Supplementary Material to

Switchable Catalysis: Modular Synthesis of Functionalized Pyrimidinones via Selective Sulfide and Halide Cross-Coupling Chemsitry

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General Methods

Analytical thin layer chromatography (TLC) was performed on Analtech 0.15 mm silica get 60-GF_{254} plates. Visualization was accomplished with exposure to UV light, exposure to Iodine or by dipping in an ethanolic phosphomolybdic acid solution followed by heating. Solvents for extraction were HPLC or ACS grade. Chromatography was performed by the method of Still with Merck silica gel 60 (230-400 mesh) with the indicated solvent system. NMR spectra were collected on Varian Unity 400, VXR-400, VXR-300 and VXR-300S spectrometers. ^{1}H NMR spectra were reported in ppm from tetramethylsilane on the δ scale. Data are reported as follows: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broadened, obs = obscured), coupling constants (Hz), and assignments or relative integration. ^{13}C NMR spectra were reported in ppm from the central deuterated solvent peak. Data are reported as follows: Chemical shift, multiplicity, coupling information, integration. Grouped shifts are provided where an ambiguity has not been resolved. LCMS were run on a hybrid Agilent HP1100-Micromass-ZMD using Agilent Eclipse (XDB-C18, 4.6 x 30 mm, 3.5-Micron) Rapid Resolution Cartridges and Alltech Adsorbosphere XL (C18, 7.5 x 3.2 mm, 5-Micron) guard columns.

Starting Materials

Copper(I) thiophene-2-carboxylate (CuTC), 3-nitrophenylboronic acid, 3-ethoxycarbonylphenylboronic acid, and 4-acetylphenylboronic acid and 3-(tributylstannyl)pyridine were purchased from Frontier Scientific, Inc. and used as received. 3-Bromophenylboronic acid, 4-(dimethylamino)phenylboronic acid, 3,4(methylenedioxy)phenylboronic acid, 4-methoxyphenylboronic acid, 2-(tributylstannyl)furan and 2-(tribuytlstannyl)thiophene were purchased from Aldrich Chemical Company and used as received. $Pd(PPh_3)_4$ was purchase from Strem Chemicals, Inc. Cu(I) 3-methylsalicylate was prepared as desribed in the literature.[1]

[1]Savarin, C.; Srogl, J.; Liebeskind, L.S. *Org. Lett.* **2001**, *3*, 91-93.

Synthesis of Scaffold 4.

***tert*-Butyl [5-bromo-2-(methylthio)-6-oxopyrimidin-1(6H)-yl]acetate (4)**. A mixture of CaH_2 (55.5 g, 1.32 mmol), tert-butyl bromoacetate (195 mL, 1.32 mmol) and 5-bromo-2-methylthiouracil[2] (97.2 g, 439.7 mmol) in anhydrous THF (2 L) were stirred at room temperature for 2 h. The reaction mixture was then heated at reflux for 16 h. This mixture was then cooled to room temperature and poured onto a slurry of ice-water (~1 L). The mixture was allowed to stir for 1 h and was then extracted with CH_2Cl_2 (3 x 500 mL). The combined extracts were washed with water and brine and dried ($MgSO_4$). Filtration and concentration afforded 133 g (90 % yield) of scaffold **4** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.06 (s, 1 H), 4.74 (s, 2 H), 2.56 (s, 3 H), 1.46 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 165.1 (s), 162.8 (s), 158.4 (s), 152.5 (d), 108.3 (s), 83.7 (s), 46.7 (t), 28.2 (q), 15.5 (q). HRMS (ESI) m/z 335.0064 (335.0060 calcd for $C_{11}H_{16}N_2O_3S^{78.9}Br$, $(M+H)^+$); m/z = 337.0081 (337.0039 calcd for $C_{11}H_{16}N_2O_3S^{80.9}Br$, $(M+H)^+$).

Suzuki Couplings of Scaffold 4.

General Procedure for Suzuki Coupling of Scaffold 4. The boronic acid (1.0 – 2.0 mmol), scaffold **4** (1 mmol), $Pd(PPh_3)_4$ (5 mol%), and Cs_2CO_3 (3.0 – 3.3 mmol) were weighed into a flask fitted with a pressure release-gas inlet. After 3 vacuum/argon cycles, dry and degassed dioxane (15 mL) was added (in some cases for which conversion was low with Cs_2CO_3, possibly due to slow transmetalation, Na_2CO_3 or K_2CO_3 was substituted and 5 mL H_2O was added to the reaction mixture). The reaction was then stirred for 12-18 h at 50-90 °C and monitored by LCMS. When the reaction was complete, the mixture was cooled to ambient temperature, and diluted with EtOAc. The filtrate was washed with 1N $NaHSO_4$, brine, and sat. $NaHCO_3$. The organic layer was dried ($MgSO_4$), filtered, and concentrated to a viscous oil or solid. The residue was purified by radial (2-4 mm plate) or flash chromatography.

***tert*-Butyl [-5-(4-methoxyphenyl)-2-(methylthio)-6-oxopyrimidin-1(6H)-yl]acetate (5a).** According to the general procedure, scaffold **4** (1.04 g, 3.10 mmol), 4-methoxyphenylboronic acid (707 mg, 4.65 mmol), Cs_2CO_3 (3.03 g, 9.30 mmol) and $Pd(PPh_3)_4$ (179 mg, 5 mol%) afforded 865 mg (77 % yield) of product **5a** as a white solid after crystallization from methanol: ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.94 (s, 1 H),

[2] Barrett, H.W.; Goodman, I.; Dittlmer, K. *J. Am. Chem. Soc.* **1948**, *70*, 1753.

7.58 (d, J = 9.2 Hz, 2 H), 6.92 (d, J = 9.2 Hz, 2 H), 4.79 (s, 2 H), 3.82 (s, 3 H), 2.63 (s, 3 H), 1.47 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 165.7 (s), 161.1 (s), 159.7 (s), 149.0 (s), 129.8 (d), 126.0 (s), 121.9 (s), 114.0 (d), 83.3 (s), 55.5 (q), 46.1 (t), 28.2 (q), 15.2 (q).
HRMS (ESI) m/z = 363.1378 (363.1373 calcd for $C_{18}H_{23}N_2O_4S$, $(M+H)^+$). LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min), retention time = 5.62 min, $(M+H)^+$ = 363; $(M+Na)^+$ = 385.

***tert*-Butyl [5-{3,4-(methylenedioxy)phenyl}-2-(methylthio)-6-oxopyrimidin-1(6H)-yl]acetate (5b).** According to the general procedure, scaffold **4** (515 mg, 1.54 mmol), 3,4-(methylenedioxy)phenylboronic acid (385 mg, 2.30 mmol), Cs_2CO_3 (1.50 g, 4.60 mmol), $Pd(PPh_3)_4$ (89.0 mg, 5 mol%) and dioxane (25 mL) afforded 461 mg (80 % yield) of product **5b** as a colorless glass, upon purification by flash column chromatography (SiO_2, CH_2Cl_2): ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.91 (s, 1 H), 7.17 (d, J = 1.60 Hz, 1 H), 7.08 (dd, J = 8.0 Hz, 2.0 Hz, 1 H), 6.83 (d, J = 8.0 Hz, 1 H), 5.96 (s, 2 H), 4.78 (s, 2 H), 2.61 (s, 3 H), 1.47 (s, 9 H). ^{13}C NMR (100 MHz, DMSO-d_6), δ 167.0 (s), 160.3 (s), 158.5 (s), 153.7 (d), 149.8 (s), 148.1 (s), 127.6 (s), 123.3 (d), 111.4 (s), 109.2 (d), 108.8 (d), 102.6 (s), 83.1 (s), 50.2 (t), 28.2 (q). HRMS (ESI) m/z = 377.1162 (377.1166 calcd for $C_{18}H_{21}N_2O_5S$, $(M+H)^+$). LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min), retention time = 6.03 min, $(M+H)^+$ = 377; $(M+Na)^+$ = 399.

Ethyl 3-[1-(2-*tert*-butoxy-2-oxoethyl)-2-(methylthio)-6-oxo-1,6-dihydropyrimidin-5-yl]benzoate (5c). According to the general procedure, scaffold **4** (500 mg, 1.49 mmol), 3-ethoxycarbonylphenylboronic acid (434 mg, 2.20 mmol), Na_2CO_3 (474 g, 4.47 mmol) and $Pd(PPh_3)_4$ (172 mg, 10 mol%), dioxane (25 mL) and argon-sparged H_2O (5 mL) afforded 449 mg (75 % yield) of product **5c** as a white solid after purification by flash column chromatography (SiO_2, 10/1 hexanes/EtOAc to 3/1): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.25 (t, J = 1.60 Hz, 1 H), 8.01 (s, 1 H), 7.99 (dt, J = 8.0 Hz, 1.20 Hz, 1 H), 7.875 (ddd, J = 8.0 Hz, 1.6 Hz, 1.2 Hz, 1 H), 7.45 (t, J = 8.0 Hz, 1 H), 4.79 (s, 2 H), 4.36 (q, J = 7.2 Hz, 2 H), 2.61 (s, 3 H), 1.47 (s, 9 H), 1.37 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 166.6 (s), 165.6 (s), 162.5 (s), 160.8 (s), 150.1 (d), 134.0 (s), 133.1 (d), 130.9 (s), 129.4 (d), 129.2 (d), 128.6 (d), 121.3 (s), 83.4 (s), 61.2 (t), 46.1 (t), 28.2 (q), 15.3 (q), 14.6 (q). HRMS (ESI) m/z = 405.1448 (405.1479 calcd for $C_{20}H_{25}N_2O_5S$, $(M+H)^+$).

***tert*-Butyl [5-(4-acetylphenyl)-2-(methylthio)-6-oxopyrimidin-1(6H)-yl]acetate (5d).** According to the general procedure, scaffold **4** (502 mg, 1.50 mmol), 4-acetylphenylboronic acid (491 mg, 2.99 mmol), K_2CO_3 (622 g, 4.50 mmol) and $Pd(PPh_3)_4$ (173 mg, 10 mol%), dioxane (25 mL) and argon-sparged H_2O (5 mL) afforded 408 mg (72 % yield) of product **5d** as a yellow solid after purification by flash column chromatography (SiO_2, 200/1 CH_2Cl_2/MeOH): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.05 (s, 1 H), 7.98 (d, J = 8.4 Hz, 2 H), 7.76 (d, J = 8.4 Hz, 2 H), 4.80 (s, 2 H), 2.64 (s, 3 H), 2.60 (s, 3 H), 1.48 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 197.9 (s), 165.5 (s), 163 (s), 160.6 (s), 150.4 (d), 138.6 (d), 136.5 (d), 128.6 (d), 128.5 (d), 120.9 (s), 83.5

(s), 46.1 (t), 28.2 (q), 26.9 (q), 15.3 (q). HRMS (ESI) m/z = 375.1378 (375.1373 calcd for $C_{19}H_{23}N_2O_4S$, $(M+H)^+$). LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min), retention time = 5.78 min, $(M+H)^+$ = 375; $(M+Na)^+$ = 397.

***tert*-Butyl [2-(methylthio)-5-(3-nitrophenyl)-6-oxopyrimidin-1(6H)-yl]acetate (5e).** According to the general procedure, scaffold **4** (500 mg, 1.50 mmol), 3-nitrophenylboronic acid (500 mg, 3.00 mmol), Na_2CO_3 (476 mg, 4.50 mmol) and $Pd(PPh_3)_4$ (173 mg, 5 mol%), dioxane (15 mL) and argon-sparged H_2O (5 mL) afforded 438 mg (77 % yield) of product **5e** as a yellow foam after purification by flash column chromatography (SiO_2, 4/1 hexane/EtOAc): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.52 (t, J = 1.6 Hz, 1 H), 8.14-8.17 (complex m, 1 H), 8.05 (s, 1 H), 8.00 (complex m, 1 H), 7.54 (t, J = 8.0 Hz, 1 H), 4.79 (s , 2 H), 2.62 (s, 3 H), 1.47 (s, 9 H).). ^{13}C NMR (100 MHz, $CDCl_3$), δ 165.4 (s), 163.6 (s), 160.6 (s), 150.6 (d), 148.5 (s), 135.4 (s), 134.5 (d), 129.5 (d), 123.3 (d), 122.9 (d), 119.8 (s), 83.7 (s), 46.2 (t), 28.2 (q), 15.4 (q). HRMS (ESI) m/z = 378.1113 (378.1118 calcd for $C_{17}H_{20}N_3O_5S$, $(M+H)^+$). LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min, retention time = 6.16 min), $(M+H)^+$ = 378; $(M+Na)^+$ = 400.

***tert*-Butyl [5-[4-(dimethylamino)phenyl]-2-(methylthio)-6-oxopyrimidin-1(6H)-yl]acetate (5f).** According to the general procedure, scaffold **4** (500 mg, 1.50 mmol), 4-(dimethylamino)phenylboronic acid (495 mg, 3.00 mmol), Na_2CO_3 (476 mg, 4.50 mmol) and $Pd(PPh_3)_4$ (173 mg, 5 mol%), dioxane (15 mL) and argon-sparged H_2O (5 mL) afforded 445 mg (79 % yield) of product **5f** as a bright yellow solid upon purification by flash column chromatography (SiO_2, 15% EtOAc in hexanes): ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.92 (s, 1 H), 7.55 (d, J = 8.8 Hz, 2 H), 6.74 (d, J = 8.8 Hz, 2 H), 4.78 (s, 2 H), 2.95 (s, 6 H), 2.58 (s, 3 H), 1.46 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 165.6 (s), 161.0 (s), 159.7 (s)150.2 (s), 147.9 (d), 129.0 (d), 122.0 (s), 121.5 (s), 82.8 (s), 45.9 (t), 40.5 (q), 27.9 (q), 14.9 (q). HRMS (ESI) m/z = 376.1714 (376.1689 calcd for $C_{19}H_{26}N_3O_3S$, $(M+H)^+$).

***tert*-Butyl [5-(3-bromophenyl)-2-(methylthio)-6-oxopyrimidin-1(6H)-yl]acetate (5g)**. According to the general procedure, scaffold **4** (500 mg, 1.49 mmol), 3-bromophenylboronic acid (307 mg, 1.53 mmol), Na_2CO_3 (474 mg, 4.47 mmol) and $Pd(PPh_3)_4$ (172 mg, 10 mol%), dioxane (25 mL) and argon-sparged H_2O (5 mL) afforded 412 mg (68 % yield) of product **5g** as a white solid upon purification by flash column chromatography (SiO_2, 5/1 hexane/EtOAc): ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.96 (s, 1 H), 7.82 (t, J = 1.6 Hz, 1 H), 7.56 (ddd, J = 7.8 Hz, 1.6 Hz, 1.2 Hz, 1), 7.44 (ddd, J = 7.8 Hz, 1.6 Hz, 1.2 Hz, 1 H), 7.24 (t, J = 7.8 Hz, 1 H), 4.78 (s, 2 H), 2.61 (s, 3 H), 1.47 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 165.5 (s), 162.7 (s), 160.6 (s), 150.1 (d), 135.7 (s), 131.4 (d), 131.1 (d), 130.0 (d), 127.1 (d), 122.6 (s), 120.7 (s), 83.5 (s), 46.1 (t), 28.2 (q), 15.3 (q). HRMS (ESI) m/z = 411.0374 (411.0373 calcd for $C_{17}H_{20}N_2O_3S^{78.9}Br$, $(M+H)^+$); 413.0348 (413.0353 calcd for $C_{17}H_{20}N_2O_3S^{80.9}Br$, $(M+H)^+$).

Stille Couplings of Scaffold 4.

General Procedure for Stille Coupling of Scaffold 4. The organostannane (1.0-1.3 mmol) and scaffold **4** (1 mmol) were weighed into a flask. The flask was flushed with argon and dry, degassed dioxane (15 mL) was added. To this solution was added $Pd(PPh_3)_4$ (5 mol%) and the mixture was stirred for 12-18 h at 80-90 °C and monitored by LCMS. When the reaction was complete, the mixture was cooled and concentrated. The residue was then purified by flash column chromatography.

***tert*-Butyl [5-(2-furyl)-2-(methylthio)-6-oxopyrimidin-1(6H)-yl]acetate (5h).** According to the general procedure: Scaffold **4** (746 mg, 2.20 mmol), 2-(tributylstannyl)furan (791 µL, 2.20 mmol), $Pd(PPh_3)_4$ (127 mg, 5 mol%) and dioxane (15 mL) afforded 488 mg (69% yield) of product **5h** as a tan solid, upon purification by flash column chromatography (SiO_2, 10/1 hexanes/EtOAc to 5/1: ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.32 (s, 1H), 7.41 (bd, J = 1.2 Hz, 1H), 7.16 (d, J = 3.2 Hz, 1 H), 6.46 (dd, J = 1.2 Hz, 3.2 Hz, 1 H), 4.79 (s, 2H), 2.60 (s, 3 H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 165.5 (s), 160.4 (s), 158.7 (s), 147.2 (s), 146.0 (d), 142.1 (d), 113.5 (s), 112.1 (d), 111.2 (d), 83.4 (s), 45.9 (t), 28.2 (q), 15.3 (q). HRMS (ESI) m/z = 323.1078 (323.1060 calcd for $C_{15}H_{19}N_2O_4S$, $(M+H)^+$). LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min), retention time = 6.09 min, $(M+H)^+$ = 323; $(M+Na)^+$ = 345.

***tert*-Butyl [2-(methylthio)-6-oxo-5-thien-2-ylpyrimidin-1(6H)-yl]acetate (5i).** A solution of scaffold **4** (1.50 g, 4.47 mmol) and 2-(tributylstannyl)thiophene (1.67 g, 4.47 mmol) in dioxane (10 mL) was flushed with argon and treated with $Pd(PPh_3)_4$ (150 mg, 3 mol%). This mixture was heated to 95 °C for 16 h and then to 105°C for an additional 16 h and concentrated. Purification by crystallization from acetonitrile and flash column chromatography of the residual mother liquor (SiO_2, 5% EtOAc in hexanes) and afforded 986 mg (65 % yield) of product **5i** as a pale yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.26 (s, 1 H), 7.58 (dd, J = 4.0 Hz, J = 1.2 Hz, 1 H), 7.33 (dd, J = 5.2 Hz, 1.2 Hz, 1 H), 7.06 (dd, J = 5.2 Hz, J = 4.0 Hz, 1 H), 4.82 (s, 2 H), 2.60 (s, 3 H), 1.47 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 165.5 (s), 160.7 (s), 159.8 (s), 147.0 (d), 134.9 (s), 127.1 (d), 126.6 (d), 124.7 (s), 116.8 (s), 83.4 (s), 46.1 (t), 28.2 (q), 15.3 (q). HRMS (ESI) m/z = 339.0844 (339.0832 calcd for $C_{15}H_{19}O_3N_2S_2$, $(M+H)^+$).

***tert*-Butyl [2-(methylthio)-6-oxo-5-pyridin-3-ylpyrimidin-1(6H)-yl]acetate (5j).** A solution of scaffold **4** (500 mg,1.50 mmol) and 3-(tributylstannyl)pyridine (662 mg, 1.80 mmol) in anhydrous toluene (15 mL) was flushed with argon and treated with $Pd(PPh_3)_4$ (173 mg, 10 mol%). The resulting mixture was refluxed for 36h (convenience) and concentrated. Purification by flash column chromatography (SiO_2, 60% EtOAc/ 40% hexanes) afforded 366 mg (73 % yield) of product **5j** as a pale yellow solid: ^{1}H NMR

(400 MHz, $CDCl_3$), δ 8.79 (s, 1 H), 8.54 (d, J = 4.0 Hz, 1 H), 8.07 (dt, J = 8.0 Hz, 1.6 Hz, 1 H), 8.00 (s, 1 H), 7.32 (dd, J = 8.0 Hz, 4.0 Hz, 1 H), 4.79 (s, 2 H), 2.61 (s, 3 H), 1.47 (s, 9 H). HRMS (ESI) m/z = 334.1222 (334.1220 calcd for $C_{16}H_{20}N_3O_3S$, $(M+H)^+$).

Liebeskind-Srogl Coupling of Scaffold 4.

General Procedure for Liebeskind-Srogl Coupling. The organoboron reagent (1.0 – 2.0 mmol), scaffold **4** (1 mmol), CuTC or CuMeSal (1.5 –2.2 equiv.), and $Pd(PPh_3)_4$ (5 mol%) were placed in a flask. After 3 vacuum/argon cycles, dry and degassed THF or dioxane (15 mL) was added. The reaction was stirred for 12-18 h at 50-60 °C and monitored by LCMS. When the reaction was complete, the mixture was cooled to ambient temperature, EtOAc was added, and the mixture was filtered through a medium frit sintered glass funnel. The filtrate was washed with 1N $NaHSO_4$, brine, and sat. $NaHCO_3$. The organic layer was dried ($MgSO_4$), filtered, and concentrated to a viscous oil or solid. The residue was purified by radial (2-4 mm plate) or flash chromatography.

***tert*-Butyl [5-bromo-2-(4-methoxyphenyl)-6-oxopyrimidin-1(6H)-yl]acetate (6a).** According to the general procedure, scaffold **4** (523 mg, 1.56 mmol), 4-methoxyphenylboronic acid (415 mg, 2.73 mmol), CuTC (446 mg, 2.34 mmol) and $Pd(PPh_3)_4$ (5 mol%) afforded 439 mg (71% yield) of **6a** as a pale yellow solid, upon purification by flash column chromatography (SiO_2, 200/1 CH_2Cl_2/MeOH): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8. 26 (s, 1H), 7.45 (d, J = 8.8 Hz, 2 H), 6.96 (d, J = 8.8 Hz, 2 H), 4.55 (s, 2 H), 3.85 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 166.4 (s), 161.8 (s), 160.4 (s), 159.0 (s), 153.1 (d), 129.9 (d), 126.1 (s), 114.5 (d), 111.8 (s), 83.4 (s), 55.7 (q), 50.1 (t), 28.1 (q).). HRMS (ESI) m/z = 395.0602 (395.0601 calcd for $C_{17}H_{20}N_2O_4{}^{78.9}Br$, $(M+H)^+$); m/z = 397.0574 (397.0583 calcd for $C_{17}H_{20}N_2O_4{}^{80.9}Br$, $(M+H)^+$) . LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min, retention time = 5.47 min), $(M+H)^+$ = 395, 397; $(M+Na)^+$ = 417, 419.

***tert*-Butyl [2-(3,4-methylenedioxy)-5-bromo-6-oxopyrimidin-1(6H)-yl]acetate (6b).** According to the general procedure, scaffold **4** (500 mg, 1.49 mmol), 3,4-(methylenedioxy)phenylboronic acid (374 mg, 2.24 mmol), CuTC (427 mg, 2.24 mmol) and $Pd(PPh_3)_4$ (86 mg, 5 mol%) afforded 453 mg (74 % yield) of **6b** as an amber solid, upon purification by flash column chromatography (SiO_2, 200/1 CH_2Cl_2/MeOH): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8. 25 (s, 1H), 7.00 (dd, J = 8.0 Hz, 2.0 Hz, 2 H), 6.96 (d, J = 2.0 Hz, 1 H), 6.86 (d, J = 8.0 Hz, 1 H), 6.04 (s, 2 H), 4.55 (s, 2 H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$), δ . HRMS (ESI) m/z = 409.0425(409.0394 calcd for $C_{17}H_{18}N_2O_5{}^{78.9}Br$, $(M+H)^+$); m/z = 411.0384 (411.0375 calcd for $C_{17}H_{18}N_2O_5{}^{80.9}Br$, $(M+H)^+$) . LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min, retention time = 5.39 min), $(M+H)^+$ = 409, 411; $(M+Na)^+$ = 431, 433.

Ethyl 3-[5-bromo-1-(2-*tert*-butoxy-2-oxoethyl)-6-oxo-1,6-dihydropyrimidin-2-yl]benzoate (6c). According to the general procedure, scaffold **4** (570 mg, 1.70 mmol), 3-ethoxycarbonylphenylboronic acid (497 mg, 2.60 mmol), CuTC (484 mg, 2.60 mmol)

and $Pd(PPh_3)_4$ (40 mg, 2 mol%) afforded 512 mg (69 % yield) of **6c** as a pale yellow solid, upon purification by flash column chromatography (SiO_2, 10/1 hexanes/EtOAc to 3/1): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8. 29 (s, 1H), 8.21 (dt, J = 8.0, 1.2 Hz, 1 H), 8.17 (broad m, 1 H), 7.68 (dt, J = 8.0 Hz, 1.2 Hz, 1 H), 7.57 (t, J = 8.0 Hz, 1 h), 4.51 (s, 2 H), 4.38 (q, J = 7.2 Hz, 2H), 1.42 (s, 9H), 1.38 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 166.0 (s), 165.5 (s), 159.4 (s), 158.6 (s), 152.9 (d), 134.1 (s), 132.2 (d), 132.0 (d), 131.7 (s), 129.4 (d), 129.1 (s), 112.8 (d), 83.8 (s), 61.7 (t), 49.1 (t), 28.1 (q), 14.5 (q). HRMS (ESI) m/z = 437.0685 (437.0707 calcd for $C_{19}H_{22}N_2O_5{}^{78.9}Br$, $(M+H)^+$); m/z = 439.0705 (439.0689 calcd for $C_{19}H_{22}N_2O_5{}^{80.9}Br$, $(M+H)^+$) . LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min, retention time = 5.87 min), $(M+H)^+$ = 437, 439; $(M+Na)^+$ = 459, 461.

***tert*-Butyl [2-(4-acetylphenyl)-5-bromo-6-oxopyrimidin-1(6H)-yl]acetate (6d).** According to the general procedure, scaffold **4** (508 mg, 1.52 mmol), 4-acetylphenylboronic acid (435 mg, 2.65 mmol), CuTC (433 mg, 2.27 mmol) and $Pd(PPh_3)_4$ (88 mg, 5 mol%) afforded 411 mg (66 % yield) of **6d** as a pale yellow solid, upon purification by flash column chromatography (SiO_2, 200/1 CH_2Cl_2/MeOH): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8. 29 (s, 1H), 8.05 (d, J = 8.8 Hz, 2 H), 7.61 (d, J = 8.8 Hz, 2 H), 4.49 (s, 2 H), 2.64 (s, 3 H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 197.2 (s), 166.1 (s), 59.3 (s), 158.5 (s), 152.9 (d), 138.9 (s), 137.8 (s), 129.0 (d), 128.5 (d), 113.0 (s), 83.8 (s), 49.1 (t), 28.1 (q). HRMS (ESI) m/z = 407.0600 (407.0601 calcd for $C_{18}H_{20}N_2O_4{}^{78.9}Br$, $(M+H)^+$); m/z = 409.0580 (409.0583 calcd for $C_{18}H_{20}N_2O_4{}^{80.9}Br$, $(M+H)^+$). LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min, retention time = 5.20 min), $(M+H)^+$ = 407, 409; $(M+Na)^+$ = 429, 431.

***tert*-Butyl [5-bromo-2-(3-nitrophenyl)-6-oxopyrimidin-1(6H)-yl]acetate (6e).** According to the general procedure, scaffold **4** (500 mg, 1.50 mmol), 3-nitrophenylboronic acid (437 mg, 2.62 mmol), CuTC (429 mg, 2.25 mmol) and $Pd(PPh_3)_4$ (87 mg, 5 mol%) afforded 360 mg (59 % yield) of **6e** as a yellow solid, upon purification by flash column chromatography (SiO_2, 200/1 CH_2Cl_2/MeOH): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.42 (apparent t, J = 2.0 Hz, 1 H), 8.38 (complex m, 1 H), 8.29 (s, 1 H), 7.87 (dt, J = 2 Hz, 1 H), 7.69 (t, J = 8.0 Hz, 1 H), 4.50 (s, 2 H), 1.43 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 165.7 (s), 158.1 (s), 157.6 (s), 152.6 (d), 148.2 (s), 135.0 (s), 134.0 (d), 130.3 (d), 125.6 (d), 123.2 (d), 113.3 (s), 84.1 (s), 49.5 (t), 27.9 (q). HRMS (ESI) m/z = 410.0337 (410.0346 calcd for $C_{16}H_{17}N_3O_5{}^{78.9}Br$, $(M+H)^+$); m/z = 412.0333 (412.0328 calcd for $C_{16}H_{17}N_3O_5{}^{80.9}Br$, $(M+H)^+$) . LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min), retention time = 5.54 min, $(M+H)^+$ = 410, 412 $(M+Na)^+$ = 432, 434.

***tert*-Butyl 5-bromo-2-[4-(dimethylamino)phenyl]-6-oxopyrimidine-1(6H)-carboxylate (6f).** According to the general procedure, scaffold **4** (500 mg, 1.50 mmol), 4-(dimethylamino)phenylboronic acid (433 mg, 2.62 mmol), CuMeSal (701 mg, 3.30 mmol) and $Pd(PPh_3)_4$ (87 mg, 5 mol%) afforded 470 mg (77 % yield) of **6f** as a bright yellow solid, upon purification by flash column chromatography (SiO_2, 200/1

CH_2Cl_2/MeOH): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.21 (s, 1 H), 7.38 (d, J = 8.8 Hz, 2 H), 6.67 (d, J = 8.8 Hz, 2 H), 4.59 (s, 2 H), 3.00 (s, 6 H), 1.44 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 166.7 (s), 161.1 (s), 159.3 (s), 153.2 (d), 152.0 (s), 129.8 (d), 111.8 (d), 110.6 (s), 83.2 (s), 50.6 (t), 40.4 (q), 28.2 (q). HRMS (ESI) m/z = 408.0907 (408.0917 calcd for $C_{18}H_{23}N_3O_3{}^{78.9}Br$, $(M+H)^+$); m/z = 410.0908 (410.0899 calcd for $C_{18}H_{23}N_3O_3{}^{80.9}Br$, $(M+H)^+$). LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min), retention time = 5.58 min, $(M+H)^+$ = 408, 410 $(M+Na)^+$ = 430, 432.

***tert*-Butyl [5-bromo-2-(3-bromophenyl)-6-oxopyrimidin-1(6H)-yl]acetate (6g).** According to the general procedure, scaffold **4** (600 mg, 1.80 mmol), 3-bromophenylboronic acid (542 mg, 2.70 mmol), CuTC (513 mg, 2.70 mmol) and $Pd(PPh_3)_4$ (104 mg, 5 mol%) afforded 600 mg (75 % yield) of **6g** as a white solid, upon purification by flash column chromatography (SiO_2, 10/1 hexanes/EtOAc to 3/1): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.27 (s, 1 H), 7.47-7.66 (m, 2 H), 7.32-7.44 (m, 2 H), 4.50 (s, 2 H), 1.44 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 166.1 (s), 158.8 (s), 158.5 (s), 152.8 (d), 135.5 (s), 134.2 (d), 131.1 (d), 130.8 (d), 126.6 (d), 123.2 (s), 112.9 (s), 83.9 (s), 49.7 (t), 28.2 (q). HRMS (ESI) m/z = 442.9572 (442.9600 calcd for $C_{16}H_{17}N_2O_3{}^{78.9}Br_2$, $(M+H)^+$); m/z = 444.9551 (444.9581 calcd for $C_{16}H_{17}N_2O_3{}^{78.9}Br{}^{80.9}Br$, M+ H^+); m/z = 446.9526 (446.9563 calcd for $C_{16}H_{17}N_2O_3{}^{80.9}Br_2$, $(M+H)^+$).

***tert*-Butyl [5-bromo-2-(2-furyl)-6-oxopyrimidin-1(6H)-yl]acetate (6h).** A mixture of scaffold **4** (815 mg, 2.40 mmol) and 2-(tributylstannyl)furan (845 µL, 2.7 mmol) in THF (15 mL) was flushed with argon and treated with CuMeSal (1.13 g, 5.26 mmol) and $Pd(PPh_3)_4$ (139 mg, 5 mol%). The resulting mixture was stirred at 54 °C for 16 h. Workup as in the general procedure afforded 670 mg (79 % yield) of **6h** as a white solid, upon purification by flash column chromatography (SiO_2, 5/1 hexanes/EtOAc): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.21 (s, 1 H), 7.57 (bs, 1 H), 7.28 (d, J = 3.6 Hz, 1 H), 6.58 (dd, J = 3.6 Hz, 1.6 Hz, 1 H), 5.07 (s, 2 H), 1.42 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 166.3 (s), 158.6 (s), 153.3 (d), 149.6 (s), 147.0 (s), 145.8 (d), 118.3 (d), 112.9 (d), 110.8 (s), 83.2 (s), 47.8 (t), 28.2 (q). HRMS (ESI) m/z = 355.0282 (355.0288 calcd for $C_{14}H_{16}N_2O_4{}^{78.9}Br$, $(M+H)^+$); m/z = 357.0257 (357.0269 calcd for $C_{14}H_{16}N_2O_4{}^{80.9}Br$, $(M+H)^+$) . LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min), retention time = 5.18 min, $(M+H)^+$ = 355, 357 $(M+Na)^+$ = 377, 379.

***tert*-Butyl (5-bromo-6-oxo-2-thien-2-ylpyrimidin-1(6H)-yl)acetate (6i).** A mixture of scaffold **4** (500 mg, 1.49 mmol) and 2-(tributylstannyl)thiophene (474 µL, 1.49 mmol) in dioxane (15 mL) was flushed with argon and treated with CuMeSal (704 mg, 3.30 mmol) and $Pd(PPh_3)_4$ (172 mg, 10 mol%). The resulting mixture was stirred at 80 °C for 16 h. Workup as in the general procedure afforded 490 mg (89 % yield) of **6i** as a yellow glass, upon purification by flash column chromatography (SiO_2, 10/1 hexanes/EtOAc): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.209 (s, 1 H), 7.558 (dd, J = 5.2 Hz, 1.2 Hz, 1 H), 7.365 (dd, J = 3.6 Hz, 1.2 Hz, 1 H), 7.095 (dd, J = 5.2 Hz, 3.6 Hz, 1 H), 4.80 (s, 2 H), 1.45 (s,

9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3 (s), 158.8 (s), 154.3 (s), 153.0 (d), 135.4 (s), 131.2 (d), 130.2 (d), 128.1 (d), 111.6 (s), 83.7 (s), 49.8 (t), 28.2 (q). HRMS (ESI) m/z = 371.0084 (371.0060 calcd for $C_{14}H_{16}N_2O_3{}^{78.9}BrS$, $(M+H)^+$); m/z = 373.0051 (373.0040 calcd for $C_{14}H_{16}N_2O_3{}^{80.9}BrS$, $(M+H)^+$). LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min) retention time = 5.50 min, $(M+H)^+$ = 371, 373 $(M+Na)^+$ = 393, 395.

***tert*-Butyl (5-bromo-6-oxo-2-pyridin-3-ylpyrimidin-1(6H)-yl)acetate (6j).** A mixture of scaffold **4** (500 mg, 1.50 mmol) and 3-(tributylstannyl)pyridine (662 mg, 1.80 mmol) in dioxane (15 mL) was flushed with argon and treated with CuMeSal (709 mg, 3.30 mmol) and $Pd(PPh_3)_4$ (173 mg, 10 mol%). The resulting mixture was stirred at 80 °C for 16 h. Workup as in the general procedure afforded 256 mg (47 % yield) of **6j** as a tan solid, upon purification by flash column chromatography (SiO_2, 52%EtOAc/48% hexanes): ^{1}H NMR (400 MHz, DMSO-d_6), δ 8.735 (dd, J = 4.8, 1.6 Hz,1 H), 8.674 (bd, J = 1.6 Hz, 1 H), 8.50 (s, 1 H), 7.924 (dt, J = 8.0 Hz, 2.0 Hz, 1 H), 7.556 (ddd, J = 8.0 Hz, 4.8 Hz, 0.8 Hz, 1 H), 4.57 (s, 2 H), 1.30 (s, 9 H). ^{13}C NMR (100MHz, DMSO-d_6) δ 166.9 (s), 158.5 (s), 158.4 (s), 153.7 (d), 152.1 (d), 149.0 (d), 136.4 (d), 130.4 (s), 124.2 (d), 112.2 (s), 83.3 (s), 49.8 (t), 28.2 (q). HRMS (ESI) m/z = 366.0433 (366.0448 calcd for $C_{15}H_{17}N_3O_3{}^{78.9}Br$, $(M+H)^+$); 368.0395 (368.0429 calcd for $C_{15}H_{17}N_3O_3{}^{80.9}Br$, $(M+H)^+$).

Synthesis of Compound 8.

***tert*-Butyl [5-(4-acetylphenyl)-2-(3-bromophenyl)-6-oxopyrimidin-1(6H)-yl]acetate (7).** A mixture of compound **6g** (188 mg, 0.42 mmol), 4-acetylboronic acid (69.0 mg, 0.42 mmol), $Pd(PPh_3)_4$ (24.0 mg, 5 mol%) and Na_2CO_3 (134 mg, 1.30 mmol) were subjected to 3 vacuum/argon cycles. Dioxane (10 mL) and argon-sparged water (3.5 mL) were added and the resulting mixture was heated to 55 °C for 16h thereafter. Workup as in the general Suzuki procedure and purification by flash column chromatography (SiO_2, 5/1 hexanes/EtOAc) afforded 158 mg (78% yield) of compound **7** as a colorless glass: ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.20 (s, 1 H), 8.05 (d, J = 8.8 Hz, 2 H), 7.83 (d, J = 8.8 Hz, 2 H), 7.72 (t, J = 1.6 Hz, 1 H), 7.67 (dt, J = 8.0 Hz, 1.2 Hz, 1 H), 7.49 (dt, J = 7.6 Hz, J = 1,2 Hz, 1 H), 7.37 (t, J = 7.6 Hz, 1 H), 4.55 (s, 2 H), 2.61 (s, 3H), 1.46 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 197.9 (s), 166.5 (s), 160.7 (s), 159.2 (s), 150.6 (d), 138.0 (s), 137.0 (s), 136.2 (s), 134.1 (d), 131.1 (d), 130.7 (d), 128.8 (d), 128.6 (d), 126.7 (d), 125.0 (s), 123.2 (s), 83.7 (s), 49.1 (t), 28.2 (q), 26.9 (q). HRMS (ESI) m/z = 483.0894 (483.0914 calcd for $C_{24}H_{24}N_2O_4{}^{78.9}Br$, $(M+H)^+$); m/z = 485.0864 (485.0897 calcd for $C_{24}H_{24}N_2O_4{}^{80.9}Br$, $(M+H)^+$). LCMS (5-95% acetonitrile gradient in 0.1% TFA over 8 min), retention time = 6.26 min, $(M+H)^+$ = 483, 485; $(M + Na)^+$ = 505, 507.

Synthesis of compound 7 from 5d. A mixture of compound **5d** (298 mg, 0.80 mmol), 3-bromophenyl boronic acid (240 mg, 1.20 mmol), $Pd(PPh_3)_4$ (46.0 mg, 5 mol%) and CuMeSal (378 mg, 1.76 mmol) were subjected to 3 vacuum/argon cycles. Dioxane (20

mL) was added and the resulting mixture was heated to 55 °C for 16h thereafter. Workup as in the general Liebeskind-Srogl procedure and purification by flash column chromatography (SiO_2, 200/1 CH_2Cl_2/MeOH) afforded 306 mg (79% yield) of compound **7.** This material was identical in all respects to the material prepared from **6g** in the previous procedure.

***tert*-Butyl [5-(4-acetylphenyl)-2-{3-[(1E)-hept-1-enyl]phenyl}-6-oxopyrimidin-1(6H)-yl]acetate (8).** A mixture of compound 7 (74.5 mg, 0.15 mmol), *trans*-1-heptenylboronic acid (32.8 mg, 0.23 mmol), $Pd(PPh_3)_4$ (9.0 mg, 5 mol%) and Na_2CO_3 (47.7 mg, 0.50 mmol) were subjected to 3 vac/argon cycles. Dioxane (10 mL) and argon-sparged water (3.0 mL) were added and the reaction was heated to 80 °C for 16h. Workup as in the general Suzuki procedure and purification by radial chromatography (SiO_2, 1000 μM plate, 5/1 hexanes/EtOAc) afforded 68.3 mg (91 % yield) of compound **8** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1 H), 8.00 (d, J = 8.8 Hz, 2 H), 7.83 (d, J = 8.8 Hz, 2 H), 7.52 (bt, could not resolve coupling, 1 H), 7.46 (bd, J = 7.6 (1 H), 7.40 (t, J = 7.6 Hz, 1 H), 7.34 (bd, J = 7.0 Hz, 2 H), 1.43 (s, 9 H), 1.27-1.32 (complex m, 6 H), 0.88 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9 (s), 166.7 (s), 160.9 (s), 150.6 (d), 139.1 (s), 138.2 (s), 136.8 (s), 134.5 (s), 133.6 (d), 129.4 (d), 128.8 (d), 128.7 (d), 128.6 (d), 128.5 (d), 126.0 (d), 125.3 (d), 124.5 (s), 83.3 (s), 49.3 (t), 33.2 (t), 31.6 (t), 29.1 (t), 28.2 (q), 26.9 (q), 22.7 (t), 14.2 (q). HRMS (ESI) m/z = 501.2710 (501.2748 calcd for $C_{31}H_{37}N_2O_4$, $(M + H)^+$). LCMS (5-95% gradient acetonitrile in 0.1% TFA over 8 min), retention time = 7.83 min, $(M + H)^+$ = 501; $(M + Na)^+$ = 523.