Supporting Information Available

Synthesis of 2-bromomethyl azoles (4). General procedure

Bromomethyl azoles were prepared from commercially available methylazoles according to literature procedure: Nagarathnam, D. *Synthesis* **1992**, 743.

3-Bromo-2-bromomethylpyrrolo[2,3-b]pyridine-1-carboxylic acid methyl ester (4a). Yellow powder; yield 82%; mp 147-148ºC; IR (KBr) 1739, 1576, 1436, 1402, 1319, 1255, 967 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.45 (dd, 1H, J = 4.8, 1.6 Hz), 7.75 (dd, 1H, J = 7.9, 1.6 Hz), 7.20 (dd, 1H, J = 4.8 , 7.9 Hz), 4.97(s, 2H), 4.05 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 150.2, 147.3, 147.0, 133.8, 128.3, 121.0, 119.7, 100.4, 54.7, 23.5; MS m/z (rel. int.) 350 (12), 349 (80), 348 (10), 347 (41), 270 (15), 269 (99), 268 (17), 267 (100). Anal Calcd for $C_{10}H_8Br_2N_2O_2$: C, 34.52; H, 2.32; N, 8.05. Found: C, 34.60; H, 2.32; N, 8.01.

3-Bromo-2-bromomethyl-4-methoxypyrrolo[2,3-b]pyridine-1-carboxylic acid methyl ester (4b). White powder; yield 80%; mp 169-170ºC; IR (KBr) 1739, 1578, 1449, 1394, 1295, 1093 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, 1H, J = 5.7 Hz), 6.67 (d, 1H, J = 5.7 Hz), 5.02 (s, 2H), 4.12 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 160.4, 150.2, 148.5, 148.2, 131.6, 110.1, 101.6, 98.1, 55.8, 54.8, 24.0; MS m/z (rel. int.) 378 (8), 376 (4), 299 (99), 297 (100), 131 (29), 59 (41). Anal Calcd for $C_{11}H_{10}Br_2N_2O_3$: C, 34.95; H, 2.67; N, 7.41. Found: C, 35.01; H, 2.67; N, 7.43.

3-Bromo-2-bromomethyl-4-chloropyrrolo[2,3-b]pyridine-1-carboxylic acid methyl ester (4c). Yellow powder, yield 65%; mp 160-161ºC; IR (KBr) 3415, 1735, 1618, 1560, 1438, 1381, 1284 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.37 (d, 1H, J = 5.3 Hz), 7.26 (d, 1H, J = 5.3 Hz), 5.06 (s, 2H), 4.17 (s, 3H); MS m/z (rel. int.) 385 (52), 384 (11), 383 (75), 305 (31), 304 (15), 303 (100), 302 (12), 301 (74). Anal Calcd for $C_{10}H_7Br_2ClN_2O_2$: C, 31.41; H, 1.84; N, 7.32. Found: C, 31.32; H, 1.84; N, 7.34.

3-Bromo-2-bromomethylindole-1-carboxylic acid methyl ester (4d). mp 119-120ºC.; mp 118-119ºC. (lit. ref. 12)

3,6-Dibromo-2-bromomethyl-5-methoxyindole-1-carboxylic acid methyl ester (4e). Yellow powder; yield 20%, mp 175-176ºC; IR (KBr) 3415, 1738, 1616, 1440, 1362, 1290, 1214 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (s, 1H), 6.93 (s, 1H), 5.02 (s, 2H), 4.11 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.6, 150.1, 133.1, 129.2, 127.7, 120.2, 111.0, 103.3, 100.3, 56.2, 54.1, 24.4; MS m/z (rel. int.) 457 (8), 455 (8), 378 (48), 377 (14), 376 (100), 374 (47), 59 (59). Anal Calcd for $C_{12}H_{10}Br_3NO_3$: C, 31.61; H, 2.21; N, 3.07. Found: C, 31.59; H, 2.21; N, 3.08.

3-Bromo-2-bromomethyl-5-chloroindole-1-carboxylic acid methyl ester (4f). White powder; yield 98%; mp 138-139ºC; IR (KBr) 3416, 2953, 1742, 1637, 1439, 1375, 1207, 1072 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, 1H, J = 9.0 Hz), 7.47, (d, 1H, J = 2.1 Hz), 7.31 (dd, 1H, J = 9.0 Hz, J = 2.1 Hz), 5.00 (s, 2H), 4.11 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 150.8, 134.2, 133.9, 129.9, 129.1, 126.9, 119.4, 117.1, 103.1, 54.4, 24.0; MS m/z (rel. int.) 381 (14), 304 (25), 303 (12), 302 (100), 300 (75), 162 (34), 127 (26), 59 (51). Anal Calcd for $C_{11}H_8Br_2ClNO_2$: C, 34.64; H, 2.11; N, 3.67. Found: C, 34.70; H, 2.10; N, 3.68.

2-Bromomethylbenzoimidazole-1-carboxylic acid methyl ester (4g). White powder; yield 52%, mp 120-121ºC; IR (KBr) 3483, 3073, 3000, 2960, 1949, 1756, 1605, 1539, 1453, 1357, 1320, 1292, 1220, 1118, 765, 749 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93-7.89 (m, 1H), 7.74-7.71 (m, 1H), 7.38-7.24 (m, 2H), 4.94 (s, 2H), 4.14 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 150.4, 150.1, 141.7, 132.7, 125.9, 124.9, 120.4, 115.0, 54.7, 24.7; MS m/z (rel. int.) 271 (97), 269 (100), 217 (19), 191 (13), 190 (17), 189 (99). Anal Calcd for $C_{10}H_9BrN_2O_2$: C, 44.75; H, 3.37; N, 10.41. Found: C, 44.75; H, 3.38; N, 10.40.

2-Bromomethylimidazole-1-carboxylic acid methyl ester (4h). White powder; yield 11%; mp 94-95ºC; IR (KBr) 3164, 1772, 1430, 1295, 1190, 821 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (s, 1H), 6.98 (s, 1H), 4.82 (s, 2H), 4.03 (s, 3H); MS m/z (rel. Int.) 220 (19), 218 (20), 149 (24), 139 (27), 94 (100), 81 (40), 79 (38), 59 (69). Anal Calcd for $C_6H_7BrN_2O_2$: C, 32.90; H, 3.22; N, 12.79. Found: C, 32.81; H, 3.21; N, 12.82.

4-Bromo-5-bromomethyl-3-methylpyrazole-1-carboxylic acid methyl ester (4i). White powder; yield 72%; mp 75-76ºC; IR (KBr) 3415, 3060, 2960, 2133, 1759, 1637, 1480, 1445, 1352, 1297, 1149, 1041, 763 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.79 (s, 2H), 4.10 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 151.7, 149.4, 140.9, 103.5, 55.2, 19.8, 12.6; MS m/z (rel. int.) 314 (4), 312 (7), 310 (4), 233 (50), 231 (51), 189 (21), 187 (23), 65 (100), 63 (49), 59 (73). Anal calcd for $C_7H_8Br_2N_2O_2$: C, 26.95; H, 2.58; N, 8.98. Found: C, 27.01; H, 2.58; N, 8.98.

Synthesis of azolopyrimidines (6). General procedure

A mixture of the bromomethyl derivative **4** (1.0 mmol), TosMIC (0.22g, 1.1 mmol) and TBAI (0.08g, 0.2 mmol) in CH_2Cl_2 (7 mL) and aqueous sodium hydroxide (7 mL) was stirred at the temperature indicated in Table 1. After the appropriate time (20min-2h), the reaction mixture was poured into water and extracted with CH_2Cl_2. The organic phase was washed with saturated NaCl solution, dried (Na_2SO_4), and concentrated under reduced pressure providing a crude product that was purified by flash chromatography (silica gel, hexane/EtOAc) to yield compounds **6a-i**.

5-Bromo-pyrido[3',2':4,5]pyrrolo[1,2-c]pyrimidine-3-carboxylic acid methyl ester (6a). Yellow powder; yield 65%; mp 208-209ºC; IR (KBr) 1732, 1637, 1618, 1567, 1523, 1439, 1286, 1011, 806 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.55 (d, 1H, J = 1.2 Hz), 8.61 (dd, 1H, J = 4.6, 1.4 Hz), 8.26 (d, 1H, J = 1.2 Hz), 8.15 (dd, 1H, J = 8.1, 1.4 Hz), 7.57 (dd, 1H, J =8.1, 4.6 Hz), 4.04 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.8, 145.1, 139.8, 138.0, 136.3, 130.3, 128.2, 122.0, 121.7, 116.0, 85.0, 53.1; MS m/z (rel. int.) 306 (99), 304 (100), 249 (43), 248 (40), 247 (44), 246 (36), 220 (25), 219 (25), 140 (40), 87 (22). Anal Calcd for $C_{12}H_8BrN_3O_2$: C, 47.08; H, 2.63; N, 13.73. Found: C, 47.13; H, 2.62; N, 13.76.

5-Bromo-6-methoxypyrido[3',2':4,5]pyrrolo[1,2-c]pyrimidine-3-carboxylic acid methyl ester (6b). Yellow powder ; yield 61%; mp 256-257ºC; IR (KBr) 1711, 1568, 1437, 1352, 1324, 1294, 1225, 1013 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.44 (d, 1H, J = 1.5 Hz), 8.42 (d, 1H, J = 5.5 Hz), 8.23 (d, 1H, J = 1.5 Hz), 6.86 (d, 1H, J = 5.5 Hz), 4.07 (s, 3H), 4.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 160.8, 159.5, 147.0, 141.2, 137.7, 135.5, 128.9, 116.4, 102.0, 82.7, 56.1, 53.0; MS m/z (rel. int.) 337 (100),

335 (97), 322 (46), 320 (45), 101 (36), 83 (36), 71 (36), 69 (53), 59 (84), 57 (93), 55 (74). Anal Calcd for $C_{13}H_{10}BrN_3O_3$: C, 46.45; H, 3.00; N, 12.50. Found: C, 46.41; H, 3.02; N, 12.51.

5-Bromo-6-chloro-pyrido[3',2':4,5]pyrrolo[1,2-c]pyrimidine-3-carboxylic acid methyl ester (6c). Yellow powder; yield 27%; mp 195-196ºC; IR (KBr) 3415, 2924, 1713, 1444, 1356, 1260, 1098 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.56 (s, 1H), 8.47 (d, 1H, *J* = 5.0 Hz), 8.33 (s, 1H), 7.55 (d, 1H, *J* = 5.0 Hz), 4.06 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 158.4, 144.6, 138.0, 130.0, 128.6, 128.2, 125.9, 123.9, 122.5, 121.1, 116.2, 53.2; MS m/z (rel. int.) 344 (24), 343 (17), 342 (100), 341 (26), 340 (76), 339 (12). Anal Calcd for $C_{12}H_7BrClN_3O_2$: C, 42.32; H, 2.07; N, 12.34. Found: C, 42.25; H, 2.07; N, 12.37.

5-Bromopyrimido[1,6-a]indole-3-carboxylic acid methyl ester (6d). Yellow powder, yield 89%, mp 260-261ºC, IR (KBr) 3427, 1729, 1456, 1372, 1217, 1095, 743 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.25 (s, 1H), 8.03 (d, 1H, *J* = 7.8 Hz), 7.82 (d, 1H, *J* = 7.6 Hz), 7.59-7.52(m, 2H), 4.02 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.2, 138.4, 135.8, 130.7, 129.0, 128.4, 126.0, 124.4, 120.1, 116.4, 111.0, 87.9, 53.0; MS m/z (rel. int.) 305 (100), 304 (28), 275 (12), 273 (12), 261 (10), 255 (17), 254 (45), 227 (35), 226 (51), 143 (33), 89 (17). Anal Calcd for $C_{13}H_9BrN_2O_2$: C, 51.17; H, 2.97; N, 9.18. Found: C, 51.09; H, 2.98; N, 9.17.

5,8-Dibromo-7-methoxypyrimido[1,6-a]indole-3-carboxylic acid methyl ester (6e). Yellow powder, yield 56%; mp 279-280ºC; IR (KBr) 3416, 1737, 1637, 1560, 1542, 1449, 897 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 9.67 (s, 1H), 8.89 (s, 1H), 7.95 (s, 1H), 7.16 (s, 1H), 3.99 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 164.3, 153.7, 140.1, 134.9, 130.8, 128.4, 123.0, 117.7, 113.8, 109.0, 98.8, 84.8, 56.6, 52.5; MS m/z (rel. int.) 415 (100), 414 (40), 413 (50), 412 (16), 385 (18), 383 (35), 331 (18), 335 (28), 334 (28). Anal Calcd for $C_{14}H_{10}Br_2N_2O_3$: C, 40.61; H, 2.43; N, 6.77. Found: C, 40.53; H, 2.43; N, 6.76.

5-Bromo-7-chloropyrimido[1,6-a]indole-3-carboxylic acid methyl ester (6f). Yellow powder, yield 58%; mp 218-219ºC; IR (KBr) 3422, 2903, 1731, 1655, 1446, 1098 cm^{-1};

^{1}H NMR (300MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.24 (s, 1H), 7.98 (d, 1H, *J* = 9.0 Hz), 7.81 (s, 1H), 7.48 (d, 1H, *J* =9.0 Hz), 4.08 (s, 3H); MS m/z (rel. int.) 343 (27), 342 (19), 341 (100), 340 (30), 339 (77), 338 (16). Anal. Calcd for $C_{13}H_8BrClN_2O_2$: C, 45.98; H, 2.37; N, 8.25. Found: C, 46.03; H, 2.37; N, 8.23.

Pyrimido[1,6-a]benzimidazole-3-carboxylic acid methyl ester (6g). Pale brown powder; yield 41%; mp 190-191ºC; IR (KBr) 3415, 1735, 1638, 1513, 1458, 1243, 754 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.39 (s, 1H), 8.43 (s, 1H), 8.10-8.01 (m, 2H), 7.70-7.51 (m, 2H), 4.05 (s, 3H); ^{13}C NMR (50MHz, $CDCl_3$) δ 164.4, 151.1, 149.3, 145.2, 141.2, 139.0, 127.8, 124.2, 121.0, 115.9, 111.1, 53.3; MS m/z (rel. int.) 227 (100), 169 (93), 168 (75), 102 (63), 76 (36), 50 (33). Anal Calcd for $C_{12}H_9N_3O_2$: C, 63.43; H, 3.99; N, 18.49. Found: C, 63.39; H, 4.00; N; 18.45.

3-Bromo-2-methylpyrazolo[1,5-c]pyrimidine-5-carboxylic acid methyl ester (6i). White powder; yield 44%; mp 180-181ºC; IR (KBr) 3424, 3071, 1724, 1616, 1532, 1470, 1337, 1277, 1204, 1048, 941, 721 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.17 (s, 1H), 3.99 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (50MHz, $CDCl_3$) δ 164.3, 155.0, 140.2, 138.5, 136.9, 114.3, 90.1, 53.1, 12.6; MS m/z (rel. int.) 272 (98), 270 (100), 269 (3), 240 (4), 238 (4), 192 (1). Anal Calcd for $C_9H_8BrN_3O_2$: C, 40.02; H, 2.99; N, 15.56. Found: C, 39.97; H, 3.00; N, 15.58.