Supporting Information:

Total Synthesis of Aigialomycin D.

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General Methods: Reagents obtained from commercial suppliers were used without further purification unless otherwise noted. THF, toluene, and methylene chloride was obtained from a dry solvent system (passed through a prepacked column of alumina) and used without further drying. All air and water sensitive reactions were performed in flame-dried glassware under a positive pressure of prepurified argon gas. NMR (^1H and ^{13}C) spectra were recorded on Bruker AMX-400 MHz or Bruker Advance DRX-500 MHz as noted individually, referenced to CDCl_3 (7.27 ppm for ^1H and 77.0 ppm for ^{13}C) or CD_3COCD_3 (2.09 ppm for ^1H and 30.6 and 205.9 ppm for ^{13}C). Infrared spectra (IR) were obtained on a Perkin-Elmer FT-IR model 1600 spectrometer. Melting point was tested on a electrothermal series IA9100 digital melting point apparatus. Optical rotations were obtained on a JASCO model DIP-370 digital polarimeter. Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F254 plates. Compounds which were not UV active were visualized by dipping the plates in para-anisaldehyde solution and heating. Preparative thin layer chromatography was performed using the

indicated solvent on Whatman (LK6F Silica gel 60 Å 250 µM or Pk6F Silica Gel 60 Å 1000 µM) TLC plate.

(2*R*, 3*S*)-Hex-5-ene-1,2,3-triol 2,3-acetonide (11**):**

To a stirring suspension of $\text{Ph}_3\text{P}^+\text{CH}_3\text{I}$ (11.2 g, 27.7 mmol) in 30 mL THF was added KHMDS (0.5 M in toluene, 46.0 mL, 23.0 mmol) at $-78\text{ }^\circ\text{C}$. The solution was warmed up to $0\text{ }^\circ\text{C}$ and stirred for 30 min before cooled down to $-78\text{ }^\circ\text{C}$. Acetonide **10**¹ (1.6 g, 9.2 mmol) in 5 mL THF was added via cannula and the solution was warmed up to r.t. overnight (10 h) before quenched with saturated aqueous NH_4Cl solution, extracted with EtOAc (100 mL X 3). The organic layers were combined and dried with anhydrous MgSO_4 , filtered, and concentrated under reduced pressure vacuum. The residue was purified on a silica gel column using petroleum ether/EtOAc (4/1) as the eluant to afford **11** as a colorless oil (1.02 g, 68%). $[\alpha]_{\text{D}}^{25}$ 54.8 (c 0.26, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 1.34 (s, 3 H), 1.46 (s, 3 H), 2.02 (b, 1 H), 2.25-2.32 (m, 1 H), 2.37-2.44 (m, 1 H), 3.65 (m, 1 H), 4.16-4.21 (m, 1 H), 4.24-4.28 (m, 1 H), 5.10-5.18 (m, 2 H), 5.79-5.89 (m, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ 25.4, 28.1, 33.6, 61.6, 76.2, 77.8, 108.3, 117.3, 134.2. LRMS (ESI) calcd for $\text{C}_9\text{H}_{16}\text{O}_3\text{Na}^+$ $[\text{M}+\text{Na}]^+$: 195.1, found 194.9. LRMS (ESI) calcd for $\text{C}_9\text{H}_{16}\text{O}_3\text{Cl}^-$ $[\text{M}+\text{Cl}]^-$: 207.1, found 207.1.

Pivalate (12):

To a solution of **11** (752 mg, 4.37 mmol), DMAP (106 mg, 0.874 mmol) and triethylamine (2.5 ml, 17.5 mmol) in CH₂Cl₂ (8 ml) was added PivCl (1.1 ml, 8.74 mmol) at 0 °C. The reaction mixture was warmed up to r.t. overnight (10h) before quenched with saturated aqueous NaHCO₃ solution, extracted with EtOAc (100 mL X 3). The organic layers were combined and dried with anhydrous MgSO₄, filtered, and concentrated under reduced pressure vacuum. The residue was purified on a silica gel column using hexanes/EtOAc (4/1) as the eluant to afford **12** as a colorless oil (984 mg, 90%). $[\alpha]_D^{25}$ 15.6 (*c* 0.32, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 1.22 (s, 9 H), 1.33 (s, 3 H), 1.47 (s, 3 H), 2.28-2.41 (m, 2 H), 4.10-4.13 (m, 2 H), 4.22-4.29 (m, 2 H), 5.10-5.17 (m, 2 H), 5.81-5.91 (m, 1 H). ¹³C NMR (100 MHz, CDCl₃) δ 25.9, 27.5, 28.4, 39.1, 63.2, 75.5, 77.8, 108.8, 117.7, 134.6, 178.5. LRMS (ESI) calcd for C₁₄H₂₄O₄Na⁺ [M+Na]⁺ 279.2, found 278.9.

Alcohol 13:

To a solution of **12** (166 mg, 0.648 mmol) in THF (1.5 mL) was added 9-BBN (0.5 M in THF, 2.8 mL, 1.425 mmol) at 0 °C. The reaction mixture was warmed up to r.t. over 4 h and H₂O (0.1 mL), NaOH (3 M, 0.7 mL) and H₂O₂ (30%, 0.2 mL) were added. The reaction mixture was diluted with H₂O 2.5 h later and acidified with citric acid (5%) till pH = 7. The mixture was extracted with EtOAc, washed with saturated aqueous Na₂S₂O₃, H₂O and brine. The organic layers were combined and dried with anhydrous MgSO₄, filtered, and concentrated under reduced pressure vacuum. The residue was purified on a silica gel column using petroleum ether /EtOAc (1/1) as the eluant to afford **13** as a colorless oil (156 mg, 88%). $[\alpha]_D^{25}$ 82.4 (*c* 0.07, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 1.21 (s, 9 H), 1.36 (s, 3 H), 1.46 (s, 3 H), 1.59-1.80 (m, 4 H), 2.30 (b, 1 H), 3.54 (m, 2 H), 4.08 (dd, *J* = 6.1, 11.5 Hz, 1 H), 4.12 (dd, *J* = 5.6, 11.5 Hz, 1 H), 4.19 (m, 1 H), 4.25 (m, 1 H). ¹³C NMR (100 MHz, CDCl₃) δ 25.5, 25.9, 27.1, 28.0, 29.9, 38.7, 62.3, 62.9, 75.3, 77.0, 108.3, 178.2. HRMS (ESI) calcd for C₁₄H₂₆O₅Na⁺ [M+Na]⁺ 297.1678, found 297.1660, Δ = -6.0 ppm.

Alkyne **16**:

To a solution of **13** (682 mg, 2.485 mmol) in CH₂Cl₂ (5 mL), DMSO (5 mL) and Et₃N (3 mL) was added SO₃-pyridine complex (1.6 g, 10.2 mmol) at 0 °C. The reaction mixture was stirred for 1 h before diluted with EtOAc and washed with HCl (0.5 N), H₂O,

saturated aqueous NaHCO_3 solution and brine. The organic layers were dried with anhydrous MgSO_4 , filtered, and concentrated under reduced pressure vacuum. The crude aldehyde **14** was used directly for next step without any further purification.

To a suspension of Zn (Nano-size power, pre-activated, 390 mg, 5.949 mmol) in THF (10 mL) was added propargyl bromide (80% in toluene, 0.53 mL, 4.759 mmol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C and a solution of aldehyde **14** thus obtained in THF (5 mL) was added and reaction mixture was warmed up to r.t. over 2 h before quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc. The organic layers were dried with anhydrous MgSO_4 , filtered, and concentrated under vacuum. To a solution of crude alcohol **15** thus obtained and 2,6-lutidine (0.6 mL, 4.76 mmol) in CH_2Cl_2 (8 mL) was added TBSOTf (0.82 mL, 3.57 mmol) and the reaction mixture was stirred for 10 h before quenched with saturated aqueous NH_4Cl solution, extracted with EtOAc (100 mL X 3). The organic layers were combined and dried with anhydrous MgSO_4 , filtered, and concentrated under reduced pressure vacuum. The residue was purified on a silica gel column using petroleum ether/EtOAc (20/1) as the eluant to afford **16** as a colorless oil (896 mg, 89% from **13**). ^1H NMR (400 MHz, CDCl_3) δ -0.02-0.05 (m, 6 H), 0.80 (s, 9 H), 1.13 (s, 9 H), 1.26 (s, 3 H), 1.36 (s, 3 H), 1.42-1.74 (m, 4 H), 1.81 (m, 1 H), 2.22-2.29 (m, 2 H), 3.78 (m, 1 H), 4.01-4.08 (m, 3 H), 4.12-4.17 (m, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ 18.0, 18.1, 24.3, 24.7, 25.6, 25.8, 27.0, 27.1, 27.2, 28.06, 28.07, 33.2, 33.3, 38.7, 62.8, 62.9, 70.1, 70.2, 70.4, 70.5, 75.2, 76.1, 77.1, 81.2, 108.20, 108.24, 178.1. HRMS (FAB) calcd for $\text{C}_{23}\text{H}_{42}\text{O}_5\text{SiH}^+$ $[\text{M}+\text{H}]^+$: 427.2880, found 427.2880, Δ = -0.1 ppm.

Enyne 18:

To a solution of **17** (87 mg, 0.254 mmol) in DMSO (1.0 mL), CH₂Cl₂ (1.0 mL) and Et₃N (1.0 mL) was added SO₃-Pyridine complex (200 mg, 2.032 mmol) at 0 °C. The reaction mixture was stirred for 2 h before diluted with EtOAc and washed with HCl (0.5 N), H₂O, saturated aqueous NaHCO₃ solution and brine. The organic layers were dried with anhydrous MgSO₄, filtered, and concentrated under reduced pressure vacuum. The crude aldehyde was used directly for next step without any further purification.

To a stirring suspension of Ph₃P⁺CH₃I (204 mg, 0.505 mmol) in 3 mL THF was added KHMDS (0.5 M in toluene, 0.9 mL, 0.454 mmol) at -78 °C. The solution was warmed up to 0 °C and stirred for 30 min before cooled down to -78 °C. Aldehyde obtained as mention above in 2 mL THF was added via cannula and the solution was warmed up to r.t. overnight (10 h) before quenched with saturated aqueous NH₄Cl solution, extracted with EtOAc (100 mL X 3). The organic layers were combined and dried with anhydrous MgSO₄, filtered, and concentrated under reduced pressure vacuum. The residue was purified on a silica gel column using petroleum ether/EtOAc (40/1) as the eluant to afford **18** as a colorless oil (73 mg, 86%). ¹H NMR (400 MHz, CDCl₃) δ -0.05 (s, 3 H), 0.02 (s, 3 H), 0.83 (s, 9 H), 1.27 (s, 3 H), 1.43 (s, 3 H), 1.43-1.78 (m, 4 H), 1.92 (b, 1 H), 2.23-2.31 (m, 2 H), 3.76 (m, 1 H), 4.05-4.10 (m, 1 H), 4.43-4.45 (m, 1 H), 5.02-5.05 (m, 2 H), 5.71-5.80 (m, 1 H). ¹³C NMR (100 MHz, CDCl₃) δ -4.30, -4.11, 18.4, 26.0, 26.1, 26.2, 26.5, 26.8, 27.7, 27.8, 28.62, 28.64, 33.2, 33.6, 70.4, 70.5, 71.07, 71.13, 78.6, 78.8, 80.2, 81.78, 81.82, 108.5, 118.6, 118.7, 134.7, 134.9. HRMS (FAB) calcd for C₁₉H₃₄O₃SiNa⁺ [M+Na]⁺: 361.2175, found 361.2175, Δ = 0.0 ppm.

Acid 19:

To a solution of **18** (586 mg, 1.731 mmol) in Et₂O (16 mL) was added BuLi (1.6 M in hexane, 1.817 mmol) at -78 °C and stirred for 5 min before quenched with dry ice and warmed up to r.t. The reaction mixture was washed with NaOH (0.1 M) and the aqueous layers were combined and acidified by HCl (0.1 M) until the pH = 2. The aqueous layer was extracted with EtOAc and the organic layers were combined and dried with anhydrous MgSO₄, filtered, and concentrated under reduced pressure vacuum and dried on high vacuum. ¹H NMR (400 MHz, CDCl₃) δ -0.03 (s, 3 H), 0.00 (s, 3 H), 0.79 (s, 9 H), 1.17 (s, 3 H), 1.40 (s, 3 H), 0.95-1.68 (m, 4 H), 2.38-2.39 (m, 2 H), 3.80 (b, 1 H), 4.06 (m, 1 H), 4.43 (m, 1 H), 5.14-5.36 (m, 2 H), 5.67-5.76 (m, 1 H), 10.5 (bs, 1 H). This crude was used directly for next step without any further purification.

Ester 20:

To a solution of acid **19** (249 mg, 0.651 mmol) in toluene (15 mL) was added alcohol **4** (0.081 mL, 0.781 mmol), PPh_3 (205 mg, 0.781 mmol), DIAD (0.154 mL, 0.781 mmol). The reaction mixture was stirred for 10 h and the solvent was removed under reduced pressure vacuum. The residue was purified on a silica gel column using petroleum ether/EtOAc (40/1) as the eluant to afford **20** as a colorless oil (255 mg, 85% for two steps). ^1H NMR (400 MHz, CDCl_3) δ -0.06-0.00 (m, 6 H), 0.80 (s, 9 H), 1.17 (d, $J = 6.2$ Hz, 3 H), 1.28 (s, 3 H), 1.38 (s, 3 H), 1.44-1.54 (m, 4 H), 2.20-2.24 (m, 1 H), 2.237-2.31 (m, 1 H), 2.35-2.37 (m, 2 H), 3.78-3.81 (m, 1 H), 4.03-4.05 (m, 1 H), 4.40-4.43 (m, 1 H), 4.94-4.96 (m, 1 H), 5.00-5.04 (m, 2 H), 5.14 (m, 1 H), 5.22 (dd, $J = 6.7, 7.1$ Hz, 1 H), 5.67-5.72 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3) δ -4.64, -4.58, -4.55, 0.0, 18.0, 19.3, 25.6, 25.7, 25.8, 26.1, 26.3, 27.6, 27.7, 28.2, 28.3, 33.3, 33.6, 40.0, 70.10, 70.12, 72.0, 74.9, 78.1, 78.3, 79.80, 79.82, 86.1, 108.2, 108.3, 118.1, 118.3, 118.4, 133.2, 134.2, 134.4, 153.2. HRMS (FAB) calcd for $\text{C}_{25}\text{H}_{42}\text{O}_5\text{SiH}^+$ $[\text{M}+\text{H}]^+$: 451.2880, found 451.2881, $\Delta = -0.3$ ppm.

Cobalt-complex **21**:

To a solution of **20** (20 mg, 0.044 mmol) in toluene (2.5 mL) was added $\text{Co}_2(\text{CO})_8$ (21.2 mg, 0.062 mmol). The reaction mixture was stirred for 30 min before filtered through

neutral alumina and concentrated under reduced pressure vacuum. The residue was purified on preparative TLC (Whatman Pk6F Silica Gel 60 Å 1000 µM) using Hexanes/EtOAc (20/1) as the eluant to afford **21** as a purple oil (30 mg, 94%). ¹H NMR (400 MHz, CDCl₃) δ 0.07-0.09 (m, 6 H), 0.90 (s, 9 H), 1.30 (d, *J* = 8.1 Hz, 3 H), 1.33 (s, 1.6 H), 1.34 (s, 1.4 H), 1.45 (s, 1.6 H), 1.47 (s, 1.4 H), 1.25-1.46 (m, 1 H), 1.58-1.89 (m, 2.5 H), 1.89-1.95 (m, 0.5 H), 2.37-2.40 (m, 2 H), 3.00-3.12 (m, 2 H), 3.82-3.86 (m, 1 H), 4.08-4.14 (m, 1 H), 4.47-4.51 (m, 1 H), 5.07-5.14 (m, 3 H), 5.21 (d, *J* = 10.4 Hz, 1 H), 5.29 (d, *J* = 17.1 Hz, 1 H), 5.73-5.84 (m, 2 H). ¹³C NMR (100 MHz, CDCl₃) δ 18.1, 19.4, 25.6, 25.8, 26.5, 27.0, 28.16, 28.2, 32.7, 33.0, 40.3, 41.9, 42.1, 71.9, 72.8, 73.0, 78.2, 169.0, 197. HRMS (FAB) calcd for C₃₁H₄₂Co₂O₁₁SiH⁺ [M+H]⁺: 737.1239, found 737.1240, Δ = -0.2 ppm.

Macrolactone **23**:

To a solution of **21** (339 mg, 0.460 mmol) in CH₂Cl₂ (80 mL) was added 2nd generation Grubbs catalyst (97 mg, 0.115 mol) in CH₂Cl₂ (15 mL) via cannula at r.t. The reaction mixture was stirred overnight and then the solvent was removed under reduced pressure vacuum and residue purified on preparative TLC (Whatman Pk6F Silica Gel 60 Å 1000

μM) using Hexanes/EtOAc (10/1) as the eluant to afford **23A** as a purple oil (123 mg, 38%). $[\alpha]_{\text{D}}^{25} -44.7$ (*c* 0.25, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 0.08 (s, 3 H), 0.09 (s, 3 H), 0.91 (s, 9 H), 1.31 (d, *J* = 6.3 Hz, 3 H), 1.35 (s, 3 H), 1.45 (s, 3 H), 1.39-1.59 (m, 2 H), 1.65-1.72 (m, 1 H), 1.93-1.97 (m, 1 H), 2.22-2.31 (m, 1 H), 2.42 (dt, *J* = 12.9, 1.83 Hz, 1 H), 3.08 (dd, *J* = 16.0, 1.5 Hz, 1 H), 3.23 (dd, *J* = 16.0, 9.4 Hz, 1 H), 3.92-3.95 (m, 1 H), 4.01-4.06 (m, 1 H), 4.40 (dd, *J* = 9.4, 5.7 Hz, 1 H), 5.53 (ddd, *J* = 15.2, 10.9, 1.52 Hz, 1 H), 5.72 (ddd, *J* = 15.2, 10.7, 3.8 Hz, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ -4.5, -4.4, 18.5, 21.2, 23.1, 26.1, 26.2, 28.8, 30.5, 41.0, 42.7, 71.6, 71.8, 79.3, 80.0, 81.3, 92.9, 108.1, 129.1, 132.6, 169.9, 198.8. HRMS (FAB) calcd for $\text{C}_{29}\text{H}_{38}\text{Co}_2\text{O}_{11}\text{SiH}^+$ $[\text{M}+\text{H}]^+$: 709.0926, found: 709.0924, Δ = 0.2 ppm.

23B (136 mg, 42%). $[\alpha]_{\text{D}}^{25} -5.9$ (*c* 0.27, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 0.12 (s, 3 H), 0.15 (s, 3 H), 0.93 (s, 9 H), 1.32 (d, *J* = 6.3 Hz, 3 H), 1.35 (s, 3 H), 1.42 (s, 3 H), 1.11-1.54 (m, 2 H), 1.67 (m, 1 H), 1.88-1.93 (m, 1 H), 2.24-2.33 (m, 1 H), 2.41-2.45 (m, 1 H), 3.05 (dd, *J* = 14.9, 9.5 Hz, 1 H), 3.18 (dd, *J* = 14.9, 2.4 Hz, 1 H), 3.54-3.59 (m, 1 H), 4.03-4.09 (m, 1 H), 4.42 (dd, *J* = 9.5 Hz, 6.0 Hz, 1 H), 5.28 (m, 1 H), 5.53 (ddd, *J* = 15.2, 7.9, 4.0 Hz, 1 H), 5.77 (ddd, *J* = 15.2, 10.5, 3.5 Hz, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ -4.3, -4.0, 18.4, 21.1, 25.8, 26.1, 26.2, 26.3, 26.9, 28.6, 32.4, 40.7, 44.6, 71.8, 73.8, 78.6, 79.8, 81.1, 93.3, 107.9, 128.6, 133.6, 169.6, 198.6. HRMS (FAB) calcd for $\text{C}_{29}\text{H}_{38}\text{Co}_2\text{O}_{11}\text{SiH}^+$ $[\text{M}+\text{H}]^+$: 709.0926, found: 709.0924, Δ = 0.2 ppm.

Macrolide 7:

To a solution of **23A** (123 mg, 0.174 mmol) in acetone (10 mL) was added CAN (475 mg, 0.868 mmol) at -10°C . After 20 min, the reaction mixture was filtered through neutral alumina and the solvent was removed under reduced pressure vacuum. The residue was purified on a silica gel column using petroleum ether/EtOAc (20/1) as the eluant to afford **7A** as a colorless oil (69 mg, 94%). $[\alpha]_{\text{D}}^{25} -124.6$ (c 0.17, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ -0.06, (s, 3 H), 0.00 (s, 3 H), 0.81 (s, 9 H), 1.24 (d, $J = 6.2$ Hz, 1 H), 1.33, (s, 3 H), 1.40 (s, 3 H), 1.59-1.81 (m, 4 H), 2.18-2.22 (m, 1 H), 2.28-2.31 (m, 1 H), 2.34-2.45 (m, 2 H), 3.90-3.93 (m, 1 H), 3.98-4.01 (m, 1 H), 4.33-4.36 (m, 1 H), 4.83-4.87 (m, 1 H), 5.42-5.53 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3) δ -4.8, 18.4, 20.6, 26.1, 26.3, 28.4, 28.8, 30.1, 36.5, 40.6, 70.0, 71.7, 78.9, 80.1, 88.5, 108.7, 129.7, 132.0, 153.8.

7B was prepared by same procedure from **23B**. **7B**: (81 mg, 95%). $[\alpha]_{\text{D}}^{25} -173.3$ (c 0.41, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 0.00, (s, 3 H), 0.01 (s, 3 H), 0.81 (s, 9 H), 1.26 (d, $J = 6.1$ Hz, 3 H), 1.34 (s, 3 H), 1.41 (s, 3 H), 1.53-1.59 (m, 2 H), 1.77-1.81 (m, 2 H), 2.19-2.24 (m, 1 H), 2.24-2.26 (m, 1 H), 2.31-2.47 (m, 2 H), 3.80 (b, 1 H), 3.91-3.93 (m, 1 H), 4.34-4.40 (m, 1 H), 4.75-4.78 (m, 1 H), 4.82-4.86 (m, 1 H), 5.43-5.60 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3) δ -5.0, -4.8, 17.9, 20.17, 20.24, 25.5, 25.6, 25.7, 25.9, 28.0,

28.2, 28.3, 28.4, 29.6, 36.0, 36.7, 40.0, 40.1, 69.5, 70.8, 71.2, 71.4, 78.5, 78.6, 79.4, 79.6, 78.8, 108.2, 129.2, 131.3, 153.0. HRMS (FAB) calcd for $C_{25}H_{42}O_5SiNa^+$ $[M+Na]^+$: 473.2699, found: 473.2700, $\Delta = 0.2$ ppm.

Resorcyclic macrolide **24**:

Macrolide **7A** (26 mg, 0.065 mmol) was transferred to a vial and 0.2 mL diene **8** was added. The vial was sealed and heated to 140 °C for 36 h. The crude mixture was purified on preparative TLC (Whatman Pk6F Silica Gel 60 Å 1000 µM) using Hexanes/EtOAc (2/1) as the eluant to afford **24A** as a colorless oil (23 mg, 74%). $[\alpha]_D^{25} -99.1$ (c 0.08, $CHCl_3$). 1H NMR (400 MHz, $CDCl_3$) δ -0.15, (s, 3 H), 0.09 (s, 3 H), 0.89 (s, 9 H), 1.36 (s, 3 H), 1.38 (s, $J = 6.1$ Hz, 1 H), 1.50 (s, 3 H), 1.25-1.39 (m, 4 H), 1.71-1.76 (m, 1 H), 2.54-2.57 (m, 2 H), 2.60-2.64 (m, 1 H), 3.63-3.68 (m, 2 H), 4.08-4.11 (m, 1 H), 4.48 (m, 1 H), 5.22-5.26 (m, 1 H), 5.54 (bs, 1 H), 5.70-5.75 (m, 2 H), 6.27 (d, $J = 2.6$ Hz, 1 H), 6.28 (d, $J = 2.6$ Hz, 1 H), 11.3 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.5, -4.1, 0.4, 14.6, 18.4, 21.3, 21.5, 24.1, 25.9, 26.3, 28.6, 32.4, 40.1, 42.4, 70.0, 73.5, 73.7, 77.7,

79.7, 101.9, 106.6, 108.7, 111.6, 130.5, 131.6, 145.7, 160.4, 165.0, 172.1. HRMS (FAB) calcd for $C_{27}H_{42}O_7SiH^+$ $[M+H]^+$: 507.2778, found: 507.2777, $\Delta = 0.2$ ppm.

24B was prepared by same procedure from **7B**. **24B**: (81 mg, 84%). $[\alpha]_D^{25} -124.2$ (c 0.42, $CHCl_3$). 1H NMR (400 MHz, $CDCl_3$) δ 0.00, (s, 3 H), 0.14 (s, 3 H), 0.99 (s, 9 H), 1.50 (s, 3 H), 1.58 (d, $J = 6.1$ Hz, 1 H), 1.40-1.67 (m, 2 H), 1.64 (s, 3 H), 1.87-1.92 (m, 2 H), 2.64-2.72 (m, 2 H), 3.09 (dd, $J = 3.8$ Hz, 2.5 Hz, 1 H), 3.45 (dd, $J = 13.8, 7.8$ Hz, 1 H), 4.02-4.04 (m, 1 H), 4.20-4.22 (m, 1 H), 4.70-4.74 (m, 1 H), 5.50-5.52 (m, 1 H), 5.76 (dd, $J = 15.5, 8.1$ Hz, 1 H), 5.93-5.95 (m, 2 H), 6.42 (m, 1 H), 6.48 (m, 1 H), 11.62 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.3, -4.0, 14.5, 18.3, 18.4, 20.5, 21.5, 25.8, 26.2, 28.3, 28.4, 28.5, 33.1, 61.1, 72.7, 73.5, 79.1, 102.1, 107.1, 108.5, 112.7, 130.1, 130.5, 144.2, 160.7, 164.9, 171.7. LRMS (ESI) calcd for $C_{27}H_{42}O_7SiNa^+$ $[M+Na]^+$: 529.2, found: 529.1. LRMS (ESI) calcd for $C_{27}H_{42}O_7SiCl^-$ $[M+Cl]^-$: 541.3, found: 541.2.

MOM ether **25**:

To a solution of **24A** (23 mg, 0.045 mmol) in CH_2Cl_2 (0.5 mL) was added diethylpropylethylamine (0.08 mL, 0.450 mmol) and MOMCl (0.018 mL, 0.227 mmol). The reaction mixture was stirred for 10 h before quenched with saturated aqueous NH_4Cl .

solution, extracted with EtOAc (100 mL X 3). The organic layers were combined and dried with anhydrous MgSO_4 , filtered, and concentrated under reduced pressure vacuum. The residue was purified on preparative TLC (Whatman Pk6F Silica Gel 60 Å 1000 μM) using Hexanes/EtOAc (2/1) as the eluant to afford **25A** as a colorless oil (21 mg, 78%). $[\alpha]_{\text{D}}^{25}$ -2.86 (*c* 0.07, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 0.00, (s, 3 H), 0.10 (s, 3 H), 0.93 (s, 9 H), 1.39 (s, 3 H), 1.39 (d, 3 H), 1.48 (s, 3 H), 1.42-1.48 (m, 1 H), 1.60-1.64 (m, 2 H), 1.72-1.77 (m, 1 H), 2.41-2.45 (m, 2 H), 2.66 (dd, *J* = 5.6, 4.6 Hz, 1 H), 2.89 (dd, *J* = 4.5, 1.6 Hz, 1 H), 3.47 (s, 3 H), 3.48 (s, 3 H), 3.97-3.98 (m, 1 H), 4.09-4.15 (m, 1 H), 4.73 (dd, *J* = 9.0, 6.0 Hz, 1 H), 5.13-5.19 (m, 4 H), 5.30-5.36 (m, 1 H), 5.57 (dd, *J* = 15.4, 9.1 Hz, 1 H), 5.70-5.77 (m, 1 H), 6.68 (d, *J* = 2.0 Hz, 1 H), 6.86 (d, *J* = 2.0 Hz, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ -4.3, -4.2, 0.5, 18.4, 21.6, 24.0, 25.9, 26.3, 28.7, 30.1, 32.3, 40.1, 40.4, 56.5, 56.6, 71.4, 71.6, 80.3, 94.7, 94.9, 101.8, 108.5, 111.4, 119.8, 130.2, 132.4, 139.4, 155.3, 158.6, 168.4.

25B was prepared by same procedure from **24B**. **25B**: (58 mg, 83%). $[\alpha]_{\text{D}}^{25}$ -16.2 (*c* 0.29, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ -0.17 (s, 3 H), -0.06 (s, 3 H), 0.81 (s, 9 H), 1.26 (s, 3 H), 1.33 (d, *J* = 6.1 Hz, 1 H), 1.38 (s, 3 H), 1.17-1.52 (m, 4 H), 2.30-2.36 (m, 2 H), 2.61 (dd, *J* = 14.2, 6.0 Hz, 1 H), 2.71 (dd, *J* = 14.2, 6.9 Hz, 1 H), 3.39 (s, 3 H), 3.40 (s, 3 H), 3.80-3.83 (m, 1 H), 4.10-4.14 (m, 1 H), 4.41 (dd, *J* = 8.9, 6.1 Hz, 1 H), 5.04-5.09 (m, 4 H), 5.20-5.23 (m, 1 H), 5.43 (dd, *J* = 15.3, 9.1 Hz, 1 H), 5.60-5.67 (m, 1 H), 6.46 (s, 1 H), 6.60 (s, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ -4.2, -3.8, 18.4, 21.3, 25.8, 26.2, 26.25, 26.3, 28.6, 33.0, 39.8, 40.0, 42.0, 56.5, 56.6, 71.7, 74.5, 78.6, 79.9, 94.7, 94.9, 101.5, 108.3,

111.2, 119.8, 131.0, 131.4, 139.2, 155.8, 158.9, 168.5. HRMS (FAB) calcd for $C_{31}H_{50}O_9SiH^+$ $[M+H]^+$: 595.3302, found: 595.3304, $\Delta = -0.3$ ppm.

Alcohol **26**:

To a solution of **25A** (21 mg, 0.035 mmol) in THF (1.4 mL) was added pyridine (0.6 mL) and HF-pyridine (30%, 0.3 mL). The reaction mixture was stirred for 10 h before quenched with MeOTf (2 mL) and stirred for 1 h. The solvent was removed under reduced pressure vacuum. The residue was purified on preparative TLC (Whatman Pk6F Silica Gel 60 Å 1000 μ M) using Hexanes/EtOAc (1/1) as the eluant to afford **26A** as a colorless oil (12 mg, 78%). $[\alpha]_D^{25} -105.2$ (*c* 0.06, $CHCl_3$). 1H NMR (400 MHz, $CDCl_3$) δ -0.05 (s, 3 H), 0.05 (s, 3 H), 1.35 (s, 3 H), 1.38 (d, $J = 6.2$ Hz, 3 H), 1.46 (s, 3 H), 1.61-1.81 (m, 4 H), 2.40-2.46 (m, 2 H), 2.70 (dd, $J = 14.1, 6.1$ Hz, 1 H), 2.81 (dd, $J = 14.1, 4.7$ Hz, 1 H), 3.46 (s, 6 H), 3.89 (b, 1 H), 4.10-4.14 (m, 1 H), 4.56 (dd, $J = 9.1, 6.1$ Hz, 1 H), 5.13-5.17 (m, 4 H), 5.32-5.37 (m, 1 H), 5.59 (dd, $J = 15.4, 9.2$ Hz, 1 H), 5.70-5.75 (m, 1 H), 6.66 (d, $J = 2.0$ Hz, 1 H), 6.70 (d, $J = 2.0$ Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 25.1, 25.7, 28.6, 30.1, 32.3, 40.0, 41.6, 56.6, 56.7, 70.5, 72.0, 80.1, 94.7,

94.9, 101.9, 108.2, 111.0, 119.7, 130.6, 132.7, 138.3, 155.8, 159.1, 168.4. HRMS (FAB) calcd for $C_{25}H_{36}O_9H^+$ $[M+H]^+$: 482.2438, found: 482.2437, $\Delta = 0.1$ ppm.

26B was prepared by same procedure from **25B**. **26B**: (20 mg, 87%). $[\alpha]_D^{25}$ -32.0 (*c* 0.10, $CHCl_3$). 1H NMR (500 MHz, $CDCl_3$) δ 1.18 (m, 2 H), 1.35 (s, 3 H), 1.37 (d, *J* = 6.2 Hz, 1 H), 1.42 (s, 3 H), 1.55-1.69 (m, 2 H), 1.98-2.06 (m, 1 H), 2.42-2.48 (m, 3 H), 2.78 (dd, *J* = 13.8, 2.4 Hz, 1 H), 3.41-3.50 (m, 6 H), 3.62-3.67 (m, 1 H), 4.19-4.25 (m, 1 H), 4.49 (dd, *J* = 9.4, 6.0 Hz, 1 H), 5.11-5.18 (m, 4 H), 5.36-5.42 (m, 1 H), 5.56 (dd, *J* = 15.4, 9.5 Hz, 1 H), 5.65-5.72 (m, 1 H), 6.57 (d, *J* = 2.0 Hz, 1 H), 6.66 (d, *J* = 2.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 25.8, 26.8, 28.6, 32.0, 39.8, 42.6, 56.5, 56.7, 72.3, 74.8, 80.3, 94.7, 94.9, 101.8, 108.6, 110.7, 108.6, 110.7, 119.5, 129.9, 132.8, 138.7, 155.9, 159.0, 168.7. HRMS (FAB) calcd for $C_{25}H_{36}O_9H^+$ $[M+H]^+$: 482.2438, found: 482.2437, $\Delta = 0.1$ ppm.

Diene 27:

A solution of Martin's sulfurane dehydration agent (140 mg, 0.208) was added into a vial containing **26B** (20 mg, 0.042) at 0 °C. The reaction mixture was warmed up to r.t. over 2 h and the crude was purified on preparative TLC (Whatman Pk6F Silica Gel 60 Å 1000

μM) using Hexanes/EtOAc (1/1) as the eluant to afford **27** as a colorless oil (16 mg, 84%). $[\alpha]_{\text{D}}^{25}$ -123.8 (*c* 0.08, CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ 1.35 (s, 3 H), 1.36 (d, *J* = 6.0 Hz, 3 H), 1.46 (s, 3 H), 1.49-1.55 (m, 1 H), 1.80-1.85 (m, 1 H), 2.07-2.11 (m, 1 H), 2.29-2.32 (m, 1 H), 2.45-2.55 (m, 2 H), 3.41-3.50 (m, 6 H), 4.16-4.21 (m, 1 H), 4.56 (dd, *J* = 9.5, 5.4 Hz, 1 H, 1 H), 5.10-5.20 (m, 4 H), 5.32-5.36 (m, 1 H), 5.59 (dd, *J* = 15.5, 9.6 Hz, 1 H), 5.70-5.77 (m, 1 H), 5.15 (m, 1 H), 6.24 (d, *J* = 15.4 Hz, 1 H), 6.80 (d, *J* = 1.8 Hz, 1 H), 6.68 (d, *J* = 1.8 Hz, 1 H). ¹³C NMR (125 MHz, CDCl₃) δ 21.1, 25.8, 28.6, 28.7, 29.0, 39.5, 71.6, 80.1, 84.3, 94.6, 102.6, 104.8, 108.3, 117.9, 124.8, 128.4, 129.3, 131.9, 132.3, 136.8, 155.1, 158.9, 167.3. HRMS (FAB) calcd for C₂₅H₃₄O₈H⁺ [M+H]⁺: 463.2332, found: 463.2333, Δ = -0.2 ppm.

To a solution of **27** (16 mg, 0.035) in MeOH (1.5 mL) was added HCl (1 N, 1.5 mL) and stirred for 2 d. The reaction was quenched with saturated aqueous NaHCO₃ solution and extracted with EtOAc. The organic layers were combined and dried over anhydrous MgSO₄, filtered and concentrated under reduced vacuum. The crude was purified on

preparative TLC (Whatman Pk6F Silica Gel 60 Å 1000 µM) using MeOH/CH₂Cl₂ (5%) as the eluant to afford **1** as a white solid (8 mg, 69%). Mp: 84.2-86.9 °C. $[\alpha]_D^{25}$ -18.0 (*c* 0.03, MeOH). IR (neat) 3346, 1643, 1607, 1311, 1261, 1166, 1017, 968. ¹H NMR (500 MHz, acetone-*d*₆) δ 1.39 (d, *J* = 6.4 Hz, 3 H), 1.58-1.61 (m, 1 H), 2.14 (m, 1 H), 2.32-2.36 (m, 2 H), 2.43-2.46 (m, 1 H), 2.57 (ddd, *J* = 14.5, 7.3, 3.1 Hz, 1 H), 3.56 (br, 1 H), 3.64 (m, 1 H), 3.76 (br, 1 H), 4.35 (brd, *J* = 4.1 Hz, 1 H), 5.41-5.47 (m, 1 H), 5.69 (dd, *J* = 15.6, 5.1 Hz, 1 H), 5.87 (dddd, *J* = 15.6, 7.4, 7.4, 1.4 Hz, 1 H), 6.10 (ddd, *J* = 15.9, 5.5, 5.7 Hz, 1 H), 6.28 (d, *J* = 2.3 Hz, 1 H), 6.53 (d, *J* = 2.3 Hz, 1 H), 7.16 (d, *J* = 15.9 Hz, 1 H), 9.10 (bs, 1 H), 11.7 (s, 1 H). ¹³C NMR (125 MHz, acetone-*d*₆) δ 19.2, 28.1, 28.8, 38.1, 73.1, 73.4, 76.7, 102.6, 104.6, 107.9, 125.6, 130.8, 133.8, 135.9, 144.5, 163.2, 166.0, 172.3. LRMS (ESI) calcd for C₁₈H₂₂O₆Na⁺ [Na+H]⁺: 357.1, found: 357.3. LRMS (ESI) calcd for C₁₈H₂₁O₆⁻ [M-H]⁻: 333.1, found: 333.1. LRMS (ESI) calcd for C₁₈H₂₂O₆Cl⁻ [M+Cl]⁻: 369.1, found: 369.0. HRMS (TOF) calcd for C₁₈H₂₂O₆Na⁺ [M+Na]⁺: 357.1314, found: 357.1325, Δ = 3.1 ppm. All the physical data are consistent with the reported value.²

Reference:

1. Barbat, J.; Gelas, J.; Horton, D. *Carbohydrate Res.* **1983**, *116*, 312-316.
2. Isaka, M.; Suyarnsestakorn, C.; Tanticharoen, M.; Kongsaree, P.; Thebtaranonth, Y. *J. Org. Chem.* **2002**, *67*, 1561-1566.

Below are the ^1H and ^{13}C spectrum of synthetic aigialomycin D (in acetone- d_6).

Table 1. ¹ H NMR Data of Aigialomycin D		
position	Isolated Aigialomycin D by Isaka ²	Synthetic Aigailomycin D
3	6.27 (d, 2.4)	6.28 (d, 2.3)
5	6.52 (d, 2.4)	6.53 (d, 2.3)
1'	7.14 (d, 15.9)	7.16 (d, 15.9)
2'	6.09 (ddd, 15.9, 5.6, 5.4)	6.10 (ddd, 15.9, 5.7, 5.5)
3'	2.31-2.34 (m)	2.32-2.36 (m)
	2.31-2.34 (m)	2.32-2.36 (m)
4'	2.14 (m)	2.14 (m)
	1.58 (m)	1.58-1.61 (m)
5'	3.62 (m)	3.64 (m)
6'	4.35 (brd, 4.3)	4.35 (brd, 4.1)
7'	5.68 (dd, 15.7, 5.0)	5.69 (dd, 15.6, 5.1)
8'	5.87 (dddd, 15.7, 7.3, 7.3, 1.2)	5.87 (dddd, 15.6, 7.4, 7.4, 1.4)
9'	2.55 (ddd, 14.6, 7.5, 3.2)	2.55 (ddd, 14.5, 7.3, 3.1)
	2.42 (m)	2.43-2.46 (m)
10'	5.42 (m)	5.41-5.47 (m)
10'-CH ₃	1.38 (d, 6.4)	1.39 (d, 6.4)
2-OH	11.65 (s)	11.7 (s)
4-OH	9.5 (br)	9.1 (br)
5'-OH	not detected	3.56 (br)
6'-OH	not detected	3.76 (br)

Deric II-48B-carbon (1) Acetone 24.0C April_04,2003_15:54 DRX 500MHz zgpg30 13C