

Supplementary Information (SI)

A Three Component One-pot Synthesis of N-amino-2-pyridone Derivatives Catalyzed by KF-Al₂O₃

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Experimental

All commercially available chemicals and reagents were purchased from Sigma Aldrich, Merck and were used without further purification. The synthesized compounds were characterized by FT-IR, ^1H NMR, ^{13}C NMR and mass spectrometry analyses. Melting points were recorded with open capillary tube method and are uncorrected. FT-IR spectra were recorded with KBr pellets using a Perkin-Elmer 400 Series FT-IR spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance II-400 instrument operating at 400 MHz for protons, 100 MHz for carbon in dimethylsulfoxide ($\text{DMSO}-d_6$) as solvent (Chemical shifts in δ with tetramethylsilane (TMS) as internal standard. Electrospray ionization (ESI) mass spectra were recorded on a Waters ZQ-4000 LC-MS spectrometer. The progress of the reaction was monitored by thin-layer chromatography (TLC) analysis on pre-coated silica gel 60 F₂₅₄ aluminum sheets (Merck), visualized under UV-light.

X-ray Crystallography

The CIF files containing the crystal structural data of **4g** and **4i** were deposited in the Cambridge Crystallographic Data Center and can be obtained free of charge on request from the Cambridge Crystallographic Data Center.

<https://www.ccdc.cam.ac.uk/structures/>

The X-ray data of **4g** and **4i** were collected with a Agilent Xcalibur (Eos, Gemini) diffractometer using graphite monochromated Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$). The data was collected and refined in CrysAlis PRO (Rigaku, 2015)¹ software and data reduction was performed using the CrysAlisPro (Rigaku, 2015) software which corrects for Lorentz polarisation. A multi-scan absorption correction was performed using CrysAlisPro (Rigaku, 2015) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm. Using Olex2², the structure was solved with the ShelXS³ structure solution program using Direct Methods and refined with ShelXL-2018⁴ using full matrix least squares on F^2 minimisation. All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model. The ORTEP view of **4 (g & i)** were illustrated by ORTEP-3⁵ as shown in **Figure 1**.

Supplementary Information (SI)

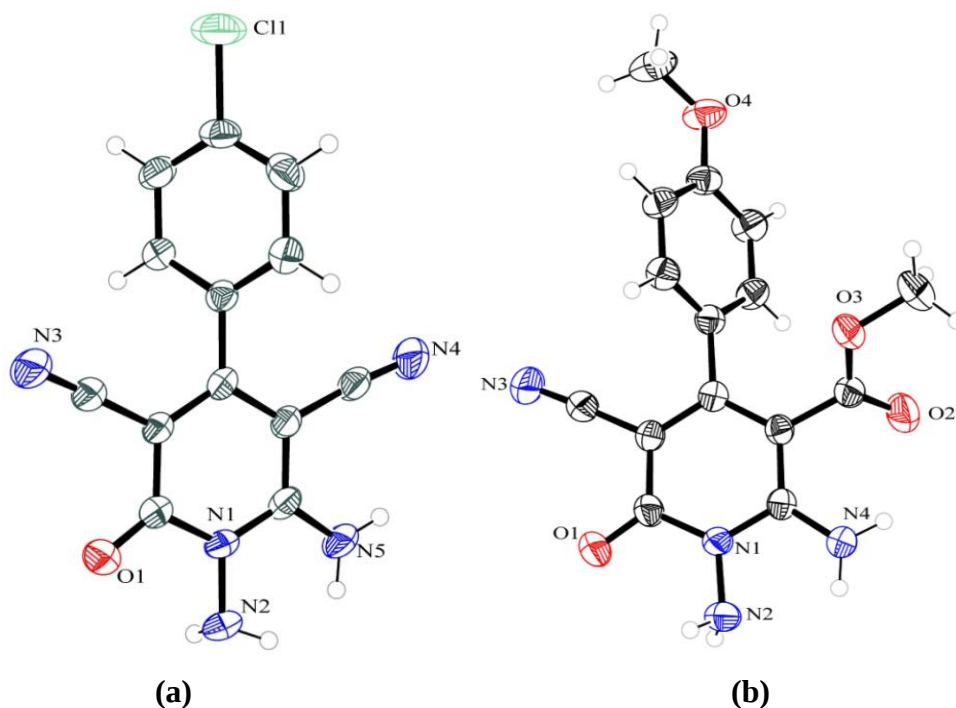


Figure 1 Ortep image of (a) **4g** (CCDC 1824530) and (b) **4i** (CCDC 1824529) showing thermal ellipsoids at 50% probability level.

Table 1 X-ray crystallography data for compound **4g** (CCDC 1824530) and (b) **4i** (CCDC 1824529).

Empirical formula	C ₁₃ H ₈ ClN ₅ O (4g)	C ₁₅ H ₁₄ N ₄ O ₄ (4i)
Formula weight	285.69	314.30
Temperature (K)	292.6(6)	295.7(6)
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	P2 ₁ /c	P2 ₁ /n
<i>a</i> (Å)	9.1112 (11)	9.3961 (7)
<i>b</i> (Å)	7.8131 (11)	14.2120 (9)
<i>c</i> (Å)	17.807 (2)	11.5460 (9)
α (°)	90	90

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β (°)	94.076 (11)	99.299 (7)
$\gamma=\alpha$ (°)	90	90
Volume (Å ³)	1264.4 (3)	1521.56 (19)
Z	4	4
ρ (calc.) (g/cm ³)	1.501	1.372
Absorption coefficient (μ) (mm ⁻¹)	0.305	0.102
F(000)	584	656
2 θ range for data collection (°)	6.638 to 52.73	6.738 to 52.74
Index ranges	-5 $\leq$ h $\leq$ 11, -9 $\leq$ k $\leq$ 8, -22 $\leq$ l $\leq$ 21	-11 $\leq$ h $\leq$ 10, -17 $\leq$ k $\leq$ 16, -14 $\leq$ l $\leq$ 14
Reflections collected	4883	5888
Independent reflections	2562 [R _{int} = 0.0305]	3109 [R _{int} = 0.0294]
Data / restraints / parameters	2562 / 0 / 182	3109 / 0 / 211
Goodness-of-fit on F ²	1.014	1.028
Final R indices [I $\geq$ 2 σ (I)]	R ₁ = 0.0532, wR ₂ = 0.1334	R ₁ = 0.0482, wR ₂ = 0.1048
R indices (all data)	R ₁ = 0.0823, wR ₂ = 0.1526	R ₁ = 0.0749, wR ₂ = 0.1189

Preparation of catalyst (KF-Al₂O₃):

The catalyst, KF-Al₂O₃ was prepared according to the method reported in the literature⁶, with some modification⁶. A mixture of potassium fluoride (5.8 g, 10 mmol) and activated neutral alumina (10 g, 10mmol) in water (10 mL) was stirred at room temperature for 12 hrs. The resulting suspension was concentrated on rotary evaporator at 60° C, and then dried in desiccators under vacuum for 12 hrs. After activation in hot oven at 140°C for 12 hrs, KF-Al₂O₃ was used for catalysis.

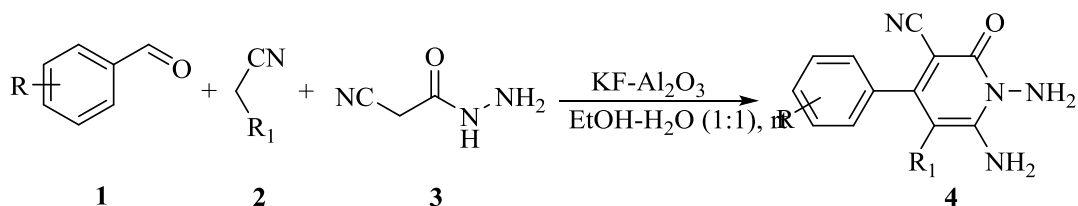
Supplementary Information (SI)

General procedure

Synthesis of Cyanoacetic hydrazide:

Cyanoacetic acid hydrazide was obtained by careful addition of 22.62 g (0.20 mol) of ethyl cyanoacetate to hydrazine hydrate (10.01 g, 0.20 mol) with stirring at 0 °C⁷. The solid cyanoacetic acid hydrazide so formed was filtered, washed with Et₂O, and dried in which a yield of 95% is obtained.

Synthesis of N-amino-2-pyridone derivatives:



2a; R₁=CN, **2b;** R₁=COOMe, **2c;** R₁=COOEt

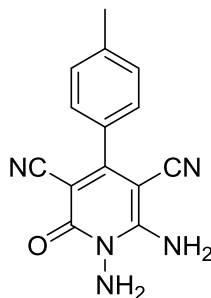
Scheme 1: Synthesis of *N*-amino-2-pyridone derivatives

A mixture of aromatic aldehydes **1** (2 mmol), active methylene compound **2** (2.1 mmol) and cyanoacetic hydrazide (2.1 mmol), 15 mol% of KF-Al₂O₃ in 1:1 EtOH-H₂O (6 mL) was stirred and the progress of the reaction was monitored by TLC. On completion, the reaction solution was filtered and washed with ethyl acetate and the catalyst was recovered and recycled. The solvent was evaporated and the solid which separated out was collected and recrystallized with ethanol to get pure product. A few members of the synthesised products were purified by column chromatography. The synthesised products were characterised from their ¹H NMR, ¹³C NMR, FT-IR and single crystal XRD analyses.

Supplementary Information (SI)

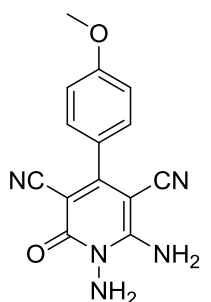
Analytical data for the *N*-amino-2-pyridone derivatives:

1,6-diamino-4-(*p*-tolyl)-3,5-dicyano-2-pyridone 4(a)



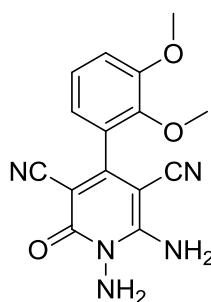
White crystals; yield: 95%, mp 237-239°C [Lit.⁸, mp 240°C]; IR (KBr): $\nu_{\max}$ 3414, 3336, 3198, 2210, 1648, 1609, 1249 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.45 (s, 2H, NH_2), 7.33 (d, $J = 7.6$ Hz, 2H, CH_{Ar}), 7.25 (d, $J = 7.6$ Hz, 2H, CH_{Ar}), 5.65 (s, 2H, NH_2), 2.39 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO- d_6) δ 159.44, 159.09, 156.32, 140.17, 136.03, 130.90, 128.81, 127.62, 119.78, 115.81, 115.31, 86.84, 74.34, 20.96 ppm; MS (ES^+) Calc. for $\text{C}_{14}\text{H}_{11}\text{N}_5\text{O}$: 265.2, found m/z 266.8 $[\text{M} + \text{H}]^+$. Anal. calc. for $\text{C}_{14}\text{H}_{11}\text{N}_5\text{O}$: C 63.39, H 4.18, N 26.40%, Found C 63.23, H 4.23, N 26.24%.

1,6-diamino-4-(4-methoxyphenyl)-3,5-dicyano-2-pyridone 4(b)



White crystals; yield: 96 %, mp 221-224°C [Lit.⁸, mp 225°C]; IR (KBr): $\nu_{\max}$ 3479, 3343, 3229, 2218, 1637, 1610, 1243 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.42 (s, 2H, NH_2), 7.45 (d, $J = 8.4$ Hz, 2H, CH_{Ar}), 7.09 (d, $J = 8.4$ Hz, 2H, CH_{Ar}), 5.64 (s, 2H, NH_2), 3.83 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.64, 159.35, 159.19, 156.62, 130.65, 129.80, 126.42, 116.65, 115.76, 113.87, 113.24, 86.06, 74.24, 55.27 ppm; MS (ES^+) calc. for $\text{C}_{14}\text{H}_{11}\text{N}_5\text{O}_2$: 281.2, found m/z 282.1 $[\text{M} + \text{H}]^+$. Anal. calc. for $\text{C}_{14}\text{H}_{11}\text{N}_5\text{O}_2$: C 59.78, H 3.94, N 24.90%, Found C 59.66, H 3.99, N 24.77%.

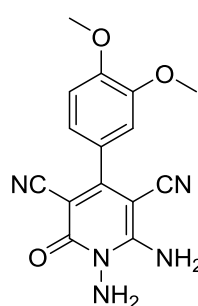
1,6-diamino-4-(2,3-dimethoxyphenyl)-3,5-dicyano-2-pyridone 4(c)



White crystals; yield: 84%, mp 252-253 °C; IR (KBr): $\nu_{\max}$ 3465, 3369, 3234, 2211, 1629, 1599, 1235 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.48 (s, 2H, NH_2), 7.20 (d, $J = 4.7$ Hz, 2H, CH_{Ar}), 6.82 (t, $J = 4.6$ Hz, 1H, CH_{Ar}), 5.65 (s, 2H, NH_2), 3.87 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO- d_6) δ 159.02, 157.62, 156.33, 152.18, 144.67, 129.05, 124.42, 120.02, 116.01, 115.09, 114.40, 87.26, 75.14, 60.52, 55.69 ppm; MS (ES^+) calc. for $\text{C}_{15}\text{H}_{13}\text{N}_5\text{O}_3$: 311.3, found m/z 312.9 $[\text{M} + \text{H}]^+$. Anal. calc. for $\text{C}_{15}\text{H}_{13}\text{N}_5\text{O}_3$: C 57.87, H 4.21, N 22.50%, Found C 57.83, H 4.23, N 22.46%.

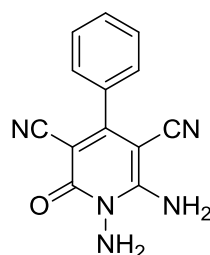
Supplementary Information (SI)

1,6-diamino-4-(3,4-dimethoxyphenyl)-3,5-dicyano-2-pyridone 4(d)



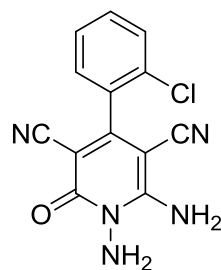
White crystals; yield: 87%, mp 243-244 °C; IR (KBr): $\nu_{\max}$ 3479, 3366, 3237, 2222, 1672, 1624, 1242 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 8.43 (s, 2H, NH_2), 7.12 – 7.07 (m, 3H, CH_{Ar}), 5.66 (s, 2H, NH_2), 3.83 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 159.41, 159.24, 156.66, 150.20, 148.06, 126.31, 121.12, 116.71, 115.82, 111.75, 111.25, 86.07, 74.31, 55.57, 55.48 ppm; MS (ES^+) calc. for $\text{C}_{15}\text{H}_{13}\text{N}_5\text{O}_3$: 311.3, found m/z 312.7 $[\text{M} + \text{H}]^+$. Anal. calc. for $\text{C}_{15}\text{H}_{13}\text{N}_5\text{O}_3$: C 57.87, H 4.21, N 22.50%, Found C 57.77, H 4.24, N 23.48%.

1,6-diamino-2-oxo-4-phenyl-3,5-dicyano-2-pyridone 4(e)



White crystals; yield: 87%, mp 238-240°C [Lit.⁸, mp 240°C]; IR (KBr): $\nu_{\max}$ 3461, 3326, 2178, 1633, 1603, 1234 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 8.51 (s, 2H, NH_2), 7.80 – 7.23 (m, 5H, CH_{Ar}), 5.67 (s, 2H, NH_2) ppm; ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 159.55, 159.24, 156.63, 134.51, 130.19, 128.57, 127.94, 116.33, 115.45, 86.34, 74.27 ppm; MS (ES^+) calc. for $\text{C}_{13}\text{H}_9\text{N}_5\text{O}$: 251.2, found m/z 252.4 $[\text{M} + \text{H}]^+$. Anal. calc. For $\text{C}_{13}\text{H}_9\text{N}_5\text{O}$: C 62.15, H 3.61, N 27.87 %, Found C 61.99, H 3.67, N 27.77%.

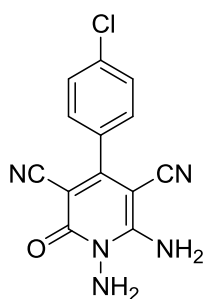
1,6-diamino-4-(2-chlorophenyl)-3,5-dicyano-2-pyridone 4(f)



Yellow crystals; yield: 93%, mp 247-249°C [Lit.⁸, mp 250°C]; IR (KBr): $\nu_{\max}$ 3413, 3310, 3220, 3202, 2217, 1639, 1607 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 8.64 (s, 2H, NH_2), 7.67 (d, $J = 7.7$ Hz, 1H, CH_{Ar}), 7.58-7.49 (m, 3H, CH_{Ar}), 5.69 (s, 2H, NH_2) ppm; ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 158.99, 157.27, 156.51, 133.69, 131.62, 130.50, 129.74, 129.67, 127.75, 115.57, 114.65, 87.03, 74.85 ppm; MS (ES^+) calc. for $\text{C}_{13}\text{H}_8\text{ClN}_5\text{O}$: 285.6, found m/z 286.9 $[\text{M} + \text{H}]^+$. Anal. calc. for $\text{C}_{13}\text{H}_8\text{ClN}_5\text{O}$: C 54.65, H 2.82, N 24.51%, Found C 54.56, H 2.87, N 24.39%.

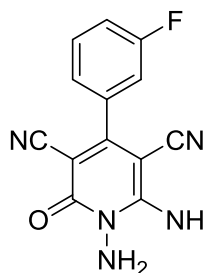
Supplementary Information (SI)

1,6-diamino-4-(4-chlorophenyl)-3,5-dicyano-2-pyridone 4(g)



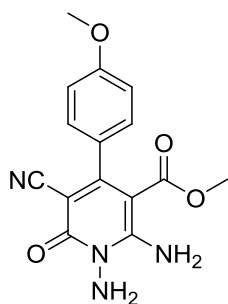
Orange crystals; yield: 96%, mp 241-243°C [Lit.⁸, mp 245°C]; IR (KBr): $\nu_{\max}$ 3481, 3319, 3203, 2185, 1635, 1599, 1260 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.53 (s, 2H, NH_2), 7.63 (d, J = 8.5 Hz, 2H, CH_{Ar}), 7.52 (d, J = 8.5 Hz, 2H, CH_{Ar}), 5.66 (s, 2H, NH_2) ppm; ^{13}C NMR (100 MHz, DMSO- d_6) δ 159.92, 159.60, 156.99, 134.87, 130.55, 128.93, 128.30, 116.69, 115.81, 86.70, 74.63 ppm; MS (ES^+) calc. for $\text{C}_{13}\text{H}_8\text{ClN}_5\text{O}$: 285.6, found m/z 286.7 [$\text{M} + \text{H}$]⁺. Anal. calc. for $\text{C}_{13}\text{H}_8\text{ClN}_5\text{O}$: C 54.65, H 2.82, N 24.51%, Found C 54.567 H 2.88, N 24.37%.

1,6-diamino-4-(3-fluorophenyl)-3,5-dicyano-2-pyridone 4(h)



Pale yellow crystals; yield: 92%, mp 236-237°C; IR (KBr): $\nu_{\max}$ 3469, 3302, 3249, 2174, 1640, 1600, 1246 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.56 (s, 2H, NH_2), 7.60 (d, J = 7.3 Hz, 1H, CH_{Ar}), 7.42-7.31 (m, 3H, CH_{Ar}), 5.68 (s, 2H, NH_2) ppm; ^{13}C NMR (100 MHz, DMSO- d_6) δ 162.83, 160.40, 159.08, 158.07, 158.05, 156.56, 136.68, 136.59, 130.98, 130.89, 124.30, 124.27, 117.14, 116.93, 116.10, 115.29, 115.22, 115.05, 86.37, 74.28 ppm; MS (ES^+) calc. for $\text{C}_{13}\text{H}_8\text{FN}_5\text{O}$: 269.2, found m/z 270.8 [$\text{M} + \text{H}$]⁺. Anal. calc. for $\text{C}_{14}\text{H}_{11}\text{N}_5\text{O}$: C 57.99, H 2.99, N 26.01%, Found C 57.96, H 3.07, N 25.67%.

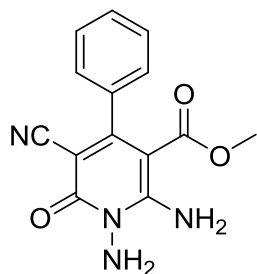
Methyl 1,6-diamino-3-cyano-4-(4-methoxyphenyl)-2-pyridone-5-carboxylate 4(i)



Pale yellow crystals; yield: 93%, mp 205-206°C [Lit.⁹, mp 203-204°C]; IR (KBr): $\nu_{\max}$ 3415, 3307, 3216, 2210, 1711, 1644, 1607, 1251, 775 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.36 (s, 2H, NH_2), 7.17 (d, J = 8.8 Hz, 2H, CH_{Ar}), 6.99 (d, J = 8.4 Hz, 2H, CH_{Ar}), 5.66 (s, 2H, NH_2), 3.80 (s, 3H, OCH_3), 3.27 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO- d_6) δ 166.38, 159.30, 159.04, 158.75, 155.53, 130.20, 128.41, 116.97, 113.30, 91.61, 87.27, 55.09, 51.37 ppm; MS (ES^+) calc. for $\text{C}_{15}\text{H}_{14}\text{N}_4\text{O}_4$: 314.3, found m/z 315.0 [$\text{M} + \text{H}$]⁺. Anal. calc. for $\text{C}_{15}\text{H}_{14}\text{N}_4\text{O}_4$: C 57.32, H 4.49, N 17.83%, Found C 57.29, H 4.54, N 17.62%.

Supplementary Information (SI)

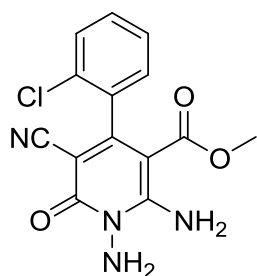
Methyl 1,6-diamino-3-cyano-4-phenyl-2-pyridone-5-carboxylate 4(j)



Yellow crystals; yield: 82%, mp 245-246°C [Lit.⁹, mp 247-248°C]; IR (KBr): $\nu_{\max}$ 3405, 3327, 3289, 3228, 2221, 1686, 1657, 1621, 1251, 743 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 8.45 (s, 2H, NH_2), 7.43-7.41 (m, 3H, CH_{Ar}), 7.23 – 7.21 (m, 2H, CH_{Ar}), 5.68 (s, 2H, NH_2), 3.21 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 166.17, 159.12, 158.92, 155.75, 138.31, 128.28, 127.87, 126.72, 116.67, 91.34, 87.41, 51.22 ppm;

MS (ES^+) calc. for $\text{C}_{14}\text{H}_{12}\text{N}_4\text{O}_3$: 284.2, found m/z 285.1 $[\text{M} + \text{H}]^+$, 307.2 $[\text{M} + \text{Na}]^+$. Anal. calc. for $\text{C}_{14}\text{H}_{12}\text{N}_4\text{O}_3$: C 59.15, H 4.26, N 19.71%, Found C 59.05, H 4.28, N 19.65%.

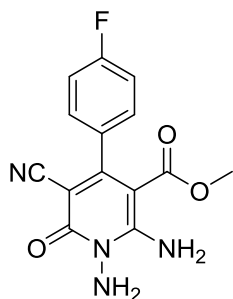
Methyl 1,6-diamino-3-cyano-4-(2-chlorophenyl)-2-pyridone-5-carboxylate 4(k)



Yellow crystals; yield: 89%, mp 251-253°C; IR (KBr): $\nu_{\max}$ 3384, 3307, 3270, 2216, 1686, 1661, 1628, 1257, 749 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 8.47 (s, 2H, NH_2), 7.53 – 7.26 (m, 4H, CH_{Ar}), 5.70 (s, 2H, NH_2), 3.25 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 165.49, 158.75, 156.54, 156.34, 137.54, 129.95, 128.77, 128.45, 126.97, 115.96, 90.74, 87.96, 51.51 ppm; MS (ES^+) calc. for $\text{C}_{14}\text{H}_{11}\text{ClN}_4\text{O}_3$: 318.7, found

m/z 319.1 $[\text{M} + \text{H}]^+$. Anal. calc. for $\text{C}_{14}\text{H}_{11}\text{ClN}_4\text{O}_3$: C 52.76, H 3.48, N 17.58%, Found C 52.68, H 3.53, N 17.52%.

Methyl 1,6-diamino-3-cyano-4-(4-fluorophenyl)-2-pyridone-5-carboxylate 4(l)

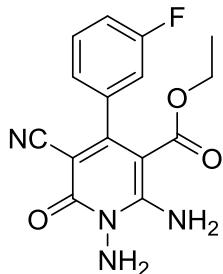


White crystals; yield: 91%, mp 248-250°C; IR (KBr): $\nu_{\max}$ 3395, 3310, 3275, 3219, 2218, 1693, 1633, 1593, 1238 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 7.99 (s, 2H, NH_2), 7.78 – 7.75 (m, 2H, CH_{Ar}), 7.30 – 7.26 (m, 2H, CH_{Ar}), 5.69 (s, 2H, NH_2), 3.26 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 166.03, 164.81, 158.81, 158.22, 155.84, 129.21, 129.13, 129.10, 129.01, 115.91, 115.69, 114.99, 114.77, 91.33, 87.67, 51.31 ppm;

MS (ES^+) calc. for $\text{C}_{14}\text{H}_{11}\text{FN}_4\text{O}_3$: 302.2, found m/z 282.7 $[\text{M} + \text{H}]^+$. Anal. calc. For $\text{C}_{14}\text{H}_{11}\text{FN}_4\text{O}_3$: C 55.63, H 3.67, N 18.54%, Found C 55.56, H 3.72, N 18.63%.

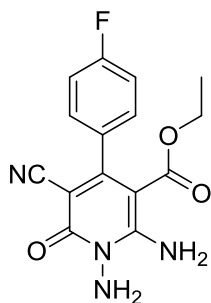
Supplementary Information (SI)

Ethyl 1,6-diamino-3-cyano-4-(3-fluorophenyl)-2-pyridone-5-carboxylate 4(m)



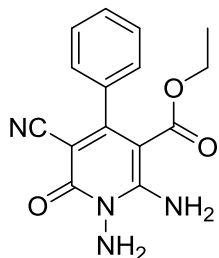
Yellow crystals; yield: 87%, mp 245-246°C; IR (KBr): $\nu_{\max}$ 3414, 3311, 3242, 3200, 2218, 1681, 1639, 1617, 1232 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.56 (s, 2H, NH_2), 7.60 (d, $J = 7.6$ Hz, 1H, CH_{Ar}), 7.41 (d, $J = 9.2$ Hz, 3H, CH_{Ar}), 5.68 (s, 2H, NH_2), 4.01 (q, $J = 7.2$ Hz, 2H, CH_2), 1.16 (t, $J = 7.2$ Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO- d_6) δ 162.83, 160.40, 159.08, 158.07, 156.56, 136.59, 130.89, 124.27, 116.93, 116.10, 115.29, 115.05, 86.37, 74.28, 14.04 ppm; MS (ES^+) calc. for $\text{C}_{15}\text{H}_{13}\text{FN}_4\text{O}_3$: 316.2, found m/z 317.7 [$\text{M} + \text{H}$] $^+$. Anal. calc. for $\text{C}_{15}\text{H}_{13}\text{FN}_4\text{O}_3$: C 56.96, H 4.14, N 17.71%, Found C 56.20, H 4.47, N 17.03%.

Ethyl 1,6-diamino-3-cyano-4-(4-fluorophenyl)-2-pyridone-5-carboxylate 4(n)



Yellow crystals; yield: 88%, mp 247-249°C; IR (KBr): $\nu_{\max}$ 3354, 3317, 3207, 2218, 1686, 1628, 1579, 1237 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.45 (s, 2H, NH_2), 7.43 (d, $J = 7.1$ Hz, 2H, CH_{Ar}), 7.22 (d, $J = 6.9$ Hz, 2H, CH_{Ar}), 5.67 (s, 2H, NH_2), 3.70 (q, $J = 7.1$ Hz, 2H, CH_2), 1.05 (t, $J = 7.0$ Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO- d_6) δ 166.03, 164.81, 158.81, 158.22, 155.84, 129.21, 129.13, 129.10, 115.69, 114.99, 114.78, 91.33, 87.68, 59.99, 12.80 ppm; MS (ES^+) calc. for $\text{C}_{15}\text{H}_{13}\text{FN}_4\text{O}_3$: 316.2, found m/z 317.4 [$\text{M} + \text{H}$] $^+$. Anal. calc. for $\text{C}_{15}\text{H}_{13}\text{FN}_4\text{O}_3$: C 56.96, H 4.14, N 17.71%, Found C 56.29, H 4.43, N 17.12%.

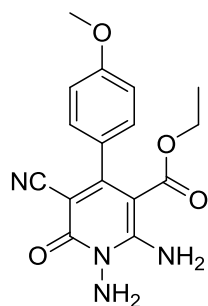
Ethyl 1,6-diamino-3-cyano-4-phenyl-2-pyridone-5-carboxylate 4(o)



Yellow crystals; yield: 85%, mp 235-237°C; IR (KBr): $\nu_{\max}$ 3474, 3365, 3230, 2219, 1669, 1624, 1581, 1240 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.45 (s, 2H, NH_2), 7.45 – 7.42 (m, 3H, CH_{Ar}), 7.22 (dd, $J = 7.3, 2.1$ Hz, 2H, CH_{Ar}), 5.67 (s, 2H, NH_2), 3.70 (q, $J = 7.1$ Hz, 2H, CH_2), 1.05 (t, $J = 7.0$ Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO- d_6) δ 166.27, 159.23, 159.03, 155.86, 138.41, 128.39, 127.98, 126.87, 126.83, 116.77, 91.45, 87.51, 60.00, 51.33, 12.81 ppm; MS (ES^+) calc. for $\text{C}_{15}\text{H}_{14}\text{N}_4\text{O}_3$: 298.3, found m/z 299.4 [$\text{M} + \text{H}$] $^+$. Anal. calc. for $\text{C}_{15}\text{H}_{14}\text{N}_4\text{O}_3$: C 60.40, H 4.73, N 18.78%, Found C 59.45, H 5.05, N 18.02%.

Supplementary Information (SI)

Ethyl 1,6-diamino-3-cyano-4-(4-methoxyphenyl)-2-pyridone-5-carboxylate 4(p)

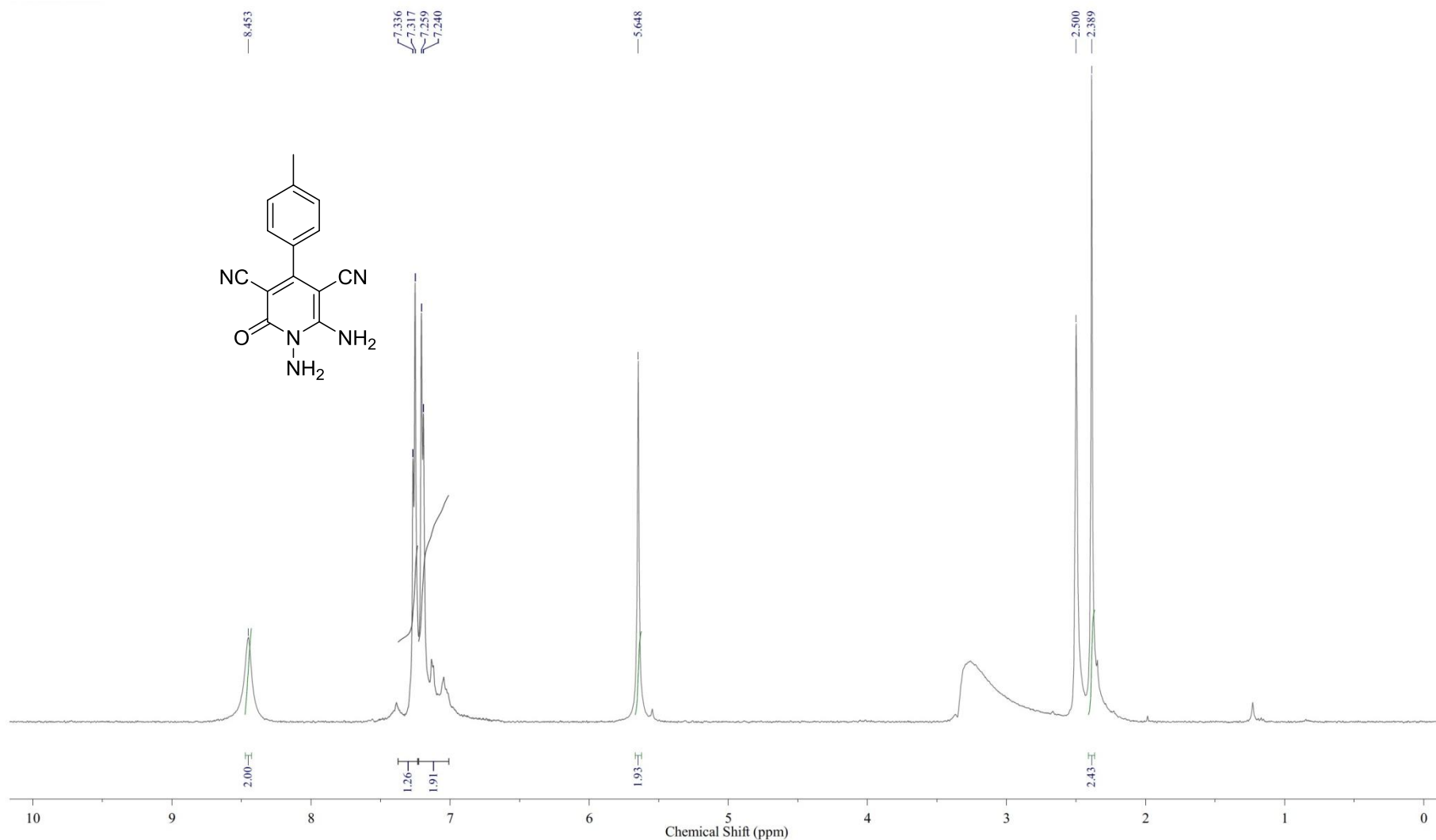


Yellow crystals; yield: 89%, mp 219-221°C; IR (KBr): $\nu_{\max}$ 3414, 3320, 3202, 2211, 1649, 1630, 1609, 1230 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.36 (s, 2H, NH_2), 7.16 (d, $J = 8.4$ Hz, 2H, CH_{Ar}), 6.98 (d, $J = 8.4$ Hz, 2H, CH_{Ar}), 5.65 (s, 2H, NH_2), 4.02 (q, $J = 7.0$ Hz, 2H, CH_2), 3.79 (s, 3H, OCH_3), 1.30 (t, $J = 7.0$ Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 166.49, 159.42, 159.14, 158.87, 155.64, 130.32, 128.52, 128.46, 117.07, 113.41, 91.72, 87.40, 60.07, 55.20, 13.03 ppm; MS (ES^+) calc. for $\text{C}_{16}\text{H}_{16}\text{N}_4\text{O}_4$: 328.3, found m/z 329.9 $[\text{M} + \text{H}]^+$.
Anal. calc. for $\text{C}_{16}\text{H}_{16}\text{N}_4\text{O}_4$: C 58.53, H 4.91, N 17.06%, Found C 57.75, H 4.98, N 16.45%.

Supplementary Information (SI)

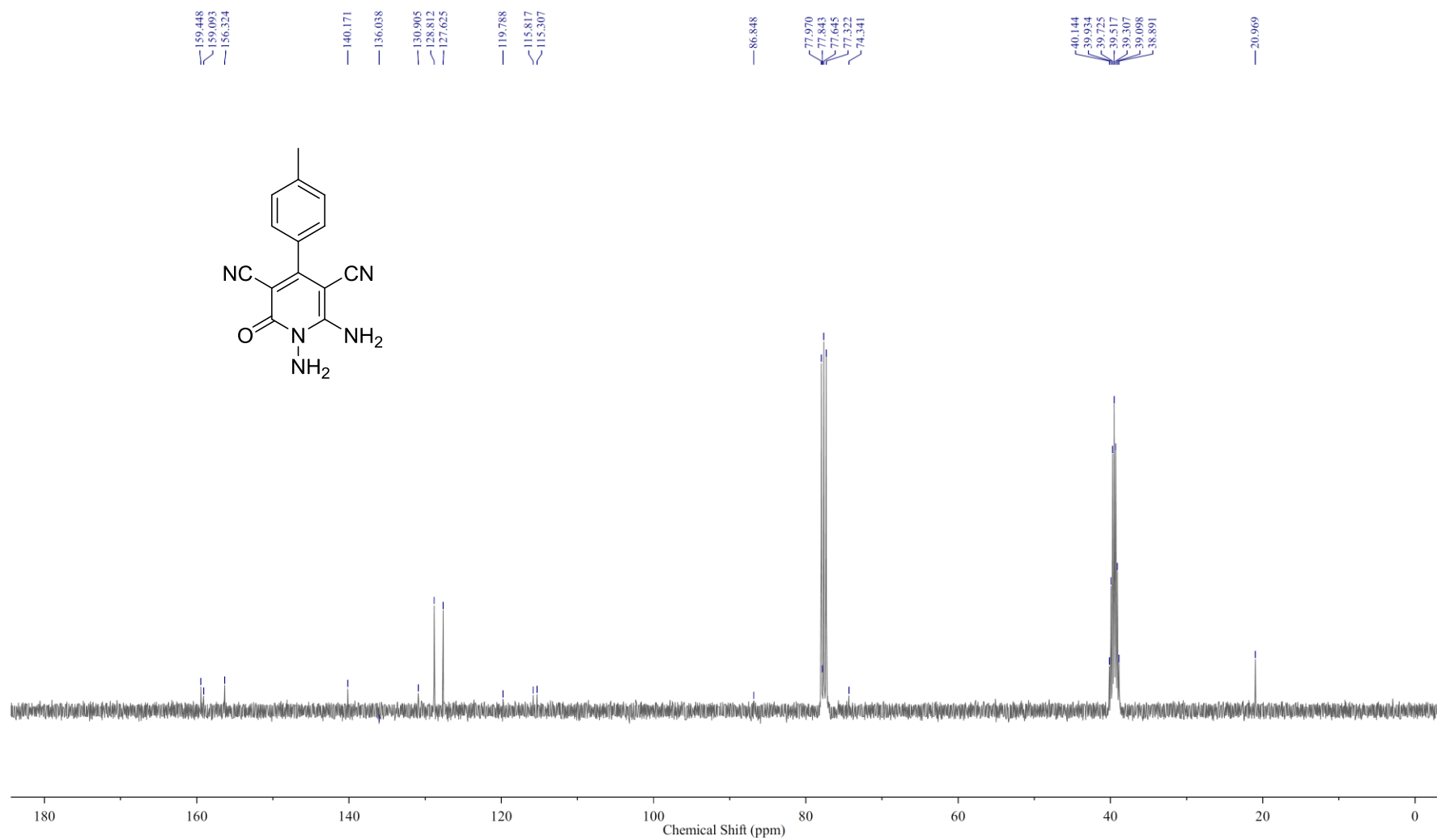
Spectral data for the *N*-amino-2-pyridone derivatives:

¹H NMR of **1,6-diamino-4-(p-tolyl)-3,5-dicyano-2-pyridone 4(a)**.



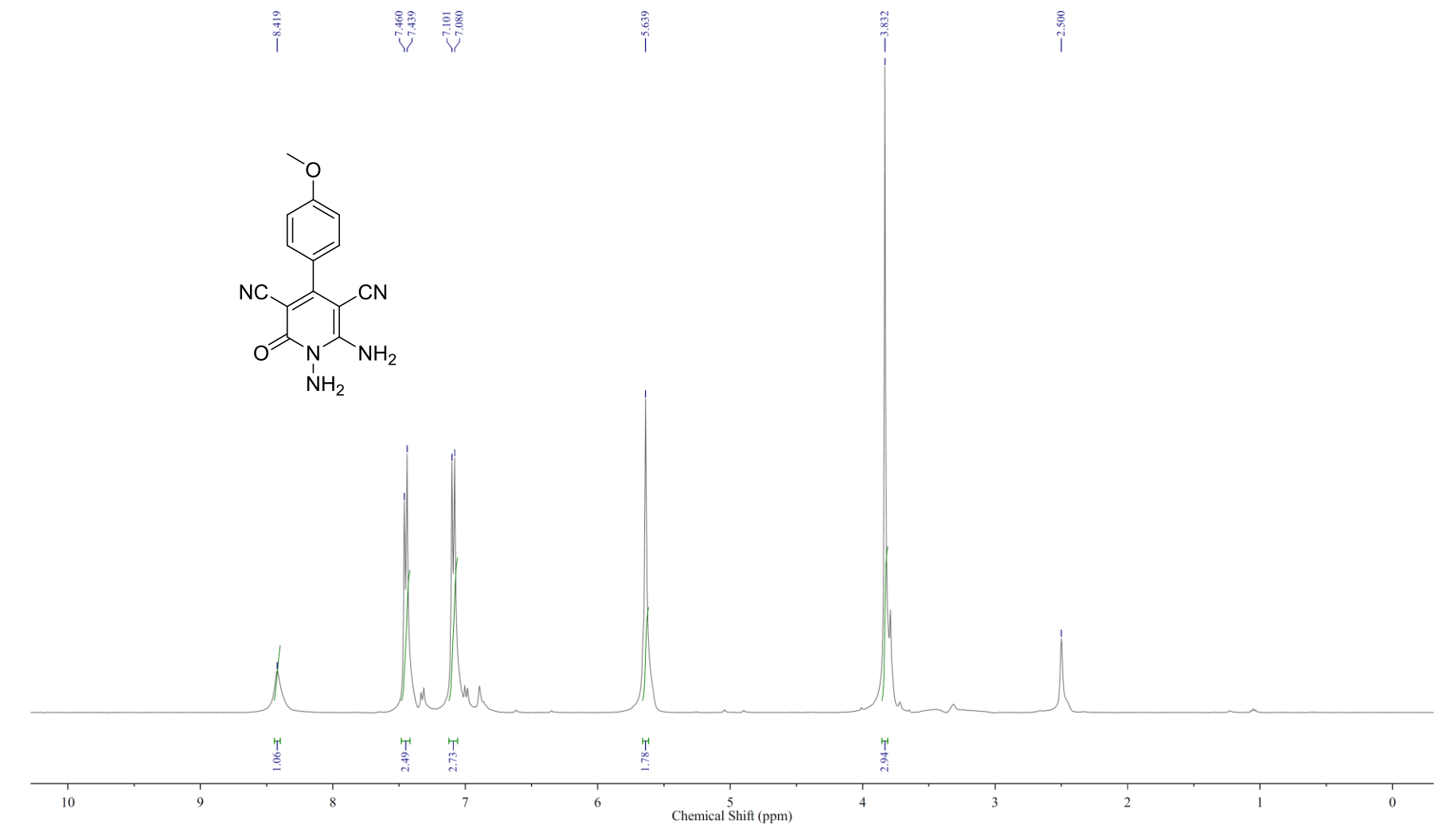
Supplementary Information (SI)

^{13}C NMR of 1,6-diamino-4-(p-tolyl)-3,5-dicyano-2-pyridone 4(a).



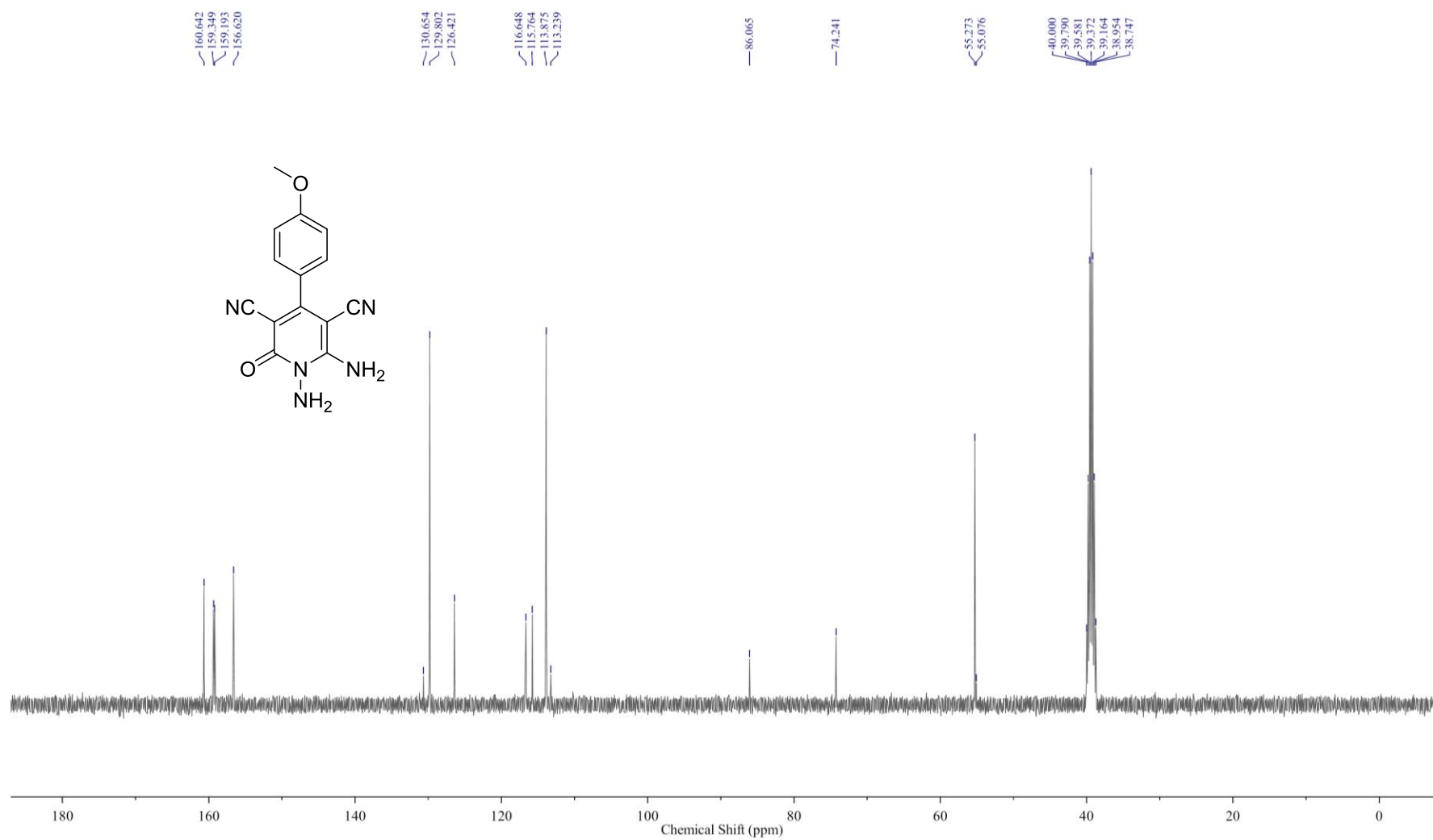
Supplementary Information (SI)

^1H NMR of **1,6-diamino-4-(4-methoxyphenyl)-3,5-dicyano-2-pyridone 4(b)**



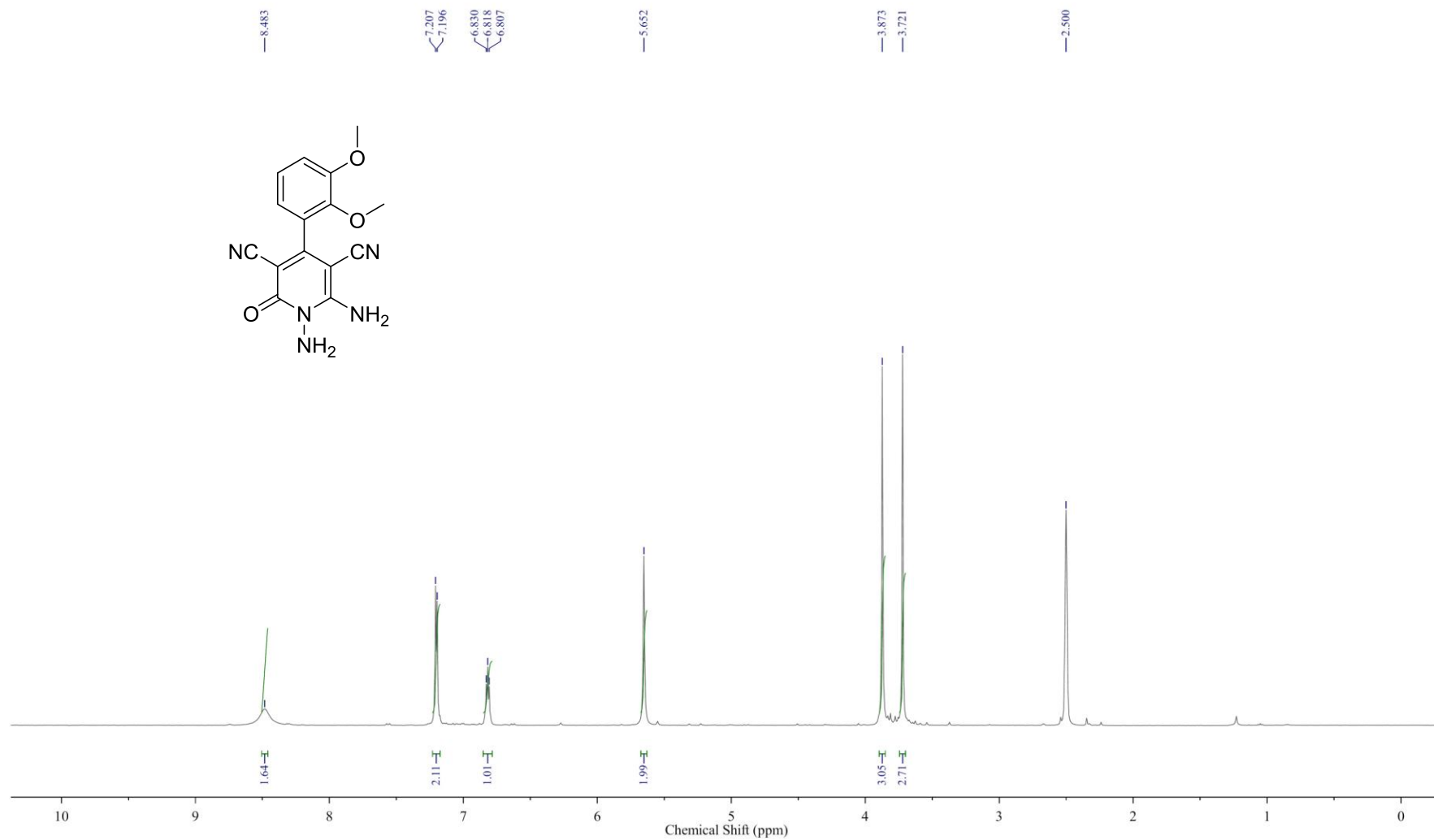
Supplementary Information (SI)

^{13}C NMR of 1,6-diamino-4-(4-methoxyphenyl)-3,5-dicyano-2-pyridone 4(b)



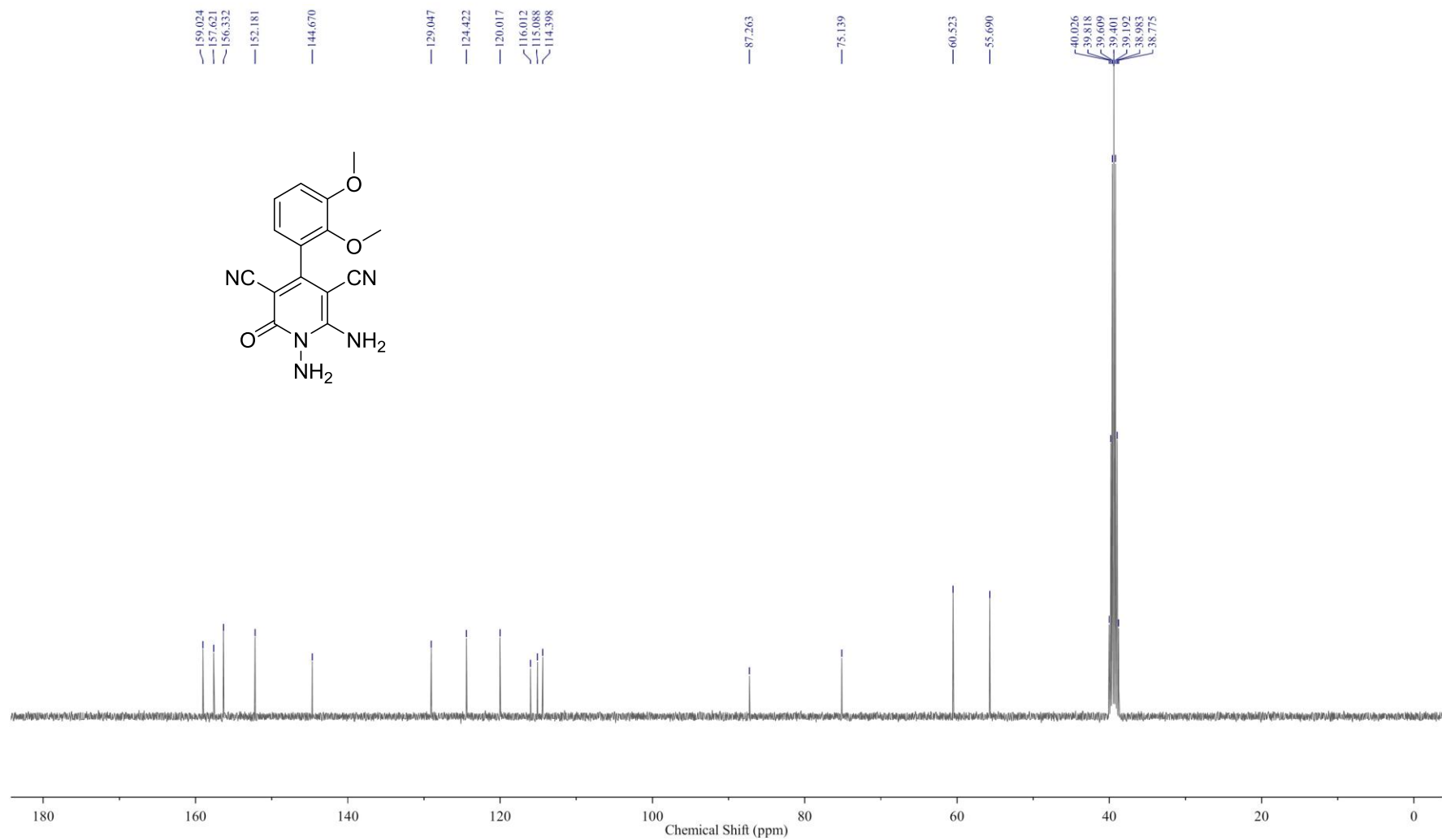
Supplementary Information (SI)

^1H NMR of 1,6-diamino-4-(2,3-dimethoxyphenyl)-3,5-dicyano-2-pyridone 4(c)



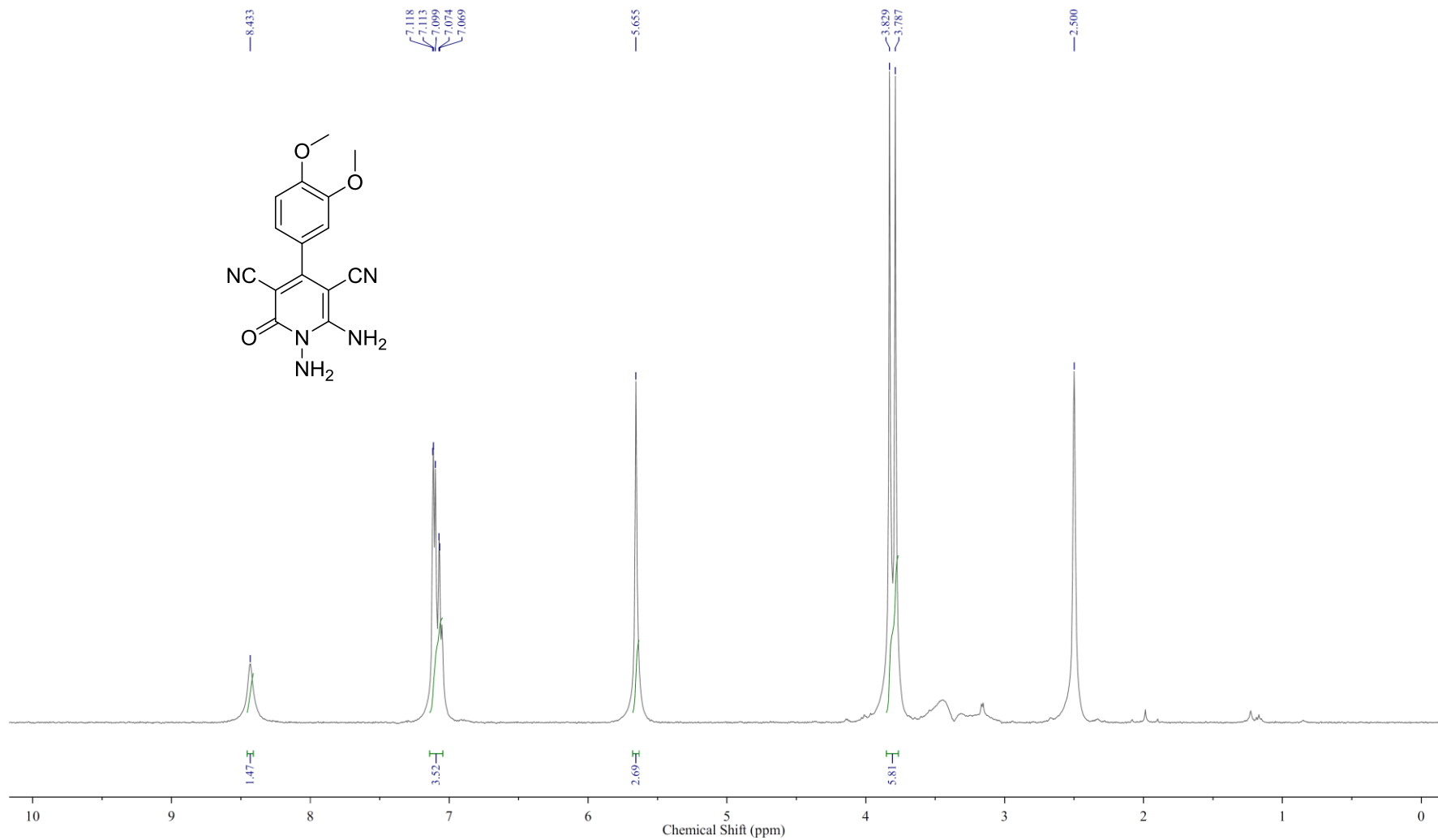
Supplementary Information (SI)

^{13}C NMR of 1,6-diamino-4-(2,3-dimethoxyphenyl)-3,5-dicyano-2-pyridone 4(c)



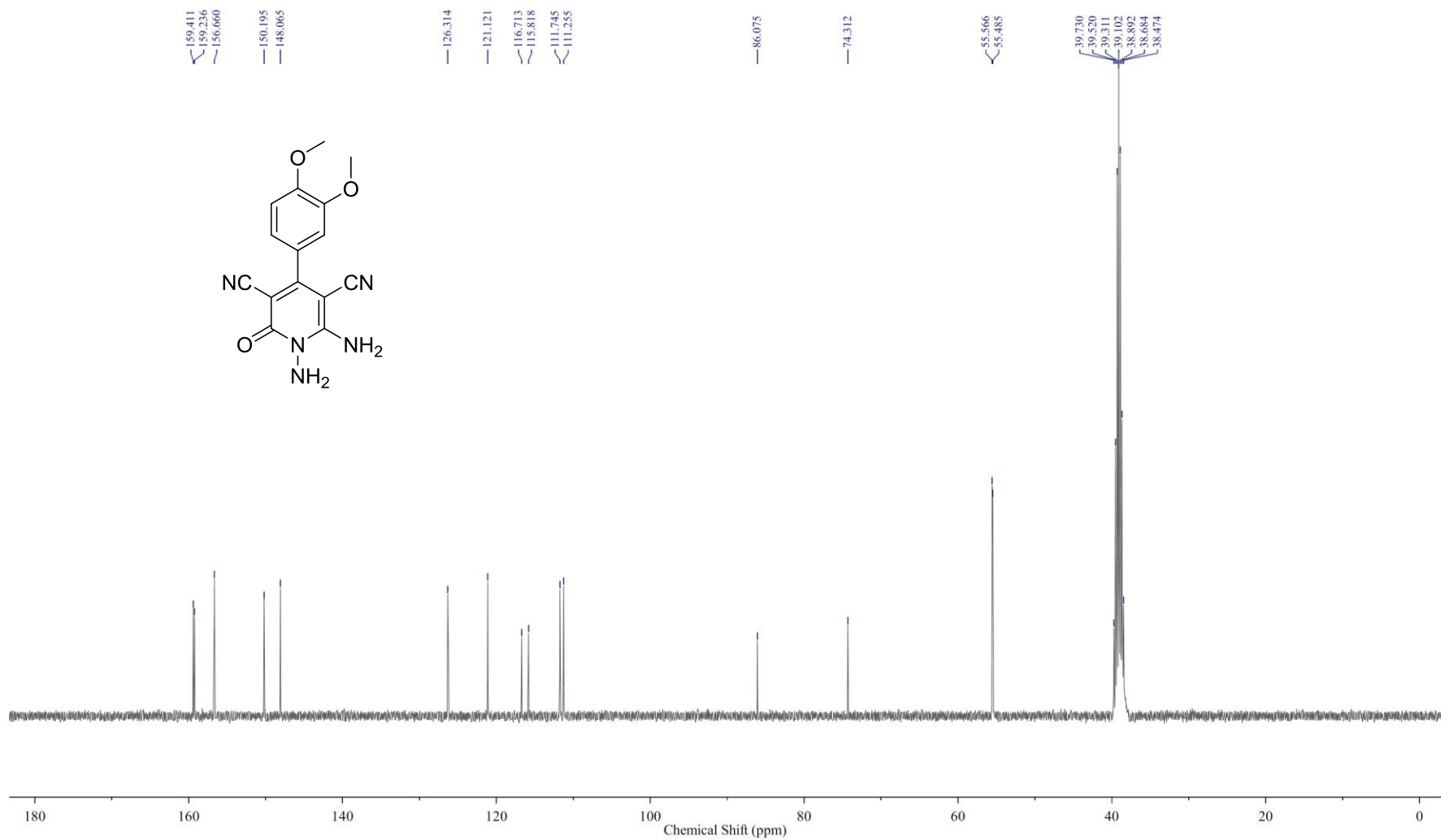
Supplementary Information (SI)

^1H NMR of 1,6-diamino-4-(3,4-dimethoxyphenyl)-3,5-dicyano-2-pyridone 4(d)



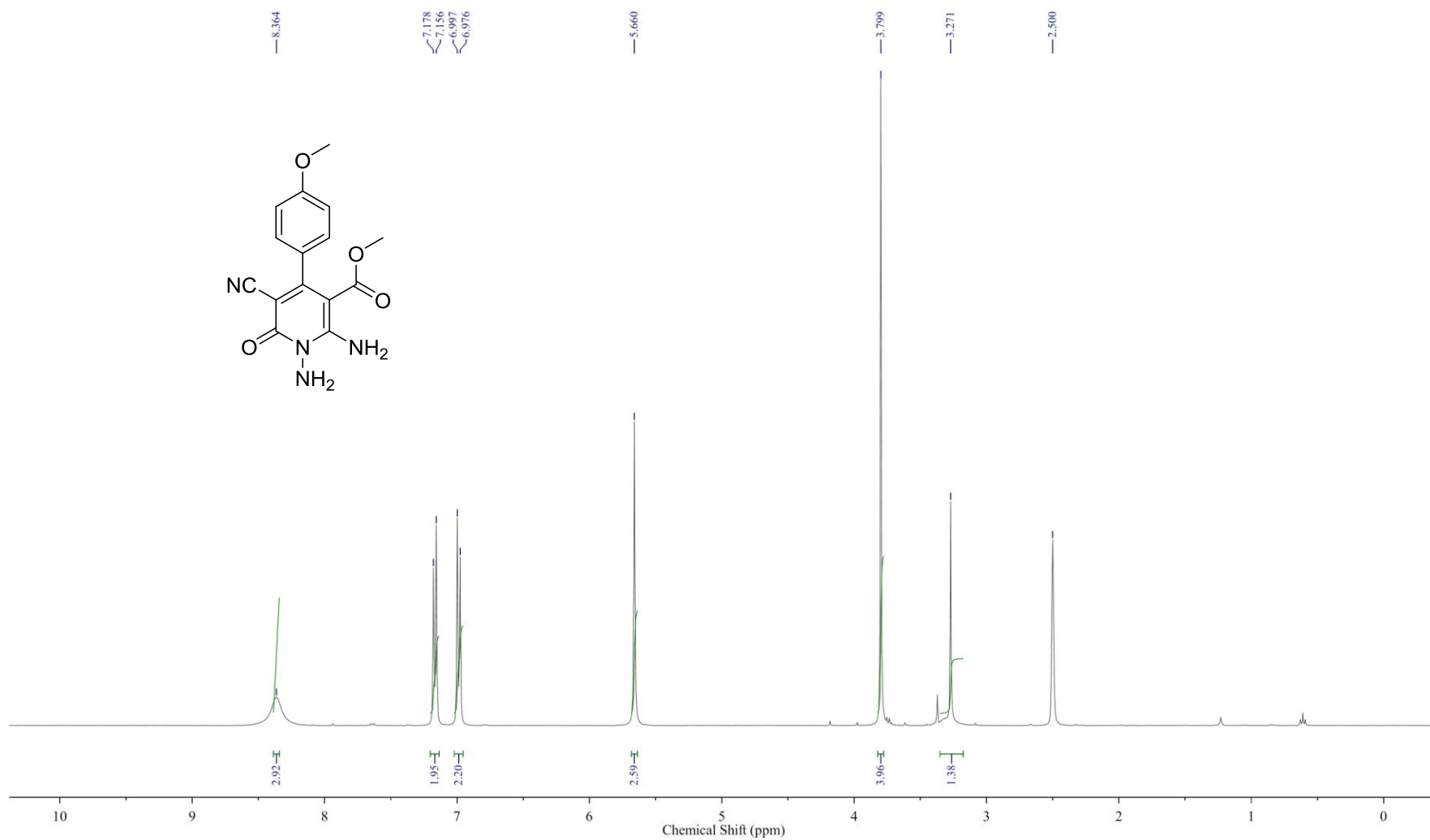
Supplementary Information (SI)

^{13}C NMR of 1,6-diamino-4-(3,4-dimethoxyphenyl)-3,5-dicyano-2-pyridone 4(d)



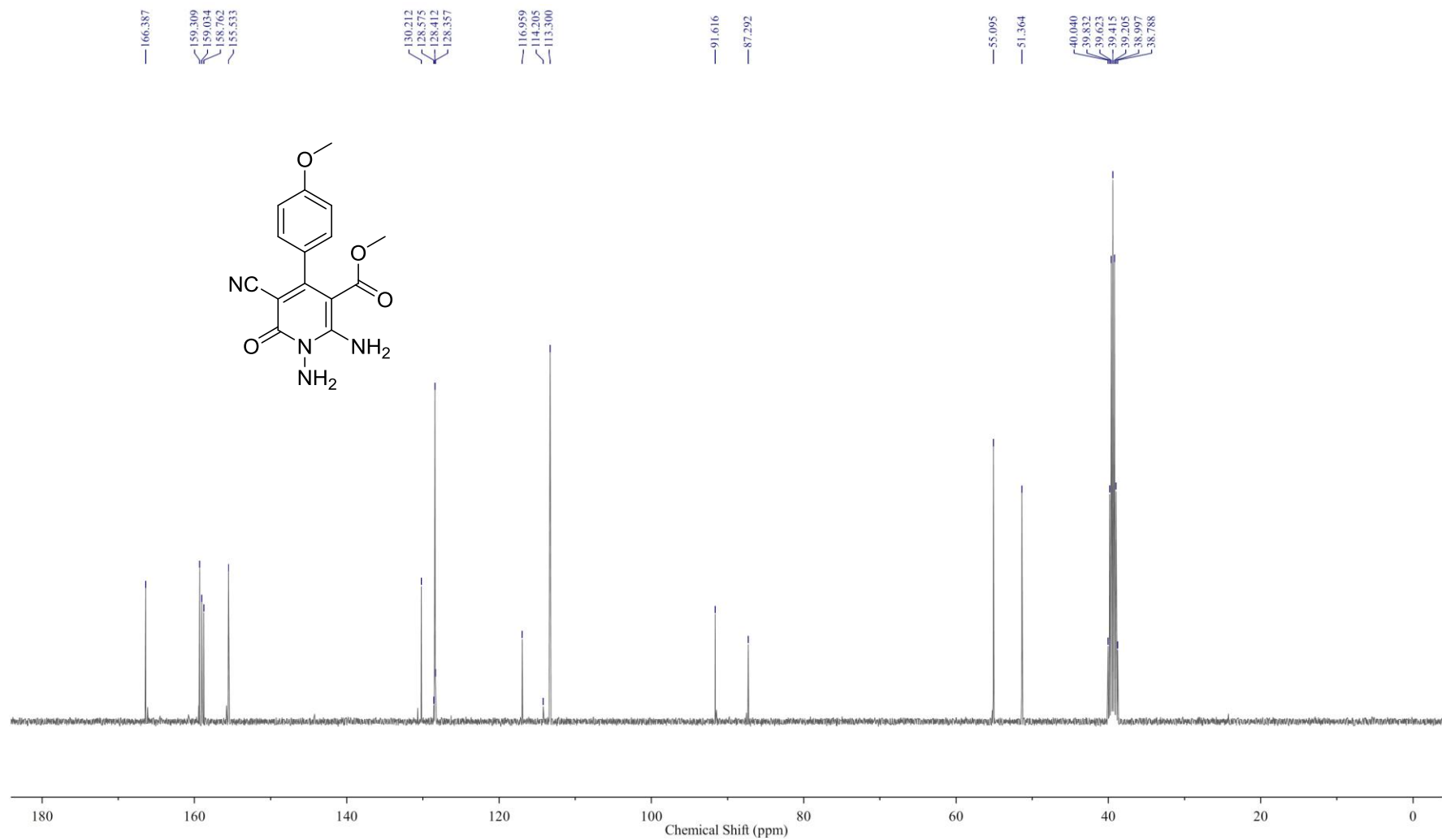
Supplementary Information (SI)

^1H NMR of methyl 1,6-diamino-3-cyano-4-(4-methoxyphenyl)-2-pyridone-5-carboxylate 4(i)



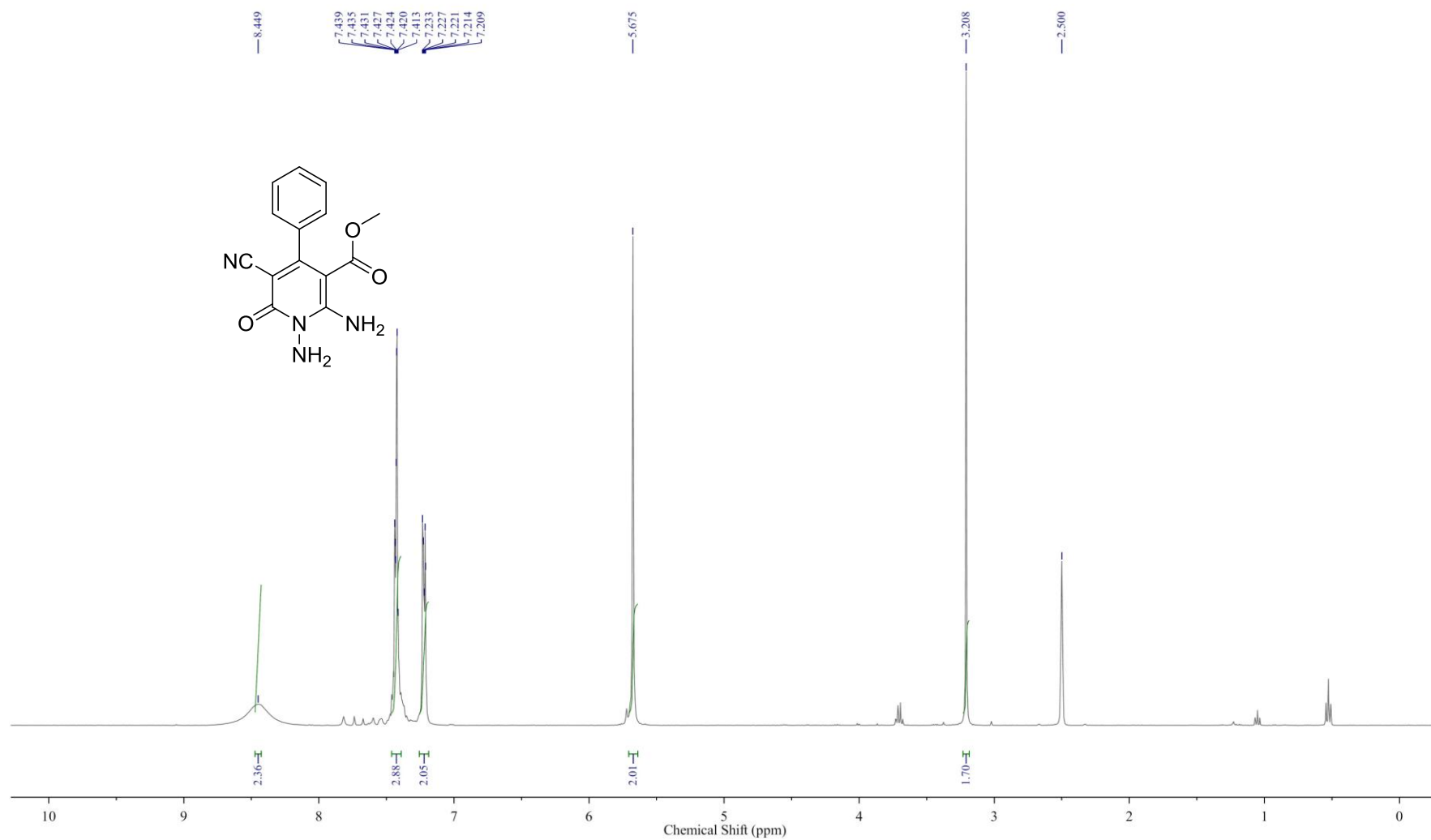
Supplementary Information (SI)

^{13}C NMR of Methyl 1,6-diamino-3-cyano-4-(4-methoxyphenyl)-2-pyridone-5-carboxylate 4(i)



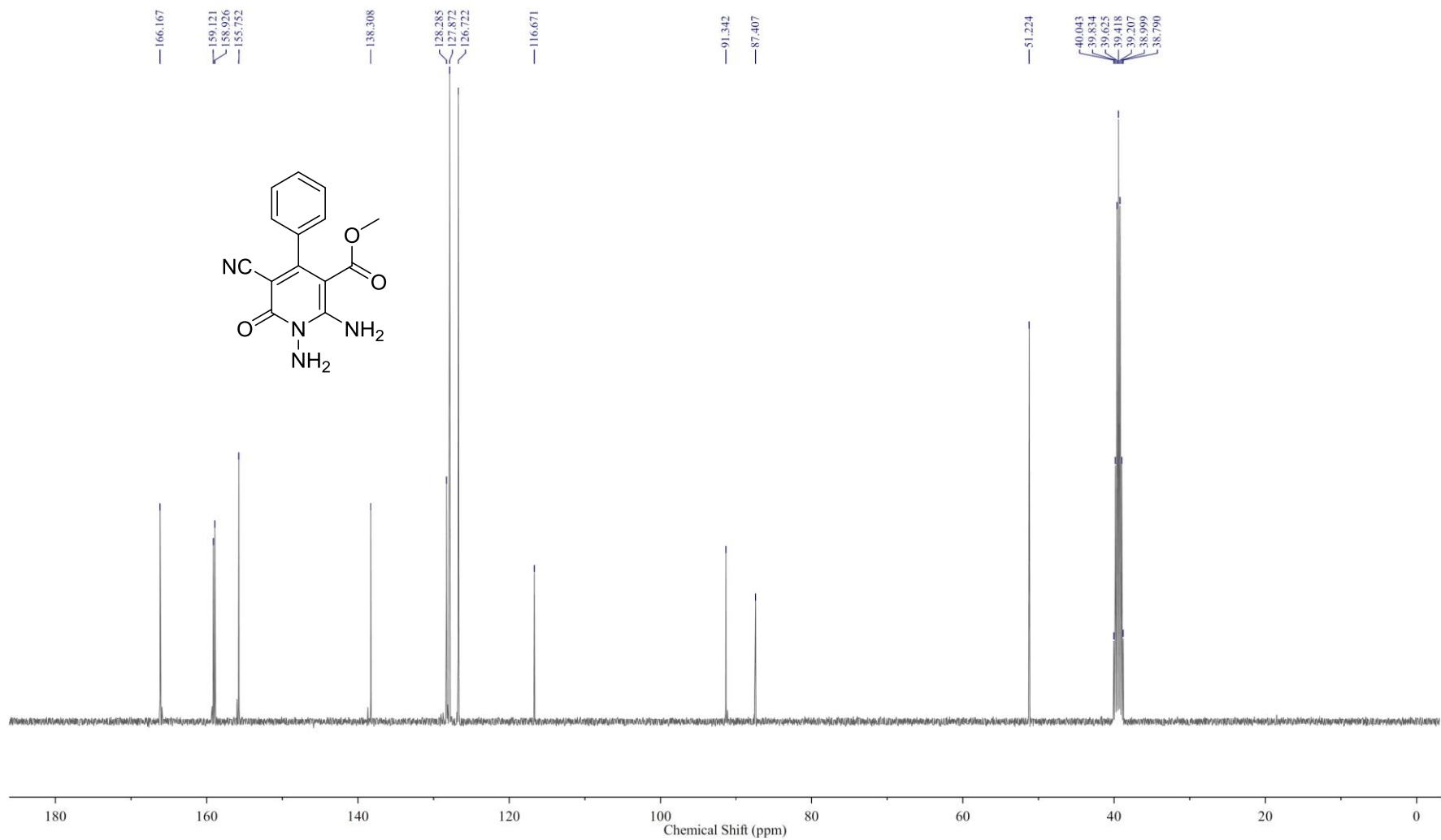
Supplementary Information (SI)

^1H NMR of Methyl 1,6-diamino-3-cyano-4-phenyl-2-pyridone-5-carboxylate 4(j)



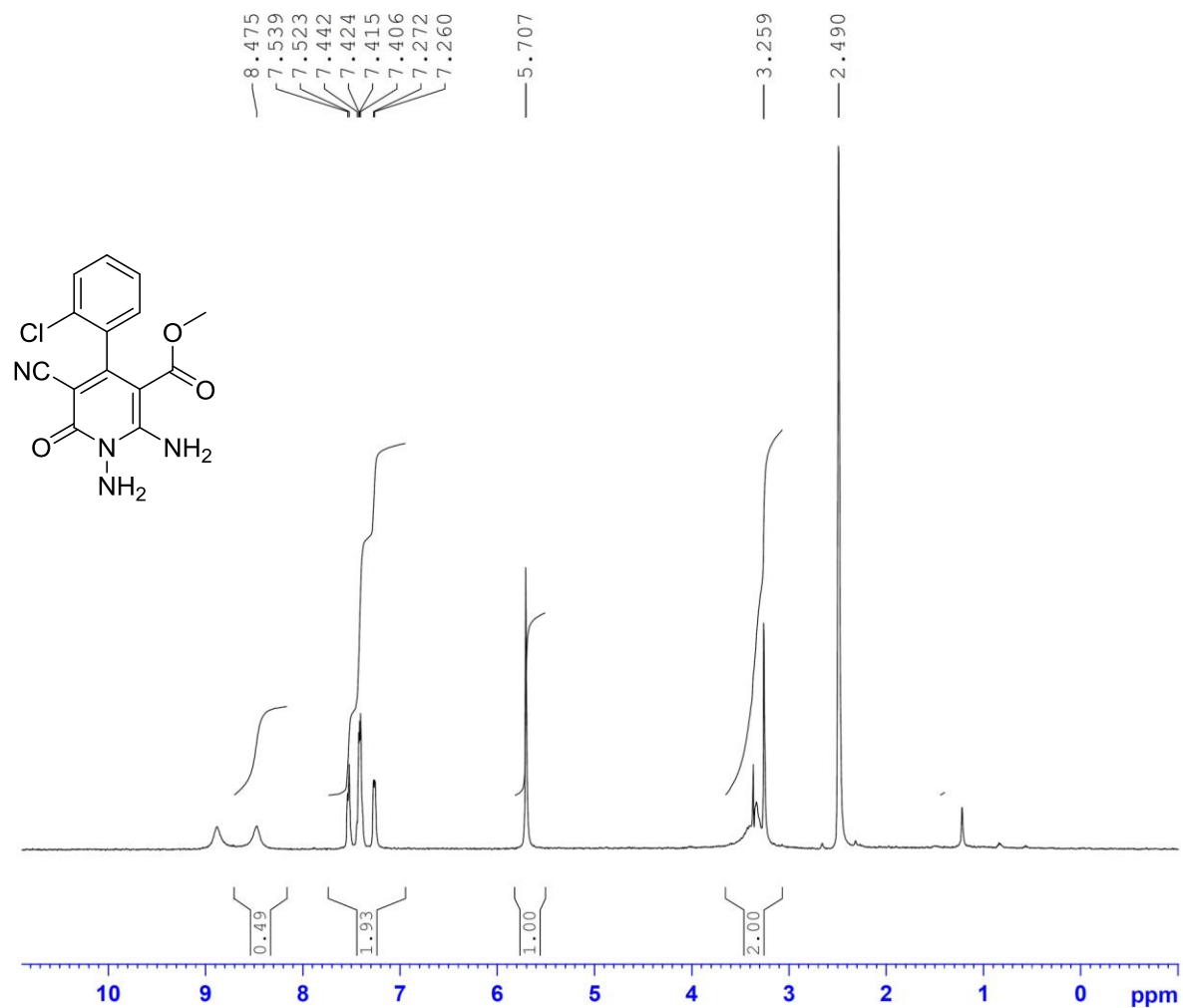
Supplementary Information (SI)

^{13}C NMR of Methyl 1,6-diamino-3-cyano-4-phenyl-2-pyridone-5-carboxylate 4(j)



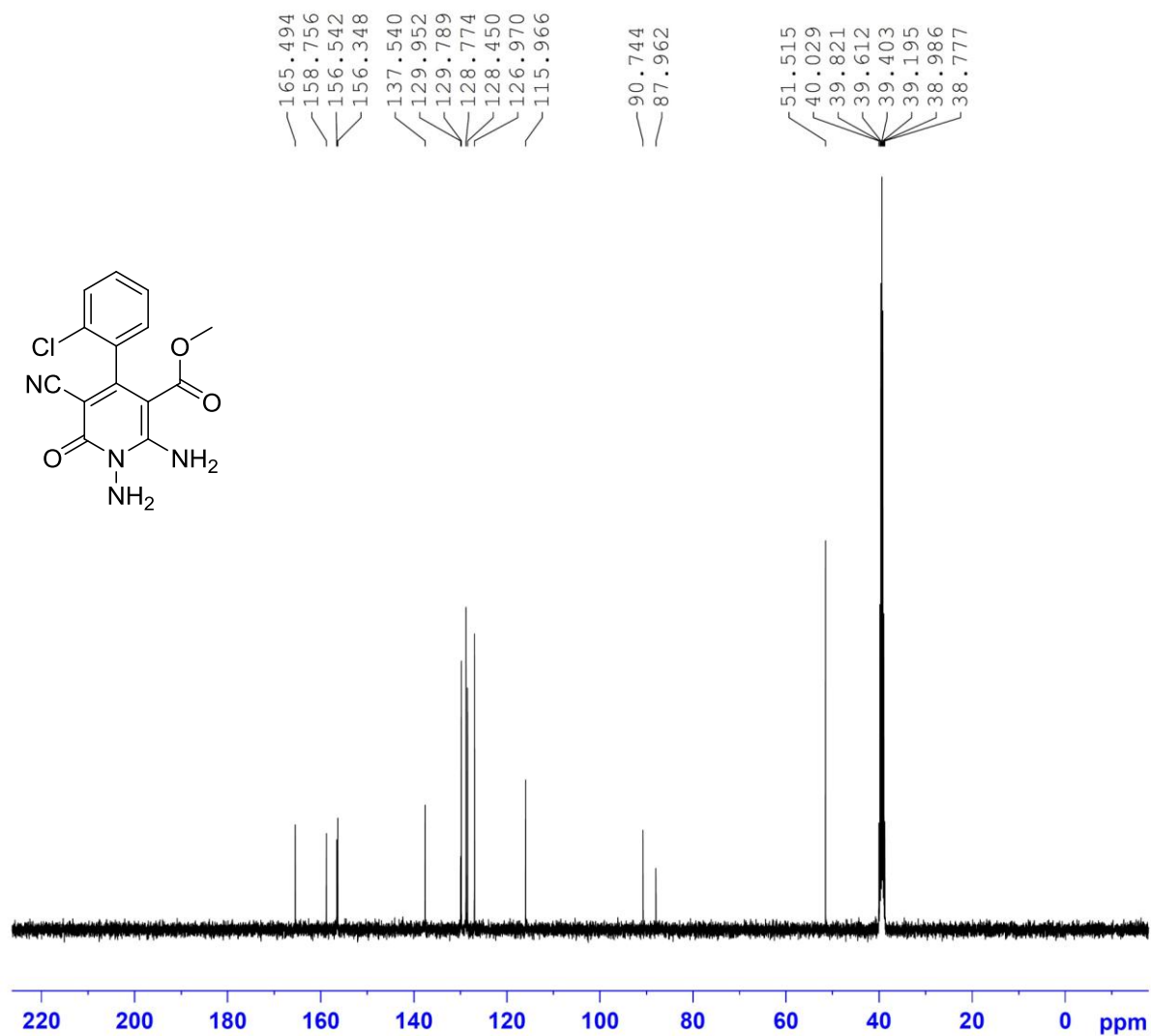
Supplementary Information (SI)

^1H NMR of Methyl 1,6-diamino-3-cyano-4-(2-chlorophenyl)-2-pyridone-5-carboxylate 4(k)



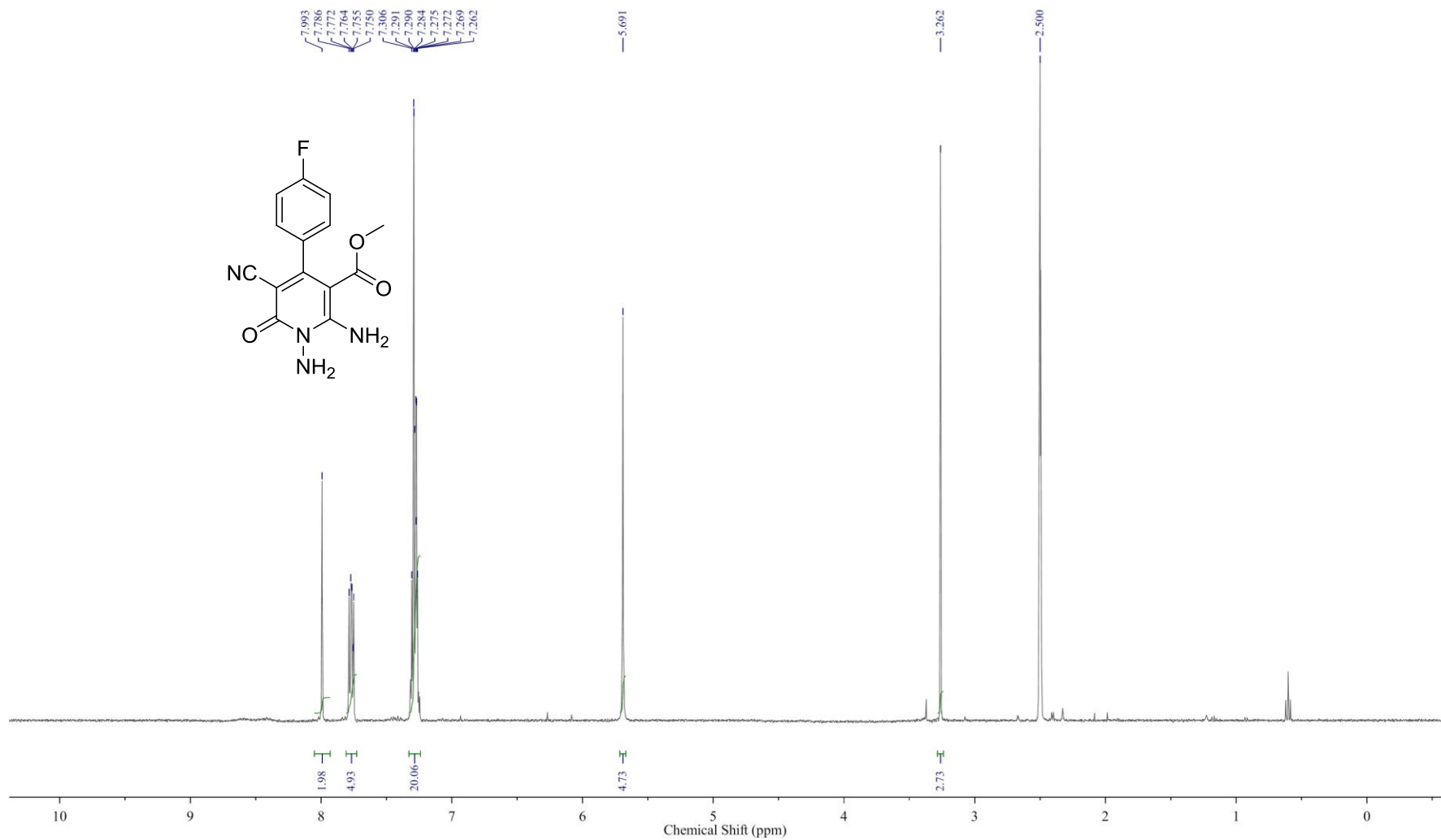
Supplementary Information (SI)

^{13}C NMR of Methyl 1,6-diamino-3-cyano-4-(2-chlorophenyl)-2-pyridone-5-carboxylate 4(k)



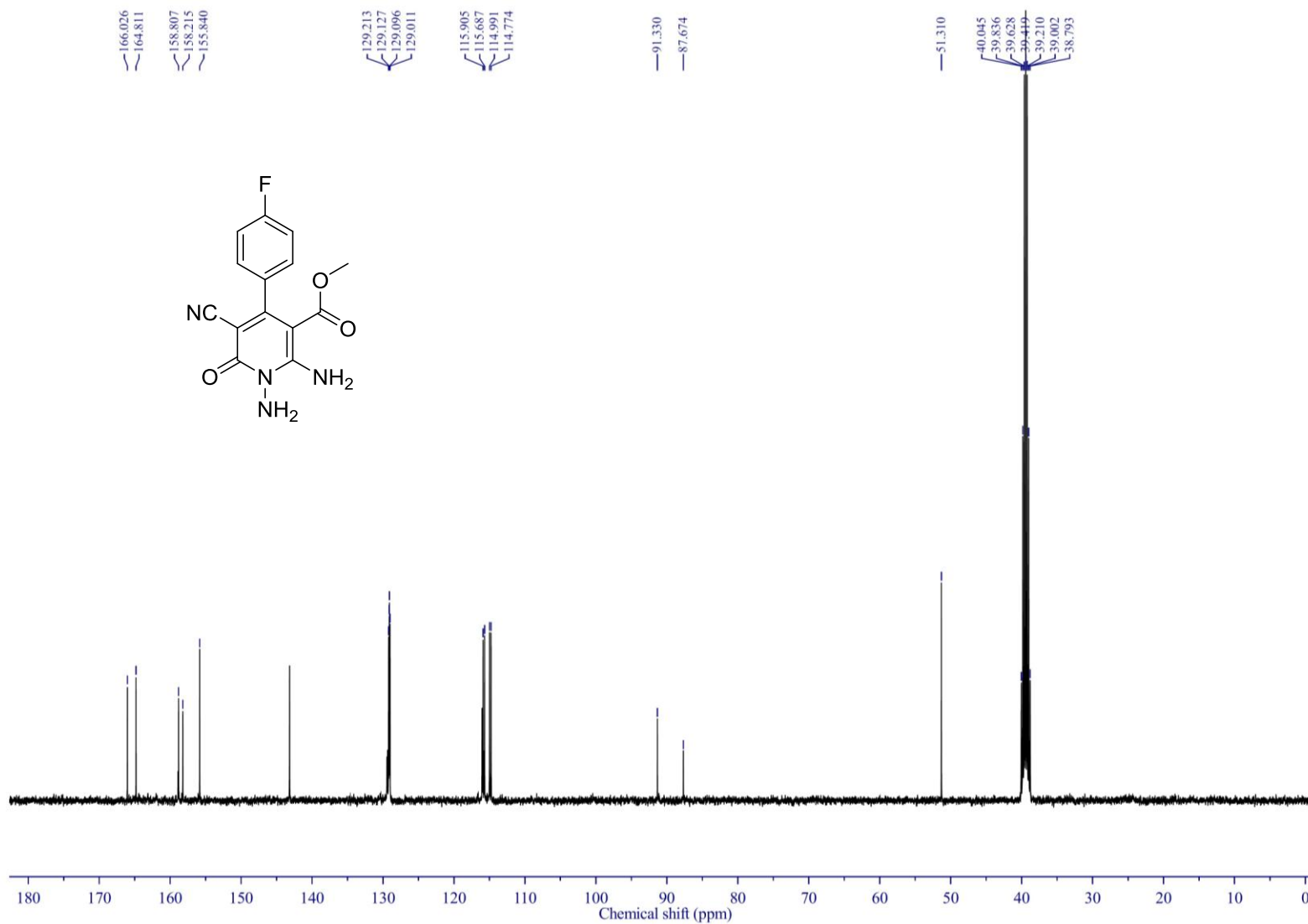
Supplementary Information (SI)

^1H NMR of Methyl 1,6-diamino-3-cyano-4-(4-fluorophenyl)-2-pyridone-5-carboxylate **4(l)**



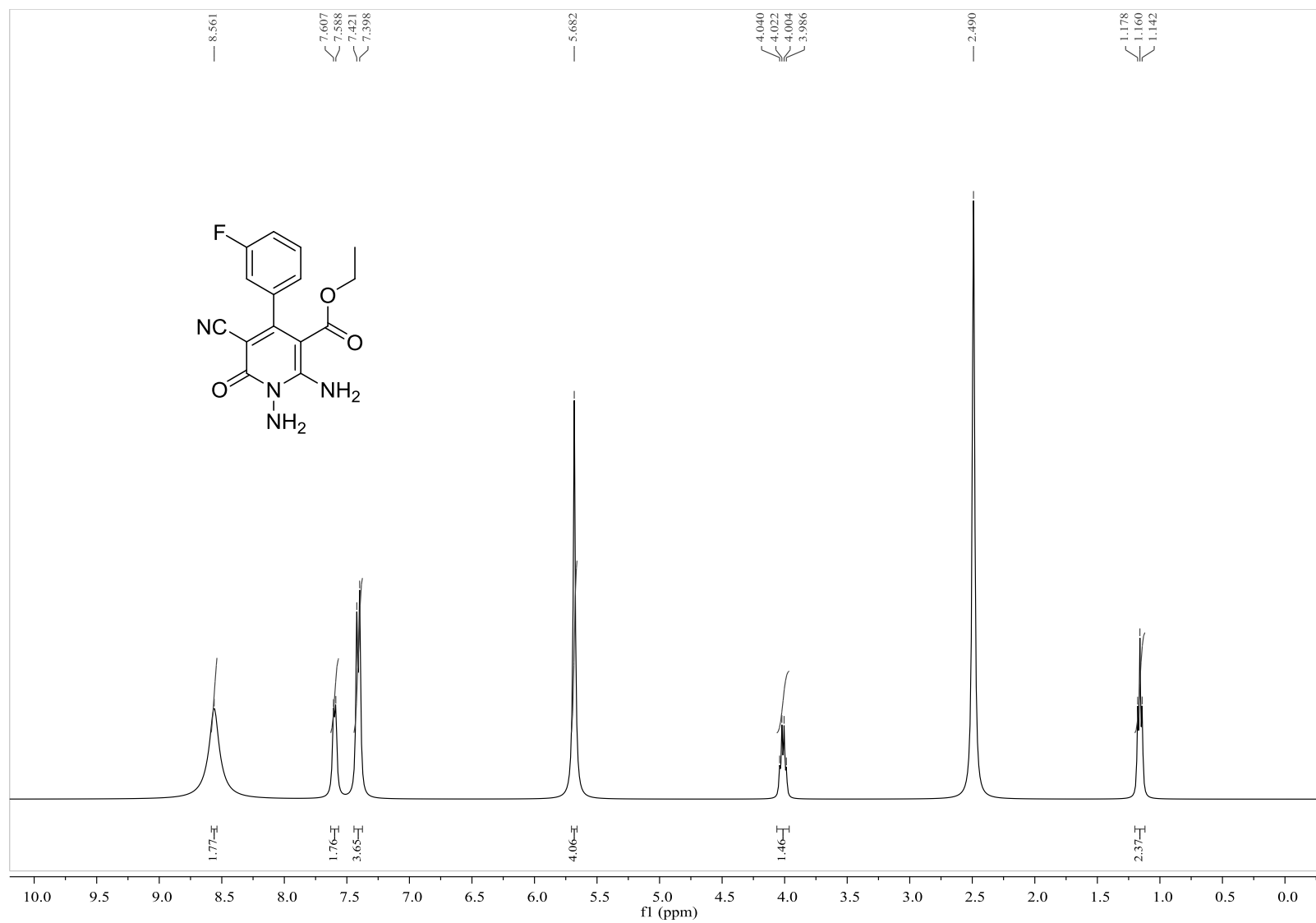
Supplementary Information (SI)

^{13}C NMR of Methyl 1,6-diamino-3-cyano-4-(4-fluorophenyl)-2-pyridone-5-carboxylate 4(l)



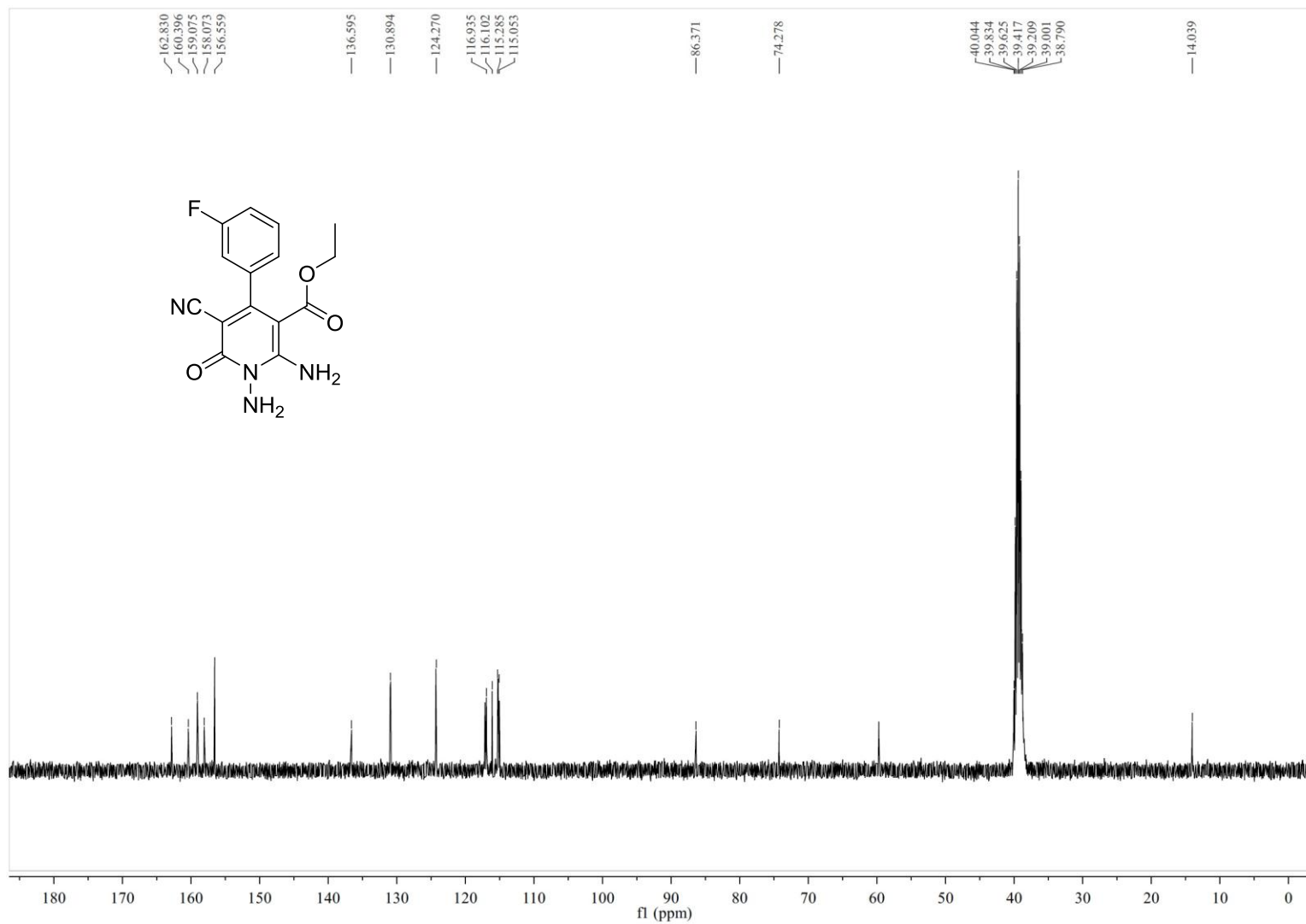
Supplementary Information (SI)

^1H NMR of ethyl 1,6-diamino-3-cyano-4-(3-fluorophenyl)-2-pyridone-5-carboxylate 4(m)



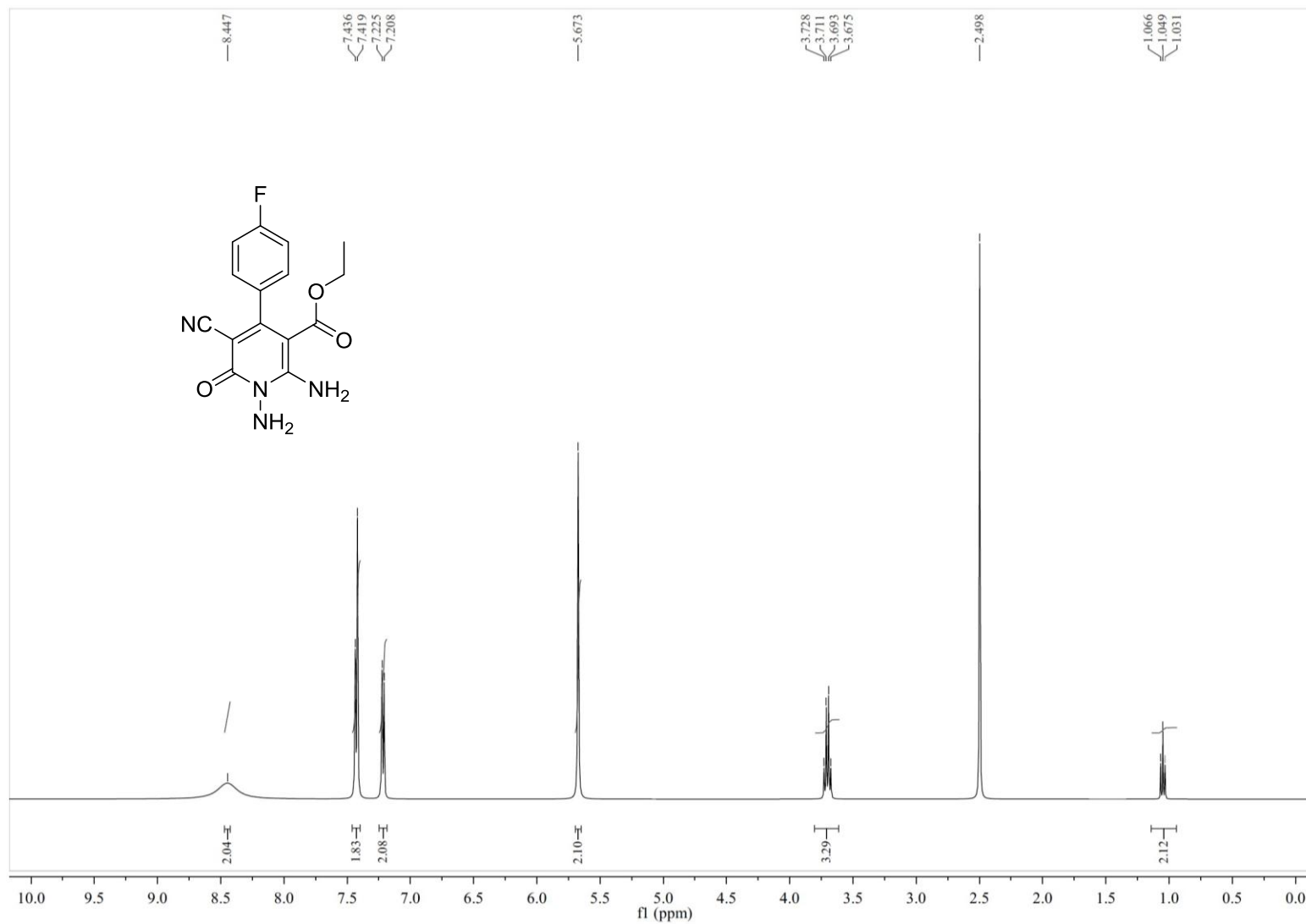
Supplementary Information (SI)

^{13}C NMR of ethyl 1,6-diamino-3-cyano-4-(3-fluorophenyl)-2-pyridone-5-carboxylate 4(m)



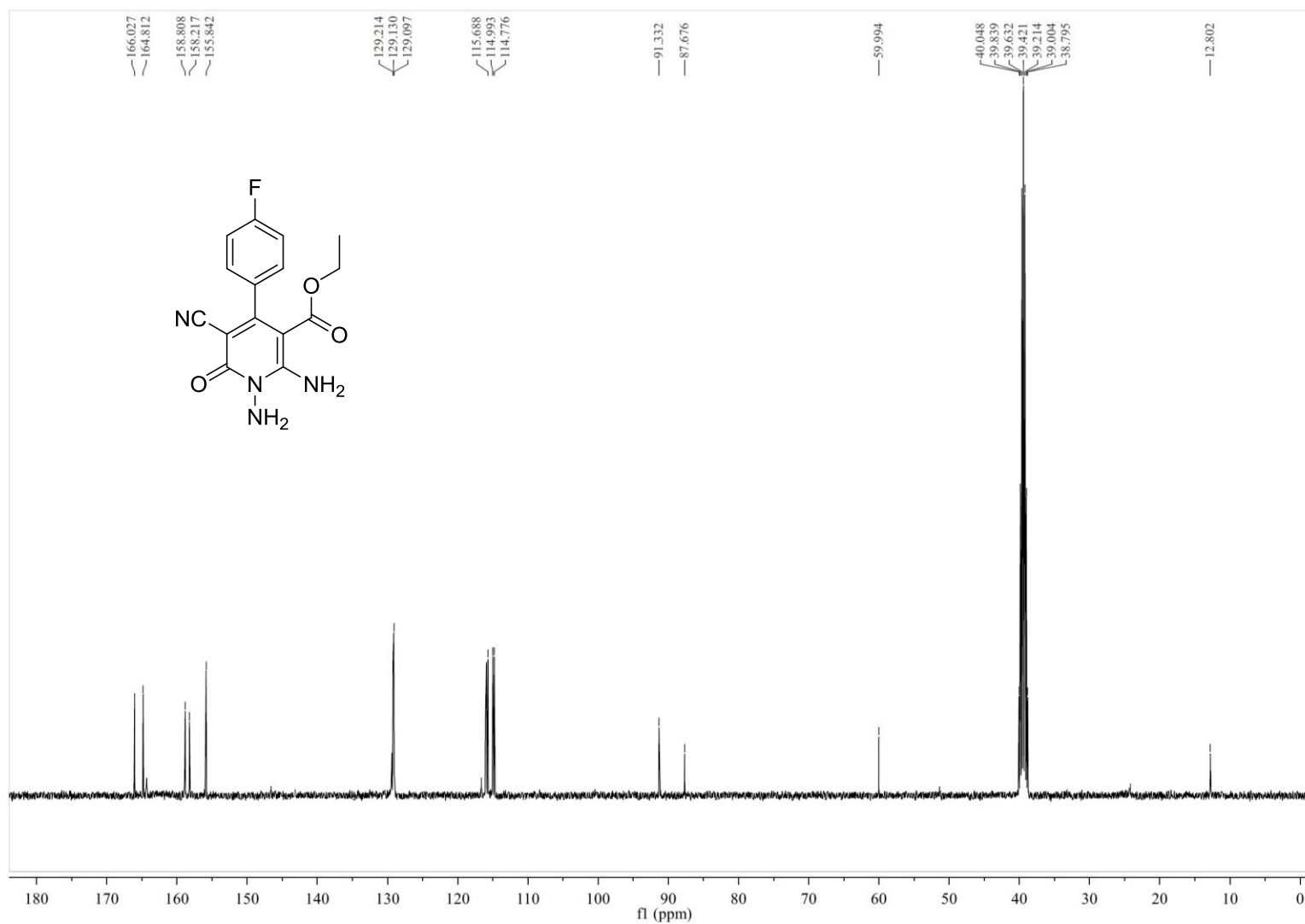
Supplementary Information (SI)

^1H NMR of ethyl 1,6-diamino-3-cyano-4-(4-fluorophenyl)-2-pyridone-5-carboxylate 4(n)



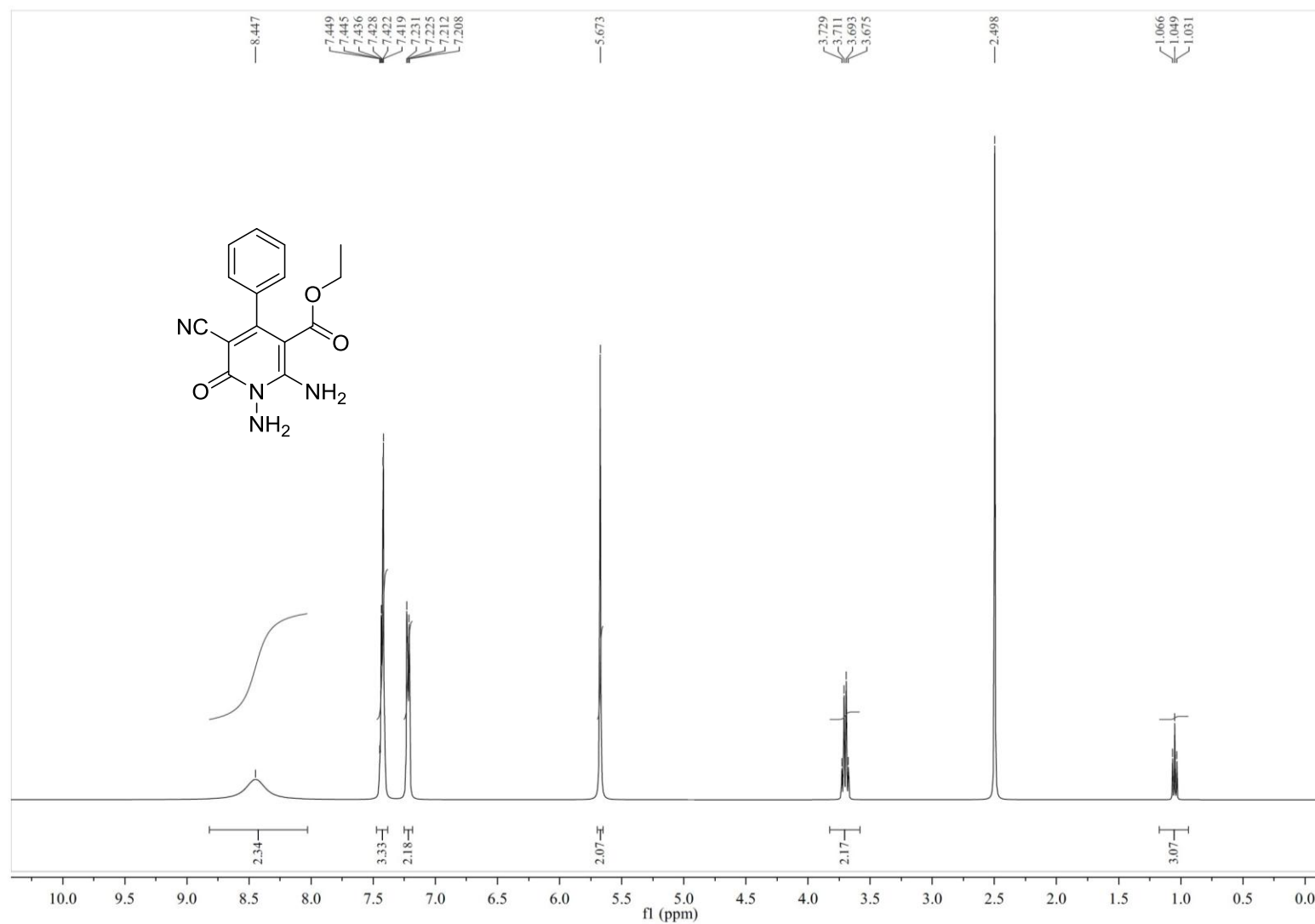
Supplementary Information (SI)

^{13}C NMR of ethyl 1,6-diamino-3-cyano-4-(4-fluorophenyl)-2-pyridone-5-carboxylate **4** (n)



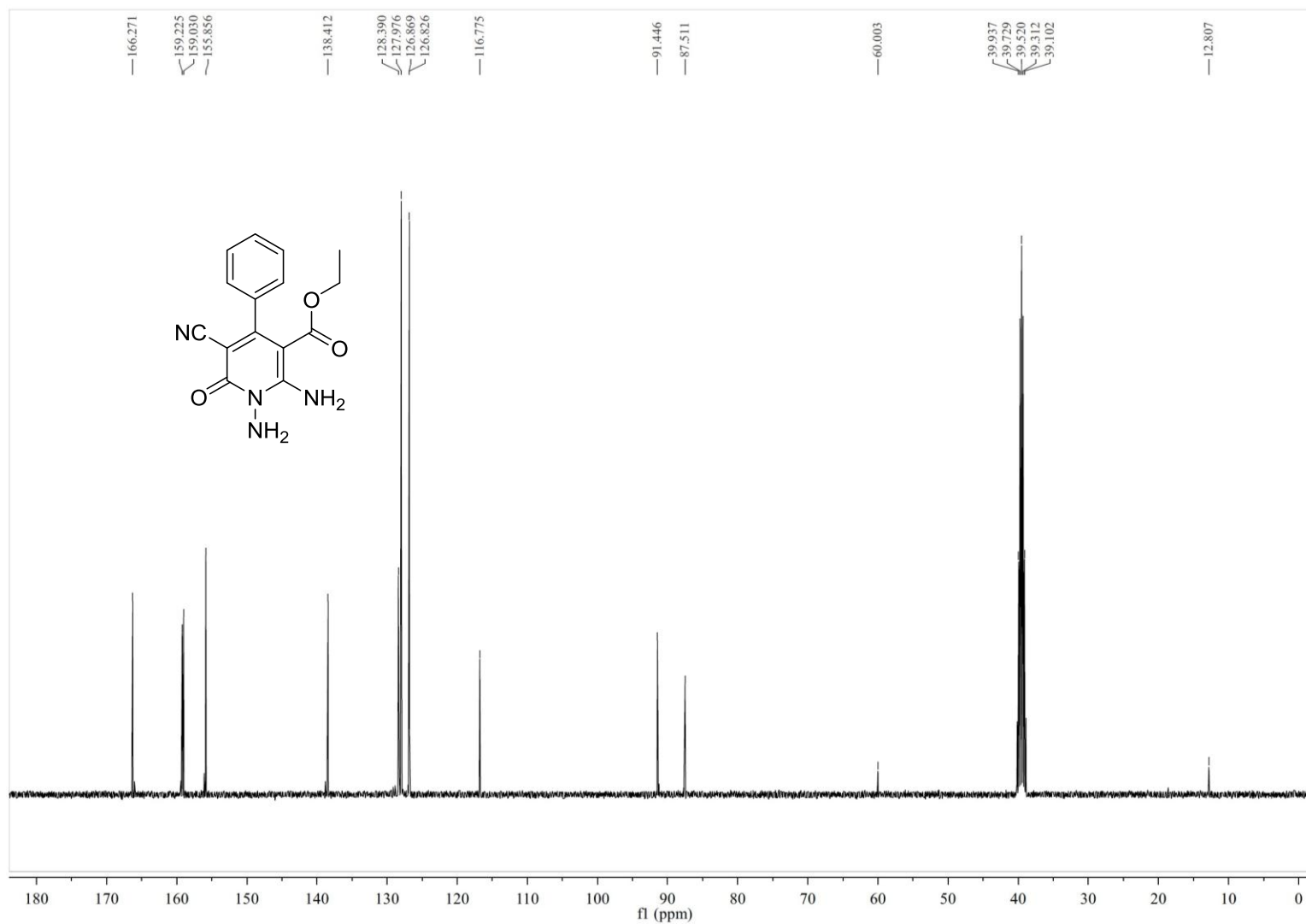
Supplementary Information (SI)

^1H NMR of ethyl 1,6-diamino-3-cyano-4-phenyl-2-pyridone-5-carboxylate **4(o)**



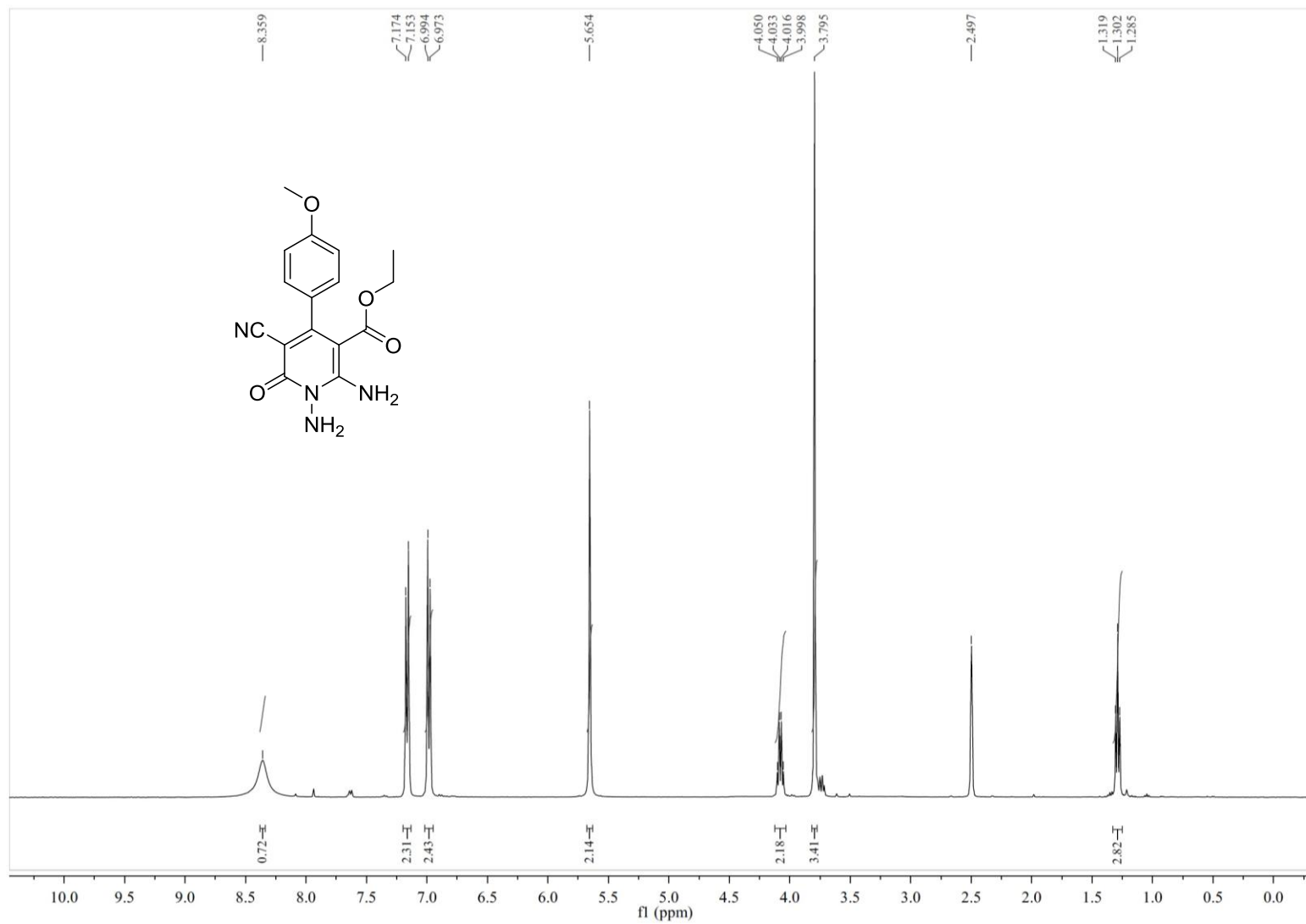
Supplementary Information (SI)

^{13}C NMR of ethyl 1,6-diamino-3-cyano-4-phenyl-2-pyridone-5-carboxylate 4(o)



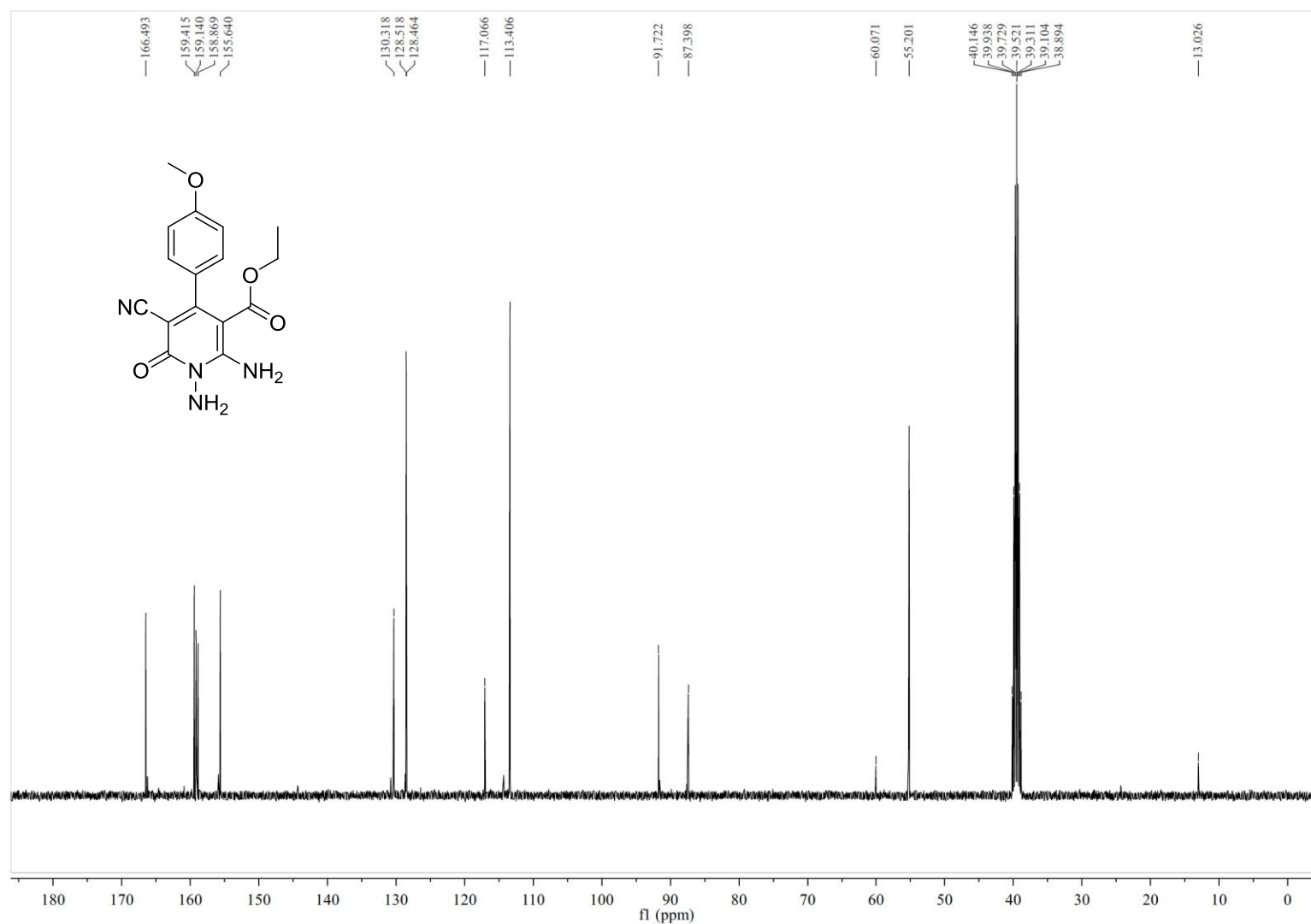
Supplementary Information (SI)

^1H NMR of ethyl 1,6-diamino-3-cyano-4-(4-methoxyphenyl)-2-yriridone-5-carboxylate 4(p)



Supplementary Information (SI)

^{13}C NMR of ethyl 1,6-diamino-3-cyano-4-(4-methoxyphenyl)-2-yriridone-5-carboxylate 4(p)



Supplementary Information (SI)

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