Supporting Information

Total Synthesis of Salinosporamide A

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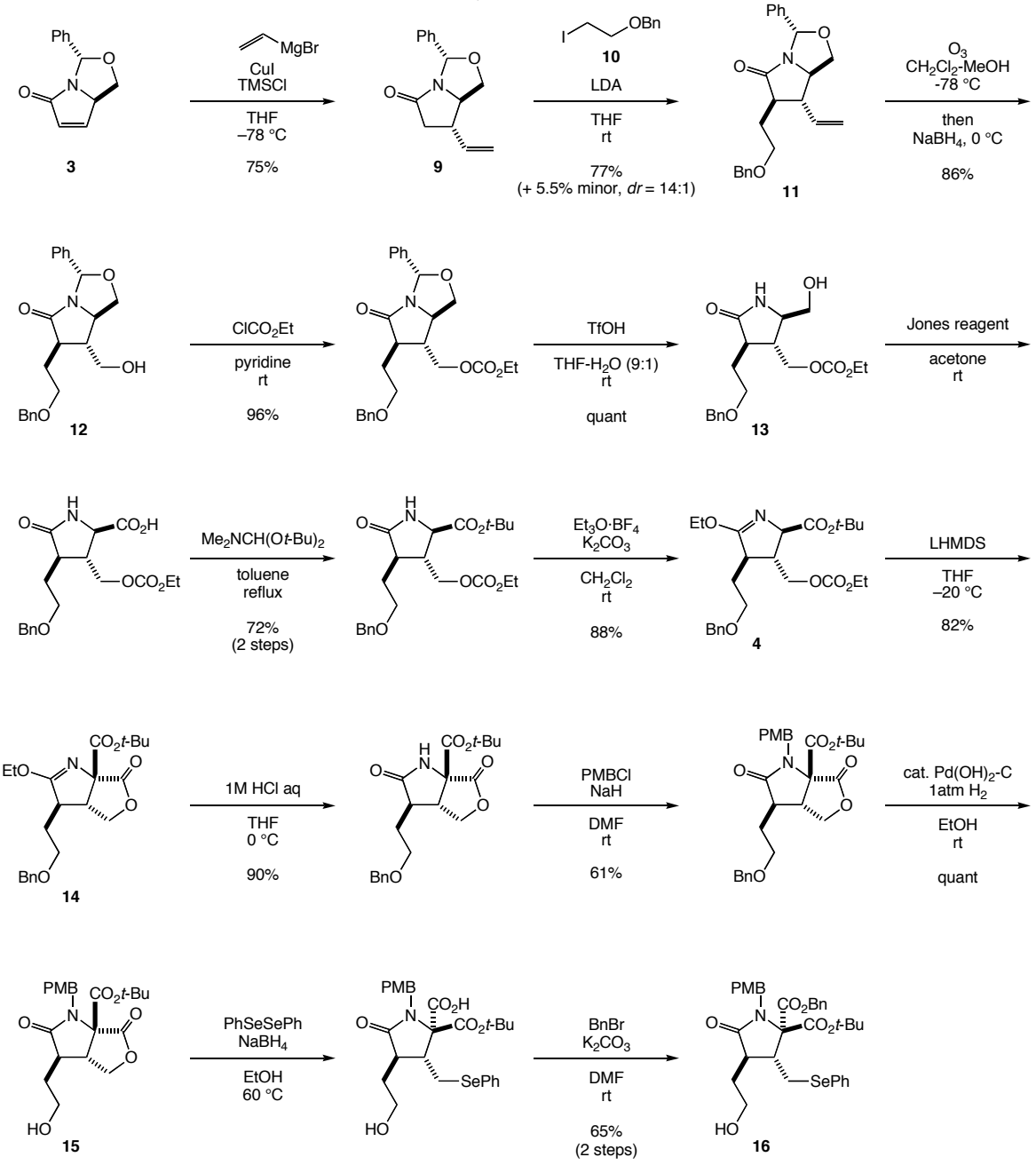
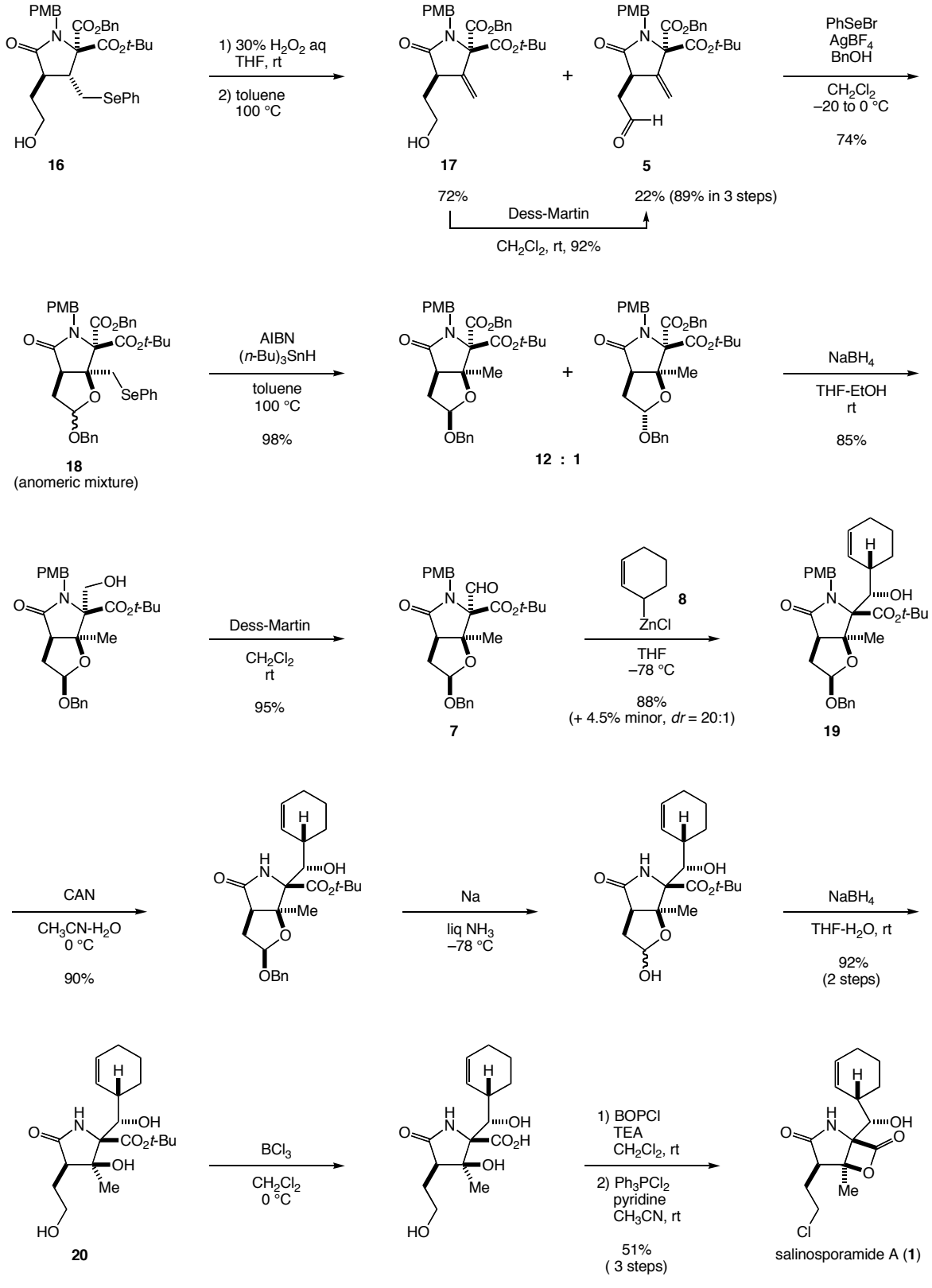
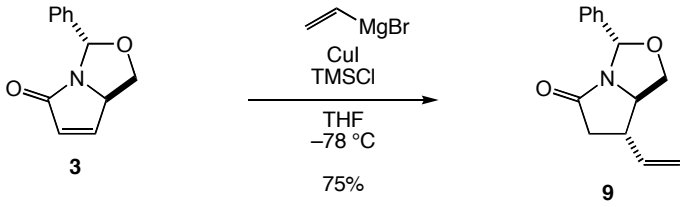



PMB
CO2Bn
CO2t-Bu
SePh
HO
16
1) 30% H2O2 aq
THF, rt
2) toluene
100 °C
17
5
72%
22% (89% in 3 steps)
Dess-Martin
CH2Cl2, rt, 92%
PhSeBr
AgBF4
BnOH
CH2Cl2
–20 to 0 °C
74%
OBn
18
(anomeric mixture)
AIBN
(n-Bu)3SnH
toluene
100 °C
98%
Me
12 : 1
NaBH4
THF-EtOH
rt
85%
OH
Dess-Martin
CH2Cl2
rt
95%
7
CHO
8
ZnCl
THF
–78 °C
88%
(+ 4.5% minor, dr = 20:1)
19
CAN
CH3CN-H2O
0 °C
90%
Na
liq NH3
–78 °C
NaBH4
THF-H2O, rt
92%
(2 steps)
20
BCl3
CH2Cl2
0 °C
1) BOPCl
TEA
CH2Cl2, rt
2) Ph3PCl2
pyridine
CH3CN, rt
51%
(3 steps)
CO2H
Cl
salinosporamide A (1)

Experimental Details

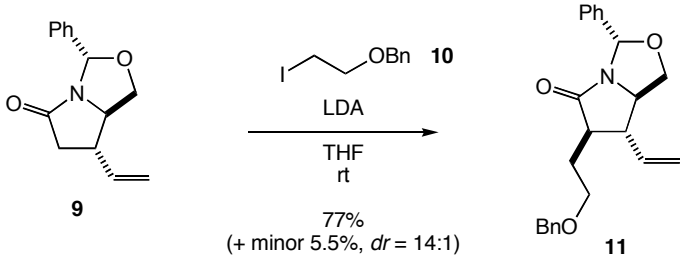
General Considerations: All glassware was dried in an oven at 150 °C prior to use. All air/moisture sensitive experiments were conducted under a slight static pressure of dry Ar unless indicated otherwise. Anhydrous benzene, toluene, Et_2O, CH_2Cl_2, THF were obtained using Solv-Tek, Inc. solvent purification system. All other solvents were of anhydrous quality purchased from Aldrich Chemicals Co. All chemicals were purchased from Aldrich Chemical Co. and used as received. Commercial grade solvents were used for routine purposes without further purification. Pyridine, triethylamine (TEA), $(i\text{-}Pr)_2NH$, and TMSCl were distilled from CaH_2 under a N_2 atmosphere prior to use. All NMR spectra were recorded on a Bruker model AMX-400 (^{1}H: 400 MHz, ^{13}C: 100 MHz) or a Bruker model DRX-500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) NMR spectrometer. Chemical shifts are reported in parts per million (ppm) from internal tetramethylsilane or the residual solvent signal of $CDCl_3$. Spectra were taken in $CDCl_3$ unless noted otherwise. The following abbreviations were used in reporting spectra: s = singlet, d = doublet, t = triplet, m = multiplet, dd = double doublet, ddd = double double doublet, br = broad, brs = broad singlet. Infrared spectra were taken on a Perkin Elmer 1600 Series FTIR Spectrometer using thin neat film deposition on NaCl plates and peaks are reported in wave numbers (cm^{-1}). High resolution mass spectra (HRMS) were taken on a Micromass Q-TOF Ultima. Column chromatography was performed with Merck silica gel 60 (40-63 mesh).



Vinyl lactam 9. Vinylmagnesium bromide (1M solution in THF, 320 ml, 320 mmol) was added to a slurry of CuI (30.5 g, 160 mmol) in THF (300 ml) at –20 °C and the resultant mixture was stirred at this temperature for 1 h. The vinyl cuprate thus prepared was cooled to –78 °C and a mixture of the enamide **3** (21.45 g, 107 mmol) and TMSCl (27.0 ml, 213 mmol) in THF (150 ml) was added slowly. After stirring at –78 °C for 2h, the reaction was quenched with saturated NH_4Cl solution, diluted with EtOAc, and filtered through a pad of Celite. The filtrate was sequentially washed with 1M HCl solution, saturated $NaHCO_3$ solution, and saturated NaCl solution. The organic layer was concentrated *in vacuo* and the residue was purified by silica gel column chromatography (40% EtOAc in hexanes) to give the vinyl lactam **9** (18.37 g, 80.1 mmol, 75%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.42-7.34 (m, 2H), 7.34-7.22 (m, 3H), 6.32 (s, 1H), 5.80 (ddd, 1H, *J*= 17.4, 10.2, 7.6 Hz), 5.15-5.02 (m, 2H), 4.12 (dd, 1H, *J*= 8.4, 6.5 Hz), 3.88 (dd, 1H, *J*= 13.2, 6.5 Hz), 3.63 (dd, 1H, *J*= 8.4, 6.5 Hz), 2.87 (m, 1H), 2.74-2.55 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 176.99, 138.61, 137.59, 129.00, 128.85, 126.40, 117.34, 87.62, 70.90, 64.29, 45.58, 40.95.
FTIR (neat) ν_{max}: 3032, 2916, 1709, 1375, 1351, 1248, 1219, 1175, 1026, 923, 741, 699.
HRMS (ESI) *m/z* calcd for $C_{14}H_{16}NO_2$ $[M+H]^+$: 230.1181, found 230.1188.
$[\alpha]^{23}_D$ –169 (c 1.6, $CHCl_3$).



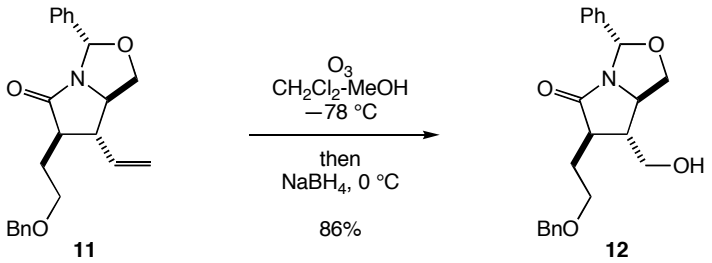
Benzyloxyethyl lactam 11. *n*-BuLi (2.5 M solution in hexanes, 20.3 ml, 50.8 mmol) was added to a solution of $(i\text{-Pr})_2NH$ in THF (100 ml) at 0 °C and the resultant mixture was stirred for 45 min. A solution of the lactam **9** (10.10 g, 44.1 mmol) in THF (50 ml) was added to the freshly prepared LDA solution at 0 °C. After stirring for 1h, the benzyloxyethyl iodide **10**[1] (19.2 ml, 116 mmol) was added and the mixture was warmed up to room temperature. After stirring for 2 h, the reaction was quenched with saturated NH_4Cl solution and partitioned between EtOAc and saturated NaCl solution. The organic layer was concentrated *in vacuo* and the residue was purified by silica gel column chromatography (40% EtOAc in hexanes) to give the benzyloxyethyl lactam **11** (12.27 g, 33.8 mmol, 77%) as a yellow oil and its diastereomer (885 mg, 2.44 mmol, 5.5%).

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.39-7.33 (m, 2H), 7.33-7.19 (m, 8H), 6.30 (s, 1H), 5.75 (ddd, 1H, *J*= 17.1, 10.3, 8.4 Hz), 5.09 (d, 1H, *J*= 17.1 Hz), 5.06 (d, 1H, *J*= 10.3 Hz), 4.43 (s, 2H), 4.06 (dd, 1H, *J*= 8.7, 6.5 Hz), 3.78 (m, 1H), 3.66-3.59 (m, 3H), 2.84 (m, 1H), 2.50 (m, 1H), 2.03 (m, 1H), 1.71 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 178.38, 138.92, 138.66, 137.34, 129.00, 128.96 (2C), 128.96 (2C), 128.10 (2C), 127.96, 126.50 (2C), 118.37, 87.61, 73.23, 70.84, 67.84, 62.23, 53.98, 47.35, 29.18.
FTIR (neat) ν_{max}: 2859, 1706, 1455, 1356, 1214, 1098, 1026, 924, 735, 698.

[1] Berlage, U.; Schmidt, J.; Peters, U.; Welzel, P. *Tetrahedron Lett.* **1987**, *28*, 3091

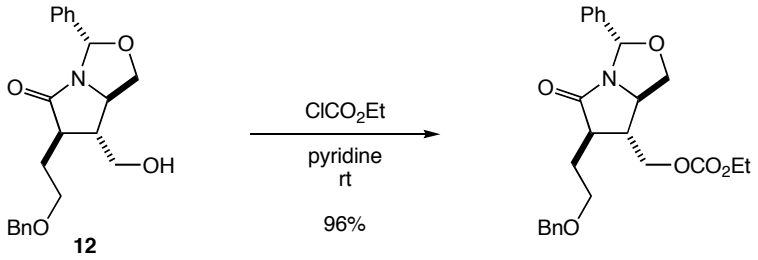
HRMS (ESI) *m/z* calcd for $C_{23}H_{26}NO_3$ $[M+H]^+$; 364.1913, found 364.1926.
$[\alpha]^{23}_D$ –85.0 (c 1.2, $CHCl_3$).

Data for the diastereomer of **11** (minor product)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.43-7.38 (m, 2H), 7.37-7.25 (m, 8H), 6.37 (s, 1H), 5.83 (ddd, 1H, *J*= 17.1, 10.3, 8.3 Hz), 5.16 (d, 1H, *J*= 10.3 Hz), 5.11 (d, 1H, *J*= 17.1 Hz), 4.52 (d, 1H, *J*= 11.7 Hz), 4.47 (d, 1H, *J*= 11.7 Hz), 4.14 (dd, 1H, *J*= 8.3, 6.6 Hz), 3.98 (m, 1H), 3.70-3.61 (m, 3H), 2.95 (m, 1H), 2.85 (m, 1H), 1.97 (m, 2H).
^{13}C NMR (125 MHz, $CDCl_3$)
δ 179.42, 138.09, 138.04, 134.18, 128.18, 128.10 (2C), 128.02 (2C), 127.43 (2C), 127.23, 125.67 (2C), 117.98, 86.94, 72.70, 69.46, 67.39, 61.47, 47.23, 46.58, 27.46.



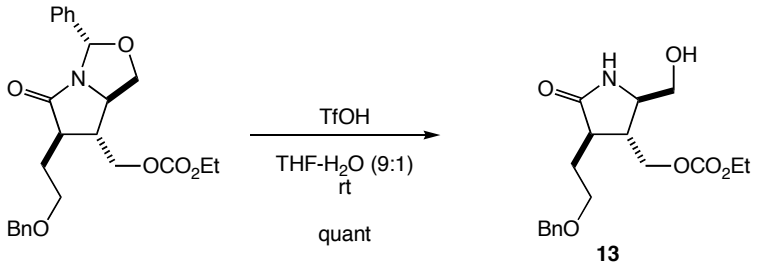
Alcohol 12. A solution of the benzyloxyethyl lactam **11** (62.2 mg, 0.171 mmol) in CH_2Cl_2-MeOH (3:1, 5.0 ml) was treated with O_3 at –78 °C. After complete consumption of the substrate, excess O_3 was removed by N_2 bubbling and the mixture was treated with $NaBH_4$ (52.2 mg, 1.38 mmol). After stirring at –78 °C for 30 min, the mixture was warmed up to 0 °C and stirred for additional 30 min. The reaction mixture was diluted with EtOAc and sequentially washed with 1M citric acid solution and saturated NaCl solution. The organic layer was concentrated *in vacuo* and the residue was purified by silica gel column chromatography (80% EtOAc in hexanes) to give the alcohol **12** (53.8 mg, 0.146 mmol, 86%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.40-7.32 (m, 2H), 7.32-7.20 (m, 8H), 6.78 (s, 1H), 4.47 (d, 1H, *J*= 12.2 Hz), 4.42 (d, 1H, *J*= 12.2 Hz), 4.15 (dd, 1H, *J*= 8.3, 6.5 Hz), 3.79 (dd, 1H, *J*= 13.4, 6.7 Hz), 3.72 (m, 1H), 3.68-3.55 (m, 3H), 3.52 (m, dd, *J*= 8.3, 7.0 Hz), 2.76 (m, 1H), 2.32 (t, 1H, *J*= 5.5 Hz), 2.22 (m, 1H), 2.16 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 178.65, 138.83, 138.13, 128.97, 128.92 (2C), 128.82 (2C), 128.32, 128.29 (2C), 126.43 (2C), 87.40, 73.61, 71.94, 69.01, 64.27, 60.27, 50.07, 45.54, 30.00.
FTIR (neat) ν_{max}: 3438, 2872, 1700, 1455, 1359, 1271, 1176, 1098, 1027, 742, 699.
HRMS (ESI) m/z calcd for $C_{22}H_{26}NO_4$ $[M+H]^+$: 368.1862, found 368.1863.
$[\alpha]^{23}_D$ –85.0 (c 0.60, $CHCl_3$).



Carbonate. The alcohol **12** (12.68 g, 34.5 mmol) was dissolved in pyridine (50 ml) and treated with $ClCO_2Et$ (4.00 ml, 41.8 mmol) at 0 °C. The reaction mixture was allowed to warm up to room temperature and stirred for 12 h. The mixture was treated with additional $ClCO_2Et$ (3.30 ml, 34.5 mmol) and stirring was continued for additional 7 h. The reaction mixture was diluted with Et_2O and poured into 2M H_2SO_4 solution. The organic layer was sequentially washed with saturated $NaHCO_3$ solution and saturated NaCl solution, and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography (40% EtOAc in hexanes) to give the carbonate (14.61 g, 33.2 mmol, 96%) as a pale yellow oil.

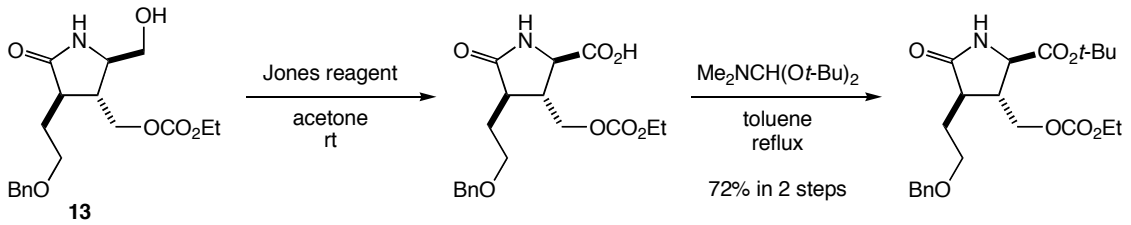
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.38-7.35 (m, 2H), 7.32-7.19 (m, 8H), 6.25 (s, 1H), 4.44 (s, 2H), 4.32 (dd, 1H, *J*= 11.0, 4.3 Hz), 4.17 (dd, 1H, *J*= 8.4, 5.5 Hz), 4.15-4.07 (m, 3H), 3.84 (dd, 1H, *J*= 13.4, 6.7 Hz), 3.61 (t, 2H, *J*= 5.5 Hz), 3.51 (dd, 1H, *J*= 8.3, 7.1 Hz), 2.77 (m, 1H), 2.35 (m, 1H), 2.13 (m, 1H), 1.74 (m, 1H), 1.23 (t, 3H, *J*= 7.1 Hz).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 177.70, 155.24, 138.69, 138.57, 129.02, 128.84 (2C), 128.80 (2C), 128.11 (2C), 128.03, 126.42 (2C), 87.42, 73.42, 71.94, 68.57, 68.15, 64.76, 60.85, 46.21, 44.91, 30.06, 14.64.
FTIR (neat) ν_{max}: 2871, 1745, 1701, 1456, 1356, 1262, 1094, 1027, 1007, 746, 700.
HRMS (ESI) m/z calcd for $C_{25}H_{30}NO_6$ $[M+H]^+$: 440.2073, found 440.2089.
$[\alpha]^{23}_D$ –63.9 (c 1.8, $CHCl_3$).



Hydroxymethyl lactam 13. The carbonate (14.61 g, 33.2 mmol) was dissolved in THF-H_2O (9:1, 400 ml) and treated with TfOH (13.5 ml, 155 mmol) at room temperature. After stirring for 18 h, the reaction mixture was diluted with EtOAc and poured into cooled

saturated $NaHCO_3$ solution. The organic layer was washed with saturated NaCl solution and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10% MeOH in $CHCl_3$) to give the hydroxymethyl lactam **13** (11.68 g, 33.2 mmol, quantitative yield) as a yellow oil.

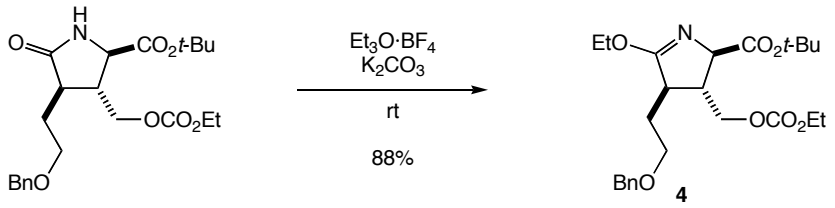
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.28-7.17 (m, 5H), 6.59 (s, 1H), 4.43 (s, 2H), 4.19 (dd, 1H, *J*= 11.0, 4.6 Hz), 4.10 (m, 2H), 3.67 (dd, 1H, *J*= 11.1, 2.9 Hz), 3.56 (m, 2H), 3.49 (m, 1H), 3.36 (dd, 1H, *J*= 11.1, 6.6 Hz), 2.89 (br, 1H), 2.36 (m, 1H), 2.23 (m, 1H), 2.08 (m, 1H), 1.72 (m, 2H), 1.23 (t, 3H, *J*= 7.1 Hz).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 178.84, 155.35, 138.60, 128.77 (2C), 128.08 (2C), 127.98, 73.34, 68.55, 68.28, 65.57, 64.68, 57.93, 41.80, 41.74, 30.96, 14.64.
FTIR (neat) ν_{max}:3280, 2871, 1745, 1684, 1456, 1368, 1262, 1092, 1007, 746, 700.
HRMS (ESI) *m/z* calcd for $C_{18}H_{26}NO_6$ $[M+H]^+$: 352.1760, found 352.1774..
$[\alpha]^{23}_D$ –9.2 (c 1.2, $CHCl_3$).



***t*-Butyl Ester.** Jones reagent (70 ml) was added to a solution of the hydroxymethyl lactam **13** (11.68 g, 33.2 mmol) in acetone (210 ml) at 0 °C and the resultant mixture was allowed to warm up to room temperature. After 3.5 h, 2-propanol (15 ml) was added to quench excess reagent and stirring was continued for additional 30 min. The mixture was partitioned between EtOAc and saturated NaCl solution. The organic layer was further washed with saturated NaCl solution and concentrated *in vacuo*. The crude carboxylic acid thus obtained was dissolved in toluene, mixed with *N,N*-dimethylformamide di-*tert*-butyl acetal (25 ml, 0.10 mol) at room temperature, and heated to reflux for 1 h. After cooling down, the mixture was partitioned between EtOAc and 5% NaCl solution. The organic layer was further washed with saturated NaCl solution and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (50% EtOAc in hexanes) to give the *t*-butyl ester (10.08 g, 23.9 mmol, 72% in 2 steps) as an orange oil.

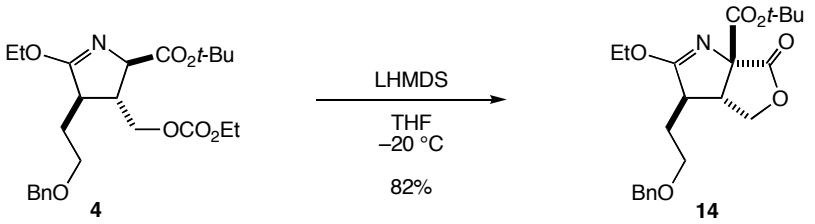
^{1}H NMR (400 MHz, $CDCl_3$)
d 7.29-7.09 (m, 5H), 6.01 (br, 1H), 4.43 (s, 2H), 4.27 (d, 1H, *J*= 4.7 Hz), 4.13 (d, 1H, *J*= 7.1 Hz), 4.09 (d, 1H, *J*= 7.1 Hz), 3.90 (d, 1H, *J*= 6.8 Hz), 3.57 (t, 2H, *J*= 6.1 Hz), 2.58 (m,

1H), 2.44 (m, 1H), 2.08 (m, 1H), 1.74 (m, 1H), 1.64 (br, 1H), 1.39 (9H), 1.23 (t, 3H, *J*= 7.1 Hz).
^{13}C NMR (100 MHz, $CDCl_3$)
177.94, 170.74, 155.32, 138.71, 128.71 (2C), 127.93 (2C), 127.88, 83.15, 73.28, 68.35, 67.41, 64.63, 56.57, 44.25, 41.22, 30.76, 28.30 (3C), 14.60.
FTIR (neat) ν_{max}: 2980, 1743, 1700, 1456, 1368, 1258, 1158, 1009.
HRMS (ESI) m/z calcd for $C_{22}H_{32}NO_7$ $[M+H]^+$: 422.2179, found 422.2191.
$[\alpha]^{23}_D$ –8.3 (c 0.63, $CHCl_3$).



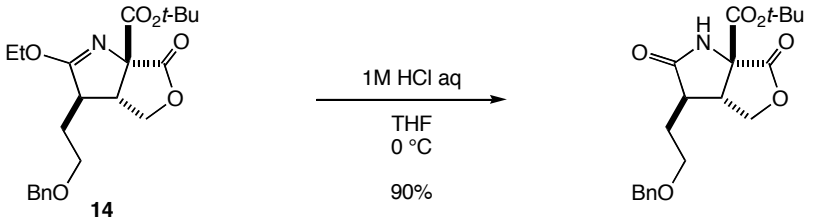
Imidate 4. A mixture of the *t*-butyl ester (9.90 g, 23.5 mmol) and powdered K_2CO_3 (13.0 g, 94.2 mmol) in CH_2Cl_2 (250 ml) was treated with Et_3OBF_4 (8.93 g, 47.0 mmol) at 0 °C and the reaction was allowed to warm up to room temperature. After stirring for 4 h, the reaction mixture was poured into saturated $NaHCO_3$ solution and extracted with EtOAc. The organic layer was washed with saturated NaCl solution and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (50% EtOAc in hexanes) to give the imidate **4** (9.33 g, 20.8 mmol, 88%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.31-7.17 (m, 5H), 4.43 (s, 2H), 4.25-4.05 (m, 7H), 3.57-3.46 (m, 2H), 2.69 (m, 1H), 2.48 (m, 1H), 2.02 (m, 1H), 1.69 (m, 1H), 1.40 (s, 9H), 1.30-1.19 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 174.73, 172.79, 155.30, 138.67, 128.60 (2C), 127.89 (2C), 127.81, 81.37, 73.18, 69.84, 68.83, 68.10, 64.71, 64.29, 44.51, 31.91, 28.32, 28.26 (3C), 14.55, 14.53.
FTIR (neat) ν_{max}:2979, 1745, 1652, 1456, 1368, 1258, 1154, 1098, 1029, 876, 791, 699.
HRMS (ESI) m/z calcd for $C_{24}H_{36}NO_7$ $[M+H]^+$: 450.2492, found 450.2506.
$[\alpha]^{23}_D$ –13.8 (c 2.9, $CHCl_3$).



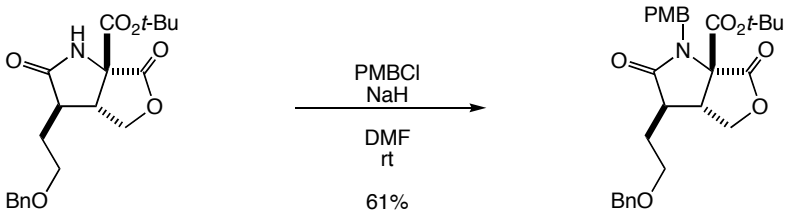
Lactone 14. A solution of the imidate **4** (2.71 g, 6.03 mmol) in THF (70 ml) was treated with LHMDS (1M in THF, 7.84 ml, 7.84 mmol) at –20 °C. After stirring for 10 min, the reaction was quenched with saturated NH_4Cl solution and partitioned between EtOAc and saturated NaCl solution. The organic layer was concentrated *in vacuo* and the residue was purified by silica gel column chromatography (40% EtOAc in hexanes) to give the lactone **14** (2.00 g, 4.96 mmol, 82%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.36-7.20 (m, 5H), 4.42 (s, 2H), 4.35-4.24 (m, 2H), 4.35 (dd, 1H, *J*= 9.5, 7.4 Hz), 4.02 (dd, 1H, *J*= 9.5, 2.5 Hz), 3.55-3.45 (m, 2H), 3.02 (m, 1H), 2.78(m, 1H), 2.08 (m, 1H), 1.61 (m, 1H), 1.40 (s, 9H), 1.24 (t, 3H, *J*= 7.1 Hz).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 176.64, 172.66, 168.31, 138.25, 128.86 (2C), 128.25, 128.10 (2C), 83.67, 79.64, 73.57, 71.71, 68.55, 66.18, 50.62, 50.35, 31.63, 28.22 (3C), 14.55.
FTIR (neat) ν_{max}: 2978, 2934, 2869, 1783, 1747, 1630, 1478, 1456, 1370, 1333, 1258, 1158, 1026, 835, 746, 700.
HRMS (ESI) m/z calcd for $C_{22}H_{30}NO_6$ $[M+H]^+$: 404.2073, found 404.2090.
$[\alpha]^{23}_D$ 28.9 (c 1.9, $CHCl_3$).



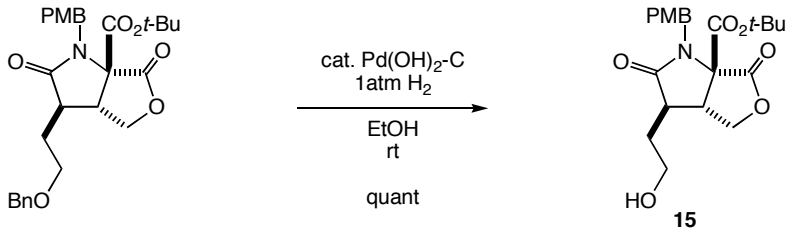
Lactam. A solution of the lactone **14** (2.10 g, 5.20 mmol) in THF (30 ml) was treated with 1M aqueous HCl (10 ml) at 0 °C. After stirring for 1 h, the reaction mixture was neutralized with saturated $NaHCO_3$ solution and extracted with EtOAc. The organic layer was washed with saturated NaCl solution and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (50% EtOAc in hexanes) to give the lactam (1.77 g, 4.72 mmol, 90%) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.40-7.23 (m, 5H), 6.38 (s, 1H), 4.47 (s, 2H), 4.44 (dd, 1H, *J*= 9.6, 6.6 Hz), 4.23 (dd, 1H, *J*= 9.6, 1.7 Hz), 3.66 (m, 1H), 3.58 (m, 1H), 3.14 (m, 1H), 2.52 (m, 1H), 2.27 (m, 1H), 1.72 (m, 1H), 1.47 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 176.39, 172.55, 166.45, 138.13, 128.92 (2C), 128.32, 128.14 (2C), 85.61, 73.66, 72.31, 69.12, 67.05, 47.97, 46.53, 30.97, 28.17 (3C).
FTIR (neat) ν_{max}: 2979, 1783, 1749, 1634, 1456, 1371, 1334, 1253, 1158, 1026, 845, 746, 700, 668.
HRMS (ESI) *m/z* calcd for $C_{20}H_{26}NO_6$ $[M+H]^+$: 376.1760, found 376.1777.
$[\alpha]^{23}_D$ 16.6 (c 0.61, $CHCl_3$).



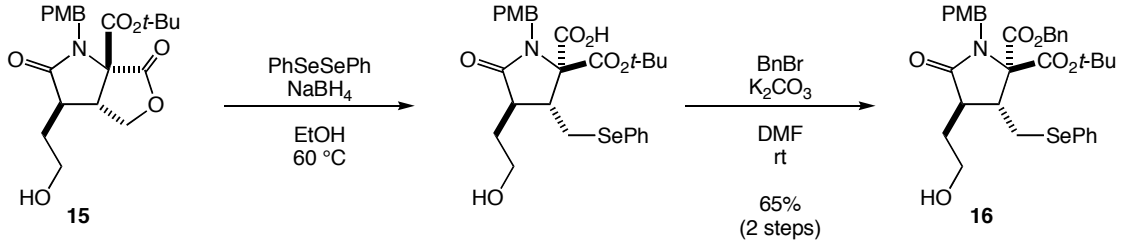
***N*-PMB lactam**. A mixture of the lactam (395 mg, 1.05 mmol) and *p*-methoxybenzyl chloride (PMBCl, 450 μl, 3.32 mmol) in DMF (4.5 ml) was treated with NaH (60% in mineral oil, 84 mg, 5.8 mmol) at 0 °C and the reaction was allowed to warm up to room temperature. After stirring for 3 h, the reaction was quenched with H_2O and partitioned between Et_2O and H_2O. The organic layer was washed with saturated NaCl solution and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (20% EtOAc in hexanes) to give the *N*-PMB lactam (322 mg, 0.650 mmol, 62%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.30-7.17 (m, 7H), 6.73 (d, 2H, *J*= 8.7 Hz), 4.69 (d, 1H, *J*= 5.2 Hz), 4.45-4.35 (m, 4H), 3.93 (dd, 1H, *J*= 9.5, 5.3 Hz), 3.70 (s, 3H), 3.62-3.50 (m, 2H), 3.11 (m, 1H), 2.44 (m, 1H), 2.12 (m, 1H), 1.64 (m, 1H), 1.33 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 175.99, 170.90, 167.27, 159.24, 138.33, 130.41 (2C), 129.17, 128.89 (2C), 128.26, 128.10 (2C), 114.02 (2C), 85.20, 73.59, 71.83, 71.05, 68.93, 55.58, 46.46, 46.11, 45.53, 31.46, 28.12 (3C).
FTIR (neat) ν_{max}: 2934, 2359, 1783, 1734, 1706, 1615, 1513, 1456, 1371, 1248, 1152, 1094, 1028, 835, 748, 700, 668.
HRMS (ESI) *m/z* calcd for $C_{28}H_{34}NO_7$ $[M+H]^+$: 496.2335, found 496.2342.
$[\alpha]^{23}_D$ 21.6 (c 0.88, $CHCl_3$).



Alcohol 15. A mixture of the *N*-PMB lactam (670 mg, 1.35 mmol) and $Pd(OH)_2$ (20% on carbon, 60.8 mg) in EtOH (30 ml) was vigorously stirred for 16 h under 1 atm hydrogen atmosphere. The catalyst was filtered off through a Celite pad and the filtrate was concentrated *in vacuo* to give the alcohol **15** (550 mg, 1.35 mmol, quantitative yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.22 (d, 2H, *J*= 8.9 Hz), 6.73 (d, 2H, *J*= 8.9 Hz), 4.72 (d, 1H, *J*= 15.2 Hz), 4.58 (dd, 1H, *J*= 9.5, 8.2 Hz), 4.42 (d, 1H, *J*= 15.2 Hz), 4.01 (dd, 1H, *J*= 9.5, 5.9 Hz), 3.80-3.72 (m, 2H), 3.71 (s, 3H), 3.19 (m, 1H), 2.53 (m, 1H), 2.38 (br, 1H), 1.92 (m, 1H), 1.70 (m, 1H), 1.40 (s, 9H)
^{13}C NMR (100 MHz, $CDCl_3$).
δ 176.73, 170.69, 167.15, 159.27, 130.25 (2C), 128.90, 114.06 (2C), 85.46, 71.69, 71.26, 60.88, 55.58, 46.47, 46.12, 45.01, 33.95, 28.11 (3C).
FTIR (neat) ν_{max}: 3458, 2935, 1784, 1734, 1690, 1684, 1652, 1615, 1514, 1456, 1395, 1372, 1280, 1250, 1152, 1034, 835, 753, 668.
HRMS (ESI) *m/z* calcd for $C_{21}H_{28}NO_7$ $[M+H]^+$: 406.1866, found 406.1885.
$[\alpha]^{23}_D$ 67.3 (c 0.52, $CHCl_3$).

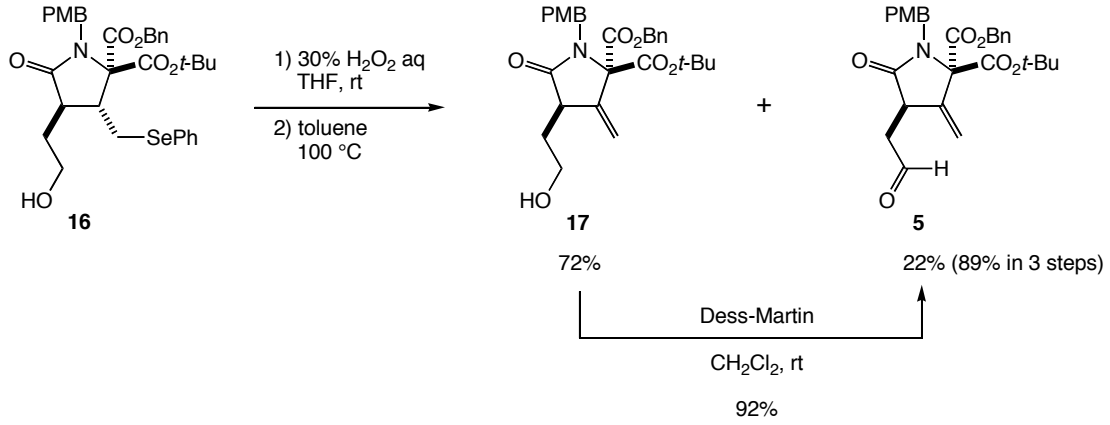


Benzyl ester 16. $NaBH_4$ (370 mg, 9.78 mmol) was added to a previously degassed (vacuum-pump-thaw) mixture of the alcohol **15** (990 mg, 2.44 mmol) and PhSeSePh (1.53 g, 4.90 mmol) in EtOH (20 ml) at room temperature. After 1 h, the mixture was heated to 60 °C and stirring was continued for 3 h. The mixture was concentrated and partitioned

between 1M KOH solution and Et_2O. The aqueous layer was acidified with 1M citric acid solution and extracted with EtOAc. The organic layer was washed with saturated NaCl solution and concentrated *in vacuo*. The crude product (yellow solid, 1.20 g) was used for the next reaction without purification.

A mixture of the crude carboxylic acid (1.20 g) and powdered K_2CO_3 (3.37 g, 24.4mmol) in DMF (15 ml) was treated with BnBr (1.16 ml, 9.75 mmol) at room temperature. After stirring for 15 h, the reaction mixture was diluted with EtOAc and sequentially washed with 5% NaCl solution and saturated NaCl solution. The organic layer was concentrated *in vacuo* and the residue was purified by silica gel column chromatography (50% EtOAc in hexanes) to give the benzyl ester **16** (1.03 g, 1.58 mmol, 65% in 2 steps) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.37-7.32 (m, 2H), 7.32-7.15 (m, 8H), 6.98 (d, 2H, *J*= 8.7 Hz), 6.72 (d, 2H, *J*= 8.7 Hz), 5.07 (d, 1H, *J*= 8.0 Hz), 4.90 (d, 1H, *J*= 8.0 Hz), 4.75 (d, 1H, *J*= 15.8 Hz), 4.35 (d, 1H, *J*= 15.8 Hz), 3.97 (dd, 1H, *J*= 8.5, 2.8 Hz), 3.68 (s, 3H), 3.60 (m, 1H), 3.46 (m, 1H), 3.10 (dd, 1H, *J*= 12.5, 5.1 Hz), 3.02 (m, 1H), 2.87 (dd, 1H, *J*= 12.5, 7.0 Hz), 2.52 (dt, 1H, *J*= 9.8, 3.2 Hz), 1.87 (m, 1H), 1.70 (m, 1H), 1.06 (s, 9H) .
^{13}C NMR (100 MHz, $CDCl_3$)
δ 178.90, 168.03, 165.58, 159.14, 134.73, 133.05 (2C), 130.40, 129.74 (2C), 129.38 (2C), 129.34, 129.20, 129.13 (2C), 128.50 (2C), 127.82, 114.21 (2C), 84.91, 75.63, 68.72, 61.75, 55.69, 46.30, 46.14, 45.83, 33.72, 27.82, 27.59 (3C).
FTIR (neat) ν_{max}: 3393, 2933, 1732, 1700, 1684, 1652, 1616, 1513, 1456, 1437, 1394, 1370, 1290, 1248, 1150, 1034, 836, 739, 693, 668.
HRMS (ESI) *m/z* calcd for $C_{34}H_{40}NO_7Se$ $[M+H]^+$: 654.1970, found 654.1959.
$[\alpha]^{23}_D$ –1.1 (c 0.88, $CHCl_3$).



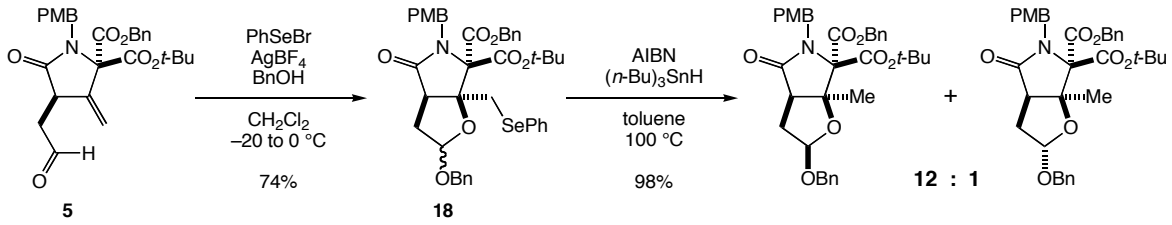
Ene-ol 17. A solution of the benzyl ester **16** (1.03 g, 1.58 mmol) in THF (25 ml) was treated with 30% aqueous H_2O_2 solution (2.50 ml) at room temperature and stirring was continued until complete consumption of the substrate (~ 4 h). The reaction mixture was cooled to 0 °C, carefully quenched with saturated Na_2SO_3 solution, and extracted with EtOAc. The organic layer was washed with saturated NaCl solution and concentrated *in vacuo* to give the corresponding selenoxide as a yellow oil, which was dissolved in toluene (60 ml) and stirred at 100 °C for 2 h. After cooling down, the reaction mixture was diluted with EtOAc, sequentially washed with saturated $NaHCO_3$ solution and saturated NaCl solution, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (50-70% EtOAc in hexanes) to give the ene-ol **17** (565 mg as a pale yellow oil, 1.14 mmol, 72%) and the ene-al **5** (174 mg as a pale yellow oil, 0.35 mmol, 22%) .

Ene-al 5. A solution of the ene-ol **17** (565 mg, 1.14 mmol) in CH_2Cl_2 (15 ml) was treated with Dess-Martin periodinane (580 mg, 1.37 mmol) at room temperature. After stirring for 1.5 h, 2-propanol (0.5 ml) was added to the reaction mixture to quench excess reagent, and stirring was continued for additional 30 min. The reaction mixture was diluted with Et_2O, filtered through a pad of Celite, and concentrated *in vacuo*. The residue was purified silica gel column chromatography (80% Et_2O in hexanes) to give the ene-al **5** (520 mg, 1.05 mmol, 92%, 694 mg in total, 89% in 3 steps from the benzyl ester **16**) as a pale yellow oil.

Data for Ene-ol **17**
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.30-7.23 (m, 3H), 7.16-7.10 (m, 2H), 7.02 (d, 2H, *J*= 8.6 Hz), 6.72 (d, 2H, *J*= 8.6 Hz), 5.54 (d, 1H, *J*= 2 Hz), 5.33 (d, 1H, *J*= 2 Hz), 4.83 (d, 1H, *J*= 12.2 Hz), 4.73 (d, 1H, *J*= 15.9 Hz), 4.67 (d, 1H, *J*= 12.2 Hz), 4.47 (d, 1H, *J*= 15.9 Hz), 3.83-3.72 (m, 2H), 3.69 (s, 3H), 3.34-3.26 (m, 2H), 2.01 (m, 1H), 1.91 (m, 1H), 2.20 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 177.49, 167.11, 166.01, 159.13, 141.09, 134.96, 129.09, 128.96 (2C), 128.89 (2C), 128.71 (2C), 115.01, 114.18 (2C), 84.64, 76.37, 68.27, 61.02, 55.67, 46.06, 44.32, 35.34, 27.77 (3C).
FTIR (neat) ν_{max}: 3393, 2933, 1731, 1700, 1684, 1652, 1615, 1513, 1456, 1437, 1394, 1369, 1290, 1248, 1150, 1034, 836, 739, 693, 668.
HRMS (ESI) *m/z* calcd for $C_{28}H_{34}NO_7$ $[M+H]^+$: 496.2335, found 496.2341.
$[\alpha]^{23}_D$ 16.9 (c 1.3, $CHCl_3$).

Data for ene-al **5**
^{1}H NMR (400 MHz, $CDCl_3$)
δ 9.72 (s, 1H), 7.28-7.23 (m, 3H), 7.15-7.08 (m, 2H), 7.04 (d, 2H, *J*= 8.6 Hz), 6.72 (d, 2H, *J*= 8.6 Hz), 5.51 (d, 1H, *J*= 2.5 Hz), 5.27 (d, 1H, *J*= 2.5 Hz), 4.80 (d, 1H, *J*= 12.2 Hz), 4.78 (d, 1H, *J*= 15.9 Hz), 4.68 (d, 1H, *J*= 12.2.Hz), 4.47 (d, 1H, *J*= 15.9 Hz), 3.70 (s, 3H), 3.64 (m, 1H), 3.00 (dd, 1H, *J*= 18.2, 4.4 Hz), 2.80 (dd, 1H, *J*= 18.2, 7.0 Hz), 1.21 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$)

δ 199.27, 175.35, 167.20, 165.63, 159.12, 140.69, 134.97, 129.20, 128.99, 128.96 (4C), 128.67 (2C), 115.26, 114.14 (2C), 84.57, 75.98, 68.26, 55.66, 46.16, 45.60, 39.79, 27.79 (3C).
FTIR (neat) ν_{max}: 2977, 1727, 1710, 1662, 1613, 1514, 1456, 1394, 1370, 1280, 1249, 1220, 1177, 1152, 1031, 995, 921, 836, 750, 699.
HRMS (ESI) *m/z* calcd for $C_{28}H_{32}NO_7$ $[M+H]^+$: 494.2179, found 494.2178.
$[\alpha]^{23}_D$ 8.1 (c 0.98, $CHCl_3$).



Benzyl glycoside 18. A mixture of the ene-al **5** (355 mg, 0.712 mmol), BnOH (298 ml, 2.88 mmol), and $AgBF_4$ (560 mg, 2.88 mmol) in CH_2Cl_2 (35 ml) was treated with PhSeBr (680 mg, 2.88 mmol) at –20 °C. After 30 min, the reaction was allowed to warm up to 0 °C and stirred for additional 1.5 h. The reaction mixture was poured into a 2:2:1 mixture of saturated NaCl, saturated $NaHCO_3$, and saturated Na_2SO_3 (25 ml) and extracted with EtOAc. The whole mixture was filtered through a pad of Celite and the organic layer was separated. Concentration *in vacuo* followed by purification of the residue by silica gel column chromatography (20% EtOAc in hexanes) gave the benzyl glycoside **18** (pale yellow oil, 403 mg, 0.533 mmol, 74%) as an inseparable anomeric mixture (12:1, determined after the next reaction).

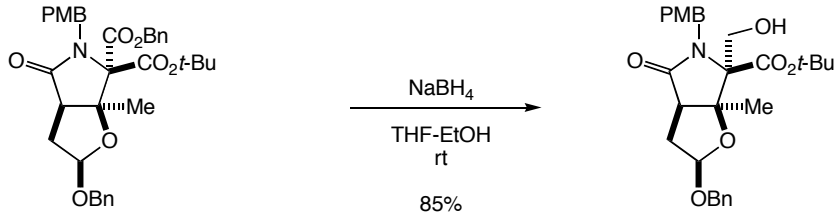
Data for the major isomer
^{1}H NMR (500 MHz, $CDCl_3$)
δ 7.31-7.04 (m, 17H), 6.61 (d, 2H, *J*= 8.6 Hz), 5.09 (s, 1H, *J*= 5.3 Hz), 4.94 (d, 1H, *J*= 14.9 Hz), 4.57 (d, 1H, *J*= 11.9 Hz), 4.49 (d, 1H, *J*= 14.9 Hz), 4.44 (d, 1H, *J*= 12.1 Hz), 4.36 (d, 1H, *J*= 12.1 Hz), 4.16 (d, 1H, *J*= 11.9 Hz), 3.71 (d, 1H, *J*= 13.3 Hz), 3.63 (s, 3H), 3.09 (d, 1H, *J*= 13.3Hz), 2.87 (d, 1H, *J*= 8.8 Hz), 2.70 (m, 1H), 2.39 (d, 1H, *J*= 13.0 Hz), 1.42 (s, 9H).
^{13}C NMR (125 MHz, $CDCl_3$)
δ 176.30, 168.28, 164.71, 159.20, 138.14, 134.51, 132.22 (2C), 131.12 (2C), 130.71, 129.56 (2C), 129.17, 129.09 (2C), 128.88 (2C), 128.73, 128.65 (2C), 128.30 (2C), 127.80, 127.42, 113.78 (2C), 104.17, 91.44, 83.77, 79.04, 69.41, 68.27, 55.60, 50.16, 45.75, 38.23, 33.16, 28.28 (3C).
FTIR (neat) ν_{max}: 2957, 2359, 1747, 1707, 1613, 1576, 1512, 1456, 1438, 1392, 1368, 1297, 1246, 1178, 1155, 1103, 1017, 950, 838, 7346, 696.

HRMS (ESI) *m/z* calcd for $C_{41}H_{44}NO_8Se$ $[M+H]^+$: 758.2232, found 758.2227.

Methyl lactam. A mixture of benzyl glycoside **18** (403 mg, 0.533 mmol, as an anomeric mixture), AIBN (8.7 mg, 0.053 mmol), and *n*-Bu_3SnH (350 μl, 1.32 mmol) in toluene (6.0 ml) was heated to 100 °C. After stirring for 2 h, the reaction mixture was cooled down and directly subjected to purification by silica gel column chromatography (30-40 % EtOAc in hexanes) to give the methyl lactam (white solid, 290 mg, 0.482 mmol, 90%) and its anomeric isomer (white solid, 24.0mg, 0.039 mmol, 7.5%).

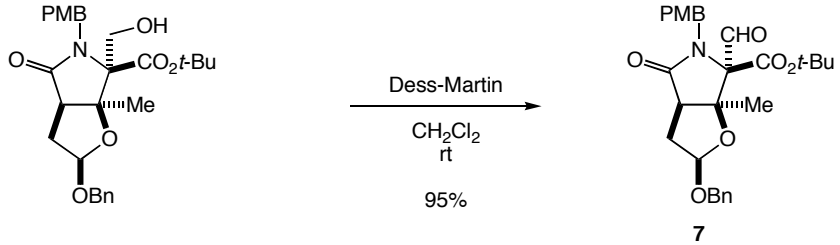
Data for the major isomer
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.35-7.11 (m, 8H), 7.25 (d, 2H, *J*= 8.6 Hz), 7.11-7.03 (m, 2H), 6.63 (d, 2H, *J*= 8.6 Hz), 5.05 (d, 1H, *J*= 5.0 Hz), 5.01 (d, 1H, *J*= 14.9 Hz), 4.59 (d, 1H, *J*= 12.0 Hz), 4.54 (d, 1H, *J*= 14.9 Hz), 4.42 (d, 1H, *J*= 12.1 Hz), 4.32 (d, 1H, *J*= 12.1 Hz), 4.18 (d, 1H, *J*= 12.0 Hz), 3.64 (s, 3H), 2.83 (d, 1H, *J*= 8.0 Hz), 2.51 (d, 1H, *J*= 13.3 Hz), 2.10 (ddd, 1H, *J*= 13.3, 8.0, 5.0 Hz), 1.44 (s, 9H), 1.33 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 75.77, 167.82, 164.69, 158.69, 137.73, 134.23, 130.75 (2C), 128.50, 128.47 (2C), 128.43, 128.29 (2C), 128.13 (2C), 127.72 (2C), 127.24, 113.26 (2C), 101.71, 88.52, 82.82, 77.83, 68.35, 67.46, 55.09, 49.91, 45.03, 34.92, 27.77 (3C), 21.25.
FTIR (neat) ν_{max}: 2944, 1746, 1706, 1653, 1616, 1558, 1512, 1456, 1393, 1300, 1248, 1159, 1097, 1024, 993, 920, 838, 750, 697.
HRMS (ESI) *m/z* calcd for $C_{35}H_{40}NO_8$ $[M+H]^+$: 602.2754, found 602.2751.
$[\alpha]^{23}_D$ –25.3 (c 0.53, $CHCl_3$).

Data for the minor isomer
^{1}H NMR (500 MHz, $CDCl_3$)
δ 7.29-7.19 (m, 8H), 7.16 (d, 2H, *J*= 8.7 Hz), 7.04-7.09 (m, 2H), 6.71 (d, 2H, *J*= 8.7 Hz), 5.18 (dd, 1H, *J*= 5.9, 4.4Hz), 5.09 (d, 1H, *J*= 14.9 Hz), 4.64 (d, 1H, *J*= 11.5 Hz), 4.52 (d, 1H, *J*= 14.9 Hz), 4.36 (d, 1H, *J*= 12.1 Hz), 4.35 (d, 1H, *J*= 11.5 Hz), 4.31 (d, 1H, *J*= 12.1 Hz), 2.97 (d, 1H, *J*= 4.4Hz), 2.69 (ddd, 1H, *J*= 14.0, 6.1, 1.1Hz), 2.19 (ddd, 1H, *J*= 13.8, 9.2, 4.3 Hz), 1.51 (s, 3H), 1.44 (s, 9H).
^{13}C NMR (125 MHz, $CDCl_3$)
δ 176.09, 167.18, 164.44, 158.94, 137.49, 134.25, 130.92 (2C), 128.58, 128.55 (2C), 128.43 (2C), 128.29 (2C), 128.22, 127.84 (2C), 127.76, 113.45 (2C), 103.69, 87.73, 83.15, 77.21, 70.11, 67.56, 55.21, 51.01, 45.02, 35.00, 27.93 (3C), 20.47.
HRMS (ESI) *m/z* calcd for $C_{35}H_{40}NO_8$ $[M+H]^+$: 602.2754, found 602.2750.
$[\alpha]^{23}_D$ 21.5 (c 2.5, $CHCl_3$).



Alcohol. A solution of the methyl lactam (major isomer, 290 mg, 0.482 mmol) in THF-EtOH (3:1, 6.0 ml) was treated with $NaBH_4$ (110 mg, 2.91 mmol) at room temperature. After stirring for 6 h, the reaction mixture was diluted with EtOAc and sequentially washed with 1M citric acid solution and saturated NaCl solution. The organic layer was concentrated *in vacuo* and the residue was purified by silica gel column chromatography (80% EtOAc in hexanes) to give the alcohol (204 mg, 0.410 mmol, 85%) as a white foam.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.32 (d, 2H, *J*= 8.6 Hz), 7.30-7.11 (m, 5H), 6.72 (d, 2H, *J*= 8.6 Hz), 5.15 (d, 1H, *J*= 15.2 Hz), 5.03 (d, 1H, *J*= 5.1 Hz), 4.65 (d, 1H, *J*= 12.0 Hz), 4.33 (d, 1H, *J*= 15.2 Hz), 4.20 (d, 1H, *J*= 12.0 Hz), 3.74 (dd, 1H, *J*= 12.8, 10.2 Hz), 3.71 (s, 3H), 3.26 (dd, 1H, *J*= 12.8, 5.2 Hz), 2.67 (d, 1H, *J*= 8.2 Hz), 2.49 (d, 1H, *J*= 13.2 Hz), 2.12 (ddd, 1H, *J*= 13.2, 8.2, 5.2 Hz), 1.48 (s, 9H), 1.40 (s, 3H), 1.01 (br, 1H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 176.10, 166.84, 159.01, 138.18, 130.80, 129.51 (2C), 128.17 (2C), 127.76 (2C), 127.20, 114.26 (2C), 101.67, 88.61, 82.35, 78.10, 68.61, 61.57, 55.19, 50.58, 44.60, 34.81, 28.11 (3C), 21.02.
FTIR (neat) ν_{max}: 33330, 2980, 1741, 1717, 1700, 1684, 1653, 1616, 1558, 1540, 1514, 1456, 1368, 1246, 1159, 1101, 1026, 920, 800, 735, 668.
HRMS (ESI) *m/z* calcd for $C_{28}H_{36}NO_7$ $[M+H]^+$: 498.2492, found 498.2495.
$[\alpha]^{23}_D$ –77.0 (c 0.40, $CHCl_3$).

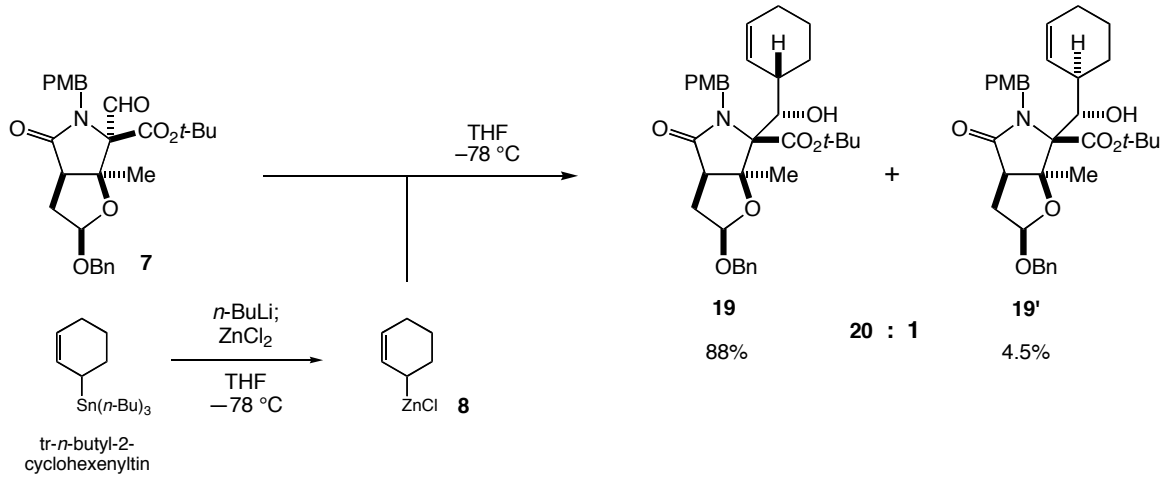


7

Aldehyde 7. A solution of the alcohol (168 mg, 0.338 mmol) in CH_2Cl_2 (8.0ml) was treated with Dess-Martin periodinane (186 mg, 0.439 mmol) at room temperature. After stirring for 1.5 h, 2-propanol (0.1 ml) was added to quench excess reagent and stirring was

continued for additional 30 min. The mixture was diluted with Et_2O, filtered through a pad of Celite, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (80% Et_2O in hexanes) to give the aldehyde **7** (159 mg, 0.321 mmol, 95%) as a white foam.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 9.34 (s, 1H), 7.27-7.22 (m, 5H), 7.08 (d, 2H, *J*= 8.7 Hz), 6.58 (d, 2H, *J*= 5.8 Hz), 5.09 (d, 1H, *J*= 5.2 Hz), 4.70 (d, 1H, *J*= 14.6 Hz), 4.68 (d, 1H, *J*= 12.3 Hz), 4.42 (d, 1H, *J*= 14.6 Hz), 4.27 (d, 1H, *J*= 12.3 Hz), 3.64 (s, 3H), 2.71 (d, 1H, *J*= 8.3 Hz), 2.53 (d, 1H, *J*= 13.4 Hz), 2.14 (ddd, 1H, *J*= 13.4, 8.3, 5.2 Hz), 1.52 (s, 9H), 1.30 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 196.67, 174.89, 164.51, 158.90, 137.74, 130.64 (2C), 128.53, 128.23 (2C), 127.65 (2C), 127.32, 113.62 (2C), 102.37, 88.64, 83.93, 81.95, 68.74, 55.10, 49.70, 45.67, 34.79, 28.09 (3C), 21.78 .
FTIR (neat) ν_{max}: 2940, 1700, 1653, 1616, 1514, 1456, 1395, 1301, 1248, 1155, 1099, 1024, 917, 810, 750, 699, 668.
HRMS (ESI) *m/z* calcd for $C_{28}H_{34}NO_7$ $[M+H]^+$: 496.2335, found 496.2361.
$[\alpha]^{23}_D$ –36.5 (c 0.34, $CHCl_3$).



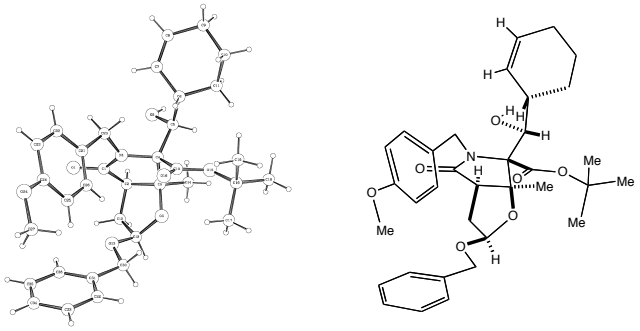
Cyclohexenyl adduct 19. A solution of tri-n-butyl-2-cyclohexenyltin[2] in (501 mg, 1.35 mmol) in THF (1.5 ml) was treated with *n*-BuLi (2.5M in hexanes, 515 µl, 1.29 mmol) at –78 °C. After 30 min, the mixture was further treated with $ZnCl_2$ (1M in Et_2O, 1.32 ml, 1.32 mmol). After 30 min, a solution of the aldehyde **7** (159 mg, 0.321 mmol) in THF (0.7 ml) was slowly added to the freshly prepared cyclohexenyl zinc reagent **8** and stirring was continued at –78 °C for 3 h.[3] The reaction was quenched with saturated NH_4Cl solution,

[2] Miyake, H.; Yamamura, K.; *Chem. Lett.* **1992**, 507-508.
[3] Reddy, L. R.; Saravanan, P.; Corey, E.; *J. J. Am. Chem. Soc.* **2004**, *126*, 6230.

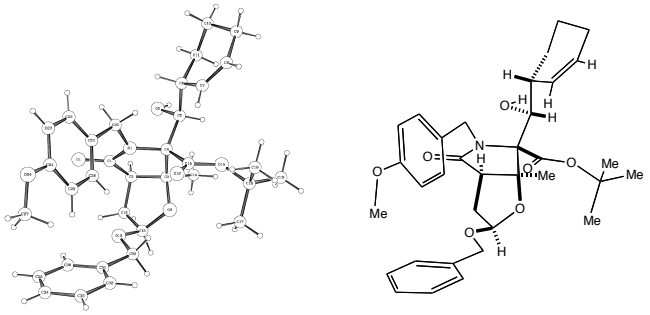
diluted with EtOAc, and sequentially washed with 1M citric acid and saturated NaCl solution. The organic layer was concentrated *in vacuo* and the residue was purified by silica gel column chromatography (50% EtOAc in hexanes) to give the cyclohexenyl adduct **19** (pale yellow oil, 163 mg, 0.282 mmol, 88%) and its diastereomer **19'** (pale yellow oil, 8.3 mg, 0.018 mmol, 4.5%). Crystals of **19** and **19'** obtained from EtOH were used for confirmation of the structures by single-crystal X-ray analysis.

Data for the major adduct **19**
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.31 (d, 2H, *J*= 8.7 Hz), 7.28-7.15 (m, 5H), 6.46 (d, 2H, *J*= 8.7 Hz), 5.84 (d, 1H, *J*= 9.7 Hz), 5.60 (d, 1H, *J*= 9.7 Hz), 5.06 (d, 1H, *J*= 5.6 Hz), 4.63 (d, 1H, *J*= 15.1 Hz), 4.56 (d, 1H, *J*= 12.6 Hz), 4.48 (d, 1H, *J*= 15.1 Hz), 4.26 (d, 1H, *J*= 12.6 Hz), 3.96 (m, 1H), 3.56 (s, 3H), 2.80 (d, 1H, *J*= 8.5 Hz), 2.44 (d, 1H, *J*= 13.6 Hz), 2.25-2.16 (m, 2H), 2.00-1.87 (m, 2H), 1.78-1.61 (m, 3H), 1.57-1.36 (m, 2H), 1.51 (s, 3H), 1.47 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 177.44, 168.07, 158.41, 138.64, 132.42, 130.80, 129.10 (2C), 128.62 (2C), 128.07 (2C), 127.64, 126.00, 113.67 (2C), 102.45, 91.60, 83.07, 80.43, 76.86, 69.30, 55.53, 50.79, 48.34, 38.73, 35.41, 29.09, 28.47 (3C), 25.48, 21.96, 20.83.
FTIR (neat) ν_{max}: 3288, 2977, 2933, 2834, 1740, 1678, 1615, 1514, 1447, 1394, 1369, 1246, 1154, 1091, 1041, 1018, 992, 912, 841, 805, 733, 698.
HRMS (ESI) *m/z* calcd for $C_{34}H_{44}NO_7$ $[M+H]^+$: 578.3118, found 578.3114.
$[\alpha]^{23}_{D}$ –34.1 (c 0.69, $CHCl_3$).

Data for the minor adduct **19'**
^{1}H NMR (500 MHz, $CDCl_3$)
δ 7.28 (d, 2H, *J*= 8.6 Hz), 7.27-7.14 (m, 5H), 6.54 (d, 2H, *J*= 8.6 Hz), 5.68 (m, 1H), 5.60 (m, 1H), 5.04 (d, 1H, *J*= 5.4 Hz), 4.74 (d, 1H, *J*= 15.4 Hz), 4.63 (d, 1H, *J*= 15.4 Hz), 4.62 (d, 1H, *J*= 12.4 Hz), 4.24 (d, 1H, *J*= 12.4 Hz), 3.93 (m, 1H), 3.61 (s, 3H), 2.84 (d, 1H, *J*= 8.3 Hz), 2.46 (d, 1H, *J*= 13.4 Hz), 2.18 (ddd, 1H, *J*= 13.4, 8.3, 5.6 Hz), 1.97-1.79 (m, 3H), 1.61-1.13 (m, 5H), 1.50 (s, 3H), 1.47 (s, 9H).
^{13}C NMR (125 MHz, $CDCl_3$)
δ 177.37, 167.76, 158.05, 138.27, 130.78, 130.68, 128.65, 128.19 (2C), 127.72 (2C), 127.19 (2C), 126.54, 113.35 (2C), 101.77, 91.66, 82.75, 79.72, 76.49, 68.87, 55.13, 50.36, 47.61, 39.14, 34.90, 28.02 (3C), 26.07, 25.29, 21.45, 19.72.
HRMS (ESI) *m/z* calcd for $C_{34}H_{44}NO_7$ $[M+H]^+$: 578.3118, found 578.3120.
$[\alpha]^{23}_{D}$ –5.9 (c 1.7, $CHCl_3$) .

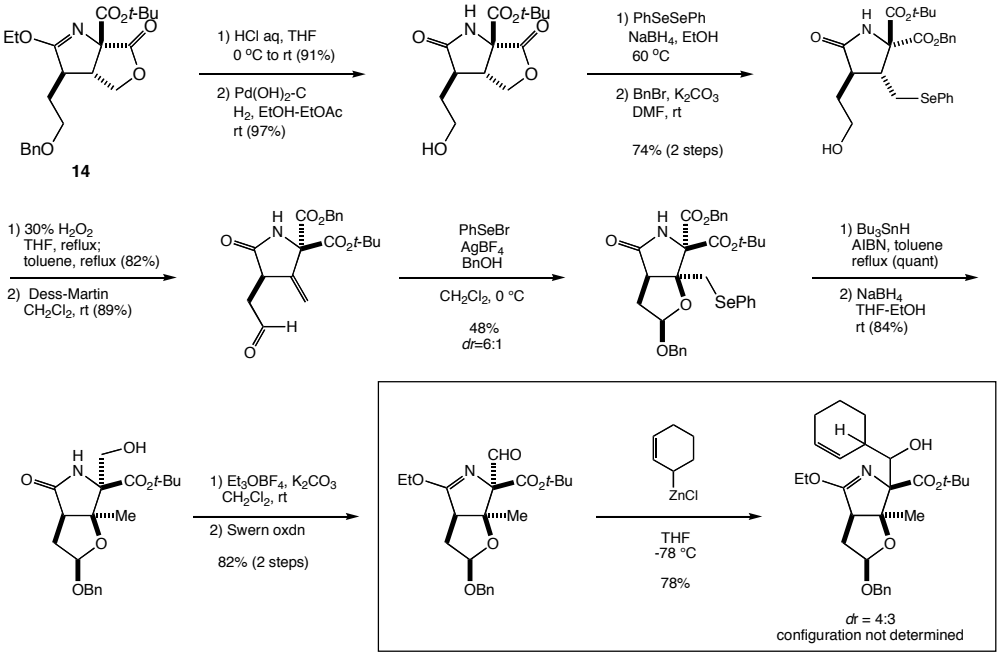


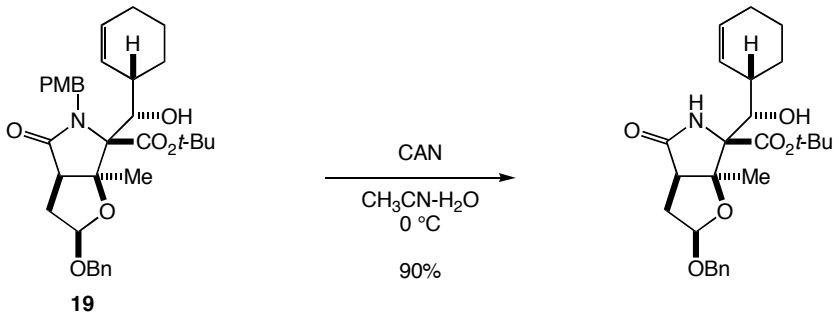
X-ray structure of the major adduct **19** at 110 K



X-ray structure of the minor adduct **19'** at 105 K

Appendix Synthesis of the imidate aldehyde and reaction with cyclohexenyl zinc chloride

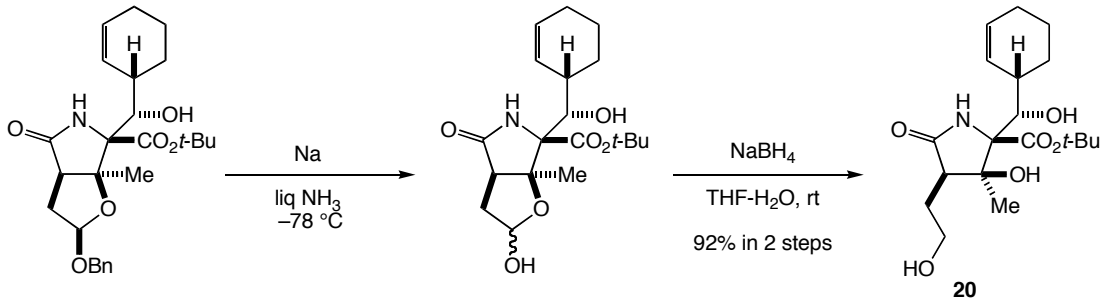




19

Lactam. A solution of ceric ammonium nitrate (CAN, 188 mg, 0.343 mmol) in H_2O (0.25 ml) was added to a solution of the cyclohexenyl adduct **19** (66.0 mg, 0.114mmol) in CH_3CN (1.2 ml) at 0 °C. After stirring for 6 h, the reaction was quenched with saturated Na_2SO_3 solution and partitioned between EtOAc and saturated $NaHCO_3$ solution. The organic layer was washed with saturated NaCl solution and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (80% EtOAc in hexanes) to give the lactam (47.3 mg, 0.103 mmol, 90%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.15-7.35 (m, 5H), 6.00 (m, 1H), 5.81 (s, 1H), 5.52 (m, 1H), 5.01 (br, 1H), 4.58 (d, 1H, *J*= 12.4 Hz), 4.37 (d, 1H, *J*= 11.2 Hz), 3.92 (d, 1H, *J*= 9.0 Hz), 2.74 d, 1H, *J*= 7.9 Hz), 2.44 (d, 1H, *J*= 13.2 Hz), 2.21 (m, 1H), 2.10 (m, 1H), 1.95 (m, 2H), 1.80-1.53 (m, 4H), 1.73 (d, 1H, *J*= 9.8 Hz), 1.49 (s, 3H & s, 9H).
^{13}C NMR (125 MHz, $CDCl_3$)
δ 177.41, 168.83, 138.43, 135.84, 128.63 (2C), 128.25, 127.67 (2C), 123.65, 101.63, 92.14, 82.96, 76.57, 75.79, 68.63, 51.02, 37.80, 35.05, 29.83, 28.41 (3C), 25.22, 21.40, 20.88.
FTIR (neat) ν_{max}: 3288, 2977, 2933, 2835, 1740, 1678, 1615, 1514, 1447, 1394, 1369, 1246, 1154, 1091, 1041, 1018, 992, 919, 841, 8.5, 733, 698.
HRMS (ESI) *m/z* calcd for $C_{26}H_{36}NO_6$ $[M+H]^+$: 458.2543, found 458.2560.
$[\alpha]^{23}_D$ –64.0 (c 0.72, $CHCl_3$).

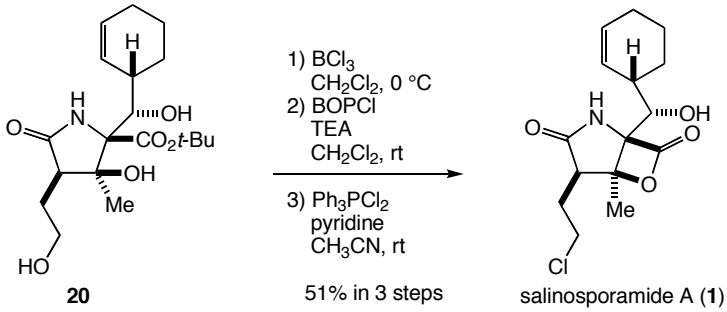


20

Triol 20. Sodium metal (Na, 81 mg, 3.5 mmol) was dissolved in liquid ammonia (8 ml) at –78 °C and the resultant dark blue mixture was stirred for 10 min. A solution of the benzyl glycoside (89.3 mg, 0.195 mmol) in THF (2 ml) was slowly added to the mixture and stirring was continued for 2 h. The reaction was quenched with NH_4Cl (solid, 300 mg) and dry ice-acetone bath was removed. All volatile materials were evaporated under N_2 stream and the white residue thus obtained was partitioned between EtOAc and saturated NaCl solution. The organic layer was further washed with saturated NaCl solution and concentrated *in vacuo* to give the crude hemiacetal (75.5 mg), which was used for the next reaction without purification.

A solution of the hemiacetal (75.5 mg) in THF-H_2O (2:1, 2.0 ml) was treated with $NaBH_4$ (22.9 mg, 0.61 mmol) at room temperature. After stirring for 30 min, the reaction mixture was diluted with EtOAc, sequentially washed with 1M citric acid and saturated NaCl solution, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10% MeOH in $CHCl_3$) to give the triol **20** (70.0 mg, 0.189 mmol, 97% in 2 steps) as a white foam.

^{1}H NMR (500 MHz, $CDCl_3$)
δ 8.74 (brs, 1H), 6.07(m, 1H), 5.79 (m, 1H), 5.28 (brs, 1H), 4.16 (d, 1H, *J*= 8.4 Hz), 3.81 (m, 1H), 3.70 (m, 1H), 2.79 (dd, 1H, *J*= 10.5, 2.1 Hz), 2.29 (m, 1H), 2.02 (m, 2H), 1.96 (m, 1H), 1.88-1.65 (m, 4H), 1.59 (m, 1H), 1.54 (s, 3H), 1.52 (s, 9H).
^{13}C NMR (125 MHz, $CDCl_3$)
δ 180 67, 171 03, 135.48, 123.17, 84.16, 81.61, 79.82, 75.53, 62.37, 52.08, 38.32, 29.33, 28.02 (3C), 26.31, 24.80, 20.38, 19.80.
FTIR (neat) ν_{max}: 3306, 2977,2930, 1713, 1684, 1669, 1371, 1288, 1253, 1156, 1046, 1019, 845, 700, 617.
HRMS (ESI) *m/z* calcd for $C_{19}H_{32}NO_6$ $[M+H]^+$: 370.2230, found 370.2240.
$[\alpha]^{23}_D$ –53.3 (c 0.39, $CHCl_3$).



20 salinosporamide A (**1**)

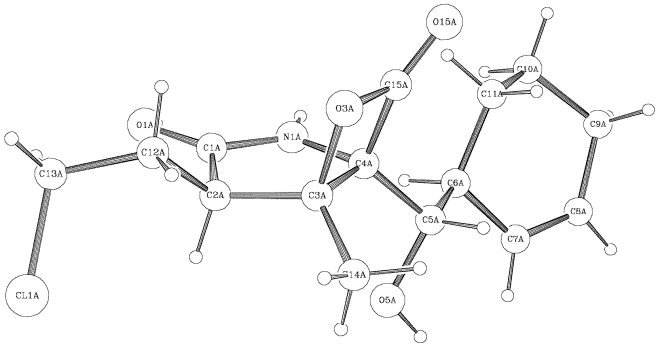
Salinosporamide A (1). A solution of the triol **20** (15.5 mg, 0.042 mmol) in CH_2Cl_2 (0.60 ml) was treated with BCl_3 (1M in CH_2Cl_2, 0.10 ml, 0.10 mmol) at 0 °C. After 30 min, the reaction was quenched by addition of MeOH (50 μl) and the resultant mixture was concentrated to a small volume. The residue was dissolved in 5% EtOH in EtOAc and washed with saturated NaCl solution (x2). The organic layer was concentrated *in vacuo*

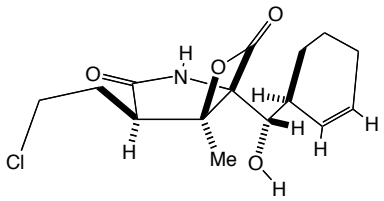
and the crude carboxylic acid (13.7 mg, as a white film) was dissolved in a mixture of CH_2Cl_2 (0.50 ml) and triethylamine (TEA, 0.10 ml). After stirring for 10 min, BOPCl (23.4 mg, 0.092 mmol) was added at room temperature and stirring was continued for 16 h. The reaction mixture was diluted with EtOAc, sequentially washed with 1M citric acid solution and saturated NaCl solution, and passed through a small pad of silica gel (EtOAc 100%). The filtrate was concentrated *in vacuo* and the residue (7.7 mg, as a white film) was dissolved in a mixture of CH_3CN (0.20 ml) and pyridine (0.20 ml). Ph_3PCl_2 (16.9 mg, 0.051 mmol) was added to the mixture at room temperature and stirring was continued for 4 h. The reaction mixture was diluted with EtOAc, sequentially washed with saturated $CuSO_4$ solution and saturated NaCl solution, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (50% EtOAc in hexanes) to give salinosporamide A (**1**) (6.8 mg, 0.022 mmol, 51% in 3 steps) as a white film. Crystallization of synthetic **1** from EtOAc/cyclohexane gave colorless needles, which were used for further confirmation of the structure by single-crystal X-ray analysis.

^{1}H NMR (500 MHz, pyridine-*d*5)
δ 10.62 (s, 1H), 6.42 (d, 1H, *J*= 10.0 Hz), 5.88 (m, 1H), 4.96 (brs, 1H), 4.26 (m, 1H), 4.13 (m, 1H), 4.02 (m, 1H), 3.18 (t, 1H, *J*= 7.1 Hz), 2.85 (m, 1H), 2.49 (m, 1H), 2.36-2.29 (m, 2H), 2.07 (s, 3H), 1.91 (m, 2H), 1.65-1.72 (m, 2H), 1.37 (m, 1H).
^{13}C NMR (125 MHz, pyridine-*d*5)
δ 176.93, 169.44, 129.09, 128.69, 86.32, 80.35, 70.99, 46.18, 43.29, 39.31, 29.01, 26.48, 25.36, 21.73, 20.00.
FTIR (neat) ν_{max}: 3389, 2926, 1826, 1702, 1432, 1385, 1226, 1080, 1022, 833, 778.
HRMS (ESI) *m/z* calcd for $C_{15}H_{21}ClNO_4$ $[M+H]^+$: 314.1159, found 314.1174.
$[\alpha]^{23}_D$ –73.0 (c 0.40, MeOH), -73.2 (c 0.49, MeOH, in lit[3]), -72.9 (c 0.55, MeOH, in lit[4]).
mp 166-167 °C (168-170 °C in lit[3], 169-171 °C in lit[4]).

X-ray structure of salinosporamide A (1) (at 100K).
The unit cell contained four independent molecules A-D with different conformations.

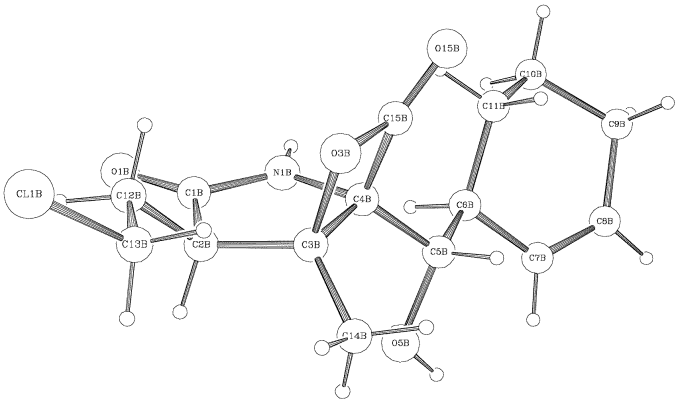
A





[4] Feling, R. H.; Buchanan, G. O.; Mincer, T. J.; Kauffman, C. A.; Jensen, P. R.; Fenical, W.; *Angew. Chem. Int. Ed.* **2003**, *42*, 355-357.

B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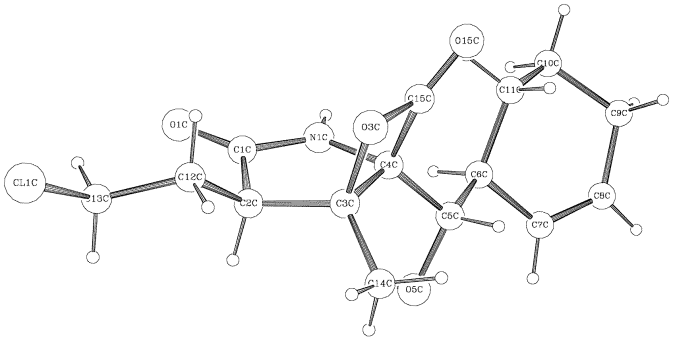
C5B
C7B
C14B
O5B

C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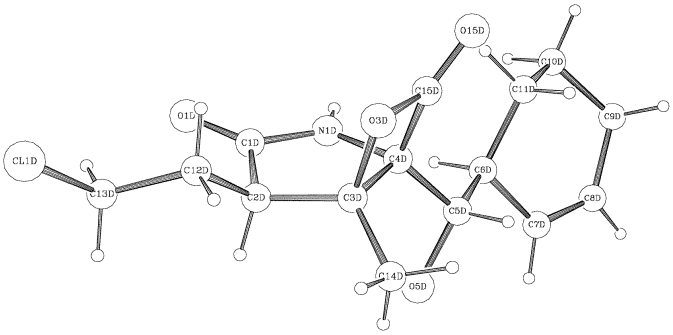
D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