Supporting Information for:

Regiocontrol of Radical Cyclization by Lewis Acids. Efficient Synthesis of Optically Active Functionalized Cyclopentanes and Cyclohexanes

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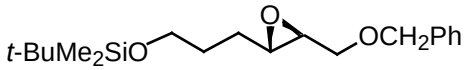
General

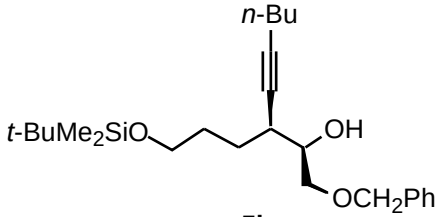
All reactions were performed under Ar atmosphere. Analytical thin layer chromatography (TLC) was performed on aluminum sheets precoated with silica gel (Merck, Kieselgel 60 F254). Visualization was accomplished by UV right (254 nm), $KMnO_4$, phosphomolybdic acid. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-2000 spectrometer at 300 and 75 MHz, respectively, with $CDCl_3$ as a solvent. Mass spectra (EI, 70eV) were measured on a Shimadzu QP-5000 GC-mass spectrometer. Infrared spectra were recorded on a JASCO FT/IR-230 spectrometer and optical rotations were measured with a JASCO DIP-370 polarimeter.



4

Compound 4: (*E*)-6-(*tert*-butyldimethylsilyl)oxyhex-2-en-1-ol (23.0 g, 100 mmol), prepared from 5-(*tert*-butyldimethylsilyl)oxy-1-pentyne, was converted to (2*S*,3*R*)-6-(*tert*-Butyldimethylsilyl)oxy-2,3-epoxyhexan-1-ol according to the procedure for the catalytic Katsuki-Sharpless asymmetric epoxidation (4A MS, L (+)-DIPT, $Ti(O\text{-}i\text{-}Pr)_4$, and TBHP in CH_2Cl_2).[1] The ee of the resulting epoxy alcohol was confirmed to be >95% by ^1H NMR analysis of its MTPA-esters. To a solution of (2*S*,3*R*)-6-(*tert*-Butyldimethylsilyl)oxy-2,3-epoxyhexan-1-ol, thus prepared, in THF (200 mL) was added portionwise sodium hydride (5.67 g, 55% in oil, 130 mmol) at 0 ^oC. The resulting mixture was warmed to room temperature and stirred for 30 min. To this was added benzyl bromide (15.5 mL, 130 mmol) and the mixture was stirred for 3 h, and then quenched by addition of saturated aqueous NH_4Cl. The mixture was extracted with ether (2 x 30 mL), dried over $MgSO_4$, filtered, concentrated and purified by column chromatography to give **4** (27.57 g) in 82% yield: ^1H NMR δ 0.06 (6H, s), 0.91 (9H, s), 1.55-1.74 (4H, m), 2.82-2.90 (1H, m), 2.92-3.00 (1H, m), 3.47 (1H, dd, J=5.7, 11.4 Hz), 3.60-3,70 (1H, m), 3.71 (1H, dd, J=3.3, 11.4 Hz), 4.54 (1H, d, J=12.0 Hz), 4.61 (1H, d, J=12.0 Hz), 7.25-7.36 (5H, m); ^{13}C NMR δ 5.3, 18.3, 25.9, 28.2, 29.1, 55.8, 56.9, 62.5, 70.3, 73.1, 127.5, 127.5, 128.2, 137.8; IR (neat) 2929, 2857, 1637, 1472, 1255, 1099 cm^{-1}.

Typical Procedure for Epoxide Ring Opening Reaction of 4.



5b

Compound 5b: To a solution of 1-hexyne (2.28 mL, 20.0 mmol) in hexanes (20 mL) was added dropwise *n*-BuLi (13.3 mL, 1.50 M in hexanes, 20.0 mmol) at 0 ^{o}C. After stirring for 30 min, Et_2AlCl (20.8 mL, 0.96 M in hexanes, 20.0 mmol) was added dropwise and the mixture was stirred at 0 ^{o}C for 30 min. To this was added Me_3Al (4.81 mL, 15% in hexanes, 10.0 mmol). After stirring for 30 min, a solution of epoxide **4** (3.37 g, 10.0 mmol) in hexanes (5 mL) was added at 0 ^{o}C, and the resulting mixture was stirred for 2 h at this temperature and then carefully quenched by addition of water (3.24 mL). The mixture was filtered through a pad of Celite with ether. The filtrate was dried over $MgSO_4$, filtered, and concentrated to afford the crude residue. The regioselectivity of epoxide ring opening was determined by ^{1}H NMR analysis of the residue. The resulting residue was chromatographed on silica gel to give a mixture of **5b** and its regioisomer in a ratio of 95 : 5 (3.26 g) in 78% combined yield. **5b**: ^{1}H NMR δ 0.04 (6h, s), 0.89 (9H, s), 0.84-0.93 (3H, m), 1.26-1.86 (8H, m), 2.13 (2H, dt, J=2.1, 6.9 Hz), 2.45-2.53 (1H, m), 3.57 (1H, dd, J=7.2, 9.3 Hz), 3.64 (2H, t, J=6.3 Hz), 3.62-3.72 (1H, m), 3.75 (1H, dd, J=2.7, 9.3 Hz), 4.58 (2H, s), 7.26-7.36 (5H, m); ^{13}C NMR δ -5.4, 13.5, 18.2, 18.3, 21.8, 25.9, 27.3, 30.3, 31.0, 35.4, 63.1, 72.5, 72.8, 73.4, 79.4, 83.5, 127.7, 127.8, 128.5, 138.13; IR (neat) 3449, 2929, 1455, 1254, 1100 cm^{-1}.

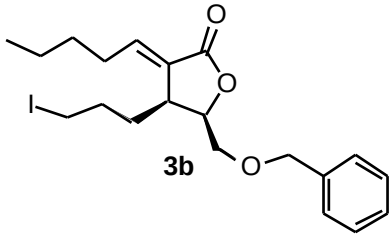
The compounds **5a**, **5c**, and **5d** were synthesized from **4** according to the similar procedure by using the corresponding alkynes. The ratio of regioisomer and combined yield of the reaction for preparing **5a**, **5c** and **5d** were 92 : 8 and 80%, 95 : 5 and 81% , and 87 : 13 and 77%, respectively.

5a: ^{1}H NMR δ 0.05 (6H, s), 0.89 (9H, s), 1.35-1.86 (4H, m), 1.77 (3H, d, J=2.4 Hz), 2.42-2.51 (2H, m), 3.57 (1H, dd, J=6.6, 9.0 Hz), 3.64 (2H, t, J=6.3 Hz), 3.60-3.71 (1H, m), 3.74 (1H, dd, J=3.0, 9.0 Hz), 4.58 (2H, s), 7.26-7.36 (5H, m); ^{13}C NMR δ -5.4, 3.4, 18.2, 25.9, 27.2, 30.3, 35.3, 63.1, 72.5, 72.7, 73.3, 78.6, 78.9, 127.7, 127.8, 128.5, 138.1; IR (neat) 3457, 2929, 1454, 1254, 1099 cm^{-1}.

5c: ^{1}H NMR δ 0.06 (6H, s), 089 (9H, s), 1.52-1.95 (4H, m), 2.55 (1H, br s), 2.74-2.81 (1H, m), 3.68 (1H, d, J=2.7 Hz), 3.64-3.72 (3H, m),3.74-3.87 (2H, m), 7.26-7.36 (10H, m); ^{13}C NMR δ -5.4, 18.2, 25.9, 27.2, 30.3, 35.9, 63.0, 72.4, 72.7, 73.4, 83.8, 89.5, 123.6, 127.8, 127.9, 128.3, 128.5, 131.7, 131.8, 138.0; IR (neat) 3449, 2928, 1471, 1254, 1099 cm^{-1}.

5d: ^{1}H NMR δ 0.06 (6H, s), 0.12 (6H, s), 0.90 (9H, s), 1.40-1.95 (4H, m), 2.50-2.59 (1H, m), 3.46-3.80 (5H, m), 4.58 (2H, s), 7.26-7.36 (5H, m); ^{13}C NMR δ -5.4, 0.1, 18.2, 25.9, 27.0, 30.2, 36.2, 63.0, 72.2, 72.6, 73.4, 87.9, 106.5, 127.7, 127.8, 128.5, 138.0; IR (neat) 2452, 2928, 2167, 1454, 1250, 1100, 840 cm^{-1}.

Typical Procedure for Conversion of 5 to 3.



Compound 3a: To a solution of alcohol **5b** (3.26 g, 7.8 mmol) in THF (16 mL) was added *n*-BuLi (6.26 mL, 1.50 M in hexanes, 9.4 mmol) at -78 ^{o}C. After stirring for 30 min, ethyl chloroformate (0.97 mL, 10.1 mmol) was added dropwise and the resulting mixture was allowed to warm to 0 ^{o}C. After stirring for 2 h, the mixture was quenched by addition of saturated aqueous NH_4Cl, extracted with ether (2 x 15 mL), washed with brine, dried over $MgSO_4$, concentrated and chromatographed on silica gel to give the corresponding ethyl carbonate **6b**. To a solution of **6b** thus obtained and Ti(O-*i*-Pr)$_4$ (3.43 mL, 11.7 mmol) in ether (40 mL) was added dropwise *i*-PrMgCl (18.0 mL, 1.30 M in ether, 23.4 mmol) at -50 ^{o}C. The resulting yellow solution was stirred for 2 h at -50 ^{o}C to -45 ^{o}C. During this period the color of the mixture became red brown. To this was added aqueous 1N HCl (30 mL) and the mixture was allowed to warm to room temperature. After stirring for 1 h, the mixture was extracted with ether (2 x 20 mL), washed with aqueous saturated $NaHCO_3$, dried over $MgSO_4$, concentrated, and passed through a silica gel short column to afford lactone **7b**. To an ice-cooled solution of **7b** thus prepared in THF (40 mL) was added aqueous HF (1.42 mL, 55%), and the mixture was allowed to warm to room temperature and stirred for 5 h. After addition of saturated aqueous $NaHCO_3$ (30 mL), the mixture was extracted with ether (2 x 30 mL), washed with brine, dried over $MgSO_4$, concentrated, and passed through a silica gel short column to give the corresponding alcohol. To an ice-cooled solution of the alcohol thus obtained and triethylamine (3.26 mL, 23.4 mmol) in CH_2Cl_2 (40 mL) was added methanesulfonyl chloride (1.21 mL, 15.6 mmol). After stirring for 3 h at room temperature, the mixture was quenched by addition of aqueous saturated $NaHCO_3$ (20 mL) at 0 ^{o}C. The mixture was extracted with ethyl acetate (2 x 20 mL), dried over $MgSO_4$, and concentrated to give the crude residue of the corresponding mesylate. A mixture of the mesylate thus synthesized, sodium iodide (5.84 g, 39.0 mmol), and acetone (40 mL) was heated to reflux for 1 h and then cooled to room temperature. After addition of water (30 mL), the mixture was extracted with ether (2 x 30 mL), dried over $MgSO_4$, concentrated and purified by column chromatography on silica gel (hexanes/ether) to give **3b** (1.72 g) in 50% overall yield from **5b**. Chemical purity of **3b** thus obtained was found to be >95% by its ^{1}H NMR and GC analyses. **3b**: ^{1}H NMR δ ; 0.92 (3H, t, J=6.9 Hz), 1.30-1.93 (8H, m), 2.15-2.23 (2H, m), 3.01 (2H, t, J=6.6 Hz), 3.06-3.18 (1H, m), 3.72 (1H, dd, J=6.9, 10.2 Hz), 3.80 (1H, dd, J=6.0, 10.2 Hz), 4.42-4.55 (1H, m), 4.56 (1H, d, J=11.7 Hz), 4.63 (1H, d, J=11.7 Hz), 6.72 (1H, dt, J=1.5, 7.8 Hz), 7.26-7.38 (5H, m); ^{13}C NMR δ 5.8, 13.7, 22.3, 29.4, 29.8, 30.4, 30.5, 38.9, 67.6, 73.7, 78.7, 128.0, 128.0, 128.6, 130.6, 137.4, 141.6, 170.7; IR (neat) 2927, 1758, 1677, 1455, 1195 cm^{-1}; $[\alpha]_D^{29}$ -57.2 (*c* 1.04, $CHCl_3$). Anal. Calcd for $C_{20}H_{27}IO_3$: C, 54.31; H, 6.15. Found: C, 53.97; H, 6.16.

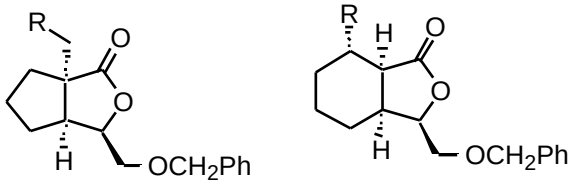
3a: ^{1}H NMR δ 1.70-1.82 (4H, m), 1.87 (3H, d, J=7.2 Hz), 3.10 (2H, t, J=6.6 Hz), 3.10-3.19 (1H, m), 3.72 (1H, dd, J=6.6, 10.2 Hz), 3.80 (1H, dd, J=6.0, 10.2 Hz), 4.47-4.56 (1H, m), 4.56 (1H, d, J=12.0 Hz), 4.63 (1H, d, J=12.0 Hz), 6.80 (1H, dq, J=1.8, 7.2 Hz), 7.30-7.37 (5H, m); ^{13}C NMR δ 5.7, 15.7, 29.3, 30.5, 38.6, 67.6, 73.6, 78.6, 127.9, 128.0, 128.5, 132.0, 136.1, 137.4, 170.4; IR (neat) 2924, 2865, 1760, 1681, 1454, 1205, 1119, 983 cm^{-1}; $[\alpha]_D^{25}$ -39.3 (*c* 1.02, $CHCl_3$). Anal. Calcd for $C_{17}H_{21}IO_3$: C, 51.01; H, 5.29. Found: C, 50.90; H, 5.23.

3c: ^{1}H NMR δ 1.51-1.95 (4H, m), 2.98 (2H, t, J=6.3 Hz), 3.68-3.77 (1H, m), 3.80 (1H, dd, J=6.9, 10.2 Hz), 3.88 (1H, dd, J=6.0, 10.2 Hz), 4.60 (1H, d, J=11.7 Hz), 4.66 (1H, d, J=11.7 Hz), 7.24-7.60 (10H, m); ^{13}C NMR δ 6.4, 29.2, 30.4, 39.4, 67.5, 73.8, 78.6, 127.9, 128.4, 128.9, 129.6, 129.7, 129.8, 130.1, 133.9, 137.0, 137.2, 171.3; IR (neat) 2930, 1756, 1649, 1542, 1189 cm^{-1}; $[\alpha]_D^{28}$ -46.9 (*c* 1.14, $CHCl_3$). Anal. Calcd for $C_{22}H_{23}IO_3$: C, 57.15; H, 5.01. Found: C, 57.19; H, 5.11.

3d: ^{1}H NMR δ 0.21 (9H, s), 1.66-1.84 (4H, m), 3.06 (2H, t, J=6.3 Hz), 3.11-3.17 (1H, m), 3.72 (1H, dd, J=6.6, 10.2 Hz), 3.79 (1H, dd, J=5.7, 10.2 Hz), 4.47-4.56 (1H, m), 4.57 (1H, d, J=9.9 Hz), 4.61 (1H, d, J=9.9 Hz), 6.87 (1H, d, J=1.8 Hz), 7.26-7.38 (5H, m); ^{13}C NMR δ −0.9, 5.8, 30.1, 30.8, 40.5, 67.5, 73.7, 78.4, 128.0, 128.4, 128.5, 137.3, 139.9, 144.7, 169.9; IR (neat) 2954, 1765, 1454, 1250, 1187, 1116, 840 cm^{-1}; $[\alpha]_D^{27}$ -46.3 (*c* 1.04, $CHCl_3$). Anal. Calcd for $C_{19}H_{27}IO_3Si$: C, 49.78; H, 5.94. Found: C, 50.17; H, 6.17.

In the case of the synthesis of **3a**, $ClTi(O\text{-}i\text{-}Pr)_3$ was used instead of $Ti(O\text{-}i\text{-}Pr)_4$ for the intramolecular nucleophilic acyl substitution reaction.

Radical Cyclization Reaction of 3 to 1 and/or 2.



1 **2**

Reaction with cat. Et$_3$B/Bu$_3$SnH Reagent. To a solution of **3** (1.0 mmol) in THF or toluene (5 mL) was added Bu_3SnH (0.35 mL, 1.3 mmol) and triethylborane (0.05 mL, 1.0 M in hexanes, 0.05 mmol) at 0 °C. The mixture was allowed to warm to room temperature and stirred at this temperature for 1-2 h. After checking completion of the reaction by TLC analysis, the mixture was concentrated by evaporation and directly subjected to column chromatography on silica gel (hexanes/ether) to give a mixture of **1** and **2**.

Reaction with cat. AIBN/Bu$_3$SnH Reagent. To a solution of **3** (1.0 mmol) in toluene (5 mL) was added Bu_3SnH (0.35 mL, 1.3 mmol) and azodiisobutyronitrile (AIBN, 49 mg, 0.3 mmol) at room temperature. The mixture was heated to 80 °C and stirred at this temperature for 3-4 h. After checking completion of the reaction by TLC analysis and cooling to room temperature, the mixture was concentrated by evaporation and directly subjected to column chromatography on silica gel (hexanes/ether) to give a mixture of **1** and **2**.

Reaction with cat. Et_3B/Bu_3SnH Reagent in the Presence of Et_2AlCl. To a solution of **3** (1.0 mmol) in toluene (5 mL) was sequentially added Et_2AlCl (1.56 mL, 0.96 M in hexanes, 1.5 mmol), Bu_3SnH (0.40 mL, 1.5 mmol), and triethylborane (0.3 mL, 1.0 M in hexanes, 0.3 mmol) at -78 °C. The mixture was gradually warmed to -20 °C over 3 h. After addition of water (0.25 mL) at -20 °C, the mixture was allowed to warm to room temperature, filtered through a pad of Celite with hexanes, and concentrated in vacuo. The resulting residue was chromatographed on silica gel to give a mixture of **1** and **2**.

In the case of the reaction with **3a** and **3b**, separation of the resulting **1** and **2** was difficult and, therefore, the following analyses were performed using a mixture of **1** and **2**.

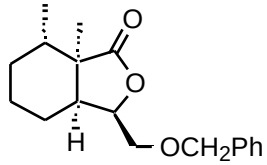
1a: ^{1}H NMR δ 0.99 (3H, t, J=7.5 Hz), 1.07-1.88 (6H, m), 2.02-2.19 (1H, m), 2.38-2.46 (1H, m), 2.49-2.61 (1H, m), 3.62 (1H, dd, J=5.1, 10.5 Hz), 3.71 (1H, dd, J=6.9, 10.5 Hz), 4.41-4.49 (1H, m), 4.54 (1H, d, J= 12.0 Hz), 4.63 (1H, d, J=12.0 Hz), 7.23-7.42 (5H, m). **2a**:^{1}H NMR δ 1.09 (3H, d, J=7.2 Hz), 1.23-1.80 (6H, m), 2.36-2.50 (2H, m), 2.45-2.61 (1H, m), 3.64 (1H, dd, J=5.1, 10.2 Hz), 3.71 (1H, dd, J=6.9, 10.2 Hz), 4.42-4.48 (1H, m), 4.52 (1H, d, J=12.0 Hz), 4.62 (1H, d, J=12.0 Hz), 7.28-7.41 (5H, m); ^{13}C NMR δ 17.6, 19.5, 22.3, 25.8, 28.5, 35.1, 47.6, 68.1, 73.5, 80.0, 127.6, 127.7, 128.3, 137.4, 176.9; IR (neat, a mixture of **1a** and **2a**) 2932, 2859, 1775, 1455, 1378, 1180, 1127 cm^{-1}. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.30; H, 8.29 (measured using a mixture of **1a** and **2a**).

1b: ^{1}H NMR δ 0.87 (3H, t, J=6.9 Hz), 1.10-1.85 (13H, m), 2.03-2.16 (1H, m), 2.45-2.61 (1H, m), 3.63 (1H, dd, J=5.1, 10.2 Hz), 3.70 (1H, dd, J=6.9, 10.2 Hz), 4.53 (1H, d, J=12.0 Hz), 4.62 (1H, d, J=12.0 Hz), 4.57-4.69 (1H, m), 7.24-7.40 (5H, m); ^{13}C NMR δ 14.0, 22.4, 25.2, 26.1, 27.5, 32.1, 36.2, 36.8, 46.4, 57.2, 69.4, 73.5, 78.4, 127.5, 127.6, 128.3, 137.4, 181.9. **2b**: ^{1}H NMR δ 0.90 (3H, t, J=6.3 Hz), 1.17-1.81 (12H, m), 2.08-2.24 (1H, m), 2.41-2.60 (2H, m), 3.63 (1H, dd, J=5.4, 10.5 Hz), 3.71 (1H, dd, J=6.9, 10.5 Hz), 4.40-4.48 (1H, m), 4.52 (1H, d, J=12.0 Hz), 4.62 (1H, d, J=12.0 Hz), 7.23-7.38 (5H, m); ^{13}C NMR δ 13.9, 17.7, 22.2, 22.5, 26.5, 29.6, 30.8, 32.3, 35.2, 46.3, 68.0, 73.5, 80.0, 127.8, 127.9, 128.5, 137.7, 177.5. IR (neat, a mixture of **1b** and **2b**) 2955, 2870, 1768, 1454, 1362, 1105 cm^{-1}. Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.68; H, 8.92 (measured using a mixture of **1b** and **2b**).

1c: ^{1}H NMR δ 1.43-1.83 (5H, m), 2.15-2.27 (1H, m), 2.62-2.73 (1H, m), 2.73 (1H, d, J=13.5 Hz), 3.28 (1H, d, J=13.5 Hz), 3.48 (1H, dd, J=5.4, 10.2 Hz), 3.55 (1H, dd, J=6.9, 10.2 Hz), 3.72 (1H, q, J=6.3 Hz), 4.44 (1H, d, J=12.0 Hz), 4.51 (1H, d, J=12.0 Hz), 7.21-7.36 (10H, m); ^{13}C NMR δ 25.8, 27.5, 38.0, 42.1, 44.8, 58.9, 69.0, 73.4, 78.2, 127.2, 127.7, 127.8, 128.4, 128.7, 129.5, 136.9, 137.9, 182.2; IR (neat) 3490, 1753, 1456, 1376, 1133 cm^{-1}; $[\alpha]D^{26}$ -13.2 (*c* 1.24, $CHCl_3$). Anal. Calcd for $C_{22}H_{24}O_3$: C, 78.54; H, 7.19. Found: C, 78.48; H, 7.16.

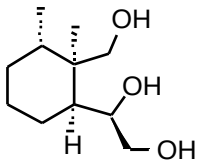
1d: ^{1}H NMR δ 0.08 (9H, s), 1.00 (1H, d, J=15.0 Hz), 1.14 (1H, d, J=15.0 Hz), 1.41-1.77 (5H, m), 2.12-2.26 (1H, m), 2.41-2.51 (1H, m), 3.63 (1H, dd, J=5.1, 10.2 Hz), 3.71 (1H, dd, J=6.9, 10.2 Hz), 4.53 (1H, d, J=12.0 Hz), 4.64 (1H, d, J=12.0 Hz), 4.71 (1H, dt, J=6.9, 6.0 Hz), 7.23-7.42 (5H, m); ^{13}C NMR δ 0.1, 24.4, 25.9, 26.7, 38.0, 49.2, 55.2, 69.6, 73.6, 77.9, 127.6, 127.7, 128.3, 137.5, 182.6; IR (neat) 2954, 2871, 1772, 1411, 1249, 1105, 841 cm^{-1}; $[\alpha]D^{28}$ -28.3 (*c* 0.92, $CHCl_3$).Anal. Calcd for $C_{19}H_{28}O_3Si$: C, 68.63; H, 8.49. Found: C, 68.66; H, 8.63.

Synthetic Transformations of 2a [Scheme 3].



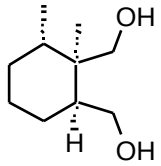
8

Compound 8: To a solution of LDA (5.75 mmol), prepared from *n*-BuLi (3.83 mL, 1.50 M in hexanes, 5.75 mmol) and *i*-Pr_2NH (0.97 mL, 6.9 mmol), in THF (9 mL) was added a solution of **2a** (630 mg, 2.3 mmol, including 8% of inseparable **1a**) in THF (1 mL) at -78 ^oC. After stirring for 1 h at this temperature, iodomethane (0.21 mL, 3.45 mmol) was added and the mixture was gradually warmed to -20 ^oC over 2 h. After addition of saturated aqueous NH_4Cl (15 mL), the mixture was extracted with ether (2 x 15 mL), dried over $MgSO_4$, concentrated, and chromatographed on silica gel (hexanes/ether) to give **8** (580 mg), which involved a small amount of inseparable **1a**. The yield of **8** was confirmed to be 87% by GC analysis using an internal standard. The resulting **8** was homogeneous on ^1H and ^{13}C NMR and GC-MS analyses, indicating almost 100% diastereoselectivity of methylation reaction. The following data for **8** was measured by using a mixture of **8** and **1a**: ^1H NMR δ 0.99 (3H, d, J=6.9 Hz), 1.18 (3H, s), 1.30-1.43 (5H, m), 1.51-1.63 (1H, m), 2.03-2.14 (1H, m), 2.20 (1H, quintet, J=5.7 Hz), 3.65 (1H, dd, J=5.1, 10.5 Hz), 3.71 (1H, dd, J=7.2, 10.5 Hz), 4.52 (1H, d, J=12.0 Hz), 4.62 (1H, d, J=12.0 Hz), 4.71 (1H, dt, J=7.2, 5.1 Hz), 7.22-7.41 (5H, m); ^{13}C NMR δ 15.3, 18.0, 19.8, 22.0, 29.7, 31.0, 41.4, 46.3, 68.7, 73.3, 78.6, 127.6, 127.7, 128.3, 137.6, 180.4; IR (neat) 2935, 1768, 1455, 1384, 1196, 1110 cm^{-1}.



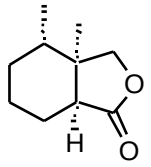
9

Triol 9: To an ice-cooled solution of **8** (380 mg, 1.32 mmol) in THF (6.5 mL) was added $LiAlH_4$ (100 mg, 2.63 mmol). The resulting mixture was stirred at room temperature for 1 h. After addition of ether (10 mL), water (1 mL), and then aqueous 15% NaOH (10 mL), the mixture was extracted with ether (2 x 15 mL), died over $MgSO_4$, and concentrated in vacuo to afford the corresponding diol. To a solution of the diol, thus obtained, in MeOH (10 mL) was added 10% Pd on carbon (50 mg) at room temperature. The mixture was stirred at this temperature under a hydrogen atmosphere (1 atm) for 3 h. The mixture was filtered to remove the catalyst through a pad of Celite with MeOH, and the filtrate was concentrated in vacuo and chromatographed on silica gel to give **9** (267 mg) in quantitative yield, where the impurity derived from **1a** could be separated. **9**: ^1H NMR δ 0.89 (3H, d, J=7.2 Hz), 0.92 (3H, s), 1.14-1.68 (8H, m), 3.03 (1H, d, J=11.4 Hz), 3.40 (1H, dd, J=3.3, 9.0 Hz), 3.51-3.68 (1H, m), 3.90 (1H, dd, J=3.3, 9.0 Hz), 4.15 (1H, d, J=11.4 Hz); ^{13}C NMR δ 14.7, 20.5, 21.0, 28.3, 37.1, 39.9, 41.3, 50.1, 65.9, 66.9, 70.0; IR (neat) 3342, 2925, 2361, 2242, 1576, 1464, 1034 cm^{-1}.



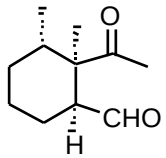
10

Diol 10: To a solution of **9**, prepared from 1.30 mmol of **8**, in ethanol/H_2O (13 mL, 1/2(v/v)) was added $NaIO_4$ (0.42 g, 1.98 mmol) at 0 ^oC. The mixture was stirred at room temperature for 1 h and then water (10 mL) was added. The mixture was extracted with ether (2 x 15 mL), washed with brine (5 mL), dried over $MgSO_4$, and concentrated to give a crude residue of the corresponding lactol, which was directly subjected to the next reaction. A solution of a half amount of the lactol (0.65 mmol), prepared above, in ethanol (4 mL) was added to a mixture of $NaBH_4$ (74 mg, 1.95 mmol) at 0 ^oC. After stirring for 2 h, ether (5 mL) and water (5 mL) were added and the mixture was extracted with ether (2 x 10 mL), washed with brine (5 mL), dried over $MgSO_4$, concentrated, and chromatographed on silica gel to give diol **10** (64 mg) in 57% overall yield from **2a**. The ^1H and ^{13}C NMR data and [α]D value of **10** thus obtained were in good agreement with those reported.[2] $[\alpha]_D^{25}$ +13.0 (*c* 0.62, $CHCl_3$), lit.,[2] $[\alpha]_D^{20}$ +13 (*c* 1.0, $CHCl_3$).



11

Lactone 11: To a solution of the lactol (0.65 mmol), prepared above, in ether (4 mL) was added a mixture of PCC (0.28 g, 1.3 mmol) and Celite (0.5 g) at 0 ^oC. The mixture was stirred at room temperature for 5 h and filtered through a pad of Celite with ether. The filtrate was concentrated and purified by column chromatography to give **11** (66 mg) in 60% overall yield from **2a**: ^1H NMR δ 0.86 (3H, d, J=6.6 Hz), 1.02 (3H, s), 1.12-1.78 (6H, m), 1.90-2.13 (1H, m), 2.24-2.35 (1H, m), 3.66 (1H, d, J=8.7 Hz), 4.08 (1H, d, J=8.7 Hz); ^{13}C NMR δ 15.9, 16.6, 20.8, 22.8, 29.2, 33.8, 42.0, 47.7, 74.8, 178.1; IR (neat) 2931, 1769, 1462, 1367, 1155, 1008 cm^{-1}; $[\alpha]_D^{29}$ +54.4 (*c* 0.88, $CHCl_3$).



12

Ketoaldehyde 12: To a solution of **8** (190 mg, 0.66 mmol) in MeOH (4 mL) was added 10% Pd on carbon (50 mg) at room temperature and the mixture was stirred at this temperature under a hydrogen atmosphere (1 atm) for 3 h. The mixture was filtered to remove the catalyst through a pad of Celite with MeOH and the filtrate was concentrated in vacuo to give the corresponding alcohol which was subjected directly to the next reaction. To a solution of the resulting alcohol in ether (5.5 mL) was added dropwise MeLi (1.45 mL, 1.14 M in ether, 1.65 mmol) at -78 ^oC. The mixture was allowed to

warm to -40 ^{o}C and stirred at this temperature for 3 h, and then quenched by addition of saturated aqueous NH_4Cl (10 mL). The mixture was extracted with ether (2 x 10 mL), washed with brine (5 mL), dried over $MgSO_4$, and concentrated in vacuo to give the crude residue of the corresponding ketodiol which was subjected to the next reaction without further purification. To a solution of the ketodiol, thus prepared, in ethanol/H_2O (6.6 mL, 1/2 (v/v)) was added $NaIO_4$ (0.21 g, 1.0 mmol) at 0 ^{o}C. The mixture was stirred at room temperature for 1 h and then water (10 mL) was added. The resulting mixture was extracted with ether (2 x 10 mL), washed with brine (5 mL), dried over MgSO4, concentrated in vacuo, and chromatographed on silica gel to give ketoaldehyde **12** (73 mg) in 56% overall yield from **2a**: ^{1}H NMR δ 1.01 (3H, d, J=6.9 Hz), 1.28 (3H, s), 1.32-1.58 (4H, m), 1.62-1.80 (1H, m), 1.81-1.97 (1H, m), 2.07-2.16 (1H, m), 2.14 (3H, s), 2.17-2.30 (1H, m), 9.80 (1H, br s); ^{13}C NMR δ 14.6, 19.0, 21.6, 23.1, 25.1, 30.2, 34.4, 51.4, 55.3, 204.6, 213.0; IR (neat) 2933, 1769, 1713, 1460, 1387, 1257 cm^{-1}; $[\alpha]D^{28}$ +48.4 (*c* 0.32, $CHCl_3$).

References

1. Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc*. **1987**, *109*, 5765.
2. Greene, A. E.; Coelho, F.; Depres, J. P.; Brocksom, T. J. *Tetrahedron Lett.* **1988**, *29*, 5661.