Supporting Information for:

Total Synthesis of Gymnocin-A

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General Methods. All reactions sensitive to air or moisture were carried out in oven-dried glassware under argon atmosphere unless otherwise noted. Anhydrous dichloromethane (CH_2Cl_2), acetonitrile (MeCN) and tetrahydrofuran (THF) were purchased from Kanto Chemical Co., Inc., Wako Pure Chemical or Aldrich and used without further drying. Trimethylsilyl chloride (TMSCl) was distilled from calcium hydride. Hexamethylphosphoramide (HMPA) was distilled from calcium hydride under reduced pressure. 2-[*N,N*-Bis(trifluoromethylsulfonyl)amino]-5-chloropyridine was distilled by Kugelrohr. All other reagents were used as supplied unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 plates (0.25-mm thickness). For column chromatography Fuji Silysia silica gel BW-300 (200-400 mesh) was used. Optical rotations were recorded on a JASCO DIP-370 digital polarimeter. ^1H and ^{13}C NMR spectra were recorded on a Varian Unity INOVA 600 or INOVA 500 spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with reference to internal residual solvent [^1H NMR, CHCl_3 (7.24), C_6HD_5 (7.15), $\text{C}_5\text{HD}_4\text{N}$ (8.71); ^{13}C NMR, CDCl_3 (77.0), C_6D_6 (128.0), $\text{C}_5\text{D}_5\text{N}$ (149.9)]. Coupling constants (*J*) are reported in hertz (Hz). The following abbreviations are used to designate the multiplicities: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Mass spectra were recorded on a JEOL TheMStation JMS-700 mass spectrometer under fast atom bombardment (FAB) conditions using *m*-nitrobenzyl alcohol (NBA) or glycerol as a matrix.

Enol Triflate 4. To a solution of lactone **5** (39.4 mg, 0.0526 mmol) in THF (2.0 mL) was added HMPA (0.045 mL, 0.259 mmol). The solution was cooled to $-78\text{ }^\circ\text{C}$ and treated with KHMDS (0.5 M in toluene, 0.32 mL, 0.16 mmol). After the resulting mixture was stirred at $-78\text{ }^\circ\text{C}$ for 20 min, 2-[*N,N*-Bis(trifluoromethylsulfonyl)amino]-5-chloropyridine (54.0 mg, 0.138 mmol) of THF solution (1.0 mL) was added. The resultant solution was stirred at $-78\text{ }^\circ\text{C}$ for 10 min, warmed to $0\text{ }^\circ\text{C}$ and stirred at $0\text{ }^\circ\text{C}$ for 1 hour. The mixture was treated with pH 7 phosphate buffer, diluted

with ether, washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (10—33% ethyl acetate/hexanes) to give enol triflate **4** (37.3 mg, 0.0423 mmol, 80%) as a colorless oil: $[\alpha]_D^{24} +63.5$ (c 0.93, benzene); ¹H NMR (600 MHz, C₆D₆) δ 4.16 (dd, *J* = 5.4, 2.4 Hz, 1H), 3.44 (ddd, *J* = 10.2, 9.6, 4.8 Hz, 1H), 3.35 (ddd, *J* = 10.2, 10.2, 4.8 Hz, 1H), 3.33-3.28 (m, 3H), 3.27-3.20 (m, 2H), 3.12-2.90 (m, 7H), 2.88-2.83 (m, 2H), 2.50 (ddd, *J* = 11.4, 4.2, 3.6 Hz, 1H), 2.45 (m, 1H), 2.38-2.35 (m, 2H), 2.24 (dd, *J* = 12.0, 3.6 Hz, 1H), 2.19 (m, 1H), 2.12 (m, 1H), 1.94 (br d, *J* = 16.2 Hz, 1H), 1.88 (m, 1H), 1.82 (dd, *J* = 12.0, 12.0 Hz, 1H), 1.76-1.54 (m, 11H), 1.43 (m, 1H), 1.33 (d, *J* = 6.6 Hz, 3H), 1.12 (s, 3H), 0.96 (s, 3H), 0.93 (s, 9H), 0.00 (s, 3H), 0.00 (s, 3H); ¹³C NMR (150 MHz, C₆D₆) δ 148.7, 120.1, 118.0, 87.5, 84.9, 83.8, 80.0, 78.8, 78.0, 77.6, 77.4, 77.24, 77.16, 76.9, 76.6, 76.2, 75.9, 72.7, 72.5, 70.8, 68.8, 45.3, 39.9, 38.3, 38.2, 37.0, 35.8 (x2), 29.80, 29.76, 29.1, 25.9 (x3), 25.5, 24.6, 18.6, 16.7, 15.4, -4.1, -4.7; HRMS (FAB) calcd for C₄₁H₆₃O₁₃F₃SiSNa [(M+Na)⁺] 903.3608, found 903.3613.

Endocyclic Enol Ether 6. Exocyclic enol ether **3** (57.2 mg, 0.0840 mmol) was treated with 9-BBN (0.2 M solution in THF, 1.3 mL, 0.26 mmol) and the resultant solution was stirred at room temperature for 2 h. The mixture was treated with 3 M aqueous Cs₂CO₃ (0.085 mL, 0.255 mmol) and stirred at room temperature for 20 min. To the mixture was added a solution of enol triflate **4** (37.3 mg, 0.0423 mmol) in DMF (4 mL) followed by Pd(PPh₃)₄ (8.8 mg, 0.0083 mmol). The resultant mixture was stirred at room temperature for 2 h before dilution with ether. The mixture was washed with water and brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (10—40% ether/hexanes) to give endocyclic enol ether **6** (48.6 mg, 0.0344 mmol, 81%) as a colorless oil: $[\alpha]_D^{26} +57.3$ (c 0.97, benzene); ¹H NMR (600 MHz, C₆D₆) δ 7.26-7.22 (m, 4H), 7.17-7.14 (m, 2H), 7.08 (m, 1H), 6.84-6.82 (m, 2H), 4.47 (ddd, *J* = 9.4, 8.4, 7.2 Hz, 1H), 4.40 (br d, *J* = 4.8, <1 Hz, 1H), 4.35 (d, *J* = 11.4 Hz, 1H), 4.27 (d, *J* = 12.0 Hz, 1H), 4.25 (d, *J* = 12.0 Hz, 1H), 4.18 (m, 1H), 4.15 (br d, *J* = 6.6, <1 Hz, 1H), 4.14 (d, *J* = 11.4 Hz, 1H), 4.11-4.07 (m, 2H), 3.65 (ddd, *J* = 8.4, 8.4, 8.4 Hz, 1H), 3.57 (ddd, *J* = 10.2, 10.2, 4.2 Hz, 1H), 3.51 (ddd, *J* = 11.4, 9.0, 4.2 Hz, 1H), 3.49-3.33 (m, 5H), 3.32 (s, 3H), 3.32-3.27 (m, 3H), 3.25-3.20 (m, 2H), 3.11-2.89 (m, 10H), 2.66 (ddd, *J* = 12.0, 4.8, 4.2 Hz, 1H), 2.53 (ddd, *J* = 11.4, 4.2, 3.6 Hz, 1H), 2.48 (ddd, *J* = 11.4, 4.2, 3.6 Hz, 1H), 2.40-2.32 (m, 4H), 2.29-2.21 (m, 4H), 2.14-2.03 (m, 4H), 1.99-1.79 (m, 11H), 1.75-1.60 (m, 10H), 1.33 (d, *J* = 6.0 Hz, 3H), 1.20 (s, 3H), 1.12 (s, 3H), 0.99 (s, 9H), 0.93 (s, 9H), 0.16 (s, 3H), 0.10 (s, 3H), -0.089 (s, 3H), -0.091 (s, 3H); ¹³C NMR (150 MHz, C₆D₆) δ 159.7, 150.9, 139.4, 131.0, 129.4 (x2), 128.4 (x2), 127.6 (x2), 127.5, 114.0 (x2), 97.0, 83.8, 82.8, 82.6, 82.4, 81.7, 81.0, 80.9, 80.6, 80.0, 79.4, 78.8, 78.7, 78.0, 77.65, 77.56, 77.5, 77.2, 77.0, 76.6, 76.2, 76.0, 74.9, 73.4, 73.0, 72.8, 72.2, 71.1, 70.8, 70.3, 68.7, 67.4, 54.7, 45.3, 40.0, 39.6, 39.0, 38.9, 38.7, 38.6, 38.3, 37.4, 37.0, 35.98, 35.97, 29.9, 29.8, 26.8, 26.1 (x3), 25.9 (x3), 25.7, 25.5, 23.1, 18.6, 18.4, 18.1, 16.7, 15.6, -4.0, -4.1, -4.7, -5.0; HRMS (FAB) calcd for C₇₉H₁₂₀O₁₈Si₂Na [(M+Na)⁺] 1435.7911, found 1435.7915.

Alcohol 7. To a solution of endocyclic enol ether **6** (15.3 mg, 0.0108 mmol) in THF (1.0

mL) cooled to 0 °C was added $\text{BH}_3\cdot\text{SMe}_2$ (2 M solution in THF, 0.045 mL, 0.090 mmol). The resulting solution was stirred at 0 °C for 10 min and then allowed to warm to room temperature. The reaction mixture was stirred at room temperature for 3.6 h. The mixture was cooled to 0 °C and treated with 3 M aqueous NaOH (0.50 mL) followed by 30% H_2O_2 (0.50 mL). After being stirred at room temperature for 1 h, the mixture was cooled to 0 °C and treated with saturated aqueous NH_4Cl . The mixture was diluted with ethyl acetate, washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (30—70% ethyl acetate/hexanes) to give alcohol **7** (11.6 mg, 75%) as a colorless oil: $[\alpha]_{\text{D}}^{24} +43.2$ (*c* 1.02, benzene); ^1H NMR (500 MHz, C_6D_6) δ 7.27-7.22 (m, 4H), 7.18-7.14 (m, 2H), 7.08 (m, 1H), 6.85-6.83 (m, 2H), 4.43 (ddd, *J* = 9.2, 8.4, 7.0 Hz, 1H), 4.35 (d, *J* = 11.3 Hz, 1H), 4.29 (d, *J* = 12.0 Hz, 1H), 4.27 (d, *J* = 12.0 Hz, 1H), 4.20 (m, 1H), 4.13 (d, *J* = 11.3 Hz, 1H), 4.13 (br d, *J* = 7.2, <1 Hz, 1H), 4.08-4.01 (m, 2H), 3.65 (ddd, *J* = 8.4, 8.4, 8.4 Hz, 1H), 3.52-3.37 (m, 7H), 3.31-3.29 (m, 2H), 3.32 (s, 3H), 3.25-3.16 (m, 4H), 3.09 (ddd, *J* = 10.1, 10.1, 4.0 Hz, 1H), 3.08-2.89 (m, 10H), 2.62 (ddd, *J* = 11.9, 4.4, 4.4 Hz, 1H), 2.53-2.47 (m, 2H), 2.40-2.32 (m, 4H), 2.25 (dd, *J* = 12.1, 4.0 Hz, 1H), 2.15 (dd, *J* = 12.1, 4.0 Hz, 1H), 2.14-1.59 (m, 28H), 1.33 (d, *J* = 5.5 Hz, 3H), 1.12 (s, 3H), 1.09 (s, 3H), 0.99 (s, 9H), 0.93 (s, 9H), 0.14 (s, 3H), 0.09 (s, 3H), 0.002 (s, 3H), -0.000 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 159.7, 139.4, 131.0, 129.5 (x2), 128.5 (x2), 127.6 (x2), 127.5, 114.0 (x2), 83.8, 83.3, 82.8, 82.6, 81.7, 81.2, 80.4, 80.3, 80.0, 79.9, 79.5, 79.4, 78.7, 78.04, 77.99, 77.6, 77.3, 77.2, 76.6, 76.5, 76.2, 76.0, 75.4, 75.0, 73.0, 72.8, 72.1, 70.94, 70.86, 70.5, 70.4, 69.0, 67.4, 54.7, 48.4, 45.4, 40.0, 39.0, 38.8, 38.6, 38.3, 38.2, 37.4, 37.0, 36.0 (x2), 29.8 (x2), 26.8, 26.1 (x3), 25.9 (x3), 25.6, 25.5, 23.7, 18.6, 18.4, 18.1, 16.7, 16.3, -4.0, -4.1, -4.7, -5.0; HRMS (FAB) calcd for $\text{C}_{79}\text{H}_{122}\text{O}_{19}\text{Si}_2\text{Na}$ $[(\text{M}+\text{Na})^+]$ 1453.8017, found 1453.8024.

Alcohol 8. To a solution of alcohol **7** (26.4 mg, 0.0184 mmol) in CH_2Cl_2 (2.0 mL) were added 2,6-lutidine (0.010 mL, 0.0858 mmol) and TESOTf (0.015 mL, 0.0668 mmol). The resultant solution was stirred at room temperature for 1 h. The mixture was diluted with ethyl acetate, washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was filtered through silica gel with 10—30% ethyl acetate/hexanes to give TES ether (32.7 mg) as a colorless oil.

To a solution of the above TES ether (32.7 mg) in CH_2Cl_2 /pH 7 phosphate buffer (6:1, v/v, 3.5 mL) at 0 °C was added DDQ (21.0 mg, 0.0925 mmol). The resultant solution was stirred at 0 °C for 3 h before the reaction was quenched with saturated aqueous NaHCO_3 at 0 °C. The reaction mixture was diluted with ethyl acetate, washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (20—50% ethyl acetate/hexanes) to give alcohol **8** (20.7 mg, 79% for the two steps) as a colorless oil: $[\alpha]_{\text{D}}^{24} +18.5$ (*c* 1.04, benzene); ^1H NMR (500 MHz, C_6D_6) δ 7.26-7.24 (m, 2H), 7.17-7.14 (m, 2H), 7.08 (m, 1H), 4.43 (ddd, *J* = 9.5, 7.1, 7.1 Hz, 1H), 4.28 (d, *J* = 12.8 Hz, 1H), 4.25 (d, *J* = 12.8 Hz, 1H), 4.16 (m, 1H), 4.12 (br d, *J* = 5.9, <1 Hz, 1H), 4.07 (ddd, *J* = 11.6, 8.9, 4.7 Hz, 1H), 3.79 (m, 1H), 3.74 (ddd, *J* = 5.9, 5.9, 5.9 Hz, 1H), 3.66-3.57 (m, 2H), 3.50-3.38 (m, 5H), 3.34-3.28 (m, 3H), 3.24-2.88 (m, 15H), 2.66 (ddd, *J* = 11.7, 4.4, 4.4 Hz, 1H), 2.51-2.47 (m,

2H), 2.40-2.30 (m, 4H), 2.25 (dd, $J = 12.0, 3.9$ Hz, 1H), 2.23-2.17 (m, 2H), 2.13-1.79 (m, 15H), 1.76-1.57 (m, 11H), 1.33 (d, $J = 5.4$ Hz, 3H), 1.13 (s, 3H), 1.11 (s, 3H), 1.01 (s, 9H), 0.97 (t, $J = 8.1$ Hz, 9H), 0.92 (s, 9H), 0.56 (q, $J = 8.1$ Hz, 6H), 0.16 (s, 3H), 0.09 (s, 3H), -0.003 (s, 3H), -0.006 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 139.4, 128.5 (x2), 127.6 (x2), 127.5, 83.8, 83.4, 83.1, 83.0, 82.5, 82.1, 81.1, 80.1 (x2), 80.0, 79.5, 78.7, 78.0, 77.61, 77.55, 77.2 (x2), 76.7, 76.5, 76.2, 75.9, 75.4, 74.9, 74.4, 73.0, 72.8, 72.1, 71.2, 70.9, 70.6, 70.3, 67.4, 49.6, 45.4, 40.0, 39.1, 38.7, 38.3, 38.2, 37.8, 37.4, 37.0, 35.96, 35.94, 30.0, 29.8, 29.6, 27.8, 26.1 (x3), 25.9 (x3), 25.6, 25.5, 18.6, 18.4, 18.1, 16.7, 16.3, 7.2 (x3), 5.5 (x3), -4.0, -4.1, -4.7, -4.9; HRMS (FAB) calcd for $\text{C}_{77}\text{H}_{128}\text{O}_{18}\text{Si}_3\text{Na}$ [(M+Na) $^+$] 1447.8306, found 1447.8304.

Ketone 9. To a solution of alcohol **8** (20.7 mg, 0.0145 mmol) in CH_2Cl_2 (4 mL) were added 4 Å molecular sieves (16.8 mg), NMO (9.3 mg, 0.0794 mmol), and TPAP (1.5 mg, 0.0042 mmol). The resulting solution was stirred at room temperature for 1.5 h. The mixture was directly subjected to flash column chromatography on silica gel (0—33% ethyl acetate/hexanes) to give ketone **9** (19.6 mg, 95%) as a colorless oil: $[\alpha]_{\text{D}}^{23} +16.2$ (c 0.98, benzene); ^1H NMR (500 MHz, C_6D_6) δ 7.27-7.25 (m, 2H), 7.18-7.15 (m, 2H), 7.09 (m, 1H), 4.42 (ddd, $J = 9.5, 8.3, 7.8$ Hz, 1H), 4.29 (d, $J = 12.7$ Hz, 1H), 4.27 (d, $J = 12.7$ Hz, 1H), 4.17 (m, 1H), 4.06-4.04 (m 2H), 3.95 (ddd, $J = 11.7, 8.8, 4.4$ Hz, 1H), 3.59 (ddd, $J = 8.3, 8.3, 8.3$ Hz, 1H), 3.55-3.49 (m, 2H), 3.49-3.39 (m, 4H), 3.32-3.26 (m, 2H), 3.24-2.88 (m, 14H), 2.83 (ddd, $J = 13.2, <1.5, <1.5$ Hz, 1H), 2.51-2.45 (m, 3H), 2.42-2.35 (m, 4H), 2.33-2.28 (m, 2H), 2.24 (dd, $J = 12.7, 4.3$ Hz, 1H), 2.16 (dd, $J = 12.7, 4.5$ Hz, 1H), 2.13-1.98 (m, 4H), 1.97-1.78 (m, 9H), 1.76-1.59 (m, 11H), 1.48 (m, 1H), 1.33 (d, $J = 5.4$ Hz, 3H), 1.13 (s, 3H), 1.11 (s, 3H), 0.98 (s, 9H), 0.95 (t, $J = 7.8$ Hz, 9H), 0.92 (s, 9H), 0.53 (q, $J = 7.8$ Hz, 6H), 0.07 (s, 3H), 0.06 (s, 3H), 0.000 (s, 3H), -0.003 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 213.5, 139.3, 128.5 (x2), 127.6 (x2), 127.5, 84.2, 83.8, 82.9, 82.8, 82.5, 80.9, 80.6, 80.2, 80.0, 79.3, 78.73, 78.67, 78.0, 77.59, 77.56, 77.24, 77.21, 76.6, 76.5, 76.2, 75.9, 75.7, 75.0, 73.0, 72.8, 71.9, 70.84, 70.76 (x2), 70.7, 67.4, 49.7, 45.4, 40.0, 38.6, 38.5, 38.3, 38.2, 37.2, 37.0, 36.7, 36.2, 36.0, 35.9, 30.0, 29.8, 29.7, 26.1 (x3), 25.9 (x3), 25.5, 25.4, 18.6, 18.3, 18.1, 16.7, 16.4, 7.1 (x3), 5.4 (x3), -4.11, -4.15, -4.7, -5.0; HRMS (FAB) calcd for $\text{C}_{77}\text{H}_{126}\text{O}_{18}\text{Si}_3\text{Na}$ [(M+Na) $^+$] 1445.8150, found 1445.8158.

Protected Hydroxy Ketone 10. To a solution of ketone **9** (19.6 mg, 0.0138 mmol) in THF (3.0 mL) were added Et_3N (0.080 mL, 0.574 mmol) and TMSCl (0.070 mL, 0.552 mmol). The reaction mixture was cooled to -78°C and treated with LiHMDS (1.0 M solution in THF, 0.10 mL, 0.10 mmol). The resultant solution was stirred at -78°C for 1.5 h before the reaction was quenched with pH 7 phosphate buffer. The mixture was diluted with ethyl acetate, washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude silyl enol ether was used in the next reaction without purification.

To a solution of the above silyl enol ether in THF/ H_2O (3:1, v/v, 6.5 mL) were added NMO (50 wt% solution in water, 0.50 mL) and OsO_4 (1g in 100 mL $t\text{-BuOH}$ solution, 0.50 mL, 0.0020 mmol). The resulting mixture was stirred at room temperature for 16 h. The mixture was diluted with ethyl acetate, washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced

pressure. The residue was purified by flash column chromatography on silica gel (0—50% ethyl acetate/hexanes) to give hydroxy ketone (20.0 mg, quant.) as a colorless oil.

To a solution of the above hydroxy ketone (20.0 mg, 0.0138 mmol) in CH_2Cl_2 (2.0 mL) were added 2,6-lutidine (0.125 mL, 1.07 mmol) and TIPSOTf (0.20 mL, 0.744 mmol). The resultant solution was stirred at room temperature for 5 h. The mixture was diluted with ethyl acetate, washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (0—50% ethyl acetate/hexanes) to give TIPS ether **10** (18.7 mg, 85% for the three steps) as a colorless oil: $[\alpha]_{\text{D}}^{24} +39.1$ (*c* 0.94, benzene); ^1H NMR (500 MHz, C_6D_6) δ 7.26-7.24 (m, 2H), 7.17-7.15 (m, 2H), 7.08 (m, 1H), 5.19 (dd, *J* = 11.9, 2.6 Hz, 1H), 4.52 (dd, *J* = 7.6, 6.6 Hz, 1H), 4.42 (ddd, *J* = 8.1, 7.7, 7.7 Hz, 1H), 4.28 (d, *J* = 12.7 Hz, 1H), 4.25 (d, *J* = 12.7 Hz, 1H), 4.17 (m, 1H), 4.03 (br d, *J* = 6.1, <1 Hz, 1H), 3.96 (ddd, *J* = 11.9, 9.2, 5.1 Hz, 1H), 3.72 (ddd, *J* = 11.4, 8.9, 5.1 Hz, 1H), 3.59 (ddd, *J* = 8.1, 8.1, 8.1 Hz, 1H), 3.50-3.35 (m, 5H), 3.31-3.17 (m, 6H), 3.14 (m, 1H), 3.10-3.04 (m, 2H), 3.02-2.88 (m, 8H), 2.57-2.52 (m, 2H), 2.52-2.46 (m, 2H), 2.43-2.34 (m, 5H), 2.29-2.21 (m, 2H), 2.20-1.98 (m, 5H), 1.91-1.59 (m, 18H), 1.33 (d, *J* = 5.1 Hz, 3H), 1.18-1.14 (m, 21H), 1.11 (s, 3H), 1.11 (s, 3H), 0.97 (t, *J* = 8.0 Hz, 9H), 0.93 (s, 9H), 0.92 (s, 9H), 0.57 (q, *J* = 8.0 Hz, 6H), 0.00 (s, 3H), 0.00 (s, 3H), -0.01 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 211.3, 139.3, 128.5 (x2), 127.6 (x2), 127.5, 84.3, 83.8, 83.3, 82.9, 82.4, 80.5, 80.1, 80.0, 79.5, 79.4, 78.7, 78.0, 77.9, 77.61, 77.56, 77.3, 77.2, 76.6, 76.5, 76.2, 76.0, 75.7, 75.0, 73.0, 72.8, 72.3, 71.8, 71.0, 70.8, 70.7, 70.6, 67.4, 49.8, 45.4, 41.2, 40.0, 38.5, 38.3, 38.22, 38.18, 37.2, 37.0, 36.3, 36.0, 35.9, 29.8, 29.7, 26.0 (x3), 25.9 (x3), 25.6, 25.5, 18.6, 18.31 (x3), 18.27 (x3), 18.0 (x2), 16.7, 16.5, 12.7 (x3), 7.1 (x3), 5.5 (x3), -4.1, -4.2, -4.7, -5.0; HRMS (FAB) calcd for $\text{C}_{86}\text{H}_{146}\text{O}_{19}\text{Si}_4\text{Na}$ [(M+Na) $^+$] 1617.9433, found 1617.9441.

Mixed Thioketal 11 and 12. To a solution of TIPS ether **10** (13.5 mg, 0.00846 mmol) in MeNO_2 (2 mL) at 0 °C were added EtSH (0.50 mL, 6.76 mmol) and $\text{Zn}(\text{OTf})_2$ (3.9 mg, 0.0107 mmol). The resultant solution was stirred at 0 °C for 45 min before the reaction was quenched with Et_3N . The mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (20—40% ethyl acetate/hexanes) to give mixed thioketal **11** (4.8 mg, 40%) and **12** (4.9 mg, 38%). **11**: $[\alpha]_{\text{D}}^{25} +52.2$ (*c* 0.34, CHCl_3); ^1H NMR (500 MHz, C_6D_6) δ 7.27-7.25 (m, 2H), 7.17-7.15 (m, 2H), 7.08 (m, 1H), 4.56-4.48 (m, 2H), 4.29 (d, *J* = 12.7 Hz, 1H), 4.27 (d, *J* = 12.7 Hz, 1H), 4.15 (m, 1H), 4.09 (br d, *J* = 4.9, <1 Hz, 1H), 4.02-3.90 (m, 3H), 3.81 (ddd, *J* = 10.8, 10.8, 4.9 Hz, 1H), 3.58 (ddd, *J* = 8.3, 8.3, 8.3 Hz, 1H), 3.51-3.39 (m, 4H), 3.25-3.13 (m, 5H), 3.09-2.81 (m, 11H), 2.79 (br d, *J* = 8.8, <1 Hz, 1H), 2.61 (m, 1H), 2.53-2.42 (m, 3H), 2.40-2.32 (m, 5H), 2.28-2.20 (m, 3H), 2.09-1.97 (m, 5H), 1.90-1.57 (m, 19H), 1.37 (ddd, *J* = 11.2 Hz, 1H), 1.25 (d, *J* = 5.9 Hz, 3H), 1.18-1.15 (m, 21H), 1.14 (s, 3H), 1.14 (t, *J* = 7.3 Hz, 3H), 1.11 (s, 3H), 1.02 (s, 9H), 0.21 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (125 MHz, $\text{pyr}-d_5$) δ 139.5, 128.7 (x2), 127.9 (x2), 127.8, 94.9, 83.9, 83.0, 82.7, 82.5, 80.1, 79.9, 79.5, 79.3, 78.5, 77.9, 77.4 (x2), 77.3, 77.1, 77.0, 76.9, 76.58, 76.57, 76.45, 76.38, 76.2, 75.0, 74.7, 73.0 (x2), 72.1, 71.3, 70.9, 70.6, 70.5, 69.7, 67.6, 45.4, 44.6, 40.8, 39.9, 39.0, 38.5, 38.2, 37.2, 37.0, 35.91, 35.85, 33.9, 30.0, 29.9, 29.8, 26.2 (x3), 25.6, 20.5, 20.1, 18.69 (x3), 18.66 (x3), 18.6, 18.3, 16.8, 16.7, 15.3, 13.0

(x3), -3.9, -4.9; HRMS (FAB) calcd for $C_{76}H_{122}O_{18}Si_2SNa [(M+Na)^+]$ 1433.7788, found 1433.7794. **12**: $[\alpha]_D^{24} +48.5$ (c 0.57, $CHCl_3$); 1H NMR (500 MHz, C_6D_6) δ 7.27-7.25 (m, 2H), 7.18-7.15 (m, 2H), 7.08 (m, 1H), 4.56-4.48 (m, 2H), 4.29 (d, $J = 12.7$ Hz, 1H), 4.27 (d, $J = 12.7$ Hz, 1H), 4.15 (m, 1H), 4.09 (br d, $J = 5.0$, <1 Hz, 1H), 4.02-3.90 (m, 3H), 3.81 (ddd, $J = 10.3$, 10.3, 5.3 Hz, 1H), 3.58 (ddd, $J = 8.5$, 8.5, 8.5 Hz, 1H), 3.51-3.40 (m, 4H), 3.31-3.29 (m, 2H), 3.25-3.13 (m, 5H), 3.08-2.84 (m, 9H), 2.79 (br d, $J = 8.5$, <1 Hz, 1H), 2.61 (m, 1H), 2.51-2.43 (m, 2H), 2.40-2.32 (m, 7H), 2.28-2.22 (m, 2H), 2.13-1.97 (m, 5H), 1.90-1.58 (m, 19H), 1.33 (d, $J = 5.3$ Hz, 3H), 1.18-1.16 (m, 21H), 1.14 (s, 3H), 1.14 (t, $J = 7.3$ Hz, 3H), 1.12 (s, 3H), 1.02 (s, 9H), 0.92 (s, 9H), 0.21 (s, 3H), 0.12 (s, 3H), 0.00 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (125 MHz, $pyr-d_5$) δ 139.5, 128.7 (x2), 127.9 (x2), 127.8, 94.9, 83.9, 83.8, 82.7, 82.5, 80.1, 79.9, 79.5, 78.6, 78.5, 77.9, 77.4 (x2), 77.3, 77.1, 77.0, 76.9, 76.5, 76.45, 76.38, 76.2, 76.0, 75.0, 74.7, 73.0 (x2), 72.6, 72.1, 70.8, 70.6, 70.5, 69.7, 67.6, 45.3, 44.6, 40.8, 39.9, 39.0, 38.44, 38.37, 38.2, 37.2, 37.0, 35.9, 35.8, 33.9, 30.0, 29.84, 29.76, 26.2 (x3), 25.9 (x3), 25.6, 20.1, 18.69 (x3), 18.67 (x3), 18.6, 18.3, 18.1, 16.8, 16.7, 15.3, 13.0 (x3), -3.9, -4.1, -4.7, -4.9; HRMS (FAB) calcd for $C_{82}H_{136}O_{18}Si_3SNa [(M+Na)^+]$ 1547.8653, found 1547.8654.

Conversion of 11 to 12. To a solution of **11** (4.7 mg, 0.0033 mmol) in CH_2Cl_2 (1.0 mL) were added 2,6-lutidine (0.025 mL, 0.215 mmol) and TBSOTf (0.030 mL, 0.134 mmol). The resultant solution was stirred at room temperature for 40 min. The mixture was diluted with ethyl acetate, washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (10–30% ethyl acetate/hexanes) to give **12** (3.6 mg, 71%).

Compound 2. To a solution of mixed thioketal **12** (11.6 mg, 0.00761 mmol) and Ph_3SnH (70.6 mg, 0.201 mmol) in toluene (3 mL) at 110 °C was added a catalytic amount of AIBN. The resultant solution was heated at 110 °C for 45 min. The reaction mixture was cooled to room temperature and directly subjected to flash column chromatography on silica gel (10–40% ethyl acetate/hexanes) to give **2** (10.9 mg, 98%) as a white solid: $[\alpha]_D^{24} +30.8$ (c 0.79, $CHCl_3$); 1H NMR (500 MHz, C_6D_6) δ 7.27-7.25 (m, 2H), 7.17-7.15 (m, 2H), 7.08 (m, 1H), 4.56 (ddd, $J = 8.8$, 8.3, 7.3 Hz, 1H), 4.29 (d, $J = 12.8$ Hz, 1H), 4.28 (m, 1H), 4.27 (d, $J = 12.8$ Hz, 1H), 4.18 (m, 1H), 4.13 (m, 1H), 4.09 (br d, $J = 4.9$, <1 Hz, 1H), 4.04-3.98 (m, 2H), 3.64 (ddd, $J = 8.3$, 8.3, 8.3 Hz, 1H), 3.51-3.40 (m, 4H), 3.32-3.28 (m, 2H), 3.27-3.11 (m, 5H), 3.08-2.86 (m, 12H), 2.67 (ddd, $J = 12.7$, 4.4, 4.4 Hz, 1H), 2.57 (m, 1H), 2.50-2.46 (m, 2H), 2.40-2.36 (m, 3H), 2.32-2.23 (m, 4H), 2.13-1.96 (m, 3H), 1.92-1.60 (m, 20H), 1.33 (d, $J = 4.8$ Hz, 3H), 1.22-1.15 (m, 21H), 1.15 (s, 3H), 1.12 (s, 3H), 1.01 (s, 9H), 0.92 (s, 9H), 0.19 (s, 3H), 0.10 (s, 3H), 0.00 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (125 MHz, $pyr-d_5$) δ 139.5, 128.7 (x2), 127.9 (x2), 127.8, 84.0, 83.8, 83.7, 83.1, 82.5, 80.1 (x2), 79.9, 78.6, 78.4, 77.9, 77.43, 77.40, 77.3, 77.1, 77.0, 76.5, 76.4, 76.3, 76.2, 76.0, 74.9, 74.7, 73.0 (x2), 72.6, 72.2, 72.1, 71.2, 70.8, 70.6, 70.5, 67.6, 45.3, 45.2, 39.9, 39.4, 39.3, 38.5, 38.4, 38.2, 37.2, 37.1, 37.0, 35.92, 35.86, 29.83, 29.80, 26.2 (x3), 25.9 (x3), 25.62, 25.55, 18.7 (x3), 18.59 (x3), 18.58, 18.2, 18.1, 16.81, 16.77, 12.9 (x3), -3.9, -4.1, -4.7, -4.9; HRMS (FAB) calcd for $C_{80}H_{132}O_{18}Si_3Na [(M+Na)^+]$ 1487.8619, found 1487.8621.

Alcohol 13. To a solution of **2** (3.9 mg, 0.0027 mmol) in THF/MeCN (1:1, v/v, 1.5 mL) were added 4 Å molecular sieves (12.3 mg) and TBAF (16.1 mg, 0.0616 mmol). The resulting mixture was stirred at room temperature for 2.5 h and heated to 70 °C for 12 h. The mixture was cooled to room temperature, extracted with CHCl₃ (5 mL x 5), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was filtered through silica gel (5—10% methanol/CHCl₃) to give triol (3.0 mg) as a white solid, which was used in the next reaction without further purification.

To a solution of the above triol (3.0 mg) in CH₂Cl₂ (2.0 mL) cooled to 0 °C were added 2,6-lutidine (0.020 mL, 0.171 mmol) and TESOTf (0.030 mL, 0.134 mmol). The resultant solution was stirred at room temperature for 50 min. The mixture was diluted with ethyl acetate, washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was filtered through silica gel (20—50% ethyl acetate/hexanes) to give TES ether (3.0 mg) as a white solid, which was used in the next reaction without further purification.

The LiDBB solution was prepared by addition of Li wire (ca. 40 mg, 5.6 mmol) to a solution of 4,4'-di-*tert*-butylbiphenyl (542.7 mg, 2.04 mmol) in THF (2.0 mL) and sonication at 0 °C for 25 min. To a solution of the above TES ether (3.0 mg) in THF cooled to -78 °C was added LiDBB solution until deep-green color persisted. The resultant solution was stirred at -78 °C for 30 min before the reaction was quenched with MeOH. The mixture was treated with NH₄Cl, diluted with CHCl₃ and stirred at room temperature for 15 min. The mixture was filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (20—70% ethyl acetate/hexanes) to give alcohol **13** (2.6 mg, 73% for the three steps) as a white solid: $[\alpha]_D^{26} +37.3$ (c 0.31, CHCl₃); ¹H NMR (500 MHz, C₆D₆) δ 4.53 (ddd, *J* = 7.7, 7.7, 7.7 Hz, 1H), 4.20 (br d, *J* = 5.1, <1 Hz, 1H), 4.09 (m, 1H), 4.07-3.95 (m, 4H), 3.62-3.53 (m, 3H), 3.50-3.42 (m, 2H), 3.38-3.32 (m, 2H), 3.27-3.17 (m, 5H), 3.09-2.91 (m, 10H), 2.85 (br d, *J* = 9.3, <1 Hz, 1H), 2.83 (br d, *J* = 8.3, <1 Hz, 1H), 2.66 (m, 1H), 2.54 (m, 1H), 2.50-2.47 (m, 2H), 2.42-2.36 (m, 3H), 2.26-2.15 (m, 4H), 2.12-2.01 (m, 2H), 1.94-1.60 (m, 21H), 1.53 (m, 1H), 1.36 (d, *J* = 5.5 Hz, 3H), 1.14 (s, 3H), 1.12 (s, 3H), 1.08 (t, *J* = 7.7 Hz, 9H), 1.07 (t, *J* = 8.0 Hz, 9H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.71 (q, *J* = 7.7 Hz, 6H), 0.70 (q, *J* = 8.0 Hz, 6H), 0.54 (q, *J* = 8.0 Hz, 6H); ¹³C NMR (125 MHz, pyr-*d*₅) δ 84.1, 83.8, 83.6, 83.1, 82.6, 80.1, 80.0, 79.9, 78.7 (x2), 77.9, 77.5, 77.43, 77.40, 77.1, 77.0, 76.5, 76.4, 76.3, 76.21, 76.16, 76.0, 75.3, 75.1, 72.5, 72.1, 72.04, 71.98, 70.8, 70.7, 70.5, 59.1, 45.32, 45.29, 40.4, 40.0, 39.4, 38.9, 38.7, 38.4, 38.2, 37.3, 37.2, 35.92, 35.85, 30.0, 29.84, 29.77, 25.6, 18.5, 16.80, 16.79, 7.4 (x3), 7.3 (x3), 7.1 (x3), 5.30 (x3), 5.28 (x3), 5.26 (x3); HRMS (FAB) calcd for C₇₀H₁₂₀O₁₈Si₃Na [(M+Na)⁺] 1355.7680, found 1355.7686.

Allyl Alcohol 14. To a solution of alcohol **13** (3.7 mg, 0.0028 mmol) in CH₂Cl₂ (1.0 mL) cooled to 0 °C were added 4 Å molecular sieves (10.9 mg), NMO (3.7 mg, 0.032 mmol), and TPAP (0.9 mg, 0.0025 mmol). The resulting solution was stirred at room temperature for 25 min. The mixture was directly subjected to column chromatography on silica gel (60% ethyl acetate/hexanes) to give aldehyde as a white solid, which was used in the next reaction without

further purification.

To a solution of the above crude aldehyde in CH_2Cl_2 (1.0 mL) was added methyl 2-(triphenylphosphoranylidene)propionate (3.5 mg, 0.010 mmol). The resulting solution was stirred at room temperature for 17.5 h. The mixture was directly subjected to column chromatography on silica gel (40% ethyl acetate/hexanes) to give crude ester as a white solid, which was used in the next reaction without further purification.

To a solution of the above crude ester in CH_2Cl_2 (1.0 mL) cooled to -78°C was added DIBAL-H (0.95 M, 0.050 mL, 0.0475 mmol). The resultant solution was stirred at -78°C for 30 min before the reaction was quenched with ethyl acetate. The reaction mixture was diluted with ethyl acetate and treated with saturated aqueous potassium sodium tartrate. The resultant mixture was vigorously stirred at room temperature until the layers were separated. The aqueous layers was separated and extracted with ethyl acetate (5 mL x 5). The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (30—80% ethyl acetate/hexanes) to give allyl alcohol **14** (2.5 mg, 66% for the three steps) as a white solid: $[\alpha]_{\text{D}}^{25} +28.8$ (c 0.21, CHCl_3); ^1H NMR (600 MHz, $\text{pyr}-d_5$) δ 5.78 (dd, $J = 5.8, 5.8$ Hz, 1H), 4.59 (ddd, $J = 7.9, 7.9, 7.9$ Hz, 1H), 4.27 (s, 2H), 4.25 (m, 1H), 4.19 (m, 1H), 4.09 (m, 1H), 4.08-4.02 (m, 3H), 3.77-3.70 (m, 3H), 3.45-3.06 (m, 19H), 2.64 (m, 1H), 2.56-2.50 (m, 5H), 2.46-2.41 (m, 4H), 2.32-2.21 (m, 4H), 2.17 (m, 1H), 2.01-1.61 (m, 20H), 1.75 (s, 3H), 1.37 (s, 3H), 1.34 (s, 3H), 1.31 (d, $J = 5.8$ Hz, 3H), 1.06 (t, $J = 8.1$ Hz, 9H), 1.05 (t, $J = 8.1$ Hz, 9H), 0.94 (t, $J = 7.9$ Hz, 9H), 0.71 (q, $J = 8.1$ Hz, 6H), 0.70 (q, $J = 8.1$ Hz, 6H), 0.58 (q, $J = 7.9$ Hz, 6H); ^{13}C NMR (150 MHz, $\text{pyr}-d_5$) δ 138.5, 120.0, 84.1, 83.8, 83.6, 83.1, 82.6, 81.1, 80.0, 79.9, 78.7, 78.6, 77.9, 77.5, 77.43 (x2), 77.40, 77.1, 77.0, 76.5, 76.4, 76.3, 76.22, 76.17, 76.0, 75.1, 72.5, 72.09, 72.05, 72.0, 70.8, 70.7, 70.5, 67.9, 45.33, 45.29, 40.0, 39.5, 38.9, 38.4, 38.2, 38.0, 37.4, 37.2, 35.9 (x2), 34.9, 29.84, 29.77, 25.57, 25.55, 18.5, 16.81, 16.79, 14.1, 7.41 (x3), 7.35 (x3), 7.1 (x3), 5.30 (x3), 5.29 (x3), 5.26 (x3); HRMS (FAB) calcd for $\text{C}_{73}\text{H}_{124}\text{O}_{18}\text{Si}_3\text{Na}$ $[(\text{M}+\text{Na})^+]$ 1395.7993, found 1395.7996.

Gymnocin-A (1). To a solution of the allyl alcohol **14** (2.5 mg, 0.0018 mmol) in THF/DMF (4:1, v/v, 1.25 mL) cooled to 0°C was added TASF (10.0 mg, 0.0363 mmol). The resultant solution was stirred at 0°C for 2.5 h, allowed to warm to room temperature and stirred for 6 h before the reaction was quenched with water. The aqueous layer was extracted with CHCl_3 (5 mL x 5) and the combined CHCl_3 layers were washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (40% acetone/benzene then 10% MeOH/ CHCl_3) to give crude tetraol as a white solid, which was used in the next reaction without further purification.

To a solution of the above tetraol in CHCl_3 (1.0 mL) was added MnO_2 (8.2 mg, 0.094 mmol). The resultant mixture was stirred at room temperature for 3 h. The mixture was directly subjected to flash column chromatography on silica gel (10% MeOH/ CHCl_3) to give gymnocin-A (**1**) (1.7 mg, 91% for the two steps) as a white solid: $[\alpha]_{\text{D}}^{26} +27.3$ (c 0.055, CHCl_3); ^1H NMR (600 MHz, CDCl_3) δ 9.37 (s, 1H), 6.47 (dd, $J = 6.6, 6.6$ Hz, 1H), 4.18 (br d, $J = 7.8, <1$ Hz, 1H), 4.15-4.11 (m, 2H), 4.01 (ddd, $J = 8.2, 8.2, 8.2$ Hz, 1H), 3.78 (ddd, $J = 9.6, 9.6, 4.8$ Hz, 1H), 3.65

(ddd, $J = 9.6, 9.6, 4.8$ Hz, 1H), 3.60 (m, 2H), 3.54-3.46 (m, 3H), 3.29-3.23 (m, 2H), 3.19-3.10 (m, 5H), 3.06-2.88 (m, 12H), 2.52-2.49 (m, 2H), 2.45 (m, 1H), 2.34-2.23 (m, 6H), 2.18-2.12 (m, 3H), 2.08-2.04 (m, 2H), 2.02-1.91 (m, 5H), 1.83-1.78 (m, 3H), 1.74-1.62 (m, 5H), 1.70 (s, 3H), 1.50-1.32 (m, 9H), 1.23 (d, $J = 5.8$ Hz, 3H), 1.20 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 195.2, 149.5, 141.0, 84.0, 83.61, 83.56, 82.7, 81.9, 80.1, 79.8, 79.6, 78.9, 78.1, 77.4, 77.2, 77.1, 77.0, 76.7 (x2), 76.5, 76.1, 76.0 (x2), 75.75, 75.71, 75.69, 75.65, 73.6, 71.50, 70.49, 70.3, 70.2, 70.1, 69.9, 44.6, 44.5, 38.5, 38.3, 37.7, 37.5, 37.4, 36.5, 36.0, 35.5, 35.2 (x2), 34.5, 29.40, 29.37, 25.1 (x2), 17.8, 16.6 (x2), 9.5; HRMS (FAB) calcd for $\text{C}_{55}\text{H}_{80}\text{O}_{18}\text{Na}$ $[(\text{M}+\text{Na})^+]$ 1051.5242, found 1051.5251.

Stereochemical Determination for Compounds **7** and **10**.

1. Determination of C22 Stereochemistry of **7**.

The stereochemistry at C22 position of alcohol **7** was unambiguously determined by conversion into the corresponding acetate **7b** and its ^1H NMR coupling constant analysis and differential NOE experiment as shown.

2. Determination of C17 Stereochemistry of **10**.

The stereochemistry at C17 position of siloxy ketone **10** was unambiguously determined by NOE between H15 and H17 on the ROESY spectrum (Figure 1). The proton signal of H15 was assigned by ^1H - ^1H COSY spectrum. The stereoselectivity of dihydroxylation of silyl enol ether, derived from ketone **9**, can be explained by approach of OsO_4 onto the double bond from the α -face in the most stable conformer **A** (Table 2).

Figure 1

Figure 2*

*TIPS and TES groups were replaced by *t*-Bu group for clarity.

^1H NMR Spectra of Gymnocin-A (600 MHz, CDCl_3)

^1H NMR Spectra of Gymnocin-A (600 MHz, CDCl_3)

synthetic

natural

^{13}C NMR Spectra of Gymnocin-A (150 MHz, CDCl_3)

synthetic

natural