Supporting Information

Library Design, Synthesis and Screening: Pyridine Dicarbonitriles as Potential Prion Disease Therapeutics

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PrP^{Sc} Inhibition Assay:

A persistently infected mouse cell line (SMB), cloned originally from scrapie infected mouse brain, but of non-neuronal origin (Clarke and Haig, 1970), was used for screening of compounds for their ability to prevent the formation of PrP^{Sc}. SMB cells were grown in tissue culture treated plastic dishes in Medium 199 (phenol red free), supplemented with 10% newborn calf serum (heat inactivated), 5% foetal calf serum (heat inactivated), and penicillin-streptomycin at 10mg/L at 37 °C in an atmosphere of 5% CO_2 in air at 95% relative humidity. Medium was changed every 3rd or 4th day, and every 7 days confluent cells were passaged using 0.05% trypsin, 0.002% EDTA, at a split ratio of 4. To assess the effects of compounds cells were distributed into 24-well cluster plates at 3 x 10^4 cells per well and incubated for 24 h to allow for cell attachment. The medium was then replaced with medium containing compounds with a final DMSO concentration of ≤0.2% (v/v). Cells were grown for 7 days at 37 °C and the medium exchanged on day 3 or 4 for medium containing compounds.

After 7 days cell viability was assessed by the MTT assay following the standard protocol supplied with the reagent (Sigma). For dot blot analyses cells were extracted using lysis buffer (10 mM Tris-HCl (pH 7.6), 100 mM NaCl, 10 mM EDTA, 0.5% (v/v) NP40 and 0.5% (w/v) sodium deoxycholate), centrifuged (1000 g, 5 min), and the post nuclear supernatant loaded onto a nitrocellulose membrane (0.45 μm) under gentle vacuum at a total cellular protein concentration of approximately 30 μg/well (determined by the Bradford assay following the protocol supplied with the reagent, Sigma). The membrane was air-dried and subjected to 75 μg/mL proteinase K digestion for 1h at 37 °C. The reaction was stopped with 1mM phenylmethylsulfonyl fluoride (PMSF) in 20mM Tris-HCl-buffered saline (TBS), the membrane washed extensively with TBS, and immersed in 3M guanidine thiocyanate in TBS for 10 min at room temperature. After further washing with TBS the membrane was blocked using 5% fat-free milk powder in phosphate buffered saline (PBS), processed with 0.2 μg/mL mouse monoclonal anti-PrP 6H4 (Prionics) and developed using an ECL kit (Amersham Pharmacia Biotech).

Experimental Spectroscopic Data:

General Information:

Infra red spectra were recorded on a Perkin-Elmer Spectrum RX1 FT-IR system equipped with a DuraSampl*IR* IITM- diamond ATR solid sample unit. All NMR spectra were recorded with tetramethylsilane as an internal standard on a Bruker AC-250 machine at 250 MHz (^{1}H) and 62.8 MHz (^{13}C), couplings (J) are given in Hz.

2-Amino-4-phenyl-6-phenylsulfanyl-pyridine-3,5-dicarbonitrile (8). υ_{max} (Solid)/cm^{-1}, 3483, 3358, 2208, 1614, 1542, 1513, 1494, 1462, 1440, 1254, 1019, 999, 752, 703, 680; δ_H/ppm (250 MHz, d^6-DMSO); 7.47-7.63 (10H, m, Ar-H), 7.83 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 87.1, 93.4, 115.0, 115.3, 127.2, 128.4, 128.7, 129.4, 129.7, 130.4, 133.9, 134.8, 158.7, 159.7, 166.1.

2-Amino-4-tert-butyl-6-phenylsulfanyl-1,4-dihydro-pyridine-3,5-dicarbonitrile (14). υ_{max} (Solid)/cm^{-1} 3337, 3210, 2963, 2176, 1636, 1482, 1440, 1393, 1312, 1240, 1173, 1023, 884, 742, 687; δ_H/ppm (250 MHz, d^6-DMSO), 0.83 (9H, s, $(CH_3)_3$), 2.78 (1H, s, CH), 5.93 (2H, bs, NH_2), 7.32-7.53 (5H, m, Ar-H), 9.40 (1H, s, NH); δ_C/ppm (62.8 MHz, d^6-DMSO), 25.9, 40.8, 47.3, 51.8, 89.6, 119.9, 122.3, 128.4, 129.8, 130.2, 131.1, 143.2, 152.9.

2-Amino-4-(4-hydroxy-phenyl)-6-(4-hydroxy-phenylsulfanyl)-pyridine-3,5-dicarbonitrile (16). υ_{max} (Solid)/cm^{-1}, 3439, 3359, 3326, 3228, 2216, 1701, 1642, 1612, 1583, 1544, 1510, 1497, 1470, 1440, 1418, 1375, 1319, 1277, 1264, 1232, 1176, 1168, 1032, 1008, 946, 848, 834, 779, 677; δ_H/ppm (250 MHz, d^6-DMSO); 6.86 (2H, dd, J = 8.5, Ar-H), 6.91 (2H, d, J = 8.6, Ar-H) 7.35 (2H, d, J = 8.6, Ar-H), 7.38 (2H, d, J = 8.9, Ar-H), 7.67 (2H, bs, NH_2), 9.99 (1H, bs, OH), 10.01 (1H, bs, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.4, 92.7, 115.0, 115.4, 115.7, 116.5, 124.2, 130.3, 137.1, 158.5, 159.0, 159.4, 159.8, 162.5, 167.6.

2-Amino-4-(3-chloro-4-hydroxy-phenyl)-6-(2-fluoro-phenylsulfanyl)-pyridine-3,5-dicarbonitrile (17). υ_{max} (Solid)/cm^{-1}, 3494, 3332, 3210, 2926, 2581, 2214, 1719, 1617, 1542, 1507, 1473, 1401, 1299, 1265, 1166, 1057, 1027, 816, 762; δ_H/ppm (250 MHz, d^6-DMSO), 7.12 (1H, d, J = 8.5, Ar-H), 7.32-7.38 (3H, m, Ar-H), 7.61-7.66 (3H, m, Ar-H), 7.80 (2H, bs, NH_2), 10.93 (1H, s, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 87.2, 94.0, 115.1, 115.4, 116.4, 116.6, 119.8, 125.2, 125.4, 128.8, 130.3, 133.1, 137.1, 149.9, 155.0, 157.2, 159.7, 164.8, 165.6.

2-Amino-6-phenylsulfanyl-4-thiophen-2-yl-pyridine-3,5-dicarbonitrile (18). υ_{max} (Solid)/cm^{-1}, 3485, 3346, 3214, 3064, 2213, 1620, 1546, 1508, 1474, 1436, 1401, 1355, 1306, 1254, 1235, 999, 827, 756, 706, 690; δ_H/ppm (250 MHz, d^6-DMSO), 7.27-7.33 (1H, m, Ar-H), 7.46-7.54 (3H, m, Ar-H), 7.56-7.64 (3H, m, Ar-H), 7.86 (2H, bs, NH_2), 7.96 (1H, d, J = 4.6, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.8, 106.9, 115.2, 115.4, 127.1, 127.9, 129.5, 129.7, 130.8, 131.3, 132.7, 134.9, 150.9, 159.8, 166.7.

2-Amino-6-(3-chloro-phenylsulfanyl)-4-phenyl-pyridine-3,5-dicarbonitrile (19). υ_{max} (Solid)/cm^{-1}, 3459, 3333, 3214, 2211, 1616, 1579, 1548, 1520, 1488, 1459, 1407, 1308, 1262, 1238, 1087, 1031, 997, 887, 806, 772, 755, 700, 680, 650; δ_H/ppm (250 MHz, d^6-DMSO), 7.49-7.61 (8H, m, Ar-H), 7.69 (1H, t, J = 1.8, Ar-H), 7.89 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 87.8, 94.3, 115.4, 115.7, 128.9, 129.2, 129.8, 130.3, 130.9, 131.6, 134.0, 134.1, 134.3, 134.6, 159.2, 160.2, 166.0.

2-Amino-4-(3-hydroxy-phenyl)-6-(4-hydroxy-phenylsulfanyl)-pyridine-3,5-dicarbonitrile (22). υ_{max} (Solid)/cm^{-1}, 3388, 3323, 3218, 2216, 1645, 1548, 1521, 1493, 1253, 1222, 1031, 870, 826; δ_H/ppm (250 MHz, d^6-DMSO); 6.87-6.96 (5H, m, Ar-H), 7.32-7.37 (3H, m, Ar-H), 7.73 (2H, bs, NH_2), 9.89 (1H, s, OH), 10.00 (1H, s, OH); δ_C/ppm (62.8 MHz, d^6-DMSO); 86.5, 92.6, 114.9, 115.0, 115.3, 116.5, 117.2, 118.4, 118.9, 130.0, 135.1, 137.2, 157.3, 158.5, 159.1, 159.7, 167.5.

2-Amino-4-(4-formyl-phenyl)-6-(4-hydroxy-phenylsulfanyl)-pyridine-3,5-dicarbonitrile (24). υ_{max} (Solid)/cm^{-1}, 3318, 3220, 2211, 1690, 1645, 1601, 1574, 1546, 1520, 1494, 1424, 1256, 1211, 1169, 818, 773; δ_H/ppm (250 MHz, d^6-DMSO); 6.87 (2H, d, J = 8.5, Ar-H), 7.38 (2H, d, J = 8.5, Ar-H), 7.78 (2H, d, J = 8.2, Ar-H), 7.86 (2H, bs, NH2), 8.09 (2H, d, J = 7.9, Ar-H), 10.04 (1H, bs, OH), 10.11 (1H, s, CHO); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.5, 92.5, 114.2, 114.7, 115.2, 116.6, 118.4, 129.4, 133.1, 137.2, 139.5, 157.5, 159.2, 159.5, 167.7, 192.8.

2-Amino-4-(3-fluoro-4-hydroxy-phenyl)-6-(4-hydroxy-phenylsulfanyl)-pyridine-3,5-dicarbonitrile (25). υ_{max} (Solid)/cm^{-1}, 3492, 3432, 3378, 3328, 3230, 2216, 1703, 1548, 1511, 1496, 1470, 1440, 1374, 1269, 1248, 1192, 1170, 1116, 1032, 946, 833, 760, 685; δ_H/ppm (250 MHz, d^6-DMSO), 6.87 (2H, d, J = 8.5, Ar-H), 7.06-7.22 (2H, m, Ar-H), 7.37 (2H, d, J = 8.5, Ar-H), 7.44 (1H, bd, J = 11.9, Ar-H), 7.74 (2H, bs, NH_2), 10.00 (1H, s, OH), 10.57 (1H, s, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.6, 92.8, 114.9, 115.2, 115.4, 116.4, 116.7, 116.9, 117.7, 125.5, 137.1, 146.7, 151.3, 157.2, 159.1, 159.6, 167.5.

2-Amino-4-(3-chloro-4-hydroxy-phenyl)-6-(4-hydroxy-phenylsulfanyl)-pyridine-3,5-dicarbonitrile (26). υ_{max} (Solid)/cm^{-1}, 3495, 3408, 3321, 3330, 2223, 1706, 1643, 1548, 1503, 1426, 1327, 1275, 1215, 1164, 1094, 1056, 1032, 921, 894, 853, 831, 778, 712, 680, 634; δ_H/ppm (250 MHz, d^6-DMSO); 6.87 (2H, d, J = 8.5, Ar-H), 7.12 (1H, d, J = 8.5, Ar-H), 7.31-7.36 (3H, m, Ar-H), 7.60 (1H, d, J = 1.8, Ar-H), 7.73 (2H, bs, NH_2), 10.00 (1H, s, OH), 10.91 (1H, s, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.6, 92.8, 114.9, 115.3, 115.6, 116.6, 119.8, 125.4, 128.8, 130.3, 133.1, 137.2, 155.0, 157.1, 159.2, 159.7, 167.6.

4-(4-Acetyl-phenyl)-2-amino-6-(4-hydroxy-phenylsulfanyl)-pyridine-3,5-dicarbonitrile (27). υ_{max} (Solid)/cm^{-1}, 3382, 3312, 3200, 2214, 1672, 1647, 1542, 1494, 1428, 1404, 1360, 1262, 1170, 1099, 1010, 962, 829, 808, 780, 724; δ_H/ppm (250 MHz, d^6-DMSO), 2.66 (3H, s, CH_3), 6.87 (2H, d, J = 8.5, Ar-H), 7.38 (2H, d, J = 8.5, Ar-H), 7.71 (2H, d, J = 8.5, Ar-H), 7.82 (2H, bs, NH_2), 8.13 (2H, d, J = 8.2, Ar-H), 10.01 (1H, s, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 26.9, 86.4, 92.4, 114.9, 115.2, 116.6, 128.4, 129.0, 137.1, 137.9, 138.3, 159.2, 159.5, 167.6, 197.6.

4-[2-Amino-3,5-dicyano-6-(4-hydroxy-phenylsulfanyl)-pyridin-4-yl]-benzoic acid methyl ester (28). υ_{max} (Solid)/cm^{-1} 3408, 3328, 3230, 2210, 1714, 1640, 1543, 1526, 1492, 1431, 1270, 1227, 1103, 1110, 965, 859, 828, 761, 705, 674; δ_H/ppm (250 MHz, d^6-DMSO), 3.89 (3H, s, OCH_3), 6.93 (2H, d, J = 8.5, Ar-H), 7.40 (2H, d, J = 8.5, Ar-H), 7.74 (2H, d, J = 8.5, Ar-H), 7.82 (2H, bs, NH_2), 8.02 (2H, d, J = 8.2, Ar-H), 10.12 (1H, s, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 52.5, 86.5, 92.5, 114.7, 114.9, 115.2, 116.6, 129.1, 129.5, 131.2, 137.2, 138.6, 157.6, 159.2, 159.5, 165.7, 167.7.

4-[2-Amino-6-(3-chloro-phenylsulfanyl)-3,5-dicyano-pyridin-4-yl]-benzoic acid methyl ester (32). υ_{max} (Solid)/cm^{-1}, 3416, 3328, 3232, 2213, 1712, 1640, 1548, 1528, 1463, 1434, 1404, 1268, 1120, 1106, 1031, 1021, 778, 709, 678; δ_H/ppm (250 MHz, d^6-DMSO), 3.91 (3H, s, CO_2CH_3), 7.49-7.61 (3H, m, Ar-H), 7.69-7.73 (3H, m, Ar-H), 7.98 (2H, bs, NH_2), 8.14 (2H, d, J = 8.2, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 52.5, 88.3, 95.1, 114.7, 115.0, 129.0, 129.3, 129.4, 129.8, 131.1, 131.3, 133.5, 133.6, 134.1, 138.4, 142.7, 157.7, 159.6, 165.6.

2-Amino-6-(2-fluoro-phenylsulfanyl)-4-(3-hydroxy-phenyl)-pyridine-3,5-dicarbonitrile (33). υ_{max} (Solid)/cm^{-1}, 3487, 3346, 3215, 2214, 1641, 1624, 1549, 1524, 1475, 1444, 1247, 1155, 1026, 940, 827, 766, 756, 702; δ_H/ppm (250 MHz, d^6-DMSO), 6.92-6.96 (3H, m, Ar-H), 7.35-7.40 (3H, m, Ar-H), 7.63-7.67 (2H, m, Ar-H), 7.81 (2H, bs, NH_2), 9.91 (1H, s, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 87.1, 92.9, 114.1, 114.9, 115.1, 115.2, 116.2, 117.3, 118.9, 125.4, 130.0, 133.1, 135.0, 137.1, 157.4, 158.7, 159.7, 160.2, 164.8.

***N*-{4-[6-Amino-3,5-dicyano-4-(2,6-difluoro-phenyl)-pyridin-2-ylsulfanyl]-phenyl}-acetamide (34).** υ_{max} (Solid)/cm^{-1} 3388, 3171, 2214, 2170, 1689, 1626, 1589, 1554, 1523, 1466, 1421, 1397, 1367, 1312, 1255, 1238, 1181, 1110, 1004, 888, 830, 788, 736, 706, 675; δ_H/ppm (250 MHz, d^6-DMSO), 2.08 (3H, s, CH_3), 7.39-7.46 (2H, m, Ar-H), 7.54 (2H, d, J = 8.5, Ar-H), 7.70-7.75 (3H, m, Ar-H), 8.07 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 24.1, 87.8, 93.9, 112.4, 112.7, 114.0, 114.3, 119.1, 119.5, 124.5, 136.0, 141.0, 147.2, 159.3, 160.4, 164.3, 167.3, 168.7.

2-Amino-6-(4-carboxy-phenylsulfanyl)-4-(4-methylester-phenyl)-pyridine-3,5-dicarbonitrile (35). υ_{max} (Solid)/cm^{-1}, 3380, 3309, 3200, 2217, 1724, 1697, 1646, 1548, 1525, 1431, 1397, 1277, 1114, 1014, 852, 801, 759, 707; δ_H/ppm (250 MHz, d^6-DMSO); 3.90 (3H, s, CO_2CH_3), 7.72 (2H, d, J = 8.2, Ar-H), 7.73 (2H, d, J = 8.6, Ar-H), 7.98 (2H, bs, NH_2), 8.01 (2H, d, J = 8.6, Ar-H), 8.13 (2H, d, J = 8.2, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO); 52.5, 87.3, 93.6, 114.7, 115.1, 126.1, 129.1, 130.1, 131.3, 132.9, 134.3, 138.4, 140.8, 157.8, 159.6, 165.6, 166.7, 166.8.

4-[2-(4-Acetylamino-phenylsulfanyl)-6-amino-3,5-dicyano-pyridin-4-yl]-benzoic acid methyl ester (36). υ_{max} (Solid)/cm^{-1}, 3520, 3368, 3131, 2218, 1711, 1682, 1652, 1588, 1523, 1432, 1397, 1368, 1317, 1295, 1255, 1180, 1110, 1012, 957, 840, 821, 764, 708, 582; δ_H/ppm (250 MHz, d^6-DMSO), 2.09 (3H, s, NHCOC<u>H</u>$_3$), 3.90 (3H, s, CO_2CH_3), 7.52 (2H, d, J = 8.9, Ar-H), 7.72 (2H, d, J = 8.6, Ar-H), 7.73 (2H, d, J = 8.9, Ar-H), 7.88 (2H, bs, NH_2), 8.14 (2H, d, J = 8.5, Ar-H), 10.21 (1H, bs, N<u>H</u>$COCH_3$); δ_C/ppm (62.8 MHz, d^6-DMSO), 24.1, 52.5, 86.7, 92.7, 106.8, 114.8, 115.1, 119.6, 129.1, 129.4, 131.2, 135.9, 138.5, 140.9, 157.6, 159.6, 165.6, 167.0, 168.7.

4-[6-Amino-3,5-dicyano-4-(3-methyl ester)-pyridin-2-ylsulfanyl]-benzoic acid methyl ester (37). υ_{max} (Solid)/cm^{-1} 3460, 3386, 3318, 3223, 2955, 2220, 1713, 1642, 1543, 1520, 1432, 1408, 1256, 1190, 1112, 1030, 1017, 968, 801, 753, 740, 713, 680, 586; δ_H/ppm (250 MHz, d^6-DMSO), 3.89 (3H, s, CO_2CH_3), 3.91 (3H, s, CO_2CH_3), 7.63-7.74 (4H, m, Ar-H), 7.92 (2H, bs, NH_2), 8.06-8.16 (4H, m, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 52.5 (2 x CH_3), 87.1, 95.0, 113.4, 114.7, 127.9, 129.0, 129.5, 130.0, 130.4, 130.8, 131.3, 135.6, 138.4, 139.6, 156.7, 157.7, 159.5, 165.5, 165.6.

4-[6-Amino-3,5-dicyano-4-(4-hydroxy-phenyl)-pyridin-2-ylsulfanyl]-benzoic acid methyl ester (38). υ_{max} (Solid)/cm^{-1}, 3405, 3324, 3229, 2218, 1704, 1645, 1608, 1594, 1554, 1531, 1512, 1438, 1294, 1279, 1268, 1179, 1112, 1014, 820, 779, 763, 728, 694, 678; δ_H/ppm (250 MHz, d^6-DMSO), 3.89 (3H, s, CO_2CH_3), 6.92 (2H, d, J = 8.6, Ar-H), 7.40 (2H, d, J = 8.5, Ar-H), 7.75 (2H, d, J = 8.6, Ar-H), 7.82 (2H, bs, NH_2), 8.02 (2H, d, J = 8.2, Ar-H), 10.12 (1H, bs, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 52.4, 87.2, 93.9, 115.3, 115.4, 115.5, 124.1, 126.2, 129.8, 130.0, 133.9, 134.3, 158.8, 159.5, 159.8, 165.7, 169.6.

2-Amino-6-(4-methylester-phenylsulfanyl)-4-(4-methylester-phenyl)-pyridine-3,5-dicarbonitrile (39). υ_{max} (Solid)/cm^{-1}, 3506, 3384, 3318, 3222, 2217, 1730, 1705, 1644, 1547, 1525, 1432, 1293, 1265, 1194, 1109, 1014, 960, 854, 801, 762; δ_H/ppm (250 MHz, d^6-DMSO), 3.89 (3H, s, CH_3), 3.90 (3H, s, CH_3), 7.68-7.80 (4H, m, Ar-H), 7.98 (2H, bs, NH_2), 8.03 (2H, d, J = 8.2, Ar-H), 8.14 (2H, d, J = 7.9, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 52.4, 52,5, 87.4, 93.6, 114.7, 115.0, 118.4, 129.1, 129.5, 129.9, 130.2, 131.3, 133.6, 134.4, 138.4, 157.8, 159.5, 164.9, 165.6.

***N*-{4-[6-Amino-3,5-dicyano-4-(3,5-difluoro-phenyl)-pyridin-2-ylsulfanyl]-phenyl}-acetamide (40).** υ_{max} (Solid)/cm^{-1} 3486, 3372, 3081, 2212, 1695, 1618, 1603, 1547, 1520, 1493, 1458, 1435, 1397, 1365, 1312, 1242, 1182, 1132, 1049, 1012, 996, 955, 872, 846, 821, 811, 774; δ_H/ppm (250 MHz, d^6-DMSO), 2.08 (3H, s, CH_3), 7.41-7.56 (5H, m, Ar-H), 7.72 (2H, d, J = 8.8, Ar-H), 7.91 (2H, bs, NH_2), 10.20 (1H, s, NH); δ_C/ppm (62.8 MHz, d^6-DMSO), 24.1, 86.9, 92.8, 112.2, 112.6, 114.6, 114.9, 119.6, 120.0, 136.0, 140.9, 141.0, 156.2, 159.4, 164.2, 166.9, 168.7, 168.8.

2-Amino-6-(3-chloro-phenylsulfanyl)-4-thiophen-2-yl-pyridine-3,5-dicarbonitrile (41). υ_{max} (Solid)/cm^{-1}, 3490, 3374, 3208, 3092, 2205, 1613, 1544, 1509, 1460, 1432, 1409, 1314, 1257, 1240, 1123, 1064, 994, 866, 774, 723, 683; δ_H/ppm (250 MHz, d^6-DMSO), 7.30 (1H, dd, J = 5.2, 3.7, Ar-H), 7.45–7.65 (4H, m, Ar-H), 7.69 (1H, t, J = 1.7, Ar-H), 7.93 (2H, bs, NH_2), 7.97 (1H, dd, J = 5.2, 1.2, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 87.1, 106.8, 115.1, 115.4, 127.9, 129.3, 129.8, 131.0, 131.20, 131.3, 132.6, 133.5, 133.6, 134.1, 150.9, 159.9, 166.1.

2-Amino-6-benzylsulfanyl-4-thiophen-2-yl-pyridine-3,5-dicarbonitrile (42). υ_{max} (Solid)/cm^{-1}, 3435, 3317, 3214, 3100, 2218, 2200, 1623, 1537, 1402, 1256, 1236, 1009, 767, 717, 696; δ_H/ppm (250 MHz, d^6-DMSO), 4.50 (2H, s, CH_2), 7.21-7.35 (4H, m, Ar-H), 7.49-7.56 (3H, m, Ar-H), 7.93 (1H, dd, J = 4.9, 1.2), 8.15 (2H, bs, NH_2); δ_C/ppm (62.5 MHz, d^6-DMSO), 33.3, 85.7, 93.1, 106.9, 115.4, 127.3, 127.9, 128.4, 129.4, 130.8, 131.2, 132.7, 137.5, 150.7, 159.7, 166.8.

***N*-[4-(6-Amino-3,5-dicyano-4-thiophen-2-yl-pyridin-2-ylsulfanyl)-phenyl]-acetamide (43)**. υ_{max} (Solid)/cm^{-1}, 3368, 3092, 2204, 1678, 1654, 1587, 1504, 1396, 1309, 1252, 1180, 1046, 1007, 837, 721; δ_H/ppm (250 MHz, d^6-DMSO), 2.09 (3H, s, CH_3), 7.25-7.35 (1H, m, Ar-H), 7.51 (2H, d, J = 9.1, Ar-H), 7.56-7.61 (1H, m, Ar-H), 7.72 (2H, d, J = 8.9, Ar-H), 7.83 (2H, bs, NH_2), 7.93-8.00 (1H, m, Ar-H), 10.20 (1H, s, NH); δ_C/ppm (62.8 MHz, d^6-DMSO), 24.1, 86.6, 92.8, 115.2, 115.4, 119.5, 119.7, 127.9, 130.8, 131.3, 132.7, 135.9, 140.9, 150.8, 159.8, 167.5, 168.7.

2-Amino-6-benzylsulfanyl-4-phenyl-pyridine-3,5-dicarbonitrile (44). υ_{max} (Solid)/cm^{-1}, 3436, 3321, 3216, 2221, 2205, 1624, 1535, 1519, 1494, 1263, 1237, 1024, 809, 772, 751, 694, 673. δ_H/ppm (250 MHz, d^6-DMSO), 4.51 (2H, s, CH_2), 7.28-7.32 (3H, m, Ar-H), 7.50-7.58 (7H, m, Ar-H), 8.18 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 33.2, 86.0, 93.2, 115.2, 115.2, 118.5, 127.3, 128.4, 128.7, 129.4, 130.3, 134.0, 137.6, 158.4, 159.6, 166.2.

2-Amino-6-benzylsulfanyl-4-(3-hydroxy-phenyl)-pyridine-3,5-dicarbonitrile (45). υ_{max} (Solid)/cm^{-1}, 3324, 3224, 2219, 1649, 1545, 1521, 1444, 1426, 1258, 1229, 1042, 863, 768, 694, 610. δ_H/ppm (250 MHz, d^6-DMSO), 4.50 (2H, s, CH_2), 6.70-7.76 (3H, m, Ar-H), 7.30-7.35 (4H, m, Ar-H), 7.50-7.54 (2H, m, Ar-H), 8.12 (2H, bs, NH_2), 9.88 (1H, s, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 33.2, 85.9, 93.1, 115.0, 115.1, 115.2, 117.2, 118.9, 127.3, 128.4, 129.4, 130.0, 135.1, 137.6, 157.3, 158.4, 159.6, 166.2.

3-(6-Amino-3,5-dicyano-4-phenyl-pyridin-2-ylsulfanyl)-benzoic acid methyl ester (48). υ_{max} (Solid)/cm^{-1}, 3455, 3346, 3330, 2214, 1732, 1638, 1548, 1521, 1438, 1410, 1296, 1270, 1236, 1127, 1094, 1073, 1000, 958, 811, 743, 701, 685, 604; δ_H/ppm (250 MHz, d^6-DMSO), 3.89 (3H, s, CH_3), 7.54-7.69 (5H, m, Ar-H), 7.85 (2H, bs, NH_2), 7.88 (1H, d, J = 8.2, Ar-H), 8.06-8.10 (2H, m, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 52.8, 87.7, 94.3, 115.5, 115.7, 128.5, 128.9, 129.2, 130.5, 130.8, 130.9, 131.3, 134.3, 136.1, 140.0, 159.2, 160.1, 165.9, 166.1.

4-(6-Amino-3,5-dicyano-4-phenyl-pyridin-2-ylsulfanyl)-benzoic acid methyl ester (49). υ_{max} (Solid)/cm^{-1}, 3401, 3323, 3229, 3063, 2214, 1704, 1644, 1528, 1438, 1294, 1278, 1282, 1197, 1181, 1111, 1013, 956, 852, 762, 750, 726, 696; δ_H/ppm (250 MHz, d^6-DMSO), 3.89 (3H, s, CH_3), 7.54-7.60 (5H, m, Ar-H), 7.76 (2H, d, J = 7.6, Ar-H), 7.92 (2H, bs, NH_2) , 8.03 (2H, d, J = 8.2, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 52.4, 87.5, 93.9, 114.9, 115.2, 128.5, 128.8, 129.8, 130.1, 130.5, 133.7, 133.9, 134.3, 158.8, 159.7, 164.9, 165.8.

2-Amino-6-(4-hydroxy-phenylsulfanyl)-4-thiophen-2-yl-pyridine-3,5-dicarbonitrile (50). υ_{max} (Solid)/cm^{-1}, 3468, 3322, 3215, 3097, 2970, 2209, 1624, 1583, 1545, 1494, 1433, 1401, 1358, 1259, 1219, 1170, 1088, 1045, 1006, 876.1, 831.0, 738 δ_H/ppm (250 MHz, d^6-DMSO), 6.87 (2H, d, J = 8.9, Ar-H), 7.29 (1H, dd, J = 4.9, 3.7, Ar-H), 7.38 (2H, d, J = 8.6, Ar-H), 7.57 (1H, dd, J = 3.7, 1.2, Ar-H), 7.80 (2H, bs, NH_2), 7.96 (1H, dd, J = 4.9, 1.2, Ar-H), 10.01 (1H, bs, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.4, 92.5, 106.8, 114.8, 115.2, 115.4, 116.6, 127.9, 131.2, 132.8, 137.1, 150.7, 159.2, 159.8, 168.1.

2-Amino-6-(3-hydroxy-phenylsulfanyl)-4-phenyl-pyridine-3,5-dicarbonitrile (51). υ_{max} (Solid)/cm^{-1}, 3320, 3224, 2214, 1974, 1646, 1582, 1523, 1496, 1474, 1441, 1301, 1260, 1218, 1077, 1036, 995, 885, 806, 784, 754, 702, 683, 649, 628; δ_H/ppm (250 MHz, d^6-DMSO), 6.85-6.89 (1H, m, Ar-H), 6.95-6.99 (2H, m, Ar-H), 7.29 (1H, t, J = 7.9, Ar-H), 7.54-7.62 (5H, m, Ar-H), 7.84 (2H, bs, NH_2), 9.81 (1H, s, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 87.1, 94.5, 115.0, 115.3, 117.0, 118.0, 121.3, 125.3, 127.7, 128.5, 128.7, 130.4, 134.0, 150.0, 157.9, 159.7, 170.6.

2-Amino-6-(4-hydroxy-phenylsulfanyl)-4-phenyl-pyridine-3,5-dicarbonitrile (52). υ_{max} (Solid)/cm^{-1}, 3469, 3330, 3213, 2214, 1619, 1581, 1544, 1519, 1495, 1423, 1263, 1221, 1169, 1045, 876, 831, 754, 701; δ_H/ppm (250 MHz, d^6-DMSO), 6.87 (2H, d, J = 8.9, Ar-H), 7.38 (2H, d, J = 8.6, Ar-H), 7.52-7.59 (5H, m, Ar-H), 7.77 (2H, bs, NH_2) , 10.01 (1H, bs, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.9, 93.5, 115.0, 115.2, 115.4, 119.4, 121.7, 127.1, 128.4, 128.7, 129.8, 130.3, 140.0, 149.7, 158.6, 159.7, 166.8.

2-Amino-6-(3-amino-phenylsulfanyl)-4-phenyl-pyridine-3,5-dicarbonitrile (53). υ_{max} (Solid)/cm^{-1}, 3344, 3207, 2971, 2209, 1647, 1623, 1593, 1545, 1520, 1478, 1441, 1421, 1307, 1257, 1236, 1157, 1076, 1037, 992, 875, 806, 781, 753, 703, 683; δ_H/ppm (250 MHz, d^6-DMSO), 5.34 (2H, bs, NH_2), 6.63-6.71 (2H, m, Ar-H), 6.80 (1H, t, J = 1.8, Ar-H), 7.11 (1H, t, J = 7.8, Ar-H), 7.53-7.60 (5H, m, Ar-H), 7.84 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 84.3, 90.5, 107.5, 112.5, 113.1, 113.4, 126.4, 126.6, 128.2, 132.0, 134.7, 148.6, 156.4, 157.6, 166.6.

2-Amino-6-(4-amino-phenylsulfanyl)-4-phenyl-pyridine-3,5-dicarbonitrile (54). υ_{max} (Solid)/cm^{-1}, 3334, 3172, 2206, 2023, 1959, 1622, 1596, 1544, 1493, 1422, 1262, 1176, 1075, 1033, 828, 781, 756, 700; δ_H/ppm (250 MHz, d^6-DMSO), 5.62 (2H, bs, NH_2), 6.62 (2H, d, J = 8.9, Ar-H), 7.19 (2H, d, J = 8.5, Ar-H), 7.48-7.59 (5H, m, Ar-H), 7.74 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.4, 109.6, 114.5, 115.2, 115.4, 115.9, 128.4, 128.7, 130.3, 134.0, 136.8, 150.6, 158.4, 159.7, 165.6.

2-Amino-6-(4-amino-phenylsulfanyl)-4-thiophen-2-yl-pyridine-3,5-dicarbonitrile (55). υ_{max} (Solid)/cm^{-1}, 3326, 3210, 2209, 1626, 1595, 1542, 1500, 1426, 1402, 1256, 1237, 1177, 1005, 827, 716. δ_H/ppm (250 MHz, d^6-DMSO), 5.63 (2H, bs, NH_2), 6.62 (2H, d, J = 8.6, Ar-H), 7.17 (2H, d, J = 8.5, Ar-H), 7.28 (H, dd, J = 4.9, 3.7, Ar-H), 7.56 (H, dd, J = 3.7, 1.2, Ar-H), 7.77 (2H, bs, NH_2), 7.95 (H, dd, J = 5.2, 1.2, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.2, 92.4, 109.5, 114.5, 115.3, 115.5, 127.9, 130.7, 131.2, 132.8, 136.7, 150.7, 156.5, 159.8, 169.1.

2-Amino-6-(3-amino-phenylsulfanyl)-4-thiophen-2-yl-pyridine-3,5-dicarbonitrile (56). υ_{max} (Solid)/cm^{-1}, 3644, 3332, 3218, 3096, 2207, 1650, 1626, 1595, 1546, 1505, 1478, 1433, 1404, 1359, 1305, 1256, 1235, 1088, 1008, 993, 891, 855, 837, 775, 766, 722. δ_H/ppm (250 MHz, d^6-DMSO), 5.34 (2H, bs, NH_2), 6.60-6.75 (2H, m, Ar-H), 6.78 (1H, t, J = 1.8, Ar-H), 7.11(1H, t, J = 7.9, Ar-H), 7.29 (H, dd, J = 5.2, 3.7, Ar-H), 7.58 (H, dd, J = 3.7, 1.2, Ar-H), 7.86 (2H, bs, NH_2), 7.96 (H, dd, J = 4.9, 1.2, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.7, 106.8, 155.2, 115.4, 115.5, 119.5, 121.7, 127.1, 127.9, 129.8, 130.8, 131.3, 132.8, 149.7, 150.8, 159.9, 167.4.

4-(6-Amino-3,5-dicyano-4-thiophen-2-yl-pyridin-2-ylsulfanyl)-benzoic acid methyl ester (57). υ_{max} (Solid)/cm^{-1}, 3423, 3326, 3226, 2206, 1702, 1635, 1537, 1511, 1436, 1400, 1354, 1277, 1254, 1236, 1180, 1117, 1015, 998, 965, 848, 832, 762, 727, 696; δ_H/ppm (250 MHz, d^6-DMSO), 3.89 (3H, s, CH_3), 7.31 (1H, dd, J = 5.2, 3.7, Ar-H), 7.60 (1H, dd, J = 3.7, 1.2, Ar-H), 7.76 (2H, d, J = 8.2, Ar-H), 7.95 (2H, bs, NH_2), 7.98 (1H, dd, J = 4.9, 1.2, Ar-H), 8.03 (2H, d, J = 8.2, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 52.4, 87.2, 93.6, 115.1, 115.4, 127.9, 129.8, 130.1, 131.0, 131.4, 132.6, 133.6, 134.4, 151.1, 159.8, 165.5, 165.7.

2-Amino-6-benzylsulfanyl-4-(4-fluoro-phenyl)-pyridine-3,5-dicarbonitrile (58). υ_{max} (Solid)/cm^{-1} 3439, 3334, 3211, 3069, 2210, 1621, 1606, 1544, 1506, 1462, 1427, 1321, 1262, 1233, 1165, 1027, 822, 694, 671; δ_H/ppm (250 MHz, d^6-DMSO), 4.51 (2H, s, CH_2), 7.25-7.44 (5H, m, Ar-H), 7.52 (2H, d, J = 6.4, Ar-H), 7.64-7.58 (2H, m, Ar-H), 8.16 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 33.2, 86.1, 93.3, 113.9, 115.2, 115.8, 127.3, 128.4, 129.4, 130.3, 131.0, 137.6, 157.5, 159.5, 165.1, 166.2.

2-Amino-4-(3-methoxy-phenyl)-6-phenylsulfanyl-pyridine-3,5-dicarbonitrile (20). υ_{max} (Solid)/cm^{-1}, 3404, 3326, 3227, 2230, 2213, 1643, 1591, 1550, 1526, 1489, 1465,

1429, 1322, 1244, 1223, 1148, 1031, 993, 834, 790, 760, 701; δ_H/ppm (250 MHz, d^6-DMSO), 3.82 (3H, s, OCH_3), 7.08-7.16 (3H, m, Ar-H), 7.46-7.53 (4H, m, Ar-H), 7.57-7.63 (2H, m, Ar-H), 7.83 (2H, bs, NH_2); δ_C/ppm (62.5 MHz, d^6-DMSO), 55.4, 87.1, 93.3, 114.1, 115.0, 115.3, 115.9, 120.5, 127.1, 129.5, 129.7, 130.0, 134.8, 135.2, 158.4, 159.1, 159.6, 166.5.

2-Amino-4-(4-methoxy-phenyl)-6-phenylsulfanyl-pyridine-3,5-dicarbonitrile (21). υ_{max} (Solid)/cm^{-1}, 3436, 3328, 3225, 2227, 2214, 1639, 1606, 1578, 1545, 1510, 1469, 1454, 1440, 1413, 1325, 1290, 1257, 1241, 1189, 1121, 1066, 1030, 1015, 836, 816, 778, 754, 704; δ_H/ppm (250 MHz, d^6-DMSO), 3.85 (3H, s, OCH_3), 7.13 (2H, d, J = 8.5, Ar-H), 7.45-7.55 (5H, m, Ar-H), 7.59-7.64 (2H, m, Ar-H), 7.78 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 55.4, 87.0, 93.4, 114.1, 115.3, 115.6, 125.8, 127.3, 129.5, 129.7, 130.3, 134.8, 158.3, 159.8, 160.9, 166.1.

2-Amino-6-(4-hydroxy-phenylsulfanyl)-4-(4-methanesulfonyl-phenyl)-pyridine-3,5-dicarbonitrile (23). υ_{max} (Solid)/cm^{-1}, 3422, 3337, 3237, 2217, 1642, 1573, 1551, 1519, 1494, 1427, 1302, 1272, 1143, 1088, 960, 832, 762, 676; δ_H/ppm (250 MHz, d^6-DMSO); 3.35 (3H, s, CH_3), 6.88 (2H, d, J = 8.6, Ar-H), 7.38 (2H, d, J = 8.9, Ar-H), 7.85 (2H, d, J = 8.2, Ar-H), 7.88 (2H, bs, NH_2), 8.05-8.2 (2H, m, Ar-H), 10.03 (1H, bs, OH); δ_C/ppm (62.8 MHz, d^6-DMSO), 43.1, 86.6, 92.5, 114.7, 114.9, 116.6, 127.9, 135.5, 137.2, 138.9, 142.4, 144.4, 157.0, 159.2, 159.9, 167.7.

2-Amino-4-(4-chloro-phenyl)-6-(3-chloro-phenylsulfanyl)-pyridine-3,5-dicarbonitrile (29). υ_{max} (Solid)/cm^{-1} 3346, 3210, 3056, 2215, 1633, 1573, 1544, 1520, 1492, 1462, 1401, 1316, 1266, 1090, 1012, 873, 837, 803, 776, 682; δ_H/ppm (250 MHz, d^6-DMSO), 7.30 (1H, t, J = 4.9, Ar-H), 7.49-7.53 (3H, m, Ar-H), 7.58-7.62 (3H, m, Ar-H), 7.86 (2H, bs, NH_2), 7.97 (1H, d, J = 5.4, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 87.4, 93.4, 114.8, 115.1, 128.9, 129.3, 129.8, 130.4, 131.1, 132.7, 133.5, 133.7, 134.0, 135.4, 157.6, 159.6, 165.5.

2-Amino-6-(3-chloro-phenylsulfanyl)-4-(3-methoxy-phenyl)-pyridine-3,5-dicarbonitrile (30). υ_{max} (Solid)/cm^{-1}, 3878, 3335, 3215, 2216, 1632, 1599, 1543, 1522, 1492, 1462, 1404, 1242, 1228, 1035, 995, 856, 775, 756, 707, 670; δ_H/ppm (250 MHz, d^6-DMSO), 3.82 (3H, s, OCH_3), 7.07-7.17 (3H, m, Ar-H), 7.46-7.61 (4H, m, Ar-H), 7.69 (1H, t, J = 1.8, Ar-H), 7.89 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 55.4, 87.4, 93.5, 114.1, 114.9, 115.2, 115.9, 120.5, 129.4, 129.8, 130.1, 131.1, 133.5, 133.6, 134.1, 135.1, 158.4, 159.1, 159.7, 165.4.

2-Amino-6-(3-chloro-phenylsulfanyl)-4-(4-methoxy-phenyl)-pyridine-3,5-dicarbonitrile (31). υ_{max} (Solid)/cm^{-1}, 3340, 3225, 2211, 1642, 1608, 1579, 1546, 1509, 1460, 1416, 1314, 1291, 1257, 1237, 1183, 1121, 1030, 996, 876, 830, 816, 775, 683, 576; δ_H/ppm (250 MHz, d^6-DMSO), 3.85 (3H, s, OCH_3), 7.13 (2H, d, J = 8.9, Ar-H), 7.48-7.62 (5H, m, Ar-H), 7.68 (1H, s, Ar-H), 7.85 (2H, bs, NH_2); δ_C/ppm (62.8 MHz, d^6-DMSO), 55.4, 87.3, 93.5, 114.1, 115.3, 115.5, 125.8, 129.5, 129.8, 130.3, 131.0, 133.5, 133.6, 134.0, 158.4, 159.8, 160.9, 165.5.

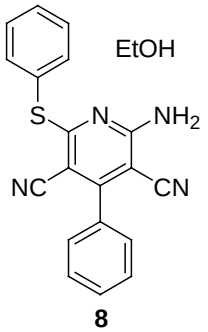
***N*-[2-(6-Amino-3,5-dicyano-4-phenyl-pyridin-2-ylsulfanyl)-ethyl]-acetamide (46).** υ_{max} (Solid)/cm^{-1}, 3374, 3333, 3182, 1646, 1625, 1526, 1259, 1042, 752, 696; δ_H/ppm (250 MHz, CD_3CN); 1.86 (3H, s, $COCH_3$), 3.32 (2H, t, J = 5.8, CH_2CH_2NH), 3.48 (2H, t, J = 6.4, CH_2CH_2NH), 6.54 (2H, bs, NH_2), 6.67 (1H, bs, NH), 7.45-7.60 (5H, m, Ar-H); δ_C/ppm (62.8 MHz, CD_3CN), 22.6, 29.9, 37.8, 85.8, 93.6, 115.2, 115.4, 128.4, 128.7, 130.3, 133.9, 158.3, 159.6, 166.8, 169.4.

4-(2-Amino-3,5-dicyano-6-pentylsulfanyl-pyridin-4-yl)-benzoic acid methyl ester (47). υ_{max} (solid)/cm^{-1}, 3429, 3335, 3233, 1711, 1693, 1529, 1430, 1263, 1237, 1116, 1042, 762; δ_H/ppm (250 MHz, CD_3CN); 0.92 (3H, t, J = 7.0, $CH_2C\underline{H}_3$), 1.30-150 (4H, m, $C\underline{H}_2C\underline{H}_2CH_3$), 1.73 (2H, qi, J = 7.3, $SCH_2C\underline{H}_2$), 3.24 (2H, t, J = 7.0, $SC\underline{H}_2CH_2$),

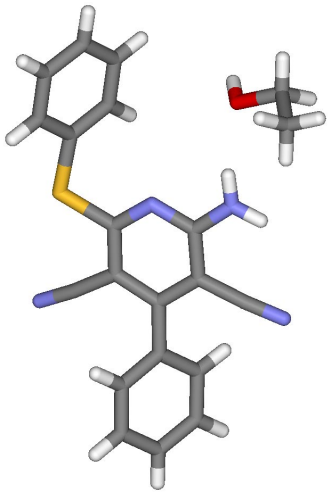
3.91 (3H, s, OCH_3), 6.48 (2H, bs, NH_2), 7.61 (2H, d, J = 8.6, ArH), 8.16 (2H, d, J = 8.6, ArH); δ_C/ppm (62.8 MHz, CD_3CN), 14.3, 23.0, 29.6, 31.1, 31.7, 53.0, 129.8, 130.6.

2-Amino-6-phenylsulfanyl-pyridine-3,5-dicarbonitrile (15). υ_{max} (Solid)/cm^{-1} 3472, 3326, 3212, 3066, 2231, 2214, 1631, 1586, 1523, 1474, 1457, 1439, 1395, 1334, 1264, 1222, 1174, 1038, 1025, 998, 941, 813, 758, 740, 707, 695, 682, 641, 590; δ_H/ppm (250 MHz, d^6-DMSO), 7.46-7.59 (5H, m, Ar-H), 7.81 (2H, bs, NH_2), 8.37 (1H, s, Py-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 86.5, 92.6, 115.3, 115.6, 127.1, 129.5, 129.6, 134.7, 147.3, 159.2, 165.6.

2-Amino-4-tert-butyl-6-phenylsulfanyl-pyridine-3,5-dicarbonitrile (13). υ_{max} (Solid)/cm^{-1} 3427, 3332, 3214, 2965, 2200, 1624, 1535, 1502, 1439, 1385, 1304, 1244, 1150, 1086, 1042, 1010, 941, 910, 832, 783; δ_H/ppm (250 MHz, d^6-DMSO), 1.60 (9H, s, $(CH_3)_3$), 7.42-7.57 (5H, m, Ar-H); δ_C/ppm (62.8 MHz, d^6-DMSO), 30.0, 37.9, 91.9, 117.1, 117.3, 127.5, 129.4, 129.6, 135.1, 161.0, 166.5, 168.5.



8



Crystal data for 2-Amino-4-phenyl-6-phenylsulfanyl-pyridine-3,5-dicarbonitrile (8): Crystal data for $C_{21}H_{18}N_4OS$; M = 374.45, crystallises from ethanol as colourless plates; crystal dimensions 0.43 x 0.23 x 0.12 mm^3. Monoclinic, *a* = 13.914(3), *b* = 10.173(3), *c* = 14.722(4) Å, β = 115.011(4)° *U* = 1888.5(8) $Å^3$, *Z* = 4, D_C = 1.317 Mg/m^3, space group $P2_1/n$ (a non-standard setting of $P2_1/c$ C_2^5 *h*', No.14), Mo-K_α radiation ($\bar{\lambda}$ = 0.71073 Å), μ(Mo-K_α) = 0.190 mm^{-1}, F(000) = 784. Data collected were measured on a Bruker Smart CCD area detector with Oxford Cryosystems low temperature system. Cell parameters were refined from the setting angles of 2981 reflections (θ range 1.69 < 27.53°). Reflections were measured from a hemisphere of data collected of frames each covering 0.3 degrees in omega. Of the 20105 reflections measured, all of which were corrected for Lorentz and polarisation effects and for absorption by semi empirical methods based on symmetry-equivalent and repeated reflections (minimum and maximum transmission coefficients 0.9229 and 0.9776), 2640 independent reflections exceeded the significance level |F|/σ(|F|) >

4.0. The structure was solved by direct methods and refined by full matrix least squares methods on F^2. Hydrogen atoms were placed geometrically and refined with a riding model (including torsional freedom for methyl groups) and with U_{iso} constrained to be 1.2 (1.5 for methyl groups) times U_{eq} of the carrier atom. Refinement converged at a final R = 0.0541(wR_2 = 0.1414, for all 4278 data, 246 parameters, mean and maximum δ/σ 0.000, 0.000) with allowance for the thermal anisotropy of all non-hydrogen atoms. Minimum and maximum final electron density -0.304 and 0.377 e.Å^{-3}. A weighting scheme w = $1/[\sigma^2(Fo^2) + (0.0526*P)^2 + 1.1352*P]$ where $P = (Fo^2 + 2 * Fc^2)/3$ was used in the latter stages of refinement. Complex scattering factors were taken from the program package SHELXTL^Y as implemented on the Pentium computer.

Crystal data for 2-amino-4-tert-butyl-6-phenylsulfanyl-1,4-dihydro-pyridine-3,5-dicarbonitrile (14): Crystal data for $C_{17}H_{18}N_4S$; M = 310.41; Crystallises from ethanol as colourless blocks; crystal dimensions 0.34 x 0.31 x 0.08 mm^3. Monoclinic, *a* = 18.559(5), *b* = 7.492(2), *c* = 12.633(4) Å, β = 102.739(5)°, *U* = 1713.4(8) Å^3, *Z* = 4, D_c = 1.203 Mg/m^3, space group $P2_1/c$ (C_{2h}^5, No.14), Mo-Kα radiation ($\bar{\lambda}$ = 0.71073 Å), μ(Mo-Kα) = 0.191 mm^{-1}, F(000) = 656. Data collected were measured on a Bruker Smart CCD area detector with Oxford Cryosystems low temperature system. Cell parameters were refined from the setting angles of 3537 reflections (θ range 2.25 < 27.66 °). Reflections were measured from a hemisphere of data collected of frames each covering 0.3 degrees in omega. Of the 18463 reflections measured, all of which were corrected for Lorentz and polarisation effects and for absorption by semi- empirical methods based on symmetry-equivalent and repeated reflections (minimum and maximum transmission coefficients 0.9380 and 0.9849) 2654 independent reflections exceeded the significance level $|F|/\sigma(|F|) > 4.0$ The structure was solved by direct methods and refined by full matrix least squares methods on F^2. Hydrogen atoms were placed geometrically and refined with a riding model (including torsional freedom for methyl groups) and with U_{iso} constrained to be 1.2(1.5 for methyl groups) times U_{eq} of the carrier atom. Refinement converged at a final R = 0.0538 (wR_2 = 0.1422, for all 3898 data, 199 parameters, mean and maximum δ/σ 0.000, 0.000) with allowance for the thermal anisotropy of all non-hydrogen atoms. Minimum and maximum final electron density -0.467 and 0.459e.Å^{-3}. A weighting scheme $w = 1/[\sigma^2 (Fo^2) + (0.0580*P)^2 + 0.7408*P]$ where $P = (Fo^2 + 2 * Fc^2)/3$ was used in the latter stages of refinement. Complex scattering factors were taken from the program package SHELXTL^Y as implemented on the Viglen Pentium computer.

Compound Purity:

Compound puruty was verified by HPLC under two conditions: HPLC 1; Luna C18 150 x 4.6 mm, 5-95% acetonitrile (0.1% TFA) in water (0.1% TFA) over 4 min, 1 mL/min, 20 µL injection. Detection was at 256 nm, run time 10 min. HPLC 2; Altima HP C18 EPS 3µ 150 x 4.6 mm, 35-98% acetonitrile (0.1% TFA) in water (0.1% TFA) over 4 min, 1.0 mL/min, 20 µL injection. Detection was at 256 nm, run time 11 min.

Table 1. Compound purity by HPLC.

Compound No.	Purity HPLC 1 [%]	Purity HPLC 2 [%]
8	99	>99
12	99	>99
13	89	90
14	96	97
15	97	97
16	98	99
17	>99	99
18	99	99
19	98	>99
20	99	>99
21	99	>99
22	96	98
23	99	99
24	94	93
25	95	98
26	84	85
27	98	95
28	97	98
29	98	>99
30	98	>99
31	98	99
32	97	96
33	98	98
34	96	93
35	97	94
36	97	97
37	96	97
38	96	98
39	93	98
40	96	98
41	98	99
42	97	98
43	98	96
44	98	98
45	95	97
46	99	>99
47	99	99
48	98	98
49	95	99

50	98	98
51	93	92
52	97	96
53	96	97
54	97	97
55	98	98
56	95	98
57	96	98
58	97	98