Electronic supplementary materials *Mendeleev Commun.*, 2027, **37**, just accepted

Smart molecules: quick assembly of functionalized 5-azaindoles from acetylenes and nicotinonitrile

Natal'ya A. Lobanova, Inna V. Tatarinova, Elena Yu. Schmidt, Igor A. Ushakov, Alexander V. Vashchenko and Boris A. Trofimov

Table of Contents

1. General Information S2
2. Optimization of the reaction parameters for the synthesis of 5-azaindole **3a** S2
3. Synthesis of 5-azaindoles **3** (*general procedure*) S3
3.1. Larger-scale synthesis of 5-azaindole **3a** S3
4. Characterization data of 5-azaindoles **3** S3
5. Synthesis of amidoximes **5** (*general procedure*) S7
6. Characterization data of amidoximes **5** S7
7. NMR spectra S9
8. X-Ray diffraction analysis S32
9. References S33

1. General Information

^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra were recorded on a Bruker AV400 instrument. The assignment of signals in the ^{1}H NMR spectra was made using COSY and NOESY experiments. Resonance signals of carbon atoms were assigned based on ^{1}H-^{13}C HSQC and ^{1}H-^{13}C HMBC experiments. Coupling constants (*J*) in hertz (Hz) were measured from one-dimensional spectra and multiplicities were abbreviated as following: s (singlet), br.s (broad singlet), m (multiplet). IR spectra were obtained on a "Bruker IFS-25" spectrometer (films) in 400-4000 cm^{-1} region. The microanalyses were performed on a FlashEA 1112 Series elemental analyzer. Mass spectra of positive electron ionization ions (70 eV) were registered on a Shimadzu GCMS-QP5050A with a DI-50 direct sample injection system (quadrupole mass analyzer, range of detected masses 34 - 650 Da). Melting points (uncorrected) were measured on a Kofler micro hot-stage apparatus. Thin layer chromatography was carried out on Merck silica gel 60 F254 pre-coated aluminium foil sheets (eluent: diethyl ether/ethanol = 10:0.1) and were visualized using UV light (254 nm). Column chromatography was carried out using slurry packed Sigma Aldrich silica gel (70-230 mesh, pore size 60 Å). DMSO was dried over molecular sieves (4 Å, 4-8 mesh). Acetylenes, nicotinonitre and other reagents and solvents are commercially available and were used without further purification.

2. Optimization of the reaction parameters for the synthesis of 5-azaindole 3a

Taking as the starting point the conditions preliminary found for selective formation of **3a** (Table S1, entry 5), first the content of $KOBu^{t}$ was increased to 1.5 equiv. (Table 2, entry 2). This allows the yield of the target product **3a** to be increased to 42%, albeit noticeable tar formation occurred, likely due to oligomerization of the reactants and intermediates. To avoid these undesirable processes and further improve the yield of **3a**, various additives were used. When $HOBu^{t}$ (10 vol% relative to DMSO) was employed, the yield of 5-azaindole **3a** became 50% (Table 2, entry 3). However, with 20 vol% of $HOBu^{t}$, the yield dropped to 33% (Table 2, entry 4). In DMSO/THF (10 vol%) mixture, the yield of **3a** reached 56% (Table 2, entry 5). At a higher THF content (25 vol%), the yield of **3a** was diminished to 38% (Table 2, entry 6). The additive of sulfolane (10 vol%) also lowered the yield of **3a** to 46% (Table 2, entry 7), the reaction mixture contained the starting acetylene **1a** (10%) and nitrile **2** (14%). The further increase of sulfolane content had a strongly negative impact on the reaction efficiency (Table 2, entry 8). In the presence of other additives (MeOH or NMP), the self-organization studied ceased completely (Table 2, entries 10 and 11) as did the reaction in pure DMF (entry 9). Since noticeable amounts of oligomers were formed in all cases, likely due to an exothermic effect up to 38 °C, the temperature of the reactant mixing was lowered to 10-12 °C, and the reaction further proceeded at room temperature. To rich 68% yield of the target product **3a**, 1.3 equiv. of acetylene **1a** were required (Table 2, entry 13). When the content of $KOBu^{t}$ was increased to two equiv. and the reaction duration was shortened to 15 min, the yield of **3a** remains the same (68%, Table 2, entry 15). Two-fold dilution of the reaction mixture (Table 2, entry 16), as well as decrease in the reactant mixing temperature (Table 2, entry 17), did not improve the reaction efficiency. In the presence of other bases, the self-organization proceeded much slower ($NaOBu^{t}$, entry 18), or stopped ($KOH \cdot 0.5H_2O$, entry 20), or the target product **3a** was formed in a low yield ($KOBu^{t}$/CsF, entry 19).

Table S1 Optimization of reaction parameters for the synthesis of 5-azaindole **3a**.[a]

entry	base	solvent/additive (vol% relative to DMSO)	**1a**:**2**:base molar ratio	T (°C)	t (min)	yield of **3a** (%)[b]
1	KOBu^t	DMSO	1:2:1	rt	60	36
2	KOBu^t	DMSO	1:2:1.5	rt	60	42
3	KOBu^t	DMSO/HOBu^t(10)	1:2:1.5	rt	60	50
4	KOBu^t	DMSO/HOBu^t(20)	1:2:1.5	rt	60	33
5	KOBu^t	DMSO/THF(10)	1:2:1.5	rt	60	56
6	KOBu^t	DMSO/THF(25)	1:2:1.5	rt	60	38
7	KOBu^t	DMSO/sulfolane(10)	1:2:1.5	rt	60	46
8	KOBu^t	DMSO/sulfolane(40)	1:2:1.5	rt	60	13
9	KOBu^t	DMF	1:2:1.5	rt	60	nd
10	KOBu^t	DMSO/MeOH(20)	1:2:1.5	rt	60	nd
11	KOBu^t	DMSO/NMP(10)	1:2:1.5	rt	60	nd
12[c]	KOBu^t	DMSO/THF(10)	1:2:1.5	10-12→rt	60	60 (55)[d]
13[c]	KOBu^t	DMSO/THF(10)	1.3:2:1.5	10-12→rt	60	68
14[c]	KOBu^t	DMSO/THF(10)	1.3:2:2	10-12→rt	30	51
15[c]	KOBu^t	DMSO/THF(10)	1.3:2:2	10-12→rt	15	68 (61)[d]
16[c,e]	KOBu^t	DMSO/THF(10)	1.3:2:2	10-12→rt	30	53[d]
17[c]	KOBu^t	DMSO/THF(10)	1.3:2:2	1-2→rt	30	25[d]
18	NaOBu^t	DMSO/THF(10)	1.3:2:2	rt	60	9
19[c,f]	KOBu^t/CsF	DMSO/THF(10)	1.3:2:2	10-12→rt	15	27[d]
20	KOH·0.5H_2O	DMSO/THF(10)	1.3:2:2	rt	60	nd

[a] *Reagents and conditions*: A solution of **1a**, KOBu^t in DMSO (3 mL) was added dropwise to a solution of **2** (2 mmol) in DMSO (3 mL) at 20-22 °C. [b] According to ^{1}H NMR data of the crude product (durene was used as an internal standard). [c] **1a** was added dropwise to a solution of KOBu^t in DMSO (3 mL)/THF (0.3 mL) at 10-12 °C for 1-2 min, then this mixture was fed dropwise to a solution of **2** in DMSO (3 mL)/THF (0.3 mL) at 10-12 °C for 1-2 min followed by stirring the reaction mixture at 20-22 °C. [d] Isolated yield of after column chromatography (SiO_2, *n*-hexane–diethyl ether with gradient from 1:1 to 0:1). [e] DMSO (12 mL). [f] CsF (1 mmol). rt=20-22 °C. nd=not detected.

3. Synthesis of 5-azaindoles 3 (*general procedure*)

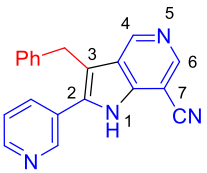
Acetylene **1** (1.3 mmol) and KOBu^t (2 mmol, 224 mg) or (1.5 mmol, 168 mg for **1e,n**) in a mixture of DMSO (3 mL)/THF (0.3 mL) were stirred at 10-12 °C for 1-2 min. Then, this mixture was added drop-wise to a solution of nicotinonitre **2** (2 mmol, 208) in a mixture of DMSO (3 mL)/THF (0.3 mL) at 10-12 °C for 1-2 min and stirred for another 15 min (60 min for **1e,n**) at 20-22 °C. The reaction mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (8 mL × 4). The organic extract was washed with H_2O (5 mL × 3) and dried over K_2CO_3. CH_2Cl_2 was evaporated in vacuum, and the residue was purified by column chromatography (SiO_2, eluent: hexane–diethyl ether with gradient from 1:1 to 0:1) to give pure 5-azaindole **3**.

3.1. Larger-scale synthesis of 5-azaindole 3a

Acetylene **1a** (13 mmol, 1.33g) and KOBu^t (20 mmol, 2.24 g) in a mixture of DMSO (30 mL)/THF (3 mL) were stirred at 10-12 °C for 2 min. Then, this mixture was added drop-wise to a solution of nitrile **2** (20 mmol, 2.08 g) in a mixture of DMSO (30 mL)/THF (3 mL) at 10-12 °C for 15 min and stirred for another 15 min at 20-22 °C. The reaction mixture was diluted with H_2O (200 mL) and extracted with CH_2Cl_2 (70 mL × 4). The organic extract was washed with H_2O (50 mL × 3) and dried over K_2CO_3. CH_2Cl_2 was evaporated in vacuum, and the residue was purified by column chromatography (SiO_2, eluent: hexane–diethyl ether with gradient from 1:1 to 0:1). **3a** was isolated as a beige powder (1.76 g, 57% yield).

4. Characterization data of 5-azaindoles 3

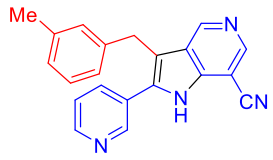
3-Benzyl-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3a**



Following the general procedure, **3a** was prepared from **1a** (1.3 mmol, 133 mg) and **2** (2 mmol, 208 mg). **3a** was isolated as a beige powder (189 mg, 61% yield). Mp 237-239

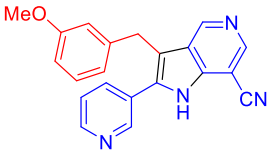
°C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.88 (br.s, 1H, NH), 8.91 (s, 1H, H4), 8.85-8.84 (m, 1H, H_{Py}), 8.66 (s, 1H, H6), 8.65-8.63 (m, 1H, H_{Py}), 8.09-8.06 (m, 1H, H_{Py}), 7.57-7.54 (m, 1H, H_{Py}), 7.25-7.23 (m, 2H, H_{Ph}), 7.18-7.14 (m, 3H, H_{Ph}), 4.31 (s, 2H, CH_2); ^{13}C{^{1}H} NMR (DMSO-d_6, 101 MHz): δ 150.0, 149.6, 146.4, 145.9, 140.9, 139.3, 136.7, 135.8, 129.1, 128.5, 127.4, 126.7, 126.0, 124.2, 116.5, 113.0, 92.5, 29.8; IR (film, ν/cm^{-1}): 3383 br (N-H), 2226 w (C≡N). Elemental analysis calcd (%) for $C_{20}H_{14}N_4$ (310.36): C, 77.40; H, 4.55; N, 18.05; found (%): C, 77.35; H, 4.53; N, 18.12; MS (EI): m/z calcd for $C_{20}H_{14}N_4$ 310.12 $[M]^{+\cdot}$; found 310.25.

3-(3-Methylbenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3b**



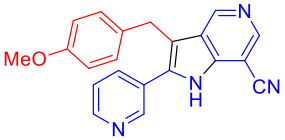
Following the general procedure, **3b** was prepared from **1b** (1.3 mmol, 151 mg) and **2** (2 mmol, 208 mg). **3b** was isolated as a yellow powder (93 mg, 29% yield). Mp 255-257 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.86 (br.s, 1H, NH), 8.88 (s, 1H, H4), 8.83-8.82 (m, 1H, H_{Py}), 8.64 (s, 1H, H6), 8.63-8.62 (m, 1H, H_{Py}), 8.07-8.04 (m, 1H, H_{Py}), 7.56-7.52 (m, 1H, H_{Py}), 7.12-7.23 (m, 1H, H_{Ph}), 6.96-6.95 (m, 2H, H_{Ph}), 6.90-6.88 (m, 1H, H_{Ph}), 4.24 (s, 2H, CH_2), 2.18 (s, 3H, Ph$\underline{CH_3}$); ^{13}C{^{1}H} NMR (DMSO-d_6, 101 MHz): δ 150.5, 150.2, 146.9, 146.5, 141.3, 139.8, 138.7, 137.2, 136.3, 129.7, 129.5, 127.9, 126.6, 126.1, 124.8, 117.0, 113.6, 93.0, 30.3, 22.1; IR (film, ν/cm^{-1}): 3399 br (N-H), 2225 w (C≡N). Elemental analysis calcd (%) for $C_{21}H_{16}N_4$ (324.39): C, 77.76; H, 4.97; N, 17.27; found (%): C, 77.70; H, 4.95; N, 17.31; MS (EI): m/z calcd for $C_{21}H_{16}N_4$ 324.14 $[M]^{+\cdot}$; found 324.20.

3-(3-Methoxybenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile) **3d**



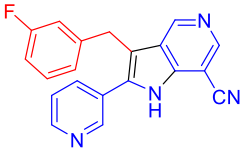
Following the general procedure, **3d** was prepared from **1d** (1.3 mmol, 172 mg) and **2** (2 mmol, 208 mg). **3b** was isolated as cream crystals (139 mg, 41% yield). Mp 219-221 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.87 (br.s, 1H, NH), 8.93 (s, 1H, H4), 8.85-8.84 (m, 1H, H_{Py}), 8.66 (s, 1H, H6), 8.65-8.64 (m, 1H, H_{Py}), 8.09-8.06 (m, 1H, H_{Py}), 7.57-7.54 (m, 1H, H_{Py}), 7.17-7.13 (m, 1H, H_{Ph}), 6.74-6.68 (m, 3H, H_{Ph}), 4.27 (s, 2H, CH_2), 3.65 (s, 3H, O$\underline{CH_3}$); ^{13}C{^{1}H} NMR (DMSO-d_6, 101 MHz): δ 159.9, 150.0, 149.6, 146.4, 145.9, 142.5, 139.3, 136.7, 135.8, 130.1, 127.4, 126.0, 124.2, 120.7, 116.5, 114.5, 113.0, 111.9, 92.5, 55.4, 29.7; IR (film, ν/cm^{-1}): 3309 br (N-H), 2227 w (C≡N). Elemental analysis calcd (%) for $C_{21}H_{16}N_4O$ (340.39): C, 74.10; H, 4.74; N, 16.46; found (%): C, 74.04; H, 4.76; N, 16.50; MS (EI): m/z calcd for $C_{21}H_{16}N_4O$ 340.13 $[M]^{+\cdot}$; found 340.20.

3-(4-Methoxybenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3e**



Following the general procedure, **3e** was prepared from **1e** (1.3 mmol, 172 mg) and **2** (2 mmol, 208 mg). **3e** was isolated as a brown powder (27 mg, 8% yield). Mp 215-218 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.84 (br.s, 1H, NH), 8.88 (s, 1H, H4), 8.85-8.84 (m, 1H, H_{Py}), 8.65-8.63 (m, 2H, H6), 8.07-8.05 (m, 1H, H_{Py}), 7.57-7.53 (m, 1H, H_{Py}), 7.06-7.03 (m, 2H, H_{Ph}), 6.81-6.79 (m, 2H, H_{Ph}), 4.22 (s, 2H, CH_2), 3.67 (s, 3H, O$\underline{CH_3}$); ^{13}C{^{1}H} NMR (DMSO-d_6, 101 MHz): δ 158.1, 149.9, 149.6, 146.3, 145.9, 139.2, 136.6, 135.6, 132.7, 129.5, 127.4, 126.0, 124.2, 116.4, 114.4, 113.5, 92.4, 55.5, 28.9; IR (film, ν/cm^{-1}): 3399 br (N-H), 2227 w (C≡N). Elemental analysis calcd (%) for $C_{21}H_{16}N_4O$ (340.39): C, 74.10; H, 4.74; N, 16.46; found (%):C, 74.05; H, 4.78; N, 16.51; MS (EI): m/z calcd for $C_{21}H_{16}N_4O$ 340.13 $[M]^{+\cdot}$; found 340.15.

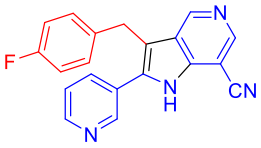
3-(3-Fluorobenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3f**



Following the general procedure, **3f** was prepared from **1f** (1.3 mmol, 156 mg) and **2** (2 mmol, 208 mg). **3f** was isolated as cream crystals (69 mg, 21% yield). Mp 227-229 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.93 (br.s, 1H, NH), 8.94 (s, 1H, H4), 8.84-8.83 (m, 1H, H_{Py}), 8.67 (s, 1H, H6), 8.65-8.63 (m, 1H, H_{Py}), 8.08-8.05 (m, 1H, H_{Py}), 7.57-7.54 (m, 1H, H_{Py}), 7.28-7.25 (m, 1H, H_{Ph}), 6.99-6.94 (m, 3H, H_{Ph}), 4.33 (s, 2H, CH_2); ^{13}C{^{1}H} NMR (DMSO-d_6, 101 MHz): δ 162.6 (d, ^1J = 243.7 Hz, C–F), 149.8, 149.4, 146.1, 145.8, 143.7 (d, ^3J = 7.1 Hz, C*i*), 139.1, 136.5, 135.8, 130.8 (d, ^3J = 8.4 Hz, C*m*), 127.1, 125.7, 124.4 (d, ^4J = 2.8 Hz, C*o*), 124.0, 116.3, 115.1 (d, ^2J = 21.3 Hz, C*p*), 113.3 (d, ^2J = 20.8 Hz, C*o*'), 112.1, 92.3, 29.2; IR (film, ν/cm^{-1}): 3398 br (N-H), 2226 w (C≡N). Elemental analysis calcd (%) for $C_{20}H_{13}FN_4$ (328.35): C, 73.16; H,

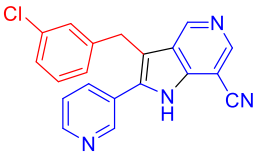
3.99; F, 5.79; N, 17.06; found (%): C, 73.10; H, 3.97; F, 5.83; N, 17.09; MS (EI): m/z calcd for $C_{20}H_{13}FN_4$ 328.11 $[M]^{+\cdot}$; found 328.15.

3-(4-Fluorobenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3g**



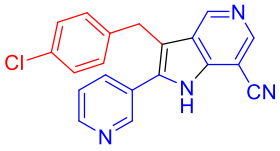
Following the general procedure, **3g** was prepared from **1g** (1.3 mmol, 156 mg) and **2** (2 mmol, 208 mg). **3g** was isolated as a beige powder (85 mg, 26% yield). Mp 227-229 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.90 (br.s, 1H, NH), 8.91 (s, 1H, H4), 8.85-8.84 (m, 1H, H_{Py}), 8.66 (s, 1H, H6), 8.65-8.64 (m, 1H, H_{Py}), 8.07-8.05 (m, 1H, H_{Py}), 7.57-7.53 (m, 1H, H_{Py}), 7.18-7.14 (m, 2H, H_{Ph}), 7.08-7.03 (m, 2H, H_{Ph}), 4.29 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 101 MHz): δ 161.2 (d, ^1J = 241.9 Hz, C-F), 150.0, 149.6, 146.3, 145.9, 139.2, 136.9 (d, ^4J = 2.8 Hz, C*i*), 136.7, 135.8, 130.2 (d, ^3J = 8.0 Hz, C*o*), 127.3, 125.9, 124.2, 116.4, 115.7 (d, ^2J = 21.1 Hz, C*m*), 112.9, 92.5, 28.9; IR (film, ν/cm^{-1}): 3422 br (N-H), 2227 w (C≡N). Elemental analysis calcd (%) for $C_{20}H_{13}FN_4$ (328.35): C, 73.16; H, 3.99; F, 5.79; N, 17.06; found (%): C, 73.11; H, 3.96; F, 5.85; N, 17.08; MS (EI): m/z calcd for $C_{20}H_{13}FN_4$ 328.11 $[M]^{+\cdot}$; found 328.15.

3-(3-Chlorobenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3h**



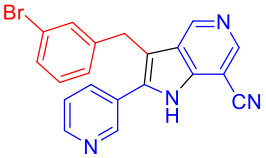
Following the general procedure, **3h** was prepared from **1h** (1.3 mmol, 178 mg) and **2** (2 mmol, 208 mg). **3h** was isolated as colorless crystals (127 mg, 37% yield). Mp 261-263 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.93 (br.s, 1H, NH), 8.95 (s, 1H, H4), 8.84-8.83 (m, 1H, H_{Py}), 8.67 (s, 1H, H6), 8.66-8.64 (m, 1H, H_{Py}), 8.08-8.05 (m, 1H, H_{Py}), 7.57-7.54 (m, 1H, H_{Py}), 7.26-7.20 (m, 3H, H_{Ph}), 7.08-7.06 (m, 1H, H_{Ph}), 4.33 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 101 MHz): δ 150.0, 149.6, 146.3, 146.0, 143.4, 139.2, 136.7, 136.0, 133.6, 130.8, 128.3, 127.2, 127.2, 126.7, 125.8, 124.2, 116.4, 112.2, 92.5, 29.3; IR (film, ν/cm^{-1}): 3404 br (N-H), 2226 w (C≡N). Elemental analysis calcd (%) for $C_{20}H_{13}ClN_4$ (344.80): C, 69.67; H, 3.80; Cl, 10.28; N, 16.25; found (%): C, 69.62; H, 3.83; Cl, 10.27; N, 16.28; MS (EI): m/z calcd for $C_{20}H_{13}ClN_4$ 344.08 $[M]^{+\cdot}$; found 344.10.

3-(4-Chlorobenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3i**



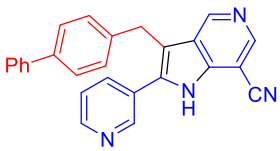
Following the general procedure, **3i** was prepared from **1i** (1.3 mmol, 178 mg) and **2** (2 mmol, 208 mg). **3i** was isolated as a beige powder (82 mg, 24% yield). Mp 266-268 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.89 (br.s, 1H, NH), 8.92 (s, 1H, H4), 8.83-8.82 (m, 1H, H_{Py}), 8.66 (s, 1H, H6), 8.65-8.63 (m, 1H, H_{Py}), 8.06-8.03 (m, 1H, H_{Py}), 7.56-7.53 (m, 1H, H_{Py}), 7.29-7.27 (m, 2H, H_{Ph}), 7.16-7.14 (m, 2H, H_{Ph}), 4.29 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 101 MHz): δ 150.0, 149.55, 146.3, 145.9, 139.9, 139.3, 136.6, 135.9, 131.2, 130.3, 128.9, 127.2, 125.9, 124.2, 116.4, 112.5, 92.5, 29.1; IR (film, ν/cm^{-1}): 3368 br (N-H), 2226 w (C≡N). Elemental analysis calcd (%) for $C_{20}H_{13}ClN_4$ (344.80): C, 69.67; H, 3.80; Cl, 10.28; N, 16.25; found (%): C, 69.63; H, 3.83; Cl, 10.25; N, 16.29; MS (EI): m/z calcd for $C_{20}H_{13}ClN_4$ 344.08 $[M]^{+\cdot}$; found 344.10.

3-(3-Bromobenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3j**



Following the general procedure, **3j** was prepared from **1j** (1.3 mmol, 234 mg) and **2** (2 mmol, 208 mg). **3j** was isolated as a cream powder (144 mg, 37% yield). Mp 267-269 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.92 (br.s, 1H, NH), 8.95 (s, 1H, H4), 8.84-8.83 (m, 1H, H_{Py}), 8.67 (s, 1H, H6), 8.65-8.64 (m, 1H, H_{Py}), 8.08-8.05 (m, 1H, H_{Py}), 7.57-7.54 (m, 1H, H_{Py}), 7.35-7.34 (m, 2H, H_{Ph}), 7.20-7.16 (m, 1H, H_{Ph}), 7.11-7.09 (m, 1H, H_{Ph}), 4.32 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 101 MHz): δ 149.5, 149.0, 145.7, 145.5, 143.2, 138.7, 136.2, 135.5, 130.7, 130.6, 129.1, 127.0, 126.7, 125.3, 123.7, 121.8, 115.9, 111.7, 92.0, 28.7; IR (film, ν/cm^{-1}): 3398 br (N-H), 2227 w (C≡N). Elemental analysis calcd (%) for $C_{20}H_{13}BrN_4$ (389.26): C, 61.71; H, 3.37; Br, 20.53; N, 14.39; found (%): C, 61.67; H, 3.39; Br, 20.51; N, 14.43; MS (EI): m/z calcd for $C_{20}H_{13}BrN_4$ 388.03 $[M]^{+\cdot}$; found 388.05.

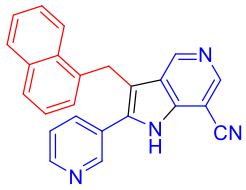
3-([1,1'-Biphenyl]-4-ylmethyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3l**



Following the general procedure, **3l** was prepared from **1l** (1.3 mmol, 231 mg) and **2** (2 mmol, 208 mg). **3l** was isolated as a cream powder (99 mg, 26% yield). Mp 265-268 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.91 (br.s, 1H, NH), 8.98 (s, 1H, H4), 8.88-8.87 (m, 1H, H_{Py}), 8.68 (s, 1H, H6), 8.66-8.64 (m, 1H, H_{Py}), 8.11-

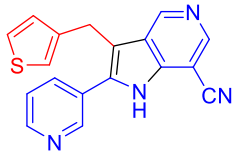
8.08 (m, 1H, H_{Py}), 7.60-7.53 (m, 5H, H_{Py}, H_{Ph}), 7.42-7.39 (m, 2H, H_{Ph}), 7.33-7.31 (m, 1H, H_{Ph}), 7.24-7.22 (m, 2H, H_{Ph}), 4.36 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 101 MHz): δ 149.5, 149.1, 145.8, 145.4, 139.8, 139.6, 138.8, 138.0, 136.1, 135.3, 128.8, 128.5, 127.2, 126.8, 126.5, 125.5, 123.7, 115.9, 112.4, 92.0, 28.8; IR (film, ν/cm^{-1}): 3409 br (N-H), 2225 w (C≡N). Elemental analysis calcd (%) for $C_{26}H_{18}N_4$ (386.46): C, 80.81; H, 4.69; N, 14.50; found (%): C, 80.77; H, 4.70; N, 14.53; MS (EI): m/z calcd for $C_{26}H_{18}N_4$ 386.15 $[M]^{+\cdot}$; found 386.20.

3-(Naphthalen-1-ylmethyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3m**



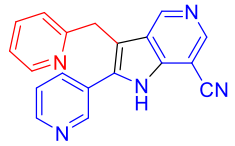
Following the general procedure, **3m** was prepared from **1m** (1.3 mmol, 198 mg) and **2** (2 mmol, 208 mg). **3m** was isolated as a beige powder (76 mg, 21% yield). Mp 256-258 ºC. ^1H NMR (DMSO-d_6, 400 MHz): δ 12.97 (br.s, 1H, NH), 8.79-8.78 (m, 1H, H_{Py}), 8.76 (s, 1H, H4), 8.64 (s, 1H, H6), 8.60-8.58 (m, 1H, H_{Py}), 8.09-8.07 (m, 1H, H_{Py}), 8.04-8.01 (m, 1H, H_{Py}), 7.95-7.92 (m, 1H, H_{Naf}), 7.79-7.77 (m, 1H, H_{Naf}), 7.53-7.48 (m, 3H, H_{Naf}), 7.35-7.31 (m, 1H, H_{Naf}), 7.07-7.06 (m, 1H, H_{Naf}), 4.73 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 101 MHz): δ 149.9, 149.4, 146.3, 145.9, 139.5, 136.4, 136.3, 136.2, 133.9, 131.9, 129.1, 127.4, 127.4, 126.7, 126.4, 126.2, 126.1, 125.7, 124.2, 124.0, 116.5, 112.05, 92.5, 27.4; IR (film, ν/cm^{-1}): 3411 br (N-H), 2226 w (C≡N). Elemental analysis calcd (%) for $C_{24}H_{16}N_4$ (360.42): C, 79.98; H, 4.47; N, 15.55; found (%): C, 79.93; H, 4.49; N, 15.58; MS (EI): m/z calcd for $C_{24}H_{16}N_4$ 360.14 $[M]^{+\cdot}$; found 360.20.

2-(Pyridin-3-yl)-3-(thiophen-3-ylmethyl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3n**



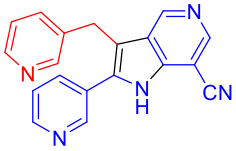
Following the general procedure, **3n** was prepared from **1n** (1.3 mmol, 140 mg) and **2** (2 mmol, 208 mg). **3n** was isolated as a beige powder (66 mg, 21% yield). Mp 228-230 ºC. ^1H NMR ($CDCl_3$, 400 MHz): δ 11.60 (br.s, 1H, NH), 8.91-8.90 (m, 1H, H_{Py}), 8.87 (s, 1H, H4), 8.62-8.61 (m, 2H, H6, H_{Py}), 7.92-7.89 (m, 1H, H_{Py}), 7.41-7.38 (m, 1H, H_{Py}), 7.29-7.26 (m, 1H, H_{Thioph}), 6.92-6.87 (m, 2H, H_{Thioph}), 4.25 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 149.7, 149.3, 146.1, 145.5, 140.2, 139.9, 136.1, 134.9, 127.7, 127.3, 126.5, 125.8, 123.9, 121.3, 115.9, 113.5, 92.5, 25.3; IR (film, ν/cm^{-1}): 3295 br (N-H), 2227 w (C≡N). Elemental analysis calcd (%) for $C_{18}H_{12}N_4S$ (316.38): C, 68.33; H, 3.82; N, 17.71; S, 10.13; found (%): C, 68.29; H, 3.84; N, 17.75; S, 10.12; MS (EI): m/z calcd for $C_{18}H_{12}N_4S$ 316.08 $[M]^{+\cdot}$; found 316.20.

3-(Pyridin-2-ylmethyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3o**



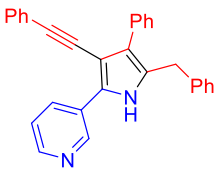
Following the general procedure, **3o** was prepared from **1o** (1.3 mmol, 134 mg) and **2** (2 mmol, 208 mg). **3o** was isolated as a cream powder (44 mg, 14% yield). Mp 218-220 ºC. ^1H NMR (DMSO-d_6, 400 MHz): δ 12.85 (br.s, 1H, NH), 9.04-9.03 (m, 1H, H_{Py}), 9.03 (s, 1H, H4), 8.66-8.65 (m, 2H, H6, H_{Py}), 8.49-8.47 (m, 1H, H_{Py}), 8.29-8.26 (m, 1H, H_{Py}), 7.73-7.68 (m, 1H, H_{Py}), 7.58-7.55 (m, 1H, H_{Py}), 7.39-7.36 (m, 1H, H_{Py}), 7.22-7.19 (m, 1H, H_{Py}), 4.38 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 101 MHz): δ 160.3, 150.0, 149.9, 149.8, 146.5, 145.9, 139.2, 137.5, 136.8, 135.9, 127.3, 126.0, 124.1, 123.4, 122.2, 116.5, 112.3, 92.4, 32.8; IR (film, ν/cm^{-1}): 3398 br (N-H), 2226 w (C≡N). Elemental analysis calcd (%) for $C_{19}H_{13}N_5$ (311.35): C, 73.30; H, 4.21; N, 22.49; found (%): C, 73.25; H, 4.23; N, 22.52; MS (EI): m/z calcd for $C_{19}H_{13}N_5$ 311.12 $[M]^{+\cdot}$; found 311.15.

2-(Pyridin-3-yl)-3-(pyridin-3-ylmethyl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3p**



Following the general procedure, **3p** was prepared from **1p** (1.3 mmol, 134 mg) and **2** (2 mmol, 208 mg). **3p** was isolated as a beige powder (47 mg, 15% yield). Mp 239-241 ºC. ^1H NMR (DMSO-d_6, 400 MHz): δ 12.93 (br.s, 1H, NH), 8.98 (s, 1H, H4), 8.86-8.85 (m, 1H, H_{Py}), 8.68 (s, 1H, H6), 8.66-8.64 (m, 1H, H_{Py}), 8.42-8.41(m, 1H, H_{Py}), 8.37-8.36 (m, 1H, H_{Py}), 8.09-8.06 (m, 1H, H_{Py}), 7.58-7.54 (m, 1H, H_{Py}), 7.48-7.46 (m, 1H, H_{Py}), 7.25-7.22 (m, 1H, H_{Py}), 4.35 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 101 MHz): δ 150.0, 149.8, 149.6, 147.3, 146.3, 146.0, 139.2, 136.8, 136.4, 136.0, 127.2, 125.8, 124.2, 124.1, 116.4, 112.1, 92.5, 27.0; IR (film, ν/cm^{-1}): 3393 br (N-H), 2226 w (C≡N). Elemental analysis calcd (%) for $C_{19}H_{13}N_5$ (311.35): C, 73.30; H, 4.21; N, 22.49; found (%): C, 73.24; H, 4.23; N, 22.51; MS (EI): m/z calcd for $C_{19}H_{13}N_5$ 311.12 $[M]^{+\cdot}$; found 311.15.

3-(5-Benzyl-4-phenyl-3-(phenylethynyl)-1H-pyrrol-2-yl)pyridine **4a**



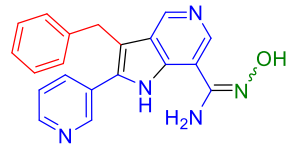
A mixture of **1a** (3 mmol, 306 mg) and KOBu^t (1 mmol, 112 mg) in DMSO (4 mL) was stirred for 2 min at rt, then, a solution of **2** (1 mmol, 104 mg) in DMSO (2 mL) was added for 10 min and stirred another 5 min. The reaction mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (8 mL × 4). The organic extract was washed with H_2O (5 mL × 3) and dried over K_2CO_3. CH_2Cl_2 was evaporated in vacuum. The crude product was purified by column chromatography on silica gel (eluent: hexane–diethyl ether with gradient from 3:1 to 0:1) to afford **4a** as a cream powder (140 mg, 52% yield, based on **1a** consumed). Unreacted **1a** (104 mg, 66% conversion) was recovered. Mp 171-173 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.95-8.93 (m, 2H, NH, H_{Py}), 8.37-8.36 (m, 1H, H_{Py}), 8.28-8.25 (m, 1H, H_{Py}), 7.65-7.63 (m, 2H, H_{Ph}), 7.48-7.44 (m, 2H, H_{Ph}), 7.40-7.21 (m, 12H, H_{Py}, H_{Ph}), 4.15 (s, 2H, CH_2); ^{13}C ($CDCl_3$, 101 MHz): δ 147.4, 146.2, 138.9, 134.3, 132.7, 131.1, 130.2, 129.5, 129.1, 129.0, 128.6, 128.3, 128.2, 127.6, 126.9, 126.6, 126.4, 124.2, 123.6, 103.4, 92.9, 85.3, 32.4; IR (film, ν/cm^{-1}): 3399 br (N-H), 2207 w (C≡C). Elemental analysis calcd (%) for $C_{30}H_{22}N_2$ (410.52): C, 87.77; H, 5.40; N, 6.82; found C, 87.85; H, 5.36; N, 6.87%. MS (EI): m/z calcd for $C_{30}H_{22}N_2$ 410.18 $[M]^{+\cdot}$; found 410.20.

5. Synthesis of amidoximes 5 (*general procedure*)

A mixture of 5-azaindole **3** (0.2 mmol), hydroxyl amine hydrochloride (0.8 mmol, 56 mg) and NaOH (0.8 mmol, 32 mg) in EtOH (8 mL) was heated at reflux for 3 h. Then, the reaction mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (10 mL × 3). The organic extract was dried over K_2CO_3. CH_2Cl_2 was evaporated in vacuum to give pure amidoxime **5**.

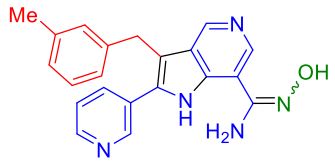
6. Characterization data of amidoximes 5

3-Benzyl-N'-hydroxy-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carboximidamide **5a**



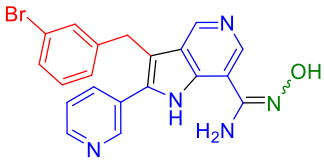
Following the general procedure, **5a** was prepared from **3a** (0.2 mmol, 62 mg). **5a** was isolated as a light brown powder (63 mg, 92% yield). Mp 235-237 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.95 (br.s, 1H, NH), 9.94 (br.s, 1H, OH), 8.80 (s, 1H, H4), 8.69 (s, 1H, H6), 8.62-8.59 (m, 2H, H_{Py}), 8.02-8.00 (m, 1H, H_{Py}), 7.55-7.52 (m, 1H, H_{Py}), 7.25-7.23 (m, 2H, H_{Ph}), 7.17-7.16 (m, 3H, H_{Ph}), 6.18 (br.s, 2H, NH_2), 4.29 (s, 2H, CH_2); ^{13}C{^{1}H} NMR (DMSO-d_6, 101 MHz): δ 150.3, 149.6, 149.1, 143.1, 141.3, 138.7, 137.0, 136.0, 133.6, 129.0, 128.5, 128.1, 126.6, 125.8, 124.3, 112.7, 112.3, 30.0. Elemental analysis calcd (%) for $C_{20}H_{17}N_5O$ (343.39): C, 69.96; H, 4.99; N, 20.40; found (%): C, 69.91; H, 5.01; N, 20.43; MS (EI): m/z calcd for $C_{20}H_{17}N_5O$ 343.14 $[M]^{+\cdot}$; found 343.10.

N'-Hydroxy-3-(3-methylbenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carboximidamide **5b**



Following the general procedure, **5b** was prepared from **3b** (0.2 mmol, 65 mg). **5b** was isolated as a beige powder (66 mg, 93% yield). Mp 249-251 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.92 (br.s, 1H, NH), 9.92 (br.s, 1H, OH), 8.79 (s, 1H, H4), 8.67 (s, 1H, H6), 8.62-8.60 (m, 1H, H_{Py}), 8.58 (m, 1H, H_{Py}), 8.02-7.99 (m, 1H, H_{Py}), 7.55-7.52 (m, 1H, H_{Py}), 7.14-7.10 (m, 1H, H_{Ph}), 6.98-6.92 (m, 3H, H_{Ph}), 6.16 (br.s, 2H, NH_2), 4.24 (s, 2H, CH_2), 2.20 (s, 3H, Ph$\underline{CH_3}$); ^{13}C{^{1}H} NMR (DMSO-d_6, 101 MHz): δ 150.4, 149.6, 149.1, 143.2, 141.2, 138.8, 138.1, 136.9, 136.0, 133.5, 129.2, 128.9, 128.2, 127.3, 125.8, 125.6, 124.4, 112.7, 112.3, 30.0, 21.6. Elemental analysis calcd (%) for $C_{21}H_{19}N_5O$ (357.42): C, 70.57; H, 5.36; N, 19.59; found (%):C, 70.51; H, 5.39; N, 19.64; MS (EI): m/z calcd for $C_{21}H_{19}N_5O$ 357.16 $[M]^{+\cdot}$; found 357.25.

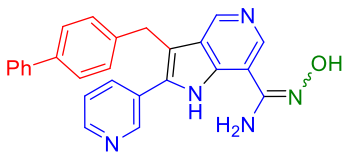
3-(3-Bromobenzyl)-N'-hydroxy-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carboximidamide **5j**



Following the general procedure, **5j** was prepared from **3j** (0.2 mmol, 78 mg). **5j** was isolated as a beige powder (77 mg, 91% yield). Mp 242-244 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.97 (br.s, 1H, NH), 9.93 (br.s, 1H, OH), 8.79 (s, 1H, H4), 8.69 (s, 1H, H6), 8.60-8.58 (m, 2H, H_{Py}), 8.01-7.99 (m, 1H, H_{Py}), 7.53-7.50 (m, 1H, H_{Py}), 7.36-7.34 (m, 2H, H_{Ph}), 7.22-7.13 (m, 2H, H_{Ph}), 6.25 (br.s, 2H, NH_2), 4.31 (s, 2H, CH_2); ^{13}C{^{1}H} NMR (DMSO-d_6, 101 MHz): δ 151.1, 149.1, 148.9, 144.9, 142.4, 135.8, 131.2, 131.1, 130.9, 129.3, 127.6, 124.2, 123.9, 122.3, 115.1,

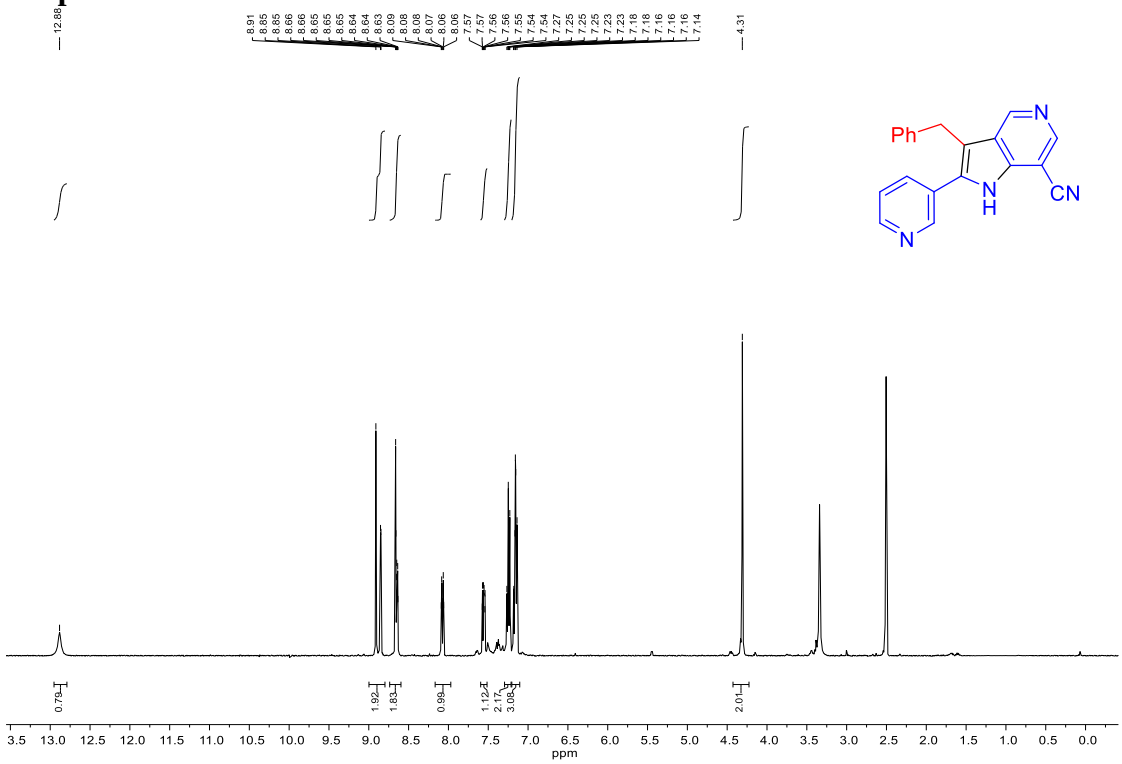
113.3, 30.0. Elemental analysis calcd (%) for $C_{20}H_{16}BrN_5O$ (422.29): C, 56.89; H, 3.82; Br, 18.92; N, 16.58; found (%): C, 56.81; H, 3.84; Br, 18.98; N, 16.57; MS (EI): m/z calcd for $C_{20}H_{16}BrN_5O$ 421.05 $[M]^{+\cdot}$; found 421.05.

3-([1,1'-biphenyl]-4-ylmethyl)-N'-hydroxy-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carboximidamide **5l**

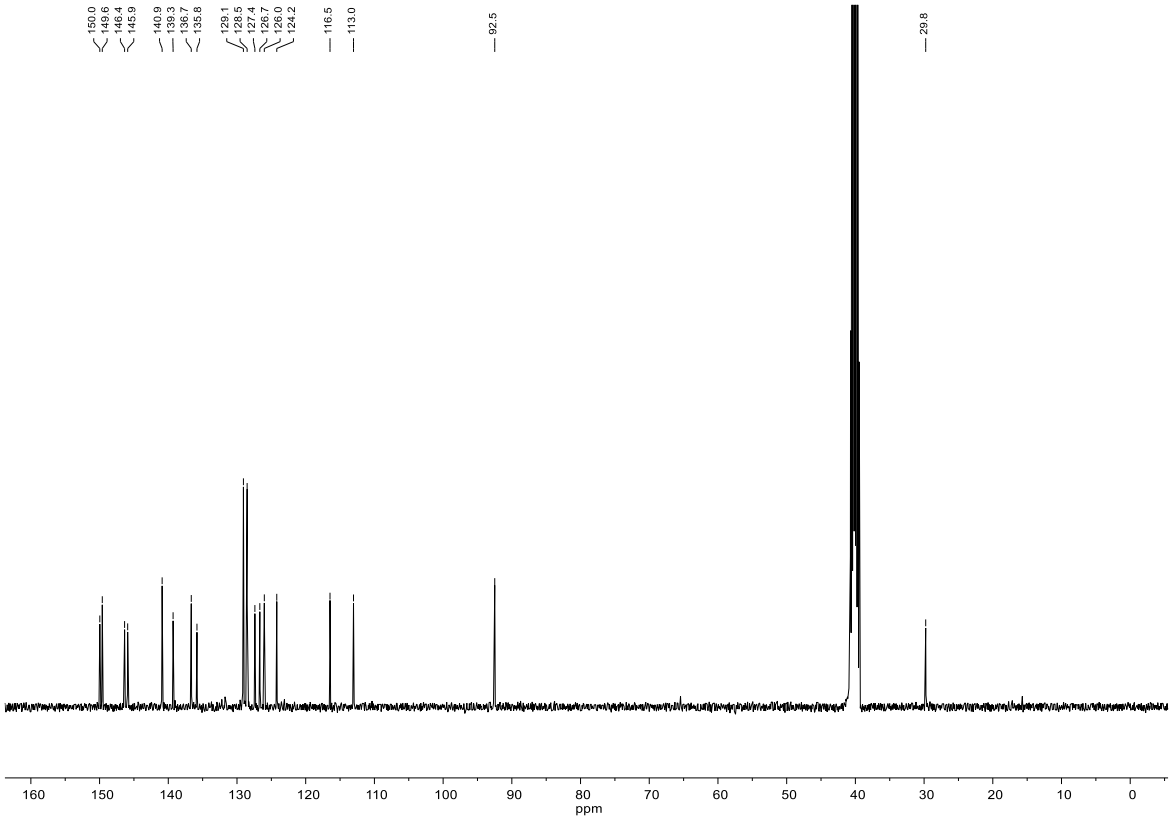


Following the general procedure, **5l** was prepared from **3l** (0.2 mmol, 77 mg). **5l** was isolated as a beige powder (81 mg, 97% yield). Mp 229-231 ºC. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.98 (br.s, 1H, NH), 9.96 (br.s, 1H, OH), 8.83 (s, 1H, H4), 8.74 (s, 1H, H6), 8.63-8.60 (m, 2H, H_{Py}), 8.05-8.02 (m, 1H, H_{Py}), 7.61-7.59 (m, 2H, H_{Py}, H_{Ph}), 7.56-7.53 (m, 3H, H_{Ph}), 7.43-7.39 (m, 2H, H_{Ph}), 7.33-7.31 (m, 1H, H_{Ph}), 7.26-7.24 (m, 2H, H_{Ph}), 6.19 (br.s, 2H, NH_2), 4.33 (s, 2H, CH_2); ^{13}C{^{1}H} NMR (DMSO-d_6, 101 MHz): δ 150.5, 148.6, 148.4, 142.2, 140.6, 140.0, 137.9, 135.3, 128.9, 128.9, 128.7, 127.3, 126.8, 126.6, 123.8, 112.7, 29.5. Elemental analysis calcd (%) for $C_{26}H_{21}N_5O$ (419.49): C, 74.44; H, 5.05; N, 16.70; found (%):C, 74.37; H, 5.08; N, 16.74; MS (EI): m/z calcd for $C_{26}H_{21}N_5O$ 419.17 $[M]^{+\cdot}$; found 419.10.

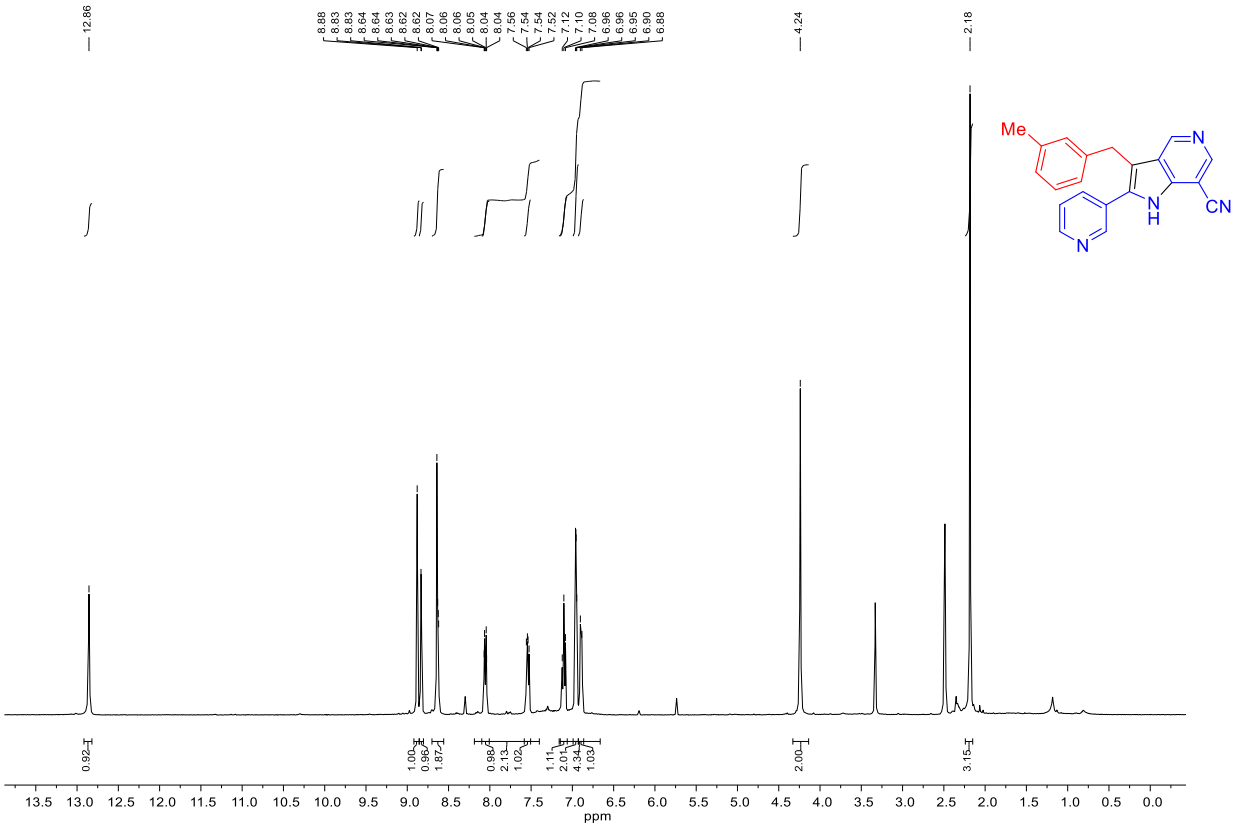
7. NMR spectra



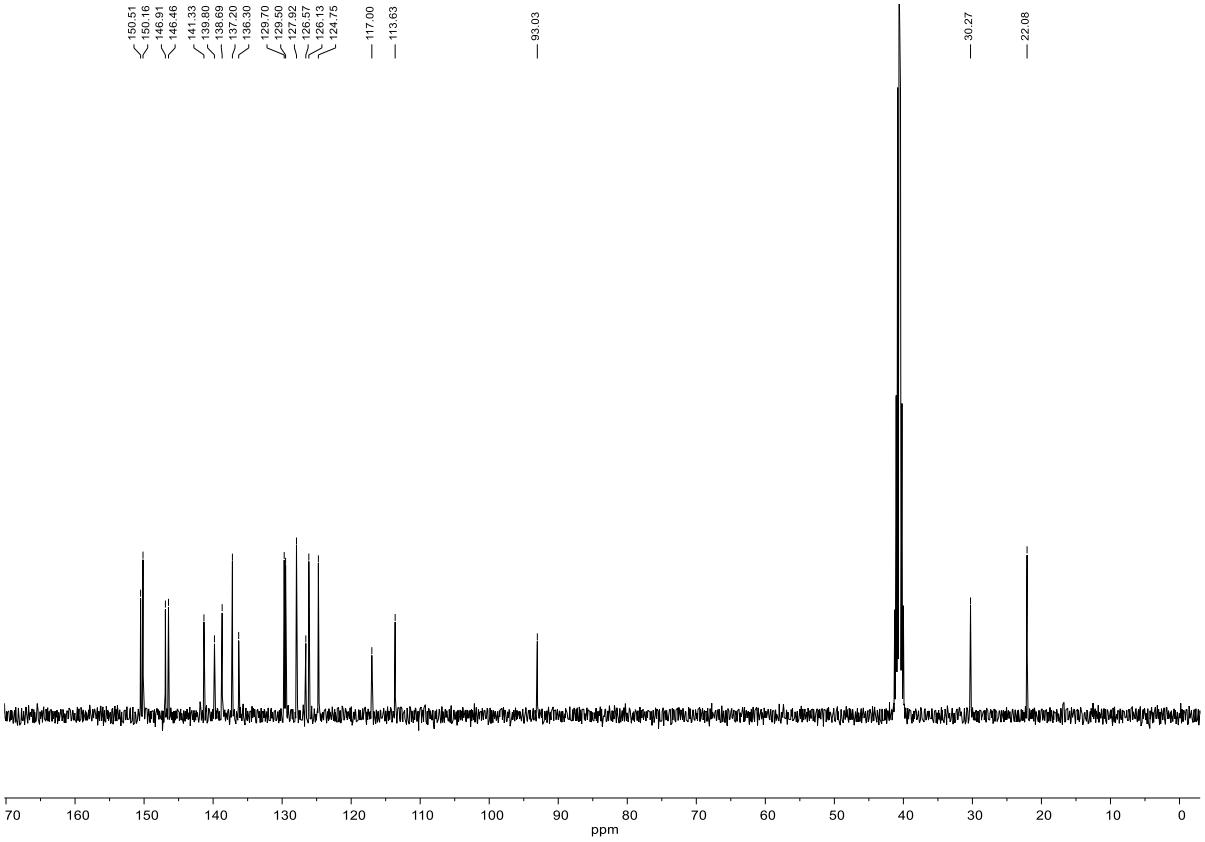
^{1}H NMR Spectrum of **3a** (400.1 MHz, DMSO-d_6)



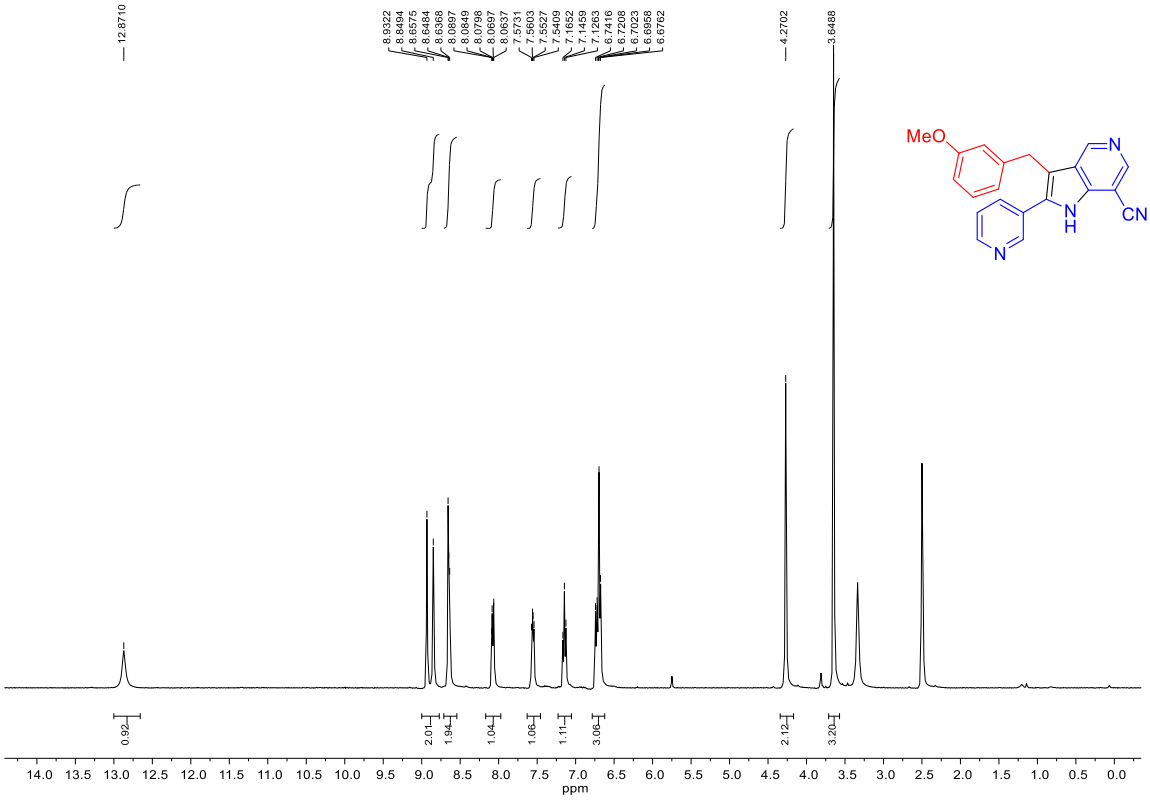
^{13}C{^{1}H} NMR Spectrum of **3a** (100.6 MHz, DMSO-d_6)



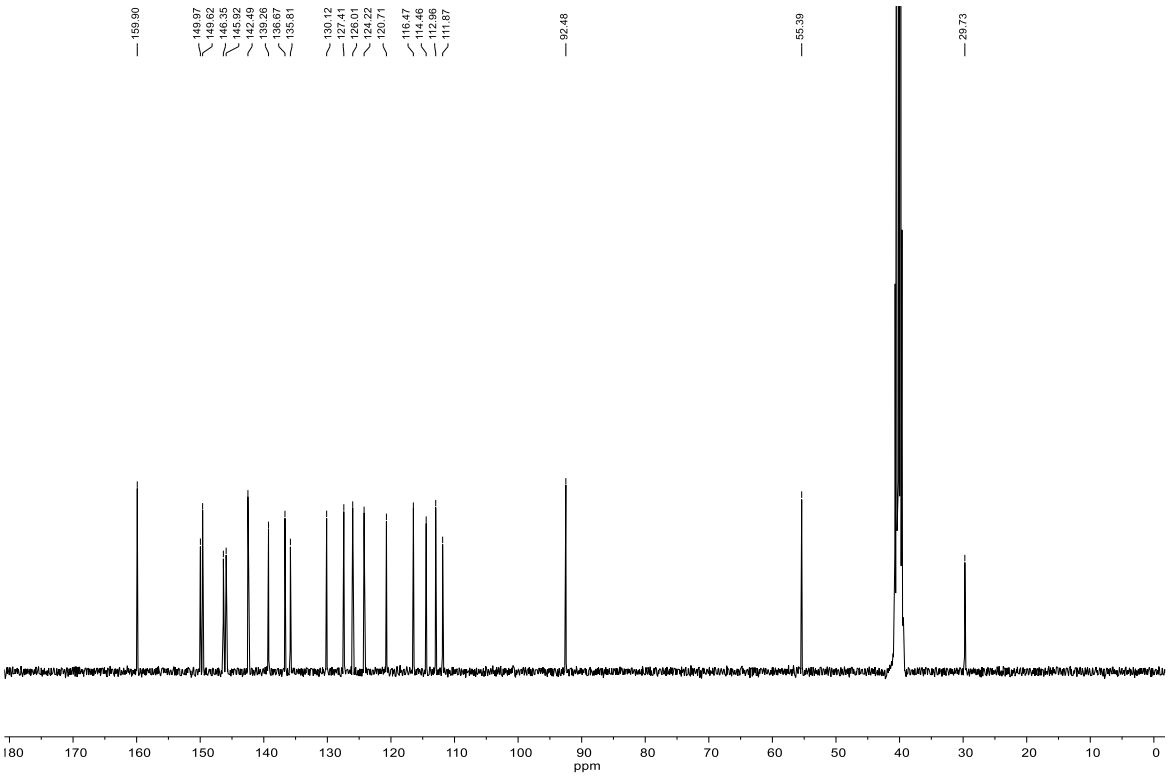
^{1}H NMR Spectrum of **3b** (400.1 MHz, DMSO-d_6)



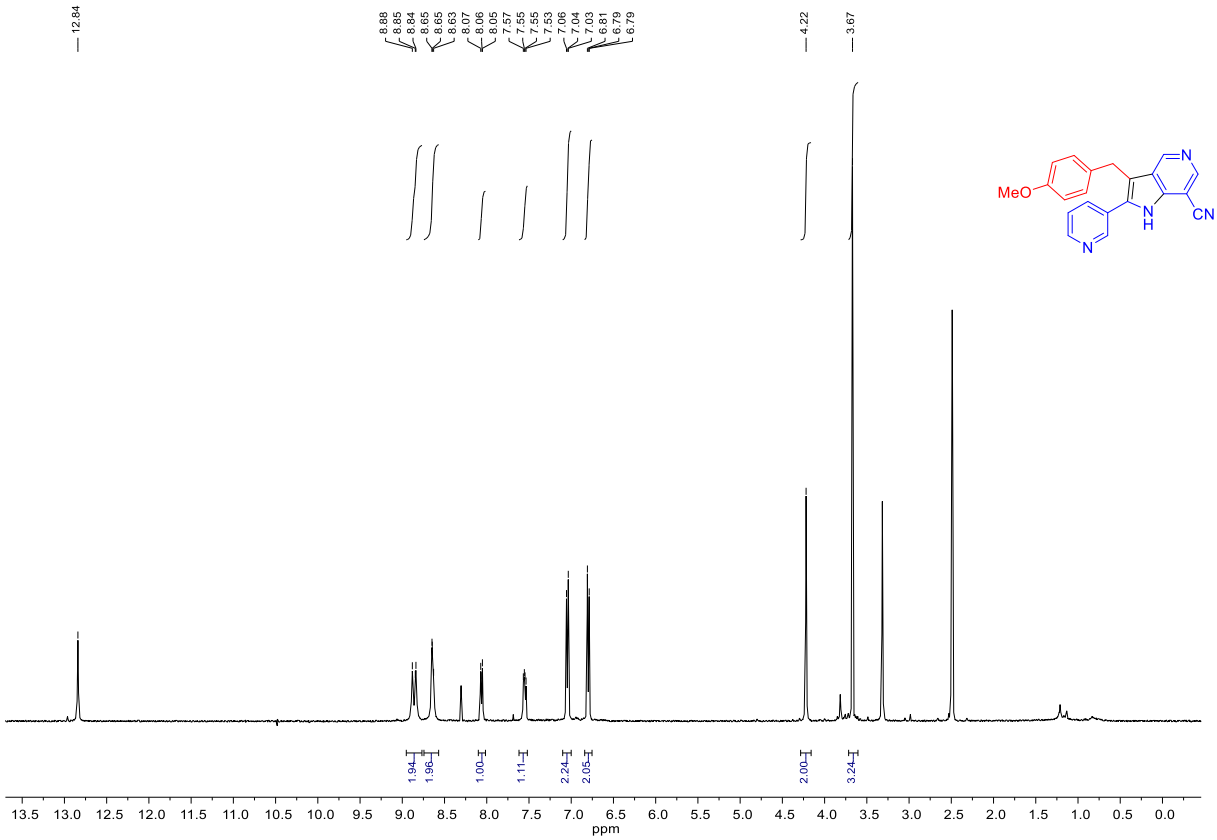
^{13}C{^{1}H} NMR Spectrum of **3b** (100.6 MHz, DMSO-d_6)



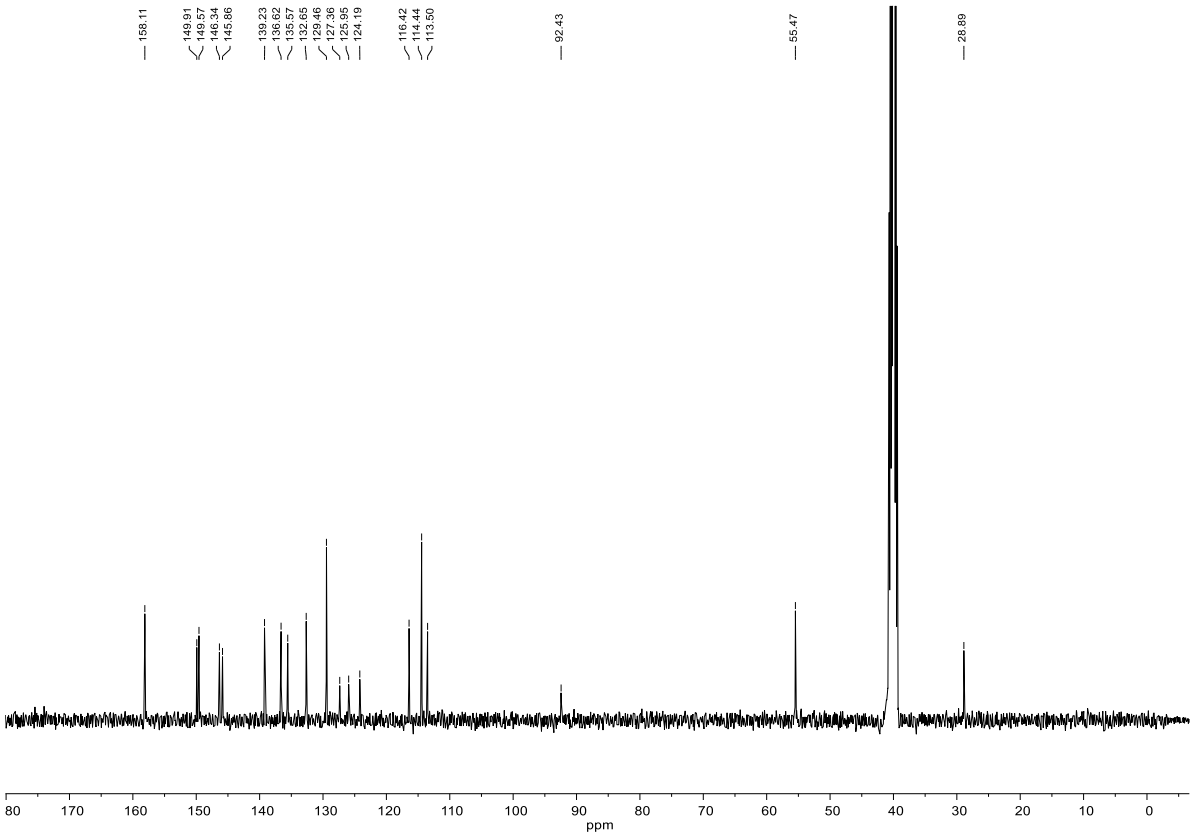
^{1}H NMR Spectrum of **3d** (400.1 MHz, DMSO-d_6)



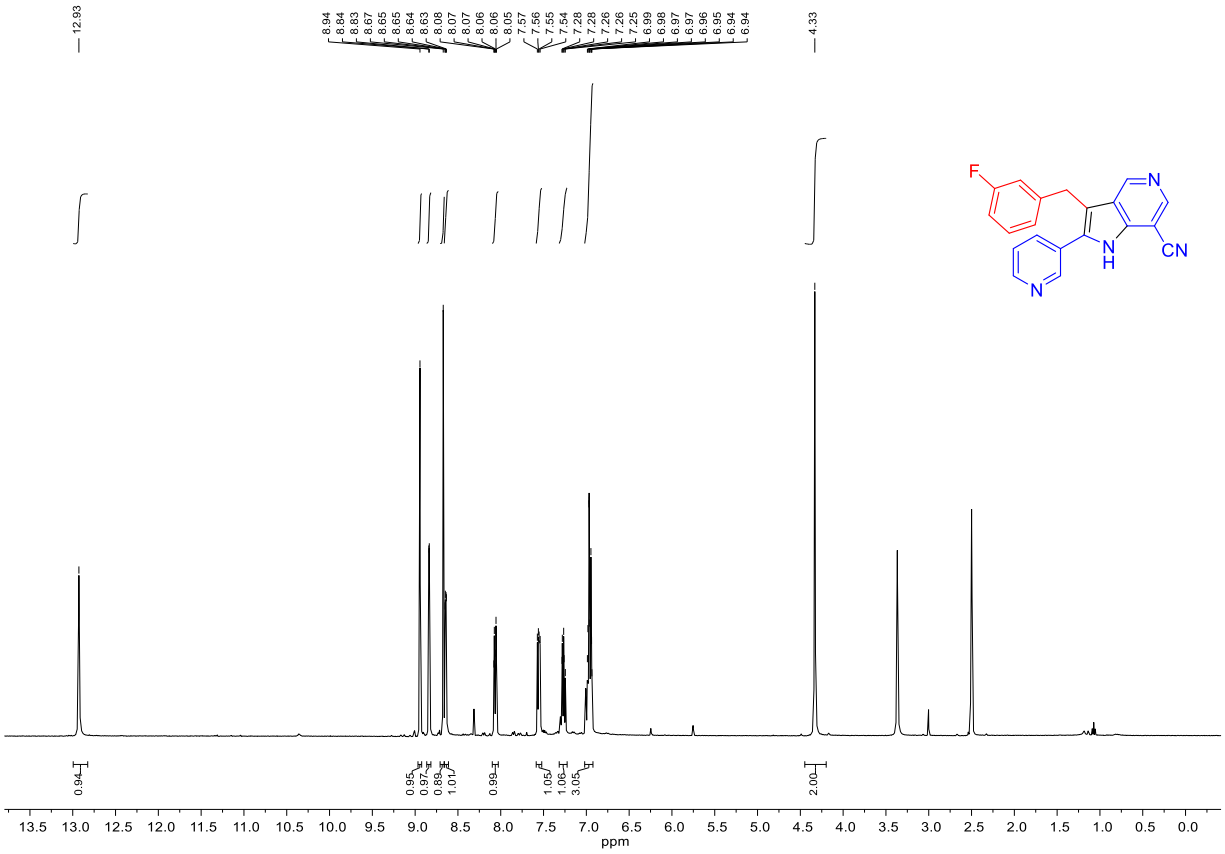
^{13}C{^{1}H} NMR Spectrum of **3d** (100.6 MHz, DMSO-d_6)



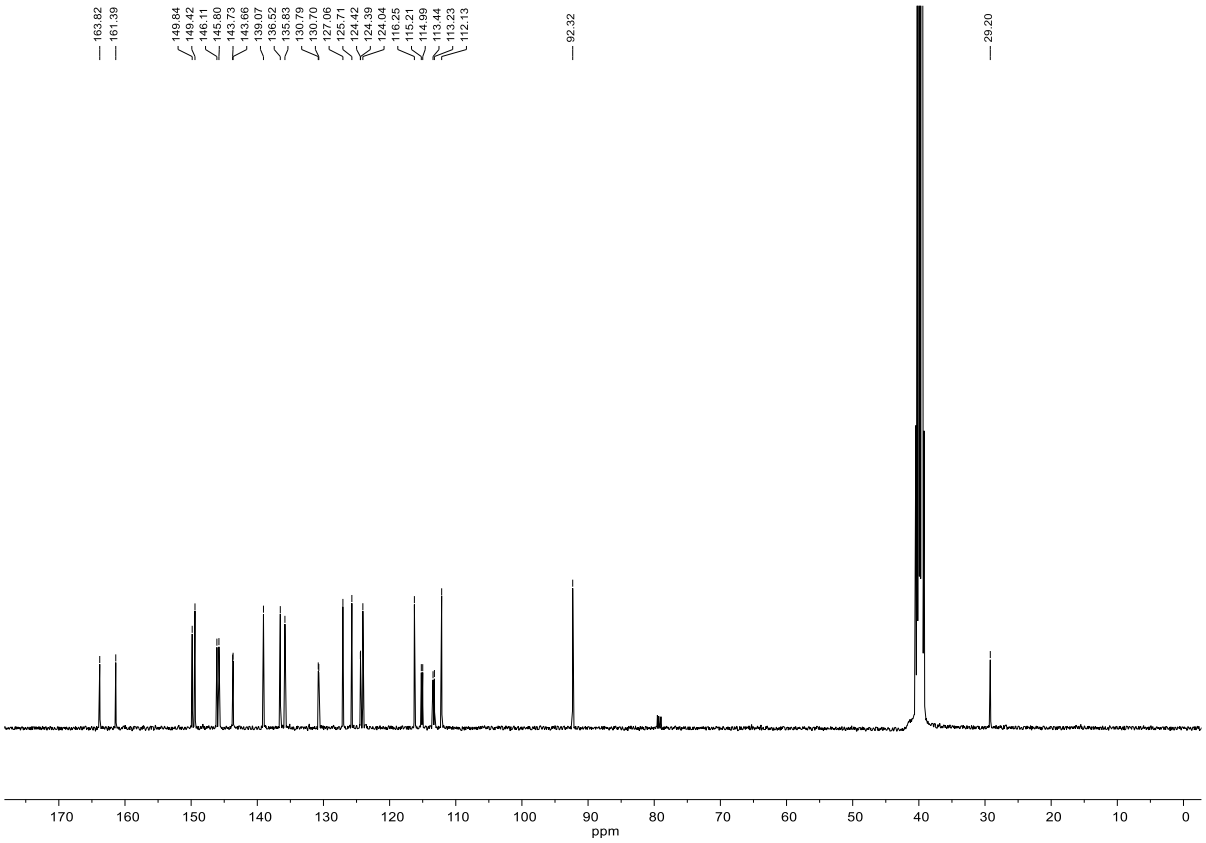
^{1}H NMR Spectrum of **3e** (400.1 MHz, DMSO-d_6)



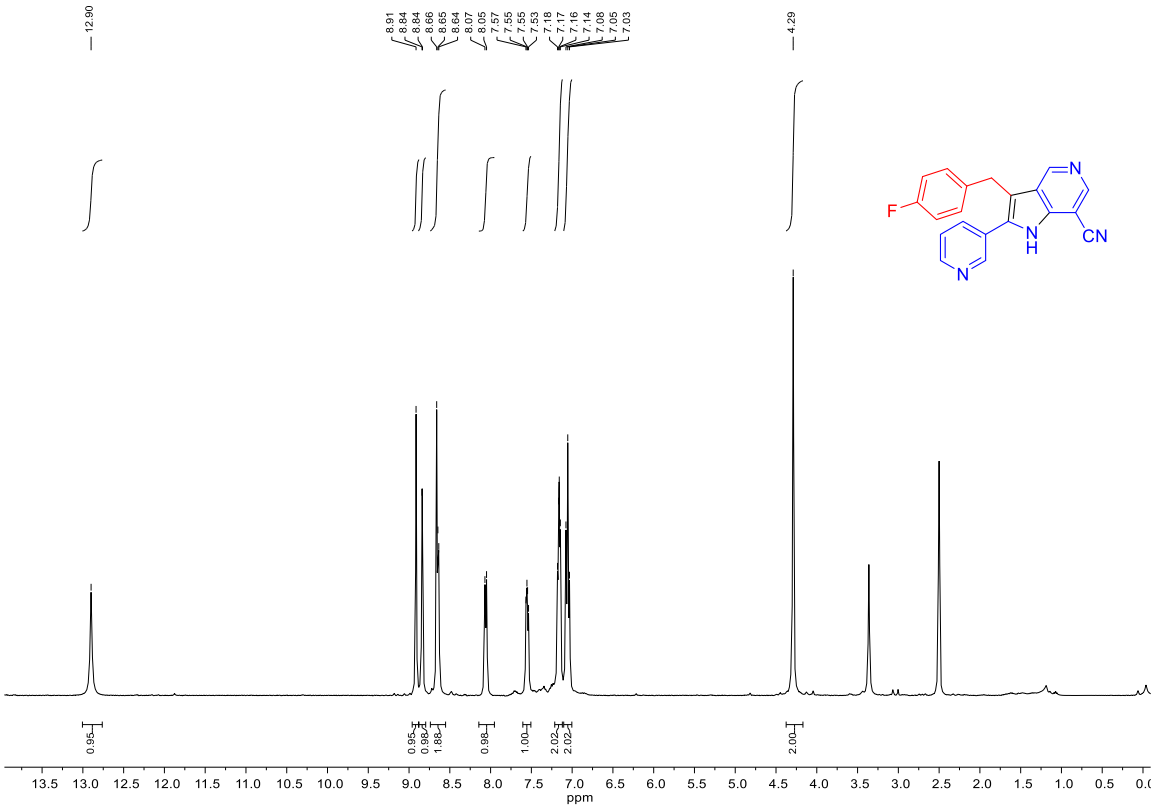
^{13}C{^{1}H} NMR Spectrum of **3e** (100.6 MHz, DMSO-d_6)



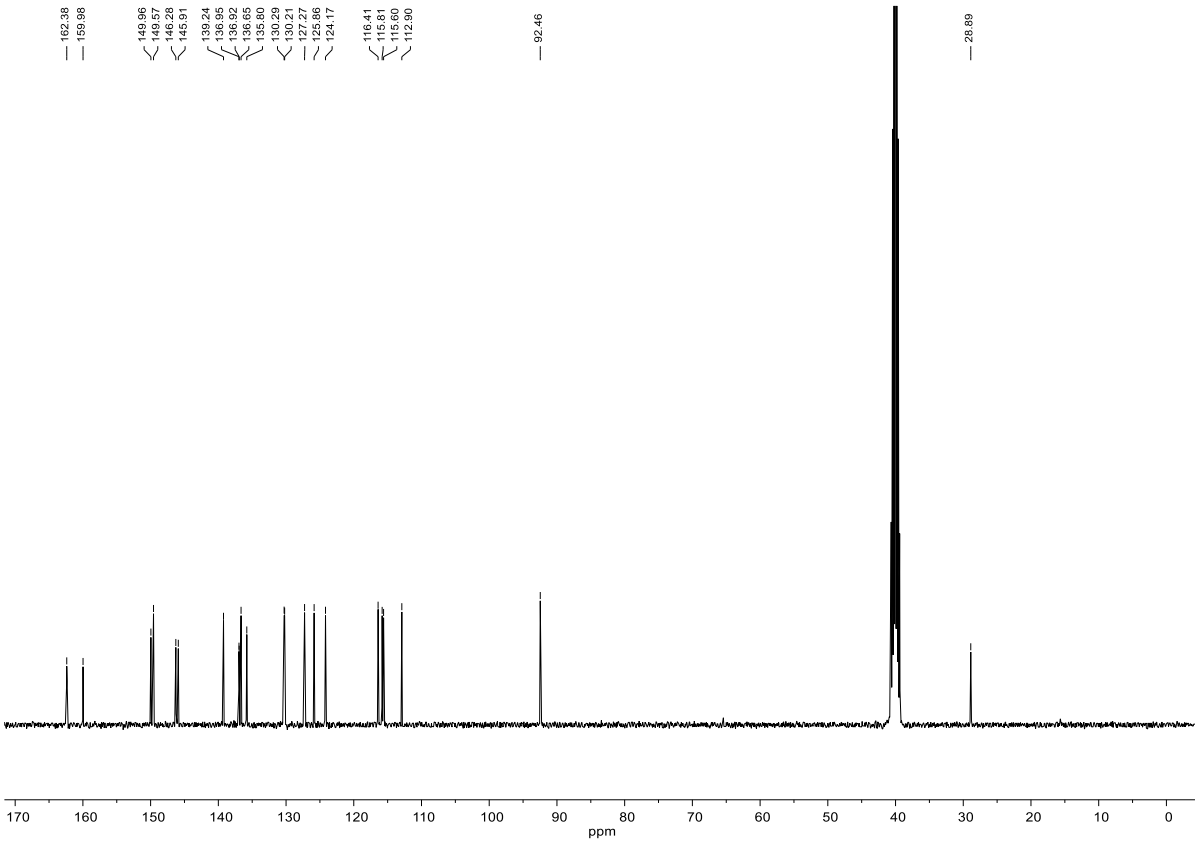
^{1}H NMR Spectrum of **3f** (400.1 MHz, DMSO-d_6)



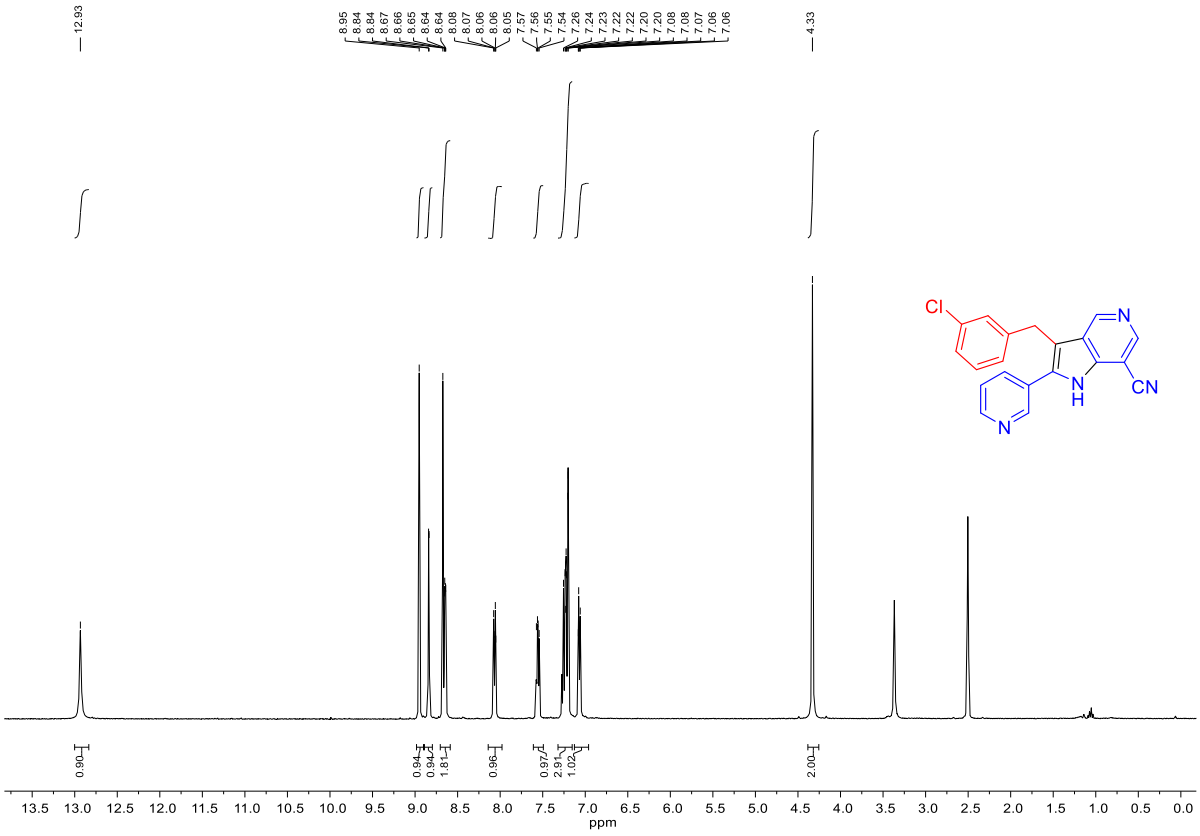
^{13}C{^{1}H} NMR Spectrum of **3f** (100.6 MHz, DMSO-d_6)



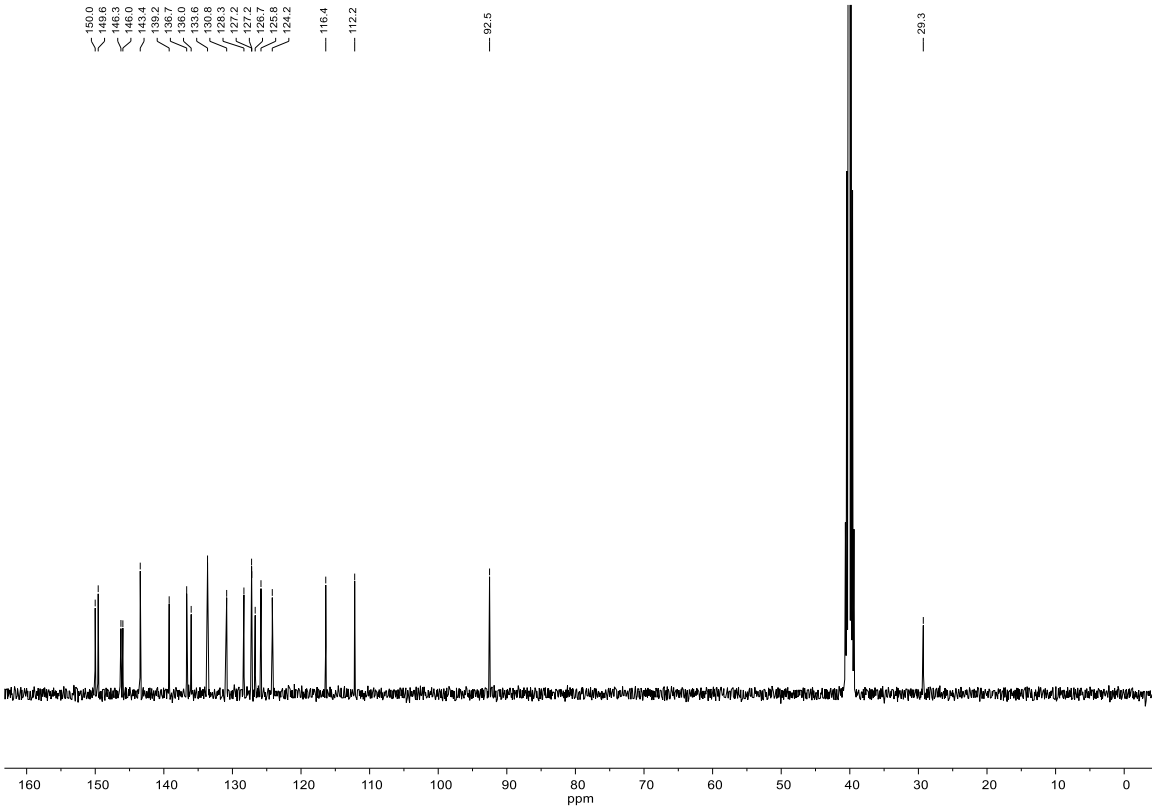
^{1}H NMR Spectrum of **3g** (400.1 MHz, DMSO-d_6)



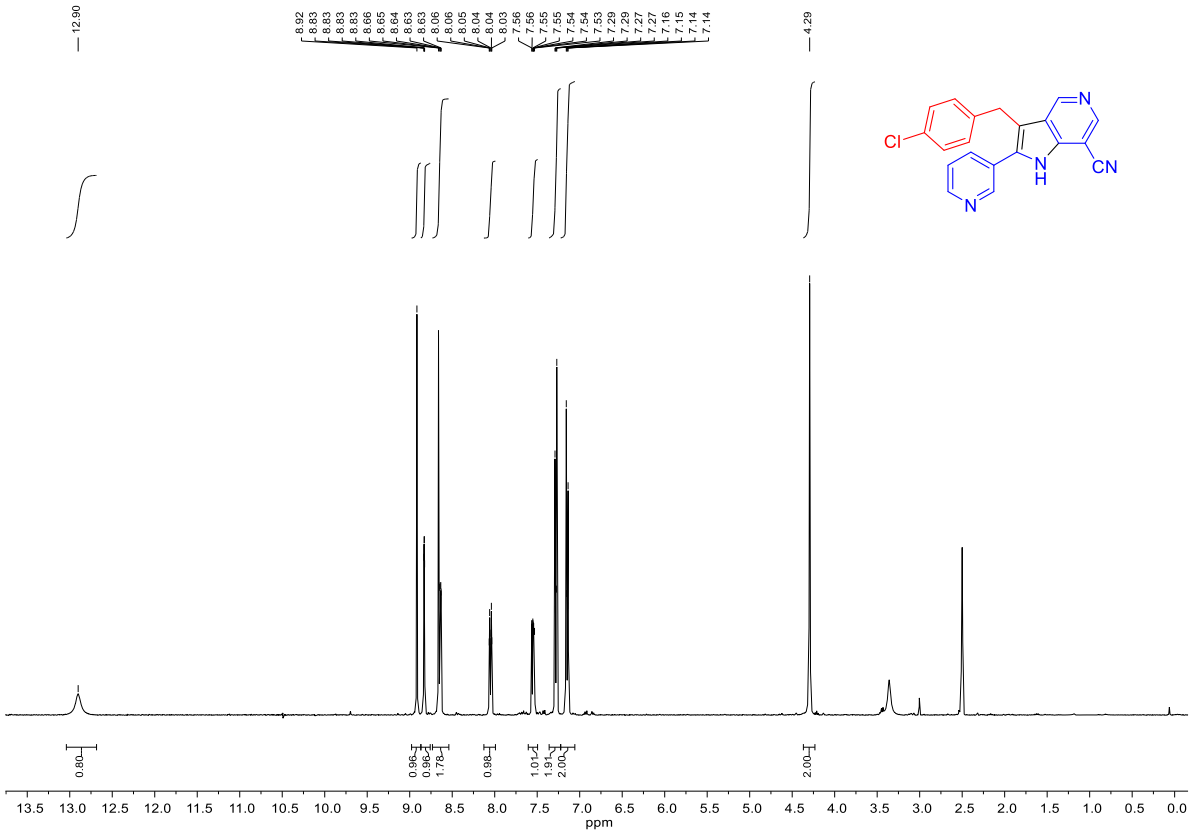
^{13}C{^{1}H} NMR Spectrum of **3g** (100.6 MHz, DMSO-d_6)



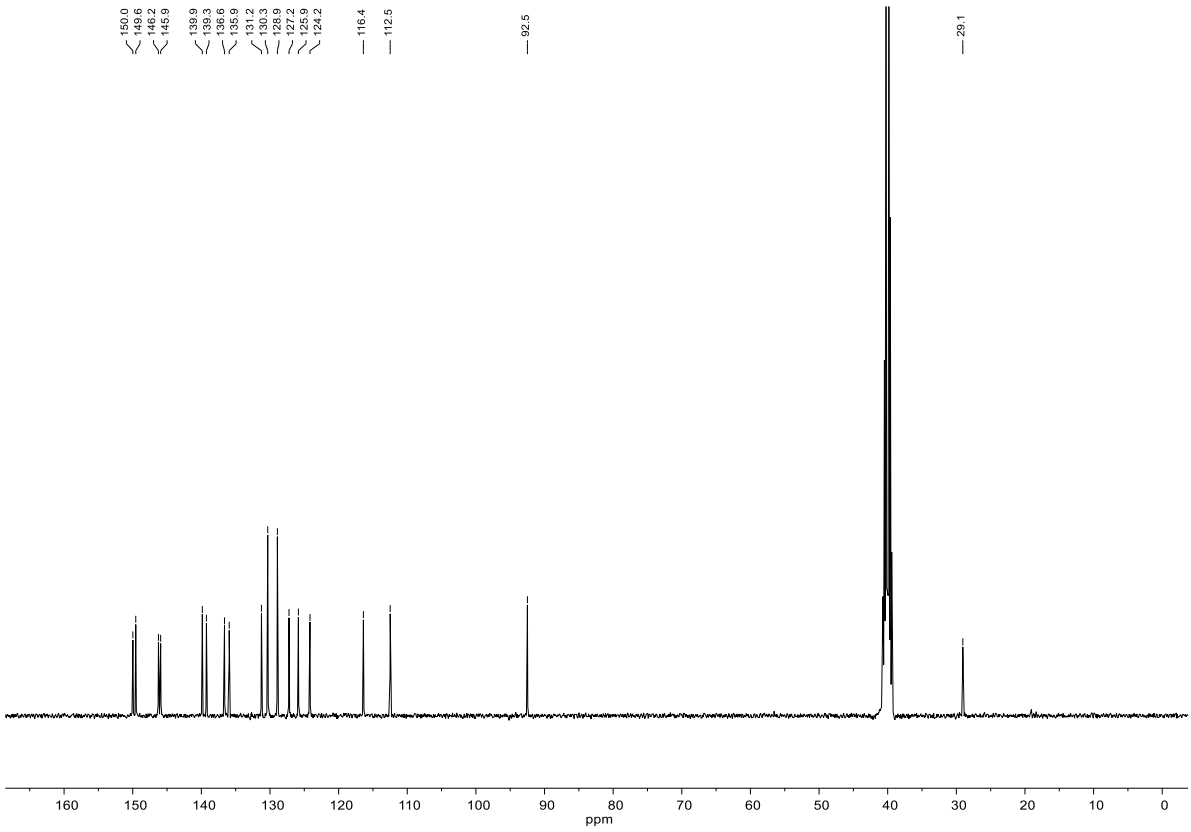
^{1}H NMR Spectrum of **3h** (400.1 MHz, DMSO-d$_6$)



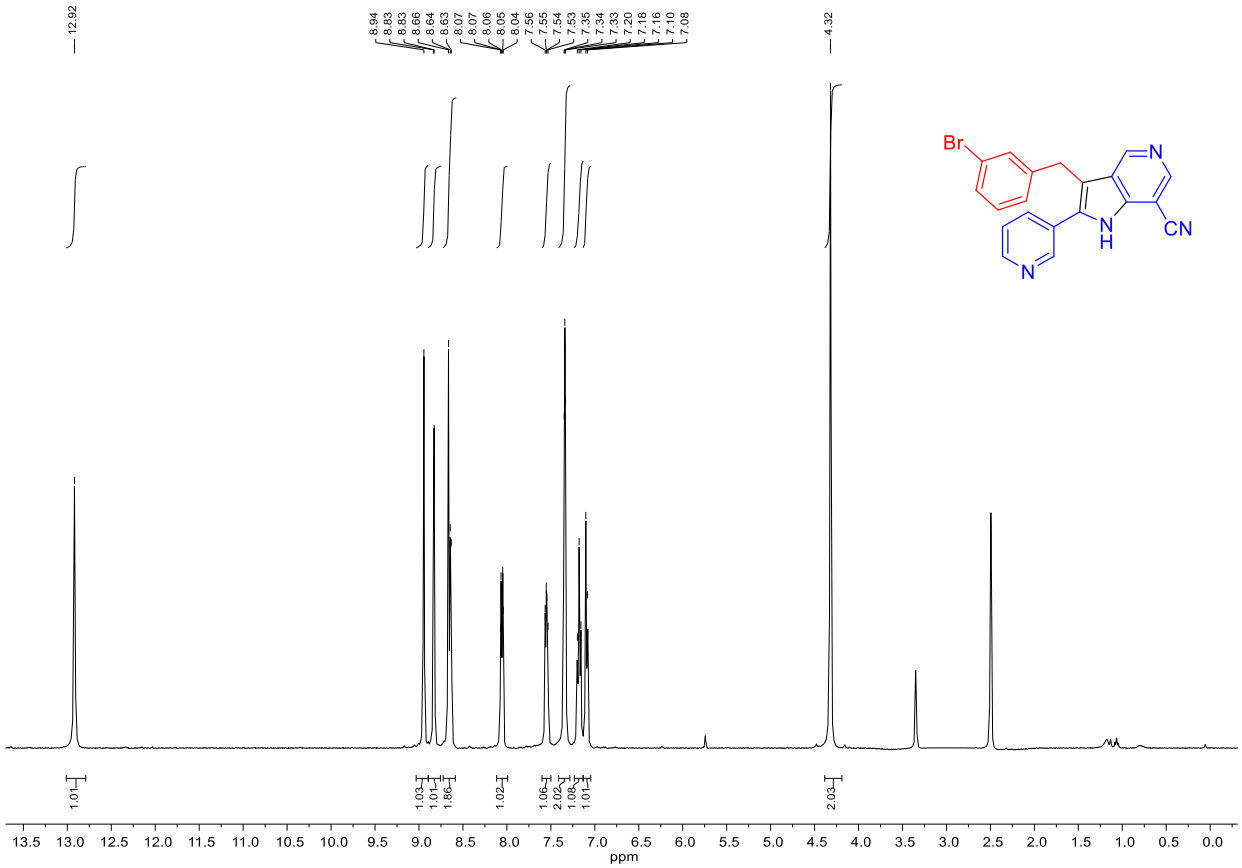
^{13}C{^{1}H} NMR Spectrum of **3h** (100.6 MHz, DMSO-d$_6$)



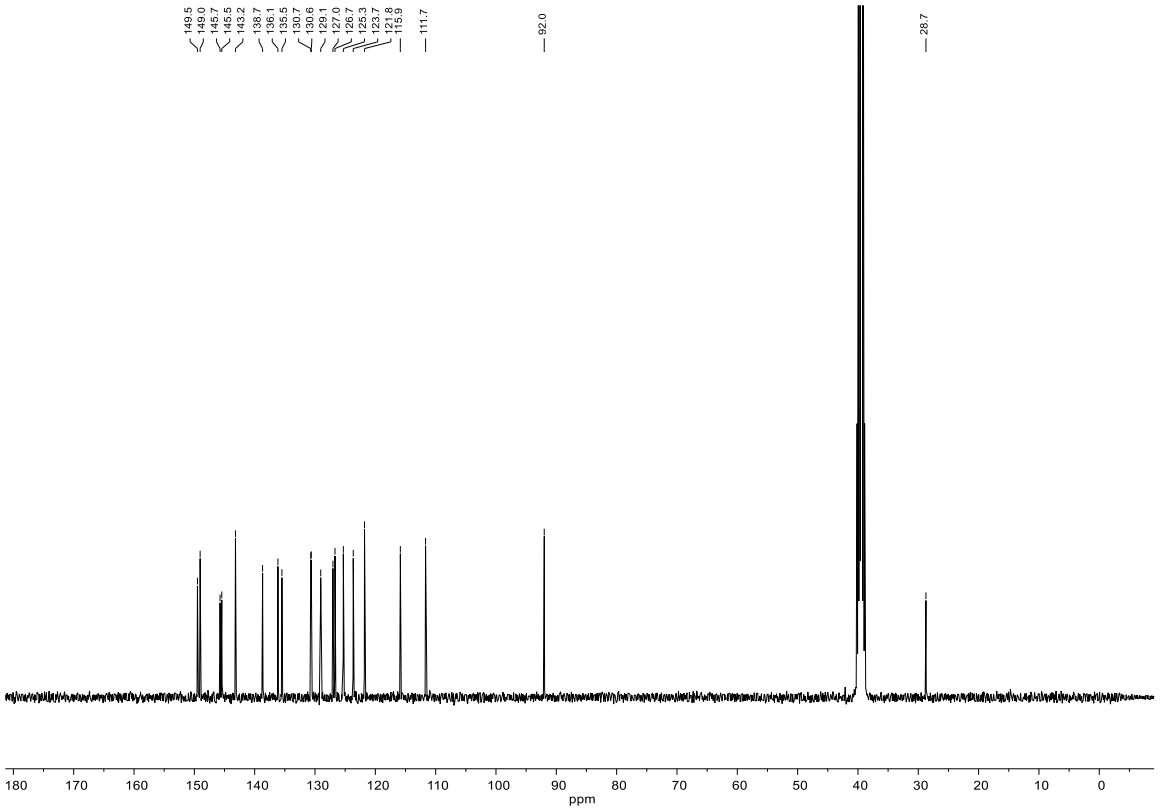
^{1}H NMR Spectrum of **3i** (400.1 MHz, DMSO-d_6)



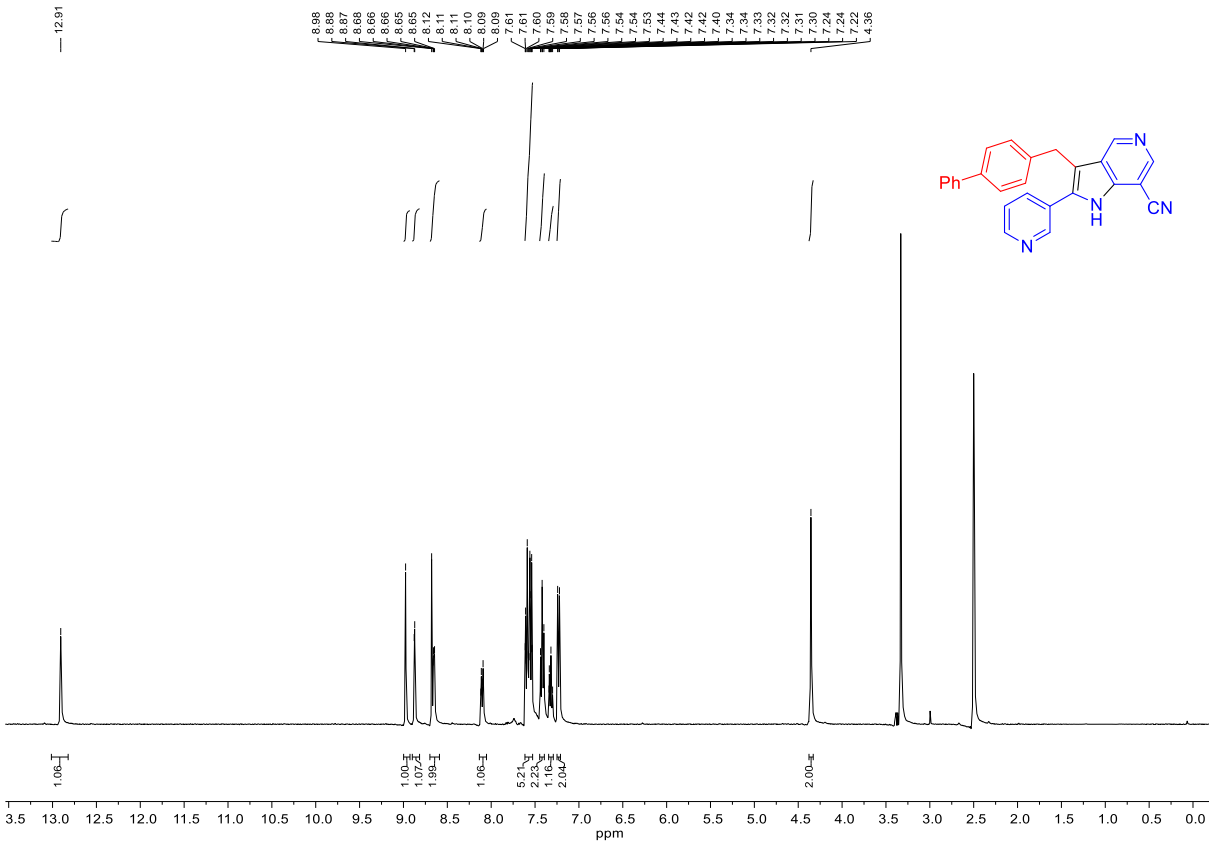
^{13}C{^{1}H} NMR Spectrum of **3i** (100.6 MHz, DMSO-d_6)



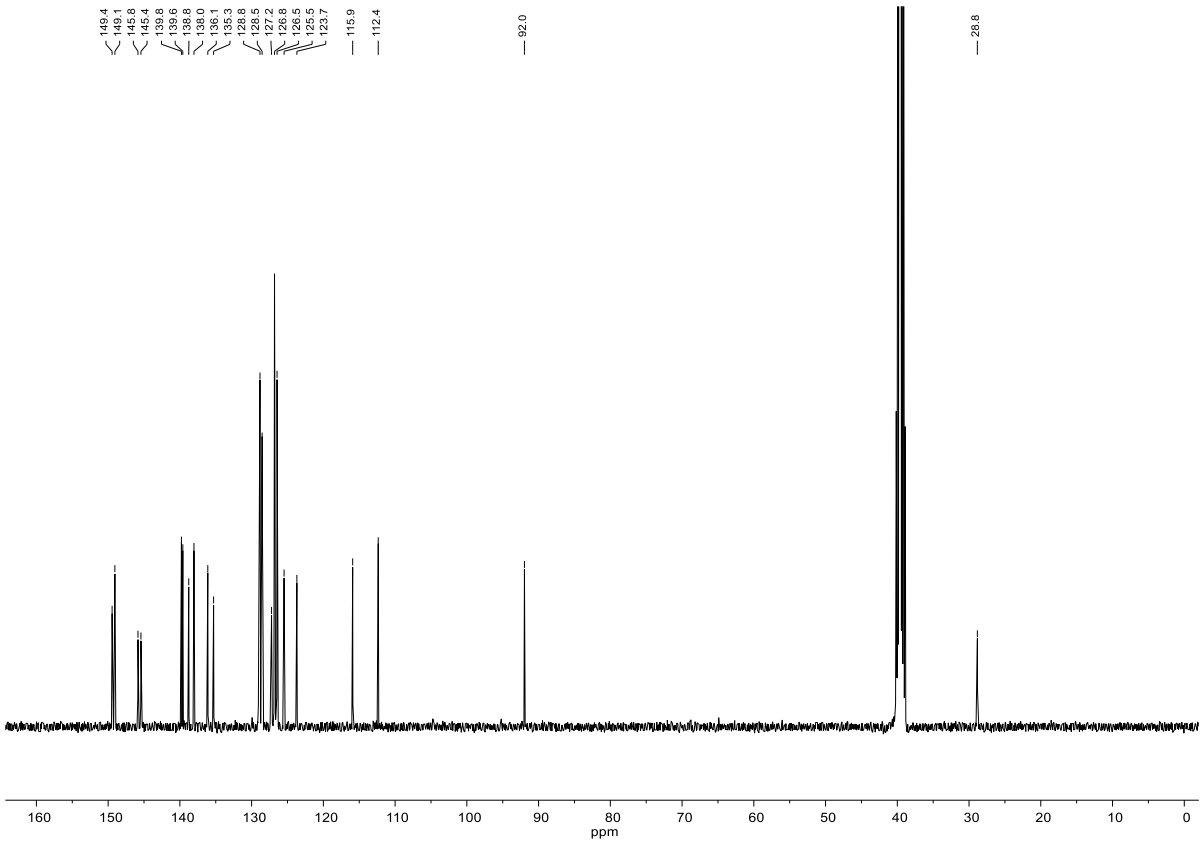
^{1}H NMR Spectrum of **3j** (400.1 MHz, DMSO-d_6)



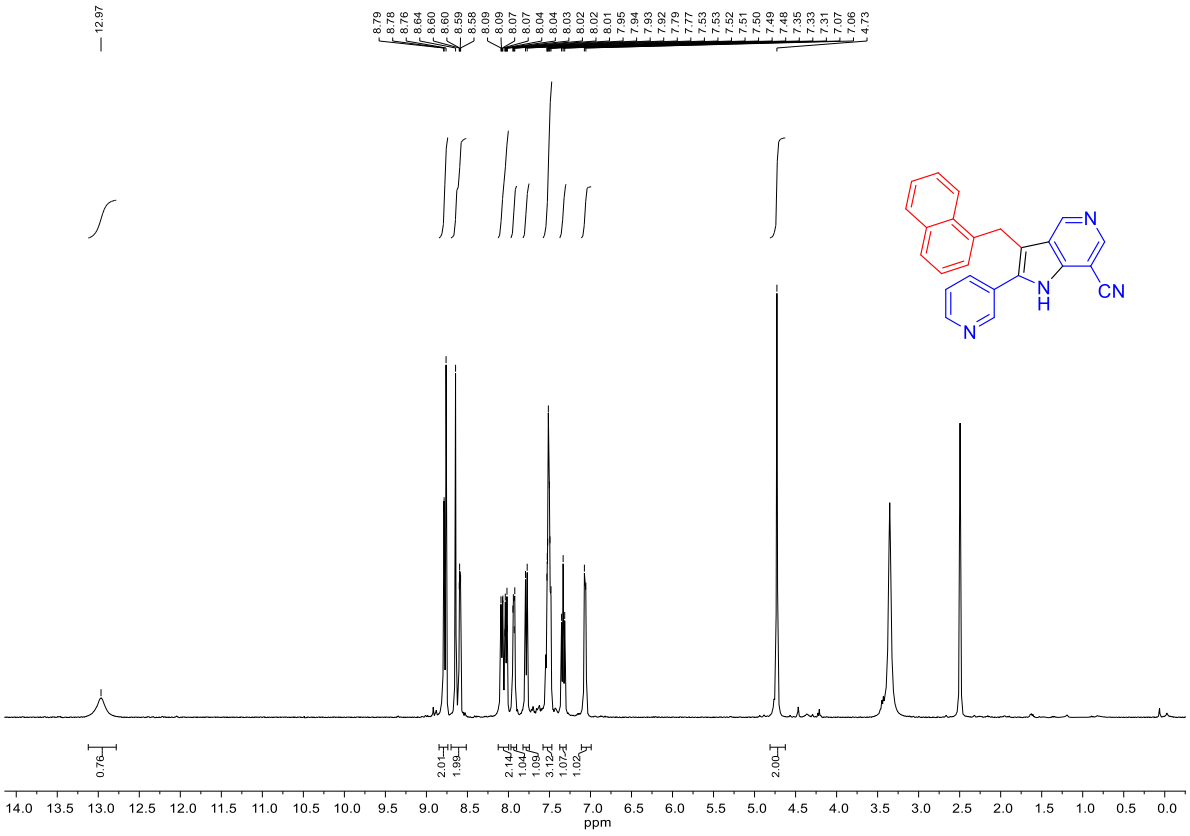
^{13}C{^{1}H} NMR Spectrum of **3j** (100.6 MHz, DMSO-d_6)



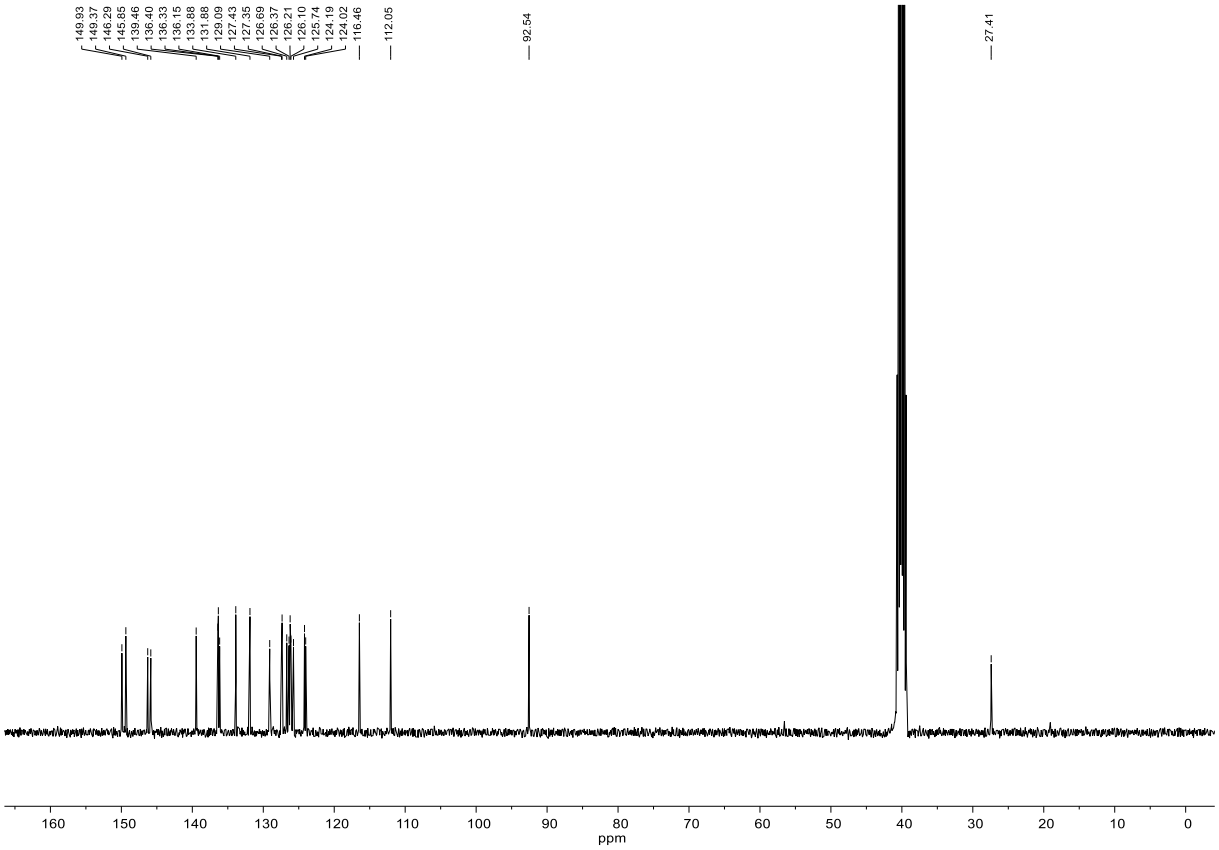
^{1}H NMR Spectrum of **3l** (400.1 MHz, DMSO-d_6)



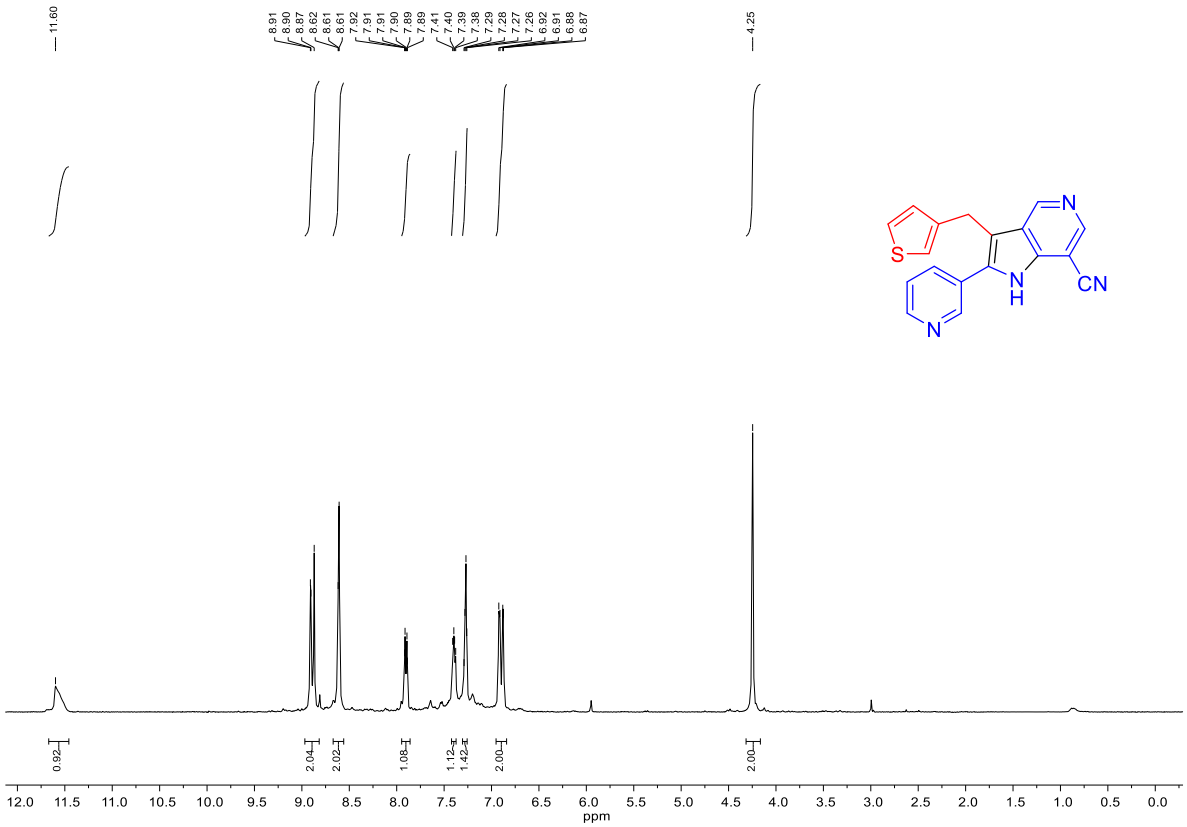
^{13}C{^{1}H} NMR Spectrum of **3l** (100.6 MHz, DMSO-d_6)



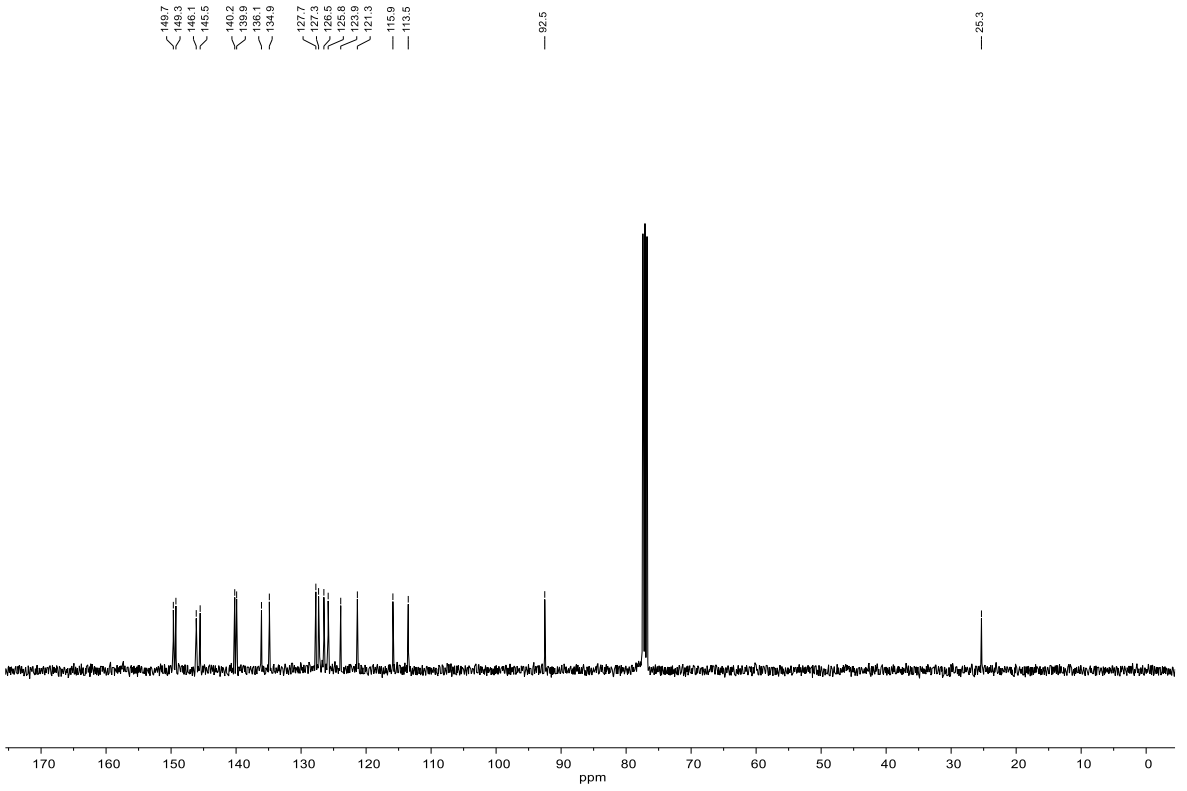
^{1}H NMR Spectrum of **3m** (400.1 MHz, DMSO-d_6)



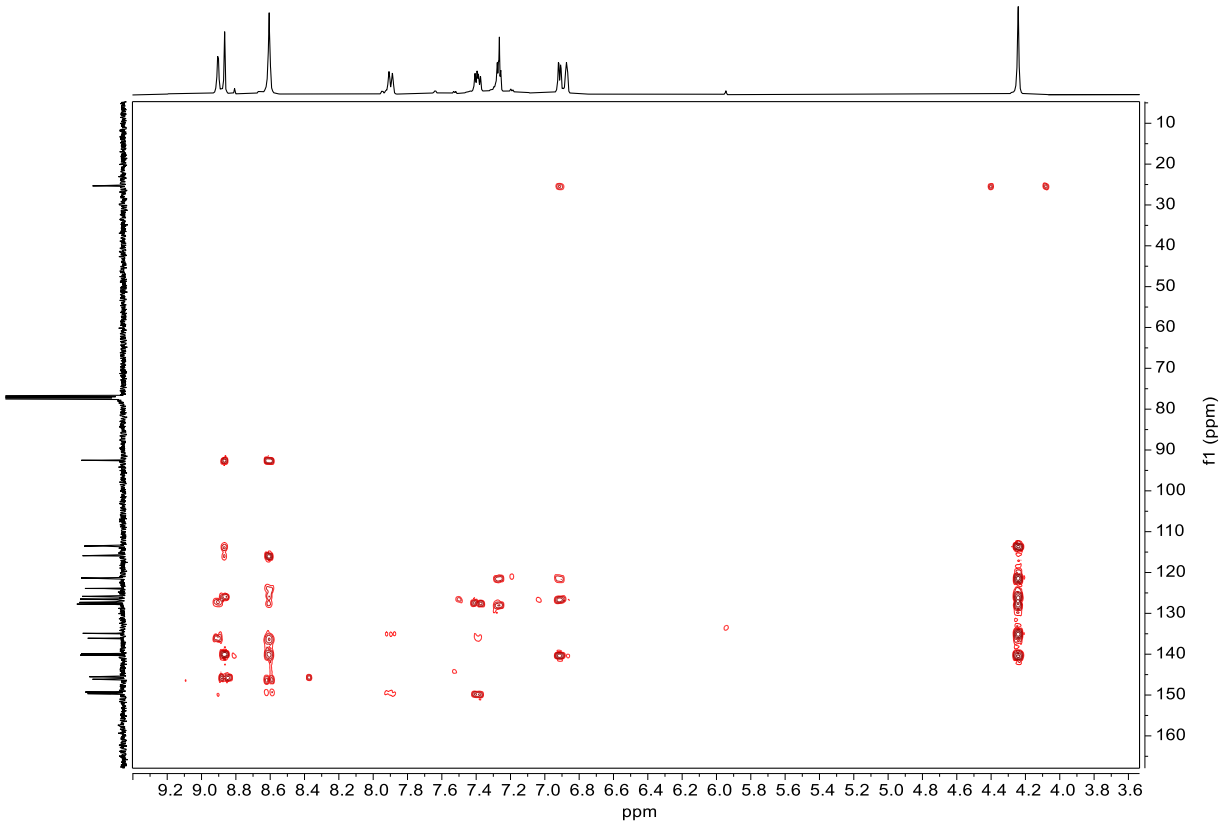
^{13}C{^{1}H} NMR Spectrum of **3m** (100.6 MHz, DMSO-d_6)



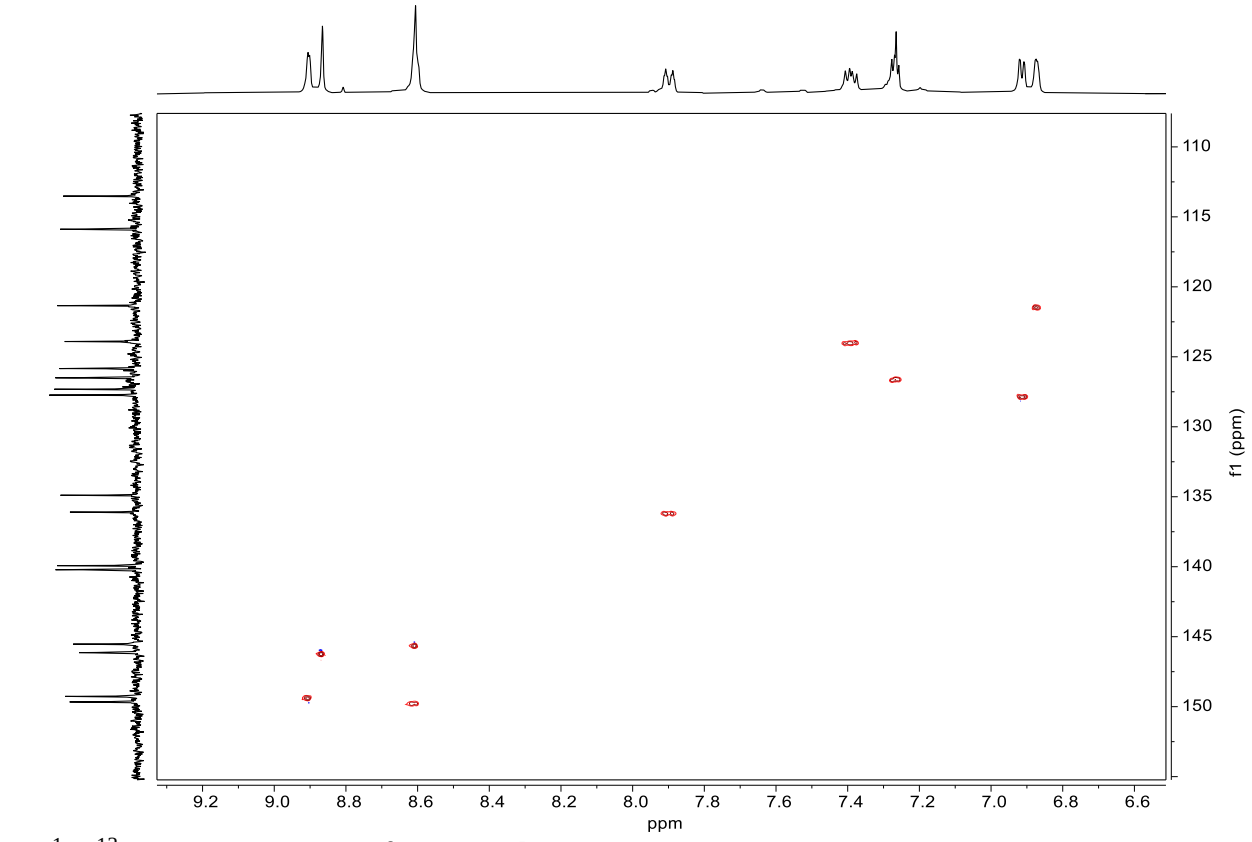
^{1}H NMR Spectrum of **3n** (400.1 MHz, $CDCl_3$)



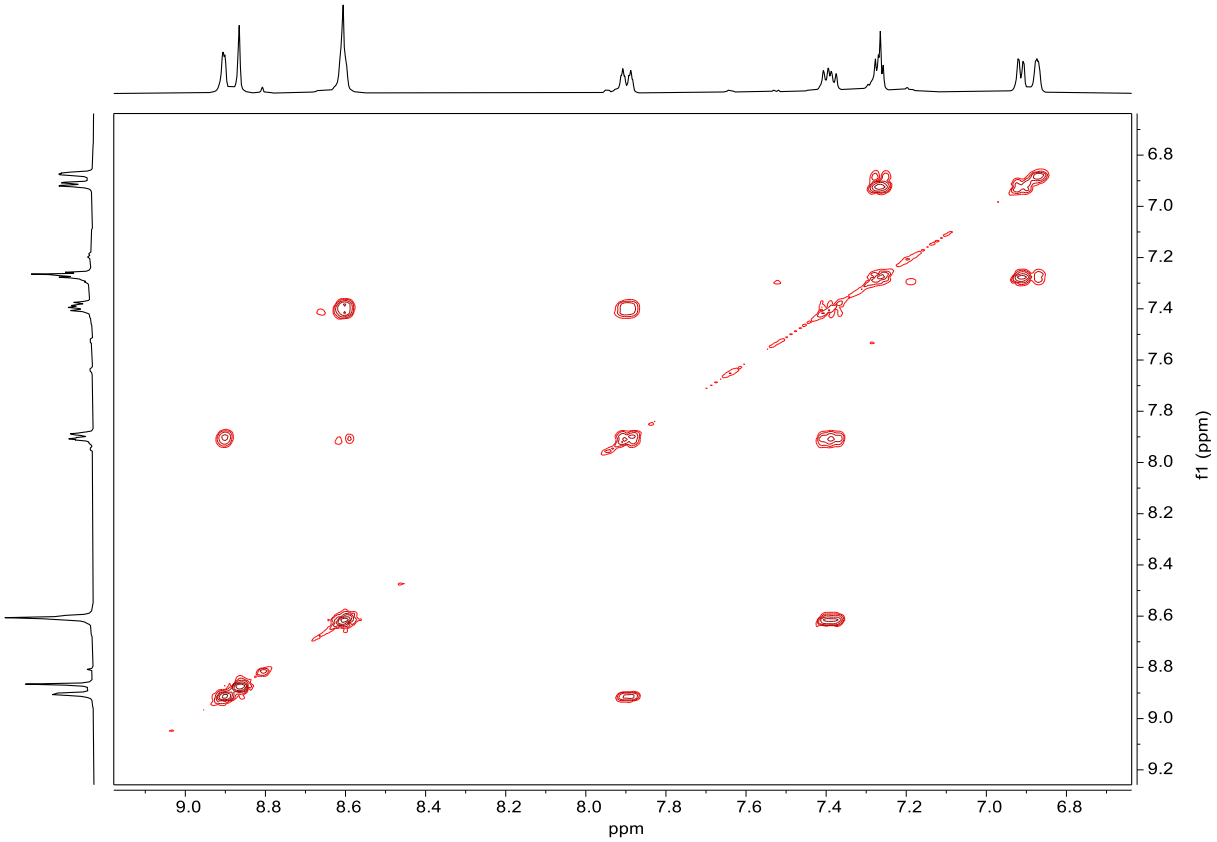
^{13}C{^{1}H} NMR Spectrum of **3n** (100.6 MHz, $CDCl_3$)



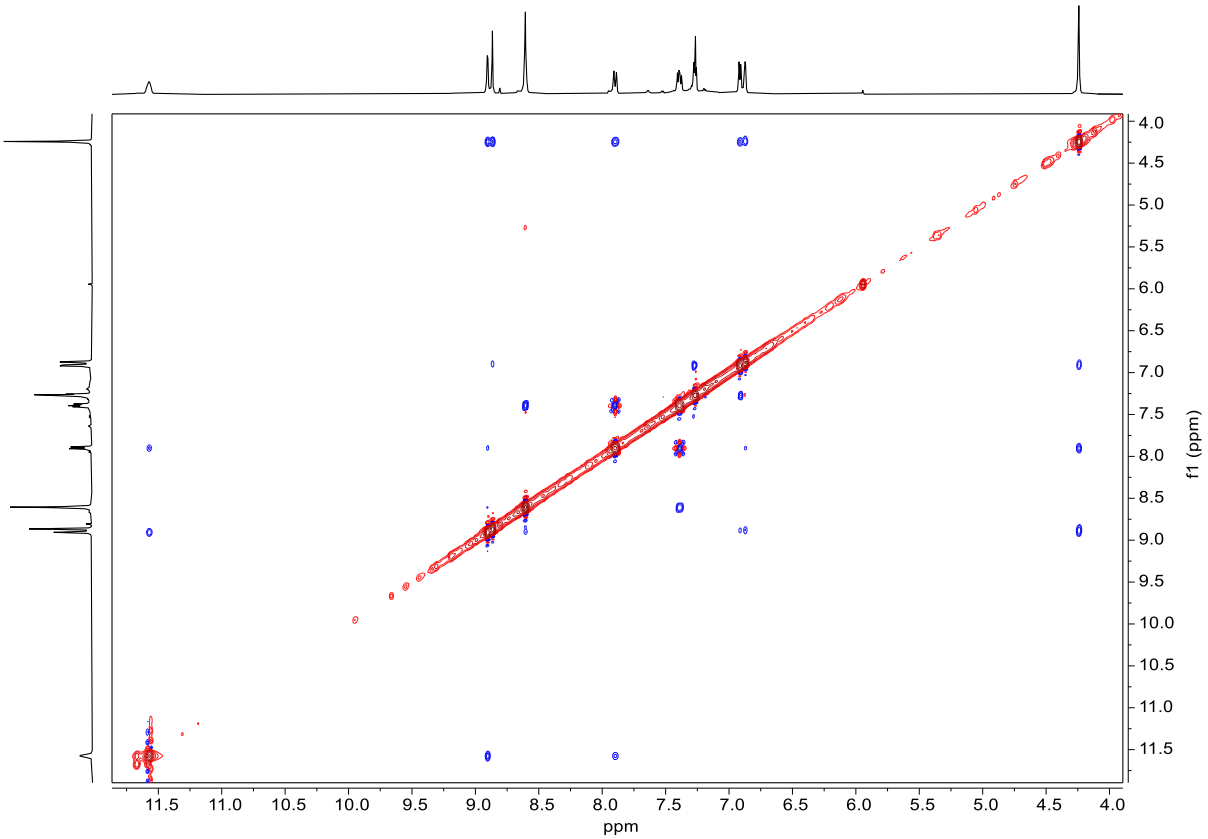
2D ^{1}H-^{13}C HMBC spectrum of **3n** ($CDCl_3$)



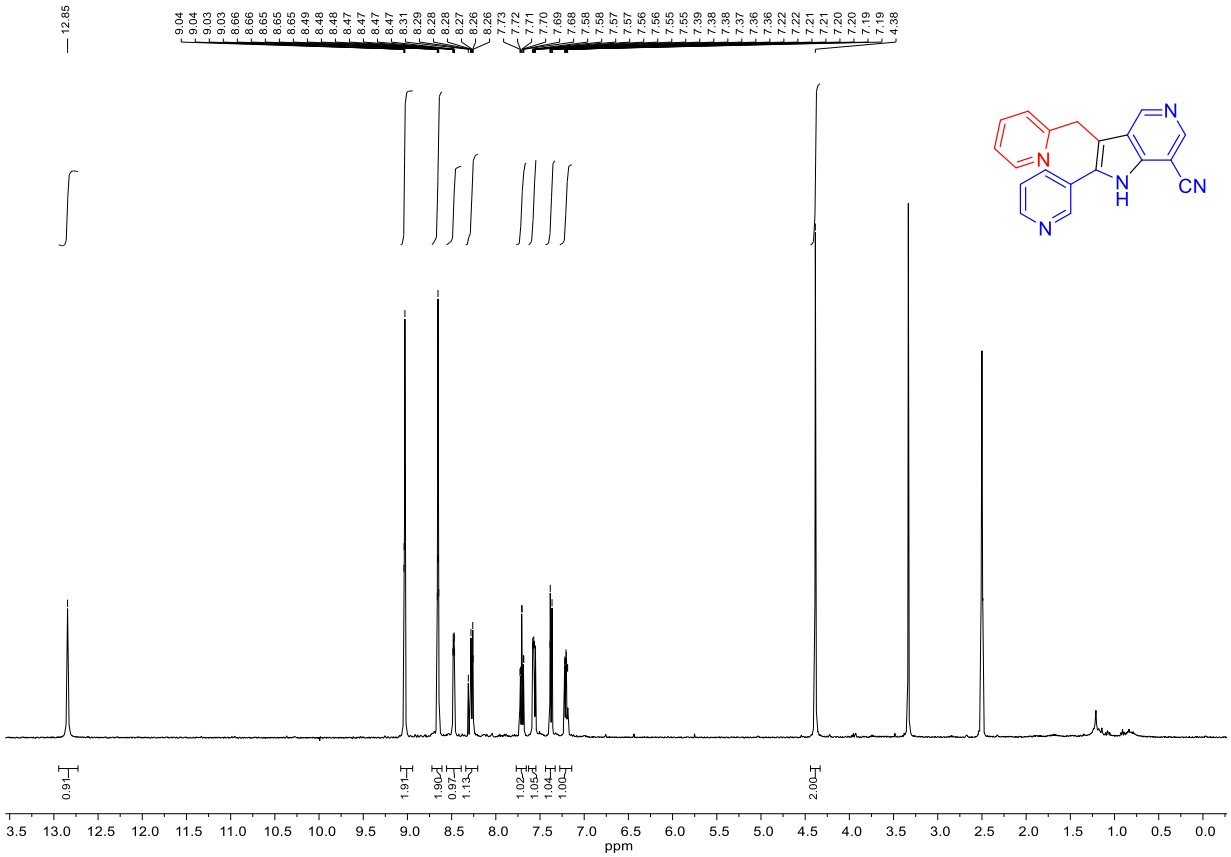
2D ^{1}H-^{13}C HSQC spectrum of **3n** ($CDCl_3$)



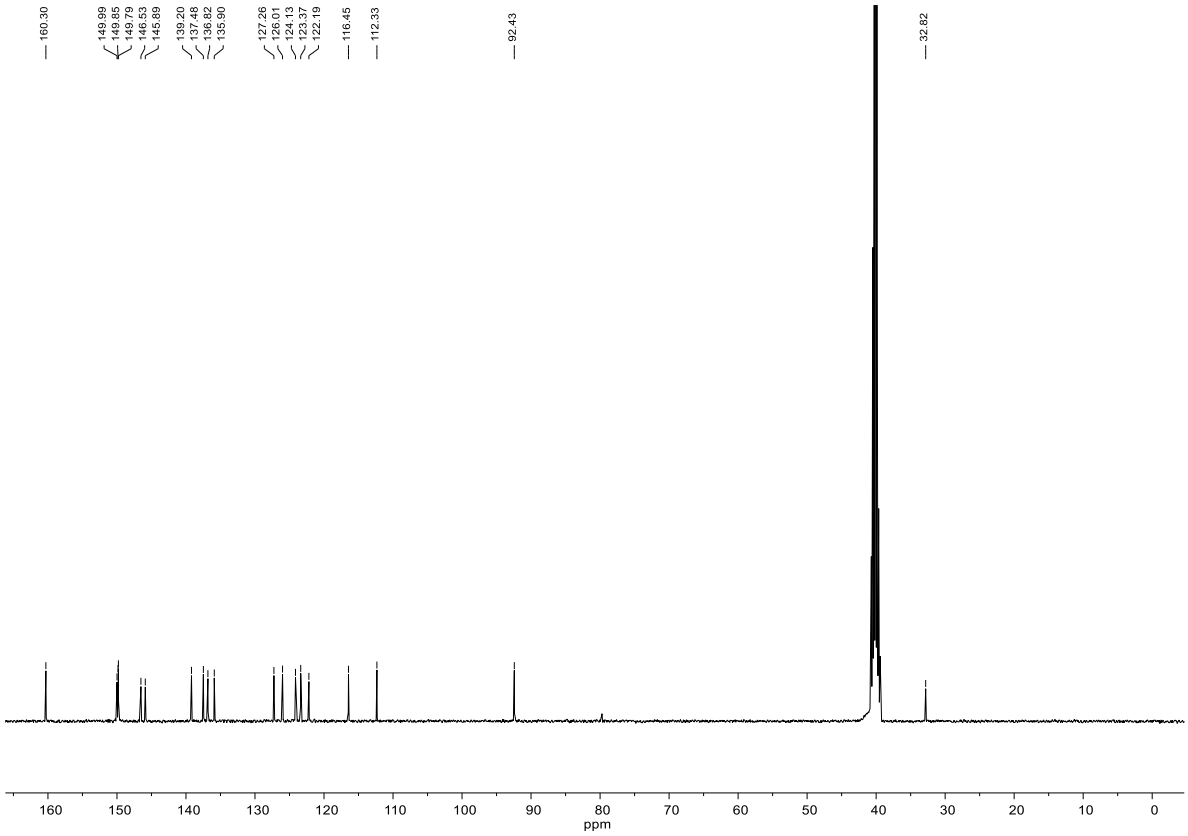
2D COSY spectrum of **3n** ($CDCl_3$)



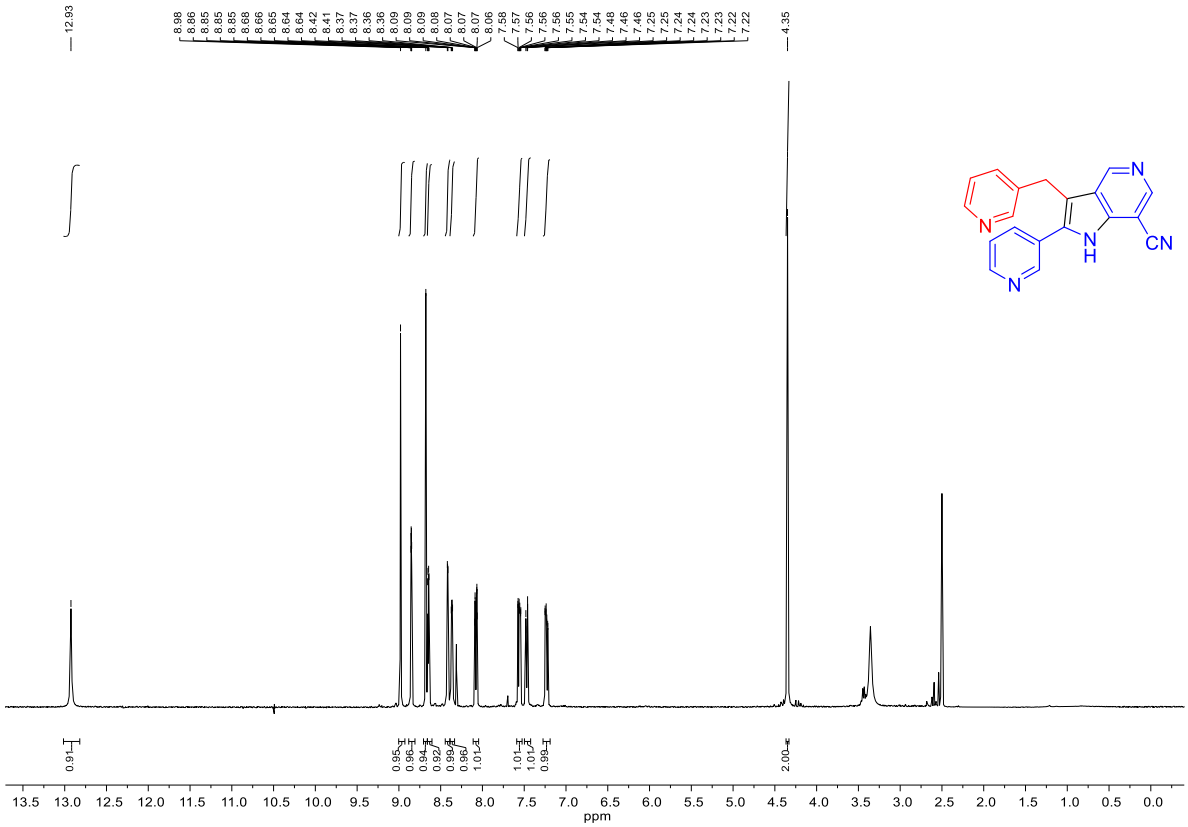
2D NOESY spectrum of **3n** ($CDCl_3$)



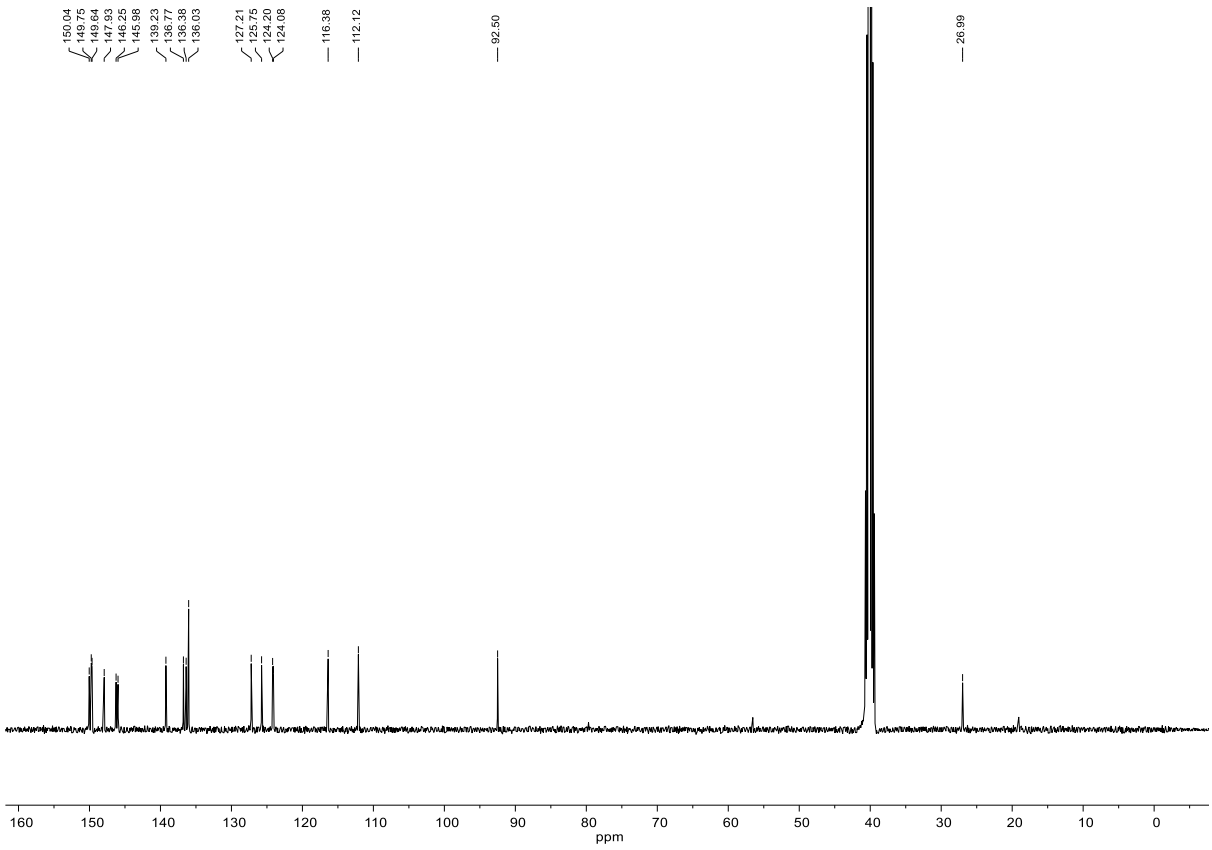
^{1}H NMR Spectrum of **3o** (400.1 MHz, DMSO-d_6)



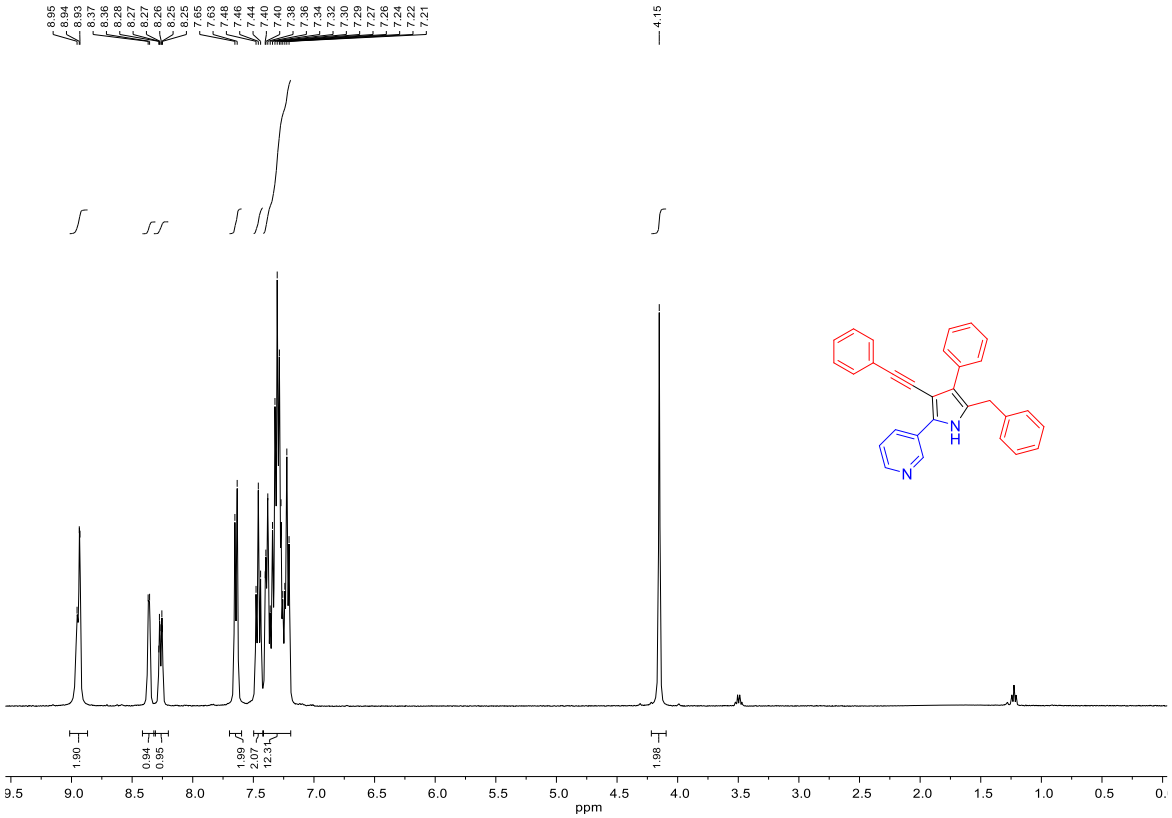
^{13}C{^{1}H} NMR Spectrum of **3o** (100.6 MHz, DMSO-d_6)



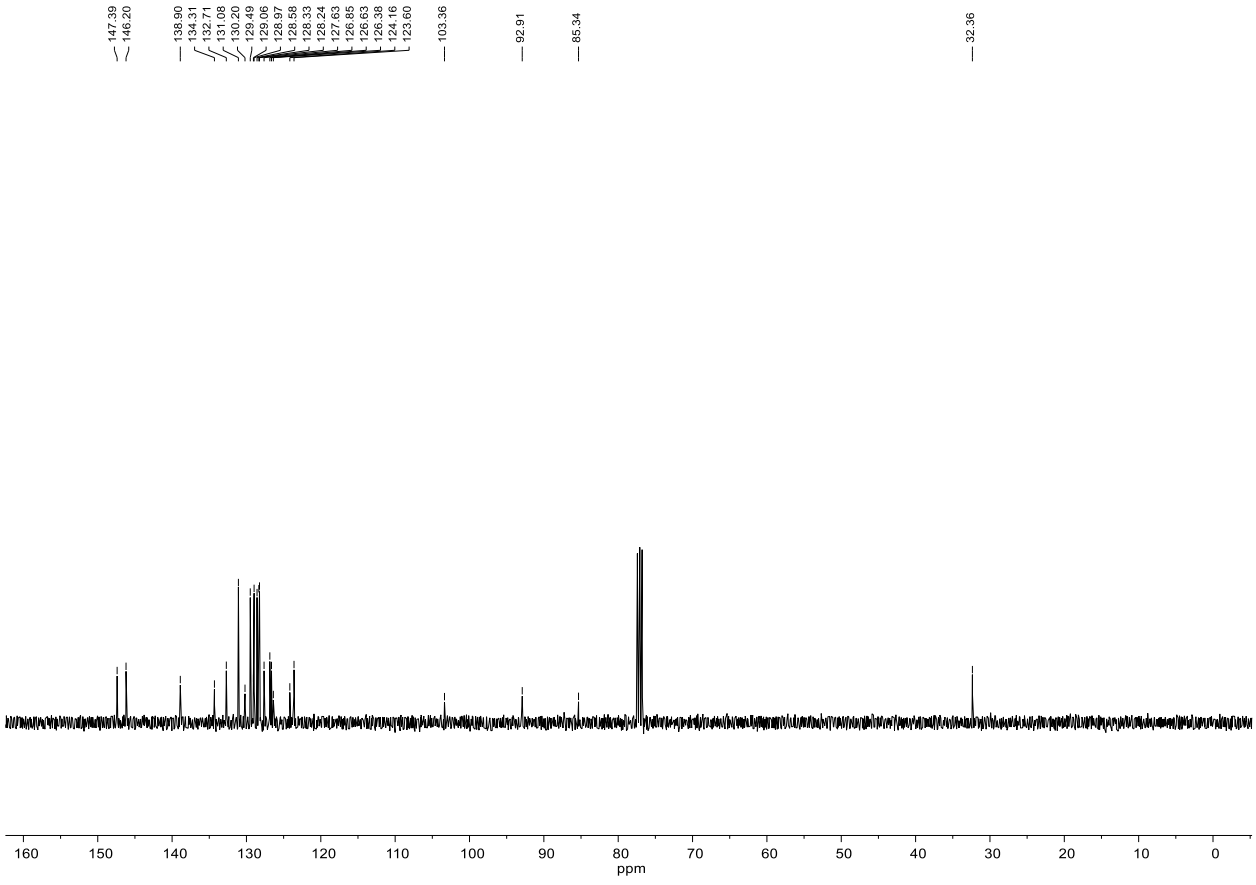
^{1}H NMR Spectrum of **3p** (400.1 MHz, DMSO-d$_6$)



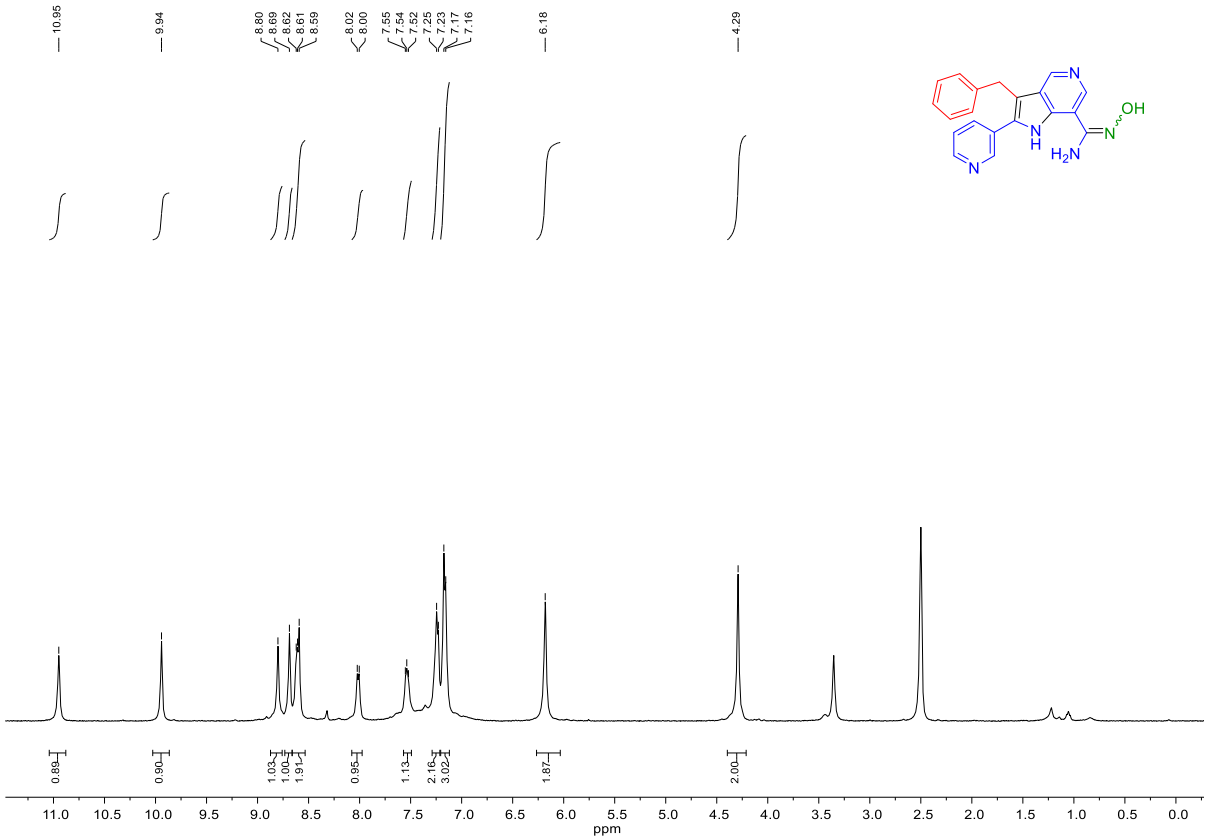
^{13}C{^{1}H} NMR Spectrum of **3p** (100.6 MHz, DMSO-d$_6$)



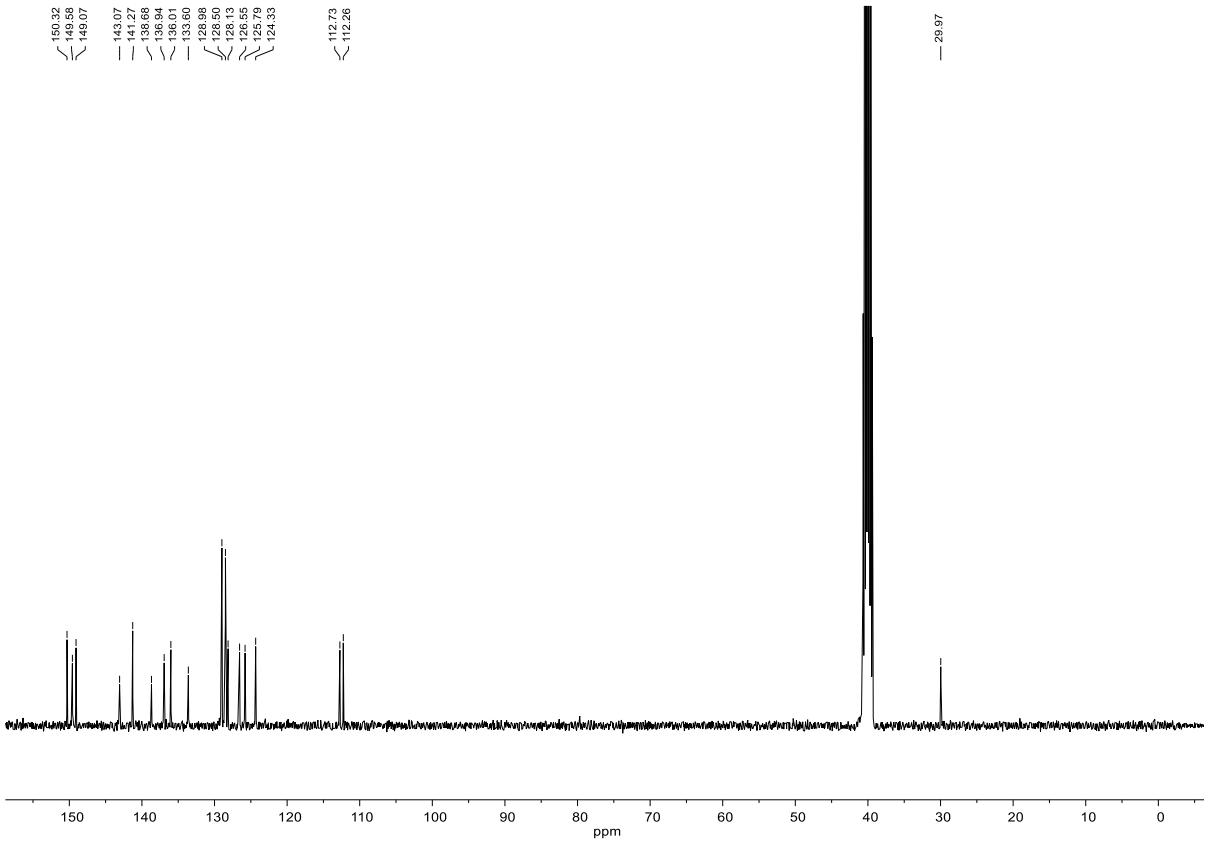
^{1}H NMR Spectrum of **4a** (400.1 MHz, $CDCl_3$)



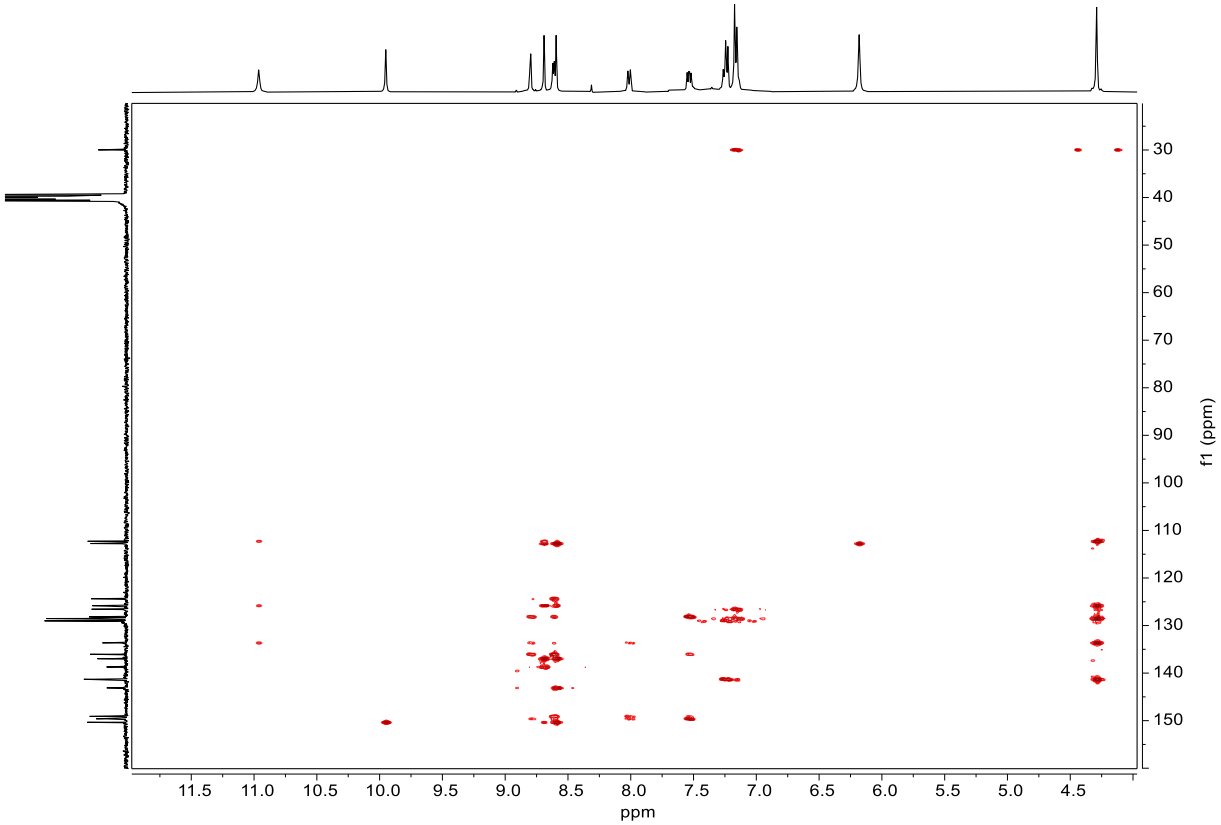
^{13}C{^{1}H} NMR Spectrum of **4a** (100.6 MHz, $CDCl_3$)



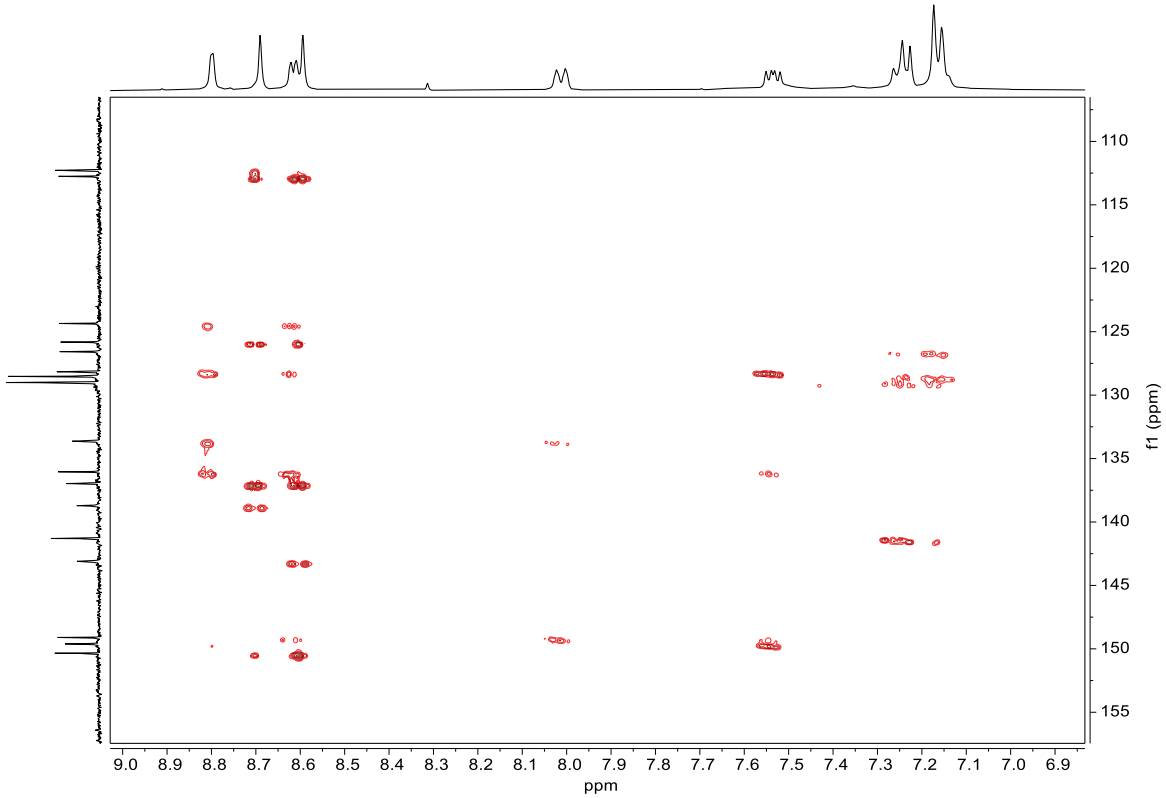
^{1}H NMR Spectrum of **5a** (400.1 MHz, DMSO-d_6)



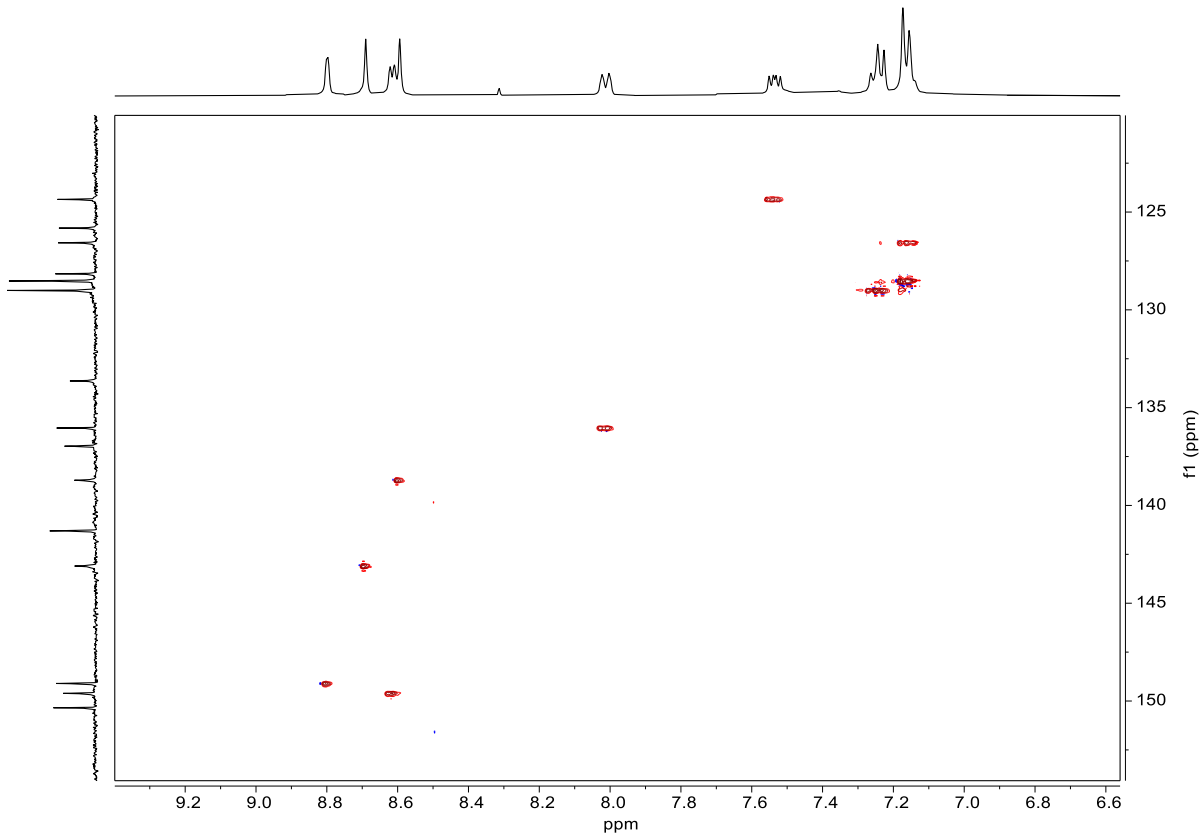
^{13}C{^{1}H} NMR Spectrum of **5a** (100.6 MHz, DMSO-d_6)



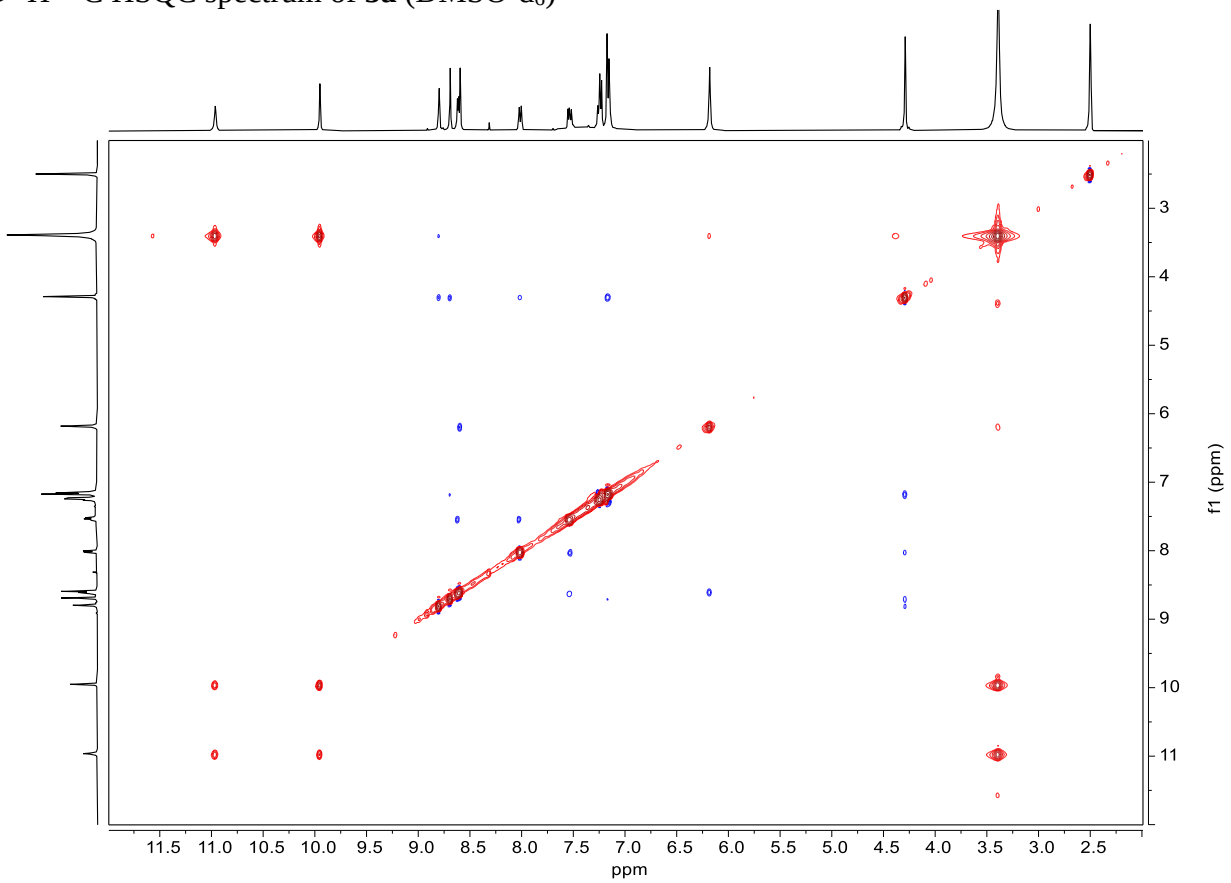
2D ^{1}H-^{13}C HMBC spectrum of **5a** (DMSO-d_6)



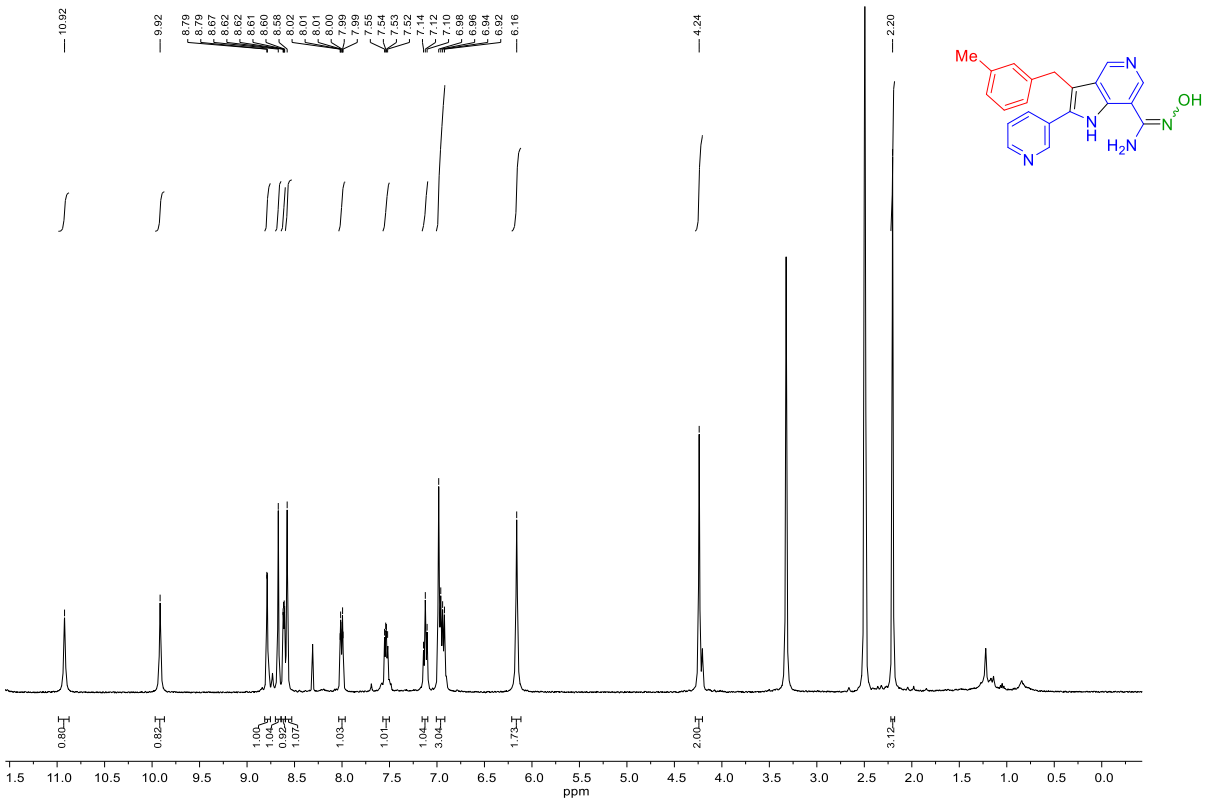
2D ^{1}H-^{13}C HMBC spectrum of **5a** (aromatic region) (DMSO-d_6)



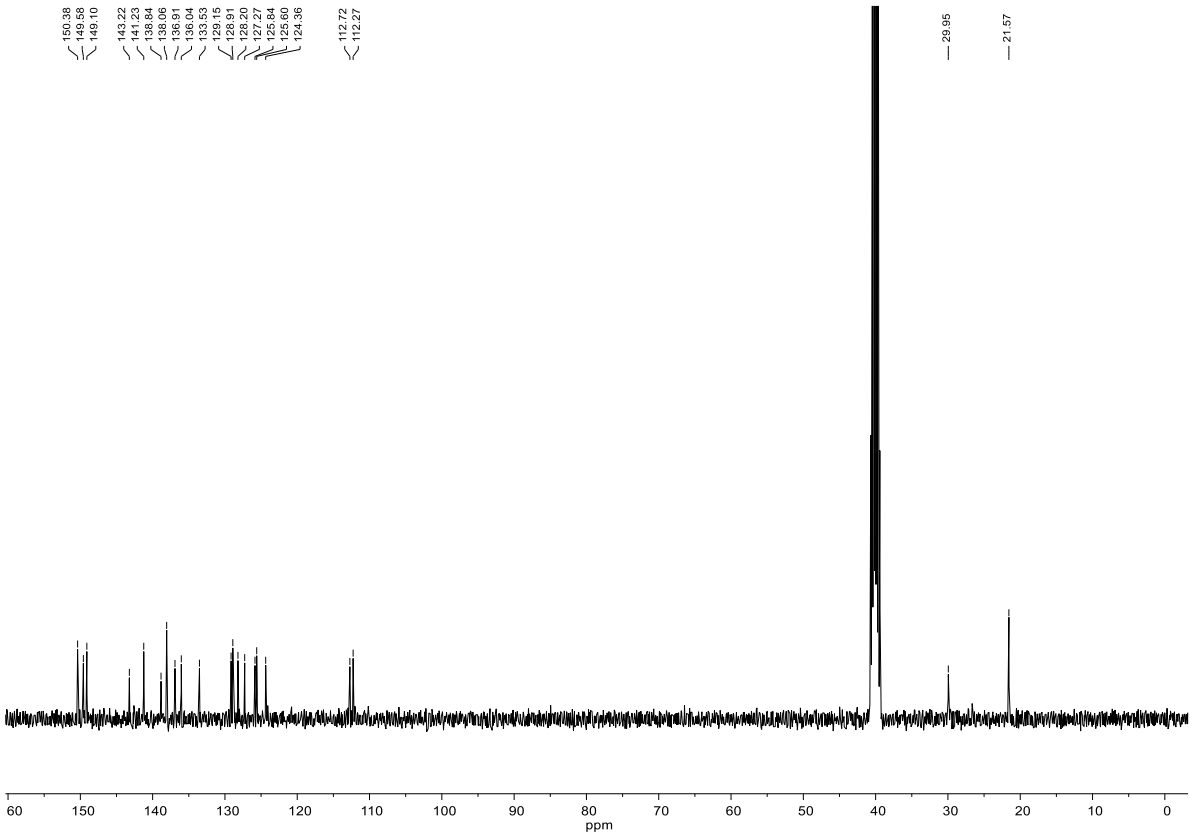
2D ^{1}H-^{13}C HSQC spectrum of **5a** (DMSO-d_6)



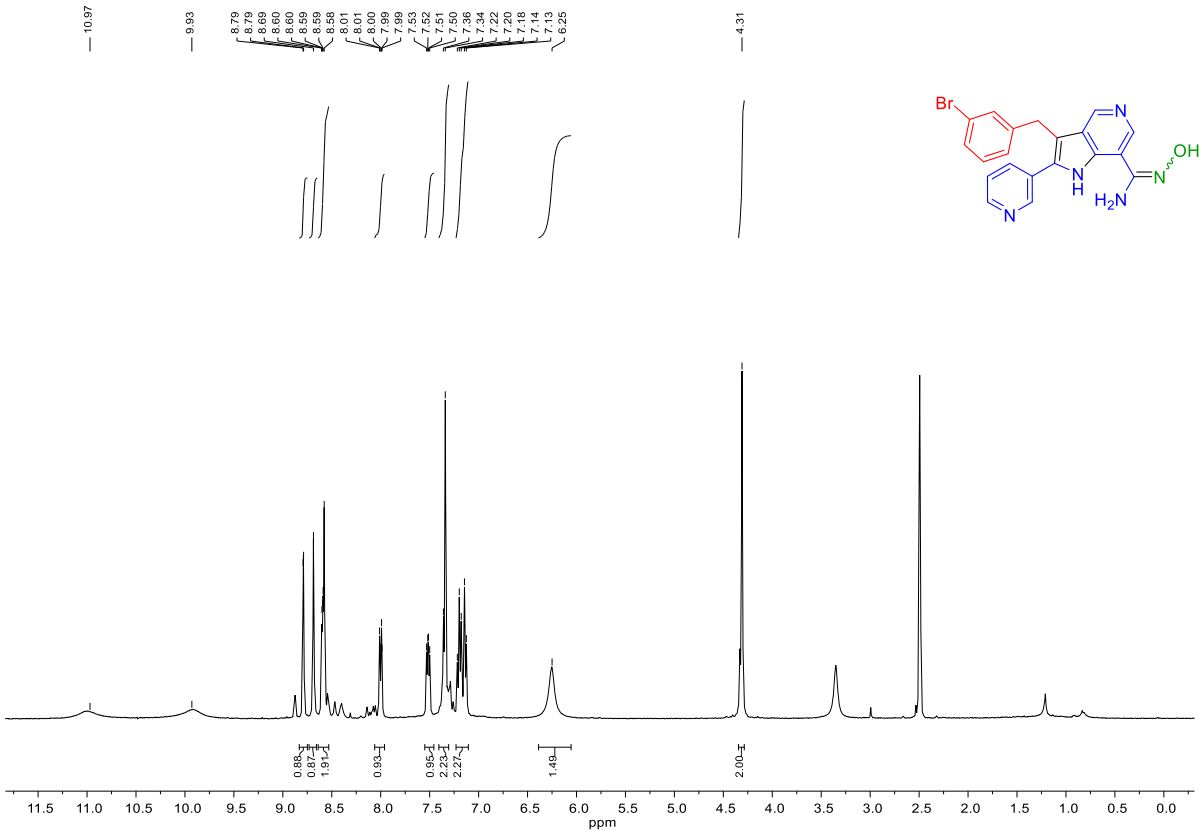
2D NOESY spectrum of **5a** (DMSO-d_6)



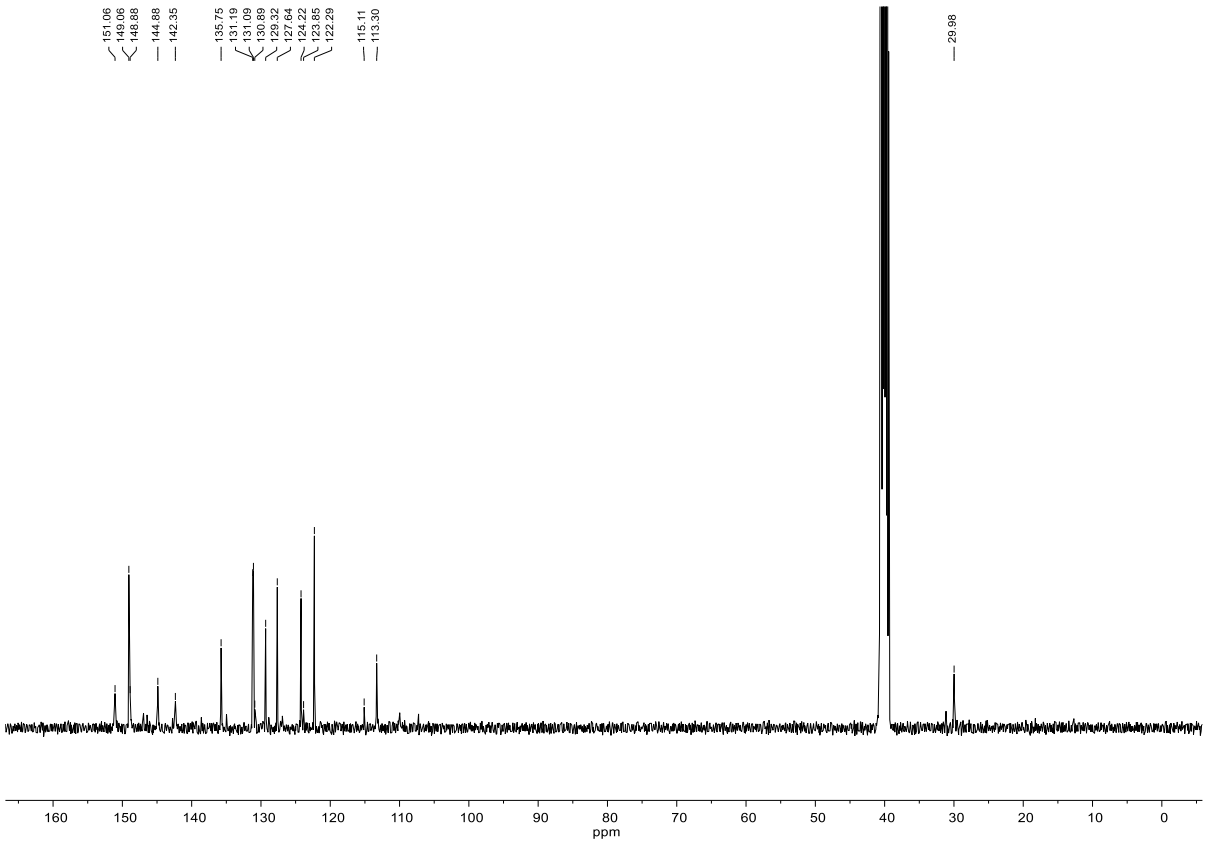
^{1}H NMR Spectrum of **5b** (400.1 MHz, DMSO-d_6)



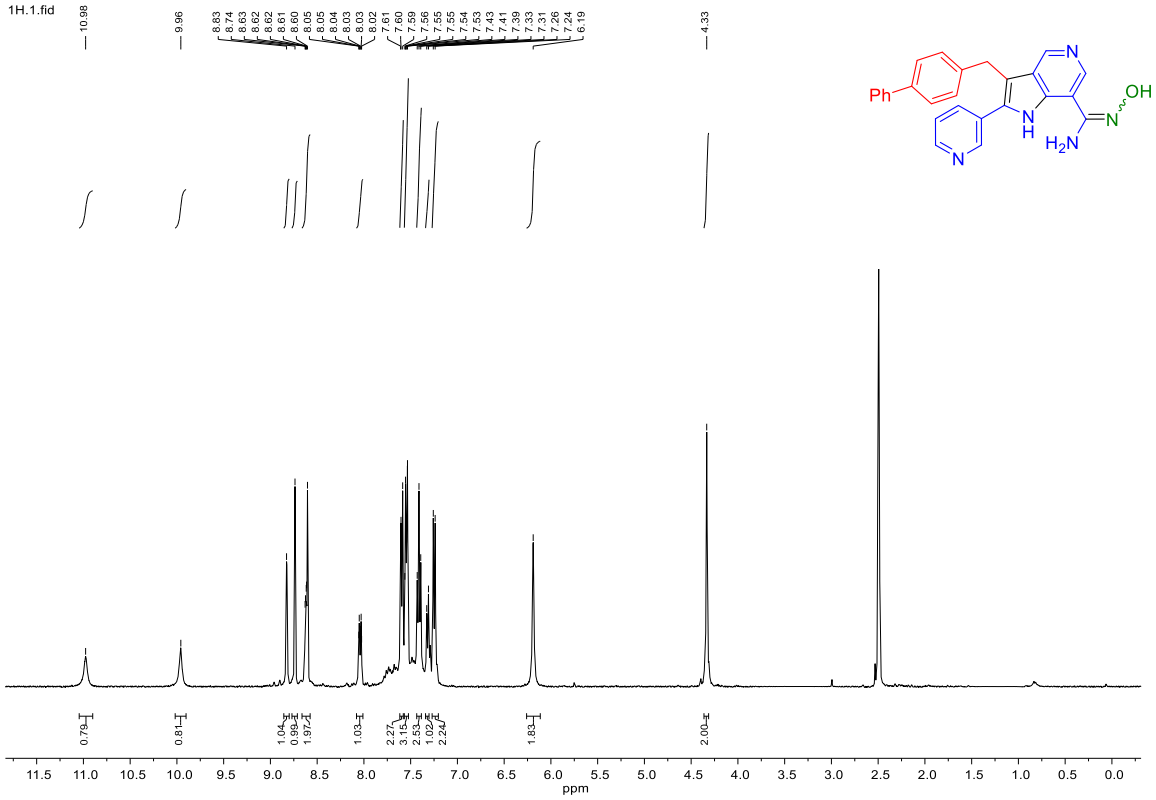
^{13}C{^{1}H} NMR Spectrum of **5b** (100.6 MHz, DMSO-d_6)



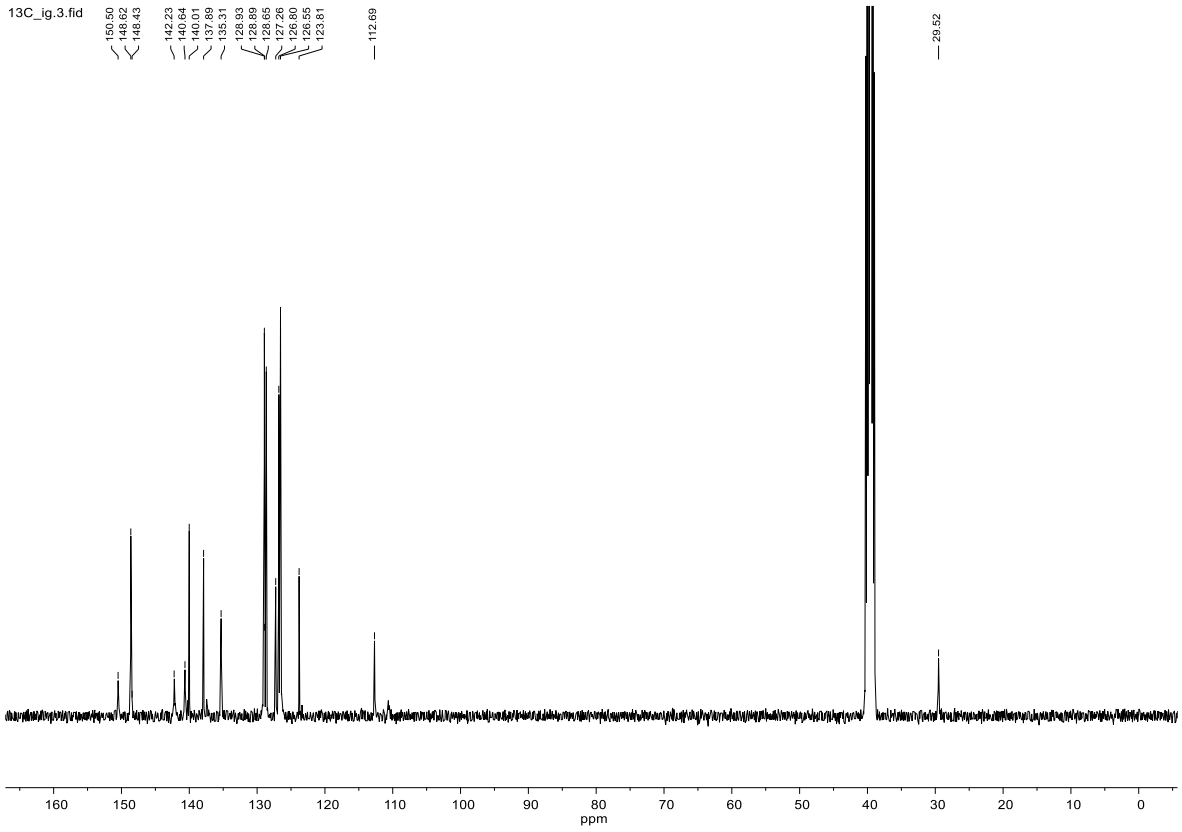
^{1}H NMR Spectrum of **5j** (400.1 MHz, DMSO-d_6)



^{13}C{^{1}H} NMR Spectrum of **5j** (100.6 MHz, DMSO-d_6)



^{1}H NMR Spectrum of **5l** (400.1 MHz, DMSO-d_6)



^{13}C{^{1}H} NMR Spectrum of **5l** (100.6 MHz, DMSO-d_6)

8. X-Ray diffraction analysis

3-(3-Fluorobenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3f**

The determination of the unit cell and the data collection for **3f** was performed on a Bruker D8 VENTURE PHOTON 100 CMOS diffractometer with MoK_α radiation (λ = 0.71073) at 293.2(2) K using the ω–φ scan technique. A specimen of $C_{20}H_{13}N_4F$, approximate dimensions 0.45 mm x 0.37 mm x 0.08 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. The integration of the data using a monoclinic unit cell with *P2₁/c* space group yielded a total of 32932 reflections to a maximum 2θ angle of 53.4, of which 3443 were independent (completeness = 100%, Rint = 5.35%, Rsig = 2.67%) and 2237 were greater than 2σ(F2). The final cell constants of **a** = 13.714(2) Å, **b** = 13.131(2) Å, **c** = 9.1025(12) Å, β = 90.879(8)º, Z= 4, volume = 1639.0(4) $Å^3$. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.966 and 0.993. All H atoms were treated by mixed method.

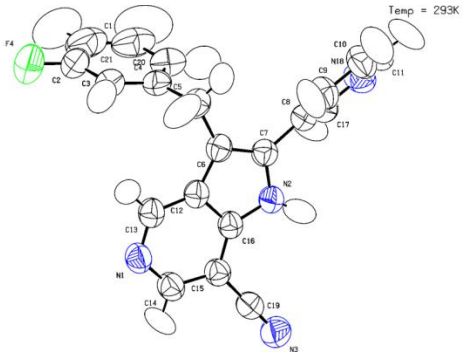


Figure S1. X-ray structure of **3f**. Thermal ellipsoids set at 50% probability.

The final anisotropic full-matrix least-squares refinement on F2 with 344 variables converged at R1 = 4.19%, for the observed data and wR2 = 11.61% for all data. The goodness-of-fit was 1.05. The largest peak in the final difference electron density synthesis was 0.18 e-/$Å^3$ and the largest hole was -0.18 e-/$Å^3$. On the basis of the final model, the calculated density was 1.331 g/cm^3 and F(000), 680 e-.

3-(3-Chlorobenzyl)-2-(pyridin-3-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile **3h**

The determination of the unit cell and the data collection for **3h** was performed with MoK_α radiation (λ = 0.71073) at 293.2(2) K using the ω–φ scan technique. A specimen of $C_{20}H_{13}ClN_4$, approximate dimensions 0.29 mm x 0.26 mm x 0.09 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. The integration of the data using a orthorhombic unit cell with *Pbca* space group yielded a total of 57675 reflections to a maximum 2θ angle of 53.6, of which 3261 were independent (completeness = 100%, Rint = 10.22%, Rsig = 4.18%) and 2079 were greater than 2σ(F2). The final cell constants of **a** = 13.349(3) Å, **b** = 9.108(2) Å, **c** = 27.934(5) Å, Z= 8, volume = 3396.2(12) $Å^3$. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.935and 0.979. All H atoms were treated by mixed method.

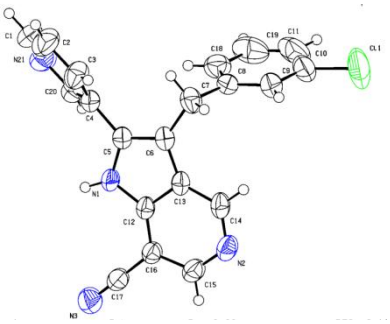


Figure S2. X-ray structure of **3h**. Thermal ellipsoids set at 50% probability.

The final anisotropic full-matrix least-squares refinement on F2 with 226 variables converged at R1 = 5.86%, for the observed data and wR2 = 14.99% for all data. The goodness-of-fit was 1.02. The largest peak in the final difference electron density synthesis was 0.27 e-/$Å^3$ and the largest hole was -0.41 e-/$Å^3$. On the basis of the final model, the calculated density was 1.349 g/cm^3 and F(000), 1424 e-.

Data were corrected for absorption effects using the multi-scan method (SADABS).[S1] The structure was solved using the Bruker SHELXTL Software Package[S2] and refined using Olex2 [S3]

package. Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC) and allocated the deposition numbers CCDC **2550666-2550667**. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

9. References

S1 G. M. Sheldrick, SADABS, Version 2016/2, Bruker AXS Inc., 2016, Germany.
S2 G. M. Sheldrick, *Acta Crystallogr*., 2008, **D64**, 112; http://doi.org/10.1107/S0108767307043930.
S3 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339; http://doi.org/10.1107/S0021889808042726.