Supplementary Information:

Spectroscopic data is reported for the compounds not detailed in the main paper together with scanned ^{1}H NMR spectra to support characterisation of those compounds that did not give satisfactory microanalysis.

Ethyl 2,4-diamino-6-(4-chlorophenyl)furo[2,3-*d*]pyrimidine-5-carboxylate 6b:
General coupling procedure A, using 4-chlorobenzeneboronic acid (1.4 eq, 2.32 mmol, 364 mg,) for 18 h afforded **6b** as a yellow fluorescent powder (204 mg, 0.61 mmol, 37%); mp 244 - 247 °C. ν_{max} (KBr)/cm^{-1} 3474, 3446, 3347, 3148, 1692, 1660, 1622, 1553, 1487, 1466, 1373, 1264, 1239, 1079, 1053, 1012, 831, 774; δ_H ($(CD_3)_2SO$) 1.15 (3H, t, *J* = 7.1), 4.26 (2H, q, *J* = 7.1), 6.68 (2H, br s, NH_2), 7.50 (2H, br s, NH_2), 7.55 (2H, d, *J* = 6.8), 7.75 (2H, d, *J* = 6.9); δ_C ($(CD_3)_2SO$) 13.9, 62.0, 91.2, 109.3, 128.4, 128.5 (2C), 131.6 (2C), 134.9, 151.9, 157.9, 160.5, 164.3, 168.2; HREIMS: calcd for $C_{15}H_{13}O_3N_4{}^{35}Cl$ (M^+): 332.0676; found: 332.0674.

Ethyl 2,4-diamino-6-(4-methoxyphenyl)furo[2,3-*d*]pyrimidine-5-carboxylate 6c:
General coupling procedure A, using 4-methoxybenzeneboronic acid (1.4 eq, 2.32 mmol, 353 mg,) for 21 h afforded **6c** as a light brown fluorescent powder (181 mg, 0.55 mmol, 33%); mp 150 - 152 °C. Found: C, 58.5; H, 5.2; N, 16.8; $C_{16}H_{16}O_4N_4$ requires C, 58.5; H, 4.9; N, 17.1%. ν_{max} (KBr)/cm^{-1} 3440, 3331, 3158, 2976, 1691, 1654, 1624, 1560, 1506, 1484, 1466, 1375, 1301, 1276, 1259, 1240, 1180, 1077, 1005, 1037, 829, 774; δ_H ($(CD_3)_2SO$) 1.16 (3H, t, CH_3, *J* = 7.1), 3.82 (3H, s, CH_3), 4.25 (2H, q, CH_2, *J* = 7.1), 6.24 (2H, br s, NH_2), 7.02 (2H, d, CH & CH, *J* = 8.9), 7.22 (2H, br s, NH_2), 7.66 (2H, d, CH & CH, *J* = 8.8); $_{\delta C}$ ($(CD_3)_2SO$) 13.6, 61.1, 90.7, 107.0, 113.4 (2C), 121.6, 130.9 (2C), 152.8, 158.6, 160.3, 161.6, 164.4, 167.7; HREIMS: calcd for $C_{16}H_{16}O_4N_4$ (M^+): 328.1172; found 328.1173.

Ethyl 2,4-diamino-6-(4-ethylphenyl)furo[2,3-*d*]pyrimidine-5-carboxylate 6d:
General coupling procedure A, using 4-ethylbenzeneboronic acid (1.4 eq, 2.32 mmol, 348 mg,) for 16 h afforded **6d** as an off-white fluorescent powder (236 mg, 0.72 mmol, 43%); mp 234 - 235 °C; ν_{max} (KBr)/cm^{-1} 3321, 3123, 2969, 2930, 2873, 1687, 1661, 1598, 1501, 1429, 1376, 1273, 1234, 1107, 1073, 1049, 989, 891, 845, 765; δ_H ($(CD_3)_2SO$) 1.13 (3H, t, *J* = 7.1), 1.20 (3H, t, *J* = 7.6), 2.69 (2H, q, *J* = 7.5), 4.26 (2H,

q, J = 7.1), 6.91 (2H, br s, NH_2), 7.33 (2H, d, CH & CH, J = 8.3), 7.65 (2H, d, CH & CH, J = 8.2), 7.78 (2H, br s, NH_2); HRFABMS: calcd for $C_{17}H_{18}O_3N_4$ ($M+H^+$): 326.1379 found 327.1459.

Ethyl 2,4-diamino-6-(4-(methylthio)phenyl)furo[2,3-*d*]pyrimidine-5-carboxylate 6e:

General coupling procedure A, using 4-(methylthio)benzeneboronic acid (1.4 eq, 2.32 mmol, 390 mg,) for 40 h afforded **6e** as a yellow fluorescent powder (149 mg, 0.43 mmol, 26%); mp 195 - 198 °C. Found: C, 56.0; H, 5.1; N, 15.6; $C_{16}H_{16}O_3N_4S$ requires C, 55.8; H, 4.7; N, 16.2%. ν_{max} (KBr)/cm^{-1} 3472, 3389, 3316, 3176, 2978, 2913, 1693, 1610, 1564, 1464, 1404, 1374, 1352, 1281, 1265, 1237, 1188, 1096, 1097, 1072, 1047, 1013, 833, 774; δ_H ($(CD_3)_2SO$) 1.17 (3H, t, J = 7.0), 2.53 (3H, s), 4.25 (2H, q, J = 7.0), 6.28 (2H, br s, NH_2), 7.23 (2H, br s, NH_2), 7.34 (2H, d, J = 8.2), 7.66 (2H, d, J = 8.2); δ_C ($(CD_3)_2SO$) 13.6, 14.2, 61.3, 90.7, 107.8, 124.7 (2C), 125.5, 129.6 (2C), 140.7, 152.1, 161.6, 164.3, 167.8; HREIMS: calcd for $C_{16}H_{16}O_3N_4S$ (M^+): 344.0943 found 344.0944.

Ethyl 2,4-diamino-6-(4-(diethoxymethyl)phenyl)furo[2,3-*d*]pyrimidine-5-carboxylate 6f:

General coupling procedure A, using 4-formylbenzeneboronic acid (1.4 eq, 2.32 mmol, 353 mg,) for 40 h afforded **6f** as a light yellow fluorescent powder (83 mg, 0.21 mmol, 16%); mp 168 - 171 °C. Found: C, 60.4; H, 6.0: N, 13.7; $C_{20}H_{24}O_5N_4$ requires C, 60.0, H, 6.0; N, 14.0%. ν_{max} (KBr)/cm^{-1} 3496, 3375, 3147, 2974, 2932, 2886, 1722, 1683, 1652, 1617, 1566, 1465, 1376, 1350, 1330, 1272, 1240, 1210, 1115, 1092, 1072, 1052, 998, 776; δ_H ($(CD_3)_2SO$) 1.12 (3H, t, CH_3, J = 7.1), 1.16 (6H, t, CH_3 & CH_3, J = 7.0), 3.53 (4H, m, CH_2 & CH_2, J = 7.0), 4.24 (2H, q, CH_2, J = 7.1), 5.56 (1H, s, CH_3), 6.29 (2H, br s, NH_2), 7.23 (2H, br s, NH_2), 7.48 (2H, d, CH &CH, J = 8.3), 7.71 (2H, d, CH & CH, J = 8.3); HRFABMS: calcd for $C_{20}H_{24}O_5N_4$ ($M+H^+$): 400.1747 found 401.1826.

2,4-Diamino-6-(4-chlorophenyl)furo[2,3-*d*]pyrimidine-5-carboxylic acid 7b:

General coupling procedure B, starting from **6b**, **7b** was isolated as a black fluorescent powder (111 mg, 0.36 mmol, 22%); mp sublimes in small needles from 250 °C, does not melt below 300 °C. ν_{max} (KBr)/cm^{-1} 3434, 3292, 3174, 2396, 1684,

1624, 1547, 1483, 1383, 1318, 1263, 1151, 1093, 1062, 1042, 1013, 836, 774; δ_H ($(CD_3)_2SO$) 6.28 (2H, br s, NH_2), 7.16 (2H, br s, NH_2), 7.52 (2H, d, *J* = 8.6), 7.77 (2H, d, *J* = 8.6); δ_C ($(CD_3)_2SO$) 91.3, 110.4, 128.2 (2C), 128.7, 131.2 (2C), 134.2, 150.6, 159.0, 161.7, 165.9, 168.1; HRFABMS: calcd for $C_{13}H_9O_3N_4{}^{35}Cl$: 304.0363; found 305.01($M+H^+$).

2,4-Diamino-6-(4-methoxyphenyl)furo[2,3-*d*]pyrimidine-5-carboxylic acid 7c:

General coupling procedure B, starting from **6c**, **7c** was isolated as a dark brown fluorescent powder (156 mg, 0.52 mmol, 31%); mp 256°C (decomp). ν_{max} (KBr)/cm^{-1} 3418, 3308, 3201, 2956, 2836, 2395, 1679, 1610, 1504, 1465, 1388, 1306, 1267, 1246, 1188, 1146, 1046, 1029, 837, 774; δ_H ($(CD_3)_2SO$) 3.81 (3H, s), 6.14 (2H, br s, NH_2), 6.99 (2H, d, *J* = 8.9), 7.01 (2H, br s, NH_2), 7.72 (2H, d, *J* = 8.8); δ_C ($(CD_3)_2SO$) 55.3, 91.4, 109.2, 113.4 (2C), 122.2, 130.7 (2C), 151.6, 158.9, 159.9, 161.3, 166.3, 167.5; HREIMS calcd for $C_{14}H_{12}O_4N_4$ (M^+); 300.0859 found 300.0856.

2,4-Diamino-6-(4-ethylphenyl)furo[2,3-*d*]pyrimidine-5-carboxylic acid 7d:

General coupling procedure B, starting from **6d**, **7d** was isolated as a light brown fluorescent powder (131 mg, 0.43 mmol, 26%); mp sublimes in crystals from 268 °C, decomposed at 297 °C. ν_{max} (KBr)/cm^{-1} 3466, 3388, 3318, 3179, 2968, 2936, 2879, 2346, 1700, 1643, 1548, 1499, 1453, 1375, 1319, 1252, 1161, 1060, 1046, 967, 948, 842, 801, 777, 607, 585, 526; δ_H ($(CD_3)_2SO$) 1.13 (3H, t, *J* = 7.1), 1.21 (3H, t, *J* = 7.6), 2.67 (2H, q, *J* = 7.5), 6.21 (2H, br s, NH_2), 7.29 (2H, br s, NH_2), 7.30 (2H, d, *J* = 8.1), 7.63 (2H, d, *J* = 8.1); δ_C ($(CD_3)_2SO$) 8.1, 28.0, 91.0, 108.6, 127.0, 127.3 (2C), 129.3 (2C), 145.4, 152.5, 158.9, 161.5, 166.0, 168.3; HRFABMS calcd for $C_{15}H_{14}O_3N_4$ ($M+H^+$); 298.1066 found 299.1142.

2,4-Diamino-6-(4-formylphenyl)furo[2,3-*d*]pyrimidine-5-carboxylic acid 7e:

General procedure B, starting from **6f**, **7e** was isolated as a dark brown fluorescent powder (90 mg, 0.30 mmol, 18%); mp decomposes at 260 °C; ν_{max} (KBr)/cm^{-1} 3447, 3329, 3158, 2846, 2736, 1691, 1602, 1499, 1426, 1387, 1306, 1213, 1177, 1051, 993, 876, 830, 804, 765, 605, 568, 535; δ_H ($(CD_3)_2SO$) 6.69 (2H, br s, NH_2), 7.70 (2H, br s, NH_2), 7.98 (4H, br s), 10.06 (1H, s, CH); δ_C ($(CD_3)_2SO$) 91.8, 111.5, 129.4 (2C),

130.3 (2C), 135.1, 136.6, 151.0, 158.2, 161.3, 168.3, 169.8, 193.1; LRMS calcd for $C_{14}H_{10}O_4N_4$ (M^+); 298.0702 found 297.00.

2,4-Diamino-*N*-(4-chlorophenyl)furo[2,3-*d*]pyrimidine-5-carboxamide 8b:

General procedure C, using 4-chloroaniline (2 eq, 2.08 mmol, 266 mg), **8b** was isolated as a light-brown powder (171 mg, 0.56 mmol, 54%); mp 225 °C, decomp. 280 °C; ν_{max} (KBr)/cm^{-1} 3483, 3391, 3323, 3179, 3132, 1667, 1620, 1572, 1551, 1538, 1509, 1492, 1468, 1391, 1311, 1243, 1119, 1089, 1012, 831, 805, 794, 748, 507; δ_H ($(CD_3)_2SO$) 6.23 (2H, br s, NH_2), 7.42 (2H, d, J = 8.8), 7.50 (2H, br s, NH_2), 7.72 (2H, d, J = 8.8), 8.30 (1H, s, CH), 10.33 (1H, br s, NH); δ_C ($(CD_3)_2SO$) 89.2, 117.1, 122.2 (2C), 127.7, 128.6 (2C), 137.2, 140.6, 159.1, 161.8, 162.0, 169.5; HRFABMS calcd for $C_{13}H_{10}O_2N_5{}^{35}Cl$ ($M+H^+$); 303.0523 found 304.0598; $C_{13}H_{10}O_2N_5{}^{37}Cl$ (M+H); 305.0494 found 306.0576.

2,4-Diamino-*N*-(4-methoxyphenyl)furo[2,3-*d*]pyrimidine-5-carboxamide 8c:

General procedure C, using *p*-anisidine (2 eq, 2.08 mmol, 254 mg), **8c** was isolated as a grey powder (177 mg, 0.59 mmol, 57%); sublimes from 210 °C, mp 272 - 275 °C; ν_{max} (KBr)/cm^{-1} 3483, 3325, 3171, 3000, 2956, 2836, 2786, 1671, 1603, 1551, 1510, 1469, 1417, 1381, 1301, 1247, 1236, 1172, 1109, 1088, 1042, 971, 892, 817, 796, 747, 731, 578, 552, 516; δ_H ($(CD_3)_2SO$) 3.75 (3H, s), 6.20 (2H, br s, NH_2), 6.94 (2H, d, J = 9.0), 7.47 (2H, br s, NH_2), 7.56 (2H, d, CH & CH, J = 9.0), 8.26 (1H, s, CH), 10.11 (1H, br s, NH); δ_C ($(CD_3)_2SO$) 55.2, 89.4, 113.9 (2C), 117.3, 122.4 (2C), 131.1, 140.0, 155.9, 159.2, 161.4, 161.9; HRFABMS calcd. For $C_{14}H_{13}O_3N_5$ 299.1018; found ($M+H^+$) 300.1098,

2,4-Diamino-*N*-(4-ethylphenyl)furo[2,3-*d*]pyrimidine-5-carboxamide 8d:

General procedure C, using 4-ethylaniline (2 eq, 2.08 mmol, 260 µl), **8d** was isolated as a grey powder (156 mg, 0.52 mmol, 50%); sublimes from 220 °C, mp 263 - 268 °C. Found: C, 60.08; H, 5.66; N, 23.15; $C_{15}H_{15}O_2N_5$ requires C, 60.60; H, 5.09; N. 23.56%. ν_{max} (KBr)/cm^{-1} 3481, 3437, 3333, 3186, 2961, 1930, 1870, 1664, 1627, 1611, 1594, 1552, 1531, 1514, 1460, 1412, 1381, 1314, 1267, 1248, 1122, 1079, 1040, 987, 979, 833, 795, 748, 726, 557; δ_H ($(CD_3)_2SO$) 1.17 (3H, t, J = 7.5), 2.58 (2H, q, J = 7.5), 6.21 (2H, br s, NH_2), 7.20 (2H, d, J = 8.5), 7.46 (2H, br s, NH_2),

7.57 (2H, d, *J* = 8.5), 8.28 (1H, s), 10.15 (1H, br s, NH); δ_C ($(CD_3)_2SO$) 15.6, 27.6, 89.4, 117.3, 120.9 (2C), 127.9 (2C), 135.8, 139.6, 140.2, 159.1, 161.6, 161.9; HR-MS calcd for $C_{15}H_{15}O_2N_5$ ($M+H^+$); 297.1226 found 298.1305.

2,4-Diamino-*N*-(4-(methylthio)phenyl)furo[2,3-*d*]pyrimidine-5-carboxamide 8e:

General procedure C, using 4-(methylthio)aniline (2 eq, 2.08 mmol, 253 µl), **8e** was isolated as a grey powder (202 mg, 0.64 mmol, 62%); mp 250 °C (decomp.). ν_{max} (KBr)/cm^{-1} 3474, 3423, 3350, 3326, 3132, 2920, 1618, 1594, 1551, 1530, 1494, 1466, 1385, 1437, 1312, 1291, 1242, 1137, 1120, 1090, 1040, 820, 803, 794; δ_H ($(CD_3)_2SO$) 2.53 (3H, s), 6.25 (2H, br s, NH_2), 7.31 (2H, d, *J* = 8.6), 7.47 (2H, br s, NH_2), 7.67 (2H, d, *J* = 8.5), 8.32 (1H, s, CH), 10.25 (1H, br s, NH); δ_C ($(CD_3)_2SO$) 15.3, 89.4, 117.3, 121.4 (2C), 126.8 (2C), 133.0, 135.6, 140.4, 159.1, 161.7, 161.9, 169.4; HRFABMS calcd for $C_{14}H_{13}O_2N_5S$ ($M+H^+$); 315.0790 found 316.0865.

Ethyl 4-(2,4-diaminofuro[2,3-*d*]pyrimidine-5-carboxamido)benzoate 8f:

General procedure C, using ethyl 4-aminobenzoate (2 eq, 2.08 mmol, 341 mg), after 15 minutes, a precipitate appeared. The reaction mixture was stirred for 1 h, and another equivalent of HBTU and the corresponding aniline were added. The reaction was stirred for 3 h at room temperature. **8f** was isolated as a brown powder (31.3 mg, 0.09 mmol, 9%); mp 215°C (decomp.). ν_{max} (KBr)/cm^{-1} 3472, 3330, 3192, 3137, 2983, 2923, 1690, 1665, 1619, 1596, 1551, 1532, 1467, 1410, 1388, 1368, 1311, 1281, 1251, 1177, 1111, 1038, 769; δ_H ($(CD_3)_2SO$) 1.32 (3H, t, *J* = 7.1), 4.30 (2H, q, CH_2, *J* = 7.0), 6.25 (2H, br s, NH_2), 7.40 (2H, br s, NH_2), 7.85 (2H, d, *J* = 8.6), 7.97 (2H, d, *J* = 8.8), 8.36 (1H, s), 10.48 (1H, br s, NH); δ_C ($(CD_3)_2SO$) 14.2, 60.5, 89.5, 117.1, 119.8 (2C), 125.0, 130.1 (2C), 141.1, 142.7, 159.0, 161.9, 162.2, 165.3, 169.5; HRFABMS calcd for $C_{16}H_{15}O_4N_5$ ($M+H^+$); 341.1124 found 342.1204.

2-Amino-4,7-dihydro-4-oxo-6-phenyl-3*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbonitrile 15a

A mixture of isopropanol and water (2:1, 10 ml) was degassed for 10 min under nitrogen. To this was added 2-amino-6-bromo-4,7-dihydro-4-oxo-3*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbonitrile **1** (0.1 g, 0.39 mmol), $PdCl_2(PPh_3)_2$ (0.014 g, 0.020 mmol,

5 mol%), potassium phenyltrifluoroborate (0.086 g, 0.47 mmol, 1.2 eq.) and *t*-butylamine (123 μl, 1.17 mmol, 3.0 eq.). The mixture was stirred at 90 °C, under nitrogen, for 96 h. Once cooled to room temperature the resulting precipitate was purified using column chromatography, using methanol:ethyl acetate (10:1) as eluant, to give **15a** as a brown solid (0.090 g, 0.36 mmol, 92%); mp >230 °C; ν_{max} (KBr)/cm^{-1} 3077, 3042, 1964, 1603, 1494, 1442, 1367, 1348, 1306, 1179, 1086, 1024, 759, 700, 578; δ_H ($(CD_3)_2SO$) 6.50 (2H, br s, NH_2), 7.43 (1H, t, J = 7.6), 7.54 (2H, dd, J = 8.2, 7.6), 7.83 (2H, d, J = 8.2), 10.74 (1H, br s, NH), 12.39 (1H, br s, NH); δ_C ($(CD_3)_2SO$) 82.3, 99.3, 100.2, 116.2, 126.2, 128.9, 129.3, 138.4, 152.2, 154.0, 157.3; HREIMS calcd for $C_{13}H_9N_5O$ (M^+); 252.0885 found 252.0880.

2-Amino-4,7-dihydro-6-(4-methoxyphenyl)-4-oxo-3*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbonitrile 15b

A mixture of isopropanol and water (2:1, 10 ml) was degassed for 10 min under nitrogen. To this was added 2-amino-6-bromo-4,7-dihydro-4-oxo-3*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbonitrile **1** (0.113 g, 0.44 mmol), $PdCl_2(PPh_3)_2$ (0.020 g, 0.028 mmol, 6.5 mol%), 4-methoxyphenylboronic acid (0.082 g, 0.54 mmol, 1.23 eq.) and *t*-butylamine (140 μl, 1.33 mmol, 3.0 eq.). The mixture was stirred at 90 °C, under nitrogen for 48 h. The resulting precipitate was triturated with methanol, filtered under reduced pressure and dried under vacuum to give **15b** as a brown solid (0.098 g, 0.35 mmol, 78%); mp >230 °C; ν_{max} (KBr)/cm^{-1} 3439, 3324, 3140, 2829, 2212, 1693, 1665, 1601, 1508, 1411, 1339, 1245, 1171, 1105, 1025, 872, 748, 691, 551; δ_H ($(CD_3)_2SO$) 3.82 (3H, s), 6.40 (2H, br s, NH_2), 7.09 (2H, d, J = 8.9), 7.77 (2H, d, J = 8.9), 10.69 (1H, br s, NH), 12.26 (1H, br s, NH); δ_C ($(CD_3)_2SO$) 55.3, 81.1, 99.9, 114.8, 116.8, 121.7, 127.7, 138.8, 152.0, 153.8, 157.3, 159.8; HREIMS calcd for $C_{14}H_{11}N_5O_2$ (M^+); 282.0991 found 282.0989.

2-Amino-6-(4-ethylphenyl)-4,7-dihydro-4-oxo-3*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbonitrile 15c

A mixture of isopropanol and water (2:1, 10 ml) was degassed for 10 min under nitrogen. To this was added 2-amino-6-bromo-4,7-dihydro-4-oxo-3*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbonitrile **1** (0.138 g, 0.54 mmol), $PdCl_2(PPh_3)_2$ (0.020 g, 0.028 mmol, 6.5 mol%), 4-ethylphenylboronic acid (0.096 g, 0.64 mmol, 1.19 eq.) and *t*-

butylamine (180 µl, 1.71 mmol, 3.2 eq.). The mixture was stirred at 90 °C, under nitrogen for 96 h. Once cooled to room temperature the resulting precipitate was triturated with methanol, filtered under reduced pressure and dried under vacuum to give **15c** as a brown solid (0.072 g, 0.26 mmol, 47%); mp >230 °C; ν_{max} (KBr)/cm^{-1} 3434, 3329, 3185, 2976, 2241, 1691, 1662, 1597, 1506, 1407, 1342, 1305, 1155, 1023, 875, 779, 691 587; δ_H ((CD$_3$)$_2$SO) 1.22 (3H, t, *J* = 7.6), 2.65 (2H, q, *J* = 7.6), 6.42 (2H, br s, NH$_2$), 7.35 (2H, d, *J* = 8.2), 7.74 (2H, d, *J* = 8.2), 10.72 (1H, br s, NH), 12.32 (1H, br s, NH); δ_C ((CD$_3$)$_2$SO) 15.4, 27.9, 81.8, 100.1, 116.6, 126.3, 126.8, 128.4, 138.7, 144.9, 152.1, 153.9, 157.3; HREIMS calcd for $C_{15}H_{13}N_5O$ (M^+); 280.1198 found 280.1194.

2-Amino-4,7-dihydro-6-(3,4-methylenedioxyphenyl)-4-oxo-3*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbonitrile 15d

A mixture of isopropanol and water (2:1, 10 ml) was degassed for 10 min under nitrogen. To this was added 2-amino-6-bromo-4,7-dihydro-4-oxo-3*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbonitrile **1** (0.126 g, 0.50 mmol), $PdCl_2(PPh_3)_2$ (0.021 g, 0.030 mmol, 6 mol%), 3,4-methylenedioxyphenylboronic acid (0.112 g, 0.68 mmol, 1.35 eq.) and *t*-butylamine (163 µl, 1.55 mmol, 3.1 eq.). The mixture was stirred at 90 °C, under nitrogen for 48 h. Once cooled, the resulting precipitate was filtered under reduced pressure and purified by trituration with hot methanol. The insoluble material was filtered, triturated with hot acetone, filtered and dried under vacuum to give **15d** as a brown solid (0.053 g, 0.18 mmol, 36%); mp >230 °C; ν_{max} (KBr)/cm^{-1} 3425, 3262, 3103, 2214, 1677, 1615, 1589, 1530, 1500, 1487, 1463, 1265, 1241, 1042, 939, 852, 776, 692; δ_H ((CD$_3$)$_2$SO) 6.11 (2H, s), 6.42 (2H, br s, NH$_2$), 7.08 (1H, d, *J* = 8.4), 7.36 (2H, 1 x dd, *J* = 1.8; 1 x s), 10.71 (1H, br s, NH), 12.24 (1H, br s, NH); δ_C ((CD$_3$)$_2$SO) 81.4, 100.0, 101.6, 106.4, 108.8, 116.6, 120.6, 123.2, 138.5, 147.7, 147.8, 151.9, 153.9, 157.3; HREIMS calcd for $C_{14}H_{10}O_3N_5$ (M^+); 296.0784 found 296.0787.

2-Amino-4,7-dihydro-6-(3-formylphenyl)-4-oxo-3*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbonitrile 15e

A mixture of isopropanol and water (2:1, 10 ml) was degassed for 10 min under nitrogen. To this was added 2-amino-6-bromo-4,7-dihydro-4-oxo-3*H*-pyrrolo[2,3-

d]pyrimidine-5-carbonitrile **1** (0.124 g, 0.49 mmol), $PdCl_2(PPh_3)_2$ (0.024 g, 0.034 mmol, 7 mol%), 3-formylphenylboronic acid (0.089 g, 0.59 mmol, 1.21 eq.) and *t*-butylamine (160 µl, 1.52 mmol, 3.1 eq.). The mixture was stirred at 90 °C, under nitrogen for 48 h. The solvent was evaporated under reduced pressure to leave a brown solid, which was triturated with hot methanol (15 ml), filtered and dried under reduced pressure to give **15e** as a brown solid (0.073 g, 0.26 mmol, 53%); mp >230 °C; ν_{max} (KBr)/cm^{-1} 3417, 3342, 3215, 3153, 2218, 1698, 1657, 1594, 1528, 1476, 1426, 1363, 1202, 1093, 845, 793, 923, 696; δ_H ($(CD_3)_2SO$) 6.50 (2H, br s, NH_2), 7.58 (1H, t, *J* = 7.6), 7.97 (1H, d, *J* = 7.6), 8.14 (1H, d, *J* = 7.9), 8.35 (1H, s), 10.07 (1H, s), 10.79 (1H, br s, NH), 12.56 (1H, br s, NH); δ_C ($(CD_3)_2SO$) 83.2, 100.5, 116.2, 126.6, 130.0 (2C), 130.2, 131.7, 136.7, 136.9, 152.4, 154.1, 157.4, 192.6**;** HREIMS calcd for $C_{14}H_{10}O_2N_5$ (M^+); 280.0834 found 280.0804.

6-Amino-2-(benzylsulfanyl)-5-(2-nitro-1-phenylethyl)-4(3*H*)-pyrimidinone 25b

Using a similar procedure as for the preparation of **25a**, in this instance using [(*E*)-2-nitroethenyl]benzene (0.26 g, 1.72 mmol); the crude product was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 1:3 to ethyl acetate 100%) to give the product **25b** as a brown solid (0.53 g, 1.39 mmol, 81%); mp 83-85 °C. Found: C, 60.3; H, 4.8: N, 14.1; S, 8.7; $C_{19}H_{18}N_4O_3S$ requires C, 59.7; H, 4.7; N, 14.6; S, 8.4%. ν_{max} (KBr)/cm^{-1} 3484, 3389, 1610, 1545, 1419, 1375, 1222, 973, 766, 698; δ_H ($(CD_3)_2SO$) 4.33 (2H, s), 4.62 (1H, t, *J* = 7.5), 5.28-5.51 (2H, m), 6.72 (2H, s, NH_2), 7.17-7.49 (10H, m), 11.78 (1H, br s); δ_C ($(CD_3)_2SO$) 33.1, 77.2, 91.4, 126.7, 127.2, 127.8, 128.1, 128.4, 129.2, 137.6, 140.2, 158.1, 160.1, 162.3; HRFABMS calcd for $C_{19}H_{18}N_4O_3S$ ($M+H^+$); 383.1178 found 383.1183.

6-Amino-2-(benzylsulfanyl)-5-[1-(4-methoxyphenyl)-2-nitroethyl]-4(3*H*)-pyrimidinone 25c

Using a similar procedure as for the preparation of **25a**, in this instance using 1-methoxy-4-[(*E*)-2-nitroethenyl]benzene (0.38 g, 2.1 mmol); the crude product was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 1:3 to ethyl acetate 100%) to give the product **25c** as a brown solid (0.68 g, 1.65 mmol, 96%); mp 88-90 °C. ν_{max} (KBr)/cm^{-1} 3486, 3385, 2835, 1610, 1546, 1510, 1420, 1249, 1030, 971; δ_H ($(CD_3)_2SO$) 3.70 (3H, s), 4.33 (2H, s), 4.54 (1H, t, *J* = 7.7), 6.68 (2H, s,

NH_2), 5.22-5.47 (2H, m), 6.80 (2H, m), 7.21-7.25 (1H, m), 7.27-7.31 (2H, m), 7.41-7.43 (4H, m), 11.77 (1H, s); δ_C ($(CD_3)_2SO$) 33.1, 38.5, 55.0, 77.5, 91.7, 113.5, 127.2, 128.4, 128.9, 129.1, 132.2, 137.6, 158.1, 159.9, 162.3; HRFABMS calcd for $C_{20}H_{20}N_4O_4S$ ($M+H^+$); 413.1284 found 413.1286.

6-Amino-2-(benzylsulfanyl)-5-{2-nitro-1-[2-(trifluoromethyl)phenyl]ethyl}-4(3*H*)-pyrimidinone 23d

Using a similar procedure as for the preparation of **25a**, in this instance using 1-[(*E*)-2-nitroethenyl]-2-(trifluoromethyl)benzene (0.19 g, 0.86 mmol) and ethyl acetate (5 ml). The crude product was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 1:3 to 1:2) to give the product **25d** as a yellow solid (0.21 g, 0.47 mmol, 55%); mp 81-83 °C. ν_{max} (KBr)/cm^{-1} 3525, 3405, 2826, 1613, 1548, 1423, 1375, 1311, 1163, 1110, 769; δ_H ($(CD_3)_2SO$) 4.34-4.80 (2H, s), 4.80 (1H, t, J = 7.5), 4.98-5.62 (2H, m), 6.16 (2H, brs, NH_2), 7.22-7.25 (1H, m), 7.41-7.43 (1H, m), 7.28-7.31 (2H, m), 7.45 (1H, t, J = 7.6), 7.59 (1H, t, J = 7.6), 7.71 (1H, d, J = 7.9), 7.90 (1H, d, J = 7.9), 11.90 (1H, br s); δ_C ($(CD_3)_2SO$) 33.2, 36.2, 75.3, 90.5, 120.5, 126.2, 126.3 (2C), 126.3 (q, $J^2_{C\text{-}F}$ 29, 2-CF_3-C_6H_4 C-2), 127.3, 127.8, 128.4, 129.2, 130.6, 132.6, 137.5, 158.6, 160.2, 162.7; HREIMS calcd for $C_{20}H_{17}F_3N_4O_3S$ (M^+); 450.0973 found 450.0976.

2-(Benzylsulfanyl)-5-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one 26b

(a) Titanium(III) chloride reaction

6-Amino-2-(benzylsulfanyl)-5-(2-nitro-1-phenylethyl)-4(3*H*)-pyrimidinone **25b** (0.53 g, 1.38 mmol) was dissolved in methanol (10 ml) and treated with one equivalent of sodium methoxide (74.5 mg). A titanium(III) chloride solution was prepared separately by adding an aqueous solution of ammonium acetate (6.3 g, 83 mmol) in water (10 ml) to titanium(III) chloride (10 ml, 8.3 mmol, 10% solution in hydrochloric acid) under nitrogen. The prepared titanium(III) chloride solution was then added carefully to the anionic solution under nitrogen with vigorous stirring. The colour changed slowly from brown to yellow. The mixture was stirred overnight at room temperature then poured into ethyl acetate (20 ml) and separated into two phases. The aqueous phase was extracted with ethyl acetate (30 ml × 3). The organic extracts were combined, washed with 5% sodium bicarbonate (20 ml) and with brine

(20 ml), then dried with anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was recrystallised from ethyl acetate and *n*-hexane to afford **26b** as a yellow solid (0.32 g, 0.96 mmol, 70%). The physical and spectroscopic data were identical to those recorded below.

(b) Tin(II) chloride reaction

To a mixture of 6-amino-2-(benzylsulfanyl)-5-(2-nitro-1-phenylethyl)-4(3*H*)-pyrimidinone **25b** (0.3 g, 0.78 mmol) in ethyl acetate (20 ml) was added tin(II) chloride dihydrate (0.61 g, 2.69 mmol). The resulting mixture was stirred in an oil bath at 85 °C for 24 h then poured into ethyl acetate (20 ml) and washed with saturated aqueous sodium bicarbonate (20 ml), 1% hydrochloric acid (10 ml) and brine (20 ml), then dried with anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 1:1 to ethyl acetate 100%) to give **26b** as a yellow solid (0.18 g, 0.55 mmol, 70%); mp 267-269 °C. Found: C, 68.5; H, 4.7; N, 12.6; $C_{19}H_{15}N_3OS$ requires C, 68.4; H, 4.5, N, 12.6%. ν_{max} (KBr)/cm^{-1} 3203, 3061, 2829, 1643, 1433, 1212, 1095, 973, 753, 694; δ_H ($(CD_3)_2SO$) 4.44 (2H, s), 7.16-7.28 (2H, m), 7.30 (1H, d, *J* = 2.2), 7.31-7.35 (4H, m), 7.46-7.48 (2H, m), 7.91-7.93 (2H, m), 11.99 (1H, s), 12.09 (1H, s); δ_C ($(CD_3)_2SO$) 33.5, 101.3, 117.6, 120.2, 125.7, 127.3, 127.9, 128.4, 129.1, 134.2, 137.3, 149.3, 153.5, 159.1; HRFABMS calcd for $C_{19}H_{15}N_3OS$ ($M+H^+$); 334.1014 found 334.1017.

2-(Benzylsulfanyl)-5-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one 26c

(a) Titanium(III) chloride reaction

6-Amino-2-(benzylsulfanyl)-5-[1-(4-methoxyphenyl)-2-nitroethyl]-4(3*H*)-pyrimidinone **25c** (0.14 g, 0.34 mmol) was dissolved in methanol (10 ml) and treated with one equivalent of sodium methoxide (18.4 mg). Titanium(III) chloride solution was prepared separately by adding of an aqueous solution of ammonium acetate (1.5 g, 20 mmol) in water (2.6 ml) to titanium(III) chloride (2.6 ml, 2.0 mmol 10% solution in hydrochloric acid) under nitrogen. The prepared titanium(III) chloride solution was then added carefully to the anionic solution under nitrogen with vigorous stirring. The colour changed slowly from brown to yellow. The mixture was stirred overnight at room temperature then poured into ethyl acetate (20 ml) and separated

into two phases. The aqueous phase was extracted with ethyl acetate (30 ml × 3). The organic extracts were combined, washed with 5% sodium bicarbonate (20 ml) and brine (20 ml), then dried with anhydrous magnesium sulfate and concentrated. The resulting residue was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 1:1) to give the product **26c** as a yellow solid (64 mg, 0.18 mmol, 52%). The physical and spectroscopic data were identical to those recorded below.

(b) Tin(II) chloride reaction

To a mixture of 6-amino-2-(benzylsulfanyl)-5-[1-(4-methoxyphenyl)-2-nitroethyl]-4(3*H*)-pyrimidinone **25c** (0.1 g, 0.24 mmol) in ethyl acetate (15 ml) was added tin(II) chloride dihydrate (0.18 g, 0.82 mmol). The resulting mixture was stirred in an oil bath at 85 °C for 24 h then poured into ethyl acetate (20 ml) and washed with saturated aqueous sodium bicarbonate (20 ml), 1% hydrochloric acid (10 ml) and brine (20 ml), then dried with anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 1:1 to ethyl acetate 100%) to give **26c** as a grey solid (41 mg, 0.1 mmol, 42%); mp 233-235 °C. ν_{max} (KBr)/cm^{-1} 3203, 2833, 1646, 1525, 1438, 1241, 1179, 1031, 970, 832; δ_H ($(CD_3)_2SO$) 3.77 (3H, s), 4.43 (2H, s), 6.88 (2H, d, *J* = 8.8), 7.19 (1H, d, *J* = 2.4), 7.24-7.49 (5H, m), 7.84 (2H, d, ArH, *J* = 8.8), 11.90 (1H, s), 12.04 (1H, s,); δ_C ($(CD_3)_2SO$) 33.5, 55.0, 101.2, 113.4, 116.5, 119.8, 126.7, 127.2, 128.4, 128.9, 129.1, 137.3, 149.1, 153.2, 157.6; HRFABMS calcd for $C_{20}H_{17}N_3O_2S$ ($M+H^+$); 364.1120 found 364.1119.

2-(Benzylsulfanyl)-5-[2-(trifluoromethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one 26d

(a) Titanium(III) chloride reaction

6-Amino-2-(benzylsulfanyl)-5-{2-nitro-1-[2-(trifluoromethyl)phenyl]ethyl}-4(3*H*)-pyrimidinone **25d** (0.16 g, 0.35 mmol) was dissolved in methanol (5 ml) and treated with one equivalent of sodium methoxide (18.9 mg). A titanium(III) chloride solution was prepared separately by adding of an aqueous solution of ammonium acetate (0.65 g, 8.4 mmol) in water (2 ml) to titanium(III) chloride (1.8 ml, 1.4 mmol, 10% solution in hydrochloric acid) under nitrogen. The prepared titanium(III) chloride solution was then added carefully to the anionic solution under nitrogen with vigorous stirring. The colour changed slowly from brown to yellow. The mixture was stirred

overnight at room temperature then poured into ethyl acetate (20 ml) and separated into two phases. The aqueous phase was extracted with ethyl acetate (30 ml × 3). The organic extracts were combined, washed with 5% sodium bicarbonate (20 ml) and brine (20 ml), then dried with anhydrous magnesium sulfate and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 2:1) to afford **26d** as a yellow solid (0.1 g, 0.25 mmol, 71%). The physical and spectroscopic data were identical to those recorded below.

(b) Tin(II) chloride reaction

To a mixture of 6-amino-2-(benzylsulfanyl)-5-{2-nitro-1-[2-(trifluoromethyl)phenyl]ethyl}-4(3*H*)-pyrimidinone **25d** (0.1 g, 0.22 mmol) in ethyl acetate (15 ml) was added tin(II) chloride dihydrate (0.15 g, 0.66 mmol). The resulting mixture was stirred in an oil bath at 85 °C for 24 h then poured into ethyl acetate (20 ml) and washed with saturated aqueous sodium bicarbonate (20 ml), 1% hydrochloric acid (10 ml) and with brine (20 ml), then dried with anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 1:2) to give **26d** as a yellow solid (45 mg, 0.11 mmol, 50%); mp 188-190 °C. ν_{max} (KBr)/cm^{-1} 3064, 1657, 1313, 1169, 1122, 1059, 1034, 972, 765, 697; δ_H ($(CD_3)_2SO$) 4.44 (1H, s), 6.89 (1H, d, CH, J = 1.9), 7.25-7.75 (9H, m), 11.99 (1H, s), 12.04 (1H, s, CH); δ_C ($(CD_3)_2SO$) 33.5, 103.1, 115.5, 118.6, 123.0 (q, $J^1_{C\text{-}F}$ 272, CF_3), 125.4 (2-CF_3-C_6H_4), 127.18 (q, $J^2_{C\text{-}F}$ 28, 2-CF_3-C_6H_4 C-2), 128.4 (2-CF_3-C_6H_4 and Ph), 129.1, 131.2, 133.5, 134.1, 137.3, 147.9, 153.7, 158.4; HRFABMS calcd for $C_{20}H_{14}F_3N_3OS$ ($M+H^+$); 402.0888 found 402.0890.

Two additional methods were used for the preparation of this compound.

(c) Microwave reaction

6-Amino-2-(benzylsulfanyl)-5-{2-nitro-1-[2-(trifluoromethyl)phenyl]ethyl}-4(3*H*)-pyrimidinone **25d** (0.1 g, 0.22 mmol) was suspended in solvent (3 ml, acetonitrile or dimethyl formamide) in a sealed vessel and then DBU (49 μL, 0.33 mmol) was added. The mixture was irradiated (average 27 W) (need to give the instrumentation in the general methods at 85 ˚C for 1 h and then ethyl acetate (30 ml) was added and evaporated to dryness. The residue was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 1:5 to 1:2) to give **26d** (green solid, 14 mg, 0.035 mmol,

16% in acetonitrile; brown solid, 21 mg, 0.052 mmol, 24% in dimethyl formamide). The physical and spectroscopic data were identical to those recorded above.

(d) Thermal reaction

To a solution of 6-Amino-2-(benzylsulfanyl)-5-{2-nitro-1-[2-(trifluoromethyl)phenyl]ethyl}-4(3*H*)-pyrimidinone **25d (**0.09 g, 0.2 mmol) in acetonitrile (5 ml) was added DBU (45μL, 0.3 mmol). The reaction mixture was stirred 2 d in an oil bath (60 ˚C) under nitrogen. Through the same work-up and purification procedure described above for the microwave reaction, the desired product **26d** was obtained as a green solid (21 mg, 0.052 mmol, 26%). The physical and spectroscopic data were identical to those recorded above.

5-Phenyl-2-(1-pyrrolidinyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one 31b

To a mixture of 2-(methylsulfanyl)-5-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one **28** (0.2 g, 0.78 mmol) in dimethylformamide (5 ml) was added 3-chlorobenzenecarboperoxoic acid (0.52 g, 2.3 mmol). The resulting mixture was stirred for 4 h at room temperature. Dimethylformamide was evaporated under vacuum and the resulting solid was washed with ether (50 ml), to afford the crude sulfone as a light pink solid (0.19 g, 84%, confirmed by MS (ES): M+1=290). The crude sulfone intermediate was heated with pyrrolidine (1 ml) in a sealed tube for 15 h at 100 °C. Pyrrolidine was removed under reduced pressure and the resulting residue was recrystallised from methanol and ether to afford **31b** as a brown solid (0.12 g, 0.43 mmol, 55%); mp > 250 °C; ν_{max} (KBr)/cm^{-1} 3439, 3126, 2956, 1646, 1519, 1344, 1127, 1078, 905, 746, 694; δ_H ($(CD_3)_2SO$) 1.88 (4H, t, *J* = 6.6), 3.43 (4H, t, *J* = 6.6), 6.98 (1H, d, *J* = 2.2), 7.11-7.29 (3H, m), 7.91-7.93 (2H, m), 9.86 (1H, br s), 11.30 (1H, br s); δ_C ($(CD_3)_2SO$) 24.9, 46.6, 96.3, 115.3, 119.4, 125.2, 127.4, 127.8, 135.0, 150.2, 152.6, 159.7; HRFABMS calcd for $C_{16}H_{16}N_4ONa$ ($M+Na^+$); 303.1222 found 303.1219.

2-Anilino-5-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one 31c.

To a mixture of 2-(methylsulfanyl)-5-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one **28** (0.2 g, 0.78 mmol) in dimethylformamide (5 ml) was added 3-chlorobenzenecarboperoxoic acid (0.52 g, 2.3 mmol). The resulting mixture was stirred for 4 h at room temperature. Dimethylformamide was evaporated under

reduced pressure and the resulting solid was washed with ether (50 ml), to afford the crude sulfone as a light pink solid (0.20 g, 89%, confirmed by MS (ES): M^++1=290). The crude sulfone intermediate was heated with aniline (1 ml) in a sealed tube for 17 h at 100 °C. Aniline was removed under reduced pressure and the residue was purified by column chromatography (silica gel/ethyl acetate:*n*-hexane = 1:3 to ethyl acetate 100%) to afford **31c** as a yellow solid (58 mg, 0.19 mmol, 24%); mp > 250 °C; ν_{max} (KBr)/cm^{-1} 3391, 2923, 2852, 1672, 1632, 1595, 1565, 1497, 1441, 1329, 1264, 1146, 855, 751, 689; δ_H ($(CD_3)_2SO$) 6.99-7.17 (3H, m), 7.27-7.34 (3H, m), 7.30 (1H, d, *J* = 2.7), 7.64-7.97 (2H, m), 8.63 (1H, s), 10.32 (1H, br s), 11.62 (1H, br s); δ_C ($(CD_3)_2SO$) 98.6, 116.2, 118.9 (2C), 119.9, 125.4, 122.1, 128.8 (6C), 127.8, 127.5, 139.1, 134.6, 148.0, 150.9, 158.7; HRFABMS calcd for $C_{18}H_{14}N_4O$ ($M+H^+$); 303.1246 found 303.1255.