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Facile Construction of Optically Active 1,3-Diols. Synthesis of (2*S*,4*R*)-7-Octene-2,4-diol and *endo*-(1*S*,3*S*,5*R*)- and *exo*-(1*R*,3*S*,5*S*)-1,3-Dimethyl-2,9-dioxabicyclo[3.3.1]nonane

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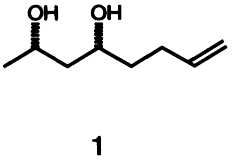
A short and stereoselective asymmetric synthesis of (2*S*,4*R*)-7-octene-2,4-diol (a key intermediate in the Bartlett synthesis of nonactic acid) and two stereoisomers of a biologically active substance isolated from Norway spruce infested by ambrosia beetle, *endo*-(1*S*,3*S*,5*R*)- and *exo*-(1*R*,3*S*,5*S*)-1,3-dimethyl-2,9-dioxabicyclo-[3.3.1]nonane, was effectively accomplished in three and four reaction steps, respectively, by starting with easily obtainable (*S*)-1-(1,3-dithian-2-yl)-2-propanol by baker's yeast asymmetric reduction. The main strategy was based on a facile construction of optically active *β*-hydroxy ketones via alkylation of the dianion of (*S*)-1-(1,3-dithian-2-yl)-2-propanol with alkyl halides, followed by their stereoselective reductions.

A 1,3-dihydroxylated structure is often found on the backbone of natural products or important key intermediates for natural products synthesis (e.g., polyoxo and polyether natural products). The compounds, (2*S*,4*R*)-7-octene-2,4-diol (**1**) and 1,3-dimethyl-2,9-dioxabicyclo[3.3.1]nonane (**2**) are typical and simple examples. The former diol is known to be a key intermediate for the Bartlett synthesis of nonactic acid[1] and the latter bicyclic acetal, which is regarded to be potentially a 1,3-diol molecule, is a host-specific substance isolated from Norway spruce infested by the ambrosia beetle (*Trypodendron lineatum* Oliv.).[2] Although these compounds have already been synthesized in optically active forms by several groups,[3] some of these syntheses require lengthy reaction steps and are laborious in spite of their synthetic importances. In a preceding communication,[4] we showed the usefulness of (*S*)-1-(1,3-dithian-2-yl)-2-propanol (**3**) as a chiral building block for the synthesis of the Bartlett diol (**1**). In this paper, we would like to describe a short and efficient asymmetric synthesis of (2*S*,4*R*)-7-octene-2,4-diol (**1**) and two stereoisomers of **2**, *endo*-(1*S*,3*S*,5*R*)- and *exo*-(1*R*,3*S*,5*S*)-1,3-dimethyl-2,9-dioxabicyclo[3.3.1]nonane (**12** and **13**), which demonstrates the usefulness of **3** for the facile construction of this type of optically active 1,3-diols.



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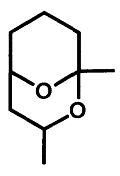

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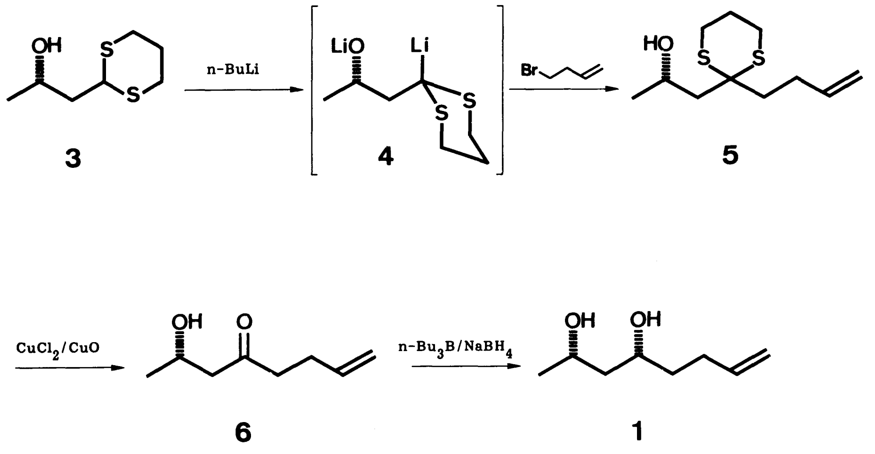
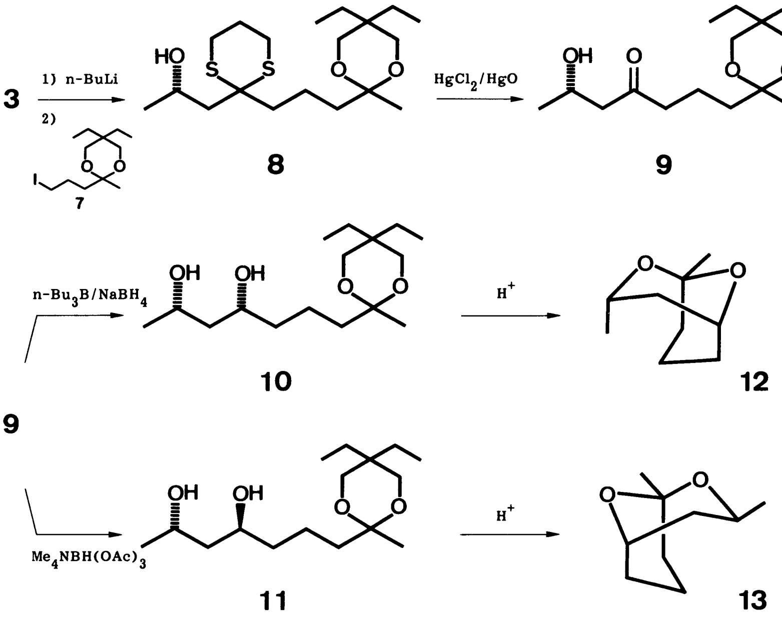
As outlined in Schemes 1 and 2, the present methodology comprises the alkylation of the dianion **4** with alkyl halides followed by the hydrolysis of the dithioacetal group and the subsequent 1,3-asymmetric induction by employing the stereoselective reduction of the resulting *β*-hydroxy ketones **6** and **9** leading to the corresponding 1,3-syn and 1,3-anti diols **1**, **10**, and **11**.

As shown in the previous communication[4] as well as in the literature,[5] optically active alcohol (*S*)-**3** was easily obtained by the baker's yeast asymmetric reduction of (1,3-dithian-2-yl)acetone in nearly quantitative yield with excellent optical purity (>99% ee). The transformation of (*S*)-**3** into the dianion **4** was



Scheme 1.



Scheme 2.

achieved by the reaction with 2.2 equiv. of *n*-BuLi in THF at −30—0 °C. When dianion **4** was treated with 1.1 equiv. of 4-bromo-1-butene in THF at −30—0 °C, the *C*-alkylation product (*S*)-**5** was obtained in high yield. (*S*)-**5** was then hydrolyzed with $CuCl_2/CuO$ in aqueous acetone[6] to give the optically active β-hydroxy ketone (*S*)-**6** in good yield without any evidence of dehydration. The stereoselective reduction of (*S*)-**6** to the syn-diol **1** was effectively accomplished using *n*-$Bu_3B/NaBH_4$[7] which produced the mixture of the Bartlett diol **1** and its C-4 epimer with high selectivity (syn:anti=97:3). They were cleanly separated by column chromatography on silica gel to give pure **1**.

We next tried the synthesis of *endo*-(1*S*,3*S*,5*R*)-**12** and *exo*-(1*R*,3*S*,5*S*)-**13** starting with the (*S*)-alcohol **3**, according to the following sequence (Scheme 2). The reaction of the dianion **4** with 1.1 equiv. of 2-(3-iodopropyl)-2-methyl-5,5-diethyl-1,3-dioxane (**7**) at −30—0 °C proceeded selectively to give (*S*)-**8** in high yield without the concomitant of *O*-alkylation product. In contrast to the case of a similar ethylene acetal analogue reported very recently,[8] the selective hydrolysis of the dithioacetal group in **8** could be easily achieved without the hydrolysis of the 2,2-diethyl-1,3-propanediyl acetal protecting group by the standard procedure using $HgCl_2/HgO$ in aqueous acetonitrile[9] to give the desired β-hydroxy ketone (*S*)-**9** in good yield. The reduction of (*S*)-**9** with *n*-$Bu_3B/NaBH_4$ satisfactorily provided the syn-diol **10** in excellent yield with high stereoselectivity (syn:anti=94:6), although the syn selective reduction of a similar ethylene acetal analogue has been reported ($Zn(BH_4)_2$: 9:1,[8] $NaBH_4/Et_2BOMe$: >99:1[3f]). On the other hand, the anti-isomer **11** could be quantitatively obtained with excellent stereoselectivity (syn:anti=6:94) by reducing (*S*)-**9** with $Me_4NBH(OAc)_3$ in acetonitrile-acetic acid[10] in sharp contrast to the poor selectivity (1:2) on the reduction of an ethylene acetal analogue by $NaBH(OAc)_3$ in acetic acid or $NaBH_4/CeCl_3$ in methanol.[8] Although the isomers of *syn*-**10** and *anti*-**11** could be separated by silica-gel column chromatography, the crude diol mixture in both cases was available for use in the final cyclization stage without separation of the minor isomer or further purification. Thus, the acid-catalyzed cyclization of the crude mixtures was performed by means of a two-layer method with hexane-2 M H_2SO_4 (1 M=1 mol dm^{-3}) to produce *endo*-**12** and *exo*-**13** in good yields, respectively. These isomers were cleanly separated by the separable-TLC technique to obtain them as pure form, respectively.

In summary, (2*S*,4*R*)-**1**, *endo*-(1*S*,3*S*,5*R*)-**12**, and *exo*-(1*R*,3*S*,5*S*)-**13** of high chemical and enantiomeric purity were obtained in 75%, 61%, and 70% overall yield, respectively. Spectroscopic data of these compounds were in good agreement with reported values. Because of the ready availability of the starting alcohol (*S*)-**3**, high overall yields of products, and simplicity of the procedure, the method can be regarded as a general and useful one for the facile construction of this type of optically active 1,3-diols.

Experimental

Optical rotations were determined with a Union Digital PM-101 polarimeter. IR spectra were obtained on a JASCO A-202 spectrophotometer. ^1H NMR spectra were measured with JEOL JNM-GX400 spectrophotometer at 400 MHz with tetramethylsilane as an internal reference. Silica gel (Merck silica gel 60, 230—400 mesh ASTM) was used for medium-pressure liquid chromatography (MPLC). Analytical and preparative TLC were carried out on Merck precoated silica gel plates (Merck silica gel 60 F_{254}).

Materials. The solvents were purified by the usual methods and were freshly distilled before use. (1,3-Dithian-2-yl)acetone was prepared from 4,4-dimethoxy-2-butanone and 1,3-propanedithiol according to the method in the literature.[11] 5-Iodo-2-pentanone was prepared by the halogen-exchange reaction of the corresponding chloride with NaI according to the method of Findlay et al.[12] Fresh baker's yeast (Oriental Yeast Co.) used was commercially available. The other reagents were supplied as high-grade commercial products and used without further purification.

***(S)*-(+)-1-(1,3-Dithian-2-yl)-2-propanol (3).** The following modified procedure gave optically pure (*S*)-**3** in excellent yield.[5] Baker's yeast (200 g) was dispersed into a solution of sucrose (40 g) and $Na_4P_2O_7$ (10 g) in distilled water (600 ml), and then stirred for 1 h at 25 °C. To the fermenting mixture was added (1,3-dithian-2-yl)acetone (8 g, 45.4 mmol) and stirred at the same temperature for 1 day. An additional baker's yeast (100 g), sucrose (20 g), $Na_4P_2O_7$ (5 g), and distilled water (300 ml) were supplied and the stirring was continued for an additional day. Ethyl acetate (500 ml) was added to the reaction mixture and the mixture was stirred for 16 h. After filtration through a Celite pad, the filtrate was extracted with ethyl acetate and the extract was dried with $MgSO_4$. The solvent was removed by evaporation under reduced pressure and the residue was diluted with CH_2Cl_2. The solution was filtered through a silica-gel pad (Wakogel C-300) and the concentration of the filtrate in vacuo gave the almost TLC-pure (*S*)-**3** in quantitative yield (>99% ee by ^{1}H NMR analysis of the alcohol with the chiral shift reagent (+)-Eu(hfc)$_3$ and of the corresponding (+)-MTPA ester[13]). Distillation of this product gave pure (*S*)-**3** as a colorless oil (7.63 g, 94%); bp 135 °C/0.1 mmHg (lit,[5] 105 °C/0.05 mmHg; 1 mmHg≈133.322 Pa); $[\alpha]_D^{25}$ +25.1° (*c* 2.0, $CHCl_3$) (lit,[5] $[\alpha]_D^{20}$ +24.7° (*c* 2.0, $CHCl_3$)); IR (neat film) 3400, 2900, 1420, 1370, 1270, 1240, 1180, 1120, 1070, 1020, 940, 900, 860, 840, and 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.23 (d, 3H, *J*=6.1 Hz), 1.81—1.95 (m, 3H), 1.98 (br, 1H), 2.13 (m, 1H), 2.81—2.96 (m, 4H), 4.13 (m, 1H), and 4.24 (dd, 1H, *J*=8.5, 5.9 Hz).

***(S)*-(+)-2-(3-Butenyl)-2-(2-hydroxypropyl)-1,3-dithiane (5).** A stirred solution of (*S*)-**3** (1.0 g, 5.6 mmol) in dry THF (8 ml) under nitrogen was cooled to −30 °C and 1.6 M solution of *n*-BuLi in hexane (8.4 ml, 13.4 mmol) was added dropwise. The mixture was stirred for 30 min at −30 °C and then for 3 h at 0 °C. The mixture was again cooled to −30 °C. 4-Bromo-1-butene (0.62 ml, 6.2 mmol) was slowly added to the solution and stirred for 1 h at −30 °C. After allowing to warm to 0 °C, the reaction mixture was stirred for additional 4 days in a refrigerator and then quenched by the addition of water. The aqueous mixture was extracted with benzene and the extract was washed successively with water, 7% aqueous KOH solution, and water. After drying the extract with $MgSO_4$, the solution was concentrated in vacuo and the residual oil was purified by MPLC (benzene/ethyl acetate 3:1 v/v) to give pure (*S*)-**5** as a colorless oil (1.18 g, 91%); $[\alpha]_D^{24}$ +25.5° (*c* 3.84, $CHCl_3$); IR (neat film) 3400, 3050, 2900, 1630, 1440, 1410, 1360, 1260, 1230, 1120, 1050, 980, 900, 860, and 780 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.20 (d, 3H, *J*=6.3 Hz), 1.88—2.22 (m, 6H), 2.33 (m, 2H), 2.81 (m, 2H), 2.97 (m, 2H), 3.50 (s, 1H), 4.16 (m, 1H), 5.00 (dq, 1H, *J*=10.1, 1.7 Hz), 5.07 (dq, 1H, *J*=17.1, 1.7 Hz), and 5.82 (m, 1H).

***(S)*-(+)-2-Hydroxy-7-octen-4-one (6).** To a solution of (*S*)-**5** (800 mg, 3.44 mmol) in 99% aqueous acetone (34 ml) was added $CuCl_2$ (925 mg, 6.88 mmol) and CuO (1.09 g, 13.76 mmol). The mixture was stirred for 3 h at room temperature. It was filtered through a Celite pad and the Celite was washed with ether. The combined filtrate and washings were concentrated under reduced pressure and the residue was diluted again with ether (30 ml). The solution was thoroughly washed with 5% aqueous $NaHCO_3$ solution and dried with $MgSO_4$. After concentration in vacuo, MPLC purification of the residue (benzene–ethyl acetate 4:1 v/v) gave pure (*S*)-**6** as a colorless heavy oil (441 mg, 90%); $[\alpha]_D^{30}$ +59.3° (*c* 2.0, $CHCl_3$) (lit,[3d] $[\alpha]_D^{22}$ −57.2° (*c* 2.27, $CHCl_3$) for (*R*)-**6**); IR (neat film) 3450, 3100, 2975, 2925, 1710, 1640, 1410, 1380, 1280, 1110, 1070, 1040, 1000, 940, 920, 840, and 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.19 (d, 3H, *J*=6.3 Hz), 2.33 (q, 2H, *J*=7.3 Hz), 2.52 (d, 1H, *J*=17.5 Hz), 2.54 (t, 2H, *J*=7.3 Hz), 2.61 (dd, 1H, *J*=17.5, 3.4 Hz), 3.19 (br, 1H), 4.23 (m, 1H), 5.02 (m, 2H), and 5.80 (m, 1H).

(2*S*,4*R*)-(+)-7-Octene-2,4-diol (1). To a solution of (*S*)-**6** (200 mg, 1.41 mmol) in dry THF (3.5 ml) was added tributylborane (1.55 ml, 1.55 mmol) and then air (4.2 ml) was slowly bubbled into the solution. The mixture was stirred for 2 h at room temperature under nitrogen. After the mixture was cooled to −78 °C, $NaBH_4$ (59 mg, 1.55 mmol) was added and then stirred for 3 h at the same temperature. The reaction mixture was allowed to warm to room temperature and the mixture of 30% H_2O_2 (7 ml), buffer solution (pH 7, 14 ml), and methanol (21 ml) was then added. The solvent was removed by evaporation under reduced pressure and the residue was extracted with CH_2Cl_2. The extract was dried with $MgSO_4$ and the solvent was removed in vacuo to yield the almost pure mixture of *syn*-**1** and its C-4 epimer in 98% yield (syn:anti=97:3 by ^{1}H NMR analysis). MPLC purification (benzene/ethyl acetate 1:2 v/v) of the mixture gave pure *syn*-**1** (187 mg, 92%); $[\alpha]_D^{26}$ +18.5° (*c* 1.13, CCl_4) (lit,[1] $[\alpha]_D^{20}$ −18.3° (*c* 0.75, CCl_4) for the enantiomer of **1**); IR (neat film) 3400, 3100, 3000, 2950, 1650, 1440, 1380, 1330, 1130, 1080, 1000, 920, and 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.21 (d, 3H, *J*=6.1 Hz), 1.46—1.64 (m, 4H), 2.16 (m, 2H), 3.11 (s, 2H), 3.88 (m, 1H), 4.05 (m, 1H), 4.98 (dq, 1H, *J*=10.0, 0.5 Hz), 5.05 (dq, 1H, *J*=17.1, 0.5 Hz), and 5.84 (m, 1H).

5,5-Diethyl-2-(3-iodopropyl)-2-methyl-1,3-dioxane (7). A mixture of 5-iodo-2-pentanone (21.2 g, 100 mmol), 2,2-diethyl-1,3-propanediol (26.4 g, 200 mmol), and *p*-toluenesulfonic acid monohydrate (1.90 g, 10 mmol) in benzene (247 ml) was refluxed in an apparatus equipped with a Dean–Stark trap for 15 h. After cooling to room temperature, 5% aqueous $NaHCO_3$ solution was added to the reaction mixture and then extracted with ether. The extract was washed with 0.1 M aqueous $Na_2S_2O_3$ solution and dried with $MgSO_4$. The solvent was removed by evaporation under reduced pressure and the residual pale yellow oil was distilled to yield pure **7** (23.7 g, 73%); bp 135 °C/0.1 mmHg; IR (neat film) 2900, 2850, 1440, 1360, 1280, 1240, 1220, 1180, 1160, 1100, 1040, 990, 920, 850, 780, 760, and 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.79 (t, 3H, *J*=7.8 Hz), 0.81 (t, 3H, *J*=7.8 Hz), 1.29 (q, 2H, *J*=7.8 Hz), 1.36 (s, 3H), 1.47 (q, 2H, *J*=7.8 Hz), 1.78 (m, 2H), 1.97 (m, 2H), 3.23 (t, 2H, *J*=6.8 Hz), and 3.52, 3.54, 3.56, 3.59 (each s, 4H).

(+)-5,5-Diethyl-2-[(*S*)-6-hydroxy-4,4-(trimethylenedithio)-heptyl]-2-methyl-1,3-dioxane (8). To a cooled and stirred solution of (*S*)-**3** (5.17 g, 29 mmol) in dry THF at −30 °C under nitrogen, was added dropwise 1.6 M hexane solution of *n*-BuLi (41 ml, 65 mmol). After stirring for 30 min at −30 °C, the mixture was allowed to slowly warm to 0 °C and then stirred for 3 h. Iodide **7** (10.5 g, 32 mmol) was added dropwise to the resulting dianion solution cooled again to −30 °C and then stirring was continued for 2 h. The reaction mixture was allowed to warm to 0 °C and stood for 2 days at 0 °C in refrigerator. The mixture was then quenched by the addition of water and the aqueous mixture was extracted with benzene. The extract was successively washed with water, 7% aqueous KOH solution, and water and then dried with $MgSO_4$. The solvent was removed in vacuo to yield almost pure (*S*)-**8** in quantitative yield; $[\alpha]_D^{30}$ +12.7° (*c* 2.18, $CHCl_3$); IR (neat film) 3450, 2950, 1720, 1460, 1420, 1380, 1280, 1250, 1220, 1190, 1100, 1060, 1000, 930, 910, 870, 790, 760, and 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.79 (t, 3H, *J*=7.6 Hz), 0.81 (t, 3H, *J*=7.6 Hz), 1.20 (d, 3H, *J*=6.3 Hz), 1.31 (q, 2H, *J*=7.6 Hz), 1.36 (s, 3H), 1.47 (q, 2H, *J*=7.6 Hz), 1.68 (m, 4H), 1.86—2.08 (m, 5H), 2.33 (dd, 1H, *J*=15.4, 9.5 Hz), 2.79 (m, 2H), 2.98 (m, 2H), 3.50, 3.53 (each d, 2H, *J*=2.2 Hz), 3.55, 3.58 (each s, 3H), and 4.14 (m, 1H).

(+)-5,5-Diethyl-2-[(*S*)-6-hydroxy-4-oxoheptyl]-2-methyl-1,3-dioxane (9). To a stirred suspension of $HgCl_2$ (14.3 g, 52.8 mmol) and HgO (11.4 g, 52.8 mmol) in acetonitrile-water (4:1 v/v, 38 ml), a solution of (*S*)-**8** (9.04 g, 24 mmol) in acetonitrile-water (4:1 v/v, 230 ml) was added dropwise under nitrogen and then stirred for 4 h at room temperature. The reaction mixture was filtered through Celite and the Celite was washed with hexane-CH_2Cl_2 (1:1 v/v). 5 M aqueous ammonium acetate solution was added to the combined filtrate and washings and filtered again through Celite. The filtrate was washed with water and saturated aqueous NaCl solution. After drying with $MgSO_4$, the solvent was removed by evaporation under reduced pressure. The residual oil was purified by MPLC (benzene/ethyl acetate 1:1 v/v) to give pure (*S*)-**9** as a colorless heavy oil (5.71 g, 83%); $[\alpha]_D^{25}$ +32.9° (*c* 2.85, $CHCl_3$); IR (neat film) 3450, 3000, 1710, 1460, 1410, 1380, 1250, 1220, 1200, 1120, 1100, 1040, 1010, 940, 860, 790, 760, and 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.79 (t, 3H, *J*=7.6 Hz), 0.81 (t, 3H, *J*=7.6 Hz), 1.19 (d, 3H, *J*=6.3 Hz), 1.28 (q, 2H, *J*=7.6 Hz), 1.36 (s, 3H), 1.48 (q, 2H, *J*=7.6 Hz), 1.69 (m, 4H), 2.46 (t, 2H, *J*=7.1 Hz), 2.50 (dd, 1H, *J*=17.6, 9.0 Hz), 2.61 (dd, 1H, *J*=17.6, 2.9 Hz), 3.16 (d, 1H, *J*=3.2 Hz), 3.50, 3.53, 3.56, 3.59 (each s, 4H), and 4.22 (m, 1H).

(+)-5,5-Diethyl-2-[(4*R*,6*S*)-4,6-dihydroxyheptyl]-2-methyl-1,3-dioxane (10). To a solution of (*S*)-**9** (716 mg, 2.5 mmol) in dry THF (6.2 ml) was added tributylborane (2.75 ml, 2.75 mmol) and then air (7.5 ml) was slowly bubbled into the solution. The mixture was stirred for 3 h at room temperature under nitrogen. After cooling to −78 °C, $NaBH_4$ (104 mg, 2.75 mmol) was added and then stirred for 3 h at the same temperature. The reaction mixture was allowed to warm to room temperature and a mixture of 30% H_2O_2 (13 ml), buffer solution (pH 7, 23 ml), and methanol (38 ml) was then added. The solvent was removed by evaporation under reduced pressure and the residue was extracted with CH_2Cl_2. The extract was dried with $MgSO_4$ and the solvent was removed in vacuo to yield an almost pure diastereomeric mixture of **10** and **11** (707 mg, 98%, **10**:**11**=94:6 by ^{1}H NMR analysis). This mixture was used for the next cyclization without further purification. TLC purification (benzene/ethyl acetate 1:1 v/v) of a part of the mixture gave pure sample of *syn*-**10**; $[\alpha]_D^{26}$ +4.1° (*c*1.02, $CHCl_3$); IR (neat film) 3400, 2950, 1460, 1380, 1360, 1330, 1240, 1200, 1150, 1130, 1100, 1080, 1060, 1030, 970, 940, 870, 840, 800, 760, and 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.79 (t, 3H, *J*=7.6 Hz), 0.81 (t, 3H, *J*=7.6 Hz), 1.21 (d, 3H, *J*=6.1 Hz), 1.28 (q, 2H, *J*=7.6 Hz), 1.36 (s, 3H), 1.49 (m, 7H), 1.59 (dt, 1H, *J*=14.4, 2.6 Hz), 1.69 (m, 2H), 3.03 (bs, 1H), and 3.18 (bs, 1H), 3.51, 3.54, 3.57, 3.60 (each s, 4H), 3.88 (m, 1H), and 4.05 (m, 1H).

(1*S*,3*S*,5*R*)-(+)-1,3-Dimethyl-2,9-dioxabicyclo[3.3.1]nonane (12). The two-layer mixture of a solution of crude *syn*-**10** (515 mg, 1.79 mmol) in hexane (6.3 ml) and 2 M H_2SO_4 (1.5 ml) was vigorously stirred for 4 days at room temperature. Saturated aqueous $NaHCO_3$ solution was carefully added to the reaction mixture and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated NaCl solution and dried with $MgSO_4$. After removal of the solvent by evaporation under reduced pressure, the pure *endo*-**12** was isolated from the residue by preparative TLC (CH_2Cl_2); 209 mg, 75%; $[\alpha]_D^{26}$ +31.1° (*c* 0.405, pentane) (lit,[3c)] $[\alpha]_D^{20}$ +37.5° (*c* 5.4, pentane)); IR (neat film) 3450, 2950, 2850, 1460, 1380, 1280, 1240, 1200, 1160, 1120, 1080, 1050, 1020, 970, and 940 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.20 (d, 3H, *J*=6.3 Hz), 1.27 (s, 3H), 1.30—1.81 (m, 6H), 2.04—2.17 (m, 2H), 3.94 (m, 1H), and 4.27 (brm, 1H).

(+)-5,5-Diethyl-2-[(4*S*,6*S*)-4,6-dihydroxyheptyl]-2-methyl-1,3-dioxane (11). To a cooled and stirred solution of tetramethylammonium triacetoxyborohydride (4.62 g, 17.5 mmol) in a mixture of dry acetonitrile (14 ml) and acetic acid (14 ml) at −40 °C was added dropwise a solution of (*S*)-**9** (1.00 g, 3.5 mmol) in dry acetonitrile (3.5 ml) under nitrogen. After the mixture was stirred for 5 h at −20 °C, it was quenched by the addition of 0.5 M aqueous sodium potassium tartarate (Rochelle salt) (52 ml) with vigorous stirring and then stirred for further 30 min. The mixture was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ solution. The organic layer was dried with Na_2SO_4 and concentrated in vacuo to yield an almost pure diastereomeric mixture of **11** and **10** in quantitative yield (**11**:**10**=94:6 by ^{1}H NMR analysis). This mixture was used for the next cyclization without further purification. TLC purification (benzene/ethyl acetate 1:1 v/v) of a part of the mixture gave pure sample of *anti*-**11**; $[\alpha]_D^{23}$ +8.7° (*c* 1.43, $CHCl_3$); IR (neat film) 3400, 3000, 1470, 1380, 1260, 1220, 1200, 1140, 1100, 1040, 1010, 940, 870, 840, 800, and 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.79 (t, 3H, *J*=7.6 Hz), 0.81 (t, 3H, *J*=7.6 Hz), 1.25 (m, 5H), 1.36 (s, 3H), 1.49—1.70 (m, 10H), 2.33 (bs, 1H), 2.40 (bs, 1H), 3.51, 3.54, 3.57, 3.60 (each s, 4H), 3.98 (m, 1H), and 4.17 (m, 1H).

(1*R*,3*S*,5*S*)-(−)-1,3-Dimethyl-2,9-dioxabicyclo[3.3.1]nonane (13). The two-layer mixture of a solution of crude *anti*-**11** (675 mg, 2.34 mmol) in hexane (8.2 ml) and 2 M H_2SO_4 (2 ml) was stirred for 3 days at room temperature. After a similar workup for *endo*-**12**, pure *exo*-**13** was isolated by preparative TLC (CH_2Cl_2); 307 mg, 84%; $[\alpha]_D^{24}$ −6.1° (*c* 0.212, pentane) (lit,[3c)] $[\alpha]_D^{20}$ +4.7° (*c* 3.2, pentane) for the enantiomer of **13**); IR (neat film) 3500, 1470, 1460, 1420, 1380, 1260, 1160, 1100, 1020, 860, and 800 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.16 (d, 3H, J=6.1 Hz), 1.32 (s, 3H), 1.53—2.20 (m, 8H), 4.21 (brm, 1H), and 4.60 (m, 1H).

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