Electronic Supplementary Information

One-pot Palladium catalyzed ligand and metal oxidant-free aerobic oxidative isocyanide insertion leading to 2-amino-substituted-4(3*H*)-quinazolinones

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Experimental Section

General: IR spectra were recorded on a Bruker Tensor 37 (FTIR) spectrophotometer. ^{1}H NMR spectra were recorded on Bruker Avance 400 (400 MHz) spectrometer at 295 K in $CDCl_3$; chemical shifts (δ in ppm) and coupling constants (J in Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) (δ_H = 0.00 ppm) or $CHCl_3$ (δ_H = 7.25 ppm). ^{13}C NMR spectra were recorded on Bruker Avance 400 (100 MHz) spectrometer at RT in $CDCl_3$; chemical shifts (δ in ppm) are reported relative to $CHCl_3$ (δ_C = 77.00 ppm). In the ^{1}H-NMR, the following abbreviations are used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, m = multiplet and br s = broad singlet, sept = septet. The assignment of signals were confirmed by ^{1}H and ^{13}C spectral data. High-resolution mass spectra (HR-MS) were recorded on an Agilent 6538 UHD Q-TOF using multimode source. Microwave experiments were carried out with CEM Discover Labmate^{TM} instrument in 10 ml vial, closed vessel, Power: 250W, Temperature: 60 °C-100 ^{o}C for 50-100 minutes. Melting points were determined using melting point apparatus manufactured by GUNA enterprises, India and are uncorrected. All small scale reactions were carried out using standard syringe-septum technique. Reactions were monitored by TLC on silica gel using a combination of hexane and ethyl acetate as eluents. Solvents were distilled prior to use.

General Procedure for the synthesis of 2-amino-substituted-4(3*H*)-quinazolinones (5a-5v):

In an oven dried schlenk tube under argon atmosphere, were added isatoic anhydride (1 equiv, 0.609 mmol), amine (1 equiv, 0.609 mmol) and activated 4Å molecular sieves (150 mg) followed by addition of dry DMSO (2 mL). The reaction mixture was stirred at 110 ^{o}C for 30 min to 4 h. The completion of first step was monitored by TLC. Once dinucleophile was formed $Pd(OAc)_2$ (5 mol%), CyNC (1.5 equiv., 0.913 mmol) were added in same pot under argon atmosphere. It was evacuated and filled with O_2 by using a balloon. The resulting reaction mixture was heated at 110 ^{o}C. Progress of the reaction was monitored by TLC, which took 15-17 h. The reaction mixture was then quenched with water and the product was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent, which afforded the desired product (**5a-5w**). All the compounds were confirmed by FTIR, ^{1}H NMR, ^{13}C NMR and HR-MS Spectral analyses. Among 22 compounds, 19 are unknown and 3 (**5a, 5i & 5m**) are known.

Spectral data of all compounds (5a-5s):

3-Benzyl-2-(cyclohexylamino)quinazolin-4(3*H*)-one (5a):[1] White solid (75%), Mp 106-108 ^{o}C.

[TLC control R*f*(**1**) = 0.30, *Rf*(**5a**) = 0.70 (petroleum ether/ethyl acetate 8:2, UV detection)]. IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3324, 3059, 2921, 1627, 1584, 1517, 1487, 1384, 1230, 1198, 1029, 951, 751, 640.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.18 (dd, 1H, J_a = 8.1 and J_b = 1.2 Hz), 7.60-7.56 (m, 1H), 7.38-7.30 (m, 4H), 7.29-7.26 (m, 1H), 7.17 (t, 1H, *J* = 7.6 Hz), 5.32 (s, 2H), 4.36 (d, 1H, *J* = 6.8 Hz), 3.99-3.91 (m, 1H), 1.83 (dd, 2H, J_a = 8.6 and J_b = 3.7 Hz), 1.53-1.46 (m, 3H), 1.40-1.29 (m, 2H), 1.18-0.98 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.2, 149.5, 149.2, 135.3, 134.4, 129.4, 128.2, 127.4, 126.6, 124.9, 122.4, 116.9, 49.7, 44.6, 42.5, 25.6, 24.2.

HR-MS (ESI+) m/z calculated for $[C_{21}H_{24}N_3O]^+$ = $[M+H]^+$: 334.1914; found: 334.1901.

2-(Cyclohexylamino)-3-(4-methoxybenzyl)quinazolin-4(3*H*)-one (5b): White solid (78%), Mp 130-132 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5b**) = 0.80 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3421, 2999, 2928, 2852, 1662, 1610, 1578, 1561, 1475, 1450, 1346, 1247, 1176, 1033, 982, 765, 693.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.18 (dd, 1H, *J*a = 7.8 and J_b = 1 Hz), 7.60-7.56 (m, 1H), 7.37 (d, 1H, *J* = 8.3 Hz), 7.21 (d, 2H, *J* = 8.8 Hz), 7.17 (m, 1H), 6.88 (d, 2H, *J* = 8.3 Hz), 5.26 (s, 2H), 4.44 (d, 1H, *J* = 6.8 Hz), 3.99-3.93 (m, 1H), 3.79 (s, 3H), 1.88-1.86 (dd, 2H, J_a = 8.1 and J_b = 3.7 Hz), 1.54-1.52 (m, 3H), 1.41-1.32 (m, 2H), 1.20-1.15 (m, 1H), 1.10-1.01 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.4, 159.7, 149.4, 149.3, 134.3, 127.9, 127.3, 127.2, 124.9, 122.3, 116.9, 114.7, 55.3, 49.7, 44.1, 32.6, 25.6, 24.3.

HR-MS (ESI+) m/z calculated for $[C_{22}H_{26}N_3O_2]^+$ = $[M+H]^+$: 364.2020; found: 364.2003.

2-(Cyclohexylamino)-3-(4-methylbenzyl)quinazolin-4(3*H*)-one (5c): White solid (78%), Mp 138–140 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5c**) = 0.70 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3422, 2926, 2853, 1659, 1562, 1475, 1346, 1224, 1147, 1069, 986, 765, 695. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.18 (dd, 1H, *J* = 7.8 Hz), 7.59-7.55 (m, 1H), 7.37 (d, 1H, *J* = 8.3 Hz), 7.18-7.16 (m, 5H), 5.28 (s, 2H), 4.4 (d, 1H, *J* = 6.8 Hz), 3.90-3.99 (m, 1H), 2.33 (s, 3H), 1.80-1.87 (m, 2H), 1.50 (d, 3H, *J* = 10.3 Hz), 1.30-1.41 (m, 2H), 1.12-1.19 (m, 1H), 0.99-1.08 (m, 1H).^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.2, 149.5, 149.3, 138.0, 134.3, 132.21, 130.0, 127.3, 126.6, 124.9, 122.4, 116.9, 49.8, 44.4, 32.5, 25.6, 24.2, 21.1.

HR-MS (ESI+) m/z calculated for $[C_{22}H_{26}N_3O]^+$ = $[M+H]^+$: 348.2070; found: 348.2056.

2-(Cyclohexylamino)-3-(3,4-dimethoxybenzyl)quinazolin-4(3*H*)-one (5d) : Orange solid (75%), Mp 100-102 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5d**) = 0.60 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3413, 2928, 2853, 1667, 1580, 1475, 1380, 1260, 1141, 1027, 766, 694.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.17 (dd, 1H, J*a* = 7.8 and J*b* = 1 Hz), 7.59-7.55 (m, 1H), 7.36 (d, 1H, J = 8.3 Hz), 7.16 (t, 1H, J = 7.6 Hz), 6.82-6.78 (m, 3H), 5.24 (s, 1H), 4.51 (d, 1H, J = 7.3 Hz), 3.95 (dt, 1H, J*a* = 6.6 and J*b* = 3.1 Hz), 3.86 (s, 3H), 3.81 (s, 3H), 1.88-1.85 (m, 2H), 1.53 (d, 3H, J = 8.3 Hz), 1.37-1.31 (m, 3H), 1.14-1.10 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.2, 149.9, 149.5, 149.4, 149.0, 134.3, 127.8, 127.3, 124.9, 122.4, 119.0, 116.9, 109.7, 56.0, 55.9, 49.8, 44.6, 32.6, 25.6, 24.8.

HR-MS (ESI+) m/z calculated for $[C_{23}H_{28}N_3O_3]^+$ = $[M+H]^+$: 394.2125; found: 394.2129.

2-(Cyclohexylamino)-3-(3-methoxybenzyl)quinazolin-4(3*H*)-one (5e): White solid (65%), Mp 108–110 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5e**) = 0.70 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm-1): υ_{max} = 3423, 2969, 2853, 1662, 1579, 1563, 1476, 1347, 1261, 1147, 1049, 985, 766, 694.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.19 (dd, 1H, J*a* = 7.8 and J*b* = 1.0 Hz), 7.62-7.57 (m, 1H), 7.38 (d, 1H, J = 8.3 Hz), 7.31-7.27 (m, 1H), 7.18 (t, 1H, J = 7.1 Hz), 6.86 (dd, 2H, J*a* = 7.1 and J*b* = 4.2 Hz), 6.82 (s, 1H), 5.30 (s, 2H), 4.41 (d, 1H, J = 6.8 Hz), 3.97 (dd, 1H, J*a* = 7.6 and J*b* = 4.2 Hz), 3.78 (s, 3H), 1.86 (dd, 2H, J*a* = 8.3 and J*b* = 3.9 Hz), 1.55-1.49 (m, 3H), 1.42-1.33 (m, 2H), 1.21-1.15 (m, 1H), 1.10-1.02 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.1, 160.5, 149.4, 149.2, 136.9, 134.3, 130.4, 127.3, 124.9, 122.4, 118.9, 116.8, 113.78, 112.2, 55.3, 49.7, 44.6, 32.5, 25.5, 24.2.

HR-MS (ESI+) m/z calculated for $[C_{22}H_{26}N_3O_2]$+ = [M+H]+: 364.2020; found: 364.2003.

2-(Cyclohexylamino)-3-(4-fluorobenzyl)quinazolin-4(3*H*)-one (5f): White solid (68%), Mp 118-120 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5f**) = 0.60 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3435, 2930, 2854, 1659, 1557, 750, 663.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.17 (dd, 1H, J_a= 8.1 and J_b = 1.2 Hz), 7.61-7.57 (m, 1H), 7.38 (d, 1H, *J* = 7.38 Hz), 7.20-7.16 (m, 1H), 7.06 (t, 2H, *J* = 8.6 Hz), 5.29 (s, 2H), 4.27 (d, 1H, *J* = 7.3 Hz), 4.00-3.94 (m, 1H), 1.90-1.86 (m, 2H), 1.52 (d, 3H, *J* = 10.3 Hz), 1.42-1.33 (m, 2H), 1.18-1.14 (m, 1H), 1.08-1.00 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.7, 163.1, 161.3, 149.4, 148.9, 134.5, 131.1, 131.0, 128.4, 128.3, 127.3, 125.0, 122.5, 116.8, 116.4, 116.2, 49.8, 43.9, 32.6, 25.6, 24.3.

HR-MS (ESI+) m/z calculated for $[C_{21}H_{23}FN_3O]^+$ = $[M+H]^+$: 352.1820; found: 352.1804.

3-(2-Chlorobenzyl)-2-(cyclohexylamino)quinazolin-4(3*H*)-one (5g): White solid (72%), Mp 108-110 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5g**) = 0.70 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3386, 2927, 2854, 1656, 1558, 1472, 1344, 1215, 1065, 830, 755, 663.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.08-8.06 (m, 1H), 7.51-7.47 (m, 1H), 7.30 (dd, 2H, J_a= 16.9 and J_b = 8.1 Hz), 7.16-7.11 (m, 1H), 7.09-7.04 (m, 3H), 5.34 (s, 2H), 4.28 (d, 1H, *J* = 7.3 Hz), 3.89 (dtd, 1H, J_a = 10.1, J_b = 6.7 and J_c = 3.9 Hz), 1.82-1.78 (m, 2H), 1.47 (d, 3H, *J* = 8.8 Hz), 1.31-1.22 (m, 2H), 1.08-1.00

(m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.2, 149.5, 148.5, 134.5, 132.6, 132.4, 129.6, 129.4, 128.2, 127.9, 127.3, 125.0, 122.4, 116.7, 50.1, 41.1, 32.7, 25.6, 24.5.

HR-MS (ESI+) m/z calculated for $[C_{21}H_{23}ClN_3O]^+ = [M+H]^+$: 368.1524; found: 368.1509.

3-(2-(1H-indol-2-yl)ethyl)-2-(cyclohexylamino)quinazolin-4(3*H*)-one (5h): Yellow solid (62%), Mp 108-110 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5h**) = 0.50 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3381, 2928, 2853, 1653, 1562, 1349, 1248, 1147, 1011, 891, 741, 663.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.40 (br s, 1H), 8.02 (d, 1H, *J* = 8.3 Hz), 7.54 (d, 1H, *J* = 7.3 Hz), 7.43-7.39 (m, 1H), 7.26 (d, 1H, *J* = 7.8 Hz), 7.18 (d, 1H, *J* = 8.3 Hz), 7.13-7.09 (m, 1H), 7.07-6.99 (m, 2H), 6.77 (s, 1H), 4.17 (t, 2H, *J* = 6.1 Hz), 3.61 (d, 1H, *J* = 7.3 Hz), 3.44-3.41 (m, 1H), 3.15 (t, 2H, *J* = 6.1 Hz), 1.44-1.33 (m, 6H), 1.16-0.99 (m, 3H), 0.80-0.74 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.3, 149.6, 149.3, 136.7, 134.2, 126.8, 126.6, 124.8, 123.2, 122.8, 120.2, 118.0, 117.1, 111.9, 111.8, 49.7, 43.5, 31.9, 25.5, 24.8, 24.1.

HR-MS (ESI+) m/z calculated for $[C_{24}H_{27}N_4O]^+ = [M+H]^+$: 387.2179; found: 387.2162.

3-Benzyl-2-(tert-butylamino)quinazolin-4(3*H*)-one (5i):[1] White solid (40%), Mp 110–112 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5i**) = 0.60 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3435, 3032, 2961, 2925, 1672, 1584, 1567, 1477, 1362, 1208, 1148, 976, 766, 695.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.18 (dd, 1H, J_a = 8.1 and J_b = 1.2 Hz), 7.58-7.56 (m, 1H), 7.38-7.31 (m, 4H), 7.26 (d, 2H, *J* = 7.3 Hz), 7.19-7.15 (m, 1H), 5.3 (s, 2H), 4.32 (s, 1H), 1.32 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.3, 149.1, 148.4, 135.5, 134.2, 129.3, 128.2, 127.3, 126.7, 125.3, 122.4, 116.9, 52.6, 44.9, 28.8.

HR-MS (ESI+) m/z calculated for $[C_{19}H_{22}N_3O]^+ = [M+H]^+$: 308.1757; found: 308.1744.

2-(Tert-butylamino)-3-cyclohexylquinazolin-4(3*H*)-one (5j): White solid (32%), Mp 82–84 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5j**) = 0.60 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3496, 2930, 2856, 1669, 1568, 1519, 1478, 1361, 1205, 1137, 953, 764, 697.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.07 (dd, 1H, J_a = 8.2 and J_b = 1.2Hz), 7.54-7.50 (m, 1H), 7.34-7.26 (m, 1H), 7.12-7.08 (m, 1H), 5.14 (br s, 1H), 4.6 (br s, 1H), 2.16-2.04 (m, 2H), 1.94-1.70 (m, 6H), 1.60-1.42 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.5, 148.7, 148.3, 133.9, 127.1, 124.8, 122.1, 52.6, 30.4, 29.3, 26.6, 25.7.

HR-MS (ESI+) m/z calculated for $[C_{18}H_{26}N_3O]^+ = [M+H]^+$: 300.2070; found: 300.2057.

3-(2-Bromophenyl)-2-(cyclohexylamino)quinazolin-4(3*H*)-one (5k): White solid (48%), Mp 162-164 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5k**) = 0.50 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3288, 2920, 2851, 1735, 1631, 1602, 1567, 1474, 1329, 1231, 1119, 1020, 957, 758, 648.

^1H NMR ($CDCl_3$, 400 MHz): δ_H = 8.13 (dd, 1H, J_a = 7.8 and J_b =1 Hz), 7.82 (dd, 1H, J_a = 8.1 and J_b = 1.2 Hz), 7.63-7.59 (m, 1H), 7.56-7.52 (m, 1H), 7.44-7.37 (m, 3H), 7.18-7.14 (m, 1H), 4.07-4.02 (m, 1H), 3.71 (d, 1H, J = 7.3Hz), 2.04-1.92 (m, 2H), 1.70-1.57 (m, 3H), 1.45-1.31 (m, 3H), 1.18-1.02 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 162.0, 149.8, 147.9, 134.7, 134.5, 134.3, 131.4, 130.9, 129.5, 127.3, 125.0, 123.6, 122.4, 117.4, 49.8, 32.9, 32.8, 29.7, 28.8, 26.4, 25.6, 24.6, 24.5.

HR-MS (ESI+) m/z calculated for $[C_{20}H_{21}BrN_3O]^+ = [M+H]^+$: 398.0863; found: 398.0879.

2-(Cyclohexylamino)-3-phenylquinazolin-4(3*H*)-one (5l): White solid (35%), Mp 158–160 °C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5l**) = 0.80 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3291, 2921, 2853, 1740, 1601, 1475, 1049, 759, 686.

^1H NMR ($CDCl_3$, 400 MHz): δ_H = 8.01 (dd, 1H, J_a = 8.1 and J_b =1.2 Hz), 7.69-7.58 (m, 2H), 7.42-7.23 (m, 2H), 7.14 (m, 1H), 4.90 (br s, 1H), 3.81 (m, 1H), 2.06 (dd, 1H, J_a = 12.2 and J_b = 2.9 Hz), 1.77-1.72 (m, 3H), 1.65-1.61 (m, 1H), 1.48-1.37 (m, 2H), 1.30-1.18 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 160.1, 150.6, 136.6, 128.7, 124.2, 123.4, 119.9, 113.2, 50.2, 32.9, 25.4, 24.6.

HR-MS (ESI+) m/z calculated for $[C_{20}H_{22}N_3O]^+ = [M+H]^+$: 320.1757; found: 320.1739.

3-Benzyl-6-chloro-2-(cyclohexylamino)quinazolin-4(3*H*)-one (5m):[1] White solid (75%), Mp 124-126 °C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5m**) = 0.70 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3324, 3059, 2921, 1627, 1584, 1384, 1230, 1198, 1065, 951, 756, 640.

^1H NMR ($CDCl_3$, 400 MHz): δ_H = 8.13 (d, 1H, J = 2.4 HZ), 7.5 (dd, 1H, J*a* = 8.8 and J*b* = 2.4 Hz), 7.38-7.24 (m, 6H), 5.3 (s, 1H), 4.39 (d, 1H, J = 7.3 Hz), 3.93-3.90 (m, 1H), 1.81 (dd, 2H, J*a* = 8.6 and J*b* = 3.7 Hz), 1.53-1.46 (m, 3H), 1.37-1.28 (m, 4H), 1.05-0.97 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 162.2, 149.3, 148.1, 135.0, 134.6, 129.5, 128.4, 127.6, 126.7, 126.6, 126.5, 117.7, 49.8, 44.7, 32.5, 29.7, 25.5, 24.2.

HR-MS (ESI+) m/z calculated for $[C_{21}H_{23}ClN_3O]^+ = [M+H]^+$: 368.1524; found: 365.1518.

6-chloro-2-(Cyclohexylamino)-3-(4-methoxybenzyl)quinazolin-4(3*H*)-one (5n): White solid (72%), Mp 98-100 °C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5n**) = 0.70 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3321, 3057, 2921, 1629, 1574, 1517, 1482, 1381, 1230, 1247, 1188, 1025, 951, 761, 643.

^1H NMR ($CDCl_3$, 400 MHz): δ_H = 8.12 (d, 1H, J = 2.4 Hz), 7.48 (dd, 1H, J*a* = 8.8 and J*b* = 2.4 Hz), 7.30-7.26 (m, 1H), 7.19 (d, 2H, J = 8.3 Hz), 6.88 (d, 2H, J = 8.8 Hz), 5.22 (s, 2H), 4.47 (d, 1H, J = 6.8 Hz), 3.93-3.89 (m, 1H), 3.78 (s, 3H), 1.85 (dd, 2H, J*a* = 8.3 and J*b* = 3.9 Hz), 1.53-1.51 (m, 3H), 1.39-1.29 (m,

3H), 1.08-0.99 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 162.2, 159.6, 149.4, 148.0, 134.6, 128.0, 127.8, 126.6, 126.5, 117.8, 114.8, 55.4, 49.9, 44.3, 32.6, 29.8, 25.5, 24.3.

HR-MS (ESI+) m/z calculated for $[C_{22}H_{25}ClN_3O_2]^+$ = $[M+H]^+$: 398.1630; found: 398.1628.

6-Chloro-2-(Cyclohexylamino)-3-(4-methylbenzyl)quinazolin-4(3*H*)-one (5o): White solid (70%), Mp 136-138 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5o**) = 0.60 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3421, 2928, 2854, 16160, 1558, 1472, 1365, 1214, 1067, 896, 754, 663.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.13 (d, 1H, *J* = 2.4 Hz), 7.50-7.48 (m, 1H), 7.30-7.26 (m, 1H), 7.17-7.12 (m, 5H), 5.25 (s, 2H), 4.44 (d, 1H, *J* = 6.8 Hz), 3.91 (dt, 1H, J_a = 6.6 and J_b = 3.1 Hz), 2.33 (s, 3H), 1.33 (dd, 2H, J_a = 8.6 and J_b = 3.7 Hz), 1.5 (d, 4H, *J* = 10.3 Hz), 1.39-1.29 (m, 2H), 1.18-1.13 (m, 1H), 1.07-1.00 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 162.2, 149.4, 148.1, 138.2, 134.6, 131.8, 130.1, 127.5, 126.6, 126.5, 126.4, 117.7, 117.8, 49.9, 44.6, 32.5, 25.5, 24.2, 21.1.

HR-MS (ESI+) m/z calculated for $[C_{22}H_{25}ClN_3O]^+$ = $[M+H]^+$: 382.1681; found: 398.1680.

6-Chloro-2-(Cyclohexylamino)-3-(3,4-dimethoxybenzyl)quinazolin-4(3*H*)-one (5p) : White solid (72%), Mp 124-126 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5p**) = 0.60 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3416, 3018, 2932, 2855, 1665, 1561, 1473, 1260, 1214, 1140, 1025, 746, 664.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.1 (d, 1H, J = 2.4 Hz), 7.47 (dd, 1H, J*a* = 8.8 and J*b* = 2.4 Hz), 7.29-7.26 (m, 1H), 6.83-6.76 (m, 3H), 5.21 (s, 2H), 4.56 (d, 1H, J =6.8 Hz), 3.94-3.87 (m, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 1.85 (d, 2H, J = 8.8 Hz), 1.53 (d, 3H, J = 8.3 Hz), 1.39-1.30 (m, 2H), 1.23-1.00 (m, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 162.3, 150.0, 149.5, 149.1, 148.1, 134.6, 127.5, 126.6, 126.5, 119.0, 117.7, 111.5, 109.7, 56.0, 55.9, 49.9, 44.7, 32.6, 25.5, 24.5.

HR-MS (ESI+) m/z calculated for $[C_{23}H_{27}ClN_3O_3]^+$ = $[M+H]^+$: 428.1735; found: 428.1735.

6-Chloro-2-(Cyclohexylamino)-3-(4-fluorobenzyl)quinazolin-4(3*H*)-one (5q): White solid (68%), Mp 124-126 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5q**) = 0.70 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3435, 2930, 2854, 1659, 1557, 1310, 1129, 1066, 894, 750, 663.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.1 (d, 1H, *J* = 2.4 Hz), 7.50-7.48 (m, 1H), 7.30 (d, 1H, *J* = 8.8 Hz), 7.26-7.21 (m, 2H), 7.05 (t, 2H, *J* = 8.6 Hz), 5.25 (s, 2H), 4.32 (d, 1H, *J* = 6.8 Hz), 3.96-3.89 (m, 1H), 1.86 (dd, 3H, J_a = 12.0 and J_b = 3.2 Hz), 1.52 (dd, 3H, J_a = 9.0 and J_b = 4.4 Hz), 1.41-1.30 (m, 2H), 1.19-1.13 (m, 1H), 1.07-0.98 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 163.8, 162.1, 149.0, 148.0, 134.7, 130.8, 130.7, 128.4, 128.3, 127.6, 126.7, 126.4, 117.6, 116.5, 116.3, 50.0, 44.0, 32.6, 25.5, 24.3.

HR-MS (ESI+) m/z calculated for $[C_{21}H_{22}ClFN_3O]^+$ = $[M+H]^+$: 386.1430; found: 386.1431.

6-chloro-3-(2-Chlorobenzyl)-2-(cyclohexylamino)quinazolin-4(3*H*)-one (5r): White solid (72%), Mp 120-122 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5r**) = 0.50 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3431, 2923, 2852, 1672, 1559, 1472, 1329, 1135, 1033, 824, 745, 622.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.12 (d, 1H, J = 2 Hz), 7.51 (dd, 1H, J*a* = 8.8 and J*b* = 2.4 Hz), 7.43 (d, 1H, J = 7.8 Hz), 7.31-7.26 (m, 2H), 7.24-7.19 (m, 2H), 7.13-7.11 (m, 1H), 5.42 (s, 2H), 4.42 (d, 1H, J = 6.8 Hz), 3.95 (dtd, 1H, J*a* = 10.1, J*b* = 6.1 and J*c* = 3.9 Hz), 1.89-1.86 (m, 2H), 1.57 (d, 3H, J = 8.3 Hz), 1.40-1.30 (m, 2H), 1.19-1.04 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 162.3, 148.6, 134.8, 132.4, 132.3, 129.7, 129.5, 128.2, 128.0, 127.6, 126.7, 126.5, 117.5, 50.2, 41.2, 32.6, 25.5, 24.5.

HR-MS (ESI+) m/z calculated for $[C_{21}H_{22}Cl_2N_3O]^+$ = $[M+H]^+$: 402.1134; found: 402.1134.

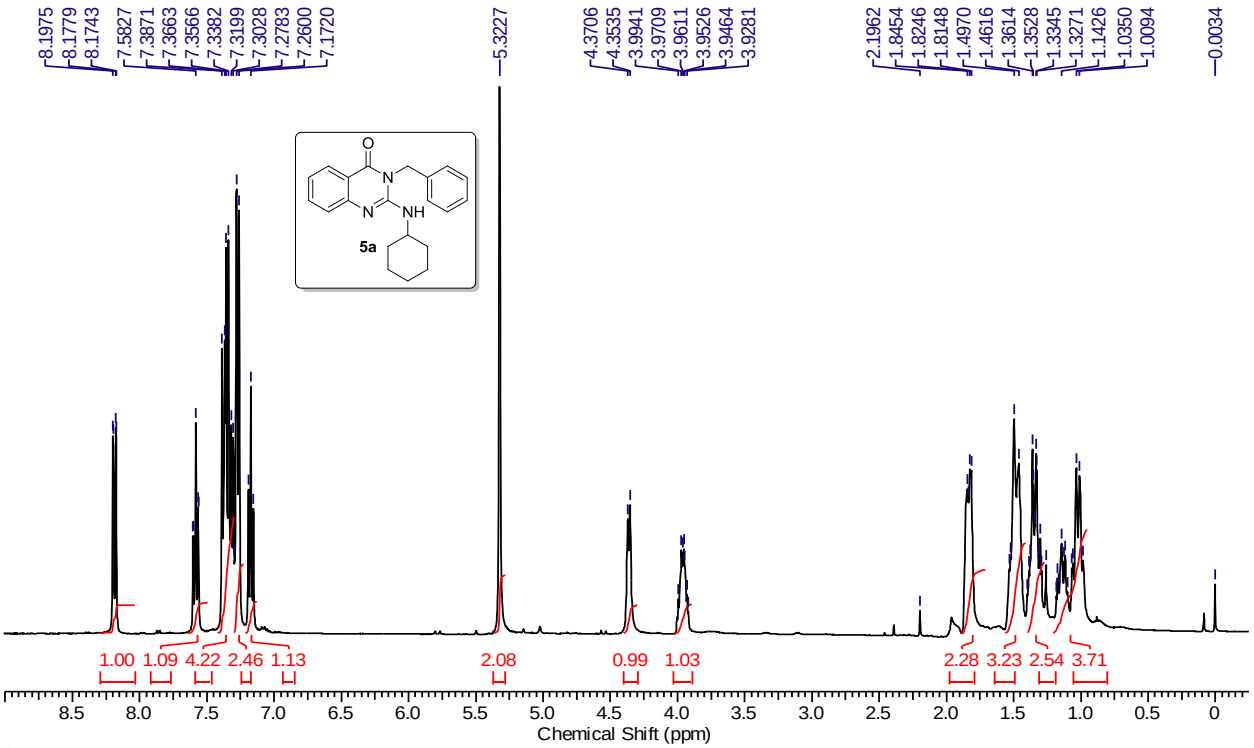
6-Chloro-3-(2-(1H-indol-2-yl)ethyl)-2-(cyclohexylamino)quinazolin-4(3*H*)-one (5s): Pale yellow (62%), Mp 142-144 ^{o}C. [TLC control R*f*(**1**) = 0.30, *Rf*(**5m**) = 0.50 (petroleum ether/ethyl acetate 8:2, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3443, 3373, 2928, 2854, 1669, 1558, 1473, 1344, 1217, 1131, 1067, 896, 749, 662.

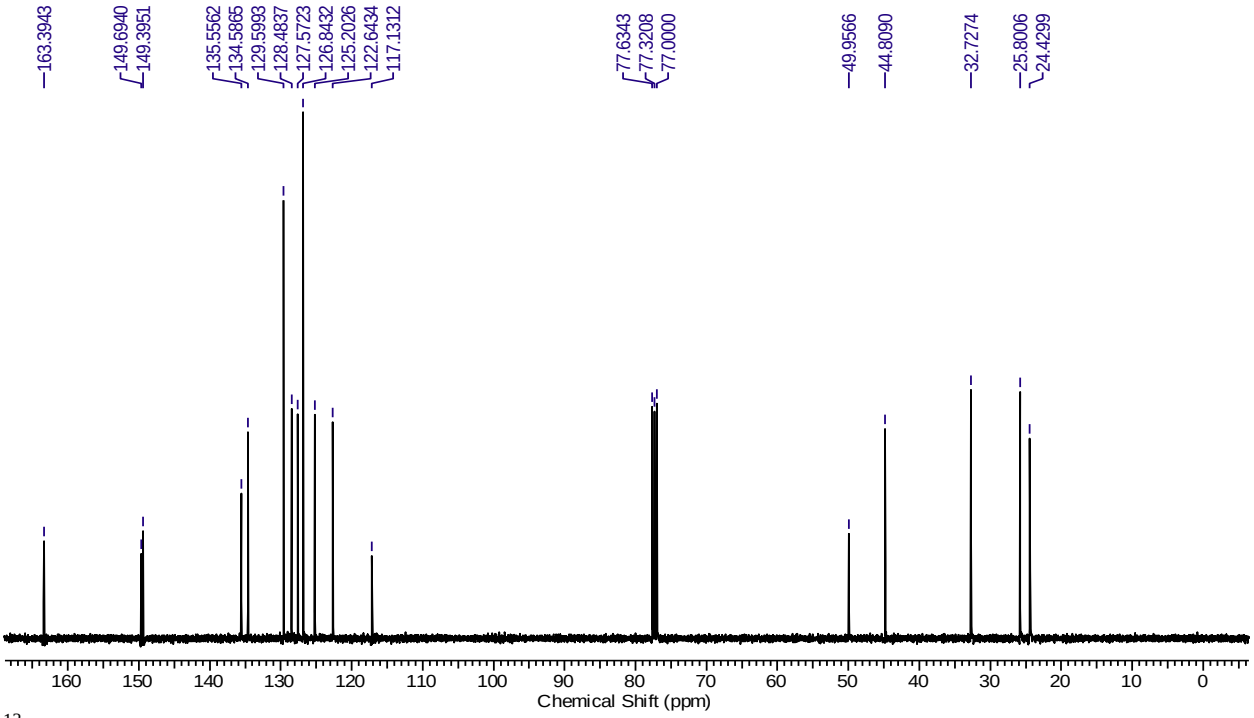
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.28 (br s, 1H), 8.08 (d, 1H, J = 2.4 Hz), 7.65 (d, 1H, J = 7.8 Hz), 7.45-7.38 (m, 2H), 7.26-7.15 (m, 3H), 6.91 (d, 1H, J = 2Hz), 4.26 (t, 2H, J = 6.1 Hz), 3.74 (d, 1H, J = 7.3 Hz), 3.5 (dtt, 1H, J*a* = 10.9, J*b* = 7.1 and J*c* = 3.6 Hz), 3.26 (t, 2H, J = 6.1 Hz), 1.52-1.41 (m, 5H), 1.26-1.09 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 162.2, 149.3, 147.9, 136.7, 134.4, 127.3, 126.5, 126.0, 123.1, 122.9, 120.4, 118.0, 117.9, 112.0, 111.9,49.8, 43.6, 31.9, 25.5, 24.8, 24.1.

HR-MS (ESI+) m/z calculated for $[C_{24}H_{26}ClN_4O]^+$ = $[M+H]^+$: 421.1790; found: 421.1788.

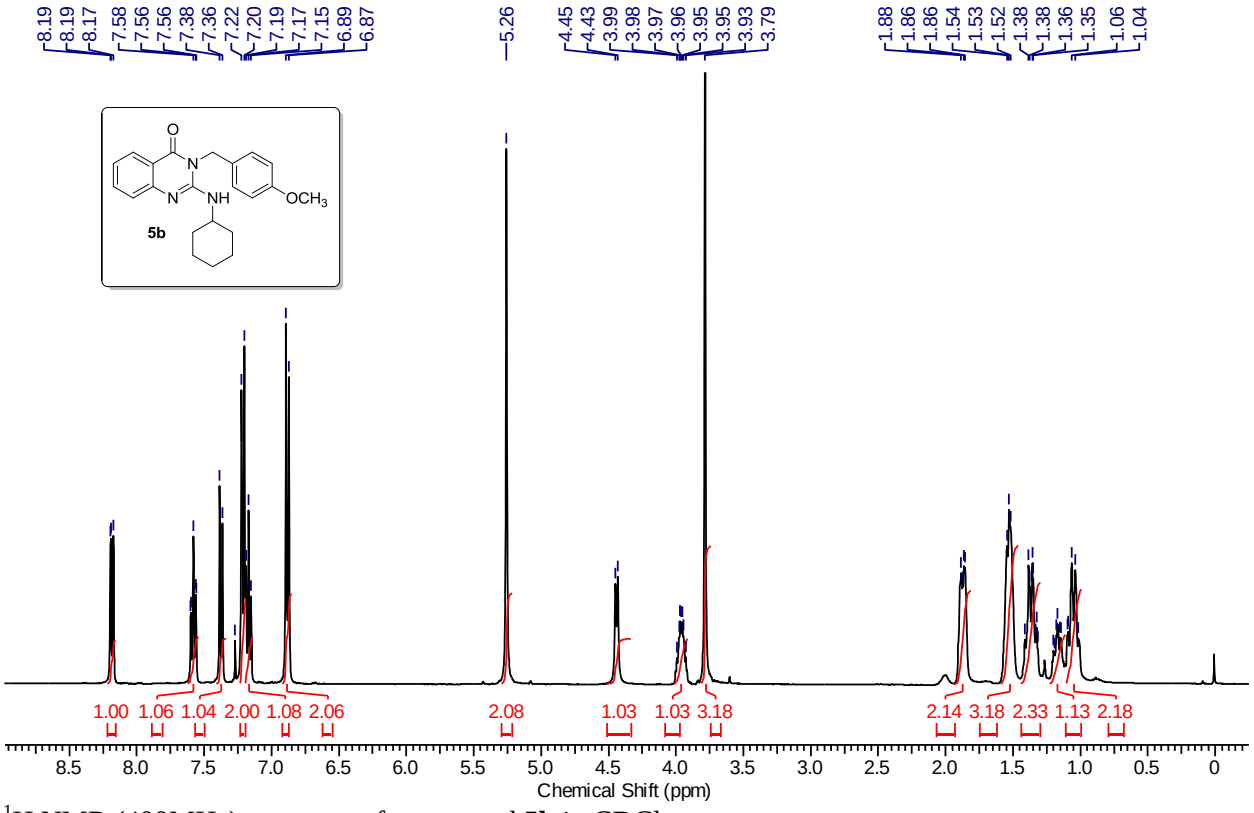
Copies of ^{1}H, ^{13}C NMR spectra of all compounds (5a-5s)



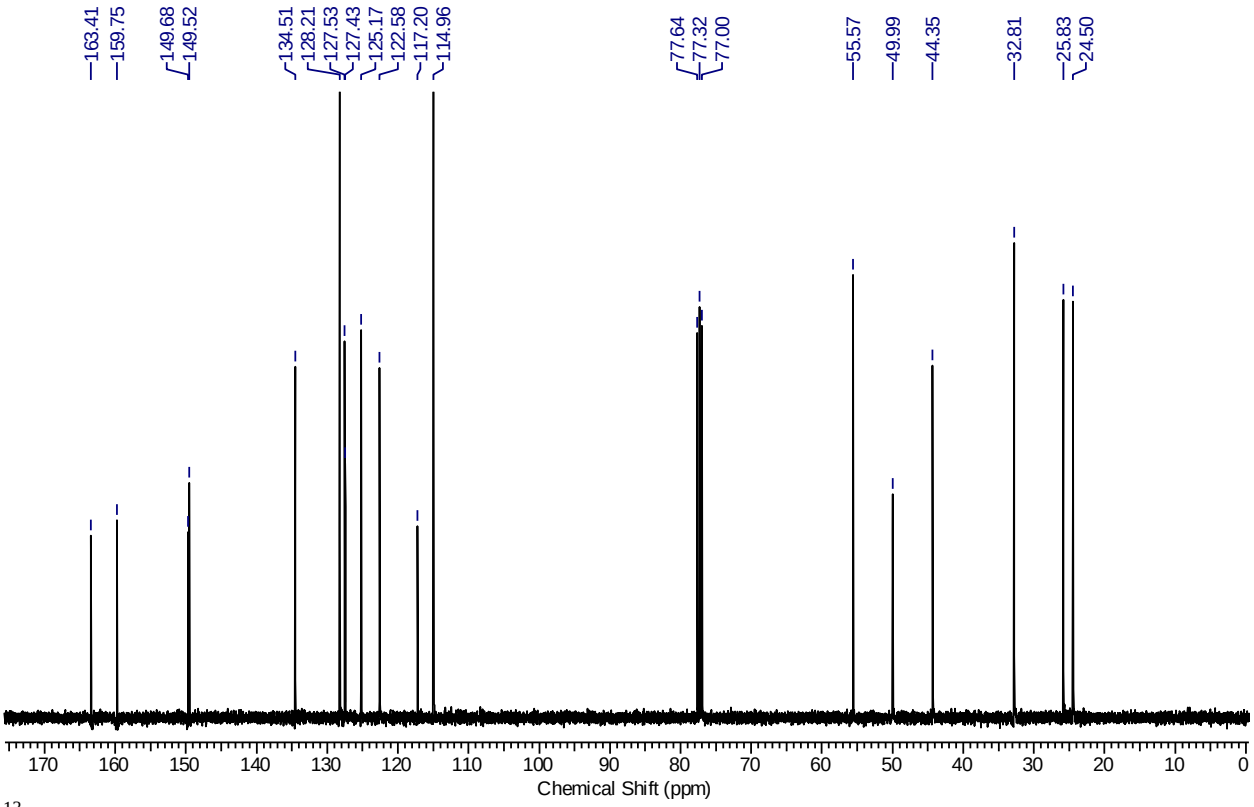
^{1}H NMR (400MHz) spectrum of compound **5a** in $CDCl_3$



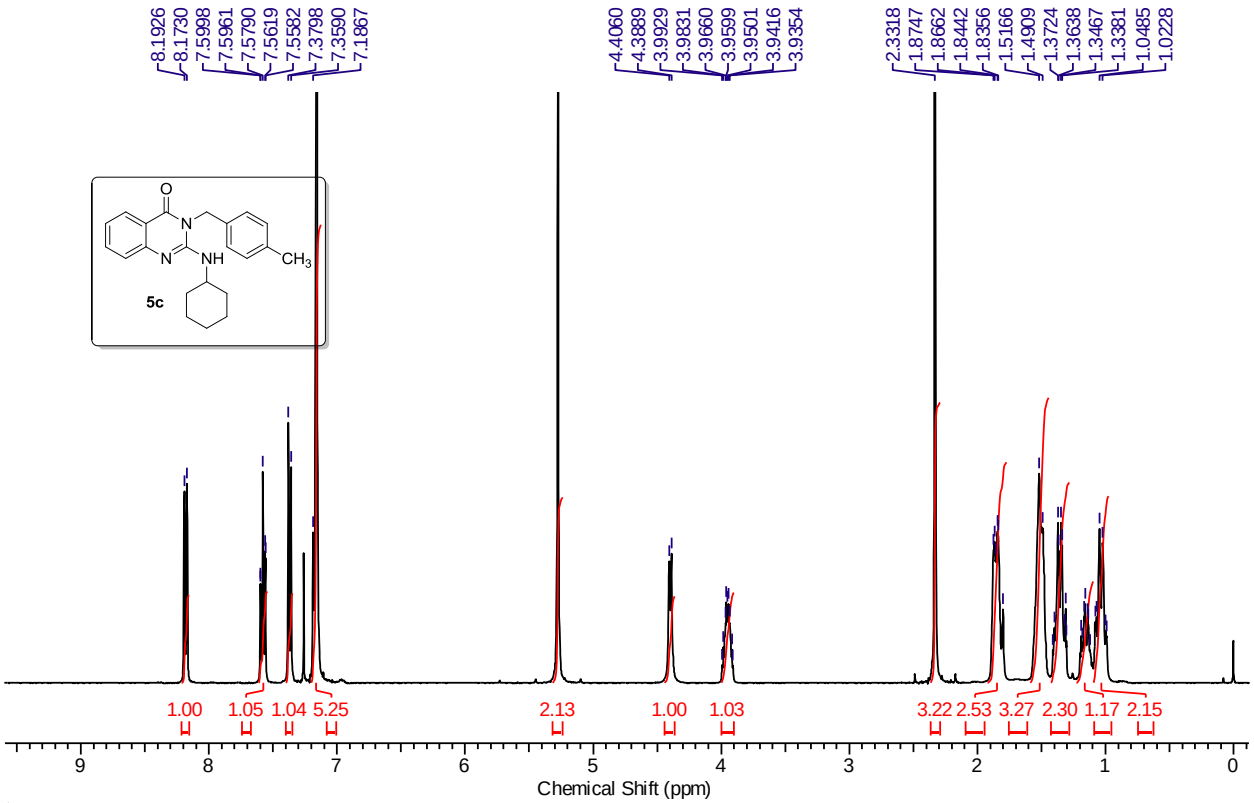
^{13}C NMR (100MHz) spectrum of compound **5a** in $CDCl_3$.



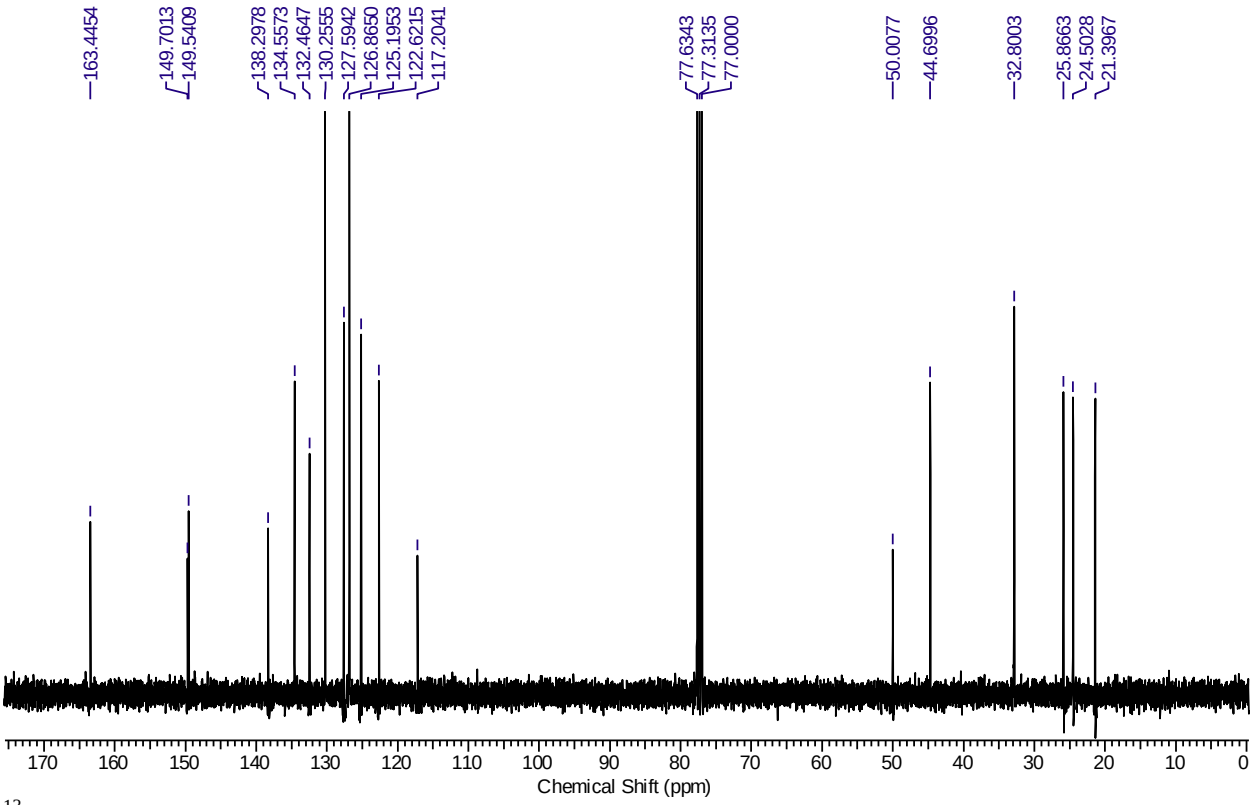
^{1}H NMR (400MHz) spectrum of compound **5b** in $CDCl_3$



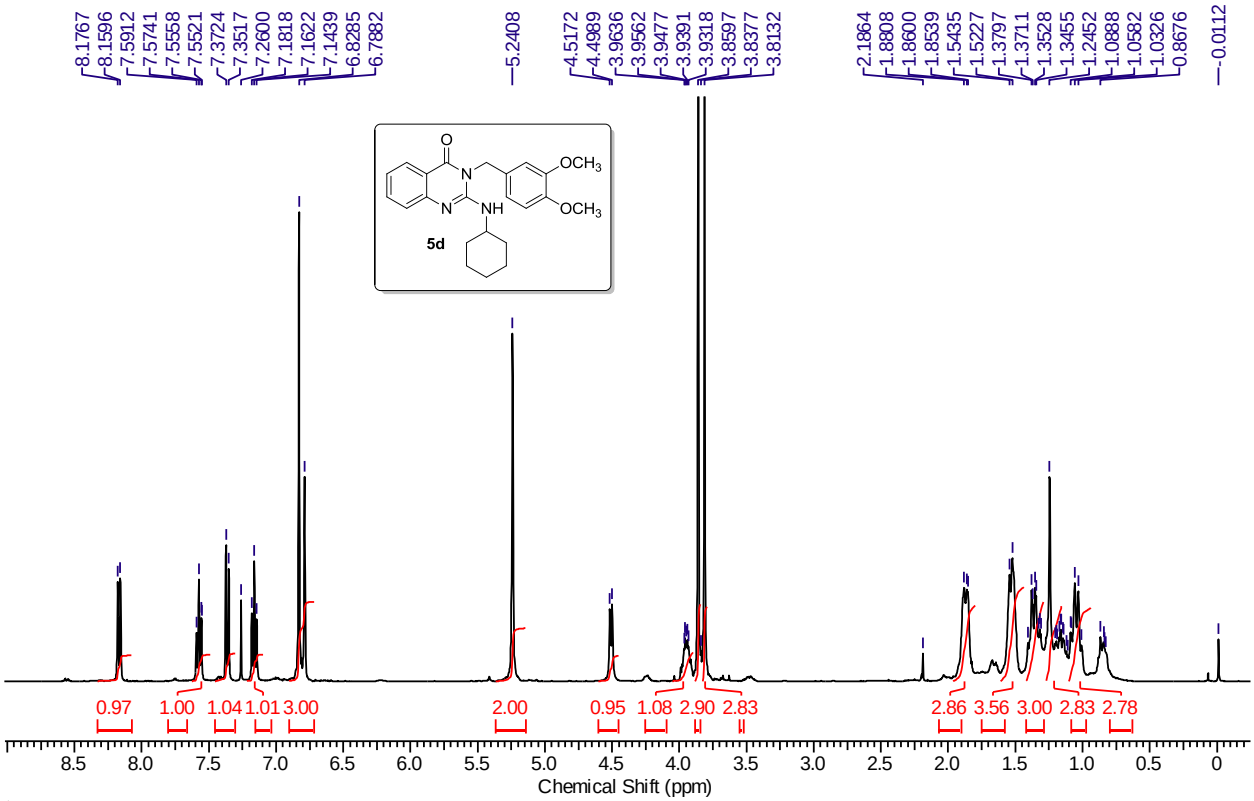
^{13}C NMR (100MHz) spectrum of compound **5b** in $CDCl_3$.



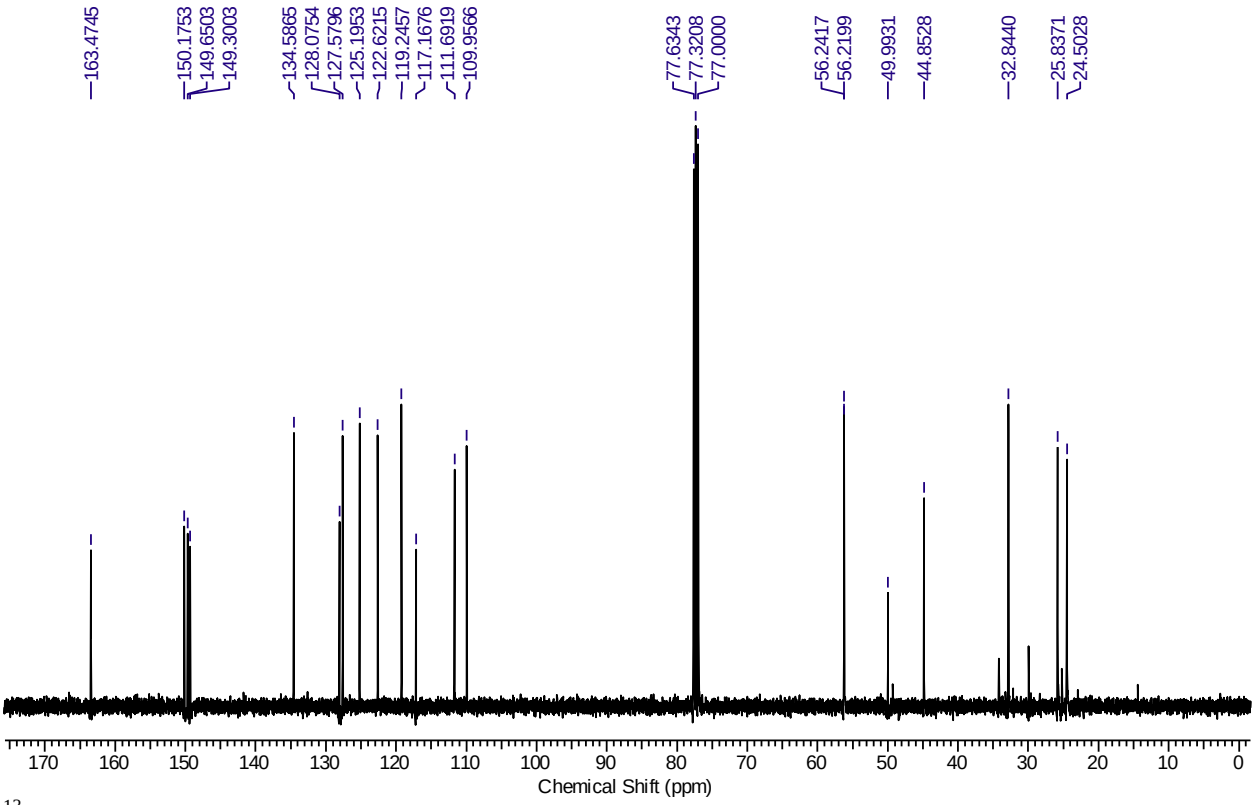
^{1}H NMR (400MHz) spectrum of compound **5c** in $CDCl_3$.



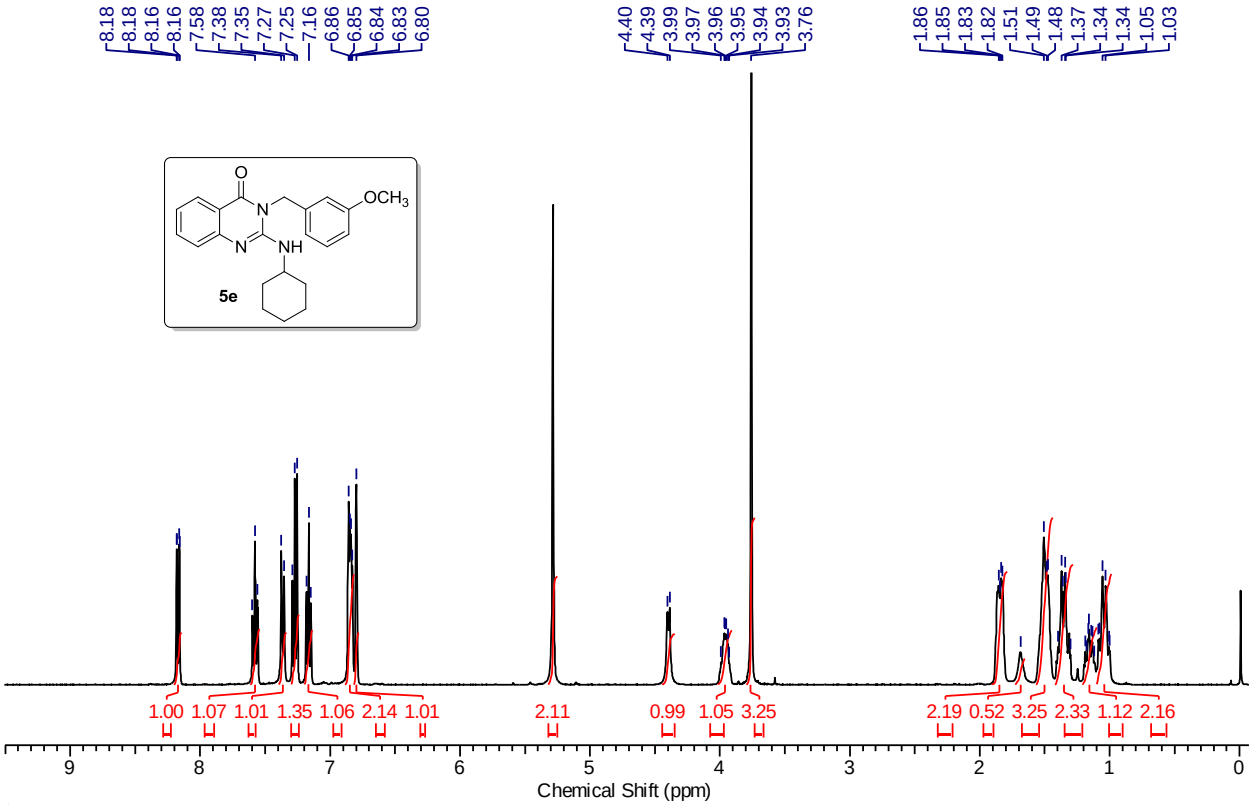
^{13}C NMR (100MHz) spectrum of compound **5c** in $CDCl_3$.



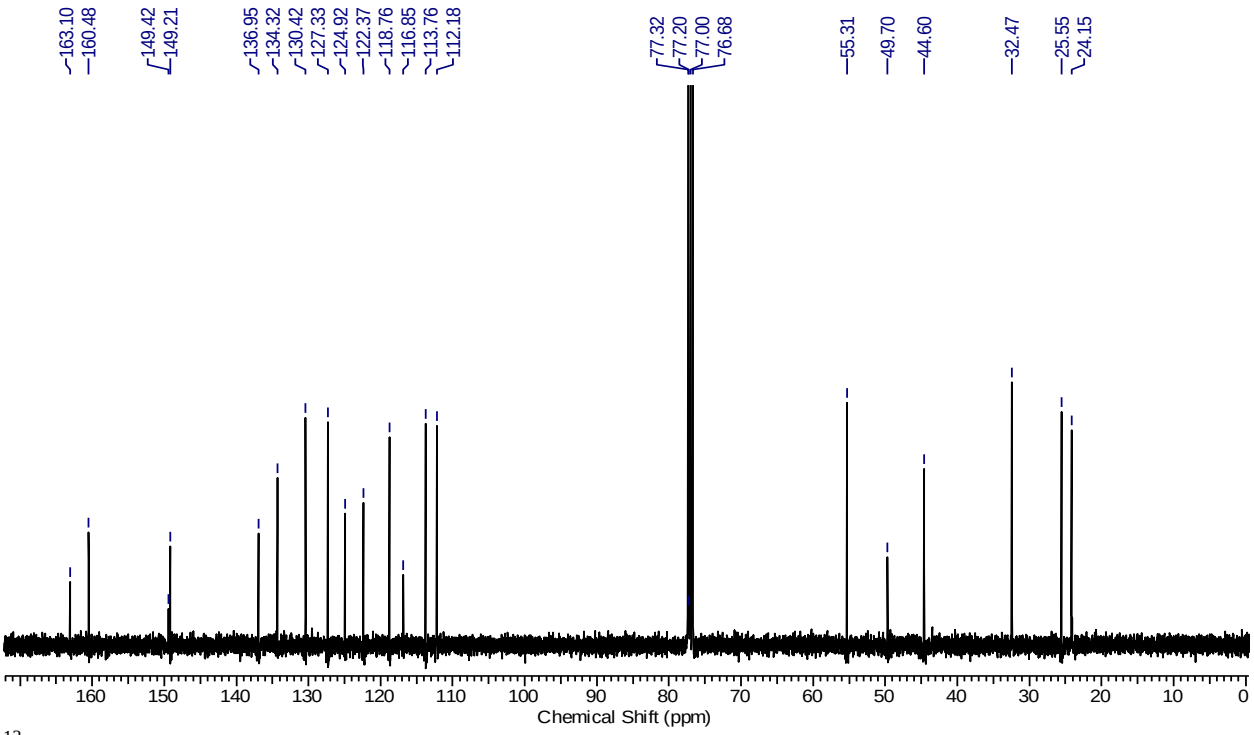
^{1}H NMR (400MHz) spectrum of compound **5d** in $CDCl_3$.



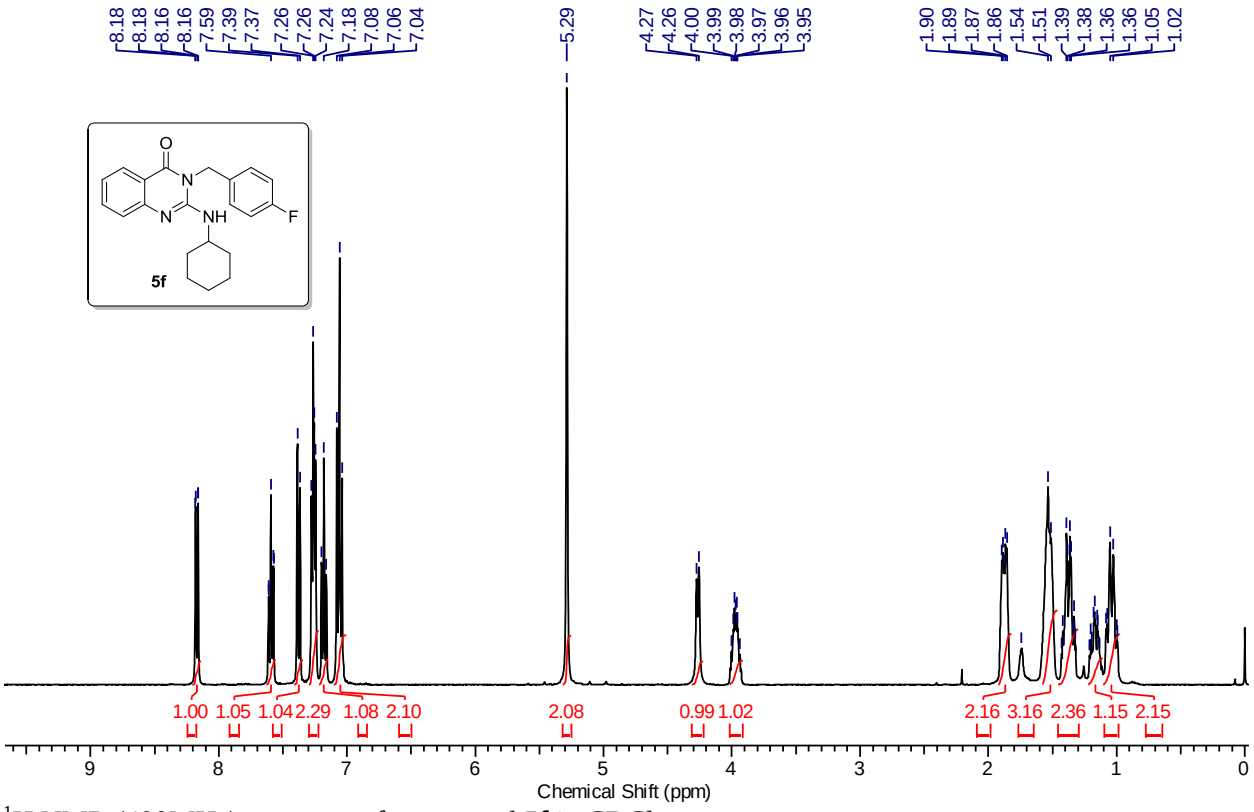
^{13}C NMR (100MHz) spectrum of compound **5d** in $CDCl_3$.



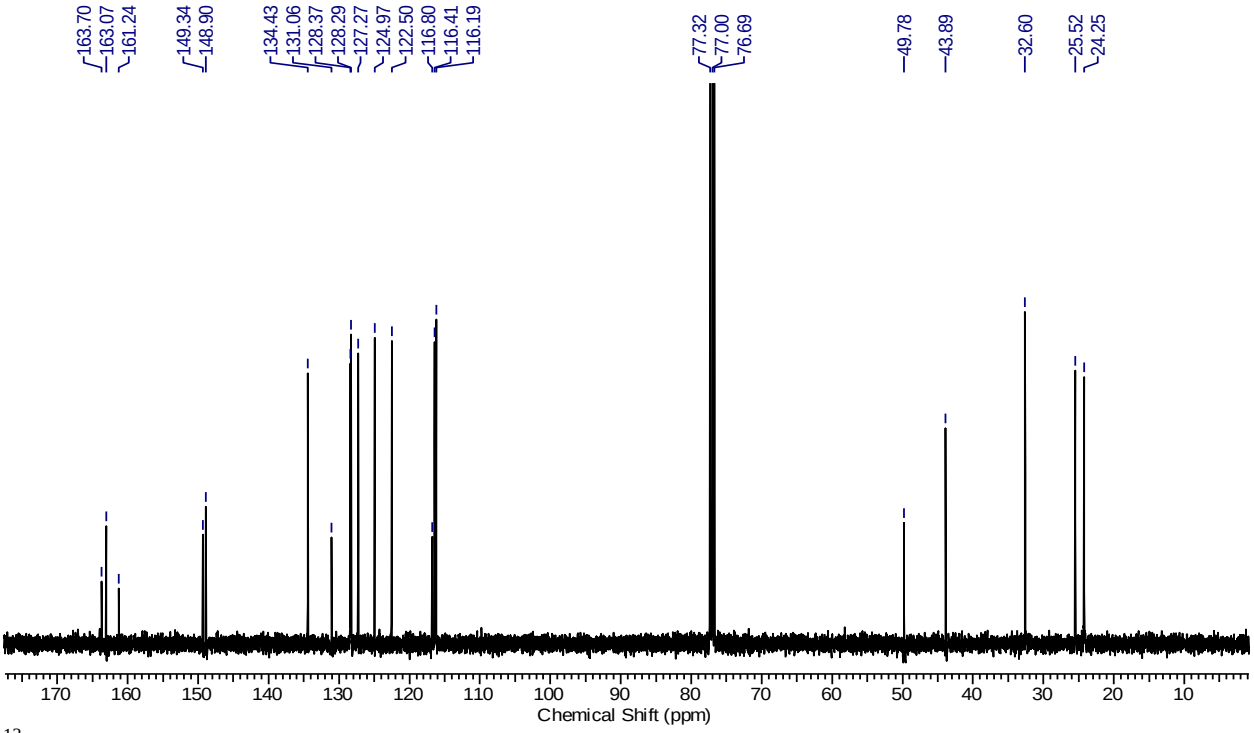
^{1}H NMR (400MHz) spectrum of compound **5e** in $CDCl_3$.



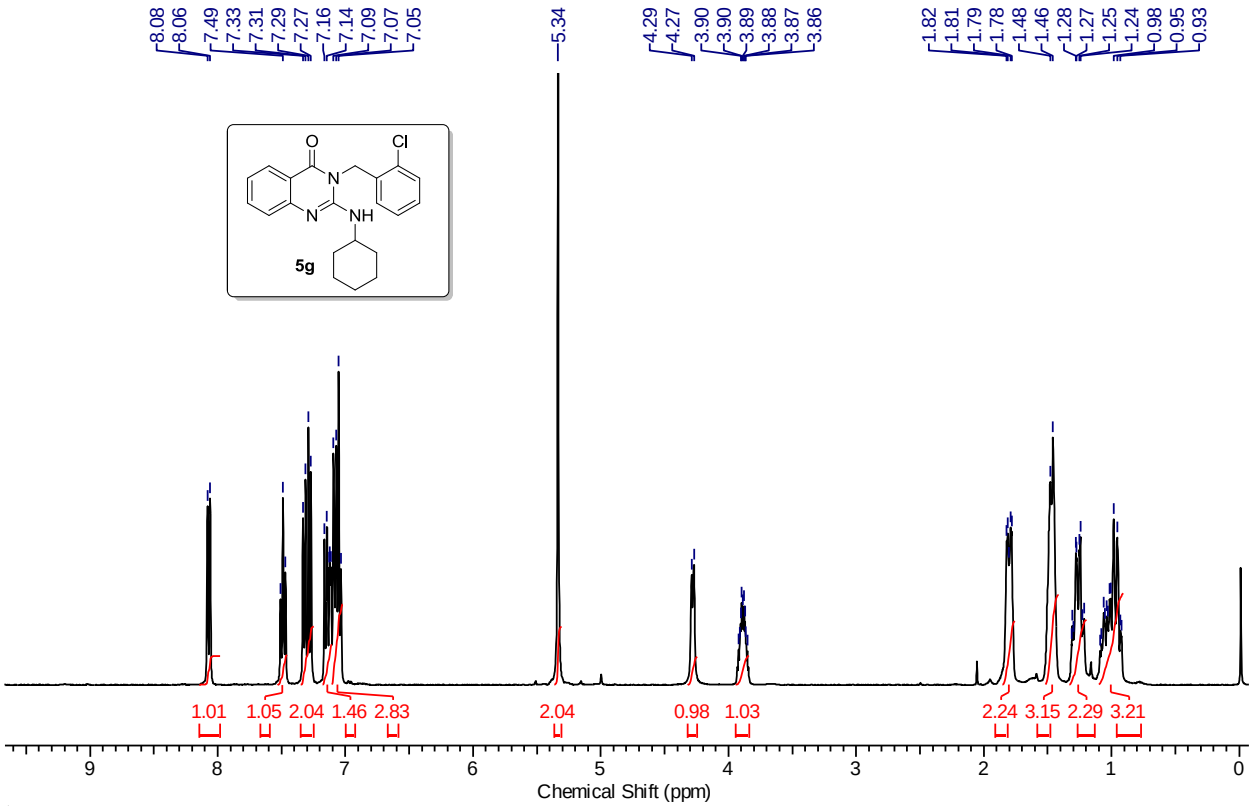
^{13}C NMR (100MHz) spectrum of compound **5e** in $CDCl_3$.



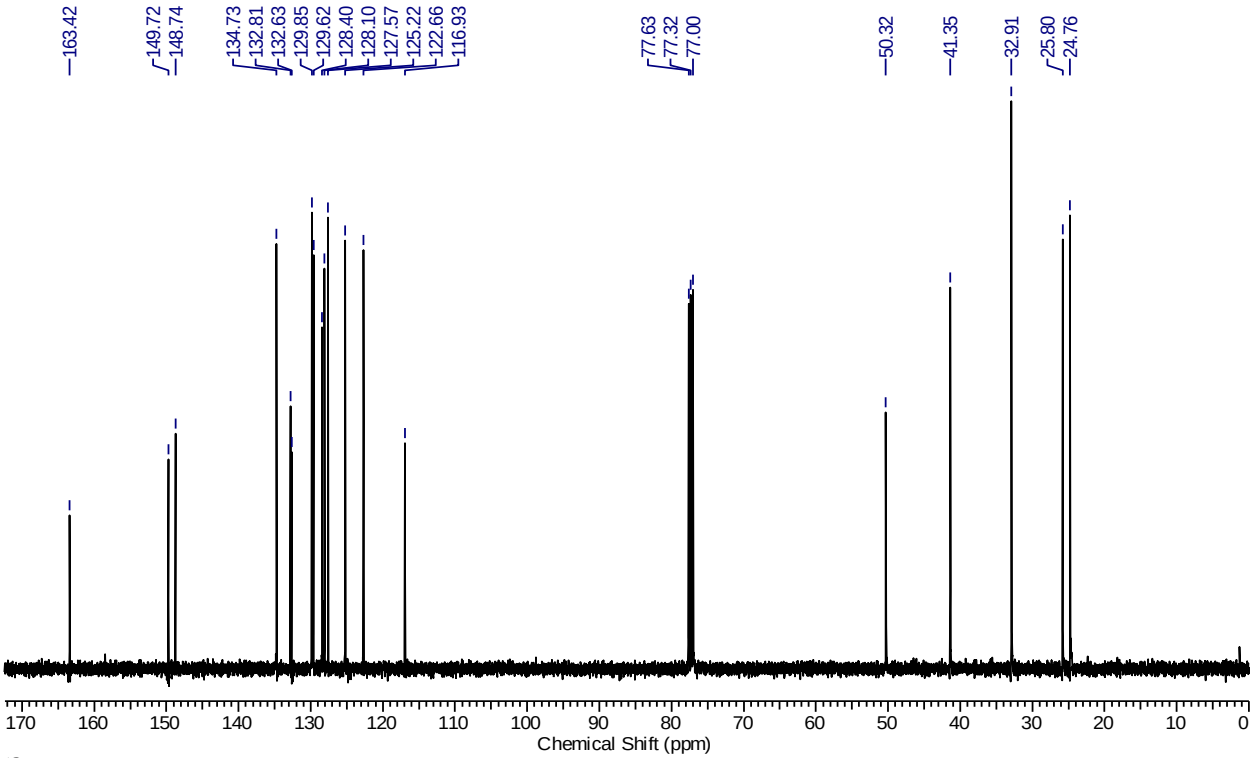
^{1}H NMR (400MHz) spectrum of compound **5f** in $CDCl_3$.



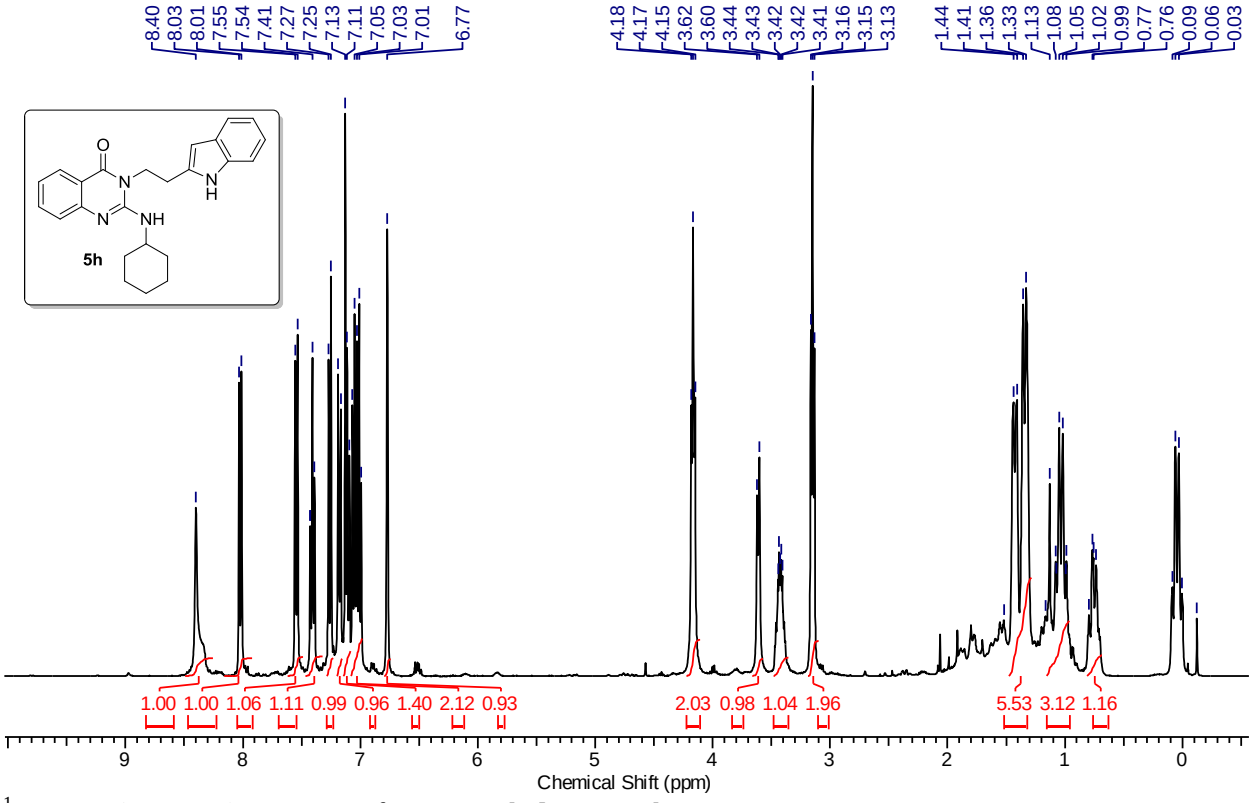
^{13}C NMR (100MHz) spectrum of compound **5f** in $CDCl_3$.



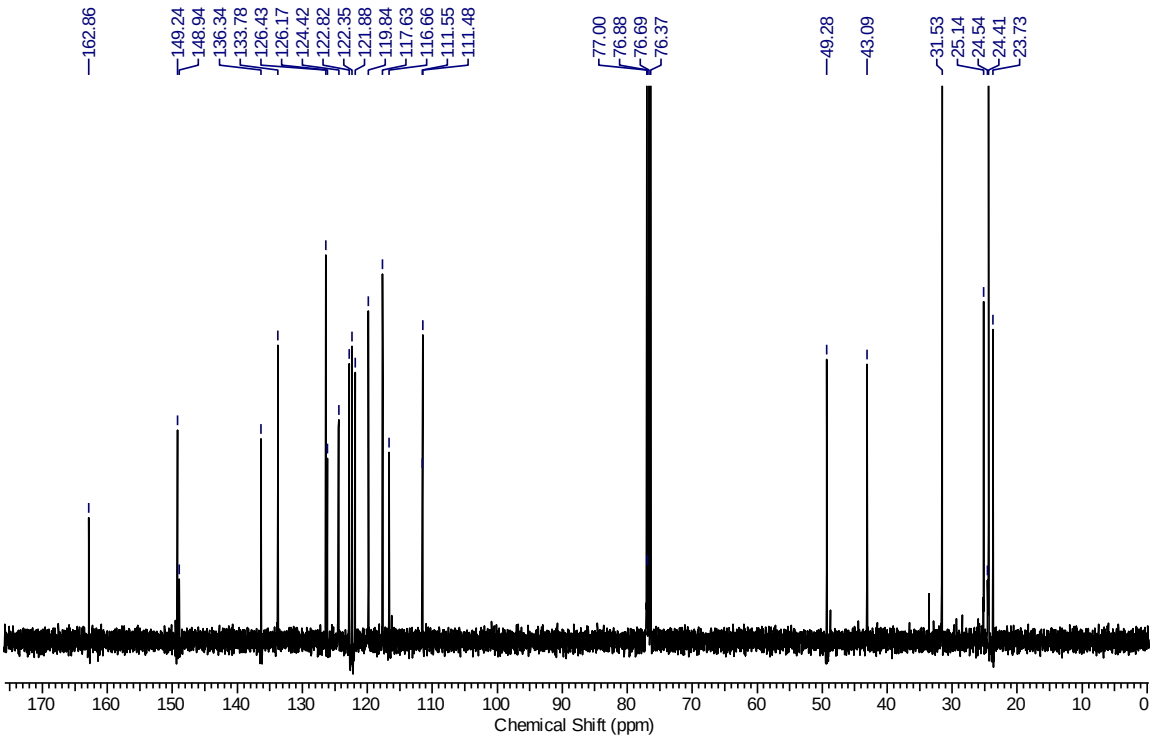
^{1}H NMR (400MHz) spectrum of compound **5g** in $CDCl_3$.



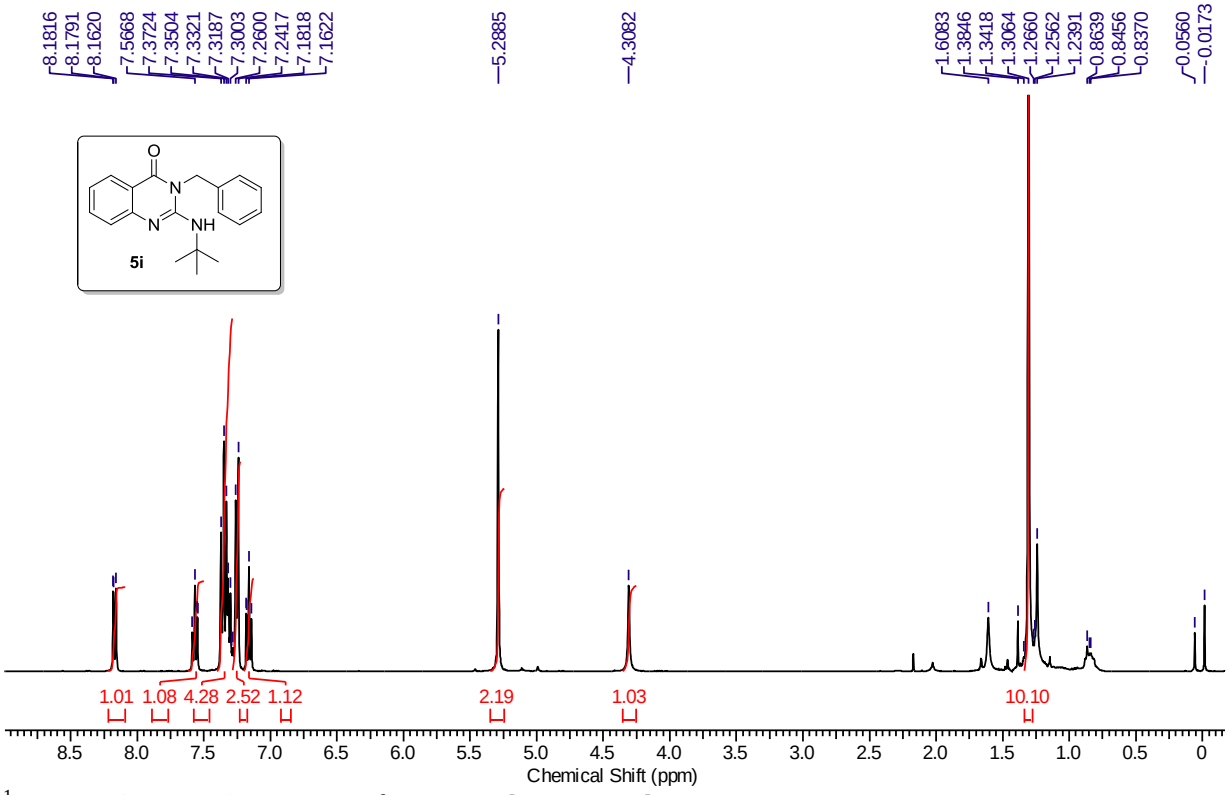
^{13}C NMR (100MHz) spectrum of compound **5g** in $CDCl_3$.



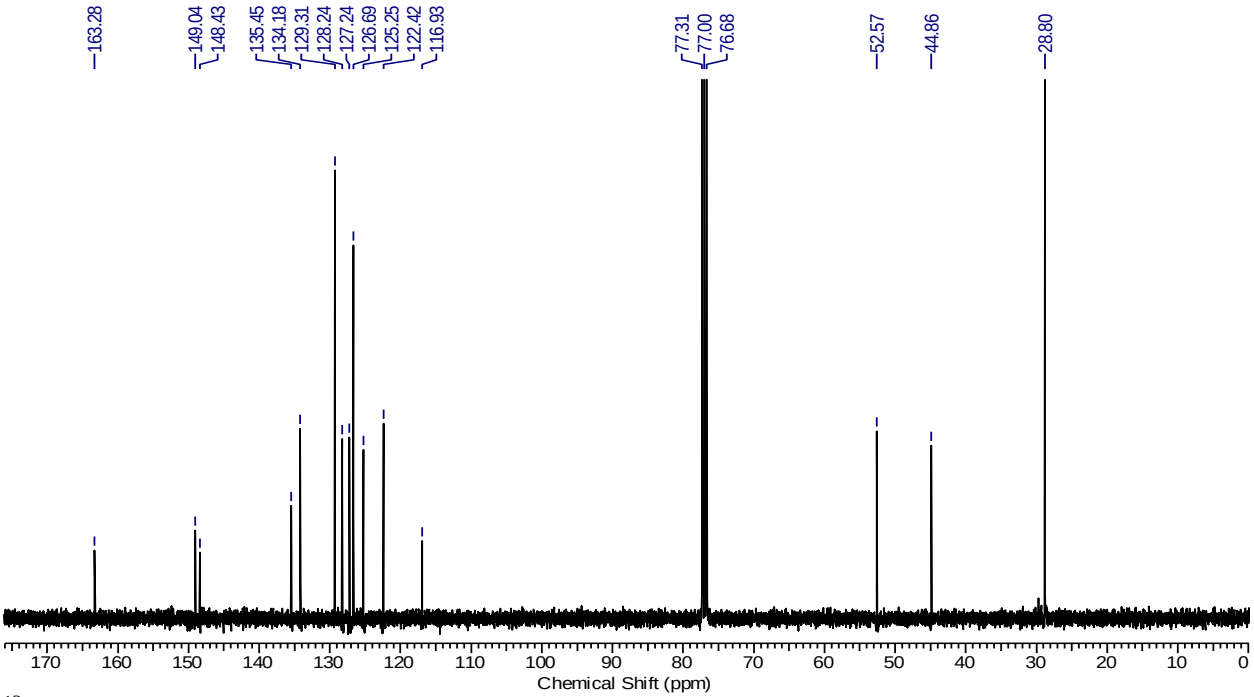
^{1}H NMR (400MHz) spectrum of compound **5h** in $CDCl_3$.



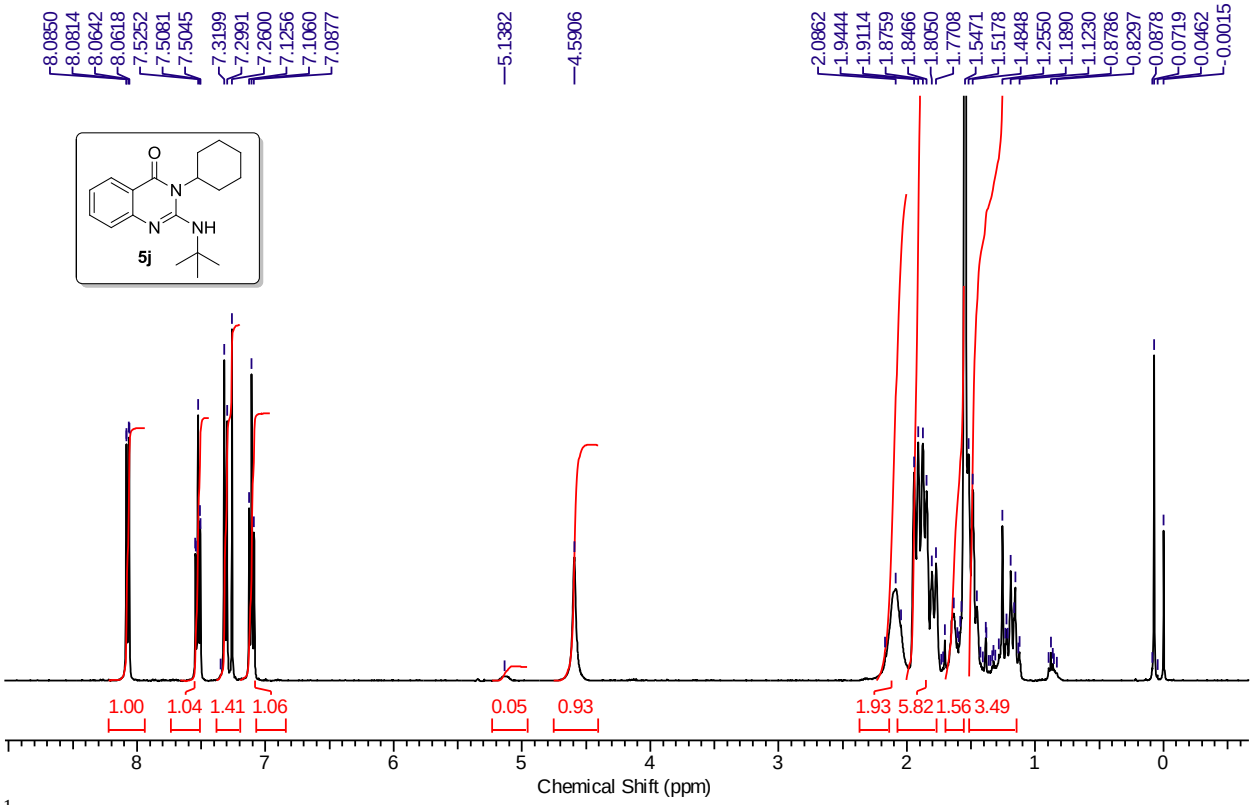
^{13}C NMR (100MHz) spectrum of compound **5h** in $CDCl_3$.



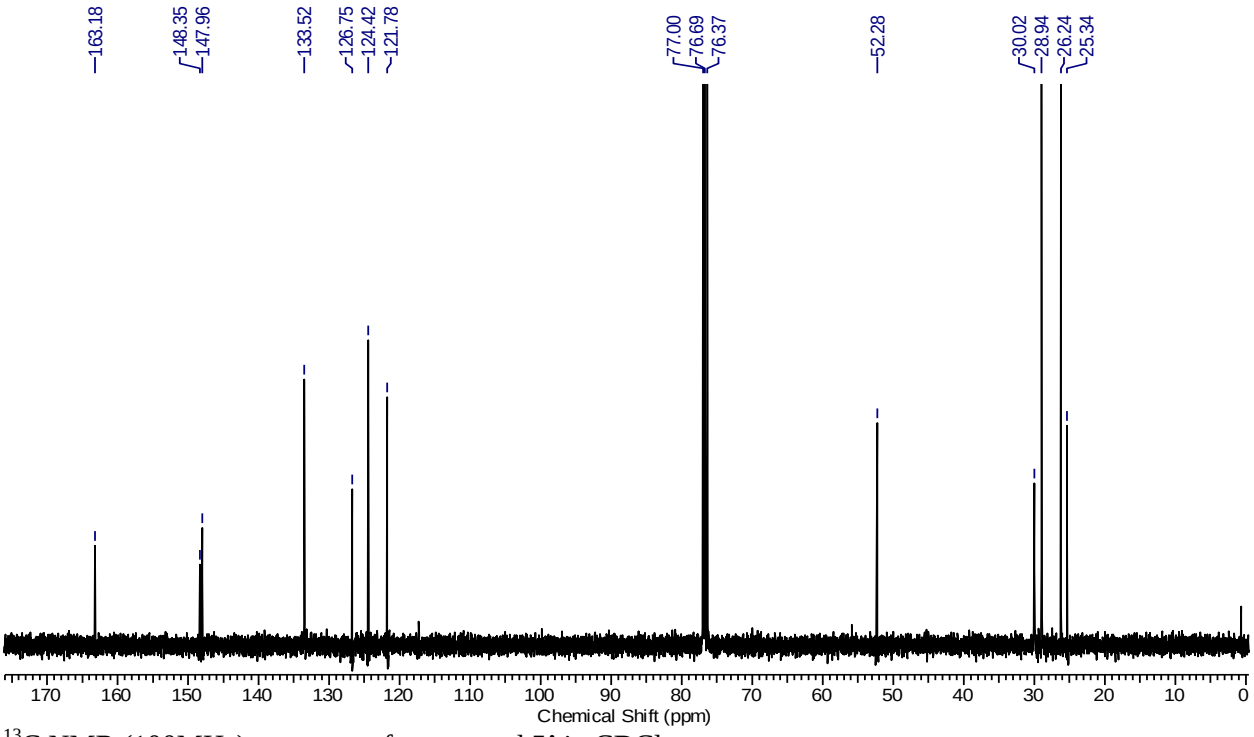
^{1}H NMR (400MHz) spectrum of compound **5i** in $CDCl_3$.



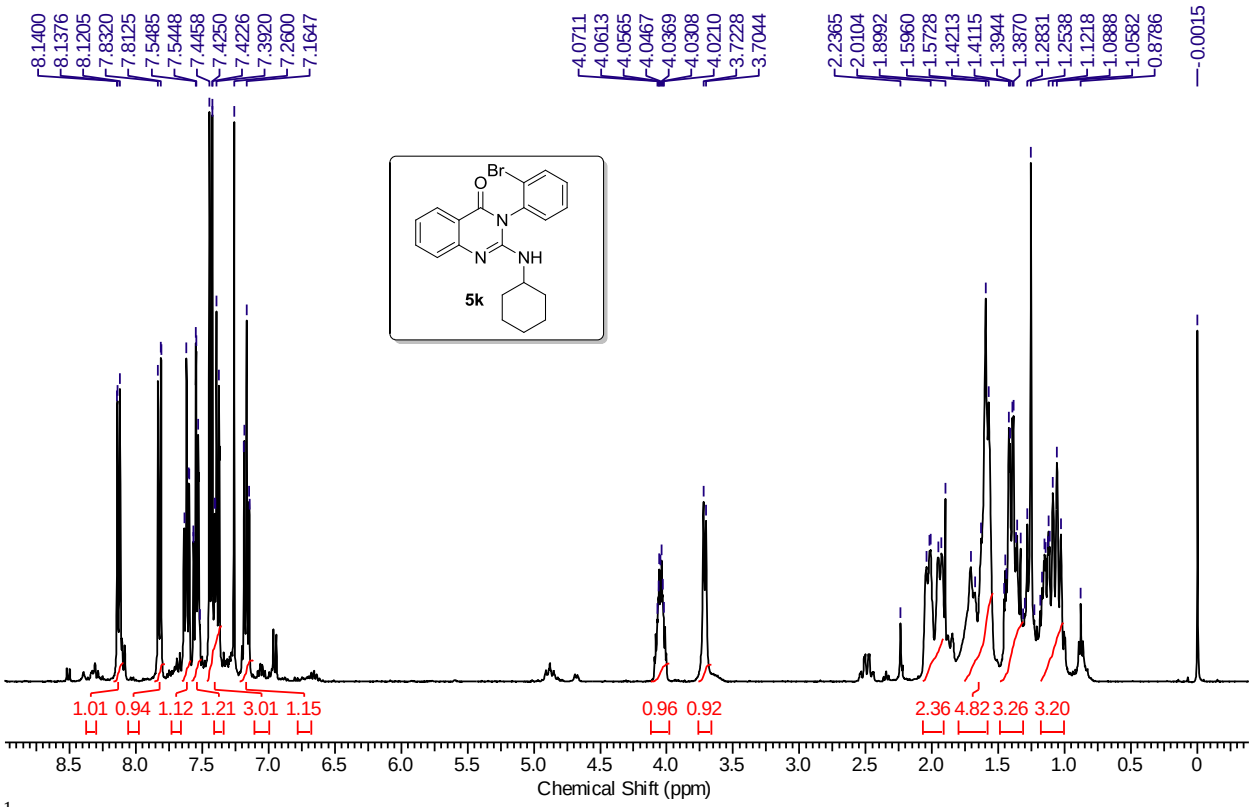
^{13}C NMR (100MHz) spectrum of compound **5i** in $CDCl_3$.



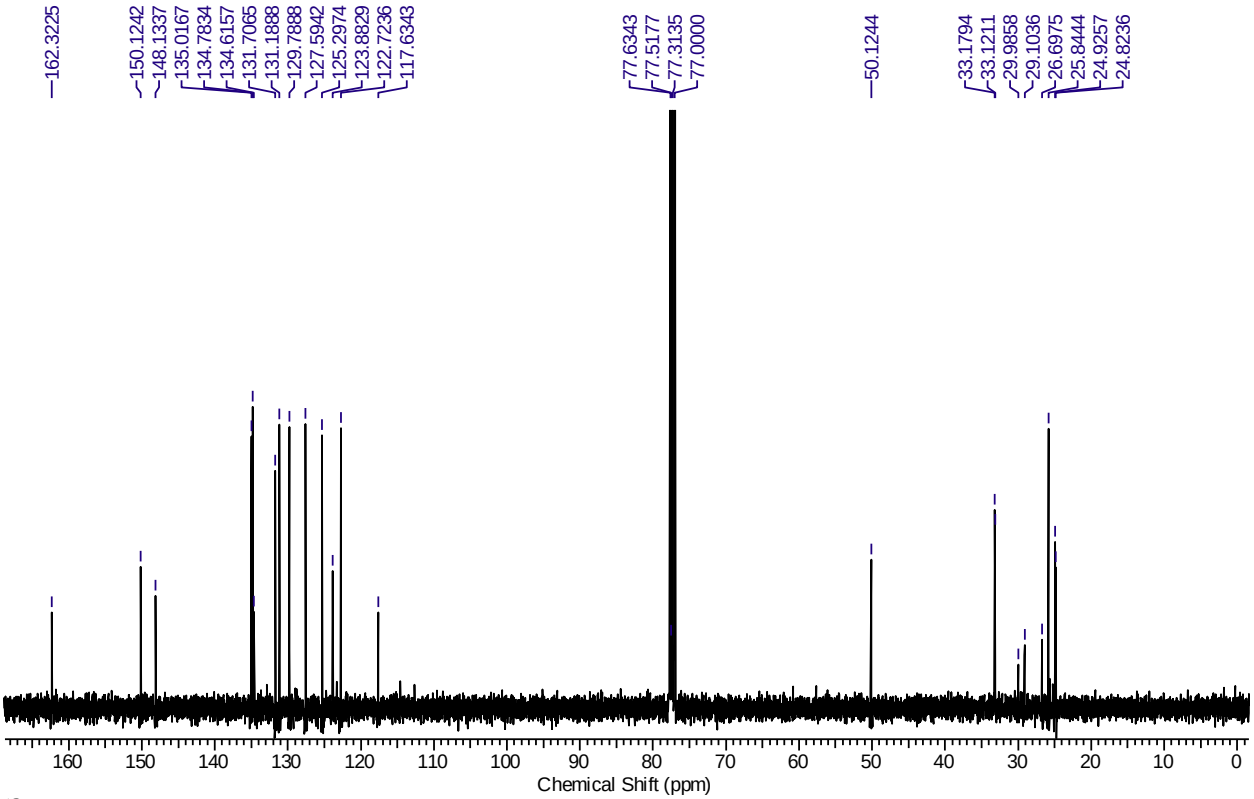
^{1}H NMR (400MHz) spectrum of compound **5j** in $CDCl_3$.



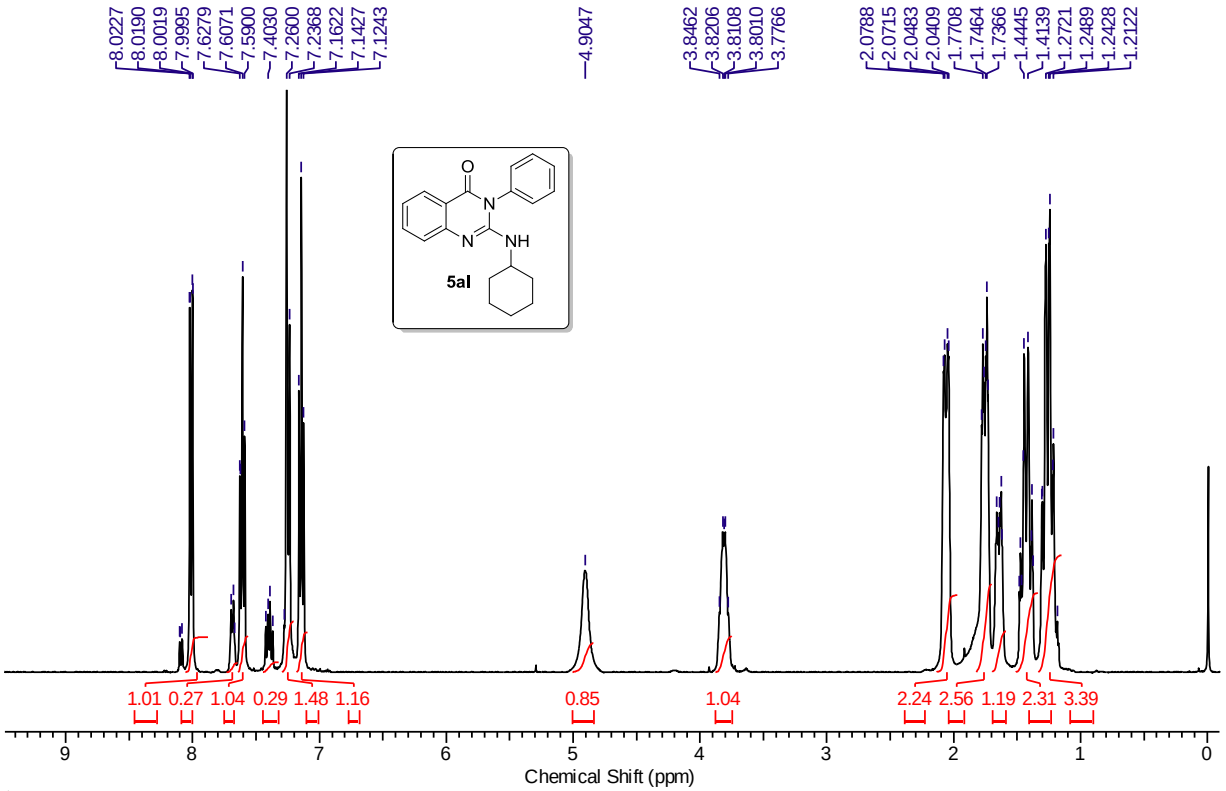
^{13}C NMR (100MHz) spectrum of compound **5j** in $CDCl_3$.



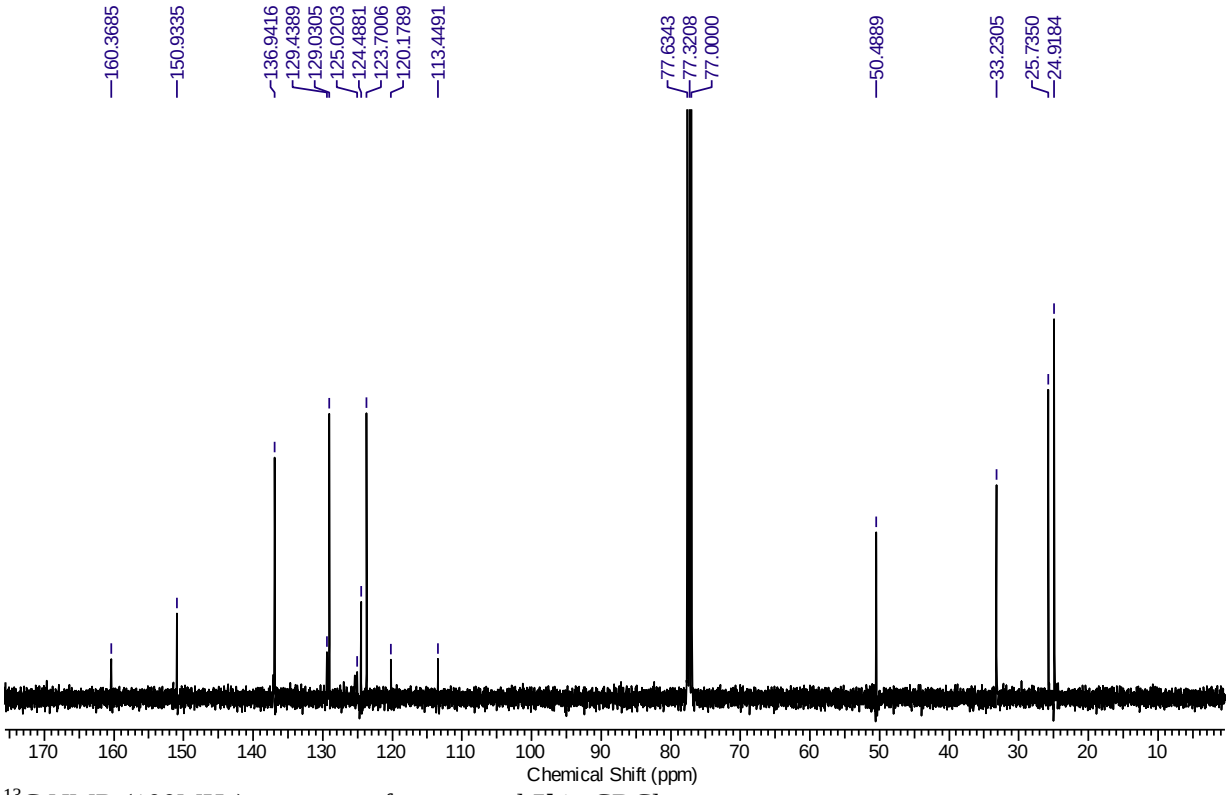
^{1}H NMR (400MHz) spectrum of compound **5k** in $CDCl_3$.



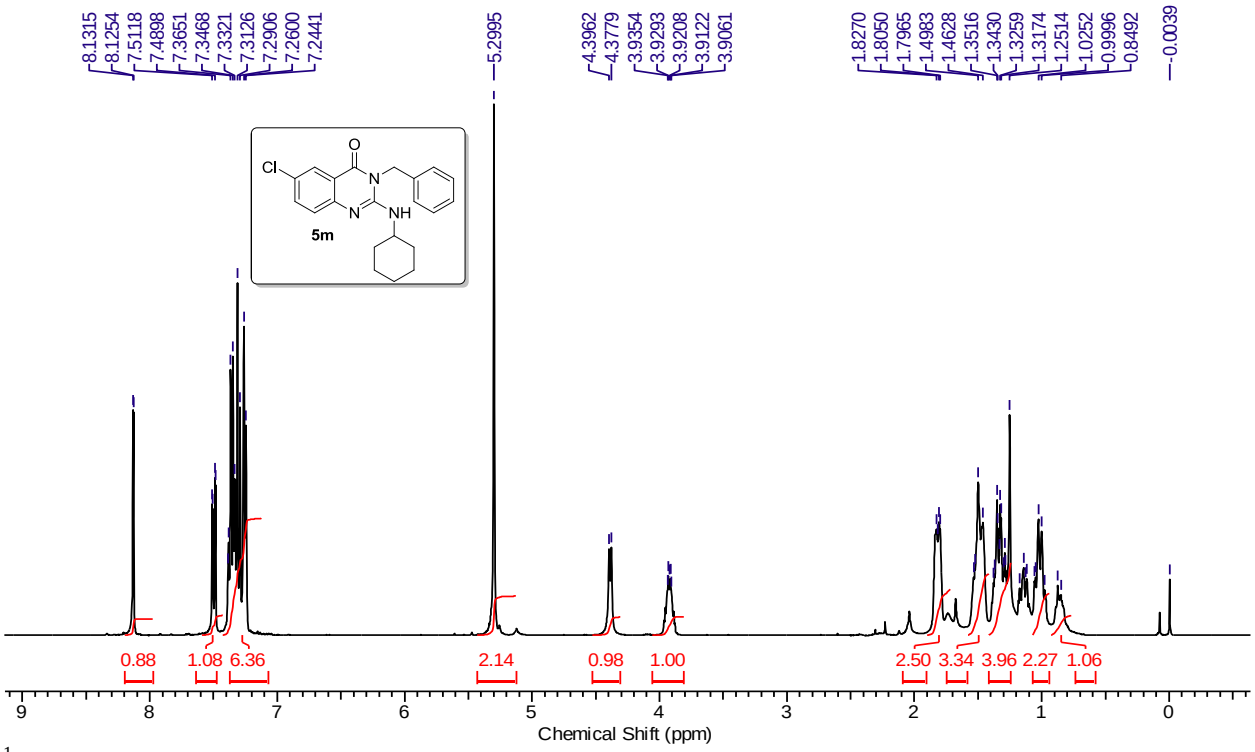
^{13}C NMR (100MHz) spectrum of compound **5k** in $CDCl_3$.



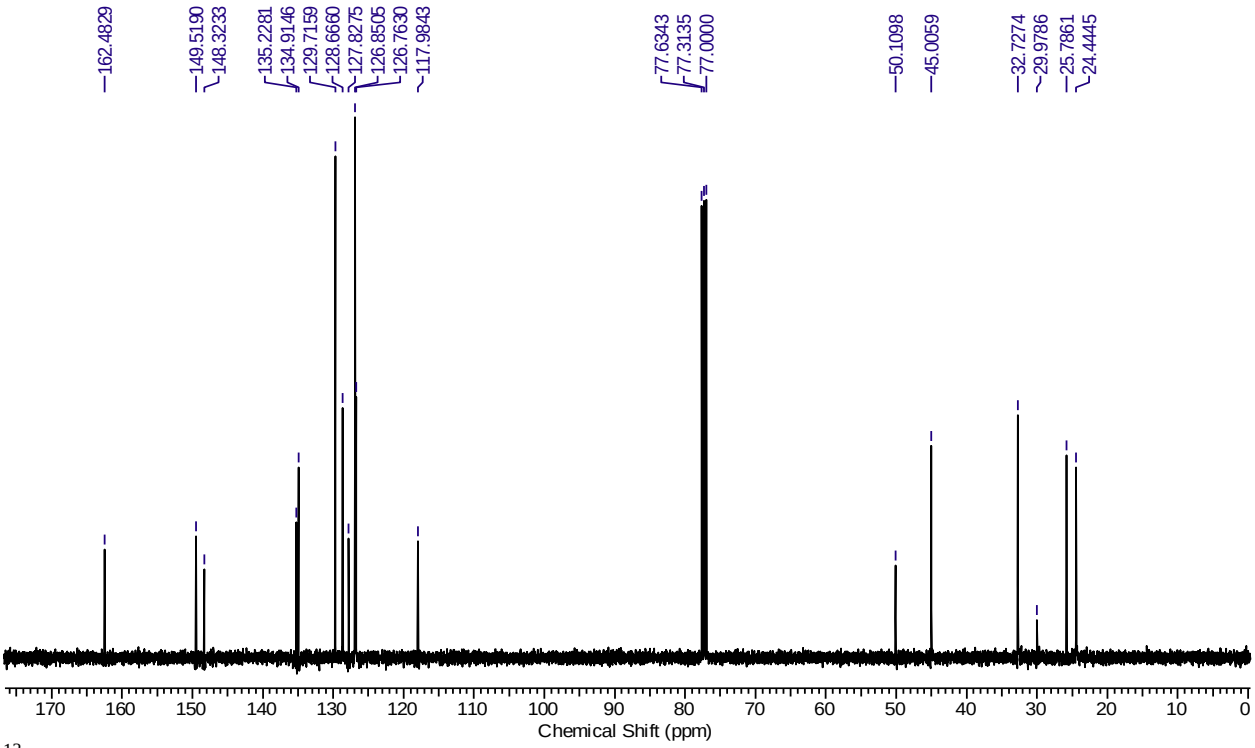
^{1}H NMR (400MHz) spectrum of compound **5l** in $CDCl_3$.



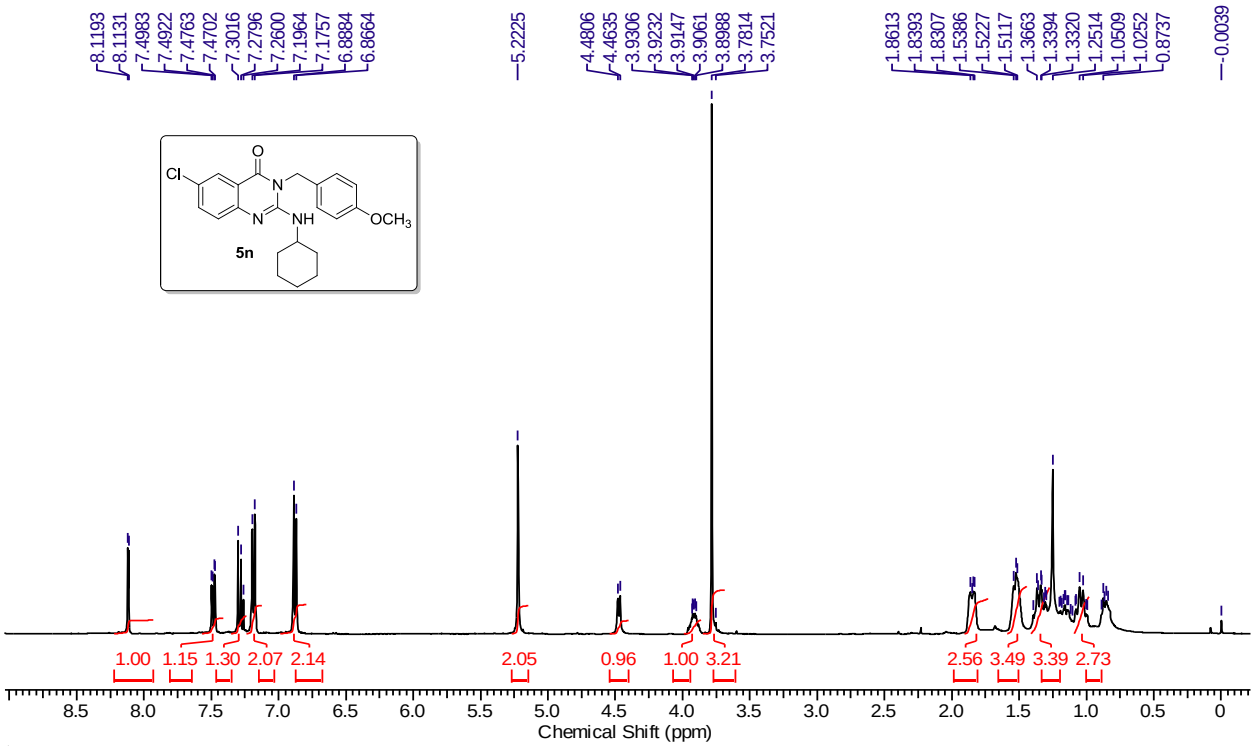
^{13}C NMR (100MHz) spectrum of compound **5l** in $CDCl_3$.



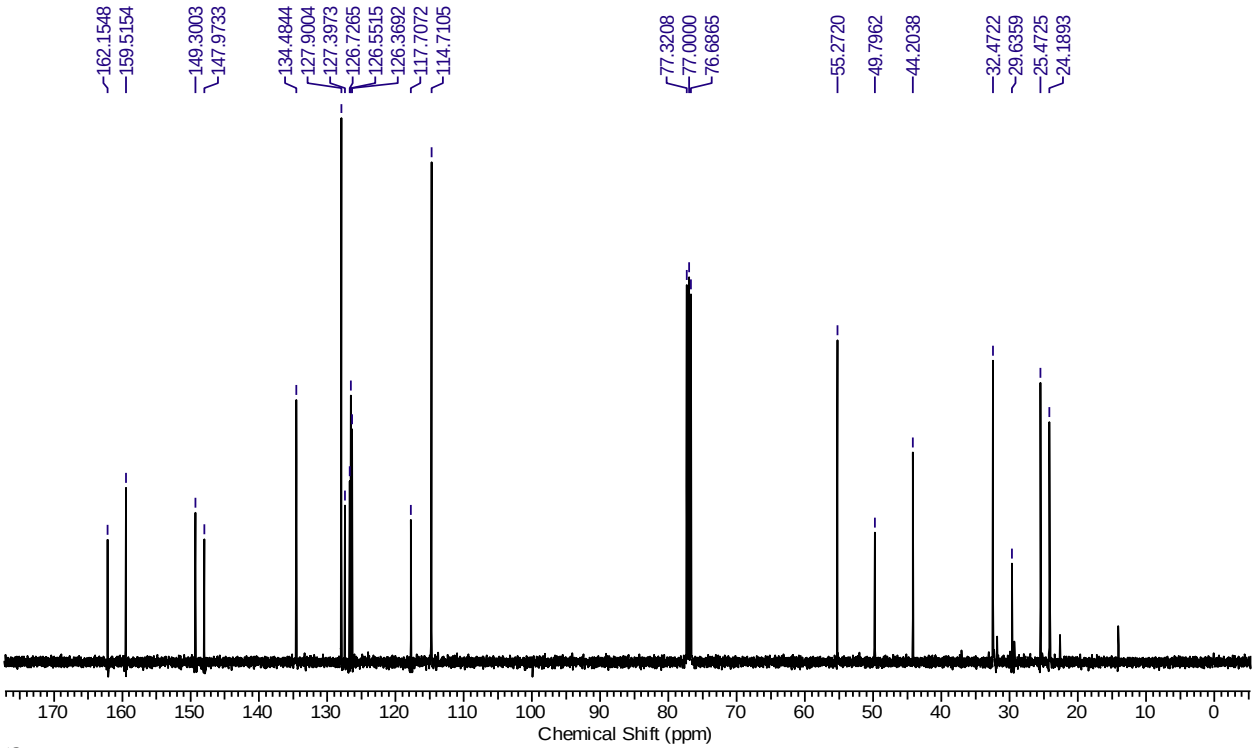
^{1}H NMR (400MHz) spectrum of compound **5m** in $CDCl_3$.



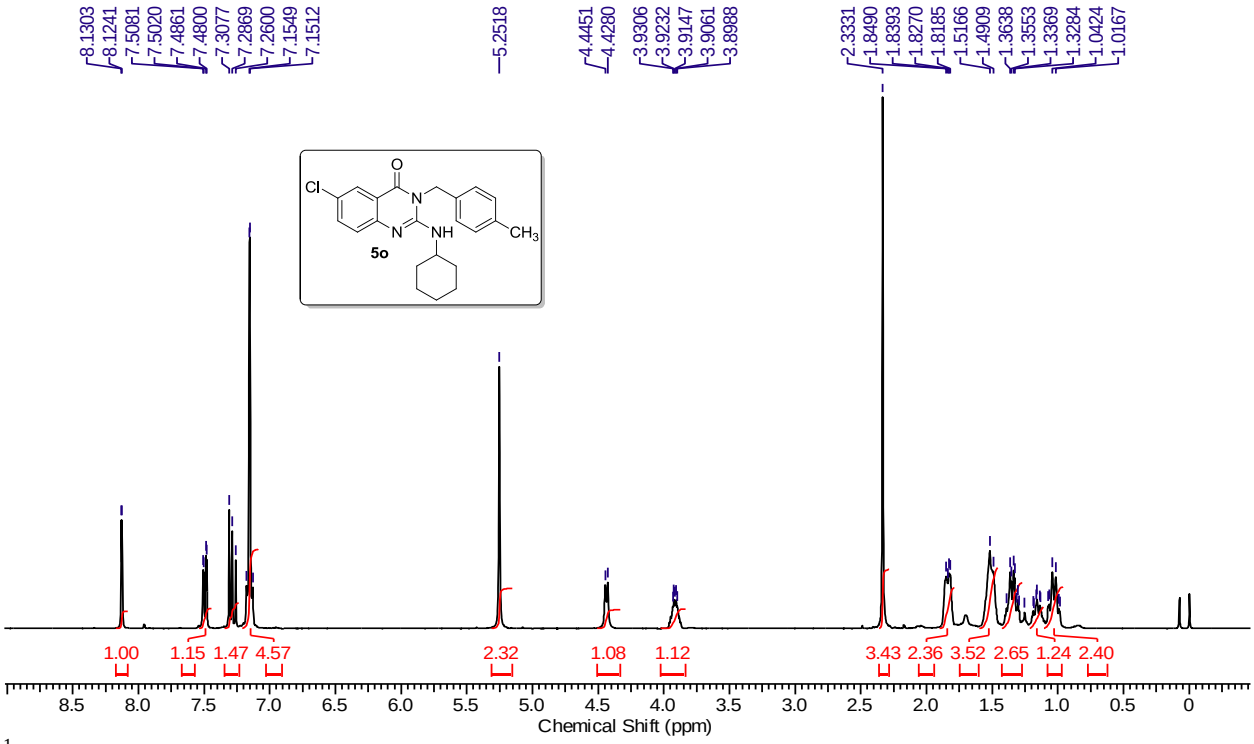
^{13}C NMR (100MHz) spectrum of compound **5m** in $CDCl_3$.



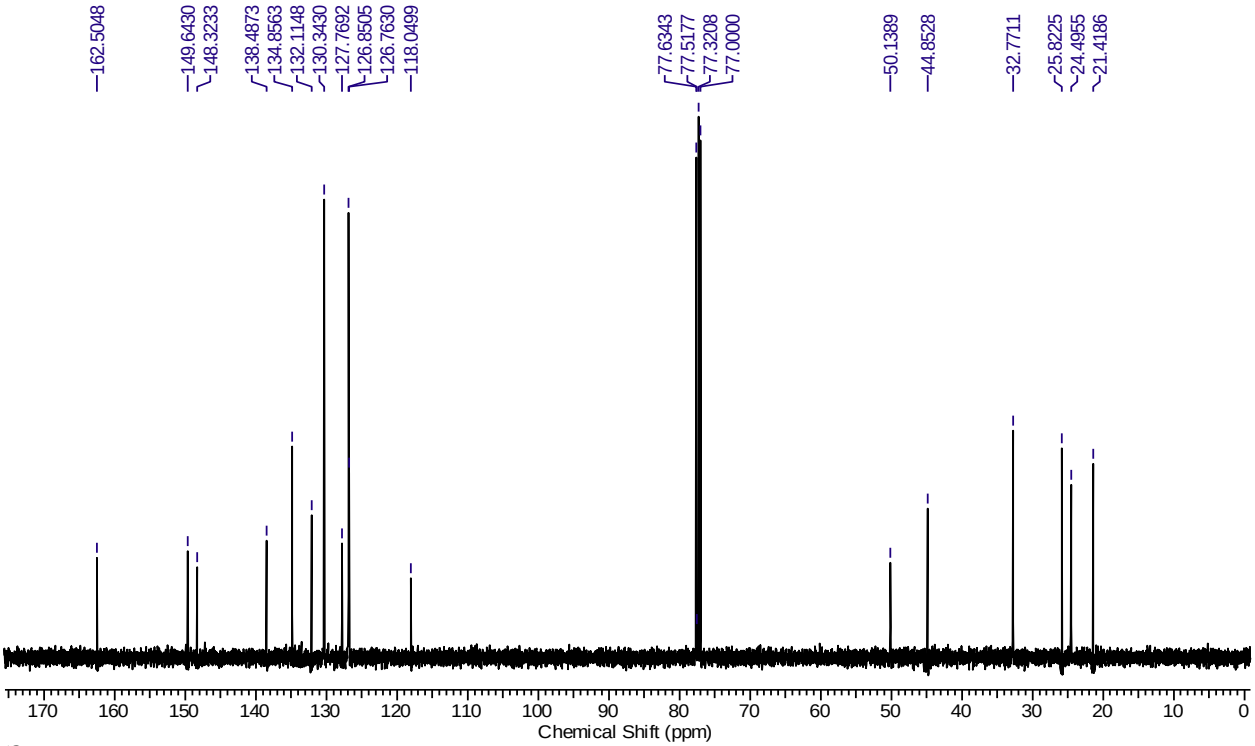
^{1}H NMR (400MHz) spectrum of compound **5n** in $CDCl_3$.



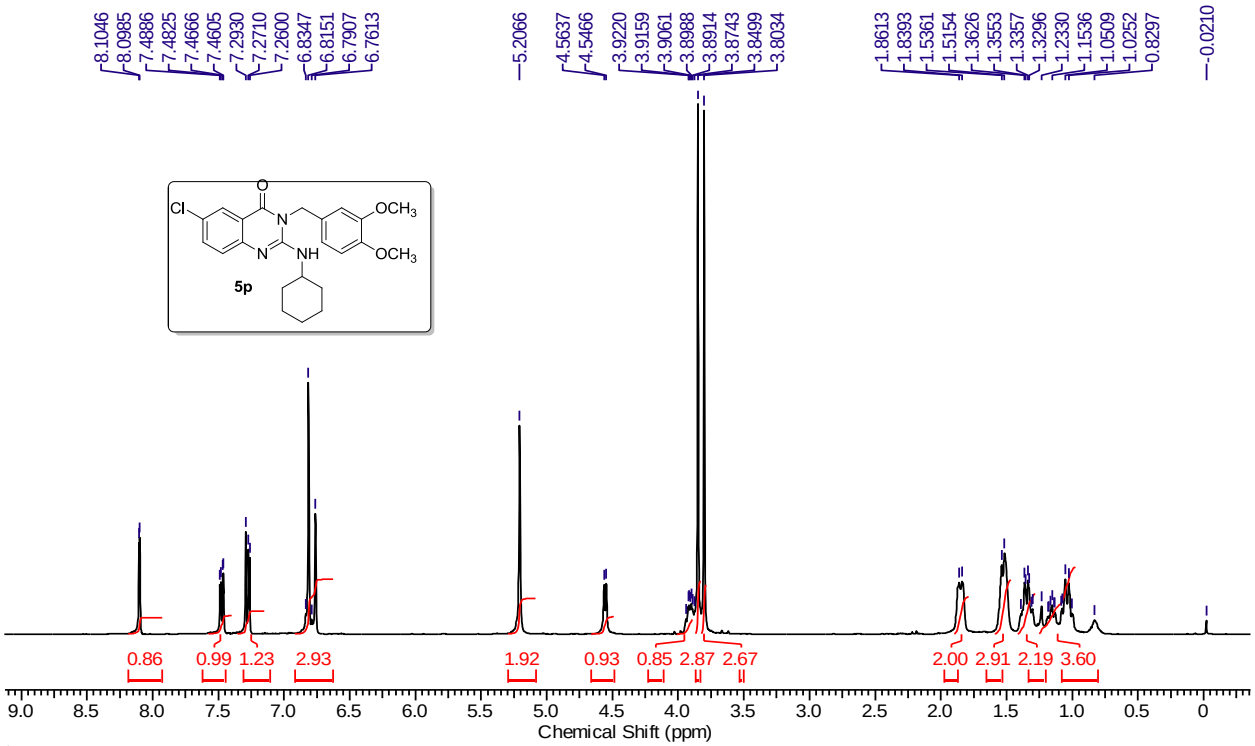
^{13}C NMR (100MHz) spectrum of compound **5n** in $CDCl_3$.



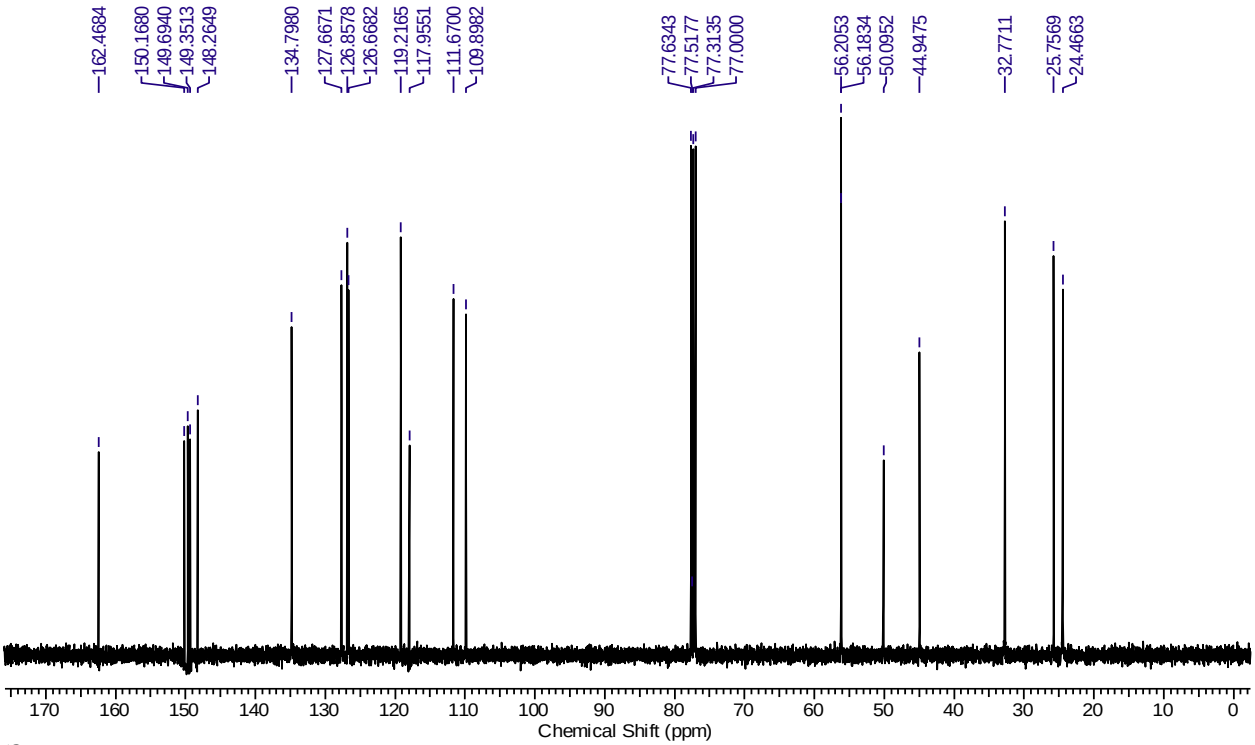
^{1}H NMR (400MHz) spectrum of compound **5o** in $CDCl_3$.



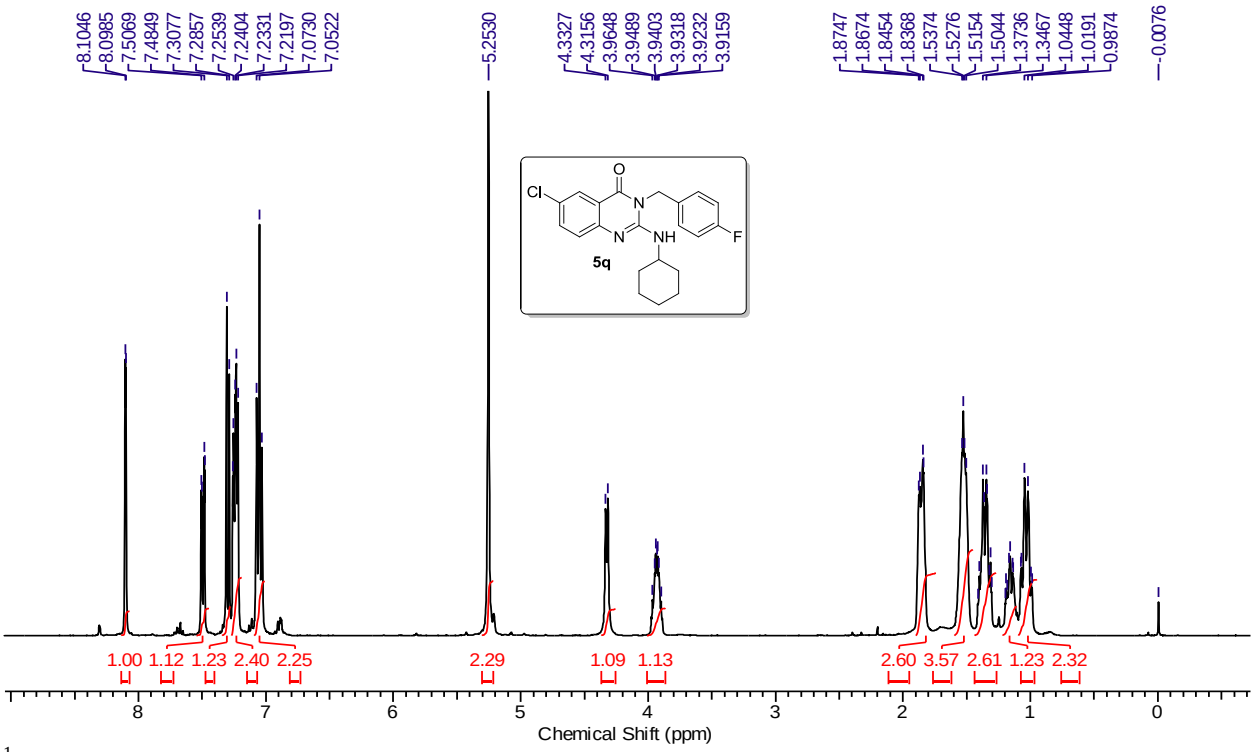
^{13}C NMR (100MHz) spectrum of compound **5o** in $CDCl_3$.



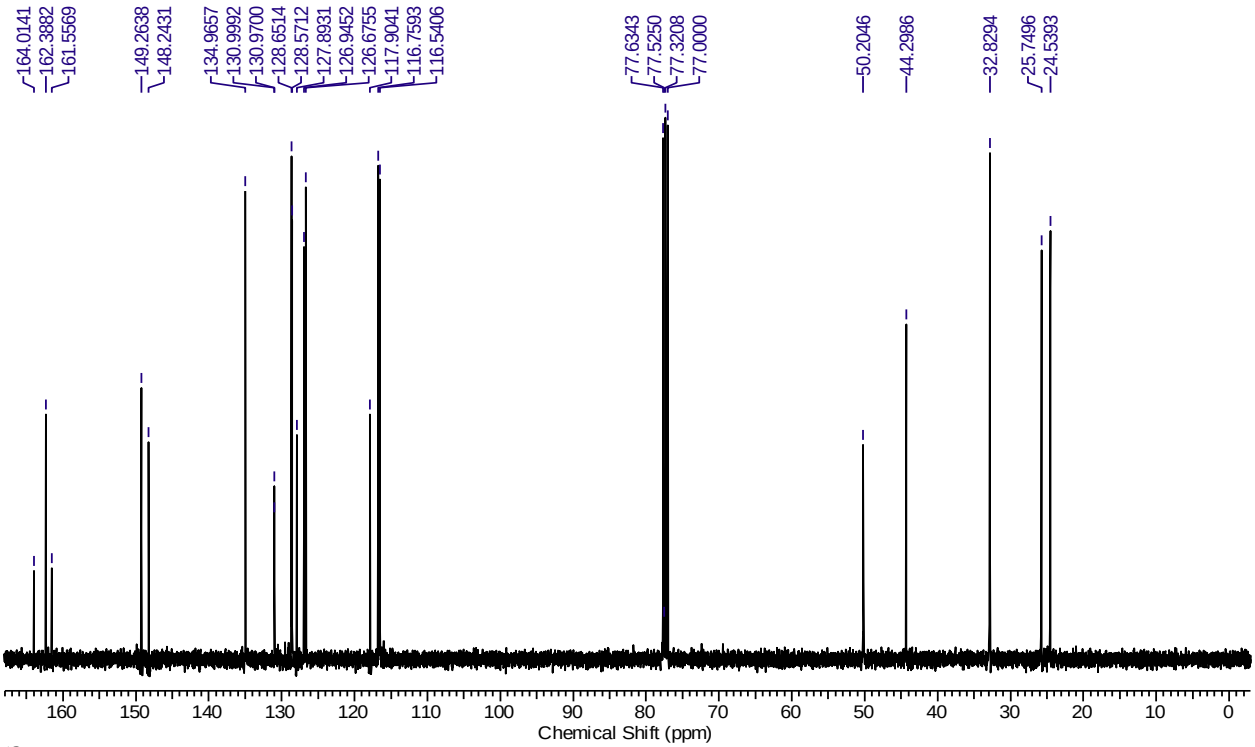
^{1}H NMR (400MHz) spectrum of compound **5p** in $CDCl_3$.



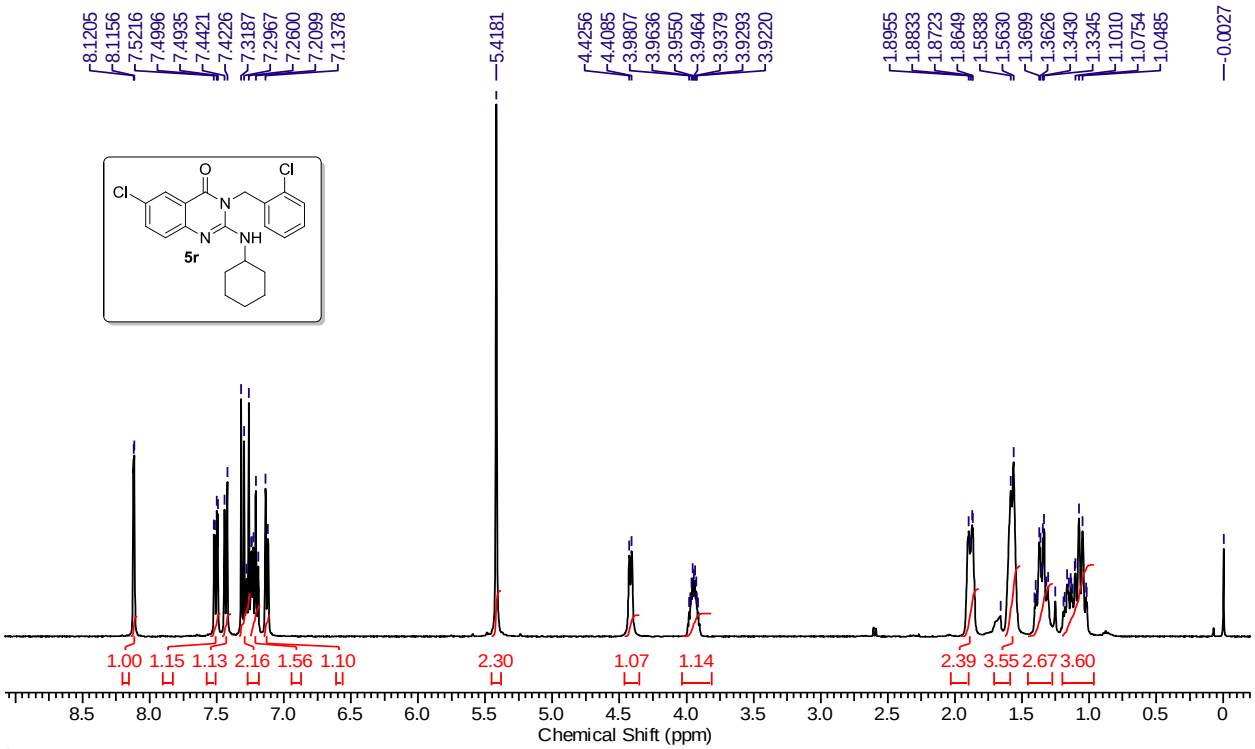
^{13}C NMR (100MHz) spectrum of compound **5p** in $CDCl_3$.



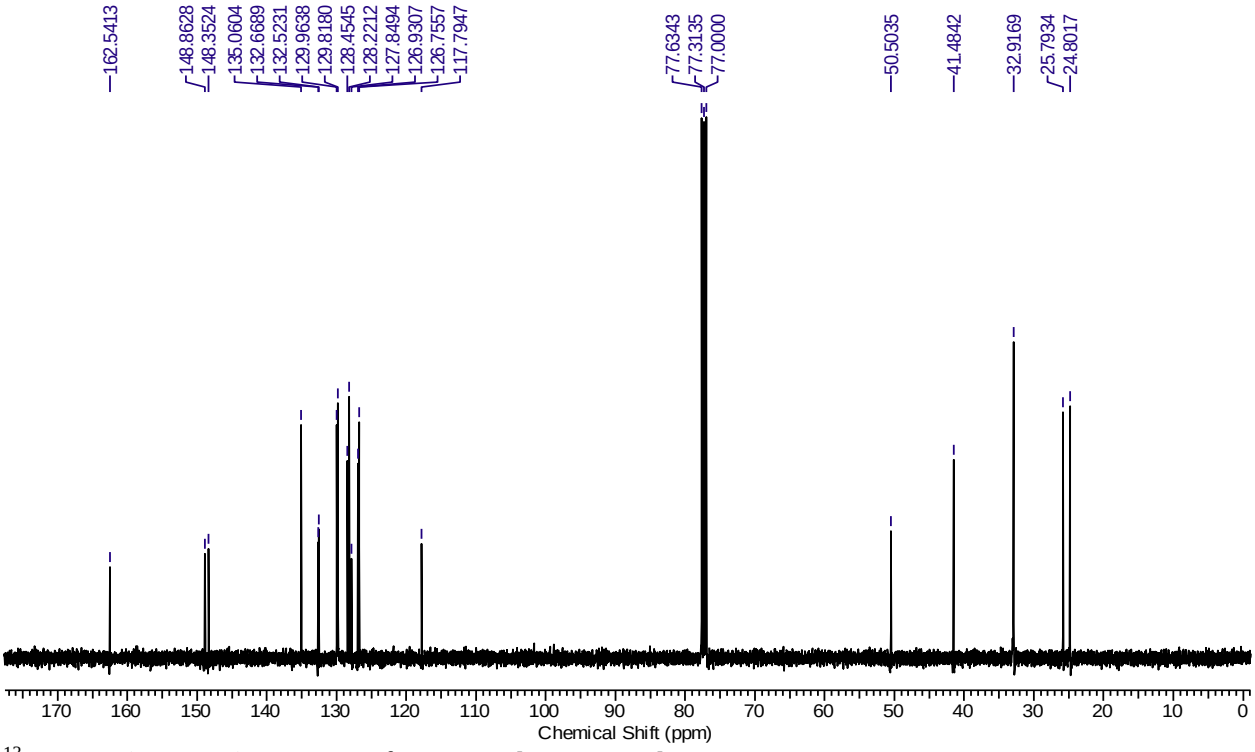
^{1}H NMR (400MHz) spectrum of compound **5q** in $CDCl_3$.



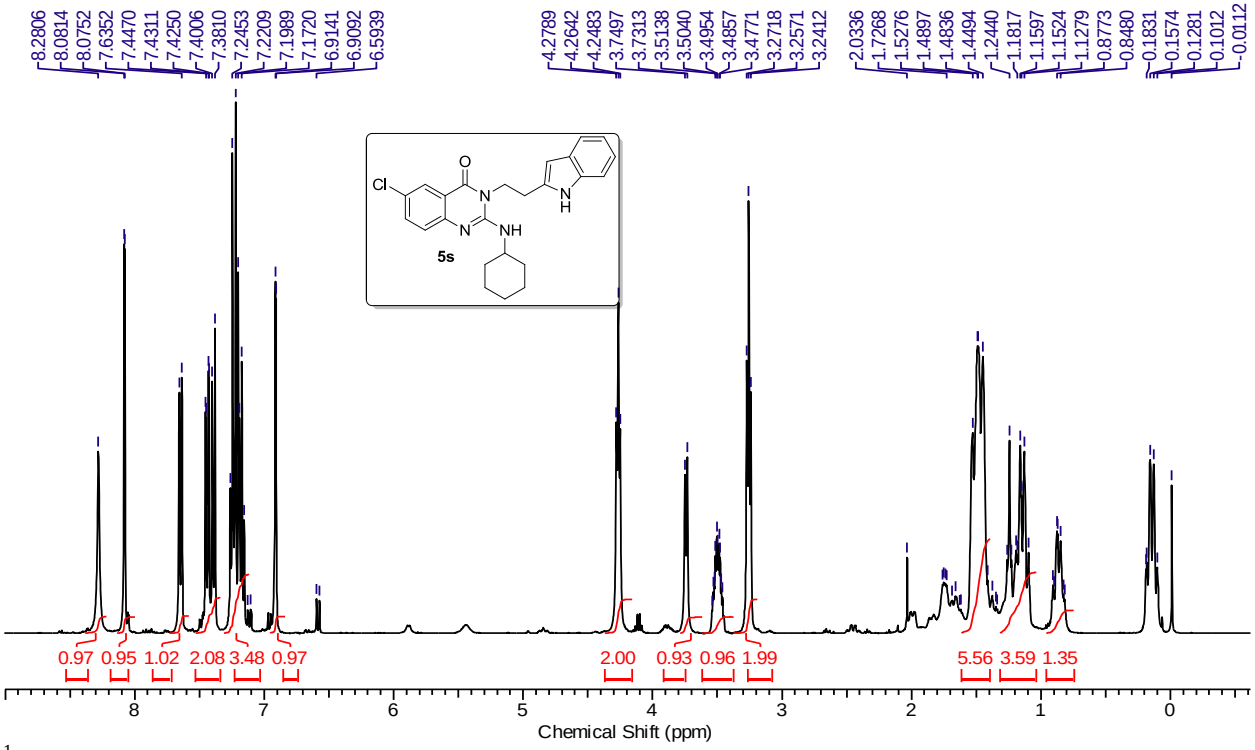
^{13}C NMR (100MHz) spectrum of compound **5q** in $CDCl_3$.



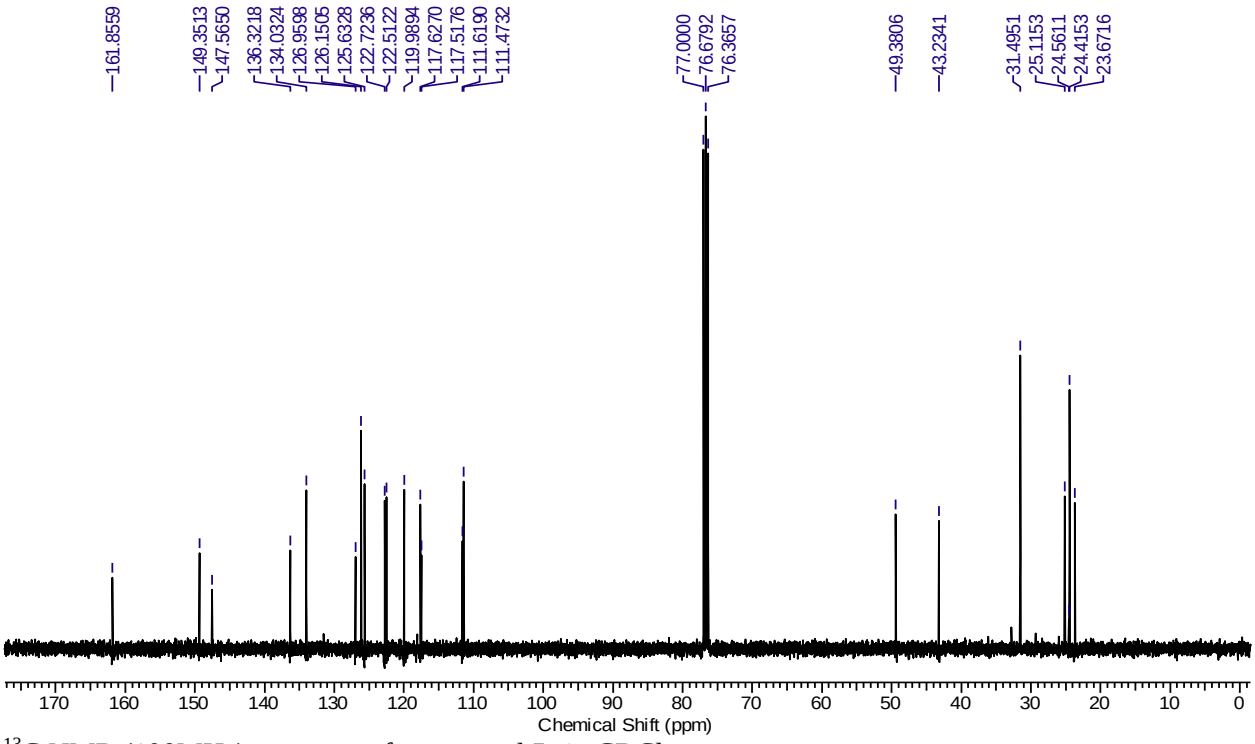
^{1}H NMR (400MHz) spectrum of compound **5r** in $CDCl_3$.



^{13}C NMR (100MHz) spectrum of compound **5r** in $CDCl_3$.



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



^{13}C NMR (100MHz) spectrum of compound **5s** in $CDCl_3$

References:

1. Ji. F, Lv. M-F, Yi. W-B and Cai. C., One-pot synthesis of 2-amino-4(3*H*)-quinazolinones via ring-opening of isatoic anhydride and palladium-catalyzed oxidative isocyanide-insertion. *Org. Biomol. Chem*., **2014**, *12*, 5766