Supporting Information

Stereoselective Syntheses of Rolliniastatin 1, Rollimembrin, and Membranacin

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EXPERIMENTAL

General Methods

All reactions were performed under argon atmosphere. ¹H and ¹³C NMR spectra were measured on 300 MHz, 400 MHz and 500 MHz spectrometers. Chemical shift values were recorded in parts per million using the residual undeuterated solvents as internal references and coupling constants in hertz. Infrared spectra (IR) were recorded on a FT-IR spectrophotometer and frequencies are given in reciprocal centimeters. Mass spectra (MS and HRMS) were recorded using chemical ionization (CI), electron impact (EI), or fast atom bombardment (FAB) method. Optical rotation data were obtained on a digital polarimeter at 589 nm (sodium D line).

The progress of reactions was checked on TLC plates, and the spots were visualized under 254 nm UV light and/or charring after dipping the TLC plate into *p*-anisaldehyde solution (ethanol 67.5 mL, *p*-anisaldehyde 1.85 mL, acetic acid 0.75 mL, and sulfuric acid 2.5 mL).

All solvents used in reactions were dried under nitrogen atmosphere. THF and toluene were distilled from Na-benzophenone. Acetonitrile and triethylamine were distilled from CaH₂. CH₂Cl₂ was distilled from P₂O₅. Dry solvents purchased from Aldrich Chem. Co. (THF, CH₂Cl₂, toluene and pyridine) were also used.

1. Synthesis of **16**: approach I

Lactone **5**

To a solution of 1,4-butanediol (**4**, 15 g, 166 mmol) in CH_2Cl_2 (30 ml) containing Et_3N (23 ml, 166 mmol) and 4-(dimethylamino)pyridine (35 mg, 0.29 mmol) was added dropwise *tert*-butylchlorodiphenylsilane (15 ml, 57.3 mmol) under argon at room temperature. The solution was stirred at room temperature for 18 h, concentrated in vacuo, and the residue was purified by flash chromatography (Hex-EtOAc, 10:1~4:1) to give alcohol **4A** (13.77g, 73% yield) as a clear oil: ^1H NMR (300 MHz, CDCl_3) δ 1.05 (s, 9H), 1.63–1.71 (m, 4H), 2.04 (s, 1H), 3.63 (t, $J = 5.84$ Hz, 2H), 3.70 (t, $J = 5.68$ Hz, 2H), 7.26–7.69 (m, 10H); ^{13}C NMR (75 MHz, CDCl_3) δ 19.6, 27.2, 29.7, 30.3, 63.3, 64.4, 128.1, 130.1, 134.0, 136.0.

A solution of oxalyl chloride (4.72ml, 54.1 mmol, 1.3 equiv) in CH_2Cl_2 (85 mL) was treated with a solution of DMSO (6.5 mL, 2.2 equiv) in CH_2Cl_2 (5 mL) at -78°C under argon in 10 min. After 15 min at -78°C , alcohol **4A** (13.66 g, 41.6 mmol) in CH_2Cl_2 (34 mL) was added in 5 min. After 15 min at -78°C , triethylamine (29 mL, 208 mmol, 5 equiv) was added in 15 min, and the mixture was allowed to warm up to room temperature. The reaction mixture was treated with 150 mL of water, and extracted with CH_2Cl_2 (2 x 100 mL). The organic extracts were washed with saturated aqueous NaCl (100 mL), and dried over MgSO_4 . The filtrate was concentrated in vacuo, and the residue was purified by flash chromatography (Hex-EtOAc, 20:1~10:1) to give aldehyde **4B** (13.51, 99% yield) as an oil: ^1H NMR (CDCl_3) δ 9.79 (d, $J = 1.68$ Hz, 1H), 7.66–7.35 (m, 10H), 3.69 (t, $J = 5.97$ Hz, 2H), 2.55 (dt, $J = 7.17, 1.65$ Hz, 2H), 1.89 (tt, $J = 7.08, 6.02$ Hz, 2H), 1.04 (s, 9H); ^{13}C NMR (CDCl_3) δ 203.0, 135.9, 134.0, 130.1, 128.1, 63.3, 41.2, 27.2, 25.6, 19.6; MS (EI) m/z 325 ($\text{M}^+ - \text{H}$), 269, 221, 199, 181, 161, 139, 131, 129, 105, 91, 77.

A mixture of **4B** (13.51 g, 41.4 mmol), monomethyl malonate (5.90 g, 50.0 mmol, 1.2 equiv.) and Et_3N (7.0 mL, 50.2mmol, 1.2 equiv.) was heated at 90°C overnight. After addition of ice (100 mL), 2 N HCl (50 mL), and EtOAc (100 mL), the mixture was extracted with EtOAc (100 mL x 2). The organic extracts were washed with saturated aqueous NaCl (100 mL), and dried over MgSO_4 . After removal of the solvent under reduced pressure, purification of the residue by flash chromatography (Hex-EtOAc, 50:1~30:1) gave ester **4C** (13.30g, 84% yield): ^1H NMR (300 MHz, CDCl_3) δ 7.67–7.64 (m, 4H), 7.42–7.25 (m, 6H), 5.59–5.55 (m, 2H), 3.69 (t, $J = 6.5$ Hz, 2H), 3.67 (s, 3H), 3.03 (d, $J = 4.9$ Hz, 2H), 2.25 (m, 2H), 1.04 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.8, 136.0, 134.3, 131.6, 130.0, 128.0, 124.0, 63.9, 52.1, 38.4, 36.3, 27.2, 19.6; MS (EI) m/z 381 ($\text{M}^+ -$

H), 325, 293, 243, 225, 213, 197, 183, 165, 153, 135, 105, 91, 77, 59.

Ester **4C** (6.70 g, 17.5 mmol) was added to a mixture of AD-mix- α (25 g, 1.4 g/mmol of **4C**) and methanesulfonamide (1.67g, 17.5 mmol) in *t*-BuOH (88 mL) and water (88 mL) at 0 °C. The solution was stirred at 0 °C for 20 h. After addition of saturated aqueous Na₂S₂O₃ (100 mL), the mixture was extracted with EtOAc. The extracts were dried over MgSO₄, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 2:1) to yield lactone **5** (6.44 g, 96% yield) as a clear oil: $[\alpha]_D^{27} -27.0$ (*c* 1.0, CHCl₃); IR (neat) ν 3452 (br.), 2932, 2858, 1766, 1472, 1428, 1164, 1110, 1014, 822, 740, 704, 615 cm⁻¹; ¹H NMR (CDCl₃) δ 7.67–7.41 (m, 10H), 4.59 (qui, *J* = 2.90 Hz, 1H), 4.50 (qui, *J* = 4.61 Hz, 1H), 3.86 (dt, *J* = 10.79, 3.95 Hz, 1H), 3.69 (dt, *J* = 10.73, 2.25 Hz, 1H), 3.55 (t, *J* = 1.86 Hz, 1H), 2.83 (ddd, *J* = 17.83, 5.73, 1.38 Hz, 1H), 2.63 (d, *J* = 17.79 Hz, 1H), 2.30 (m, 1H), 2.10 (ddt, *J* = 14.60, 4.81, 2.09 Hz, 1H), 1.07 (s, 9H); ¹³C NMR (CDCl₃) δ 175.7, 135.9, 135.9, 132.5, 132.3, 130.6, 128.4, 84.1, 69.1, 60.8, 38.5, 31.1, 27.2, 19.4; MS (EI) *m/z* 327 (M⁺-*t*Bu), 309, 297, 279, 249, 225, 207, 199, 183, 163, 139, 117, 105, 91, 77. The enantiomeric purity of **5** was determined to be 86% e.e. by ¹H NMR analysis of its *O*-acetyl mandelate derivative.¹

Tosylate **6**

A solution of lactone **5** (6.3g, 16.5 mmol) in THF (35 mL) was slowly added to a suspension of LiAlH₄ (626 mg, 1.0 equiv) in THF (35 mL) at -78 °C. The reaction mixture was warmed to room temperature, and after 30 min, treated with diluted H₂SO₄ (3 wt. %, 58mL) at 0 °C. The mixture was extracted with EtOAc (100 mL x 4). The combined organic extracts were dried over MgSO₄. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography (Hex-EtOAc, 1:2~0:1) to yield triol **5A** (4.67 g, 73% yield) as a clear oil: $[\alpha]_D^{25} + 1.9$ (*c* 1.0, CHCl₃); IR (neat) ν 3382 (br.), 2930, 2858, 1472, 1428, 1390, 1110, 822, 738, 702 cm⁻¹; ¹H NMR (CDCl₃) δ 7.68–7.37 (m, 10H), 3.91–3.72 (m, 6H), 3.73 (br. s, 1H), 3.13 (d, *J* = 4.32, 1H), 2.70 (br. s, 1H), 1.88–1.65 (m, 4H), 1.06 (s, 9H); ¹³C NMR (CDCl₃) δ 135.94, 135.91, 133.23, 133.14, 130.34, 130.36, 130.33, 128.25, 74.48, 74.44, 63.18, 61.37, 35.54, 35.28, 27.21, 19.43; MS (EI) *m/z* 387 (M⁺-H), 313, 257, 235, 223, 211, 206, 199, 181, 169, 157, 139, 134, 115, 97, 77, 57.

To a solution of **5A** (4.95 g, 12.7 mmol) in CH₂Cl₂ (50 mL) in ice bath, benzaldehyde dimethylacetal (2.26 mL, 15.3 mmol) and (±)-camphorsulfonic acid (74 mg, 2.5 mol%) were added. After stirring the mixture for 1 h at room temperature, saturated aqueous NaHCO₃ (10 mL) was added and the mixture was extracted with CH₂Cl₂ (20 mL x 2). The combined organic extracts were

dried over MgSO_4 and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (Hex-EtOAc, 6:1~3:1) to yield acetal **5B** (4.83 g, 80%): $[\alpha]_D^{23} -2.6$ (*c* 1.00, CHCl_3); IR (neat) ν 3496, 2958, 2930, 2856, 1472, 1428, 1392, 1110, 1024, 822, 740, 700 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.69–7.34 (m, 15H), 5.51 (s, 1H), 4.30 (ddd, $J = 11.40, 5.07, 1.11$ Hz, 1H), 3.95–3.80 (m, 5H), 2.85 (d, $J = 3.45$ Hz, 1H), 2.04–1.88 (m, 1H), 1.82–1.70 (m, 2H), 1.54–1.48 (dm, $J = 13.2$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 138.9, 136.0, 133.9, 130.1, 129.3, 128.6, 128.1, 126.5, 101.6, 80.3, 72.2, 67.1, 61.8, 34.8, 27.3, 27.2, 19.5; MS (EI) m/z 476 (M^+), 417, 401, 313, 295, 275, 255, 235, 229, 205, 199, 183, 181, 163, 139, 135, 117, 105, 91, 77, 57. Its dioxolane by-product was also obtained (0.55 g, 11%).

A solution of acetal **5B** (4.46 g, 9.36 mmol) in THF (31 mL) was treated with Bu_4NF (1.0 M in THF, 10.3 mL, 1.1 equiv) at room temperature, and the mixture was stirred for 3 h. Water (10 mL) was added, and the aqueous phase was extracted with EtOAc (50 mL x 3). The organic extracts were dried over MgSO_4 and the solvent was evaporated. Purification of the residue by flash chromatography (Hex-EtOAc, 1:2) afforded diol **5C** (2.21 g, 99%) as a white solid: mp 88.9–90.2 $^\circ\text{C}$; $[\alpha]_D^{25} +5.8$ (*c* 1.00, CHCl_3); IR (neat) ν 3274, 2954, 2924, 2862, 1364, 1232, 1156, 1116, 1094, 1030, 974, 730, 694 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.50–7.35 (m, 5H), 5.54 (s, 1H), 4.31 (ddd, $J = 11.44, 5.12, 1.24$ Hz, 1H), 3.97 (dt, $J = 11.61, 2.59$ Hz, 1H), 3.87–3.76 (m, 4H), 2.86 (d, $J = 2.98$ Hz, 1H), 2.63 (t, $J = 5.43$ Hz, 1H), 1.90 (ddt, $J = 12.94, 11.07, 5.14$ Hz, 1H), 1.76 (q, $J = 5.55$ Hz, 2H), 1.51 (dq, $J = 13.2, 1.90$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 138.6, 129.4, 128.7, 126.5, 101.7, 80.4, 74.1, 66.9, 61.3, 34.0, 27.3; MS (EI) m/z 238 (M^+), 237, 164, 163, 146, 133, 120, 115, 107, 106, 105, 97, 91, 79, 77, 71, 57.

To a solution of **5C** (2.23 g, 9.37 mmol) and triethylamine (1.96 mL, 14.1 mmol) in dry CH_2Cl_2 (20 mL) was added *p*-toluenesulfonyl chloride (1.87 g, 9.83 mmol) at 0 $^\circ\text{C}$. The reaction mixture was stirred for 12 h at 0 $^\circ\text{C}$, and then it was treated with aqueous 1 N HCl (10 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (20 mL x 2). The combined organic layers were washed with brine, dried over MgSO_4 , and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hex-EtOAc, 2:1) to give tosylate **6** (3.08 g, 84% yield) as an oil: ^1H NMR (CDCl_3) δ 7.80 (d, $J = 8.31$ Hz, 2H), 7.46–7.31 (m, 7H), 5.49 (s, 1H), 4.28 (dd, $J = 4.19, 11.57$ Hz, 1H), 4.23 (dd, $J = 7.26, 5.25$ Hz, 2H), 3.92 (dt, $J = 12.13, 2.42$ Hz, 1H), 3.75–3.62 (m, 2H), 2.43 (s, 3H), 1.98–1.73 (m, 3H), 1.44 (dd, $J = 13.20, 1.17$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 145.2, 138.6, 133.4, 130.3, 129.4, 128.7, 128.3, 126.5, 101.6, 79.9, 70.3, 67.8, 66.9, 32.2, 27.3, 22.0.

Iodide 8

To a solution of tosylate **6** (1.85 g, 4.72 mmol) and (–)-(*S*)-ethynyl *p*-tolyl sulfoxide (**7**, 1.16 g, 7.08 mmol, 1.5 equiv) in dry CH₂Cl₂ (16 mL) was added *N*-methylmorpholine (0.52 mL, 14.1 mmol) at 0 °C. After stirring for 12 h at ambient temperature, aqueous 1 N HCl (10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (20 mL x 2). The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. Charcoal (3 g) was added to the solution of the residue in ethyl acetate. The mixture was filtered through a pad of silica gel, which was washed with ethyl acetate. The solution was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel (Hex-EtOAc, 1:2) to give tosylate **6A** (3.08 g, 84%) as an oil: $[\alpha]_D^{25} +104.0$ (*c* 1.02, CHCl₃); IR (neat) ν 2968, 2924, 2860, 1618, 1360, 1176, 1110, 1032, 924, 812, 758, 700, 662 cm⁻¹; ¹H NMR (CDCl₃) δ 7.78 (d, *J* = 8.32 Hz, 2H), 7.47–7.35(m, 7H), 7.24 (d, *J* = 8.30 Hz, 2H), 7.17 (d, *J* = 8.19 Hz, 2H), 7.11 (d, *J* = 12.46 Hz, 1H), 5.75 (d, *J* = 12.47 Hz, 1H), 5.45 (s, 1H), 4.30 (dd, *J* = 11.61, 4.20 Hz, 1H), 4.22 (qui, *J* = 5.11 Hz, 1H), 4.11–4.03 (m, 2H), 3.98–3.90 (m, 2H), 2.46 (s, 3H), 2.37 (s, 3H), 2.16–1.78 (m, 3H), 1.47 (dd, *J* = 12.95, 1.08 Hz, 1H); ¹³C NMR (CDCl₃) δ 159.0, 145.7, 142.3, 141.0, 138.4, 132.9, 130.6, 130.2, 129.5, 128.7, 128.3, 126.5, 124.6, 113.3, 101.7, 82.1, 78.3, 66.7, 66.3, 29.9, 27.0, 22.1, 21.7.

To a solution of **6A** (2.62 g, 4.71 mmol) in acetone (50 mL) was added NaI (2.12 g, 14.1 mmol, 3.0 equiv) at room temperature. The reaction mixture was heated under reflux for 3 h. The mixture was concentrated under reduced pressure, and water and ethyl acetate was added. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (20 mL x 2). The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (Hex-EtOAc, 1:1) provided iodide **8** (2.30g, 95% yield, 86% de) as a white solid. The solid was recrystallized from ethyl acetate to give a pure sample of **8** (1.94 g, 81% yield, >98% de): mp 139.5–140.7 °C; $[\alpha]_D^{25} +85.7$ (*c* 0.50, CHCl₃); IR (neat) ν 3020, 2922, 2856, 1598, 1450, 1362, 1212, 1098, 1028, 996, 882, 852, 812, 750, 698, 592, 522 cm⁻¹; ¹H NMR (CDCl₃) δ 7.50–7.16 (m, 10H), 5.81 (d, *J* = 12.5 Hz, 1H), 5.49 (s, 1H), 4.32 (dd, *J* = 11.5, 4.1 Hz, 1H), 4.14 (q, *J* = 6.4 Hz, 1H), 4.04–3.92 (m, 2H), 3.33 (dt, *J* = 10.4, 5.3 Hz, 1H), 3.20 (dt, *J* = 9.9, 7.8 Hz, 1H), 2.37 (s, 3H), 2.17–2.09 (m, 2H), 1.91 (dq, *J* = 12.2, 5.1 Hz, 1H), 1.49 (dd, *J* = 13.0, 1.4 Hz, 1H); ¹³C NMR (CDCl₃) δ 159.30, 142.44, 140.93, 138.37, 130.13, 129.52, 128.72, 126.45, 124.60, 113.35, 85.69, 78.16, 66.72, 33.82, 27.13, 21.70, 1.06; HRMS (CI)

calcd for C₂₂H₂₆IO₄S (M⁺+H) 513.0597, found 513.0604.

Oxolane 9

To a stirred solution of **8** (1.54 g, 3.01 mmol) in dry toluene (120 mL, 0.025 M) were added tributylstannane (972 μ L, 3.61 mmol) and triethylborane (4.52 mL, 1.0 M solution in hexane) in sequence at -20°C . The resulting mixture was stirred for 30 min under air at the same temperature. Concentration and flash chromatography on silica gel (Kanto, Silica gel 60, Spherical; Hex-EtOAc, 1:2~0:1) furnished 2,5-disubstituted oxolane products (1.14g, 98 %) as a white solid: it was a 88:1 mixture of 2,5-*cis*- and 2,5-*trans*-disubstituted oxolane derivatives determined by HPLC analysis (Licrosorb, Hibar RT 250-4, Si 60, 5 μ m, hexane/EtOAc= 50:50, flow rate; 2 mL/min, column temperature; 24.1°C , detection at 254 nm). The solid was recrystallized from ethyl acetate-hexane to afford a pure sample of oxolane **9** (1.08g, 93%): mp $161.5\text{--}162.5^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{24} -153.3$ (c 1.00, CHCl₃); IR (neat) ν 2954, 2918, 2892, 1494, 1448, 1402, 1368, 1220, 1140, 1116, 1076, 1028, 918, 810, 760, 716, 622, 514 cm^{-1} ; ^1H NMR (CDCl₃) δ 7.46–7.18 (m, 9H), 5.53 (s, 1H), 4.52 (m, 1H), 4.33 (dd, J = 11.3, 4.2, 1H), 4.13 (dt, J = 6.8, 3.5 Hz, 1H), 3.97 (dt, J = 11.9, 2.2 Hz, 1H), 3.86 (dt, J = 11.6, 2.9 Hz, 1H), 2.97 (dd, J = 12.8, 8.9 Hz, 1H), 2.82 (dd, J = 12.9, 3.9 Hz, 1H), 2.38 (s, 3H), 2.27–1.97 (m, 3H), 1.73 (m, 1H), 1.47 (dd, J = 13.3, 1.2 Hz, 1H); ^{13}C NMR (CDCl₃) δ 141.96, 141.42, 139.11, 130.23, 129.02, 128.57, 126.37, 124.15, 101.58, 81.47, 78.79, 74.14, 67.40, 64.95, 31.77, 27.61, 26.98, 21.76; MS (EI) m/z 246 [M⁺–(CH₃C₆H₄SOH (140))], 163, 155 (100), 138, 107, 105, 95, 91, 83, 79, 77, 57; HRMS (CI) calcd for C₂₂H₂₇O₄S (M⁺+H) 387.1630, found 387.1635.

X-ray analysis. The X-ray data were collected on an Enraf-Nonius CAD4 automated diffractometer equipped with a Mo X-ray tube at room temperature.

Crystal data for **9**: C₂₂H₂₆O₄S, Mw=386.49, monoclinic, space group p2(1) (No. 4), $a=9.601(2)$, $b=21.070(2)$, $c=9.898(2)$ Å, $\alpha=90.00(2)$, $\beta=90.86(2)$, $\gamma=90.00(2)^{\circ}$, $V=2002.1(6)$ Å³, $Z=4$, $\rho_{\text{calcd}}=1.282$ Mg/m³, $F(000)=824$, $\mu=0.186\text{mm}^{-1}$, $\lambda(\text{MoK}\alpha)=0.71073$ Å, $T=293(2)$ K, $1.93<\theta<25.16$, reflections collected 3247, unique 3064 ($R_{\text{int}}=0.0329$), observed 3007 ($I>2\sigma(I)$), final R factors $R_1=0.0403$, $wR_2=0.1046$, GOF=1.051, parameters refined 487.

The structure solution and refinement of the data were handled with the SHELXS-86 and SHELXL-97 programs. CCDC 263911 (compound **9**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via WWW.ccdc.cam.ac.uk/data_request/cif.

Aldehyde **10**

To an acetonitrile solution (10 mL) of **9** (640.0 mg, 1.66 mmol) was added *sym*-collidine (1.1 mL, 8.30 mmol) and trifluoroacetic anhydride (467 μ L, 3.31 mmol) under nitrogen at 0 °C. After stirring at the same temperature for 20 min, solid KOAc (975 mg, 9.93 mmol, 6 equiv) and water (320 μ L, 10.7 eq.) were added to the reaction mixture. The resulting suspension was stirred at 0 °C for 1.5 h. Saturated aqueous NaHCO₃ solution was added to the mixture at 0 °C and the solution was extracted with ethyl acetate. The organic phase was washed with 1 N HCl, brine, saturated aqueous NaHCO₃, and brine. The organic layer was then dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (Hex-EtOAc, 1:1) afforded aldehyde **10** (374.7 mg, 86%) as a colorless oil: IR (neat) ν 3442, 2960, 2924, 2856, 1730, 1454, 1370, 1310, 1244, 1216, 1106, 1022, 758, 700 cm⁻¹; ¹H NMR (CDCl₃) δ 9.75 (d, J = 1.6 Hz, 1H), 7.47–7.33 (m, 5H), 5.53 (s, 1H), 4.34–4.21 (m, 2H), 4.19 (dt, J = 6.9, 4.7 Hz, 1H), 3.98 (dt, J = 12.0, 2.4 Hz, 1H), 3.91 (ddd, J = 11.6, 4.6, 2.4 Hz, 1H), 2.20–1.76 (m, 4H), 1.48 (dd, J = 13.2, 1.3 Hz, 1H); ¹³C NMR (CDCl₃) δ 204.07, 138.76, 129.23, 128.62, 126.53, 101.94, 84.00, 82.88, 79.49, 67.19, 28.28, 27.54, 27.43; MS (EI) m/z 261 (M⁺–H), 233, 216, 188, 175, 163 (100), 139, 127, 107, 105, 97, 91, 79, 69, 55.

Alcohol **11**

To a stirred solution of **10** (292.1 mg, 1.11 mmol) in THF (7 mL) was added *n*-decylmagnesium bromide (1.0 M in THF, 4.45 mL, 4 equiv, prepared from Mg (162.3 mg, 6.68 mmol), 1-bromodecane (924 μ L, 4.45 mmol) and a catalytic amount of I₂) under argon at 0 °C. The reaction mixture was stirred for 1 h, and allowed to warm to room temperature. After 8 h at room temperature, saturated aqueous NH₄Cl was added at 0 °C and the mixture was extracted with ethyl acetate. The organic layers were washed with brine and dried over MgSO₄, filtered and

concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (Hex-EtOAc, 7:1 ~ 3:1) gave alcohol **11** (256 mg, 57%) followed by the *threo* epimer (135 mg, 30%).

Alcohol 11: $[\alpha]_D^{25} +12.8$ (*c* 0.96, CHCl₃); IR (neat) ν 3506 (br), 2924, 2854, 1464, 1366, 1306, 1242, 1216, 1106, 1082, 1024, 754, 698 cm⁻¹; ¹H NMR (CDCl₃) δ 7.49–7.31 (m, 5H), 5.51 (s, 1H), 4.31 (dd, *J* = 11.4, 4.3 Hz, 1H), 4.03–3.83 (m, 5H), 2.58 (br. s, 1H), 2.13 (dq, *J* = 12.4, 5.1 Hz, 1H), 1.99–1.73 (m, 4H), 1.46 (dd, *J* = 13.2, 1.2 Hz, 1H), 1.4–1.1 (m, 18H), 0.88 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (CDCl₃) δ 138.69, 129.21, 128.65, 126.51, 102.08, 83.30, 81.06, 79.22, 72.41, 67.35, 33.04, 32.29, 30.09, 30.00, 29.94, 29.71, 28.10, 27.97, 26.35, 24.25, 23.07, 14.50; MS (EI) *m/z* 404 (M⁺), 297, 280, 267, 263, 241, 235, 216, 205, 188, 175 (100), 172, 163, 160, 159, 127, 107, 105, 97, 91, 85, 83, 81, 79, 71, 69, 57, 55; HRMS (EI) calcd for C₂₅H₄₀O₄ (M⁺) 404.2927, found 404.2923.

Epimer (*threo*) of 11: $[\alpha]_D^{25} +11.4$ (*c* 1.00, CHCl₃); IR (neat) ν 2924, 2854, 1460, 1372, 1308, 1242, 1216, 1108, 1024, 756, 698 cm⁻¹; ¹H NMR (CDCl₃) δ 7.50–7.31 (m, 5H), 5.51 (s, 1H), 4.32 (ddd, *J* = 11.4, 4.0, 1.1 Hz, 1H), 4.04 (m, 1H), 3.96 (dt, *J* = 12.0, 2.6 Hz, 1H), 3.90–3.82 (m, 2H), 3.36 (br. s, 1H), 2.65 (br. s, 1H), 2.16 (dq, 12.4, 5.0 Hz, 1H), 2.04–1.78 (m, 4H), 1.49–1.15 (m, 19H), 0.88 (t, *J* = 6.7, 3H); ¹³C NMR (CDCl₃) δ 138.74, 129.27, 128.65, 126.53, 102.09, 83.15, 81.24, 79.19, 74.51, 67.39, 34.71, 32.31, 30.12, 30.04, 29.74, 28.53, 28.07, 27.59, 26.23, 23.09, 14.51; MS (EI) *m/z* 404 (M⁺), 297, 281, 263, 241, 235, 216, 205, 188, 175 (100), 172, 163, 160, 159, 127, 107, 105, 97, 91, 85, 83, 81, 79, 71, 69, 57, 55.

Tosylate 12

To a solution of alcohol **11** (367.2 mg, 0.91 mmol) in 5 mL CH₂Cl₂ and 0.5 mL of DMF were added imidazole (309 mg, 4.54 mmol) and TBSCl (547 mg, 3.63 mmol). After 18 h, the reaction mixture was partitioned between 30 ml of saturated aqueous NH₄Cl solution and 50 ml of ether. The aqueous layer was extracted twice with 30 ml of ether. The combined organic layers were washed with 30 ml of a saturated aqueous NaCl solution, and dried with MgSO₄. The mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (Hex-EtOAc, 20:1) to afford TBS ether **11A** (470.7 mg, 100%) as a colorless oil: $[\alpha]_D^{25} +20.8$ (*c* 1.0, CHCl₃); IR (neat) ν 2926, 2854, 1464, 1364, 1250, 1108, 1088, 1028, 836, 774, 696 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.49 (dd, *J* = 7.5, 1.9 Hz, 2H), 7.37–7.29 (m, 3H), 5.50 (s, 1H), 4.29 (dd, *J* = 11.3, 4.5 Hz, 1H), 4.01–3.79 (m, 4H), 3.74 (q, *J* = 5.0 Hz, 1H), 2.00–1.62 (m, 5H),

1.51~1.2 (m, 19H), 0.89 (s, 9H), 0.88 (t, $J = 7.1$ Hz, 3H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 138.69, 128.66, 128.15, 126.25, 101.37, 82.18, 80.88, 79.55, 73.13, 66.91, 34.97, 31.92, 29.98, 29.63, 29.35, 27.18, 26.97, 26.00, 25.91, 24.83, 18.18, 14.14, -4.09, -4.31; MS (EI) m/z 461, 369, 355, 337, 285, 263, 227, 185, 171, 162, 131, 115, 97, 75, 73.

To a solution of **11A** (458.7 mg, 0.88 mmol) in ethyl acetate (20 mL) was added palladium on activated carbon (46 mg, 10% w/w). The mixture was stirred under hydrogen atmosphere for 18 h and then filtered through a pad of celite. After solvent evaporation, flash chromatography of the residue on silica gel (Hex-EtOAc, 2:1) gave 1,3-diol **11B** (372.5 mg, 98% yield): $[\alpha]_D^{25} + 13.1$ (c 1.02, CHCl_3); IR (neat) ν 3368, 2926, 2856, 1464, 1252, 1072, 836, 774 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.88~3.74 (m, 5H), 3.67 (m, 1H), 2.76 (s, OH, 2H), 1.97~1.56 (m, 6H), 1.52~1.40 (m, 2H), 1.38~1.2 (m, 16H), 0.89 (s, 9H), 0.88 (t, $J = 7.0$ Hz, 3H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 82.24, 82.16, 74.42, 73.04, 60.97, 35.48, 34.99, 31.89, 29.91, 29.57, 29.32, 27.76, 25.90, 25.78, 24.94, 22.67, 18.11, 14.10, -4.10, -4.29; MS (EI) m/z 429 ($\text{M}^+ - \text{H}$), 411, 355, 337, 285, 263, 245, 227, 171, 157, 149, 131, 115, 101, 75, 73; HRMS (CI) calcd for $\text{C}_{24}\text{H}_{51}\text{O}_4\text{Si}$ ($\text{M}^+ + \text{H}$) 431.3557, found 431.3552.

To a solution of **11B** (354.8 mg, 0.82 mmol) and triethylamine (276 μL , 1.98 mmol) in dry CH_2Cl_2 (3 mL, 0.3 M) was added *p*-toluenesulfonyl chloride (220.0 mg, 1.2 mmol) at 0 $^\circ\text{C}$. The reaction mixture was stirred for 12 h at 0 $^\circ\text{C}$, and then it was treated with aqueous 1 N HCl (5 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (20 mL x 2). The combined organic layers were washed with brine, dried over MgSO_4 , and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 5:1) to give tosylate **12** (452.6 mg, 94% yield) as an oil: $[\alpha]_D^{25} + 3.8$ (c 1.01, CHCl_3); IR (neat) ν 3560, 2926, 2854, 1466, 1362, 1254, 1178, 1078, 968, 914, 836, 774, 664 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.79 (d, $J = 8.3$ Hz, 2H), 7.34 (d, $J = 8.1$ Hz, 2H), 4.23~4.18 (m, 2H), 3.85~3.72 (m, 3H), 3.69 (q, $J = 6.2$ Hz, 1H), 3.50 (m, 1H), 2.45 (s, 3H), 2.40 (d, $J = 5.5$ Hz, OH, 1H), 1.95~1.56 (m, 6H), 1.50~1.20 (m, 18H), 0.88 (t, $J = 6.4$ Hz, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 144.66, 133.10, 129.82, 127.94, 82.13, 81.78, 72.97, 70.61, 67.65, 35.01, 33.42, 31.90, 29.91, 29.58, 29.34, 27.79, 25.90, 25.63, 24.95, 22.69, 21.65, 18.10, 14.13, -4.07, -4.34; MS (EI) m/z 391, 373, 355, 337, 299, 285 (100), 271, 227, 193, 157, 115, 75, 73, 57; HRMS (CI) calcd for $\text{C}_{31}\text{H}_{57}\text{O}_6\text{SSi}$ ($\text{M}^+ + \text{H}$) 585.3645, found 585.3628.

Tosylate 13

To a solution of **12** (444.9 mg, 0.76 mmol) and (–)-(S)-ethynyl *p*-tolyl sulfoxide **7** (250.0 mg, 1.52 mmol, 2.0 equiv) in dry CH₂Cl₂ (8 mL) was added *N*-methylmorpholine (83.6 μL, 0.76 mmol, 1.0 equiv) at 0 °C. After stirring for 12 h at ambient temperature, (–)-(S)-ethynyl *p*-tolyl sulfoxide **7** (250.0 mg, 2.0 equiv) and *N*-methylmorpholine (83.6 μL, 1.0 equiv) were added three times at eight-hour intervals. After stirring for 8 h at ambient temperature, aqueous 1 N HCl (10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. Charcoal (3 g) was added to the ethyl acetate solution of the residue. The mixture was stirred for 10 min, filtered through a pad of silica gel, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hex-EtOAc, 5:1~1.5:1) to give alcohol **12** (97.9 mg, 22% recovery) and tosylate **13** (310.7 mg, 54% yield): $[\alpha]_D^{25} + 70.6$ (*c* 1.30, CHCl₃); IR (neat) ν 2924, 2854, 1618, 1464, 1362, 1180, 1082, 1042, 926, 834, 774, 662 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.79 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.9 Hz, 2H), 7.10 (d, *J* = 12.4 Hz, 1H), 5.72 (d, *J* = 12.4 Hz, 1H), 4.19 (qui, *J* = 5.0 Hz, 1H), 4.04 (td, *J* = 9.6, 4.6 Hz, 1H), 3.88 (m, 1H), 3.77 (qui, *J* = 6.4 Hz, 2H), 3.65 (q, *J* = 5.0 Hz, 1H), 2.48 (s, 3H), 2.40 (s, 3H), 2.06~1.80 (m, 5H), 1.55~1.40 (m, 3H), 1.36~1.2 (m, 16H), 0.88 (m, 9H+3H), 0.05 (s, 3H), 0.03 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 158.73, 145.25, 142.25, 140.54, 132.63, 130.17, 129.74, 127.88, 124.37, 112.97, 82.91, 82.20, 80.87, 73.30, 65.98, 34.83, 31.90, 31.10, 30.02, 29.69, 29.62, 29.34, 27.68, 26.06, 25.91, 24.56, 22.68, 21.69, 21.31, 18.11, 14.11, –4.06, –4.13; HRMS (FAB) calcd for C₄₀H₆₅O₇S₂Si (M⁺+H) 749.3941, found 749.3942.

Bis-oxolane **14**

The substitution reaction as described for **8** and flash chromatography (Hex-EtOAc, 3:1) converted **13** (292.3mg, 0.39 mmol) into iodide **13A** (251.3 mg, 91%): $[\alpha]_D^{22} + 47.7$ (*c* 1.01, CHCl₃); IR (neat) ν 2926, 2854, 1618, 1464, 1378, 1252, 1216, 1178, 1082, 1042, 834, 808, 776 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 12.3 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 2H), 5.84 (d, *J* = 12.4 Hz, 1H), 3.97 (m, 1H), 3.89~3.79 (m, 2H), 3.70 (q, *J* = 4.9 Hz, 1H), 3.31 (m, 1H), 3.18 (td, *J* = 9.7, 6.1 Hz, 1H), 2.40 (s, 3H), 2.2~1.8 (m, 5H), 1.6~1.42 (m, 3H), 1.40~1.2 (m, 16H), 0.89 (s, 9H), 0.88 (t, *J* = 6.8 Hz, 3H), 0.07 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 159.18, 142.26, 140.51, 129.72, 124.39, 112.81, 86.64, 82.20, 80.59, 73.26, 35.03, 34.89, 31.89, 29.99, 29.66, 29.62, 29.34, 27.80, 25.95, 25.84, 24.68, 22.68, 21.33, 18.13, 14.14, 1.25, -4.00, -4.09.

To a stirred solution of **13A** (230.0 mg, 0.33 mmol) in dry toluene (13 mL, 0.025 M) were added tributylstannane (0.114 mL, 0.42 mmol, 1.3 equiv) and triethylborane (0.49 mL, 1.5 equiv, 1.0 M solution in hexane) at -20 °C. The resulting mixture was stirred for 30 min under air at the same temperature. Concentration and flash chromatography of the residue on silica gel (Kanto, Silica gel 60, Spherical; Hex-EtOAc, 3:1~2:1) provided bis-oxolane **14** (183.3 mg, 97% yield): $[\alpha]_D^{25} - 56.1$ (*c* 1.00, CHCl₃); IR (neat) ν 2926, 2854, 1494, 1464, 1386, 1252, 1086, 1054, 836, 808, 774 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.39 (qui, *J* = 6.3 Hz, 1H), 3.87 (q, *J* = 6.7 Hz, 1H), 3.83~3.68 (m, 3H), 2.94 (ABX, *J* = 12.9, 7.2 Hz, 1H), 2.90 (ABX, *J* = 13.1, 5.6 Hz, 1H), 2.41 (s, 3H), 2.15~1.52 (m, 8H), 1.50~1.2 (m, 18H), 0.88 (m, 9H+3H), 0.06 (s, 3H), 0.05 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 141.59, 141.36, 129.94, 123.85, 82.27, 81.81, 81.79, 73.84, 73.39, 64.12, 34.93, 31.90, 31.26, 29.94, 29.60, 29.33, 27.84, 26.16, 25.96, 24.70, 22.68, 21.39, 18.14, 14.12, -4.05, -4.28; HRMS (FAB) calcd for C₃₃H₅₉O₄SSi (M⁺+H) 579.3903, found 579.3908.

Aldehyde **15**

To an acetonitrile solution (4.5 mL) of **14** (145.8 mg, 0.252 mmol) were added pyridine (102.7 μ L, 1.26 mmol, 5 equiv) and trifluoroacetic anhydride (71 μ L, 0.503 mmol, 2 equiv) under argon at 0 °C. After stirring at the same temperature for 30 min, solid KOAc (148 mg, 1.51 mmol, 6 equiv)

and water (50 μ L) were added to the reaction mixture. The resulting suspension was stirred at 0 $^{\circ}$ C for 2 h. Saturated aqueous NaHCO_3 solution was added to the mixture at 0 $^{\circ}$ C and the solution was extracted with ethyl acetate. The organic phase was washed with 1 N HCl, brine, saturated aqueous NaHCO_3 , and brine. The organic layer was dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography (Hex-EtOAc, 5:1) afforded aldehyde **15** (90.0 mg, 79%) as a colorless oil: $[\alpha]_D^{20} + 42.8$ (*c* 0.86, CHCl_3); IR (neat) ν 2926, 2856, 1736, 1464, 1252, 1070, 836, 774 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.68 (d, *J* = 1.65 Hz, 1H), 4.23 (dt, *J* = 6.7, 1.6 Hz, 1H), 3.94 (dt, *J* = 8.7, 6.5 Hz, 1H), 3.78 (m, 1H), 3.70 (m, 2H), 2.05 (m, 2H), 1.94–1.67 (m, 5H), 1.54–1.32 (m, 4H), 1.3–1.15 (m, 15H), 0.82 (m, 9H+3H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 203.54, 83.50, 83.41, 82.40, 82.06, 73.24, 35.00, 31.89, 29.87, 29.58, 29.32, 28.01, 27.93, 25.95, 24.84, 22.66, 18.12, 14.09, –4.05, –4.35; MS (EI) *m/z* 453 ($\text{M}^+ - \text{H}$), 439, 425, 397, 379, 355, 337, 305, 285 (100), 269, 257, 227, 211, 185, 169, 157, 143, 125, 95, 75, 73, 55; HRMS (FAB) calcd for $\text{C}_{26}\text{H}_{51}\text{O}_4\text{Si}$ ($\text{M}^+ + \text{H}$) 455.3557, found 455.3553.

Homoallylic alcohol **16**

To a solution of **15** (86.3 mg, 0.19 mmol) and $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ (147 mg, 0.57 mmol, 3 equiv) in CH_2Cl_2 (3 mL) was added allyltributylstannane (118 μ L, 0.38 mmol, 2 equiv) at 0 $^{\circ}$ C. After stirring for 2 h at room temperature, dichloromethane (10 mL) and saturated aqueous NH_4Cl solution (5 mL) were added to the reaction mixture. The aqueous phase was extracted with CH_2Cl_2 (10 mL x 2), and the combined organic extracts were washed with brine, dried over MgSO_4 , and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Kanto, Silica gel 60, Spherical; Hex-EtOAc, 9:1) to give homoallylic alcohol **16** (90.3 mg, 96% yield) as a colorless oil: $[\alpha]_D^{20} + 14.3$ (*c* 0.88, CHCl_3); IR (neat) ν 3448, 2926, 2856, 1464, 1252, 1064, 910, 836, 774 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.84 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.08–4.98 (m, 2H), 3.83–3.77 (m, 2H), 3.75–3.63 (m, 3H), 3.42 (q, *J* = 5.9 Hz, 1H), 2.71 (br. s, 1H, OH), 2.21 (m, 2H), 1.93–1.37 (m, 10H), 1.34–1.15 (m, 16H), 0.82 (m, 9H+3H), 0.00 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 135.12, 116.84, 82.30, 81.89, 81.79, 81.58, 73.87, 73.60, 38.77, 34.93, 31.90, 29.95, 29.61, 29.34, 28.37, 28.01, 27.87, 26.74, 25.95, 24.54, 22.67, 18.14, 14.10, –4.17, –4.29; MS (EI) *m/z* 481, 455, 439, 421, 403, 369, 355, 337, 323, 305, 285, 271, 249, 227, 211, 185, 171, 125, 97, 75, 73, 55; MS (FAB) *m/z* 497 ($\text{M}^+ + \text{H}$), 439, 365, 355, 347, 311, 285, 211, 185, 171, 139, 125, 115, 109, 97, 75, 73, 55; HRMS (FAB) calcd for $\text{C}_{29}\text{H}_{57}\text{O}_4\text{Si}$ ($\text{M}^+ + \text{H}$) 497.4026, found 497.4024.

2. Synthesis of **16**: approach II

Homoallylic alcohol **23**

Homoallylic alcohol **23** was prepared from D-malic acid (**17**) and (+)-(R)-ethynyl *p*-tolyl sulfoxide **19** via the known ten-step sequence reported previously for the synthesis of *ent*-**23**.²

23: $[\alpha]_{\text{D}}^{25} + 8.7$ (*c* 1.01, CHCl_3); IR (neat) ν 3458 (br.) 2866, 1640, 1452, 1366, 1294, 1208, 1074, 912, 738, 698 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.38–7.25 (m, 5H), 5.88 (ddt, $J = 17.2, 10.1, 7.0$ Hz, 1H), 5.14–5.05 (m, 2H), 4.58, 4.56 (ABq, $J = 12.2$ Hz, 2H), 4.20–4.12 (m, 1H), 3.93–3.85 (m, 1H), 3.59 (ABX, $J = 10.0, 3.9$ Hz, 1H), 3.48 (m, 1H), 3.45 (ABX, $J = 10.0, 4.6$ Hz, 1H), 2.84 (br. s, 1H), 2.27 (dt, $J = 7.0, 1.1$ Hz, 2H), 1.97–1.80 (m, 4H); ^{13}C NMR (CDCl_3) δ 138.36, 135.50, 128.83, 128.14, 117.38, 82.41, 78.88, 74.24, 73.77, 72.73, 39.35, 28.49, 28.42; MS m/z 262 (M^+), 244, 221, 191, 173, 155, 141, 129, 113, 101, 99, 91 (100), 83, 71, 65, 57, 55; HRMS (CI) calcd for $\text{C}_{16}\text{H}_{23}\text{O}_3$ ($\text{M}^+ + \text{H}$) 263.1647, found 263.1643.

Tosylate **24**

Homoallylic alcohol **23** (1.620 g, 6.18 mmol) in acetone-water (3:1, 20 mL) was treated with OsO₄ (78.5 mg, 0.31 mmol) and 4-methylmorpholine *N*-oxide (2.17 g, 18.52 mmol) at room temperature. After stirring for 1.5 h, acetone was removed under reduced pressure. Ethanol (30 mL) and NaIO₄ (3.960 g, 18.50 mmol) were added to the residue at room temperature, and vigorous stirring was continued for 1 h. The reaction mixture was cooled to 0 °C and NaBH₄ (0.700 g, 18.50 mmol) was added. After 30 min, the reaction was quenched by addition of saturated aqueous NH₄Cl solution (50 mL). The resulting mixture was extracted with ether (70 mL x 3) and the combined organic extracts were washed with saturated NaHSO₃ solution (40 mL) and brine (40 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. Flash chromatography of the residue (EtOAc/MeOH, 1:0~20:1) provided diol **23A** (1.467 g, 89%): [α]_D²³ +8.5 (*c* 1.01, CHCl₃); IR (neat) ν 3406 (br.), 2870, 1452, 1366, 1202, 1072, 738, 698 cm⁻¹; ¹H NMR (CDCl₃) δ 7.38–7.25 (m, 5H), 4.58, 4.55 (ABq, *J* = 12.0 Hz, 2H), 4.17 (m, 1H), 3.90 (m, 1H), 3.80 (m, 2H), 3.65 (m, 1H), 3.61 (ABX, *J* = 10.0, 3.7 Hz, 1H), 3.45 (ABX, *J* = 10.0, 4.4 Hz, 1H), 3.31 (d, *J* = 5.9 Hz, 1H, OH), 3.01 (br. s, 1H), 2.0–1.6 (m, 6H); ¹³C NMR (CDCl₃) δ 137.78, 128.47, 127.82, 82.77, 78.54, 73.99, 73.43, 72.32, 60.85, 35.97, 28.12, 27.88; MS *m/z* 266 (M⁺), 221, 217, 191, 173, 160, 145, 127, 107, 101, 91, 83, 71, 65, 57; HRMS (CI) calcd for C₁₅H₂₃O₄ (M⁺+H) 267.1596, found 267.1597.

Diol **23A** (1.797 g, 6.75 mmol) was converted into the corresponding tosylate **24** by the procedure as described for **12** in 90% yield (2.55 g) as an oil after flash chromatography (Hex-EtOAc, 1:1): [α]_D²⁵ –5.9 (*c* 1.0, CHCl₃); IR (neat) ν 3444, 2868, 1598, 1454, 1358, 1176, 1096, 964, 912, 816, 742, 698, 662 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.4–7.21 (m, 7H), 4.53 (ABq, *J* = 12.7, 2H), 4.20–4.09 (m, 3H), 3.80 (m, 1H), 3.59 (ABX, *J* = 10.0, 3.6 Hz, 1H), 3.49 (qui, *J* = 4.3 Hz, 1H), 3.42 (ABX, *J* = 10.0, 4.3 Hz, 1H), 2.64 (br. s, 1H, OH), 2.43 (s, 3H), 1.95–1.73 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 144.66, 137.78, 133.16, 129.83, 128.45, 127.90, 127.81, 127.78, 82.31, 78.61, 73.38, 72.19, 70.33, 67.93, 33.88, 28.13, 27.80, 21.63; MS (FAB) *m/z* 421 (M⁺+H), 391, 313, 279, 249, 191, 159, 149, 141, 137, 136, 91, 69, 57, 55, 43; HRMS (FAB) calcd for C₂₂H₂₈O₆S (M⁺+H) 421.1685, found 421.1683.

Iodide **25**

To a solution of **24** (2.477 g, 5.89 mmol) and (–)-(S)-ethynyl *p*-tolyl sulfoxide **7** (2.902 g, 17.67 mmol, 3.0 equiv) in dry CH₂Cl₂ (39 mL, 0.15 M) was added *N*-methylmorpholine (0.652 mL, 5.90 mmol, 1.0 equiv) at 0 °C. After stirring for 12 h at ambient temperature, aqueous 1 N HCl (20 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hex-EtOAc, 1:1) to give tosylate **24A** (2.75 g, 80%): [α]_D²³ + 100.1 (*c* 1.00, CHCl₃); IR (neat) ν 2866, 1620, 1452, 1358, 1176, 1084, 1038, 926, 812, 760, 664 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.38–7.20 (m, 9H), 7.14 (d, *J* = 12.4 Hz, 1H), 5.68 (d, *J* = 12.4 Hz, 1H), 4.54 (s, 2H), 4.15 (sxt, *J* = 5.1 Hz, 1H), 4.02 (dt, *J* = 9.6, 4.8 Hz, 1H), 3.91 (m, 1H), 3.49, 3.45 (ABX, *J* = 10.2, 5.2, 4.3 Hz, 2H), 2.46 (s, 3H), 2.38 (s, 3H), 2.04–1.60 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 158.71, 145.23, 142.25, 140.49, 138.04, 132.60, 130.13, 129.75, 128.47, 127.88, 127.75, 127.71, 124.38, 112.69, 82.41, 81.00, 78.96, 73.40, 72.39, 66.17, 30.78, 27.84, 27.64, 21.68, 21.31; MS (FAB) *m/z* 585 (M⁺+H), 568, 536, 495, 493, 477, 413, 403, 313, 273, 231, 183, 141, 139, 134, 123, 105, 97, 91, 55, 43; HRMS (FAB) calcd for C₃₁H₃₇O₇S₂ (M⁺+H) 585.1981, found 585.1990.

To a solution of **24A** (2.104 g, 3.60 mmol) in acetone (36 mL) was added NaI (1.618 g, 10.79 mmol, 3 equiv) at room temperature. The reaction mixture was heated under reflux for 9 h. The mixture was concentrated under reduced pressure, and the residue was partitioned between ethyl acetate and saturated aqueous NaCl and Na₂S₂O₃ solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (30 mL). The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hex-EtOAc, 3:2) to give iodide **25** (1.810 g, 93%) as a colorless oil: [α]_D²⁵ + 65.6 (*c* 1.00, CHCl₃); IR (neat) ν 2864, 1618, 1492, 1452, 1370, 1214, 1176, 1082, 1038, 810, 738, 698 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.49 (d, *J* = 8.2 Hz, 2H), 7.36–7.14 (m, 8H), 5.80 (d, *J* = 12.5 Hz, 1H), 4.56 (s, 2H), 4.17 (m, 1H), 3.99 (m, 2H), 3.53, 3.48 (ABX, *J* = 10.1, 4.9, 4.0 Hz, 2H), 3.28 (ddd, *J* = 10.0, 6.5, 4.8 Hz, 1H), 3.14 (dt, *J* = 9.6, 6.2 Hz, 1H), 2.38 (s, 3H), 2.17–1.65 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 159.06, 142.30, 140.49, 138.07, 129.74, 128.46, 127.75, 127.73, 124.42, 112.61, 86.02, 80.75, 78.96, 73.45, 72.52, 34.77, 27.90, 27.74, 21.31, 1.21; MS (FAB) *m/z* 542, 541 (M⁺+H), 524, 492, 449, 413, 379, 297, 269, 223, 183, 139, 91, 55, 43; HRMS (FAB) calcd for C₂₄H₃₀IO₄S (M⁺+H) 541.0910, found 541.0918.

Bis-oxolane 26

To a stirred solution of iodide **25** (1.736 g, 3.21 mmol) in dry toluene (128 mL, 0.025 M) were added tributylstannane (1.04 mL, 3.87 mmol, 1.2 equiv) and triethylborane (4.8 mL, 1.5 equiv, 1.0 M solution in hexane) at -20°C . The resulting mixture was stirred for 30 min under air at the same temperature. Concentration and flash chromatography of the residue on silica gel (Kanto, Silica gel 60, Spherical; Hex-EtOAc, 1:2~0:1) furnished the simple reduction product (66 mg, 5% yield) and bis-oxolane **26** (1.265 g, 95% yield): $[\alpha]_{\text{D}}^{24} - 86.7$ (*c* 1.01, CHCl_3); IR (neat) ν 2870, 1494, 1452, 1384, 1206, 1086, 1046, 810, 738, 698 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.50 (d, $J = 8.2$ Hz, 2H), 7.31–7.22 (m, 7H), 4.53, 4.51 (ABq, $J = 12.2$ Hz, 2H), 4.39 (qui, $J = 6.6$ Hz, 1H), 4.14 (qui, $J = 5.8$ Hz, 1H), 3.94–3.83 (m, 2H), 3.48, 3.44 (ABX, $J = 9.8, 5.4, 5.0$ Hz, 2H), 2.87 (d, $J = 6.4$ Hz, 2H), 2.40 (s, 3H), 2.10–1.61 (m, 8H); ^{13}C NMR (75 MHz, CDCl_3) δ 141.59, 141.36, 138.36, 129.94, 128.33, 127.61, 127.53, 123.89, 81.77, 81.71, 78.58, 73.71, 73.22, 72.79, 64.22, 31.34, 28.31, 27.84, 27.64, 21.40; MS (FAB) m/z 415 ($\text{M}^+ + \text{H}$), 397, 325, 307, 293, 275, 223, 207, 154, 139, 91, 55, 43; HRMS (FAB) calcd for $\text{C}_{24}\text{H}_{31}\text{O}_4\text{S}$ ($\text{M}^+ + \text{H}$) 415.1943, found 415.1940.

Aldehyde 27

To an acetonitrile solution (22 mL) of **26** (1.095 g, 2.64 mmol) were added pyridine (0.861 mL, 10.6 mmol, 4.0 equiv) and trifluoroacetic anhydride (0.559 mL, 3.96 mmol, 1.5 equiv) under argon at 0°C . After stirring at the same temperature for 20 min, solid KOAc (1.554 g, 15.84 mmol, 6 equiv) and water (0.728 mL, 15 equiv) were added to the reaction mixture. The resulting suspension was stirred at 0°C for 80 min. Saturated aqueous NaHCO_3 solution was added to the mixture at 0°C and the solution was extracted with ethyl acetate. The organic phase was washed with 1 N HCl,

brine, saturated aqueous NaHCO_3 , and brine. The organic layer was then dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography (Hex-EtOAc, 1:1~1:2) afforded aldehyde **27** (598 mg, 78%) as a colorless oil: $[\alpha]_D^{25} + 71.4$ (c 1.00, CHCl_3); IR (neat) ν 3422, 2870, 1730, 1452, 1366, 1194, 1070, 738, 698 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.71 (d, $J = 1.7\text{ Hz}$, 1H), 7.34–7.26 (m 5H), 4.56 (s, 2H), 4.26 (dt, $J = 9.7, 3.5\text{ Hz}$, 1H), 4.16 (m, 1H), 4.03 (td, $J = 7.7, 6.1\text{ Hz}$, 1H), 3.88 (td, $J = 7.6, 6.0\text{ Hz}$, 1H), 3.52, 3.48 (ABX, $J = 10.0, 5.3, 5.3\text{ Hz}$, 2H), 2.11 (td, $J = 8.2, 1.9\text{ Hz}$, 1H), 2.01–1.61 (m, 7H); ^{13}C NMR (75 MHz, CDCl_3) δ 203.60, 138.36, 128.33, 127.67, 127.55, 83.51, 83.10, 81.98, 78.66, 73.36, 72.66, 28.25, 27.95, 27.92, 27.66; MS (EI) m/z 290 (M^+), 272, 261, 191, 181, 169, 155, 141, 129, 125, 107, 91 (100), 79, 65, 55.

Alcohol **28**

A solution of **27** (495.3 mg, 1.71 mmol) in ether (6 mL) was added dropwise to a solution of *n*-decylmagnesium bromide (8.53 mL, 5 equiv, 1 M in ether) at $-78\text{ }^\circ\text{C}$. After stirring for 2 h, the reaction mixture was allowed to warm to room temperature. The reaction mixture was then treated with saturated aqueous NH_4Cl (10 mL) and ether (10 mL). The aqueous layer was extracted twice with ether (20 mL). The combined organic layers were washed with brine, dried over MgSO_4 , and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hex-EtOAc, 3:1) to afford a mixture (*threo*:*erythro* = 1.7:1 by ^{13}C NMR) of epimeric alcohols **27A** (604 mg, 82% yield).

A solution of oxalyl chloride (0.262 mL, 3.00 mmol, 1.8 equiv) in CH_2Cl_2 (8 mL) under argon was treated with a solution of DMSO (0.369 mL, 3.11 equiv) in CH_2Cl_2 (2 mL) in 10 min at $-78\text{ }^\circ\text{C}$. After 15 min at $-78\text{ }^\circ\text{C}$, a solution of **27A** (722.4 mg, 1.67 mmol) in CH_2Cl_2 (8 mL) was added in 5 min. After 15 min at $-78\text{ }^\circ\text{C}$, triethylamine (1.91 mL, 13.7 mmol, 8.2 equiv) was added in 15 min, and the mixture was allowed to warm to room temperature. The reaction was quenched by addition of 20 mL of water, and the reaction mixture was extracted twice with CH_2Cl_2 (20 mL). The combined organic layers were washed with saturated aqueous NaCl (15 mL), and dried over MgSO_4 . The filtrate was concentrated in vacuo, and the residue was purified by flash chromatography on silica gel (Hex-EtOAc, 5:1) to give ketone **27B** (686.2 mg, 95% yield): ^1H NMR (300 MHz, CDCl_3) δ 7.35–7.24 (m, 5H), 4.49 (s, 2H), 4.25 (dd, $J = 8.3, 6.0\text{ Hz}$, 1H), 4.10 (qui, 1H), 3.85 (m,

2H), 3.47 (ABX, $J = 9.8, 5.1$ Hz, 1H), 3.40 (ABX, $J = 9.8, 5.3$ Hz, 1H), 2.6–2.4 (m, 2H), 2.0–1.4 (m, 8 H), 1.3–1.0 (m, 16 H), 0.81 (t, $J = 6.6$ Hz, 3H).

To a solution of **27B** (686.2 mg, 1.59 mmol) in THF (17 mL) at -78 °C, L-Selectride (4.78 mL, 3.0 equiv, 1 M in THF) was added. After stirring for 2 h at -78 °C, 2 N NaOH (10 mL) and 30% H_2O_2 (10 mL) were added at 0 °C. The mixture was stirred for 1 h and then treated with water (25 mL) and ethyl acetate (25 mL). The aqueous layer was extracted with ethyl acetate (30 mL). The combined organic layers were washed with saturated aqueous NaHCO_3 and saturated aqueous NaCl, and dried over MgSO_4 . Removal of the solvent gave a crude mixture (*threo:erythro* = 19:81 by ^{13}C NMR, 8:92 by GLC) of the epimeric alcohols. Purification of the residue by flash chromatography on silica gel (hexane/ethyl acetate, 5:1~3:1) gave alcohol **28** (536 mg, 78% yield) and its *threo* epimer (125 mg, 18% yield).

Alcohol 28: $[\alpha]_{\text{D}}^{25} + 19.6$ (c 0.94, CHCl_3); IR (neat) ν 3464, 2924, 2854, 1458, 1366, 1074, 734, 698 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.35–7.24 (m, 5H), 4.55 (s, 2H), 4.13 (m, 1H), 3.93–3.73 (m, 4H), 3.53, 3.50 (ABX, $J = 9.7, 4.9, 4.8$ Hz, 2H), 2.99 (br. s, 1H), 2.0–1.7 (m, 8H), 1.48–1.15 (m, 18H), 0.88 (t, $J = 6.7$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 138.38, 128.29, 127.71, 127.49, 82.98, 81.66, 80.87, 78.46, 73.33, 72.44, 72.19, 32.72, 31.91, 29.73, 29.63, 29.59, 29.34, 28.73, 28.17, 27.91, 26.08, 23.98, 22.69, 14.12; MS (EI) m/z 432 (M^+), 323, 311, 293, 275, 261, 241, 217, 205, 191, 173, 160, 141, 129, 111, 91 (100), 71, 55; HRMS (CI) calcd for $\text{C}_{27}\text{H}_{45}\text{O}_4$ ($\text{M}^+\text{+H}$) 433.3318, found 433.3317.

Epimer (*threo*) of 28: $[\alpha]_{\text{D}}^{25} + 15.4$ (c 1.59, CHCl_3); IR (neat) ν 3452, 2924, 2854, 1456, 1192, 1076, 734, 696 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.34–7.23 (m, 5H), 4.55, 4.53 (ABq, $J = 12.3$ Hz, 2H), 4.13 (qui, $J = 5.7$ Hz, 1H), 3.95–3.82 (m, 3H), 3.52, 3.48 (ABX, $J = 8.6, 4.1, 3.8$ Hz, 2H), 3.35 (m, 1H), 2.85 (br. s, 1H), 1.98–1.7 (m, 8H), 1.5–1.15 (m, 18H), 0.88 (t, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 138.34, 128.32, 127.71, 127.53, 82.60, 81.72, 81.26, 78.52, 74.45, 73.32, 72.55, 34.37, 31.91, 29.77, 29.66, 29.34, 28.33, 28.24, 27.82, 25.89, 22.69, 14.11; MS (EI) m/z 432 (M^+), 414, 323, 311, 291, 275, 261, 241, 217, 205, 191, 173, 160, 141, 129, 91, 71, 55.

Aldehyde 15

To a stirred solution of **28** (533.4 mg, 1.23 mmol) in CH_2Cl_2 (8 mL) and DMF (2 mL) were added imidazole (420 mg, 6.17 mmol) and TBSCl (743 mg, 4.93 mmol). After 8 h at room

temperature, the reaction mixture was concentrated and a mixture of hexane and ethyl acetate (2:1, 20 mL) was added. The reaction mixture was quenched with aqueous NH_4Cl (10 mL), and aqueous layer was extracted twice with a mixture of hexane and ethyl acetate (2:1, 20 mL). The combined organic layers were washed three times with brine, dried over MgSO_4 , and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (Hex-EtOAc, 15:1) afforded TBS ether **28A** (670.3 mg, 99% yield): $[\alpha]_D^{24} + 20.3$ (*c* 1.38, CHCl_3); IR (neat) ν 2926, 2856, 1462, 1364, 1252, 1088, 836, 774, 734 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.28–7.18 (m, 5H), 4.51, 4.49 (ABq, $J = 12.2$ Hz, 2H), 4.08 (qui, $J = 5.8$ Hz, 1H), 3.82–3.63 (m, 4H), 3.50, 3.38 (ABX, $J = 9.7, 5.8, 4.8$ Hz, 2H), 1.83–1.31 (m, 10H), 1.30–0.80 (m, 16H), 0.83 (m, 9H+3H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 138.51, 128.31, 127.63, 127.49, 82.20, 78.37, 73.39, 73.35, 72.91, 35.00, 31.92, 29.94, 29.63, 29.35, 28.45, 27.85, 27.66, 25.99, 25.89, 24.84, 18.16, 14.12, –4.00, –4.31; MS (EI) m/z 546 (M^+), 489, 425, 397, 381, 355, 330, 305, 285, 261, 227, 171, 155, 131, 115, 91, 73, 55; HRMS (CI) calcd for $\text{C}_{33}\text{H}_{59}\text{O}_4\text{Si}$ (M^++H) 547.4182, found 547.4183.

TBS ether **28A** (670.3 mg, 1.23 mmol) was dissolved in ethyl acetate (20 mL) and palladium on activated carbon (62 mg, 10% w/w) was added. The mixture was stirred under hydrogen atmosphere for 14 h and then filtered through a pad of celite. After solvent evaporation, purification of the residue by flash chromatography on silica gel (Hex-EtOAc, 3:1) yielded alcohol **28B** (543.6 mg, 98% yield): $[\alpha]_D^{26} + 6.5$ (*c* 0.91, CHCl_3); IR (neat) ν 3450 (br. s), 2926, 2856, 1464, 1252, 1062, 836, 774 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 4.02 (m, 1H), 3.84–3.64 (m, 4H), 3.42 (dd, $J = 11.5, 4.0$ Hz, 1H), 2.24 (br. s, 1H, OH), 1.90–1.32 (m, 10H), 1.30–1.15 (m, 16H), 0.82 (m, 9H+3H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 82.31, 82.17, 82.04, 79.89, 73.42, 65.13, 34.95, 31.90, 29.92, 29.61, 29.33, 28.64, 28.09, 27.05, 26.08, 25.96, 24.74, 22.68, 18.14, 14.11, –4.11, –4.32; MS (EI) m/z 441, 425, 399, 381, 369, 355, 307, 285 (100), 271, 227, 201, 183, 171, 157, 131, 115, 101, 75, 73, 57; HRMS (FAB) calcd for $\text{C}_{26}\text{H}_{53}\text{O}_4\text{Si}$ (M^++H) 457.3713, found 457.3717.

A solution of oxalyl chloride (0.187 mL, 2.14 mmol, 1.8 equiv) in CH_2Cl_2 (6 mL) was treated with a solution of DMSO (0.263 mL, 3.71 mmol, 3.11 equiv) in CH_2Cl_2 (2 mL) in 10 min at -78°C under argon. After stirring for 15 min at -78°C , a solution of **28B** (543.6 mg, 1.19 mmol) in CH_2Cl_2 (6 mL) was added in 5 min. After 15 min at -78°C , triethylamine (1.36 mL, 9.76 mmol, 8.2 equiv) was added in 15 min, and the mixture was allowed to warm to room temperature. The reaction mixture was treated with water (20 mL), and extracted twice with CH_2Cl_2 (20 mL). The combined organic layers were washed with saturated aqueous NaCl (15 mL) and dried over MgSO_4 . The filtrate was concentrated in vacuo, and the residue was purified by flash chromatography on silica gel (Hex-EtOAc, 5:1) to give aldehyde **15** (530.1 mg, 98% yield): $[\alpha]_D^{25} + 51.2$ (*c* 0.78, CHCl_3).

Homoallylic alcohol 16

To a solution of the aldehyde **15** (prepared from **28**, 519.5 mg, 1.14 mmol) and $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ (590.0 mg, 2.28 mmol, 2 equiv) in CH_2Cl_2 (8 mL) was added allyltributylstannane (0.531 mL, 1.71 mmol, 1.5 equiv) at 0 °C. After stirring for 3 h at room temperature, the organic layer was washed with aqueous 1 N HCl, extracted with CH_2Cl_2 (30 mL x 2), dried over MgSO_4 , and concentrated. The residue was purified by flash chromatography on silica gel (Kanto, Silica gel 60, Spherical; Hex-EtOAc, 9:1) to give homoallylic alcohol **16** (547.2 mg, 96% yield) as a colorless oil: $[\alpha]_D^{25} + 12.0$ (*c* 0.80, CHCl_3).

The absolute stereochemistry of **16** at the two carbinol centers was determined by preparing the (*R*)- and (*S*)-MTPA diesters from **16** by Mosher's method.³ The positive $\Delta\delta^{S-R}$ values of H-3 and H-12, and negative $\Delta\delta^{S-R}$ values of H-6 and H-14 indicated the *R* configuration for C-4 and *S* configurations for C-13 respectively.⁴

Bis-(S)-MTPA ester of 16: ^1H NMR (300 MHz, CDCl_3) δ 7.62–7.35 (m, 10H), 5.80 (m, 1H), 5.18 (m, 2H, CH-4,13), 5.19–5.06 (m, 2H), 4.06 (dt, $J = 7.7, 5.4$ Hz, 1H, CH-5), 3.98 (q, $J = 6.1$ Hz, 1H, CH-12), 3.74–3.63 (m, 2H, CH-8,9), 3.57 (s, 3H), 3.54 (s, 3H), 2.60–2.36 (m, 2H, CH_2 -3), 1.91–1.45 (m, 8H), 1.42–1.1 (m, 18H), 0.88 (t, $J = 6.7$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.19, 166.15, 133.21, 132.32, 132.48, 129.50, 129.45, 128.28, 128.16, 127.68, 127.54, 118.50, 82.14 (2C), 79.52, 78.88, 77.69, 77.36, 55.70, 55.34, 34.95, 31.89, 30.96, 29.56, 29.49, 29.40, 29.30, 27.55, 27.28, 27.22, 26.42, 24.97, 22.67, 14.09.

Bis-(R)-MTPA ester of 16: ^1H NMR (300 MHz, CDCl_3) δ 7.64–7.35 (m, 10H), 5.65 (m, 1H, CH-1), 5.15 (m, 1H, CH-4), 5.14 (m, 1H, CH-13), 5.05–4.95 (m, 2H, CH_2 -2), 4.00 (q, J = 6.8 Hz, 1H, CH-5), 3.90 (q, J = 6.1 Hz, 1H, CH-12), 3.69 (dt, J = 8.2, 6.1 Hz, 1H, CH-9), 3.58 (m, 1H, CH-8), 3.58 (s, 1H), 3.55 (s, 3H), 2.47–2.22 (m, 2H, CH_2 -3), 2.0–1.4 (m, 10H), 1.4–1.15 (m, 16H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.18, 165.93, 132.59, 132.39, 129.41 (2C), 128.69, 128.68, 128.27, 128.22, 127.69, 127.46, 118.41, 82.12, 81.93, 79.47, 79.20, 78.01, 77.52, 55.59, 55.40, 35.21, 31.89, 31.50, 29.58, 29.52, 29.45, 29.31, 27.68, 27.21, 26.83, 25.11, 22.67, 14.09.

3. Synthesis of Rolliniastatin 1 (**1**)

Iodide **36**

To a suspension of magnesium turnings (319 mg, 13.12 g-atom) in THF (2 mL) was added iodine (catalytic amount), and a solution of 8-bromo-1-octene (1.10 mL, 6.55 mmol) in THF (4 mL) was added dropwise with a gentle heating. After the addition, the mixture was stirred for an additional 30 min with an occasional heating with a heat gun, and diluted with THF (10 mL). The reaction mixture was allowed to settle down and the clear supernatant solution was transferred via syringe to a solution of Li_2CuCl_4 (4.4 mL of a 0.10M solution in THF, 0.1 equiv) at -40°C . After the reaction mixture was stirred for 30 min, a pre-cooled (-40°C) solution of (*R*)-(-)-glycidyl tosylate (**35**, 1.0 g, 43.8 mmol) in THF (10 mL) was added via syringe. After 3 h at -40°C , the mixture was poured into a mixture of saturated NH_4Cl and ethyl acetate (20 mL). After separation of the phases, the aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over MgSO_4 , and concentrated. The residue was purified by flash chromatography (hexane/ethyl acetate, 6:1~4:1) to provide 10,11-epoxy-1-undecene (34 mg, 5% yield) and tosylate **35A** (898.8 mg, 60% yield) as a white solid: mp $39.4\text{--}39.9^\circ\text{C}$; $[\alpha]_D^{23} -7.5$ (*c* 1.02, CHCl_3); IR (neat) ν 3534, 2926, 2854, 1598, 1454, 1360, 1176, 1098, 968, 910, 814, 666 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.80 (d, $J = 8.3$ Hz, 2H), 7.36 (d, $J = 8.0$ Hz, 2H), 5.80 (ddt, $J = 16.9, 10.2, 6.7$ Hz, 1H), 5.02–4.90 (m, 2H), 4.03 (dd, $J = 9.6, 2.7$ Hz, 1H), 3.88 (dd, $J = 9.6, 7.0$ Hz, 1H), 3.84 (m, 1H), 2.45 (s, 3H), 2.21 (d, $J = 2.4$ Hz, 1H, OH), 2.03 (m, 2H), 1.41–1.2 (m, 12H); ^{13}C NMR (CDCl_3) δ 145.04, 139.10, 132.72, 129.94, 127.96, 114.18, 73.99, 69.47, 33.74, 32.64, 29.36, 29.97, 28.85, 25.18, 21.64; MS (FAB) m/z 341($\text{M}^+\text{+H}$), 325, 185, 173, 169, 155, 151, 139, 109, 95, 81, 69, 55, 43; HRMS (FAB) calcd for $\text{C}_{18}\text{H}_{29}\text{O}_4\text{S}$ ($\text{M}^+\text{+H}$) 341.1787, found 341.1785.

TBSOTf (0.643 mL, 2.80 mmol) was added to a solution of **35A** (476.8 mg, 1.40 mmol) and 2,6-lutidine (0.489 mL, 4.20 mmol) in dry CH_2Cl_2 at -78°C . The mixture was stirred at the same temperature for 1 h and then worked up with water and CH_2Cl_2 . The organic layer was dried over MgSO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (Hex-EtOAc, 20:1) gave TBS ether **35B** (610 mg, 96% yield) as a colorless oil: $[\alpha]_D^{22} +2.8$ (*c* 1.01, CHCl_3); IR (neat) ν 2928, 2856, 1598, 1464, 1366, 1254, 1178, 1100, 978, 910, 836, 778, 664 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.78 (d, $J = 8.3$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 5.79 (ddt, $J = 16.9, 10.2, 6.7$ Hz, 1H), 5.02–4.89 (m, 2H), 3.91–3.76 (m, 3H), 2.44 (s, 3H), 2.02 (q, $J = 7.0$ Hz, 2H), 1.4–1.2 (m, 12H), 0.83 (s, 9H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (CDCl_3) δ 144.72, 139.10, 133.06, 129.79, 127.96, 114.17, 73.20, 69.97, 34.03, 33.75, 29.51, 29.28, 28.96, 28.86, 25.74, 24.72, 21.60, 18.01, $-4.57, -4.82$; MS (EI) m/z 453 ($\text{M}^+\text{+H}$), 439, 397, 329, 269, 229 (100), 165, 149, 117,

91, 73; HRMS (FAB) calcd for C₂₄H₄₃O₄SiS (M⁺+H) 455.2651, found 455.2657.

To a solution of **35B** (510.4 mg, 1.12 mmol) in acetone (11 mL) was added NaI (1.68 g, 11.21 mmol) and NaHCO₃ (94.2 mg, 1.12 mmol). The reaction mixture was heated under reflux for 40 h. The solvent was removed under reduced pressure, and the residue was dissolved in water and extracted with ethyl acetate (20 mL x 2). The combined organic layers were washed with aqueous Na₂S₂O₃ and then with brine, dried over MgSO₄, and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (hexane) afforded iodide **36** (441.4 mg, 96 % yield) as a colorless oil: $[\alpha]_D^{22} +9.5$ (*c* 1.02, CHCl₃); IR (neat) ν 2928, 2856, 1640, 1464, 1254, 1184, 1086, 910, 836, 776 cm⁻¹; ¹H NMR (CDCl₃) δ 5.75 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 4.96–4.84 (m, 2H), 3.47 (qui, *J* = 5.3 Hz, 1H), 3.12 (d, *J* = 5.1 Hz, 2H), 1.98 (q, *J* = 6.9 Hz, 2H), 1.6–1.15 (m, 12H), 0.84 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ¹³C NMR (CDCl₃) δ 139.18, 114.16, 71.44, 36.89, 33.79, 29.48, 29.38, 29.03, 28.89, 25.84, 24.91, 18.09, 14.12, -4.36, -4.56; MS (EI) *m/z* 409 (M⁺-H), 395, 353, 285, 269, 255, 241, 229, 215, 201, 185, 109, 95, 81, 75, 67, 55; HRMS (CI) calcd for C₁₇H₃₆IOSi (M⁺+H) 411.1580, found 411.1579.

Olefin **30**

A solution of diisopropylamine (0.278 mL, 2.28 mmol) in THF (8 mL) was treated with *n*-BuLi (1.54 mL of a 1.6 M solution in hexane, 2.46 mmol) at 0 °C for 15 min and then cooled to -78 °C. Lactone **37** (434.9 mg, 2.09 mmol) in THF (3 mL) was added dropwise via syringe and the mixture was stirred at 0 °C for 30 min. Iodide **36** (779.1 mg, 1.90 mmol) in dry HMPA (1.98 mL, 11.38 mmol) was added, and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with ether and the organic layer was washed with saturated aqueous NH₄Cl, 10% Na₂S₂O₃, water and brine. The organic layer was dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 9:1) to yield iodide **36** (98.3 mg, 13% recovery), and a phenyl sulfide (originated from simple substitution of the iodide moiety, 113 mg, 15% yield), and olefin **30** (626.8 mg, 67% yield) as a colorless oil (3:1 inseparable mixture): ¹H NMR of the major isomer (CDCl₃) δ 7.46–7.14 (m, 5H), 5.69 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 4.91–4.79 (m, 2H), 4.40 (sxt, *J* = 6.6 Hz, 1H), 4.14 (m, 1H), 2.93 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.98–1.69 (m, 5H), 1.35–1.10 (m, 12H+3H), 0.78 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H); ¹³C NMR of the major isomer (CDCl₃) δ 177.57, 139.17, 136.70, 130.44, 129.62, 128.99, 114.16, 73.32, 69.49, 55.45, 41.23, 39.52, 38.53, 33.79, 29.72, 29.40, 29.00, 28.90, 26.01, 24.42, 21.34, 18.03, -3.82; MS (EI) *m/z* 489 (M⁺-H), 475, 433 (100), 391, 361, 323, 283, 269, 251, 237, 213, 199, 185, 169, 155, 135, 109, 95, 75, 73, 55; HRMS (CI) calcd for C₂₈H₄₇O₃SSi (M⁺+H) 491.3015, found 491.3015.

Olefin **31**

A solution of homoallylic alcohol **16** (63.9 mg, 0.129 mmol) and olefin **30** (252.5 mg, 0.514 mmol) in dry CH₂Cl₂ (2 mL) was transferred to a flame-dried 10 mL two neck round-bottom flask equipped with a condenser and a magnetic stirring bar under argon at 45 °C. A solution of the first-generation Grubbs catalyst (10.5 mg, 0.012 mmol) in dry CH₂Cl₂ (1 mL) was injected via syringe. After 18 h at the same temperature, additional catalyst (10.5 mg, 0.012 mmol) in dry CH₂Cl₂ (3 mL) was added. The reaction mixture was stirred for 18 h at 45 °C, cooled to room temperature, and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 20:1~5:1) to afford alcohol **16** (10.7 mg, 17% recovery) and olefin **31** (97.1 mg, 79% yield) as an oil: ¹H NMR of the major isomer (CDCl₃) δ 7.51–7.25 (m, 5H), 5.42 (m, 2H), 4.46 (sxt, *J* = 6.5 Hz, 1H), 4.18 (m, 1H), 3.82–3.63 (m, 5H), 3.37 (q, *J* = 5.8 Hz, 1H), 2.99 (dd, *J* = 14.0, 7.6 Hz, 1H), 2.2–1.3 (m, 15H+OH), 1.3–1.1 (m, 33H), 0.82 (m, 18H+3H), 0.10 (s, 3H), 0.06 (s, 3H), 0.00 (s, 6H); ¹³C NMR of major isomer (CDCl₃) δ 177.57, 136.69, 133.13, 130.43, 129.61, 128.97, 126.07, 82.29, 81.91, 81.77, 81.69, 74.28, 73.57, 73.31, 69.50, 55.43, 41.22, 39.52, 38.54, 37.47, 34.91, 32.66, 31.91, 29.95, 29.61 (overlapped), 29.45, 29.34, 29.13, 28.38, 28.00, 27.84, 26.65, 26.00, 25.96 (overlapped), 24.57, 24.46, 22.68, 21.33, 20.38, 18.14, 18.02, 14.12, –3.81, –4.15, –4.28.

Alcohol **31A**

To a solution of olefin **31** (93.2 mg, 0.097 mmol) and *p*-toluenesulfonylhydrazide (1.212 g, 6.507 mmol) in DME (15 mL) under reflux was added a solution of sodium acetate (661.3 mg,

8.06mmol) in water (12 mL) in 4 h via syringe pump. After cooling to room temperature, the reaction mixture was poured into water and extracted with ethyl acetate (20 mLx2). The combined organic extracts were washed with water, brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 7:1) to afford alcohol **31A** (85.1 mg, 91% yield) as an oil: ¹H NMR of the major isomer (CDCl₃) δ 7.52–7.24 (m, 5H), 4.46 (sxt, *J* = 6.7 Hz, 1H), 4.19 (m, 1H), 3.9–3.6 (m, 6H), 3.31 (m, 1H), 2.99 (dd, *J* = 14.0, 7.6 Hz, 1H), 2.3–1.1 (m, 53H), 0.9–0.7 (m, 21H), 0.10 ~ –0.03 (m, 12H); ¹³C NMR of major isomer (CDCl₃) δ 177.56, 136.69, 129.60, 128.97, 128.92, 82.75, 82.31, 81.81, 81.69, 74.43, 73.61, 73.31, 69.53, 55.45, 41.24, 39.54, 38.56, 34.93, 34.15, 31.91, 29.96, 29.8 ~ 29.5 (overlapped), 29.34, 28.36, 28.04, 27.97, 26.69, 26.01, 25.96 (overlapped), 25.81, 24.58, 24.47, 22.68, 21.32, 18.14, 18.02, 14.10, –3.81 (2), –4.16, –4.28; MS (FAB) *m/z* 961 (*M*⁺+H), 903, 829, 753, 697, 679, 661, 551, 455, 403, 311, 285, 227, 185, 169, 97, 81, 73, 55, 43; HRMS (FAB) calcd for C₅₅H₁₀₁O₇SSi₂ (*M*⁺+H) 961.6807, found 961.6813.

Butenolide **31B**

Magnesium monoperoxyphthalate hexahydrate (MMPP, 34.4 mg, 0.056 mmol, purity 80%) was added to a solution of **31A** (82.4 mg, 0.086 mmol) in THF-MeOH (2 mL/2 mL) at 0 °C. The mixture was stirred at room temperature for 2 h. The mixture was concentrated and filtered through a pad of silica gel, which was washed with a mixture of hexane and ethyl acetate (2:1). The filtrate was concentrated under reduced pressure, and the crude sulfoxide was dissolved in toluene (5 mL). The mixture was stirred at 90 °C for 1 h, and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 7:1~6:1) to afford butenolide **31B** (64.7 mg, 89% yield) as an oil: [α]_D²⁵ + 15.8 (*c* 0.95, CHCl₃); IR (neat) ν 3452, 2928, 2856, 1760, 1464, 1254, 1072, 836, 776 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.06 (s, 1H), 4.94 (dq, *J* = 5.6, 1.3 Hz, 1H), 3.89 (qui, *J* = 5.7 Hz, 1H), 3.84–.62 (m, 5H), 3.31 (q, *J* = 5.1 Hz, 1H), 2.65 (br. s, 1H), 2.36 (d, *J* = 6.0 Hz, 2H), 1.91–1.5 (m, 10H), 1.35 (d, *J* = 6.8 Hz, 3H), 1.4–1.15 (m, 36H), 0.85–0.75 (m, 18H+3H), 0.08 (s, 6H), –0.04 (s, 3H), –0.06 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 174.01, 151.43, 130.87, 82.74, 82.29, 81.79, 81.67, 77.44, 74.41, 73.60, 70.19, 36.96, 34.91, 34.14, 32.74, 31.90, 29.95, 29.71, 29.95 (overlapped), 29.33, 28.36, 28.03, 27.97, 25.95, 25.87 (overlapped), 25.80, 25.13, 24.56, 22.67, 18.96, 18.13, 18.03, 14.10, –4.17, –4.29, –4.46; MS (FAB) *m/z* 851 (*M*⁺+H),

833, 793, 775, 719, 701, 661, 643, 569, 551, 533, 425, 355, 311, 285, 227, 211, 185, 169, 95, 83, 75, 73, 67, 55, 43; HRMS (FAB) calcd for $C_{49}H_{95}O_7Si_2$ ($M^+ + H$) 851.6616, found 851.6627.

(+)-Rolliniastatin 1 (1)

Butenolide **31B** (47.7 mg, 0.056 mmol) was dissolved in MeOH (2 mL) and treated with a solution of 5% (v/v) acetyl chloride in MeOH (2 mL) and the mixture was stirred for 1 h at room temperature. The solution was diluted with CH_2Cl_2 and neutralized by the addition of solid $NaHCO_3$. The mixture was filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (ethyl acetate) to yield (+)-rolliniastatin 1 (**1**) (31.8 mg, 91% yield): $[\alpha]_D^{24} +22.5$ (c 0.52, CH_2Cl_2) {lit.⁵ $[\alpha]_D^{28} +25.2$ (c 1.03, CH_2Cl_2); lit.⁶ $[\alpha]_D^{20} +25$ (c 0.51, CH_2Cl_2)}; IR (neat) ν 3424 (br. s), 2924, 2854, 1752, 1462, 1320, 1196, 1068 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, J = 1.3 Hz, 1H, CH-35), 5.06 (dq, J = 6.8, 1.4 Hz, 1H, CH-36), 3.92–3.82 (m, 6H, CH-4, 16, 19, 20, 23, 24), 3.41 (m, 1H, CH-15), 2.95 (br. s, 2H, OH), 2.53 (ddt, J = 15.1, 3.3, 1.65 Hz, 1H, CH₂-3a), 2.40 (dd, J = 15.2, 8.3 Hz, 1H, CH₂-3b), 1.74–1.99 (m, 8H, CH₂-17, 18, 21, 22), 1.43 (d, J = 6.8 Hz, 3H, CH₃-37), 1.20–1.55 (m, 30H, CH₂-7~13, 26~33), 0.88 (t, J = 6.9 Hz, 3H, CH₃-34); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.58, 151.73, 131.19, 83.03, 82.93, 81.12, 80.98, 77.93, 73.99, 71.90, 69.96, 37.39, 34.21, 33.30, 32.76, 31.88, 29.68, 29.62, 29.59, 29.55, 29.52, 29.49, 29.46, 29.30, 28.73, 28.41, 27.87, 25.99, 25.73, 25.54, 23.72, 22.65, 19.09, 14.08; MS (FAB) m/z 623 ($M^+ + H$), 605, 577, 563, 549, 535, 523, 521, 509, 507, 495, 369, 311, 237, 154, 149, 137, 123, 121, 109, 107, 97, 95, 93, 83, 81, 79, 69, 57, 55, 43, 41; HRMS (FAB) calcd for $C_{37}H_{67}O_7$ ($M^+ + H$) 623.4887, found 623.4888.

4. Synthesis of Rollimembrin (2)

Iodide 39

To a mixture of (*R*)-epichlorohydrin (**38**, 0.391 mL, 5.00 mmol) and CuCN (44.8 mg, 0.05 mmol) in THF (10 mL) at $-40\text{ }^{\circ}\text{C}$ was added slowly a solution of 5-hexenyl magnesium bromide (0.47 M) in THF (16 mL) prepared from Mg (243 mg, 13.12 g-atom) and 6-bromo-1-hexene (1.0 mL, 7.46 mmol). The mixture was stirred at $-40\text{ }^{\circ}\text{C}$ for 3 h and poured into a mixture of saturated aqueous NH_4Cl and ethyl acetate. After separation of the phases, the aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over MgSO_4 , and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hex-Et₂O, 5:1) to give chlorohydrin **38A** (745.8 mg, 84% yield): $[\alpha]_D^{28} -1.9$ (*c* 1.01, CHCl_3); IR (neat) ν 3382 (br), 2930, 2856, 1640, 1434, 1050, 996, 910, 740 cm^{-1} ; ^1H NMR (CDCl_3) δ 5.80 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.03–4.92 (m, 2H), 3.80 (m, 1H), 3.63, 3.48 (ABX, *J* = 11.1, 7.1, 3.2 Hz, 2H), 2.18 (d, *J* = 4.8 Hz, 1H), 2.05 (q, *J* = 6.8 Hz, 2H), 1.6–1.3 (m, 8H); ^{13}C NMR (CDCl_3) δ 138.91, 114.35, 71.42, 50.56, 34.16, 33.64, 28.94, 28.73, 25.36; MS (EI) *m/z* 158 ($\text{M}^+ - \text{H}_2\text{O}$), 143, 127, 123, 116, 109, 105, 95, 81, 79, 67 (100), 55, 54; MS (CI) 177 ($\text{M}^+ + \text{H}$), 159, 141, 123 (100), 109, 95, 81; HRMS (CI) calcd for $\text{C}_9\text{H}_{18}\text{ClO}$ ($\text{M}^+ + \text{H}$) 177.1046, found 177.1047.

To a solution of **38A** (732.4 mg, 4.15 mmol) in acetone (28 mL) was added NaI (6.21 g, 41.43 mmol). The reaction mixture was stirred vigorously under reflux for 48 h. Solvent was removed under reduced pressure, and the residue was dissolved in water and extracted with ethyl acetate (20 mL x 2). The combined organic layers were washed with aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and brine, dried over MgSO_4 , and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (Hex-EtOAc, 7:1) afforded iodohydrin **38B** (1.036 g, 93% yield) as a colorless oil: $[\alpha]_D^{26} -6.7$ (*c* 1.03, CHCl_3); IR (neat) ν 3376 (br), 2928, 2854, 1640, 1414, 1182, 996, 910 cm^{-1} ; ^1H NMR (CDCl_3) δ 5.80 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.03–4.91 (m, 2H), 3.51 (m, 1H), 3.39, 3.23 (ABX, *J* = 10.1, 6.8, 3.5 Hz, 2H), 2.05 (m, 3H), 1.6–1.3 (m, 8H); ^{13}C NMR (CDCl_3) δ 138.91, 114.38, 70.95, 36.55, 33.64, 28.90, 28.73, 25.52, 25.16, 16.71; MS (EI) *m/z* 211 ($\text{M}^+ - 57$), 196, 184, 171, 155, 141, 123, 109, 97, 81 (100), 67, 55; MS (CI) 269 ($\text{M}^+ + \text{H}$), 251, 209, 141, 123 (100), 109, 95, 81, 67; HRMS (FAB) calcd for $\text{C}_9\text{H}_{18}\text{IO}$ ($\text{M}^+ + \text{H}$) 269.0403, found 269.0396.

TBSOTf (1.74 mL, 7.56 mmol) was added to a solution of **38B** (1.014 g, 3.78 mmol) and 2,6-lutidine (1.32 mL, 11.34 mmol) in dry CH_2Cl_2 (13 mL) at $-78\text{ }^{\circ}\text{C}$. The mixture was stirred at the

same temperature for 1 h and then worked up with water and CH₂Cl₂. The organic layer was dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash chromatography (hexane) to give iodide **39** (1.374 g, 95% yield) as a colorless oil: $[\alpha]_D^{24} + 10.1$ (c 1.01, CHCl₃); IR (neat) ν 2930, 2856, 1640, 1464, 1254, 1082, 910, 836, 776 cm⁻¹; ¹H NMR (CDCl₃) δ 5.74 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 4.96–4.85 (m, 2H), 3.85 (dq, J = 6.0, 5.2 Hz, 1H), 3.12 (d, J = 5.1 Hz), 1.98 (q, J = 6.9 Hz, 1H), 1.6–1.2 (m, 8H), 0.84 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ¹³C NMR (CDCl₃) δ 138.99, 114.30, 71.42, 36.84, 33.69, 29.01, 28.82, 25.84, 24.76, 18.08, 13.98, -4.36, -4.56; MS (EI) m/z 381 (M⁺-H), 367, 325, 285, 255, 241, 229, 215, 185, 171, 153, 139, 123, 115, 101, 81 (100), 75, 67, 55; MS (CI) 383 (M⁺+H), 367, 325, 285, 255, 251, 209, 133, 123, 95, 81; HRMS (CI) calcd for C₁₅H₃₂IOSi (M⁺+H) 383.1267, found 383.1264.

Olefin **33**

To a solution of LDA (1.56 mL, 2.0 M solution in heptane/THF/ethylbenzene, purchased from Aldrich) was added lactone **37** (597.7 mg, 2.87 mmol) in THF (3 mL) via syringe and the mixture was stirred at 0 °C for 30 min. A solution of **39** (997.5 mg, 2.61 mmol) in dry HMPA (2.72 mL, 15.65 mmol) was added and the mixture was stirred at room temperature for 24 h. The solution was diluted with ether and washed with saturated aqueous NH₄Cl, 10% Na₂S₂O₃, water, and brine. The organic layer was dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 20:1) to give olefin **33** (927.1 mg, 77% yield) as a colorless oil (3:1 inseparable mixture): IR (neat) ν 2930, 2856, 1766, 1468, 1382, 1342, 1254, 1184, 1052, 1004, 908, 834, 776 cm⁻¹; ¹H NMR of the major isomer (CDCl₃) δ 7.46–7.18 (m, 5H), 5.67 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 4.9–4.7 (m, 2H), 4.40 (sxt, J = 6.6 Hz, 1H), 4.14 (m, 1H), 2.93 (dd, J = 14.0, 7.6 Hz, 1H), 1.93–1.68 (m, 5H), 1.4–1.0 (m, 8H), 1.11 (d, J = 6.3 Hz, 3H), 0.78 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H); ¹³C NMR of major isomer (CDCl₃) δ 177.56, 138.96, 136.69, 130.43, 129.62, 128.99, 114.29, 73.32, 69.47, 55.41, 41.22, 39.54, 38.47, 33.65, 29.25, 28.81, 26.01, 24.29, 21.34, 18.02, -3.82; MS (EI) m/z 461 (M⁺-H), 447, 405 (100), 363, 333, 295, 279, 255, 237, 214, 199, 169, 155, 135, 109, 74, 73; HRMS (FAB) calcd for C₂₆H₄₃O₃SSi (M⁺+H) 463.2702, found 463.2693.

Olefin 34

A solution of homoallylic alcohol **16** (34.7 mg, 0.070 mmol) and olefin **33** (129.3 mg, 0.279 mmol) in dry CH_2Cl_2 (2 mL) was placed via syringe in a flame-dried 10 mL two neck round-bottom flask equipped with a condenser and a magnetic stirring bar under argon at 45 °C. A solution of the second-generation Grubbs catalyst (5.9mg, 0.007 mmol) in dry CH_2Cl_2 (1 mL) was injected via syringe. The reaction mixture was stirred for 24 h at 45 °C, cooled to room temperature, and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 20:1~5:1) to afford olefin **34** (48.2 mg, 74% yield) as an oil: IR (neat) ν 3460, 2928, 2856, 1768, 1466, 1254, 1184, 1060, 836, 776 cm^{-1} ; ^1H NMR of the major isomer (CDCl_3) δ 7.52–7.24 (m, 5H), 4.41 (m, 2H), 4.46 (sxt, $J = 6.7$ Hz, 1H), 4.18 (m, 1H), 3.84–3.63 (m, 5H), 3.36 (q, $J = 5.9$ Hz, 1H), 2.98 (dd, $J = 14.0, 7.6$ Hz, 1H), 2.65 (br. s, 1H), 2.29–1.50 (m, 15H), 1.42–1.15 (m, 29H), 0.84–0.80 (m, 18H + 3H), 0.10 (s, 3H), 0.06 (s, 3H), 0.00 (s, 6H); ^{13}C NMR (CDCl_3) δ 136.69, 129.61, 128.98, 82.30, 81.86, 81.78, 81.66, 74.27, 73.58, 73.30, 39.55, 34.94, 31.91, 29.96, 29.62, 29.34, 28.37, 28.01, 27.85, 26.66, 26.00, 25.96, 24.57, 22.68, 21.33, 18.15, 18.02, 14.11, –3.81, –4.14, –4.27; MS (FAB) m/z 931 ($\text{M}^+\text{+H}$), 873, 799, 723, 649, 631, 477, 425, 355, 323, 311, 285, 227, 185, 169, 137, 135, 132, 129, 115, 105, 97, 95, 74, 73 (100), 55; HRMS (FAB) calcd for $\text{C}_{53}\text{H}_{95}\text{O}_7\text{SSi}_2$ ($\text{M}^+\text{+H}$) 931.6337, found 931.6313.

Alcohol 34A

A solution of sodium acetate (292 mg, 3.560 mmol) in water (4 mL) was added via syringe

pump to a solution of **34** (40.0 mg, 0.043 mmol) and *p*-toluenesulfonylhydrazide (536 mg, 2.878 mmol) in DME (8 mL) under reflux in 4 h. After cooling to room temperature, the reaction mixture was poured into water and extracted with ethyl acetate. The combined organic extracts were washed with water, brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 7:1) to afford alcohol **34A** (30.4 mg, 76% yield) as an oil: IR (neat) ν 3460, 2928, 2856, 1768, 1464, 1254, 1184, 1064, 836, 774 cm⁻¹; ¹H NMR of the major isomer (CDCl₃) δ 7.51–7.24 (m, 5H), 4.44 (sxt, *J* = 6.6 Hz, 1H), 4.19 (m, 1H), 3.87–3.63 (m, 5H), 3.31 (q, *J* = 5.6 Hz, 1H), 2.99 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.98–1.53 (m, 12H), 1.5–1.15 (m, 37H), 0.82 (m, 18H+3H), 0.10 (s, 3H), 0.06 (s, 3H), 0.00 (s, 6H); ¹³C NMR (CDCl₃) δ 176.56, 136.69, 129.61, 128.98, 128.93, 82.73, 82.30, 81.82, 81.68, 74.42, 73.60, 73.31, 69.51, 55.45, 55.06, 41.23, 39.52, 38.55, 34.94, 34.14, 29.96, 29.72, 29.62, 29.34, 28.36, 28.05, 27.98, 26.68, 26.01, 25.96, 24.57, 22.68, 21.32, 18.14, 18.02, 14.11, -3.81, -4.15, -4.28; MS (FAB) *m/z* 933 (*M*⁺+H), 875, 801, 786, 651, 633, 523, 425, 355, 311, 285, 227, 185, 169, 149, 143, 137, 135, 121, 95, 74, 73, 55; HRMS (FAB) calcd for C₅₃H₉₇O₇SSi₂ (*M*⁺+H) 933.6494, found 933.6517.

Butenolide **34B**

Magnesium monoperoxyphthalate hexahydrate (MMPP, 14.6 mg, 0.024 mmol, purity 80%) was added to a solution of **34A** (33.8 mg, 0.036 mmol) in THF-MeOH (2 mL/2 mL) at 0 °C. The mixture was stirred at room temperature for 2 h. The mixture was concentrated and filtered through a pad of silica gel, which was washed with a mixture of hexane and ethyl acetate (2:1). The filtrate was concentrated under reduced pressure, and the crude sulfoxide was dissolved in toluene (5 mL). The mixture was stirred at 90 °C for 1 h and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 6:1~5:1) to give butenolide **34B** (24.8 mg, 89% yield) as an oil: $[\alpha]_D^{25} +16.8$ (*c* 0.86, CHCl₃); IR (neat) ν 3460, 2928, 2856, 1758, 1464, 1254, 1070, 836, 774 cm⁻¹; ¹H NMR (CDCl₃) δ 7.12 (s, 1H), 5.00 (qd, *J* = 6.8, 1.1 Hz, 1H), 3.94 (qui, *J* = 5.6 Hz, 1H), 3.90–3.68 (m, 5H), 3.36 (q, *J* = 5.6 Hz, 1H), 2.42 (d, *J* = 5.4 Hz, 2H), 1.92–1.54 (m, 8H), 1.5–1.2 (m, 34H), 1.41 (d, *J* = 6.8 Hz, 3H), 0.9–0.8 (m, 18H+3H), 0.05 (s, 6H), 0.04 (s, 3H), 0.01 (s, 3H); ¹³C NMR (CDCl₃) δ 174.01, 151.43, 130.87, 82.73, 82.31, 81.81, 81.67, 77.45, 74.41, 73.60, 70.20, 36.96, 34.94, 34.14, 32.75, 31.90, 29.96, 29.73, 29.61, 29.34, 28.35, 28.03, 27.97, 26.69, 25.95, 25.87, 25.79, 25.15, 24.57, 22.67, 18.97, 18.14, 18.04, 14.10, -4.17, -4.29, -4.46; MS (FAB)

m/z 823 ($M^+ + H$), 765, 691, 677, 615, 541, 523, 425, 355, 311, 285, 211, 169, 95, 74, 73 (100), 55;
HRMS (FAB) calcd for $C_{47}H_{91}O_7Si_2$ ($M^+ + H$) 823.6303, found 823.6310.

(+)-Rollimembrin (2)

Butenolide **34B** (24.8 mg, 0.030 mmol) was dissolved in MeOH (2 mL) and treated with a solution of 5% (v/v) acetyl chloride in MeOH (2 mL) and the reaction mixture was stirred for 1 h at room temperature. The solution was diluted with CH_2Cl_2 and neutralized by the addition of solid $NaHCO_3$. The mixture was filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (ethyl acetate) to yield rollimembrin (**2**, 17.3 mg, 97% yield): $[\alpha]_D^{25} +24.4$ (c 0.63, MeOH) {lit.⁷ $[\alpha]_D +17.5$ (c 0.4, MeOH)}; IR (neat) ν 3424 (br. s), 2924, 2854, 1752, 1462, 1320, 1068 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, $J = 1.17$ Hz, 1H, CH-33), 5.06 (dq, $J = 6.8, 1.3$ Hz, CH-34), 3.80–3.94 (m, 6H, CH-4, 14, 17, 18, 21, 22), 3.41 (m, 1H, CH-13), 2.39 (dd, 1H, $J = 15.1, 8.1$ Hz, CH_2 -3a), 2.53 (ddt, 1H, $J = 15.1, 3.3, 1.7$ Hz, CH_2 -3b), 1.73–1.99 (m, 8H, CH_2 -15, 16, 19, 20), 1.43 (d, $J = 6.8$ Hz, 3H, CH_3 -35), 1.2–1.5 (m, 34H, CH_2 -5~12, 23~31), 0.88 (t, $J = 6.6$ Hz, 3H, CH_3 -32); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.55, 151.71, 131.22, 83.04, 82.90, 81.12, 80.97, 77.92, 73.99, 71.94, 69.98, 37.39, 34.24, 33.33, 32.80, 31.89, 29.69, 29.60, 29.46, 29.43, 29.31, 28.74, 28.43, 27.90, 25.72, 23.75, 26.00, 25.53, 22.66, 19.10, 14.08; MS (FAB) m/z 595 ($M^+ + H$), 581, 541, 523, 423, 391, 333, 311, 307, 289, 283, 267, 265, 263, 249, 241, 211, 197, 167, 154, 149, 138, 137, 136, 109, 107, 97, 91, 83, 81, 77, 69, 68, 57, 55; HRMS (FAB) calcd for $C_{35}H_{63}O_7$ ($M^+ + H$) 595.4574, found 595.4579.

5. Synthesis of Membranacin (3)

Olefin 41

To a solution of lactone **37** (400.0 mg, 1.92 mmol) in THF (7 mL) was added dropwise lithium diisopropylamide (1.3 mL, 2.6 mmol, 2.0 M solution in heptane/THF/ethylbenzene, purchased from Aldrich) via syringe at $-78\text{ }^{\circ}\text{C}$ and the reaction mixture was stirred $0\text{ }^{\circ}\text{C}$ for 30 min. Bromide **40** (672 mg, 2.88 mmol) in dry HMPA (2.0 mL, 11.5 mmol) was then added, and the reaction mixture was stirred at room temperature for 24 h. The solution was diluted with ether and washed with saturated aqueous NH_4Cl , 10% $\text{Na}_2\text{S}_2\text{O}_3$, water, and brine. The organic layer was dried over MgSO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 20:1) to give olefin **41** (514.6 mg, 74% yield) as a colorless oil (4:1 inseparable mixture): ^1H NMR of the major isomer (300 MHz, CDCl_3) δ 7.57~7.34 (m, 5H), 5.81 (ddt, $J = 16.9, 10.2, 6.7$ Hz, 1H), 5.03~4.90 (m, 2H), 4.48 (sxt, $J = 6.6$ Hz, 1H), 2.51 (dd, $J = 13.9, 7.6$ Hz, 1H), 2.07 (q, $J = 7.0$ Hz, 2H), 1.96 (dd, $J = 14.0, 6.9$ Hz, 1H), 1.82~1.53 (m, 2H), 1.40~1.2 (m, 14H), 1.18 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR of major isomer (75 MHz, CDCl_3) δ 177.09, 136.83, 130.52, 129.68, 128.99, 114.13, 73.19, 56.28, 40.16, 36.51, 33.79, 29.57, 29.42, 29.33, 29.07, 28.91, 24.66, 21.51; MS (EI) m/z 360 ($\text{M}^+ + \text{H}$), 251, 233, 208 (100), 190, 178, 163, 150, 135, 110, 109, 95, 81, 69, 67, 55; HRMS (EI) calcd for $\text{C}_{22}\text{H}_{32}\text{O}_2\text{S}$ (M^+) 360.2123, found 360.2125.

Olefin 42

A solution of homoallylic alcohol **16** (64.1 mg, 0.13 mmol) and olefin **41** (186.1 mg, 0.52 mmol) in dry CH_2Cl_2 (4 mL) was placed via syringe in a flame-dried 10 mL two neck round-bottom flask equipped with a condenser and a magnetic stirring bar under argon at $45\text{ }^{\circ}\text{C}$. A solution of the second-generation Grubbs catalyst (11.0 mg, 0.013 mmol, 0.1 equiv) in dry CH_2Cl_2 (1 mL) was injected via syringe. The reaction mixture was stirred for 20 h at $45\text{ }^{\circ}\text{C}$, cooled to room temperature,

and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 9:1~1:1) to afford alcohol **16** (5.4 mg, 8% recovery), the **16**-homocoupled product (14.4 mg, 12% yield), and olefin **42** (79.1 mg, 74% yield) as an oil: ^1H NMR of the major isomer (CDCl_3) δ 7.57~7.31 (m, 5H), 5.48 (m, 2H), 4.48 (sxt, $J = 6.7$ Hz, 1H), 3.90~3.69 (m, 5H), 3.42 (q, $J = 5.7$ Hz, 1H), 2.70 (br. s, OH, 1H), 2.51 (dd, $J = 13.9, 7.6$ Hz, 1H), 2.36~1.43 (m, 17H), 1.38~1.2 (m, 30H), 1.18 (d, $J = 6.3$ Hz, 3H), 0.88 (m, 9H+3H), 0.06 (s, 6H); ^{13}C NMR of major isomer (CDCl_3) δ 177.10, 136.84, 133.15, 130.50, 129.68, 129.00, 126.08, 82.29, 81.85, 81.77, 81.61, 74.29, 73.59, 73.19, 56.28, 40.14, 37.49, 36.51, 34.95, 32.66, 31.91, 29.96, 29.62, 29.46, 29.35, 29.18, 28.38, 28.01, 27.86, 26.71, 25.97, 24.67, 24.56, 22.69, 21.51, 18.15, 14.12, -4.14, -4.27; HRMS (FAB) calcd for $\text{C}_{49}\text{H}_{85}\text{O}_6\text{SSi}$ ($\text{M}^+ + \text{H}$) 829.5836, found 829.5841.

Alcohol 42A

A solution of sodium acetate (624 mg, 7.606 mmol) in water (10 mL) was added via syringe pump to a solution of **42** (76.0 mg, 0.092 mmol) and *p*-toluenesulfonylhydrazide (1.143 g, 6.140 mmol) in DME (13 mL) under reflux in 4 h. After cooling to room temperature, the reaction mixture was poured into water and extracted with ethyl acetate. The combined organic extracts were washed with water, brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex-EtOAc, 6:1) to give alcohol **42A** (69.7mg, 92% yield) as an oil: ^1H NMR of the major isomer (CDCl_3) δ 7.57~7.31 (m, 5H), 4.49 (sxt, $J = 6.7$ Hz, 1H), 3.90~3.60 (m, 5H), 3.37 (q, $J = 5.1$ Hz, 1H), 2.69 (br. s, OH, 1H), 2.52 (dd, $J = 13.9, 7.6$ Hz, 1H), 2.04~1.89 (m, 10H), 1.63~1.2 (m, 41H), 1.18 (d, $J = 6.3$ Hz, 3H), 0.88 (m, 9H+3H), 0.06 (s, 6H); ^{13}C NMR of major isomer (CDCl_3) δ 177.12, 136.84, 130.50, 129.68, 128.99, 82.70, 82.29, 81.80, 81.62, 74.43, 73.61, 73.19, 56.28, 40.12, 36.50, 34.94, 34.17, 31.91, 29.96, 29.76, 29.62, 29.50, 29.35, 28.37, 28.06, 27.99, 26.76, 25.96, 25.82, 24.67, 24.55, 22.69, 21.51, 18.14, 14.13, -4.16, -4.27.

Butenolide **42B**

Magnesium monoperoxyphthalate hexahydrate (MMPP, 35.6 mg, 0.057 mmol, purity 80%) was added to a solution of **42A** (68.4 mg, 0.083 mmol) in THF–MeOH (2 mL/2 mL) at room temperature. The mixture was stirred at room temperature for 1 h. The mixture was concentrated and filtered through a pad of silica gel, which was washed with a mixture of hexane and ethyl acetate (2:1). The filtrate was concentrated under reduced pressure, and the crude sulfoxide was dissolved in toluene (10 mL). The reaction mixture was stirred at 90 °C for 1 h and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex–EtOAc, 5:1) to afford butenolide **42B** (50.1 mg, 84% yield) as an oil: $[\alpha]_D^{21} + 19.6$ (*c* 0.49, CHCl₃); IR (neat) ν 3458, 2926, 2854, 1758, 1454, 1318, 1252, 1196, 1072, 836, 776 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.99 (d, *J* = 1.2 Hz, 1H), 5.00 (dq, *J* = 6.7, 1.4 Hz, 1H), 3.90–3.65 (m, 5H), 3.37 (q, *J* = 5.5 Hz, 1H), 2.70 (br. s, OH, 1H), 2.26 (t, *J* = 7.6 Hz, 2H), 1.96–1.69 (m, 8H), 1.66–1.2 (m, 40H), 1.41 (d, *J* = 6.8 Hz, 3H), 0.88 (m, 9H+3H), 0.06 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 173.88, 148.85, 134.31, 82.70, 82.28, 81.79, 81.62, 77.39, 74.42, 73.60, 34.93, 34.16, 31.91, 29.96, 29.75, 29.62, 29.52, 29.34, 29.32, 29.18, 28.36, 28.05, 27.98, 27.39, 26.75, 25.95, 25.81, 25.17, 24.55, 22.68, 19.22, 18.13, 14.12, –4.17, –4.29; HRMS (FAB) calcd for C₄₃H₈₁O₆Si (M⁺+H) 721.5802, found 721.5806.

(+)-Membranacin (**3**)

Butenolide **42B** (44.2 mg, 0.061 mmol) was dissolved in MeOH (2 mL) and the solution was treated with a solution of 5% (v/v) acetyl chloride in MeOH (2 mL). The reaction mixture was

stirred for 1 h at room temperature. The solution was concentrated under reduced pressure, and the residue was purified by flash chromatography (Hex-EtOAc, 1:1~0:1) to yield membranacin (**3**) (35.7 mg, 96% yield): $[\alpha]^{22}_{\text{D}} +28.8$ (c 0.35, CHCl_3); $[\alpha]^{23}_{\text{D}} +37.7$ (c 0.32, MeOH); {lit.⁸ $[\alpha]_{\text{D}} +22.5$ (c 0.2, MeOH)}; IR (neat) ν 3452 (br. s), 2924, 2852, 1756, 1464, 1318, 1196, 1070, 1028, 954, 878 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.99 (q, $J = 1.5$ Hz, 1H), 5.00 (qq, $J = 6.8, 1.7$ Hz, 1H), 3.93~3.81 (m, 5H), 3.42 (dt, $J = 7.7, 4.8$ Hz, 1H), 3.01 (br. s, OH, 2H), 2.26 (m, 2H), 2.01~1.71 (m, 8H), 1.60~1.2 (m, 40H), 1.41 (d, $J = 6.8$ Hz, 3H), 0.88 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 173.92, 148.87, 134.31, 83.05, 82.96, 81.14, 81.01, 77.41, 74.03, 71.89, 34.23, 32.78, 31.91, 29.70, 29.62, 29.58, 29.51, 29.33, 29.32, 29.18, 28.75, 28.44, 27.89, 27.38, 26.02, 25.80, 25.17, 23.73, 22.68, 19.22, 14.12; HRMS (FAB) calcd for $\text{C}_{37}\text{H}_{67}\text{O}_6$ ($\text{M}^+ + \text{H}$) 607.4938, found 607.4959.

6. References

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