Supporting Information
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Synthesis and Structure–Activity Relationship of Vicenistatin, a Cytotoxic 20-Membered Macrolactam Glycoside


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General Remarks

All reactions were carried out under an argon atmosphere using flame-dried or oven-dried glassware, unless otherwise noted, and monitored with analytical TLC (Merck Kieselgel 60 F254) or NH-TLC (FUJI SILYSIA CHEMICAL Co., Ltd.). Dehydrated tetrahydrofuran (THF) and dichromomethane (DCM) were purchased from Kanto Chemical Co., Inc. Other solvents were dehydrated and distilled according to standard protocols. Reagents were obtained from commercial suppliers and used without further purification, unless otherwise noted. NMR spectra were measured on a JEOL JNM-AL400 (400 MHz), a JEOL ECP-500 (500 MHz), and a JEOL ECA-600 spectrometer (600 MHz). Chemical shifts were reported in the δ scale relative to tetramethylsilane (TMS) as 0.00 ppm for \(^1\)H (CDCl\textsubscript{3}) and residual CHCl\textsubscript{3} (7.26 ppm for \(^1\)H and 77.00 ppm for \(^13\)C), pyridine (7.19 ppm for \(^1\)H and 123.5 ppm for \(^13\)C), DMSO (2.49 ppm for \(^1\)H and 39.7 ppm for \(^13\)C) as internal references. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, sept = septet, br = broad. The infrared (IR) spectra were recorded on JASCO FT/IR-410 and JASCO IR-700. Mass spectra (MS) were measured on JEOL JMS-DX303 (EI), JEOL JMS-700 (EI), JEOL JMS-T 100GC (EI), and JEOL JMS 700 (FAB). Melting points were taken with Yazawa BY-2 and are uncorrected. The optical rotations were determined on JASCO DIP-370 Digital Polarimeter at room temperature, using the sodium D line. Silica gel column chromatography, flash column chromatography, and amine silica gel column chromatography were carried out with silica gel 60N (Kanto Chemical Co., Inc., spherical, neutral, 63-210 µm), silica gel (Kanto Chemical Co., Inc., spherical, neutral, 40-50 µm), and Chromatorex NHDM 1020 (Fuji Silysia Chemical Co., Ltd., 100-200 mesh), respectively.

Homoallyl alcohol 6: To a stirred solution of \(\text{Cp}_2\text{ZrCl}_2\) (589 mg, 2.02 mmol) in wet DCM (6 mL) was added Me\textsubscript{3}Al (2.0 M in heptane, 6.05 mL, 12.1 mmol) at room temperature. The reaction mixture was cooled to 0 °C and to the mixture was added a solution of 4 (500 mg, 4.03 mmol) in DCM (4 mL) via cannula. After stirring at room temperature for 3 hr, the reaction mixture was cooled to 0 °C and to the mixture was added a solution of I\textsubscript{2} (1.23 g, 4.84 mmol) in THF (5 mL) using a syringe. The reaction mixture was stirred at room temperature for 2 hr and then quenched by slow addition of water at 0 °C. The mixture was extracted twice with Et\textsubscript{2}O. The combined organic extracts were washed with brine, dried (MgSO\textsubscript{4}), and concentrated. The residue was purified by flash chromatography (AcOEt-hexane = 1 : 15) to give 6 (688 mg, 2.59 mmol, 64%) as a pale yellow oil.

6: IR (neat): 3341, 2913, 1433, 1376, 1267, 1139, 1045, 753 cm\textsuperscript{-1}; \(^1\)H-NMR (400 MHz, CDCl\textsubscript{3}) δ 5.93 (s, 1H), 5.22 (t, \(J = 7.0\) Hz, 1H), 3.64 (t, \(J = 6.6\) Hz, 2H), 2.87 (s, 2H), 2.31 (dd, \(J = 7.0, 6.6\) Hz,
**Alcohol (−)-7:** To a stirred solution of 6 (2.06 g, 7.74 mmol) in DCM (35 mL) was added Dess-Martin periodinane (3.60 g, 8.52 mmol) at room temperature. The reaction mixture was stirred at room temperature for 1 hr and then concentrated. To the residue was added hexane and the mixture was filtered through Celite. The filtrate was concentrated in vacuo to give crude aldehyde (1.86 g, <7.05 mmol) as pale yellow oil. This material was used without further purification. To a stirred solution of t-BuOK (1.58 g, 14.1 mmol, freshly dried by heating with a heat gun under vacuum) in THF (12 mL) was added cis-2-butene (ca. 4 mL) at −78 °C. Then n-BuLi (1.56 M in hexane, 7.68 mL, 12.0 mmol) was added dropwise to the reaction mixture at −78 °C. The reaction mixture was stirred to −50 °C for 10 min. To the mixture was added (+)-Ipc2BOMe (3.78 g, 12.0 mmol) in THF (20 mL) via cannula at −78 °C and the resulting mixture was stirred at the same temperature for 30 min. After BF3·OEt2 (1.48 mL, 12.0 mmol) was added to the reaction mixture at −78 °C, crude aldehyde (1.86 g, <7.05 mmol) prepared above was added to the mixture via a syringe at the same temperature. The resulting mixture was slowly warmed to 0 °C, then cooled again to −78 °C. After MeOH (4.5 mL), saturated aqueous NaHCO3 (45 mL), and 30% aqueous H2O2 (22 mL) were added, the resulting mixture was stirred at room temperature overnight. The resulting mixture was extracted twice with Et2O. The combined organic extracts were washed with brine, dried (MgSO4), and concentrated. The residue was purified by flash chromatography (AcOEt-hexane = 1 : 20) to give (−)-7 (1.16 g, 3.63 mmol, 47% for 2 steps, 100 % de, 94% ee) as pale yellow oil.

(−)-7: [α]D$^2^0$ = −21.6 ($c$ 1.24, CHCl3); IR (neat): 3419, 2972, 2911, 1638, 1434, 1375, 1267, 1139, 1094, 1040, 998, 915, 884, 758, 667 cm$^{-1}$; 1H-NMR (400 MHz, CDCl3) δ 5.94 (s, 1H), 5.80 (m, 1H), 5.28 (t, $J = 6.7$ Hz, 1H), 5.09 (d, $J = 17.6$ Hz, 1H), 5.08 (d, $J = 10.4$ Hz, 1H), 3.55-3.49 (m, 1H), 2.88 (s, 2H), 2.32-2.12 (m, 3H), 1.76 (s, 3H), 1.55 (s, 3H), 1.49 (d, $J = 4.4$ Hz, 1H), 1.05 (d, $J = 4.1$ Hz, 3H); 13C-NMR (100 MHz, CDCl3) δ 145.9, 140.9, 134.7, 123.6, 115.2, 76.0, 74.5, 49.9, 43.1, 33.1, 23.2, 15.7, 14.4; LRMS (EI) m/z 320 (M$^+$), 109 (100%); HRMS (EI) Calcd. C13H21OI (M$^+$): 320.0635. Found: 320.0614.
Optical purity of (−)-7 was determined by chiral HPLC analysis (HPLC conditions: column; CHIRALCEL OD-H, eluent; hexane-i-PrOH = 199 : 1, flow rate; 0.5 mL/min, detection; UV 254 nm, retention time; 21.5 min for (−)-7 and 69.6 min for (+)-7).

Enal (−)-16: To a stirred solution of (−)-7 (113 mg, 353 µmol) in DCM (3.5 mL) were added acrolein (0.236 mL, 3.53 mmol) and Hoveyda-Grubbs second generation catalyst (22 mg, 35.3 µmol) at room temperature. The reaction mixture was stirred at room temperature for 3 hr and then concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 2) to give crude 8 (37 mg) as a pale yellow oil. To a stirred solution of crude 8 (37 mg, <102 µmol) in DCM (1 mL) were added 2,6-lutidine (71 µL, 613 µmol) and TMSCl (39 µL, 307 µmol) at room temperature. The reaction mixture was stirred at room temperature for 40 min, then quenched with water. The resulting mixture was extracted twice with Et2O. The combined organic extracts were washed with brine, dried (MgSO4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 10) to give (−)-16 (43 mg, 102 µmol, 29% for 2 steps) as a pale yellow oil.

(−)-16: [α]D28 = −46.9 (c 0.89, CHCl3); IR (neat): 2959, 1693, 1250, 1142, 840 cm⁻¹; ¹H-NMR (400 MHz, CDCl3) δ 9.53 (d, J = 7.9 Hz, 1H), 6.88 (dd, J = 15.9, 7.2 Hz, 1H), 6.11 (dd, J = 15.9, 7.9 Hz, 1H), 5.93 (s, 1H), 5.21 (t, J = 6.9 Hz, 1H), 3.52 (dt, J = 6.5, 5.2 Hz, 1H), 2.85 (s, 2H), 2.59-2.54 (m, 1H), 2.24-2.10 (m, 2H), 1.76 (s, 3H), 1.52 (s, 3H), 1.09 (d, J = 4.1 Hz, 3H), 0.11 (s, 9H); ¹³C-NMR (100 MHz, CDCl3) δ 160.5, 145.4, 133.5 132.0, 122.8, 75.7, 74.7, 49.4, 42.0, 32.9, 23.0, 15.4, 13.5, 0.00; LRMS (EI) m/z 420 (M⁺), 185 (100%); HRMS (EI) Calcd. C₁₇H₂₉O₂Si (M⁺): 420.0979. Found: 420.0963.

Alcohol (−)-19: To a stirred solution of 18 (87 mg, 473 µmol) in MeOH (2 mL) was added K₂CO₃ (131 mg, 946 µmol) at room temperature. The reaction mixture was stirred for 6 hr. After quenched with H₂O, the mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 2) to give (−)-19 (51 mg, 455 µmol, 96%) as a colorless oil.
(−)-19: \([\alpha]_D^{25}\) –13.9 (c 0.82, CHCl₃); IR (neat): 3300, 2929, 2874, 1040 cm⁻¹; \(^1\)H-NMR (400 MHz, CDCl₃) δ 3.55-3.47 (m, 2H), 2.34-2.17 (m, 2H), 1.95 (t, J = 2.7 Hz, 1H), 1.84-1.76 (m, 1H), 1.75-1.65 (m, 1H), 1.43-1.34 (m, 1H), 0.95 (d, J = 6.7 Hz, 3H); \(^13\)C-NMR (100 MHz, CDCl₃) δ 84.4, 68.3, 67.3, 34.6, 31.7, 16.0, 15.9; LRMS (EI) m/z 112 (M⁺), 79 (100%); HRMS (EI) Calcd. C₇H₁₂O (M⁺): 112.0888. Found: 112.0890.

Vinyl stannane (−)-20: To a stirred solution of Pd₂(dba)₃·CHCl₃ (10.4 mg, 10 µmol) and Cy₃P·HBF₄ (15 mg, 40.7 µmol) in degassed DCM (10 mL) was added i-Pr₂NEt (36 µL, 202 µmol) at room temperature. The reaction mixture was stirred for 20 min. A solution of (−)-19 (100 mg, 893 µmol) in degassed DCM (2 mL) and Bu₃SnH (0.323 mL, 1.20 mmol) were added dropwise to the mixture. The resulting mixture was stirred for 2 hr, and then concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 10) to give (−)-20 (266 mg, 0.658 mmol, 74%, gem isomer : trans isomer = 1 : 20) as a colorless oil. This material was used in the next reaction without further purification. Small amount of this material was purified further to give pure trans isomer.

(−)-20: \([\alpha]_D^{25}\) –5.0 (c 0.68, CHCl₃); IR (neat): 3328, 2956, 2925, 2871, 2852, 1598, 1462, 1376, 1042, 989 cm⁻¹; \(^1\)H-NMR (400 MHz, CDCl₃) δ 6.02-5.77 (m, 2H), 3.52 (ddd, J = 10.5, 5.9, 5.6 Hz, 1H), 3.44 (ddd, J = 10.5, 6.1, 5.9 Hz, 1H), 2.26-2.08 (m, 2H), 1.69-1.61 (m, 1H), 1.56-1.38 (m, 7H), 1.35-1.18 (m, 7H), 0.95-0.77 (m, 18H); \(^13\)C-NMR (100 MHz, CDCl₃) δ 149.2, 127.3, 68.2, 35.3, 32.4, 29.3, 29.2, 27.1, 16.6, 13.8, 9.5; LRMS (EI) m/z 347 (M⁺–n-Bu), 347 (100%); HRMS (EI) Calcd. C₁₅H₃₁OSn (M⁺–n-Bu): 347.1396. Found: 347.1397.

Phosphonate (−)-17: To a stirred solution of Ph₃P (345 mg, 1.32 mmol) in THF (4 mL) was added DIAD (259 µL, 1.32 mmol) at 0 °C. The reaction mixture was stirred at the same temperature for 20 min. A solution of (−)-20 (gem isomer : trans isomer = 1 : 20, 266 mg, 658 µmol) in THF (1.5 mL) and DPPA (295 µL, 1.32 mmol) were added to the mixture. The resulting mixture was allowed to warm to room temperature over 2 hr, and then quenched with H₂O. The mixture was extracted twice with hexane. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 :
10) to give the corresponding azide (232 mg, 651 μmol, 82%, *gem* isomer : *trans* isomer = 1 : 20) as a colorless oil. Analytical sample was prepared from pure *trans* isomer (−)-20.

azide: [α]D27 +24.6 (c 0.64, CHCl3); IR (neat): 2957, 2925, 2871, 2852, 2097, 1598, 1461, 1376, 1283, 990 cm⁻¹; ¹H-NMR (400 MHz, CDCl3) δ 5.99-5.81 (m, 2H), 3.22 (dd, J = 12.0, 5.8 Hz, 1H), 3.12 (dd, J = 12.0, 6.8 Hz, 1H), 2.22-2.09 (m, 2H), 1.76-1.69 (m, 1H), 1.55-1.39 (m, 7H), 1.33-1.22 (m, 7H), 0.96 (d, J = 6.8 Hz, 3H), 0.95-0.78 (m, 15H); LRMS (EI) m/z 372 (M⁺–n-Bu), 344 (100%); HRMS (EI) Calcd. C15H30N3Sn (M⁺–n-Bu): 372.1460. Found: 372.1458.

A solution of azide (1.27 g, 2.97 mmol), 5% Lindlar catalyst (255 mg, 20% w/w) and quinoline (526 µl, 4.45 mmol) in MeOH (15 mL) was stirred for 2 hr under H2 atmosphere at room temperature. The reaction mixture was filtered through Celite. The filtrate was concentrated to give crude amine as a pale yellow oil, which was used without further purification. To a stirred solution of crude amine and 21 (1.46 g, 7.42 mmol) in DCM were added EDCI (1.42 g, 7.42 mmol) and HOBt (1.00 g, 7.42 mmol) at room temperature. After stirred at the same temperature for 5 min, the reaction was cooled to 0 °C, Et3N (2.07 mmol, 14.8 mmol) was added. The resulting mixture was allowed to warm to room temperature and stirred for 10 hr. The reaction was quenched with H2O, and the mixture was extracted twice with AcOEt. The combined organic extracts were washed with brine, dried (MgSO4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt) to give (−)-17 (1.39 g, 2.39 mmol, 80% for 2 steps, *gem* isomer : *trans* isomer = 1 : 20) as a colorless oil. Analytical sample was prepared from pure (−)-20.

(−)-17: [α]D27 −2.7 (c 0.48, CHCl3); IR (neat): 3296, 2957, 2925, 2871, 2852, 1654, 1557, 1457, 1245, 1029, 968 cm⁻¹; ¹H-NMR (400 MHz, CDCl3) δ 6.77 (brs, 1H), 5.98-5.80 (m, 2H), 4.14 (dq, J = 7.6, 7.1 Hz, 4H), 3.23 (dd, J = 13.3, 5.9, 5.6 Hz, 1H), 3.11 (ddd, J = 13.3, 6.6, 6.4 Hz, 1H), 2.84 (d, J = 20.2 Hz, 1H), 2.23-2.08 (m, 2H), 1.71-1.63 (m, 1H), 1.52-1.44 (m, 7H), 1.36-1.25 (m, 13H), 0.93 (d, J = 6.6 Hz, 3H), 0.92-0.77 (m, 15H); ¹³C-NMR (100 MHz, CDCl3) δ 163.7, 148.9, 127.5, 62.7, 45.7, 35.7, 35.3, 34.4, 33.5, 32.9, 29.2, 27.3, 17.5, 16.4, 13.8, 9.5; LRMS (EI) m/z 524 (M⁺–n-Bu), 524 (100%); HRMS (EI) Calcd. C21H43NO4PSn (M⁺–n-Bu): 524.1952. Found: 524.1953.

**Tetraene (−)-24:** To a cooled (−78 °C) solution of (−)-17 (gem isomer : *trans* isomer = 1 : 20, 56 mg, 96.9 μmol) in THF (1 mL)
was added potassium bis(trimethylsilylamide (211 µL, 106 µmol). The resulting solution was stirred for 5 min. Then, a solution of (-)-16 (37 mg, 88.1 µmol) in THF (2 mL) was added via a syringe at the same temperature. The resulting mixture was allowed to warm to 0 °C over 20 min. Saturated aqueous NH₄Cl was added, and the mixture was allowed to warm to room temperature. The resulting mixture was extracted twice with Et₂O and the combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 6) to give (-)-25 (53 mg, 62.6 µmol, 71%, gem isomer : trans isomer = 1 : 20) as a colorless oil. Analytical sample was prepared from pure (-)-17.

(-)-24: [α]D²⁷ -37.5 (c 0.38, CHCl₃); IR (neat): 3282, 2956, 2924, 2870, 2852, 1656, 1627, 1551, 1461, 1375, 1250, 998, 839 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.19 (dd, J = 14.9, 10.5 Hz, 1H), 6.10 (dd, J = 15.4, 10.5 Hz, 1H), 6.00 (dd, J = 15.4, 7.6 Hz, 1H), 5.92-5.84 (m, 3H), 5.77 (d, J = 14.9 Hz, 1H), 5.43 (brs, 1H), 5.23 (t, J = 7.0 Hz, 1H), 3.57 (dt, J = 5.8, 5.6 Hz, 1H), 3.28 (ddd, J = 13.6, 6.0, 5.8 Hz, 1H), 3.18 (ddd, J = 13.6, 6.8, 6.3 Hz, 1H), 2.85 (s, 2H), 2.37-2.29 (m, 1H), 2.26-2.08 (m, 4H), 1.77 (s, 3H), 1.72-1.63 (m, 1H), 1.52-1.45 (m, 10H), 1.35-1.26 (m, 7H), 1.02 (d, J = 6.8 Hz, 3H), 0.93-0.84 (m, 15H); ¹³C-NMR (99 MHz, CDCl₃) δ 163.7, 148.9, 127.5, 62.7, 45.7, 35.7, 35.3, 34.4, 33.5, 32.9, 29.2, 27.3, 17.5, 16.4, 13.8, 9.5; LRMS (FAB) m/z 524 (M⁺+H), 73 (100%); HRMS (FAB) Calcd. C₃₈H₇¹NO₃SiSn (M⁺+H): 848.3316. Found: 848.3367.

Macrolactam (+)-25: A solution of (-)-24 (27 mg, 31.9 µmol), Pd(dba)₂-CHCl₃ (6.6 mg, 6.38 µmol), Ph₃As (9.8 mg, 31.9 µmol) and i-Pr₂NEt (56 µL, 319 µmol) in DMF (15 mL) was stirred at room temperature for 2 hr. The resulting mixture was extracted twice with Et₂O and the combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 4) to give crude (+)-25 (3.1 mg, 7.23 µmol, < 23%) as a white powder.

(+)-25: [α]D²⁶ +56.8 (c 0.12, CHCl₃); IR (neat): 3316, 2955, 1656, 1627, 1616, 1262, 1251, 1070, 992, 887, 841, ¹H-NMR (400 MHz, pyridine-d₅) δ 8.40 (brs, 1H), 7.56 (dd, J = 14.6, 11.5 Hz, 1H), 6.75 (dd, J = 14.1, 11.5 Hz, 1H), 6.23 (d, J = 15.1 Hz, 1H), 6.21 (m, 1H), 5.93 (m, 2H), 5.68 (ddd, J = 14.6, 8.5, 6.1 Hz, 1H), 5.20 (t, J = 7.4 Hz, 1H), 3.93 (m, 1H), 3.47 (m, 1H), 3.09 (brd, J = 13.4 Hz, 1H), 2.70 (d, J = 14.1 Hz, 1H), 2.63 (d, J = 14.4 Hz, 1H), 2.41-2.32 (m, 4H), 2.15-2.07 (m, 1H), 1.91 (s, 3H), 1.81 (m, 1H), 1.55 (s, 3H), 1.08 (d, J = 6.6 Hz, 1H), 0.85 (d, J = 6.8 Hz, 1H), 0.20 (s, 9H); ¹³C-NMR (150 MHz, pyridine-d₅) δ 166.3, 143.3, 140.3, 134.6, 134.0, 132.5, 128.5, 128.3, 127.7,
124.5, 121.9, 77.2, 49.7, 47.4, 43.3, 38.2, 33.6, 35.1, 28.2, 19.3, 18.3, 17.4, 17.2, 0.5; LRMS (FAB) m/z 429 (M⁺), 154 (100%); HRMS (FAB) Calcd. C_{43}H_{71}NO_{2}Si (M⁺): 429.3063. Found: 429.3065.

Enal (−)-26: A solution of (−)-8 (1.14 g, 3.26 mmol), tributyl(vinyl)tin (1.58 mL, 5.40 mmol) and Ph₃P (284 mg, 1.08 mmol) in THF (15 mL) was deaerated, then added Pd₂(dba)₃·CHCl₃ (280 mg, 270 µmol) at room temperature. The reaction mixture was stirred at that temperature for 1 hr and quenched with saturated aqueous NaHCO₃. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:4) to give crude tetraene as a colorless oil.

Phthalimide (−)-28: To a stirred solution of Ph₃P (422 mg, 1.61 mmol) in THF (8 mL) was added DIAD (316 µL, 1.61 mmol) at 0 °C and the mixture was stirred at that temperature for 20 min. Then (−)-18 (90 mg, 804 µmol) and phthalimide (236 mg, 1.61 mmol) were added to the solution. The resulting mixture was warmed to room temperature, stirred for 2 hr and concentrated. The residue was...
purified by silica gel column chromatography (AcOEt-hexane = 1:8) to give phthalimide (195 mg, 804 μmol, 100%) as a colorless crystal.

**Phthalimide**: Mp 58-60 °C (recrystalized from hexane); [α]_D^{25} –57.1 (c 0.61, CHCl₃); IR (neat) 3252, 2923, 2853, 1772, 1698, 1463, 1401, 1377 cm⁻¹; H-NMR (400 MHz, CDCl₃) δ 7.85 (dd, J = 5.6, 3.1 Hz, 2H), 7.72 (dd, J = 13.5, 6.8 Hz, 1H), 3.60 (dd, J = 13.5, 7.5 Hz, 1H), 2.33 (m, 1H), 2.23 (dt, J = 2.7, 7.9 Hz, 1H), 2.15 (m, 1H), 1.93 (t, J = 2.7 Hz, 1H), 1.65 (m, 1H), 1.40 (ddt, J = 14.0, 5.3, 8.5 Hz, 1H), 0.94 (d, J = 6.8 Hz, 3H); C NMR (100 MHz, CDCl₃) δ 168.6, 133.9, 132.0, 123.2, 83.9, 68.6, 43.6, 32.9, 31.9, 16.9, 16.0; LRMS (EI) m/z 241 (M⁺), 160 (100%); HRMS (EI) Calcd. C₁₅H₁₅NO₂ (M⁺) 241.1103. Found: 241.1097.

A solution of phthalimide (195 mg, 809 μmol), quinoline (143 μL, 1.21 mmol) and Lindlar catalyst (39 mg, 20% w/w) in AcOEt (8 mL) was stirred under H₂ atmosphere at room temperature for 2.5 hr and filtered through Celite. The filtrate was concentrated and the residue was purified by silica gel column chromatography (AcOEt-hexane = 1:4) to give (−)-28 (178 mg, 733 μmol, 91%) as a white powder.

(−)-28: [α]_D^{20} –14.0 (c 0.59, CHCl₃); IR (neat): 3470, 3276, 2963, 2930, 1774, 1714, 1640, 1614, 1467, 1434, 1397, 1381, 1359 cm⁻¹; H-NMR (400 MHz, CDCl₃) δ 7.84 (dd, J = 5.1, 3.2 Hz, 2H), 7.71 (dd, J = 5.1, 3.2 Hz, 2H), 5.78 (ddt, J = 16.8, 10.2, 6.6 Hz, 1H), 5.01 (d, J = 17.2 Hz, 1H), 4.94 (d, J = 10.0 Hz, 1H), 3.59 (dd, J = 13.4, 6.6 Hz, 1H), 3.51 (dd, J = 13.4, 7.8 Hz, 1H), 2.19 (m, 1H), 2.03 (m, 2H), 1.49 (m, 1H), 1.26 (m, 1H), 0.92 (d, J = 6.8 Hz, 3H); C NMR (100 MHz, CDCl₃) δ 168.2, 138.2, 133.6, 131.8, 122.9, 114.4, 43.9, 33.4, 32.0, 30.9, 17.2; LRMS (EI) m/z 243 (M⁺), 160 (100%); HRMS (EI) Calcd. C₁₅H₁₇NO₂ (M⁺) 243.1259. Found: 243.1261.

**Phosphonate (−)-27**: A solution of (−)-28 (178 mg, 733 μmol) and 80% hydrazine (133 μL, 2.20 mmol) in EtOH (7 mL) was stirred at reflux for 3 hr and filtered through Celite. The filtrate was added 10% aqueous HCl and stirred at room temperature for 30 min. The mixture was concentrated and freeze-dried to give crude amine hydrochloride salt. To a stirred solution of crude amine hydrochloride salt and 21 (718 mg, 3.66 mmol) in DCM (15 mL) were added EDCI (702 mg, 3.66 mmol) and HOBt (495 mg, 3.66 mmol) at room temperature and the mixture was stirred at that temperature for 5 min. The solution was added triethylamine (1.81 mL, 11.0 mmol) and stirred for 10 hr, then quenched with H₂O. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were
washed with brine, dried (MgSO\textsubscript{4}), and concentrated. The residue was purified by silica gel column chromatography (AcOEt) to give (−)-27 (208 mg, 0.531 mmol, 72% for 2 steps) as a colorless oil.

(−)-27: [α]\textsubscript{D}\textsuperscript{27} −1.07 (c 0.48, CHCl\textsubscript{3}); IR (neat) 3294, 3076, 2978, 2929, 2872, 1659, 1556, 1443, 1392, 1300, 1245 cm\textsuperscript{−1}; \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) 6.83 (brs, 1H), 5.79 (ddt, \( J = 17.1, 10.2, 6.6 \) Hz, 1H), 5.00 (dd, \( J = 17.1, 1.5 \) Hz, 1H), 4.94 (d, \( J = 10.2 \) Hz, 1H), 4.14 (quint., \( J = 7.3 \) Hz, 4H), 3.22 (m, 1H), 3.11 (m, 1H), 2.84 (d, \( J = 20.2 \) Hz, 2H), 2.16-2.01 (m, 2H), 1.68 (m, 1H), 1.51-1.42 (m, 1H), 1.34 (t, \( J = 7.1 \) Hz, 6H), 1.28-1.20 (m, 1H), 0.93 (d, \( J = 6.6 \) Hz, 1H); \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) \( \delta \) 163.5, 137.8, 113.7, 76.7, 61.9, 44.9, 35.1, 33.8, 32.8, 32.1, 30.5, 16.8, 15.8; LRMS (FAB) \( m/z \) 292 (M\textsuperscript{+}+H, 100%); HRMS (FAB) Calcd. C\textsubscript{13}H\textsubscript{27}NO\textsubscript{4}P (M\textsuperscript{+}+H): 292.1678. Found: 292.1684.

**Hexaene (−)-29:** To a stirred solution of (−)-27 (63 mg, 162 \( \mu \)mol) in THF (1 mL) were added LHMDS (1.6 M in THF, 110 \( \mu \)L, 176 \( \mu \)mol). The reaction mixture was stirred for 5 min. To the solution was added (−)-26 (47 mg, 147 \( \mu \)mol) in THF (1.5 mL) at −78 °C. The reaction mixture was warmed up to 0 °C, then quenched with saturated aqueous NH\textsubscript{4}Cl. The resulting mixture was extracted twice with Et\textsubscript{2}O. The combined organic extracts were washed with brine, dried (MgSO\textsubscript{4}), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 10) to give (−)-29 (57 mg, 125 \( \mu \)mol, 85%) as a colorless oil.

(−)-29: [α]\textsubscript{D}\textsuperscript{27} −42.2 (c 0.33, CHCl\textsubscript{3}); IR (neat): 3281, 3080, 2959, 2916, 1658, 1628, 1555 cm\textsuperscript{−1}; \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) 7.19 (dd, \( J = 14.9, 10.3 \) Hz, 1H), 6.56 (dt, \( J = 16.8, 10.5 \) Hz, 1H), 6.10 (dd, \( J = 15.4, 10.5 \) Hz, 1H), 6.01 (dd, \( J = 15.1, 7.3 \) Hz, 1H), 5.87 (d, \( J = 11.0 \) Hz, 1H), 5.78 (ddt, \( J = 17.3, 10.3, 6.6 \) Hz, 1H), 5.76 (d, \( J = 15.1 \) Hz, 1H), 5.50 (brt, \( J = 5.5 \) Hz, 1H), 5.21 (t, \( J = 6.3 \) Hz, 1H), 5.11 (dd, \( J = 16.8, 1.7 \) Hz, 1H), 5.03-4.93 (m, 3H), 3.57 (dt, \( J = 11.7, 5.6 \) Hz, 1H), 3.28 (dt, \( J = 13.4, 6.8 \) Hz), 3.17 (dt, \( J = 13.4, 6.7 \) Hz, 1H), 2.71 (s, 1H), 2.35 (m, 1H), 2.20-2.05 (m, 1H), 1.68 (s, 3H), 1.49 (s, 1H), 1.47 (m), 1.25 (m, 1H), 1.02 (d, \( J = 6.6 \) Hz, 1H), 0.92 (d, \( J = 6.6 \) Hz, 3H), 0.09 (s, 9H); \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) \( \delta \) 166.3, 145.4, 141.0, 138.5, 137.5, 134.5, 133.3, 127.8, 127.0, 122.9, 122.3, 114.9, 114.5, 75.9, 50.4, 45.4, 42.5, 33.8, 33.5, 32.9, 31.0, 17.4, 16.1, 15.8, 14.9, 0.37; LRMS (EI) \( m/z \) 457 (M\textsuperscript{+}), 221 (100%); HRMS (EI) Calcd. C\textsubscript{28}H\textsubscript{47}NO\textsubscript{2}Si (M\textsuperscript{+}): 457.3363. Found: 457.3363.
**Hexaene (−)-30:** To a stirred solution of (−)-29 (136 mg, 298 µmol) in DCM (2 mL) were added Et₃N (1.66 mL, 11.9 mmol), Boc₂O (2.74 mL, 11.9 mmol) and DMAP (145 mg, 1.19 mmol) at room temperature. The reaction mixture was stirred at room temperature for 11 hr, then quenched with H₂O. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 50) to give (−)-30 (139 mg, 250 µmol, 91%) as a colorless oil.

(−)-30: [α]D²⁷ −42.1 (c 0.87, CHCl₃); IR (neat) 2963, 1728, 1674, 1633, 1602, 1456 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.27 (dd, J = 15.0, 10.9 Hz, 1H), 6.79 (d, J = 16.8, 10.5 Hz, 1H), 6.58 (dt, J = 16.9, 10.6 Hz, 1H), 6.21 (dd, J = 15.5, 11.1 Hz, 1H), 6.07 (dd, J = 15.2, 7.7 Hz, 1H), 5.87 (d, J = 11.1 Hz, 1H), 5.79 (dd, J = 16.9, 10.4, 6.5 Hz, 1H), 5.11 (t, J = 6.8 Hz, 1H), 5.07 (d, J = 16.9 Hz, 1H), 5.02-4.91 (m, 3H), 3.62-3.55 (m, 3H), 2.71 (s, 2H), 2.36 (m, 1H), 2.20-2.10 (m, 3H), 1.86 (m, 1H), 1.68 (s, 3H), 1.52 (s, 9H), 1.50 (s, 3H), 1.43 (m, 1H), 1.26-1.20 (m, 2H), 1.02 (d, J = 6.7 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H), 0.07 (s, 9H); ¹³C-NMR (100 MHz, CDCl₃) δ 168.9, 153.6, 146.3, 143.4, 137.2, 134.4, 133.2, 128.4, 126.9, 123.0, 122.8, 114.8, 114.2, 82.6, 75.9, 50.4, 50.2, 42.6, 33.8, 33.7, 32.3, 31.1, 28.0, 17.2, 16.2, 15.9, 14.9, 0.47; LRMS (EI) m/z 557 (M⁺), 337 (100%); HRMS (EI) Calcd. C₃₃H₅₅NO₃Si (M⁺) 557.3897. Found: 557.3908.

**Pentaene 32:** A solution of (−)-30 (60 mg, 108 µmol), p-quinone (4.7 mg, 43.1 µmol) and Grubbs first generation catalyst (31) (17.7 mg, 21.5 µmol) in DCE (108 mL) was stirred at reflux for 1 hr. The mixture was cooled down to room temperature and directly purified by silica gel column chromatography (CHCl₃) to give 32 (37 mg, 69.9 µmol, 65%, 14E : 14Z = 5 : 1) as a colorless oil.

32: IR (neat) 2958, 2926, 1725, 1677, 1368, 1251, 1145, 1078, 841 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ (14E) 7.25 (dd, J = 14.6, 11.4 Hz, 1H), 6.60 (d, J = 14.6 Hz, 1H), 6.31 (dd, J = 14.8, 11.0 Hz, 1H), 6.18 (dd, J = 15.0, 11.4 Hz, 1H), 5.87 (dd, J = 15.0, 9.2 Hz, 1H), 5.68 (d, J = 11.0 Hz, 1H), 5.41 (ddd, J = 14.8, 8.7, 5.7 Hz, 1H), 4.97 (dd, J = 7.2, 7.2 Hz, 1H), 4.03 (dd, J = 13.6, 9.6 Hz, 1H), 3.34 (dt, J = 2.0, 8.4 Hz, 1H), 3.26 (dd, J = 13.8, 5.4 Hz, 1H), 2.63 (d, J = 15.0 Hz, 1H), 2.55 (d, J = 15.0 Hz, 1H), 2.31-2.19 (m, 3H), 2.10 (m, 1H), 2.00 (m, 1H), 1.85 (m, 1H), 1.78 (s, 3H), 1.57-1.35 (m, 2H), 1.51 (s, 12H), 1.03 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H), 0.16 (s, 9H); ¹³C-NMR
(125 MHz, CDCl₃) δ 169.3, 153.7, 145.5, 143.8, 134.9, 133.5, 131.5, 128.2, 127.9, 127.0, 123.4, 120.8, 82.4, 77.1, 49.3, 48.6, 47.2, 37.8, 32.6, 31.9, 29.7, 28.1, 19.4, 17.6, 17.3, 17.0, 0.4; LRMS (EI) m/z 529 (M⁺), 429 (100%); HRMS (EI) Calcd. C₃₁H₅₅NO₄S (M⁺): 529.3585. Found: 529.3609.

**p-Bromobenzoate 33:** To a stirred solution of 32 (107 mg, 202 µmol) in MeOH (2 mL) and Et₂O (2 mL) was added 2% aqueous HCl (1.47 mL, 1.01 mmol). The reaction mixture was stirred at room temperature for 1 hr, then quenched with saturated aqueous NaHCO₃. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 6) to give the corresponding alcohol (84 mg, 184 µmol, 91%) as a colorless oil.

alcohol: IR (neat) 3457, 2961, 2927, 1724, 1672, 1368, 1146 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ (14E) 7.26 (dd, J = 15.3, 11.0 Hz; 1H), 6.65 (d, J = 15.3 Hz; 1H), 6.30 (dd, J = 15.2, 11.0 Hz; 1H), 6.22 (dd, J = 15.2, 11.0 Hz; 1H), 5.89 (dd, J = 15.2, 9.8 Hz; 1H), 5.69 (d, J = 11.0 Hz; 1H), 5.44 (ddd, J = 15.2, 8.8, 6.3 Hz; 1H), 4.96 (dd, J = 7.5, 7.0 Hz, 1H), 4.01 (dd, J = 13.3, 9.8 Hz, 1H), 3.45 (m, 1H), 3.31 (dd, J = 14.0, 5.0 Hz, 1H), 2.65 (d, J = 15.0 Hz, 1H), 2.57 (d, J = 15.0 Hz, 1H), 2.33-2.26 (m, 3H), 2.10 (m, 1H), 1.97 (m, 1H), 1.89 (m, 1H), 1.78 (s, 3H), 1.63 (m, 1H), 1.58 (s, 3H), 1.52 (s, 9H), 1.39 (m, 1H), 1.12 (d, J = 7.0 Hz, 3H), 0.90 (d, J = 6.5 Hz, 3H); ¹³C-NMR (125 MHz, CDCl₃) δ (14E) 169.3, 153.7, 144.7, 143.5, 136.2, 133.3, 131.9, 128.8, 127.5, 127.4, 123.8, 119.5, 82.5, 76.1, 48.9, 48.7, 46.4, 35.7, 32.6, 32.1, 28.3, 28.1, 18.5, 17.7, 17.5, 17.1; LRMS (EI) m/z 458 (M⁺+H), 262 (100%); HRMS (EI) Calcd. C₂₉H₄₅NO₄ (M⁺+H): 458.3268. Found: 458.3298.

To a stirred solution of alcohol (84 mg, 184 µmol) in pyridine (2 mL) was added p-BrBzCl (202 mg, 919 µmol). The reaction mixture was stirred at room temperature for 5 hr, then quenched with saturated aqueous NaHCO₃. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by flash silica gel column chromatography (AcOEt-hexane = 1 : 40) to give (14E)-ester 33 (76 mg, 119 µmol, 65%) as a colorless oil, and crude (14Z)-ester (17 mg, 26.6 µmol, <14%) as a colorless oil.

33: [α]D²⁵ −117.6 (c 0.67, CHCl₃); IR (neat) 2972, 2928, 1719, 1676, 1268, 1145, 678 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.91 (d, J = 8.4 Hz; 1H), 7.59 (d, J = 8.4 Hz; 1H), 7.30 (dd, J = 14.8,
11.2 Hz; 1H), 6.69 (d, J = 14.8 Hz; 1H), 6.33 (dd, J = 14.8, 10.9 Hz; 1H), 6.28 (dd, J = 15.0, 11.2 Hz; 1H), 5.93 (dd, J = 15.0, 9.6 Hz; 1H), 5.69 (d, J = 10.9 Hz; 1H), 5.45 (ddd, J = 14.8, 8.4, 5.4 Hz; 1H), 5.02 (dd, J = 7.2, 14.8 Hz; 1H), 4.83 (br, 1H), 4.06 (dd, J = 13.6, 9.6 Hz; 1H), 3.29 (dd, J = 13.6, 4.8 Hz; 1H), 2.65 (d, J = 15.2 Hz; 1H), 2.64 (m, 1H), 2.53 (d, J = 15.2 Hz; 1H), 2.45 (m, 1H), 2.36 (m, 1H), 1.99 (m, 1H), 1.87 (m, 1H), 1.81 (s, 3H), 1.58 (s, 3H), 1.52 (s, 9H), 1.52-1.36 (m, 2H), 1.08 (d, J = 6.4 Hz; 3H), 0.91 (d, J = 6.8 Hz; 3H); 13C-NMR (100 MHz, CDCl3) δ (14E) 169.1, 165.1, 153.7, 143.2, 136.7, 133.3, 131.7, 131.1, 129.4, 128.0, 127.7, 127.4, 124.2, 118.9, 82.5, 78.7, 49.0, 48.5, 44.0, 33.5, 32.4, 32.0, 28.1, 28.0, 18.5, 17.5, 17.4, 17.1; LRMS (EI) m/z 639 (M+), 339 (100%); HRMS (EI) Calcd. C35H46NO5Br (M+) 639.2527. Found: 639.2565.

**TMS ether (+)-25**: To a stirred solution of (14E)-33 (7.3 mg, 11.4 μmol) in DCM (1 mL) was added 2.6-lutidin (13 μL, 114 μmol) and TMSOTf (10 μL, 57.1 μmol). The reaction mixture was stirred at room temperature for 5 hr, then quenched with saturated aqueous NaHCO3. The resulting mixture was extracted twice with Et2O. The combined organic extracts were washed with brine, dried (MgSO4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 10) to give crude lactam (<5.9 mg) as a white powder.

A solution of crude lactam (<5.9 mg) and K2CO3 (45 mg, 0.326 mmol) in MeOH (1 mL) and CHCl3 (1 mL) was stirred at room temperature for 36.5 hr. The resulting mixture was concentrated and the residue was purified by silica gel column chromatography (MeOH-CHCl3 = 1 : 4) to give crude alcohol (<4.3 mg) as a white powder.

To a stirred solution of crude alcohol (<4.3 mg) in DCM (3 mL) were added Et3N (31 μL, 219 μmol), TMSCl (14 μL, 109 μmol) at room temperature. The reaction mixture was stirred at room temperature for 2 hr, then quenched with saturated aqueous NaHCO3. The resulting mixture was extracted twice with Et2O. The combined organic extracts were washed with brine, dried (MgSO4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 4) to give (+)-20 (4.3 mg, 10 μmol, 88% for 3 steps) as a white powder.

**Cyclic carbamate (−)-34**: To a stirred solution of (+)-3 (1.00 g, 7.81 mmol) in DCM (26 mL) was added benzoyl isocyanate (1.18 mL, 9.37 mmol) at room temperature. After stirring for 1 h, the reaction mixture was concentrated. The
residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 2) to give carbamate (2.14 g, 7.78 mmol, 100%) as a colorless oil.

carbamate: $[\alpha]_D^{27} +22.7$ (c 0.16, CHCl$_3$); IR (neat): 3276, 3000, 1758, 1517, 1491, 1195 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) δ 8.05 (s, 1H), 7.81 (d, $J = 7.3$ Hz, 2H), 7.59 (t, $J = 7.3$ Hz, 1H), 7.48 (t, $J = 7.6$ Hz, 2H), 5.80 (ddd, $J = 17.1$, 9.9, 7.2 Hz, 1H), 5.17 (m, 2H), 4.83 (brq, $J = 4.2$ Hz, 1H), 2.98 (m, 1H), 2.67 (dd, $J = 5.6$ Hz, 2H), 2.54 (m, 2H), 1.33 (d, $J = 5.1$, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 165.0, 150.2, 132.8, 131.9, 128.6, 127.7, 118.7, 74.7, 59.2, 52.7, 35.9, 16.9; LRMS (EI) m/z 275 (M$^+$), 105 (100%).

To a stirred solution of carbamate (429 mg, 1.56 mmol) in DCM (5 mL) was added DBU (58.3 µL, 390 µmol) at room temperature. After the reaction mixture was refluxed for 2 hr, the mixture was concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 3) to give $(-)-34$ (384 mg, 1.40 mmol, 90%) as a colorless oil.

$(-)-34$: $[\alpha]_D^{29} -19.1$ (c 2.97, CHCl$_3$); IR (neat): 3269, 2980, 1758, 1601, 1451, 1381, 1268, 1112 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) δ 8.03 (d, $J = 7.3$ Hz, 2H), 7.57 (t, $J = 7.4$ Hz, 1H), 7.45 (t, $J = 7.7$ Hz, 2H), 5.83 (ddt, $J = 17.1$, 10.2, 6.6 Hz, 1H), 5.64 (s, 1H), 5.29 (dt, $J = 6.1$, 6.1 Hz, 1H), 5.25 (m, 2H), 4.76 (m, 1H), 4.09 (t, $J = 6.7$ Hz, 1H), 2.58 (m, 1H), 2.46 (m, 1H), 1.43 (d, $J = 6.4$ Hz, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 165.1, 159.6, 133.2, 132.2, 129.5, 128.4, 118.5, 78.7, 69.4, 58.4, 33.5, 16.4; LRMS (EI) m/z 276 (M$^+$+H), 105 (100%); HRMS (EI) Calcd. C$_{15}$H$_{18}$NO$_4$ (M$^+$+H): 276.1236. Found: 276.1222.

**Tetrahydropyran (+)-35:** To a stirred solution of NaH (60% in mineral oil, 69.8 mg, 2.91 mmol), which was washed by hexane (1 mL) twice, in THF (2 mL) was added $(-)-34$ (668 mg, 2.43 mmol), which was used after azeotropic removal of water, in THF (2 mL) via cannula at room temperature. After the reaction mixture was stirred for 30 min, Mel (227 µL, 3.65 mmol) was added to the mixture dropwise and the mixture was stirred for another 3 hr. After the reaction completed, saturated aqueous NH$_4$Cl was added to the reaction mixture. The resulting mixture was concentrated in vacuo, and extracted twice with AcOEt. The combined organic extracts were washed with brine, dried (MgSO$_4$), and concentrated. The residue was purified by silica gel column chromatography (EtO$_2$O-hexane = 2 : 1) to give methylated cyclic carbamate (665 mg, 2.30 mmol, 95%) as a colorless oil.
methylated cyclic carbamate: [α]D^29 +24.4 (c 0.40, CHCl3); IR (neat): 2980, 2360, 1759, 1719, 1434, 1401, 1274 cm^-1; ¹H-NMR (400 MHz, CDCl3) δ 8.01 (d, J = 8.5 Hz, 2H), 7.61 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 7.9 Hz, 2H), 5.90 (ddt, J = 17.1, 10.4, 6.6 Hz, 1H), 5.47 (dq, J = 6.5, 1.4 Hz, 1H), 5.26 (m, 2H), 4.63 (dt, J = 8.2, 7.2 Hz, 1H), 3.92 (dd, J = 7.7, 1.4 Hz, 1H), 3.08 (s, 3H), 2.61 (m, 2H), 1.42 (d, J = 6.5 Hz, 3H); ¹³C-NMR (100 MHz, CDCl3) δ 165.5, 158.0, 133.5, 132.1, 129.6, 128.6, 119.0, 76.0, 70.2, 62.7, 33.5, 31.3, 15.2; LRMS (EI) m/z: 290 (M^+H), 140 (100%); HRMS (El) Calcd. C_{16}H_{39}NO_4 (M^+H): 290.1392. Found: 290.1372.

To a stirred solution of methylated cyclic carbamate (600 mg, 2.08 mmol) in MeOH (7 mL) was added NaOMe (56.2 mg, 1.04 mmol) at room temperature. The reaction mixture was stirred at the same temperature for 1 hr and then quenched by an addition of saturated aqueous NH_4Cl. The mixture was extracted twice with AcOEt. The combined organic extracts were washed with water and brine, dried (MgSO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt) to give alcohol (329 mg, 1.78 mmol, 90%) as a colorless oil.

alcohol: [α]D^33 +4.16 (c 0.89, CHCl3); IR (neat): 3336, 1721, 1409, 1144 cm^-1; ¹H-NMR (400 MHz, CDCl3) δ 5.82 (ddtt, J = 17.4, 10.4, 6.6 Hz, 1H), 5.17 (m, 2H), 4.57 (dt, J = 5.7, 8.4 Hz, 1H), 4.14 (m, 1H), 3.71 (dd, J = 7.7, 2.7 Hz, 1H), 3.02 (s, 3H), 2.52 (m, 2H), 1.28 (d, J = 6.3 Hz, 3H); ¹³C-NMR (100 MHz, CDCl3) δ 158.6, 132.8, 129.0, 128.2, 125.2, 118.3, 66.7, 64.6, 33.4, 31.5, 18.7; LRMS (El) m/z 185 (M^+), 140 (100%); HRMS (El) Calcd. C_{16}H_{39}NO_4 (M^+): 185.1052. Found: 185.1053.

O_3 gas was bubbled through a cooled (−20 °C) solution of alcohol (637 mg, 3.44 mmol) in MeOH (8.6 mL) for 15 min. N_2 gas was then bubbled through the mixture for 15 min at the same temperature. To the reaction mixture were added Me_3S and p-TsOH•H_2O, and the mixture was refluxed. After the reaction completed, the reaction mixture was allowed to cool to room temperature and concentrated. The residue was extracted twice with AcOEt. The combined organic extracts were washed with water and brine, dried (MgSO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt) to give (+)-35 (616 mg, 3.06 mmol, 89%, α : β = 1 : 1) as a colorless oil.

(+)-35: [α]D^31 +38.5 (c 0.13, CHCl3); IR (neat): 2937, 1755, 1430, 1395 cm^-1; ¹H-NMR (400 MHz, CDCl3) δ 4.75 (t, J = 6.3 Hz, 1H), 4.72 (m, 1H), 4.64 (dd, J = 8.2, 2.7 Hz, 1H), 4.57 (dddd, J = 9.7, 8.5, 5.6 Hz, 1H), 3.92 (dddd, J = 12.3, 8.7, 6.3 Hz, 1H), 3.68 (dddd, J = 12.6, 8.2, 6.3 Hz, 1H), 3.47 (s, 3H), 4.41 (t, J = 8.6 Hz, 1H), 3.72 (s, 3H), 3.25 (dd, J = 8.2, 6.8 Hz, 1H), 2.96 (s, 3H), 2.90 (s, 3H), 2.34-2.27 (m, 2H), 1.97-1.89 (m, 2H), 1.41 (d, J = 6.3 Hz, 3H), 1.38 (d, J = 6.3 Hz, 3H); ¹³C-NMR (100 MHz, CDCl3) δ 158.3, 157.8, 98.9, 96.6, 72.6, 71.1, 69.6, 65.2, 61.7, 60.3, 56.1, 55.0, 31.8,
Glycosyl fluoride (+)-36: To a stirred solution of (+)-35 (74.5 mg, 370 \( \mu \)mol) and phenyl trimethylsilyl sulfide (350 \( \mu \)L, 1.86 mmol) in DCM (1.2 mL) was added trimethylsilyl trifluoromethanesulfonate (110 \( \mu \)L, 614 \( \mu \)mol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 30 min. The mixture was quenched with saturated aqueous NaHCO\(_3\) and extracted twice with AcOEt. The combined organic extracts were washed with brine, dried (MgSO\(_4\)), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 2 : 1) to give thioglycoside (93.7 mg, 336 \( \mu \)mol, 91%) as a colorless oil.

Thioglycoside: \([\alpha]_D^{27} +114\) (c 1.87, CHCl\(_3\)); IR (neat): 3487, 2934, 1768, 1583 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.47 (m, 4H), 7.33-7.24 (m, 6H), 5.46 (dd, \(J = 8.3, 6.6\) Hz, 1H), 4.95 (dd, \(J = 12.0, 2.4\) Hz, 1H), 4.64 (m, 2H), 4.19 (dq, \(J = 8.5, 6.2\) Hz, 1H), 3.60 (dq, \(J = 8.8, 6.1\) Hz, 1H), 3.47 (t, \(J = 8.4\) Hz, 1H), 3.20 (dd, \(J = 8.8, 6.3\) Hz, 1H), 2.93 (s, 3H), 2.91 (s, 3H), 2.54-2.44 (m, 2H), 2.12-1.98 (m, 2H), 1.42 (d, \(J = 6.3\) Hz, 3H), 1.38 (d, \(J = 6.1\) Hz, 3H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.9, 157.5, 134.3, 133.0, 131.4, 128.8, 128.7, 127.5, 127.3, 80.9, 80.0, 74.9, 72.8, 70.0, 66.2, 61.8, 59.6, 32.2, 31.3, 31.1, 31.0, 21.2, 20.5; LRMS (EI) \(m/z\) 279 (M\(^+\)), 170 (100%); HRMS (EI) Calcd. C\(_{14}\)H\(_{17}\)NO\(_3\)S (M\(^+\)) : 279.0929. Found : 279.0910.

To a stirred solution of thioglycoside (32.7 mg, 117 \(\mu\)mol) in DCM (1.2 mL) were added NBS (46.0 mg, 258 \(\mu\)mol) and DAST (100 \(\mu\)L, 756 \(\mu\)mol) at \(-15\) °C. The reaction mixture was stirred for 1 hr. After the reaction was quenched with saturated aqueous NaHCO\(_3\), the mixture was allowed to warm to room temperature, and then extracted twice with AcOEt. The combined organic extracts were washed with brine, dried (Na\(_2\)SO\(_4\)), and concentrated. The residue was purified by amine silica gel column chromatography (NH-silica gel, AcOEt-hexane = 2 : 3) to give (+)-36 (15.8 mg, 83.6 \(\mu\)mol, 71%), \(\alpha : \beta = 1 : 1\) as a colorless oil.
\[ J = 6.3 \text{ Hz}, 3\text{H}; \] \text{LRMS (El) } m/z 189 (M^+), 99 (100\%); \text{HRMS (El) Calcd. } C_{8}H_{11}NO_{3}F (M^+\text{-H}): 188.0723. \text{ Found: 188.0719.}

**Fmoc carbamate 39:** A solution of (+)-35 (69 mg, 343 \( \mu \)mol) and 30\% aqueous NaOH (0.7 mL, 5.25 mmol) in MeOH (1 mL) was stirred at reflux for 20 min. After the reaction mixture was cooled to room temperature and neutralized with 10\% aqueous HCl, the mixture was concentrated and added H\(_2\)O (3.5 mL) and THF (7.5 mL). To the resulting mixture was added K\(_2\)CO\(_3\) at 0 \( ^\circ \)C, the reaction mixture was stirred at the same temperature for 30 min. After FmocCl (264 mg, 1.02 mmol) was added to the reaction mixture, the mixture was warmed to room temperature and extracted twice with Et\(_2\)O. The combined organic extracts were washed with brine, dried (MgSO\(_4\)), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 1) to give 39 (118 mg, 297 \( \mu \)mol, 87\%) as a colorless oil.

39: IR (neat): 3448, 2932, 1750, 1698, 1450, 1312, 1125 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.78-7.30 (m, 8H), 4.84 (d, \( J = 9.7 \text{ Hz}, 1\text{H} \)), 4.81 (d, \( J = 2.9 \text{ Hz}, 1\text{H} \)), 4.73 (d, \( J = 3.1 \text{ Hz}, 1\text{H} \)), 4.57 (dq, \( J = 19.1, 5.2 \text{ Hz}, 2\text{H} \)), 4.44 (d, \( J = 1.2 \text{ Hz}, 2\text{H} \)), 4.42 (s, 1H), 4.26 (t, \( J = 7.0 \text{ Hz}, 1\text{H} \)), 4.23 (t, \( J = 5.0 \text{ Hz}, 1\text{H} \)), 4.09 (m, 1H), 3.91 (d, \( J = 10.6 \text{ Hz}, 1\text{H} \)), 3.60 (d, \( J = 9.5 \text{ Hz}, 1\text{H} \)), 3.52 (d, \( J = 9.7 \text{ Hz}, 1\text{H} \)), 3.41 (s, 3H), 3.37 (s, 3H), 3.26 (brd, \( J = 10.5, 1\text{H} \)), 3.00 (s, 3H), 2.91 (s, 3H), 2.05 (dd, \( J = 14.4, 1.9 \text{ Hz}, 1\text{H} \)), 1.99 (dt, \( J = 14.2, 3.3\text{Hz}, 1\text{H} \)), 1.90 (dd, \( J = 14.0, 2.8 \text{ Hz}, 1\text{H} \)), 1.61 (dt, \( J = 6.8, 3.4 \text{ Hz}, 1\text{H} \)), 1.22 (d, \( J = 6.1 \text{ Hz}, 3\text{H} \)), 1.18 (d, \( J = 6.3 \text{ Hz}, 3\text{H} \)), 1.03 (d, \( J = 6.0 \text{ Hz}, 3\text{H} \)); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \( \delta \) 143.9, 141.3, 128.9, 128.1, 127.6, 127.0, 125.2, 125.0, 124.5, 119.8, 98.9, 69.1, 67.5, 60.7, 55.3, 47.4, 36.6, 36.4, 18.2; LRMS (El) m/z 397 (M\(^+\)), 178 (100\%); HRMS (El) Calcd. C\(_{23}\)H\(_{27}\)NO\(_3\) (M\(^+\)): 397.1889. Found: 397.1903.

**Diacetate 37:** After a solution of 39 (320 mg, 806 \( \mu \)mol) in AcOH (20 mL) and H\(_2\)O (4 mL) was stirred at 95 \( ^\circ \)C for 30 min, the reaction mixture was concentrated and added pyridine (8 mL) and DMAP (158 mg, 1.29 mmol). The mixture was added AcCl (1.22 mL, 12.9 mmol) at 0 \( ^\circ \)C and then the resulting mixture was warmed to room temperature and stirred for 1 hr. The reaction mixture was added water at 0 \( ^\circ \)C and extracted with AcOEt. The combined organic extracts were washed with brine, dried (MgSO\(_4\)), and
concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 1) to give 37 (397 mg, 765 µmol, 95%) as a colorless oil.

37: $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 169.2, 166.2, 144.0, 141.4, 127.8, 127.1, 124.9, 124.5, 119.9, 91.6, 90.3, 79.4, 76.7, 68.8, 67.5, 67.1, 54.1, 47.4, 35.2, 34.9, 32.7, 32.4, 21.3, 21.2, 18.5, 18.2; LRMS (EI) m/z 467 (M$^+$), 178 (100%); HRMS (EI) Calcd. C$_{26}$H$_{29}$NO$_7$ (M$^+$): 467.1944. Found: 467.1933.

TIPS ether (+)-38: To a stirred solution of 39 (69.6 mg, 175 µmol) in pyridine (1 mL) was added TIPSOTf (141 µL, 526 µmol) at room temperature. The reaction mixture was stirred at room temperature overnight and quenched with saturated aqueous NaHCO$_3$. The resulting mixture was extracted twice with Et$_2$O. The combined organic extracts were washed with brine, dried (MgSO$_4$), and concentrated. This material was used without further purification. A solution of crude TIPS ether in AcOH (5 mL) and H$_2$O (1 mL) was stirred at 90 °C for 2 hr. The reaction mixture was concentrated and the residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 2) to give hemiacetal (76 mg, 141 µmol, 80% for 2 steps) (α : β = 1 : 1) as a colorless amorphous.

hemiacetal: [α]$_D^{20}$ +61.5 (c 1.04, CHCl$_3$); IR (neat): 3403, 2944, 2866, 1688, 1678, 1450, 1159, 1083, 739 cm$^{-1}$; $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 157.0, 156.1, 144.2, 144.1, 144.0, 141.5, 141.3, 127.8, 127.7, 127.65, 127.60, 127.1, 127.01, 127.00, 125.01, 125.00, 124.9, 124.8, 124.4, 124.3, 124.2, 120.2, 120.0, 119.9, 119.85, 119.81, 119.74, 119.71, 92.2, 92.1, 91.9, 91.8, 67.9, 67.6, 66.6, 66.4, 62.5, 62.4, 59.84, 59.77, 59.54, 59.47, 47.4, 37.0, 36.7, 36.5, 31.8, 31.64, 31.61, 31.4, 18.9, 18.5, 18.1, 18.0, 17.89, 17.86, 17.80, 12.93, 12.89, 12.7, 12.6; LRMS (FAB) m/z 540 (M$^+$+H), 179 (100%); HRMS (FAB) Calcd. C$_{31}$H$_{46}$NO$_5$Si (M$^+$+H): 540.3142. Found: 540.3130.

To a stirred solution of hemiacetal (40 mg, 74.2 µmol) in DCM (2 mL) was added DAST (15 µL, 110 µmol) at 0 °C. The reaction mixture was stirred at that temperature for 5 min and quenched with saturated aqueous NaHCO$_3$. The resulting mixture was extracted twice with Et$_2$O. The combined organic extracts were washed with brine, dried (MgSO$_4$), and concentrated. The residue was purified by NH-silica gel column chromatography (AcOEt-hexane = 1 : 8) to give (+)-38 (40 mg, 73.9 µmol, 100%) (α : β = 1 : 1) as a colorless oil.
(+)-38: \([\alpha]_D^{29} +75.6\ (c\ 0.80,\ CHCl_3)\); IR (neat): 2944, 2866, 1700, 1318, 1155, 1108, 1074, 741 cm\(^{-1}\); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 156.9, 156.8, 156.2, 155.9, 144.1, 144.02, 143.99, 143.94, 143.91, 143.85, 141.44, 141.40, 141.27, 141.25, 141.24, 127.64, 127.59, 127.56, 127.53, 127.1, 127.03, 127.01, 126.97, 126.94, 126.92, 124.95, 124.91, 124.78, 124.72, 124.33, 124.25, 124.23, 124.15, 119.93, 119.91, 119.89, 119.84, 119.80, 119.7, 106.6, 106.3, 104.3, 104.0, 71.2, 70.4, 70.3, 67.6, 67.5, 67.0, 66.8, 66.7, 66.4, 60.3, 60.0, 59.9, 59.7, 47.31, 47.27, 47.22, 41.1, 40.7, 36.9, 36.5, 31.57, 31.52, 31.46, 31.3, 18.92, 18.90, 18.82, 18.81, 18.1, 17.98, 17.97, 17.93, 17.92, 17.87, 17.83, 12.9, 12.68, 12.67, 12.4; LRMS (FAB) m/z 542 (M\(^{+}\)+H), 179 (100%); HRMS (FAB) Calcd. C\(_{31}\)H\(_{45}\)NO\(_4\)FSi (M\(^{+}\)+H): 542.3099. Found: 542.3102.

**Synthesis of vicenistatin (1) and \(\alpha\)-vicenistatin (40) from 36 and (+)-25:** A solution of 36 (9.3 mg, 49.0 \(\mu\)mol), (+)-25 (4.2 mg, 9.79 \(\mu\)mol) and activated MS4Å (50 mg) in DCM (1 mL) was stirred at room temperature for 30 min. To the mixture was added TMSOTf (0.294 M in DCM, 100 \(\mu\)L, 29.4 \(\mu\)mol) at \(-78^\circ\)C. After the reaction mixture was warmed to 0 \(^\circ\)C, saturated aqueous NaHCO\(_3\) was added to the mixture. The resulting mixture was allowed to warm to room temperature over 20 min, and then extracted twice with CHCl\(_3\). The combined organic extracts were dried (MgSO\(_4\)), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 2 : 1) to give protected vicenistatin (2.8 mg). A solution of protected vicenistatin (2.8 mg) in 5.0 M aqueous KOH (2 mL) and MeOH (3 mL) was stirred at room temperature for 1 week. After the reaction mixture was neutralized with 10% aqueous HCl, the mixture was concentrated. The residue was purified by silica gel column chromatography (MeOH-CHCl\(_3\)= 1 : 9) to give 1 (0.5 mg, 1.0 \(\mu\)mol 10% for 2 steps) as a white powder and 40 (0.9 mg, 1.8 \(\mu\)mol 18% for 2 steps) as a white powder.

1: [\(\alpha\]_D\(^{26}\) \(-1.2\ (c\ 0.06,\ MeOH),\ lit.\]^1 \[\alpha\]_D\(^{22}\) \(-3\ (c\ 0.1,\ MeOH);\ IR (neat): 3294, 2923, 1655, 1625, 1459, 1377, 1158, 1098, 993 cm\(^{-1}\); \(^1\)H-NMR (500 MHz, pyridine-\(d_5\)) \(\delta\) 8.52 (brd, 1H), 7.59 (dd, \(J = 14.7, 11.0\) Hz, 1H), 6.79 (dd, \(J = 14.7, 11.5\) Hz, 1H), 6.24 (d, \(J = 15.1\) Hz, 1H), 6.21 (dd, \(J = 15.1, 11.0\) Hz, 1H), 5.95 (d, \(J = 10.5\) Hz, 1H), 5.86 (dd, \(J = 14.7, 10.1\) Hz, 1H), 5.69 (dd, \(J = 14.2, 9.2, 5.0\) Hz, 1H), 5.29 (dd, \(J = 9.5, 3.0\) Hz, 1H), 5.21 (t, \(J = 7.5\) Hz, 1H), 4.38 (m, 1H), 4.00 (m, 2H), 3.37 (m, 1H), 3.05 (m, 1H), 2.74 (d, \(J = 15.1\) Hz, 1H), 2.62 (d, \(J = 15.1\) Hz, 1H), 2.43 (s, 3H), 2.23 (dd, \(J = 9.5, 3.0\) Hz, 1H), 1.94 (s, 3H), 1.90 (m, 1H), 1.69 (s, 3H), 1.51 (d, \(J = 6.4\) Hz, 3H), 1.08 (d, \(J = 6.4\) Hz, 3H), 0.83 (d, \(J = 6.9\) Hz, 3H); \(^{13}\)C-NMR (150 MHz, pyridine-\(d_5\)) \(\delta\) 166.1, 143.1, 140.1, 133.8,
filtrate was concentrated then concentrated. To the residue was added TBAF (1.0 M in THF, 73 µL) as a white powder. The reaction mixture was stirred at that temperature for 2 hr, then quenched with saturated aqueous NaHCO₃. The resulting mixture was extracted twice with AcOEt. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. This material was used without further purification. To a stirred solution of crude glycosyl adduct in THF (2 mL) was added TBAF (1.0 M in THF, 73 µL, 73 µmol) at room temperature. After the reaction mixture was stirred at that temperature for 2 hr, directly purified by silica gel column chromatography (MeOH-CHCl₃ = 1 : 20) to give 1 (1.5 mg, 3.0 µmol 12% for 2 steps) as a white powder and 40 (2.3 mg, 4.6 µmol 19% for 2 steps) as a white powder.

**Synthesis of vicenistatin (1) and α-vicenistatin (40) from 38 and (+)-25**: To a stirred solution of (+)-25 (10.5 mg, 24.5 µmol), 38 (40 mg, 73.9 µmol) in DCM (1 mL) was added TMSOTf (8.9 µL, 49 µmol) at −40 °C. The reaction mixture was stirred at that temperature for 2.5 hr, then quenched with saturated aqueous NaHCO₃. The resulting mixture was extracted twice with AcOEt. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. This material was used without further purification. To a stirred solution of crude glycosyl adduct in THF (2 mL) was added TBAF (1.0 M in THF, 73 µL, 73 µmol) at room temperature. After the reaction mixture was stirred at that temperature for 2 hr, directly purified by silica gel column chromatography (MeOH-CHCl₃ = 1 : 20) to give 1 (1.5 mg, 3.0 µmol 12% for 2 steps) as a white powder and 40 (2.3 mg, 4.6 µmol 19% for 2 steps) as a white powder.

**Homoallyl alcohol (−)-43**: To a stirred solution of 6 (2.15 g, 8.08 mmol) in DCM (40 mL) was added Dess-Martin periodinane (4.10 g, 9.70 mmol) at room temperature. The reaction mixture was stirred at room temperature for 1.5 hr and then concentrated. To the residue was added hexane and the mixture was filtered through Celite. The filtrate was concentrated in vacuo to give crude aldehyde (2.10 g, <7.95 mmol) as pale yellow oil.
This material was used without further purification. To a stirred solution of (+)-Ipc₂BOMe (3.80 g, 11.9 mmol) in Et₂O (24 mL) was added allylmagnesium bromide (1.0 M in Et₂O, 11.9 mL, 11.9 mmol) at −78 °C. The mixture was stirred to room temperature for 40 min. And crude aldehyde (2.10 g, <7.95 mmol) prepared above was added to the mixture via a syringe at −78 °C. The resulting mixture was slowly warmed to 0 °C, then cooled again to −78 °C. After MeOH (4.6 mL), saturated aqueous NaHCO₃ (46 mL), and 30% aqueous H₂O₂ (23 mL) were added, the resulting mixture was stirred at room temperature overnight. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by flash chromatography (AcOEt–hexane = 1 : 20) to give (−)-43 (1.88 g, 6.14 mmol, 76% for 2 steps, 100 % de, 92% ee) as pale yellow oil.

(−)-43: [α]D²⁰ = −5.8 (c 1.4, CHCl₃); IR (neat): 3389, 2977, 2911, 1434, 1267, 1138, 1042, 915 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 5.94 (s, 1H), 5.83 (ddt, J = 16.4, 11.3, 7.2 Hz, 1H), 5.27 (t, J = 6.1 Hz, 1H), 5.14 (dd, J = 16.4, 1.3 Hz, 1H), 5.13 (dd, J = 11.3, 1.3 Hz, 1H), 3.68 (m, 1H), 2.88 (s, 2H), 2.31 (ddd, J = 13.9, 4.9, 4.6 Hz, 1H), 2.23 (dd, J = 7.1, 6.6 Hz, 1H), 2.16 (dd, J = 13.9, 7.7 Hz, 1H), 1.76 (s, 3H), 1.72 (br, 1H), 1.55 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 145.9, 134.8, 134.6, 123.0, 118.0, 76.1, 70.6, 50.0, 41.4, 35.6, 23.3, 15.8; LRMS (EI) m/z 306 (M⁺), 109 (100%); HRMS (EI) Calcd. C₁₂H₁₉OI (M⁺): 306.0481. Found: 306.0465.

Optical purity of (−)-43 was determined by chiral HPLC analysis (HPLC conditions: column; CHIRALCEL OD-H, eluent; hexane-i-PrOH = 199 : 1, flow rate; 0.5 mL/min, detection; UV 254 nm, retention time; 27.3 min for (−)-43 and 50.1 min for (+)-43).

Enal (+)-44: To a stirred solution of (−)-43 (838 mg, 2.74 mmol) in DCM (13 mL) were added acrolein (1.83 mL, 27.4 mmol) and Hoveyda-Grubbs second generation catalyst 13 (34 mg, 54.8 µmol) at room temperature. The reaction mixture was stirred at room temperature for 3 hr and then concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 4) to give enal (+)-44 (799 mg, 2.30 mmol, 84%) as a pale yellow oil.

(+)-44: [α]D²⁰ = +2.3 (c 0.82, CHCl₃); IR (neat): 3434, 2910, 1687, 1432, 1268, 1136, 1054, 975 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 9.53 (d, J = 7.9 Hz, 1H), 6.93 (dt, J = 15.6, 7.2 Hz, 1H), 6.19 (dd, J = 15.6, 7.9 Hz, 1H), 5.95 (s, 1H), 5.25 (t, J = 7.3 Hz, 1H), 3.86 (m, 1H), 2.89 (s, 2H), 2.55 (m, 1H), 2.47 (ddd, J = 14.7, 7.2, 1.2 Hz, 1H), 2.28 (dd, J = 7.6, 7.0 Hz, 1H), 1.77 (s, 3H), 1.57 (s, 3H);
$^{13}$C-NMR (100 MHz, CDCl$_3$) δ 193.9, 154.7, 145.8, 136.4, 135.1, 122.2, 76.7, 70.5, 50.2, 40.2, 36.5, 23.7, 16.2; LRMS (FAB) m/z 335 (M$^+$+H), 153 (100%); HRMS (FAB) Calcd. C$_{13}$H$_{20}$O$_2$I (M$^+$+H): 335.0508. Found: 335.0526.

**TMS ether (+)-41:** A solution of (+)-44 (895 mg, 2.20 mmol), tributyl(vinyl)tin (1.58 mL, 5.40 mmol) and Ph$_3$P (284 mg, 1.08 mmol) in THF (44 mL) was degaerated, then added Pd$_2$(dba)$_3$·CHCl$_3$ (280 mg, 270 µmol) at room temperature. The reaction mixture was stirred at that temperature for 1 hr and quenched with saturated aqueous NaHCO$_3$. The resulting mixture was extracted twice with Et$_2$O. The combined organic extracts were washed with brine, dried (MgSO$_4$), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 4) to give tetratriene (518 mg, 2.21 mmol) as a colorless oil.

To a stirred solution of crude tetratriene in DCM (19 mL) were added 2,6-lutidine (1.29 mL, 11.1 mmol) and TMSCl (700 µL, 5.54 mmol) at room temperature. The reaction mixture was stirred at room temperature for 4 hr, then quenched with saturated aqueous NaHCO$_3$. The resulting mixture was extracted twice with Et$_2$O. The combined organic extracts were washed with brine, dried (MgSO$_4$), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 10) to give (+)-41 (481 mg, 1.57 mmol, 85% for 2 steps) as a colorless oil.

(+)-41: [α]$_D^{23}$+1.25 (c 1.50, CHCl$_3$); IR (neat) 3357, 3434, 2912, 1687 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) δ 6.94 (dt, $J$ = 15.6, 7.2 Hz, 1H), 6.57 (ddd, $J$ = 16.8, 10.6, 10.6 Hz, 1H), 6.19 (ddt, $J$ = 8.0, 15.6, 1.4 Hz, 1H), 5.88 (d, $J$ = 10.8 Hz, 1H), 5.23 (dt, $J$ = 1.6, 7.4 Hz, 1H), 5.12 (dd, $J$ = 16.8, 1.6 Hz, 1H), 5.02 (d, $J$ = 10.0 Hz, 1H), 3.86 (m, 1H), 2.75 (s, 1H), 2.46-2.60 (m, 2H), 2.29 (m, 2H), 1.68 (s, 3H), 1.58 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 193.7, 154.6, 137.5, 136.7, 134.7, 133.1, 121.1, 115.3, 70.3, 50.4, 39.8, 36.2, 16.2, 16.1; LRMS (EI) m/z 216 (M$^+$-H$_2$O), 107 (100%); HRMS (EI) Calcd. C$_{15}$H$_{20}$O (M$^+$-H$_2$O): 216.1514. Found: 216.1502.

**Phosphonate 42:** To a stirred solution of 5-hexen-1-ol (45) (1.50 g, 15 mmol), Ph$_3$P (5.90 g, 22.5 mmol) and phthalimide (3.31 g, 22.5 mmol) in THF (60 mL) was added DIAD (4.43 mL, 22.5 mmol) at –20 °C. Then, the mixture was stirred at that temperature for 10 min and concentrated. The residue was purified by silica gel.
column chromatography (AcOEt-hexane = 1 : 4) to give phthalimide (3.45 g, 15 mmol, 100%) as a colorless oil.

phthalimide: IR (neat) 3075, 2937, 2860, 1772, 1714, 1437, 1396, 1370 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.84 (dd, J = 5.3, 3.1 Hz, 2H), 7.71 (dd, J = 5.3, 3.1 Hz, 2H), 5.78 (ddt, J = 16.9, 10.1, 6.8 Hz, 1H), 5.00 (d, J = 16.9 Hz, 1H), 4.95 (d, J = 10.1 Hz, 1H), 3.69 (t, J = 7.2 Hz, 2H), 2.10 (dt, J = 6.8, 7.1 Hz, 2H), 1.70 (m, 2H), 1.46 (m, 2H); ¹³C-NMR (100 MHz, CDCl₃) δ 168.4, 138.2, 133.8, 132.1, 123.1, 114.8, 37.8, 33.2, 28.0, 26.1; LRMS (EI) m/z 229 (M⁺), 160 (100%); HRMS (EI) Calcd. C₁₄H₁₅NO₂ (M⁺): 229.1103. Found: 229.1083.

A solution of phthalimide (571 mg, 2.49 mmol) and 80% hydrazine (3.63 mL, 12.5 mmol) in EtOH (12 mL) was stirred at reflux for 2 hr and filtered through Celite. The filtrate was added 10% aqueous HCl and stirred at room temperature for 1 hr. The mixture was concentrated and freeze-dried to give crude amine hydrochloride salt. To a stirred solution of crude amine hydrochloride salt and diethylphosphonoacetic acid (21) (1.95 g, 9.96 mmol) in DCM (24 mL) were added EDCI (1.91 g, 9.96 mmol) and HOBt (1.35 g, 9.96 mmol) at room temperature and the mixture was stirred at that temperature for 5 min. The solution was added triethylamine (4.16 mL, 29.9 mmol) and stirred for 15 hr, then quenched with H₂O. The resulting mixture was extracted twice with DCM. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt) to give 42 (635 mg, 2.29 mmol, 92% for 2 steps) as a colorless oil.

42: IR (neat) 3292, 2930, 1655, 1559 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 6.88 (brs, 1H), 5.77 (ddt, J = 16.9, 10.1, 6.8 Hz, 1H), 5.00 (dd, J = 16.9, 1.5 Hz, 1H), 4.95 (dd, J = 10.1, 1.5 Hz, 1H), 4.14 (quint., J = 7.3 Hz, 4H), 3.27 (dd, J = 12.6, 6.8 Hz, 2H), 2.84 (d, J = 20.5 Hz, 2H), 2.07 (dt, J = 7.0, 7.0 Hz, 2H), 1.53 (m, 2H), 1.44 (m, 2H), 1.34 (t, J = 7.1 Hz, 6H); ¹³C-NMR (100 MHz, CDCl₃) δ 163.8, 138.3, 114.7, 62.6, 39.6, 35.6, 34.2, 33.2, 28.7, 25.9, 16.3; LRMS (EI) m/z 277 (M⁺), 179 (100%); HRMS (EI) Calcd. C₁₂H₂₄NO₄P (M⁺): 277.1443. Found: 277.1440.

Hexaene (−)-46: To a stirred solution of (−)-27 (133 mg, 457 µmol) in THF (2 mL) were added KHMDS (0.5 M in toluene, 841 µL, 421 µmol), and (+)-41 (117 mg, 381 µmol) in THF (1.5 mL) at −78 °C. The reaction mixture was warmed up to 0 °C over 20 min, then quenched with saturated aqueous NH₄Cl. The resulting mixture was extracted twice with Et₂O. The
combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 10) to give (−)-46 (118 mg, 266 µmol, 70%) as a colorless oil.

(−)-46: [α]D₂⁰⁻2.1 (c 0.43, CHCl₃); IR (neat): 3282, 2957, 2916, 1658, 1631, 1615, 1552, 1251, 998, 841 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.20 (dd, J = 14.6, 10.5 Hz, 1H), 6.58 (ddd, J = 17.0, 10.8, 10.5 Hz, 1H), 6.15 (dd, J = 15.3, 10.5 Hz, 1H), 6.06 (dt, J = 15.3, 6.9 Hz, 1H), 5.87 (d, J = 10.8 Hz, 1H), 5.80 (m, 1H), 5.76 (d, J = 14.6 Hz, 1H), 5.49 (brt, J = 5.8, 1H), 5.20 (t, J = 7.2 Hz, 1H), 5.11 (d, J = 17.0 Hz, 1H), 5.02 (d, J = 17.2 Hz, 1H), 5.01 (d, J = 10.5 Hz, 1H), 4.95 (d, J = 10.0 Hz, 1H), 3.73 (tt, J = 6.4, 5.6 Hz, 1H), 3.29 (ddd, J = 13.4, 6.8, 6.0 Hz, 1H), 3.16 (ddd, J = 13.4, 6.8, 6.0 Hz, 1H), 2.72 (s, 2H), 2.34-2.02 (m, 4H), 2.19 (dd, J = 6.9, 6.8 Hz, 2H), 1.68 (s, 3H), 1.52 (s, 3H), 1.46 (m, 1H), 1.25 (m, 1H), 0.92 (d, J = 6.8 Hz, 3H), 0.09 (s, 9H); ¹³C-NMR (100 MHz, CDCl₃) δ 166.3, 140.7, 139.1, 138.5, 137.3, 134.9, 133.2, 130.4, 127.0, 122.5, 122.3, 114.9, 114.5, 72.1, 50.3, 45.4, 40.6, 36.2, 33.5, 32.8, 31.0, 17.4, 16.1, 15.8, 0.3; LRMS (EI) m/z 443 (M⁺), 308 (100%); HRMS (EI) Calcd. C₂₅H₄₈NO₂Si (M⁺): 443.3217. Found: 443.3216.

Tetraene (−)-47: To a stirred solution of 42 (209 mg, 754 µmol) in THF (4 mL) were added KHMDS (0.5 M in toluene, 1.38 mL, 691 µmol), and (−)-26 (201 mg, 628 µmol) in THF (2 mL) at −78 °C. The reaction was warmed up to 0 °C over 20 min, then quenched with saturated NH₄Cl eq. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 50) to give (−)-47 (205 mg, 463 µmol, 74%) as a colorless oil.

(−)-47: [α]D₂⁰⁻44.8 (c 1.08, CHCl₃); IR (neat): 3279, 2958, 2929, 1656, 1628, 1614, 1555, 1251, 999, 840 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.18 (dd, J = 14.5, 10.2 Hz, 1H), 6.58 (ddd, J = 16.8, 10.8, 10.4 Hz, 1H), 6.10 (dd, J = 14.5, 10.2 Hz, 1H), 6.01 (dd, J = 14.5, 7.8 Hz, 1H), 5.87 (d, J = 10.8 Hz, 1H), 5.79 (ddt, J = 17.2, 10.0, 7.0 Hz, 1H), 5.74 (d, J = 14.5 Hz, 1H), 5.45 (brt, J = 4.6 Hz, 1H), 5.21 (t, J = 7.2 Hz, 1H), 5.11 (d, J = 16.8 Hz, 1H), 5.03-4.99 (m, 2H), 4.96 (d, J = 10.0 Hz, 1H), 3.57 (dt, J = 5.6, 5.8 Hz, 2H), 3.33 (dt, J = 6.4, 6.6 Hz, 1H), 2.71 (s, 2H), 2.34 (m, 1H), 2.22-2.12 (m, 2H), 2.08 (dt, J = 7.0, 7.0 Hz, 2H), 1.68 (s, 3H), 1.59-1.53 (m, 2H), 1.50 (s, 3H), 1.47-1.40 (m, 2H), 1.02 (d, J = 6.4 Hz, 3H), 0.09 (s, 9H); ¹³C-NMR (100 MHz, CDCl₃) δ 166.2, 145.5, 141.1, 138.3, 137.5, 134.5, 133.4, 127.8, 127.0., 122.9, 122.2, 114.9, 114.7, 75.9, 50.4, 42.5, 39.4, 33.8, 33.3, 29.1,
26.1, 16.2, 15.9, 14.9, 0.4; LRMS (EI) m/z 443 (M⁺), 207 (100%); HRMS (EI) Calcd. C_{27}H_{45}NO_{2}Si (M⁺): 443.3217. Found: 443.3200.

**Tetraene (−)-48:** To a stirred solution of 42 (320 mg, 1.15 mmol) in THF (11.5 mL) were added LiHMDS (1.6 M in THF, 788 µL, 1.26 mmol), and (+)-41 (322 mg, 1.05 mmol) in THF (6 mL) at −78 °C. The reaction mixture was warmed up to 0 °C over 20 min, then quenched with saturated NH₄Cl eq. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 20) to give (−)-48 (355 mg, 827 µmol, 79%) as a colorless oil.

(−)-48: [α]_D^{23} −7.7 (c 0.40, CHCl₃); IR (neat) 3278, 2925, 1657, 1630, 1551 cm⁻¹; ~H-NMR (400 MHz, CDCl₃) δ 7.19 (dd, J = 15.0, 10.4 Hz, 1H), 6.58 (ddd, J = 17.2, 10.9, 10.6 Hz, 1H), 6.14 (dd, J = 15.0, 10.4 Hz, 1H), 6.06 (dt, J = 15.0, 7.2 Hz, 1H), 5.87 (d, J = 10.9 Hz, 1H), 5.79 (ddt, J = 16.9, 10.1, 6.8 Hz, 1H), 5.75 (d, J = 15.0 Hz, 1H), 5.54 (brs, 1H), 5.22 (t, J = 7.2 Hz, 1H), 5.11 (d, J = 17.2 Hz, 1H), 4.99-4.94 (m, 1H), 3.73 (dd, J = 11.4, 6.3 Hz, 1H), 3.23 (dt, J = 6.4, 6.8 Hz, 2H), 2.72 (s, 2H), 2.27 (m, 2H), 2.20 (t, J = 6.8 Hz, 2H), 2.08 (dt, J = 6.8, 7.1 Hz, 2H), 1.68 (s, 3H), 1.52 (s, 3H), 1.55 (m, 2H), 1.44 (m, 1H), 0.09 (s, 9H); ~C-NMR (100 MHz, CDCl₃) δ 166.2, 140.9, 139.3, 138.4, 137.5, 135.0, 133.4, 130.4, 127.1, 122.6, 122.2, 115.0, 114.8, 72.1, 50.4, 40.7, 39.4, 36.3, 33.3, 29.1, 26.2, 16.3, 15.9, 0.32; LRMS (EI) m/z 414 (M⁺–CH₃), 294 (100%); HRMS (EI) Calcd. C_{25}H_{40}NO_{2}Si (M⁺–CH₃): 414.2828. Found: 414.2827.

**Hexaene (−)-49:** To a stirred solution of (−)-46 (118 mg, 266 µmol) in DCM (4 mL) were added Et₃N (1.8 mL, 13.3 mmol), Boc₂O (1.8 mL, 7.99 mmol) and DMAP (163 mg, 1.33 mmol) at room temperature. After the reaction mixture was stirred at room temperature for 12.5 hr, then added Et₃N (370 µL, 2.66 mmol) and Boc₂O (305 µL, 1.33 mmol). The solution was stirred for 2 hr and quenched with H₂O. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 50) to give (−)-49 (110 mg, 202 µmol, 76%) as a colorless oil.
(--)-49: [α]D$^{28}$ = -5.7 (c 0.47, CHCl$_3$); IR (neat): 2960, 2931, 1727, 1675, 1369, 1251, 1144, 1085, 841 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.27 (dd, J = 15.2, 11.3 Hz, 1H), 6.77 (d, J = 15.2 Hz, 1H), 6.58 (ddd, J = 17.2, 11.0, 10.4 Hz, 1H), 6.24 (dd, J = 15.1, 11.3 Hz, 1H), 6.10 (dt, J = 15.1, 7.2 Hz, 1H), 5.87 (d, J = 11.0 Hz, 1H), 5.79 (ddt, J = 17.2, 10.4, 6.8 Hz, 1H), 5.20 (t, J = 7.0 Hz, 1H), 5.11 (dd, J = 17.2, 1.8 Hz, 1H), 5.01 (dd, J = 10.4, 1.8 Hz, 1H), 5.00 (dd, J = 17.2, 2.0 Hz, 1H), 4.93 (d, J = 10.4 Hz, 1H), 3.72 (tt, J = 6.4, 6.4 Hz, 1H), 3.63 (dd, J = 13.4, 6.6 Hz, 1H), 3.58 (dd, J = 13.4, 8.2 Hz, 1H), 2.72 (s, 2H), 2.36-2.17 (m, 2H), 2.19 (dd, J = 6.8, 6.4 Hz, 2H), 2.13 (m, 1H), 2.02 (m, 1H), 1.86 (m, 1H), 1.68 (s, 3H), 1.50 (s, 12H), 1.43 (m, 1H), 1.22 (m, 1H), 0.86 (d, J = 6.8 Hz, 3H), 0.10 (s, 9H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 166.1, 153.7, 143.2, 140.1, 138.7, 137.4, 134.9, 133.3, 131.0, 127.1, 123.1, 122.5, 114.9, 114.3, 82.7, 72.1, 50.4, 50.3, 40.7, 36.2, 33.7, 32.3, 31.1, 28.0, 17.2, 16.1, 15.9, 0.3; LRMS (EI) m/z 543 (M$^+$), 308 (100%); HRMS (EI) Calcd. C$_{32}$H$_{53}$NO$_5$Si (M$^+$): 543.3741. Found: 543.3732.

**Hexaene (--)-50:** To a stirred solution of (--)-47 (54 mg, 122 µmol) in DCM (2 mL) were added Et$_3$N (850 µL, 6.09 mmol), Boc$_2$O (840 µL, 3.66 mmol) and DMAP (74 mg, 609 µmol) at room temperature. The reaction mixture was stirred at room temperature overnight, then quenched with H$_2$O. The resulting mixture was extracted twice with Et$_2$O. The combined organic extracts were washed with brine, dried (MgSO$_4$), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 50) to give (--)-50 (62 mg, 114 µmol, 94%) as a colorless oil.

(--)-50: [α]D$^{27}$ = -39.1 (c 1.24, CHCl$_3$); IR (neat): 2962, 2931, 1729, 1675, 1367, 1251, 1146, 841 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.27 (dd, J = 14.4, 11.2 Hz, 1H), 6.81 (d, J = 16.8 Hz, 1H), 6.58 (ddd, J = 17.0, 10.8, 10.6 Hz, 1H), 6.21 (dd, J = 15.0, 10.6 Hz, 1H), 6.07 (ddd, J = 15.2, 8.0 Hz, 1H), 5.87 (d, J = 11.6 Hz, 1H), 5.79 (ddt, J = 17.2, 10.2, 6.8 Hz, 1H), 5.21 (t, J = 6.8 Hz, 1H), 5.11 (d, J = 17.0 Hz, 1H), 5.03-4.98 (m, 2H), 4.95 (d, J = 10.2 Hz, 1H), 3.70 (dd, J = 7.6, 7.2 Hz, 2H), 3.57 (dt, J = 6.0, 5.6 Hz, 1H), 2.72 (s, 2H), 2.36 (m, 1H), 2.20-2.12 (m, 2H), 2.07 (dt, J = 7.2, 7.0 Hz, 2H), 1.68 (s, 3H), 1.59-1.56 (m, 2H), 1.53 (s, 9H), 1.51 (s, 3H), 1.43-1.36 (m, 2H), 1.02 (d, J = 6.8 Hz, 3H), 0.09 (s, 9H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 168.8, 153.5, 146.5, 143.6, 138.5, 137.5, 134.6, 133.3, 128.5, 127.0, 123.1, 123.0, 114.9, 114.6, 82.7, 76.0, 50.5, 44.6, 42.6, 33.8, 33.4, 28.3, 28.0, 26.2, 16.2, 15.9, 14.9, 0.4; LRMS (EI) m/z 543 (M$^+$), 323 (100%); HRMS (EI) Calcd. C$_{32}$H$_{53}$NO$_5$Si (M$^+$): 543.3741. Found: 543.3769.
**Hexaene (−)-51:** To a stirred solution of (−)-48 (369 mg, 860 μmol) in DCM (8.6 mL) were added Et₃N (2.4 mL, 17.2 mmol), Boc₂O (1.98 mL, 8.6 mmol) and DMAP (105 mg, 860 μmol) at room temperature. The reaction mixture was stirred at room temperature for 8 hr, then quenched with H₂O. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 4) to give carbamate (−)-51 (456 mg, 860 μmol, 100%) as a colorless oil.

(−)-51: [α]D²⁷ −5.2 (c 0.90, CHCl₃); IR (neat): 2931, 2929, 1724, 1674, 1368, 1351, 1251, 1146, 1078, 842 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.27 (dd, J = 14.9, 11.0 Hz, 1H), 6.79 (d, J = 14.9 Hz, 1H), 6.58 (ddd, J = 17.0, 10.8, 10.5 Hz, 1H), 6.24 (dd, J = 15.1, 11.0 Hz, 1H), 6.11 (dt, J = 15.1, 7.4 Hz, 1H), 5.87 (d, J = 10.8 Hz, 1H), 5.79 (ddt, J = 16.8, 10.2, 6.6 Hz, 1H), 5.20 (t, J = 6.8 Hz, 1H), 5.11 (dd, J = 17.0, 1.7 Hz, 1H), 5.02–4.93 (m, 3H), 3.74-3.66 (m, 3H), 2.72 (s, 2H), 2.33–2.24 (m, 2H), 2.19 (dd, J = 6.8, 6.4 Hz, 2H), 2.07 (dt, J = 7.2, 7.2 Hz, 2H), 1.68 (s, 3H), 1.64–1.57 (m, 2H), 1.53 (s, 12H), 1.54 (m, 1H), 1.40 (tt, J = 7.6, 7.2 Hz, 2H), 0.08 (s, 9H), ¹³C-NMR (100 MHz, CDCl₃) δ 168.7, 153.3, 143.2, 140.1, 138.5, 134.9, 133.3, 131.0, 127.0, 123.1, 122.5, 114.9, 114.5, 82.7, 72.2, 50.5, 44.7, 40.8, 36.3, 33.4, 28.4, 28.1, 26.3, 16.2, 16.0, 0.4; LRMS (EI) m/z 529 (M⁺), 309 (100%); HRMS (EI) Calcd. C₃₁H₅₁NO₄Si (M⁺): 529.3587. Found: 529.3576.

**Lactam 52:** A solution of (−)-49 (189 mg, 348 μmol), p-quinone (15 mg, 139 μmol) and Grubbs first generation catalyst (57 mg, 69.6 μmol) in DCE (350 mL) was stirred at reflux for 1 hr. The mixture was cooled down to room temperature, concentrated in half, and directly purified by silica gel column chromatography (AcOEt-hexane = 1 : 50) to give 52 (104 mg, 202 μmol, 58%, 14E : 14Z = 5 : 1) as a colorless amorphous.

52: IR (neat): 2957, 2929, 1724, 1674, 1368, 1351, 1251, 1146, 1078, 842 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) (14E) δ 7.24 (dd, J = 15.0, 11.3 Hz, 1H), 6.53 (d, J = 15.0 Hz, 1H), 6.25 (dd, J = 14.8, 11.0 Hz, 1H), 6.18 (dd, J = 15.4, 11.3 Hz, 1H), 6.02 (m, 1H), 5.65 (d, J = 11.0 Hz, 1H), 5.43 (ddd, J = 14.8, 8.8, 5.8 Hz, 1H), 4.97 (dd, J = 7.2, 7.2 Hz, 1H), 3.85 (dd, J = 14.0, 10.0 Hz, 1H), 3.76 (m, 1H), 3.43 (dd, J = 14.0, 4.8 Hz, 1H), 2.63 (d, J = 14.8 Hz, 1H), 2.57 (d, J = 14.8 Hz, 1H), 2.39-2.08 (m,
silica gel column chromatography (AcOEt was cooled down to room temperature µ (100%); HRMS (EI) Calcd. C 49.7, 46.4, 42.9, 37.0, 30.5, 28.1, 26.7, 25.2, 18.9, 16.9, 16.8, 0.3 2H),

14.2, 14.0, 7.2, 6.8 Hz), 1.54 (m, 1H), 1.46 (m, 1H), 1.52 (s, 9H), 1.54-1.46 (m, 2H), 1.44 (s, 3H), 1.29 (m, 1H), 1.04 (d, J = 6.4 Hz, 3H), 0.15 (s, 9H); 13C-NMR (100 MHz, CDCl3) (14E) δ 168.9, 153.6, 145.3, 144.1, 134.7, 133.9, 130.9, 128.4, 128.3, 126.4, 122.8, 121.0, 82.3, 76.4, 49.7, 46.4, 42.9, 37.0, 30.5, 28.1, 26.7, 25.2, 18.9, 16.9, 16.8, 0.3; LRMS (EI) m/z 515 (M+), 415 (100%); HRMS (EI) Calcd. C30H46NO4Si (M+): 515.3428. Found: 515.3448.

Lactam 53: A solution of (−)-50 (21.5 mg, 39.6 µmol), p-quinone (1.7 mg, 15.8 µmol) and Grubbs first generation catalyst (6.5 mg, 7.9 µmol) in DCE (40 mL) was stirred at reflux for 1 hr. The mixture was cooled down to room temperature, concentrated in half, and directly purified by silica gel column chromatography (AcOEt-hexane = 1 : 40) to give 53 (10 mg, 19.4 µmol, 49%, 14E : 14Z = 4 : 1) as a colorless oil.

53: IR (neat): 2959, 1720, 1676, 1367, 1250, 1147, 1071, 841 cm⁻¹; 1H-NMR (400 MHz, CDCl3) (14E) δ 7.26 (dd, J = 15.2, 11.4 Hz, 1H), 6.53 (d, J = 15.2 Hz, 1H), 6.29 (dd, J = 15.2, 10.8 Hz, 1H), 6.15 (dd, J = 15.2, 11.4 Hz, 1H), 5.87 (dd, J = 15.2, 9.2 Hz, 1H), 5.69 (d, J = 10.8 Hz, 1H), 5.39 (ddd, J = 15.2, 7.2, 6.8 Hz, 1H), 5.07 (dd, J = 7.2, 6.8 Hz, 1H), 4.06 (ddd, J = 14.0, 6.4, 6.4 Hz, 1H), 3.49 (ddd, J = 14.0, 6.4, 6.4 Hz, 1H), 3.43 (m, 1H), 2.62 (d, J = 14.2 Hz, 1H), 2.57 (d, J = 14.2 Hz, 1H), 2.31-2.24 (m, 3H), 2.15-2.10 (m, 2H), 1.77 (s, 3H), 1.61 (m, 1H), 1.52 (s, 9H), 1.54-1.46 (m, 2H), 1.44 (s, 3H), 1.29 (m, 1H), 1.04 (d, J = 6.4 Hz, 3H), 0.15 (s, 9H); 13C-NMR (100 MHz, CDCl3) (14E) δ 168.9, 153.6, 145.3, 144.1, 134.7, 133.9, 130.9, 128.4, 128.3, 126.4, 122.8, 121.0, 82.3, 76.4, 49.7, 46.4, 42.9, 37.0, 30.5, 28.1, 26.7, 25.2, 18.9, 16.9, 16.8, 0.3; LRMS (EI) m/z 515 (M+), 415 (100%); HRMS (EI) Calcd. C30H46NO4Si (M+): 515.3428. Found: 515.3436.

Lactam 54: A solution of (−)-51 (30 mg, 56.7 µmol), p-quinone (2.5 mg, 22.7 µmol) and Grubbs first generation catalyst (9.3 mg, 11.3 µmol) in DCE (57 mL) was stirred at reflux for 12 hr. The mixture was cooled down to room temperature, concentrated, and purified by silica gel column chromatography (AcOEt-hexane = 1 : 20) to give 54 (15.5 mg, 30.9 µmol, 55%, 14E : 14Z = 5 : 1) as a colorless oil.

54: IR (neat) 3325, 2927, 2360, 1656, 1627, 1537, 1249 cm⁻¹; 1H-NMR (400 MHz, CDCl3) (14E) δ 7.26 (m, 1H), 6.50 (d, J = 14.8 Hz, 1H), 6.27 (dd, J = 15.6, 10.8 Hz, 1H), 6.16 (dd, J = 14.8, 11.2 Hz,
Lactam (−)-55: To a stirred solution of 52 (31.9 mg, 61.9 μmol) in DCM (2 mL) were added 2,6-lutidine (43 μL, 372 μmol), TMSOTf (34 μL, 186 μmol) at room temperature. The reaction mixture was stirred at that temperature for 9 hr, then quenched with saturated aqueous NaHCO₃. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 4) to give (−)-55 (12.4 mg, 29.9 μmol, 48%) as a white powder.

(−)-55: [α]D⁰ −77.5° (c 0.21, CHCl₃); IR (neat): 3320, 2952, 2917, 1658, 1631, 1250, 1053, 993, 842 cm⁻¹; ¹H-NMR (400 MHz, pyridine-ｄ₅) δ 8.45 (brd, J = 5.6, 4.4 Hz, 1H), 7.53 (dd, J = 14.8, 10.8 Hz, 1H), 6.67 (dd, J = 14.7, 11.1 Hz, 1H), 6.24 (m, 1H), 6.24 (d, J = 14.8 Hz, 1H), 6.02 (ddd, J = 15.2, 7.8, 7.2 Hz, 1H), 5.94 (d, J = 11.1 Hz, 1H), 5.70 (ddd, J = 14.7, 7.8, 6.8 Hz, 1H), 5.12 (dd, J = 7.6, 6.8 Hz, 1H), 3.90 (m, 1H), 3.53 (ddd, J = 13.4, 8.8, 7.8 Hz, 1H), 3.38 (dd, J = 13.4, 4.4, 4.0 Hz, 1H), 2.68 (d, J = 14.2 Hz, 1H), 2.62 (d, J = 14.2 Hz, 1H), 2.41-2.26 (m, 5H), 2.14 (m, 1H), 1.85 (m, 1H), 1.85 (s, 3H), 1.58 (m, 1H), 1.54 (s, 3H), 1.39 (m, 1H), 0.84 (d, J = 6.8 Hz, 3H), 0.17 (s, 9H); ¹³C-NMR (100 MHz, pyridine-ｄ₅) δ 168.0, 166.2, 143.7, 139.1, 138.3, 136.6, 134.9, 134.8, 134.5, 134.2, 132.4, 132.1, 131.8, 130.5, 128.0, 127.6, 126.3, 126.0, 123.9, 121.4, 120.4, 117.1, 71.6, 70.8, 49.6, 49.3, 47.5, 44.4, 43.0, 39.7, 37.9, 35.0, 34.1, 33.8, 33.0, 32.7, 29.5, 29.0, 19.1, 18.1, 17.4, 17.2, 16.9, 0.11, 0.08; LRMS (EI) m/z 415 (M⁺, 100%); HRMS (EI) Calcd. C₂₉H₄₅NO₅Si (M⁺): 415.2904. Found: 415.2874.

Lactam (+)-56: To a stirred solution of 53 (10 mg, 15.6 μmol) in DCM (1 mL) were added 2,6-lutidine (18 μL, 0.156 mmol), TMSOTf (14 μL, 78.2 μmol) at room overnight. The reaction mixture was stirred at that temperature overnight, then quenched with saturated aqueous NaHCO₃. The resulting mixture was extracted twice with Et₂O. The combined organic
extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 4) to give (+)-**56** (4.8 mg, 11.6 μmol, 60%) as a white powder.

(+)-**56**: [α]ᵢ²⁷ +115.9 (c 0.33, CHCl₃); IR (neat): 3300, 2924, 2853, 1656, 1627, 1614, 1543, 1456, 1020, 994, 964 cm⁻¹; ¹H-NMR (400 MHz, pyridine-ｄ₅) (major) δ 8.27 (brs, 1H), 7.53 (dd, J = 15.0, 11.2 Hz, 1H), 6.67 (dd, J = 15.2, 10.8 Hz, 1H), 6.22 (dd, J = 15.0 Hz, 1H), 6.20 (m, 1H), 5.95 (d, J = 10.8 Hz, 1H), 5.87 (dd, J = 15.4, 9.0 Hz, 1H), 5.70 (ddd, J = 15.2, 7.4, 7.0 Hz, 1H), 5.28 (ddd, J = 7.6, 6.8 Hz, 1H), 4.05 (m, 1H), 3.52 (m, 1H), 3.12 (m, 1H), 2.67 (s, 2H), 2.40-2.12 (m, 5H), 1.86 (s, 3H), 1.65 (m, 1H), 1.64-1.52 (m, 2H), 1.52 (s, 3H), 1.08 (d, J = 6.8 Hz, 3H), 0.19 (s, 9H); ¹³C-NMR (100 MHz, pyridine-ｄ₅) δ 167.9, 166.1, 144.6, 143.8, 142.1, 139.2, 135.1, 134.6, 134.5, 134.1, 132.3, 131.8, 129.5, 129.0, 128.4, 127.8, 125.9, 125.8, 124.1, 121.3, 120.0, 117.2, 76.0, 75.1, 49.9, 49.8, 45.8, 43.4, 41.9, 38.3, 36.5, 34.6, 31.3, 30.9, 30.1, 27.4, 26.7, 24.9, 18.7, 18.2, 17.3, 16.7, 16.5, 0.3; LRMS (EI) m/z 415 (M⁺, 100%); HRMS (EI) Calcd. C₂₅H₄₁NO₂Si (M⁺): 415.2904. Found: 415.2898.

**Lactam** (--)-**57**: To a stirred solution of **54** (22 mg, 43.9 μmol) in DCM (440 μL) were added 2,6-lutidine (51 μL, 439 μmol), TMSOTf (32 μL, 176 μmol) at room temperature. The reaction mixture was stirred at that temperature for 2 hr, then quenched with saturated aqueous NaHCO₃. The resulting mixture was extracted twice with Et₂O. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1 : 4) to give (--)-**57** (7.8 mg, 19.4 μmol, 44%) as a white powder.

(--)-**57**: [α]ᵢ²² +45.5 (c 1.05, CHCl₃); IR (neat) 3325, 2927, 2360, 1656, 1627, 1537, 1249 cm⁻¹; ¹H-NMR (400 MHz, pyridine-ｄ₅) (major) δ 8.30 (brd, J = 5.6, 4.8 Hz, 1H), 7.51 (dd, J = 15.1, 11.4 Hz, 1H), 6.64 (dd, J = 15.0, 11.2 Hz, 1H), 6.22 (d, J = 15.1 Hz, 1H), 6.18 (m, 1H), 5.99 (ddd, J = 15.6, 8.4, 7.2 Hz, 1H), 5.94 (d, J = 11.2 Hz, 1H), 5.71 (ddd, J = 15.0, 7.6, 7.2 Hz, 1H), 5.20 (dd, J = 7.2, 6.8 Hz, 1H), 3.92 (m, 1H), 3.73 (ddd, J = 14.0, 6.0, 6.0 Hz, 1H), 3.45 (m, 1H), 2.65 (s, 2H), 2.54 (m, 1H), 2.43-2.16 (m, 5H), 1.83 (s, 3H), 1.79 (s, 3H), 1.64-1.53 (m, 3H), 1.53 (s, 3H), 1.48 (s, 1H), 1.41 (m, 1H), 0.17 (9H, s); ¹³C-NMR (100 MHz, pyridine-ｄ₅) (major) δ 166.6, 139.7, 136.7, 134.8, 134.2, 132.4, 130.9, 128.2, 127.4, 124.9, 121.3, 72.0, 49.7, 43.5, 38.3, 37.6, 30.7, 28.0, 26.2, 17.3,
17.2, 0.2; LRMS (FAB) m/z 402 (M^+H, 100%); HRMS (FAB) Calcd. C_{29}H_{40}NO_5Si (M^+H): 402.2828. Found: 402.2805.

**20-demethyl vicenistatin [(−)-58]** and **20-demethyl α-vicenistatin [(−)-61]**: To a stirred solution of (−)-55 (12.3 mg, 29.6 μmol), 38 (c.a. 59.3 μmol) in DCM (1 mL) was added TMSOTf (11 μL, 59.3 μmol) at −40 °C. The reaction mixture was stirred at that temperature for 2 hr, then quenched with saturated aqueous NaHCO_3. The resulting extract was extracted twice with AcOEt. The combined organic extracts were washed with brine, dried (MgSO_4), and concentrated. This material was used without further purification. To a stirred solution of crude glycosyl adduct in THF (2 mL) was added TBAF (1.0 M in THF, 89 μL, 89 μmol) at room temperature. After the reaction mixture was stirred at that temperature for 2 hr, directly purified by silica gel column chromatography (MeOH-CHCl_3 = 1 : 20) and preparative layer chromatography (MeOH-CHCl_3 = 1 : 50) to give (−)-58 (1.6 mg, 3.3 μmol 11% for 2 steps) as a white powder and (−)-61 (1.2 mg, 2.5 μmol 8% for 2 steps) as a white powder.

(−)-58: [α]_D^{26} −18.1 (c 0.06, MeOH); IR (neat): 3312, 2922, 2852, 1657, 1629, 1612, 1014, 994 cm\(^{-1}\); \(^1\)H-NMR (500 MHz, pyridine-d_5) (major) δ 8.39 (brddd, J = 6.5, 5.0 Hz, 1H), 7.49 (dd, J = 14.7, 11.5 Hz, 1H), 6.66 (dd, J = 14.3, 11.0 Hz, 1H), 6.21 (d, J = 14.7 Hz, 1H), 6.18 (dd, J = 15.2, 11.3 Hz, 1H), 5.96 (ddd, J = 15.2, 8.0, 7.0 Hz, 1H), 5.92 (d, J = 11.0 Hz, 1H), 5.69 (ddd, J = 14.3, 6.8, 5.5 Hz, 1H), 5.19 (d, J = 3.5 Hz, 1H), 5.08 (dd, J = 8.0, 7.0 Hz, 1H), 4.23 (m, 1H), 4.10 (dq, J = 9.8, 6.2 Hz, 1H), 3.90 (m, 1H), 3.53 (ddd, J = 13.3, 9.0, 8.3 Hz, 1H), 3.39 (ddd, J = 13.3, 4.5, 4.0 Hz, 1H), 2.66 (d, J = 14.3 Hz, 1H), 2.58 (d, J = 14.3 Hz, 1H), 2.45 (s, 3H), 2.43-2.12 (m, 6H), 1.94 (ddd, J = 14.5, 4.0, 3.8 Hz, 1H), 1.86 (m, 1H), 1.82 (s, 3H), 1.55 (m, 1H), 1.52 (s, 3H), 1.49 (d, J = 6.2 Hz, 3H), 1.40 (m, 1H), 0.84 (d, J = 6.5 Hz, 3H); \(^1^3\)C-NMR (125 MHz, pyridine-d_5) (major) δ 166.4, 139.7, 136.4, 133.9, 132.6, 131.0, 128.7, 128.2, 127.5, 124.9, 121.0, 96.0, 76.4, 65.1, 64.6, 62.9, 49.7, 44.0, 41.3, 36.6, 34.1, 33.9, 33.5, 33.2, 28.6, 19.2, 18.6, 17.17, 17.15; LRMS (FAB) m/z 487 (M^+H), 154 (100%); HRMS (FAB) Calcd. C_{29}H_{40}N_2O_4 : (M^+H) 487.3528. Found: 487.3538.

(−)-61: [α]_D^{26} −88.2 (c 0.08, MeOH); IR (neat): 3285, 2919, 2875, 1655, 1627, 1612, 994 cm\(^{-1}\); \(^1\)H-NMR (500 MHz, pyridine-d_5) (major) δ 8.41 (brddd, J = 6.3, 4.3 Hz, 1H), 7.53 (dd, J = 15.3, 11.5 Hz, 1H), 6.67 (dd, J = 14.7, 11.2 Hz, 1H), 6.21 (d, J = 14.7 Hz, 1H), 6.19 (dd, J = 14.2, 11.5 Hz, 1H), 5.96 (ddd, J = 14.2, 8.5, 6.5 Hz, 1H), 5.92 (d, J = 11.2 Hz, 1H), 5.69 (ddd, J = 14.7, 8.5, 5.5 Hz, 1H), 5.36 (d, J = 7.6 Hz, 1H), 5.17 (dd, J = 6.0, 5.6 Hz, 1H), 4.34 (m, 1H), 4.02-3.96 (m, 2H), 3.60 (ddd,
J = 13.0, 9.0, 9.0 Hz, 1H), 3.32 (ddd, J = 13.0, 4.0, 4.0 Hz, 1H), 2.86 (m, 1H), 2.67 (d, J = 14.3 Hz, 1H), 2.63 (m, 1H), 2.59 (d, J = 14.3 Hz, 1H), 2.40 (s, 3H), 2.42-2.35 (m, 3H), 2.24 (dd, J = 9.5, 2.5 Hz, 1H), 2.11 (m, 1H), 1.95-1.87 (m, 2H), 1.83 (s, 3H), 1.57 (s, 3H), 1.51 (d, J = 6.0 Hz, 3H), 1.40 (m, 1H), 0.84 (d, J = 7.0 Hz, 3H); $^{13}$C-NMR (125 MHz, pyridine-$d_5$) (major) δ 166.4, 139.8, 136.8, 134.9, 134.1, 132.5, 130.8, 128.2, 127.5, 124.7, 121.7, 97.4, 78.1, 70.5, 65.2, 63.3, 49.6, 44.0, 40.3, 39.8, 36.8, 34.0, 33.4, 33.2, 28.4, 19.6, 18.4, 17.4, 17.2; LRMS (EI) m/z 486 (M$^+$), 144 (100%); HRMS (EI) Calcd. C$_{20}$H$_{40}$N$_2$O$_4$ : (M$^+$) 486.3455. Found: 486.3433.

23-Demethyl vicenistatin [(+)-59] and 23-demethyl α-vicenistatin [(+)-62]: To a stirred solution of (+)-56 (9.7 mg, 23.4 µmol), 38 (c.a. 46.7 µmol) in DCM (1 mL) was added TMSOTf (8.5 µL, 46.7 µmol) at −40 °C. The reaction mixture was stirred at that temperature for 75 min, then quenched with saturated aqueous NaHCO$_3$. The resulting mixture was extracted twice with AcOEt. The combined organic extracts were washed with brine, dried (MgSO$_4$), and concentrated. This material was used without further purification.

To a stirred solution of crude glycosyl adduct in THF (2 mL) was added TBAF (1.0 M in THF, 70 µL, 70 µmol) at room temperature. After the reaction mixture was stirred at that temperature for 1 hr, directly purified by silica gel column chromatography (MeOH-CHCl$_3$ = 1 : 20) to give (+)-59 (0.8 mg, 1.6 µmol 7% for 2 steps) as a white powder and (+)-62 (1.8 mg, 3.7 µmol 15% for 2 steps) as a white powder.

(+)-59: [α]$^0_{D}$ +179.2 (c 0.09, MeOH); IR (neat): 3514, 3297, 2926, 1658, 1630, 1086, 1016, 999 cm$^{-1}$; 1H-NMR (500 MHz, pyridine-$d_5$) (major) δ 8.32 (brd, J = 7.5, 4.5 Hz, 1H), 7.52 (dd, J = 15.3, 11.3 Hz, 1H), 6.67 (dd, J = 15.0, 11.0 Hz, 1H), 6.23 (d, J = 15.0 Hz, 1H), 6.20 (dd, J = 15.0, 11.0 Hz, 1H), 5.93 (d, J = 10.5 Hz, 1H), 5.91 (dd, J = 14.8, 8.7 Hz, 1H), 5.69 (dd, J = 15.0, 7.3, 7.0 Hz, 1H), 5.22 (d, J = 4.0 Hz, 1H), 5.16 (dd, J = 7.5, 6.5 Hz, 1H), 4.24 (m, 1H), 4.16 (m, 1H), 3.97 (m, 1H), 3.67 (m, 1H), 3.20 (m, 1H), 2.66 (d, J = 13.8 Hz, 1H), 2.61 (d, J = 13.8 Hz, 1H), 2.45 (m, 1H), 2.43 (s, 3H), 2.31-2.19 (m, 5H), 1.97 (ddd, J = 14.5, 4.0, 3.5 Hz, 1H), 1.84 (s, 3H), 1.64 (m, 1H), 1.57-1.49 (m, 3H), 1.52 (s, 3H), 1.50 (d, J = 6.5 Hz, 3H), 1.17 (d, J = 6.5 Hz, 3H); $^{13}$C-NMR (125 MHz, pyridine-$d_5$) (major) δ 166.4, 142.5, 139.8, 135.0, 134.1, 132.3, 129.0, 128.4, 127.4, 125.0, 121.1, 94.2, 79.5, 65.4, 64.6, 62.7, 49.7, 44.2, 37.5, 36.5, 34.0, 30.70, 30.67, 28.1, 26.2, 19.2, 18.9, 17.3, 17.1; LRMS (FAB) m/z 487 (M$^+$+H), 154 (100%); HRMS (FAB) Calcd. C$_{20}$H$_{46}$N$_2$O$_4$ : (M$^+$+H) 487.3528. Found: 487.3533.
(+)-62: [α]D30 +111.6 (c 0.06, MeOH); IR (neat): 3304, 2923, 1655, 1626, 1544, 1092, 992 cm⁻¹;
1H-NMR (500 MHz, pyridine-d₅) (major) δ 8.31 (br, 1H), 7.56 (m, 1H), 6.71 (dd, J = 15.3, 10.8 Hz, 1H), 6.23 (d, J = 15.2 Hz, 1H), 6.19 (dd, J = 14.9, 11.3 Hz, 1H), 5.94 (d, J = 10.8 Hz, 1H), 5.84 (dd, J = 14.9, 9.5 Hz, 1H), 5.70 (ddd, J = 15.3, 7.0, 6.5 Hz, 1H), 5.29-5.25 (m, 2H), 4.38 (m, 1H), 4.16 (m, 1H), 3.99 (m, 1H), 3.41 (m, 1H), 3.11 (m, 1H), 2.95 (dd, J = 14.0, 8.5 Hz, 1H), 2.69 (d, J = 14.5 Hz, 1H), 2.63 (d, J = 14.5 Hz, 1H), 2.45-2.36 (m, 3H), 2.40 (s, 3H), 2.23 (dd, J = 9.5, 3.0 Hz, 1H), 2.14-2.08 (m, 2H), 1.91 (m, 1H), 1.88 (s, 3H), 1.65 (s, 3H), 1.62-1.48 (m, 4H), 1.50 (d, J = 6.5 Hz, 3H), 1.08 (d, J = 6.5 Hz, 3H); 13C-NMR (125 MHz, pyridine-d₅) (major) δ 166.5, 142.9, 140.1, 134.8, 134.3, 132.3, 128.8, 128.7, 128.4, 124.7, 122.0, 100.8, 85.6, 70.5, 65.2, 63.2, 49.5, 45.7, 39.4, 37.2, 36.0, 34.0, 30.6, 28.1, 26.2, 19.6, 18.8, 17.7, 17.3; LRMS (FAB) m/z 487 (M⁺+H), 154 (100%); HRMS (FAB) Calcd. C₂₀H₁₄N₂O₄ : (M⁺+H) 487.3528. Found: 487.3530.

20,23-Didemethyl vicenistatin [(−)-60] and 20,23-didemethyl vicenistatin [(−)-63]: To a stirred solution of (−)-57 (11.8 mg, 29.4 μmol), 38 (58.9 μmol) in DCM (1 mL) was added TMSOTf (11 μL, 58.9 μmol) at −40 °C. The reaction mixture was stirred at that temperature for 40 min, then quenched with saturated aqueous NaHCO₃. The resulting mixture was extracted twice with AcOEt. The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. This material was used without further purification. To a stirred solution of crude glycosyl adduct in THF (2 mL) was added TBAF (1.0 M in THF, 88 μL, 88 μmol) at room temperature. After the reaction mixture was stirred at that temperature for 2 hr, directly purified by silica gel column chromatography (MeOH-CHCl₃ = 1 : 20) to give (−)-60 (2.9 mg, 6.1 μmol 21% for 2 steps) as a white powder and (+)-63 (2.7 mg, 5.7 μmol 19% for 2 steps) as a white powder.

(−)-60: [α]D28 −28.8 (c 0.05, MeOH); IR (neat): 3296, 2926, 2853, 1656, 1628, 1258, 1159, 1073, 1031, 995 cm⁻¹; 1H-NMR (500 MHz, pyridine-d₅) (major) δ 8.31 (brdd, J = 6.0, 5.5 Hz, 1H), 7.51 (dd, J = 15.0, 11.0 Hz, 1H), 6.64 (dd, J = 14.8, 10.8 Hz, 1H), 6.21 (d, J = 15.0 Hz, 1H), 6.18 (m, 1H), 5.95 (dd, J = 15.0, 7.5 Hz, 1H), 5.92 (d, J = 10.8 Hz, 1H), 5.71 (ddd, J = 14.8, 7.5, 7.0 Hz, 1H), 5.36 (d, J = 9.5 Hz, 1H), 5.20 (dd, J = 7.0, 7.0 Hz, 1H), 4.40 (m, 1H), 4.01 (m, 2H), 3.41 (m, 2H), 2.65 (d, J = 14.5 Hz, 1H), 2.61 (d, J = 14.5 Hz, 1H), 2.51-2.28 (m, 6H), 2.43 (s, 3H), 1.92 (m, 1H), 1.82 (s, 3H), 1.56 (s, 3H), 1.52 (d, J = 5.5 Hz, 3H); 13C-NMR (125 MHz, pyridine-d₅) (major) δ; LRMS (FAB) m/z 473 (M⁺+H), 154 (100%); HRMS (FAB) Calcd. C₂₂H₁₂O₄ : (M⁺+H) 473.3377. Found: 473.3397.
(+)-63: $[\alpha]_D^{30} +31.6 (c 0.13, MeOH)$; IR (neat): 3294, 2925, 2852, 1657, 1630, 1610, 998 cm$^{-1}$; $^1$H-NMR (500 MHz, pyridine-$d_5$) (major) $\delta$ 8.31 (brdd, $J = 6.0, 5.5$ Hz, 1H), 7.48 (dd, $J = 14.7, 10.3$ Hz, 1H), 6.64 (dd, $J = 15.0, 11.0$ Hz, 1H), 6.20 (d, $J = 14.7$ Hz, 1H), 6.19 (m, 1H), 5.96 (dd, $J = 15.0, 7.5$ Hz, 1H), 5.92 (d, $J = 11.0$ Hz, 1H), 5.71 (dd, $J = 15.0, 7.0, 6.5$ Hz, 1H), 5.18 (m, 1H), 5.11 (dd, $J = 8.0, 7.5$ Hz, 1H), 4.21 (m, 1H), 4.07 (m, 1H), 3.93 (m, 1H), 3.73 (m, 1H), 3.45 (m, 1H), 2.62 (brs, 2H), 2.53-2.16 (m, 8H), 2.43 (s, 3H), 1.93 (m, 1H), 1.81 (s, 3H), 1.58 (s, 3H), 1.55 (d, $J = 6.5$ Hz, 3H); $^{13}$C-NMR (125 MHz, pyridine-$d_5$) (major) $\delta$ 166.6, 139.6, 136.4, 134.1, 132.4, 131.1, 128.2, 127.4, 125.0, 120.8, 95.9, 76.1, 65.2, 64.7, 62.9, 49.7, 41.1, 37.5, 36.6, 34.0, 33.7, 30.7, 28.1, 26.2, 19.2, 17.2; LRMS (FAB) m/z 473 (M$^+$+H), 154 (100%); HRMS (FAB) Calcd. C$_{28}$H$_{45}$N$_2$O$_4$: (M$^+$+H) 473.3377. Found: 473.3336.

Cytotoxicity Assay.

3Y1, U87 and HeLa cells were seeded in 96-well culture plates (3 $\times$ 10$^3$ cells per well) containing 100 $\mu$L of DMEM medium per well. After 24 hr, drugs were added to the wells (final concentration: 100, 30, 10, 3, 1, 0.3, 0.1 $\mu$M). After 48 hr, 10 $\mu$L of WST-8 was added to each well and absorbance at 450 nm was measured using a microplate reader.