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Asymmetric synthesis of the δ-lactone moiety in mevinic acid derivatives using an enzymatic procedure

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Abstract: Asymmetric induction into *meso*-1,3-diacetoxy-5-cycloheptene **4** by PFL-catalyzed hydrolysis afforded monoacetate (1*S*,3*R*)-**5** of 96% enantiomeric excess (e.e.), which was converted into a synthetic equivalent **14** of the δ-lactone moiety in mevinic acid derivatives. © 1997 Published by Elsevier Science Ltd. All rights reserved.

Mevinic acid derivatives[1] such as compactin, mevinolin, synvastatin and pravastatin have attracted much synthetic attention because of their biological activities as inhibitors of HMG CoA reductase. We report here an asymmetric synthesis of a versatile unit for the lactone moiety[2] of the above compounds by using an enzymatic procedure. The target lactol derivative **14** with a 2-iodoethyl substituent at the C6-position would be applicable as a useful electrophile to construct the mevinic acid derivatives.

Diastereoselective preparation of substrate for enzymatic chiral induction

As a substrate for enzymatic chiral induction, we designed seven-membered 1,3-diacetate **4**,[2b] which was synthesized from 3,5-cycloheptadienol[3] **1** in a diastereoselective manner. That is to say, monoepoxidation of **1** with *m*-chloroperbenzoic acid (1.1 equiv.) in CH_2Cl_2 at room temperature predominantly gave *cis*-epoxyalcohol **2a** (95% yield) accompanied with *trans*-epoxyalcohol **2b** (4% yield), which were easily separated by silica-gel column chromatography. Stereochemistry of **2a** was deduced based on NOESY spectrum, in which NOEs were observed between C1–Hα and C3–Hα, and between C3–Hα and C4–Hα. Reduction of **2a** with $LiAlH_4$ afforded the desired *cis*-5-cyclohepten-1,3-diol **3a** (45%). In the 270 MHz ^{1}H NMR spectrum of **3a**, C2-protons were differently observed at δ 1.67 (1H, C2β–H, dt, J=12.3, 10.9 Hz) and δ 2.30 (m, C2α–H). On the other hand, those of **3b** derived from **2b** by a similar $LiAlH_4$ reduction were equivalently observed at δ 2.02 (2H, t, J=5.9 Hz) based on its C_2-symmetric structure. Thus, the stereochemistry of **3a,b** was unambiguously determined. Acetylation of **3a** in the usual manner gave the corresponding diacetate **4** (99%) (Scheme 1).

PFL-Catalyzed asymmetric hydrolysis

Lipase-catalyzed asymmetric hydrolysis of **4** was studied using three kinds of lipases such as *Pseudomonas fluorescence* lipase (PFL),[4,5] Lipase A, and Lipase A-6. Among them, PFL-catalyzed hydrolysis gave the best result in both chemical yield and enantiomeric excess (e.e.) of the monoacetate (−)-**5** (72% yield, 96% e.e.) (Scheme 2). The enantiomeric excess of the hydrolyzed products was determined by ^{1}H NMR spectra after conversion into the corresponding Mosher's esters [(+)-MTPA esters].[6] The ^{1}H NMR spectra of (+)-MTPA ester derived from (±)-**5** showed the methyl proton signals at δ 2.03 (s, 1.5H) and 2.01 (s, 1.5H), while the corresponding signal from (−)-**5** was observed at δ 2.03 (s) and 2.01 (s) in the ratio of 98 to 2. The absolute configuration of (−)-**5** was determined as follows. The obtained (−)-**5** (96% e.e.) was converted into *trans*-1,3-bis(benzoyloxy)cycloheptane (+)-**8** *via* a four-step sequence: i. hydrogenation of the double bond of (−)-**5**; ii. inversion of the hydroxy

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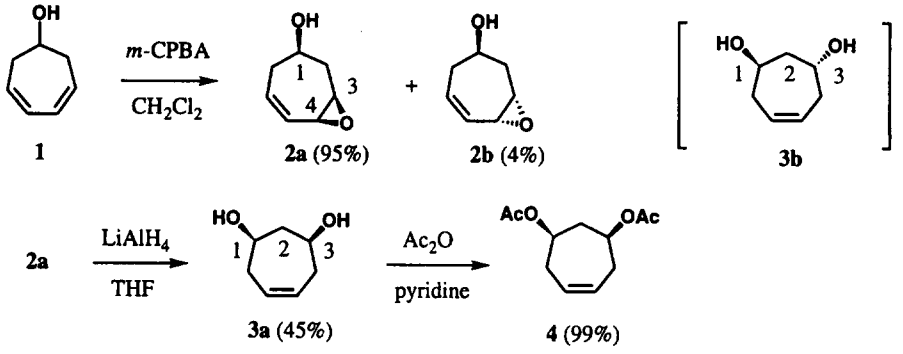
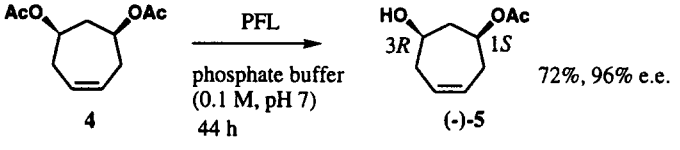
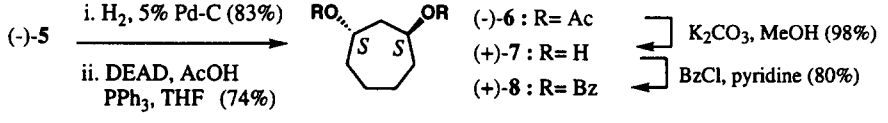


Scheme 1. Diastereoselective preparation of substrate **4** for enzymatic hydrolysis.



Scheme 2.



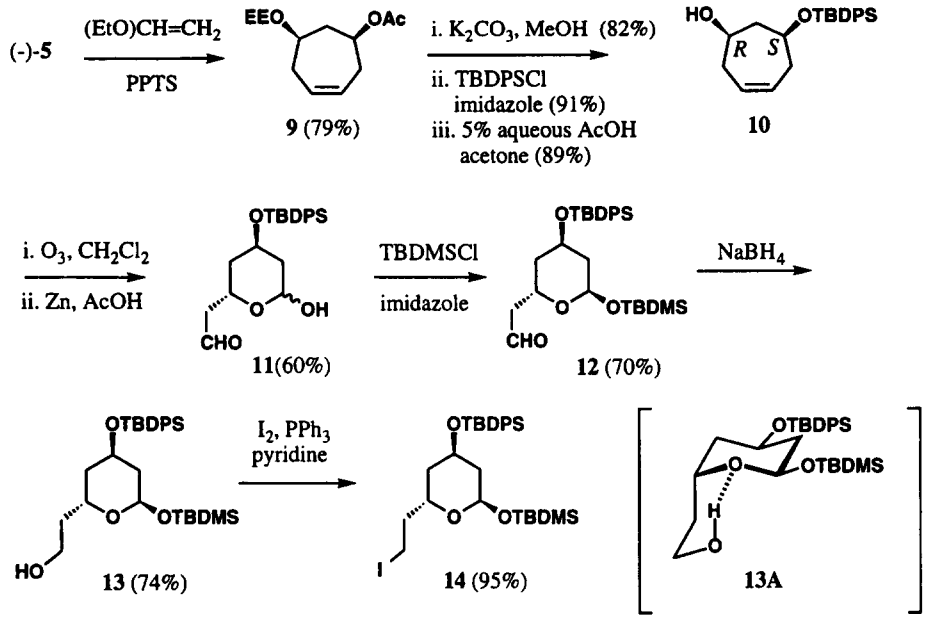
Scheme 3.

group by Mitsunobu reaction into (−)-**6**; iii. solvolysis of the acetate into (+)-**7**; iv. benzoylation of the hydroxy group. The CD spectrum of (+)-**8** showed the positive first Cotton effect[7] ($\Delta\epsilon$=+13.6, 232.4 nm, MeOH),[8] from which the absolute stereochemistry of (+)-**8** was determined to be *S,S* and that of monoacetate (−)-**5** was 1*S*,3*R* (Scheme 3).[2b,9]

Preparation of a synthetic equivalent for the δ-lactone moiety in mevinic acids

For the synthesis of the target **14**, the conversion of the acetate function in (−)-**5** into the *tert*-butyldiphenylsilyl (TBDPS) ether in **10** is necessary. This conversion was achieved by a four-step sequence in good yields: i. protection of the hydroxy group in (−)-**5** as 1-ethoxyethyl ether **9**; ii. solvolysis of the acetate function; iii. protection of the *S*-hydroxy group as a TBDPS ether; iv. chemoselective deprotection of the ethoxyethyl ether. Ozonolysis of **10** and subsequent treatment with Zn/AcOH gave the hemiacetal **11** in 60% yield as a 1:1 diastereomeric mixture at the C2-position. Protection of the hemiacetal function in **11** as a TBDMS ether gave the sole product **12** in 70% yield. This result suggests that *O*-silylation proceeded from only (2*S*)-**11** to afford the sterically stable **12** accompanied with a shift of equilibrium between diastereomeric hemiacetals **11**.

The compound **12** was converted into the corresponding alcohol **13** by $NaBH_4$ reduction. Compound **13** resisted usual sulfonylation by *p*-TsCl and/or MsCl in the presence of 4-dimethylaminopyridine, which allows us to consider the hydrogen-bonded structure of **13A**. Direct iodination of **13** was achieved by using I_2/PPh_3/pyridine to give the target molecule **14** in 95% yield (Scheme 4). In the ^1H NMR spectrum of **14**, C2–H was observed at δ 5.30 (dd, *J*=9.4, 2.1 Hz), C4–H at δ 4.22 (tt,



Scheme 4. Preparation of a synthetic equivalent for the δ-lactone in mevinic acids.

J=9.0, 2.8 Hz) and C6–H at δ 4.26 (m, W_H=7.5 Hz), which suggests the C2- and C4-substituents are in equatorial orientation and the C6-substituent in axial orientation. Synthetic application of **14** for mevinic acid derivatives is currently under investigation.

Experimental

IR spectra were measured with a JASCO A-202 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-GX-270 or JEOL JNM-FX-100 spectrometer. EIMS spectra were taken on a JEOL JMS-D 300 spectrometer and FDMS spectra were taken on a JEOL JMS-DX 300 spectrometer. Specific rotation was measured on a JASCO DIP-360 polarimeter. Melting points were uncorrected. For O_3 oxidation, Ishii ozone generator (7,800 V, O_2 flow rate; 0.5 mL/min) was used. THF was distilled from Na/benzophenone before use. Benzene and CH_2Cl_2 were distilled from P_2O_5. PFL (Amano PS), Lipase A and Lipase A-6 were gifted by courtesy of Amano Pharmaceutical Corp. (Japan), and were used as received.

(1RS,3RS,4SR)-3,4-Epoxy-5-cyclohepten-1-ol (2a) and (1RS,3SR,4RS)-3,4-epoxy-5-cyclohepten-1-ol (2b)

A solution of *m*-CPBA (80%) (22.3 g, 104 mmol) in CH_2Cl_2 (200 mL) was added to the stirred solution of 3,5-cycloheptadien-1-ol **1** (13.4 g, 122 mmol) in CH_2Cl_2 (300 mL) at 0°C. After being stirred at 0°C for 5 h, the reaction mixture was filtered. The filtrate was washed with aqueous 5% $NaHCO_3$ and brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with AcOEt afforded **2a** (14.6 g, 95%) and **2b** (0.7 g, 4%).

2a: A colorless oil. IR (neat) 3400, 2900, 1651, 1420, 1260, 1120, 1040 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 5.75 (m, 2H), 4.36 (m, 1H), 3.20 (m, 2H), 2.90 (dd, J=4.3, 14.5 Hz, 1H), 2.77 (dd, J=7.9, 14.5 Hz, 1H), 2.40–2.70 (m, 2H), 1.80 (m, 1H). EIMS *m/z* 126 (M^+), 108 (M^+-H_2O).

2b: A colorless oil. IR (neat) 3400, 2900, 1650, 1420, 1060, 1040 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 5.84 (m, 1H), 5.61 (m, 1H), 4.65 (m, 1H), 4.38 (dd, J=6.3, 8.6 Hz, 1H), 4.23 (d, J=4.6 Hz, 1H), 2.66 (m,

1H), 2.17 (ddd, *J*=2.0, 6.3, 13.8 Hz, 1H), 1.96–2.15 (m, 2H), 1.65 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 128.0 (d), 124.4 (d), 79.8 (d), 77.9 (d), 73.4 (d), 41.5 (t), 33.5 (t). EIMS *m/z* 126 (M^+), 108 (M^+-H_2O).

(1RS,3SR)-5-Cycloheptene-1,3-diol (3a)

A solution of **2a** (14.6 g, 116 mmol) in THF (20 mL) was added to the stirred suspension of $LiAlH_4$ (3.46 g, 96.3 mmol) in THF (220 mL) at 0°C. After being stirred at room temperature for 20 h, the reaction was quenched with 15% aqueous NaOH. Resulting precipitate was filtered off through Celite. The filtrate was dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 50% AcOEt in hexane afforded **3a** (6.7 g, 45%) as colorless crystals. mp 129–130°C (Et_2O–hexane). IR (nujol) 3200, 1630, 1030, 1000 cm^{-1}; ^{1}H NMR (CD_3OD) δ 5.78 (m, 2H), 3.50 (tt, *J*=3.3, 9.9 Hz, 2H), 2.15–2.45 (m, 5H), 1.67 (dt, *J*=12.3, 10.9 Hz, 1H). EIMS *m/z* 110 (M^+-H_2O).

(1RS,3SR)-1,3-Diacetoxy-5-cycloheptene (4)

Ac_2O (15 mL) was added to the stirred solution of *cis*-diol **3a** (3.0 g, 23.4 mmol) in pyridine (24 mL) at 0°C. After being stirred at room temperature for 20 min, the reaction mixture was poured into ice water and extracted with AcOEt. The extracts were successively washed with 5% aqueous $NaHCO_3$, brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 20% AcOEt in hexane afforded **4** (4.7 g, 99%) as a colorless oil. IR (neat) 1730, 1630, 1220, 1000 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 5.77 (m, 2H), 4.72 (m, 2H), 2.28–2.45 (m, 5H), 2.03 (s, 6H), 1.90 (dt, *J*=10.9, 11.2 Hz, 1H). EIMS *m/z* 212 (M^+).

(1S,3R)-1-Acetoxy-5-cyclohepten-3-ol (−)-(5)

PFL (500 mg) was added to a suspension of **4** (500 mg) in acetone (10 mL) and 0.1 M phosphate buffer (100 mL, pH 7.0). The whole was stirred at 30°C for 44 h and then extracted with CH_2Cl_2. (When a spot of the corresponding diol **3a** appeared on TLC, reaction was quenched by extraction.) The CH_2Cl_2 extract was dried over $MgSO_4$, and then concentrated *in vacuo* to leave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 30% AcOEt in hexane afforded (−)-**5** (289 mg, 72%) as a colorless oil. $[\alpha]_D^{26}$ −49.0 (*c* 1.45, $CHCl_3$). IR (neat) 3400, 2950, 1730, 1250, 1025 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 5.77 (m, 2H), 4.75 (m, 1H), 3.73 (m, 1H), 2.28–2.45 (m, 5H), 2.04 (s, 3H), 1.88 (dt, *J*=10.2, 12.9 Hz, 1H), 1.72 (br s, 1H). EIMS *m/z* 170 (M^+), 152 (M^+-H_2O). HRMS for $C_9H_{14}O_3$ M^+ 170.0943, found 170.0937.

Determination of absolute configuration of (−)-5

Hydrogenation of (−)-**5** (203 mg) in MeOH catalyzed by 5% Pd–C (150 mg) was performed in a usual manner (room temperature, 3 h) and subsequent purification by silica-gel column chromatography (20% AcOEt in hexane) gave (−)-3-acetoxycycloheptanol (171 mg, 83%) as a colorless oil. $[\alpha]_D^{21}$ −9.26 (*c* 1.30, $CHCl_3$). Diethyl azodicarboxylate (1.65 g) was added to a mixture of (−)-3-acetoxycycloheptanol (163 mg), triphenylphosphine (1.24 g), and acetic acid (0.38 mL) in THF (5 mL) at 0°C. The whole was stirred for 3 h at room temperature. The reaction mixture was diluted with Et_2O and washed with brine, and then dried over $MgSO_4$. Purification by silica-gel column chromatography gave (−)-**6** (149 mg, 74%) as a colorless oil. $[\alpha]_D^{20}$ −9.21 (c 1.16, $CHCl_3$). IR (neat) 2940, 1730, 1440, 1370, 1235, 1025 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 5.08 (m, 2H), 2.04 (s, 6H), 2.00–1.30 (m, 10H). FDMS *m/z* 215 (M^++1).

Solvolysis of (−)-**6** (73 mg) in MeOH (1 mL) using K_2CO_3 (10 mg) (room temperature, 15 h) and subsequent purification by silica-gel column chromatography (10% hexane in AcOEt) gave (+)-**7** (43.6 mg, 98%) as a colorless oil. $[\alpha]_D^{23}$ +16.0 (*c* 1.64, $CHCl_3$). IR (neat) 3375, 2925, 1450, 1215, 1020 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 4.08 (m, 2H), 3.48 (brs, 2H), 2.00 (t, *J*=5.3 Hz, 2H), 1.94–1.50 (m, 8H). EIMS *m/z* 112 (M^+-H_2O). Usual benzoylation of (+)-**7** (33 mg) using benzoyl chloride in pyridine gave corresponding dibenzoate (+)-**8** (69 mg, 80%) as a colorless oil. $[\alpha]_D^{24}$ +93.1 (*c* 0.59, $CHCl_3$).

IR (neat) 2925, 1710, 1450, 1270, 1110 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.05 (m, 4H), 7.40–7.60 (m, 6H), 5.48 (m, 2H), 2.34 (t, *J*=5.6 Hz, 2H), 2.13 (m, 2H), 1.55–2.00 (m, 6H). CD Δε=+13.6 (232.4 nm, MeOH). EIMS *m/z* 339 (M^++1), 338 (M^+), 216. HRMS for $C_{21}H_{22}O_4$ M^+ 338.1502, found 338.1518.

(1S,3R)-(−)-1-Acetoxy-3-(1-ethoxyethyl)oxy-5-cycloheptene (9)

Pyridinium *p*-toluenesulfonate (100 mg) was added to a stirred solution of ethyl vinyl ether (558 mg, 7.76 mmol) and (−)-**5** (1.10 g, 6.47 mmol) in CH_2Cl_2 (30 mL) at 0°C. After being stirred at room temperature for 2 h, the reaction mixture was diluted with CH_2Cl_2, and washed with brine then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 10% AcOEt in hexane afforded **9** (1.24 g, 79%) as a colorless oil. IR (neat) 2975, 2925, 1720, 1430, 1360, 1230, 1120, 1080, 1010, 940, 840, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 5.77 (m, 2H), 4.73 (ddd, *J*=10.9, 5.8, 5.3 Hz, 1H), 4.64 (m, 1H), 3.63 (m, 1H), 3.48 (m, 2H), 2.33 (m, 5H), 2.03 (s, 3H), 1.82 (m, 1H), 1.29 (d, *J*=5.7 Hz, 1.5H), 1.30 (d, *J*=5.1 Hz, 1.5H), 1.20 (t, *J*=7.1 Hz, 1.5H), 1.19 (t, *J*=7.1 Hz, 1.5H). FABMS *m/z* 243 (M^++1).

*(1R,3S)-3-*tert*-Butyldiphenylsiloxy-5-cyclohepten-1-ol (10)*

A solution of **9** (1.20 g, 4.96 mmol) and K_2CO_3 (208 mg, 1.49 mmol) in MeOH (20 mL) was stirred at room temperature for 3 h. After removal of the solvent, the residue was diluted with brine and extracted with AcOEt. The combined extracts were washed with 2% aqueous HCl, 5% aqueous $NaHCO_3$ and brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was dissolved in DMF (2 mL). This solution was added to a stirred solution of imidazole (328 mg, 4.87 mmol) and TBDPSCl (1.39 g, 4.87 mmol) in DMF (20 mL) at 0°C. After being stirred at room temperature for 2 h, the reaction mixture was diluted with benzene and washed with brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was dissolved in a mixure of acetone (22 mL) and 5% aqueous AcOH (22 mL). After being stirred at room temperature for 2 h, the reaction mixture was diluted with AcOEt, washed with 5% aqueous $NaHCO_3$ and brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 5% AcOEt in hexane afforded **10** (1.2 g, 66%) as a colorless oil. $[\alpha]_D^{23}$ −24.9 (*c* 1.37, $CHCl_3$). IR (neat) 3350, 2940, 1420, 1370, 1240, 1110 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.67 (m, 4H), 7.40 (m, 6H), 5.72 (dt, *J*=10.5, 5.8 Hz, 1H), 5.60 (dt, *J*=10.5, 5.8 Hz, 1H), 3.83 (m, 1H), 3.68 (brs, 1H), 2.56 (brs, 1H), 2.41 (ddd, *J*=14.7, 8.5, 6.1 Hz, 1H), 2.29–2.01 (m, 5H), 1.06 (s, 9H). FABMS *m/z* 367 (M^++1).

*(2RS,4R,6S)-4-*tert*-Butyldiphenylsiloxy-2-hydroxy-6-(2-oxoethyl)-1-oxacyclohexane (11)*

Ozone gas was bubbled into a solution of **10** (300 mg, 1.24 mmol) in CH_2Cl_2 (5 mL) at −78°C until reaction mixture showed blue color continuously. Zn (1 g, 15.30 mmol) and AcOH (5 mL) was added to the reaction mixture at −78°C. The reaction mixture was gradually warmed to room temperature while being stirred. After 3 h, the reaction mixture was diluted with CH_2Cl_2 and filtered. The filtrate was washed with brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 20% AcOEt in hexane afforded **11** (190 mg, 60%) as a colorless oil. $[\alpha]_D^{27}$ −13.9 (*c* 0.93, $CHCl_3$). IR (neat) 3425, 3075, 2925, 2950, 1720, 1420, 1360, 1100, 1040 cm^{-1}. ^1H NMR ($CDCl_3$) δ 9.79 (m, 1H), 7.65 (m, 4H), 7.40 (m, 6H), 5.62 (d, *J*=10.5 Hz, 0.5H), 5.27 (m, 1H), 4.89 (m, 0.5H), 4.59 (m, 0.5H), 4.25 (m, 1.5H), 2.61 (m, 1H), 2.46 (m, 1H), 2.18–1.18 (m, 4H), 1.12 (m, 9H). FABMS *m/z* 381 (M^++1−H_2O).

*(2R,4R,6S)-2-*tert*-Butyldimethylsiloxy-4-*tert*-butyldiphenylsiloxy-6-(2-oxoethyl)-1-oxa-cyclohexane (12)*

A solution of imidazole (67 mg, 0.99 mmol) and TBDMSCl (198 mg, 1.34 mmol) in CH_2Cl_2 (1 mL) was added to the stirred solution of **11** (180 mg, 0.66 mmol) in CH_2Cl_2 (1 mL) at 0°C. After being stirred at room temperature for 15 h, the reaction mixture was diluted with CH_2Cl_2, washed

with brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 4% AcOEt in hexane afforded **12** (162 mg, 70%) as a colorless oil. $[\alpha]_D^{27}$ −8.62 (*c* 0.24, $CHCl_3$). IR (neat) 2950, 1730, 1460, 1430, 1380, 1250, 1160, 1110, 1040 cm^{-1}. ^1H NMR ($CDCl_3$) δ 9.82 (m, 1H), δ 7.65 (m, 4H), 7.38 (m, 6H), 5.31 (m, 1H), 4.54 (m, 1H), 4.24 (m, 1H), 3.52 (m, 1H), 2.58 (m, 1H), 1.73–1.10 (m, 4H), 1.09 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H). FABMS *m/z* 512 (M^+).

*(2R,4R,6R)-2-*tert*-Butyldimethylsiloxy-4-*tert*-butyldiphenylsiloxy-6-(2-hydroxyethyl)-1-oxacyclohexane (13)*

$NaBH_4$ (42.3 mg, 1.12 mmol) was added to the stirred solution of **12** (145 mg, 0.37 mmol) in MeOH (3 mL) at 0°C, and the reaction mixture was stirred at room temperature for 7 h. After addition of acetone (1 mL), the solution was diluted with brine, and extracted with AcOEt. The AcOEt extract was washed with brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 12% AcOEt in hexane afforded **13** (107 mg, 74%) as a colorless oil. $[\alpha]_D^{27}$ +7.85 (*c* 0.83, $CHCl_3$). IR (neat) 3450, 2970, 2850, 1470, 1390, 1250, 1120, 1040 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.64 (m, 4H), 7.38 (m, 6H), 5.30 (dd, *J*=9.4, 2.1 Hz, 1H), 4.26 (t, *J*=2.7 Hz, 1H), 4.16 (m, 1H), 3.33 (m, 2H), 2.34 (m, 1H), 2.04 (m, 2H), 1.86–1.29 (m, 4H), 1.09 (s, 9H), 0.92 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H). FABMS *m/z* 514 (M^+), 457 (M^+−*t*-Bu). HRMS for $C_{29}H_{46}O_4Si_2$ M^+ 514.2949, found 514.2934.

*(2R,4R,6S)-2-*tert*-Butyldimethylsiloxy-4-*tert*-butyldiphenylsiloxy-6-(2-iodoethyl)-1-oxacyclohexane (14)*

A mixture of Ph_3P (134 mg, 0.51 mmol) and I_2 (131 mg, 0.51 mmol) in CH_2Cl_2 (1 mL) was stirred for 1 h at room temperature, to which a solution of **13** (20.0 mg, 0.051 mmol) and pyridine (0.08 mL) in CH_2Cl_2 (0.5 mL) was added dropwise at 0°C. The whole was stirred for 3 h at room temperature. The reaction mixture was diluted with 5% aqueous $Na_2S_2O_3$, and extracted with ether. The ether extract was washed with brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 2% AcOEt in hexane afforded **14** (24.4 mg, 95%) as a colorless oil. $[\alpha]_D^{22}$ +11.2 (*c* 1.20, $CHCl_3$). IR (neat) 2950, 1465, 1425, 1390, 1360, 1250, 1155, 1100, 1040 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.60–7.71 (m, 4H), 7.35–7.46 (m, 6H), 5.30 (dd, *J*=2.1, 9.4 Hz, 1H), 4.26 (m, W_H=7.5 Hz, 1H), 4.22 (tt, *J*=9.0, 2.8 Hz, 1H), 3.80 (m, 2H), 2.46 (m, 1H), 1.30–1.85 (m, 5H), 1.08 (s, 9H), 0.91 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H). FABMS *m/z* 624 (M^+), 567 (M^+−*t*-Bu). HRMS for $C_{29}H_{45}O_3ISi_2$ M^+ 624.1951, found 624.1954.

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8. The second negative Cotton effect was not observed because of the strong positive background.
9. Based on a Dreiding stereomodel examination, the sign of exiton chirality attributable to the two benzoyloxy groups of (+)-**8** did not change among the reasonable conformations, which means that *S,S*-configuration of **8** results the positive exiton chirality. Our result concerning with the absolute configuration of (−)-**5** is agreed with that of Lautans *et al.* (ref. 2b) based on ^{1}H NMR spectra of corresponding Mosher's ester.

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