Supporting Information
For

Ethyl 2-chlorooxazole-4-carboxylate: A versatile intermediate for the synthesis of substituted oxazoles

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Compound **2**. 2-Aminooxazole **1**[13] (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 (hexane:ether, 3:1) and gave compound **2** (14.5 g, 83%). ^{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 **3**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (t, *J* = 7 Hz, 3H), 4.35 (q, *J* = 7 Hz, 2H), 8.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 61.6, 134.9, 135.7, 148.9, 159.8.

Compound **4**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, *J* = 7 Hz, 3H), 4.37 (q, *J* = 7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 61.8, 130.4, 133.1, 134.3, 159.1.

Representative procedure for Suzuki coupling reaction:

Compound **5a**. A stirred solution of phenylboronic acid (61 mg, 0.5 mmol), $Pd(PPh_3)_4$ (20 mg), 2 M potassium carbonate solution (0.5 ml, 1.0 mmol), **2** (88 mg, 0.5 mmol) in toluene (5 ml) was heated under a nitrogen atmosphere at 90 ^{o}C for 1 h. The solution was cooled and partitioned between ethyl acetate (10 ml) and 2 M sodium hydroxide solution (5 ml). The aqueous layer was further extracted with ethyl acetate (2 x 10 ml), and the combined organics were washed with brine (10 ml), dried ($MgSO_4$) and evaporated. . The residue was purified by flash chromatography (hexane:ether, 3:1) and gave compound **5a** (95 mg, 87%). ^{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.

Representative procedure for Stille coupling reaction:

Compound **5b**. A stirred solution of vinyltributyltin (150 mg, 0.5 mmol), $Pd(PPh_3)_2Cl_2$ (22 mg), **2** (88 mg, 0.5 mmol) in dioxane (5 ml) was heated under a nitrogen atmosphere at 100 ^{o}C for 4 h. The solution was cooled and partitioned between ethyl acetate (10 ml) and water (10 ml). The aqueous layer was further extracted with ethyl acetate (2 x 10 ml), and the combined organics were washed with brine (10 ml), dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography (hexane:ether, 3:1) and gave compound **5b** (73 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, *J* = 7 Hz, 3H), 4.36 (q, *J* = 7 Hz, 2H), 5.70 (d, *J* = 11 Hz, 1H), 6.24 (d, *J* = 17.5 Hz, 1H), 6.60 (dd, *J* = 11 and 17.5 Hz, 1H), 8.14 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 61.1 122.5, 123.9, 134.2, 143.3, 161.0, 161.2.

Representative procedure for Negishi coupling reaction:

Compound **5c**. A stirred solution of 0.5 M 2-pyridylzinc bromide in THF (2.0 ml, 1.0 mmol), $Pd(PPh_3)_4$ (20 mg), **2** (88 mg, 0.5 mmol) in THF (5 ml) was heated under a nitrogen atmosphere at 65 ^{o}C for 4 h. The solution was cooled and partitioned between ethyl acetate (10 ml) and water (10 ml). The aqueous layer was further extracted with ethyl acetate (2 x 10 ml), and the combined organics were washed with brine (10 ml), dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography (hexane:ether, 2:3) and

gave compound **5c** (80 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (t, *J* = 7 Hz, 3H), 4.41 (q, *J* = 7 Hz, 2H), 7.38-7.42 (m, 1H), 7.83 (dt, *J* = 1.5 and 8 Hz, 1H), 8.26 (d, *J* = 8 Hz, 1H), 8.35 (s, 1H), 8.71-8.73 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 61.4, 122.8, 125.4, 134.8, 137.1, 144.7, 145.1, 150.0, 160.9, 161.0.

Compound **6**. A solution of **5a** (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 (hexane:ether, 3:1) and gave compound **6** (2.54 g, 86%). ^{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.

Compound **7a**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, *J* = 7 Hz, 3H), 4.46 (q, *J* = 7 Hz, 2H), 7.48-7.51 (m, 6H), 8.10-8.17 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 61.4, 126.3, 126.8, 127.1, 128.2, 128.3, 128.5, 128.7, 130.2, 131.0, 155.0, 159.7, 162.2.

Compound **7b**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (t, *J* = 7 Hz, 3H), 3.96 (s, 3H), 4.00 (s, 3H), 4.46 (q, *J* = 7 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 1H), 7.49-7.50 (m, 3H), 7.76 (dd, *J* = 2 and 8.5 Hz, 1H), 7.89 (d, *J* = 8 Hz, 1H), 8.14-8.16 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 55.9, 56.0, 61.4, 110.7, 111.5, 119.7, 121.8, 126.4, 126.7, 127.1, 128.7, 130.9, 148.6, 150.7, 155.2, 158.9, 162.5.

Compound **7c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, *J* = 7 Hz, 3H), 4.46 (q, *J* = 7 Hz, 2H), 5.63 (dd, *J* = 1 and 11.5 Hz, 1H), 6.13 (dd, *J* = 1 and 18 Hz, 1H), 7.26 (dd, *J* = 11.5 and 18 Hz, 1H), 7.47-7.50 (m, 3H), 8.12-8.14 (m, 2H).

Compound **7d**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (t, *J* = 7 Hz, 3H), 4.46 (q, *J* = 7 Hz, 2H), 7.37 (ddd, *J* = 1, 5 and 7.5 Hz, 1H), 7.47-7.51 (m, 3H), 7.84 (dt, *J* = 1.5 and 8 Hz, 1H), 8.21-8.23 (m, 2H), 8.31 (d, *J* = 8 Hz, 1H), 8.80 (brd, *J* = 5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 61.7, 124.3, 125.2, 126.1, 127.2, 128.7, 130.4, 131.3, 136.4, 146.4, 149.8, 153.2, 160.9, 162.1.

Representative procedure for Sonogashira coupling reaction:

Compound **7e**. A stirred solution of phenylacetylene (62 mg, 0.6 mmol), $Pd(PPh_3)_2Cl_2$ (18 mg), **6** (89 mg, 0.3 mmol), CuI (10 mg) and triethylamine (0.6 ml) was heated under a nitrogen atmosphere at 80 ^{o}C for 16 h. The solution was cooled and partitioned between ethyl acetate (10 ml) and water (10 ml). The aqueous layer was further extracted with ethyl acetate (2 x 10 ml), and the combined organics were washed with brine (10 ml), dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography (hexane:ether, 3:1) and gave compound **7e** (73 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (t, *J* = 7 Hz, 3H), 4.47 (q, *J* = 7 Hz, 2H), 7.41-7.43 (m, 3H), 7.48 –7.50 (m, 3H), 7.62-7.64 (m, 2H), 8.14-8.17 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 61.5, 76.2, 101.7, 121.2, 126.1, 127.1, 128.6, 128.8, 129.9, 131.4, 131.8, 135.5, 138.2, 160.9, 161.1.

Compound **8**. A solution of **7a** (630 mg, 2.15 mmol) and sodium hydroxide (120 mg, 3.0 mmol) in ethanol (20 ml) was stirred at room temperature overnight. The ethanol was evaporated and the residue acidified 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 compound **8** (553 mg, 97%). ^{1}H NMR (400 MHz, DMSO) δ 7.53-7.58 (m, 6H), 8.08-8.13 (m, 4H), 13.28 (brs, 1H). ^{13}C NMR (100 MHz, DMSO) δ 126.0, 126.4, 126.8, 128.4, 128.5, 128.6, 129.3, 130.3, 131.3, 153.9, 158.7, 163.1.

Compound **9**. To a solution of **8** (500 mg, 1.9 mmol) and potassium hydroxide (162 mg, 2.2 mmol) in water (10 ml) was added a solution of silver nitrate (340 mg, 2.2 mmol) in water (10 ml). The reaction mixture was stirred at room temperature for 2 h and filtered. The salt was washed with water, air dried, and finally dried

under vacuum at 60 ^{o}C overnight. The salt was suspended in carbon tetrachloride (20 ml) under a nitrogen atmosphere, and bromine (320 mg, 2.0 mmol) was added dropwise. The reaction mixture was heated under 75 ^{o}C for 1.5 h and then filtered. The filtrate was partitioned between 2 M sodium hydroxide (20 ml) and dichloromethane (50 ml) and the aqueous layer was further extracted with dichloromethane (2 x 50 ml). The combined organics were washed with brine (50 ml), dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography (hexane:ether, 9:1) and gave compound **9** (450 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.5 Hz, 1H), 7.47-7.51 (m, 5H), 8.01 (d, *J* = 7.5 Hz, 2H), 8.08-8.15 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.6, 125.3, 126.3, 126.9, 128.7, 128.7, 128.8, 130.9, 146.0, 159.9 (one peak is overlapping).

Compound **10a**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.44 (m, 5H), 7.48-7.50 (m, 4H), 7.70 (dd, *J* = 1.5 and 8 Hz, 2H), 7.75 (dd, *J* = 1.5 and 8 Hz, 2H), 8.17 (dd, *J* = 2 and 7.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.4, 126.5, 127.3, 128.1, 128.2, 128.5, 128.6, 128.7, 128.8, 128.9, 130.3, 132.5, 136.7, 145.5, 160.1.

Compound **10b**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.47 (dd, *J* = 2 and 11 Hz, 1H), 6.25 (dd, *J* = 2 and 17 Hz), 6.94 (dd, *J* = 11 and 17 Hz), 7.39-7.43 (m, 1H), 7.46-7.51 (m, 5H), 7.71 (dd, *J* = 1.5 and 8 Hz, 1H), 8.01 (dd, *J* =1.5 and 8.5 Hz, 1H), 8.09-8.11 (m, 1H), 8.14-8.16 (m, 1H).

Compound **10c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (t, *J* = 7 Hz, 1H), 7.39-7.53 (m, 6H), 7.75-7.79 (m, 1H), 7.96 (d, *J* = 8 Hz, 1H), 8.03 (d, *J* = 8 Hz, 2H), 8.19 (brd, *J* = 8 Hz, 2H), 8.69 (brd, *J* = 5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 122.8, 123.1, 126.5, 127.2, 127.4, 128.4, 128.6, 128.7, 128.9, 130.5, 136.2, 136.5, 148.0, 149.3, 152.0, 159.9.

Compound **10d**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.42 (m, 4H), 7.49-7.53 (m, 5H), 7.62-7.64 (m, 2H), 8.14-8.17 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.5, 95.3, 119.6, 122.5, 125.1, 126.6, 126.7, 127.7, 128.4, 128.5, 128.8, 129.0, 129.7, 130.8, 131.7, 151.9, 159.9.

Compound **11**. A solution of **7b** (140 mg, 0.4 mmol) and sodium hydroxide (20 mg, 0.5 mmol) in ethanol (4 ml) was stirred at room temperature overnight. The ethanol was evaporated and the residue acidified with 2 M hydrochloric acid and extracted with ethyl acetate (3 x 10 ml). The combined organics were washed with brine (10 ml), dried ($MgSO_4$), evaporated and gave **11** (123 mg, 95%). ^{1}H NMR (400 MHz, DMSO) δ 3.83 (s, 3H), 3.84 (s, 3H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.57-7.58 (m, 3H), 7.74 (dd, *J* = 2 and 8.5 Hz, 1H), 7.85 (d, *J* = 2 Hz, 1H), 8.08-8.10 (m, 2H), 13.16 (brs, 1H). ^{13}C NMR (100 MHz, DMSO) δ 55.6, 55.6, 111.5, 111.8, 119.1, 121.7, 126.1, 126.3, 127.4, 129.2, 131.1, 148.3, 150.5, 154.3, 158.0, 163.3.

Compound **12**. A solution of **11** (108 mg, 0.33 mmol) in DMF (1 ml) and water (1 ml), was heated at 150 ^{o}C for 60 h. The solution was cooled and partitioned between ethyl acetate (10 ml) and 2 M sodium hydroxide (10 ml). The aqueous layer was further extracted with ethyl acetate (2 x 10 ml), and the combined organics were washed with brine (10 ml), dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography (hexane:ether, 1:1) and gave compound **12** (69 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 (s, 3H), 3.99 (s, 3H), 6.94 (d, *J* = 8.5 Hz, 1H), 7.20 (d, *J* = 2 Hz, 1H), 7.30 (dd, *J* = 2 and 8.5 Hz, 1H), 7.34 (s, 1H), 7.45-7.55 (m, 3H), 8.10 (dd, *J* = 2 and 8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.9, 56.0, 107.4, 111.4, 117.2, 121.0, 122.2, 126.1, 127.5, 128.8, 130.2, 149.3, 149.4, 151.3, 160.6.