Supplementary Information

Electrocatalytic assisted one pot three component reaction for construction of highly substituted pyridine

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Experimental

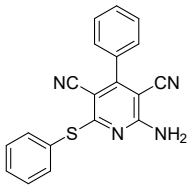
General Information: All chemicals were reagent grade and purchased from Aldrich, Alfa Aesar, Merck, Spectrochem and Qualigens and were used without further purification. The reactions were monitored using pre-coated Aluminium TLC plates of silica gel G/UV-254 of 0.25 mm thickness (Merck 60 F-254). NMR spectra were recorded on a Bruker Avance-II 400FT spectrometer at 300 or 500 MHz (^{1}H) and 75 or 125 MHz (^{13}C) in DMSO or $CDCl_3$ using TMS as an internal reference. Mass spectra (EIMS) were obtained on a Waters UPLC-TQD mass spectrometer. IR spectra were recorded on a Thermo Scientific Nicolet iS5 FT-IR spectrometer. Elemental analyses were carried out in a Thermo Scientific (FLASH 2000) CHN Elemental Analyser. Melting points were determined by open glass capillary method and were uncorrected.

General procedure for the synthesis of Electrocatalytic assisted one pot three component reaction for construction of highly substituted pyridine:

The suspension of benzaldehyde 1 (11.0 mmol) and malononitrile 2 (22 mmol) were electrolyzed in an undivided cell using $LiClO_4$ (electrolyte, .1 M), EtOH (20.0 mL), as solvent and platinum as the working and counter electrodes at constant potential (2.0 volt). The reaction mixture was electrolyzed until benzaldehyde was completely consumed (30 minutes). Thiophenol 3 (1 mmol) was added, and the reaction mixture was stirred for a period of time until completion of the reaction (TLC). The solvent was evaporated under reduced pressure and reaction mixture was

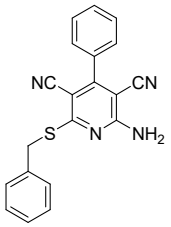
added by water (10 mL) and extracted with ethyl acetate (50 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The resulting crude product was purified by silica gel chromatography using a mixture of hexane/ethyl acetate as eluent to afford an analytically pure sample of product **4 a-o)**.

2-amino-4-phenyl-6-(phenylthio) pyridine-3,5-dicarbonitrile (4a):



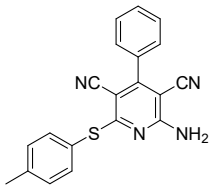
Compound 4a: Colourless solid, mp 217-219 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d6) δ: 7.47 -7.38 (m, 10H), 7.25 (broad, 2H); ^{13}C NMR (75 MHz): δ 167.4, 160.0, 158.1, 135.1 (2c), 134.0, 130.5 (2c), 130.0, 129.5, 129 (2c), 128.5 (2c), 127.5, 114.2 (2c), 93.9, 87.3; IR (KBr): 3480, 3350, 3215, 2220, 1622, 1580, 1550, 1521, 1263, 760, 700 cm-1 ; Mass (ESI): m/z 351 (M + Na)+

2-Amino-6-benzylsulfanyl-4-phenyl-pyridine-3,5-dicarbonitrile (4b):



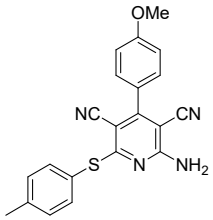
Compound **4b:** (Solid). ^{1}H NMR (300 MHz, DMSO-d6) δ: 8.18 (2H, bs, NH2) 7.58-7.50 (7H, m, Ar-H), 7.32-7.28 (3H, m, Ar-H), 4.51 (2H, s, CH_2); ^{13}C NMR (75 MHz): 166.2, 159.5, 159.3,137.5, 129.9, 128.5, 128.3, 127.1, 117.5, 115.0, 93.0, 85.9, 33.2 ppm IR (KBr): 3436, 3321, 3216, 2221, 2205, 1624, 1535, 1519, 1494, 1263, 1237, 1024, 809, 772, 751, 694, 673 cm^{-1}. Mass (ESI): m/z 365 (M + Na)+

2-Amino-4-(4-cyanophenyl)-6-(4-methylphenylsulfanyl)-3,5-pyridinedicarbonitrile (4c):



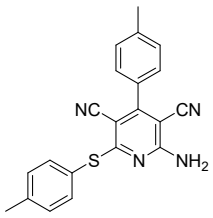
Compound **4c:** White solid; mp 272 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.73-7.70 (d, J = 8 Hz, 2H, Ar-H), 7.50-7.40 (m, 4H, Ar-H), 7.30- 7.28 (d, J = 8 Hz, 2H, Ar-H), 5.49 (s, 2H, NH2), 2.40 (s, 3H, CH3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 165.0, 156.2, 155.4, 136.5, 135.5, 134.5, 134.0, 133.9, 131.4, 130.3, 128.0, 115.8, 115.0, 94.5, 87.2.; Anal. Calcd for $C_{21}H_{13}N_5S$: C, 68.65; H, 3.57; N, 19.06%. Found: C: 68.78; H, 3.44; N, 18.95%. IR (KBr) v: 3479, 3352, 3215, 2218, 1634, 1551, 1498, 1256, cm^{-1} Mass (ESI): m/z 365 $(M + Na)^+$

2-(p-tolylthio)-6-amino-4-(4-methoxyphenyl)pyridine-3,5-dicarbonitrile (4d):



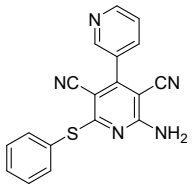
Compound **4d:** Pale yellow solid; Melting point 230–233°C; ^{1}H NMR (DMSO-d6, 200 MHz) δ: 7·43 (d, J = 8·2 Hz, 2H), 7·37 (d, J = 7·5 Hz, 2H), 7·19 (d, J = 8·2 Hz, 2H), 7·0 (d, J = 7·5 Hz, 2H), 6·74 (s, br, 2H), 3·85 (s, 3H), 2·38 (s, 3H); ^{13}C NMR (DMSO-d6, 75 MHz): δ 166·5; 160·8, 159·5, 158·1, 139·3, 135·0, 131·3, 130·2, 129·9, 128·0, 125·8, 123·5,115·5, 115·3, 114·0, 113·8, 93·1, 86·8, 55·3, 21·0; Mass (ESI): m/z 395 $(M + Na)^+$; IR (KBr) v 3463, 3323, 3215, 2221, 1632, 1603, 1545, 1508, 1258, 1179, 1028, 811 cm^{-1}

2-(p-tolylthio)-6-amino-4-p-tolylpyridine-3,5-dicarbonitrile (4e):



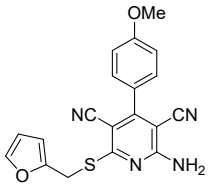
Compound **4e :** Colorless solid; mp 222°C; 1H NMR (CDCl3, 400 MHz) δ: 7.59–7.41 (m, 4H, Ar-H); 7.36-7.25 (m, 4H, Ar-H), 5.44 (s, 2H, NH2), 2.11 (s, 3H, CH3), 2.41 (s, 3H, CH3): ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 167.6, 160.0, 156.2, 136.1, 135.2, 134.6, 131.8, 131.4, 130.0, 129.7, 129.2, 128.9, 126.6, 115.5, 114.2, 96.3, 86.1, 17.1, 15.7; Anal. Calcd for $C_{21}H_{16}N_4S$: C, 70.76; H, 4.52; 15.72%. Found: C, 70.52; H, 4.65; N, 15.84%: IR (KBr) v: 3442, 3357, 3198, 2211, 1616, 1572, 1533, 1481, 1252, cm^{-1}

2-amino-6-(phenylthio)-4-(pyridin-3-yl)pyridine-3,5-dicarbonitrile (4f):



Compound **4f:** Light-yellow solid, mp 305-306 ^{1}H NMR (DMSO-d6) δ 8.77 (dd, J = 1.83 Hz, J = 4.78Hz, 1H); 8.76 (dd, J = 1.53 Hz, J = 4.88 Hz, 1H), 8.03 (dd, J = 1.53 Hz, J = 7.93 Hz, 1H), 7.80 (bs, 2H), 7.62 (dd, J = 4.88 Hz, J = 7.93 Hz, 1H), 7.60 (m, 2H), 7.51 (m, 3H); ^{13}C NMR (75 MHz): 168.2, 160.5, 159.3, 148.9, 147.3, 137.5, 128.5, 128.3, 127.1, 117.5, 115.0, 93.0, 85.9 ppm; IR (KBr) 3376, 3248, 3152, 2218, 2212, 1708, 1656, 1646, 1582, 1550, 1520, 1420, 1268, 1072, 1054, 1028, 810, 756, 728 cm^{-1} . Anal. Calcd for $C_{18}H_{11}N_5S$ (329.387): C, 65.63; H, 3.37; N, 21.27; S, 9.73. Found: C, 65.80; H, 3.35; N, 21.20; S 9.62.

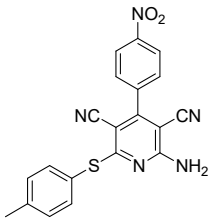
2-((furan-2-yl)methylthio)-6-amino-4-(4-methoxyphenyl)pyridine-3,5-dicarbonitrile (4g):



Compound **4g**: Pale yellow solid; Melting point 217–218°C; ^{1}H NMR (DMSO-d6, 200 MHz) δ7·62-7·37 (m, 5H), 7·04 (d, J = 8·8 Hz, 2H), 6·44 (d, J = 2·9 Hz, 1H), 6·29 (t, J = 2·2, 2·9 Hz, 1H), 4·51 (s, 2H), 3·88 (s, 3H); ^{13}C NMR (DMSO-d6, 75 MHz) δ 165·4; 160·7, 159·6, 158·1, 149·8, 142·7, 130·1, 125·7, 115·3, 114·0, 113·6, 110·7, 108·9, 93·4, 85·9, 55·2, 25·9; Mass (ESI): m/z 369 (M + Na)+ ; HRMS (ESI): Anal. Calcd. for

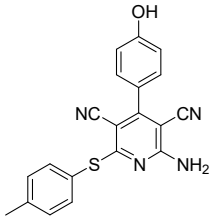
$C_{19}H_{14}N_4ONaS$: 369·0786; Found: 369·0776. IR (KBr): 3459, 3324, 3209, 2363, 2214, 1616, 1541, 1506, 1459, 1247, 1170, 1016, 826, 743 cm^{-1}.

2-Amino-4-(4-nitrophenyl)-6-(4-methylphenylsulfanyl)-3, 5-pyridinedicarbonitrile: (4h)



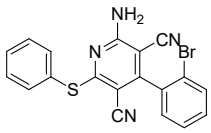
Compound **4h:** Yellow solid; mp 301°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.41-8.39 (d, J = 8 Hz, 2H); 7.68-7.66 (d, J = 7.8 Hz, 2H), 7.45-7.43 (d, J = 8 Hz, 2H), 7.28-7.26 (d, J = 7.8 Hz, 2H), 5.50 (s, 2H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 165.1.; 158.2, 156.1, 137.3, 136.2, 135.5, 134.9, 134.1, 132.9, 131.3, 125.3, 116.9, 115.1, 96.2, 86.8, 18.9, Anal. Calcd for $C_{20}H_{13}N_5O_2S$: C, 62.01; H, 3.38; N, 18.08%. Found: C, 61.85; H, 3.26; N, 18.16%; IR (KBr) v: 3472, 3332, 3218, 2215, 1626, 1541, 1509, 13.44, 1262, cm^{-1}

2-Amino-4-(4-methylphenyl)-6-(4-methylphenylsulfanyl)- 3,5-pyridinedicarbonitrile (4i)



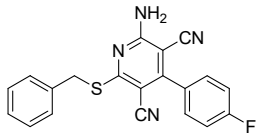
Compound **4i:** Colorless solid; mp 222°C; ^{1}H NMR (CDCl3, 400 MHz) δ: 7.59-7.41 (m, 4H, Ar-H); 7.36-7.25 (m, 4H, Ar-H), 5.44 (s, 2H, NH2), 2.11 (s, 3H, CH3), 2.41 (s, 3H, CH3), ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 167.6.; 158.9, 156.2, 136.1, 135.2, 134.6, 131.8, 131.4, 130.1, 129.7, 129.2, 129.1, 126.6, 115.5, 114.2, 96.3, 86.1, 17.1, 15.7 Anal. Calcd for $C_{21}H_{16}N_4S$: C, 70.76; H, 4.52; 15.72%. Found: C, 70.52; H, 4.65; N, 15.84% IR (KBr) v: 3442, 3357, 3198, 2211, 1616, 1572, 1533, 1481, 1252, cm^{-1}.

2-Amino-4-(2-bromo- phenyl)-6-phenylsulfanyl-pyridine-3,5-dicarbonitrile: (4j)



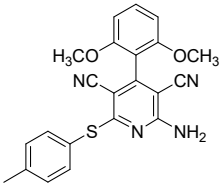
Compound **4j** Colourless solid, mp (CH_3CN) 242-244 o C; ^{1}H NMR (300 MHz, DMSO-d6): δ 7.91 (broad, 2H); 7.80 (d, J = 7.8 Hz, 1H), 7.60-7.43 (m, 8H), ^{13}C NMR (75 MHz): δ 166.4, 159.8, 158.4, 135.5, 135.3 (2C), 133.3, 132.4, 130.5, 130.2, 129.9, 128.8, 127.2, 121.1, 114.9, 114.6, 94.2, 88.2.; HRMS Calcd for $C_{19}H_{11}BrN_4S$: [M+H]+ , 406.9966; Found: 406.9961. IR (KBr): 3440, 3336, 3217, 2214, 1627, 1596, 1542, 1263, 758 cm$^{-1.}$

2-Amino-6-benzylsulfanyl-4-(4-fluoro-phenyl)-pyridine-3,5-dicarbonitrile :(4k)



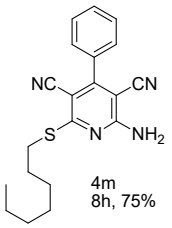
Compound **4k**: δH/ppm (250 MHz, d6 -DMSO), 8.16 (2H, bs, NH_2), 7.64-7.58 (2H, m, Ar-H), 7.52 (2H, d, J = 6.4, Ar-H), 7.44-7.25 (5H, m, Ar-H), 4.51 (2H, s), ^{13}C NMR (75 MHz, d6 -DMSO), 166.2, 165.1, 159.5, 157.5, 137.6, 131.0, 130.3, 129.4, 128.4, 127.3, 115.8, 115.2, 113.9, 93.3, 86.1, 33.2. IR (KBr): (Solid)/cm^{-1} 3439, 3334, 3211, 3069, 2210, 1621, 1606, 1544, 1506, 1462, 1427, 1321, 1262, 1233, 1165, 1027, 822, 694, 671.

2-(p-tolylthio)-6-amino-4-(2,6-dimethoxyphenyl)pyridine-3,5-dicarbonitrile: (4l)



Compound **4l :** Colourless solid; Melting point 202–203°C. ^{1}H NMR (DMSO-d6, 200 MHz) δ 7·66 (s, 1H); 7·45 (d, J = 8·1 Hz, 2H), 7·24 (d, J = 8·1 Hz, 2H), 6·7 (d, J = 8·8 Hz, 2H), 6·62 (s, br, 2H), 3·85 (s, 6H), 2·42 (s, 3H), ^{13}C NMR (DMSO-d6, 75 MHz) δ 165·8; 159·5, 156·6, 153·9, 139·5, 135·0, 132·2, 130·0, 123·2, 114·9, 114·7, 110·8, 104·5, 94·8, 88·8, 56·0, 20·8.; Mass (ESI): m/z 425 (M + Na)+ ; HRMS (ESI): Anal. Calcd. for $C_{22}H_{18}N_4O_2NaS$: 425·1048; Found: 425·1037; IR (KBr) ν 3440, 3343, 3220, 2212, 2180, 1630, 1593, 1541, 1465, 1253, 1106, 1021, 768 cm^{-1}

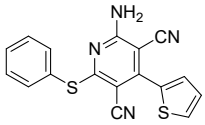
2-Amino-6-(Heptylthio)-4-phenylpyridine-3,5-dicarbonitrile: (4m)



4m
8h, 75%

Compound 4m : white crystal, mp 148 °C 1H NMR (400 MHz, CDCl3) δ 7.73–7.37 (m, 5H), 5.63 (s, 2H), 3.20 (t, J = 7.3 Hz, 2H), 1.73 (t, J = 7.5 Hz, 2H), 1.45 (t, J = 7.5 Hz, 2H), 1.40–1.21 (m, 6H), 0.89 (t, J = 7.5 Hz, 3H). LRMS m/z (ESI) calc. for $C_{20}H_{22}N_4S$ [M + H]+ : 351.

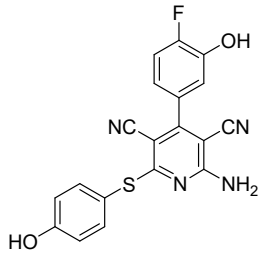
2-Amino-6-(phenylsulfanyl)-4-(3-thienyl)-3,5-pyridinedicarbonitrile: (4n)



Compound 4n: White solid; mp 235-236 ^{o}C (CH_3CN); ^{1}H NMR (DMSO-d6) δ 8.04 (dd, J = 1.22 Hz, J = 3.05 Hz, 1H); 7.77 (dd, J = 1.22 Hz, J = 3.05 Hz, 1H), 7.65 (bs, 2H), 7.60 (m, 2H), 7.50 (m, 3H), 7.39 (dd, J = 1.22 Hz, J = 4.89 Hz, 1H). ^{13}C NMR: δ 168·4; 162·7, 160·6, 158·1, 149·8, 142·7, 130·1, 128·7, 116·3, 114·0, 113·6, 111·7, 110·9, 97·4, 88·9 PPm.

Anal. Calcd for $C_{17}H_{10}N_4S_2$ (334.427): C, 61.05; H, 3.02; N, 16.76; S, 19.17. Found: C, 60.90; H, 2.98; N, 16.83; S, 19.31. IR (KBr) 3472, 3352, 3216, 2216, 1624, 1550, 1512, 1476, 1440, 1366,1306, 1262, 1024, 830, 790, 772, 756, 708, 692 cm −1

2-Amino-4-(3-fluoro-4-hydroxy-phenyl)-6-(4-hydroxy-phenylsulfanyl)-pyridine3,5-dicarbonitrile: (4o)



Compound 4o:; ^{1}H NMR (250 MHz, d6 -DMSO), 10.57 (1H, s, OH); 10.00 (1H, s, OH), 7.74 (2H, bs, NH_2), 7.44 (1H, bd, J = 11.9, Ar-H), 7.37 (2H, d, J = 8.5, Ar-H), 7.06-7.22 (2H, m, Ar-H), 6.87 (2H, d, J = 8.5, Ar-H), ^{13}C NMR (75 MHz, d6 -DMSO), 167.5, 159.6, 159.1, 157.2, 151.3, 146.7, 137.1, 125.5, 117.7, 116.9, 116.7, 116.4, 115.4, 115.2, 114.9, 92.8, 86.6 ppm, IR (KBr) 3492, 3432, 3378, 3328, 3230, 2216, 1703, 1548, 1511, 1496, 1470, 1440, 1374, 1269, 1248, 1192, 1170, 1116, 1032, 946, 833, 760, 685 cm^{-1}; ESIMS Calcd for $C_{19}H_{11}FN_4O_2S$: $[M+ Na]^+$ = 401