applied sciences

MDPI

Supplementary Materials

1. General Information

1.1 Chemistry

All analytical grade chemicals were purchased from Supelco, Fisher and Fluka chemical companies. The X-ray powder diffraction (XRD) was carried out on a Bruker D8 Advance X-ray diffractometer with Cu-Kα radiation 1.5406 Å radiation at 40 kV and 40 mA in the Bragg-Brentano geometry (θ-2θ). The samples were analysed by FT-IR spectroscopy (using a SHIMADZU IRAffinity-1S in the range of 4000-400cm^{-1}). Scanning electron microscope (SEM) studies were performed on a HIROX SH-4000M. The TEM micrographs were performed on an FEI microscope at 120 kV. NMR studies were performed with a Bruker AVANCE 300 (^{1}H 300 MHz/^{13}C 75 MHz) spectrometer and JNM-ECZ500R/S1 FT NMR SYSTEM (JEOL) (^{1}H 500 MHz/^{13}C 125 MHz) spectrometer. The GC/MS analysis was performed using a Shimadzu GC-2010 gas chromatograph and interfaced with a Shimadzu QP2010 Plus mass spectrometer (software version 2.50 SU1). A DB-5 capillary column (30 m x 0.25 mm i.d., film thickness 0.25 µm; SGE, Ltd.) was used with the carrier gas helium adjusted to a linear velocity of 36.5 cm.s^{-1}. The MS transfer line temperature was set to 300°C; MS ionization temperature was set to 200°C. The split ratio was set to 1:40. Mass spectra were recorded at 70 eV, the mass range was 45-400 m/z. Melting points were determined in open capillary type on Stuart melting point SMP30. The elemental analyses were carried out with a EUROVECTOR EA3100 CHNS instrument. All the reactions were monitored by thin-layer chromatography (TLC) performed on Merck precoated silica gel of 60-120 mesh plates, and the compound were visualized with UV light at 254 nm.

1.2 Antibacterial and antifungal assay

Microbial Strains:

Ten microbial strains were used in the antimicrobial activity assay, which included eight American Type Culture Collection (ATCC) strains. ATCC strains were: *Escherichia coli* ATCC 25922 (*E. coli*), *Pseudomonas aeruginosa* ATCC 27853 (*P. aeruginosa*), *Staphylococcus aureus* ATCC 25923 (*S. aureus*), *Bacillus subtillis* ATCC6633 *(B. subtillis), staphylococcus epidermidis* ATCC12228 *(S. epidermidis), Enterococcus faecalis* ATCC29212 *(E. faecalis),* et *Klebsiella pneumonia* ATCC13883 *(K. pneumoniae)* and one fungal strain *Candida albicans* ATCC10231 *(C. albicans).*

Antimicrobial effect Screening:

Antibacterial and antifungal activities of the nine molecules were evaluated using the disc diffusion method in Mueller-Hinton Agar (MHA) as described by Kuete and al.

[1] with slight modifications. From the fresh cultures, a liquid bacterial suspension was prepared with a standard density of 0.5 McFarland (1×10^6 CFU/mL). Thereafter, 500 µL of the liquid was transferred to the petri dish containing MHA. The liquid was carefully distributed on the surface of MHA and let dry for 30 minutes at room temperature. Subsequently, we placed in each petri dish: a commercial antibiotic/antifungal disc for which the bacterium/fungus is susceptible which serves as a positive control, an empty sterile cellulose disc (6mm in diameter) soaked in sterile distilled water as a negative control and three discs each with 10 µL of one molecule suspension. The dishes were incubated 18-24h at 37°C then inhibition zone diameters were measured.

Minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC):

To determine Minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) for the active molecules, we used the antimicrobial micro-dilution broth test according to standards using a 96-well Elisa microplate [2].

2. Experimental Section

Methods:

2.1 Typical procedure for the synthesis of 2-amino-3-cyanopyridine derivatives 5.

In a 50 ml round bottom flask containing a mixture of aromatic aldehyde **1** (0.001 mol), malononitrile **2** (0.0726 gr, 0.0011 mol), methyl ketone or cyclohexanone **3** (0.001 mol), ammonium acetate (0.1156 gr, 0.0015 mol) and (1.92 mol, 0.05 gr) nanocatalyst $Na_2CaP_2O_7$ were stirred and heated to 80°C in an oil bath for 30 min under atmospheric air. The addition of excess ammonium acetate was used to shift the equilibrium in favor of imine 2′ which improves the yield of the reaction The progress of the reactions was monitored with thin-layer chromatography (TLC) using eluent (*n*-hexane-ethyl acetate, 8:2). After completion of the reaction, the mixture is cooled to room temperature. Acetone (25 mL) was added to the reaction mixture and stirred. Afterward, the reaction mixture was then filtered off by vacuum filtration. The recovered catalyst was washed with acetone, and the filtrate was concentrated by rotary evaporation.. The corresponding solid product was obtained through recrystallized with hydrated ethanol (96%) affording the pure 2-amino-3-cyanopyridine derivatives **5**. These derivatives were characterized by their melting points, spectroscopy FT-IR, ^{1}H-NMR, and ^{13}C-NMR.

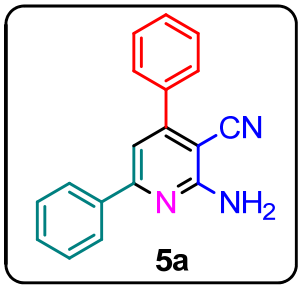
2.2 Typical procedure for the synthesis of pyrido[2,3-*d*]pyrimidine derivatives 6.

In a 100 ml flask, a mixture of 2-amino-3-cyanopyridine derivatives **5** (0.001 mol) and formamide (25 ml) was heated at 180-200°C in an oil bath for 16h. After completion of the reaction, the mixture is cooled to room temperature and 20 ml of cool water has been added stirring for 15 min. The isolated solid was filtered off, washed with water and recrystallized from ethanol affording the pure pyrido[2,3-*d*] pyrimidine derivatives **6.**

3. Compounds Characterization

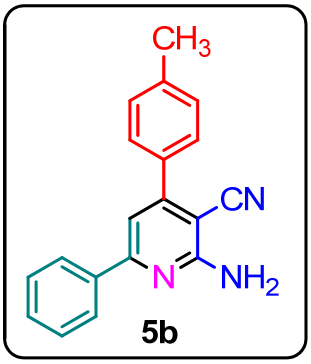
3.1 Spectral data of 2-amino-3-cyanopyridine 5

4-Phenyl-6-phenyl-2-amino-3-cyanopyridine 5a



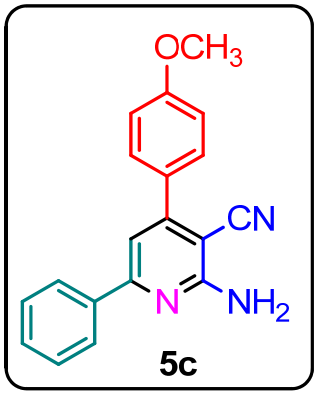
White solid, mp 183-186°C; FTIR (KBr) υ(cm^{-1}): 3464-3304 (NH_2), 3180 (Ar-H), 2206 (CN); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 5.45 (s, 2H, NH_2), 7.22 (m, 1H, H_{Ar}), 7.48 (m, 8H, H_{Ar}), 8.01 (m, 2H, H_{Ar}); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 88.33 (C_3), 111.31 (C_5), 117.16 (CN), 127.36 (C_{Ar}), 128.20 (C_{Ar}), 128.43 (C_{Ar}), 128.83 (C_{Ar}), 128.97 (C_{Ar}), 129.86 (C_{Ar}), 130.23 (C_{Ar}), 136.9 (C_{Ar}), 137.97 (C_{Ar}), 155.17 (C_4), 159.87 (C_6), 160.29 (C_2). These results are similar to the data published in the literature [3].

4-(4-Methylphenyl)-6-phenyl-2-amino-3-cyanopyridine 5b



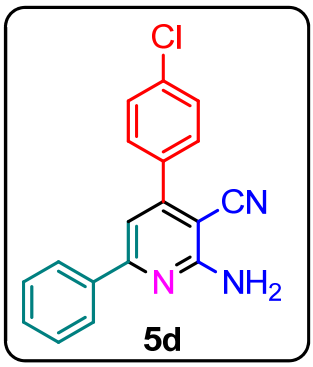
Yellow solid, mp 172-175°C; FTIR (KBr): υ(cm^{-1}): 3500-3306 (NH_2), 3215 (Ar-H), 2228 (CN); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 2.48 (s, 3H, CH_3), 5.45 (s, 2H, NH_2), 7.23(m, 1H), 7.38-7.36 (m, 2H, H_{Ar}), 7.60-7.50 (m, 5H, H_{Ar}), 8.05-8.02 (m, 2H, H_{Ar}); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 21.40 (CH_3), 88.26 (C_3), 111.20 (C_5), 117.34 (CN), 127.16 (C_{Ar}), 127.35 (C_{Ar}), 128.10 (C_{Ar}), 128.72 (C_{Ar}), 128.83 (C_{Ar}), 129.02 (C_{Ar}), 129.67 (C_{Ar}), 129.86 (C_{Ar}), 130.01 (C_{Ar}), 130.16 (C_{Ar}), 134.07 (C_{Ar}), 138.07 (C_{Ar}), 140.11(C_{Ar}-CH_3), 155.18 (C_4), 159.77 (C_6), 160.33 (C_2). These results are described by the literature [4].

4-(4-Methoxyphenyl)-6-phenyl-2-amino-3-cyanopyridine 5c



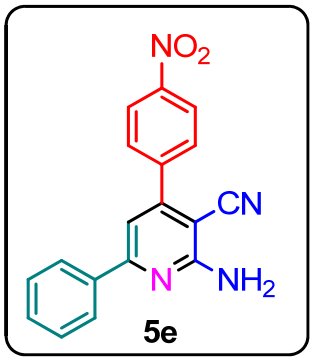
Yellow solid, mp 182-183°C; FTIR (KBr) υ(cm^{-1}): 3466-3307 (NH_2), 3184(Ar-H), 2206(CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 3.80 (s, 3H, OCH_3), 6.92 (s, 2H, NH_2), 7.02 – 7.10 (m, 2H, H_{Ar}), 7.20 (s, 1H, H_{Ar}), 7.40 – 7.49 (m, 3H, H_{Ar}), 7.58 – 7.65 (m, 2H, H_{Ar}), 8.03 – 8.11 (m, 2H, H_{Ar}). ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 55.89 (OCH_3), 86.90 (C_3), 109.58 (C_5), 114.70 (C_{Ar}), 117.88 (CN), 127.76 (C_{Ar}), 129.18 (C_{Ar}), 129.60 (C_{Ar}), 130.41 (C_{Ar}), 130.59 (C_{Ar}), 138.18 (C_{Ar}), 155.02 (C_4), 159.02 (C_6), 160.96 (C_2), 161.50 (CAr-O). These results are following the literature [5].

4-(4-Chlorophenyl)-6-phenyl-2-amino-3-cyanopyridine 5d



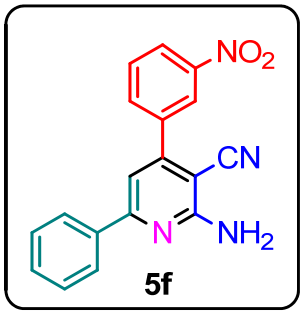
White solid: mp 239-241°C; FTIR (KBr) υ(cm^{-1}): 3446-3315 (NH_2), 3151(Ar-H), 2215(CN). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.38(s, 2H, NH_2).7.18-7.08(m, 1H), 7.51-7.38(m, 7H), 7.92-7.89(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 88.03 (C_3), 111.00(C_5), 116.95(CN), 127.36(C_{Ar}), 128.40(C_{Ar}), 128.60(C_{Ar}), 128.87(C_{Ar}), 128.99(C_{Ar}), 129.28(C_{Ar}), 129.55(C_{Ar}), 129.77(C_{Ar}), 130.37(C_{Ar}), 135.33(C_{Ar}), 136.16(C_{Ar}), 137.79 ($C_{Ar\text{-}Cl}$), 153.86(C_4), 160.09(C_6), 160.30(C_2). These results are also found in the literature [3].

4-(4-Nitrophenyl)-6-phenyl-2-amino-3-cyanopyridine 5e



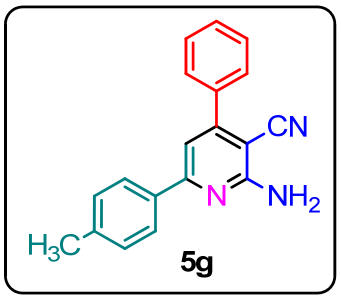
Green solid, mp 221-223°C; FTIR (KBr) υ(cm^{-1}): 3460-3352 (NH_2), 3244 (Ar-H), 2208 (CN). ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 6.80 (s, 1H, NH_2), 6.92 (s, 1H, NH_2), 7.12 (s, 1H, H_{Ar}), 7.29 (s, 1H, H_{Ar}), 7.39 – 7.53 (m, 2H, H_{Ar}), 7.55 – 7.63 (m, 1H, H_{Ar}), 7.89 (dd, J=17.90, 8.37 Hz, 2H, H_{Ar}), 8.08 (dd, J=6.71, 2.94 Hz, 1H, H_{Ar}), 8.32 (dd, J=16.80, 8.35 Hz, 2H, H_{Ar}); ^{13}C NMR(DMSO-d_6, 126 MHz) δ (ppm): 94.38 (C_3), 109.67 (C_5), 116.36 (CN), 124.24 (C_{Ar}), 127.83 (C_{Ar}), 129.12 (C_{Ar}), 129.22 (C_{Ar}), 130.14 (C_{Ar}), 130.54 (C_{Ar}), 130.86 (C_{Ar}), 137.73 (C_{Ar}), 148.54 (C-NO_2), 153.29 (C_4), 154.60 (C_6), 161.29 (C_2). These results are reported in the literature [3].

4-(3-Nitrophenyl)-6-phenyl-2-amino-3-cyanopyridine 5f



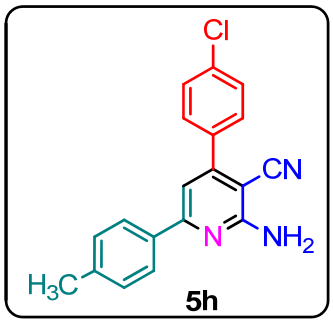
Yellow solid, mp 202-204°C; FTIR (KBr) υ(cm^{-1}): 3465-3349 cm-1 (NH_2), 3214 (Ar-H), 2223 (CN); ^{1}H NMR(DMSO-d_6, 500 MHz) δ (ppm): 6.90 (d, J=13.84 Hz, 3H, NH_2), 7.43 – 7.55 (m, 3H), 7.57 – 7.66 (m, 2H), 7.79 (t, J=8.01 Hz, 1H), 8.08 (ddd, J=7.73, 1.84, 1.01 Hz, 1H), 8.32 (ddd, J=8.30, 2.29, 0.99 Hz, 1H), 8.43 (t, J=2.00 Hz, 1H); ^{13}C NMR(DMSO-d_6, 126 MHz) δ (ppm): 94.60 (C3), 95.43 (C5), 116.41 (CN), 119.18 (CAr), 124.00 (CAr), 124.69 (CAr), 129.16 (CAr), 129.25 (CAr), 130.12 (CAr), 130.89 (CAr), 135.87 (CAr), 137.78 (CAr), 139.36 (CAr), 147.91 (C-NO_2), 148.34 (C_4), 150.73 (C_6), 154.61 (C_2). The literature confirmed these results [6].

4-Phenyl-6-(4-methylphenyl)-2-amino-3-cyanopyridine 5g



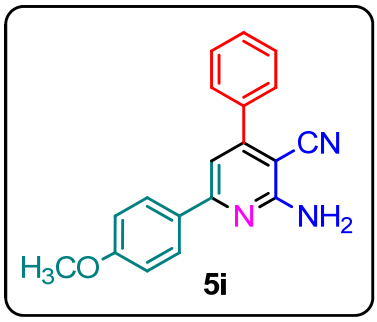
Yellow solid, mp 166-168°C; FTIR (KBr) υ(cm^{-1}): 3481-3300 (NH_2), 3182 (Ar-H), 2203 (CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 2.29 (s, 3H, CH_3), 6.95 (s, 2H, NH_2), 7.18 (s, 1H, H_{Ar}), 7.21 – 7.26 (m, 2H, H_{Ar}), 7.44 – 7.54 (m, 3H, H_{Ar}), 7.58 – 7.65 (m, 2H, H_{Ar}), 7.95 – 8.01 (m, 2H, H_{Ar}); ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 21.43 (CH_3), 86.81 (C_3), 109.43 (C_5), 117.71(CN), 127.71 (C_{Ar}), 128.85 (C_{Ar}), 129.26 (C_{Ar}), 129.79 (C_{Ar}), 130.08 (C_{Ar}), 135.28 (C_{Ar}), 137.58 ($C_{Ar\text{-}Cl}$), 140.46 ($C_{Ar\text{-}CH3}$), 155.31 (C_4), 159.15 (C_6), 161.41 (C_2). These results are mentioned in the literature [7].

4-(4-chlorophenyl)-6-(4-methylphenyl)-2-amino-3-cyanopyridine 5h



Yellow solid, mp 175-177°C; FTIR (KBr) υ(cm^{-1}): 3422-3297 (NH_2), 3130 (Ar-H), 2212 (CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 2.31 (s, 3H, CH_3), 6.98 (s, 2H, NH_2), 7.19 (s, 1H, HAr), 7.25 (d, J=7.96 Hz, 2H, H_{Ar}), 7.55 – 7.60 (m, 2H, H_{Ar}), 7.62 – 7.67 (m, 2H, H_{Ar}), 7.95 – 8.02 (m, 2H, H_{Ar}); ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 21.45 (CH_3), 86.60 (C_3), 109.31 (C_5), 117.51 (CN), 127.74 (C_{Ar}), 129.29 (C_{Ar}), 129.80 (C_{Ar}), 130.80 (C_{Ar}), 135.01 (C_{Ar}), 135.18 (C_{Ar}), 136.35 ($C_{Ar\text{-}Cl}$), 140.57 ($C_{Ar\text{-}CH3}$), 154.04 (C_4), 159.25 (C_6), 161.34 (C_2).

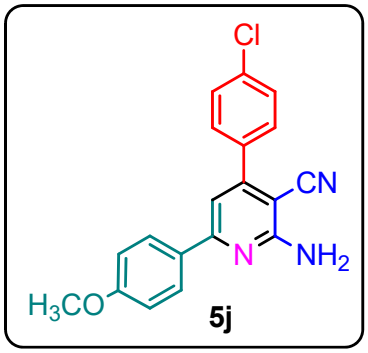
4-(phenyl)-6-(4-methoxyphenyl)-2-amino-3-cyanopyridine 5i



Yellow solid, mp 167-169°C; FTIR (KBr) υ(cm^{-1}): 3414-3307 (NH_2), 3140 (Ar-H), 2211 (CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 3.77 (s, 3H, OCH_3), 6.91 (s, 2H, NH_2), 6.96

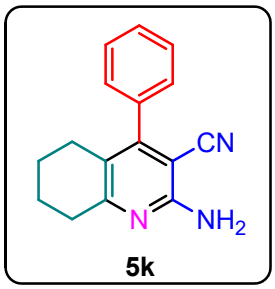
– 7.04 (m, 2H, H_{Ar}), 7.17 (s, 1H, H_{Ar}), 7.44 – 7.56 (m, 3H, H_{Ar}), 7.57 – 7.65 (m, 2H, H_{Ar}), 8.04 – 8.10 (m, 2H, H_{Ar}); ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 55.83(OCH_3), 86.21(C_3), 108.98(C_5), 114.54(C_{Ar}), 117.80 (CN), 128.85 (C_{Ar}), 129.26 (C_{Ar}), 129.39 (C_{Ar}), 130.06 (C_{Ar}), 130.39 (C_{Ar}), 137.66 (C_{Ar}), 155.22 (C_4), 158.84 (C_6), 161.36 (C_2), 161.53 (C_{Ar}-O). These results are agreed with the literature [4,7].

4-(4-chlorophenyl)-6-(4-methoxyphenyl)-2-amino-3-cyanopyridine 5j



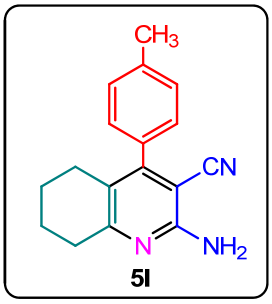
Yellow solid, mp 186-187°C; FTIR (KBr) υ(cm^{-1}): 3454-3360 (NH_2), 3228 (Ar-H), 2206 (CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 3.77 (s, 3H, OCH_3), 6.95 (s, 2H, NH_2), 6.96 – 7.02 (m, 2H, H_{Ar}), 7.17 (s, 1H, H_{Ar}), 7.53 – 7.60 (m, 2H, H_{Ar}), 7.61 – 7.67 (m, 2H, H_{Ar}), 8.02 – 8.09 (m, 2H, H_{Ar}); ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 50.80 (OCH_3), 88.66 (C_3), 113.13 (C_5), 117.31 (CN), 118.97 (C_{Ar}), 120.83 (C_{Ar}), 127.28 (C_{Ar}), 128.53 (C_{Ar}), 129.67 (C_{Ar}), 133.94 (C_{Ar}), 138.47 ($C_{Ar\text{-}Cl}$), 144.12 (C_4), 154.58 (C_6), 158.45 (C_2), 161.38 (C_{Ar}-O). The literature confirmed these results [5].

4-phenyl-5,6,7,8-tetrahydro-benzo[5,6-*b*]-2amino-3-cyanopyridine 5k



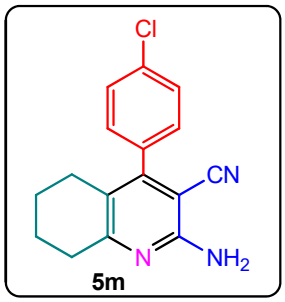
Yellow solid, mp 233-235°C; FTIR (KBr) υ(cm^{-1}): 3488-3364 (NH_2), 2949-2911 (CH_2), 2201 (CN); ^{1}H NMR (300 MHz, CDCl3) δ (ppm): 1.52 – 1.68 (m, 2H, CH_2), 1.68 – 1.83 (m, 2H, CH_2), 2.26 (t, J=6.29 Hz, 2H, CH_2), 2.74 (t, J=6.50 Hz, 2H, CH_2), 5.12 (s, 2H, NH_2), 7.13 – 7.25 (m, 2H H_{Ar}), 7.28 – 7.48 (m, 3H, H_{Ar}); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 22.55 (CH_2), 22.86 (CH_2), 26.47 (CH_2), 33.32 (CH_2), 90.09 (C_3), 116.69 (CN), 120.82 (C_5), 128.09 (C_{Ar}), 128.70 (C_{Ar}), 128.85 (C_{Ar}), 136.18 (C_{Ar}), 154.55 (C_4), 157.15 (C_2), 161.43 (C_6). These results are mentioned in the literature [4].

4-(4-Methylphenyl)-5,6,7,8-tetrahydro-benzo[5,6-*b*]-2amino-3-cyanopyridine 5l



Yellow solid, mp 252-254°C; FTIR (KBr) υ(cm^{-1}): 3488-3364 (NH_2), 2933-2905 (CH_2), 2201 (CN); ^{1}HNMR (DMSO-d_6, 500 MHz) δ (ppm): 1.49–1.56 (m, 2H, CH_2), 1.68 (td, J=6.24, 2.76 Hz, 2H, CH_2), 2.16 (t, J=6.32 Hz, 2H, CH_2), 2.31 (dd, J=16.00, 1.47 Hz, 3H, CH_3), 2.62 – 2.68 (m, 2H, CH_2), 6.48 (s, 2H, NH_2), 7.12 (dd, J=8.00, 1.66 Hz, 2H, H_{Ar}), 7.23 – 7.28 (m, 2H, H_{Ar}). ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 21.38 (CH_3), 22.63 (CH_2), 22.99 (CH_2), 26.41 (CH_2), 33.33 (CH_2), 88.66 (C_3), 117.31 (CN), 118.97 ($C_{4'}$), 120.83 (C_{Ar}), 128.53 (C_{Ar}), 129.67 (C_{Ar}), 133.94 (C_{Ar}), 138.47 (C_{Ar}), 154.58 (C_4), 158.45 (C_2), 161.38 ($C_{8'}$). The literature confirmed these results [8].

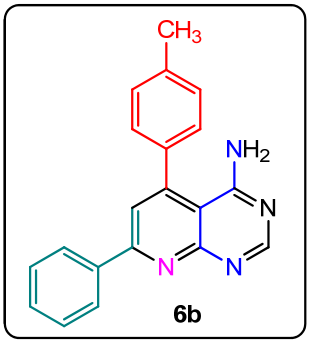
4-(4-chlorophenyl)-5,6,7,8-tetrahydro-benzo[5,6-*b*]-2amino-3-cyanopyridine 5m



Yellow solid, mp 246-249°C; FTIR (KBr) υ(cm^{-1}): 3463-3310 (NH_2), 3172-3109 (CH_2), 2206 (CN). ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 1.50 – 1.58 (m, 2H, CH_2), 1.64 – 1.73 (m, 2H, CH_2), 2.14 (t, J=6.34 Hz, 2H, CH_2), 2.65 (t, J=6.50 Hz, 2H, CH_2), 6.56 (s, 2H, NH_2), 7.26 – 7.32 (m, 2H, H_{Ar}), 7.49 – 7.56 (m, 2H, H_{Ar}); ^{13}C NMR (DMSO-d_6, 126 MHz): δ (ppm) 22.57(CH_2), 22.93(CH_2), 26.30(CH_2), 33.35(CH_2), 88.33(C_3), 117.11(CN), 118.78($C_{4'}$), 129.24(C_{Ar}), 130.68(C_{Ar}), 133.97(C_{Ar}), 135.72(C_{Ar}), 153.25(C_4), 158.41(C_2), 161.71($C_{8'}$). These results are mentioned in the literature [3].

3.2 Spectral data of pyrido[2,3-*d*]pyrimidine 6

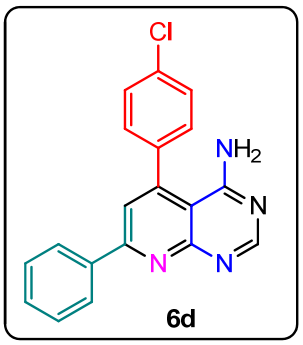
7-phenyl-5-(*p*-tolyl)pyrido[2,3-*d*]pyrimidin-4-amine 6b



6b

Yellow solid, mp 302-305°C; FTIR (KBr) υ(cm^{-1}): 3532-3340 (NH_2), 3316 (Ar-H), 1605-1524 (C=C, C=N); ^{1}H NMR(DMSO-d_6, 500 MHz) δ (ppm): 2.39 (s, 3H, CH_3), 6.36 (s, 1H, NH_2), 7.19 (s, 2H, H_{Ar}), 7.29 (s, 2H, H_{Ar}), 7.37 – 7.43 (m, 1H, H_{Ar}), 7.48 (d, J=7.72 Hz, 1H, H_{Ar}), 7.54 (d, J=5.34 Hz, 1H, H_{Ar}), 7.91 (d, J=13.48 Hz, 1H, H_{Ar}), 8.01 (s, 1H, H_{Ar}), 8.25 – 8.31 (m, 1H, H_{Ar}), 8.76 (s, 1H, $H_{Ar\text{-}C=N}$), 9.38 – 9.42 (m, 1H,NH_2). ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 21.49 (CH_3), 105.27 ($C_{4'}$), 122.63 (C_6), 129.3 (C_{Ar}), 129.69 (C_{Ar}), 130.47 (C_{Ar}), 132.02 (C_{Ar}), 134.05 (C_{Ar}), 136.83 ($C_{\text{-}CH3}$), 140.36 (C_5), 151.59 (C_7), 161.84 (C=N), 163.53 (C-NH_2), 164.06 ($C_{8'}$).MS, m/z (%): 311 [M^+ -1] (100); Analysis calculated for $C_{20}H_{16}N_4$ (%): C, 76.90; H, 5.16; N, 17.94. Found: C, 76.71, H, 4.98, N, 17.75.

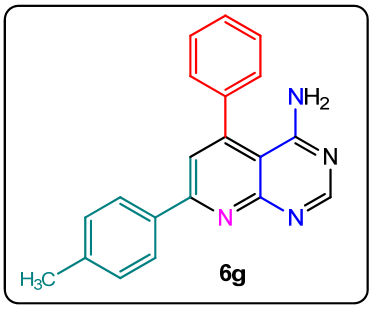
5-(4-chlorophenyl)-7-phenylpyrido[2,3-*d*]pyrimidin-4-amine 6c



6d

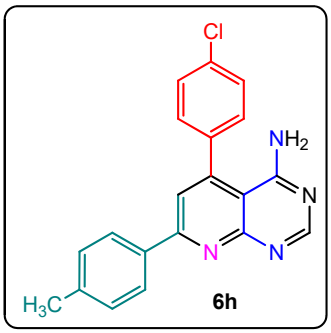
Brown solid, mp 324-328°C; FTIR (KBr) υ(cm^{-1}): 3412-3357 (NH_2), 3108 (Ar-H), 1611-1497 (C=C, C=N); ^{1}H NMR(DMSO-d_6, 500 MHz) δ (ppm): 7.16 (s, 1H, NH_2), 7.26 (s, 1H, H_{Ar}), 7.36 (s, 1H, H_{Ar}), 7.58 (dt, J=5.37, 3.44 Hz, 2H, H_{Ar}), 7.67 (s, 3H, H_{Ar}), 8.13 (s, 1H, H_{Ar}), 8.32 (dd, J=7.63, 2.21 Hz, 2H, H_{Ar}), 8.85 (s, 1H, HAr), 9.85 (s, 1H, NH2); ^{13}C NMR(DMSO-d6, 126 MHz) δ (ppm): 104.75 (C4'), 129.76 (C_6), 129.90 (C_{Ar}), 131.72 (C_{Ar}), 134.97 (C_{Ar}), 135.73 (C_{Ar}), 136.42 (C-Cl), 150.54 (C_5), 153.33 (C_7), 162.24 (C=N), 163.53 (C-NH_2), 164.19 ($C_{8'}$); MS, m/z (%): 331 [M^+ -1] (100); Analysis calculated for $C_{19}H_{13}ClN_4$ (%): C, 68.57; H, 3.94; N, 16.84. Found: C, 68.72, H, 3.74, N, 17.01.

5-phenyl-7-(p-tolyl)pyrido[2,3-*d*]pyrimidin-4-amine 6g



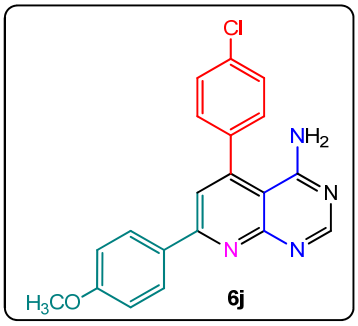
Orange, mp 307-311°C; FTIR (KBr) υ(cm^{-1}): 3521-3341 (NH_2), 3321 (Ar-H), 1610-1534 (C=C, C=N); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 2.34 (s, 3H, CH_3), 7.13 – 7.18 (m, 1H, H_{Ar}), 7.31 (d, J=7.78 Hz, 2H, NH_2), 7.36 – 7.44 (m, 1H, H_{Ar}), 7.55 (d, J=14.83 Hz, 5H, H_{Ar}), 7.79 (s, 1H, H_{Ar}), 8.16 (d, J=7.79 Hz, 2H, H_{Ar}), 8.52 (s, 1H, $H_{Ar\text{-}C=N}$); ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 21.48(CH_3) , 105.86 ($C_{4'}$), 120.43 (C_6), 128.14 (C_{Ar}), 129.06 (C_{Ar}), 129.70 (C_{Ar}), 129.92 (C_{Ar}), 130.09 (C_{Ar}), 135.21 (C_{Ar}), 138.90 (C_{Ar}), 141.05 (C-CH_3), 150.23 (C_5), 158.89 (C_7), 160.76 (C=N), 162.77 (C-NH_2), 163.52 ($C_{8'}$); MS, m/z (%): 311 [M^+ -1] (100); Analysis calculated for $C_{20}H_{16}N_4$ (%): C, 76.90; H, 5.16; N, 17.94. Found: C, 76.81, H, 4.97, N, 18.17.

5-(4-chlorophenyl)-7-(p-tolyl)pyrido[2,3-*d*]pyrimidin-4-amine 6h



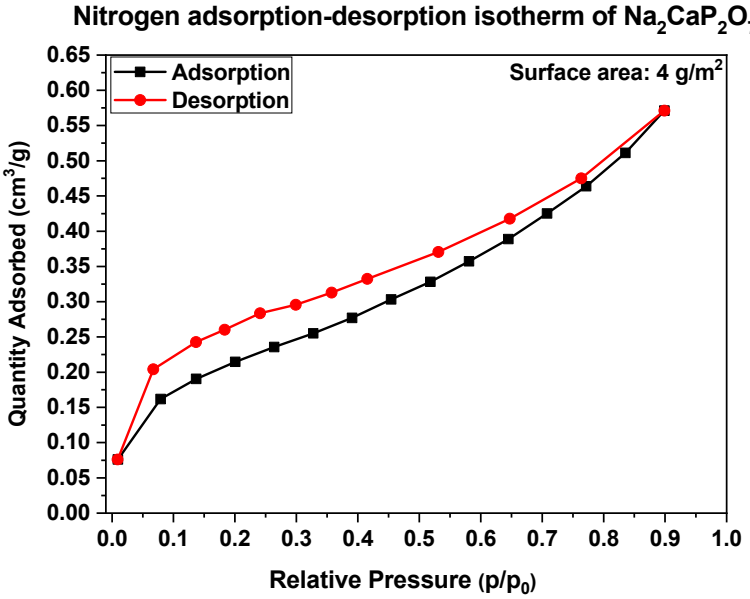
Brown solid, mp 299-304°C; FTIR (KBr) υ(cm^{-1}): 3515-3309 (NH_2), 3099 (Ar-H), 1608-1524 (C=C, C=N); ^{1}H NMR(DMSO-d6, 500 MHz) δ (ppm): 2.46(s, 3H, CH_3), 6.97 (s, 1H, NH_2), 7.42 (s, 5H, $H_{Ar\text{-}NH2}$), 7.57 (d, J=8.16 Hz, 1H, H_{Ar}), 7.59 – 7.68 (m, 1H, H_{Ar}), 7.93 (d, J=13.54 Hz, 4H, H_{Ar}); ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 21.44 (CH_3), 109.33 ($C_{4'}$), 117.50 (C_6), 127.74 (C_{Ar}), 129.30 (C_{Ar}), 129.57 (C_{Ar}), 129.82 (C_{Ar}), 130.80 (C_{Ar}), 135.02 (C_{Ar}), 135.18 (C_{Ar}), 136.35 ($C_{Ar\text{-}Cl}$), 140.59 (C_5), 154.06 (C_7), 159.27 (C=N), 161.33 (C-NH_2), 163.58 ($C_{8'}$); MS, m/z (%): 345 [M^+ -1] (100); Analysis calculated for $C_{20}H_{15}ClN_4$ (%):C, 69.26; H, 4.36; N, 16.15. Found: C, 69.35, H, 4.52, N, 16.02.

5-(4-chlorophenyl)-7-(4-methoxyphenyl)pyrido[2,3-*d*]pyrimidin-4-amine 6j



Green solid, mp 254-258°C; FTIR (KBr) υ(cm-1): 3515-3309 (NH_2), 3099 (Ar-H), 1608-1524 (C=C, C=N); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 3.80 (s, 3H, OCH_3), 7.01 – 7.08 (m, 2H, NH_2), 7.35 – 7.49 (m, 1H, H_{Ar}), 7.55 – 7.60 (m, 2H, H_{Ar}), 7.60 – 7.66 (m, 2H, H_{Ar}), 7.78 (s, 1H, H_{Ar}), 7.93 (dd, J=13.52, 1.77 Hz, 1H, H_{Ar}), 8.18 – 8.28 (m, 2H, H_{Ar}), 8.50 (s, 1H, H_{Ar}); ^{13}C NMR (DMSO-d_6, 126 MHz) δ (ppm): 55.90 (OCH_3), 105.30 ($C_{4'}$), 114.84 (C_6), 120.29 (C_{Ar}), 129.56 (C_{Ar}), 129.85 (C_{Ar}), 130.27 (C_{Ar}), 131.26 (C_{Ar}), 134.78 (C_{Ar}), 137.51 (C_{Ar}), 148.83 ($C_{Ar\text{-}Cl}$), 158.79 (C_5), 160.29 (C7), 160.49 (C=N), 161.98 ($C_{Ar\text{-}O}$), 162.62 (C-NH_2), 163.53 ($C_{8'}$); MS, m/z (%): 361 [M^+ -1] (70), 346 [M^+ -16] (100); Analysis calculated for $C_{20}H_{15}ClN_4O$ (%): C, 66.21; H, 4.17; N, 15.44. Found: C, 66.26, H, 4.37, N, 15.31.

3.3 BET nitrogen adsorption-desorption isotherm of $Na_2CaP_2O_7$:



3.4 Copies of ^{1}H-NMR and ^{13}C-NMR spectral data of the different synthesized products and the MS of the new compounds 6b-6j:

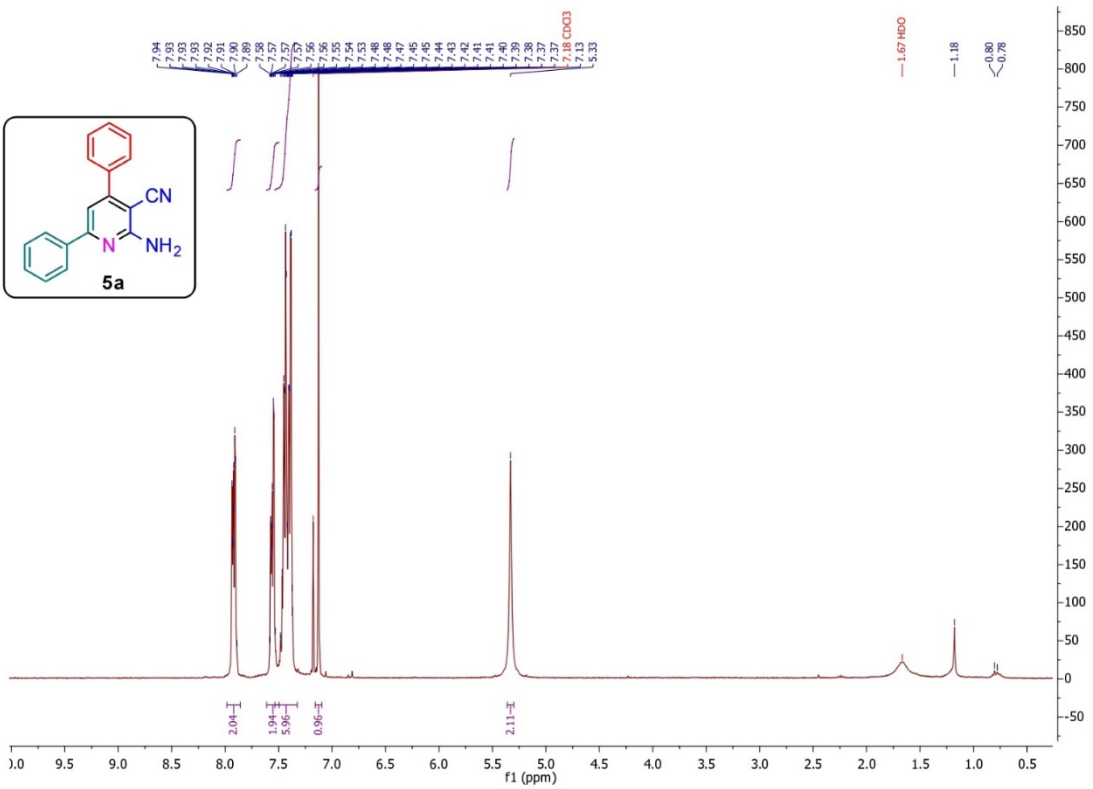


Figure S1: The ^{1}H-NMR spectrum of compound **5a.**

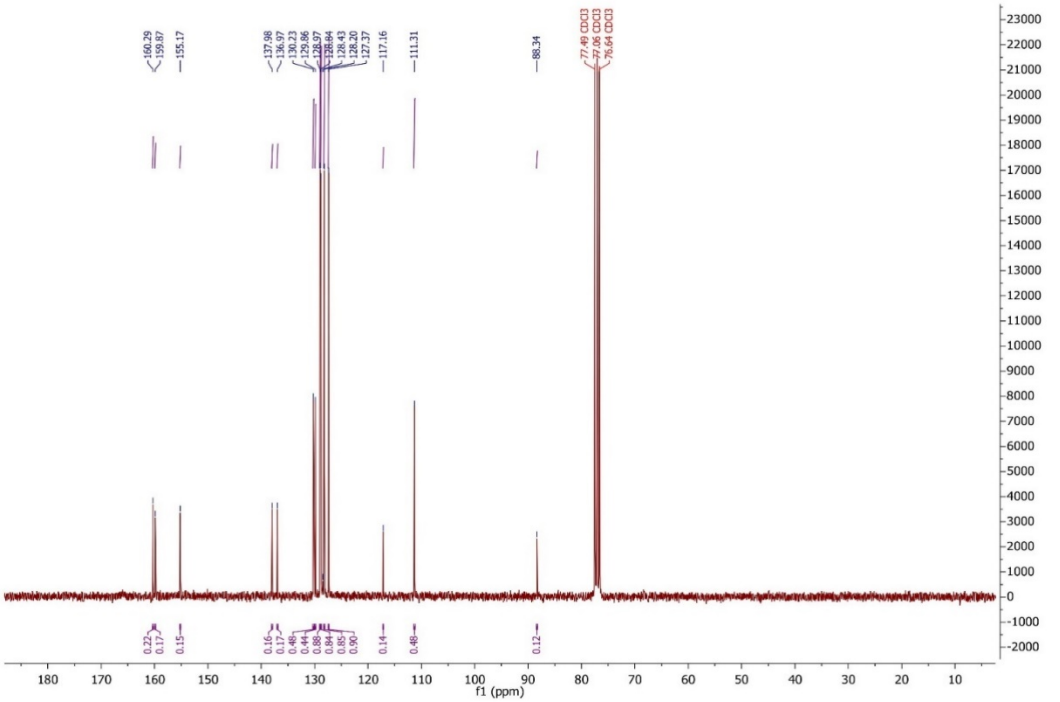


Figure S2: The ^{13}C-NMR spectrum of compound **5a.**

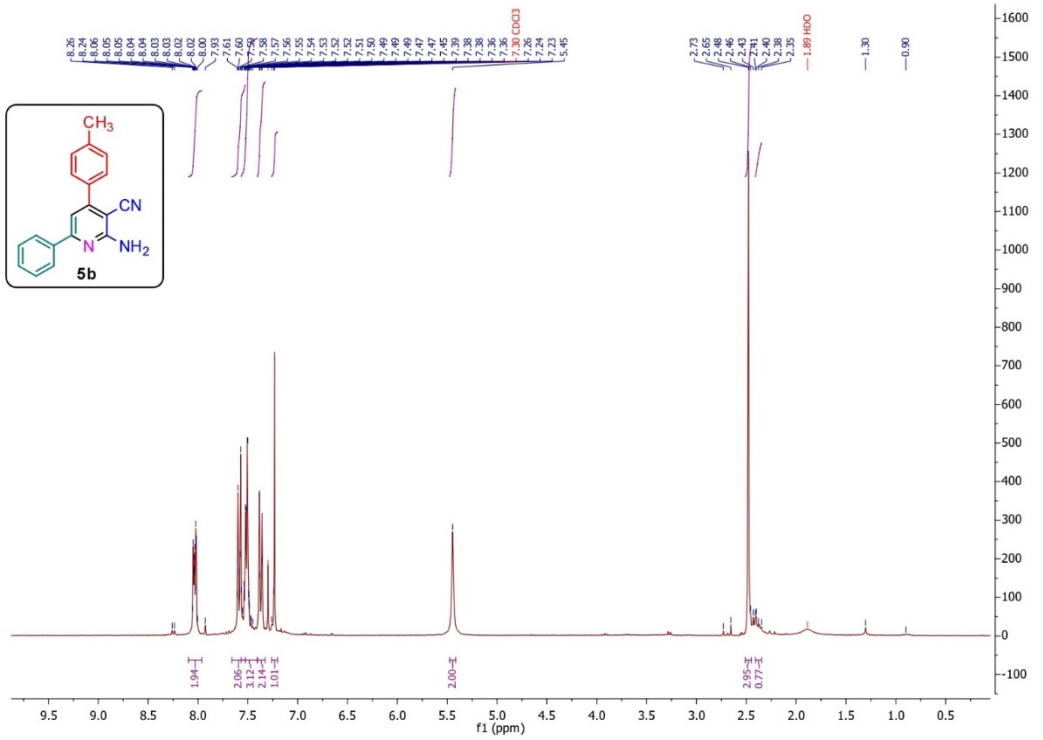


Figure S3: The ^{1}H-NMR spectrum of compound **5b.**

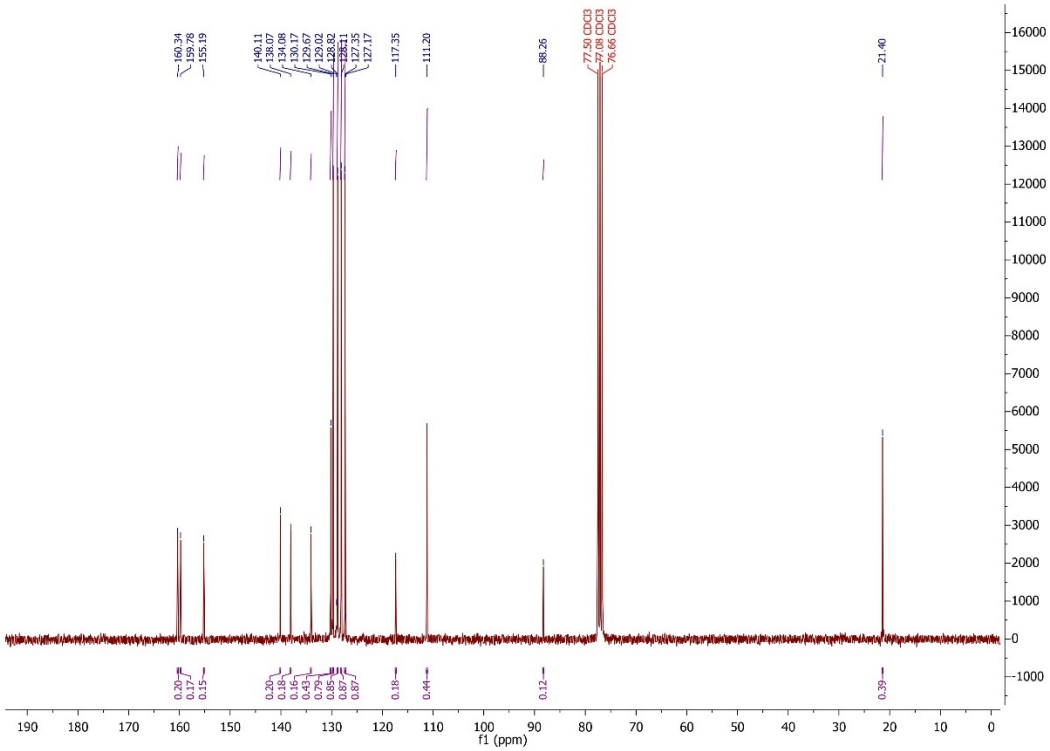


Figure S4: The ^{13}C-NMR spectrum of compound **5b.**

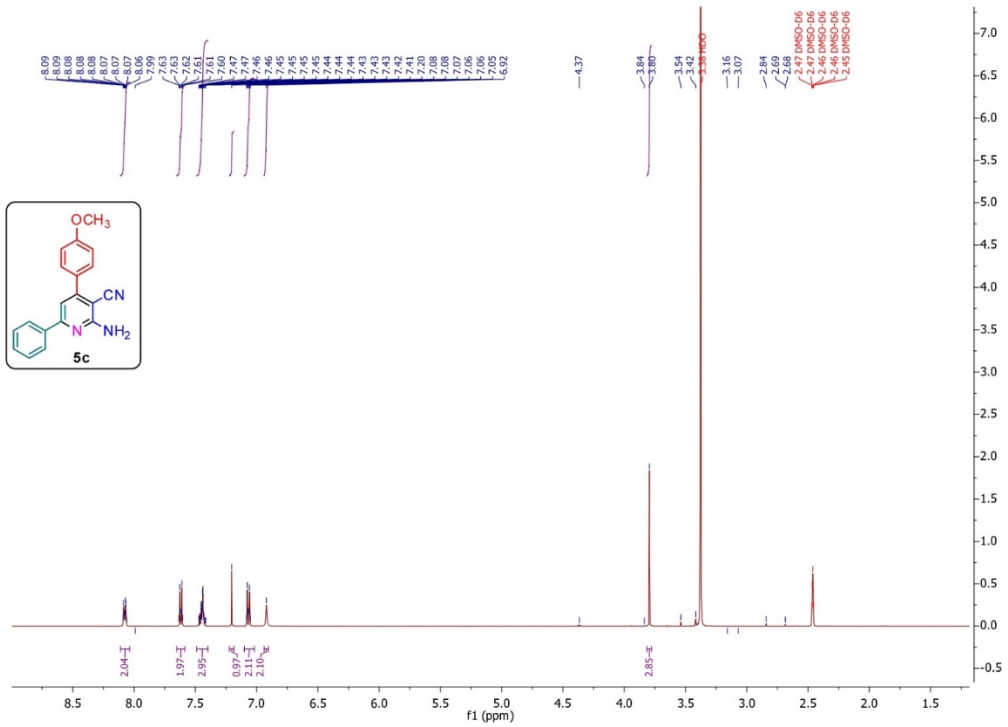


Figure S5: The ^{1}H-NMR spectrum of compound **5c.**

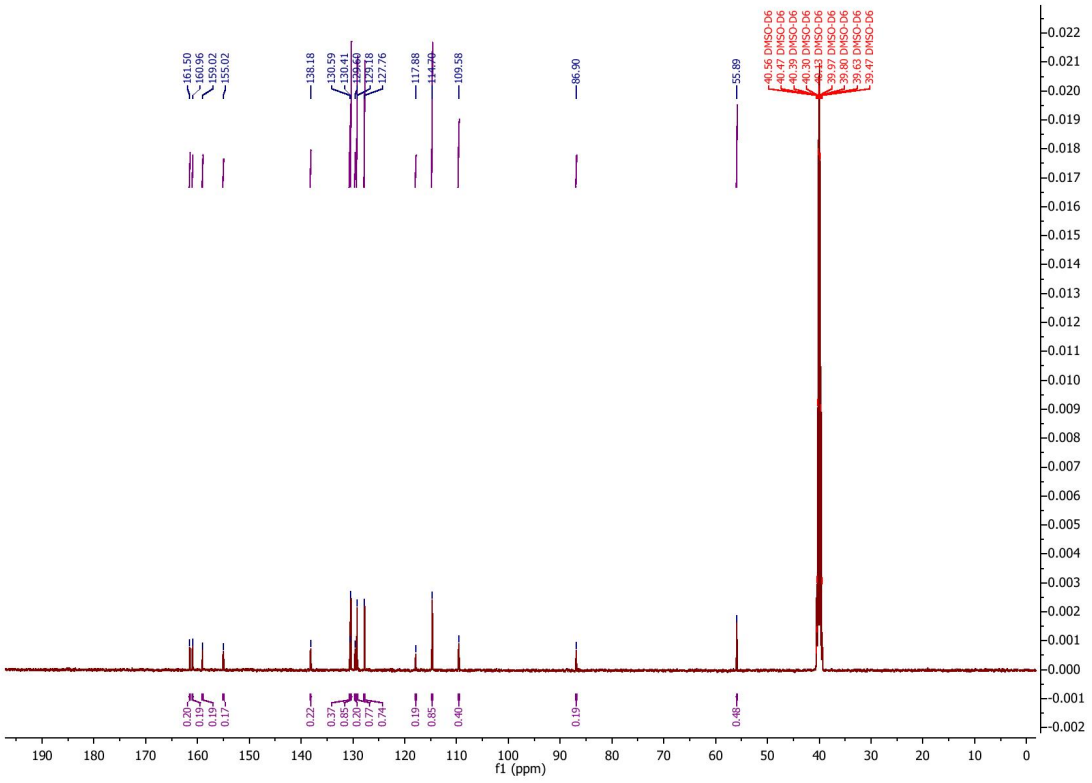


Figure S6: The ^{13}C-NMR spectrum of compound **5c.**

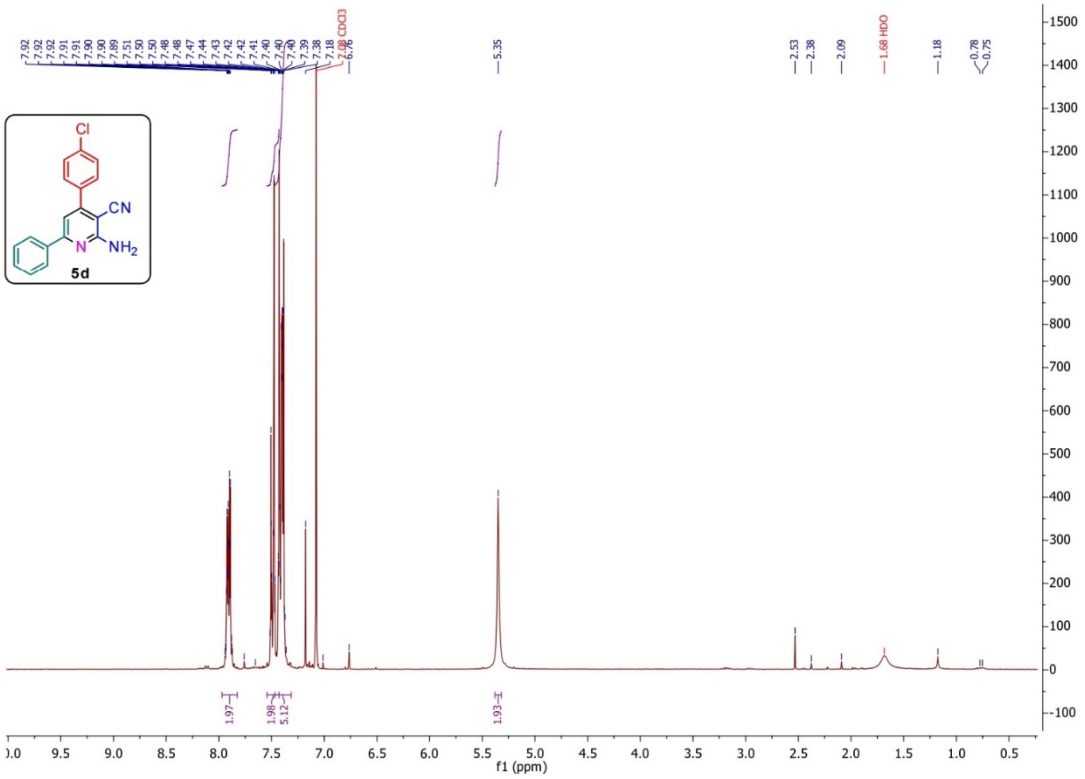


Figure S7: The ^{1}H-NMR spectrum of compound **5d.**

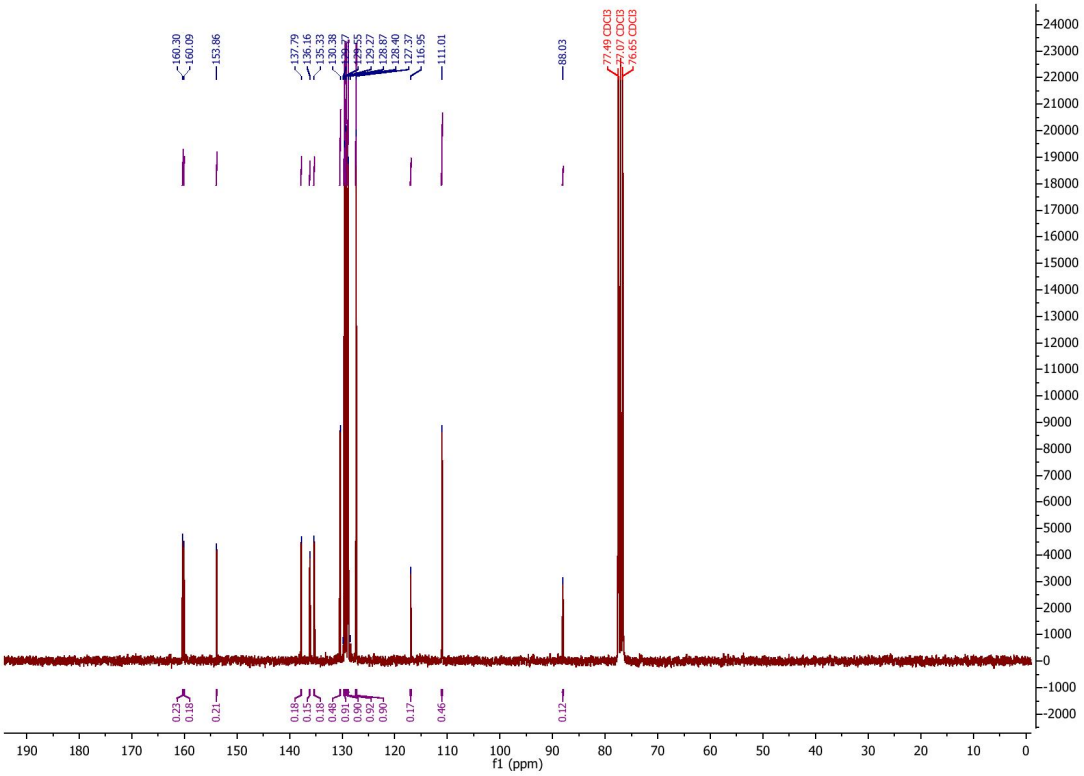


Figure S8: The ^{13}C-NMR spectrum of compound **5d.**

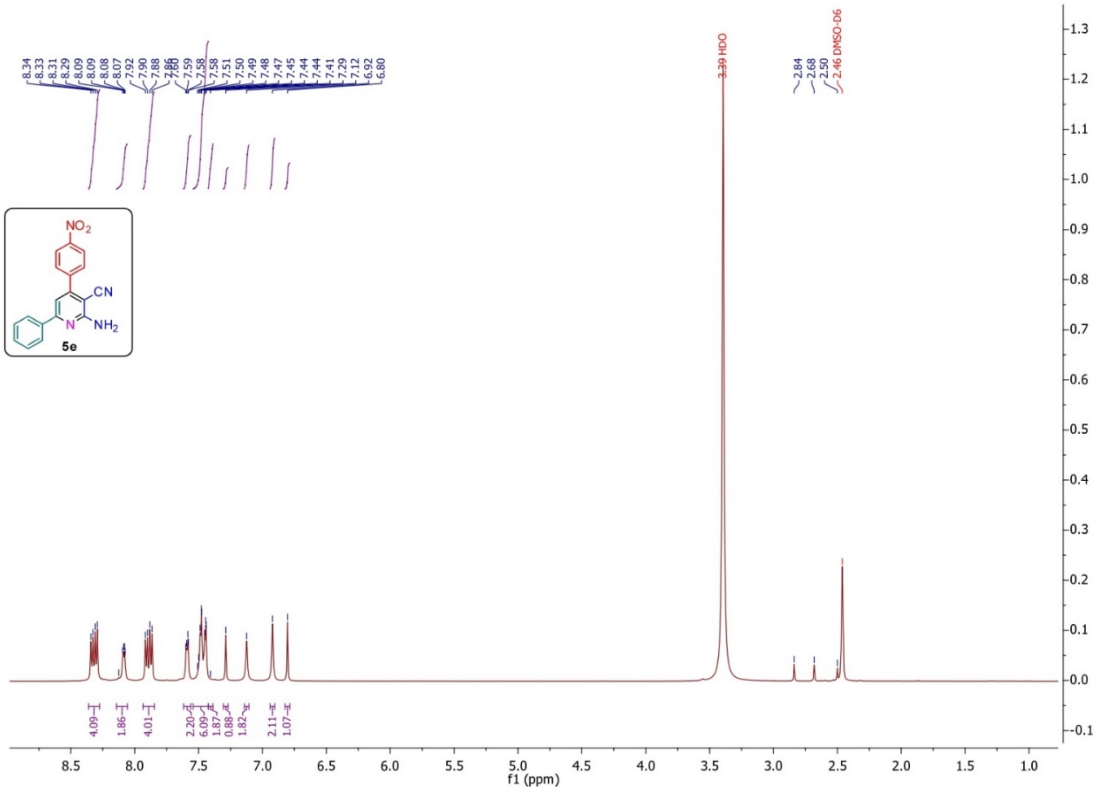


Figure S9: The ^{1}H-NMR spectrum of compound **5e.**

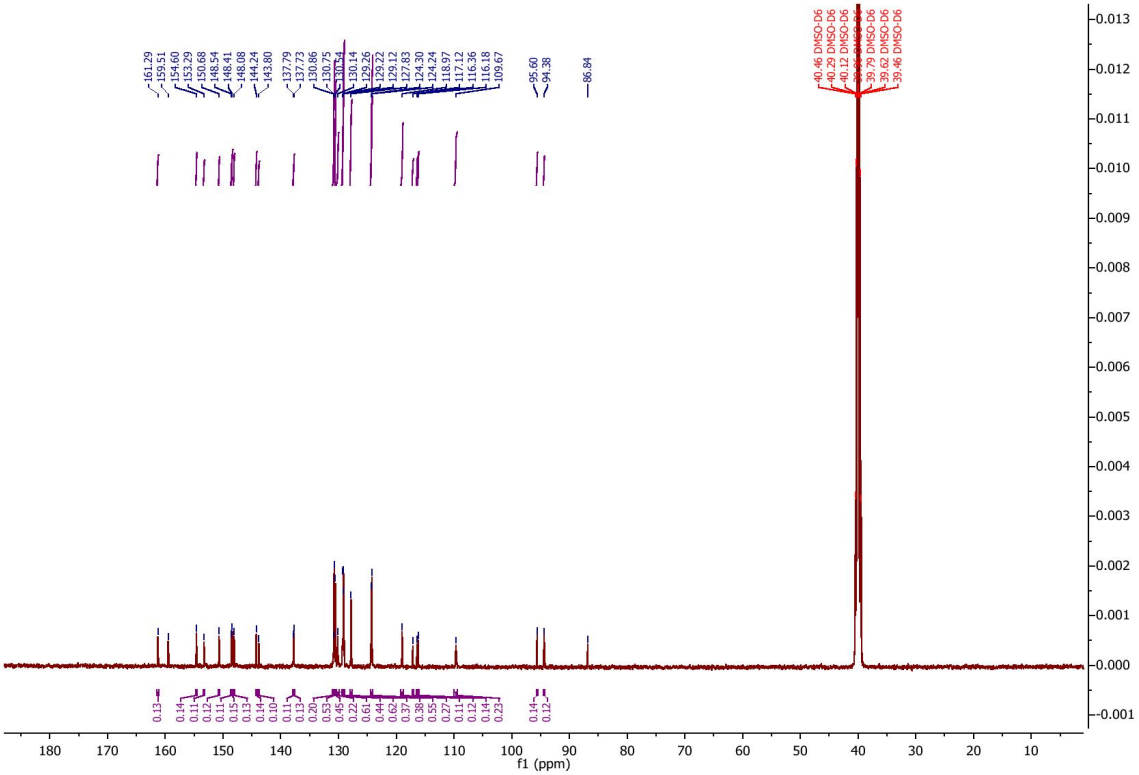


Figure S10: The ^{13}C-NMR spectrum of compound **5e.**

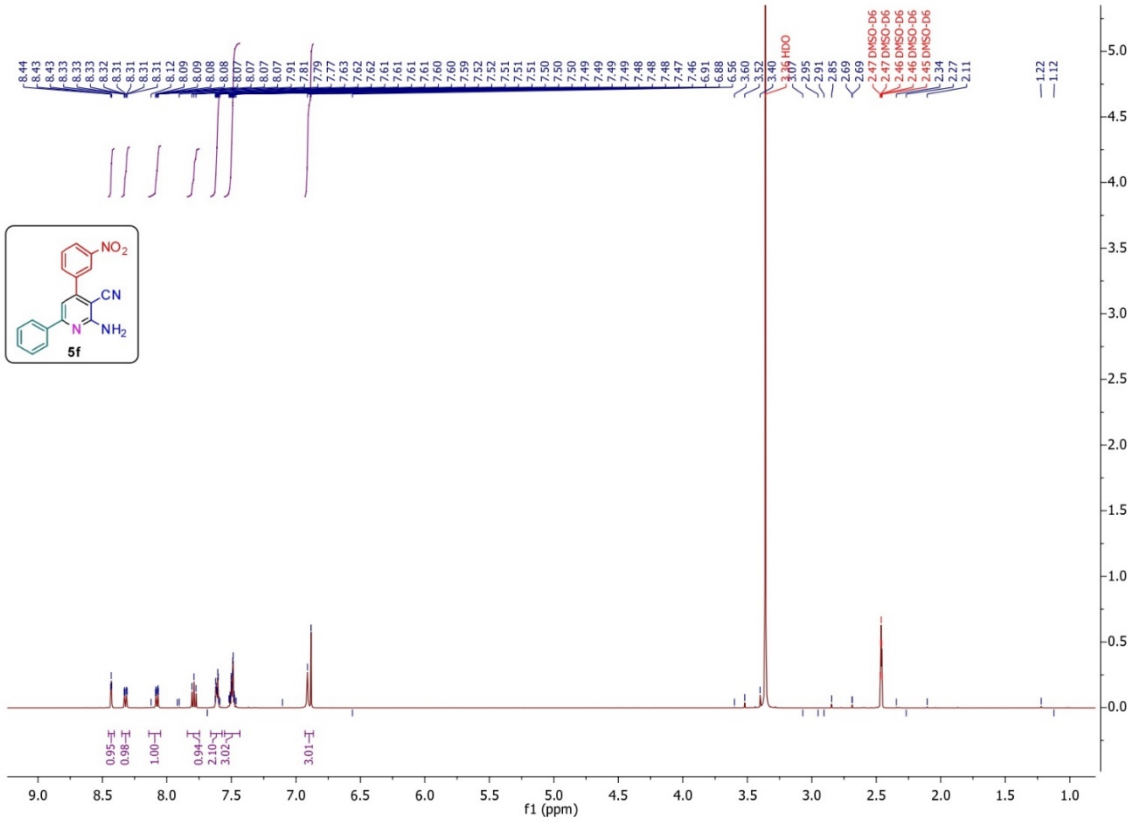


Figure S11: The ^{1}H-NMR spectrum of compound **5f.**

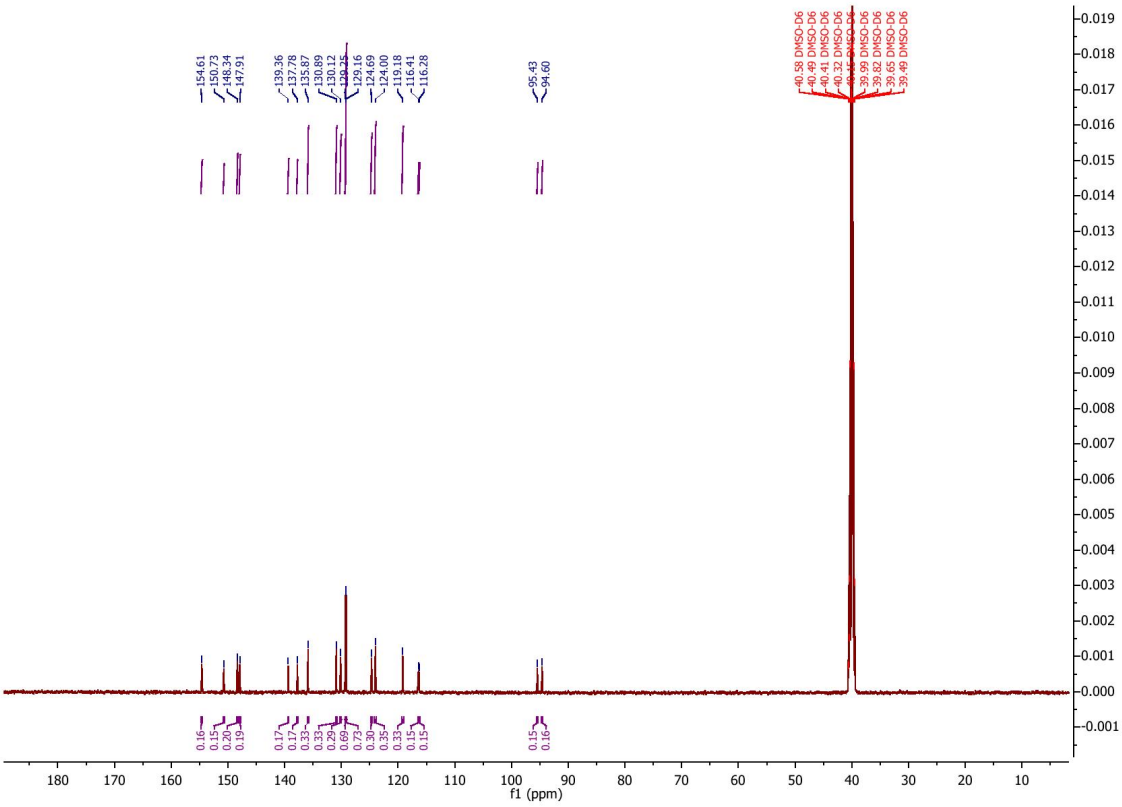


Figure S12: The ^{13}C-NMR spectrum of compound **5f.**

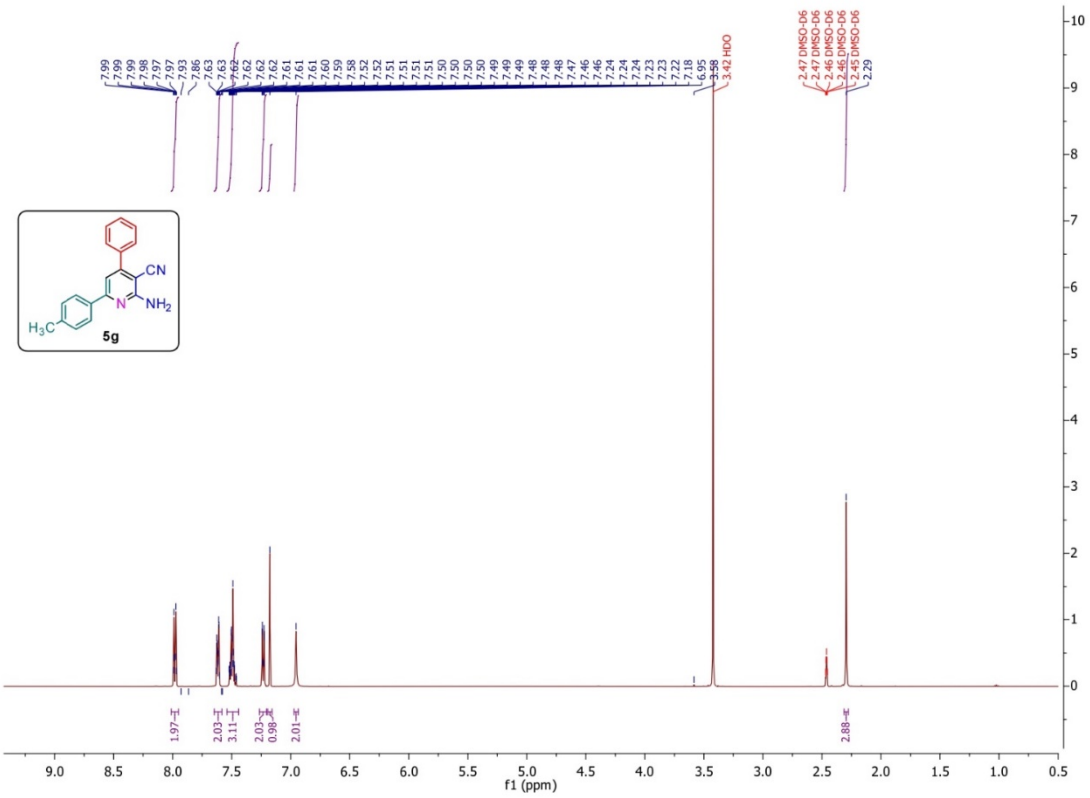


Figure S13: The ^{1}H-NMR spectrum of compound **5g.**

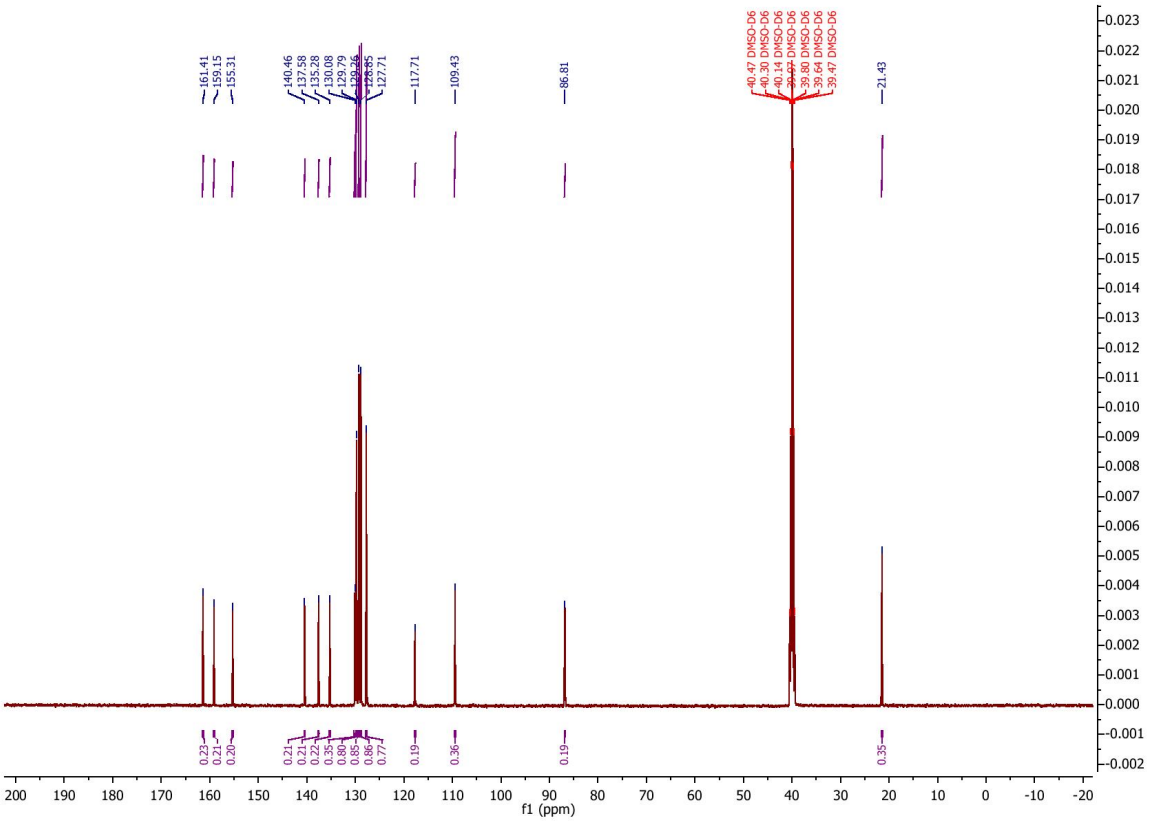


Figure S14: The ^{13}C-NMR spectrum of compound **5g.**

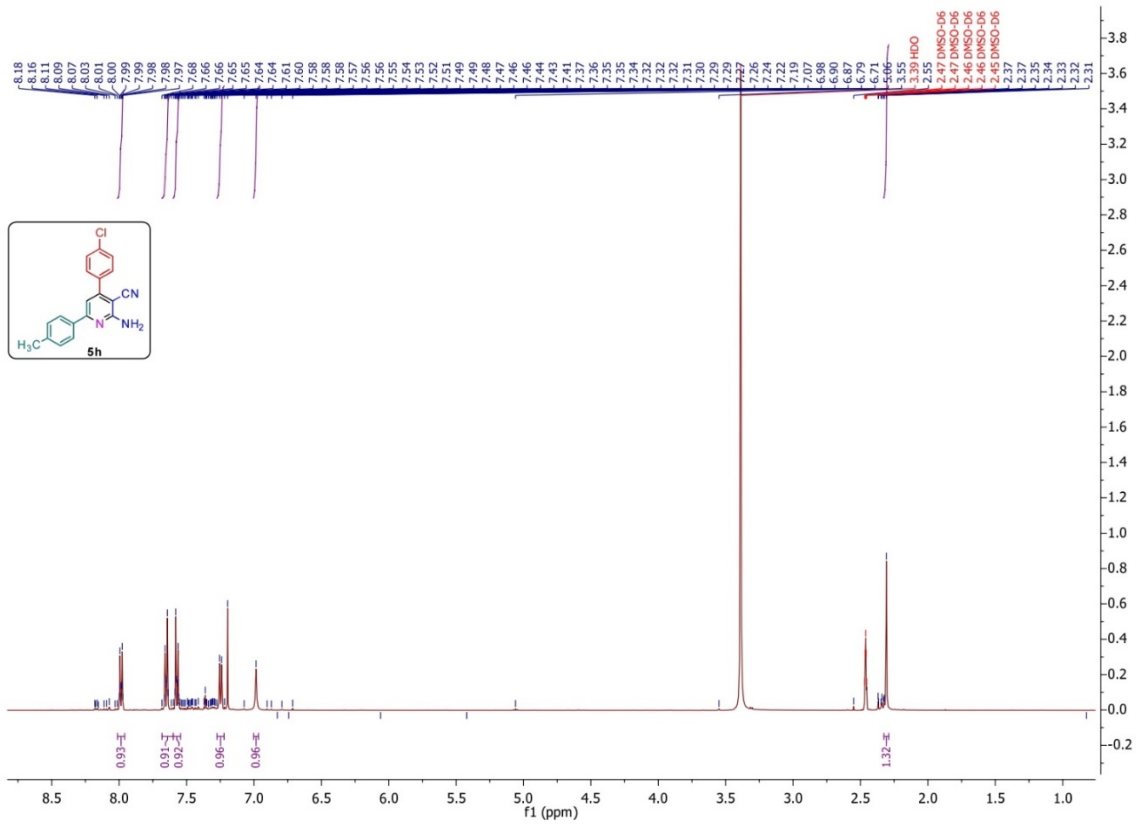


Figure S15: The ^{1}H-NMR spectrum of compound **5h.**

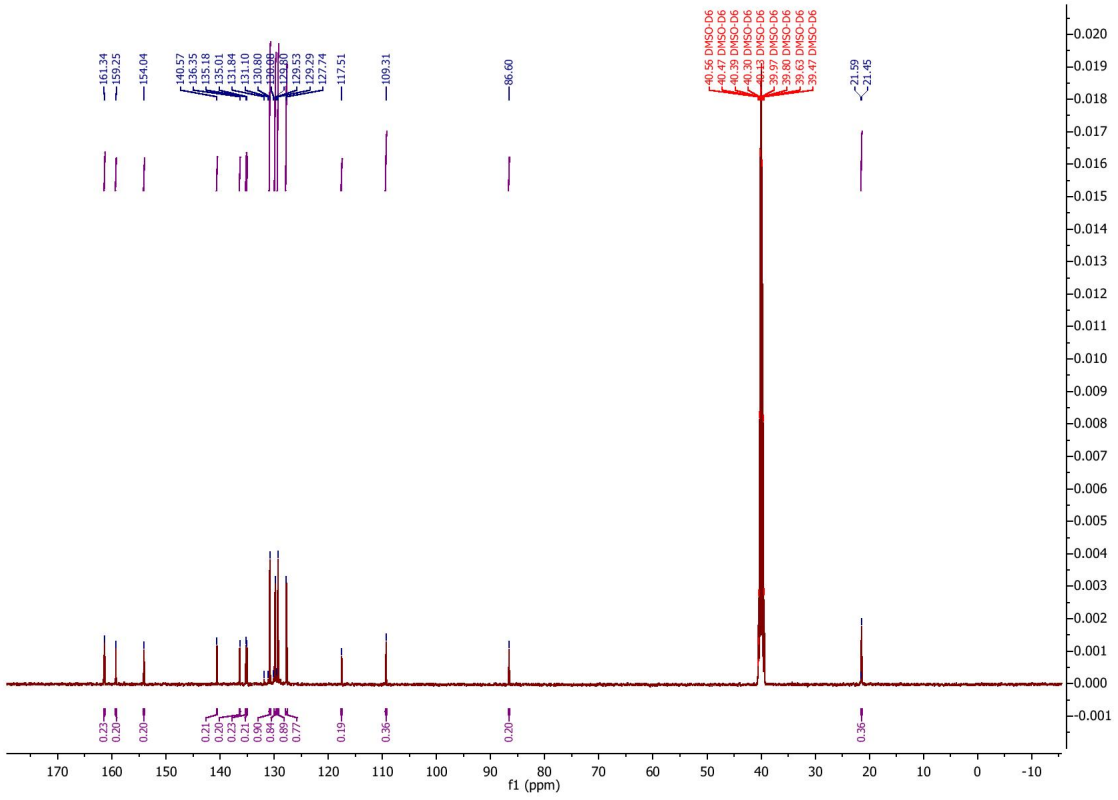


Figure S16: The ^{13}C-NMR spectrum of compound **5h.**

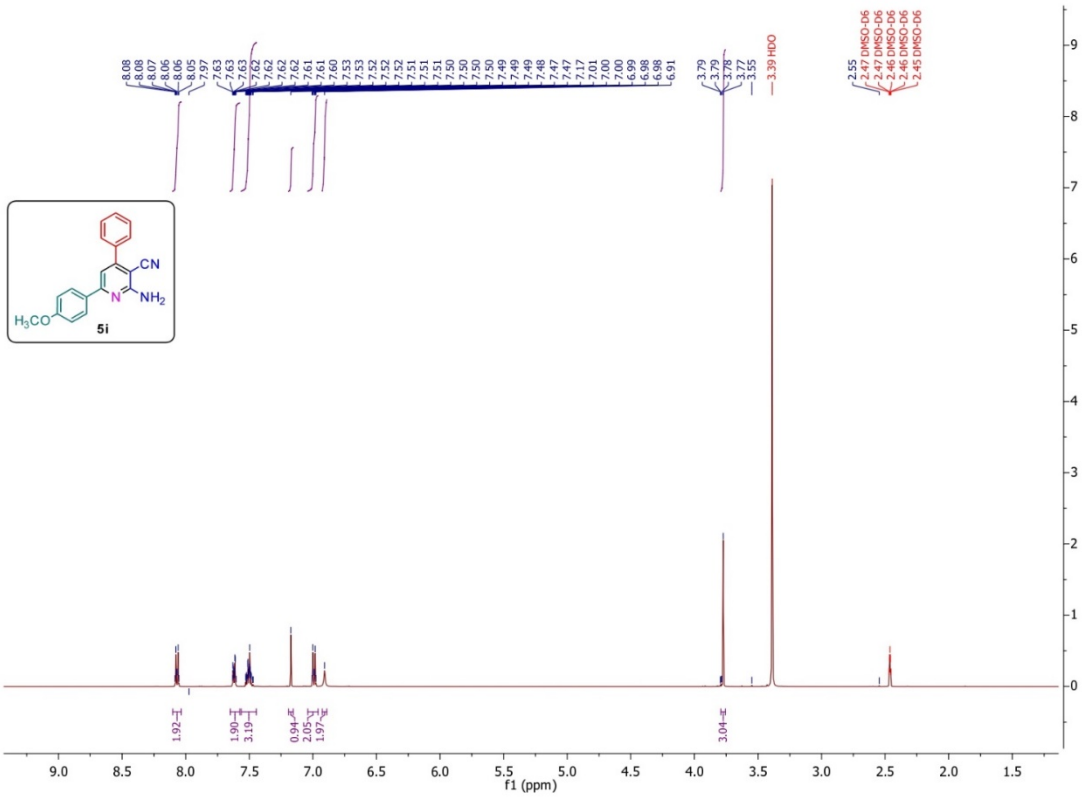


Figure S17: The ^{1}H-NMR spectrum of compound **5i.**

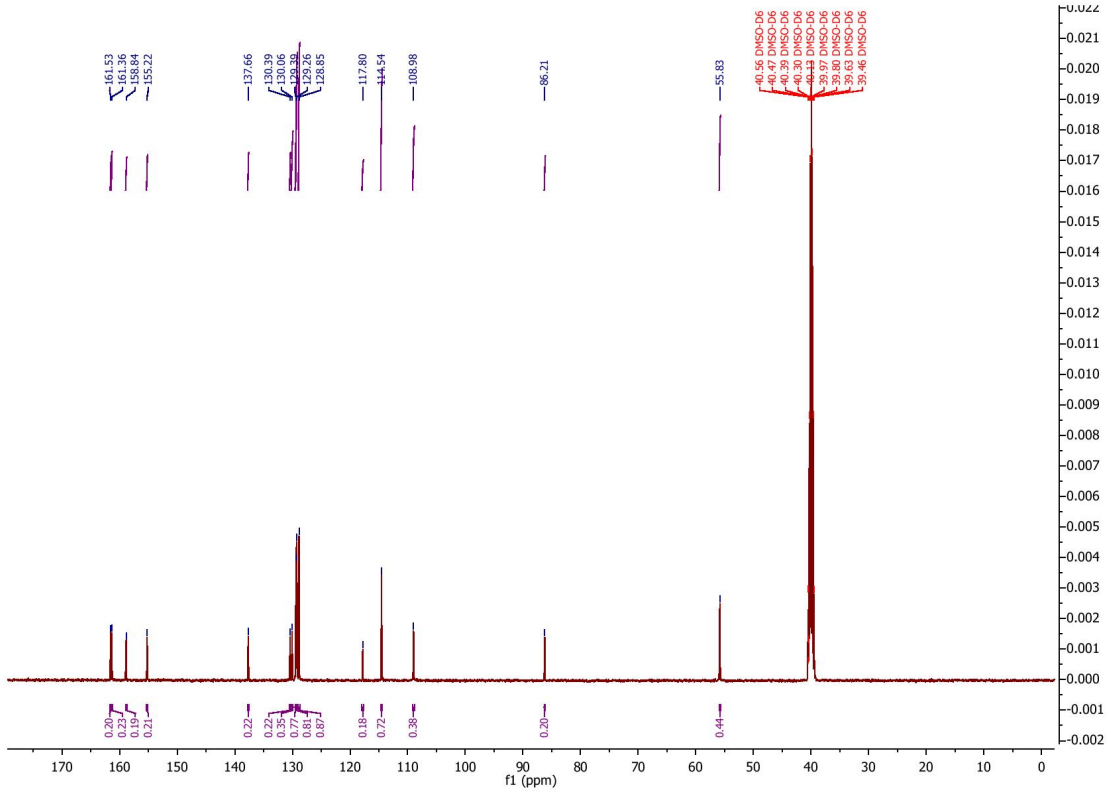


Figure S18: The ^{13}C-NMR spectrum of compound **5i.**

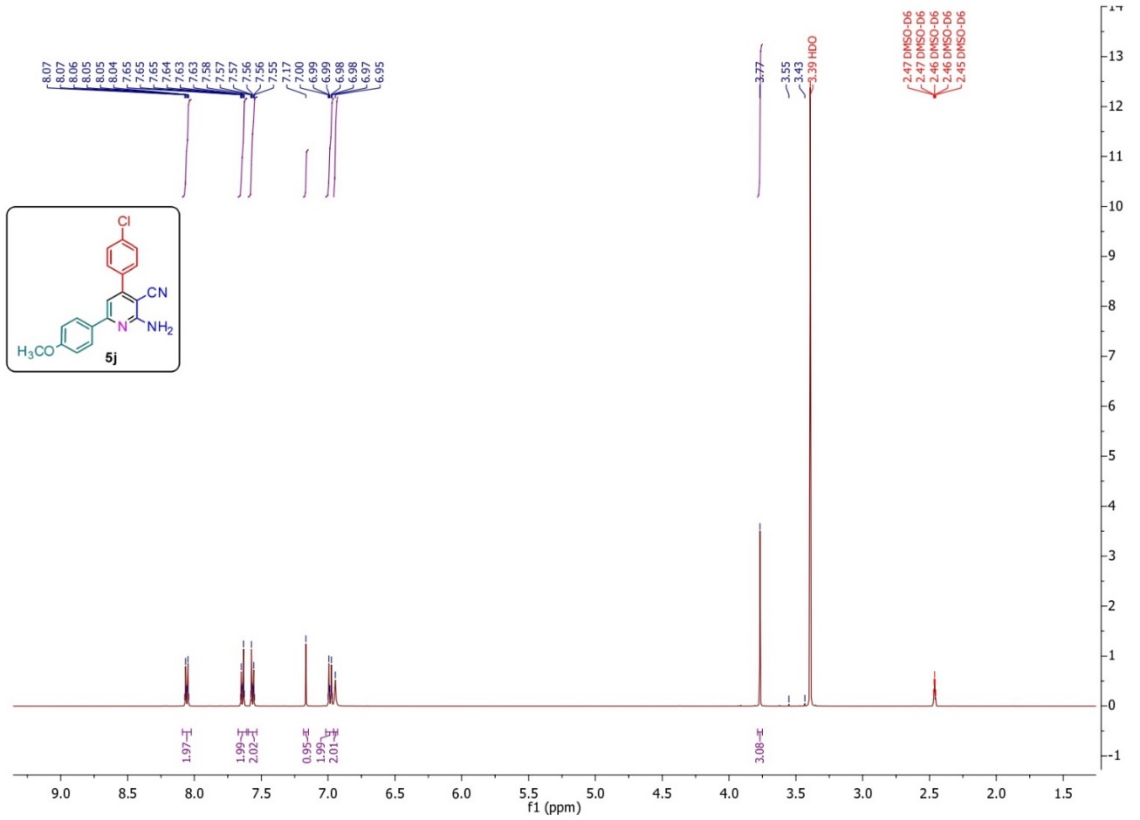


Figure S19: The ^{1}H-NMR spectrum of compound **5j.**

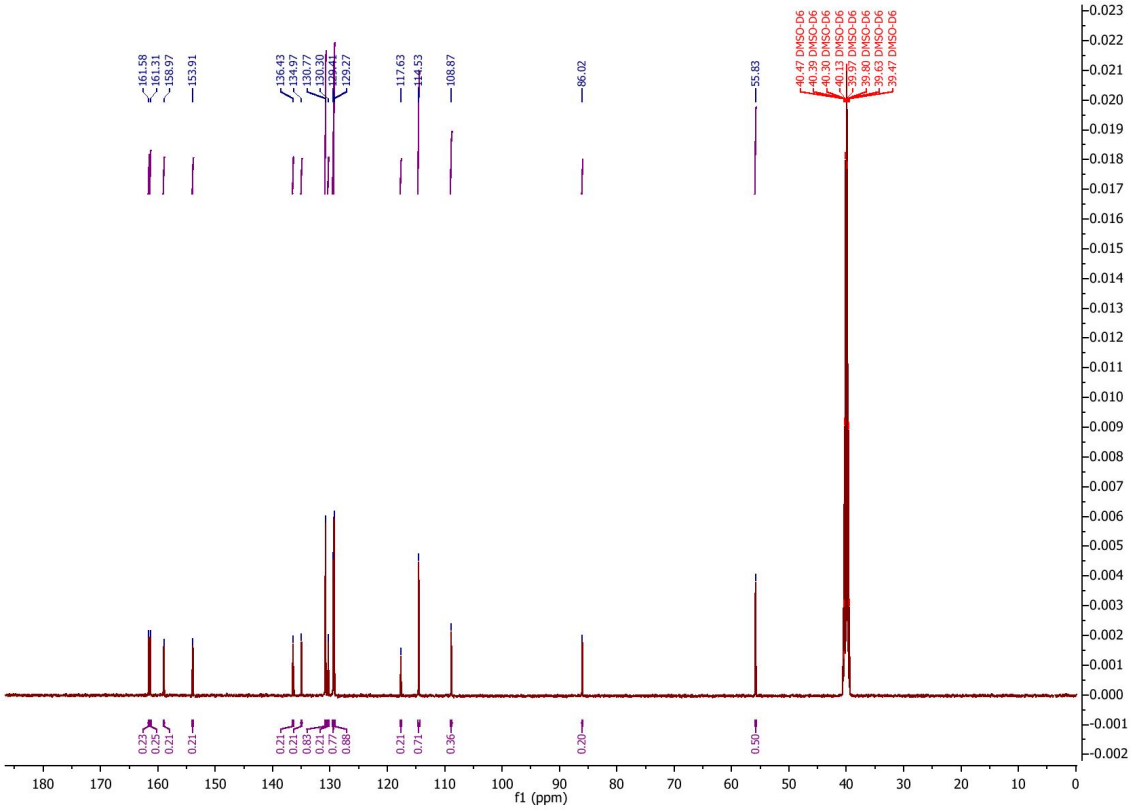


Figure S20: The ^{13}C-NMR spectrum of compound **5j.**

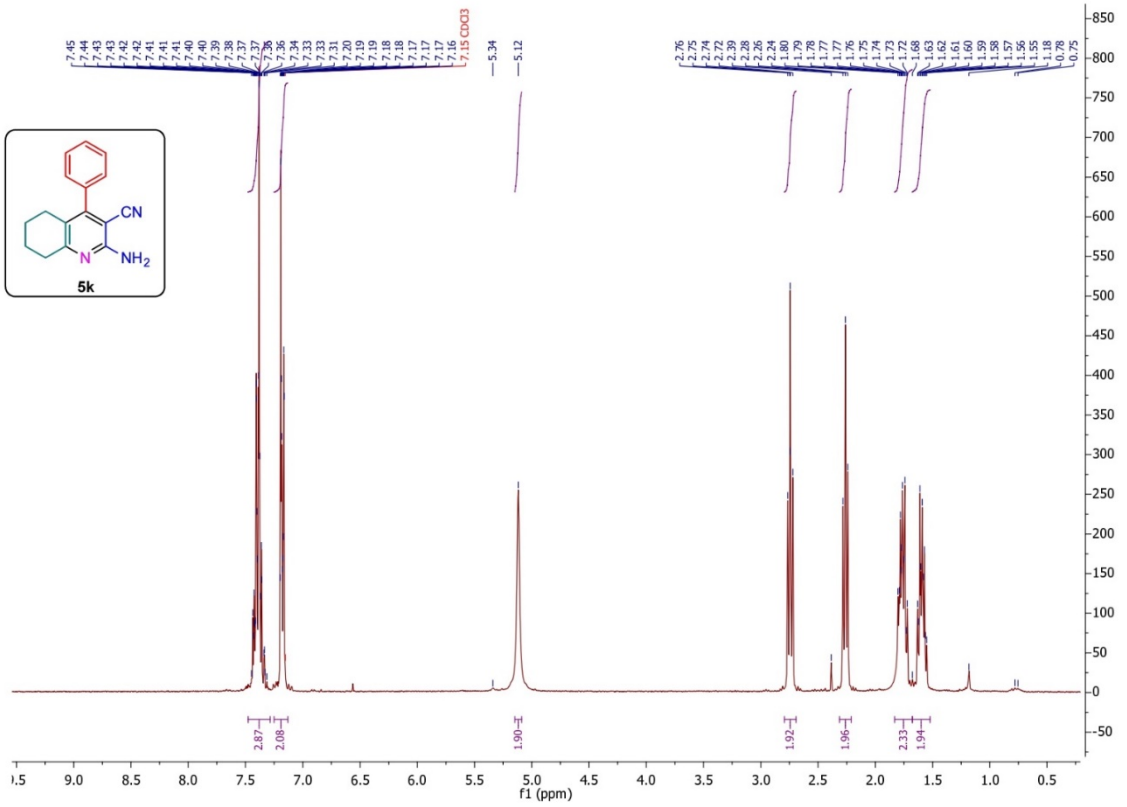


Figure S21: The ^{1}H-NMR spectrum of compound **5k.**

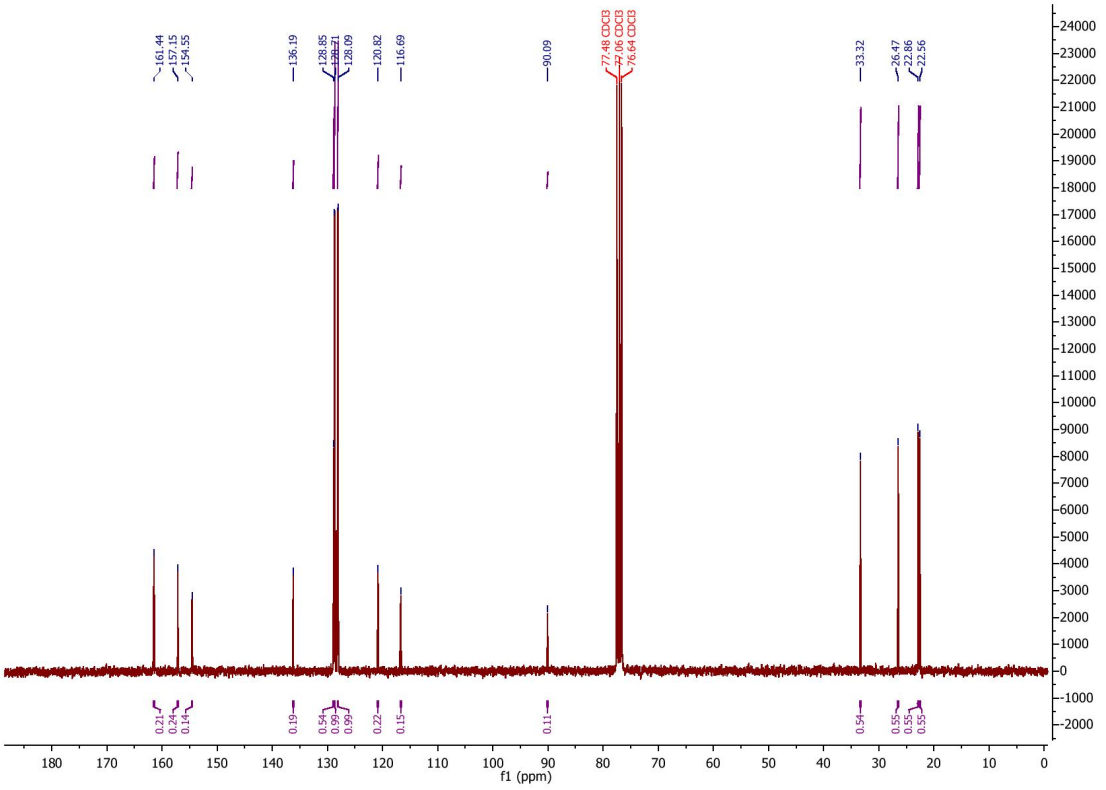


Figure S22: The ^{13}C-NMR spectrum of compound **5k.**

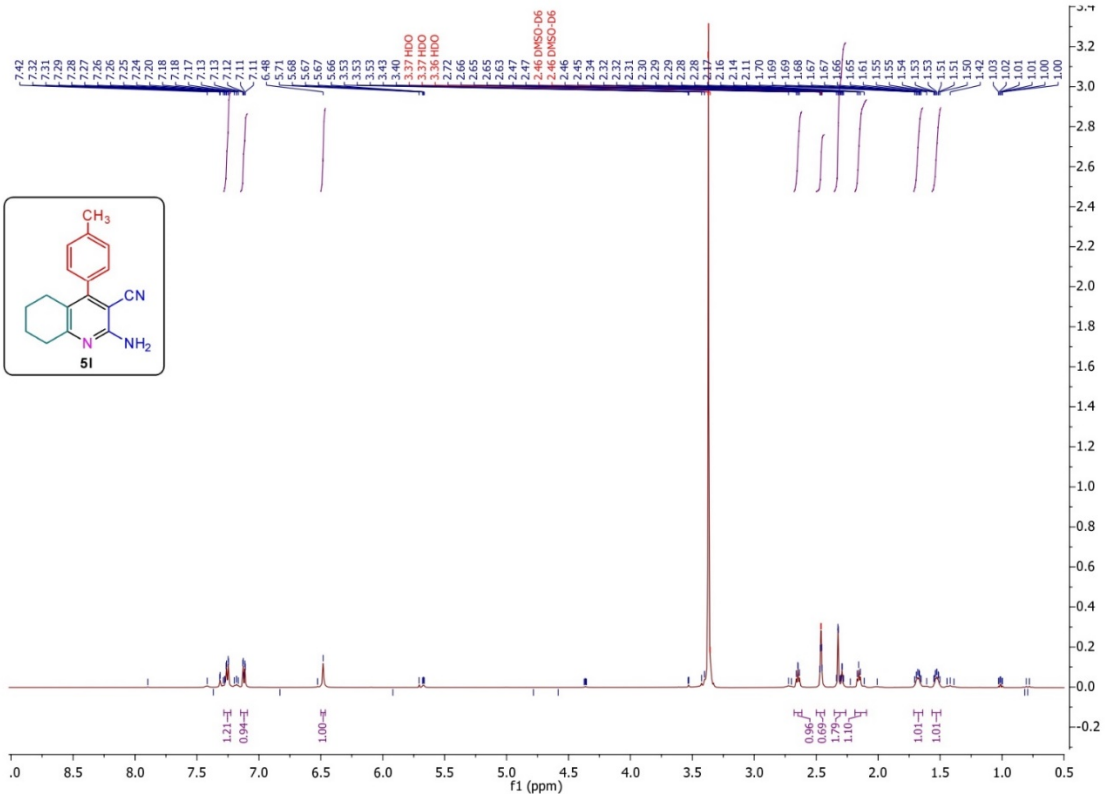


Figure S23: The ^{1}H-NMR spectrum of compound **5l.**

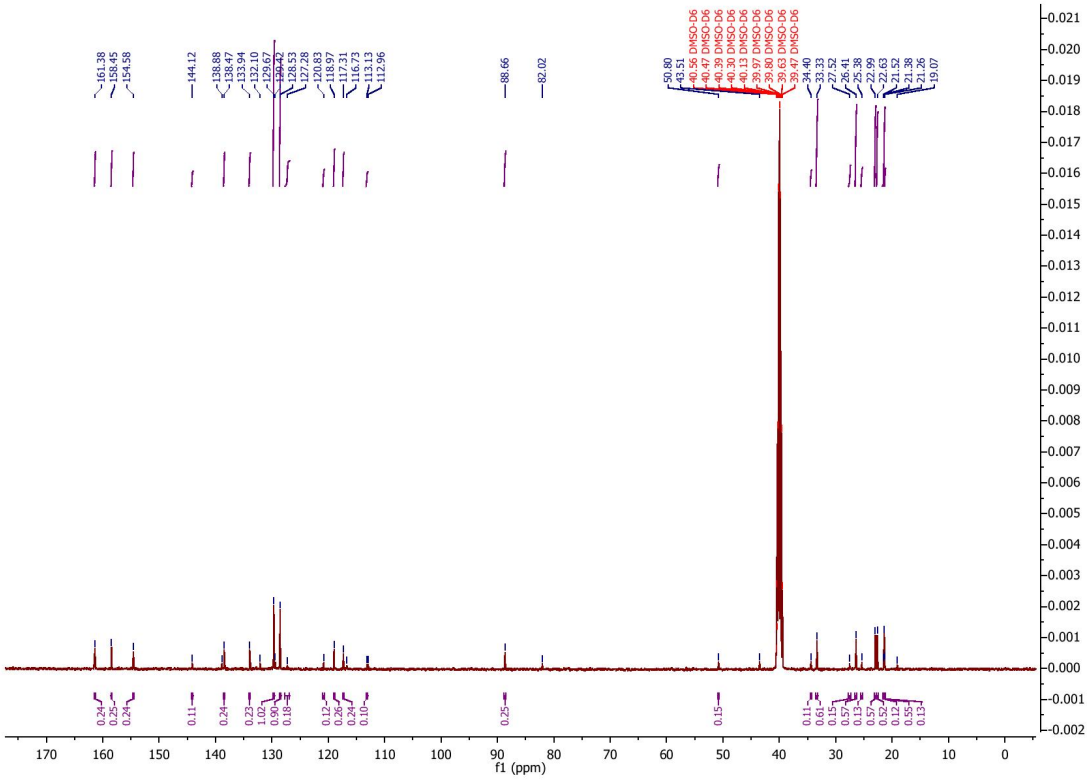


Figure S24: The ^{13}C-NMR spectrum of compound **5l.**

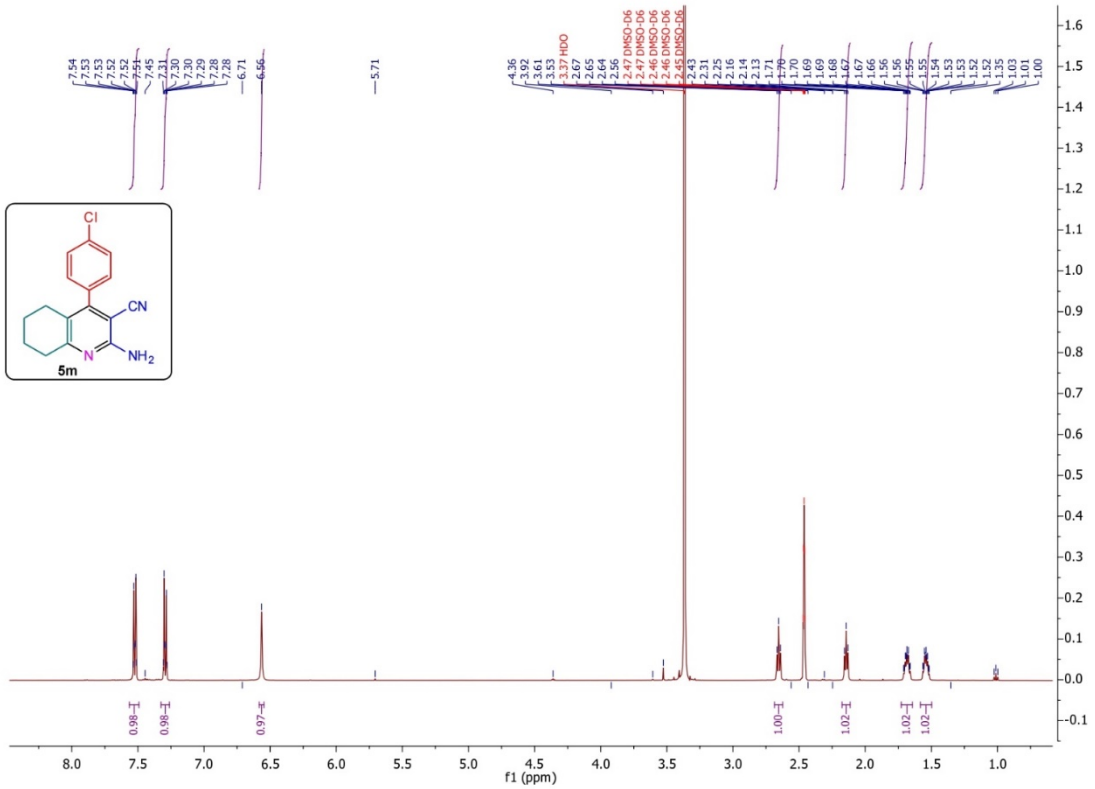


Figure S25: The ^{1}H-NMR spectrum of compound **5m.**

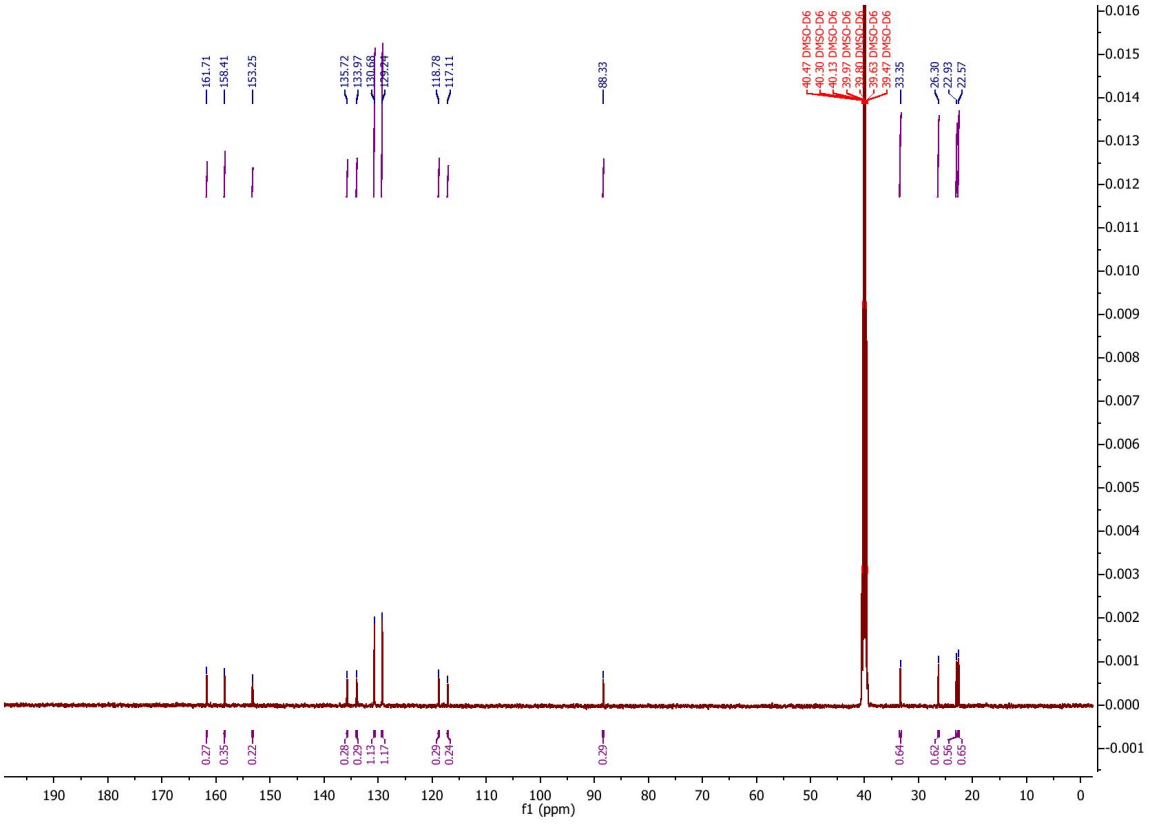


Figure S26: The ^{13}C-NMR spectrum of compound **5m.**

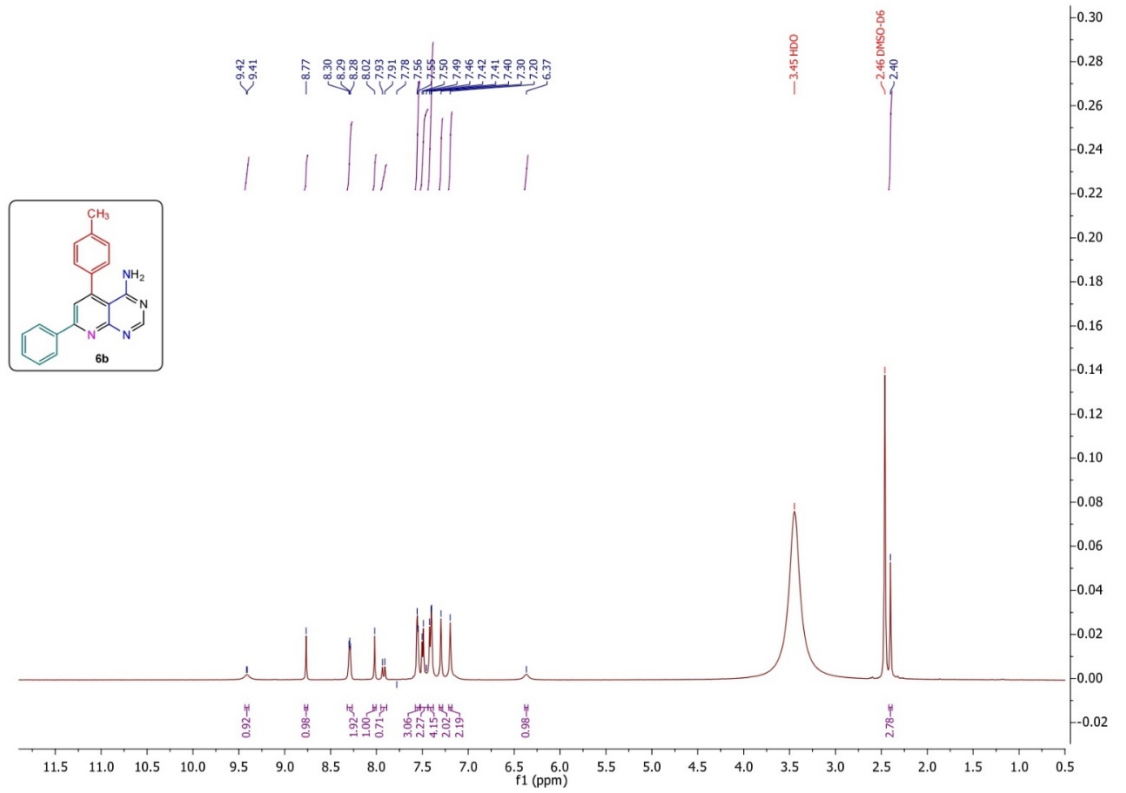


Figure S27: The ^{1}H-NMR spectrum of compound **6b.**

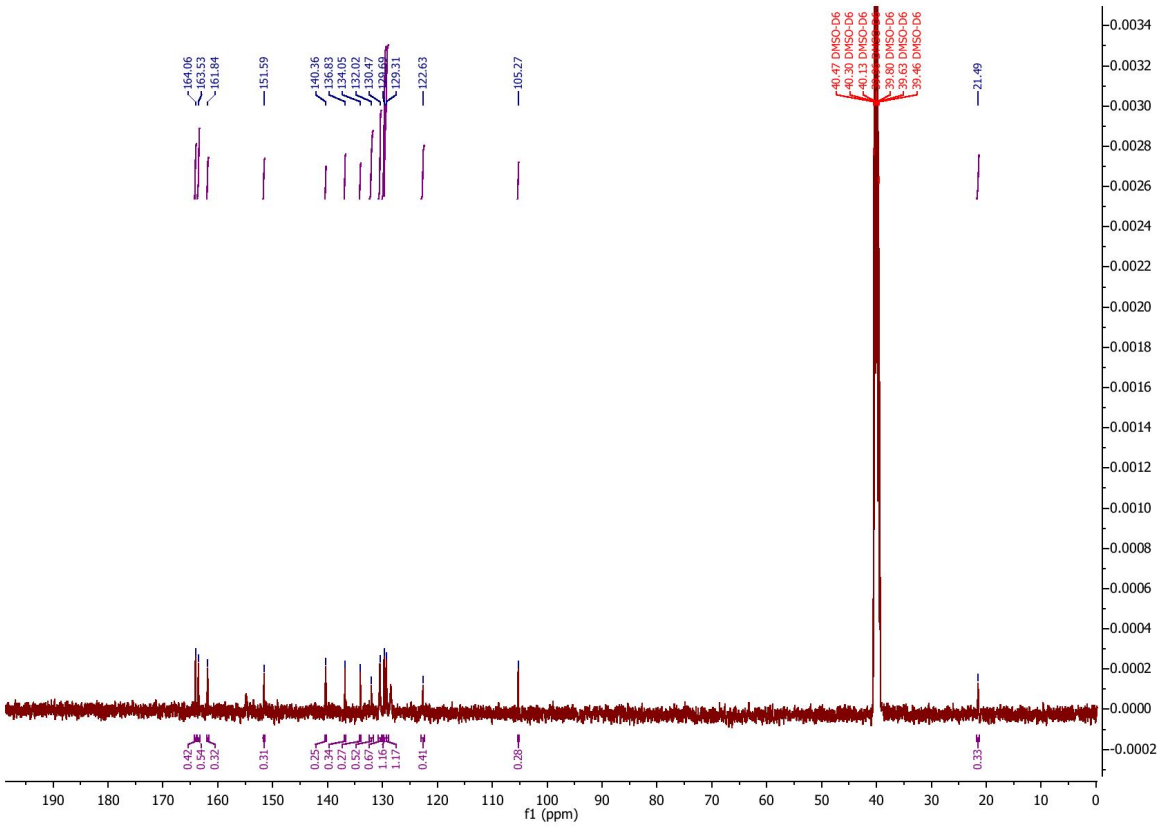


Figure S28: The ^{13}C-NMR spectrum of compound **6b.**

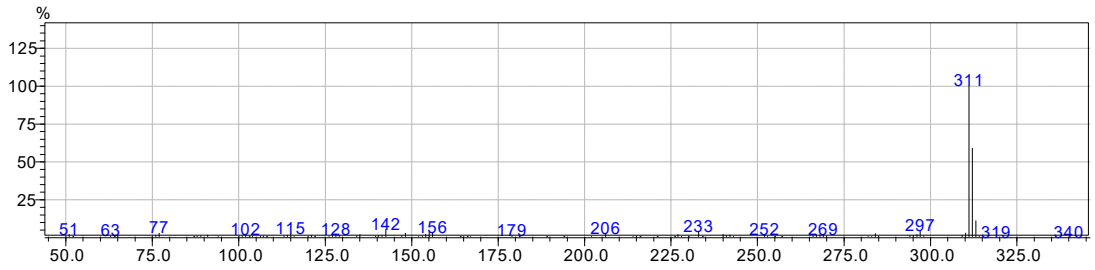


Figure S29: The MS spectrum of compound **6b.**

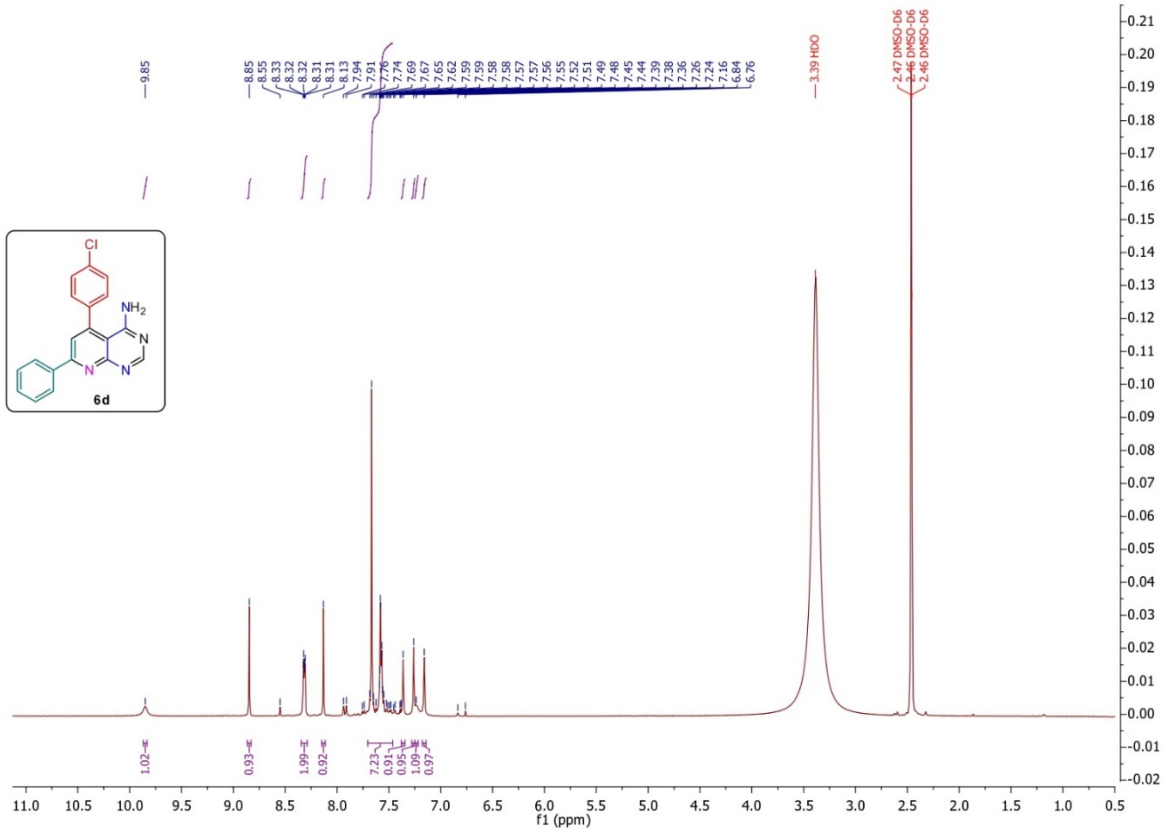


Figure S30: The ^{1}H-NMR spectrum of compound **6d.**

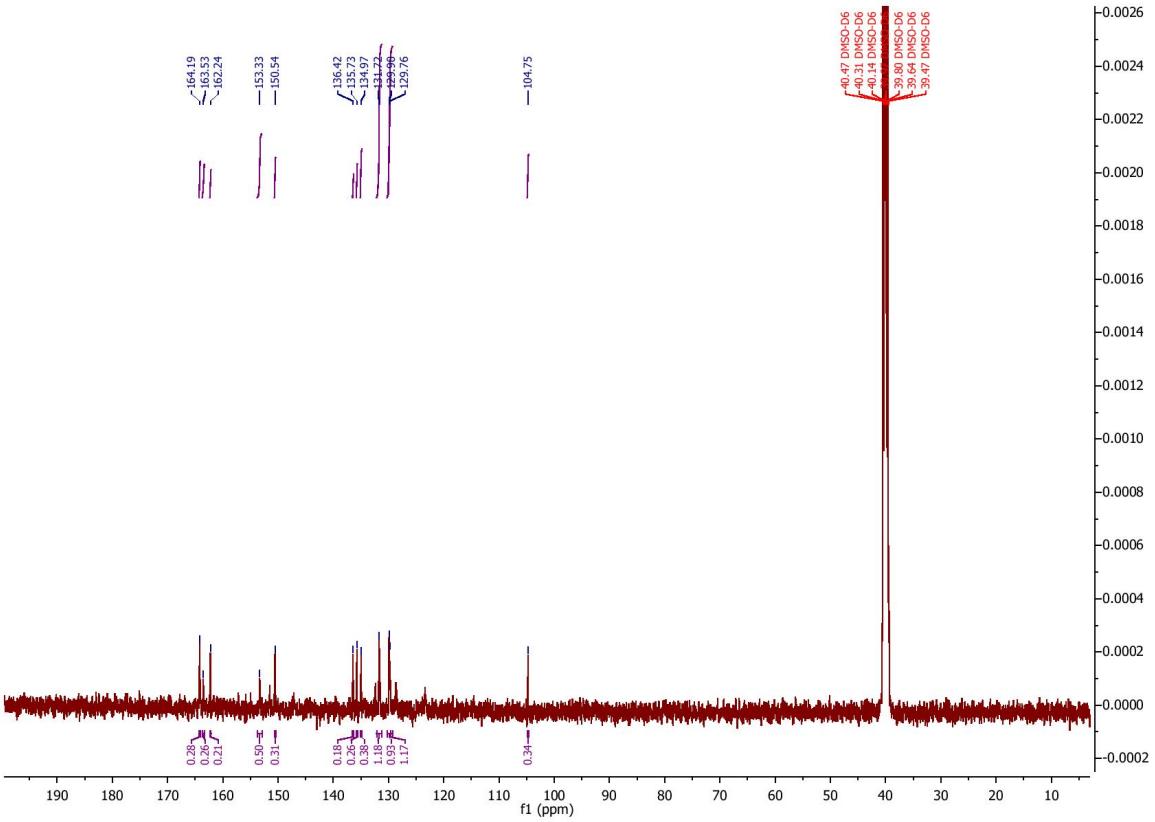


Figure S31: The ^{13}C-NMR spectrum of compound **6d.**

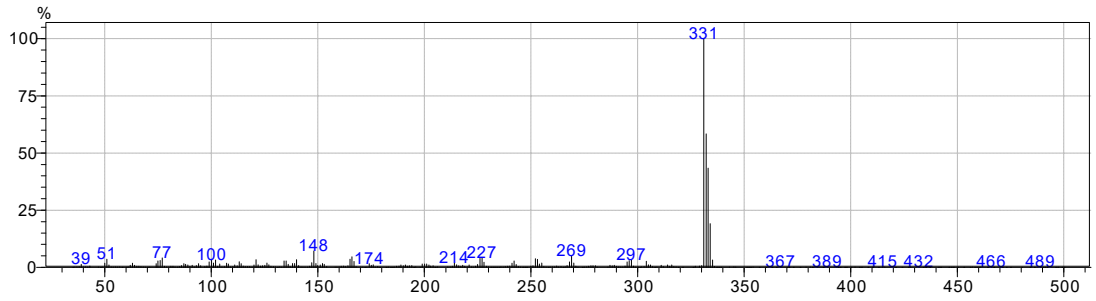


Figure S32: The MS spectrum of compound **6d.**

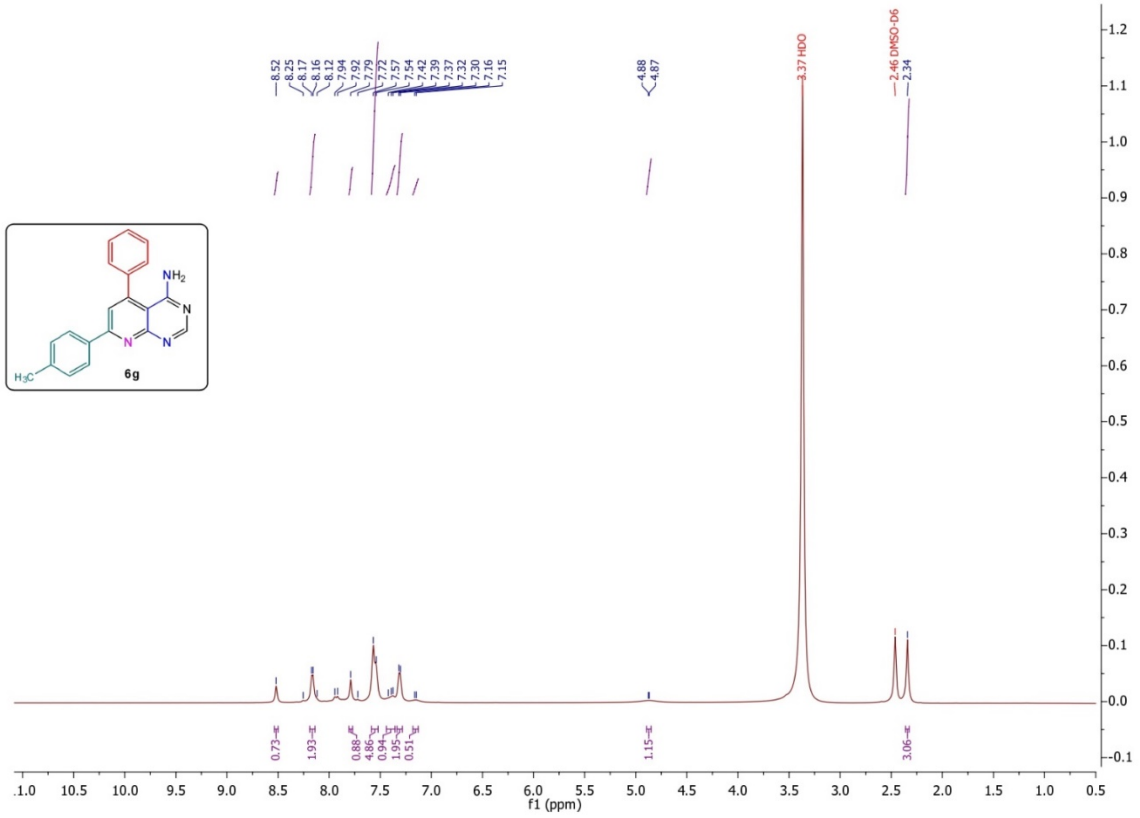


Figure S33: The ^{1}H-NMR spectrum of compound **6g.**

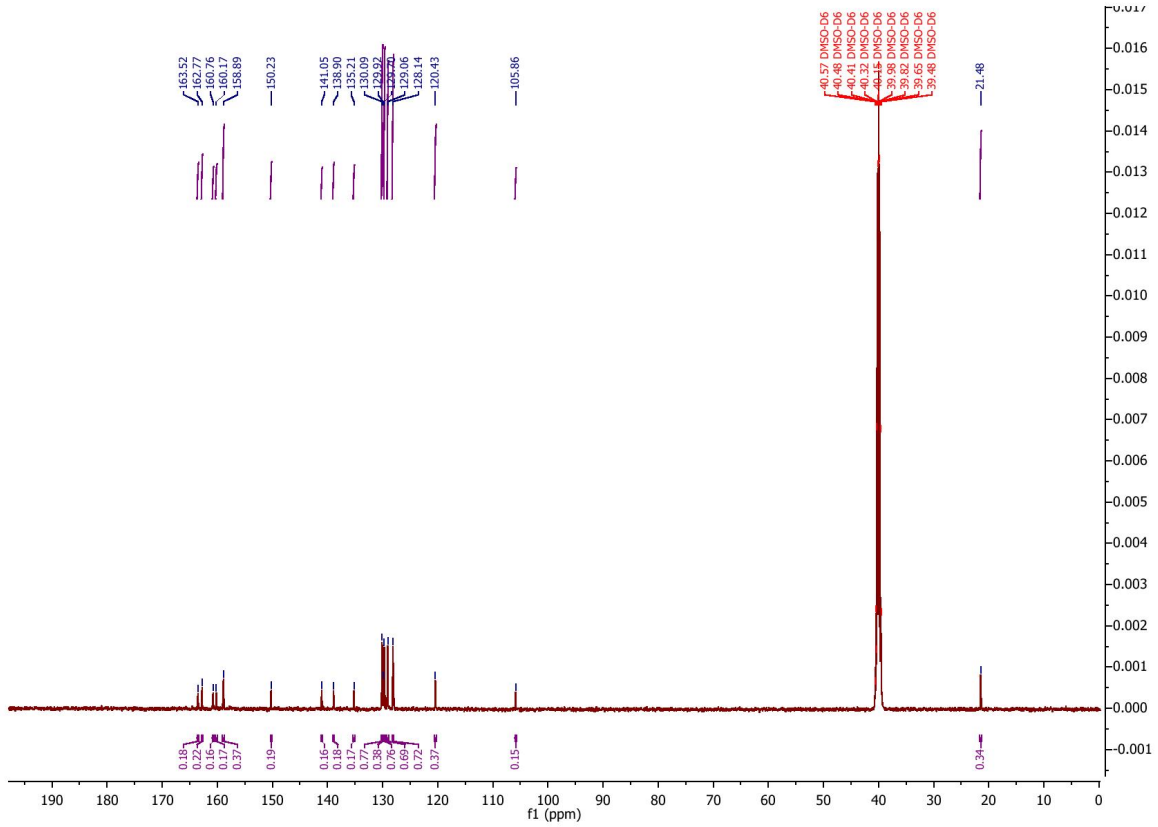


Figure S34: The ^{13}C-NMR spectrum of compound **6g.**

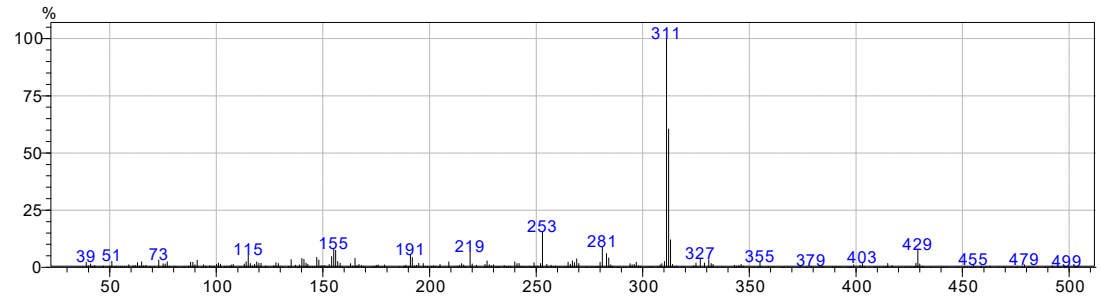


Figure S35: The MS spectrum of compound **6g.**

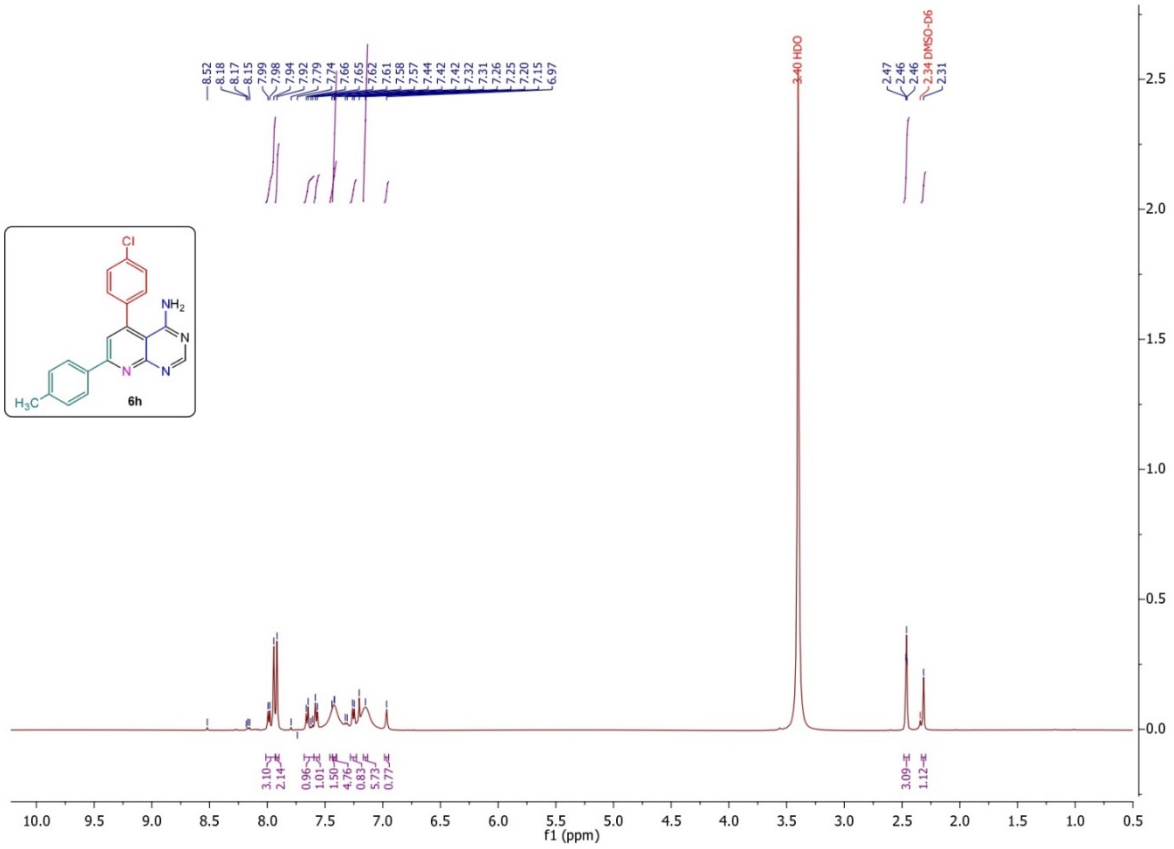


Figure S36: The ^{1}H-NMR spectrum of compound **6h.**

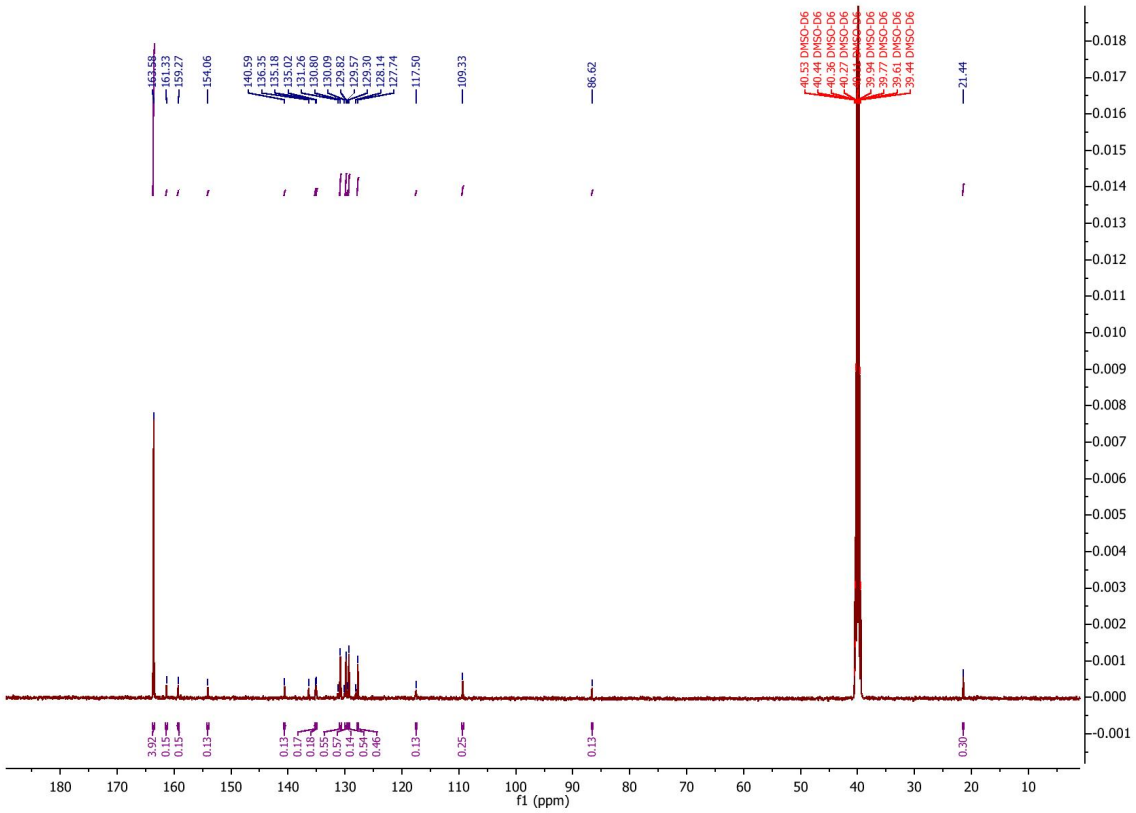


Figure S37: The ^{13}C-NMR spectrum of compound **6h.**

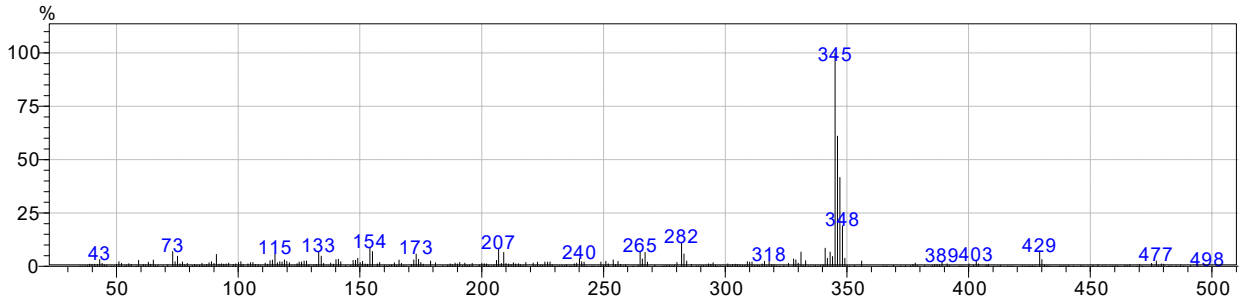


Figure S38: The MS spectrum of compound **6h.**

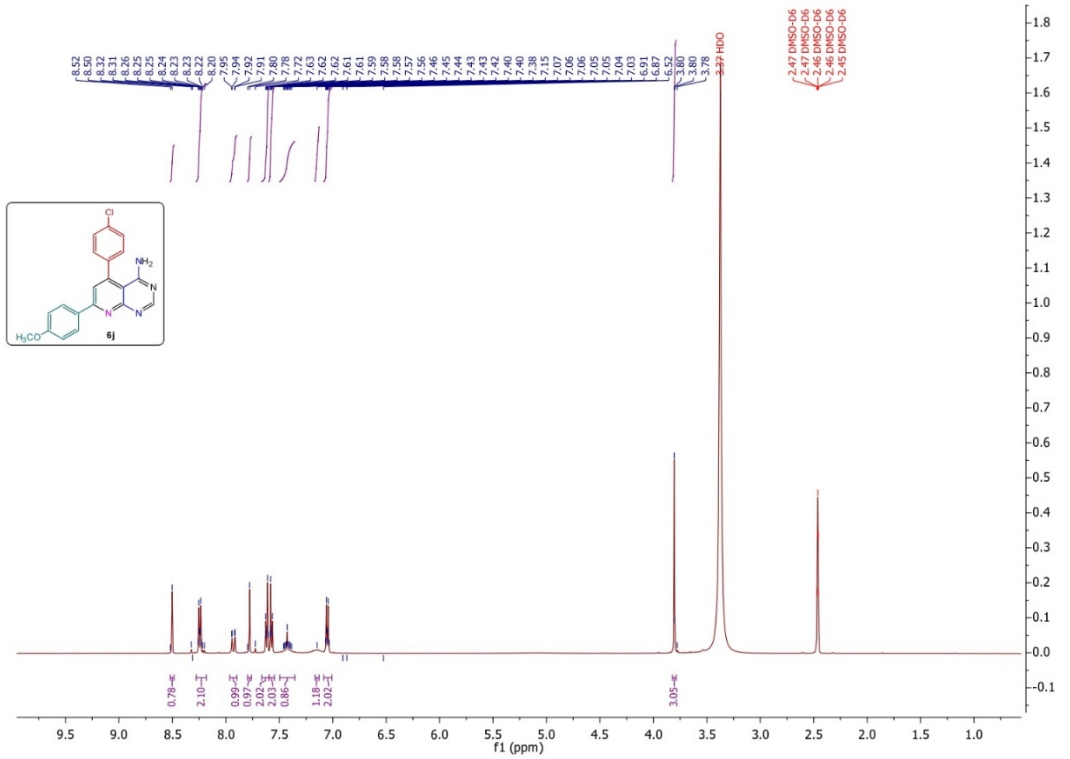


Figure S39: The ^{1}H-NMR spectrum of compound **6j.**

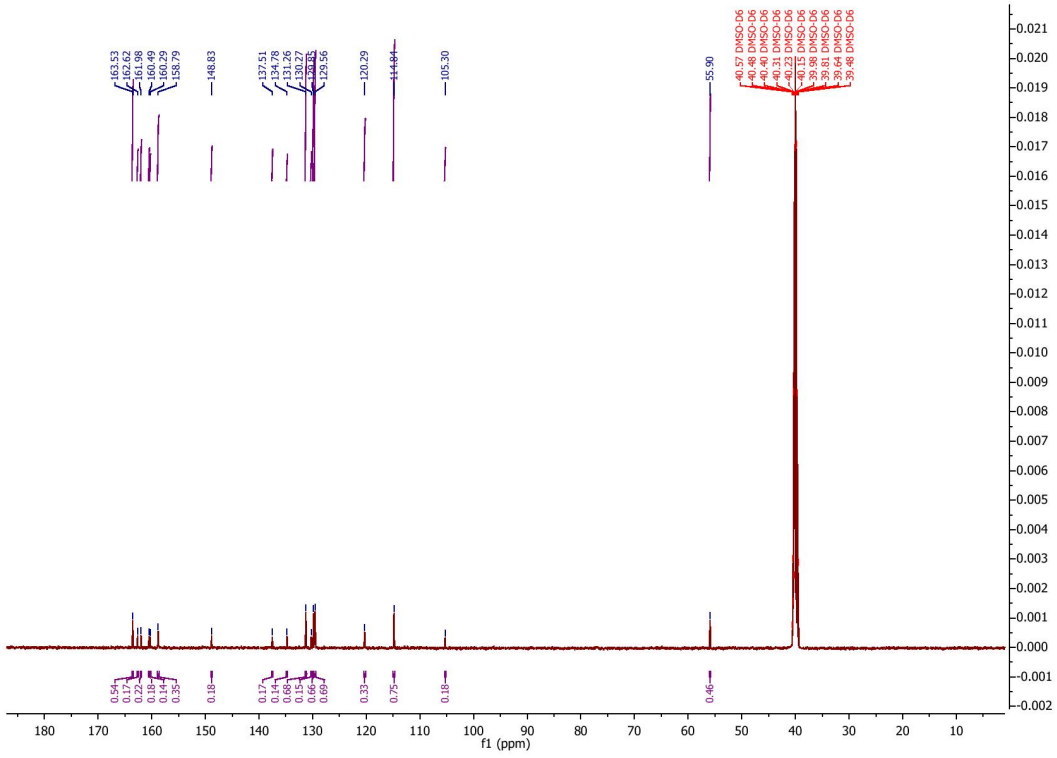


Figure S40: The ^{13}C-NMR spectrum of compound **6j.**

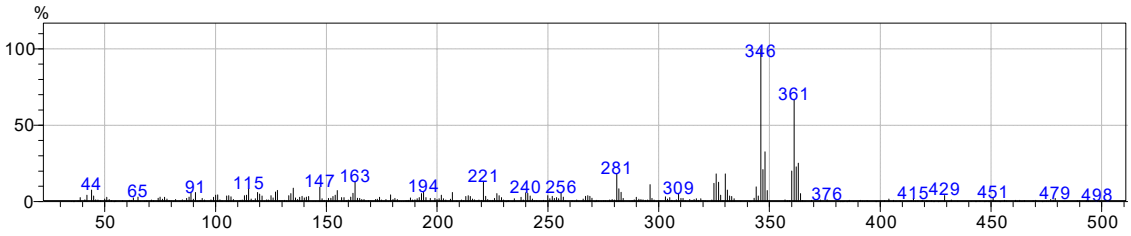


Figure S41: The MS spectrum of compound **6j.**

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