Design, Synthesis, and Structure-activity Relationships for Chimeric Inhibitors of Hsp90

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Supporting Information

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General Methods. NMR spectra were recorded on a 400 and 500 MHz spectrometer. Chemical shifts are reported in ppm. IR were reported on a FTIR spectrometer. MS and HRMS were performed on a high/low resolution mass spectrometer. Tetrahydrofuran, diethyl ether, and dichloromethane were dried using solvent drying system. The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2).

Procedure for syntheses

2,3,6-trimethoxybenzaldehyde (**2).** 1,2,4-trimethoxy benzene (9.04 g, 53.8 mmol) was dissolved in anhydrous ether (200 mL) and the solution was heated to reflux before ^{n}BuLi (25.8 mL, 64.6 mmol) was cautiously added over 20 min. The resulting slurry was refluxing for 2 h and cooled to rt. DMF (16.6 mL, 215.2 mmol) was slowly added dropwise to the solution over 15 min before heating to reflux for 2 h. The mixture was cooled to rt and quenched with 6 N HCl. The organic layer was extracted with ether (3 × 150 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **2** as a brown oil (8.17g, 78%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.50 (S, 1H), 7.10 (d, *J* = 9.1 Hz, 1H), 6.66 (d, *J* = 9.1 Hz, 1H), 3.93 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 190.2, 155.3, 152.5, 147.2, 120.1, 119.5, 106.6, 64.5, 57.1, 56.6; IR (film) ν_{max} 2941, 2838, 2764, 1693, 1583, 1486cm^{-1}; HRMS (FAB^{+}) *m/z* 197.0819 (M + H, $C_{10}H_{13}O_4$ requires *m/z* 197.0814).

2-(2,3,6-trimethoxyphenyl)ethanol (**4).** 1,2,4-trimethoxy benzene (10 g, 59.5 mmol) was dissolved in anhydrous ether (200 mL) and the solution was heated to reflux before ^{n}BuLi (28.6 mL, 71.4 mmol) was cautiously added over 20 min. The resulting slurry was

maintained at reflux for 2 h and cooled to rt. Ethylene oxide (11.9 mL, 239 mmol) covered with dry ice in syringe was cautiously dropped to the solution over 3 min followed by refluxing the reaction for another 2 h before the reaction was cooled to rt and quenched with 6 N HCl. The organic layer was extracted with ether (3 × 150 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 15% EtOAc in hexanes) to give **4** as a yellow oil (10.3 g, 81%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.75 (d, *J* = 8.9 Hz, 1H), 6.59 (d, *J* = 8.9 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.80 (s, 3H), 3.79 (t, *J* = 6.4 Hz, 2H), 2.99 (t, *J* = 6.4 Hz, 2H), 2.21 (s, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.6, 148.6, 147.6, 122.2, 110.8, 105.9, 63.5, 61.2, 56.6, 56.3, 27.7; IR (film) v_{max} 3420, 2939, 2361, 1593, 1488, 1256, 1103, 794, 721cm^{-1}; HRMS (FAB$^+$) *m/z* 213.1117 (M + H, $C_{11}H_{17}O_4$ requires *m/z* 213.1127).

1-(2,3,6-trimethoxyphenyl)propan-2-ol (5). 1,2,4-trimethoxy benzene (7 g, 41.7 mmol) was dissolved in anhydrous ether (180 mL) and the solution was heated to reflux. ^{n}BuLi (31.2 mL, 1.6 M) was cautiously added to the refluxing solution over 10 min. The milky solution was refluxed for 2 h before cooling to the rt. Propylene oxide (11.62 mL, 166 mmol) was added at the rt and the solution was heated to reflux. After 35 min at reflux, the reaction was cooled to rt, quenched by the addition of saturated aqueous ammonium chloride and extracted with EtOAc (3 × 150 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 5% EtOAc in hexanes) to give **5** as a yellow oil (9.13 g, 97%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.75 (d, *J* = 8.9 Hz, 1H), 6.58 (d, *J* = 8.9 Hz, 1H), 4.00 (m, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.78 (s, 3H), 2.93 (m, 1H), 2.90 (m, 1H), 2.61

(s, 1H), 1.22 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.6, 148.5, 147.6, 122.1, 110.8, 105.9, 69.0, 61.0, 56.5, 56.3, 33.7, 23.8; IR (film) ν_{max} 3417, 2968, 2936, 1487, 1256, 1110, 793, 723cm^{-1}; HRMS (FAB$^+$) *m/z* 226.1214 (M^+, $C_{12}H_{18}O_4$ requires *m/z* 226.1205).

Ethyl 3-(2,3,6-trimethoxyphenyl)acrylate (5.1). NaH (60% in mineral oil, 536 mg, 13.4 mmol) was cautiously added into toluene (62 mL) and the flask was cooled to 0 °C. Triethyl phosphonoacetate (1.48 mL, 7.41 mmol) was added dropwise to the slurry and then warmed to the rt and stirred for 15 min. 2,3,6-Trimethoxyl benzaldehyde (1.5 g, 7.65 mmol) was added to the mixture and stirred for 12 h. The reaction was quenched by the addition of saturated aqueous ammonium chloride and then extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 5% EtOAc in hexanes) to give **5.1** as a yellow oil (340 mg, 78%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (d, *J* = 16.3 Hz, 1H), 6.99 (d, *J* = 17.0 Hz, 1H), 6.91 (dd, *J1* = 9 Hz, *J2* = 17.6 Hz, 1H), 6.62 (dd, *J1* = 9 Hz, *J2* = 17.6 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.7, 154.0, 150.1, 147.4, 136.0, 122.6, 118.5, 114.7, 106.1, 61.3, 60.7, 57.3, 56.9, 14.6; IR (film) ν_{max} 2939, 2837, 1709, 1626, 1582, 1488, 1257cm^{-1}; HRMS (FAB$^+$) *m/z* 266.1161 (M^+, $C_{14}H_{18}O_5$ requires *m/z* 266.1154).

3-(2,3,6-trimethoxyphenyl)propan-1-ol (6). Compound **5.1** (7.5 g, 28.2 mmol) was dissolved in EtOAc (150 mL) before Pd/C (0.75 g, 10% w/w) was added to the flask and stirred under hydrogen environment for 12 h. The solution was filtered through celite, and the filtrate concentrated. The residue was purified via chromatography (SiO_2, 5%

EtOAc in hexanes) to give a yellow oil (6.20 g, 82%). The oil (6 g, 22.4 mmol) was dissolved in CH_2Cl_2 (200 mL) at 0 °C. DIBAL-H (49.3 mL, 49.3 mmol, 1M in toluene) was added to the reaction and stirred for 1 h. The reaction was quenched by the addition of saturated aqueous sodium potassium tartrate at 0 °C, which was stirred 6 h at rt. The reaction was extracted with CH_2Cl_2 (3 × 100 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **6** as a yellow oil (4.96 g, 98%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.73 (d, *J* = 8.9 Hz, 1H), 6.57 (d, *J* = 8.9 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.78 (s, 3H), 3.48 (t, *J* = 5.8 Hz, 2H), 2.78 (t, J = 6.8 Hz, 2H), 1.97 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.6, 148.3, 147.5, 124.3, 110.3, 105.9, 61.6, 61.3, 56.5, 56.3, 33.2, 19.6; IR (film) ν_{max} 3439, 3053, 2939, 2835, 1593, 1487; HRMS (FAB$^+$) *m/z* 227.1291 (M + H, $C_{12}H_{19}O_4$ requires *m/z* 227.1283).

2,3,6-trimethoxy-5-nitrobenzaldehyde (3). Compound **2** (6.3 g, 32.2 mmol) was dissolved in glacial acetic acid (32 mL) and warmed to 60 °C before a premixed solution of 70% HNO_3 (16.8 mL) and acetic acid (63.8 mL) was slowly added to the mixture. The resulting orange-yellow solution was stirred for 0.5 h at 60 °C and then cooled to rt. H_2O (55 mL) was added and crystals appeared upon cooling to -20 °C for 12 h. The resulting crystals were filtered and washed with ice-cold H_2O (3 × 50 mL) to afford **3** as a yellow solid (4.1 g, 53%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.40 (s, 1H), 7.65 (s, 1H), 4.07 (s, 3H), 4.00 (s, 3H), 3.96 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 188.5, 156.1, 149.2, 149.1, 139.4, 125.6, 113.2, 65.2, 62.9, 57.0; IR (film) ν_{max} 3052, 2986, 1702, 1527, 1481, 1264; HRMS (FAB$^+$) *m/z* 242.0676 (M + H, $C_{10}H_{12}NO_6$ requires *m/z* 242.0665).

(2,3,6-trimethoxy-5-nitrophenyl)methanol (7). Compound **3** (1.2 g, 5.0 mmol) was dissolved in methanol (30 mL) before $NaBH_4$ (0.23 g, 6.0 mmol) was added to the solution and stirred for 4.5 h at rt. The reaction was quenched by the addition of saturated aqueous ammonium chloride (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **7** as a yellow oil (1.06 g, 88%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.71 (s, 1H), 4.77 (d, *J* = 6.7 Hz, 2H), 4.02 (s, 3H), 3.96 (s, 3H), 3.93 (s, 3H), 2.40 (t, *J* = 6.7 Hz, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.1, 148.9, 147.8, 138.5, 130.5, 109.1, 64.2, 62.1, 56.8, 55.7; IR (film) v_{max} 3582, 3056, 2946, 2839, 1579, 1524, 1427; HRMS (FAB$^+$) *m/z* 244.0830 (M + H, $C_{10}H_{14}NO_6$ requires *m/z* 244.0821).

2-(2,3,6-trimethoxy-5-nitrophenyl)ethanol (8). Compound **4** (4.5 g, 21.2 mmol) was dissolved in glacial acetic acid (22.8 mL) before a premixed solution of 70% HNO_3 (12.0 mL) and acetic acid (45.5 mL) was added to the mixture and warmed to 60 °C. The resulting orange-yellow solution was stirred for 0.5 h at 60 °C. The solution was neutralized with solid sodium bicarbonate at 0 °C until the pH = 7 and then extracted with EtOAc (3 × 150 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was directly used for the next step. The residue (3.34 g) was dissolved in H_2O (22 mL), methanol (22 mL) and THF (68 mL) and stirred for 5 min before LiOH (2.6 g, 60.6 mmol) was added to the reaction. The reaction was stirred for 3 h before quenching with saturated aqueous ammonium chloride (150 mL) and extracted with EtOAc (3 × 150 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2,

10% EtOAc in hexanes) to give **8** as a yellow solid (2.9 g, two steps 53%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43 (s, 1H), 3.95 (s, 3H), 3.88 (s, 3H), 3.84 (s, 3H), 3.82 (dd, *J*1 = 6.5 Hz, *J*2 = 5.5 Hz, 2H), 3.01 (t, *J* = 6.6 Hz, 2H), 2.02 (t, J = 5.4 Hz, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ153.0, 148.9, 148.0, 138.9, 129.0, 107.8, 63.2, 62.9, 61.5, 56.6, 28.4; IR (film) v_{max} 3403, 2945, 1576, 1519, 1244; HRMS (FAB$^+$) *m/z* 257.0906 (M^+, $C_{11}H_{15}NO_6$ requires *m/z* 257.0899).

1-(2,3,6-trimethoxy-5-nitrophenyl)propan-2-ol (9). Compound **5** (11.5 g, 50.9 mmol) was dissolved in glacial acetic acid (54.7 mL) before a premixed solution of 70% HNO_3 (28.8 mL) and acetic acid (109.2 mL) was added to the mixture and warm to 60 °C. The orange-yellow solution was stirred for 1 h at 60 °C. The solution was neutralized with sodium bicarbonate at 0 °C until the pH = 7 and then extracted with EtOAc (3 × 200 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was directly used for the next step. The residue was dissolved in methanol (100 mL) before $NaBH_4$ (1.24 g, 32.6 mmol) was added to mixture and stirred for 4 h. The organic layer was evaporated before adding ammonium chloride (100 mL). The slurry was extracted with EtOAc (3 × 150 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 8% EtOAc in hexanes) to give **9** as a yellow solid (5.84 g, two steps 42%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (s, 1H), 4.09 (m, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.87 (s, 3H), 2.91 (m, 2H), 2.21 (s, OH), 1.28 (dd, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.9, 148.9, 148.0, 138.5, 129.2, 107.9, 68.7, 63.0, 61.4, 56.6, 34.5, 24.2; IR (film) υ_{max} 3411, 2973, 2943, 1577, 1521, 1481, 1341, 1245, 1112, 1041cm^{-1}; HRMS (FAB$^+$) *m/z* 271.1057 (M^+, $C_{12}H_{17}NO_6$ requires *m/z* 271.1056).

3-(2,3,6-trimethoxy-5-nitrophenyl)propan-1-ol (10). Compound **6** (5 g, 22.1 mmol) was dissolved in glacial acetic acid (25.3 mL) before a premixed solution of 70% HNO_3 (13.4 mL) and acetic acid (50.6 mL) was added to the stirring solution and warmed to 60 °C. The resulting orange-yellow solution was stirred for 1 h at 60 °C. The mixture was neutralized with solid sodium bicarbonate at 0 °C until the pH = 7. The solution was extracted with EtOAc (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was directly used for the next step. The residue (2.5 g) was dissolved in H_2O (10 mL), methanol (10 mL) and THF (30 mL). The reaction was stirred for 5 min before LiOH (1.86 g, 77.5 mmol) was added. The mixture was stirred for 3 h before quenching with saturated aqueous ammonium chloride (100 mL). The mixture was extracted with EtOAc (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **10** as a yellow solid (2.1 g, two steps 78%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40 (s, 1H), 3.95 (s, 3H), 3.90 (s, 3H), 3.88 (s, 3H), 3.59 (d, *J* = 4.6 Hz, 2H), 2.81 (t, *J* = 7.3 Hz, 2H), 2.10 (s, OH), 1.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ152.8, 148.9, 147.7, 138.9, 131.8, 107.4, 63.2, 62.0, 61.5, 56.6, 32.9, 21.0; IR (film) ν_{max} 3418, 3056, 2944, 1577, 1426, 1267; HRMS (FAB$^+$) *m/z* 278.1219 (M + Li, $C_{12}H_{17}NO_6Li$ requires *m/z* 278.1216).

2,3,6-Trimethoxy-5-nitrobenzyl 5-chloro-2,4-dihydroxybenzoate (11). 2, 4-dihydroxy-5-chloro-benzoic acid (500 mg, 2.66 mmol) was dissolved in DMF: THF (1:1, 20 mL) before DMAP (490 mg, 4.01 mmol), DCC (822 mg, 3.99 mmol) and compound **7** (646 mg, 2.66 mmol) were added. The mixture was warmed to 50 °C and stirred for 12 h before saturated aqueous ammonium chloride (20 mL) was added. The mixture was

extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **11** as a pale yellow solid (450 mg, 41%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.8 (s, 1H), 7.70 (s, 1H), 7.63 (s, 1H), 6.64 (s, 1H), 6.02 (s, 1H), 5.47 (s, 2H), 4.01 (s, 3H), 3.96 (s, 3H), 3.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 162.8, 157.8, 154.3, 149.2, 139.0, 130.3, 124.8, 112.0, 110.6, 107.0, 104.6, 104.5, 64.4, 62.7, 57.4, 56.7; IR (film) υ_{max} 3320, 3056, 2988, 1671, 1487, 1266cm^{-1}; HRMS (FAB$^+$) *m/z* 431.0857 (M + NH_4, $C_{17}H_{20}N_2O_9Cl$ requires *m/z* 431.0857).

2,3,6-Trimethoxy-5-nitrophenethyl 5-chloro-2,4-dihydroxybenzoate (12). Triphenylphosphine (869 mg, 3.32 mmol) was added to a solution of DIAD (0.653 mL, 3.32 mmol) in THF (1 mL) at rt until the reaction became turbid. Compound **8** (568 mg, 2.21 mmol) was added to the reaction and stirred for 30 min before the addition of 2,4-dihydroxy-5-chloro-benzoic acid (500 mg, 2.66 mmol). The resulting slurry was stirred at rt for 12 h. Saturated aqueous ammonium chloride (30 mL) was added and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in toluene) to give **12** as a pale yellow solid (406 mg, 43%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.80 (s, 1H), 7.82 (s, 1H), 7.47 (s, 1H), 6.60 (s, 1H), 6.02 (s, 1H), 4.47 (t, 2H), 4.00 (s, 3H), 3.92 (s, 3H), 3.91 (s, 3H), 3.20 (t, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 162.7, 157.6, 153.2, 148.7, 148.3, 138.6, 130.7, 127.0, 111.8, 108.5, 107.1, 104.4, 64.5, 63.2, 61.6, 56.7, 24.5; IR (film) υ_{max} 3321, 3056, 2986,

1728, 1423, 1266cm^{-1}; HRMS (ES$^+$) *m/z* 445.1017 (M + NH_4, $C_{18}H_{22}N_2O_9Cl$ requires *m/z* 445.1014).

3-(2,3,6-Trimethoxy-5-nitrophenyl)propyl 5-chloro-2,4-dihydrobenzoate (13). Triphenylphosphine (363 mg, 1.38 mmol) was added to a solution of DIAD (0.273 mL, 1.39 mmol) in THF (1mL) at rt until the reaction became turbid. Then compound **10** (250 mg, 0.92 3mmol) was added to the mixture and stirred for 30 min before adding 2,4-dihydroxy-5-chloro-benzoic acid (208 mg, 1.11 mmol). The resulting slurry was stirred at rt for 12 h. Saturated aqueous ammonium chloride (15 mL) was added and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in toluene) to give **13** as a pale yellow solid (175 mg, 43%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.90 (s, 1H), 7.72 (s, 1H), 7.42 (s, 1H), 6.60 (s, 1H), 6.05 (s, OH), 4.38 (t, *J* = 8.0 Hz, 2H), 3.96 (s, 3H), 3.89 (s, 3H), 3.88 (s, 3H), 2.86 (t, *J* = 8.0 Hz, 2H), 2.07 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 162.2, 157.3, 152.5, 148.5, 147.4, 138.3, 130.9, 130.0, 111.4, 107.3, 106.6, 104.2, 65.2, 62.8, 61.1, 56.2, 28.8, 21.4; IR (film) υ_{max} 3289, 2934, 2867, 1459, 1248, 1067cm^{-1}; HRMS (FAB$^+$) *m/z* 442.0890 (M + H, $C_{19}H_{21}NO_9Cl$ requires *m/z* 442.0905).

2-(2,3,6-Trimethoxy-5-nitrophenyl)propyl 5-chloro-2,4-dihydroxybenzoate (14). 2, 4-dihydroxy-5-chloro-benzoic acid (500 mg, 2.66 mmol) was dissolved in DMF: THF (1:1, 20 mL) before DMAP (490 mg, 3.99 mmol), DCC (822 mg, 3.99 mmol) and compound **9** (720 mg, 2.66 mmol) were added. The mixture was warmed to 50 °C and stirred for 12 h before saturated aqueous ammonium chloride (30mL) was added. The mixture was extracted with EtOAc (3 × 50 mL) and the combined organic layers were

dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in toluene) to give **14** as a pale yellow solid (492 mg, 42%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.90 (s, 1H), 7.84 (s, 1H), 7.44 (s, 1H), 7.20 (s, 1H), 6.55 (s, 1H), 5.45 (m, 1H), 4.00 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H), 3.20 (m, 1H), 3.05 (m, 1H), 1.40 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 162.7, 157.5, 153.2, 148.6, 148.3 138.4, 130.8, 127.1, 111.7, 108.5, 107.3, 104.4, 72.2, 62.9, 61.2, 56.7, 30.5, 20.3; IR (film) υ_{max} 3315, 3055, 2986, 1667, 1483, 1266cm^{-1}; HRMS (EI$^+$) *m/z* 442.0902 (M + H, $C_{19}H_{21}NO_9Cl$ requires *m/z* 442.0905).

3-Amino-2,5,6-trimethoxybenzyl 5-chloro-2,4-dihydroxybenzoate (15). Compound **11** (440 mg, 1.07 mmol) was dissolved in ethanol (10.7 mL) at rt before PtO_2 (44 mg, 10% w/w) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and the filtrate concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give **15** as a brown solid (329 mg, 81%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.97 (s, 1H), 7.74 (s, 1H), 6.62 (s, 1H), 6.46 (s, 1H), 5.43 (s, 2H), 3.86 (s, 3H), 3.81 (s, 3H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 162.8, 157.5, 150.1, 141.0, 139.9, 136.5, 130.4, 122.5, 111.6, 107.2, 104.5, 102.4, 62.2, 61.5, 58.3, 56.4; IR (film) υ_{max} 3512, 3054, 2987, 1671, 1489, 1264cm^{-1}; HRMS (EI$^+$) HRMS (FAB$^+$) *m/z* 383.0783 (M$^+$, $C_{17}H_{18}NO_7Cl$ requires *m/z* 383.0772).

3-Amino-2,5,6-trimethoxyphenethyl 5-chloro-2,4-dihydroxybenzoate (16). Compound **12** (490 mg, 1.15 mmol) was dissolved in ethanol (11.0 mL) at rt before PtO_2 (49 mg, 10% w/w) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and filtrate concentrated. The residue

was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give **16** as a brown solid (311 mg, 68%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.90 (s, 1H), 7.88 (s, 1H), 6.61 (s,1H), 6.31 (s, 1H), 4.50 (t, *J* = 7.4 Hz, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 3.77 (s, 3H), 3.12 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 162.7, 157.1, 150.1, 140.3, 139.6, 136.2, 130.8, 124.6, 111.5, 107.5, 104.4, 100.1, 65.3, 61.5, 60.5, 56.4, 24.5; IR (film) υ_{max} 3506, 3054, 2987, 1672, 1489, 1422, 1266cm^{-1}; HRMS (FAB$^+$) *m/z* 397.0942 (M^+, $C_{18}H_{20}NO_7Cl$ requires *m/z* 397.0928).

3-(3-Amino-2,5,6-trimethoxyphenyl)propyl 5-chloro-2,4-dihydroxybenzoate (17). Compound **13** (200 mg, 0.45 mmol) was dissolved in ethanol (4.5 mL) at rt before PtO_2 (20 mg, 10% w/w) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and filtrate concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give **17** as a brown solid (171 mg, 92%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.90 (s, 1H), 7.88 (s, 1H), 6.62 (s,1H), 6.27 (s, 1H), 4.80 (t, *J* = 8.0 Hz, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 2.80 (t, *J* = 8.0 Hz, 2H), 2.07 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 167.9, 162.8, 157.3, 150.0, 139.2, 136.1, 130.5, 130.4, 128.9, 111.6, 104.5, 99.3, 65.9, 61.4, 60.4, 56.2, 29.6, 21.6; IR (film) υ_{max} 3575, 3054, 2987, 1671, 1489, 1422, 1265cm^{-1}; HRMS (EI$^+$) *m/z* 411.1078 (M^+, $C_{19}H_{22}NO_7Cl$ requires *m/z* 411.1085).

2-(3-Amino-2,5,6-trimethoxyphenyl)propyl 5-chloro-2,4-dihydroxybenzoate (18). Compound **14** (450 mg, 1.02 mmol) was dissolved in ethanol (10.0 mL) at rt before PtO_2 (45 mg, 10% w/w) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and the filtrate concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give

18 as a brown solid (302 mg, 72%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.97 (s, 1H), 7.85 (s, 1H), 6.59 (s, 1H), 6.33 (s, 1H), 5.64 (m, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.10 (m, 1H), 2.98 (m, 1H), 1.36 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 162.7, 157.2, 150.0, 140.7, 140.0, 135.2, 130.8, 124.9, 111.4, 107.8, 104.3, 100.6, 72.9, 61.3, 60.4, 56.4, 29.8, 20.1; IR (film) υ_{max} 3550, 3520, 3053, 2985, 1667, 1620, 1422, 1172, 896cm^{-1}; HRMS (EI^{+}) *m/z* 412.1151 (M + H, $C_{19}H_{23}NO_7Cl$ requires *m/z* 412.1163).

3-Formamido-2,5,6-trimethoxybenzyl 5-chloro-2,4-dihydroxybenzoate (19). Compound **15** (110 mg, 0.287 mmol) was dissolved in CH_2Cl_2 (2 mL) at 0 °C before PhOCHO (70.1 mg, 0.373 mmol) was added to mixture. The reaction was warmed to 30 °C and stirred for 12 h. After concentration, the residue was purified via column chromatography (SiO_2, 25% EtOAc in hexanes) to give **19** as a yellow solid (96.8 mg, 82%): ^{1}H NMR (CD_3OD, 400 MHz) δ 8.36 (s, 1H), 8.06 (s, 1H), 7.64 (s, 1H), 7.54 (s, 1H), 6.47 (s, 1H), 5.40 (s, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 3.77 (s 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 162.2, 160.7, 160.6, 149.5, 145.4, 142.8, 131.0, 127.2, 122.3, 113.2, 107.5, 105.0, 104.2, 62.9, 62.0, 57.6, 56.3; IR (film) υ_{max} 3054, 2987, 1657, 1612, 1527, 1384, 1265, 895, 738cm^{-1}; HRMS (EI^{+}) *m/z* 429.1058 (M + NH_4, $C_{18}H_{22}N_2O_8Cl$ requires *m/z* 429.1065).

3-Formamido-2,5,6-trimethoxyphenethyl 5-chloro-2,4-dihydroxybenzoate (20). Compound **16** (50 mg, 0.126 mmol) was dissolved in CH_2Cl_2 (0.1 mL) at 0 °C before PhOCHO (30.7 mg, 0.164 mmol) was added to the mixture. The reaction was warmed to 30 °C and stirred for 12 h. After concentration, the residue was purified via column chromatography (SiO_2, 25% EtOAc in hexanes) to give **20** as a yellow solid (47.6 mg,

89%): ^{1}H NMR (CD_3OD, 400 MHz) δ 8.33 (s, 1H), 7.90 (s, 1H), 7.73 (s 1H), 7.67 (s 1H), 6.44 (s 1H), 4.50 (t, *J* = 7.4 Hz, 2H), 3.75 (s 3H), 3.36 (s, 3H), 3.35 (s, 3H), 3.15 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (CD_3OD, 125 MHz) δ 169.0, 161.5, 160.3, 159.4, 148.9, 144.1, 142.0, 130.9, 126.5, 123.9, 112.3, 105.1, 105.0, 103.5, 64.2, 61.3, 60.7, 56.0, 24.0; IR (film) u_{max} 3054, 2986, 1754, 1692, 1606, 1421, 1266, 896, 739cm^{-1}; HRMS (EI^{+}) *m/z* 425.0889 (M^{+}, $C_{19}H_{20}NO_8Cl$ requires *m/z* 425.0877).

3-(3-Formamido-2,5,6-trimethoxyphenyl)propyl 5-chloro-2,4-dihydroxybenzoate (21). Compound **17** (310 mg, 0.754 mmol) was dissolved in CH_2Cl_2 (0.5 mL) at 0 °C before PhOCHO (166.3 mg, 0.98 mmol) was added to the mixture. The reaction was warmed to 30 °C and stirred for 12 h. After concentration, the residue was purified via column chromatography (SiO_2, 25% EtOAc in hexanes) to give **21** as a yellow solid (288 mg, 87%): ^{1}H NMR (CD_3OD, 400 MHz) δ 8.39 (s, 1H), 7.76 (s, 1H), 7.72 (s 1H), 6.63 (s, 1H), 4.37 (t, *J* = 8.0 Hz, 2H), 3.88 (s, 3H), 3.59 (s, 3H), 3.55 (s, 3H), 2.79 (t, *J* = 8.0 Hz, 2H), 2.06 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ 169.8, 168.0, 163.5, 162.2, 160.9, 149.3, 144.3, 130.8, 128.6, 126.9, 113.7, 113.3, 104.7, 104.3, 65.1, 61.3, 59.9, 56.1, 29.5, 21.6; IR (film) u_{max} 3054, 2987, 1422, 1265cm^{-1}. HRMS (ES^{+}) *m/z* 440.1104 (M + H, $C_{20}H_{23}NO_8Cl$ requires *m/z* 440.1112).

2-(3-Formamido-2,5,6-trimethoxyphenyl)propyl 5-chloro-2,4-dihydroxybenzoate (22). Compound **18** (140 mg, 0.34 mmol) was dissolved in CH_2Cl_2 (0.2 mL) at 0 °C before PhOCHO (75 mg, 0.442 mmol) was added to the mixture. The reaction was warmed to 30 °C and stirred for 12 h. After concentration, the residue was purified via column chromatography (SiO_2, 25% EtOAc in hexanes) to give **22** as a yellow solid (121 mg, 81%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.80 (s, 1H), 8.32 (s, 1H), 7.90 (s, 1H),

7.85 (s 1H), 6.55 (s 1H), 5.41 (m, 1H), 3.84 (s 3H), 3.83 (s, 3H), 3.72(s, 3H), 3.12 (m, 1H), 2.98 (m, 1H), 1.35 (m, 3H); ^{13}C NMR (CD_3OD, 100 MHz) δ 169.2, 162.0, 160.8, 159.4, 149.3, 146.1, 144.7, 142.5, 131.4, 126.8, 124.5, 112.5, 105.6, 103.9, 72.3, 61.5, 61.0, 56.2, 31.0, 19.9; IR (film) υ_{max} 3055, 2986, 1667, 1516, 1463cm^{-1}. HRMS (ES^+) *m/z* 440.1100 (M + H, $C_{20}H_{23}NO_8Cl$ requires *m/z* 440.1112).

2-Methoxy-3,6-bis(methoxymethoxy)benzaldehyde (25). 2-methoxy-1,4-bis-methoxymethoxy-benzene (6 g, 26.3 mmol) was dissolved in THF (100 mL) before addition of TMEDA (4.8 mL, 31.6 mmol) and then cooled to 0 °C. ^{n}BuLi (12.7 mL, 31.6 mmol) was added dropwise to the mixture and stirred at rt for 4 h before DMF (8.1 mL, 105 mmol) was added. After stirring for 2 h, the reaction was quenched with 0.5 M HCl solution until the pH = 7. The slurry was extracted with EtOAc (3 × 150 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give **8** as a yellow oil (5.19 g, 77%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ10.50 (s, 1H), 7.29 (d, *J* = 9.2 Hz, 1H), 6.90 (d, *J* = 9.2 Hz, 1H), 5.20 (s, 2H), 5.16 (s, 2H), 3.94 (s, 3H), 3.52 (s, 3H), 3.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 189.8, 154.1, 152.8, 145.6, 124.3, 121.2, 111.5, 96.5, 95.8, 62.6, 56.8, 56.5; IR (film) υ_{max} 3055, 2958, 2829, 1689, 1599, 1483, 1394, 1203, 1089, 703cm$^-$1; HRMS (ES^+) *m/z* 257.1029 (M + H, $C_{12}H_{17}O_6$ requires *m/z* 257.1025).

(2-Methoxy-3,6-bis(methoxymethoxy)phenyl)methanol (26). Compound **25** (1 g, 3.9 mmol) was dissolved in methanol (35 mL) before $NaBH_4$ (298 mg, 7.8 mmol) was added to the mixture at rt. The slurry was stirred for 20 min before quenching with saturated aqueous ammonium chloride (100 mL) and extracted with EtOAc (3 × 100 mL). The

combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 16% EtOAc in hexanes) to give **26** as a yellow oil (1.0 g, 99%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.02 (d, *J* = 9.2 Hz, 1H), 6.80 (d, *J* = 9.2 Hz, 1H), 5.15 (s, 2H), 5.14 (s, 2H), 4.75 (s, 2H), 3.89 (s, 3H), 3.50 (s, 3H), 3.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.9, 149.0, 145.3, 124.7, 117.1, 110.5, 95.7, 95.5, 61.6, 56.2, 56.1, 55.3; IR (film) υ_{max} 3460, 3053, 2938, 1593, 1267, 1205, 1010, 946 cm^{-1}; HRMS (ES$^+$) *m/z* 281.1008 (M + Na, $C_{12}H_{18}O_6Na$ requires *m/z* 281.1001).

2-(2-methoxy-3,6-bis(methoxymethoxy)phenyl)ethanol (27). 2-methoxy-1, 4-bis-methoxymethoxy-benzene (5 g, 21.9 mmol) was dissolved in THF (100 mL) before the addition of TMEDA (4.0 mL, 26.4 mmol). The flask was cooled to 0 °C before ^{n}BuLi (10.6 mL, 26.4 mmol) was added dropwise. After stirring at rt for 4 h, the mixture was cooled to 0 °C before the addition of ethylene oxide (5.5 mL, 110 mmol). After stirring for 2 h, the reaction was quenched with 0.5 M HCl solution until the pH = 7. The slurry was extracted with EtOAc (3 × 150 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give **27** as a yellow oil (4.83 g, 81%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.97 (d, *J* = 9.2 Hz, 1H), 6.75 (d, *J* = 9.2 Hz, 1H), 5.16 (s, 2H), 5.15 (s, 2H), 3.88 (s, 3H), 3.82 (t, *J* = 6.6 Hz, 2H), 3.52 (s, 3H), 3.50 (s, 3H), 2.99 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.3, 149.5, 145.6, 122.9, 115.8, 110.1, 96.1, 95.4, 63.3, 61.3, 56.6, 56.5, 28.1; IR (film) υ_{max} 3426, 2940, 2827, 1593, 1491, 1250, 1090, 1065, 917, 804cm^{-1}; HRMS (ES$^+$) *m/z* 273.1338 (M + H, $C_{13}H_{21}O_6$ requires *m/z* 273.1338).

Ethyl 3-(2-methoxy-3,6-bis(methoxymethoxy)phenyl)acrylate (25.1). NaH (60% in mineral oil, 1.4 g, 34.3 mmol) was added to toluene (150 mL) and the flask was cooled to 0 °C. Triethyl phosphonoacetate (3.75 mL, 18.7 mmol) was added dropwise to the slurry before the mixture was warmed to rt and stirred for 15 min. Compound **25** (4 g, 15.6 mmol) was added and stirred for 12 h. The reaction was quenched by addition of saturated aqueous ammonium chloride (100 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **25.1** as a yellow solid (4.38 g, 86%):^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (d, *J* = 9.1 Hz, 1H), 7.10 (d, *J* = 9.1 Hz, 1H), 6.92 (m, 2H), 5.21 (s, 2H), 5.17 (s, 2H), 4.28 (q, 4H), 3.87 (s, 3H), 3.53(s, 3H), 3.49 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.6, 152.5, 150.9, 145.6, 135.9, 122.7, 119.7, 119.4, 110.5, 96.3, 95.3, 61.3, 60.7, 56.7, 56.6, 14.8; IR (film) υ_{max} 3055, 2985, 2939, 1637, 1483, 1180, 1029cm^{-1}; HRMS (ES$^+$) *m/z* 327.1438 (M + H, $C_{16}H_{23}O_7$ requires *m/z* 327.1444).

1-(2-Methoxy-3,6-bis(methoxymethoxy)phenyl)pentan-2-ol (29). 2-methoxy-1,4-bis-methoxymethoxy-benzene (1 g, 4.4 mmol) was dissolved in THF (44 mL) before addition of TMEDA (0.8 mL, 5.3 mmol). The solution was cooled to 0 °C and ^{n}BuLi (3.3 mL, 5.3 mmol) was added dropwise. The mixture was stirred at rt for 4 h before it was cooled to 0 °C and 1,2-epoxypentane (0.91 mL, 8.8 mmol) was added. After stirring for 2 h, the reaction was quenched with 0.5 M HCl solution until the pH = 7. The mixture was extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 15% EtOAc in hexanes) to give **29** as a yellow oil (1.18 g, 86%):

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.96 (d, *J* = 9.0 Hz, 1H), 6.80 (d, *J* = 9.0 Hz, 1H), 5.14 (s, 2H), 5.12 (s, 2H), 3.86 (s, 3H), 3.81 (m, 1H), 3.51 (s, 3H), 3.47 (s, 3H), 2.94 (m, 1H), 2.78 (m, 1H), 2.56 (s, OH), 1.47 (m, 4H), 0.94 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.3, 149.4, 145.7, 123.3, 115.7, 110.0, 96.1, 95.4, 72.6, 61.1, 56.5, 56.4, 40.2, 32.5, 19.4, 14.5; IR (film) ν_{max} 3583, 3053, 2958, 1593, 1465, 1205, 1153, 1056, 946cm^{-1}; HRMS (ES$^+$) *m/z* 315.1811 (M + H, $C_{16}H_{27}O_6$ requires *m/z* 315.1808).

3-(2-Methoxy-3,6-bis(methoxymethoxy)phenyl)propan-1-ol (30). Compound **25.1** (5.8 g, 17.8 mmol) was dissolved in EtOAc (100 mL) before Pd/C (0.58g, 10% w/w) was added to the mixture and stirred under a hydrogen atmosphere for 12 h. The mixture was filtered through celite and the filtrate concentrated. The residue was purified via column (SiO_2, 5% EtOAc in hexanes) to afford a yellow oil compound (4.6 g, 79%). This compound was dissolved in CH_2Cl_2 (150 mL) at 0 °C before DIBAL-H (32.2mL, 32.2 mmol) was added to the mixture and stirred for 1 h. The reaction was quenched by addition of saturated aqueous sodium potassium tartrate (100 mL) at 0 °C and stirred for 6 h. The mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **30** as a yellow oil (3.69 g, 92%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.94 (d, *J* = 8.9 Hz, 1H), 6.78 (d, *J* = 8.9 Hz, 1H), 5.15 (s, 2H), 5.14 (s, 2H), 3.86 (s, 3H), 3.47 (s, 3H), 3.42 (s, 3H), 3.41 (m, 2H), 2.78 (t, *J* = 7.0 Hz, 2H), 2.65 (s, OH), 1.97 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.2, 149.2, 145.5, 125.2, 115.3, 110.0, 96.1, 95.4, 61.7, 61.5, 56.6, 56.5, 32.4, 20.0; IR (film) υ_{max} 3518, 3382, 3053, 2941, 1602, 1485, 1259, 1151, 1016, 921 cm^{-1}; HRMS (ES$^+$) *m/z* 287.1488 (M + H, $C_{14}H_{23}O_6$ requires *m/z* 287.1495).

(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)methanol (31). Compound **26** (1 g, 3.9 mmol) was dissolved in CH_3CN (8 mL) and stirred at -10 °C before the addition of ammonium nitrate (327 mg, 4.1 mmol). $(CF_3CO)_2O$ (2.16 mL, 15.6 mmol) was added to the mixture and stirred for 15 min at rt. The reaction was quenched by addition of saturated aqueous sodium bicarbonate (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was dissolved with THF-MeOH-H_2O (3:1:1, 20 mL) before LiOH (490 mg, 11.4 mmol) was added and stirred for 5 min. The mixture was quenched by addition of saturated aqueous sodium bicarbonate (5 mL). The mixture was extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **31** as a brown oil (524 mg, 45 %):^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75 (s, 1H), 5.24 (s, 2H), 5.13 (s. 2H), 4.69 (s, 2H), 4.02 (s, 3H), 3.66 (s, 3H), 3.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.9, 147.1, 146.6, 139.4, 132.0, 113.3, 102.3, 95.8, 62.5, 58.3, 57.0, 54.8; IR (film) υ_{max} 3055, 2943, 1575, 1521, 1425, 1265, 1110, 1035cm^{-1}; HRMS (ES$^+$) *m/z* 304.1018 (M + H, $C_{12}H_{18}NO_8$ requires *m/z* 304.1032).

2-(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)ethanol (32). Compound **27** (50 mg, 0.18 mmol) was dissolved in THF (2.5 mL) and stirred at -10 °C before the addition of ammonium nitrate (15 mg, 0.19 mmol). $(CF_3CO)_2O$ (151 mg, 0.72 mmol) was added to the mixture and stirred for 15 min at rt. The reaction was quenched by addition of saturated aqueous sodium bicarbonate (50 mL) and extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was dissolved with THF-MeOH-H_2O (3:1:1, 1.5 mL) before LiOH (45 mg,

1.2 mmol) was added and stirred for 5 min. The mixture was quenched by addition of saturated aqueous $NaHCO_3$ (3 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **32** as a yellow solid oil (35.5 mg, 61%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.65 (s, 1H), 5.23 (s, 2H), 5.08 (s, 2H), 3.97 (s. 3H), 3.86 (t, *J* = 8 Hz, 2H), 3.61 (s, 3H), 3.52 (s, 3H), 3.04 (t, *J* = 8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 153.1, 146.2, 145.9, 139.6, 129.1, 111.5, 101.9, 95.4, 62.2, 61.1, 57.7, 56.5, 28.4; IR (film) ν_{max} 3398, 2940, 2828, 1521, 1475, 1149, 1051, 925 cm^{-1}; HRMS (ES$^+$) *m/z* 340.1007 (M + Na, $C_{13}H_{19}NO_8Na$ requires *m/z* 340.1008).

3-(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)propan-1-ol (**33)** Compound **30** (1 g, 3.5 mmol) was dissolved in CH_3CN (7 mL) and stirred at -10 °C before addition of ammonium nitrate (294 mg, 3.68 mmol). $(CF_3CO)_2O$ (1.94 mL, 14 mmol) was added to the mixture and stirred for 15 min at rt. The mixture was quenched by addition of saturated aqueous sodium bicarbonate (50 mL) and extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was dissolved with THF-MeOH-H_2O (3:1:1, 15 mL) before LiOH (440 mg, 10.5 mmol) was added and stirred for 5 min. The mixture was quenched by addition of saturated aqueous sodium bicarbonate (5 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give **33** as a brown oil (775 mg, 67%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63 (s, 1H), 5.22 (s, 2H), 5.02 (s, 2H), 3.94 (s, 3H), 3.59 (t, *J* = 6.2 Hz, 2H), 3.56 (s, 3H), 3.51 (s, 3H), 2.86

(t, *J* = 7.4 Hz, 2H), 2.08 (s, OH), 1.84 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.2, 146.6, 145.6, 140.1, 132.3, 111.3, 102.2, 95.8, 62.1, 61.7, 58.3, 57.0, 32.8, 21.4; IR (film) v_{max} 3400, 2940, 1571, 1521, 1474, 1343, 1292, 1152, 1055, 929cm^{-1}; HRMS (FAB$^+$) *m/z* 331.1254 (M^+, $C_{14}H_{21}NO_8$ requires *m/z* 331.1267).

1-(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)pentan-2-ol (35). Compound **29** (0.84 g, 2.7 mmol) was dissolved in CH_3CN (10 mL) and stirred at -10 °C before addition of ammonium nitrate (749 mg, 9.2 mmol). $(CF_3CO)_2O$ (11.7 mL, 9.2 mmol) was added to the mixture and it stirred for 15 min at rt. The mixture was quenched by addition of saturated aqueous sodium bicarbonate (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was dissolved with THF-MeOH-H_2O (3:1:1, 15 mL) before LiOH (276 mg, 11.5 mmol) was added and stirred for 5 min. The mixture was quenched by addition of saturated aqueous sodium bicarbonate (5 mL) and extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give **35** as a brown oil (557 mg, 58%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66 (s, 1H), 5.24 (s, 2H), 5.12 (d, *J* = 6.4 Hz, 1H), 5.05 (d, *J* = 6.4 Hz, 1H), 3.97 (s, 3H), 3.87 (m, 1H), 3.61 (s, 3H), 3.53 (s, 3H), 2.91 (m, 2H), 2.46 (m, OH), 1.55 (m, 2H), 1.45 (m, 2H), 0.97 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.4, 146.6, 146.4, 139.8, 130.1, 111.7, 102.3, 95.8, 71.8, 61.4, 58.0, 56.9, 41.0, 33.4, 19.3, 14.5; IR (film) v_{max} 3468, 3053, 2985, 1578, 1477, 1155, 1022, 897cm^{-1}; HRMS (FAB$^+$) *m/z* 360.1672 (M + H, $C_{16}H_{26}NO_8$ requires *m/z* 360.1658).

2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrobenzyl 5-chloro-2,4-dihydroxybenzoate (36). 2,4-dihydroxy-5-chloro-benzoic acid (149 mg, 0.79 mmol) was dissolved in DMF: THF (1:3, 8 mL) before DMAP (145 mg, 1.19 mmol), DCC (245 mg, 1.19 mmol) and compound **31** (239 mg, 0.79 mmol) were added. The mixture was warmed to 50 °C and stirred for 12 h before addition of saturated aqueous ammonium chloride (20 mL) and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give **36** as a pale yellow solid (125 mg, 33%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.82 (s, 1H), 7.65 (s, 1H), 6.56 (s, 1H), 5.46 (s, 2H), 5.26 (s, 2H), 5.07 (s, 2H), 3.99 (s, 3H), 3.54 (s, 3H), 3.53 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.6, 162.3, 157.4, 154.1, 146.3, 146.2, 139.4, 129.9, 124.8, 114.0, 111.4, 106.2, 104.1, 102.3, 95.4, 61.8, 57.9, 57.3, 56.6; IR (film) υ_{max} 3401, 3103, 2945, 1673, 1580, 1485, 1300, 1155, 1047, 952, 785cm^{-1}; HRMS (ES$^+$) *m/z* 474.0792 (M + H, $C_{19}H_{21}NO_{11}Cl$ requires *m/z* 474.0803).

3-Methoxy-2,6-bis(methoxymethoxy)-5-nitrophenethyl 5-chloro-2,4-dihydroxybenzoate (37). 2,4-dihydroxy-5-chloro-benzoic acid (147 mg, 0.78 mmol) was dissolved in DMF: THF (1:3, 8 mL) before DMAP (143mg, 1.17 mmol), DCC (241 mg, 1.17 mmol) and compound **32** (248 mg, 0.78 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h before addition of saturated aqueous ammonium chloride (30 mL) and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **37** as a pale yellow solid (194 mg, 51%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.80 (s, 1H), 7.86 (s, 1H), 7.71 (s,

1H), 6.63 (s, 1H), 5.94 (s, 1H), 5.25 (s, 2H), 5.09 (s, 2H), 4.51 (t, *J* = 5.6 Hz, 2H), 4.02 (s, 3H), 3.60 (s, 3H), 3.55 (s, 3H), 3.26 (t, *J* = 5.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 162.7, 157.6, 153.6, 146.4, 146.3, 139.6, 130.7, 127.8, 112.5, 111.7, 107.1, 104.4, 102.3, 95.8, 64.6, 61.7, 58.2, 57.0, 24.9; IR (film) u_{max} 3411, 3108, 2955, 1670, 1614, 1480, 1342, 1260, 1158, 1111, 922, 794, 712cm^{-1}; HRMS (ES$^+$) *m/z* 505.1247 (M + NH_4, $C_{20}H_{26}N_2O_{11}Cl$ requires *m/z* 505.1225).

3-(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)propyl 5-chloro-2,4-dihydroxybenzoate (38). 2,4-dihydroxy-5-chloro-benzoic acid (245 mg, 1.3 mmol) was dissolved in DMF: THF (1:3, 14 mL) before DMAP (238 mg, 1.95 mmol), DCC (402 mg, 1.95 mmol) and compound **33** (431 mg, 1.3 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h. The mixture was quenched by addition of saturated aqueous ammonium chloride (20 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **38** as a pale yellow solid (364 mg, 56%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (s, 1H), 7.63 (s, 1H), 6.59 (s, 1H), 5.22 (s, 2H), 5.04 (s, 2H), 4.38 (t, *J* = 6.1 Hz, 2H), 3.97 (s, 3H), 3.57 (s, 3H), 3.52 (s, 3H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.07 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 162.7, 158.0, 153.3, 146.6, 145.8, 139.8, 131.8, 130.5, 111.9, 111.6, 106.8, 104.6, 102.2, 95.8, 65.6, 61.6, 58.2, 56.9, 29.0, 22.3; IR (film) u_{max} 3053, 2986, 1525, 1421,1155, 1043, 939cm^{-1}; HRMS (ES$^+$) *m/z* 502.1093 (M + H, $C_{21}H_{25}NO_{11}Cl$ requires *m/z* 502.1116).

1-(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)pentan-2-yl 5-chloro-2,4-dihydroxybenzoate (40). 2,4-dihydroxy-5-chloro-benzoic acid (209 mg, 1.1 mmol) was

dissolved in DMF: THF (1:3, 11 mL) before DMAP (201 mg, 1.65 mmol), DCC (340 mg, 1.65 mmol) and compound **35** (400 mg, 1.1 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h. The mixture was quenched by addition of saturated aqueous ammonium chloride (20 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **40** as a pale yellow solid (301 mg, 51%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (s, 1H), 7.63 (s, 1H), 6.57 (s, 1H), 5.42 (m, 1H), 5.19 (m, 2H), 5.06 (m, 2H), 4.00 (s, 3H), 3.61 (s, 3H), 3.50 (s, 3H), 3.21 (m, 1H), 3.11 (m, 1H), 1.69 (m, 2H), 1.45 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.1, 162.8, 157.5, 153.6, 146.2, 139.6, 130.7, 130.6, 127.9, 112.4, 111.6, 107.2, 104.3, 102.2, 95.9, 75.2, 61.6, 58.3, 56.9, 36.7, 30.1, 19.1, 14.3; IR (film) ν_{max} 3055, 2986, 1668, 1525, 1421, 1265, 1157cm^{-1}; HRMS (ES$^+$) *m/z* 530.1426 (M + H, $C_{23}H_{29}NO_{11}Cl$ requires *m/z* 530.1429).

3-Amino-6-methoxy-2,5-bis(methoxymethoxy)benzyl 5-chloro-2,4-dihydroxybenzoate (41). Compound **36** (102 mg, 0.22 mmol) was dissolved in ethanol (2.2 mL) at the rt before PtO_2 (5.0 mg) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and the filtrate concentrated. The residue was purified via column chromatography (SiO_2, 15% EtOAc in hexanes) to give **41** as a brown solid (60 mg, 63%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66 (s, 1H), 6.69 (s, 1H), 6.50 (s, 1H), 5.38 (s, 2H), 5.16 (s, 2H), 4.95 (s, 2H), 3.79 (s, 3H), 3.55 (s, 3H), 3.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 162.5, 158.4, 147.9, 141.6, 139.5, 136.9, 130.7, 123.1, 112.2, 106.6, 106.3, 104.5, 100.7, 95.7, 62.4, 58.5,

58.0, 56.6; IR (film) ν_{max} 3512, 3053, 2986, 1672, 1421, 1159, 894, 739cm^{-1}; HRMS (ES$^+$) *m/z* 444.1057 (M + H, $C_{19}H_{23}NO_9Cl$ requires *m/z* 444.1061).

3-Amino-5-methoxy-2,6-bis(methoxymethoxy)phenethyl 5-chloro-2,4-dihydroxybenzoate (42). Compound **37** (190 mg, 0.39 mmol) was dissolved in ethanol (3.9 mL) at the rt before PtO_2 (10 mg) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and the filtrate concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **42** as a brown solid (152 mg, 85%): ^{1}H NMR ($CDCl_3$ 400 MHz) δ 7.67 (s, 1H), 6.49 (s, 1H), 6.35 (s, 1H), 5.10 (s, 2H), 4.94 (s, 2H), 4.39 (m, 2H), 3.78 (s, 3H), 3.55 (s, 3H), 3.46 (s, 3H), 3.06 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 162.7, 157.5, 147.9, 140.9, 139.2, 136.6, 130.8, 125.3, 111.6, 107.3, 104.4, 104.1, 100.1, 95.8, 65.2, 61.7, 57.9, 56.6, 24.9; IR (film) ν_{max} 3362, 3055, 2945, 2833, 1667, 1619, 1449, 1267 cm^{-1}; HRMS (ES$^+$) *m/z* 458.1215 (M + H, $C_{20}H_{25}NO_9Cl$ requires *m/z* 458.1218).

3-(3-Amino-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propyl 5-chloro-2,4-dihydroxybenzoate (43). Compound **38** (280 mg, 0.56 mmol) was dissolved in ethanol (5.6 mL) at the rt before PtO_2 (14 mg, 5% w/w) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and the filtrate concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **43** as a brown solid (216 mg, 82%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (s, 1H), 6.55 (s, 1H), 6.52 (s, 1H), 5.15 (s, 2H), 4.95 (s, 2H), 4.35 (t, *J* = 6.1 Hz, 2H), 3.79 (s, 3H), 3.58 (s, 3H), 3.51 (s, 3H), 2.78 (t, *J* = 7.4 Hz, 2H), 2.06 (m, 2H); ^{13}C NMR ($CDCl_3$ 100 MHz) δ 169.0, 162.4, 156.9, 149.7, 139.5, 138.8, 135.8, 130.1, 128.5, 111.1, 107.0, 104.1, 103.0, 98.8, 95.0, 65.5, 61.0, 58.2, 55.8, 29.2, 21.2;

IR (film) ν_{max} 3510, 3055, 2983, 1670, 1524, 1487, 1155, 1045cm^{-1}; HRMS (ES$^+$) *m/z* 472.1357 (M + H, $C_{21}H_{27}NO_9Cl$ requires *m/z* 472.1374).

1-(3-Amino-6-methoxy-2,5-bis(methoxymethoxy)phenyl)pentan-2-yl 5-chloro-2,4-dihydroxybenzoate (45). Compound **40** (200 mg, 0.38 mmol) was dissolved in ethanol (3.8 mL) at the rt before PtO_2 (10 mg, 5% w/w) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and the filtrate concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **45** as a brown solid (158 mg, 84%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.90 (s, 1H), 6.57 (s, 1H), 6.50 (s, 1H), 5.42 (m, 1H), 5.14 (m, 2H), 4.99 (m, 2H), 3.81 (s, 3H), 3.63 (s, 3H), 3.49 (s, 3H), 3.03 (m, 2H), 1.65 (m, 2H), 1.39 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 162.6, 157.6, 147.8, 141.0, 139.3, 136.3, 130.9, 125.6, 111.6, 107.4, 104.3, 104.1, 100.1, 95.8, 75.8, 61.4, 57.9, 56.6, 36.4, 30.1, 19.2, 14.3; IR (film) ν_{max} 3518, 3053, 2939, 1697, 1517, 1155, 1036, 894cm^{-1}; HRMS (ES$^+$) *m/z* 500.1691 (M + H, $C_{23}H_{31}ClNO_9$ requires *m/z* 500.1687).

3-Formamido-6-methoxy-2,5-bis(methoxymethoxy)benzyl 5-chloro-2,4-dihydroxybenzoate (46). Compound **41** (61 mg, 0.14 mmol) was dissolved in CH_2Cl_2 (1.5 mL) at 0 °C before PhOCHO (85.4 mg, 0.7 mmol) was added. The reaction was warmed to 30 °C and stirred for 12 h. After evaporation of organic solvent, the residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **46** as a yellow solid (46 mg, 71%) a mixture of rotamers: ^{1}H NMR (CD_3OD, 400 MHz) δ 10.65 (s, 1H), 8.35 (s, 1H), 8.34 (s, 1H), 8.20 (s, 1H), 7.65 (s, 1H), 6.55 (s, 1H), 5.45 (s, 2H), 5.25 (s, 2H), 5.05 (s, 2H), 3.85 (s, 3H), 3.60 (s, 3H), 3.55 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 162.9, 162.7, 159.3, 157.8, 147.3, 146.4, 142.2, 130.4, 130.3, 127.4,

127.2, 122.7, 112.0, 111.9, 109.5, 106.8, 104.6, 101.8, 101.7, 96.0, 95.9, 62.3, 58.1, 58.0, 57.0, 56.9; IR (film) ν_{max} 3053, 2986, 1697, 1487, 1157, 1047cm^{-1}; HRMS (ES$^+$) *m/z* 472.1023 (M + H, $C_{20}H_{23}NO_{10}Cl$ requires *m/z* 472.1010).

3-Formamido-6-methoxy-2,5-bis(methoxymethoxy)phenethyl 5-chloro-2,4-dihydroxybenzoate (47). Compound **42** (106 mg, 0.23 mmol) was dissolved in CH_2Cl_2 (2.3 mL) at 0 °C before PhOCHO (20 0mg, 1.64 mmol) was added. The reaction was warmed to 30 °C and stirred for 12 h. After evaporation of organic solvent, the residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **47** as a yellow solid (102 mg, 91%): ^{1}H NMR (CD_3CN, 500 MHz) δ 10.70 (s, 1H), 8.37 (s, 1H), 8.31 (s, 1H), 8.03 (s, 1H), 7.80 (s, 1H), 6.54 (s, 1H), 5.19 (s, 2H), 5.02 (s, 2H), 4.53 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 3.59 (s, 3H), 3.50 (s, 3H), 3.19 (t, *J* = 6.2 Hz, 2H); ^{13}C NMR (CD_3CN, 125 MHz) δ 168.8, 161.8, 159.3, 158.4, 130.9, 128.2, 126.9, 125.1, 117.0, 116.9, 111.7, 109.2, 106.3, 103.8, 100.5, 95.5, 64.3, 60.4, 57.0, 55.6, 24.2; IR (film) υ_{max} 3275, 2959, 2828, 1666, 1611, 1431, 1336, 1255, 1156, 1020, 961, 731cm^{-1}; HRMS (ES$^+$) *m/z* 503.1449 (M + NH_4, $C_{21}H_{28}N_2O_{10}Cl$ requires *m/z* 503.1432).

3-(3-Formamido-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propyl 5-chloro-2,4-dihydroxybenzoate (48). Compound **43** (150 mg, 0.32 mmol) was dissolved in CH_2Cl_2 (3.2 mL) at 0 °C before PhOCHO (137 mg, 1.13 mmol) was added. The reaction was warmed to 30 °C and stirred for 12 h. After evaporation of organic solvent, the residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **48** as a yellow solid (137 mg, 86%) a mixture of rotamers: ^{1}H NMR ($CDCl_3$ 400 MHz) δ 8.33 (s, 1H), 8.25 (s, 1H), 7.95(s, 1H), 7.73 (s, 1H), 6.53 (s, 1H), 5.14 (s, 2H), 4.95 (s, 2H), 4.36 (t, *J* = 5.0 Hz, 2H), 3.82 (s, 3H), 3.53 (s, 3H), 3.47 (s, 3H), 2.84 (t, *J* = 6 Hz, 2H), 2.05

(m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.0, 168.9, 162.4, 162.2, 158.8, 157.5, 147.7, 146.8, 145.8, 144.8, 142.1, 140.9, 130.0, 129.9, 128.4, 126.7, 126.4, 111.4, 111.3, 108.4, 106.5, 106.0, 104.2, 104.1, 100.8, 100.7, 95.6, 95.5, 65.2, 61.1, 57.5, 57.4, 56.6, 56.4, 28.9, 28.8, 21.9, 21.8; IR (film) υ_{max} 3392, 3053, 2986, 1608, 1373, 1161, 1045, 894cm^{-1}; HRMS (ES$^+$) *m/z* 500.1310 (M + H, $C_{22}H_{27}NO_{10}Cl$ requires *m/z* 500.1323).

1-(3-Formamido-6-methoxy-2,5-bis(methoxymethoxy)phenyl)pentan-2-yl 5-chloro-2,4-dihydroxybenzoate (50). Compound **45** (200 mg, 0.40 mmol) was dissolved in CH_2Cl_2 (40 mL) at 0 °C before PhOCHO (182 mg, 1.5 mmol) was added. The reaction was warmed to 30 °C and stirred for 12 h. After evaporation of organic solvent, the residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **50** as a yellow solid (177 mg, 84%) as a mixture of rotamers: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.46 (s, 1H), 8.09 (s, 1H), 7.84 (s, 1H), 6.58 (s, 1H), 5.39 (m, 1H), 5.18 (m, 2H), 5.00 (m, 2H), 3.89 (s, 3H), 3.62 (s, 3H), 3.51 (s, 3H), 3.03 (d, *J* = 6.7 Hz, 2H), 1.64 (m, 2H), 1.38 (m, 2H), 0.94 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 169.1, 162.7, 162.6, 159.3, 157.7, 157.6, 147.8, 147.0, 146.7, 145.6, 143.2, 141.8, 130.7, 126.9, 126.6, 125.0, 111.6, 109.6, 107.3, 107.2, 107.1, 104.4, 101.2, 101.1, 96.0, 95.9, 75.5, 75.3, 61.4, 58.0, 57.8, 56.9, 56.8, 36.5, 36.3, 30.2, 30.1, 19.2, 14.3; IR (film) ν_{max} 3392, 2986, 1697, 1529, 1396, 1155, 1113, 960cm^{-1}; HRMS (ES$^+$) *m/z* 528.1644 (M + H, $C_{24}H_{31}NO_{10}Cl$ requires *m/z* 528.1636).

3-Formamido-2,5-dihydroxy-6-methoxybenzyl 5-chloro-2,4-dihydroxybenzoate (51). Ester **46** (20 mg, 0.04 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and CH_3CN (0.2 mL) at 25 ºC before addition of sodium iodide (60 mg, 0.4 mmol) and trimethylsilyl chloride (50.8 μM, 0.4 mmol). The turbid solution was stirred for 15 min before saturated

$Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **51** (14.8 mg, 91%) as a red oil: ^{1}H NMR (CD_3CN, 400 MHz) δ 10.80 (s, 1H), 9.58 (s, 1H), 8.30 (s, 1H), 7.81 (s, 1H), 7.70 (s, 1H), 7.22 (s, 1H), 6.58 (s, 1H), 6.57 (s, 1H), 5.48(s, 2H), 3.85(s, 3H); ^{13}C NMR (CD_3CN, 100 MHz) δ 170.1, 163.6, 163.1, 161.5, 160.3, 146.2, 144.0, 132.1, 131.7, 118.9, 111.7, 106.5, 104.9, 104.7, 61.9, 58.8; IR (film) ν_{max} 3257, 2966, 2919, 2848, 1665, 1614, 1491, 1388, 1209cm^{-1}; HRMS (ES^+) *m/z* 384.0502 (M + H, $C_{16}H_{15}NO_8Cl$ requires *m/z* 384.0486).

3-Formamido-2,5-dihydroxy-6-methoxyphenethyl 5-chloro-2,4-dihydroxybenzoate (52). Ester **47** (20 mg, 0.041 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and CH_3CN (0.2 mL) at 25 ºC before the addition of sodium iodide (60 mg, 0.4 mmol) and trimethylsilyl chloride (50.8 μM, 0.4 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **52** (14.1 mg, 86%) as a red oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.70 (s,1H), 8.55 (s, 1H), 8.29 (s, 1H), 8.15 (s, 1H), 8.05 (s, OH), 7.85 (s, 1H), 6.65 (s, 1H), 6.45 (s, 1H), 6.44 (s, 1H), 4.45 (t, *J* = 6.6 Hz, 2H), 3.75 (s, 3H), 3.10 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (CD_3CN 100 MHz) δ 170.3, 163.2, 162.2, 159.8, 146.4, 144.2, 141.7, 132.3, 123.7, 122.5, 113.0, 109.3, 107.6, 105.1, 65.6, 62.0, 25.2; IR (film) υ_{max} 3304, 2960, 2925, 2853, 1670, 1614, 1491, 1393, 1250cm^{-1}; HRMS (ES^+) *m/z* 415.0922 (M + NH_4, $C_{17}H_{20}N_2O_8Cl$ requires *m/z* 415.0908).

3-(3-Formamido-2,5-dihydroxy-6-methoxyphenyl)propyl 5-chloro-2,4-dihydroxybenzoate (53). Ester **48** (20 mg, 0.040 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and CH_3CN (0.2 mL) at 25 ºC before addition of sodium iodide (60 mg, 0.4 mmol) and trimethylsilyl chloride (50.8 μM, 0.4 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added. The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **53** (13.5 mg, 82%) as a red oil: ^{1}H NMR (CD_3COCD_3, 500 MHz) δ 10.90 (s, 1H), 9.58 (s, 1H), 8.23 (s, 1H), 6.83 (s, 1H), 6.59 (s, 1H), 4.37 (t, *J* = 6.4 Hz, 2H), 3.78 (s, 3H), 2.89 (t, *J* = 7.4 Hz, 2H), 2.09 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR (CD_3CN, 125 MHz) δ 169.6, 162.5, 160.9, 159.6, 144.9, 143.5, 140.2, 131.2, 125.1, 122.2, 112.3, 107.8, 106.1, 104.2, 65.7, 60.5, 21.4, 14.0; IR (film) ν_{max} 3283, 2955, 2935, 2858, 1670, 1619, 1393, 1250 cm^{-1}; HRMS (ES$^+$) *m/z* 434.0621 (M + Na, $C_{18}H_{18}NO_8ClNa$ requires *m/z* 434.0619).

1-(3-Formamido-2,5-dihydroxy-6-methoxyphenyl)pentan-2-yl 5-chloro-2,4-dihydroxybenzoate (55). Ester **50** (30 mg, 0.057 mmol) was dissolved in CH_2Cl_2 (0.3 mL) and CH_3CN (0.3 mL) at 25 ºC before addition of sodium iodide (85 mg, 0.57 mmol) and trimethylsilyl chloride (72.4 μM, 0.57 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added. The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **55** (21.7 mg, 87%) as a red oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.72 (s, 1H), 8.30 (s, 1H), 7.86 (m, 3H), 7.31 (s, 1H), 6.62 (s, 1H), 6.40 (s, 1H), 5.96 (s, 1H),

5.10 (m, 1H), 3.82 (s, 3H), 3.16 (m, 1H), 3.05 (m, 1H), 1.74 (m, 2H), 1.51 (m, 1H), 1.36 (m, 1H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 162.8, 160.1, 157.9, 144.0, 142.8, 139.9, 130.7, 121.9, 119.4, 112.0, 108.2, 106.9, 104.6, 76.8, 61.7, 36.0, 30.0, 19.3, 14.3; IR (film) ν_{max} 3512, 3392, 3055, 2985, 1618, 1373, 1161, 1045, 896cm^{-1}; HRMS (ES$^+$) *m/z* 440.1134 (M + H, $C_{20}H_{23}NO_8Cl$ requires *m/z* 440.1112).

2-(5-Formamido-2-methoxy-3,6-dioxocyclohexa-1,4-dienyl)ethyl 5-chloro-2,4-dihydroxybenzoate (56). Compound **52** (18 mg, 0.046 mmol) was dissolved in EtOAc (0.4 mL) before $Pd(OAc)_2$ (36 mg, 200% w/w) was added and stirred for 30 min. The mixture was filtered through silica gel pad and the filtrate concentrated, the residue was purified via prepared TLC (SiO_2, 250 μM, 50% EtOAc in hexane) to afford **56** (11.3 mg, 63%) as a brown solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.75 (s,1H), 8.62 (s, 1H), 8.30 (s, 1H), 7.75 (s, 1H), 7.43 (s, OH), 6.63 (s, 1H), 5.91 (s, 1H), 4.44 (t, *J* = 5.2 Hz, 2H), 4.21 (s, 3H), 2.98 (t, *J* = 5.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 184.0, 182.0, 168.9, 161.5, 161.1, 159.2, 157.0, 138.5, 130.8, 123.0, 114.1, 112.3, 105.0, 103.5, 63.0, 61.5, 22.5; IR (film) υ_{max} 3054, 2987, 2928, 1598, 1422, 1264cm^{-1}; HRMS (ES$^+$) *m/z* 413.0740 (M + NH_4, $C_{17}H_{18}N_2O_8Cl$ requires *m/z* 413.0752).

1-(5-Formamido-2-methoxy-3,6-dioxocyclohexa-1,4-dienyl)pentan-2-yl 5-chloro-2,4-dihydroxybenzoate (58). Compound **55** (17 mg, 0.039mmol) was dissolved in EtOAc (0.4 mL) before $Pd(OAc)_2$ (34 mg, 200% w/w) was added and stirred for 30 min. The mixture was filtered through silica gel pad and the filtrate concentrated, the residue was purified via prepared TLC (SiO_2, 250 μM, 50% EtOAc in hexane) to afford **58** (11.5 mg, 68%) as a brown solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.80 (s, 1H), 8.59 (a, 1H), 8.23 (s, 1H), 7.74 (s, 1H), 7.36 (s, 1H), 6.60 (s, 1H), 5.26 (m, 1H), 4.14 (s, 3H), 3.78 (m,

1H), 2.82 (m, 1H), 2.64 (m, 1H), 1.66 (m, 2H), 1.42 (m, 2H), 0.98 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 183.7, 182.5, 168.7, 162.5, 159.4, 157.1, 136.8, 130.0, 129.9, 122.9, 114.2, 111.2, 106.7, 104.2, 74.2, 61.8, 36.5, 27.9, 18.7, 14.2; IR (film) ν_{max} 3603, 3398, 2972, 1664, 1616, 1379, 1161, 1122, 946cm^{-1}; HRMS (ES$^+$) *m/z* 455.1218 (M + NH_4, $C_{20}H_{24}N_2O_8Cl$ requires *m/z* 455.1221).

3-(2-Azidoethyl)-2-methoxy-1,4-bis(methoxymethoxy)-5-nitrobenzene (**59.1)**. Compound **27** (1.2 g, 4.41 mmol), triphenylphosphine (2.87 g, 11.0 mmol) and diisopropylazodicarboxylate (2.16 mL, 11.0 mmol) were dissolved in THF (20 mL) and stirred at 0 °C for 15 min before diphenyl phosphoryl azide (2.4 mL, 11.0 mmol) was added and stirred at rt for 12 h. The reaction was quenched by addition of saturated aqueous ammonium chloride (100 mL). The organic layer was removed and the aqueous layer extracted with EtOAc (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 15% EtOAc in hexanes) afforded **59.1** (1.46 g, 97%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (s, 1H), 5.24 (s, 2H), 5.07 (s, 2H), 4.00 (s, 3H), 3.60 (s, 3H), 3.53 (s, 3H), 3.47 (t, *J* = 7.6 Hz, 2H), 3.06 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.6, 146.5, 146.3, 139.6, 128.4, 112.2, 102.5, 95.8, 61.7, 58.2, 57.0, 50.7, 25.3; IR (film) ν_{max} 3053, 2986, 2253, 2102, 1526, 1477, 1357cm^{-1}; HRMS (ES$^+$) *m/z* 365.1068 (M + Na, $C_{13}H_{18}N_4O_7Na$ requires *m/z* 365.1073).

2-(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)ethanamine (59). The azide **59.1** (0.33 g, 0.96 mmol) and sodium sulfide (0.487 g, 2.02 mmol) were dissolved in methanol (3.3 mL) before triethylamine (14 μL, 0.096 mmol) was added and the mixture stirred for 12 h before the addition of saturated aqueous ammonium chloride (30 mL).

The organic layer was removed and the aqueous layer extracted with EtOAc (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 30% EtOAc in hexanes) afforded **59** (0.15 g, 51%) as the yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.54 (s, 1H), 5.17 (s, 2H), 4.98 (s, 2H), 3.81 (s, 3H), 3.64 (s, 3H), 3.54 (s, 3H), 3.46 (t, *J* = 7.7 Hz, 2H), 2.96 (t, *J* = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.9, 140.6, 138.9, 136.6, 126.0, 103.7, 100.1, 95.8, 61.6, 57.9, 56.6, 51.3, 25.3; IR (film) ν_{max} 3448, 3373, 2935, 2902, 1612, 1491, 1155, 1059cm^{-1}; HRMS (ES$^+$) *m/z* 317.1352 (M + H, $C_{13}H_{21}N_2O_7$ requires *m/z* 317.1349).

2,4-Bis(benzyloxy)-5-chloro-*N*-(2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenethyl)benzamide (**60)**. 2,4-bis(benzyloxy)-5-chlorobenzoic acid (200 mg, 0.543 mmol) was dissolved in THF (5 mL) before DCC (134 mg, 0.652 mmol) and compound **59** (257 mg, 0.81 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h before the addition of saturated aqueous ammonium chloride (30 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 6% EtOAc in hexanes) to give **60** as a yellow solid (228 mg, 63%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.10 (s, NH), 8.34 (s, 1H), 8.28 (s, 1H), 7.39 (m, 10H), 6.60 (s, 1H), 5.29 (s, 2H), 5.26 (s, 2H), 5.12 (s, 2H), 4.77 (s, 2H), 3.90 (s, 3H), 3.57 (s, 3H), 3.43 (s, 3H), 3.43 (t, *J* = 8.0 Hz, 2H), 2.98 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.3, 157.7, 156.5, 147.1, 145.1, 141.1, 136.0, 135.8, 135.5, 134.0, 129.4, 129.2, 129.1, 128.7, 127.9, 127.4, 125.4, 116.7, 116.2, 109.7, 100.5, 100.4, 95.9, 72.5, 71.4, 61.5, 58.2, 57.0, 51.1, 25.3; IR (film) υ_{max} 3053, 2985, 1697,

1332, 1155, 960cm^{-1}; HRMS (ES$^+$) *m/z* 667.2072 (M + H, $C_{34}H_{36}N_2O_{10}Cl$ requires *m/z* 667.2058).

5-Chloro-*N*-(3-formamido-6-methoxy-2,5-bis(methoxymethoxy)phenethyl)-2,4-dihydroxybenzamide (62). Compound **60** (100 mg, 0.15 mmol) was dissolved in EtOAc (2 mL) before Pd/C (10 mg, 10 w/w %) was added. The mixture was stirred under a hydrogen atmosphere for 48 h. The solution was filtered through celite and the filtrate concentrated. The residue was dissolved in CH_2Cl_2 (2.0 mL) at 0 °C before PhOCHO (97.6 mg, 0.8 mmol) was added. The reaction was warmed to 30 °C and stirred for 12 h. After concentration, the residue was purified via column chromatography (SiO_2, 10% e EtOAc in hexanes) to give **62** as a yellow solid (17.4 mg, 69% for two steps, based on recovery of starting material): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.46 (s, 1H), 7.91 (s, 1H), 7.61 (s, 1H), 7.53 (s, 2H), 6.46 (s, 1H), 5.18 (s, 2H), 4.99 (s, 2H), 3.89 (s, 3H), 3.59 (s, 3H), 3.52 (m, 2H), 3.50 (s, 3H), 2.98 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.9, 167.5, 164.4, 164.0, 161.2, 150.4, 149.2, 145.7, 132.0, 130.6, 115.4, 113.6, 112.1, 107.9, 104.4, 99.3, 64.7, 61.0, 59.9, 43.3, 28.2; IR (film) ν_{max} 3325, 3053, 2935, 1670, 1488, 1394, 1155, 1093, 1045, 894cm^{-1}; HRMS (ES$^+$) *m/z* 485.1306 (M + H, $C_{21}H_{26}N_2O_9Cl$ requires *m/z* 485.1327).

5-Chloro-*N*-(3-formamido-2,5-dihydroxy-6-methoxyphenethyl)-2,4-dihydroxybenzamide (63). Ester **62** (20 mg, 0.04 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and CH_3CN (0.2 mL) at 25 ºC before addition of sodium iodide (62.0 mg, 0.4 mmol) and trimethylsilyl chloride (50.8 μM, 0.4 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried

(Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **63** (12.4 mg, 76%) as a red oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.16 (s, 1H), 7.60 (s, 1H), 7.44 (s, 1H), 6.98 (s, 1H), 6.43 (d, *J* = 5.2 Hz, 1H), 3.82 (s, 3H), 3.50 (t, *J* = 7.0 Hz, 2H), 2.99 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.1, 164.3, 164.2, 161.2, 147.9, 146.5, 142.8, 132.1, 125.8, 125.6, 115.6, 112.0, 111.9, 107.9, 64.6, 44.0, 27.6; IR (film) ν_{max} 3691, 3337, 2985, 1604, 1373, 1159, 1045, 894cm^{-1}; HRMS (ES$^+$) *m/z* 419.0612 (M + Na, $C_{17}H_{17}N_2O_7ClNa$ requires *m/z* 419.0622).

5-Chloro-*N*-(2-(5-formamido-2-methoxy-3,6-dioxocyclohexa-1,4-dienyl)ethyl-2,4-dihydroxybenzamide (64). Compound **63** (10 mg, 0.025 mmol) was dissolved in EtOAc (0.3 mL) before $Pd(OAc)_2$ (20 mg, 200% w/w) was added and stirred for 30 min. The solution was filtered through silica gel and the filtrated concentrated, the residue was purified via preparative TLC (SiO_2, 250 μM, 50% EtOAc in hexane) to afford **64** as a brown solid (5.6 mg, 56%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.50 (s, 1H), 7.55 (s, 1H), 6.43 (s, 1H), 4.06 (s, 3H), 3.45 (t, *J* = 8 Hz, 2H), 2.71 (t, *J* = 8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 184.3, 182.7, 168.9, 161.5, 160.1, 157.2, 156.8, 137.9, 128.4, 125.4, 113.9, 111.6, 108.4, 103.9, 61.2, 37.8, 23.1; IR (film) ν_{max} 3398, 2985, 1637, 1610, 1115, 1095, 941cm^{-1}; HRMS (ES$^+$) *m/z* 395.0641 (M + H, $C_{17}H_{16}N_2O_7Cl$ requires *m/z* 395.0646).

5-Bromo-2,4-dihydroxybenzoic acid (65). 2,4-dihydroxybenzoic acid (3 g, 19.6 mmol) was dissolved in acetic acid (21 mL) before bromine (1.1 mL, 23.3 mmol) dissolved in acetic acid (18 mL) was added dropwise and stirred for 4 h. The mixture was diluted with water (100 mL) and quenched with saturated aqueous $Na_2S_2O_3$. The mixture was extracted rigorously with EtOAc until the extracts showed no sign of product. The

combined EtOAc layers were dried over Na_2SO_4, filtered and concentrated. The solid was recrystallized from a 50% acetonitrile in toluene to afford **65** as a yellow solid (3.6 g, 80%): ^{1}H NMR (DMSO, 400 MHz) δ 7.79 (s, 1H), 6.44 (s, 1H); ^{13}C NMR (DMSO, 100 MHz) δ 171.3, 163.0, 159.7, 134.3, 108.7, 103.7, 99.2; IR (film) v_{max} 3495, 3350, 1654, 1612, 1186, 1159, 1045, 842cm^{-1}; HRMS (ES$^-$) *m/z* 230.9291 (M - H, $C_7H_4BrO_4$ requires *m/z* 230.9293).

2,4-dihydroxy-5-iodobenzoic acid (66). 2,4-hydroxybenzoic acid (3 g, 19.5 mmol) was dissolved in acetic acid (24 mL) before iodine monochloride (3.87 g, 23.4 mmol) dissolved in acetic acid (10.3 mL) was added dropwise and stirred for 4 h. The mixture was diluted with water and quenched with aqueous saturated $Na_2S_2O_3$. The mixture was extracted rigorously with EtOAc until the extracts showed no sign of product. The combined EtOAc layers were dried over Na_2SO_4, filtered and concentrated. The solid was recrystallized from a 50% acetonitrile in toluene to afford white solid (3.76 g, 69%): ^{1}H NMR (DMSO, 400 MHz) δ 11.3 (s, 1H), 8.01 (s, 1H), 6.43 (s, 1H); ^{13}C NMR (DMSO, 100 MHz) δ 171.1, 163.5, 163.0, 141.5, 107.6, 102.6, 73.6; IR (film) v_{max} 3446, 3386, 1656, 1612, 1442, 1164, 1045, 933cm^{-1}; HRMS (ES$^+$) *m/z* 280.9320 (M + H, $C_7H_6IO_4$ requires *m/z* 280.9311).

1-(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)propan-2-yl 5-bromo-2,4-dihydroxybenzoate (67). Compound **65** (102 mg, 0.44 mmol) was dissolved in DMF: THF (1:1, 4 mL) before DMAP (53.7 mg, 0.44 mmol), DCC (90.6 mg, 0.44 mmol) and compound **34** (122 mg, 0.34 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h before the addition of saturated aqueous ammonium chloride (15 mL). The mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were

dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **67** as a pale yellow solid (94.5 mg, 51%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (s, 1H), 7.66 (s, 1H), 6.59 (s, 1H), 5.40 (m, 1H), 5.21 (m, 2H), 5.09 (m, 2H), 4.02 (s, 3H), 3.62 (s, 3H), 3.51 (s, 3H), 3.25 (m, 1H), 3.10 (m, 1H), 1.43 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 163.3, 158.3, 153.6, 146.4, 146.3, 139.6, 134.0, 127.8, 112.4, 108.1, 104.1, 102.3, 100.9, 95.8, 72.4, 61.6, 58.2, 56.9, 31.5, 20.4; IR (film) ν_{max} 3496, 3055, 2939, 1664,1525, 1479, 1224, 1157, 1111, 1049cm^{-1}; HRMS (FAB$^+$) *m/z* 546.0623 (M + H, $C_{21}H_{25}NO_{11}Br$ requires *m/z* 546.0611).

1-(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)propan-2-yl 2,4-dihydroxy-5-iodobenzoate (68). Compound **66** (779 mg, 2.79 mmol) was dissolved in DMF: THF (1:1, 28 mL) before DMAP (464 mg, 3.81 mmol), DCC (784 mg, 3.81 mmol) and compound **34** (912 mg, 2.54 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h before addition of saturated aqueous ammonium chloride (50 mL). The mixture was extracted with EtOAc (3 × 60 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **68** as a pale yellow solid (783 mg, 52%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.85 (s, 1H), 8.22 (s, 1H), 7.66 (s, 1H), 6.57 (s, 1H), 5.39 (m, 1H), 5.21 (m, 2H), 5.10 (m, 2H), 4.03 (s, 3H), 3.63 (s, 3H), 3.51 (s, 3H), 3.25 (m, 1H), 3.10 (m, 1H), 1.43 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.6, 164.2, 160.6, 153.6, 146.4, 146.3, 140.4, 139.5, 127.8, 112.4, 109.1, 103.3, 102.3, 95.9, 74.1, 72.4, 61.6, 58.2, 57.0, 31.6, 20.5; IR (film) ν_{max} 3470, 2985, 1664,

1527, 1475, 1371, 1222, 1155, 1047, 1026cm^{-1}; HRMS (FAB$^+$) *m/z* 594.0472 (M + H, $C_{21}H_{25}NO_{11}I$ requires *m/z* 594.0472).

1-(3-Amino-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propan-2-yl 5-bromo-2,4-dihydroxybenzoate (69). Compound **67** (180 mg, 0.33 mmol) was dissolved in ethanol (3.3 mL) at the rt before PtO_2 (18.0 mg) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and the filtrate concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **69** as a brown solid (127 mg, 71%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.93 (s, 1H), 8.05 (s, 1H), 6.53 (s, 1H), 6.51 (s, 1H), 5.41 (m, 1H), 5.13 (m, 2H), 5.01 (m, 2H), 3.82 (s, 3H), 3.64 (s, 3H), 3.50 (s, 3H), 3.10 (m, 1H), 3.00 (m, 1H), 1.38 (d, *J* = 5.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 163.2, 158.2, 147.8, 141.0, 139.4, 136.3, 134.1, 125.5, 108.3, 104.2, 104.1, 100.7, 100.1, 95.9, 72.9, 61.5, 57.9, 56.6, 31.6, 20.3; IR (film) ν_{max} 3393, 3303, 2985, 1650, 1421, 1373, 1155, 1047, 896cm^{-1}; HRMS (FAB$^+$) *m/z* 516.0849 (M + H, $C_{21}H_{27}NO_9Br$ requires *m/z* 516.0869).

1-(3-Amino-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propan-2-yl 2,4-dihydroxy-5-iodobenzoate (70). $SnCl_2{\cdot}H_2O$ (216 mg, 0.96 mmol) was added to a suspension of compound **68** (108 mg, 0.18 mmol) in anhydrous ethanol (0.75 mL). The mixture was heated to reflux before sodium borohydide (0.361 mg, 9.54 μmol) dissolved in EtOH (0.4 mL) was added dropwise. The mixture was stirred at reflux for 20 min before cooling to rt. The reaction was quenched by the addition of saturated aqueous sodium potassium tartrate and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **37** as a pale yellow solid

(64.5 mg, 63%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.92 (s, 1H), 8.24 (s, 1H), 6.56 (s, 1H), 6.51 (s, 1H), 5.42 (m, 1H), 5.12 (m, 2H), 5.01 (s, 2H), 3.83 (s, 3H), 3.64 (s, 3H), 3.50 (s, 3H), 3.10 (m, 1H), 3.01 (m, 1H), 1.39 (d, *J* = 5.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.6, 164.3, 160.5, 147.8, 141.1, 140.4, 139.3, 136.4, 125.4, 121.5, 109.5, 104.4, 103.3, 100.0, 96.1, 73.0, 61.4, 57.9, 56.5, 31.6, 20.2; IR (film) ν_{max} 3416, 3053, 1612, 1421, 1373,1155, 975, 896cm^{-1}; HRMS (FAB^{+}) *m/z* 564.0729 (M + H, $C_{21}H_{27}NO_9I$ requires *m/z* 564.0730).

1-(3-Formamido-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propan-2-yl 5-bromo-2,4-dihydroxybenzoate (71). Compound **69** (100 mg, 0.19 mmol) was dissolved in CH_2Cl_2 (1.9 mL) at 0 °C before PhOCHO (230 mg, 1.9 mmol) was added. The reaction was warmed to 30 °C and stirred for 12 h. After concentration, the residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **71** as a pale yellow solid (87.5 mg, 83%) as a mixture of rotamers: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.89 (s, 1H), 8.52 (s, 0.5H), 8.49 (s, 1H), 8.09 (s, 1H), 8.00 (s, 1H), 6.96 (s, 1H), 6.58 (s, 1H), 5.39 (m, 1H), 5.21 (m, 2H), 5.02 (m, 2H), 3.90 (s, 3H), 3.63 (s, 3H), 3.52 (s, 3H), 3.06 (m, 1H), 3.01 (m, 1H), 1.38 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 168.8, 163.2, 163.2, 162.9, 159.4, 158.7, 147.9, 147.1, 146.8, 145.7, 143.2, 141.9, 134.0, 126.8, 126.5, 125.0, 109.7, 108.0, 107.9, 107.5, 104.3, 101.2, 101.1, 100.8, 100.7, 96.0, 95.9, 72.4, 72.3, 61.4, 58.0, 57.8, 56.9, 56.8, 31.6, 31.5, 20.4, 20.2; IR (film) ν_{max} 3055, 2937, 1697, 1666, 1616, 1425, 1371, 1155, 1112, 1027, 970cm^{-1}; HRMS (FAB^{+}) *m/z* 544.0811 (M + H, $C_{22}H_{27}NO_{10}Br$ requires *m/z* 544.0818).

1-(3-Formamido-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propan-2-yl 2,4-dihydroxy-5-iodobenzoate (72). Compound **70** (100 mg, 0.18 mmol) was dissolved in

CH_2Cl_2 (1.8 mL) at 0 °C before PhOCHO (217 mg, 1.8 mmol) was added. The reaction was warmed to 30 °C and stirred for 12 h. After concentration, the residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **72** as a yellow solid (79.6 mg, 76%) as a mixture of rotomers: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.42 (m, 1H), 8.10 (s, 0.5H), 7.73 (m, 1H), 6.94 (s, 0.5H), 6.39 (m, 1H), 6.37 (s, 1H), 5.45 (m, 1H), 5.19 (m, 2H), 5.02 (m, 2H), 3.90 (s, 3H), 3.59 (s, 3H), 3.51 (s, 3H), 3.08 (m, 1H), 3.01 (m, 1H), 1.34 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ170.0, 169.9, 163.9, 163.4, 163.2, 159.7, 147.8, 147.0, 147.0, 145.9, 143.5, 142.1, 132.3, 126.8, 126.7, 126.3, 125.2, 109.7, 108.3, 107.5, 106.2, 106.0, 106.0, 103.4, 101.2, 101.1, 95.9, 71.6, 71.5, 61.5, 61.4, 57.9, 57.7, 56.9, 56.8, 31.7, 31.4, 20.4, 20.1; IR (film) ν_{max} 3342, 3282, 2985, 1701, 1605, 1375, 1151, 1049, 976cm^{-1}; HRMS (FAB$^+$) *m/z* 592.0682 (M + H, $C_{22}H_{27}NO_{10}I$ requires *m/z* 592.0680).

1-(3-formamido-2,5-dihydroxy-6-methoxyphenyl)propan-2-yl 5-bromo-2,4-dihydroxybenzoate (73). Ester **71** (20 mg, 0.037 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and CH_3CN (0.2 mL) at 25 ºC before the addition of sodium iodide (55.2 mg, 0.37 mmol) and trimethylsilyl chloride (47.0 μM, 0.37 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **73** (10.2 mg, 61%) as a red oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.17 (s, 1H), 7.95 (d, *J* = 6.4 Hz, 1H), 7.00 (s, 1H), 6.39 (s, 1H), 5.43 (m, 1H), 3.83 (s, 3H), 3.17 (m, 1H), 3.04 (m, 1H), 1.39 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 162.8, 161.0, 160.8, 144.9, 143.3, 140.0, 134.5, 122.0,

120.8, 108.8, 106.4, 103.1, 100.4, 72.4, 60.0, 30.6, 19.2; IR (film) ν_{max} 3400, 2985, 1664, 1473, 1331, 1159, 1047, 941cm^{-1}; HRMS (ES$^+$) *m/z* 478.0123 (M + Na, $C_{18}H_{18}NO_8BrNa$ requires *m/z* 478.0113).

1-(3-Formamido-2,5-dihydroxy-6-methoxyphenyl)propan-2-yl 2,4-dihydroxy-5-iodobenzoate (74). Ester **72** (10 mg, 0.017 mmol) was dissolved in CH_2Cl_2 (0.1 mL) and CH_3CN (0.1 mL) at 25 ºC before the addition of sodium iodide (25.5 mg, 0.17 mmol) and trimethylsilyl chloride (22.0 μM, 0.17 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **74** (7.0 mg, 83%) as a red oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.17 (s, 1H), 7.72 (s, 1H), 7.00 (s, 1H), 6.63 (m, 1H), 6.25 (m, 1H), 5.43 (m, 3H), 3.82 (s, 3H), 3.14 (m, 1H), 3.05 (m, 1H), 1.39 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.1, 164.4, 163.9, 161.0, 145.0, 143.3, 140.0, 132.0, 122.0, 121.0, 108.8, 107.9, 105.0, 102.3, 71.8, 60.0, 30.7, 19.2; IR (film) ν_{max} 3404, 2985, 1649, 1471, 1375, 1117, 1045, 896cm^{-1}; HRMS (FAB$^+$) *m/z* 525.9991 (M + Na, $C_{18}H_{18}NO_8INa$ requires *m/z* 525.9975).

1-(5-Formamido-2-methoxy-3,6-dioxocyclohexa-1,4-dienyl)propan-2-yl 5-bromo-2,4-dihydroxybenzoate (75). Compound **73** (16 mg, 0.035 mmol) was dissolved in EtOAc (0.3 mL) before $Pd(OAc)_2$ (32 mg, 200% w/w) was added and stirred for 30 min. The solution was filtered through silica gel and the filtrate concentrated. The residue was purified via preparative TLC (SiO_2, 250 μM, 50% EtOAc in hexane) to afford **75** as a brown solid (9.4 mg, 59%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.80 (s, 1H), 8.61 (s, 1H),

8.34 (s, 1H), 7.85 (s, 1H), 7.35 (s, 1H), 6.61 (s, 1H), 5.95 (m, 1H), 5.32 (m, 1H), 4.20 (s, 3H), 2.96 (m, 1H), 2.78 (m, 1H), 1.43 (d, J = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 183.7, 182.5, 168.4, 163.1, 159.4, 157.9, 157.2, 136.8, 133.2, 122.6, 114.3, 107.6, 103.9, 100.5, 71.2, 61.9, 29.3, 20.2; IR (film) ν_{max} 3400, 3329, 3053, 1610, 1477, 1421, 1375, 1112, 846cm^{-1}; HRMS (FAB$^+$) *m/z* 454.0121 (M + H, $C_{18}H_{17}NO_8Br$ requires *m/z* 454.0138).

1-(5-Formamido-2-methoxy-3,6-dioxocyclohexa-1,4-dienyl)propan-2-yl 2,4-dihydroxy-5-iodobenzoate (76). Compound **74** (22 mg, 0.044 mmol) was dissolved in EtOAc (0.5 mL) before $Pd(OAc)_2$ (44 mg, 200% w/w) was added and stirred for 30 min. The solution was filtered through silica gel and the filtrate concentrated. The residue was purified via preparative TLC (SiO_2, 250 μM, 50% EtOAc in hexane) to afford **76** as a brown solid (15.5 mg, 71%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.80 (s, 1H), 8.50 (s, 1H), 8.23 (s, 1H), 7.57 (s, 1H), 7.19 (s, 1h), 6.30 (s, 2H), 5.25 (m, 1H), 4.05 (s, 3H), 2.87 (m, 1H), 2.70 (m, 1H), 1.32 (d, J = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 183.8, 182.5, 169.4, 163.7, 162.0, 159.6, 157.3, 136.8, 131.9, 123.0, 114.3, 107.8, 106.0, 103.1, 70.4, 61.8, 29.4, 20.3; IR (film) ν_{max} 3396, 3278, 2941, 1662, 1421, 1332, 1151, 1045, 896cm^{-1}; HRMS (ES$^+$) *m/z* 501.9986 (M + H, $C_{18}H_{17}NO_8I$ requires *m/z* 501.9999).

5-Ethyl-2,4-bis(methoxymethoxy)benzaldehyde (78). Dimethylformamide (3 mL, 38.2 mmol) and phosphorus oxychloride (4 mL, 43.1 mmol) were mixed at 0 °C and stirred for 15 min before 2,4-dihydroxy 5-ethyl benzaldehyde (2 g, 14.5 mmol) dissolved in dimethylformamide (5 mL) was added. The mixture was stirred for 10 h and quenched by the addition of saturated aqueous sodium bicarbonate (100 mL). The solution was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic layers were dried

(Na_2SO_4), filtered, and concentrated. The residue was dissolved in THF (120 mL) and the solution was cooled to 0 °C before NaH (60% in mineral oil, 2.32 g, 58 mmol) was cautiously added. The mixture was stirred at rt for 4 h before quenching by the addition of saturated aqueous ammonium chloride (100 mL). The solution was extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **78** as a brown oil (2.83 mg, 77% for two steps): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.30 (s, 1H), 7.66 (s, 1H), 6.88 (s, 1H), 5.26 (s, 4H), 3.52 (s, 3H), 3.49 (s, 3H), 2.59 (q, *J* = 7.5 Hz, 2H), 1.18 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 189.0, 161.6, 160.4, 128.9, 127.6, 120.0, 100.7, 95.3, 94.5, 57.0, 56.8, 23.1, 14.5; IR (film) ν_{max} 3055, 2935, 2873, 2773, 1606, 1581, 1396, 1209, 1116, 1057, 993cm^{-1}; HRMS (ES$^+$) *m/z* 272.1495 (M + NH_4, $C_{13}H_{22}NO_5$ requires *m/z* 272.1498).

5-Ethyl-2,4-bis(methoxymethoxy)benzoic acid (79). $NaH_2PO_4{\cdot}H_2O$ (1.52 g, 11.0 mmol) and H_2O (12 mL) were added to aldehyde **78** (0.4 g, 1.57 mmol). *Tert*-butyl alcohol (4 mL), 2-methyl-2-butene (3.34 mL, 22.0 mmol) and 90 % sodium chlorite (1.42 g, 14.1 mmol) were added to the mixture and stirred at rt for 4 h. The mixture was diluted with H_2O (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to give **79** as a clear liquid (387 mg, 91%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (s, 1H), 6.94 (s, 1H), 5.36 (s, 2H), 5.24 (s, 2H), 3.53 (s, 3H), 3.46 (s, 3H), 2.58 (q, *J* = 7.5 Hz, 2H), 1.16 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.7, 160.4, 156.4, 133.9, 128.4, 111.5, 101.2, 96.5, 94.6,

57.5, 56.8, 23.1, 14.5; IR (film) ν_{max} 3435, 2935, 1651, 1493, 1442, 1373, 1188, 1064, 989cm^{-1}; HRMS (ES$^+$) *m/z* 293.1013 (M + Na, $C_{13}H_{18}O_6Na$ requires *m/z* 293.1001).

1-(2-Methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)propan-2-yl 5-ethyl-2,4-bis(methoxymethoxy)benzoate (80). Compound **79** (670 mg, 2.48 mmol) was dissolved in THF (25 mL) before DMAP (464 mg, 3.81 mmol), DCC (784 mg, 3.81 mmol) and compound **34** (700 mg, 1.95 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h and quenched by the addition of saturated aqueous ammonium chloride (100 mL). The solution was extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **80** as a pale yellow solid (670 mg, 59%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.62 (s, 1H), 7.61 (s, 1H), 6.85 (s, 1H), 5.40 (m, 1H), 5.20 (s, 2H), 5.19 (s, 2H), 5.16 (s, 2H), 5.06 (s, 2H), 3.98 (s, 3H), 3.57 (s, 3H), 3.51 (s, 3H), 3.50 (s, 3H), 3.49 (s, 3H), 3.15 (m, 1H), 2.95 (m, 1H), 2.58 (m, 2H), 1.36 (t, *J* = 6.2 Hz, 3H), 1.18 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.3, 159.1, 157.3, 153.7, 146.4, 139.7, 139.6, 132.5, 128.6, 127.1, 114.8, 112.0, 103.4, 102.2, 96.2, 95.8, 94.5, 70.5, 61.6, 58.1, 56.9, 56.8, 56.7, 31.8, 23.2, 20.7, 14.8; IR (film) ν_{max} 3055, 2939, 1610, 1577, 1477, 1438, 1242, 1108, 975cm^{-1}; HRMS (ES$^+$) *m/z* 584.2340 (M + H, $C_{27}H_{38}NO_{13}$ requires *m/z* 584.2343).

1-(3-Amino-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propan-2-yl 5-ethyl-2,4-bis(methoxymethoxy)benzoate (81). Compound **80** (200 mg, 0.34 mmol) was dissolved in EtOAc (3.4 mL) at the rt before Pd/C (20 mg, 10% w/w) was added. The reaction was stirred under a hydrogen atmosphere for 12 h. The solution was filtered through celite and the filtrate concentrated. The residue was purified via column

chromatography (SiO_2, 10% EtOAc in hexanes) to give **81** as a brown solid (157 mg, 83%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60 (s, 1H), 6.85 (s, 1H), 6.50 (s, 1H), 5.43 (m, 1H), 5.22 (s, 2H), 5.17 (s, 2H), 5.13 (s, 2H), 4.98 (s, 2H), 3.78 (s, 3H), 3.60 (s, 3H), 3.51 (s, 3H), 3.50 (s, 3H), 3.47 (s, 3H), 3.09 (m, 1H), 2.94 (m, 1H), 2.60 (q, *J* = 7.5 Hz, 2H), 1.36 (t, *J* = 6.2 Hz, 3H), 1.18 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.3, 159.1, 157.3, 153.7, 146.4, 139.7, 139.6, 132.5, 128.6, 127.1, 114.8, 112.0, 103.4, 102.2, 96.2, 95.8, 94.5, 70.5, 61.6, 58.1, 56.9, 56.8, 56.7, 31.8, 23.2, 20.7, 14.8; IR (film) ν_{max} 3458, 3368, 2983, 1610, 1579, 1463, 1423, 1352, 1242, 1209, 1053, 922cm^{-1}; HRMS (ES$^+$) *m/z* 553.2529 (M^+, $C_{27}H_{39}NO_{11}$ requires *m/z* 553.2523).

1-(3-Formamido-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propan-2-yl 5-ethyl-2,4-bis(methoxymethoxy)benzoate (82). Compound **81** (25 mg, 0.045 mmol) was dissolved in CH_2Cl_2 (0.5 mL) at 0 °C before PhOCHO (61.0 mg, 0.5 mmol) was added. The reaction was warmed to 30° C and stirred for 12 h. After concentration, the residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **82** as a yellow solid (20.5 mg, 78%), a mixture of rotamers: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.52 (s, 0.5H), 8.40 (m, 1H), 8.37 (s, 0.5H), 8.05 (s, 1H), 7.55 (s, 0.5 H), 7.53 (s, 1H), 6.94 (s, 0.5H), 6.85 (s, 1H), 5.40 (m, 1H), 5.19 (s, 2H), 5.18 (s, 2H), 5.17 (s, 2H), 4.99 (m, 2H), 3.85 (s, 3H), 3.58 (s, 3H), 3.51 (s, 3H), 3.49 (s, 3H), 3.47 (s, 3H), 3.08 (m, 1H), 2.95 (m, 1H), 2.57 (m, 2H), 1.32 (t, *J* = 6.6 Hz, 3H), 1.17 (t, *J* =7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.6, 162.5, 159.1, 159.0, 157.2, 157.1, 147.9, 147.0, 145.7, 143.1, 141.9, 132.4, 127.3, 127.0, 126.9, 125.6, 115.2, 109.2, 106.8, 103.5, 101.3, 101.2, 96.3, 96.0, 95.9, 94.6, 70.7, 70.6, 61.4, 61.3, 57.8, 57.6, 56.9, 56.8, 56.7, 56.6, 31.7, 31.6, 23.3,

20.5, 20.3, 14.8; IR (film) ν_{max} 3053, 2986, 1697, 1610, 1421,1047, 991cm^{-1}; HRMS (FAB$^+$) *m/z* 582.2530 (M + H, $C_{28}H_{40}NO_{12}$ requires *m/z* 582.2551).

1-(3-Benzamido-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propan-2-yl 5-ethyl-2,4-bis(methoxymethoxy)benzoate (83). Compound **81** (100 mg, 0.18mmol) was dissolved in THF (2 mL) before DCC (67 mg, 0.325 mmol) and benzoic acid (33.1 mg, 0.27 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h. The reaction was quenched by the addition of saturated aqueous ammonium chloride (10 mL). The solution was extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **83** as a pale yellow solid (79.0 mg, 67%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.28 (s, 1H), 8.30 (s, 1H), 7.93 (s, 1H), 7.90 (s, 1H), 7.49 (m, 4H), 6.85 (s, 1H), 5.40 (m, 1H), 5.24 (s, 2H), 5.20 (s, 2H), 5.17 (s, 2H), 5.07 (m, 2H), 3.89 (s, 3H), 3.53 (s, 3H), 3.49 (s, 3H), 3.48 (s, 3H), 3.45 (s, 3H), 3.05 (m, 1H), 2.95 (m, 1H), 2.55 (m, 2H), 1.33 (d, *J* = 6.3 Hz, 3H), 1.14 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 165.6, 159.0, 157.1, 147.2, 145.3, 142.5, 135.6, 132.4, 132.1, 129.0, 128.3, 127.5, 127.0, 125.5, 115.2, 108.8, 103.5, 101.6, 96.3, 96.0, 94.5, 70.8, 61.4, 57.7, 56.9, 56.8, 56.6, 34.3, 31.7, 23.3, 20.3, 14.8; IR (film) ν_{max} 3055, 2983, 1674, 1579, 1494, 1467, 1423, 1350, 1242, 1049, 921cm^{-1}; HRMS (ES$^+$) *m/z* 658.2861 (M + H, $C_{34}H_{44}NO_{12}$ requires *m/z* 658.2864).

1-(3-Formamido-2,5-dihydroxy-6-methoxyphenyl)propan-2-yl 5-ethyl-2,4-dihydroxybenzoate (84). Ester **82** (23.5 mg, 0.04 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and CH_3CN (0.2 mL) at 25 ºC before the addition of sodium iodide (109.2 mg, 0.728 mmol) and trimethylsilyl chloride (102.3 μM, 0.79 mmol). The turbid solution was

stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **84** (14.3 mg, 87%) as a red oil: ^{1}H NMR (CD_3OD, 400 MHz) δ 8.15 (s, 1H), 7.55 (s, 1H), 6.99 (s, 1H), 6.23 (s, 1H), 5.40 (m, 1H), 3.81 (s, 3H), 3.14 (m, 1H), 3.02 (m, 1H), 2.51 (m, 2H), 1.36 (t, *J* = 6.2 Hz, 3H), 1.15 (m, 3H); ^{13}C NMR (CD_3OD, 100 MHz) δ 170.3, 162.3, 162.0, 161.0, 144.9, 143.3, 140.0, 130.5, 123.3, 122.0, 121.0, 108.7, 104.4, 101.7, 71.6, 59.9, 30.7, 22.6, 19.2, 13.7; IR (film) ν_{max} 3350, 2964, 1610, 1578, 1242, 1082, 991cm^{-1}; HRMS (ES$^+$) *m/z* 406.1496 (M + H, $C_{20}H_{24}NO_8$ requires *m/z* 406.1502).

1-(3-Benzamido-2,5-dihydroxy-6-methoxyphenyl)propan-2-yl 5-ethyl-2,4-dihydroxybenzoate (85). Ester **83** (45 mg, 0.068 mmol) was dissolved in CH_2Cl_2 (0.3 mL) and CH_3CN (0.3 mL) at 25 ºC before the addition of sodium iodide (184.9 mg, 1.23 mmol) and trimethylsilyl chloride (173.2 μM, 1.34 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **85** (26.0 mg, 79%) as a red oil: ^{1}H NMR (CD_3OD, 400 MHz) δ 7.93 (m, 2H), 7.58 (m, 2H), 7.50 (m, 2H), 6.91 (s, 1H), 6.22 (s, 1H), 5.43 (m, 1H), 3.84 (s, 3H), 3.20 (m, 1H), 3.05 (m, 1H), 2.48 (q, *J* = 7.5 Hz, 2H), 1.38 (d, *J* = 6.2 Hz, 3H), 1.11 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (CD_3OD, 100 MHz) δ 170.3, 165.1, 162.3, 162.0, 161.0, 144.9, 143.3 (2), 140.0, 130.5, 123.3, 122.0 (2), 121.0, 108.7 (2), 104.4, 101.7, 71.6, 59.9, 30.7, 22.6, 19.2, 13.8; IR (film) ν_{max} 3398,

2985, 1670, 1527, 1373, 1153, 1093, 955cm^{-1}; HRMS (ES$^+$) *m/z* 482.1809 (M + H, $C_{26}H_{28}NO_8$ requires *m/z* 482.1815).

***tert*-Butoxy(2-methoxyphenoxy)diphenylsilane (88)**. 2-methoxyphenol (2 g, 16.1 mmol) was dissolved in THF (100 mL) and stirred at 0 ºC. NaH (60% in mineral oil, 0.46 g, 32.2 mmol) was added cautiously and stirred for 30 min. Diphenyl *tert*-butylsilyl chloride (8.8 g, 32.2 mmol) was added to the slurry and the mixture was stirred for 12 h before the addition of saturated aqueous ammonium chloride (100 mL). The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 8% EtOAc in hexanes) to afford **88** (45.3 mg, 79%) as clear oil (5.12 g, 84%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (m, 4H), 7.37 (m, 6H), 6.75 (m, 4H), 3.57 (s, 3H), 1.13 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.0, 145.5, 135.8, 134.1, 130.0, 127.9, 121.9, 121.0, 120.7, 112.8, 55.8, 27.1, 20.2; IR (film) ν_{max} 3070, 2931, 1589, 1504, 1427, 1226, 1114, 923cm^{-1}; HRMS (ES$^+$) *m/z* 379.1716 (M + H, $C_{23}H_{27}O_3Si$ requires *m/z* 379.1729).

1-Methoxy-3-(methoxymethoxy)benzene (89). 2-methoxyphenol (2 g, 16.1 mmol) was dissolved in THF (100 mL) and stirred at 0 ºC. NaH (60% in mineral oil, 0.46 g, 32.2 mmol) was added and stirred for 30 min. Chloromethyl methyl ether (5.4 mL, 6 mmol/mL, 32.2 mmol) was added to the slurry and the mixture was stirred for 12 h before the addition of saturated aqueous ammonium chloride (100 mL). The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 8% EtOAc in hexanes) to afford **89** (2.46 g, 91%) as clear oil: ^{1}H

NMR ($CDCl_3$, 400 MHz) δ 7.23 (t, *J* = 8.2 Hz, 1H), 6.69 (m, 2H), 6.60 (dd, *J* = 2.2 Hz, 8.2 Hz, 1H), 5.20 (s, 2H), 3.82 (s, 3H), 3.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.2, 158.9, 130.3, 108.8, 107.9, 103.0, 94.8, 56.4, 55.7; IR (film) ν_{max} 2985, 2960, 1508, 1466, 1188, 1078, 1007, 923cm^{-1}; HRMS (ES^+) *m/z* 191.0679 (M + Na, $C_9H_{12}O_3Na$ requires *m/z* 191.0684).

1-(3-*tert*-Butoxydiphenylsiloxy)-2-methoxyphenyl)propan-2-ol (90). Compound **88** (1.5 g, 3.97 mmol) was dissolved in THF (40 mL) before the addition of TMEDA (0.76 mL, 5.0 mmol). The solution was cooled to 0 ºC before ^{n}BuLi (1.9 mL, 4.76 mmol) was added dropwise to the stirred solution. The reaction was warmed to 25 ºC and stirred for 4 h. Upon cooling to 0 ºC, propylene oxide (0.56 mL, 7.94 mmol) was added and the mixture stirred for 2 h. The reaction was quenched by the addition of aqueous 0.5 M HCl to pH = 7. The aqueous layer was extracted with EtOAc (3 × 100 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to afford **90** (1.36 g, 79%) as a yellow oil: ^1H NMR ($CDCl_3$, 400 MHz) δ7.80 (m, 4H), 7.43 (m, 6H), 6.73 (d, J = 7.3 Hz, 1H), 6.64 (t, J = 7.8 Hz, 1H), 6.48 (d, J = 7.8 Hz, 1H), 4.10 (m, 1H), 4.00 (s, 3H), 2.84 (m, 2H), 2.48 (s, OH), 1.28 (d, J = 6.1 Hz, 3H), 1.19 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.1, 149.0, 135.6, 132.9, 132.8, 130.0, 127.9, 123.8, 123.6, 119.4, 68.6, 60.8, 40.4, 26.7, 23.2, 19.6; IR (film) ν_{max} 3421, 2931, 1595, 1473, 1375, 1112, 1047, 995cm^{-1}; HRMS (ES^+) *m/z* 437.2146 (M + H, $C_{26}H_{33}O_4Si$ requires *m/z* 437.2148).

1-(2-Methoxy-6-(methoxymethoxy)phenyl)propan-2-ol (91). Compound **89** (2.1 g, 12.5 mmol) was dissolved in THF (30 mL) before the addition of TMEDA (2.3 mL, 15.1

mmol). The solution was cooled to 0 ºC before ^{n}BuLi (7.55 mL, 15.1 mmol) was added dropwise to the stirred solution. The reaction was warmed to 25 ºC and stirred for 4 h. Upon cooling to 0 ºC, propylene oxide (3.5 mL, 50.0 mmol) was added and the mixture stirred for 2 h. The reaction was quenched by the addition of aqueous 0.5 M HCl to pH = 7. The aqueous layer was extracted with EtOAc (3 × 100 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 20% EtOAc in hexanes) to afford **91** (2.3 g, 82%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.16 (t, *J* = 8.3 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.61 (d, *J* = 8.3 Hz, 1H), 5.21 (m, 2H), 4.06 (m, 1H), 3.90 (s, 3H), 3.49 (s, 3H), 2.94 (m, 2H), 2.42 (s, OH), 1.24 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.0, 156.6, 128.0, 116.6, 107.4, 105.0, 94.9, 68.9, 56.6, 56.1, 33.1, 23.7; IR (film) ν_{max} 3439, 2968, 1595, 1471, 1256, 1153, 1014, 935cm^{-1}; HRMS (ES$^+$) *m/z* 249.1099 (M + Na, $C_{12}H_{18}O_4Na$ requires *m/z* 249.1103).

1-(2-Methoxy-6-(methoxymethoxy)phenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (92). 2,4-dihydroxy-5-chloro-benzoic acid (120 mg, 0.64 mmol) was dissolved in DMF: THF (1:3, 8 mL) before DMAP (140 mg, 1.15 mmol), DCC (237 mg, 1.15 mmol) and compound **91** (231 mg, 1.02 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h before the addition of saturated aqueous ammonium chloride (10 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **92** as a pale yellow solid (116 mg, 46%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.00 (s, 1H), 7.83 (s, 1H), 7.15 (m, 1H), 6.75 (d, J = 8.3 Hz, 1H), 6.57 (m, 2H), 5.43 (m, 1H), 5.22 (s, 2H), 3.82 (s, 3H), 3.51

(s, 3H), 3.18 (m, 1H), 3.04 (m, 1H), 1.40 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 162.6, 159.1, 157.1, 156.7, 130.7, 128.3, 114.9, 111.3, 107.9, 107.0, 104.6, 104.3, 94.8, 72.9, 56.6, 56.0, 29.8, 20.3; IR (film) ν_{max} 3406, 2985, 1668, 1604, 1481, 1299, 1159, 1070, 968cm^{-1}; HRMS (ES$^+$) *m/z* 419.0873 (M + Na, $C_{19}H_{21}O_7ClNa$ requires *m/z* 419.0874).

1-(3-*tert*-Butoxydiphenylsilyloxy)-2-methoxyphenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (93). 2,4-dihydroxy-5-chloro-benzoic acid (14 mg, 0.07 mmol) was dissolved in DMF: THF (1:3, 1 mL) before DMAP (12.4 mg, 0.10 mmol), DCC (21 mg, 0.10 mmol) and compound **90** (20 mg, 0.045 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h before the addition of saturated aqueous ammonium chloride (2 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **93** as a pale yellow solid (19.4 mg, 43%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83 (s, 1H), 7.70 (m, 4H), 7.38 (m, 6H), 6.68 (m, 1H), 6.58 (m, 2H), 6.38 (m, 1H), 5.90 (s, OH), 5.40 (m, 1H), 3.98 (s, 3H), 3.06 (m, 1H), 2.96 (m, 1H), 1.36 (d, *J* = 6.3 Hz, 3H), 1.10 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.5, 162.4, 156.8, 149.3, 148.8, 135.5, 132.7, 131.3, 130.1, 129.9, 127.8, 123.4, 123.3, 119.6, 111.1, 107.3, 104.0, 72.8, 60.8, 36.5, 26.6, 19.8, 19.5; IR (film) ν_{max} 3404, 3072, 2827, 1585, 1475, 1390, 1265, 1095, 1010, 937cm^{-1}; HRMS (ES$^+$) *m/z* 607.1926 (M + H, $C_{33}H_{36}ClO_7Si$ requires *m/z* 607.1919).

1-(2-Hydroxy-6-methoxyphenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (94). Ester **92** (22 mg, 0.056 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and CH_3CN (0.2 mL) at 25 ºC before the addition of sodium iodide (83.3 mg, 0.56 mmol) and trimethylsilyl

chloride (71 μM, 0.55 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **94** (16.8 mg, 86%) as a red oil:^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.87 (s, 1H), 7.10 (m, 1H), 6.62 (s, 1H), 6.50 (m, 2H), 5.19 (m, 1H), 3.81 (s, 3H), 3.15 (m, 1H), 3.01 (m, 1H), 1.44 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 162.8, 159.1, 157.6, 155.9, 130.7, 128.6, 111.7, 111.6, 109.1, 107.3, 104.5, 103.2, 73.7, 56.0, 29.8, 20.0; IR (film) ν_{max} 3490, 3080, 2915, 1665, 1620, 1480, 1475, 1110, 920cm^{-1}; HRMS (ES$^+$) *m/z* 353.0799 (M + H, $C_{17}H_{18}O_6Cl$ requires *m/z* 353.0792).

1-(3-Hydroxy-2-methoxyphenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (95). Ester **93** (22.4 mg, 0.038 mmol) was dissolved in THF (.4 mL) at rt before tetrabutyl ammonium fluoride (0.076 mL, 0.076 mmol) was cautiously added and stirred for 3 h. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate (5 mL). The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **95** (11.8 mg, 91%) as a red oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.90 (s, 1H), 7.79 (s, 1H), 6.95 (m, 1H), 6.85 (d, J = 6.7 Hz, 1H), 6.74 (d, J = 7.6 Hz, 1H), 6.59 (s, 1H), 5.42 (m, 1H), 3.83 (s, 3H), 3.07 (m, 1H), 2.95 (m, 1H), 1.35 (d, J = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.4, 161.3, 155.9, 148.0, 144.7, 128.9, 123.9, 121.4, 113.5, 110.0, 106.0, 107.0, 103.0, 71.3, 60.2, 35.1, 13.1; IR (film) ν_{max} 3413, 2925, 2853, 1666, 1618, 1487, 1473,

1298, 1157, 738cm^{-1}; HRMS (ES$^+$) *m/z* 353.0778 (M + H, $C_{17}H_{18}O_6Cl$ requires *m/z* 353.0792).

1-(2-Methoxy-3,6-bis(methoxymethoxy)phenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (96). 2, 4-dihydroxy-5-chloro-benzoic acid (520 mg, 2.8 mmol) was dissolved in DMF: THF (1:3, 20 mL) before DMAP (512 mg, 4.2 mmol), DCC (864 mg, 4.2 mmol) and compound **27** (800 mg, 2.9 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h before the addition of saturated aqueous ammonium chloride (20 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **96** as a pale yellow solid (668 mg, 53%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.00 (s, 1H), 7.87 (s, 1H), 6.97 (d, *J* = 9.0 Hz, 1H), 6.78 (d, *J* = 9.0 Hz, 1H), 6.57 (s, 1H), 6.20 (s, 1H), 5.44 (m, 1H), 5.16 (m, 2H), 5.12 (m, 2H), 3.91 (s, 3H), 3.51 (s, 3H), 3.50 (s, 3H), 3.16 (m, 1H), 3.04 (m, 1H), 1.39 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 162.6, 157.3, 151.6, 149.9, 145.4, 130.8, 121.2, 116.7, 111.4, 109.5, 107.7, 104.4, 96.3, 95.2, 72.7, 61.2, 56.6, 56.5, 30.7, 20.3; IR (film) ν_{max} 3325, 2937, 1666, 1618, 1485, 1371, 1251, 1153, 1051, 950cm^{-1}; HRMS (ES$^+$) *m/z* 457.1252 (M + H, $C_{21}H_{26}O_9Cl$ requires *m/z* 457.1265).

1-(2-Methoxy-3,6-bis(methoxymethoxy)-5-propionamidophenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (97). Compound **44** (80 mg, 0.17 mmol) was dissolved in THF (1.7 mL) before DCC (52.5 mg, 0.25 mmol) and propionic acid (16.4 mg, 0.22 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h before the addition of saturated aqueous ammonium chloride (10 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated.

The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **97** as a pale yellow solid (31 mg, 35%), a mixture of rotomers: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.43 (s, 1H), 8.11 (s, 1H), 7.84 (s, 1H), 6.55 (s, 1H), 5.36 (m, 1H), 5.18 (m, 2H), 4.97 (m, 2H), 3.86 (s, 3H), 3.62 (s, 3H), 3.48 (s, 3H), 3.00 (m, 1H), 2.98 (m, 1H), 2.38 (m, 2H), 1.34 (dd, *J* = 3.0 Hz, 6.3 Hz, 3H), 1.23 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.6, 169.1, 162.7, 157.7, 147.1, 144.9, 141.9, 130.8, 128.0, 124.6, 111.6, 109.0, 107.3, 104.4, 101.3, 95.9, 72.5, 61.4, 57.9, 56.9, 31.5, 31.3, 20.1, 10.0; IR (film) ν_{max} 3369, 2985, 1610, 1421, 1247, 1045, 896cm^{-1}; HRMS (ES$^+$) *m/z* 528.1618 (M + H, $C_{24}H_{31}NO_{10}Cl$ requires *m/z* 528.1636).

1-(3-Benzamido-6-methoxy-2,5-bis(methoxymethoxy)phenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (98). Compound **44** (80 mg, 0.17 mmol) was dissolved in THF (1.7 mL) before DCC (52.5 mg, 0.25 mmol) and benzoic acid (27 mg, 0.22 mmol) were added. The reaction was warmed to 50 °C and stirred for 12 h before the addition of saturated aqueous ammonium chloride (5 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 10% EtOAc in hexanes) to give **98** as a pale yellow solid (63 mg, 65%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.90 (s, 1H), 8.21 (d, J = 7.1 Hz, 1H), 8.06 (s, 1H), 7.66 (d, J = 7.4 Hz, 1H), 7.53 (m, 2H), 6.92 (s, 1H), 6.50 (s, 1H), 5.44 (m, 1H), 5.11 (m, 2H), 4.98 (m, 2H), 3.80 (s, 3H), 3.62 (s, 3H), 3.49 (s, 3H), 3.10 (m, 1H), 3.00 (m, 1H), 1.39 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.8, 164.0, 161.5, 152.6, 147.8, 140.8, 139.1, 136.6, 134.5, 131.8, 130.9, 129.1, 128.9, 125.3, 117.6, 113.2, 112.5, 104.0, 100.0, 95.8, 73.6, 61.4, 57.9, 56.6, 31.5, 20.2;

IR (film) ν_{max} 3327, 3053, 2935, 1697, 1610, 1375, 1110, 1049, 972cm^{-1}; HRMS (ES$^+$) *m/z* 576.1629 (M + H, $C_{28}H_{31}NO_{10}Cl$ requires *m/z* 576.1636).

1-(3,6-dihydroxy-2-methoxyphenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (99). Ester **96** (40 mg, 0.088 mmol) was dissolved in CH_2Cl_2 (0.5 mL) and CH_3CN (0.5 mL) at 25 ºC before the addition of sodium iodide (132 mg, 0.88 mmol) and trimethylsilyl chloride (111 μM, 0.88 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **99** (29 mg, 92%) as a clear oil: ^{1}H NMR (CD_3OD, 400 MHz) δ 7.55 (d, *J* = 8.7 Hz, 1H), 6.41 (d, *J* = 8.7 Hz, 1H), 6.24 (d, *J* = 8.7 Hz, 1H), 6.14 (m, 1H), 5.20 (m, 1H), 4.27 (s, OH), 3.62 (s, 3H), 2.88 (m, 1H), 2.81 (m, 1H), 1.16 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 164.0, 163.5, 149.3, 147.3, 142.8, 132.3, 118.5, 115.0, 110.8, 108.3, 105.6, 102.7, 72.2, 60.7, 30.7, 19.9; IR (film) ν_{max} 3400, 3053, 2935, 1645, 1618, 1485, 1373, 1186, 972, 806, 703 cm^{-1}; HRMS (ES$^+$) *m/z* 369.0738 (M + H, $C_{17}H_{18}O_7Cl$ requires *m/z* 369.0741).

1-(2,5-dihydroxy-6-methoxy-3-propionamidophenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (100). Ester **97** (20 mg, 0.038 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and CH_3CN (0.2 mL) at 25 ºC before the addition of sodium iodide (57 mg, 0.38 mmol) and trimethylsilyl chloride (50 μM, 0.38 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column

chromatography (SiO_2, 50% EtOAc in hexanes) to afford **100** (14.5 mg, 87%) as a clear oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.80 (s, 1H), 7.85 (s, 1H), 7.55 (s, 1H), 6.89 (s, 1H), 6.58 (s, 1H), 5.29 (m, 1H), 3.80 (s, 3H), 3.09 (m, 2H), 2.46 (m, 2H), 1.40 (t, *J* = 6.2 Hz, 3H), 1.26 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.3, 169.6, 162.7, 157.6, 144.4, 142.7, 141.0, 130.8, 122.6, 120.6, 111.7, 108.0, 107.3, 104.4, 73.1, 61.8, 31.3, 30.7, 20.1, 10.3; IR (film) ν_{max} 3342, 3060, 2933, 1664, 1616, 1535, 1371, 788, 704 cm^{-1}; HRMS (ES$^+$) *m/z* 438.0958 (M - H, $C_{20}H_{21}NO_8Cl$ requires *m/z* 438.0956).

1-(3-Benzamido-2,5-dihydroxy-6-methoxyphenyl)propan-2-yl 5-chloro-2,4-dihydroxybenzoate (101). Ester **98** (20 mg, 0.035 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and CH_3CN (0.2 mL) at 25 ºC before the addition of sodium iodide (52 mg, 0.35 mmol) and trimethylsilyl chloride (45 μM, 0.35 mmol). The turbid solution was stirred for 15 min before saturated $Na_2S_2O_3$ (10 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified via column chromatography (SiO_2, 50% EtOAc in hexanes) to afford **101** (15.4 mg, 91%) as a brown oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.90 (s, 1H), 8.21 (m, 2H), 7.89 (s, 1H), 7.67 (m, 1H), 7.54 (m, 2H), 6.94 (s, 1H), 5.53 (s, 1H), 5.31 (m, 1H), 5.08 (s, OH), 4.19 (s, 3H), 2.91 (m, 1H), 2.76 (m, 1H), 1.42 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 183.8, 182.3, 168.8, 164.0, 161.6, 159.0, 152.8, 147.1, 134.5, 131.5, 130.9, 129.1, 128.8, 121.6, 117.8, 113.4, 112.1, 100.5, 72.4, 62.3, 29.5, 20.5; IR (film) ν_{max} 3510, 3390, 2933, 1745, 1676, 1593, 1479, 1211, 908 cm^{-1}; HRMS (ES$^+$) *m/z* 486.0955 (M - H, $C_{24}H_{21}NO_8Cl$ requires *m/z* 486.0956).

Methyl 4,6-bis(tert-butyldimethylsilyloxy)-3-chloro-2-(hex-5-enyl)benzoate (110b). To a solution of **109** (3.69 g, 8.3 mmol) in THF (20 mL) was added Lithium diisopropylamide (LDA) (5.1 mL, 2 M in THF/Heptanes, 10.2 mmol) at –40^{o}C. After 10 min, to the mixture was slowly added 5-bromo-1-pentene (2.03 mL, 17.2 mmol) and stirred at –40^{o}C before a saturated aqueous NH_4Cl (5 mL) was added. The aqueous layer was extracted with EtOAc (3 $\times$ 50 mL). The combined organic layers were washed with H_2O (20 mL), saturated aqueous NaCl (20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified via chromatography (SiO_2, 2% EtOAc in hexanes) to afford **110b** (3.49g, 82% yield) as a colorless solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 6.30(s, 1H), 5.80(m, 1H), 4.94 (m, 2H), 3.86(s, 3H), 2.64(t,2 H, J = 8.0 Hz), 2.06(m, 2H), 1.56(tt, 2H, J = 7.1, 6.8 Hz), 1.45(tt, 2H, J = 7.0, 6.6 Hz), 0.98(s, 3H), 0.97(s, 9H), 0.23 (s, 6H), 0.21(s, 6H); ^{13}C NMR (CDCl3, 100 MHz) δ 168.72, 153.21, 151.57, 140.27, 139.22, 121.42, 118.94, 114.79, 109.42, 52.51, 33.84, 32.31, 29.44, 29.41, 26.05, 25.86, 18.76, 18.42, -3.96, -4.00; IR (film) ν_{max} 2946, 2931, 2855, 1738, 1582, 1450, 1408, 1356, 1254, 1199, 1108 cm^{-1}; HRMS (TOF-ES+) found 513.2604 ($M+H^+$), calcd 513.2623 for $C_{26}H_{46}O_4Si_2Cl$.

3-Chloro-2- (5-hexenyl)-4,6-dihydroxybenzoic acid (111b). To a solution of **110b** (5.6 g, 11 mmol) in THF (15 mL), MeOH (5 mL), and H_2O (5 mL) was added LiOH (1.3 g, 32 mmol) at rt. Affer 1hr, the The solvent was removed and EtOAc (100 mL) was added. The solution was washed with H_2O (2 $\times$ 50 mL), saturated aqueous NaCl (50 mL), dried (Na_2SO_4), filtered, and concentrated. The crude product was filtered through a plug of silica gel (15% EtOAC in hexanes). The eluent was concentrated and dissolved in HMPA (5 mL) before freshly prepared lithium 1-propanethiolate (48 mL, 24 mmol, 0.5 M

in HMPA) was added at rt. After 2.5 h, aqueous HCl (20 mL, 4 M) was added at 0 ^{o}C and stirred for 30 min. The mixture was diluted with EtOAc (200 mL) and the organic phase washed with aqueous HCl (3 $\times$ 20 mL, 2 M) and H_2O (3 $\times$ 20 mL). The solvent was removed before an aqueous solution of NaOH (30 mL, 2M) was added at 0 ^{o}C .The mixture was washed with EtOAc (2 $\times$ 20 mL) and treated with aqueous HCl (2 M) until pH = 3. The acidified aqueous phase was extracted with EtOAc (2 $\times$ 80 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated to afford **111b** (2.3 g, 76%) as a colorless solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 6.59(s, 1H), 5.82(m, 1H), 4.98(m, 2H), 3.18(t,2 H, J = 6.7 Hz), 2.13(m, 2H), 1.56-1.67(m,4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.41, 164.35, 157.16, 145.49, 138.73, 114.55, 114.24, 104.82, 102.37, 33.41, 32.70, 29.16, 29.09 IR (film) ν_{max} 3380, 3076, 2980, 1639, 1265, 1162 cm^{-1}; HRMS (TOF-ES+) found 271.0748 (M+H^{+}), calcd 271.0737 for $C_{13}H_{16}O_4Cl$.

2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenethyl 2-(but-3-enyl)-3-chloro-4,6-dihydroxybenzoate (116c). To a mixture of **32** (634mg, 2.0 mmol) and PPh_3 (524 mg, 2.0 mmol) in THF (14 mL) was added diisopropyl azodicarboxylate (404 mg, 2.0 mmol) at 0 ^{o}C. After 10 min, a solution of **104** (484 mg, 2.0 mmol) in THF (2 mL) was added to the mixture at 0 ^{o}C and warmed to rt. stirring for 10h. The solvent was removed under reduced pressure and the residue was purified via chromatography (SiO_2, 25% EtOAc in hexanes) to afford **116c** (974 mg, 90%) as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.70 (s, 1H), 6.57 (s, 1H), 5.78(m, 1H), 5.24 (s, 2H), 5.03 (s, 2H), 4.96(m, 2H), 4.54 (t, J = 7.3 Hz, 2 H), 3.99 (s, 3H), 3.57 (s, 3H), 3.52 (s, 3H), 3.24 (t, J = 7.5 Hz, 2 H), 3.09 (t, J = 8.2 Hz, 2 H), 2.21 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 163.4, 156.9, 153.6, 146.5, 146.4, 143.5, 139.6, 138.0, 127.5, 115.1, 114.3, 112.4, 107.0,

102.8, 102.4, 95.7, 64.8, 61.7, 58.2, 56.9, 33.5, 32.4, 25.0; IR (film) ν_{max} 3390, 2954, 1656, 1526, 1477, 1309, 1242, 1157 cm^{-1}; HRMS (TOF-ES+) found 564.1234 ($M+Na^+$), calcd 564.1249 for $C_{24}H_{28}NO_{11}ClNa$.

3-(2-chloro-3,5-dihydroxy-6-((2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenethoxy)carbonyl)phenyl)propanoic acid (118c). 116c (350 mg, 0.65 mmol) was dissolved in dioxane (4.5 mL) and water (1.5 mL) before 2, 6-lutidine (278 mg, 2.60 mmol), OsO_4 (4 wt. % in water, 3.0 mg, 0.01 mmol), and $NaIO_4$ (556 mg, 2.60 mmol) were added at rt. The slurry was stirred for 2 h and filtered through a plug of celite. Water (3 mL) and EtOAc (15 mL) was added to the eluent and the aqueous phase extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with H_2O (15 mL), saturated aqueous NaCl (15 mL), and dried (Na_2SO_4). The residue was redissolved in ^tBuOH (3.0 mL), 2-methyl-2-butene (3.0 mL) and water (0.6 mL). $NaClO_2$ (81 mg, 0.90 mmol) and NaH_2PO_4 (166 mg, 1.2 mmol) were added to the solution and stirred for 30 min at rt. Saturated aqueous NaH_2PO_4 (3 mL) was added and the aqueous layer extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with H_2O (10 mL), saturated aqueous NaCl (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified via chromatography (SiO_2, 40% EtOAc in hexanes) to afford **118c** (302 mg, 83% 2 steps) as a pale yellow solid: ^1H NMR ($CDCl_3$, 400MHz) δ 7.66 (s, 1H), 6.58 (s, 1H), 5.24 (s, 2H), 5.02 (s, 2H), 4.58(t, J = 6.9 Hz, 2 H), 3.98 (s, 3H), 3.54 (m, 6H), 3.26 (m, 4 H), 2.48 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.5, 170.6, 163.3, 156.8, 153.8, 146.4, 146.3, 141.6, 139.6, 127.6, 114.4, 113.0, 107.2, 103.3, 102.2, 95.8, 65.1, 61.7, 58.2, 57.0, 33.5, 28.4, 24.8; IR (film) ν_{max} 3380,

2956,1709, 1650, 1524, 1475, 1306, 1240, 1157 cm^{-1}; HRMS (TOF-ES+) found 582.1015 ($M+Na^+$), calcd 582.0990 for $C_{23}H_{26}NO_{13}ClNa$.

2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenethyl 3-chloro-4,6-dihydroxy-2-(pent-4-enyl)benzoate (116e). To a mixture of **32** (634mg, 2.0 mmol) and PPh_3 (524 mg, 2.0 mmol) in THF (14 mL) was added diisopropyl azodicarboxylate (404 mg, 2.0 mmol) at 0 ^oC. After 10 min, a solution of **111a** (514 mg, 2.0 mmol) in THF (2 mL) was added to the mixture at 0 ^oC and warmed to rt. stirring for 10h. The solvent was removed under reduced pressure and the residue was purified via chromatography (SiO_2, 25% EtOAc in hexanes) to afford **116e** (1.0 g, 90%) as a pale yellow solid: ^1H NMR ($CDCl_3$, 400MHz) δ 7.70 (s, 1H), 6.55 (s, 1H), 6.13 (bs, 1H), 5.75(m, 1H), 5.23 (s, 2H), 5.04 (s, 2H), 4.96(m, 2H), 4.54 (t, J = 7.3 Hz, 2 H), 3.99 (s, 3H), 3.57 (s, 3H), 3.52 (s, 3H), 3.25 (t, J = 7.8 Hz, 2 H), 3.00 (t, J = 8.2 Hz, 2 H), 2.06 (m, 2H), 1.56 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 163.5, 156.5, 153.6, 146.5, 146.4, 144.2, 139.7, 138.4, 127.5, 115.3, 114.1, 112.5, 107.2, 102.6, 102.4, 95.8, 64.8, 61.7, 58.2, 56.9, 34.4, 32.8, 28.9, 25.0 ; IR (film) ν_{max} 3390, 2954, 1656, 1526, 1477, 1309, 1242, 1157 cm^{-1}; HRMS (TOF-ES+) found 578.1393 ($M+Na^+$), calcd 578.1405 for $C_{25}H_{30}NO_{11}ClNa$.

4-(2-chloro-3,5-dihydroxy-6-((2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenethoxy)carbonyl)phenyl)butanoic acid (118e). 116e (361 mg, 0.65 mmol) was dissolved in dioxane (4.5 mL) and water (1.5 mL) before 2, 6-lutidine (278 mg, 2.60 mmol), OsO_4 (4 wt. % in water, 3.0 mg, 0.01 mmol), and $NaIO_4$ (556 mg, 2.60 mmol) were added at rt. The slurry was stirred for 2 h and filtered through a plug of celite. Water (3 mL) and EtOAc (15 mL) was added to the eluent and the aqueous phase extracted with EtOAc (3 $\times$ 15 mL). The combined organic layers were washed with H_2O

(15 mL), saturated aqueous NaCl (15 mL), and dried (Na_2SO_4). The residue was redissolved in ^tBuOH (3.0 mL), 2-methyl-2-butene (3.0 mL) and water (0.6 mL). $NaClO_2$ (81 mg, 0.90 mmol) and NaH_2PO_4 (166 mg, 1.2 mmol) were added to the solution and stirred for 30 min at rt. Saturated aqueous NaH_2PO_4 (3 mL) was added and the aqueous layer extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with H_2O (10 mL), saturated aqueous NaCl (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified via chromatography (SiO_2, 40% EtOAc in hexanes) to afford **118e** (291 mg, 78% 2 steps) as a pale yellow solid: ^1H NMR ($CDCl_3$, 400MHz) δ 7.71 (s, 1H), 6.57 (s, 1H), 5.24 (s, 2H), 5.03(s, 2H), 4.57(t, J = 7.0 Hz, 2 H), 3.99 (s, 3H), 3.59 (s, 3H), 3.53 (s, 3H), 3.25 (t, J = 7.3 Hz, 2H), 3.06 (m, 2H), 2.33 (t, J = 7.3 Hz, 2H), 1.80 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.0, 170.9, 163.6, 156.6, 153.8, 146.5, 146.1, 143.0, 139.6, 127.6, 114.2, 112.8, 107.1, 103.0, 102.1, 95.8, 64.9, 61.7, 58.3, 57.0, 34.2, 32.4, 24.9, 24.8, ; IR (film) ν_{max} 3360, 2927, 1709, 1650, 1524, 1475, 1306, 1240, 1157 cm^{-1}; HRMS (TOF-ES+) found 596.1155 ($M+Na^+$), calcd 596.1147 for $C_{24}H_{28}NO_{13}ClNa$.

MOM-protected Desmethyl Butyl-Radanamycin (120e). 118e (63 mg, 0.11 mmol) was dissolved in EtOH (2.0 mL) before 10% palladium on carbon (12 mg) was added. The mixture was purged with argon before H_2 gas was added. The heterogeneous mixture was stirred for 3 h and then filtered through a plug of celite. The eluent was concentrated and the residue redissoved in DMF (10 mL) before slow addition to a mixture of HATU (125 mg, 0.33 mmol), HOBt (45 mg, 0.33 mmol), and diisopropyl ethylamine (0.17 mL, 0.99 mmol) in DMF (100 mL) over 4 hours. Upon addition, the solution was heated at 70 ^oC for 15 h. The The solvent was removed by distillation at

reduced pressure. EtOAC (20 mL) was added to the residue and the resulting solution was washed with saturated aqueous NH_4Cl (3 × 5 mL), H_2O (5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 20% hexanes in EtOAc) to afford **120e** (45 mg, 77% yield, 2 steps) as a colorless solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.28 (s, 1H), 6.99 (s, 1H), 6.50 (s, 1H), 5.18 (dd, *J* = 6.2, 23.0 Hz, 2H), 5.10 (m, 1H), 4.80 (dd, *J* = 6.5, 24.1 Hz, 2H), 4.12 (m, 1H), 3.96 (s, 3H), 3.54 (s, 3H), 3.50 (s, 3H), 3.25 (m, 1H), 3.04 (m, 2H), 2.71 (m, 1H), 2.19 (m, 1H), 1.94 (m, 1H), 1.82 (m, 1H), 1.79 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.3, 171.9, 163.2, 156.8, 149.3, 148.9, 147.6, 143.2, 127.8, 126.7, 116.6, 114.2, 106.9, 102.9, 100.8, 95.8, 67.6, 61.4, 58.2, 56.8, 34.5, 32.3, 25.9, 25.2; IR (film) ν_{max} 3163, 2920, 1643, 1597, 1478, 1128, 1018 cm^{-1}; HRMS (TOF-ES+) found 526.1470 ($M+H^+$), calcd 526.1480 for $C_{24}H_{29}NO_{10}Cl$.

Desmethyl Butyl Radanamycin (121e). MOM-protected radanamycin **120e** (41 mg, 0.078 mmol) was dissolved in CH_3CN (1.2 mL) and CH_2Cl_2 (1.2 mL) before NaI (88 mg, 0.78 mmol) and TMSCl (0.104 mL, 0.78 mmol) were added at rt. Upon addition, the solution turned cloudy and yellow. After 20 minutes, a saturated aqueous solution of $Na_2S_2O_4$ (2 mL) was added to the mixture and stirred for 10 min. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic layers were washed with H_2O (2 × 5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 10% MeOH in CH_2Cl_2) to afford **121e** (27 mg, 80% yield) as a colorless solid: ^{1}H NMR (acetone-d_6, 400MHz) δ 7.72 (s, 1H), 6.68 (s, 1H), 6.48 (s, 1H), 4.77 (m, 1H), 4.58 (m, 1H), 3.93 (s, 3H), 3.40 (m, 1H), 3.00 (m, 2H), 2.78 (m, 1H), 2.69 (m, 1H), 1.98 (m, 1H), 1.82 (m, 1H),

1.59 (m, 1H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 175.8, 169.8, 159.4, 156.9, 147.3, 146.2, 143.4, 142.0, 121.1, 120.8, 115.9, 113.2, 110.5, 102.4, 66.7, 60.2, 34.9, 31.7, 26.4, 24.1; IR (film) ν_{max} 3520, 3336, 3002, 1704, 1649, 1444, 1367 1239, 1172 cm^{-1}; HRMS (TOF-ES+) found 438.0949 (M+H$^+$), calcd 438.0956 for $C_{20}H_{21}NO_8Cl$.

2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenethyl 3-chloro-2-(hex-5-enyl)-4,6-dihydroxybenzoate (116f). To a mixture of **32** (634mg, 2.0 mmol) and PPh_3 (524 mg, 2.0 mmol) in THF (14 mL) was added diisopropyl azodicarboxylate (404 mg, 2.0 mmol) at 0 ^{o}C. After 10 min, a solution of **111b** (542 mg, 2.0 mmol) in THF (2 mL) was added to the mixture at 0 ^{o}C and warmed to rt. stirring for 10h. The solvent was removed under reduced pressure and the residue was purified via chromatography (SiO_2, 25% EtOAc in hexanes) to afford **116f** (1.0 g, 90%) as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.70 (s, 1H), 6.54 (s, 1H), 5.76(m, 1H), 5.24 (s, 2H), 5.02 (s, 2H), 4.94(m, 2H), 4.54 (t, J = 7.4 Hz, 2 H), 3.99 (s, 3H), 3.57 (s, 3H), 3.53 (s, 3H), 3.25 (t, J = 7.3 Hz, 2 H), 2.99 (t, J = 8.0 Hz, 2 H), 2.02 (m, 2H), 1.51 (m, 2H), 1.40 (m, 2H); ^{13}C NMR (CDC_{l3}, 100 MHz) δ 171.0, 163.5, 156.5, 153.6, 146.5, 146.4, 144.3, 139.6, 139.0, 127.5, 115.0, 114.1, 112.4, 107.1, 102.6, 102.4, 95.8, 64.8, 61.7, 58.2, 57.0, 33.9, 33.1, 29.6, 29.4, 25.0; IR (film) ν max 3365, 2930, 1656, 1526, 1477, 1309, 1242, 1157 cm-*1*; HRMS (TOF-ES+) found 592.1552 (M+Na+), calcd 592.1562 for $C_{26}H_{32}NO_{11}ClNa$.

5-(2-chloro-3,5-dihydroxy-6-((2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenethoxy)carbonyl)phenyl)pentanoic acid (118f). 116f (370 mg, 0.65 mmol) was dissolved in dioxane (4.5 mL) and water (1.5 mL) before 2, 6-lutidine (278 mg, 2.60 mmol), OsO_4 (4 wt. % in water, 3.0 mg, 0.01 mmol), and $NaIO_4$ (556 mg, 2.60 mmol) were added at rt. The slurry was stirred for 2 h and filtered through a plug of celite.

Water (3 mL) and EtOAc (15 mL) was added to the eluent and the aqueous phase extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with H_2O (15 mL), saturated aqueous NaCl (15 mL), and dried (Na_2SO_4). The residue was redissolved in ^tBuOH (3.0 mL), 2-methyl-2-butene (3.0 mL) and water (0.6 mL). $NaClO_2$ (81 mg, 0.90 mmol) and NaH_2PO_4 (166 mg, 1.2 mmol) were added to the solution and stirred for 30 min at rt. Saturated aqueous NaH_2PO_4 (3 mL) was added and the aqueous layer extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with H_2O (10 mL), saturated aqueous NaCl (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified via chromatography (SiO_2, 40% EtOAc in hexanes) to afford **118f** (305 mg, 80% 2 steps) as a pale yellow solid: ^1H NMR ($CDCl_3$, 400MHz) δ 7.82 (s, 1H), 6.79(s, 1H), 5.44 (s, 2H), 5.07 (s, 2H), 4.55(t, J = 6.8 Hz, 2 H), 3.98 (s, 3H), 3.57 (m, 3H), 3.52 (s, 2H), 3.03 (t, J = 8.2 Hz, 2H), 2.99 (m, 2H), 2.33 (t, J = 7.2 Hz, 2H), 1.62 (m, 2H), 1.53 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 179.8, 170.9, 163.3, 156.7, 153.6, 146.4, 146.2, 143.8, 139.6, 127.6, 114.2, 112.4, 107.0, 102.8, 102.3, 95.7, 64.9, 61.7, 58.2, 57.0, 34.0, 32.8, 29.1, 25.2, 25.0, ; IR (film) ν_{max} 3155, 2927, 1709, 1650, 1524, 1475, 1306, 1240, 1159 cm^{-1}; HRMS (TOF-ES+) found 610.1299 ($M+Na^+$), calcd 610.1303 for $C_{25}H_{30}NO_{13}ClNa$.

MOM-protected desmethyl pentenyl Radanamycin (120f). 118f (65 mg, 0.11 mmol) was dissolved in EtOH (2.0 mL) before 10% palladium on carbon (12 mg) was added. The mixture was purged with argon before H_2 gas was added. The heterogeneous mixture was stirred for 3 h and then filtered through a plug of celite. The eluent was concentrated and the residue redissoved in DMF (10 mL) before slow addition to a mixture of HATU (125 mg, 0.33 mmol), HOBt (45 mg, 0.33 mmol), and diisopropyl ethyl

amine (0.17 mL, 0.99 mmol) in DMF (100 mL) over 4 hours. Upon addition, the solution was heated at 70 ^{o}C for 15 h. The The solvent was removed by distillation at reduced pressure. EtOAC (20 mL) was added to the residue and the resulting solution was washed with saturated aqueous NH_4Cl (3 $\times$ 5 mL), H_2O (5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 20% hexanes in EtOAc) to afford **120f** (47mg, 80% yield, 2 steps) as a colorless solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.41 (s, 1H), 7.04 (s, 1H), 6.51 (s, 1H), 5.17 (m, 2H), 4.91 (m, 1H), 4.88 (m, 1H), 4.80 (m, 1H), 4.56 (m, 1H), 3.83 (s, 3H), 3.51 (s, 6H), 3.26 (m, 1H), 3.11 (m, 1H), 2.70 (m, 2H), 2.40 (m, 1H), 2.22 (m, 1H), 1.43 (m, 1H), 1.20 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.7, 171.8, 163.9, 156.8, 148.9, 148.8, 147.6, 144.1, 127.2, 127.0, 116.2, 114.2, 106.4, 102.7, 100.9, 95.7, 65.6, 61.6, 57.7, 56.7, 34.2, 31.6, 28.4, 25.0, 24.8; IR (film) $\nu_{max\ max}$ 3126, 2923, 1650, 1596, 1487, 1128, 1018 cm^{-1}; HRMS (TOF-ES+) found 540.1648 ($M+H^+$), calcd 540.1636 for $C_{25}H_{31}NO_{10}Cl$.

Desmethyl pentenyl Radanamycin (121f). MOM-protected radanamycin **120f** (42 mg, 0.078 mmol) was dissolved in CH_3CN (1.2 mL) and CH_2Cl_2 (1.2 mL) before NaI (88 mg, 0.78 mmol) and TMSCl (0.104 mL, 0.78 mmol) were added at rt. Upon addition, the solution turned cloudy and yellow. After 20 minutes, a saturated aqueous solution of $Na_2S_2O_4$ (2 mL) was added to the mixture and stirried for 10 min. The aqueous phase was extracted with EtOAc (3 $\times$ 5 mL) and the combined organic layers were washed with H_2O (2 $\times$ 5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 10% MeOH in CH_2Cl_2) to afford **121f** (31 mg, 88% yield) as a colorless solid: ^{1}H NMR (acetone-d_6,

400MHz) δ 10.52 (bs, 1H), 9.33 (bs, 1H), 8.19 (bs, 1H), 7.84 (s, 1H), 6.75 (s, 1H), 6.46 (s, 1H), 5.11 (m, 1H), 4.61 (m, 1H), 3.66 (s, 3H), 3.38 (m, 1H), 2.99 (m, 1H), 2.51 (m, 1H), 2.22 (m, 1H), 2.12 (m, 2H), 1.58 (m, 1H), 1.37 (m, 2H), 1.16 (m, 1H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 176.6, 169.9, 159.7, 156.9, 147.8, 146.0, 143.6, 142.5, 120.6, 120.1, 115.7, 113.2, 110.0, 102.2, 63.5, 60.4, 33.4, 30.8, 28.5, 25.4, 24.2; IR (film) ν_{max} 3320, 3132, 3002, 1706, 1656, 1367, 1307, 1240, 1142 cm^{-1}; HRMS (TOF-ES+) found 452.1117 (M+H$^+$), calcd 452.1112 for $C_{21}H_{23}NO_8Cl$.

Desmethyl pentenyl Radanamycin quinone (122f). To a solution of **121f** (45 mg, 0.1 mmol) in EtOAc(2 mL) and MeOH(0.4 mL) was added 10% palladium on carbon (42 mg) and stirred in open air at rt. After 2h, the mixture was filtered through a plug of celite. The eluent was concentrated and the residue was purified via chromatography (SiO_2, 4% MeOH in CH_2Cl_2) to afford **122f** (36 mg, 80% yield) as a yellow solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.30 (s, 1H), 8.99 (s, 1H), 8.84 (s, 1H), 6.91 (s, 1H), 6.46 (s, 1H), 4.63 (t, J = 5.5 Hz, 2H), 4.06 (s, 3H), 2.97 (t, J = 5.9 Hz, 2H), 2.80 (J = 7.9 Hz, 2H), 2.61 (J = 6.5 Hz, 2H), 1.89 (m, 2H), 1.43 (m, 2H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 185.2, 183.7, 173.8, 173.7, 166.8, 157.9, 156.8, 143.6, 140.9, 126.8, 113.9, 111.7, 110.8, 102.6, 64.3, 61.3, 37.2, 31.4, 28.0, 27.1, 23.6; IR (film) ν_{max} 2577, 3320, 2957, 2891, 1716, 1659, 1607, 1400, 1232, 1119, 1057 cm^{-1}; HRMS (TOF-ES+) found 450.0946 (M+H$^+$), calcd 450.0956 for $C_{21}H_{21}NO_8Cl$.

1-(2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)propan-2-yl 3-chloro-2-(hex-5-enyl)-4,6-dihydroxybenzoate (116i). To a mixture of **111b** (350 mg, 1.29 mmol) and **34** (555 mg, 1.68 mmol) in THF (18 mL) was added DCC (399 mg, 1.94 mmol) and DMAP (205 mg, 1.68 mmol) at rt. After 10 min, the mixture was heated to 50 ^{o}C for 10

h. The solvent was removed and the residue dissolved in EtOAC (40 mL), washed with saturated aqueous NH_4Cl (10 mL), H_2O (10 mL) and saturated aqueous NaCl (10 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 25% EtOAc in hexanes) to afford **116i** (504 mg, 68% yield) as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.68(s, 1H), 6.53(s, 1H), 5.65(m, 1H), 5.60(m, 1H), 5.22(s, 2H), 5.05(s, 2H), 4.96(m, 2H), 3.97(s, 3H), 3.56(s, 2H), 3.52(s, 2H), 3.21(d, 2H, J = 6.5 Hz), 3.10(m,1 H), 3.01(m, 1H), 2.07(t, 2 H, J = 6.8 Hz), 1.51-1.61(m,4 H), 1.36(d, 3H, J = 6.4 Hz); ^{13}C NMR (CDCl3, 100 MHz) δ 170.6, 163.4, 156.3, 153.6, 146.4, 146.3, 144.2, 139.6, 139.0, 127.4, 115.0, 114.0, 112.4, 107.4, 102.5, 102.3, 95.9, 61.5, 58.3, 56.9, 34.1, 33.1, 31.2, 29.7, 29.6, 19.8; IR (film) ν_{max} 3290, 2974, 1656, 1526, 1477, 1309, 1242, 1157 cm^{-1}; HRMS (TOF-ES+) found 606.1713 ($M+Na^+$), calcd 606.1718 for $C_{27}H_{34}Cl\ NO_{11}Na$.

5-(2-chloro-3,5-dihydroxy-6-((1-(2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)propan-2-yloxy)carbonyl)phenyl)pentanoic acid (118i). 116i (256 mg, 0.44 mmol) was dissolved in dioxane (3.0 mL) and water (1.0 mL) before 2, 6-lutidine (188 mg, 1.76 mmol), OsO_4 (4 wt. % in water, 3.0 mg, 0.01 mmol), and $NaIO_4$ (377 mg, 1.76 mmol) were added at rt. The slurry was stirred for 2 h and filtered through a plug of celite. Water (3 mL) and EtOAc (15 mL) was added to the eluent and the aqueous phase extracted with EtOAc (3 $\times$ 15 mL). The combined organic layers were washed with H_2O (15 mL), saturated aqueous NaCl (15 mL), and dried (Na_2SO_4). The residue was redissolved in ^{t}BuOH (3.0 mL), 2-methyl-2-butene (3.0 mL) and water (0.6 mL). $NaClO_2$ (81 mg, 0.90 mmol) and NaH_2PO_4 (166 mg, 1.2 mmol) were added to the solution and stirred for 30 min at rt. Saturated aqueous NaH_2PO_4 (3 mL) was added and

the aqueous layer extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with H_2O (10 mL), saturated aqueous NaCl (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified via chromatography (SiO_2, 40% EtOAc in hexanes) to afford **118i** (200 mg, 79% 2 steps) as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 500MHz) δ 7.58(s, 1H), 6.44(s, 1H), 5.53(m, 1H), 5.60(m, 1H), 5.13(s, 2H), 4.79(d, 1H, J = 5.1 Hz), 4.62(d, 1H, J = 5.1 Hz), 3.78(s, 3H), 3.45(s, 3H), 3.37(dd, 1H, J = 3.2, 11.1 Hz), 3.26(s, 3H), 2.93(m,1 H), 2.89(m, 1H), 2.62(m, 1H), 2.35(m, 1 H), 2.13(m, 1 H), 1.32(m, 2H), 1.23(d, 3H, J = 6.7 Hz), 0.94 (m 1H); ^{13}C NMR (CDCl3, 125 MHz) δ 176.4, 171.3, 163.2, 156.3, 148.9, 148.7, 146.9, 143.8, 126.7, 124.7, 115.6, 114.0, 106.7, 102.3, 100.6, 95.4, 73.0, 61.0, 57.0, 56.3, 38.7, 34.0, 30.7, 28.0, 24.4, 18.7; IR (film) ν_{max} 3099, 2933, 1709, 1650, 1524, 1475, 1309, 1240, 1157 cm^{-1}; HRMS (TOF-ES+) found 624.1454 ($M+Na^+$), calcd 624.1460 for $C_{26}H_{32}Cl\,NO_{13}Na$.

MOM-protected pentenyl Radanamycin (120i). 118i (75 mg, 0.12 mmol) was dissolved in EtOH (2.0 mL) before 10% palladium on carbon (15 mg) was added. The mixture was purged with argon before H_2 gas was added. The heterogeneous mixture was stirred for 3 h and then filtered through a plug of celite. The eluent was concentrated and the residue redissoved in DMF (10 mL) before slow addition to a mixture of HATU (137 mg, 0.36 mmol), HOBt (49 mg, 0.36 mmol), and diisopropyl ethyl amine (0.19 mL, 1.08 mmol) in DMF (110 mL) over 4 hours. Upon addition, the solution was heated at 70 ^{o}C for 15 h. The The solvent was removed by distillation at reduced pressure. EtOAC (20 mL) was added to the residue and the resulting solution was washed with saturated aqueous NH_4Cl (3 × 5 mL), H_2O (5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via

chromatography (SiO_2, 20% hexanes in EtOAc) to afford **120i** (57mg, 80% yield, 2 steps) as a colorless solid: ^{1}H NMR ($CDCl_3$, 500MHz) δ 7.40(s, 1H), 6.94(s, 1H), 6.42(s, 1H), 5.38(m, 1H), 5.13(s, 2H), 4.95(s, 2H), 3.88(s, 3H), 3.46(s, 2H), 3.43(s, 2H), 3.12(d, 2H, J = 5.2 Hz), 2.96(m,1 H), 2.92(m, 1H), 2.30(t, 2 H, J = 5.8 Hz), 1.65(m, 2 H), 1.53(m, 2 H), 1.28(d, 3H, J = 6.4 Hz); ^{13}C NMR (CDCl3, 125 MHz) δ 178.5, 165.9, 162.8, 155.9, 153.1, 145.8, 145.6, 143.0, 139.1, 126.8, 113.5, 112.0, 106.9, 102.2, 101.6, 95.3, 72.0, 61.0, 57.8, 56.4, 33.6, 32.3, 30.6, 28.7, 24.8, 19.2; IR (film) ν_{max} 3123, 2920, 1648, 1597, 1487, 1128, 1018 cm^{-1}; HRMS (TOF-ES+) found 554.1770 ($M+H^+$), calcd 554.1793 for $C_{26}H_{33}Cl\,NO_{10}$.

Pentenyl Radanamycin (121i). MOM-protected radanamycin **120i** (80 mg, 0.144 mmol) was dissolved in CH_3CN (1.5 mL) and CH_2Cl_2 (1.5 mL) before NaI (216 mg, 1.44 mmol) and TMSCl (0.182 mL, 1.44 mmol) were added at rt. Upon addition, the solution turned cloudy and yellow. After 20 minutes, a saturated aqueous solution of $Na_2S_2O_4$ (2 mL) was added to the mixture and stirried for 10 min. The aqueous phase was extracted with EtOAc (3 $\times$ 5 mL) and the combined organic layers were washed with H_2O (2 $\times$ 5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 10% MeOH in CH_2Cl_2) to afford **121i** (61 mg, 90% yield) as a colorless solid: ^{1}H NMR (acetone-d_6, 500MHz) δ 9.03(s, 1H), 8.15(s, 1H), 7.81(s, 1H), 7.75(s, 1H), 6.70(s, 1H), 6.45(s, 1H), 5.90(m, 1H), 3.58(s, 1H), 3.14(m, 1H), 2.89(m, 1H), 2.23(m, 2H), 2.05(m, 1H), 1.64(m, 2H), 1.41-1.50(m, 4H), 1.12(m, 1H), 1.00(m, 1H); ^{13}C NMR (Acetone-d_6, 125 MHz) δ 177.1, 168.0, 155.1, 154.9, 148.3, 146.2, 144.0, 139.7, 121.1, 120.9, 116.8, 116.0, 112.3, 102.5, 70.0, 60.7, 33.3, 31.8, 30.9, 28.5, 26.1, 21.0; IR (film) ν_{max} 3320, 3132, 3002, 1706, 1656, 1367,

1307, 1240, 1142 cm^{-1}; HRMS (TOF-ES+) found 488.1093 ($M+Na^+$), calcd 488.1088 for $C_{22}H_{24}Cl\ NO_8Na$.

Pentenyl Radanamycin quinone (122i). To a solution of **121i** (30 mg, 0.06 mmol) in EtOAc (2 mL) and MeOH(0.4 mL) was added 10% palladium on carbon (30 mg) and stirred in open air at rt. After 2h, the mixture was filtered through a plug of celite. The eluent was concentrated and the residue was purified via chromatography (SiO_2, 4% MeOH in CH_2Cl_2) to afford **122i** (21 mg, 75% yield) as a yellow solid: ^{1}H NMR (acetone-d, 500MHz) δ 9.18(s, 1H), 8.86(s, 1H), 8.84(s, 1H), 6.92(s, 1H), 6.44(s, 1H), 5.40(m, 1H), 4.03(s, 3H), 2.96(m, 1H), 2.74(m, 1H), 2.67(m, 2H), 2.53(m, 1H), 1.95(m, 1H), 1.85(m, 1H), 1.65(m, 1H), 1.49(d, 3H, J = 5.1 Hz), 1.18(m, 2H); ^{13}C NMR (Acetone-d_6, 125 MHz) δ185.6, 184.3, 174.3, 166.8, 158.0, 157.2, 157.1, 144.0, 141.5, 127.0, 114.2, 111.9, 103.0, 73.0, 61.8, 37.7, 31.8, 30.9, 27.7, 21.7, 14.5; IR (film) ν_{max} 3467, 3310, 2993, 2898, 1717, 1659, 1609, 1400, 1233, 1120, 1057 cm^{-1}; HRMS (TOF-ES+) found 464.1100 ($M+H^+$), calcd 464.1112 for $C_{22}H_{23}Cl\ NO_8$.

Compound (116g). To a mixture of **33** (662 mg, 2.0 mmol) and PPh_3 (524 mg, 2.0 mmol) in THF (14 mL) was added diisopropyl azodicarboxylate (404 mg, 2.0 mmol) at 0 ^oC. After 10 min, a solution of **111b** (542 mg, 2.0 mmol) in THF (2 mL) was added to the mixture at 0 ^oC and warmed to rt. stirring for 10h. The solvent was removed under reduced pressure and the residue was purified via chromatography (SiO_2, 25% EtOAc in hexanes) to afford **116g** (958 mg, 82%) as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 500MHz) δ 7.65 (s, 1H), 6.56 (s, 1H), 6.13 (m, 1H), 5.79 (m, 1H), 5.21 (s, 2H), 5.02 (s, 2H), 4.94 (m, 2H), 4.42 (t, J = 6.7 Hz), 3.96 (s, 3H), 3.56 (s, 2H), 3.54 (s, 2H), 3.11 (t, J = 8.0 Hz, 2H), 2.87 (t, J = 7.7 Hz, 2H), 2.10 (m, 4H), 1.58 (m, 2H), 1.51 (m, 2H); ^{13}C

NMR ($CDCl_3$, 125 MHz) δ 170.4, 162.9, 156.0, 152.8, 146.0, 145.3, 143.8, 139.4, 138.4, 131.0, 114.4, 113.5, 111.5, 106.8, 102.2, 101.7, 95.6, 65.5, 61.0, 57.6, 56.4, 33.4, 32.5, 29.2, 29.1, 28.6, 21.6; IR (film) ν_{max} 3160, 2735, 1656, 1526, 1477, 1309, 1242, 1157 cm^{-1}; HRMS (TOF-ES+) found 601.2171 ($M+NH_4^+$), calcd 601.2164 for $C_{27}H_{38}Cl\ N_2O_{11}$.

Compound (118g). 116g (380 mg, 0.65 mmol) was dissolved in dioxane (4.5 mL) and water (1.5 mL) before 2, 6-lutidine (278 mg, 2.60 mmol), OsO_4 (4 wt. % in water, 3.0 mg, 0.01 mmol), and $NaIO_4$ (556 mg, 2.60 mmol) were added at rt. The slurry was stirred for 2 h and filtered through a plug of celite. Water (3 mL) and EtOAc (15 mL) was added to the eluent and the aqueous phase extracted with EtOAc (3 $\times$ 15 mL). The combined organic layers were washed with H_2O (15 mL), saturated aqueous NaCl (15 mL), and dried (Na_2SO_4). The residue was redissolved in ^tBuOH (3.0 mL), 2-methyl-2-butene (3.0 mL) and water (0.6 mL). $NaClO_2$ (81 mg, 0.90 mmol) and NaH_2PO_4 (166 mg, 1.2 mmol) were added to the solution and stirred for 30 min at rt. Saturated aqueous NaH_2PO_4 (3 mL) was added and the aqueous layer extracted with EtOAc (3 $\times$ 15 mL). The combined organic layers were washed with H_2O (10 mL), saturated aqueous NaCl (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified via chromatography (SiO_2, 40% EtOAc in hexanes) to afford **118g** (313 mg, 80% 2 steps) as a pale yellow solid: ^1H NMR ($CDCl_3$, 400MHz) δ 7.63 (s, 1H), 6.55 (s, 1H), 5.23(s, 2H), 5.05 (s, 2H), 4.43 (d, J = 6.8 Hz, 2H), 3.95 (s, 3H), 3.57 (s, 3H), 3.53 (s, 3H), 3.10 (t, J = 8.0 Hz, 2H), 2.84 (t, J = 7.9 Hz, 2H), 2.40 (m, 2H), 2.07 (m, 2H), 1.76 (m, 2H), 1.64 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.4, 170.9, 163.5, 156.5, 153.2, 146.5, 145.7, 143.6, 139.8, 131.5, 114.1, 111.9, 107.1, 102.8, 102.1, 95.8, 66.0, 61.6, 58.2, 57.0, 33.9, 32.9, 29.4, 29.0, 25.3, 22.0; IR (film) ν_{max} 3080, 2926, 1709,

1650, 1524, 1475, 1306, 1240, 1158 cm^{-1}; HRMS (TOF-ES+) found 624.1439 ($M+Na^+$), calcd 624.1460 for $C_{26}H_{32}Cl\ NO_{13}Na$.

Macrocycle (120g). 118g (66 mg, 0.11 mmol) was dissolved in EtOH (2.0 mL) before 10% palladium on carbon (12 mg) was added. The mixture was purged with argon before H_2 gas was added. The heterogeneous mixture was stirred for 3 h and then filtered through a plug of celite. The eluent was concentrated and the residue redissoved in DMF (10 mL) before slow addition to a mixture of HATU (125 mg, 0.33 mmol), HOBt (45 mg, 0.33 mmol), and diisopropyl ethyl amine (0.17 mL, 0.99 mmol) in DMF (100 mL) over 4 hours. Upon addition, the solution was heated at 70 ^oC for 15 h. The The solvent was removed by distillation at reduced pressure. EtOAC (20 mL) was added to the residue and the resulting solution was washed with saturated aqueous NH_4Cl (3 $\times$ 5 mL), H_2O (5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 20% hexanes in EtOAc) to afford **120g** (44 mg, 72% yield, 2 steps) as a colorless solid: ^1H NMR ($CDCl_3$, 500MHz) δ 8.23 (s, 1H), 6.97 (s, 1H), 6.42 (s, 1H), 5.26 (m, 2H), 5.13 (s, 2H), 4.52 (m, 2H), 3.88 (s, 3H), 3.60 (m, 2H), 3.51(s, 3H), 3.49 (s, 3H), 2.98 (m, 1H), 2.87 (m, 2H), 2.69 (m, 1H), 2.34 (m, 2H), 2.26 (m, 1H), 1.89 (m, 1H), 1.74 (m, 1H), 1.50 (m, 2H), 1.24 (m, 1H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.1, 171.0, 163.1, 156.8, 148.9, 148.3, 147.6, 143.7, 129.6, 127.3, 115.4, 114.2, 106.9, 102.7, 100.6, 95.7, 64.6, 61.5, 58.0, 56.8, 33.4, 32.3, 29.8, 28.0, 25.6, 21.5; IR (film) ν_{max} 3133, 2929, 1651, 1597, 1487, 1128, 1018 cm^{-1}; HRMS (TOF-ES+) found 554.1770 ($M+H^+$), calcd 554.1793 for $C_{26}H_{33}Cl\ NO_{10}$.

Macrocycle (121g). MOM-protected radanamycin **120g** (43 mg, 0.078 mmol) was dissolved in CH_3CN (1.2 mL) and CH_2Cl_2 (1.2 mL) before NaI (88 mg, 0.78 mmol) and TMSCl (0.104 mL, 0.78 mmol) were added at rt. Upon addition, the solution turned cloudy and yellow. After 20 minutes, a saturated aqueous solution of $Na_2S_2O_4$ (2 mL) was added to the mixture and stirred for 10 min. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic layers were washed with H_2O (2 × 5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 10% MeOH in CH_2Cl_2) to afford **121g** (36 mg, 73% yield) as a colorless solid: ^{1}H NMR (acetone-d_6, 400 MHz) δ 6.63 (s, 1H), 6.47 (s, 1H), 6.44 (s, 1H), 6.41 (s, 1H), 4.10 (m, 2H), 3.81 (s, 3H), 3.79 (m, 2H), 3.40 (m, 2H), 2.23(m, 2H), 2.10 (m, 2H), 1.62 (m, 4H); ^{13}C NMR (Acetone-d_6, 125 MHz) δ 174.8, 173.3, 164.7, 157.2, 144.9, 144.5, 143.2, 142.6, 123.2, 121.4, 114.3, 108.2, 102.6, 101.9, 64.2, 59.9, 36.7, 32.9, 31.4, 26.5, 25.2, 20.2; IR (film) ν_{max} 3340, 3132, 2998, 1706, 1656, 1450, 1308, 1240, 1142 cm^{-1}; HRMS (TOF-ES+) found 488.1104 ($M+Na^+$), calcd 488.1088 for $C_{22}H_{24}Cl\,NO_8Na$.

4-(2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)butyl 3-chloro-2-(hex-5-enyl)-4,6-dihydroxybenzoate (116h). To a mixture of **114** (690 mg, 2.0 mmol) and PPh_3 (524 mg, 2.0 mmol) in THF (14 mL) was added diisopropyl azodicarboxylate (404 mg, 2.0 mmol) at 0 ^{o}C. After 10 min, a solution of **111b** (542 mg, 2.0 mmol) in THF (2 mL) was added to the mixture at 0 ^{o}C and warmed to rt. stirring for 10h. The solvent was removed under reduced pressure and the residue was purified via chromatography (SiO_2, 25% EtOAc in hexanes) to afford **116h** (1.0 mg, 84%) as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.60 (s, 1H), 6.52 (s, 1H), 5.74 (m, 1H), 5.22 (s, 2H), 5.01 (s,

2H), 4.93 (m, 2H), 4.39 (t, J = 6.4 Hz), 3.93 (s, 3H), 3.55 (s, 2H), 3.52 (s, 2H), 3.06 (t, J = 7.9 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 2.07 (m, 2H), 1.84 (m, 2H), 1.67 (m, 2H), 1.48 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 163.6, 156.4, 153.2, 146.6, 145.7, 144.2, 140.0, 139.0, 132.4, 115.0, 114.0, 111.4, 107.0, 102.6, 102.2, 95.8, 66.1, 61.6, 58.2, 56.9, 34.0 (2), 33.2, 29.7, 28.9, 26.7, 25.0; IR (film) ν_{max} 3105, 2919, 1656, 1526, 1477, 1309, 1242, 1157 cm^{-1}; HRMS (TOF-ES+) found 620.1872 ($M+Na^+$), calcd 620.1875 for $C_{27}H_{38}Cl\ N_2O_{11}$.

5-(2-chloro-3,5-dihydroxy-6-((4-(2-methoxy-3,6-bis(methoxymethoxy)-5-nitrophenyl)butoxy)carbonyl)phenyl)pentanoic acid (118h). 116h (389 mg, 0.65 mmol) was dissolved in dioxane (4.5 mL) and water (1.5 mL) before 2, 6-lutidine (278 mg, 2.60 mmol), OsO_4 (4 wt. % in water, 3.0 mg, 0.01 mmol), and $NaIO_4$ (556 mg, 2.60 mmol) were added at rt. The slurry was stirred for 2 h and filtered through a plug of celite. Water (3 mL) and EtOAc (15 mL) was added to the eluent and the aqueous phase extracted with EtOAc (3 $\times$ 15 mL). The combined organic layers were washed with H_2O (15 mL), saturated aqueous NaCl (15 mL), and dried (Na_2SO_4). The residue was redissolved in ^{t}BuOH (3.0 mL), 2-methyl-2-butene (3.0 mL) and water (0.6 mL). $NaClO_2$ (81 mg, 0.90 mmol) and NaH_2PO_4 (166 mg, 1.2 mmol) were added to the solution and stirred for 30 min at rt. Saturated aqueous NaH_2PO_4 (3 mL) was added and the aqueous layer extracted with EtOAc (3 $\times$ 15 mL). The combined organic layers were washed with H_2O (10 mL), saturated aqueous NaCl (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified via chromatography (SiO_2, 40% EtOAc in hexanes) to afford **118h** (279 mg, 72% 2 steps) as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.60 (s, 1H), 6.42 (s, 1H), 5.42 (s, 2H), 5.22 (s, 2H), 4.39 (t, J = 7.8 Hz, 2H),

3.94 (s, 3H), 3.56 (s, 3H), 3.52(s, 3H), 3.05 (t, J = 7.8 Hz, 2H), 2.76 (t, J = 7.5 Hz, 2H), 2.35 (m, 2H), 1.84 (m, 2H), 1.59 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 179.7, 171.2, 163.4, 156.8, 153.2, 146.6, 145.6, 143.7, 140.0, 132.4, 114.1, 111.4, 106.8, 102.8, 102.1, 95.7, 66.2, 61.6, 58.2, 56.9, 34.3, 32.8, 29.4, 28.9, 26.6, 25.3, 24.9; IR (film) ν_{max} 3370, 2967, 1709, 1650, 1524, 1475, 1306, 1240, 1157 cm^{-1}; HRMS (TOF-ES+) found 638.1609 ($M+Na^+$), calcd 638.1616 for $C_{27}H_{34}Cl\,NO_{13}Na$.

Macrocycle (120h). 118h (34 mg, 0.05 mmol) was dissolved in EtOH (1.0 mL) before 10% palladium on carbon (5 mg) was added. The mixture was purged with argon before H_2 gas was added. The heterogeneous mixture was stirred for 3 h and then filtered through a plug of celite. The eluent was concentrated and the residue redissoved in DMF (5 mL) before slow addition to a mixture of HATU (63 mg, 0.16 mmol), HOBt (23 mg, 0.16 mmol), and diisopropyl ethylamine (0.08 mL, 0.50 mmol) in DMF (25 mL) over 4 hours. Upon addition, the solution was heated at 70 ^oC for 15 h. The The solvent was removed by distillation at reduced pressure. EtOAC (20 mL) was added to the residue and the resulting solution was washed with saturated aqueous NH_4Cl (3 $\times$ 5 mL), H_2O (5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 20% hexanes in EtOAc) to afford **120h** (24 mg, 76% yield, 2 steps) as a colorless solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.26 (s, 1H), 6.92 (s, 1H), 6.49 (s, 1H), 5.22 (m, 1H), 5.16 (m, 1H), 4.95 (m, 1H), 4.84 (m, 1H), 4.29 (m, 1H), 4.00 (m, 1H), 3.90 (s, 3H), 3.58 (s, 2H), 3.52 (s, 3H), 3.12 (m, 1H), 2.94 (m, 1H), 2.84 (m, 1H), 2.71 (m, 1H), 2.14 (m, 1H), 1.92 (m, 1H), 1.62 (m, 4H), 1.44 (m, 4H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.0, 171.3, 164.0, 156.7, 148.7, 148.5, 147.8, 143.9, 130.1, 126.6, 115.2, 114.2, 106.4, 102.7, 100.7, 95.7, 66.8, 61.5, 58.3, 56.8, 33.5

(2), 29.9, 26.8, 26.5, 25.3, 24.2; IR (film) ν_{max} 3153, 2999, 1649, 1596, 1487, 1128, 1018 cm^{-1}; HRMS (TOF-ES+) found 568.1963 ($M+H^+$), calcd 568.1949 for $C_{27}H_{35}Cl NO_{10}$.

Macrocycle (121h). MOM-protected radanamycin **120h** (24 mg, 0.039 mmol) was dissolved in CH_3CN (0.6 mL) and CH_2Cl_2 (0.6 mL) before NaI (44 mg, 0.39 mmol) and TMSCl (0.05 mL, 0.39 mmol) were added at rt. Upon addition, the solution turned cloudy and yellow. After 20 minutes, a saturated aqueous solution of $Na_2S_2O_4$ (1 mL) was added to the mixture and stirried for 10 min. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic layers were washed with H_2O (2 × 5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 10% MeOH in CH_2Cl_2) to afford **121h** (18 mg, 73% yield) as a colorless solid: ^1H NMR ($CDCl_3$, 400MHz) δ 7.78 (s, 1H), 7.65 (s, 1H), 6.60 (s, 1H), 6.60 (s, 1H), 6.43 (s, 1H), 4.35 (m, 1H), 4.10 (m, 1H), 3.84 (s, 3H), 3.21 (m, 1H), 3.09 (m, 2H), 2.92 (m, 1H), 2.44 (m, 1H), 2.21 (m, 1H), 1.47-1.88 (m, 8H); ^{13}C NMR ($CDCl_3$, 200 MHz) δ 174.8, 170.8, 162.6, 157.9, 146.5, 145.5, 143.7, 143.2, 122.9, 120.5, 114.4, 107.9, 106.1, 102.0, 66.5, 59.9, 32.8, 32.5, 29.5, 26.4, 26.3, 24.8, 22.6; IR (film) ν_{max} 3360, 3232, 3001, 1711, 1656, 1470, 1308, 1249, 1138 cm^{-1}; HRMS (TOF-ES+) found 502.1258 ($M+Na^+$), calcd 502.1245 for $C_{23}H_{36}Cl NO_8Na$.

2,3,6-trimethoxy-5-nitrophenethyl-2-(but-3-enyl)-3-chloro-4,6-dihydroxybenzoate (116a). To a mixture of **8** (155mg, 0.6 mmol) and PPh_3 (157 mg, 0.6 mmol) in THF (4 mL) was added diisopropyl azodicarboxylate (121 mg, 0.6 mmol) at 0 ^oC. After 10 min, a solution of **104** (150 mg, 0.6 mmol) in THF (1 mL) was added to the mixture at 0 ^oC and warmed to rt. stirring for 10h. The solvent was removed under reduced pressure and the

residue was purified via chromatography (SiO_2, 20% EtOAc in hexanes) to afford **116a** (250 mg, 87%) as a yellow solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.46 (s, 1H), 6.54 (s, 1H), 5.78 (m, 1H), 4.97 (m, 2H), 4.50 (t, J = 7.4 Hz, 2H), 3.97 (s, 3H), 3.91 (s, 3H), 3.89 (s, 3H), 3.18 (t, J = 7.4 Hz, 2H), 3.09 (t, J = 7.8 Hz, 2H), 2.23 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 163.5, 156.7, 153.2, 148.8, 148.2, 143.4, 138.7, 138.1, 126.9, 115.1, 114.2, 108.4, 107.0, 102.8, 64.8, 63.2, 61.6, 56.7, 33.6, 32.4, 24.6; IR (film) ν_{max} 3437, 2947, 1657, 1521, 1470, 1430, 1310, 1250, 1116, 1092 cm^{-1}; HRMS (TOF-ES+) found 504.1022 (M+Na$^+$), calcd 504.1037 for $C_{22}H_{24}NO_9Cl$.

2,3,6-trimethoxy-5-nitrophenethyl-3-chloro-4,6-dihydroxy-2-(3-oxopropyl)benzoate (117a). 116a (226 mg, 0.47 mmol) was dissolved in dioxane (3 mL) and water (1 mL) before OsO_4 (4 wt. % in water, 3 mg, 0.01 mmol), and $NaIO_4$ (377 mg, 1.76 mmol) were added at rt. The slurry was stirred for 2 h and filtered through a plug of celite. Water (3 mL) and EtOAc (15 mL) was added to the eluent and the aqueous phase extracted with EtOAc (3 $\times$ 15 mL). The combined organic layers were washed with H_2O (15 mL), saturated aqueous NaCl (15 mL), and dried (Na_2SO_4). The residue was purified via chromatography (SiO_2, 20% EtOAc in hexanes) to afford **117a** (213 mg, 94%) as a yellow solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 11.38 (s, 1H), 9.76 (s, 1H), 7.46 (s, 1H), 6.59 (s, 1H), 6.06 (s, 1H), 4.50 (t, J = 7.2 Hz, 2H), 3.98(s, 3H), 3.92 (s, 3H), 3.88 (s, 3H), 3.31 (t, J = 7.6 Hz, 2H), 3.14 (t, J = 7.2 Hz, 2H), 2.66 (t, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.6, 170.4, 163.4, 157.0, 153.1, 148.8, 148.0, 141.9, 138.6, 126.8, 114.3, 108.4, 107.0, 103.3, 65.0, 63.2, 61.6, 56.7, 43.4, 25.7, 24.5; IR (film) ν_{max} 3400, 2945, 2849, 1720, 1658, 1520, 1481, 1425, 1310, 1250, 1115, 1092 cm^{-1}; HRMS (TOF-ES+) found 501.1269 (M+ NH_4^+), calcd 501.1276 for $C_{21}H_{26}N_2O_{10}Cl$.

3-(2-chloro-3,5-dihydroxy-6-((2,3,6-trimethoxy-5-nitrophenethoxy)carbonyl)phenyl)propanoic acid (118a). 117a was redissolved in ^{t}BuOH (1.2 mL), 2-methyl-2-butene (1.2 mL) and water (0.2 mL) before $NaClO_2$ (31 mg, 0.34 mmol) and NaH_2PO_4 (63 mg, 0.45mmol) were added to the solution at rt. The mixture was stirred for 30 min at rt. Saturated aqueous NaH_2PO_4 (2 mL) was added and the aqueous layer extracted with EtOAc (3 $\times$ 15 mL). The combined organic layers were washed with H_2O (10 mL), saturated aqueous NaCl (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified via chromatography (SiO_2, 40% EtOAc in hexanes) to afford **118a** (107 mg, 95%) as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 500MHz) δ 7.46 (s, 1H), 6.60 (s, 1H), 4.56 (t, J = 7.1 Hz, 2H), 3.98(s, 3H), 3.92 (s, 3H), 3.88 (s, 3H), 3.33 (t, J = 8.1 Hz, 2H), 3.20 (t, J = 7.1 Hz, 2H), 2.56 (t, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.3, 170.0, 163.1, 156.1, 152.7, 148.3, 147.6, 140.8, 138.2, 126.4, 113.8, 108.0, 106.9, 102.9, 64.6, 62.7, 61.0, 56.2, 32.8, 27.9, 24.0; IR (film) ν_{max} 3500, 2945, 1708, 1659, 1521, 1483, 1309, 1298, 1200, 1114, 1092 1027 cm^{-1}; HRMS (TOF-ES+) found 522.0795 (M+ Na^+), calcd 522.0779 for $C_{21}H_{22}NO_{11}ClNa$.

3-(2-((3-amino-2,5,6-trimethoxyphenethoxy)carbonyl)-6-chloro-3,5-dihydroxyphenyl)propanoic acid (119a). 118a (100 mg, 0.20 mmol) was dissolved in EtOH (2.0 mL) before 10% palladium on carbon (10 mg) was added. The mixture was purged with argon before H_2 gas was added. The heterogeneous mixture was stirred for 3 h and then filtered through a plug of celite. The The solvent was removed under reduced pressure and the residue was purified via chromatography (SiO_2, 60% EtOAc in hexanes) to afford **119a** (86 mg, 92%) as a colorless solid: ^{1}H NMR (CD_3OD, 400MHz) δ 6.44 (s, 1H), 6.40 (s, 1H), 4.48 (t, J = 7.7 Hz, 2H), 3.78(s, 3H), 3.74 (s, 3H),

3.72 (s, 3H), 3.24 (t, J = 7.9 Hz, 2H), 3.11 (t, J = 7.7 Hz, 2H), 2.50 (t, J = 8.0 Hz, 2H); ^{13}C NMR (CD_3OD, 125 MHz) δ 169.8 (2), 160.4, 157.5, 149.5, 140.8, 139.4, 139.3, 136.3, 123.5, 113.5, 107.8, 101.7, 100.0, 64.7, 60.0, 59.1, 54.9, 33.2, 27.6, 23.6; IR (film) ν_{max} 3480, 2943, 1708, 1654, 1605, 1492, 1315, 1250, 1119, 1089, 1020, 1007cm^{-1}; HRMS (TOF-ES+) found 470.1220 ($M+H^+$), calcd 470.1218 for $C_{21}H_{25}NO_9Cl$.

Desmethyltrimethoxy Radanamycin (120a). 119a (82 mg, 0.18 mmol) was dissolved in DMF (10 mL) before slow addition to a mixture of HATU (133 mg, 0.35 mmol), HOBt (47 mg, 0.35 mmol), and diisopropyl ethyl amine (90 uL, 0.7 mmol) in DMF (190 mL) over 4 hours. Upon addition, the solution was heated at 70 ^{o}C for 15 h. The The solvent was removed by distillation at reduced pressure. EtOAC (30 mL) was added to the residue and the resulting solution was washed with saturated aqueous NH_4Cl (3 $\times$ 5 mL), H_2O (5 mL), saturated aqueous NaCl (5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified via chromatography (SiO_2, 20% hexanes in EtOAc) to afford **120a** (68 mg, 84% yield) as a colorless solid: ^{1}H NMR ($CDCl_3$, 400MHz) δ 11.98 (s, 1H), 6.91 (s, 1H), 6.68 (s, 1H), 6.53 (s, 1H), 6.18 (s, 1H), 4.64 (m, 1H), 4.39 (m, 1H), 4.10 (m, 1H), 3.95 (s, 3H), 3.85 (s, 3H), 3.69 (s, 3H), 3.37 (t, J = 5.2 Hz, 1H), 3.10 (m, 2H), 2.12 (m, 1H), 1.96 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.3, 172.0, 164.0, 156.2, 150.5, 149.5, 146.8, 142.2, 125.7, 125.5, 114.0, 110.6, 106.6, 102.8, 67.3, 61.1(2), 56.0, 33.8, 28.0, 23.0; IR (film) ν_{max} 3000, 2850, 1645, 1635, 1487, 1456, 1320, 1236, 1100, 1080 cm^{-1}; HRMS (TOF-ES+) found 452.1106 ($M+H^+$), calcd 452.1112 for $C_{21}H_{23}NO_8Cl$.

Cell Culture

MCF-7 cells were maintained in a 1:1 mixture of Dulbecco's Modified Eagle's Medium and Ham's F-12 supplemented with sodium pyruvate (1 mM), l-glutamine (2 mM), streptomycin (500 μg/ml), penicillin (100 units/ml) and 10% fetal bovine serum. They were cultured at 37 ˚C in a humidified incubator under 5% CO_2 in air.

Anti-proliferation Assay

MCF-7 cells were plated in 96-well microtitier plates (Corning # 3595) at 20,000 cells/well in growth medium (99 μL) and allowed to attach for 24 h at 37 ˚C in a humidified incubator under 5% CO_2 in air. Inhibitors were dissolved in DMSO and 1μL aliquots were added to the assay mixture to produce the total volume 100 μL. A 96-well microtitre plate containing the individual assays was incubated at 37 ˚C for 72 h. PMS-TMS solution (Promega Part# TB 169) 20 μL was added to each well and incubated for 4 h prior to measurement of resorufin absorbance at 490 nm. Absorbance of the blank was subtracted from the absorbance of the inhibitor to give a corrected value for each inhibitor. The mean value of each triplicate assay at each concentration was regressed according to the equation $\%Activity = 100/\{1+([I]/IC_{50})^k\}$. Thus, after three separate experiments, the overall IC_{50} values for those inhibitors were obtained.

Protein Degradation Assay

SkBr3 cells (3×10^3) were seeded in black, clear-bottom microtiter plates (Corning 3603) in 99 μl McCoy's modified 5A media and allowed to attach overnight at 37 ˚C in a humidified incubator under 5% CO_2. Each of the compounds, geldanamycin and vehicle (DMSO) (100 μL) were added to each well for a final concentration of 80 to 0.1 μM of inhibitor (1% DMSO final concentration). After inoculation, the cells were allowed

to incubate 24 hrs, each well was washed with ice-cold PBS (2 × 125 μl). Methanol (100 μL at -20°C) was added to each well, and then the plate was put in a cold room (-4 °C) for 10 min. Each well was washed again with ice-cold PBS (2 × 125 μl) followed by adding 200 μl blocking buffer (5% bovine serum albumin) and incubating at room temperature for 1 hr. Again each well was washed again with ice-cold PBS (2 × 125 μl) before primary antibody (100 μl, 1:500, Her-2 rabbit polyclonal IgG, Zymed Laboratories Inc., San Francisco, CA) was added and the plate was put in a cold room (-4 °C) overnight. Each well was washed again with ice-cold PBS (2 × 125 μl) and a horseradish peroxidase-conjugated secondary antibody (100 μl, 1:1000, Amersham, Piscataway, NJ) was added and incubated at room temperature for 2 hrs. Each well was then washed again with ice-cold PBS (3 × 125 μl) before adding chemiluminescent substrate solution (100 μl) (Pierce 34080) and allowed left there for 5 min. the plate was read in LumiCound reader (Packard). Each well was scanned for 1 s. The background (the wells containing normal IgG and the corresponding HRP-linked secondary antibody) was deducted from other values. The readings were then plotted against drug concentrations to give the IC_{50} values for each compound.

Western Blot Analysis of Hsp90 Client Protein Degradation

MCF-7 cells (1×10^6) were cultured in a Tissue Culture Dish (Becton Dickinson) in 3 ml media and allowed to attach overnight at 37 ˚C in a humidified incubator under 5% CO_2. **101**, **121g**, **121i** or vehicle (DMSO) was added in an additional 2 ml media to each dish for a final concentration of 80 to 0.1 μM of inhibitor (1% DMSO final concentration). After inoculation, the cells were allowed to incubate 24 h, before the cells were harvested by washing with PBS, scraped into 5 ml PBS on ice, and pelleted (400 × g, 4˚C). PBS was

removed and the pellets resuspended in lysis buffer (150 µl, 50 mM Tris, pH 7.5, 1% NP-40, 150 mM NaCl, 2.5 mM Na_3VO_4, 10 mM PMSF, 10 µM aprotinin, 10µM leupeptin, and 10µM soybean trypsin inhibitor) and transferred to 1.5 ml centrifuge tubes. Samples were incubated for 1 h at 4 ˚C with intermittent agitation. Lysates were cleared by centrifugation at 14000 × rpm for 10 minutes at 4 ˚C. The supernatants were collected and comprised the experimental samples. The protein concentration of each sample was determined by a BSA assay (Pierce, Rockford, IL). Equal amounts of protein were resolved on a 9% polyacrylamide gel (100 V, 100 mA) and transferred to a nitrocellulose membrane (30 V, 3 h). Bands were visualized with Ponceau to confirm protein transfer. Blots were blocked with 5% nonfat milk in PBST (3 × 20 mL), probed with primary antibody (1:500, Her-2 rabbit polyclonal IgG, Zymed Laboratories Inc., San Francisco, CA; 1:1000, Hsp70 rabbit polyclonal IgG, Upstate Cell Signaling Solutions Biotechnology; 1:1000, Akt1/2 rabbit polyclonal IgG, Santa Crutz Biotechnology; 1:2500, Actin polyclonal IgG, Santa Crutz Biotechnology: 2.5 h). The blots were washed (3 × 10 mL) with Milk/PBST, incubated with a horseradish peroxidase-conjugated secondary antibody (Amersham, Piscataway, NJ: 1 h) then washed with Milk/PBST (1 × 10 mL), followed by PBST (2 × 10 mL). Protein bands were visualized by chemiluminescence using the ECL detection reagents (Amersham, Piscataway, NJ).