Supplementary Material

Nano-Structured $Na_2CaP_2O_7$: a New and Efficient Catalyst for One-Pot Synthesis of 2-Amino-3-Cyanopyridine Derivatives and Evaluation of Their Antibacterial Activity

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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. Melting points were determined in open capillary type on Stuart melting point SMP30. 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.

A mixture of aromatic aldehyde **1** (1.0 mmol), malononitrile **2** (1.0 mmol), methyl ketone or cyclohexanone **1** (1.0 mmol), ammonium acetate (1.5 mmol) and (0.05 g) nanocatalyst $Na_2CaP_2O_7$ were stirred and heated to 80°C in an oil bath for 30 min. 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. Then the catalyst separates from the mixture by vacuum filtration and then washed with acetone. The solvent was evaporated and 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.

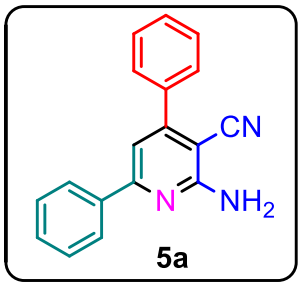
2.2 Typical procedure for the synthesis of pyrido[2,3-*d*]pyrimidine derivatives 6.

In a 100 ml flask, a mixture of 2-amino-3-cyanopyridine derivatives **5** (1 mmol) 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

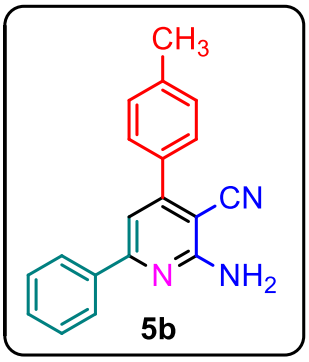
3.1 Spectral data of 2-amino-3-cyanopyridine 5

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



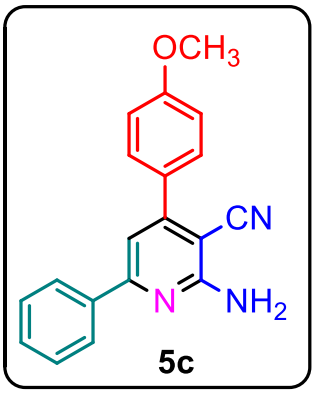
White solid, mp 183-186°C; FTIR (KBr) υ(cm^{-1}): 3464-3304 (NH_2), 3180 (Ar-H), 2206 (CN); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 5.45 (s, 2H, NH_2), 7.22 (m, 1H, H_{Ar}), 7.48 (m, 8H, H_{Ar}), 8.01 (m, 2H, H_{Ar}); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 88.33 (C_3), 111.31 (C_5), 117.16 (CN), 127.36 (C_{Ar}), 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



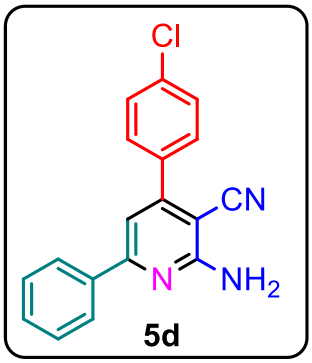
Yellow solid, mp 172-175°C; FTIR (KBr): υ(cm^{-1}): 3500-3306 (NH_2), 3215 (Ar-H), 2228 (CN); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 2.48 (s, 3H, CH_3), 5.45 (s, 2H, NH_2), 7.23(m, 1H), 7.38-7.36 (m, 2H, H_{Ar}), 7.60-7.50 (m, 5H, H_{Ar}), 8.05-8.02 (m, 2H, H_{Ar}); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 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



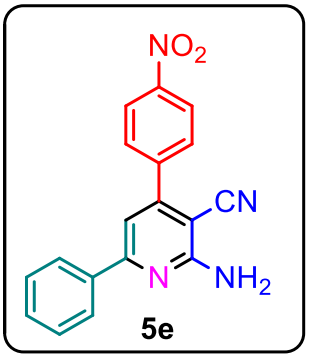
Yellow solid, mp 182-183°C; FTIR (KBr) υ(cm^{-1}): 3466-3307 (NH_2), 3184(Ar-H), 2206(CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 3.80 (s, 3H, OCH_3), 6.92 (s, 2H, NH_2), 7.02 – 7.10 (m, 2H, H_{Ar}), 7.20 (s, 1H, H_{Ar}), 7.40 – 7.49 (m, 3H, H_{Ar}), 7.58 – 7.65 (m, 2H, H_{Ar}), 8.03 – 8.11 (m, 2H, H_{Ar}). ^{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



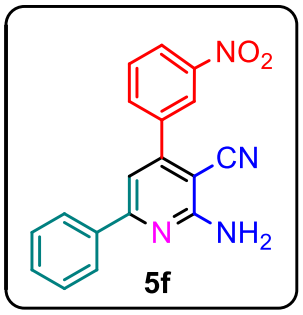
White solid: mp 239-241°C; FTIR (KBr) υ(cm^{-1}): 3446-3315 (NH_2), 3151(Ar-H), 2215(CN). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.38(s, 2H, NH_2).7.18-7.08(m, 1H), 7.51-7.38(m, 7H), 7.92-7.89(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 88.03 (C_3), 111.00(C_5), 116.95(CN), 127.36(C_{Ar}), 128.40(C_{Ar}), 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



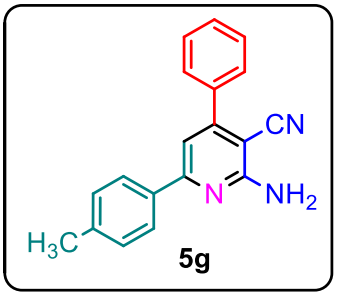
Green solid, mp 221-223°C; FTIR (KBr) υ(cm^{-1}): 3460-3352 (NH_2), 3244 (Ar-H), 2208 (CN). ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 6.80 (s, 1H, NH_2), 6.92 (s, 1H, NH_2), 7.12 (s, 1H, H_{Ar}), 7.29 (s, 1H, H_{Ar}), 7.39 – 7.53 (m, 2H, H_{Ar}), 7.55 – 7.63 (m, 1H, H_{Ar}), 7.89 (dd, J=17.90, 8.37 Hz, 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



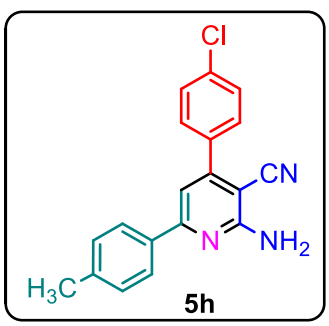
Yellow solid, mp 202-204°C; FTIR (KBr) υ(cm^{-1}): 3465-3349 cm-1 (NH_2), 3214 (Ar-H), 2223 (CN); ^{1}H NMR(DMSO-d_6, 500 MHz) δ (ppm): 6.90 (d, J=13.84 Hz, 3H, NH_2), 7.43 – 7.55 (m, 3H), 7.57 – 7.66 (m, 2H), 7.79 (t, J=8.01 Hz, 1H), 8.08 (ddd, J=7.73, 1.84, 1.01 Hz, 1H), 8.32 (ddd, J=8.30, 2.29, 0.99 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



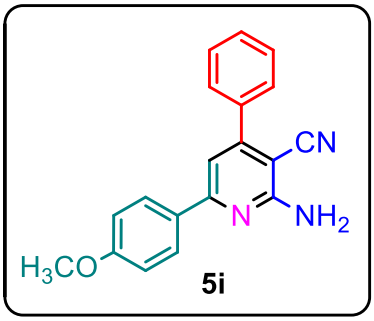
Yellow solid, mp 166-168°C; FTIR (KBr) υ(cm^{-1}): 3481-3300 (NH_2), 3182 (Ar-H), 2203 (CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 2.29 (s, 3H, CH_3), 6.95 (s, 2H, NH_2), 7.18 (s, 1H, H_{Ar}), 7.21 – 7.26 (m, 2H, H_{Ar}), 7.44 – 7.54 (m, 3H, H_{Ar}), 7.58 – 7.65 (m, 2H, H_{Ar}), 7.95 – 8.01 (m, 2H, 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



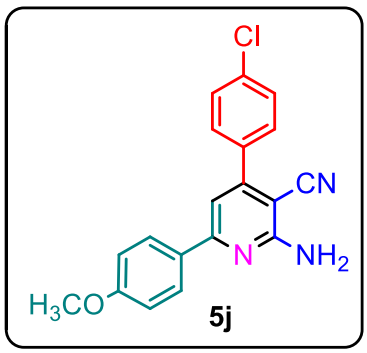
Yellow solid, mp 175-177°C; FTIR (KBr) υ(cm^{-1}): 3422-3297 (NH_2), 3130 (Ar-H), 2212 (CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 2.31 (s, 3H, CH_3), 6.98 (s, 2H, NH_2), 7.19 (s, 1H, HAr), 7.25 (d, J=7.96 Hz, 2H, H_{Ar}), 7.55 – 7.60 (m, 2H, H_{Ar}), 7.62 – 7.67 (m, 2H, H_{Ar}), 7.95 – 8.02 (m, 2H, 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



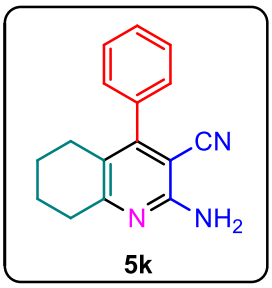
Yellow solid, mp 167-169°C; FTIR (KBr) υ(cm^{-1}): 3414-3307 (NH_2), 3140 (Ar-H), 2211 (CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 3.77 (s, 3H, OCH_3), 6.91 (s, 2H, NH_2), 6.96 – 7.04 (m, 2H, H_{Ar}), 7.17 (s, 1H, H_{Ar}), 7.44 – 7.56 (m, 3H, H_{Ar}), 7.57 – 7.65 (m, 2H, H_{Ar}), 8.04 – 8.10 (m, 2H, 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



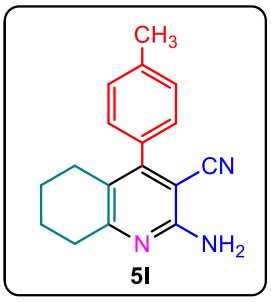
Yellow solid, mp 186-187°C; FTIR (KBr) υ(cm^{-1}): 3454-3360 (NH_2), 3228 (Ar-H), 2206 (CN); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 3.77 (s, 3H, OCH_3), 6.95 (s, 2H, NH_2), 6.96 – 7.02 (m, 2H, H_{Ar}), 7.17 (s, 1H, H_{Ar}), 7.53 – 7.60 (m, 2H, H_{Ar}), 7.61 – 7.67 (m, 2H, H_{Ar}), 8.02 – 8.09 (m, 2H, 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



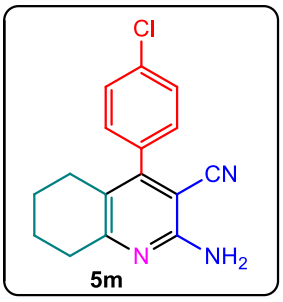
Yellow solid, mp 233-235°C; FTIR (KBr) υ(cm^{-1}): 3488-3364 (NH_2), 2949-2911 (CH_2), 2201 (CN); ^{1}H NMR (300 MHz, CDCl3) δ (ppm): 1.52 – 1.68 (m, 2H, CH_2), 1.68 – 1.83 (m, 2H, CH_2), 2.26 (t, J=6.29 Hz, 2H, CH_2), 2.74 (t, J=6.50 Hz, 2H, CH_2), 5.12 (s, 2H, NH_2), 7.13 – 7.25 (m, 2H H_{Ar}), 7.28 – 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].

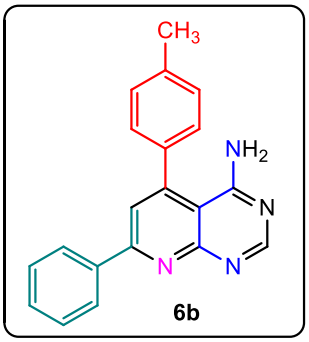
4-(4-chlorophenyl)-5,6,7,8-tetrahydro-benzo[5,6-*b*]-2amino-3-cyanopyridine 5m



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].

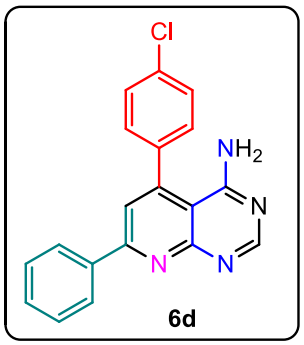
3.2 Spectral data of pyrido[2,3-*d*]pyrimidine 6

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



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 ($C_{8'}$).

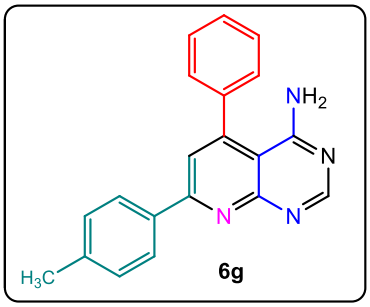
5-(4-chlorophenyl)-7-phenylpyrido[2,3-*d*]pyrimidin-4-amine 6c



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}),

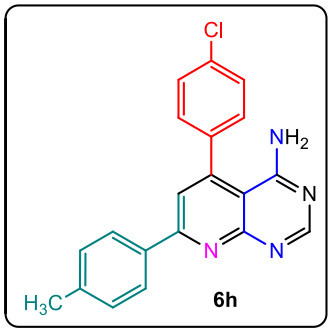
134.97 (C_{Ar}), 135.73 (C_{Ar}), 136.42 (C-Cl), 150.54 (C_5), 153.33 (C_7), 162.24 (C=N), 163.53 (C-NH_2), 164.19 ($C_{8'}$).

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



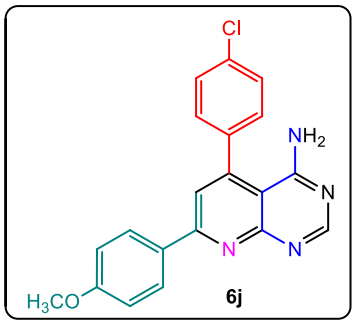
Orange, mp 307-311°C; FTIR (KBr) υ(cm^{-1}): 3521-3341 (NH_2), 3321 (Ar-H), 1610-1534 (C=C, C=N); ^{1}H NMR (DMSO-d_6, 500 MHz) δ (ppm): 2.34 (s, 3H, CH_3), 7.13 – 7.18 (m, 1H, H_{Ar}), 7.31 (d, J=7.78 Hz, 2H, NH_2), 7.36 – 7.44 (m, 1H, H_{Ar}), 7.55 (d, J=14.83 Hz, 5H, H_{Ar}), 7.79 (s, 1H, H_{Ar}), 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 ($C_{8'}$).

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 ($C_{8'}$).

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



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 ($C_{8'}$).

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