Studies toward the total synthesis of scyphostatin: first entry to the highly functionalized cyclohexenone segment

– Supporting Information –

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Genaral Procedure.

All reaction were carried out using oven dried glassware and standard syringe, cannula, and septa techniques. Routine monitorings of reaction were carried out using glass-supported Merck Silica gel 60 F_{254} TLC plates. Flash column chromatography was performed on Merck silica gel F_{254} (230-400 mesh) with indicated solvents.

Materials.

All solvents and reagents were used as supplied with following exceptions. Tetrahydrofuran and ether were freshly distilled from sodium/benzophenone under argon. Toluene and ethanol were distilled from sodium under argon. Dichloromethane, carbon tetrachloride, and *N*,*N*-dimethylformamide were distilled from calcium hydride under argon.

Instrumentation.

Measurements of optical rotations were performed with a JASCO P-1020 automatic digital polarimeter. Melting points were taken on a Yanaco MP-3 micro melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured with a Brucker DRX-500 (500 MHz) spectrometer. Chemical shifts were expressed in ppm using tetramethylsilane (δ=0) as an internal standard. The following abbreviations are used: singlet (s), doublet (d), triplet (t), multiplet (m), and broad (br). Infrared (IR) spectral measurements were carried out with a JASCO FT/IR-5300 spectrometer. Low resolution mass (MS) spectra were taken with a Hitachi RMU-6MG spectrometer, and high resolution mass (HRMS) spectra were obtained on a Hitachi M-80A spectrometer.

Coupling product 6.

Lithium bis(trimethylsilyl)amide in tetrahydrofuran (1.0 M solution, 5.30 ml, 5.3 mmol) was added dropwise to a stirred solution of bromo ether **5**[1] (800 mg, 2.4 mmol) in dry tetrahydrofuran (40 ml) at -78°C under argon. After 30 min, a solution of (*R*)-*N*-(*p*-toluenesulfonyl)-*N*,*O*-isopropylidene serinal (**3**) (2.06 g, 7.2 mmol) in dry tetrahydrofuran (12 ml) was added slowly at -78°C, and the stirring was continued for 1 h at the same temperature. The reaction was quenched with saturated aqueous ammonium chloride (10 ml), and the mixture was diluted with ether (400 ml). The organic layer was washed successively with saturated aqueous ammonium chloride, saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 2:1→1:1) to give **6** (1.23 g, 95%) as a colorless caramel: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38 (3H, s), 1.39 (3H, s), 1.44 (3H, s), 1.67 (0.3H, s), 1.68 (2.7H, s), 1.79 (1H, d, J=11.3 Hz), 1.85 (1H, d, J=11.3 Hz), 2.25 (1H, d, J=5.2 Hz), 2.35 (1H, dd, J=1.8, 5.2 Hz), 2.41 (3H, s), 2.43 (1H, t, J=4.4 Hz), 2.45 (1H, s), 2.70 (1H, d, J=6.8 Hz) , 2.85 (0.1H, t, J=2.4 Hz), 2.90 (0.9H, t, J=2.3 Hz), 3.76 (1H, dd, J=6.4, 9.8Hz), 4.20 (1H, d, J=6.5 Hz), 4.39 (1H, d, J=7.0 Hz), 4.51 (1H, dd, J=1.3, 9.8 Hz), 4.55 (1H, t, J=2.3 Hz), 4.59 (1H, t, J=2.8 Hz), 5.05 (1H, d, J=3.1 Hz), 7.30 (2H, d, J=8.2 Hz), 7.68 (2H, d, J=8.2 Hz); IR (neat) 550, 590, 680, 730, 820, 830, 880, 940, 1030, 1100, 1150, 1230, 1250, 1340, 1370, 1380, 1460, 1710, 2880, 2940, 2990, 3440 cm^{-1}; HREIMS m/z calcd for $C_{27}H_{33}NO_8S$ (M^+), 531.1903, found 531.1924.

Methyl xanthate 7.

Sodium bis(trimethylsilyl)amide in tetrahydrofuran (1.0 M solution, 1.10 ml, 1.1 mmol) was added dropwise to a stirred solution of **6** (378 mg, 0.71 mmol) in dry tetrahydrofuran (35 ml) at -78°C under argon. After 30 min, carbon disulfide (0.852 ml, 14 mmol) was added slowly, and stirring was continued for 1 h at the same temperature. The mixture was gradually warmed up to -50°C over 1 h, and then iodomethane (0.537 ml, 7.1 mmol) was added slowly at -78°C. After 1 h, the mixture was gradually warmed up to -50°C over 1 h. The reaction was quenched with saturated aqueous ammonium chloride (3 ml), and then the mixture was diluted with ether (300 ml). The organic layer was washed successively with saturated aqueous sodium thiosulfate, saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 2:1) to give **7** (389 mg, 88%) as a colorless caramel: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (3H, s), 1.41 (3H, s), 1.47 (3H, s), 1.50 (3H, s), 1.79 (1H, d, J=11.4 Hz), 1.84 (1H, d, J=11.4 Hz), 2.25 (1H, d, J=5.2 Hz), 2.42 (4H, s), 2.72 (1H, dd, J=1.9, 5.2 Hz), 2.88 (1H, t, J=2.4 Hz), 3.78 (1H, dd, J=7.0, 9.5 Hz), 4.47 (1H, dd, J=1.4, 9.6 Hz), 4.50 (1H, t, J=2.7 Hz), 4.52 (1H, t, J=2.3 Hz), 4.57 (1H, d, J=2.8 Hz), 4.65 (1H, d, J=5.9 Hz), 6.89 (1H, s), 7.30 (2H, d, J=8.2 Hz), 7.69

(2H, d, J=8.2 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 19.31, 20.27, 21.50, 24.11, 25.84, 27.68, 28.69, 29.32, 30.46, 32.45, 41.44, 47.53, 58.63, 64.72, 75.56, 79.45, 80.87, 82.88, 87.40, 96.79, 109.44, 128.21 (two carbons), 129.59 (two carbons), 137.46, 143.41, 205.60, 214.03; IR (neat) 520, 550, 590, 650, 680, 730, 820, 880, 910, 940, 1060, 1100, 1150, 1180, 1210, 1350, 1370, 1460, 1710, 2880, 2940, 2990 cm^{-1}; HREIMS m/z calcd for $C_{29}H_{35}NO_8S_3$ (M^+), 621.1523, found 621.1528.

Deoxygenated product 8.

Tributyltin hydride (0.330 ml, 1.2 mmol) and triethylborane in hexane (1.0 M solution, 0.630 ml, 0.63 mmol) were added successively to a stirred solution of **7** (384 mg, 0.62 mmol) in dry toluene (24 ml) at room temperature. After 1 h, the mixture was concentrated *in vacuo* to afford a residue, which was purified by column chromatography (hexane-ethyl acetate, 1:0→2:1) to give **8** (303 mg, 95%) as a colorless caramel: $[\alpha]_D^{20}$ +49.1 (*c* 1.04, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.34 (3H, s), 1.37 (3H, s), 1.40 (3H, s), 1.67 (3H, s), 1.79 (1H, d, J=11.4 Hz), 1.84 (1H, d, J=11.4 Hz), 2.20 (1H, dd, J=10.9, 14.7 Hz), 2.29 (1H, d, J=5.3 Hz), 2.41 (3H, s), 2.46 (1H, s), 2.51 (1H, dd, J=1.8, 5.3 Hz), 2.57 (1H, d, J=14.7 Hz), 2.88 (1H, t, J=2.4 Hz), 3.67 (1H, dd, J=5.3, 10.8 Hz), 4.14 (1H, d, J=8.9 Hz), 4.15 (1H, dd, J=5.3, 10.8Hz), 4.33 (1H, d, J=2.9 Hz), 4.58 (2H, m), 7.28 (2H, d, J=8.3 Hz,), 7.65 (2H, d, J=8.3 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$)δ 20.00, 21.48, 23.96, 26.78, 27.80, 30.31, 30.53, 31.69, 41.38, 44.48, 46.96, 55.73, 69.24, 76.30, 83.45, 84.90, 84.92, 96.59, 109.70, 127.47 (two carbons), 129.60 (two carbons), 138.03, 143.20, 207.22; IR (neat) 520, 550, 600, 650, 680, 710, 840, 880, 920, 940, 1030, 1060, 1240, 1300, 1340, 1370, 1450, 1710, 2880, 2940, 2990 cm^{-1}; CIMS (isobutane) m/z 516 [$(M+H)^+$], 500 [$(M+H-CH_4)^+$]; HREIMS m/z calcd for $C_{26}H_{30}NO_7S$ [$(M-Me)^+$], 500.1740, found 500.1733.

Cyclic carbamate 10.

1.0 M Hydrochloric acid (1.36 ml, 1.4 mmol) was added to a stirred solution of **8** (320 mg, 0.62 mmol) in tetrahydrofuran (15 ml) at room temperature, and the mixture was heated at 55°C for 6 h. After cooling, the mixture was neutralized with saturated aqueous sodium hydrogen carbonate and extracted with ether (3 x 60 ml). The combined extracts were washed with brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 2:1) to give an equilibrium mixture[2] of **9a** and **9b** (290 mg) as a colorless caramel.

Trichloromethyl chloroformate (1.23 ml, 6.2 mmol) was added dropwise to a stirred solution of the above mixture **9a** and **9b** (290 mg, 0.61 mmol) in dry tetrahydrofuran (30 ml) containing pyridine (1.96 ml, 24 mmol) at 0°C, and the mixture was allowed to warm up to room temperature. After 2 h, the reaction was quenched with saturated aqueous sodium hydrogen carbonate (5 ml), and the mixture was diluted with ether (300 ml). The organic layer was washed successively with 3% aqueous hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of

the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 3:2) to give **10** (209 mg, 67% from **8**) as a colorless caramel: $[\alpha]_D^{20}$ +27.5 (*c* 1.16, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.36 (3H, s), 1.39 (3H, s), 1.82 (1H, d, J=11.6 Hz), 1.87 (1H, d, J=11.6 Hz), 2.02-2.09 (1H, m), 2.25 (1H, dd, J=1.8, 5.2 Hz), 2.34 (1H, d, J=5.2 Hz), 2.45 (3H, s), 2.50 (1H, s), 2.90 (1H, t, J=2.2 Hz), 2.92 (1H, d, J=14.6 Hz), 4.33 (1H, d, J=3.0 Hz), 4.37-4.44 (2H, m), 4.57 (1H, d, J=5.4 Hz), 4.60 (1H, t, J=2.8 Hz), 4.62 (1H, t, J=2.2 Hz), 7.33 (2H, d, J=8.4 Hz), 7.86 (2H, d, J=8.4Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 20.60, 21.71, 26.76, 27.82, 30.27, 30.45, 32.12, 41.33, 43.25, 46.61, 54.57, 68.64, 76.18, 83.33, 83.89, 84.12, 110.25, 128.46 (two carbons), 129.84 (two carbons), 134.69, 145.70, 152.26, 205.82; IR(neat) 540, 580, 620, 670, 750, 810, 840, 880, 920, 940, 990, 1030, 1070, 1090, 1140, 1170, 1220, 1250, 1300, 1370, 1600, 1710, 1790, 2880, 2940, 2990 cm^{-1}; HREIMS m/z calcd for $C_{25}H_{27}NO_8S$ (M^+), 501.1456, found 501.1481.

γ-Iodo ketone 11.

Iodotrimethylsilane (68 μl, 0.48 mmol) was added dropwise to a stirred solution of **10** (210 mg, 0.42 mmol) in carbon tetrachloride-dichloromethane (10:1) (22 ml) at -20°C under argon. After 1h, the reaction was quenched with saturated aqueous sodium thiosulfate (2 ml), and then the mixture was diluted with ether (200 ml). The organic layer was washed successively with 20% aqueous sodium thiosulfate, saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 3:2) to give **11** (195 mg, 74%) as a colorless caramel: $[\alpha]_D^{20}$ +152.8 (*c* 1.04, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.35 (3H, s), 1.41 (3H, s), 1.85 (1H, d, J=11.3 Hz), 2.05 (1H, dd, J=10.7, 14.6 Hz), 2.29 (1H, d, J=11.1 Hz), 2.45 (3H, s), 2.89-2.95 (3H, m), 2.97-3.04 (2H, m), 3.80 (1H, d, J=2.4 Hz), 4.29 (1H, t, J=3.7 Hz), 4.42 (1H, t, J=9.0 Hz), 4.45 (1H, d, J=4.1 Hz), 4.56 (1H, dd, J=4.4, 9.3 Hz), 4.77-4.83 (1H, m), 4.85 (1H, d, J=5.3 Hz), 7.37 (2H, d, J=8.3 Hz), 7.96 (2H, d, J=8.3 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 21.67, 27.05, 28.01, 32.16, 36.73, 39.85, 40.69, 46.90, 47.88, 48.32, 54.53, 68.83, 75.62, 80.76, 81.02, 89.26, 111.47, 128.48 (two carbons), 129.79 (two carbons), 134.84, 145.52, 152.45, 210.30; IR (neat) 540, 570, 610, 670, 760, 820, 920, 1050, 1090, 1130, 1170, 1310, 1370, 1450, 1600, 1700, 1790, 2990 cm^{-1}; EIMS m/z 629 (M^+), 614 [$(M\text{-}Me)^+$]; HRCIMS (isobutane) m/z calcd for $C_{25}H_{28}INO_8S$ [$(M+H)^+$], 630.0658, found 630.0693.

***endo*-Alcohol 12.**

Zinc powder (300 mg, 4.6 mmol) and acetic acid (0.264 ml, 4.6 mmol) were successively added to a stirred solution of **11** (194 mg, 0.31 mmol) in tetrahydrofuran-methanol (1:1) (20 ml) at room temperature. The mixture was gradually warmed to 60°C and stirred for 1 h at the same temperature. After cooling, the mixture was diluted with ether (200 ml) and filtrated. The filtrate was washed with saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue,

which was purified by column chromatography (hexane-ethyl acetate, 3:2) to give **12** (148 mg, 95%) as a colorless caramel: $[\alpha]_D^{20}$ +155.9 (*c* 1.00, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.41 (1H, d, J=8.4 Hz), 1.50 (3H, s), 1.53 (3H, s), 1.56 (1H, d, J=8.4 Hz), 1.94 (1H, s), 2.30 (1H, dd, J=10.5, 14.2 Hz), 2.44 (3H, s), 2.72 (1H, dd, J=2.1, 14.2 Hz), 3.01 (1H, s), 3.14 (1H, s), 3.25 (1H, dt, J=3.2, 11.6 Hz), 3.44 (1H, dd, J=3.6, 11.6 Hz), 4.17 (1H, t, J=8.8Hz), 4.36 (1H, dd, J=5.1, 8.8 Hz), 4.44 (1H, s), 4.59 (1H, d, J=4.3 Hz), 4.90-4.95 (1H, m), 6.20 (1H, br dd, J=3.0, 5.3 Hz), 6.49 (1H, br dd, J=3.1, 5.5 Hz), 7.34 (2H, d, J=8.3 Hz), 7.95 (2H, d, J=8.3 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 21.68, 26.32, 27.21, 41.08, 43.07, 43.66, 45.50, 46.08, 51.23, 54.78, 67.93, 69.22, 82.93, 84.01, 112.46, 128.47 (two carbons), 129.75 (two carbons), 132.93, 134.90, 139.55, 145.47, 152.84, 207.68; IR (neat) 540, 580, 610, 670, 700, 760, 820, 850, 920, 1050, 1090, 1120, 1170, 1210, 1250, 1310, 1380, 1450, 1600, 1720, 1780, 2940, 2990, 3540 cm^{-1}; HREIMS m/z calcd for $C_{25}H_{29}NO_8S$ (M^+), 503.1611, found 503.1595.

Cyclohexenone 13.

A stirred solution of **12** (148 mg, 0.29 mmol) in diphenyl ether (15 ml) was heated at 230°C for 2 h. After cooling, the mixture was concentrated *in vacuo* to afford a residue, which was purified by column chromatography (hexane-ethyl acetate, 1:0→1:1) to give **13** (75.9 mg, 59%) as a colorless caramel: $[\alpha]_D^{20}$ +80.9 (*c* 1.05, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.27 (3H, s), 1.40 (3H, s), 2.09 (1H, dd, J=11.0, 14.5 Hz), 2.20 (1H, d, J=5.3 Hz), 2.44 (3H, s), 2.92 (1H, dd, J=2.2, 14.5 Hz), 4.19 (1H, t, J=1.7 Hz), 4.45 (2H, d, J=6.2 Hz), 4.57-4.63 (1H, m), 4.72 (1H, br t, J=4.7 Hz), 6.19 (1H, d, J=10.2 Hz), 6.90 (1H, ddd, J=1.9, 4.8, 10.1 Hz), 7.34 (2H, d, J=8.2 Hz), 7.87 (2H, d, J=8.2 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 21.70, 26.63, 27.19, 39.02, 54.27, 64.13, 69.19, 79.99, 83.18, 109.89, 127.99, 128.44 (two carbons), 129.90 (two carbons), 134.46, 144.66, 145.81, 152.51, 198.00; IR (neat) 540, 570, 600, 670, 760, 820, 910, 1040, 1090, 1130, 1170, 1230, 1380, 1490, 1600, 1680, 1790, 2930, 3480 cm^{-1}; CIMS (isobutane) m/z 438 [$(M+H)^+$]; HREIMS m/z calcd for $C_{19}H_{20}NO_8S$ [$(M-Me)^+$], 422.0908, found 422.0926.

Mesylate 14.

Methanesulfonyl chloride (73 μl, 0.93 mmol) was added to a stirred solution of **13** (68 mg, 0.16 mmol) in pyridine (7 ml) containing 4-dimethylaminopyridine (38 mg, 0.31 mmol) at 0°C, and stirring was continued for 4 h at room temperature. The reaction was quenched with saturated aqueous sodium hydrogen carbonate (1 ml), and the mixture was diluted with ether (80 ml). The organic layer was successively washed with 3% aqueous hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 1:1) to give **14** (67 mg, 83%) as a colorless caramel: $[\alpha]_D^{20}$ +47.3 (*c* 1.07, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.27 (3H, s),

1.42 (3H, s), 2.10 (1H, dd, J=10.8, 14.3 Hz), 2.45 (3H, s), 2.91 (1H, dd, J=2.2, 14.3 Hz), 3.19 (3H, s), 4.34 (1H, t, J=1.8 Hz), 4.43 (1H, dd, J=4.8, 9.4 Hz), 4.46 (1H, t, J=9.3 Hz), 4.55-4.60 (1H, m), 5.58 (1H, dd, J=1.7, 4.9 Hz), 6.34 (1H, d, J=10.1 Hz), 6.89 (1H, ddd, J=1.9, 5.0, 10.2 Hz), 7.36 (2H, d, J=8.2 Hz), 7.88 (2H, d, J=8.3 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 21.71, 26.75, 27.08, 38.50, 39.07, 53.96, 68.89, 69.68, 79.82, 80.94, 121.02, 128.44 (two carbons), 129.94 (two carbons), 130.88, 134.40, 138.93, 145.84, 152.20, 196.51; IR (neat) 540, 570, 600, 620, 670, 730, 760, 820, 860, 950, 990, 1060, 1090, 1130, 1170, 1230, 1370, 1600, 1690, 1790, 2930, 2990 cm^{-1}; CIMS (isobutane) m/z 516 [$(M+H)^+$]; HREIMS m/z calcd for $C_{20}H_{22}NO_{10}S2$ [$(M-Me)^+$], 500.0684, found 500.0696.

Diol 15.

A solution of **14** (59 mg, 0.11 mmol) in trifluoroacetic acid-water (4:1) (3 ml) was stirred at 0°C for 5 h. The mixture was concentrated *in vacuo* to give **15** (54 mg, 100%) as a colorless caramel: $[\alpha]_D^{20}$ +25.9 (*c* 1.22, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 2.25 (1H, dd, J=10.0, 14.7 Hz), 2.25-2.70 (1H, br s), 2.45 (3H, s), 2.70 (1H, br s), 2.98 (1H, d, J=14.7 Hz), 3.18 (3H, s), 4.20-4.27 (2H, m), 4.30 (1H, dd, J=4.4, 9.3 Hz), 4.45 (1H, t, J=8.8 Hz), 5.47 (1H, t, J=3.5 Hz), 6.38 (1H, d, J=10.2 Hz), 6.89 (1H, ddd, J=1.3, 4.1, 10.2 Hz), 7.37 (2H, d, J=8.3 Hz), 7.87 (2H, d, J=8.3 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 21.73, 38.79, 40.18, 53.56, 70.42, 74.84, 74.98, 77.29, 128.47 (two carbons), 129.27, 130.02 (two carbons), 134.22, 140.62, 146.11, 152.36, 197.96; IR (neat) 540, 570, 670, 730, 760, 820, 850, 940, 1090, 1170, 1360, 1600, 1700, 1780, 2360, 2930, 3480 cm^{-1}; HRCIMS (isobutane) m/z calcd for $C_{18}H_{22}NO_{10}S_2$ [$(M+H)^+$], 470.0682, found 470.0658. This material was directly used for the next reaction without further purification.

Epoxycyclohexenone 2.

0.1 M Aqueous sodium hydroxide (3 ml, 0.30 mmol) was added dropwise to a stirred solution of **15** (54 mg, 0.11 mmol) in dichloromethane (7 ml) at 0°C. After 30 min, the mixture was extracted with ether (3 x 40 ml). The combined extracts were washed with brine and dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 1:1) to give **2** (33 mg, 75%) as a white solid. Recrystallization from dichloromethane-hexane (1:2) afforded colorless prisms, mp 218-221°C: $[\alpha]_D^{20}$ +153.3 (*c* 0.93, acetone); ^{1}H-NMR (500 MHz, CD_2Cl_2) δ 2.34 (1H, dd, J=10.5, 14.2 Hz), 2.45 (3H, s), 2.51 (1H, dd, J=1.1, 14.2 Hz), 3.49 (1H, br s), 3.64-3.68 (2H, m), 4.13-4.18 (1H, m), 4.34 (1H, dd, J=4.6, 9.4 Hz), 4.44 (1H, t, J=9.1 Hz), 6.33-6.37 (1H, m), 7.26-7.29 (1H, m), 7.38 (2H, d, J=8.3 Hz), 7.80 (2H, d, J=8.3 Hz); ^{13}C-NMR (125 MHz, CD_2Cl_2) δ 21.87, 40.69, 48.59, 53.68, 56.51, 70.53, 77.29, 128.70 (two carbons), 130.27 (two carbons), 130.28, 134.74, 145.91, 146.60, 152.43, 197.94; IR (neat) 540, 570, 600, 670, 760, 840, 990, 1090, 1170, 1370, 1690, 1780, 2360, 2930, 3460 cm^{-1}; HRCIMS (isobutane) m/z calcd for $C_{17}H_{18}NO_7S$ [$(M+H)^+$], 380.0802, found

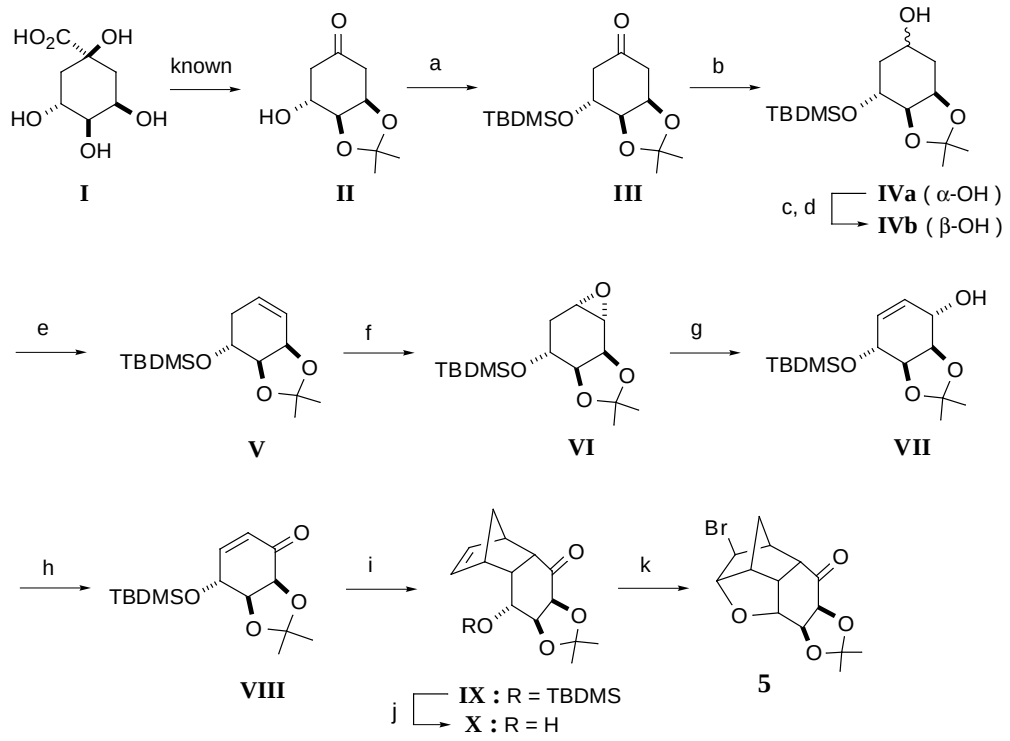
380.0786.

X-Ray diffraction study of 2.

$C_{17}H_{17}NO_7S$: colorless crystal [0.20 x 0.22 x 0.11 mm, grown from dichloromethane-hexane (1:2)], $C_{17}H_{17}NO_7S$, *M* 379.00, orthorhombic, space group $P2_12_12_1$, a=18.400(4)Å, b=25.316(6)Å, c=7.300(2)Å, *V*=3400(1)Å, *Z*=8, *D*=1.48 g/cm^3, *F*(000)=1583, *T*=293K. A Mac Science MXC18 diffractometer and graphite monochromated CuKα radiation, *l*=1.54178Å, was used for all measurements. Cell constants and an orientation matrix for data collection were obtained from a least-squares refinement using the setting angle of 20 carefully centered reflections.

References

1. The starting material **5** has been previously prepared starting from commercially available (–)-quinic acid (**I**), as shown in the following Scheme, in our preliminary communication (*see*, Izuhara, T.; Katoh, T. *Tetrahedron Lett.* **2000**, *41*, 7651-7655). Experimental procedure and characterization data for all new compounds depicted in this Scheme are as follows.



(a) TBDMSCl, imidazole, DMF, rt, 98% (b) $NaBH_4$, THF-H_2O, rt, 53% for **IVa**, 44% for **IVb** (c) DEAD, Ph_3P, benzoic acid, THF, rt, 98% (d) KOH, MeOH, rt, 100% (e) DEAD, Ph_3P, THF, rt, 67% (f) *m*CPBA, $NaHCO_3$, CH_2Cl_2, rt, 92% (g) Se_2Ph_2, $NaBH_4$,EtOH, 0°C→reflux; H_2O_2, THF, 0°C→reflux, 78% (h) Dess-Martin periodinane, CH_2Cl_2, rt, 95% (i) cyclopentadiene, Et_2AlCl, CH_2Cl_2, -78→0°C, 97% (j) TBAF, THF, 0°C, 75% (k) NBS, CH_2Cl_2, 0°C, 86%

Preparation of alcohol II.

Preparation of **II** was carried out starting from (–)-quinic acid (**I**) through a three-step sequence of reactions according to the reported procedure (*see*, Wang, Z-X.; Miller, S. M.; Anderson, O. P.; Shi, Y. *J. Org. Chem*. **1999**, *64*, 6443-6458).

Preparation of *tert*-butyldimethylsilyl ether III.

tert-Butyldimethylsilyl chloride (24.4 g, 0.16 mol) was added to a stirred solution of **I** (10.0 g, 54 mmol) in dry *N*,*N*-dimethylformamide (120 ml) containing imidazole (14.7 g, 0.22 mol) at room temperature. After 15 h, the mixture was diluted with ethyl acetate (1000 ml). The organic layer was successively washed with 3% aqueous hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 14:1) to give **III** (16.2 g, 98%) as a colorless oil: $[\alpha]_D^{20}$ +105.3 (*c* 1.00, $CHCl_3$); ^{1}H-NMR (500 MHz, CD_2Cl_2) δ 0.05 (3H, s, Si-Me), 0.09 (3H, s, Si-Me), 0.86 (9H, s, Si-*t*-Bu), 1.35 (3H, s, C-Me), 1.44 (3H, s, C-Me), 2.37 (1H, ddd, J=1.9, 3.4, 17.5 Hz, C4-H or C6-H), 2.63 (1H, dd, J=2.5, 8.4 Hz, C4-H or C6-H), 2.67 (1H, dd, J=2.5, 8.4 Hz, C4-H or C6-H), 2.76 (1H, dd, J=3.4, 17.5 Hz, C4-H or C6-H), 4.16 (1H, dd, J=2.5, 5.2 Hz, C2-H), 4.22 (1H, dt, J=2.1, 7.2 Hz, C1-H), 4.69 (1H, quint, J=3.0 Hz, C3-H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ -5.04, -3.60, 17.85, 23.86, 25.62 (three carbons), 26.30, 40.14, 41.91, 68.73, 72.40, 75.14, 108.68, 207.69; IR (neat) 440, 520, 690, 780, 810, 840, 870, 910, 980, 1010, 1060, 1090, 1140, 1180, 1210, 1250, 1380, 1470, 1720, 2860, 2930, 2960 cm^{-1}; CIMS (isobutane) m/z 301 ($[M+H]^+$); HREIMS m/z calcd for $C_{14}H_{25}O_4Si$ $[(M-Me)^+]$, 285.1521, found 285.1523.

Preparation of α-alcohol IVa and β-alcohol IVb.

Sodium borohydride (1.30 g, 34 mmol) in water (15 ml) was added dropwise to a stirred solution of **III** (9.40 g, 31 mmol) in dry tetrahydrofuran (400 ml) at -5°C, and stirring was continued for 1 h at room temperature. The reaction was quenched with saturated aqueous ammonium chloride (30 ml), and then the mixture was diluted with ethyl acetate (1200 ml). The organic layer was washed with saturated aqueous ammonium chloride and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* gave a residue, which was separated by column chromatography (hexane-ethyl acetate, 5:1→3:1) to give **IVb** (4.16 g, 44%) as a less polar product and **IVa** (5.02 g, 53%) as a more polar product.

IVb: colorless oil; $[\alpha]_D^{20}$ -33.7 (*c* 1.02, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.08 (3H, s, Si-Me), 0.09 (3H, s, Si-Me), 0.88 (9H, s, Si-*t*-Bu), 1.35 (3H, s, C-Me), 1.52 (3H, s, C-Me), 1.57 (3H, s, C-Me), 1.70-1.77 (1H, m, C4-H), 1.87-1.94 (1H, m, C4-H), 2.05 (2H, t, J=4.4 Hz, C6-H2), 2.27 (1H, d, J=8.2 Hz, OH), 3.90 (1H, t, J=5.2 Hz, C2-H), 4.04 (1H, br dd, J=8.2, 10.7 Hz, C5-H), 4.09 (1H, quint, J=3.8 Hz, C3-H), 4.41 (1H, dd, J=4.6,

9.7 Hz, C1-H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ -4.81, -4.72, 17.98, 25.69, 25.77 (three carbons), 28.23, 33.77, 37.87, 65.27, 68.67, 74.10, 78.93, 108.60; IR (neat) 520, 660, 780, 840, 910, 940, 960, 1000, 1050, 1070, 1120, 1150, 1220, 1250, 1380, 1460, 2860, 2890, 2930, 2960, 2990, 3440 cm^{-1}; EIMS m/z 287 ($[M-Me]^+$); CIMS (isobutane) m/z 303 ($[M+H]^+$).

IVa: colorless needles; $[\alpha]_D^{20}$ -41.7 (*c* 1.01, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.11 (3H, s, Si-Me), 0.12 (3H, s, Si-Me), 0.90 (9H, s, Si-*t*-Bu), 1.35 (3H, s, C-Me), 1.46 (3H, s, C-Me), 1.60 (1H, quint, C4-H), 1.80-1.88 (1H, m, C6-H), 2.00 (1H, dt, J=2.3, 13.7 Hz, C4-H), 2.20 (1H, dt, J=4.0, 14.1 Hz, C6-H), 2.24 (1H, d, J=7.1 Hz, OH), 3.92 (1H, t, J=5.0 Hz, C2-H), 3.95 (1H, quint, J=4.8 Hz, C3-H), 4.00-4.05 (1H, m, 4.09 (1H, m, C5-H), 4.40 (1H, dd, J=4.8, 9.8 Hz, C1-H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ -4.91, -4.71, 17.96, 25.77 (three carbons), 25.87, 28.08, 35.50, 37.67, 65.11, 71.08, 72.69, 78.87, 108.46; IR (neat) 520, 660, 780, 840, 910, 940, 960, 1000, 1050, 1070, 1120, 1150, 1220, 1250, 1380, 1460, 2860, 2890, 2930, 2960, 2990, 3440 cm^{-1}; EIMS m/z 287 ($[M-Me]^+$); CIMS (isobutane) m/z 303 ($[M+H]^+$).

Conversion of α-alcohol IVa to β-alcohol IVb.

Diethyl azodicarboxylate in toluene (40% solution, 14.5 ml, 34 mmol) was added dropwise to a stirred solution of **IVa** (5.00 g, 17 mmol) in dry tetrahydrofuran (150 ml) containing triphenylphosphine (8.68 g, 34 mmol) and benzoic acid (4.15 g, 34 mmol) at 0°C under argon. The mixture was stirred for 3 h at room temperature. Concentration of the mixture *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 13:1) to give the corresponding benzoate (6.61 g, 98%) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.09 (3H, s, Si-Me), 0.10 (3H, s, Si-Me), 0.90 (9H, s, Si-*t*-Bu), 1.53 (3H, s, C-Me), 1.55 (3H, s, C-Me), 1.90-2.10 (3H, m, C4-H_2 + C6-H), 2.24 (1H, dt, J=5.1, 14.5 Hz, C6-H), 3.95 (1H, t, J=5.1 Hz, C2-H), 4.19 (1H, quint, J=3.7 Hz, C3-H), 4.43 (1H, q, J=5.5 Hz), 5.30-5,35 (1H, m, C5-H), 7.43 (2H, t, J=7.9 Hz, Ph-H(*m*)), 7.55 (1H, t, J=7.5Hz, Ph-H(*p*)), 8.05 (2H, d, J=7.5 Hz, Ph-H(*o*)); IR (neat) 520, 710, 780, 840, 920, 940, 970, 1010, 1030, 1070, 1110, 1220, 1280, 1370, 1380, 1450, 1540, 1600, 1720, 1780, 2860, 2890, 2930 cm^{-1}; EIMS m/z 391 ($[M-Me]^+$); CIMS (isobutane) m/z 406 ($[M+H]^+$).

2.0 M Aqueous potassium hydroxide solution (22.4 ml, 45 mmol) was added dropwise to a stirred solution of the above benzoate (6.50 g, 16 mmol) in methanol (280 ml) at room temperature. After 3 h, the mixture was concentrated *in vacuo* to give a residue, which was diluted with ethyl acetate (800 ml). The organic layer was washed with brine and then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 3:1) to give **IVb** (4.82 g, 100%) as a colorless oil. The IR, ^{1}H-NMR, and mass spectra of this material were identical with those recorded for preparation of **IVb**.

Preparation of olefin V.

Diethyl azodicarboxylate in toluene (40% solution, 21.6 ml, 50 mmol) was added dropwise to a stirred solution of **IVb** (5.00 g, 17 mmol) in dry tetrahydrofuran (150 ml) containing triphenylphosphine (13.1 g, 50 mmol) at room temperature. After 3 h, the mixture was concentrated *in vacuo* to afford a residue, which was purified by column chromatography (hexane-ethyl acetate, 13:1) to give **V** (3.15 g, 67%) as a colorless oil: $[\alpha]_D^{20}$ -87.1 (*c* 1.05, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.07 (3H, s, Si-Me), 0.10 (3H, s, Si-Me), 0.89 (9H, s, Si-*t*-Bu), 1.38 (3H, s, C-Me), 1.46 (3H, s, C-Me), 1.97-2.04 (1H, m, C4-H), 2.25-2.32 (1H, m, C4-H), 3.80-3.85 (1H, m, C3-H), 3.98 (1H, t, J=7.2 Hz, C2-H), 4.60 (1H, d, J=6.2 Hz, C1-H), 5.77-5.83 (2H, m, C5-H + C6-H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ -4.90, -4.85, 18.00, 25.80 (three carbons), 28.19, 34.04, 67.86, 68.41, 72.81, 78.00, 108.59, 128.26, 129.58; IR (neat) 670, 780, 840, 910, 1010, 1060, 1120, 1220, 1250, 1380, 1460, 1690, 1730, 2860, 2930, 2960 cm^{-1}; CIMS (isobutane) m/z 285 ($[M+H]^+$); HREIMS m/z calcd for $C_{14}H_{25}O_3Si$ $[(M-Me)^+]$, 269.1570, found 269.1570.

Preparation of epoxide VI.

3-Chloroperoxybenzoic acid (7.53 g, 45 mmol) was added to a stirred solution of **V** (4.95 g, 17 mmol) in dry dichloromethane (180 ml) containing sodium hydrogen carbonate (7.53 g, 45 mmol) at 0°C, and stirring was continued for 24 h at room temperature. The reaction was diluted with ethyl acetate (500 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* gave a residue, which was purified by column chromatography (hexane-ethyl acetate, 13:1) to give **VI** (4.81 g, 92%) as a colorless oil: $[\alpha]_D^{20}$ -29.1 (*c* 1.04, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.06 (3H, s, Si-Me), 0.07 (3H, s, Si-Me), 0.88 (9H, s, Si-*t*-Bu), 1.38 (3H, s, C-Me), 1.46 (3H, s, C-Me), 1.90 (1H, ddd, J=1.6, 6.1, 15.6 Hz, C4-H), 2.18 (1H, ddd, J =4.0, 5.1, 15.4 Hz, C4-H), 3.14 (1H, d, J=3.6 Hz, C6-H), 3.23 (1H, br s, C5-H), 3.87 (1H, dd, J=5.7, 11.2 Hz, C3-H), 3.94 (1H, t, J=5.7 Hz, C2-H), 4.53 (1H, d, J=5.7 Hz, C1-H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ -4.77, -4.75, 17.96, 25.71 (three carbons), 25.97, 28.03, 29.36, 51.31, 51.68, 66.33, 71.81, 76.81, 109.29; IR (neat) 510, 710, 780, 840, 870, 910, 940, 1000, 1110, 1220, 1250, 1380, 1470, 2860, 2890, 2930, 2990 cm^{-1}; CIMS (isobutane) m/z 301 ($[M+H]^+$); HREIMS m/z calcd for $C_{14}H_{25}O_4Si$ $[(M-Me)^+]$, 285.1522, found 285.1508.

Preparation of allylic alcohol VII.

Sodium borohydride (663 mg, 18 mmol) was added in small portions to a stirred suspension of diphenyl diselenide (2.74 g, 8.8 mmol) in dry ethanol (30 ml) at 0°C under argon. After 30 min, a solution of **VI** (4.80 g, 16 mmol) in dry ethanol (30 ml) was added dropwise to the above mixture at room temperature. The mixture was heated at reflux for 1 h. After cooling, the mixture was diluted with dry tetrahydrofuran (24 ml). Hydrogen peroxide in water (30% solution, 19.5 ml, 0.17 mol) was added at 0°C. The

mixture was stirred for 5 min and slowly heated at reflux for 1 h. After cooling, the mixture was diluted with ether (600 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* gave a residue, which was separated by column chromatography (hexane-ethyl acetate, 3:1) to give **VII** (3.74 g, 78%) as a colorless oil: $[\alpha]_D^{20}$ -42.4 (*c* 1.03, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.11 (3H, s, Si-Me), 0.13 (3H, s, Si-Me), 0.90 (9H, s, Si-*t*-Bu), 1.34 (3H, s, C-Me), 1.40 (3H, s, C-Me), 2.90 (1H, d, J=8.3 Hz, OH), 4.12 (1H, quint, J=4.1 Hz, C1-H), 4.21 (1H, t, J=3.8 Hz, C4-H), 4.29 (1H, dd, J=4.1, 7.5 Hz, C3-H), 4.33 (1H, dd, J=4.1, 7.5 Hz, C2-H), 5.95 (1H, dd, J=4.1, 9.8 Hz, C5-H), 6.07 (1H, dd, J=4.1, 9.8 Hz, C6-H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ -4.81, -4.75, 18.02, 24.56, 25.76 (three carbons), 26.64, 67.90, 68.70, 78.83, 78.95, 108.65, 132.28, 132.31; IR (neat) 410, 480, 520, 640, 660, 690, 780, 840, 890, 940, 960, 990, 1010, 1060, 1120, 1160, 1210, 1250, 1380, 1460, 1640, 2860, 2900, 2930, 2960, 2990, 3050, 3450 cm^{-1}; CIMS (isobutane) m/z 301 ($[M+H]^+$); HREIMS m/z calcd for $C_{14}H_{25}O_4Si$ $[(M-Me)^+]$, 285.1520, found 285.1534.

Preparation of enone VIII.

Dess-Martin periodinane (14.5 g, 34 mmol) was added in small portions to a stirred solution of **VII** (5.15 g, 17 mmol) in dry dichloromethane (200 ml) at room temperature. After 2 h, the mixture was diluted with ethyl acetate (800 ml). The organic layer was washed successively with 20% aqueous sodium thiosulfate, saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 7:1) to give **VIII** (4.86 g, 95%) as white solid. Recrystallization from dichloromethane-hexane afforded colorless prisms, mp 55-56°C: $[\alpha]_D^{20}$ -84.7 (*c* 1.02, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.14 (3H, s, Si-Me), 0.17 (3H, s, Si-Me), 0.92 (9H, s, Si-*t*-Bu), 1.40 (3H, s, C-Me), 1.43 (3H, s, C-Me), 4.39-4.42 (1H, m, C5-H or C6-H), 4.44 (1H, d, J=5.9 Hz, C5-H or C6-H), 4.52-4.55 (1H, m, C4-H), 6.08 (1H, d, J=10.3 Hz, C2-H), 6.76 (1H, ddd, J=0.9, 3.8, 10.3 Hz, C3-H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ -4.74, -4.73, 18.08, 25.70 (three carbons), 25.88, 27.43, 67.07, 74.36, 79.64, 110.17, 127.87, 148.47, 194.53; IR (KBr) 470, 520, 630, 670, 730, 780, 840, 890, 940, 980, 1010, 1080, 1170, 1250, 1330 cm^{-1}; EIMS m/z 298 ($[M]^+$), 283 ($[M-Me]^+$), 241 ($[M-t\text{-}Bu]^+$). *Anal* calcd for $C_{15}H_{26}O_4Si$: C, 60.37; H, 8.78, found: C, 60.03; H, 8.56.

Preparation of cyclopentadiene adduct IX.

Diethylaluminum chloride in hexane (1.0 M solution, 2.68 ml, 0.27 mmol) was added dropwise to a stirred solution of **VIII** (4.00 g, 13 mmol) and cyclopentadiene (11.1 ml, 0.13 mol) in dry dichloromethane (140 ml) at -78°C under argon. The mixture was gradually warmed up to 0°C over 1h, and stirring was continued for 1 h at 0°C. The mixture was diluted with ether (600 ml). The organic layer was washed with saturated

aqueous sodium hydrogen carbonate and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* gave a residue, which was purified by column chromatography (hexane-ethyl acetate, 6:1) to give **IX** (4.74 g, 97%) as white solid. Recrystallization from dichloromethane-hexane afforded colorless prisms, mp 88-90°C; $[\alpha]_D^{20}$ +46.7 (*c* 1.01, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.08 (3H, s, Si-Me), 0.09 (3H, s, Si-Me), 0.89 (6H, s, Si-*t*-Bu), 1.30 (3H, s, C-Me), 1.37 (1H, d, J=8.4 Hz), 1.47 (3H, s, C-Me), 1.54 (1H, d, J=8.4 Hz), 2.90 (1H, ddd, J=3.3, 5.6, 10.2 Hz), 3.08 (1H, s), 3.11 (1H, s), 3.18 (1H, dd, J=3.8, 10.2 Hz), 3.99 (1H, t, J=6.2 Hz), 4.12 (1H, d, J=8.3 Hz), 4.22 (1H, dd, J=7.0, 8.3 Hz), 6.12 (1H, dd, J=3.0, 5.6 Hz), 6.20 (1H, dd, J=3.0, 5.6 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ -4.93, -4.53, 18.01, 24.01, 25.75 (three carbons), 26.54, 45.21, 45.71, 46.58, 49.59, 51.59, 71.55, 78.06, 79.68, 109.89, 133.14, 136.98, 208.66; IR (KBr) 560, 680, 730, 780, 840, 850, 900, 940, 970, 1010, 1040, 1080, 1110, 1160, 1210, 1260, 1380, 1460, 1720, 2860, 2900, 2930, 2960 cm^{-1}; CIMS m/z 365 ($[M+H]^+$), 349 ($[M-Me]^+$), 307 ($[M-t\text{-}Bu]^+$), 249 ($[M-TBDMS]^+$). *Anal* calcd for $C_{20}H_{32}O_4Si$: C, 65.89; H, 8.85, found: C, 65.57; H, 8.56.

Preparation of alcohol X.

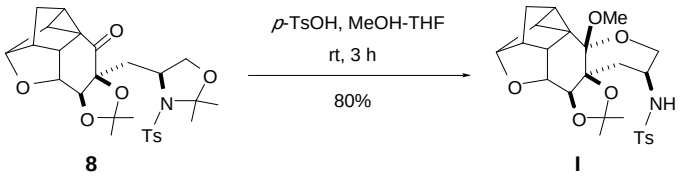
Tetrabutylammonium fluoride in tetrahydrofuran (1.0 M solution, 15.0 ml, 15 mmol) was added to a stirred solution of **IX** (3.51 g, 9.6 mmol) in dry tetrahydrofuran (100 ml) at 0°C, and stirring was continued for 2 h at room temperature. The mixture was diluted with ether (600 ml). The organic layer was successively washed with saturated aqueous ammonium chloride, saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* gave a residue, which was purified by column chromatography (hexane-ethyl acetate, 5:3) to give **X** (1.81 g, 75%) as white solid. Recrystallization from dichloromethane-hexane afforded colorless needles, mp 125-126°C; $[\alpha]_D^{20}$ +112.9 (*c* 1.00, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.34 (3H, s, C-Me), 1.42 (1H, d, J=8.1 Hz), 1.53 (3H, s, C-Me), 1.58 (1H, d, J=8.1 Hz), 2.07 (1H, br s, OH), 3.08-3.20 (3H, m), 3.38 (1H, br dd, J=3.8, 11.0 Hz), 4.14 (1H, br t, J=4.1 Hz), 4.16 (1H, d, J=8.0 Hz), 4.42 (1H, dd, J=6.0, 8.0 Hz), 6.27 (1H, br dd, J=2.5, 5.3 Hz), 6.38 (1H, dd, J=3.3, 5.7 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 23.87, 26.40, 44.55 (two carbons), 45.33, 48.39, 51.72, 70.28, 78.09, 79.68, 110.99, 134.89, 137.41, 208.56; IR (KBr) 550, 740, 860, 890, 1040, 1060, 1160, 1210, 1260, 1380, 1630, 1710, 2940, 2980, 3440 cm^{-1}; EIMS m/z 250 ($[M]^+$), 235 ($[M-Me]^+$). *Anal* calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25, found: C, 67.35; H, 7.24.

Preparation of bromo ether 5.

N-Bromosuccinimide (2.78 g, 16 mmol) was added in small portions to a stirred solution of **X** (3.02 g, 12 mmol) in dry dichloromethane (200 ml) at 0°C, and stirring was continued for 1 h at room temperature. The mixture was diluted with ether (600 ml). The organic layer was washed successively with 20% aqueous sodium thiosulfate,

saturated aqueous sodium hydrogen carbonate, and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 4:1) to give **5** (3.41 g, 86%) as white solid. Recrystallization from ether-hexane afforded colorless plates, mp 121-122°C, $[\alpha]_D^{20}$ +65.9 (*c* 1.00, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.33 (3H, s, C-Me), 1.52 (3H, s, C-Me), 1.67 (1H, d, J=11.2 Hz), 2.19 (1H, d, J=11.2 Hz), 2.82 (1H, br d, J=3.1 Hz), 2.97 (1H, br t, J=3.5 Hz), 3.00-3.10 (2H, m), 3.82 (1H, d, J=1.2 Hz), 3.88 (1H, t, J=1.9 Hz), 4.28 (1H, d, J=6.3 Hz), 4.44 (1H, dd, J=1.2, 5.3 Hz), 4.54 (1H, dd, J=1.9, 6.3 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 24.71, 26.61, 33.72, 41.44, 42.68, 46.10, 47.52, 55.04, 77.46, 77.71, 78.06, 87.30, 111.25, 207.01; IR (KBr) 540, 710, 750, 770, 810, 840, 860, 890, 940, 970, 1060, 1090, 1160, 1210, 1270, 1310, 1380, 1460, 1720, 1790, 2890, 2940, 2990 cm^{-1}; EIMS m/z 330 ($[M+2]^+$, ^{81}Br), 328 ($[M]^+$, ^{79}Br), 315 ($[M-Me]^+$, ^{81}Br), 313 ($[M-Me]^+$, ^{79}Br). *Anal* calcd for $C_{14}H_{17}O_4Br$: C, 51.08; H, 5.21, Br, 24.27, found: C, 51.33; H, 5.23, Br, 24.50.

2. When deprotection of acetonide moiety of the side chain in **8** was performed in methanolic media [*p*-TsOH, MeOH-THF (1:1), rt, 3 h], as shown in the following scheme, the corresponding methyl acetal **I** was obtained in 80% yield as the sole product. This result strongly indicates the formation of hemiacetal **9b** under acidic conditions. Experimental procedure and characterization data for **I** are described below.



8 **I**

p-Toluenesulfonic acid (1.00 mg, 5.3 μmol) was added to a stirred solution of **8** (5.00 mg, 9.7 μmol) in methanol-tetrahydrofuran (1:1) (1 ml) at room temperature. After 3 h, the mixture was diluted with ether (40 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate and brine, then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 3:2) to give **I** (3.80 mg, 80%) as colorless caramel: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.14 (1H, dd, J=1.6, 5.2 Hz), 1.26 (1H, t, J=7.5 Hz), 1.33 (3H, s, C-Me), 1.49 (3H, s, C-Me), 1.68 (1H, dd, J=1.1, 5.2 Hz), 1.76 (2H, s), 1.98 (1H, dd, J=7.9, 14.5 Hz), 2.20 (1H, s), 2.35 (1H, t, J=2.4 Hz), 2.43 (3H, s, Ts-Me), 3.21 (3H, s, OMe), 3.42 (1H, dd, J=9.4, 11.7 Hz), 3.64 (1H, dd, J=8.9, 11.7 Hz), 3.84 (1H, quint, J=9.2 Hz), 3.95 (1H, d, J=2.1 Hz), 4.31 (2H, s), 5.16 (1H, d, J=10.6 Hz),

7.29(2H, d, J=8.0 Hz, Ph), 7.73 (2H, d, J=8.2 Hz, Ph); IR (neat) 550, 570, 660, 710, 820, 840, 890, 950, 970, 1040, 1060, 1100, 1120, 1160, 1100, 1120, 1160, 1220, 1250, 1300, 1330, 1370, 1420, 2940, 2980 cm^{-1}; EIMS m/z 489 ($[M]^+$), 474 ($[M\text{-}Me]^+$), 458 ($[M\text{-}OMe]^+$).