

Supporting Information for:-

A novel one-pot multi-component synthesis of 3, 3'-disubstituted oxindoles and spirooxindoles scaffold via Sn-catalyzed C(sp³)-H functionalization of azaarenes by sequential Knoevenagel-Michael-Cyclization reaction †

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1. General Information

All reactions were carried out with the open atmosphere in flame-dried glassware. All reactions were carried out with the open atmosphere in flame-dried glassware. DMF solvent was used LR grade and all reagents, solvents were purchased from commercial suppliers and Sigma Aldrich, Alfa easer, Avra synthesis. All these commercially available chemicals were used without further purification. The variety of 2-methyl benziimidazole were synthesized from commercially available various *o*-Phenylenediamine by using the following literature procedure.¹

Analytical thin layer chromatography was performed on TLC Silica gel 60 F254. And routine monitoring of reaction was performed by TLC using 0.25 mm E. Merck pre-coated silica gel TLC plates (60 F254) using UV light to visualize the course of the reactions or KMnO₄ staining solutions followed by heating. Column Chromatography was performed on silica gel (60-120 mesh) by standard techniques eluting with solvents as indicated.

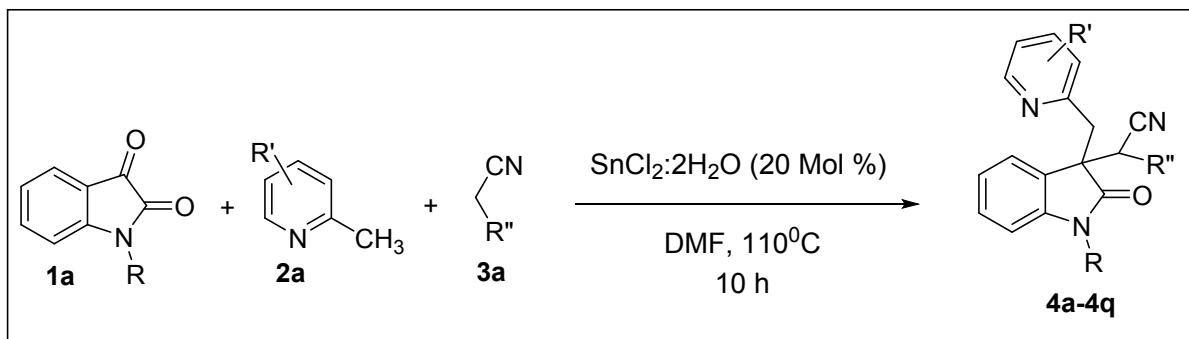
All compounds were fully characterized by using ¹H and ¹³C NMR, the spectra were recorded at 200, 400, 500 MHz and 50 MHz spectrometer using CDCl₃ as solvent at room temperature. The compound 4q and 5d were characterized by single crystal X-ray analysis of their structural configuration. Chemical shifts (δ) are reported in ppm with TMS as internal standard. Abbreviations for signal couplings are: s, singlet; d, doublet; t, triplet; m, multiplet. q, quartet etc.

(a) Mayo, M. S.; Bao, M.; Yu, X.; Zhou, X.; Feng, X.; Yamamoto, Y. *Org. Lett.* **2014**, *16*, 764-767. (b) Lee, J. J.; Kim, J.; Jun, Y. M.; Lee, B. M.; Kim, B. H. *Tetrahedron*. **2009**, *65*, 8821-8831

2. General Procedures for the Optimization of the Reaction Conditions

To a 10 ml round bottom flask equipped with a magnetic stir bar was added **1a** (1 mmol), **2a** (1.2 mmol), **3a** (1.2 mmol) and Catalysts (20 mol %) were taken and added solvents (5 mL), later RBF was capped with condenser. The reaction mixture was reflux at oil bath temperature, and the progress of the reaction was monitored by TLC with reaction time as shown in reaction optimization condition (**Table No.1**). After the completion of the reaction, the reaction mixture was diluted with 10 mL water and 10 mL ethyl acetate, stirred for 10 minutes. The organic layer and aqueous layer were separated. The organic layer was dried over anhydrous Na₂SO₄. The solvent was evaporated and the crude residue was purified by column chromatography on silica gel to afford the corresponding desired compound (**4a**) in moderate to good yields.

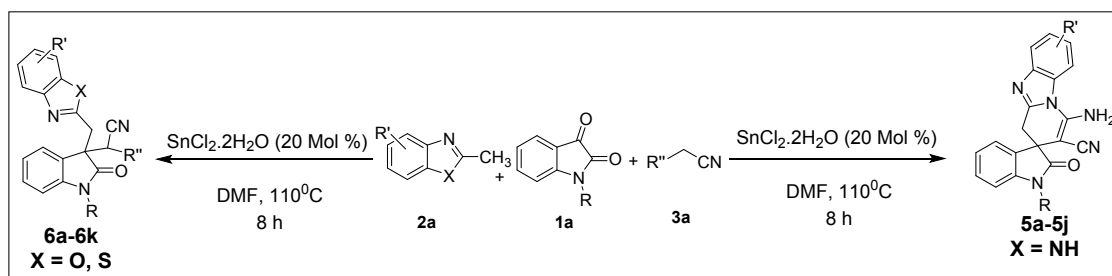
3. General Experimental Procedures for the Synthesis of **4a** to **4q**



To a 10 ml round bottom flask equipped with a magnetic stir bar was added isatins **1a** (1 mmol), azaarenes **2a** (1.2 mmol), malononitrile or ethylcyanoacetate **3a** (1.2 mmol), SnCl₂·2H₂O (20 mol %) and DMF (5 mL), and RBF was capped with condenser. The resultant reaction solution was kept stirring at 110 °C in oil bath. The completion of the reaction was monitored by TLC. The completion of the reaction was observed in 8 to 10 h for **4a-4q**. After the completion of the reaction, the reaction mixture was diluted with 10 mL water and 10 mL ethyl acetate, stirred for 10 minutes. Thereafter the organic layer and aqueous layer were separated. The

organic layer was dried over anhydrous Na_2SO_4 . The solvent was evaporated and the crude residue was purified by column chromatography on silica gel to afford the corresponding desired compounds derivative (**4a-4q**) in moderate to good yields.

4. General Procedure for Cascade Reaction for the Synthesis for **5a-5j** and **6a-6k**



To a 10 ml round bottom flask equipped with a magnetic stir bar was added isatins **1a** (1 mmol), malononitrile or ethylcyanoacetate **3a** (1.2 mmol), $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (20 mol %) and DMF (5 mL), and the reaction mixture was stirred at ambient condition for 30 minutes followed by addition of 2-(azaaryl)methanes **2a** (1.2 mmol). The resultant solution containing RBF equipped with condenser was kept for stirring at 110°C in oil bath. The completion of the reaction was monitored by TLC. The completion of the reaction was observed in 6 to 8 h for **5a-5j**. After the completion of the reaction, the reaction mixture was diluted with 10 mL water and 10 mL ethyl acetate, stirred for 10 minutes. Thereafter the organic layer and aqueous layer were separated. The organic layer was dried over anhydrous Na_2SO_4 . The solvent was evaporated and the crude residue was purified by column chromatography on silica gel to afford the corresponding desired compounds derivative of (**5a-5j** and **6a-6k**) in moderate to good yields.

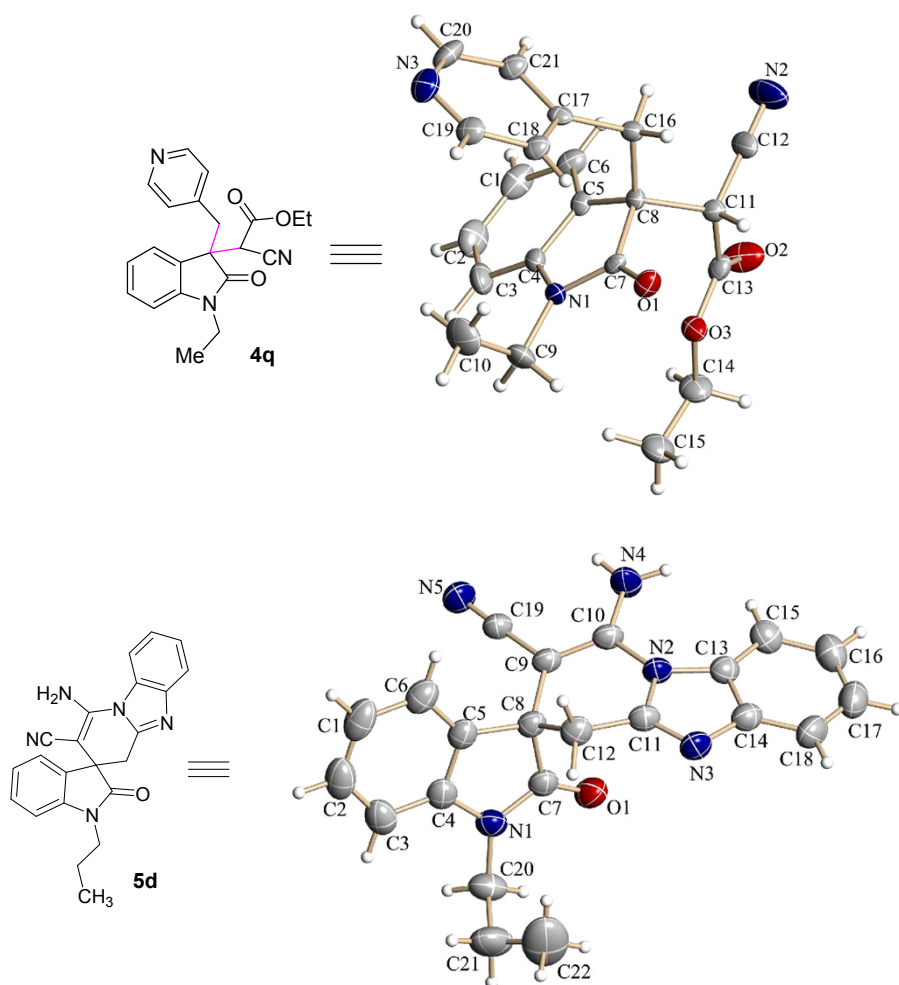
5. Single Crystal X-ray data for Compound 4q, 5d

X-ray intensity data measurements of compound 4q and 5d were carried out on a Bruker SMART APEX II CCD diffractometer with graphite-monochromatized ($\text{MoK}_\alpha = 0.71073 \text{ \AA}$) radiation. The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of cell constants and an orientation matrix were calculated from three sets of 36 frames. Data were collected with ω scan width of 0.5° at different settings of φ and 2θ with a frame time of 10 secs for 4q, while 7secs for the 5d keeping the sample-to-detector distance fixed at 5.00 cm. The X-ray data collection was monitored by APEX2 program (Bruker, 2006).¹ All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2006). SHELX-97 was used for structure solution and full matrix least-squares refinement on F^2 .² All the hydrogen atoms were placed in geometrically idealized position and constrained to ride on their parent atoms. An ORTEP view of both compounds were drawn with 30% probability displacement ellipsoids and H atoms are shown as small spheres of arbitrary radii.

Crystal data of 4q $\text{C}_{21}\text{H}_{21}\text{N}_3\text{O}_3$, $M = 363.41$, colorless needle, $0.46 \times 0.20 \times 0.10 \text{ mm}^3$, monoclinic, space group $P21/c$, $a = 13.9952(17) \text{ \AA}$, $b = 9.1123(12) \text{ \AA}$, $c = 15.2436(19) \text{ \AA}$, $\beta = 97.909(9)^\circ$, $V = 1925.5(4) \text{ \AA}^3$, $Z = 4$, $T = 296(2) \text{ K}$, $2\theta_{\text{max}} = 50.00^\circ$, $D_{\text{calc}} (\text{g cm}^{-3}) = 1.254$, $F(000) = 768$, $\mu (\text{mm}^{-1}) = 0.085$, 12212 reflections collected, 3344 unique reflections ($R_{\text{int}} = 0.1768$), 2728 observed ($I > 2\sigma(I)$) reflections, multi-scan absorption correction, $T_{\text{min}} = 0.9618$, $T_{\text{max}} = 0.9915$, 246 refined parameters, $S = 1.187$, $R1 = 0.1164$, $wR2 = 0.1985$ (all data $R = 0.1388$, $wR2 = 0.2103$), maximum and minimum residual electron densities; $\Delta\rho_{\text{max}} = 0.326$, $\Delta\rho_{\text{min}} = -0.312 (\text{e \AA}^{-3})$

Crystal data of 5d $\text{C}_{22}\text{H}_{19}\text{N}_5\text{O}$, $M = 369.42$, colorless plate, $0.51 \times 0.43 \times 0.20 \text{ mm}^3$, monoclinic, space group $P21/c$, $a = 12.3799(12) \text{ \AA}$, $b = 13.0555(12) \text{ \AA}$, $c = 11.5532(11) \text{ \AA}$, $\beta = 98.570(5)^\circ$, $V = 1846.4(3) \text{ \AA}^3$, $Z = 4$, $T = 296(2) \text{ K}$, $2\theta_{\text{max}} = 54.00^\circ$, $D_{\text{calc}} (\text{g cm}^{-3}) = 1.329$, $F(000) = 776$, $\mu (\text{mm}^{-1}) = 0.086$, 19861 reflections collected, 4016 unique reflections ($R_{\text{int}} = 0.0516$), 3086 observed ($I > 2\sigma(I)$) reflections, multi-scan absorption correction, $T_{\text{min}} = 0.9576$, $T_{\text{max}} = 0.9831$, 255 refined parameters, $S = 1.123$, $R1 = 0.0551$, $wR2 = 0.1569$ (all data $R = 0.0700$, $wR2 = 0.1701$), maximum and minimum residual electron densities; $\Delta\rho_{\text{max}} = 0.561$, $\Delta\rho_{\text{min}} = -0.299 (\text{e \AA}^{-3})$.

6. ORTEP Diagram for Compound 4q, 5d

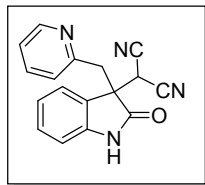


References

- (1) Bruker (2006). *APEX2*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA. (2) G. M. Sheldrick, *Acta Crystallogr.*, 2008, **A64**, 112. (3) L. J. Farrugia, *J. Appl. Cryst.* 1997, **30**, 565–565.

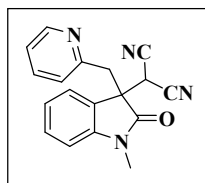
7. Spectral Data for Products 4a to 4q, 5a-5j and 6a-6k:-

2-(2-oxo-3-(pyridine-2-ylmethyl)indolin-3-yl)malononitrile (4a)



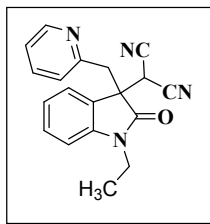
Yield: 82%; Off White solid, mp 152-154 °C; ¹H NMR (200 MHz, DMSO-*d*₆) δ ppm: 10.94 (s, 1H), 8.34 (d, *J*=4.80 Hz, 1H), 7.60 (dt, *J*=7.71 Hz, 1H), 7.25-7.13 (m, 3H), 7.08-6.93 (m, 2H), 6.80 (d, *J*=8.34 Hz, 1H), 5.83 (s, 1H), 3.50 (d, *J*=1.77 Hz, 2H); ¹³C NMR (200 MHz, DMSO-*d*₆) δ 175.2, 154.8, 148.7, 142.4, 136.4, 129.9, 125.8, 124.4, 124.2, 122.2, 121.9, 111.9, 110.0, 51.5, 40.8, 29.8. FTIR (CHCl₃, cm⁻¹) 3393, 2099, 1622, 1473, 1439, 1337, 1219, 1153, 1114, 1051, 1000, 932, 751, 666, 497.

2-(1-methyl-2-oxo-3-(pyridine-2-ylmethyl)indolin-3-yl)malononitrile (4b)



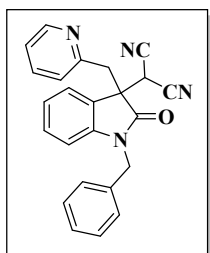
Yield: 86%; Off White solid, mp 98-100 °C; ¹H NMR (200 MHz, CDCl₃) δ ppm 8.44 (d, *J*=4.04 Hz, 2 H) 7.53 (td, *J*=7.64, 1.77 Hz, 1 H) 7.27 - 7.40 (m, 3 H) 6.96 - 7.15 (m, 3 H) 6.85 (d, *J*=7.83 Hz, 1 H) 5.06 (s, 1 H) 3.50 (s, 2 H) 3.23 (s, 3 H); ¹³C NMR (50 MHz, CDCl₃) δ ppm: 173.5, 154.5, 149.00, 143.8, 136.4, 130.4, 125.3, 124.3, 124.2, 123.4, 122.4, 111.1, 110.0, 108.8, 52.0, 41.3, 29.9, 26.7. HRMS (ESI) calculated [M+H]⁺ for C₁₈H₁₅ON₄ : 303.1240, found: 303.1238. FTIR (CHCl₃, cm⁻¹) 3433, 2090, 1641, 1473, 1377, 1217, 1100, 1023, 770, 496.

2-(1-ethyl-2-oxo-3-(pyridine-2-ylmethyl)indolin-3-yl)malononitrile (4c)



Yield: 84%; Off White solid, mp 124-126 °C; **¹H NMR (200 MHz, CDCl₃)** δ ppm: 8.40 (dd, *J*=4.93, 0.88 Hz, 1 H) 7.42 - 7.56 (m, 2 H) 7.29-7.37 (ms, 1 H) 6.96 - 7.164(m, 3 H) 6.85 (d, *J*=7.83 Hz, 1 H) 4.97 (s, 1 H) 3.77 (q, *J*=7.20 Hz, 2 H) 3.53 (s, 2 H) 1.22 (t, *J*=7.20 Hz, 3 H); **¹³C NMR (50 MHz, CDCl₃)** δ ppm: 173.1, 154.4, 148.9, 142.8, 136.4, 130.4, 125.4, 124.0, 123.2, 122.3, 111.1, 109.9, 108.9, 51.8, 41.3, 35.2, 30.1, 12.1. **FTIR (CHCl₃, cm⁻¹)** 3224, 2982, 2936, 1717, 1612, 1594, 1571, 1489, 1469, 1438, 1375, 1351, 1223, 1137, 1102, 1079, 1051, 1028, 998, 753.

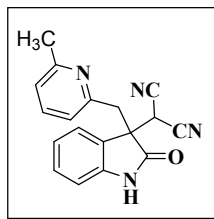
2-(1-benzyl-2-oxo-3-(pyridine-2-ylmethyl)indolin-3-yl)malononitrile (4d)



Yield: 88%; Off white solid, mp 132-134 °C; **¹H NMR (200 MHz, CDCl₃)** δ ppm: 8.26 (dd, *J*=4.80, Hz, 1 H) 7.35 - 7.41 (m, 2 H) 7.09 - 7.26 (m, 6 H) 6.87 - 7.05 (m, 3 H) 6.63 (d, *J*=7.7 Hz, 1 H) 4.93 (s, 1 H) 4.84 (d, *J*=3.66 Hz, 2 H) 3.50 (s, 2 H); **¹³C NMR (50 MHz, CDCl₃)** δ ppm: 173.6, 154.2, 148.9, 143.0, 136.7, 134.7, 130.4, 128.8, 127.8, 127.4, 125.1, 124.4, 124.3, 123.4, 122.4, 111.1, 110.1, 110.0, 52.1, 44.5, 41.4, 30.3. **HRMS (ESI)** calculated [M+H]⁺ for C₂₄H₁₉ON₄ : 379.1553, found: 379.1550. **FTIR (CHCl₃, cm⁻¹)** 3413, 3020, 2925, 2357, 1718, 1675, 1652, 1614, 1595, 1577, 1537, 1489, 1468, 1457, 1437, 1370, 1303, 1216, 1174, 1158,

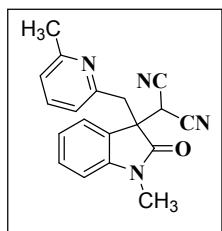
1098, 1079, 1029, 931, 755, 696, 668, 503.

2-(3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (4e)



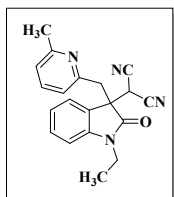
Yield: 84%; Off White solid, mp 201-203 °C; ¹H NMR (200 MHz, DMSO-*d*₆) δ ppm: 10.92 (s, 1 H) 7.48 (t, *J*=7.64 Hz, 1 H) 7.14 - 7.27 (m, 2 H) 6.99 (t, *J*=7.77 Hz, 2 H) 6.81 - 6.91 (m, 2 H) 5.80 (s, 1 H) 3.44 (d, *J*=4.4 Hz, 2 H) 2.31 (s, 3 H); ¹³C NMR (50 MHz, CDCl₃) δ ppm: 175.8, 157.3, 154.3, 143.0, 137.0, 130.1, 126.4, 124.7, 122.0, 121.7, 121.2, 112.4, 110.2, 51.6, 30.1, 24.0. HRMS (ESI) calculated [M+H]⁺ for C₁₈H₁₅ON₄: 303.1240, found: 303.1237. FTIR (CHCl₃, cm⁻¹) 3304, 2925, 2852, 2447, 1709, 1620, 1456, 1185, 1119, 770, 692, 649, 489.

2-(1-methyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (4f)



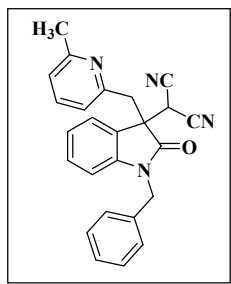
Yield: 90%; White solid, mp 112-114 °C; ¹H NMR (200 MHz, CDCl₃) δ ppm: 7.55-7.30 (m, 3H), 7.16-7.02 (m, 2H), 6.91-6.87 (m, 2H), 5.06 (s, 1H), 3.57 (s, 2H), 3.30 (s, 3H), 2.49 (s, 3H); ¹³C NMR (50 MHz, CDCl₃) δ ppm: 173.0, 156.8, 152.7, 143.3, 136.4, 129.7, 124.8, 123.5, 122.7, 121.3, 120.6, 108.0, 51.1, 40.1, 29.3, 26.0, 23.4. HRMS (ESI) calculated [M+H]⁺ for C₁₉H₁₇ON₄ : 317.1397, found: 317.1393. FTIR (CHCl₃, cm⁻¹) 3308, 3023, 3061, 2895, 2854, 2255, 1718, 1613, 1595, 1578, 1493, 1471, 1458, 1425, 1376, 1356, 1311, 1258, 1217, 1158, 1131, 1094, 1024, 996, 934, 900, 821, 753, 687, 666, 626, 602, 586, 542.

2-(1-ethyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (4g)



Yield: 89%; Brown solid, mp 111-113 °C; ¹H NMR (200 MHz, CDCl₃) δ ppm: 7.45-7.27 (m, 3 H) 6.97 - 7.12 (m, 2 H) 6.80 - 6.88 (m, 2 H) 5.01 (s, 1 H) 3.60 - 3.97 (m, 2 H) 3.49 (s, 3 H) 2.44 (s, 3 H) 1.28 (m, 3 H); ¹³C NMR (50 MHz, CDCl₃) δ ppm: 168.2, 164.9, 164.5, 162.7, 159.9, 155.1, 150.3, 148.7, 148.4, 147.80, 137.1, 137.0, 134.1, 129.3, 129.3, 129.0, 128.7, 128.1, 127.5, 127.2, 126.2, 125.9, 125.2, 124.9, 124.6, 124.4, 124.2, 122.1, 121.9, 120.2, 117.8, 116.8, 116.7, 116.2, 115.8, 115.1, 112.8, 59.2, 46.7, 45.3, 40.3, 36.9, 24.5, 14.5, 13.9. HRMS (ESI) calculated [M+H]⁺ for C₂₀H₁₉ON₄ : 331.1553, found: 331.1552. FTIR (CHCl₃, cm⁻¹) 3419, 3063, 3023, 2983, 1936, 2897, 2590, 2255, 1714, 1613, 1595, 1578, 1489, 1457, 1469, 1375, 1352, 1311, 1225, 1158, 1137, 1101, 1028, 997, 934, 903, 877, 821, 753, 698, 685, 666, 604, 589, 555, 492.

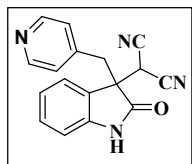
2-(1-benzyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (4h)



Yield: 91%; White solid, mp 141-143 °C; ¹H NMR (200 MHz, CDCl₃) δ ppm: 7.37 - 7.50 (m, 2 H) 7.27 (m, 6 H) 7.06 (dd, *J*=17.37, 7.64 Hz, 2 H) 6.68-6.81 (dd, *J*=18.19, 7.7 Hz, 2 H) 5.10 (s, 1 H) 4.77 - 5.06 (m, 2 H) 3.44 - 3.61 (d, 2 H) 2.43 (s, 3 H); ¹³C NMR (50 MHz, CDCl₃) δ ppm: 173.6, 157.6, 153.3, 142.9, 136.8, 134.7, 130.2, 128.7, 127.7, 127.1, 125.4, 124.3, 123.2, 121.9,

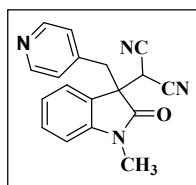
121.3, 111.1, 110.2, 109.8, 51.9, 44.4, 41.3, 29.9, 24.1. **FTIR** (CHCl_3 , cm^{-1}) 3407, 3037, 2925, 2845, 2593, 1711, 1612, 1455, 1370, 1216, 1173, 1098, 1029, 755, 642, 487.

2-(2-oxo-3-(pyridine-4-ylmethyl)indolin-3-yl)malononitrile (4i)



Yield: 84%; Brown solid, mp 169-171 °C; **^1H NMR (200 MHz, $\text{DMSO}-d_6$)** δ ppm: 10.9 (s, 1 H) 8.32 (d, $J=5.9$ Hz, 2 H) 7.59 - 7.71 (m, 1 H) 7.12 - 7.41 (m, 2 H) 6.73 - 6.93 (m, 3 H) 5.83 (s, 1 H) 3.29 - 3.40 (d, 2 H); **^{13}C NMR (50 MHz, $\text{DMSO}-d_6$)** δ ppm: 174.5, 150.1, 149.1, 142.7, 142.0, 130.4, 124.9, 124.6, 123.1, 122.4, 111.8, 111.4, 110.2, 52.5, 29.6. **HRMS (ESI)** calculated $[\text{M}+\text{H}]^+$ for $\text{C}_{17}\text{H}_{13}\text{ON}_4$: 289.1084, found: 289.1082. **FTIR** (CHCl_3 , cm^{-1}) 3363, 3020, 1716, 1621, 1473, 1417, 1339, 1216, 1114, 813, 754, 670, 629, 501.

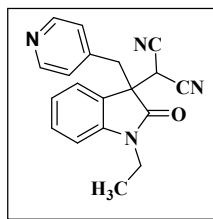
2-(1-methyl-2-oxo-3-(pyridine-4-ylmethyl)indolin-3-yl)malononitrile (4j)



Yield: 77%; Red solid, mp 116-118 °C; **^1H NMR (200 MHz, CDCl_3)** δ ppm: 8.34 - 8.37 (m, 2 H) 7.71 - 7.82 (m, 1 H) 7.41 - 7.49 (m, 1 H) 7.27 - 7.35 (m, 1 H) 6.75 - 6.85 (m, 3 H) 4.46 (s, 1 H) 3.29 - 3.46 (m, 2 H) 3.08 (s, 3 H); **^{13}C NMR (50 MHz, CDCl_3)** δ ppm: 172.6, 154.9, 149.4, 143.7, 141.8, 138.8, 134.7, 132.3, 131.1, 124.8, 124.0, 123.9, 110.6, 109.3, 53.4, 39.9, 30.2, 26.4. **HRMS (ESI)** calculated $[\text{M}+\text{H}]^+$ for $\text{C}_{18}\text{H}_{15}\text{ON}_4$: 303.1240, found: 303.1238. **FTIR** (CHCl_3 , cm^{-1}) 3316, 3059, 3026, 2931, 2890, 2255, 2199, 1945, 1715, 1612, 1562, 1492, 1472, 1418, 1376, 1356, 1308, 1260, 1222, 1159, 1131, 1096, 1024, 997, 913, 877, 846, 798, 813, 754, 689,

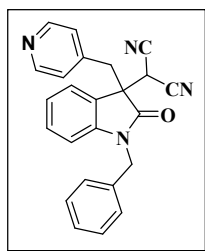
666, 618, 598, 569, 541, 484.

2-(1-ethyl-2-oxo-3-(pyridine-4-ylmethyl)indolin-3-yl)malononitrile (4k)



Yield: 82%; Yellow solid, mp 128-130 °C; ¹H NMR (200 MHz, CDCl₃) δ ppm: 8.41 (dd, *J*=4.9, 1 H) 7.42 - 7.56 (m, 2 H) 7.27 - 7.37 (m, 1 H) 6.95 - 7.14 (m, 3 H) 6.85 (d, *J*=7.83 Hz, 1 H) 4.97 (s, 1 H) 3.77 (q, 2 H) 3.53 (s, 2 H) 1.22 (t, *J*=7.20 Hz, 3 H); ¹³C NMR (50 MHz, CDCl₃) δ ppm: 173.0, 154.4, 148.8, 142.8, 136.4, 130.3, 125.4, 124.4, 124.2, 123.1, 122.3, 111.1, 109.9, 108.9, 51.8, 41.2, 35.2, 30.1, 12.1. **FTIR (CHCl₃, cm⁻¹)** 3422, 3020, 2986, 2939, 2897, 2401, 2256, 1716, 2256, 1716, 1614, 1596, 1488, 1470, 1438, 1376, 1352, 1288, 1216, 1151, 1137, 1103, 1051, 1028, 930, 895, 754, 685, 668, 630, 591, 484.

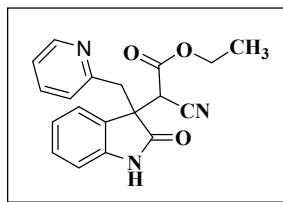
2-(1-benzyl-2-oxo-3-(pyridine-4-ylmethyl)indolin-3-yl)malononitrile (4l)



Yield: 86%; Off white solid, mp 121-123 °C; ¹H NMR (200 MHz, CDCl₃) δ ppm: 8.21 (d, *J*=6.06 Hz, 2 H) 7.65 - 7.79 (m, 1 H) 7.07 - 7.27 (m, 5 H) 6.76 (d, *J*=6.06 Hz, 2 H) 6.63 - 6.69 (m, 2 H) 6.51 - 6.59 (m, 1 H) 4.71 - 4.79 (d, 1 H) 4.48 - 4.58 (m, 2 H) 3.40 - 3.48 (d, 1 H) 3.24 (d, 1 H); ¹³C NMR (50 MHz, CDCl₃) δ ppm: 172.6, 148.9, 143.1, 142.5, 133.8, 131.2, 128.9, 127.9, 126.5, 125.2, 124.0, 123.9, 123.8, 110.6, 109.4, 53.3, 44.2, 39.9, 30.7. **HRMS (ESI)**

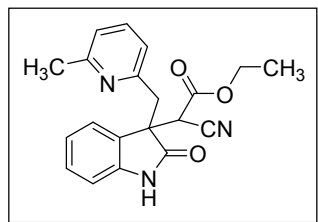
calculated $[M+H]^+$ for $C_{24}H_{19}ON_4$: 379.1553, found: 379.1551. **FTIR** ($CHCl_3$, cm^{-1}) 3444, 3020, 2400, 1716, 1644, 1523, 1488, 1470, 1419, 1379, 1215, 1046, 928, 848, 771, 669, 501.

Ethyl 2-cyano-2-(2-oxo-3-(pyridine-4-ylmethyl)indolin-3-yl)acetate (4m)



Yield: 74%; Orange solid, mp 167-169 °C; **1H NMR (200 MHz, $DMSO-d_6$)** δ ppm: 10.5 (d, $J=15.9$ Hz, 1 H) 8.26 - 8.35 (m, 1 H) 7.42 - 7.57 (m, 2 H) 7.04 - 7.17 (m, 2 H) 6.82 - 7.01 (m, 2 H) 6.67 (dd, $J=7.58$, 1 H) 5.08 (s, 1 H) 3.90 (dq, $J=14.7$, 2 H) 3.45 - 3.57 (d, 2 H) 0.89 - 1.03 (t, 3 H); **^{13}C NMR (200 MHz, $CDCl_3$)** δ ppm: 173.9, 162.8, 152.1, 143.5, 129.9, 126.0, 125.2, 123.9, 122.9, 121.2, 114.7, 108.5, 63.0, 51.0, 43.9, 34.9, 11.8. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{19}H_{18}O_3N_3$: 336.1343, found: 336.1338. **FTIR** ($CHCl_3$, cm^{-1}) 3661, 3445, 1733, 1651, 1542, 1536, 1497, 1474, 771.

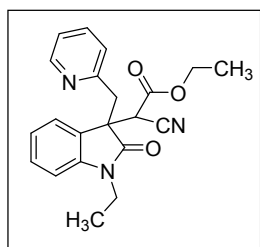
Ethyl 2-cyano-2-(3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)acetate (4n)



Yield: 83%; White solid, mp 93-95 °C; **1H NMR (200 MHz, $CDCl_3$)** δ ppm: 10.54 (s, 1H), 10.46 (s, 1H), 7.46-7.37 (m, 2H), 7.20-6.85 (m, 8H), 6.75-6.63 (m, 4H), 5.04 (s, 1H), 4.91 (s, 1H), 4.09-3.90 (m, 4H), 3.45-3.39 (m, 4H), 2.23 (s, 6H), 1.04-0.90 (m, 6H); **^{13}C NMR (200 MHz, $CDCl_3$)** δ ppm: 176.6, 176.1, 163.8, 163.5, 156.5, 154.6, 154.1, 142.5, 136.1, 128.9, 127.7, 124.5, 123.8, 121.1, 121.0, 120.9, 115.8, 109.3, **HRMS (ESI)** calculated $[M+H]^+$ for

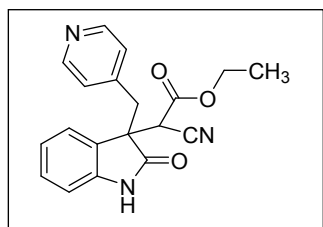
C₂₀H₂₀O₃N₃: 350.1499, found: 350.1497. **FTIR (CHCl₃, cm⁻¹)** 3252, 3064, 3020, 2926, 2252, 1727, 1621, 1595, 1578, 1542, 1473, 1457, 1393, 1370, 1335, 1219, 1157, 1114, 1097, 1070, 1022, 936, 855, 806, 753, 666, 610, 534, 499.

Ethyl 2-cyano-2-(1-ethyl-2-oxo-3-(pyridine-2-ylmethyl)indolin-3-yl)acetate (4o)



Yield: 80 %; Pink solid, mp 130-132 °C; **¹H NMR (200 MHz, CDCl₃)** δ ppm 8.32 - 8.38 (m, 1 H) 7.54 - 7.72 (m, 1 H) 7.30 - 7.47 (m, 1 H) 7.00 - 7.30 (m, 3 H) 6.85 - 6.89 (m, 1 H) 6.61 - 6.72 (m, 1 H) 4.48 (m, 1 H) 3.92 - 4.07 (m, 2 H) 3.40 - 3.80 (m, 4 H) 0.99 - 1.27 (m, 6 H); **¹³C NMR (50 MHz, CDCl₃)** δ ppm: 174.5, 163.4, 162.6, 154.5, 154.1, 148.2, 147.2, 143.0, 142.7, 137.4, 136.0, 129.4, 129.2, 126.9, 126.4, 125.1, 125.0, 124.4, 124.0, 122.4, 122.0, 114.8, 113.5, 108.2, 107.9, 62.6, 51.5, 44.1, 43.8, 34.7, 13.5, 11.8. **HRMS (ESI)** calculated [M+H]⁺ for C₂₁H₂₂O₃N₃: 364.1656, found: 364.1653. **FTIR (CHCl₃, cm⁻¹)** 3420, 3020, 2986, 2939, 2401, 2552, 1947, 1748, 1716, 1614, 1594, 1572, 1490, 1469, 1438, 1376, 1353, 1216, 1136, 1102, 1079, 1050, 1020, 929, 897, 853, 755, 688, 668, 628, 575, 553, 492.

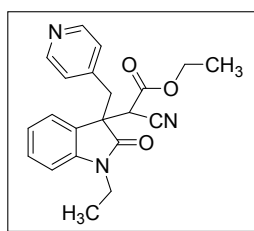
Ethyl 2-cyano-2-(2-oxo-3-(pyridine-4-ylmethyl)indolin-3-yl)acetate (4p)



Yield: 81%; Orange solid, mp 167-169 °C; **¹H NMR (200 MHz, CDCl₃)** δ ppm: 10.56 (s, 1H),

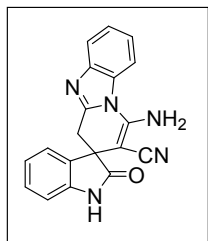
8.27 (t, $J=4.29$ Hz, 3H), 7.60 (d, $J=7.20$ Hz, 1H), 7.21-7.17 (m, 1H), 6.83-6.76 (m, 3H), 5.07 (s, 1H), 3.96 (q, 2H), 3.16-3.09 (m, 2H), 0.90 (t, $J=7.20$ Hz, 3H); ^{13}C NMR (200 MHz, CDCl_3) δ ppm: 177.30, 175.69, 163.29, 148.97, 144.13, 141.80, 129.52, 126.64, 125.10, 121.82, 117.31, 115.60, 109.66, 62.31, 52.42, 50.49, 44.21, 35.79, 30.78, 24.69, 13.28. **HRMS (ESI)** calculated $[\text{M}+\text{H}]^+$ for $\text{C}_{19}\text{H}_{18}\text{O}_3\text{N}_3$: 336.1343, found: 336.1340. **FTIR (CHCl_3 , cm^{-1})** 3430, 3021, 2401, 2255, 1945, 1716, 1622, 1562, 1473, 1444, 1417, 1370, 1333, 1219, 1174, 1114, 1095, 1072, 1020, 962, 930, 875, 850, 840, 821, 768, 625, 591, 579, 510, 491.

Ethyl 2-cyano-2-(1-ethyl-2-oxo-3-(pyridine-4-ylmethyl)indolin-3-yl)acetate (4q)



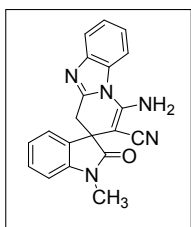
Yield: 85%; Pink solid, mp 144-146 °C; ^1H NMR (200 MHz, CDCl_3) δ ppm: 8.29 (d, $J=6.06$ Hz, 2H), 7.75 (d, $J=7.58$ Hz, 1H), 7.35-7.27 (m, 1H), 7.16 (t, $J=7.58$ Hz, 1H), 6.81-6.72 (m, 2H), 6.62 (d, $J=7.74$ Hz, 1H), 4.38 (s, 1H), 4.05-3.94 (m, 2H), 3.63-3.40 (m, 4H), 1.01 (t, $J=7.07$ Hz, 3H), 0.86 (t, $J=7.20$ Hz, 3H); ^{13}C NMR (200 MHz, CDCl_3) δ ppm: 174.0, 162.3, 148.2, 143.3, 129.9, 126.1, 125.3, 123.6, 122.8, 114.5, 108.5, 62.9, 51.9, 43.9, 42.0, 34.7, 13.5, 11.6. **HRMS (ESI)** calculated $[\text{M}+\text{H}]^+$ for $\text{C}_{21}\text{H}_{22}\text{O}_3\text{N}_3$: 364.1656, found: 364.1655. **FTIR (CHCl_3 , cm^{-1})** 3428, 3021, 2400, 2090, 1643, 1614, 1489, 1469, 1417, 1376, 1215, 1136, 1101, 1018, 928, 850, 756, 688, 668, 501.

1-amino-2'-oxo-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-carbonitrile (5a)



Yield: 80%; Brown solid, mp 255-256 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ ppm: 10.6 (s, 1 H) 7.95 (d, *J*=8.24 Hz, 1 H) 7.67 (d, *J*=7.63 Hz, 1 H) 7.32 - 7.39 (m, 2 H) 7.24 - 7.30 (m, 3 H) 6.95 - 7.00 (m, 2 H) 6.90 (d, *J*=7.93 Hz, 1 H) 3.54 (d, *J*=15.87 Hz, 1 H) 3.29 (d, *J*=16.17 Hz, 1 H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ ppm: 177.8, 152.5, 149.9, 142.7, 141.3, 131.0, 130.7, 129.0, 123.8, 123.7, 123.5, 122.1, 119.3, 118.0, 113.5, 109.9, 64.5, 47.0, 33.1. HRMS (ESI) calculated [M+H]⁺ for C₁₉H₁₄ON₅ : 328.1193, found: 328.1189. FTIR (CHCl₃, cm⁻¹) 3400, 3020, 2927, 2184, 1641, 1456, 1217, 1095, 769, 666.

1-amino-1'-methyl-2'-oxo-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-carbonitrile (5b)



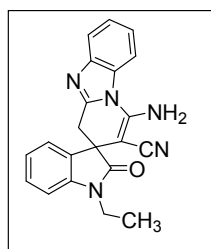
Yield: 84%; Off white solid, mp 173-174 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ ppm: 7.94 (d, *J*=7.93 Hz, 1 H) 7.67 (d, *J*=7.63 Hz, 1 H) 7.33 - 7.40 (m, 5 H) 7.07 - 7.10 (m, 3 H) 3.61 (d, *J*=15.87 Hz, 1 H) 3.28 (d, *J*=15.87 Hz, 1 H) 3.12 (s, 3 H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ ppm: 175.9, 152.6, 149.9, 142.9, 142.6, 131.0, 129.9, 129.1, 123.7, 123.6, 123.5, 122.7, 119.3, 117.9, 113.5, 109.0, 64.2, 46.6, 33.1, 26.2. MALDI TOF/TOF *m/z* calcd for C₂₀H₁₅N₅O [M + K⁺] 380.0914, observed 380.0771. FTIR (CHCl₃, cm⁻¹) 3435, 2103, 1638, 1352, 1215, 753,

670, 506.

D₂O, Exchanged ¹H NMR and DEPT of Compound (5b):-

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm: 7.85 - 7.87 (d, 1 H) 7.59 - 7.62 (m, 1 H) 7.30 - 7.34 (m, 3 H) 7.02 - 7.04 (m, 3 H) 3.55 (d, 1 H) 3.19 (d, 1 H) 3.05 (s, 3 H); **¹³C NMR (126 MHz, DMSO-*d*₆)** δ ppm: 129.6, 124.2, 124.1, 123.9, 123.2, 119.7, 114.0, 109.5, 72.2, 51.7, 39.9, 26.6.

1-amino-1'-ethyl-2'-oxo-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-carbonitrile (5c)



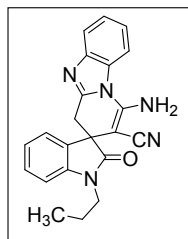
Yield: 83%; White to brownish color solid, mp 114-116 °C; **¹H NMR (500 MHz, DMSO-*d*₆)** δ ppm: 7.93 - 7.94 (d, 1 H) 7.67 (d, 1 H) 7.33 - 7.40 (m, 5 H) 7.15 (d, 1 H) 7.07 (m, 2 H) 3.61 - 3.73 (m, 2 H) 3.55 (d, 1 H) 3.28 (d, 1 H) 1.15 (t, *J*=7.17 Hz, 3 H); **¹³C NMR (126 MHz, DMSO-*d*₆)** δ ppm: 175.6, 152.5, 149.9, 142.7, 141.8, 131.0, 130.2, 129.2, 123.8, 123.7, 123.6, 122.7, 119.3, 117.8, 113.5, 109.1, 64.4, 46.6, 34.3, 33.0, 12.4. **MALDI TOF/TOF** *m/z* calcd for C₂₁H₁₇N₅O [M + K⁺] 394.1070, observed 394.1104.

D₂O, Exchanged ¹H NMR and DEPT of Compound (5c):-

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm: 7.89 - 7.91 (m, 1 H) 7.64 - 7.66 (d, 1 H) 7.32 - 7.40 (m, 3 H) 7.10 - 7.12 (m, 1 H) 6.99 - 7.06 (m, 2 H) 3.59 - 3.70 (m, 2 H) 3.56 (d, 1 H) 3.24 (d, 1 H) 1.11 (t, 3 H); **¹³C NMR (126 MHz, DMSO-*d*₆)** δ ppm: 129.6, 124.2, 124.2, 124.0, 123.1, 119.7, 114.0, 109.5, 34.7, 33.4, 12.9.

1-amino-2'-oxo-1'-propyl-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-

carbonitrile (5d)

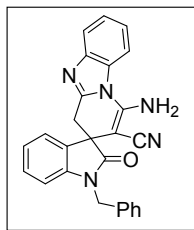


Yield: 86%; White to brownish color solid, mp 216-217 °C; **¹H NMR (500 MHz, DMSO-*d*₆)** δ ppm: 7.95 (d, *J*=7.93 Hz, 1 H) 7.67 (d, *J*=7.63 Hz, 1 H) 7.33 - 7.40 (m, 5 H) 7.15 (d, *J*=7.63 Hz, 1 H) 7.03 - 7.07 (m, 2 H) 3.63 - 3.69 (m, 1 H) 3.56 - 3.61 (m, 2 H) 3.27 (d, *J*=15.87 Hz, 1 H) 1.59 - 1.64 (m, 2 H) 0.85 (t, *J*=7.32 Hz, 3 H); **¹³C NMR (126 MHz, DMSO-*d*₆)** δ ppm: 176.5, 153.0, 150.3, 143.1, 142.6, 131.4, 130.5, 129.6, 124.2, 124.1, 124.0, 123.1, 119.7, 118.3, 114.0, 109.7, 64.9, 47.1, 41.3, 40.3, 33.6, 20.6, 11.4. **HRMS (ESI)** calculated [M+H]⁺ for C₂₂H₂₀N₅O: 370.1662, found: 370.1656. **FTIR (CHCl₃, cm⁻¹)** 3357, 2963, 2927, 2872, 2193, 1698, 1651, 1607, 1461, 1435, 1417, 1363, 1328, 1275, 1219, 1230, 1194, 1158, 1143, 1101, 1037, 998, 903, 865, 849, 834, 822, 801, 766, 752, 713, 694, 615, 569, 490.

D₂O, Exchanged ¹H NMR and DEPT of Compound (5d):-

¹H NMR (400 MHz, DMSO-*d*₆) δ ppm: 7.86 - 7.88 (m, 1 H) 7.60 - 7.62 (m, 1 H) 7.27 - 7.36 (m, 3 H) 7.06 (d, 1 H) 7.01 (m, 2 H) 3.50 - 3.61 (m, 3 H) 3.19 (d, 1 H) 1.50 - 1.59 (m, 2 H) 0.77 (t, *J*=7.56 Hz, 3 H); **¹³C NMR (126 MHz, DMSO-*d*₆)** δ ppm: 129.6, 124.2, 124.1, 124.0, 123.1, 119.7, 114.0, 109.7, 41.3, 33.6, 20.6, 11.4.

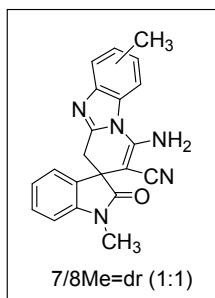
1-amino-1'-benzyl-2'-oxo-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-carbonitrile (5e)



Yield: 91%; Off white to brown solid, mp 235-236 °C; **¹H NMR (400 MHz, DMSO-*d*₆)** δ ppm: 7.91 (d, 1 H) 7.62 (m, 1 H) 7.23 - 7.34 (m, 10 H) 7.01 - 7.06 (m, 2 H) 6.91 (d, *J*=7.79 Hz, 1 H) 4.92 (d, 1 H) 4.79 (d, 1 H) 3.65 (d, *J*=16.03 Hz, 1 H) 3.27 (d, 1 H); **¹³C NMR (101 MHz, CDCl₃)** δ ppm 172.7, 162.3, 152.7, 143.3, 135.0, 134.3, 131.0, 128.7, 127.8, 127.1, 126.3, 125.5, 124.3, 124.2, 123.9, 123.3, 121.5, 110.6, 110.4, 109.6, 51.7, 44.6, 37.8.

HRMS (ESI) calculated [M+H]⁺ for C₂₆H₂₀N₅O : 418.1662, found: 418.1661. **FTIR (CHCl₃, cm⁻¹)** 3320, 3177, 3021, 2989, 2924, 2401, 2194, 1697, 1659, 1614, 1556, 1487, 1460, 1434, 1415, 1377, 1348, 1312, 1278, 1216, 1158, 1106, 1076, 1025, 999, 928, 875, 852, 761, 694, 667, 622, 553, 479.

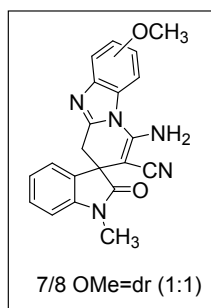
1-amino-1',7-dimethyl-2'-oxo-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-carbonitrile (5f)



Yield: 90%; off white solid, mp 258-260 °C; mixture of diastereoisomers (dr 1:1); **¹H NMR (500 MHz, DMSO-*d*₆)** δ ppm 7.79 - 7.81 (d, 1 H) 7.76 (s, *J*=8.24 Hz, 1 H) 7.54 (d, 1 H) 7.46 (s, 1 H) 7.35-7.38 (t, *J*=7.17 Hz, 2 H) 7.27 (br. s., 4 H) 7.16-7.20 (dd, *J*=15.41, 8.09 Hz, 2 H) 7.05 - 7.09 (m, 4 H) 7.00 - 7.05 (m, 2 H) 3.55 (dd, *J*=15.87, 2.44 Hz, 2 H) 3.27 (dd, *J*=15.87, 5.19 Hz, 2 H)

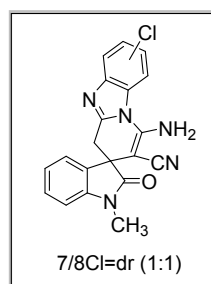
3.12 (s, 6 H) 2.49 (s, 3 H) 2.44 (s, 3 H); ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ ppm: 175.9, 154.6, 152.6, 149.8, 149.2, 143.0, 142.8, 140.7, 133.2, 132.8, 131.1, 130.0, 129.1, 129.0, 124.8, 124.7, 123.5, 122.7, 119.2, 118.8, 118.0, 113.5, 113.0, 109.0, 63.9, 63.8, 46.6, 33.2, 33.1, 26.2, 21.4, 20.9. **HRMS (ESI)** calculated $[\text{M}+\text{H}]^+$ for $\text{C}_{21}\text{H}_{18}\text{N}_5\text{O}$: 356.1506, found: 356.1503.

1-amino-7-methoxy-1'-methyl-2'-oxo-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-carbonitrile (5g)



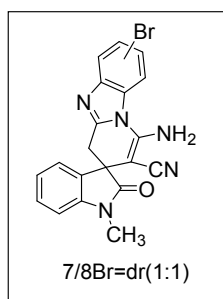
Yield: 88%; off white solid, mp 270-271 °C; mixture of diastereoisomers (dr 1:1); ^1H NMR (200 MHz, $\text{DMSO}-d_6$) δ ppm 7.723- 7.82 (m, 1 H) 7.46 - 7.66 (m, 3 H) 7.16 - 7.40 (m, 7 H) 6.92 – 7.09 (m, 7 H) 3.86 (s, 3 H) 3.82 (s, 3 H) 3.46 - 3.57 (m, 2 H) 3.17 - 3.28 (m, 2 H) 3.11 (s, 6 H); ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ ppm: 175.9, 152.7, 152.6, 149.8, 149.2, 143.0, 142.8, 140.7, 133.2, 132.8, 131.1, 130.0, 129.1, 129.0, 124.8, 124.7, 123.5, 122.9, 119.2, 118.8, 118.0, 113.9, 113.0, 109.0, 63.9, 63.8, 58.7, 46.7, 33.2, 33.1, 26.2.

1-amino-7-chloro-1'-methyl-2'-oxo-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-carbonitrile (5h)



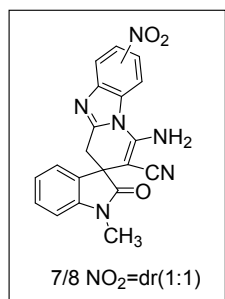
Yield: 88%; pale brown solid, mp 283-284 °C; mixture of diastereoisomers (dr 1:1); **¹H NMR (400 MHz, CDCl₃)** δ ppm: 7.98 (s, 1 H) 7.94 (d, *J*=8.80 Hz, 1 H) 7.74 (s, 1 H) 7.69 (d, *J*=8.56 Hz, 1 H) 7.36 - 7.45 (m, 8 H) 7.08 - 7.14 (m, 6 H) 3.626(d, *J*=15.89 Hz, 2 H) 3.29 (d, *J*=15.89 Hz, 2 H) 3.12 (s, 6 H); **¹³C NMR (101 MHz, DMSO-*d*₆)** δ ppm: 176.0, 152.5, 152.4, 151.9, 151.3, 143.9, 143.1, 141.7, 131.7, 130.0, 129.8, 129.5, 128.3, 128.1, 123.9, 123.0, 120.6, 119.0, 117.9, 115.1, 113.8, 109.3, 65.2, 65.0, 46.7, 33.2, 26.4. **HRMS (ESI)** calculated [M+H]⁺ for C₂₀H₁₅ClN₅O : 376.0960, found: 376.0957.

1-amino-7-bromo-1'-methyl-2'-oxo-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-carbonitrile (5i)



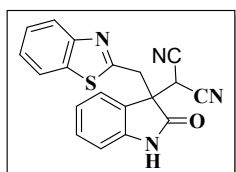
Yield: 85%; pale brow solid, mp 78-80 °C; mixture of diastereoisomers (dr 1:1); **¹H NMR (200 MHz, DMSO-*d*₆)** δ ppm: 8.12 (s, 1 H) 7.87 - 7.97 (m, 2 H) 7.51 - 7.66 (m, 3 H) 7.35 - 7.41 (m, 6 H) 7.08 - 7.13 (m, 8 H) 3.70 (dd, *J*=15.92 Hz, 2 H) 3.23-3.32 (dd, *J*=16.0 Hz, 2 H) 3.12 (s, 6 H); **¹³C NMR (50 MHz, DMSO-*d*₆)** δ ppm: 175.8, 152.2, 151.5, 150.9, 150.7, 142.9, 131.9, 129.6, 129.2, 126.4, 123.7, 122.8, 117.7, 116.4, 109.0, 65.1, 46.5, 33.0, 26.2. **HRMS (ESI)** calculated [M+Na]⁺ for C₂₀H₁₄BrNaN₅O : 442.0274, found: 442.0275.

1-amino-1'-methyl-7-nitro-2'-oxo-4H-spiro[benzo[4,5]imidazo[1,2-a]pyridine-3,3'-indoline]-2-carbonitrile (5j)



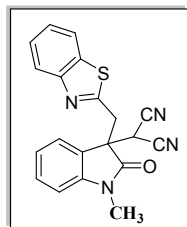
Yield: 88%; brown solid, mp 270-271 °C; mixture of diastereoisomers (dr 1:1); **¹H NMR (400 MHz, DMSO-*d*₆)** δ ppm: 8.81 (d, *J*=2.01 Hz, 1 H) 8.52 (d, *J*=2.26 Hz, 1 H) 8.25 - 8.32 (m, 2 H) 8.13 (d, *J*=9.03 Hz, 1 H) 7.89 (d, *J*=9.03 Hz, 1 H) 7.53 - 7.61 (m, 4 H) 7.37-7.41 (td, *J*=7.78 Hz, 2 H) 7.25 (d, *J*=7.28 Hz, 2 H) 7.09 - 7.14 (m, 4 H) 3.81 (dd, *J*=16.19, 6.90 Hz, 2 H) 3.33 (d, *J*=5.77 Hz, 1 H) 3.18 - 3.22 (d, 1 H) 3.11 (s, 6 H); **¹³C NMR (101 MHz, DMSO-*d*₆)** δ ppm: 175.8, 155.5, 154.0, 151.9, 151.9, 147.2, 143.7, 143.4, 143.0, 142.3, 135.2, 130.3, 129.4, 129.2, 123.9, 122.9, 119.5, 119.2, 119.2, 117.4, 114.9, 114.2, 110.4, 109.1, 66.2, 65.9, 46.4, 46.3, 33.0, 26.2. **HRMS (ESI)** calculated [M+H]⁺ for C₂₀H₁₅N₆O₃ : 387.1200, found: 387.1196.

2-(3-(benzo[d]thiazol-2-ylmethyl)-2-oxoindolin-3-yl)malononitrile (6a)



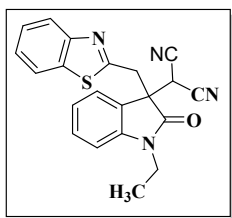
Yield: 84%; Off White solid, mp 188-190 °C; **¹H NMR (200 MHz, DMSO-*d*₆)** δ ppm: 11.11 (s, 1H), 8.00-7.86 (m, 2H), 7.55-7.27 (m, 4H), 7.10 (t, *J*=7.45 Hz, 1H), 6.87 (d, *J*=7.71 Hz, 1H), 5.92 (s, 1H), 4.00 (d, *J*=14.53 Hz, 1H), 3.86 (d, *J*=14.65 Hz, 1H); **¹³C NMR (200 MHz, DMSO-*d*₆)** δ ppm: 174.4, 163.7, 152.0, 142.7, 134.9, 130.7, 126.2, 125.3, 125.0, 124.6, 122.5, 122.1, 111.8, 111.4, 110.4, 51.2, 36.9, 29.8. **HRMS (ESI)** calculated [M+H]⁺ for C₁₉H₁₃ON₄S: 345.0805, found: 364.0805.

2-(3-(benzo[d]thiazol-2-ylmethyl)-2-oxoindolin-3-yl)malononitrile (6b)



Yield: 86%; Off white solid, mp 153-155 °C; ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.88 - 7.98 (d, 1 H) 7.77 (d, *J*=7.7 Hz, 1 H) 7.35 - 7.52 (m, 4 H) 7.11 - 7.17 (m, 1 H) 6.88 - 6.90 (d, 1 H) 5.11 (s, 1 H) 3.73 - 3.90 (m, 2 H) 3.29 (s, 3 H); ¹³C NMR (101 MHz, CDCl₃) δ ppm: 173.0, 162.9, 153.0, 144.2, 137.8, 135.2, 132.4, 131.3, 128.4, 127.3, 126.6, 125.8, 124.7, 124.6, 124.1, 123.5, 122.2, 121.7, 121.0, 110.9, 109.9, 109.5, 51.9, 37.6, 30.4, 30.0, 27.2. HRMS (ESI) calculated [M+H]⁺ for C₂₀H₁₅ON₄S: 359.0961, found: 359.0961. FTIR (CHCl₃, cm⁻¹) 3407, 3020, 2926, 2401, 1722, 1615, 1508, 1493, 1472, 1457, 1435, 1377, 1354, 1312, 1215, 1226, 1092, 1024, 931, 855, 758, 668, 491.

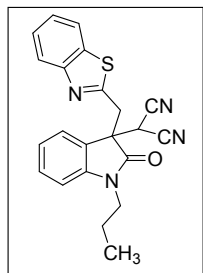
2-(3-(benzo[d]thiazol-2-ylmethyl)-1-ethyl-2-oxoindolin-3-yl)malononitrile (6c)



Yield: 83%; Off white solid, mp 160 °C; ¹H NMR (200 MHz, CDCl₃) δ ppm: 7.84 (d, *J*=8.59 Hz, 1H), 7.68 (d, *J*=7.20 Hz, 1H), 7.46 (d, *J*=7.45 Hz, 1H), 7.36-7.19 (m, 3H), 7.04 (t, *J*=7.45 Hz, 1H), 6.70 (d, *J*=7.85 Hz, 1H), 4.95 (s, 1H), 3.85-3.64 (m, 4H), 1.17 (t, *J*=7.20 Hz, 3H); ¹³C NMR (200 MHz, CDCl₃) δ ppm: 172.3, 162.6, 152.6, 143.1, 134.9, 131.0, 126.3, 125.5, 124.5, 123.6, 123.1, 110.6, 109.3, 51.4, 37.3, 35.5, 30.3, 12.2. HRMS (ESI) calculated [M+H]⁺ for C₂₁H₁₇ON₄S: 373.1118, found: 373.1114. FTIR (CHCl₃, cm⁻¹) 3434, 2098, 2400, 2090, 1700,

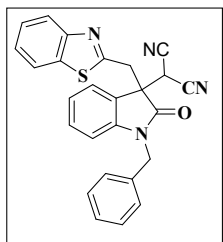
1642, 1488, 1468, 1375, 1351, 1312, 1216, 1128, 939, 755, 495.

2-(3-(benzo[d]thiazol-2-ylmethyl)-2-oxo-1-propylindolin-3-yl)malononitrile (6d)



Yield: 82%; Off white solid, mp 157 °C; ¹H NMR (200 MHz, CDCl₃) δ ppm: 7.93 (d, *J*=7.58 Hz, 1H), 7.76 (d, *J*=7.07 Hz, 1H), 7.54 (d, *J*=7.45 Hz, 1H), 7.48-7.32 (m, 3H), 7.13 (t, *J*=7.58 Hz, 1H), 6.89 (d, *J*=7.83 Hz, 1H), 5.07 (s, 1H), 3.92-3.65 (m, 4H), 1.70 (q, *J*=7.33 Hz, 2H), 0.93 (t, *J*=7.33 Hz, 3H); ¹³C NMR (200 MHz, CDCl₃) δ ppm: 172.6, 162.6, 152.6, 143.6, 134.9, 130.9, 126.3, 125.5, 124.4, 123.6, 123.1, 121.4, 110.7, 109.63, 109.5, 51.5, 42.4, 37.4, 30.2, 20.6, 11.5. HRMS (ESI) calculated [M+H]⁺ for C₂₂H₁₉ON₄S: 387.1274, found: 387.1272. FTIR (CHCl₃, cm⁻¹) 3409, 3064, 3022, 2972, 2935, 2878, 2808, 2594, 2256, 2212, 1945, 1714, 1614, 1487, 1468, 1434, 1372, 1316, 1216, 1152, 1112, 1061, 1029, 1015, 990, 931, 875, 754, 693, 669, 632, 603, 569, 500.

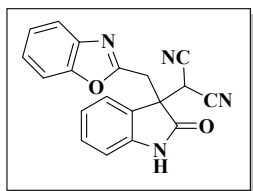
2-(3-(benzo[d]thiazol-2-ylmethyl)-1-benzyl-2-oxoindolin-3-yl)malononitrile (6e)



Yield: 89%; Off white solid, mp 166-168 °C; ¹H NMR (200 MHz, CDCl₃) δ ppm: 8.01 – 8.13 (m, 1 H) 7.93 (dd, *J*=7.8, 1 H) 7.72 - 7.78 (d, 1 H) 7.42 - 7.68 (m, 4 H) 7.25 - 7.38 (m, 5 H) 6.91 (d, *J*=7.5, 1 H) 4.52 – 4.98 (m, 3 H) 3.96 - 4.15 (m, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ ppm:

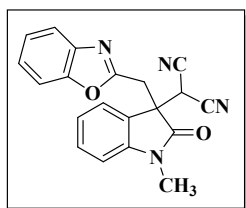
172.7, 162.3, 152.7, 143.3, 135.0, 134.3, 131.0, 128.7, 127.8, 127.1, 126.3, 125.5, 124.3, 124.2, 123.9, 123.3, 121.8, 121.5, 110.6, 110.4, 109.6, 51.7, 44.6, 37.8, 30.4. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{26}H_{19}ON_4S$: 435.1274, found: 435.11273. **FTIR ($CHCl_3$, cm^{-1})** 3420, 3067, 3020, 2925, 2400, 2090, 1720, 1615, 1488, 1469, 1456, 1436, 1371, 1312, 1261, 1215, 1177, 1016, 929, 879, 758, 697, 669.

2-3(-(benzo[d]oxazol-2-ylmethyl)-2-oxoindolin-3-yl)malononitrile (6f)



Yield: 82%; Off White solid, mp 188-190 °C; **1H NMR (200 MHz, $DMSO-d_6$)** δ ppm: 11.1 (s, 1 H) 7.86 - 8.07 (m, 2 H) 7.27 - 7.55 (m, 4 H) 7.07 - 7.14 (m, 1 H) 6.89 (d, $J=7.7$ Hz, 1 H) 5.92 (s, 1 H) 3.84 - 4.05 (m, 2 H); **^{13}C NMR (50 MHz, $DMSO-d_6$)** δ ppm: 174.8, 164.0, 152.4, 143.1, 135.2, 131.1, 126.6, 126.4, 125.7, 125.5, 125.0, 122.9, 122.4, 112.1, 111.8, 110.8, 51.6, 37.3, 30.2. **MALDI TOF/TOF** m/z calcd for $C_{19}H_{12}N_4O_2$ $[M + K^+]$ 367.0597, observed 367.0674. **FTIR ($CHCl_3$, cm^{-1})** 3419, 2918, 2184, 1721, 1642, 1468, 1316, 1216, 1184, 1118, 758, 691, 666, 502.

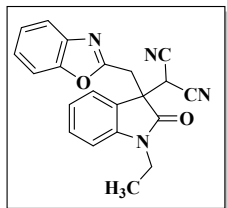
2-(3(-(benzo[d]oxazol-2-ylmethyl)-2-oxoindolin-3-yl)malononitrile (6g)



Yield: 85%; White solid, mp 158-160 °C; **1H NMR (200 MHz, $CDCl_3$)** δ ppm: 7.97 (d, $J=7.7$ Hz, 1 H) 7.80 (d, $J=7.5$ Hz, 1 H) 7.34 - 7.54 (m, 4 H) 7.10 - 7.18 (m, 1 H) 6.92 (d, $J=7.8$ Hz, 1

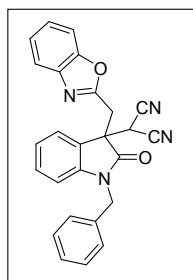
H) 5.13 (s, 1 H) 3.96 (q, 2 H) 3.29 (s, 3 H); ^{13}C NMR (50 MHz, CDCl_3) δ ppm: 172.7, 162.6, 152.9, 143.9, 134.9, 131.0, 126.3, 125.5, 124.4, 124.3, 123.7, 123.2, 121.4, 110.6, 109.6, 109.2, 51.5, 37.3, 30.12, 26.8. FTIR (CHCl_3 , cm^{-1}) 3417, 2927, 1716, 1647, 1494, 1469, 1377, 1245, 1159, 1124, 728, 755, 503.

2-(3-(benzo[d]oxazol-2-ylmethyl)-1-ethyl-2-oxoindolin-3-yl)malononitrile (6h)



Yield: 86%; White solid, mp 155-156 °C; ^1H NMR (200 MHz, CDCl_3) δ ppm: 7.95 (dd, $J=7.89$ Hz, 1 H) 7.75 - 7.79 (d, 1 H) 7.53-7.57 (dd, $J=7.52$ Hz, 1 H) 7.32 - 7.57 (m, 3 H) 7.09 - 7.17 (m, 1 H) 6.86.91 (d, $J=7.83$ Hz, 1 H) 5.04 (s, 1 H) 3.72 - 3.95 (m, 4 H) 1.22 (t, 3 H); ^{13}C NMR (50 MHz, CDCl_3) δ ppm: 172.3, 162.5, 152.7, 143.1, 134.9, 130.9, 126.2, 125.4, 124.6, 124.4, 123.5, 123.2, 121.4, 110.6, 109.5, 109.3, 51.3, 37.3, 35.4, 30.2, 12.2. FTIR (CHCl_3 , cm^{-1}) 3411, 3019, 2925, 2400, 2343, 2279, 1843, 1767, 1714, 1701, 1696, 1653, 1645, 1544, 1539, 1520, 1468, 1456, 1436, 1377, 1215, 929, 762, 669.

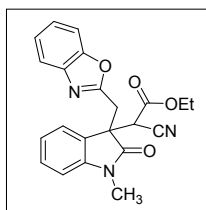
2-(3-(benzo[d]oxazol-2-ylmethyl)-1-benzyl-2-oxoindolin-3-yl)malononitrile (6i)



Yield: 90%; White solid, mp 162 °C; ^1H NMR (200 MHz, CDCl_3) δ ppm: 7.82 (d, $J=8.34$ Hz, 1H), 7.66 (d, $J=7.45$ Hz, 1H), 7.54 (d, $J=7.45$ Hz, 1H), 7.42-7.16 (m, 3H), 7.09-6.97 (m, 6H),

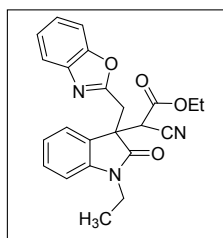
6.62 (d, $J=7.58$ Hz, 1H), 5.37 (s, 1H), 4.94 (d, $J=15.79$ Hz, 1H), 4.76 (d, $J=15.79$ Hz, 1H), 3.88 (s, 2H); **^{13}C NMR (200 MHz, CDCl_3)** δ ppm: 172.3, 162.1, 152.0, 142.8, 134.6, 133.9, 130.4, 128.1, 127.2, 126.5, 125.6, 124.9, 123.7, 123.1, 122.6, 120.9, 109.8, 51.0, 43.9, 37.2, 29.8.

ethyl 2-(3-(benzo[d]oxazol-2-ylmethyl)-1-methyl-2-oxoindolin-3-yl)-2-cyanoacetate (6j)



Yield: 76%; White solid, mp 173-175 °C, **^1H NMR (200 MHz, $\text{DMSO}-d_6$)** δ ppm:: 7.37 - 7.46 (m, 2 H) 6.85 - 7.18 (m, 4 H) 6.63 - 6.81 (m, 2 H) 4.92 - 5.04 (m, 1 H) 3.90 - 4.09 (m, 2 H) 3.37 (m, 2 H) 2.29 (s, 3 H) 0.90 - 1.15 (t, 3 H); **^{13}C NMR (50 MHz, $\text{DMSO}-d_6$)** δ ppm:: 176.6, 176.1, 163.7, 163.4, 162.3, 156.6, 156.5, 154.5, 154.1, 142.5, 136.2, 136.1, 128.8, 128.7, 128.4, 127.6, 127.5, 124.5, 123.8, 121.1, 121.0, 120.9, 120.7, 120.5, 115.8, 62.1, 51.7, 44.2, 43.0, 42.8, 23.7, 13.3. **FTIR (CHCl_3 , cm^{-1})** 3422, 3030, 2967, 2927, 2400, 2256, 1721, 1615, 1508, 1457, 1493, 1472, 1426, 1376, 1354, 1311, 1281, 1127, 1093, 1059, 1024, 930, 893, 853, 756, 668, 633, 601, 570, 541, 485.

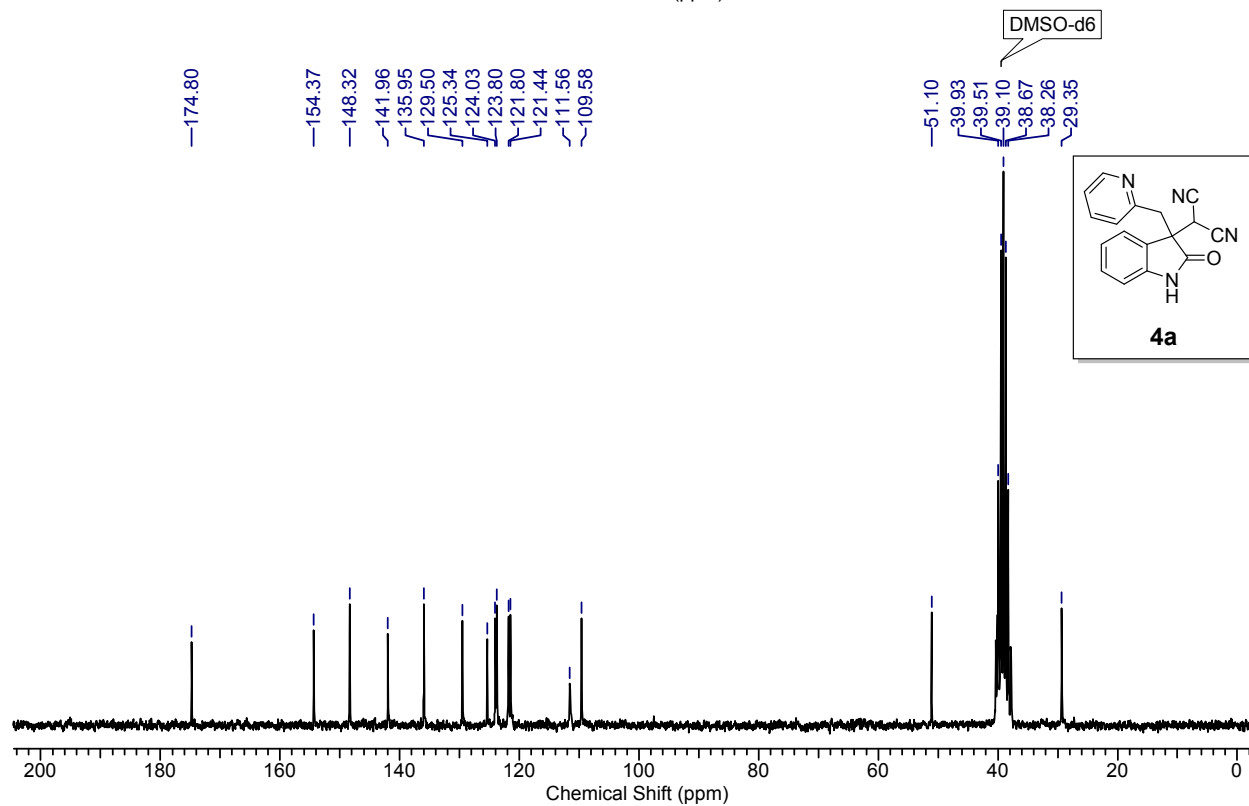
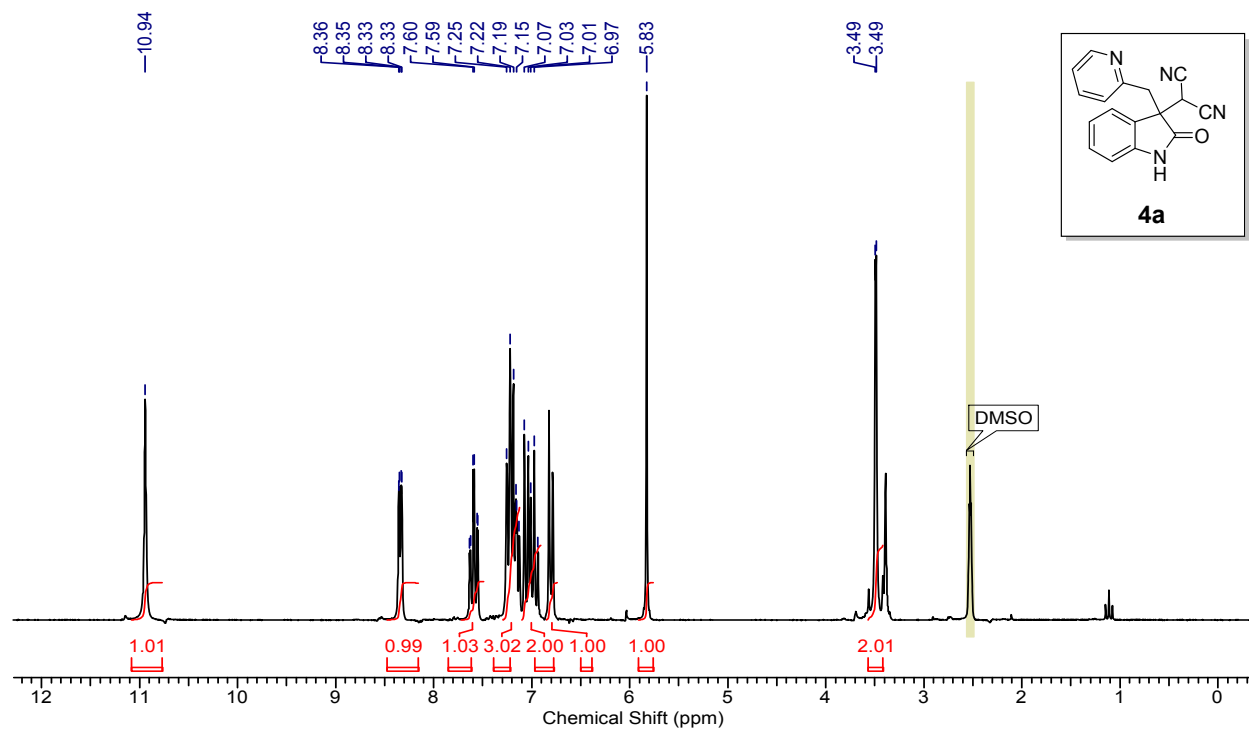
ethyl 2-(3-(benzo[d]oxazol-2-ylmethyl)-1-ethyl-2-oxoindolin-3-yl)-2-cyanoacetate (6k)

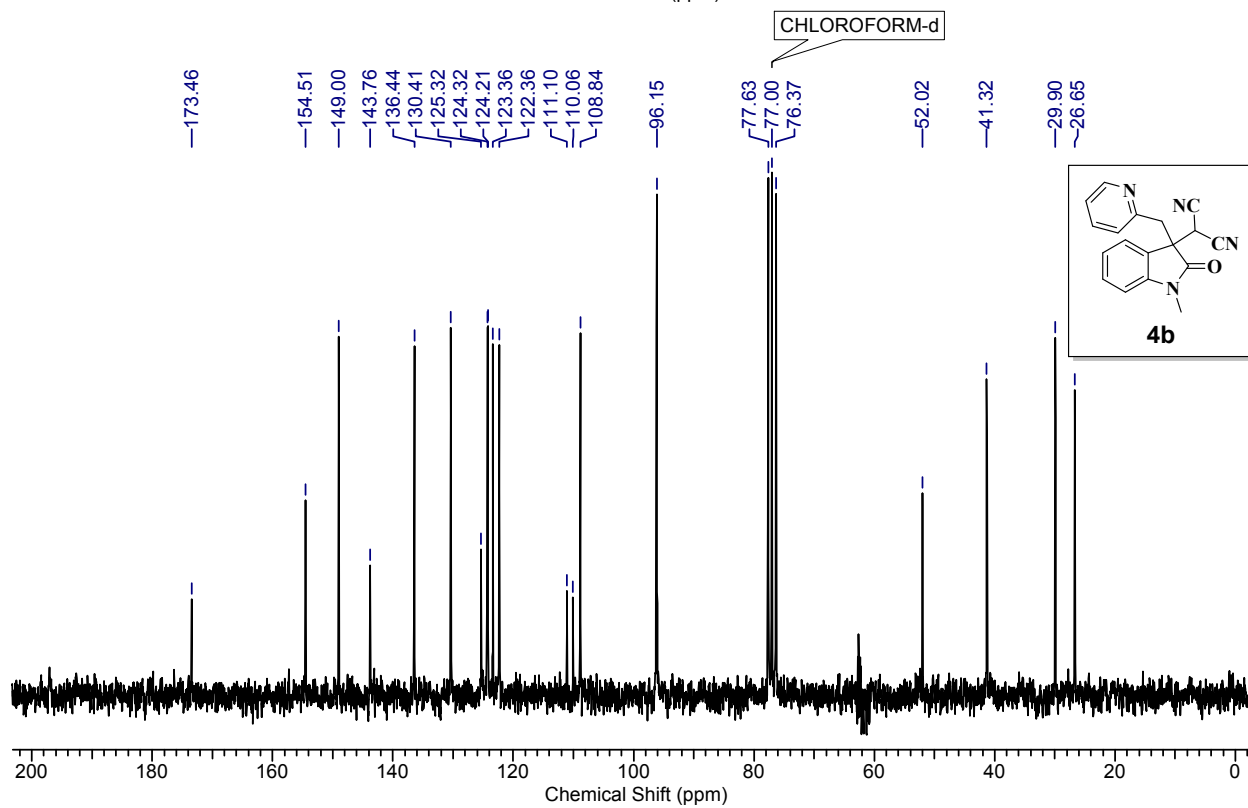
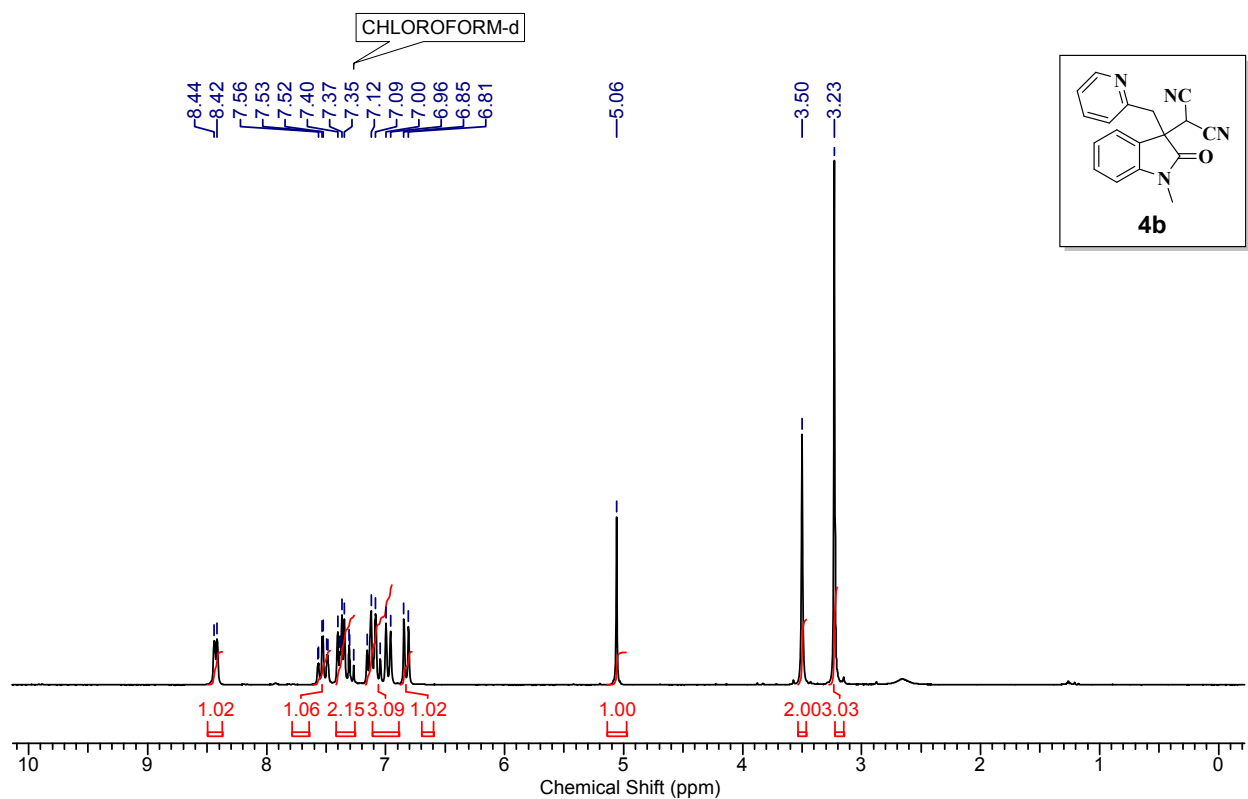


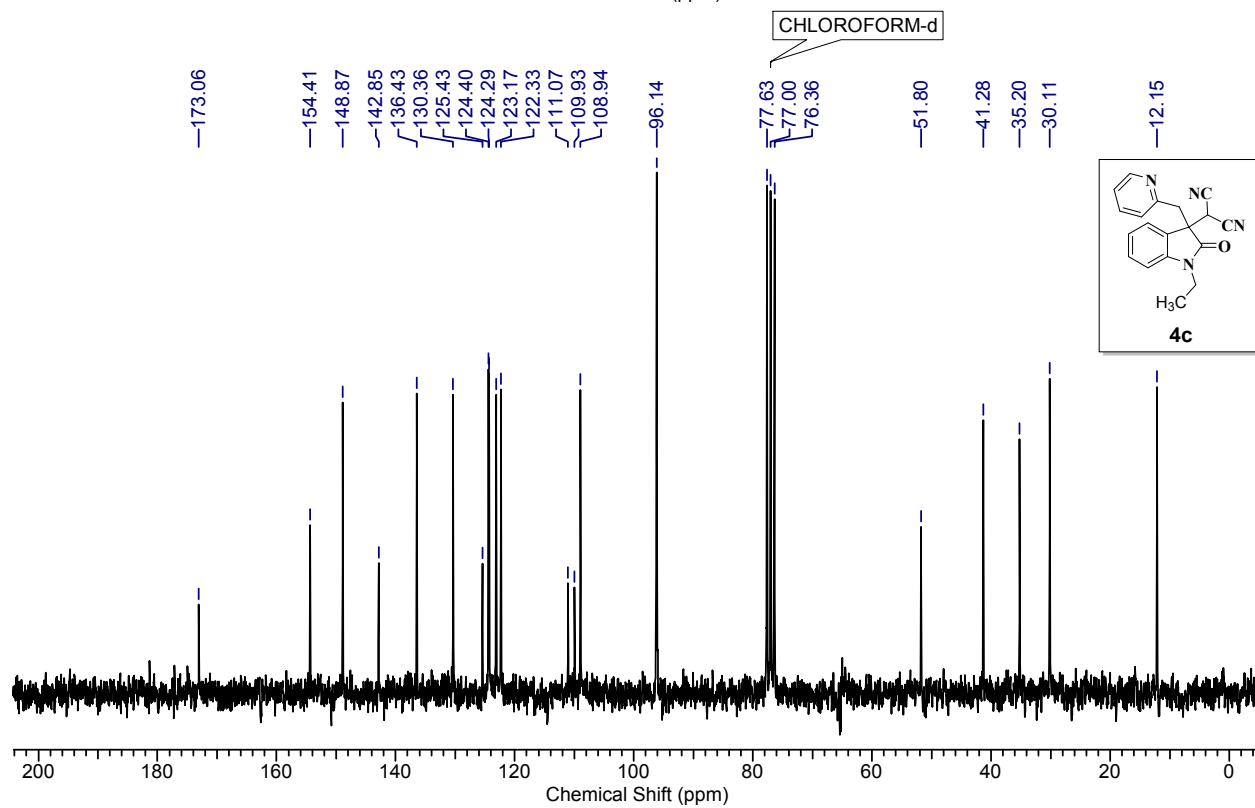
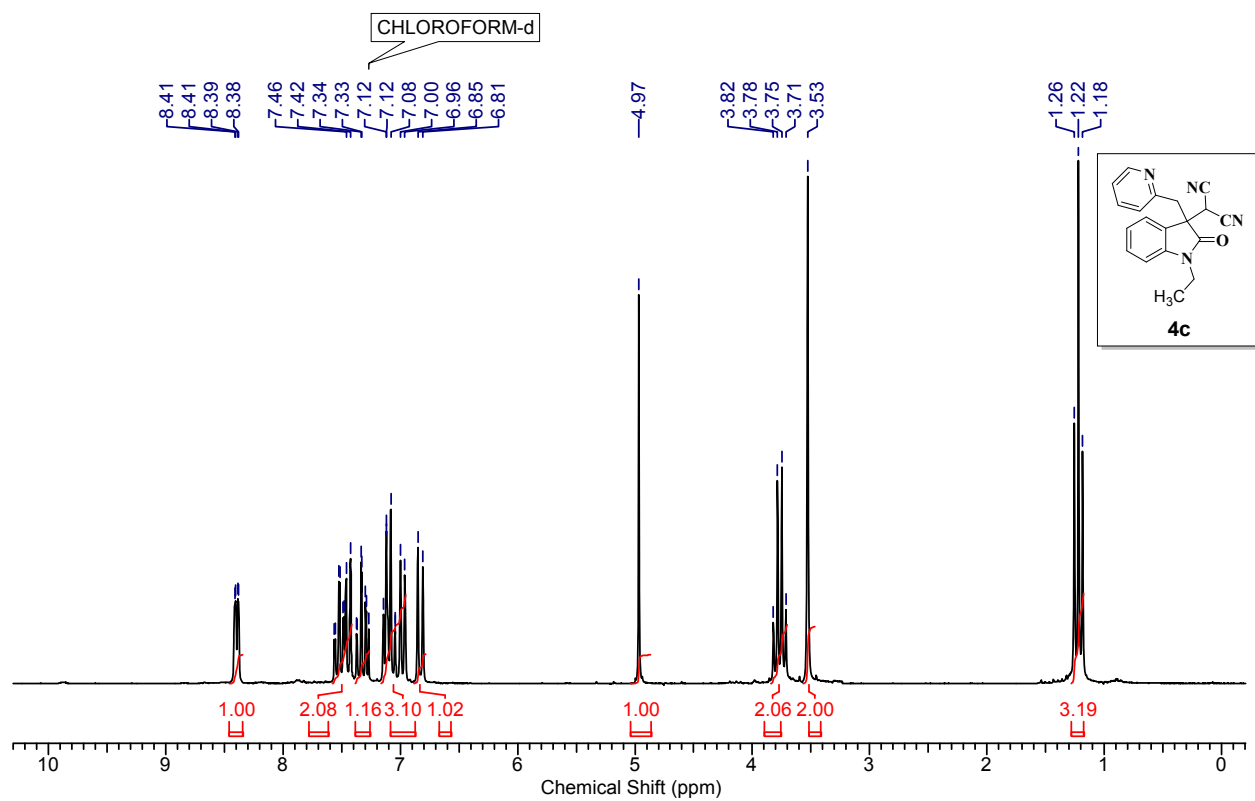
Yield: 80%; White solid, mp 180-181 °C, **^1H NMR (200 MHz, CDCl_3)** δ ppm: 7.89 (d, $J=7.83$ Hz, 1 H) 7.65 - 7.71 (m, 1 H) 7.23 - 7.36 (m, 3 H) 7.06 - 7.13 (m, 1 H) 6.69 (d, $J=7.71$ Hz, 1 H) 4.51 (s, 1 H) 3.92 - 4.03 (m, 2 H) 3.85 (d, $J=4.42$ Hz, 2 H) 3.48 - 3.73 (m, 2 H) 0.94 (td, $J=7.20$

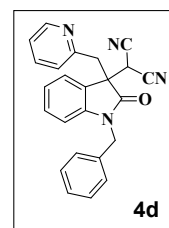
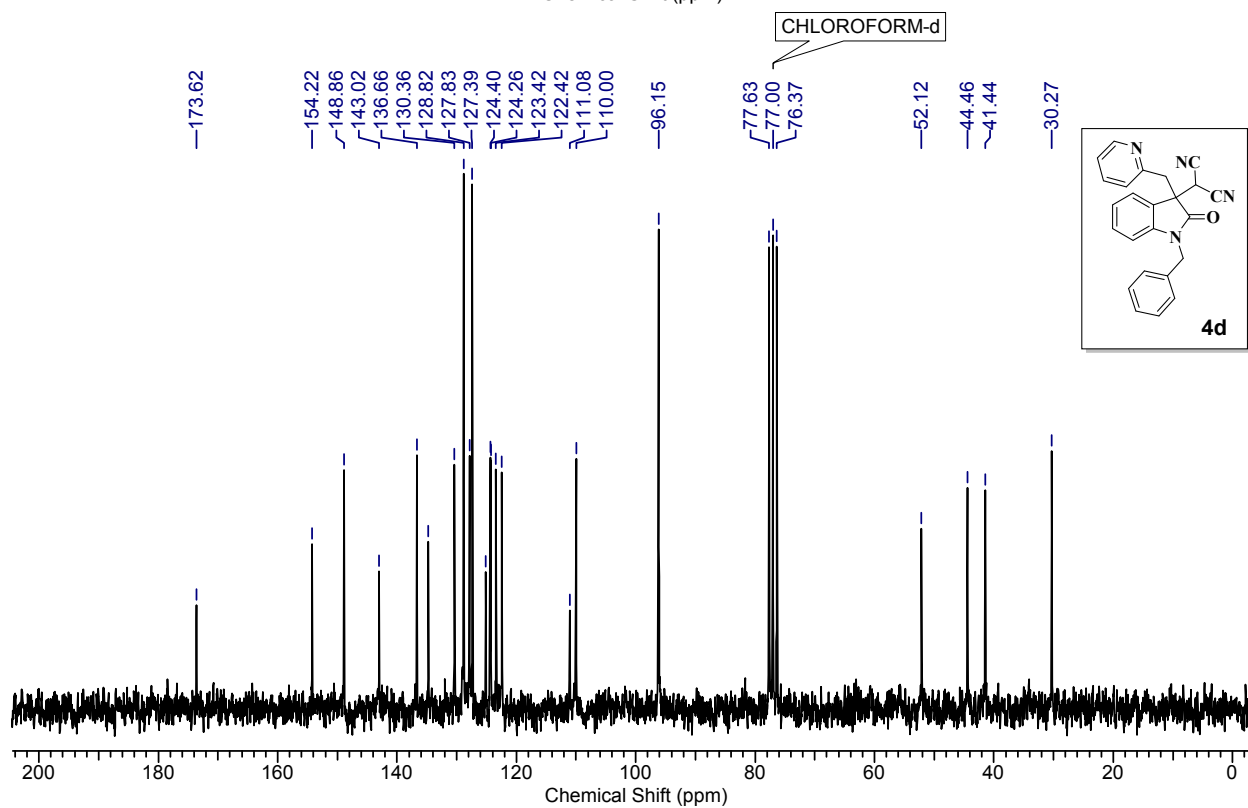
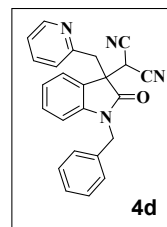
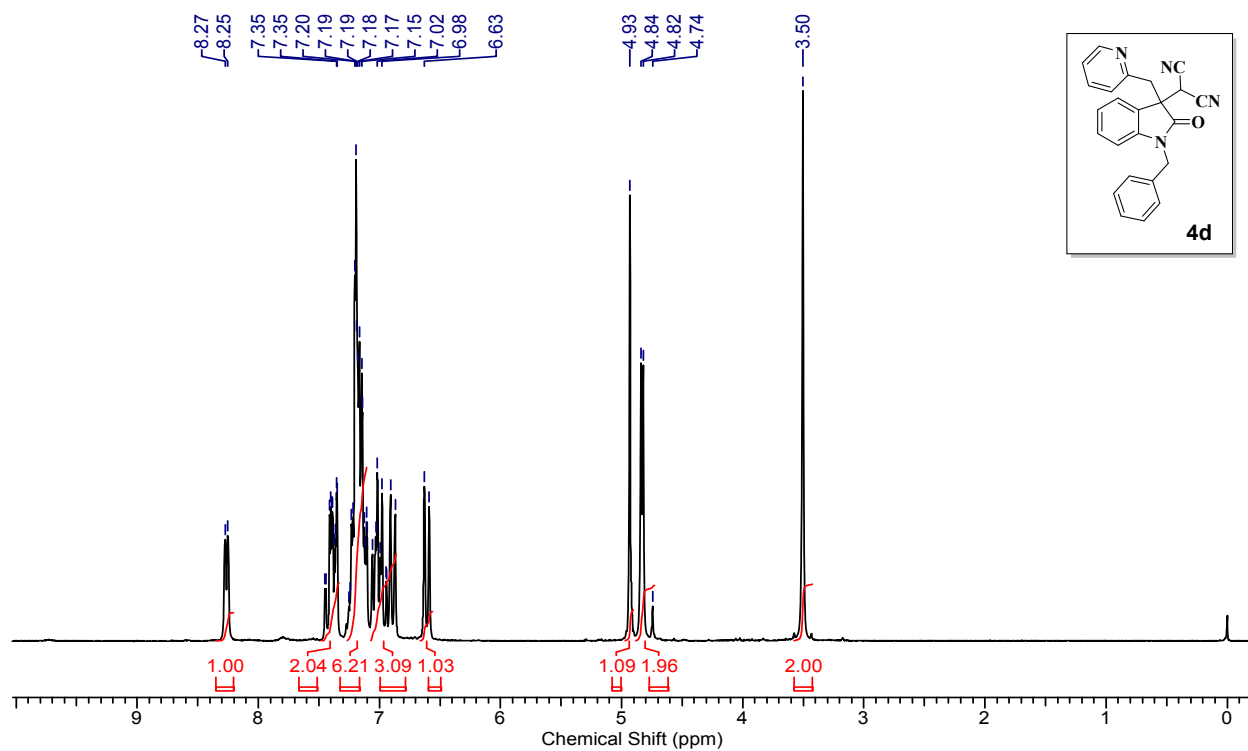
Hz, 6 H); **¹³C NMR (50 MHz, CDCl₃)** δ ppm: 174.0, 164.5, 162.9, 162.4, 152.1, 143.5, 143.2, 135.1, 130.0, 126.3, 126.2, 126.0, 125.5, 125.2, 125.0, 124.0, 122.9, 121.4, 121.3, 114.7, 113.5, 108.8, 108.6, 63.1, 51.1, 44.0, 43.4, 40.1, 35.0, 13.8, 13.5, 12.3, 12.0, 11.9. **MALDI TOF/TOF** m/z calcd for C₂₃H₂₁N₃O₄ [M + K⁺] 442.1169, observed 442.1179. **FTIR (CHCl₃, cm⁻¹)** 3421, 3020, 2985, 2938, 2401, 2254, 1946, 1909, 1845, 1747, 1715, 1614, 1562, 1541, 1513, 1489, 1470, 1376, 1353, 1313, 1218, 11260, 1129, 1100, 1080, 1017, 929, 854, 770, 666, 624, 554, 470.

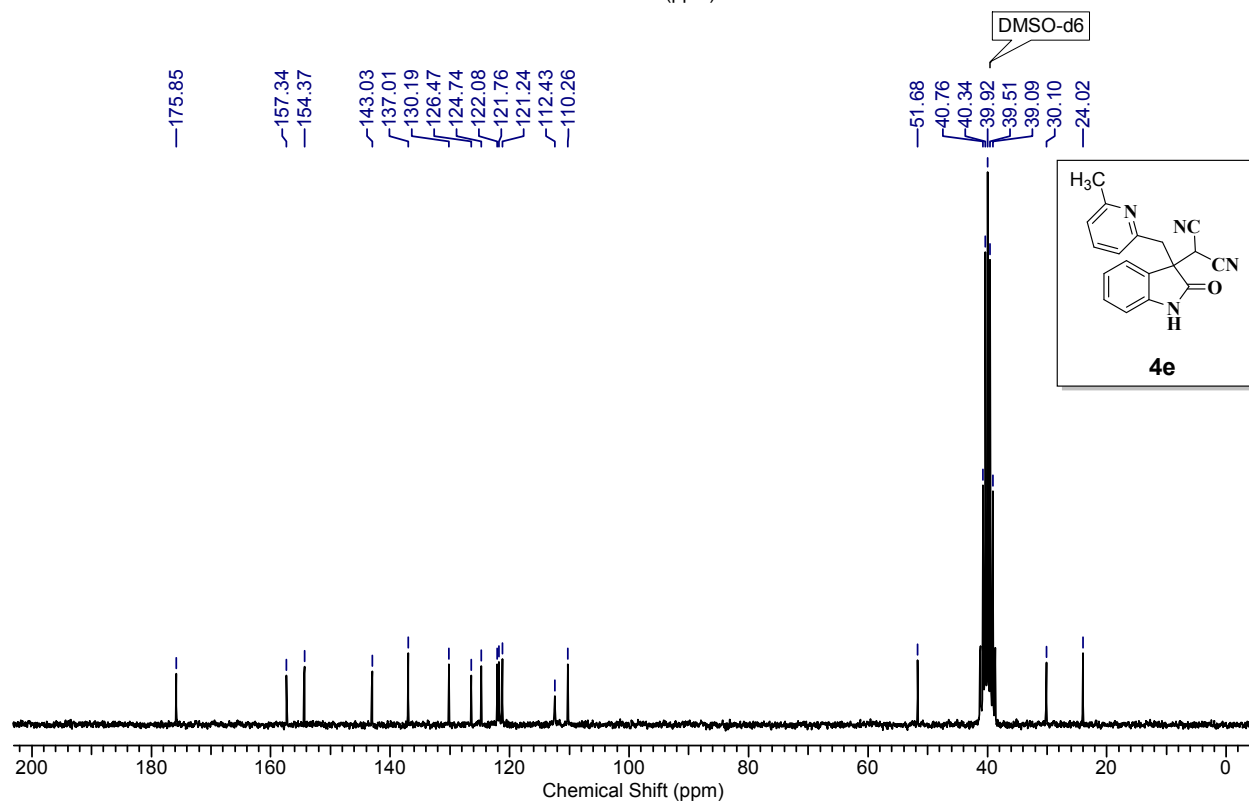
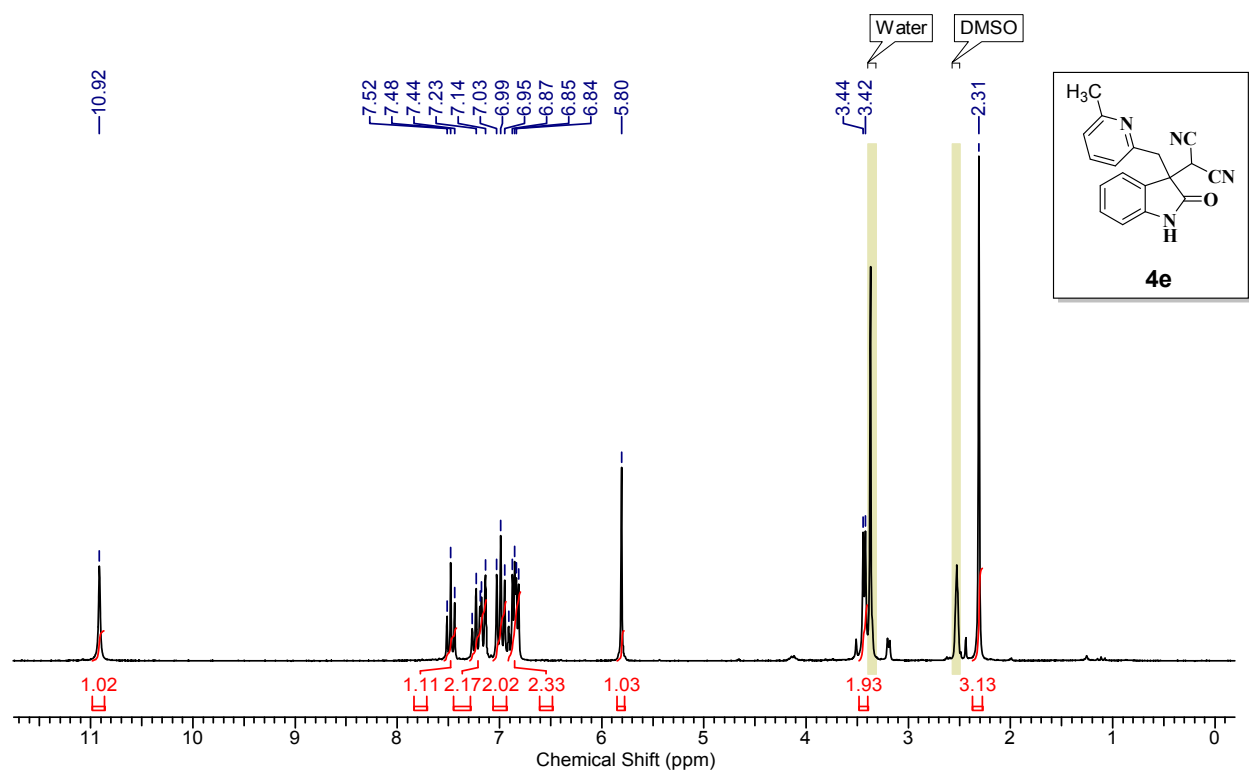
8. ^1H NMR and ^{13}C NMR Spectra of Product:-

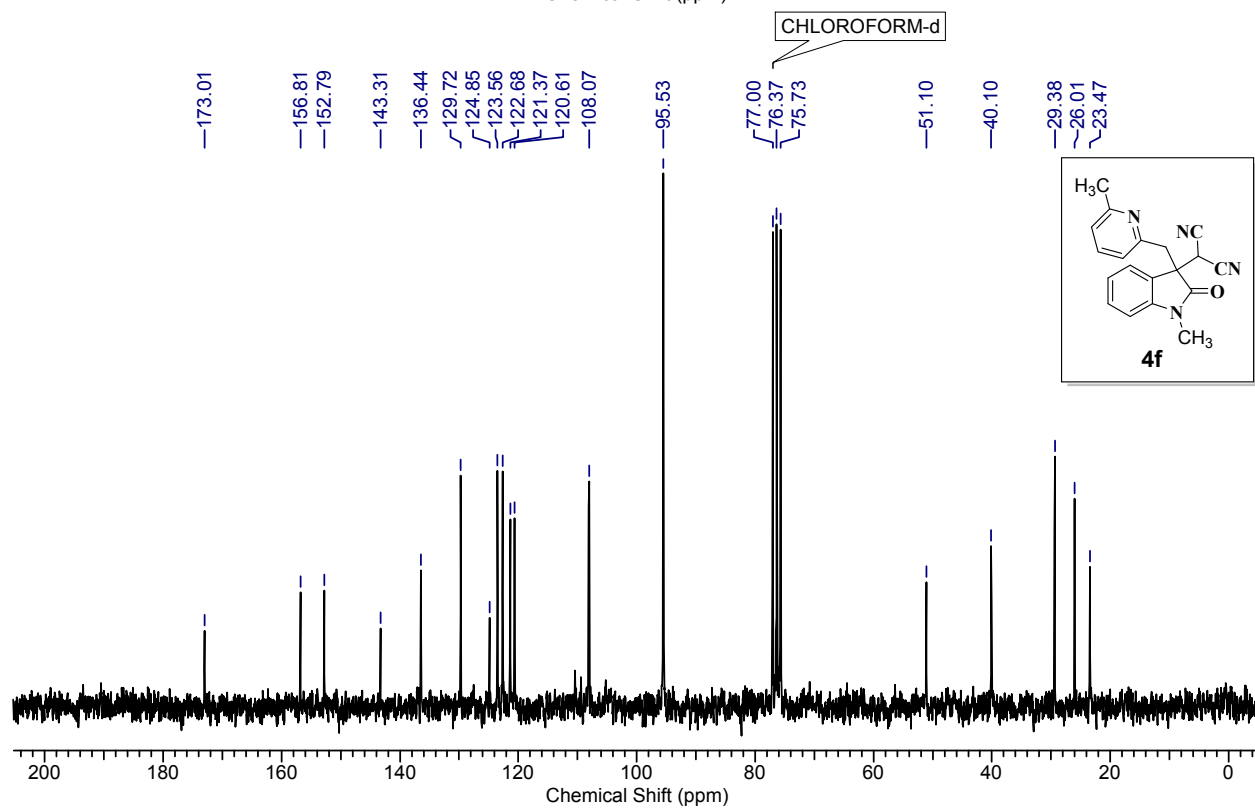
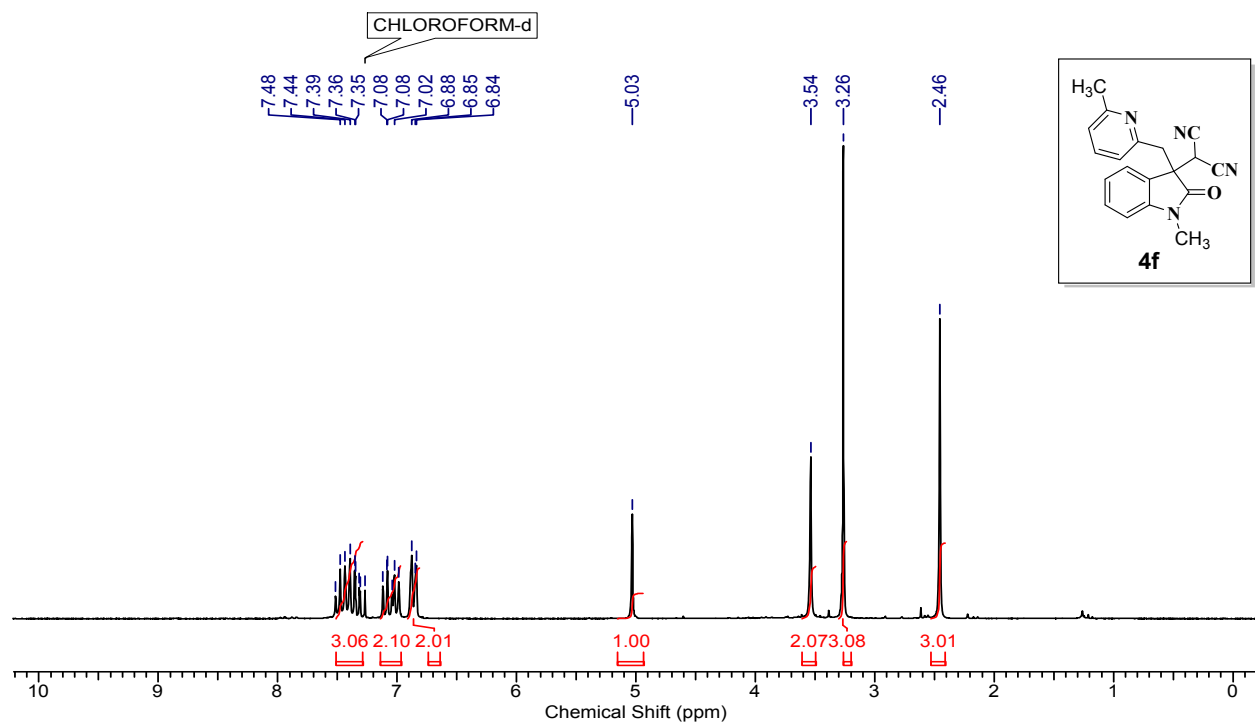


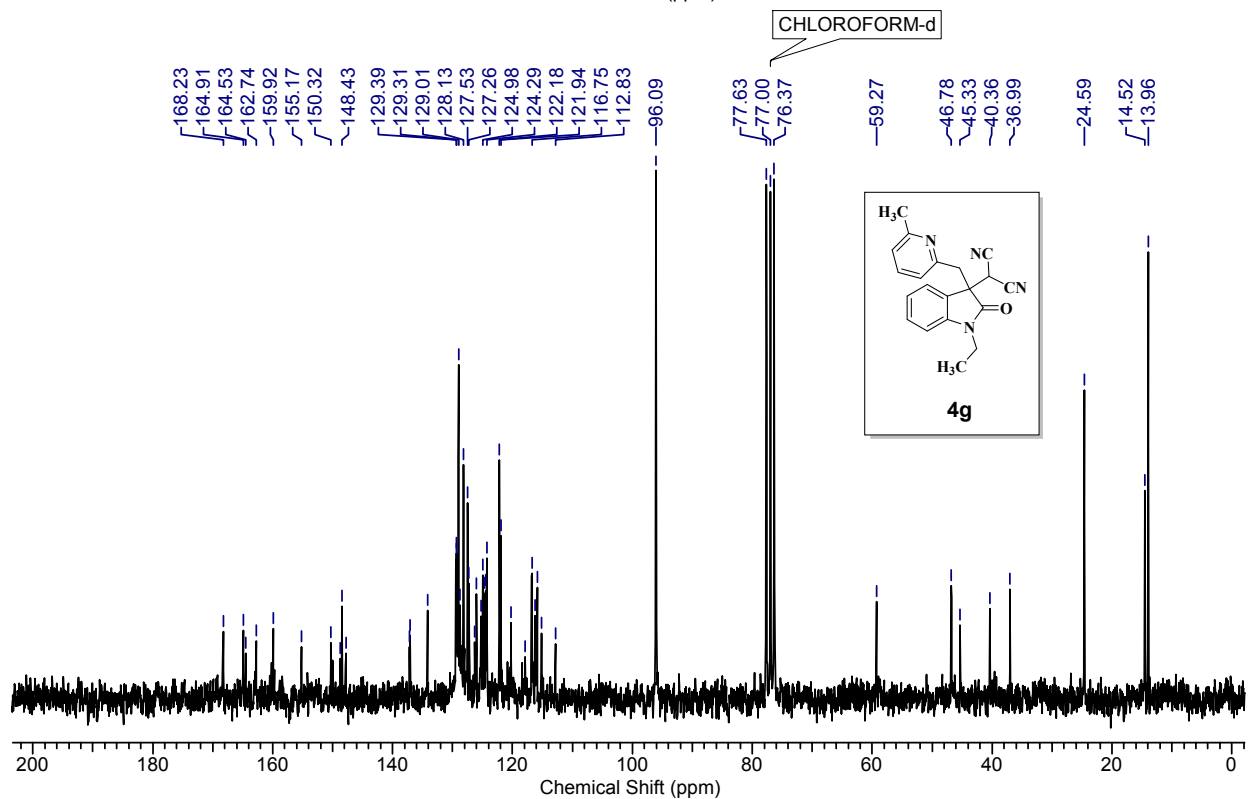
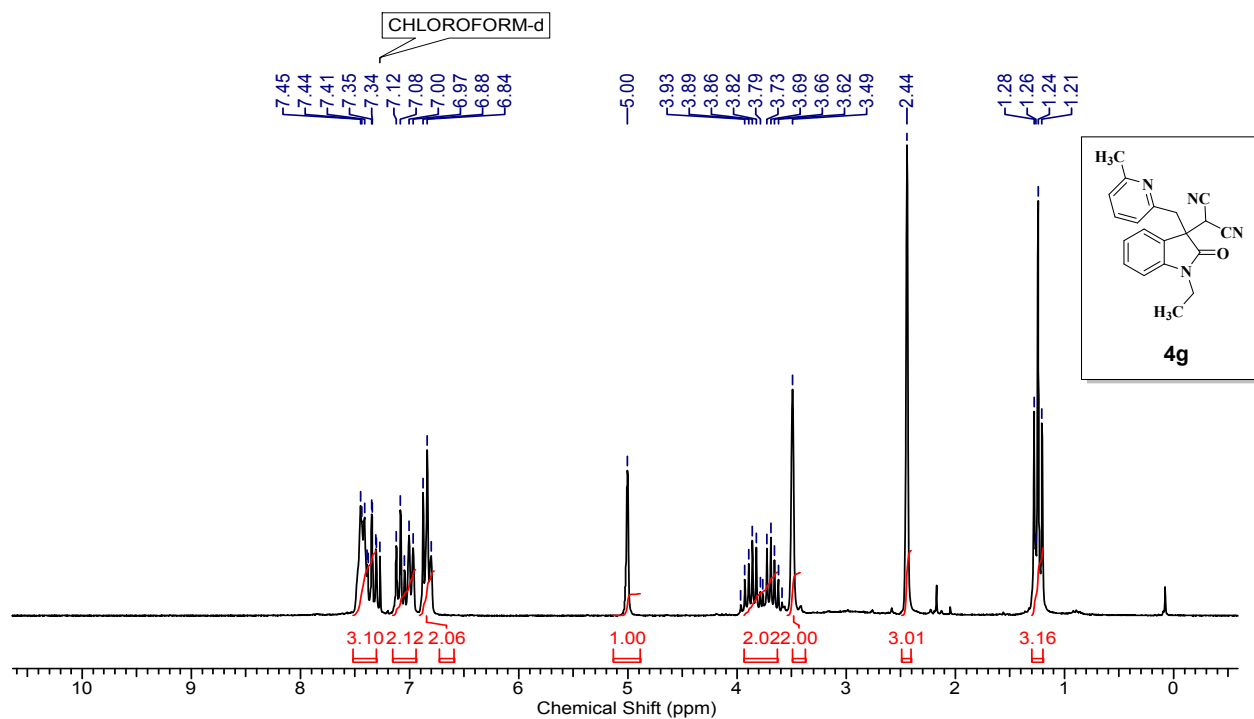


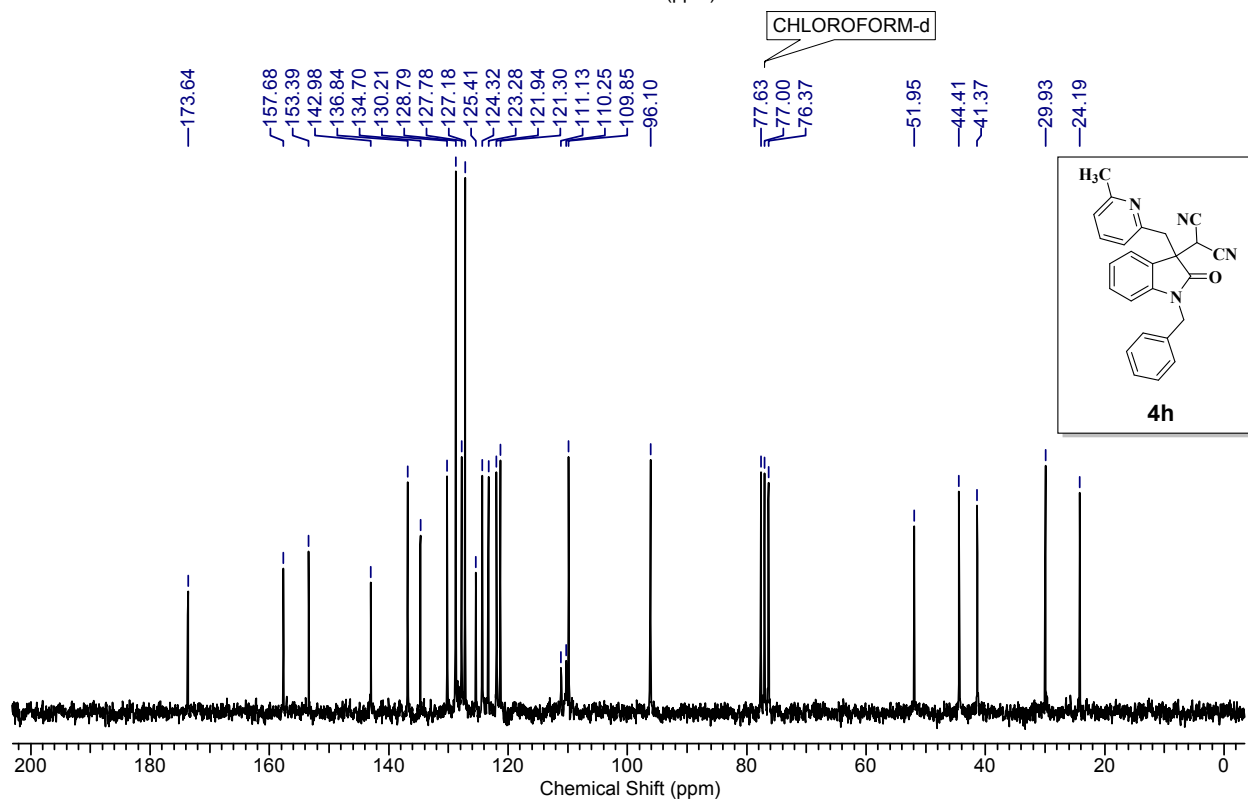
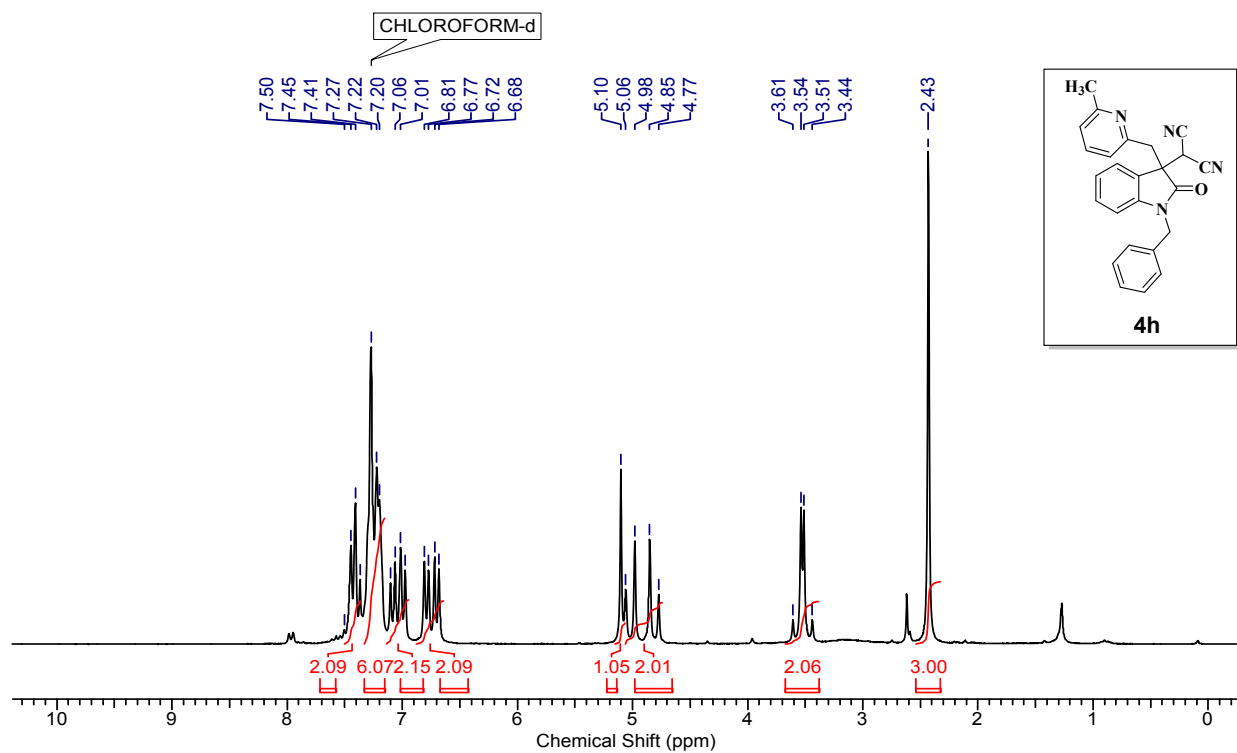


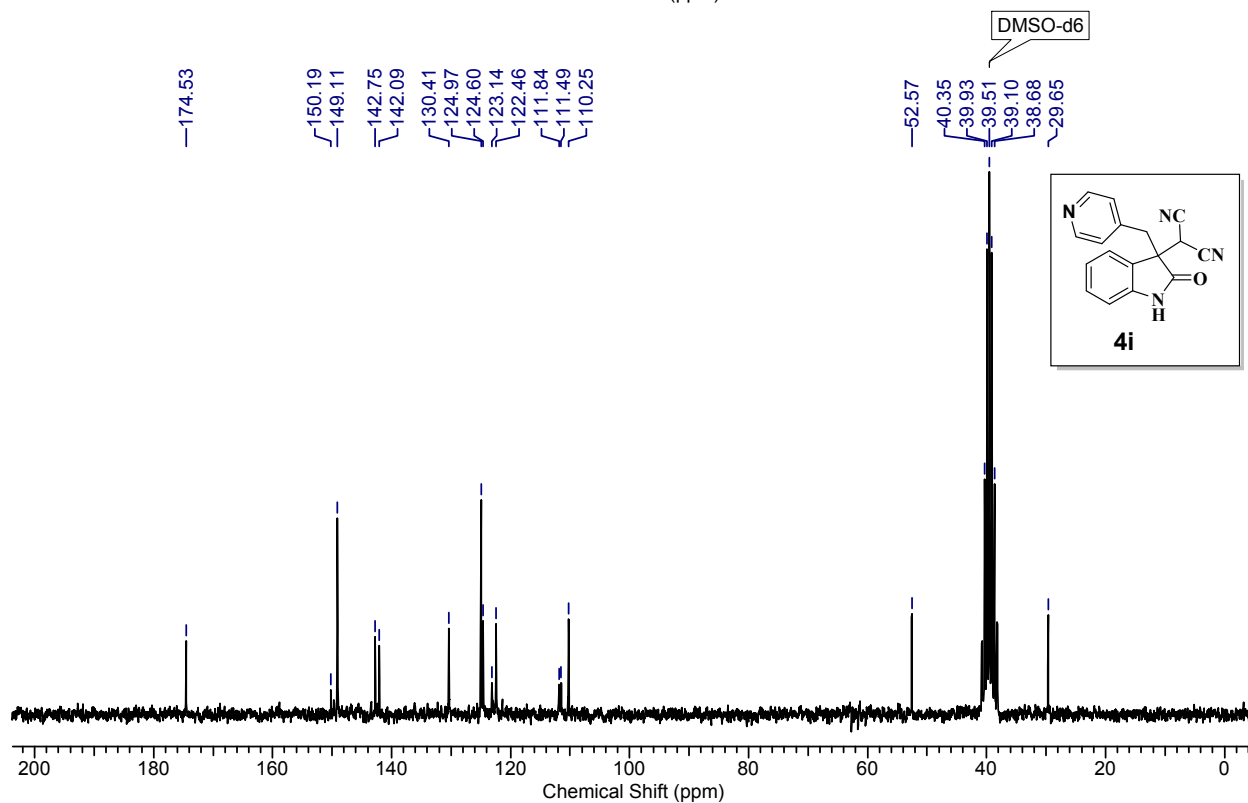
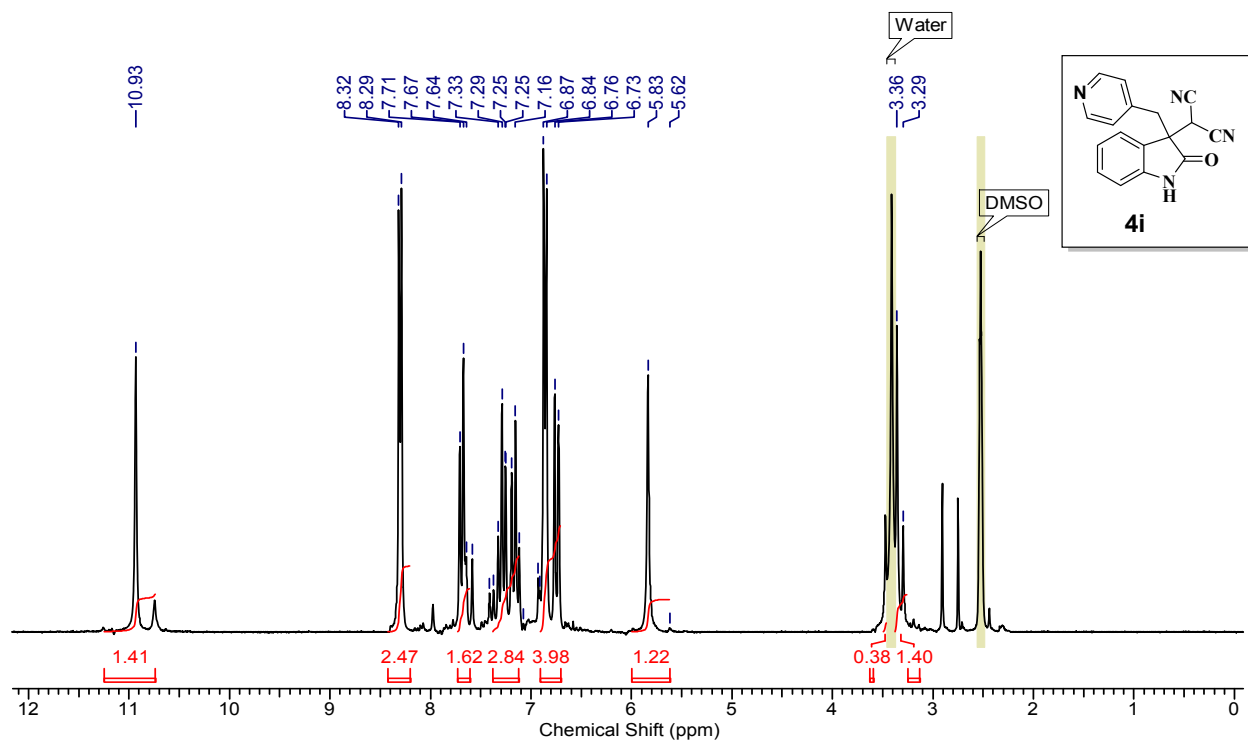


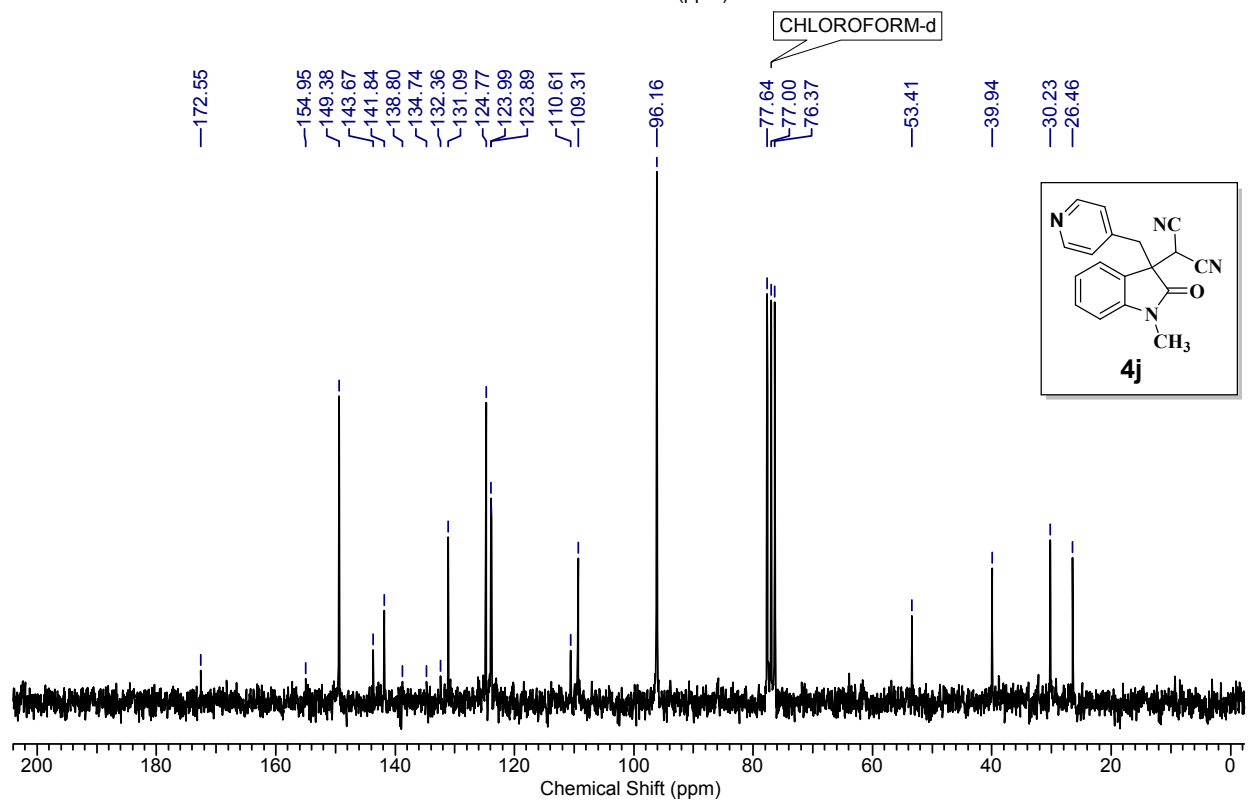
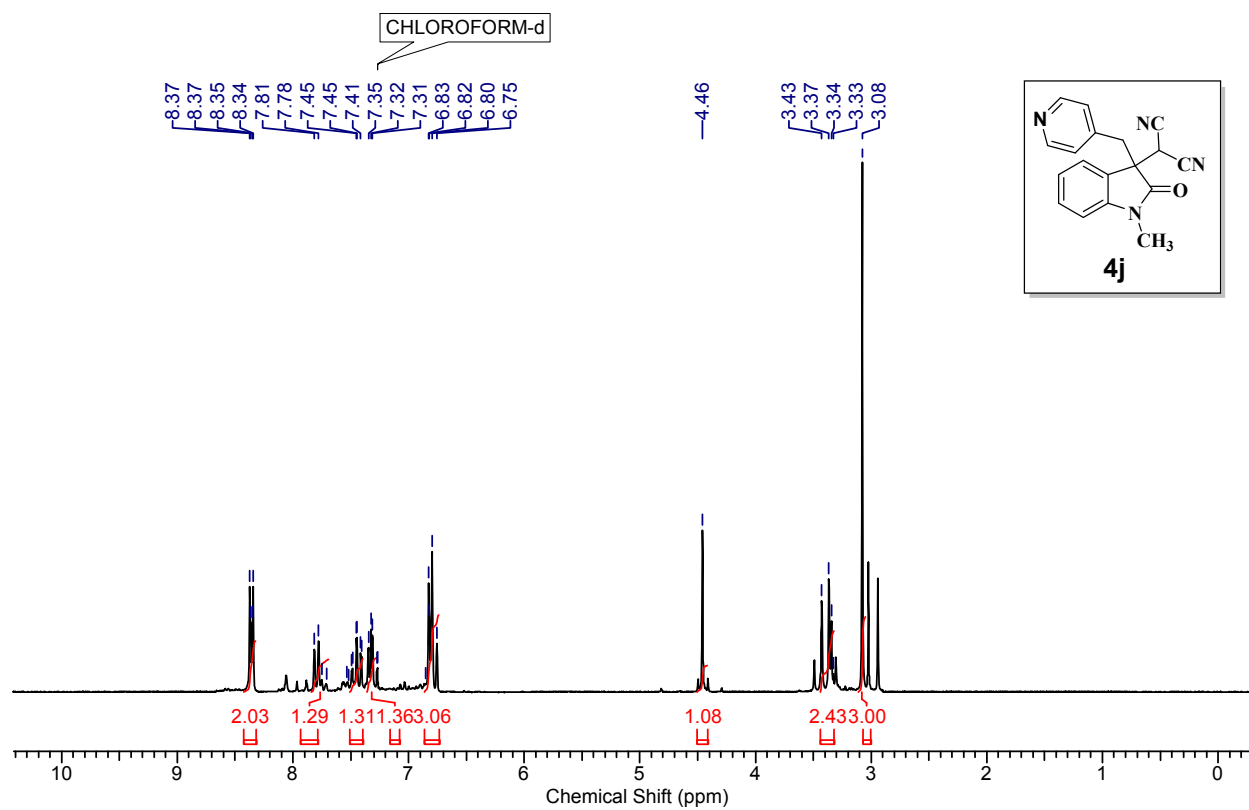


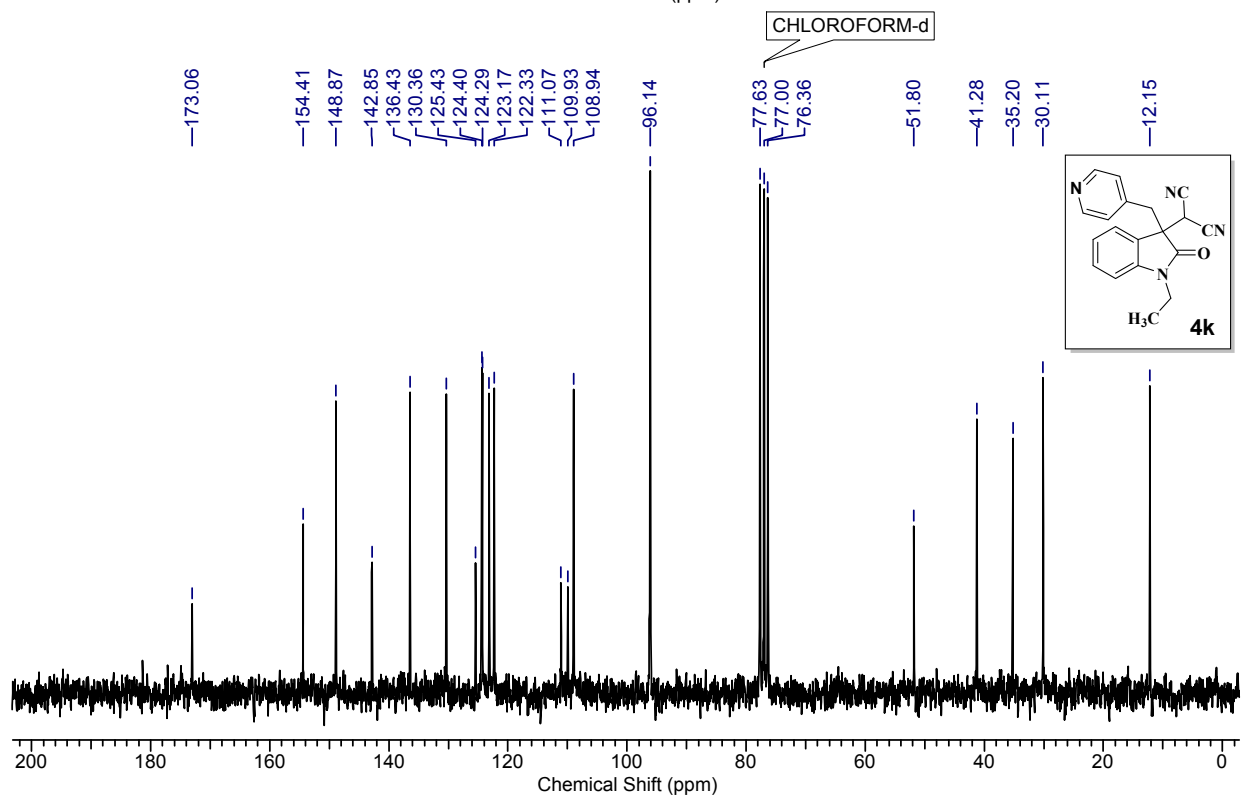
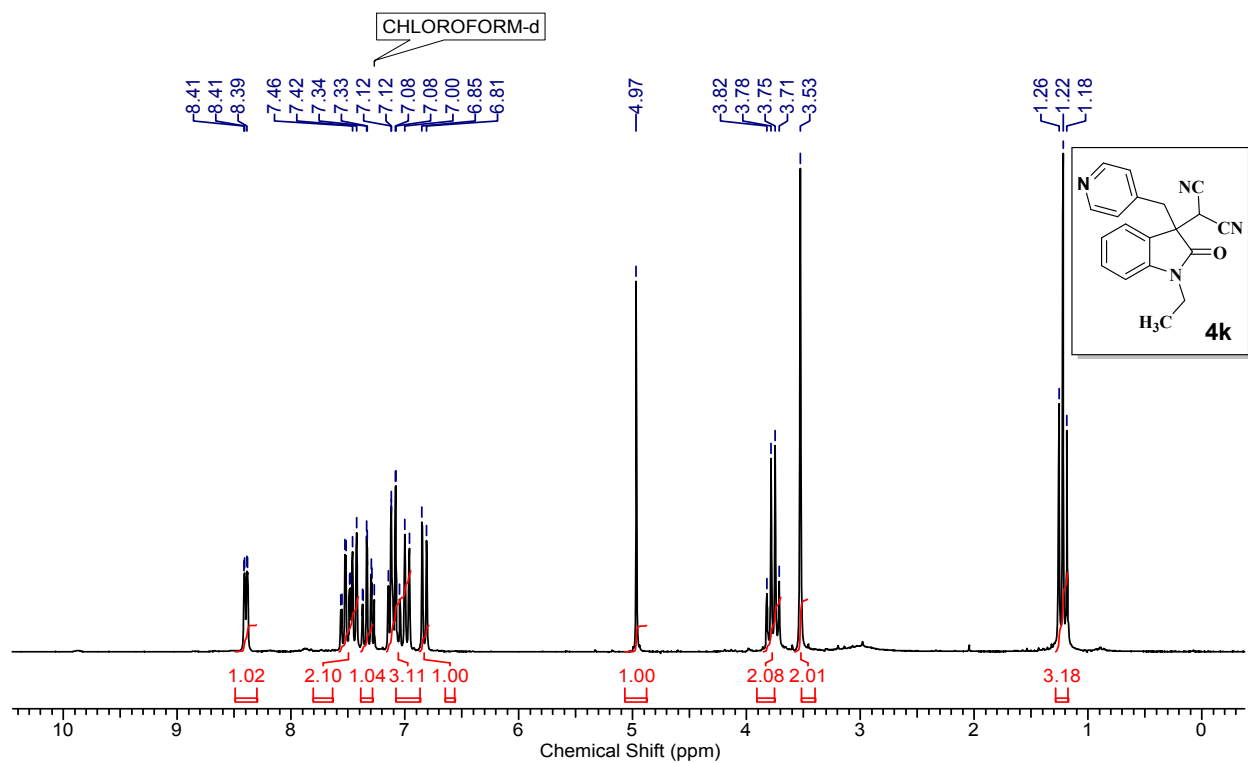


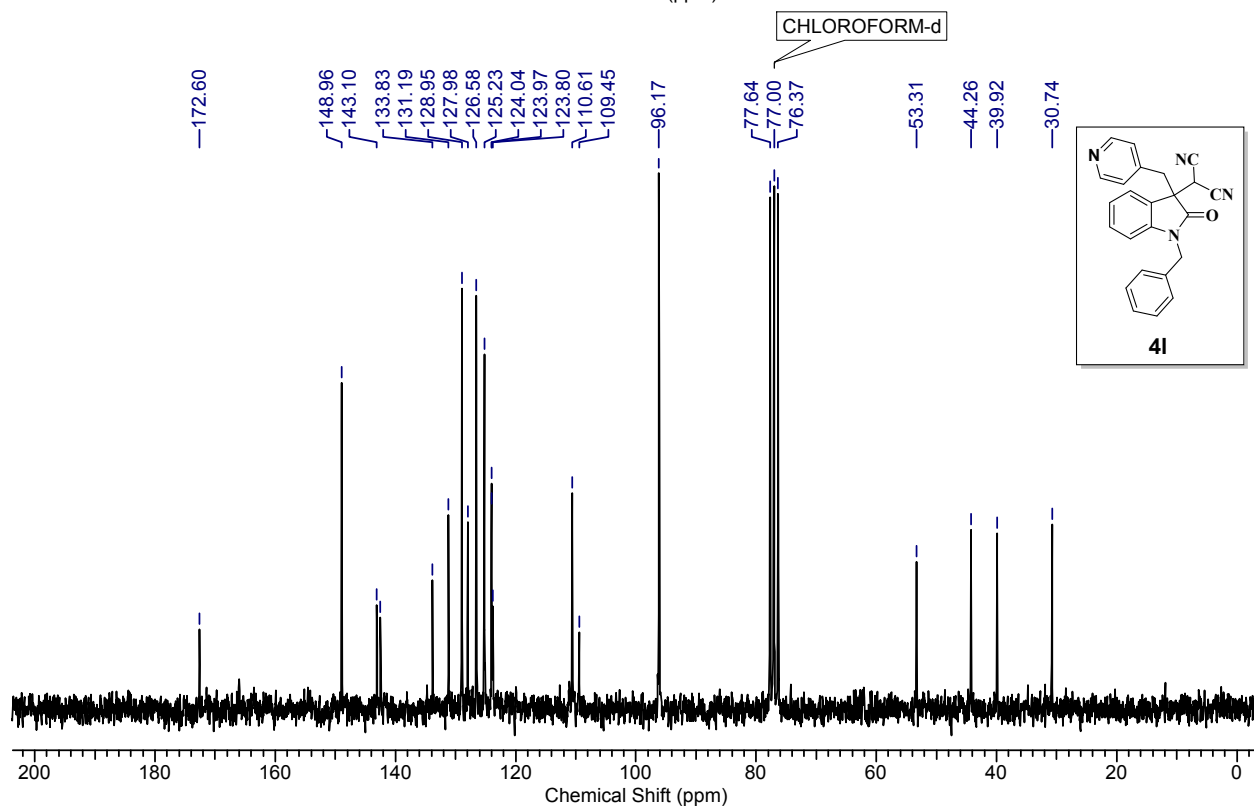
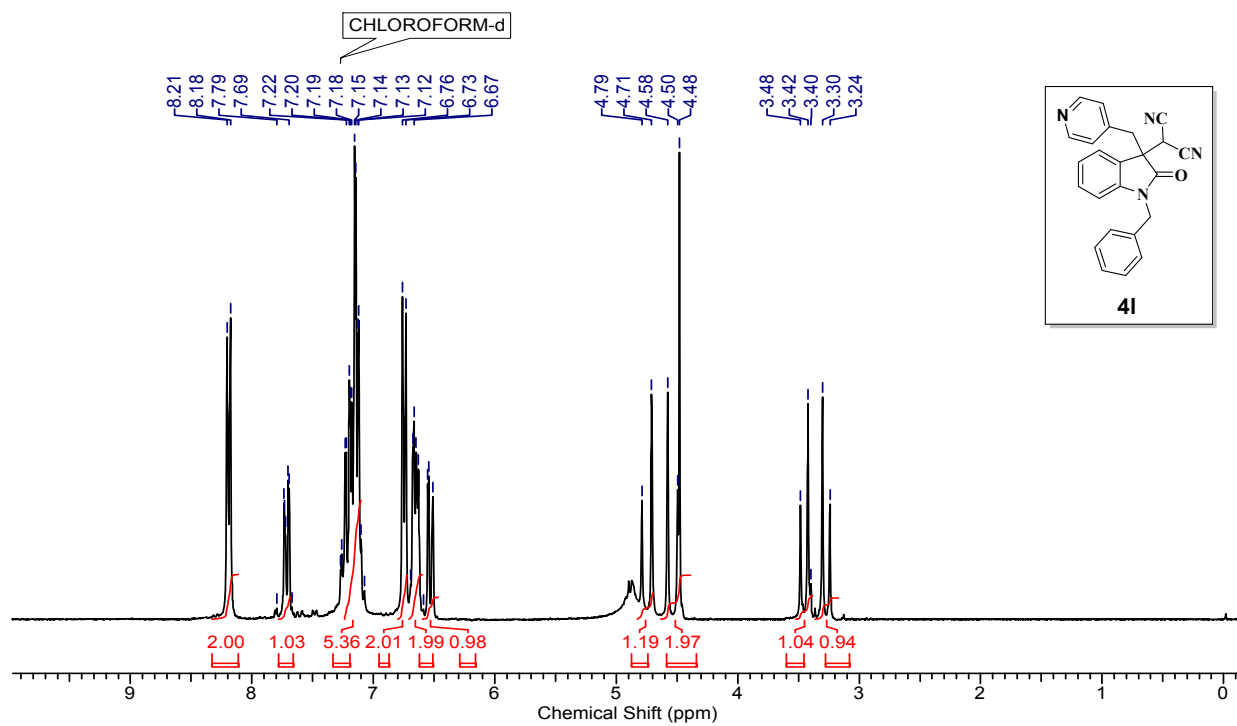


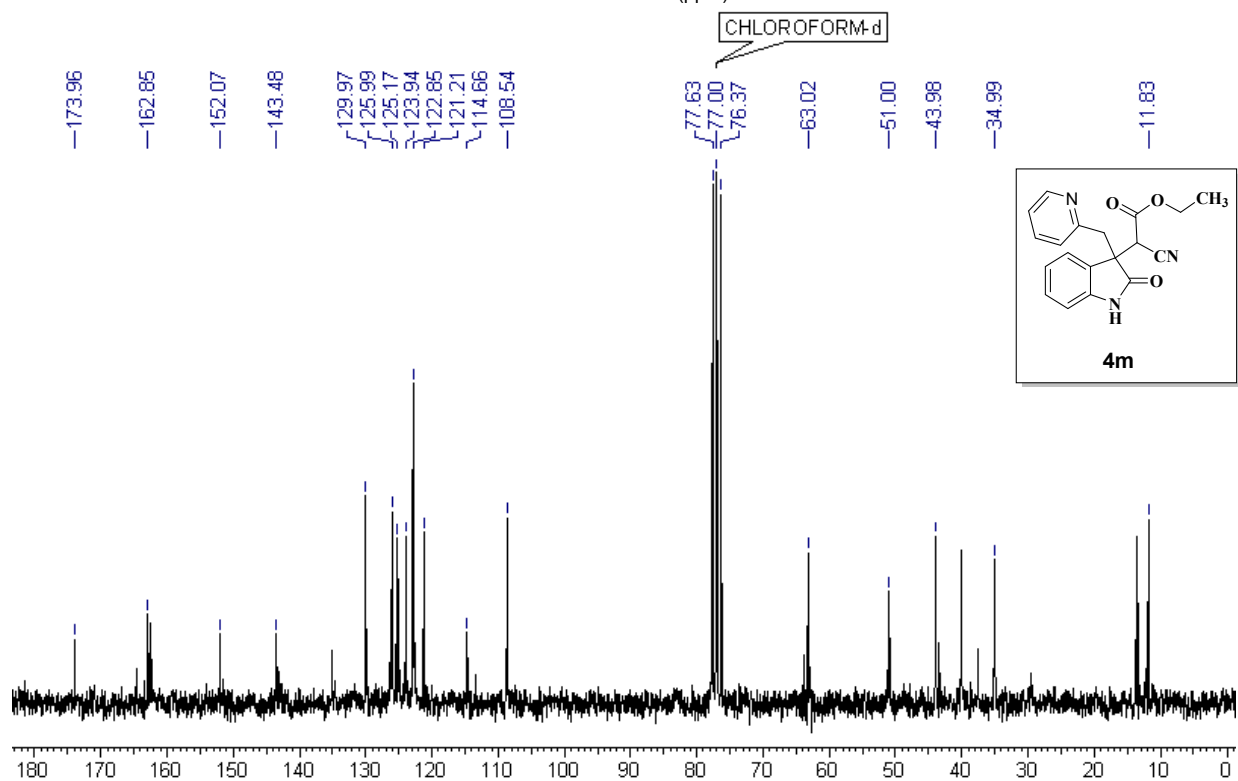
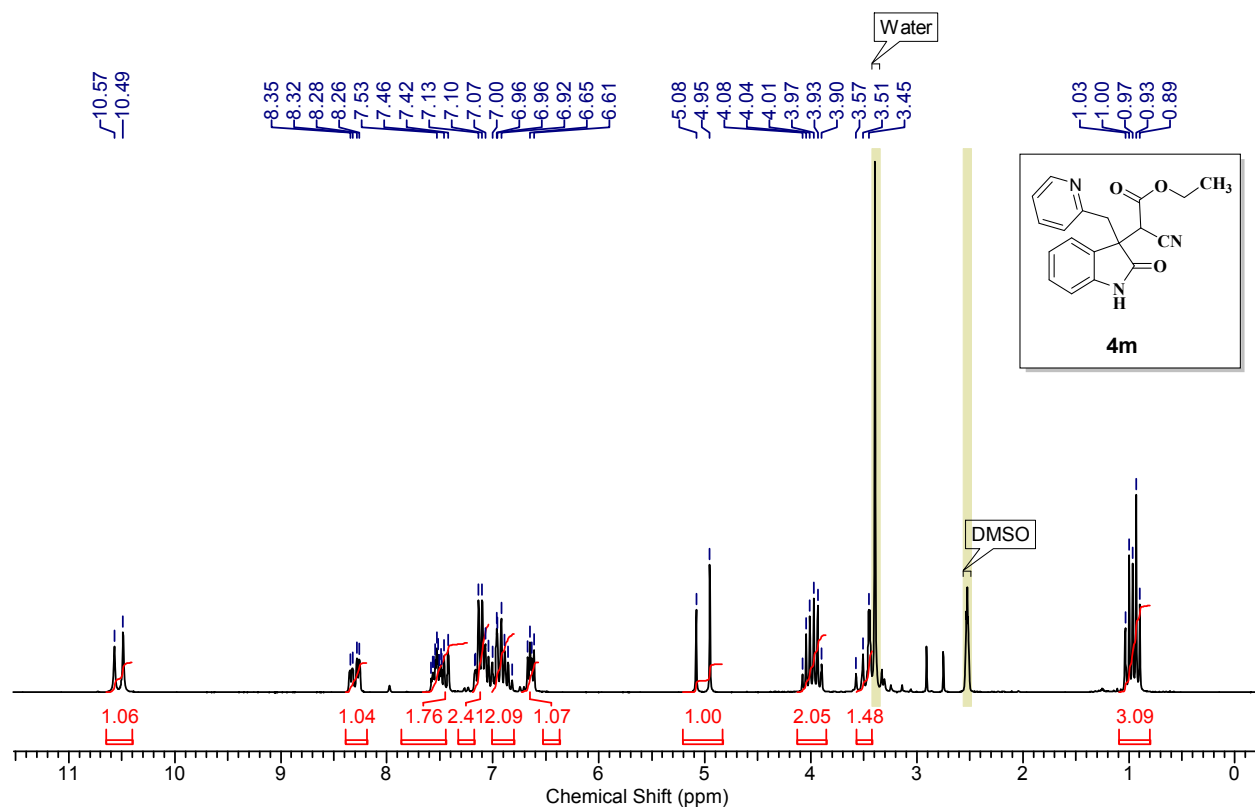


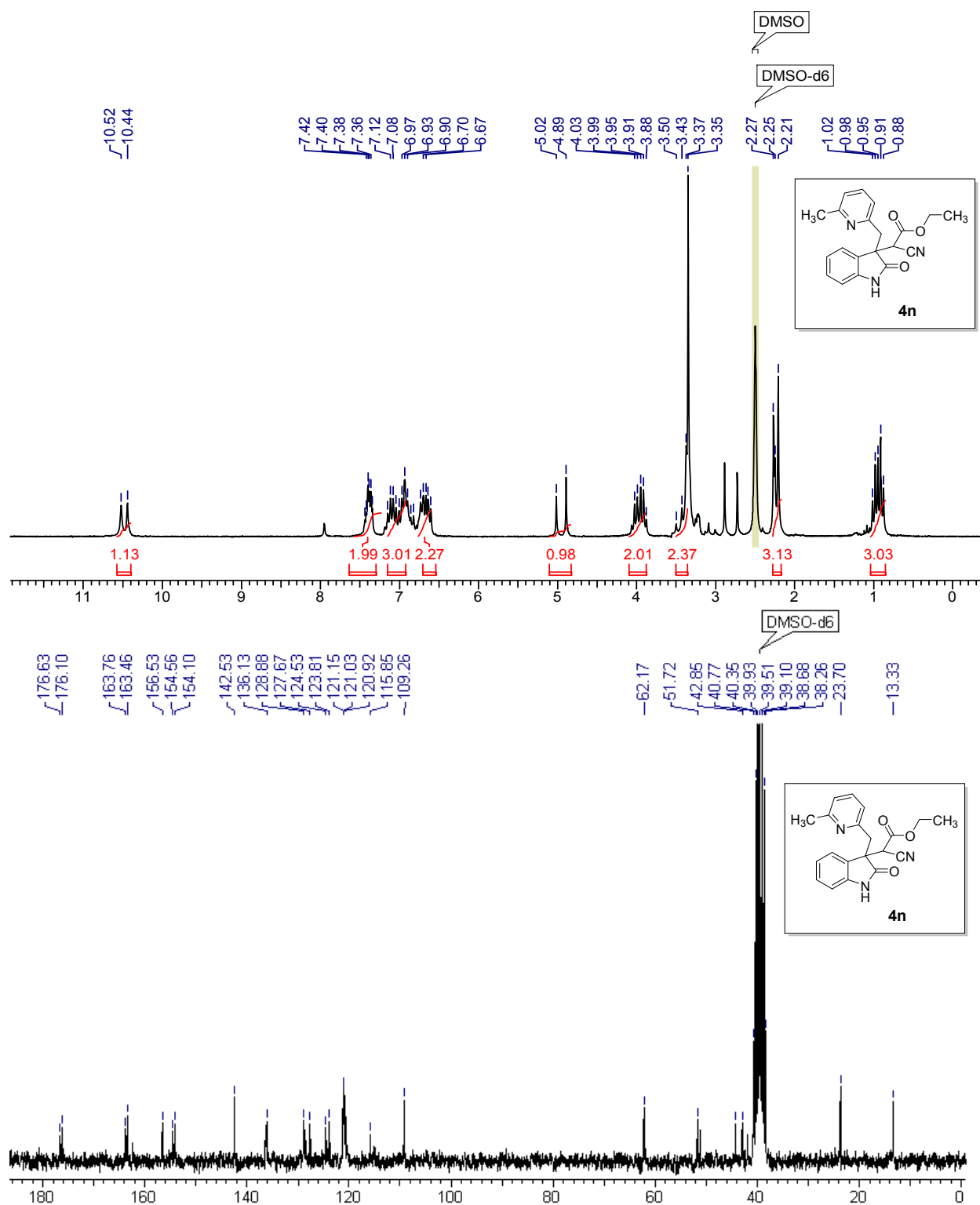


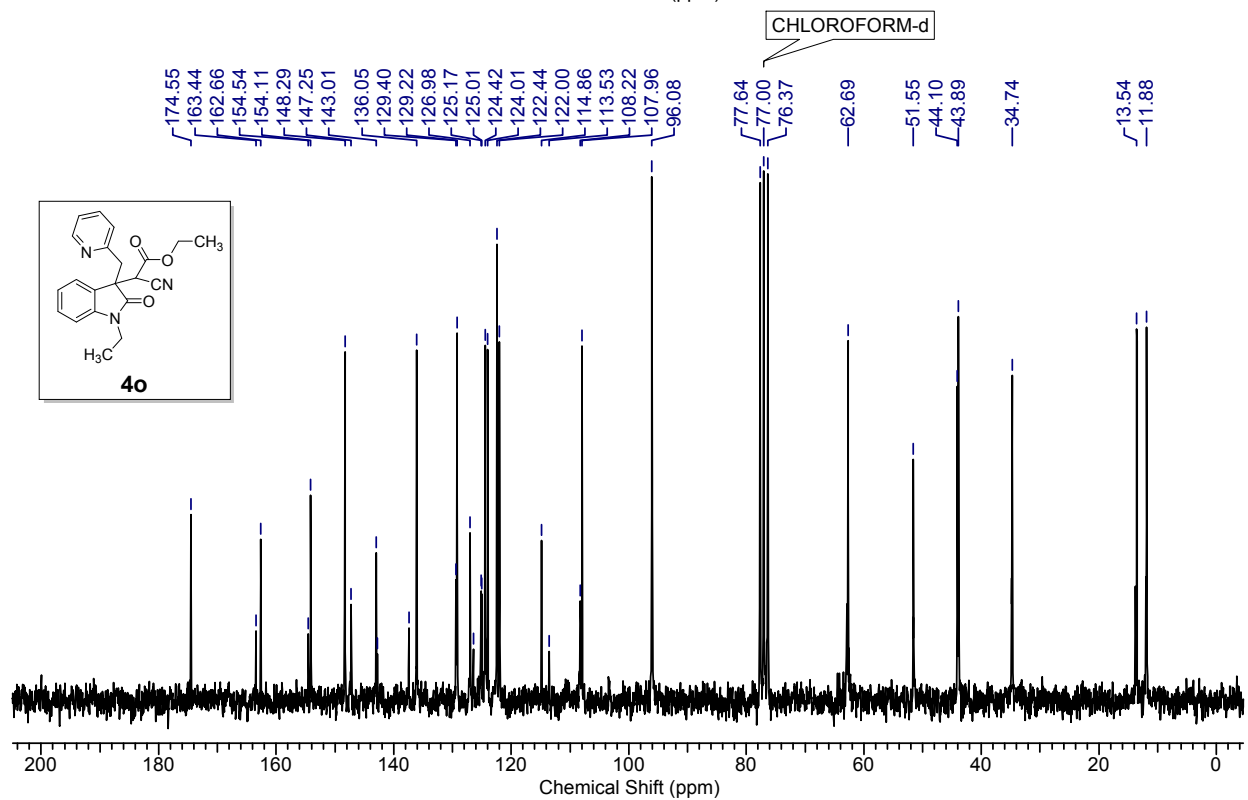
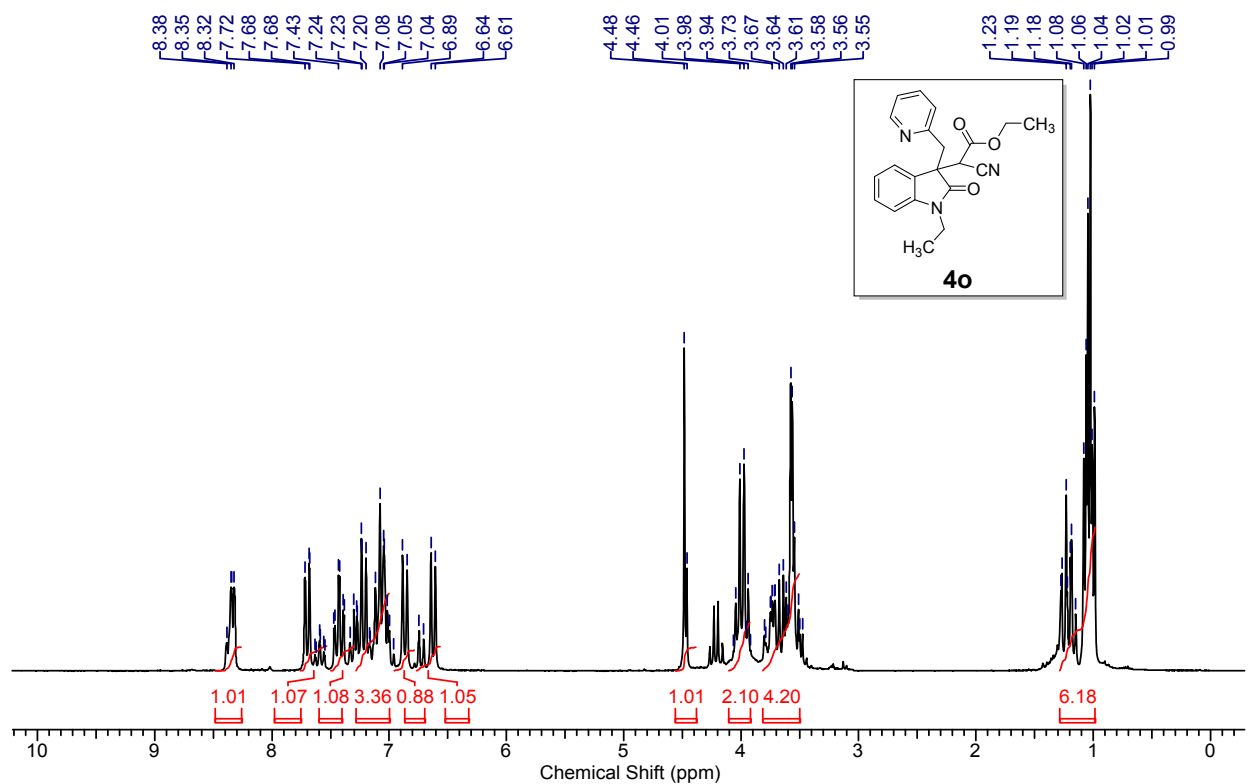


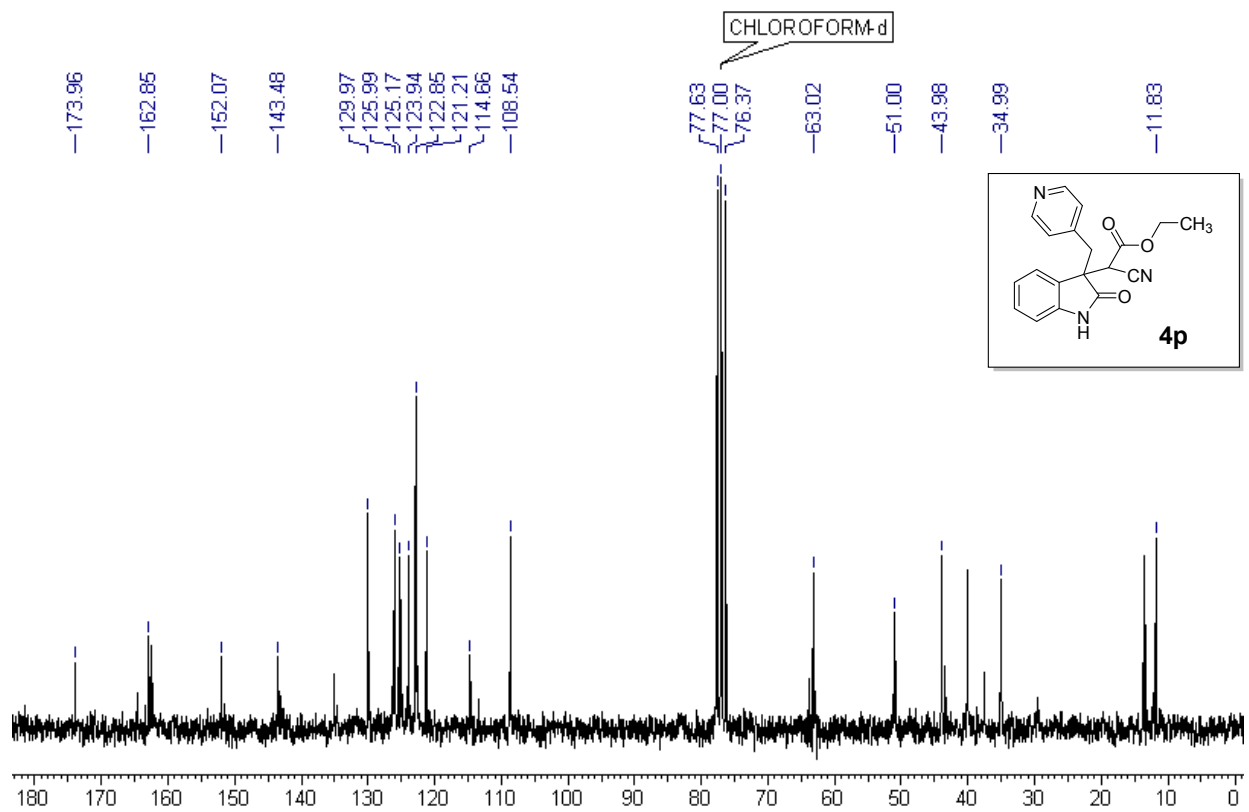
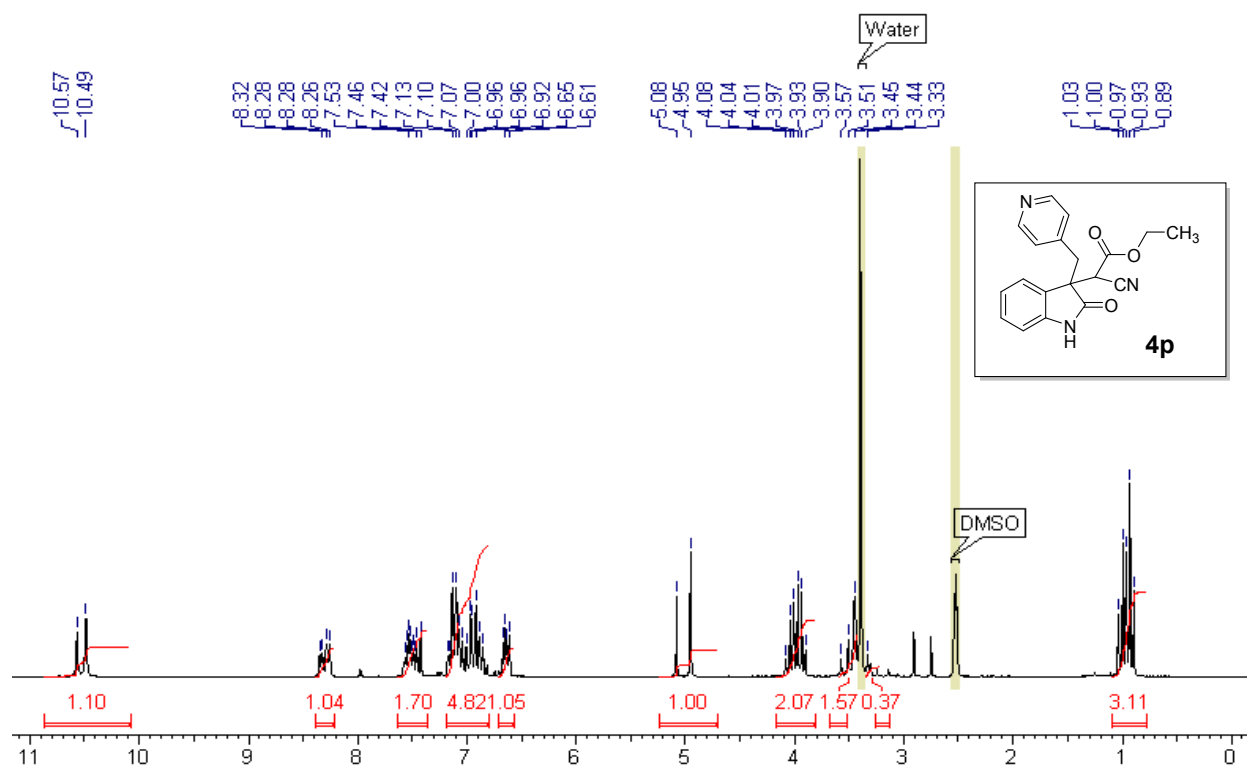


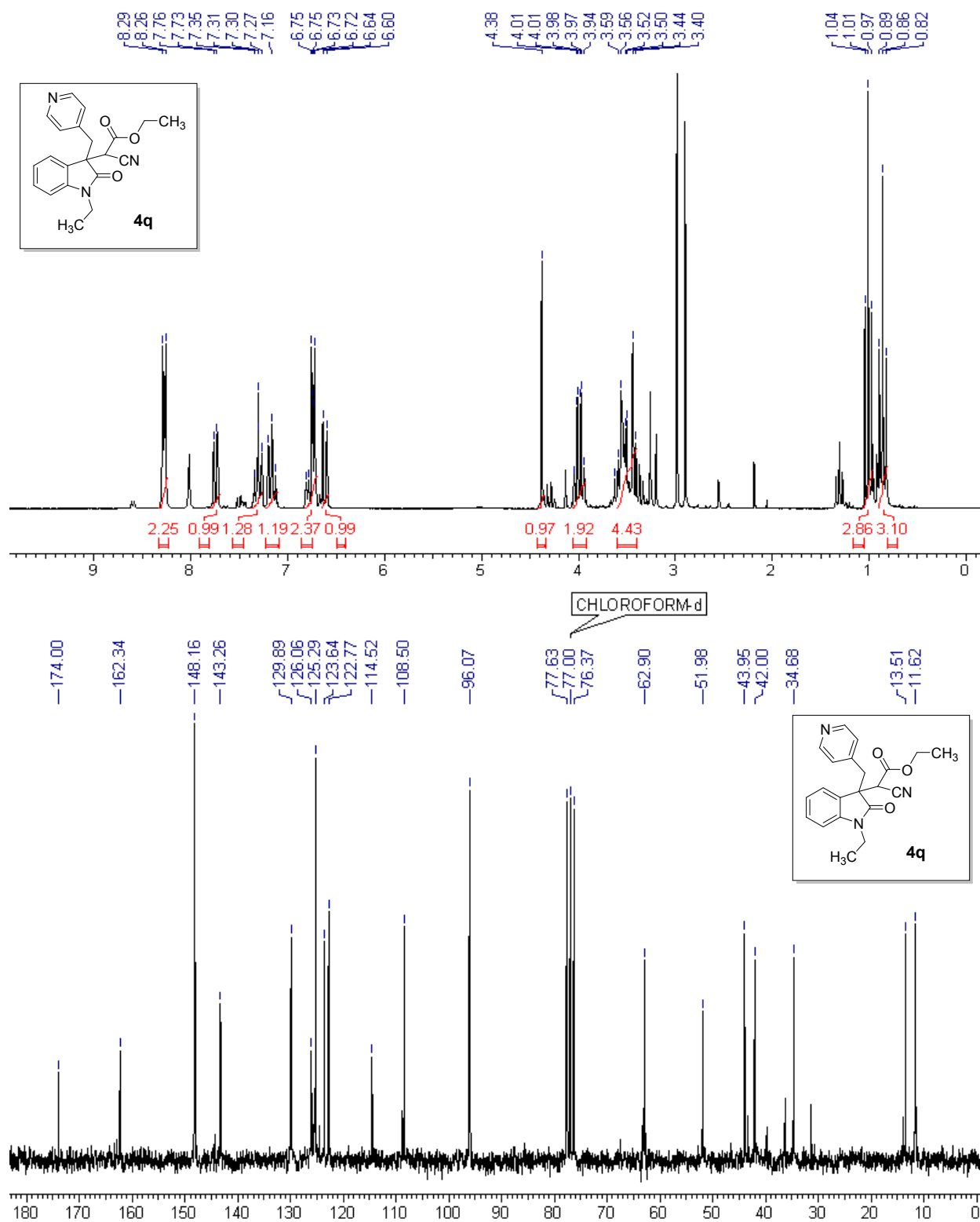


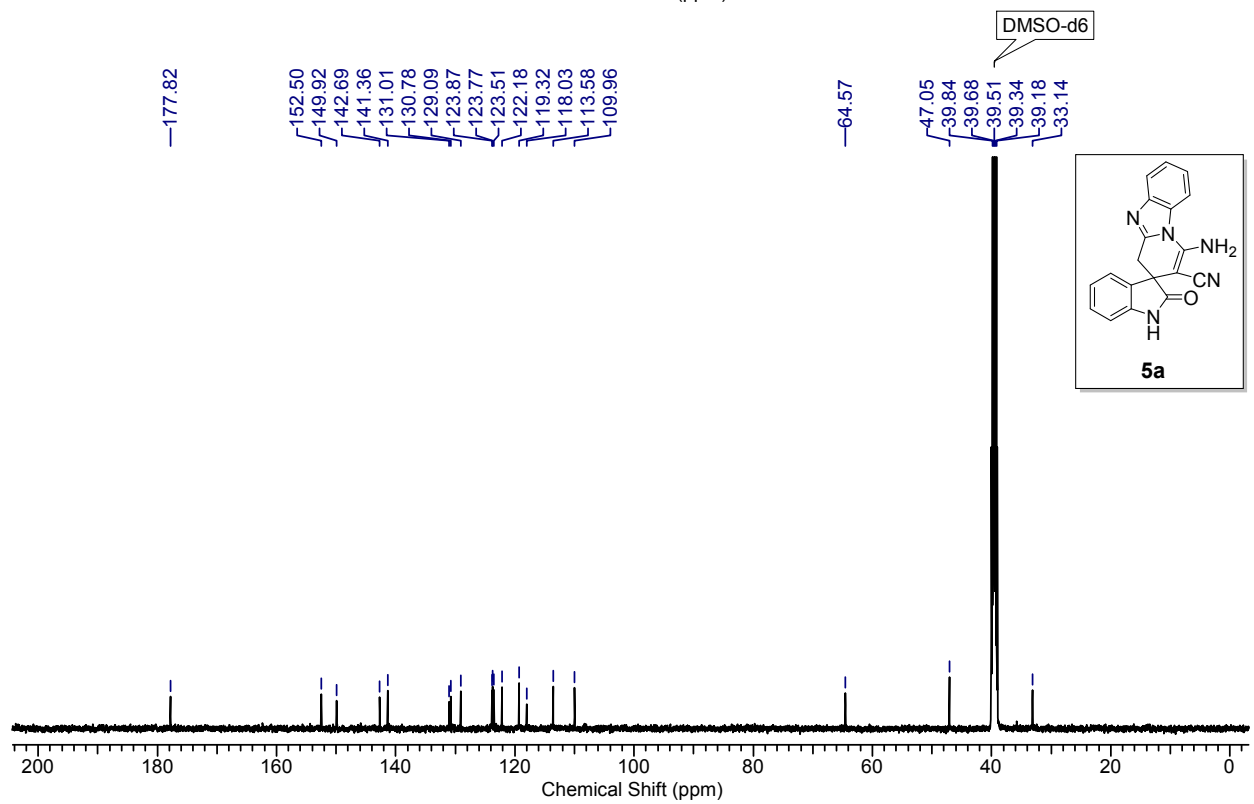
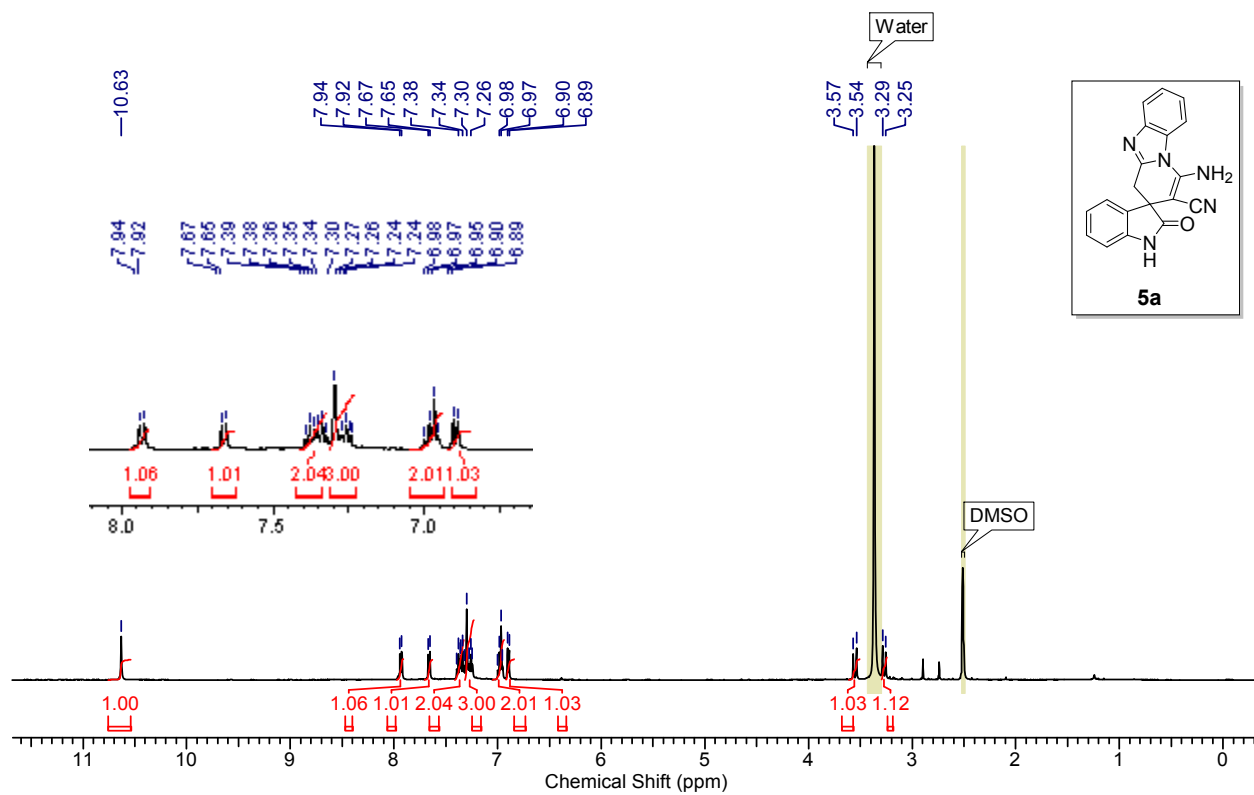


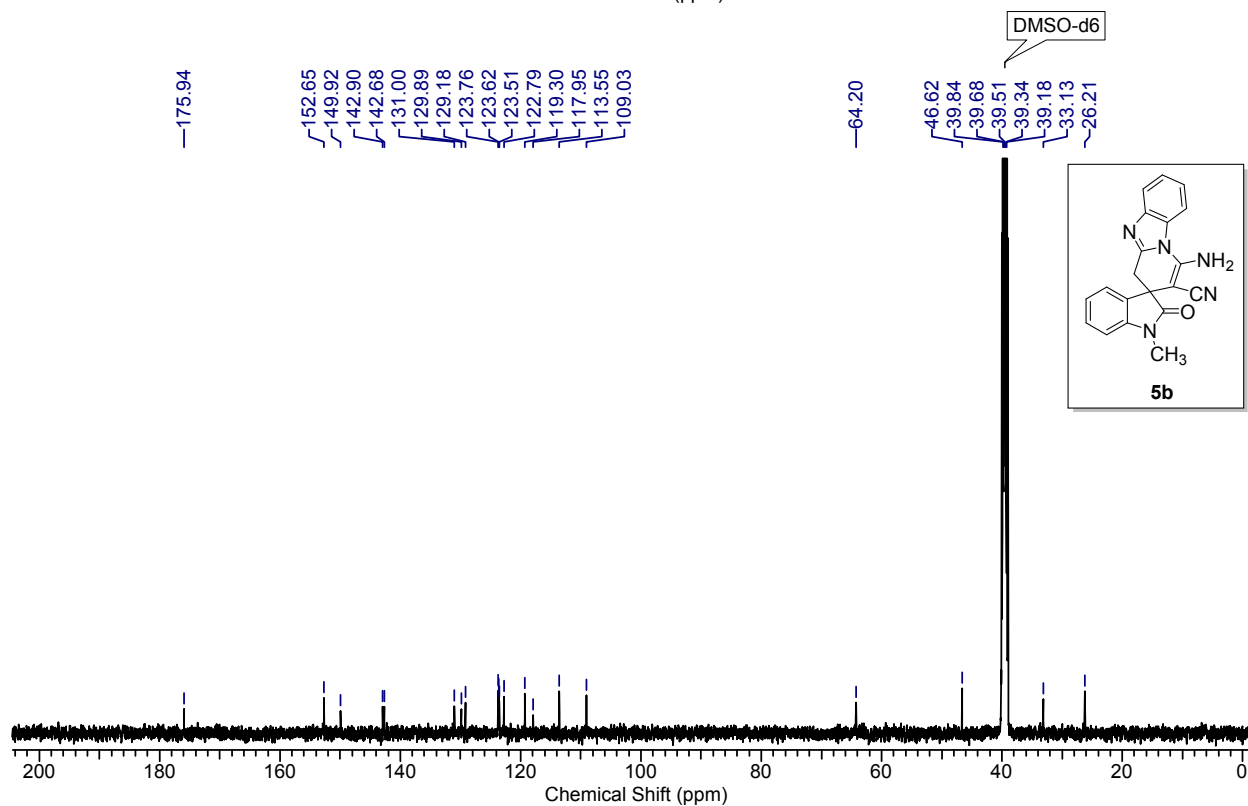
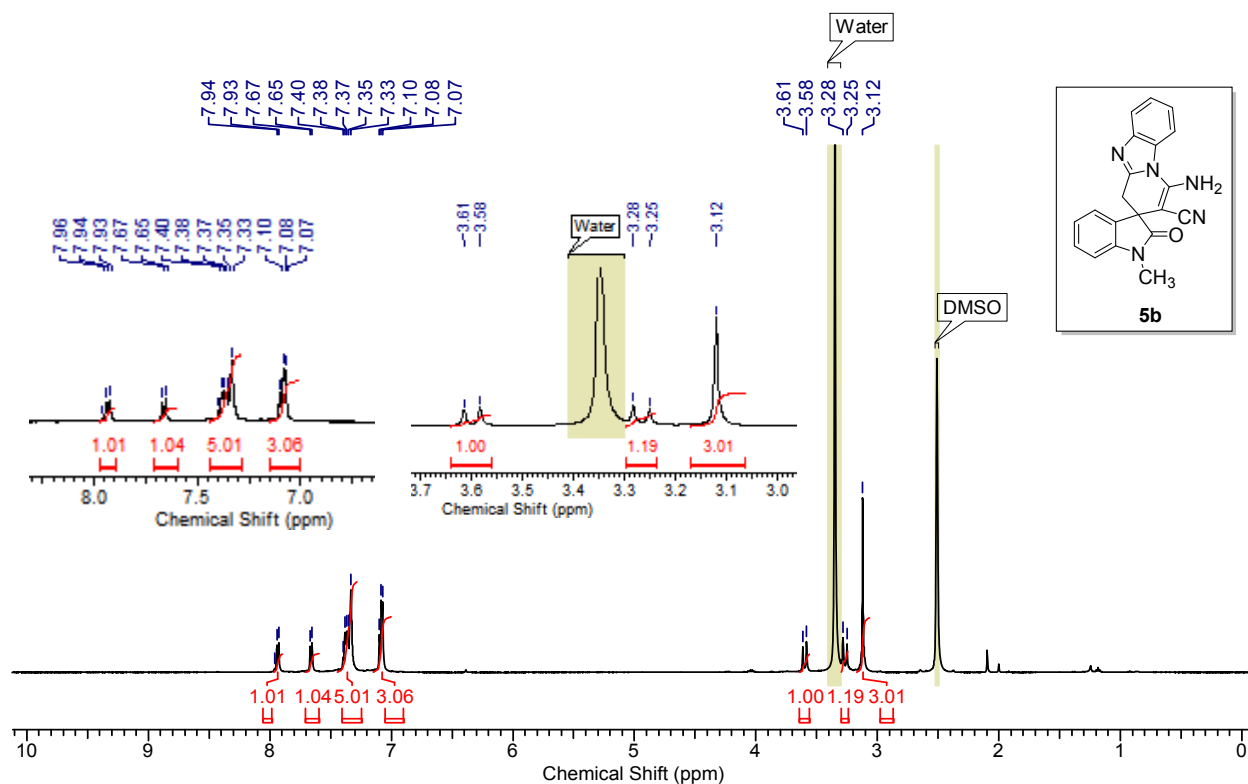




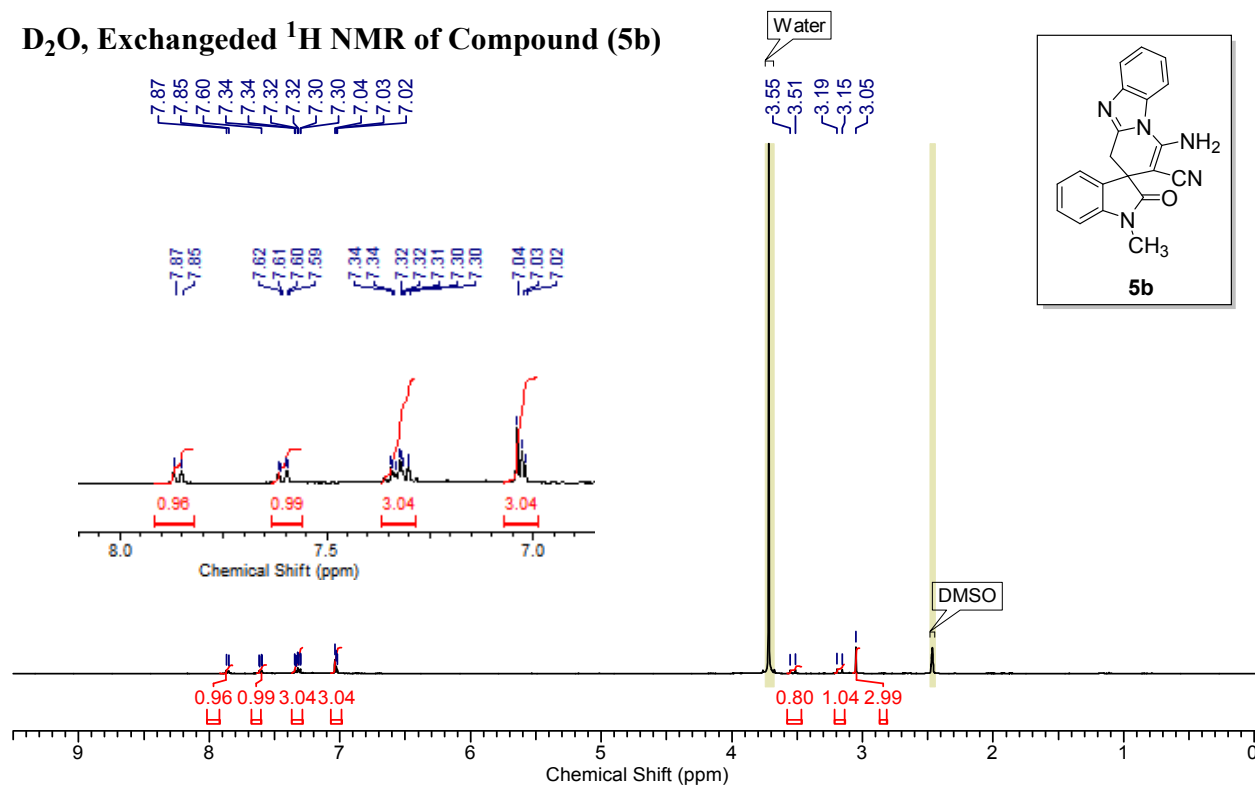




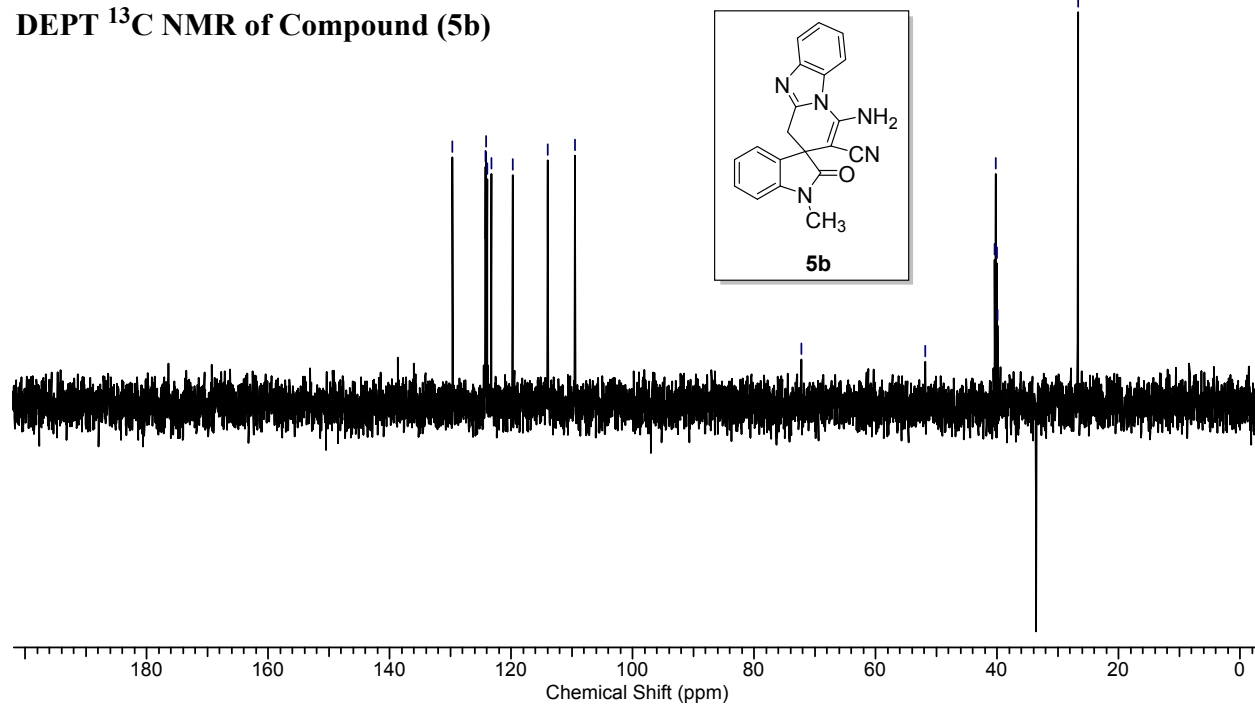


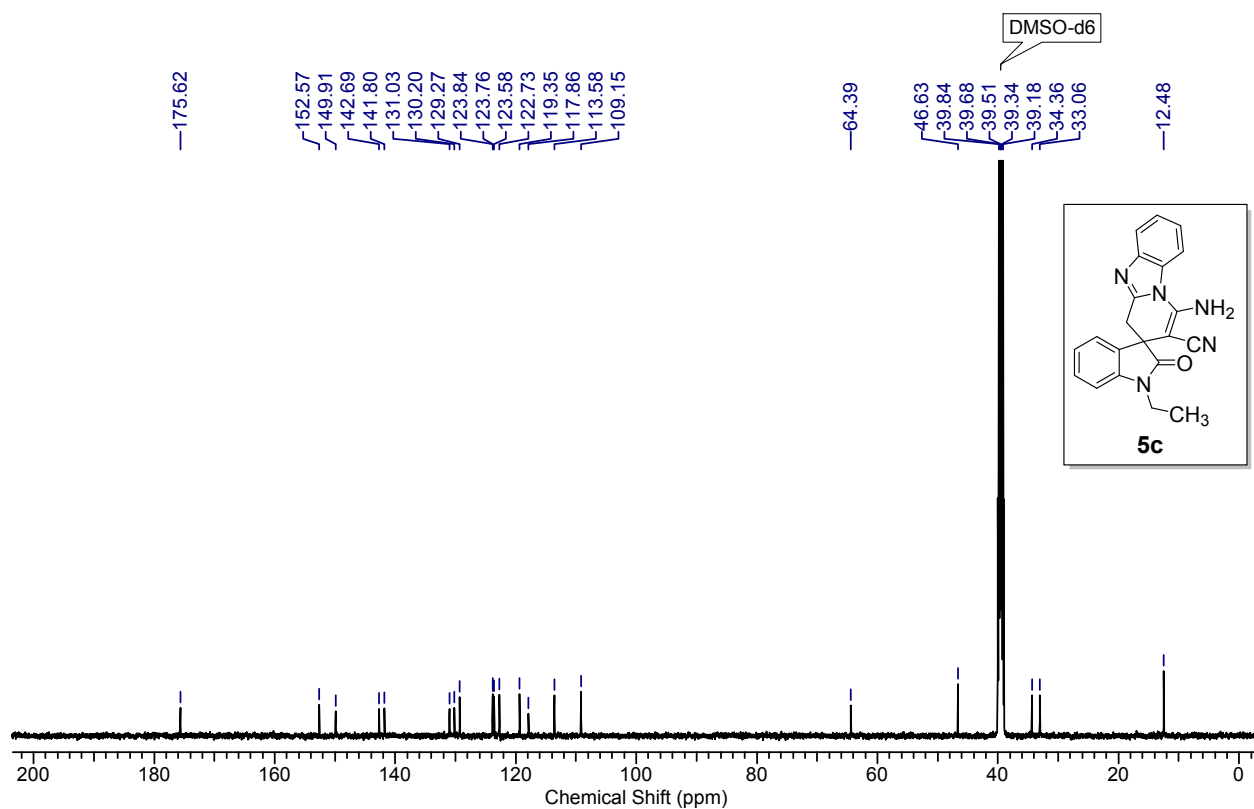
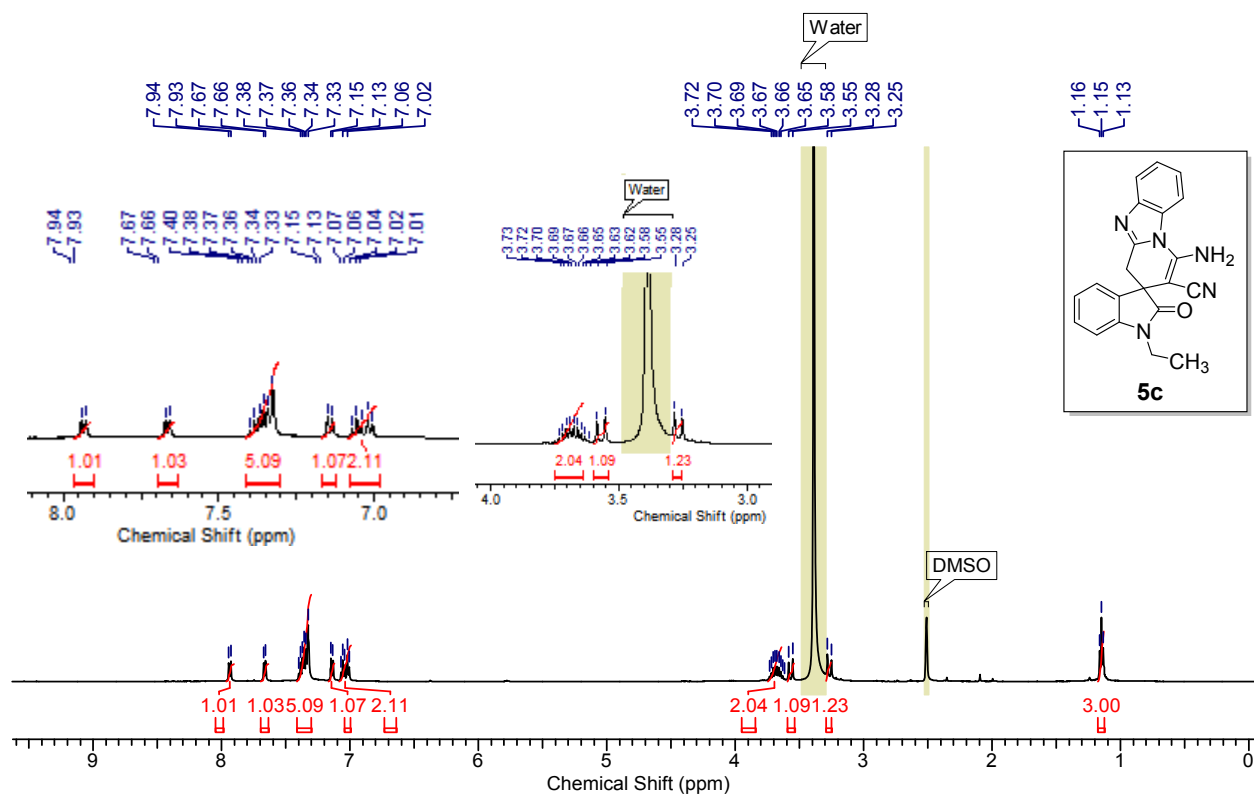


D₂O, Exchanged ¹H NMR of Compound (5b)

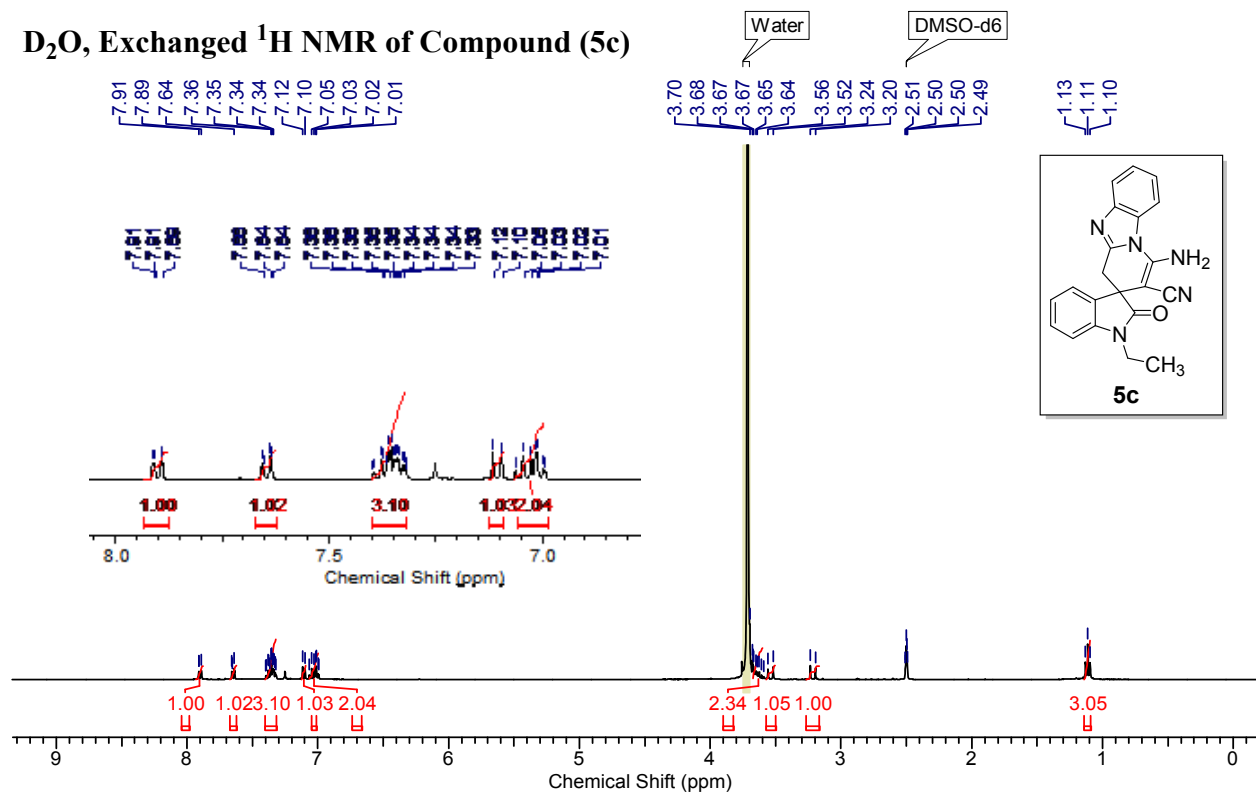


DEPT ¹³C NMR of Compound (5b)

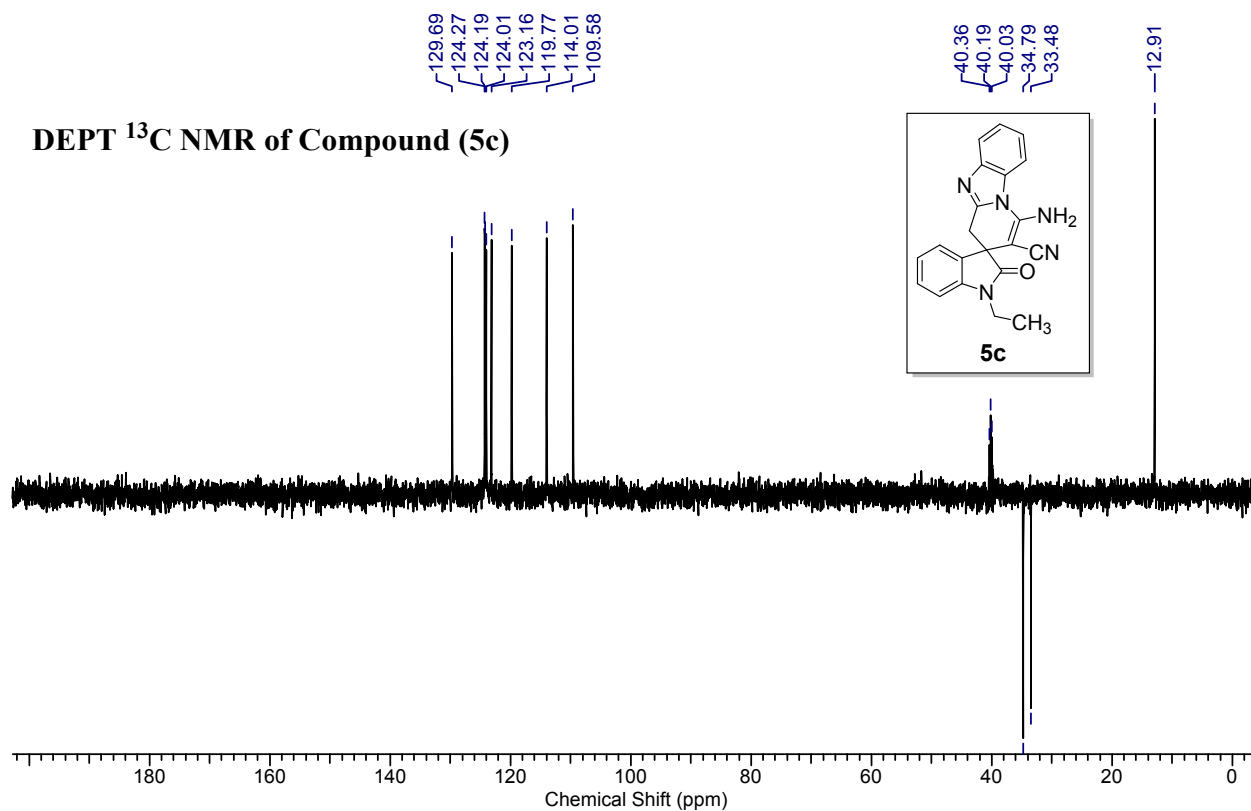


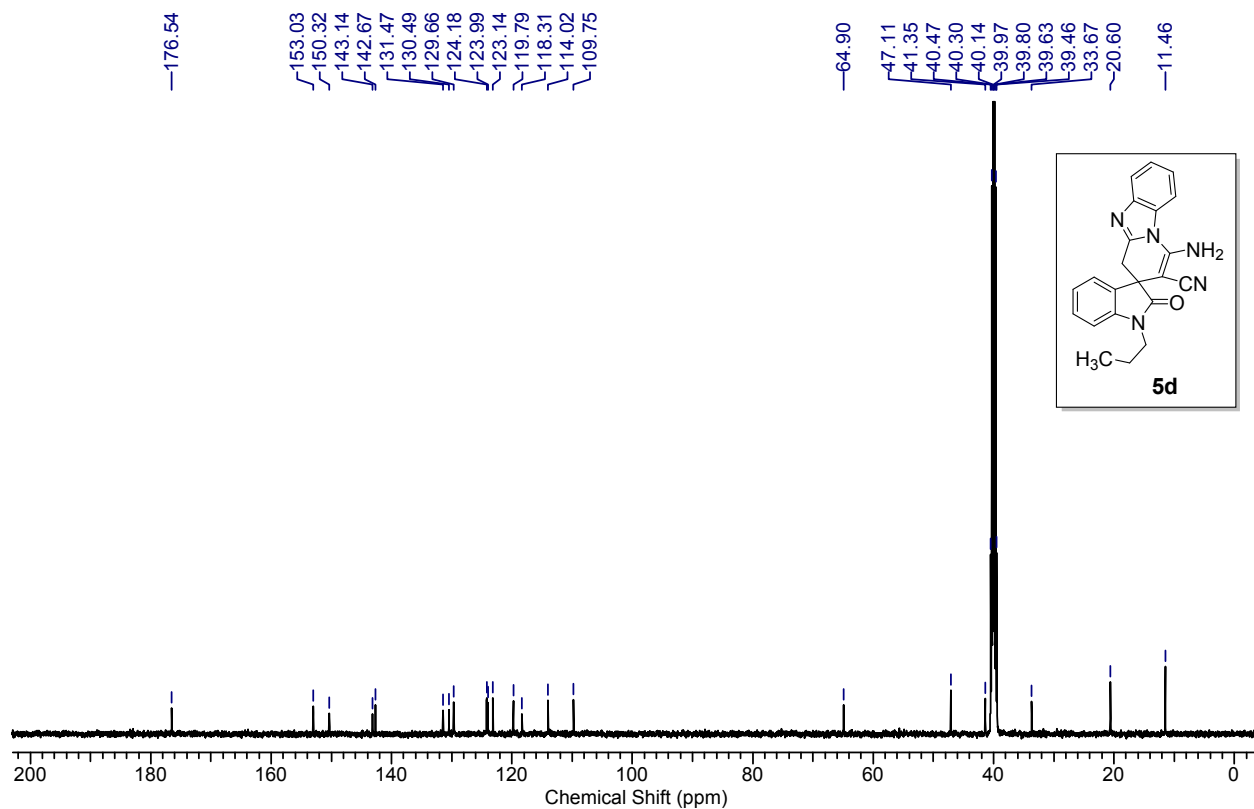
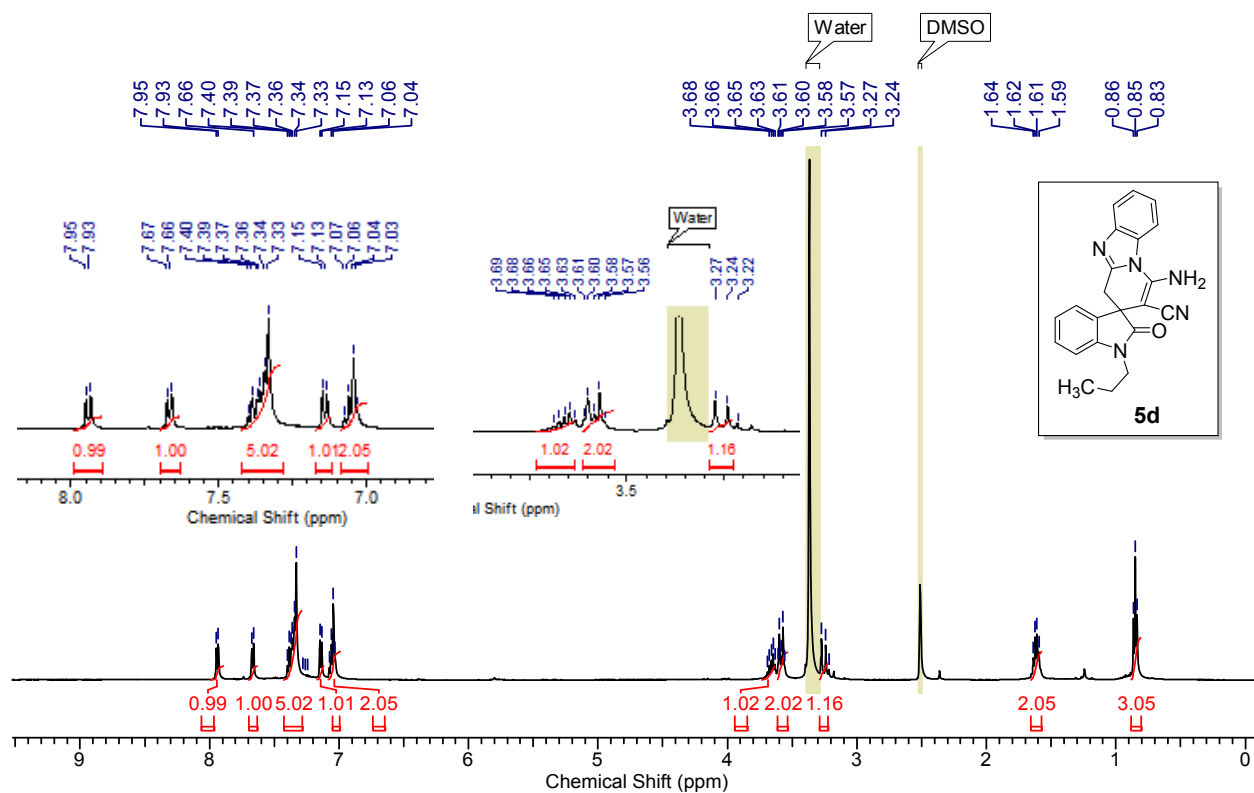


D₂O, Exchanged ¹H NMR of Compound (5c)

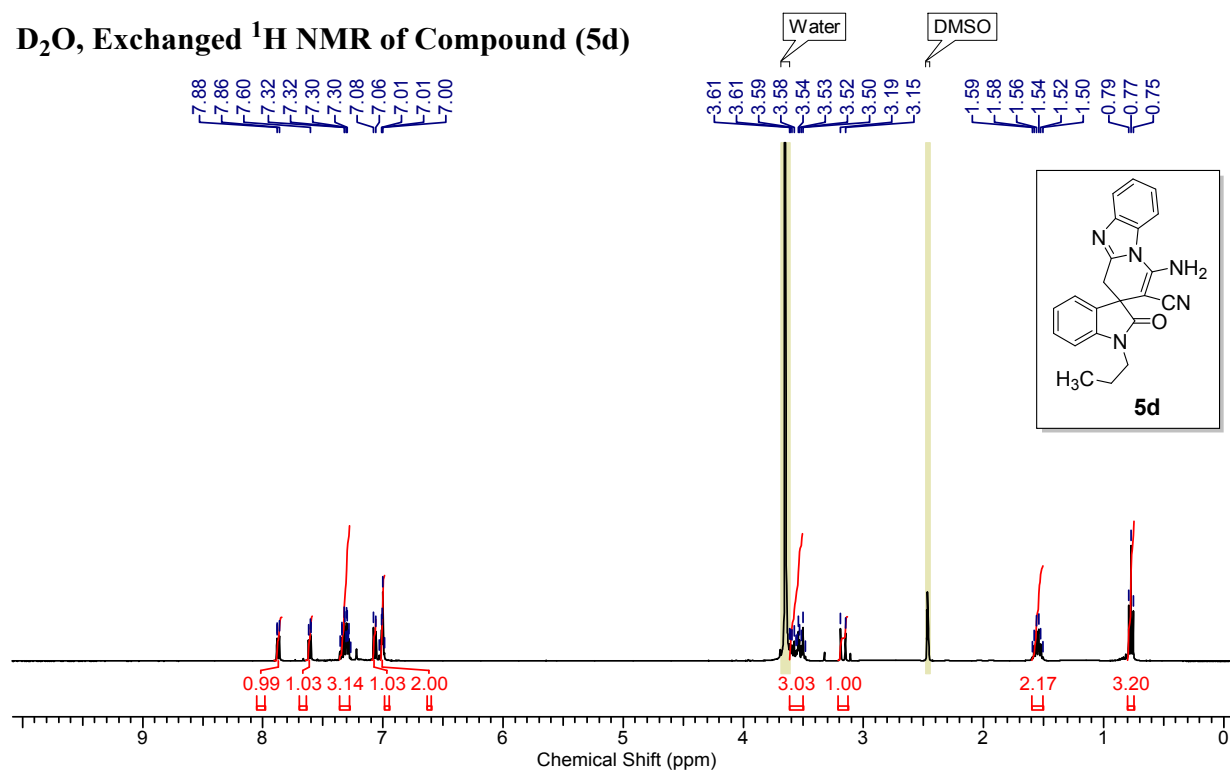


DEPT ¹³C NMR of Compound (5c)





D₂O, Exchanged ¹H NMR of Compound (5d)



DEPT ¹³C NMR of Compound (5d)

