Supporting Information

Catalytic Asymmetric Synthesis of Both *Syn*- and *Anti*-3,5-Dihydroxy Esters: Application to 1,3-Polyol/ α -Pyrone Natural Product Synthesis

Shin-ya Tosaki, Tetsuhiro Nemoto, Takashi Ohshima, and Masakatsu Shibasaki*

Experimental Procedures, Characterization of the Products and Detailed Experimental Data

General: Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ^1H NMR and 125.65 MHz for ^{13}C NMR. Chemical shifts in CDCl_3 were reported downfield from TMS (= 0 ppm) for ^1H NMR. For ^{13}C NMR, chemical shifts were reported downfield from TMS (= 0 ppm) or in the scale relative to CHCl_3 (77.00 ppm for ^{13}C NMR) as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. EI mass spectra were measured on JEOL JMS-DX303 or JMS-BU20 GCmate. ESI mass spectra were measured on Waters micromass ZQ. The enantiomeric excess (ee) was determined by HPLC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, 880-PU or PU-980; detector, 875-UV or UV-970, measured at 254 nm; column, DAICEL CHIRALPAK AD-H, DAICELCHIRALCEL OJ-H; mobile phase, hexane–2-propanol; flow rate, 1 mL/min. Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise stated. $\text{Ln}(\text{O}-i\text{-Pr})_3$ was purchased from Kojundo Chemical Laboratory Co., LTD., 5-1-28, Chiyoda, Sakado-shi, Saitama 350-0214, Japan (fax: +(81)-492-84-1351). MS 4A (Molecular Sieve UOP type 4A, powder) was purchased from Fluka. Other reagents were purified by the usual methods.

1. Catalytic Asymmetric Synthesis of *Syn*- and *Anti*-3,5-Dihydroxy Esters.

For the known compound **1**, **2**, and **8**, see: *Chem. Pharm. Bull.* **1990**, *38*, 2890. For the known compound **4** and **5**, see: *J. Am. Chem. Soc.* **2001**, *123*, 9474.

General Procedure for the Synthesis of β - Alkyl-Substituted 4-Phenyl Imidazolides.

5-Phenyl-2-pentenoic acid (1.76 g, 10 mmol) was added in small portions to thionyl chloride (2 ml, 27.4 mmol) at room temperature. After being stirred for 30 min, the reaction mixture

was heated to 50 °C and stirred until the evolution of gas was ceased. The mixture was cooled to room temperature and concentrated to give crude acid chloride. To a stirred solution of 4-phenylimidazole (1.51 g, 10.5 mmol) in THF (30 ml) was added *n*-butyllithium (6.62 ml, 10 mmol, 1.51 M solution in hexane) at –78 °C. After being stirred for 40 min, a THF (10 ml) solution of the crude acid chloride was added slowly to the reaction mixture at the same temperature. After 15 min, the reaction was quenched with saturated aqueous NaHCO₃ and extracted with CH₂Cl₂ (2 x 50 ml). The combined organic layers were washed with brine, and dried over MgSO₄. After concentration *in vacuo*, recrystallization of the obtained residue from CH₂Cl₂–Et₂O at room temperature afforded **5** (2.30 g, 76%) as a white solid.

General Procedure for the Catalytic Asymmetric Epoxidation of Carboxylic Acid Imidazoles Using the Pr–BINOL–Ph₃As=O Complex.

To a mixture of (*S*)-BINOL (7.2 mg, 0.025 mmol), triphenylarsine oxide (8.1 mg, 0.025 mmol) and MS 4A (250 mg; MS 4A was not dried (1000 mg/mmol of starting material).) in dry THF (2.5 mL) was added a solution of Pr(O-*i*-Pr)₃ (0.125 mL, 0.025 mmol, 0.2 M solution in THF) at room temperature. After being stirred for 45 min at the same temperature, TBHP (0.12 mL, 0.6 mmol, 5 M solution in decane) was added. After being stirred for 10 min, imidazolid **5** (75.6 mg, 0.25 mmol) was added directly and the mixture was stirred at room temperature. After the starting material was consumed completely, excess MeOH (0.5 mL) was added to the reaction mixture and the resulting mixture was stirred for 3 h, and then quenched by the addition of 2% aqueous citric acid solution at 0 °C. The mixture was extracted with ethyl acetate (2 x 10 mL) and the combined organic layers were washed with 2% aqueous Na₂S₂O₃ and brine, and dried over Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 50:1) to give epoxy ester **4** (51.6 mg, 87%) as a colorless oil. The enantiomeric excess of **4** was determined by chiral stationary-phase HPLC analysis (DAICEL CHIRALPAK AD-H, *i*-PrOH/hexane 2/98, flow rate 1.0 mL/min, *t*_R 8.9 min (2*R*,3*S*)-isomer and 10.3 min (2*S*,3*R*)-isomer, detection at 254 nm); [α]_D²⁵ –34.7 (*c* 0.82, CHCl₃, 86% ee).

General Procedure for the Synthesis of α,β-Unsaturated Amides.

5-Phenyl-2-pentenoic acid (1.76 g, 10 mmol) was added in small portions to thionyl chloride

(2 mL, 27.4 mmol) at room temperature. After being stirred for 30 min, the reaction mixture was heated to 50 °C and stirred until the evolution of gas was ceased. The mixture was cooled to room temperature and concentrated to give crude acid chloride. To a stirred solution of the crude acid chloride in THF (50 mL) was added methylamine (2.44 mL, 33 mmol, 40 wt. % in water) at 0 °C. After being stirred for 2 h at room temperature, the reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (2 x 20 mL) and the combined organic layers were washed with brine, and then dried over Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 3:1 to 2:1) to give **7** (1.882 g, 81% for 2 steps) as a white solid. IR (KBr) ν 3303, 2924, 1668, 1624, 1557, 1498, 1454, 1410, 1353, 1159, 959, 697 cm⁻¹; ¹H NMR (CDCl₃) δ 7.29–7.16 (m, 5H), 6.85 (dt, *J* = 15.3, 7.0 Hz, 1H), 5.76 (dt, *J* = 15.3, 1.1 Hz, 1H), 5.53 (br-s, 1H), 2.85 (d, *J* = 4.9 Hz, 3H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.49 (ddt, *J* = 7.6, 7.0, 1.1 Hz, 2H); ¹³C NMR (CDCl₃) δ 166.5, 143.2, 141.0, 128.4 (x 2), 128.3 (x 2), 126.1, 124.0, 34.6, 33.7, 26.2; ESI-MS *m/z* 212 [M+Na⁺], 189 [M+H⁺].

General Procedure for the Catalytic Asymmetric Epoxidation of α,β -Unsaturated Amides Using the Sm-BINOL-Ph₃As=O Complex.

To a mixture of (*S*)-BINOL (14.3 mg, 0.05 mmol), triphenylarsine oxide (16.1 mg, 0.05 mmol) and MS 4A [500 mg (1000 mg/mmol of starting material); MS 4A was not dried.] in dry THF (5 mL) was added a solution of Sm(O-*i*-Pr)₃ (0.5 mL, 0.05 mmol, 0.1 M solution in THF) at room temperature. After being stirred for 45 min at the same temperature, TBHP (0.12 mL, 0.6 mmol, 5 M solution in decane) was added. After being stirred for 10 min, amide **7** (94.6 mg, 0.5 mmol) was added directly and the mixture was stirred at room temperature. After complete consumption of the starting material (8 h), the reaction mixture was diluted with ethyl acetate and quenched with 2% aqueous citric acid. The water layer was extracted with ethyl acetate (10 mL), the combined organic layers were washed with brine, and dried over Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash chromatography (SiO₂, hexane/ethyl acetate = 4/1 to 3/1) to give epoxy amide **6** (101.9 mg, 99%) as a white yellow solid. IR (KBr) ν 3294, 3124, 1656, 1580, 1450, 1267, 902, 742, 695 cm⁻¹; ¹H NMR (CDCl₃) δ 7.33–7.27 (m, 2H), 7.23–7.19 (m, 3H), 6.09 (br-s, 1H), 3.23 (d, *J* = 2.1 Hz, 1H), 2.96 (ddd, *J* = 6.6, 4.3, 2.1 Hz, 1H), 2.79 (d, *J* = 5.0 Hz, 3H), 2.83–2.73 (m, 2H), 2.06–1.99 (m, 1H), 1.89–1.80 (m, 1H), ; ¹³C NMR (CDCl₃) δ 169.2, 140.7, 128.8 (x 2), 128.6 (x 2), 126.5, 59.2, 55.7, 33.7, 32.0, 25.7; ESI-MS *m/z* 228 [M+Na⁺]. The enantiomeric excess of **6** was determined by chiral stationary-phase HPLC analysis [DAICEL CHIRALPAK AS-H, *i*-PrOH/hexane 1/4, flow rate 0.6 mL/min, *t*_R 26.0 min

((2*S*,3*R*)-isomer) and 35.5 min ((2*R*,3*S*)-isomer), detection at 254 nm]; $[\alpha]_D^{27} +12.2$ (*c* 1.50 CHCl₃, >99% ee).

The Conversion of α,β -Epoxy Methyl Amides to α,β -Epoxy Methyl Ester.

Martin Sulfurane (983 mg, 1.46 mmol) and **7** (100 mg, 0.487 mmol) were combined in a grove box, and then dissolved in dry THF (4.8 mL). After being stirred for 3 h at room temperature, NaOMe (0.334 mL, 1.46 mmol, 25 wt % solution in MeOH) was added to the reaction mixture. After being stirred for 30 min, the reaction was diluted with ethyl acetate and quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (2 x 10 mL) and the combined organic layers were washed with brine, and dried over Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 20:1 to 3:1) to give **4** [65 mg, 65% (conv. 98%)] as a pale yellow oil, with recovery of **7** (34 mg, 34%). The enantiomeric excess of **4** was determined by chiral stationary-phase HPLC analysis (DAICEL CHIRALPAK AD-H, *i*-PrOH/hexane 2/98, flow rate 1.0 mL/min, *t_R* 8.9 min (2*R*,3*S*)-isomer and 10.3 min (2*S*,3*R*)-isomer, detection at 254 nm); $[\alpha]_D^{25} -39.9$ (*c* 0.82, CHCl₃, 99% ee).

Ethyl (4*R*,5*S*)-4,5-epoxy-3-oxo-5-phenethylpentanoate (3): To a stirred solution of ethyl acetate (2.15 mL, 2.15 mmol, 1 M solution in THF) in THF (2.0 mL) was added LHMDS (1.79 mL, 1.79 mmol, 1M solution in THF) at $-78\text{ }^{\circ}\text{C}$. After the mixture was stirred for 15 min, THF solution of **4** (184.9 mg, 0.896 mmol in 3 mL of THF) was added slowly over 5 min at the same temperature. The reaction temperature was gradually warmed up from $-78\text{ }^{\circ}\text{C}$ to $-20\text{ }^{\circ}\text{C}$ in 2 h. The resulting mixture was quenched with saturated aqueous ammonium chloride, diluted with H₂O, and then extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with brine, and dried over Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 30:1 to 20:1) to give **3** (204.1 mg, 87%) as a pale yellow oil. IR (neat) ν 2983, 2932, 1718, 1654, 1454, 1319, 1226, 1030, 701 cm⁻¹; ¹H NMR (CDCl₃) δ 7.32–7.18 (m, 5H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.35 (d, *J* = 16.2 Hz, 1H), 3.31 (d, *J* = 16.2 Hz, 1H), 3.29 (d, *J* = 1.8 Hz, 1H), 3.16 (dt, *J* = 1.8, 5.3 Hz, 1H), 2.86–2.74 (m, 2H), 2.00–1.93 (m, 2H), 1.28 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (CDCl₃) δ 199.9, 166.6, 140.2, 128.6 (x 2), 128.3 (x 2), 126.3, 61.6, 59.6, 57.7,

43.8, 33.4, 31.9, 14.0; EI-MS m/z 262 [M^+]; $[\alpha]_D^{21} +22.4$ (c 0.78, CHCl_3 , 99% ee).

Ethyl (5S)-5-hydroxy-3-oxo-7-phenylheptanoate (8): To a stirred suspension of NaBH_4 (39 mg, 1.03 mmol) in EtOH (0.72 mL) was added PhSeSePh (161.4 mg, 0.517 mmol) at 0 °C, and then the mixture was stirred at room temperature. After 30 min, an EtOH solution of **4** (45.2 mg, 0.172 mmol in 1 mL of EtOH) was added slowly, and the yellow solution was stirred for 30 min. After the starting material was consumed completely, the reaction was diluted with ethyl acetate, washed with brine, and the organic layer was dried over Na_2SO_4 . After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate 4:1) to give **8** (38.5 mg, 85%) as a pale yellow oil. $[\alpha]_D^{23} +9.35$ (c 1.25, CHCl_3 , 99% ee).

Ethyl (3S,5S)-3,5-dihydroxy-7-phenylheptanoate (1): To a stirred solution of **8** (25.2 mg, 0.095 mmol) in THF (0.6 mL) and MeOH (0.15 mL) was added $\text{BEt}_2(\text{OMe})$ (0.104 mL, 0.104 mmol in THF solution) at -78 °C and the mixture was stirred at the same temperature. After 1 h, NaBH_4 (4.5 mg, 0.119 mmol) was added and the reaction was kept stirring for 3 h at -78 °C, then for 1 h at -20 °C. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with brine, and then dried over Na_2SO_4 . After concentration *in vacuo*, the residue was azeotroped a few times with MeOH and the obtained crude residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate 3:1) to give *syn*-3,5-dihydroxy ester **1** [20.0 mg, 79% isolated yield, (*syn:anti* = >20:1)] as a colorless oil. $[\alpha]_D^{22} +4.63$ (c 0.67, CHCl_3 , 99% ee). The enantiomeric excess of **1** was determined after conversion of **1** into the corresponding acetonide-protected compound (dimethoxypropane, cat. TsOH, rt, 98%). Acetonide-protected compound of **1**: IR (neat) ν 2991, 2940, 1737, 1496, 1455, 1380, 1199, 1167, 1028, 700 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.29–7.26 (m, 3H), 7.19–7.17 (m, 2H), 4.29–4.24 (m, 1H), 4.18–4.11 (m, 2H), 3.84–3.78 (m, 1H), 2.74 (ddd, J = 5.2, 9.0, 14.0 Hz, 1H), 2.65 (ddd, J = 8.0, 8.3, 14.0 Hz, 1H), 2.52 (dd, J = 6.9, 15.4 Hz, 1H), 2.36 (dd, J = 6.3, 15.4 Hz, 1H), 1.787–1.79 (m, 1H), 1.72–1.54 (m, 3H), 1.43 (s, 3H), 1.40 (s, 3H), 1.25 (dt, J = 0.6, 7.2 Hz, 3H); ^{13}C NMR (CDCl_3) δ 171.0, 141.9, 128.5 (x 2), 128.3 (x 2), 125.8, 98.8, 67.6, 66.0, 60.4, 41.5, 37.8, 36.5, 31.0, 30.1, 19.7, 14.2; EI-MS m/z 306 [M^+]. The enantiomeric excess of the acetonide-protected compound was determined by chiral stationary-phase HPLC analysis

(DAICEL CHIRALCEL OJ-H, *i*-PrOH/hexane 1/99, flow rate 1.0 mL/min, t_R 14.4 min (3*R*,5*R*)-isomer and 17.7 min (3*S*,5*S*)-isomer, detection at 254 nm); $[\alpha]_D^{23}$ -27.4 (*c* 1.08, CHCl₃, 99% ee).

Ethyl (3*R*,5*S*)-3,5-dihydroxy-7-phenylheptanoate (2): To a stirred solution of tetramethylammonium triacetoxyborohydride (235 mg, 0.906 mmol) in anhydrous acetonitrile (0.5 mL) was added acetic acid (0.5 mL) and the mixture was stirred at room temperature for 30 min. The mixture was cooled to 0 °C, and an acetonitrile solution of **8** (40.0 mg, 0.151 mmol in 0.5 mL of acetonitrile) was added. The mixture was stirred at the same temperature for 3 h. The reaction was quenched with 0.5 N aqueous sodium potassium tartrate and the mixture was diluted with CH₂Cl₂, washed with saturated aqueous Na₂CO₃. The aqueous layer was back extracted with CH₂Cl₂ (4 x 5 mL), and the combined organic layers were washed with saturated aqueous Na₂CO₃. The aqueous layer was back extracted with CH₂Cl₂ (4 x 5 mL), and the combined organic layers were dried with Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 3:1) to give a mixture of *syn*- and *anti*-3,5-dihydroxy ester **1** and **2** [36.3 mg, 89%, (*syn:anti* = 1:9)]. The mixture fraction was purified by preparative thin-layer chromatography and **2** was isolated as a white solid (30.0 mg, 80%). $[\alpha]_D^{21}$ -15.5 [*c* 0.89, CHCl₃ (99% ee)]. The enantiomeric excess of **2** was determined after conversion of **2** into the corresponding acetonide-protected compound (dimethoxypropane, cat. TsOH, rt, 96%). Acetonide-protected compound of **2**: IR (neat) ν 2986, 2937, 1738, 1496, 1455, 1380, 1224, 1187, 1025, 700 cm⁻¹; ¹H NMR (CDCl₃) δ 7.29–7.26 (m, 3H), 7.19–7.16 (m, 2H), 4.29–4.25 (m, 1H), 4.17–4.11 (m, 2H), 3.79–3.75 (m, 1H), 2.77 (ddd, *J* = 5.5, 9.5, 13.8 Hz, 1H), 2.61 (ddd, *J* = 7.2, 8.9, 13.8 Hz, 1H), 2.50 (dd, *J* = 8.3, 15.3 Hz, 1H), 2.41 (dd, *J* = 5.2, 15.3 Hz, 1H), 1.88–1.82 (m, 1H), 1.76–1.59 (m, 3H), 1.38 (s, 3H), 1.33 (s, 3H), 1.25 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (CDCl₃) δ 170.9, 141.9, 128.4 (x 2), 128.3 (x 2), 125.8, 100.6, 65.6, 63.5, 60.4, 40.8, 37.9, 37.4, 31.6, 24.7, 24.6, 14.2; EI-MS *m/z* 306 [*M*⁺]. The enantiomeric excess of the acetonide-protected compound was determined by chiral stationary-phase HPLC analysis (DAICEL CHIRALCEL OJ-H, *i*-PrOH/hexane 2/98, flow rate 1.0 mL/min, t_R 8.7 min (3*R*,5*S*)-isomer and 11.6 min (3*S*,5*R*)-isomer, detection at 254 nm); $[\alpha]_D^{22}$ +17.4 (*c* 0.70, CHCl₃, 99% ee).

2. Catalytic Asymmetric Synthesis of 9a, 9b.

2-1. Catalytic Asymmetric Epoxidation of α,β -Unsaturated Amides 14a and 14b.

The compounds **14a** and **14b** were prepared according to the general procedure for the synthesis of α,β -unsaturated amides. The compounds **13a** and **13b** were prepared according to the general procedure for the catalytic asymmetric epoxidation of α,β -unsaturated amides.

7-Phenyl-hept-2-enoic acid methylamide (14a): white solid; IR (KBr) ν 3301, 3026, 2931, 2855, 1627, 1159, 977, 746, 701 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.29–7.23 (m, 2H), 7.19–7.15 (m, 3H), 6.81 (dt, J = 6.7, 15.3 Hz, 1H), 5.73 (d, J = 15.3 Hz, 1H), 5.51 (br-s, 1H), 2.86 (d, J = 4.0 Hz, 3H), 2.61 (t, J = 7.6 Hz, 2H), 2.21–2.17 (m, 2H), 1.67–1.61 (m, 2H), 1.51–1.46 (m, 2H); ^{13}C NMR (CDCl_3) δ 166.9, 144.4, 142.2, 128.3 (x 2), 128.2 (x 2), 125.7, 123.4, 35.6, 31.8, 30.9, 27.8, 26.2; ESI-MS m/z 240 $[\text{M}+\text{Na}^+]$, 218 $[\text{M}+\text{H}^+]$.

1-Morpholin-4-yl-7-phenyl-hept-2-en-1-one (14b): pale yellow oil; IR (neat) 2926, 2855, 1658, 1620, 1432, 1268, 1230, 1116, 975, 749, 701 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.29–7.26 (m, 2H), 7.19–7.15 (m, 3H), 6.89 (dt, J = 15.0, 7.0 Hz, 1H), 6.17 (d, J = 15.0 Hz, 1H), 3.67–3.39 (m, 8H), 2.62 (t, J = 7.5 Hz, 2H), 2.25–2.21 (m, 2H), 1.68–1.62 (m, 2H), 1.54–1.48 (m, 2H); ^{13}C NMR (CDCl_3) δ 165.6, 146.9, 142.2, 128.3 (x 2), 128.2 (x 2), 125.7, 119.5, 66.8 (x 2), 46.0, 42.2, 36.7, 32.4, 31.0, 27.8; EI-MS m/z 273 $[\text{M}^+]$.

(2S,3R)-3-(4-Phenyl-butyl)-oxirane-2-carboxylic acid methylamide (13a): white solid; IR (KBr) ν 3277, 3107, 3026, 2936, 2853, 1662, 1567, 1451, 1412, 1268, 1162, 893, 749, 697 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.23–7.29 (m, 2H), 7.18–7.15 (m, 3H), 6.11 (br-s, 1H), 3.22 (d, J = 2.1 Hz, 1H), 2.92 (dt, J = 6.0, 2.1 Hz, 1H), 2.79 (d, J = 5.2 Hz, 3H), 2.62 (t, J = 7.3 Hz, 2H), 1.74–1.48 (m, 6H); ^{13}C NMR (CDCl_3) δ 169.2, 142.1, 128.4 (x 2), 128.3 (x 2), 125.8, 59.6, 55.4, 35.7, 31.6, 31.0, 25.4, 25.2; ESI-MS m/z 256 $[\text{M}+\text{Na}^+]$. The enantiomeric excess of **13a** was determined by chiral stationary-phase HPLC analysis [DAICEL CHIRALPAK AS-H, *i*-

PrOH/hexane 1/4, flow rate 1.0 mL/min, t_R 13.5 min (2*S*,3*R*)-isomer and 24.7 min (2*R*,3*S*)-isomer, detection at 254 nm]; $[\alpha]_D^{25} -21.8$ (*c* 1.29 CHCl₃, 99% ee).

1-Morpholin-4-yl-[(2*S*,3*R*)-3-(4-phenyl-butyl)-oxiranyl]-methanone (13b): colorless oil; IR (neat) ν 2928, 2857, 1659, 1465, 1274, 1239, 749, 701 cm⁻¹; ¹H NMR (CDCl₃) δ 7.29–7.26 (m, 2H), 7.19–7.16 (m, 3H), 3.69–3.56 (m, 8H), 3.33 (d, *J* = 2.1 Hz, 1H), 3.15 (ddd, *J* = 6.4, 4.6, 2.1 Hz, 1H), 2.63 (t, *J* = 7.6 Hz, 2H), 1.72–1.48 (m, 6H); ¹³C NMR (CDCl₃) δ 166.1, 142.1, 128.3 (x 2), 128.3 (x 2), 125.8, 66.7 (x 2), 58.2, 53.9, 45.3, 42.3, 35.7, 31.4, 31.0, 25.4; EI-MS *m/z* 289 [M⁺]. The enantiomeric excess of **13b** was determined by chiral stationary-phase HPLC analysis [DAICEL CHIRALPAK AS-H, *i*-PrOH/hexane 1/4, flow rate 1.0 mL/min, t_R 32.3 min (2*S*,3*R*)-isomer and 58.1 min (2*R*,3*S*)-isomer, detection at 254 nm]; $[\alpha]_D^{24} +20.0$ (*c* 0.79 CHCl₃, 99% ee).

2-2. Synthetic Routes towards γ,δ -Epoxy β -Keto Amide 16.

Route A

(2*S*,3*R*)-3-(4-Phenyl-butyl)-oxirane-2-carboxylic acid methyl ester (15): Martin Sulfurane (1020 mg, 1.52 mmol) and **13a** (100 mg, 0.487 mmol) were combined in a grove box, and then dissolved in dry THF (5 mL). After being stirred for 3 h at room temperature, NaOMe (0.347 mL, 1.52 mmol, 25 wt % solution in MeOH) was added to the reaction mixture. After being stirred for 30 min, the reaction was diluted with ethyl acetate and quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (2 x 10 mL) and the combined organic layers were washed with brine, and dried over Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 20:1 to 3:1) to give **15** [84.3 mg, 71% (conv. 97%)] as a pale yellow oil, with recovery of **13a** (31.7 mg, 27%). IR (neat) ν 3025, 2935, 2858, 1755, 1453, 1291, 1250, 1030, 700 cm⁻¹; ¹H NMR (CDCl₃) δ 7.34 (m, 2H), 7.24 (m, 3H), 3.84 (s, 3H), 3.29 (d, *J* = 2 Hz, 1H), 3.22 (ddd, *J* = 6, 5, 2 Hz, 1H), 2.69 (t, *J* = 7.5 Hz, 2H), 1.78–1.55 (m, 6H); ¹³C NMR (CDCl₃) δ 169.7, 142.1, 128.34 (x 2), 128.29 (x 2), 125.8, 58.4, 52.9, 52.4, 35.7, 31.3, 31.0, 25.3; EI-MS *m/z* 234 [M⁺]. The enantiomeric excess of **15** was determined by chiral stationary-phase HPLC analysis [DAICEL CHIRALPAK AD-H, *i*-PrOH/hexane 1/99, flow rate 1.0 mL/min, t_R 12.1 min (2*R*,3*S*)-isomer and 14.0 min (2*S*,3*R*)-

isomer, detection at 254 nm]; $[\alpha]_{\text{D}}^{24} +24.6$ (c 1.68, CHCl_3 , 99% ee). The absolute stereochemistry was determined by Mosher's method after conversion to the corresponding β -hydroxy ester. Detailed data are shown in section 4-4.

γ,δ -Epoxy β -keto amide (16): To a stirred solution of *N*-methoxy-*N*-methylacetamide (0.361 mL, 3.40 mmol) in THF (14 mL) was added LHMDs (3.20 mL, 3.20 mmol, 1.0 M solution in THF) at -78°C . After being stirred for 20 min, a THF solution of **15** (398 mg, 1.70 mmol in 7 mL of THF) was added to the reaction mixture at the same temperature. The reaction was slowly warmed to -30°C over a period of 2 h. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (2 x 10 mL) and the combined organic layers were washed with brine, and dried over Na_2SO_4 . After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate 3:1) to give **16** (464 mg, 89%) as a pale yellow oil. IR (neat) ν 2936, 2858, 1724, 1643, 1454, 1359, 1185, 1009, 749, 701 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.27 (m, 2H), 7.17 (m, 3H), 3.66 (s, 3H), 3.59 (d, $J = 16$ Hz, 1H), 3.41 (d, $J = 16$ Hz, 1H), 3.30 (d, $J = 1.5$ Hz, 1H), 3.20 (s, 3H), 3.15 (m, 1H), 2.62 (t, $J = 7.5$ Hz, 2H) 1.74–1.46 (m, 6H); ^{13}C NMR (CDCl_3) δ 200.9, 167.6, 142.0, 128.34 (x 2), 128.29 (x 2), 125.8, 61.3, 59.6, 58.1, 42.3, 35.6, 32.1, 31.6, 30.9, 25.3; EI-MS m/z 305 [M^+]; $[\alpha]_{\text{D}}^{26} -21.1$ (c 0.87, CHCl_3 , 99% ee).

Route B

γ,δ -Epoxy β -keto amide (16): To a stirred solution of *N*-methoxy-*N*-methylacetamide (28 μL , 0.263 mmol) in THF (0.75 mL) was added LHMDs (0.25 mL, 0.25 mmol, 1.0 M solution in THF) at -78°C . After being stirred for 20 min, a THF solution of **13b** (30.5 mg, 0.105 mmol in 0.4 mL of THF) was added to the reaction mixture at the same temperature. The reaction was slowly warmed to -50°C over a period of 1 h and stirred for 70 h. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (2 x 5 mL) and the combined organic layers were washed with brine, and dried over Na_2SO_4 . After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate 3:1) to give **16** [19.3 mg, 60% (conv. 85%)] as a pale yellow oil, with recovery of **13b** (8.7 mg, 29%).

2-3. Total Synthesis of 9a and 9b.

δ -Hydroxy β -keto amide: To a stirred suspension of NaBH_4 (227 mg, 6.00 mmol) in EtOH (5 mL) was added PhSeSePh (936 mg, 3.00 mmol) at 0 °C. The reaction was allowed to warm to room temperature, and then stirred for 20 min. An EtOH solution of **16** (305 mg, 1.00 mmol in 3 mL of EtOH) was added to the reaction mixture. After being stirred for 10 min, the reaction was diluted with ethyl acetate and poured into water. The aqueous layer was extracted with ethyl acetate (2 x 10 mL) and the combined organic layers were washed with brine, and then dried over Na_2SO_4 . After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate 1:2) to give the corresponding δ -hydroxy β -keto amide (259 mg, 84%) as a pale yellow oil. IR (neat) ν 3429, 2934, 1715, 1650, 1454, 1194, 749, 701 cm^{-1} ; ^1H NMR (CDCl_3): δ 7.28 (m, 2H), 7.18 (m, 3H), 4.08 (m, 1H), 3.68 (s, 3H) 3.61 (s, 2H), 3.22 (s, 3H), 2.72–2.62 (m, 4H), 1.68–1.39 (m, 6H); ^{13}C NMR (CDCl_3): δ 204.8, 167.8, 142.5, 128.3 (x 2), 128.2 (x 2), 125.6, 67.5, 61.4, 49.8, 48.2, 36.3, 35.8, 32.0, 31.3, 25.1; EI-MS m/z 307 [M^+]; $[\alpha]_{\text{D}}^{27}$ –18.8 (c 1.21, CHCl_3 , 99% ee)

Benzyliden acetal of β,δ -hydroxy amide (17b**):** To a stirred solution of δ -hydroxy β -keto amide (69.1 mg, 0.225 mmol) in THF (1.3 mL) and MeOH (0.44 mL) was added $\text{BeEt}_2(\text{OMe})$ (0.45 mL, 0.45 mmol, 1.0 M solution in THF) at –78 °C. After being stirred for 15 min, NaBH_4 (30 mg, 0.79 mmol) was added and stirred for 5 h at the same temperature. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with brine, and then dried over Na_2SO_4 . After concentration *in vacuo*, the residue was azeotroped a few times with MeOH to give crude diol. To a solution of the crude diol in toluene (1.0 mL) was added benzaldehyde dimethyl acetal (0.084 mL, 0.563 mmol) and PPTS (2.8 mg, 0.011 mmol) at room temperature, and then the mixture was allowed to reflux. After being stirred for 10 h, the reaction was diluted with ether and poured into saturated aqueous NaHCO_3 . The aqueous layer was extracted with ether (2 x 5 mL) and the combined organic layers were washed with brine, and then dried over Na_2SO_4 . After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate 5:1) to give **17b** (66.2 mg, 74% in 2 steps) as a yellow oil. IR (neat) ν 2936, 2857, 1661, 1454, 1343, 1120, 1026, 752, 700 cm^{-1}

¹H NMR (CDCl₃) δ 7.48 (m, 2H), 7.36–7.27 (m, 5H), 7.18 (m, 3H), 5.56 (s, 1H), 4.38 (m, 1H), 3.85 (m, 1H) 3.68 (s, 3H), 3.20 (s, 3H), 2.98 (dd, *J* = 17.5, 5.5 Hz, 1H) 2.63 (t, *J* = 7.5 Hz, 2H), 2.55 (dd, *J* = 17.5, 6 Hz, 1H), 1.81–1.40 (m, 8H); ¹³C NMR (CDCl₃) δ 171.4, 142.6, 138.7, 128.5 (x 2), 128.4 (x 2), 128.2 (x 2), 128.1 (x 2), 126.1, 125.6, 100.6, 76.6, 73.5, 61.4, 38.2, 37.0, 35.8, 35.7, 32.0, 31.4, 24.7; EI-MS *m/z* 397 [*M*⁺]. The enantiomeric excess of **17b** was determined by chiral stationary-phase HPLC analysis (DAICEL CHIRALPAK AD-H, *i*-PrOH/hexane 1/9, flow rate 1.0 mL/min, *t_R* 7.9 min (3*S*, 5*S*)-isomer and 10.0 min (3*R*, 5*R*)-isomer, detection at 254 nm); [α]_D²⁷ +21.8 (*c* 0.92, CHCl₃, 99% ee).

Homoallylketone (11b): To a stirred solution of **17b** (77.9 mg, 0.196 mmol) in THF (1.6 mL) was added allylmagnesium bromide (0.39 mL, 0.39 mmol, 1M solution in Et₂O) at 0 °C. After being stirred for 30 min at the same temperature, the reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (2 x 4 mL) and the combined organic layers were washed with brine, and then dried over Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 20:1) to give **11b** (64.2 mg, 87%) as a colorless oil. IR (neat) ν 2934, 2857, 1715, 1454, 1346, 1128, 1026, 921, 752, 699 cm⁻¹; ¹H NMR (CDCl₃) δ 7.45 (m, 2H), 7.37–7.29 (m, 5H), 7.18 (m, 3H), 5.92 (ddt, 17.5, 10.5, 7 Hz, 1H), 5.53 (s, 1H), 5.20 (dd, *J* = 10.5, 1.5 Hz, 1H), 5.14 (dd, *J* = 17.5, 1.5 Hz, 1H), 4.32 (m, 1H), 3.83 (m, 1H), 3.24 (ddd, *J* = 7, 1.5, 1.5 Hz, 2H), 2.89 (dd, *J* = 16, 6.5 Hz, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.57 (dd, *J* = 16, 6 Hz, 1H), 1.72–1.35 (m, 8H); ¹³C NMR (CDCl₃) δ 206.4, 142.5, 138.5, 130.1, 128.6 (x 2), 128.4 (x 2), 128.2 (x 2), 128.1 (x 2), 126.0, 125.6, 119.1, 100.5, 76.6, 73.0, 48.8, 48.2, 36.7, 35.8, 35.6, 31.4, 24.6; EI-MS *m/z* 378 [*M*⁺]; [α]_D³⁰ –2.1 (*c* 1.36, CHCl₃, 99% ee)

Homoallyl alcohol (18b): To a stirred solution of **11b** (22.2 mg, 0.0586 mmol) in THF (0.6 mL) was added L-Selectride (0.117 mL, 0.117 mmol, 1.0 M solution in THF) at –100 °C. After being stirred for 2 h at the same temperature, the reaction was quenched with H₂O₂ (30 wt. % solution in water) and 1 M NaOH. The mixture was allowed to warm to room temperature and diluted with ether. The aqueous layer was extracted with ether (2 x 3 mL) and the combined organic layers were washed with 2% aqueous Na₂S₂O₃, brine, and then dried

over Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 10:1) to give **18b** [13.3 mg, 60% (conv. 97%), inseparable mixture of *syn,syn*- and *syn,anti*-diastereomer (7:1)] as a colorless oil.

IR (neat) ν 3522, 2935, 2857, 1454, 1342, 1104, 1026, 914, 752, 698 cm⁻¹; ¹H NMR (CDCl₃) *syn,syn*-diastereomer: δ 7.46 (m, 2H), 7.36–7.27 (m, 5H), 7.18 (m, 3H), 5.84 (ddt, *J* = 17.5, 10.5, 7 Hz), 5.55 (s, 1H), 5.12 (m, 2H), 4.08 (m, 1H), 3.97 (m, 1H), 3.82 (m, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.26 (m, 2H), 1.80–1.43 (m, 10H); ¹³C NMR (CDCl₃) *syn,syn*-diastereomer: δ 142.5, 138.3, 134.7, 128.7 (x 2), 128.4 (x 2), 128.3 (x 2), 128.2 (x 2), 126.0, 125.6, 117.6, 100.6, 77.3, 76.8, 70.4, 42.0, 37.1, 35.8, 35.6, 31.4, 24.6; EI-MS *m/z* 380 [M⁺]; [α]_D²³ –0.93 (c 1.40, CHCl₃, 99% ee, 7 : 1 mixture of *syn,syn*- and *syn,anti*-diastereomer)

Acryloyl ester (19): To a stirred solution of **18b** (21.1 mg, 0.0554 mmol) in CH₂Cl₂ (0.55 mL) was added acryloyl chloride (9.0 μ L, 0.11 mmol) and *i*-Pr₂NEt (20 mL, 0.115 mmol) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 3 h. The reaction was diluted with ether and poured into saturated aqueous NaHCO₃. The aqueous layer was extracted with ether and the combined organic layers were washed with brine, and then dried over Na₂SO₄. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 25:1) to give **19** (21.8 mg, 91%, inseparable mixture of *syn,syn*- and *syn,anti*-diastereomer) as a colorless oil. IR (neat) ν 2934, 2857, 1721, 1404, 1194, 1026, 699 cm⁻¹; ¹H NMR (CDCl₃) *syn,syn*-diastereomer: δ 7.40 (m, 2H), 7.28–7.18 (m, 5H), 7.10 (m, 3H), 6.30 (dd, *J* = 17.5, 1.5 Hz, 1H), 6.01 (dd, *J* = 17.5, 10.5 Hz, 1H), 5.73 (dd, *J* = 10.5, 1.5 Hz, 1H), 5.70 (ddt, *J* = 17.5, 10.5, 7 Hz, 1H), 5.40 (s, 1H), 5.14 (m, 1H), 5.02 (m, 2H), 3.83 (m, 1H), 3.70 (m, 1H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.00 (m, 1H), 1.70 (m, 1H), 1.63–1.29 (m, 8H); ¹³C NMR (CDCl₃) *syn,syn*-diastereomer: δ 165.7, 142.6, 138.7, 133.2, 130.7, 128.6 (x 2), 128.5, 128.4 (x 2), 128.2 (x 2), 128.1 (x 2), 126.1, 125.6, 118.2, 100.6, 76.6, 74.0, 70.4, 39.8, 38.9, 36.8, 35.8, 35.7, 31.4, 24.7; EI-MS *m/z* 434 [M⁺]; [α]_D²³ +4.6 (c 1.09, CHCl₃, 99% ee, mixture of *syn,syn*- and *syn,anti*-diastereomer)

α,β -Unsaturated lactone (20): **19** (19.9 mg, 0.0458 mmol) was dissolved in 6.5 mL of CH₂Cl₂. After degassing, Grubbs' catalyst (1.5 mg, 1.8 μ mol) was added to the mixture at

room temperature. The reaction was allowed to reflux for 9 h. After the solvent being removed, the obtained residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate 4:1) to give **20** (15.7 mg, 84%, separable mixture of *syn,syn*- and *syn,anti*-diastereomer) as a colorless oil. *syn,syn*-diastereomer: IR (neat) ν 2929, 2857, 1730, 1245, 1119, 1026, 699 cm⁻¹; ¹H NMR (CDCl₃) δ 7.46 (m, 2H), 7.38–7.24 (m, 5H), 7.18 (m, 3H), 6.90 (m, 1H), 6.04 (dd, J = 10, 1.5 Hz, 1H), 5.52 (s, 1H), 4.68 (m, 1H), 4.16 (m, 1H), 3.83 (m, 1H), 2.63 (t, J = 7.5 Hz, 2H), 2.55–2.39 (m, 2H), 2.22 (m, 1H), 1.92 (m, 1H), 1.73–1.43 (m, 8H); ¹³C NMR (CDCl₃) δ 164.3, 145.3, 142.5, 138.6, 128.6 (x 2), 128.4 (x 2), 128.2 (x 2), 128.1 (x 2), 126.0, 125.6, 121.2, 100.5, 77.2, 74.6, 72.5, 40.3, 36.5, 35.8, 35.7, 31.4, 29.3, 24.7; EI-MS m/z 406 [M⁺]; [α]_D²⁷ –47.6 (c 1.21, CHCl₃, 99% ee).

9a and 9b: **20** (9.0 mg, 0.022 mmol) was dissolved in 0.5 mL of an 80 % solution of AcOH and the solution was heated to 60 °C. After being stirred for 5 h, the reaction was diluted with ethyl acetate and then poured into saturated aqueous NaHCO₃. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with brine, and then dried over Na₂SO₄. After concentration *in vacuo*, crude diol was obtained. To a stirred solution of the crude diol in CH₂Cl₂ (0.2 mL) was added triethyl orthoacetate (10 μ L, 0.055 mmol) and PPTS (0.5 mg, 2 μ mol) at room temperature. After the reaction being stirred until all of the starting material was consumed (1 h), water (1 μ L) was added to the reaction and the mixture was stirred for 1 h. The reaction mixture was directly purified by flash column chromatography (SiO₂, hexane/ethyl acetate 1:1) to give **9a** and **9b** (6.0 mg, 76% in 2 steps) as a yellow oil. **Migration of an acetyl group between 9a and 9b takes place easily. Thus, the ratio of obtained 9a and 9b was not determined.** IR (neat) ν 3453, 2933, 1730, 1375, 1246, 1035 cm⁻¹; ¹H NMR (CDCl₃) **9a**: δ 7.27 (m, 2H), 7.18 (m, 3H), 6.89 (m, 1H), 6.02 (d, J = 9.5 Hz, 1H), 4.95 (m, 1H), 4.65 (m, 1H), 3.89 (m, 1H), 2.61 (t, J = 7.5 Hz, 2H), 2.41 (m, 2H), 2.20–1.31 (m, 10H), 2.04 (s, 3H); ¹H NMR (CDCl₃) **9b**: δ 7.27 (m, 2H), 7.18 (m, 3H), 6.89 (m, 1H), 6.02 (d, J = 9.5 Hz, 1H), 5.23 (m, 1H), 4.51 (m, 1H), 3.70 (m, 1H), 2.62 (t, J = 7.5 Hz, 2H), 2.42–2.22 (m, 2H), 2.20–1.31 (m, 10H), 2.06 (s, 3H); ¹³C NMR (CDCl₃) **9a**: δ 171.3, 163.8, 145.2, 142.3, 128.4 (x 2), 128.3 (x 2), 125.7, 121.3, 76.7, 72.4, 67.1, 42.3, 41.7, 35.7, 34.6, 31.1, 29.4, 24.8, 21.3; ¹³C NMR (CDCl₃) **9b**: 171.3, 163.8, 144.7, 142.3, 128.4 (x 2), 128.3 (x 2), 125.7, 121.4, 75.1, 69.2, 69.0, 41.7, 39.3, 37.7, 35.8, 31.3, 29.2, 25.0, 21.3; EI-MS m/z 360 [M⁺]; [α]_D²⁶ –29.7 (c 0.60, MeOH, 99% ee) for a mixture of synthetic **9a** and **9b** ; lit. (ref 17) [α]_D +35 (c 0.05, MeOH) for **9a** and [α]_D +35 (c 0.05, MeOH) for **9b**.

Diacetate (21): To a stirred solution of a mixture of **9a** and **9b** (2.4 mg, 6.7 μmol) in pyridine (0.1 mL) was added Ac_2O (2.5 μL , 0.027 mmol) and catalytic amount of DMAP. After being stirred for 30 min, the reaction mixture was diluted with ethyl acetate and the solution was quenched with saturated aqueous NaHCO_3 . The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with 1N HCl, brine, and then dried over Na_2SO_4 . After concentration *in vacuo*, the residue was purified by preparative thin-layer chromatography (SiO_2 , hexane/ethyl acetate 1:2) to give **21** (2.4 mg, 89%) as a yellow oil. IR (neat) ν 2931, 1730, 1372, 1240, 1038 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.27 (m, 2H), 7.18 (m, 3H), 6.88 (m, 1H), 6.01 (dd, $J = 9.75$, 2 Hz, 1H), 5.04 (m, 1H), 4.93 (m, 1H), 4.48 (m, 1H), 2.60 (t, $J = 7.5$ Hz, 2H), 2.45–2.27 (m, 2H), 2.06 (s, 3H), 2.04 (s, 3H), 2.16–1.78 (m, 4H), 1.62 (m, 4H), 1.34 (m, 2H); ^{13}C NMR (CDCl_3) δ 170.8, 170.7, 163.8, 144.7, 142.3, 128.4 (x 2), 128.3 (x 2), 125.7, 121.4, 74.9, 70.8, 67.9, 39.0, 39.0, 35.7, 34.1, 31.1, 29.1, 24.7, 21.2, 21.2; EI-MS m/z 402 [M^+].

In confirmation of the stereochemistry, minor isomer of **20** was also converted to the corresponding diacetate by the same procedure.

IR (neat) ν 2930, 2857, 1724, 1248, 1120, 1026, 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.46 (m, 2H), 7.37–7.27 (m, 5H), 7.19 (m, 3H), 6.88 (ddd, $J = 10$, 5.5, 3 Hz, 1H), 6.03 (dd, $J = 10$, 1.5 Hz, 1H), 5.50 (s, 1H), 4.80 (m, 1H), 4.23 (m, 1H), 3.82 (m, 1H), 2.63 (t, $J = 7.5$ Hz, 2H), 2.36 (m, 2H), 1.94 (m, 1H), 1.86 (m, 1H), 1.73–1.37 (m, 8H); ^{13}C NMR (CDCl_3) δ 164.4, 145.1, 142.6, 138.7, 128.6 (x 2), 128.4 (x 2), 128.3 (x 2), 128.2 (x 2), 126.1, 125.6, 121.4, 100.4, 76.7, 74.0, 72.0, 41.6, 37.2, 35.8, 35.7, 31.4, 30.0, 24.7; EI-MS m/z 406 [M^+]; $[\alpha]_{\text{D}}^{27} -2.1$ (c 0.28, CHCl_3 , 99% ee)

IR (neat) ν 2931, 1731, 1373, 1240, 1023 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.27 (m, 2H), 7.19 (m, 3H), 6.85 (ddd, $J = 10$, 5.5, 3 Hz, 1H), 6.02 (dd, $J = 10$, 1.5 Hz, 1H), 5.14 (m, 1H), 4.92 (m,

1H), 4.48 (m, 1H), 2.60 (t, $J = 7.5$ Hz, 2H), 2.35–2.31 (m, 2H), 2.10–1.78 (m, 4H), 2.04 (s, 3H), 2.04 (s, 3H), 1.60 (m, 4H), 1.32 (m, 2H); ^{13}C NMR (CDCl_3) δ 170.8, 170.3, 163.6, 144.5, 142.3, 128.4 (x 2), 128.3 (x 2), 125.7, 121.6, 74.5, 70.7, 68.0, 39.4, 38.8, 35.7, 34.0, 31.1, 29.6, 24.7, 21.2, 21.2; MS m/z 402 [M^+].

3. Catalytic Asymmetric Synthesis of the Intermediate for Use in Aimi's Total Synthesis of Strictifolione 10.

2-([4R,6S]-2,2-Dimethyl-6-phenethyl-[1,3]dioxan-4-yl)-ethanol (22): To a stirred solution of **2** (22.8 mg, 0.086 mmol) in dimethoxypropane (0.6 mL) was added TsOH (1.6 mg, 0.008 mmol) at room temperature. After 2 h, the reaction was diluted with ethyl acetate (10 mL). The solution was washed with saturated aqueous NaHCO_3 and brine, and then dried over Na_2SO_4 . After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate 30:1) to give the corresponding acetonide-protected compound (25.2 mg, 96%). To a suspension of lithium aluminum hydride (6.6 mg, 0.175 mmol) in THF (0.3 mL) was added a THF solution of the acetonide-protected compound (22.4 mg, 0.073 mmol in 0.7 mL of THF) at 0 °C. After being stirred for 1 h, the reaction was quenched with excess MeOH, and diluted with ethyl acetate. The mixture was washed with 0.1N aqueous HCl, saturated aqueous NaHCO_3 , brine, and then dried over Na_2SO_4 . After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate 2:1) to give alcohol **22** as a colorless oil (18.6 mg, 96%). $[\alpha]_{\text{D}}^{23} +23.1$ (c 1.07, CHCl_3 , 99% ee). lit. (ref. 22); $[\alpha]_{\text{D}}^{25} +24.9$ (c 1.70, CHCl_3).

4. Detailed Experimental Data

4-1. Examination of Catalytic Asymmetric Epoxidation of Imidazolid

entry	Ln	time (h)	yield (%)	ee (%)
1	La	1.5	86	83
2	Pr	1.5	87	85
3*	Pr	4	82	86
4	Sm	6	81	79
5	Gd	3	81	67
6	Dy	3	79	77
7	Yb	20	78	68

*entry 3: (S)-Pr-BINOL-Ph₃P=O complex (1:1:3) (10 mol%) was used.

entry	Ln	time (h)	yield (%)	ee (%)
1	La	1	93	79
2	Pr	1.5	88	86
3*	Pr	7	92	88
4	Sm	5	88	65
5	Gd	8	84	49
6	Dy	2	85	76
7	Yb	18	71	56

*entry 3: (S)-Pr-BINOL-Ph₃P=O complex (1:1:3) (10 mol%) was used.

4-2. Examination of Reductive Epoxide Opening Reaction

entry	condition	yield of 8	yield of S1
1	SmI ₂ (2 eq), THF-MeOH, -78 °C ^{S1}	ca. 30%	-
2	SmI ₂ (2 eq), Me ₂ NCH ₂ CH ₂ OH (2 eq), HMPA (5 eq), THF, rt ^{S2}	52%	30%
3	Cp ₂ TiCl (2.5 eq), THF-MeOH, -78 °C to 0 °C ^{S3}	66%	10%
4	PhSeSePh (3 eq), NaBH ₄ (6 eq), EtOH, rt ^{S3}	85%	-

S1) Molander, G. A.; Hahn, G. *J. Org. Chem.* **1986**, 51, 2596.

S2) Otsubo, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, 28, 4437.

S3) Hardouin, C.; Chevallier, F.; Rousseau, B.; Doris, E. *J. Org. Chem.* **2001**, 66, 1046.

4-3. Examination of Diastereoselective Reduction of β,γ-Unsaturated Ketone 11a and 11b

entry	condition	yield	syn:anti
1	NaBH ₄ , MeOH, 0 °C	ca. 80%	1.5:1
2	L-Selectride, THF, -78 °C		2:1
3	TiCl ₄ (2.0 eq), NaBH ₃ CN (3.5 eq), CH ₂ Cl ₂ -THF, -78 °C	70%	3:1

entry	condition	yield (conv.)	syn:anti
1	L-Selectride, THF, -78 °C		4:1
2	L-Selectride, THF, -100 °C	60% (97%)	7:1
3	TiCl ₄ (2.0 eq), NaBH ₃ CN (3.5 eq), CH ₂ Cl ₂ -THF, -78 °C	80%	4:1
3	TiCl ₄ (2.0 eq), NaBH ₃ CN (3.5 eq), CH ₂ Cl ₂ -THF, -100 °C	ca. 75%	2:1

4-4. Determination of the Absolute Stereochemistry of **15** by Mosher's Method

The absolute stereochemistry of **15** was determined to be 2*S*,3*R*.