A Radical-Based Approach for the Construction of the Tetracyclic Structure of Resiniferatoxin

Koichi Murai, Shun-ichiroh Katoh, Daisuke Urabe and Masayuki Inoue*

Graduate School of Pharmaceutical Sciences
*The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan
Fax: (+81)3-5841-0568
E-mail: inoue@mol.f.u-tokyo.ac.jp

Supporting Information

51 page

Contents:

1. Experimental S2
2. $^1$H and $^{13}$C NMR spectra of newly synthesized compounds S26
**Supporting Information**

**General:** All reactions sensitive to air or moisture were carried out under argon atmosphere in dry solvents under anhydrous conditions, unless otherwise noted. THF, CH₂Cl₂, DMF and Et₂O were purified by Glass Contour solvent dispensing system (Nikko Hansen & Co., Ltd., Osaka, Japan). All other reagents were used as supplied. Analytical thin-layer chromatography (TLC) was performed using E. Merck Silica gel 60 F254 pre-coated plates. Flash chromatography was performed using 40-50 μm Silica-gel 60N (Kanto Chemical Co., Inc.), 40-63 μm Silica-gel 60 (Merck) or 32-53 μm Silica-gel BW-300 (Fuji Silysia Chemical Ltd.). Melting points were measured on Yanaco MP-J3 micro melting point apparatus, and are uncorrected. Optical rotations were measured on JASCO DIP-1000 Digital Polarimeter at room temperature using the sodium D line. Infrared (IR) spectra were recorded on JASCO FT/IR-4100 spectrometer. ¹H and ¹³C NMR spectra were recorded on JEOL JNM-ECX-500, JNM-ECA-500, or JNM-ECS-400 spectrometer. Chemical shifts were reported in ppm on the δ scale relative to CHCl₃ (δ = 7.26 for ¹H NMR), CDCl₃ (δ = 77.0 for ¹³C NMR), C₆D₆H (δ = 7.16 for ¹H NMR), C₆D₆ (δ = 128.0 for ¹³C NMR), CD₃HOD (δ = 3.31 for ¹H NMR) and CD₂OD (δ = 49.0 for ¹³C NMR) as internal references. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broaden peak. The numbering of compounds corresponds to that of natural product. High resolution mass spectra were measured on BRUKER DALTONICS microTOF II or JEOL JMS-T100LP instrument.

**Lactol 9.** Concentrated H₂SO₄ (88 µL, 1.7 mmol) was added to a solution of D-ribose (5.00 g, 33.3 mmol) in acetone (130 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 3 h, and was neutralized by addition of solid Ca(OH)₂ (2 g). The insoluble salts were removed by passing the mixture through a pad of Celite. The filter cake was washed with acetone (100 mL), and the filtrate was concentrated to afford crude S₁ (6.75 g), which was used for the next reaction without further purification. The above crude S₁ was dissolved in H₂O (130 mL), and the solution was cooled to 0 °C. NaBH₄ (2.14 g, 56.6 mmol) in H₂O (90 mL) was added to the solution. The reaction mixture was stirred at 0 °C for 30 min, and then the pH of the reaction mixture
was adjusted to 6 by adding AcOH. NaIO₄ (6.28 g, 29.3 mmol) was added to the mixture, and the combined mixture was stirred at 0 °C for 80 min. Then, the reaction mixture was concentrated. The residue was partitioned between EtOAc (100 mL) and H₂O (50 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (150 mL ×3). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Merck silica gel 60 g, hexane/Et₂O 2:1 to 0:1) to afford lactol 9 (4.23 g, 26.4 mmol) in 79% yield over 2 steps. All the spectral data were identical with those reported previously.¹

Pivaloate 10. A solution of lactol 9 (15.6 g, 97.5 mmol) in THF (160 mL) was cooled to 0°C. Isopropenylmagnesium bromide (0.5 M solution in THF, 500 mL, 250 mmol) was added by an addition funnel over 40 min to the solution, and the reaction mixture was stirred at 0°C for 1 h. The mixture was poured into saturated aqueous NH₄Cl (500 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (300 mL ×3). The combined organic layers were washed with brine (300 mL), dried over Na₂SO₄, filtered, and concentrated. The crude mixture was passed through a short pad of silica gel (Kanto silica gel, 200 g) with EtOAc (500 mL). The filtrate was concentrated to afford crude diol S₂, which was used for the next reaction without further purification.

PivCl (14 mL, 110 mmol) was added to a mixture of the above crude diol S₂, Et₃N (33 mL, 240 mmol) and DMAP (1.19 g, 9.74 mmol) in CH₂Cl₂ (330 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 3 min, and was poured into H₂O (300 mL). The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (200 mL ×3). The combined organic layers were washed with saturated aqueous NaHCO₃ (100 mL ×3) and brine (200 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Kanto silica gel 500 g, hexane/EtOAc 30:1 to 3:1) to afford pivaloate 10 (20.8 g, 72.7 mmol) in 75% yield over 2 steps: white

Supporting Information

crystal; m.p. 62-63 °C; [α]D<sup>19</sup> -0.27 (c 1.00, CHCl₃): IR (neat) ν<sub>max</sub> 3503, 2980, 1711, 1458, 1370, 1289, 1170, 1081, 1046 cm⁻¹; <sup>1</sup>H NMR (400 MHz, C₆D₆) δ 1.19 (3H, s, acetonide), 1.22 (9H, s, COC(CH₃)₃), 1.39 (3H, s, acetonide), 1.72 (3H, s, H18), 3.94 (1H, br d, J = 9.2 Hz, H9), 4.02 (1H, dd, J = 9.2, 6.0 Hz, H8), 4.38 (1H, ddd, J = 7.8, 6.0, 3.7 Hz, H14), 4.49 (1H, dd, J = 11.9, 7.8 Hz, H13a), 4.58 (1H, dd, J = 11.9, 3.7 Hz, H13b), 4.84 (1H, s, C=CH₂H₃), 4.96 (1H, s, C=CH₂H₃); <sup>13</sup>C NMR (100 MHz, C₆D₆) δ 17.8, 25.5, 27.3, 28.0, 38.8, 63.8, 73.8, 76.2, 77.8, 108.9, 113.7, 145.7, 177.9; HRMS (ESI) calcd for C₁₅H₂₆O₅Na, 309.1672 (M+Na⁺), found 309.1678.

Determination of the C9 stereochemistry: Acetonide S₃. PPTS (9.6 mg, 38 µmol) was added to a solution of diol S₂ (16 mg, 79 µmol) in CH₂Cl₂ (0.8 mL) and 2-methoxy-1-propene (36 µL, 0.38 mmol) at room temperature. The reaction mixture was stirred at room temperature for 5 min, and was quenched with saturated aqueous NaHCO₃ (1.5 mL). The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (1 mL ×3). The combined organic layers were washed with brine (2 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified twice by flash chromatography (1<sup>st</sup>: Kanto silica gel 2 g, hexane/EtOAc 20:1 to 1:1; 2<sup>nd</sup>: Kanto silica gel 1 g, CH₂Cl₂/EtOAc 1:0 to 0:1) to afford S₃ (9.8 mg, 40 µmol) in 51% yield: colorless oil; [α]D<sup>19</sup> +37 (c 0.49, CHCl₃); IR (neat) ν<sub>max</sub> 2989, 1380, 1217, 1163, 1085, 1049 cm⁻¹; <sup>1</sup>H NMR (400 MHz, C₆D₆) δ 1.21 (3H, s, acetonide), 1.27 (3H, s, acetonide), 1.33 (3H, s, acetonide), 1.50 (3H, s, acetonide), 1.87 (3H, s, H18), 3.62 (1H, dd, J = 14.2, 1.4 Hz, H13a), 3.71 (1H, dt, J = 5.5, 1.8 Hz, H14), 3.85 (1H, dd, J = 14.2, 1.8 Hz, H13b), 3.89 (1H, dd, J = 9.6, 5.5 Hz, H8), 4.40 (1H, d, J = 9.6 Hz, H9), 5.00 (1H, t, J = 1.8 Hz, C=CH₃H₃), 5.15 (1H, s, C=CH₃H₃); <sup>13</sup>C NMR (100 MHz, C₆D₆) δ 18.8, 23.9, 25.0, 26.0, 28.7, 58.7, 73.5, 77.2, 78.0, 101.3, 108.2, 114.0, 143.9; HRMS (ESI) calcd for C₁₃H₂₂O₄Na, 265.1410 (M+Na⁺), found 265.1399.
Supporting Information

**TBS ether 11.** A solution of pivaloate 10 (18.9 g, 66.1 mmol) in CH₂Cl₂ (220 mL) was cooled to 0 °C, and then Et₃N (18.4 mL, 132 mmol) and TBSOTf (15.6 mL, 66.0 mmol) were successively added. The reaction mixture was stirred at 0 °C for 10 min, and was poured into H₂O (200 mL). The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (200 mL ×3). The combined organic layers were washed with H₂O (200 mL) and brine (200 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Merck silica gel 600 g, hexane/EtOAc 50:1 to 5:1) to afford TBS ether 11 (24.9 g, 62.1 mmol) in 94% yield: colorless oil; [α]D₂¹ -30 (c 1.00, CHCl₃); IR (neat) ν max 2957, 2932, 2859, 1732, 1462, 1371, 1254, 1160, 1086 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 0.05 (3H, s, CH₃ of TBS), 0.16 (3H, s, CH₃ of TBS), 0.96 (9H, s, t-Bu of TBS), 1.22 (9H, s, COC(CH₃)₃), 1.23 (3H, s, acetonide), 1.45 (3H, s, acetonide), 1.69 (3H, s, H18), 4.12 (1H, dd, J = 8.2, 6.0 Hz, H8), 4.26 (1H, d, J = 8.2 Hz, H9), 4.38 (1H, ddd, J = 8.2, 6.0, 2.3 Hz, H14), 4.47 (1H, dd, J = 11.9, 2.3 Hz, H13b), 4.85 (1H, t, J = 1.4 Hz, C=CH₂H₈), 4.99 (1H, s, C=CH₂H₈); ¹³C NMR (100 MHz, C₆D₆) δ -5.2, -4.0, 17.2, 18.3, 25.6, 26.0, 27.4, 28.0, 38.8, 64.4, 75.5, 76.0, 77.7, 108.8, 115.0, 145.1, 177.9; HRMS (ESI) calcd for C₂₁H₄₀O₅SiNa, 423.2537 (M+Na⁺), found 423.2525.

**Alcohol 12.** DIBAL-H (1.0 M in hexane, 124 mL, 124 mmol) was added dropwise to a solution of 11 (24.9 g, 62.2 mmol) in CH₂Cl₂ (210 mL) -78 °C. The reaction mixture was stirred at -78 °C for 45 min, and was poured into a mixture of EtOAc and saturated aqueous Rochelle’s salt (300 mL, 1:1). The mixture was stirred at room temperature for 12 h. The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (200 mL ×3). The combined organic layers was washed with H₂O (200 mL ×2) and brine (200 mL), dried over Na₂SO₄, filtered, and concentrated. The crude residue was combined with another batch of alcohol 12 that was synthesized from 11.
Supporting Information

(32.0 g, 79.8 mmol) by the same procedure described above. The combined crude was purified by recrystallization from Et₂O/hexane to afford 12 (27.8 g, 87.7 mmol) in 62% yield as a white needle. The mother liquid was concentrated and purified by flash chromatography (Merck silica gel 600 g, hexane/EtOAc 50:1 to 5:1) to afford 12 (12.4 g, 39.2 mmol) in 28% yield. The combined yield of the reactions was 90%: m.p. 54-56 °C; [α]D <sup>19</sup> -19 (c 1.00, CHCl₃); IR (neat) ν <sub>max</sub> 3488, 2954, 2932, 2858, 1463, 1371, 1253, 1220, 1078 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 0.05 (3H, s, C₃H₃ of TBS), 0.10 (3H, s, C₃H₃ of TBS), 0.94 (9H, s, t-Bu of TBS), 1.23 (3H, s, acetonide), 1.39 (3H, s, acetonide), 1.67 (3H, s, H₁₈), 2.32 (1H, ddd, J = 7.8, 6.0, 6.0 Hz, OH), 3.85 (1H, ddd, J = 11.4, 6.0 Hz, H₁₃a), 3.91 (1H, ddd, J = 11.4, 7.8, 4.6 Hz, H₁₃b), 4.10 (1H, dd, J = 8.2, 6.4 Hz, H₈), 4.23 (1H, ddd, J = 6.4, 6.0, 4.6 Hz, H₁₄), 4.35 (1H, d, J = 8.2 Hz, H₉), 4.83 (1H, m, C=CH₂H₁₈), 5.00 (1H, s, C=CH₂H₁₈); ¹³C NMR (100 MHz, C₆D₆) δ -5.1, -4.1, 17.4, 18.3, 25.5, 26.0, 28.0, 61.7, 75.4, 77.8, 78.5, 108.2, 114.9, 145.1; HRMS (ESI) calcd for C₁₆H₃₂O₄SiNa, 339.1962 (M+Na⁺), found 339.1974.

Diene 13. DMSO (1.1 mL, 16 mmol) in CH₂Cl₂ (16 mL) was added dropwise to a solution of (COCl)₂ (540 µL, 6.4 mmol) in CH₂Cl₂ (40 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 10 min. To the mixture was added a solution of alcohol 12 (1.01 g, 3.19 mmol) in CH₂Cl₂ (8 mL). The resultant mixture was stirred at -78 °C for 1 h, and then Et₃N (3.1 mL, 22 mmol) was added at -78 °C. The reaction mixture was allowed to warm to 0 °C, stirred for 1 h, and was quenched with H₂O (80 mL). The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (50 mL ×3). The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, filtered, and concentrated to afford crude aldehyde S₄, which was used for the next reaction without further purification.

Vinylmagnesium bromide (1.0 M in THF, 4.0 mL, 4.0 mmol) was added dropwise to the above crude aldehyde S₄ in THF (44 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 10 min, and was quenched with saturated aqueous NH₄Cl (50 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (30 mL ×3). The combined organic layers were washed with brine (60 mL), dried over
Supporting Information

Na₂SO₄, filtered, and concentrated. The crude residue was purified by flash chromatography (Merck silica gel 20 g, hexane/EtOAc 30:1 to 2:1) to afford diene 13 (854 mg, 2.49 mmol) in 78% yield over 2 steps: crystal: m.p. 48-51 °C; [α]_D^{20} -29 (c 1.01, CHCl₃); IR (neat) νmax 3567, 3486, 2954, 2931, 2858, 1462, 1372, 1253, 1069 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.07 (3H, s, CH₃ of TBS), 0.14 (3H, s, CH₃ of TBS), 0.90 (9H, s, t-Bu of TBS), 1.36 (3H, s, acetonide), 1.52 (3H, s, acetonide), 1.78 (3H, s, H18), 2.85 (1H, d, J = 6.8 Hz, OH), 4.09 (1H, dd, J = 7.0, 1.4 Hz, H9), 4.25 (1H, dd, J = 7.0, 7.0 Hz, H8), 4.43 (1H, m, H13), 4.61 (1H, d, J = 7.0 Hz, H14), 5.01 (1H, d, J = 1.4 Hz, C=CH₂H₈), 5.13 (1H, s, C=CH₂H₈), 5.18 (1H, ddd, J = 10.5, 1.6, 1.6 Hz, CH=CH₂H₈), 5.30 (1H, ddd, J = 17.4, 1.6, 1.6 Hz, CH=CH₂H₈), 5.93 (1H, ddd, J = 17.4, 10.5, 5.5 Hz, H12); ¹³C NMR (100 MHz, CDCl₃) δ -5.3, -4.3, 17.6, 18.2, 24.6, 25.8, 26.5, 70.0, 75.0, 77.2, 79.4, 108.1, 114.9, 115.2, 138.6, 144.1; HRMS (ESI) calcd for C₁₈H₃₄O₄SiNa, 365.2119 (M+Na⁺), found 365.2108.

Allyl alcohol 14. A mixture of diene 13 (4.38 g, 12.8 mmol) and 1,4-benzoquinone (28 mg, 260 µmol) in toluene (210 mL) was heated to 80 °C. Hoveyda-Grubbs 2nd generation catalyst A (80 mg, 130 µmol) in toluene (50 mL) was added by an addition funnel over 5.5 h, and the resultant mixture was stirred at 80 °C for further 3 h. The reaction mixture was passed through a short pad of silica gel (Merck silica gel) and the filter cake was washed with a mixture of CH₂Cl₂ and acetone (2:1). The filtrate was concentrated, and the residue was purified by flash chromatography (Merck silica gel 100 g, hexane/EtOAc 20:1 to 2:1) to afford allyl alcohol 14 (3.20 g, 10.3 mmol) in 80% yield as a green oil. The green color was attributed to the residual ruthenium catalyst although the isolated compound was sufficiently pure from the ¹H NMR. The product was isolated as a single diastereomer, however the stereochemistry at the C13 position was not determined: [α]_D^{29} -51 (c 1.00, CHCl₃); IR (neat) νmax 3453, 2931, 2857, 1378, 1254, 1209, 1135, 1066 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.08 (3H, s, CH₃ of TBS), 0.10 (3H, s, CH₃ of TBS), 0.90 (9H, s, t-Bu of TBS), 1.33 (3H, s, acetonide), 1.43 (3H,
s, acetonide), 1.81 (3H, s, H18), 2.09 (1H, br s, OH), 4.21 (1H, dd, J = 7.8, 4.6 Hz, H14), 4.30 (1H, dd, J = 7.8, 3.6 Hz, H8), 4.39 (1H, d, J = 3.6 Hz, H9), 4.45 (1H, m, H13), 5.59 (1H, m, H12); 13C NMR (100 MHz, CDCl3) δ -4.7, -4.5, 18.2, 20.3, 24.6, 25.8, 26.4, 69.2, 69.6, 76.9, 80.0, 109.7, 125.5, 140.9; HRMS (ESI) calcd for C16H30O4SiNa, 337.1806 (M+Na+), found 337.1791.

**Enone 15.** TPAP (107 mg, 304 µmol) was added to a mixture of 14 (1.87 g, 5.95 mmol), NMO (1.04 g, 8.92 mmol) and 4Å MS (3 g, activated by drying in oven at 120 ℃ for 3 h) in CH2Cl2 (60 mL) at room temperature. The resultant suspension was stirred at room temperature for 1 h, and was filtered through a pad of Celite with a mixture of CH2Cl2/acetone (200 mL, 5:1). The filtrate was concentrated, and the residue was passed through a pad of silica gel (Kanto silica gel 100 g, CH2Cl2/acetone 5:1) to remove the residual ruthenium catalyst. The fractions containing the product were collected and concentrated. The concentrate was further purified by flash chromatography (Merck silica gel 30 g, hexane/Et2O 5:1 to 1:2) to afford enone 15 (1.70 g, 5.44 mmol) in 91% yield: colorless oil; [α]D24 -40 (c 0.94, CHCl3); IR (neat) νmax 2931, 2857, 1675, 1379, 1234, 1135, 1102, 1065 cm⁻¹; 1H NMR (400 MHz, CDCl3) δ -4.7, -4.5, 18.2, 20.3, 24.6, 25.8, 26.4, 69.2, 69.6, 76.9, 80.0, 109.7, 125.5, 140.9; HRMS (ESI) calcd for C16H28O4SiNa, 335.1649 (M+Na+), found 335.1640.

**Ketone 16.** A solution of enone 15 (1.70 g, 5.44 mmol) and Pd/C (10 wt% Pd on 15O, NMO, NOE 118
carbon, 170 mg) in EtOAc (27 mL) was exposed to H₂ atmosphere (1 atm), and was stirred at room temperature for 30 min. Then, the reaction mixture was passed through a pad of Celite. The filter cake was washed with EtOAc (100 mL), and the filtrate was concentrated to afford keone 16 (1.60 g, 5.09 mmol) in 94% yield, which was used in the next reaction without further purification: white crystal; m.p. 102-104 °C; [α]D<sup>25</sup> -0.017 (c 1.07, CHCl₃); IR (neat) ν<sub>max</sub> 2928, 1726, 1460, 1377, 1257, 1167, 1107 cm⁻¹; <sup>1</sup>H NMR (400 MHz, CDCl₃) δ 0.04 (3H, s, CH₃ of TBS), 0.06 (3H, s, CH₃ of TBS), 0.85 (9H, t-Bu of TBS), 1.07 (3H, d, J = 6.4 Hz, H18), 1.34 (3H, s, acetonide), 1.51 (3H, s, acetonide), 2.07 (1H, dd, J = 17.0, 10.1 Hz, H12a), 2.16-2.22 (1H, m, H11), 2.37 (1H, dd, J = 17.0, 7.4 Hz, H12b), 3.99 (1H, d, J = 3.7 Hz, H9), 4.36 (1H, d, J = 9.6 Hz, H14), 4.48 (1H, dd, J = 9.6, 3.7 Hz, H8); <sup>13</sup>C NMR (100 MHz, CDCl₃) δ -4.7, -3.7, 18.1, 18.6, 24.2, 25.8, 26.0, 31.3, 40.1, 70.1, 77.2, 78.4, 110.1, 205.9; HRMS (ESI) calcd for C₁₆H₃₆O₄SiNa, 337.1806 (M+Na⁺), found 337.1811.

Alcohol 16. A oven-dried 3-neck round-bottom flask was charged with 2-bromopropene (2.6 mL, 29 mmol) and THF (80 mL), and the solution was cooled to -78 °C. t-BuLi (1.65 M solution in pentane, 37 mL, 61 mmol) was added dropwise by an addition funnel, and the resultant canary yellow solution was stirred at -78 °C for 30 min. The mixture was then treated with LaCl₃·2LiCl (0.6 M solution in THF, 50 mL, 30 mmol). The resultant burgundy mixture was further stirred at -78 °C for 30 min, and a solution of alcohol 16 (4.75 g, 15.1 mmol) in THF (20 mL) was added dropwise via cannula. The reaction mixture was stirred at -78 °C for 30 min, and was poured into a stirring mixture of saturated aqueous NH₄Cl (200 mL) and EtOAc (60 mL). The mixture was filtered through a pad of Celite with EtOAc (80 mL). The aqueous phase was separated and extracted with EtOAc (100 mL ×3). The combined organic layers were washed with brine (150 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Merck silica gel 200 g, hexane/EtOAc 100:1 to 1:1) to afford alcohol 17 (4.71 g, 13.2 mmol) in 87% yield: crystal; m.p. 57-60 °C; [α]D<sup>28</sup> -31 (c 0.83, CHCl₃); IR (neat) ν<sub>max</sub> 3417, 2929, 2360, 1366, 1255,
Supporting Information

1039 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 0.13 (3H, s, CH\(_3\) of TBS), 0.17 (3H, s, CH\(_3\) of TBS), 0.94 (9H, s, t-Bu of TBS), 1.05 (3H, d, \(J = 6.8\) Hz, H18), 1.36 (3H, s, acetonide), 1.54 (3H, s, acetonide), 1.57 (1H, dd, \(J = 14.6, 10.5\) Hz, H12a), 1.64-1.71 (1H, m, H11), 1.82 (3H, s, H17), 2.00 (1H, dd, \(J = 14.6, 7.8\) Hz, H12b), 4.12 (1H, dd, \(J = 5.0, 1.8\) Hz, H9), 4.18 (1H, d, \(J = 8.2\) Hz, H14), 4.23 (1H, dd, \(J = 8.2, 5.0\) Hz, H8), 4.72 (1H, s, OH), 4.93 (1H, m, H16a), 5.17 (1H, m, H16b); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) -4.9, -4.2, 18.4, 19.1, 19.6, 25.2, 25.9, 26.2, 30.6, 40.3, 71.1, 73.3, 75.6, 77.2, 109.7, 111.5, 147.7; HRMS (ESI) calcd for C\(_{19}\)H\(_{36}\)O\(_4\)SiNa, 379.2275 (M+Na\(^+\)), found 379.2256.

Diol S5. TBAF (1.0 M in THF, 45 mL, 45 mmol) was added to a solution of alcohol 17 (7.76 g, 21.7 mmol) in THF (70 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 10 min, and was quenched with saturated aqueous NH\(_4\)Cl (70 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (20 mL x3). The combined organic layers were washed with brine (20 mL), dried over Na\(_2\)SO\(_4\), filtered, and concentrated. The residue was purified by flash chromatography (Merck silica gel 120 g, hexane/EtOAc 5:1 to 1:2) to afford diol S5 (4.65 g, 19.2 mmol) in 88% yield: crystal; m.p. 113-117 °C; [\(\alpha\)]\(_D\)\(^{24}\) -53 (c 1.04, CHCl\(_3\)); IR (neat) \(\nu\)\(_{max}\) 3387, 2928, 1455, 1382, 1261, 1212, 1162 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CD\(_3\)OD) \(\delta\) 1.09 (3H, d, \(J = 6.8\) Hz, H18), 1.39 (3H, s, acetonide), 1.53 (3H, s, acetonide), 1.53 (1H, dd, \(J = 14.6, 9.6\) Hz, H12a), 1.65-1.75 (1H, m, H11), 1.82 (3H, s, H17), 1.88 (1H, dd, \(J = 14.6, 8.2\) Hz, H12b), 3.84 (1H, dd, \(J = 5.5, 2.3\) Hz, H9), 4.30 (1H, dd, \(J = 8.2, 5.5\) Hz, H8), 4.38 (1H, d, \(J = 8.2\) Hz, H14), 4.90 (1H, m, H16a), 5.09 (1H, s, H16b); \(^{13}\)C NMR (100 MHz, CD\(_3\)OD) \(\delta\) 19.0, 19.5, 24.7, 26.2, 31.1, 38.7, 70.5, 75.6, 77.1, 77.3, 110.0, 111.9, 149.5; HRMS (ESI) calcd for C\(_{13}\)H\(_{22}\)O\(_4\)Na, 265.1410 (M+Na\(^+\)), found 265.1419.
TIPS ether S8. IBX (3.87 g, 13.8 mmol) was added to a solution of diol S5 (2.23 g, 9.21 mmol) in DMSO (61 mL) was added. The reaction mixture was stirred at 80 °C for 30 min, cooled to room temperature, and then quenched with saturated aqueous NaHCO₃ (50 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Merck silica gel) to afford an inseparable mixture of ketones 18 and S6 (2.09 g, 8.70 mmol), which was used for the next reaction without further purification.

DOWEX 50Wx8 (200-400 mesh, 10.5 g) was added to a solution of the above mixture of ketones 18 and S6 in THF/H₂O (87 mL, 3:1). The reaction mixture was stirred at 80 °C for 12 h, and was cooled to room temperature. The resin was removed by the filtration through a pad of Celite with acetone (200 mL). The filtrate was concentrated to afford crude triol S7, which was used for the next reaction without further purification. For a characterization, a small amount of triol S7 was purified by flash chromatography (Merck silica gel, hexane/EtOAc 1:1 to 1:3): [α]D24 ± -4.3 (c 1.74, CHCl₃); IR (neat) νmax 3400, 2971, 2933, 1726, 1450, 1129, 1027 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.10 (3H, d, J = 6.4 Hz, H18), 1.96 (3H, s, H17), 2.01 (1H, dd, J = 14.2 Hz, H12a), 2.32 (1H, ddd, J = 14.2, 6.4, 2.3 Hz, H12b), 2.50 (1H, ddq, J = 14.2, 6.4, 6.4 Hz, H11), 2.88 (1H, s, OH), 3.41 (1H, d, J = 2.3 Hz, OH), 3.93 (1H, d, J = 4.1 Hz, OH), 4.22 (1H, m, H8), 4.43 (1H, m, H14), 5.24 (1H, s, H16a), 5.31 (1H, s, H16b); ¹³C NMR (100 MHz, CDCl₃) δ 13.5, 18.8, 38.7, 39.3, 73.9, 74.5, 76.8, 114.8, 144.0, 210.7; HRMS (ESI) calcd for C₁₀H₁₆O₄Na, 223.0941 (M+Na⁺), found 223.0945.

TIPSOTf (4.7 mL, 18 mmol) were added to a solution of the above crude S7 and Et₃N (4.8 mL, 35 mmol) in CH₂Cl₂ (44 mL) at 0 °C. The reaction mixture was stirred at
Supporting Information

0 °C for 3 h, and was quenched with H₂O (50 mL). The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (10 mL × 3). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Merck silica gel 100 g, hexane/EtOAc 6:1 to 4:1) to afford TIPS ether S₈ (1.98 g, 5.56 mmol) in 60% yield over 3 steps: white solid; m.p. 46-47 °C; [α]D²⁴ -16 (c 0.51 CHCl₃); IR (neat) νmax 3463, 2943, 2868, 1739, 1464, 1165, 1011 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.04-1.17 (24H, m, H₁₈, (Si(CH₃)₂)₃), 1.95 (1H, dd, J = 13.3, 13.3 Hz, H₁₂a), 1.97 (3H, s, H₁₇), 2.29 (1H, ddd, J = 13.3, 5.9, 1.8 Hz, H₁₂b), 2.35 (1H, dqq, J = 13.3, 6.4, 5.9 Hz, H₁₁), 2.76 (1H, s, OH), 2.90 (1H, s, OH), 4.36 (1H, br s, H₈), 4.43 (1H, d, J = 3.2 Hz, H₁₄), 5.25 (1H, d, J = 0.9 Hz, H₁₆a), 5.27 (1H, s, H₁₆b); ¹³C NMR (100 MHz, CDCl₃) δ 12.2, 13.9, 17.9, 19.0, 38.8, 39.7, 74.0, 75.8, 78.5, 114.6, 144.3, 208.2; HRMS (ESI) calcd for C₁₉H₃₆O₄SiNa, 379.2275 (M+Na⁺), found 379.2282.

Orthoester 2₁. (+)-CSA (97 mg, 420 µmol) was added to a solution of TIPS ether S₈ (1.49 g, 4.17 mmol) and trimethyl orthoacetate (3.8 mL, 30 mmol) in benzene (42 mL). The mixture was heated to 50 °C for 30 min, and was allowed to cool to room temperature. Then, saturated aqueous NaHCO₃ (40 mL) was added, and the organic layer was separated. The aqueous layer was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine (40 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was azeotropically dried with toluene to afford a 8.3 : 1 diastereomixture of crude 1₉, which was used for the next reaction without further purification.

A oven-dried 3-neck round-bottom flask was charged with ethyl vinyl ether (2.8 mL, 29 mmol) and THF (33 mL), and the solution was cooled to -78 °C. After t-BuLi (1.65 M solution in pentane, 13 mL, 21 mmol) was injected dropwise into the flask, the dry
ice-acetone bath was replaced with an ice bath and the reaction flask was allowed to warm to 0 °C. The canary yellow solution turned colorless after stirred at 0 °C for 15 min. The resultant colorless solution was cooled to -78 °C, and was treated with LaCl$_3$·2LiCl (0.6 M solution in THF, 35 mL, 21 mmol). The resultant amber-colored solution was further stirred at -78 °C for 15 min, then a solution of the above crude 19 in THF (9 mL) was added dropwise via cannula. The mixture was stirred at -78 °C for 10 min and at 0 °C for 5 min, and was poured into a stirring mixture of saturated aqueous NH$_4$Cl (50 mL) and EtOAc (20 mL). The white precipitate was filtered through a pad of Celite with EtOAc (200 mL). The filtrate was concentrated to ca.100 mL. The aqueous phase was separated and extracted with EtOAc (30 mL x3). The combined organic layers were washed with brine (50 mL), dried over Na$_2$SO$_4$, filtered, and concentrated to afford crude alcohol 20 (1.6 g), which was used for the next reaction without further purification.

(+)-CSA (97 mg, 420 µmol) was added to a solution of the above crude alcohol 20 in a mixture of benzene and triethyl orthoformate (42 mL, 5:1). The reaction mixture was stirred at room temperature for 30 min. Saturated aqueous NaHCO$_3$ (60 mL) was added to the mixture, and the organic layer was separated. The aqueous layer was extracted with EtOAc (40 mL x3). The combined organic layers were washed with brine (50 mL), dried over Na$_2$SO$_4$, filtered, and concentrated. The residue was purified by flash chromatography (Kanto silica gel 50 g, hexane/EtOAc 20:1) to afford orthoester 21 (1.52 g, 3.36 mmol) in 80% yield over 3 steps: colorless oil: [α]$_D^{24}$ +87 (c 0.96, MeOH); IR (neat) $\nu_{\text{max}}$ 2941, 2867, 1402, 1302, 1158, 1107 cm$^{-1}$; $^1$H NMR (400 MHz, C$_6$D$_6$) $\delta$ 1.10-1.15 (3H, m, SiCH(CH$_3$)$_2$ x 3), 1.11 (3H, t, $J = 7.3$ Hz, CH$_2$CH$_3$), 1.17 (9H, d, $J = 6.4$ Hz, SiCH(CH$_3$) x 3), 1.21 (9H, d, $J = 6.4$ Hz, SiCH(CH$_3$) x 3), 1.29 (3H, d, $J = 7.3$ Hz, H$_{18}$), 1.63 (1H, d, $J = 14.6$ Hz, H$_{12a}$), 1.71 (3H, br s, H$_{17}$), 1.78 (3H, s, CCH$_3$), 1.83 (1H, dd, $J = 14.6$, 9.2 Hz, H$_{12b}$), 2.48 (1H, dq, $J = 9.2$, 7.3 Hz, H$_{11}$), 3.43 (1H, dq, $J = 9.6$, 7.3 Hz, CH$_3$H$_8$CH$_3$), 3.57 (1H, dq, $J = 9.6$, 7.3 Hz, CH$_3$H$_8$CH$_3$), 4.00 (1H, d, $J = 3.2$ Hz, H$_8$), 4.18 (1H, d, $J = 1.4$ Hz, (EtO)C=CH$_3$H$_8$), 4.42 (1H, d, $J = 3.2$ Hz, H$_{14}$), 4.84 (1H, d, $J = 1.4$ Hz, H$_{16a}$), 4.85 (1H, d, $J = 1.4$ Hz, (EtO)C=CH$_3$H$_8$), 5.14 (1H, d, $J = 1.4$ Hz, H$_{16b}$); $^{13}$C NMR (100 MHz, C$_6$D$_6$) $\delta$ 13.4, 14.5, 17.7, 18.4, 18.5, 19.2, 21.5, 33.0, 33.6, 62.7, 67.4, 80.4, 82.1, 83.9, 85.4, 110.9, 118.5, 146.7, 160.1; HRMS (ESI) calcd for C$_{25}$H$_{44}$O$_5$SiNa, 475.2850 (M+Na$^+$), found 475.2878.
**Supporting Information**

O,Se-Acetal 27. m-CPBA (75% purity, 283 mg, 1.23 mmol) was added to a solution of 21 (1.11 g, 2.46 mmol) in a mixture of CH₃CN/H₂O (35 mL, 2:1) at 10 °C. The equal amount of m-CPBA was added to the reaction mixture at 10 °C in every 20 min twice. Once TLC indicated the disappearance of 21, the reaction temperature was carefully raised to 15~17 °C. After completion of the reaction was indicated on TLC, saturated aqueous NaHCO₃ (5 mL) was added. The organic layer was separated, and the aqueous layer was extracted with Et₂O (10 mL × 3). The combined organic layer was washed with saturated aqueous NaHCO₃ (10 mL × 2), saturated aqueous NH₄Cl (10 mL × 2), saturated aqueous NaHCO₃ (10 mL), and brine (10 mL), dried over Na₂SO₄, filtered, and concentrated to afford crude hydroxyketone 22, which was used for the next reaction without further purification. For a characterization, a small amount of hydroxyketone 22 was purified by flash chromatography (Fuji Silysia silica gel, hexane/EtOAc 10:1): white crystal m.p. 58-60 °C; [α]D₂⁴ +108 (c 0.78, MeOH); IR (neat) νmax 3535, 2944, 2867, 1718, 1461, 1400, 1305, 1263, 1154, 1077 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 0.92 (3H, d, J = 7.3 Hz, H₁₈), 0.96-1.04 (3H, m, SiC(H(CH₃))₂ x 3), 1.07 (9H, d, J = 6.9 Hz, SiCH(CH₃) x 3), 1.10 (9H, d, J = 6.9 Hz, SiCH(CH₃) x 3), 1.42 (1H, d, J = 14.6 Hz, H₁₂a), 1.60 (3H, s, H₁₇), 1.62 (3H, s, CCH₃), 1.68 (1H, dd, J = 14.6, 9.2 Hz, H₁₂b), 2.51 (1H, dq, J = 9.2, 7.3 Hz, H₁₁), 3.14 (1H, t, J = 4.6, OH), 3.90 (1H, d, J = 3.2 Hz, H₁₄), 4.28 (1H, d, J = 3.2 Hz, H₈), 4.57 (1H, dd, J = 21.1, 4.6 Hz, COCH₃H₉OH), 4.79 (1H, s, H₁₆a), 4.86 (1H, dd, J = 21.1, 4.6 Hz, COCH₃H₉OH), 5.03 (1H, s, H₁₆b); ¹³C NMR (100 MHz, C₆D₆) δ 13.0, 17.8, 18.0, 18.1, 19.0, 20.9, 33.1,
Supporting Information

35.4, 69.0, 69.2, 79.8, 86.1, 88.0, 111.3, 118.5, 145.7, 212.9; HRMS (ESI) calcd for C_{23}H_{40}O_{6}SiNa, 463.2486 (M+Na^+), found 463.2476.

Me_3BnNOH (40% in MeOH, 4.5 mL, 9.9 mmol) and TBHP (70% in H_2O, 1.2 mL, 8.7 mmol) were successively added to a solution of crude hydroxyketone 22 in THF (7.4 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 10 min, and was allowed to warm to room temperature. After 1.5 h, solid NH_4Cl (2.63 g) and H_2O (1 mL) were added to the reaction mixture. The suspension was stirred for 20 min, then Na_2SO_4 was added. The insoluble salts were filtered through a pad of Celite with EtOAc (200 mL). The filtrate was concentrated, and the resultant residue was diluted with EtOAc (10 mL). White precipitate formation was observed. The precipitate was removed by passing the mixture through a pad of Celite with EtOAc (200 mL) and acetone (100 mL). The filtrate was concentrated. Toluene (30 mL) was added to the concentrate, and excess TBHP was removed azeotropically under reduced pressure twice to afford crude carboxylic acid 23, which was used for the next reaction without further purification.

MsCl (0.38 mL, 4.9 mmol) was added to a solution of the above crude carboxylic acid 23 and Et_3N (3.4 mL, 2.5 mmol) in CH_2Cl_2 (25 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 15 min, and was quenched with saturated aqueous NaHCO_3 (10 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (10 mL ×3). The combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated to afford crude mesylate 24, which was used for the next reaction without further purification.

2-mercaptopyridine N-oxide sodium salt (733 mg, 4.92 mmol) and DMAP (60 mg, 0.49 mmol) were successively added to a solution of the above crude mesylate 24 in toluene (25 mL) at room temperature. The reaction flask was wrapped with aluminum foil, and the mixture was stirred at room temperature for 1 h. [HRMS (ESI) of Barton ester 25, calcd for C_{27}H_{41}NO_6SSiNa, 558.2316 (M+Na^+), found 558.2327] Then, (PhSe)_2 (1.53 g, 4.92 mmol) was added to the reaction mixture. The aluminum foil was removed, and the reaction mixture was stirred under photo irradiation (a medium pressure mercury lamp, 100 W) at room temperature for 30 min. Saturated aqueous NaHCO_3 (10 mL) was added to the reaction mixture, and the organic layer was separated. The aqueous layer was extracted with EtOAc (10 mL ×3). The combined organic layer was washed with H_2O (10 mL ×2) and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated to afford crude O,Se-acetal 26, which was used for the next reaction without purification. For a characterization, a small amount of O,Se-acetal 26
was purified by flash chromatography (Kanto silica gel, hexane/EtOAc 20:1 to 5:1): colorless oil; [α]_D^{24} +88 (c 0.61, MeOH); IR (neat) ν_{max} 2942, 2867, 1463, 1400, 1154, 1069 cm⁻¹; \(^1\)H NMR (400 MHz, C₆D₆) δ 1.16-1.22 (21H, m, Si(CH(CH₃)₂)₃), 1.28 (3H, d, J = 6.9 Hz, H18), 1.48 (1H, d, J = 14.2 Hz, H12a), 1.63 (3H, s, H17), 1.67 (3H, s, CCH₃), 1.67 (1H, dd, J = 14.2, 8.7 Hz, H12b), 2.11 (1H, dq, J = 8.7, 6.9 Hz, H11), 3.89 (1H, d, J = 2.7 Hz, H8), 4.45 (1H, d, J = 2.7 Hz, H14), 4.80 (1H, m, H16a), 5.03 (1H, s, H16b), 7.03-7.07 (3H, m, aromatic); 13C NMR (100 MHz, C₆D₆) δ 13.6, 18.5, 18.6, 19.0, 19.2, 21.0, 34.8, 39.3, 70.7, 80.7, 85.3, 92.0, 111.2, 119.5, 128.7, 130.6, 136.5, 146.0; HRMS (ESI) calcd for C₂₇H₄₂O₄SeSiNa, 561.1910 (M+Na⁺), found 561.1904.

TBAF (1.0 M solution in THF, 3.0 mL, 3.0 mmol) was added to a solution of the above crude 26 in THF (25 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 10 min, and was quenched with saturated aqueous NH₄Cl (10 mL). The mixture was extracted with EtOAc (10 mL × 3). The combined organic layers were washed with H₂O (10 mL) and brine (10 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Kanto silica gel 30 g, hexane/EtOAc 10:1 to 5:1) to afford O,Se-acetal 27 (373 mg, 0.980 mmol) in 40% yield over 5 steps: yellow oil; [α]_D^{24} +95.7 (c 1.45, MeOH); IR (neat) ν_{max} 3467, 2934, 1438, 1398, 1302, 1170, 1124, 1102, 1070 cm⁻¹; \(^1\)H NMR (400 MHz, C₆D₆) δ 1.25 (1H, dd, J = 14.6, 8.7 Hz, H12a), 1.43 (1H, d, J = 14.6 Hz, H12b), 1.43 (3H, s, H17), 1.50 (3H, d, J = 7.3 Hz, H18), 1.60 (3H, s, CCH₃), 1.88 (1H, dq, J = 8.7, 7.3 Hz, H11), 3.14 (1H, dd, J = 10.0, 3.2 Hz, H8), 3.21 (1H, m, OH), 4.15 (1H, dd, J = 3.2, 1.4 Hz, H14), 4.71 (1H, m, H16a), 4.85 (1H, s, H16b), 7.00-7.06 (3H, m, aromatic); 13C NMR (100 MHz, C₆D₆) δ 18.7, 18.8, 20.8, 33.7, 36.7, 67.0, 80.4, 85.5, 93.6, 111.2, 119.5, 129.1, 138.4, 145.5. Two peaks overlap with solvent peak; HRMS (ESI), calcd for C₁₈H₂₂O₄SeNa, 405.0576 (M+Na⁺), found 405.0580.

**Acetate 6a.** Ac₂O (95 µL, 1.0 mmol), pyridine (0.33 mL, 4.0 mmol), and DMAP (2.5 mg, 0.20 µmol) were successively added to a solution of O,Se-acetal 27 (38 mg, 0.10 mmol) in CH₂Cl₂ (1.0 mL) at room temperature. The mixture was stirred at room temperature for 15 min, and then was washed with H₂O (10 mL) and brine (10 mL), filtered, and concentrated. The residue was purified by flash chromatography (Kanto silica gel 80 g, hexane/EtOAc 10:1 to 5:1) to afford acetate 6a (29 mg, 0.077 mmol) in 21% yield over 5 steps: yellow oil; [α]_D^{24} +95.7 (c 1.45, MeOH); IR (neat) ν_{max} 3467, 2934, 1438, 1398, 1302, 1170, 1124, 1102, 1070 cm⁻¹; \(^1\)H NMR (400 MHz, C₆D₆) δ 1.22-1.28 (21H, m, Si(CH(CH₃)₂)₃), 1.28 (3H, d, J = 6.9 Hz, H18), 1.48 (1H, d, J = 14.2 Hz, H12a), 1.63 (3H, s, H17), 1.67 (3H, s, CCH₃), 1.67 (1H, dd, J = 14.2, 8.7 Hz, H12b), 2.11 (1H, dq, J = 8.7, 6.9 Hz, H11), 3.89 (1H, d, J = 2.7 Hz, H8), 4.45 (1H, d, J = 2.7 Hz, H14), 4.80 (1H, m, H16a), 5.03 (1H, s, H16b), 7.03-7.07 (3H, m, aromatic); 13C NMR (100 MHz, C₆D₆) δ 13.6, 18.5, 18.6, 19.0, 19.2, 21.0, 34.8, 39.3, 70.7, 80.7, 85.3, 92.0, 111.2, 119.5, 128.7, 130.6, 136.5, 146.0; HRMS (ESI) calcd for C₂₇H₄₄O₆SeSiNa, 613.2059 (M+Na⁺), found 613.2053.
Supporting Information

temperature for 24 h, and was quenched with saturated aqueous NaHCO₃ (5 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (5 mL x 3). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Kanto silica gel 10 g, hexane/EtOAc 20:1) to afford acetate 6a (37 mg, 87 µmol) in 87% yield: colorless oil; [α]D²⁵ +88.0 (c 1.43, MeOH); IR (neat) ν max 2977, 2936, 1735, 1439, 1401, 1376, 1239, 1100 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 1.46 (3H, d, J = 6.8 Hz, H₁₈), 1.47-1.49 (2H, m, H₁₂), 1.48 (3H, s, H₁₇), 1.65 (3H, s, CCH₃), 1.78 (3H, s, Ac), 1.87 (1H, m, H₁₁), 4.41 (1H, d, J = 3.6 Hz, H₁₄), 4.72 (1H, m, H₁₆a), 4.89 (1H, d, J = 3.6 Hz, H₈), 4.90 (1H, s, H₁₆b), 7.10-7.04 (3H, m, aromatic), 7.74-7.77 (2H, m, aromatic); ¹³C NMR (100 MHz, C₆D₆) δ 18.8, 18.9, 20.7, 20.9, 34.0, 37.3, 69.7, 78.4, 85.5, 88.9, 111.6, 119.9, 128.6, 129.0, 129.4, 137.0, 145.3, 170.2; HRMS (ESI) calcd for C₂₀H₂₄O₅SeNa, 447.0681 (M+Na⁺), found 447.0673.

Acetate 6b. A solution of O,Se-acetal 27 (373 mg, 0.980 mmol) in DMSO/Ac₂O (9.8 mL, 4:1) was stirred at 35 °C for 2 h. Then, the reaction mixture was cooled to 0 °C, and was quenched with saturated aqueous NaHCO₃ (15 mL). EtOAc (10 mL) was added, and the organic layer was separated. The aqueous layer was extracted with EtOAc (10 mL x 3). The combined organic layer was washed with H₂O (10 mL × 2) and brine (10 mL), dried over Na₂SO₄, filtered, and concentrated to afford crude ketone S⁹, which was used for the next reaction without purification.

CeCl₃·7H₂O (728 mg, 1.95 mmol) and NaBH₄ (74 mg, 2.0 mmol) were successively added to a solution of the above crude ketone S⁹ in MeOH (14 mL) at -78 °C. The reaction mixture was stirred for 10 min at -78 °C, and was quenched with saturated aqueous NH₄Cl (10 mL). EtOAc (5 mL) was added, and the organic layer was separated. The aqueous layer was extracted with EtOAc (10 mL × 3). The combined
Supporting Information

organic layer was washed with brine (10 mL), dried over Na₂SO₄, filtered, and concentrated to afford crude alcohol 28, which was used for the next reaction without purification. For a characterization, a small amount of alcohol 28 was purified by flash chromatography (Kanto silica gel, hexane/EtOAc 20:1 to 5:1): white solid; m.p. 99-101 °C; [α]D²⁴ +47 (c 0.36, MeOH); IR (neat) νmax 3490, 2928, 1441, 1398, 1298, 1109, 1073, 1038 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 1.53 (3H, d, J = 7.3 Hz, H18), 1.58 (1H, d, J = 13.7 Hz, H12a), 1.61 (3H, s, H17), 1.64 (3H, s, CCH₃), 1.79 (1H, br s, OH), 2.26 (1H, dq, J = 9.2, 7.3 Hz, H11), 2.53 (1H, dd, J = 13.7, 9.2 Hz, H12b), 3.83 (1H, br s, H8), 4.03 (1H, d, J = 2.3 Hz, H14), 4.80 (1H, m, H16a), 5.11 (1H, m, H16b), 7.01-7.07 (3H, m, aromatic), 7.66-7.69 (2H, m, aromatic); ¹³C NMR (100 MHz, C₆D₆) δ 18.9, 20.2, 20.4, 34.1, 34.4, 69.5, 78.1, 84.9, 92.6, 111.1, 119.6, 127.4, 128.8, 128.9, 137.1, 146.2; HRMS (ESI) calcd for C₁₈H₂₂O₄SeNa, 405.0576 (M+Na⁺), found 405.0573.

Ac₂O (0.46 mL, 4.9 mmol), pyridine (1.6 mL, 20 mmol) and DMAP (24 mg, 0.20 mmol) were successively added to a solution of the above crude alcohol 28 in CH₂Cl₂ (10 mL). The reaction mixture was stirred at room temperature for 12 h, and was quenched with saturated aqueous NaHCO₃ (10 mL). The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (10 mL ×3). The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Kanto silica gel 20 g, hexane/EtOAc 20:1 to 10:1) to afford acetate 6b (350 mg, 0.83 mmol) in 84% over 3 steps: colorless oil; [α]D²² +4.4 (c 0.39, MeOH); IR (neat) νmax 2969, 2934, 1750, 1440, 1399, 1373, 1223, 1064 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 1.59 (3H, s, H17), 1.66 (3H, d, J = 6.9 Hz, H18), 1.70 (3H, s, CCH₃), 1.73 (3H, s, Ac), 1.74 (1H, d, J = 12.4 Hz, H12a), 2.33 (1H, dd, J = 12.4, 9.2 Hz, H12b), 2.36 (1H, dq, J = 9.2, 6.9 Hz, H11), 4.20 (1H, d, J = 2.3 Hz, H14), 4.85 (1H, m, H16a), 5.11 (1H, s, H16b), 5.50 (1H, d, J = 2.3 Hz, H8), 7.13-7.18 (3H, m, aromatic), 7.92-7.95 (2H, m, aromatic); ¹³C NMR (100 MHz, C₆D₆) δ 18.7, 20.0, 20.1, 20.4, 34.4, 34.8, 70.4, 76.9, 84.6, 88.3, 111.3, 119.7, 127.0, 128.8, 129.2, 138.2, 145.8, 168.4; HRMS (ESI) calcd for C₂₀H₂₄O₅SeNa, 447.0681 (M+Na⁺), found 447.0677.
**General procedure A: Compound 31bb.** A two-neck round-bottomed flask equipped with a reflux condenser was charged with 6b (49 mg, 115 µmol), 7b (123 mg, 580 µmol), V-40 (7 mg, 29 µmol) and chlorobenzene (0.8 mL). A separate pear-shaped flask was charged with 8 (348 mg, 580 µmol), V-40 (7 mg, 29 µmol) and chlorobenzene (0.4 mL). Both solutions were degassed by freeze-thaw procedure (x3). The latter solution was added to the refluxing former mixture by a syringe pump over 30 min, and then the reaction mixture was concentrated to afford crude 5bb, which was used for the next reaction without purification.

A mixture of the above crude 5bb and K$_2$CO$_3$ (14 mg, 100 µmol) in MeOH (2.3 mL) was stirred at room temperature for 3 h. Upon completion of the reaction indicated by ESI-MS, the reaction was quenched with saturated aqueous NH$_4$Cl (10 mL). The aqueous layer was extracted with EtOAc (10 mL x3). The combined organic layers were washed with brine (10 mL), dried over Na$_2$SO$_4$, filtered, and concentrated. The residue was purified by flash chromatography (a column consecutively packed with Kanto silica gel 20 g and 10% (w/w) KF contained Kanto silica gel 7 g, hexane/EtOAc 10:1 to 5:1) to afford 31bb (40 mg, 65 µmol) in 56% yield over 2 steps: colorless oil; [α]$_D^{22}$ +131 (c 0.54, MeOH); IR (neat) ν$_{max}$ 3432, 2931, 2855, 1693, 1399, 1110 cm$^{-1}$; $^1$H NMR (400 MHz, C$_6$D$_6$) δ 1.17 (9H, s, t-Bu of TBDPS), 1.23 (3H, d, $J = 7.3$ Hz, H18), 1.64 (1H, d, $J = 13.7$ Hz, H12a), 1.71 (3H, s, H17), 1.72 (3H, s, CCH$_3$), 2.14 (1H, dq, $J = 9.2$, 7.3 Hz, H11), 2.24 (1H, dd, $J = 15.1$, 4.6 Hz, H5a), 2.43 (1H, dd, $J = 15.1$, 6.0 Hz, H5b), 2.54 (1H, dd, $J = 13.7$, 9.2 Hz, H12b), 3.03 (2H, m, H4 and 10), 3.54 (1H, m, H8), 3.73 (1H, m, H14), 4.09 (1H, d, $J = 14.6$ Hz, H20a), 4.24 (1H, d, $J = 14.6$ Hz,
Supporting Information

H20b), 4.89 (2H, m, H7a and 16a), 5.21 (1H, s, H16b), 5.38 (1H, s, H7b), 5.97 (1H, d, J = 5.5 Hz, H2), 7.22-7.24 (6H, m, aromatic), 7.46 (1H, dd, J = 5.5, 2.3 Hz, H1), 7.76-7.79 (4H, m, aromatic); 13C NMR (100 MHz, C6D6) δ 18.5, 19.1, 19.5, 20.9, 27.0, 30.3, 35.01, 35.04, 45.8, 52.3, 66.4, 68.2, 78.9, 82.4, 84.7, 110.9, 112.0, 118.5, 130.0, 133.79, 133.82, 134.5, 135.87, 135.89, 145.1, 146.8, 166.8, 211.7. Two peaks overlap with solvent peak; HRMS (ESI) calcd for C37H46O6SiNa, 637.2956 (M+Na+), found 637.2982.

**Compound 30aa.** According to the general procedure A, 30aa (1.4 mg, 2.3 µmol) was synthesized from 6a (11 mg, 26 µmol) in 9% yield over 2 steps by using 7a (27 mg, 0.13 mmol), 8 (76 mg, 0.13 mmol), V-40 (3.0 mg, 12 µmol), chlorobenzene (0.26 mL), K2CO3 (1.8 mg, 13 µmol), and MeOH (1.3 mL). The crude residue was purified by flash chromatography (a column consecutively packed with Kanto silica gel 5 g and 10% (w/w) KF contained Kanto silica gel 3 g, hexane/EtOAc 10:1 to 5:1): colorless oil; [α]D24 +12 (c 0.10, MeOH); IR (neat) νmax 2926, 2855, 1740, 1402, 1110 cm⁻¹; 1H NMR (400 MHz, C6D6) δ 1.00 (3H, d, J = 7.3 Hz, H18), 1.19 (9H, s, t-Bu of TBDPS), 1.31-1.41 (2H, m, H11 and 12a), 1.52 (3H, s, H17), 1.58 (3H, s, CCH3), 1.52-1.60 (1H, m, H12b), 1.75 (1H, dd, J = 14.2, 10.5 Hz, H5a), 2.21 (1H, d, J = 8.7 Hz, H10), 2.30 (1H, dd, J = 14.2, 5.0 Hz, H5b), 2.45 (1H, dd, J = 19.2, 8.7 Hz, H2a), 2.84 (1H, dd, J = 19.2, 5.0 Hz, H2b), 2.88 (1H, d, J = 10.5, 5.0 Hz, H4), 3.21 (1H, d, J = 3.2 Hz, H8), 4.09 (1H, d, J = 14.2 Hz, H20a), 4.19 (1H, d, J = 14.2 Hz, H20b), 4.23 (1H, d, J = 3.2 Hz, H14), 4.69 (1H, dd, J = 8.7, 5.0 Hz, H1), 4.76 (1H, s, H16a), 4.84 (1H, s, H7a), 4.98 (1H, s, H16b), 5.38 (1H, s, H7b), 7.21-7.25 (6H, m, aromatic), 7.76-7.81 (4H, m, aromatic); 13C NMR (100 MHz, C6D6) δ 18.1, 18.8, 19.5, 20.8, 27.0, 34.7, 35.7, 36.4.
Two peaks overlap with solvent peak; HRMS (ESI) calcd for C\textsubscript{37}H\textsubscript{46}O\textsubscript{6}SiNa, 637.2956 (M\textsuperscript{+Na\textsuperscript{+}}), found 637.2957.

**Compound 30ab.** According to the general procedure A, 30ab (7.6 mg, 12 µmol) was synthesized from 6a (15 mg, 34 µmol) in 36% yield over 2 steps by using 7b (36 mg, 0.17 mmol), 8 (102 mg, 0.17 mmol), V-40 (4.2 mg, 17 µmol), chlorobenzene (0.68 mL), K\textsubscript{2}CO\textsubscript{3} (2.4 mg, 17 µmol), and MeOH (1.7 mL). The crude residue was purified by flash chromatography (a column consecutively packed with Kanto silica gel 8 g and 10% (w/w) KF contained Kanto silica gel 4 g, hexane/EtOAc 10:1 to 5:1): colorless oil; [α]\textsubscript{D}\textsuperscript{20} +23 (c 0.30, MeOH); IR (neat) ν\textsubscript{max} 2928, 2855, 1743, 1430, 1399, 1296, 1108 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, C\textsubscript{6}D\textsubscript{6}) δ 1.14 (3H, d, J = 6.4 Hz, H\textsubscript{18}), 1.18 (9H, s, t-Bu of TBDPS), 1.42-1.53 (3H, m, H\textsubscript{11} and 12), 1.59 (3H, s, H17), 1.69 (1H, m, H4), 1.76 (3H, s, C\textsubscript{CH}\textsubscript{3}), 1.77 (1H, dd, J = 18.8, 5.0 Hz, H2a), 2.05 (1H, dd, J = 14.5, 6.9 Hz, H5a), 2.23 (1H, dd, J = 9.6, 5.0 Hz, H10), 2.46 (1H, d, J = 14.5 Hz, H5b), 2.47 (1H, d, J = 18.8 Hz, H2b), 3.01 (1H, d, J = 2.8 Hz, H8), 4.01 (1H, d, J = 14.7 Hz, H20a), 4.22 (1H, d, J = 2.8 Hz, H14), 4.26 (1H, d, J = 14.7 Hz, H20b), 4.83 (1H, br s, H16a), 4.85 (1H, t, J = 5.0 Hz, H1), 4.96 (1H, s, H7a), 5.08 (1H, s, H16b), 5.51 (1H, s, H7b), 7.18-7.23 (6H, m, aromatic), 7.76-7.79 (4H, m, aromatic); \textsuperscript{13}C NMR (100 MHz, C\textsubscript{6}D\textsubscript{6}) δ 18.7, 19.1, 19.5, 21.3, 27.0, 31.7, 33.4, 35.2, 44.7, 46.4, 52.2, 66.7, 75.6, 76.6, 82.2, 86.0, 86.8, 110.9, 112.7, 118.1, 130.1, 133.66, 133.74, 135.8, 135.9, 144.9, 146.2, 216.3. Two peaks overlap with solvent peak; HRMS (ESI) calcd for C\textsubscript{37}H\textsubscript{46}O\textsubscript{6}SiNa, 637.2956 (M\textsuperscript{+Na\textsuperscript{+}}), found 637.2955.
**Compound 31ba.** According to the general procedure A, 31ba (10 mg, 16 µmol) was synthesized from 6b (26 mg, 61 µmol) in 27% yield over 2 steps by using 7a (64 mg, 0.30 mmol), 8 (181 mg, 0.30 mmol), V-40 (7.5 mg, 30 µmol), chlorobenzene (1.5 mL), K₂CO₃ (4.2 mg, 30 µmol), and MeOH (3.0 mL). The crude residue was purified by flash chromatography (a column consecutively packed with Kanto silica gel 10 g and 10% (w/w) KF contained Kanto silica gel 5 g, hexane/EtOAc 10:1 to 5:1): colorless oil; [α]D²⁰ -44 (c 0.18, MeOH); IR (neat) νmax 3445, 2931, 2857, 1692, 1399, 1298, 1110 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 1.19 (9H, s, t-Bu of TBDPS), 1.17 (3H, d, J = 8.2 Hz, H18), 1.56 (3H, s, CCH₃), 1.64 (1H, d, J = 13.7 Hz, H12a), 1.71 (3H, s, H17), 2.06 (1H, m, H11), 2.43-2.60 (4H, m, H12b, 4 and 5), 2.99 (1H, br s, H10), 3.32 (1H, m, H8), 3.82 (1H, d, J = 7.7 Hz, H14), 4.21 (1H, d, J = 14.6 Hz, H20a), 4.29 (1H, d, J = 14.6 Hz, H20b), 4.88 (1H, m, H16a), 5.02 (1H, s, H7a), 5.20 (1H, s, H16b), 5.47 (1H, s, H7b), 5.77 (1H, dd, J = 5.9, 2.3 Hz, H2), 7.07 (1H, m, H1), 7.22-7.24 (6H, m, aromatic), 7.78-7.82 (4H, m, aromatic); ¹³C NMR (100 MHz, C₆D₆) δ 18.5, 19.1, 19.5, 20.6, 27.1, 30.1, 34.9, 35.0, 46.3, 51.5, 66.6, 68.6, 78.6, 82.7, 84.7, 110.9, 111.9, 118.4, 127.9, 128.1, 130.0, 132.3, 134.0, 135.91, 135.93, 146.2, 146.8, 164.1, 210.4; HRMS (ESI) calcd for C₃₇H₄₆O₆SiNa, 637.2956 (M+Na⁺), found 637.2984.
Supporting Information

**Xanthate 4bb.** CS$_2$ (5.0 µL, 83 µmol) and NaH (50-70% in oil, 3.5 mg, ca. 88 µmol) were successively added to a solution of 31bb (27 mg, 44 µmol) in THF (2.2 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 10 min, and then MeI (5.0 µL, 80 µmol) was added. The mixture was allowed to warm to room temperature and stirred for further 2 h. The reaction mixture was quenched with saturated aqueous NH$_4$Cl (5 mL). The mixture was extracted with EtOAc (5 mL × 3). The combined organic layers were washed with brine (5 mL), dried over Na$_2$SO$_4$, filtered, and concentrated. The residue was purified by flash chromatography (Kanto silica gel 15 g, hexane/EtOAc 20:1) to afford xanthate 4bb (19 mg, 27 µmol) in 61% yield: yellow oil; [α]$_D^{20}$ +137 (c 0.38, MeOH); IR (neat) ν$_{max}$ 2962, 2932, 2857, 1712, 1400, 1198, 1108 cm$^{-1}$; $^1$H NMR (400 MHz, C$_6$D$_6$) δ 1.19 (9H, s, t-Bu of TBDPS), 1.25 (3H, d, $J$ = 7.3 Hz, H18), 1.58 (3H, s, H17), 1.69 (3H, s, CCH$_3$), 1.70 (1H, d, $J$ = 14.2 Hz, H12a), 1.97 (3H, s, C(=S)SCH$_3$), 2.20 (1H, dq, $J$ = 9.2, 7.3 Hz, H11), 2.23 (1H, dd, $J$ = 14.7, 6.9 Hz, H5a), 2.35 (1H, dd, $J$ = 14.2, 9.2 Hz, H12b), 2.43 (1H, dd, $J$ = 14.7, 5.9 Hz, H5b), 2.59 (1H, dd, $J$ = 6.9, 5.9 Hz, H4), 2.98 (1H, br s, H10), 4.17 (1H, d, $J$ = 14.7 Hz, H20a), 4.35 (1H, d, $J$ = 14.7 Hz, H20b), 4.53 (1H, m, H14), 4.81 (1H, m, H16a), 4.93 (1H, s, H7a), 5.14 (1H, m, H16b), 5.41 (1H, m, H7b), 5.91 (1H, s, H8), 5.96 (1H, dd, $J$ = 5.9, 1.8 Hz, H2), 7.21-7.24 (6H, m, aromatic), 7.28 (1H, dd, $J$ = 5.9, 2.8 Hz, H1), 7.77-7.80 (4H, m, aromatic); $^{13}$C NMR (100 MHz, C$_6$D$_6$) δ 18.6, 18.9, 19.2, 19.5, 20.5, 27.0, 31.3, 35.1, 35.8, 45.2, 52.2, 66.5, 75.1, 77.3, 81.8, 84.5, 111.4, 112.1, 119.0, 128.5, 130.0, 133.85, 133.95, 135.4, 135.9, 145.2, 145.8, 163.1, 207.9, 214.1. Two peaks overlap with solvent peak; HRMS (ESI) caled for C$_{39}$H$_{48}$O$_6$S$_2$SiNa, 727.2544 (M+Na$^+$), found 727.2551.
Compound 33. A flask was charged with xanthate 4bb (60 mg, 85 µmol), n-Bu₃SnH (115 µL, 428 µmol) and V-40 (10 mg, 43 µmol) and degassed xylene (10 mL). The mixture was heated under microwave irradiation at 180 °C for 5 min. The reaction mixture was then concentrated, and the residue was purified by flash chromatography (a column consecutively packed with Kanto silica gel 8 g and 10% (w/w) KF contained Kanto silica gel 3 g, hexane/EtOAc 5:1) to afford 33 (30 mg, 50 µmol) in 59% yield: colorless oil; [α]D° 19 +120 (c 0.17, MeOH); IR (neat) νmax 3007, 2934, 2858, 1708, 1399, 1296, 1108 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 0.80 (1H, ddd, J = 13.7, 13.7, 8.7 Hz, H5a), 1.16-1.19 (1H, m, H8), 1.17 (9H, s, t-Bu of TBDPS), 1.18 (3H, d, J = 6.9 Hz, H18), 1.45-1.55 (2H, m, H7a and 11), 1.55 (3H, s, CCH₃), 1.56 (1H, d, J = 14.2 Hz, H12a), 1.69 (3H, s, H17), 1.72 (1H, dd, J = 14.2, 8.2 Hz, H12b), 2.03 (1H, br dd, J = 10.6, 4.1 Hz, H7b), 2.07 (1H, m, H10), 2.46 (1H, m, H6), 2.55 (1H, ddd, J = 13.7, 4.6, 4.6 Hz, H5b), 3.03 (1H, ddd, J = 13.7, 4.6, 4.6 Hz, H4), 3.47 (1H, dd, J = 10.1, 8.2 Hz, H20a), 3.59 (1H, dd, J = 10.1, 6.0 Hz, H20b), 4.00 (1H, d, J = 2.3 Hz, H14), 4.85 (1H, t, J = 1.8 Hz, H16a), 5.03 (1H, s, H16b), 5.96 (1H, dd, J = 6.0, 2.8 Hz, H2), 7.09 (1H, dd, J = 6.0, 1.8 Hz, H1), 7.22-7.28 (6H, m, aromatic), 7.78-7.81 (4H, m, aromatic); ¹³C NMR (100 MHz, C₆D₆) δ 18.9, 19.5, 20.9, 21.4, 27.1, 31.4, 33.3, 35.4, 36.8, 37.1, 38.8, 46.2, 56.7, 69.1, 77.8, 84.0, 84.7, 110.7, 118.4, 129.99, 130.03, 133.1, 134.1, 134.3, 135.97, 136.04, 147.2, 160.3, 207.6. Two peaks overlap with solvent peak; HRMS (ESI) calcd for C₃₇H₄₆O₅SiNa, 621.3007 (M+Na⁺), found 621.3012.

Compound 3. A plastic test tube was charged with 33 (6.8 mg, 11 µmol) and CH₃CN (1.1 mL). HF·pyridine (ca. 70% HF, 20 µL, 770 µmol for HF) was added to the
solution at 0 °C. While the mixture was stirred at room temperature for 2 h, additional HF-pyridine (100 µL) was added three times every 30 min. The reaction mixture was carefully quenched with saturated aqueous NaHCO₃ (10 mL). The mixture was extracted with EtOAc (5 mL ×3). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (Kanto silica gel 10 g, hexane/EtOAc 5:1) to afford 3 (2.3 mg, 6.4 µmol) in 58% yield: colorless oil; [α]D²¹ + 130 (c 0.21, MeOH); IR (neat) νmax 3418, 2934, 1705, 1449, 1400, 1295, 1132 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 0.74 (1H, ddd, J = 13.8, 13.8, 10.1 Hz, H₅a), 1.12 (1H, m, H₈), 1.15 (3H, d, J = 6.9 Hz, H₁₈), 1.30 (1H, m, H₇a), 1.48 (1H, dq, J = 8.2, 6.9 Hz, H₁₁), 1.52 (1H, d, J = 14.2 Hz, H₁₂a), 1.53 (3H, s, CCH₃), 1.63 (3H, s, H₁₇), 1.67 (1H, dd, J = 14.2, 8.2 Hz, H₁₂b), 1.92 (1H, dd, J = 15.1, 2.3 Hz, H₇b), 2.12-2.20 (2H, m, H₆ and 10), 2.51 (1H, ddd, J = 13.8, 4.1, 4.1 Hz, H₅b), 3.05 (1H, ddd, J = 13.8, 4.1, 4.1 Hz, H₄), 3.11-3.17 (1H, m, H₂₀a), 3.19-3.24 (1H, m, H₂₀b), 3.94 (1H, s, H₁₄), 4.83 (1H, t, J = 1.8 Hz, H₁₆a), 4.99 (1H, s, H₁₆b), 5.98 (1H, dd, J = 6.0, 2.8 Hz, H₂), 7.08 (1H, d, J = 6.0 Hz, H₁); ¹³C NMR (100 MHz, C₆D₆) δ 18.9, 20.7, 21.4, 31.9, 33.8, 35.1, 36.9, 37.4, 38.9, 46.4, 56.5, 68.2, 77.8, 83.9, 84.7, 110.7, 118.3, 133.0, 147.1, 160.4, 207.7; HRMS (ESI) calcd for C₂₁H₂₈O₅Na, 383.1829 (M+Na⁺), found 383.1835.

**Molecular modeling**

The 3D structure of 28, in which Se atom was replaced with S atom, was built by the molecular mechanics simulation using a 1000-steps of mixed torsional/low-mode sampling conformational search and PRCG energy minimization with MM3* (MacroModel 9.9). S2

![3D structure model of 28 (Se Atom was replaced with S atom)](image)
