Green Chemistry

Supporting Information

A Facile protocol for the Synthesis of 3-Aminoimidazo-Fused Heterocycles *via* Groebke-Blackburn-Bienayme Reaction Under Catalyst-Free and Solvent-Free Conditions

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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 were 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. The GC–MS analyses were performed using a Thermo scientific TRACE GC ULTRA gas chromatograph–mass spectrometry instrument (Thermo scientific DSQ-II). The ion source was EI source. He as the carrier gas at a constant flow rate of 1 mL/min, with an injection volume of 1 µL sample was used. The temperature was ramped up from 40-250 °C, with ramp rate of 20 ^{o}C/min. The ionization voltage was 70 eV, and the source temperature was 250 ^{o}C. The scanning scope was 0-500. Melting points were measured using melting point apparatus manufactured by GUNA enterprises, india and are uncorrected.

All small scale reactions were carried out in 5 ml stoppered round bottom flask (RBF). Reactions were monitored by silica gel TLC plates, using a mixture of petroleum ether and ethyl acetate as eluents. All solvents were distilled prior use; petroleum ether with a boiling range of 60 to 80 ^{o}C, dichloromethane (DCM), ethanol (EtOH), ethyl acetate, purchased from locally available commercial sources were used. Aromatic aldehydes and amines were purchased from locally available commercial sources and few of them from Sigma Aldrich. Cyclohexyl and tertiary butyl isocyanides were prepared according to literature procedure.[1]

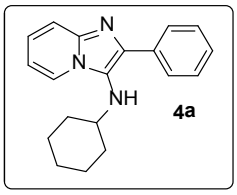
General Procedure for the Synthesis of 3-Aminoimidazo-fused Heterocycles *via* Groebke-Blackburn-Bienayme Reaction:

2-Aminoheterocycle **1** (1 mmol), aldehyde **2** (1 mmol) and isocyanide **3** (1 mmol) were taken in a 5 ml RBF and the mixture was stirred for appropriate time at 160 ^{o}C in oil bath until the starting materials were completely consumed. The products were recrystallized using EtOH. Some of the compounds (**4d, 4h, 4l, 4q & 4z**) which were viscous in nature was purified by column chromatography on silica (petroleum ether/ethyl acetate). All the compounds were confirmed by FTIR, ^{1}H NMR, ^{13}C NMR and HR-MS Spectral analyses. Among 26 compounds, 16 (**4f, 4g, 4k-4m, 4o and 4p-4z**) are unknown and 10 (**4a-4e, 4h-4j, 4n and 4r**) are known.

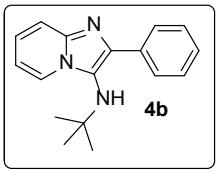
Scale-up reaction: Procedure for the Synthesis of *N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyridine-3-amine (4a).

2-Aminoheterocycle **1** (10.62 mmol), aldehyde **2** (10.62 mmol) and isocyanide **3** (10.62 mmol) were taken in a 25 ml RBF and the mixture was stirred for 2 h at 160 ^{o}C in oil bath. The product was recrystallized using EtOH and further confirmed by FTIR, ^{1}H NMR, ^{13}C NMR and HR-MS Spectral analyses. Yield 93%, and Mp is 176–178 ^{o}C**.**

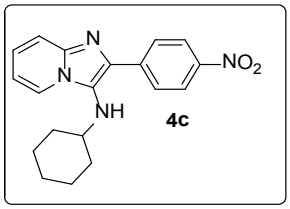
Spectral Data of all Compounds (4a-z)



***N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyridine-3-amine (4a):**[2] White solid (97%), Mp 176-178 °C**.** IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3239 (NH), 2918 (sp^2-CH), 2848 (sp^3-CH), 1561, 1443, 1363 (CN), 1333, 1225, 735. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.31 (d, 1H, J = 6.8 Hz), 8.05 (d, 2H, J = 7.3 Hz), 7.58 (d, 1H, J = 8.8 Hz), 7.48-7.44 (m, 2H), 7.35-7.27 (m, 1H), 7.15 (dd, 1H, J_a= 8.6 and J_b = 7.1 Hz), 6.8 (t, 1H, J = 6.6 Hz), 3.17 (d, 1H, J = 3.4 Hz), 2.98-2.95 (m, 1H), 1.82 (d, 1H, J = 12.2 Hz), 1.71-1.69 (m, 2H), 1.29-1.25 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C =141.4, 134.2, 128.6, 127.4, 127.0, 125.0, 124.1, 122.8, 117.3, 111.7, 57.0, 34.2, 25.8, 24.9. HR-MS (ESI+) m/z calculated for $[C_{19}H_{22}N_3]^+$ = $[M+H]^+$: 292.1808; found: 292.1800.

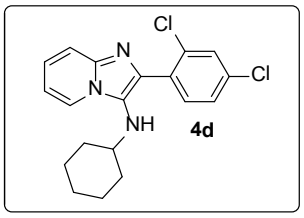


***N*-(*tert*-butyl)-2-phenylimidazo[1,2-*a*]pyridine-3-amine (4b):**[3] White solid (95%), Mp 160-162 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3313 (NH), 2962 (sp^2-CH), 2924 (sp^3-CH), 1600, 1506, 1441, 1360 (CN), 1331, 1206, 1027, 746. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.23 (d, 1H, J = 6.8 Hz), 7.92-7.90 (m, 2H), 7.54 (d, 1H, J = 9.3 Hz), 7.43 (t, 2H, J = 7.8 Hz), 7.33-7.27 (m, 1H), 7.15-7.10 (m, 1H), 6.76 (t, 1H, J = 6.8 Hz), 3.13 (br s, 1H), 1.03 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 142.0, 139.5, 135.3, 128.3, 127.4, 124.0, 123.5, 117.3, 111.3, 56.4, 30.3. HR-MS (ESI+) m/z calculated for $[C_{17}H_{20}N_3]^+$ = $[M+H]^+$: 266.1652; found: 266.1644.

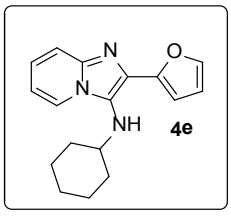


***N*-cyclohexyl-2-(4-nitrophenyl)imidazo[1,2-*a*]pyridine-3-amine (4c):**[3b, 4] Rust color solid (98%), Mp 203-205 °C. IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3242 (NH), 2919 (sp^2-CH),

2849 (sp^3-CH), 1596 (-NO_2), 1509, 1445, 1367 (CN), 1327, 1111, 858, 737. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.33-8.27 (m, 4H), 8.06 (d, 1H, J = 6.8 Hz), 7.5 (d, 1H, J = 9.3 Hz), 7.21-7.17 (m, 1H), 6.8 (t, 1H, J = 6.4 Hz), 3.09 (d, 1H, J = 4.9 Hz), 3.00-2.94 (m, 1H), 1.87-1.82 (m, 3H), 1.73-1.71 (m, 2H), 1.31-1.16 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 146.5, 142.1, 141.2, 134.4, 127.2, 126.5, 124.9, 123.9, 122.7, 117.9, 12.7, 57.1, 34.3, 25.6, 24.8. HR-MS (ESI+) m/z calculated for $[C_{19}H_{21}N_4O_2]^+ = [M+H]^+$: 337.1659; found: 337.1653.

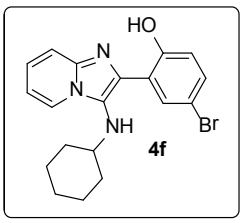


***N*-cyclohexyl-2-(2,4-dichlorophenyl)imidazo[1,2-*a*]pyridine-3-amine (4d):**[4, 5] Viscous brown oil (96%). IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3242 (NH), 2925 (sp^2-CH), 2852 (sp^3-CH), 1550, 1476, 1364 (CN), 1349, 1101, 920 (C-Cl), 826 (C-Cl), 753. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.14 (d, 1H, J = 6.8 Hz), 7.62 (d, 1H, J = 8.3 Hz), 7.54-7.49 (m, 2H), 7.35 (dd, 1H, J_a = 8.6 and J_b = 2.2 Hz), 7.15 (dd, 1H, J_a = 8.6 and J_b = 7.1 Hz), 6.81 (t, 1H, J = 6.6 Hz), 3.2 (d, J = 6.8 Hz), 2.66 (dd, 1H, J_a = 6.1 and J_b = 3.7 Hz), 1.66 (d, 2H, J = 11.7), 1.58 (d, 2H, J = 4.9 Hz), 1.18-0.97 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C =141.8, 134.3, 134.1, 133.3, 132.8, 129.3, 127.4, 126.5, 123.9, 122.9, 117.7, 56.4, 33.9, 25.62, 24.6. HR-MS (ESI+) m/z calculated for $[C_{19}H_{20}Cl_2N_3]^+ = [M+H]^+$: 360.1029; found: 360.1024.

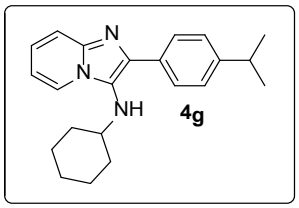


***N*-cyclohexyl-2-(furan-2-yl)imidazo[1,2-*a*]pyridine-3-amine (4e):**[6] Creamish-yellow solid (95%), Mp 121-122 ^{o}C. IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3225 (NH), 2925 (sp^2-CH), 2852 (sp^3-CH), 1545, 1492, 1351 (CN), 1340, 1091 (C-O-C), 1011, 741, 728. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.05 (d, 1H, 6.8 Hz), 7.55 (dd, 2H, J_a = 4.9 and J_b = 3.9 Hz), 7.14-7.09 (m, 1H), 6.87 (d, 1H, J = 3.4 Hz), 6.77 (t, 1H, J = 6.6 Hz), 6.53 (dd, J_a = 3.2 and J_b = 1.7 Hz), 3.62 (d, 1H, J =6.8 Hz), 3.00-2.92 (m, 1H), 1.9 (d, 2H, J = 12.2 Hz), 1.75-1.73 (m, 2H), 1.33-1.13 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 150.5, 141.8, 128.1, 125.5, 123.9, 122.8, 111.6, 111.5, 106.4, 57.0, 34.1, 25.77, 25.0. HR-MS (ESI+) m/z calculated for $[C_{17}H_{20}N_3O]^+$ =

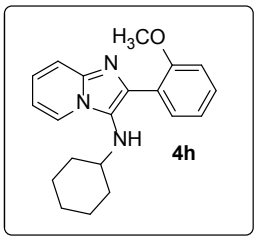
$[M+H]^+$: 282.1601; found: 282.1593.



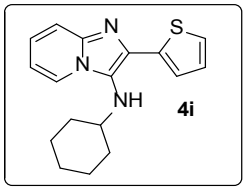
4-Bromo-2-(3-(cyclohexylamino)imidazo[1,2-*a*]pyridin-2-yl)phenol (4f): Off-white solid (90%), Mp 152-154 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3346 (OH), 3068 (NH), 2926 (sp^2-CH), 2852 (sp^3-CH), 1635, 1475, 1365 (CN), 1346, 1280, 1242, 1082, 811 (C-Br), 736. ^1H NMR ($CDCl_3$, 400 MHz): δ_H = 13.23 (br s, 1H), 8.46-8.25 (m, 1H), 8.11-8.05 (m, 1H), 7.47 (d, 1H, J = 9.3 Hz), 7.28-7.21 (m, 2H), 6.91-6.87 (m, 2H), 3.03-2.98 (m, 2H), 1.84 (d, 2H, J = 12.2 Hz), 1.75-1.73 (m, 2H), 1.38-1.27 (m, 3H), 1.24-1.14 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 156.6, 139.5, 134.8, 131.5, 129.0, 125.0, 123.7, 122.3, 119.3, 119.1, 116.7, 112.7, 110.5, 57.0, 34.1, 25.6, 24.8. HR-MS (ESI+) m/z calculated for $[C_{19}H_{21}BrN_3O]^+ = [M+H]^+$: 386.0863; found: 386.0852.



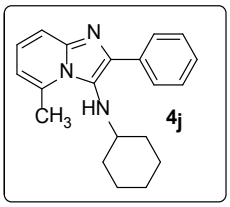
***N*-cyclohexyl-2-(4-isopropylphenyl)imidazo[1,2-*a*]pyridin-3-amine (4g):** White solid (89%), Mp 160-162 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3258 (NH), 2957, 2926 (sp^2-CH), 2852 (sp^3-CH), 1630, 1504, 1448, 1361 (CN), 1344, 1226, 1100, 841, 753. ^1H NMR ($CDCl_3$, 400 MHz): δ_H = 8.11 (d, 1H, 6.8 Hz), 7.97 (d, 2H, J = 8.3 Hz), 7.53 (d, 1H, J = 8.8 Hz), 7.31 (d, 2H, J = 8.3 Hz), 7.12-7.08 (m, 1H), 6.77-6.74 (m, 1H), 3.10-2.99 (br s, 1H), 2.99-2.92 (m, 2H), 1.83 (d, 2H, J = 12.2 Hz), 1.71-1.69 (m, 2H), 1.3 (d, 6H, J = 6.8 Hz), 1.25-1.13 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 147.9, 141.5, 136.6, 132.0, 126.9, 126.6, 124.7, 123.6, 122.7, 117.3, 111.3, 56.9, 34.1, 33.9, 25.8, 24.8, 24.0. HR-MS (ESI+) m/z calculated for $[C_{22}H_{28}N_3]^+ = [M+H]^+$: 334.2278; found: 334.2272.



***N*-cyclohexyl-2-(2-methoxyphenyl)imidazo[1,2-*a*]pyridine-3-amine (4h):**[4] Viscous brown oil (86%) . IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3346 (NH), 2925 (sp^2-CH), 2851 (sp^3-CH), 1558, 1493, 1363 (CN), 1346, 1234, 1114, 1021 (C-O-C), 744. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.06 (d, 1H, *J* = 6.8 Hz), 7.85 (d, 1H, *J* = 7.3 Hz), 7.5 (d, 1H, *J* = 8.8 Hz), 7.29 (t, 1H, *J* = 7.3 Hz), 7.10-7.00 (m, 2H), 6.95 (d, 1H, *J* = 7.8 Hz), 6.71-6.68 (m, 1H), 3.91 (br s, 1H), 3.82 (s, 3H), 2.62 (br s, 1H), 1.66 (d, 2H, *J* = 9.3 Hz), 1.52 (br s, 2H), 1.04-0.97 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 155.8, 141.8, 133.4, 131.7, 128.8, 127.3, 124.3, 122.9, 122.6, 121.6, 117.3, 111.6, 111.2, 56.3, 56.0, 34.1, 25.7, 24.7. HR-MS (ESI+) m/z calculated for $[C_{20}H_{24}N_3O]^+ = [M+H]^+$: 322.1914; found: 322.1908.

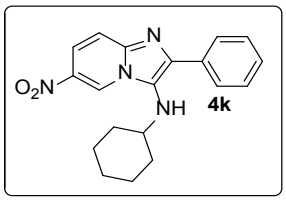


***N*-cyclohexyl-2-(thiophen-2-yl)imidazo[1,2-*a*]pyridine-3-amine (4i):**[6b] Greenish grey solid (84%), Mp 165-166 °C. IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3255 (NH), 2922 (sp^2-CH), 2849 (sp^3-CH), 1501, 1444, 1354 (CN), 1338, 1244, 753, 737. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.17 (d, 1H, *J* = 6.8 Hz), 7.74-7.61 (m, 1H), 7.63 (d, 1H, *J* = 8.8 Hz), 7.34-7.27 (m, 1H), 7.2 (t, 1H, *J* = 7.6 Hz), 7.13-7.09 (m, 1H), 6.85 (t, 1H, *J* = 6.6 Hz), 3.34 (br s, 1H), 3.09 (d, 1H, *J* = 2.9 Hz), 1.88 (d, 2H, *J* = 12.2 Hz), 1.75-1.63 (m, 3H), 1.39-1.16 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 140.6, 127.7, 125.8, 125.4, 125.3, 124.0, 123.2, 116.1, 112.7, 57.0, 34.2, 25.7, 24.9. HR-MS (ESI+) m/z calculated for $[C_{17}H_{20}N_3S]^+ = [M+H]^+$: 298.1372; found: 298.1364.

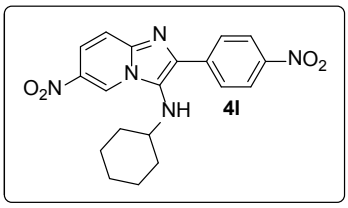


***N*-cyclohexyl-5-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-amine (4j):**[7] Golden red solid (93%), Mp 76-78 °C. IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3328 (NH), 3052, 2919 (sp^2-CH), 2850 (sp^3-CH), 1551, 1508, 1445, 1390 (CN), 1364, 1222, 1070, 763. ^{1}H NMR ($CDCl_3$, 400

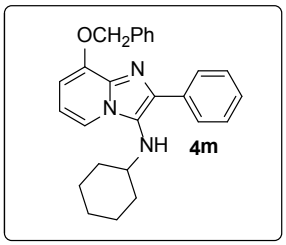
MHz): δ_H = 7.95-7.93 (m, 2H), 7.46-7.41 (m, 3H), 7.34-7.29 (m, 1H), 7.01 (dd, 1H, J_a = 8.8 and J_b = 6.8 Hz), 6.43 (d, 1H, J = 6.4 Hz), 3.12 (br s, 1H), 2.95 (s, 3H), 2.76 (br s, 1H), 1.69 (br s, 2H), 1.59 (br s, 2H), 1.06-0.99 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 143.2, 139.0, 136.3, 135.0, 128.4, 127.8, 127.2, 126.7, 124.0, 58.9, 33.2, 25.8, 24.9, 20.1. HR-MS (ESI+) m/z calculated for $[C_{20}H_{24}N_3]^+ = [M+H]^+$: 306.1965; found: 306.1957.



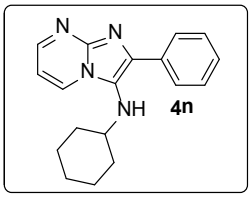
***N*-cyclohexyl-6-nitro-2-phenylimidazo[1,2-*a*]pyridine-3-amine (4k):** Golden yellow solid (80%), Mp 158-160 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3269 (NH), 2926 (sp^2-CH), 2850 (sp^3-CH), 1636, 1538, 1500 (NO_2), 1428, 1350 (CN), 1324 (NO_2), 1183, 818, 749. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 9.24 (d, 1H, J = 2.4 Hz), 8.01 (d, 2H, J = 7.3 Hz), 7.99 (dd, 1H, J_a = 9.8 and J_b = 2.4 Hz), 7.57 (d, 1H, 9.8 Hz), 7.51-7.46 (m, 2H), 7.41-7.37 (m, 1H), 3.24 (d, 1H, J = 4.4 Hz), 3.06-2.98 (m,1H), 1.82 (d, 2H, J = 12.7 Hz), 1.73-1.66 (m, 3H), 1.33-1.17 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 141.3, 139.9, 136.9, 133.2, 128.3, 127.2, 127.0, 123.1, 118.0, 117.0. HR-MS (ESI+) m/z calculated for $[C_{19}H_{20}N_4O_2]^+ = [M+H]^+$: 337.1659; found: 337.1652.



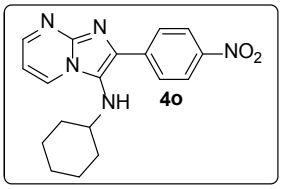
***N*-cyclohexyl-6-nitro-2-(4-nitrophenyl)imidazo[1,2-*a*]pyridine-3-amine (4l):** Viscous brown oil (83%). IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3363 (NH), 2927 (sp^2-CH), 2852 (sp^3-CH), 1635, 1540 (NO_2), 1503, 1477, 1449, 1397 (CN), 1347, 1314, 1180, 749. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 9.25 (d, 1H, J = 1.5 Hz), 7.94 (dd, 1H, J_a = 9.8 and J_b = 2.4 Hz), 7.6 (dd, 2H, J_a = 8.8 and J_b = 6.4 Hz), 7.54 (d, 1H, J = 2 Hz), 7.44-7.36 (m, 2H), 3.30 (d, 1H, J = 6.4 Hz), 2.72-2.69 (m, 1H), 1.69-1.66 (m, 2H), 1.61 (m, 2H), 1.15-1.03 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 141.3, 137.2, 135.3, 133.2, 133.0, 131.4, 129.6, 127.6, 123.4, 118.1, 117.3, 56.8, 33.8, 25.4, 25.5. HR-MS (ESI+) m/z calculated for $[C_{19}H_{20}N_5O_4]^+ = [M+H]^+$: 382.1510; found: 382.1502.



8-(Benzyloxy)-*N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyridin-3-amine (4m): Viscous brown oil (85%). IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3319 (NH), 2929 (sp^2-CH), 2853 (sp^3-CH), 1649, 1544, 1448, 1370 (CN), 1313, 1273, 1117, 1070 (C-O-C), 733, 694. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.10-8.06 (m, 2H), 7.73 (d, 1H, J = 6.4 Hz), 7.54-7.48 (m, 2H), 7.47-7.42 (m, 2H), 7.39-7.35 (m, 3H), 7.33-7.29 (m, 2H), 6.59 (t, 1H, J = 7.3 Hz), 6.4 (d, 1H, J = 7.3 Hz), 5.4 (s, 2H), 2.96-2.92 (m, 1H), 1.82-1.74 (m, 2H), 1.67 (d, 3H, J = 4.4 Hz), 1.25-1.20 (m, 3H), 1.15-1.13 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 147.5, 136.3, 134.2, 128.2, 128.0, 127.6, 127.0, 126.9, 126.8, 125.5, 115.7, 110.9, 102.1, 56.6, 33.9, 25.4, 24.5. HR-MS (ESI+) m/z calculated for $[C_{26}H_{27}N_3O]^+ = [M+H]^+$: 398.2227; found: 398.2221.

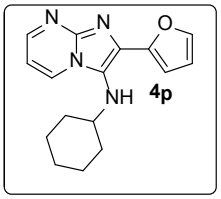


***N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyrimidin-3-amine (4n):**[8] Brown color solid (86%), Mp 162-163 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3317 (NH), 2927 (sp^2-CH), 2852 (sp^3-CH), 1612, 1560, 1475, 1447, 1318 (CN), 1193, 803, 763. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.5 (dd, 1H, J_a = 4.2 and J_b = 2.2 Hz), 8.43 (dd, 1H, J_a = 6.8 and J_b = 2 Hz), 8.3 (d, 2H, J = 4.9 Hz), 8.11 (d, 2H, J = 7.3 Hz), 7.48 (t, 2H, J = 7.6 Hz), 7.38-7.34 (m, 1H), 6.85 (dd, 1H, J_a = 6.8 and J_b = 3.9 Hz), 6.63 (t, 1H, 4.9Hz), 5.02 (br s, 1H), 3.16 (br s, 1H), 3.00 (d, 1H, 3.4 Hz), 1.82 (d, 2H, 10.8 Hz), 1.72 (br s, 2H), 1.31-1.16 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 143.2, 138.9, 136.7, 133.5, 128.9, 128.7, 127.3, 126.6, 56.9, 34.9, 25.6, 24.8. . HR-MS (ESI+) m/z calculated for $[C_{18}H_{21}N_4]^+ = [M+H]^+$: 293.1761; found: 293.1750.

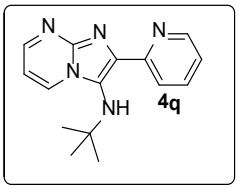


***N*-cyclohexyl-2-(4-nitrophenyl)imidazo[1,2-*a*]pyrimidin-3-amine (4o):** Yellow solid (94%), decomposed at 242 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3202 (NH), 2920 (sp^2-CH), 2849

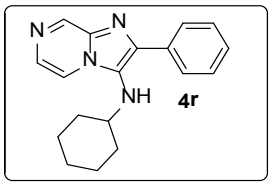
(sp^3-CH), 1595, 1511 (NO_2), 1340 (CN), 1312, 1237, 1109, 863, 720. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.55 (dd, 1H, J_a = 4.2 and J_b = 2.2 Hz), 8.4 (dd, 1H, J_a =6.8 and J_b = 2.5 Hz), 8.39-8.36 (m, 2H), 8.31-8.29 (m, 2H), 6.89 (dd, 1H, J_a = 6.8 and J_b = 3.9 Hz), 3.15 (d, 1H, J = 4.9 Hz), 3.02-2.96 (m, 1H), 1.83 (d, 2H, J = 12.7 Hz), 1.74-1.72 (m, 2H), 1.66-1.61 (m, 2H), 1.32-1.25 (m, 2H), 1.22-1.14 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 150.1, 140.1, 130.1, 127.0, 123.5, 108.2, 57.0, 33.9, 25.2, 24.4. HR-MS (ESI+) m/z calculated for $[C_{18}H_{20}N_5O_2]^+$ = $[M+H]^+$: 338.1612; found: 338.1608.



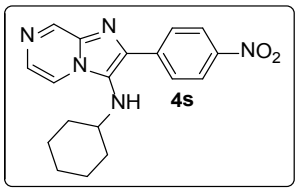
***N*-cyclohexyl-2-(furan-2-yl)imidazo[1,2-*a*]pyrimidin-3-amine (4p):** Brown solid (90%), Mp 118-120 ^{o}C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3269 (CN), 2925 (sp^2-CH), 2851 (sp^3-CH), 1627, 1536, 1498, 1359 (CN), 1322, 1239, 1007, 762, 734. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.45 (dd, 1H, J_a = 4.2 and J_b = 2.2 Hz), 8.33 (dd, 1H, J_a = 6.8 and J_b = 2.0 Hz), 7.51 (dd, 1H, J_a = 1.0 and J_b = 1 Hz), 7.00 (d, 1H, J = 3.4 Hz), 6.81 (dd, 1H, J_a = 6.6 and J_b = 4.2 Hz), 6.56-6.53 (m, 1H), 3.68 (br s, 1H), 2.97-2.93 (m, 1H), 1.89-1.86 (m, 2H), 1.73 (dd, 2H, J_a = 9 and J_b = 3.2 Hz), 1.29-1.12 (m, 6H) . ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 150.1, 149.1, 144.9, 142.0, 130.8, 129.8, 123.8, 111.8, 108.1, 107.9, 57.4, 34.1, 25.7, 24.9. HR-MS (ESI+) m/z calculated for $[C_{16}H_{19}N_4O]^+$ = $[M+H]^+$: 283.1553; found: 283.15329.



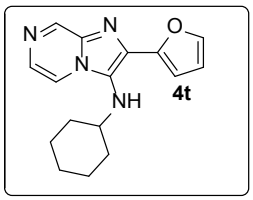
***N*-(*tert*-butyl)-2-(pyridine-2-yl)imidazo[1,2-*a*]pyrimidin-3-amine (4q):** Viscous yellow oil (85%). IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3308 (NH), 2957 (sp^2-CH), 2922, 2852 (sp^3-CH), 1575, 1435, 1331 (CN), 1219, 1039, 754. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.68 (d, 1H, J = 3.4 Hz), 8.61 (d, 1H, J = 6.4 Hz), 8.52 (d, 1H, J = 2 Hz), 8.36-8.33 (m, 1H), 7.88 (t, 1H, J = 7.6 Hz), 6.87 (dd, 1H, J_a = 6.8 and J_b = 4.4 Hz), 5.59-5.53 (m, 2H), 1.1 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 152.9, 150.4, 147.4, 144.4, 137.9, 134.6, 132.0, 129.0, 127.2, 122.9, 122.7, 108.3, 57.2, 29.9. HR-MS (ESI+) m/z calculated for $[C_{15}H_{18}N_5]^+$ = $[M+H]^+$: 268.1557; found: 268.15384.



***N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyrazin-3-amine (4r):**[9] Off-white solid (95%), Mp 141-142 °C**.** IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3245 (NH), 2923 (sp^2-CH), 2850 (sp^3-CH), 1495, 1443, 1353 (CN), 1317, 1186, 768, 690. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.98 (s, 1H), 8.0 (d, 3H, 6.8 Hz), 7.84 (d, 1H, J = 4.4 Hz), 7.49-7.46 (m, 2H), 7.39-7.35 (m, 1H), 3.29 (br s, 1H), 3.00 (br s, 1H), 1.81 (d, 2H, J = 10.3 Hz), 1.71-1.69 (m, 2H), 1.28-1.13 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 143.2, 138.9, 136.7, 133.5, 128.9, 128.7, 127.3, 126.6, 56.9, 34.9, 25.6, 24.8. HR-MS (ESI+) m/z calculated for $[C_{18}H_{21}N_4]^+ = [M+H]^+$: 293.1761; found: 293.1754.

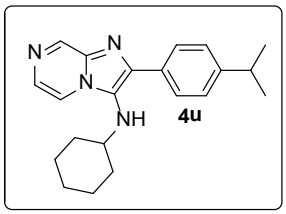


***N*-cyclohexyl-2-(4-nitrophenyl)imidazo[1,2-*a*]pyrazin-3-amine (4s):** Olive solid (94%), Mp 221-222 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3250 (NH), 2925 (sp^2-CH), 2852 (sp^3-CH), 1597, 1513 (NO_2), 1341 (CN), 1315 (NO_2), 1202, 1109, 859, 721. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 9.02 (d, 1H, J = 1.5 Hz), 8.35-8.30 (m, 4H), 7.98 (dd, 1H, J_a = 4.9 and J_b = 1.5 Hz), 7.89 (d, 1H, J = 4.4 Hz), 3.17 (d, 1H, J = 4.9), 3.0-3.01 (m, 1H), 1.84 (d, 2H, J = 12.2 Hz), 1.73 (dd, 2H, J_a = 8.6 and J_b = 3.2 Hz), 1.32-1.15 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 146.8, 143.9, 139.8, 136.8, 136.1, 129.1, 127.3, 123.7, 115.1, 56.9, 34.1, 25.1, 24.5. HR-MS (ESI+) m/z calculated for $[C_{18}H_{20}N_5O_2]^+ = [M+H]^+$: 338.1612; found: 338.1605.

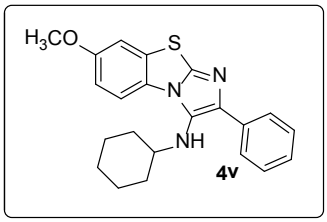


***N*-cyclohexyl-2-(furan-2-yl)imidazo[1,2-*a*]pyrazin-3-amine (4t):** Light brown solid (91%), Mp 132-134 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3283 (NH), 2966 (sp^2-CH), 2853 (sp^3-CH), 1630, 1501, 1443, 1361 (CN), 1337, 1205, 1027, 751, 698. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.92 (d, 1H, J = 1.5 Hz), 7.97-7.91 (m, 1H), 7.81 (d, 1H, J = 4.9 Hz), 7.52 (d, 1H, J = 2 Hz), 6.93 (dd, 1H, J_a = 3.4 and J_b = 1 Hz), 6.54 (dd, 1H, J_a = 3.4 and J_b = 2 Hz), 3.77 (br s, 1H), 4.3 (br s, 1H), 1.88-1.85 (m, 2H), 1.73 (dd, 2H, J_a = 9.3 and J_b = 3.4 Hz), 1.33-1.14 (m, 6H). ^{13}C

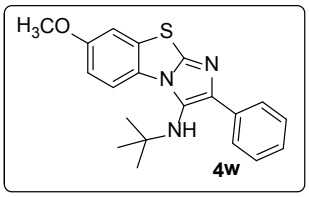
NMR ($CDCl_3$, 100 MHz): δ_C = 149.6, 143.2, 142.2, 137.0, 129.0, 127.0, 115.6, 111.8, 107.8, 56.9, 34.2, 25.6, 24.9. HR-MS (ESI+) m/z calculated for $[C_{16}H_{19}N_4O]^+ = [M+H]^+$: 283.1553; found: 283.1545.



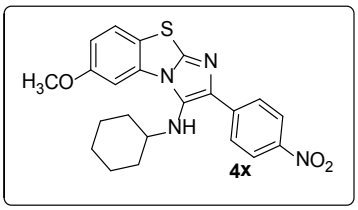
***N*-cyclohexyl-2-(4-isopropylphenyl)imidazo[1,2-*a*]pyrazin-3-amine (4u):** Light brown solid (90%), Mp 108-110 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3248 (NH), 2955 (sp^2-CH), 2924, 2852 (sp^3-CH), 1546, 1500, 1448, 1349 (CN), 1287, 1198, 841, 731. ^1H NMR ($CDCl_3$, 400 MHz): δ_H = 8.97 (d, 1H, J = 1.5 Hz), 8.0-7.98 (m, 1H), 7.95-7.93 (m, 2H), 7.83 (d, 1H, J = 4.9), 7.34 (d, 2H, J = 8.3 Hz), 3.22 (br s, 1H), 3.03 (br s, 1H), 2.96 (sept, 1H, J = 6.8 Hz), 1.83 (d, 2H, J = 10.3 Hz), 1.71 (dd, 2H, J_a = 8.8 and J_b = 2.9 Hz), 1.3 (d, 6H, J = 6.8 Hz), 1.25-1.12 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C =149.0, 143.1, 139.0, 136.7, 131.0, 128.9, 127.2, 126.9, 126.3, 115.5, 56.9, 34.3, 33.9, 29.7, 25.6, 24.8, 23.9. HR-MS (ESI+) m/z calculated for $[C_{21}H_{27}N_4]^+ = [M+H]^+$: 335.2230; found: 335.2230.



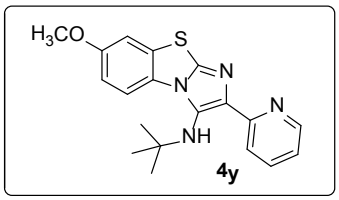
***N*-cyclohexyl-6-methoxy-2-phenylbenzo[*d*]imidazo[2,1-*b*]thiazol-3-amine (4v):** Reddish orange solid (90%), Mp 60-62 °C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3305 (NH), 2928 (sp^2-CH), 2852 (sp^3-CH), 1663, 1600, 1570, 1545, 1468, 1446, 1396 (CN), 1262, 1178, 1027 (C-O-C), 828, 700. ^1H NMR ($CDCl_3$, 400 MHz): δ_H = 7.95 (d, 1H, J = 8.8), 7.88 (dd, 2H, J_a = 8.3 and J_b = 1 Hz), 7.43-7.39 (m, 2H), 7.28-7.24 (m, 1H), 7.16 (d, 1H, J = 2.4), 6.97 (dd, 1H, J_a = 8.8 and J_b = 2.4 Hz), 3.86 (s, 3H), 3.18 (br s, 1H), 2.94 (br s, 1H), 1.89 (d, 2H, J = 10.3 Hz), 1.68-1.66 (m, 2H), 1.26-1.11 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 156.6, 142.8, 137.4, 134.7, 131.6, 129.3, 128.5, 127.5, 126.6, 126.3, 114.3, 112.8, 108.5, 57.4, 55.9, 33.7, 25.8, 24.9. HR-MS (ESI+) m/z calculated for $[C_{22}H_{24}N_3OS]^+ = [M+H]^+$: 378.1635; found: 378.1616.



***N*-(*tert*-butyl)-6-methoxy-2-phenylbenzo[*d*]imidazo[2,1-*b*]thiazol-3-amine (4w):** Off-white solid (90%), Mp 147-152 ^{o}C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3284 (NH), 2964 (sp^2-CH) 2964, 2922 (sp^3-CH), 2852, 1602, 1550, 1490, 1440, 1364 (CN), 1298, 1230, 1192, 1066, 1026 (C-O-C), 907, 728, 695. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.21 (d, 1H, J = 8.8 Hz), 7.76-7.73 (m, 2H), 7.41-7.37 (m, 2H), 7.29-7.24 (m, 1H), 7.16 (d, 1H, J = 2.4 Hz), 6.96 (dd, 1H, J_a = 9 and J_b = 2.7 Hz), 3.85 (s, 3H), 3.17 (br s, 1H), 1.03 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 156.6, 143.3, 140.6, 135.4, 131.6, 128.3, 127.9, 127.7, 126.9, 115.1, 112.3, 108.3, 56.5, 55.8, 29.9. HR-MS (ESI+) m/z calculated for $[C_{20}H_{22}N_3OS]^+ = [M+H]^+$: 352.1478; found: 352.1469.

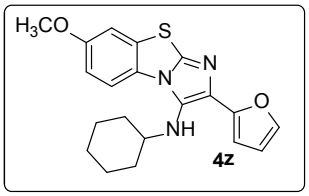


***N*-cyclohexyl-6-methoxy-2-(4-nitrophenyl)benzo[*d*]imidazo[2,1-*b*]thiazol-3-amine (4x):** Orange solid (95%), Mp 180-190 ^{o}C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3334 (NH), 2926 (sp^2-CH), 2851 (sp^3-CH), 1594, 1492 (NO_2), 1332 (CN), 1265, 1232, 1108, 1035 (C-O-C), 853, 707. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.17-8.14 (m, 2H), 8.09-8.04 (m, 2H), 7.79 (d, 1H, J = 8.8 Hz), 7.15 (d, 1 H, J = 2.4 Hz), 6.97 (dd, 1H, J_a = 8.8 and J_b = 2.4 Hz), 3.81 (s, 3H), 3.12 (d, 1H, J = 4.4 Hz), 2.94-2.92 (m, 1H), 1.87 (d, 2H, J = 12.7 Hz), 1.70-1.68 (m, 2H), 1.26-1.19 (m, 4H), 1.16-1.2 (m, 2H) . ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 157.1, 145.7, 144.0, 141.1, 135.5, 131.7, 130.9, 126.9, 126.0, 123.8, 114.2, 113.1, 108.7, 57.4, 55.9, 33.8, 32.6, 25.6, 24.9, 22.6, 14.1. HR-MS (ESI+) m/z calculated for $[C_{22}H_{23}N_4OS]^+ = [M+H]^+$: 423.1485; found: 423.1474.



***N*-(*tert*-butyl)-6-methoxy-2-(pyridin-2-yl)benzo[*d*]imidazo[2,1-*b*]thiazol-3-amine (4y):** Reddish brown solid (90%), Mp 120-122 ^{o}C. IR (MIR-ATR, 4000-600 cm^{-1}): υ_{max} = 3302

(NH), 3054 (sp^2-CH), 2964, 2219 (sp^3-CH), 1588, 1541, 1498, 1473, 1435, 1364 (CN), 1263, 1230, 1197, 1165, 1039 (C-O-C), 907, 728, 645. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.49 (d, 1H, J = 4.9 Hz), 8.23 (dd, 1H, J_a = 9.3 and J_b = 1 Hz), 7.94 (d, 1H, J =7.8 Hz), 7.70-7.66 (m, 1H), 7.11-7.05 (m, 2H), 6.92 (dd, 1H, J_a = 8.8 and J_b = 2.4 Hz), 5.02 (br s, 1H), 3.8 (s, 3H), 1.05 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 156.8, 154.9, 148.2, 143.0, 136.5, 136.4, 133.2, 131.6, 127.8, 121.0, 120.3, 115.9, 112.3, 108.3, 57.2, 55.8, 29.5. HR-MS (ESI+) m/z calculated for $[C_{19}H_{21}N_4OS]^+ = [M+H]^+$: 353.1431; found: 353.14054.

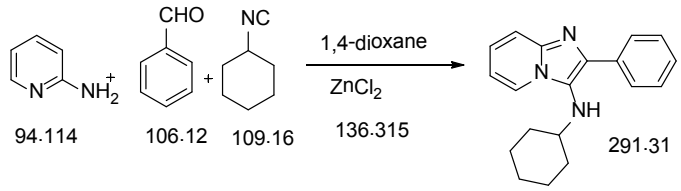


***N*-cyclohexyl-2-(furan-2-yl)-6-methoxybenzo[*d*]imidazo[2,1-*b*]thiazol-3-amine (4z)**: Viscous brown oil (81%). IR (MIR-ATR, 4000-600 cm-1): υ_{max} = 3353 (NH), 2923 (sp^2-CH), 2851 (sp^3-CH), 1603, 1543, 1496, 1462, 1348 (CN), 1263, 1230, 1167, 1040 (C-O-C), 805, 730. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 7.89 (dd, 1H, J_a = 9.3 and J_b = 1.5 Hz), 7.42 (d, 1H, J = 1.5 Hz), 7.15 (s, 1H), 6.99-6.96 (m, 1H), 6.65-6.64 (m, 1H), 6.49-6.48 (m, 1H), 3.85 (s, 3H), 3.63 (m, 1H), 2.96-2.91 (m, 1H), 2.04-1.98 (m, 2H), 1.75-1.73 (m, 2H), 1.33-1.14 (m, 6H) . ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 156.8, 150.4, 143.0, 140.4, 131.6, 129.9, 128.6, 127.1, 114.4, 113.0, 111.3, 108.5, 104.6, 58.0, 55.9, 33.7, 29.7, 25.9, 25.2. HR-MS (ESI+) m/z calculated for $[C_{20}H_{22}N_3O_2S]+ = [M+H]+$: 368.1427; found: 368.1420.

E-Factor and Mass Intensity Calculations

Comparison of present protocol for the synthesis *N*-cyclohexyl-2-phenylimidazo[1,2-*a*] pyridine-3-amine with reported methods

A) Calculation for the synthesis of *N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyridine-3-amine in 1,4-dioxane.[10]



Raw Materials Used		Crude Product and Waste	
2-Aminopyridine	200 mg	Product	482.99 mg
Benzaldehyde	225.50 mg	Waste	3478.96 mg
Cyclohexyl isocyanide	231.96 mg		
$ZnCl_2$	14.48 mg		
1,4-dioxane	3290 mg		
Total	3961.95 mg	Total	3961.95 mg

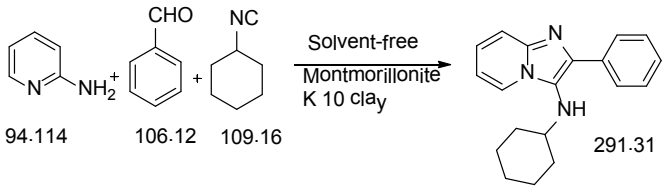
E-Factor (E) = (3478.96 of waste produced / 482.99 of crude product) = 7.20

Mass Intensity = (3961.95 of raw material used / 482.99 of crude product) = 8.20

Considerations**:**

1. Solvent was not recovered, it is considered as waste in calculations.
2. Calculation did not consider organic solvents used for column chromatography.

B) Calculation for the synthesis of *N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyridine-3-amine in presence of Montmorillonite as a catalyst.[11]



Raw Materials Used		Crude Product and Waste	
2-Aminopyridine	200 mg	Product	532.52 mg
Benzaldehyde	225.50 mg	Waste	231.33 mg
Cyclohexyl isocyanide	231.96 mg		
Montmorillonite K10 clay	106.38 mg		
Total	763.85 mg	Total	763.85 mg

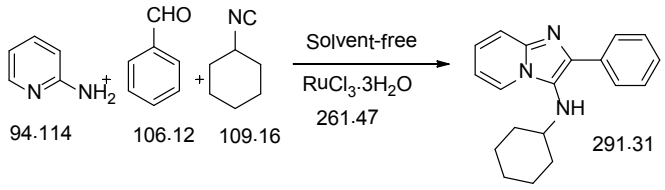
E-Factor (E) = (231.33 of waste produced / 532.52 of crude product) = 0.43

Mass Intensity = (763.85 of raw material used / 532.52 of crude product) = 1.43

Considerations:

1. DCM used for clay wash is not considered in calculations.
2. Calculation did not consider organic solvents used for column chromatography.

C) Calculation for the synthesis of *N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyridine-3-amine in presence of $RuCl_3$ as a catalyst.[13]



Raw Materials Used		Crude Product and Waste	
2-amino-pyridine	200 mg	Product	551.10 mg
Benzaldehyde	225.50 mg	Waste	179.81 mg
Cyclohexyl isocyanide	277.70 mg		
$RuCl_3.3H_2O$	27.71 mg		
Total	730.91 mg	Total	730.91 mg

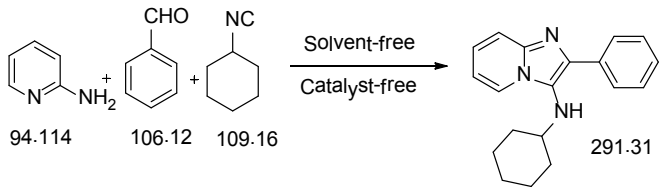
E-Factor (E) = (179.81 of waste produced / 551.10 of crude product) = 0.32

Mass Intensity = (730.91 of raw material used / 551.10 of crude product) = 1.32

Considerations:

1. Ether or petroleum ether used to remove catalyst from reaction mixture is not considered in calculations.
2. Calculation did not consider solvent used for crystallization.

D) Our protocol: Calculation for the synthesis of *N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyridine-3-amine in solvent-free and catalyst-free conditions.



Raw Materials Used		Crude Product and Waste	
2-Aminopyridine	200 mg	Product	600.65 mg
Benzaldehyde	225.50 mg	Waste	56.82 mg
Cyclohexyl isocyanide	231.96 mg		
Total	657.47 mg	Total	657.82 mg

E-Factor (E) = (56.47 of waste produced / 600.65 of crude product) = 0.09

Mass Intensity = (657.82 of raw material used / 600.65 of crude product) = 1.09

Considerations:

1. In calculation did not consider EtOH used in crystallization.

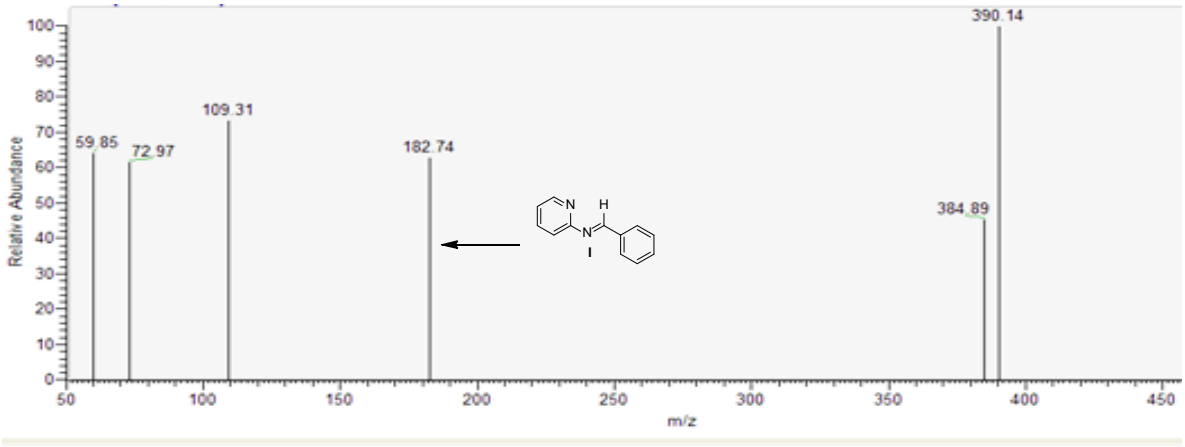
Conclusion:

Among above all the methods our method is very efficient because E-Factor is almost zero and mass intensity is nearly one.

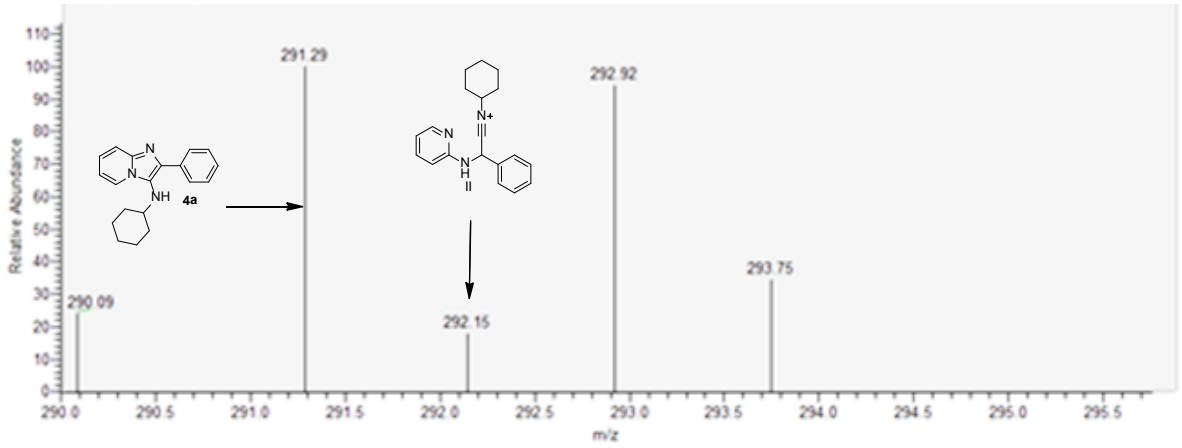
Studies to probe Reaction Course Using GC-MS for the synthesis of *N*-cyclohexyl-2-phenylimidazo[1,2-*a*]pyridine-3-amine (4a):

GC-MS was recorded for the reaction mixture at various time intervals. When the sample was injected after 30 min of commencement of the reaction, it showed the fragment ion peak m/z 182 corresponding to imine **I** (graph A). The sample injected after 90 min showed fragment ion peaks m/z 292 and 291 corresponding to nitrilium ion **II** and product **4a** respectively (graph B). After completion of the reaction (2h), the injected sample showed the fragment ion peak m/z 291 corresponding to product **4a** (graph C).

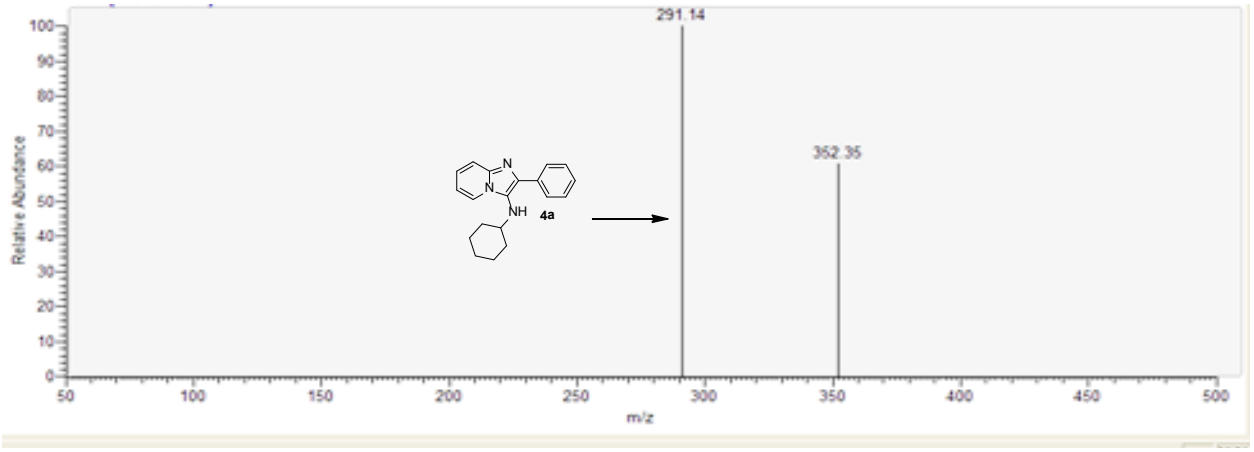
A) GC-MS spectrum for the reaction mixture recorded at 30 minutes.



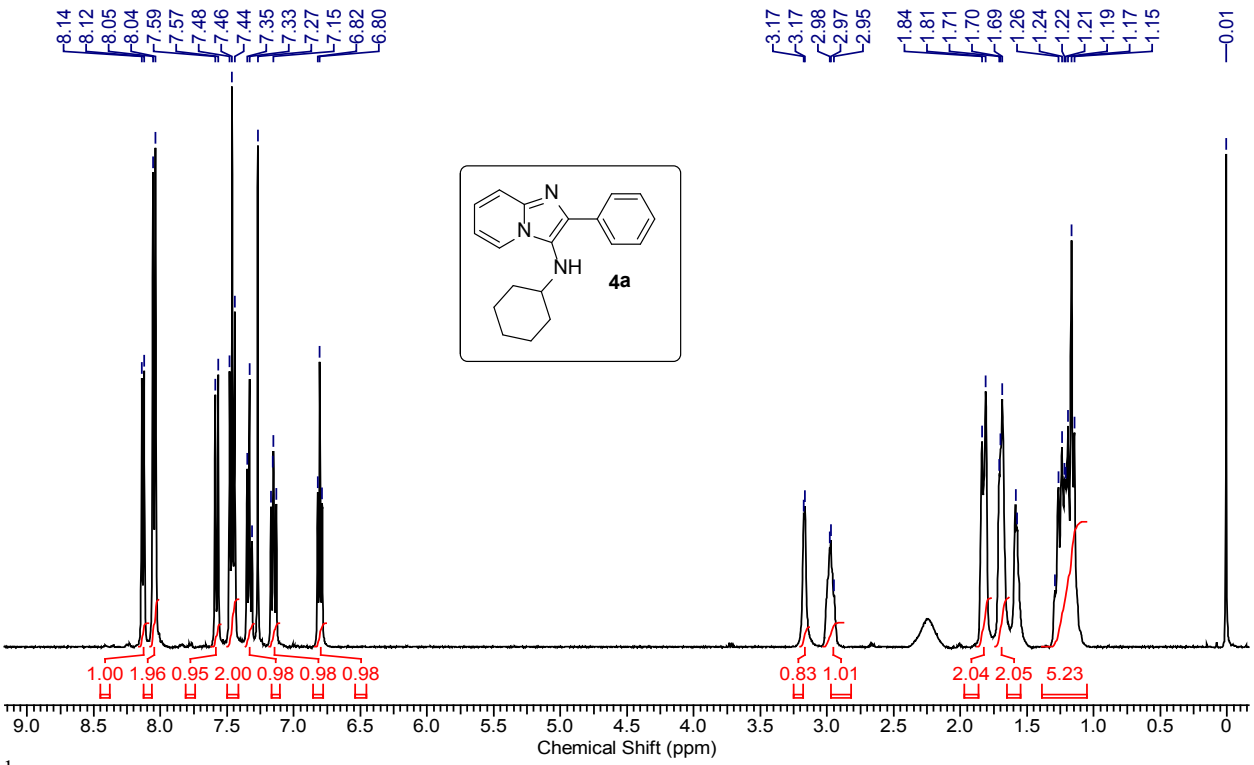
B) GC-MS spectrum for the reaction mixture recorded at 90 minutes.



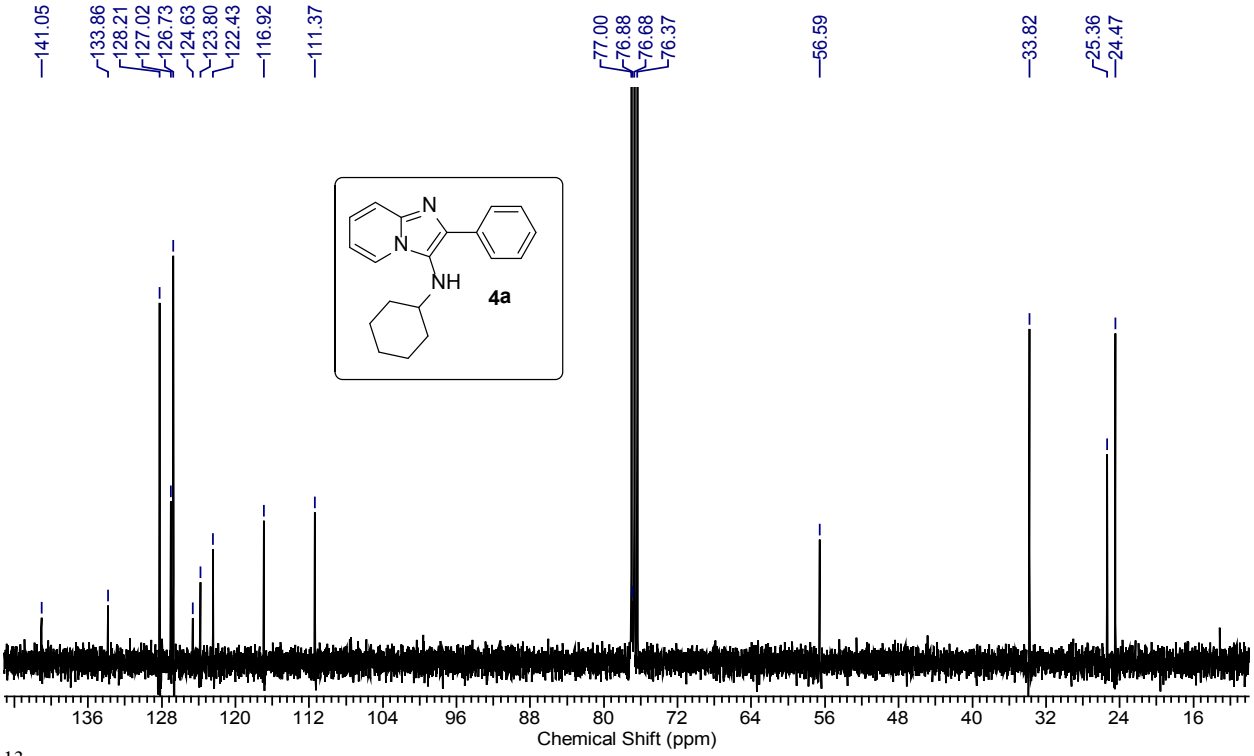
C) GC-MS spectrum for the reaction mixture after 2 hour.



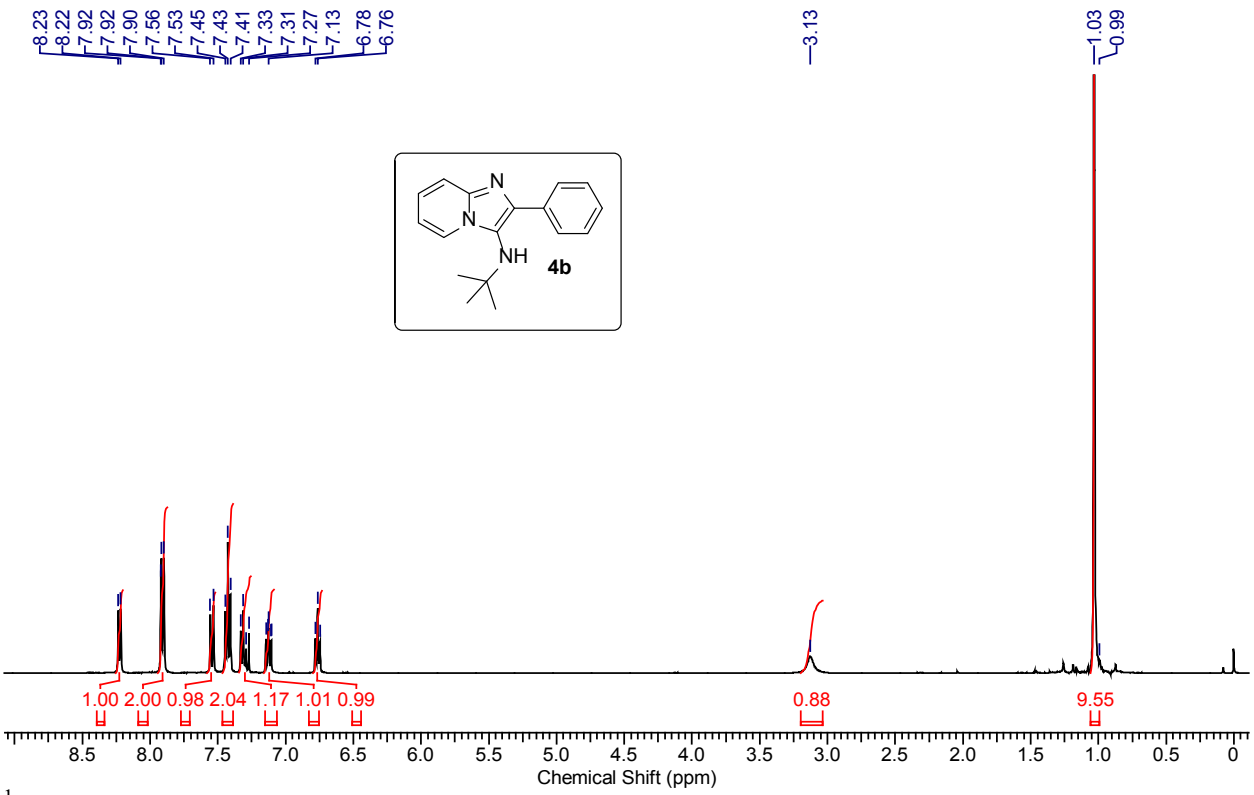
Copies of ^{1}H, ^{13}C NMR Spectra of all Compounds (4a-z)



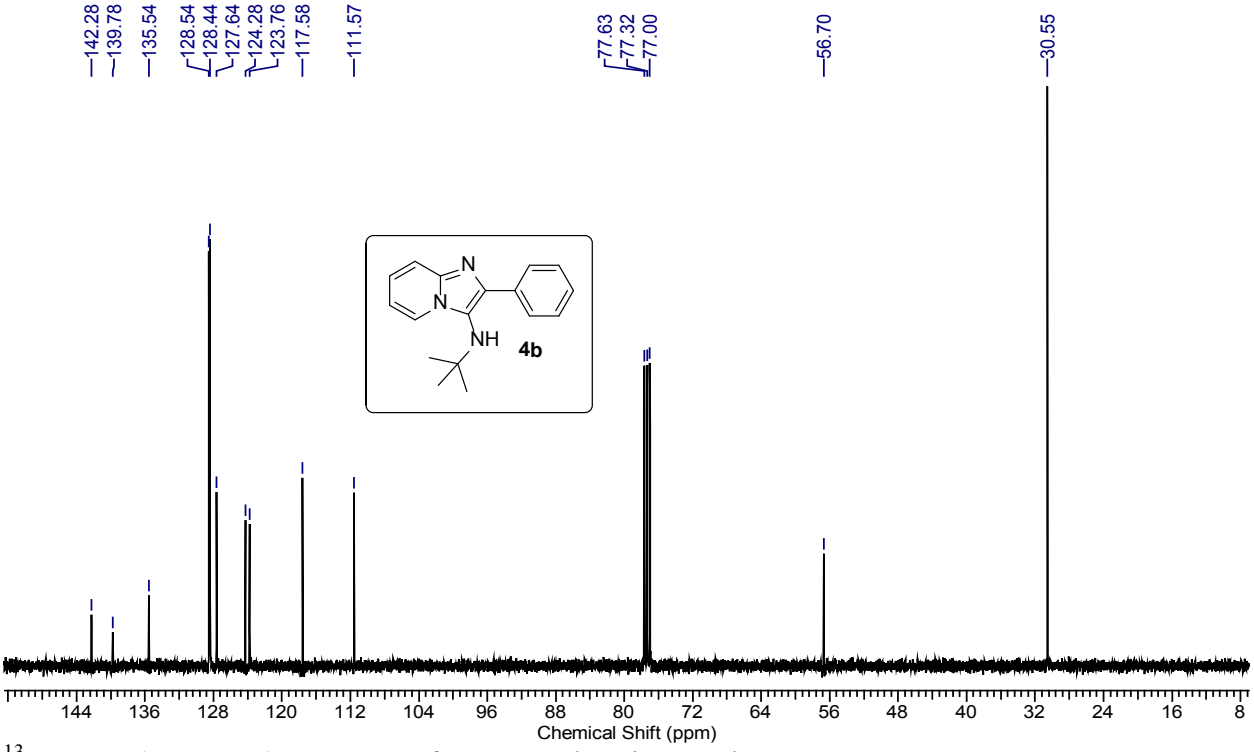
^{1}H NMR (400 MHz) spectrum of compound **4a** in $CDCl_3$



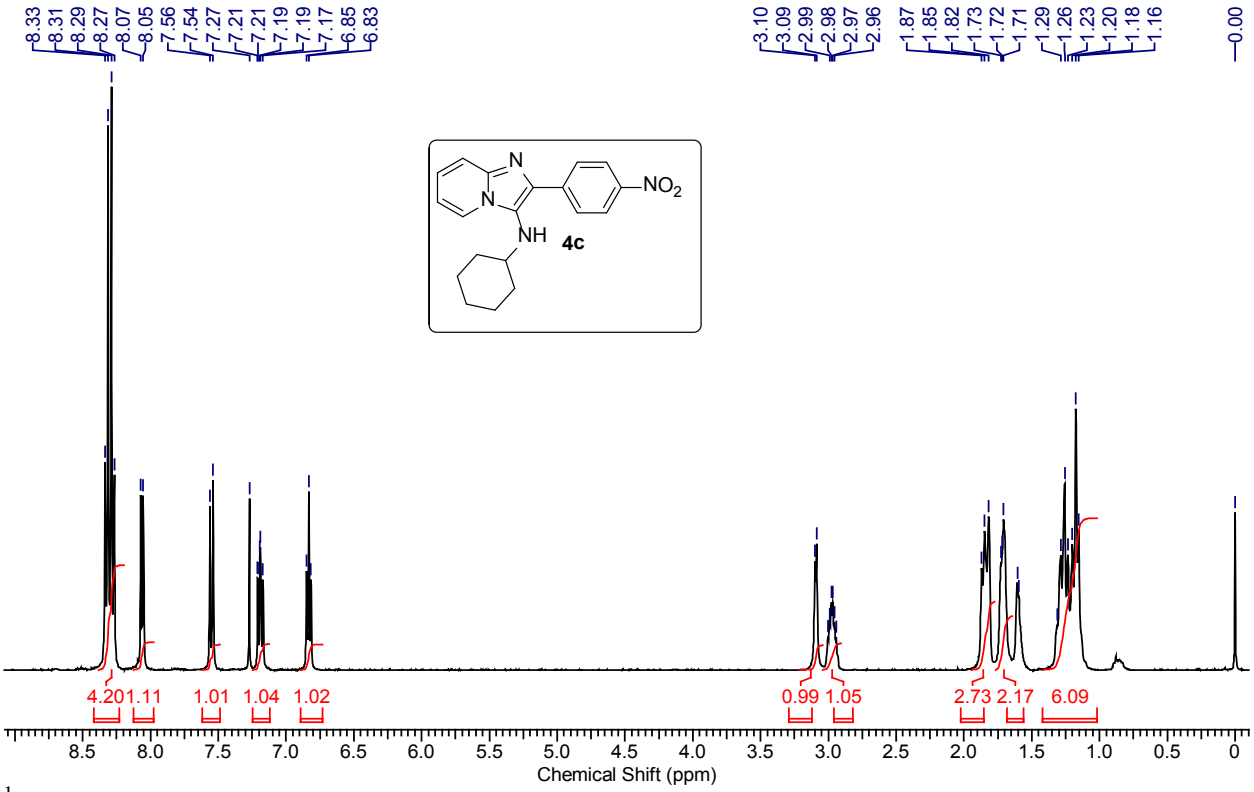
^{13}C NMR (100 MHz) spectrum of compound **4a** in $CDCl_3$



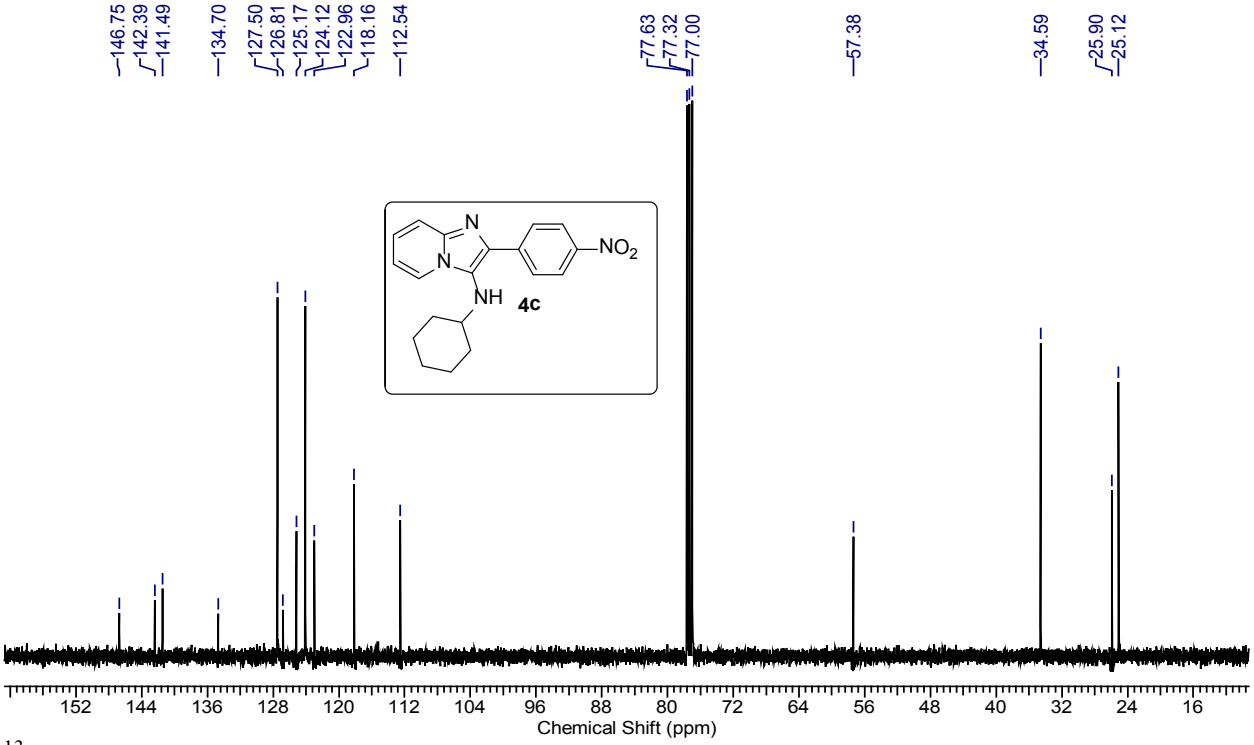
^{1}H NMR (400 MHz) spectrum of compound **4b** in $CDCl_3$



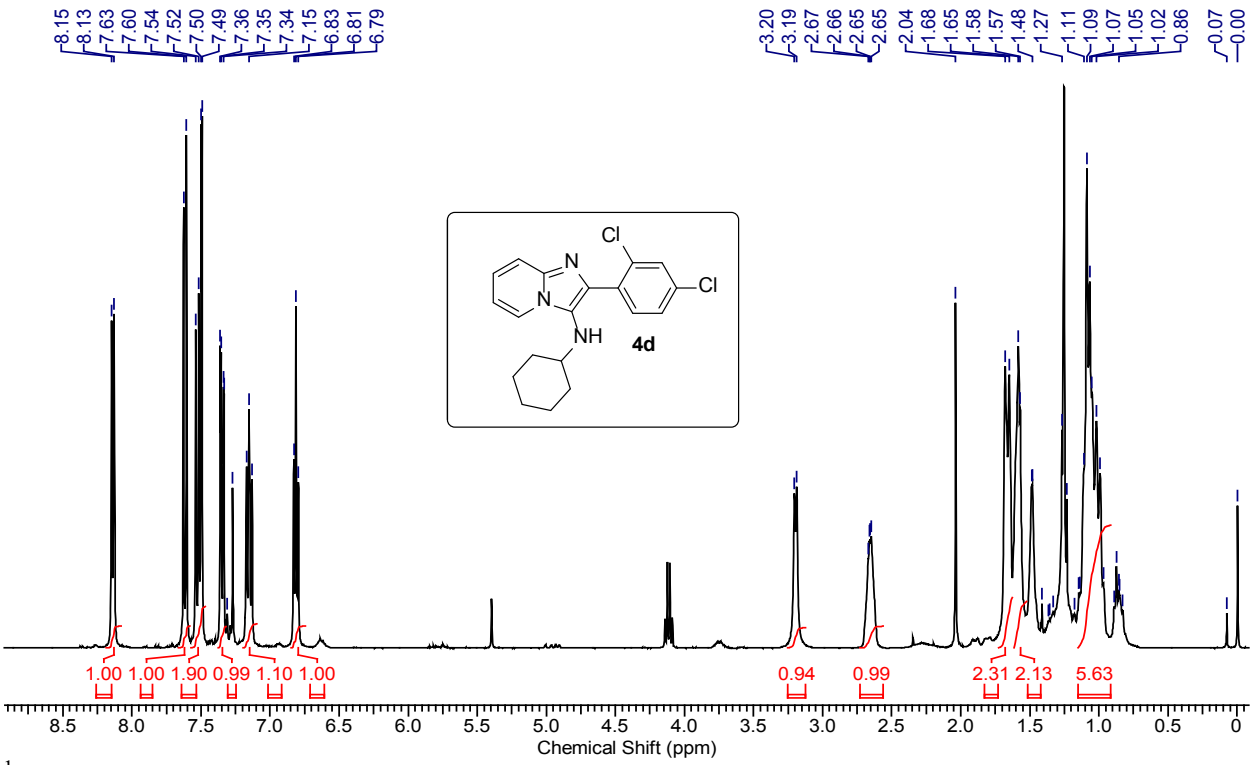
^{13}C NMR (100 MHz) spectrum of compound **4b** in $CDCl_3$



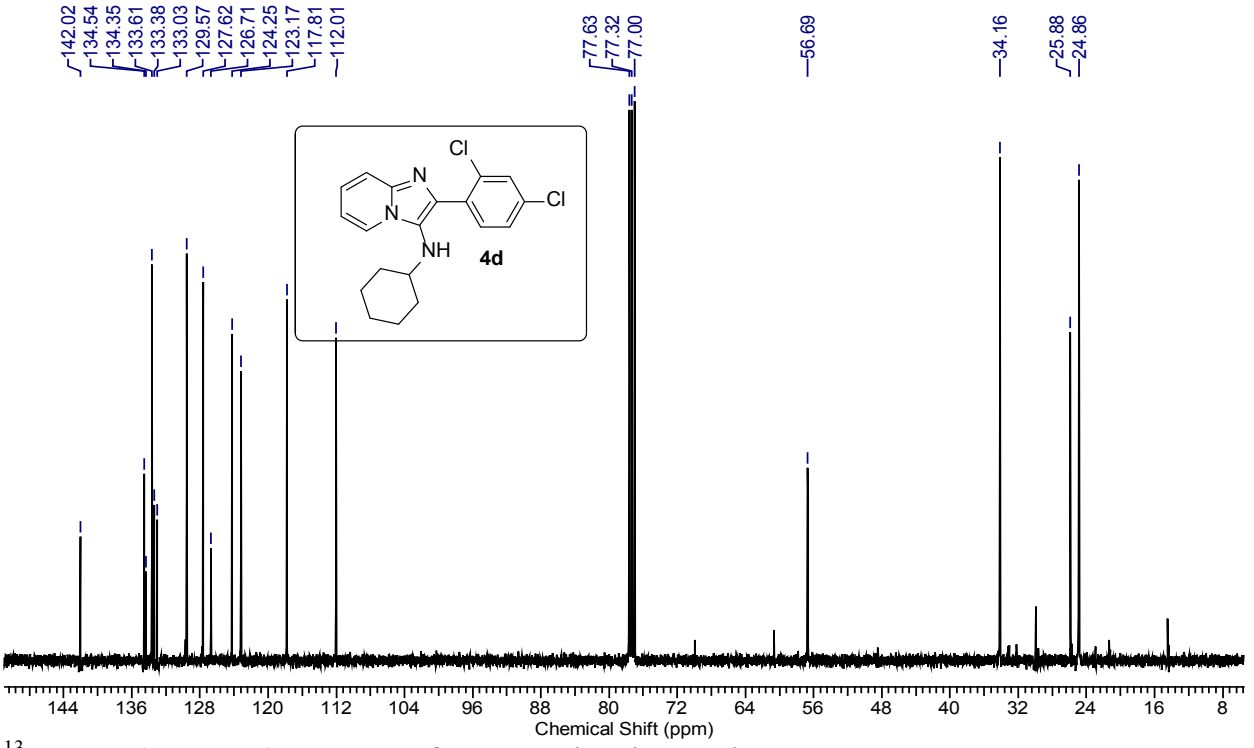
^{1}H NMR (400 MHz) spectrum of compound **4c** in $CDCl_3$



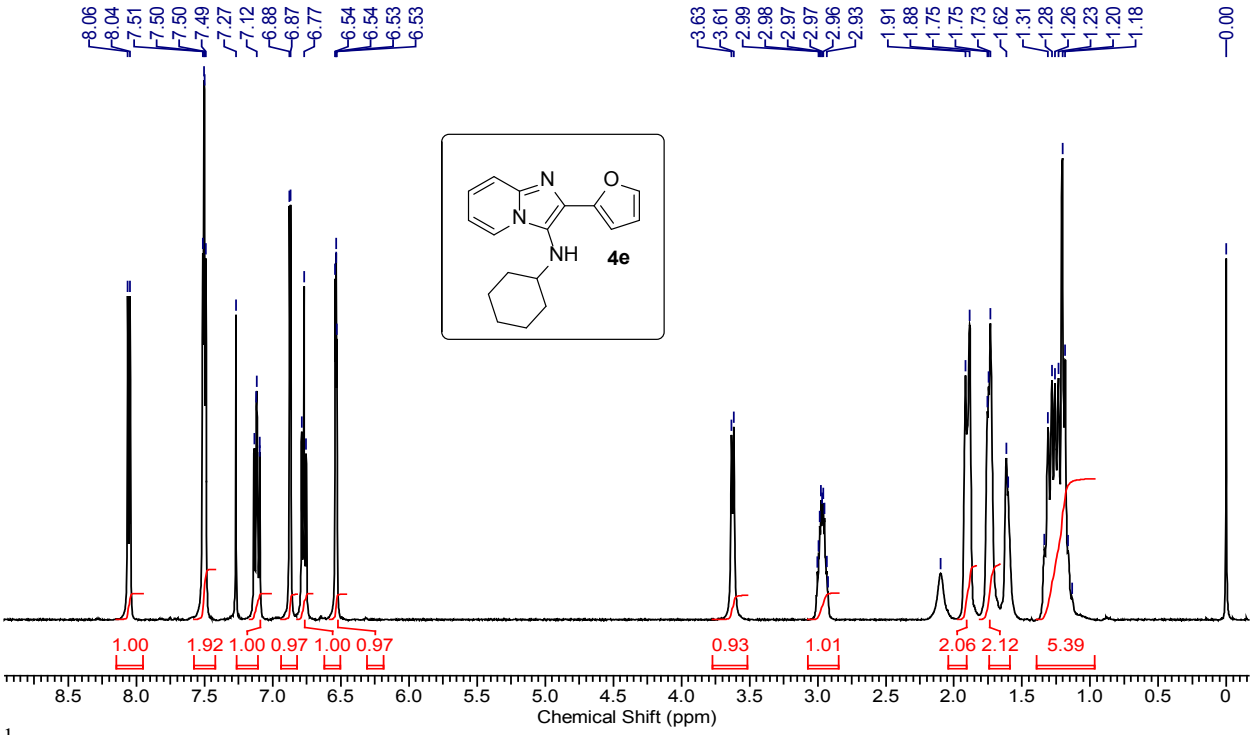
^{13}C NMR (100 MHz) spectrum of compound **4c** in $CDCl_3$



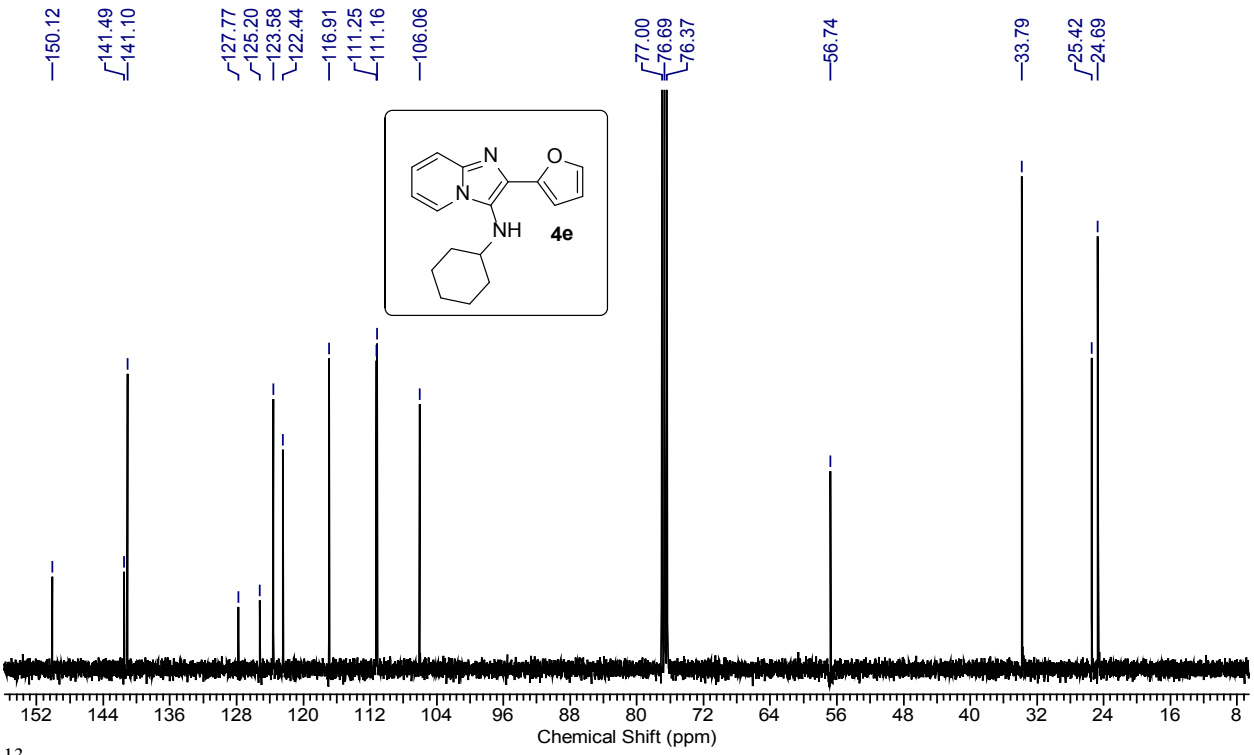
^{1}H NMR (400 MHz) spectrum of compound **4d** in $CDCl_3$



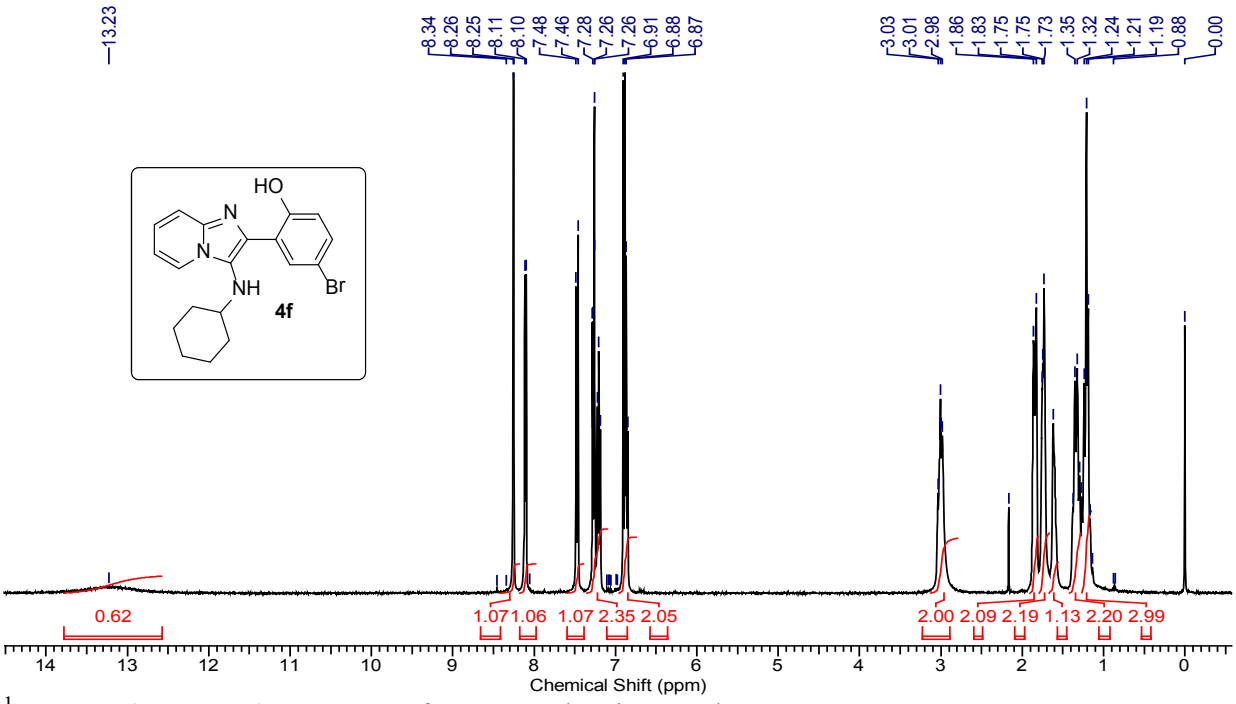
^{13}C NMR (100 MHz) spectrum of compound **4d** in $CDCl_3$



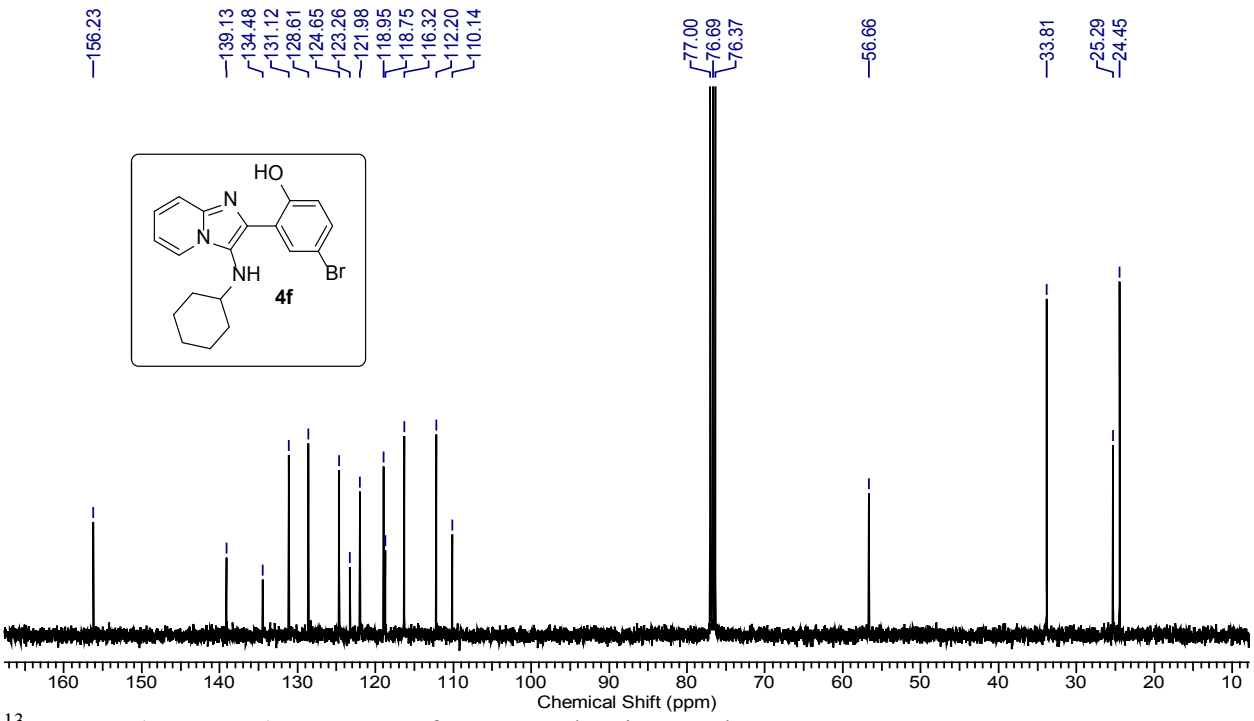
^{1}H NMR (400 MHz) spectrum of compound **4e** in $CDCl_3$



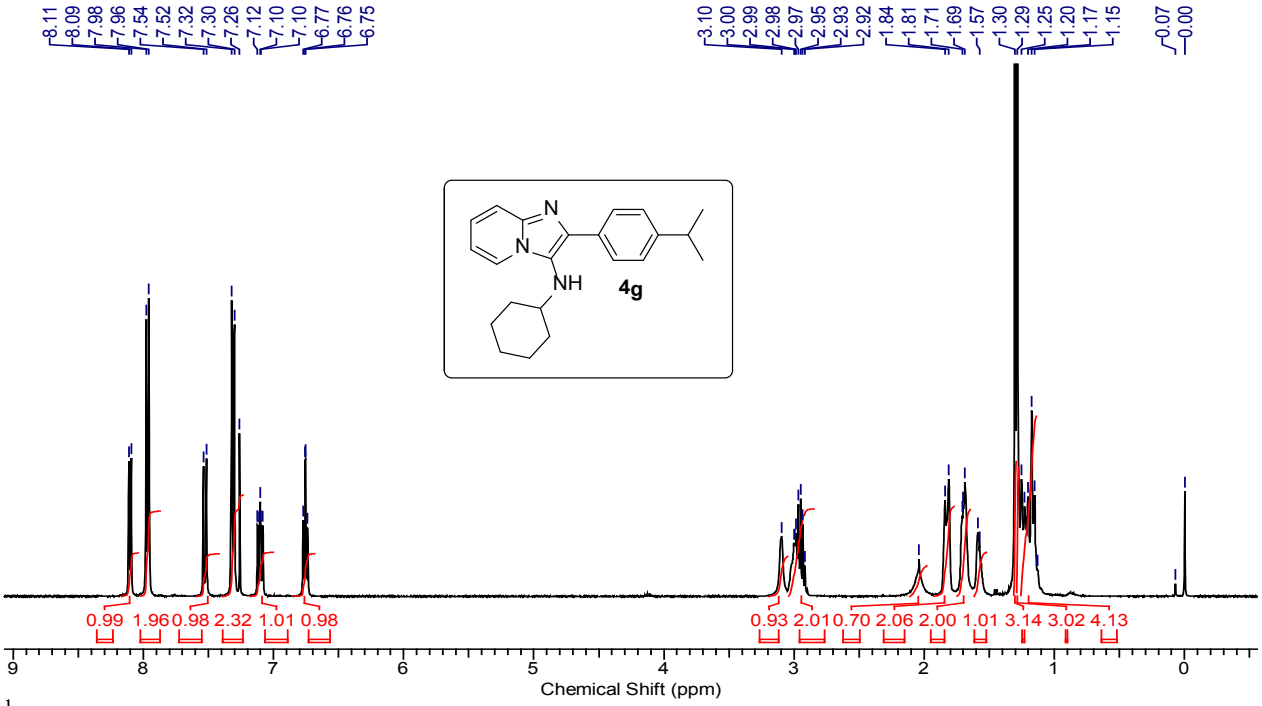
^{13}C NMR (100 MHz) spectrum of compound **4e** in $CDCl_3$



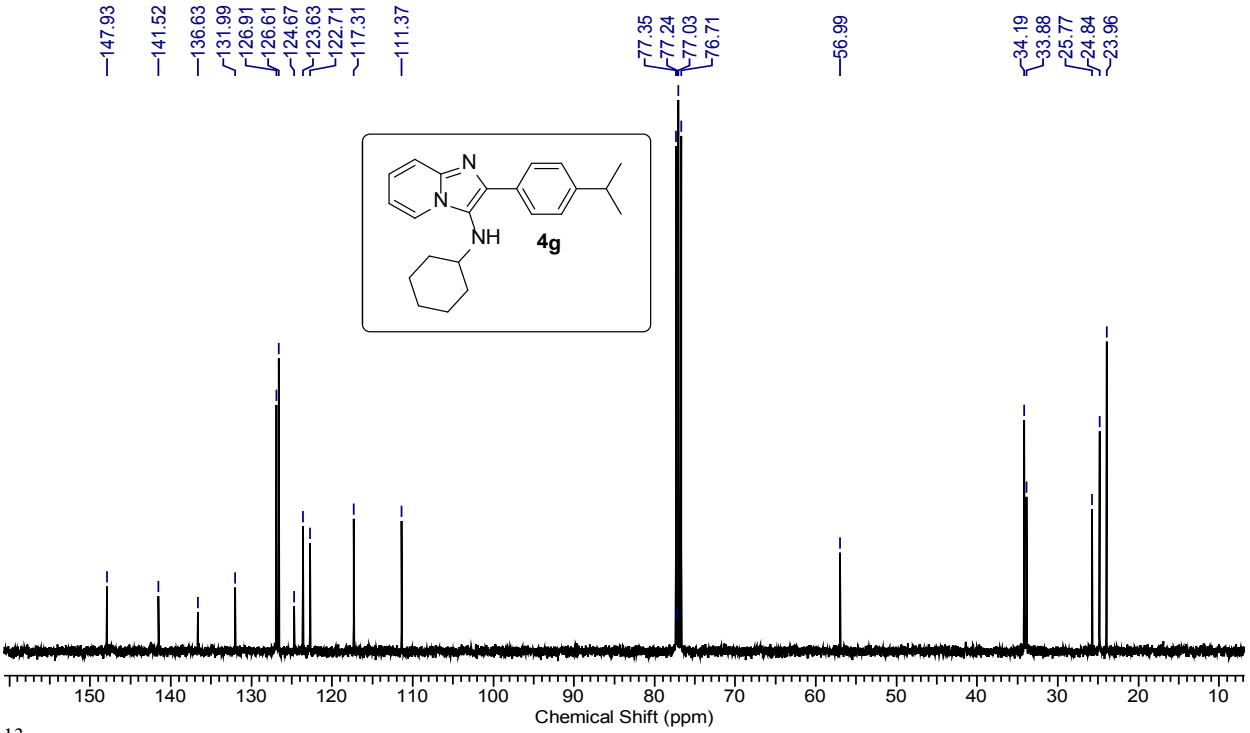
^{1}H NMR (400 MHz) spectrum of compound **4f** in $CDCl_3$



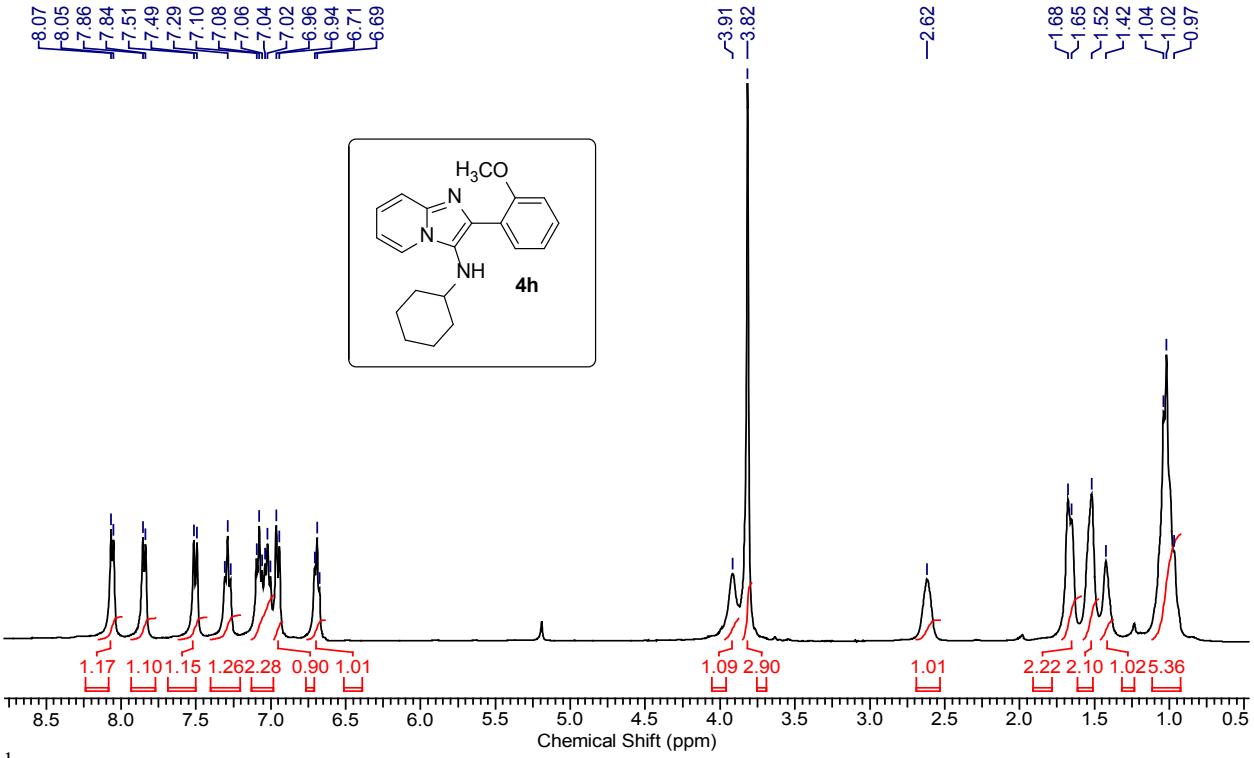
^{13}C NMR (100 MHz) spectrum of compound **4f** in $CDCl_3$



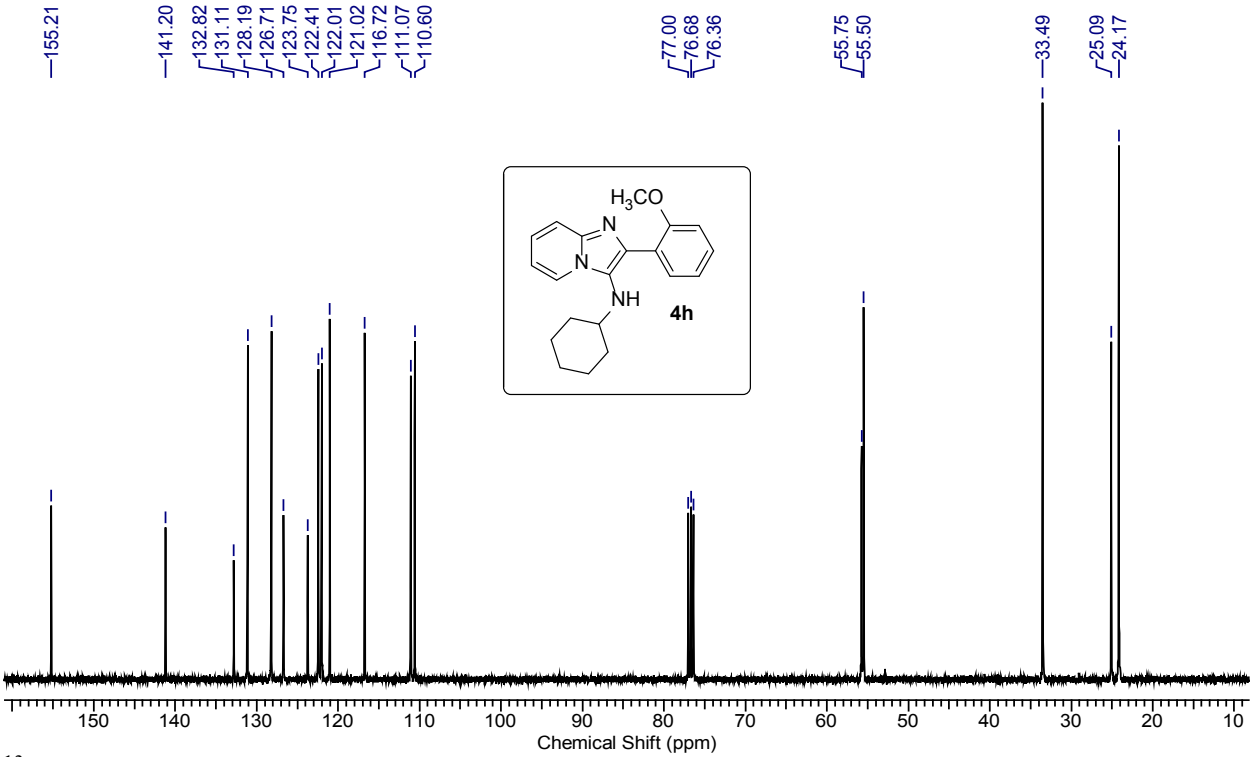
^{1}H NMR (400 MHz) spectrum of compound **4g** in $CDCl_3$



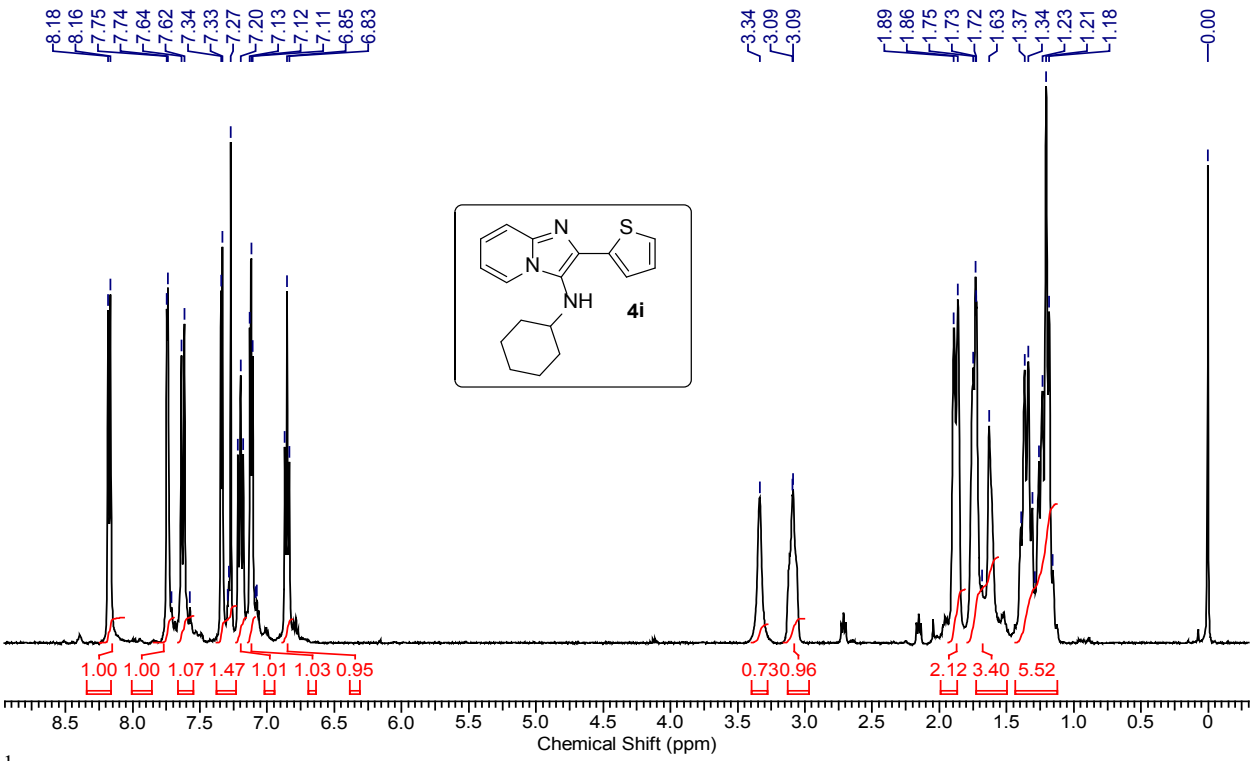
^{13}C NMR (100 MHz) spectrum of compound **4g** in $CDCl_3$



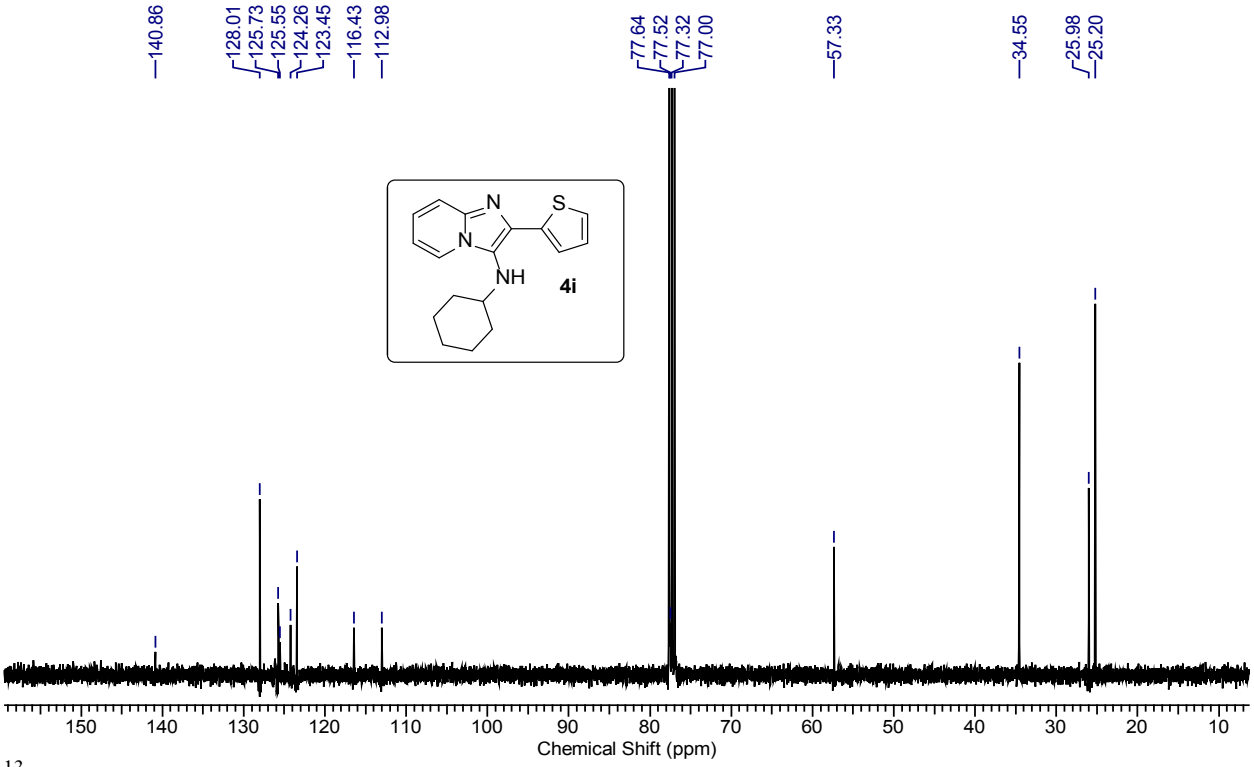
^{1}H NMR (400 MHz) spectrum of compound **4h** in $CDCl_3$



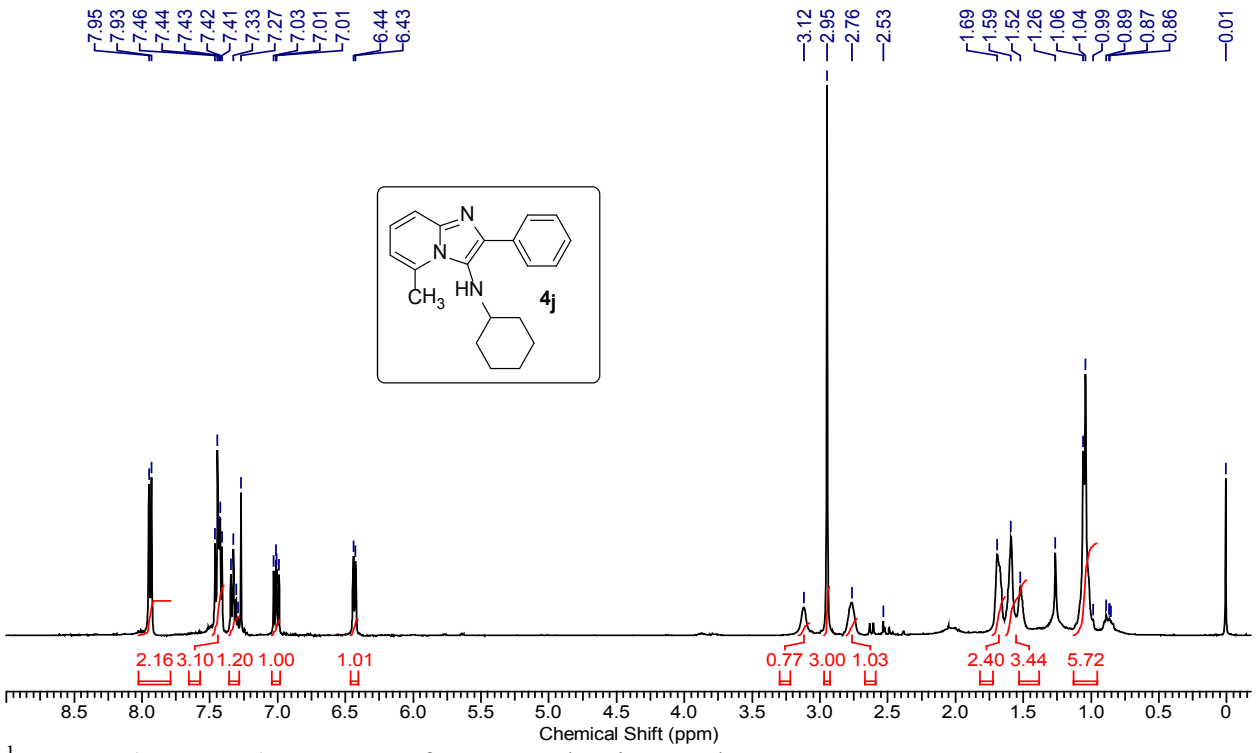
^{13}C NMR (100 MHz) spectrum of compound **4h** in $CDCl_3$



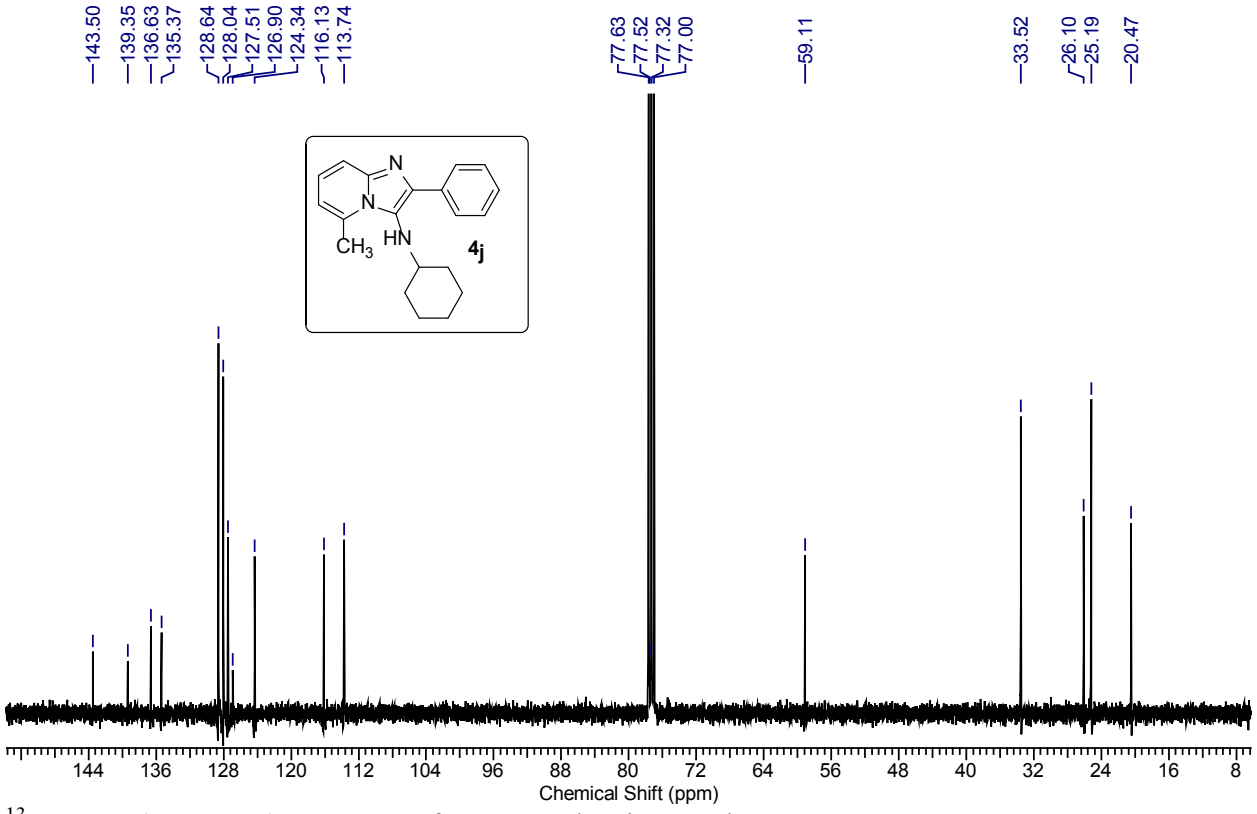
^{1}H NMR (400 MHz) spectrum of compound **4i** in $CDCl_3$



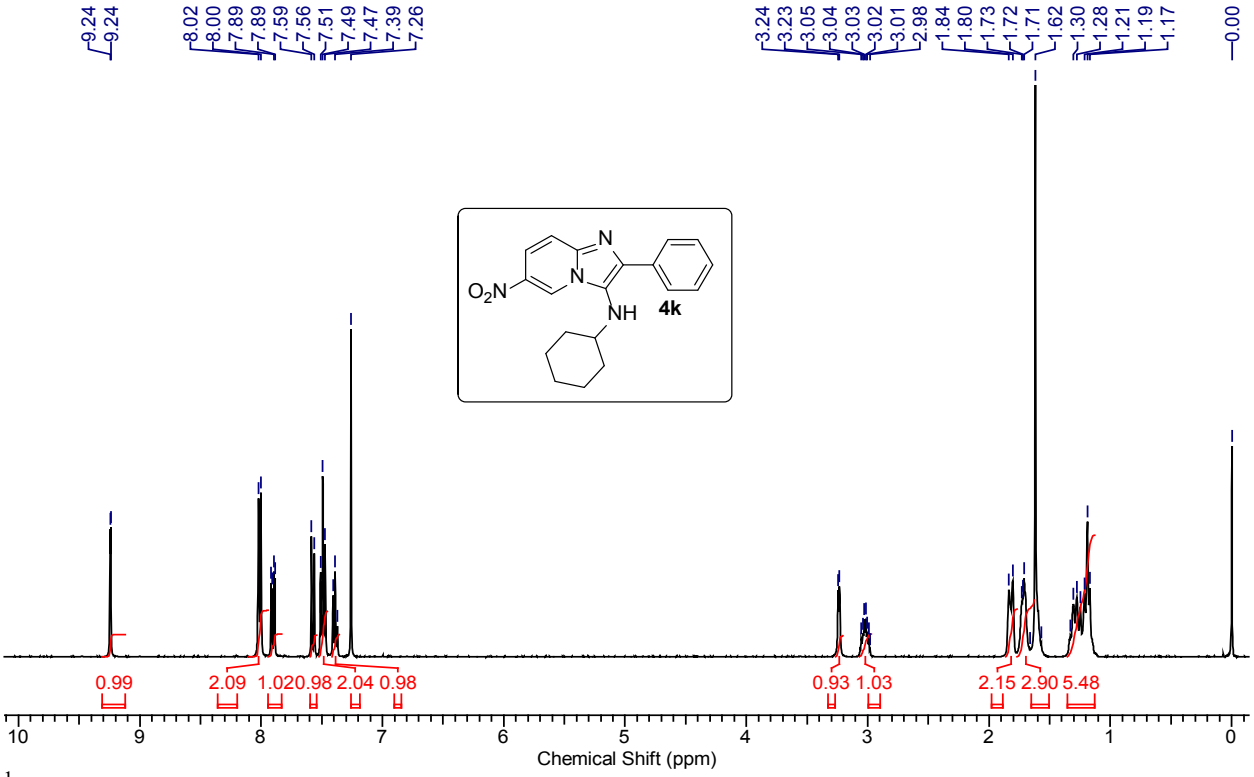
^{13}C NMR (100 MHz) spectrum of compound **4i** in $CDCl_3$



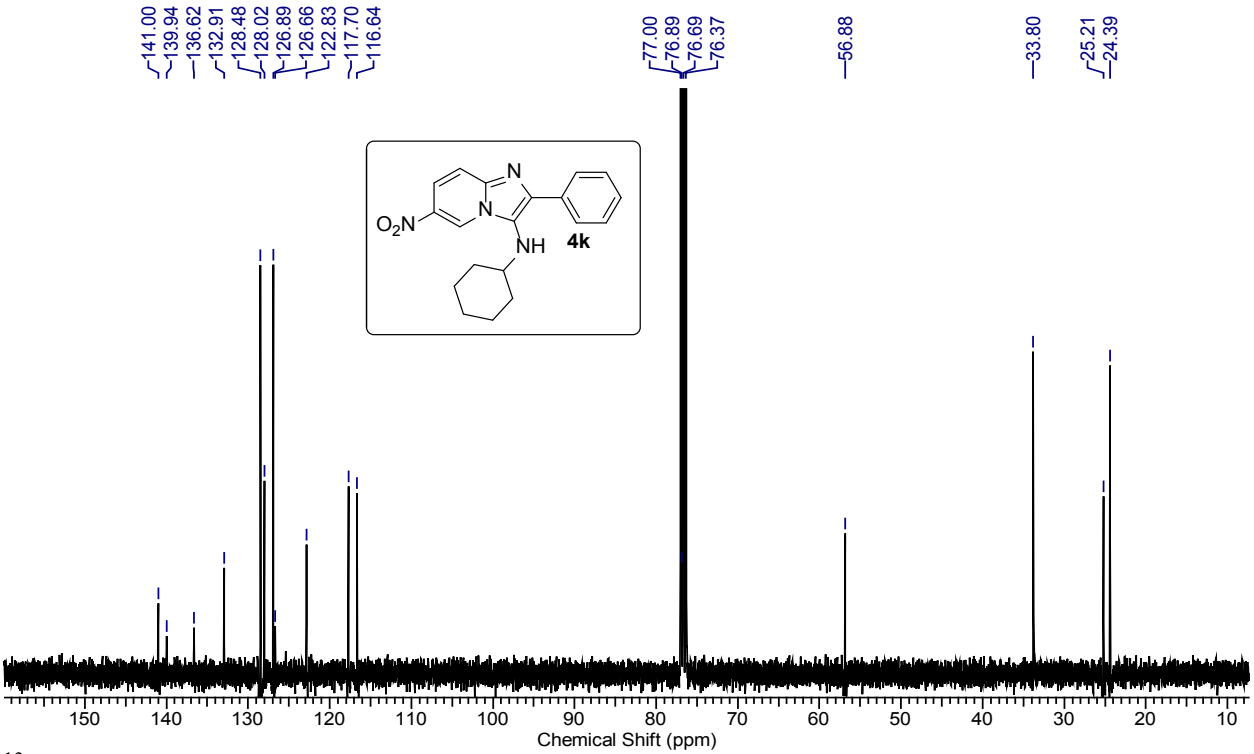
^{1}H NMR (400 MHz) spectrum of compound **4j** in $CDCl_3$



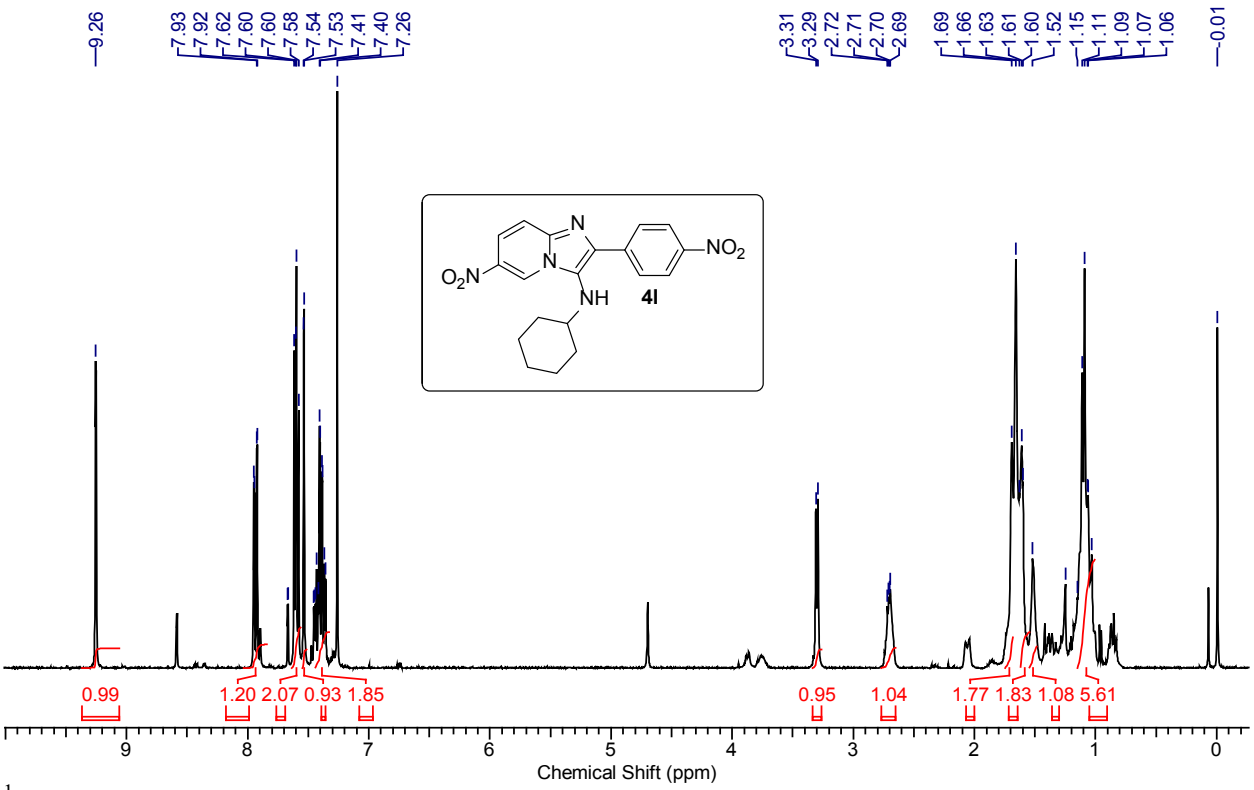
^{13}C NMR (100 MHz) spectrum of compound **4j** in $CDCl_3$



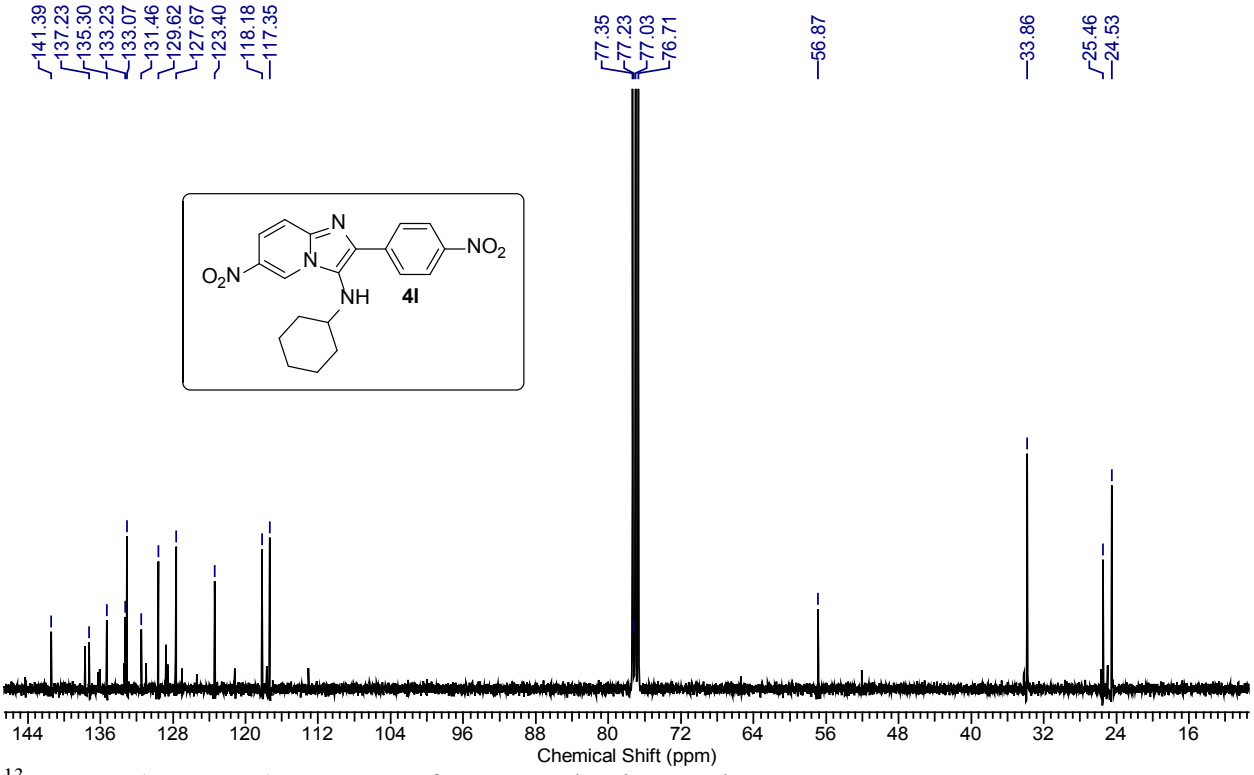
^{1}H NMR (400 MHz) spectrum of compound **4k** in $CDCl_3$



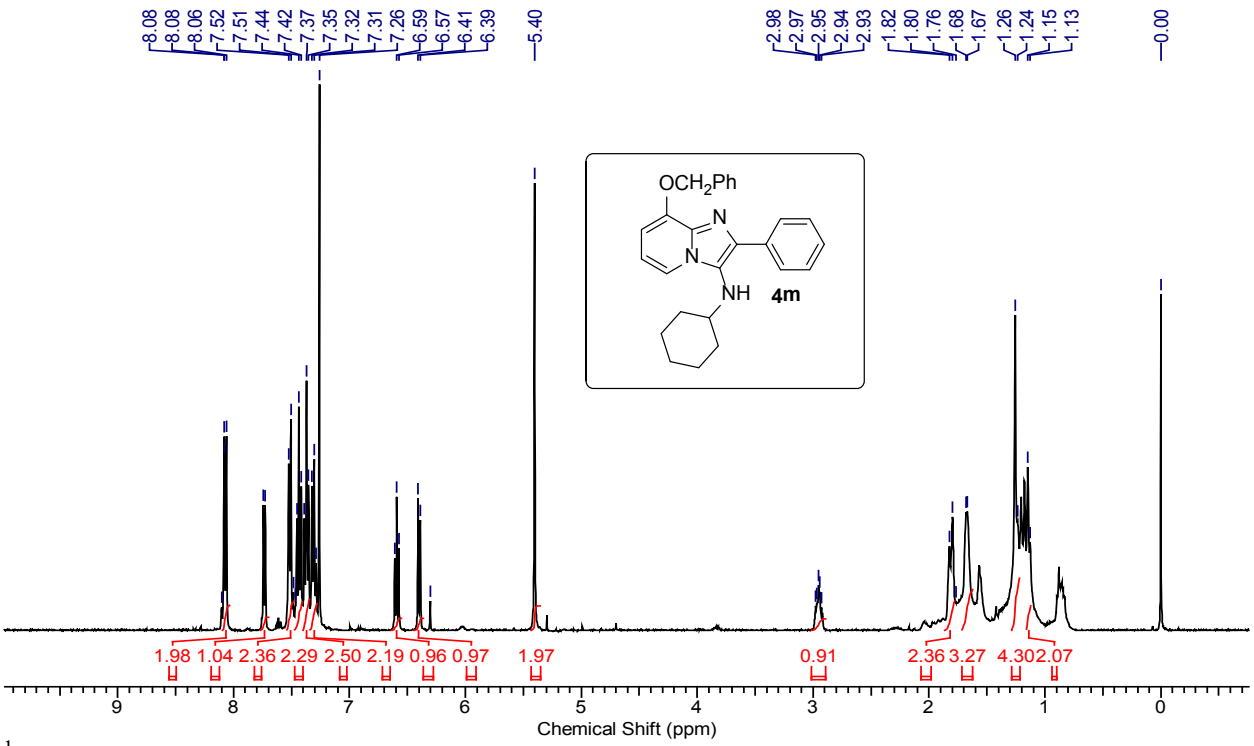
^{13}C NMR (100 MHz) spectrum of compound **4k** in $CDCl_3$



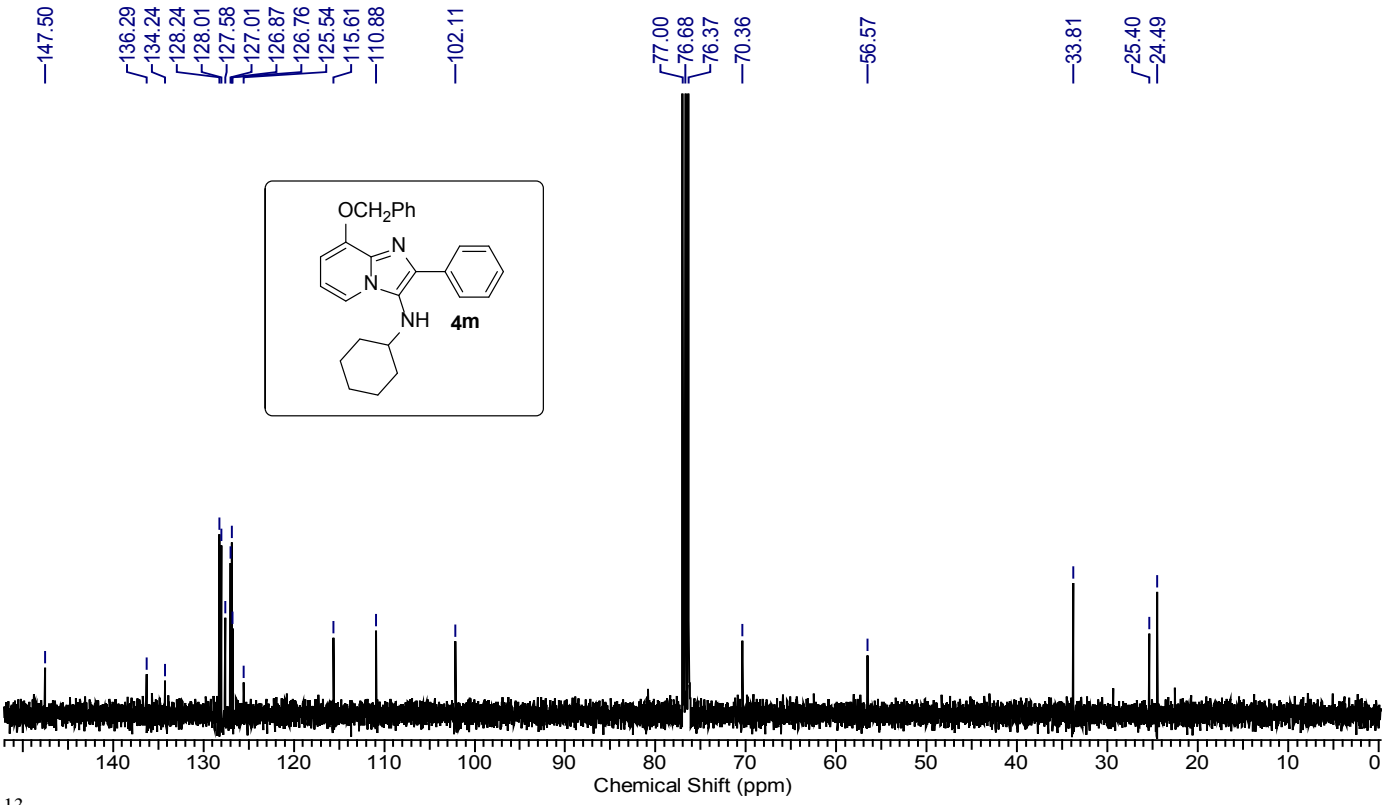
^{1}H NMR (400 MHz) spectrum of compound **4l** in $CDCl_3$



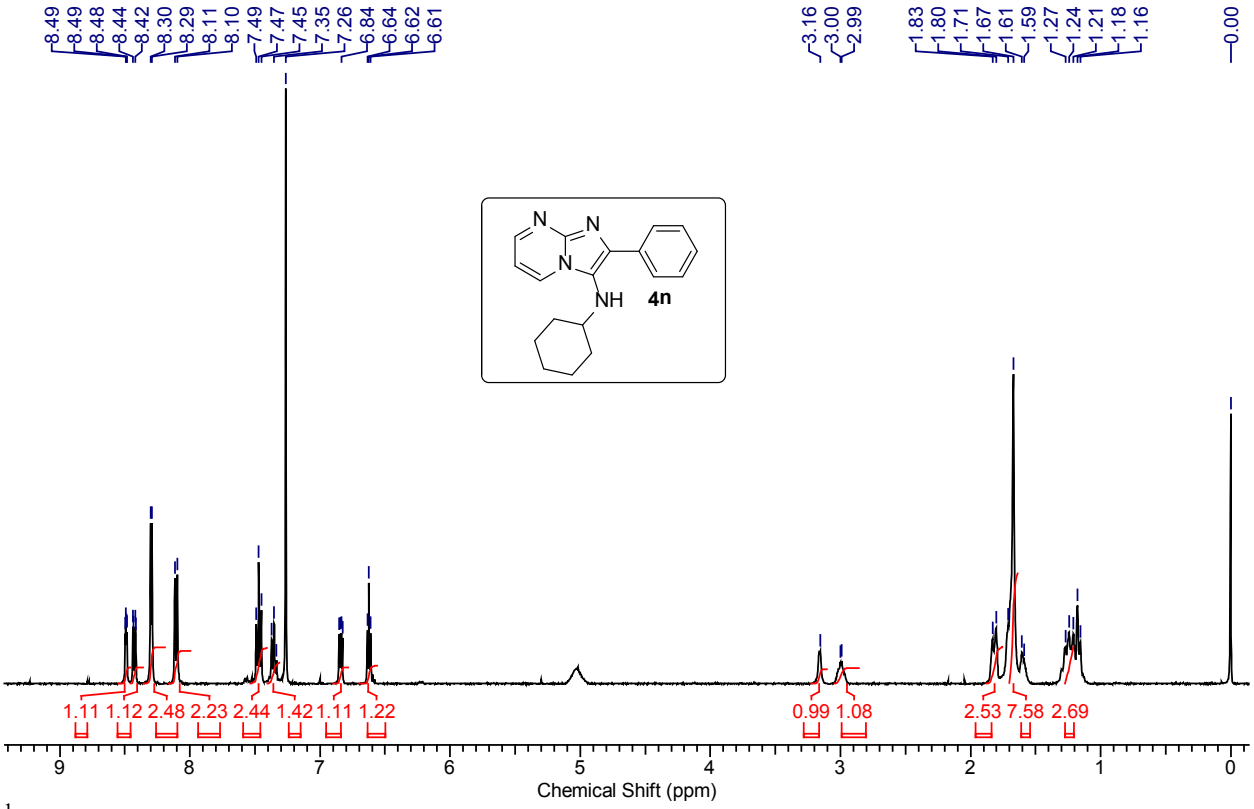
^{13}C NMR (100 MHz) spectrum of compound **4l** in $CDCl_3$



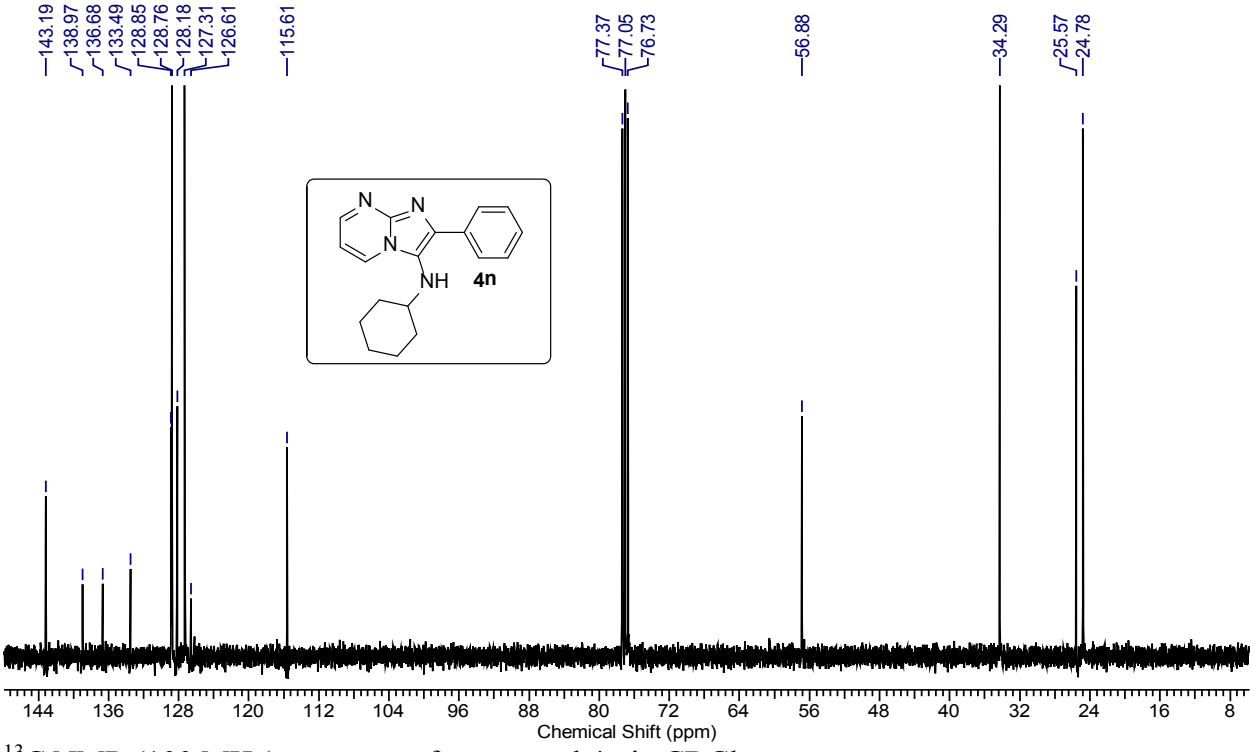
^{1}H NMR (400 MHz) spectrum of compound **4m** in $CDCl_3$



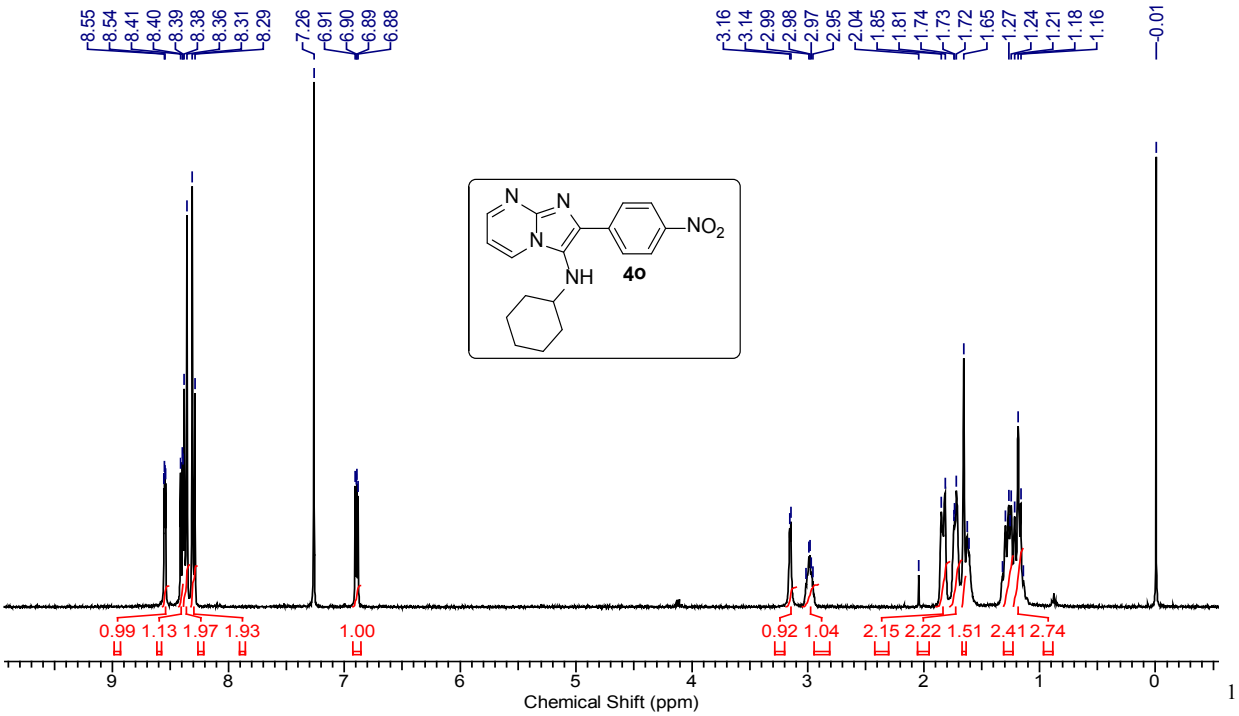
^{13}C NMR (100 MHz) spectrum of compound **4m** in $CDCl_3$



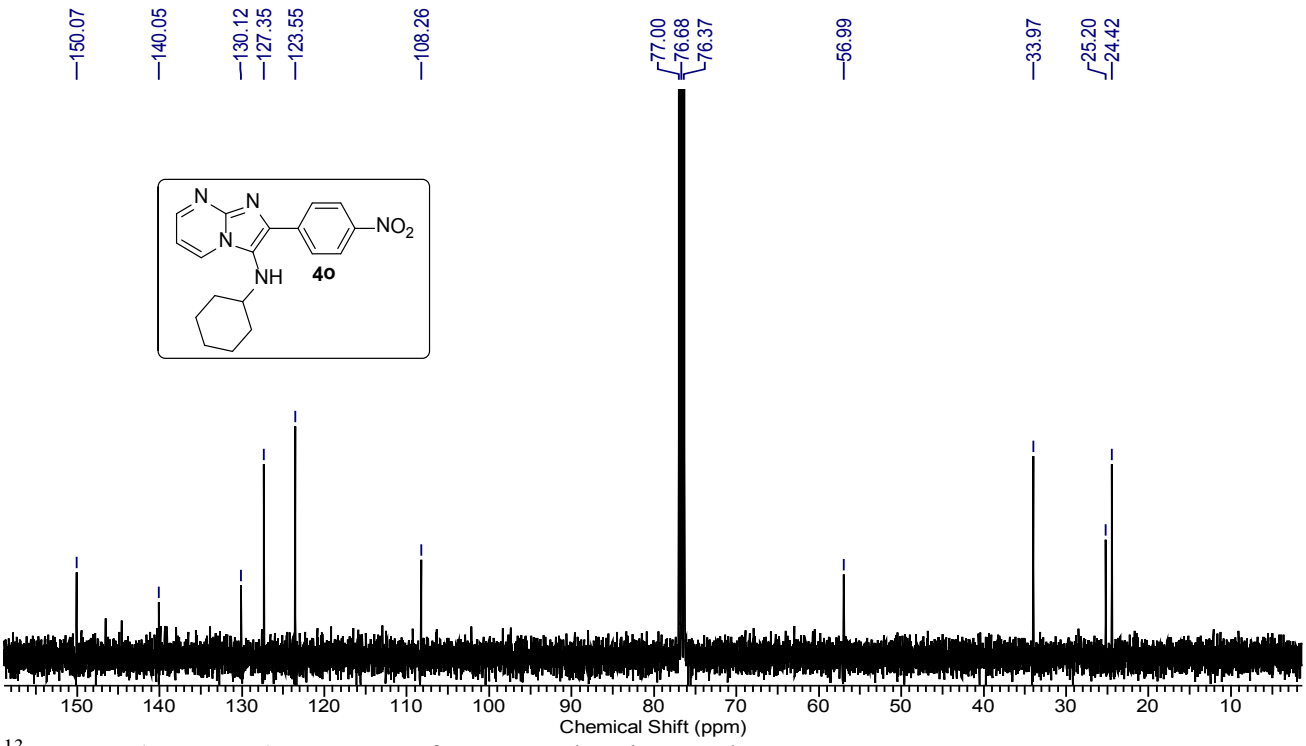
^{1}H NMR (400 MHz) spectrum of compound **4n** in $CDCl_3$



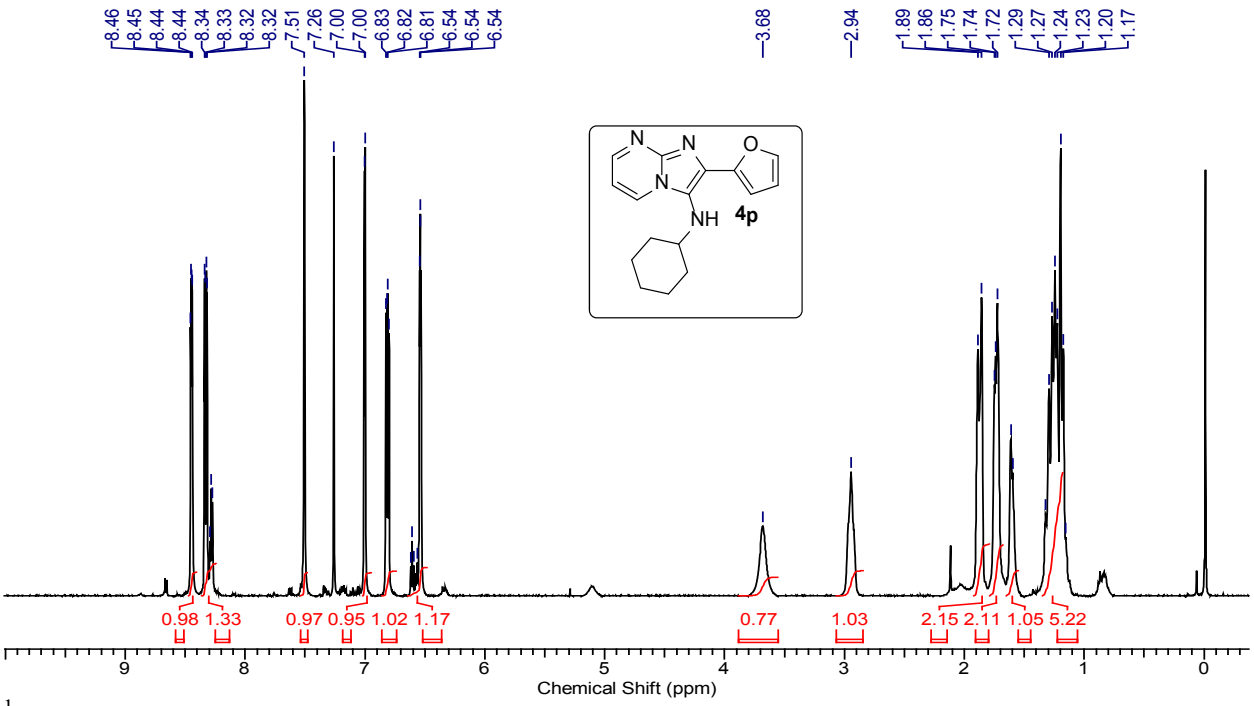
^{13}C NMR (100 MHz) spectrum of compound **4n** in $CDCl_3$



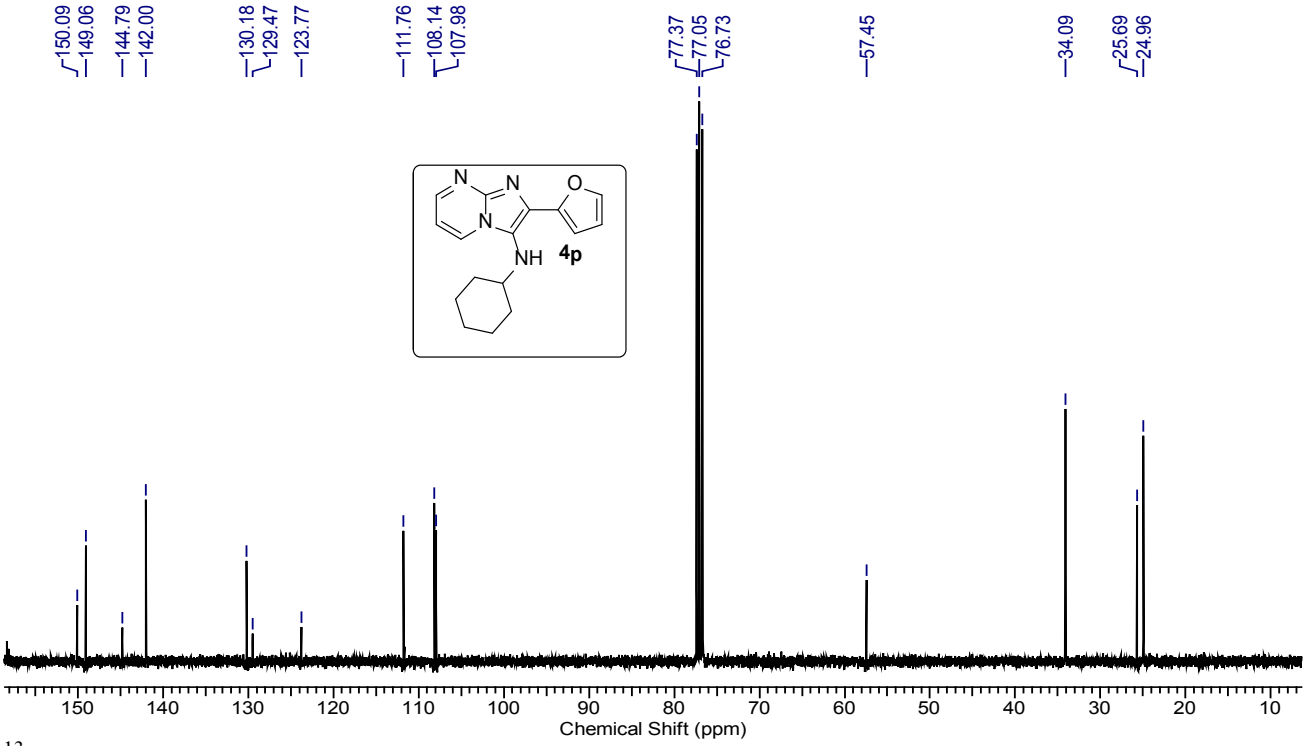
H NMR (400 MHz) spectrum of compound **4o** in $CDCl_3$



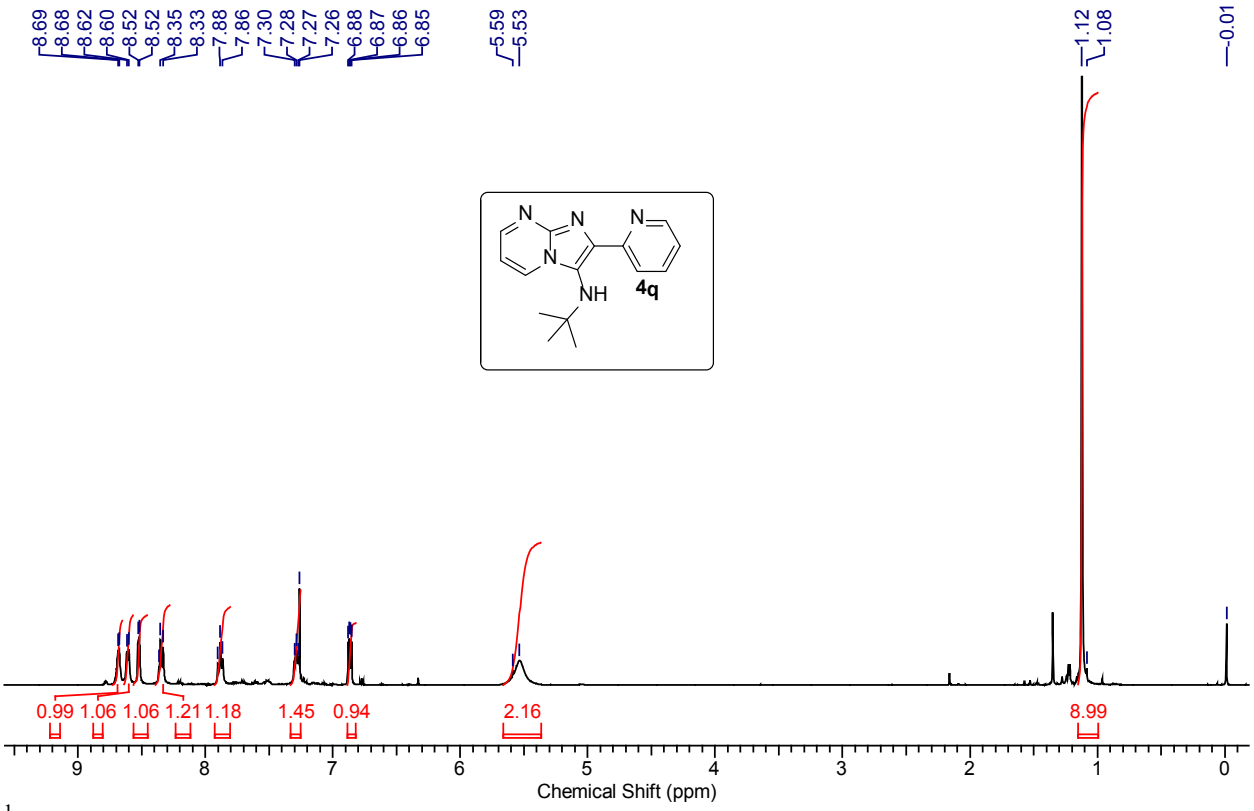
^{13}C NMR (100 MHz) spectrum of compound **4o** in $CDCl_3$



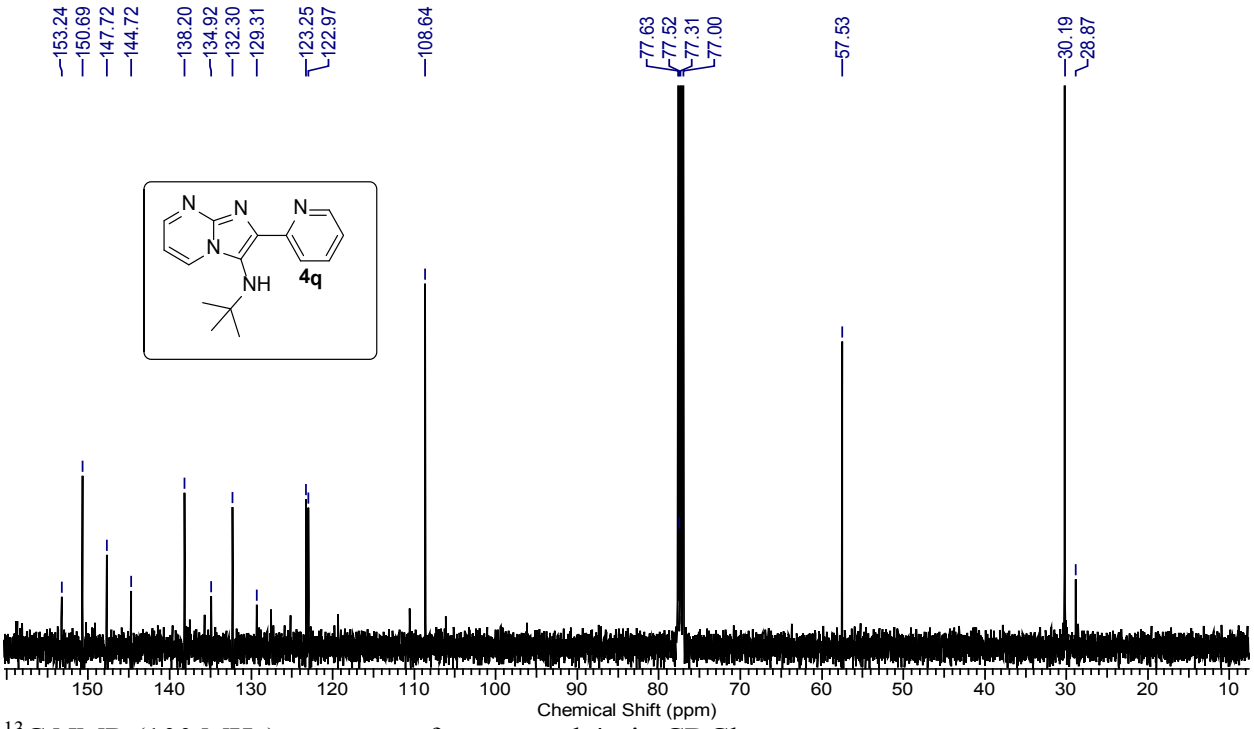
^{1}H NMR (400 MHz) spectrum of compound **4p** in $CDCl_3$



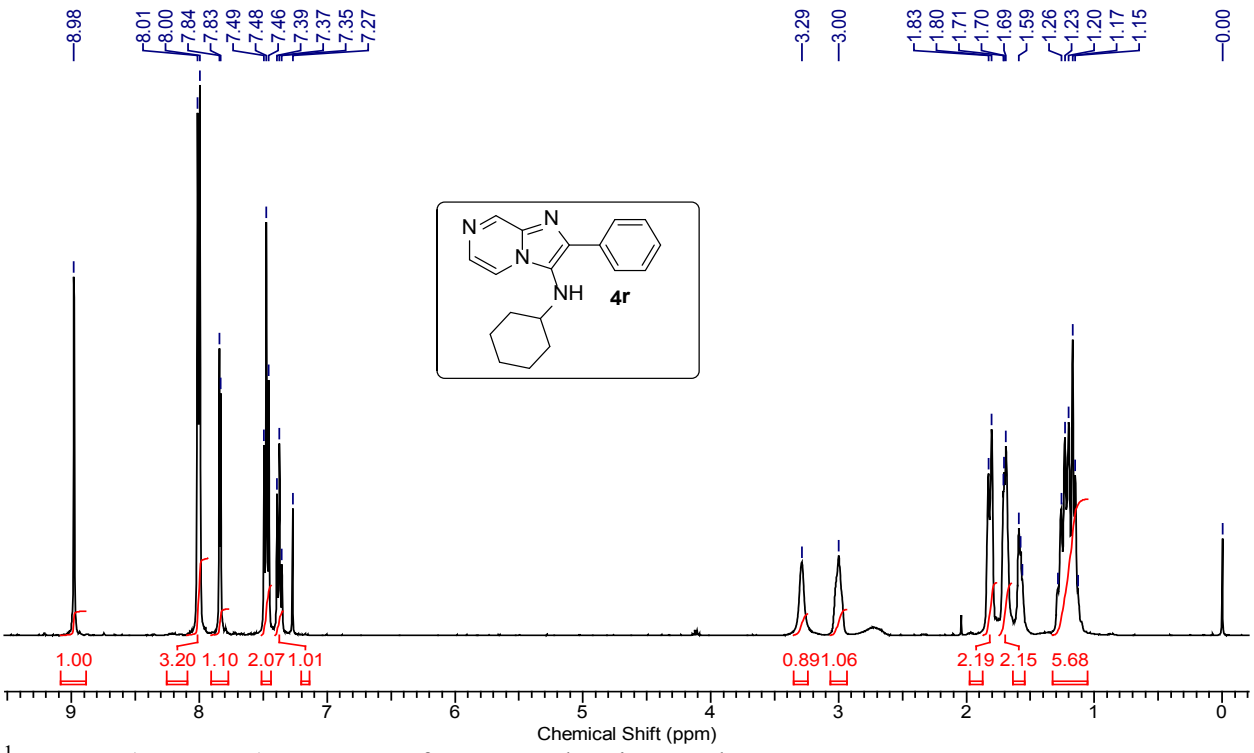
^{13}C NMR (100 MHz) spectrum of compound **4p** in $CDCl_3$



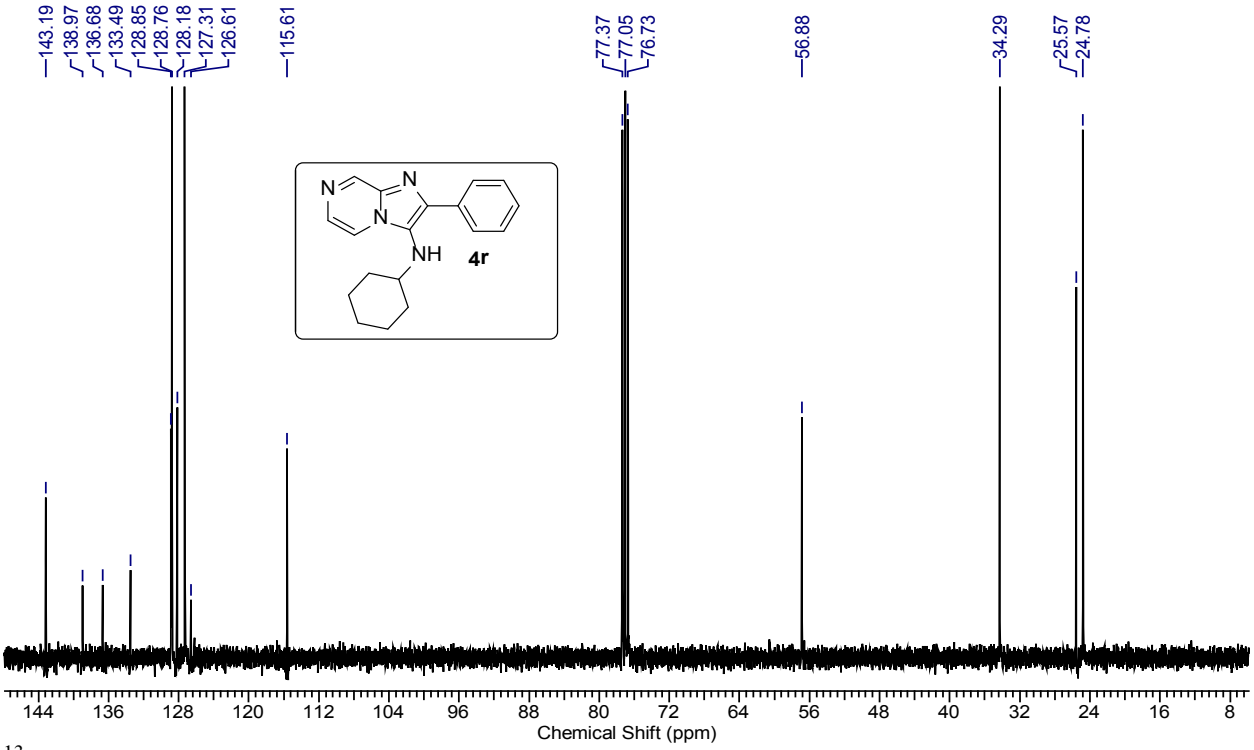
^{1}H NMR (400 MHz) spectrum of compound **4q** in $CDCl_3$



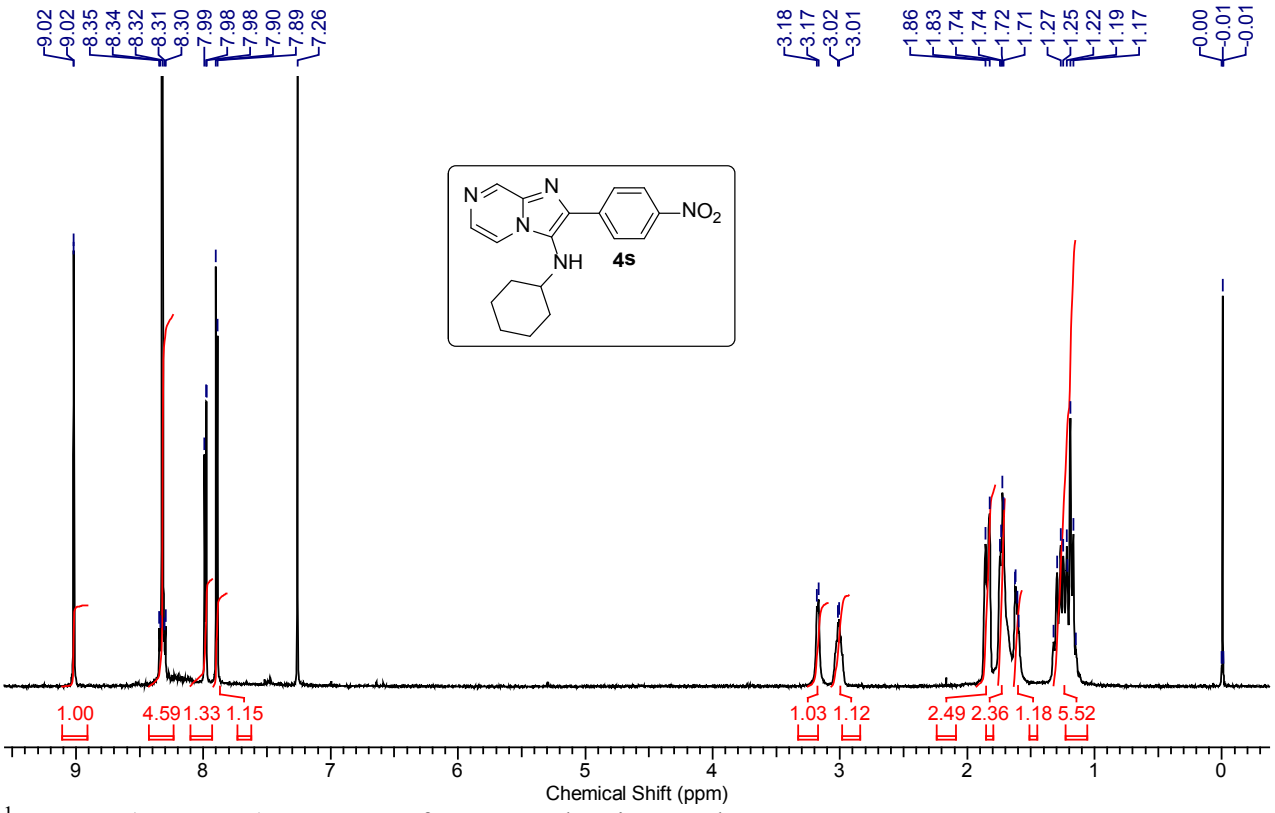
^{13}C NMR (100 MHz) spectrum of compound **4q** in $CDCl_3$



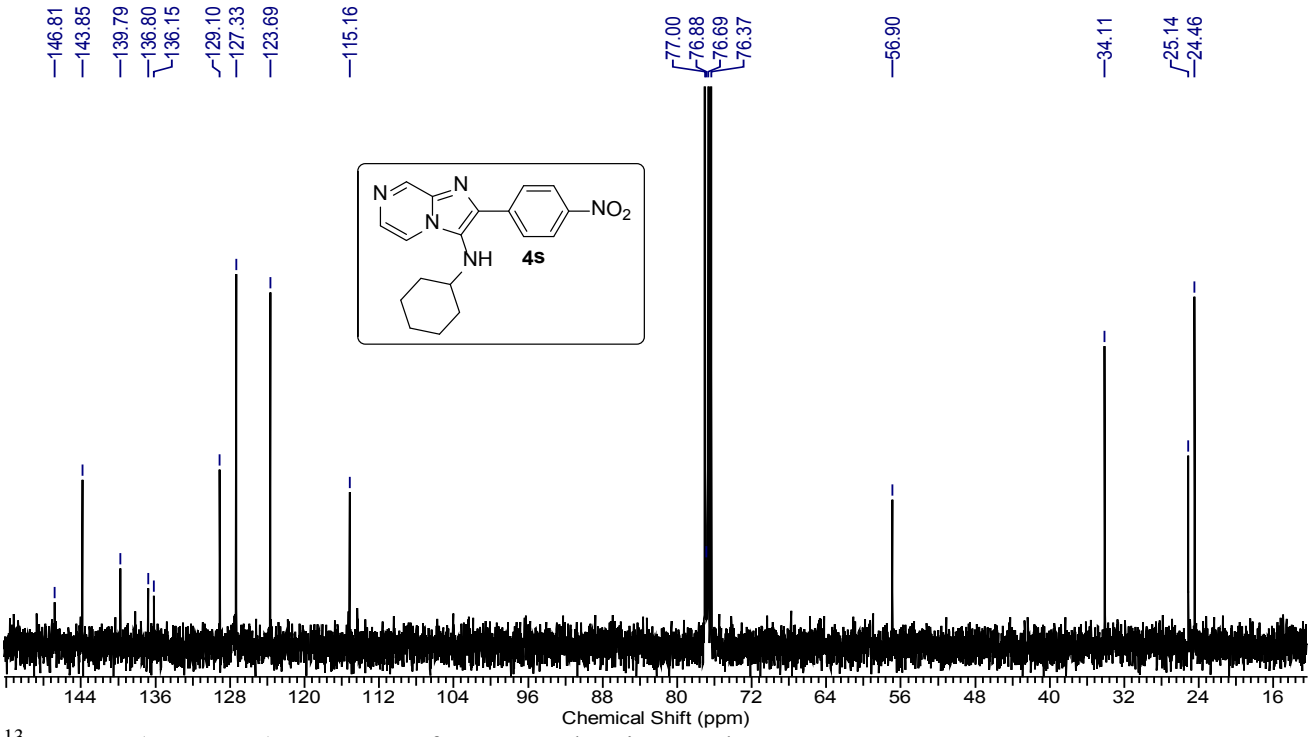
^{1}H NMR (400 MHz) spectrum of compound **4r** in $CDCl_3$



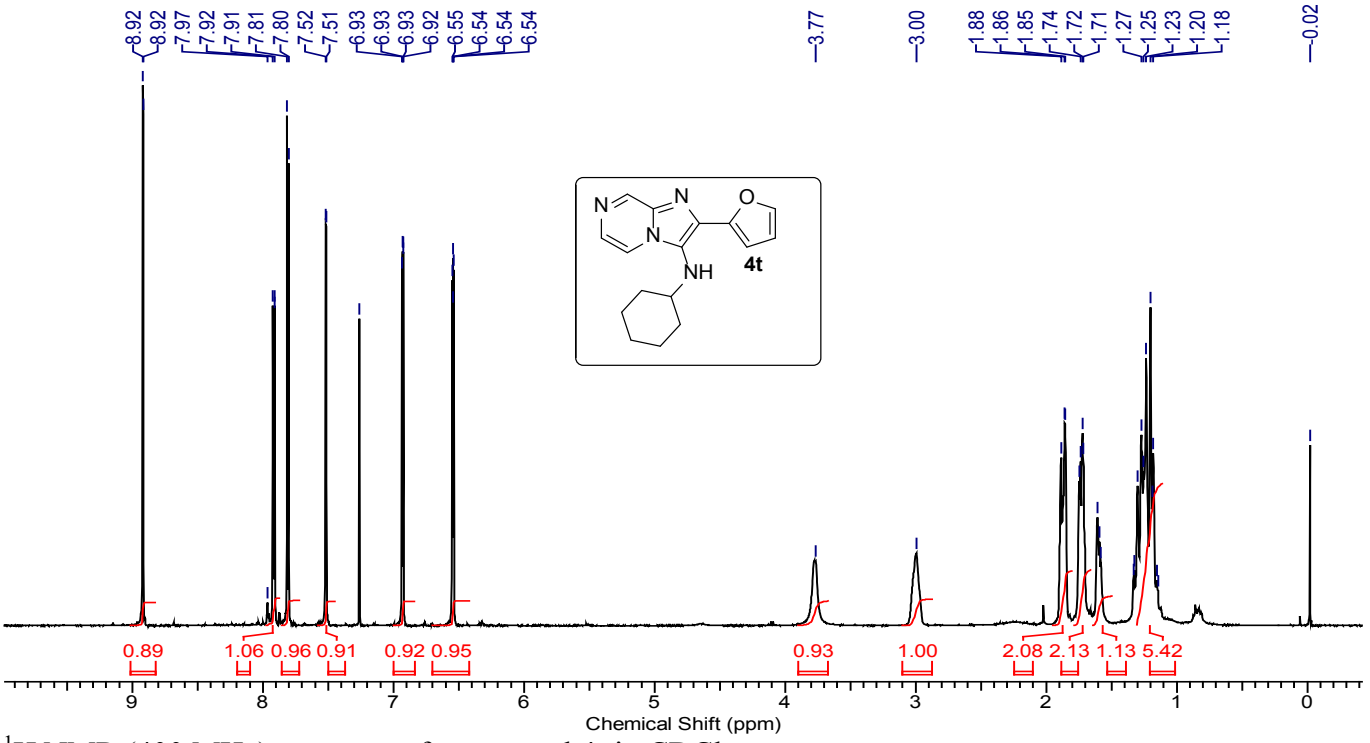
^{13}C NMR (100 MHz) spectrum of compound **4r** in $CDCl_3$



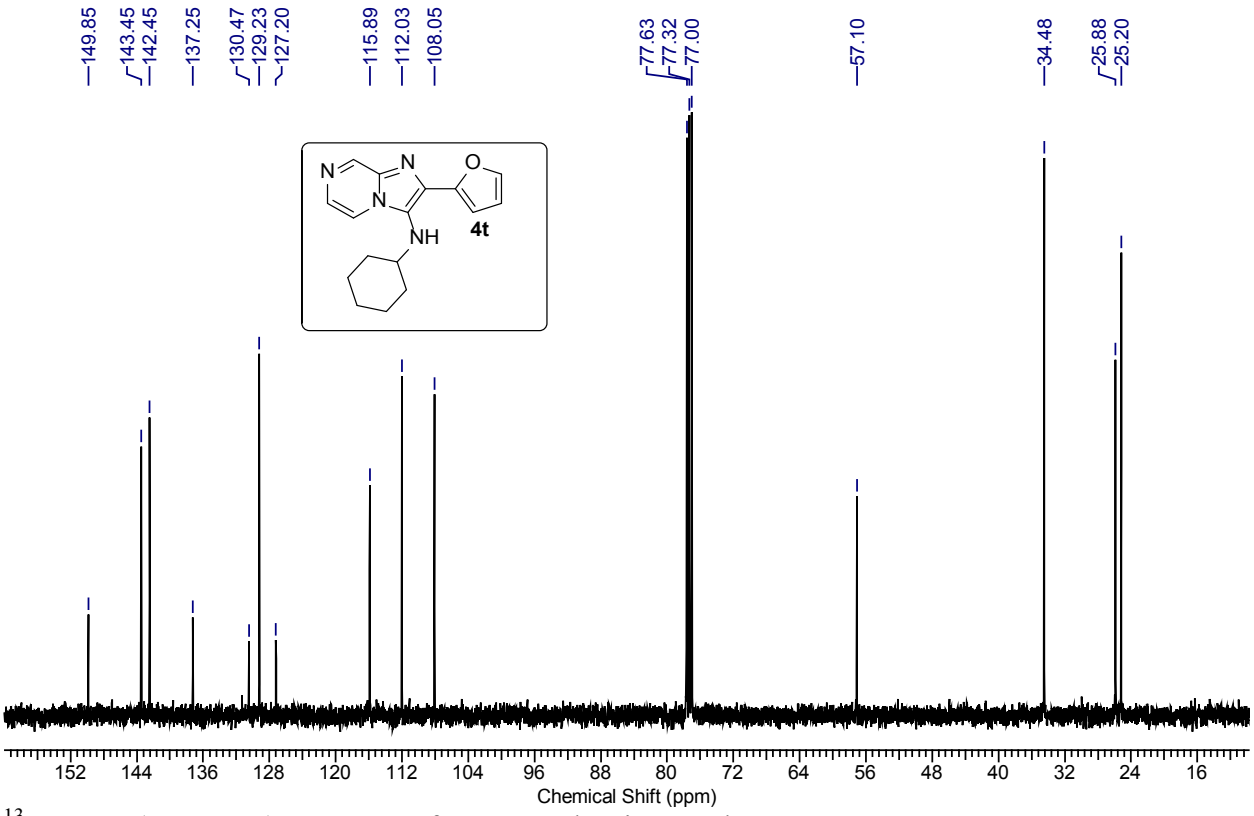
^{1}H NMR (400 MHz) spectrum of compound **4s** in $CDCl_3$



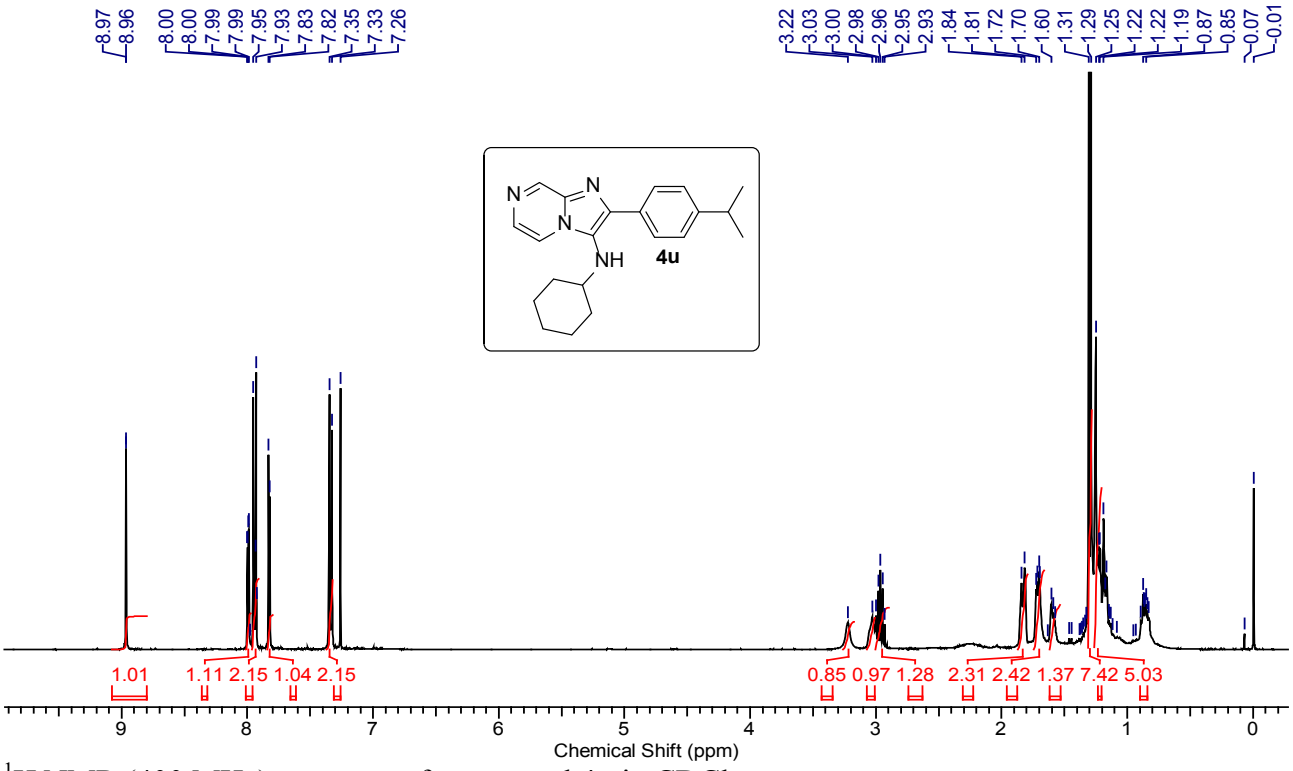
^{13}C NMR (100 MHz) spectrum of compound **4s** in $CDCl_3$



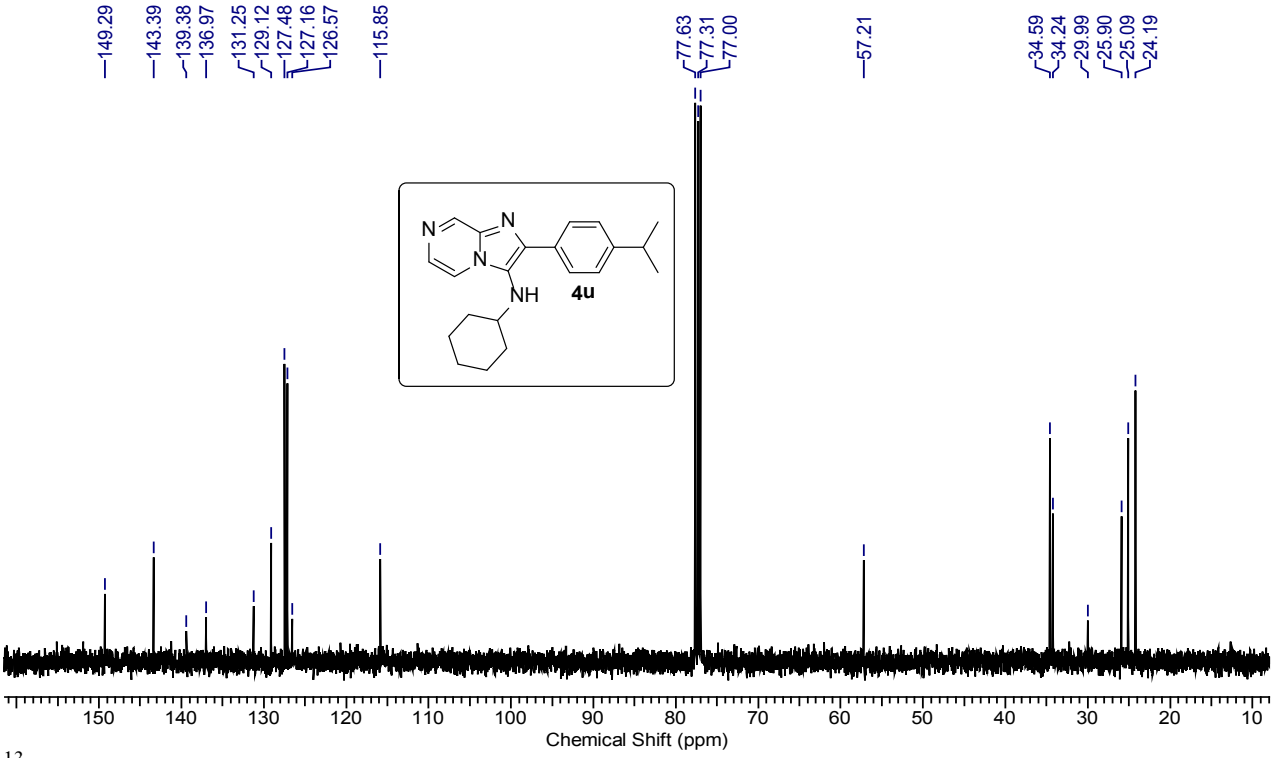
^{1}H NMR (400 MHz) spectrum of compound **4t** in $CDCl_3$



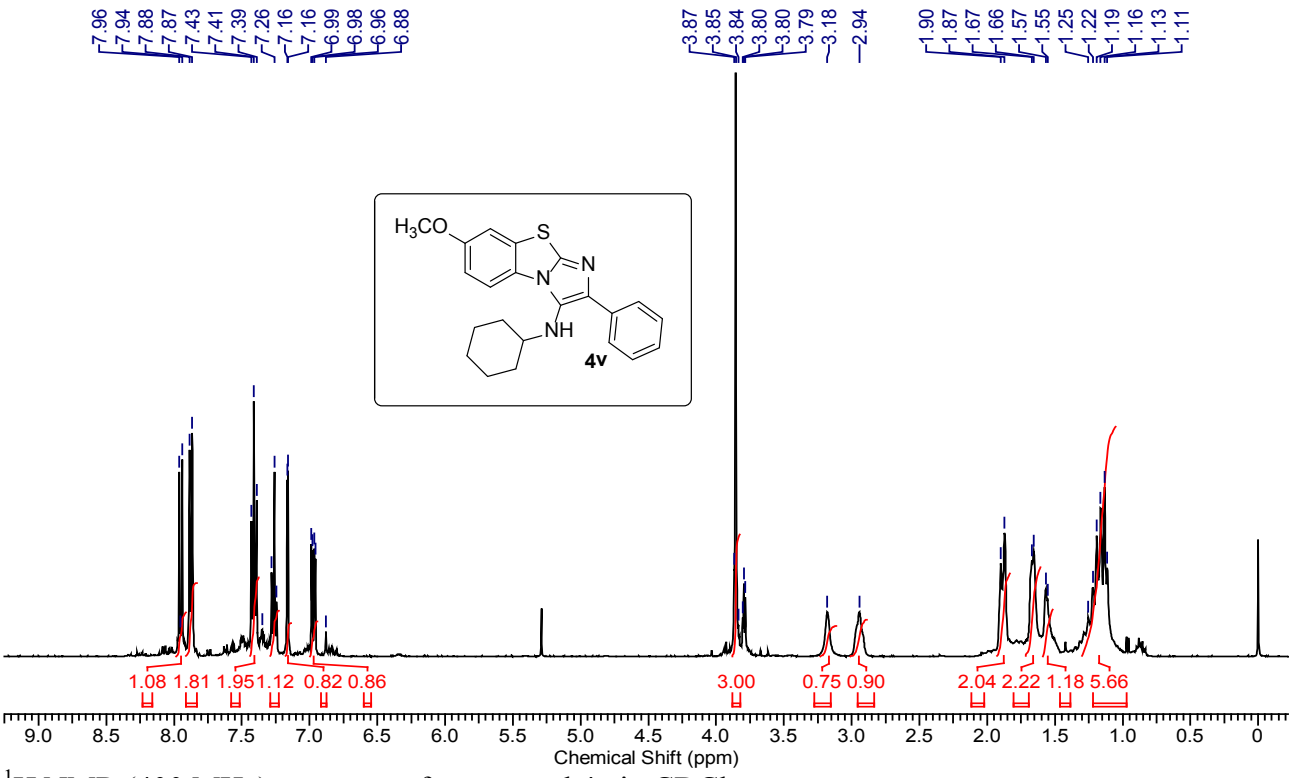
^{13}C NMR (100 MHz) spectrum of compound **4t** in $CDCl_3$



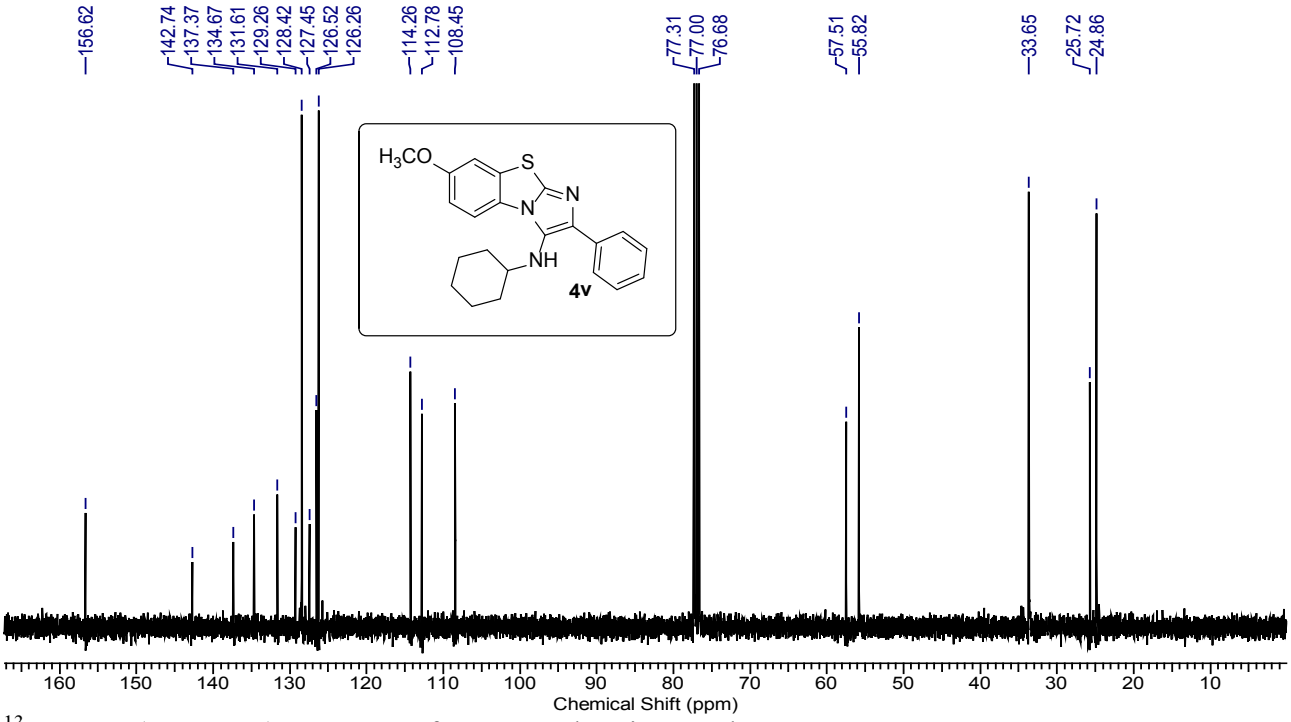
^{1}H NMR (400 MHz) spectrum of compound **4u** in $CDCl_3$



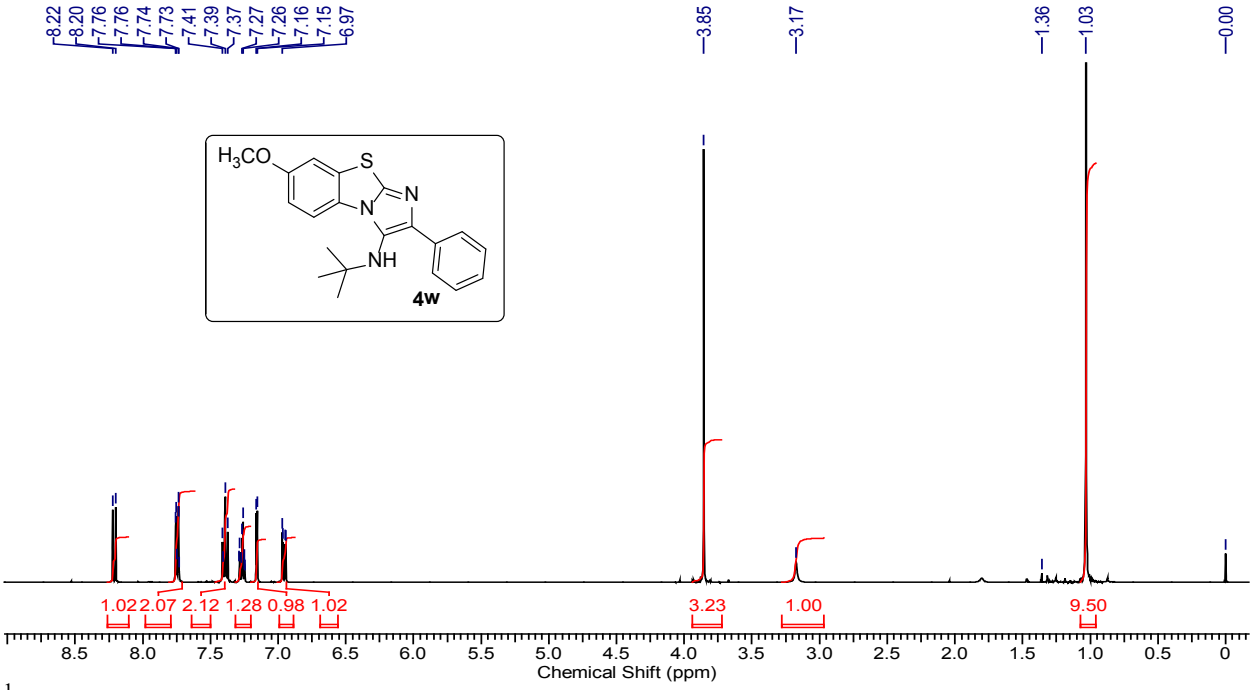
^{13}C NMR (100 MHz) spectrum of compound **4u** in $CDCl_3$



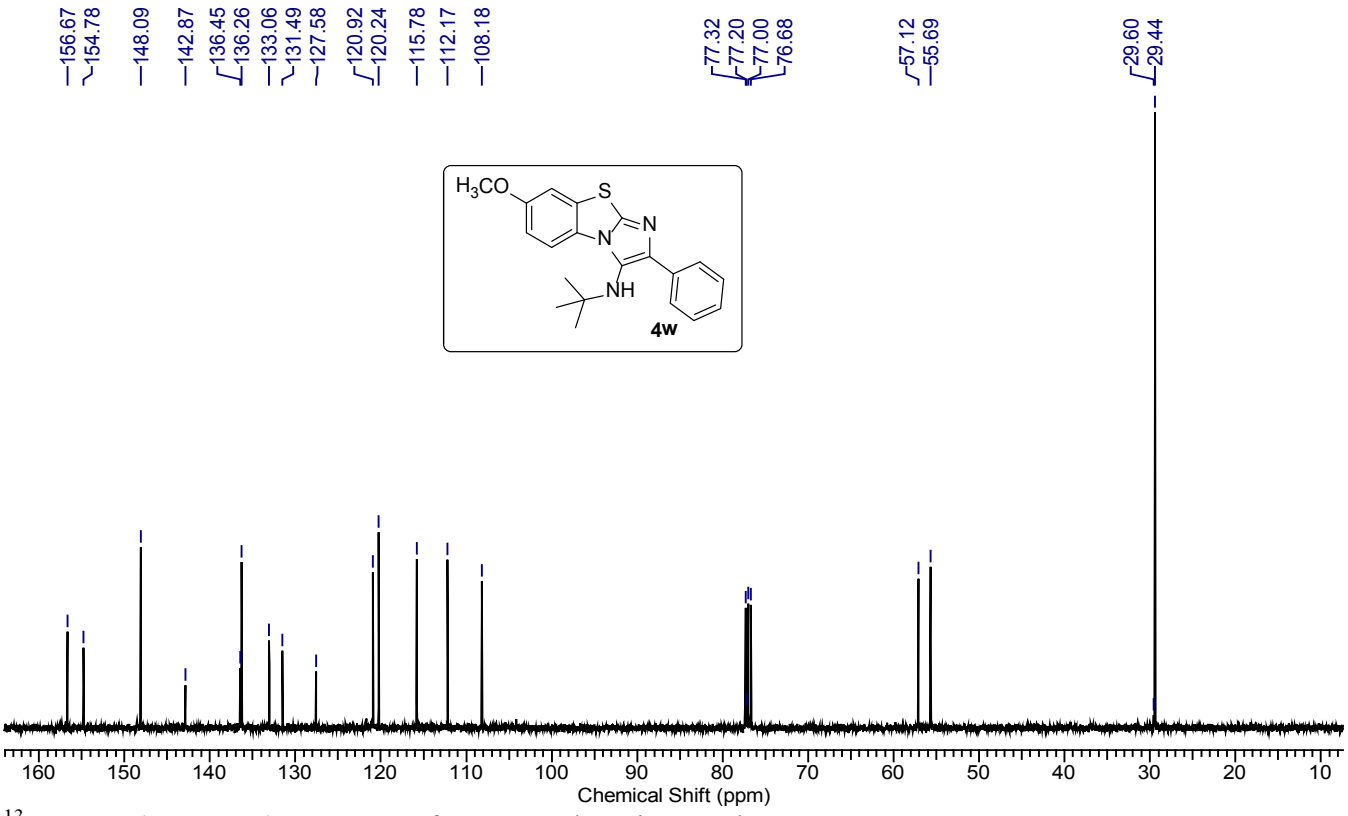
^{1}H NMR (400 MHz) spectrum of compound **4v** in $CDCl_3$



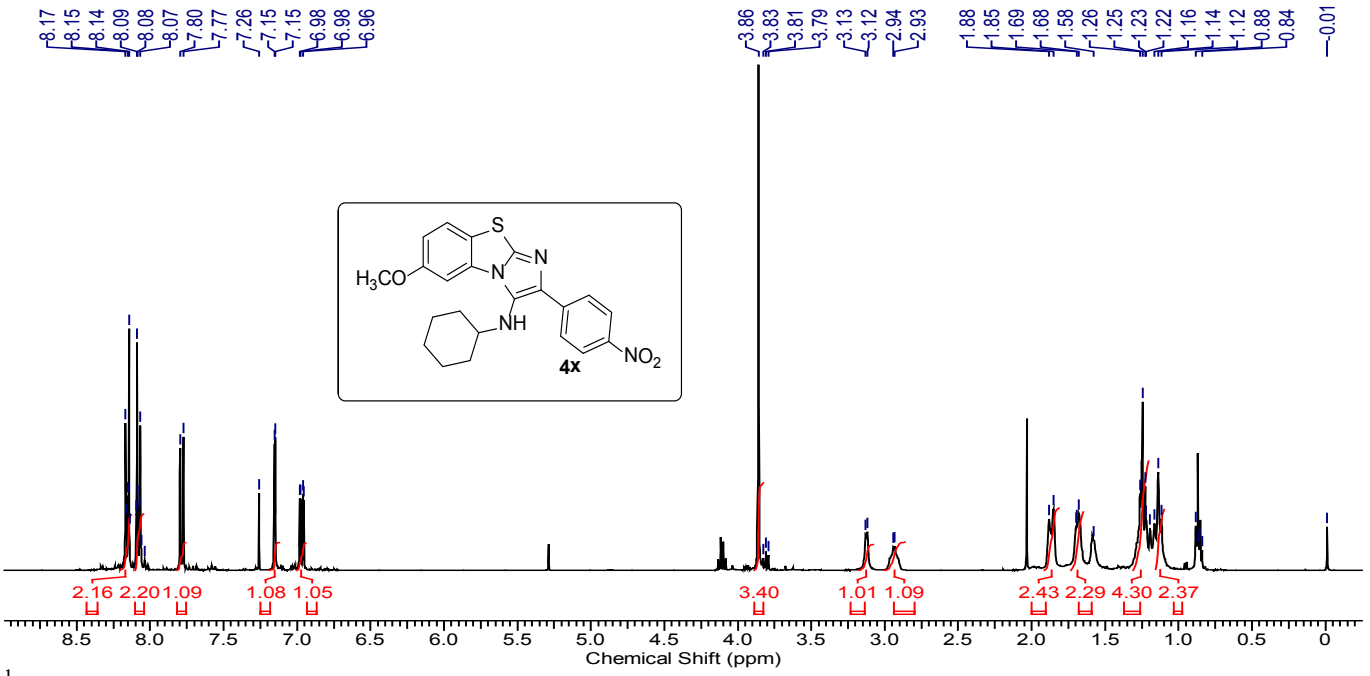
^{13}C NMR (100 MHz) spectrum of compound **4v** in $CDCl_3$



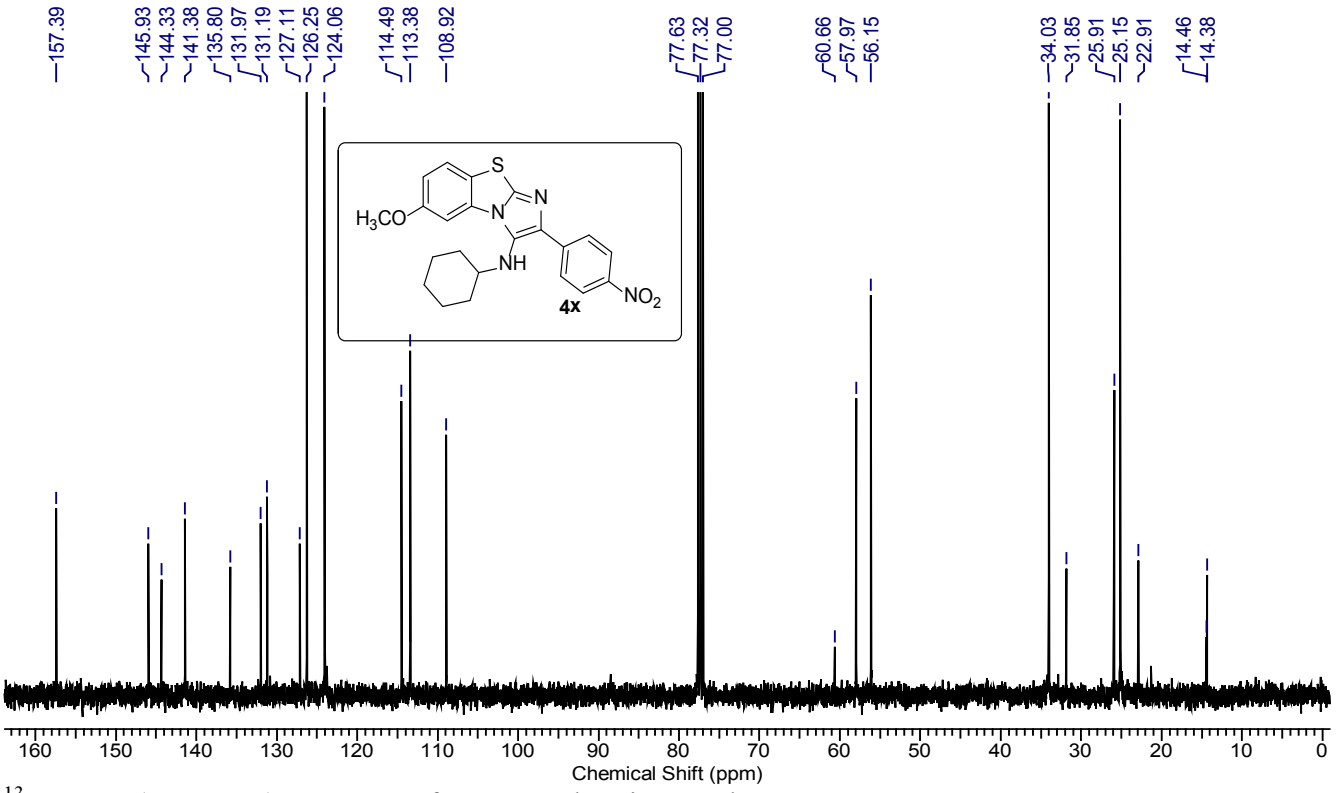
^{1}H NMR (400 MHz) spectrum of compound **4w** in $CDCl_3$



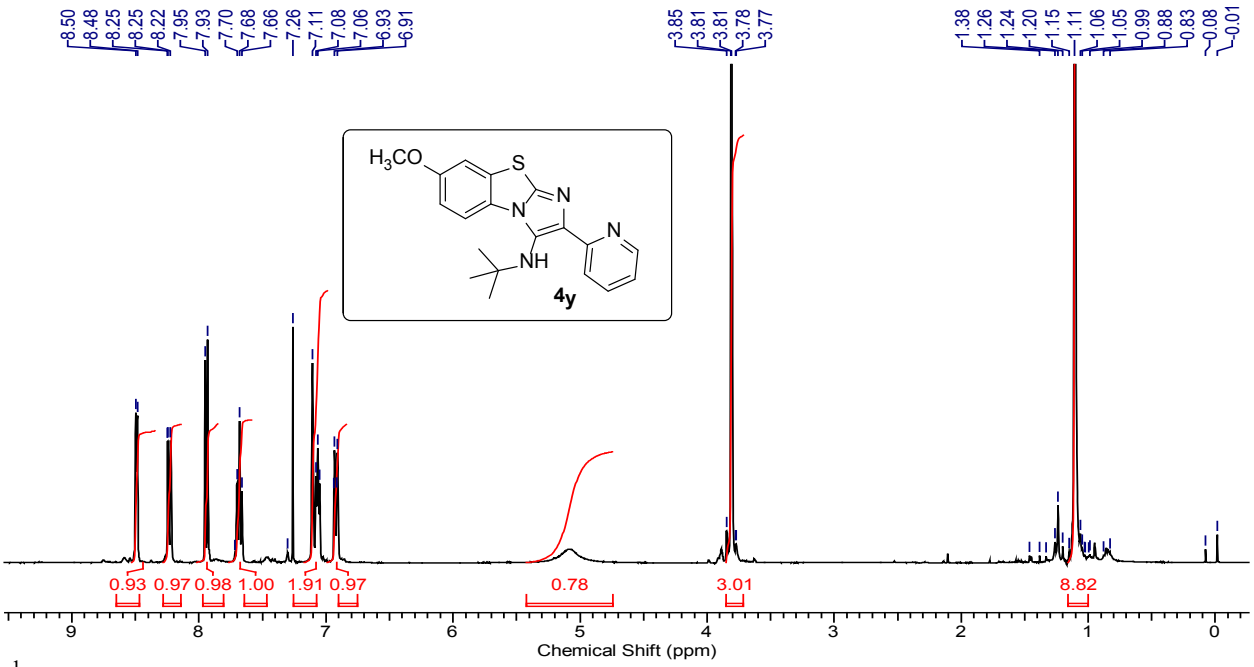
^{13}C NMR (100 MHz) spectrum of compound **4w** in $CDCl_3$



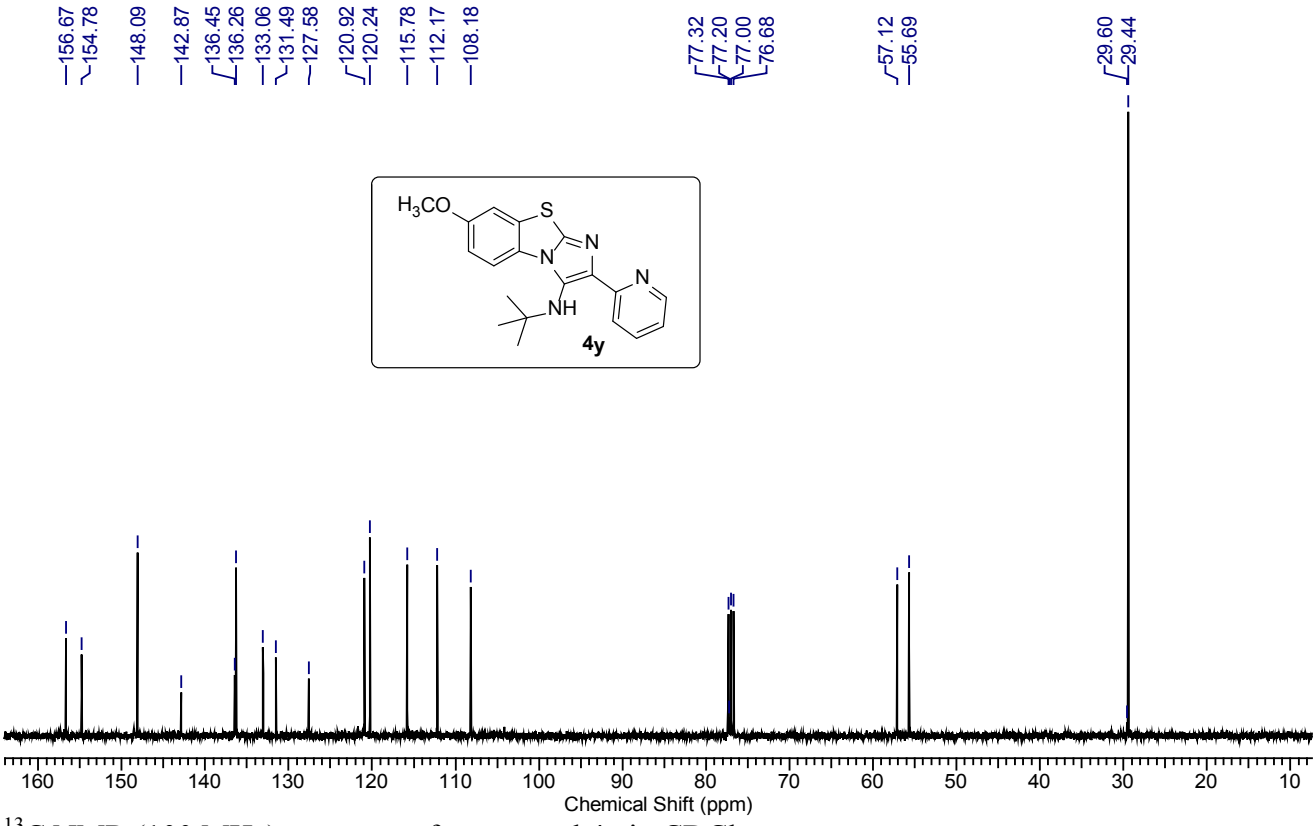
^{1}H NMR (400 MHz) spectrum of compound **4x** in $CDCl_3$



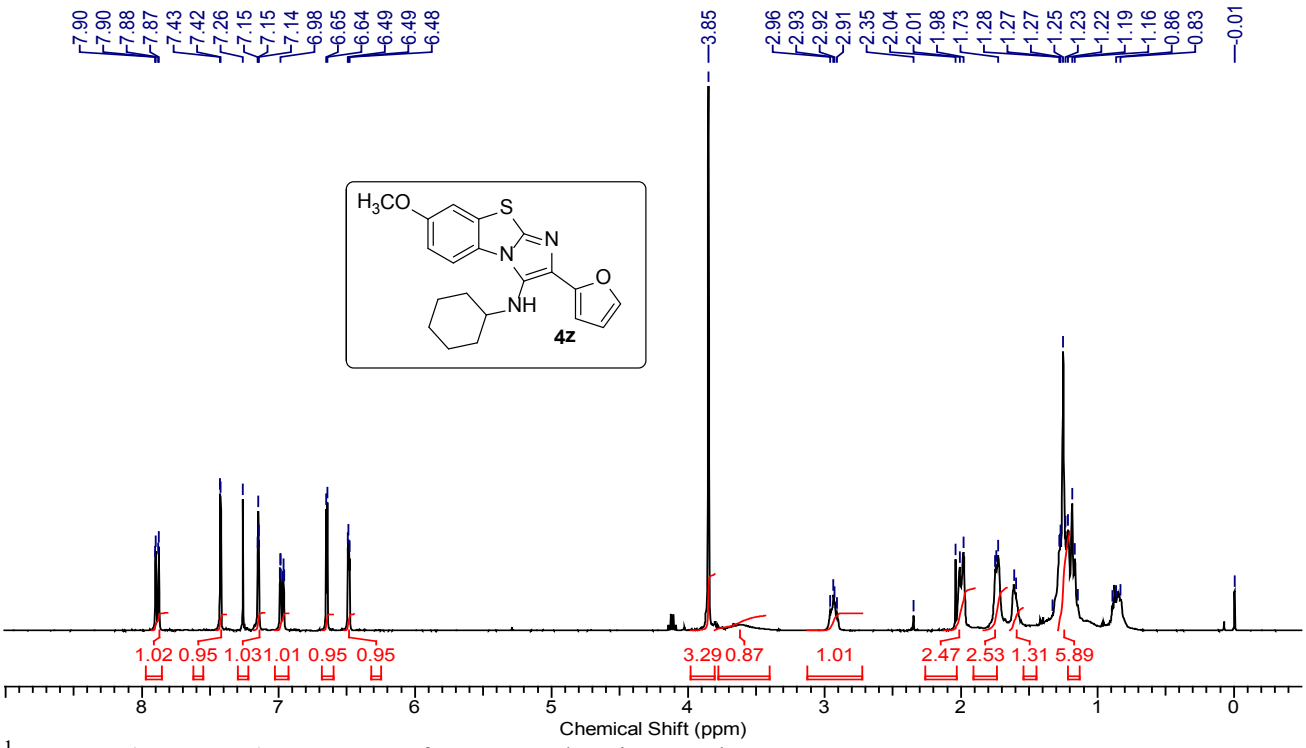
^{13}C NMR (100 MHz) spectrum of compound **4x** in $CDCl_3$



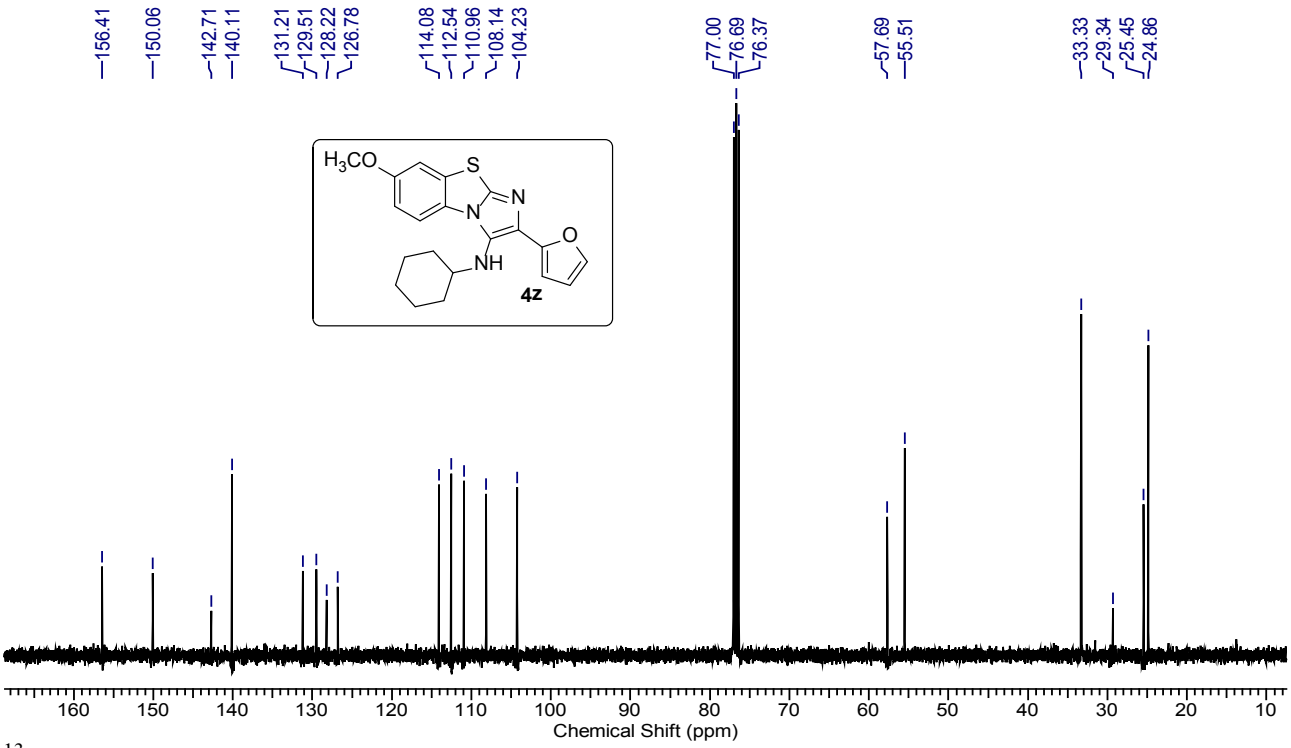
^{1}H NMR (400 MHz) spectrum of compound **4y** in $CDCl_3$



^{13}C NMR (100 MHz) spectrum of compound **4y** in $CDCl_3$



^{1}H NMR (400 MHz) spectrum of compound **4z** in $CDCl_3$



^{13}C NMR (100 MHz) spectrum of compound **4z** in $CDCl_3$

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