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Note

Syntheses of Highly Oxygen-functionalized Derivatives of Dihydrodihydroxyphthalic Acid in Enantiomerically Enriched Forms

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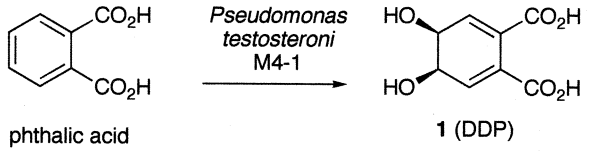
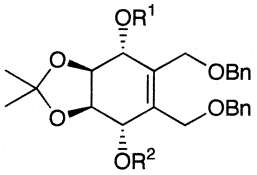
Starting from dihydrodihydroxyphthalic acid (DDP), (1*R*, 2*S*, 5*R*, 6*S*)-(-)-3,4-bis(benzyloxymethyl)-5-hydroxy-8,8-dimethyl-6,8-dioxabicyclo[4.3.0]non-3-en-2-yl chloroacetate (>95%*e.e.*), a highly oxygen-functionalized derivative, was prepared by a combination of chemical and enzymatic reactions. The key step for asymmetrization was hydrolysis of the corresponding meso bis-chloroacetate with pig pancreatic lipase.

Key words: dihydrodihydroxyphthalic acid; photooxygenation; pig pancreatic lipase; meso substrate; hydrolysis

Omori and co-workers have reported the production of 4,5-dihydro-4,5-dihydroxyphthalic acid (DDP, **1**) from phthalic acid by microbial dihydroxylation with *Pseudomonas testosteroni* M4-1 (scheme **1**).[1] Their extensive study on the incubation conditions with a mutant strain enabled the accumulation of **1** (10 g/l) in the broth, starting from phthalic acid (8.3 g/l). Microbial dihydroxylation is an elaborate process for preparing enantiomerically enriched forms of poly-hydroxylated compounds which have been utilized as intermediates in natural product syntheses.[2,3] However, the utilization of DDP itself has so far been very limited, due to its instability under various conditions for the conversion of its functional groups.[4] In this paper, we describe the preparation of some new derivatives starting from **1**. One of our eventual goals is a highly oxygenated cyclohexene in an enantiomerically enriched form (**2**, scheme **1**).



phthalic acid — **1** (DDP)



2

Scheme 1

The first attempt was the esterification of **3a**, which had never been achieved by conventional methods such as acid-catalyzed esterification or treatment with diazomethane.[4] This problem was solved by using the reaction between the corresponding cesium salt[5] and methyl iodide; adjusting the pH value (*ca.* 11) at the step of salt formation by adding an excess amount of cesium carbonate was essential to obtain a high yield (93%) of **3b**. The reduction of two unsaturated ester groups of **3b** to diol **4a** conld only be achieved (36%) by diisobutylaluminum hydride in a mixture of dichloromethane-toluene (2:1). Any attempt by using other conventional reductants (or direct reduction of **3a**) resulted in the production of a complex mixture. Diol **4a** was protected as dibenzyl ether to give **4b** (76%). Photooxygenation in the presence of tetraphenylporphyrin (TPP)[6] and then

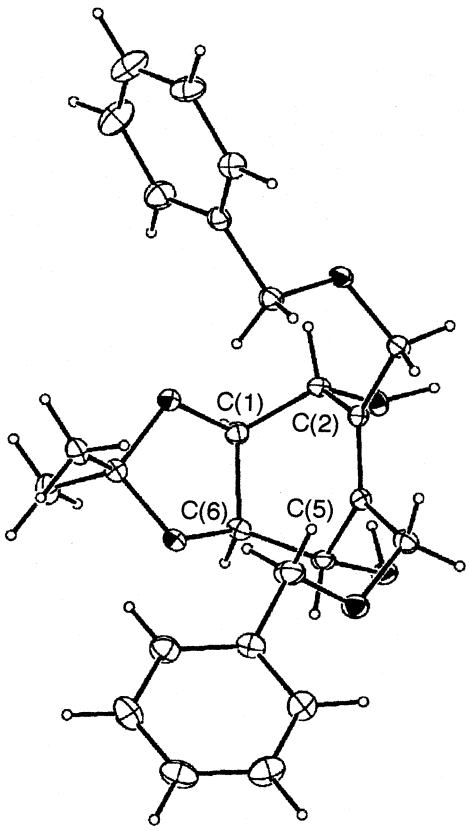


Fig. 1. Molecular Structure of **2a**.

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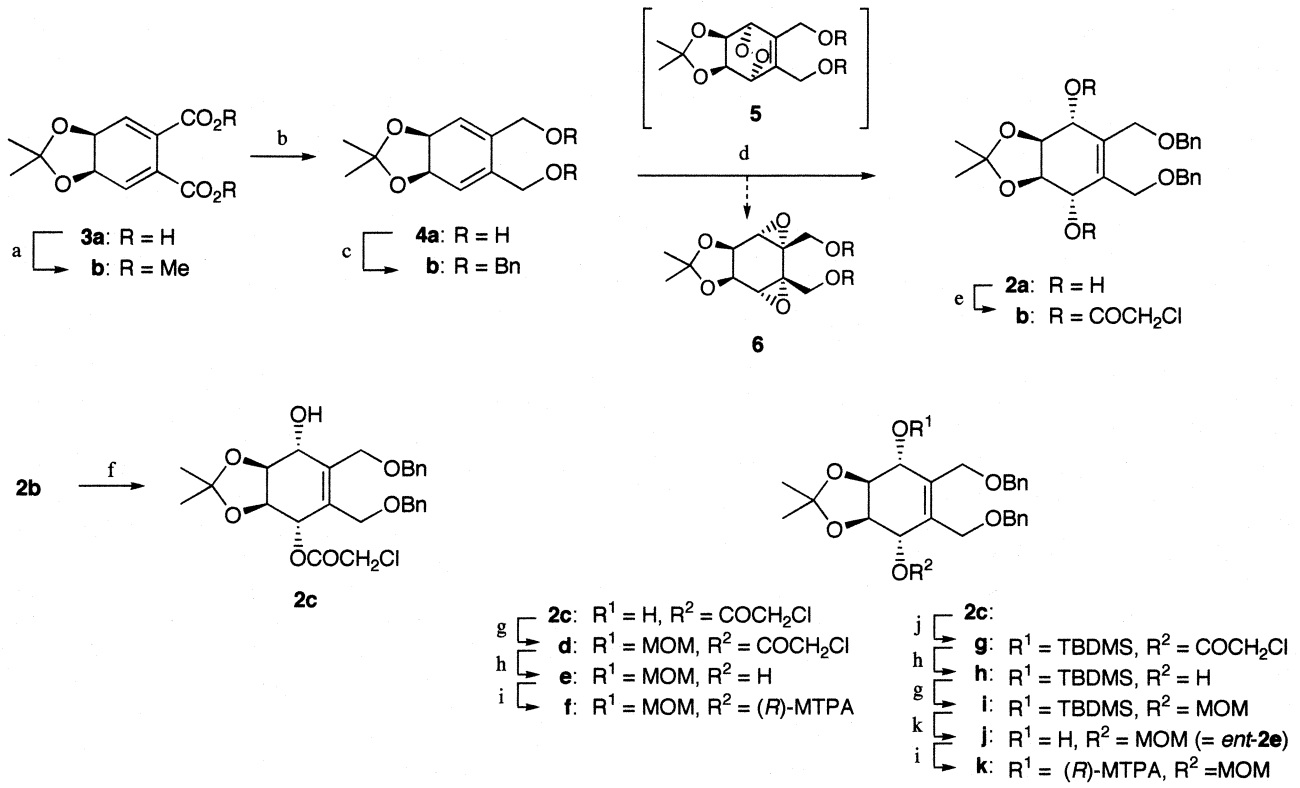

Scheme 2 a: Cs_2CO_3, MeI/DMF (93%); b: DIBAL-H/CH_2Cl_2-toluene (36%); c: NaH, benzyl bromide, TBAI/THF (76%); d: hν, O_2, TPP/CCl_4, then thiourea/MeOH (68%); e: $(ClCH_2CO)_2O$, DMAP/pyridine (96%); f: porcine pancreatic lipase/phosphate buffer-DMF (45%); g: MOMCl, *i*-Pr_2EtN/CH_2Cl_2; h: K_2CO_3/MeOH (83% of **2e** from **2c**); i: MTPA-Cl [from (*R*)-acid]/pyridine; j: TBDMS-Cl, imidazole/DMF; k: TBAF/THF (52% of **2j** from **2c**).

immediate reduction of the corresponding endoperoxide **5** with thiourea afforded diol **2a** (68%, scheme 2). It was necessary to stop the photooxygenation within 10 min due to the instability of **5**, as a more prolonged reaction caused the formation of diepoxide **6**.[cf.6] The orientation of the newly introduced dihydroxyl group was unambigiously determined by an X-ray analysis as depicted in Fig. 1.

Asymmetrization[3] of *meso*-form **2a** was realized by the pig pancreatic lipase-catalyzed hydrolysis of corresponding bis-chloroacetate **2b** (scheme 2). Product **2c** could successfully be converted to both the enantiomers of methoxymethyl ether **2e** and **2j** *via* **2d** and **2g-2i**, respectively.

The absolute configuration based on the modified Mosher method[7] of **2c** as illustrated in scheme 2 was elucidated by comparing the ^{1}H-NMR spectra of (*R*)-MTPA esters **2f** and **2k**. The upfield shift of the signals (geminal dimethyl protons on acetonide and the proton at the C-1 position, circled in Fig. 2) of (*R*)-MTPA ester **2f** over **2k** consistently indicates the (1*R*, 2*S*, 5*R*, 6*S*)-absolute configuration of (−)-**2c**. The stereochemical outcome of the lipase-catalyzed hydrolysis agrees well with those observed previously with analogous substrates.[3] The enantiomeric excess (>95%) of **2e** and **2j** could also be evaluated from the ^{1}H-NMR spectra of the (*R*)-MTPA esters.

In conclusion, we have disclosed a new synthetic application of DDP (**1**) by establishing a chemo-enzymatic pathway.

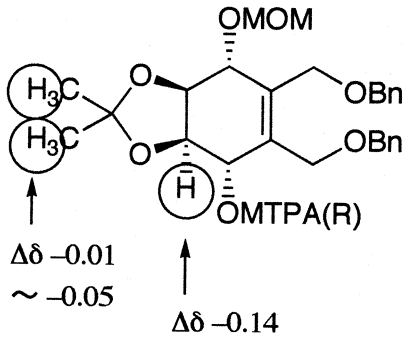

Fig. 2. Determination of the Absolute Configuration of **2c**: $\Delta\delta = \delta H(\mathbf{2f}) - \delta H(\mathbf{2k})$.

Experimental

Dimethyl (1R, 6S*)-8,8-dimethyl-7,9-dioxabicyclo [4.3.0]nona-2,4-diene-3,4-dicarboxylate* (**3b**). Free carboxylic acid **3a**[4] was firstly isolated in a crystalline state, mp 181.2–182.0°C; IR ν_{max} cm^{-1}: 3000, 2930, 2650, 2550, 1710, 1640, 1450, 1380, 1300, 1260, 1220, 1160, 1070, 1040, 905, 860, 790; ^{1}H-NMR (DMSO-d_6) δ: 1.28 (3H, s), 1.32 (3H, s), 4.79 (2H, dd, J=1.5, 1.5 Hz), 6.45 (2H, dd, J=1.5, 2.4 Hz); ^{13}C-NMR (DMSO-d_6) δ 24.59, 26.47, 69.26, 105.30, 129.11. 130.69, 167.40. *Anal.* Found: C, 55.12; H, 5.18%. Calcd. for $C_{11}H_{12}O_6$: C, 55.00; H, 5.04%). To a stirred solution of **3a** (1.14 g,

4.75 mmol) in water (10 ml), cesium carbonate (3.10 g, 9.51 mmol) was added until the pH of the solution reached 11, and the resulting mixture was lyophilized. The residual solid was finely powdered and suspended in dry DMF (50 ml). To this was added methyl iodide (6.74 g, 47.5 mmol), and the mixture was stirred for 16 hr at room temperature. The mixture was quenched by adding a 10% aqueous $Na_2S_2O_3$ solution and extracted with ether. The organic solution was successively washed with water and brine, and dried over Na_2SO_4. The solvent was removed to give **3b** as a solid (1.19 g, 93%), IR ν_{max} cm^{-1}: 3000, 2950, 2650, 2550, 1730, 1650, 1440, 1250, 1160, 1060, 1040, 970, 950, 890, 850, 810, 760; ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, s), 1.32 (3H, s), 4.79 (2H, dd, J=1.5, 1.5 Hz), 6.45 (2H, dd, J=1.5, 2.4 Hz); MS m/z (%): 252 (8), 236 (32), 220 (50), 209 (83), 192 (72), 178 (100), 166 (74), 150 (87), 134 (25), 121 (25), 108 (18), 92 (22), 77 (26), 59 (38), 43 (55). This was employed in the next step without further purification.

(1R,6S*)-8,8-Dimethyl-7,9-dioxabicyclo[4.3.0]nona-2,4-diene-3,4-dimethanol (***4a***).* To a solution of **3b** (1.08 g, 4.03 mmol) in CH_2Cl_2 (36 ml), a 1.01 M solution of DIBAL-H in toluene (18 ml) was added over 20 min at −78°C, and the mixture was stirred for 30 min at this temperature. The mixture was quenched by slowly adding a phosphate buffer solution (0.5 M, pH 7.5, 5 ml), allowed to warm to room temperature, and further stirred for 2 hr. The mixture was concentrated *in vacuo*, and the resulting residue was washed with a mixture of ethyl acetate-ethanol (5:1). The solvent was removed *in vacuo*, and the residue was purified by silica gel flash column chromatography (3 g). Elution with hexane-ethyl acetate (3:1) afforded crude diol **4a** (308 mg, 36%) as an oil, IR ν_{max} cm^{-1}: 3420, 3000, 2950, 2900, 1730, 1690, 1450, 1380, 1210, 1170, 1040, 870; ^{1}H-NMR ($CDCl_3$) δ: 1.39 (3H, s), 1.40 (3H, s), 3.04 (^{1}H, br, s), 4.23 (2H, d, J=12.7 Hz), 4.36 (2H, d, J=12.7 Hz), 4.67 (2H, dd, J=1.4, 1.9 Hz), 5.94 (2H, d, J=1.4 Hz). This was employed in the next step without further purification, because of its instability.

(1R, 6S*)-8,8-Dimethyl-3,4-bis(benzyloxymethyl)-7,9-dioxabicyclo[4.3.0]nona-2,4-diene (***4b***).* To a suspension of sodium hydride (125 mg, 60% in mineral oil, 3.2 mmol) in dry tetrahydrofuran (10 ml) at 0°C were added **4a** (320 mg, 1.51 mmol), benzyl bromide (684 mg, 4.00 mmol) and tetrabutylammonium iodide (150 mg, 0.406 mmol), and the mixture was stirred at room temperature for 30 min. Stirring was continued at 40°C for 4 hr. After cooling, the mixture was quenched by adding a saturated aqueous NH_4Cl solution and extracted with ether. After the solvent had been removed, the residue was purified by silica gel column chromatography (10 g). Elution with toluene-ethyl acetate (2:1) afforded **4b** (450 mg, 76%) as a yellow oil, IR ν_{max} cm^{-1}: 3000, 2950, 2870, 1500, 1380, 1370, 1240, 1210, 1070, 1030, 870, 740, 700; ^{1}H-NMR ($CDCl_3$) δ: 1.37 (3H, s), 1.40 (3H, s), 4.16 (2H, d, J=12.4 Hz), 4.21 (2H, d, J=12.4 Hz), 4.48 (4H, s), 4.68 (2H, d, J=1.5 Hz), 5.98 (2H, dd, J=1.5, 2.4 Hz), 7.27–7.35 (10H, m, aromatic). This was employed in the next step without further purification due to its highly unstable nature.

(1R, 2S*, 5R*, 6S*)-3,4-Bis(benzyloxymethyl)-8,8-dimethyl-7,9-dioxabicyclo[4.3.0]non-3-ene-2,5-diol (***2a***).* A mixture of **4b** (390 mg, 0.994 mmol) and TPP (20 mg) in CCl_4 (50 ml) was irradiated by a high-pressure mercury lamp (540 W) with bubbling of oxygen for 15 min. The solvent was removed *in vacuo*, and the residue was purified by silica gel flash column chromatography (8 g). Elution with hexane-ethyl acetate (3:1) afforded *endo*-peroxide **5** as an oil, which was immediately dissolved in MeOH (5 ml). To this mixture, thiourea (114 mg, 1.50 mmol) was added, and the mixture stirred for 30 min. The solvent was removed *in vacuo*, the residue was purified by silica gel column chromatography (8 g). Elution with toluene-ethyl acetate (3:2) afforded **2a** (288 mg, 68%) as a solid. An analytical sample was obtained by recrystallizing it from diisopropyl ether, mp 84.2–84.8°C; IR ν_{max} cm^{-1}: 3200, 2860, 1500, 1450, 1370, 1260, 1210, 1160, 1110, 1100, 1070, 1010, 960, 860, 750, 700, 620; 1H-NMR ($CDCl_3$) δ: 1.33 (3H, s), 1.34 (3H, s), 3.13 (2H, d, J=6.8 Hz), 4.06 (2H, d, J=11.7 Hz), 4.30 (2H, d, J=11.7 Hz), 4.37 (2H, dd, J=1.5, 6.8 Hz), 4.48 (2H, d, J=11.7 Hz), 4.52 (2H, d, J=11.7 Hz), 4.53 (2H, dd, J=1.5, 1.5 Hz), 7.29–7.46 (10H, m, aromatic); ^{13}C-NMR δ: 24.09, 26.26, 67.30, 69.02, 72.25, 77.00, 77.25, 108.50, 127.87, 128.49, 137.39, 137.59. *Anal.* Found: C, 70.23; H, 7.30%. Calcd. for $C_{25}H_{30}O_6$: C, 70.40; H, 7.09%. Single-crystal X-ray diffraction measurements were performed with a Rigaku AFC-5 four-circle diffractometer with Mo Kα radiation. The crystal data are as follows: $C_{25}H_{30}O_6$, M_r=426.51, monoclinic, $P2_1/c$, a=10.329 (3), b=28.175 (4), c=7.899 (4) Å, β=95.53 (4)°, V=2288.1 (13) Å^3, Z=4, D_m not determined, D_x=1.238 Mg m^{-3}, R=0.062 for 2201 reflections.[8] The molecular structure is shown in Fig. 1.

(1R, 2S*, 5R*, 6S*)-3,4-Bis(benzyloxymethyl)-8,8-dimethyl-7,9-dioxabicyclo[4.3.0]non-3-en-2,5-ylene bischloroacetate (***2b***).* This was prepared in a conventional manner from diol **2a** in a 96% yield, IR ν_{max} cm^{-1}: 2930, 2850, 1760, 1450, 1410, 1370, 1310, 1210, 1160, 1120, 1060, 980, 860, 790, 740, 700; ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, s), 1.39 (3H, s), 3.95 (2H, d, J=14.9 Hz), 4.00 (2H, d, J=14.9 Hz), 4.13 (2H, d, J=15.0 Hz), 4.16 (1H, d, J=15.0 Hz), 4.40 (2H, d, J=11.8 Hz), 4.48 (2H, d, J=1.0 Hz), 4.50 (2H, d, J=11.8 Hz), 5.73 (1H, d, J=1.0 Hz), 7.28-7.35 (10H, m, aromatic); ^{13}C-NMR δ: 24.38, 26.33, 40.79, 66.64, 70.35, 72.16, 74.63, 109.28, 127.72, 127.75, 128.40, 135.81, 137.71, 166.53. *Anal.* Found: C, 60.24; H, 5.61%. Calcd. for $C_{29}H_{32}O_8Cl_2$: C, 60.11; H, 5.57%.

*(1R,2S,5R,6S)-(−)-3,4-Bis(benzyloxymethyl)-5-hydroxy-8,8-dimethyl-6,8-dioxabicyclo[4.3.0]non-3-en-2-yl chloroacetate (***2c***).* A mixture of **2b** (548 mg, 0.946 mmol), porcine pancreatic lipase (Sigma L-3176, 5.4 g), DMF (27 ml) and a phosphate buffer (pH 7.1, 0.2 M, 27 ml) was stirred at 30°C for 16 hr. After filtering through a pad of Celite to remove the insoluble materials, the

mixture was extracted with ethyl acetate. The organic solution was washed with brine, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (10 g). Elution with hexane-ethyl acetate (3:1) afforded (−)-**2c** as an oil (214 mg, 45%), $[\alpha]_D^{23}$-19.2° (*c* 1.02, chloroform); IR ν_{max} cm^{-1}: 3450, 3000, 2930, 1750, 1500, 1450, 1380, 1205, 1160, 1120, 1060, 1030, 970, 870, 740, 700; ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, s), 1.39 (3H, s), 2.71 (1H, d, J=7.8 Hz), 3.95 (1H, d, J=15.2 Hz), 4.01 (1H, d, J=15.2 Hz), 4.04 (1H, d, J=12.0 Hz), 4.11 (1H, d, J=12.0 Hz), 4.17 (1H, d, J=12.0 Hz), 4.29 (1H, d, J=12.0 Hz), 4.39 (1H, d, J=11.9 Hz), 4.42–445 (6H, m), 4.54 (1H, d, J=11.7 Hz), 5.69 (1H, d, J=2.7 Hz), 7.26–7.34 (10H, m, aromatic). HRMS: found, 483.1593; calcd. for $C_{27}H_{29}O_6Cl$, 483.1572 (M^+-1-H_2O). Further elution of the chromatograph afforded diol **2a** (190 mg, 47%).

*(1R,2S,5R,6S)-(+)-3,4-Bis(benzyloxymethyl)-5-methoxymethoxy-8,8-dimethyl-6,8-dioxabicyclo[4.3.0]non-3-ene-2-ol (***2e***).* To a solution of (−)-**2c** (50 mg, 0.099 mmol) and diisopropylethylamine (40 mg, 0.31 mmol) in dry dichloromethane (1 ml) was added dropwise chloromethyl methyl ether (MOMCl, 24 mg, 0.30 mmol) while ice-cooling. After removing the ice bath, the mixture was stirred at room temperature for 3 hr, before being poured into ice-cooled water and extracted twice with ether (15 ml). The extract was concentrated *in vacuo*, and the residue was dissolved in methanol (1 ml). To this was added potassium carbonate (10 mg), and the resulting mixture was stirred for 10 min at room temperature. The mixture was concentrated *in vacuo*, and the residue was purified by preparative thin-layer chromatography [Wako-gel B-5F, 20 cm × 20 cm × 0.75 mm, developed with hexane-ethyl acetate (2:1)] to give **2e** as an oil (39 mg, 83%), $[\alpha]_D^{22}$+18.3° (*c* 1.00, chloroform); IR ν_{max} cm^{-1}: 3500, 3030, 2930, 1500, 1450, 1390, 1370, 1280, 1210, 1160, 1120, 1060, 1020, 920, 870, 750, 710; ^{1}H-NMR ($CDCl_3$) δ: 1.26 (3H, s), 1.29 (3H, s), 3.10–3.30 (1H, br.s), 3.30 (3H, s), 4.05 (1H, d, J=12.4 Hz), 4.10 (1H, d, J=12.4 Hz), 4.13 (1H, d, J=12.4 Hz), 4.20 (1H, d, J=12.4 Hz), 4.30 (1H, d, J=2.2 Hz), 4.35 (1H, d, J=11.8 Hz), 4.39 (1H, d, J=11.8 Hz), 4.40 (1H, d, J=2.7 Hz), 4.47 (1H, d, J=11.8 Hz), 4.49 (1H, d, J=11.8 Hz), 4.57 (1H, d, J=2.2, 7.2 Hz), 4.60 (1H, dd, J=2.7, 7.2 Hz), 4.63 (1H, d, J=6.7 Hz), 4.71 (1H, d, J=6.7 Hz), 7.20–7.30 (10H, m, aromatic). HRMS: found, 469.2250; calcd. for $C_{27}H_{33}O_7$: 469.2224 (M^+-1).

(*R*)-MTPA ester derivative **2f** was prepared *via* a conventional procedure from (+)-**2e**. **2f**: ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, s), 1.37 (3H, s), 3.17 (3H, s), 3.47 (3H, s), 4.11 (1H, d, J=11.8 Hz), 4.14 (1H, d, J=12.2 Hz), 4.15 (1H, d, J=11.8 Hz), 4.19 (1H, d, J=12.2 Hz), 4.36 (1H, d, J=11.7 Hz), 4.39 (1H, d, J=12.7 Hz), 4.41 (1H, d, J=2.2 Hz, H-5), 4.41 (1H, dd, J=2.2, 6.8 Hz, H-1), 4.49 (1H, d, J=7.1 Hz), 4.50 (1H, dd, J=2.2, 6.8 Hz, H-6), 4.50 (1H, d, J=12.7 Hz), 4.54 (1H, d, J=7.1 Hz), 5.82 (1H, d, J=2.2 Hz, H-2), 7.26–7.34 (10H, m, aromatic), 7.51–7.54 (5H, m, aromatic). The proton assignment was fully confirmed by decoupling experiments, except for one of the methylene protons (δ 4.1–4.5, 1H, d, J should be 11.7 Hz) due to the complexity of the signals.

*(1S,2R,5S,6R)-(−)-3,4-Bis(benzyloxymethyl)-5-methoxymethoxy-8,8-dimethyl-6,8-dioxabicyclo[4.3.0]non-3-ene-2-ol (***2j***=ent-***2e***).* To a solution of (−)-**2c** (100 mg, 0.199 mmol) and imidazole (40 mg, 0.59 mmol) in dry DMF (2 ml) was added *t*-butyldimethylsilyl chloride (60 mg, 0.40 mmol), and the mixture was stirred at room temperature overnight. The mixture was poured into water and extracted with ether (20 ml). The extract was concentrated *in vacuo*, and the residue was dissolved in dichloromethane (1 ml). To this was added diisopropylethylamine (75 mg, 0.58 mmol), and the resulting mixture was stirred in an ice bath. To this was added MOMCl (33 mg, 0.41 mmol), and the mixture was stirred overnight at room temperature. The reaction mixture was worked-up in the same manner as that for **2e**. The crude product was dissolved in a tetrabutylammonium fluoride solution (1.0 M in THF, 3 ml), and the mixture was stirred for 30 min. This was poured into water (3 ml) and extracted three times with ether (20 ml). The extract was concentrated *in vacuo*, and the residue was purified by preparative thin-layer chromatography [three plates of 20 cm × 20 cm × 0.75 mm, developed with hexane-ethyl acetate (2:1)] to give **2j** as an oil (49 mg, 52% from **2c**), $[\alpha]_D^{22}$-18.3° (*c* 0.890, chloroform). HRMS; found, 453.2274; calcd. for $C_{27}H_{33}O_6$, 453.2274 (M^+-OH). Its IR and NMR spectra were identical with those of **2e**. MTPA ester **2k** was prepared from (−)-**2j**. **2k**: ^{1}H-NMR ($CDCl_3$) δ: 1.36 (3H, s), 1.39 (3H, s), 3.23 (3H, s), 3.54 (3H, s), 3.92 (1H, d, J=11.9 Hz), 4.06 (1H, d, J=11.9 Hz), 4.10 (1H, d, J=12.2 Hz), 4.16 (1H, d, J=12.2 Hz), 4.27 (1H, d, J=11.8 Hz), 4.34 (1H, d, J=11.8 Hz), 4.41 (1H, d, J=11.8 Hz), 4.46 (2H, d, J=2.5 Hz, H-5), 4.48 (1H, d, J=11.8 Hz), 4.49 (1H, dd, J=2.5, 6.9 Hz, H-6), 4.54 (1H, d, J=6.9 Hz), 4.55 (1H, dd, J=2.5, 6.9 Hz, H-1), 4.59 (1H, d, J=6.9 Hz), 5.79 (1H, d, J=2.5 Hz, H-2), 7.26–7.34 (10H, m, aromatic), 7.51–7.55 (5H, m, aromatic). The proton assignment was fully confirmed by decoupling experiments, except for one of the methylene protons (δ 4.1–4.5, 1H, d, J should be 11.8 Hz) due to the complexity of the signals. As no signal due to contamination was apparent in the spectra of **2f** and **2k**, *e.e.s* of **2c**, **2e** and **2j** was concluded to be over 95%, for each.

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References

1) T. Omori, M. Matsubara, S. Matsuda, and T. Kodama, *Appl. Microbial. Biotechnol.*, **35**, 431–435 (1991).

2) Recent report and reviews: D. R. Boyd, N. D. Sharma, H. Dalton, and D. A. Clarke, *Chem. Commun.*, **1996**, 45–46; M. G. Banwell and J. R. Dupuche, *Chem. Commun.*, **1996**, 869–870; S. V. Ley, *Pure Appl. Chem.*, 62, 2031–2034 (1990); H. A. J. Carless, *Tetrahedron: Asymmetry*, **3**, 795–826 (1992); E. Schoffers, A. Golebiowski, and C. R. Johnson, *Tetrahedron*, **52**, 3769–3826 (1996); T. Hudlicky and A. J. Thorpe, *Chem. Commun.*, **1996**, 1993–2000.

3) C. R. Johnson, P. A. Plé, and J. P. Adams, *J. Chem. Soc., Chem,. Commun.*, **1991**, 1006–1007; C. R. Johnson and S. J. Bis, *Tetrahedron Lett.*, **33**, 7287 (1992); L. Dumortier, P. Liu, S. Dobbelaere, J. Van der Eycken, and M. Vandewalle, *Synlett*, **1992**, 243–245; L. Pingli and M. Vandewalle, *Tetrahedron*, **50**, 7061–7074 (1994); L. Pingli and M. Vandewalle, *Synlett*, **1994**, 228–230; G. Nicolosi, A. Patti, M. Piattelli, and C. Sanfilippo, *Tetrahedron Lett.*, **36**, 6545–6546 (1995).

4) M. Ueda, K. Ohta, and M. Matsubara, Jpn. Kokai Tokkyo Koho JP 94,321,949 (*Chemical Abstracts* **122**, 187562n, (1995).

5) S.-S. Wang, B. F. Gisin, D. P. Winter, R. Makofske, I. D. Kulesha, C. Tzougraki, and J. Meinenhofer, *J. Org. Chem.*, **42**, 1286–1290 (1977).

6) Y. Sütbeyaz, H. Seçen, and M. Balci, *J. Chem. Soc., Chem. Commun.*, **1988**, 1330–1331; M. Balci, *Pure Appl. Chem.*, **69**, 97–104 (1997).

7) I. Ohtani, T. Kusumi, Y. Kashman, and H. Kakisawa, *J. Am. Chem. Soc.*, **113**, 4092–4096 (1991).

8) Tables of atomic parameters, bond lengths and bond angles have been deposited with Cambridge Crystallographic Data Centre.