Supporting Information

Asymmetric Total Synthesis of Bacillariolide III, A Marine Oxylipin

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General Experimental

Unless noted otherwise, all starting materials and reagents were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran and Et₂O were distilled from sodium benzophenone ketyl. Dichloromethane, triethylamine, acetonitrile and pyridine were freshly distilled from calcium hydride. All solvents used for routine isolation of products and chromatography were reagent grade and glass distilled. Reaction flasks were dried at 100 °C. Air and moisture sensitive reactions were performed under an argon atmosphere. Flash column chromatography was performed using silica gel 60 (230-400 mesh, Merck) with the indicated solvents. Thin-layer chromatography was performed using 0.25 mm silica gel plates (Merck). Melting points were measured on a Büchi melting point apparatus and are uncorrected. Optical rotations were measured with JASCO DIP-1000 digital polarimeter at ambient temperature using 100 mm cell of 2 mL capacity. Infrared spectra were recorded on a Perkin-Elmer 1710 FT-IR spectrometer. Mass spectra were obtained with VG Trio-2 GC-MS instrument. High-resolution mass spectra were obtained with JEOL JMS-AX 505WA instrument. ¹H and ¹³C NMR spectra were recorded on either a JEOL JNM-GCX 400 or JEOL JNM-LA 300 spectrometer as solutions in deuteriochloroform (CDCl₃). Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane and are referenced to the deuterated solvent (CHCl₃). ¹H-NMR data were reported in the order of chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and/or multiple resonance), number of protons, and coupling constant in hertz (Hz).

Methyl (*E*,4*R*)-4-*tert*-butyldimethylsilyloxy-6-hydroxy-2-hexenoate (7):

To a solution of trimethyl phosphonoacetate (4.5 mL, 28 mmol) in THF (50 mL) at $-78\text{ }^{\circ}\text{C}$ was added *n*-BuLi (1.6M solution in hexanes, 17 mL, 28 mmol) dropwise over 30 min. After stirring for 1 h at $-78\text{ }^{\circ}\text{C}$, a solution of TBS-protected (*R*)-(-)- α -hydroxy- γ -butyrolactone **6**¹ (5.0 g, 23 mmol) in THF (10 mL) was added to this mixture, which was followed by the addition of DIBAL (1.0 M solution in toluene, 25 mL, 25 mmol) dropwise over 1 h. The resulting mixture was slowly warmed to $0\text{ }^{\circ}\text{C}$, and then quenched with excess $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$. The mixture was stirred for an additional 2 h, after which it was extracted with EtOAc and the combined organic layers were washed with H_2O , and brine, dried over MgSO_4 , and concentrated in vacuo. Purification via flash column chromatography (EtOAc:hexanes = 1:3) of the residue afforded 5.3 g (85%) of the unsaturated ester **7** as a colorless oil: $[\alpha]_{\text{D}}^{20} +25.8$ (c 3.7, CH_2Cl_2) [lit.² 90% purity $[\alpha]_{\text{D}} +11.1$ (c 1.0, CH_2Cl_2)]; $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ 6.83 (dd, 1H, $J = 4.6, 15.6\text{ Hz}$), 5.91 (dd, 1H, $J = 1.7, 15.6\text{ Hz}$), 4.56-4.50 (m, 1H), 3.76-3.60 (m, 2H), 3.68 (s, 3H), 1.90-1.79 (m, 1H), 1.73-1.63 (m, 1H), 0.86 (s, 9H), 0.00 (2s, 6H); $^{13}\text{C-NMR}$ (CDCl_3 , 75MHz) δ 166.8, 150.2, 120.0, 70.4, 59.4, 51.5, 38.6, 25.7, 18.0, $-4.6, -5.1$; IR (neat) 3445, 2953, 2857, 1726, 1659 cm^{-1} ; LRMS (EI) m/z 217 ($\text{M}^+ - t\text{C}_4\text{H}_9$); HRMS (EI) calcd for $\text{C}_9\text{H}_{17}\text{O}_4\text{Si}$ ($\text{M}^+ - t\text{C}_4\text{H}_9$) 217.0895, found 217.0885.

(3*R*,4*E*)-3-*tert*-Butyldimethylsilyloxy-6-hydroxy-4-hexenyl-4-methyl benzenesulfonate (8):

(i) Tosylation of 7. To a solution of the alcohol **7** (7.4 g, 27 mmol) and Et_3N (5.7 mL, 40 mmol) in CH_2Cl_2 (100 mL) at $0\text{ }^{\circ}\text{C}$ were added *p*-toluenesulfonyl chloride (5.2 g, 27 mmol) and DMAP (0.60 g, 4.9 mmol). After stirring for 3 h at ambient temperature, the mixture was diluted with CH_2Cl_2 , and saturated aqueous NH_4Cl . The mixture was extracted with CH_2Cl_2 , and the combined organic layers were washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo. Purification via flash column chromatography (EtOAc:hexanes = 1:5) of the residue afforded 11 g (99%) of the tosylate as a clear and colorless oil: $[\alpha]_{\text{D}}^{20} +18.4$ (c 0.25, CH_2Cl_2); $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ 7.78 (d, 2H, $J = 8.3\text{ Hz}$), 7.34 (d, 2H, $J = 8.0$

¹ (a) Shiuey, S. J.; Partridge, J. J.; Uskokovic, M. R. *J. Org. Chem.* **1988**, 53, 1040. (b) Mulzer, J.; Mantoulidis, A.; Ohler, E. *J. Org. Chem.* **2000**, 65, 7456.

² Hassan, H. H. A. M.; Tamm, Ch. *Helv. Chim. Acta.* **1997**, 79, 527.

Hz), 6.81 (dd, 1H, $J = 4.8, 15$ Hz), 5.91 (dd, 1H, $J = 1.7, 15$ Hz), 4.43-4.37 (m, 1H), 4.18-4.02 (m, 2H), 3.73 (s, 3H), 2.45 (s, 3H), 1.95-1.75 (m, 2H), 0.85 (s, 9H), 0.00 (s, 6H); ^{13}C -NMR (CDCl_3 , 75MHz) δ 166.6, 149.4, 144.8, 132.9, 129.8, 127.9, 120.3, 67.8, 66.4, 51.6, 36.3, 25.6, 21.6, 17.9, -4.5, -5.2; IR (neat) 2953, 2857, 1725, 1363, 1177 cm^{-1} ; LRMS (EI) m/z 371 ($\text{M}^+ - t\text{C}_4\text{H}_9$); HRMS (EI) calcd for $\text{C}_{16}\text{H}_{23}\text{O}_6\text{Si}_1\text{Si}_1$ ($\text{M}^+ - t\text{C}_4\text{H}_9$) 371.0984, found 371.0944.

(ii) DIBAL reduction of the ester. To a solution of the above ester (6.7 g, 16 mmol) in CH_2Cl_2 (100 mL) at -78°C was added DIBAL (1.0 M solution in toluene, 39 mL, 39 mmol) dropwise over 30 min. After stirring for 1 h at -40°C , the reaction mixture was quenched by slow addition of MeOH. A saturated aqueous potassium sodium tartrate solution was added and the mixture was stirred at ambient temperature for 2 h. After separation of the organic layers, the aqueous phase was extracted with CH_2Cl_2 . The combined organic layers were washed with brine, dried over MgSO_4 , and concentrated in vacuo. Purification via flash column chromatography (EtOAc:hexanes = 1:2) of the residue afforded 6.0 g (96%) of the desired alcohol **8** as a colorless oil: $[\alpha]_{\text{D}}^{20} +10.0$ (c 0.25, CH_2Cl_2); ^1H -NMR (CDCl_3 , 300MHz) δ 7.79 (d, 2H, $J = 8.3$ Hz), 7.34 (d, 2H, $J = 8.3$ Hz), 5.74 (td, 1H, $J = 5.1, 15.6$ Hz), 5.60 (dd, 1H, $J = 6.0, 15.4$ Hz), 4.26 (q, 1H, $J = 6.0$ Hz), 4.20-4.05 (m, 4H), 2.45 (s, 3H), 1.82 (q, 1H, $J = 6.3$ Hz), 1.48 (bs, 1H), 0.83 (s, 9H), 0.00 (s, 6H); ^{13}C -NMR (CDCl_3 , 75MHz) δ 144.7, 133.4, 133.1, 129.8, 129.6, 127.8, 69.0, 67.2, 62.8, 37.1, 25.7, 21.5, 18.0, -4.5, -5.2; IR (neat) 3413, 2928, 2856, 1361, 1176 cm^{-1} ; LRMS (EI) m/z 603 ($\text{M}^+ - t\text{C}_4\text{H}_9$); HRMS (EI) calcd for $\text{C}_{15}\text{H}_{23}\text{O}_5\text{SSi}$ ($\text{M}^+ - t\text{C}_4\text{H}_9$) 343.1035, found 343.1041.

Methyl (5R,6E)-5-tert-butyldimethylsilyloxy-2-phenylsulfonyl-8-tetrahydro-2H-pyran-2-yloxy-6-octenoate (9):

(i) Protection of the alcohol. To a mixture of the alcohol **8** (4.8 g, 12 mmol) and dihydropyran (1.6 mL, 18 mmol) in CH_2Cl_2 (100 mL) at ambient temperature was added pyridinium *p*-toluenesulfonic acid (0.30 g, 1.2 mmol). After stirring for 3 h, the reaction mixture was concentrated in vacuo. Purification via flash column chromatography (EtOAc:hexanes = 1:5) of the residue afforded 5.8 g (100%) of the THP-protected tosylate as a colorless oil: ^1H -NMR (CDCl_3 , 300MHz) δ 7.79 (d, 2H, $J = 8.3$ Hz), 7.34 (d, 2H, $J = 8.3$ Hz), 5.71-5.56 (m, 2H), 4.61 (s, 1H), 4.27-4.18 (m, 1H), 4.16-4.04 (m, 3H), 3.98-3.92 (m, 1H), 3.90-3.82 (m, 1H), 3.52-3.47 (m, 1H), 2.46 (s, 3H), 1.88-1.53 (m, 8H), 0.83 (s, 9H), 0.00 (s, 6H); IR (neat) 2951, 2856, 1363, 1177 cm^{-1} ; LRMS (EI) m/z 427 ($\text{M}^+ - t\text{C}_4\text{H}_9$).

(ii) Alkylation of the tosylate. To a suspension of NaH (60% in mineral oil, 1.3 g, 32 mmol) in DMF (2 mL) at 0 °C was added dropwise a solution of methyl benzenesulfonylacetate (6.9 g, 32 mmol) in DMF (10 mL). After stirring for 2 h, a solution of the tosylate (5.6 g, 12 mmol) in DMF (25 mL) was added. The resulting solution was warmed to 80 °C, and stirred for 15 h. The reaction mixture was quenched by an addition of saturated aqueous NH₄Cl and the reaction mixture was diluted with EtOAc. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over MgSO₄, and concentrated in vacuo. Purification via flash column chromatography (EtOAc:hexanes = 1:2) of the residue afforded 5.3 g (87%) of the alkylated product **9** as a colorless oil: ¹H-NMR (CDCl₃, 300MHz) δ 7.87 (d, 2H, *J* = 7.3 Hz), 7.69 (t, 1H, *J* = 7.4 Hz), 7.57 (t, 2H, *J* = 7.5 Hz), 5.72-5.56 (m, 2H), 4.61 (m, 1H), 4.22-4.09 (m, 2H), 4.06-3.94 (m, 2H), 3.89-3.83 (m, 1H), 3.70 and 3.69 (2s, 3H), 3.52-3.49 (m, 1H), 4.22-3.83 (m, 10H), 0.86 and 0.84 (2s, 9H), 0.00 (2s, 6H); IR (neat) 2950, 2856, 1744, 1324, 1149 cm⁻¹; LRMS (EI) *m/z* 425 (M⁺ – OTHP); HRMS (EI) calcd for C₂₁H₃₃O₅SSi (M⁺ – OTHP) 425.1818, found 425.1818.

Ethyl (*E*)-3-(2*R*)-6-oxo-5-phenylsulfonyltetrahydro-2*H*-pyran-2-yl-2-propenyl carbonate (5**):**

(i) Deprotection of both THP and TBS group. To a solution of **9** (4.4 g, 8.4 mmol) in MeOH (50 mL) at ambient temperature was added camphorsulfonic acid (0.19 g, 0.84 mmol). After stirring for 5 h, the reaction mixture was concentrated in vacuo. Purification via flash column chromatography (CH₂Cl₂:MeOH = 15:1) of the residue afforded 2.5 g (92%) of a diol as a colorless oil: ¹H-NMR (CDCl₃, 300MHz) δ 7.81-7.78 (m, 2H), 7.65-7.59 (m, 1H), 7.53-7.38 (m, 2H), 5.80-5.71 (m, 1H), 5.65-5.56 (m, 1H), 4.10-4.00 (m, 3H), 3.98-3.95 (m, 1H), 3.58 and 3.57 (s, 3H), 2.15-1.94 (m, 2H), 1.53-1.44 (m, 2H); IR (neat) 3366, 2951, 1735, 1314, 1147 cm⁻¹; LRMS (EI) *m/z* 310 (M⁺ – H₂O).

(ii) Lactonization of the dihydroxy ester. To a solution of the above diol (1.2 g, 3.7 mmol) in CH₃CN (50 mL) at ambient temperature was added DBU (0.67 mL, 4.5 mmol). After stirring for 2 h, the reaction mixture was concentrated in vacuo. Purification via flash column chromatography (EtOAc:hexanes:MeOH = 30:15:2) of the residue afforded 0.88 g (80%) of the valerolactone as a colorless oil: ¹H-NMR (CDCl₃, 300MHz) δ 7.88-7.84 (m, 2H), 7.65-7.59 (m, 1H), 7.54-7.48 (m, 2H), 5.95-5.84 (m, 1H), 5.77-5.63 (m, 1H), 5.01 and 4.87 (m, 1H),

4.12 (d, 2H, $J = 4.2$ Hz), 4.05 (dd, 1/2H, $J = 7.1, 8.9$ Hz), 3.98 (dd, 1/2H, $J = 5.4, 7.1$ Hz), 2.79-2.53 (m, 1H), 2.42-2.05 (m, 2H), 1.97-1.91 and 1.73-1.60 (m, 1H); IR (neat) 3522, 2926, 1730, 1447, 1309, 1146, 1082 cm^{-1} ; LRMS (EI) m/z 278 ($\text{M}^+ - \text{H}_2\text{O}$); HRMS (EI) calcd for $\text{C}_{14}\text{H}_{14}\text{O}_4\text{S}$ ($\text{M}^+ - \text{H}_2\text{O}$) 278.0613, found 278.0604.

(iii) Preparation of the allylic carbonate. To a solution of the above-mentioned valerolactone (1.2 g, 4.1 mmol) in CH_2Cl_2 (50 mL) at 0°C were added pyridine (0.49 mL, 6.1 mmol) and ethyl chloroformate (0.47 mL, 4.9 mmol). After stirring for 3 h at ambient temperature, the reaction was quenched by an addition of saturated aqueous NH_4Cl and the reaction mixture was diluted with CH_2Cl_2 . The reaction mixture was extracted with CH_2Cl_2 and the combined organic layers were washed with brine, dried over MgSO_4 , and concentrated in vacuo. Purification via flash column chromatography ($\text{EtOAc}:\text{hexanes} = 1:5$) of the residue afforded 1.4 g (95%) of **5** as a colorless oil: $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ 7.87-7.84 (m, 2H), 7.64-7.59 (m, 1H), 7.53-7.48 (m, 2H), 5.90-5.69 (m, 2H), 5.02 and 4.83 (m, 1H), 4.62-4.51 (m, 2H), 4.18-4.09 (m, 2H), 4.07-3.96 (m, 1H), 2.80-2.72 and 2.67-2.54 (m, 1H), 2.41-2.05 (m, 2H), 1.97-1.89 and 1.70-1.58 (m, 1H), 1.21-1.27 (m, 3H); IR (neat) 2983, 1741, 1447, 1309, 1259, 1147 cm^{-1} ; LRMS (EI) m/z 391 ($\text{M}^+ + \text{Na}$), 369 ($\text{M}^+ + \text{H}$).

(1R,4S,7R)-4-Phenylsulfonyl-7-vinyl-2-oxabicyclo[2.2.1]heptan-3-one (4):

To a refluxing solution of the allylic carbonate **5** (1.0 g, 2.7 mmol) in CH_2Cl_2 (45 mL) was added a solution of $\text{Pd}(\text{PPh}_3)_4$ (0.16 g, 0.014 mmol) in CH_2Cl_2 (5 mL). After stirring for 30 min, the reaction mixture was cooled to ambient temperature, and concentrated in vacuo. Purification via flash column chromatography ($\text{EtOAc}:\text{hexanes}:\text{CH}_2\text{Cl}_2 = 1:4:1$) of the residue afforded 0.65 g (88%) of the desired bicyclic lactone **4** and 20 mg of the minor isomer **4'** as a white solid, respectively. Major isomer **4**: $[\alpha]_{\text{D}}^{28} -7.97$ (c 0.29, CH_2Cl_2); $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ 8.06-8.03 (m, 2H), 7.64-7.59 (m, 1H), 7.52-7.47 (m, 2H), 5.78 (ddd, 1H, $J = 8.7, 10.4, 17.0$ Hz), 5.37 (d, 1H, $J = 17.0$ Hz), 5.27 (d, 1H, $J = 10.5$ Hz), 4.64 (s, 1H), 3.15 (d, 1H, $J = 8.7$ Hz), 2.49 (dt, 1H, $J = 4.8, 11.9$ Hz), 2.12-2.02 (m, 1H), 1.90 (ddd, 1H, $J = 4.8, 9.0, 13.4$ Hz), 1.73 (ddd, 1H, $J = 3.9, 9.0, 13.1$ Hz); $^{13}\text{C-NMR}$ (CDCl_3 , 75MHz) δ 168.6, 136.8, 134.4, 130.3, 129.2, 128.7, 121.5, 83.2, 74.0, 58.7, 28.1, 27.5; IR (neat) 1787, 1321, 1157, 1117 cm^{-1} ; LRMS (EI) m/z 279 ($\text{M}^+ + \text{H}$); HRMS (EI) calcd for $\text{C}_{14}\text{H}_{14}\text{O}_4\text{S}$ (M^+) 278.0613, found 278.0602. Minor isomer **4'**: $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ 7.87 (d, 2H, $J = 7.3$ Hz),

7.60 (t, 1H, $J = 7.3$ Hz), 7.74 (t, 2H, $J = 7.3$ Hz), 5.81 (ddd, 1H, $J = 8.2, 10.2, 17.2$ Hz), 5.29 (d, 1H, $J = 10.0$ Hz) 5.25 (d, 1H, $J = 16.8$ Hz), 4.58 (s, 1H), 3.02 (d, 1H, $J = 7.8$ Hz), 2.71-2.57 (m, 1H), 2.22-2.11 (m, 1H), 2.00-1.88 (m, 2H).

(3*R*,3*aS*,4*R*,6*aR*)-4-Hydroxy-6*a*-phenylsulfonyl-3-vinylhexahydro-1*H*-cyclopenta [c]furan-1-one (12**):**

(i) Ozonolysis of the vinyl lactone. A solution of the bicyclic lactone **4** (0.10 g, 0.36 mmol) in CH₂Cl₂ (10 mL) was cooled to -78 °C, and ozone was bubbled through it at -78 °C until the solution turned light blue. To this solution was added Me₂S (0.53 mL, 7.2 mmol) at -78 °C. The reaction mixture was stirred at room temperature for 12 h, after which it was concentrated under reduced pressure to afford the crude aldehyde.

(ii) Vinyl addition of the above crude aldehyde. To a solution of the above aldehyde in anhydrous THF solution (2 mL) was added vinylmagnesium bromide (1.0 M solution in THF, 0.43 mL, 0.43 mmol) at -78 °C. After the resulting mixture was stirred at the same temperature for 5 h, the reaction was quenched by an addition of saturated aqueous NH₄Cl. The mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over MgSO₄, and concentrated in vacuo. Purification via flash column chromatography (EtOAc:hexanes = 1:1) of the residue afforded 27 mg (25%) of **12** as a white solid: ¹H-NMR (CDCl₃, 600MHz) δ 7.87 (d, 2H, $J = 7.3$ Hz), 7.66 (t, 1H, $J = 7.3$ Hz), 7.54 (t, 2H, $J = 7.3$ Hz), 6.23 (ddd, 1H, $J = 5.0, 10.8, 17.4$ Hz), 5.55 (ddd, 1H, $J = 1.2, 1.4, 17.5$ Hz), 5.39 (ddd, 1H, $J = 1.2, 1.6, 10.8$ Hz), 5.35 (dddd, 1H, $J = 1.4, 1.6, 3.8, 5.0$ Hz), 4.53 (dd, 1H, $J = 1.7$ Hz), 3.55 (dt, 1H, $J = 1.7, 3.8$ Hz), 2.28-2.24 (m, 2H), 1.86-1.84 (m, 2H); LRMS (EI) m/z (M⁺) 308.

(1*R*,4*R*,7*S*)-7-Vinyl-2-oxabicyclo[2.2.1]heptan-3-one (13):

To a mixture of the bicyclic lactone **4** (0.60 g, 2.2 mmol) and boric acid (1.3 g, 22 mmol) in MeOH (30 mL) was added 6% Na/Hg (4.1 g, 11 mmol) in one portion. After stirring for 3 h, the resulting mixture was quenched by an addition of saturated aqueous NH₄Cl. The mixture was extracted with Et₂O and the combined organic layers were washed with a solution of saturated aqueous NaHCO₃, H₂O, and brine, dried over MgSO₄, and concentrated in vacuo. Purification via flash column chromatography (Et₂O:hexanes = 1:2) of the residue afforded 260 mg (88%) of the desulfonylated lactone **11** as a colorless oil: $[\alpha]_D^{20} +17.9$ (*c* 0.24, CH₂Cl₂); ¹H-NMR (CDCl₃, 300MHz) δ 5.78 (ddd, 1H, *J* = 6.7, 10.5, 17.2 Hz), 5.26 and 5.21 (td, 1H, *J* = 1.2, 17.2 Hz), 5.21 and 5.18 (td, 1H, *J* = 1.1, 10.4 Hz), 4.68 (s, 1H), 2.06-1.85 (m, 3H), 1.81-1.69 (m, 1H); ¹³C-NMR (CDCl₃, 100MHz) δ 177.5, 132.1, 119.0, 83.6, 55.2, 46.6, 28.5, 22.9; IR (neat) 2952, 1781, 1045, 948 cm⁻¹; LRMS (EI) *m/z* 139 (*M*⁺ + H); HRMS (EI) calcd for C₈H₁₁O₂ (*M*⁺ + H) 139.0759, found 139.0759.

(3*S*,3*aS*,4*R*,6*aS*)-4-Hydroxy-3-vinylhexahydro-1*H*-cyclopenta[*c*]furan-1-one (3):

(i) Preparation of the vinylcerium reagent. Cerium chloride (0.19 g, 0.79 mmol) was dried at 140 °C for 3 h in vacuo. Anhydrous THF (2 mL) was added to this solid at 0 °C, and the mixture was stirred for 12 h at room temperature. To this suspension was added vinylmagnesium bromide (1.0 M solution in THF, 0.72 mL, 0.72 mmol) at −78 °C and the resulting mixture was stirred for 1 h.

(ii) Ozonolysis of 13. A solution of bicyclic lactone **13** (50 mg, 0.36 mmol) in CH₂Cl₂ (10 mL) was cooled to −78 °C, and ozone was bubbled through it at −78 °C until the solution turned light blue. To this solution was added Me₂S (0.55 mL, 7.5 mmol) at −78 °C. The reaction mixture was stirred at room temperature for 12 h, after which it was concentrated under reduced pressure to afford the crude aldehyde.

(iii) Vinyl addition of the crude aldehyde. A solution of the crude aldehyde in anhydrous THF (2 mL) was added to the above prepared vinylcerium reagent solution dropwise at -78°C . After stirring for 5 h at the same temperature, the reaction mixture was diluted with saturated aqueous NH_4Cl and EtOAc. The suspension was filtered through a pad of Celite, which was then rinsed with EtOAc. The filtrate was diluted with EtOAc and the combined organic layers were washed with brine, dried over MgSO_4 , and concentrated in vacuo. Purification via flash column chromatography (EtOAc:hexanes = 1:2 $\rightarrow$ 1:1) of the residue afforded 39 mg (65%) of the vinylated lactone **3** and 5 mg of the undesired isomer **3'** as a colorless oil, respectively. Major isomer **3**: $[\alpha]_{\text{D}}^{20} -4.91$ (c 0.20, CH_2Cl_2); $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ 5.83 (ddd, 1H, $J = 5.6, 10.4, 17.0$ Hz), 5.29 (d, 1H, $J = 17.3$ Hz), 5.21 (d, 1H, $J = 10.4$ Hz), 5.10-5.13 (m, 1H), 4.34 (dd, 1H, $J = 6.5, 1.4$ Hz), 3.01 (dt, 1H, $J = 2.9, 9.5$ Hz), 2.62 (ddd, 1H, $J = 2.9, 6.5, 9.5$ Hz), 2.09-1.82 (m, 3H), 1.65-1.56 (m, 1H); $^{13}\text{C-NMR}$ (CDCl_3 , 100MHz) δ 180.1, 136.8, 115.9, 78.2, 74.0, 49.4, 34.2, 26.1; IR (neat) 3463, 2924, 1747, 616 cm^{-1} ; LRMS (EI) m/z 168 (M^+). Minor isomer **3'**: $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ 5.83 (ddd, 1H, $J = 5.6, 10.4, 17.0$ Hz), 5.29 (d, 1H, $J = 17.3$ Hz), 5.14 (d, 1H, $J = 10.4$ Hz), 5.10-5.13 (m, 1H), 4.34 (dd, 1H, $J = 6.6, 11.5$ Hz), 3.01 (dt, 1H, $J = 2.9, 9.5$ Hz), 2.62 (ddd, 1H, $J = 2.9, 6.6, 9.5$ Hz), 2.09-1.82 (m, 3H), 1.65-1.56 (m, 1H); $^{13}\text{C-NMR}$ (CDCl_3 , 100MHz) δ 180.1, 136.8, 115.9, 78.2, 74.0, 49.4, 34.2, 26.1; IR (neat) 3463, 2924, 1747, 616 cm^{-1} ; LRMS (EI) m/z 168 (M^+).

(3S,3aS,4R,6aS)-1-Oxo-3-vinylhexahydro-1H-cyclopenta[c]furan-4-yl-4-pentenoate (14**):**

To a mixture of the alcohol **3** (20 mg, 0.12 mmol), DMAP (3.0 mg, 0.024 mmol), and Et_3N (42 μL , 0.30 mmol) in CH_2Cl_2 (2 mL) at 0°C was added pentenoyl chloride (27 μL , 0.24 mmol). After stirring for 3 h at ambient temperature, the mixture was diluted with CH_2Cl_2 and saturated aqueous NH_4Cl . The mixture was extracted with CH_2Cl_2 , and the combined organic layers were washed with brine, dried over MgSO_4 , and concentrated in vacuo. Purification via flash column chromatography (EtOAc:hexanes = 1:3) of the residue afforded 29 mg (98%) of the pentenoate **14** as a colorless oil: $[\alpha]_{\text{D}}^{24} +9.85$ (c 0.22, CH_2Cl_2); $^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ 5.82-5.67 (m, 2H), 5.28-5.12 (m, 3H), 5.03-4.92 (m, 2H), 4.82-4.79 (m, 1H), 3.09-3.01 (m, 1H), 2.83 (ddd, 1H, $J = 3.1, 6.8, 9.6$ Hz), 2.40-2.29 (m, 4H), 1.99-1.92 (m, 3H), 1.73-1.65 (m, 1H); $^{13}\text{C-NMR}$ (CDCl_3 , 100MHz) δ 179.4, 172.4, 136.2, 136.1, 116.3, 115.8,

78.3, 75.9, 47.7, 42.5, 33.4, 31.0, 28.6, 25.8; IR (neat) 3463, 2924, 1747, 616 cm^{-1} ; LRMS (FAB) m/z 251 ($\text{M}^+ + \text{H}$); HRMS (EI) calcd for $\text{C}_{14}\text{H}_{19}\text{O}_4$ ($\text{M}^+ + \text{H}$) 251.1283, found 251.1275.

(2a*S*,4a*R*,10a*S*,10b*S*)-2a,3,4,4a,7,8,10a,10b-Octahydro-1,5-dioxacyclonona[*cd*]pentalene-2,6-dione (2):

To a refluxing solution of the dien **14** (15 mg, 0.060 mmol) in CH_2Cl_2 (280 mL) was added a solution of the 2nd generation Grubbs' catalyst (10 mg, 0.012 mmol) in CH_2Cl_2 (20 mL).³ After stirring for 10 min, the reaction mixture was cooled to ambient temperature, and solvent volume was then reduced to 2 mL in vacuo. The reaction mixture was treated with DMSO (0.10 mL, 1.4 mmol) overnight.⁴ The mixture was concentrated in vacuo and purification via column chromatography (EtOAc:hexanes = 1:1) of the residue afforded 11 mg (84%) of the desired 9-membered lactone **2** as a colorless oil: $[\alpha]_{\text{D}}^{25} -1.83$ (c 0.24, CH_2Cl_2); ^1H -NMR (CDCl_3 , 500 MHz) δ 5.67 (dd, 1H, $J = 7.9, 11.2$ Hz), 5.64 (dt, 1H, $J = 6.1, 9.5, 11.3$ Hz), 5.30 (dt, 1H, $J = 6.8, 9.4$ Hz), 5.17 (t, 1H, $J = 7.9$ Hz), 3.16-3.11 (m, 1H), 3.03-2.98 (m, 1H), 2.77-2.69 (m, 1H), 2.63 (ddd, 1H, $J = 3.2, 5.0, 13.3$ Hz), 2.30-2.25 (m, 1H), 2.17-2.10 (m, 3H), 2.1-1.9 (m, 2H); ^{13}C -NMR (CDCl_3 , 100MHz) δ 179.0, 172.8, 131.9, 128.7, 76.0, 74.7, 50.7, 43.3, 33.4, 28.6, 25.6, 25.0; IR (neat) 3375, 2924, 1775, 1740, 1105, 1026 cm^{-1} ; LRMS (EI) m/z 222 (M^+); HRMS (CI $^+$) calcd for $\text{C}_{12}\text{H}_{15}\text{O}_4$ ($\text{M}^+ + \text{H}$) 223.0970, found 223.0972.

Bacillariolide III (1):

To a solution of the 9-membered lactone **2** (5.0 mg, 0.023 mmol) in THF/ H_2O (5:1, 1 mL) at ambient temperature was added $\text{LiOH} \cdot \text{H}_2\text{O}$ (3.0 mg, 0.071 mmol). After stirring for 1 h, the reaction mixture was treated with trifluoroacetic acid (15 μL , 0.19 mmol). The mixture was

³ Yamamoto, K.; Biswas, K.; Gaul, C.; Danishefsky, S. J. *Tetrahedron. Lett.* **2003**, 44, 3297.

⁴ Ahn, Y. M.; Yang, K.; Georg, G. I. *Org. Lett.* **2001**, 3, 1411.

concentrated in vacuo and purification via silica gel (Hexanes : THF : AcOH = 10:10:0.5) and ODS column chromatography (H₂O:CH₃CN:AcOH = 90:10:0.3) of the residue afforded 3.9 mg (71%) of bacillariolide III (**1**) as a colorless oil: $[\alpha]_{\text{D}}^{20} -27.1$ (*c* 0.20, MeOH) [lit.⁵ $[\alpha]_{\text{D}}^{24} -25.3$ (*c* 0.28, MeOH)]; ¹H-NMR (CD₃OD, 500MHz) δ 5.58-5.54 (dt, 1H, *J* = 7.4, 9.6 Hz), 5.53-5.47 (m, 2H), 4.28 (dd, 1H, *J* = 6.3, 11.3 Hz), 3.14 (dt, 1H, *J* = 6.6, 9.5 Hz), 2.59 (t, 1H, *J* = 7.1 Hz), 2.46-2.39 (m, 2H), 2.35 (t, 2H, *J* = 6.7 Hz), 1.94 (dd, 2H, *J* = 6.6, 15.0 Hz), 1.81-1.75 (m, 1H), 1.60-1.53 (m, 1H); ¹³C-NMR (CD₃OD, 100MHz) δ 183.5, 183.4, 134.0, 130.3, 76.5, 74.5, 51.8, 44.6, 36.0, 34.5, 27.1, 25.1; IR (neat) 3649, 2962, 1736, 1436, 1261, 1094 cm⁻¹; LRMS (EI) *m/z* 241 (M⁺ + H).

⁵ Zheng, N.; Shimizu, Y. *Chem. Commun.* **1997**, 399.

NAME Current Data Parameters
EXPNO 2
PROCNO 1

===== CHANNEL f1 =====
NUC1 ¹H
P1 10.40 usec
PL1 6.00 dB
SFO1 400.1317206 MHz

F2 - Acquisition Parameters
Date_ 20100905
Time 14.54
INSTRUM spect
PROBHD 5 mm HLLHNU
PULPROG zgpg30
TD 65536
FIDRES 0.0012
AQ 0.184844 sec
RG 327.5
DM 135.200 usec
DE 1.500 usec
TE 300.2 K
DO 0.00000000 sec
D1 2.00000000 sec
D11 0.00027040 sec
D12 0.00027040 sec

F1 - Processing parameters
SI 32768
SF 400.1317206 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

2D NMR plot parameters
CQ2 15.00 cm
CQ1 15.00 cm
F2P1D 8.3871 ppm
F2C1D 2558.67 Hz
F2P1F -0.321 ppm
F2C1F -120.20 Hz
F1P1D 3660.87 Hz
F1C1D -0.321 ppm
F1P1F -120.20 Hz
F2P1M 0.81617 ppm/cn
F2C1M 246.54632 Hz/cn
F1P1M 0.81617 ppm/cn
F1C1M 246.54632 Hz/cn

Current Data Parameters
NAME 180225-081
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20010828
Time 10:48
INSTRUM spect
PROBHD 5 mm T1 1H/
PULPROG zgpg30
TO 32768
SOLVENT CDCl3
NS 64
DS 16
SWH 5009.315 Hz
FIDRES 0.143829 Hz
AQ 2.726347 sec
RG 1448.2
RW 1448.2 Hz
OW 83.200 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
C1 0.00000000 sec
C8 0.00000000 sec
C18 0.00000000 sec
C20 0.34849598 sec

===== CHANNEL f1 =====
NUC1 1H
P1 9.80 usec
PL1 0.00 dB
RG1 655.00 usec
P12 19.80 usec
PL2 0.00 dB
RG2 120.00 dB
PL3 0.00 dB
RG3 120.00 dB
P14 0.00 usec
PL4 0.00 dB
RG4 120.00 dB
P15 64.53 dB
RG5 1000
SPR1 1.000
SPR2 1.000
SPR3 1.000
SPR4 1.000
SPR5 1.000
SPR6 1.000
SPR7 1.000
SPR8 1.000
SPR9 1.000
SPR10 1.000
SPR11 1.000
SPR12 1.000
SPR13 1.000
SPR14 1.000
SPR15 1.000
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SPR78 1.000
SPR79 1.000
SPR80 1.000
SPR81 1.000
SPR82 1.000
SPR83 1.000
SPR84 1.000
SPR85 1.000
SPR86 1.000
SPR87 1.000
SPR88 1.000
SPR89 1.000
SPR90 1.000
SPR91 1.000
SPR92 1.000
SPR93 1.000
SPR94 1.000
SPR95 1.000
SPR96 1.000
SPR97 1.000
SPR98 1.000
SPR99 1.000
SPR100 1.000

F2 - Processing parameters
SI 32768
SF 500.130029 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00

10 usec plot parameters
CX 20.00 cm
F1P 9.815 dBm
F1 5770.53 Hz
F2P -0.389 dBm
F2 -238.65 Hz
PRINCM 0.50069 dB/cm
HZCM 300.48077 Hz/cm

Current Data Parameters

NAME	EXPNO	PROCNO
NAME	12	1
EXPNO	12	1
PROCNO	1	1

F2 - Acquisition Parameters

NAME	VALUE
DATE_	20030221
TIME	12.14
PROBHD	5 mm MSL500
PULPROG	zgpg30
TD	1024
SOLVENT	CDCl3
NS	18
DS	4
SWH	3914.156 Hz
FIDRES	3.74448 Hz
AQ	0.1315796 sec
RG	512
IN	130.400 usec
DE	16.600 usec
TE	300.0 K
D0	0.00000000 sec
D1	2.00000000 sec
TD0	0.00000000 sec

===== CHANNEL f1 =====

NAME	VALUE
NUC1	13C
PC1	9.50 usec
PL1	5.00 dB
PR01	400.1315621 MHz

F1 - Acquisition parameters

NAME	VALUE
NUC1	13C
PC1	9.50 usec
PL1	5.00 dB
PR01	400.1315621 MHz
FIDRES	30.431395 Hz
SN	9.583 ppm

F2 - Processing parameters

NAME	VALUE
SI	32768
SF	400.1360005 MHz
WDW	EM
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

F1 - Processing parameters

NAME	VALUE
SI	1024
WDW	EM
SSB	0
LB	0.00 Hz
GB	0

2D NMR plot parameters

NAME	VALUE
CH2	15.00 cm
CH1	15.00 cm
PC10	8.46 usec
PC11	3478.77 Hz
PC12	-0.889 ppm
PC13	-355.58 Hz
PC14	8.698 ppm
PC15	3480.47 Hz
PC16	-37.884 ppm
PC17	0.53885 ppm/cm
PC18	255.62372 Hz/cm
PC19	0.53885 ppm/cm
PC20	255.62372 Hz/cm

[illegible]

¹H-NMR of Synthetic sample

¹H-NMR (ODS) of Y. Yamada group