Supporting Information

Sonochemistry in organocatalytic domino reaction: An expedient scalable multicomponent access to structurally functionalized 2-amino-3-cyano-dihydropyrano[3,2-*b*]pyrans, Spiro[indoline-3,4′-pyrano[3,2-*b*]pyrans], and Spiro-indenoquinoxaline-pyranopyrans at ambient conditions

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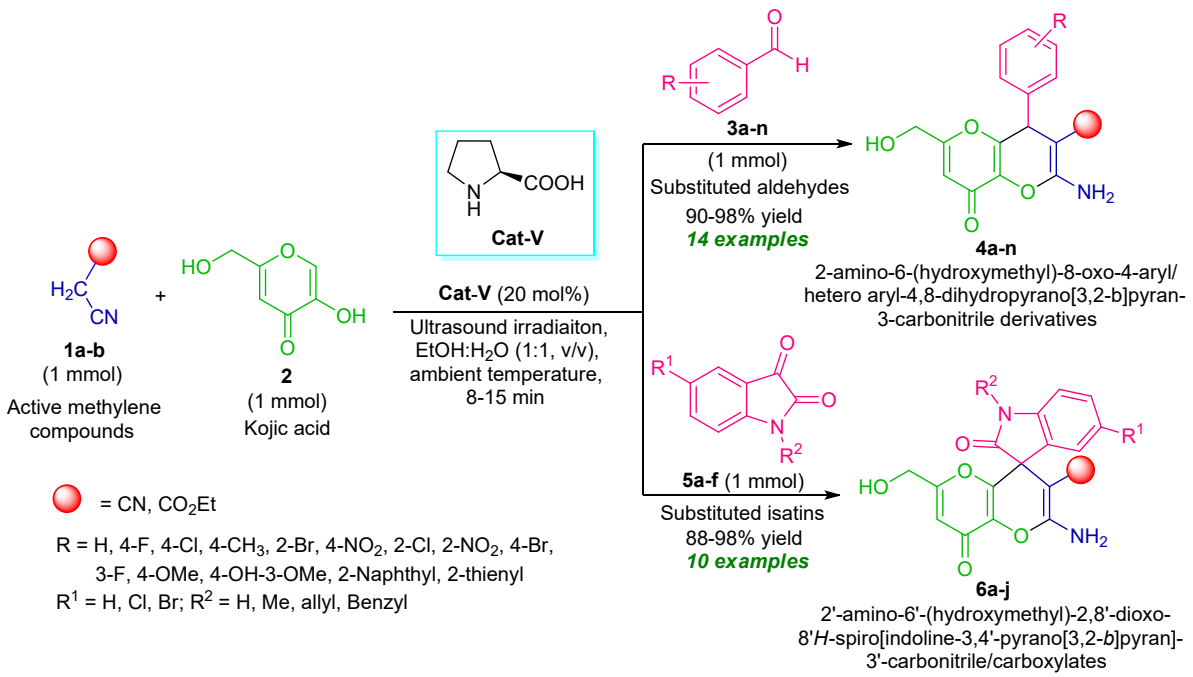
General Experimental Detail

All commercially available chemicals were used without further purification. Thin Layer Chromatography (TLC) was executed utilizing silica gel 60 F254 (Merck) plates. Proton nuclear magnetic resonance spectra (^{1}H NMR spectra) were obtained on Bruker 500 MHz FT-NMR spectrometers and 400 MHz FT-NMR in $CDCl_3$ and DMSO solvents. ^{13}C NMR spectra were recorded at 125 MHz and 100 MHz. Chemical shifts are reported in parts per million (ppm) relative to the TMS signal. Multiplicity is indicated as follows: s (singlet); bs (broad singlet); d (doublet); t (triplet); q (quartet); m (multiplet); dd (doublet of doublets), etc. Sonication was performed using an ultrasonic bath cleaner (model: SB-3200DT) with an operating frequency of 40 kHz and nominal power of 180 W. TOF and quadrupole mass analyzer types are used for the HRMS measurements The IR spectra were recorded using an FT-IR spectrometer (Shimadzu) in the range of 400–4000cm^{-1}.

1. General Procedure for the synthesis of amino-substituted dihydropyrano[3,2-*b*]pyran 4 and spiro[indoline-3,4′-pyrano[3,2-b]pyran] 6:

An oven-dried round bottom flask charged with a mixture of active methylene compounds 1 (1 mmol), kojic acid 2 (1 mmol), carbonyl compound such as aryl aldehydes **3**, or substituted isatin **5** and 20 mol% of L-proline (**Cat-V**) in aqueous ethanolic solution (1:1, v/v) was subjected to

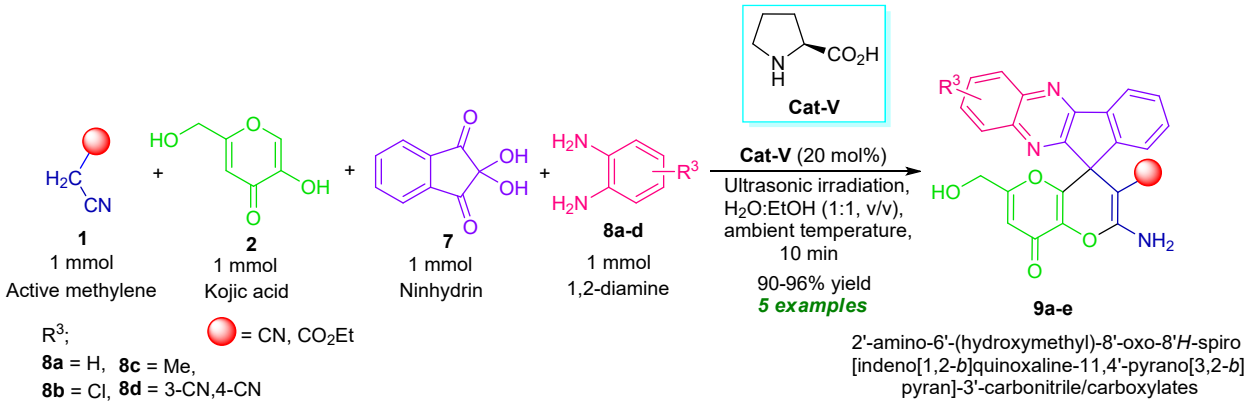


Scheme S1 Ultrasound-assisted domino one-pot three-component reaction of active methylene **1** and kojic acid **2**, with substituted aldehydes **3** or isatins **5** by using L-proline as organocatalyst

ultrasound irradiation (40 kHz, 180 W) at ambient temperature for the indicated time. The progress of the reaction was monitored by TLC (thin layer chromatography); however, the same can be inferred by visualizing the disappearance of the color of the starting material. After the complete consumption of starting material, as indicated by the TLC, the reaction mixture was filtered off by using filter paper and washed with dilute water, and the crude solid product was recrystallized from ethanol to give analytically pure products **4**, and **6** (**Scheme S1**).

2. General procedure for the synthesis of spiro[indeno[1,2-*b*]quinoxaline-11,4´-pyrano[3,2-*b*]pyran] 9:

A mixture of active methylene compound **1** (1 mmol), kojic acid **2** (1 mmol), ninhydrin **7** (1 mmol), 1,2-diamine **8** (1 mmol), and 20 mol% of L-proline (**Cat-V**) in presence of aqueous ethanol (1:1, v/v) was irradiated under ultrasound (40 kHz, 180 W) at ambient temperature for the required time. After the complete consumption of starting material as indicated by TLC, the residue was poured on ice water and the solid was filtered. The crude product was further washed with cold ethanol to afford analytically pure products **9** (**Scheme S2**).

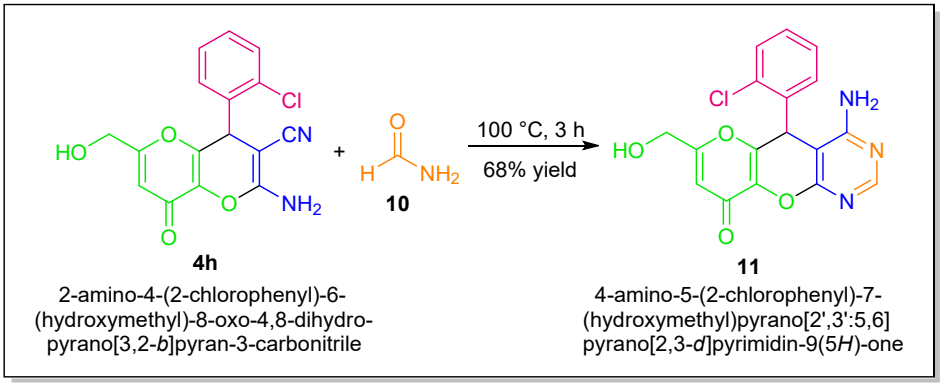


Scheme S2: Organocatalytic one-pot four-component reaction of active methylene **1**, kojic acid **2**, ninhydrin **7**, and 1,2-diamine **8** under ultrasonic irradiation in aqueous ethanol

3. General procedure for the synthesis of 4-amino-5-(2-chlorophenyl)-7-(hydroxymethyl)pyrano[2',3':5,6]pyrano[2,3-d]pyrimidin-9(5*H*)-one 11:

In a round bottom flask containing formamide **10** (0.02 mmol), the so-formed product **4h** was added, and the mixture was stirred at 100 °C for 3 hours. The reaction mixture was poured on ice

and cooled to ambient temperature. The formed solid mixture was then filtered off and washes with water and cooled methanol to afford the product **11** in 68% yields.



Scheme S3: Reaction of pyrano[3,2-*b*]pyran **4h** and formamide for the synthesis of 4-amino pyrimidine derivative **11**

4. Recyclability of the reaction medium for the synthesis of 6a and 9a

The catalyst could be recovered from the solid reaction mixture after separating the product by filtration and the filtrate containing the catalyst and water was directly reused for further reaction. After four consecutive cycles, we observed that there was no considerable change in yields of the products which demonstrated the effectiveness and efficiency of the catalyst for the present work.

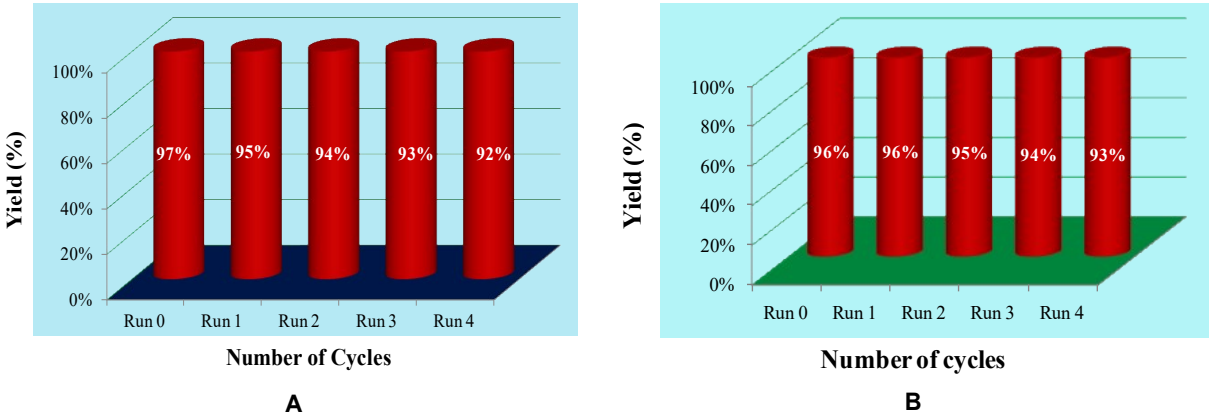
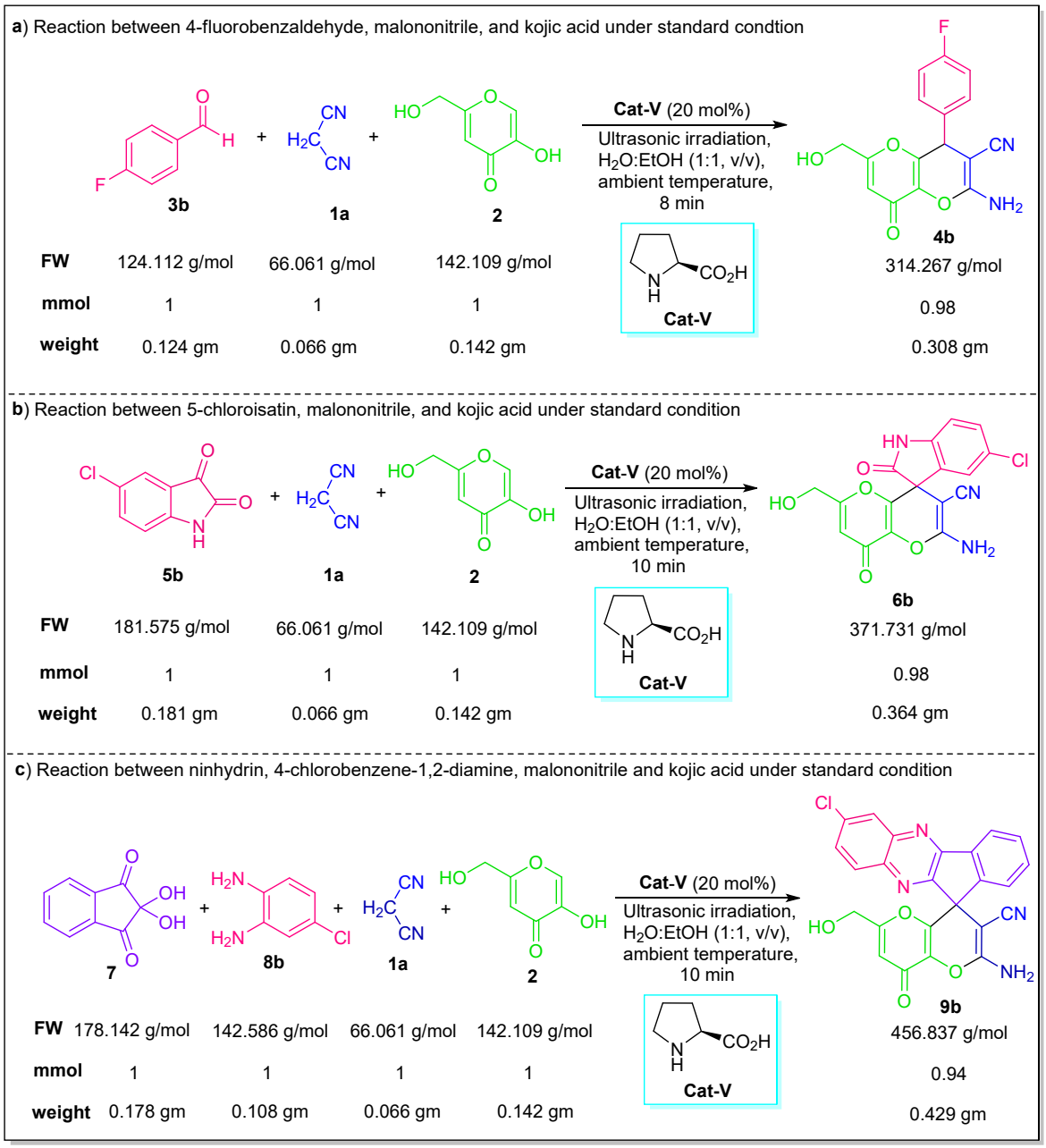


Figure S1: Recyclability experiment for the synthesis of (**A**) 2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile (**6a**), and (**B**) 2′-amino-6′-(hydroxymethyl)-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile (**9a**).

5. Green Chemistry Metrics calculation

Several green chemistry metrics such as Atom Economy (AE), atom efficiency, E-factor, Reaction Mass Efficiency (RME), Process Mass Intensity (PMI), Carbon Efficiency (CE) are calculated for the present study (**Table S1**). The schematic representation of the obtained value for the synthesis of compounds **4b** (**Scheme S4a**), **6b** (**Scheme S4b**), and **9b** (**Scheme S4c**) to calculate the green chemistry metrics are presented below-



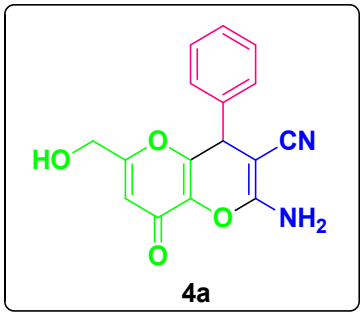
Scheme S4: Materials used in the synthetic purpose and the obtained value of their representative products

Table S1: Green chemistry metrics value for compounds **4b**, **6b**, and **9b**

Sl No	Green Metrics	Compound 4b	Compound 6b	Compound 9b
1	**Atom economy (AE) (%)** = Mol. Wt. of product ÷ Σ (MW of stoichiometric reactants) × 100%	314.267 g/mol ÷ (124.112 g/mol + 66.061 g/mol + 142.109 g/mol) × 100% = 94.57%	371.731 g/mol ÷ (181.575 g/mol + 66.061 g/mol + 142.109 g/mol) × 100% = 95.38%	456.837 g/mol ÷ (178.126 g/mol + 142.586 g/mol + 66.061 g/mol + 142.109 g/mol) × 100% = 86.38%
2	**Atom efficiency (%)** = (Yield × AE)/100	(98% × 94.57%)/ 100 = 92.68%	(98% × 95.38%)/ 100 = 93.47%	(94% × 86.38%)/100 = 81.19%
3	**E-factor** = [mass of waste]/mass of product Mass of waste = total mass of raw materials - Total mass of product	[(0.124 + 0.066 + 0.142) – 0.308]/0.308 = 0.07	[(0.181 + 0.066 + 0.142)] – 0.364/0.364 = 0.06	[(0.178 + 0.142 + 0.066 + 0.142) – 0.429]/ 0.429 = 0.23
4	**Reaction mass efficiency (RME) (%)** = mass of product / Σ (mass of stoichiometric reactants) × 100%	0.308 ÷ (0.124 + 0.066 + 0.142) × 100% = 92.77%	0.364 ÷ (0.181 + 0.066 + 0.142) × 100% = 93.58%	0.429 ÷ (0.178 + 0.142 + 0.066 + 0.142) × 100% = 81.25%
5	**Process mass intensity (PMI)** = Σ (mass of stoichiometric reactants + solvent) / mass of product	[0.124 + 0.066 + 0.142 + 0.018 + 0.046] ÷ 0.308 = 1.28	[0.181 + 0.066 + 0.142 + 0.018 + 0.046] ÷ 0.364 = 1.24	[0.160 + 0.142 + 0.066 + 0.142 + 0.018 + 0.046] ÷ 0.429 = 1.37
6	**Carbon efficiency (CE) (%)** (Amount of carbon in product/Total carbon present in reactant) × 100%	[0.98 × 16/ (1 × 7 + 1 × 3 + 1 × 6)] × 100% = 98%	[0.98 × 17/ (1 × 8 + 1 × 3 + 1 × 6)] × 100% = 98%	[0.94 × 24/ (1 × 9 + 1 × 6 + 1 × 3 + 1 × 6)] × 100% = 94%

6. Characterization data for the product (4a-4n), (6a-6j), (9a-9e), and 11:

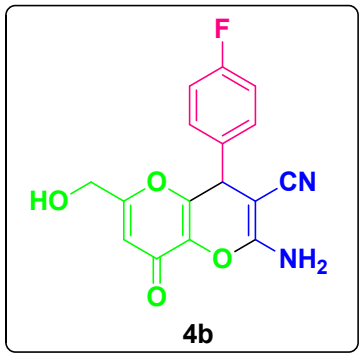
2-amino-6(hydroxymethyl)-8-oxo-4-phenyl-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4a:



4a

95% yield, white solid. R_f = 0.45 (40% EtOAc/Hexane); M.P. 221-224 °C. IR (KBr) υ_{max} (cm^{-1}): 3361, 3351, 3340, 3280, 3064, 2218, 1646, 985. ^1H NMR (500 MHz, $CDCl_3$+ DMSO-d_6) δ 7.38 (t, *J* = 7.1 Hz, 2H), 7.30 (t, *J* = 9.9 Hz, 3H), 7.10 (s, 2H), 6.34 (s, 1H), 5.64 (t, *J* = 5.9 Hz, 1H), 4.69 (s, 1H), 4.25 (dd, *J* = 15.9, 5.8 Hz, 1H), 4.15 (dd, *J* = 15.8, 5.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 169.83, 168.15, 159.41, 148.61, 140.19, 136.29, 128.62, 127.68, 127.50, 119.07, 111.12, 59.19, 55.56, 40.62. HRMS (ESI^+): m/z calculated for [$C_{16}H_{12}N_2O_4$ + H^+]: 297.0875; found 297.0888

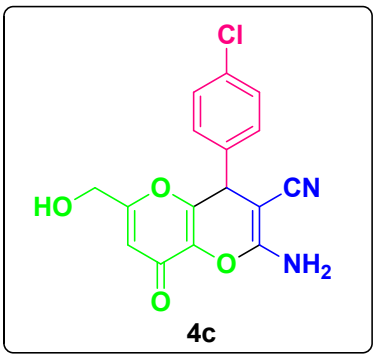
2-amino-4-(-fluorophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4b:



4b

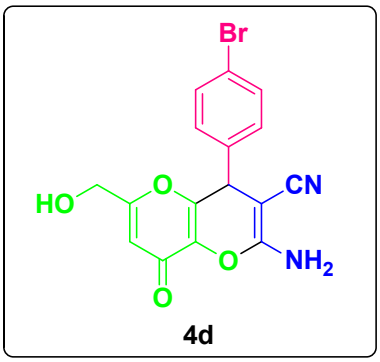
98% yield, white solid. R_f = 0.4 (40% EtOAc/Hexane); M.P. 247-249 °C. IR (KBr) υ_{max} (cm^{-1}): 3330, 3253, 3204, 2286, 1654, 980. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 7.55 (s, 1H), 7.38 – 7.22 (m, 2H), 7.07 (t, *J* = 8.3 Hz, 2H), 6.43 (d, *J* = 27.0 Hz, 2H), 5.52 (t, *J* = 6.0 Hz, 1H), 4.67 (s, 1H), 4.32 (dd, *J* = 15.7, 6.0 Hz, 1H), 4.23 (dd, *J* = 16.0, 5.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$+ DMSO-d_6) δ 169.95, 168.20, 162.78, 160.83, 159.40, 148.30, 136.20, 135.92, 129.38, 118.93, 115.51, 115.34, 111.12, 59.23, 55.52, 40.02. HRMS (ESI^+): m/z calculated for [$C_{16}H_{11}FN_2O_4$ + H^+]: 315.0781; found 315.0786

2-amino-4-(4-chlorophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4c:



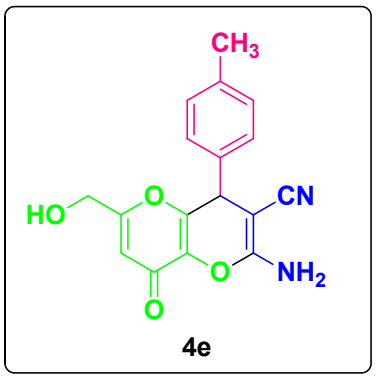
97% yield, white solid. R_f = 0.4 (40% EtOAc/Hexane); M.P. 199-202 °C. IR (KBr) υ_{max} (cm^{-1}): 3357, 3290, 3152, 2215, 1676, 1590, 876. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 7.37 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 6.96 (s, 2H), 6.38 (s, 1H), 5.64 (s, 1H), 4.70 (s, 1H), 4.28 (d, J = 18.3 Hz, 1H), 4.18 (d, J = 15.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 170.39, 170.06, 168.45, 159.52, 148.21, 138.85, 136.37, 133.18, 129.31, 128.77, 119.02, 111.22, 59.84, 59.29, 55.25, 13.98. HRMS (ESI^+): m/z calculated for [$C_{16}H_{11}ClN_2O_4$ + H^+]: 331.0486; found 331.0468

2-amino-4-(4-bromophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4d:



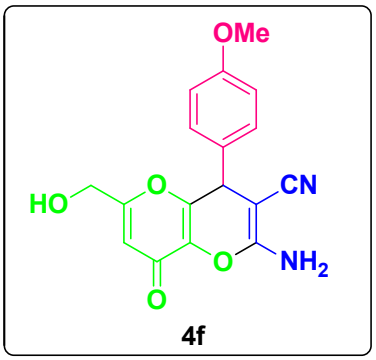
96% yield, white solid. R_f = 0.4 (40% EtOAc/Hexane); M.P. 223-225 °C. IR (KBr) υ_{max} (cm^{-1}): 3365, 3280, 3145, 2220, 1652, 802. ^1H NMR (500 MHz, DMSO-d_6) δ 7.60 (d, J = 1.8 Hz, 1H), 7.59 (s, 1H), 7.31 (s, 2H), 7.28 (s, 1H), 7.26 (s, 1H), 6.33 (s, 1H), 5.70 (t, J = 6.1 Hz, 1H), 4.85 (s, 1H), 4.20 (dd, J = 15.8, 5.7 Hz, 1H), 4.13 (dd, J = 15.7, 5.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 169.80, 168.32, 159.47, 148.17, 139.73, 136.41, 131.75, 129.83, 121.37, 119.09, 111.28, 59.21, 55.02, 48.87. HRMS (ESI^+): m/z calculated for [$C_{16}H_{11}BrN_2O_4$ + H^+]: 374.9980; found 374.9969

2-amino-6-(hydroxymethyl)-8-oxo-4-(*p*-tolyl)-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4e:



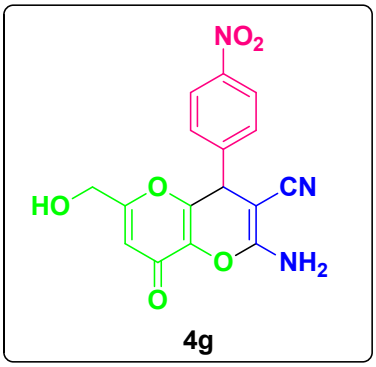
90% yield, creamy solid. R_f = 0.45 (40% EtOAc/Hexane); M.P. 204-206 °C. IR (KBr) υ_{max} (cm^{-1}): 3350, 3260, 3125, 2232, 1620, 870. ^1H NMR (500 MHz, DMSO-d_6) δ 7.22 (s, 2H), 7.18 (dd, *J* = 18.1, 8.1 Hz, 4H), 6.32 (s, 1H), 5.69 (t, *J* = 6.1 Hz, 1H), 4.74 (s, 1H), 4.20 (dd, *J* = 16.5, 6.2 Hz, 1H), 4.12 (dd, *J* = 16.1, 5.7 Hz, 1H), 2.29 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 169.76, 168.10, 159.31, 148.78, 137.34, 137.09, 136.15, 129.23, 127.39, 119.12, 111.03, 59.13, 55.56, 20.67. HRMS (ESI^+): m/z calculated for [$C_{17}H_{14}N_2O_4$ + H^+]: 311.1032; found 311.1022

2-amino-6-(hydroxymethyl)-4-(4-methoxyphenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4f:



92% yield, white solid. R_f = 0.45 (40% EtOAc/Hexane); M.P. 220-222 °C. IR (KBr) υ_{max} (cm^{-1}): 3420, 3360, 3280, 3191, 2962, 2230, 1649, 1632. ^1H NMR (500 MHz, $CDCl_3$+ DMSO-d_6) δ 7.21 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.58 (d, *J* = 13.6 Hz, 2H), 6.41 (s, 1H), 5.58 (t, *J* = 6.0 Hz, 1H), 4.61 (s, 1H), 4.30 (dd, *J* = 16.0, 6.1 Hz, 1H), 4.21 (dd, *J* = 16.0, 6.1 Hz, 1H), 3.79 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$+ DMSO-d_6) δ 170.19, 168.17, 159.21, 158.87, 148.87, 136.07, 131.75, 128.56, 118.96, 114.66, 113.86, 111.07, 59.33, 56.42, 55.45, 54.85. HRMS (ESI^+): m/z calculated for [$C_{17}H_{14}N_2O_5$ + H^+]: 327.0981; found 327.0997

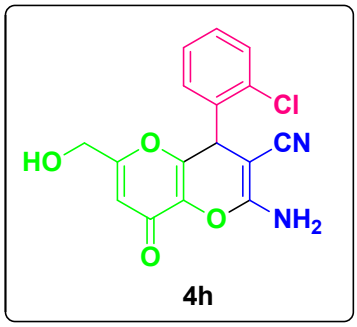
2-amino-6-(hydroxymethyl)-4-(4-nitrophenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4g:



4g

94% yield, light pink solid. R_f = 0.4 (40% EtOAc/Hexane); M.P. 230-232 °C. IR (KBr) υ_{max} (cm^{-1}): 3538, 3454, 3329, 3176, 2194, 1670, 1649, 1520, 1352. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 8.25 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 2H), 6.99 (s, 2H), 6.42 (s, 1H), 5.63 (d, *J* = 5.7 Hz, 1H), 4.88 (s, 1H), 4.29 (dd, *J* = 16.1, 5.4 Hz, 1H), 4.19 (dd, *J* = 16.2, 5.4 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.68, 168.48, 159.46, 148.09, 147.84, 147.24, 136.79, 129.42, 124.33, 119.13, 111.58, 59.14, 54.74, 30.79. HRMS (ESI^+): m/z calculated for [$C_{16}H_{11}N_3O_6$ + H^+]: 342.0726; found 342.0714

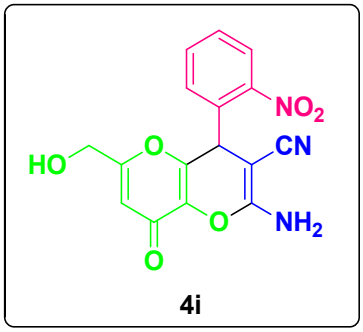
2-amino-4-(2-chlorophenyl)-6(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4h:



4h

96% yield, white solid. R_f = 0.42 (40% EtOAc/Hexane); M.P. 211-213 °C. IR (KBr) υ_{max} (cm^{-1}): 3386, 3351, 3274, 3145, 2217, 1613, 925. ^1H NMR (500 MHz, $CDCl_3$+ DMSO-d_6) δ 7.71 (d, *J* = 5.6 Hz, 1H), 7.45 – 7.27 (m, 4H), 6.66 (s, 2H), 6.44 (s, 1H), 5.56 (t, *J* = 5.6 Hz, 1H), 5.27 (s, 1H), 4.30 (dd, *J* = 16.1, 6.0 Hz, 1H), 4.19 (dd, *J* = 16.2, 6.0 Hz, 1H).^{13}C NMR (126 MHz, $CDCl_3$+ DMSO-d_6) δ 169.69, 168.22, 159.61, 147.74, 137.18, 136.75, 132.80, 130.04, 129.61, 129.12, 127.48, 118.66, 111.11, 59.10, 54.68, 37.67. HRMS (ESI^+): m/z calculated for [$C_{16}H_{11}ClN_2O_4$ + H^+]: 331.0486; found 331.0458

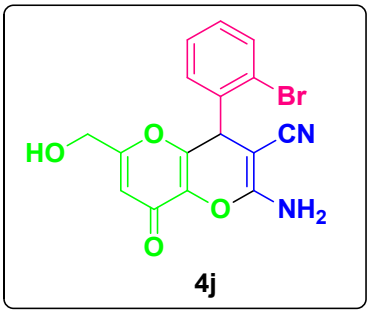
2-amino-6-(hydroxymethyl)-4-(2-nitrophenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4i:



4i

94% yield, white solid. R_f = 0.42 (40% EtOAc/Hexane); M.P. 224-226 °C. IR (KBr) υ_{max} (cm^{-1}): 3380, 3318, 3212, 3140, 2192, 1676, 1529, 1354. ^1H NMR (500 MHz, $CDCl_3$+ DMSO-d_6) δ 7.60 (s, 1H), 7.37 (d, *J* = 7.3 Hz, 2H), 7.31 (dd, *J* = 15.5, 6.9 Hz, 2H), 6.43 (d, *J* = 10.8 Hz, 2H), 5.51 (t, *J* = 5.8 Hz, 1H), 4.65 (s, 1H), 4.31 (dd, *J* = 15.8, 5.9 Hz, 1H), 4.21 (dd, *J* = 16.1, 5.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 169.58, 168.41, 159.96, 149.19, 147.33, 136.67, 133.86, 133.58, 130.86, 129.37, 124.75, 118.78, 111.32, 59.04, 53.56, 35.86. HRMS (ESI^+): m/z calculated for [$C_{16}H_{11}N_3O_6$ + H^+]: 342.0726; found 342.0705

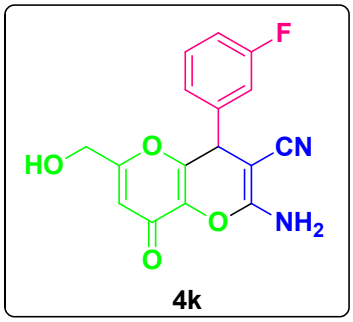
2-amino-4-(2-bromophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4j:



4j

95% yield, white solid. R_f = 0.42 (40% EtOAc/Hexane); M.P. 234-236 °C. IR (KBr) υ_{max} (cm^{-1}): 3373, 3265, 3,178, 2210, 1,698, 810. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 7.60 (d, *J* = 7.9 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.78 (s, 2H), 6.43 (s, 1H), 5.58 (t, *J* = 5.6 Hz, 1H), 5.30 (s, 1H), 4.29 (dd, *J* = 16.2, 5.8 Hz, 1H), 4.18 (dd, *J* = 16.2, 5.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 170.26, 168.72, 159.78, 148.22, 139.01, 136.83, 133.13, 130.41, 129.72, 128.41, 123.27, 118.88, 111.30, 59.34, 55.25, 40.14. HRMS (ESI^+): m/z calculated for [$C_{16}H_{11}BrN_2O_4$ + H^+]: 374.9980; found 374.9961

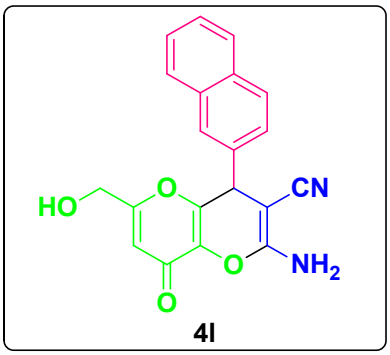
2-amino-4-(3-flurophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4k:



4k

98% yield, white solid. R_f = 0.42 (40% EtOAc/Hexane); M.P. 220-222 °C. IR (KBr) υ_{max} (cm^{-1}): 3463, 3425, 3325, 3220, 2214, 1642. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 7.35 (d, *J* = 16.9 Hz, 3H), 7.10 (d, *J* = 7.4 Hz, 1H), 6.51 (s, 1H), 5.82 (s, 2H), 5.15 (s, 1H), 4.66 (s, 1H), 4.38 – 4.31 (m, 1H), 4.30 – 4.23 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$+ DMSO-d_6) δ 170.37, 168.47, 163.60, 161.64, 159.59, 148.21, 142.34, 136.46, 130.37, 123.49, 118.89, 114.79, 111.38, 59.47, 55.66, 40.44. HRMS (ESI^+): m/z calculated for [$C_{16}H_{11}FN_2O_4$ + H^+]: 315.0781; found 315.0767

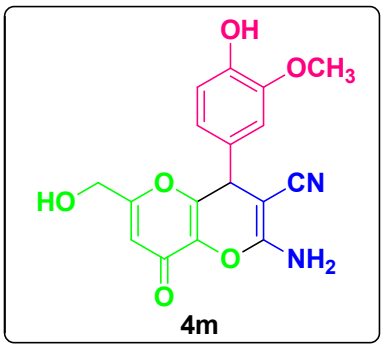
2-amino-6-(hydroxymethyl)-4-(naphthalene-2-yl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4l:



4l

94% yield, white solid. R_f = 0.45 (40% EtOAc/Hexane); M.P. 248-250 °C. IR (KBr) υ_{max} (cm^{-1}): 3393, 3299, 3193, 3061, 2961, 2188, 1644, 1592, 1412, 1267, 1216, 1090. ^1H NMR (500 MHz, DMSO-d_6) δ 8.35 (d, *J* = 7.8 Hz, 1H), 8.02 – 7.98 (m, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.64 – 7.52 (m, 3H), 7.43 (d, *J* = 6.5 Hz, 1H), 7.28 (s, 2H), 6.33 (s, 1H), 5.77 (s, 1H), 5.61 (t, *J* = 6.1 Hz, 1H), 4.09 (dd, *J* = 15.9, 5.6 Hz, 1H), 3.93 (dd, *J* = 15.9, 5.6 Hz, 1H).^{13}C NMR (126 MHz, $CDCl_3$+ DMSO-d_6) δ 169.97, 168.12, 159.66, 149.18, 136.48, 133.45, 130.90, 128.39, 126.46, 126.19, 125.64, 125.35, 122.57, 122.57, 118.93, 111.14, 65.17, 59.10, 56.04, 14.91. HRMS (ESI^+): m/z calculated for [$C_{20}H_{14}N_2O_4$ + H^+]: 347.1032; found 347.1052

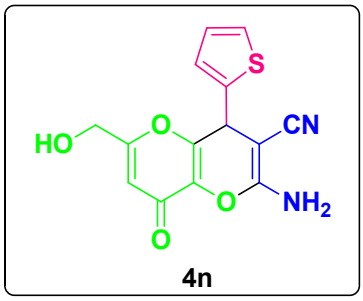
2-amino-4-(4-hydroxy-3-methoxyphenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4m:



4m

96% yield, white solid. R_f = 0.4 (40% EtOAc/Hexane); M.P. 218-220 °C. IR (KBr) υ_{max} (cm^{-1}): 3380, 3320, 3185, 2848, 2228, 1610, 975. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 8.91 (s, 1H), 6.95 (s, 2H), 6.86 – 6.76 (m, 2H), 6.69 (s, 1H), 6.35 (s, 1H), 5.65 (s, 1H), 4.58 (s, 1H), 4.24 (d, *J* = 19.8 Hz, 1H), 4.19 (d, *J* = 16.1 Hz, 1H), 3.83 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 170.16, 168.30, 159.51, 149.34, 147.75, 146.32, 136.22, 131.47, 120.22, 119.49, 115.72, 111.46, 111.34, 59.47, 56.09, 55.74, 40.35. HRMS (ESI^+): m/z calculated for [$C_{17}H_{14}N_2O_6$ + H^+]: 343.0930; found 343.0914

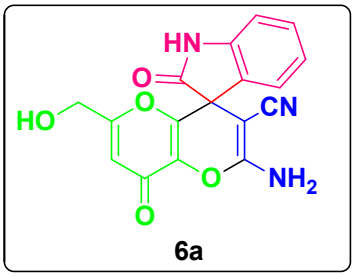
2-amino-6-(hydroxymethyl)8-oxo-4-(thiophen-2-yl)-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile, 4n:



4n

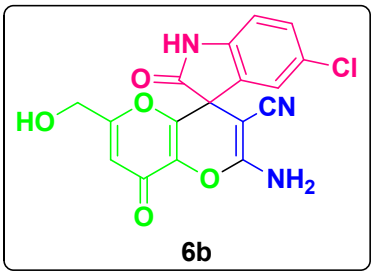
97% yield, white solid. R_f = 0.42 (40% EtOAc/Hexane); M.P. 235-237 °C. IR (KBr) υ_{max} (cm^{-1}): 3410, 3350, 3282, 2162, 1620, 840. ^1H NMR (500 MHz, $CDCl_3$+ DMSO-d_6) δ 7.43 (s, 2H), 7.29 (d, *J* = 4.8 Hz, 1H), 7.02 (d, *J* = 30.6 Hz, 1H), 6.49 (s, 1H), 6.19 (s, 1H), 5.42 (t, *J* = 5.9 Hz, 1H), 4.97 (s, 1H), 4.49 – 4.23 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) ^{13}C NMR (126 MHz, DMSO) δ 169.76, 168.20, 159.52, 147.81, 144.39, 135.75, 126.97, 125.65, 118.98, 111.18, 59.21, 55.49, 35.79, 30.54. HRMS (ESI^+): m/z calculated for [$C_{14}H_{10}N_2O_4S$ + H^+]: 303.0440; found 303.0448

2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile, 6a:



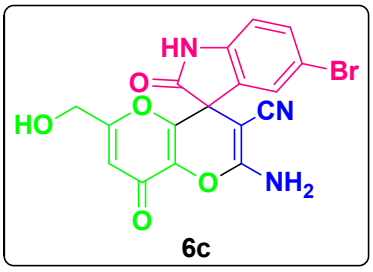
97% yield, white solid. R_f = 0.25 (90% EtOAc/ Hexane); M.P. 235-237 °C. IR (KBr) υ_{max} (cm^{-1}): 3436, 3298, 3173, 2204, 1716, 1634, 1597, 1475, 1226, 1051. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 10.66 (s, 1H), 7.78 (s, 2H), 7.28 (t, J = 7.5 Hz, 1H), 7.18 (d, J = 7.4 Hz, 1H), 7.07 – 7.01 (m, 1H), 6.94 (d, J = 7.4 Hz, 1H), 6.43 (s, 1H), 5.56 (t, J = 5.8 Hz, 1H), 4.17 (dd, J = 16.5, 5.9 Hz, 1H), 4.08 (dd, J = 15.4, 6.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 175.39, 169.47, 168.31, 159.94, 145.59, 141.59, 137.74, 130.18, 129.56, 124.49, 122.52, 117.05, 111.27, 110.21, 59.02, 54.97, 51.13. HRMS (ESI^+): m/z calculated for [$C_{17}H_{11}N_3O_5$ + H^+]: 338.0777; found 338.0763

2′-amino-5-chloro-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile, 6b:



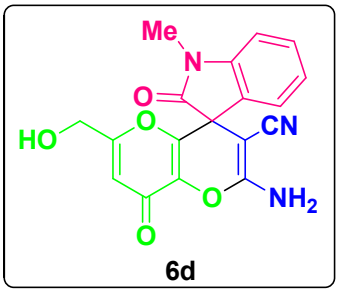
95% yield, white solid, R_f = 0.3 (90% EtOAc/Hexane); M.P. 296-298 °C. IR (KBr) υ_{max} (cm^{-1}): 3310, 3190, 2204, 1738, 1636, 1590, 1480, 1444, 1215, 1060, 1031. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 10.71 (s, 1H), 7.54 (s, 1H), 7.26 (d, J = 8.3 Hz, 1H), 7.16 (s, 1H), 6.91 (d, J = 8.3 Hz, 1H), 6.74 (s, 2H), 6.49 (s, 1H), 5.49 (t, J = 6.1 Hz, 1H), 4.21 (dd, J = 16.2, 6.0 Hz, 1H), 4.14 (dd, J = 16.4, 5.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 175.17, 169.74, 168.57, 160.05, 144.90, 140.26, 137.86, 131.63, 129.63, 127.39, 124.70, 116.82, 111.60, 111.36, 59.18, 54.86, 51.31. HRMS (ESI^+): m/z calculated for [$C_{17}H_{10}ClN_3O_5$ + H^+]: 372.0387; found 372.0372

2′-amino-5-bromo-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile, 6c:



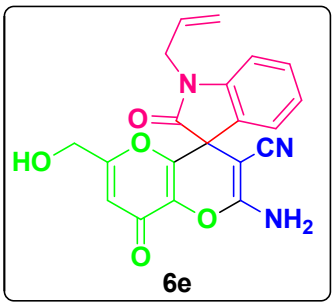
97% yield, white solid. R_f = 0.3 (90% EtOAc/Hexane); M.P. 220-222 °C. IR (KBr) υ_{max} (cm^{-1}): 3350, 3195, 2205, 1732, 1646, 1471, 1440, 1297, 1215, 1072, 1033. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 10.80 (s, 1H), 7.69 (d, J = 6.4 Hz, 2H), 7.41 (d, J = 6.6 Hz, 1H), 7.04 (s, 1H), 6.87 (d, J = 7.9 Hz, 1H), 6.46 (s, 1H), 5.55 (d, J = 5.4 Hz, 1H), 4.19 (dd, J = 16.2 Hz, 1H), 4.14 (dd, J = 6.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 180.18, 174.97, 173.78, 165.22, 150.08, 145.87, 143.04, 137.69, 137.15, 132.60, 121.95, 119.94, 117.28, 116.56, 64.40, 60.25, 56.40. HRMS (ESI^+): m/z calculated for [$C_{17}H_{10}BrN_3O_5$ + H^+]: 415.9882; found 415.9870

2′-amino-6′-(hydroxymethyl)-1-methyl-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile, 6d:



90% yield, White solid. R_f = 0.2 (90% EtOAc/Hexane); M.P. 270-272 °C. IR (KBr) υ_{max} (cm^{-1}): 3340, 3190, 3070, 2987, 2205, 1720, 1645, 1612, 1490, 1228, 1035. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 7.50 (d, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.09 (d, *J* = 7.1 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 6.45 (s, 1H), 5.40 – 5.34 (m, 1H), 4.17 (dd, *J* = 16.0, 5.7 Hz, 1H), 4.05 (dd, *J* = 16.3, 5.7 Hz, 1H), 2.60 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6) δ 175.74, 169.72, 168.28, 167.04, 159.91, 147.23, 143.29, 136.56, 132.44, 128.68, 122.81, 122.49, 110.93, 107.70, 73.55, 59.01, 50.39, 26.43. HRMS (ESI^+): m/z calculated for [$C_{18}H_{13}N_3O_5$ + H^+]: 352.0933; found 352.0915

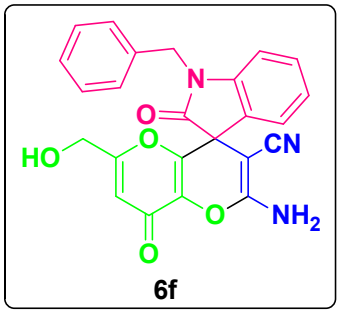
1-allyl-2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile, 6e:



6e

88% yield, light pink solid. R_f = 0.3 (90% EtOAc/Hexane); M.P. 220-222 °C. IR (KBr) υ_{max} (cm^{-1}): 3401, 3321, 2960, 2198, 1721, 1648, 1608, 1485, 1402. ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 7.97 (s, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.39 – 7.30 (m, 3H), 7.19 (t, *J* = 7.2 Hz, 2H), 6.40 (s, 1H), 5.66 (s, 1H), 4.58 (s, *J* = 18.0 Hz, 2H), 4.14 – 4.05 (m, 1H), 4.05 – 3.96 (m, 1H), 2.57 (d, *J* = 1.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6) δ 173.71, 170.14, 169.11, 160.58, 145.69, 141.59, 138.01, 130.54, 129.50, 125.06, 124.32, 117.18, 111.71, 110.30, 77.17, 74.45, 59.25, 54.59, 51.17, 29.95. HRMS (ESI^+): m/z calculated for [$C_{20}H_{15}N_3O_5$ + H^+]: 378.1090; found 378.1108

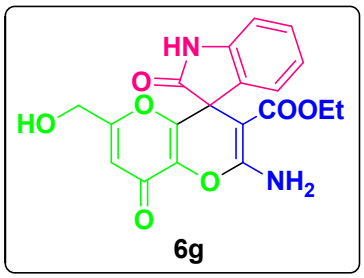
2′-amino-1-benzyl-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile, 6f:



6f

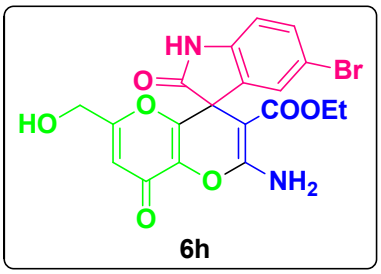
96% yield, white solid. R_f = 0.21 (90% EtOAc/Hexane); M.P. 234-236 °C. IR (KBr) υ_{max} (cm^{-1}): 3428, 3326, 2931, 2190, 1705, 1635, 1610, 1486, 1468, 1207. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 7.57 (s, 2H), 7.34 (s, 4H), 7.26 (d, J = 7.5 Hz, 2H), 7.12 (d, J = 7.1 Hz, 1H), 6.80 (s, 2H), 6.49 (s, 1H), 5.50 (s, 1H), 5.12 (d, J = 15.8 Hz, 1H), 4.88 (d, J = 16.2 Hz, 1H), 4.15 (s, 1H), 4.10 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 174.10, 169.58, 168.49, 160.22, 145.42, 142.05, 137.78, 135.03, 129.92, 129.54, 128.50, 127.41, 126.72, 124.65, 123.55, 117.11, 111.47, 109.78, 59.05, 54.61, 50.97, 43.53. HRMS (ESI^+): m/z calculated for [$C_{24}H_{17}N_3O_5$ + H^+]: 428.1246; found 428.1220

Ethyl 2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate, 6g:



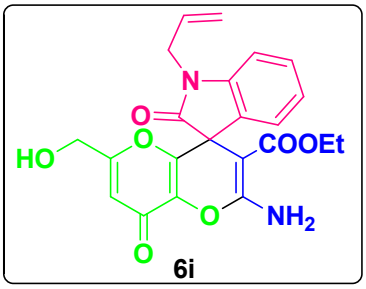
94% yield, white solid. R_f = 0.2 (90% EtOAc/Hexane); M.P. 283-285 °C. IR (KBr) υ_{max} (cm^{-1}): 3438, 3290, 2916, 1720, 1688, 1656, 1640, 1619, 1522, 1474, 1295, 1210. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 10.22 (s, 1H), 7.55 (s, 2H), 7.19 (t, J = 7.3 Hz, 1H), 7.03 (d, J = 6.4 Hz, 1H), 6.94 (t, J = 7.4 Hz, 1H), 6.89 (t, J = 6.8 Hz, 1H), 6.44 (s, 1H), 5.42 (t, J = 5.8 Hz, 1H), 4.24 – 4.17 (m, 1H), 4.09 (d, J = 15.9 Hz, 1H), 3.91-3.79 (m, 2H), 0.85 (t, J = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 177.69, 169.93, 168.35, 167.05, 159.94, 147.71, 142.08, 136.53, 133.50, 128.38, 123.01, 121.74, 110.98, 109.37, 73.50, 59.13, 51.16, 50.27, 12.93. HRMS (ESI^+): m/z calculated for [$C_{19}H_{16}N_2O_7$ + H^+]: 358.1036; found 358.1052

Ethyl 2′-amino-5-bromo-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate, 6h:



96% yield, pale yellow solid. R_f = 0.25 (90% EtOAc/Hexane); M.P. 296-298 °C. IR (KBr) υ_{max} (cm^{-1}): 3398, 3326, 2986, 2854, 1735, 1642, 1526, 1474, 1215, 1130, 1036. ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 10.55 (s, 1H), 7.94 (s, 2H), 7.37 – 7.24 (m, 1H), 7.13 (d, *J* = 1.4 Hz, 1H), 6.90 – 6.76 (m, 1H), 6.40 (s, 1H), 5.53 (s, 1H), 4.21 – 4.12 (m, 1H), 4.12 – 4.04 (m, 1H), 3.38 (d, *J* = 14.1 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6) δ 177.01, 169.80, 168.34, 167.07, 159.95, 146.92, 141.13, 136.53, 135.31, 131.26, 125.97, 113.79, 111.08, 73.20, 59.72, 59.14, 51.26, 50.34, 13.81. HRMS (ESI^+): m/z calculated for [$C_{19}H_{15}BrN_2O_7$ + H^+]: 463.0141; found 463.0167

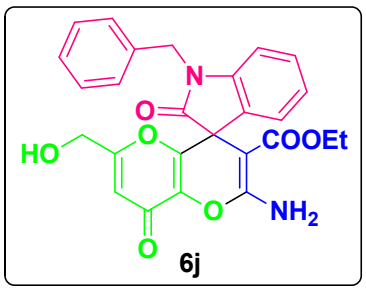
Ethyl 1-allyl-2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate, 6i:



6i

95% yield, white solid. R_f = 0.25 (90% EtOAc/Hexane); M.P. 230-232 °C. IR (KBr) υ_{max} (cm^{-1}): 3400, 3290, 2986, 2207, 1745, 1680, 1646, 1620, 1608, 1594, 1468, 1225, 1091, 1027. ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.02 (s, 2H), 7.91 (d, *J* = 2.2 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.09 (dt, *J* = 16.0, 7.3 Hz, 3H), 6.36 (s, 1H), 5.57 (t, *J* = 6.1 Hz, 1H), 4.70 – 4.58 (m, 1H), 4.48 (d, *J* = 17.7 Hz, 1H), 4.11 (dd, *J* = 16.4, 5.9 Hz, 1H), 3.98 (dd, *J* = 16.4, 6.1 Hz, 1H), 3.87 (tt, *J* = 14.2, 7.0 Hz, 1H), 3.79 – 3.68 (m, 1H), 0.71 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6) δ 174.69, 169.55, 168.31, 166.64, 160.02, 146.94, 141.37, 136.30, 132.51, 128.46, 122.85, 122.76, 110.82, 108.43, 76.62, 72.85, 72.74, 58.81, 58.69, 50.53, 29.07, 13.29. HRMS (ESI^+): m/z calculated for [$C_{22}H_{20}N_2O_7$ + H^+]: 425.1349; found 425.1328

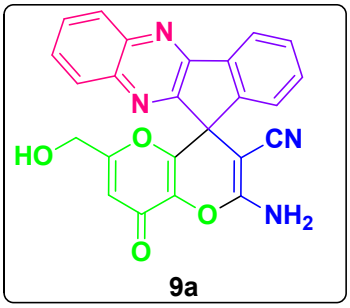
Ethyl 2′-amino-1-benzyl-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate, 6j:



6j

97% yield, white solid. R_f = 0.21 (90% EtOAc/Hexane); M.P. 240-242 °C. IR (KBr) υ_{max} (cm^{-1}): 3384, 3286, 3070, 2986, 1692, 1676, 1650, 1624, 1610, 1520, 1225, 1092. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 7.96 (s, 2H), 7.45 – 7.34 (m, 2H), 7.34 – 7.27 (m, 1H), 7.26 – 7.18 (m, 1H), 7.17 – 7.09 (m, 1H), 7.05 – 6.97 (m, 1H), 6.80 (dd, *J* = 7.7, 2.8 Hz, 1H), 6.42 (s, 1H), 5.61 (dd, *J* = 7.6, 4.5 Hz, 1H), 4.58 (dd, *J* = 15.7, 2.7 Hz, 1H), 4.17 – 4.07 (m, 1H), 4.07 – 3.96 (m, 1H), 3.86 – 3.77 (m, 1H), 3.76 – 3.67 (m, 1H), 0.79 (t, 2H). ^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6) δ 175.65, 169.39, 168.24, 166.73, 160.01, 147.25, 142.60, 136.48, 135.79, 132.72, 128.59, 128.29, 127.20, 126.88, 123.08, 122.57, 111.13, 108.39, 73.12, 58.92, 58.76, 50.59, 43.39, 13.27. HRMS (ESI^+): m/z calculated for [$C_{26}H_{22}N_2O_7$ + H^+]: 475.1505; found 475.1530

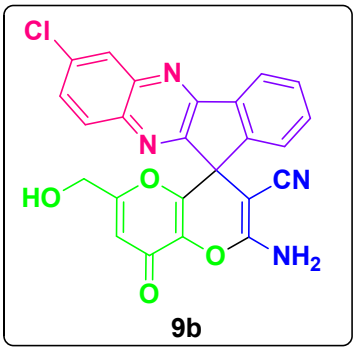
2′-amino-6′-(hydroxymethyl)-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano]3,2-*b*]pyran]-3′-carbonitrile, 9a:



9a

96% yield, white solid. R_f = 0.3 (90% EtOAc/Hexane); M.P. 278-280 °C. IR (KBr) υ_{max} (cm^{-1}): 3467, 3277, 3233, 3152, 2194, 1679, 1661, 1633, 1597, 1426, 1339, 1228, 1208, 1062. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 8.20 (t, *J* = 7.4 Hz, 2H), 8.14 (d, *J* = 7.9 Hz, 1H), 8.05 (s, 1H), 7.86 (t, *J* = 7.4 Hz, 1H), 7.80 (t, *J* = 7.3 Hz, 1H), 7.70 (s, 3H), 7.47 (s, 2H), 6.35 (s, 1H), 5.42 (t, *J* = 5.8 Hz, 1H), 3.81 (d, *J* = 5.8 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 168.99, 167.79, 161.09, 159.59, 152.32, 147.45, 146.36, 141.93, 140.59, 137.50, 135.81, 131.97, 129.50, 128.33, 121.47, 116.63, 110.72, 58.27, 55.59, 50.06. HRMS (ESI^+): m/z calculated for [$C_{24}H_{14}N_4O_4$ + H^+]: 423.1093; found 423.1093

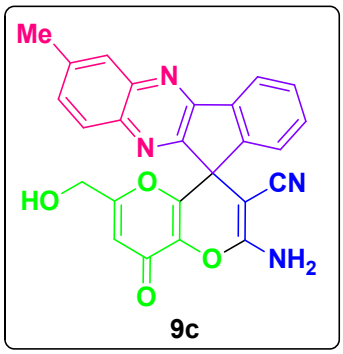
2′-amino-7-chloro-6′-(hydroxymethyl)-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile, 9b:



9b

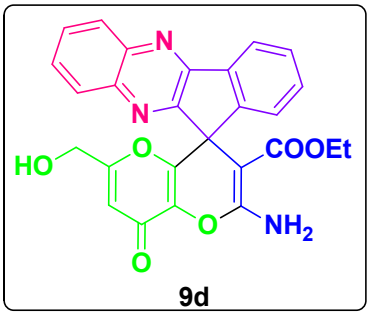
94% yield, light green powder. R_f = 0.25 (90% EtOAc/Hexane); M.P. 248-250 °C. IR (KBr) υ_{max} (cm^{-1}): 3410, 3280, 3255, 3080, 2198, 1690, 1650, 1560, 1525, 1410, 1351, 1220, 1053, 900, 769. ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 8.23 – 8.17 (m, 2H), 8.12 (d, *J* = 9.3 Hz, 1H), 7.95 (s, 1H), 7.72 (dd, *J* = 31.6, 8.7 Hz, 3H), 7.40 (s, 2H), 6.37 (s, 1H), 5.43 (s, 1H), 3.81 (dd, *J* = 23.2, 8.4 Hz, 2H). HRMS (ESI^+): m/z calculated for [$C_{24}H_{13}ClN_4O_4$ + H^+]: 457.0704; found 457.0704

2′-amino-6′-(hydroxymethyl)-7-methyl-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11-4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile, 9c:



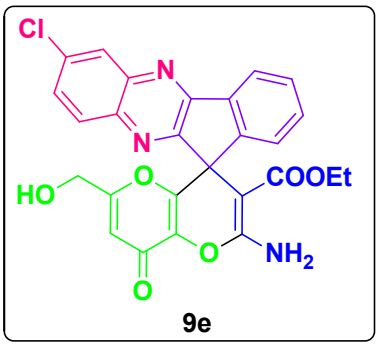
90% yield, pale yellow solid. R_f = 0.2 (90% EtOAc/Hexane); M.P. 260-262 °C. IR (KBr) υ_{max} (cm^{-1}): 3397, 3310, 3250, 2951, 2833, 2190, 1710, 1670, 1646, 1621, 1579, 1453, 1409, 1353, 1208, 1136, 1062. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) 8.20 (s, 1H), 8.02 – 7.94 (m, 1H), 7.69 – 7.56 (m, 5H), 6.72 (s, 2H), 6.43 (s, 1H), 5.30 (s, 1H), 3.85 (s, 2H), 2.64 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d_6) δ 170.00, 168.43, 160.23, 160.16, 152.78, 147.74, 147.22, 142.58, 140.71, 139.61, 138.04, 136.48, 132.10, 131.34, 129.87, 128.49, 127.72, 125.13, 121.94, 117.03, 111.17, 58.94, 57.03, 50.32, 21.40. HRMS (ESI^+): m/z calculated for [$C_{25}H_{16}N_4O_4$ + H^+]: 437.1250; found 437.1265

Ethyl 2′-amino-6′-(hydroxymethyl)-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate, 9d:



95% yield, white solid. R_f = 0.25 (90% EtOAc/Hexane); M. P. 296-298 °C. IR (KBr) υ_{max} (cm^{-1}): 3435, 3390, 3290, 2961, 2914, 2713, 1981, 1720, 1688, 1656, 1640, 1522, 1474, 1295, 1210. ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.22 – 8.10 (m, 2H), 8.05 (d, J = 8.1 Hz, 1H), 7.81 – 7.67 (m, 4H), 7.55 (ddd, J = 19.9, 6.6, 3.3 Hz, 3H), 6.34 (d, J = 1.0 Hz, 1H), 5.25 (d, J = 5.6 Hz, 1H), 3.76 (dd, J = 14.2, 8.3 Hz, 2H), 3.46 – 3.31 (m, 2H), 0.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6) δ 169.27, 167.50, 166.12, 159.61, 153.71, 150.16, 148.23, 141.03, 139.94, 136.22, 135.96, 135.13, 131.02, 128.55, 128.01, 127.88, 123.36, 120.76, 112.43, 110.16, 73.92, 58.14, 57.79, 49.94, 49.17, 11.90. HRMS (ESI^+): m/z calculated for [$C_{26}H_{19}N_3O_6$ + H^+]: 470.1352; found 470.1375

Ethyl 2′-amino-6′-(hydroxymethyl)-7-chloro-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate, 9e:

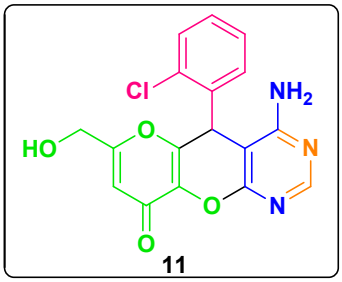


9e

93% yield, white solid. R_f = 0.2 (90% EtOAc/Hexane); M. P. 284-286 °C. IR (KBr) υ_{max} (cm^{-1}): 3437, 3390, 3154, 2975, 1740, 1686, 1670, 1646, 1619, 1520 1474, 1221, 1124, 1091. ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.12 – 8.08 (m, 2H), 8.03 (d, *J* = 2.2 Hz, 1H), 7.82 (s, 2H), 7.71 (t, *J* = 11.0 Hz, 1H), 7.58 (dd, *J* = 5.6, 2.6 Hz, 3H), 6.42 (d, *J* = 7.6 Hz, 1H), 5.58 (s, 1H), 4.44 (s, 2H), 4.35 (s, 1H), 4.08 (qd, *J* = 7.1, 3.0 Hz, 1H), 1.24 (t, 3H). ^{13}C NMR (101 MHz, $CDCl_3$ + DMSO-d_6) δ 173.47, 167.30, 161.61, 160.80, 153.62, 152.92, 148.12, 146.82, 142.08, 140.84, 140.37, 139.83, 139.02, 136.46, 131.56, 130.75, 129.74, 128.50, 128.07, 127.77, 124.57, 121.30, 108.81, 76.81, 59.80, 21.18. HRMS (ESI^+): m/z calculated for [$C_{26}H_{18}ClN_3O_6$ + H^+]: 504.0962; found 504.0990

Spectral data for the product 11

4-amino-5-(2-chlorophenyl)-7-(hydroxymethyl)pyrano[2',3':5,6]pyrano[2,3-*d*]pyrimidin-9(5*H*)-one, 11:



11

68% yield, brown solid. M. P. 284-286 °C. IR (KBr) υ_{max} (cm^{-1}): 3461, 3350, 3078, 2950, 2820, 2760, 1750, 1690, 1646, 1531, 1421, 1351, 1132, 1031. ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.60 (s, 1H), 6.45 (s, 1H), 5.56 (d, *J* = 5.7 Hz, 1H), 5.31 (s, 1H), 4.31 (dd, *J* = 16.2, 6.0 Hz, 1H), 4.20 (dd, *J* = 16.0, 5.6 Hz, 1H). HRMS (ESI^+): m/z calculated for [$C_{17}H_{12}ClN_3O_4$ + H^+]: 358.0595; found 358.0615

7. Copies of ^{1}H NMR and ^{13}C NMR spectra for product (4a-4n), (6a-6j), (9a-9e) and 11:

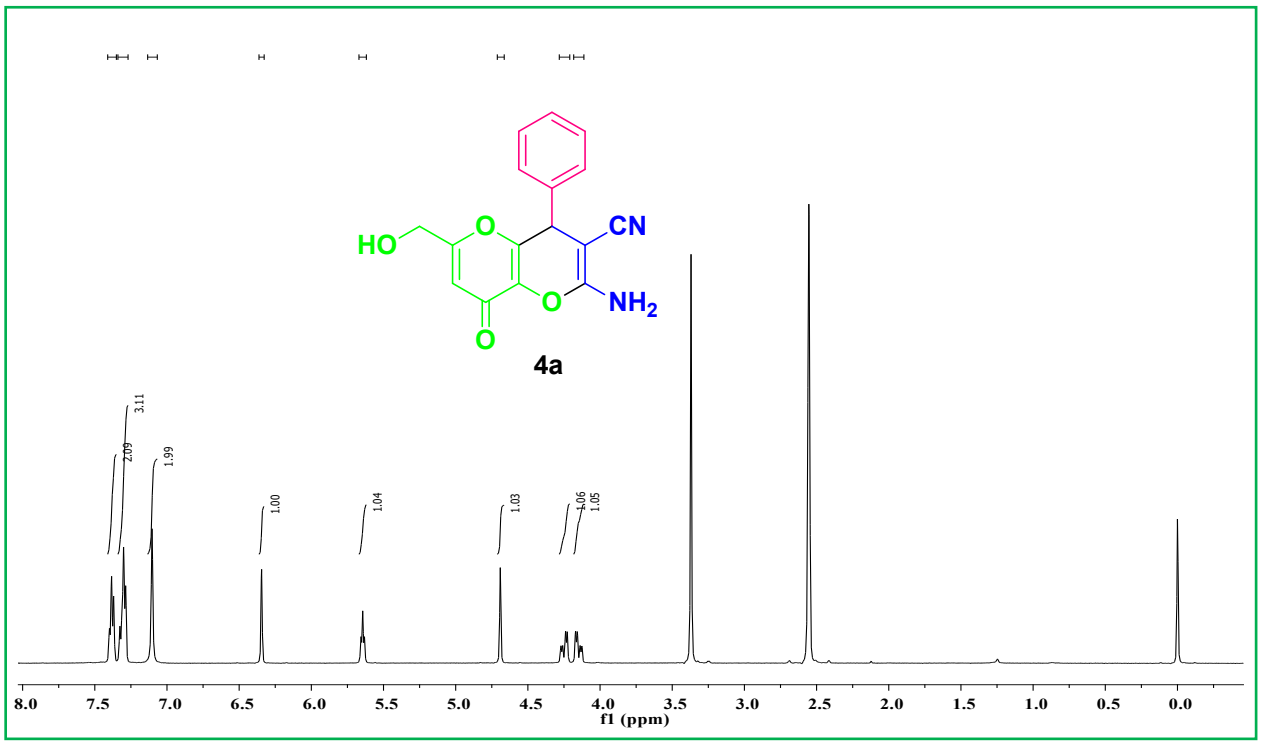


Figure S2: ^{1}H NMR spectra of 2-amino-6(hydroxymethyl)-8-oxo-4-phenyl-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4a**

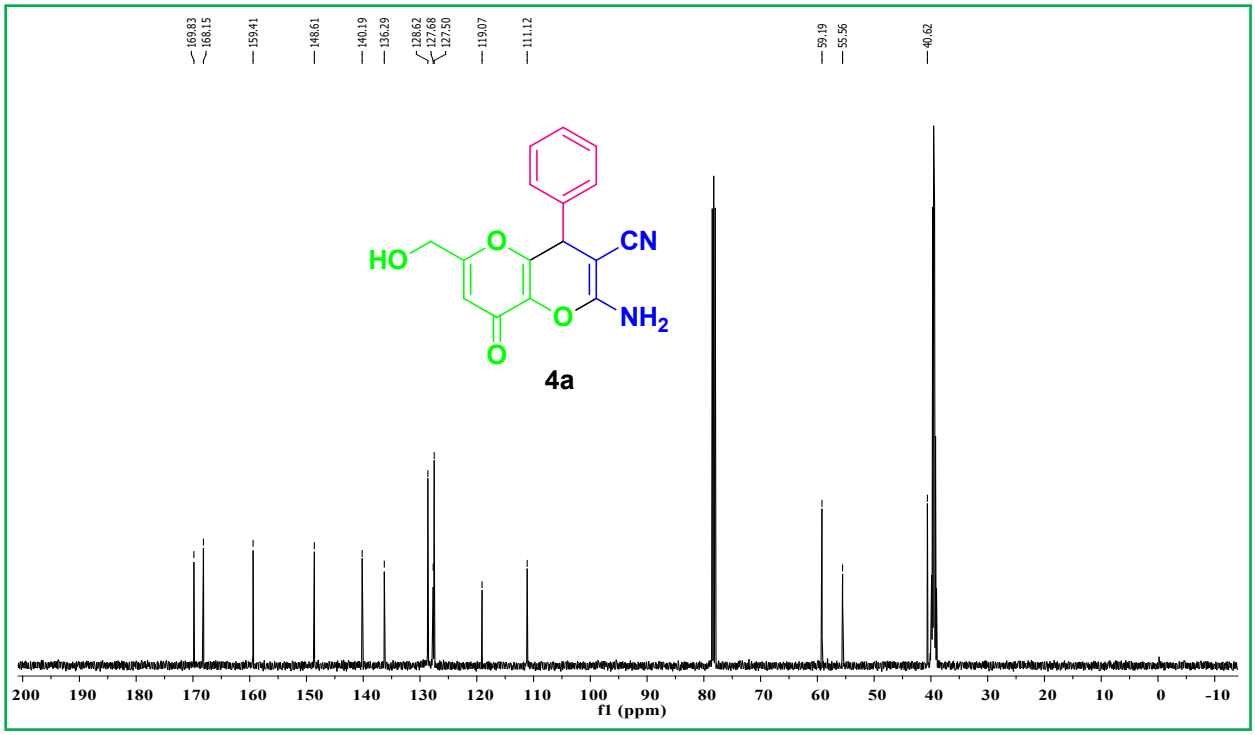


Figure S3: ^{13}C NMR spectra of 2-amino-6(hydroxymethyl)-8-oxo-4-phenyl-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4a**

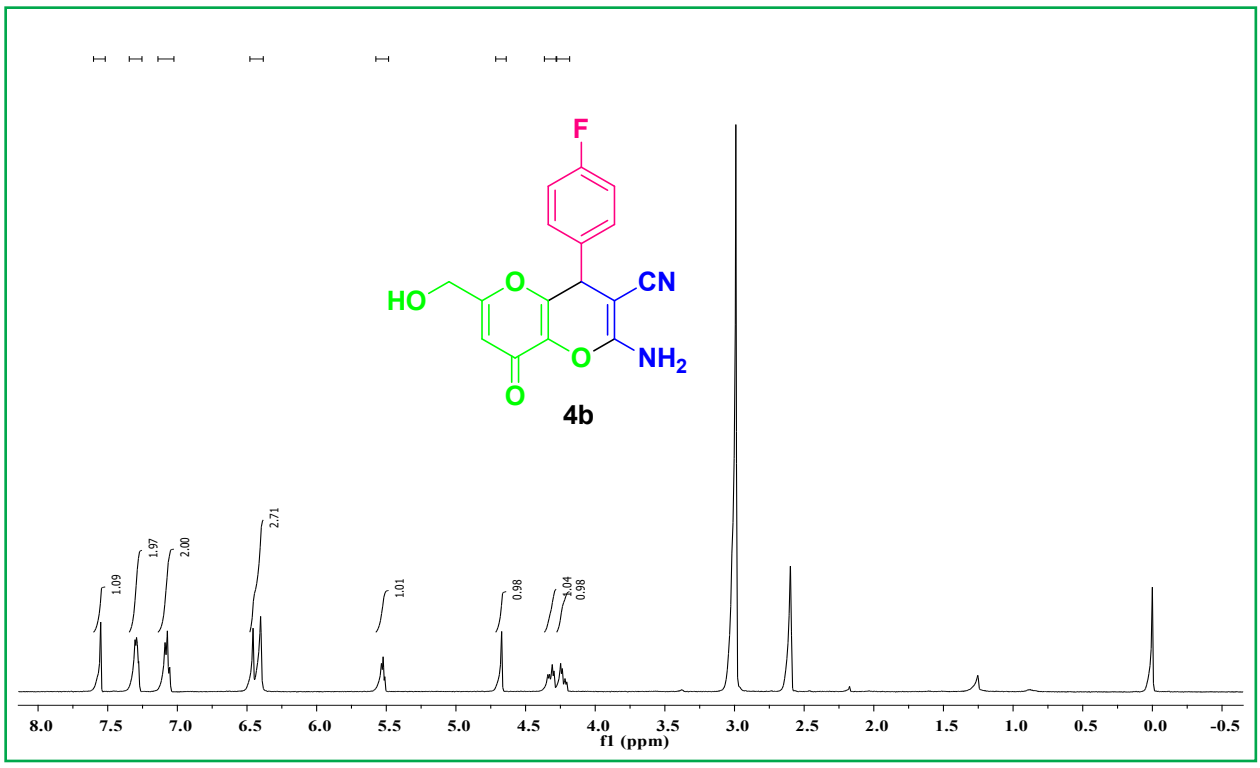


Figure S4: [1]H NMR Spectra of 2-amino-4-(-fluorophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4b**

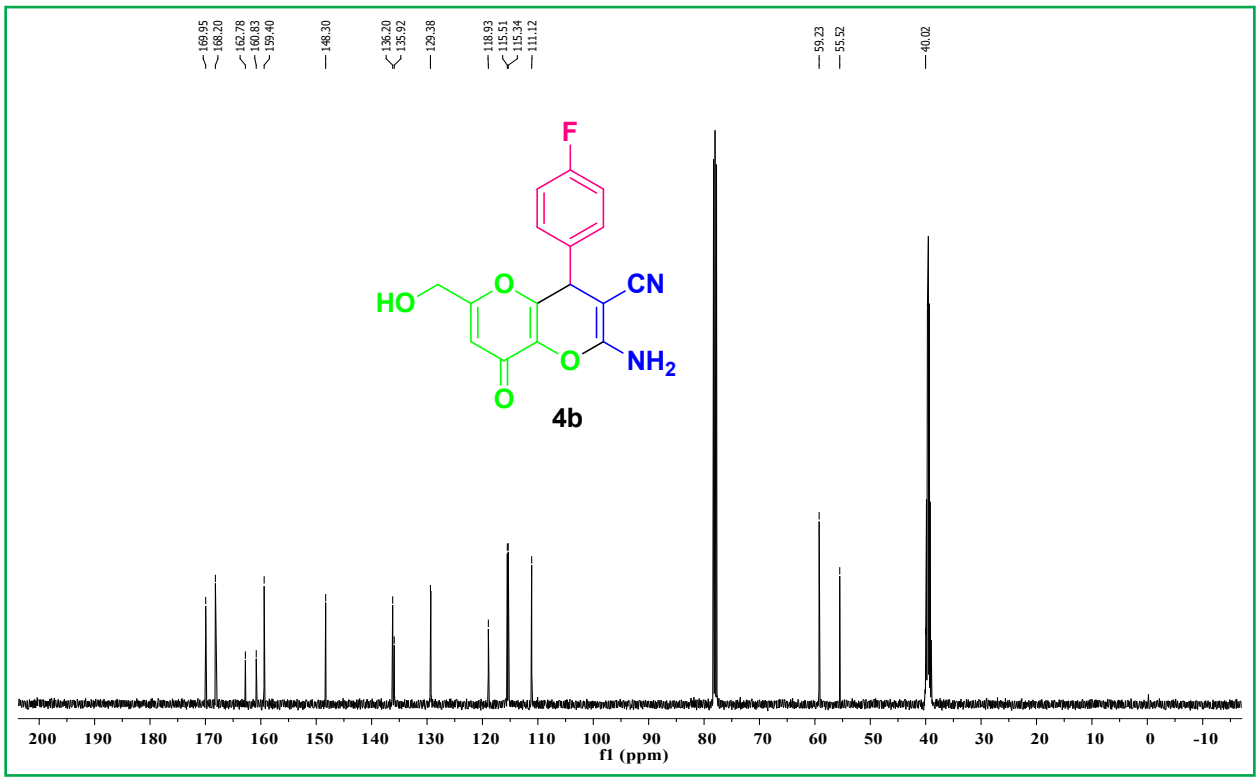


Figure S5: [13]C NMR spectra of -amino-4-(-fluorophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4b**

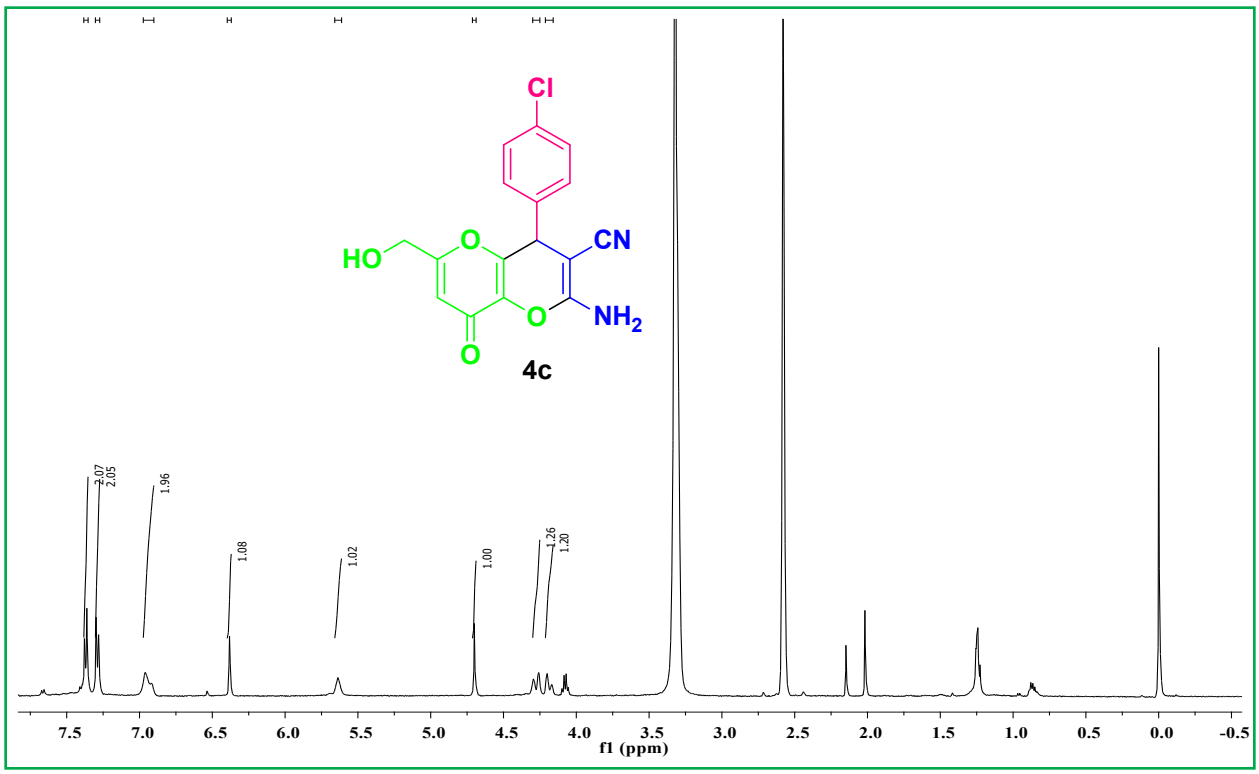


Figure S6: [1]H NMR spectra of 2-amino-4-(4-chlorophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4c**

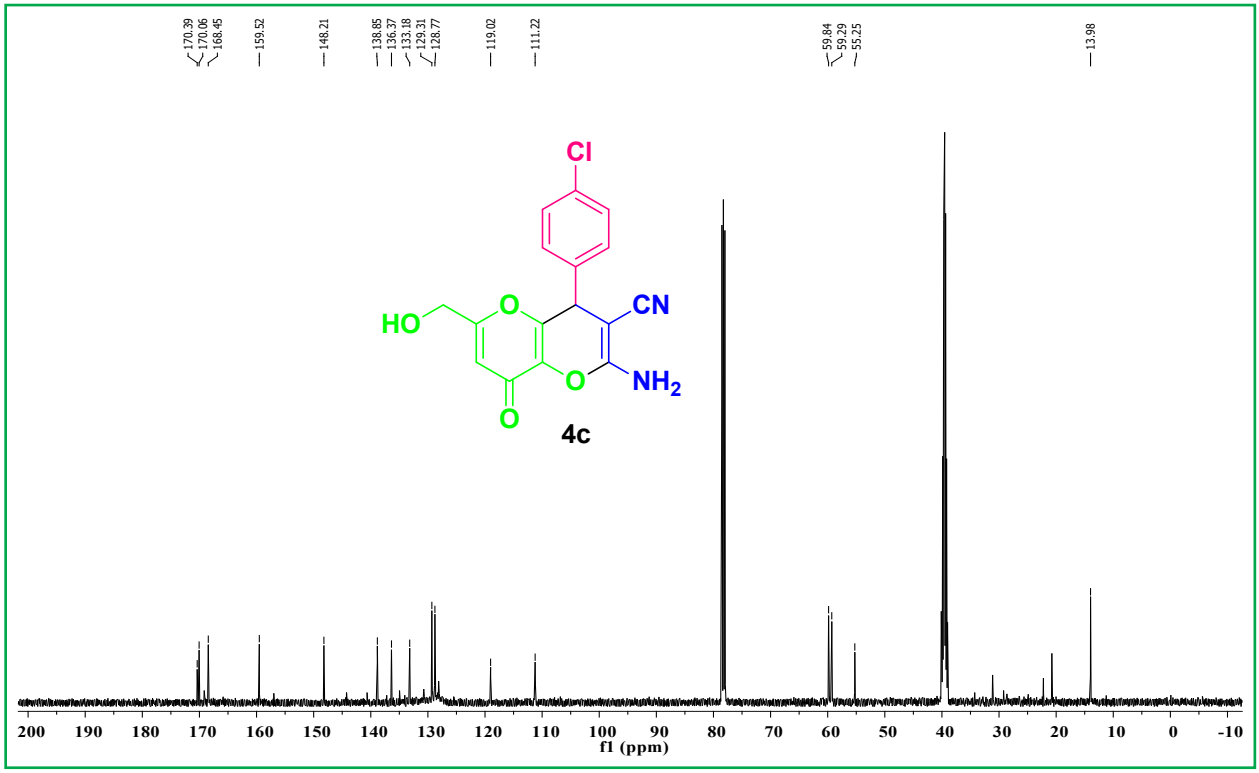


Figure S7: [13]C NMR spectra of 2-amino-4-(4-chlorophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4c**

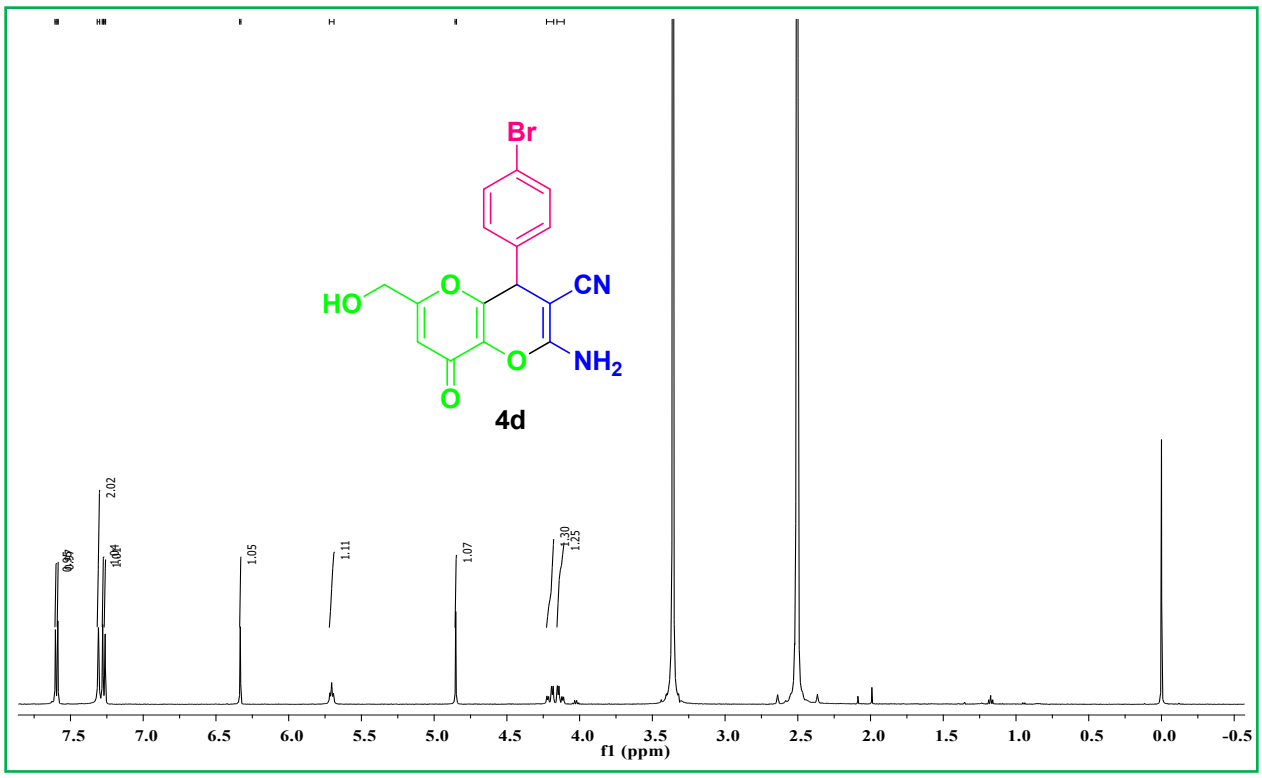


Figure S8: ^{1}H NMR spectra of 2-amino-4-(4-bromophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4d**

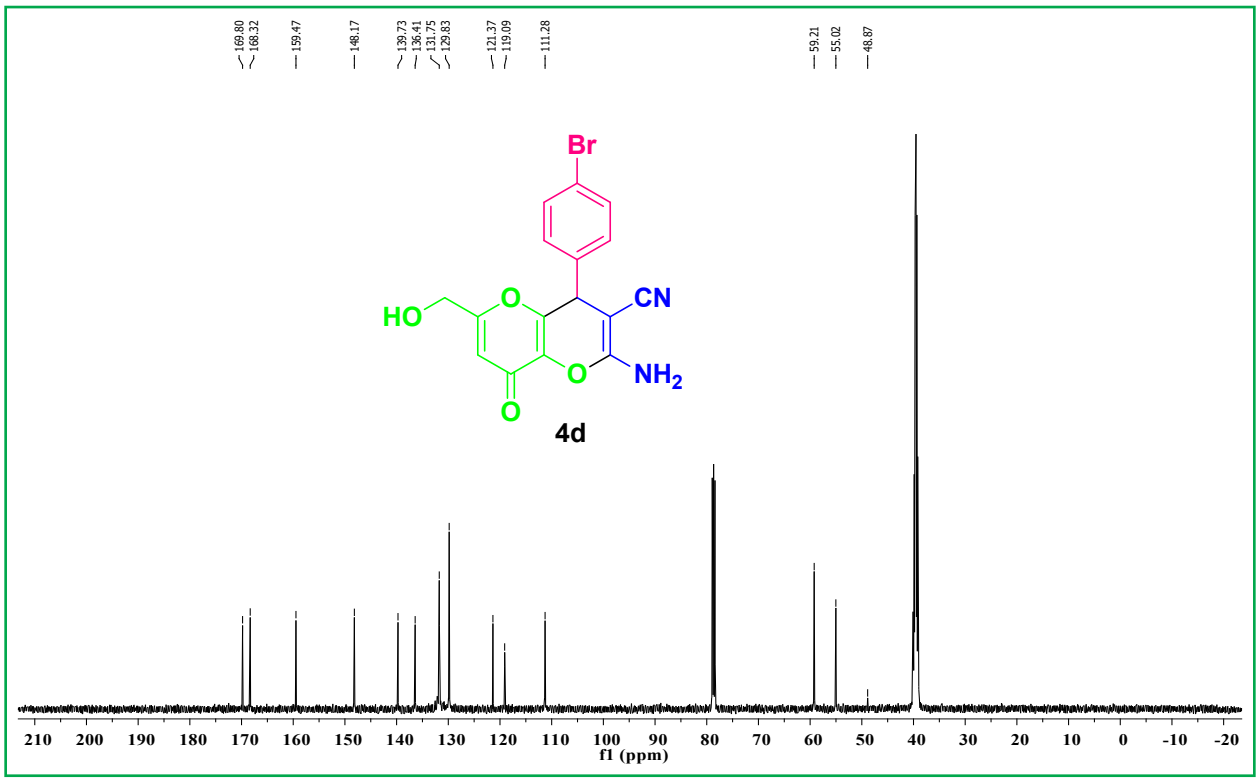


Figure S9: ^{13}C NMR spectra of 2-amino-4-(4-bromophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4d**

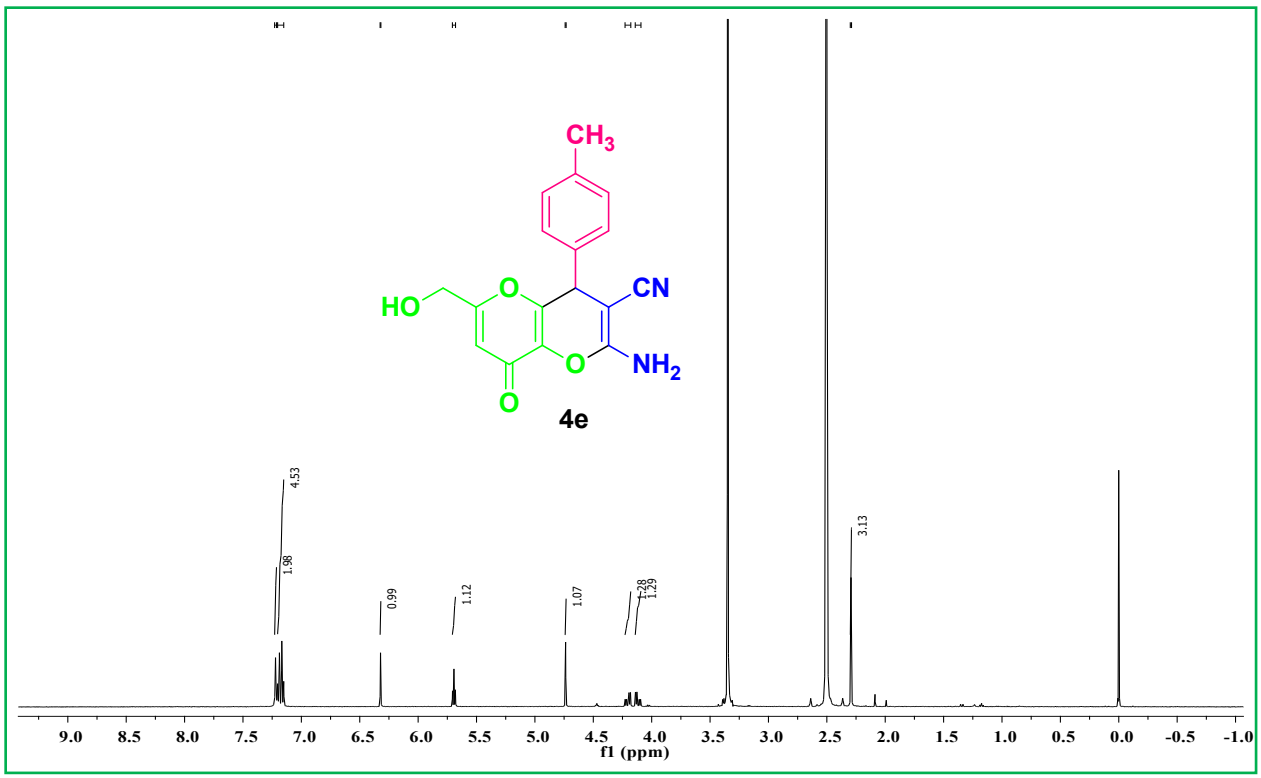


Figure S10: ^{1}H NMR spectra of 2-amino-6-(hydroxymethyl)-8-oxo-4-(*p*-tolyl)-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4e**

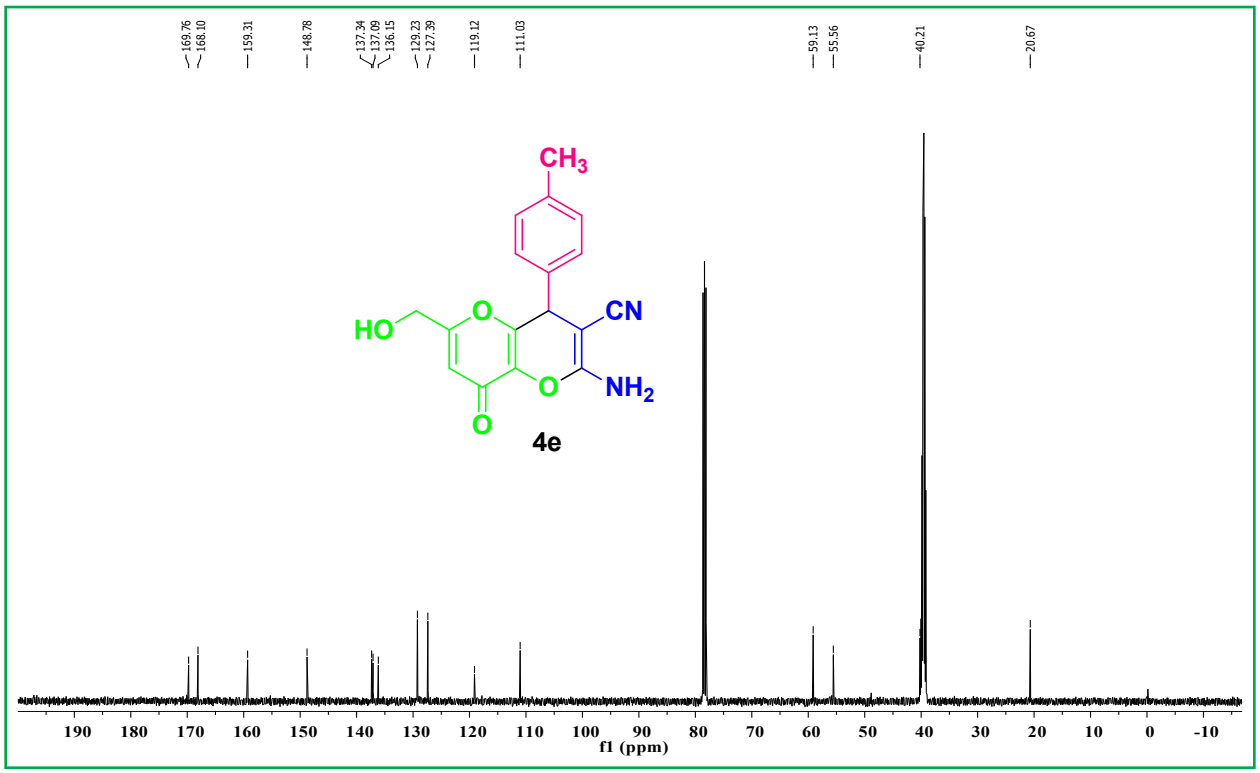


Figure S11: ^{13}C NMR spectra of 2-amino-6-(hydroxymethyl)-8-oxo-4-(p-tolyl)-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4e**

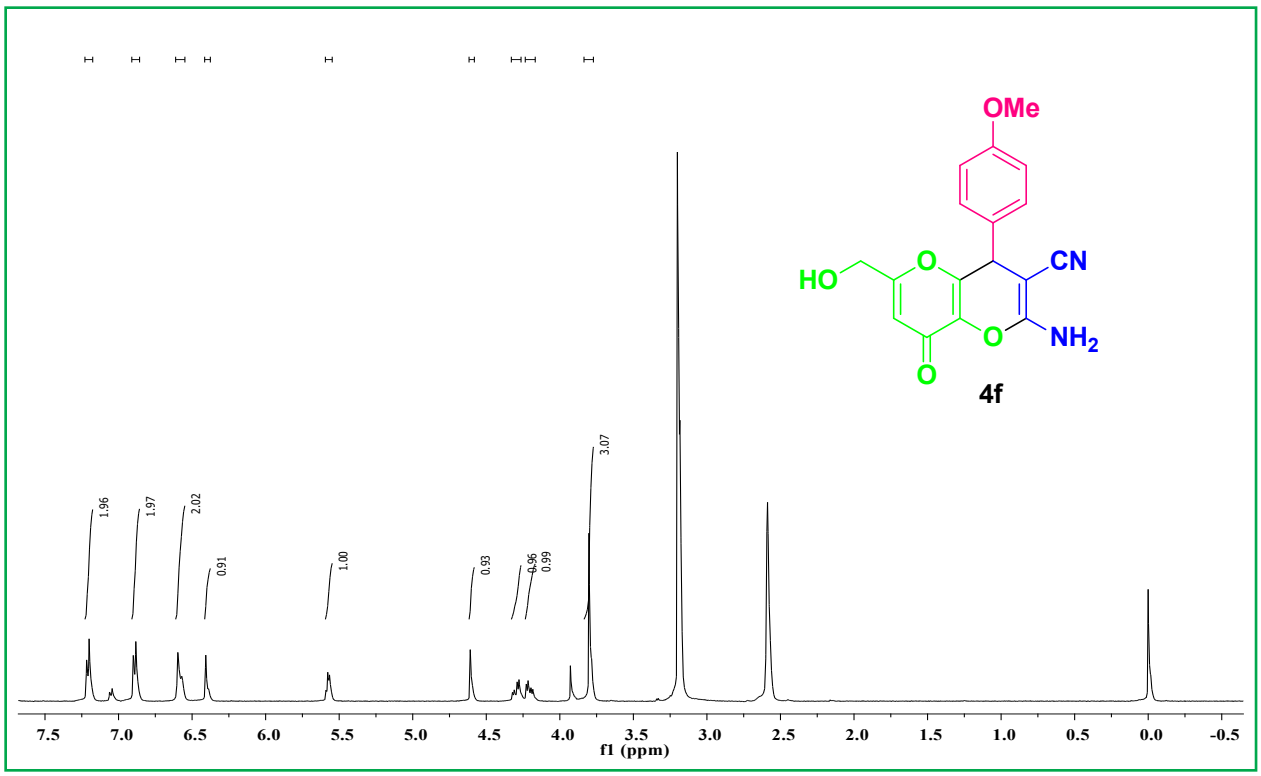


Figure S12: ^{1}H NMR spectra of 2-amino-6-(hydroxymethyl)-4-(4-methoxyphenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4f**

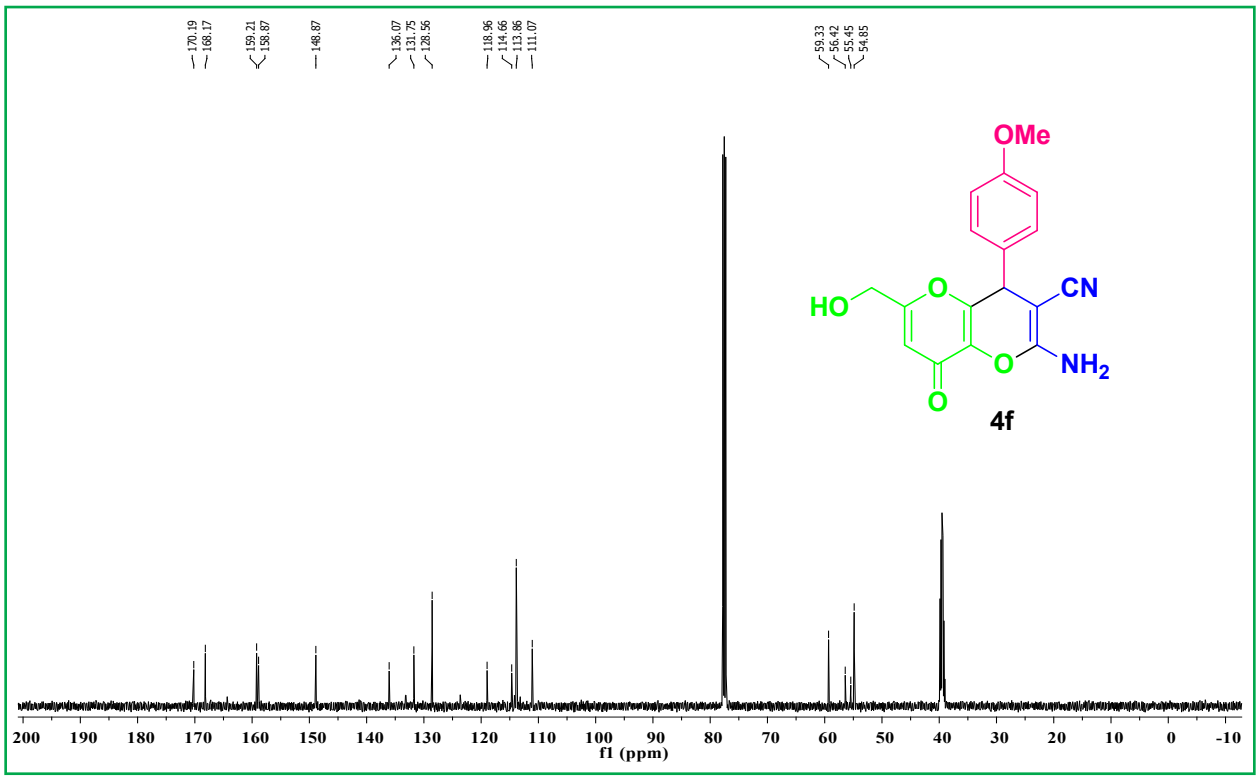


Figure S13: ^{13}C spectra of 2-amino-6-(hydroxymethyl)-4-(4-methoxyphenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4f**

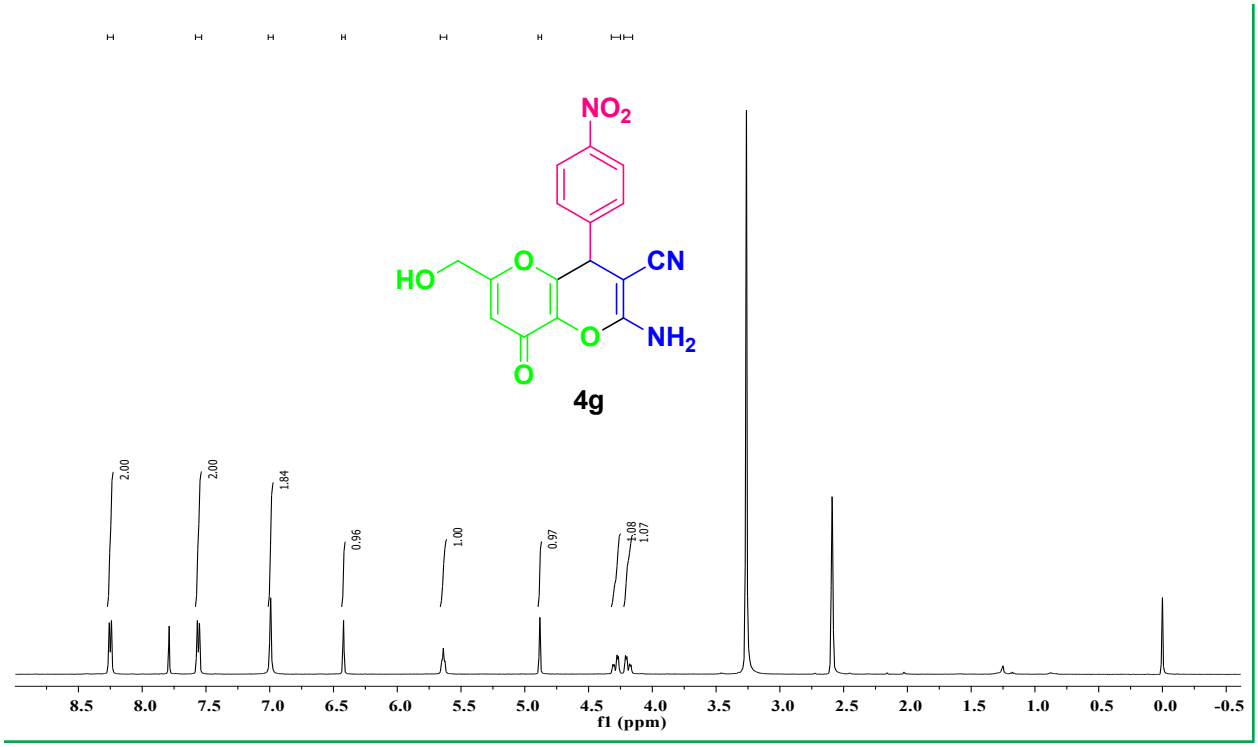


Figure S14: ^{1}H NMR spectra of 2-amino-6-(hydroxymethyl)-4-(4-nitrophenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4g**

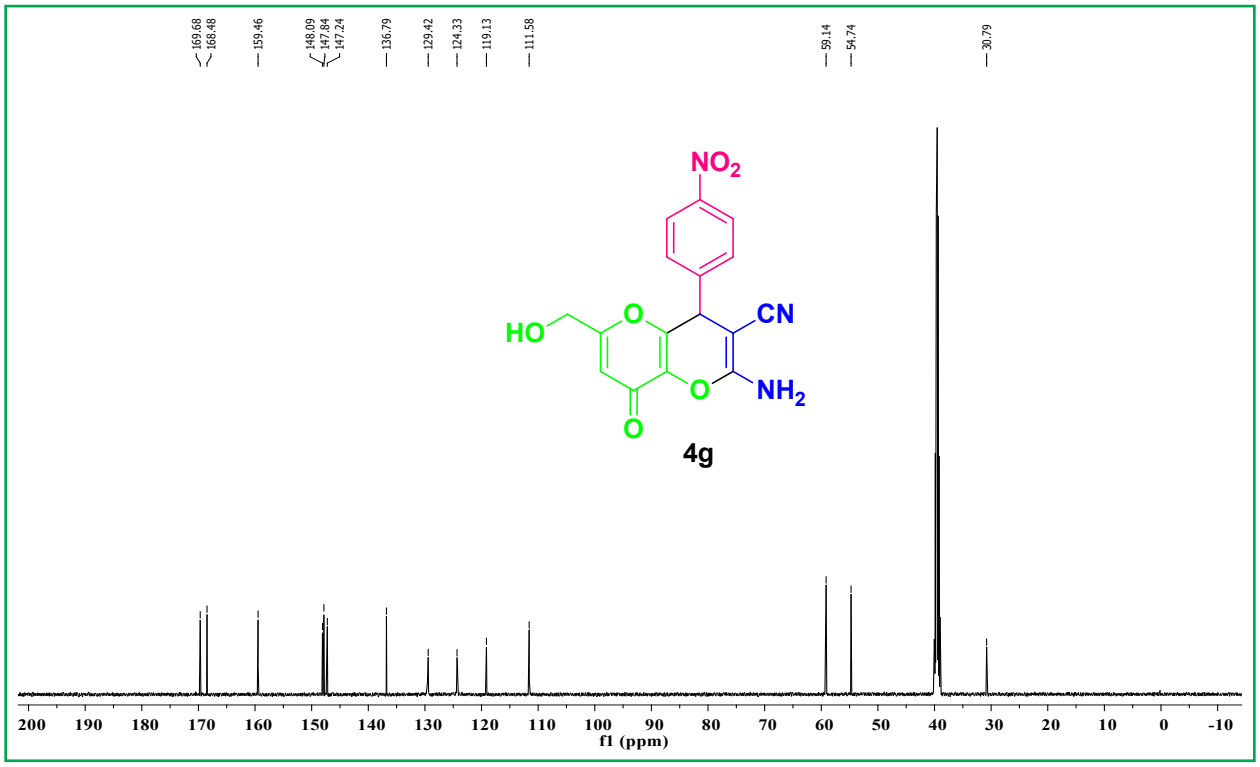


Figure S15: ^{13}C NMR spectra of 2-amino-6-(hydroxymethyl)-4-(4-nitrophenyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4g**

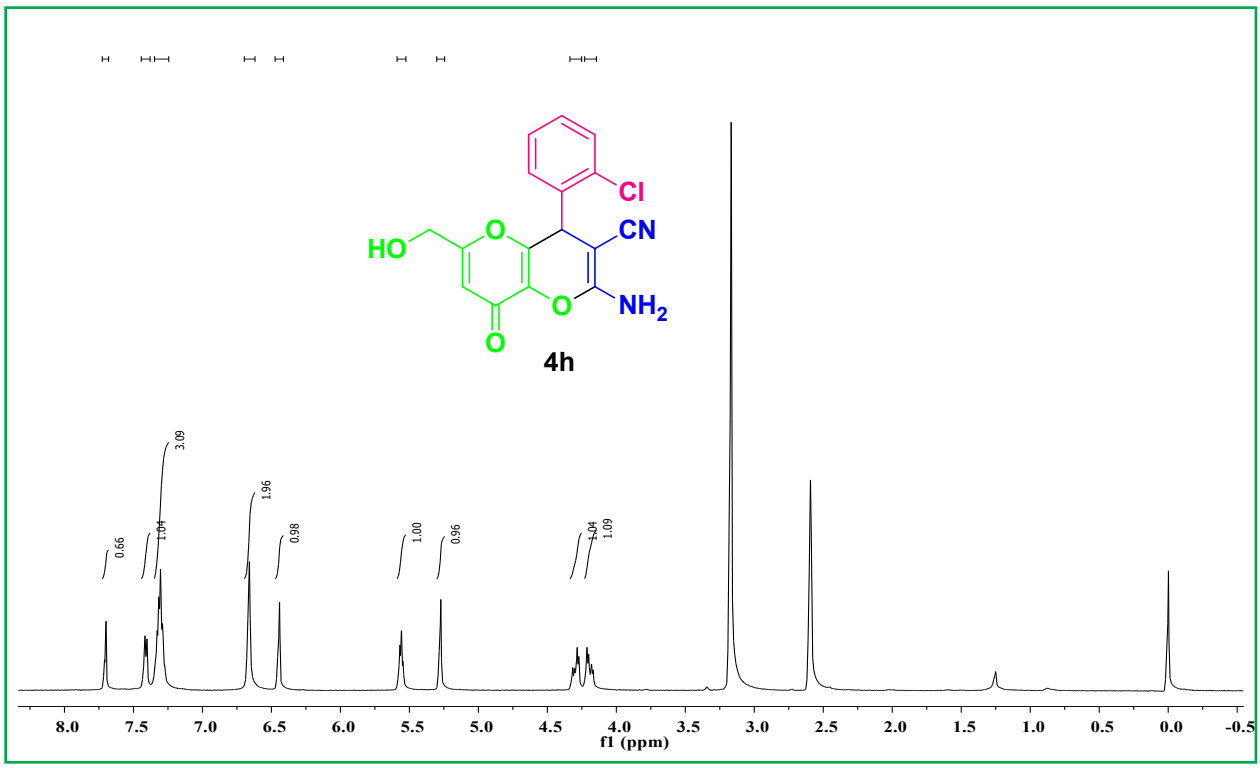


Figure S16: [1]H NMR spectra of 2-amino-4-(2-chlorophenyl)-6(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4h**

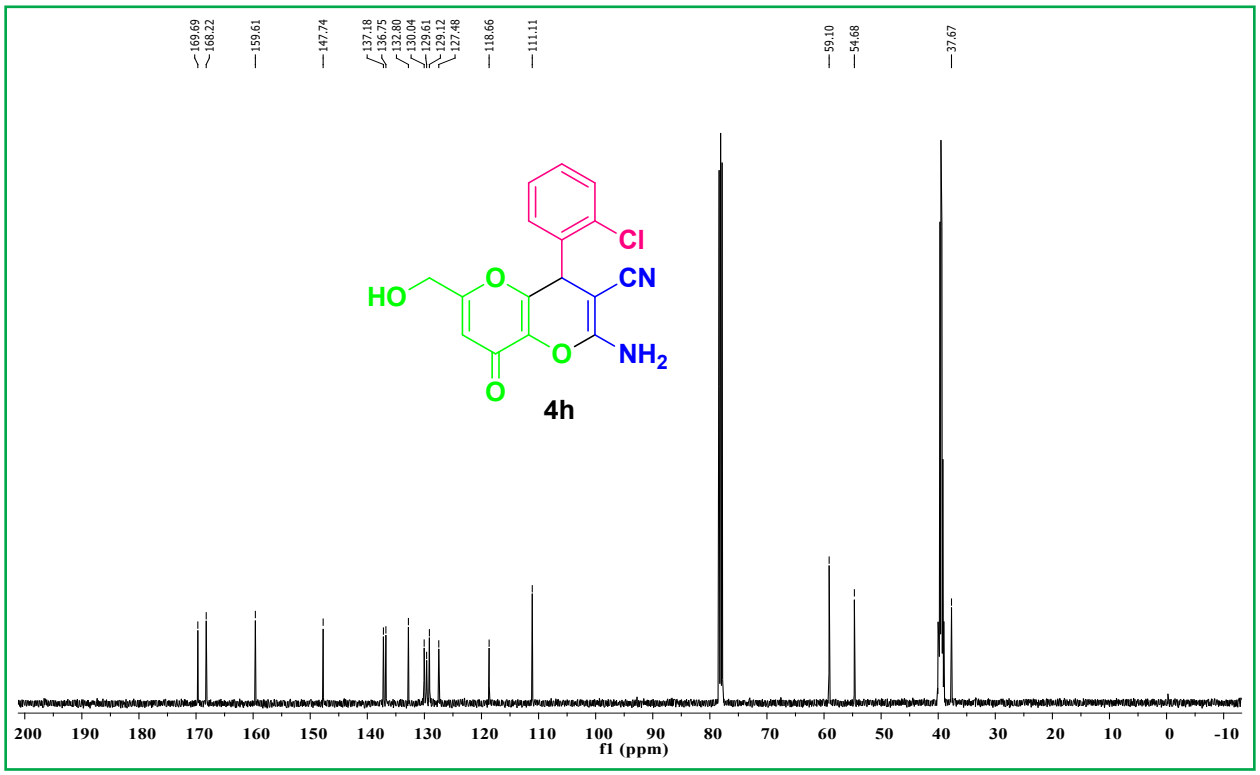


Figure S17: [13]C spectra of 2-amino-4-(2-chlorophenyl)-6(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4h**

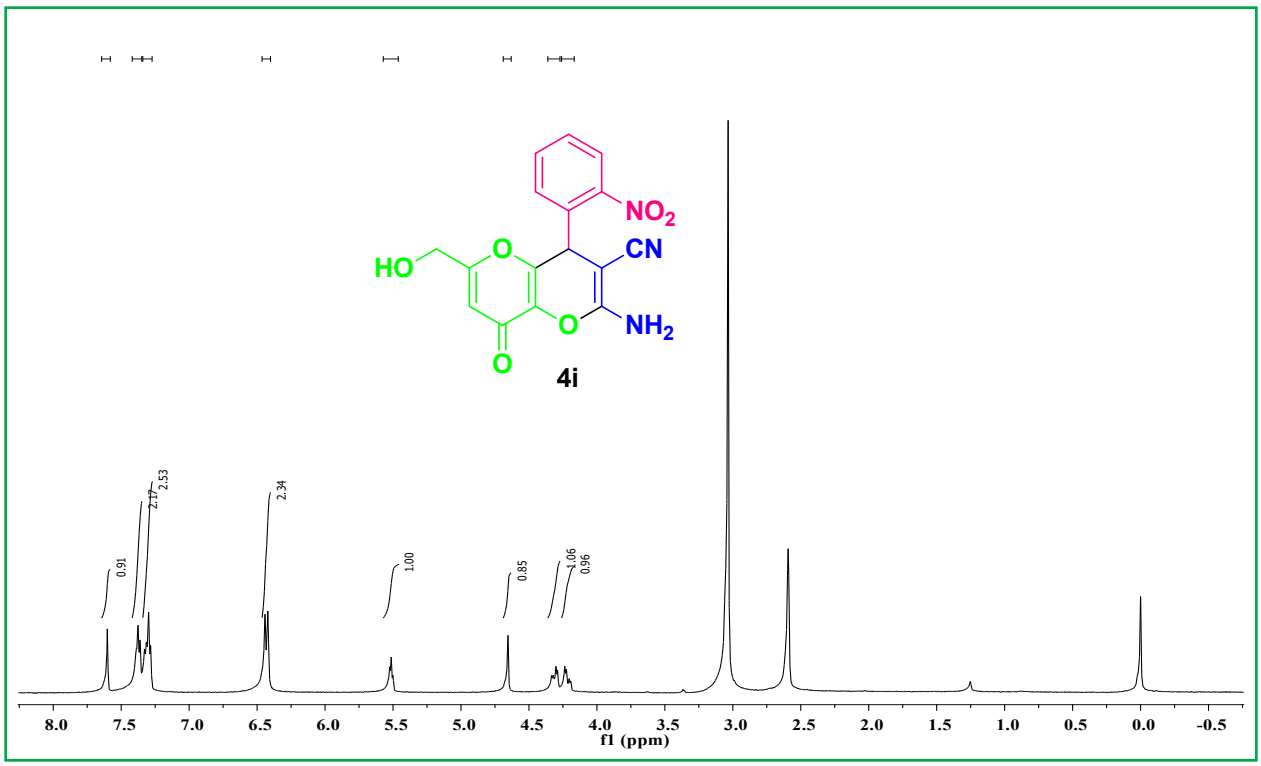


Figure S18: ^{1}H NMR spectra of 2-amino-6-(hydroxymethyl)-4-(2-nitrophenyl)-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4i**

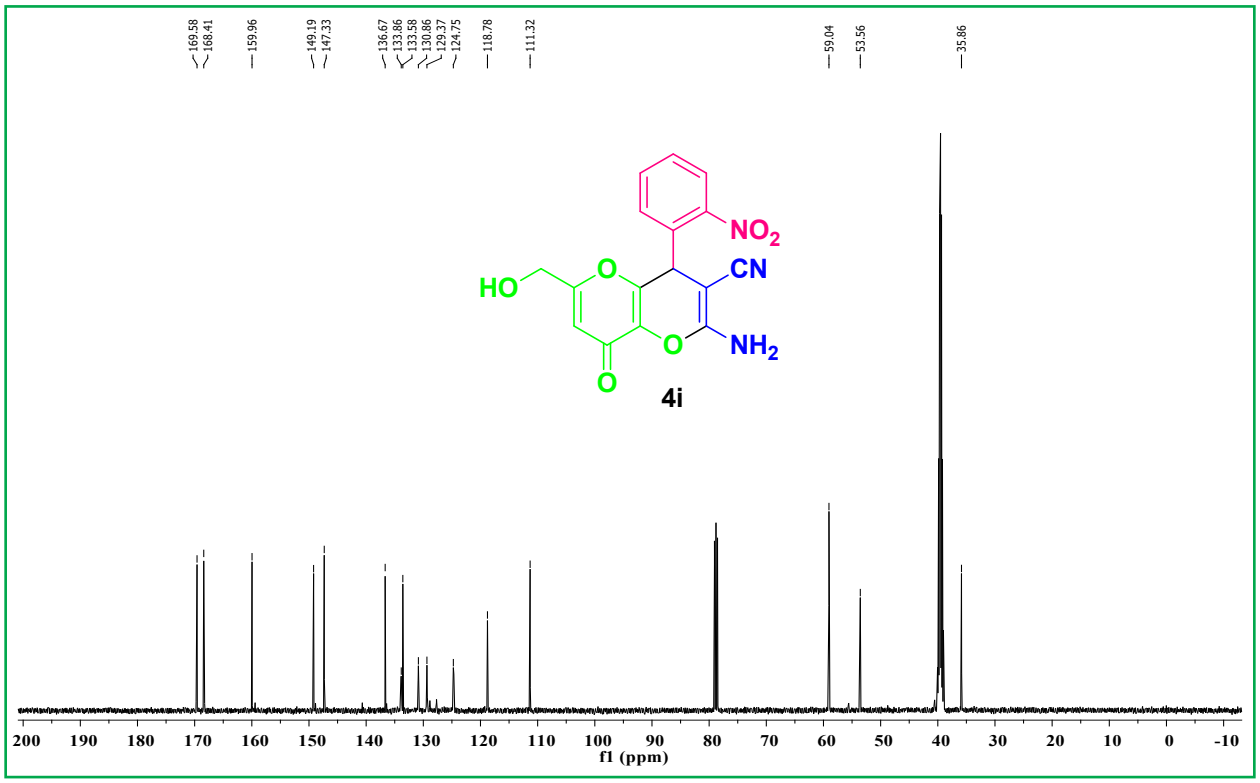


Figure S19: ^{13}C NMR spectra of 2-amino-6-(hydroxymethyl)-4-(2-nitrophenyl)-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4i**

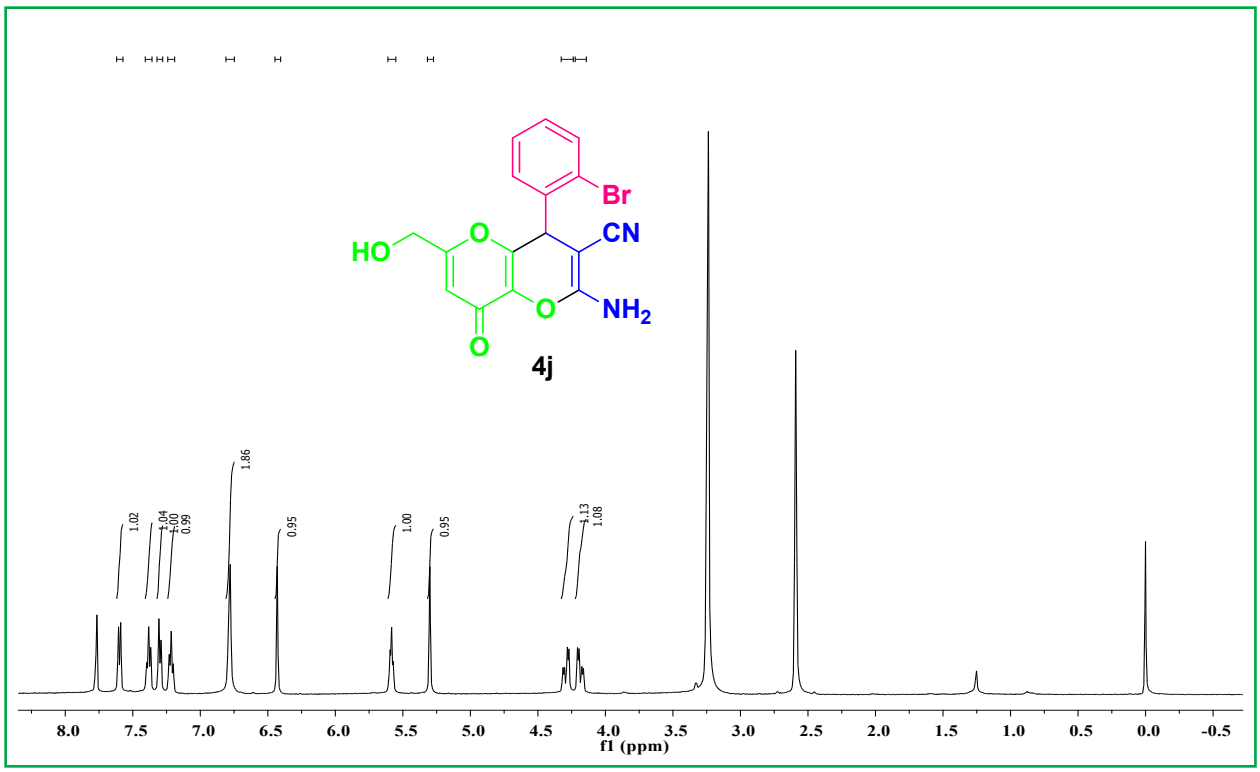


Figure S20: [1]H NMR spectra of 2-amino-4-(2-bromophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4j**

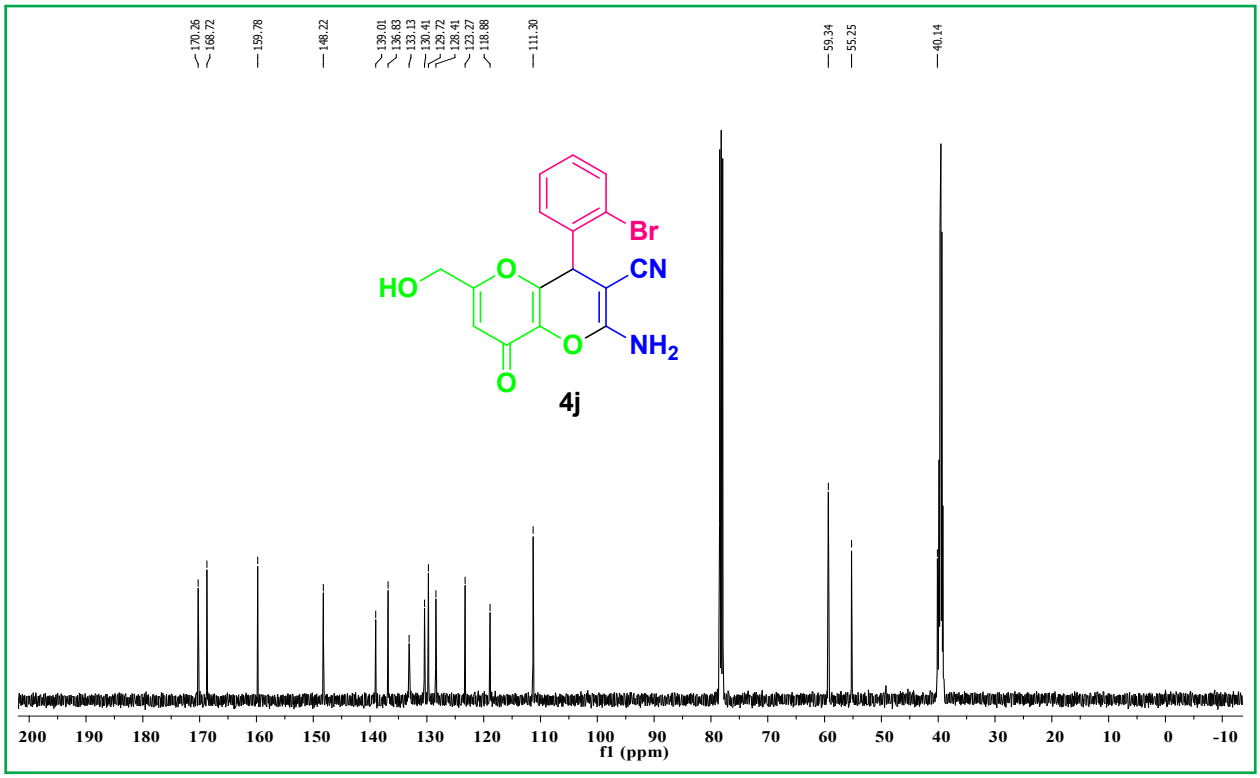


Figure S21: [13]C NMR spectra of 2-amino-4-(2-bromophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4j**

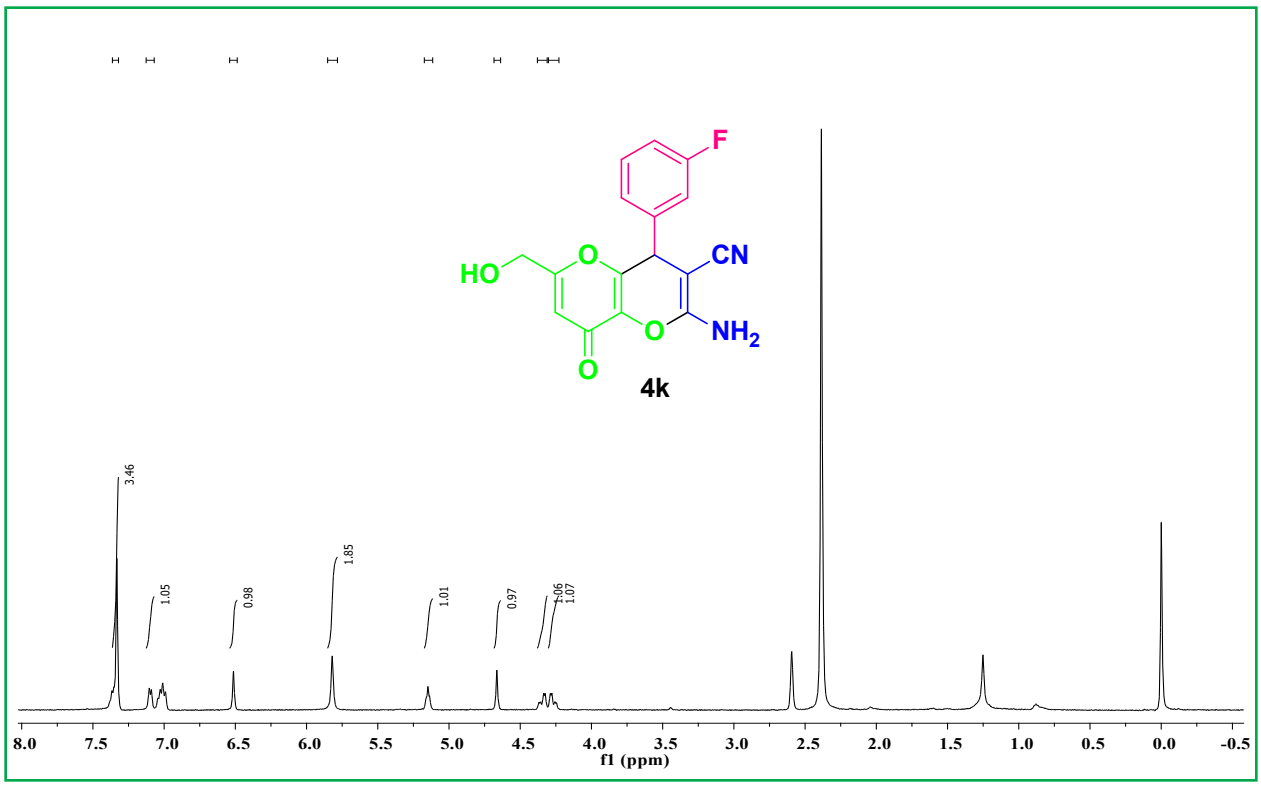


Figure S22: [1]H NMR spectra of 2-amino-4-(3-flurophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4k**

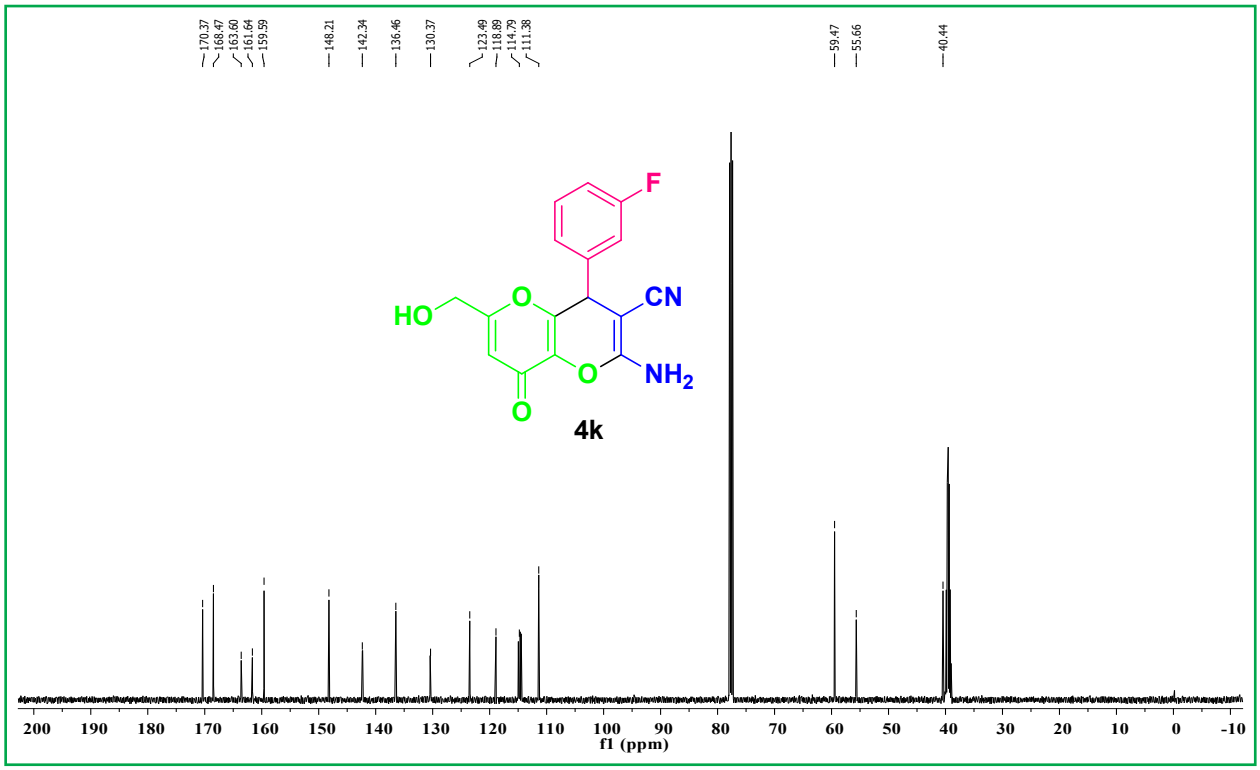


Figure S23: [13]C NMR Spectra of 2-amino-4-(3-flurophenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4k**

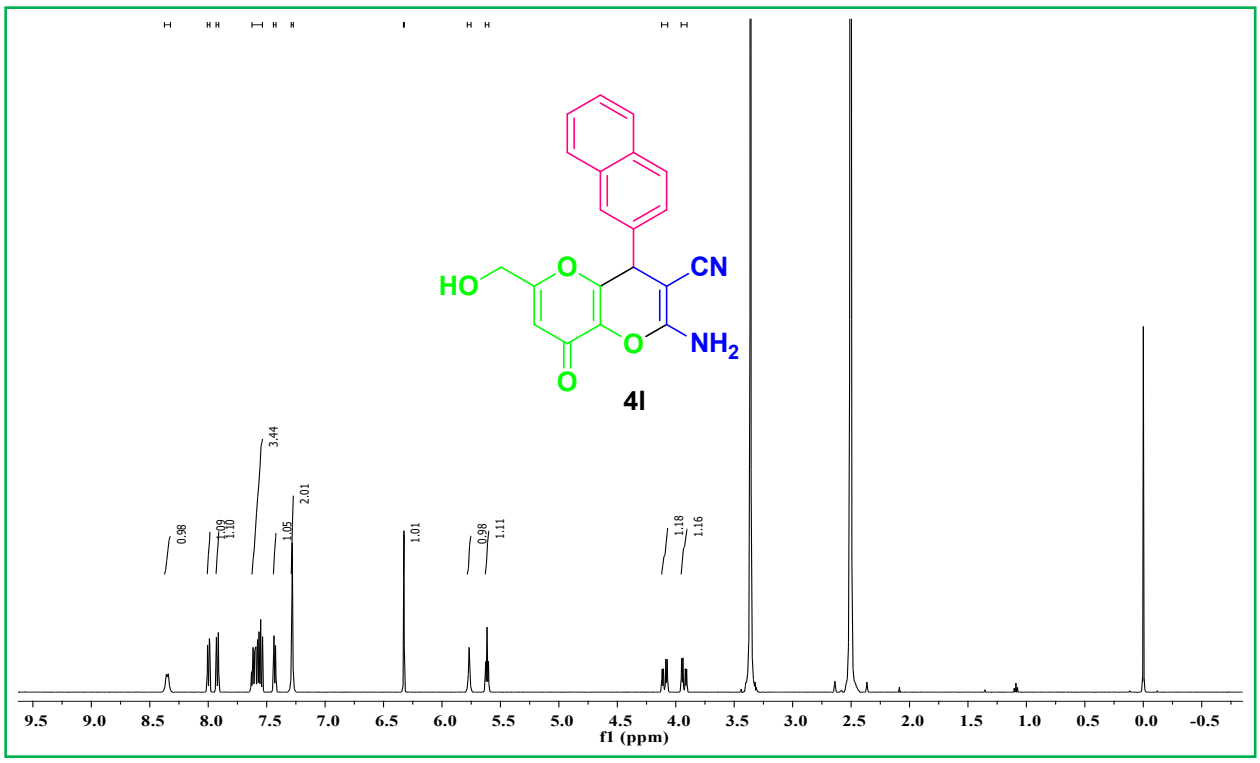


Figure S24: [1]H NMR spectra of 2-amino-6-(hydroxymethyl)-4-(naphthalene-2-yl)-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4l**

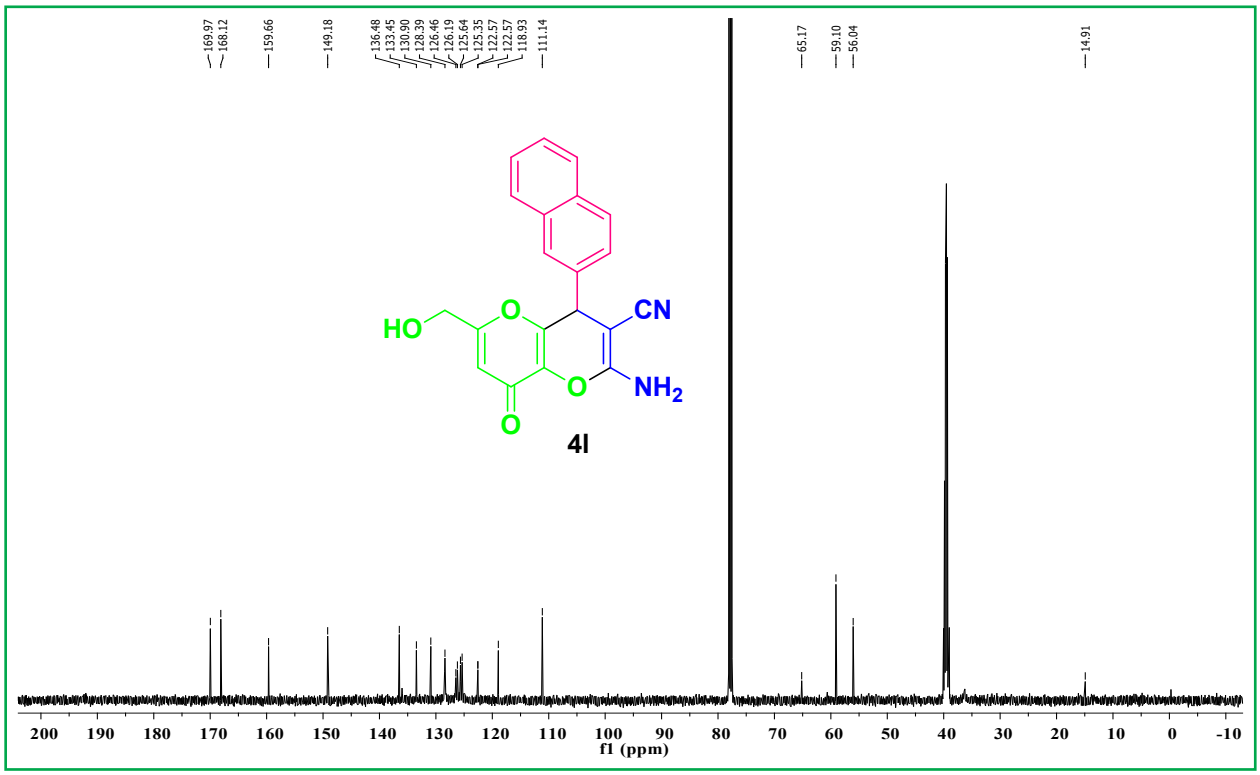


Figure S25: [13]C NMR spectra of 2-amino-6-(hydroxymethyl)-4-(naphthalene-2-yl)-8-oxo-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile **4l**

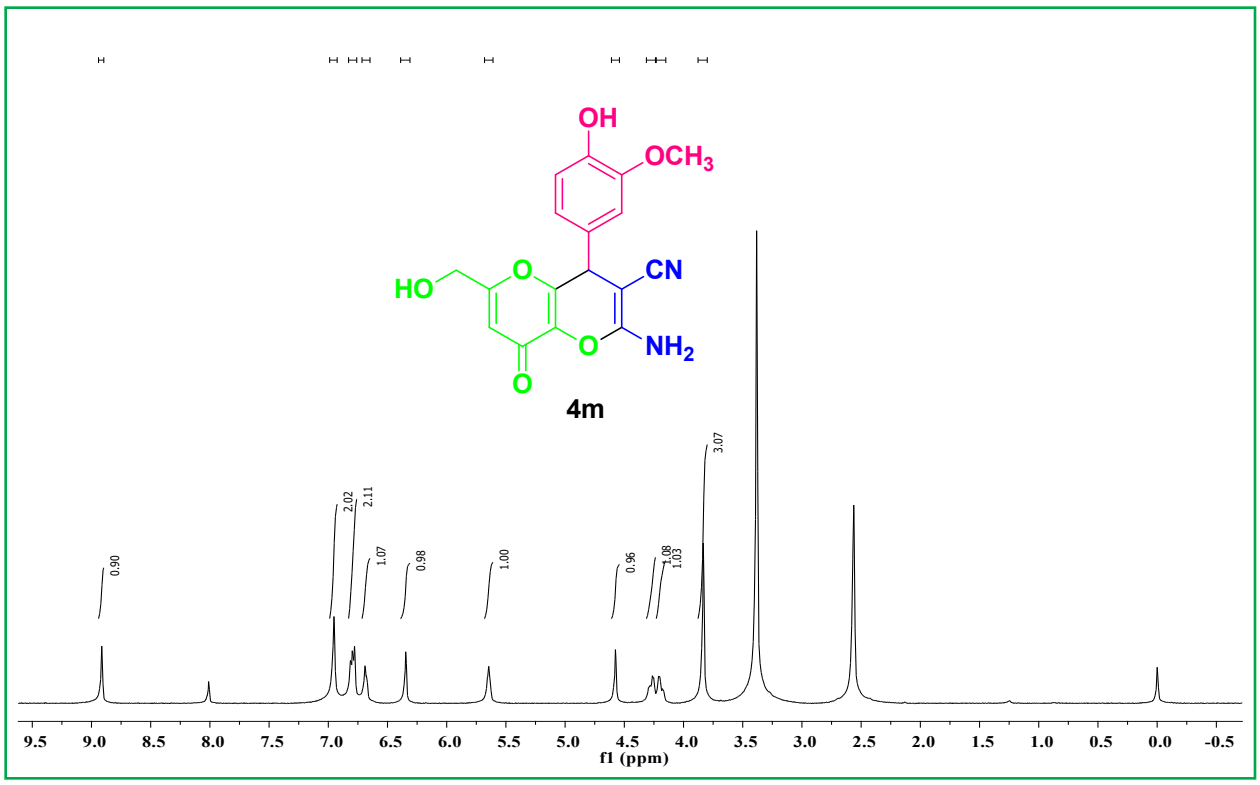


Figure S26: ^{1}H NMR spectra of 2-amino-4-(4-hydroxy-3-methoxyphenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4m**

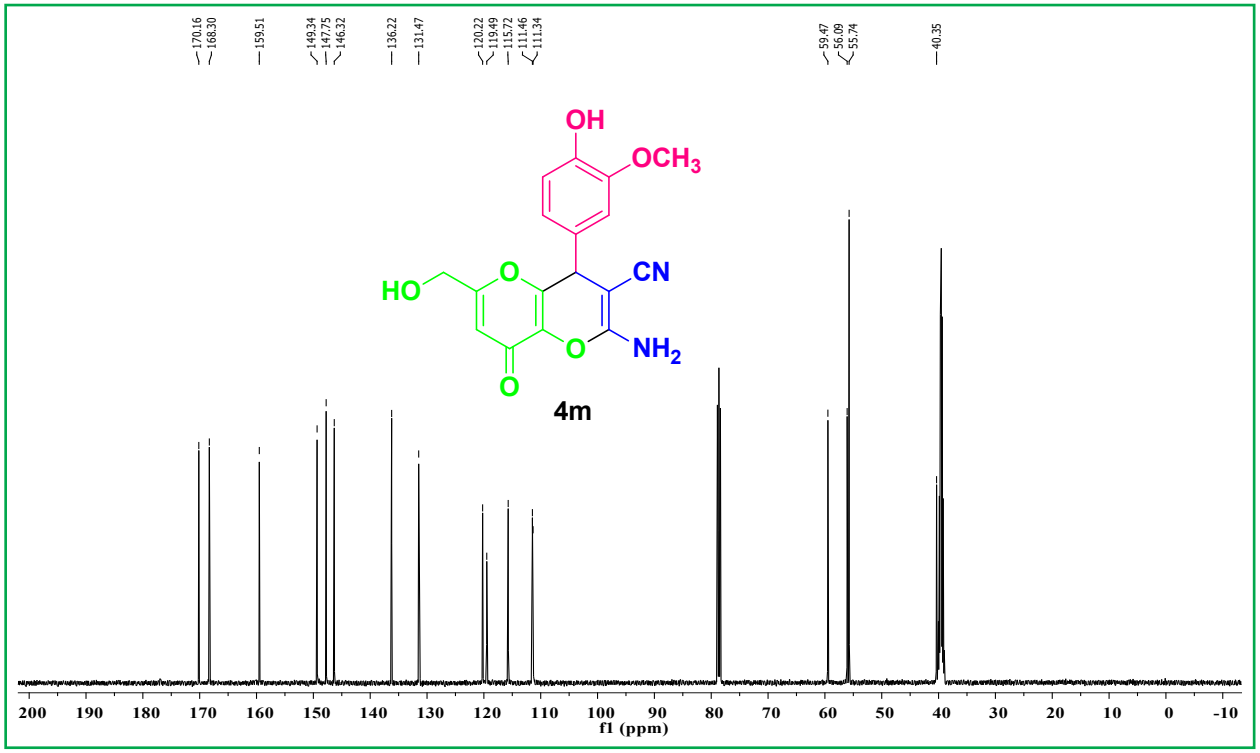


Figure S27: ^{13}C NMR spectra of 2-amino-4-(4-hydroxy-3-methoxyphenyl)-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4m**

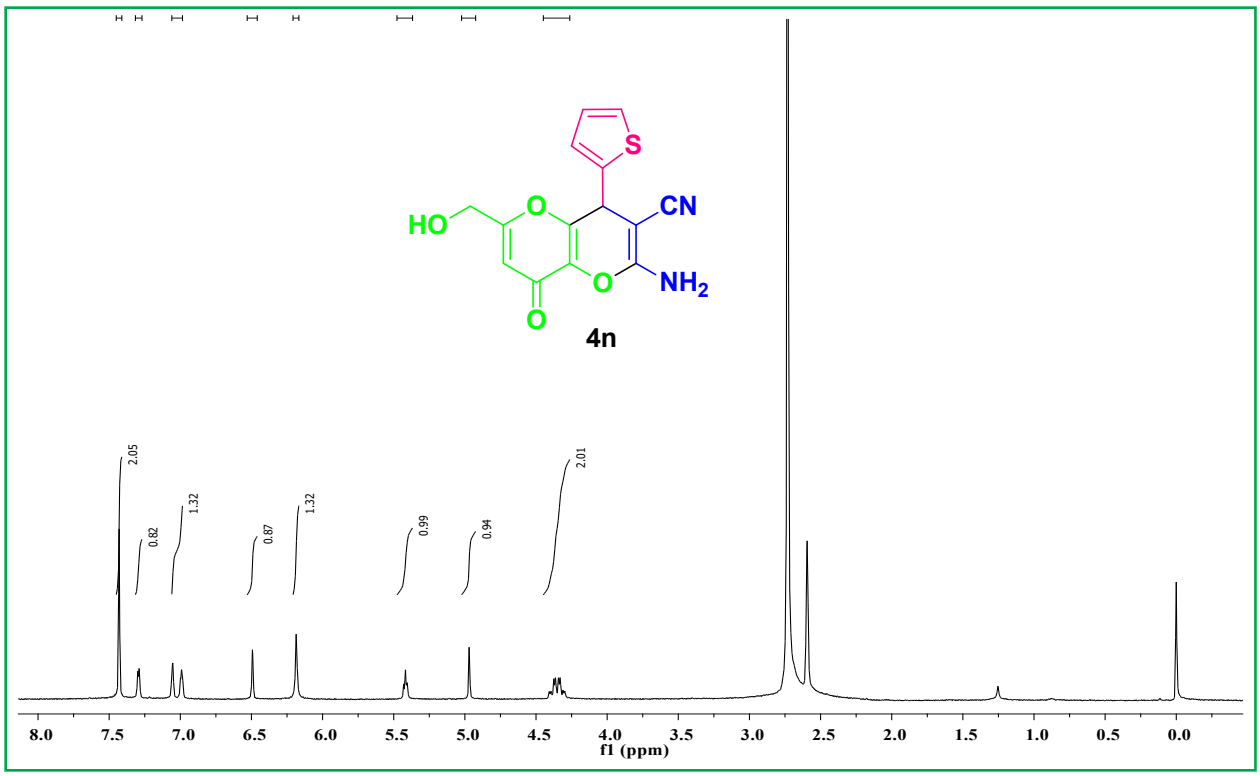


Figure S28: [1]H NMR spectra of 2-amino-6-(hydroxymethyl)8-oxo-4-(thiophen-2-yl)-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4n**

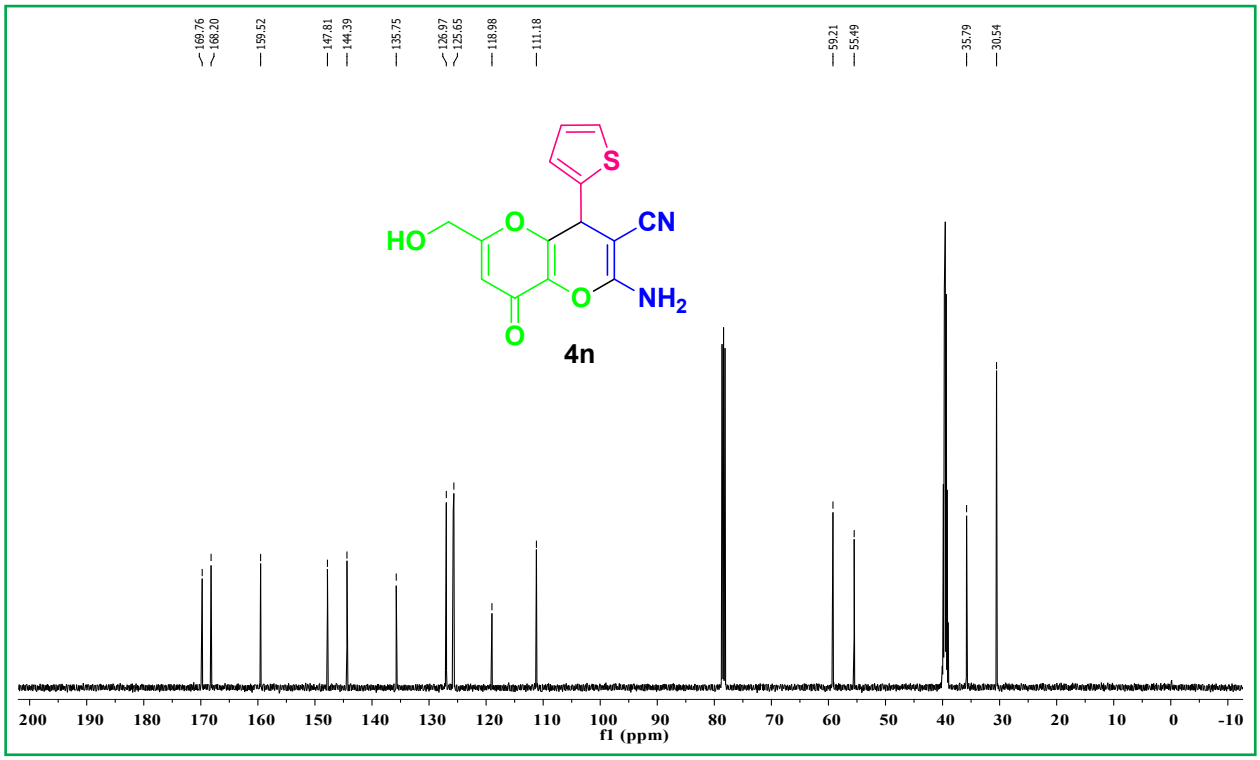


Figure S29: [13]C NMR spectra of 2-amino-6-(hydroxymethyl)8-oxo-4-(thiophen-2-yl)-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile **4n**

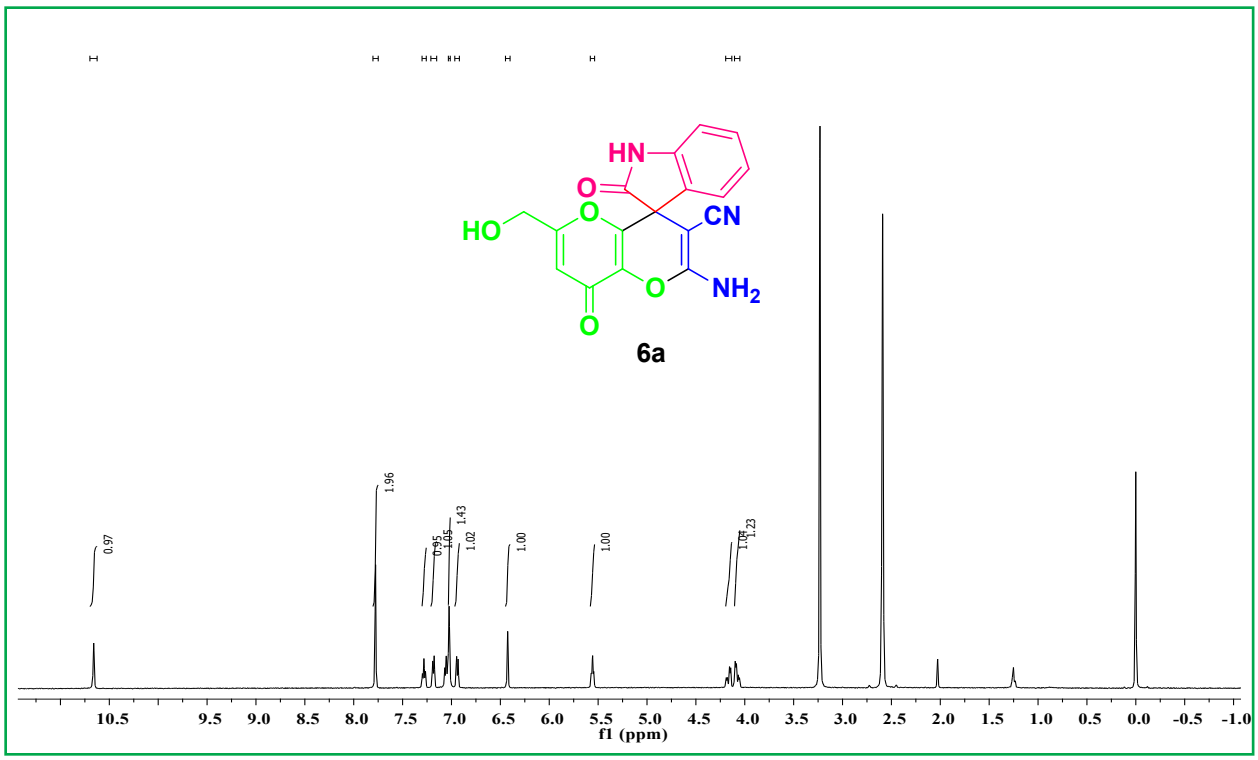


Figure S30: [1]H NMR spectra of 2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6a**

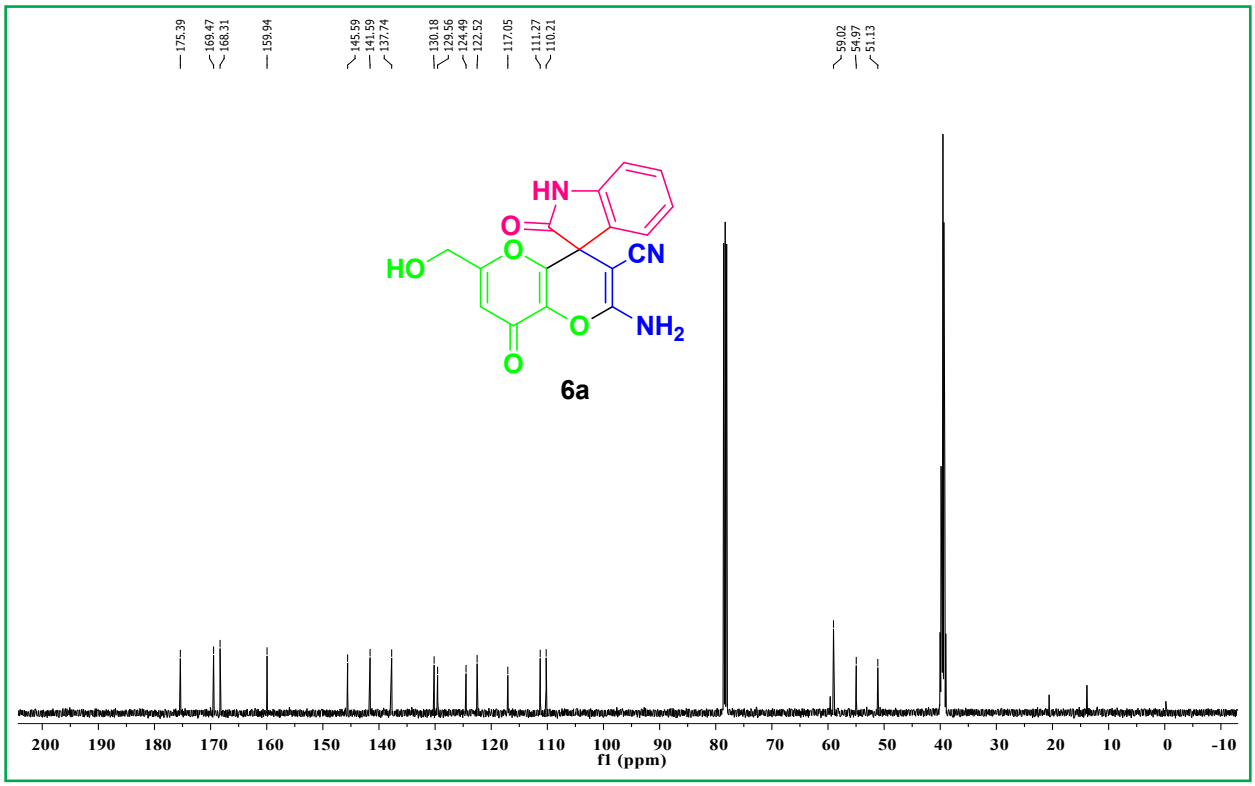


Figure S31: [13]C NMR spectra of 2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6a**

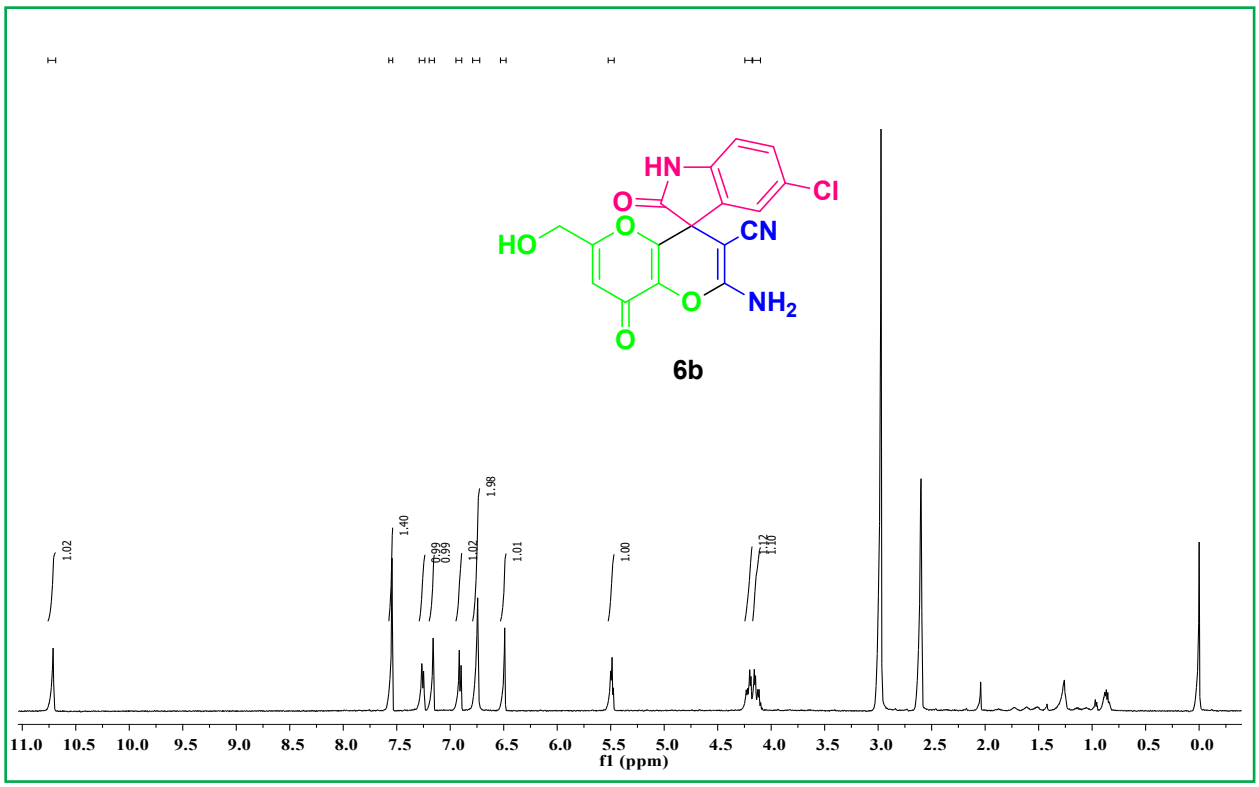


Figure S32: [1]H NMR spectra of 2′-amino-5-chloro-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6b**

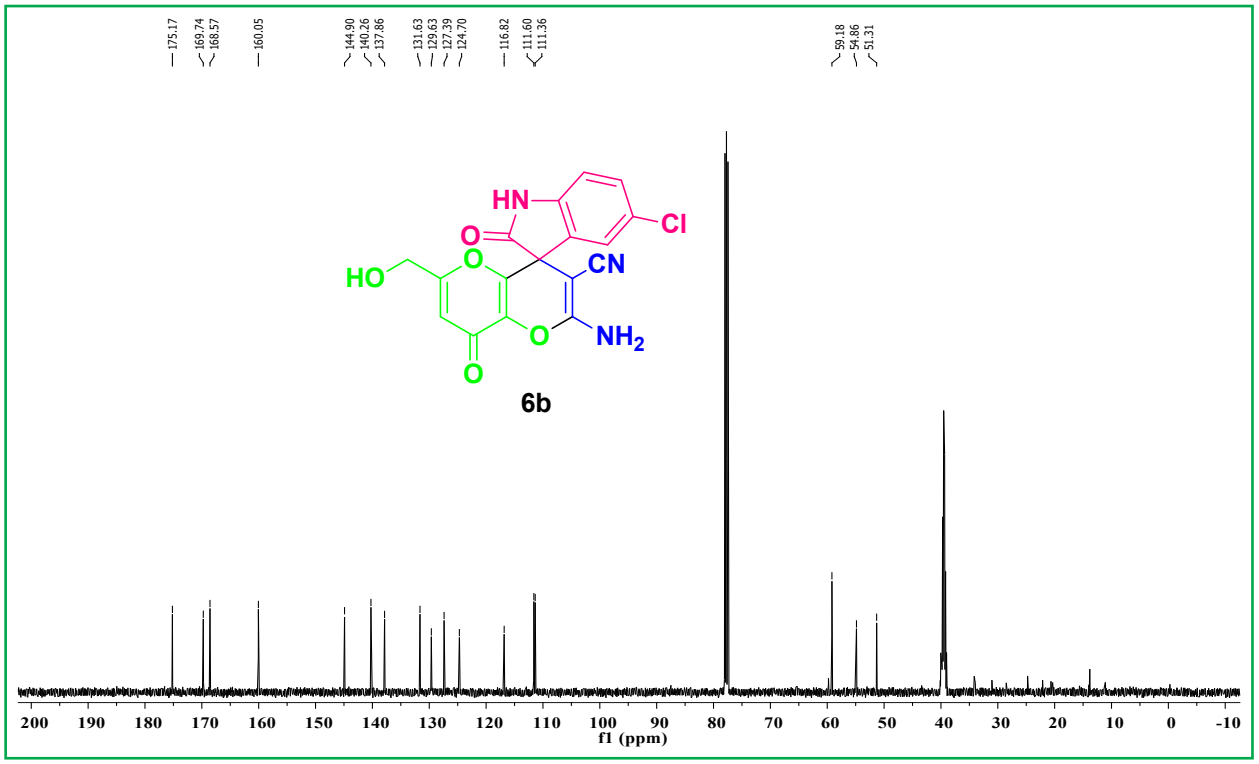


Figure S33: [13]C NMR spectra of 2′-amino-5-chloro-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6b**

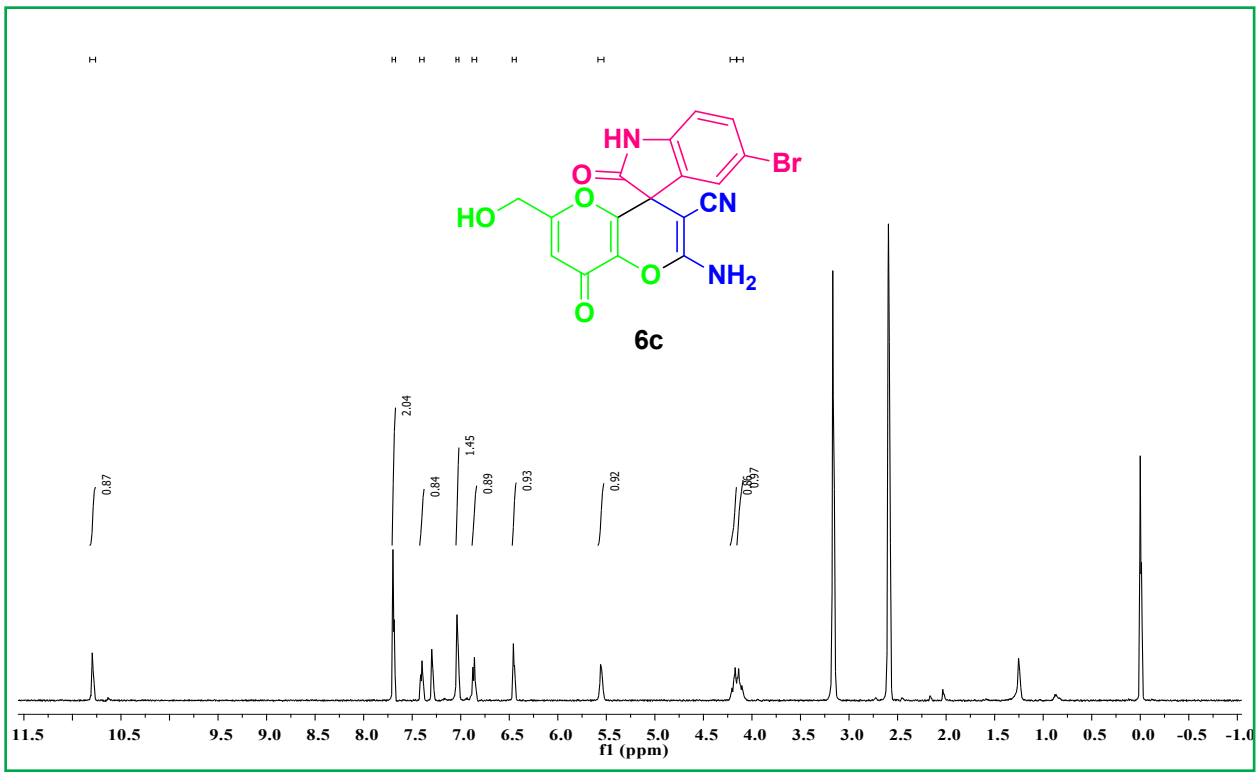


Figure S34: [1]H NMR spectra of 2′-amino-5-bromo-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6c**

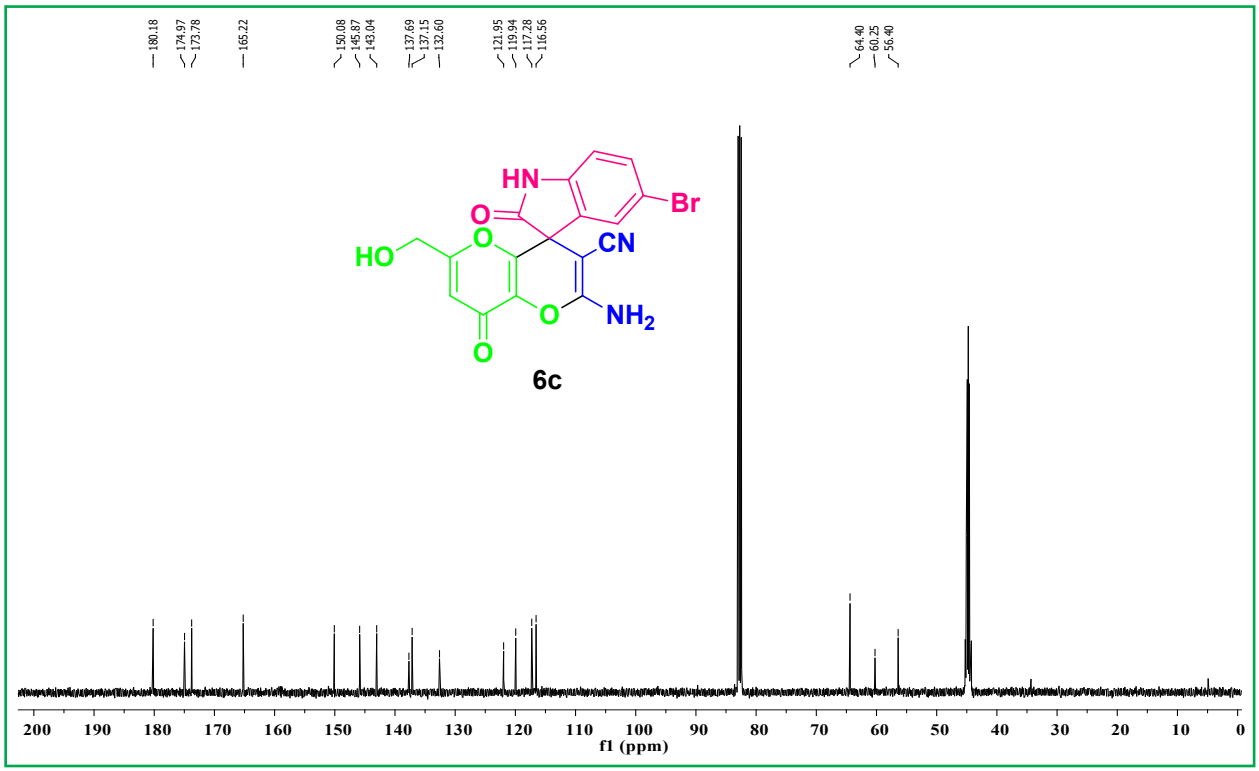


Figure S35: [13]C NMR spectra of 2′-amino-5-bromo-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6c**

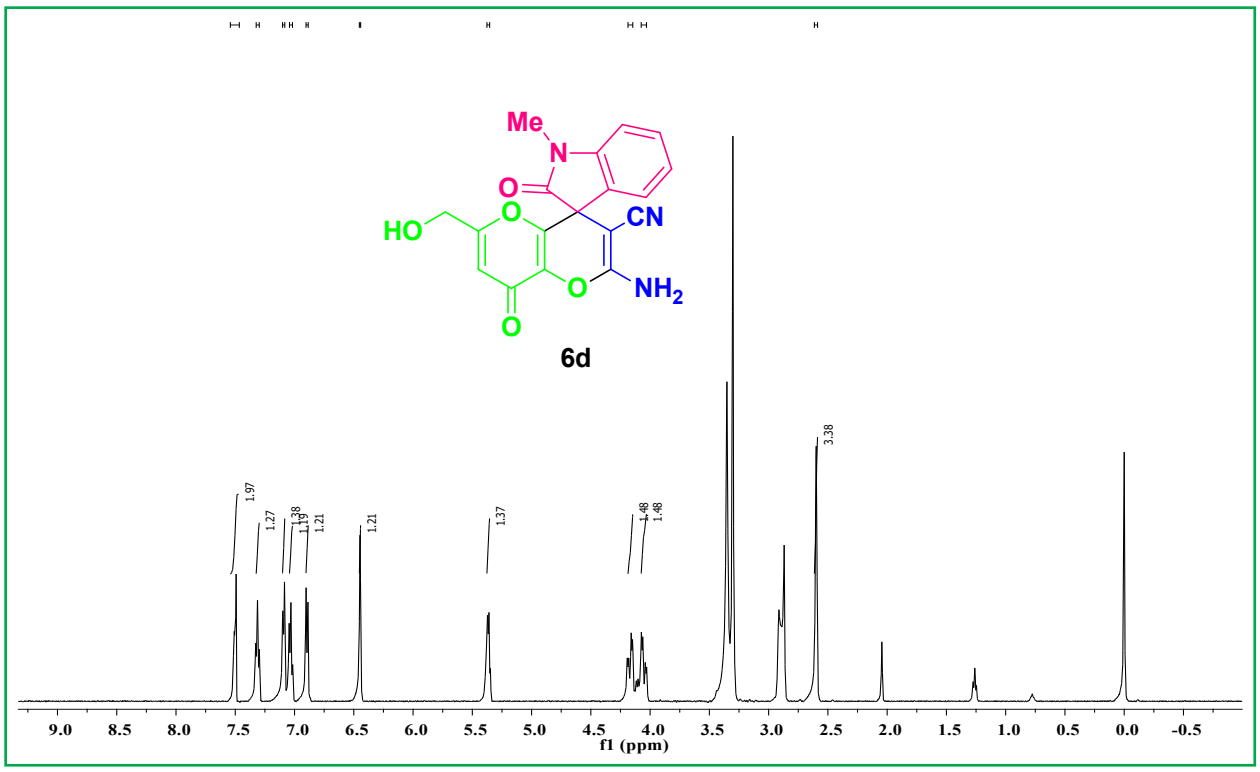


Figure S36: [1]H NMR spectra of 2′-amino-6′-(hydroxymethyl)-1-methyl-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6d**

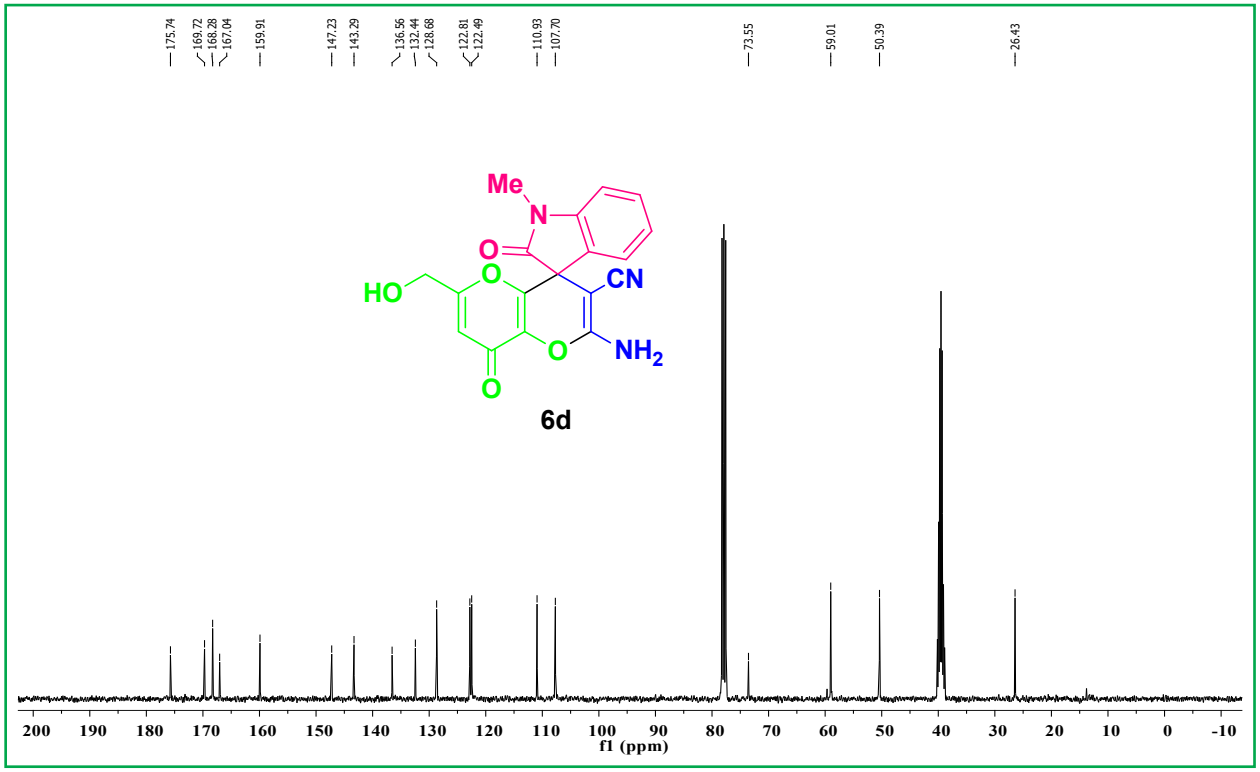


Figure S37: [13]C NMR spectra of 2′-amino-6′-(hydroxymethyl)-1-methyl-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6d**

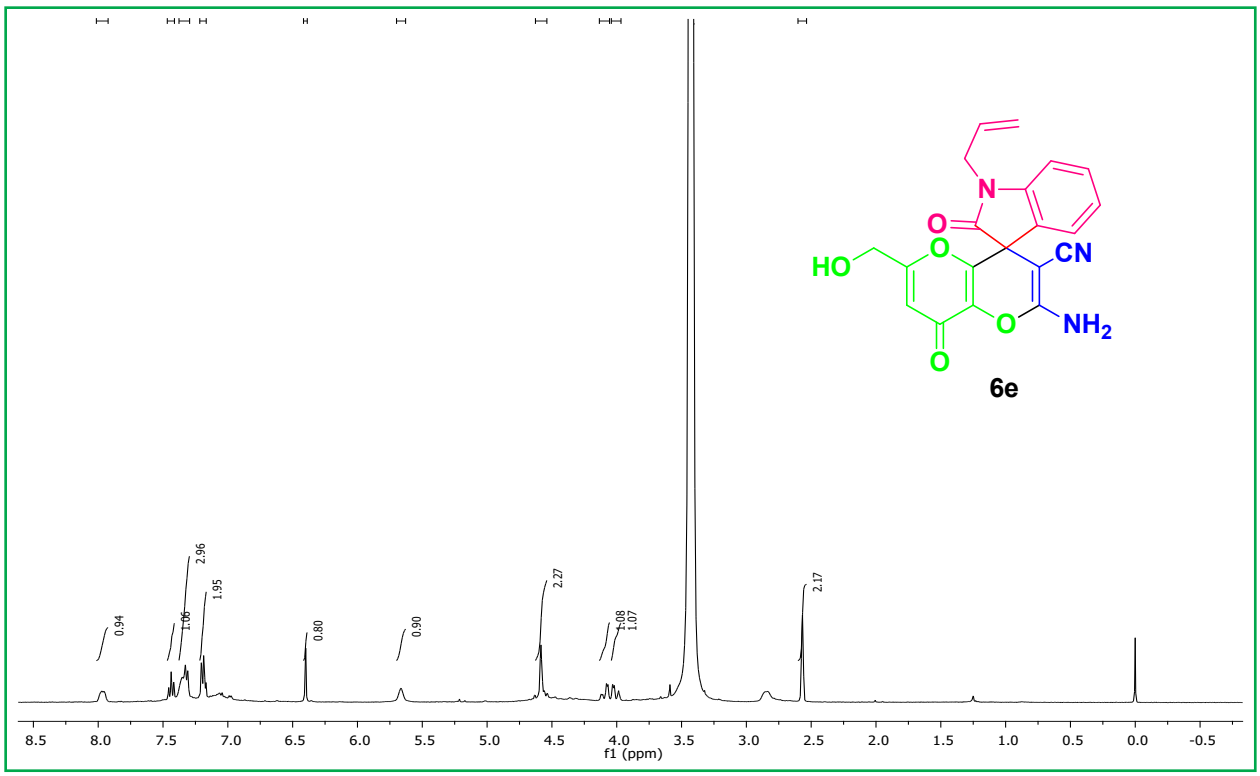


Figure S38: [1]H NMR spectra of 1-allyl-2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6e**

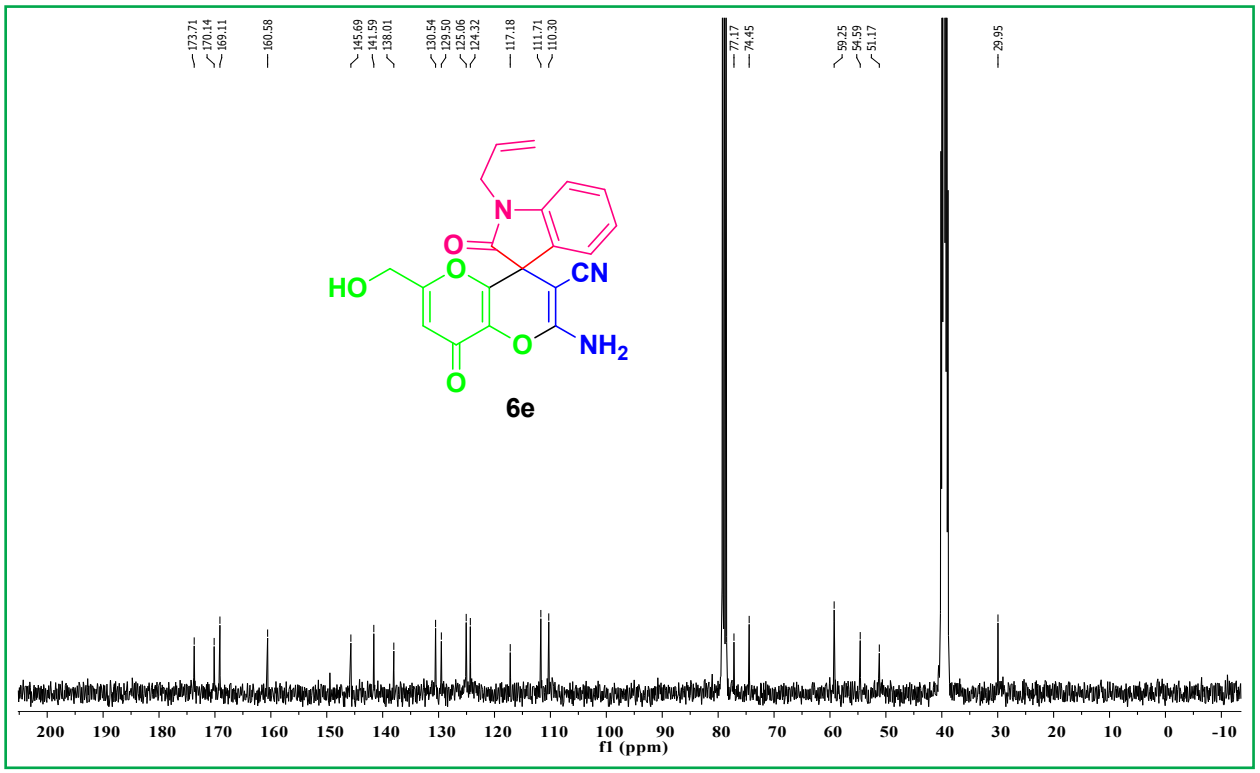


Figure S39: [13]C NMR spectra of 1-allyl-2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6e**

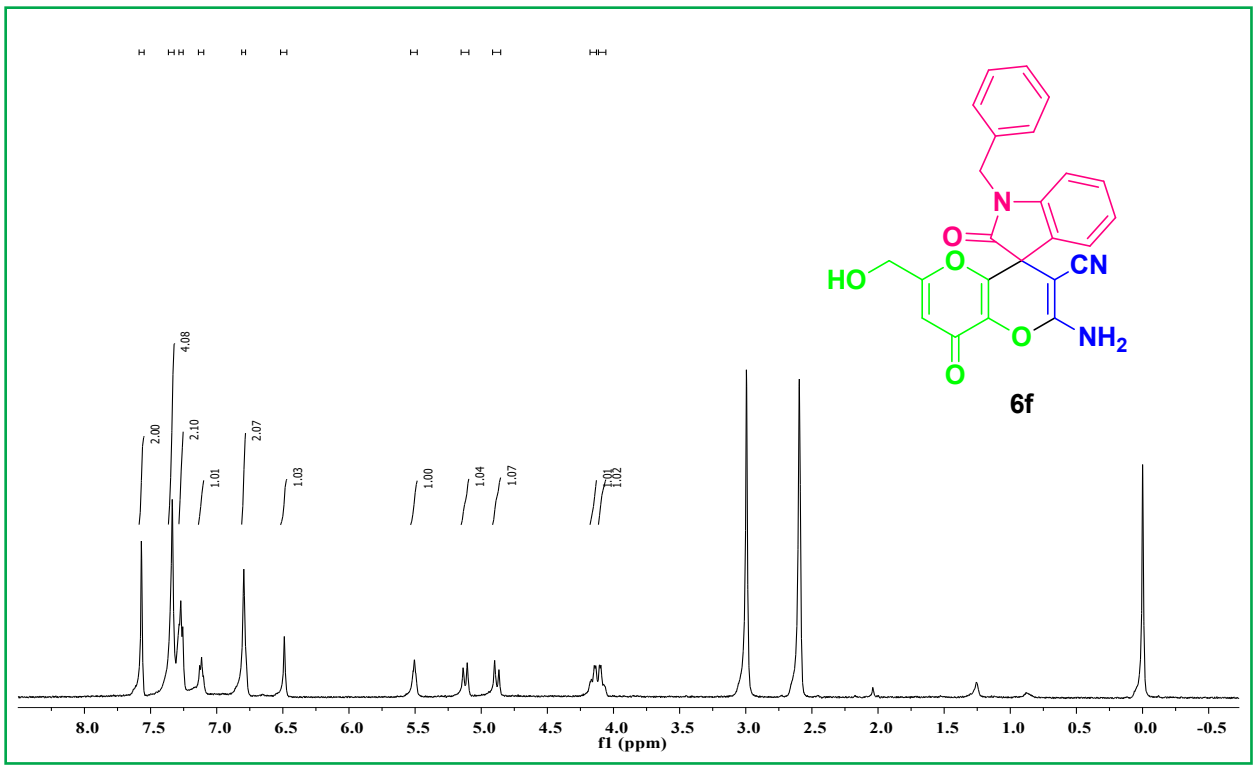


Figure S40: [1]H NMR spectra of 2′-amino-1-benzyl-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6f**

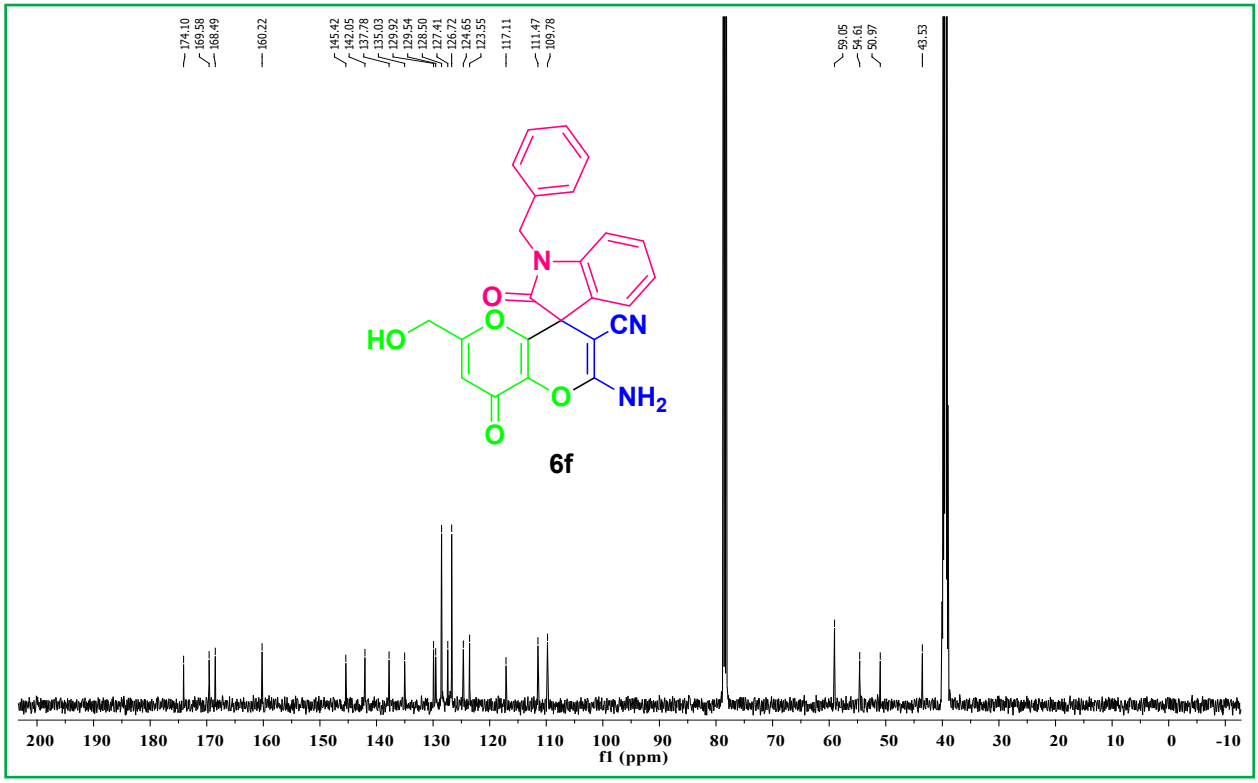


Figure S41: [13]C NMR spectra of 2′-amino-1-benzyl-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **6f**

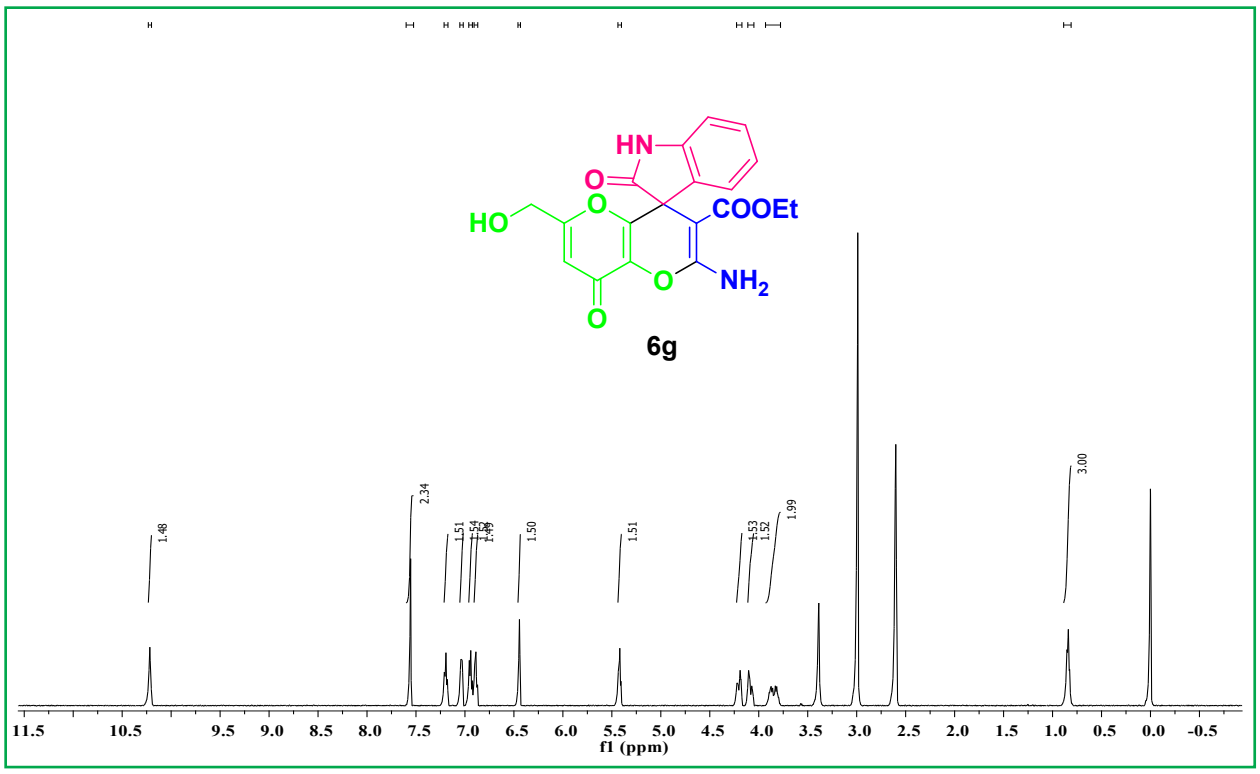


Figure S42: [1]H NMR spectra of Ethyl 2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **6g**

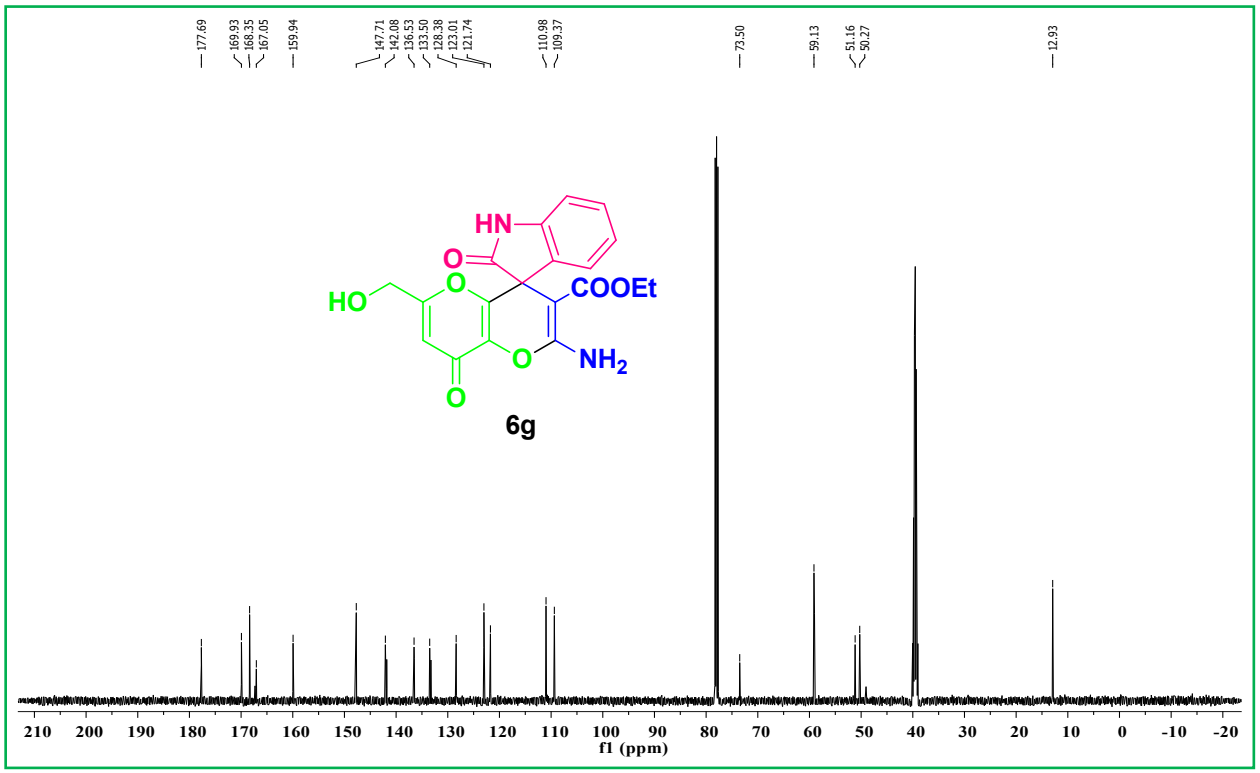


Figure S43: [13]C NMR spectra of Ethyl 2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **6g**

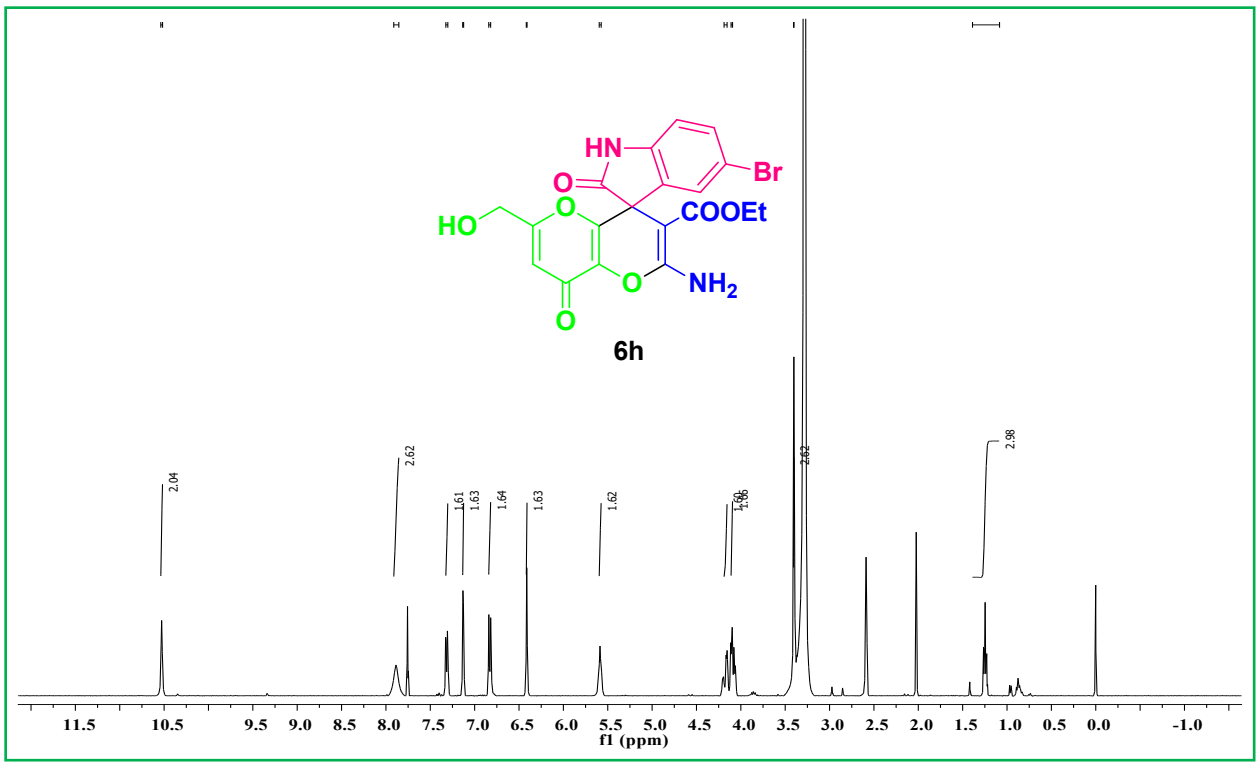


Figure S44: ^{1}H NMR spectra of Ethyl 2′-amino-5-bromo-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **6h**

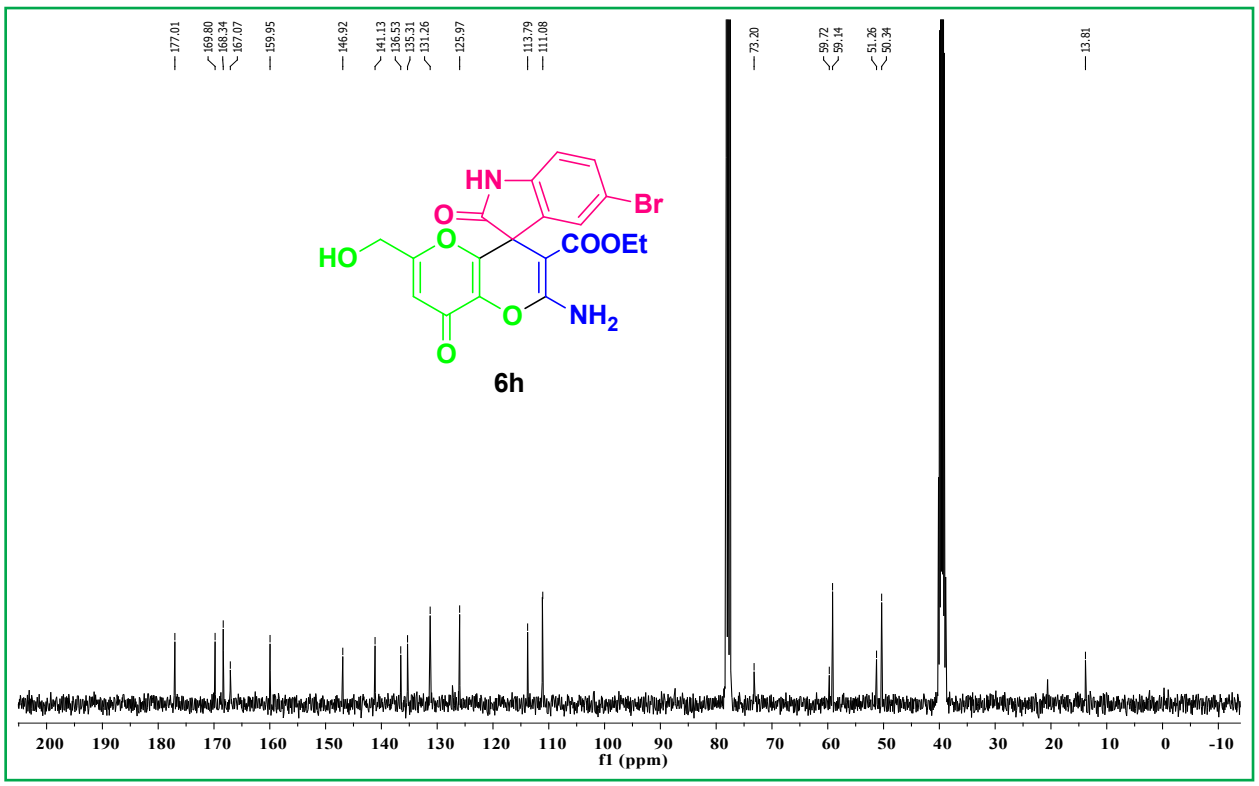


Figure S45: ^{13}C NMR spectra of Ethyl 2′-amino-5-bromo-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **6h**

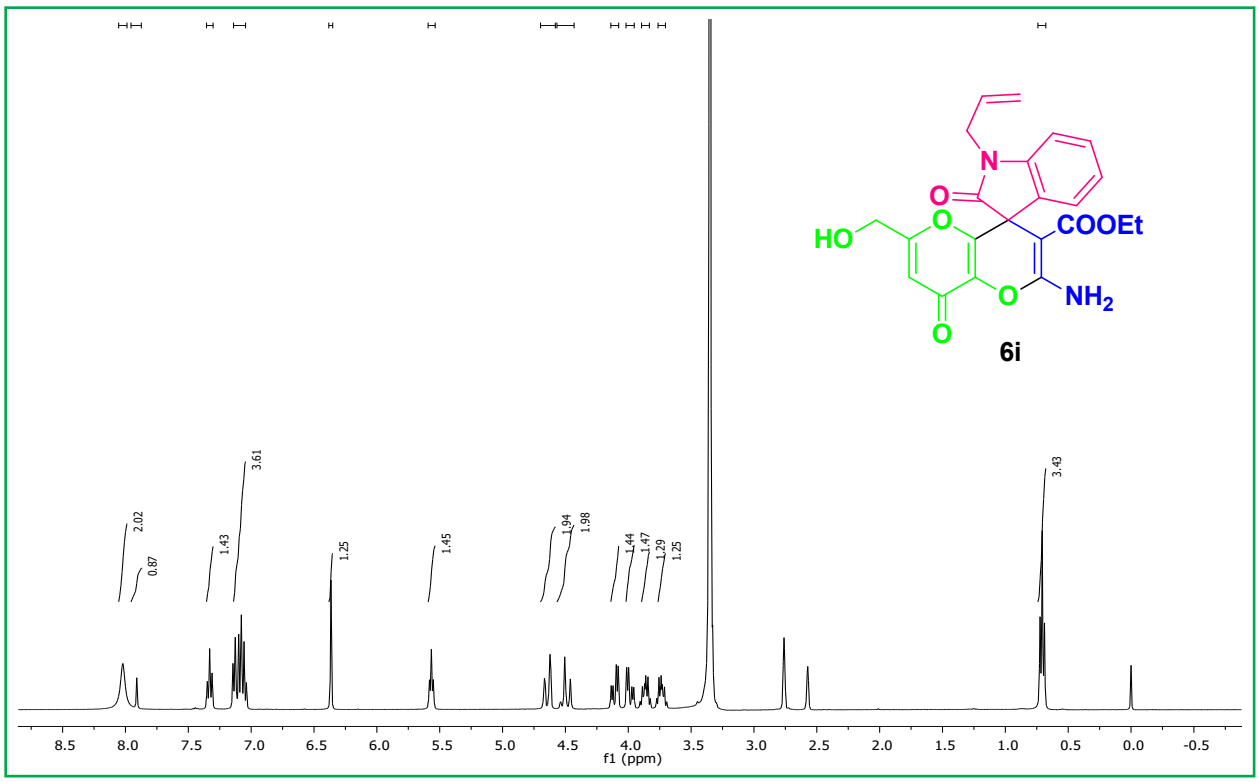


Figure S46: [1]H NMR spectra of Ethyl 1-allyl-2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **6i**

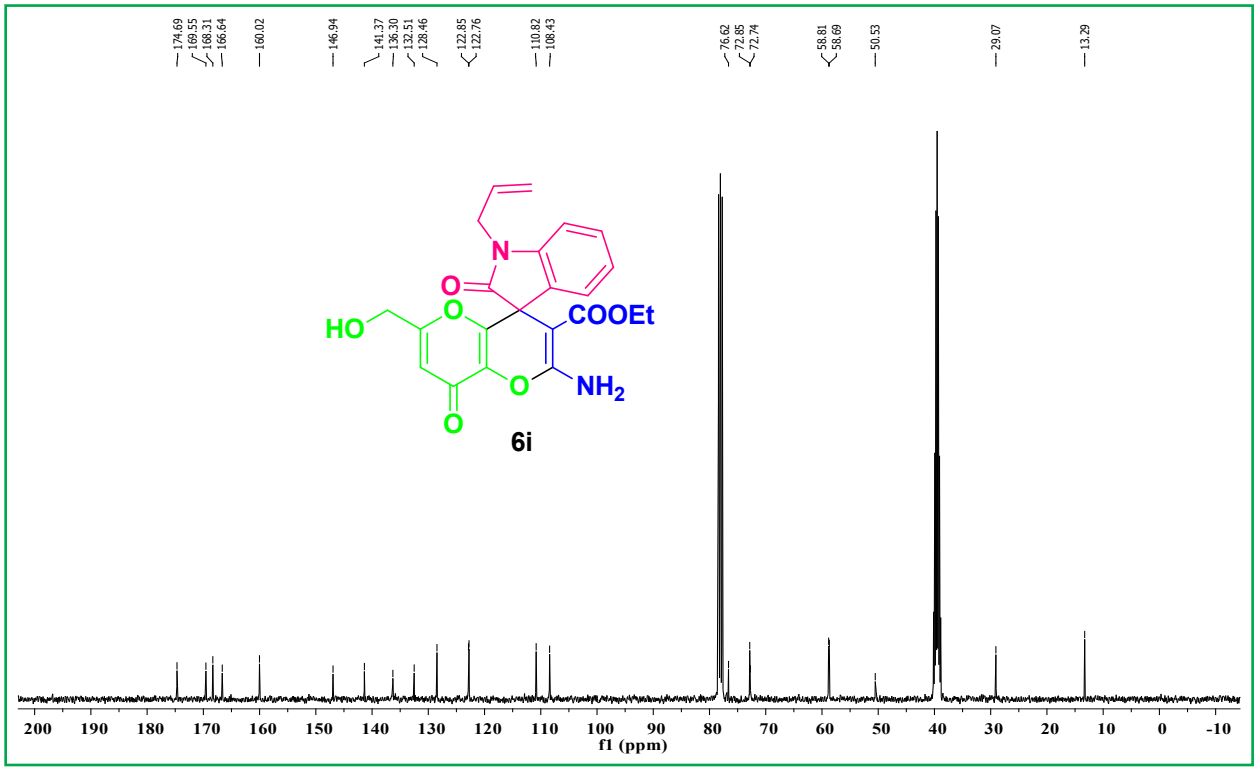


Figure S47: [13]C NMR spectra of Ethyl 1-allyl-2′-amino-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **6i**

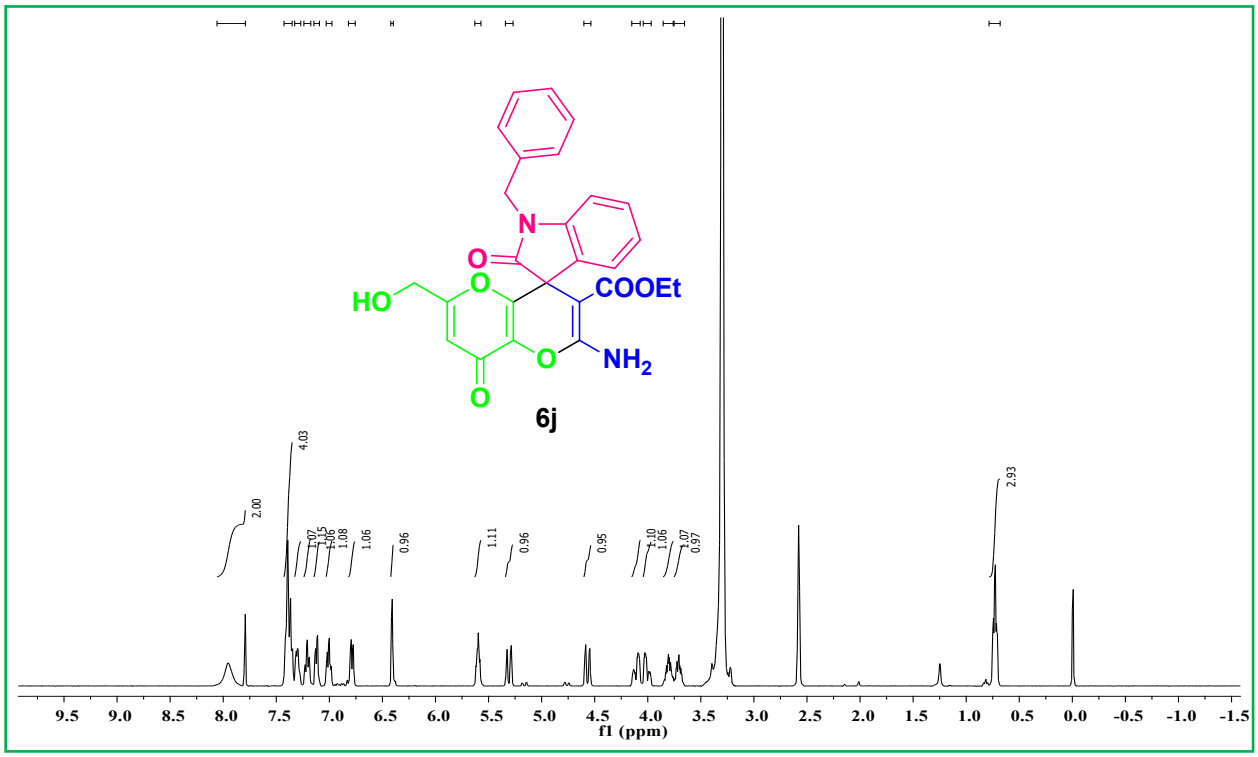


Figure S48: [1]H NMR spectra of Ethyl 2′-amino-1-benzyl-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **6j**

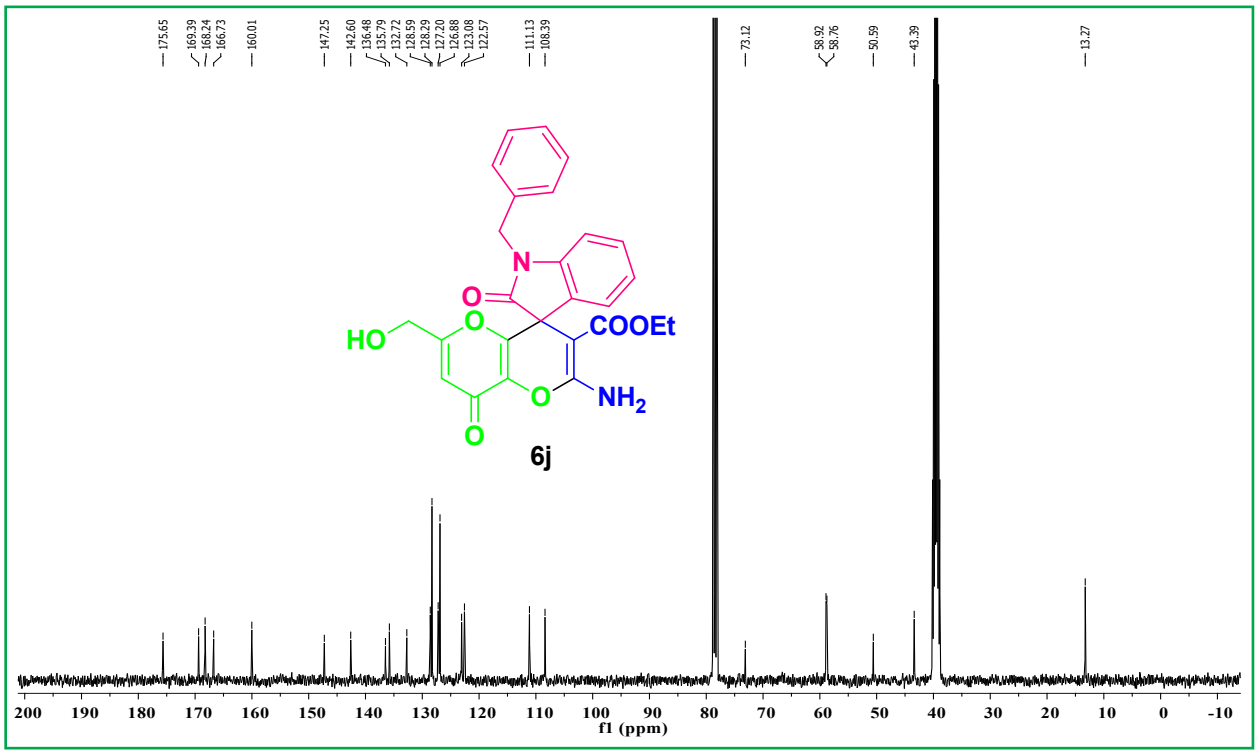


Figure S49: [13]C NMR spectra of Ethyl 2′-amino-1-benzyl-6′-(hydroxymethyl)-2,8′-dioxo-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **6j**

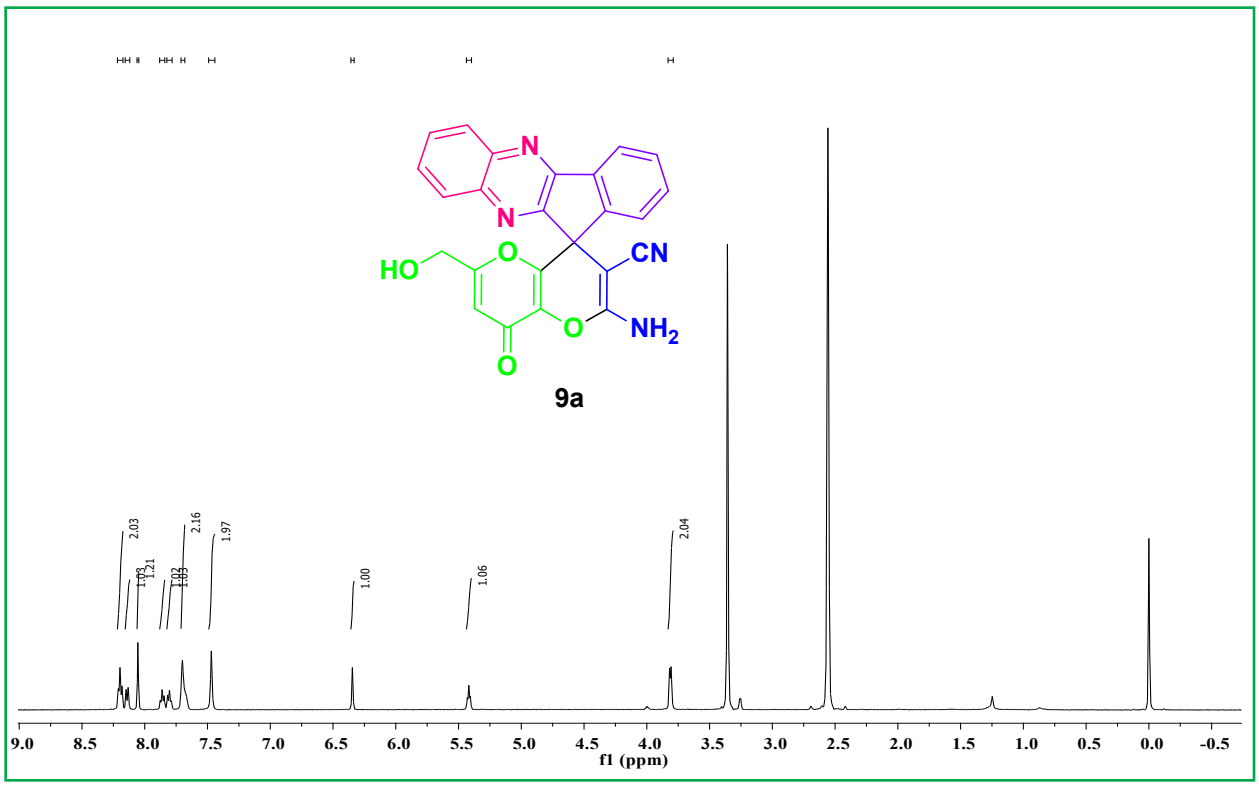


Figure S50: [1]H NMR spectra of 2′-amino-6′-(hydroxymethyl)-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano]3,2-*b*]pyran]-3′-carbonitrile **9a**

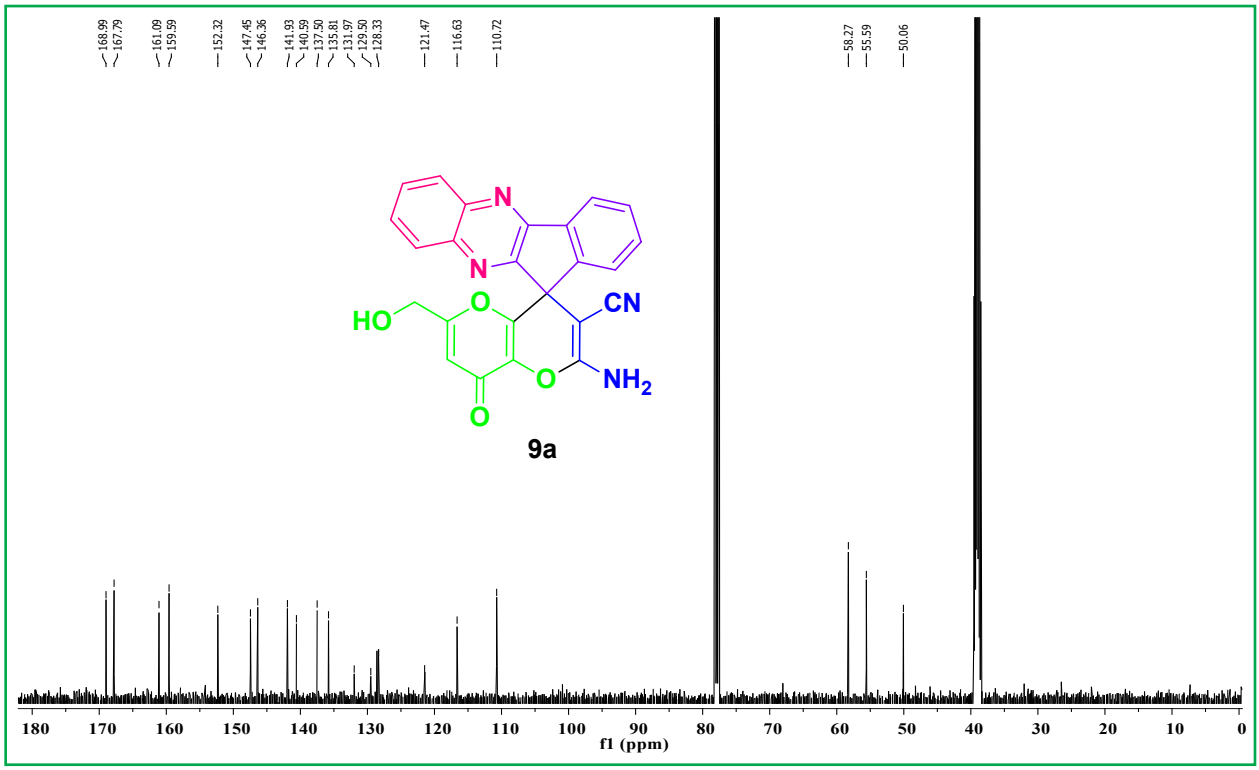


Figure S51: [13]C NMR spectra of 2′-amino-6′-(hydroxymethyl)-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano]3,2-*b*]pyran]-3′-carbonitrile **9a**

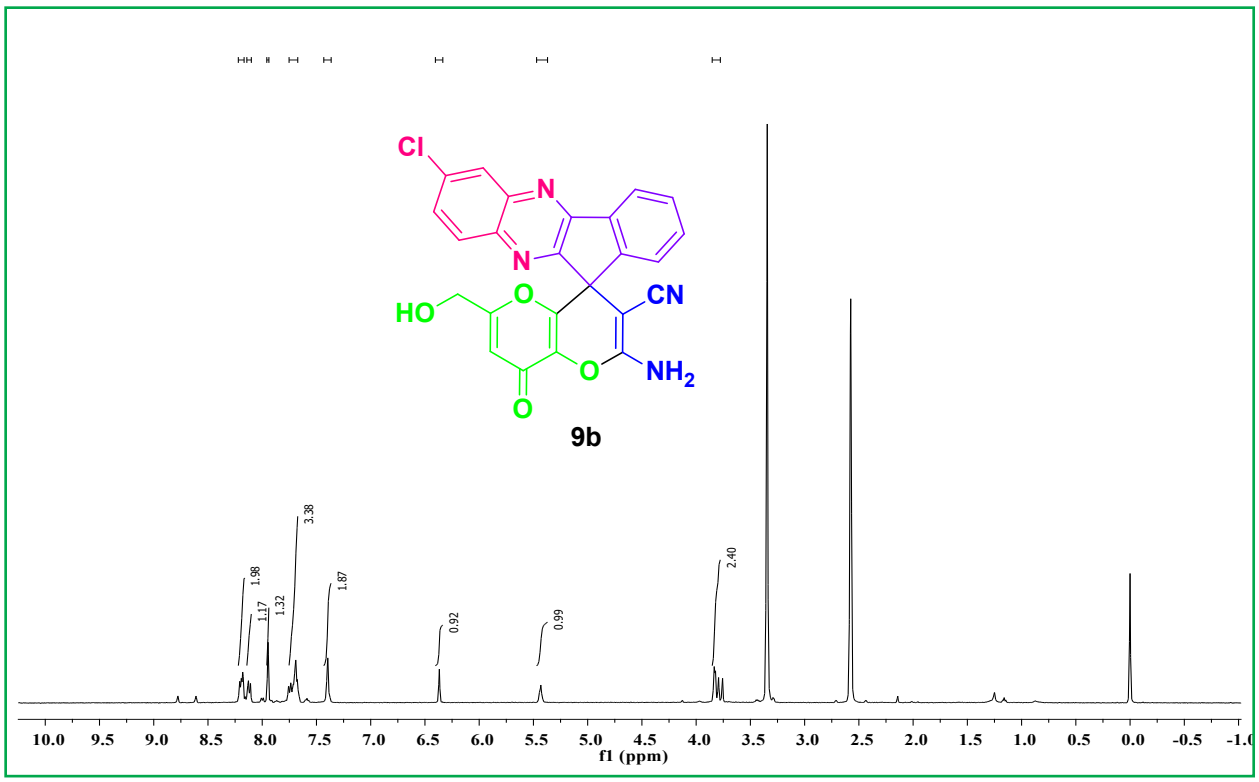


Figure S52: ^{1}H NMR spectra of 2′-amino-7-chloro-6′-(hydroxymethyl)-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **8b**

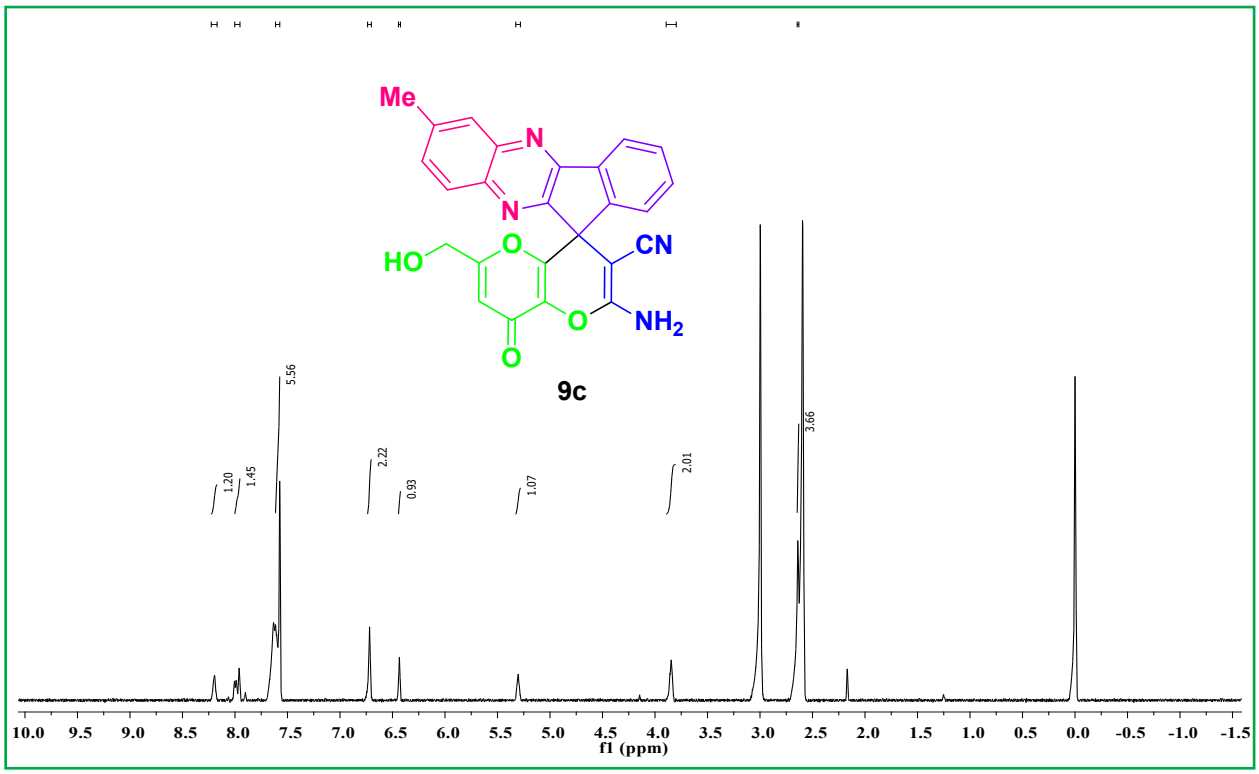


Figure S53: ^{1}H NMR spectra of 2′-amino-6′-(hydroxymethyl)-7-methyl-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11-4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **9c**

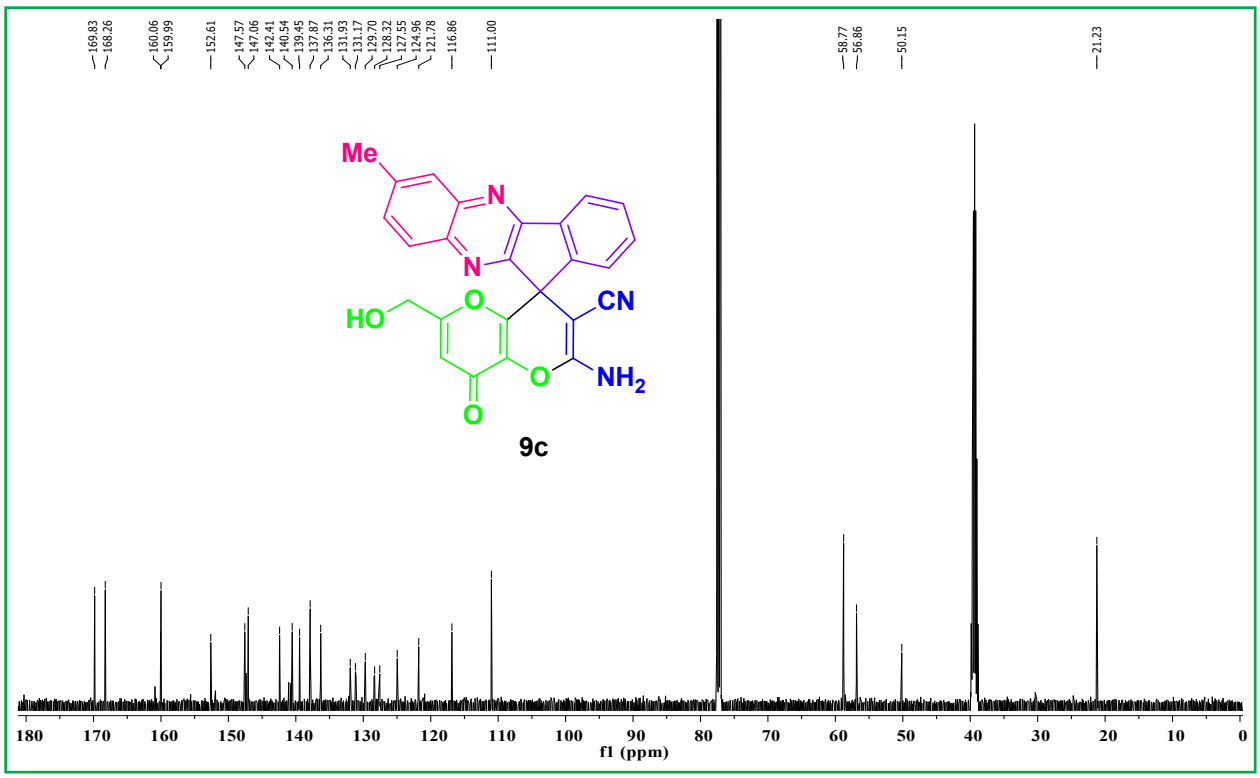


Figure S54: ^{13}C NMR spectra of 2′-amino-6′-(hydroxymethyl)-7-methyl-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11-4′-pyrano[3,2-*b*]pyran]-3′-carbonitrile **9c**

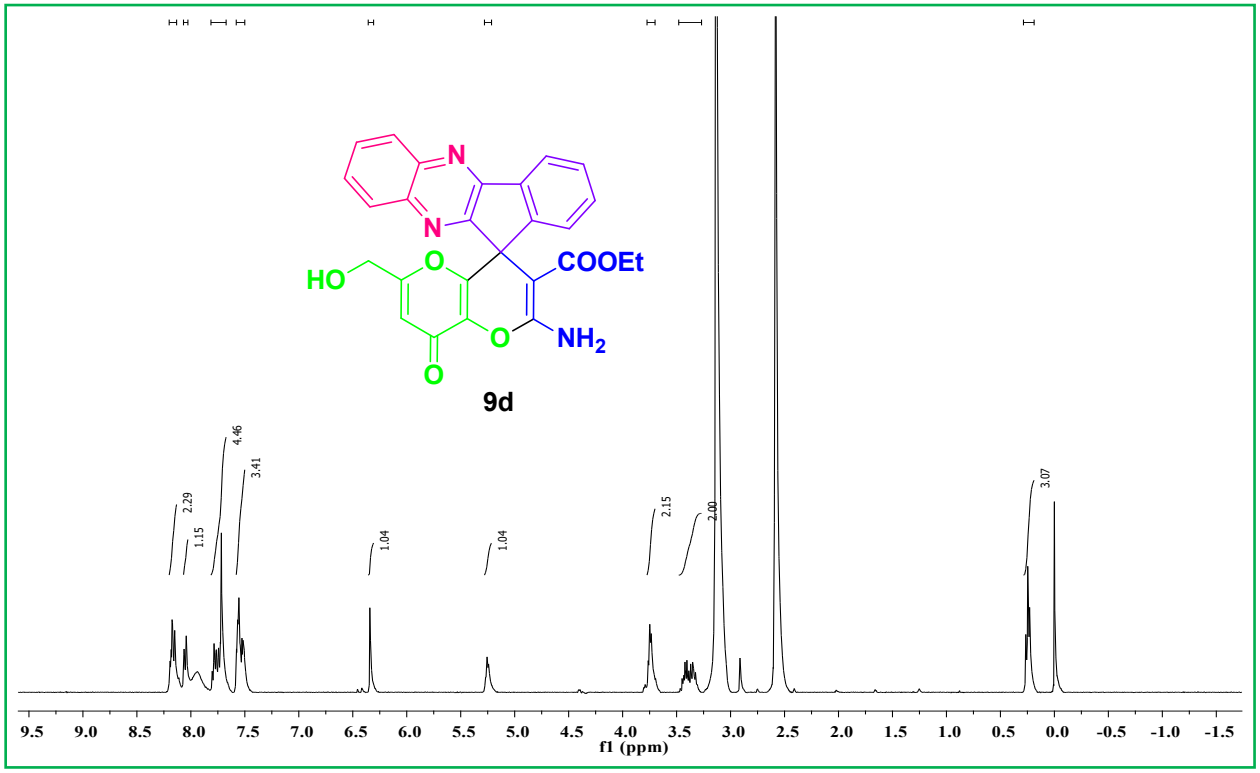


Figure S55: ^{1}H NMR spectra of Ethyl 2′-amino-6′-(hydroxymethyl)-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **9d**

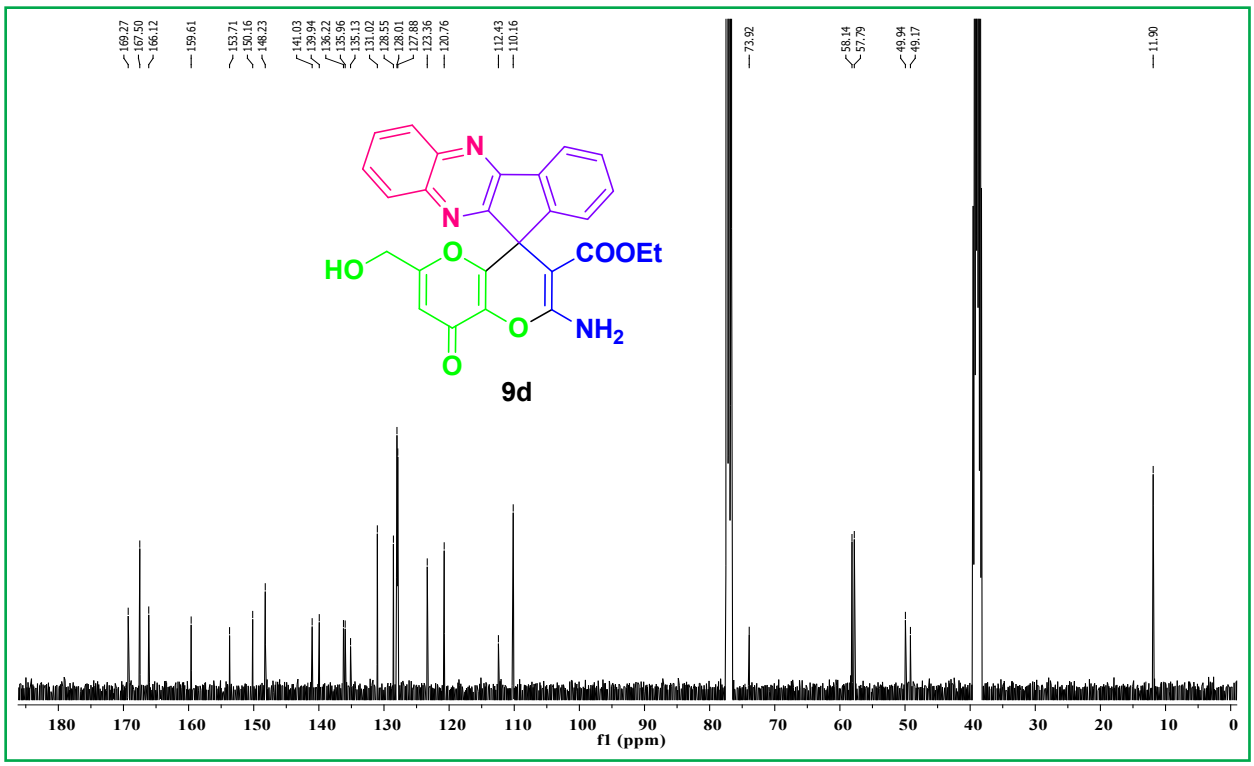


Figure S56: ^{13}C NMR spectra of Ethyl 2′-amino-6′-(hydroxymethyl)-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **9d**

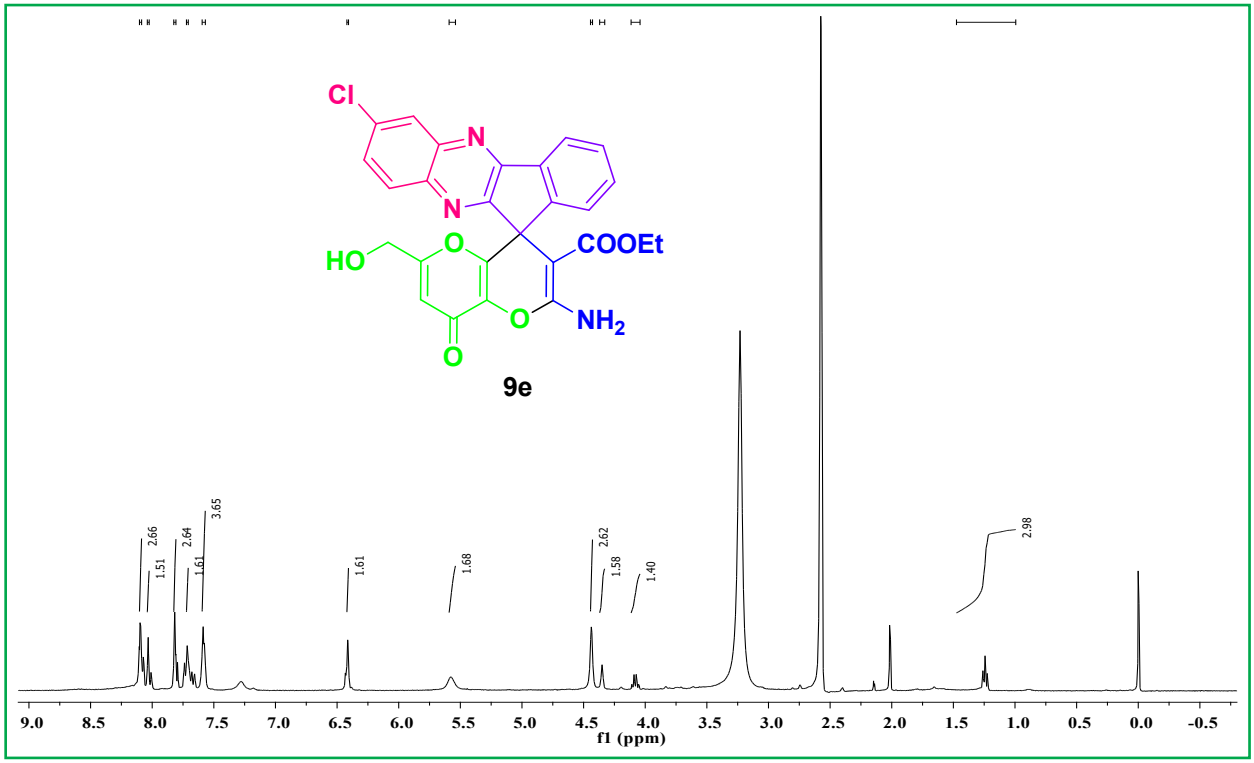


Figure S57: ^{1}H NMR spectra of Ethyl 2′-amino-6′-(hydroxymethyl)-7-chloro-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **9e**

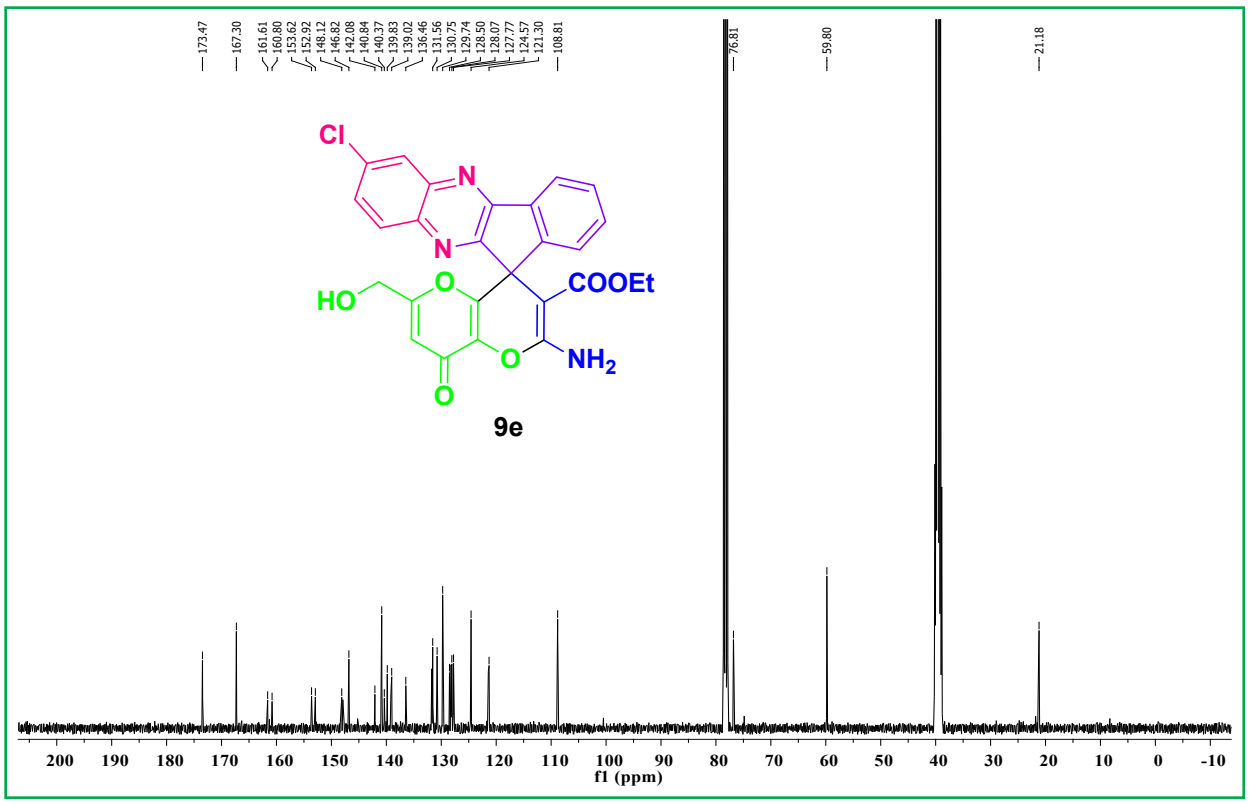


Figure S58: ^{13}C NMR spectra of Ethyl 2′-amino-6′-(hydroxymethyl)-7-chloro-8′-oxo-8′*H*-spiro[indeno[1,2-*b*]quinoxaline-11,4′-pyrano[3,2-*b*]pyran]-3′-carboxylate **9e**

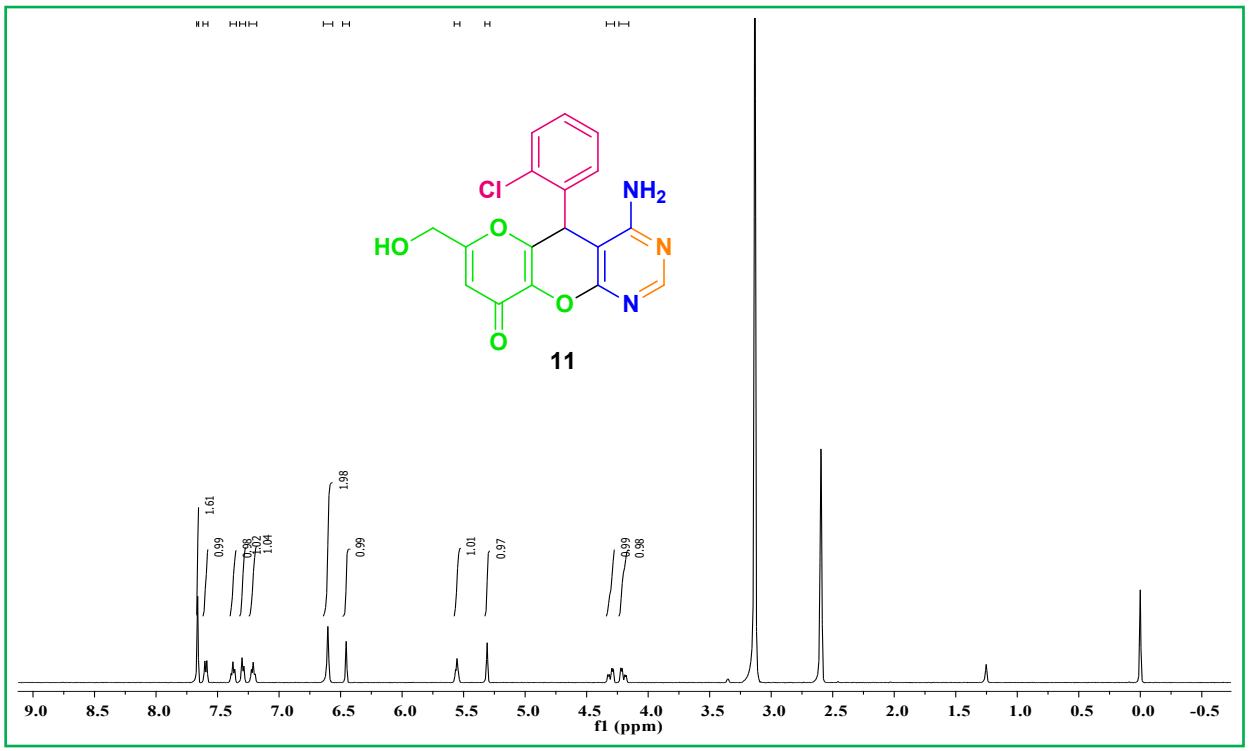


Figure S59: 4-amino-5-(2-chlorophenyl)-7-(hydroxymethyl)pyrano[2',3':5,6]pyrano[2,3-*d*]pyrimidin-9(5*H*)-one **11**