Regioselectivity in the Stille coupling reactions of 3,5-dibromo-2-pyrone.

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Experimental Section

General methods. ^1H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra at 100 MHz, with either TMS(=0) or residual CHCl_3 in the CDCl_3 solvent (7.24) as internal standards. J values are reported in Hz. High resolution mass spectra were measured by using FAB method. Flash column chromatography was performed with Kieselgel 60 Art 9385 (230-400 mesh). All solvents used were purified according to standard procedures.

Typical procedure : A mixture of 30 mg (0.12 mmol) of 3,5-dibromo-2-pyrone, 52 mg (0.14 mmol) of tributylphenyltin, 7 mg (5 mol%) of $\text{Pd}(\text{PPh}_3)_4$, 2 mg (10 mol%) of CuI and 1 mL of toluene was heated at 100°C for 0.5 h. Upon cooling to rt, the reaction mixture was treated with saturated KF (aq.), diluted with Et_2O , and filtered through a plug of Celite. The filtrate was dried over MgSO_4 , concentrated and purified by column chromatography (hexanes : EtOAc = 20 : 1) provided 28 mg of **2a** in 94% yield.

5-Bromo-3-phenyl-pyran-2-one (2a): ^1H NMR (400MHz, CDCl_3) δ 7.63-7.60 (m, 2H), 7.57 (d, J = 2.4 Hz, 1H), 7.45 (d, J = 2.0 Hz, 1H), 7.43-7.39 (m, 3H); ^{13}C NMR (100MHz, CDCl_3) δ 159.2, 148.1, 141.7, 133.2, 129.2, 129.1, 128.4, 128.1, 101.2; FT-IR (CHCl_3) 3083, 1727, 1609 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_{11}\text{H}_8\text{BrO}_2$ 250.9708, found 250.9704.

3-Bromo-5-phenyl-pyran-2-one (3a): ^1H NMR (400MHz, CDCl_3) δ 7.99 (d, J = 2.4 Hz, 1H), 7.67 (d, J = 2.4 Hz, 1H), 7.46-7.34 (m, 5H); ^{13}C NMR (100MHz, CDCl_3) δ 157.5, 146.8, 144.9, 132.0, 129.1, 128.5, 125.9, 121.3, 112.4 ; FT-IR (CHCl_3) 3082, 1728, 1644 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_{11}\text{H}_8\text{BrO}_2$ 250.9708, found 250.9690.

5-Bromo-3-(1-ethoxy-vinyl)-pyran-2-one (2b): ^1H NMR (400MHz, CDCl_3) δ 7.78 (d, $J = 2.8$ Hz, 1H), 7.52 (d, $J = 2.8$ Hz, 1H), 5.73 (d, $J = 2.4$ Hz, 1H), 4.59 (d, $J = 2.4$ Hz, 1H), 3.87 (q, $J = 6.8$ Hz, 2H), 1.39 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100MHz, CDCl_3) δ 157.5, 151.1, 147.8, 140.2, 122.6, 101.1, 91.0, 63.1, 14.5; FT-IR (CHCl_3) 3060, 2863, 1721, 1647 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_9\text{H}_{10}\text{BrO}_3$ 244.9813, found 244.9809.

3-Bromo-5-(1-ethoxy-vinyl)-pyran-2-one (3b): ^1H NMR (400MHz, CDCl_3) δ 7.89 (d, $J = 2.4$ Hz, 1H), 7.77 (d, $J = 2.4$ Hz, 1H), 4.39 (d, $J = 4.0$ Hz, 1H), 4.23 (d, $J = 4.0$ Hz, 1H), 3.87 (q, $J = 7.2$ Hz, 2H), 1.38 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100MHz, CDCl_3) δ 157.7, 152.8, 147.6, 142.5, 117.2, 111.6, 83.4, 63.7, 14.5; FT-IR (CHCl_3) 3035, 2943, 1724, 1647 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_9\text{H}_{10}\text{BrO}_3$ 244.9813, found 244.9794.

5-Bromo-3-trimethylsilanylethynyl-pyran-2-one (2c): ^1H NMR (400MHz, CDCl_3) δ 7.67 (d, $J = 2.4$ Hz, 1H), 7.53 (d, $J = 2.4$ Hz, 1H), 0.25 (s, 9H); ^{13}C NMR (100MHz, CDCl_3) δ 158.1, 148.9, 147.6, 114.2, 104.6, 100.2, 96.5, -0.2; FT-IR (CHCl_3) 2927, 2150, 1741, 1600 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_{10}\text{H}_{12}\text{BrO}_2\text{Si}$ 270.9790, found 270.9789.

5-Bromo-3-furan-2-yl-pyran-2-one (2d): ^1H NMR (400MHz, CDCl_3) δ 7.70 (d, $J = 2.4$ Hz, 1H), 7.50 (d, $J = 2.4$ Hz, 1H), 7.49 (d, $J = 1.2$ Hz, 1H), 7.30 (d, $J = 3.2$ Hz, 1H), 6.50 (dd, $J = 3.2, 1.2$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ 156.8, 146.3, 146.0, 143.8, 135.6, 118.9, 113.6, 112.4, 101.4; FT-IR (CHCl_3) 3084, 1739, 1611 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_9\text{H}_5\text{BrO}_3$ 240.9500, found 240.9485.

3-Bromo-5-furan-2-yl-pyran-2-one (3d): ^1H NMR (400MHz, CDCl_3) δ 7.98 (d, $J = 2.4$ Hz, 1H), 7.85 (d, $J = 2.4$ Hz, 1H), 7.43 (dd, $J = 2.0, 0.8$ Hz, 1H), 6.48 – 6.45 (m, 2H); ^{13}C NMR (100MHz, CDCl_3) δ 157.2, 145.7, 145.1, 142.8, 141.8, 112.8, 112.7, 111.6, 106.4; FT-IR (CHCl_3) 3084, 1734, 1611 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_9\text{H}_6\text{BrO}_3$ 240.9500, found 240.9525.

5-Bromo-3-thiophen-2-yl-pyran-2-one (2e): ^1H NMR (400MHz, CDCl_3) δ 7.71 (dd, $J = 3.6, 1.0$ Hz, 1H), 7.62 (d, $J = 2.4$ Hz, 1H), 7.52 (d, $J = 2.4$ Hz, 1H), 7.43 (dd, $J = 5.2, 1.0$ Hz, 1H), 7.09 (dd, $J = 5.2, 3.6$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ 158.2, 146.6,

137.1, 134.2, 128.6, 127.5, 127.4, 122.9, 101.2 ; FT-IR (CHCl₃) 3094, 1714, 1598, 1422 cm⁻¹ ; HRMS (FAB) m/z (M+1) calcd for C₉H₆BrO₂S 256.9272, found 256.9260.

3-Bromo-5-thiophen-2-yl-pyran-2-one (3e): ¹H NMR (400MHz, CDCl₃) δ 7.97 (d, *J* = 2.0 Hz, 1H), 7.73 (d, *J* = 2.4 Hz, 1H), 7.31 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.11 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.07 (dd, *J* = 5.2, 3.6 Hz, 1H); ¹³C NMR (100MHz, CDCl₃) δ 156.9, 145.4,

143.8, 133.6, 127.8, 125.5, 124.3, 115.6, 112.4 ; FT-IR (CHCl₃) 3164, 1720, 1515 cm⁻¹; HRMS (FAB) m/z (M+1) calcd for C₉H₆BrO₂S 256.9272, found 256.9090.

5-Bromo-3-pyridin-2-yl-pyran-2-one (2f): ¹H NMR (400MHz, CDCl₃) δ 8.64-8.62 (m, 1H), 8.47 (d, *J* = 3.2 Hz, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 7.76 (td, *J* = 8.0, 2.0 Hz, 1H), 7.66 (d, *J* = 2.8, 1H), 7.28 (ddd, *J* = 7.2, 4.8, 1.2 Hz, 1H); ¹³C NMR (100MHz,

CDCl₃) δ 159.1, 149.6, 149.3, 149.2, 144.4, 136.6, 125.8, 123.7, 123.6, 101.9; FT-IR (CHCl₃) 3067, 1726, 1653 cm⁻¹; HRMS (FAB) m/z (M+1) calcd for C₁₀H₇BrNO₂ 251.9660, found 251.9659.

3-Bromo-5-pyridin-2-yl-pyran-2-one (3f): ¹H NMR (400MHz, CDCl₃) δ 8.63-8.61 (m, 1H), 8.49 (d, *J* = 2.4 Hz, 1H), 8.13 (d, *J* = 2.4 Hz, 1H), 7.75 (td, *J* = 8.0, 2.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.27 (ddd, *J* = 7.9, 4.8, 1.2 Hz, 1H); ¹³C NMR (100MHz,

CDCl₃) δ 157.6, 149.8, 149.7, 148.9, 143.6, 137.1, 123.1, 120.4, 118.9, 112.3 ; FT-IR (CHCl₃) 3067, 1724, 1654 cm⁻¹ ; HRMS (FAB) m/z (M+1)) calcd for C₁₀H₇BrNO₂ 251.9660, found 251.9674.

4-(5-Bromo-2-oxo-2H-pyran-3-yl)-benzonitrile (2g): ¹H NMR (400MHz, CDCl₃) δ 7.78 – 7.76 (m, 2H), 7.72 – 7.70 (m, 2H), 7.65 (d, *J* = 2.4 Hz, 1H), 7.54 (d, *J* = 2.4 Hz, 1H); ¹³C NMR (100MHz, CDCl₃) δ 158.6, 149.4, 143.3, 137.5, 132.1, 128.7, 127.1, 118.2, 112.9, 101.0 ; FT-IR (CHCl₃) 3049, 2226,

1714, 1601 cm⁻¹ ; HRMS (FAB) m/z (M+1)) calcd for C₁₂H₇BrNO₂ 275.9660, found 275.9672.

4-(5-Bromo-6-oxo-6H-pyran-3-yl)-benzonitrile (3g): ¹H NMR (400MHz, CDCl₃) δ 7.98 (d, *J* = 2.0 Hz, 1H), 7.76 (d, *J* = 2.0 Hz, 1H), 7.75 – 7.73 (m, 2H), 7.51 – 7.48 (m, 2H); ¹³C NMR (100MHz, CDCl₃) δ 156.9, 147.9, 143.6, 136.7, 133.0, 126.5, 119.8, 117.9, 113.3, 112.5 ; FT-IR (CHCl₃) 3008, 2232,

1737, 1629 cm⁻¹ ; HRMS (FAB) m/z (M+1) calcd for C₁₂H₇BrNO₂ 275.9660, found 275.9661.

4-(5-Bromo-2-oxo-2H-pyran-3-yl)-benzoic acid methyl

ester (2h): ^1H NMR (400MHz, CDCl_3) δ 8.01 – 8.06 (m, 2H), 7.73 – 7.70 (m, 2H), 7.61 (d, $J = 2.4$ Hz, 1H), 7.52 (d, $J = 2.4$ Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (100MHz, CDCl_3) δ 166.2, 158.9, 148.9, 142.8, 137.4, 130.6, 129.6, 128.1, 128.0, 101.1, 52.4 ; FT-IR (CHCl_3) 3150, 1728, 1613 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_{13}\text{H}_{10}\text{BrO}_4$ 308.9762, found 308.9761.

4-(5-Bromo-6-oxo-6H-pyran-3-yl)-benzoic acid methyl

ester (3h): ^1H NMR (400MHz, CDCl_3) δ 8.11 – 8.09 (m, 2H), 8.02 (d, $J = 2.4$ Hz, 1H), 7.76 (d, $J = 2.4$ Hz, 1H), 7.46 – 7.43 (m, 2H), 3.94 (s, 3H); ^{13}C NMR (100MHz, CDCl_3) δ 166.0, 157.2, 147.6, 144.2, 136.5, 130.5, 130.2, 125.8, 120.4, 112.9, 52.4 ; FT-IR (CHCl_3) 3073, 1739, 1715, 1616 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_{13}\text{H}_{10}\text{BrO}_4$ 308.9762, found 308.9751.

5-Bromo-3-(4-methoxy-phenyl)-pyran-2-one (2i):

^1H NMR (400MHz, CDCl_3) δ 7.61 – 7.59 (m, 2H), 7.54 (d, $J = 2.4$ Hz, 1H), 7.40 (d, $J = 2.4$ Hz, 1H), 6.94 – 6.92 (m, 2H), 3.84 (s, 3H); ^{13}C NMR (100MHz, CDCl_3) δ 160.3, 159.6, 147.3, 140.3, 129.5, 128.7, 125.5, 113.9, 101.4, 55.4; FT-IR (CHCl_3) 3084, 2943, 1725, 1610 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_{12}\text{H}_{10}\text{BrO}_3$ 280.9813, found 280.9812.

3-Bromo-5-(4-methoxy-phenyl)-pyran-2-one (3i):

^1H NMR (400MHz, CDCl_3) δ 7.96 (d, $J = 2.4$ Hz, 1H), 7.61 (d, $J = 2.4$ Hz, 1H), 7.28 – 7.26 (m, 2H), 6.96 – 6.93 (m, 2H), 3.84 (s, 3H); ^{13}C NMR (100MHz, CDCl_3) δ 159.7, 157.6, 146.0, 145.1, 127.1, 124.3, 121.0, 114.5, 112.2, 55.3 ; FT-IR (CHCl_3) 3078, 2943, 1725, 1618 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_{12}\text{H}_{10}\text{BrO}_3$ 280.9813, found 280.9810.

3-Bromo-5-vinyl-pyran-2-one (3j):

^1H NMR (400MHz, CDCl_3) δ 7.95 (d, $J = 2.4$ Hz, 1H), 7.47 (d, $J = 2.4$ Hz, 1H), 6.33 (dd, $J = 17.6, 11.2$ Hz, 1H), 5.52 (d, $J = 17.6$ Hz, 1H), 5.31 (d, $J = 11.2$ Hz, 1H) ; ^{13}C NMR (100MHz, CDCl_3) δ 157.5, 147.9, 141.4, 127.0, 118.3, 115.2, 112.9 ; FT-IR (CHCl_3) 3191, 1718, 1651 cm^{-1} ; HRMS (FAB) m/z (M+1) calcd for $\text{C}_7\text{H}_6\text{BrO}_2$ 200.9551, found 200.9566.

3-Pallado-5-bromo-2-pyrone (5a; Pd-Br): ^1H NMR (400MHz, CDCl_3) δ 7.71 – 7.66 (m, 12H), 7.37 – 7.30 (m, 18H), 6.53 – 6.51 (m, 1H), 6.37 (d, $J = 2.4$ Hz, 1H); ^{13}C

NMR (100MHz, CDCl₃) δ 160.8 (t, J = 3.0 Hz), 153.6 (t, J = 6.0 Hz), 147.1 (t, J = 5.3 Hz), 143.0, 134.6 (t, J = 6.1 Hz), 130.35 (t, J = 23.5 Hz), 130.2, 127.9 (t, J = 5.3 Hz), 101.1.; FT-IR (CHCl₃) 3061.0, 3011.1, 1716.5, 1688.3, 1598.0, 1481.6, 1435.1 cm⁻¹

ORTEP representation of the X-ray crystal structure of **5a**

3-Pallado-5-bromo-2-pyrone (5b; Pd-I): ^1H NMR (400MHz, CDCl_3) δ 7.71 – 7.66 (m, 12H), 7.37 – 7.30 (m, 18H), 6.53 – 6.51 (m, 1H), 6.37 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ 160.8 (t, $J = 3.0$ Hz), 153.6 (t, $J = 6.0$ Hz), 147.1 (t, $J = 5.3$ Hz), 143.0, 134.6 (t, $J = 6.1$ Hz), 130.35 (t, $J = 23.5$ Hz), 130.2, 127

ORTEP representation of the X-ray crystal structure of **5b**

5-Pallado-3-bromo-2-pyrone (6): ^1H NMR (400MHz, CDCl_3) δ 7.68 – 7.63 (m, 12H), 7.42 – 7.33 (m, 18H), 6.48 (dd, $J = 1.2, 0.8$ Hz, 1H), 6.26 (dd, $J = 1.2, 0.8$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ 158.3, 150.4, 143.9, 134.5 (t, $J = 6.4$ Hz), 130.7, 129.8 (t, $J = 23.9$ Hz), 128.3 (t, $J = 5.3$ Hz), 125.2, 110.5; FT-IR (CHCl_3) 3057.0, 1732.8, 1717.2, 1704.6, 1482.4, 1435.4 cm^{-1} .

ORTEP representation of the X-ray crystal structure of **6**