Supporting Information

Dicarbofunctionalization of Unactivated Alkenes *via* Organo Photoredox Catalysis in Water: Access to Cyanoalkylated Fused Quinazolinones

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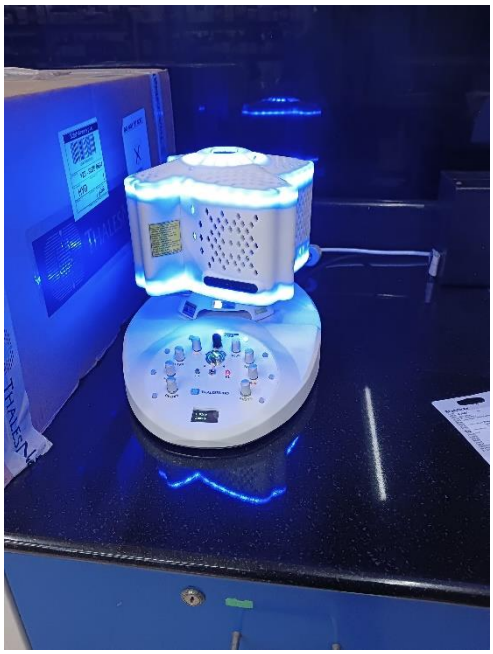
1. General information:

Unless otherwise noted, reagents obtained from commercial suppliers were used without further purification. All solvents were dried and distilled according to standard procedures. Reactions were monitored by silica gel thin-layer chromatography (TLC). Silica gel (100-200 mesh) packed in glass column was used for the column chromatography. NMR spectra were recorded at 400, 500 MHz (H), at 101, 126 MHz (C) and at 376 MHz (F) respectively. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 and C: δ = 77.0 ppm) as internal standard, and coupling constants (J) are measured in hertz (Hz). High-resolution mass spectra (HRMS) were recorded using ESI-TOF techniques. All photoredox-catalyzed reactions were carried out in *Thales Nano photocube* (4 × 32 W blue LED). All 3-quinazolin-4(3H)-one and oxime esters were prepared using existing methods. [1-5]



2. Analytical data of the newly synthesized oxime esters 2j and 2l:

(1,2,5)-2-Isopropyl-5-methylcyclohexyl 3-(((4-(trifluoromethyl)benzoyl)oxy)imino)cyclobutane-1-carboxylate (2j)

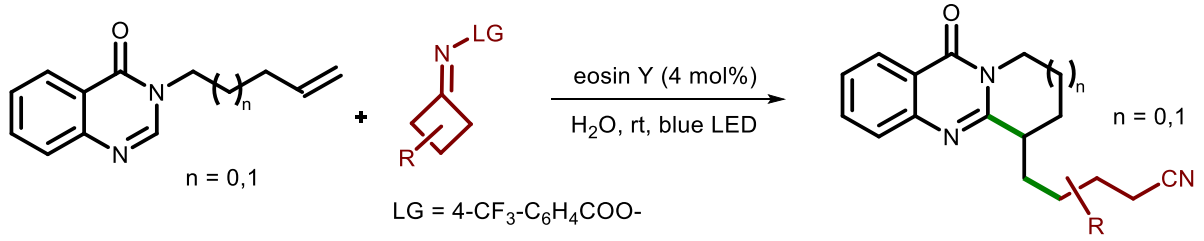
Yellow syrup (47% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 7.9 Hz, 2H), 4.75 (td, *J* = 10.9, 4.4 Hz, 1H), 3.45 – 3.35 (m, 4H), 3.32 – 3.20 (m, 1H), 2.06 – 1.94 (m, 1H), 1.90 – 1.80 (m, 1H), 1.75 – 1.64 (m, 2H), 1.58 – 1.47 (m, 1H), 1.46 – 1.36 (m, 1H), 1.13 – 0.95 (m, 2H), 0.94 – 0.88 (m, 7H), 0.77 (dd, *J* = 7.0, 1.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 165.5, 165.4, 162.7, 135.0 (q, *J* = 33.3 Hz), 132.2, 130.7, 130.2, 125.7 (q, *J* = 3.4 Hz), 123.6 (q, *J* = 274.7 Hz), 75.5, 47.1, 47.1, 41.0, 40.9, 35.9, 35.8, 35.8, 35.7, 34.3, 31.5, 31.4, 31.4, 26.5, 23.5, 22.1, 20.9, 16.5, 16.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2; HRMS (ESI) calcd for $C_{23}H_{29}F_3NO_4^+$ $[M+H]^+$ = 440.2043, found = 440.2012.

Methyl (2,4a,6a,6b,10,12a,14b)-2,4a,6a,6b,9,9,12a-heptamethyl-10-((3-(((4-(trifluoromethyl)benzoyl)oxy)imino)cyclobutane-1-carbonyl)oxy)-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14b-octadecahydropicene-2-carboxylate (2l)

Yellow syrup (49% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 5.71 – 5.50 (m, 2H), 4.60 (dd, *J* = 10.3, 6.1 Hz, 1H), 3.69 (s, 3H), 3.42 (d, *J* = 7.4 Hz, 4H), 3.31 (dd, *J* = 15.7, 7.7 Hz, 1H), 2.15 – 1.82 (m, 7H), 1.78 – 1.67 (m, 3H), 1.65 – 1.27 (m, 9H), 1.22 (s, 3H), 1.13 (s, 6H), 1.08 – 1.01 (m, 1H), 0.99 (s, 3H), 0.91 (d, *J* = 8.7 Hz, 6H), 0.83 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.8, 172.9, 165.4, 162.7, 154.1, 146.5, 135.0 (q, *J* = 33.7 Hz), 132.2, 130.7, 130.2, 125.7 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.5 Hz), 121.5, 116.2, 82.0, 51.8, 51.4, 46.6, 44.4, 42.9, 42.9, 40.6, 38.8, 38.5, 38.2, 36.9, 35.9, 35.8, 32.2, 31.7, 31.6, 31.6, 31.3, 28.6, 28.6, 28.4, 27.4, 25.7, 25.4, 24.4, 21.1, 20.2, 18.3, 17.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2; HRMS (ESI) calcd for $C_{44}H_{57}F_3NO_6^+$ $[M+H]^+$ = 769.4398, found = 769.4376.

3. Dicarbofunctionalization of alkenes using cycloketone oxime esters:

3.1) General procedure for the organophotocatalyzed dicarbofunctionalization to access cyanoalkylated quinazolinones:



To an oven dried vial equipped with a magnetic stir bar was added quinazolin-4(3H)-one **1** (0.3 mmol), oxime ester **2** (0.6 mmol) and eosin Y (0.012 mmol). Later, 1.0 mL of H_2O was added via syringe with gentle stirring. The tube was sealed and stirred in *Thales Nano photocube* (4 × 32 W blue LED) for 12 hours. After completion of reaction, the reaction mixture was diluted with dichloromethane (15.0 mL), and washed successively with water (10 mL × 2), aq. $NaHCO_3$ solution (10 mL × 2) and brine solution (10 mL × 2). The organic layer was dried over anhydrous sodium sulfate, concentrated and purified via flash chromatography on silica gel to get the desired compound **3**.

3.2) Analytical data of the cyanoalkylated compounds:

5-(11-Oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3a)

Yellow syrup (60.0 mg, 71% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 7.9 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 4.27 – 4.13 (m, 1H), 4.04 – 3.88 (m, 1H), 3.02 – 2.81 (m, 1H), 2.41 (t, *J* = 7.0 Hz, 2H), 2.26 – 2.08 (m, 2H), 2.06 – 1.91 (m, 2H), 1.85 – 1.57 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 157.5, 147.2, 134.2, 126.8, 126.7, 126.4, 120.2, 119.8, 42.0, 40.3, 32.5, 26.3, 25.5, 24.8, 20.3, 17.2; HRMS (ESI) calcd for $C_{17}H_{20}N_3O^+$ $[M+H]^+$ = 282.1601, found = 282.1610.

5-(3-Chloro-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3b)

Yellow syrup (57.7 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.6 Hz, 1H), 7.63 (d, *J* = 1.9 Hz, 1H), 7.37 (dd, *J* = 8.6, 2.0 Hz, 1H), 4.28 – 4.14 (m, 1H), 4.04 – 3.88 (m, 1H), 2.97 – 2.82 (m, 1H), 2.50 – 2.36 (m, 2H), 2.27 – 2.09 (m, 2H), 2.08 – 1.89 (m, 2H), 1.82 – 1.59 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 158.8, 148.4, 140.3, 128.2, 126.9, 126.5, 119.7, 118.7, 42.1, 40.4, 32.4, 26.3, 25.5, 24.8, 20.4, 17.2; HRMS (ESI) calcd for $C_{17}H_{19}ClN_3O^+$ $[M+H]^+$ = 316.1211, found = 316.1213.

5-(3-Bromo-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3c)

Yellow syrup (53.0 mg, 49% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 8.4, 6.3 Hz, 1H), 7.82 (d, *J* = 4.6 Hz, 1H), 7.64 – 7.46 (m, 1H), 4.28 – 4.13 (m, 1H), 4.04 – 3.89 (m, 1H), 2.88 (s, 1H), 2.51 – 2.35 (m, 2H), 2.26 – 2.10 (m, 2H), 2.09 – 1.91 (m, 2H), 1.85 – 1.61 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8, 158.8, 148.4, 129.7, 129.6, 128.9, 128.3, 119.7, 119.1, 42.1, 40.4, 32.4, 26.3, 25.5, 24.8, 20.4, 17.3; HRMS (ESI) calcd for $C_{17}H_{19}BrN_3O^+$ $[M+H]^+$ = 360.0706, found = 360.0709.

5-(3-Fluoro-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3d)

Yellow syrup (39.5 mg, 44% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 8.9, 6.2 Hz, 1H), 7.32 – 7.22 (m, 1H), 7.19 – 7.05 (m, 1H), 4.28 – 4.10 (m, 1H), 4.03 – 3.88 (m, 1H), 2.99 – 2.77 (m, 1H), 2.47 – 2.37 (m, 2H), 2.28 – 2.10 (m, 2H), 2.08 – 1.90 (m, 2H), 1.82 – 1.59 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5 (d, *J* = 245.93 Hz), 161.6, 158.8, 149.5 (d, *J* = 13.21 Hz), 129.5 (d, *J* = 11.12 Hz), 119.7, 117.1, 115.2 (d, *J* = 25.5, Hz), 112.0 (d, *J* = 21.3, Hz), 42.0, 40.4, 32.4, 26.3, 25.5, 24.8, 20.4, 17.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -103.7; HRMS (ESI) calcd for $C_{17}H_{19}FN_3O^+$ $[M+H]^+$ = 300.1507, found = 300.1509.

5-(2-Methyl-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3e)

Yellow syrup (52.2 mg, 59% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.02 (m, 1H), 7.52 (d, *J* = 1.3 Hz, 2H), 4.27 – 4.12 (m, 1H), 4.02 – 3.90 (m, 1H), 2.95 – 2.83 (m, 1H), 2.46 (d, *J* = 0.7 Hz, 3H), 2.40 (dd, *J* = 9.1, 5.1 Hz, 2H), 2.24 – 2.07 (m, 2H), 2.06 – 1.90 (m, 2H), 1.80 – 1.59 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 156.6, 145.3, 136.5, 135.8, 126.6, 126.0, 119.9, 119.8, 42.0, 40.2, 32.5, 26.3, 25.5, 24.9, 21.4, 20.4, 17.2; HRMS (ESI) calcd for $C_{18}H_{22}N_3O^+$ $[M+H]^+$ = 296.1757, found = 296.1762.

5-(2-Chloro-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3f)

Yellow syrup (40.6 mg, 43% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 2.1 Hz, 1H), 7.63 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.57 (d, *J* = 8.7 Hz, 1H), 4.28 – 4.16 (m, 1H), 4.02 – 3.90 (m, 1H), 2.96 – 2.80 (m, 1H), 2.41 (t, *J* = 6.9 Hz, 2H), 2.24 – 2.09 (m, 2H), 2.05 – 1.91 (m, 2H), 1.81 – 1.60 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 157.8, 145.8, 134.7, 131.9, 128.6, 126.0, 121.2, 119.7, 42.2, 40.3, 32.4, 26.3, 25.5, 24.8, 20.3, 17.2; HRMS (ESI) calcd for $C_{17}H_{19}ClN_3O^+$ $[M+H]^+$ = 316.1211, found = 316.1203.

5-(2-Bromo-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3g)

Yellow syrup (44.2 mg, 41% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 2.3 Hz, 1H), 7.78 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.51 (d, *J* = 8.7 Hz, 1H), 4.27 – 4.14 (m, 1H), 4.04 – 3.88 (m, 1H), 2.95 – 2.81 (m, 1H), 2.41 (t, *J*=7.0 Hz, 2H), 2.25 – 2.07 (m, 2H), 2.04 – 1.91 (m, 2H), 1.81 – 1.58 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 158.0, 146.1, 137.4, 129.3, 128.7, 121.6, 119.7, 42.3, 40.3, 32.4, 26.3, 25.5, 24.8, 20.3, 17.2; HRMS (ESI) calcd for $C_{17}H_{19}BrN_3O^+$ $[M+H]^+$ = 360.0706, found = 360.0694.

5-(2-Iodo-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3h)

Yellow syrup (76.9 mg, 63% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.0 Hz, 1H), 7.96 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 4.25 – 4.13 (m, 1H), 4.00 – 3.90 (m, 1H), 2.96 – 2.82 (m, 1H), 2.41 (t, *J* = 7.0 Hz, 2H), 2.26 – 2.09 (m, 2H), 2.07 – 1.91 (m, 2H), 1.82 – 1.59 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 158.3, 146.5, 143.0, 135.6, 128.7, 121.9, 119.7, 90.5, 42.3, 40.3, 32.4, 26.3, 25.5, 24.7, 20.3, 17.2; HRMS (ESI) calcd for $C_{17}H_{19}IN_3O^+$ $[M+H]^+$ = 408.0567, found = 408.0581.

5-(11-Oxo-2-phenyl-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3i)

Yellow syrup (78.2 mg, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.1 Hz, 1H), 7.98 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.77 – 7.66 (m, 3H), 7.52 – 7.44 (m, 2H), 7.42 – 7.33 (m, 1H), 4.32 – 4.17 (m, 1H), 4.07 – 3.94 (m, 1H), 3.04 – 2.83 (m, 1H), 2.42 (t, *J* = 7.0 Hz, 2H), 2.28 – 2.10 (m, 2H), 2.09 – 1.93 (m, 2H), 1.83 – 1.61 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 157.4, 146.7, 139.2, 133.2, 129.1, 127.8, 127.4, 127.3, 124.6, 120.5, 119.8, 42.1, 40.4, 32.5, 26.3, 25.6, 24.9, 20.4, 17.3; HRMS (ESI) calcd for $C_{23}H_{24}N_3O^+$ $[M+H]^+$ = 358.1914, found = 358.1915.

5-(2-(4-Chlorophenyl)-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3j)

Yellow syrup (65.7 mg, 56% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 2.0 Hz, 1H), 7.93 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.49 – 7.38 (m, 2H), 4.32 – 4.15 (m, 1H), 4.08 – 3.92 (m, 1H), 3.02 – 2.85 (m, 1H), 2.50 – 2.38 (m, 2H), 2.29 – 2.11 (m, 2H), 2.10 – 1.93 (m, 2H), 1.86 – 1.60 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 157.6, 146.8, 138.4, 137.9, 134.0, 132.9, 129.2, 128.5, 127.6, 124.5, 120.6, 119.8, 42.2, 40.4,

32.5, 26.3, 25.5, 24.9, 20.4, 17.2; HRMS (ESI) calcd for $C_{23}H_{23}ClN_3O^+$ $[M+H]^+$ = 392.1524, found = 392.1534.

5-(4-Methyl-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3k)

Yellow syrup (46.9 mg, 53% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 7.0 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 4.38 – 4.11 (m, 1H), 4.04 – 3.85 (m, 1H), 2.95 – 2.82 (m, 1H), 2.58 (s, 3H), 2.46 – 2.36 (m, 2H), 2.28 – 2.19 (m, 1H), 2.18 – 2.09 (m, 1H), 2.06 – 1.91 (m, 2H), 1.82 – 1.58 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 155.9, 145.9, 135.4, 134.6, 125.9, 124.4, 120.2, 119.8, 41.6, 40.3, 32.4, 26.4, 25.7, 25.4, 20.8, 17.4, 17.3; HRMS (ESI) calcd for $C_{18}H_{22}N_3O^+$ $[M+H]^+$ = 296.1757, found = 296.1763.

5-(1-Chloro-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3l)

Yellow syrup (54.8 mg, 58% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.47 (m, 2H), 7.45 – 7.36 (m, 1H), 4.24 – 4.06 (m, 1H), 4.02 – 3.85 (m, 1H), 2.95 – 2.78 (m, 1H), 2.50 – 2.36 (m, 2H), 2.24 – 2.08 (m, 2H), 2.05 – 1.88 (m, 2H), 1.83 – 1.57 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4, 158.2, 149.8, 133.9, 133.7, 133.5, 129.0, 126.2, 119.7, 117.4, 42.3, 40.3, 32.4, 26.3, 25.5, 24.8, 20.4, 17.2; HRMS (ESI) calcd for $C_{17}H_{19}ClN_3O^+$ $[M+H]^+$ = 316.1211, found = 316.1213.

5-(3,4-Dimethyl-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (3m)

Yellow syrup (60.3 mg, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.1 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 4.35 – 4.12 (m, 1H), 3.98 – 3.86 (m, 1H), 2.95 – 2.80 (m, 1H), 2.53 (s, 3H), 2.46 – 2.37 (m, 5H), 2.30 – 2.08 (m, 2H), 2.06 – 1.91 (m, 2H), 1.84 – 1.56 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7, 155.5, 145.6, 142.9, 133.2, 128.3, 123.5, 119.8, 118.2,

41.6, 40.3, 32.3, 26.4, 25.7, 25.4, 21.0, 20.8, 17.3, 13.0; HRMS (ESI) calcd for $C_{19}H_{24}N_3O^+$ $[M+H]^+$ = 310.1914, found = 310.1933.

5-(9-Oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3n)

Yellow syrup (60.9 mg, 76% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 – 8.23 (m, 1H), 7.78 – 7.63 (m, 2H), 7.50 – 7.39 (m, 1H), 4.39 – 4.17 (m, 1H), 4.13 – 3.90 (m, 1H), 3.33 – 3.17 (m, 1H), 2.56 – 2.46 (m, 1H), 2.42 (t, *J* = 6.9 Hz, 2H), 2.24 – 2.12 (m, 1H), 1.99 – 1.86 (m, 1H), 1.83 – 1.74 (m, 2H), 1.72 – 1.59 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 161.1, 149.3, 134.3, 127.1, 126.5, 126.4, 120.9, 119.6, 44.9, 43.7, 31.5, 26.5, 26.4, 25.4, 17.2; HRMS (ESI) calcd for $C_{16}H_{18}N_3O^+$ $[M+H]^+$ = 268.1444, found = 268.1441.

5-(6-Chloro-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3o)

Yellow syrup (56.9 mg, 63% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.5 Hz, 1H), 7.66 (d, *J* =2 .0 Hz, 1H), 7.39 (dd, *J* = 8.6, 2.0 Hz, 1H), 4.34 – 4.20 (m, 1H), 4.05 – 3.91 (m, 1H), 3.30 – 3.16 (m, 1H), 2.55 – 2.45 (m, 1H), 2.44 – 2.39 (m, 2H), 2.23 – 2.07 (m, 1H), 1.99 – 1.86 (m, 1H), 1.82 – 1.58 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.6, 160.5, 150.3, 140.4, 127.9, 127.0, 126.8, 119.6, 119.4, 45.0, 43.8, 31.3, 26.5, 26.3, 25.4, 17.2; HRMS (ESI) calcd for $C_{16}H_{17}ClN_3O^+$ $[M+H]^+$ = 302.1055, found = 302.1055.

5-(6-Fluoro-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3p)

Yellow syrup (59.1 mg, 69% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.9, 6.2 Hz, 1H), 7.30 (dd, *J* = 9.8, 2.5 Hz, 1H), 7.19 – 7.11 (m, 1H), 4.32 – 4.20 (m, 1H), 4.10 – 3.93 (m, 1H), 3.30 – 3.16 (m, 1H), 2.53 – 2.45 (m, 1H), 2.42 (t, *J* = 6.9 Hz, 2H), 2.21 – 2.10 (m, 1H), 1.99 – 1.86 (m, 1H), 1.82 – 1.72 (m, 2H), 1.72 – 1.57 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5 (d, *J* = 255.4 Hz), 162.6, 160.4, 151.6 (d, *J* = 13.4 Hz), 129.1 (d, *J* = 10.7 Hz), 127.9 (d, *J* = 443.0 Hz), 119.5, 117.6, 113.8 (dd, *J* = 268.5 Hz), 44.9, 43.8, 31.4, 26.5, 26.3, 25.4, 17.2; ^{19}FNMR (376 MHz, $CDCl_3$) δ -103.9; HRMS (ESI) calcd for $C_{16}H_{17}FN_3O^+$ $[M+H]^+$ = 286.1350, found = 286.1351.

5-(7-Methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3q)

Yellow syrup (61.6 mg, 73% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.60 – 7.50 (m, 2H), 4.33 – 4.20 (m, 1H), 4.10 – 3.90 (m, 1H), 3.27 – 3.15 (m, 1H), 2.51 – 2.44 (m, 4H), 2.41 (t, *J* = 6.9 Hz, 2H), 2.23 – 2.10 (m, 1H), 1.97 – 1.86 (m, 1H), 1.82 – 1.71 (m, 2H), 1.71 – 1.57 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 160.4, 147.3, 136.6, 135.7, 126.9, 125.9, 120.6, 119.6, 44.8, 43.6, 31.5, 26.5, 26.4, 25.4, 21.4, 17.2; HRMS (ESI) calcd for $C_{17}H_{20}N_3O^+$ $[M+H]^+$ = 282.1601, found = 282.1602.

5-(7-Bromo-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3r)

Yellow syrup (64.2 mg, 62% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 2.3 Hz, 1H), 7.79 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.54 (d, *J* = 8.7 Hz, 1H), 4.33 – 4.22 (m, 1H), 4.06 – 3.93 (m, 1H), 3.28 – 3.15 (m, 1H), 2.55 – 2.45 (m, 1H), 2.42 (t, *J* = 6.9 Hz, 2H), 2.23 – 2.09 (m, 1H), 1.99 – 1.87 (m, 1H), 1.83 – 1.59 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 159.9, 148.2, 137.4, 129.1, 129.0, 122.3, 119.9, 119.6, 45.0, 43.8, 31.4, 26.5, 26.4, 25.4, 17.2; HRMS (ESI) calcd for $C_{16}H_{17}BrN_3O^+$ $[M+H]^+$ = 346.0549, found = 346.0548.

5-(7-Iodo-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3s)

Yellow syrup (75.5 mg, 64% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.1, 1H), 7.97 (dd, *J* = 8.6, 2.1, 1H), 7.40 (d, *J* = 8.6, 1H), 4.36 – 4.20 (m, 1H), 4.10 – 3.93 (m, 1H), 3.29 – 3.15 (m, 1H), 2.55 – 2.44 (m, 1H), 2.42 (t, *J* = 6.9 Hz, 2H), 2.20 – 2.10 (m, 1H), 1.98 – 1.87 (m, 1H), 1.83 – 1.56 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9, 159.6, 148.7, 143.0, 135.3, 129.0, 122.6, 119.6, 90.7, 45.1, 43.8, 31.4, 26.5, 26.4, 25.4, 17.2; HRMS (ESI) calcd for $C_{16}H_{17}IN_3O^+$ $[M+H]^+$ = 394.0411, found = 394.0405.

5-(7-(4-Chlorophenyl)-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3t)

Yellow syrup (60.0 mg, 53% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 2.1 Hz, 1H), 7.93 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.67 – 7.55 (m, 2H), 7.48 – 7.36 (m,

2H), 4.39 – 4.21 (m, 1H), 4.09 – 3.92 (m, 1H), 3.32 – 3.20 (m, 1H), 2.56 – 2.45 (m, 1H), 2.42 (t, *J* = 6.9 Hz, 2H), 2.25 – 2.10 (m, 1H), 2.03 – 1.87 (m, 1H), 1.84 – 1.60 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 161.1, 148.7, 138.2, 138.1, 134.1, 132.9, 129.3, 128.5, 127.8, 124.3, 121.2, 119.6, 45.0, 43.8, 31.5, 26.5, 26.4, 25.4, 17.3; HRMS (ESI) calcd for $C_{22}H_{21}ClN_3O^+$ $[M+H]^+$ = 378.1368, found = 378.1361.

5-(8-Chloro-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3u)

Yellow syrup (61.4 mg, 68% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.52 (m, 2H), 7.41 (dd, *J* = 5.3, 3.7 Hz, 1H), 4.34 – 4.20 (m, 1H), 4.05 – 3.92 (m, 1H), 3.33 – 3.14 (m, 1H), 2.53 – 2.44 (m, 1H), 2.41 (t, *J* = 6.8 Hz, 2H), 2.21 – 2.07 (m, 1H), 1.98 – 1.84 (m, 1H), 1.82 – 1.56 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8, 159.2, 151.9, 134.2, 133.6, 129.2, 126.5, 119.5, 118.2, 45.2, 43.8, 31.3, 26.3, 26.3, 25.4, 17.2; HRMS (ESI) calcd for $C_{16}H_{17}ClN_3O^+$ $[M+H]^+$ = 302.1055, found = 302.1048.

5-(5-Methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3v)

Yellow syrup (37.1 mg, 44% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.9 Hz, 1H), 7.57 (d, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 4.40 – 4.19 (m, 1H), 4.10 – 3.90 (m, 1H), 3.32 – 3.14 (m, 1H), 2.60 (s, 3H), 2.54 – 2.44 (m, 1H), 2.42 (t, *J* = 6.7 Hz, 2H), 2.22 – 2.10 (m, 1H), 1.96 – 1.85 (m, 1H), 1.83 – 1.59 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 159.8, 148.0, 135.7, 134.8, 125.9, 124.1, 120.8, 119.6, 44.7, 43.6, 31.6, 26.8, 26.4, 25.5, 17.7, 17.3; HRMS (ESI) calcd for $C_{17}H_{20}N_3O^+$ $[M+H]^+$ = 282.1600, found = 282.1602.

5-(5-Methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentanenitrile (3w)

Yellow syrup (51.5 mg, 61% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.0 Hz, 1H), 7.79 – 7.63 (m, 2H), 7.49 – 7.40 (m, 1H), 4.21 – 4.12 (m, 1H), 4.10 – 4.03 (m, 1H), 2.40 – 2.32 (m, 2H), 2.26 – 2.16 (m, 1H), 2.12 – 1.99 (m, 1H), 1.91 – 1.70 (m, 2H), 1.72 – 1.57 (m, 3H), 1.49 – 1.36 (m, 4H); δ

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.2, 161.2, 149.6, 134.2, 127.3, 126.5, 126.3, 120.9, 119.6, 46.7, 43.4, 37.9, 32.7, 25.8, 24.4, 23.6, 17.2; HRMS (ESI) calcd for $C_{17}H_{20}N_3O^+$ $[M+H]^+$ = 282.1601, found = 282.1627.

5-(11-Oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)-3-phenylpentanenitrile (4a) (1:1 diastereomers)

Yellow syrup (86.8 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.17 (m, 1H), 7.76 – 7.67 (m, 1H), 7.63 – 7.56 (m, 1H), 7.46 – 7.38 (m, 1H), 7.38 – 7.32 (m, 2H), 7.31 – 7.21 (m, 3H), 4.27 – 4.07 (m, 1H), 4.02 – 3.84 (m, 1H), 3.10 – 2.98 (m, 1H), 2.94 – 2.79 (m, 1H), 2.67 – 2.63 (m, 2H), 2.16 – 1.85 (m, 6H), 1.76 – 1.50 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 162.2, 157.2, 147.4, 141.7, 141.5, 134.2, 129.1, 127.7, 127.6, 127.3, 127.3, 126.9, 126.9, 126.7, 126.3, 120.3, 120.3, 118.6, 42.6, 42.4, 42.3, 42.0, 41.7, 40.4, 40.2, 32.3, 31.1, 30.9, 25.5, 25.2, 25.1, 24.9, 20.4, 20.3; HRMS (ESI) calcd for $C_{23}H_{24}N_3O^+$ $[M+H]^+$ = 358.1914, found = 358.19169.

3-(2-Bromophenyl)-5-(11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (4b) (1:1 diastereomers)

Yellow syrup (99.2 mg, 76% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 – 8.20 (m, 1H), 7.76 – 7.67 (m, 1H), 7.66 – 7.54 (m, 2H), 7.47 – 7.29 (m, 3H), 7.18 – 7.07 (m, 1H), 4.30 – 4.11 (m, 1H), 4.01 – 3.85 (m, 1H), 3.70 – 3.58 (m, 1H), 2.98 – 2.85 (m, 1H), 2.80 – 2.57 (m, 2H), 2.19 – 1.93 (m, 6H), 1.77 – 1.59 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.3, 162.2, 157.2, 157.1, 147.3, 140.3, 140.1, 134.2, 133.5, 133.5, 129.1, 128.2, 127.9, 127.7, 126.9, 126.8, 126.7, 126.4, 125.7, 125.1, 125.0, 120.3, 120.3, 118.1, 72.4, 62.0, 54.8, 42.0, 41.6, 40.3, 40.1, 31.2, 30.9, 30.6, 30.6, 25.4, 24.9, 24.0, 23.7, 20.6, 20.5; HRMS (ESI) calcd for $C_{23}H_{23}BrN_3O^+$ $[M+H]^+$ = 436.1019, found = 436.1035.

3-(2-(11-Oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)ethyl)heptanenitrile (4c) (1:1 diastereomers)

Yellow syrup (67.8 mg, 67% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 7.8 Hz, 1H), 7.89 – 7.55 (m, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 4.31 – 4.08 (m, 1H), 4.07 – 3.78 (m, 1H), 3.00 – 2.74 (m, 1H), 2.50 – 2.31 (m, 2H), 2.24 – 2.08 (m, 2H), 2.06 – 1.86 (m, 2H), 1.86 – 1.19 (m, 11H), 0.90 (dd, *J* = 5.8, 3.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 157.4, 147.4, 137.0, 134.2, 127.4, 126.9, 126.9, 126.7, 126.3, 120.3, 119.1, 118.9, 116.2, 46.7, 42.1, 41.9, 40.6, 40.5, 36.8, 35.6, 35.4, 33.5, 33.1, 31.0, 30.9, 30.3, 30.2, 29.0, 28.8, 24.9, 24.9, 22.9, 22.0, 21.7, 20.5, 20.5, 14.1; HRMS (ESI) calcd for $C_{21}H_{28}N_3O^+$ $[M+H]^+$ = 338.2227, found = 338.2223.

Benzyl 2-(cyanomethyl)-4-(11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)butanoate (4d) (1:1 diastereomers)

Yellow syrup (88.4 mg, 71% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.0 Hz, 1H), 7.77 – 7.66 (m, 1H), 7.60 (d, *J* = 10.0 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.38 – 7.27 (m, 5H), 5.32 – 5.10 (m, 2H), 4.28 – 4.14 (m, 1H), 3.98 – 3.83 (m, 1H), 2.97 – 2.79 (m, 2H), 2.78 – 2.61 (m, 2H), 2.24 – 2.01 (m, 3H), 2.00 – 1.85 (m, 3H), 1.73 – 1.51 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 162.2, 156.8, 156.8, 147.3, 135.3, 134.2, 128.8, 128.7, 128.6, 127.0, 126.7, 126.4, 120.3, 117.9, 117.8, 67.4, 41.8, 41.7, 41.6, 40.1, 40.0, 30.1, 29.8, 29.1, 28.9, 25.1, 24.9, 20.5, 20.4, 19.6, 19.2; HRMS (ESI) calcd for $C_{25}H_{26}N_3O_3^+$ $[M+H]^+$ = 416.1969, found = 416.1965.

4-Benzyl-5-(11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanenitrile (4e) (1:1 diastereomers)

Yellow syrup (86.9 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.21 (m, 1H), 7.77 – 7.68 (m, 1H), 7.65 – 7.59 (m, 1H), 7.50 – 7.37 (m, 1H), 7.33 – 7.26 (m, 2H), 7.25 – 7.12 (m, 3H), 4.36 – 4.16 (m, 1H), 3.96 – 3.64 (m, 1H), 3.08 – 2.72 (m, 2H), 2.71 – 2.48 (m, 2H), 2.42 – 2.34 (m, 1H), 2.31 – 2.09 (m, 3H), 2.10 – 1.85 (m, 2H), 1.84 – 1.71 (m, 2H), 1.70 – 1.56 (m, 1H), 1.54 – 1.39 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 162.1, 157.7, 157.6, 147.4, 147.4, 139.9, 139.6, 134.2, 129.2, 128.7, 126.9, 126.8, 126.5, 126.3, 120.4, 120.2, 119.7, 41.5,

41.1, 41.0, 40.0, 38.0, 37.8, 37.2, 37.1, 37.0, 36.2, 29.9, 29.6, 25.5, 25.4, 20.3, 20.1, 15.1, 15.0; HRMS (ESI) calcd for $C_{24}H_{26}N_3O^+$ $[M+H]^+$ = 372.2070, found = 372.2073.

2-(2-(11-Oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)ethoxy)acetonitrile (4f)

Yellow syrup (30.6 mg, 36% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.0 Hz, 1H), 7.78 – 7.66 (m, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.42 (dd, *J* = 7.9, 7.1 Hz, 1H), 4.43 – 4.22 (m, 3H), 3.99 – 3.77 (m, 3H), 3.13 – 2.92 (m, 1H), 2.65 – 2.44 (m, 1H), 2.25 – 2.12 (m, 1H), 2.10 – 1.88 (m, 3H), 1.73 – 1.57 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 157.1, 147.4, 134.2, 128.0, 127.0, 126.8, 126.4, 120.4, 116.2, 69.8, 56.4, 41.5, 37.1, 32.6, 25.4, 20.5; HRMS (ESI) calcd for $C_{16}H_{18}N_3O_2^+$ $[M+H]^+$ = 284.1394, found = 284.1396.

5,5-dimethyl-6-(11-Oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)hexanenitrile (4h)

Yellow syrup (36.8 mg, 38% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.70 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.49 – 7.36 (m, 1H), 4.40 – 4.14 (m, 1H), 4.11 – 3.84 (m, 1H), 3.02 – 2.81 (m, 1H), 2.48 – 2.29 (m, 3H), 2.13 – 2.07 (m, 1H), 2.04 – 1.95 (m, 2H), 1.94 – 1.80 (m, 1H), 1.75 – 1.61 (m, 2H), 1.57 – 1.31 (m, 3H), 1.01 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 158.8, 147.5, 134.1, 126.9, 126.7, 126.2, 120.2, 120.0, 44.4, 41.3, 41.2, 37.1, 33.9, 28.1, 27.7, 27.4, 20.7, 20.3, 18.0; HRMS (ESI) calcd for $C_{20}H_{26}N_3O^+$ $[M+H]^+$ = 324.2070, found = 324.2067.

2-(3-((11-Oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)methyl)cyclopentyl)acetonitrile (4i) (1:1 diastereomers)

Yellow syrup (62.6 mg, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.70 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.41 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 4.30 – 4.16 (m, 1H), 4.03 – 3.88 (m, 1H), 2.99 – 2.82 (m, 1H), 2.41 – 2.34 (m, 2H), 2.31 – 2.08 (m, 4H), 2.10 – 1.84 (m, 5H), 1.75 – 1.56 (m, 3H), 1.50 – 1.28 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 157.9, 157.8, 147.5, 134.1, 126.9, 126.7, 126.2, 120.3, 119.4, 41.9,

41.8, 40.3, 39.8, 39.7, 39.5, 39.4, 39.3, 38.5, 37.7, 37.6, 37.1, 36.3, 36.3, 36.2, 35.3, 35.2, 33.6, 32.4, 32.2, 32.1, 31.1, 31.0, 30.9, 25.0, 24.9, 24.8, 23.4, 23.4, 23.2, 20.2; HRMS (ESI) calcd for $C_{20}H_{24}N_3O^+$ $[M+H]^+$ = 322.1914, found = 322.1913.

(1,2,5)-2-isopropyl-5-methylcyclohexyl 2-(cyanomethyl)-4-(11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)butanoate (4j) (1:1 diastereomers)

Yellow syrup (94.5 mg, 68% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 – 8.06 (m, 1H), 7.74 – 7.45 (m, 2H), 7.33 (t, *J* = 7.5 Hz, 1H), 4.73 – 4.56 (m, 1H), 4.23 – 4.06 (m, 1H), 3.91 – 3.76 (m, 1H), 2.92 – 2.77 (m, 1H), 2.78 – 2.66 (m, 1H), 2.65 – 2.48 (m, 2H), 2.17 – 1.98 (m, 2H), 1.97 – 1.82 (m, 4H), 1.81 – 1.72 (m, 2H), 1.70 – 1.47 (m, 4H), 1.46 – 1.23 (m, 2H), 1.04 – 0.84 (m, 2H), 0.84 – 0.71 (m, 7H), 0.69 – 0.58 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.2, 162.1, 157.1, 147.1, 134.3, 126.8, 126.6, 120.2, 117.9, 117.9, 117.8, 75.8, 75.7, 75.71, 47.1, 47.0, 42.2, 42.0, 41.9, 40.9, 40.9, 40.1, 34.2, 31.5, 30.2, 29.3, 29.1, 26.4, 26.3, 26.3, 25.1, 23.4, 23.2, 23.2, 22.1, 21.0, 20.9, 20.4, 19.8, 19.7, 19.5, 19.4, 16.3, 16.2, 16.1; HRMS (ESI) calcd for $C_{28}H_{38}N_3O_3^+$ $[M+H]^+$ = 464.2908, found = 464.2880.

(3,8,9,10,13,14,17)-10,13-Dimethyl-17-(6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-(cyanomethyl)-4-(11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)butanoate (4k) (1:1 diastereomers)

Yellow syrup (112.7 mg, 54% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.76 – 7.68 (m, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.48 – 7.37 (m, 1H), 5.38 (s, 1H), 4.78 – 4.58 (m, 1H), 4.32 – 4.20 (m, 1H), 4.10 – 3.89 (m, 1H), 2.96 – 2.85 (m, 1H), 2.84 – 2.59 (m, 3H), 2.35 (d, *J* = 7.4 Hz, 2H), 2.27 – 2.10 (m, 2H), 2.04 – 1.93 (m, 5H), 1.92 – 1.73 (m, 5H), 1.72 – 1.41 (m, 11H), 1.40 – 1.26 (m, 5H), 1.20 – 1.04 (m, 7H), 1.01 (d, *J* = 3.6 Hz, 4H), 0.91 (d, *J* = 6.4 Hz, 3H), 0.86 (dd, *J* = 6.6, 1.7 Hz, 6H), 0.68 (d, *J* = 1.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 162.3, 156.9, 147.4, 139.3, 134.3, 127.0, 126.8, 126.4, 123.2, 120.4, 117.9, 108.1, 75.4, 56.8, 56.3, 50.1, 42.5, 41.9, 40.2, 40.1, 39.9, 39.7, 38.2, 37.0, 36.7, 36.3,

35.9, 32.0, 31.9, 30.1, 30.1, 29.9, 28.4, 28.2, 27.9, 25.2, 25.0, 24.4, 24.0, 23.0, 22.7, 21.2, 20.6, 19.7, 19.5, 19.4, 18.9, 12.0; HRMS (ESI) calcd for $C_{45}H_{66}N_3O_3^+$ $[M-H]^+$ = 694.4942, found = 694.4942.

Methyl 10-((2-(cyanomethyl)-4-(11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)butanoyl)oxy)-2,4a,6a,6b,9,9,12a-heptamethyl-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14b-octadecahydropicene-2-carboxylate (4l) (1:1 diastereomers)

Yellow syrup (141.9 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.71 (ddd, *J* = 8.4, 7.1, 1.5 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 5.73 – 5.45 (m, 2H), 4.68 – 4.54 (m, 1H), 4.34 – 4.17 (m, 1H), 4.05 – 3.87 (m, 1H), 3.69 (s, 3H), 2.99 – 2.82 (m, 2H), 2.78 – 2.63 (m, 2H), 2.24 – 1.83 (m, 10H), 1.81 – 1.29 (m, 13H), 1.26 (d, *J* = 10.4 Hz, 3H), 1.19 (d, *J* = 8.5 Hz, 3H), 1.12 (s, 6H), 1.06 – 0.99 (m, 1H), 0.97 (d, *J* = 1.4, 3H), 0.94 – 0.92 (m, 3H), 0.91 – 0.87 (m, 4H), 0.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7, 172.3, 162.3, 156.8, 154.0, 147.4, 146.5, 134.2, 126.9, 126.8, 126.4, 121.5, 120.4, 117.9, 116.2, 82.3, 51.8, 51.4, 46.5, 44.4, 42.9, 42.8, 42.2, 41.8, 40.6, 40.2, 38.7, 38.5, 38.0, 36.9, 32.2, 31.7, 31.3, 30.2, 29.8, 29.1, 28.6, 28.6, 27.4, 25.7, 25.4, 25.3, 25.1, 24.4, 21.1, 20.5, 20.1, 19.5, 18.3, 17.0; HRMS (ESI) calcd for $C_{49}H_{66}N_3O_5^+$ $[M+H]^+$ = 776.4997, found = 776.4963.

4) Gram-scale experiment:

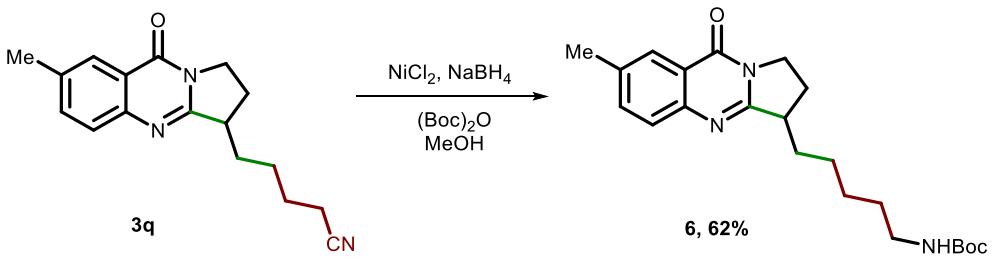
To an oven dried 25mL vial equipped with a magnetic stir bar was charged with quinazolin-4(3H)-one **1a** (1.0 g, 4.7 mmol), oxime ester **2a** (2.4 g, 9.4 mmol) and eosin Y (121 mg, 0.19 mmol). Later, 15.7 mL of H_2O was then added via syringe and sonicated for a while. The tube was sealed and stirred under *Thales Nano photocube* (4 × 32 W blue LED) for 12 h. After completion of reaction, the reaction mixture was diluted with DCM (25.0 mL), and washed successively with water (25 mL × 2), aq. $NaHCO_3$ solution (25 mL × 2) and brine solution (25

mL × 2). The organic layer was dried over anhydrous sodium sulfate, concentrated and purified via flash column chromatography on silica gel to get the desired compound **3a** (0.89 g, 68%).

5) Synthetic applications:

tert-Butyl(5-(7-methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)pentyl)carbamate (6):

A mixture of **3q** (28.1 mg, 0.1 mmol), $NiCl_2$ (32.4 mg, 0.25 mmol), $(Boc)_2O$ (130.9 mg, 0.6mmol) in dry methanol (4 mL) was cooled to 0 °C. Then, $NaBH_4$ (26.48 mg, 0.7 mmol) was added in small portions. The mixture was allowed to stir overnight at room temperature. The reaction was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc. The combined organic phase was dried over anhydrous sodium sulfate, concentrated and purified via flash chromatography on silica gel to get the desired compound **6** in 62% yield.

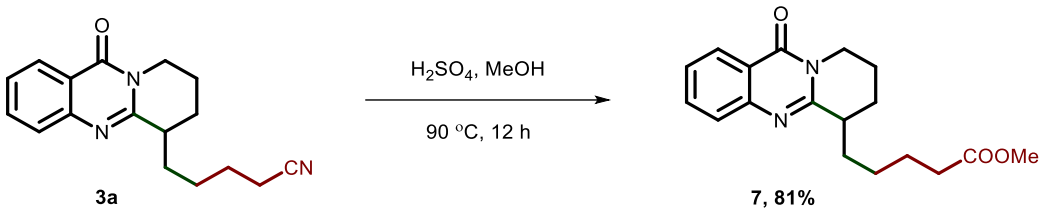


Yellow syrup (23.8 mg, 62%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.55 (dt, *J* = 8.2, 5.0 Hz, 2H), 4.54 (s, 1H), 4.32 – 4.18 (m, 1H), 4.10 – 3.96 (m, 1H), 3.31 – 3.01 (m, 3H), 2.52 – 2.39 (m, 4H), 2.20 – 2.07 (m, 1H), 1.97 – 1.82 (m, 1H), 1.66 – 1.46 (m, 7H), 1.44 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 160.9, 156.1, 147.4, 136.4, 135.7, 126.9, 125.9, 120.6, 79.3, 44.9, 43.9, 40.6, 32.4, 32.1, 28.6, 26.9, 26.8, 26.5, 22.8, 21.4, 14.3; HRMS (ESI) calcd for $C_{22}H_{32}N_3O_3^+$ $[M+H]^+$ = 386.2438, found = 386.2458.

Methyl 5-(11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-b]quinazolin-6-yl)pentanoate (7):

Compound **3a** (30 mg, 0.1 mmol) was treated with 0.4 mL conc. H_2SO_4 in 4.0 mL methanol and was heated to 90 °C for 12 h. After completion, the mixture was neutralized by saturated $NaHCO_3$, extracted with EtOAc, dried over anhydrous sodium sulfate, evaporated under

vacuum and purified by silica gel flash column chromatography to give compound in 81% yield.

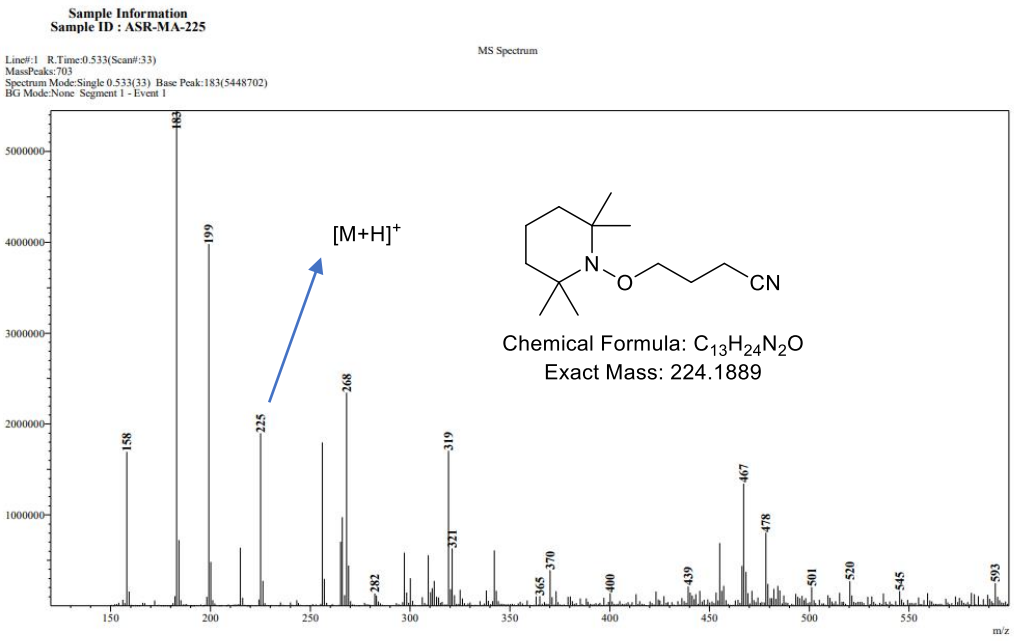


Yellow syrup (25.5 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 7.9 Hz, 1H), 7.77 – 7.59 (m, 2H), 7.41 (t, *J* = 7.5 Hz, 1H), 4.26 – 4.09 (m, 1H), 4.06 – 3.92 (m, 1H), 3.66 (s, 3H), 3.02 – 2.85 (m, 1H), 2.36 (t, *J* = 7.4 Hz, 2H), 2.27 – 1.86 (m, 4H), 1.82 – 1.61 (m, 4H), 1.59 – 1.41 (m, 2H); ^{13}C NMR (126 MHz, CDCl3) δ 174.2, 162.3, 157.9, 134.2, 126.7, 126.3, 120.2, 51.6, 42.2, 40.4, 34.1, 33.2, 26.7, 25.0, 24.6, 20.3; HRMS (ESI) calcd for $C_{18}H_{23}N_2O_3^+$ $[M+H]^+$ = 315.1703, found = 315.1698.

6) Control experiments for mechanistic studies:

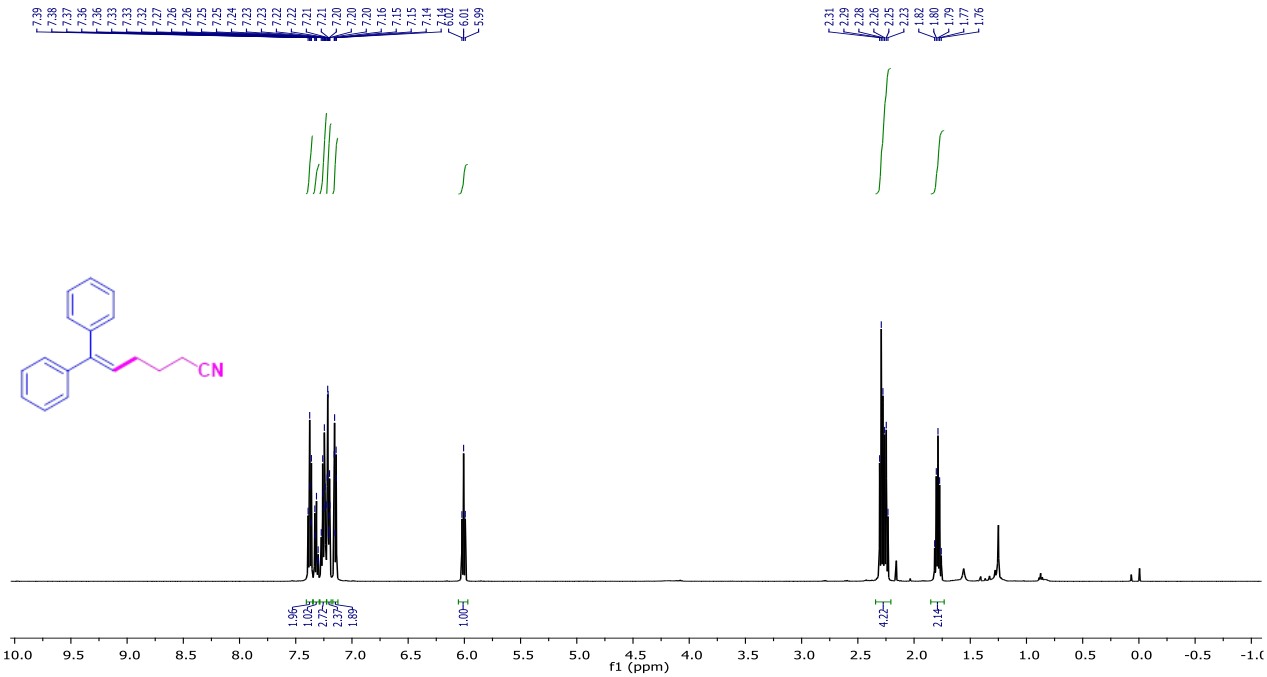
6.1) Radical inhibition/trapping experiments:

(i) To an oven dried vial equipped with a magnetic stir bar was added quinazolin-4(3H)-one **1a** (64.3 mg, 0.3 mmol), oxime ester **2a** (154.2 mg, 0.6 mmol), TEMPO (93.8 mg, 0.6 mmol) and eosin Y (7.8 mg, 0.012 mmol). The tube was sealed with a septum, evacuated and back filled with nitrogen three times. 1 mL of H_2O was then added via syringe with gentle stirring. The tube was sealed and stirred under *Thales Nano photocube* (4 × 32 W blue LED) for 12 h. After completion of reaction, the reaction mixture was diluted with DCM (20 mL), and washed successively with water (15 mL ×2), aq. $NaHCO_3$ solution (10 mL×2) and brine solution (10 mL×2). The organic layer was dried over anhydrous sodium sulfate, concentrated. In this reaction, the formation of product 3aa was completely suppressed. The cyanoalkyl-TEMPO adduct **8** was characterized by ESI-MS.

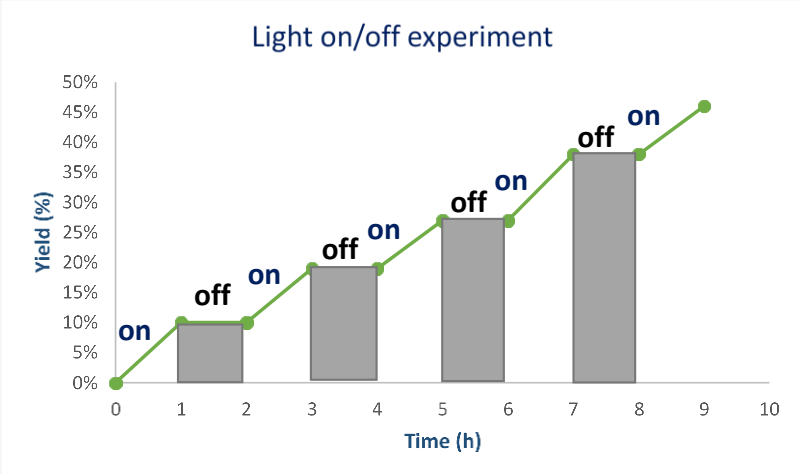


(ii) To an oven-dried sealed tube equipped with a magnetic stir bar was charged with quinazoline-4(3H)-one **1a** (64.3 mg, 0.3 mmol), oxime ester **2a** (154.2 mg, 0.6 mmol), 1,1- diphenylethylene (0.1 mL, 0.6 mmol), eosin Y (7.8 mg, 0.012 mmol), and H_2O (1.0 mL). The tube was sealed and stirred under *Thales Nano photocube* (4 × 32 W blue LED) for 12 h, no corresponding product 3a was detected and the heck-type product **9** was isolated in 65% yield, indicating that this photo-induced cyanoalkylation/cyclisation protocol may proceed through a radical-based mechanism. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.35 – 7.30 (m, 1H), 7.29 – 7.23 (m, 3H), 7.21 (dt, *J* = 7.9, 1.7 Hz, 2H), 7.15 (dd, *J* = 8.1, 1.2 Hz, 2H), 6.01 (t, *J* = 7.4 Hz, 1H), 2.27 (dt, *J* = 22.4, 7.4 Hz, 4H), 1.79 (p, *J* = 7.3 Hz, 2H).

^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (9)



5.2) Light on/off experiment:



Quinazolin-4(3H)-one **1a** (64.3 mg, 0.3 mmol), oxime ester **2a** (154.2 mg, 0.6 mmol), eosin Y (7.8 mg, 0.012 mmol) and internal standard 1,3,5-trimethoxy benzene (50.5 mg, 0.3 mmol) were weighed in a vial. Later 1.0 mL of H_2O was added via syringe and the vial was sealed with a septum. Then this sealed vial was irradiated with blue LED alternately over 1hour (i.e.

the reaction mixture was under light for 1hour followed by in the absence of light for the next 1hour). After each 1hour of interval, some aliquot was removed from the reaction mixture and analyzed by ^{1}H nmr to determine the yield. As shown in the above graph, there was no progress in this transformation when the light was switched off. The results of this experiment indicate that continuous irradiation is necessary for this transformation, indicating that the possibility of a radical chain mechanism is highly unlikely in this scenario.

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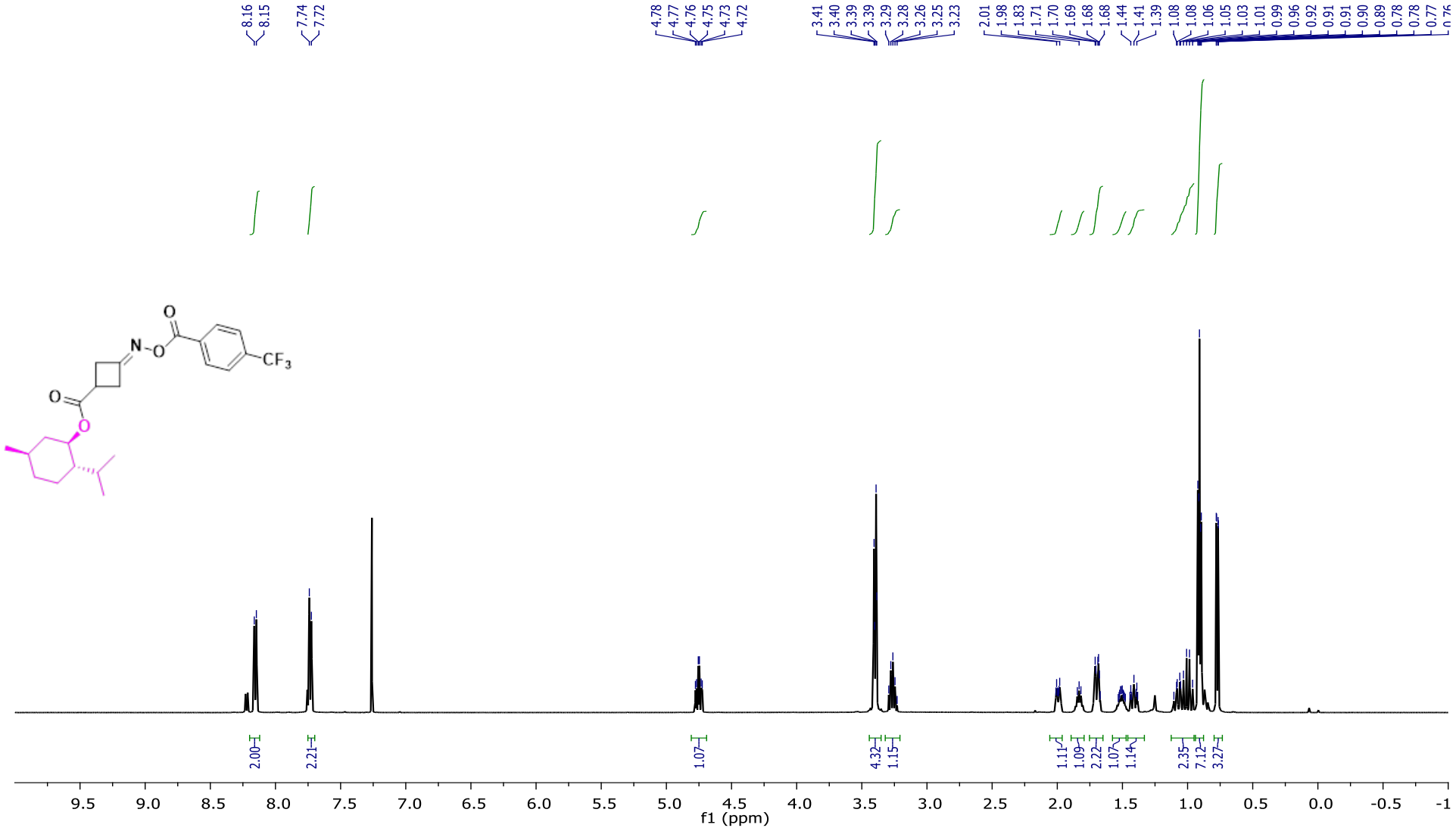
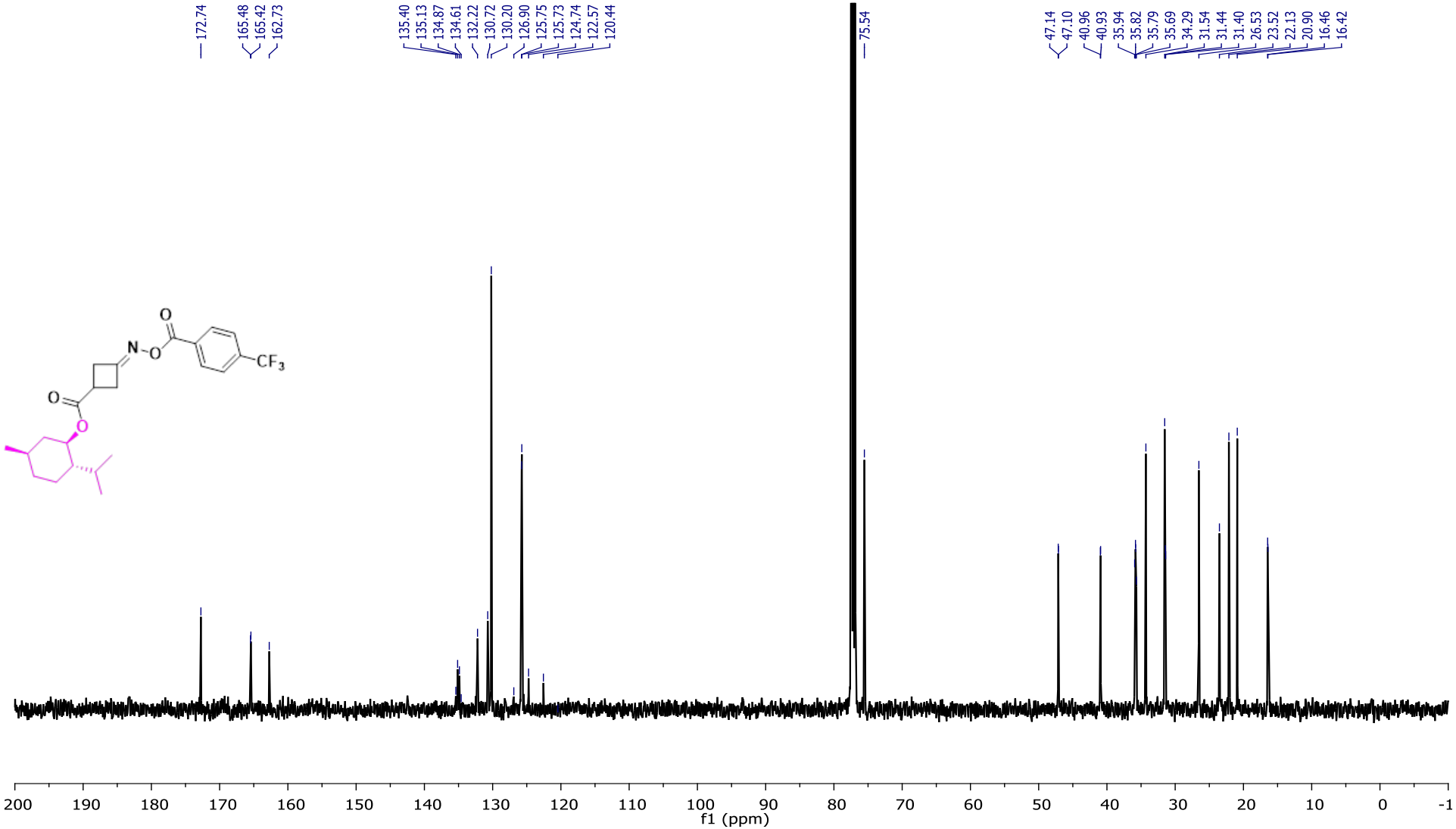
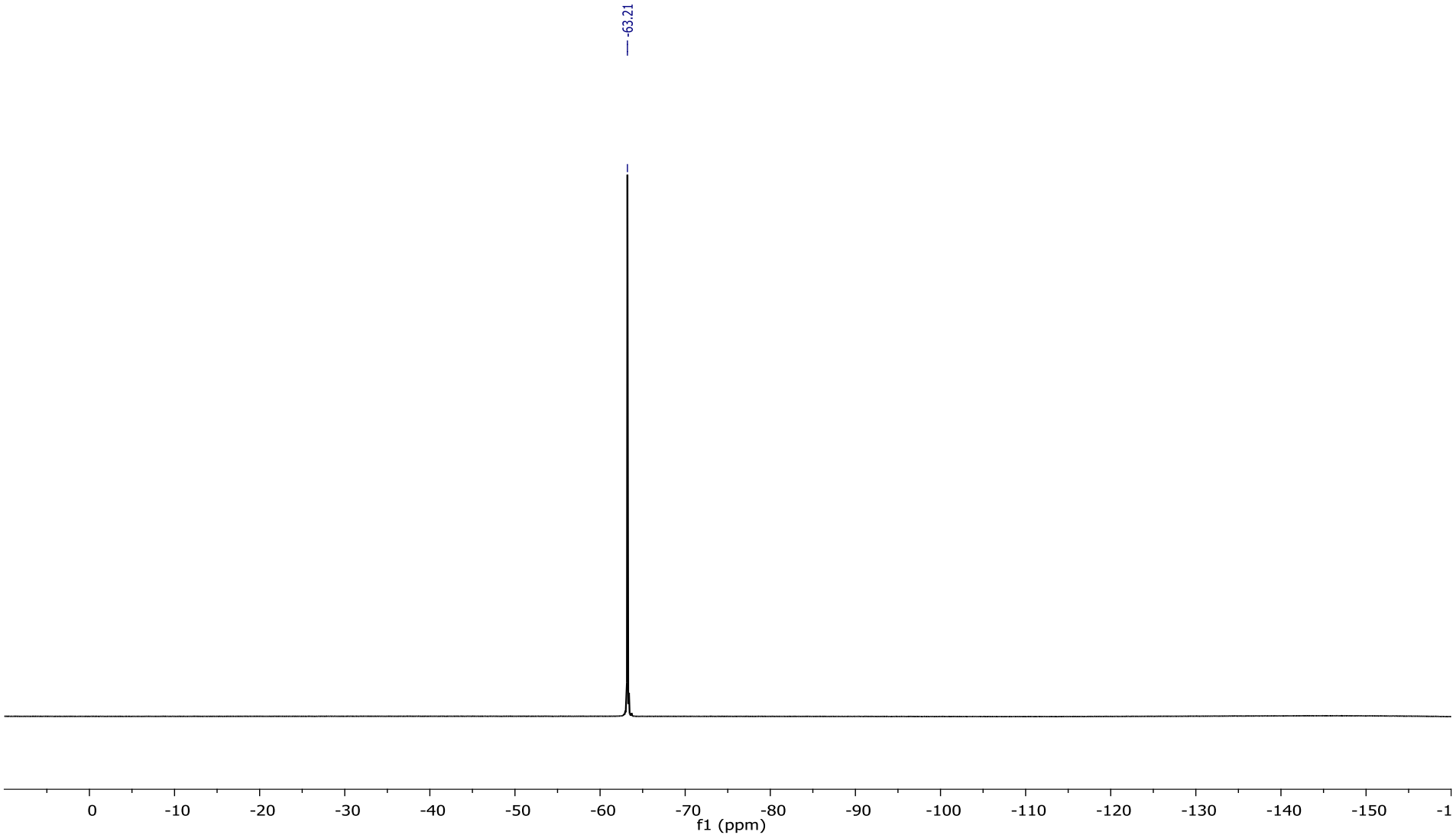
^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (2j)



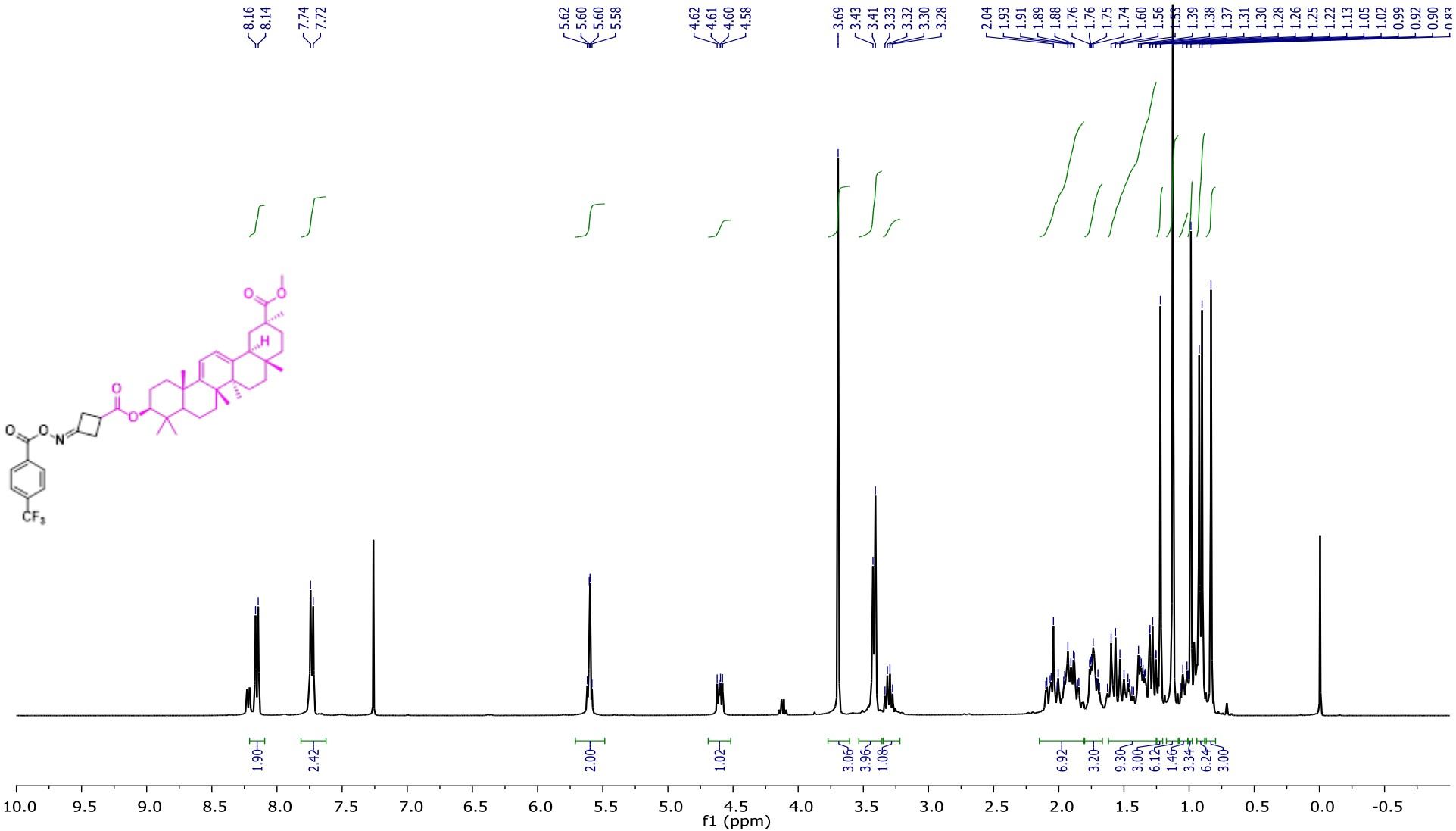
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (2j)



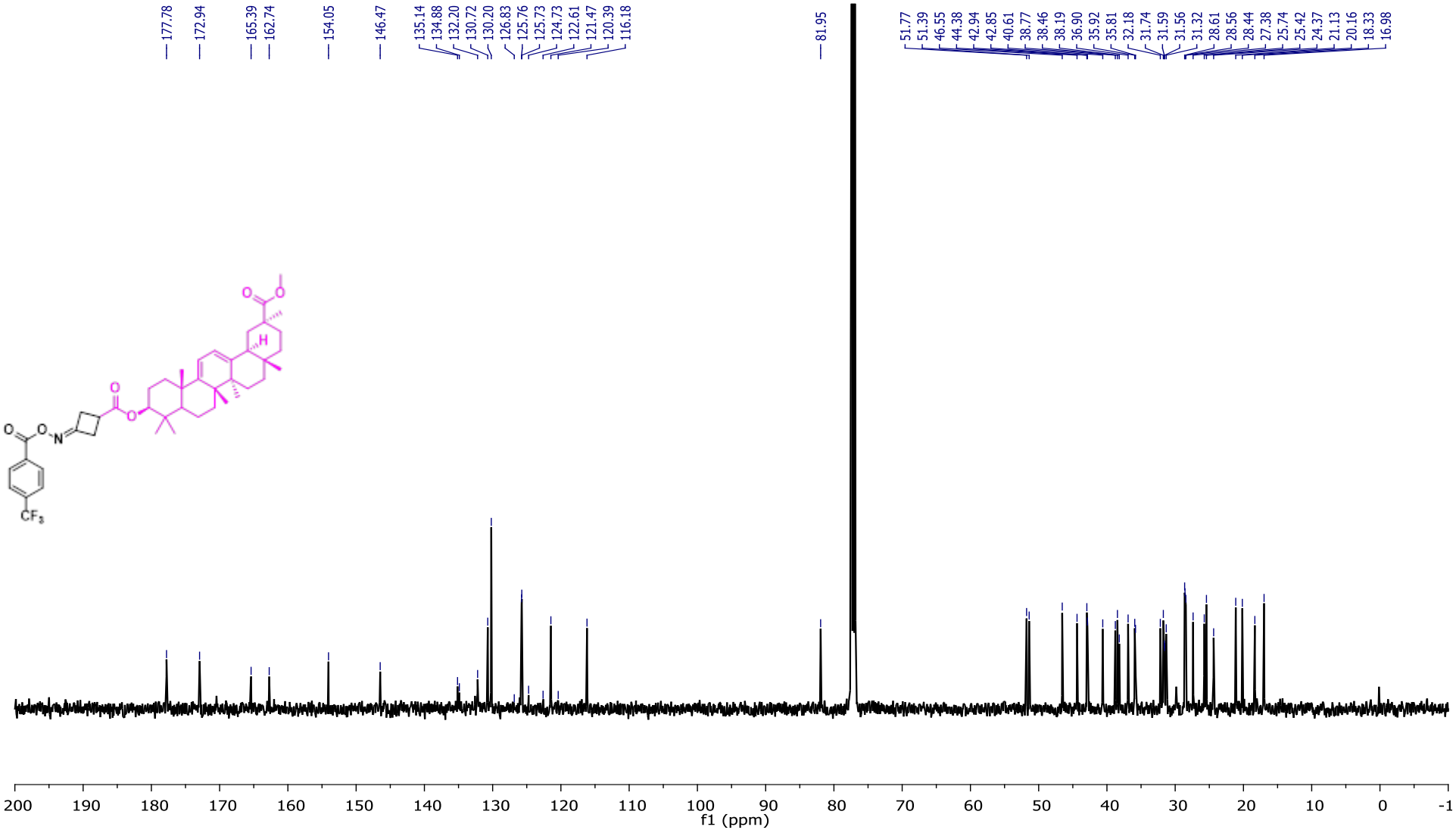
^{19}FNMR (376 MHz, $CDCl_3$) Spectrum of Compound (2j)



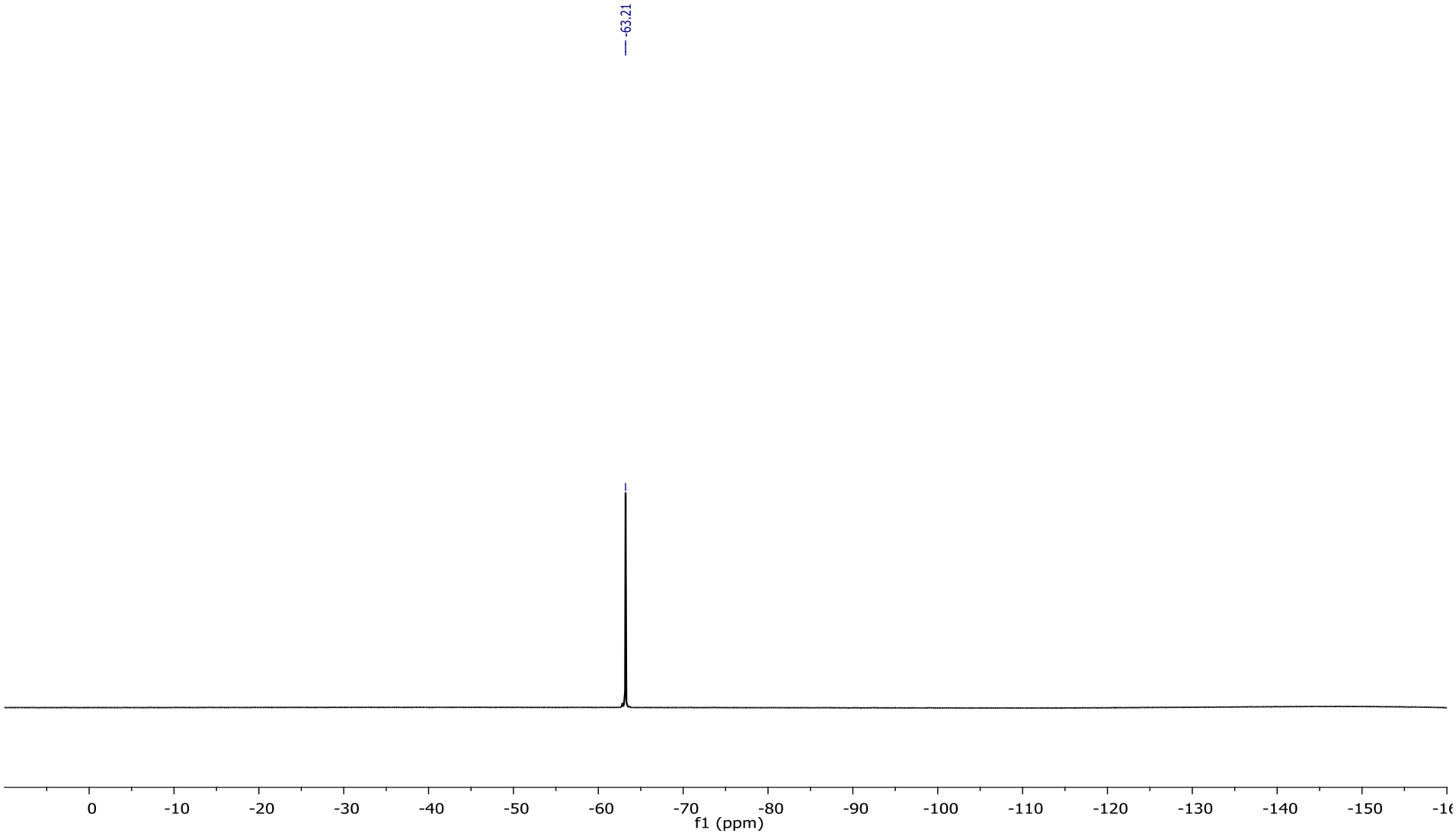
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (2l)



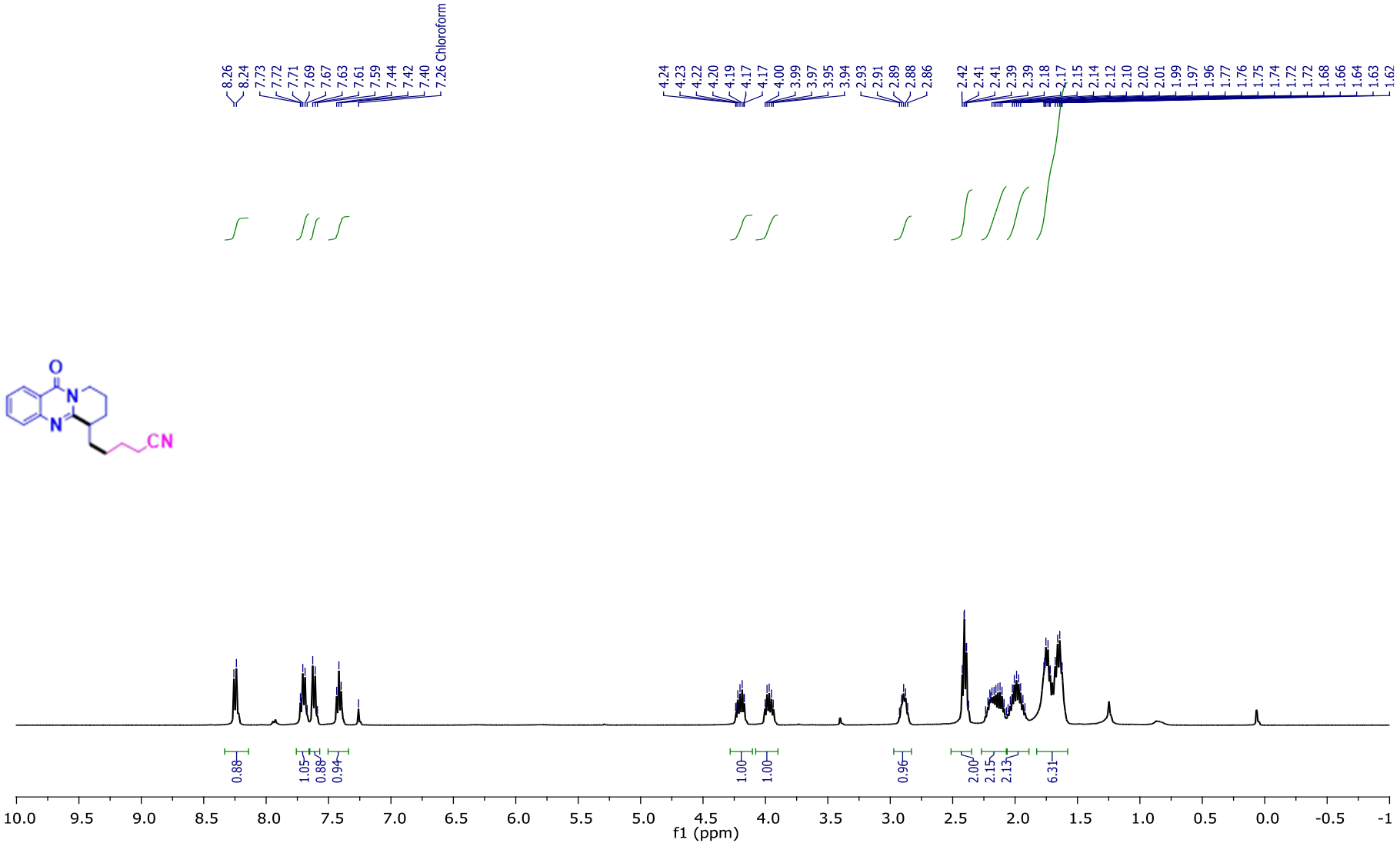
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (2l)



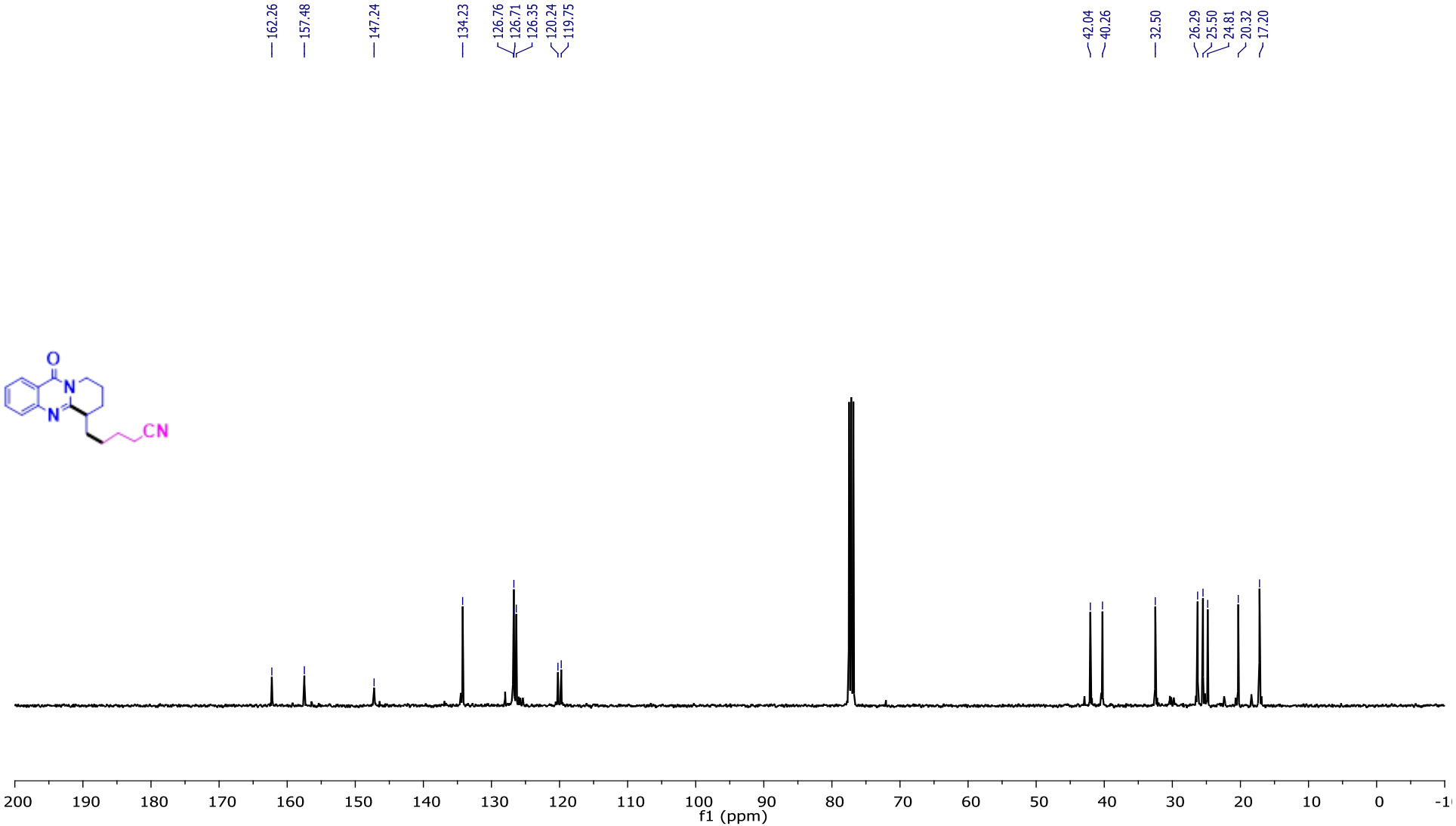
^{19}FNMR (376 MHz, $CDCl_3$) Spectrum of Compound (2l)



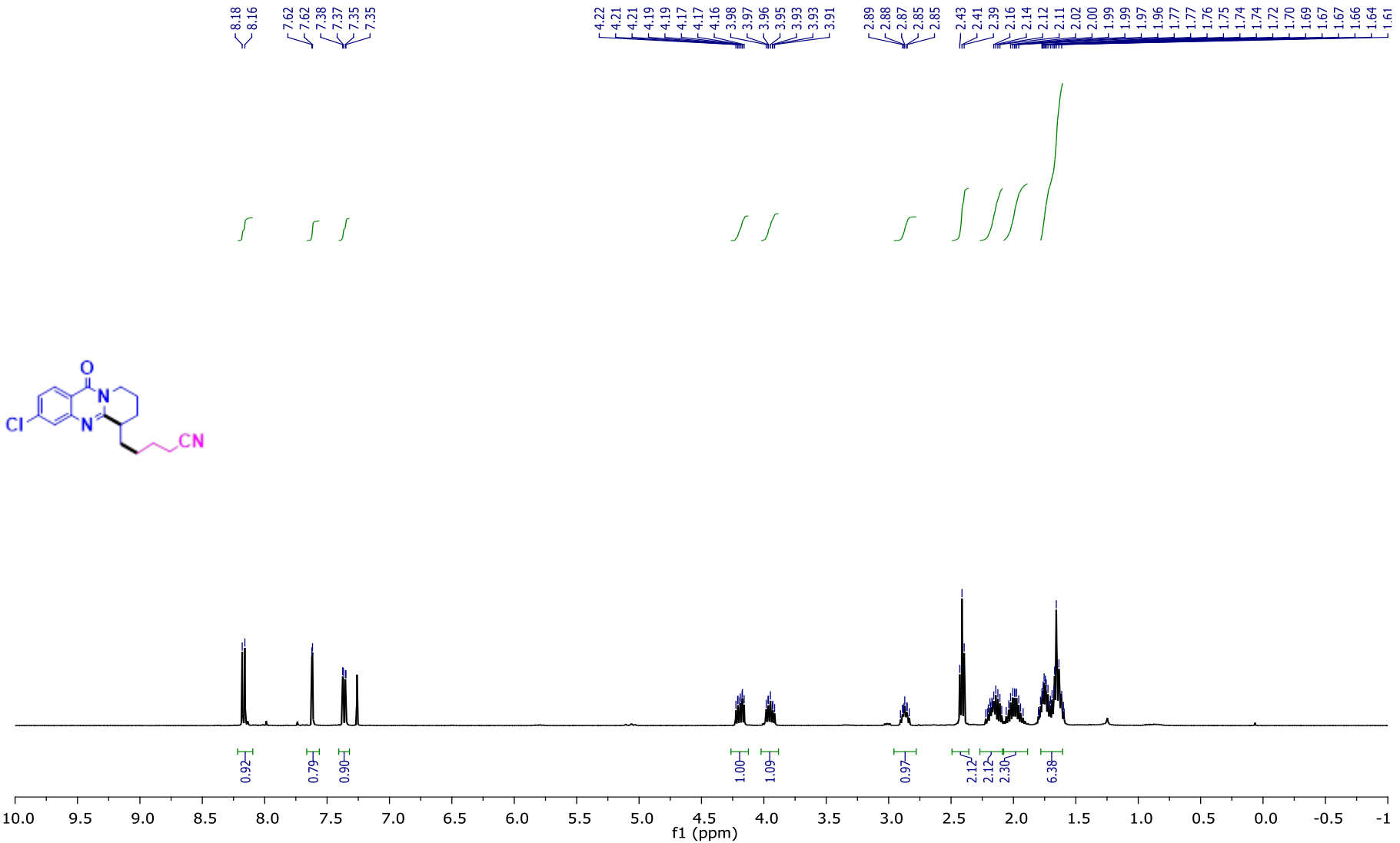
[1]HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3a)



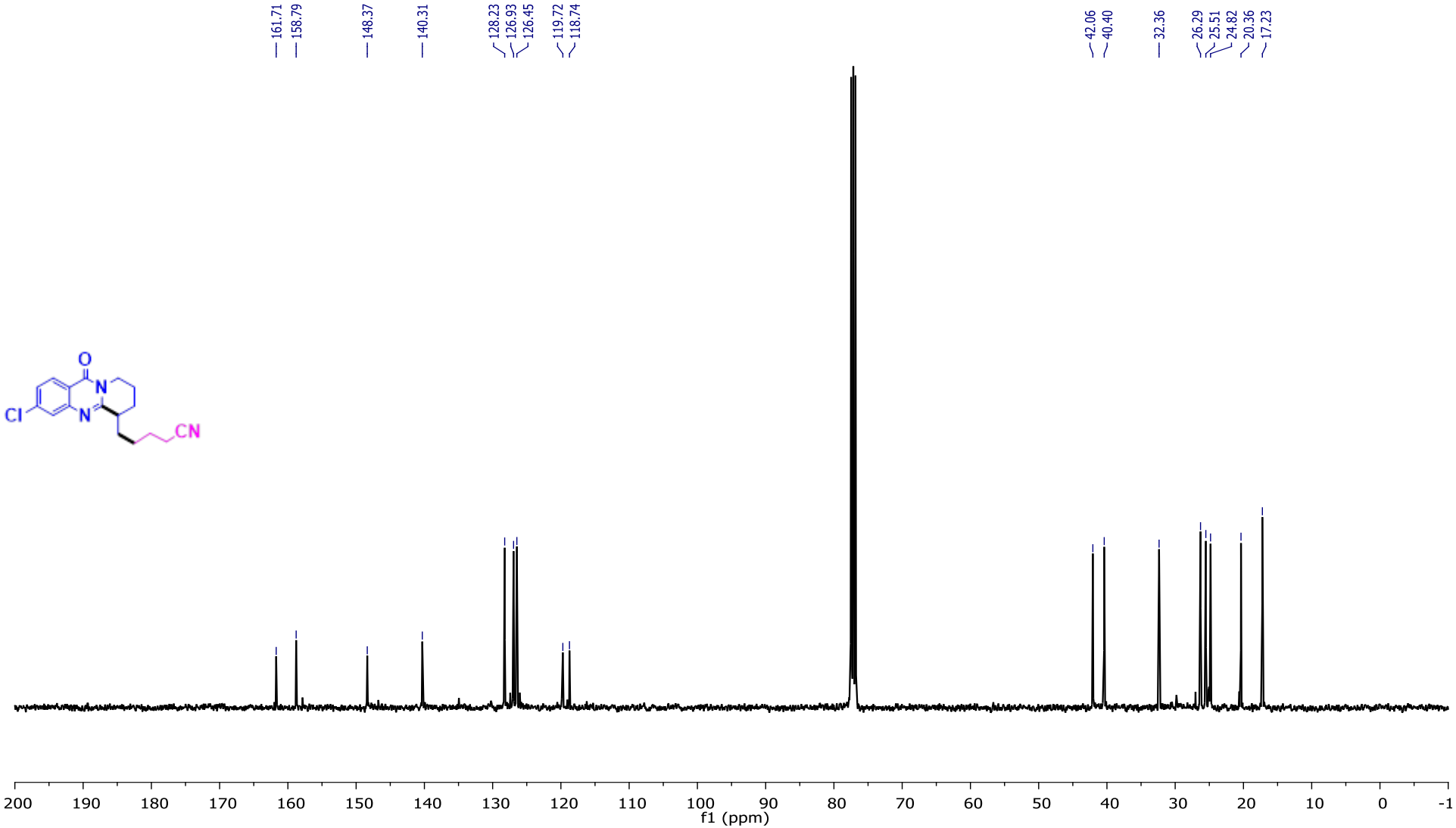
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3a)



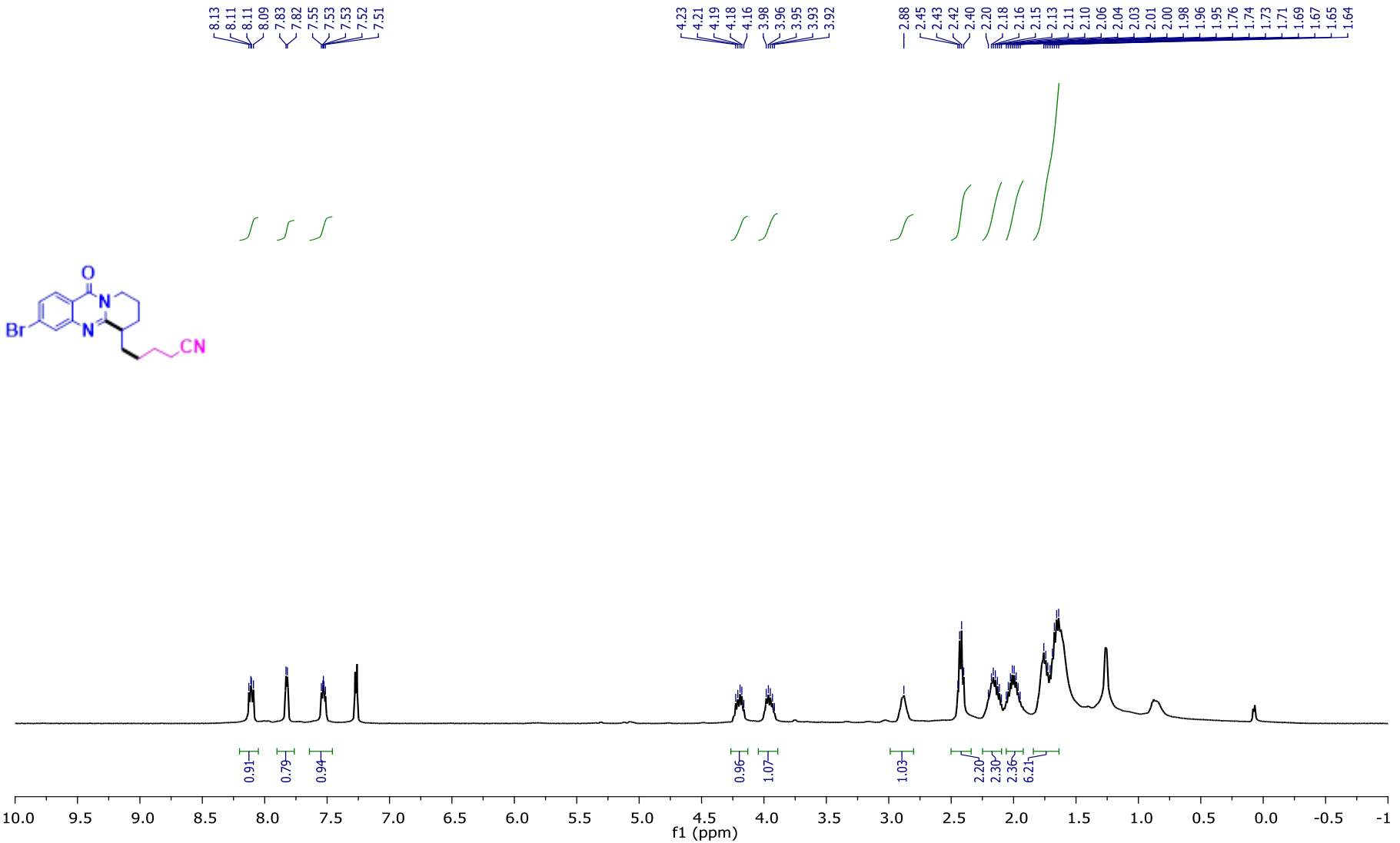
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3b)



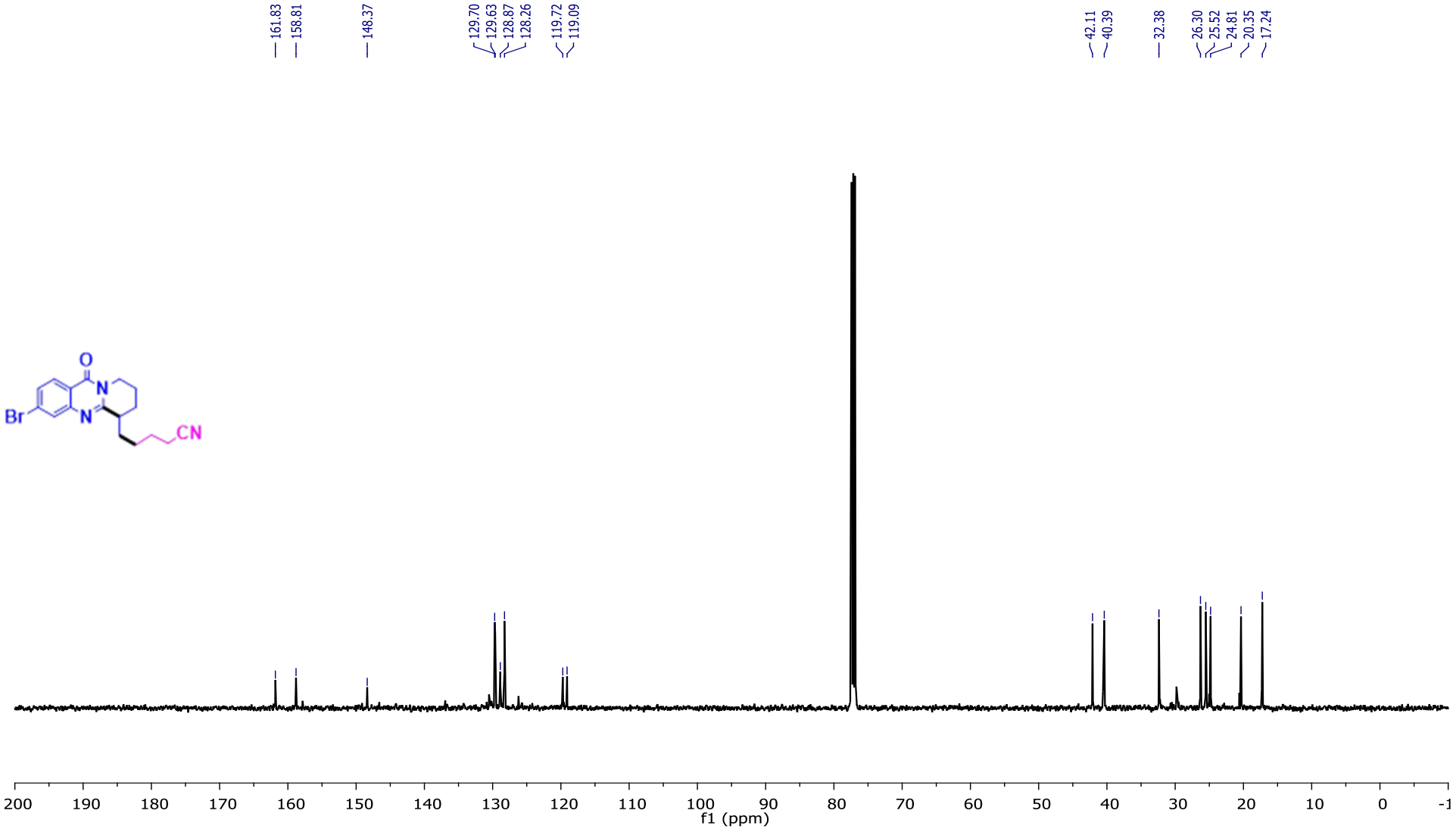
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3b)



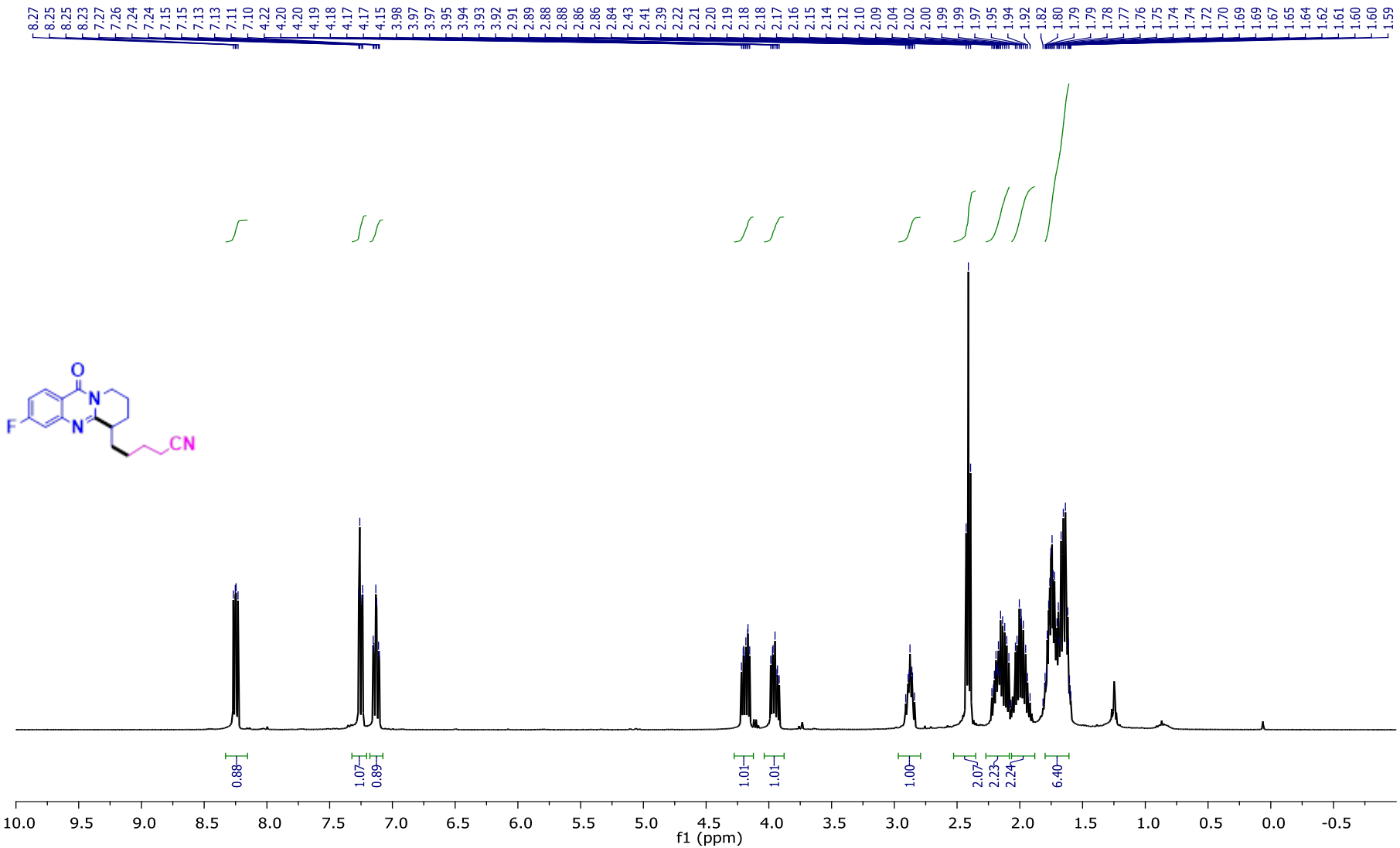
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3c)



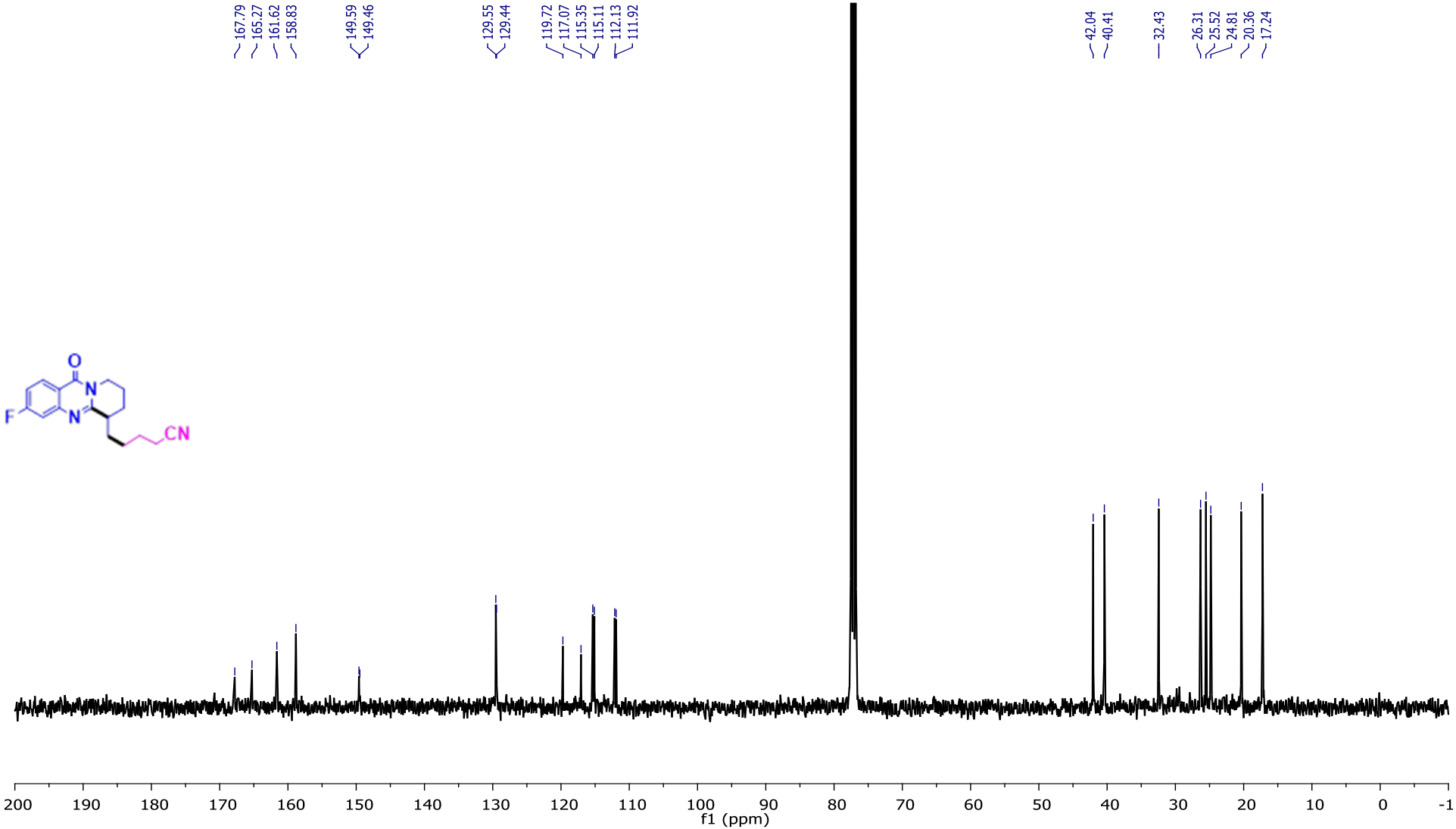
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (3c)



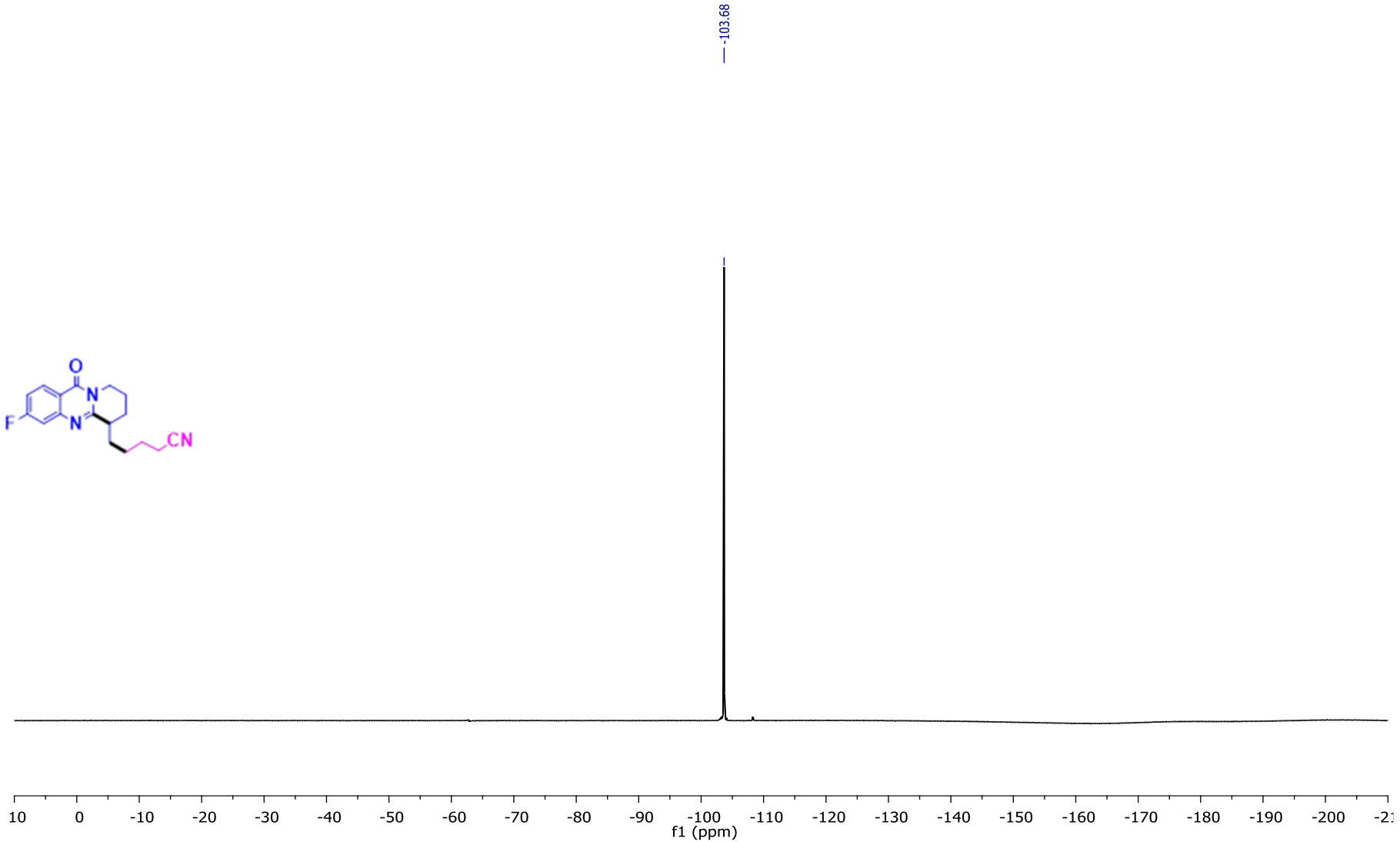
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3d)



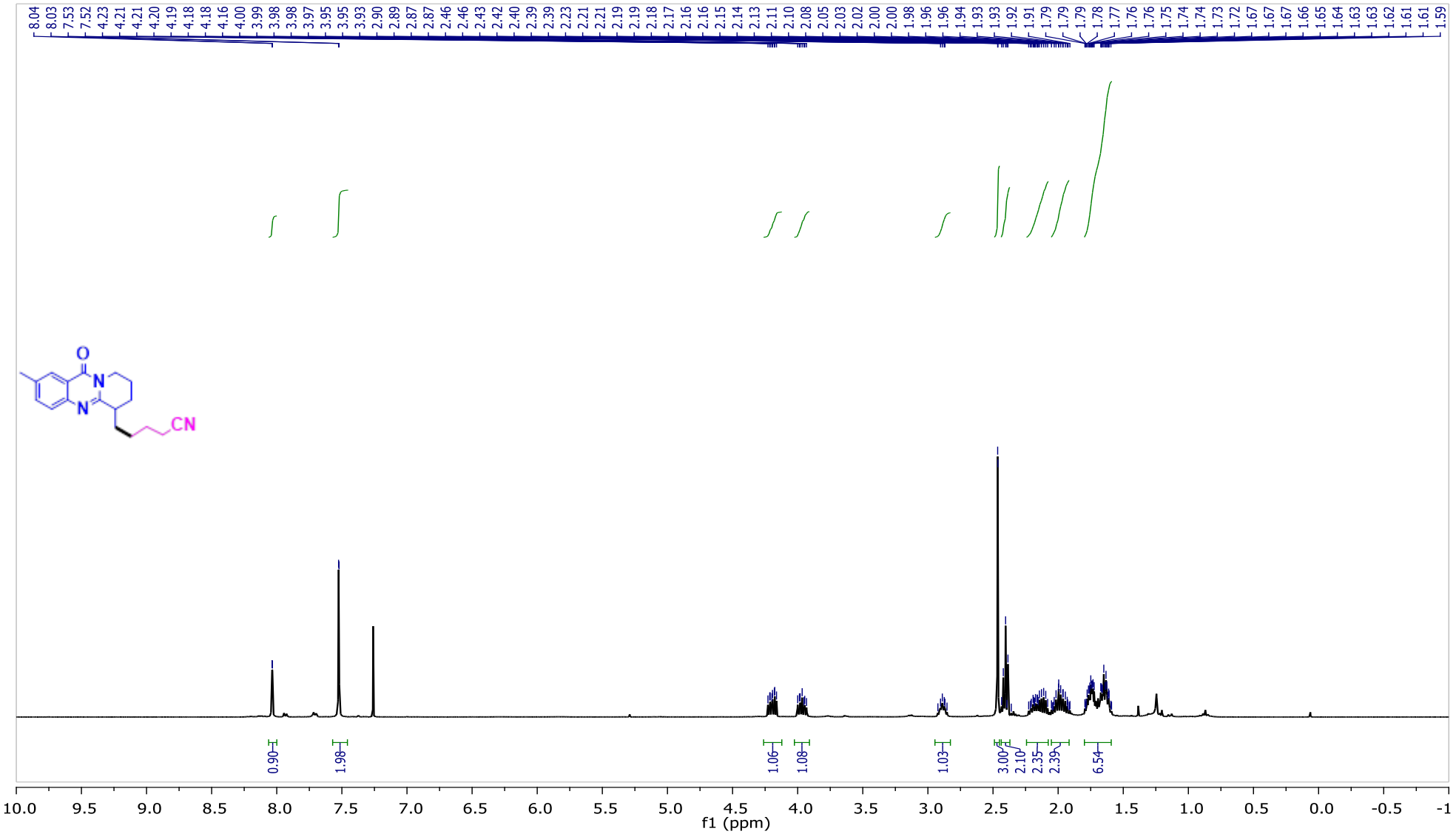
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3d)



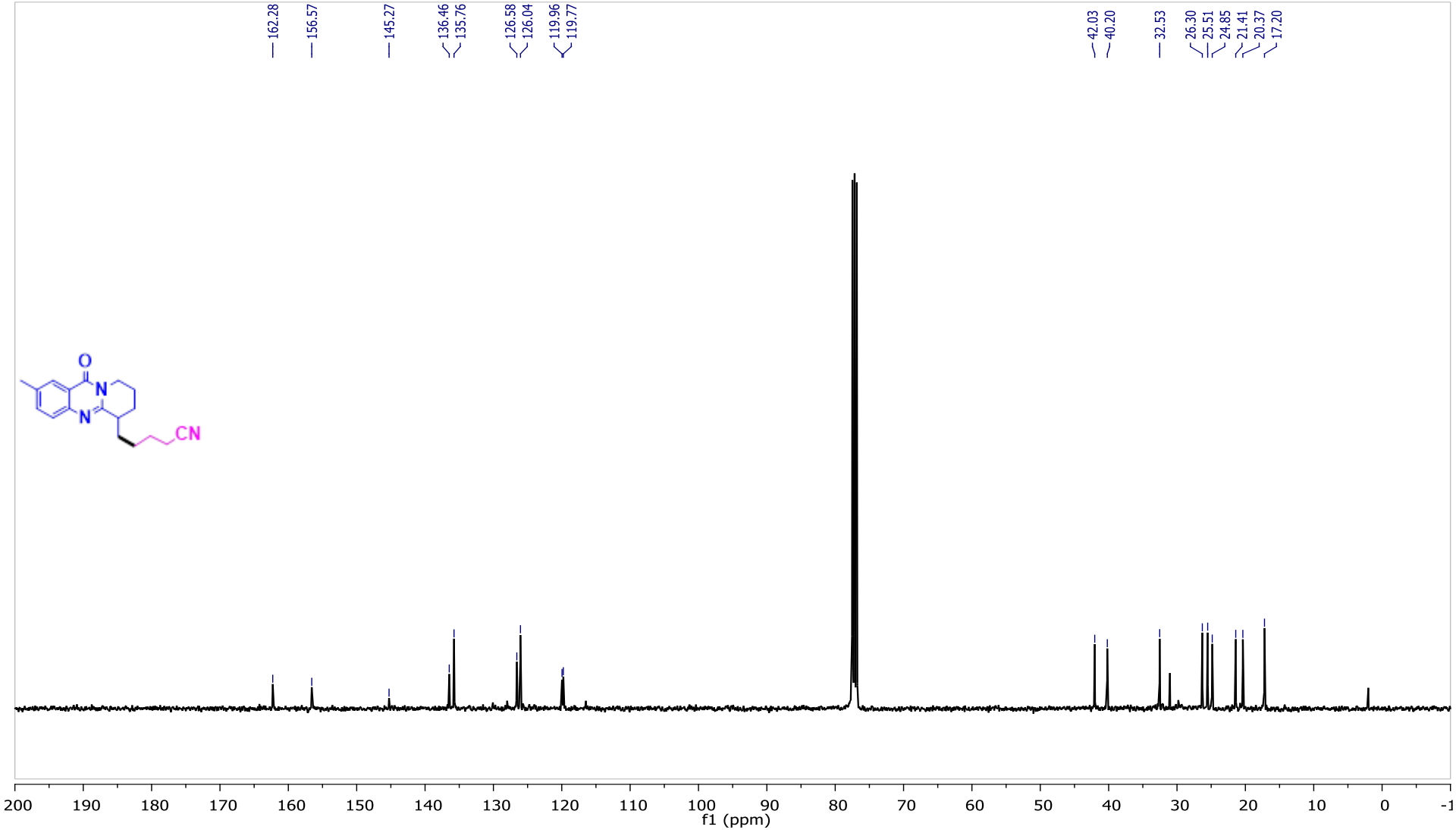
^{19}FNMR (376 MHz, $CDCl_3$) Spectrum of Compound (3d)



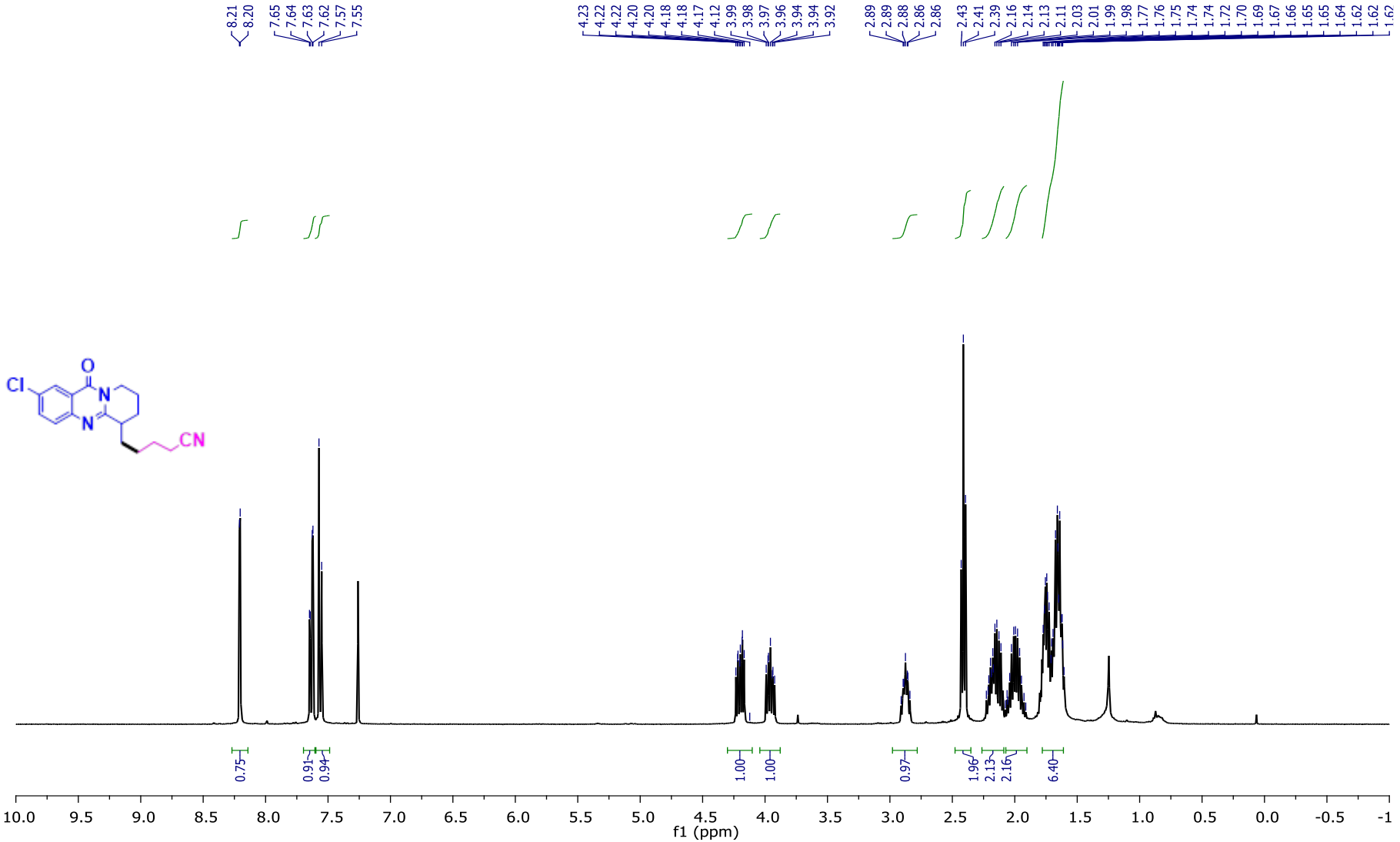
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3e)



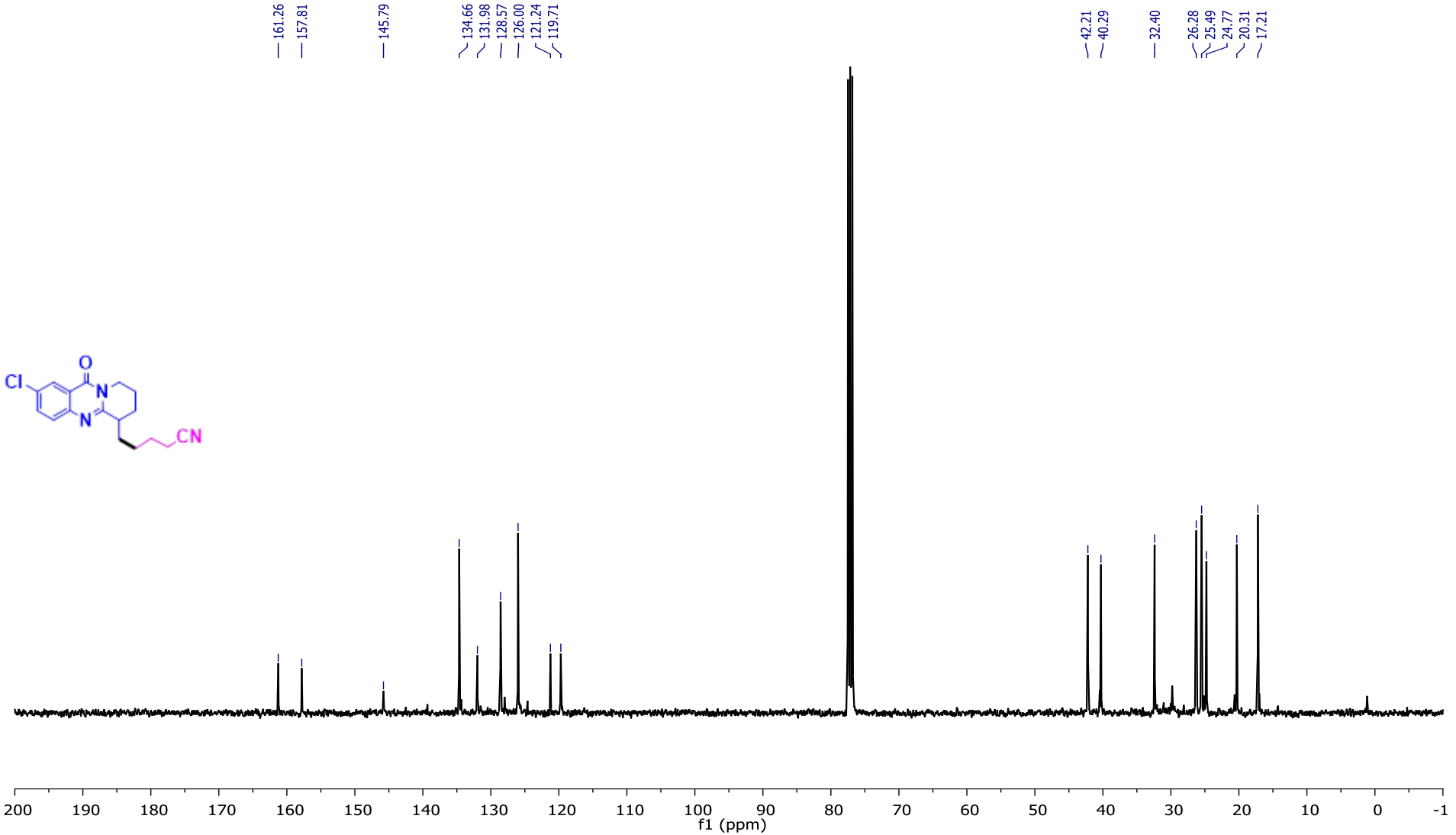
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3e)



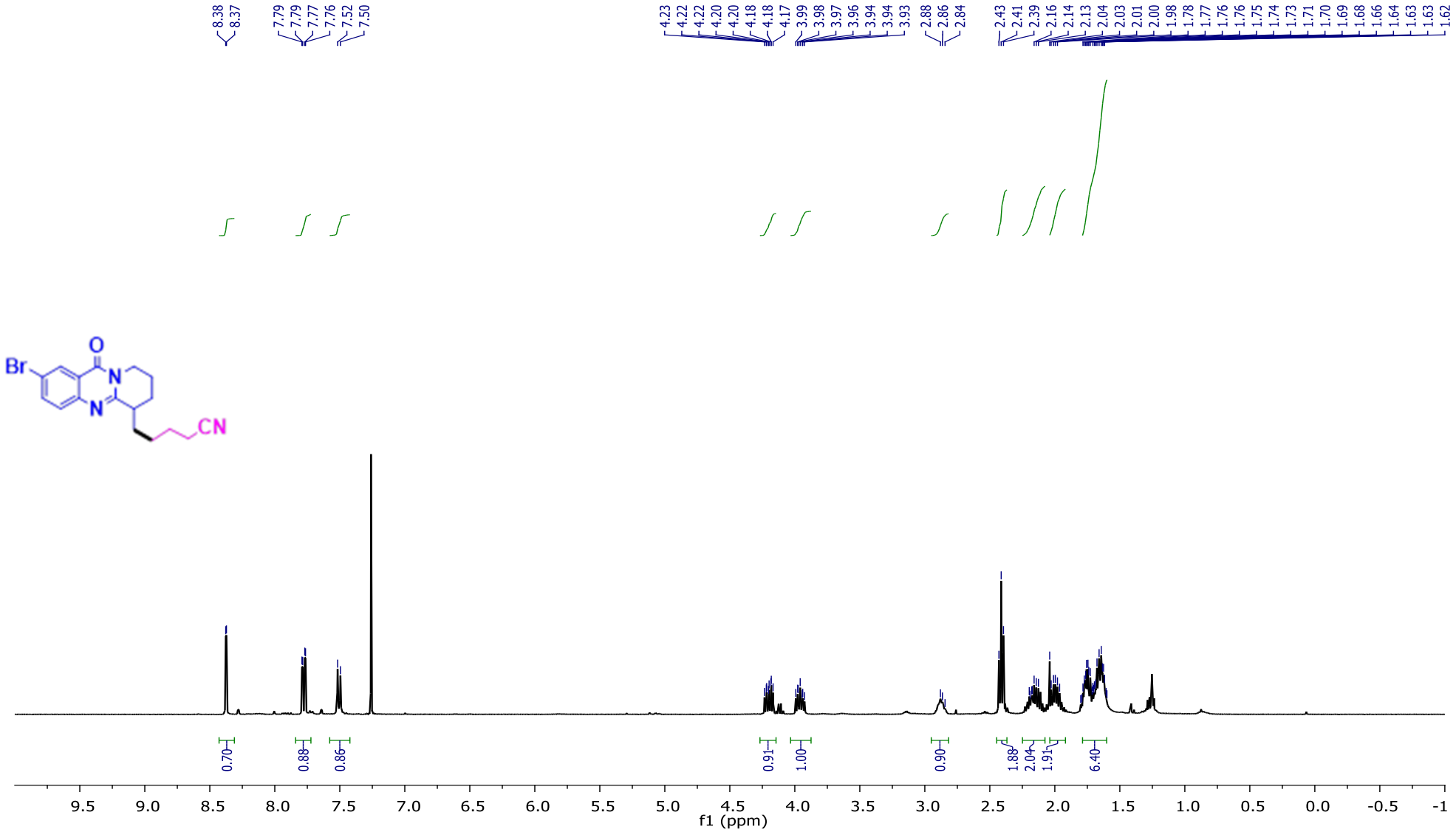
^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (3f)



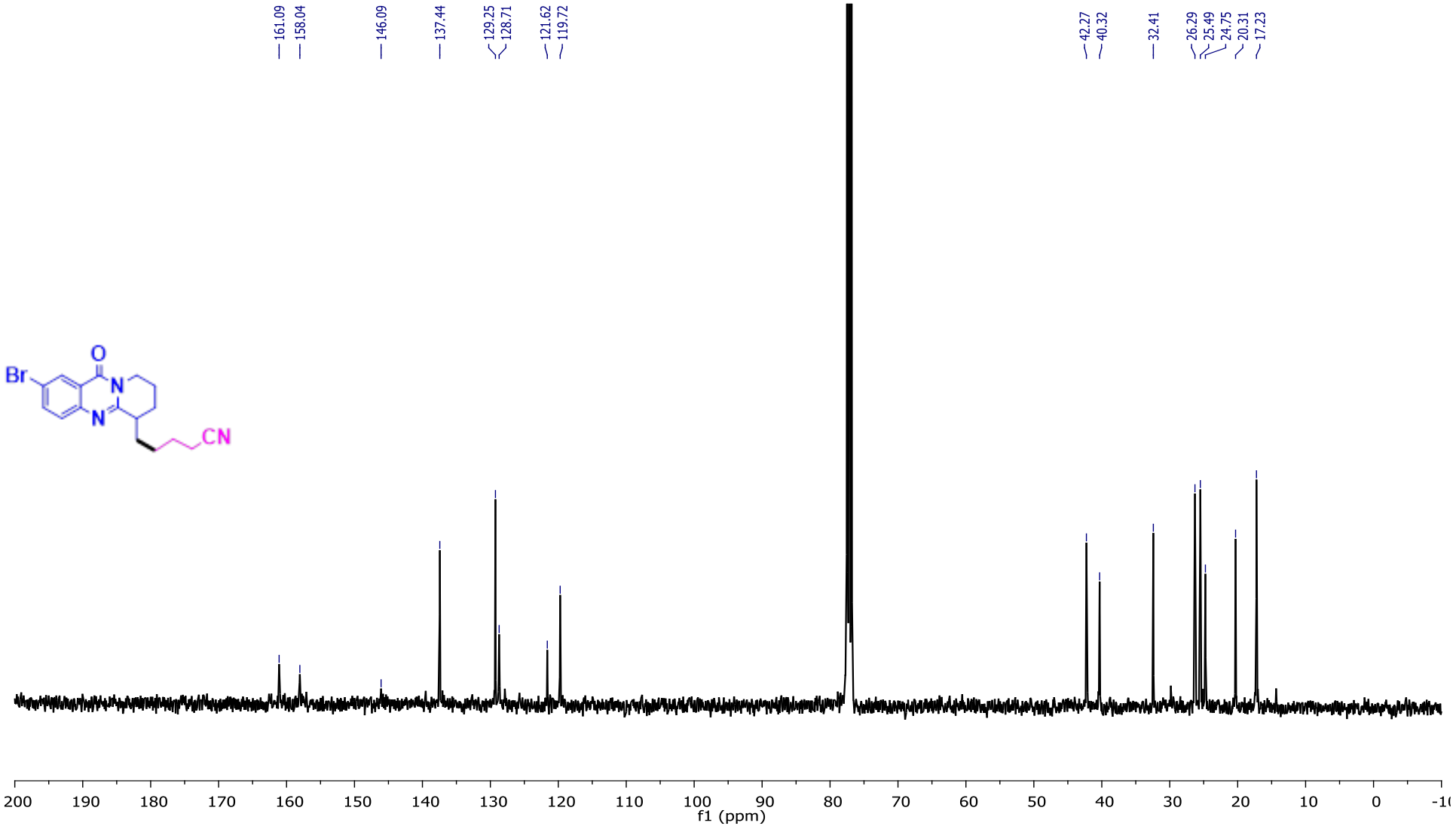
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3f)



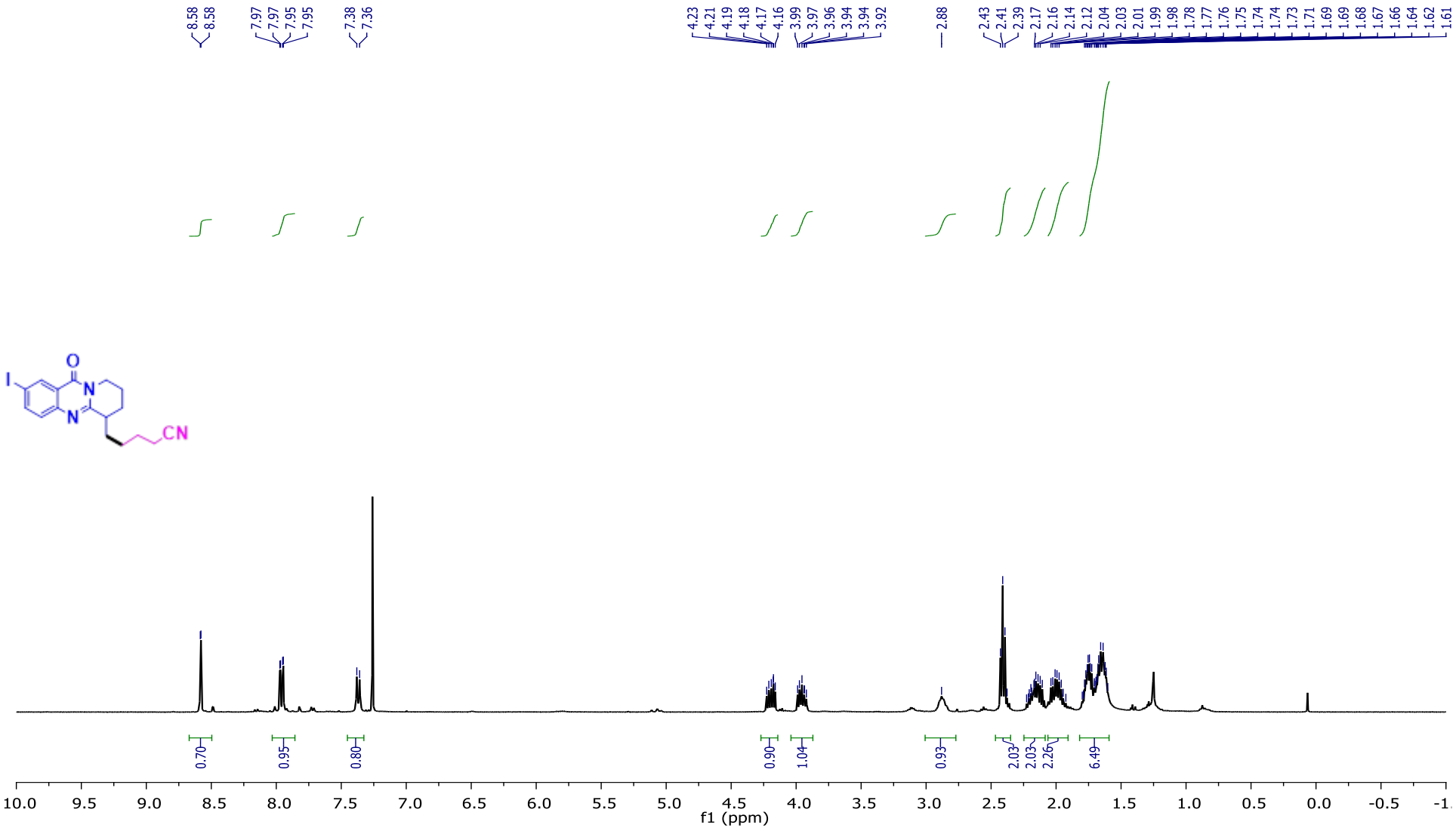
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3g)



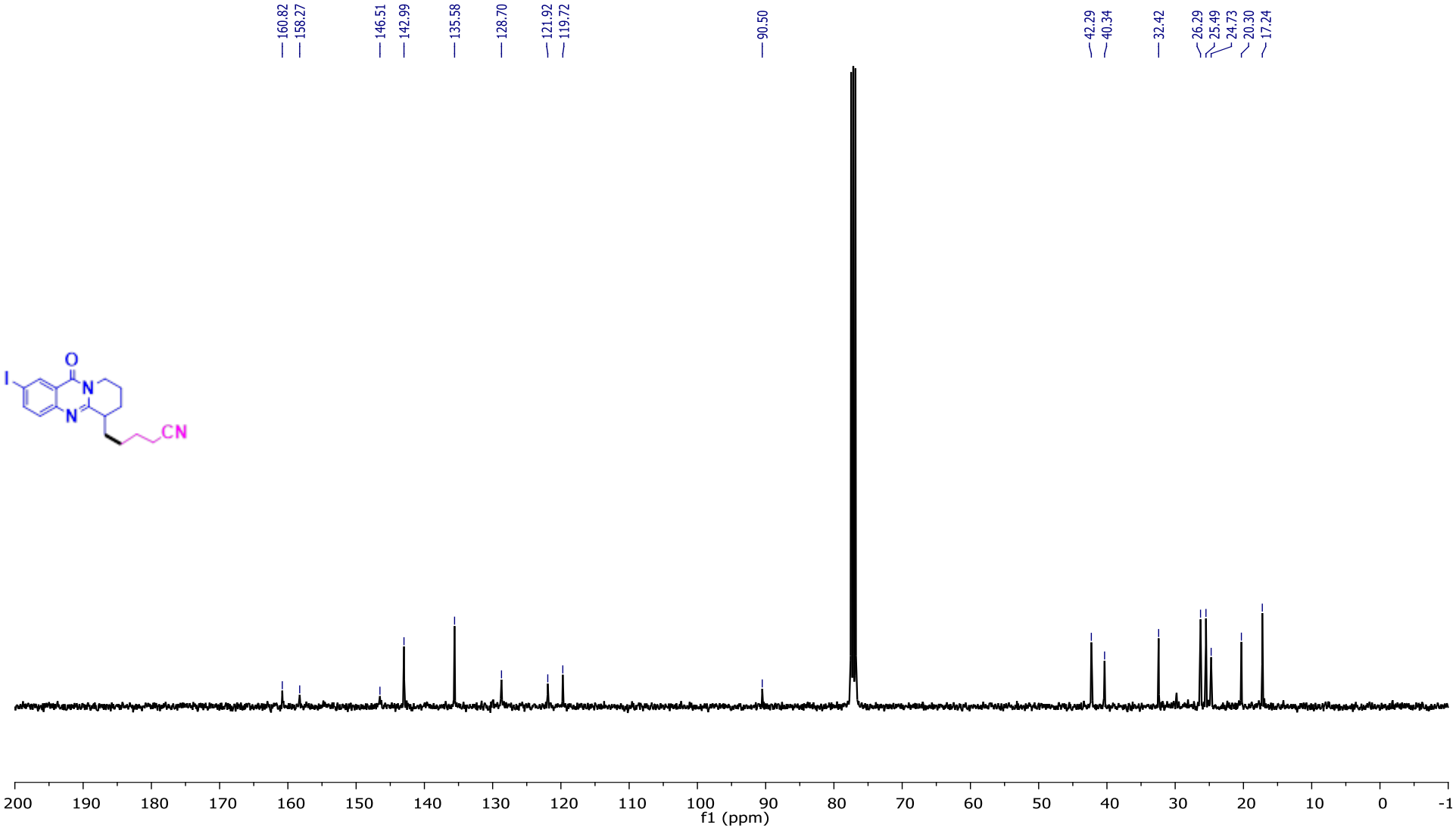
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3g)



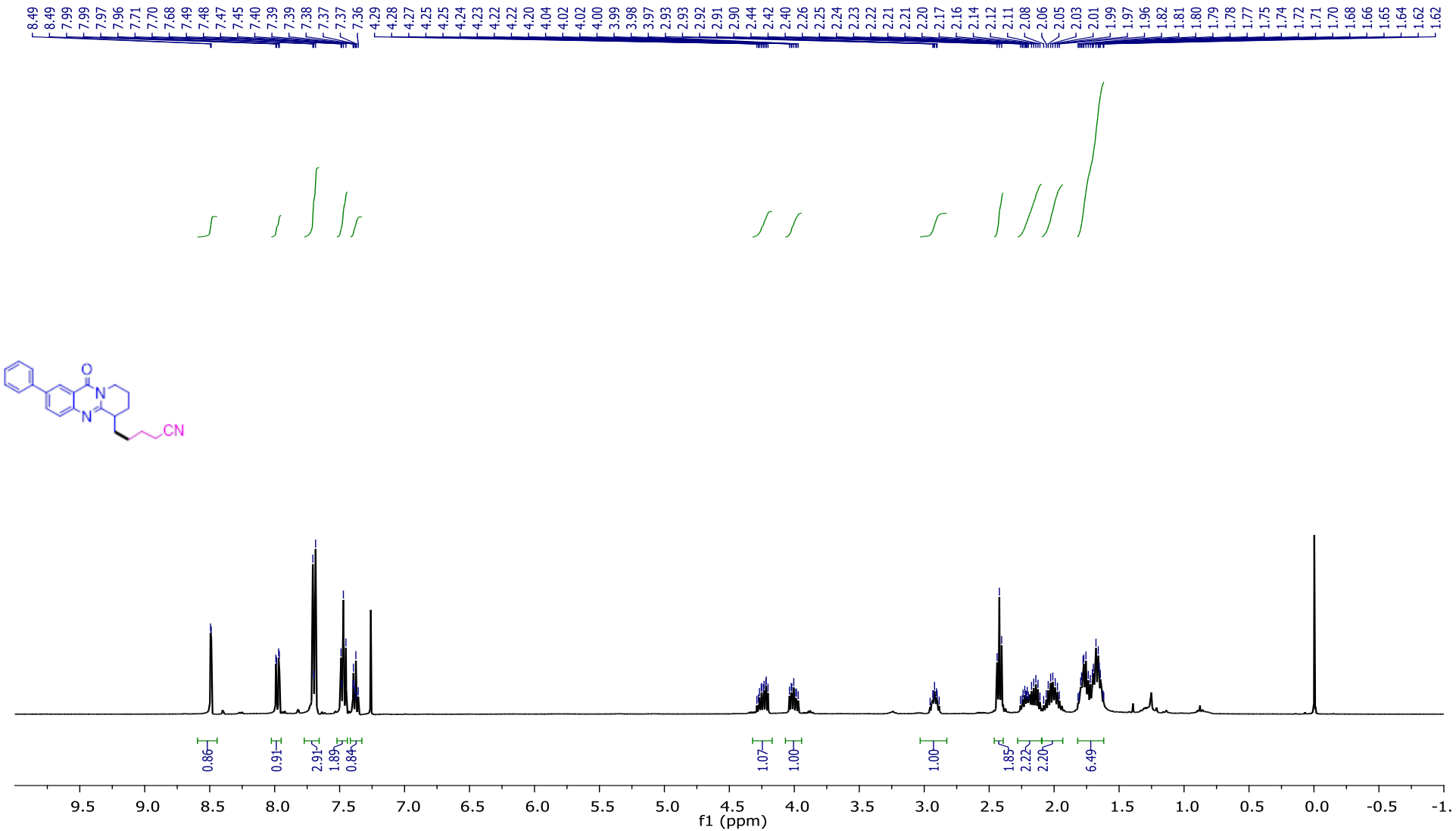
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3h)



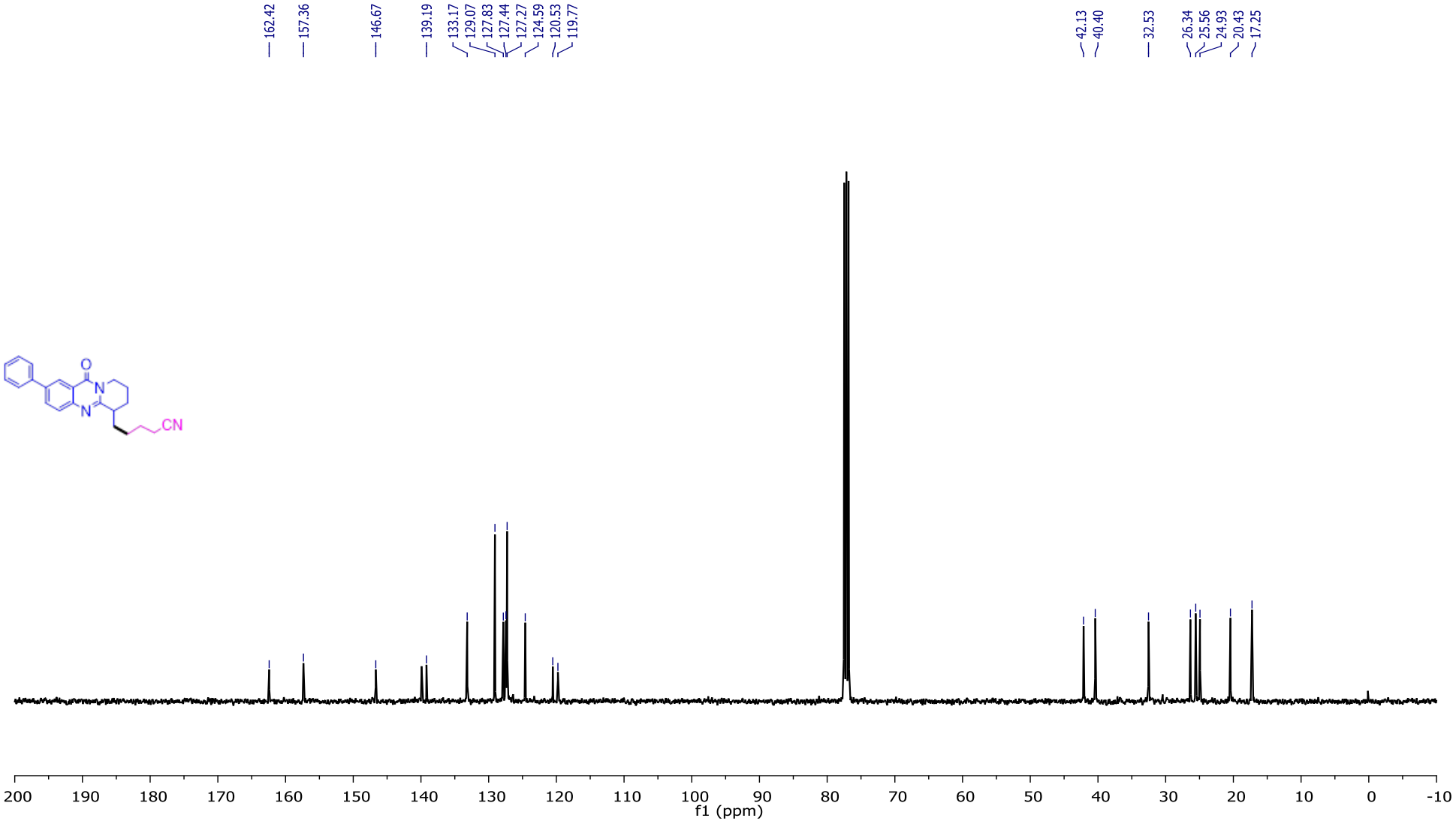
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3h)



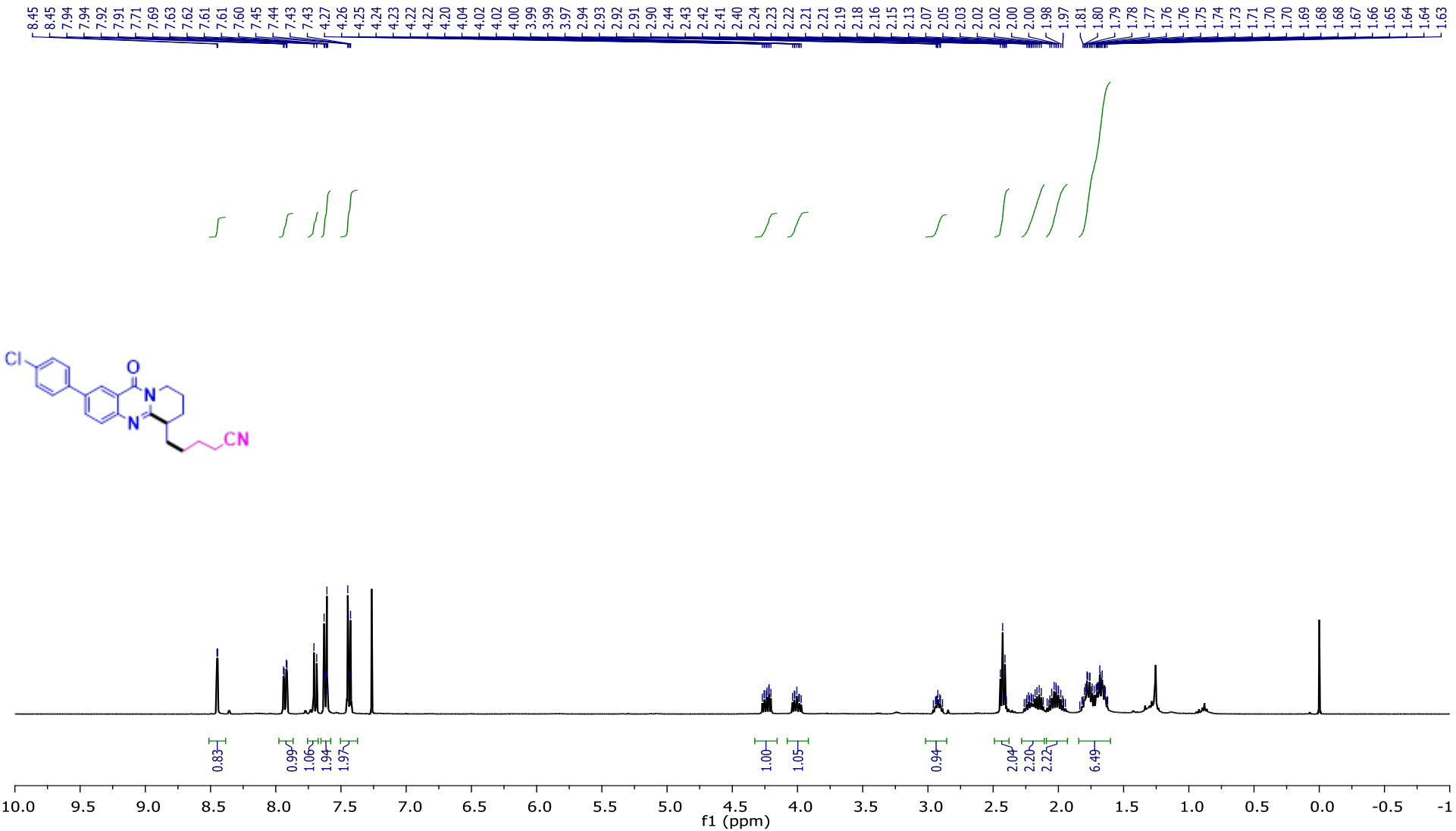
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3i)



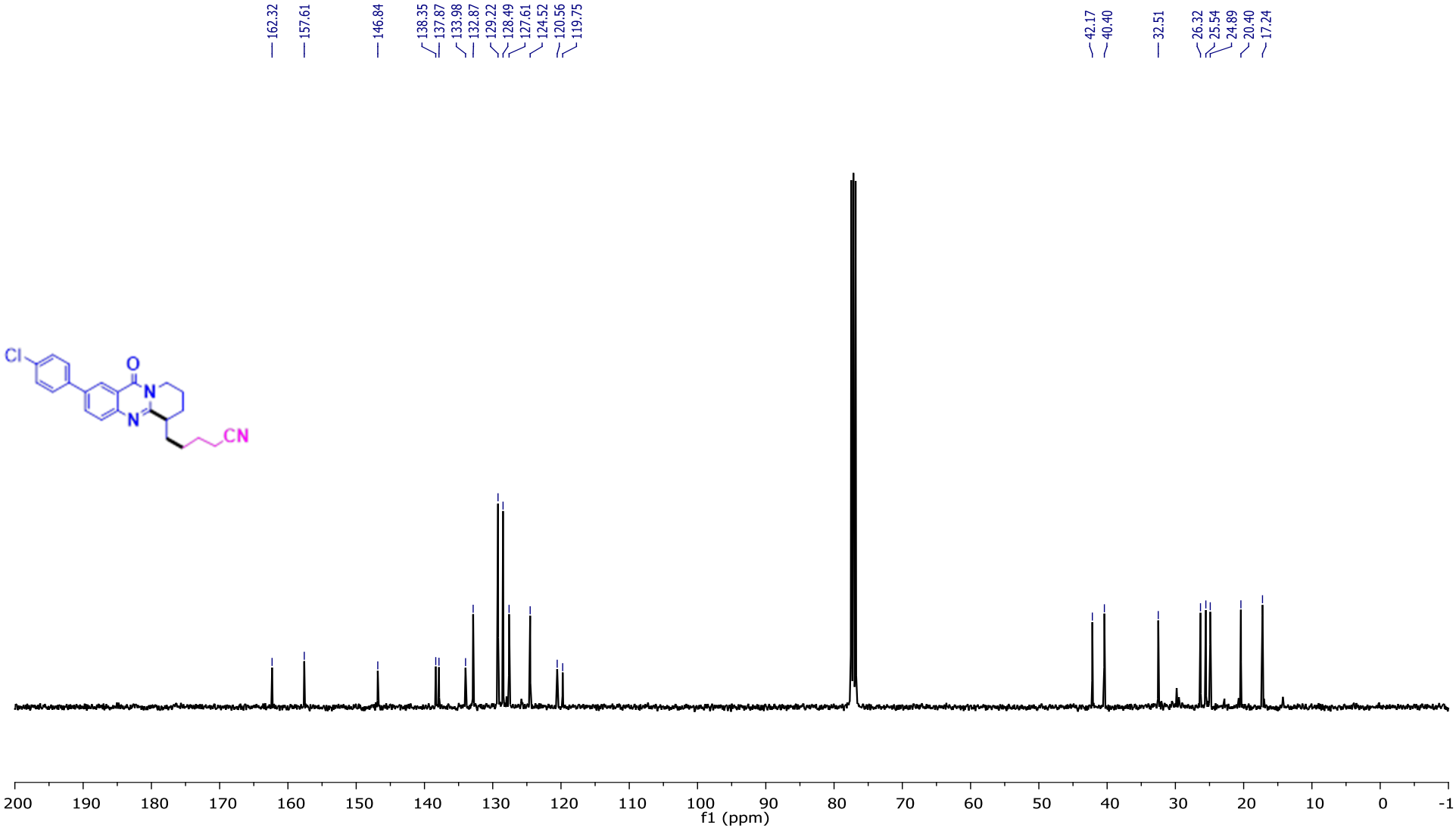
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3i)



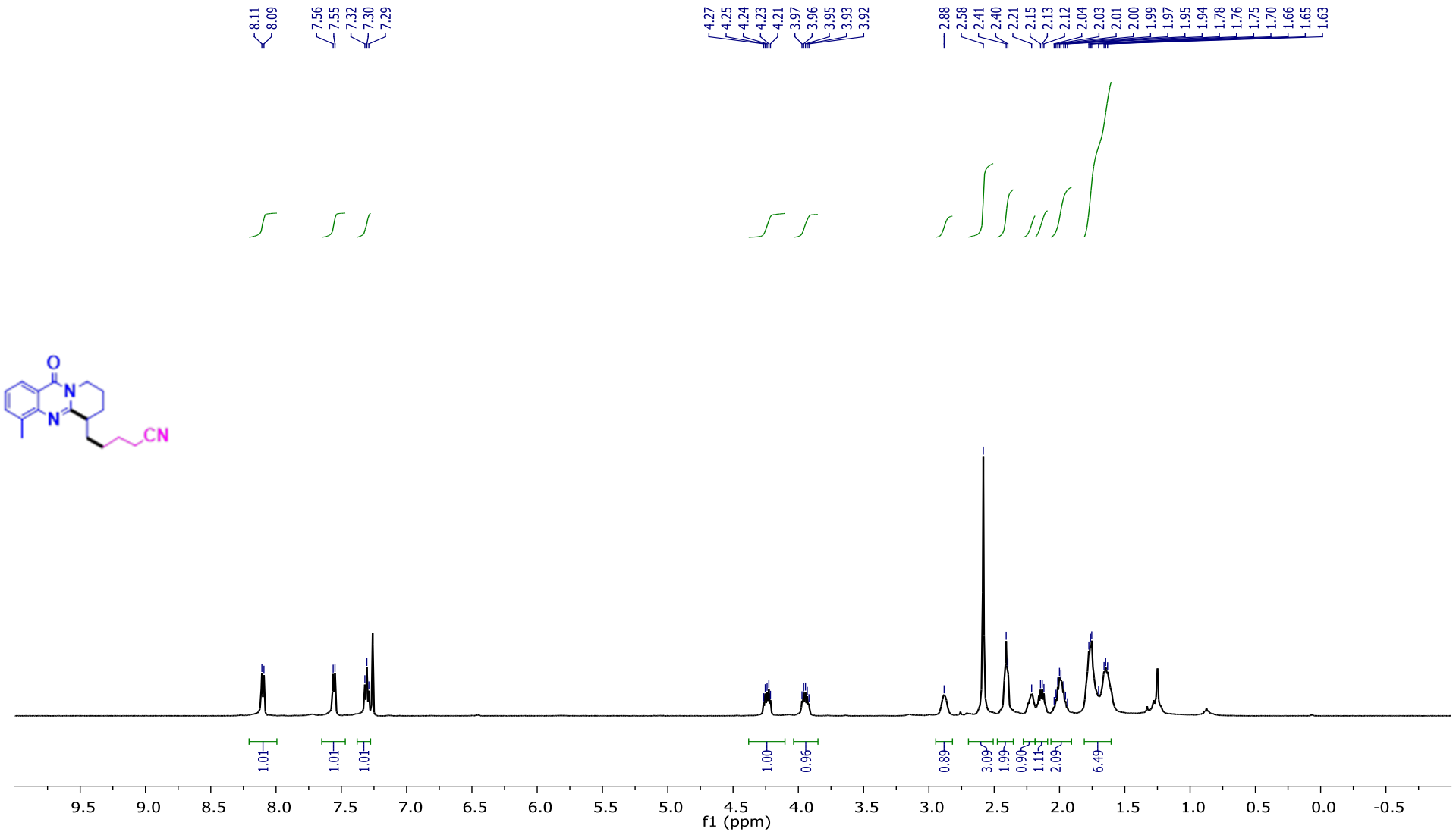
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3j)



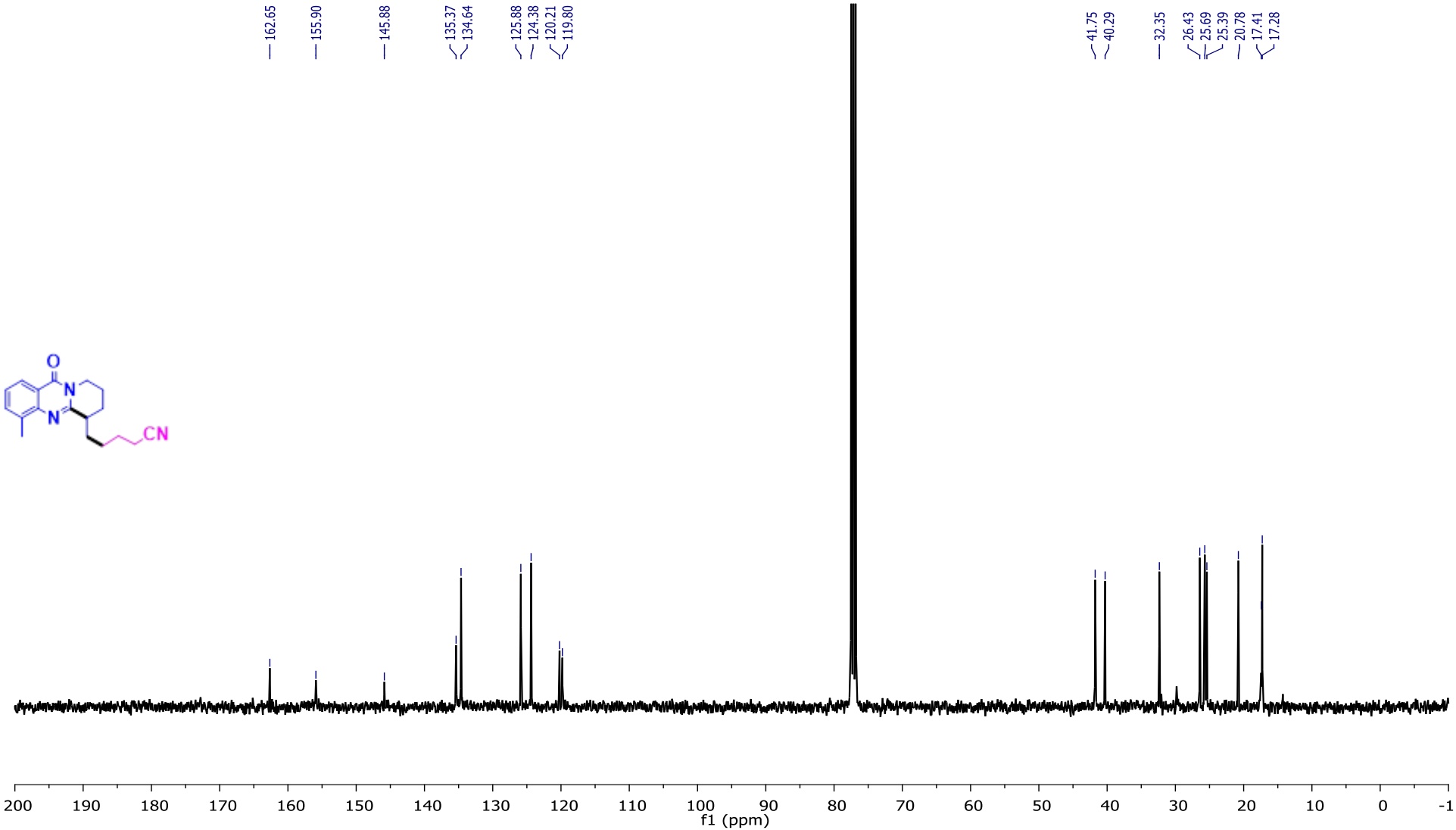
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3j)



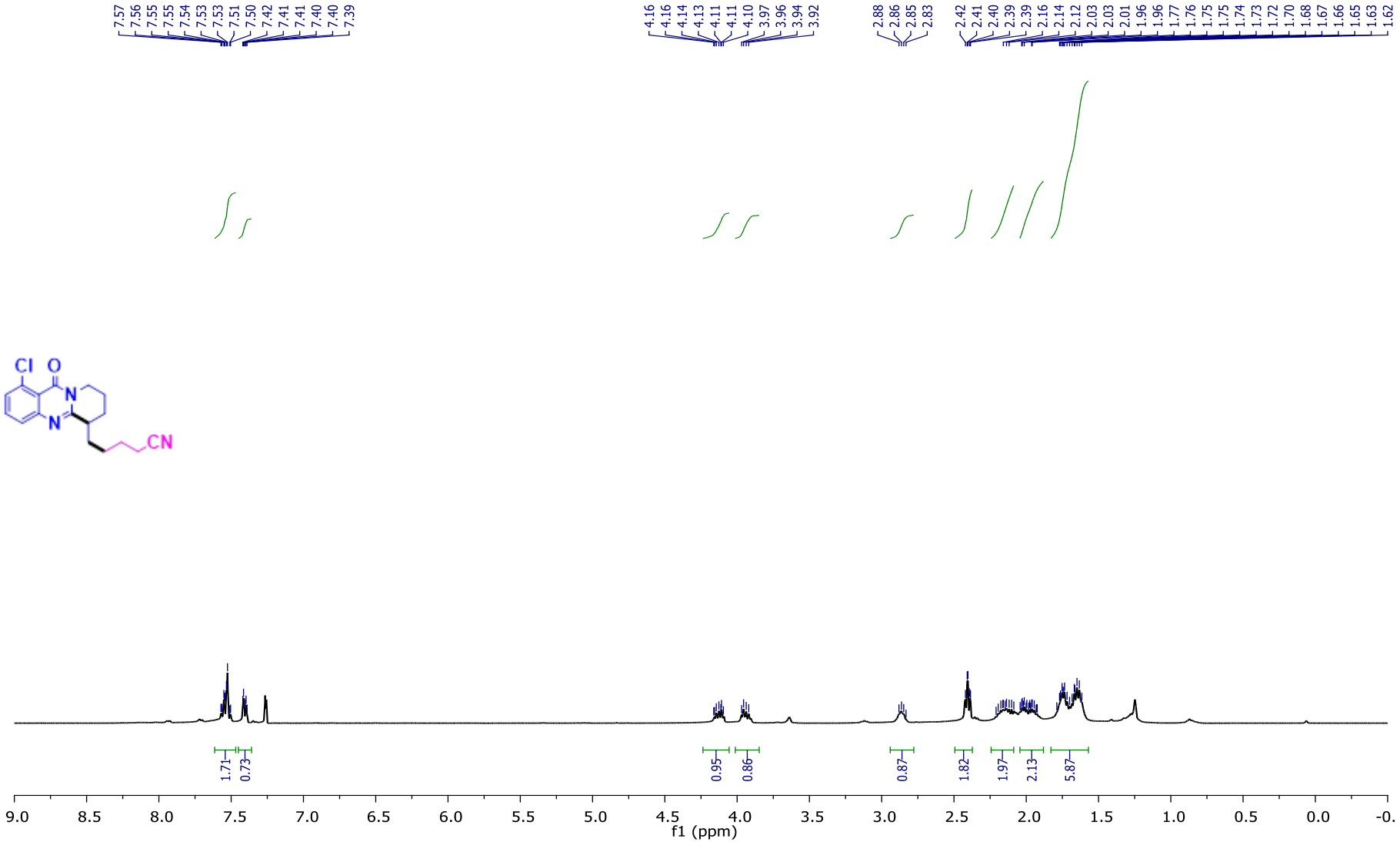
^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (3k)



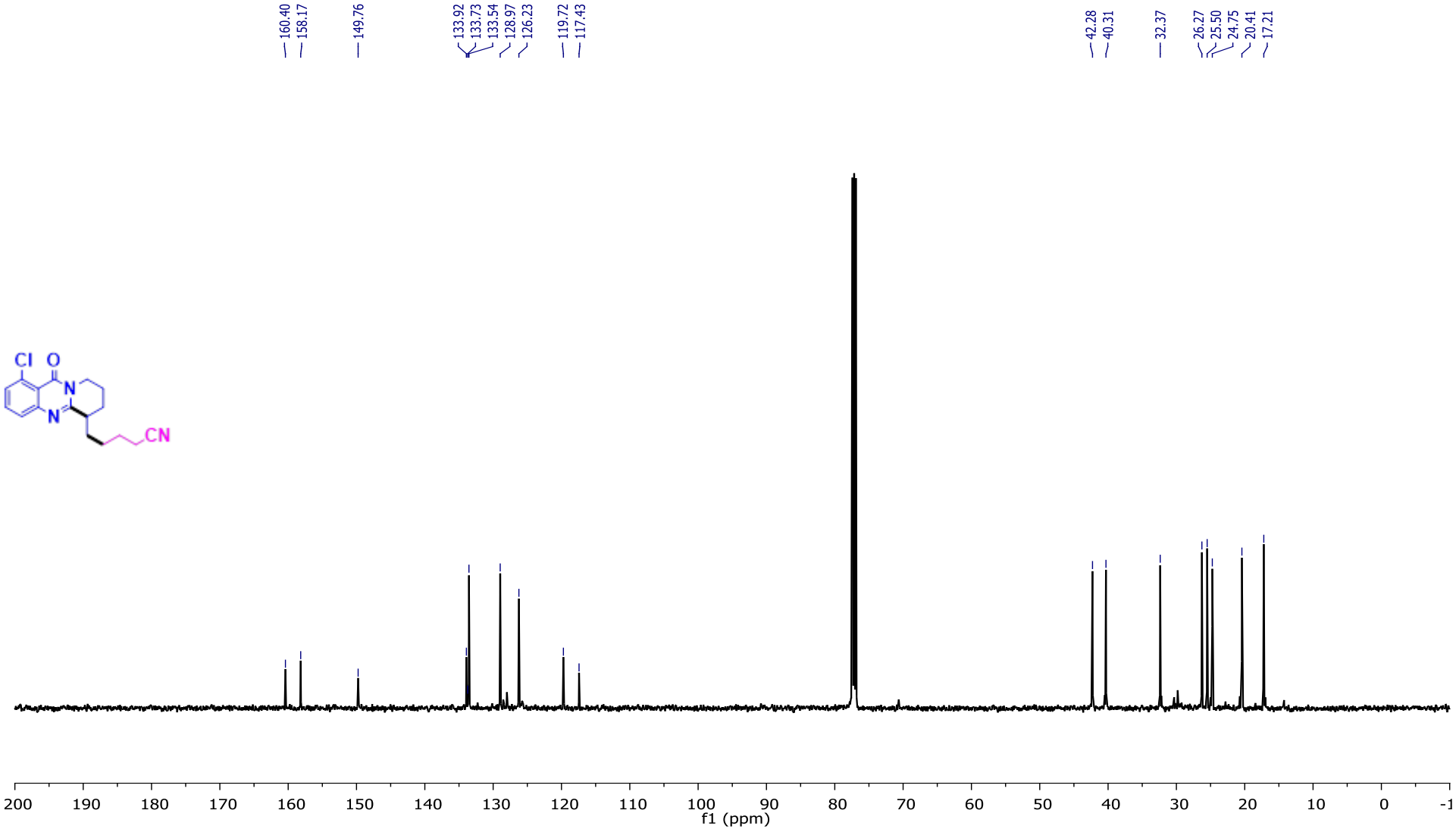
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3k)



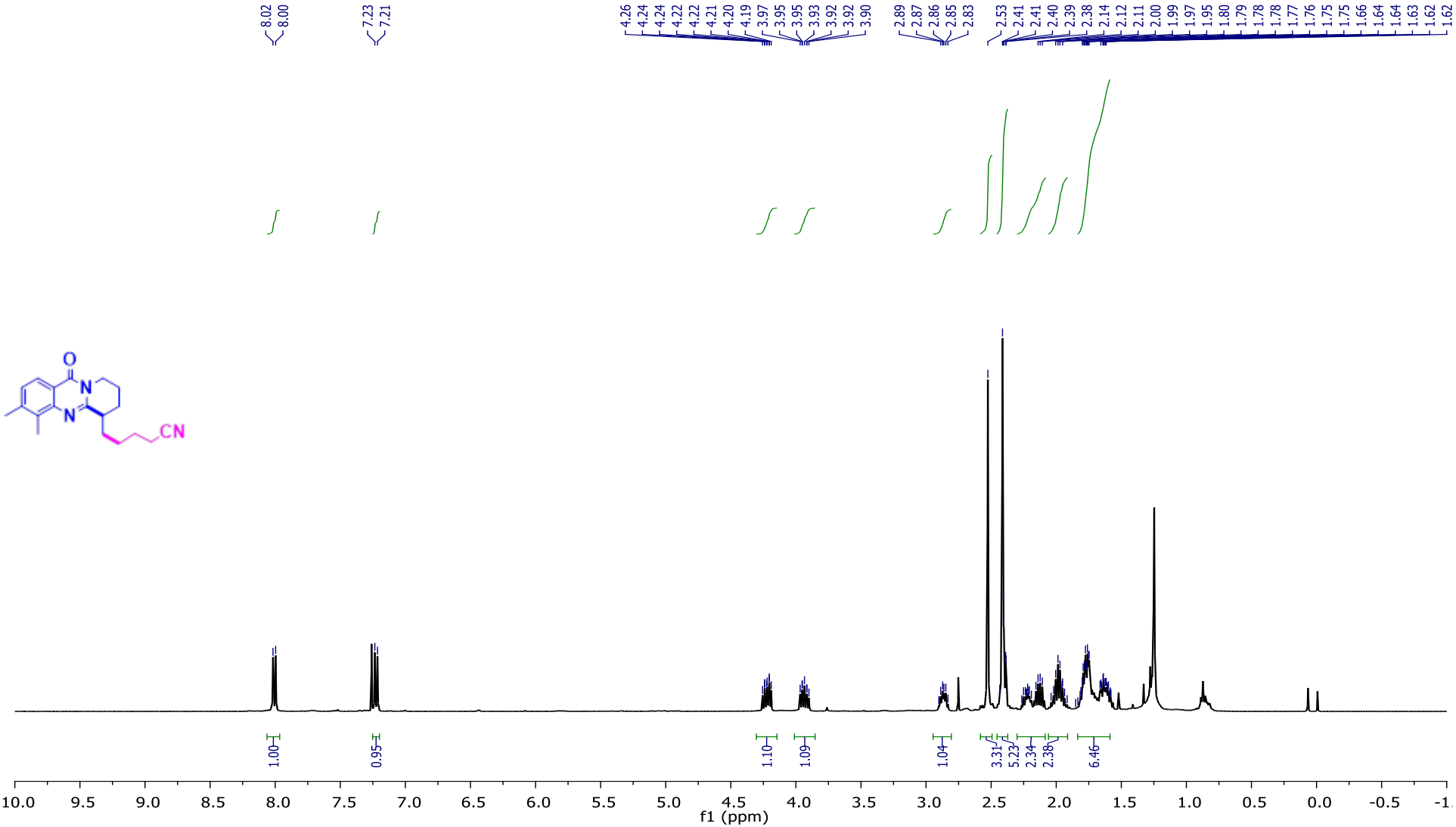
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3l)



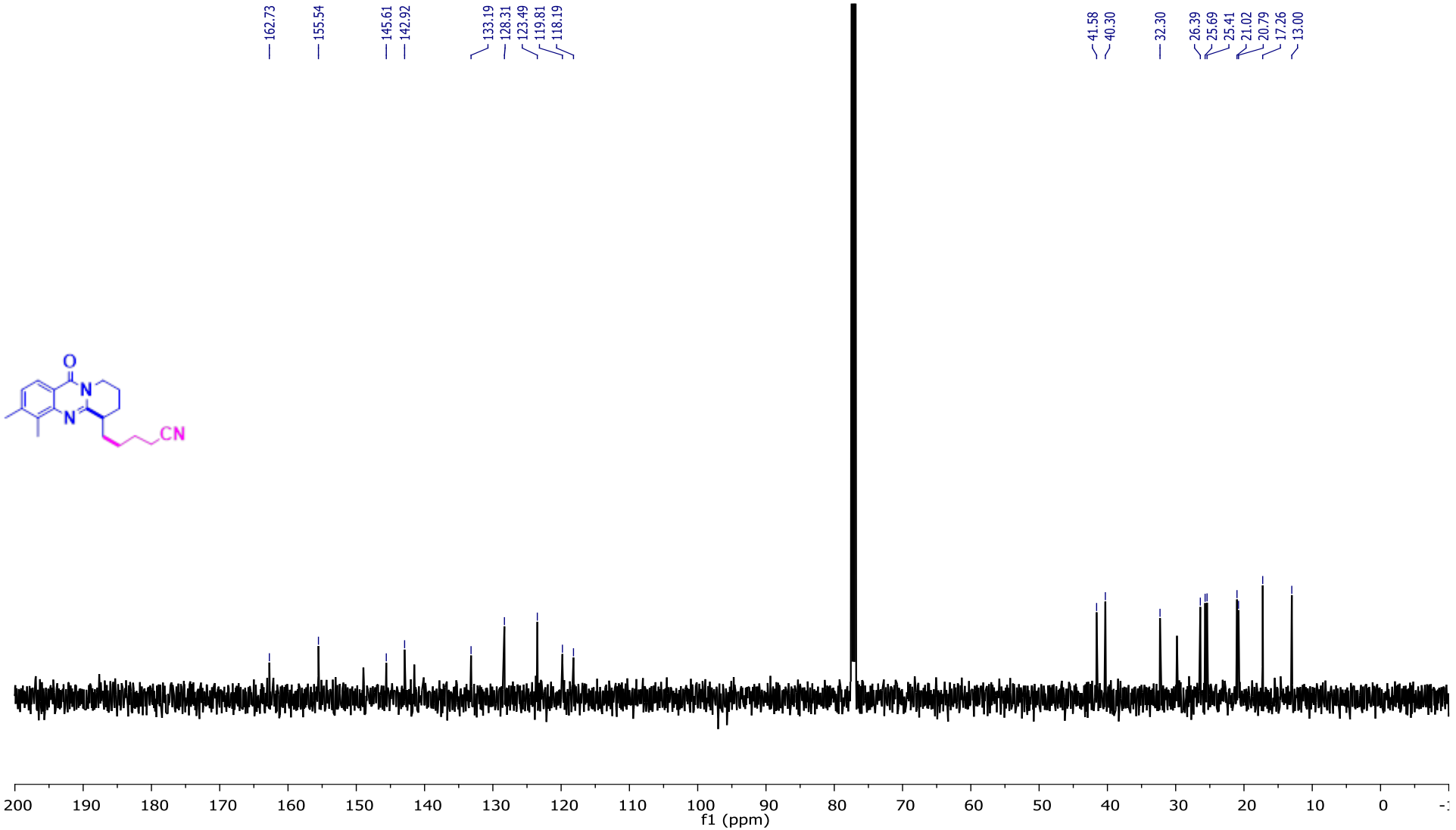
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (3l)



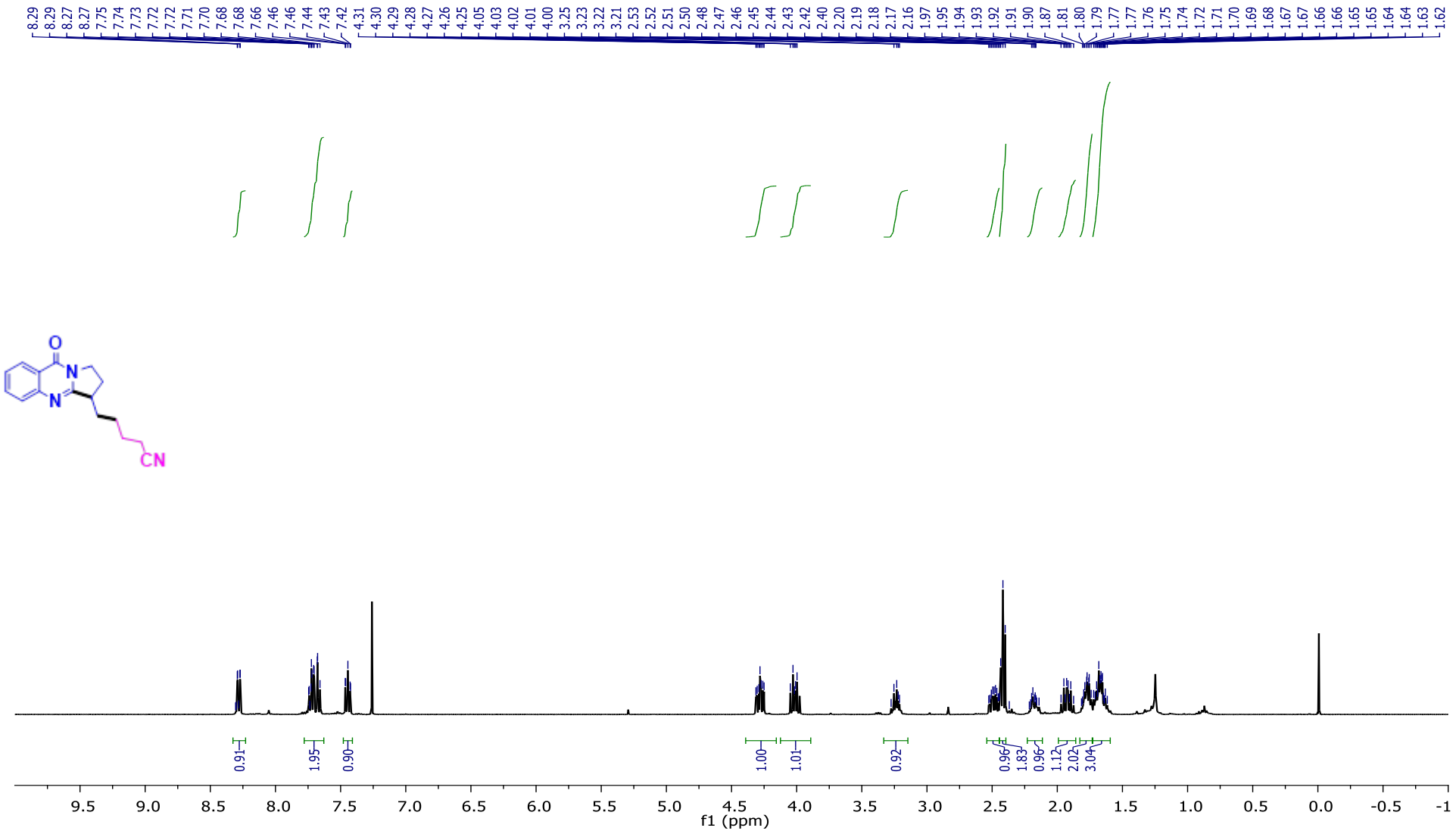
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3m)



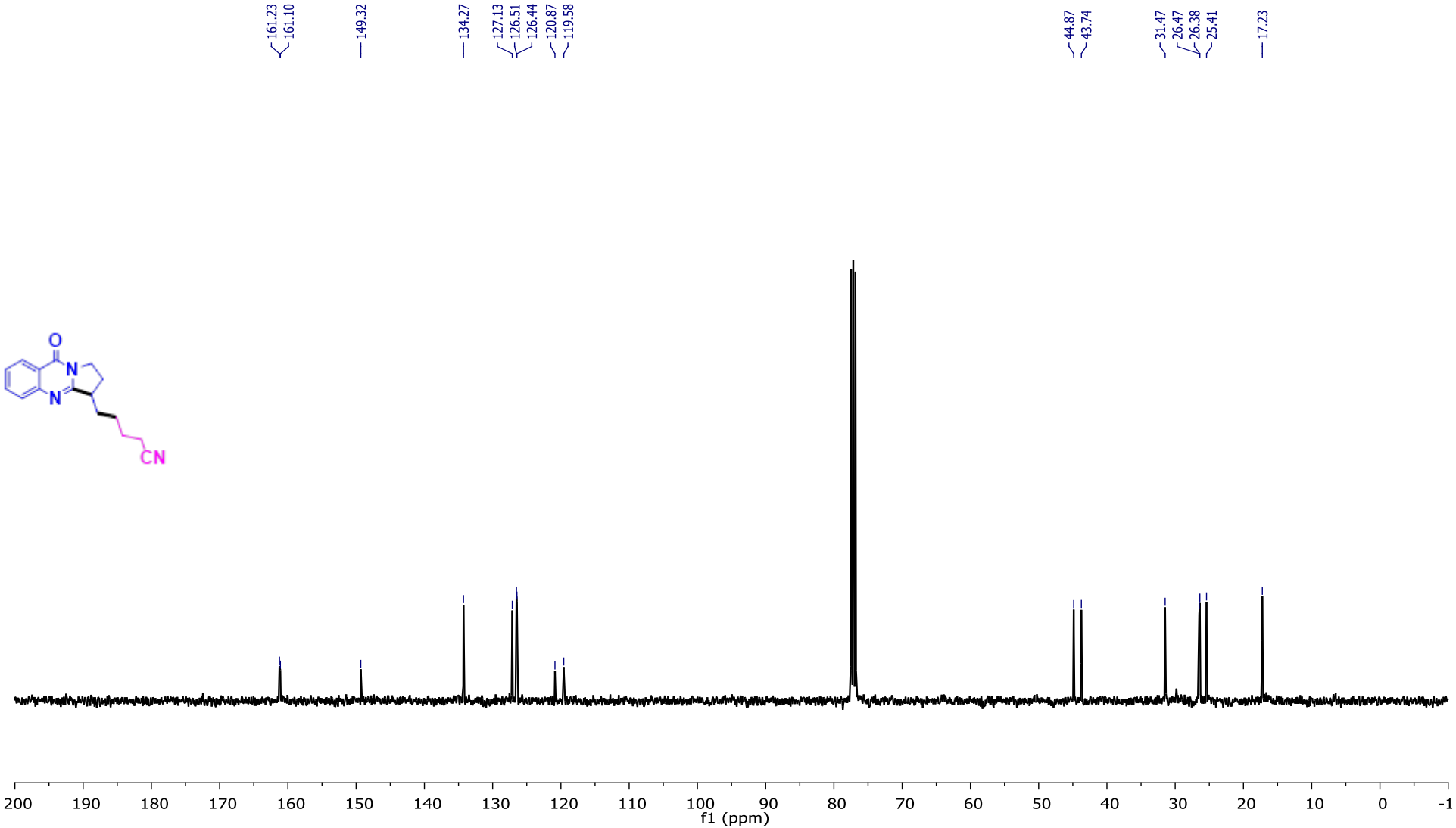
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (3m)



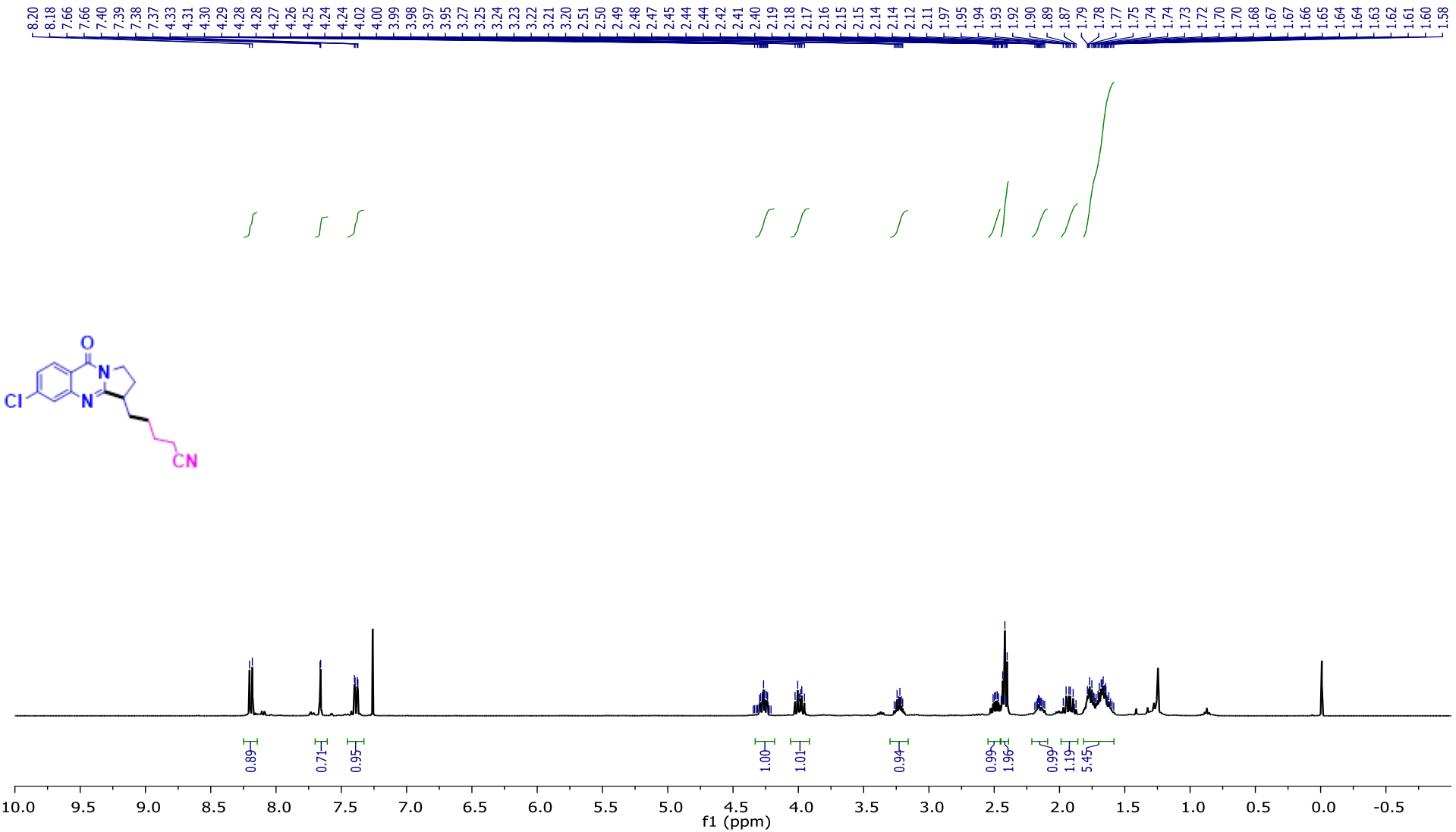
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3n)



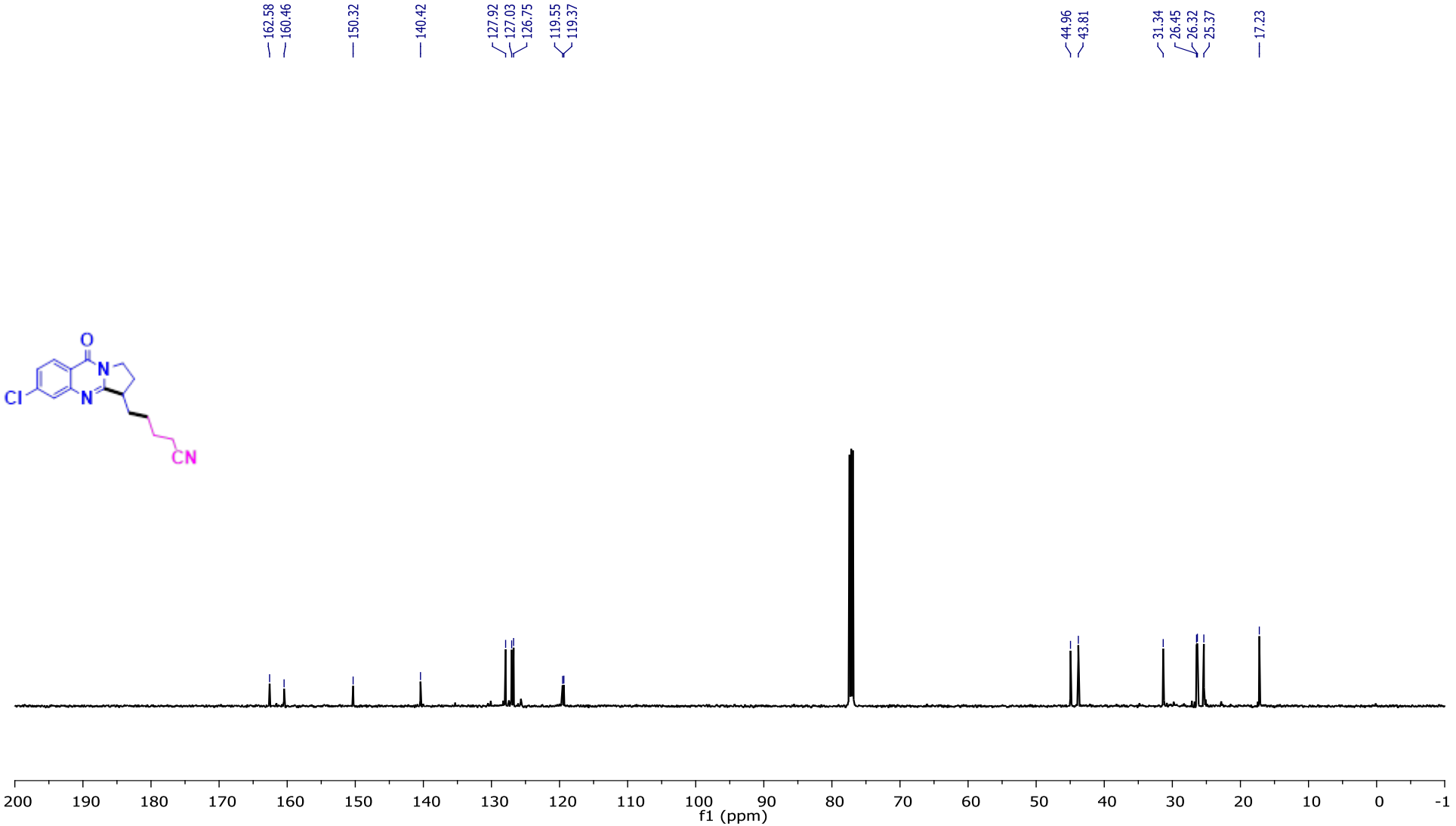
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3n)



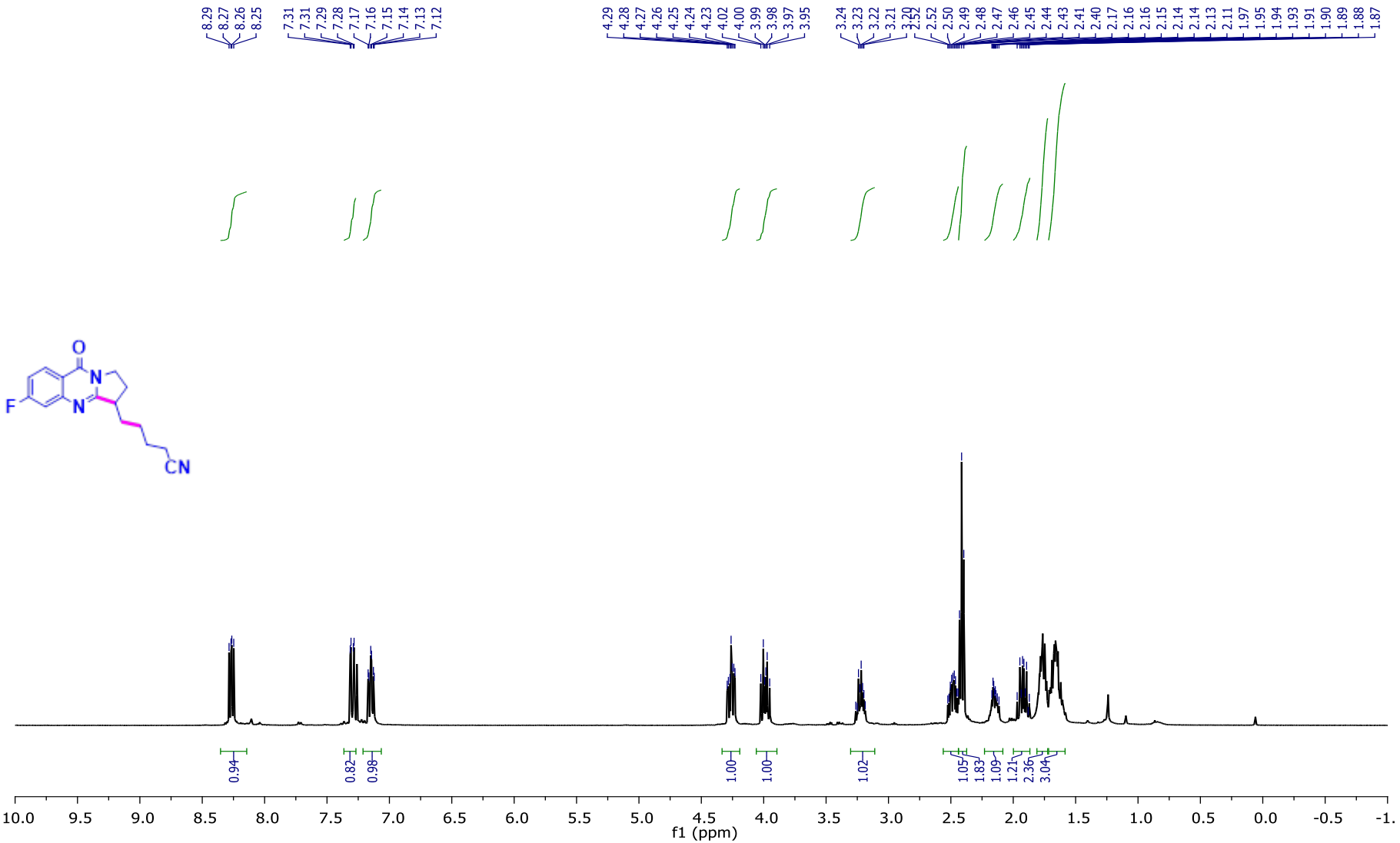
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3o)



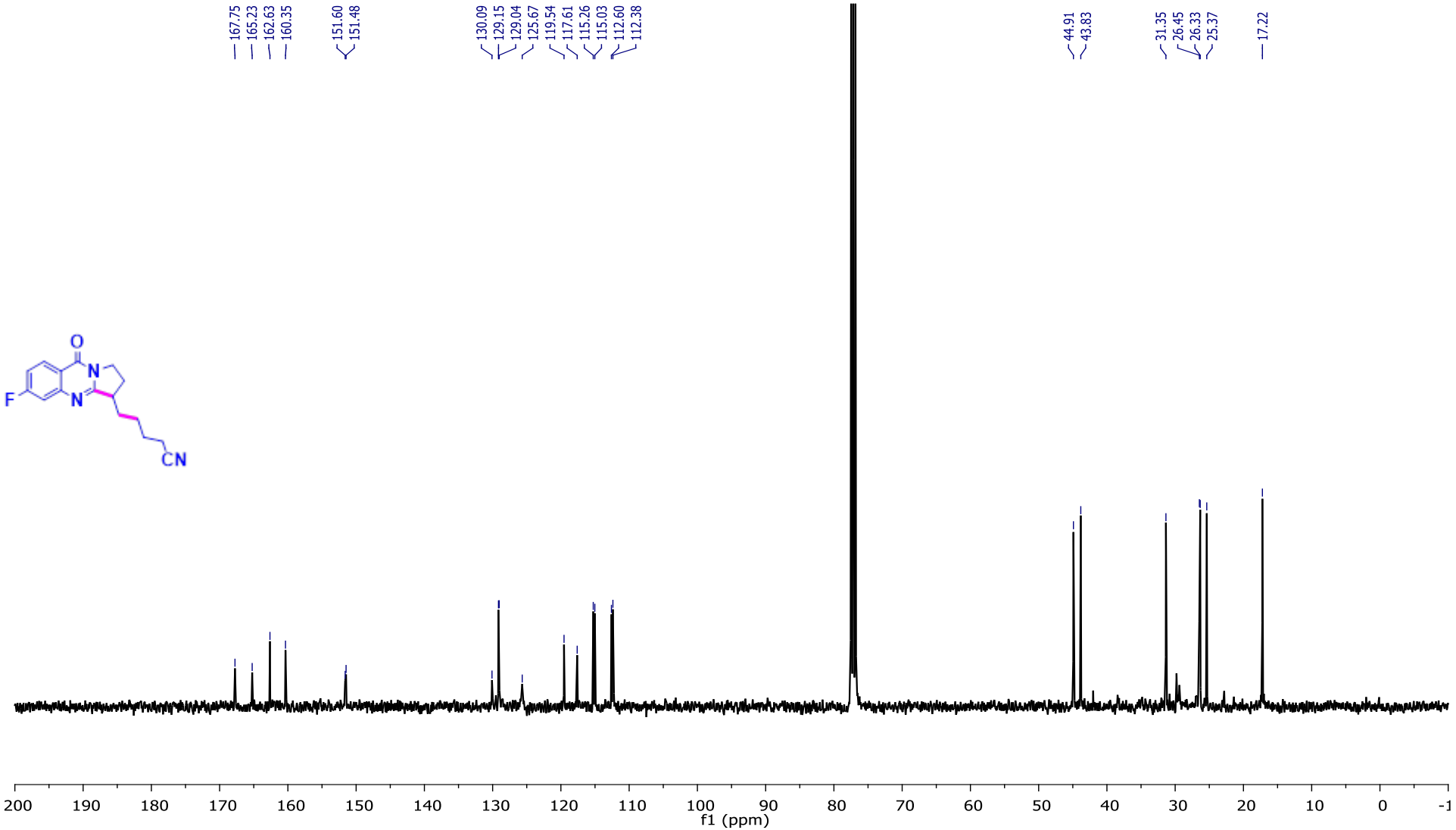
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (3o)



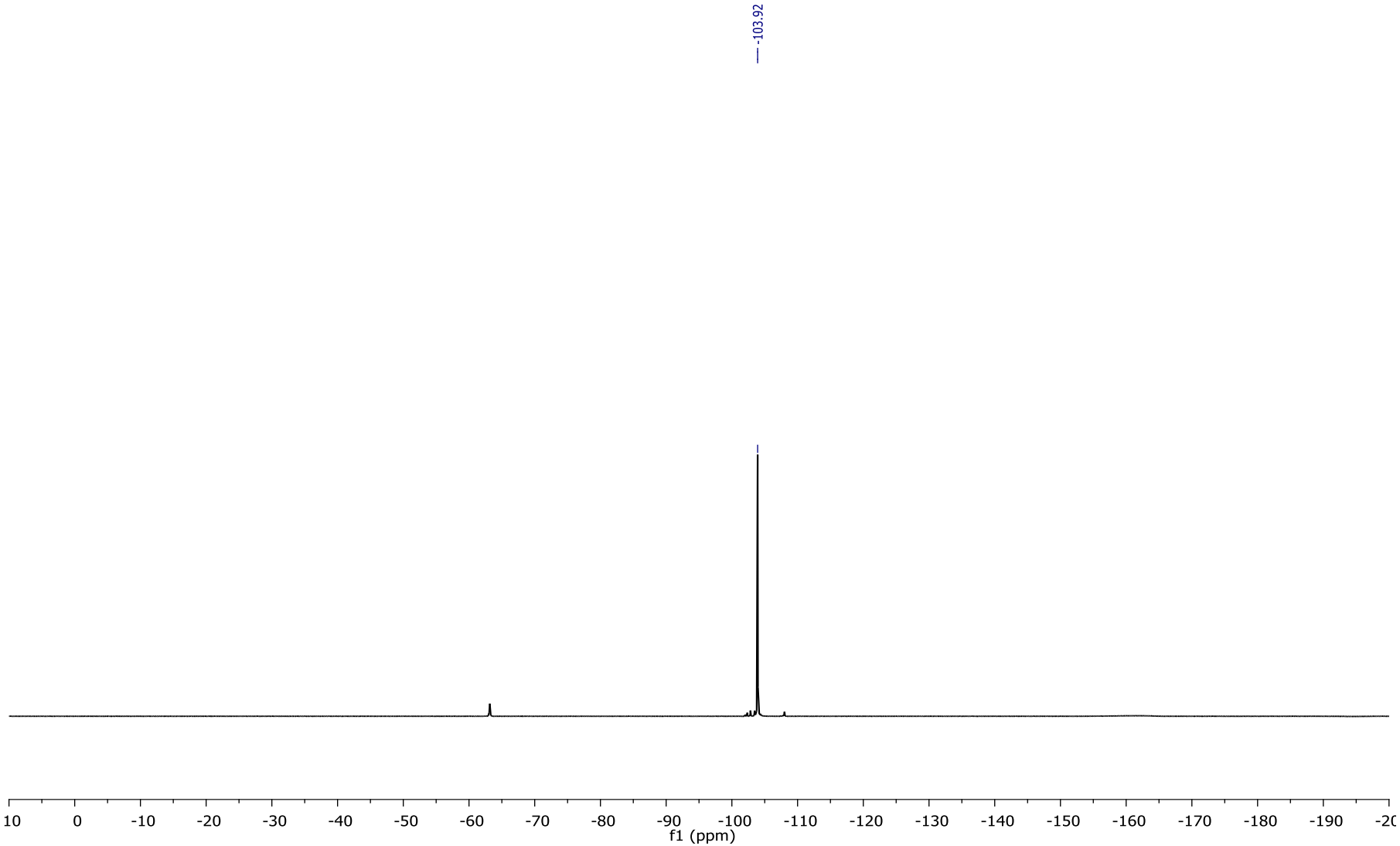
[1]HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (3p)



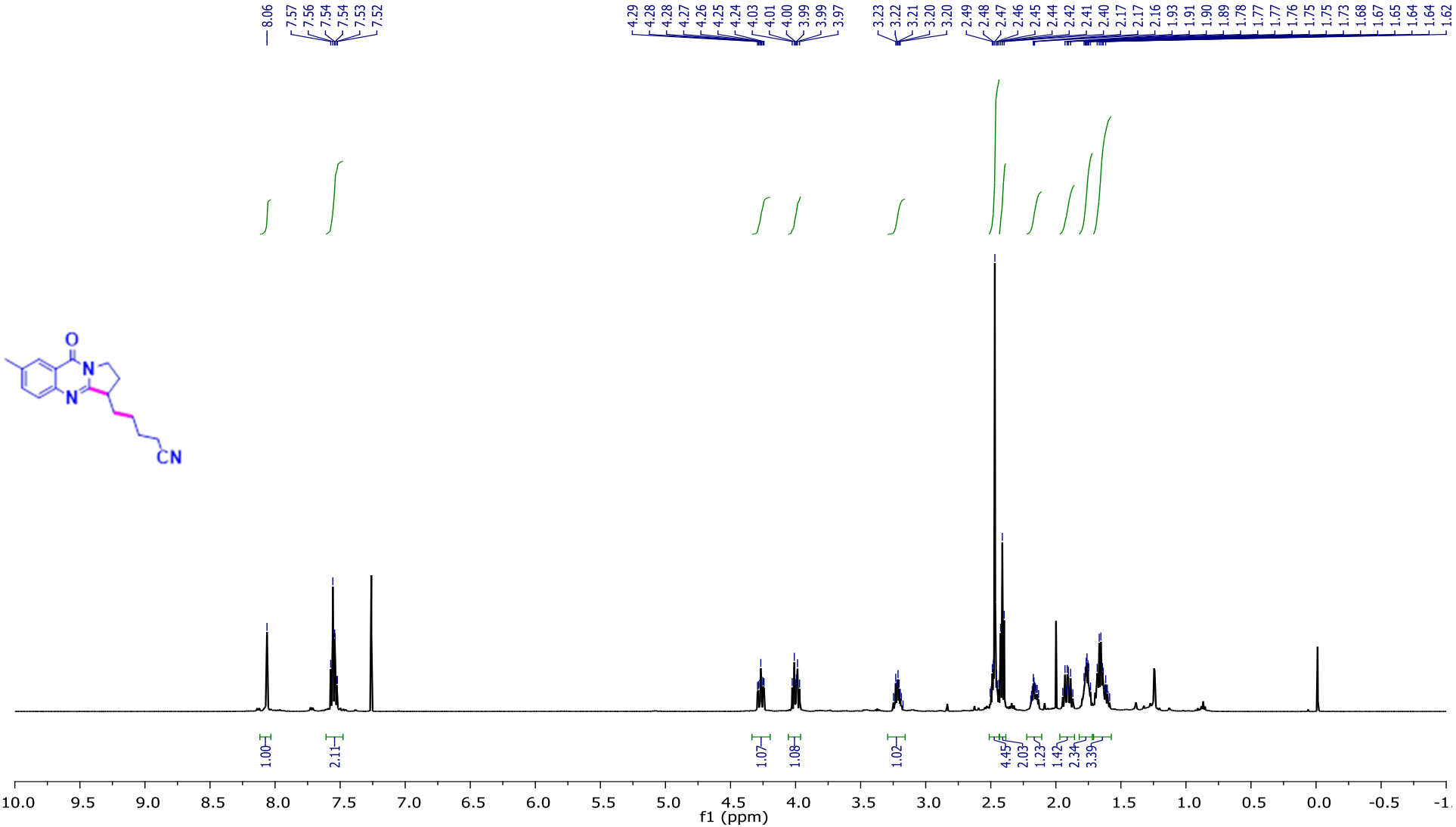
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3p)



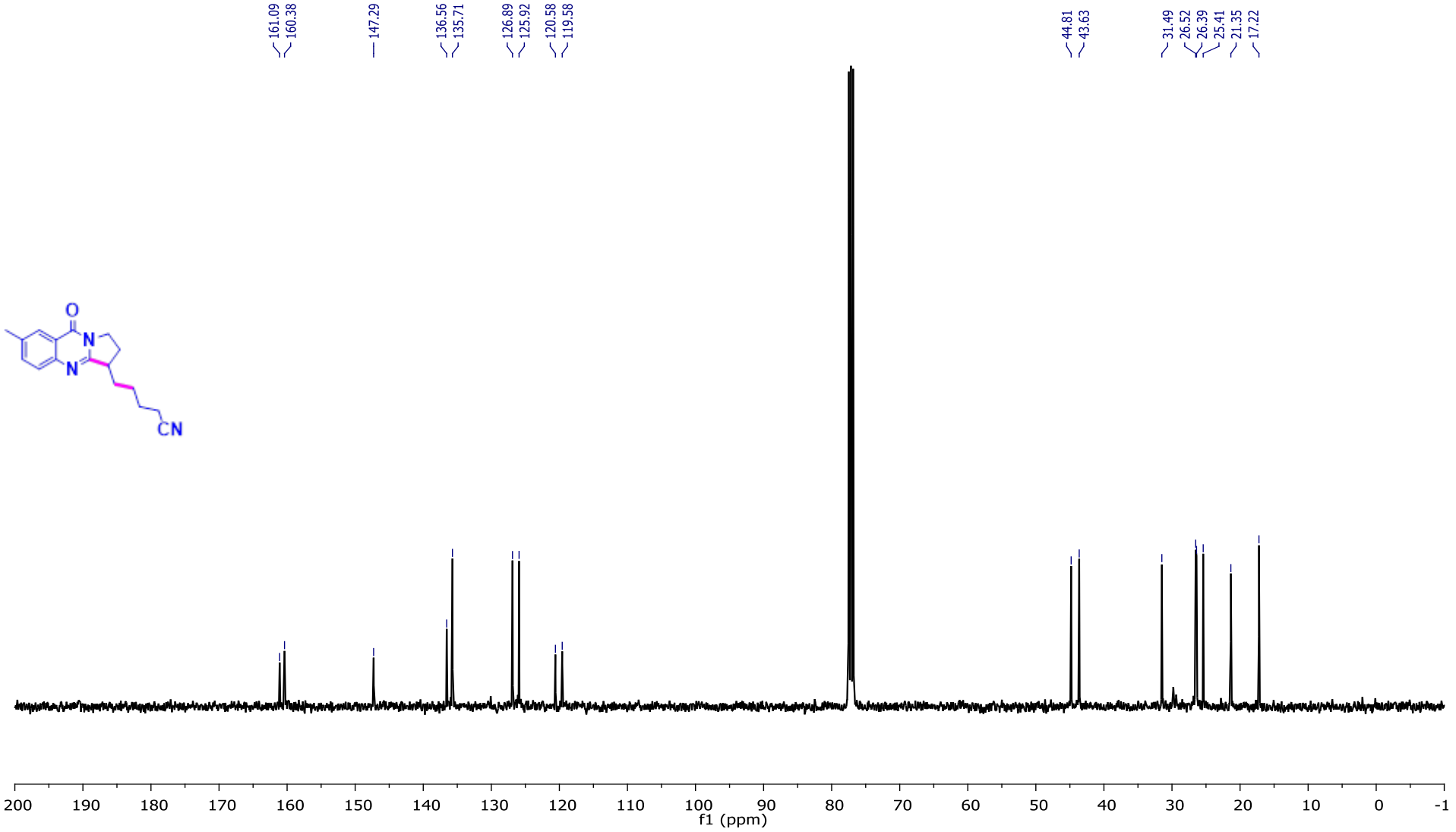
^{19}FNMR (376 MHz, $CDCl_3$) Spectrum of Compound (3p)



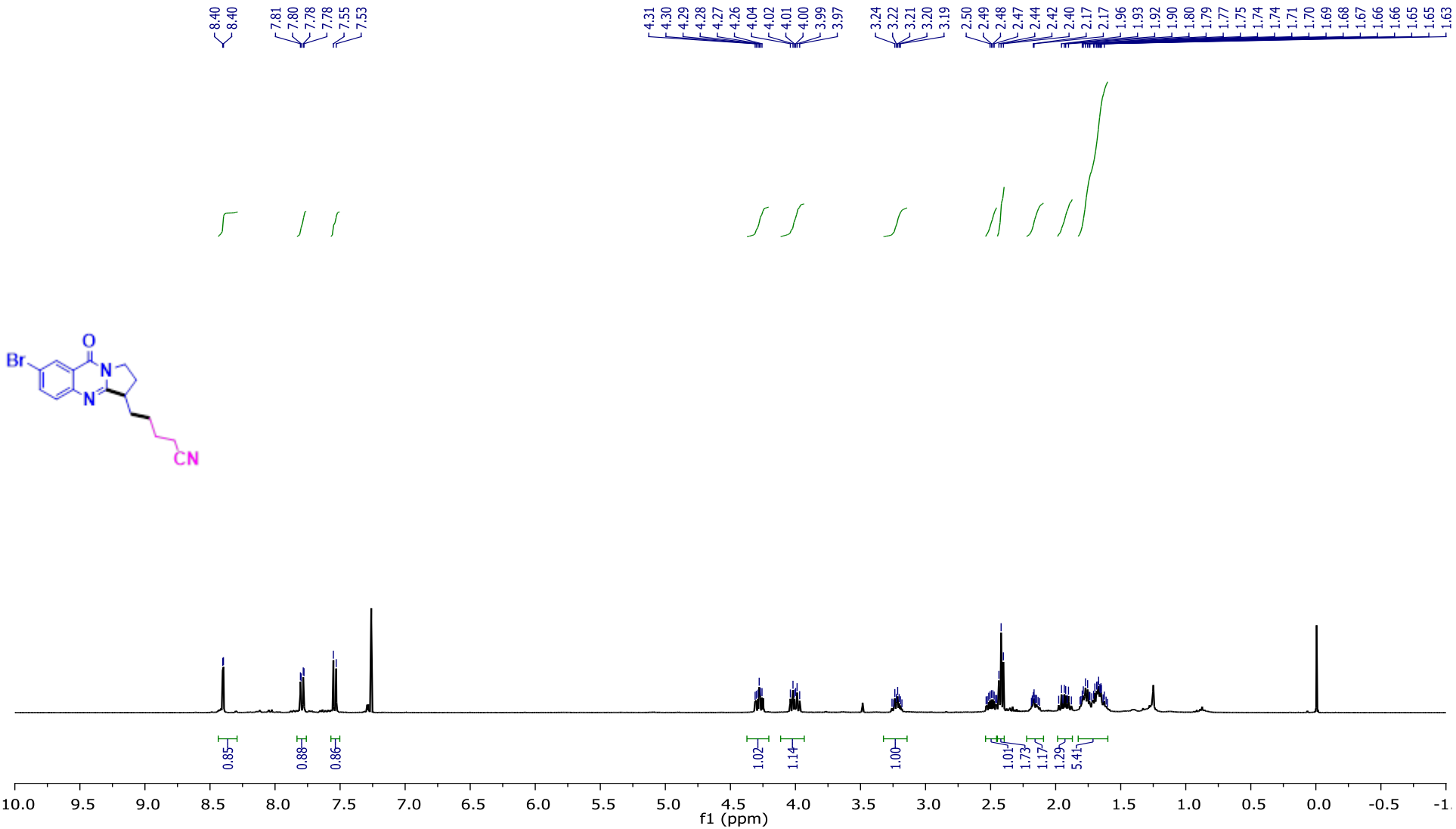
^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (3q)



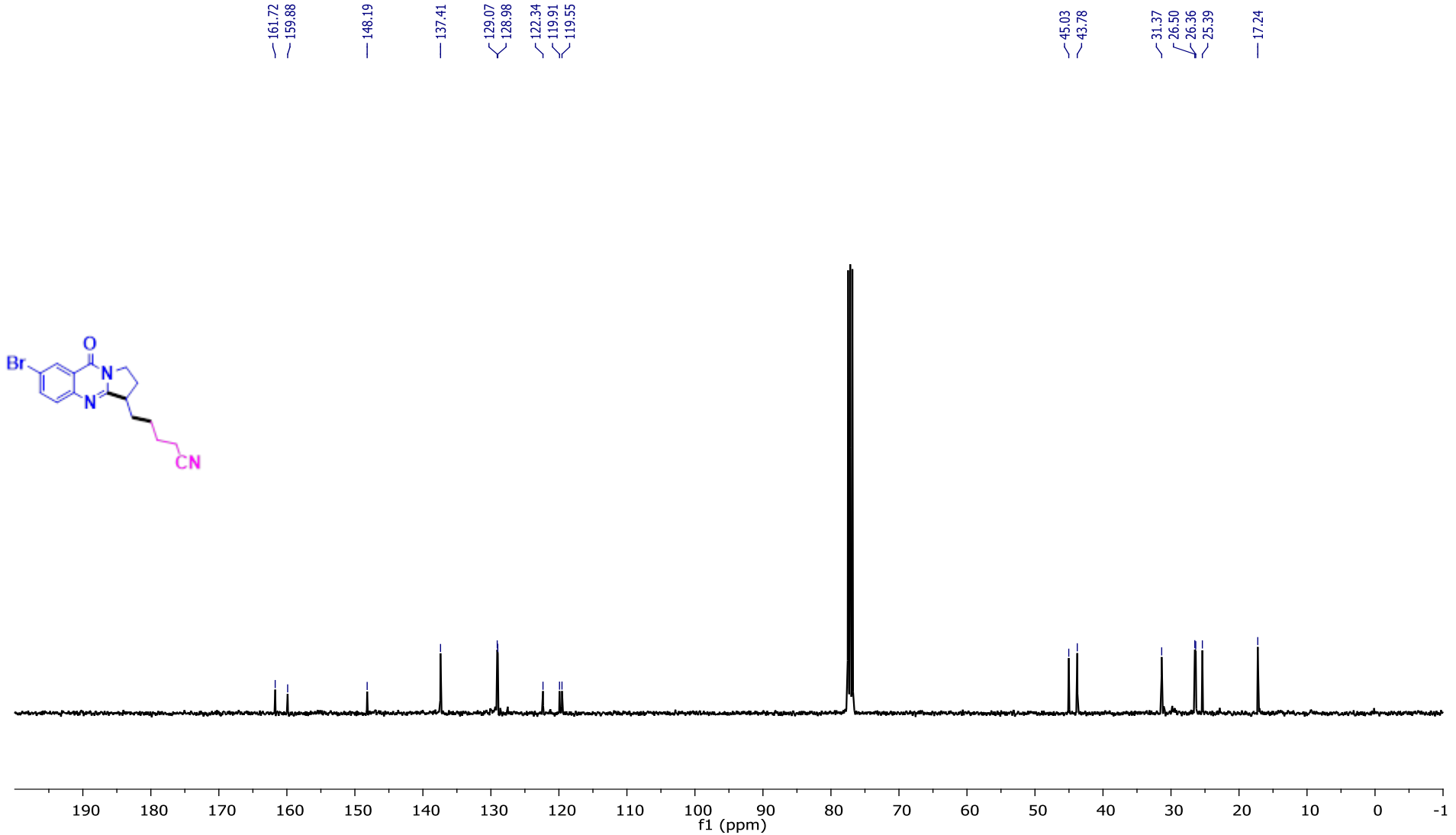
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3q)



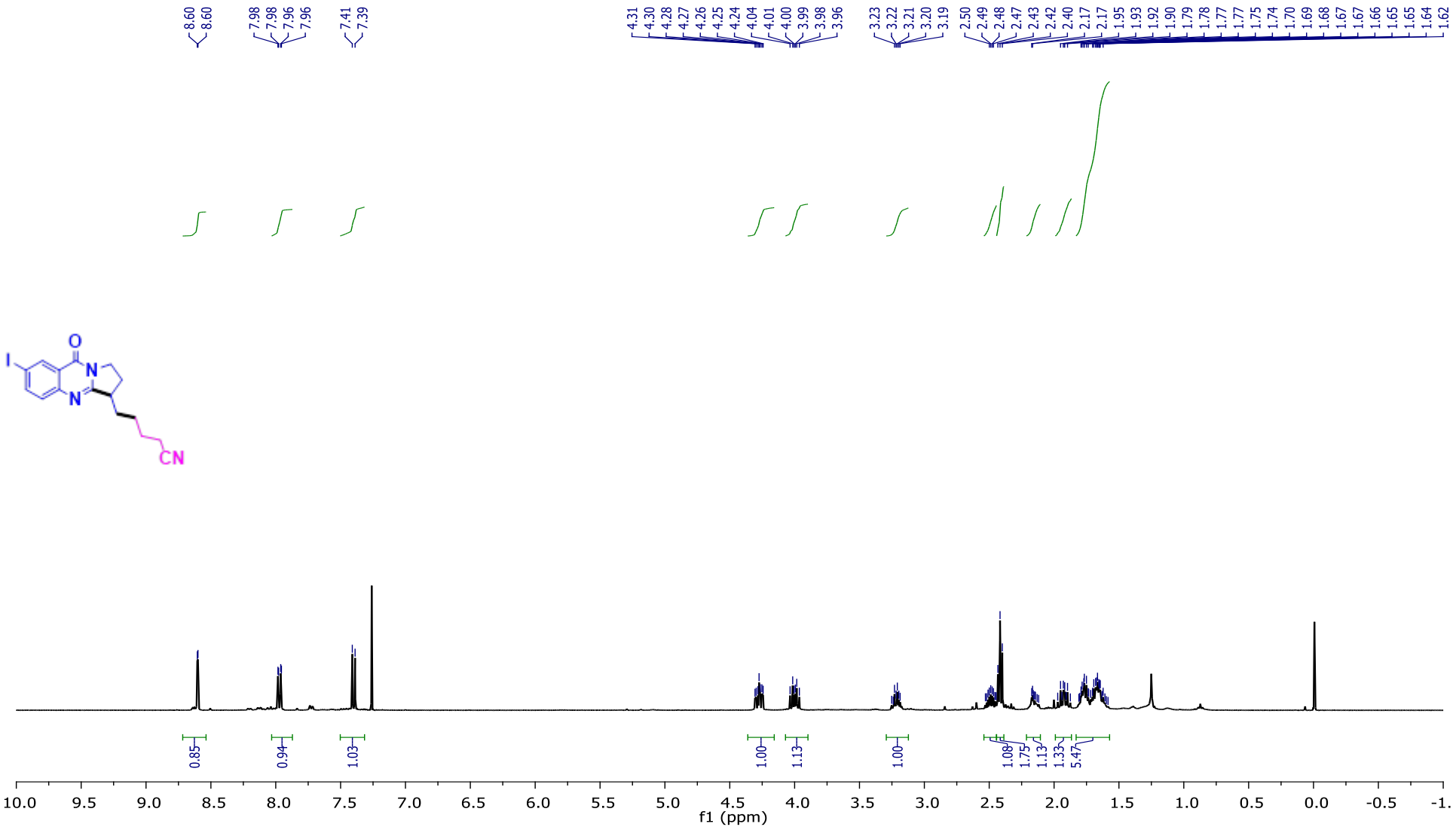
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3r)



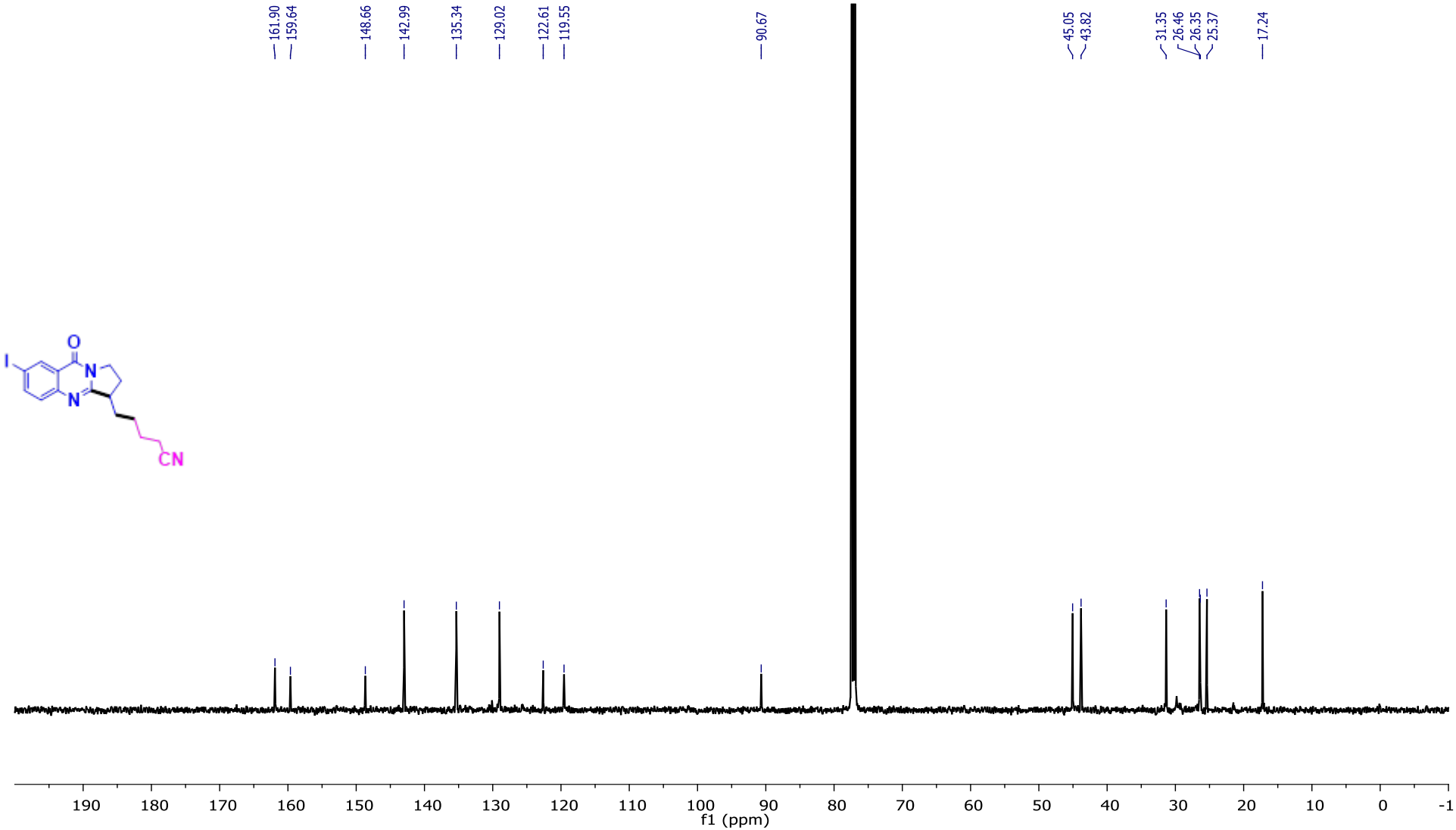
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3r)



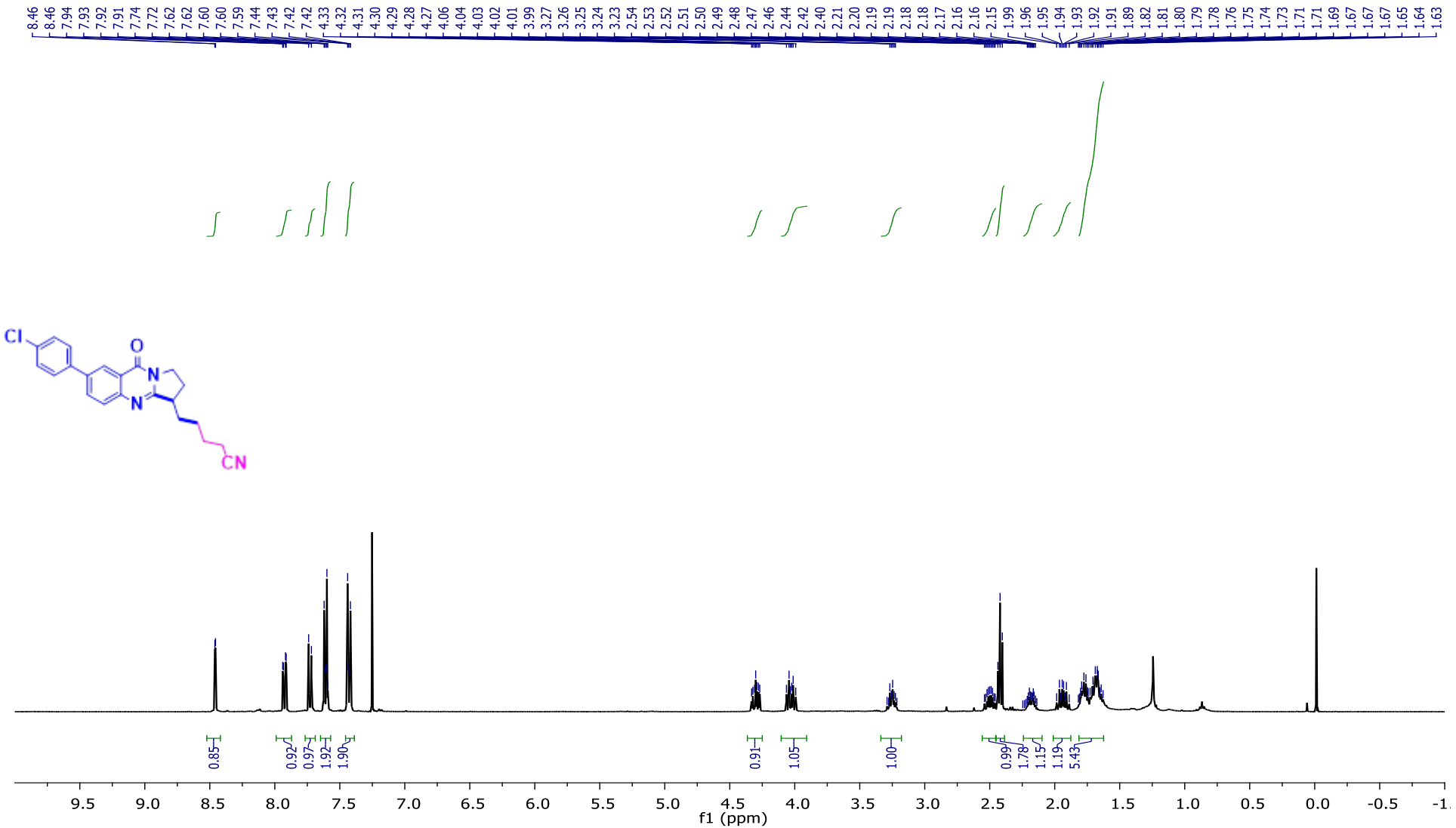
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3s)



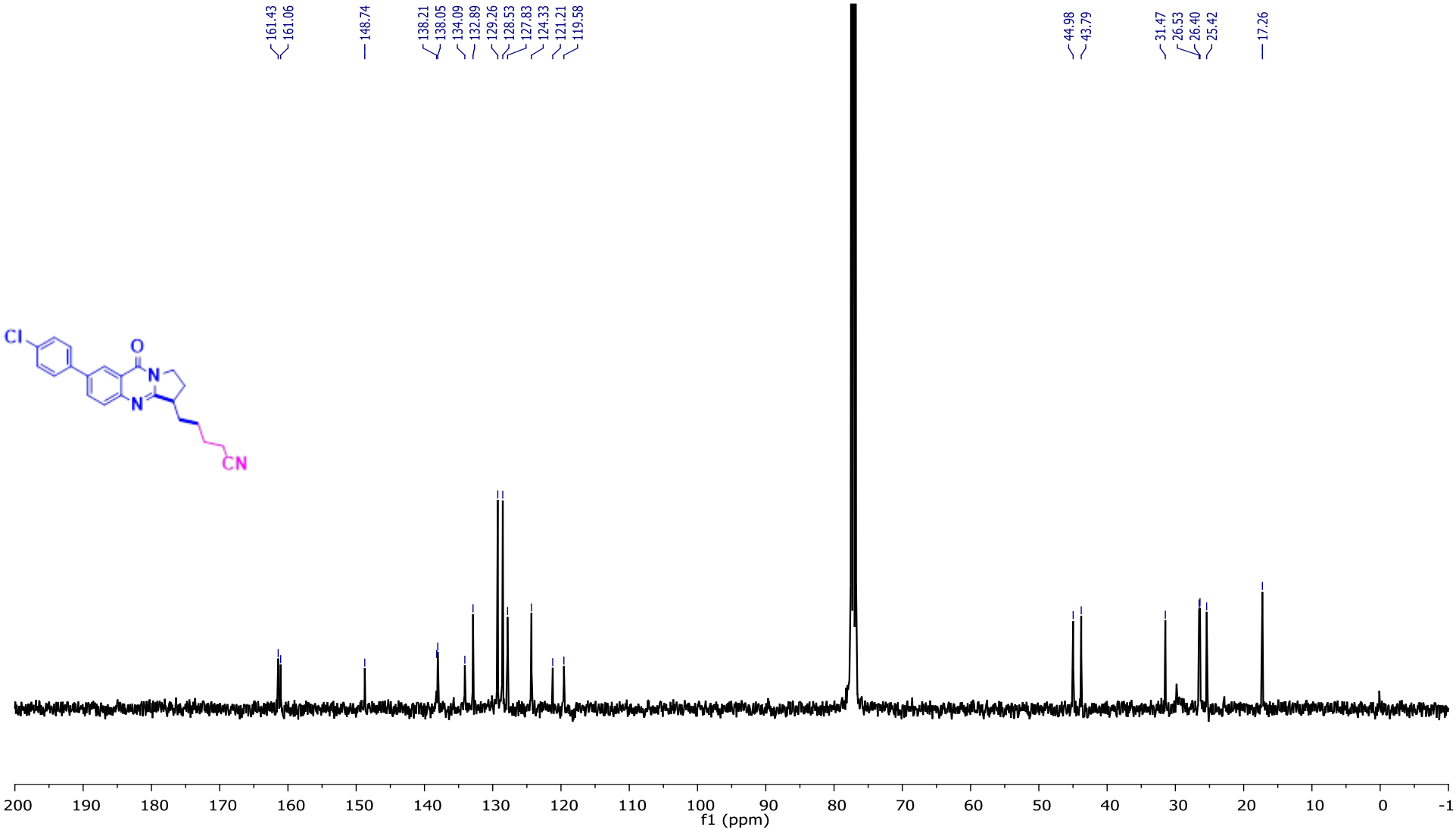
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (3s)



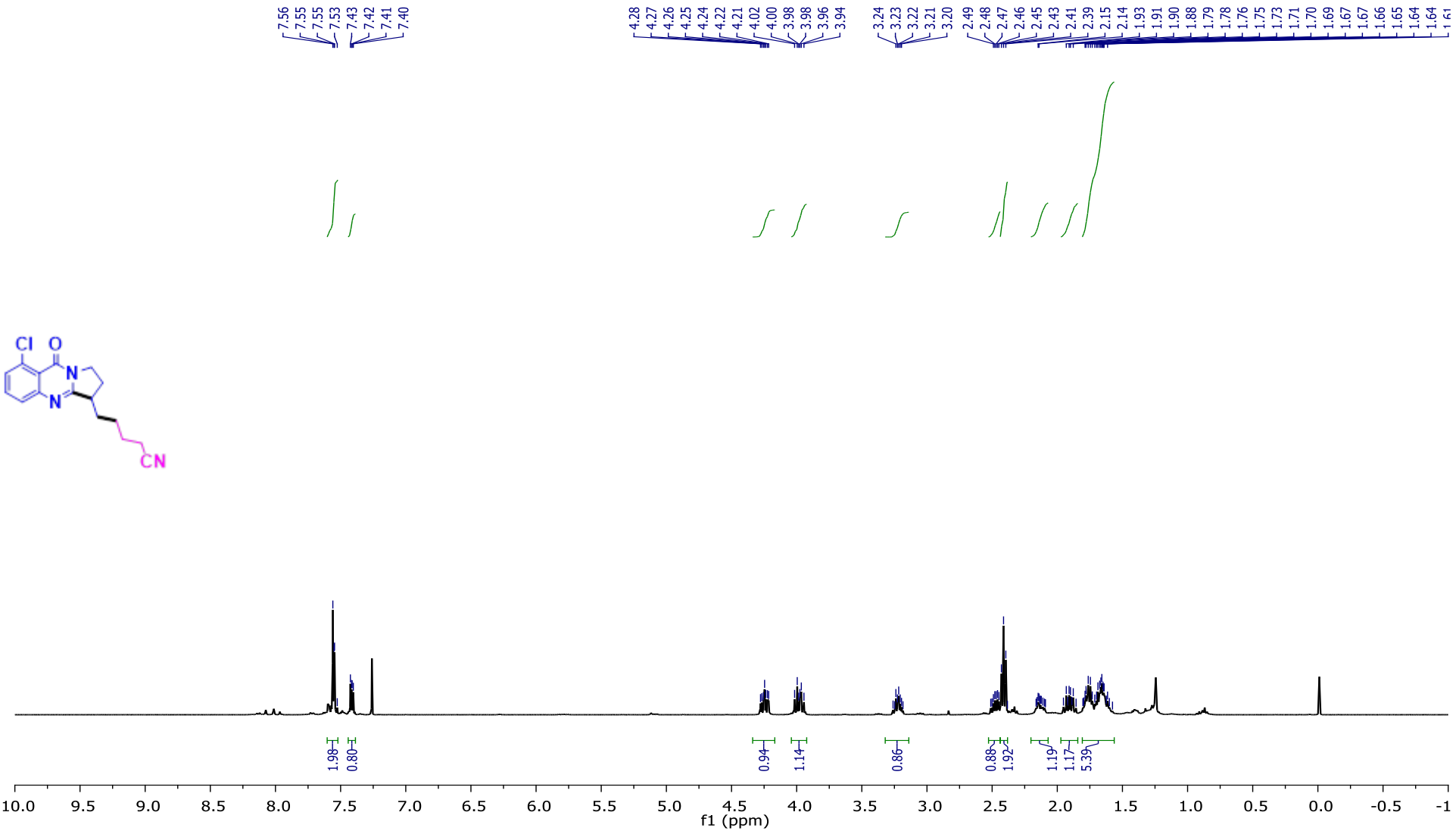
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3t)



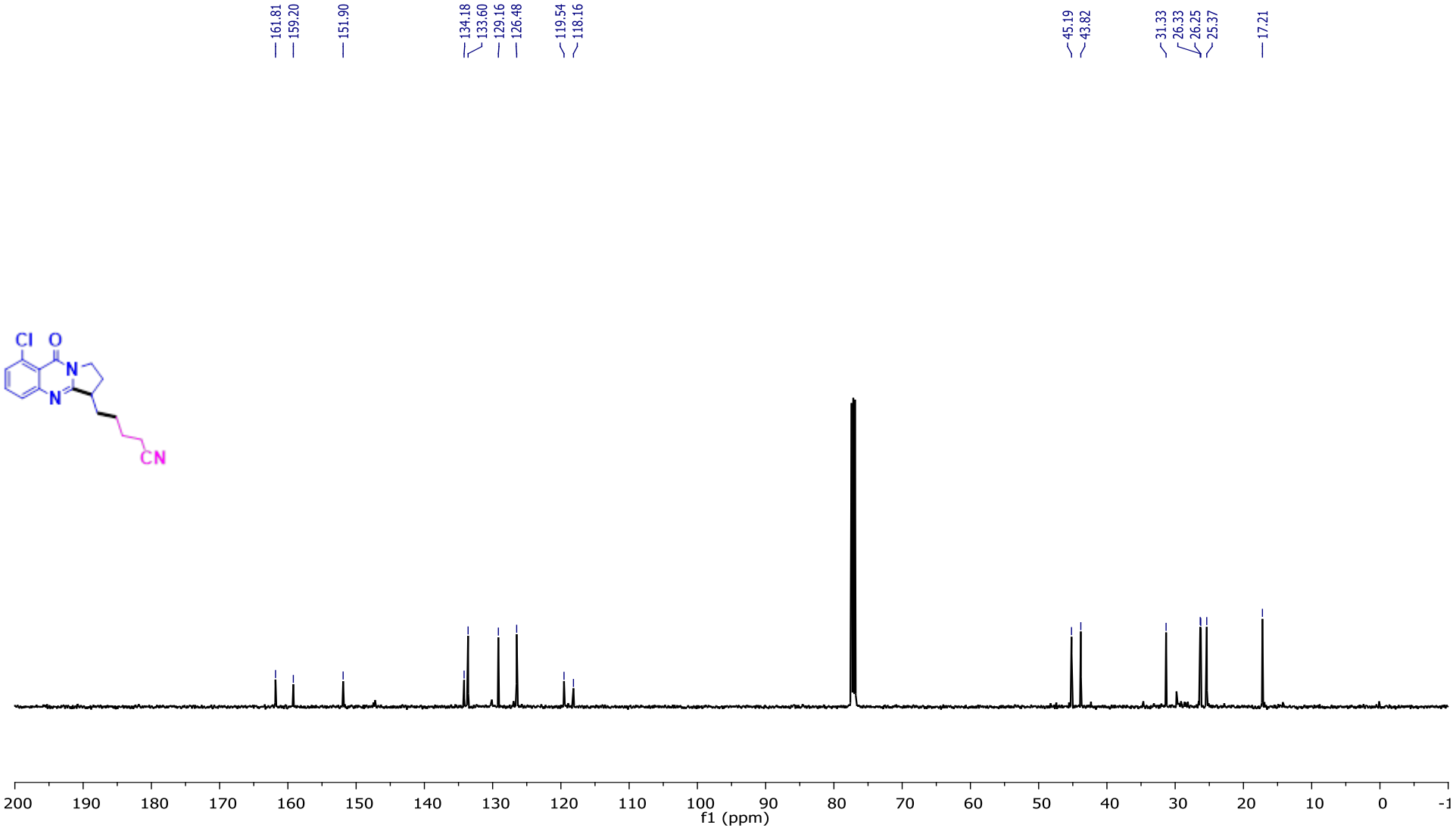
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3t)



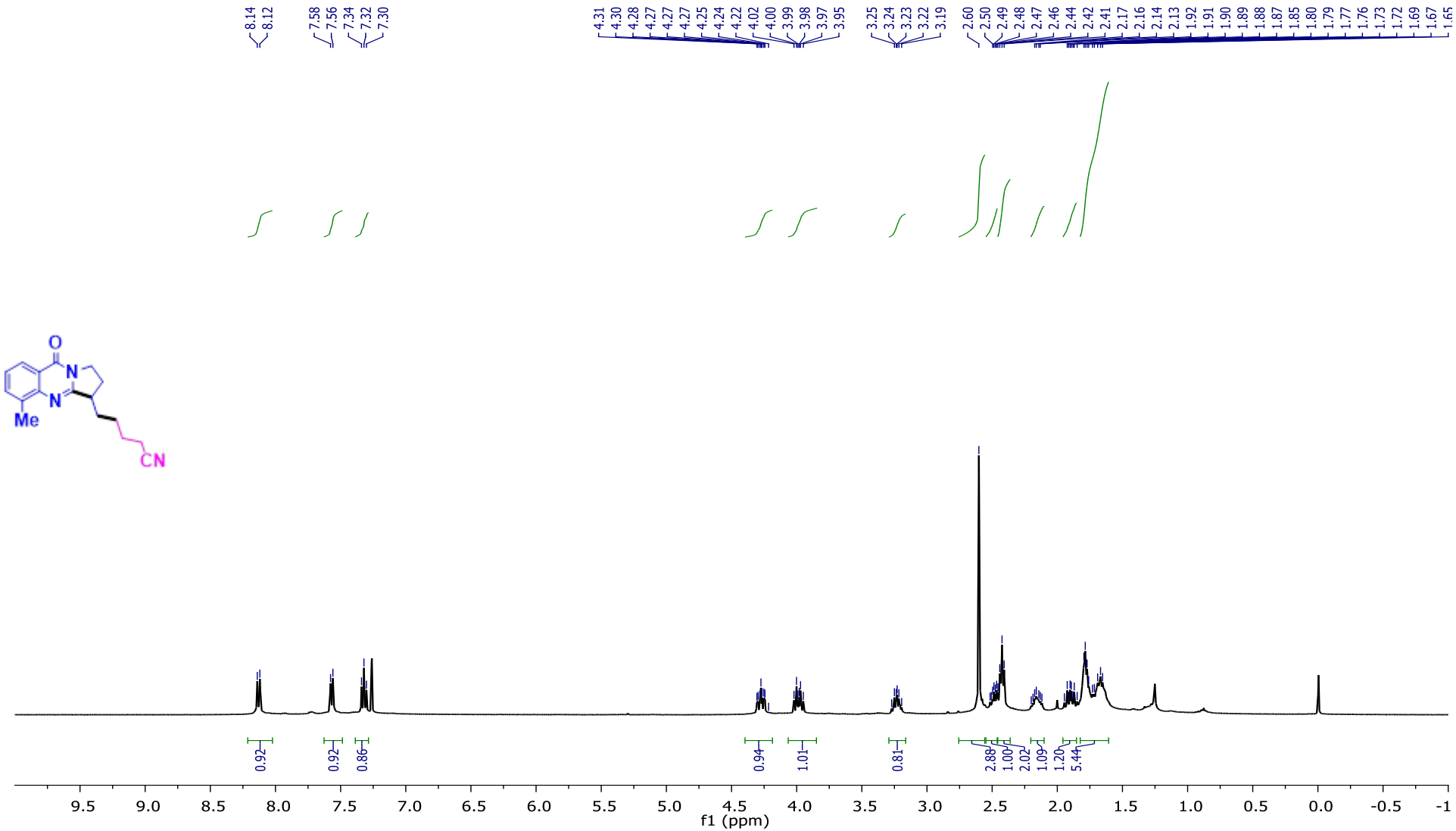
[1]HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3u)



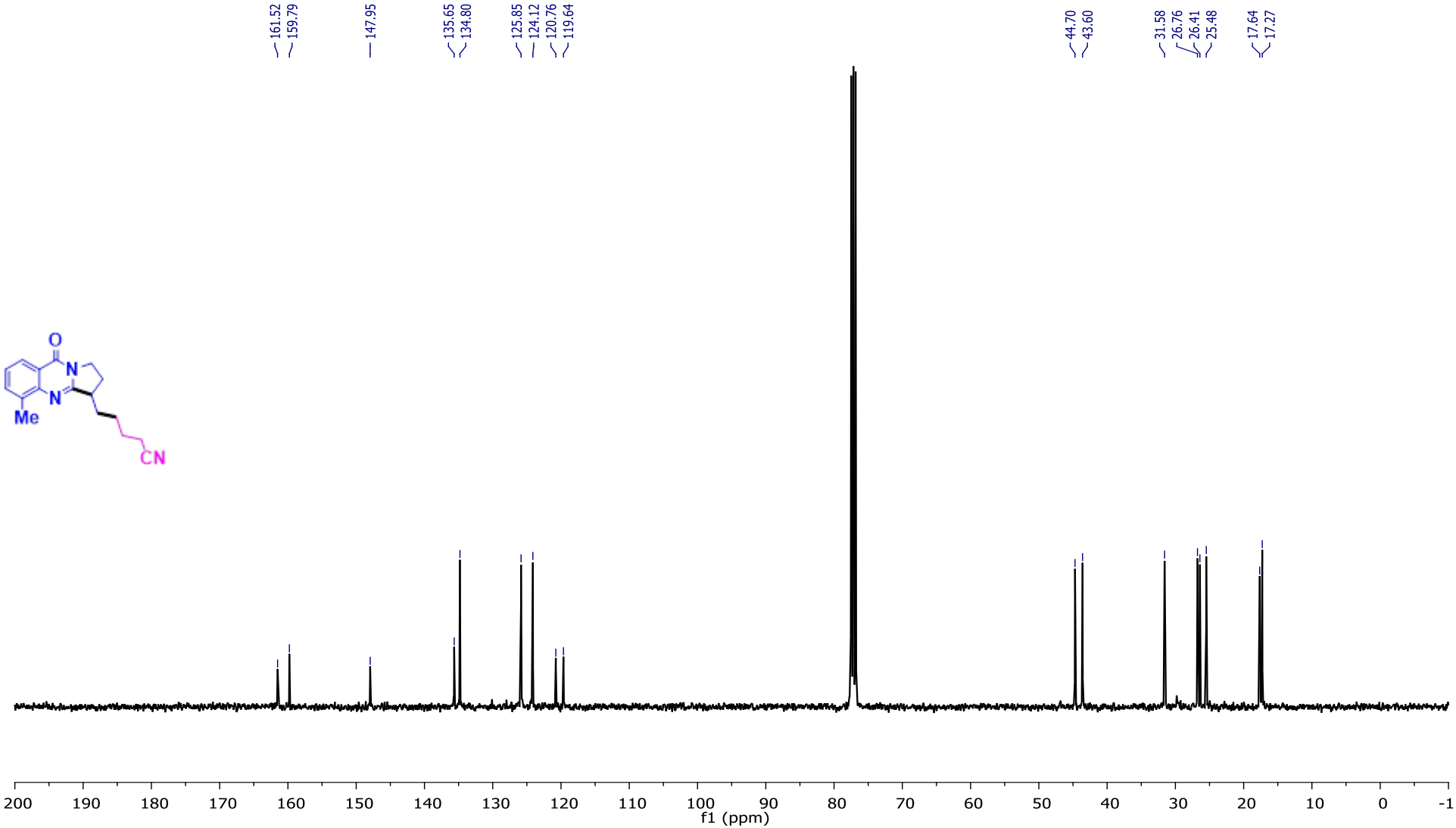
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (3u)



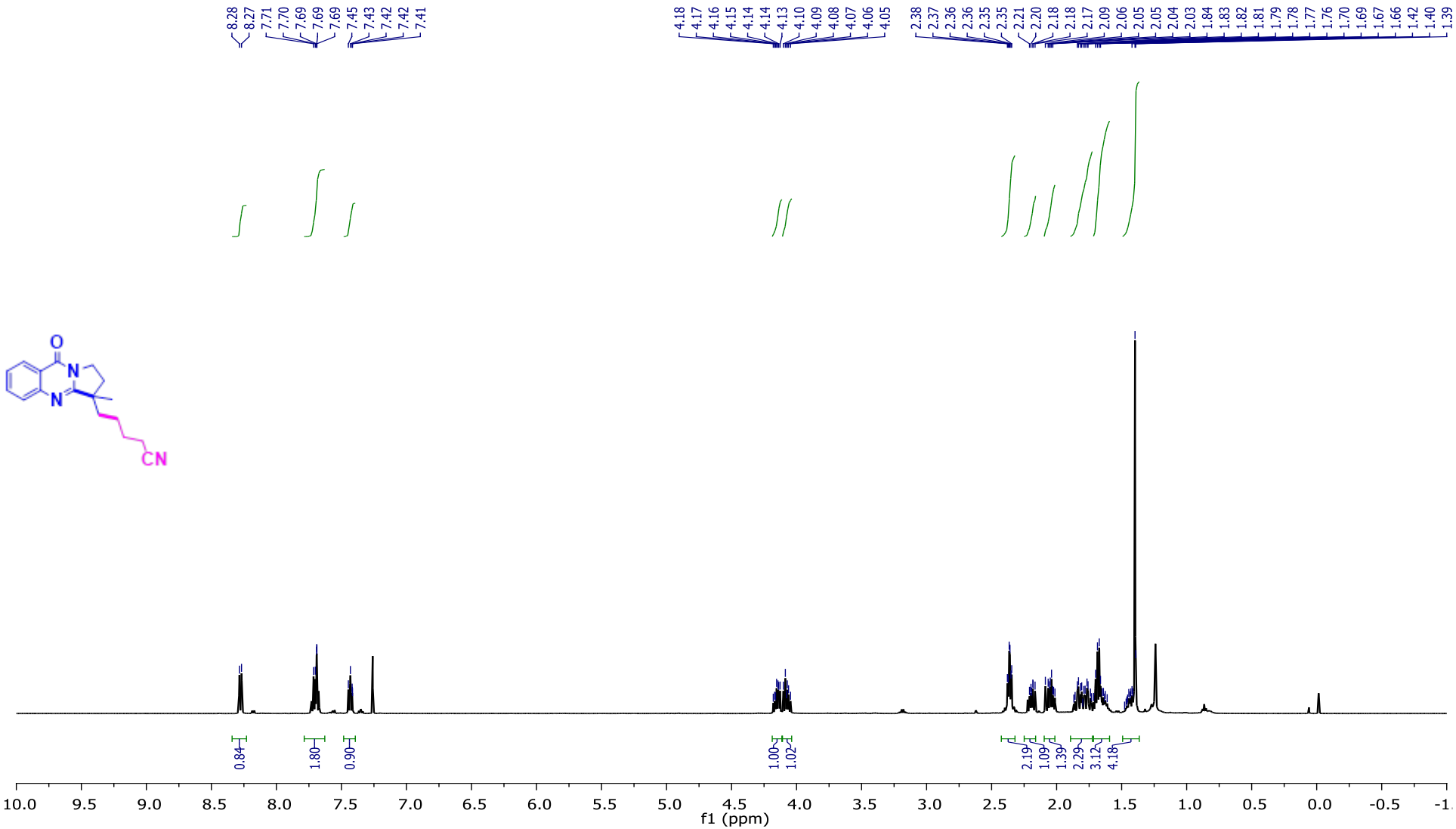
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (3v)



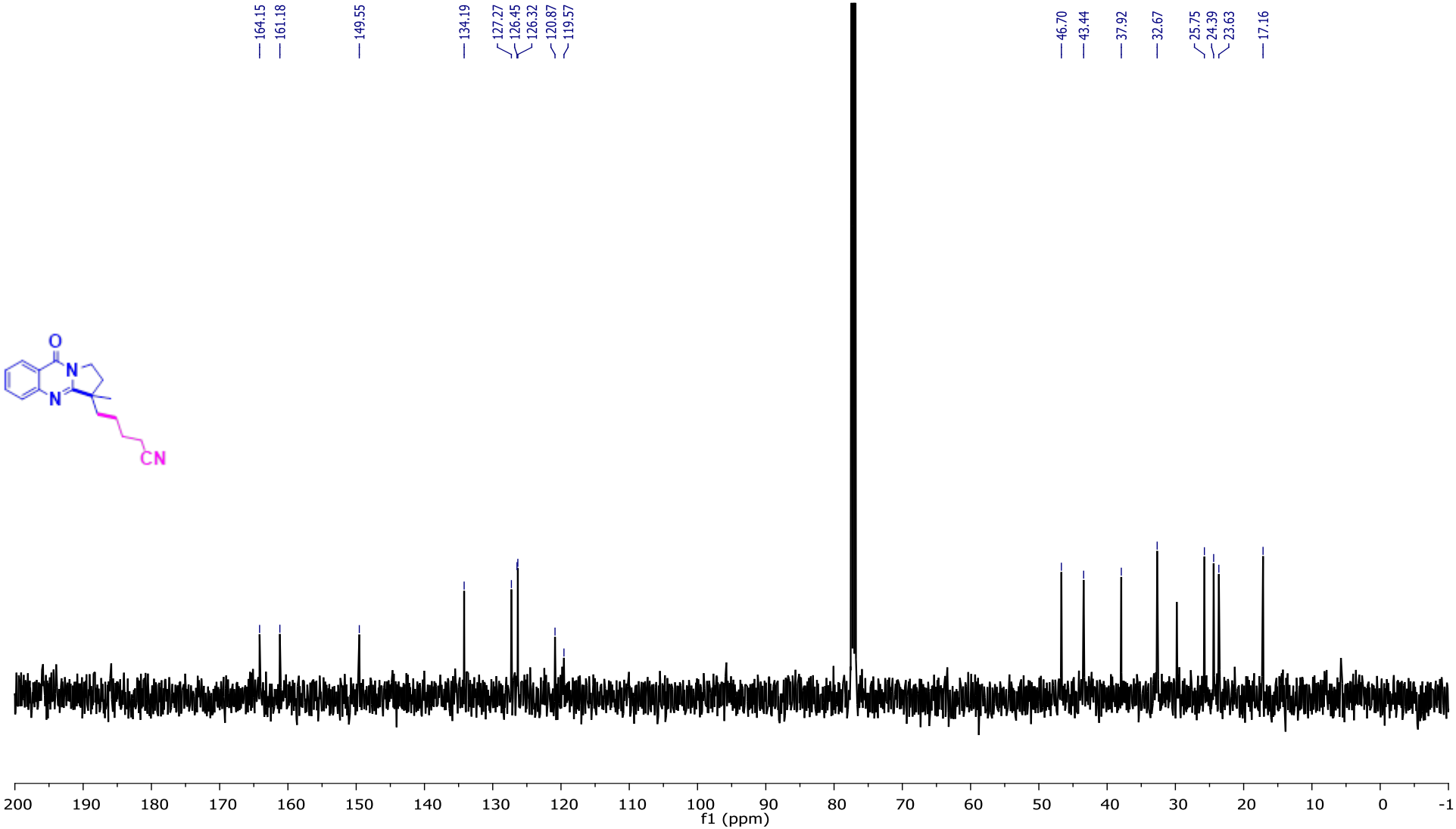
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (3v)



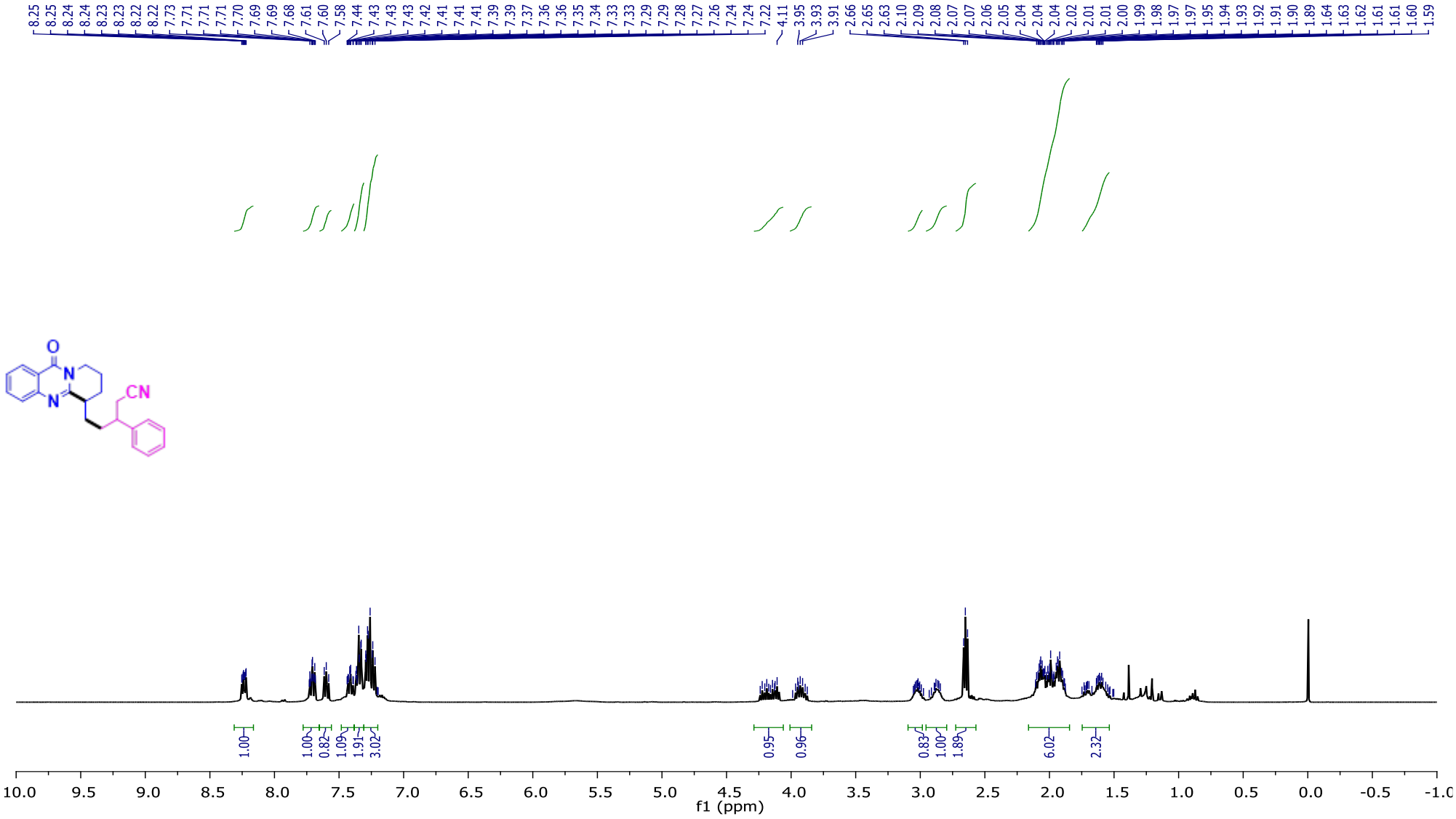
^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (3w)



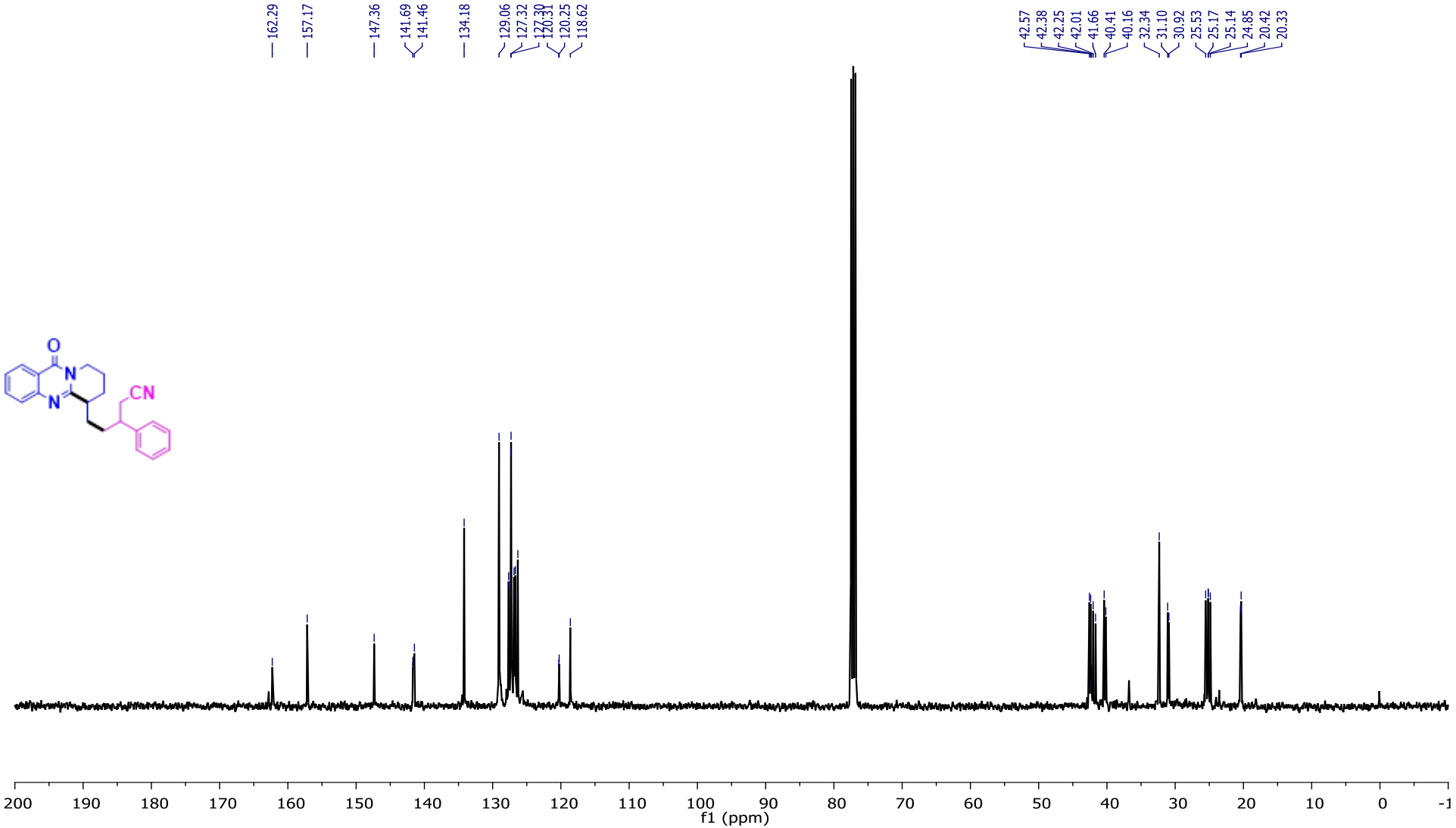
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (3w)



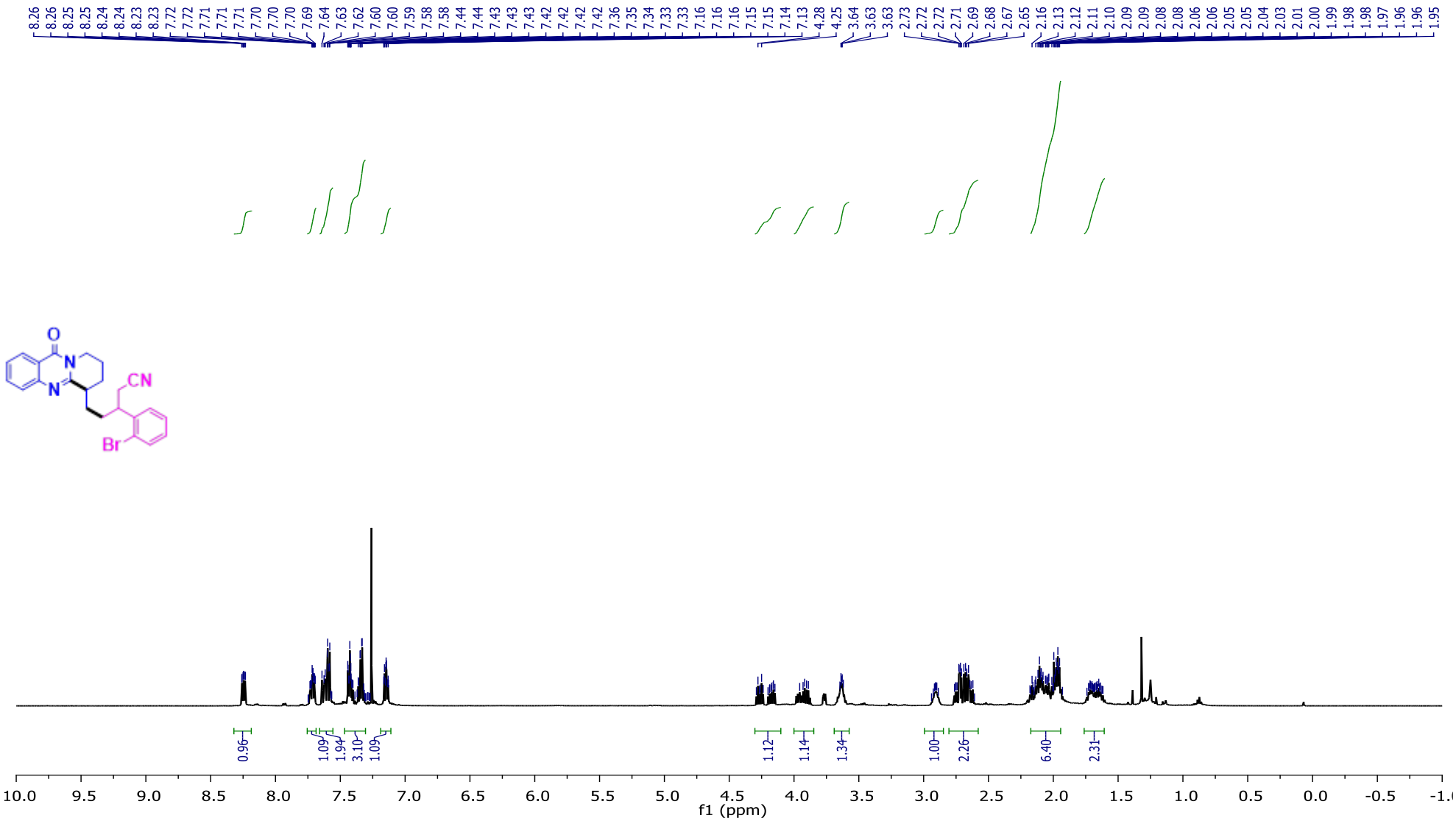
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (4a)



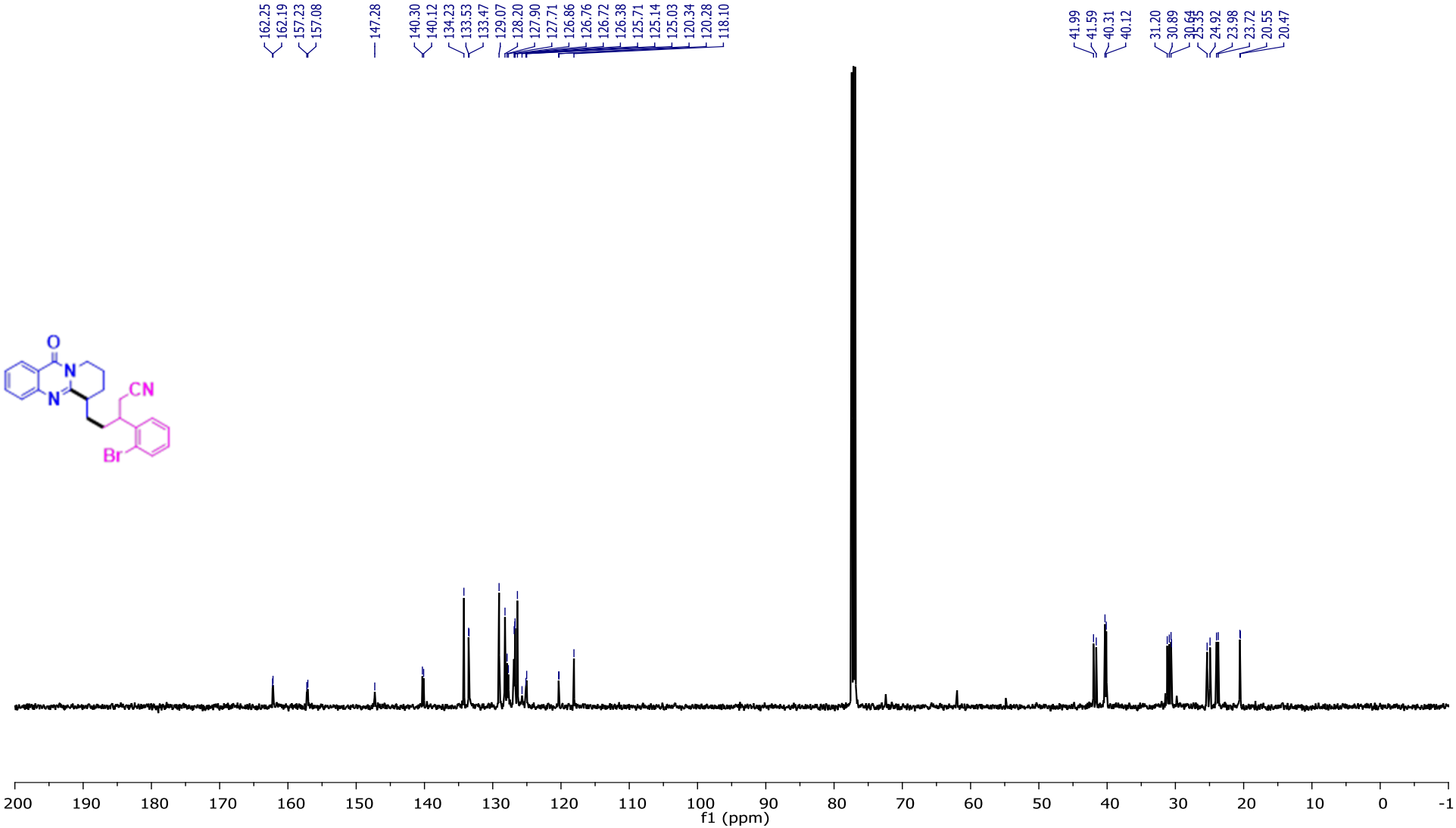
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4a)



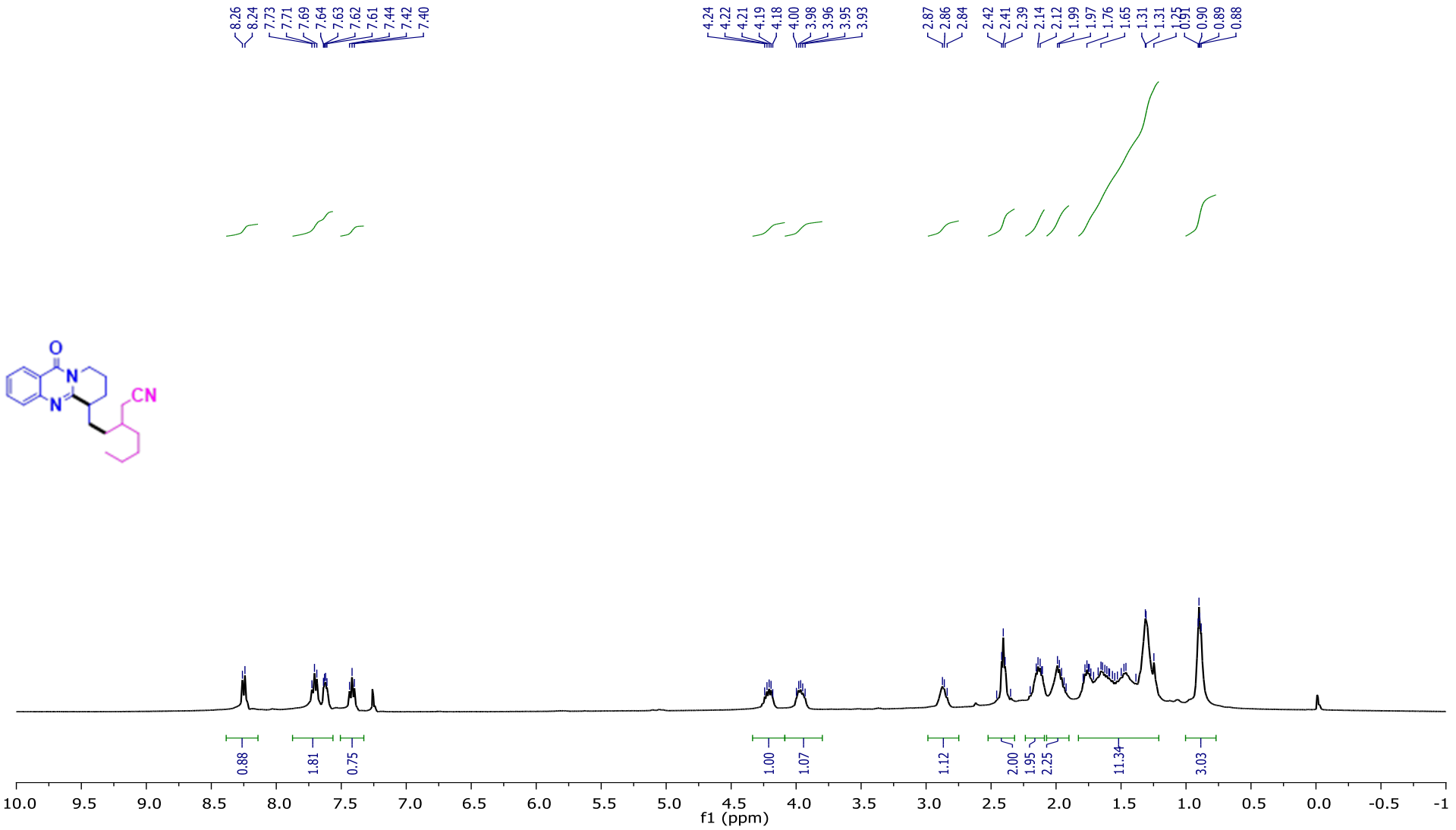
^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (4b)



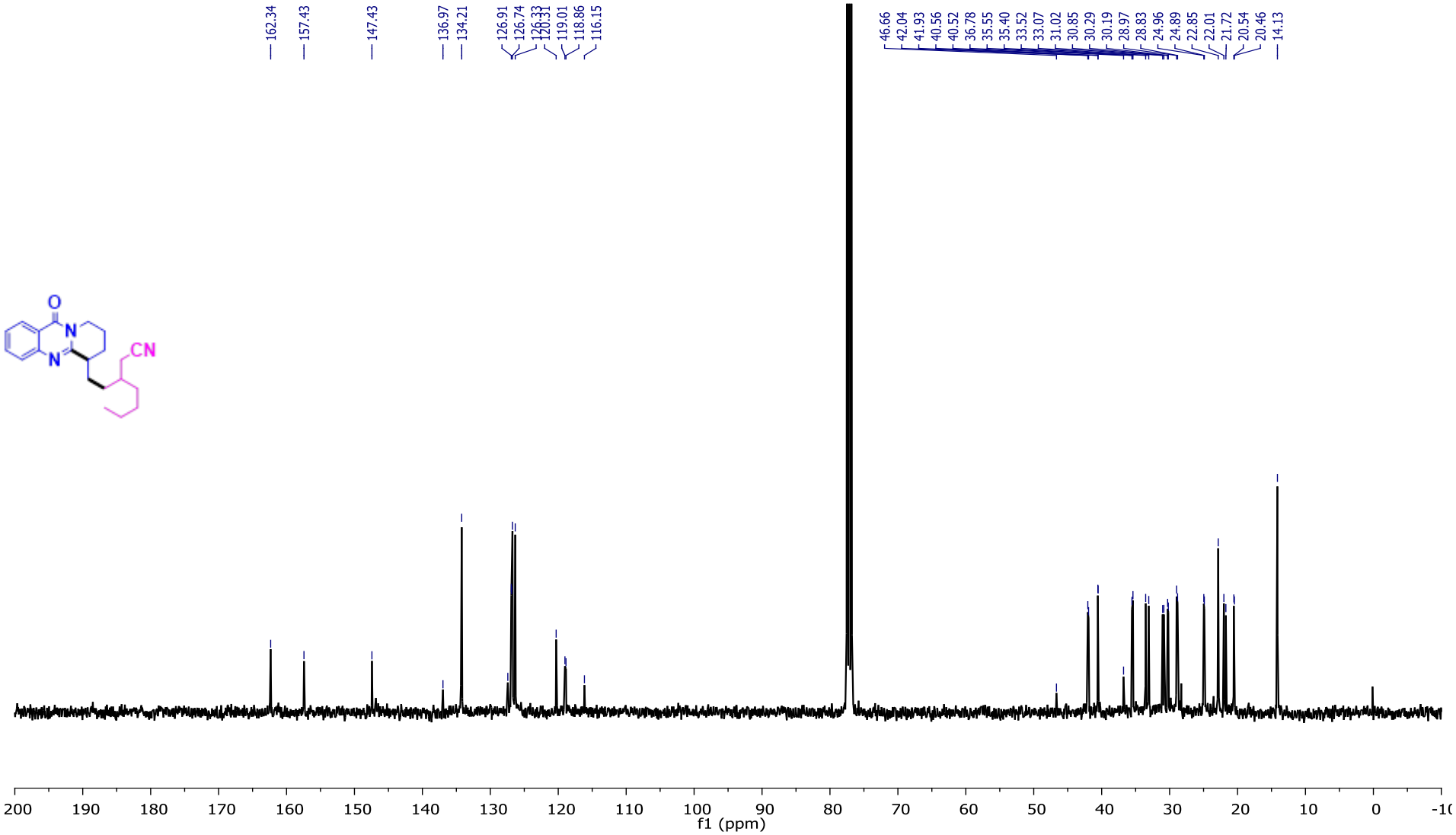
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound (4b)



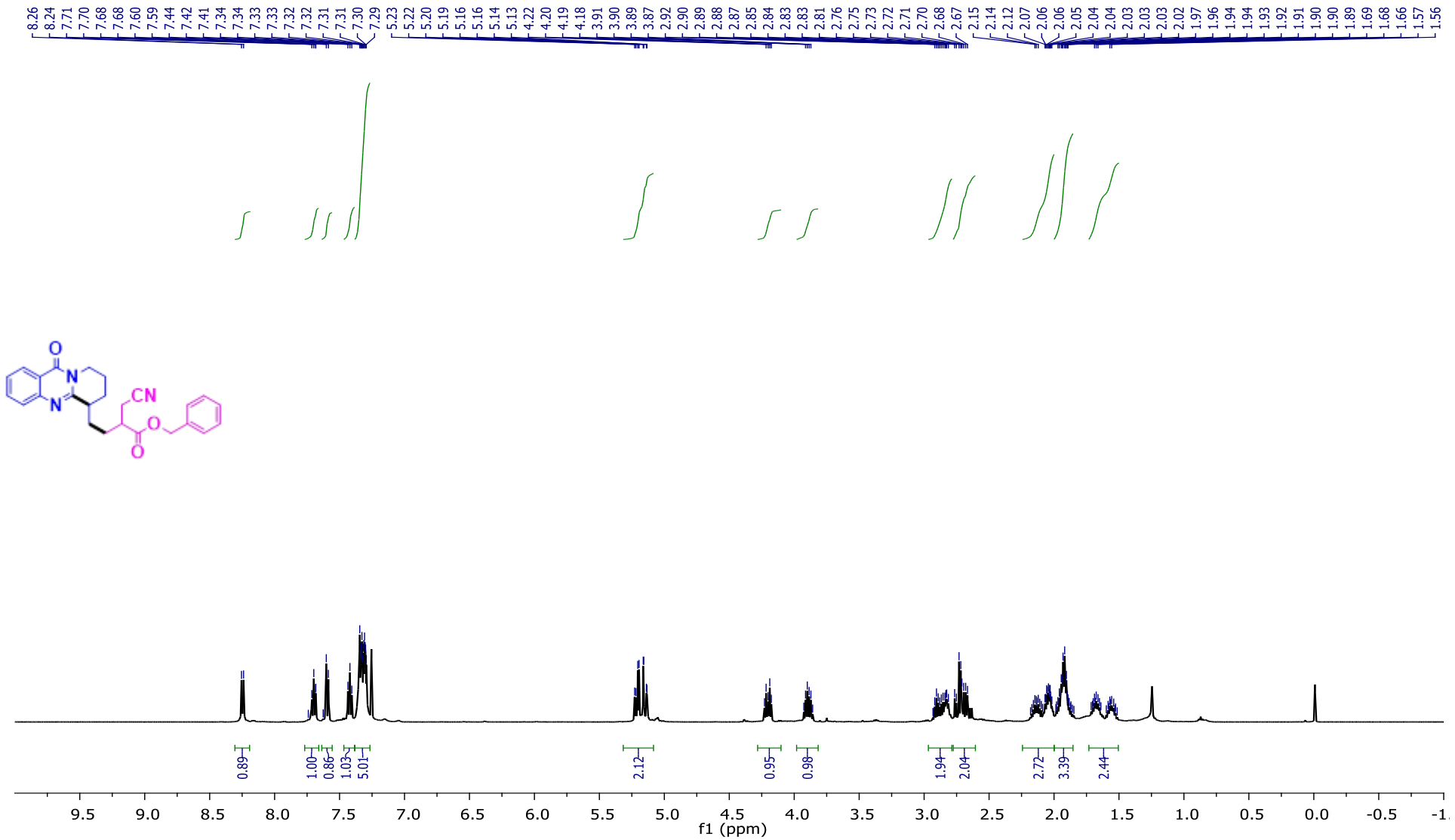
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (4c)



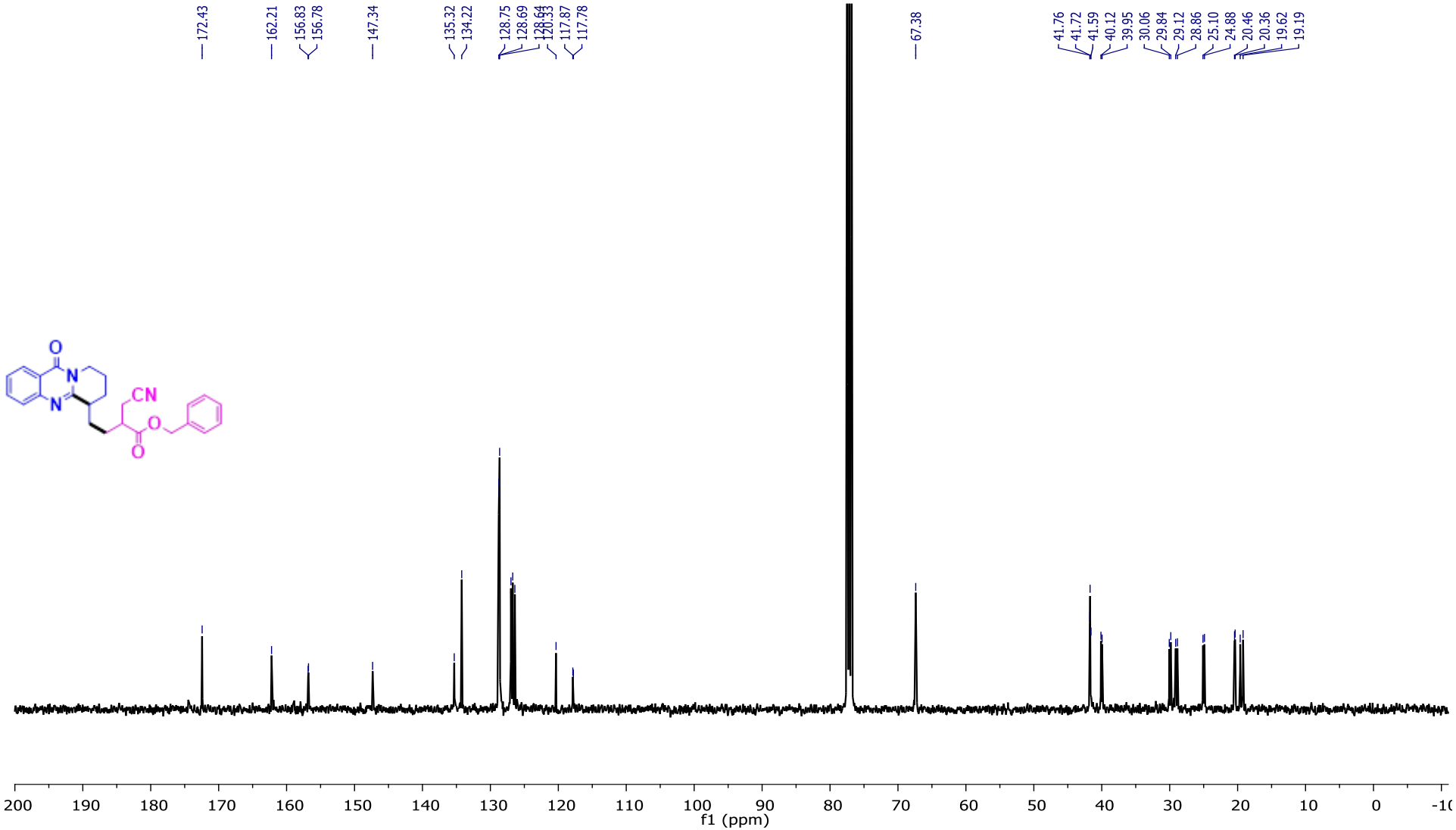
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4c)



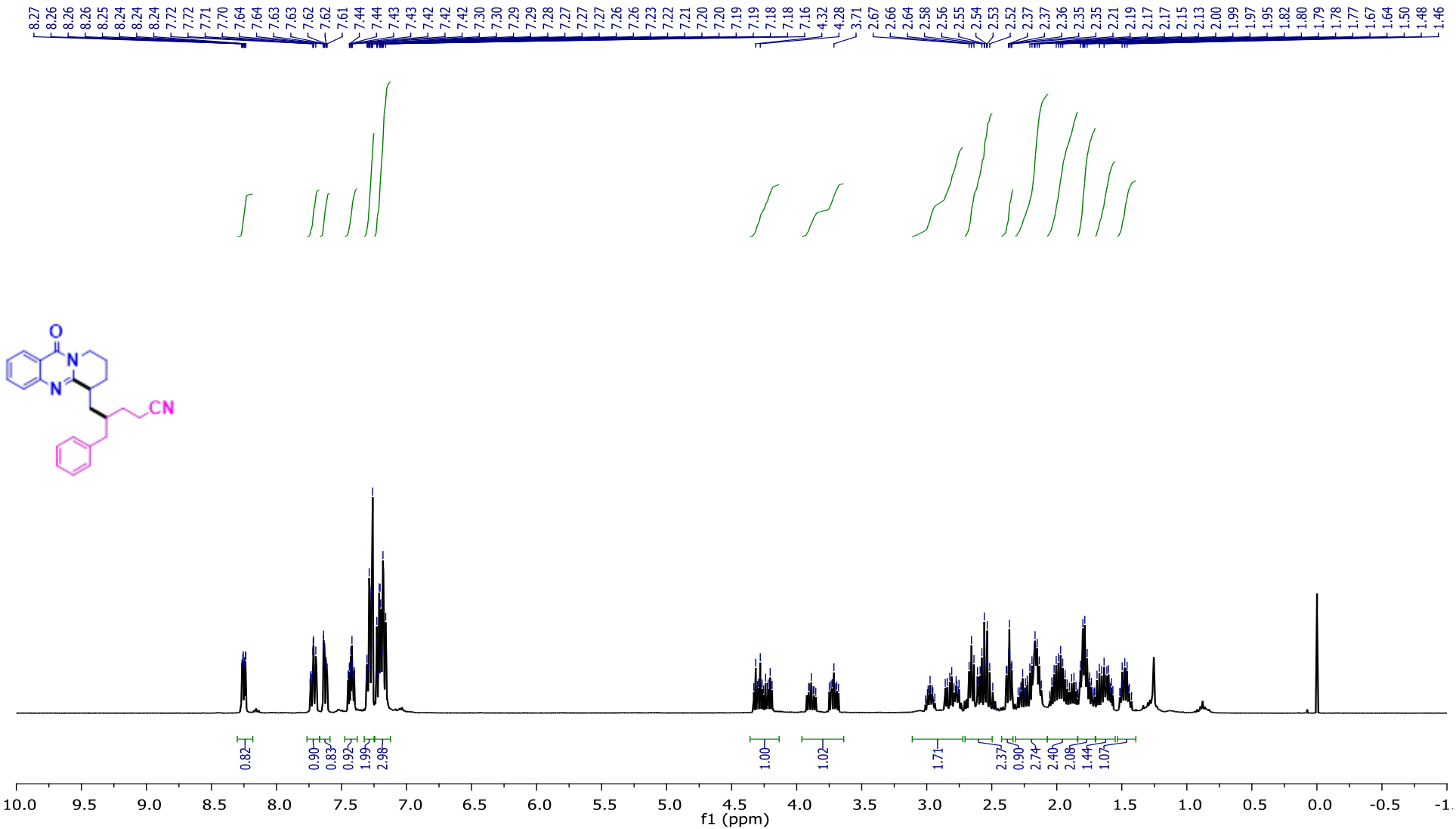
^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (4d)



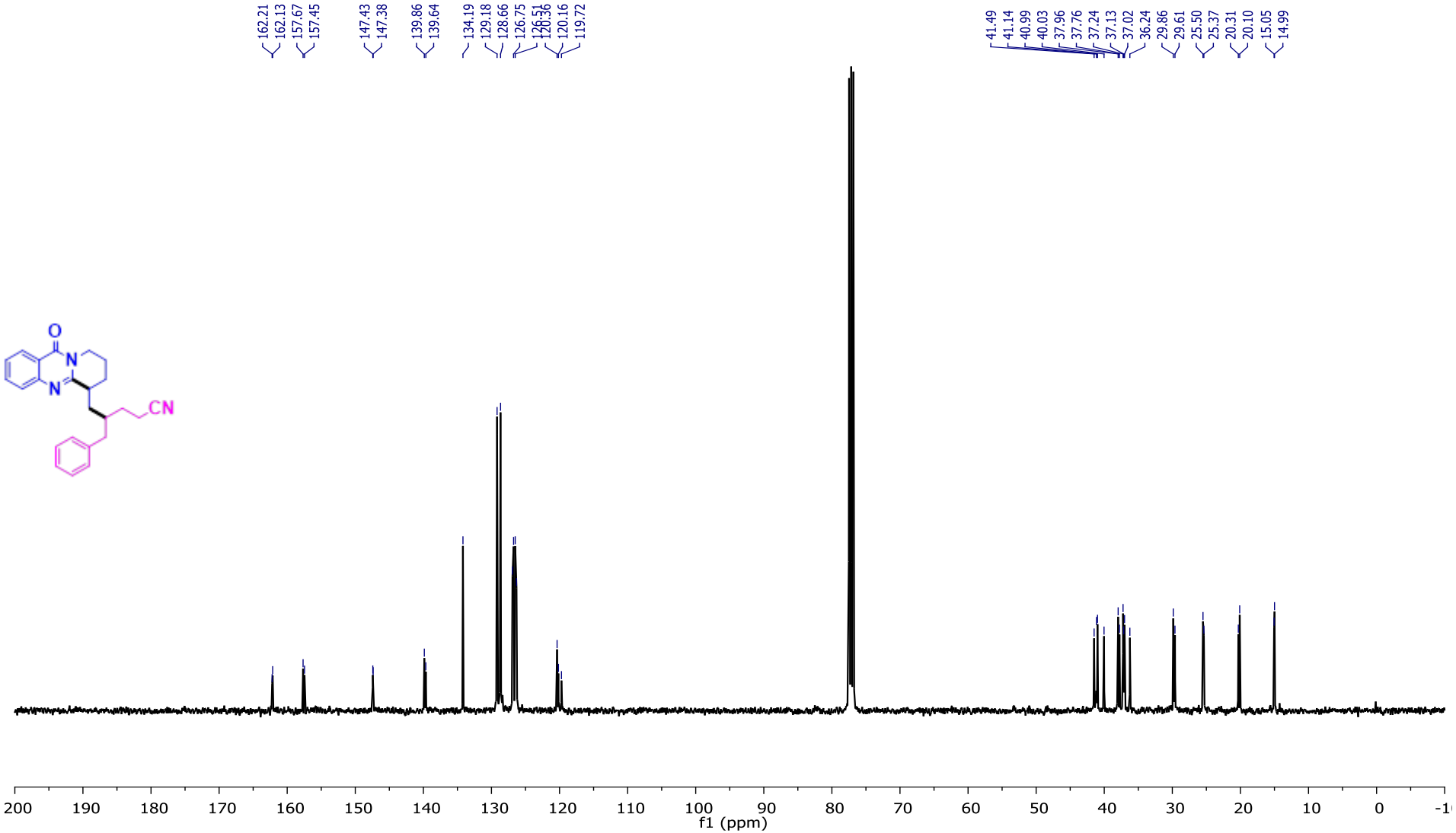
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4d)



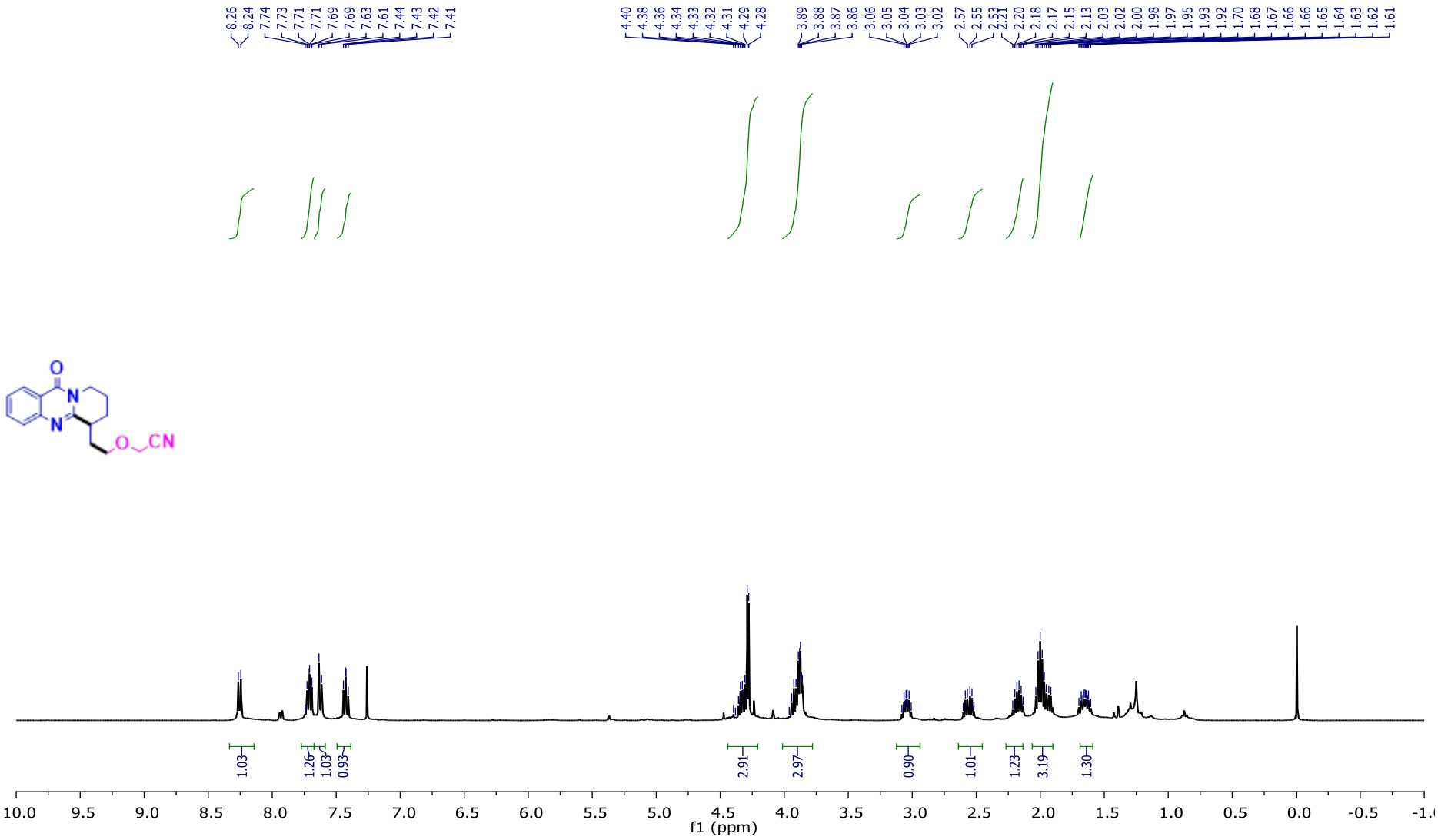
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (4e)



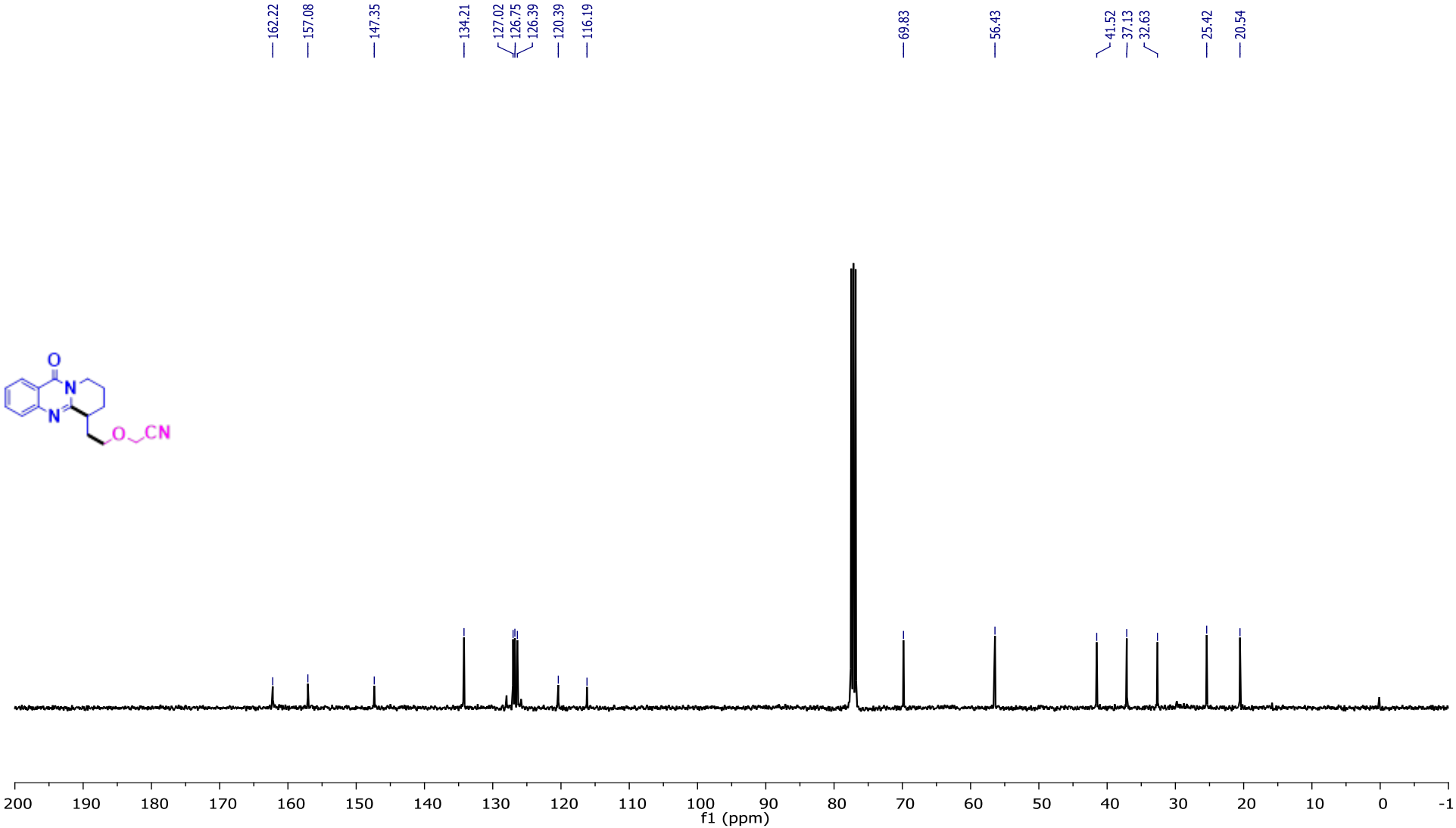
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4e)



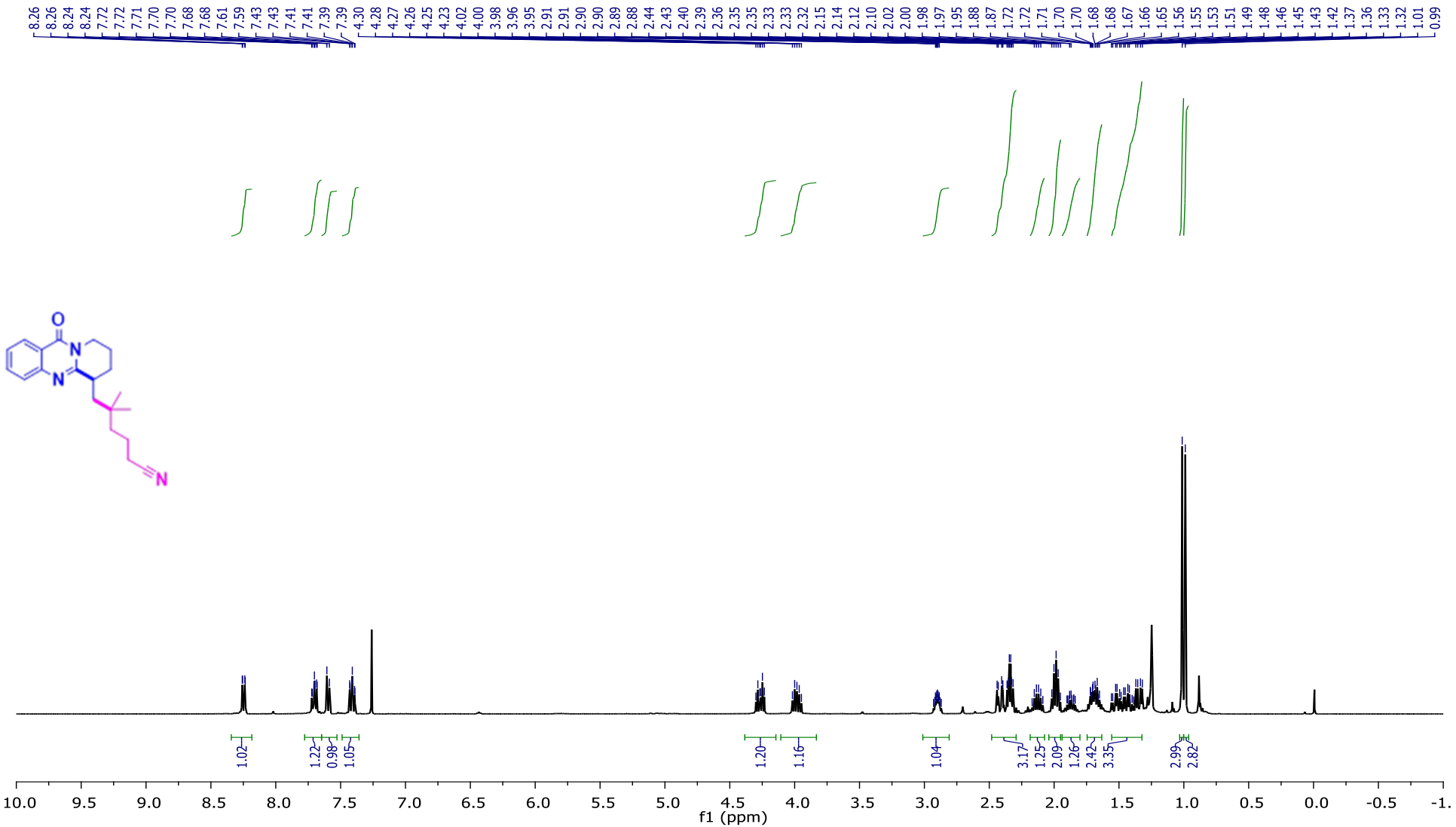
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (4f)



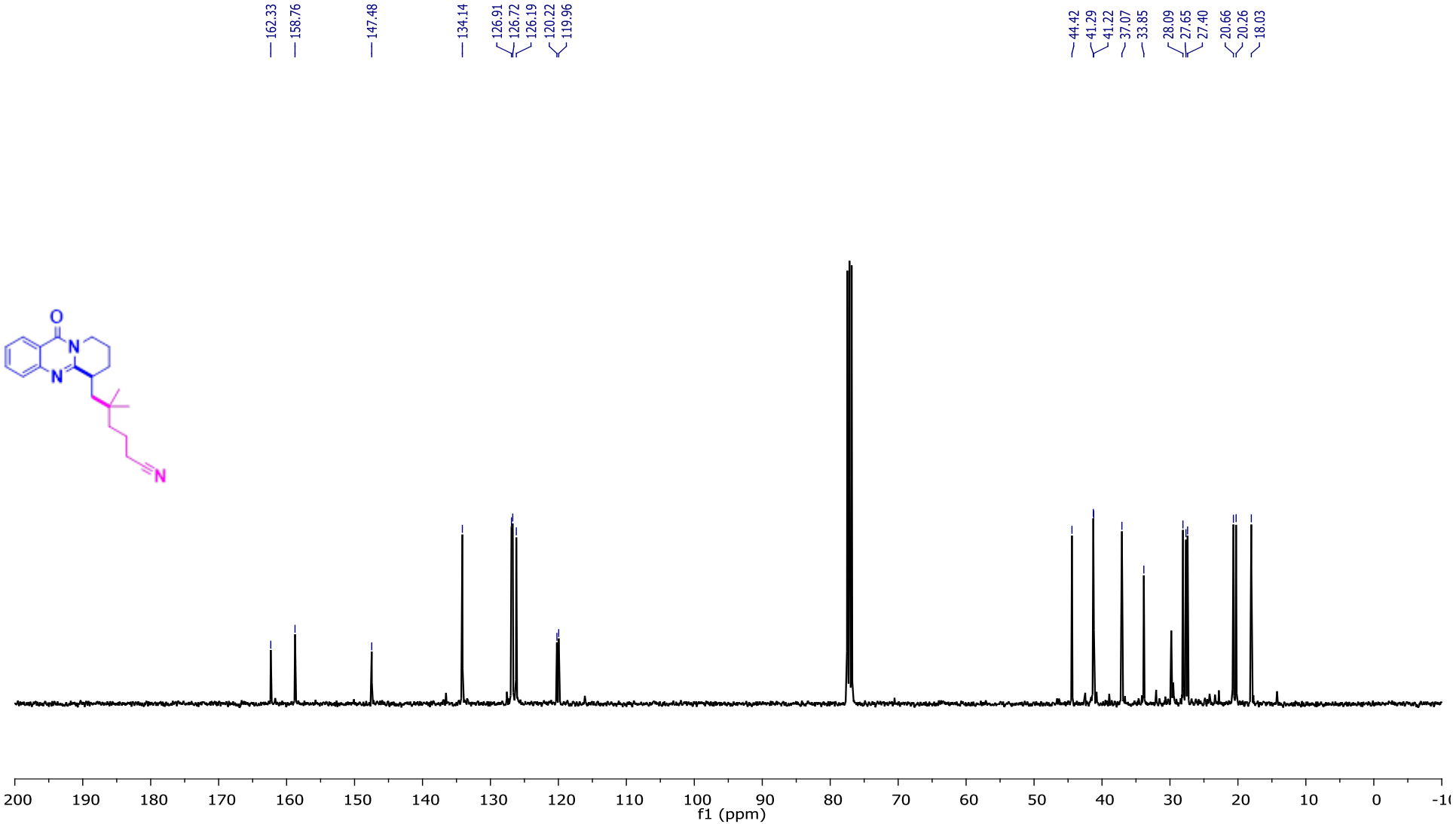
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4f)



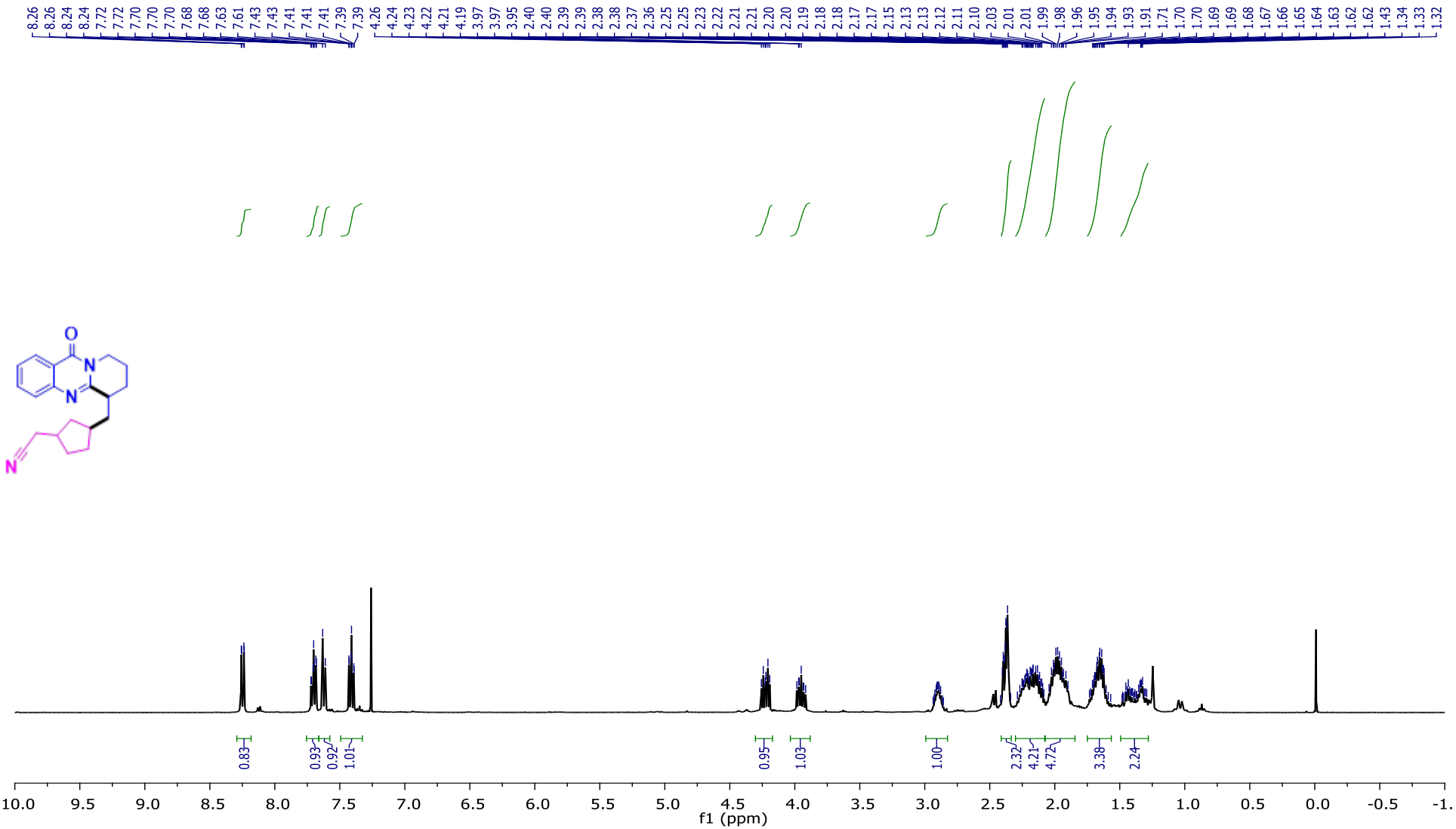
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (4h)



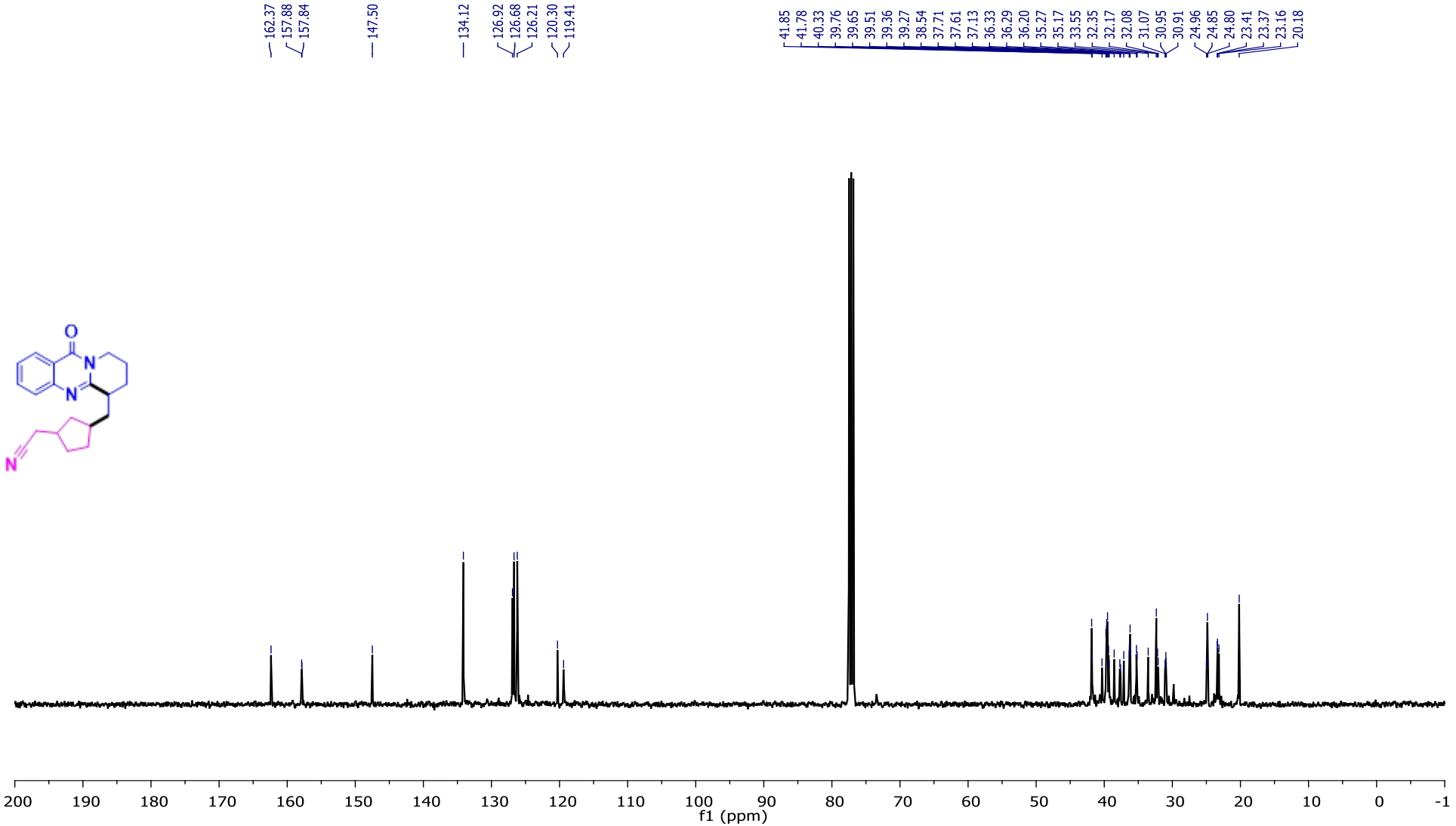
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4h)



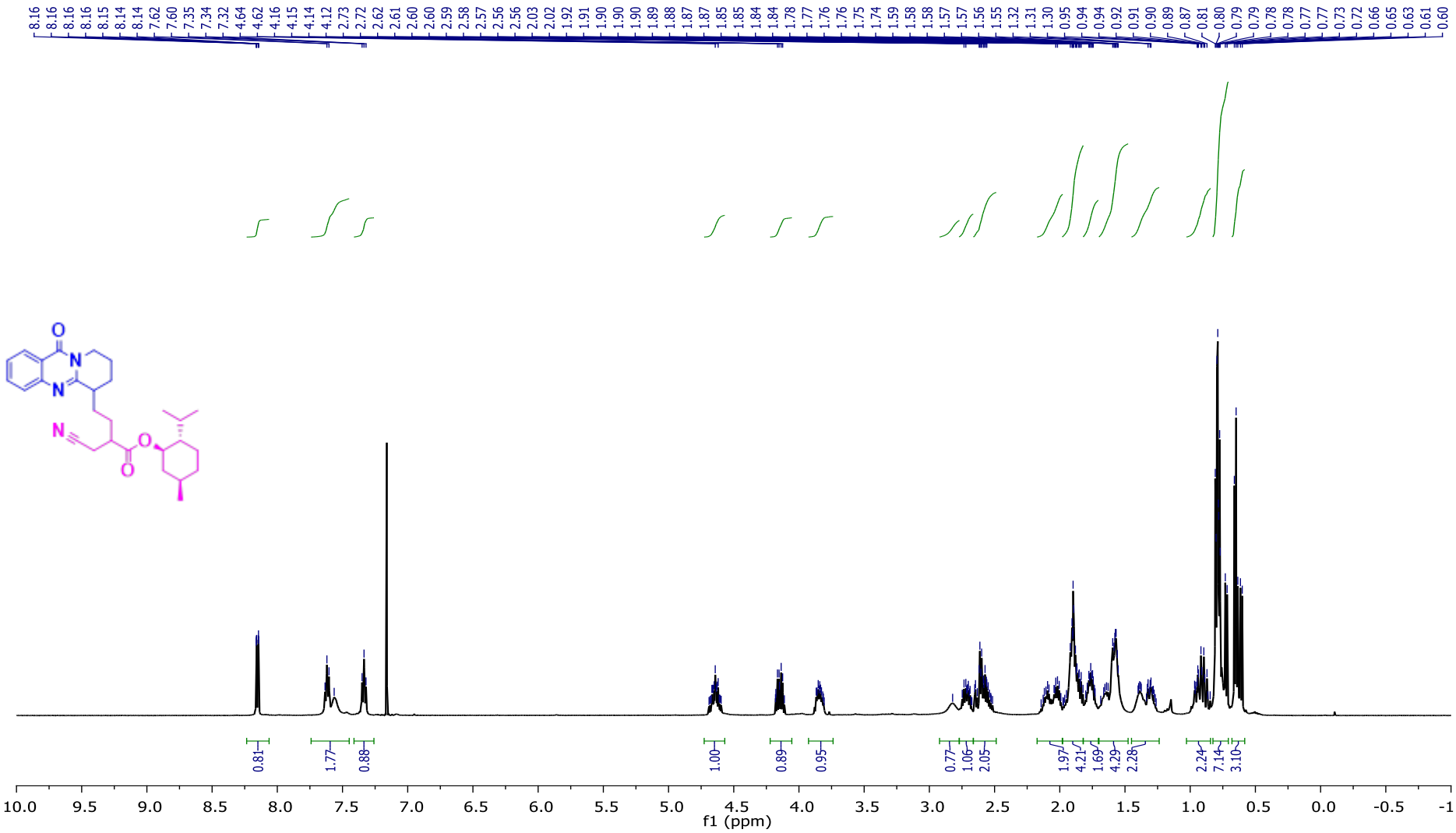
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (4i)



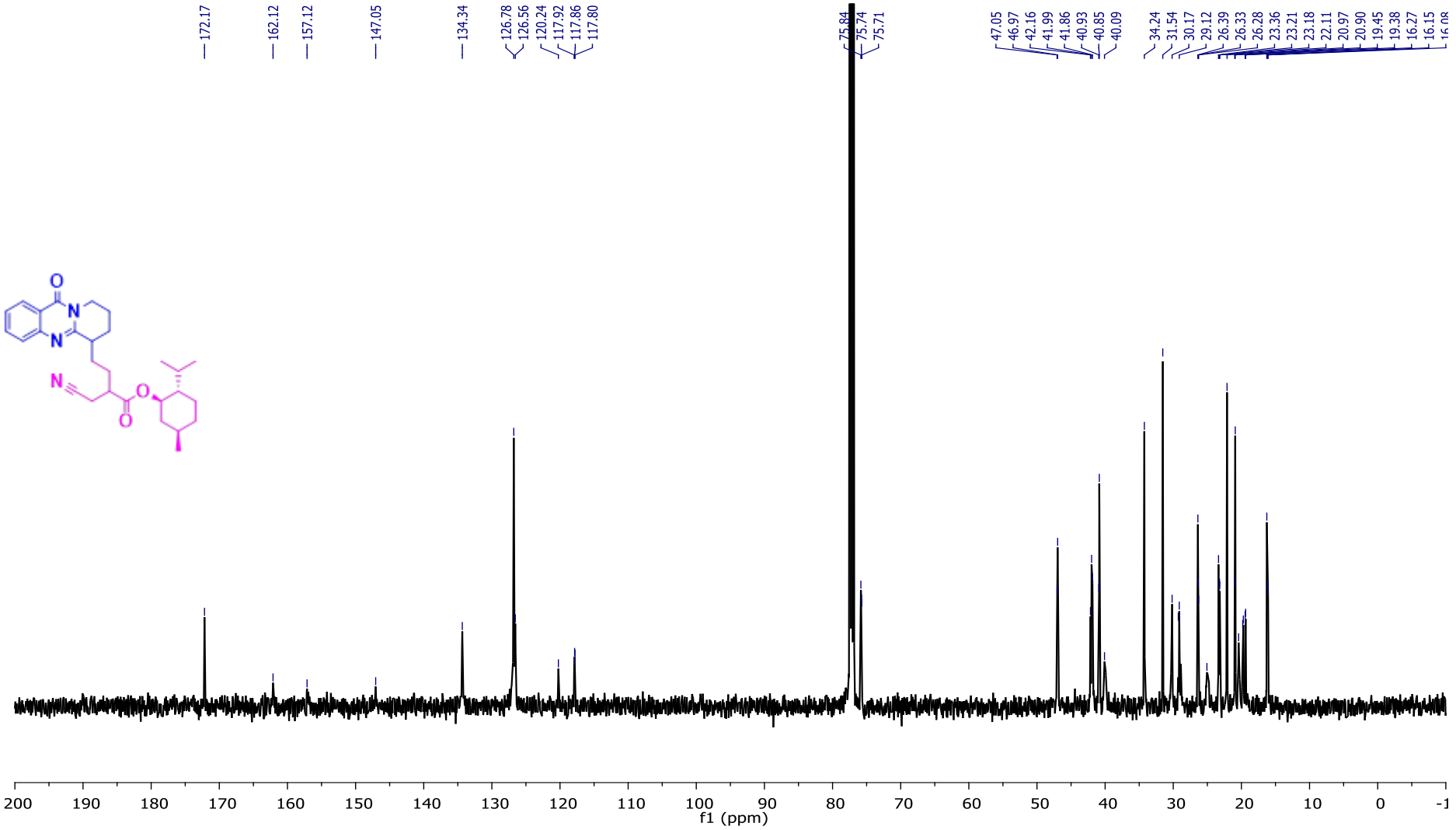
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4i)



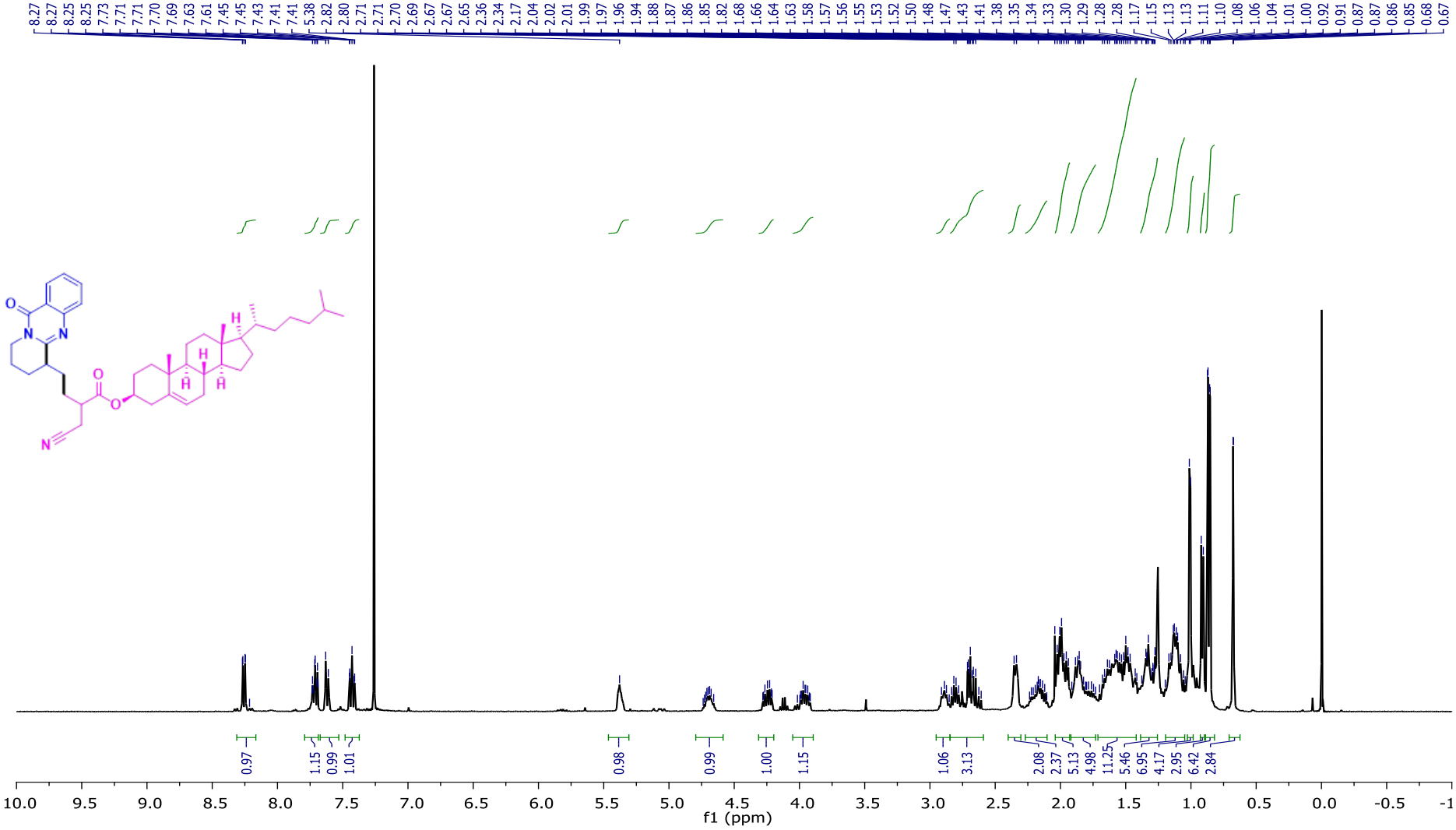
^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (4j)



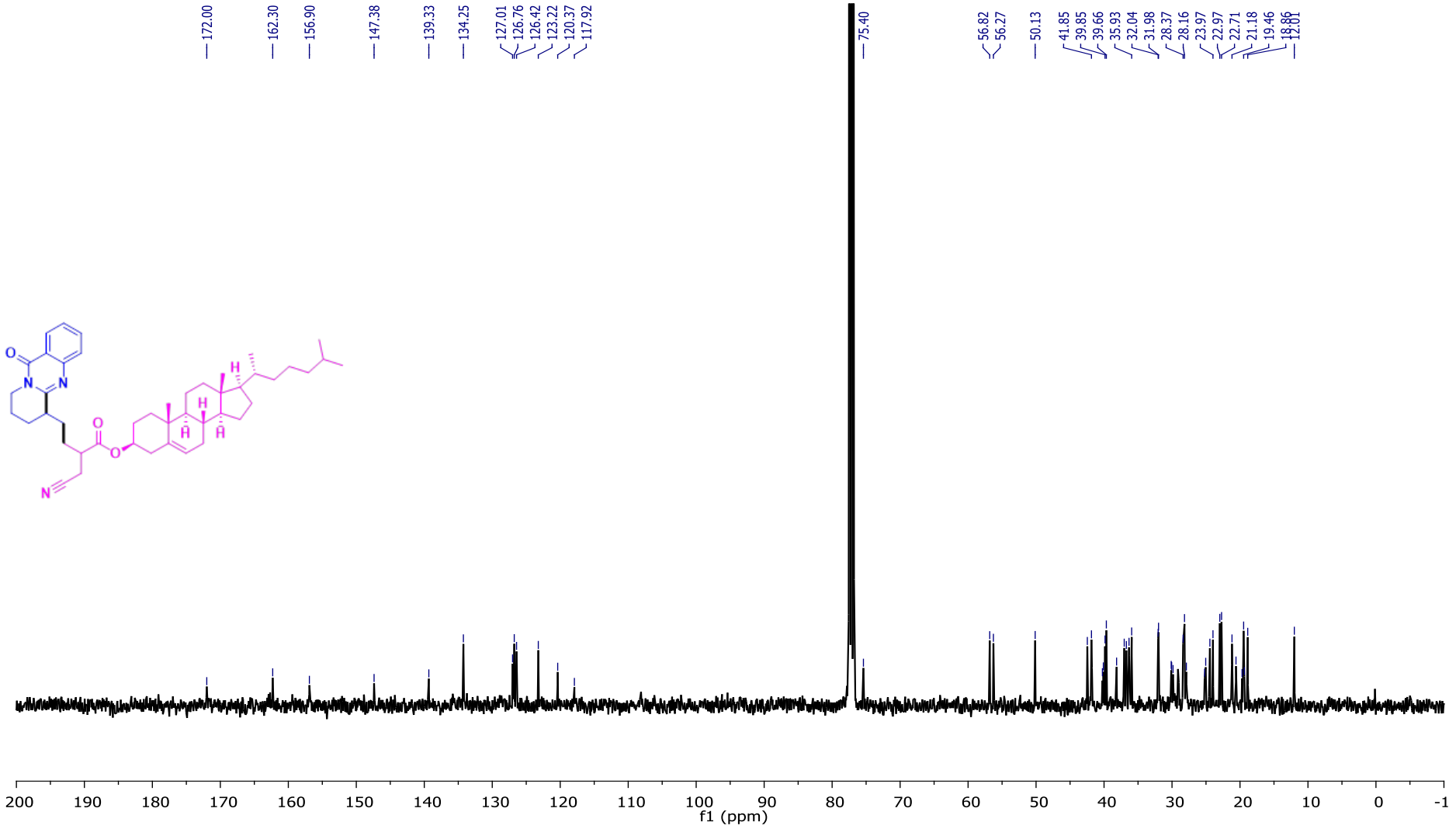
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4j)



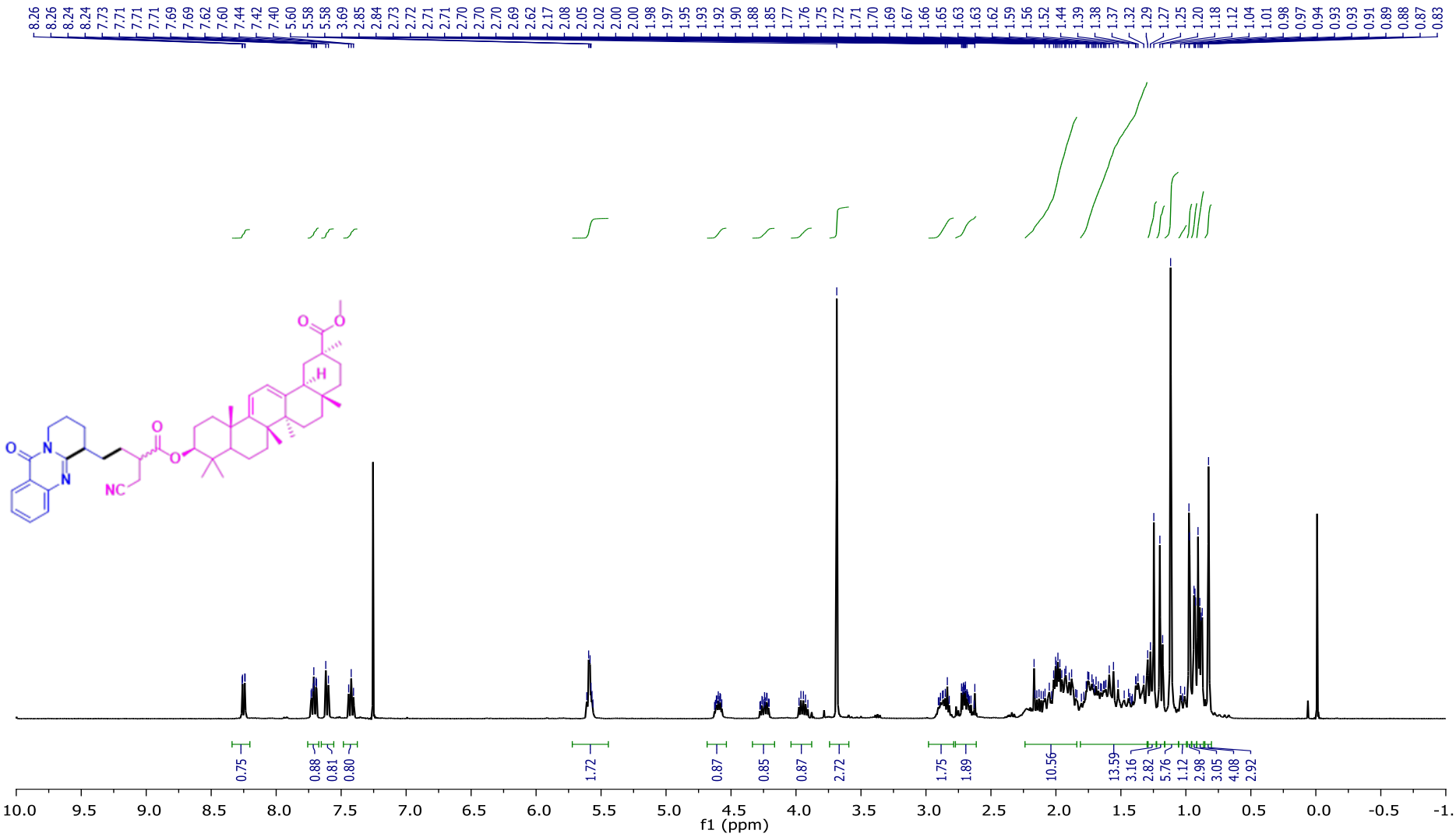
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (4k)



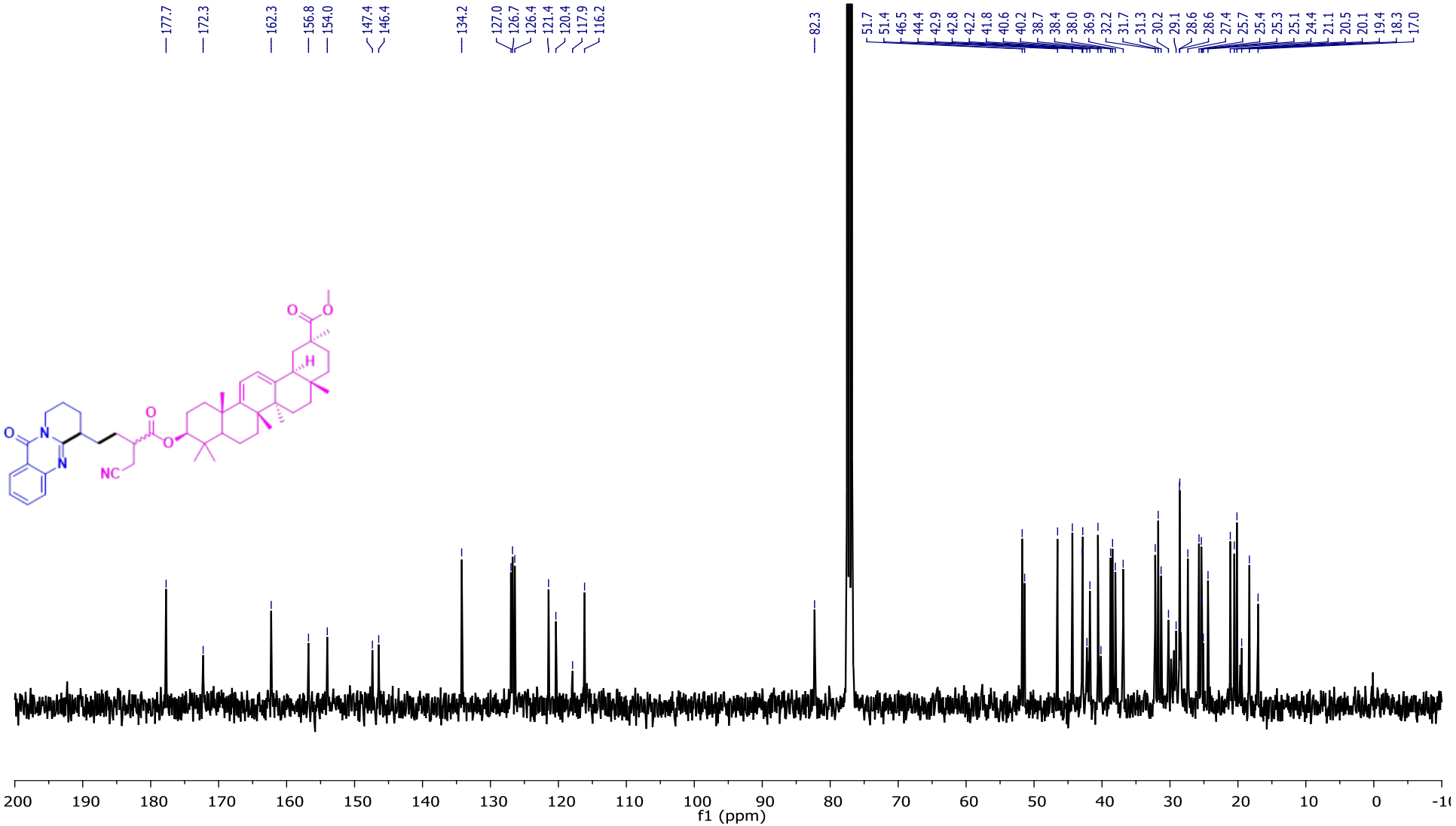
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4k)



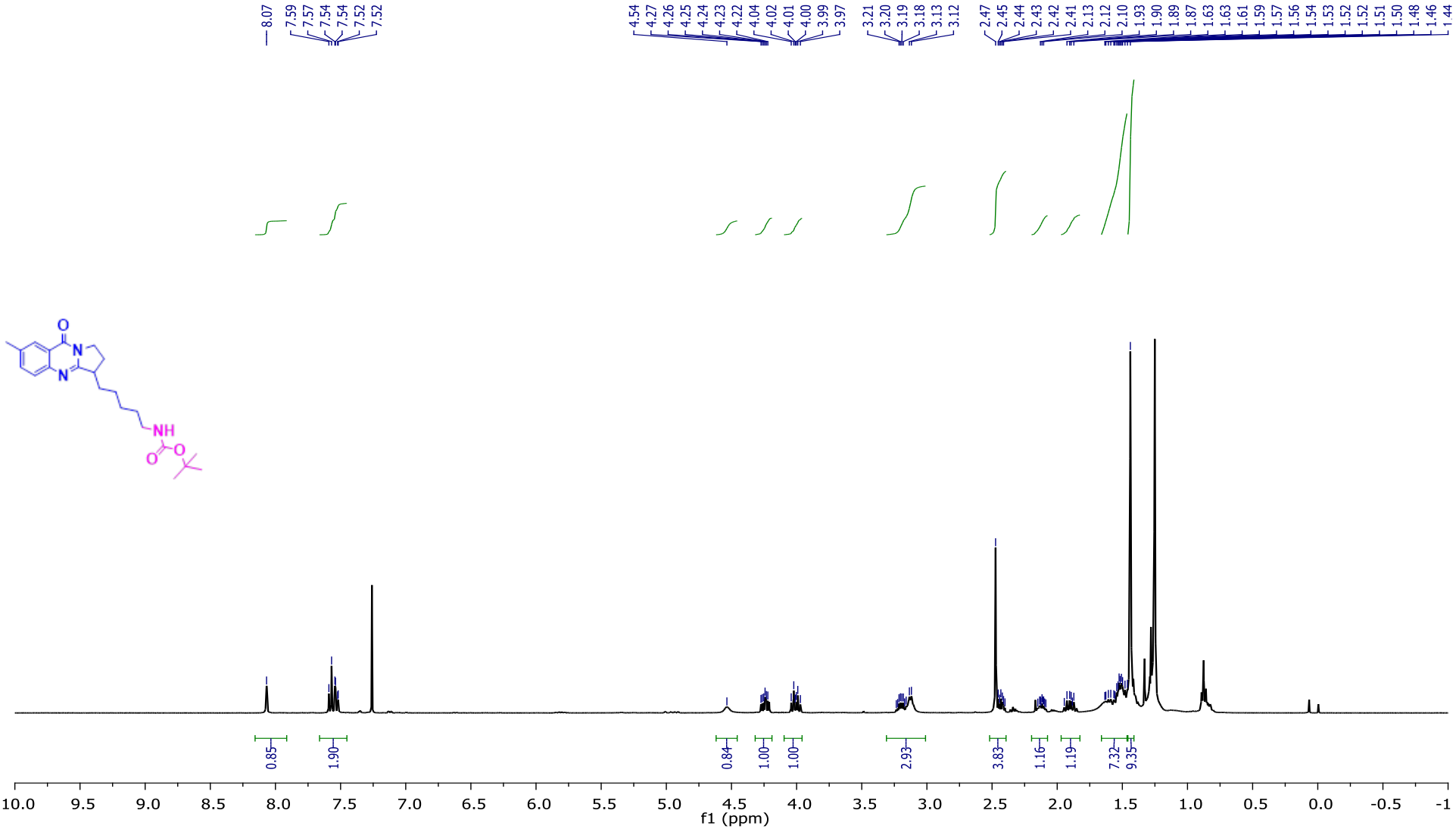
^{1}HNMR (400 MHz, $CDCl_3$) Spectrum of Compound (4l)



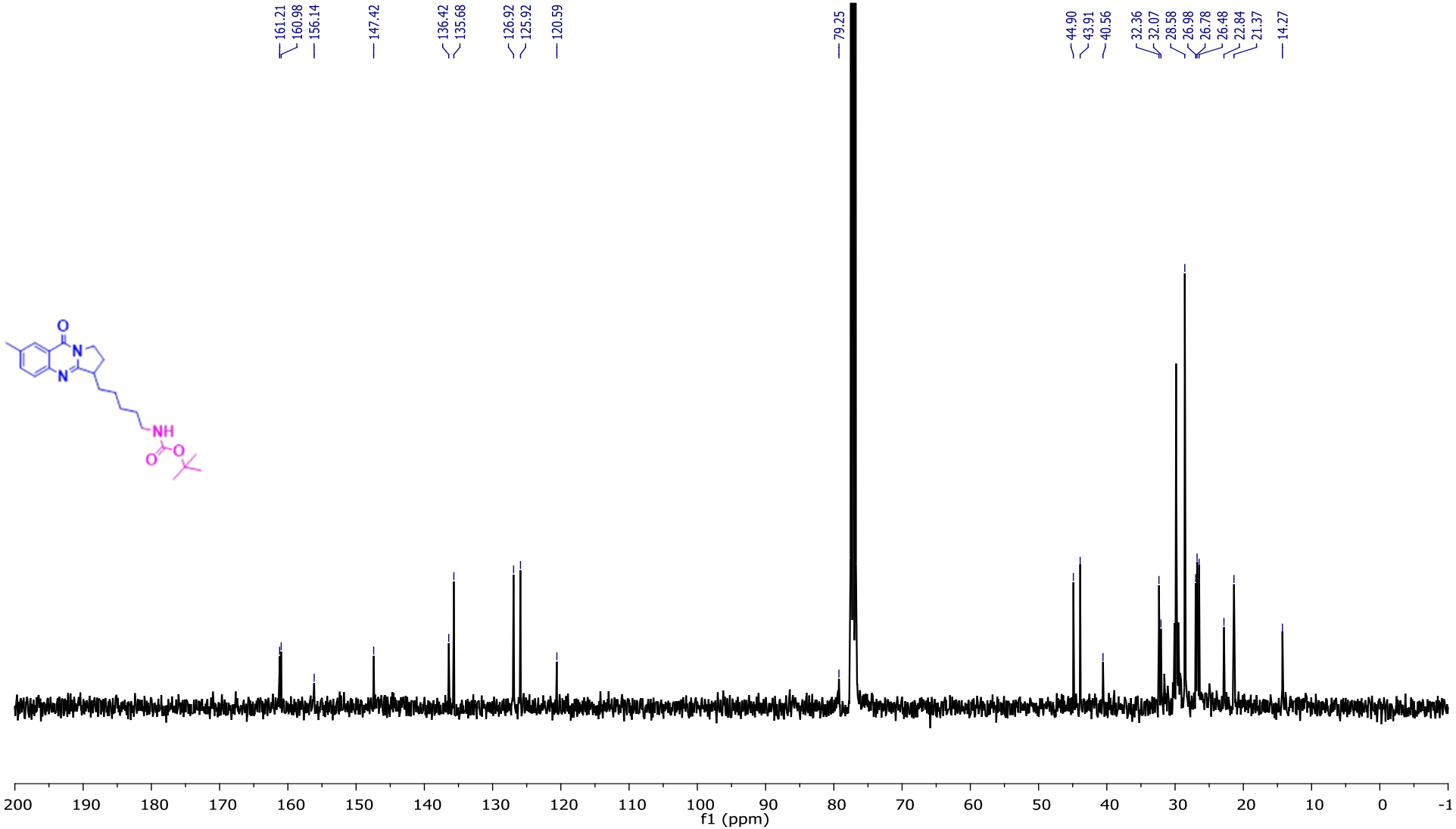
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (4l)



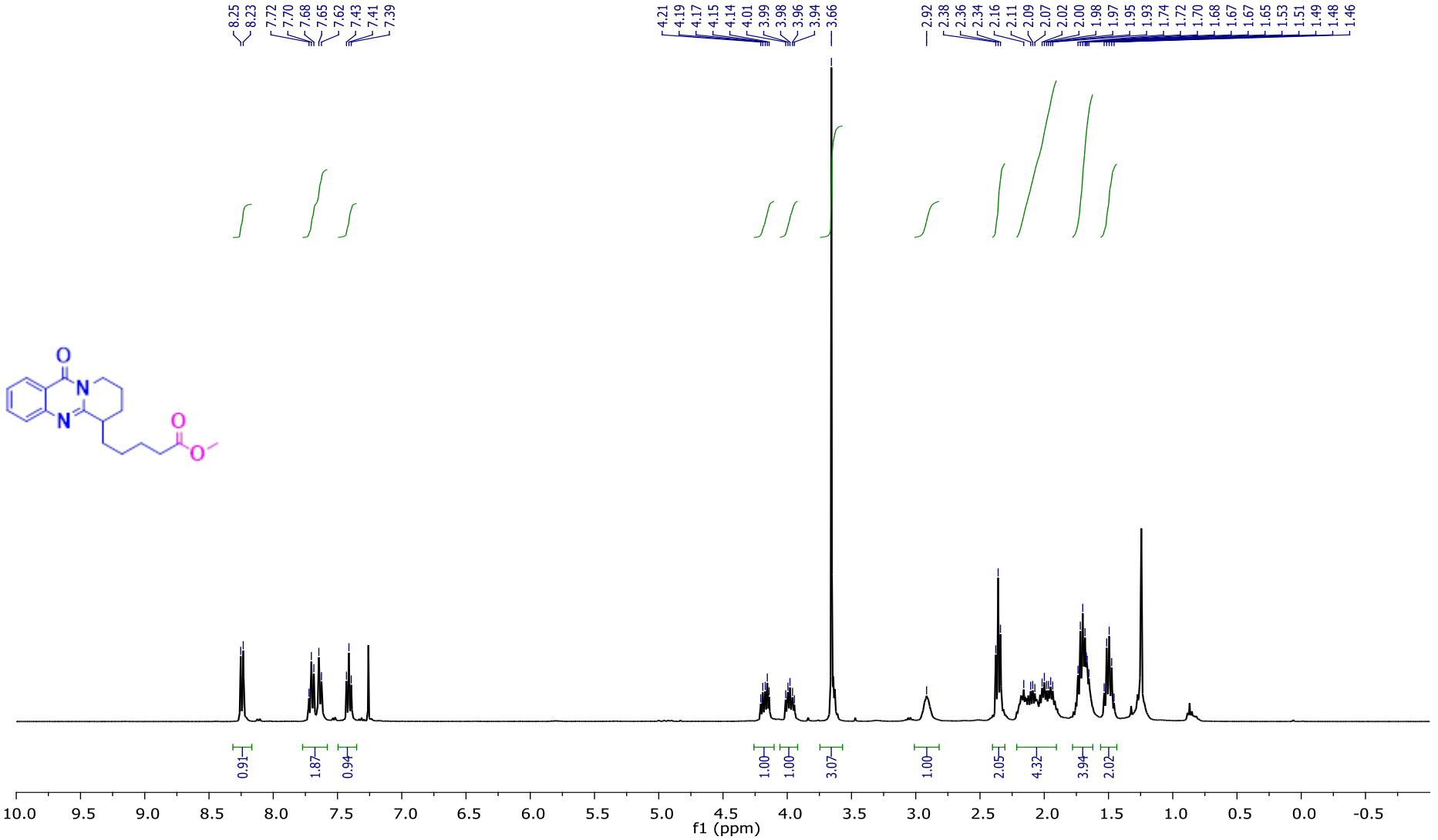
^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (6)



^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (6)



^{1}HNMR (500 MHz, $CDCl_3$) Spectrum of Compound (7)



^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound (7)