SUPPORTING INFORMATION

An Approach to Total Synthesis of the Marine Ascidian Metabolite Perophoramidine via a Halogen-Selective Tandem Heck/Carbonylation Strategy

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3-(2-Methoxybenzylidene)dihydrofuran-2-one (6). 3-(Triphenyl-λ 5-phosphanylidene)dihydrofuran-2-one (**4**, 5.42 g, 15.6 mmol) was added to *o*-anisaldehyde (**5**, 1.90 mL, 15.7 mmol) in toluene (75 mL). The reaction mixture was then refluxed for 8 h and cooled with stirring to rt overnight. The volatile organics were removed under reduced pressure to afford an off-white solid. The crude product was absorbed onto silica gel and purified by flash silica gel column chromatography (1:1 EtOAc: hexanes) to afford the benzylidene lactone **6** (3.11 g, 98 %) as a colorless solid (mp 86–87 ^{o}C). IR (KBr) 2962, 2908, 2837, 1748, 1485, 1457, 923, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.16 (td, *J* = 7.2, 2.8 Hz, 2H), 3.82 (s, 3H), 4.40 (t, *J* = 7.2 Hz, 2H), 6.92 (d, *J* = 8.3 Hz, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.96 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 158.4, 131.3, 131.1, 128.9, 123.6, 123.3, 120.4, 110.9, 65.5, 55.5, 27.5; HRMS-APCI: $[M+H]^+$ calcd for $C_{12}H_{12}O_3$, 205.0859; found, 205.0856.

***N*-(2,4-Dichloro-6-iodophenyl)-2-(2-hydroxyethyl)-3-(2-methoxyphenyl)-acrylamide (8)**. $AlMe_3$ (14.5 mL, 2.0 M in hexane, 29.0 mmol) was added to a two-neck flask containing benzene (20 mL) and the mixture was cooled to 0 ^{o}C. 2,4-Dichloro-6-iodoaniline (**7**, 7.89 g, 27.4 mmol, Lancaster) in benzene (45 mL) was slowly introduced via syringe. The reaction mixture was slowly warmed to rt over 45 min. Lactone **6** (5.08 g, 24.9 mmol) dissolved in benzene (20 mL) was added dropwise via syringe to the reaction mixture over 20 min and the resulting mixture was then refluxed for 15 h. The solution was cooled to 0 ^{o}C and 1N HCl (5 mL) was slowly added dropwise to the dark mixture. After complete addition of the acid, the reaction mixture was stirred at rt for 30 min. The organic layer was removed

and the aqueous layer was extracted with EtOAc (2 x 80 mL). The combined organics were dried over $MgSO_4$ and the volatile organics were removed *in vacuo* to afford the acrylamide **8** as a purple foam (11.6 g, 95 %), which did not require further purification for the next step. ^{1}H NMR (360 MHz, $CDCl_3$) d 2.80 (br s, 1H), 2.84 (t, *J* = 5.8 Hz, 2H), 3.86 (s, 3H), 3.90 (t, *J* = 5.6 Hz, 2H), 6.93 (d, *J* = 8.5 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 7.32-7.36 (m, 2H), 7.50 (d, *J* = 2.2 Hz, 1H), 7.67 (br s, 1H), 7.81 (d, *J* = 2.2 Hz, 1H), 7.97 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) d 157.7, 137.8, 135.9, 135.6, 134.6, 133.5, 133.2, 130.5, 130.4, 130.2, 124.4, 111.4, 100.4, 62. 8, 55.9, 31.9; HMRS-APCI: $[M+H-H_2O]^+$ calcd for $C_{18}H_{16}Cl_2INO_3$, 473.9525; found, 473.9546.

2-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-*N*-(2,4-dichloro-6-iodophenyl)-3-(2-methoxyphenyl)-acrylamide (9). TBSCl (4.32 g, 28.7 mmol) was added in a single portion to the above acrylamide **8** (11.6 g, 23.5 mmol) and imidazole (3.60 g, 52.9 mmol) in DMF (25 mL) and the mixture was stirred at rt for 60 min. Water (50 mL) was added and the aqueous phase was extracted with ether (3 x 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified via flash column silica gel chromatography (1:3 EtOAc: hexanes) to afford the desired TBS ether **9** (13.9 g, 98 %) as a brown solid (dec 108 ^{o}C). IR (KBr) 3197, 2976, 2939, 1640, 1421, 1294, 636 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) d 0.06 (s, 6H), 0.85 (s, 9H), 2.88 (t, *J* = 5.5 Hz, 2H), 3.84 (s, 3H), 3.94 (t, *J* = 5.6 Hz, 2H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.96 (t, *J* =7.5 Hz, 1H), 7.30 (td, *J* = 7.7, 1.5 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 2.2 Hz, 1H), 7.79 (m, 2H), 8.74 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) d 167.8, 157.7, 137.5, 136.4, 135.0, 134.1, 134.0, 133.5, 130.2, 130.0, 124.8, 120.4, 110.8, 100.8, 63.7, 55.7, 31.8, 26.1, 18.5, -5.2; HRMS-APCI: $[M+H]^+$ calcd for $C_{24}H_{30}Cl_2INO_3Si$, 606.0490; found, 606.0503.

2-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-*N*-(2,4-dichloro-6-iodphenyl)-3-(2-methoxyphenyl)-*N*-methylacrylamide (10). LiHMDS (600 mL, 1.0 M in THF, 0.60 mmol) was slowly added to the amide **9** (220 mg, 0.36 mmol) in THF (3 mL) at 0 ^{o}C. The solution was stirred for an additional 20 min at this temperature before MeI (50 mL, 0.80 mmol) was introduced. The reaction solution was warmed to rt and stirred for 1 h. Saturated aqueous $NaHCO_3$ (10 mL) was slowly added and the organic layer was removed. The aqueous phase was extracted with EtOAc (2 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (1:5 EtOAc: hexanes) to afford the *N*-

methyl amide **10** (220 mg, 98 %) as red oil. IR (thin film) 2949, 2851, 1649, 1534, 1461, 1245, 1085 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of rotamers) d 0.06 (s, 6H, *minor*), 0.07 (s, 6H, *major*), 0.89 (s, 9H, *minor*), 0.91 (s, 9H, *major*), 2.36-2.69 (m, 2H, *minor*), 2.85-2.89 (m, 2H, *major*), 3.25 (s, 3H, *minor*), 3.44 (s, 3H, *major*), 3.70 (s 3H, *minor*), 3.85 (s, 3H, *major*), 3.90-3.95 (4H, *major and minor*), 6.78-6.81 (m, 1H, *major*), 6.90-7.01 (m, 2H, *major*), 7.20-7.36 (m, 6H, *major and minor*), 7.47 (d, *J* = 2.3 Hz, 1H, *minor*), 7.53 (d, *J* = 2.3 Hz, 1H, *major*), 7.65 (d, *J* = 7.5 Hz, 1H, *major*), 7.81-7.84 (m, 2H, *major and minor*); ^{13}C NMR (75 MHz, $CDCl_3$) d 172.6, 172.2, 157.9, 157.5, 142.1, 138.4, 138.2, 135.1, 134.5, 133.8, 133.7, 132.9, 131.7, 130.9, 130.8, 130.7, 130.5, 129.9, 129.8, 129.7, 129.6, 124.9, 120.6, 120.5, 110.7, 101.8, 100.2, 63.3, 61.5, 55.9, 55.4, 38.6, 36.0, 33.8, 33.0, 26.5, 26.3, 18.8, 18.7, -4.8, -4.9; HRMS-APCI: $[M+H]^+$ calcd for $C_{25}H_{32}Cl_2INO_3Si$, 620.0646; found, 620.0640.

2-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-*N*-(2,4-dichloro-6-iodphenyl)-3-(2-methoxyphenyl)-*N*-methoxymethylacrylamide (11). LiHMDS (4.2 mL, 1.0 M in THF, 4.2 mmol) was slowly added to the amide **9** (1.7 g, 2.9 mmol) in THF (30 mL) at 0 ^{o}C. The solution was stirred for an additional 20 min at this temperature before MOMCl (0.38 mL, 5.0 mmol) was introduced. The reaction solution was warmed to rt and stirred for 1 h. Saturated aqueous $NaHCO_3$ (20 mL) was slowly added and the organic layer was removed. The aqueous phase was extracted with EtOAc (2 x 30 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (1:5 EtOAc: hexanes) to afford the MOM amide **11** (1.6 g, 87 %) as a yellow oil. IR (thin film) 3065, 2950, 2853, 1664, 1595, 1440, 1367, 1288, 1254, 1105 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of rotamers) d 0.03 (s, 6H, *minor*), 0.06 (s, 6H, *major*), 0.88 (s, 9H, *minor*), 0.91 (s, 9H, *major*), 2.67-2.73 (m, 2H), *minor*), 2.85 (t, *J* = 5.6 Hz, 2H, *major*), 3.32 (s, 3H, *major*), 3.60 (s, 3H, *minor*), 3.71 (s, 3H, *minor*), 3.85-3.96 (m, 7 H, *major and minor*), 5.10 (AB_q, *J* = 26.9, 10.2 Hz, 2H, *major*), 5.20 (AB_q, *J* = 114.2, 10.6 Hz, 2H, *minor*), 6.79 (m, 1H, *minor*), 6.90-7.0 (m, 3H, *major and minor*), 7.20-7.33 (m, 4H, *major and minor*), 7.48 (d, *J* = 2.3 Hz, 1H, *minor*), 7.53 (s, 1H), 7.55 (d, *J*= 2.3 Hz, 1H, *major*), 7.59 (m, 1H, *major*), 7.85-7.89 (m, 2H, *major and minor*); ^{13}C NMR (75 MHz, $CDCl_3$) d 172.7, 172.5, 157.5, 157.3, 140.5, 138.5, 134.8, 134.3, 134.2, 133.1, 131.9, 131.1, 130.7, 130.6, 130.5, 129.7, 129.5, 129.4, 124.7, 124.2, 120.3, 120.2, 110.5, 102.2, 101.2, 83.0, 80.2, 63.0, 61.2, 59.1, 56.7, 55.5, 55.1, 33.7, 32.9, 26.1, 26.0, 18.5, 18.4, -5.0, -5.1; HRMS-APCI: $[M+H]^+$ calcd for $C_{26}H_{34}Cl_2INO_4Si$, 650.0752; found, 650.0749.

{3-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-5,7-dichloro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-3-yl}-(2-methoxyphenyl)acetic Acid Methyl Ester (12). $Pd(OAc)_2$ (3.1 mg, 0.014 mmol), P(*o*-Tol)$_3$ (14 mg, 0.046 mmol), Bu_4NBr (101 mg, 0.31 mmol) and TEA (100 mL, 0.72 mmol) were added to the *N*-methyl acrylamide **10** (91 mg, 0.15 mmol) in DMA (2 mL) and MeOH (1 mL). The reaction flask was equipped with a balloon of carbon monoxide, flushed three times with CO and heated under an atmosphere of CO for 12 h. The reaction mixture was cooled to rt and saturated aqueous $NaHCO_3$ (10 mL) was added. The aqueous phase was extracted with EtOAc (3 x 20 mL) and the combined extracts were dried over $MgSO_4$. The volatile organics were removed *in vacuo* and the resulting oil was purified by flash silica gel column chromatography (1:5 EtOAc: hexanes) to afford the desired lactam **12** (60 mg, 74 %) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) d -0.15 (s, 6H), 0.74 (s, 9H), 1.75 (dt, *J* = 13.7, 5.4 Hz, 1H), 2.36 (dt, *J* = 13.6, 7.3 Hz, 1H), 3.14 (m, 2H), 3.49 (s, 3H), 3.57 (s, 3H), 3.76 (br s, 3H), 4.75 (br s, 1H), 6.43 (d, *J*= 2.0 Hz, 1H), 6.91-6.98 (m, 2H), 7.05 (br d, *J* = 7.0 Hz, 1H), 7.18 (d, *J* = 2.0 Hz, 1H), 7.34 (td, *J* = 7.4, 1.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) d 179.7, 172.1, 157.9, 140.4, 134.1, 132.8, 130.2, 129.8, 126.7, 124.4, 122.6, 120.5, 115.7, 111.3, 59.3, 55.7, 52.4, 39.3, 30.4, 26.2, 18.6, -5.3; HRMS-APCI: $[M+H]^+$ calcd for $C_{27}H_{35}Cl_2NO_5Si$, 552.1734; found, 552.1747.

{3-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-5,7-dichloro-1-methoxymethyl-2-oxo-2,3-dihydro-1*H*-indol-3-yl}-(2-methoxyphenyl)acetic Acid Methyl Ester (13). $Pd(OAc)_2$ (27.8 mg, 0.124 mmol), P(*o*-Tol)$_3$ (112 mg, 0.368 mmol), Bu_4NBr (794 mg, 2.46 mmol) and TEA (1.40 mL, 10.0 mmol) were added to the *N*-methyl acrylamide **11** (1.60 g, 2.46 mmol) in DMA (27 mL) and MeOH (14 mL). The reaction flask was equipped with a balloon of carbon monoxide, flushed three times with CO and heated under an atmosphere of CO for 12 h. The reaction mixture was cooled to rt and saturated aqueous $NaHCO_3$ (30 mL) was added. The aqueous phase was extracted with EtOAc (3 x 40 mL) and the combined extracts were dried over $MgSO_4$. The volatile organics were removed *in vacuo* and the resulting oil was purified by flash silica gel column chromatography (1:5 EtOAc: hexanes) to afford the desired lactam **13** (1.26 g, 88 %) as an oil. ^{1}H NMR (360 MHz, $CDCl_3$) d -0.16 (s, 3H), -0.14 (s, 3H), 0.74 (s, 9H), 1.75-1.83 (m, 1H), 2.29-2.37 (m, 1H), 3.08-3.11 (m, 2H), 3.18-3.25 (m, 1H), 3.46 (s, 3H), 3.48 (s, 3H), 3.78 (br s, 3H), 4.78 (br s, 1H), 5.41 (AB_q, *J* = 3.5, 10.7 Hz, 2H), 6.48 (d, *J* = 2.0 Hz, 1H), 6.94-7.00 (m, 2H), 7.09 (br d, *J* = 7.0 Hz, 1H), 7.22 (d, *J* = 2.0 Hz, 1H), 7.37 (td, *J* = 8.3, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) d 180.2, 171.8, 157.7, 138.6, 133.8, 132.1, 130.1, 129.8, 127.3, 124.2,

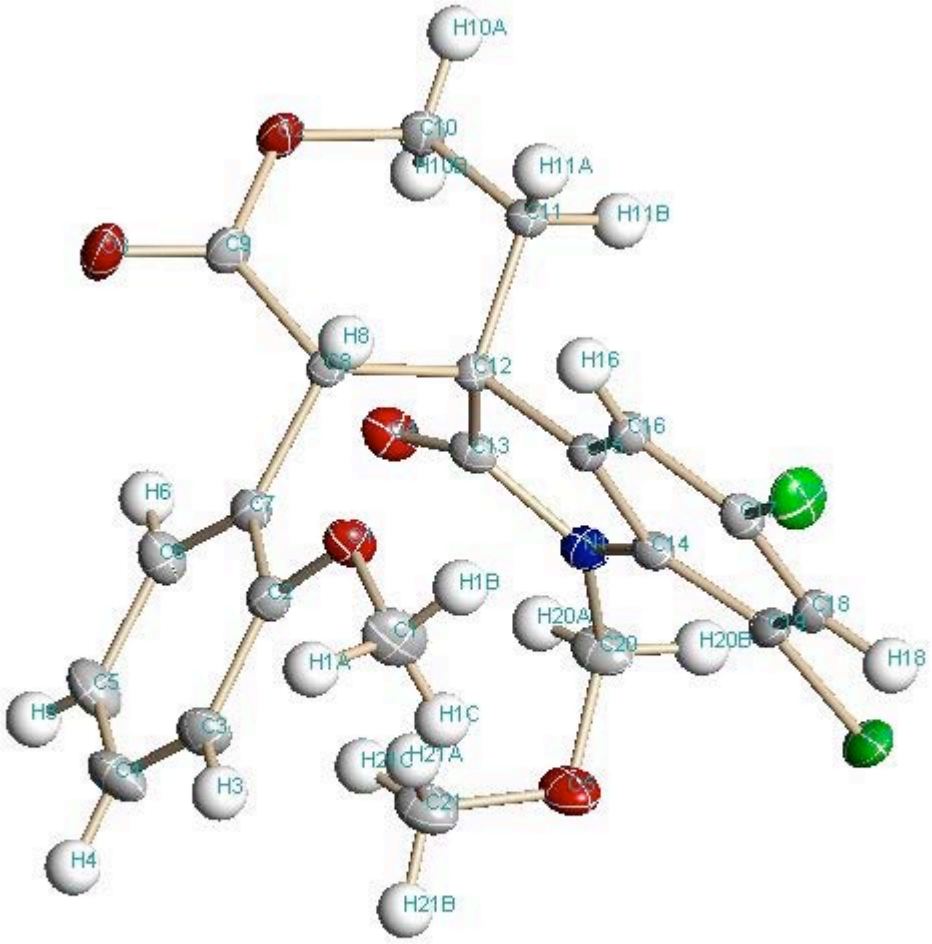
122.1, 120.3, 116.1, 111.2, 72.4, 59.0, 56.9, 55.3, 52.2, 39.6, 25.9, 18.3, -5.4; HRMS-APCI: $[M+Na]^+$ calcd for $C_{31}H_{41}Cl_2NO_6Si$, 644.1972; found, 644.1952.

Synthesis of *N*-Methyl Lactam Lactone 14. TBAF (2.3 mL, 1.0 M in THF, 2.3 mmol) and NH_4F (91 mg, 2.5 mmol) were added to lactam **12** (254 mg, 0.46 mmol) in THF (15 mL) at 0 °C. The reaction solution was stirred for 1 h and the volatile organics were removed under reduced pressure. The reaction vessel was equipped with a Dean-Stark trap and TsOH (40 mg) and benzene (15 mL) were added. The solution was heated at reflux for 12 h and cooled to rt. Saturated aqueous $NaHCO_3$ (10 mL) was added and the organic layer was removed. The aqueous layer was extracted with EtOAc (2 x 15 mL) and the combined organic extracts were dried over $MgSO_4$. The volatile organics were removed under reduced pressure and the resulting oil was purified by flash silica gel column chromatography (1:3 EtOAc: hexanes) to give the oily lactone **14** (151 mg, 81 %) as separable 3:1 mixture of C4 epimers. *Major C4 Epimer:* ^{1}H NMR (400 MHz, $CDCl_3$) d 2.10 (dt, *J* = 14.4, 4.4 Hz, 1H), 2.43 (ddd, *J* = 14.4, 9.4, 5.6 Hz, 1H), 3.25 (s, 3H), 3.51 (s, 3H), 4.52 (dt, *J* = 11.6, 4.6 Hz, 1H), 4.79 (br s, 1H), 4.99 (td, *J* = 6.6, 4.4 Hz, 1H), 6.52 (d, *J* = 8.3 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 7.02-7.07 (m, 2H), 7.11 (br d, *J* = 7.1 Hz, 1H), 7.20 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) d 176.9, 170.7, 156.0, 137.5, 133.6, 130.3, 130.2, 129.4, 127.4, 123.3, 120.6, 120.3, 115.3, 109.9, 64.7, 54.9, 52.1, 45.3, 31.9, 29.4, 20.9, 14.3; *Minor C4 Epimer*: ^{1}H NMR (400 MHz, $CDCl_3$) d 2.09-2.13 (m, 1H), 2.24-2.29 (m, 1H), 3.32 (s, 3H), 3.53 (s, 3H), 4.60-4.66 (m, 2H), 4.77-4.81 (m, 1H), 6.64 –6.71 (m, 4H), 7.10-7.14 (m, 2H); HMRS-APCI: $[M+H]^+$ calcd for $C_{20}H_{17}Cl_2NO_4$, 406.0607; found, 406.0628.

Synthesis of *N*-MOM Lactam Lactone 15. 12 N HCl (1 mL) was added to the lactam **13** (460 mg, 0.79 mmol) in MeOH (4 mL) and the reaction solution was stirred for 1 h. A catalytic amount of TsOH (10 mg) and benzene (15 mL) were then added and the reaction vessel was equipped with a Dean-Stark trap. The solution was heated at reflux for 12 h and cooled to rt. Saturated aqueous $NaHCO_3$ (10 mL) was added and the organic layer was removed. The aqueous layer was extracted with EtOAc (2 x 15 mL) and the combined organic extracts were dried over $MgSO_4$. The volatile organics were removed under reduced pressure and the resulting oil was purified by flash silica gel chromatography (1:3 EtOAc: hexanes) to give the lactone **15** (271 mg, 79 %) as white crystals (mp 184–186 °C). IR (KBr) 3063, 2956, 2837, 1740, 1725, 1492, 1464, 1081, 1013, 755 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) d 2.17 (dt, *J* = 14.5, 4.0 Hz, 1H), 2.56 (ddd, *J* = 14.8, 10.4, 5.4 Hz, 1H), 3.17 (s, 3H), 3.61 (s, 3H), 4.57-4.62 (m, 1H),

4.91 (br s, 1H), 4.99-5.06 (m, 1H), 5.20 (AB_q, *J* = 32.9, 10.7 Hz, 2H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 7.10-7.28 (m, 3H), 7.34 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) d 178.0, 170.6, 156.6, 136.6, 134.2, 131.4, 130.8, 129.8, 128.6, 123.8, 121.5, 120.8, 116.6, 110.4, 72.0, 64.8, 56.9, 55.3, 52.8, 44.3, 33.5; HMRS-APCI: $[M+H-MOM]^+$ calcd for $C_{22}H_{23}Cl_2NO_5$, 404.0456; found, 404.0462.

Crystals for X-ray analysis of *N*-MOM lactam lactone **15** were grown via slow evaporation from CH_2Cl_2. An ORTEP representation is shown below.



3-(4-Bromobenzylidene)dihydrofuran-2-one (16). 3-(Triphenyl-l 5-phosphanylidene)dihydrofuran-2-one (**4**, 1.04 g, 3.01 mmol) was added to 4-bromobenzaldehyde (559 mg, 3.02 mmol) in toluene (20 mL). The reaction mixture was then refluxed for 8 h and cooled with stirring to rt overnight. The volatile organics were removed under reduced pressure to afford an green oil, which was absorbed onto silica gel and purified by flash column chromatography (1:2 EtOAc: hexanes) to afford the benzylidene lactone **16** (640 mg, 84 %) as white needles (mp 151–152 ^{o}C). IR (KBr) 3450, 3054, 2989, 2929, 1725, 1645, 1484, 819, 694 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) d 3.18 (td, *J* = 7.3, 2.9 Hz, 2H), 3.86 (s, 3H), 4.42 (t, *J* = 7.3 Hz, 2H), 6.91-7.01 (m, 2H), 7.33-7.40 (m, 2H), 7.98 (t, *J* = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) d 172.6, 135.7, 133.9, 132.6, 131.7, 124.8, 124.6, 65.8, 27.8; HRMS-APCI: $[M+H]^+$ calcd for $C_{11}H_9BrO_2$, 252.9859; found, 252.9864.

***N*-(2,4-Dichloro-6-iodophenyl)-2-(2-hydroxyethyl)-3-(4-bromophenyl)acrylamide (17)**. $AlMe_3$ (1.2 mL, 2.0 M in hexane, 2.4 mmol) was added to a two-neck flask containing benzene (2 mL) and the mixture was cooled to 0 ^{o}C. 2,4-Dichloro-6-iodoaniline (**7**, 634 mg, 2.2 mmol) in benzene (3 mL) was slowly introduced via syringe and the reaction mixture was slowly warmed to rt over 45 min. Lactone **16** (506 mg, 2.0 mmol) dissolved in benzene (10 mL) was added dropwise via syringe over 20 min and the reaction mixture was then refluxed for 15 h. The mixture was cooled to 0 ^{o}C and 1N HCl (10 mL) was slowly added dropwise. After complete addition of the acid, the reaction mixture was stirred at rt for 30 min. The organic layer was removed, the aqueous layer was extracted with EtOAc (2 x 20 mL) and the combined organics were dried over $MgSO_4$. The volatile organics were removed *in vacuo* and the resulting oil was purified via flash silica gel column chromatography (1:2 EtOAc: hexanes) to afford the acrylamide **17** (732 mg, 67 %) as an oil. ^{1}H NMR (360 MHz, $CDCl_3$) d 2.80 (br s, 1H), 2.89 (t, *J* = 5.8 Hz, 2H), 3.98 (t, *J* = 5.7 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 2.3 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 2.3 Hz, 1H), 8.56 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) d 168.9, 137.7, 136.5, 136.1, 136.0, 134.6, 134.5, 133.3, 132.2, 131.2, 131.1, 130.4, 100.3, 62.7, 31.4; HMRS-APCI: $[M+H]^+$ calcd for $C_{17}H_{13}BrCl_2INO_2$, 539.8624; found, 539.8628.

2-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-*N*-(2,4-dichloro-6-iodphenyl)-3-(4-bromophenyl)-*N*-methylacrylamide (18). TBSCl (82 mg, 0.54 mmol) was added in a single portion to the acrylamide **17** (211 mg, 0.39 mmol) and imidazole (68 mg, 0.91 mmol) in DMF (2 mL) and the mixture was stirred at rt for 60 min. Water (10 mL) was added and the aqueous phase was extracted with ether (3 x 20 mL).

The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified via flash silica gel column chromatography (1:4 EtOAc: hexanes) to afford the desired TBS ether (185 mg, 72 %) as a foam. IR (KBr) 3231, 2928, 2854, 1661, 1494, 1254, 1073, 928, 854, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) d 0.09 (s, 6H), 0.87 (s, 9H), 2.93 (t, *J* = 5.4 Hz, 2H), 4.01 (t, *J* = 5.3 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 2.2 Hz, 1H), 7.53 (d, *J* = 8.5 Hz, 2H), 7.55 (br s, 1H), 7.76 (d, *J* = 2.2 Hz, 1H), 8.96 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) d 167.9, 137.7, 136.9, 136.4, 136.3, 134.8, 134.6, 133.7, 132.1, 131.3, 130.4, 122.9, 100.9, 64.0, 31.7, 26.3, 18.7, -4.9; HRMS-APCI : $[M+H]^+$ calcd for $C_{23}H_{27}BrCl_2INO_2Si$, 653.9489; found, 653.9478.

LiHMDS (420 mL, 1.0 M in THF, 0.42 mmol) was slowly added to the above TBS ether (185 mg, 0.28 mmol) in THF (5 mL) at 0 °C. The solution was stirred for an additional 20 min at this temperature before MeI (40 mL, 0.64 mmol) was added. The reaction solution was warmed to rt and stirred for 1 h. Saturated aqueous $NaHCO_3$ (10 mL) was slowly added and the organic layer was removed. The aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash silica gel chromatography (1:5 EtOAc: hexanes) to afford the *N*-methyl amide **18** (169 mg, 90 %) as an oil. ^1H NMR (360 MHz, $CDCl_3$) (mixture of rotamers) d 0.03 (s, 9H, *minor*), 0.10 (s, 9H, *major*), 0.86 (s, 9H, *minor*), 0.91 (s, 9H, *major*), 2.50-2.65 (m, 2H, *minor*), 2.82-2.86 (m, 2H, *major*), 3.20 (s, 3H, *minor*), 3.36 (s, 3H, *major*), 3.83-3.96 (m, 4H, *major and minor*), 6.69 (s, 1H, *minor*), 6.95 (s, 1H, *major*), 7.04 (d, *J* = 8.4 Hz, 2H, *minor*), 7.38-7.51 (m, 6H, *major and minor*), 7.78 (d, *J* = 2.3 Hz, 1H, *minor*), 7.81 (d, *J* = 2.3 Hz, 1H, *major*); ^{13}C NMR (100 MHz, $CDCl_3$) (mixture of rotamers) d 172.3, 171.8, 143.6, 141.6, 138.6, 138.2, 135.7, 135.3, 135.1, 134.7, 134.6, 134.3, 134.2, 134.1, 133.6, 132.5, 131.9, 131.8, 131.3, 131.2, 130.9, 130.8, 122.5, 122.4, 101.6, 100.1, 62.7, 61.2, 38.5, 35.8, 32.9, 30.1, 26.4, 26.3, 18.7, 18.6, -4.8, -4.9; HRMS-APCI: $[M+H]^+$ calcd for $C_{24}H_{29}BrCl_2INO_2Si$, 667.9645; found, 667.9701.

(4-Bromophenyl)-{3-[2-(*tert*-butyldimethylsilanyloxy)ethyl]-5,7-dichloro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-3-yl}acetic Acid Methyl Ester (19). $Pd(OAc)_2$ (6.0 mg, mmol), P(*o*-Tol)$_3$ (24 mg, mmol), Bu_4NBr (131 mg, 2.46 mmol) and TEA (150 mL, 10.0 mmol) were added to the *N*-methyl acrylamide **18** (137 mg, 0.21 mmol) in DMA (2 mL) and MeOH (1 mL). The reaction flask was equipped with a balloon of carbon monoxide, flushed three times with CO and heated under an atmosphere of CO for 12 h. The reaction mixture was cooled to rt and saturated aqueous $NaHCO_3$ (10

mL) was added. The aqueous phase was extracted with EtOAc (3 x 20 mL) and the combined extracts were dried over $MgSO_4$. The volatile organics were removed *in vacuo* and the resulting oil was purified by flash silica gel column chromatography (1:5 EtOAc: hexanes) to afford the desired lactam **19** (93 mg, 74 %) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) d -0.15 (s, 6H), 0.74 (s, 6H), 1.74-1.79 (m, 1H), 2.21-2.29 (m, 1H), 3.16-3.24 (m, 2H), 3.51 (s, 3H), 3.54 (s, 3H), 4.19 (s, 1H), 6.30 (d, *J* = 2.0 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 2.0 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) d 179.1, 171.2, 140.4, 133.2, 132.7, 132.5, 132.1, 131.9, 131.8, 131.7, 127.2, 124.2, 124.0, 123.3, 116.1, 59.1, 57.8, 57.7, 52.7, 52.6, 30.4, 18.6, -5.35; HRMS-APCI: $[M+H]^+$ calcd for $C_{26}H_{32}BrCl_2NO_4Si$, 600.0734; found, 600.0728.

Synthesis of *N*-Methyl Lactam Lactone 20. 12 N HCl (1 mL) was added to the lactam **19** (460 mg, 0.79 mmol) in MeOH (4 mL) and the solution was stirred at rt for 1 h. A catalytic amount of TsOH (10 mg) and benzene (15 mL) were then added and the reaction vessel was equipped with a Dean-Stark trap. The reaction mixture was heated at reflux for 12 h and cooled to rt. Saturated aqueous $NaHCO_3$ (10 mL) was added and the organic layer was removed. The aqueous phase was extracted with EtOAc (2 x 15 mL) and the combined organic extracts were dried over $MgSO_4$. The volatile organics were removed under reduced pressure and the resulting oil was purified by flash silica gel column chromatography (1:3 EtOAc: hexanes) to give the lactone **20** (271 mg, 79 %) as an inseparable 5:1 mixture of C4 epimers. ^{1}H NMR (360 MHz, $CDCl_3$) d 2.08 (dt, *J* = 14.6, 3.8 Hz, 1H, *major*), 2.11-2.15 (m, 1H, *minor*), 2.39 (ddd, *J* = 15.3 10.4, 5.3 Hz, 1H, *major*), 2.45-2.52 (m, 1H, *minor*), 3.13 (s, 3H, *minor*), 3.18 (s, 3H, *major*), 3.82 (s, 1H, *major*), 4.22 (s, 1H, *minor*) 4.72 (dt, *J* = 10.7, 5.2 Hz, 1H, *major*), 4.50-4.70 (m, 2H, *minor*), 5.00 (td, *J* = 11.5, 4.1 Hz, 1H, *major*), 6.62 (d, *J* = 8.5 Hz, 2H, *minor*), 6.68 (d, *J* = 8.5 Hz, 2H, *major*), 7.07-7.26 (m, 8H, *major and minor*); ^{13}C NMR (100 MHz, $CDCl_3$) d 176.5, 169.4, 138.1, 135.7, 134.5, 134.2, 133.9, 132.6, 132.1, 131.7, 131.5, 131.4, 131.3, 130.2, 128.9, 128.8, 124.6, 123.5, 122.8, 121.8, 116.9, 65.8, 65.3, 64.9, 54.7, 52.8, 51.5, 32.1, 29.7, 27.8; HRMS-APCI: $[M+Na]^+$ calcd for $C_{19}H_{14}BrCl_2NO_3$, 475.9431; found, 475.9412.

Allylation of *N*-MOM Lactam Lactone 15. NaH (60 % dispersion in mineral oil, 24 mg, mmol) was slowly added to the *N*-MOM lactone **15** (130 mg, 0.30 mmol) in DMF (1 mL) at 0 ^{0}C. The reaction mixture was stirred for 20 min and allyl bromide (60 mL, 0.70 mmol) was added. The solution was warmed at 70 ^{o}C with stirring for 12 h, cooled to rt and saturated aqueous $NaHCO_3$ (10 mL) was added

slowly. The aqueous phase was extracted with Et_2O (3 x 20 mL) and the combined organic extracts were dried over $MgSO_4$. The volatile organics were removed *in vacuo* and the crude oil was purified by flash silica gel column chromatography (1:3 EtOAc: hexanes) to afford the oily allyl lactone **23** (93 mg, 65 %) as a single diastereoisomer. ^{1}H NMR (300 MHz, $CDCl_3$) d 1.67 (ddd, *J* = 14.2, 5.5, 1.5 Hz, 1H), 2.49-2.60 (m, 2H), 2.94 (dd, *J* = 15. 3, 5.6 Hz, 1H), 3.42 (s, 3H), 3.73 (br s, 3H), 4.55 (ddd, *J* = 11.3, 7.1, 1.6 Hz, 1H), 4.86-5.04 (m, 3H), 5.44 (s, 2H), 5.65 (br s, 1H), 5.88-5.98 (m, 1H), 6.75-6.85 (m, 1H), 6.88 (t, *J* = 7.3 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 7.21 (d, *J* = 1.9 Hz, 1H), 7.33-7.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) d 177.4, 172.2, 158.2, 137.0, 136.1, 133.6, 132.7, 130.9, 130.7, 130.4, 130.3, 128.0, 126.3, 125.4, 120.9, 120.6, 72.2, 64.5, 57.2, 54.7, 39.1, 29.0; HMRS-APCI: $[M+H]^+$ calcd for $C_{25}H_{27}Cl_2NO_4$, 476.1390; found, 476.1387.