH), 1.98 (s, 3H, CH_3), 3.14 (s, 3H, CH_3), 3.39 (s, 1H, CH), 5.17 (s, 1H, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ =11.4, 19.3, 28.0, 28.2, 29.5, 31.9, 34.7, 36.5, 38.4, 48.4, 111.0, 115.3, 134.8, 162.6. HRMS (TOF ES^+): *m/z* calcd for $C_{15}H_{23}N_2O$ [$(M+H)^+$], 247.1805; found, 247.1803.

9-Ethyl-4-methyl-2-oxo-3-azaspiro[5.5]undec-4-ene-1-carbonitrile (3h)



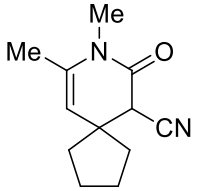
White solid; Mp: 148.8–149.3 °C; IR (KBr): 3431, 3236, 3121, 2934, 2865, 1688, 1624, 1450, 1373, 1123, 816, 549, 509 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 0.88 (t, J =6.7 Hz, 3H, CH_3), 1.12–1.19 (m, 2H, CH_2), 1.29–1.37 (m, 4H, CH_2), 1.44–1.49 (m, 1H, CH), 1.66–1.72 (m, 3H, CH_2), 1.88 (s, 3H, CH_3), 2.00–2.02 (m, 1H, CH_2), 3.61 (s, 1H, CH), 4.79 (s, 1H, CH), 8.43 (s, 1H, NH); ^{13}C NMR (150 MHz, $CDCl_3$): δ =11.6, 18.7, 26.5, 26.7, 27.7, 31.1, 32.4, 37.1, 37.8, 42.1, 110.5, 115.3, 131.5, 163.8. HRMS (TOF ES^+): *m/z* calcd for $C_{14}H_{21}N_2O$ [$(M+H)^+$], 233.1648; found, 233.1649.

9-Methyl-7-oxo-8-azaspiro[4.5]dec-9-ene-6-carbonitrile (3i)



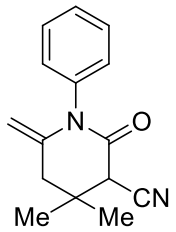
White solid; Mp: 165.2–165.8 °C; IR (KBr): 3281, 2960, 2870, 1672, 1447, 1385, 1264, 1114, 786, 611 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.63–1.74 (m, 8H, CH_2), 1.81 (s, 3H, CH_3), 3.50 (s, 1H, CH), 4.82 (s, 1H,CH), 8.38 (s, 1H,NH); ^{13}C NMR (150 MHz, $CDCl_3$): δ =18.6, 23.9, 24.2, 36.0, 37.3, 44.8, 45.2, 111.5, 115.6, 131.1, 164.1. HRMS (TOF ES^+): *m/z* calcd for $C_{11}H_{15}N_2O$ [$(M+H)^+$], 191.1179; found, 191.1183.

8,9-Dimethyl-7-oxo-8-azaspiro[4.5]dec-9-ene-6-carbonitrile (3j)



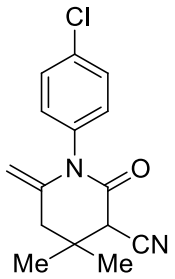
White solid; Mp: 144.2–144.9 °C; IR (KBr): 3434, 2962, 1679, 1626, 1447, 1370, 1259, 1121, 774, 658, 609, 566 cm^{-1}; ^1H NMR (600 MHz, $CDCl_{36}$): δ = 1.65–1.86 (m, 8H, CH_2), 1.96 (s, 3H, CH_3), 3.15 (s, 3H, CH_3), 3.55 (s, 1H, CH), 5.05 (s, 1H,CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ =19.0, 23.9, 24.1, 29.5, 35.9, 37.0, 44.0, 45.3, 114.9, 115.9, 134.5, 162.6. HRMS (TOF ES^+): *m/z* calcd for $C_{12}H_{17}N_2O$ [$(M+H)^+$], 205.1335; found, 205.1335.

4,4-Dimethyl-6-methylene-2-oxo-1-phenylpiperidine-3-carbonitrile (4a)



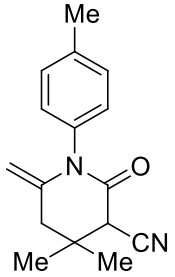
White solid; Mp: 166.6–166.9 °C; IR (KBr): 3435, 2968, 2836, 1668, 1628, 1498, 1375, 1325, 1123, 762, 700, 600 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.29 (s, 6H, CH_3), 2.55–2.66 (m, 2H, CH_2), 3.62 (s, 1H, CH), 3.81 (s, 1H, CH_2), 4.23 (s, 1H, CH_2), 7.13 (d, *J* = 7.6 Hz, 2H, ArH), 7.40–7.48 (m, 3H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 22.8, 27.6, 32.7, 42.3, 48.7, 97.6, 115.3, 128.4, 128.6, 129.8, 137.7, 142.4, 161.2. HRMS (TOF ES^+): *m/z* calcd for $C_{15}H_{17}N_2O$ [$(M+H)^+$], 241.1335; found, 241.1335.

1-(4-Chlorophenyl)-4,4-dimethyl-6-methylene-2-oxopiperidine-3-carbonitrile (4b)



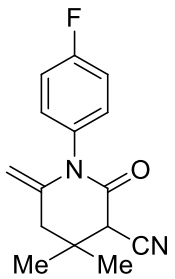
White solid; Mp: 179.2–179.9 °C; IR (KBr): 3442, 2961, 1676, 1628, 1487, 1372, 1291, 1096, 843, 792, 724, 599, 517 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.28 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 2.55–2.66 (m, 2H, CH_2), 3.62 (s, 1H, CH), 3.83 (s, 1H, CH_2), 4.26 (s, 1H, CH_2), 7.08 (d, J = 8.5 Hz, 2H, ArH), 7.45 (d, J = 8.5 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 22.8, 27.7, 32.8, 42.2, 48.7, 97.8, 115.1, 129.9, 130.1, 134.6, 136.1, 142.3, 161.3. HRMS (TOF ES^+): *m/z* calcd for $C_{15}H_{16}ClN_2O$ [$(M+H)^+$], 275.0946; found, 275.0940.

4,4-Dimethyl-6-methylene-2-oxo-1-(p-tolyl)piperidine-3-carbonitrile (4c)



White solid; Mp: 188.1–188.8 °C; IR (KBr): 3442, 2971, 2835, 1625, 1510, 1366, 1120, 768, 660, 602, 554, 522, 498, 436 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.28 (s, 6H, CH_3), 2.39 (s, 3H, CH_3), 2.54–2.65 (m, 2H, CH_2), 3.60 (s, 1H, CH), 3.85 (s, 1H, CH_2), 4.22 (s, 1H, CH_2), 7.00 (d, J = 8.2 Hz, 2H, ArH), 7.27 (d, J = 8.0 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.2, 22.8, 27.7, 32.7, 42.2, 48.7, 97.5, 115.4, 128.0, 130.4, 135.0, 138.5, 142.5, 161.2. HRMS (TOF ES^+): *m/z* calcd for $C_{16}H_{19}N_2O$ [$(M+H)^+$], 255.1492; found, 255.1490.

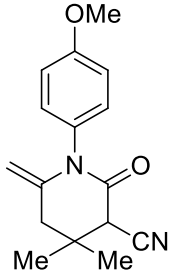
1-(4-Fluorophenyl)-4,4-dimethyl-6-methylene-2-oxopiperidine-3-carbonitrile (4d)



White solid; Mp: 182.6–183.0 °C; IR (KBr): 3442, 2966, 1626, 1513, 1370, 1114, 836, 766, 688, 601, 533 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.28 (s, 3H, CH_3),

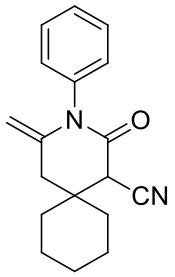
1.29 (s, 3H, CH_3), 2.56–2.66 (m, 2H, CH_2), 3.62 (s, 1H, CH), 3.82 (s, 1H, CH_2), 4.26 (s, 1H, CH_2), 7.10–7.27 (m, 4H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 22.8, 27.7, 32.8, 42.2, 48.7, 97.6, 116.8 (d, J = 22.5 Hz), 130.2 (d, J = 9.0 Hz), 133.4, 142.5, 161.4 (d, J = 12.0 Hz), 163.1. HRMS (TOF ES$^+$): *m/z* calcd for $C_{15}H_{16}FN_2O$ [(M+H)$^+$], 259.1241; found, 259.1240.

1-(4-Methoxyphenyl)-4,4-dimethyl-6-methylene-2-oxopiperidine-3-carbonitrile (4e)



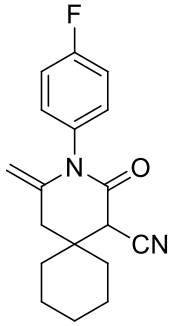
White solid; Mp: 144.4–144.8 °C; IR (KBr): 3441, 2964, 1677, 1624, 1512, 1369, 1255, 1111, 867, 768, 660, 606, 556 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.28 (s, 6H, CH_3), 2.54–2.64 (m, 2H, CH_2), 3.61 (s, 1H, CH), 3.86 (s, 3H, OCH_3), 4.23 (s, 1H, CH_2), 6.97 (d, J = 8.8 Hz, 2H, ArH), 7.03 (d, J = 8.8 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 22.8, 27.7, 32.7, 42.2, 48.7, 55.5, 97.5, 115.0, 115.4, 129.3, 130.2, 142.6, 159.4, 161.4. HRMS (TOF ES$^+$): *m/z* calcd for $C_{16}H_{19}N_2O_2$ [(M+H)$^+$], 271.1441; found, 271.1439.

4-Methylene-2-oxo-3-phenyl-3-azaspiro[5.5]undecane-1-carbonitrile (5a)



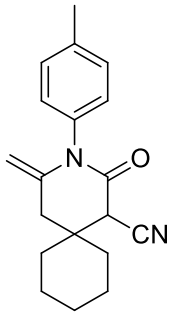
White solid; Mp: 162.4–162.8 °C; IR (KBr): 3440, 2962, 2931, 2877, 1674, 1627, 1477, 1364, 1266, 1199, 1124, 799, 723, 690, 606, 528, 436 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.26–1.71 (m, 10H, CH_2), 2.49–3.01 (m, 2H, CH_2), 3.66 (s, 1H, CH), 3.82 (s, 1H, CH_2), 4.27 (s, 1H, CH_2), 7.13 (d, J = 7.5 Hz, 2H, ArH), 7.39–7.49 (m, 3H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.3, 21.5, 25.3, 31.9, 34.6, 35.2, 36.9, 97.8, 115.3, 128.4, 128.6, 129.8, 137.7, 142.1, 161.1. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{21}N_2O$ [(M+H)$^+$], 281.1648; found, 281.1644.

3-(4-Fluorophenyl)-4-methylene-2-oxo-3-azaspiro[5.5]undecane-1-carbonitrile (5b)



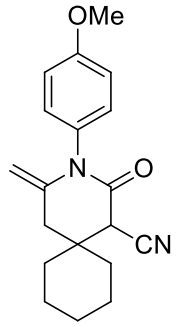
White solid; Mp: 167.9–168.6 °C; IR (KBr): 3439, 2937, 1631, 1508, 1368, 1214, 1119, 672, 605, 543 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.30–1.70 (m, 10H, CH_2), 2.45–3.01 (m, 2H, CH_2), 3.65 (s, 1H, CH), 3.83 (s, 1H, CH_2), 4.28 (s, 1H, CH_2), 7.01 (d, J = 8.2 Hz, 2H, ArH), 7.26 (t, J = 4.0 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.2, 21.3, 21.5, 25.3, 31.9, 34.5, 35.1, 36.9, 48.1, 97.6, 115.4, 128.0, 130.4, 135.0, 138.5, 142.1, 161.1. HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{20}FN_2O$ [$(M+H)^+$], 299.1554; found, 299.1549.

4-Methylene-2-oxo-3-(*p*-tolyl)-3-azaspiro[5.5]undecane-1-carbonitrile (5c)



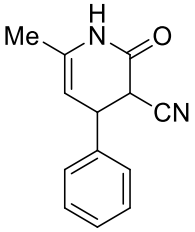
White solid; Mp: 174.4–174.7 °C; IR (KBr): 3441, 2936, 2867, 1677, 1630, 1514, 1454, 1372, 1302, 1112, 836, 767, 706, 661, 602, 558 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.52–1.70 (m, 10H, CH_2), 2.39 (s, 3H, CH_3), 2.44–2.99 (m, 2H, CH_2), 3.64 (s, 1H, CH), 3.85 (s, 1H, CH_2), 4.25 (s, 1H, CH_2), 7.10–7.18 (m, 4H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.3, 21.4, 25.3, 31.9, 34.6, 35.2, 36.9, 48.1, 97.8, 115.1, 116.8 (d, J = 22.5 Hz), 130.2 (d, J = 7.5 Hz), 133.4, 142.1, 161.4 (d, J = 30.0 Hz), 163.1. HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{23}N_2O$ [$(M+H)^+$], 295.1805; found, 295.1800.

3-(4-Methoxyphenyl)-4-methylene-2-oxo-3-azaspiro[5.5]undecane-1-carbonitrile (5d)



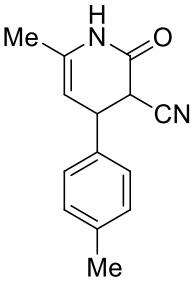
White solid; Mp: 171.9–172.3 °C; IR (KBr): 3436, 2972, 1683, 1614, 1512, 1435, 1390, 1342, 1276, 1227, 1154, 841, 808, 761, 671, 544 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.52–1.70 (m, 10H, CH_2), 2.44–2.99 (m, 2H, CH_2), 3.64 (s, 1H, CH), 3.83 (s, 3H, OCH_3), 3.87 (s, 1H, CH_2), 4.26 (s, 1H, CH_2), 6.97 (d, J = 8.8 Hz, 2H, ArH), 7.04 (t, J = 8.9 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.3, 21.5, 25.3, 31.9, 34.5, 35.1, 36.9, 48.1, 55.5, 97.6, 115.0, 115.3, 129.3, 130.2, 142.3, 159.4, 161.3. HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{23}N_2O_2$ [$(M+H)^+$], 311.1754; found, 311.1746.

6-Methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyridine-3-carbonitrile (6a)



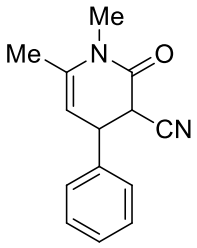
White solid; Mp: 162.2–163.7 °C; IR (KBr): 3434, 3235, 3172, 3121, 2962, 1678, 1622, 1389, 1273, 1193, 1121, 767, 700, 612, 561, 521 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 1.96 (s, 3H, CH_3), 3.93 (t, J =5.6 Hz, 1H, CH), 3.98 (d, J =6.8 Hz, 1H, CH), 5.13 (d, J =5.2 Hz, 1H, CH), 7.26–7.38 (m, 5H, ArH), 7.92 (s, 1H, NH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 19.0, 41.1, 41.4, 103.7, 114.8, 128.0, 128.4, 129.1, 134.1, 136.9, 162.7. HRMS (TOF ES^+): *m/z* calcd for $C_{13}H_{13}N_2O$ [$(M+H)^+$], 213.1022; found, 213.1024.

6-Methyl-2-oxo-4-(p-tolyl)-1,2,3,4-tetrahydropyridine-3-carbonitrile (6b)



White solid; Mp: 160.5–161.0 °C; IR (KBr): 3439, 3233, 1618, 1457, 1339, 1145, 675 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 1.93 (s, 3H, CH_3), 2.34 (d, J =9.0 Hz, 3H, CH_3), 3.65 (t, J =12.0 Hz, 1H, CH), 3.96 (d, J =11.9 Hz, 1H, CH), 4.94 (s, 1H, CH), 7.17–7.18 (m, 4H, ArH), 7.50 (s, 1H, NH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 18.9, 21.1, 42.7, 42.8, 104.3, 115.9, 127.5, 129.7, 129.8, 133.8, 136.5, 138.0, 163.3. HRMS (TOF ES^+): *m/z* calcd for $C_{14}H_{15}N_2O$ $[(M+H)^+]$, 227.1179; found, 227.1180.

1,6-Dimethyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyridine-3-carbonitrile (6c)



White solid; Mp: 102.5–103.1 °C; IR (KBr): 3440, 1671, 1454, 1371, 1134, 771, 710, 668, 508 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 2.06 (d, J =1.2 Hz, 3H, CH_3), 3.20 (t, J =3.6 Hz, 3H, CH_3), 3.71 (d, J =11.6 Hz, 1H, CH), 3.90 (d, J =11.6 Hz, 1H, CH), 5.13 (d, J =1.3 Hz, 1H, CH), 7.27 (q, J =2.7 Hz, 2H, ArH), 7.30–7.33 (m, 1H, ArH), 7.37 (t, J =7.5 Hz, 2H, ArH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 19.4, 29.8, 41.7, 43.2, 107.2, 116.0, 127.5, 128.2, 129.2, 137.3, 139.2, 161.8. HRMS (TOF ES^+): *m/z* calcd for $C_{14}H_{15}N_2O$ $[(M+H)^+]$, 227.1179; found, 227.1181.

X-ray Structure and Data[2] of 2a and 4a.

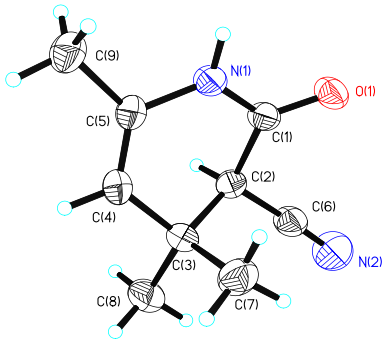


Figure S1. X-Ray crystal structure of **2a**

Table S1. Crystal data and structure refinement for **2a**

Identification code	1
Empirical formula	C9 H12 N2 O
Formula weight	164.21
Temperature	293.15 K
Wavelength	0.71073 Å
Crystal system	Monoclinic, P2(1)/c
Space group	P 1 21/c 1
Unit cell dimensions	a = 6.4219(12) Å α= 90°. b = 10.741(2) Å β= 95.887(3)°. c = 13.507(3) Å γ = 90°.
Volume	926.8(3) $Å^3$
Z	4
Density (calculated)	1.177 Mg/m^3
Absorption coefficient	0.079 mm^{-1}
F(000)	352
Theta range for data collection	3.032 to 24.972°.
Index ranges	-7<=h<=7, -11<=k<=12, -15<=l<=15
Reflections collected	5110
Independent reflections	1621 [R(int) = 0.0704]
Completeness to theta = 25.242°	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.981324 and 0.401939
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1621 / 0 / 113
Goodness-of-fit on F^2	0.900
Final R indices [I>2sigma(I)]	R1 = 0.0500, wR2 = 0.1048
R indices (all data)	R1 = 0.1226, wR2 = 0.1279
Extinction coefficient	0.034(5)
Largest diff. peak and hole	0.123 and -0.149 $e.Å^{-3}$

Table S2. Bond lengths [A] and angles [deg] for **2a**

Cl(1)-C(14)	1.353(5)	C(4)-N(1)-C(1)	112.4(3)
O(1)-C(2)	1.224(5)	O(2)-N(2)-O(3)	121.1(4)
O(2)-N(2)	1.235(4)	O(2)-N(2)-C(3)	119.9(4)
O(3)-N(2)	1.256(5)	O(3)-N(2)-C(3)	119.0(4)
N(1)-C(4)	1.324(5)	C(4)-N(3)-C(11)	129.1(4)
N(1)-C(1)	1.455(5)	C(3)-C(2)-C(1)	105.2(3)
N(2)-C(3)	1.392(5)	N(2)-C(3)-C(2)	125.4(4)
N(3)-C(4)	1.327(5)	N(2)-C(3)-C(4)	124.8(4)
N(3)-C(11)	1.429(5)	C(2)-C(3)-C(4)	109.5(4)
C(1)-C(5)	1.513(6)	N(1)-C(4)-N(3)	125.3(4)
C(1)-C(2)	1.534(6)	N(1)-C(4)-C(3)	109.3(3)
C(2)-C(3)	1.424(6)	N(3)-C(4)-C(3)	125.4(4)
C(3)-C(4)	1.425(6)	C(6)-C(5)-C(10)	118.5(4)
C(5)-C(6)	1.382(7)	C(6)-C(5)-C(1)	122.5(4)
C(5)-C(10)	1.386(6)	C(10)-C(5)-C(1)	118.9(4)
C(6)-C(7)	1.403(6)	C(5)-C(6)-C(7)	120.6(5)
C(7)-C(8)	1.356(8)	C(8)-C(7)-C(6)	120.2(5)
C(8)-C(9)	1.399(8)	C(7)-C(8)-C(9)	120.3(5)
C(9)-C(10)	1.390(6)	C(10)-C(9)-C(8)	119.0(5)
C(11)-C(12)	1.373(6)	C(5)-C(10)-C(9)	121.3(5)
C(11)-C(16)	1.387(6)	C(12)-C(11)-C(16)	119.8(4)
C(12)-C(13)	1.379(6)	C(12)-C(11)-N(3)	118.2(4)
C(13)-C(14)	1.369(7)	C(16)-C(11)-N(3)	121.9(4)
C(14)-C(15)	1.362(7)	C(11)-C(12)-C(13)	121.1(4)
C(15)-C(16)	1.391(6)	C(14)-C(13)-C(12)	118.1(4)
N(1)-C(1)-C(5)	114.1(3)	Cl(1)-C(14)-C(15)	118.8(4)
N(1)-C(1)-C(2)	103.2(3)	Cl(1)-C(14)-C(13)	118.6(4)
C(5)-C(1)-C(2)	110.8(3)	C(15)-C(14)-C(13)	122.5(4)
O(1)-C(2)-C(3)	131.9(4)	C(14)-C(15)-C(16)	119.0(4)
O(1)-C(2)-C(1)	122.9(4)	C(11)-C(16)-C(15)	119.5(4)

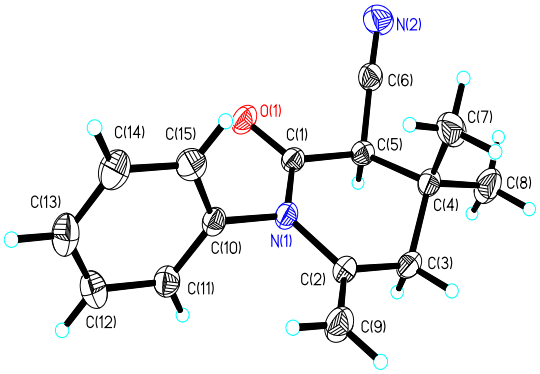


Figure S2. X-Ray crystal structure of **4a**

Table S3. Crystal data and structure refinement for **4a**

dentification code	180908ysj_0m
Empirical formula	C15 H16 N2 O
Formula weight	240.30
Temperature	296.15 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 7.3319(11) Å b = 11.5409(16) Å c = 16.169(2) Å
Volume	1350.8(3) $Å^3$
Z	4
Density (calculated)	1.182 Mg/m^3
Absorption coefficient	0.075 mm^{-1}
F(000)	512
Crystal size	0.15x 0.12x 0.10 mm^3
Theta range for data collection	2.552 to 27.783°.
Index ranges	-9<=h<=9, -10<=k<=14, -21<=l<=18
Reflections collected	8001
Independent reflections	3095 [R(int) = 0.0300]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6809
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3095 / 0 / 165
Goodness-of-fit on F^2	1.020
Final R indices [I>2sigma(I)]	R1 = 0.0473, wR2 = 0.1176
R indices (all data)	R1 = 0.0799, wR2 = 0.1354
Extinction coefficient	n/a

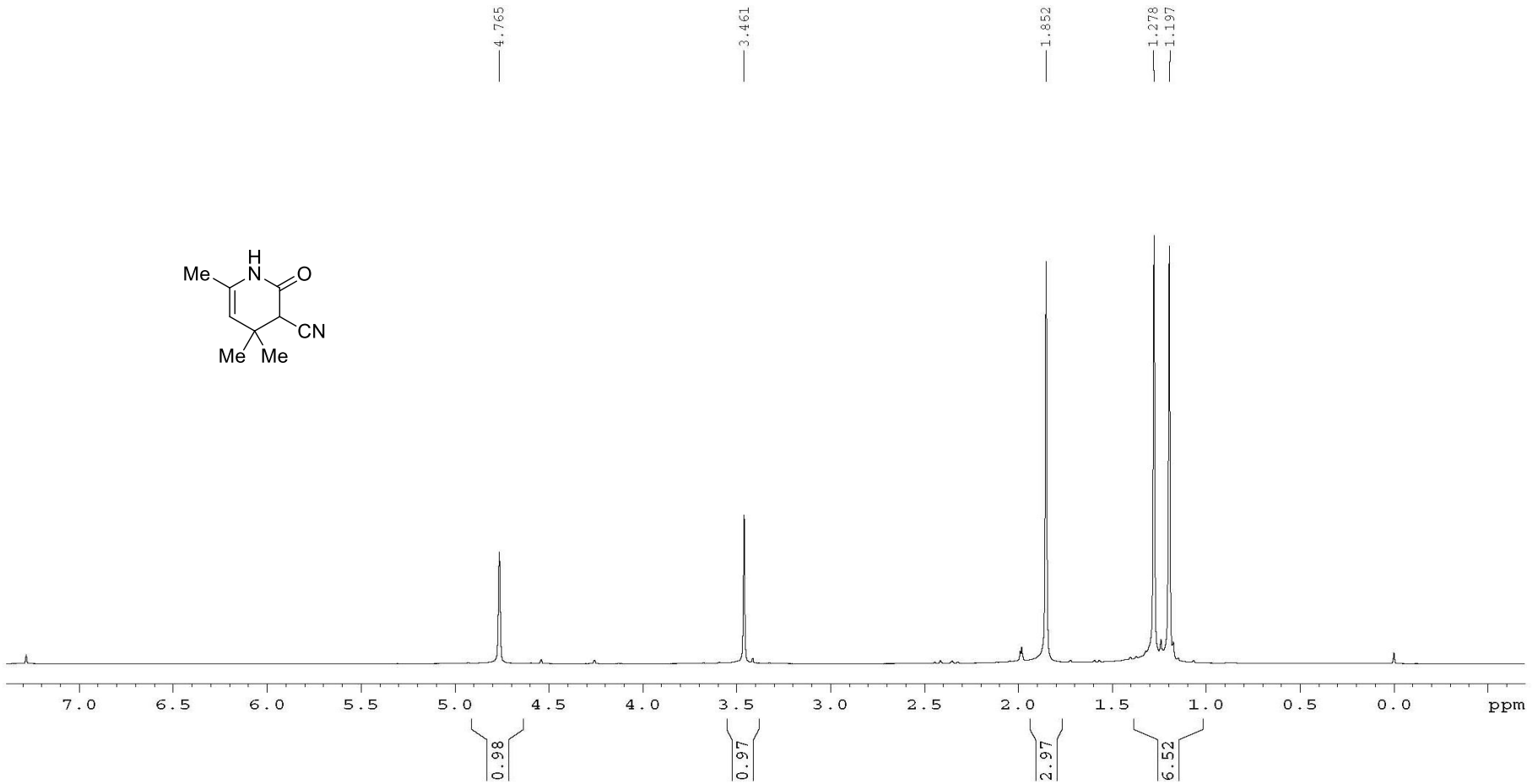


Figure S3. ^{1}H NMR (500 MHz, $CDCl_3$) spectra of compound **2a**

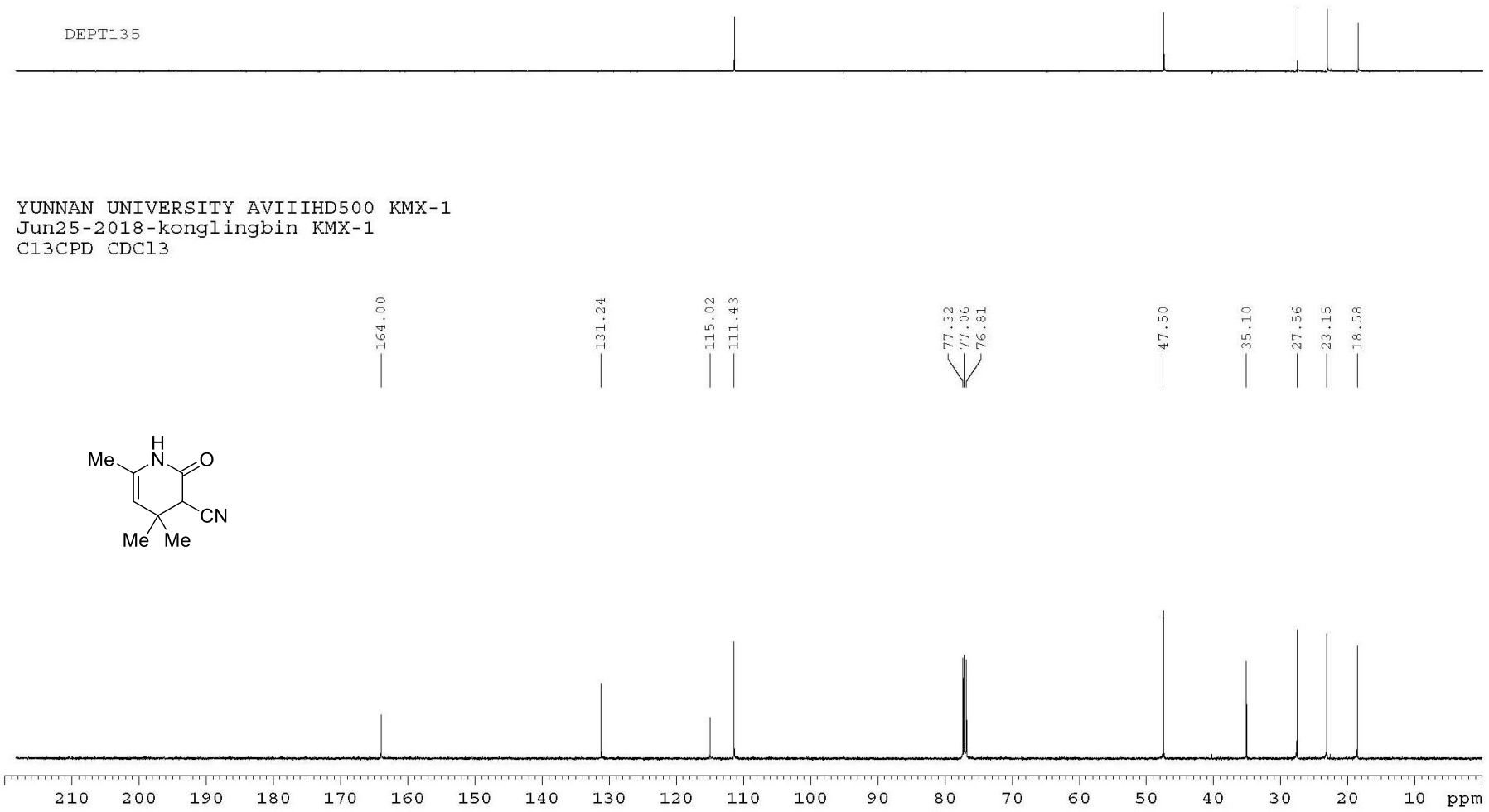


Figure S4. ^{13}C NMR (125 MHz, $CDCl_3$) spectra of compound **2a**

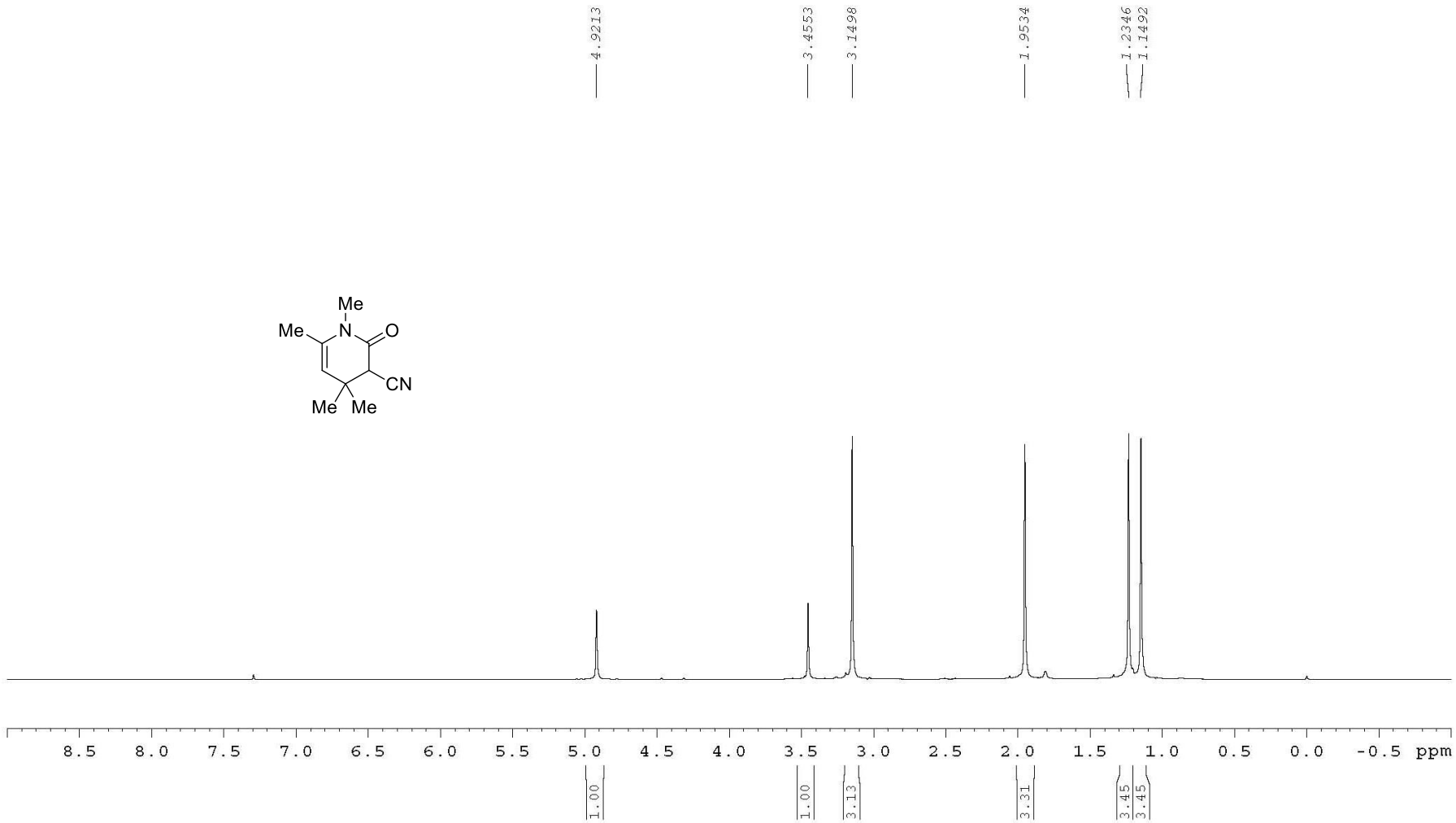


Figure S5. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **2b**

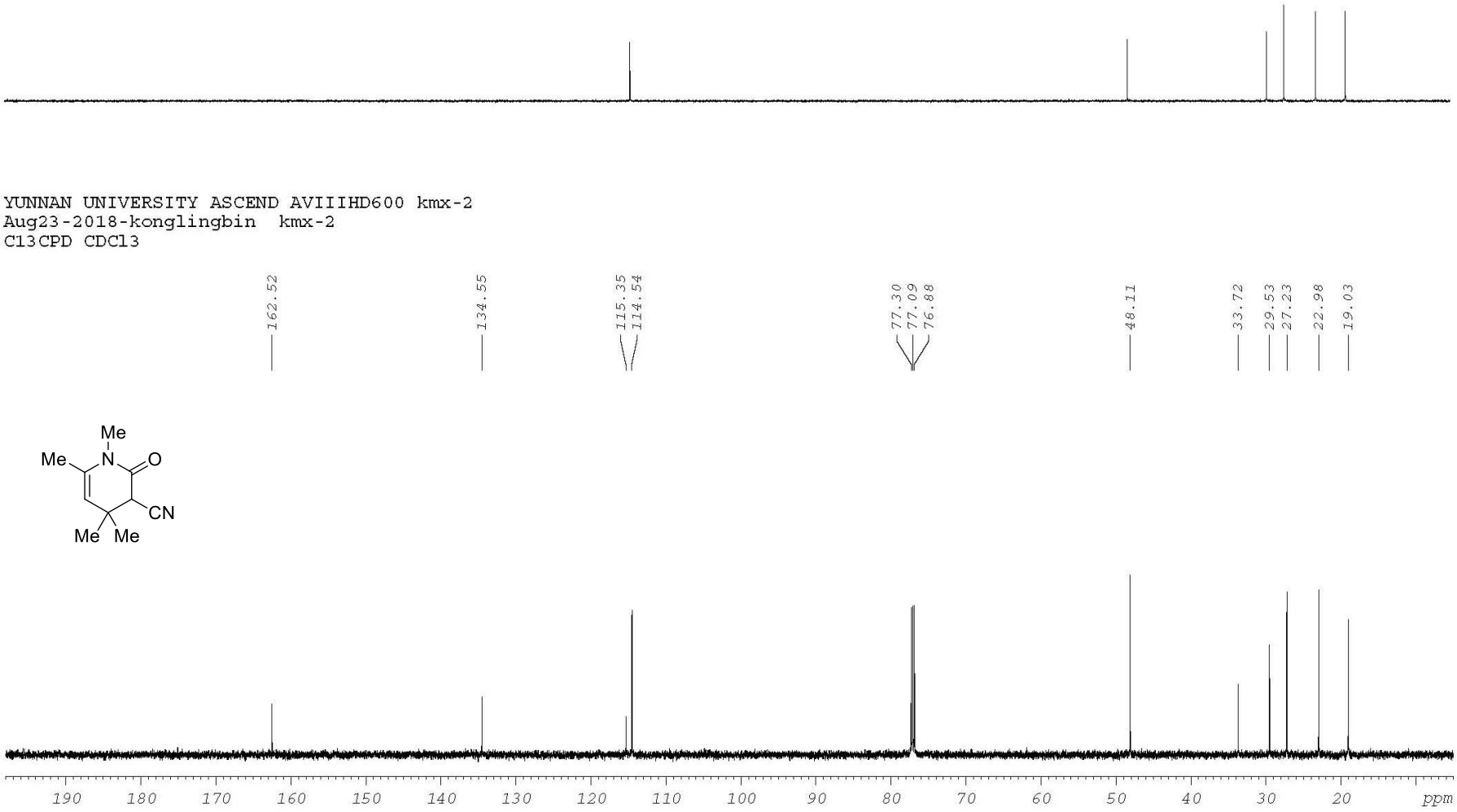


Figure S6. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **2b**

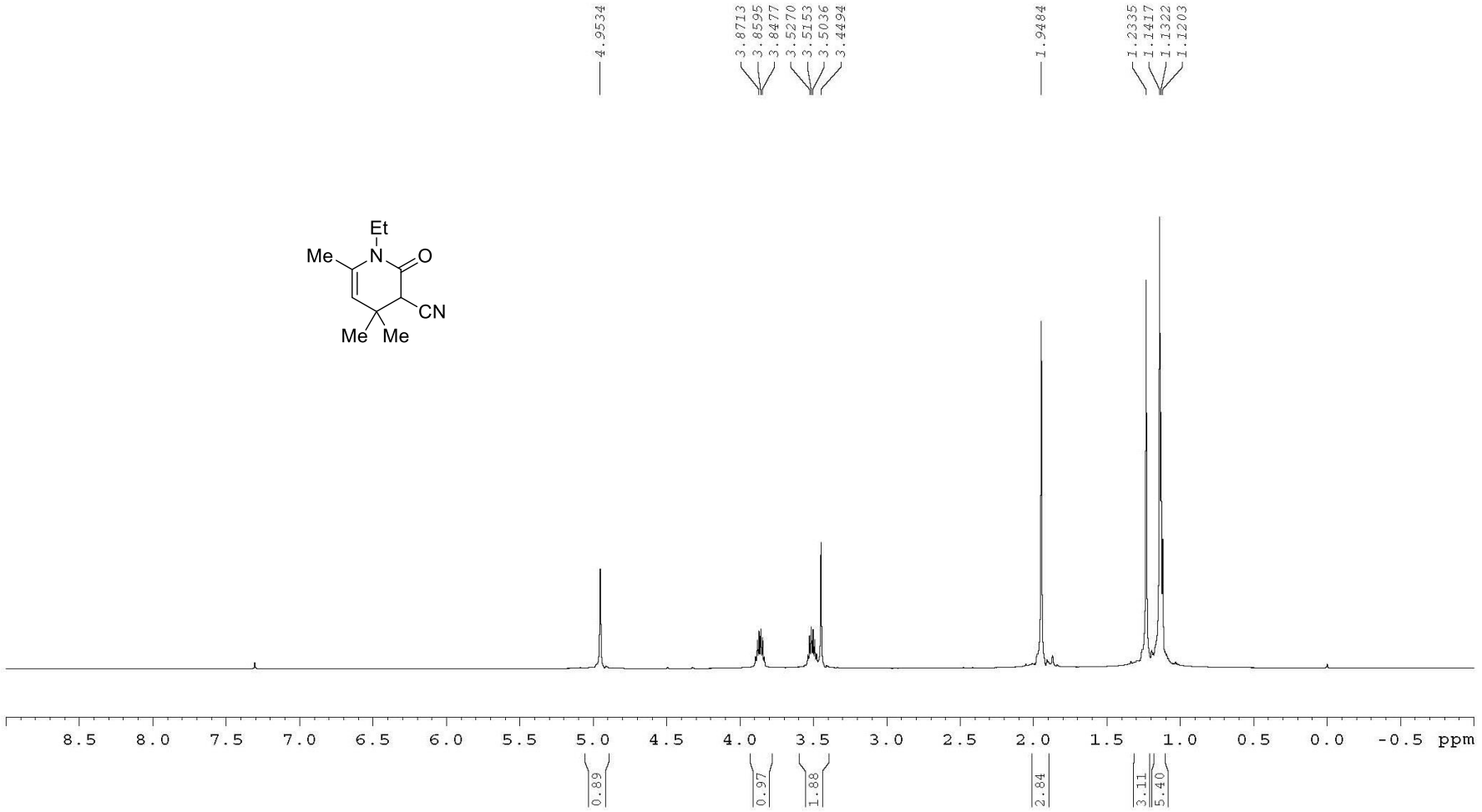


Figure S7. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **2c**

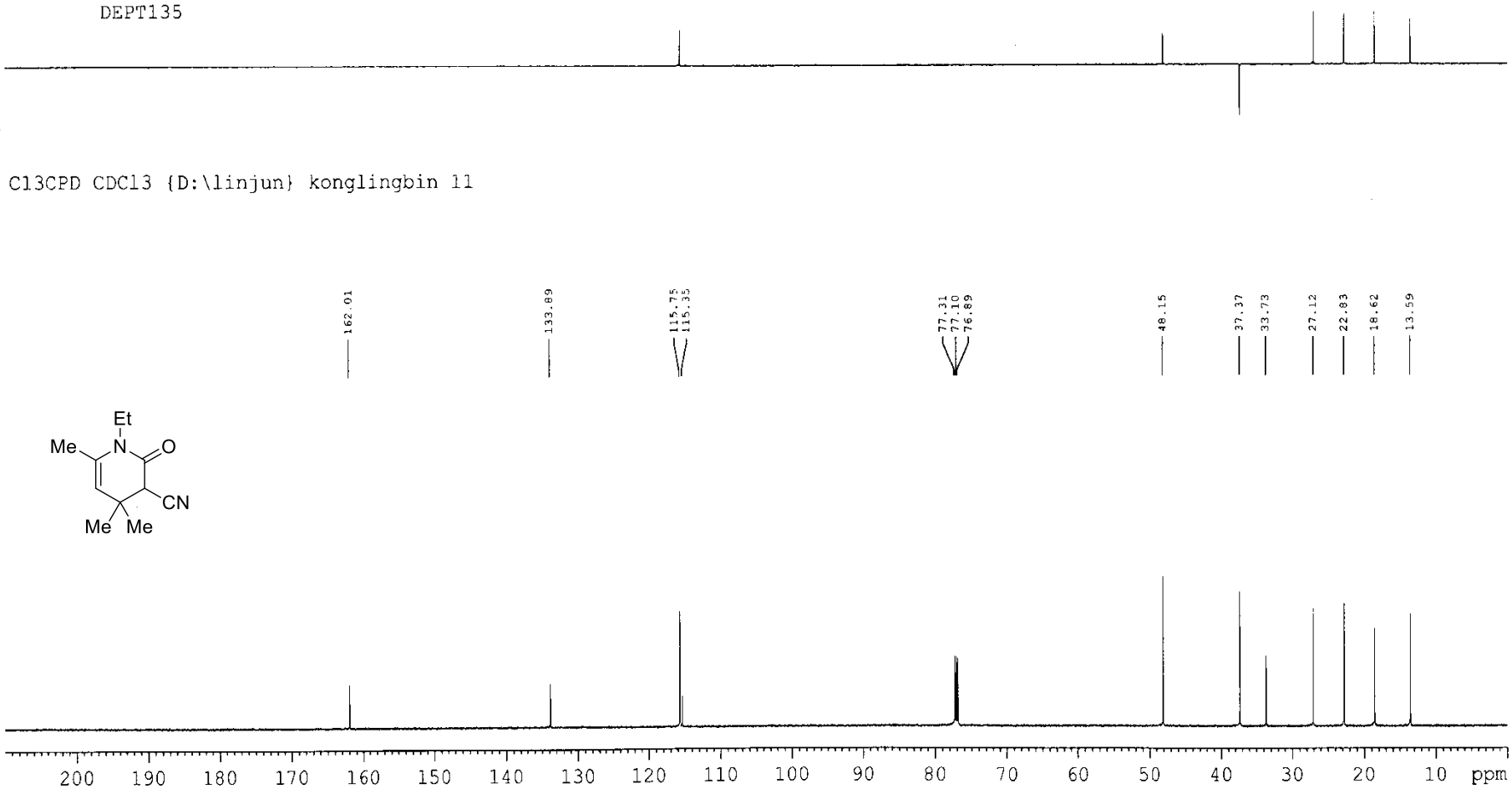


Figure S8. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **2c**

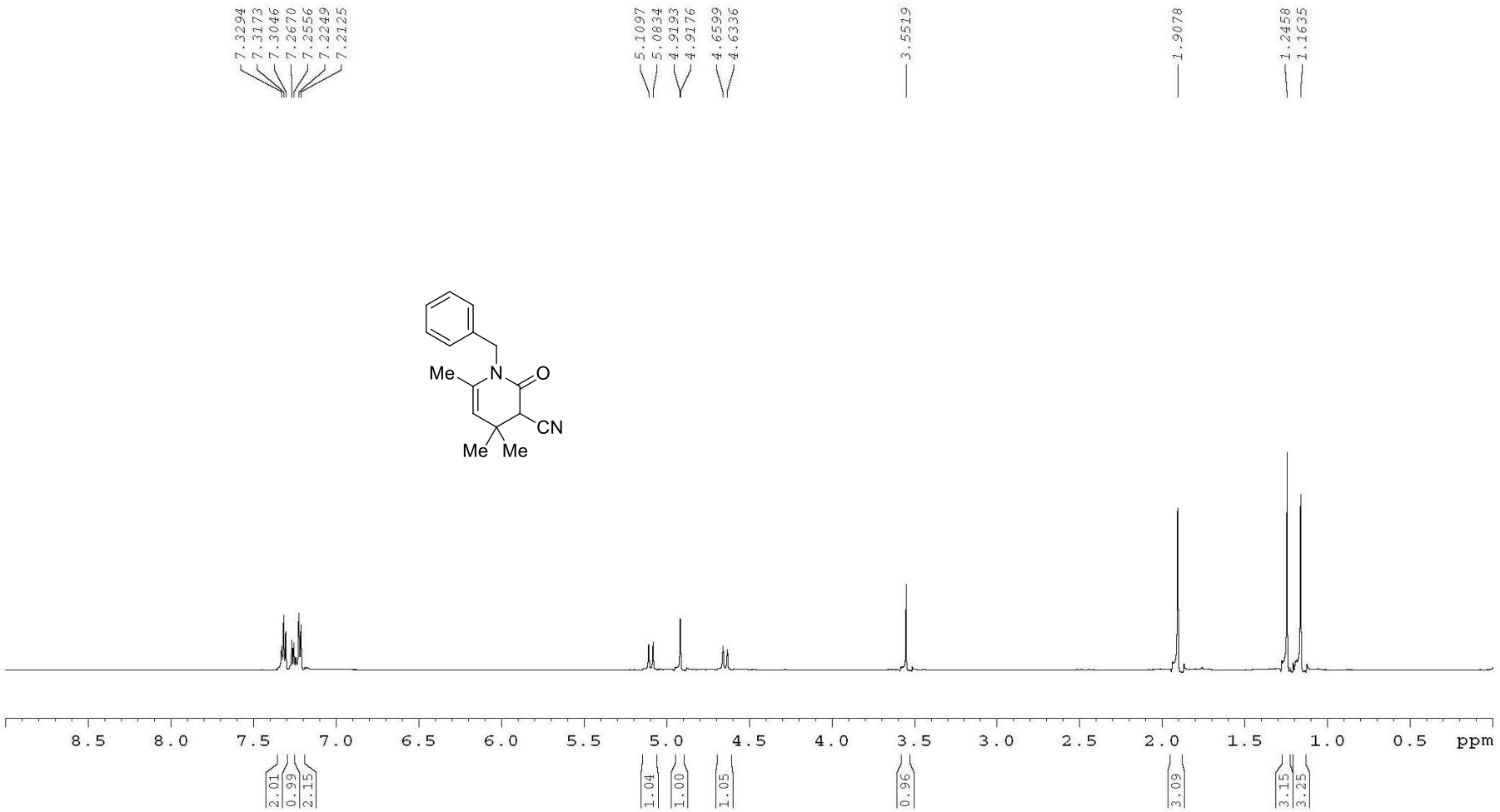


Figure S9. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **2d**

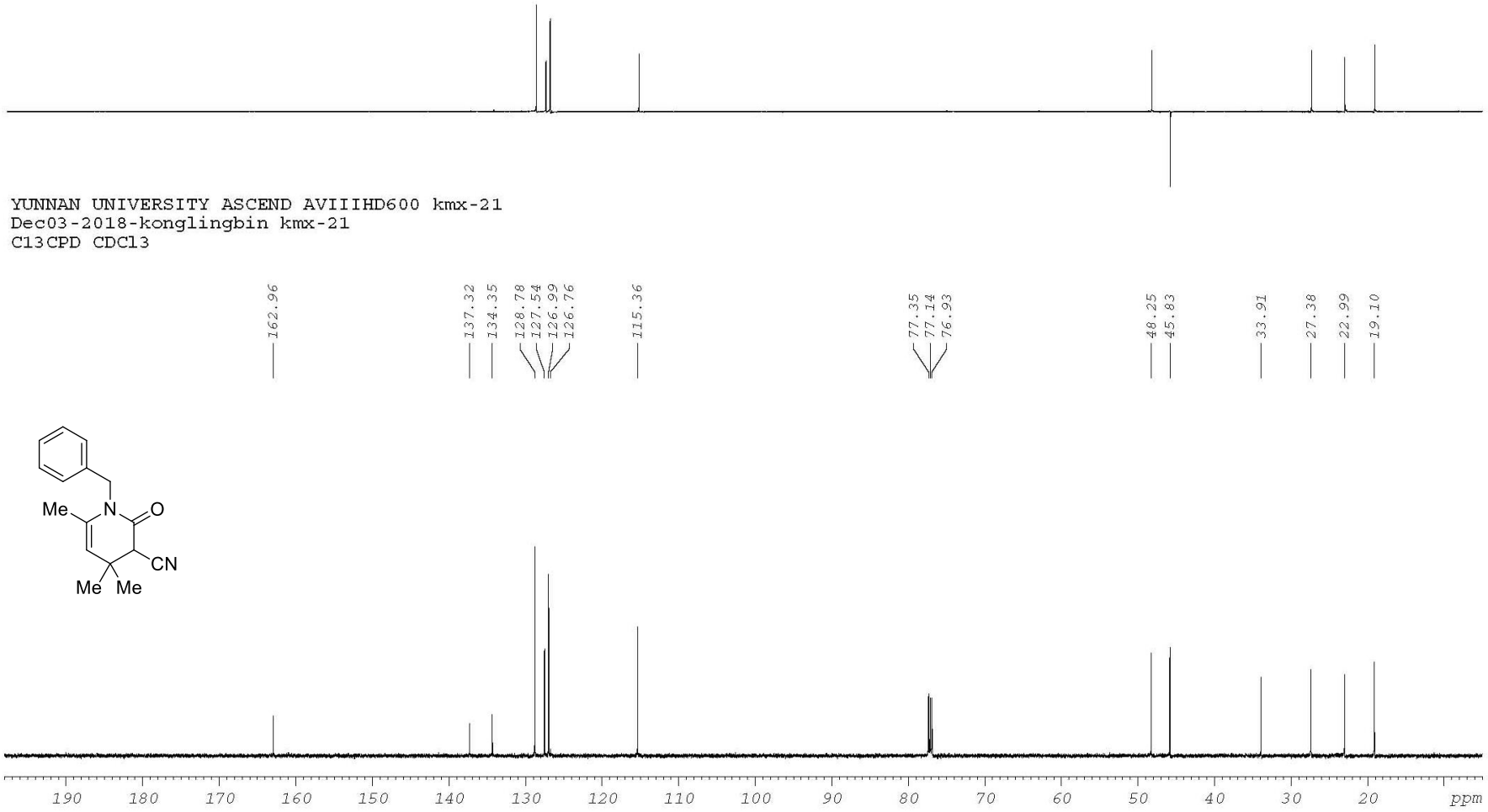


Figure S10. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **2d**

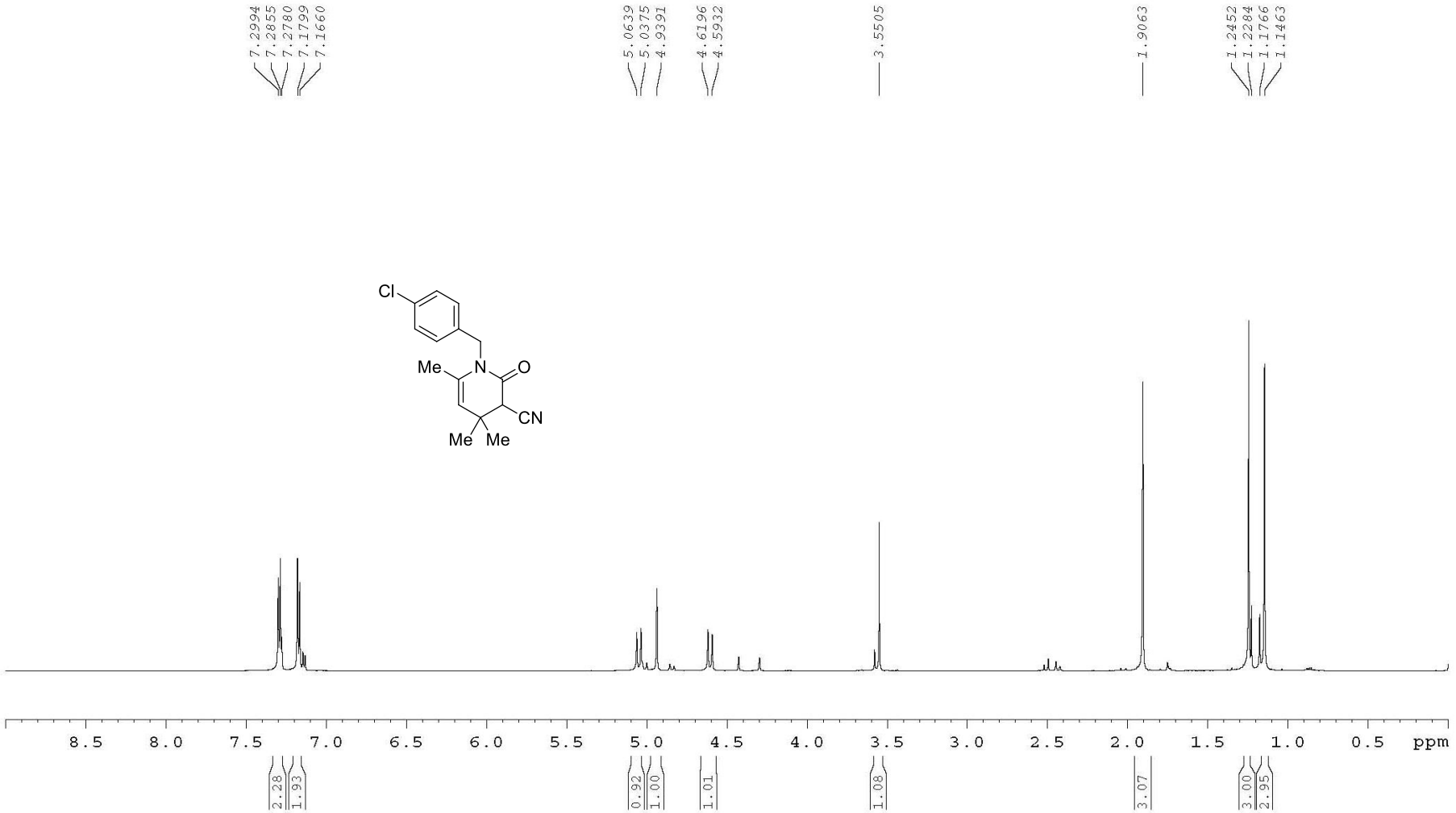


Figure S11. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **2e**

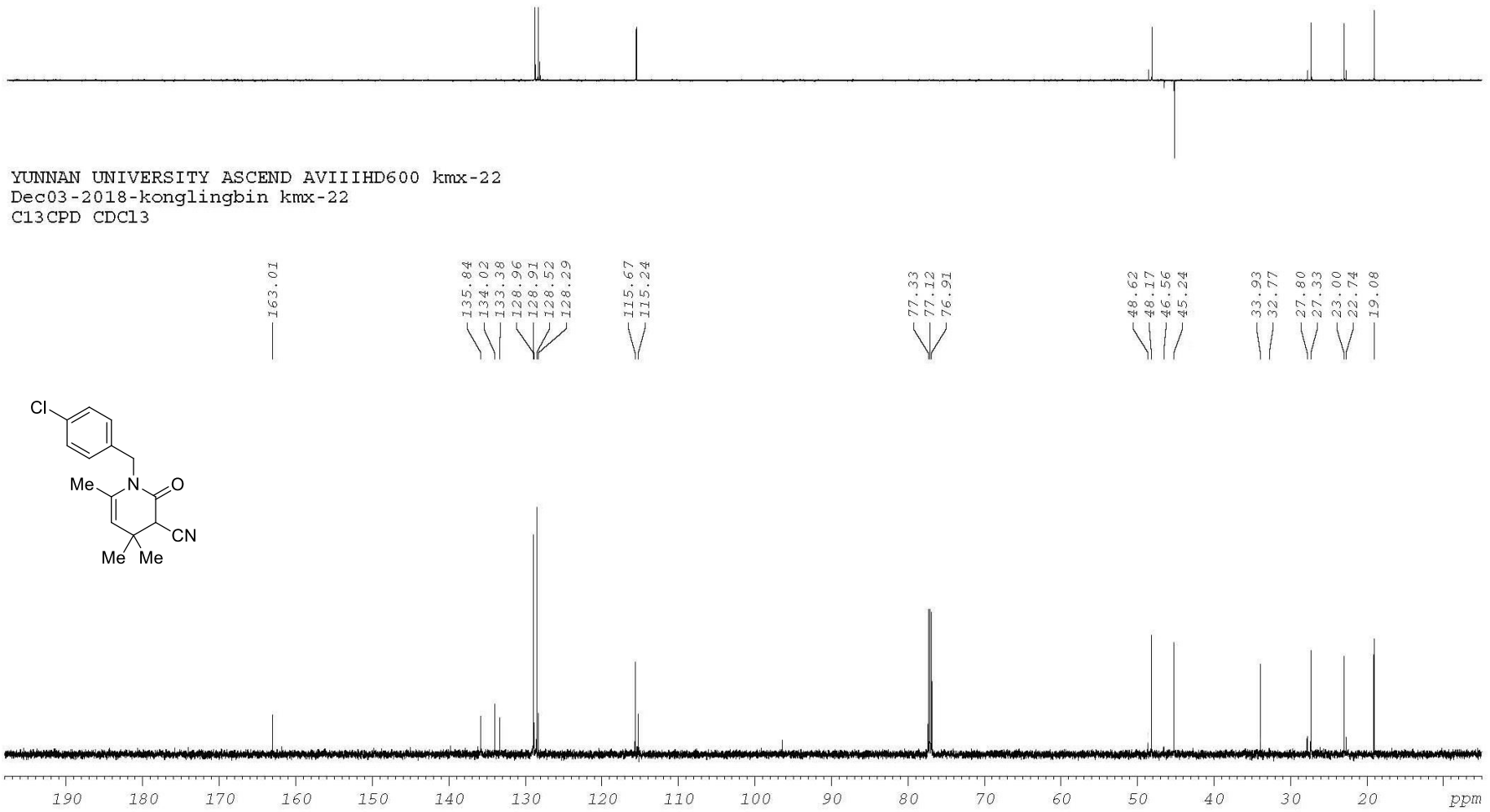


Figure S12. ^{13}C NMR (125 MHz, $CDCl_3$) spectra of compound **2e**

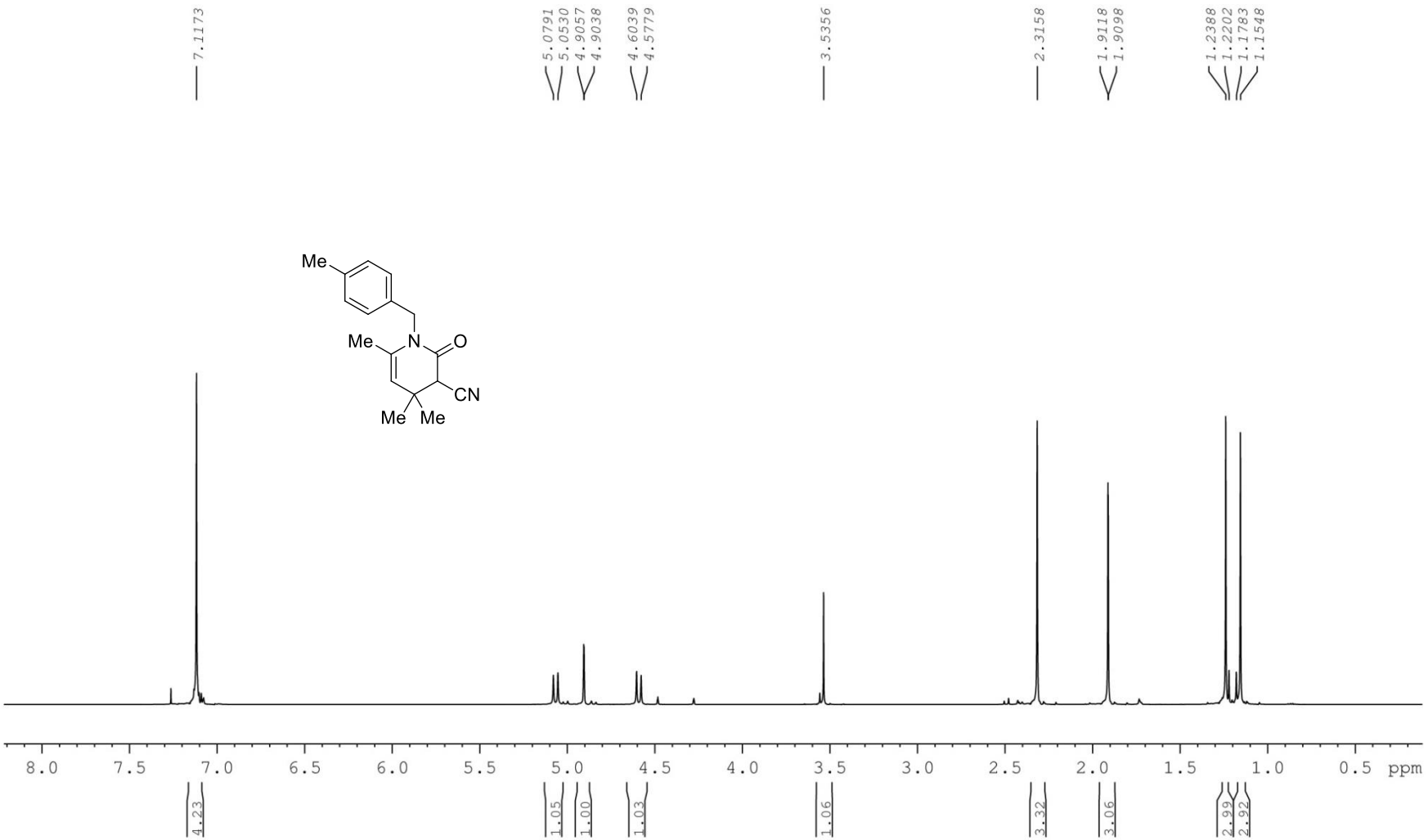


Figure S13. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **2f**

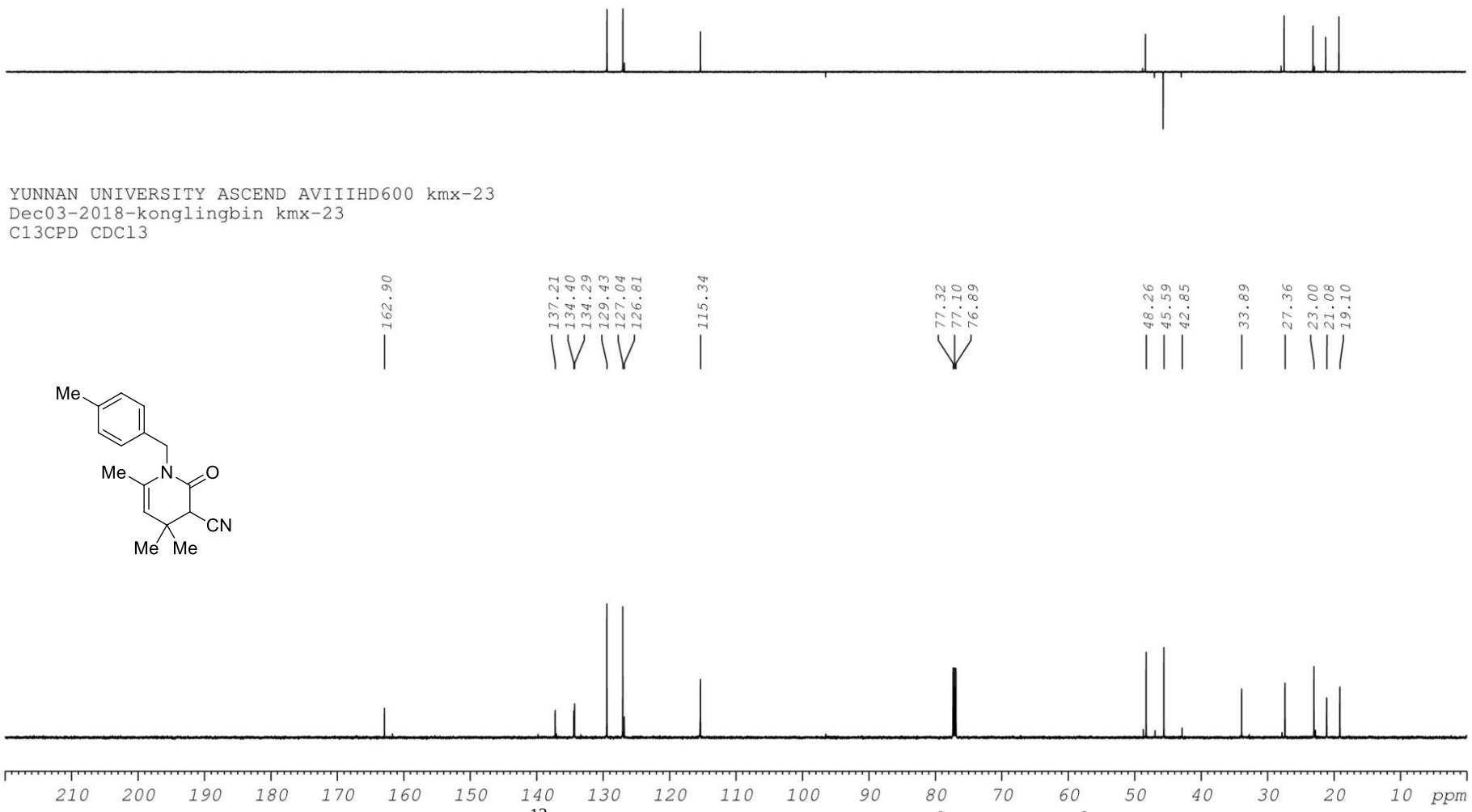


Figure S14. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **2f**

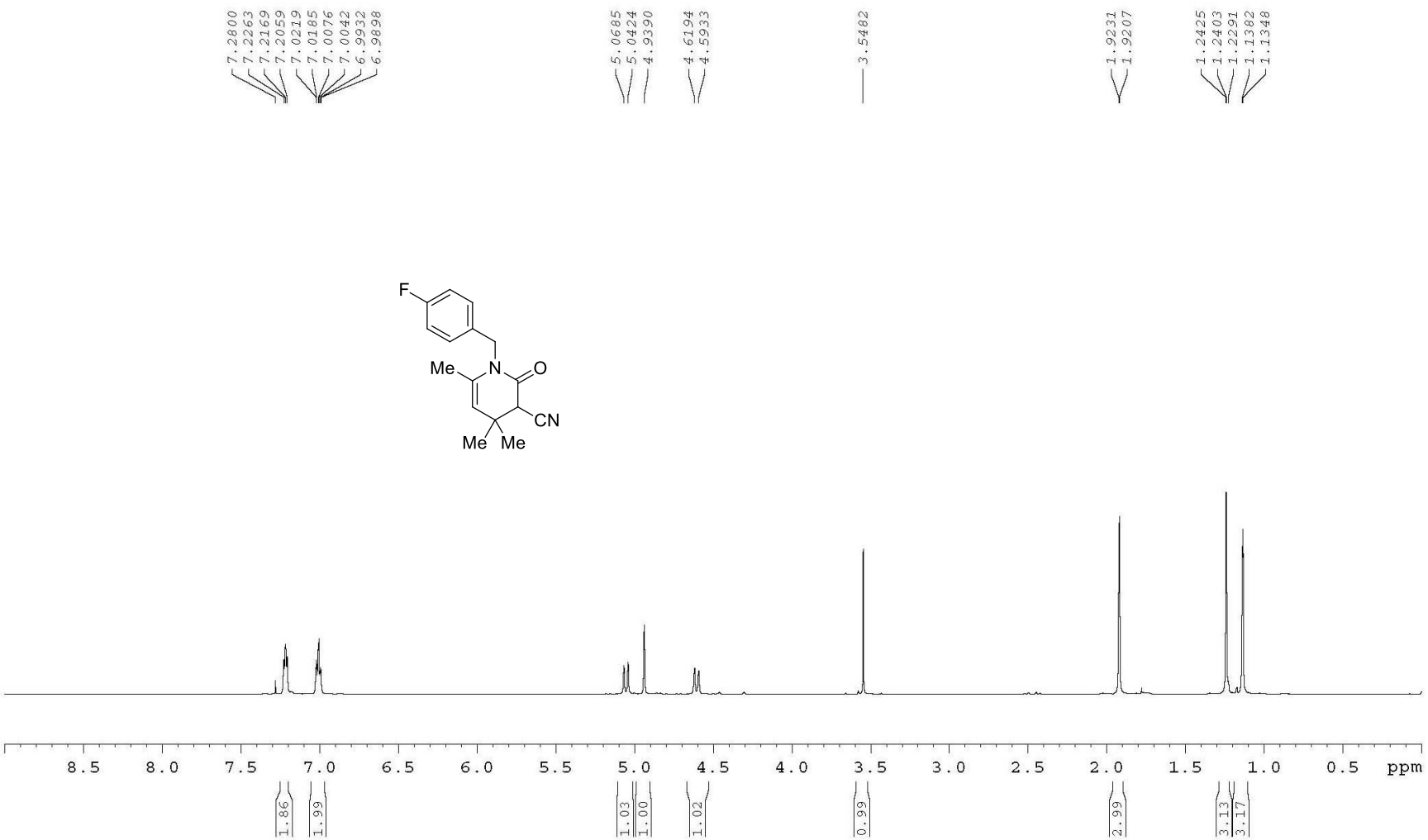


Figure S15. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **2g**

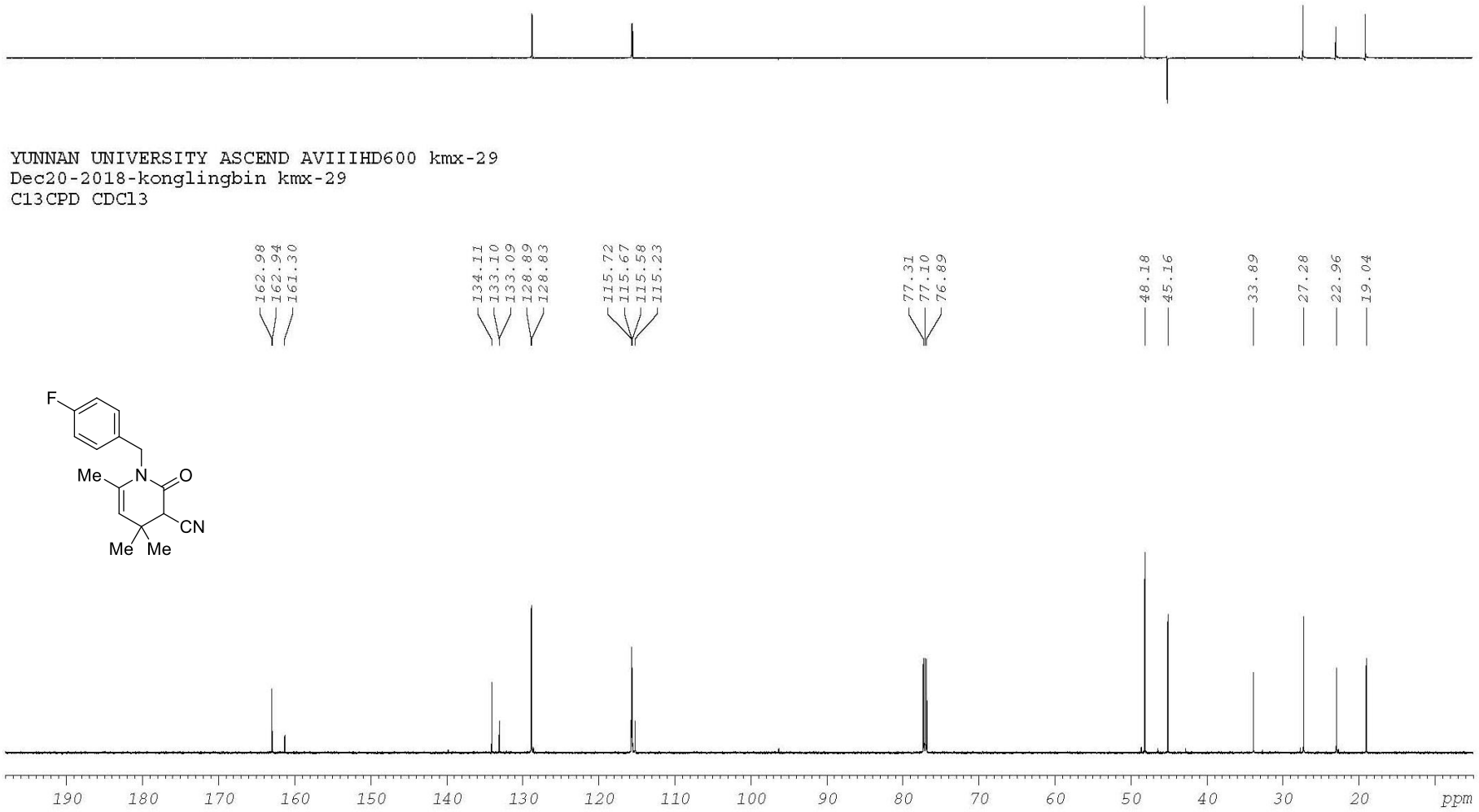


Figure S16. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **2g**

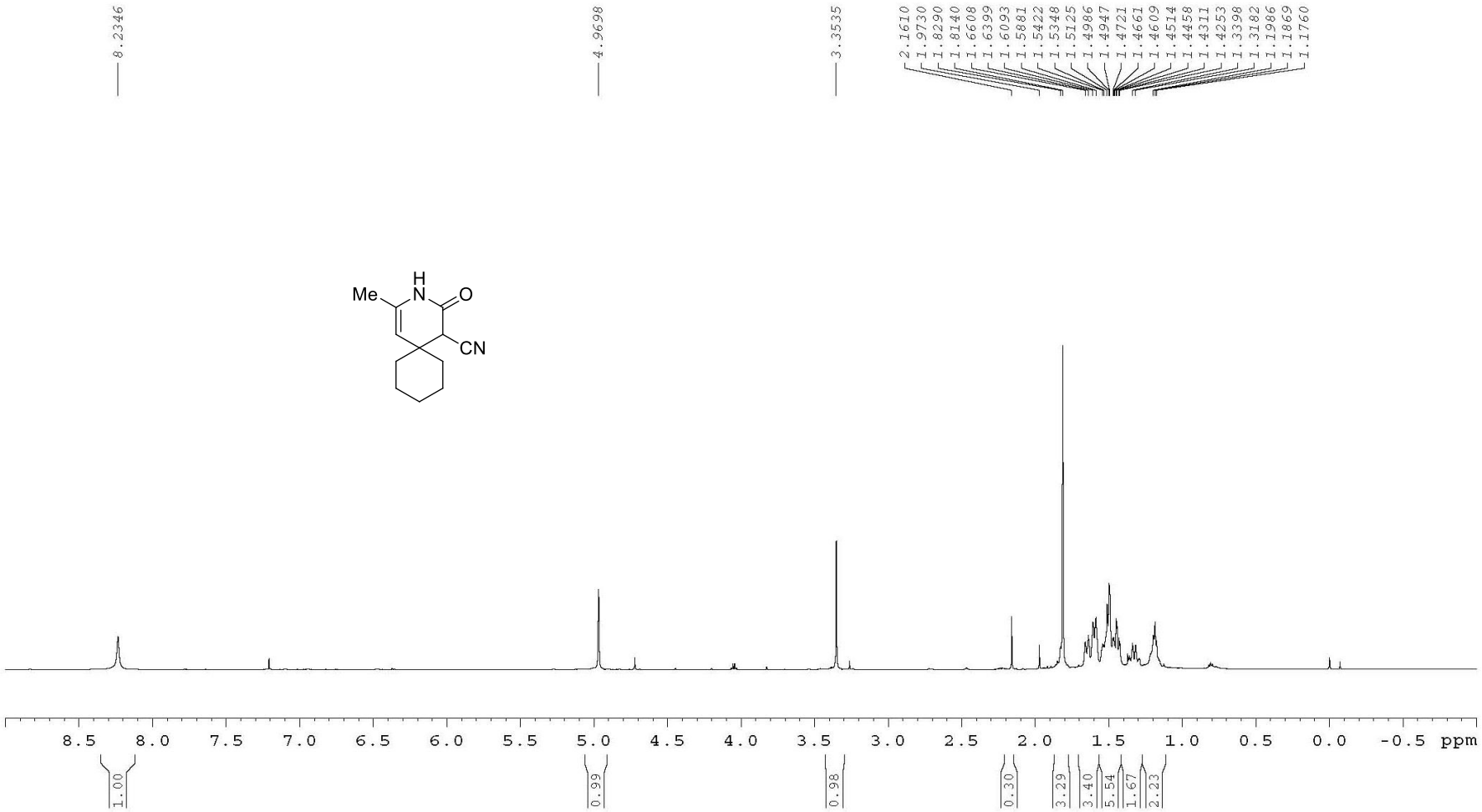


Figure S17. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3a**

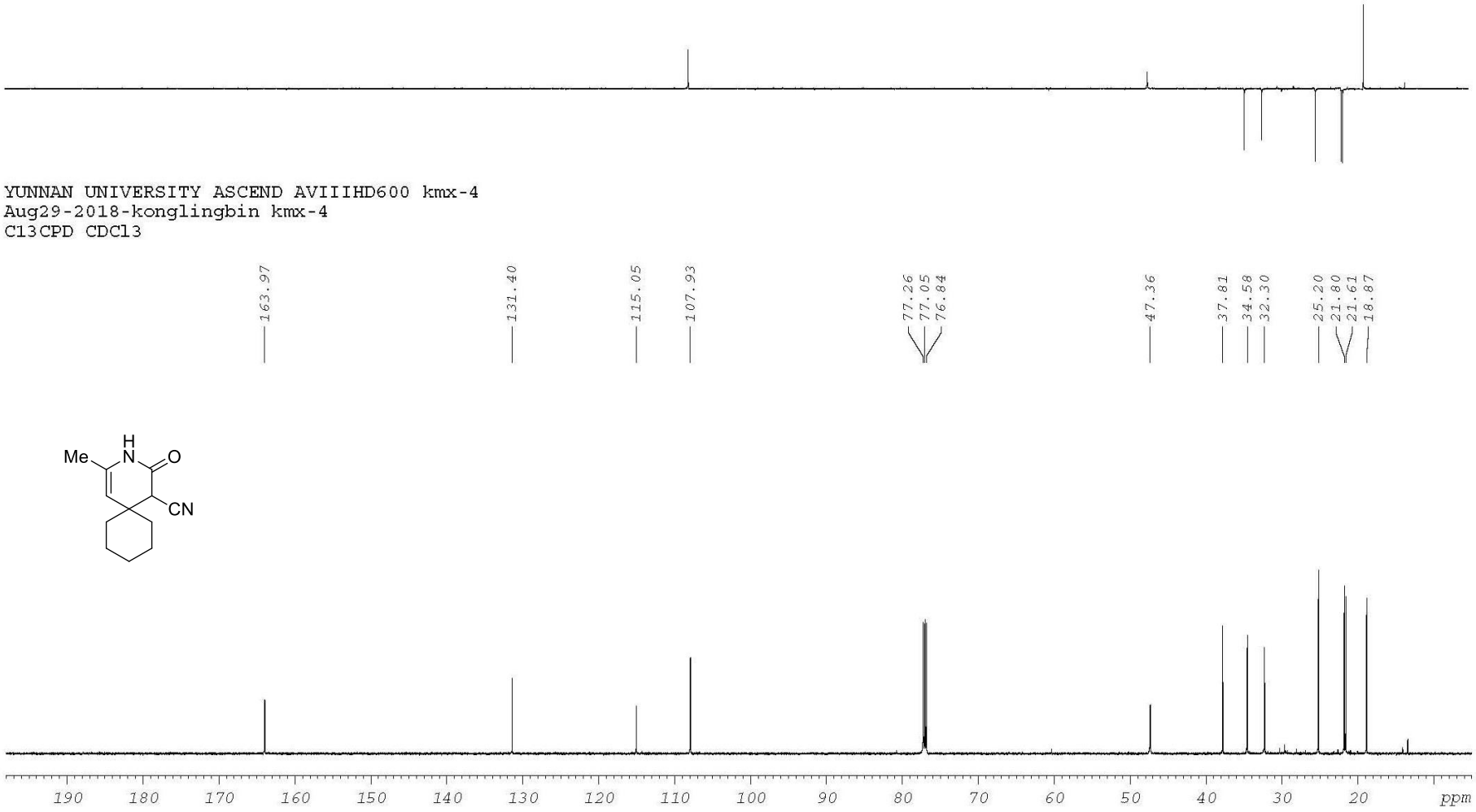


Figure S18. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3a**

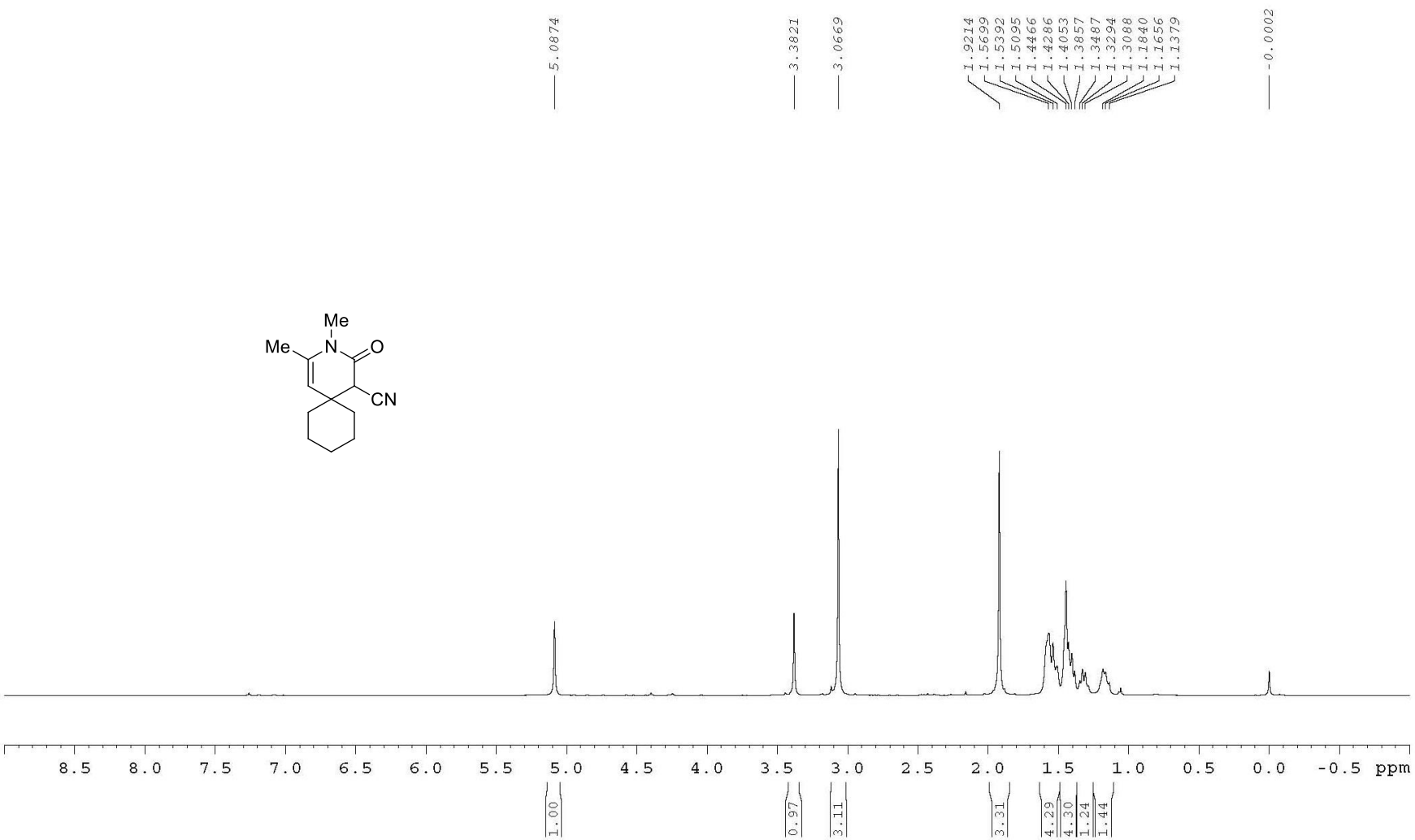


Figure S19. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3b**

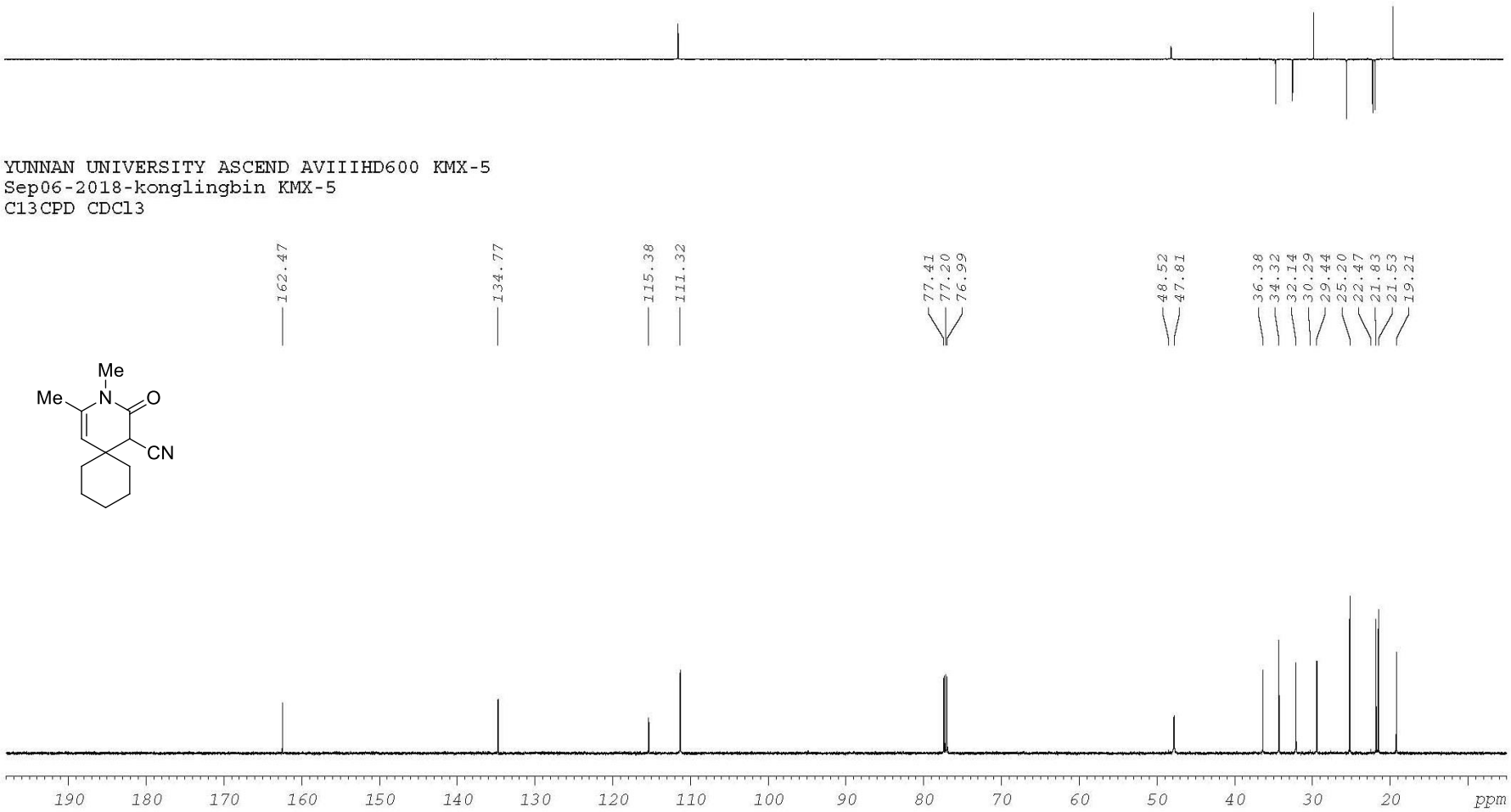


Figure S20. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3b**

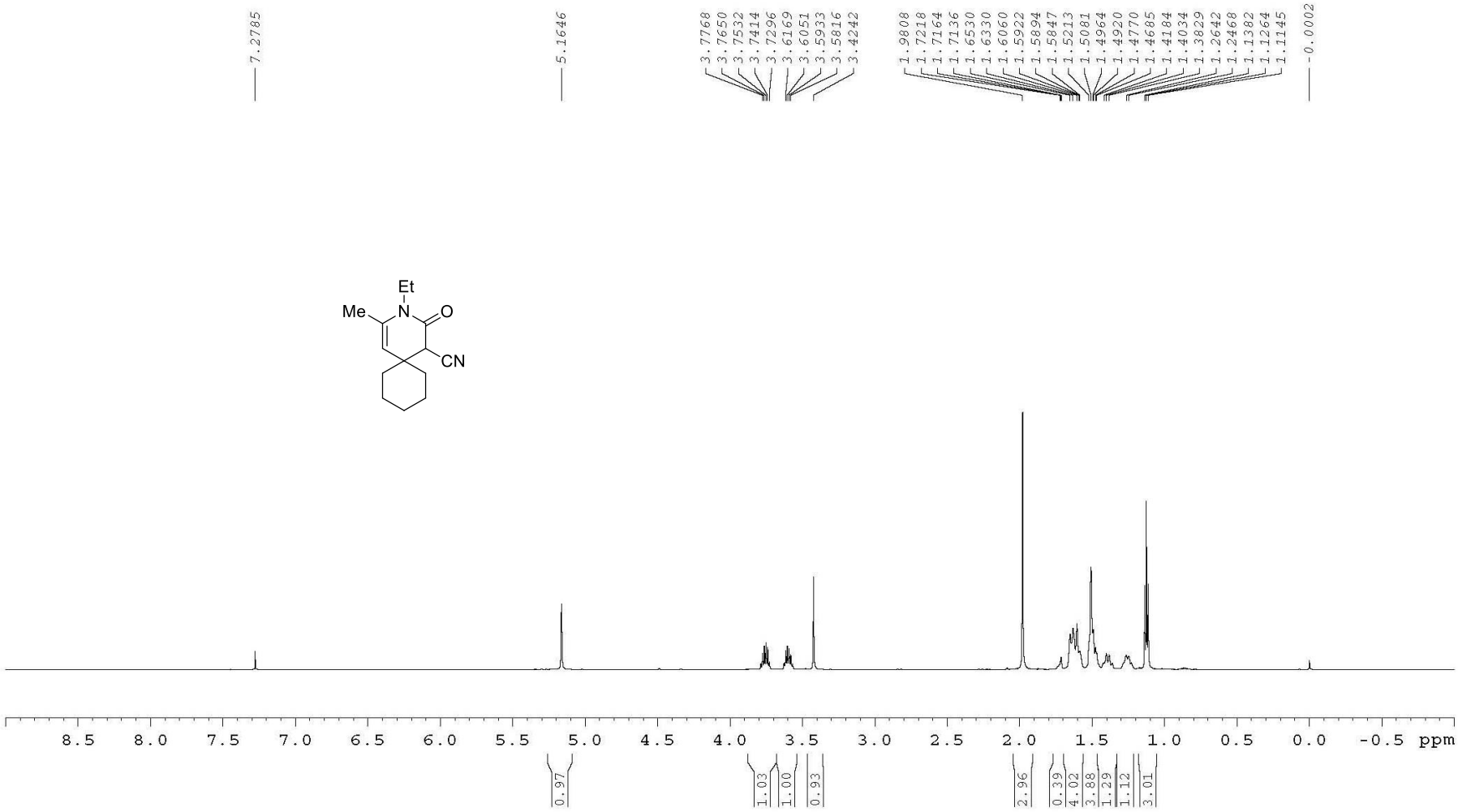


Figure S21. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3c**

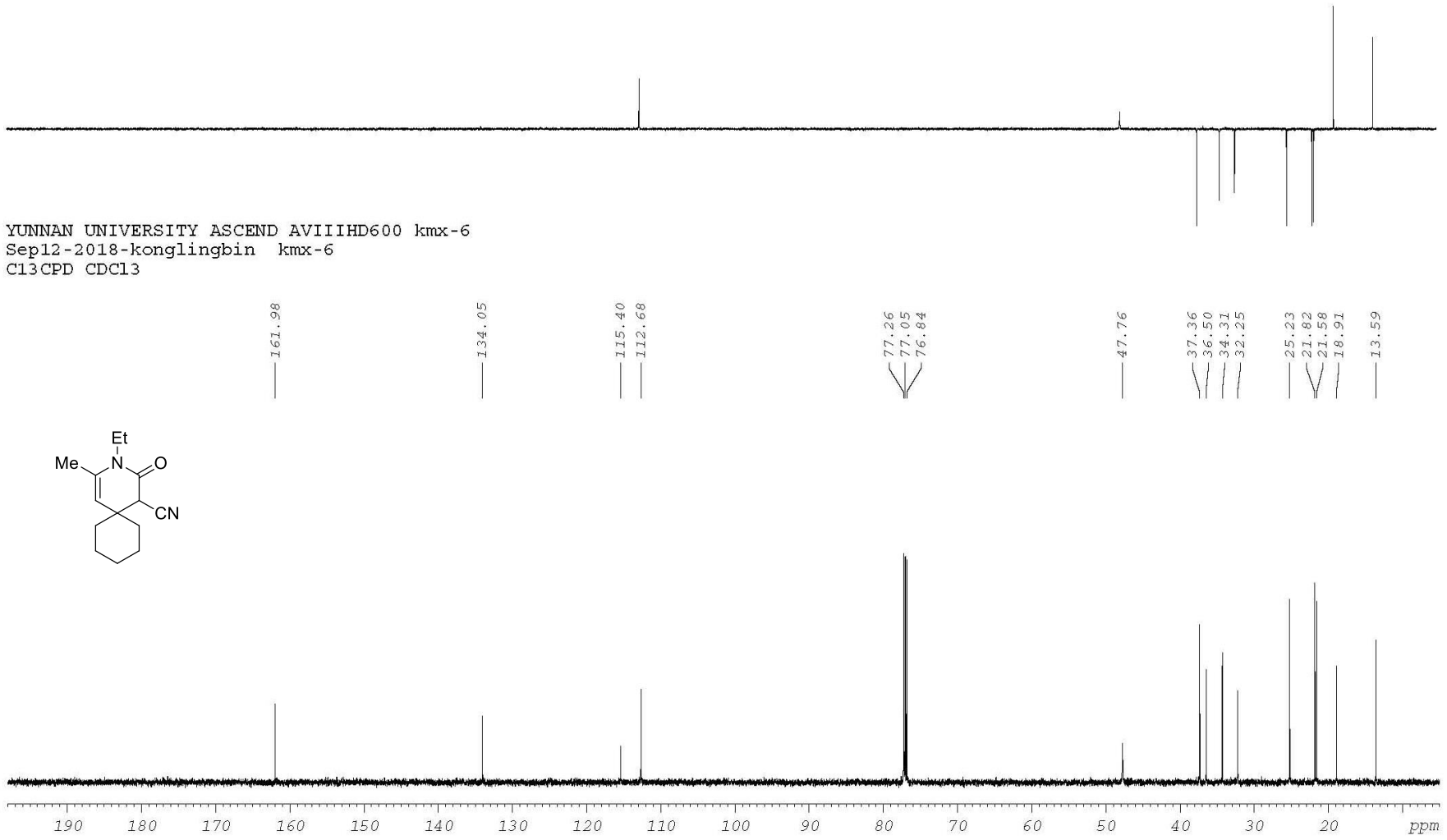


Figure S22. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3c**

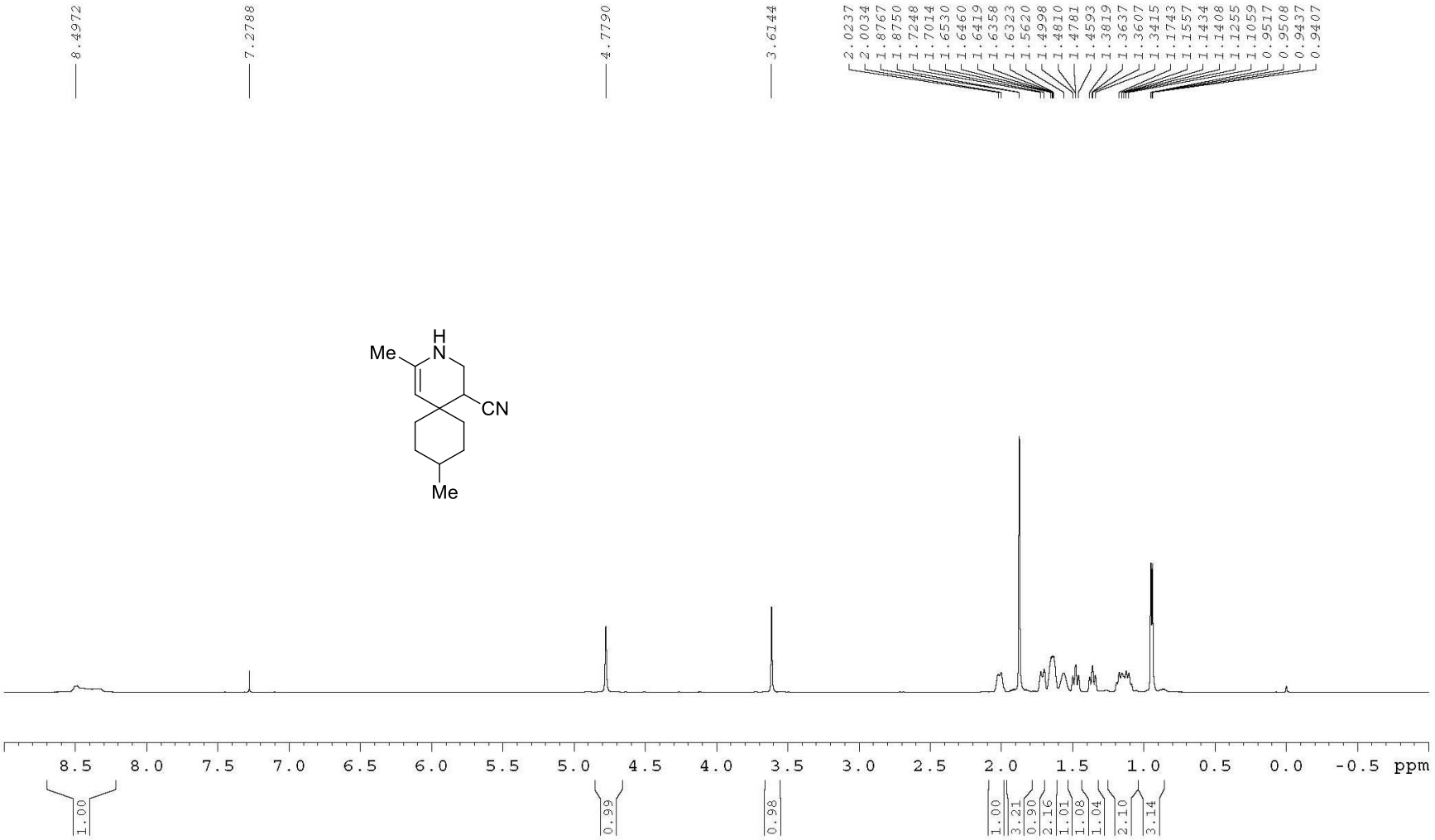


Figure S23. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3d**

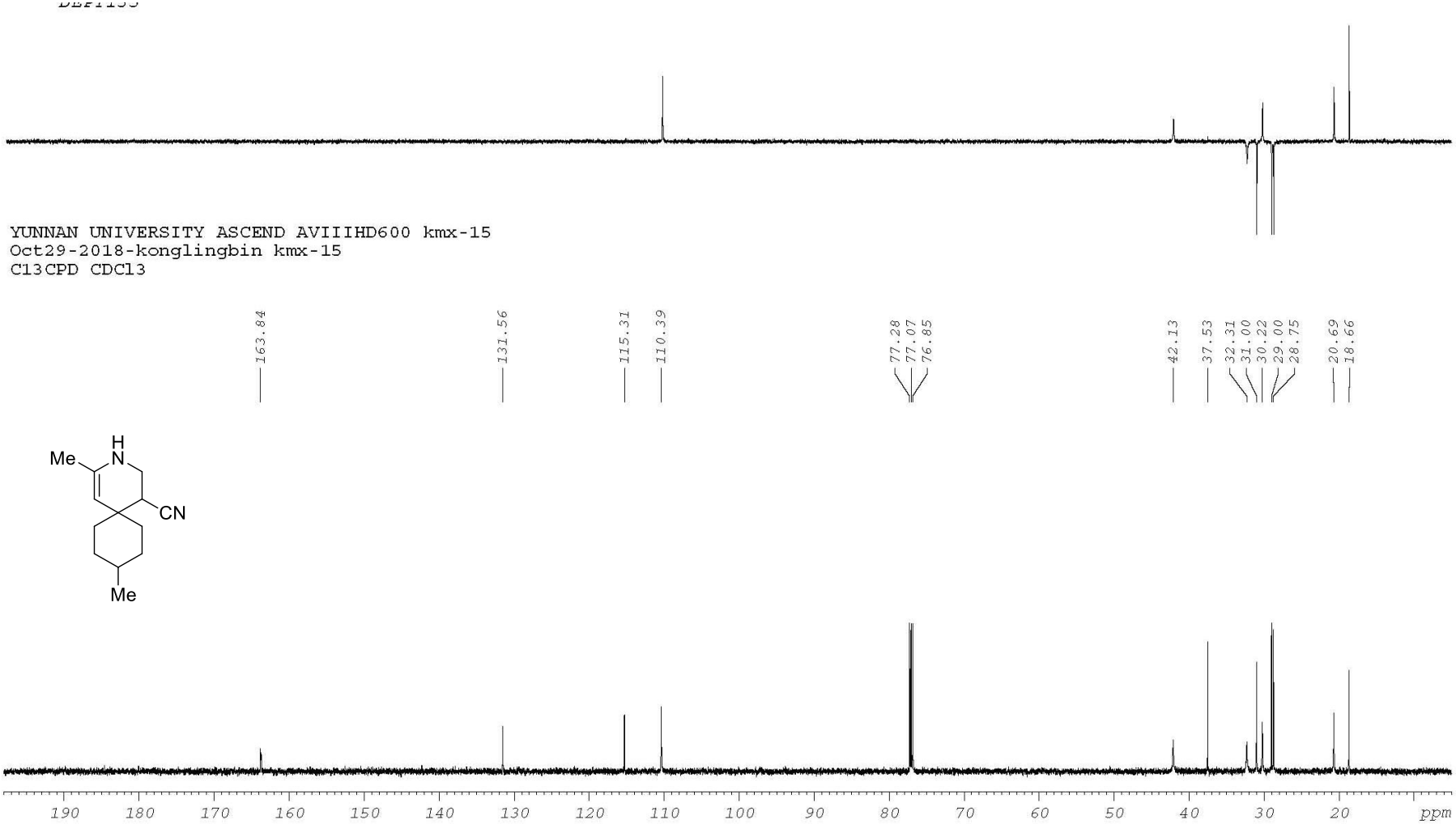


Figure S24. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3d**

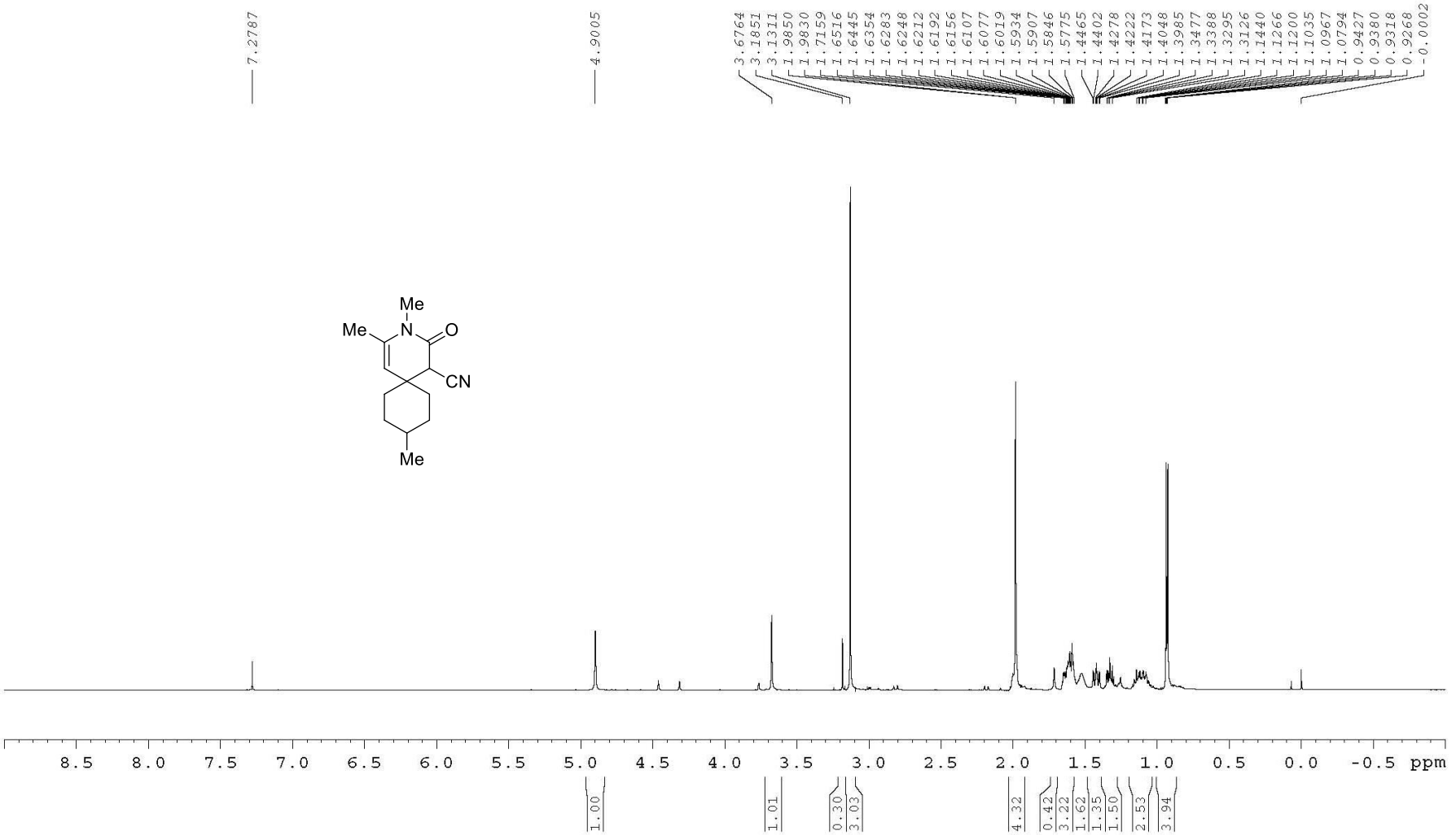


Figure S25. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3e**

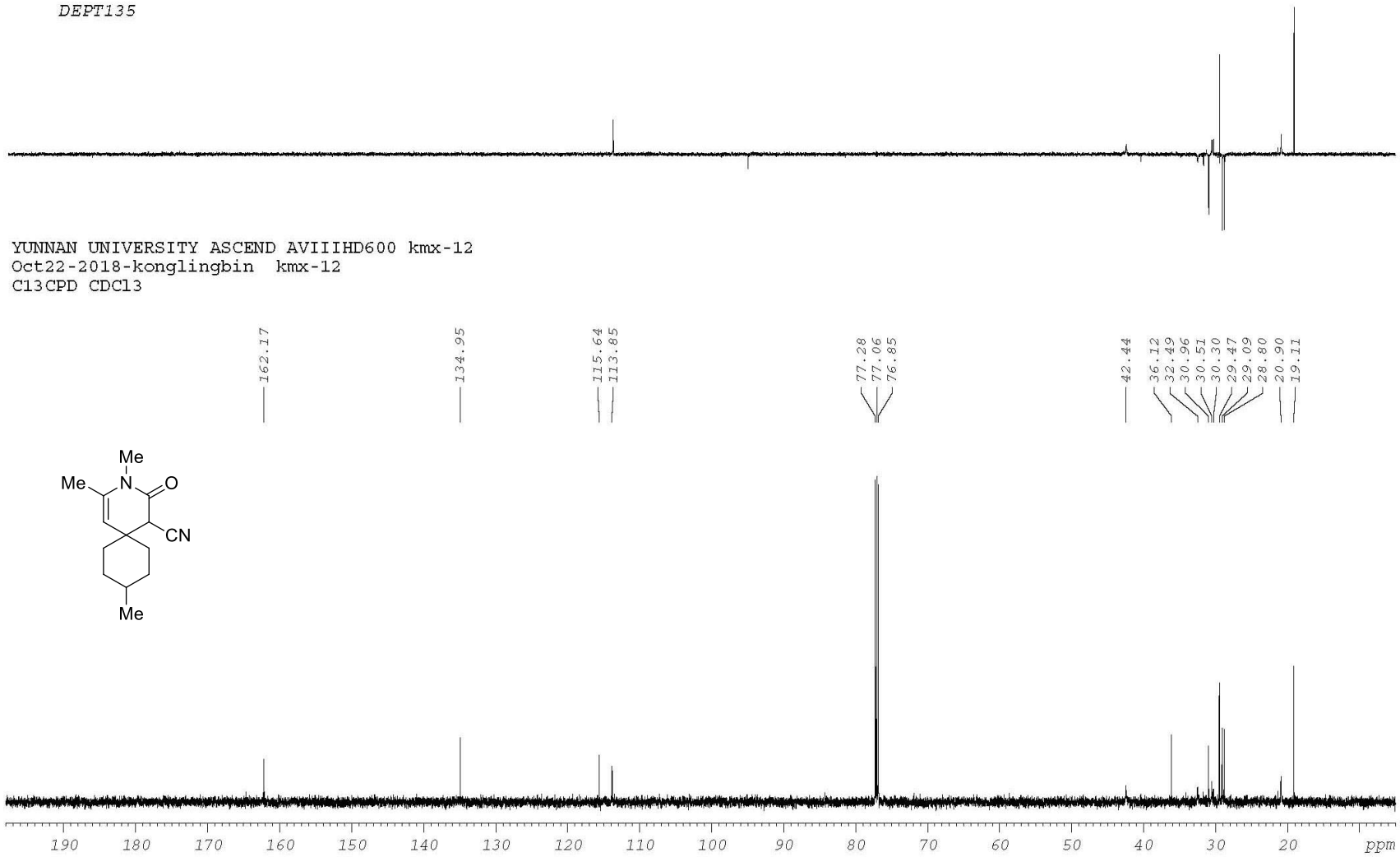


Figure S26. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3e**

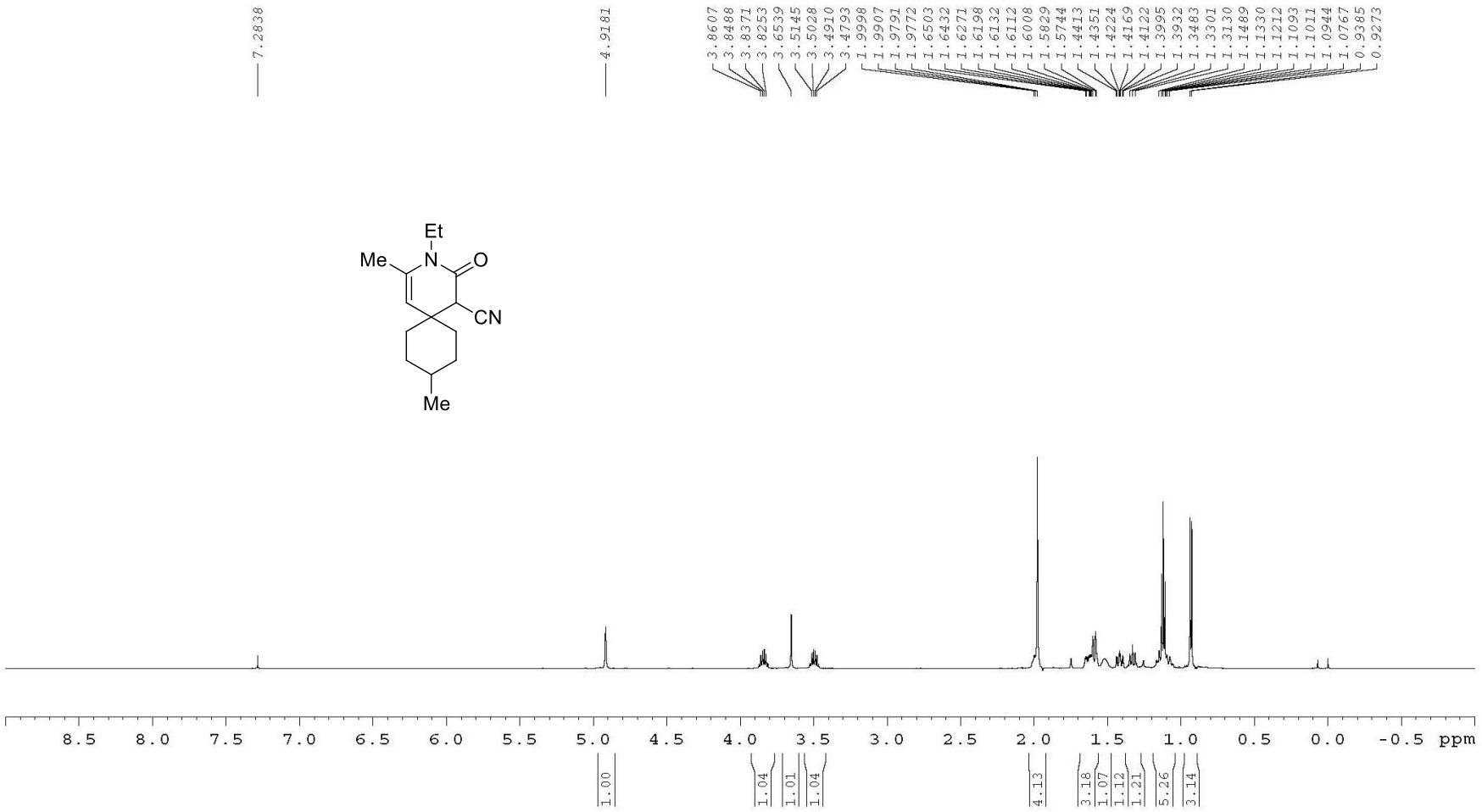


Figure S27. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3f**

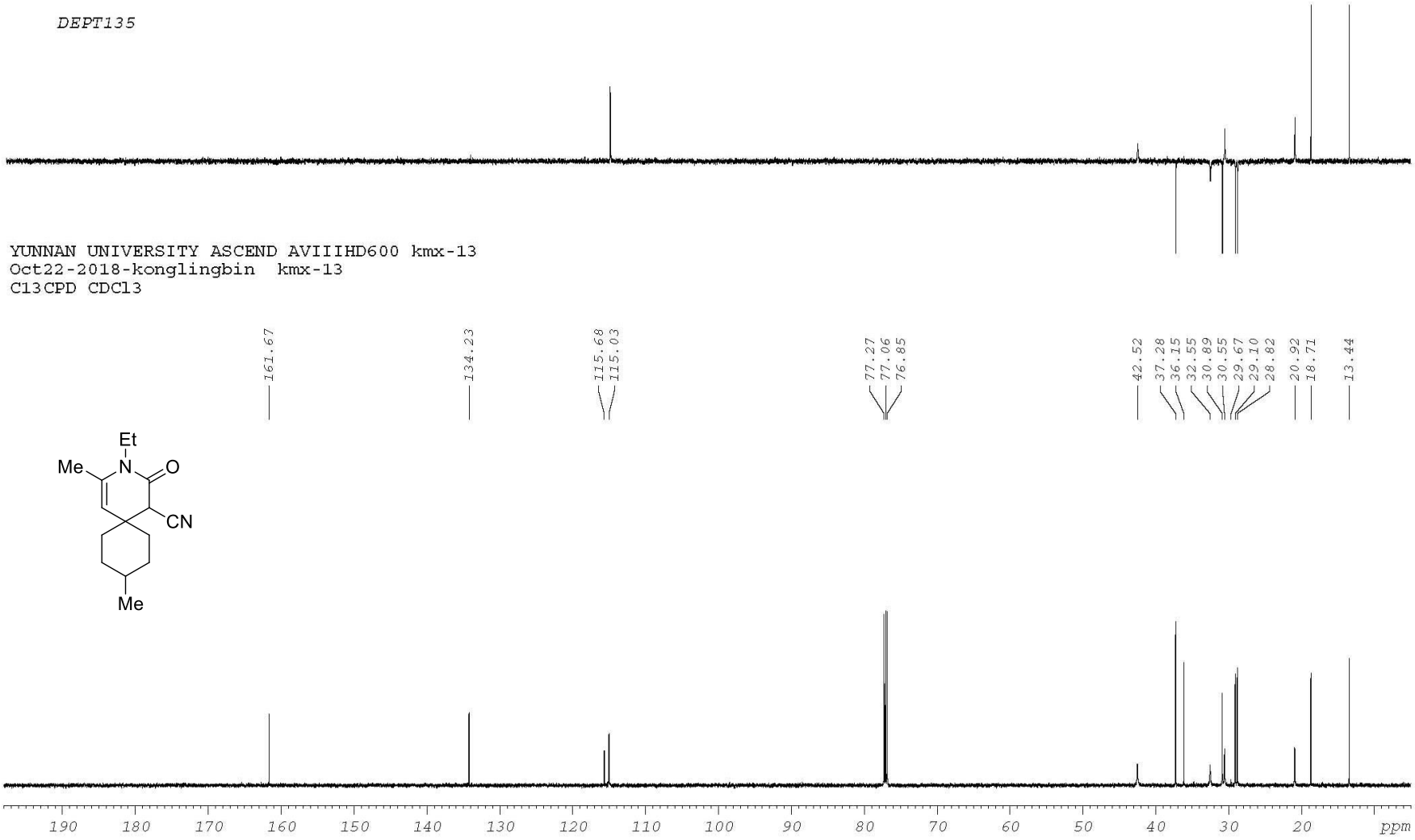


Figure S28. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3f**

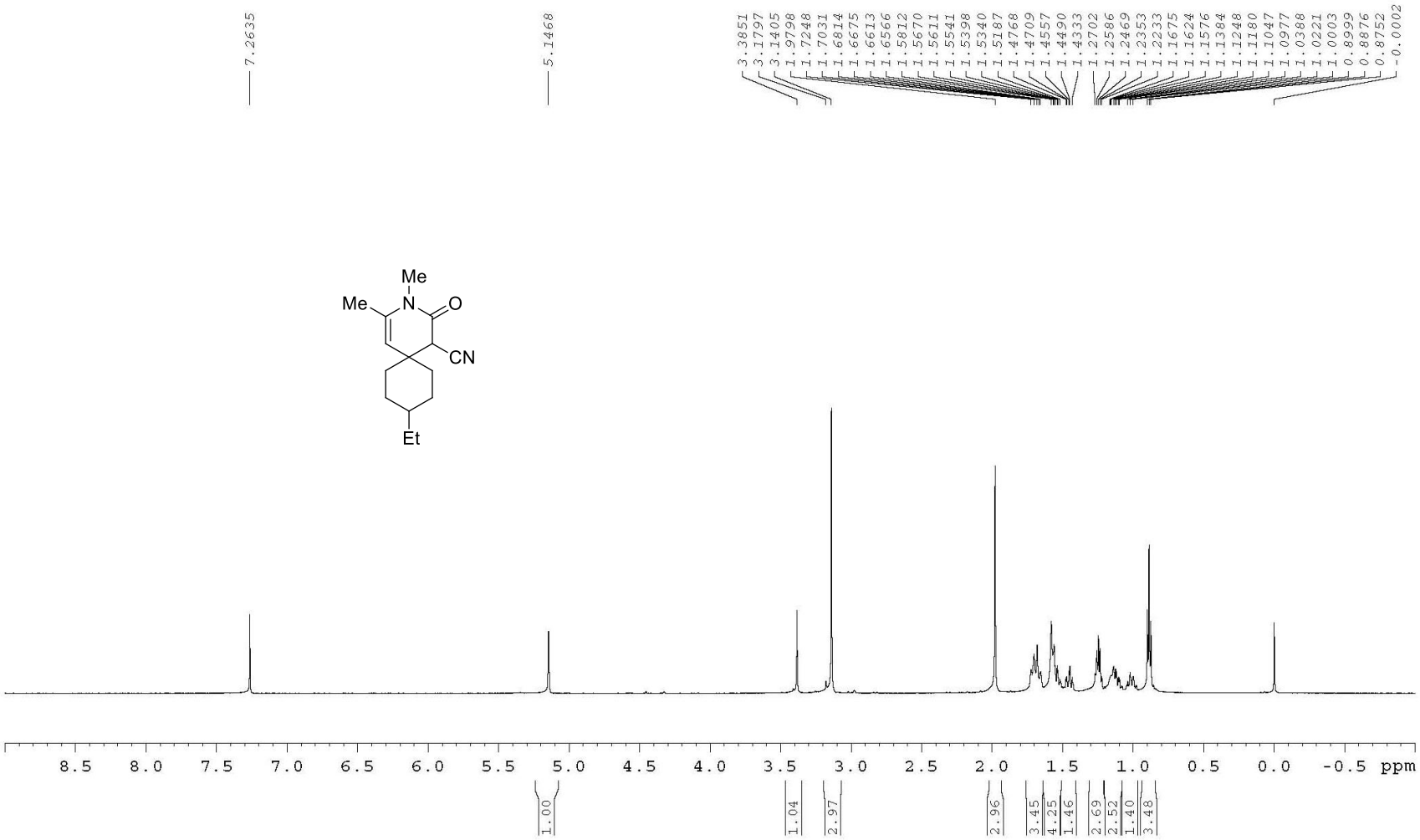


Figure S29. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3g**

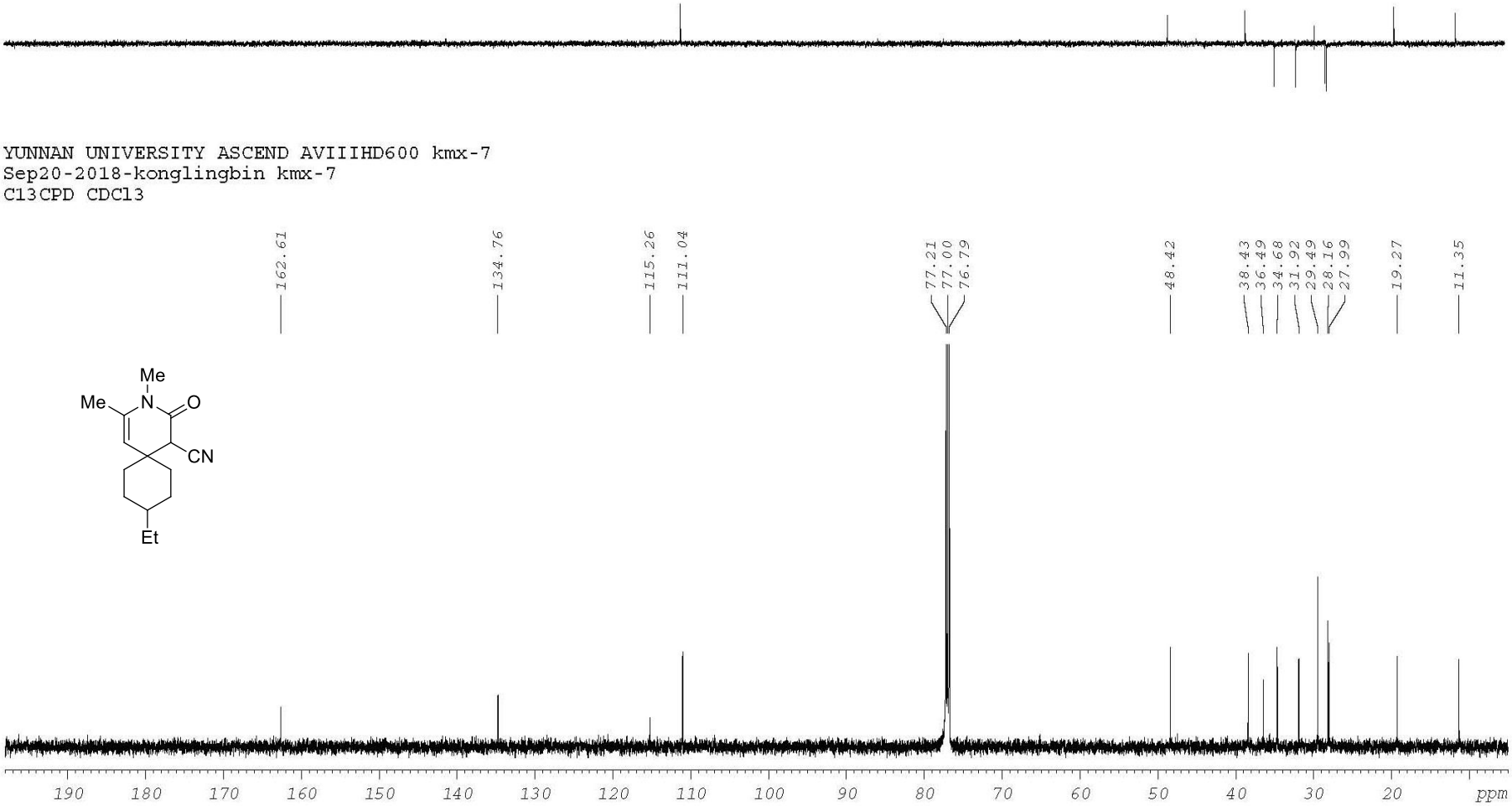


Figure S30. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3g**

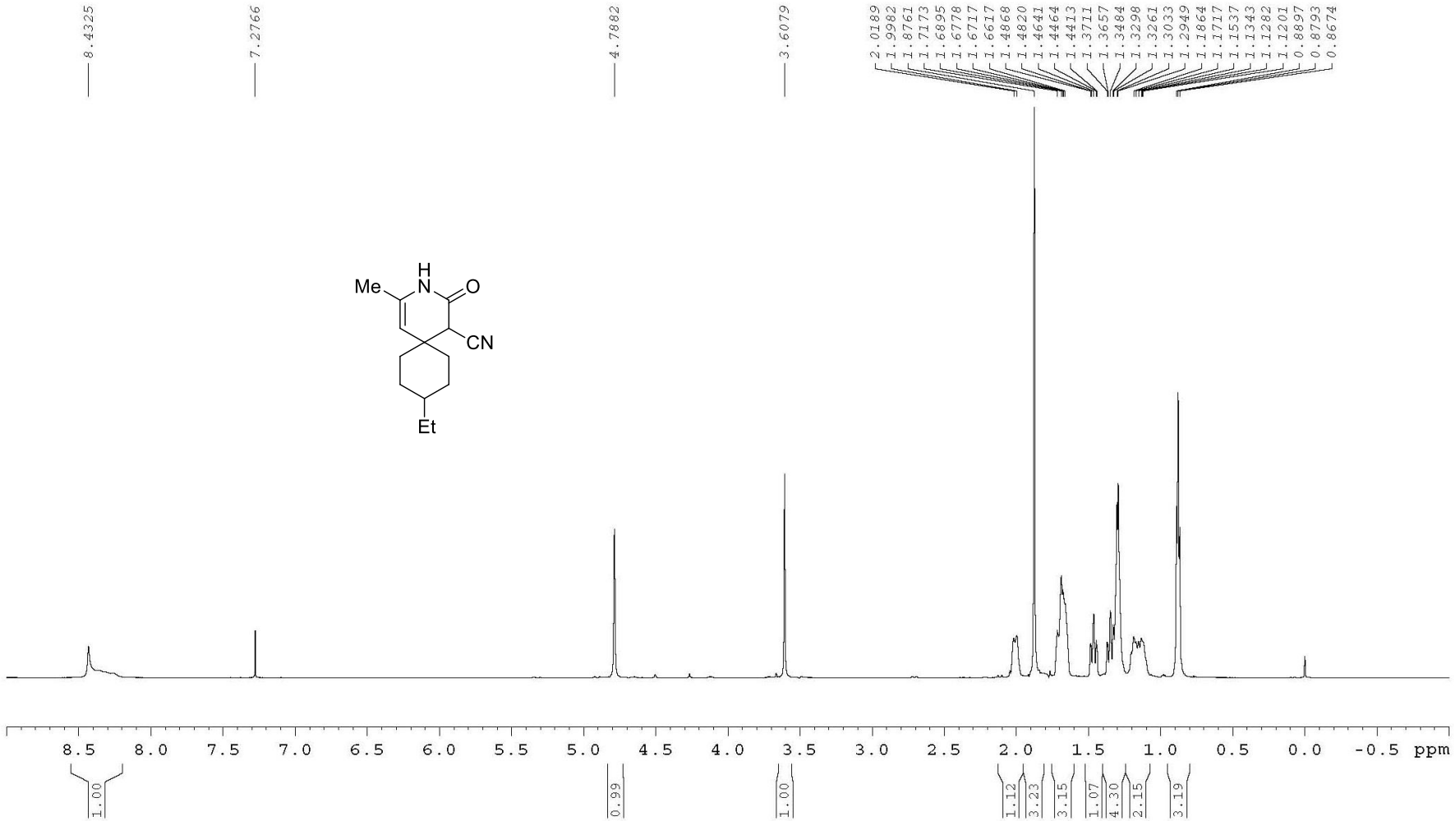


Figure S31. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3h**

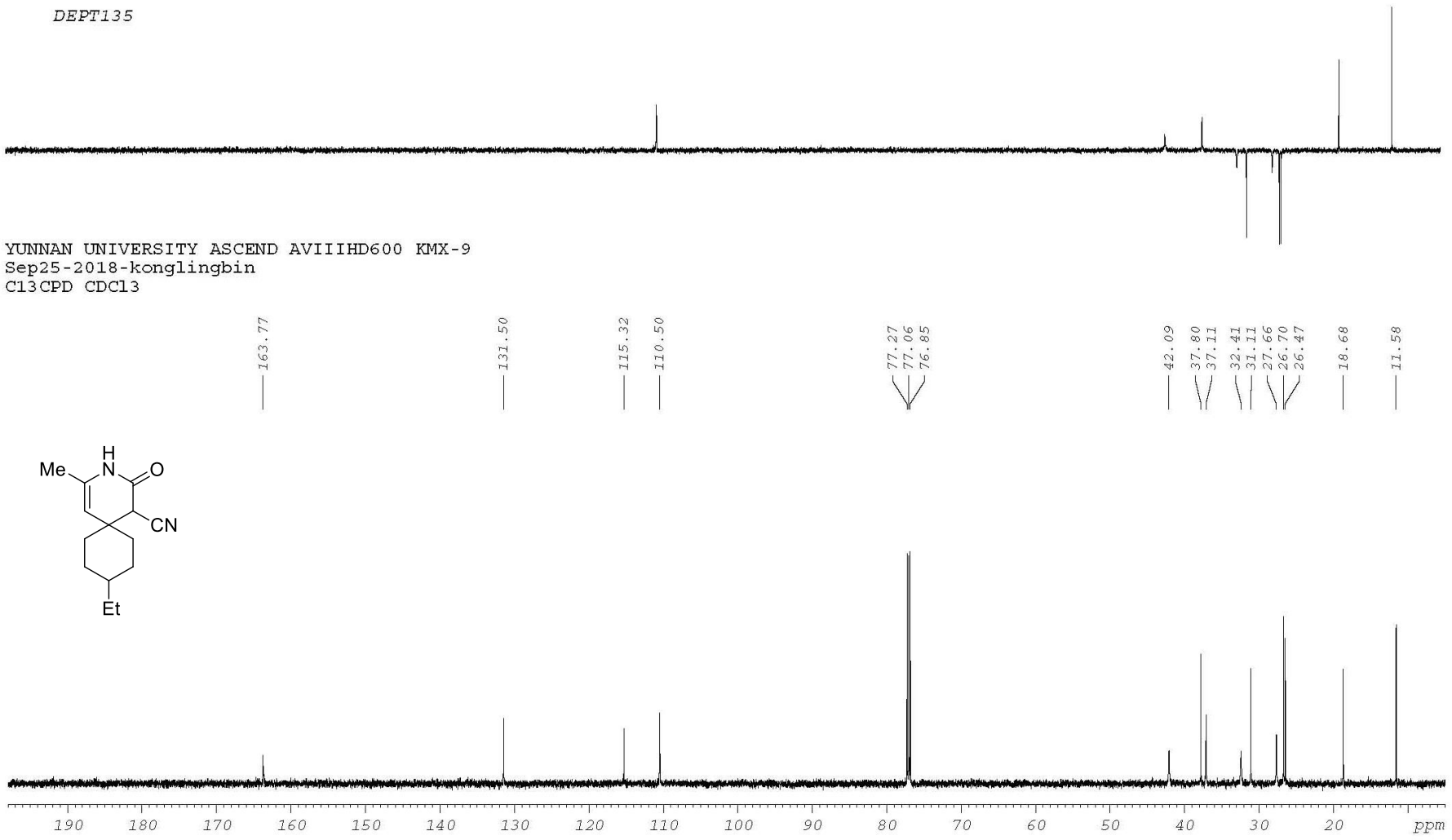


Figure S32. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3h**

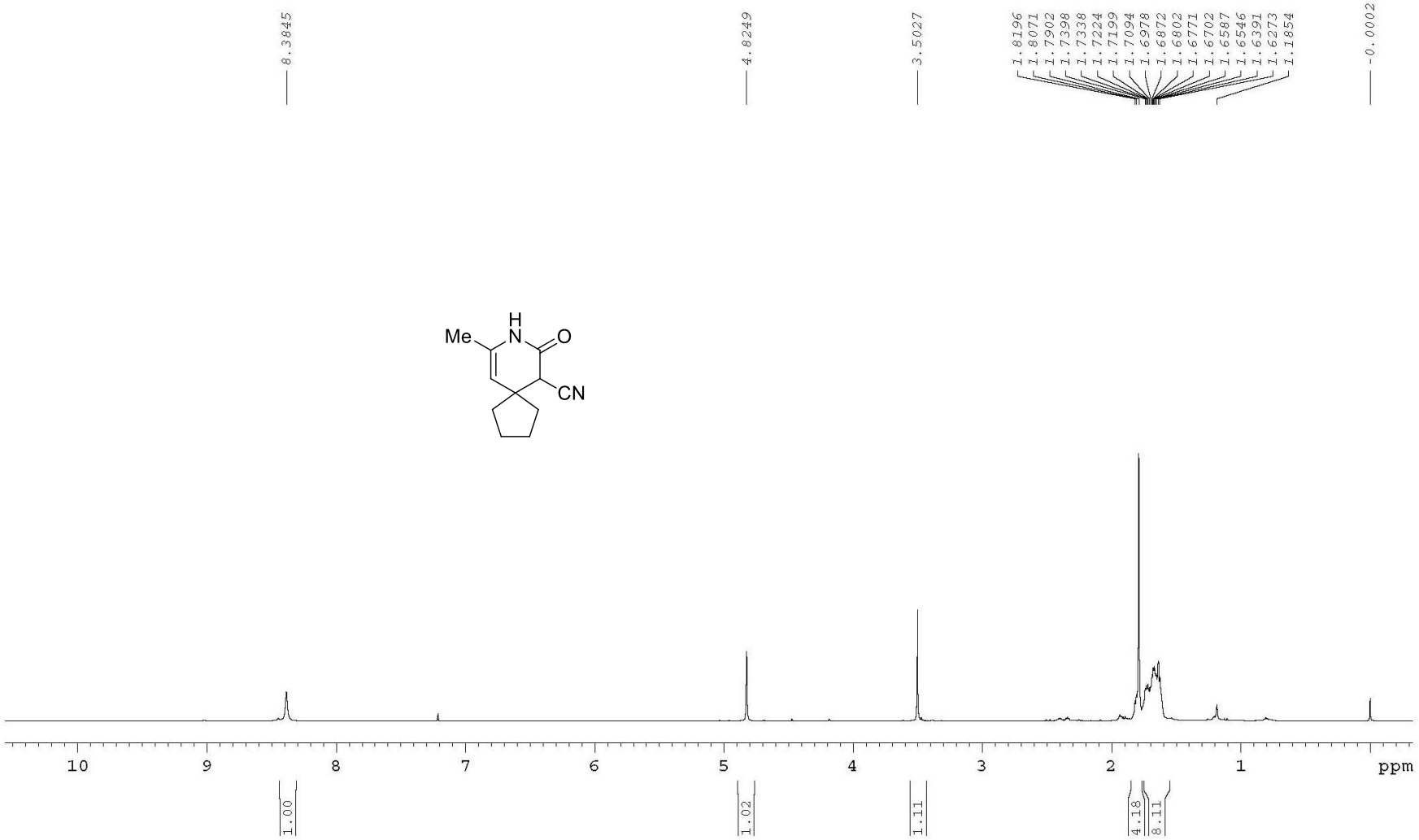


Figure S33. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3i**

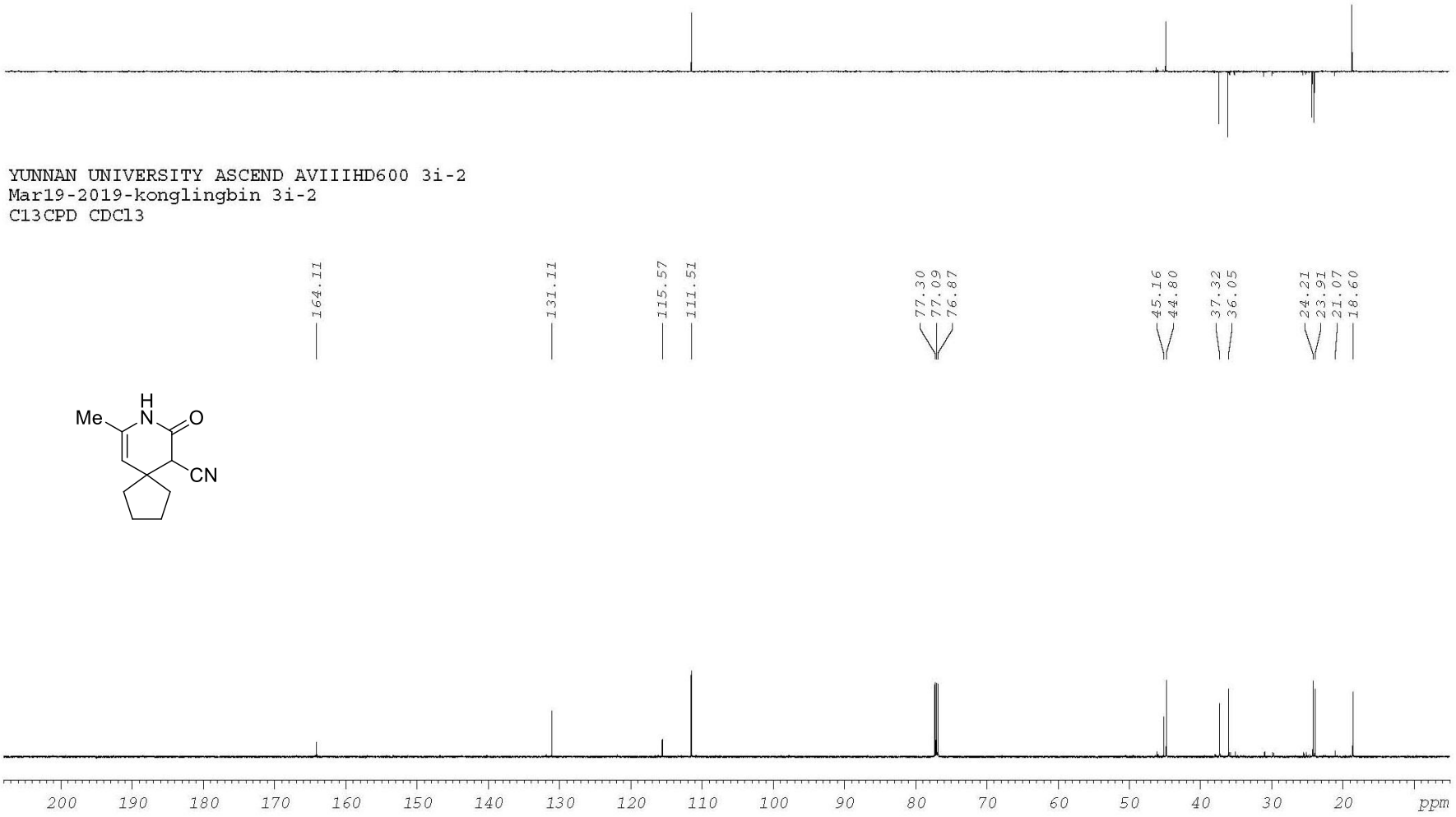


Figure S34. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3i**

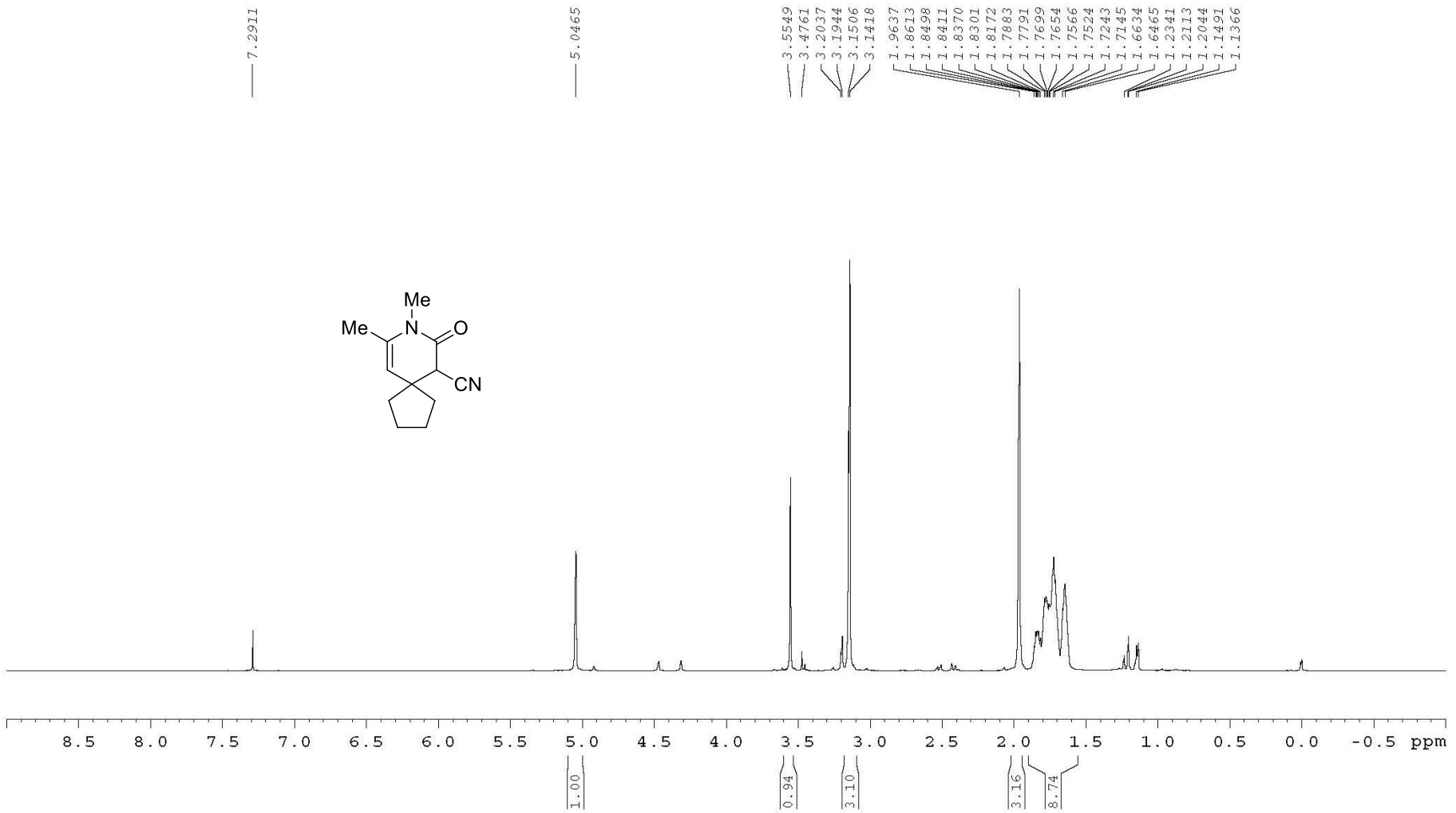


Figure S35. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3j**

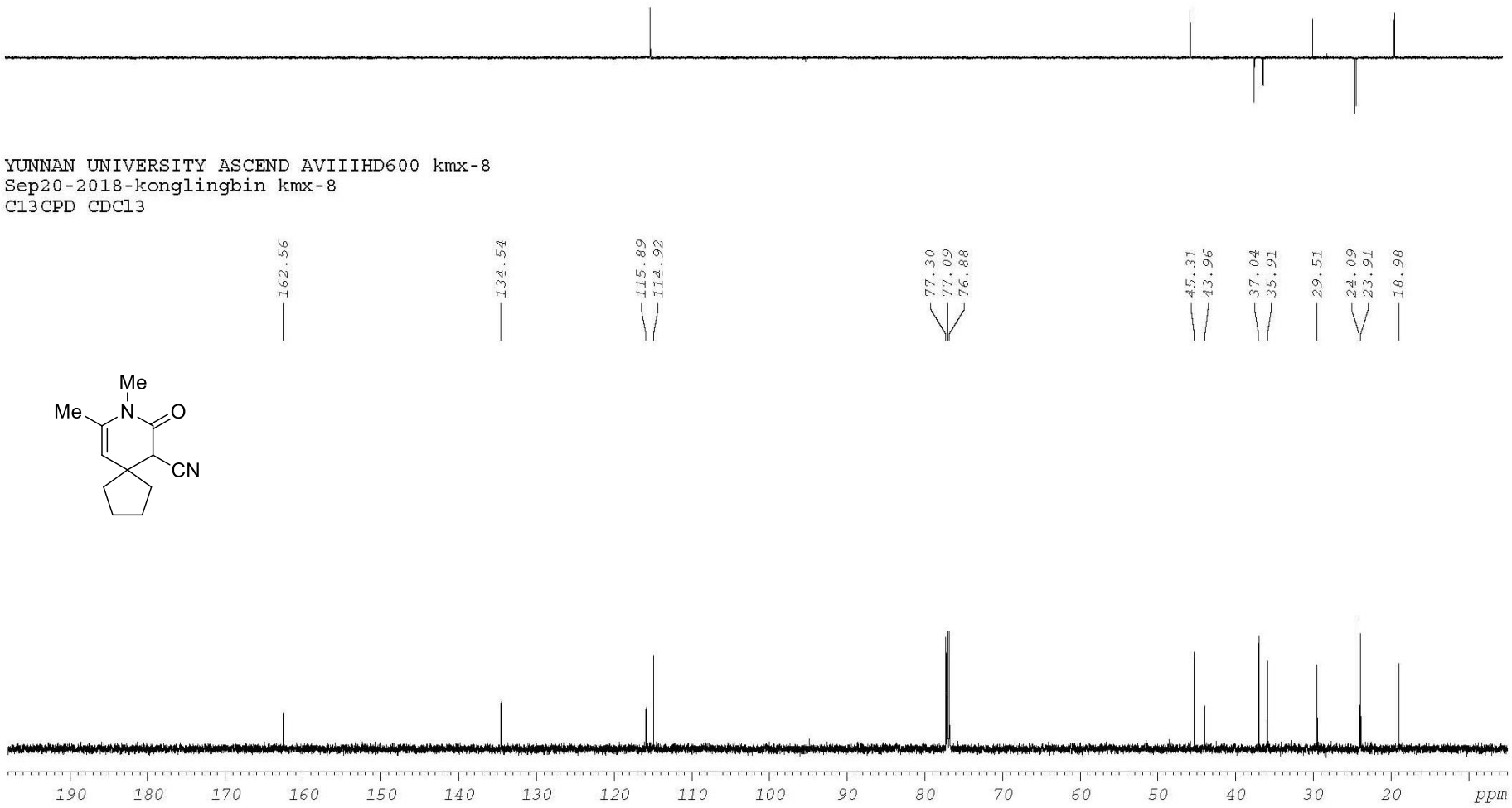


Figure S36. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3j**

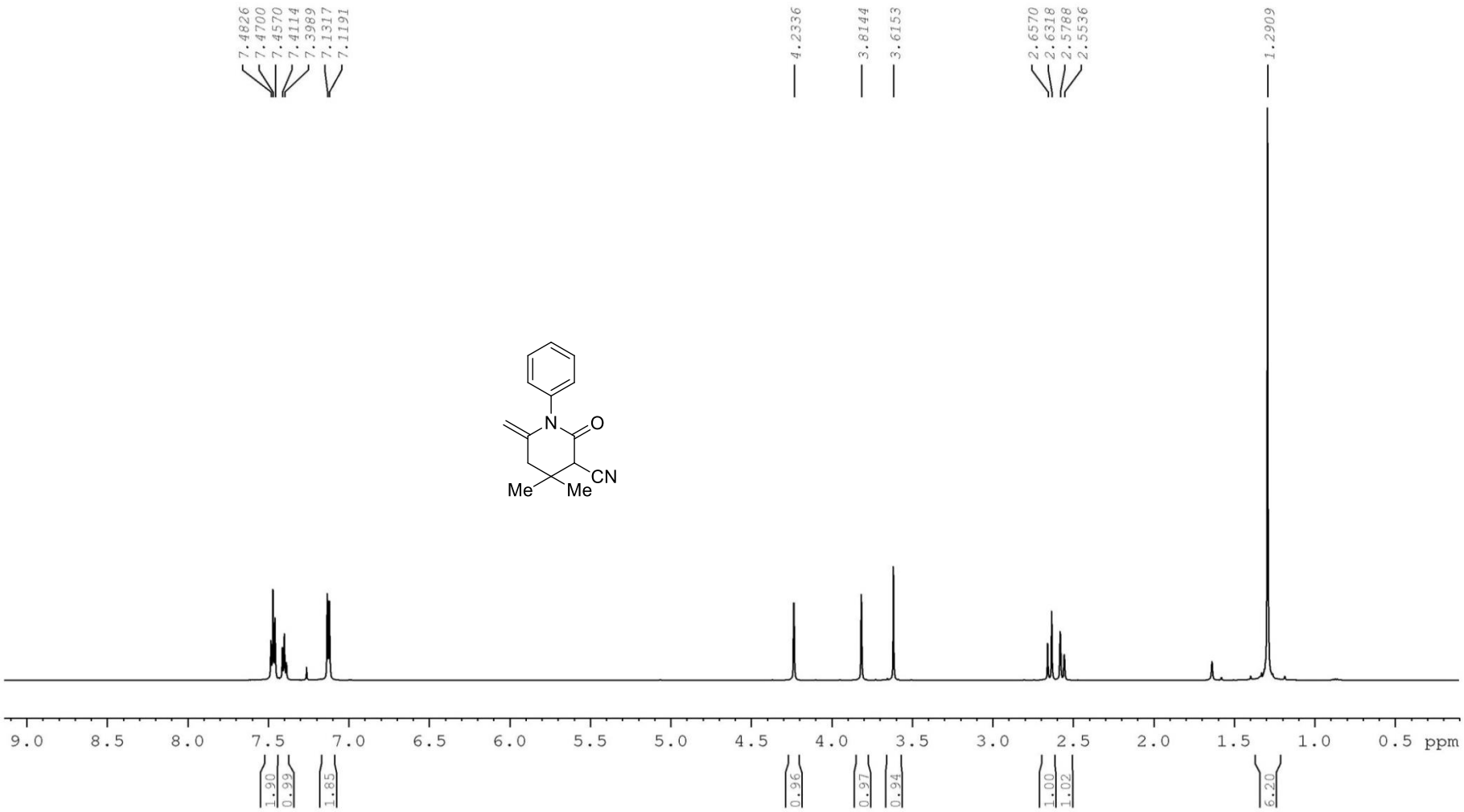


Figure S37. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4a**

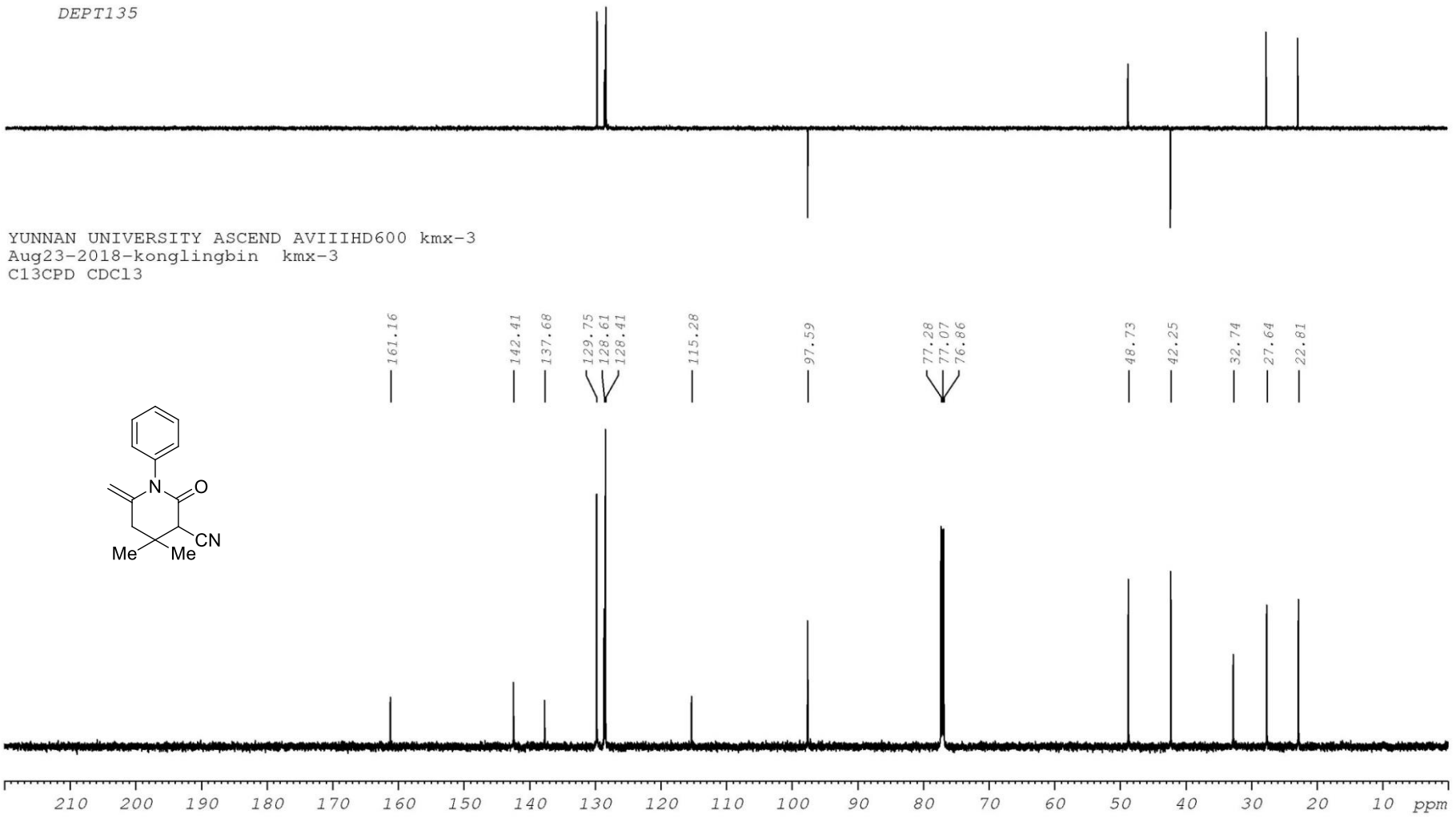


Figure S38. ^{13}C NMR (150MHz, $CDCl_3$) spectra of compound **4a**

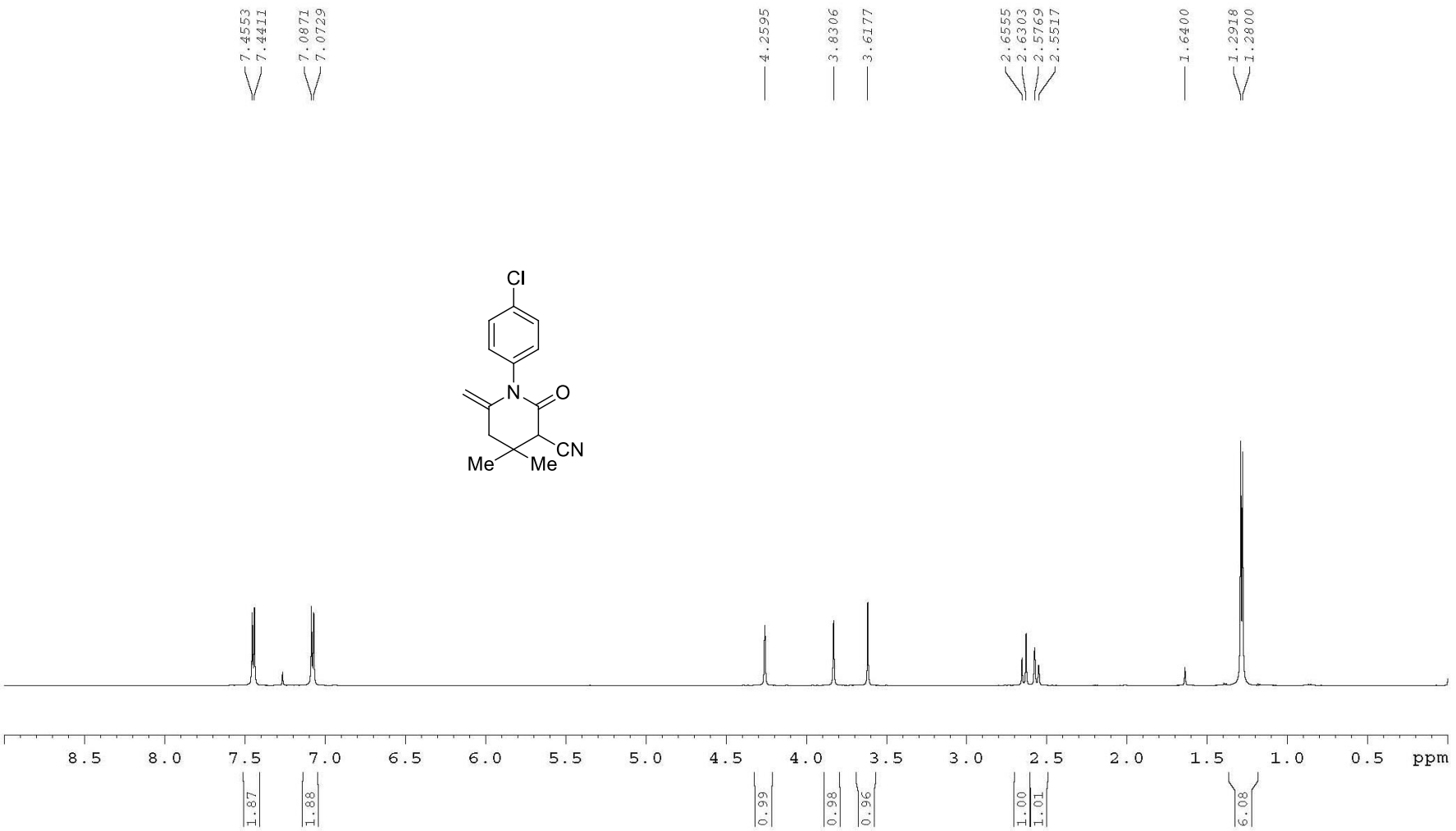


Figure S39. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4b**

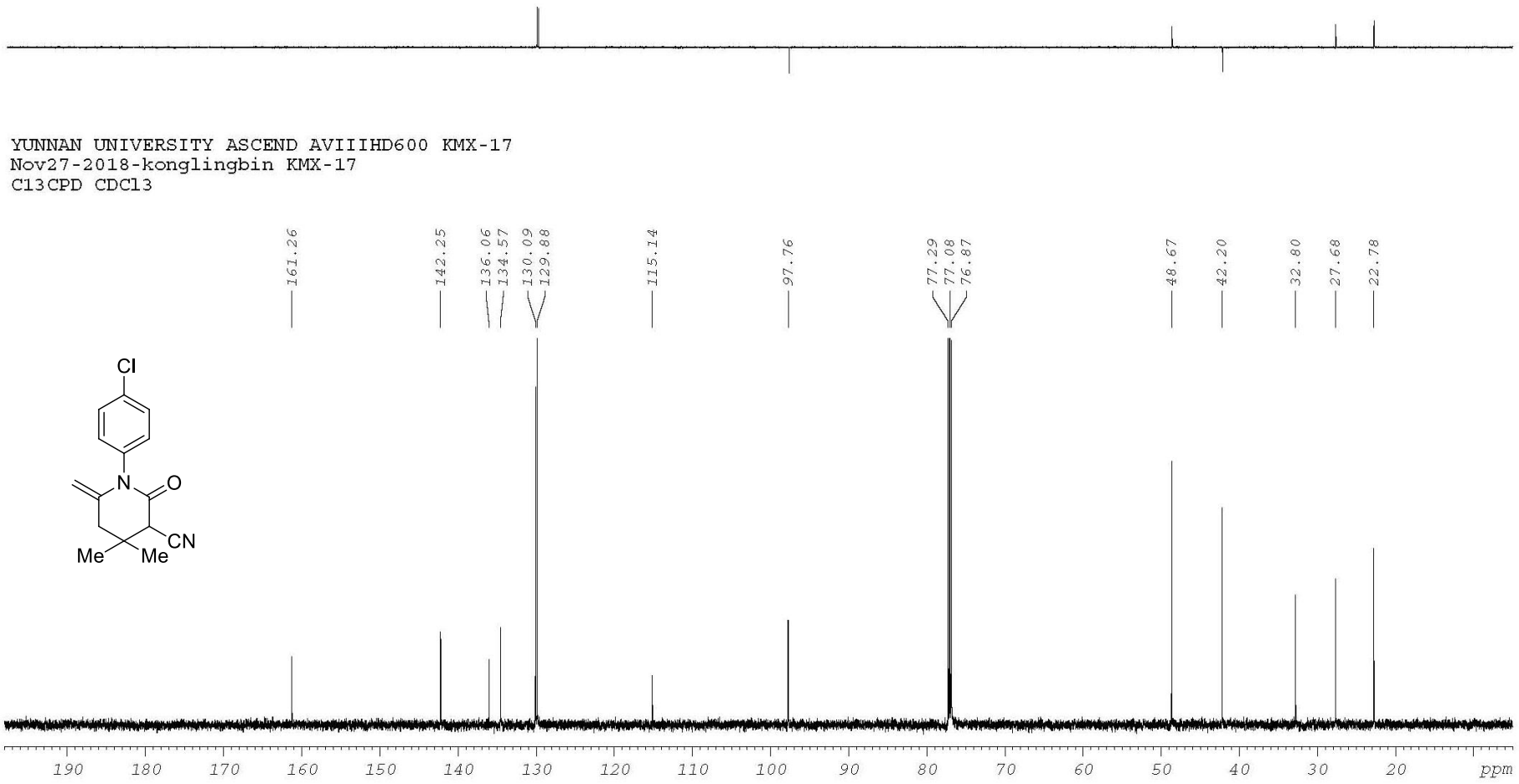


Figure S40. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4b**

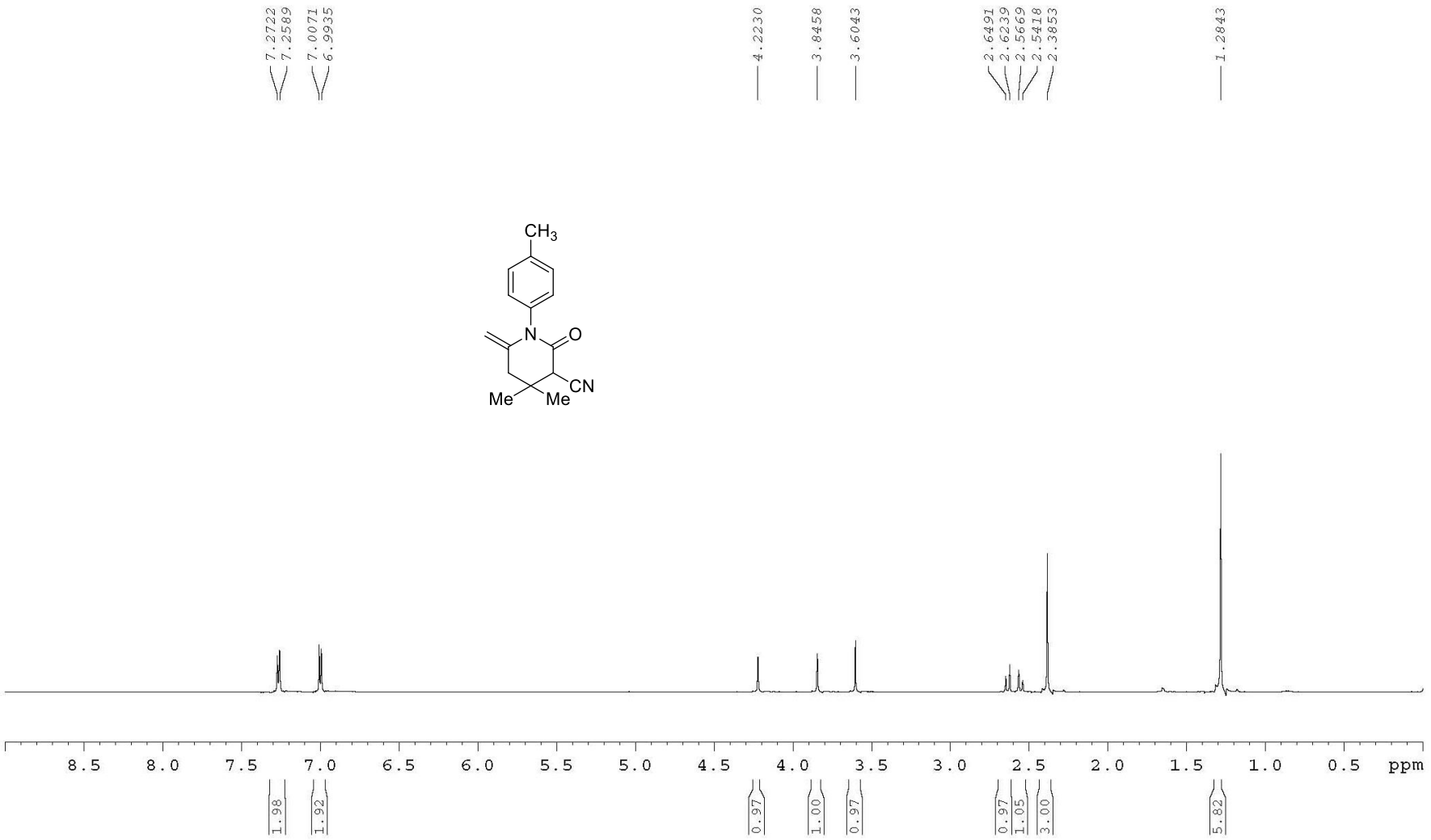


Figure S41. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4c**

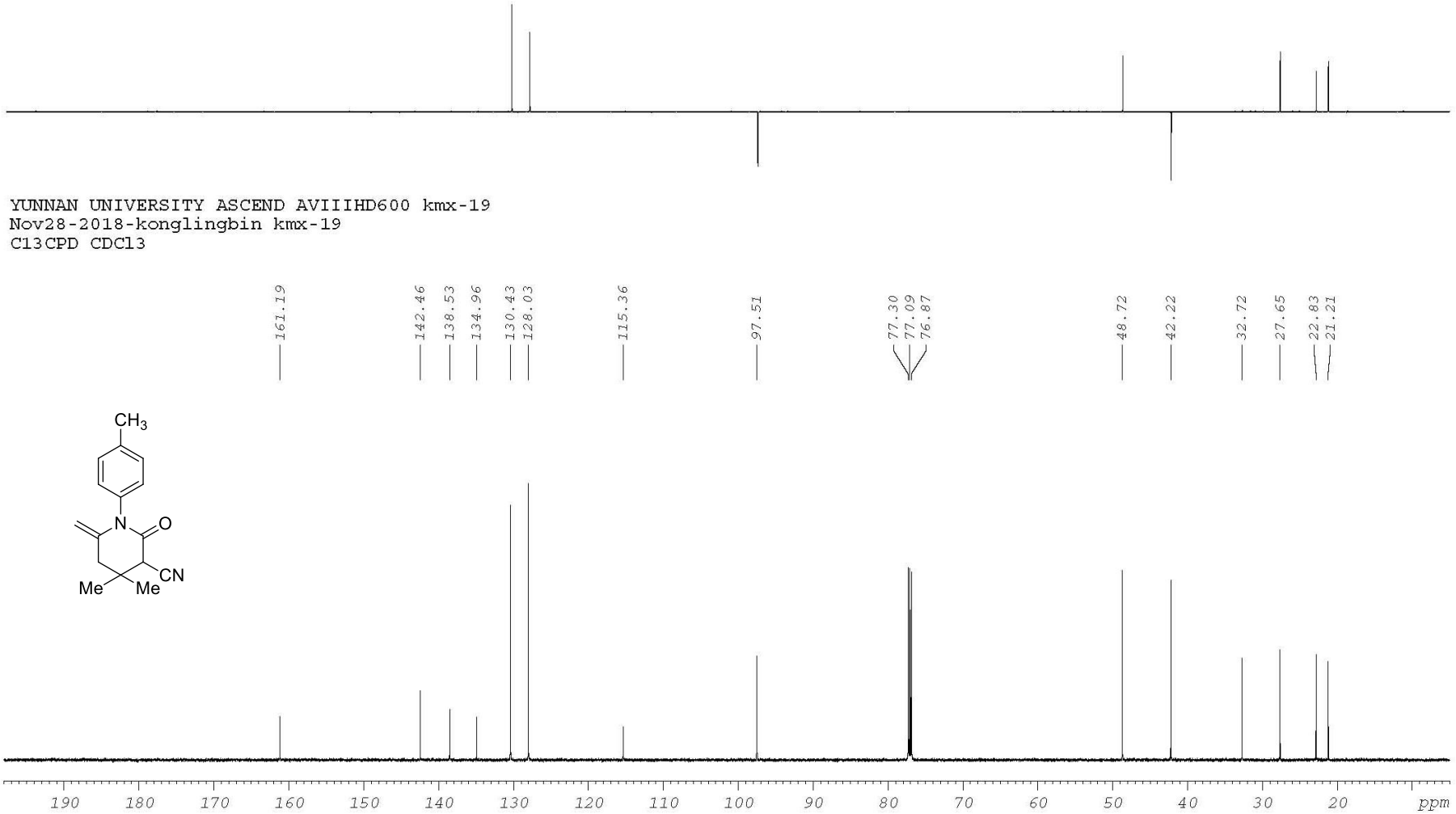


Figure S42. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound**4c**

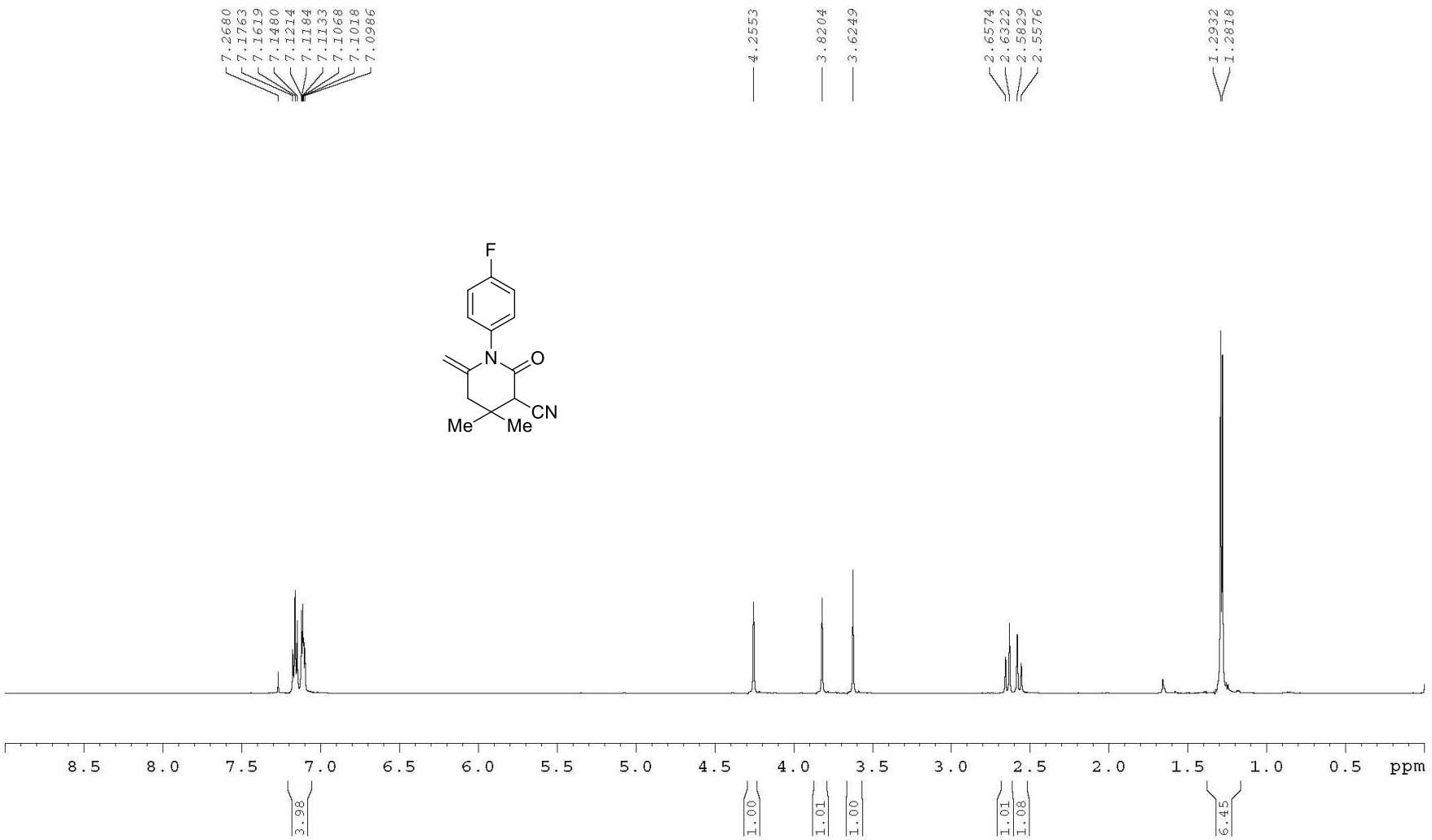


Figure S43. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4d**

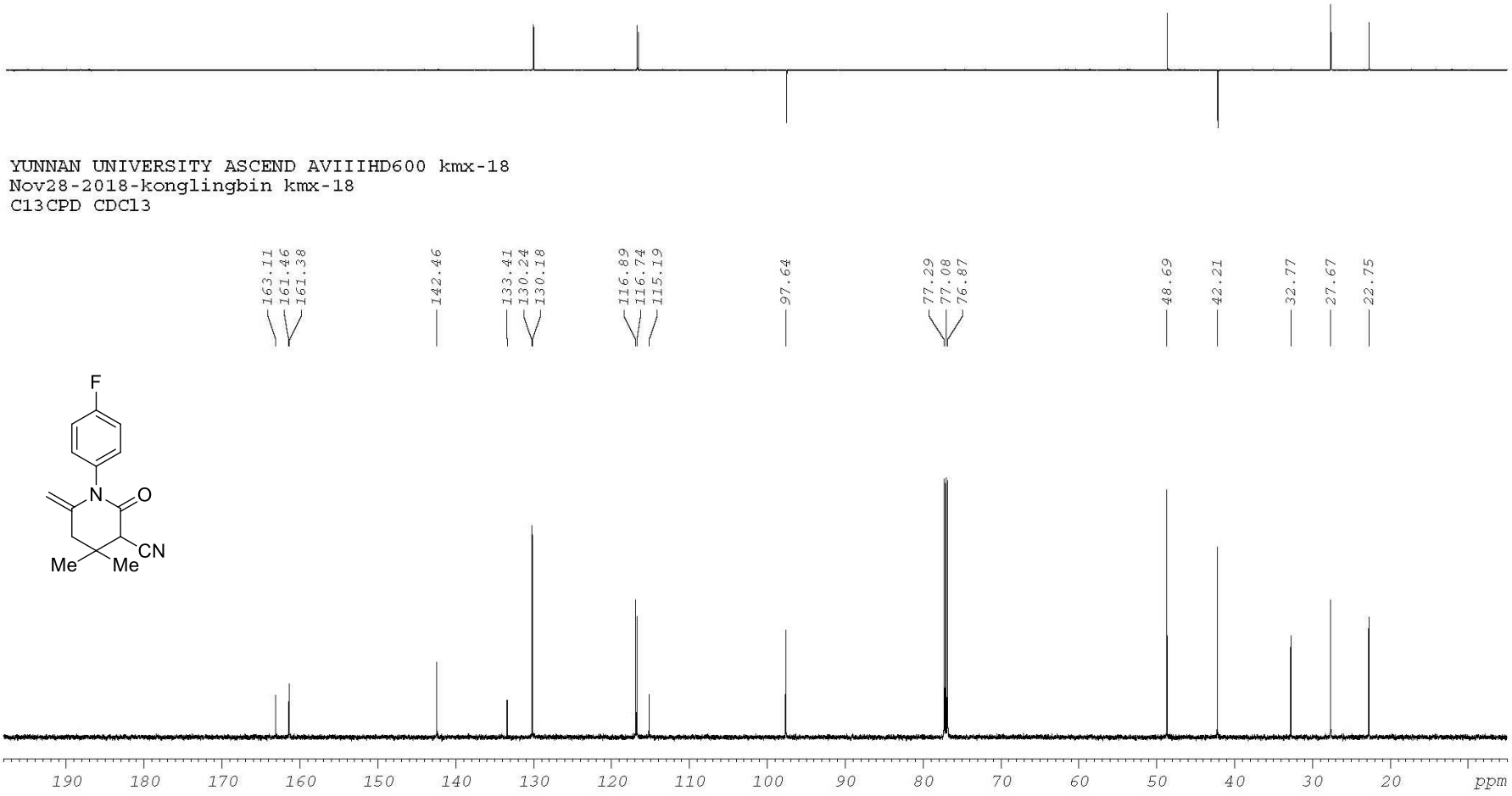


Figure S44. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4e**

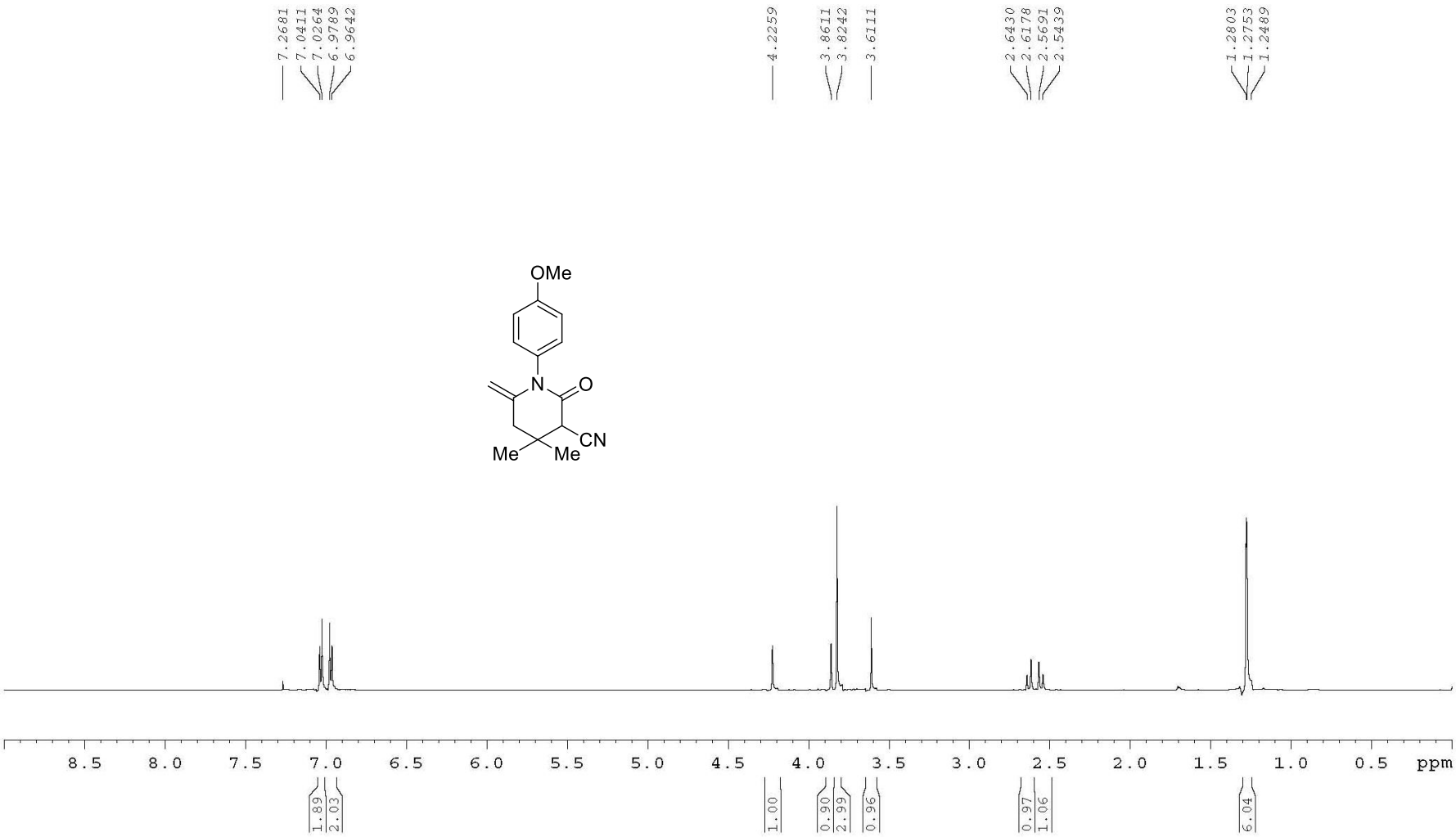


Figure S45. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4e**

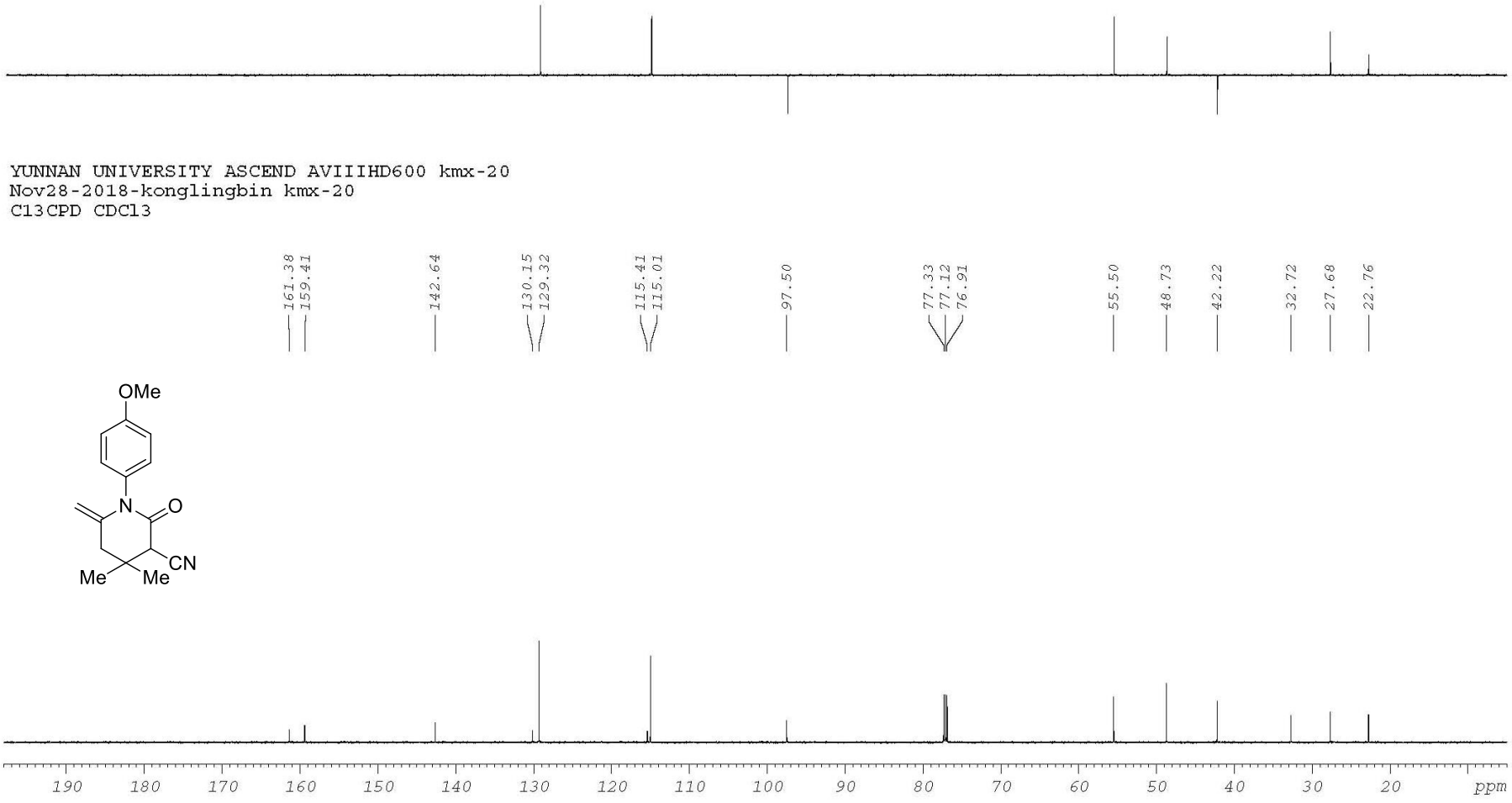


Figure S46. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4e**

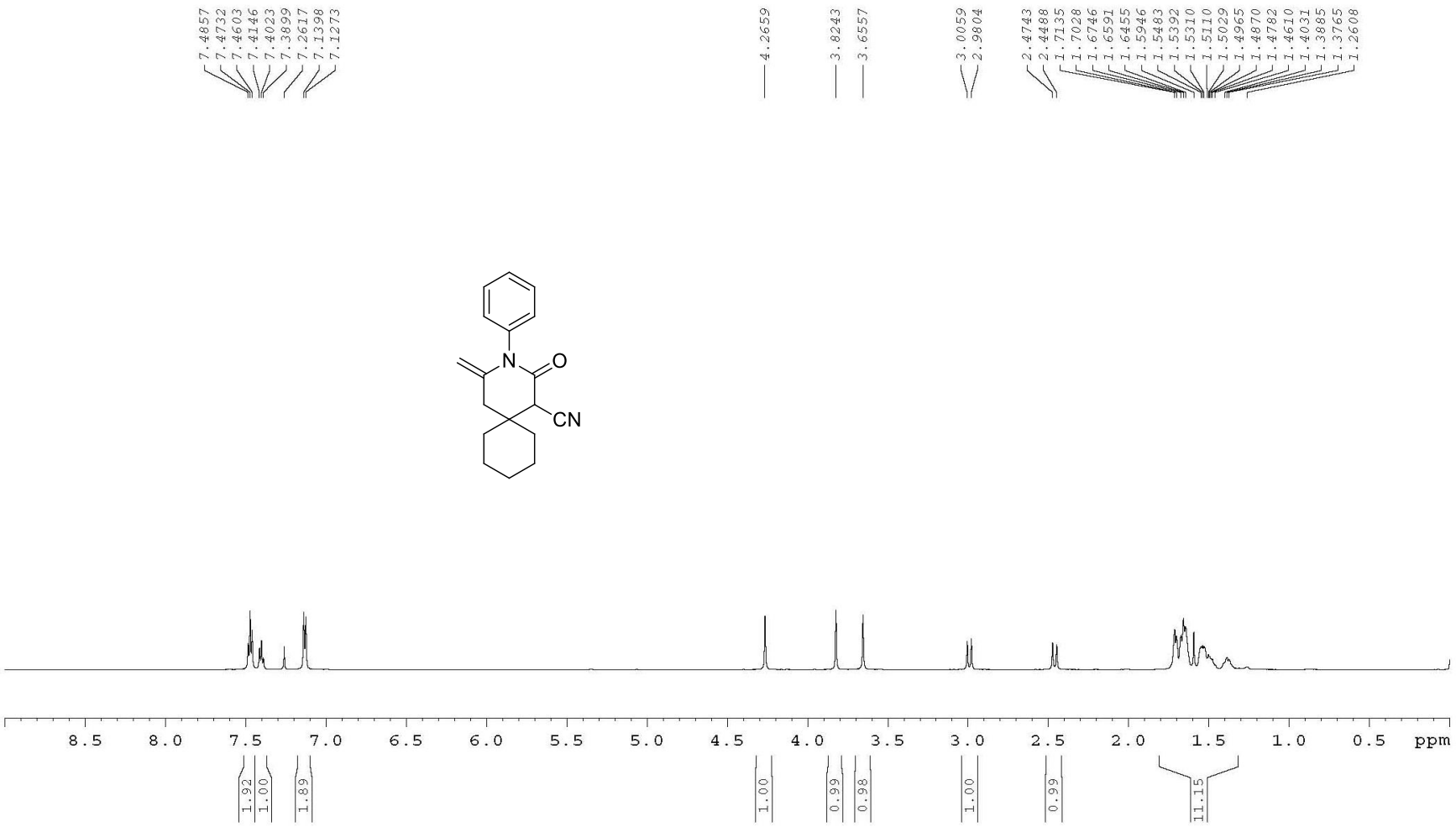


Figure S47. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5a**

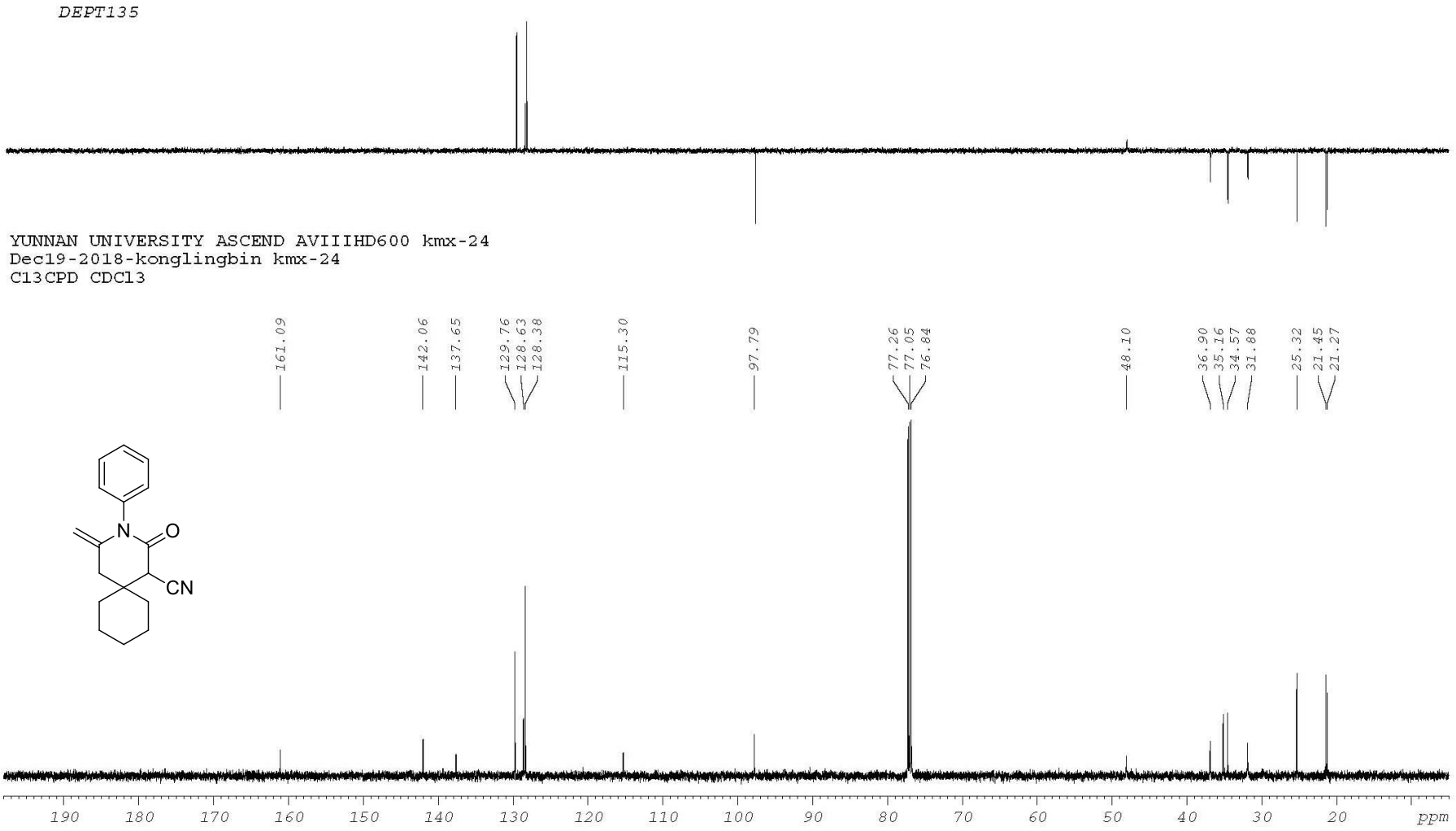


Figure S48. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5a**

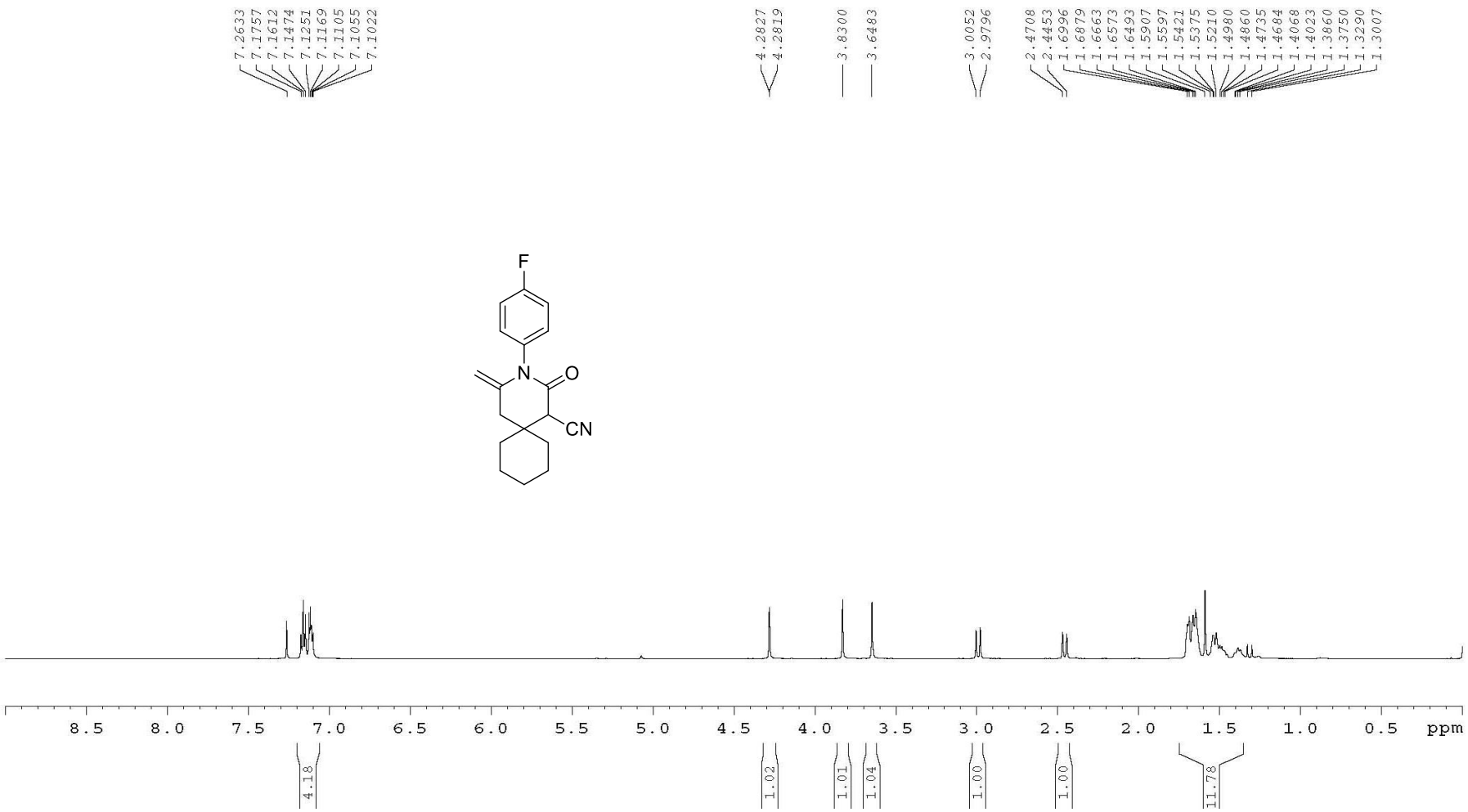


Figure S49. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5b**

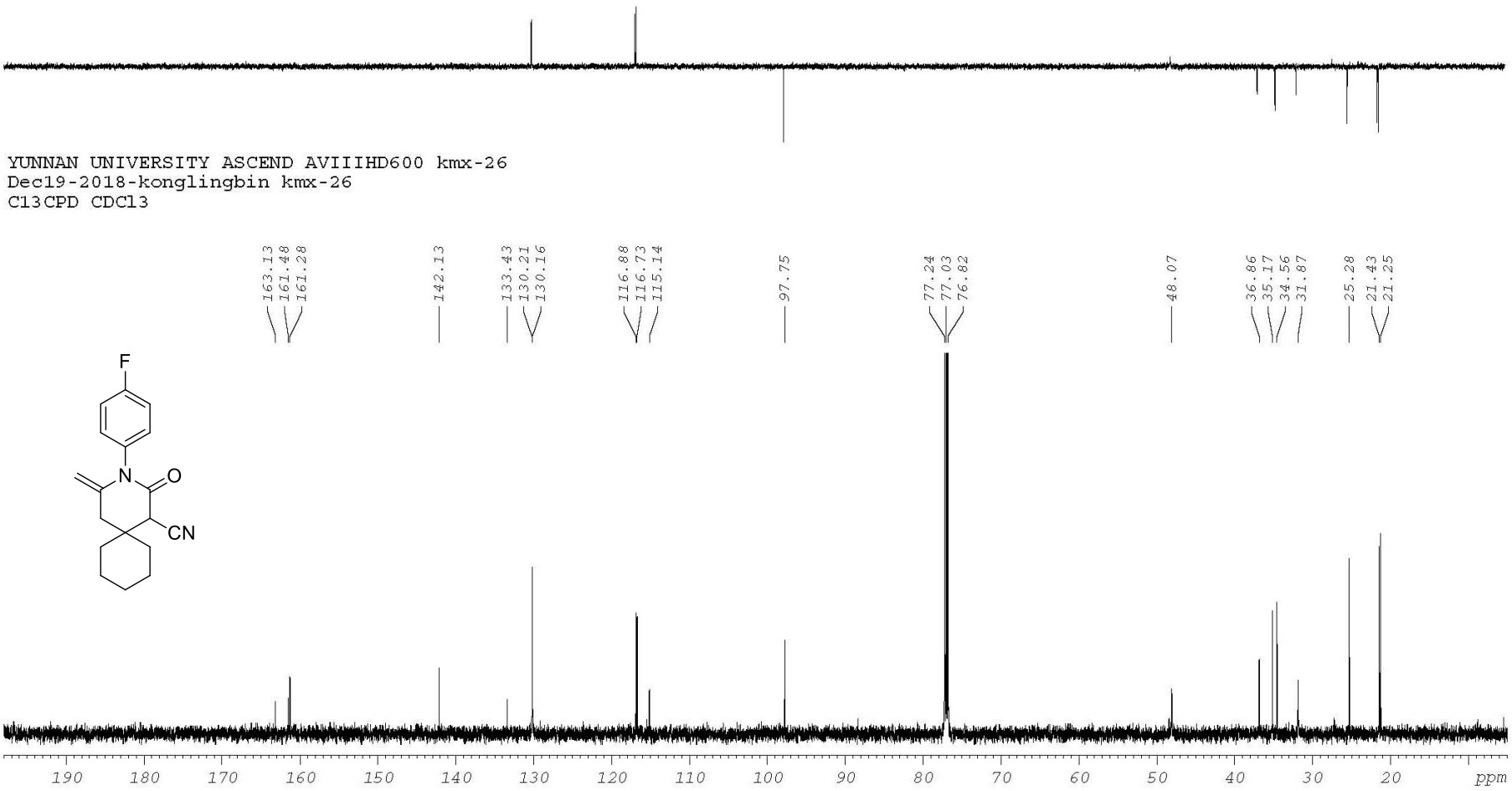


Figure S50. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5b**

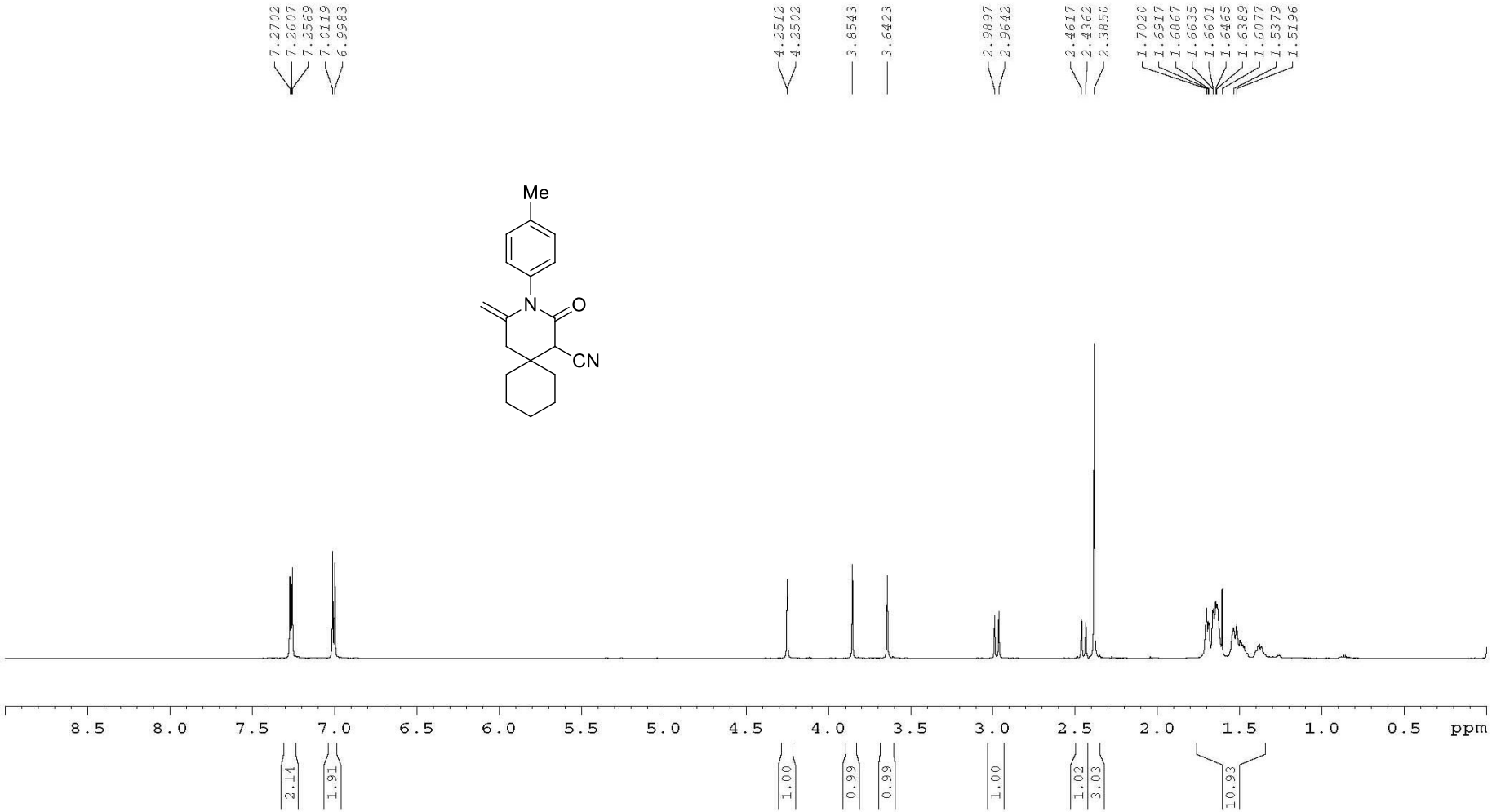


Figure S51. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5c**

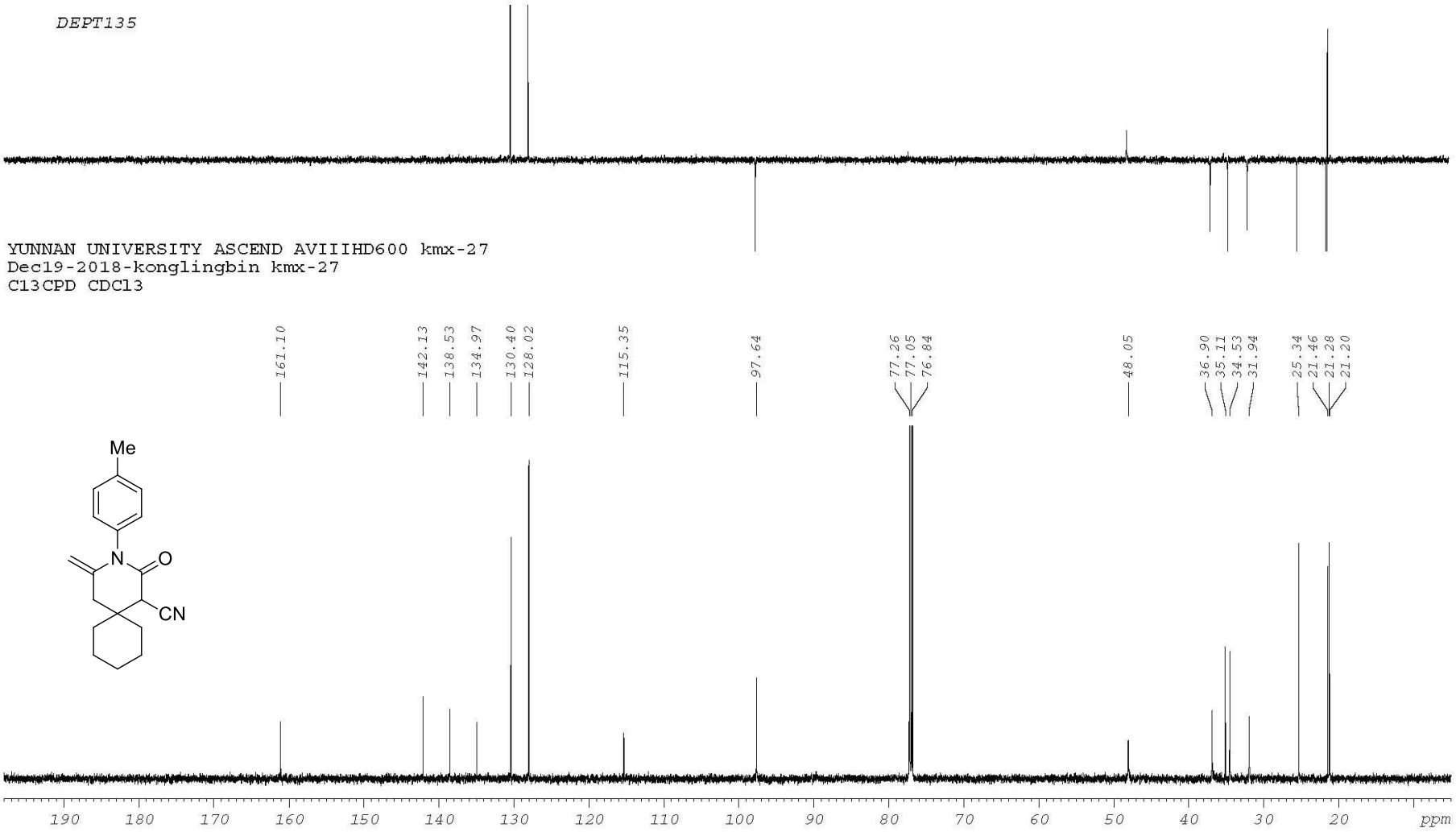


Figure S52. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5c**

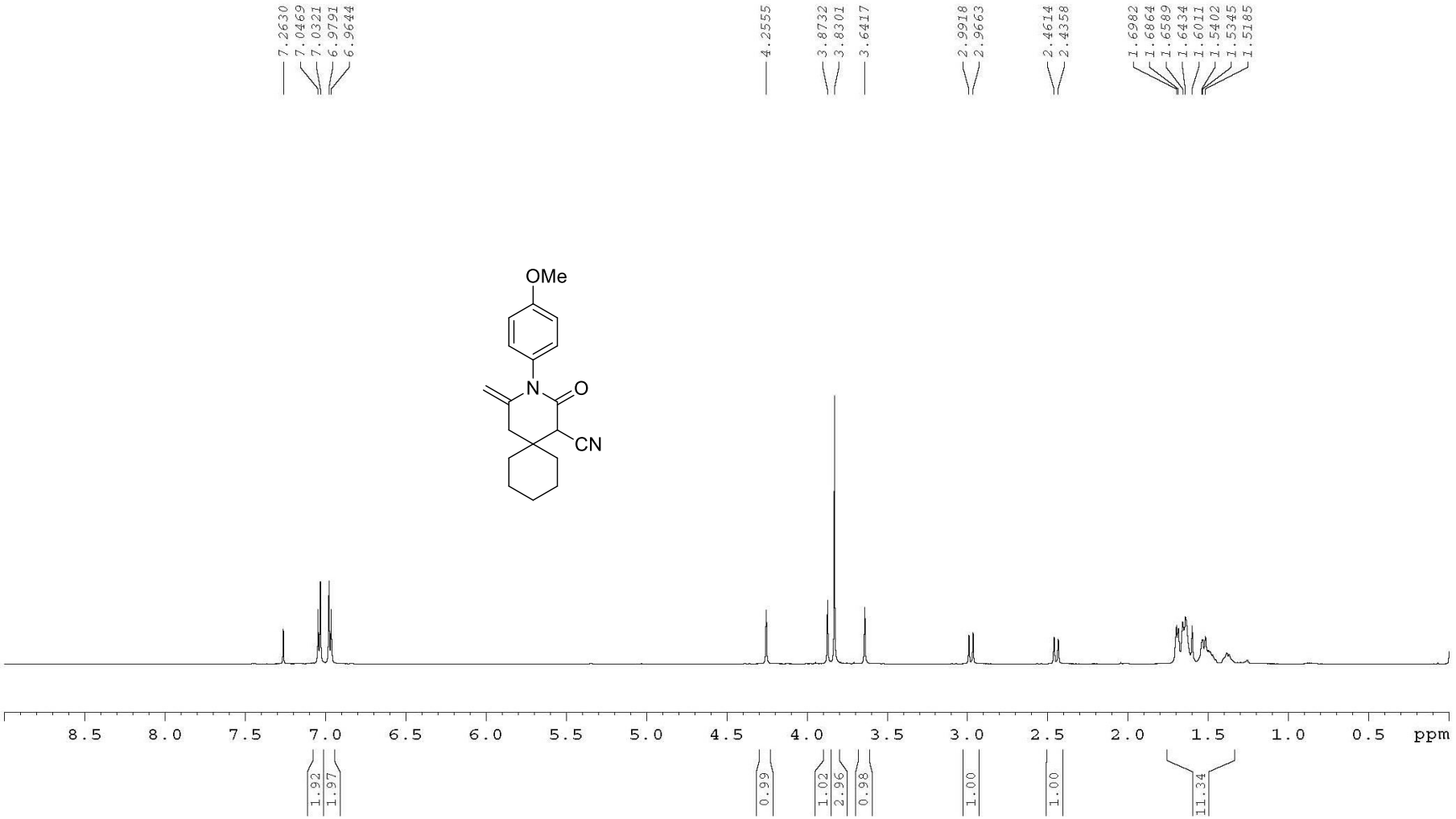


Figure S53. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5d**

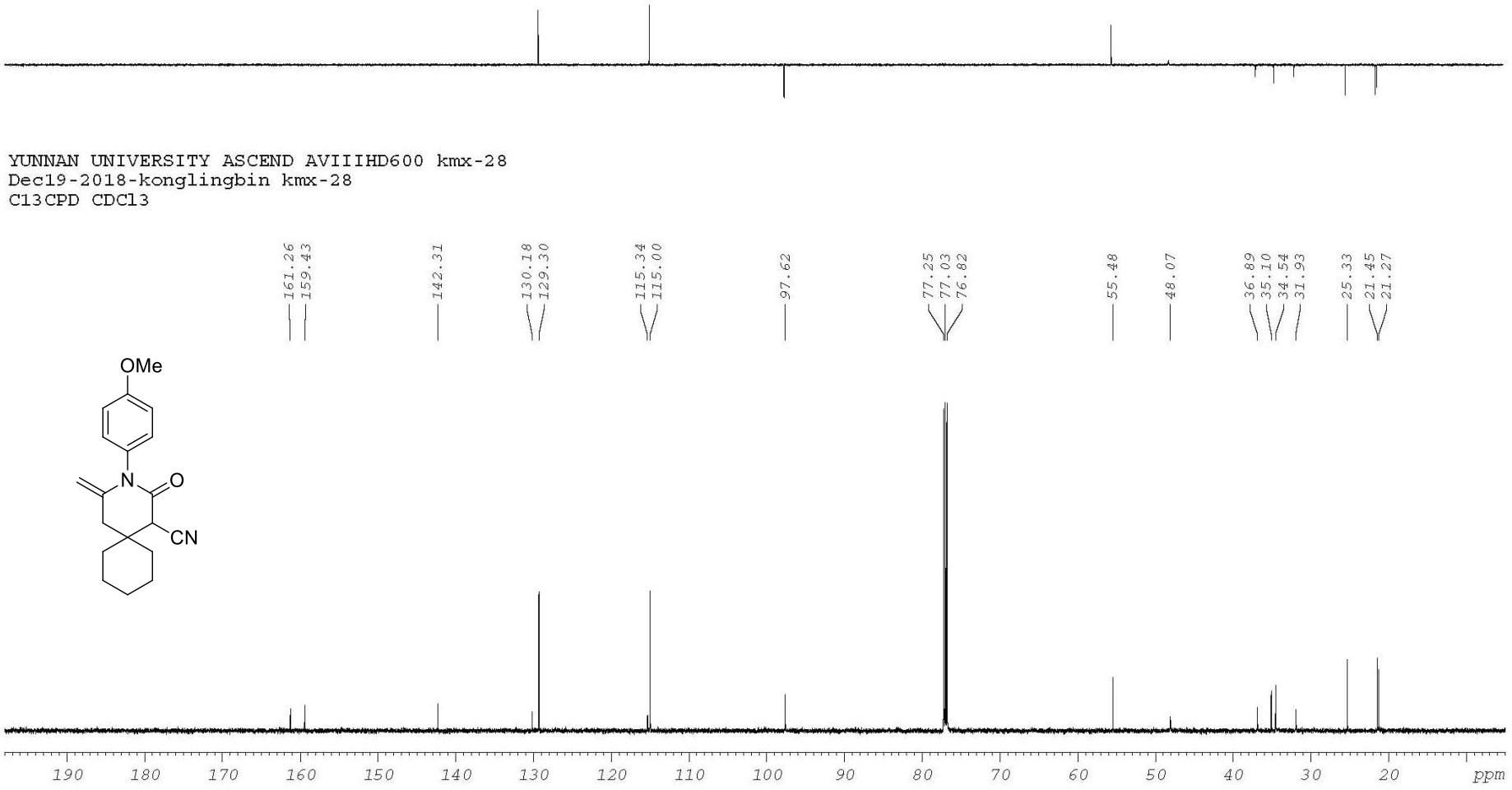


Figure S54. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5d**

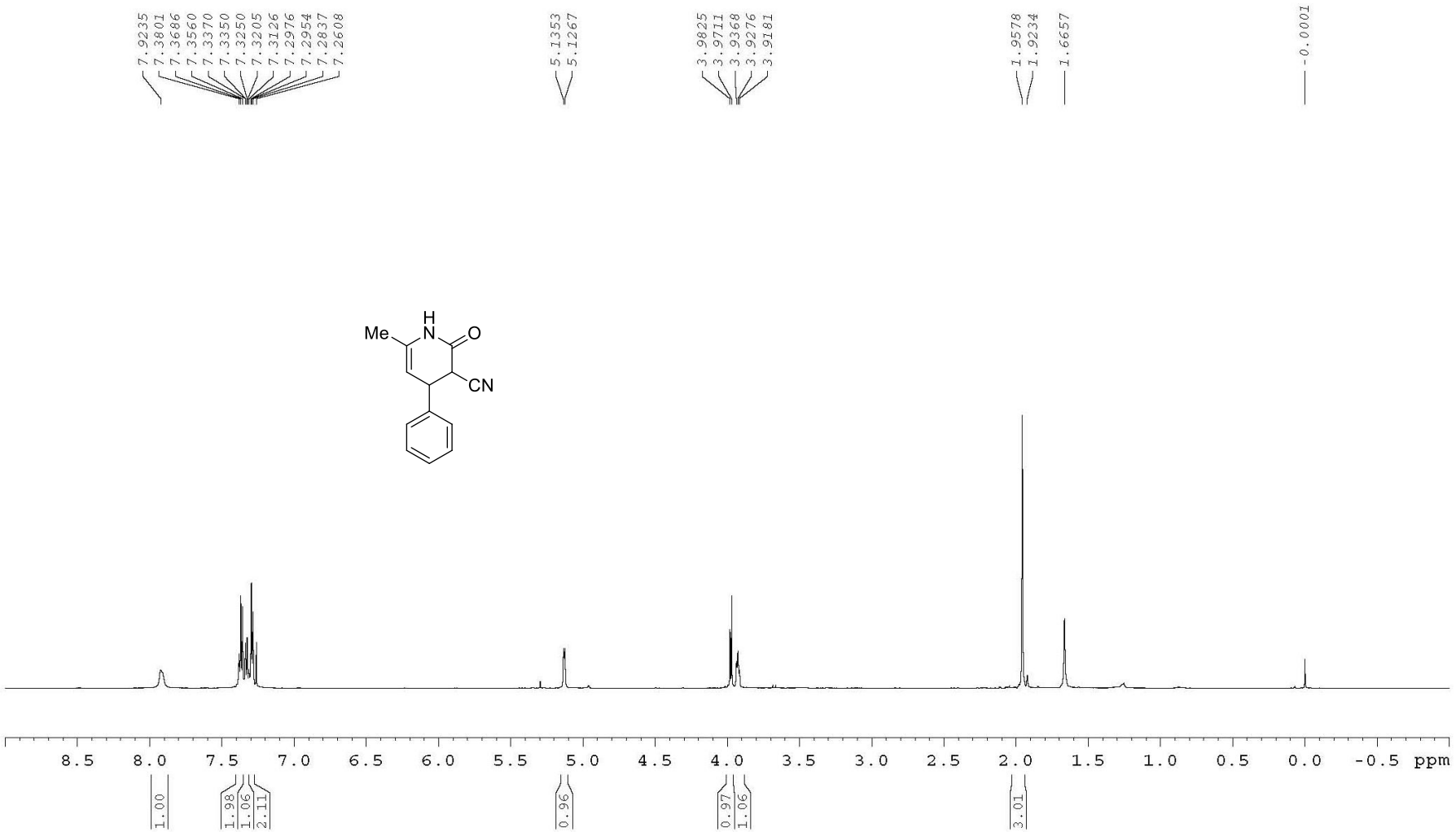


Figure S55. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **6a**

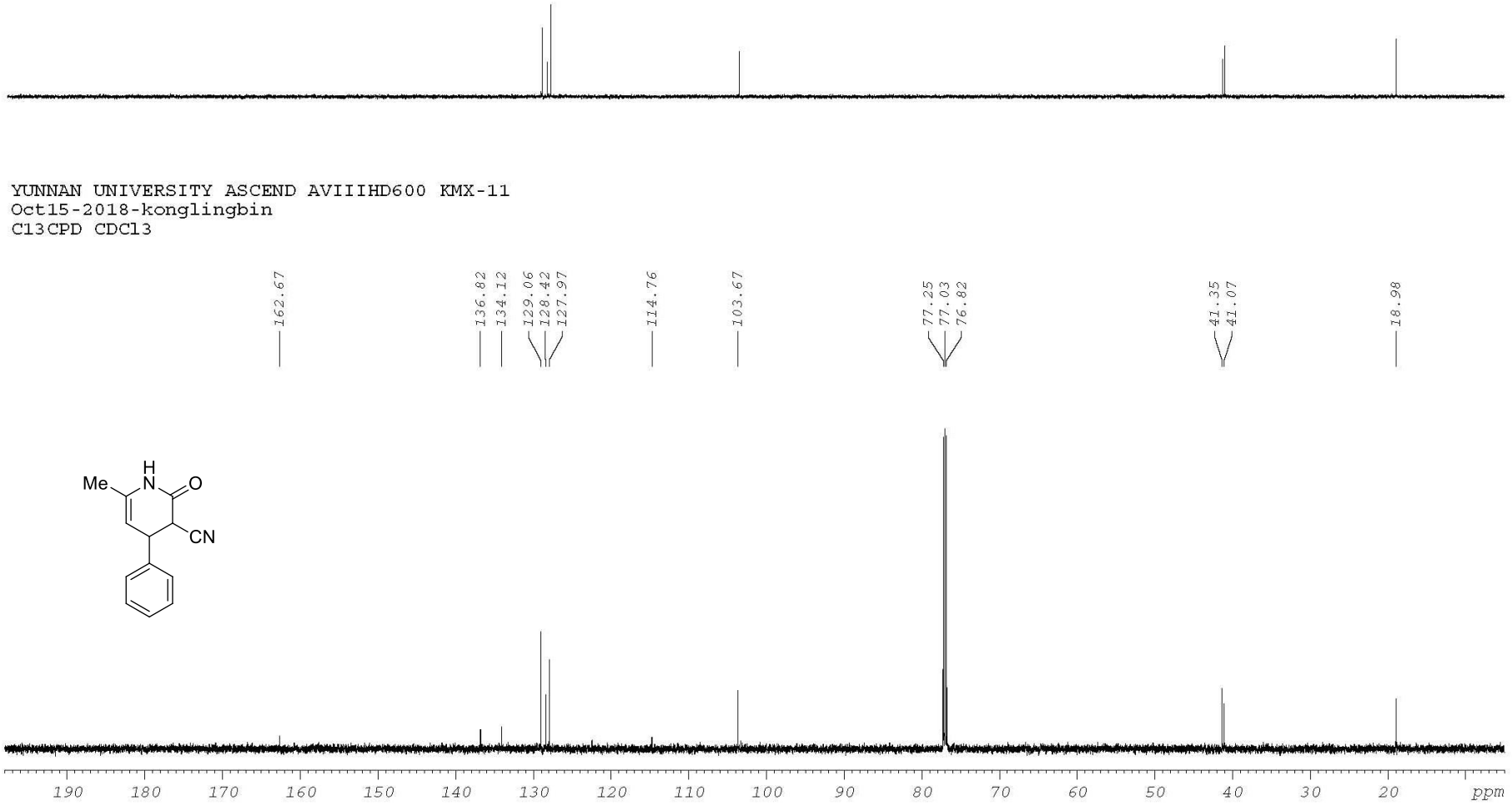


Figure S56. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **6a**

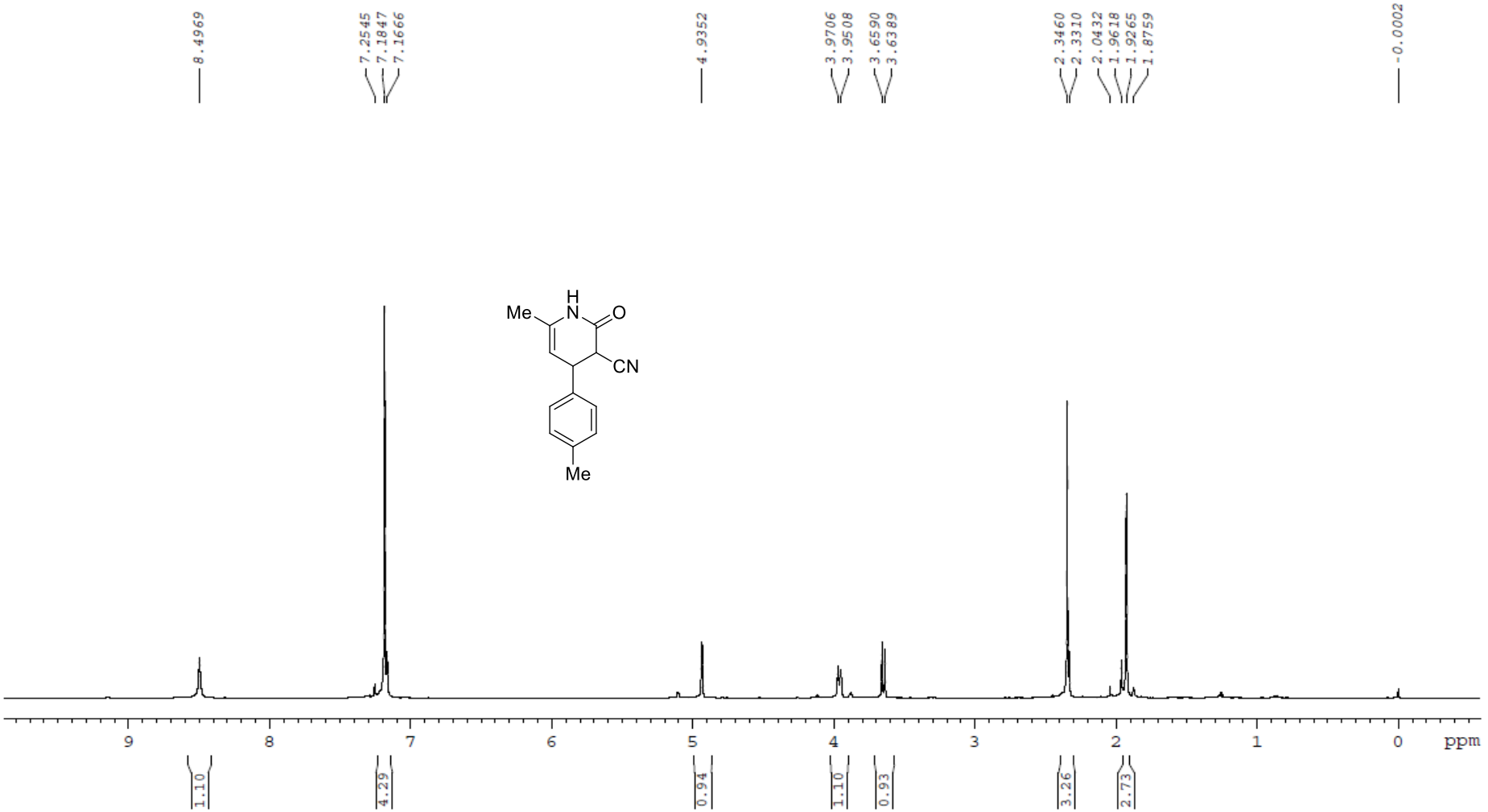


Figure S57. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **6b**

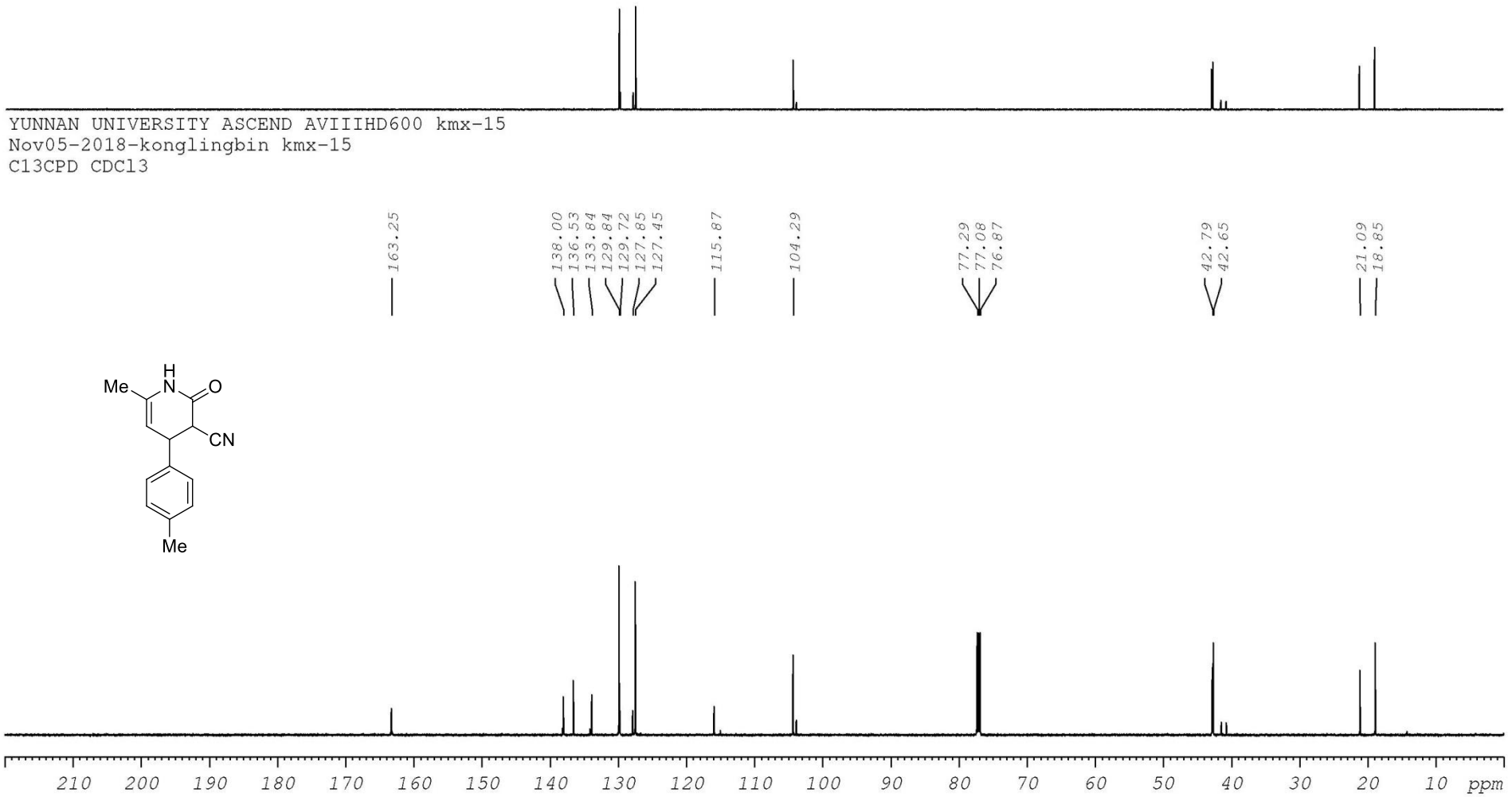


Figure S58. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **6b**

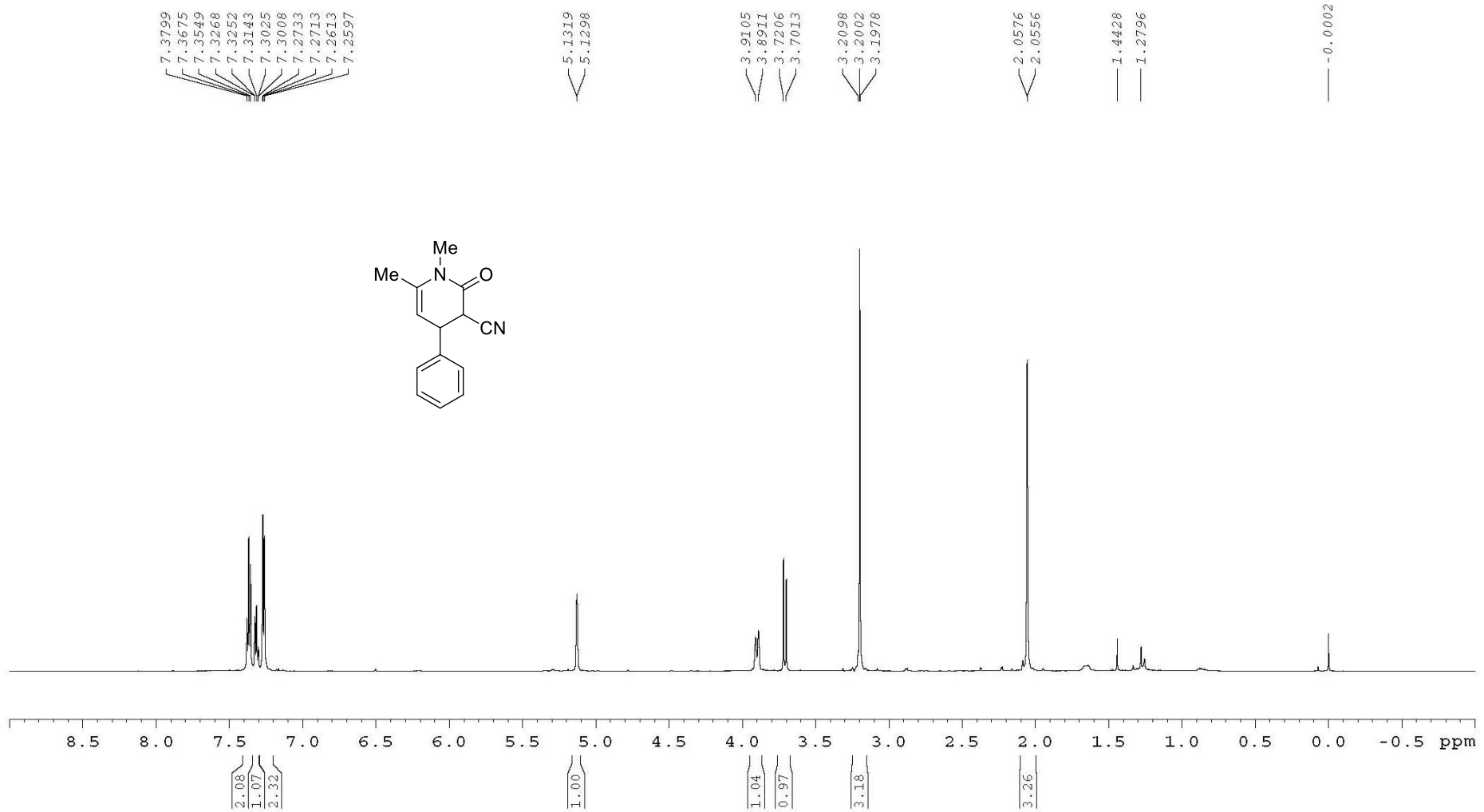


Figure S59. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **6c**

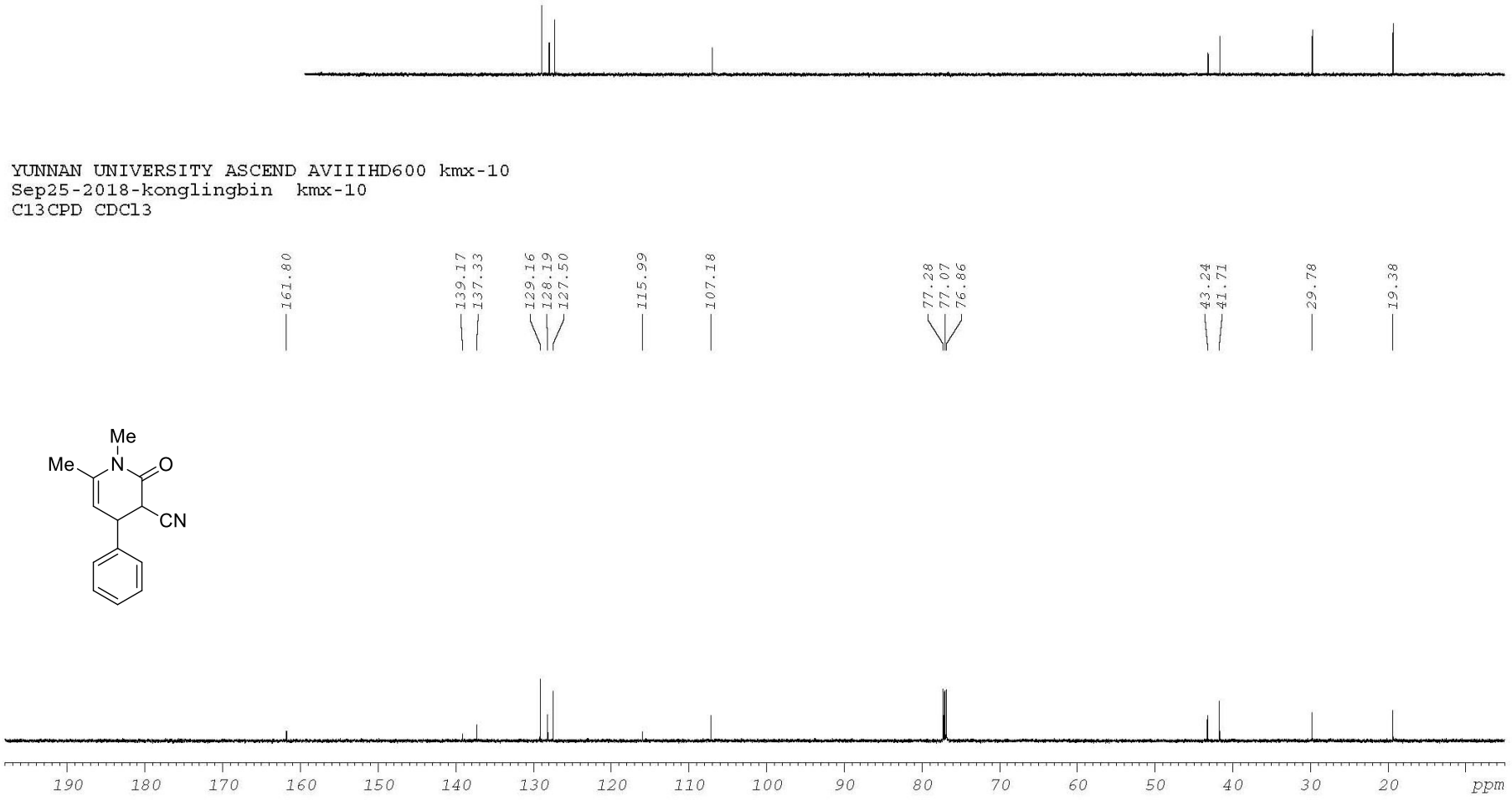


Figure S60. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **6c**

References and Notes

1. K. M. Al-Zaydi, R. M. Borik and M. H. Elnagdi. *Green Chemistry Letters and Reviews* 2012, **5**, 241-250.