Supporting Information for

Synthesis of 2-Aryl-oxazolo[4,5-*c*]quinoline-4(5*H*)-ones and 2-Aryl-thiazolo[4,5-*c*]quinoline-4(5*H*)-ones

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Yields refer to isolated, chromatographically homogeneous material (HPLC and TLC) whose spectral data (including 400 MHz ^{1}H NMR, 100 MHz ^{13}C NMR, and mass spectra) are consistent with the proposed structures.

Compound **4**. Ethyl 2-aminooxazole-4-carboxylate[1] (15.6 g, 0.1 mol) was added in portions to a solution of *tert*-butyl nitrite (20 ml, 0.15 mol) and copper(II) chloride (20 g, 0.15 mol) in acetonitrile (450 ml) at 60 ^{o}C. The mixture was then heated at 80 ^{o}C for 2 h. The mixture was cooled and partitioned between dichloromethane (500 ml), water (250 ml), and concentrated hydrochloric acid (25 ml). The aqueous layer was further extracted with dichloromethane and the combined organics washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography, eluting with hexane:ether, 3:1, and gave **4** (14.5 g, 83%). M.p. 97-98 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, *J* = 7 Hz, 3H), 4.34 (q, *J* = 7 Hz, 2H), 8.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 61.8, 135.3, 145.6, 148.4, 160.2.

Compound **6**. A stirred solution of phenylboronic acid (244 mg, 2.0 mmol), $Pd(PPh_3)_4$ (80 mg), 2 M potassium carbonate solution (2.0 ml, 4.0 mmol), **4** (352 mg, 2.0 mmol) in toluene (20 ml) was heated under a nitrogen atmosphere at 90 ^{o}C for 1 h. The solution was cooled and partitioned between ethyl acetate (30 ml) and 2 M sodium hydroxide solution (15 ml). The aqueous layer was further extracted with ethyl acetate (2 x 25 ml), and the combined organics were washed with brine (30 ml), dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography, eluting with hexane:ether, 3:1, and gave **6** (380 mg, 87%). M.p. 62 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7 Hz, 3H), 4.40 (q, *J* = 7 Hz, 2H), 7.43-7.45 (m, 3H), 8.08 (dd, *J* = 2 and 7.5 Hz, 2H), 8.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 61.2, 126.3, 126.7, 128.7, 131.0, 134.6, 143.6, 161.3, 162.3.

Compound **7**. A mixture of oxazole **6** (280 mg, 1.28 mmol), 2-iodonitrobenzene (622 mg, 2.5 mmol), palladium acetate (18 mg, 0.08 mmol), triphenyl phosphine (31 mg, 0.12 mmol), calcium carbonate (978 mg, 3.0 mmol), and DMF (8 ml) was flushed with nitrogen and heated at 140 ^{o}C for 3 h. The cooled mixture was diluted with ethyl acetate (50 ml) and washed with water (3 x 25 ml), brine (25 ml), dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography, eluting with hexane:ether, 3:2, and gave **7** (359 mg, 83%) as a pale yellow, crystalline material (recrystallized from ethanol). M.p. 144-145 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, *J* = 7 Hz, 3H), 4.31 (q, *J* = 7 Hz, 2H), 7.46-7.50 (m, 3H), 7.67-7.71 (m, 1H), 7.76 (d, *J* = 4 Hz, 2H), 8.11 (d, *J* = 7.5 Hz, 2H), 8.17 (d, *J* = 8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 61.4, 122.6, 124.7, 126.0, 126.9, 128.8, 130.0, 131.2, 131.3, 132.5, 132.8, 148.4, 150.8, 161.2, 161.3. LRMS m/z (relative intensity) 339(M + 1, 70%), 362(M + 23, 35%).

Compound **8**. A mixture of **7** (338 mg, 1.0 mmol), 10% palladium on activated carbon (75 mg), and methanol (25 ml) was stirred under a hydrogen atmosphere (hydrogen filled balloon) for 1 h. After adding further methanol (30 ml) the mixture was briefly heated to reflux with a heat gun and filtered hot through Celite. The volatiles were removed by evaporation and gave **8** as a grey/white powder (308 mg, 100%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (t, *J* = 7 Hz, 3H), 4.20 (q, *J* = 7 Hz, 2H), 5.43 (s, 2H), 6.57 (t, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 7.5 Hz, 1H), 7.55 (br s, 3H), 8.01 (br s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 60.3, 110.4, 114.9, 115.3, 126.3, 126.6, 128.8, 129.1, 130.9, 131.2, 131.7, 147.6, 154.8, 159.3, 161.2. LRMS m/z (relative intensity) 309(M + 1, 100%).

Compound **9**. A mixture of **8** (308 mg, 1.0 mmol), DME (20 ml), and 2 M potassium carbonate solution (2.0 ml, 4.0 mmol) were heated to reflux for 8 h. The solvent was reduced in volume by evaporation and water (15 ml) added. The solid was collected by filtration and recrystallized from ethanol and gave **9** as a fluffy white solid (201 mg, 77%). M.p. 345-348 ^{o}C (decomposition). ^{1}H NMR (400 MHz, DMSO) δ 7.34 (t, *J* = 7.0 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.58-7.62 (m, 4H), 8.02 (d, *J* = 7.5 Hz, 1H), 8.20 (br s, 2H), 12.01 (s, 1H). 13C NMR (100 MHz, DMSO) δ 109.8, 116.2, 120.9, 122.5, 125.9, 126.9, 129.3, 129.9, 130.3, 131.8, 137.4, 153.1, 156.9, 161.4. LRMS m/z (relative intensity) 263(M + 1, 30%).

Compound **10**. A solution of **6** (2.17 g, 10 mmol), *N*-bromosuccinimide (7.12 g, 40 mmol) in chloroform (80 ml) was heated at reflux for 48 h. The solution was cooled and partitioned with saturated aqueous sodium bicarbonate (100 ml). The aqueous layer was further extracted with dichloromethane and the combined organics washed with brine, dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography, eluting with hexane:ether, 3:1, and gave **10** (2.54 g, 86%). M.p. 75 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (t, *J* = 7 Hz, 3H), 4.44 (q, *J* = 7 Hz, 2H), 7.44-7.50 (m, 3H), 8.04-8.07 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 61.6, 125.6, 126.6, 128.1, 128.8, 131.5, 131.8, 160.6, 162.6. LRMS m/z (relative intensity) 296 and 298(M + 1, 60%).

Compound **11**. A solution of **6** (217 mg, 1.0 mmol) and sodium hydroxide (48 mg, 1.2 mmol) in ethanol (10 ml) was stirred at room temperature overnight. The ethanol was evaporated and the residue acidified (*ca* pH 5) with 2 M hydrochloric acid and extracted with ethyl acetate (3 x 25 ml). The combined organics were washed with brine (30 ml), dried ($MgSO_4$), evaporated and gave **11** (169 mg, 89%). M.p. 215 ^{o}C. ^{1}H NMR (400 MHz, DMSO) δ 7.54-7.56 (m, 3H), 7.98-8.00 (m, 2H), 8.83 (s, 1H), 13.14 (br s, 1H). ^{13}C NMR (100 MHz, DMSO) δ 126.2, 126.30, 129.3, 131.3, 134.6, 145.4, 161.2, 162.1. LRMS m/z (relative intensity) 190(M + 1, 100%), 213(M + 23, 90%).

Compound **12**. A solution of **11** (189 mg, 1.0 mmol), BOP (486, 1.0 mmol), triethylamine (112, 1.1 mmol), 2-iodoaniline (219 mg, 1.0 mmol) in dichloromethane (10 ml) was stirred at room temperature overnight. The mixture was partitioned between ethyl acetate (40 ml) and saturated sodium bicarbonate (20 ml) and the layers separated. The aqueous layer was extracted with ethyl acetate (2 x 25 ml) and the combined organics washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography, eluting with hexane:ether, 4:1, and gave **12** (304 mg, 78%) as a white solid. M.p. 147-148 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.51-7.52 (m, 3H), 7.84 (d, *J* = 8 Hz,

1H), 8.11 (m, 2H), 8.34 (s, 1H), 8.45 (d, J = 8 Hz, 1H), 9.40 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 89.6, 121.4, 125.9, 126.4, 126.7, 128.9, 129.2, 131.2, 137.3, 138.1, 139.0, 141.4, 158.6, 161.5. LRMS m/z (relative intensity) 391(M + 1, 95%), 413(M + 23, 100%).

Compound **13**. Ethyl 2-amino-5-chloro-4-thiazole-carboxylate[2] (2.06 g, 10 mmol) was added in portions to a solution of *tert*-butyl nitrite (1.54 g, 15 mmol) and copper(II) bromide (2.68 g, 12 mmol) in acetonitrile (100 ml) at 60 °C. The mixture was then heated at 80 °C for 2 h. The mixture was cooled and partitioned between dichloromethane (150 ml) and 1 M hydrochloric acid (100 ml). The aqueous layer was further extracted with dichloromethane and the combined organics washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography, eluting with hexane:ether, 5:1, and gave **13** (2.21g, 82%) as a pale yellow solid. M.p. 56 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (t, J = 7 Hz, 3H), 4.44 (q, J = 7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 62.0, 132.5, 136.5, 141.4, 159.3. LRMS m/z (relative intensity) 271(M + 1, 100%).

Compound **2**. A stirred solution of 3,4-dimethoxyphenylboronic acid (91 mg, 0.5 mmol), $Pd(PPh_3)_4$ (20 mg), 2 M potassium carbonate solution (0.5 ml, 1.0 mmol), and **13** (135 mg, 0.5 mmol) in DME (5 ml) was heated under a nitrogen atmosphere at 80 °C for 4 h. TLC indicated that no starting material **13** remained and the reaction mixture was removed from the heat source and 2-aminophenylboronic acid (102 mg, 0.75 mmol) and $Pd(PPh_3)_4$ (20 mg) were added and the reaction mixture was reheated to 80 °C for 4 h. The solution was cooled and partitioned between ethyl acetate (20 ml) and 2 M sodium hydroxide solution (15 ml). The aqueous layer was further extracted with ethyl acetate (2 x 25 ml), and the combined organics washed with brine (30 ml), dried ($MgSO_4$), and evaporated. The solid was recrystallized from ether and ethanol and gave **2** (96 mg, 69%) as a white solid. M.p. 312-314 °C (decomposition). ^{1}H NMR (400 MHz, DMSO) δ 3.84 (s, 3H), 3.89 (s, 3H), 7.12 (d, J = 8 Hz, 1H), 7.26 (d, J = 7 Hz, 1H), 7.43 (d, J = 8 Hz, 1H), 7.51 (t, J = 7 Hz, 1H), 7.59 (m, 2H), 7.78 (d, J = 7 Hz, 1H), 11.99 (s, 1H). ^{13}C NMR (100 MHz, C_5D_5N) δ 56.2, 56.4, 110.9, 112.6, 116.5, 116.8, 121.7, 123.2, 126.2, 126.9, 130.5, 138.2, 142.8, 146.6, 153.0, 158.4, 167.5 (one peak obscured). LRMS m/z (relative intensity) 339(M + 1, 60%). HRMS (M + H, 339.0804. $C_{18}H_{15}N_2O_3S$ requires 339.0803).

Reference for experimental

1. Crank, G.; Foulis, M. J. *J. Med. Chem.* **1971**, *14*, 1075.

2. South, M. S. *J. Het. Chem.* **1991**, *28*, 1003.