Supporting Information

A Diastereoselective Construction of functionalized dihydro-pyridazine based Spirooxindole Scaffold *via* C-3 Umpolung of Isatin *N*,*N*′-Cyclic Azomethine Imine

F. Matloubi-Mogaddam*, M. Eslami, A. Siahpoosh, H. Golfam

Laboratory of Organic Synthesis and Natural Products, Department of Chemistry,

Sharif University of Technology, Azadi Street, PO Box 111559516

Tehran, Iran

E-mail Address: matloubi@sharif.edu

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1. General data

Materials and methods

All solvents and starting materials were purchased from Merck and Sigma-Aldrich used without any additional purification. Analytical TLC was carried out using Merck 0.2 mm silica gel 60 F-254 Al-plates. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-500 machine using DMSO-d6 as solvent and TMS as an internal standard at room temperature (DMSO-d_6 ^{1}HNMR: δ=2.50 ppm and ^{13}CNMR: δ=39.52 ppm). Chemical shifts were reported in ppm scale. FT-IR spectra of samples were obtained on ABB Bomem MB100 spectrometer with potassium bromide (KBr) pellets. Melting points were determined using an Electrothermal 9100 apparatus and are uncorrected. CHN analysis was done by LECO Truspec. X-ray diffraction was carried out on a STOE IPDS 2T diffractometer with graphite monochromated MoKα radiation. A single crystal suitable for X-ray analysis was obtained from DMSO solution.

2. Typical procedure for the synthesis of 1a-c

Isatin *N*,*N*′-cyclic azomethine imine 1,3-dipoles were synthesized according to the previously reported method.[1] To the solution of hydrazine monohydrate (2.42 mL, 50 mmol) in 30 mL anhydrous ethanol cooled to 0 °C was added ethyl acrylate (5.85 mL, 55 mmol) dropwise over 1h period. Then the reaction mixture was heated under reflux condition for 8 h and the volatile components and solvent were removed under reduced pressure. Finally, the pyrazolidin-3-one was obtained as yellow oil, which was dissolved in 20 mL of anhydrous ethanol, and *N*-allyl isatin (4.67 g, 25 mmol) was added. The crude reaction mixture was stirred overnight at room temperature. After completion of reaction, the solid product was collected by filteration and purified by flash chromatography eluting with MeOH/CH_2Cl_2 (1:100) to afford **1a** as a red solid (1.17 g, 4.6 mmol, 46%).

Data for 2-(1-benzyl-2-oxoindolin-3-ylidene)-5-oxopyrazolidin-2-ium-1-ide 1b:

Red solid; m.p 198-200 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.74 (2H, t, *J* = 7.0 Hz, CH_2), 4.99 (2H, t, *J* = 7 Hz, CH_2), 5.02 (2H, s, *N*-CH_2), 7.06 (1H, d, *J* = 8.0 Hz, H-Ar), 7.16 (1H, t, *J* = 7.5 Hz, H-Ar), 7.34 (6H, m, H-Ar), 8.02 (1H, d, *J* = 7.5 Hz, H-Ar).

3. Typical procedure for the synthesis of 2a-i

In a 25 mL round bottom flask equipped with a magnetic bar, aldehyde (3 mmol), malononitrile (238 mg, 3.6 mmol), and morpholine (20 µl) were added to ethanol (5 mL). Then, the reaction mixture was stirred at room temperature until completion of the reaction. The reaction progress was monitored by TLC (EtOAc/n-hexane, 1:3) as well as precipitating out of the products from the reaction mixture. After completion of the reaction, the solid products **2a-i** were filtered, washed with cold ethanol (2 mL) to obtain essentially pure products.

4. Typical procedure for the synthesis of 4a-p

A reaction vial was charged with a mixture of isatin *N*,*N*′-cyclic azomethine imine 1,3-dipoles (0.5 mmol), 2-arylidenemalononitrile (0.5 mmol), DABCO (20 mol%), 1.0 ml DCM as solvent and stirred at room temperature for 12h. The progress of the reaction was monitored by TLC (1:3 n-hexan:Ethyl acetate). After completion of the reaction, the organic

pure products were simply filtered, dried in air and directly characterized by ^{1}HNMR, ^{13}CNMR, FT-IR, HRMS, melting point and X-ray crystal analysis.

5. Spectra Data for compounds 4a-p

Data for 1-allyl-8'-amino-1',2-dioxo-6'-phenyl-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4a:

White solid; Yield 90% (184 mg); m.p 250-252 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.83 (2H, AB_q), 4.42 (1H, d, *J* = 17.0 Hz), 4.74 (1H, s), 4.82 (1H, d, *J* = 10.0 Hz), 5.30 (1H, m), 5.69 (1H, s), 6.74 (1H, d, *J* = 7.0 Hz, H-Ar), 6.88 (2H, br s, H-Ar), 7.12 (2H, br s, H-Ar), 7.16 (1H, d, *J* = 6.0 Hz, H-Ar), 7.27 (1H, t, *J* = 7.0 Hz, H-Ar), 7.33 (1H, br s, H-Ar), 7.39 (1H, t, *J* = 7.5 Hz, H-Ar), 7.74 (2H, br s, NH_2), 7.83 (1H, d, *J* = 7.0 Hz, H-Ar); ^{13}C NMR (125 M Hz, DMSO-d_6) δ 41.6, 46.5, 58.5, 67.1, 101.2, 110.2, 117.1, 119.5, 121.9, 123.7, 125., 128.2, 128.4, 130.0, 130.9, 131.9, 134.3, 142.5, 143.2, 150.1, 165.3, 169.0; IR (KBr) ν (cm^{-1}) 3452, 3304, 3145, 3078, 2875, 2191, 1689, 1625, 1579; HRMS calcd. for $(C_{24}H_{19}N_5O_2+H)^+$, 410.1617, found 410.1606.

Data for 1-allyl-8'-amino-1',2-dioxo-6'-(p-tolyl)-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4b:

white solid; Yield 88% (186 mg); m.p 253-255 °C; ^{1}H NMR (500c MHz, DMSO-d_6) δ 2.17 (3H, s, CH_3), 3.93 (2H, AB_q, *N*-CH_2), 4.34 (1H, d, *J* = 16.5 Hz), 4.68(1H, s), 4.84 (1H, d, *J* = 9.5 Hz), 5.31 (1H, m), 5.68 (1H, s), 6.74 (3H, m, H-Ar), 6.92 (2H, m, H-Ar), 7.28 (2H, m, H-Ar), 7.39 (1H, s), 7.72 (2H, br s, NH_2), 7.82 (1H, d, *J* = 6.0 Hz, H-Ar); ^{13}C NMR (125 M Hz, DMSO-d_6) δ 20.0, 41.5, 46.2, 58.7, 67.1, 101.2, 110.3, 116.8, 119.5, 122.2, 123.7, 125.8, 128.8, 129.9, 130.9, 131.3, 131.8, 137.7, 142.5, 143.4, 150.0, 165.3, 169.1; IR (KBr) *v* (cm^{-1}) 3451, 3354, 3176, 2942, 2770, 2192, 1675, 1667; HRMS calcd. for $(C_{25}H_{21}N_5O_2+H)^+$, 424.1773, found 424.1761.

Data for 1-allyl-8'-amino-1',2-dioxo-6'-(m-tolyl)-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4c:

white solid; Yield 91% (192 mg); m.p 254-258 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.09 (3H, s, CH_3), 3.92 (2H, AB_q,CH_2), 4.42 (1H, d, *J* = 17.5 Hz), 4.68 (1H, s), 4.86 (1H, d, *J* = 11.5 Hz), 5.32 (1H, m), 5.68 (1H, d, *J* = 4.0 Hz), 6.68 (2H, m, H-Ar), 6.74 (2H, d, *J* = 7.5 Hz, H-Ar), 6.97 (2H, s, H-Ar), 7.27 (1H, s, H-Ar), 7.26 (1H, t, *J* = 7.5 Hz, H-Ar), 7.32 (1H, d, *J* = 3.5 Hz), 7.39 (1H, t, *J* = 7.5 Hz, H-Ar), 7.73 (2H, br s, NH_2), 7.82 (1H, d, *J* = 7.5 Hz, H-Ar); ^{13}C NMR (125 MHz, DMSO-d_6) δ δ 21.3, 41.6, 46.6, 58.5, 67.1, 101.1, 110.2, 116.9, 119.5, 122.1, 123.7, 125.8, 127.3, 128.0, 129.0, 130.5, 131.0, 131.8, 134.2, 137.3, 142.5, 143.4, 150.1, 165.3, 169.3; IR (KBr) ν (cm-1) 3371, 3331, 3196, 2187, 1726, 1685, 1631, 1581, 1188; HRMS calcd. for $(C_{25}H_{21}N_5O_2+H)^+$, 424.1774, found 424.1773.

Data for 1-allyl-8'-amino-6'-(4-methoxyphenyl)-1',2-dioxo-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4d:

white solid; Yield 89% (202 mg); m.p 240-242 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.64 (3H, s, OCH_3), 3.96 (2H, AB_q, *N*-CH_2), 4.43 (1H, d, *J* = 17.5 Hz), 4.68 (1H, s), 4.86 (1H, d, *J* = 10.0 Hz), 5.35 (1H, m), 5.68 (1H, d, *J*=2.5 Hz), 6.68 (2H, m, H-Ar), 6.78 (3H, m, H-Ar), 7.26 (1H, d, *J* = 7.5 Hz, H-Ar), 7.27 (1H, s), 7.40 (1H, t, *J* = 7.5 Hz, H-Ar), 7.71 (2H, br s, NH_2), 7.81 (1H, d, *J* = 6.0 Hz, H-Ar); ^{13}C NMR (125 M Hz, DMSO-d_6) δ 36.0, 41.6, 45.9, 55.4, 67.2, 101.1, 110.3, 113.7, 117.0, 119.4, 122.3, 123.7, 125.7, 126.1, 131.0, 131.1, 131.8,

142.5, 143.4, 150.0, 159.4, 165.3, 169.2; IR (KBr) ν (cm^{-1}) 3377, 3302, 3238, 3165, 3076, 2962, 2193, 1737, 1697, 1608, 1577; HRMS calcd. for $(C_{25}H_{21}N_5O_3+H)^+$, 440.1728, found 440.1712.

Data for 1-allyl-8'-amino-6'-(2-methoxyphenyl)-1',2-dioxo-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4e:

white solid; Yield 87% (197 mg); m.p 244-246 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.68 (3H, s, OCH_3), 4.00 (2H, AB_q, *N*-CH_2), 4.62 (1H, d, *J* = 17.0 Hz), 4.94 (1H, d, *J* = 10.5 Hz), 5.10 (1H, s), 5.43 (1H, m), 5.66 (1H, d, *J* = 3.5), 6.71 (1H, d, *J* = 8.0 Hz, H-Ar), 6.77 (1H, d, *J* = 8.0 Hz H-Ar), 7.85 (1H, t, *J* = 7 Hz, H-Ar), 7.13-7.21 (3H, m, H-Ar), 7.27 (1H, d, *J* = 3.5 Hz), 7.35 (1H, t, *J* = 7.5 Hz, H-Ar), 7.64 (1H, d, *J* = 7.0 Hz, H-Ar), 7.72 (2H, s br, NH_2); ^{13}C NMR (125 M Hz, DMSO-d6) δ 37.9, 41.8, 55.3, 58.4, 66.9, 100.9, 109.9, 111.0, 117.4, 119.5, 120.5, 122.2, 122.5, 123.9, 126.3, 129.6, 130.0, 131.2, 131.4, 142.4, 142.9, 150.2, 157.4, 165.3, 169.1; IR (KBr) ν (cm^{-1}) 3437, 3288, 3147, 3084, 2968, 2846, 2191, 1726, 1685, 1625, 1606, 1182; HRMS calcd. for $(C_{25}H_{21}N_5O_3+H)^+$, 440.1728, found 440.1715.

Data for 1-allyl-8'-amino-6'-(4-chlorophenyl)-1',2-dioxo-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-a]pyridazine]-7'-carbonitrile 4f:

white solid; Yield 77% (170 mg); m.p 260-262 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.96 (2H, AB_q, *N*-CH_2), 4.42 (1H, d, *J* = 16.5 Hz), 4.78 (1H, br s), 4.88 (1H, br s), 5.36 (1H, br s), 5.69 (1H, br s), 6.79-76.91 (3H, m, H-Ar), 7.21-7.41 (5H, m, H-Ar), 7.78 (3H, m, H-Ar); ^{13}C NMR (125 M Hz, DMSO-d_6) δ 41.5, 45.9, 57.8, 66.9, 101.3, 110.4, 116.9, 119.4, 121.8, 123.9, 125.8, 128.3, 130.9, 131.8, 132.0, 133.2, 133.5, 142.7, 143.2, 150.2, 165.3, 168.9; IR (KBr) ν (cm^{-1}) 3361, 3378, 3103, 2189, 1726, 1683, 1629, 1579, 1197,759; HRMS calcd. for $(C_{24}H_{18}N_5O_2Cl+Na)^+$, 466.1052, found 466.0982.

Data for 1-allyl-8'-amino-6'-(2-chlorophenyl)-1',2-dioxo-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4g:

white solid; Yield 83% (184 mg); m.p 262-264 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.09 (2H, AB_q, *N*-CH_2), 4.75 (1H, d, *J* = 17.5 Hz), 5.01 (1H, d, *J* = 10.5 Hz), 5.11 (1H, s), 5.53 (1H, m), 5.70 (1H, d, *J* = 3.5 Hz), 6.86 (1H, d, *J* = 8.0 Hz, H-Ar), 7.19 (1H, t, *J* = 7.5 Hz, H-Ar), 7.24 (2H, m, H-Ar), 7.33 (2H, m, Hz, H-Ar), 7.40 (1H, t, *J* = 8 Hz, H-Ar), 7.71 (1H, d, *J* = 7.5 Hz, H-Ar), 7.83 (2H, br s, NH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 42.0 42.4, 57.9, 66.7, 101.1, 110.3, 117.8, 119.2, 121.8, 123.5, 126.3, 127.6, 129.7, 130.2, 131.1, 131,4, 131,9, 132.6, 134.3, 142.7, 142.7, 150.1, 165.3, 168.9; IR (KBr) ν (cm^{-1}) 3444, 3290, 3147, 2189, 1724, 1625, 1579, 1180, 763; HRMS calcd. for $(C_{24}H_{18}N_5O_2Cl+Na)^+$, 466.1041, found 466.0982.

Data for 1-allyl-8'-amino-6'-(2,4-dichlorophenyl)-1',2-dioxo-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4h:

white solid; Yield 86% (206 mg); m.p 250-252 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.12 (2H, AB_q, *N*-CH_2), 4.78 (1H, d, *J* = 17 Hz), 5.03 (2H, m), 5.59 (1H, m), 5.70 (1H, d, *J* = 3.0 Hz), 6.92 (1H, d, *J* = 8.0 Hz, H-Ar), 7.20 (1H, t, *J* = 7.0 Hz, H-Ar), 7.39 (5H, m, H-Ar), 7.68 (1H, d, *J* = 7.0 Hz, H-Ar), 7.88 (2H, br s, NH_2); ^{13}C NMR (125 MHz, DMSO-d6) δ 42.1, 42.2, 57.4, 66.5, 101.3, 110.4, 117.7, 119.1, 121.8, 123.6, 126, 127.9, 129.0, 131.0, 131.9, 132.0, 132.8, 134.0, 135.3, 142.5, 142.8, 150.1, 165.3, 168.6; IR (KBr) ν (cm^{-1}) 3454, 3288, 3142, 3086, 2191, 1726, 1716, 1629, 1577, 1190; HRMS calcd. for $(C_{24}H_{17}N_5O_2Cl_2+H)^+$,

478.0824, found 478.0831.

Data for 1-allyl-8'-amino-1',2-dioxo-6'-(thiophen-2-yl)-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4i:

white solid; Yield 84% (174 mg); m.p 244-245 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.98 (2H, AB_q, *N*-CH_2), 4.62 (1H, d, *J* = 17.5 Hz), 4.95 (1H, d, *J* = 10.5 Hz), 5.08 (1H, s), 5.42 (1H, m), 5.69 (1H, *J* = 3.5 HZ), 6.67 (1H, s), 6.83 (2H, m, H-Ar), 7.30 (1H, t, *J* = 7.5 Hz, H-Ar), 7.32 (2H, m, H-Ar), 7.44 (1H, t, *J* = 8.0 Hz, H-Ar), 7.74 (2H, br s, NH_2), 7.79 (1H, d, *J* = 7.5 Hz, , H-Ar); ^{13}C NMR (125 MHz, DMSO-d_6) δ 41.6, 41.9, 58.9, 66.9, 101.3, 110.4, 117.7, 119.3, 122.3, 123.9, 125.7, 126.7, 126.8, 128.5, 131.1, 132.0, 136.8, 142.9, 143.7, 149.8, 165.3, 168.9; IR (KBr) *v* 3388, 3284, 2191, 1720, 1718, 1625, 1606, 1188, 765; HRMS calcd. for $(C_{22}H_{17}N_5O_2S+H)^+$, 416.1186, found 416.1169.

Data for 8'-amino-1-benzyl-1',2-dioxo-6'-phenyl-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4j:

Wite solid; Yield 91% (208 mg); m.p 281-282 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.54 (2H, AB_q, *N*-CH_2), 4.81 (1H, s), 5.73 (1H, s), 6.63 (1H, d, *J* = 7.5 Hz), 6.67 (2H, d, *J* = 5.5 Hz, H-Ar), 6.96 (2H, br s, H-Ar), 7.12-7.33 (9H, m, H-Ar), 7.74 (2H, s br, NH_2), 7.87 (1H, d, *J* = 7.0 Hz, H-Ar); ^{13}C NMR (125 MHz, DMSO-d_6) δ 42.9, 46.2, 58.7, 67.2, 101.5, 110.4, 119.5, 121.9, 124.0, 126.0, 126.9, 127, 128.4, 128.5, 128.9, 130.1, 132.0, 134.2, 135.1, 142.6, 143.3, 149.9, 165.4, 169.4; IR (KBr) *v* (cm^{-1}) 3390, 3284, 3143, 3062, 2189, 1728, 1720, 1679, 1197, 767; HRMS calcd. for $(C_{28}H_{21}N_5O_2+H)^+$, 460.1773, found 460.1768.

Data for 8'-amino-1-benzyl-1',2-dioxo-6'-(*p*-tolyl)-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4k:

White solid; Yield 90% (213 mg); m.p 286-287 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.22 (3H, s, CH_3), 4.56 (2H, AB_q, *N*-CH_2), 4.75 (1H, s), 5.71 (1H, d, *J* = 3.5 Hz), 6.65 (1H, d, *J* = 7.5 Hz, H-Ar), 6.72 (2H, d, *J* = 7.5 Hz, H-Ar), 6.83 (2H, br, s, , H-Ar), 6.92 (2H, d, *J* = 7.5 Hz, , H-Ar), 7.16 (2H, t, *J* = 7.5 Hz, H-Ar), 7.20-7.26 (3H, m, H-Ar), 7.33 (1H, t, *J* = 7.5 Hz, H-Ar), 7.70 (2H, br s, NH_2), 7.85 (1H, t, *J* = 7 Hz); ^{13}C NMR (125 M Hz, DMSO-d_6) δ 21.1, 43.0, 45.8, 58.9, 67.2, 101.4, 110.4, 119.5, 122.1, 124.0, 125.9, 127.1, 127.7, 128.7, 129.0, 130.0, 131.3, 131.9, 135.3, 137.7, 142.5, 143.4, 150.0, 165.4, 169.4; IR (KBr) *v* (cm^{-1}) 3388, 3282, 2187, 1724, 1722, 1627, 1573, 1191,759; HRMS calcd. for $(C_{29}H_{23}N_5O_2+H)^+$, 474.1930, found 474.1923.

Data for 8'-amino-1-benzyl-1',2-dioxo-6'-(m-tolyl)-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4l:

White solid; Yield 89% (210 mg); m.p 254-256 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.09 (3H, s, CH_3), 4.69 (2H, AB_q, CH_2), 5.18 (1H, s), 5.72 (1H, s), 6.80 (1H, d, *J* = 7.5 Hz, H-Ar), 6.97 (2H, br s, H-Ar), 7.19 (2H, m, H-Ar), 7.24 (4H, m, H-Ar), 7.29 (1H, br s), 8.35 (2H, t, *J* = 8.0 Hz, H-Ar), 7.76 (3H, m, H- Ar, NH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 31.1, 42.1, 43.3, 58.2, 66.8, 101.4, 110.3, 119.2, 121.5, 123.6, 126.7, 127.5, 127.7, 127.9, 129.0, 129.8 130.2, 131.4, 132.1, 132.5, 134.2, 135.4, 142.6, 142.8, 150.0, 165.4, 169.3; IR (KBr) *v* (cm^{-1}) 3367, 3298, 3142, 2187, 1726, 1687, 1631, 1608, 1191; EI-MS: m/z (%) = 474.60.

Data for 8'-amino-1-benzyl-6'-(2-methoxyphenyl)-1',2-dioxo-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4m:

White solid; Yield 87% (213 mg); m.p 250-252 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.37 (3H, s, OCH_3), 4.60 (2H, AB_q, *N*-CH_2), 5.08 (1H, s), 5.70 (1H, d, *J* = 3.5 Hz), 6.63 (1H, d, *J*

= 8.0 Hz, H-Ar), 6.73 (1H, d, *J* = 8.5 Hz, H-Ar), 6.82 (3H, m, H-Ar), 7.20 (6H, m, H-Ar), 7.27 (1H, d, *J* = 4.0 Hz), 7.29 (1H, t, *J* = 8.0 Hz, H-Ar), 7.68 (1H, d, *J* = 7.5 Hz, H-Ar), 7.72 (2H, br s, NH_2); ^{13}C NMR (125 M Hz, DMSO-d_6) δ 37.6, 43.1, 55.3, 58.7, 67.0, 101.2, 110.0, 111.1, 119.5, 120.7, 122.0, 122.4, 123.2, 126.6, 127.2, 127.7, 128.9, 129.7, 130.4, 131.5, 135.5, 142.4, 142.9, 150.2, 157.4, 165.4, 169.5; IR (KBr) *ν* (cm^{-1}) 3440, 3304, 3062, 2956, 2841, 2197, 1732, 1681, 1627, 1573, 1182; HRMS calcd. for $(C_{29}H_{23}N_5O_3+H)^+$, 490.1884, found 490.1871.

Data for 8'-amino-1-(4-chlorobenzyl)-1',2-dioxo-6'-phenyl-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4n:

White solid; Yield 85% (210 mg); m.p 256-258 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.54 (2H, AB_q, *N*-CH_2), 4.81 (1H, s), 5.73 (1H, s), 6.67 (3H, t, *J* = 9.0 Hz, H-Ar), 6.94 (2H, br s, Hz, H-Ar), 7.12 (2H, br s, H-Ar), 7.26 (5H, m, H-Ar), 7.35 (1H, t, *J* = 8.0 Hz, H-Ar), 7.75 (2H, br s, NH_2), 7.87 (1H, d, *J* = 7.5 Hz, H-Ar); ^{13}C NMR (125 MHz, DMSO-d_6) δ 42.3, 46.2, 58.6, 67.7, 101.6, 110.3, 119.5, 121.1, 124.0, 126.1, 128.4, 128.5, 128.8, 129.1, 130.1, 132.2, 132.0, 132.7, 132.4, 142.7, 143.1, 150.1, 165.4, 169.3; IR (KBr) *ν* (cm^{-1}) 3446, 3298, 3126, 2196, 1732, 1685, 1629, 1579, 1188, 758, EI-MS: m/z (%) = 493.50.

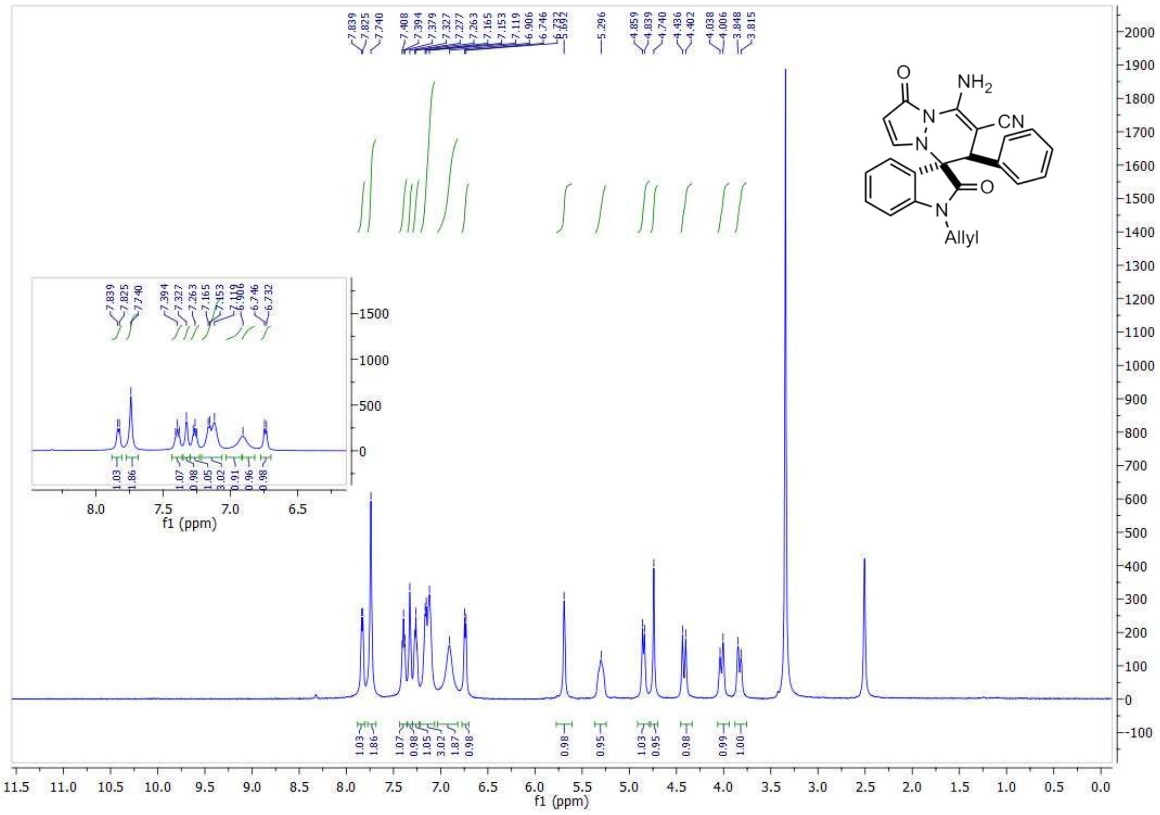
Data for 8'-amino-1-(4-chlorobenzyl)-6'-(4-chlorophenyl)-1',2-dioxo-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4o:

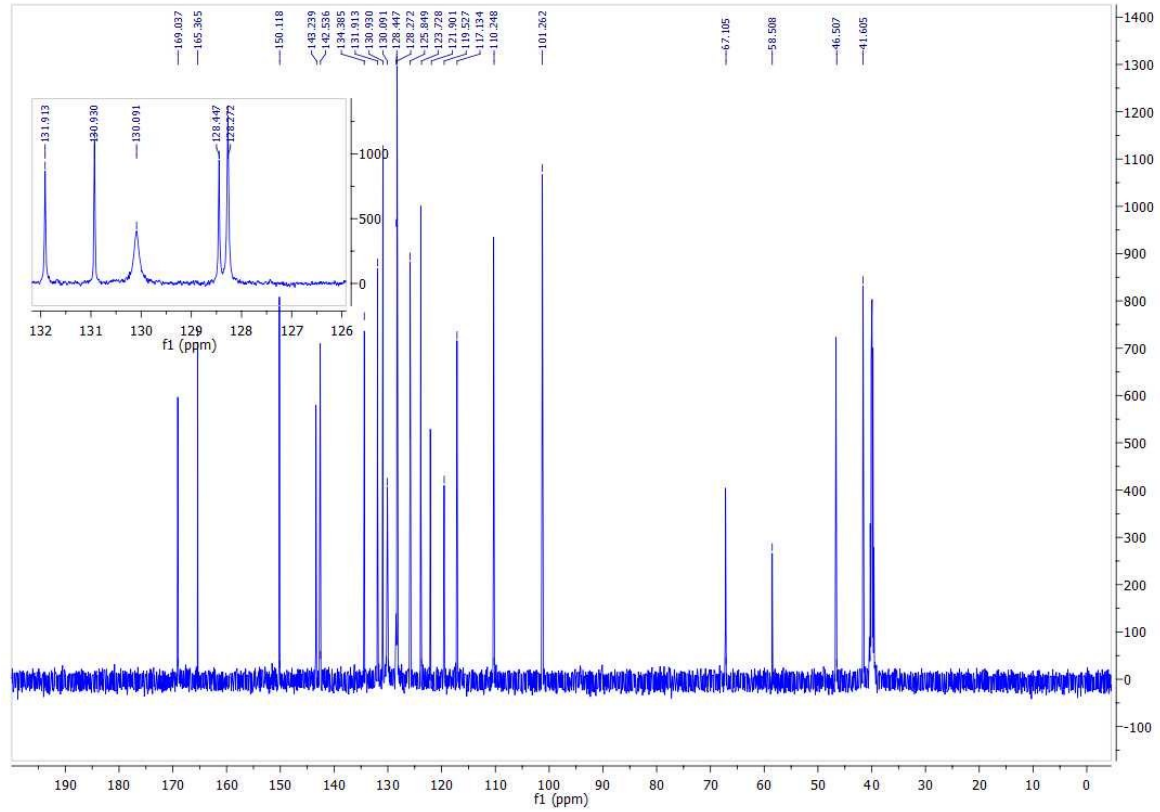
White solid; Yield 90% (237 mg); m.p 214-216 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.58 (2H, AB_q, *N*-CH_2), 4.84 (1H, s), 5.74 (1H, d, *J* = 3.5 Hz), 6.78 (3H, m, H-Ar), 6.92 (2H, br, s, , H-Ar), 7.17 (2H, d, *J* = 7.0 Hz, H-Ar), 7.27 (4H, m, H-Ar), 7.39 (1H, t, *J* = 7.5 Hz, H-Ar), 7.78 (2H, br s, NH_2), 7.86 (1H, d, *J* = 7.5 Hz, , H-Ar); ^{13}C NMR (125 M Hz, DMSO-d_6) δ 42.4, 45.5, 58.0, 66.9, 101.7, 110.4, 119.4, 121.8, 124.2, 126.1, 128.5, 128.7, 129.3, 131.9, 132.2, 132.50, 133.3, 133.4, 134.5, 142.8, 143.1, 150.2, 165.4, 168.1; IR (KBr) *ν* (cm^{-1}) 3363, 3273, 3143, 3070, 2187, 1722, 1683, 1633, 1571, 1191, 754, 599, EI-MS: m/z (%) = 527.60.

Data for 8'-amino-1-(4-chlorobenzyl)-6'-(2-chlorophenyl)-1',2-dioxo-1'*H*,6'*H*-spiro[indoline-3,5'-pyrazolo[1,2-*a*]pyridazine]-7'-carbonitrile 4p:

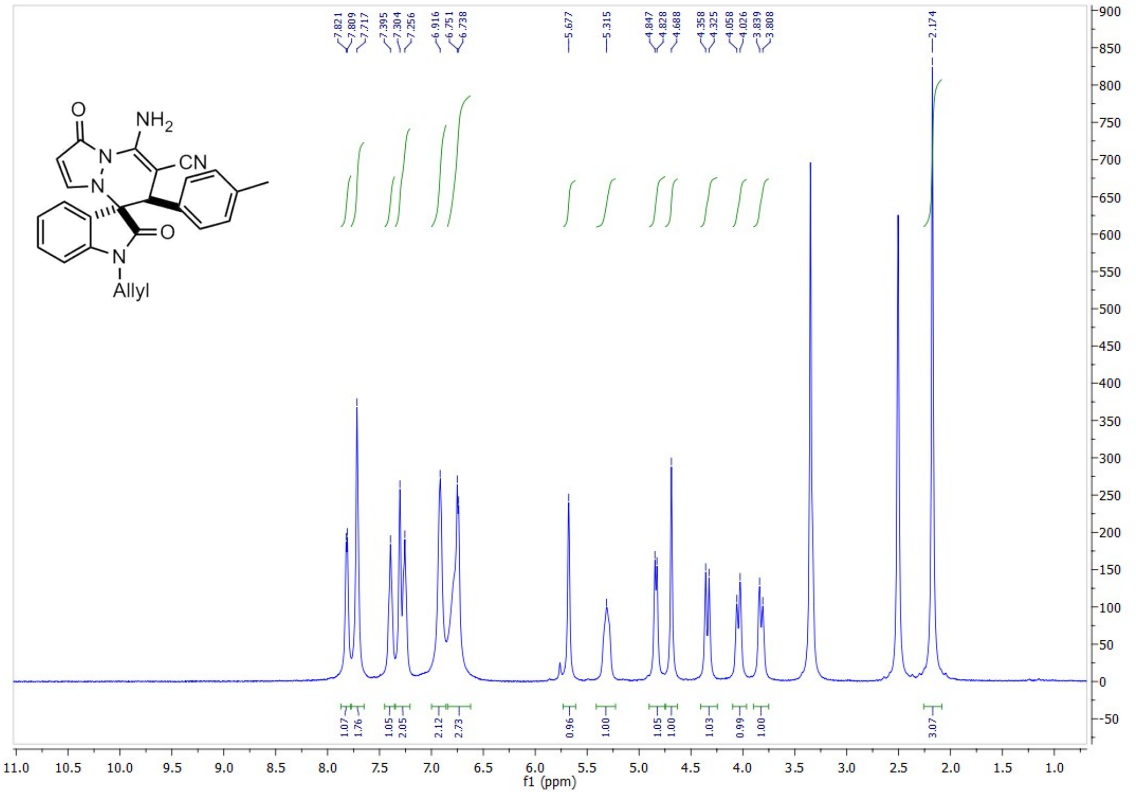
White solid; Yield 86% (226 mg); m.p 262-264 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.70 (2H, AB_q, *N*-CH_2), 5.14 (1H, s), 5.74 (1H, d, *J* = 4.0 Hz), 6.94 (1H, d, *J* = 8.0 Hz, H-Ar), 7.04 (2H, d, *J* = 8.5 Hz, H-Ar), 7.22 (2H, m, H-Ar), 7.32 (3H, m, H-Ar), 7.40 (1H, t, *J* = 7.5 Hz, H-Ar), 7.43 (1H, d, *J* = 2.0 Hz), 7.76 (1H, d, *J* = 7.0 Hz, H-Ar), 7.86 (2H, br s, NH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 41.7, 42.7, 57.6, 66.5, 101.6, 110, 119.1, 121.4, 123.8, 126.8, 128.0, 128.9, 129.1, 129.9, 131.7, 132.2, 132.2, 132.7, 132.9, 134.0, 134.6, 135.1, 142.6, 142.9, 150.1, 165.4, 169.1; IR (KBr) *ν* (cm^{-1}) 3375, 3290, 3176, 2925, 2191, 1728, 1720, 1641, 1608, 1191, 837, 754, EI-MS: m/z (%) = 527.70.

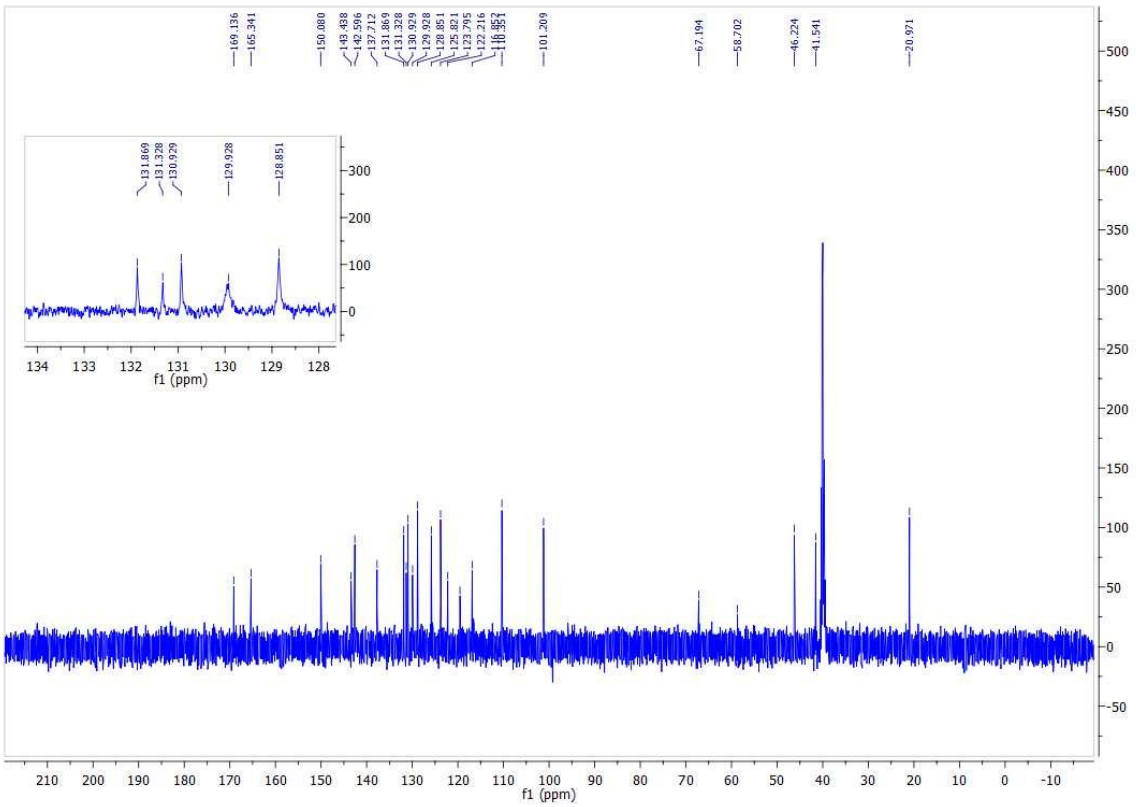
^{1}H and ^{13}C NMR spectra of compound 4a:



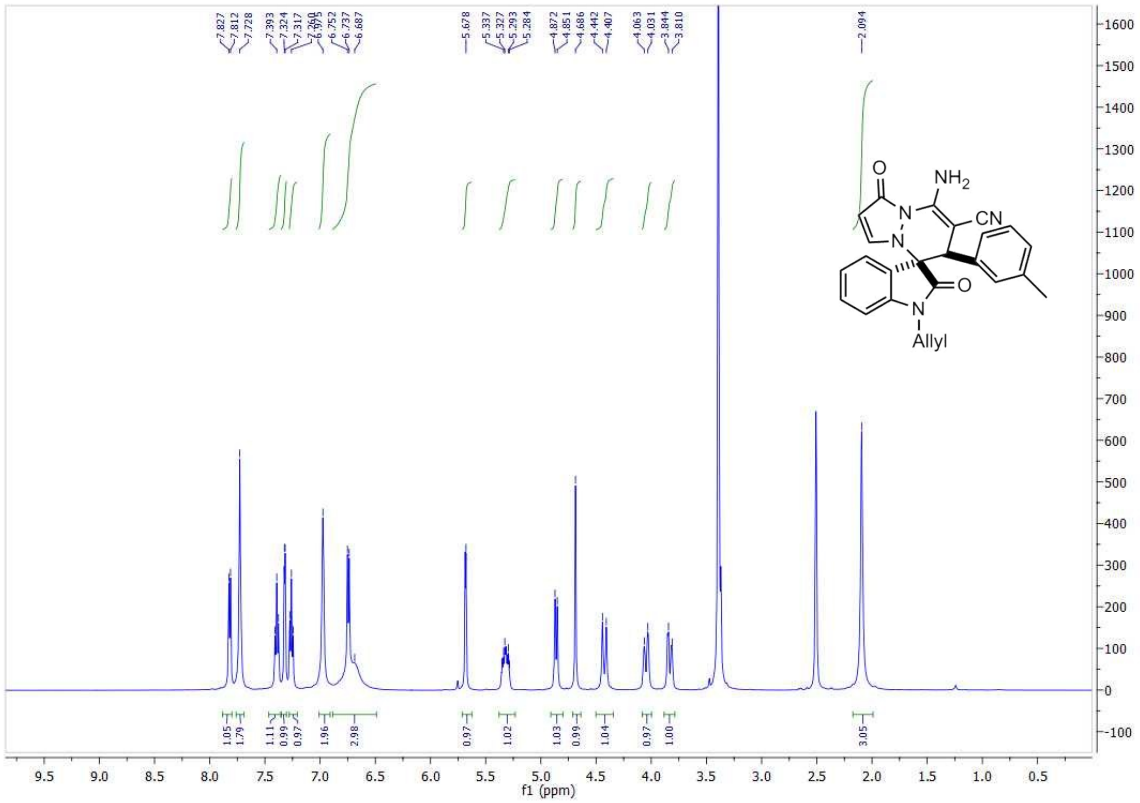


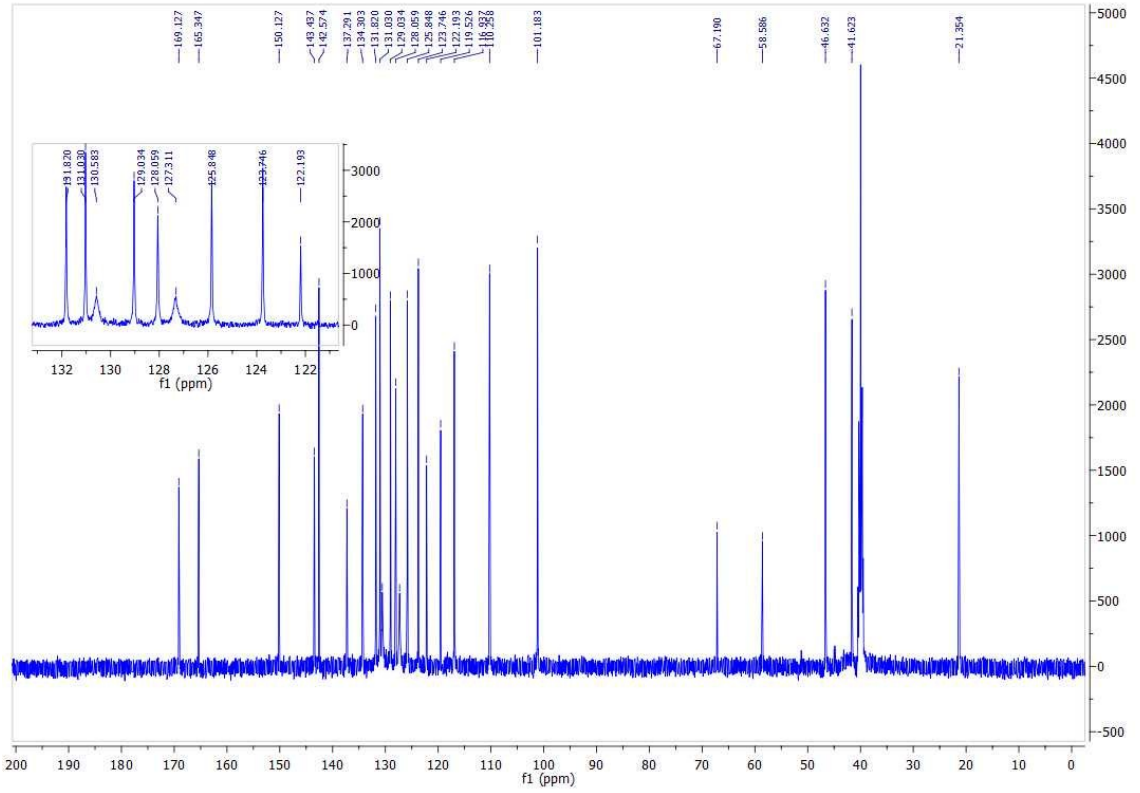
^{1}H and ^{13}C NMR spectra of compound 4b:



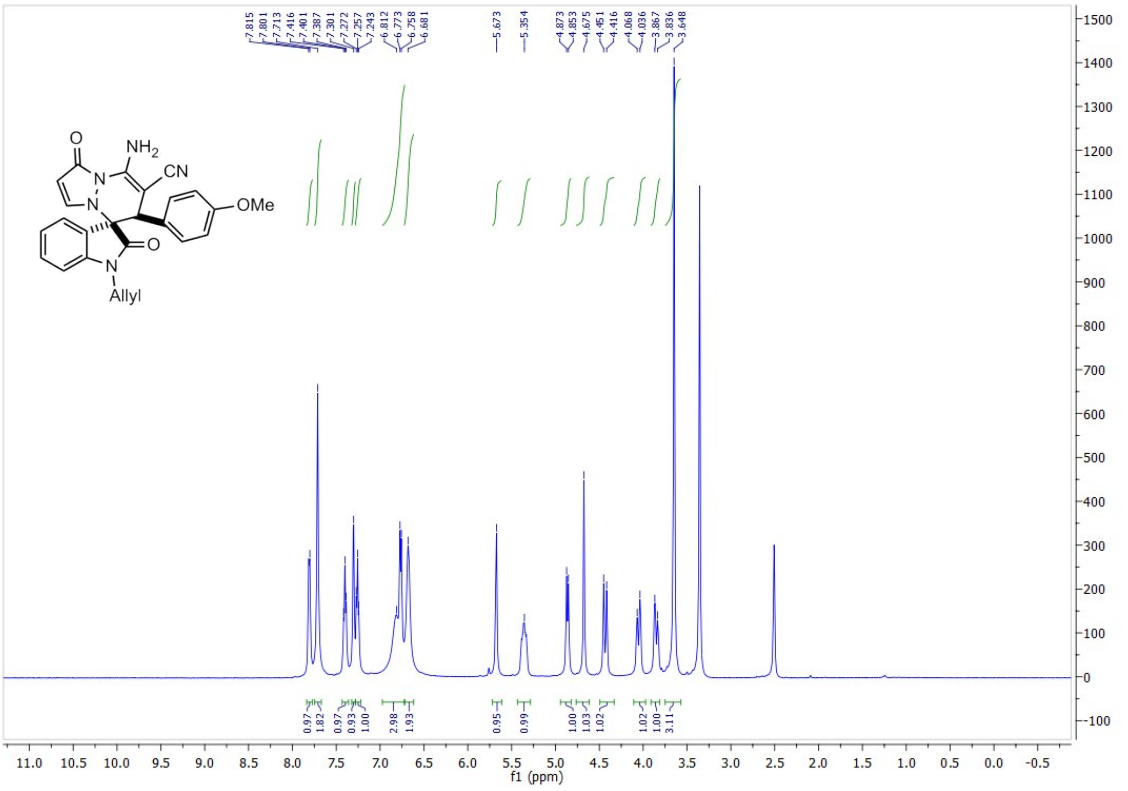


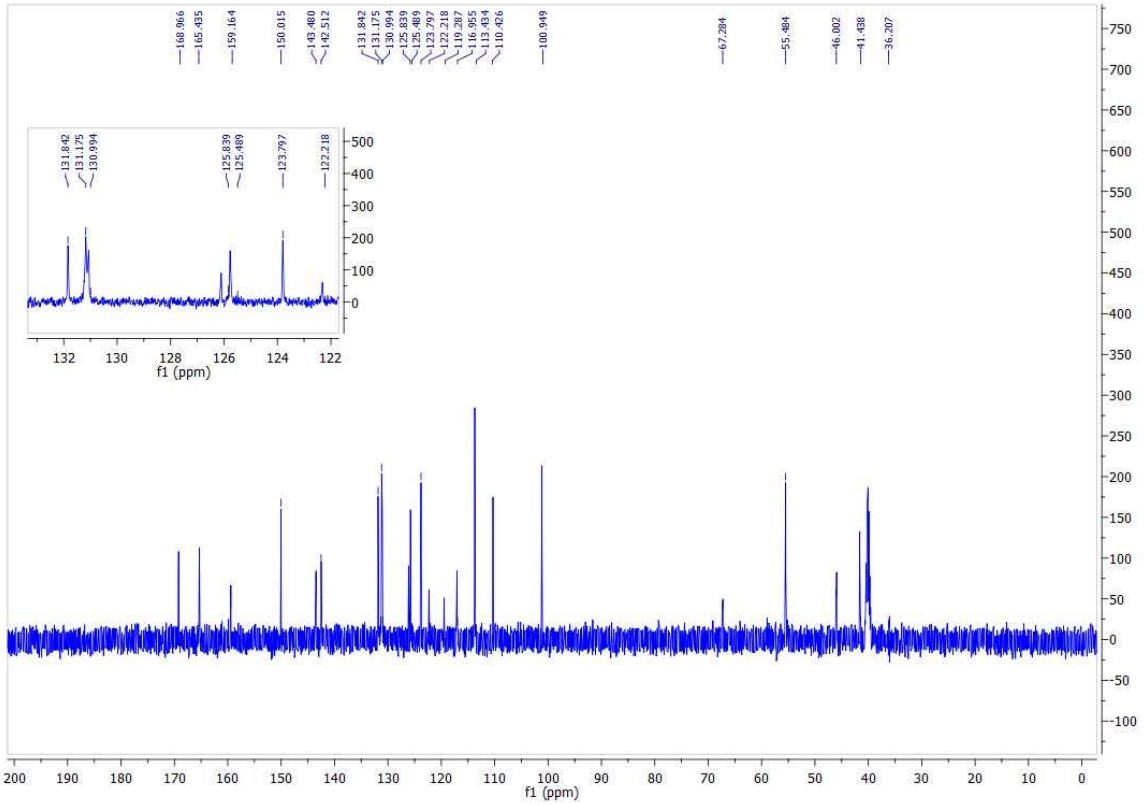
^{1}H and ^{13}C NMR spectra of compound 4c:



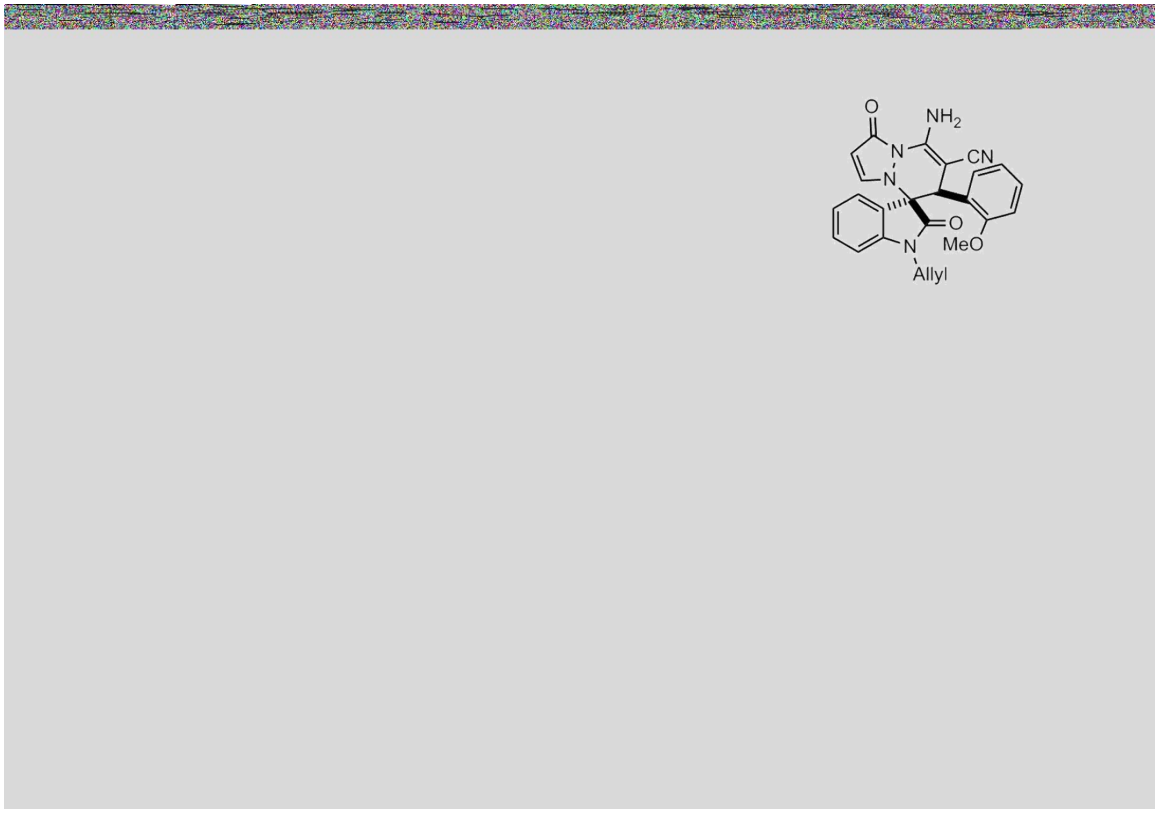


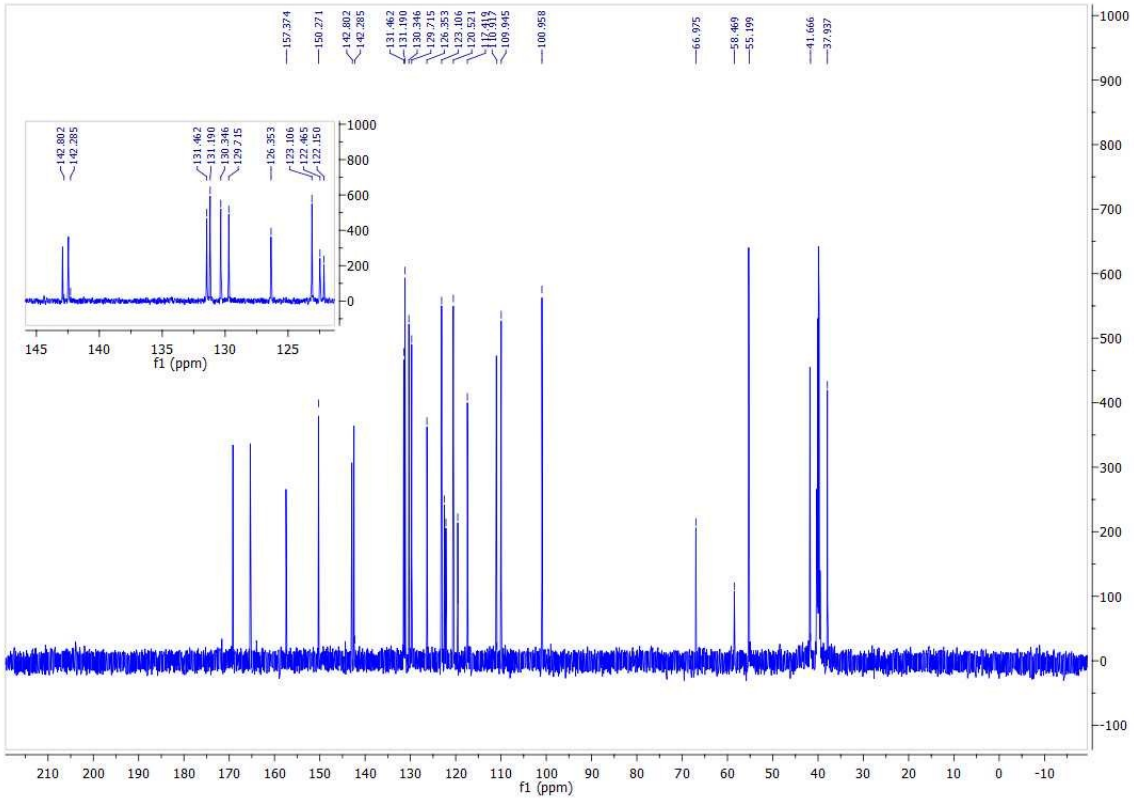
^{1}H and ^{13}C NMR spectra of compound 4d:



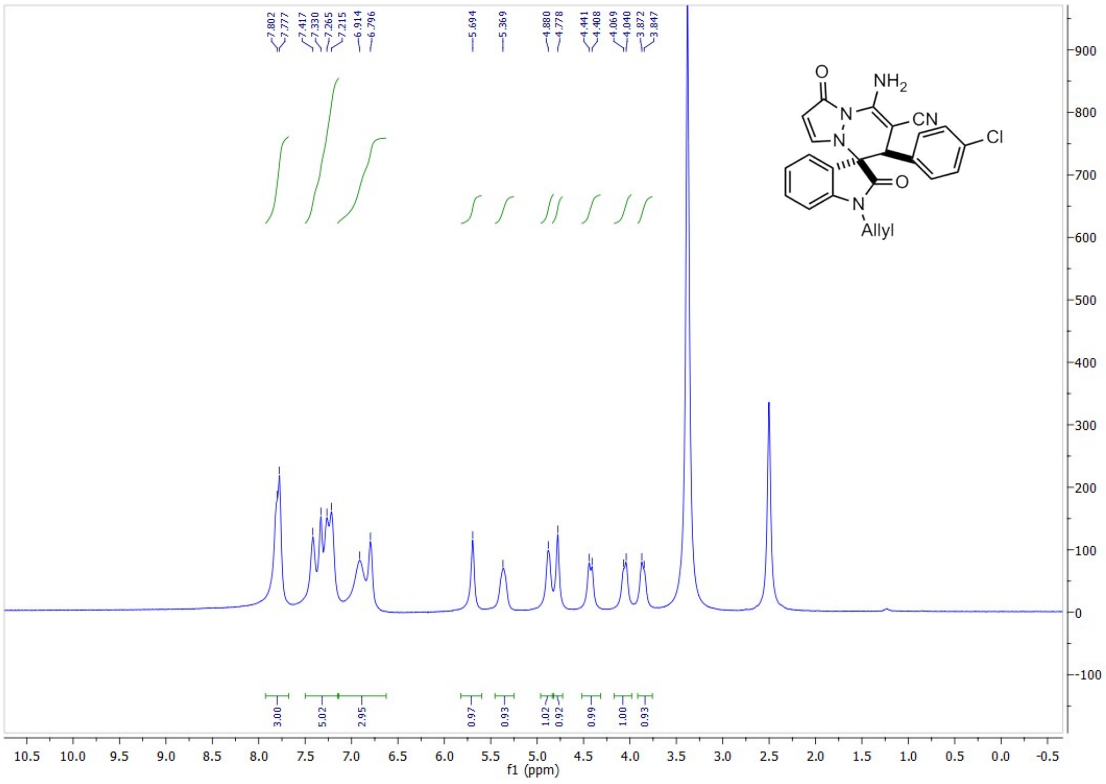


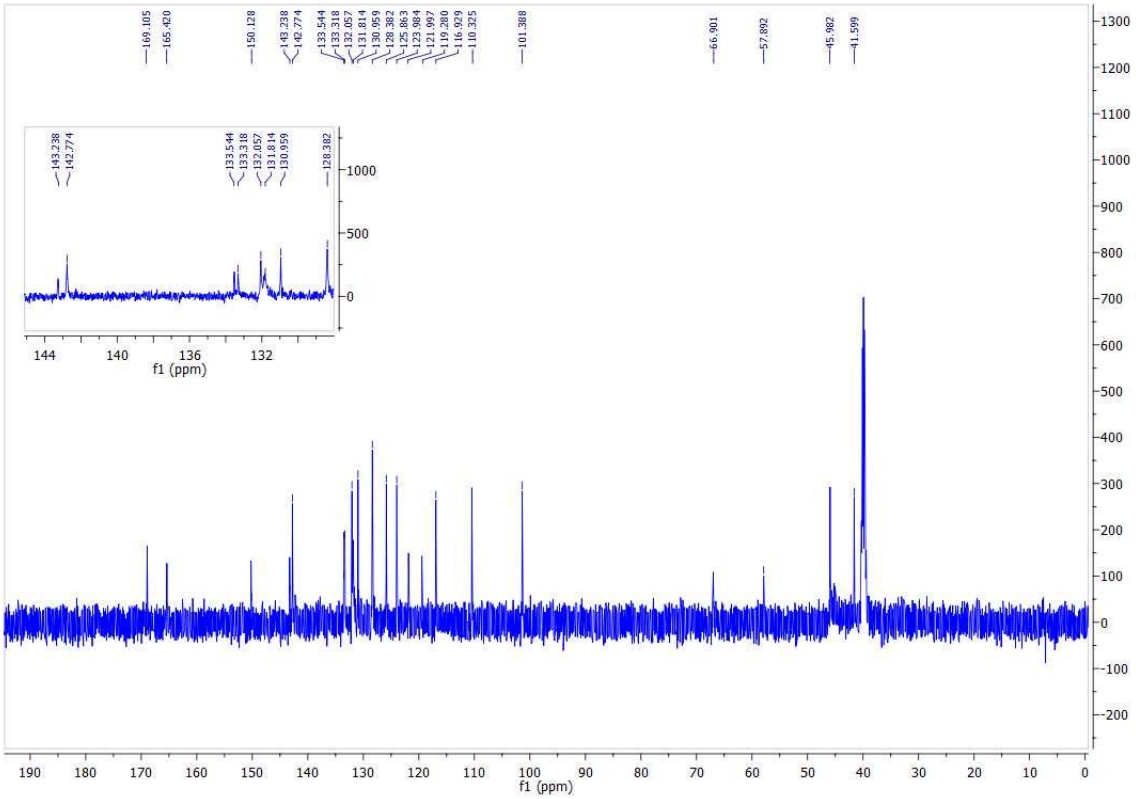
^{1}H and ^{13}C NMR spectra of compound 4e:



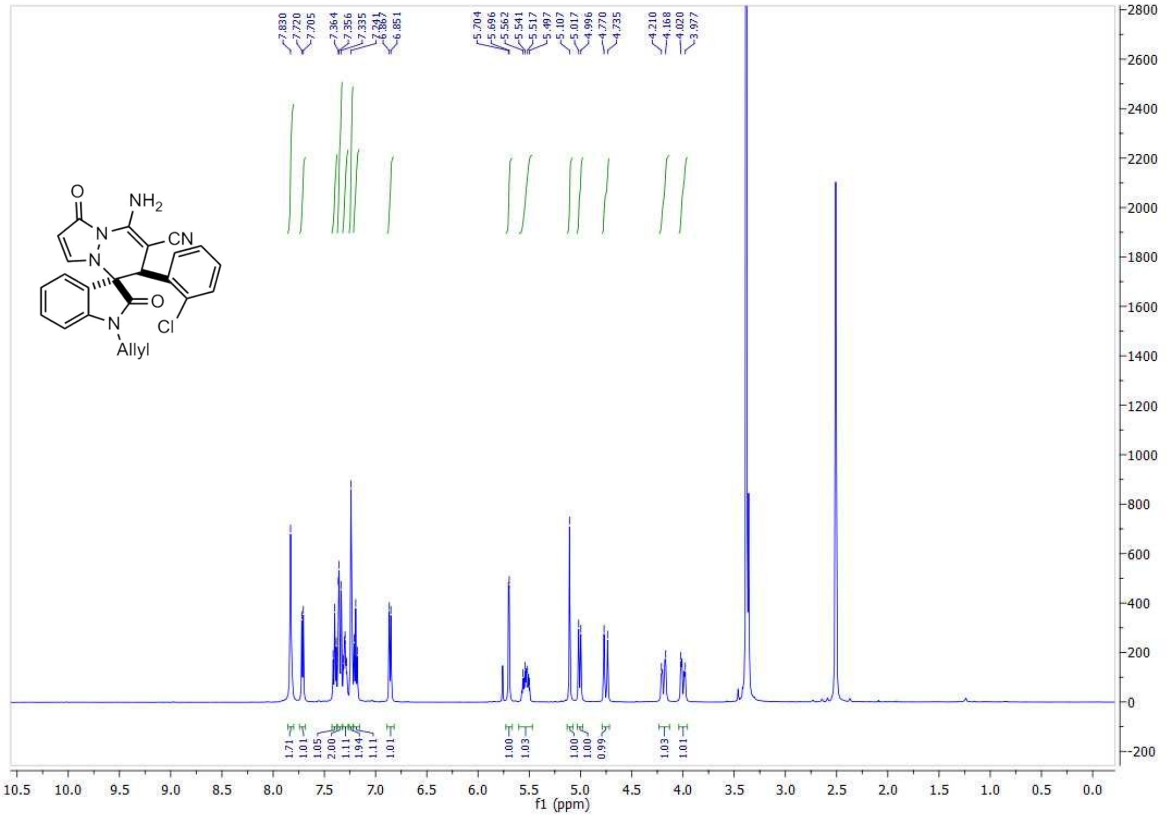


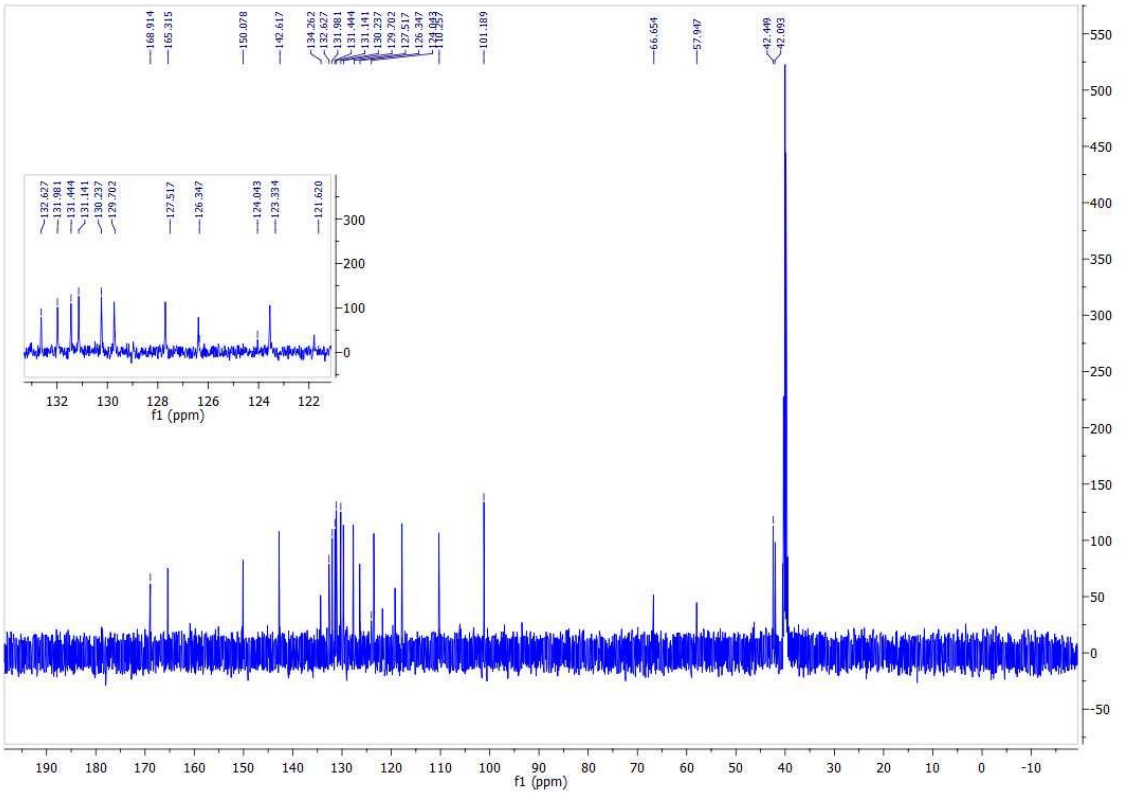
^{1}H and ^{13}C NMR spectra of compound 4f:



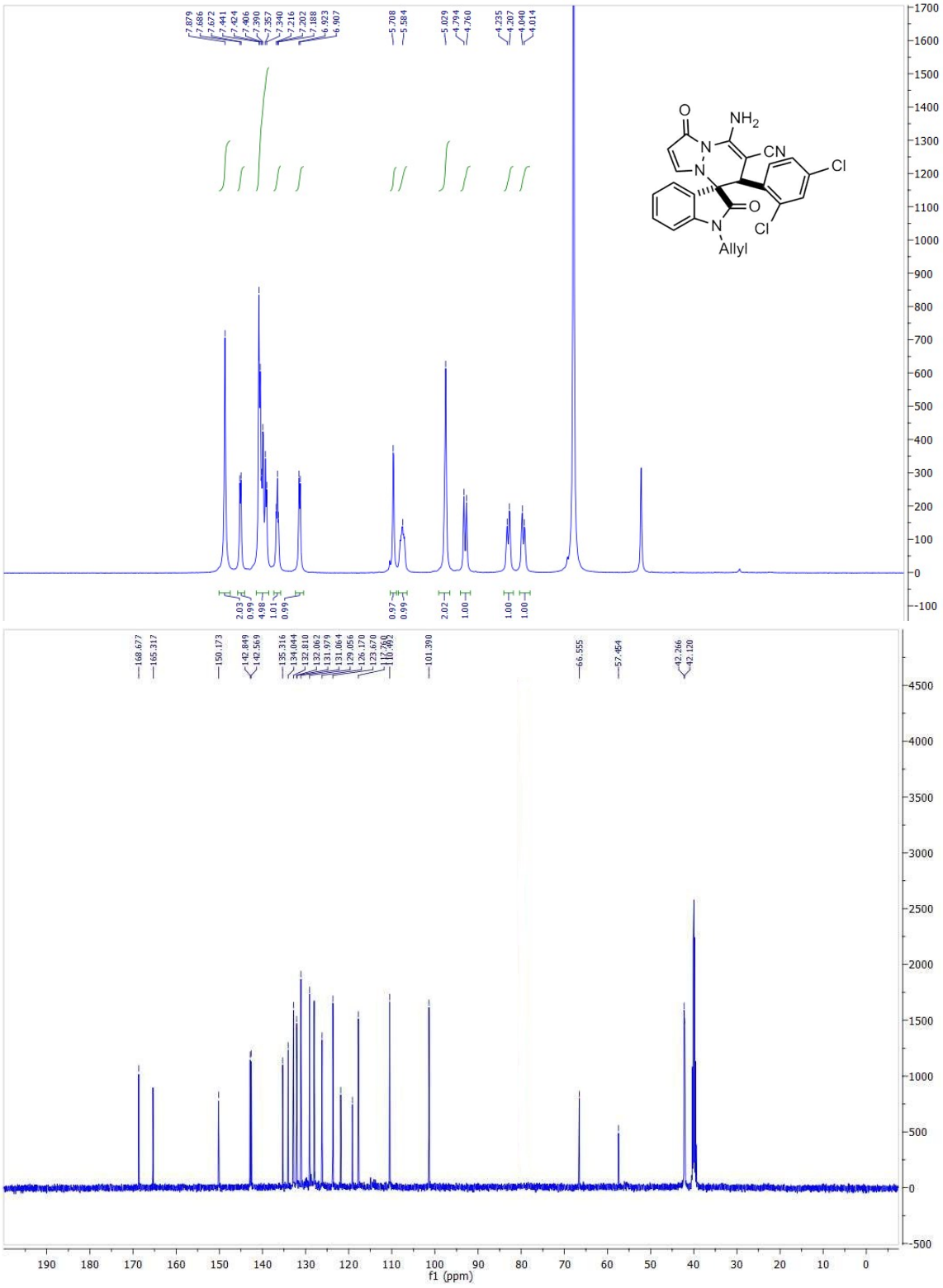


^{1}H and ^{13}C NMR spectra of compound 4g:

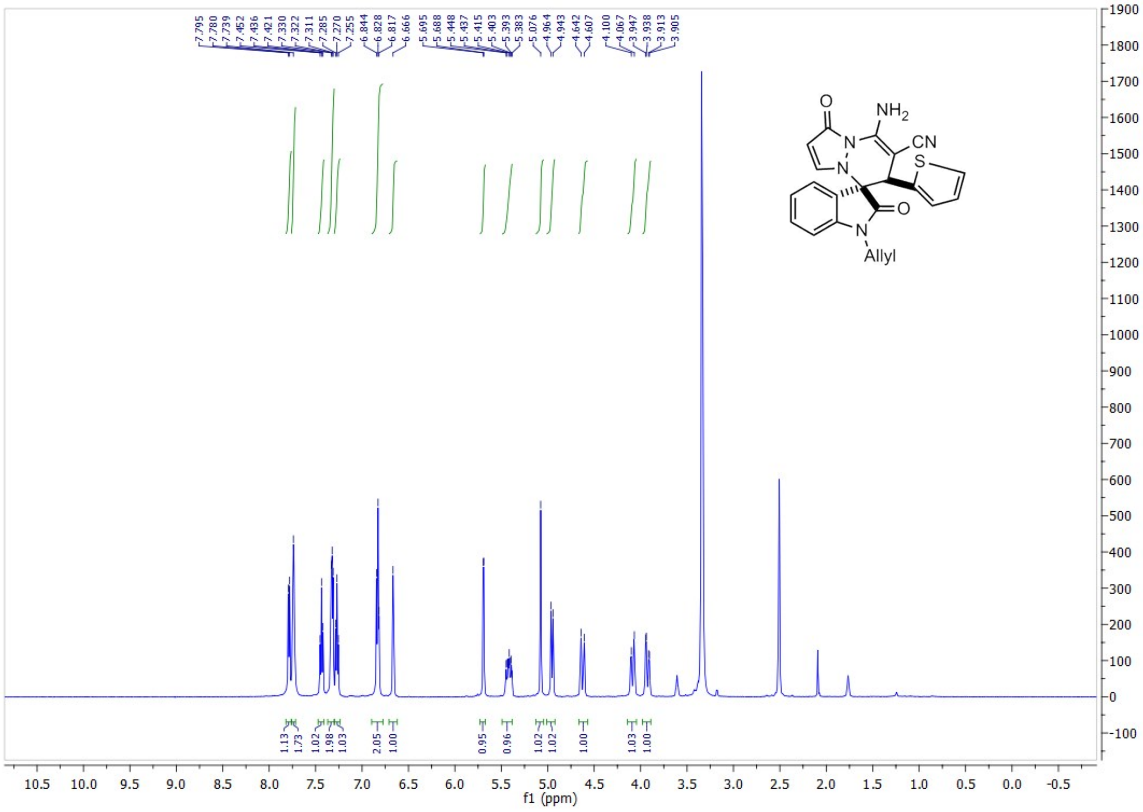


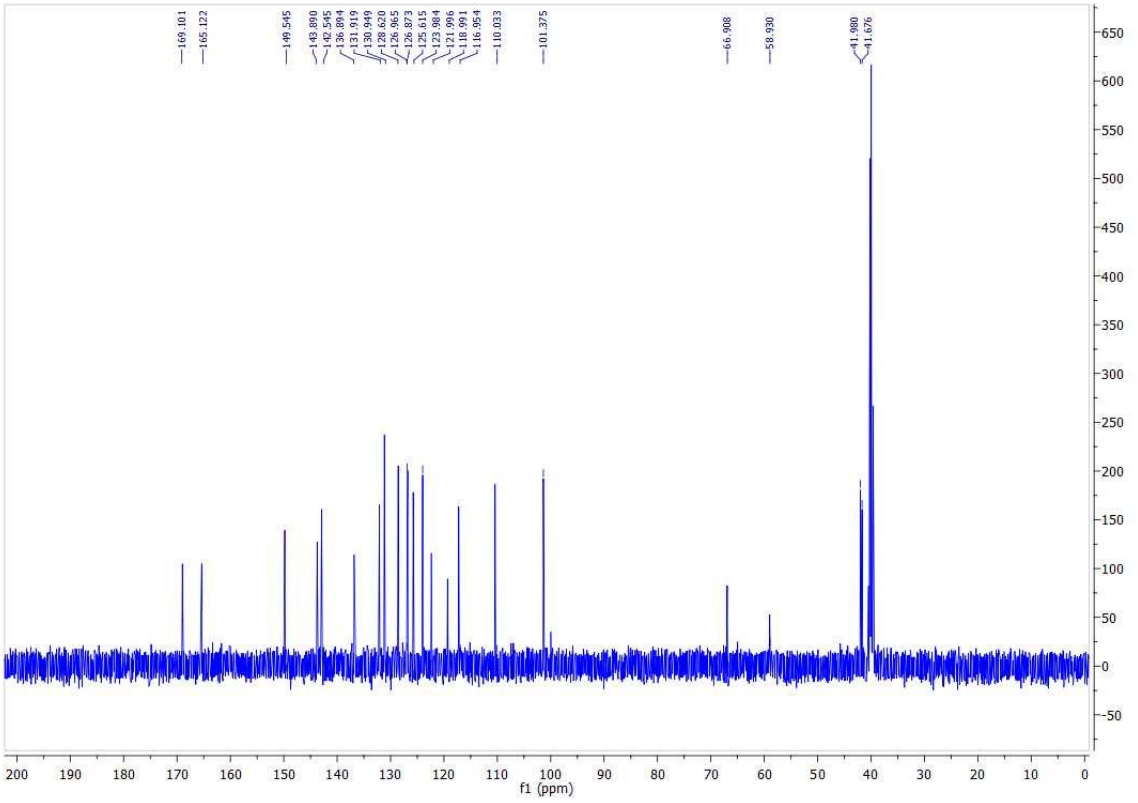


^{1}H and ^{13}C NMR spectra of compound 4h:

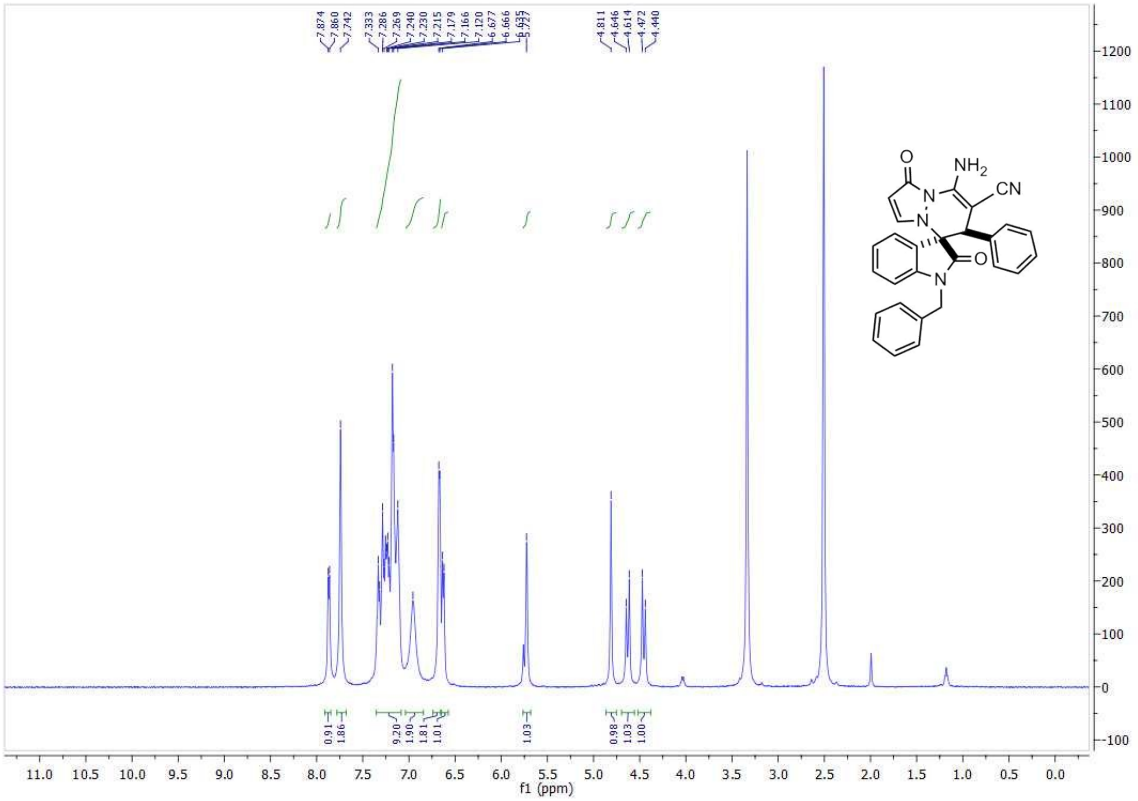


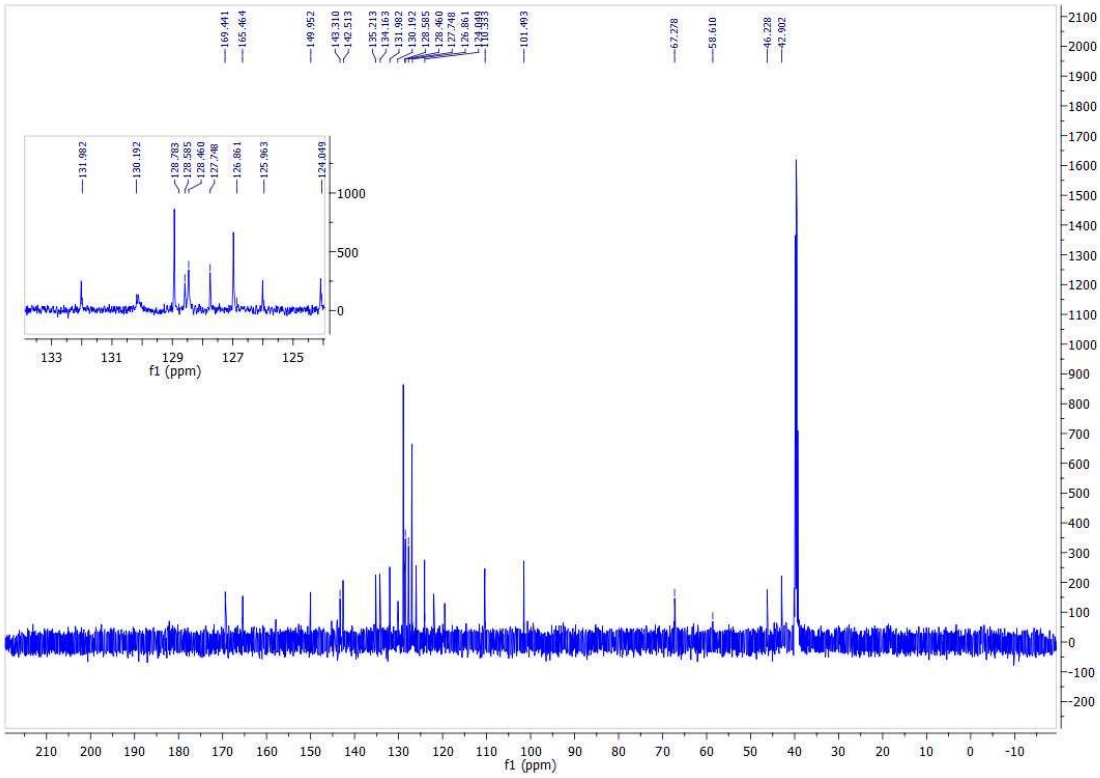
^{1}HNMR and ^{13}CNMR spectra of compound 4i:



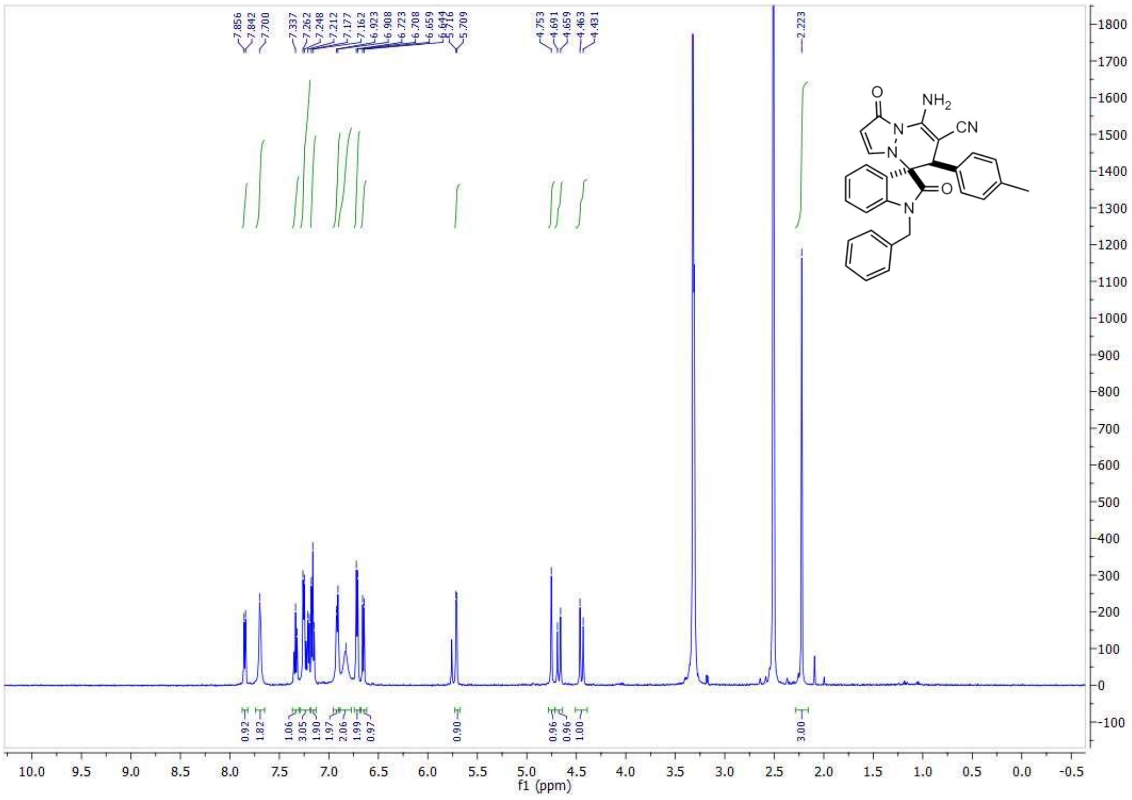


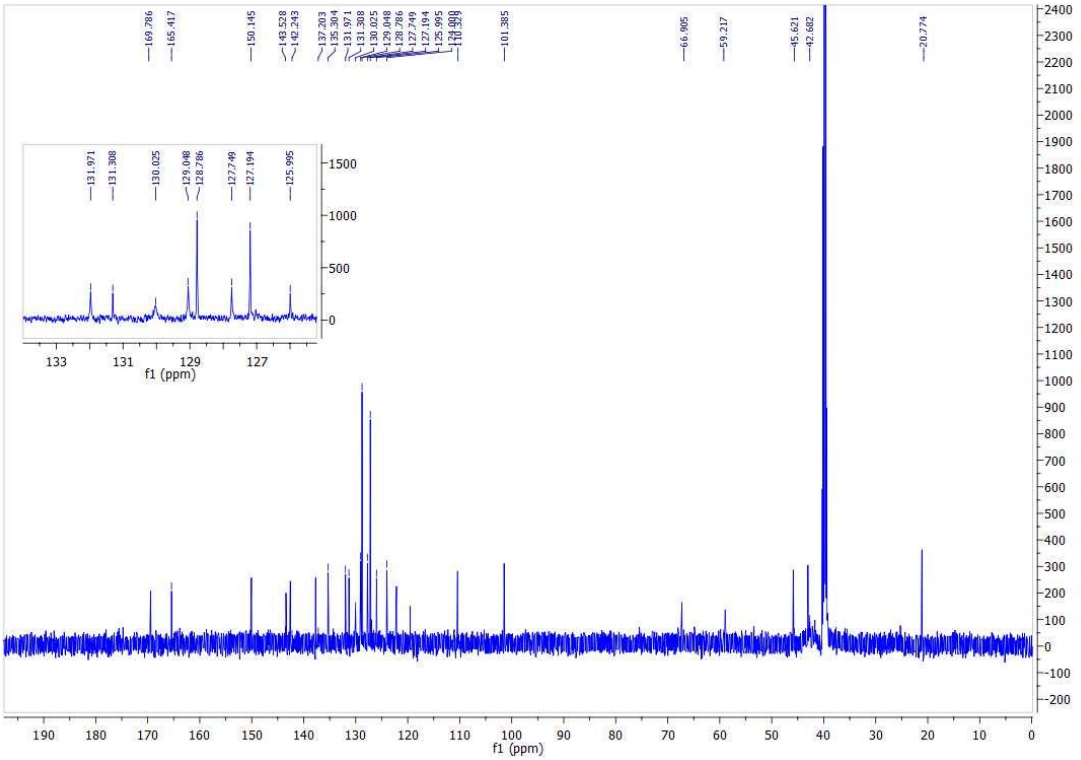
^{1}H and ^{13}C NMR spectra of compound 4j:



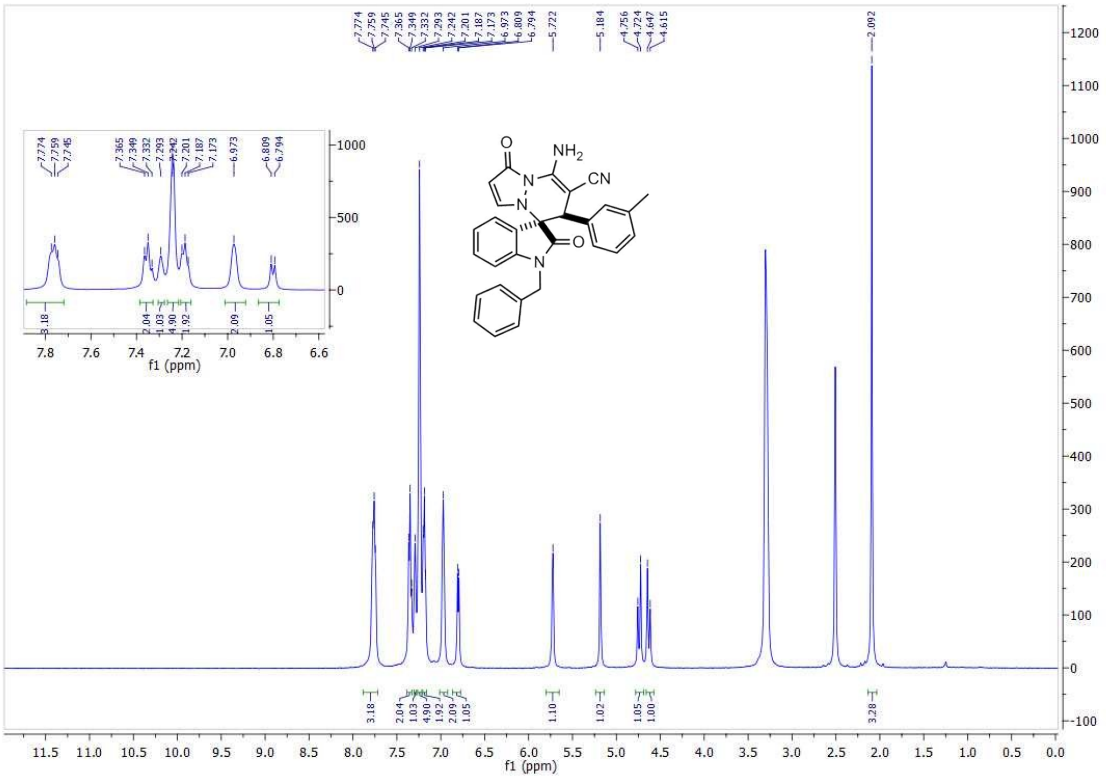


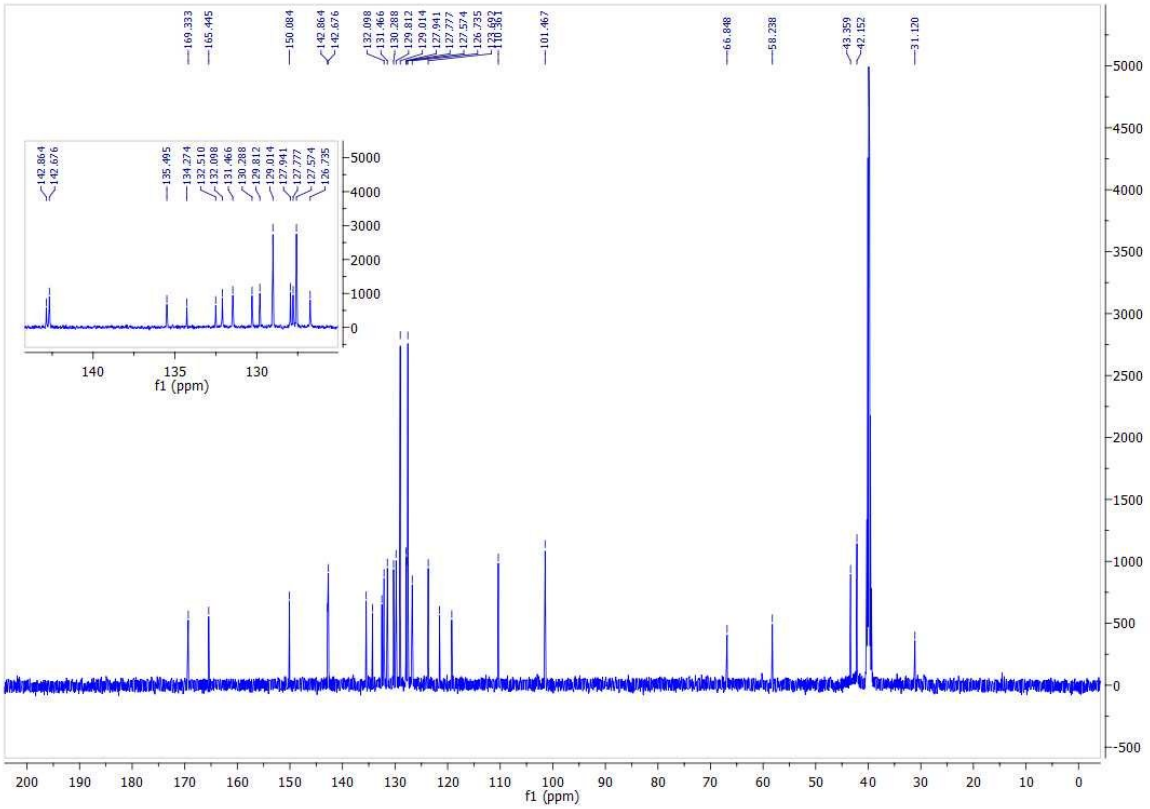
^{1}HNMR and ^{13}CNMR spectra of compound 4k:



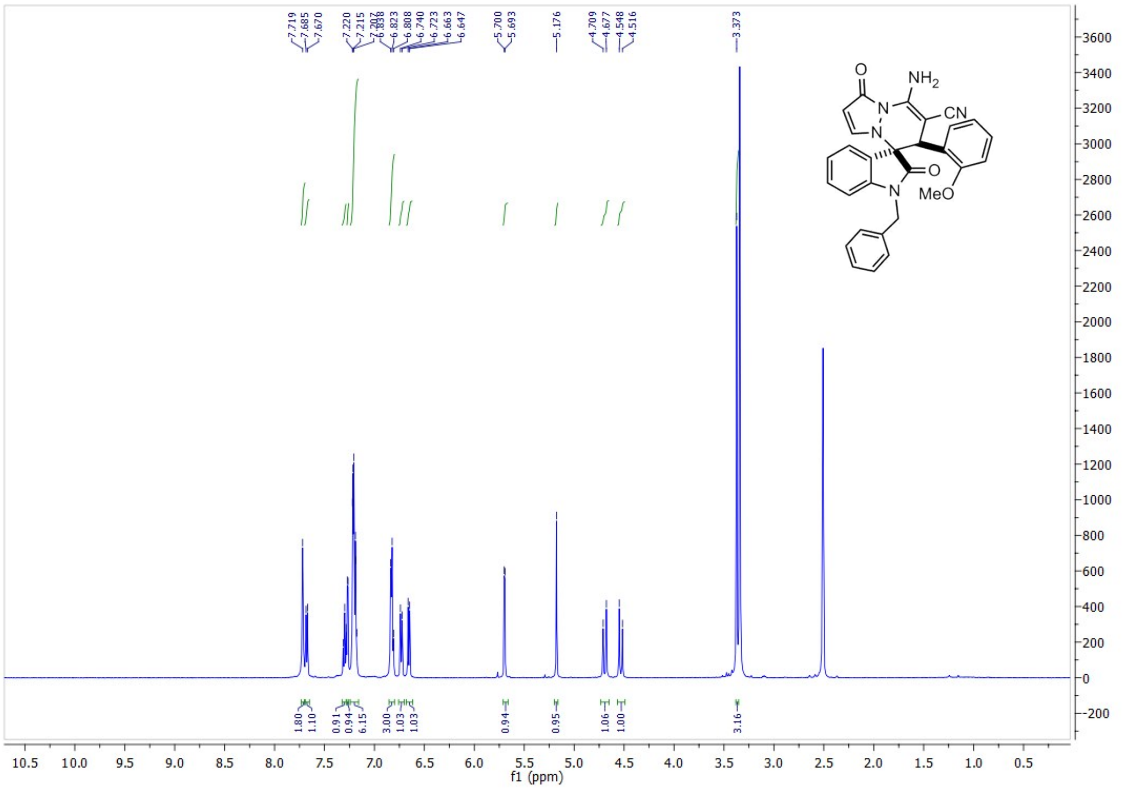


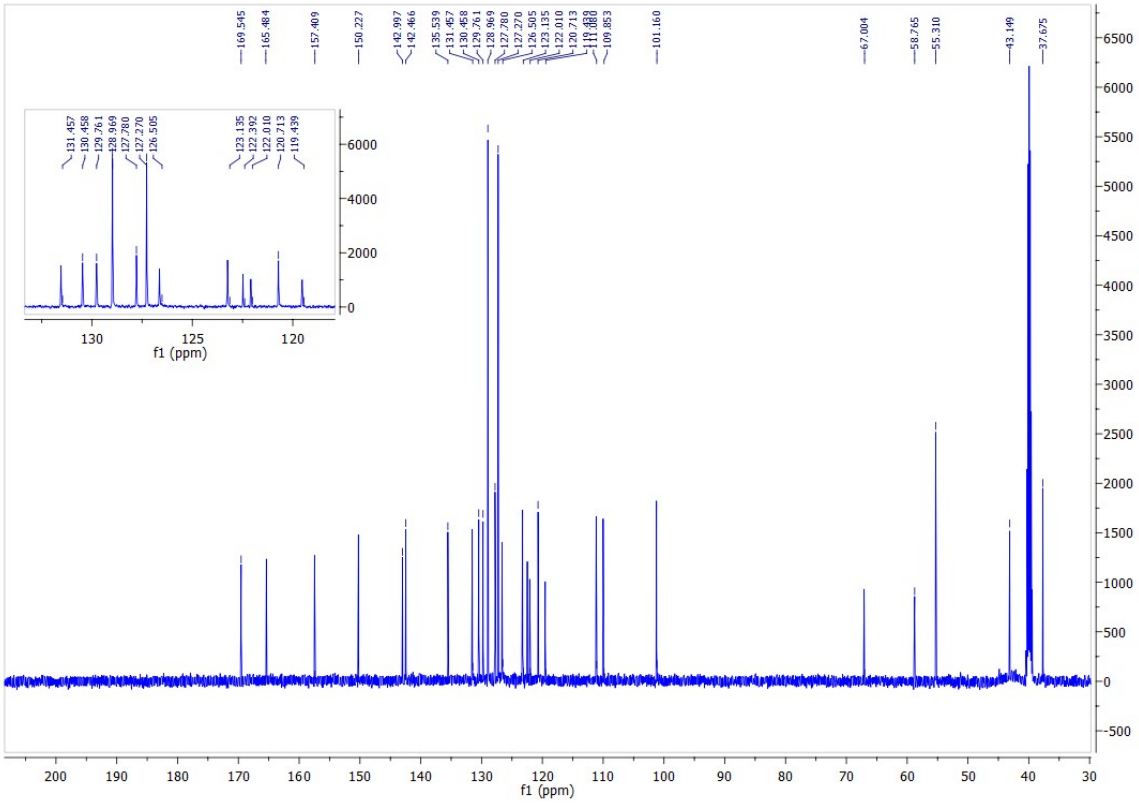
^{1}H and ^{13}C NMR spectra of compound 4l:



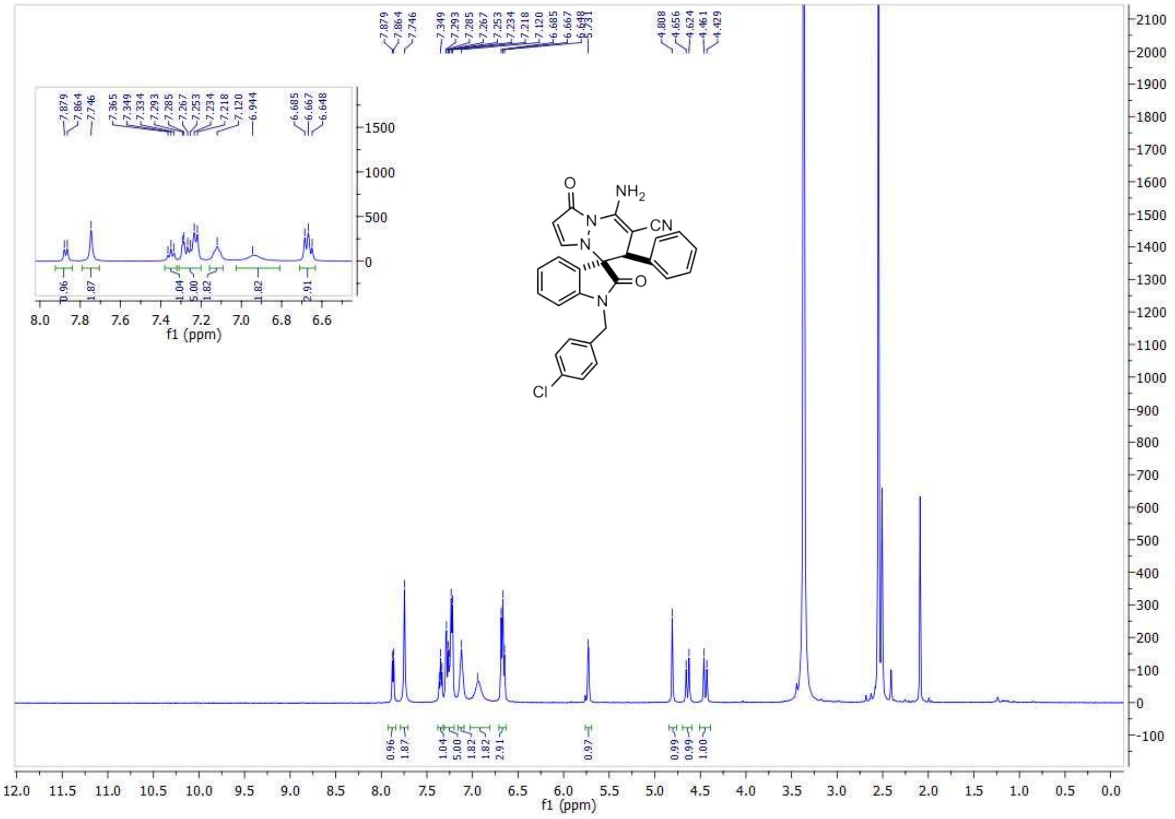


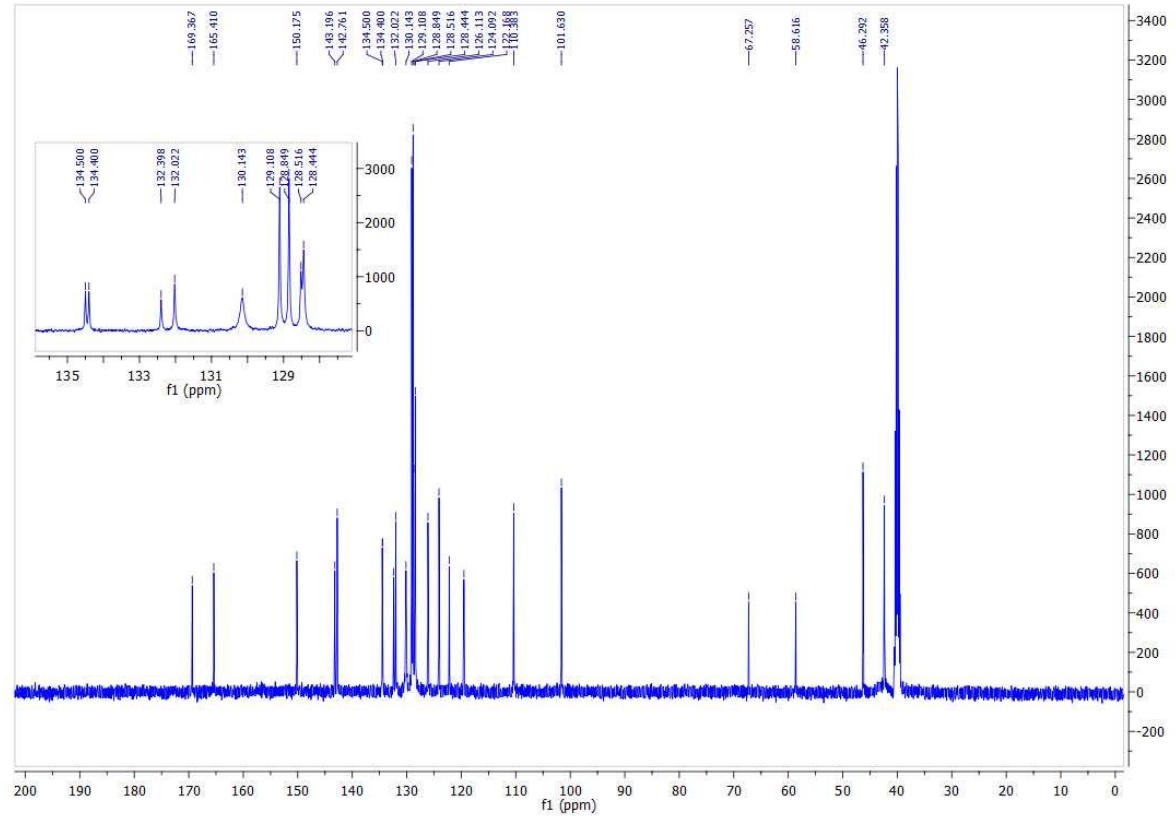
^{1}H and ^{13}C NMR spectra of compound 4m:



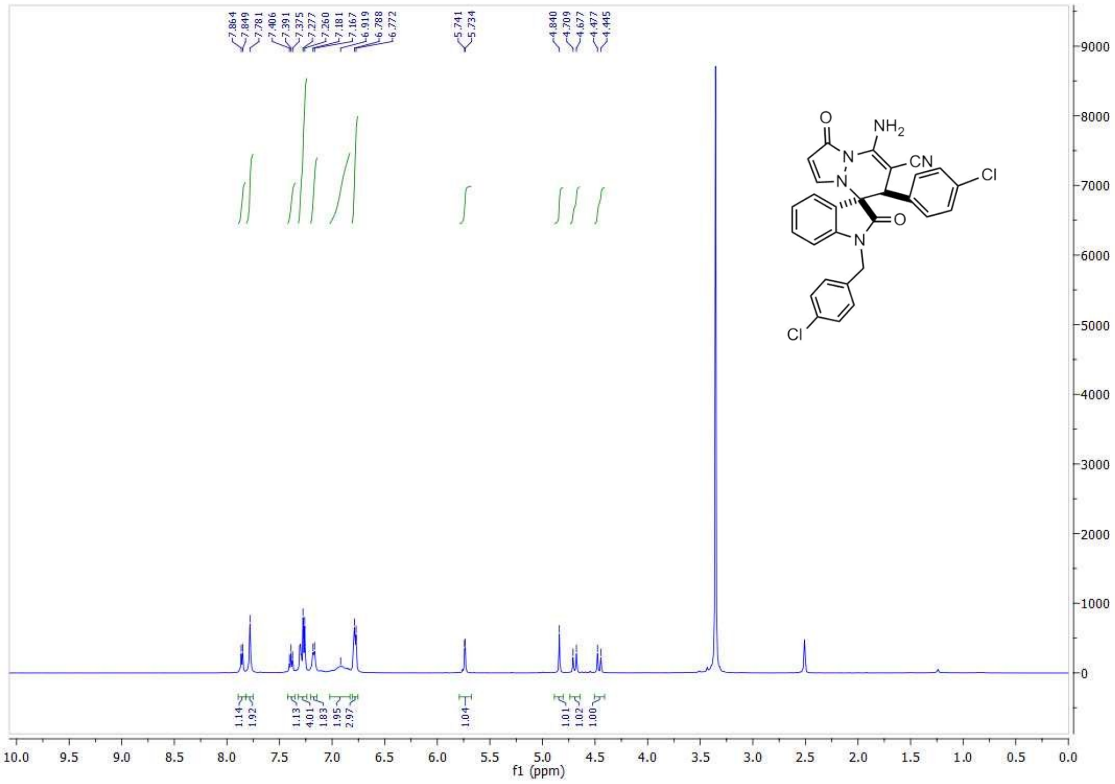


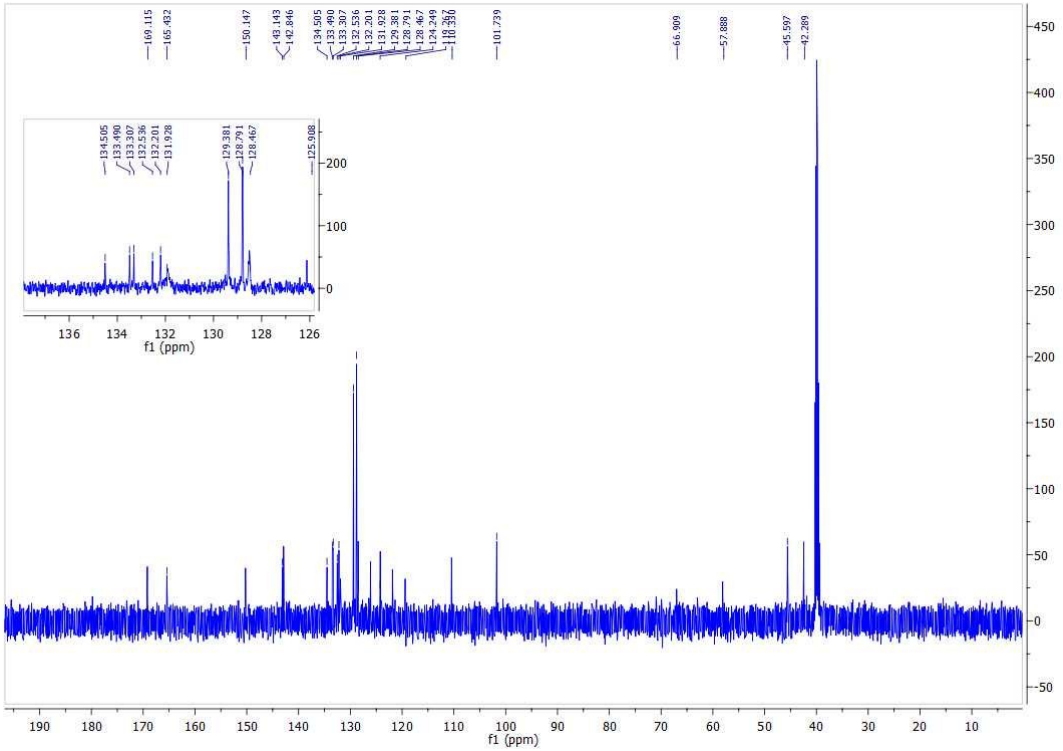
^{1}H and ^{13}C NMR spectra of compound 4n:



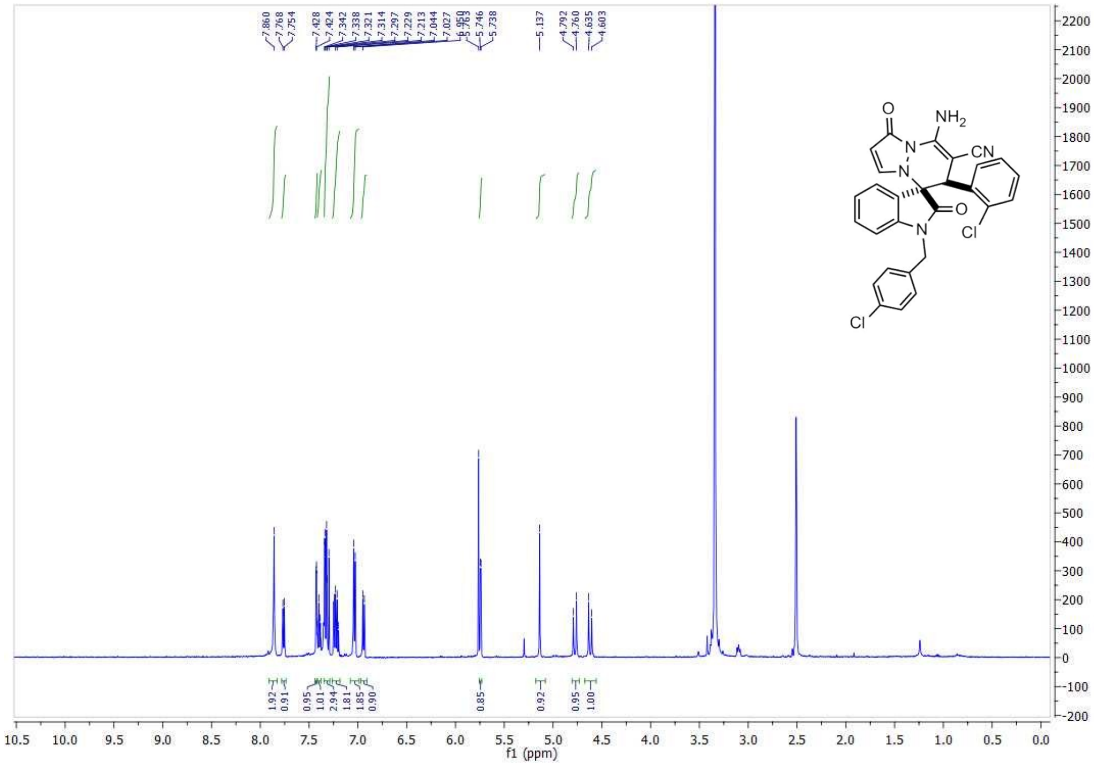


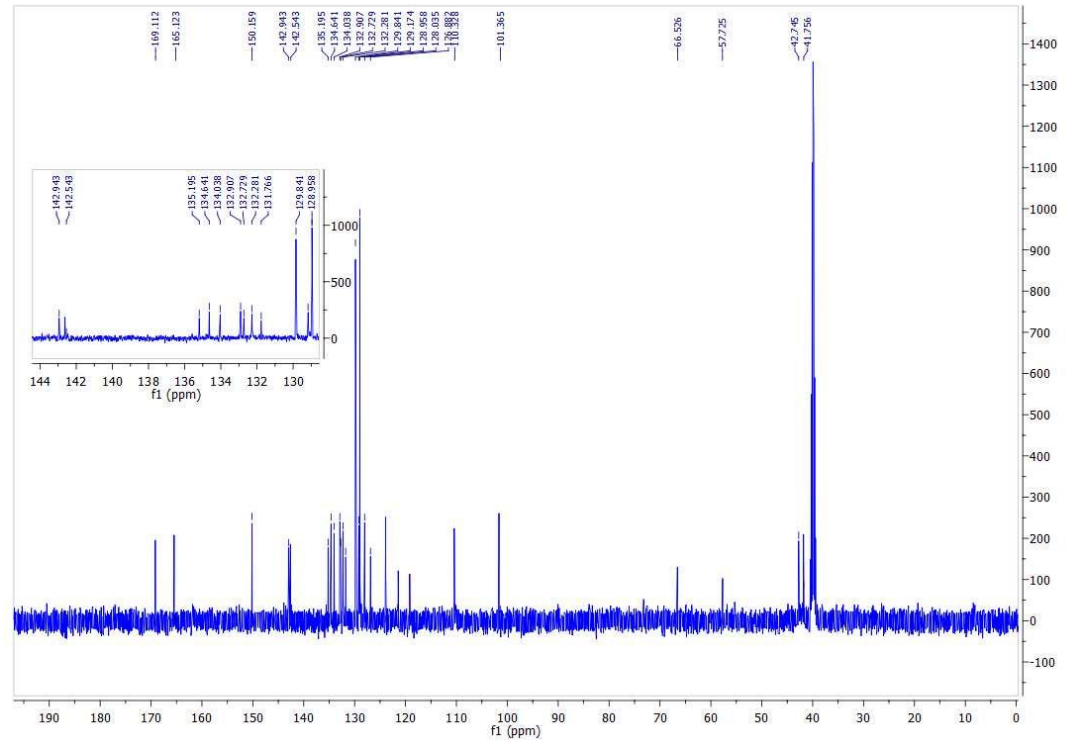
^{1}H and ^{13}C NMR spectra of compound 4o:





^{1}H and ^{13}C NMR spectra of compound 4p:





1. X. Wang, L. Wu, P. Yang, X-J. Song, H-X. Ren, L. Peng, L-X. Wang, *Org. lett.* 2017**, 19**, 3051-3054.