Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting information

Synthesis of Novel Chromeno [*1,6*] Naphthyridine Derivatives in PEG-400 via Catalyst-Free, One-Pot, Multicomponent Reactions

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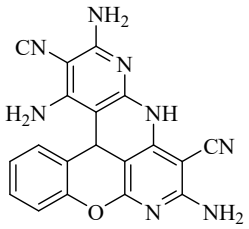
General information: All reagents were purchased from commercial suppliers and used without further purification. All experiments were carried out air atmospher. Flash chromatography was carried out with Merck silica gel 60 (63-200 mesh). Analytical TLC was performed with Merck silica gel 60 F_{254} plates, and the products were visualized by ^{1}H NMR and ^{13}C NMR (300 MHz and 75 MHz, respectively) spectra were recorded in DMSO-d6. Chemical shifts (δ) are reported in ppm using TMS as internal standard, and spin-spin coupling constants (J) are given in Hz. Melting points were determined in open-end capillary tubes on a Büchi B-540 melting point apparatus and are uncorrected.

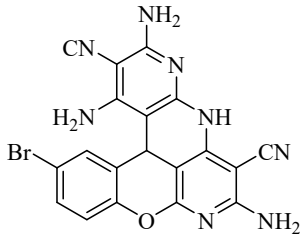
General procedure for the synthesis of Chromeno [1,6] Naphthyridine

Compound **3a-e** (1 mmol) was added to a stirred mixture of salicylaldehyde derivatives (1 mmol), malononitrile dimer (1 mmol) in PEG-400 (3 mL) and the reaction mixture stirred at 80 °C to complete the formation of related chromeno[1,6]naphthyridine (monitored by TLC). After completion of the reaction, water (3 mL) was added to the reaction mixture; the precipitate was filtrated and recrystallized from hot ethanol to afford the pure products.

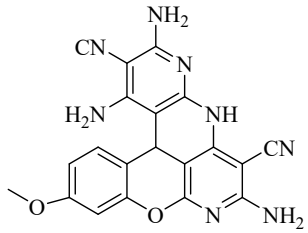
Spectrum information of Novel Chromeno [*1,6*] Naphthyridine derivatives



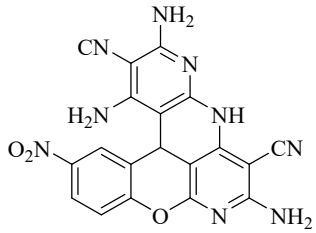
1,3,7-triamino-2-isocyano-5,13b-dihydrochromeno[4,3,2-de]pyrido[2,3-b][1,6] naphthyridine-6-carbonitrile(4a). green powder, M.P.=94°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.09 (s, 2H, NH_2), 5.33 (s, 1H, CH), 6.55 (s, 2H, NH_2), 6.99 (s, 2H, NH_2), 7.08-7.11 (m, 1H, CH aromatic), 7.12-7.14 (m, 1H, CH aromatic), 7.18-7.20 (m, 1H, CH aromatic), 7.26-7.30 (m, 1H, CH aromatic), 8.93 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 24.3, 61.2, 75.5, 85.2, 99.6, 115.2, 117.0, 117.1, 123.2, 125.2, 128.8, 129.3, 131.1, 131.6, 151.7, 152.9, 158.3, 160.5, 161.0. HRMS m/z calcd for $C_{19}H_{12}N_8O$ $[M]^+$ 368.11, found 368.1. *Anal.* Calcd for $C_{19}H_{12}N_8O$: C, 61.95; H, 3.28; N, 30.42%. Found: C, 61.92; H, 3.21; N, 30.45%.



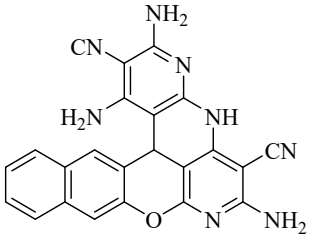
1,3,7-triamino-12-bromo-2-isocyano-5,13b-dihydrochromeno[4,3,2-de]pyrido[2,3-b][1,6]naphthyridine-6-carbonitrile(4b). green powder, M.P.=94°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.02 (s, 2H, NH_2), 5.36 (s, 1H, CH), 6.63 (s, 2H, NH_2), 7.00 (s, 2H, NH_2), 7.14 (d, J = 6.0 Hz, 1H, CH aromatic), 7.30-7.31 (m, 1H, CH aromatic), 7.46-7.48 (m, 1H, CH aromatic), 8.90 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 36.5, 74.1, 94.5, 96.5, 99.9, 115.0, 117.2, 118.6, 124.8, 131.9, 132.8, 147.3, 149.9, 150.4, 155.6, 157.5, 159.2, 160.7, 168.1. *Anal.* Calcd for $C_{19}H_{11}BrN_8O$: C, 51.02; H, 2.48; N, 25.05%. Found: C, 51.06; H, 2.42; N, 25.01%.



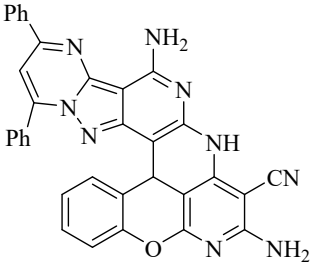
1,3,7-triamino-2-isocyano-11-methoxy-5,13b-dihydrochromeno[4,3,2-de]pyrido[2,3-b][1,6]naphthyridine-6-carbonitrile(4c). green powder, M.P.=96°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.09 (s, 2H, NH_2), 3.82 (s, 3H, CH_3), 5.32 (s, 1H, CH), 6.55 (s, 2H, NH_2), 6.57-6.63 (m, 1H, CH aromatic), 6.88 (s, 1H, CH aromatic), 6.99 (s, 2H, NH_2), 7.03-7.06 (m, 1H, CH aromatic), 8.93 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 30.5, 55.6, 74.1, 94.5, 96.8, 99.5, 102.9, 108.3, 115.0, 120.9, 129.3, 147.3, 149.9, 152.2, 155.6, 157.5, 159.2, 160.3, 160.7, 168.0. HRMS m/z calcd for $C_{20}H_{14}N_8O_2$ $[M]^+$ 398.12, found 398.1. *Anal.* Calcd for $C_{20}H_{14}N_8O_2$: C, 60.30; H, 3.54; N, 28.13%. Found: C, 60.33; H, 3.51; N, 28.11%.



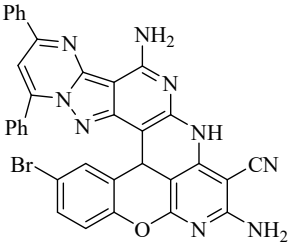
1,3,7-triamino-2-isocyano-12-nitro-5,13b-dihydrochromeno[4,3,2-de]pyrido[2,3-b][1,6]naphthyridine-6-carbonitrile(4d). green powder, M.P.=92°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.08 (s, 2H, NH_2), 5.16 (s, 1H, CH), 6.62 (s, 2H, NH_2), 6.91 (s, 2H, NH_2), 7.22 (s, 1H, CH aromatic), 8.12 (d, J = 3.0 Hz, 1H, CH aromatic), 8.27 (s, 1H, CH aromatic), 8.91 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 30.1, 74.1, 94.4, 95.0, 99.9, 115.0, 118.3, 123.7, 124.2, 124.5, 142.1, 147.2, 149.9, 155.4, 155.7, 157.5, 159.2, 160.7, 168.3. *Anal.* Calcd for $C_{19}H_{11}N_9O_3$: C, 55.21; H, 2.68; N, 30.50%. Found: C, 55.18; H, 2.65; N, 30.54%.



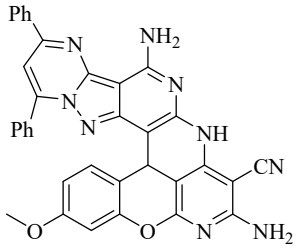
1,3,7-triamino-2-isocyano-5,15b-dihydrobenzo[6,7]chromeno[4,3,2-de]pyrido[2,3-b][1,6]naphthyridine-6-carbonitrile(4e). green powder, M.P.=93°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.07 (s, 2H, NH_2), 5.32 (s, 1H, CH), 6.57 (s, 2H, NH_2), 6.91 (s, 2H, NH_2), 7.45-7.47 (m, 2H, CH aromatic), 7.60 (d, J = 3.0 Hz, 1H, CH aromatic), 7.67-7.68 (s, 1H, CH aromatic), 7.81-7.83 (m, 2H, CH aromatic), 8.94 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 30.1, 74.3, 94.5, 96.5, 99.9, 112.4, 115.0, 122.7, 125.9, 126.6, 127.2, 127.4, 128.2, 130.3, 134.3, 147.3, 149.6, 149.9, 155.6, 157.5, 159.3, 160.7, 168.5. HRMS m/z calcd for $C_{23}H_{14}N_8O$ $[M]^+$ 418.13, found 418.1. *Anal.* Calcd for $C_{23}H_{14}N_8O$: C, 66.02; H, 3.37; N, 26.78%. Found: C, 66.05; H, 3.31; N, 26.71%.



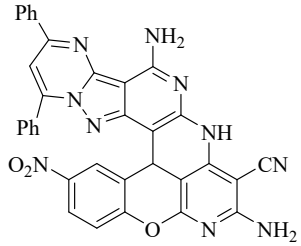
2,6-diamino-8,10-diphenyl-4,12c-dihydrochromeno[4,3,2-de]pyrimido[1'',2'':1',5']pyrazolo[3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-3-carbonitrile(4f). red powder, M.P.=98°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.08 (s, 2H, NH_2), 5.28 (s, 1H, CH), 7.07-7.10 (m, 1H, CH aromatic), 7.12-7.14 (m, 1H, CH aromatic), 7.22-7.24 (m, 1H, CH aromatic), 7.26-7.30 (m, 1H, CH aromatic), 7.44-7.52 (m, 5H, CH aromatic), 7.53-7.54 (m, 1H, CH aromatic), 7.60-7.63 (m, 2H, CH aromatic), 7.81 (s, 1H, CH aromatic), 7.87 (s, 2H, NH_2), 8.32-8.34 (m, 2H, CH aromatic), 8.67 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 33.6, 74.1, 87.9, 98.8, 102.7, 106.9, 115.0, 117.7, 123.2, 125.3, 127.4, 127.5, 129.1, 129.2, 129.3, 129.8, 132.7, 134.6, 142.1, 145.8, 149.9, 151.0, 151.2, 154.8, 155.0, 159.2, 160.7, 162.0. *Anal.* Calcd for $C_{34}H_{21}N_9O$: C, 71.44; H, 3.70; N, 22.05%. Found: C, 71.41; H, 3.64; N, 22.08%.



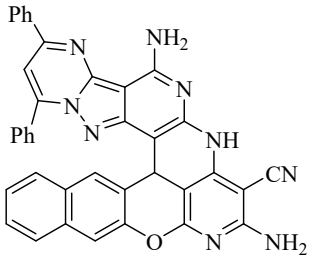
2,6-diamino-14-bromo-8,10-diphenyl-4,12c-dihydrochromeno[4,3,2-de]pyrimido [1'',2'':1',5']pyrazolo[3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-3-carbonitrile(4g). red powder, M.P.=98°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.04 (s, 2H, NH_2), 5.28 (s, 1H, CH), 7.14 (d, J = 6.0 Hz, 1H, CH aromatic), 7.31 (s, 1H, CH aromatic), 7.44-7.49 (m, 5H, CH aromatic), 7.50-7.54 (m, 2H, CH aromatic), 7.60-7.63 (m, 2H, CH aromatic), 7.83 (s, 1H, CH aromatic), 7.89 (s, 2H, NH_2), 8.32-8.35 (m, 2H, CH aromatic), 8.68 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 35.6, 71.4, 85.2, 98.9, 102.8, 104.8, 108.2, 113.0, 113.2, 113.4, 117.3, 119.9, 122.4, 122.8, 125.5, 126.4, 128.2, 130.5, 132.8, 133.5, 135.9, 137.7, 152.5, 152.8, 153.0, 155.5, 159.6, 160.7, 162.0. *Anal.* Calcd for $C_{34}H_{20}BrN_9O$: C, 62.78; H, 3.10; N, 19.38%. Found: C, 62.71; H, 3.13; N, 19.35%.



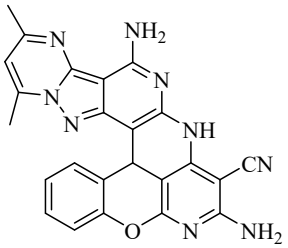
2,6-diamino-15-methoxy-8,10-diphenyl-4,12c-dihydrochromeno[4,3,2-de]pyrimido [1'',2'':1',5']pyrazolo[3',4':4,5] pyrido[2,3-b][1,6]naphthyridine-3-carbonitrile(4h). red powder, M.P.=96°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.00 (s, 2H, NH_2), 3.82 (s, 3H, OCH_3), 5.48 (s, 1H, CH), 6.62 (d, J = 3.0 Hz, 1H, CH aromatic), 7.02 (s, 1H, CH aromatic), 7.24 (d, J = 6.0 Hz, 1H, CH aromatic), 7.47-7.51 (m, 4H, CH aromatic), 7.54-7.58 (m, 2H, CH aromatic), 7.85 (s, 1H, CH aromatic), 8.08-8.12 (m, 2H, CH aromatic), 8.24 (s, 2H, NH_2), 8.32-8.35 (m, 2H, CH aromatic), 8.94 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 36.5, 55.6, 73.5, 88.5, 97.1, 103.1, 103.2, 109.7, 111.0, 115.3, 120.1, 126.8, 127.2, 129.0, 129.2, 129.7, 129.8, 130.5, 131.9, 133.1, 146.2, 147.2, 148.6, 148.9, 152.2, 152.7, 157.0, 160.6, 160.8, 161.7, 162.6. *Anal.* Calcd for $C_{35}H_{23}N_9O_2$: C, 69.87; H, 3.85; N, 20.95%. Found: C, 69.85; H, 3.88; N, 20.91%.



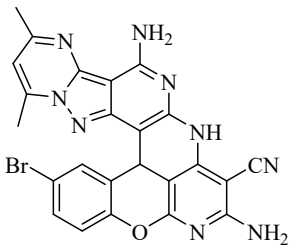
2,6-diamino-14-nitro-8,10-diphenyl-4,12c-dihydrochromeno[4,3,2-de]pyrimido [1'',2'':1',5']pyrazolo[3',4':4,5] pyrido [2,3-b][1,6]naphthyridine-3-carbonitrile(4i). red powder, M.P.=92°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.04(s, 2H, NH_2), 5.29 (s, 1H, CH), 7.21 (d, J = 6.0 Hz, 1H, CH aromatic), 7.44-7.49 (m, 4H, CH aromatic), 7.50-7.54 (m, 2H, CH aromatic), 7.60-7.63 (m, 2H, CH aromatic), 7.81 (s, 1H, CH aromatic), 7.87 (s, 2H, NH_2), 8.10-8.13 (m, 1H, CH aromatic), 8.27-8.28 (m, 1H, CH aromatic), 8.32-8.34 (m, 2H, CH aromatic), 8.66 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 37.4, 77.4, 87.4, 99.1, 107.2, 109.8, 112.3, 112.4, 113.2, 113.5, 117.2, 120.8, 122.7, 122.8, 125.4, 126.5, 132.8, 133.5, 133.9, 134.0, 135.8, 148.6, 148.7, 152.4, 152.5, 154.7, 155.1, 159.7, 162.4. *Anal.* Calcd for $C_{34}H_{20}N_{10}O_3$: C, 66.23; H, 3.27; N, 22.72%. Found: C, 66.21; H, 3.28; N, 22.79%.



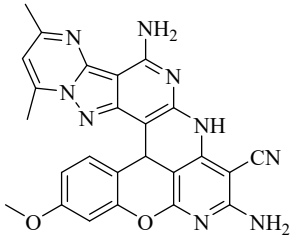
1,5-diamino-16,18-diphenyl-3,13b-dihydrobenzo[6,7]chromeno[4,3,2-de]pyrimido [1'',2'':1',5']pyrazolo[3',4':4,5] pyrido[2,3-b][1,6]naphthyridine-4-carbonitrile(4j). red powder, M.P.=99°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.08(s, 2H, NH_2), 5.30 (s, 1H, CH), 7.43-7.54 (m, 8H, CH aromatic), 7.60-7.63 (m, 3H, CH aromatic), 7.67-7.69 (m, 1H, CH aromatic), 7.81-7.83 (m, 3H, CH aromatic), 7.88 (s, 2H, NH_2), 8.32-8.34 (m, 2H, CH aromatic), 8.67 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 31.4, 75.2, 86.2, 97.4, 102.0, 107.2, 109.5, 112.2, 113.2, 113.4, 114.6, 115.4, 117.2, 120.9, 121.6, 122.7, 125.4, 127.5, 128.0, 133.5, 133.9, 137.4, 137.9, 148.6, 148.7, 151.6, 152.4, 153.5, 154.9, 158.7, 159.7, 162.6, 163.5. *Anal.* Calcd for $C_{38}H_{23}N_9O$: C, 73.42; H, 3.73; N, 20.28%. Found: C, 73.45; H, 3.81; N, 20.22%.



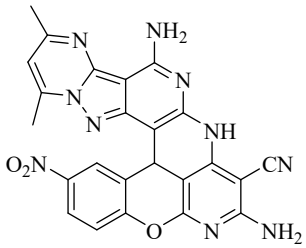
2,6-diamino-8,10-dimethyl-4,12c-dihydrochromeno[4,3,2-de]pyrimido [1'',2'':1',5']pyrazolo[3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-3-carbonitrile(4k). red powder, M.P.=90°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 2.65 (s, 6H, CH_3), 3.07 (s, 2H, NH_2), 5.26 (s, 1H, CH), 6.98-6.99 (m, 1H, CH aromatic), 7.07-7.10 (m, 1H, CH aromatic), 7.12-7.14 (m, 1H, CH aromatic), 7.22-7.24 (m, 1H, CH aromatic), 7.26-7.30 (m, 1H, CH aromatic), 7.86 (s, 2H, NH_2), 8.66 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 16.8, 23.3, 32.3, 74.1, 81.6, 98.8, 102.5, 109.5, 115.0, 117.7, 123.2, 125.3, 129.1, 129.2, 146.4, 147.1, 149.5, 149.9, 151.0, 155.0, 157.0, 159.2, 160.7, 161.4. HRMS m/z calcd for $C_{24}H_{17}N_9O$ $[M]^+$ 447.16, found 447.1. *Anal.* Calcd for $C_{24}H_{17}N_9O$: C, 64.42; H, 3.83; N, 28.17%. Found: C, 64.40; H, 3.81; N, 28.14%.



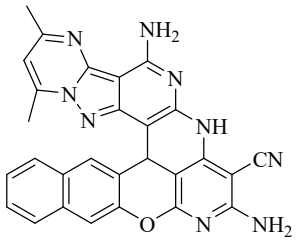
2,6-diamino-14-bromo-8,10-dimethyl-4,12c-dihydrochromeno[4,3,2-de]pyrimido [1'',2'':1',5']pyrazolo[3',4':4,5] pyrido[2,3-b][1,6]naphthyridine-3-carbonitrile(4l). red powder, M.P.=94°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 2.60 (s, 6H, CH_3), 3.18 (s, 2H, NH_2), 5.28 (s, 1H, CH), 6.98-6.99 (m, 1H, CH aromatic), 7.14 (d, J = 6.0 Hz, 1H, CH aromatic), 7.31 (s, 1H, CH aromatic), 7.46-7.48 (m, 1H, CH aromatic), 7.87 (s, 2H, NH_2), 8.67 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 16.3, 23.4, 31.6, 73.9, 82.0, 99.1, 102.4, 110.5, 115.3, 117.4, 123.7, 125.3, 129.0, 129.4, 145.4, 146.9, 149.7, 149.9, 151.1, 155.3, 156.7, 159.0, 160.9, 162.0. *Anal.* Calcd for $C_{24}H_{16}BrN_9O$: C, 54.77; H, 3.06; N, 23.95%. Found: C, 54.72; H, 3.01; N, 23.91%.



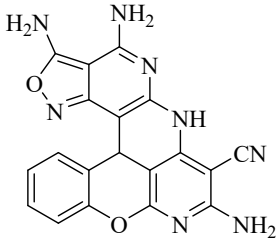
2,6-diamino-15-methoxy-8,10-dimethyl-4,12c-dihydrochromeno[4,3,2-de]pyrimido [1'',2'':1',5']pyrazolo[3',4':4,5] pyrido[2,3-b][1,6]naphthyridine-3-carbonitrile(4m). red powder, M.P.=97°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 2.75 (s, 6H, CH_3), 3.02 (s, 2H, NH_2), 3.82 (s, 3H, CH_3), 5.36 (s, 1H, CH), 6.57-6.59 (m, 1H, CH aromatic), 6.88 (d, J = 3.0 Hz, 1H, CH aromatic), 6.98-6.99 (m, 1H, CH aromatic), 7.06 (d, J = 6.0 Hz, 1H, CH aromatic), 7.77 (s, 2H, NH_2), 8.77 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 16.5, 23.0, 31.8, 55.6, 74.0, 81.7, 98.7, 102.4, 102.9, 108.3, 109.5, 115.1, 121.0, 129.4, 146.5, 147.0, 149.4, 149.7, 152.1, 155.3, 157.3, 159.2, 160.3, 160.4, 161.5. HRMS m/z calcd for $C_{25}H_{19}N_9O_2$ $[M]^+$ 477.17, found 477.1. *Anal.* Calcd for $C_{25}H_{19}N_9O_2$: C, 62.89; H, 4.01; N, 26.40%. Found: C, 62.85; H, 4.04; N, 26.43%.



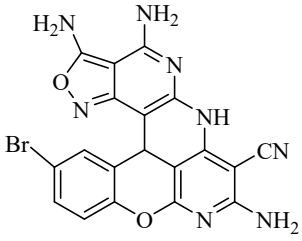
2,6-diamino-8,10-dimethyl-14-nitro-4,12c-dihydrochromeno[4,3,2-de]pyrimido [1'',2'':1',5']pyrazolo[3',4':4,5] pyrido[2,3-b][1,6]naphthyridine-3-carbonitrile(4n). red powder, M.P.=92°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 2.26 (s, 6H, CH_3), 3.52 (s, 2H, NH_2), 5.38 (s, 1H, CH), 7.15-7.18 (m, 1H, CH aromatic), 7.35-7.41 (m, 1H, CH aromatic), 7.65-7.72 (m, 2H, CH aromatic), 7.83 (s, 2H, NH_2), 8.66 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 15.9, 21.3, 31.4, 78.6, 82.2, 97.0, 101.4, 110.4, 115.4, 117.7, 121.6, 126.0, 127.1, 137.6, 138.2, 138.3, 148.1, 148.6, 153.9, 155.0, 157.4, 159.2, 160.1, 161.0. *Anal.* Calcd for $C_{24}H_{16}N_{10}O_3$: C, 58.54; H, 3.27; N, 28.44%. Found: C, 58.51; H, 3.29; N, 28.42%.



1,5-diamino-16,18-dimethyl-3,13b-dihydrobenzo[6,7]chromeno[4,3,2-de]pyrimido [1'',2'':1',5']pyrazolo[3',4':4,5] pyrido[2,3-b][1,6]naphthyridine-4-carbonitrile(4o). red powder, M.P.=98°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 2.59 (s, 6H, CH_3), 3.34 (s, 2H, NH_2), 5.16 (s, 1H, CH), 7.15-7.19 (m, 2H, CH aromatic), 7.37-7.46 (m, 4H, CH aromatic), 7.71 (s, 2H, NH_2), 7.81-7.84 (m, 1H, CH aromatic), 8.67 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 16.2, 24.5, 32.2, 76.4, 84.0, 99.0, 102.4, 109.5, 112.3, 115.6, 125.9, 127.3, 128.6, 129.8, 130.5, 131.0, 133.1, 133.5, 144.5, 145.0, 149.2, 149.3, 149.4, 151.3, 155.8, 159.1, 160.6, 161.3. HRMS m/z calcd for $C_{28}H_{19}N_9O$ $[M]^+$ 497.17, found 497.1. *Anal.* Calcd for $C_{28}H_{19}N_9O$: C, 67.60; H, 3.85; N, 25.34%. Found: C, 67.62; H, 3.81; N, 25.30%.

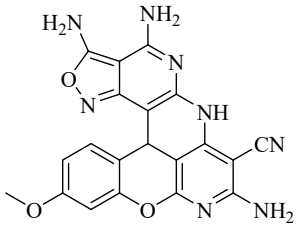


3,4,8-triamino-6,14b-dihydrochromeno[4,3,2-de]isoxazolo[3',4':4,5]pyrido[2,3-b][1,6] naphthyridine-7-carbonitrile (4p). red powder, M.P.=93°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.09 (s, 2H, NH_2), 5.26 (s, 1H, CH), 6.53 (s, 2H, NH_2), 7.15-7.19 (m, 1H, CH aromatic), 7.32-7.46 (m, 2H, CH aromatic), 7.67 (s, 2H, NH_2), 7.73-7.81 (m, 1H, CH aromatic), 8.50 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 31.2, 75.1, 84.0, 98.0, 102.1, 127.2, 128.5, 128.8, 128.9, 129.8, 130.8, 149.6, 151.6, 152.9, 157.4, 158.3, 159.2, 161.0, 165.5. *Anal.* Calcd for $C_{28}H_{19}N_9O$: C, 67.60; H, 3.85; N, 25.34%. Found: C, 67.62; H, 3.81; N, 25.30%.

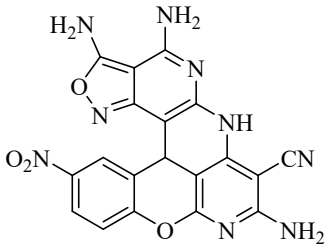


3,4,8-triamino-13-bromo-6,14b-dihydrochromeno[4,3,2-de]isoxazolo[3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-7-carbonitrile (4q). red powder, M.P.=95°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.62 (s, 2H, NH_2), 5.67 (s, 1H, CH), 6.15 (s, 2H, NH_2), 7.06 (d, J = 6.0 Hz, 1H, CH aromatic), 7.14-7.19 (m, 1H, CH aromatic), 7.55 (s, 2H, NH_2), 7.72 (d, J = 6.0 Hz, 1H, CH aromatic), 8.58 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 30.1, 72.6, 82.8, 98.3, 102.9, 125.8, 128.7, 129.0, 130.5, 131.8, 135.3, 149.7, 150.3, 151.2, 156.6, 157.7, 159.0, 160.3,

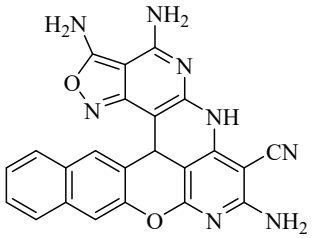
164.9. *Anal.* Calcd for $C_{19}H_{11}BrN_8O_2$: C, 49.26; H, 2.39; N, 24.19%. Found: C, 49.22; H, 2.35; N, 24.11%.



3,4,8-triamino-12-methoxy-6,14b-dihydrochromeno[4,3,2-de]isoxazolo[3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-7-carbonitrile(4r). red powder, M.P.=96°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 2.25 (s, 3H, CH_3), 3.18 (s, 2H, NH_2), 5.46 (s, 1H, CH), 6.07 (s, 2H, NH_2), 7.05-7.08 (m, 1H, CH aromatic), 7.42-7.47 (m, 1H, CH aromatic), 7.61 (s, 2H, NH_2), 7.83-7.88 (m, 1H, CH aromatic), 8.87 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 31.1, 54.5, 76.9, 87.8, 99.3, 102.0, 104.5, 109.3, 114.8, 126.0, 130.5, 148.4, 150.7, 151.4, 155.0, 157.9, 158.9, 160.0, 160.3, 164.6. *Anal.* Calcd for $C_{20}H_{14}N_8O_3$: C, 57.97; H, 3.41; N, 27.04%. Found: C, 57.93; H, 3.45; N, 27.01%.

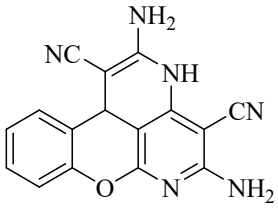


3,4,8-triamino-13-nitro-6,14b-dihydrochromeno[4,3,2-de]isoxazolo[3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-7-carbonitrile (4s). red powder, M.P.=95°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.47 (s, 2H, NH_2), 5.24 (s, 1H, CH), 6.53 (s, 2H, NH_2), 7.31-7.36 (m, 2H, CH aromatic), 7.59 (s, 2H, NH_2), 7.71-7.74 (m, 1H, CH aromatic), 8.50 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 31.0, 74.1, 86.7, 99.4, 102.4, 115.0, 118.3, 123.4, 124.2, 124.5, 142.1, 149.9, 151.8, 155.4, 156.7, 158.1, 159.2, 160.7, 165.2. *Anal.* Calcd for $C_{19}H_{11}N_9O_4$: C, 53.15; H, 2.58; N, 29.36%. Found: C, 53.17; H, 2.54; N, 29.37%.

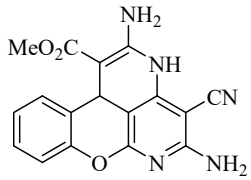


1,5,16-triamino-3,13b-dihydrobenzo[6,7]chromeno[4,3,2-de]isoxazolo[3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-4-carbonitrile (4t). red powder, M.P.=94°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.08 (s, 2H, NH_2), 5.27 (s, 1H, CH), 6.49 (s, 2H, NH_2), 7.43-7.49 (m, 2H, CH aromatic), 7.60 (d, J = 3.0 Hz, 1H, CH aromatic), 7.67-7.69 (m, 1H, CH aromatic), 7.72 (s, 2H, NH_2), 7.81-7.83 (m, 2H, CH aromatic), 8.51 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm)

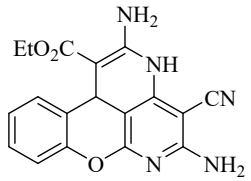
32.0, 72.7, 87.5, 98.5, 102.8, 113.1, 117.3, 123.0, 125.4, 126.6, 128.5, 129.1, 130.3, 131.1, 132.3, 147.2, 148.3, 152.6, 154.5, 157.9, 159.6, 160.6, 167.4. *Anal.* Calcd for $C_{23}H_{14}N_8O_2$: C, 63.59; H, 3.25; N, 25.79%. Found: C, 63.53; H, 3.28; N, 25.72%.



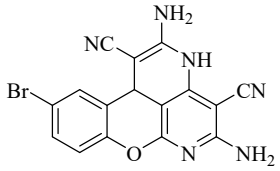
2,5-diamino-3,11b-dihydrochromeno[4,3,2-de][1,6]naphthyridine-1,4-dicarbonitrile (4u). orange powder, M.P.=90°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.06 (s, 2H, NH_2), 4.88 (s, 1H, CH), 5.89 (s, 2H, NH_2), 7.07-7.12 (m, 2H, CH aromatic), 7.21-7.23 (m, 1H, CH aromatic), 7.28-7.32 (m, 1H, CH aromatic), 8.43 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 32.6, 57.5, 76.1, 98.5, 115.0, 117.3, 120.6, 123.4, 123.9, 129.1, 129.2, 150.6, 152.1, 153.2, 160.5, 160.9. *Anal.* Calcd for $C_{16}H_{10}N_6O$: C, 63.57; H, 3.33; N, 25.80%. Found: C, 63.51; H, 3.27; N, 25.81%.



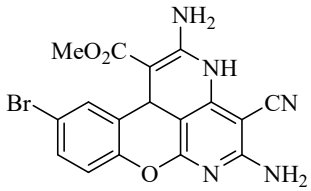
methyl 2,5-diamino-4-cyano-3,11b-dihydrochromeno[4,3,2-de][1,6]naphthyridine-1-carboxylate (4v). orange powder, M.P.=93°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.05 (s, 2H, NH_2), 3.63 (s, 3H, OCH_3), 5.82 (s, 1H, CH), 6.78 (s, 2H, NH_2), 7.24-7.36 (m, 2H, CH aromatic), 7.42-7.48 (m, 2H, CH aromatic), 7.98 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 21.1, 51.1, 78.0, 78.4, 95.0, 115.4, 118.6, 122.5, 124.7, 129.5, 130.2, 149.9, 152.1, 155.4, 160.5, 161.2, 162.2. *Anal.* Calcd for $C_{17}H_{13}N_5O_3$: C, 60.89; H, 3.91; N, 20.89%. Found: C, 60.85; H, 3.97; N, 20.82%.



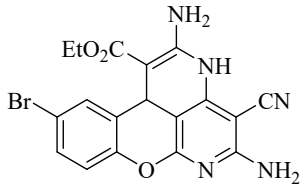
ethyl 2,5-diamino-4-cyano-3,11b-dihydrochromeno[4,3,2-de][1,6]naphthyridine-1-carboxylate (4w). orange powder, M.P.=88°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 1.19 (t, J = 3 Hz, 3H, CH_3), 3.08 (s, 2H, NH_2), 4.07 (q, J = 12, 6 Hz, 2H, CH_2), 4.98 (s, 1H, CH), 6.66 (s, 2H, NH_2), 6.76-6.87 (m, 2H, CH aromatic), 7.02-7.06 (m, 1H, CH aromatic), 7.45-7.50 (m, 1H, CH aromatic), 8.17 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 15.1, 26.8, 60.0, 77.6, 78.7, 96.7, 114.6, 116.0, 120.4, 126.3, 128.2, 135.0, 148.2, 148.6, 155.2, 158.2, 160.3, 161.5. *Anal.* Calcd for $C_{18}H_{15}N_5O_3$: C, 61.89; H, 4.33; N, 20.05%. Found: C, 61.88; H, 4.30; N, 20.09%.



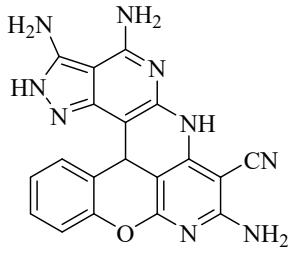
2,5-diamino-10-bromo-3,11b-dihydrochromeno[4,3,2-de][1,6]naphthyridine-1,4-dicarbonitrile (4x). orange powder, M.P.=92°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.06 (s, 2H, NH_2), 4.89 (s, 1H, CH), 5.89 (s, 2H, NH_2), 7.14 (d, J = 3 Hz, 1H, CH aromatic), 7.50-7.56 (m, 2H, CH aromatic), 8.43 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 33.0, 57.4, 76.1, 98.6, 115.0, 118.0, 118.1, 120.6, 122.0, 132.1, 132.8, 150.6, 150.7, 153.2, 160.5, 160.7. *Anal.* Calcd for $C_{16}H_9BrN_6O$: C, 50.41; H, 2.38; N, 22.05%. Found: C, 50.44; H, 2.32; N, 22.08%.



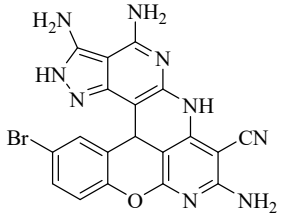
methyl 2,5-diamino-10-bromo-4-cyano-3,11b-dihydrochromeno[4,3,2-de][1,6] naphthyridine-1-carboxylate(4y). orange powder, M.P.=90°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.06 (s, 2H, NH_2), 3.61 (s, 3H, OCH_3), 5.02 (s, 1H, CH), 6.75 (s, 2H, NH_2), 7.32-7.51 (m, 2H, CH aromatic), 7.67-7.73 (m, 1H, CH aromatic), 7.99 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 28.4, 50.7, 76.2, 77.6, 98.2, 113.1, 117.3, 119.3, 123.0, 131.1, 132.3, 151.8, 152.6, 154.5, 159.6, 160.1, 163.9. *Anal.* Calcd for $C_{17}H_{12}BrN_5O_3$: C, 49.29; H, 2.92; N, 16.91%. Found: C, 49.27; H, 2.94; N, 16.95%.



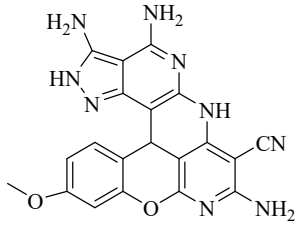
ethyl 2,5-diamino-10-bromo-4-cyano-3,11b-dihydrochromeno[4,3,2-de][1,6]naphthyridine-1-carboxylate(4z). orange powder, M.P.=89°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 0.87 (t, J = 3 Hz, 3H, CH_3), 3.11 (s, 2H, NH_2), 4.09 (q, J = 12, 6 Hz, 2H, CH_2), 5.09 (s, 1H, CH), 6.75 (s, 2H, NH_2), 7.13-7.24 (m, 2H, CH aromatic), 7.33-7.39 (m, 1H, CH aromatic), 8.11 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 14.2, 22.4, 60.0, 76.9, 79.1, 97.8, 102.0, 116.0, 117.1, 119.8, 125.6, 129.7, 132.0, 148.6, 150.1, 155.7, 160.0, 161.5, 166.7. *Anal.* Calcd for $C_{18}H_{14}BrN_5O_3$: C, 50.48; H, 3.30; N, 16.35%. Found: C, 50.49; H, 3.34; N, 16.37%.



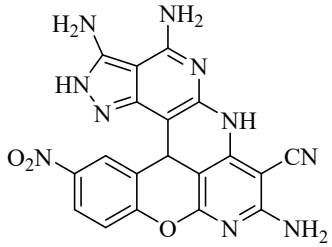
3,4,8-triamino-6,14b-dihydro-2H-chromeno[4,3,2-de]pyrazolo[3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-7-carbonitrile (4aa). red powder, M.P.=97°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.12 (s, 2H, NH_2), 5.28 (s, 1H, CH), 6.23 (s, 2H, NH_2), 7.07-7.14 (m, 2H, CH aromatic), 7.19 (s, 2H, NH_2), 7.22-7.30 (m, 2H, CH aromatic), 8.77 (s, 1H, NH), 9.04 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 36.5, 74.1, 79.3, 98.6, 100.2, 115.0, 117.7, 123.2, 125.3, 129.1, 129.2, 144.3, 149.4, 149.9, 151.0, 154.3, 155.4, 159.2, 160.7. *Anal.* Calcd for $C_{19}H_{13}N_9O$: C, 59.53; H, 3.42; N, 32.88%. Found: C, 59.50; H, 3.44; N, 32.83%.



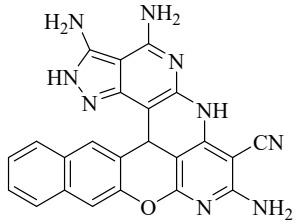
3,4,8-triamino-13-bromo-6,14b-dihydro-2H-chromeno[4,3,2-de]pyrazolo [3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-7-carbonitrile (4ab). red powder, M.P.=95°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.18 (s, 2H, NH_2), 5.26 (s, 1H, CH), 6.21 (s, 2H, NH_2), 7.14 (d, J = 6 Hz, 1H, CH aromatic), 7.25 (s, 2H, NH_2), 7.31 (t, J = 3 Hz, 3H, CH_3), 7.47 (d, J = 6 Hz, 1H, CH aromatic), 8.78 (s, 1H, NH), 9.00 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 31.8, 74.1, 79.3, 98.9, 100.3, 115.0, 117.2, 118.6, 124.0, 131.9, 132.8, 144.3, 149.4, 149.9, 150.4, 154.3, 155.4, 159.2, 160.7. *Anal.* Calcd for $C_{19}H_{12}BrN_9O$: C, 49.37; H, 2.62; N, 27.27%. Found: C, 49.30; H, 2.63; N, 27.21%.



3,4,8-triamino-12-methoxy-6,14b-dihydro-2H-chromeno[4,3,2-de]pyrazolo [3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-7-carbonitrile (4ac). red powder, M.P.=94°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.09 (s, 2H, NH_2), 3.82 (s, 3H, CH_3), 5.25 (s, 1H, CH), 6.21 (s, 2H, NH_2), 6.58 (d, J = 6 Hz, 1H, CH aromatic), 6.88 (s, 1H, CH aromatic), 7.06 (d, J = 6 Hz, 1H, CH aromatic), 7.19 (s, 2H, NH_2), 8.77 (s, 1H, NH), 8.95 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 31.3, 55.7, 74.8, 79.1, 97.8, 101.8, 103.8, 110.2, 114.4, 120.4, 129.2, 145.5, 149.6, 149.9, 151.6, 152.7, 155.3, 159.3, 160.2, 161.8. *Anal.* Calcd for $C_{20}H_{15}N_9O_2$: C, 58.11; H, 3.66; N, 30.49%. Found: C, 58.14; H, 3.63; N, 30.47%.



3,4,8-triamino-13-nitro-6,14b-dihydro-2H-chromeno[4,3,2-de]pyrazolo[3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-7-carbonitrile (4ad). red powder, M.P.=95°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.11 (s, 2H, NH_2), 5.29 (s, 1H, CH), 6.31 (s, 2H, NH_2), 7.13-7.24 (m, 2H, CH aromatic), 7.33-7.39 (m, 2H, CH aromatic), 7.45 (s, 2H, NH_2), 8.76 (s, 1H, NH), 8.88 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 31.1, 75.1, 80.5, 98.8, 102.0, 115.4, 120.7, 125.6, 126.0, 129.7, 139.1, 145.5, 148.6, 149.7, 154.7, 155.7, 156.4, 160.0, 161.5. *Anal.* Calcd for $C_{19}H_{12}N_{10}O_3$: C, 53.27; H, 2.82; N, 32.70%. Found: C, 53.24; H, 2.80; N, 32.74%.



1,5,16-triamino-13b,15-dihydro-3H-benzo[6,7]chromeno[4,3,2-de]pyrazolo [3',4':4,5]pyrido[2,3-b][1,6]naphthyridine-4-carbonitrile (4ae). red powder, M.P.=93°C. ^{1}H-NMR (300 MHZ, DMSO-d_6): δ (ppm) 3.15 (s, 2H, NH_2), 5.30 (s, 1H, CH), 6.30 (s, 2H, NH_2), 7.19 (s, 2H, NH_2), 7.43-7.49 (m, 2H, CH aromatic), 7.61 (s, 1H, CH aromatic), 7.67-7.69 (m, 1H, CH aromatic), 7.81-7.83 (m, 2H, CH aromatic), 8.77 (s, 1H, NH), 8.92 (s, 1H, NH). ^{13}C-NMR (75 MHZ, DMSO-d_6): δ (ppm) 31.3, 74.1, 78.4, 97.8, 101.8, 111.9, 114.0, 123.3, 124.3, 126.1, 127.3, 128.2, 129.2, 131.6, 133.8, 145.1, 149.1, 149.7, 149.9, 155.7, 156.4, 158.9, 161.8. *Anal.* Calcd for $C_{23}H_{15}N_9O$: C, 63.74; H, 3.49; N, 29.08%. Found: C, 63.71; H, 3.47; N, 29.6%.

^{1}H NMR and ^{13}C NMR spectrum of the synthesized compounds

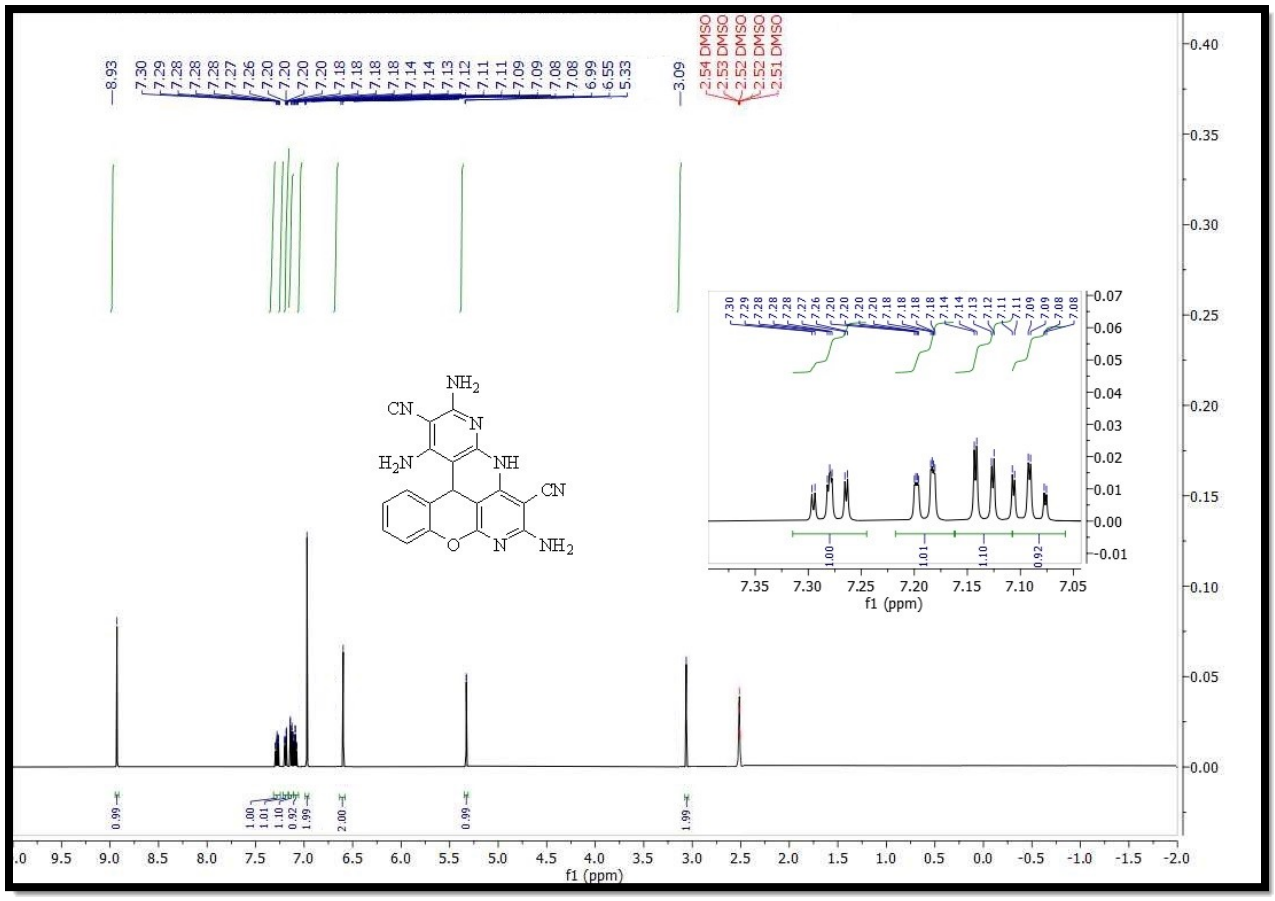


Figure 1: ^{1}H-NMR spectrum of compound **4a**

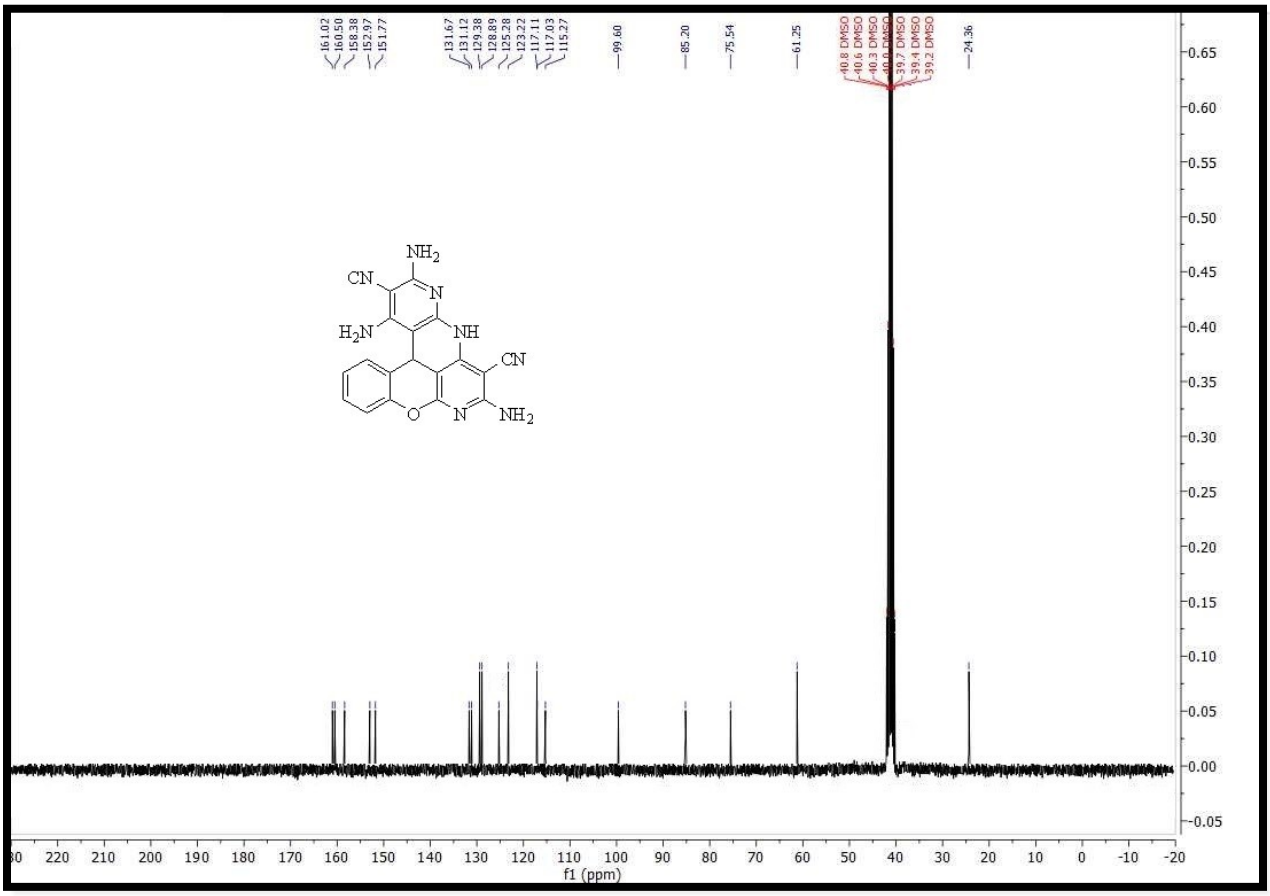


Figure 2: ^{13}C-NMR spectrum of compound **4a**

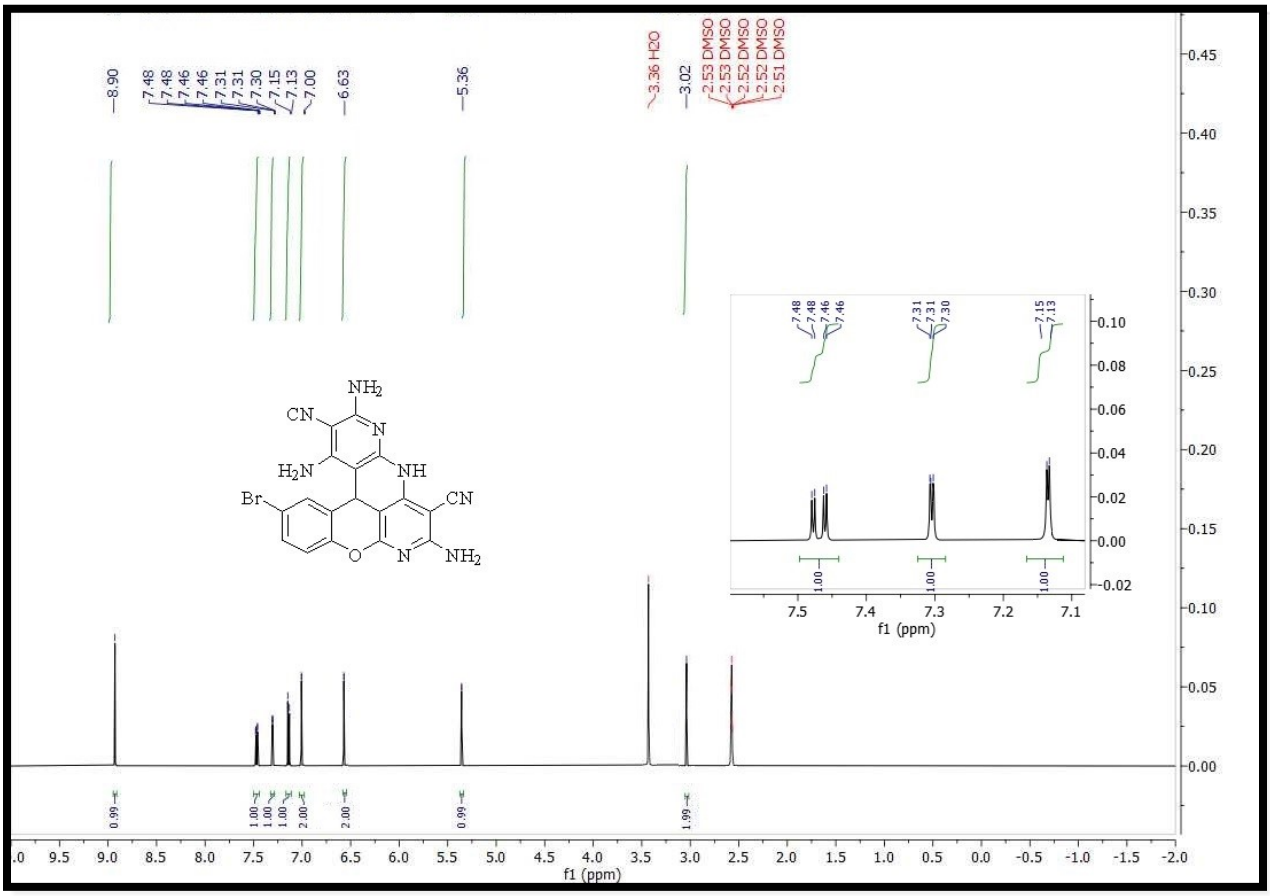


Figure 3: ^{1}H-NMR spectrum of compound **4b**

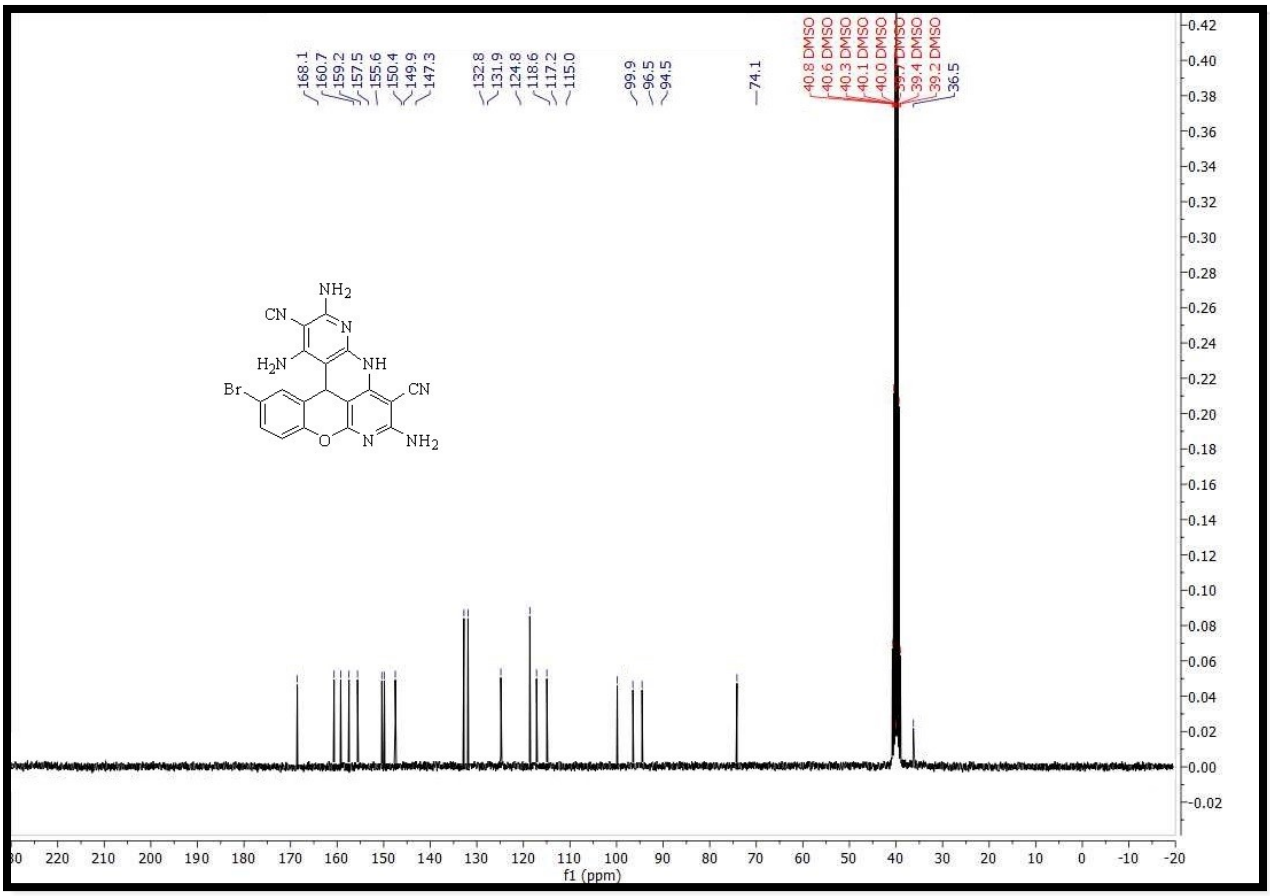


Figure 4: ^{13}C-NMR spectrum of compound **4b**

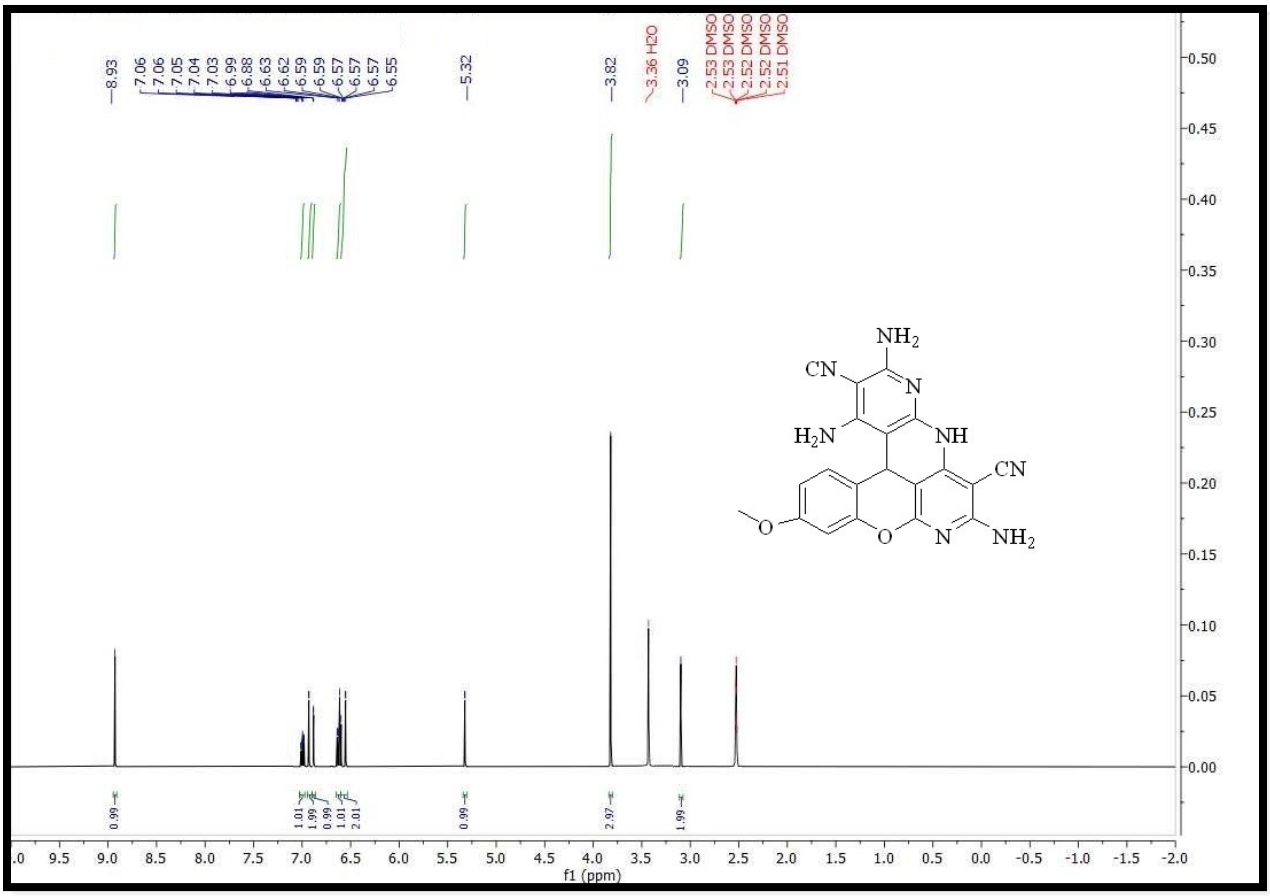


Figure 5: ^{1}H-NMR spectrum of compound **4c**

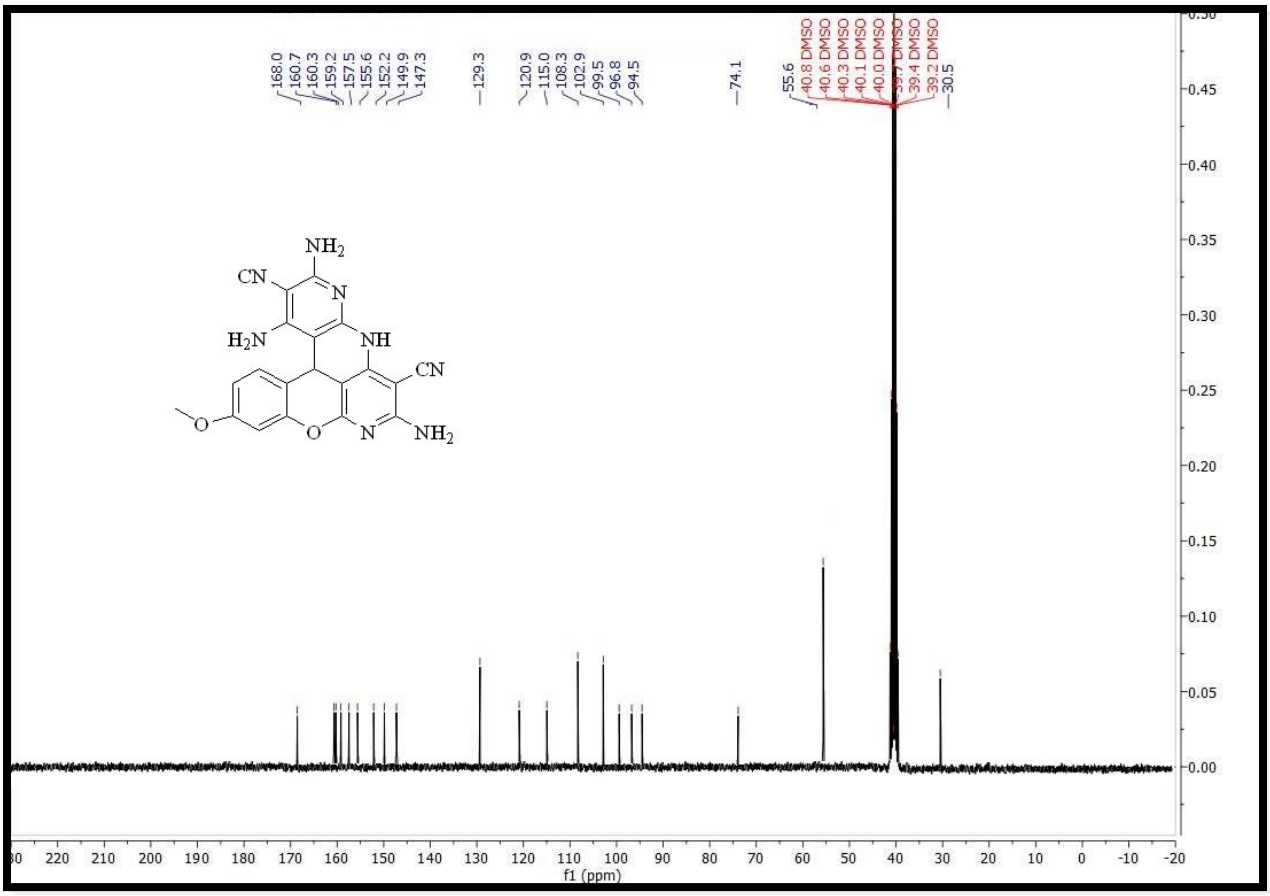


Figure 6: ^{13}C-NMR spectrum of compound **4c**

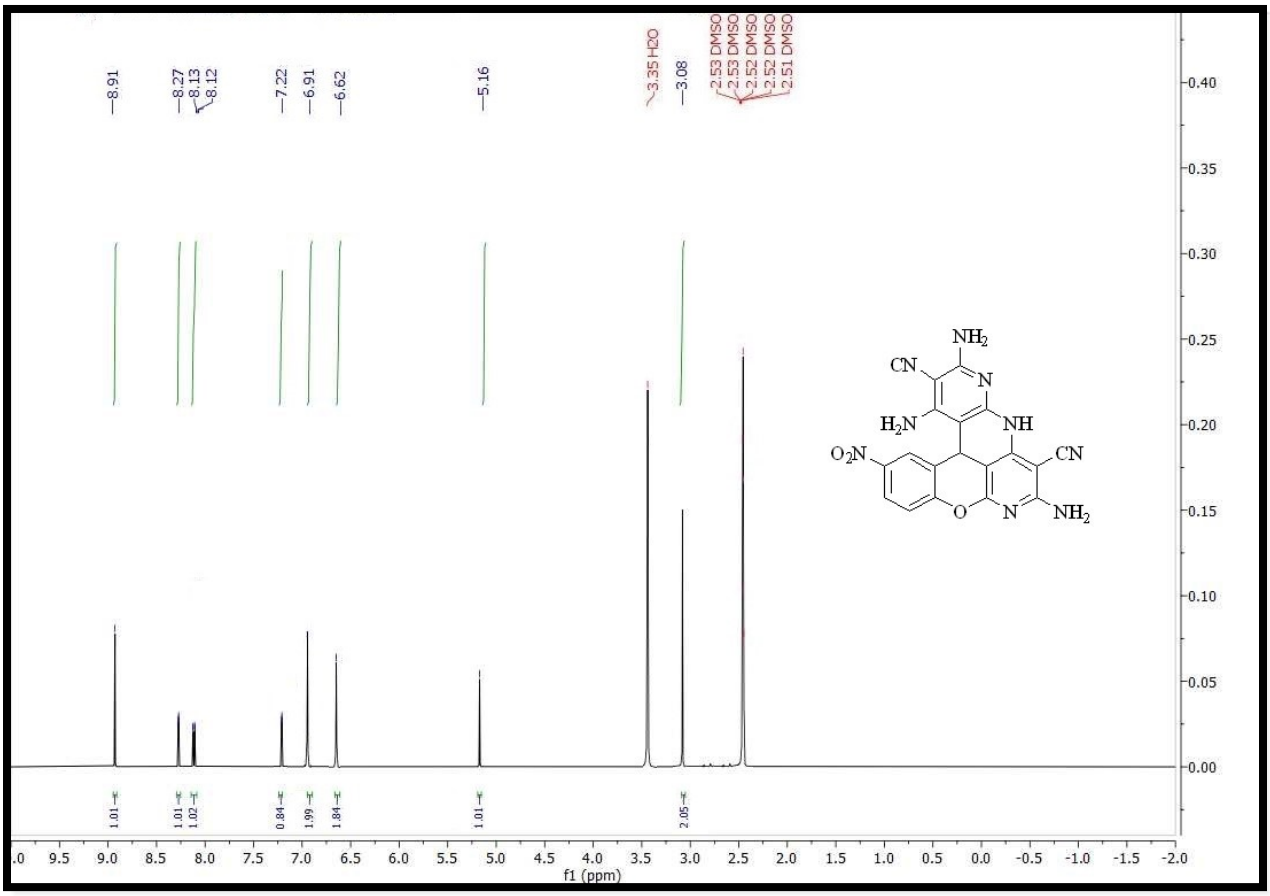


Figure 7: ^{1}H-NMR spectrum of compound **4d**

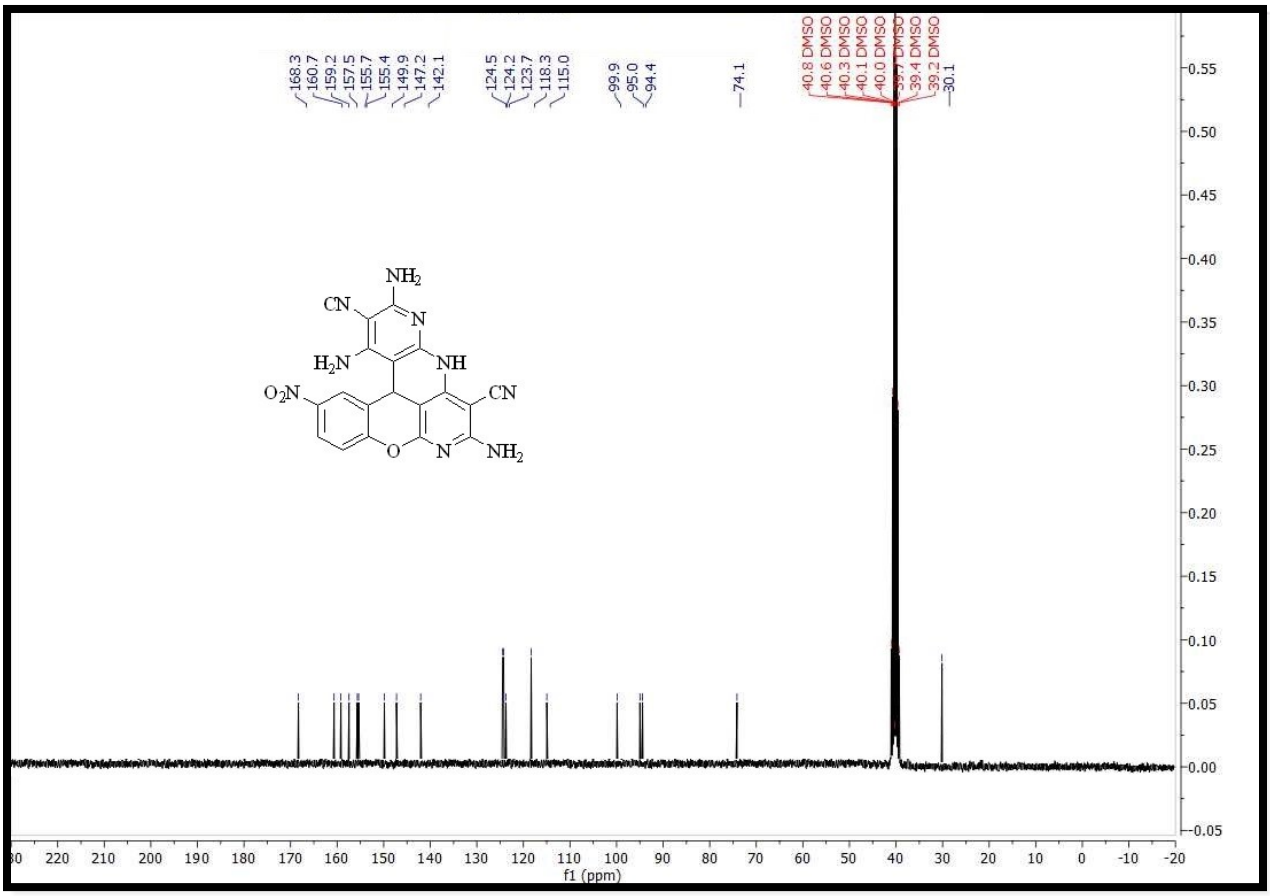


Figure 8: ^{13}C-NMR spectrum of compound **4d**

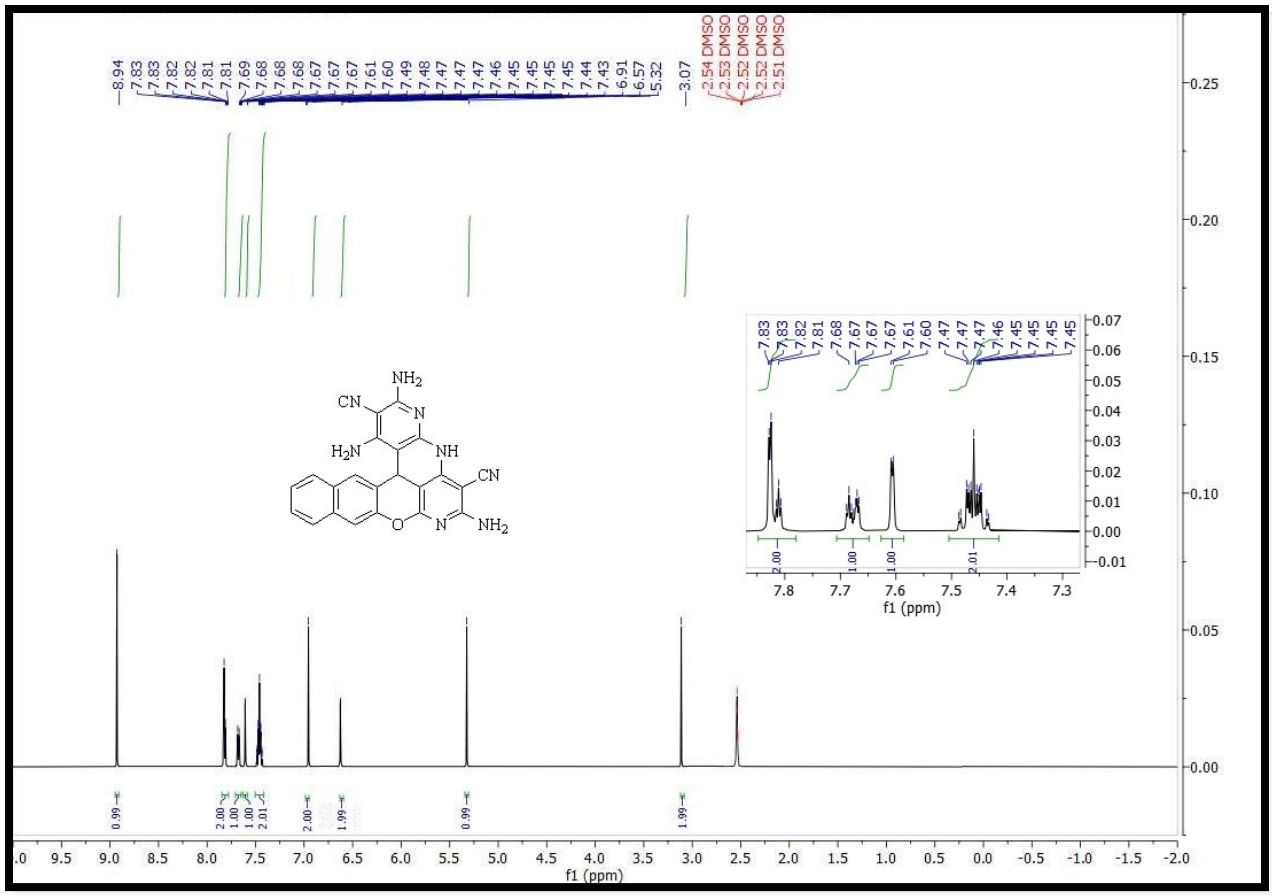


Figure 9: ^{1}H-NMR spectrum of compound **4e**

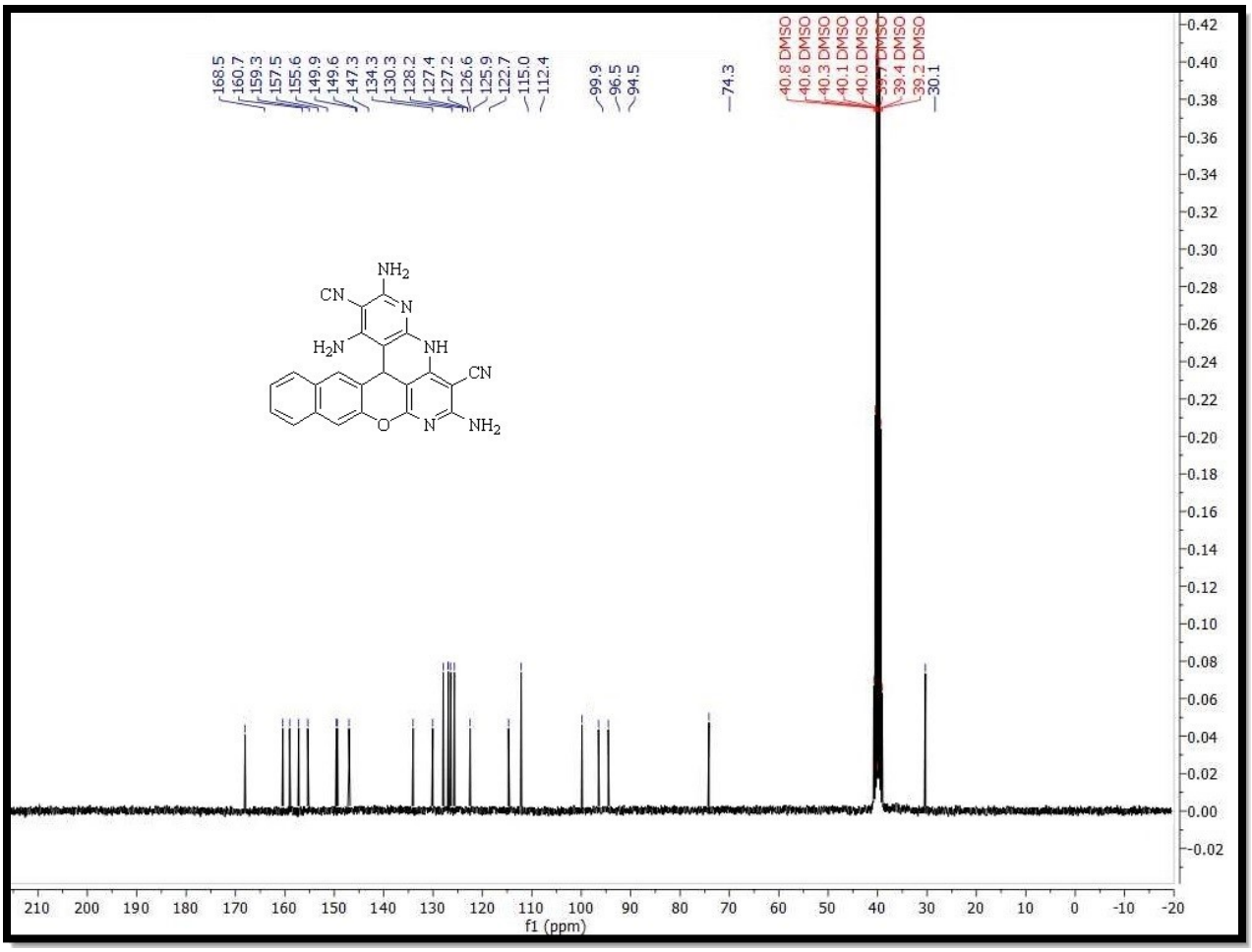


Figure 10: ^{13}C-NMR spectrum of compound **4e**

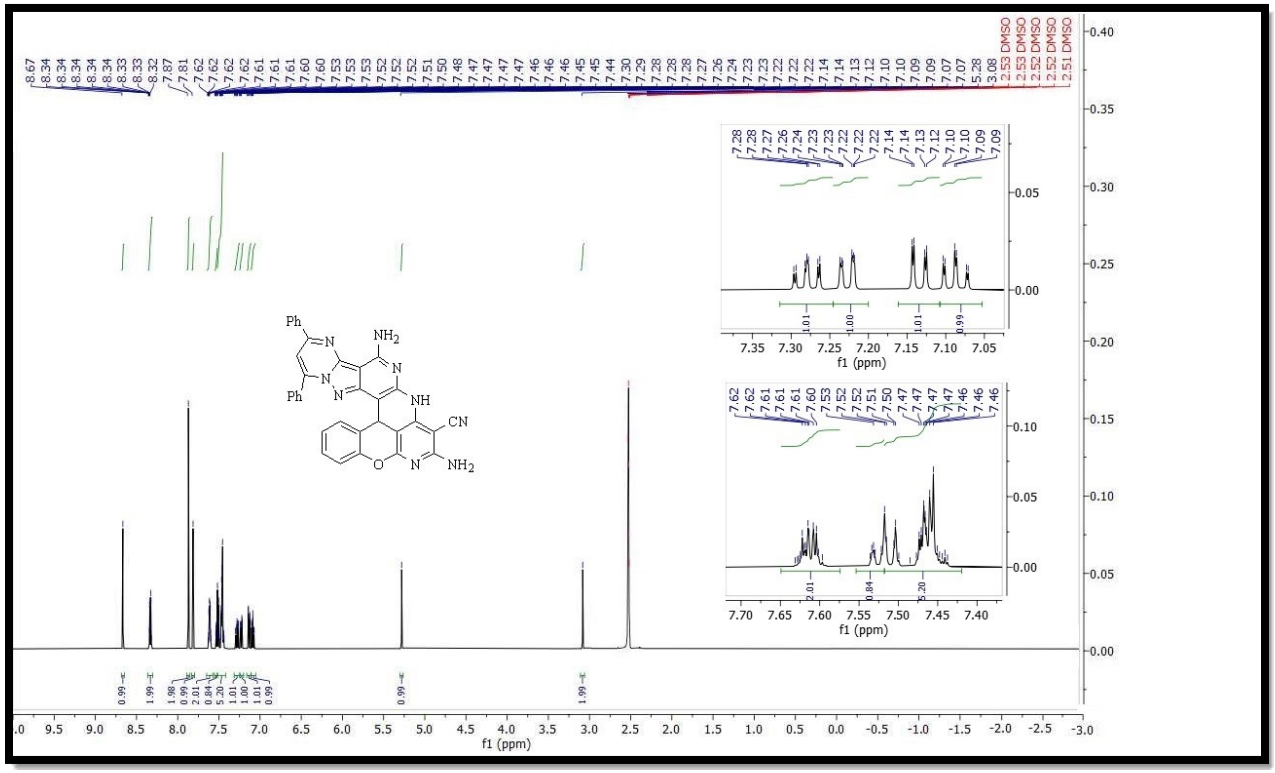


Figure 11: [1]H-NMR spectrum of compound **4f**

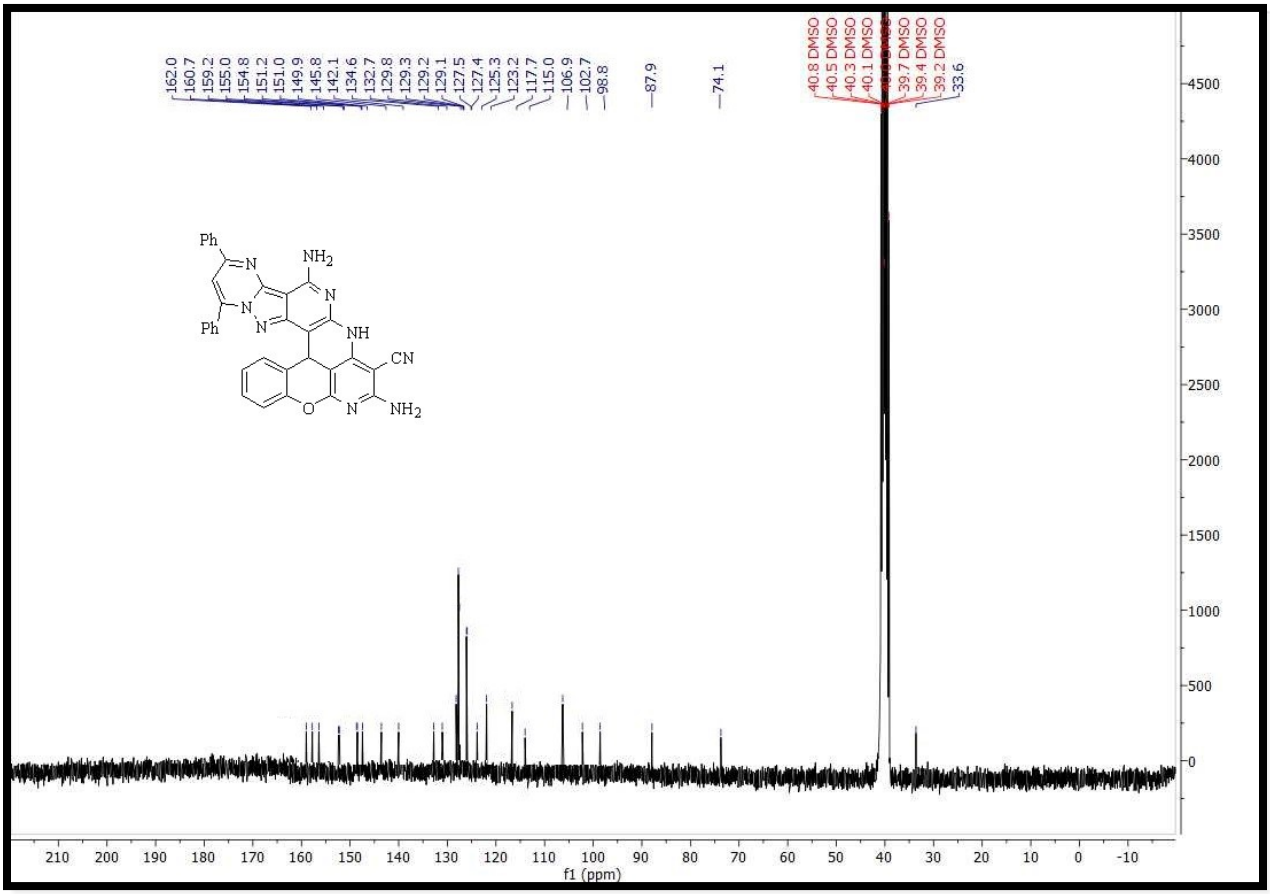


Figure 12: ^{13}C-NMR spectrum of compound **4f**

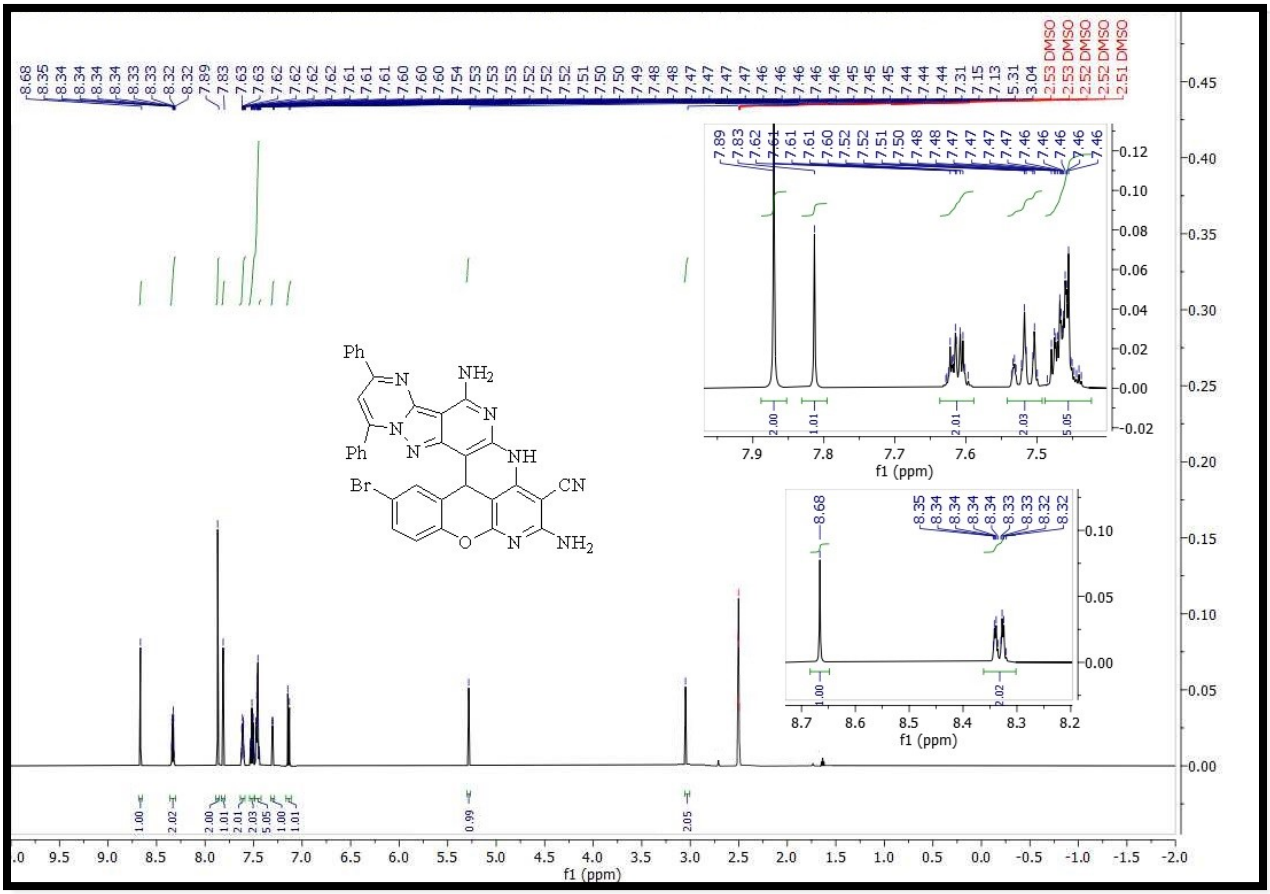


Figure 13: [1]H-NMR spectrum of compound **4g**

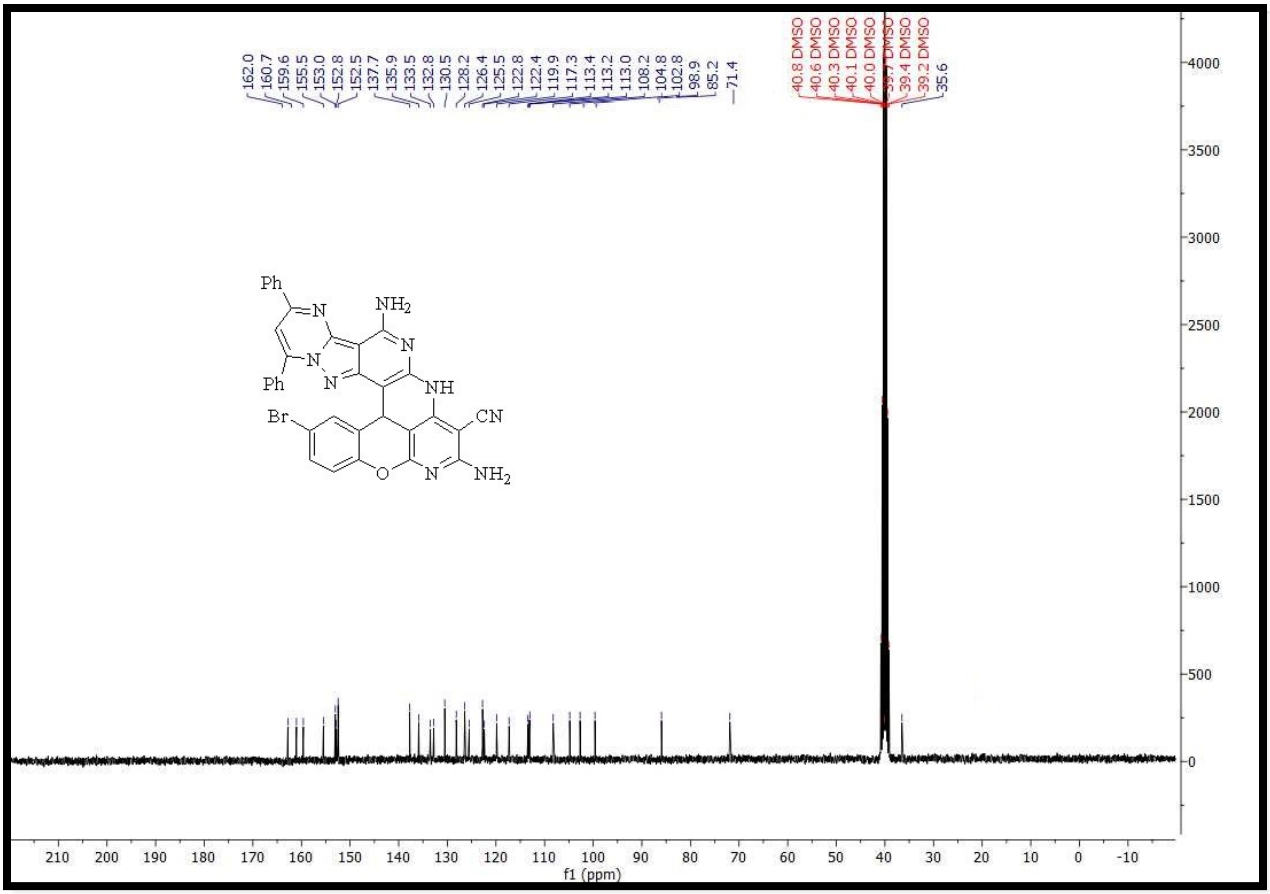


Figure 14: ^{13}C-NMR spectrum of compound **4g**

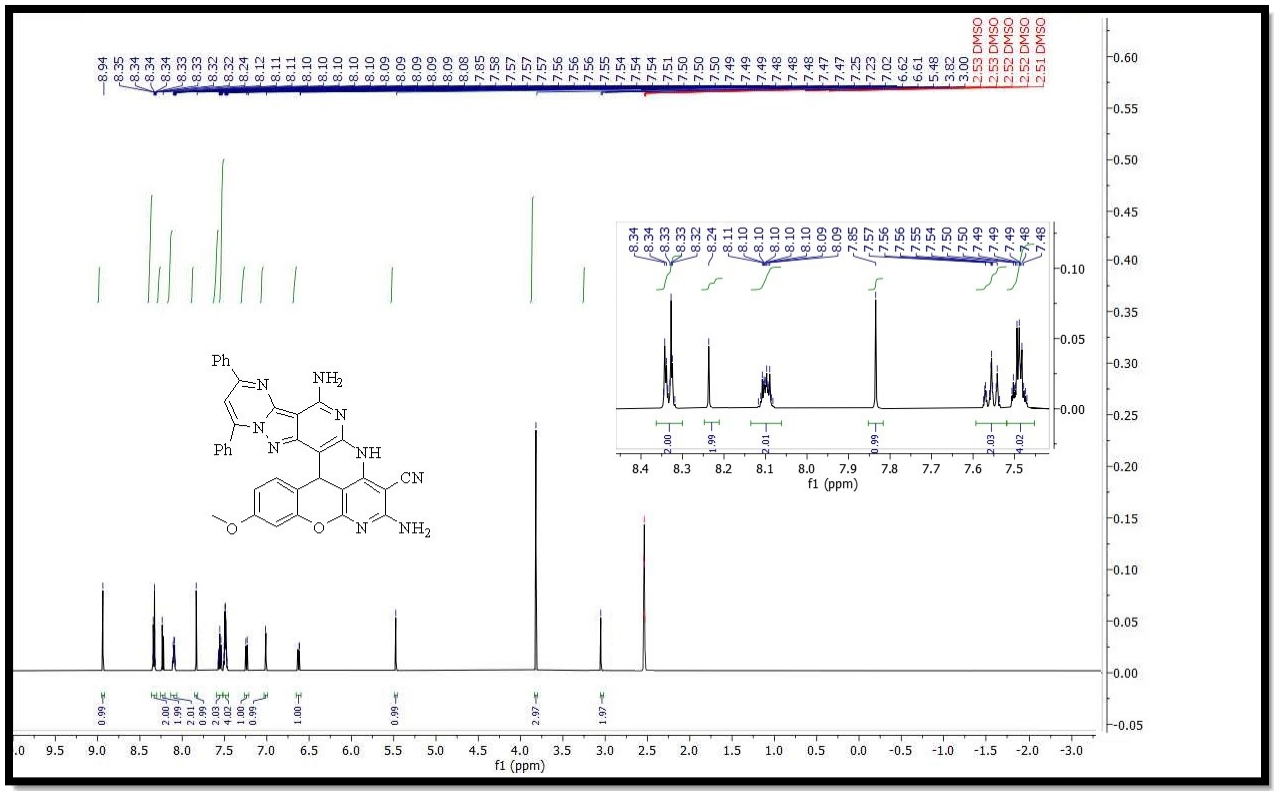


Figure 15: [1]H-NMR spectrum of compound **4h**

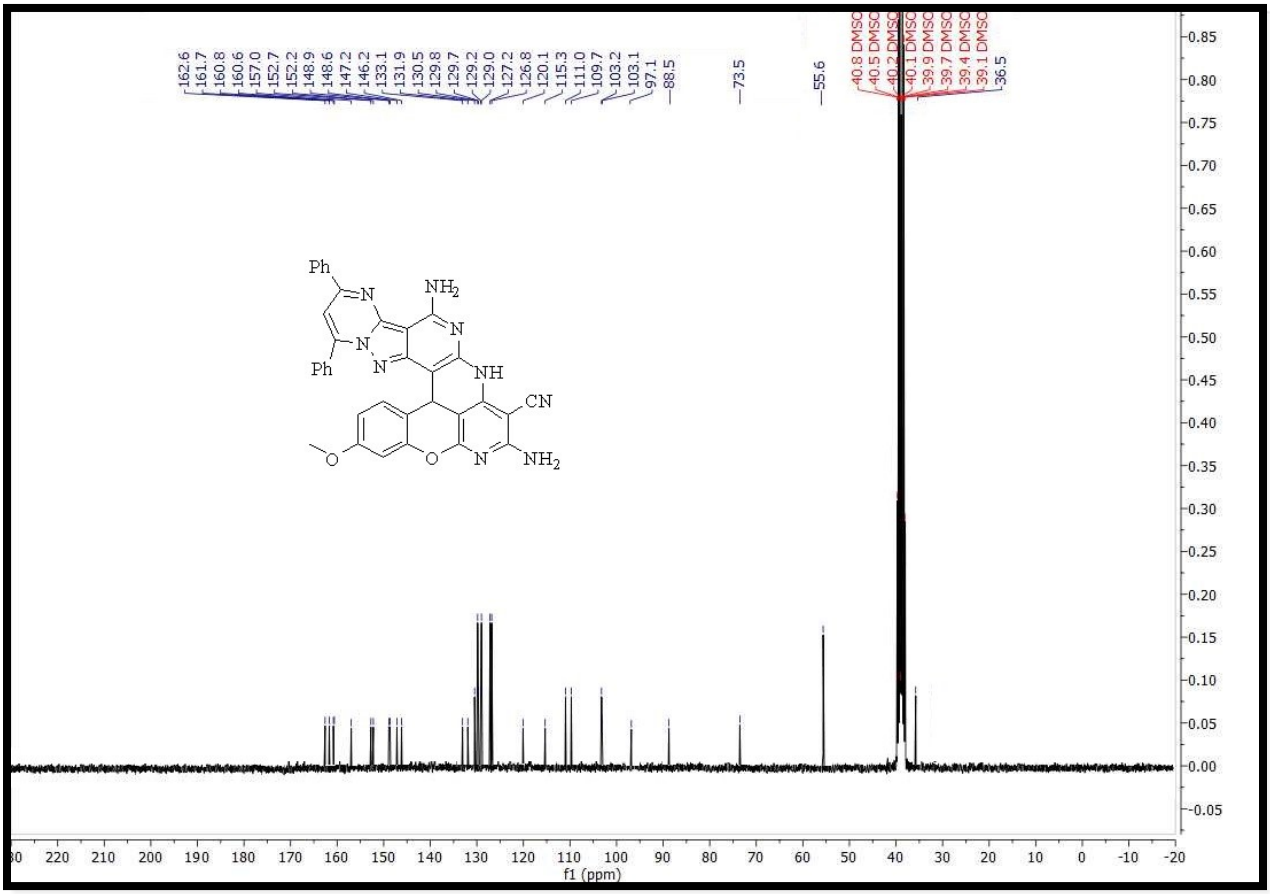


Figure 16: ^{13}C-NMR spectrum of compound **4h**

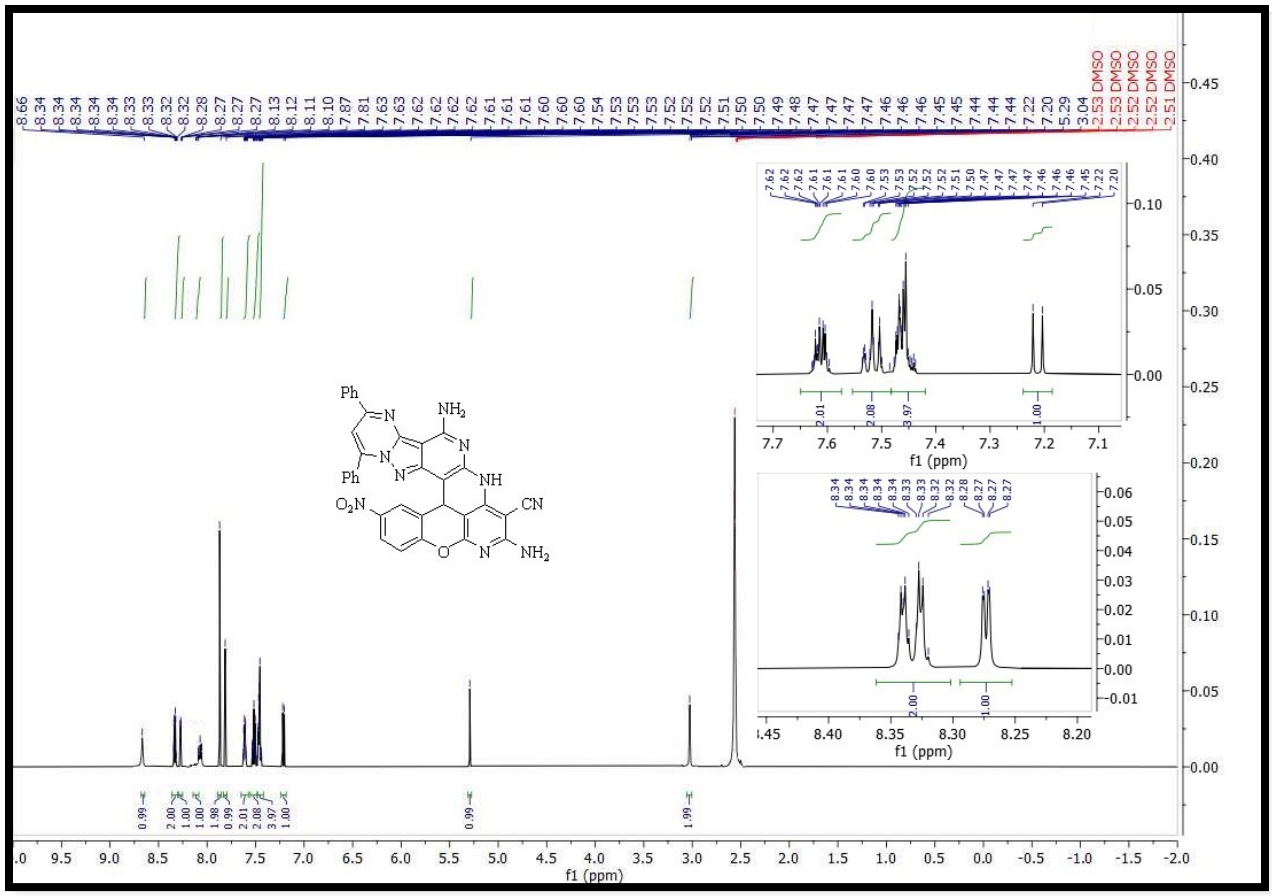


Figure 17: [1]H-NMR spectrum of compound **4i**

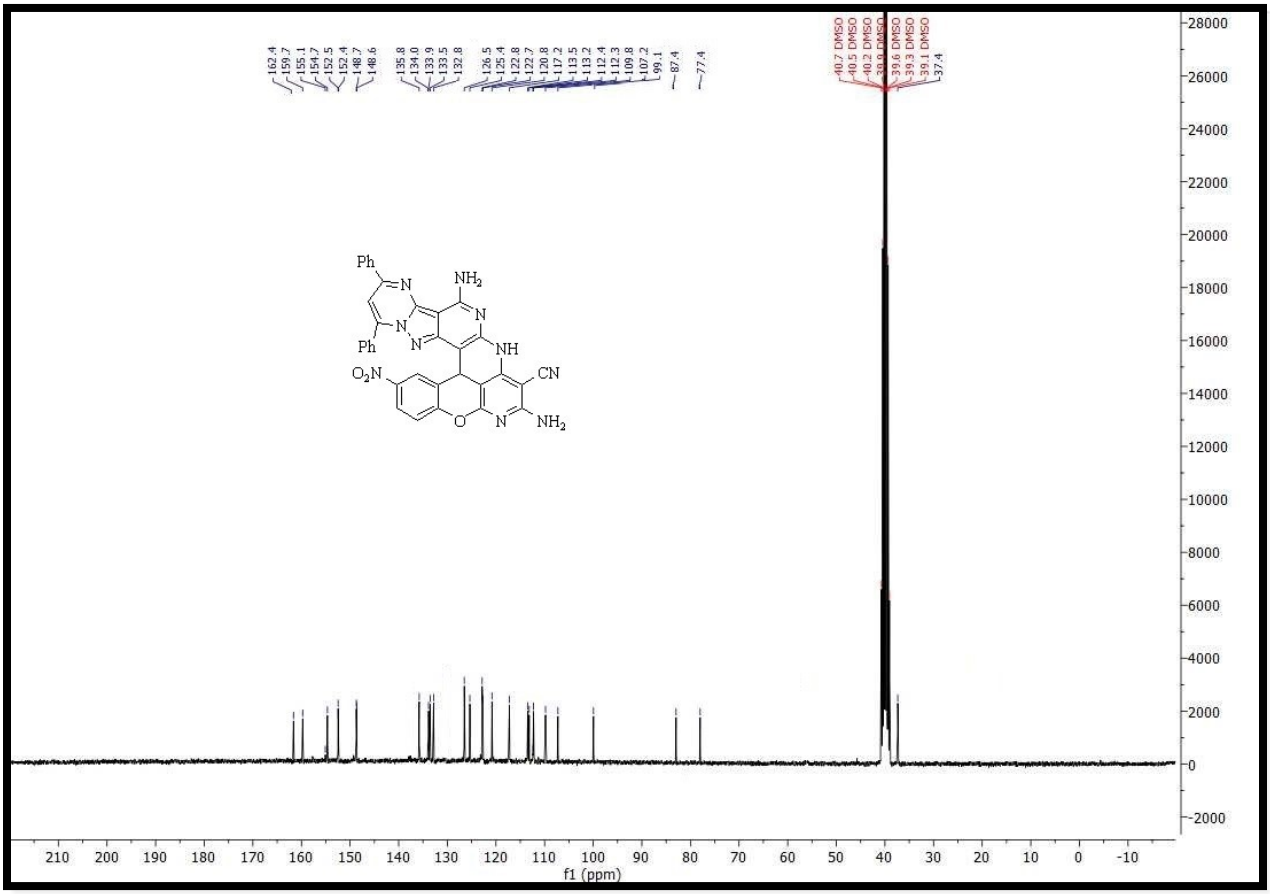


Figure 18: ^{13}C-NMR spectrum of compound **4i**

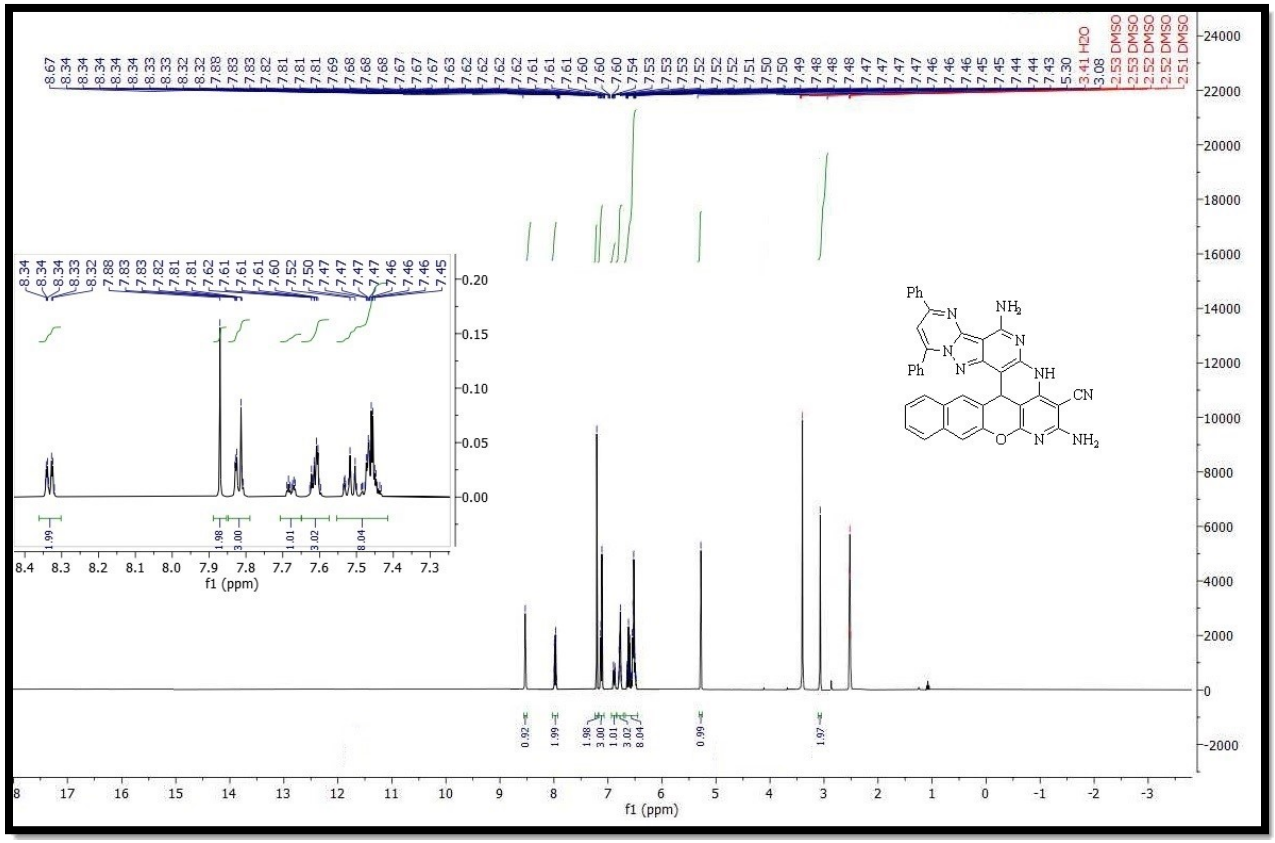


Figure 19: ^{1}H-NMR spectrum of compound **4j**

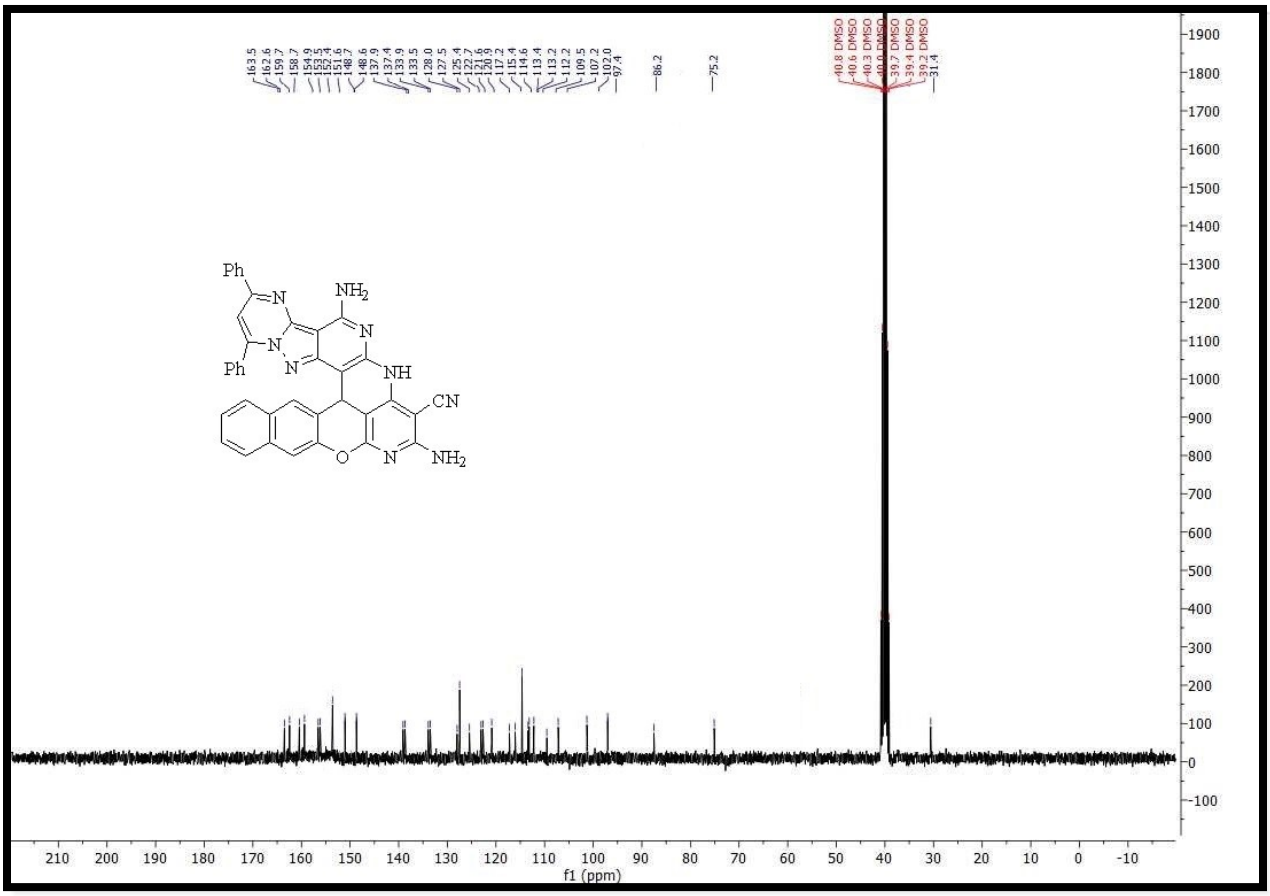


Figure 20: ^{13}C-NMR spectrum of compound **4j**

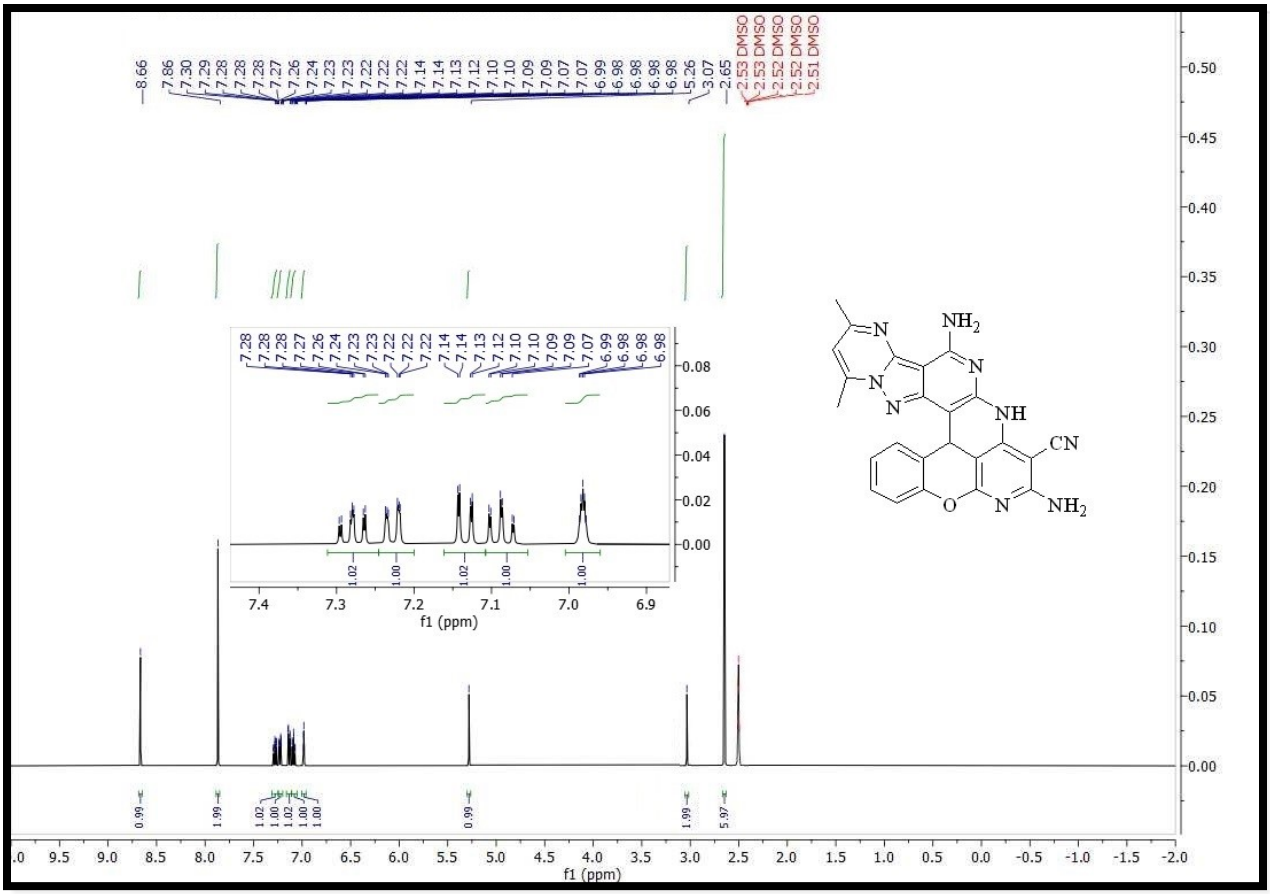


Figure 21: [1]H-NMR spectrum of compound **4k**

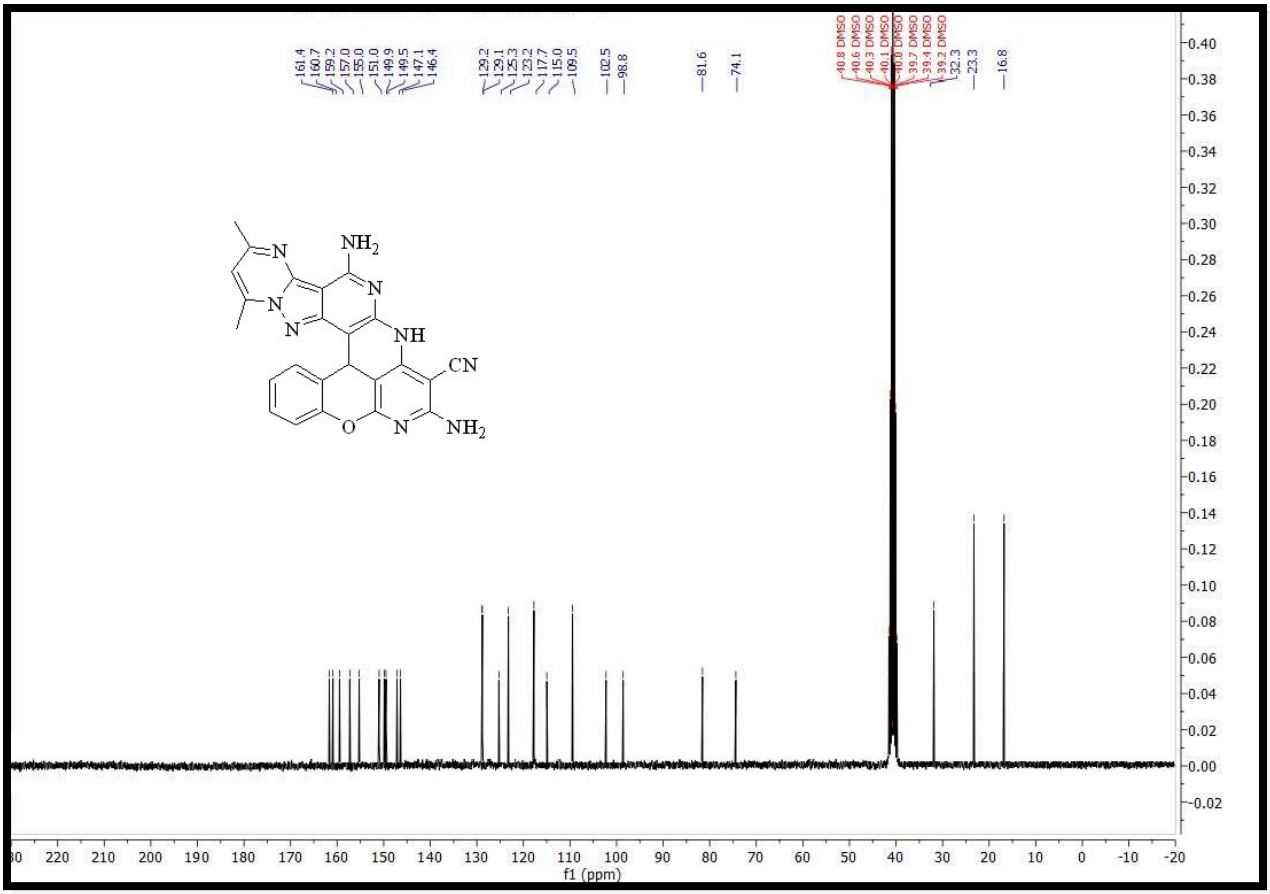


Figure 22: ^{13}C-NMR spectrum of compound **4k**

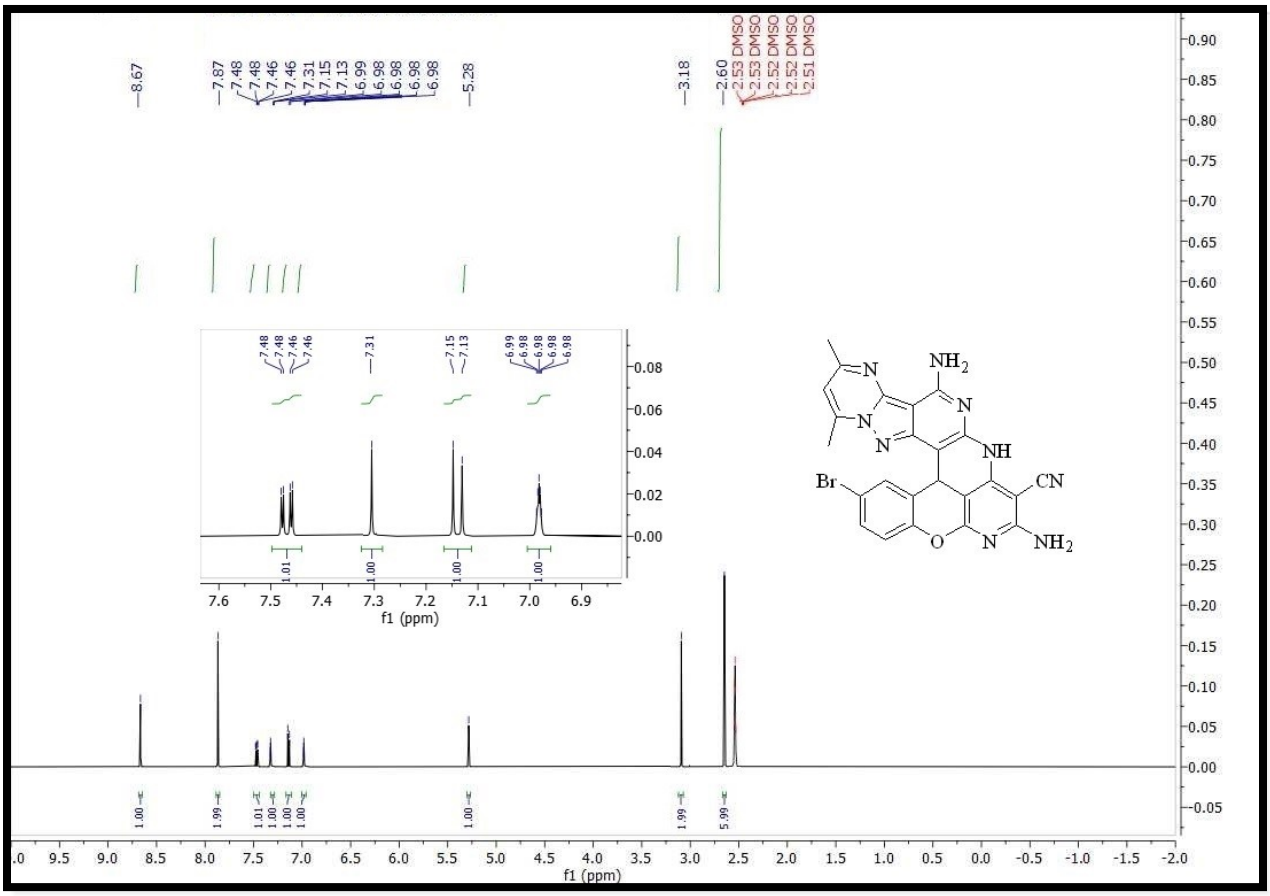


Figure 23: ^{1}H-NMR spectrum of compound **4l**

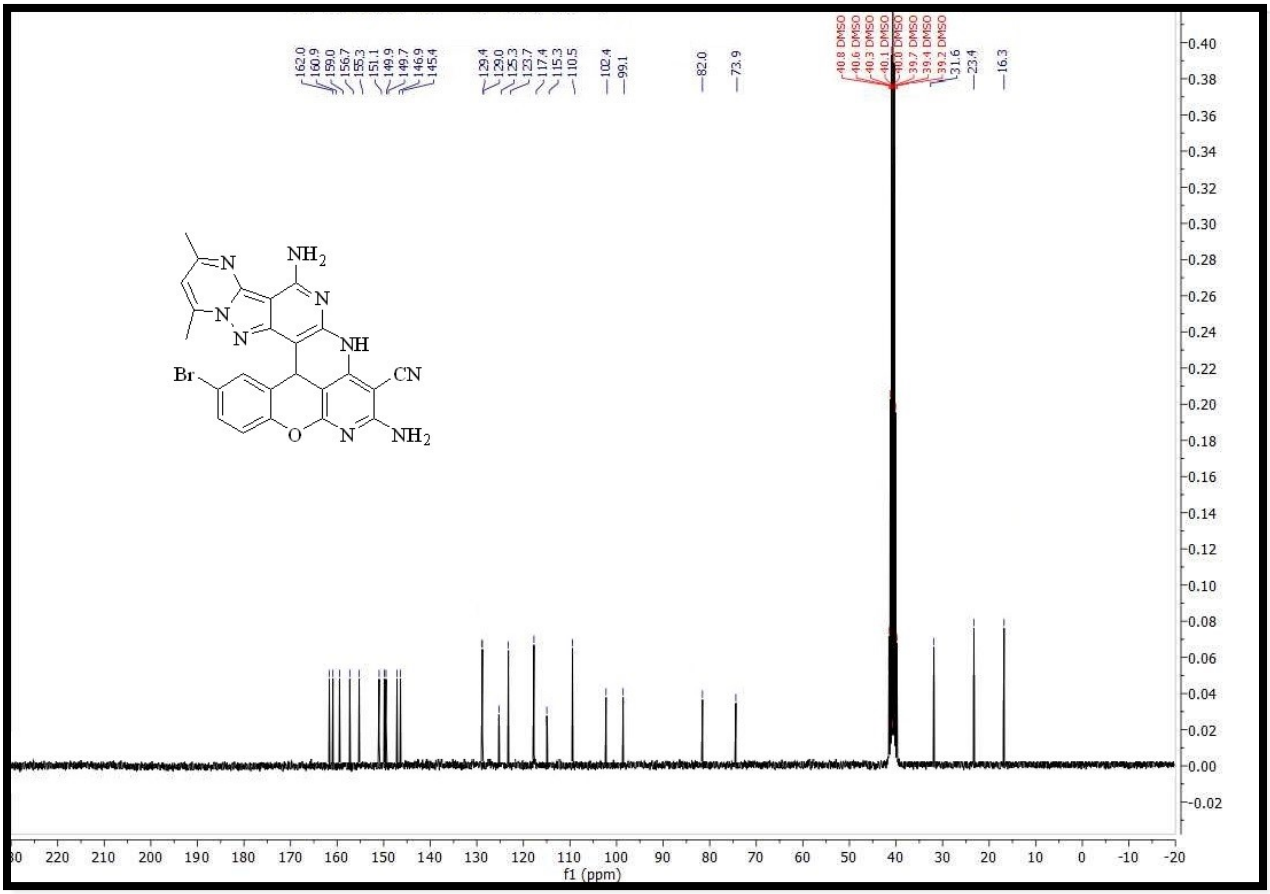


Figure 24: ^{13}C-NMR spectrum of compound **4l**

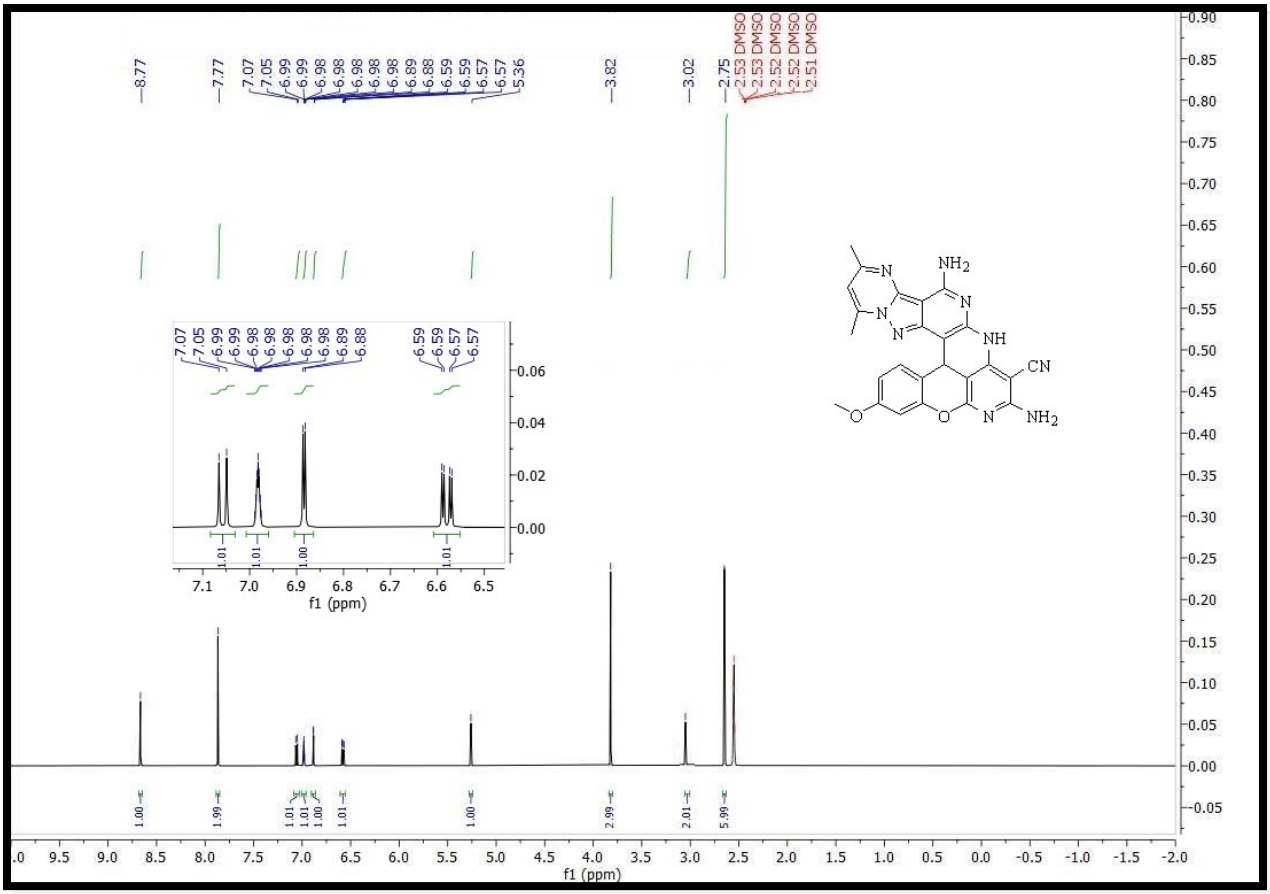


Figure 25: [1]H-NMR spectrum of compound **4m**

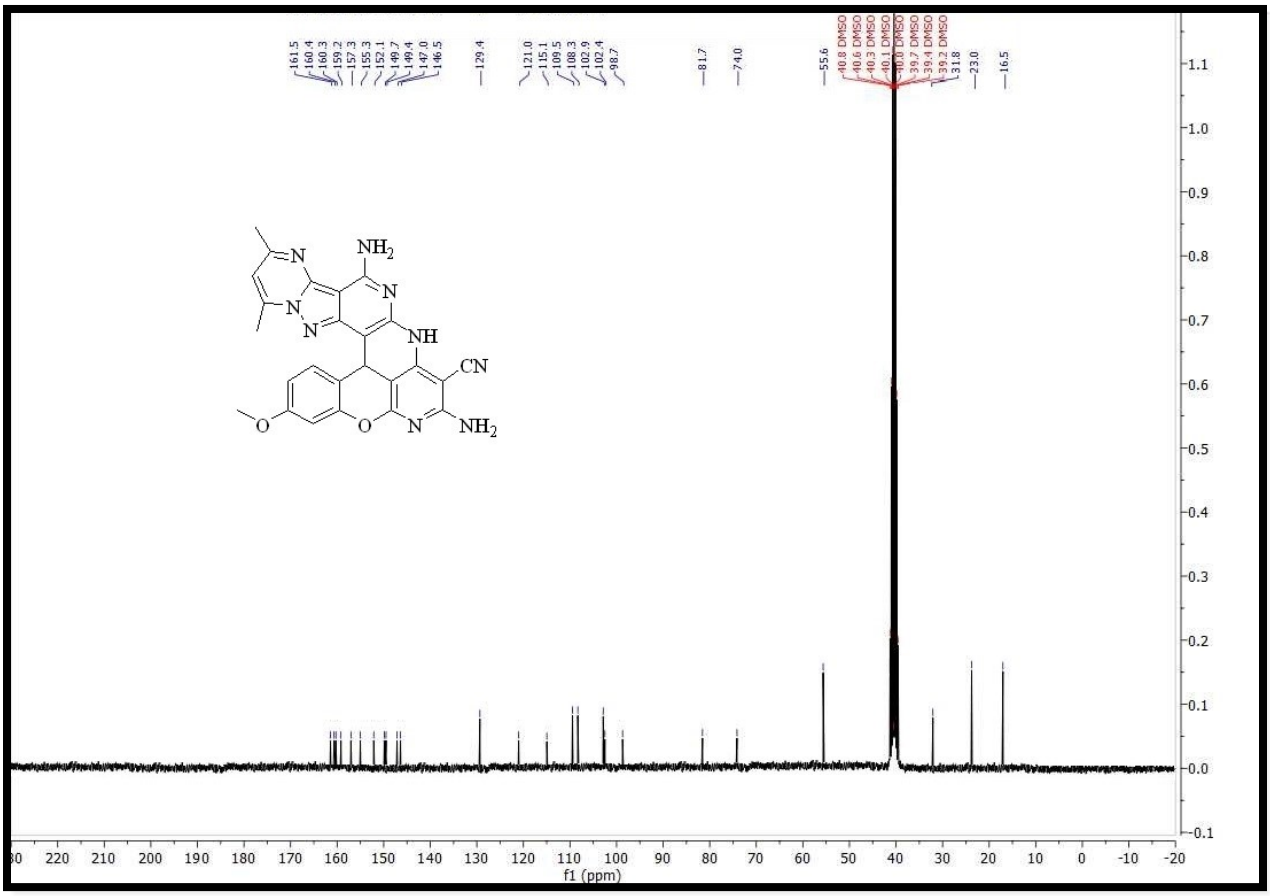


Figure 26: ^{13}C-NMR spectrum of compound **4m**

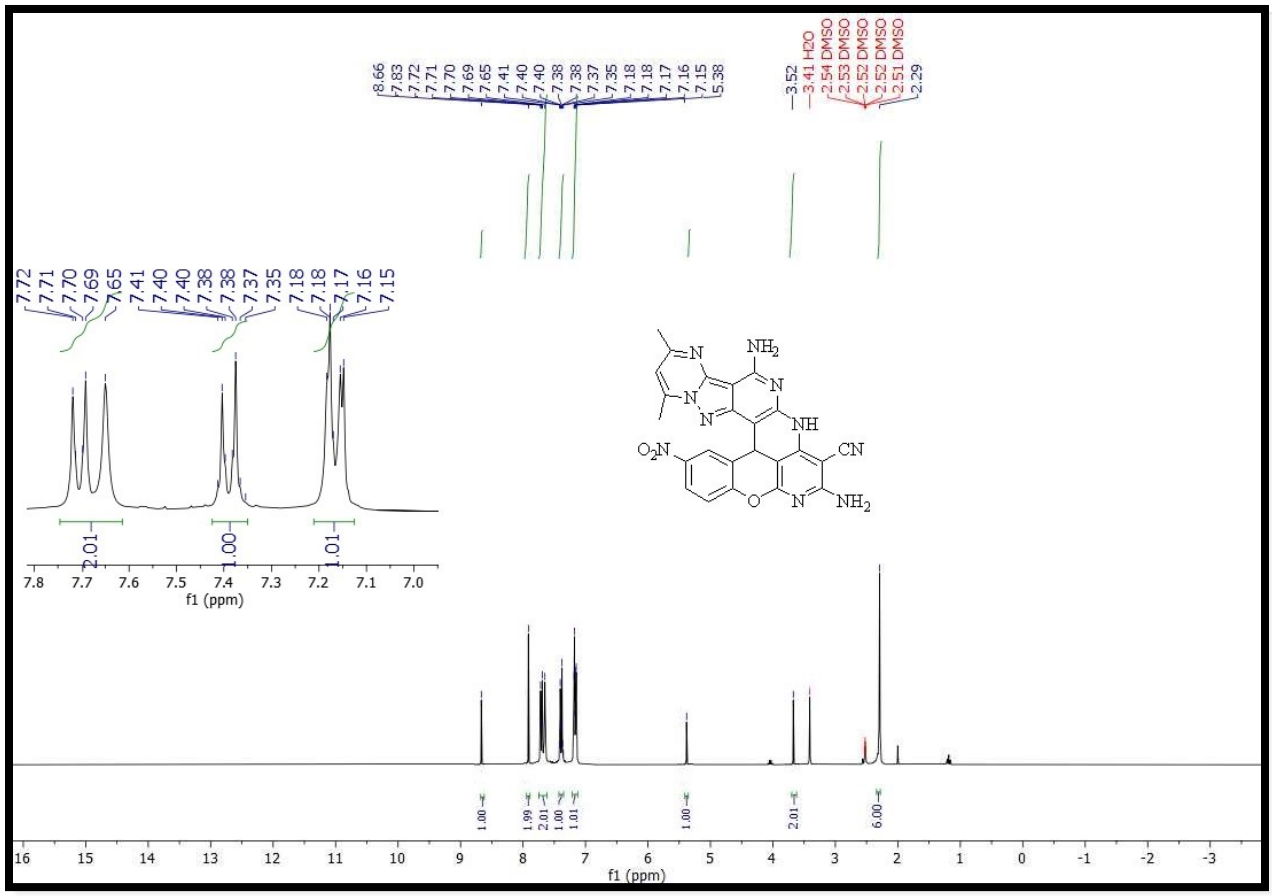


Figure 27: [1]H-NMR spectrum of compound **4n**

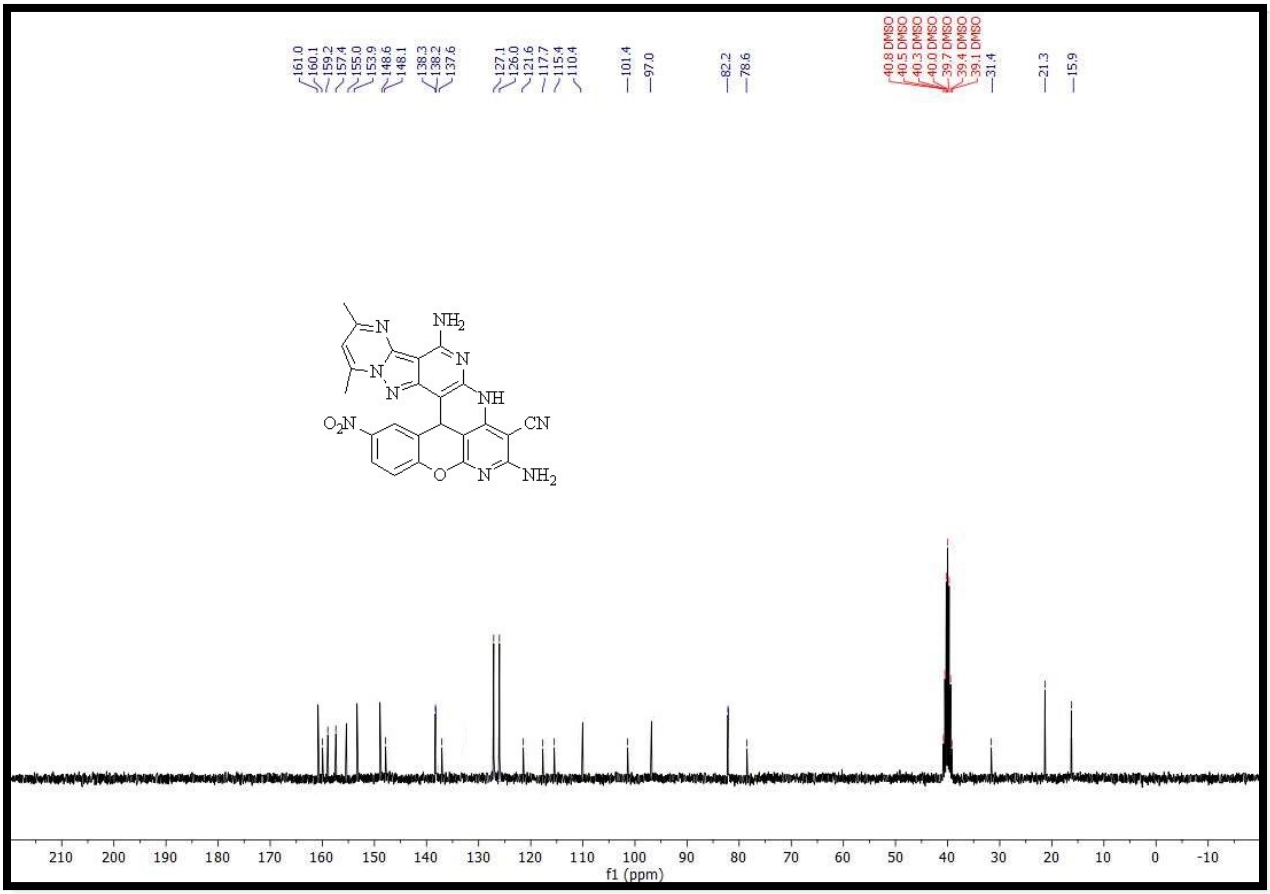


Figure 28: ^{13}C-NMR spectrum of compound **4n**

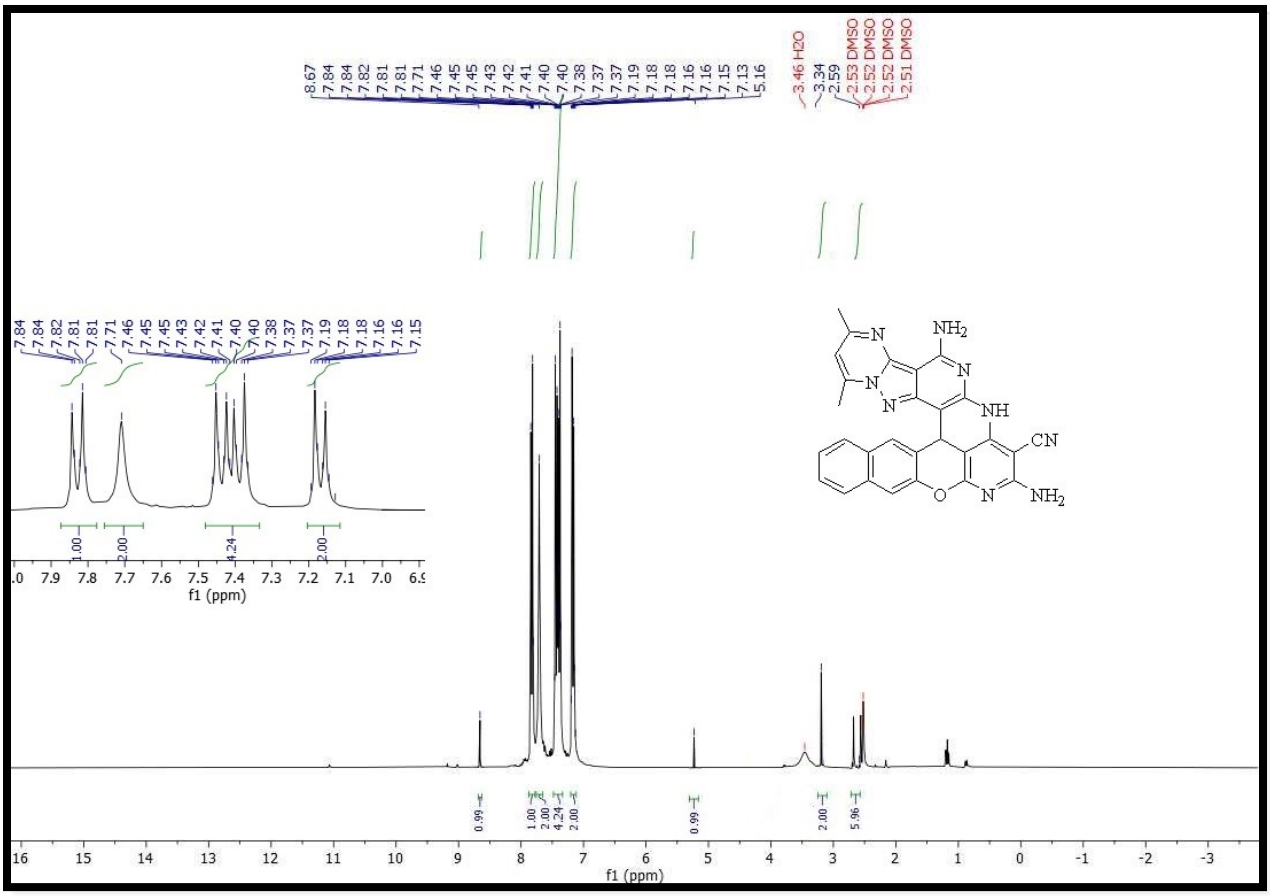


Figure 29: [1]H-NMR spectrum of compound **4o**

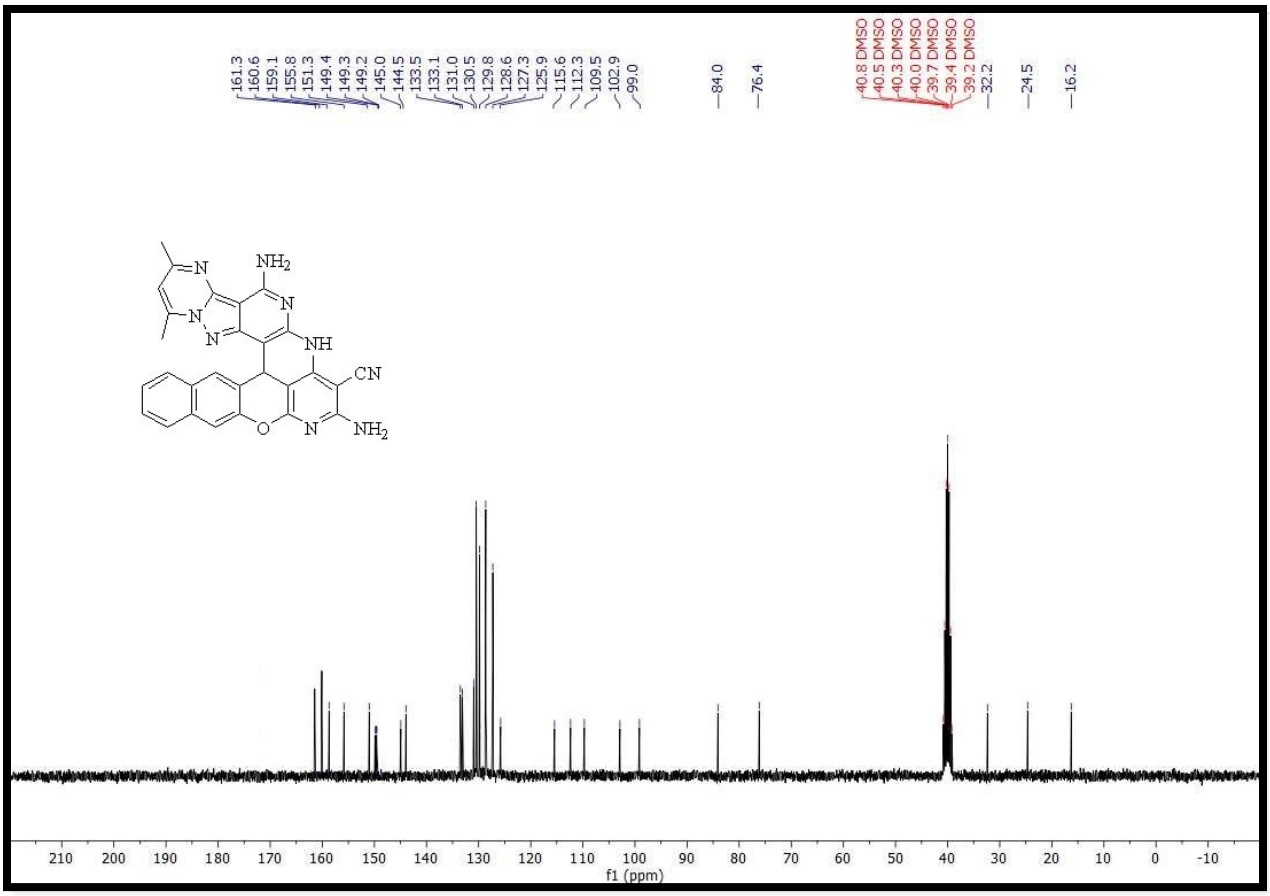


Figure 30: ^{13}C-NMR spectrum of compound **4o**

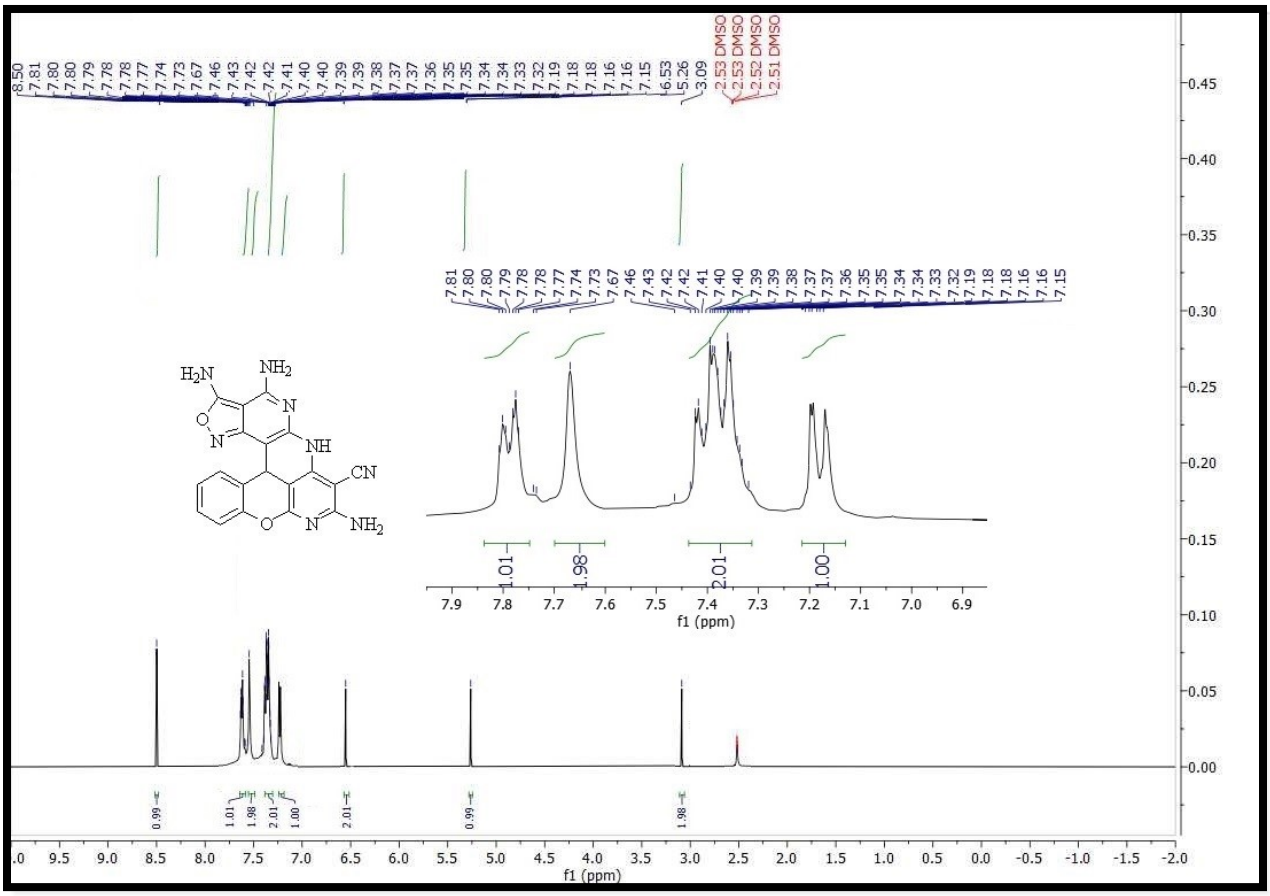


Figure 31: [1]H-NMR spectrum of compound **4p**

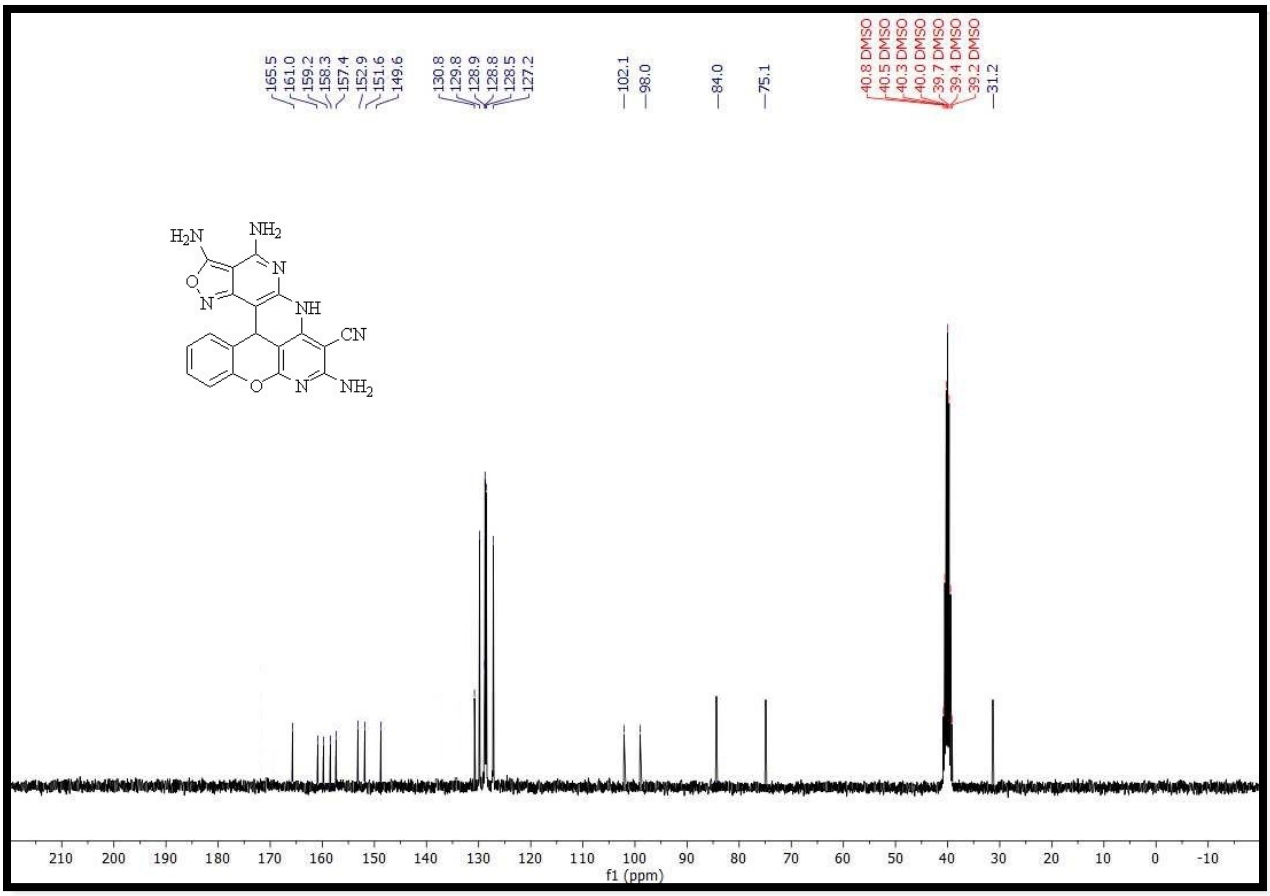


Figure 32: ^{13}C-NMR spectrum of compound **4p**

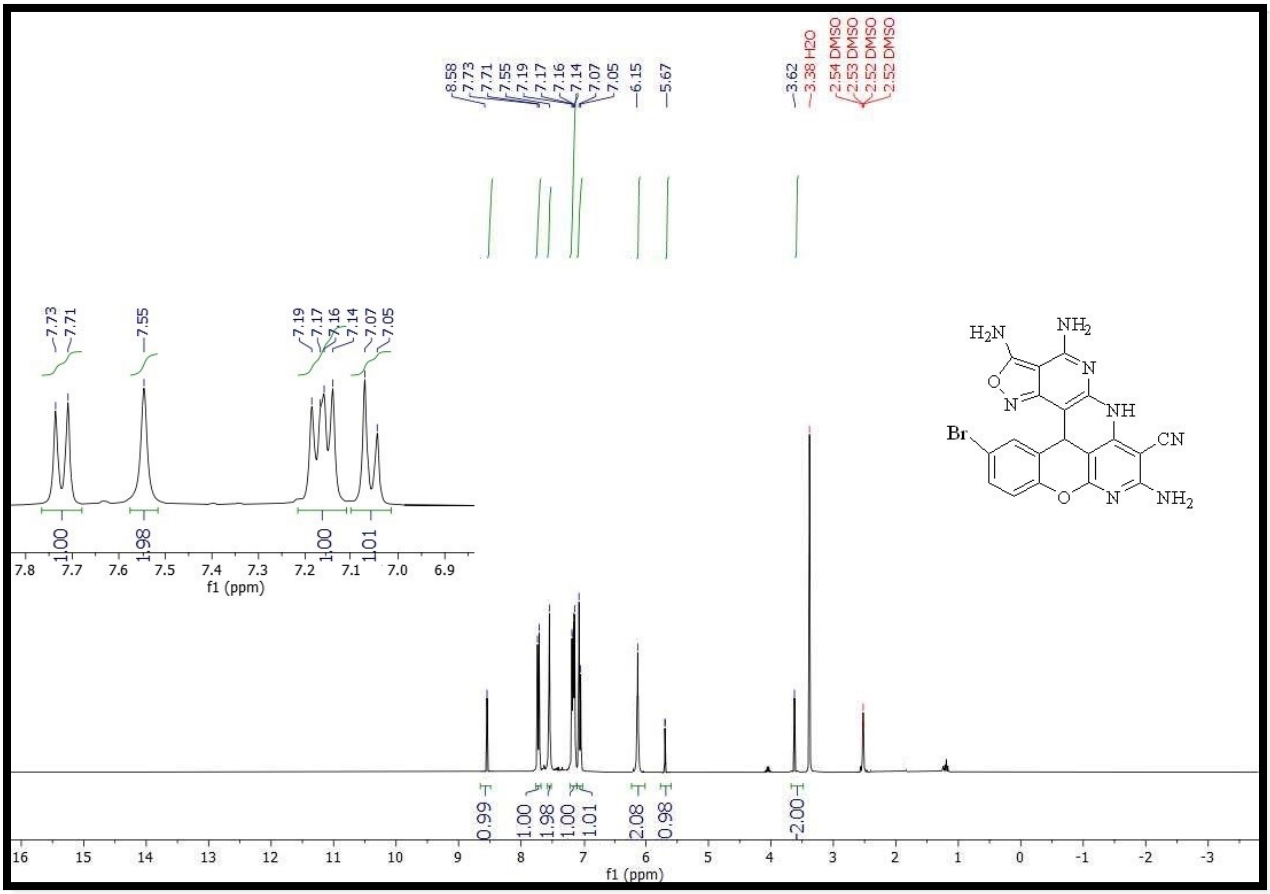


Figure 33: [1]H-NMR spectrum of compound **4q**

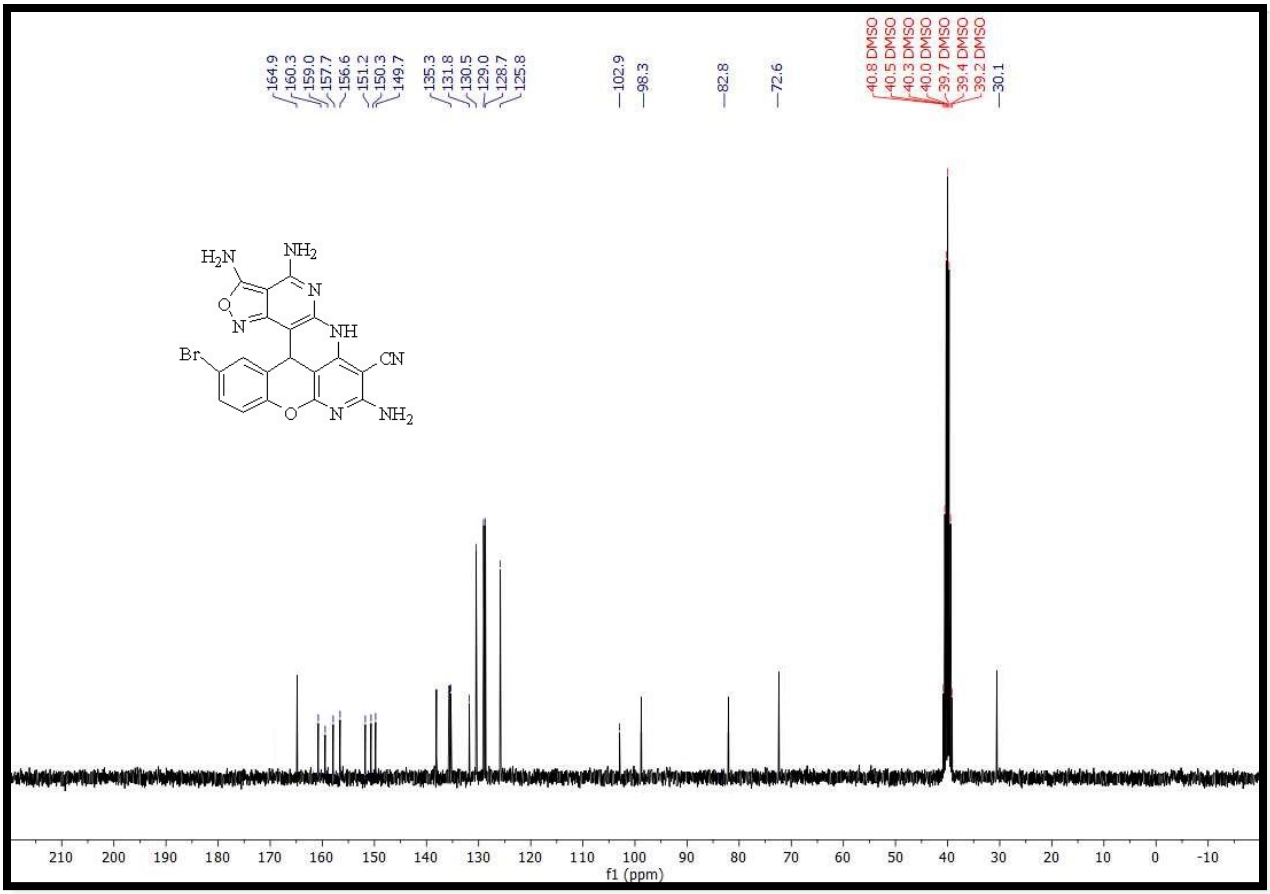


Figure 34: ^{13}C-NMR spectrum of compound **4q**

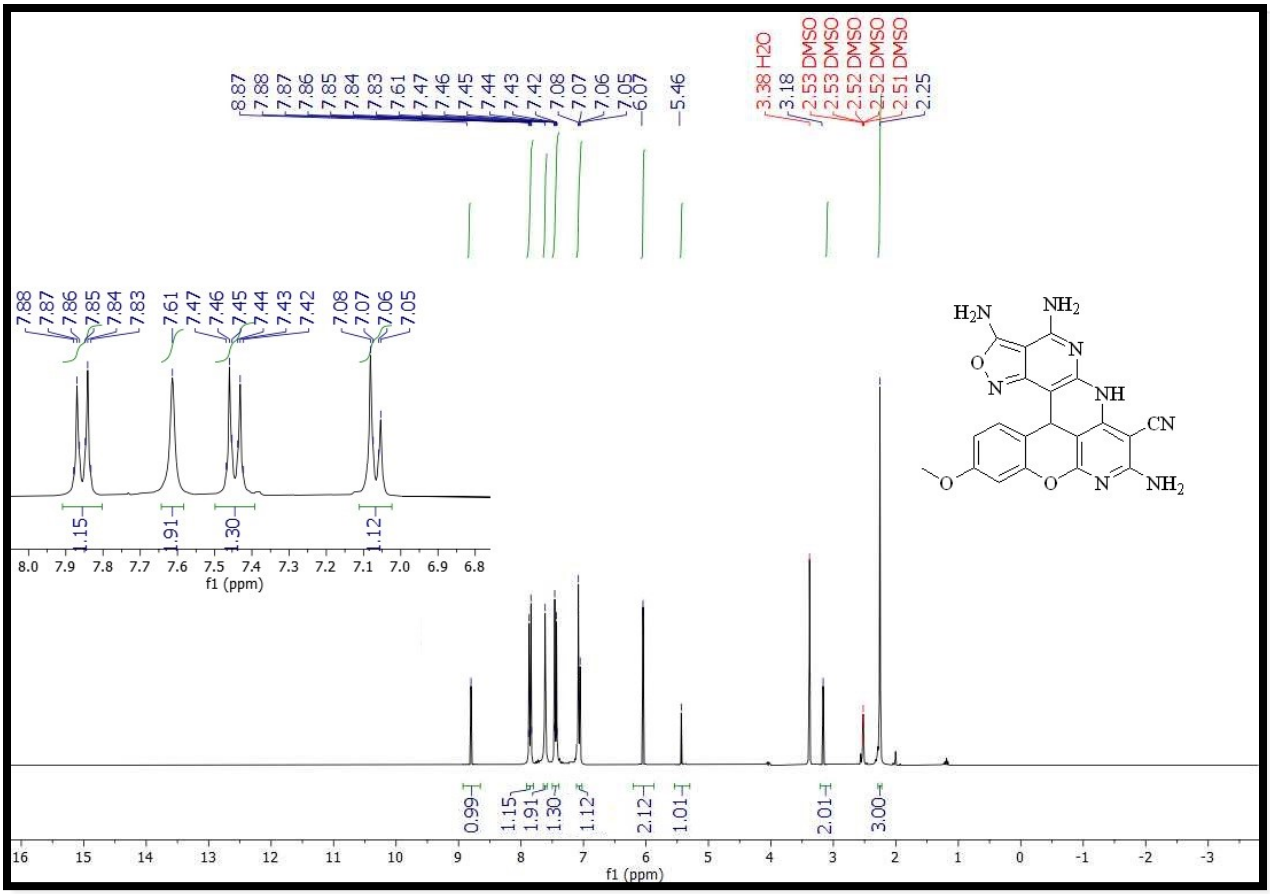


Figure 35: [1]H-NMR spectrum of compound **4r**

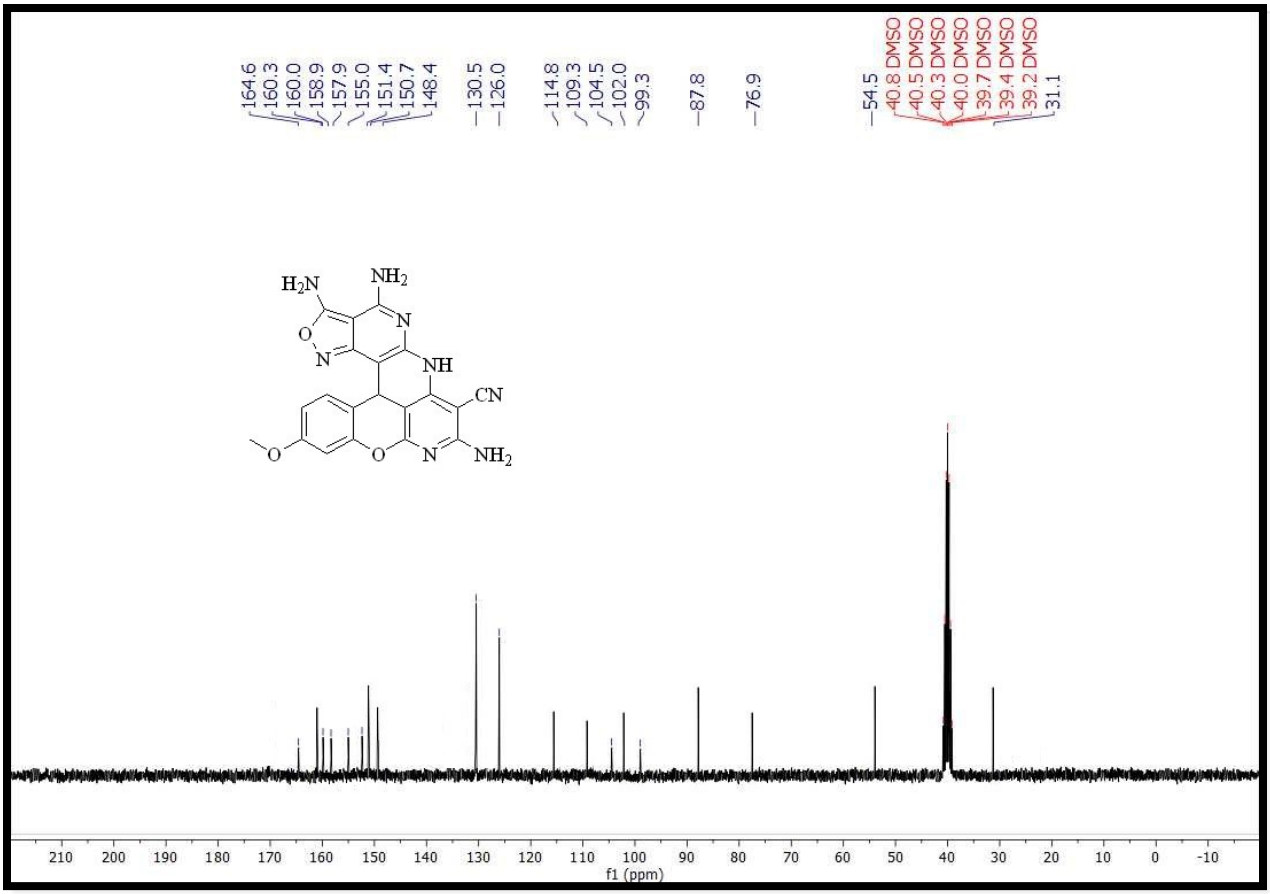


Figure 36: ^{13}C-NMR spectrum of compound **4r**

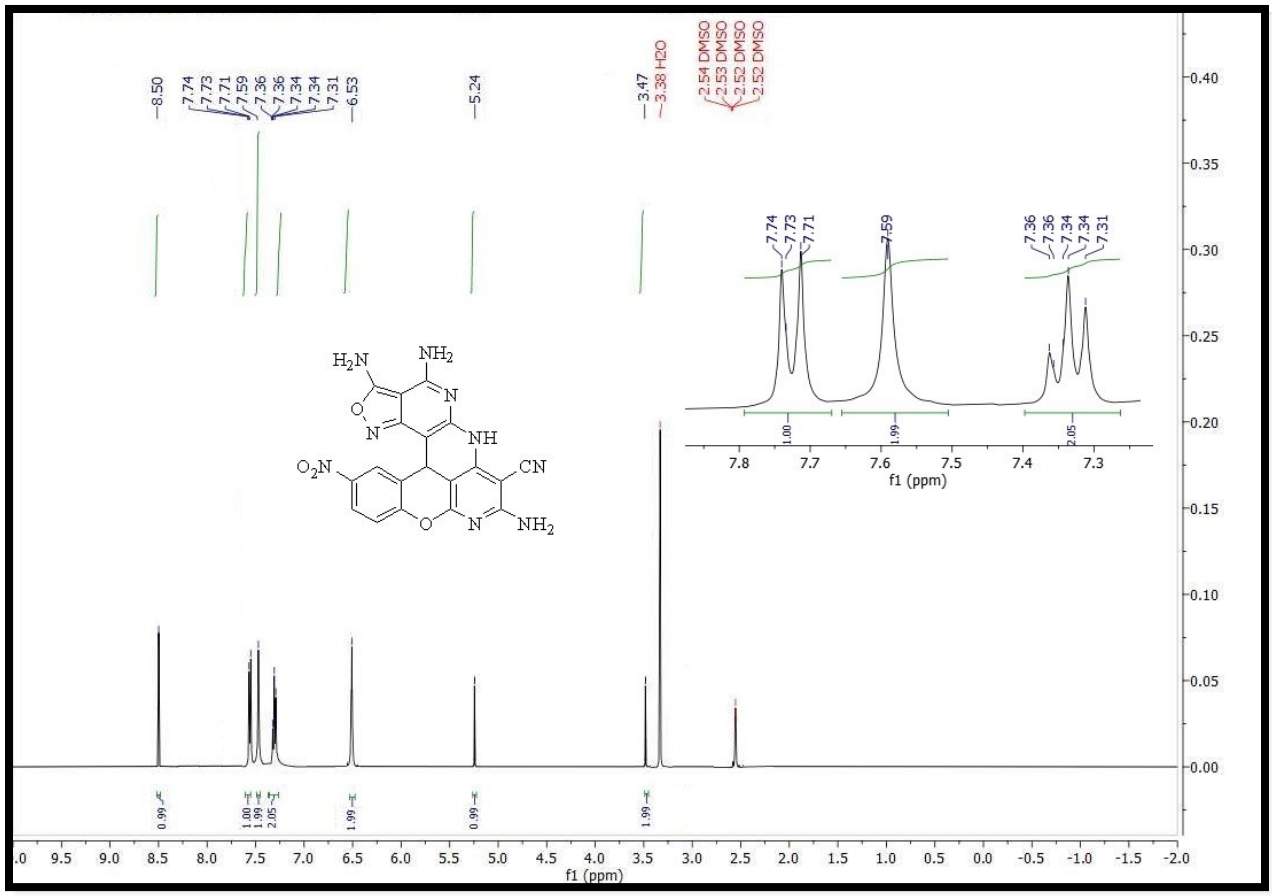


Figure 37: ^{1}H-NMR spectrum of compound **4s**

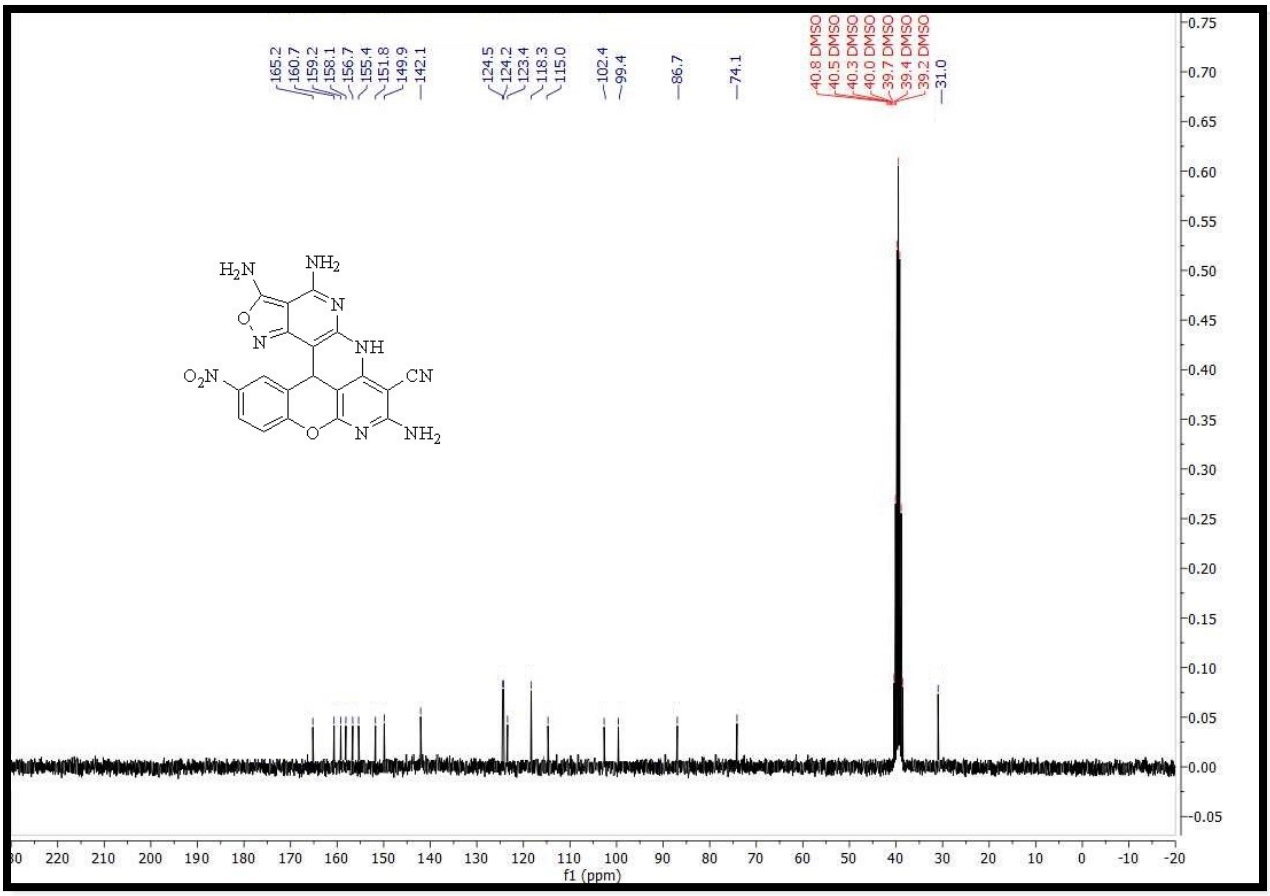


Figure 38: ^{13}C-NMR spectrum of compound **4s**

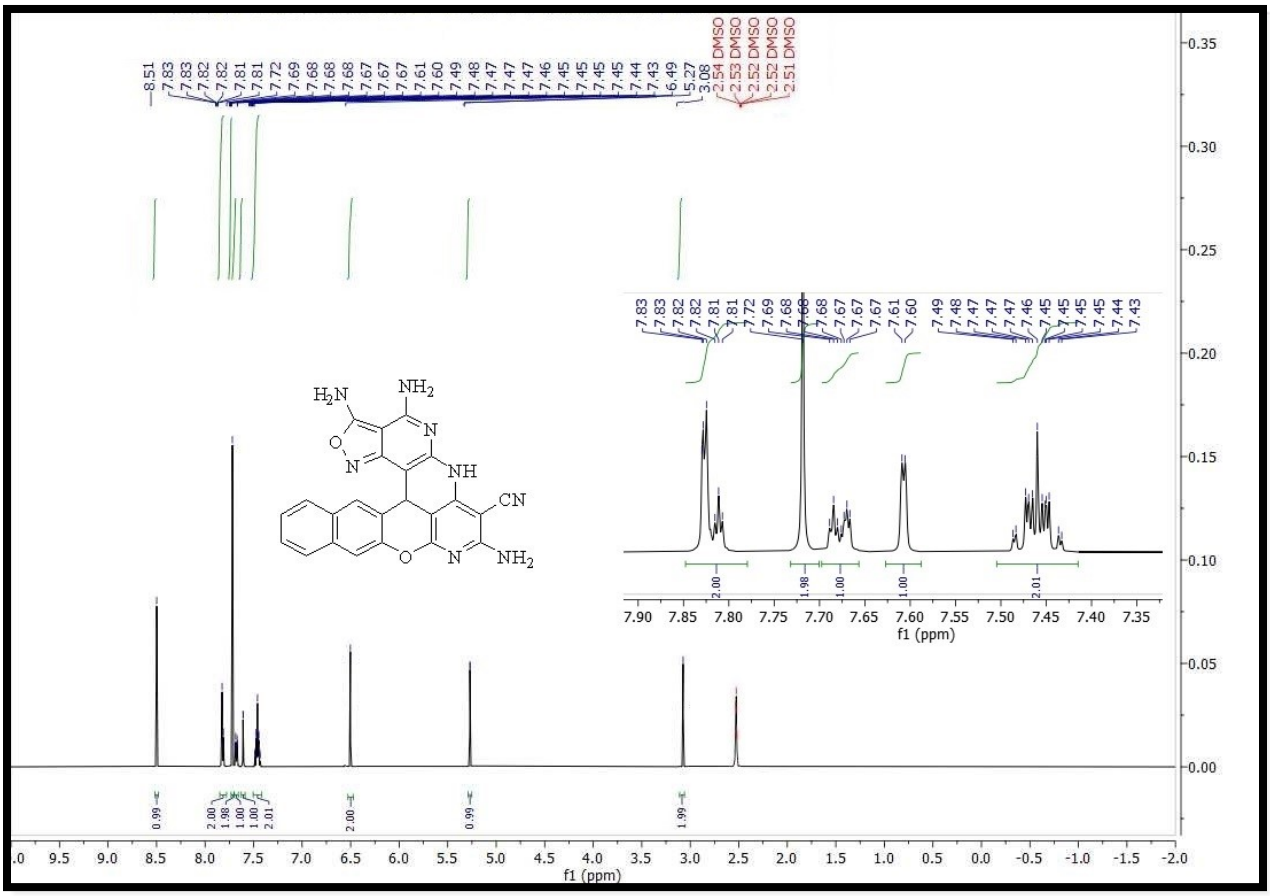


Figure 39: [1]H-NMR spectrum of compound **4t**

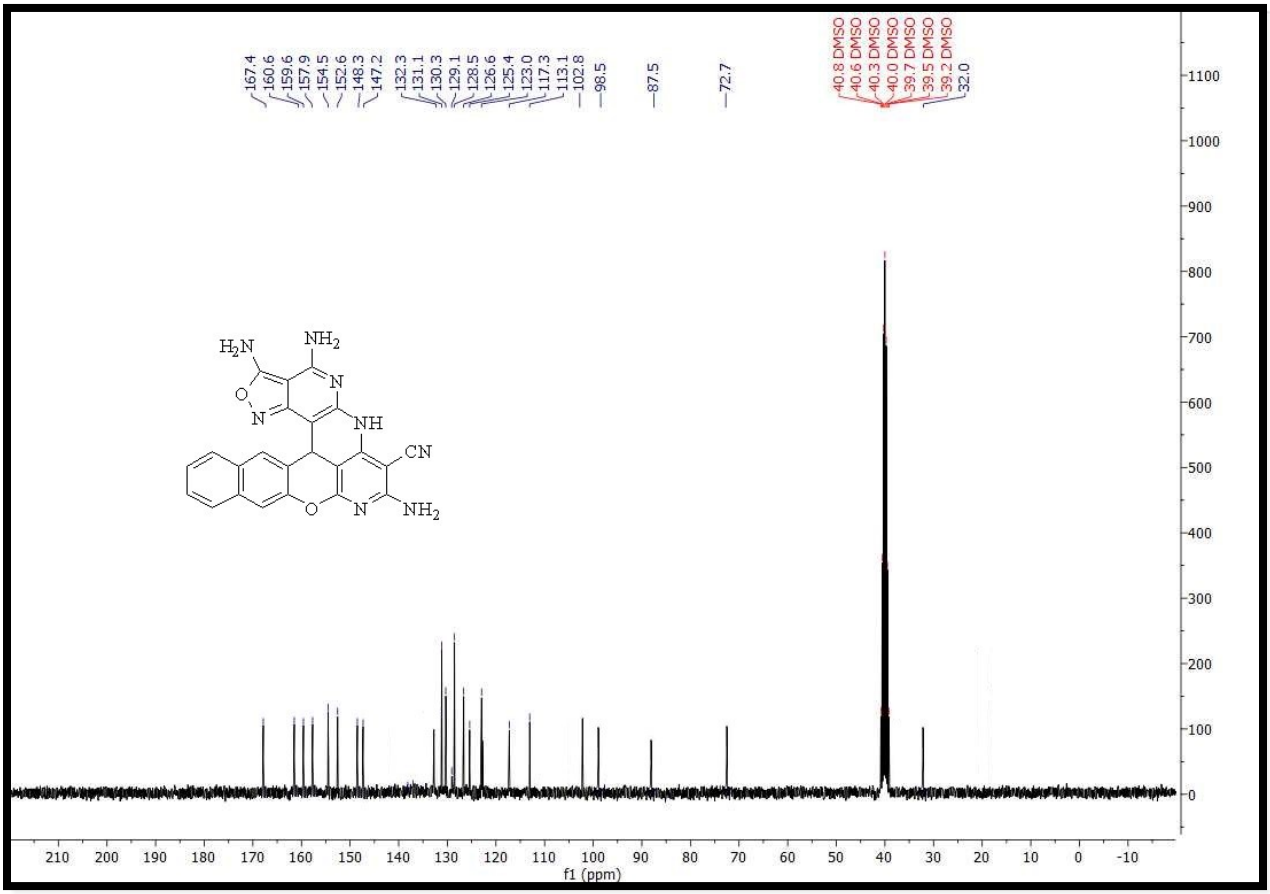


Figure 40: ^{13}C-NMR spectrum of compound **4t**

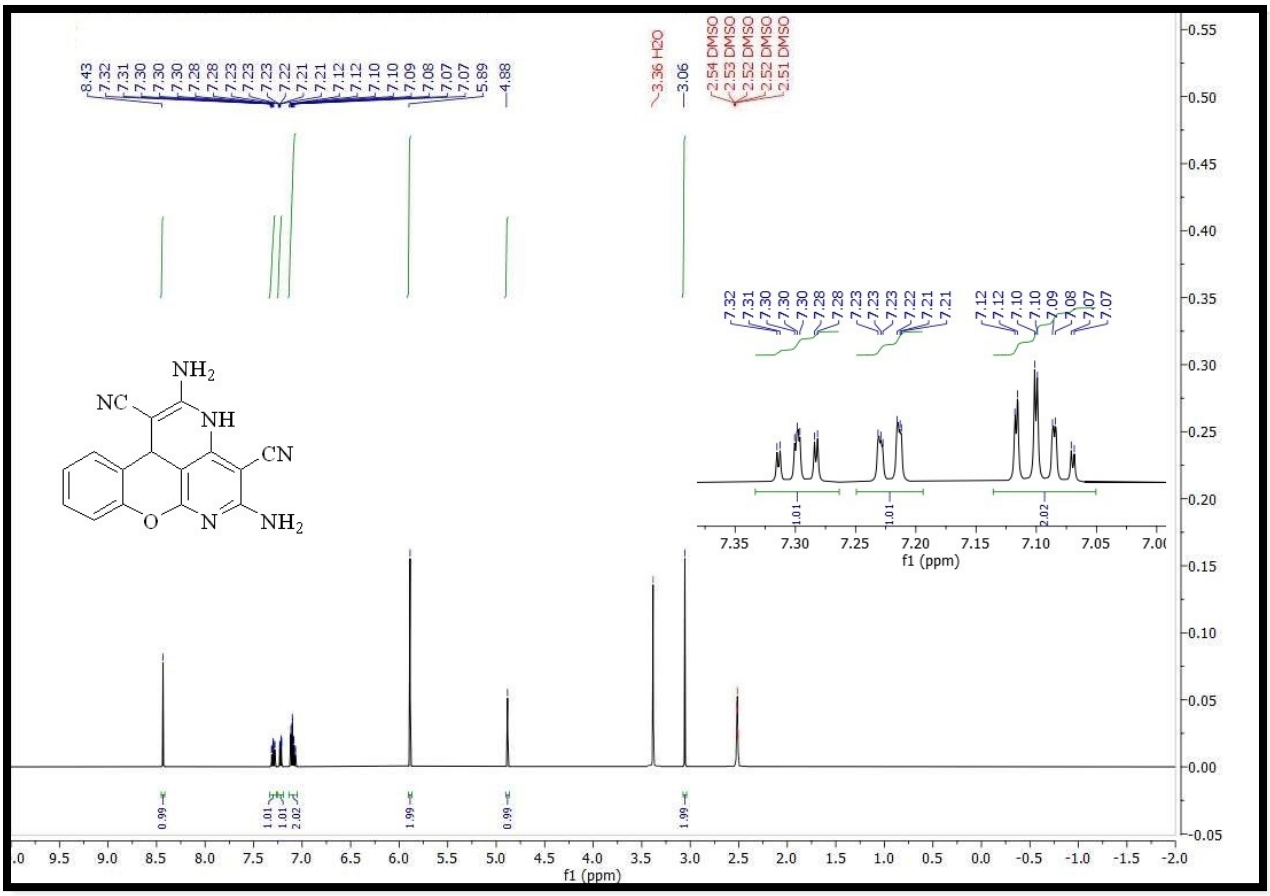


Figure 41: [1]H-NMR spectrum of compound **4u**

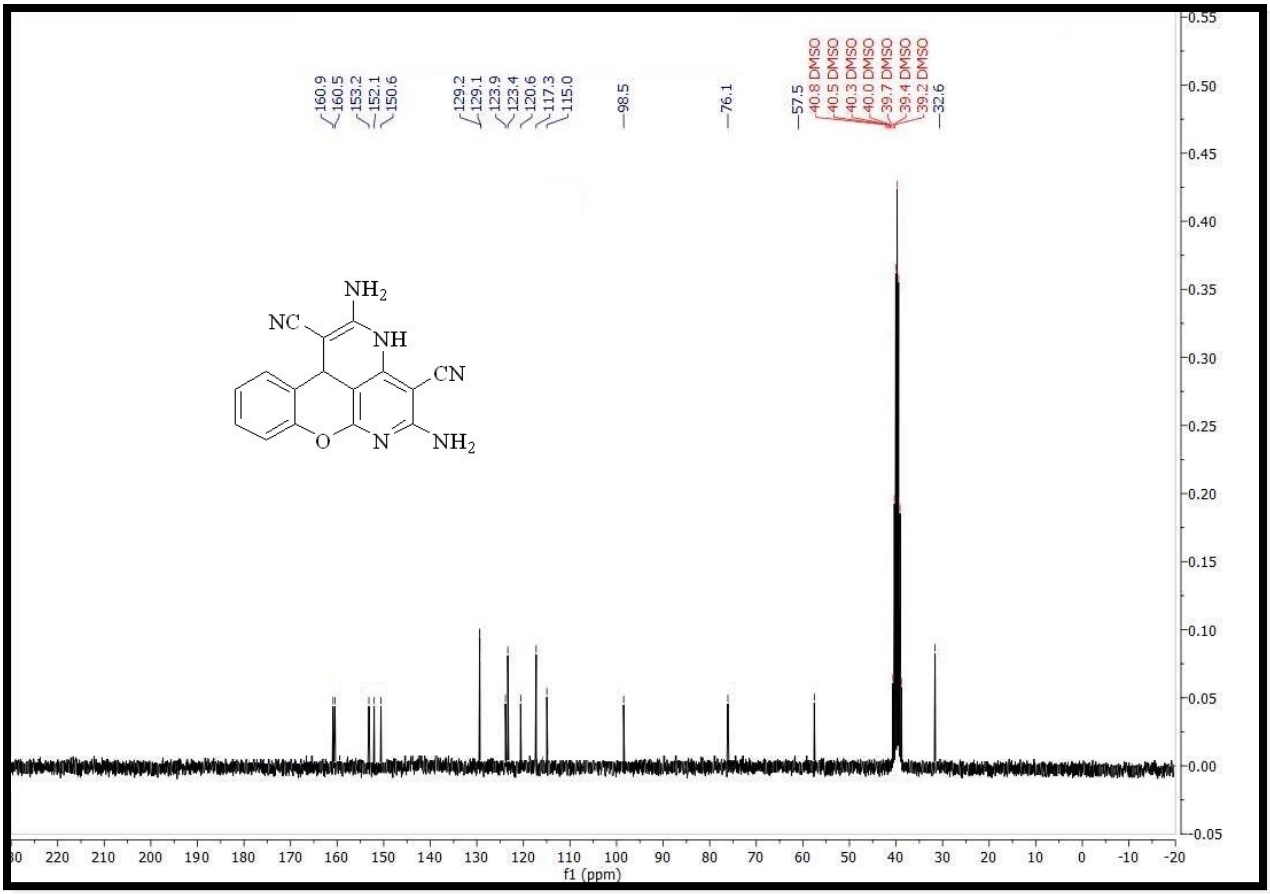


Figure 42: ^{13}C-NMR spectrum of compound **4u**

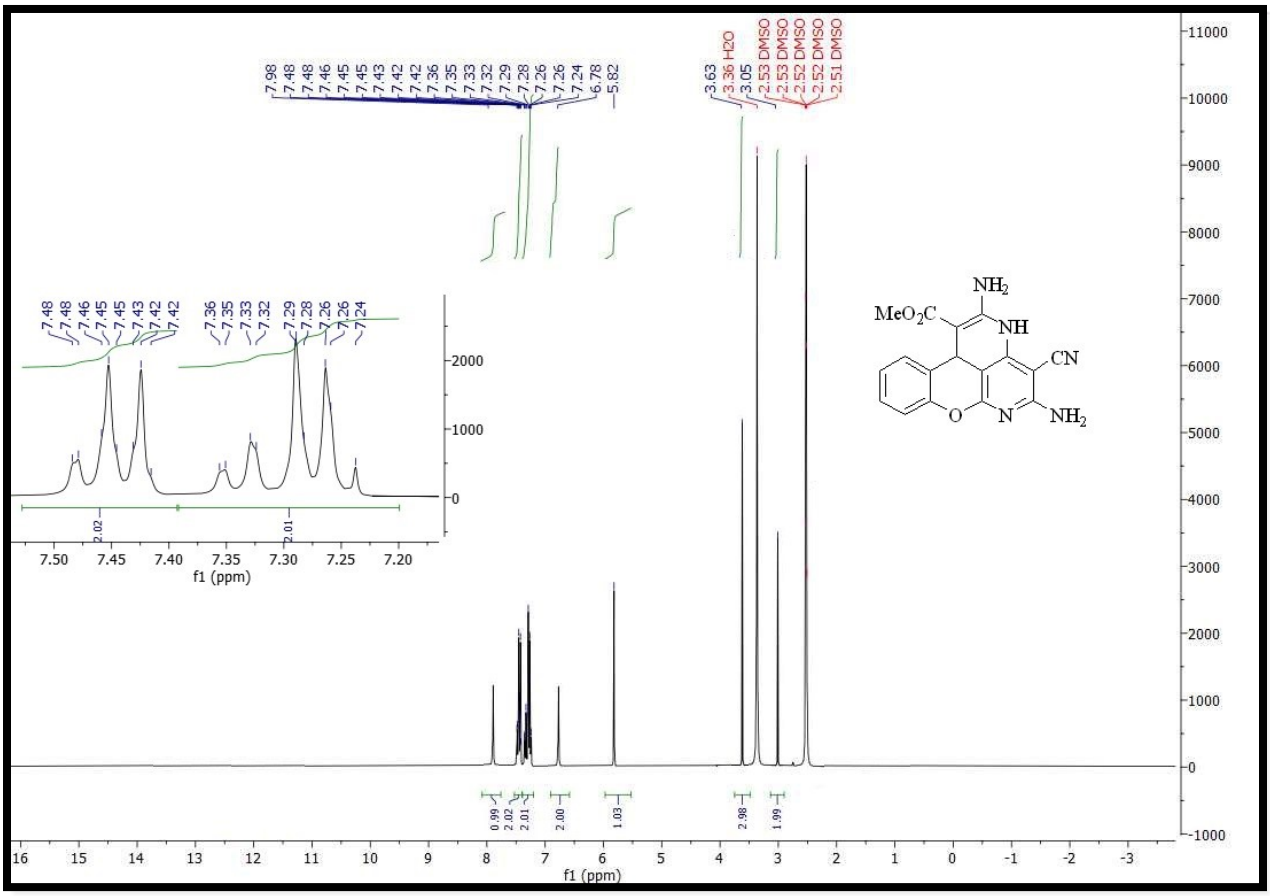


Figure 43: [1]H-NMR spectrum of compound **4v**

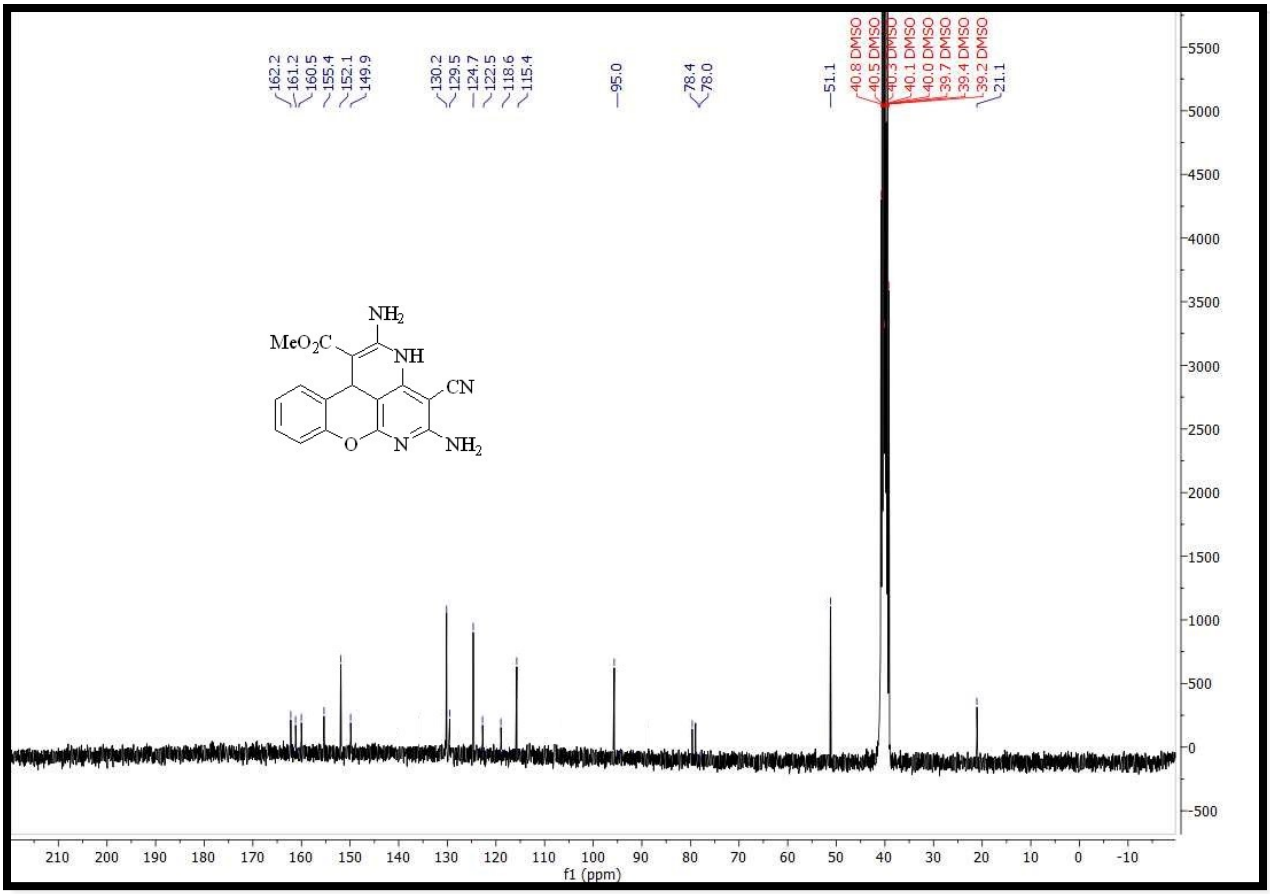


Figure 44: ^{13}C-NMR spectrum of compound **4v**

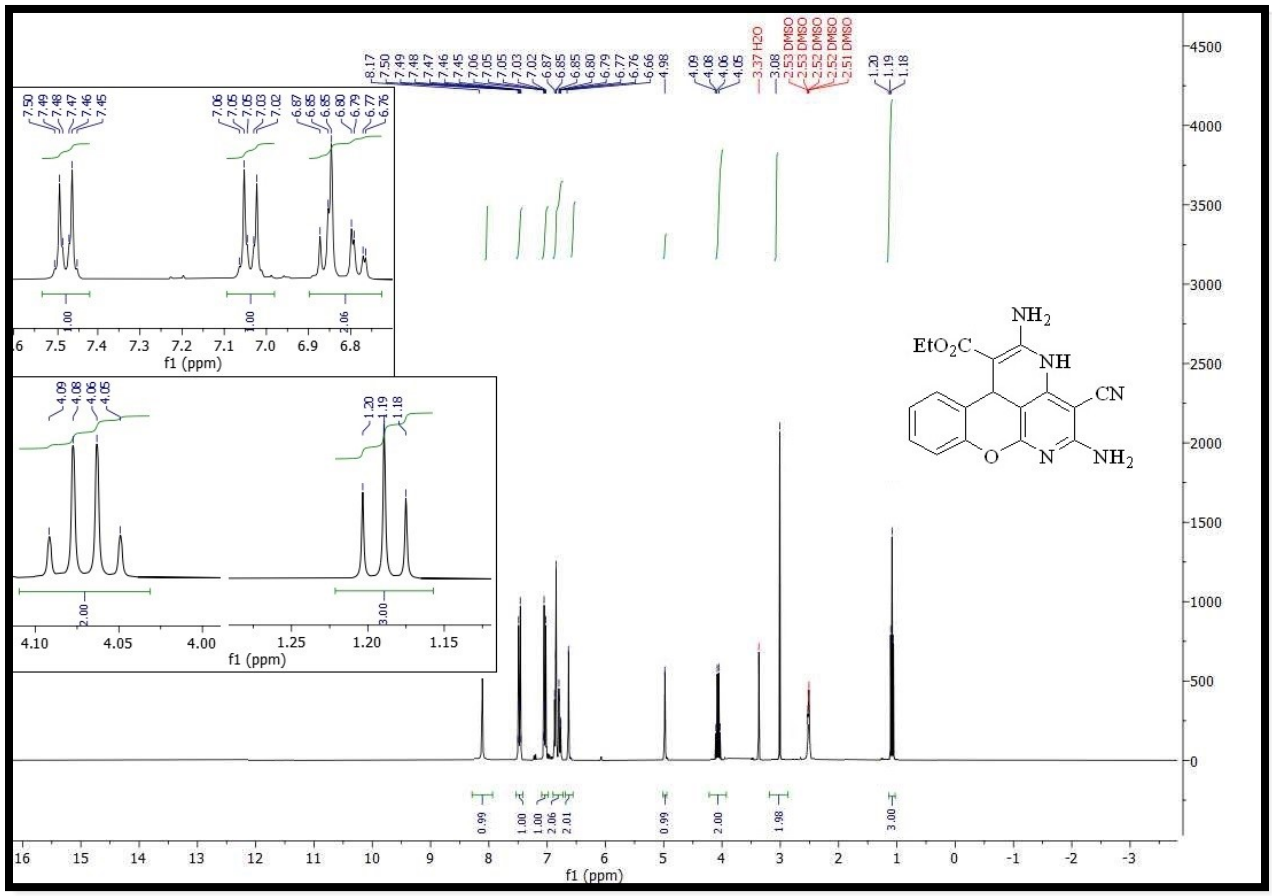


Figure 45: ^{1}H-NMR spectrum of compound **4w**

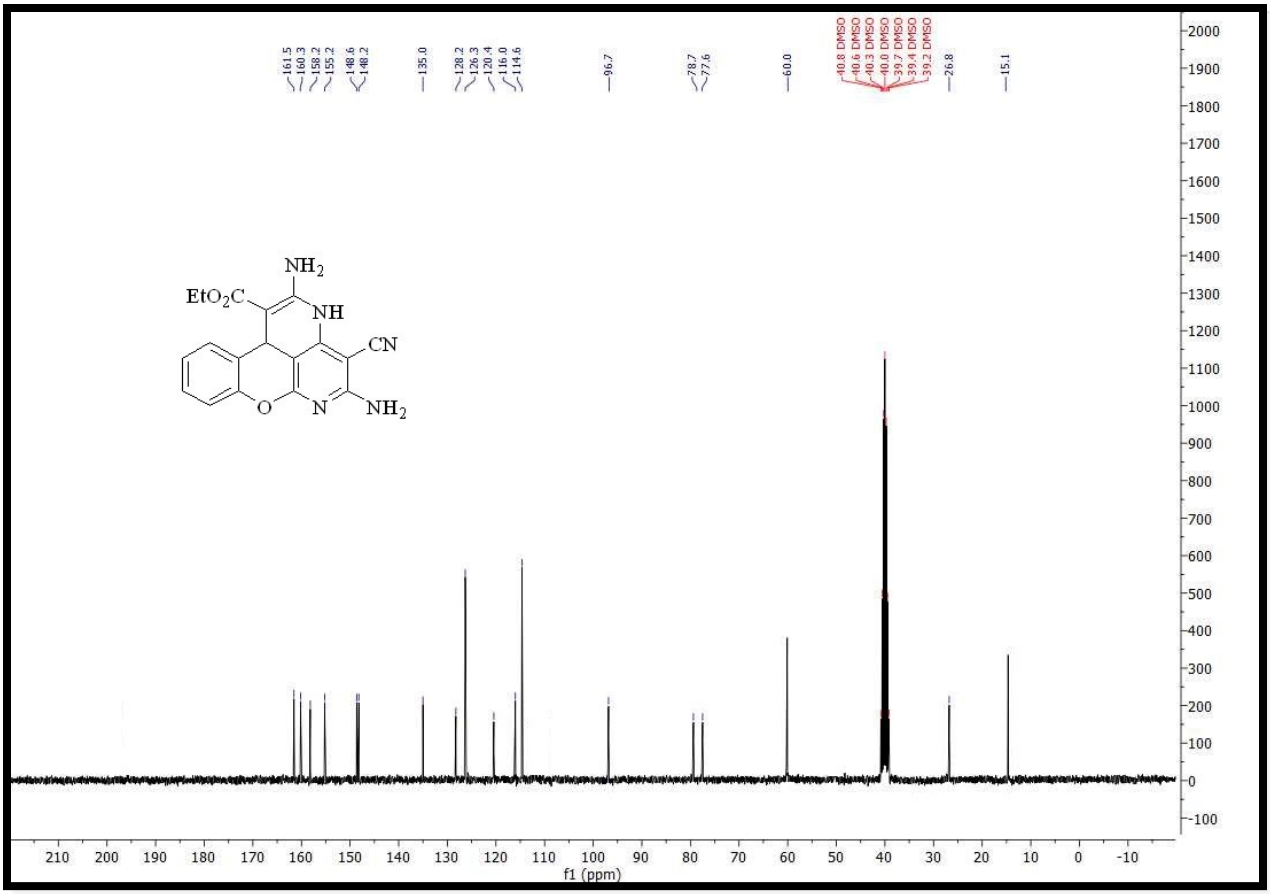


Figure 46: ^{13}C-NMR spectrum of compound **4w**

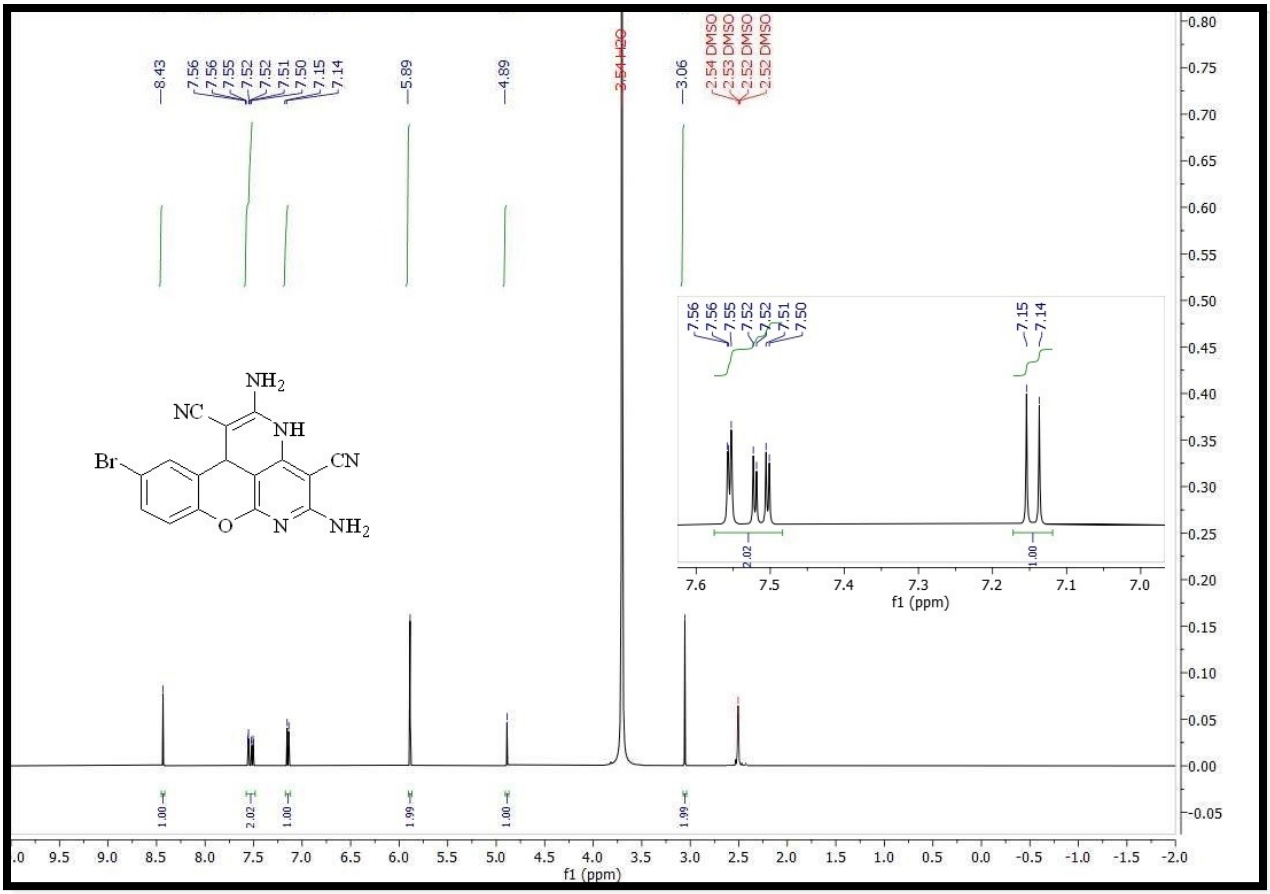


Figure 47: [1]H-NMR spectrum of compound **4x**

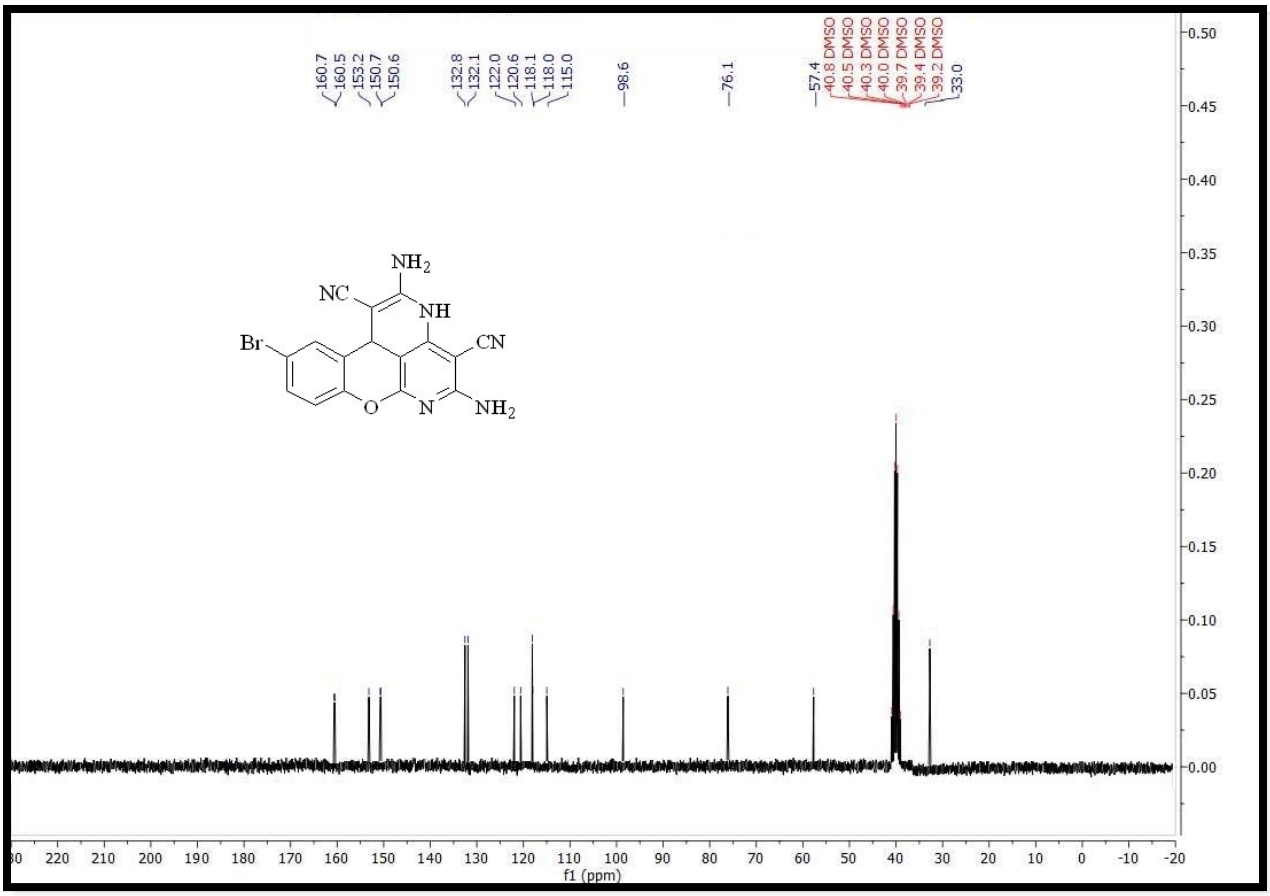


Figure 48: ^{13}C-NMR spectrum of compound **4x**

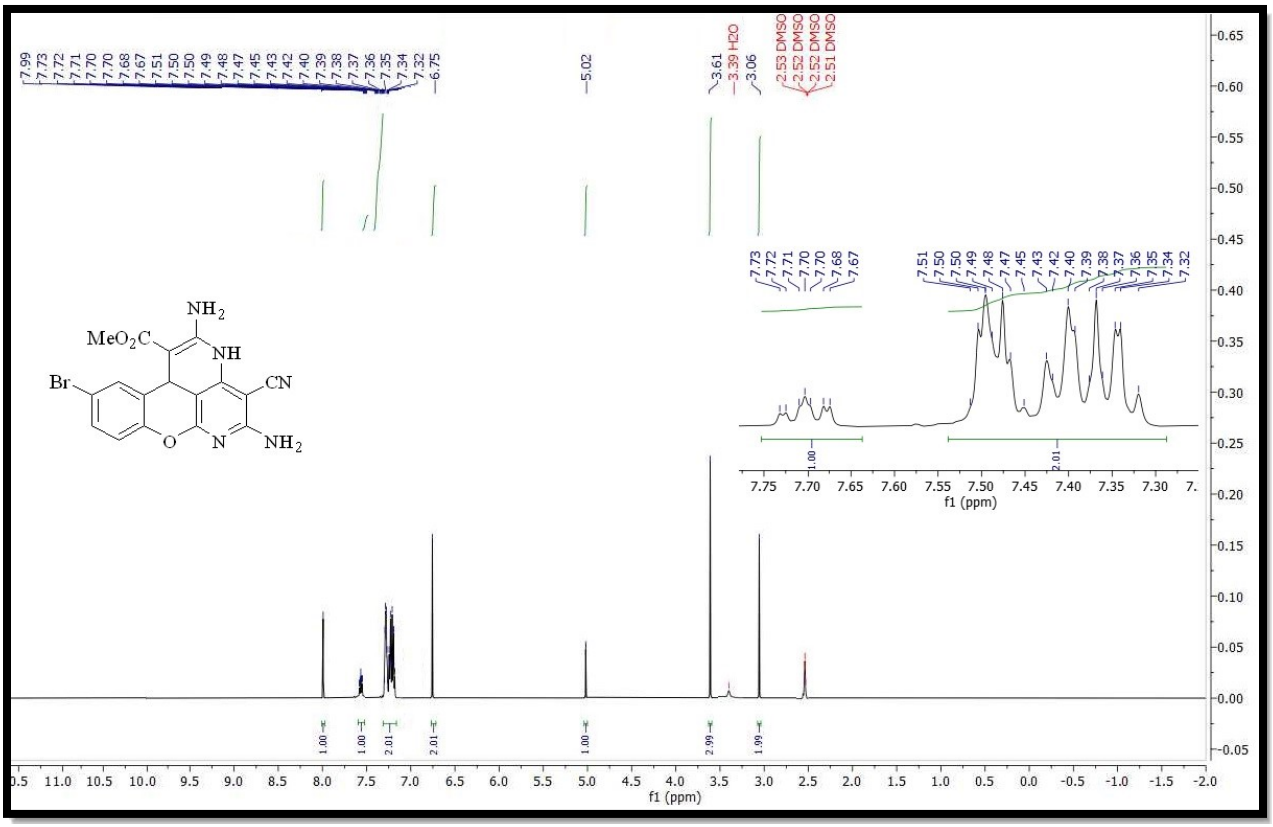


Figure 49: ^{1}H-NMR spectrum of compound **4y**

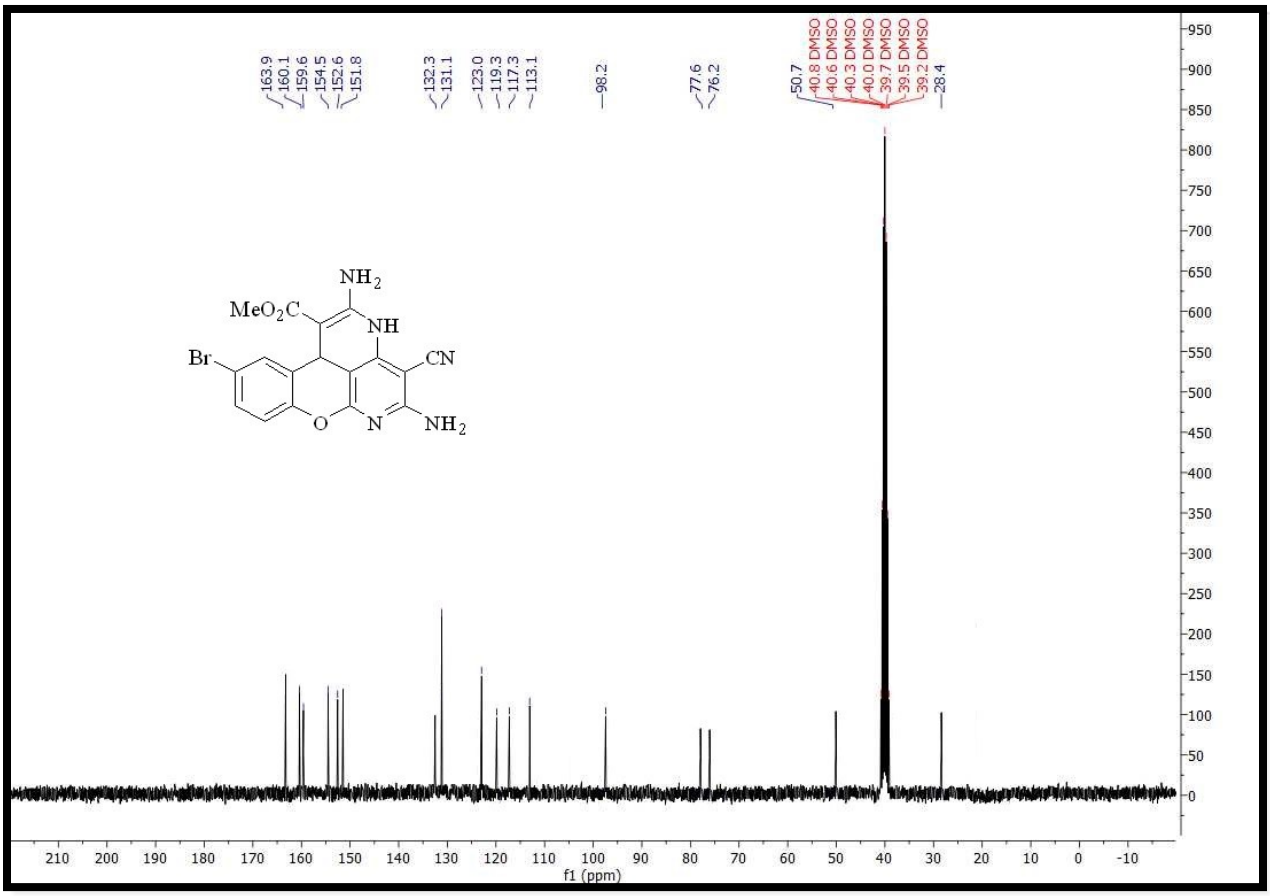


Figure 50: ^{13}C-NMR spectrum of compound **4y**

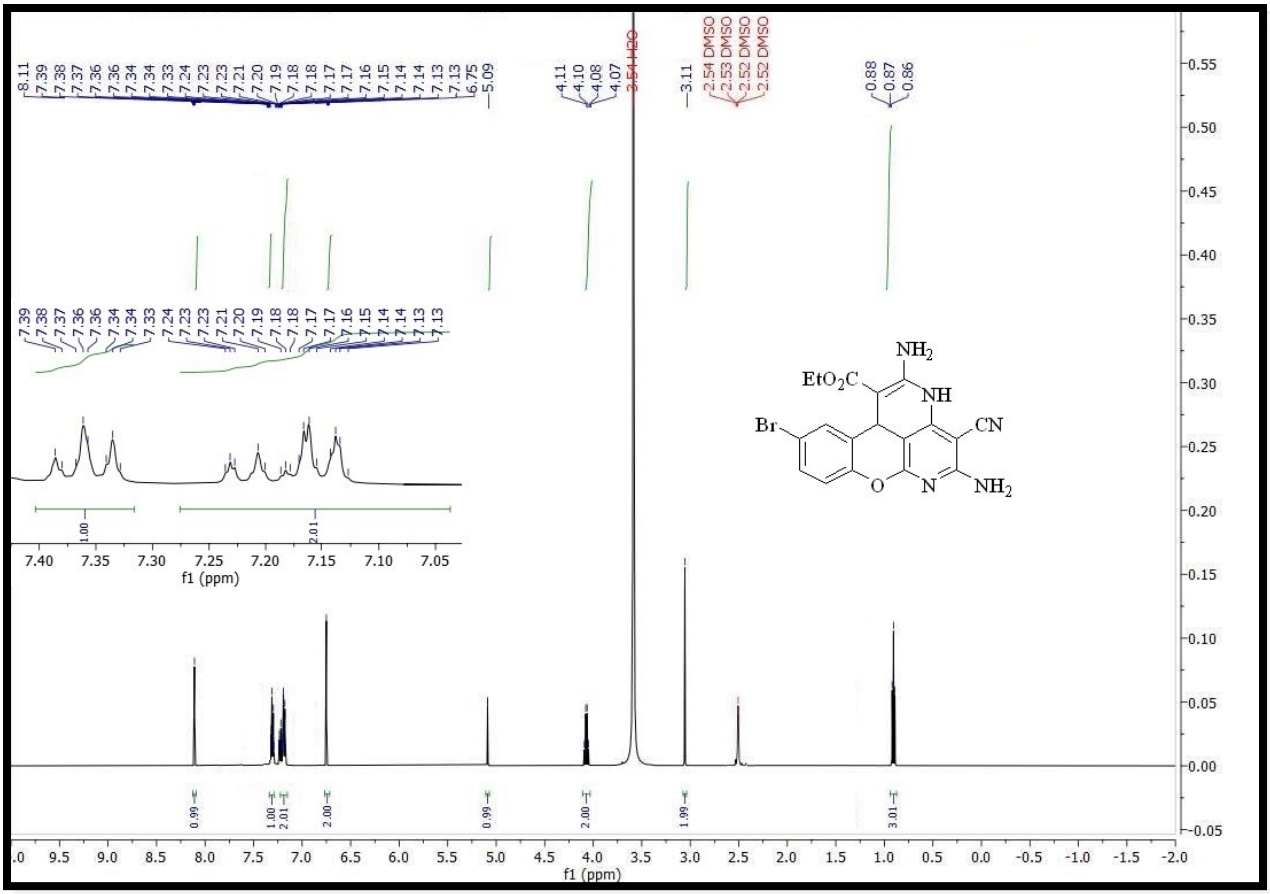


Figure 51: [1]H-NMR spectrum of compound **4z**

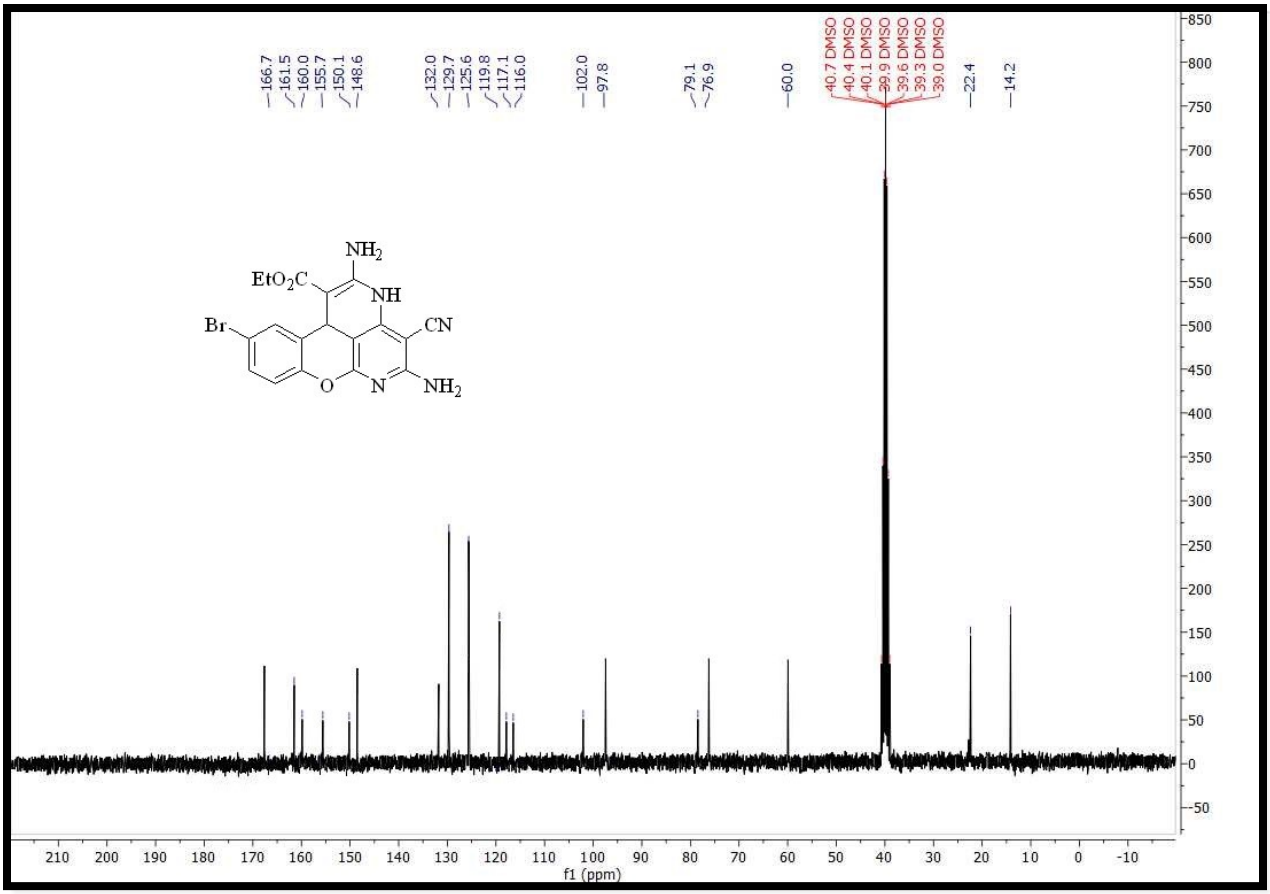


Figure 52: ^{13}C-NMR spectrum of compound **4z**

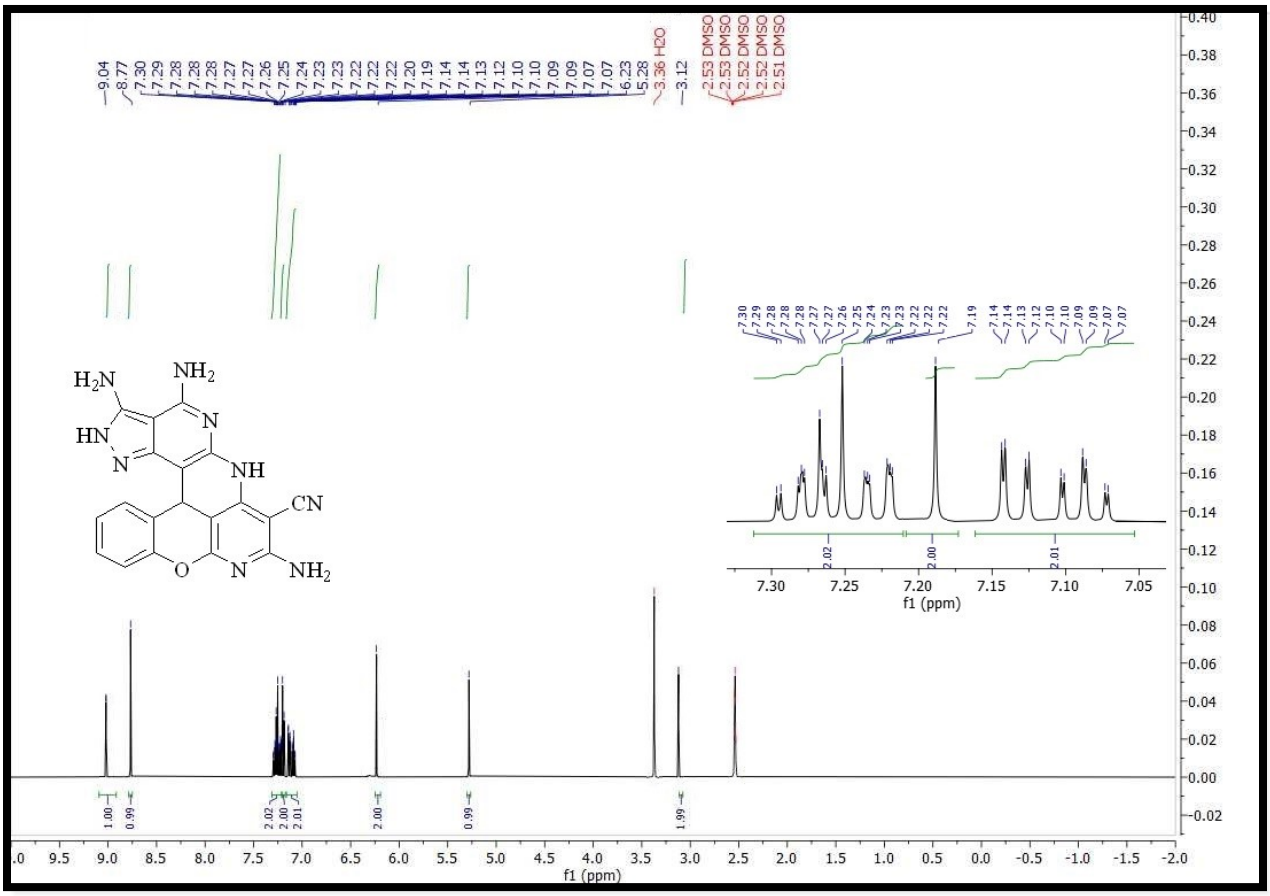


Figure 53: ^{1}H-NMR spectrum of compound **4aa**

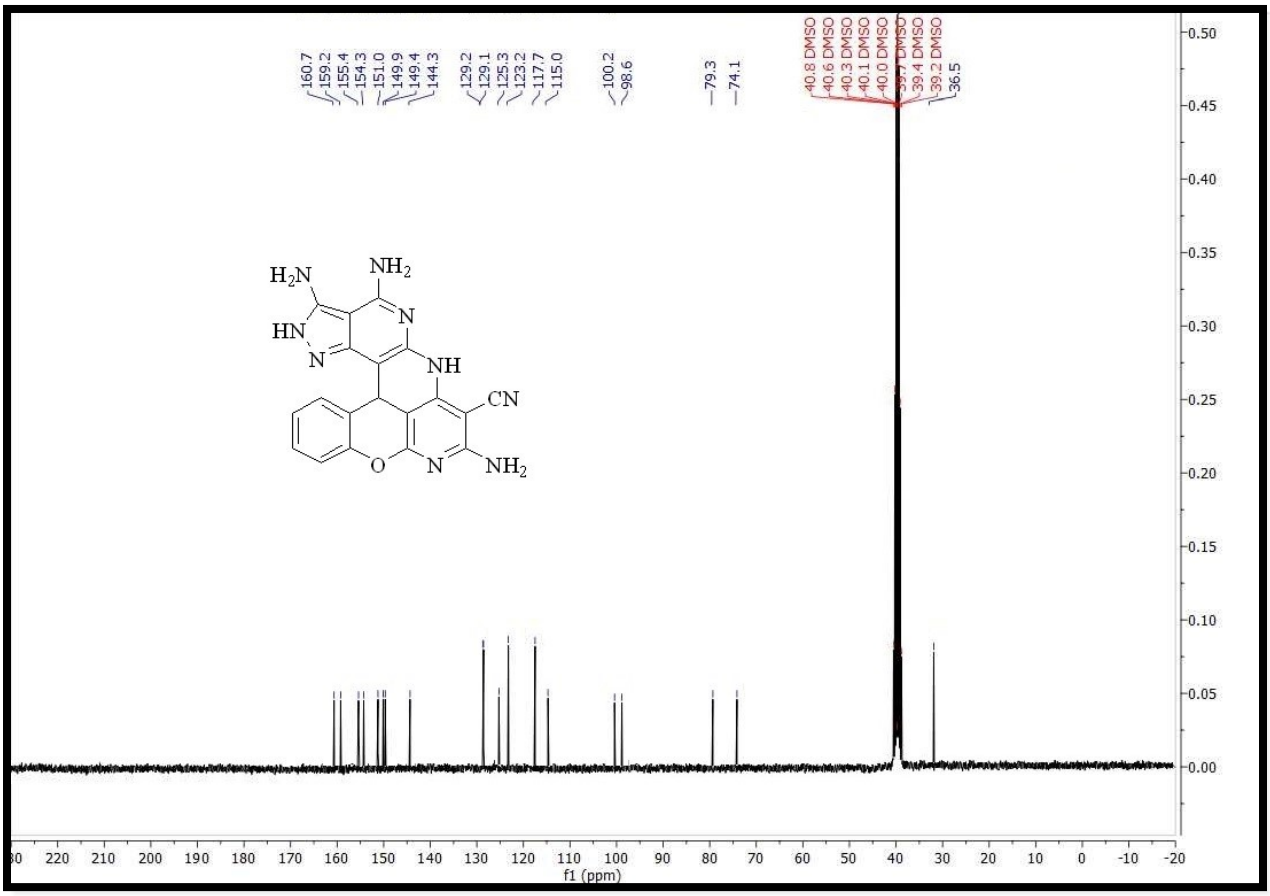


Figure 54: ^{13}C-NMR spectrum of compound **4aa**

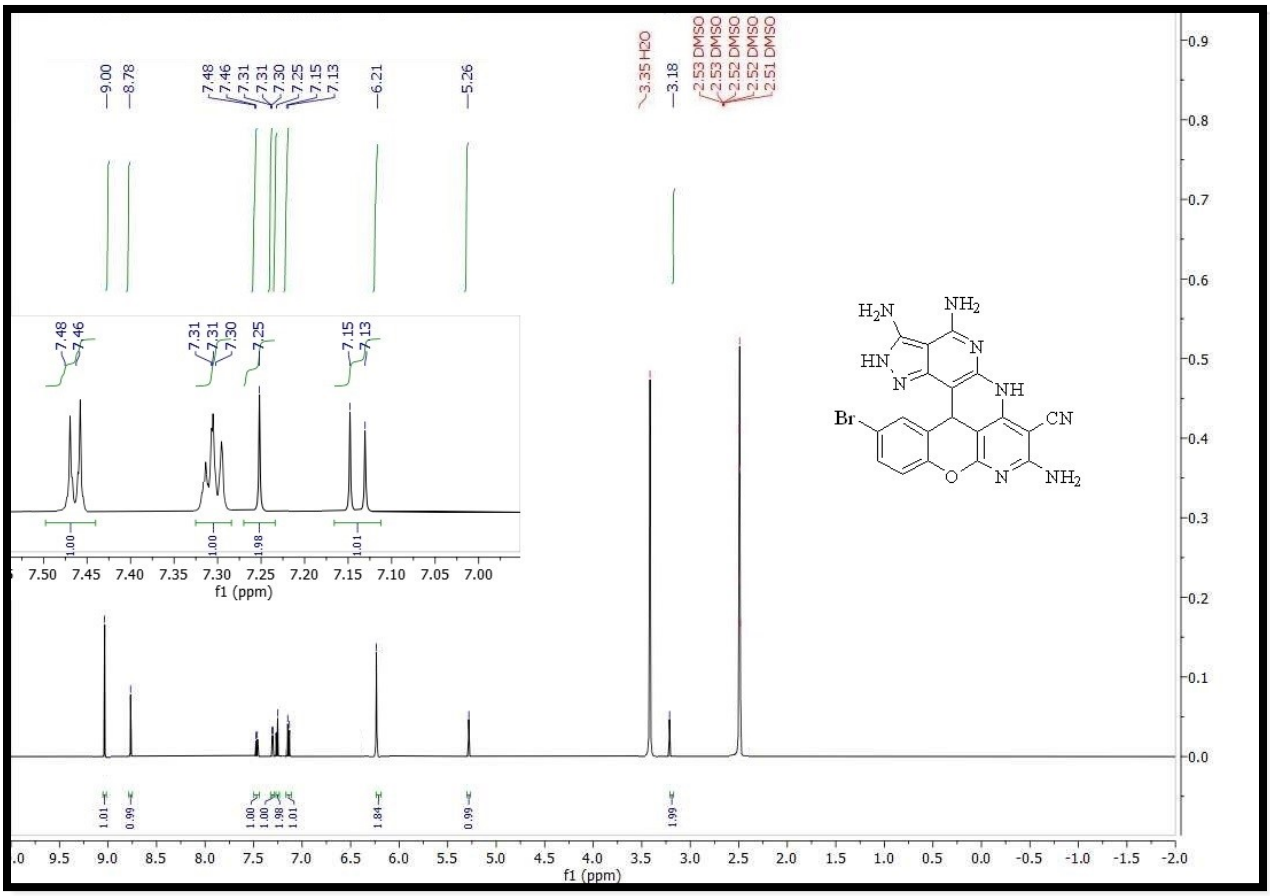


Figure 55: ^{1}H-NMR spectrum of compound **4ab**

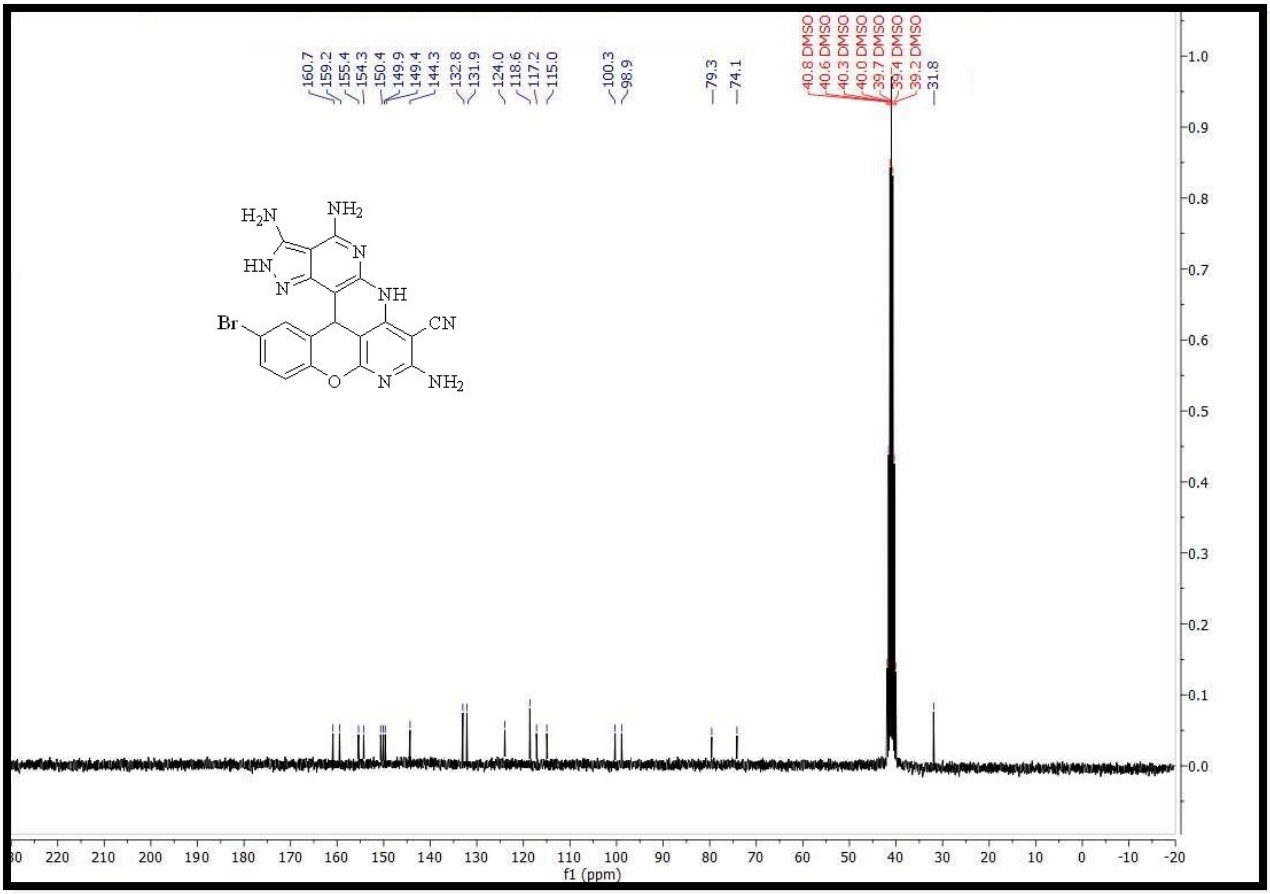


Figure 56: ^{13}C-NMR spectrum of compound **4ab**

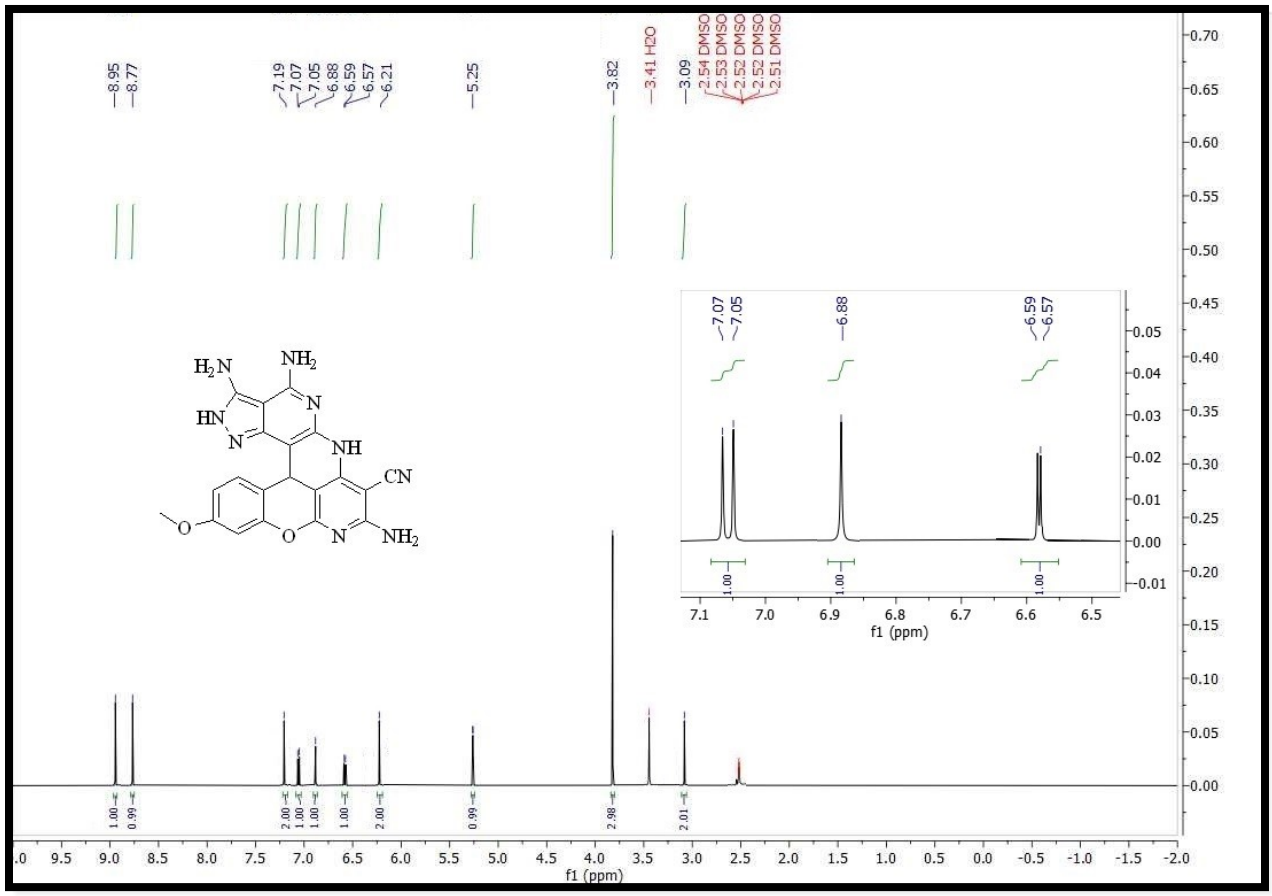


Figure 57: ^{1}H-NMR spectrum of compound **4ac**

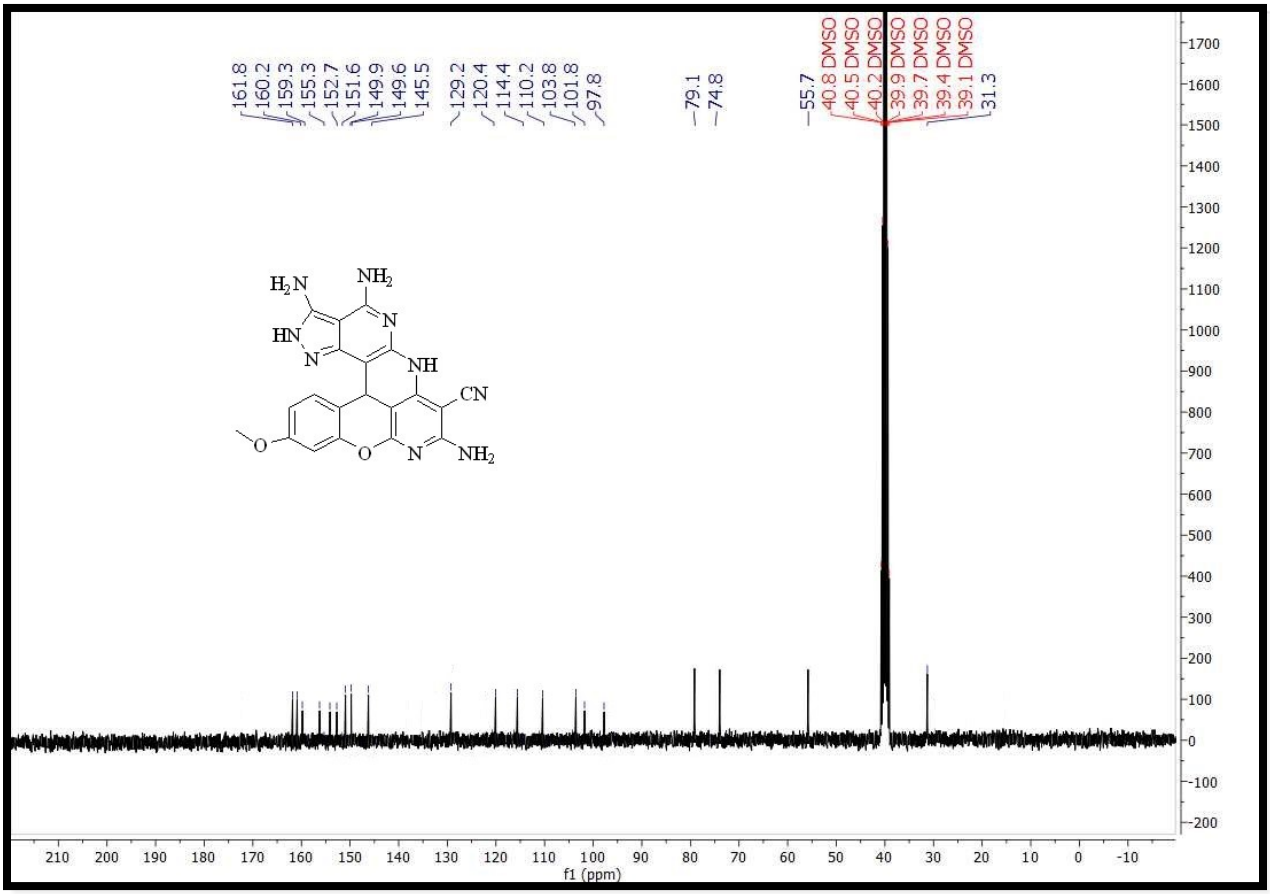


Figure 58: ^{13}C-NMR spectrum of compound **4ac**

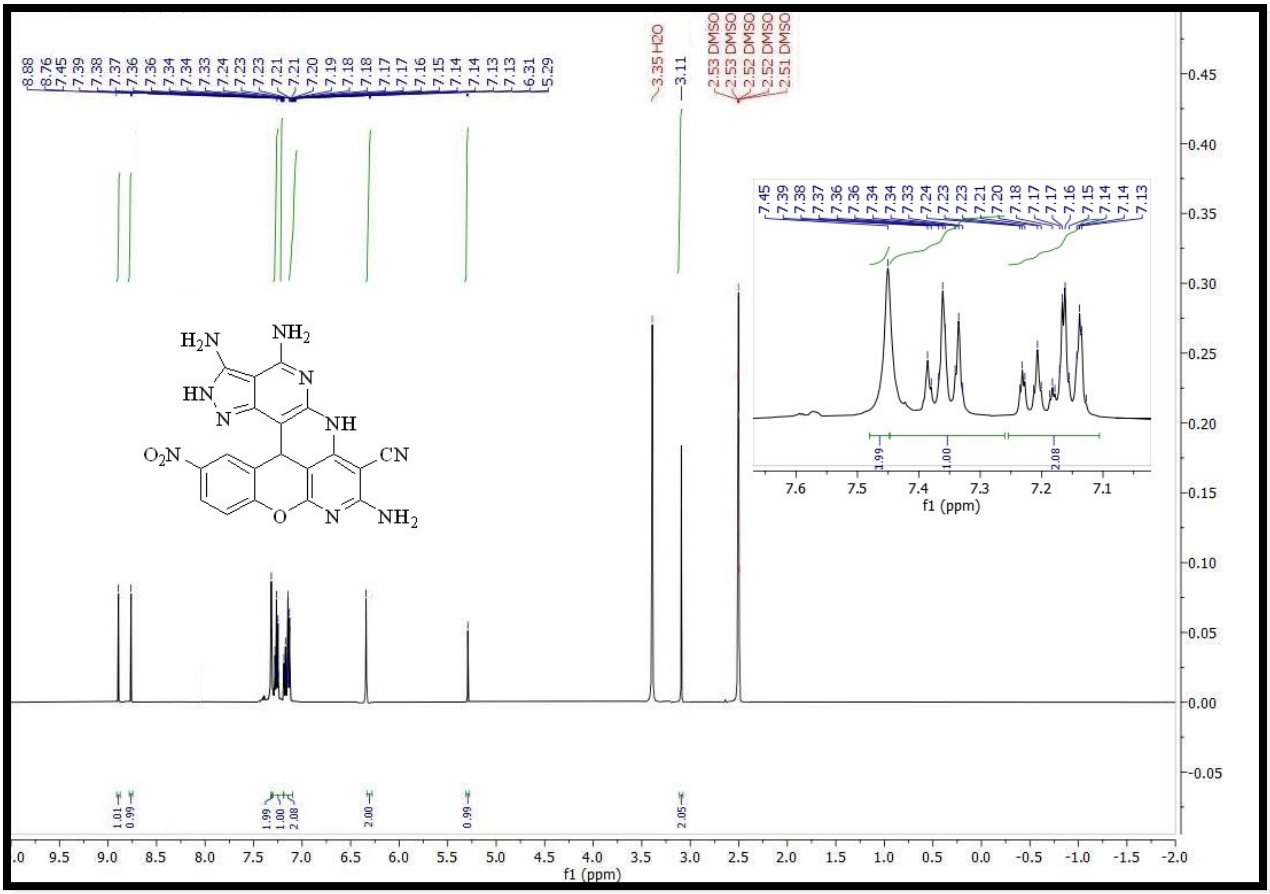


Figure 59: ^{1}H-NMR spectrum of compound **4ad**

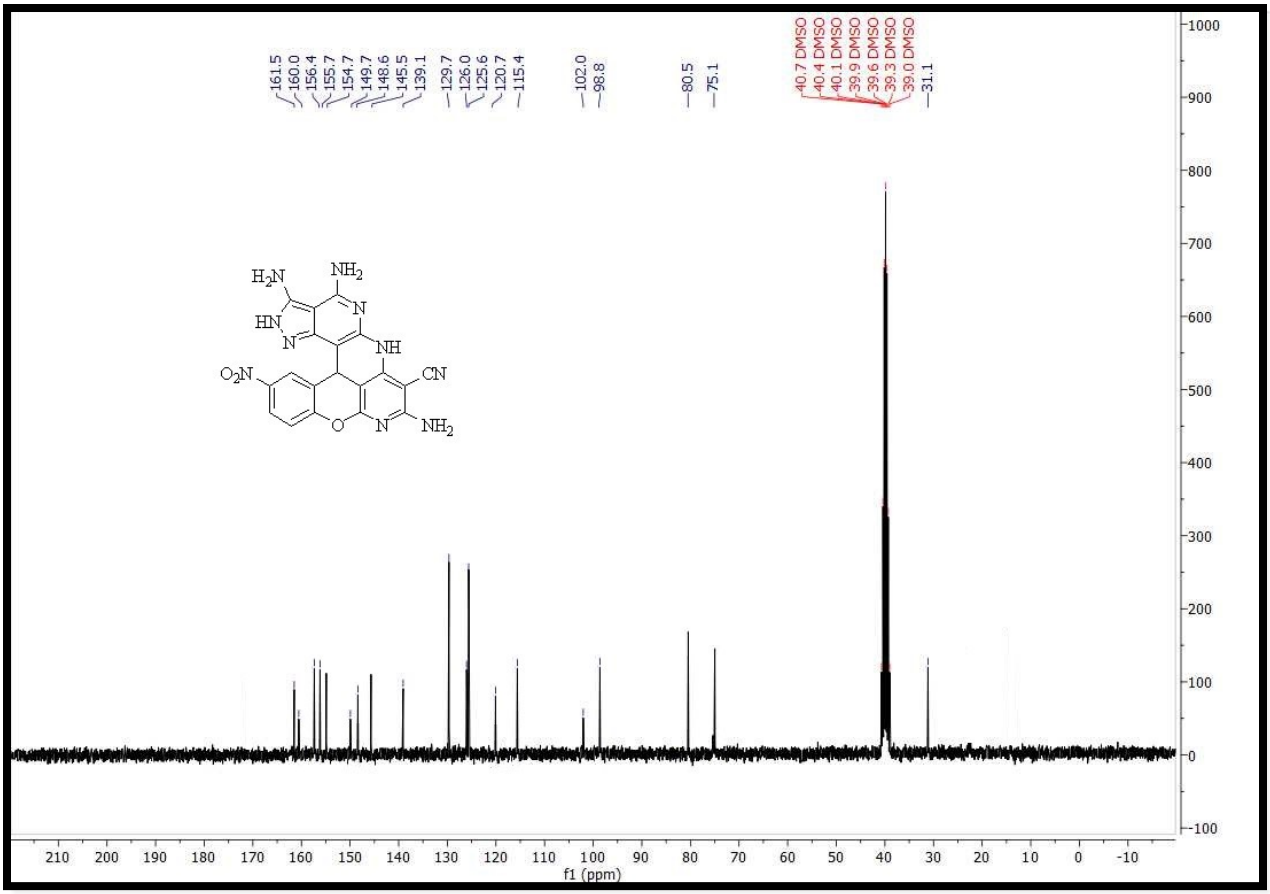


Figure 60: ^{13}C-NMR spectrum of compound **4ad**

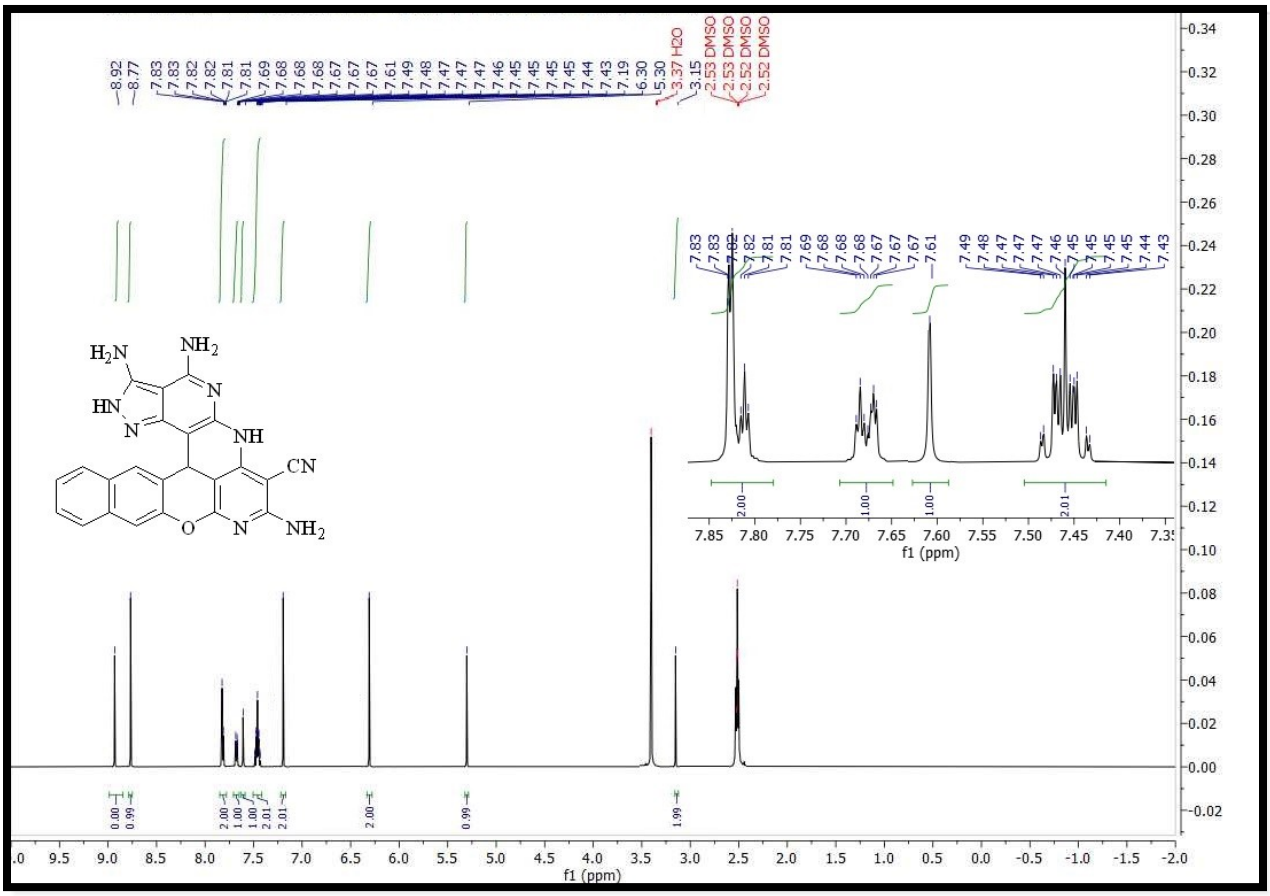


Figure 61: ^{1}H-NMR spectrum of compound **4ae**

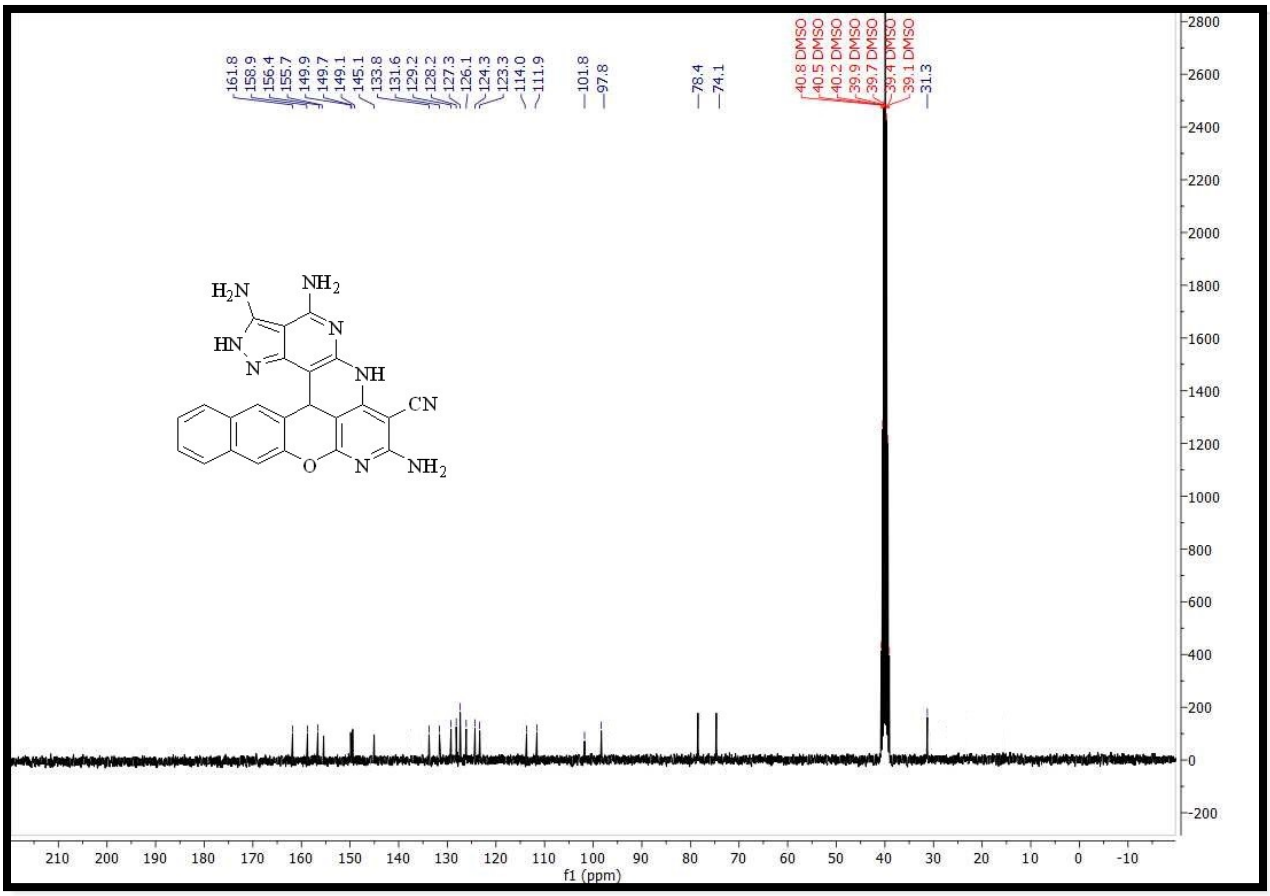


Figure 62: ^{13}C-NMR spectrum of compound **4ae**