Stereoselective Synthesis of Optically Active 4-Ethyl-3,5-dihydroxy-2-methylpentyl Derivatives. A Basic Building Block with Three Contiguous Chiral Centers of Polyether Antibiotics[1)]

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Optically active 4-ethyl-3,5-dihydroxy-2-methylpentyl derivatives, the iodide (4), phenyl sulfone (5), and phenyl sulfoxide (6), which are chiral synthons for an essential structural unit of polyether antibiotics, were stereoselectively synthesized starting from commercially available methyl (2*S*)-3-hydroxy-2-methylpropionate (7) in good overall yield (33% for 18 steps).

Keywords polyether antibiotic; stereoselective synthesis; chiral synthon; asymmetric epoxidation; organocopper reagent; protecting group

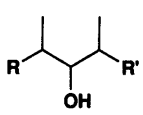
Stereoselective construction of many chiral centers by means of acyclic as well as cyclic stereocontrol is the most important issue in the synthesis of complex natural products such as macrolide and polyether antibiotics, and hence, a large number of enantioselective and diastereoselective reactions have been reported. The structural unit (**1**) with three chiral centers bearing methyl, hydroxy and methyl groups in frequently found in polyketide derived natural products represented by macrolide and polyether antibiotics. There are four possible diastereoisomers of **1**, and satisfactory methods for the selective synthesis of each isomer have been developed by several groups, beginning with Kishi's work.[2)] Compared with **1**, the structural unit (**2**) with ethyl, hydroxy and methyl groups is generally found only as a minor structural unit in polyketide-derived natural products. Many polyether antibiotics represented by salinomycin, lasalocid A, and lysocellin, however, have **2** as an essential unit, and **3** is a typical chiral structure.

In the course of the total synthesis of isolasalocid A and lasalocid A, we reported that a stereoselective synthesis of chiral synthons, the iodide (**4**) and sulfone (**5**), corresponding to **3**, and **5** was successfully used to obtain the C13–C17 part of isolasalocid A and lasalocid A.[1,3)] The synthesis of **5** from D-glucose, however, required no less than 24 reaction steps, and the overall yield was only 8%.[1)] In the present paper, we report an improved synthesis of **4** and **5** starting from methyl (2*S*)-3-hydroxy-2-methylpropionate (**7**).

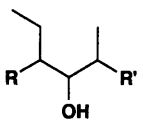
The (*S*)-ester (**7**) was first converted to the (*E*,*R*)-allyl alcohol (**8**) according to the procedure reported by Barrett *et al.* in 86% overall yield in 5 steps.[4)] Sharpless asymmetric epoxidation[5)] of **8** in the presence of diethyl (+)-tartrate readily gave the epoxide (**9**) with over 20 : 1 selectivity in excellent yield. When **9** was treated with vinylmagnesium bromide in the presence of 10 mol% of cuprous iodide[6)] at −20 °C, completely regio- and stereoselective vinylation with epoxide ring opening proceeded to give **10**, probably *via* **11**.[7)] No regioisomer was obtained, presumably owing to the steric hindrance of the methyl group of **9**. After tosylation of the primary alcohol and acetylation of the secondary alcohol, the resulting **12** was treated with lithium dimethyl cuprate in the usual way to give **13**, which was easily converted to **14** *via* three conventional reactions; oxidation with osmium tetroxide and sodium periodate, and reduction with lithium aluminum hydride. Protection of the diol of **14** as an acetonide and subsequent reductive removal of the benzyloxymethyl (BOM) protecting group with sodium in liquid ammonia gave the known alcohol (**15**),[1)] which was readily converted to the iodide (**4**) and sulfone (**5**).[1)] Thus, a new and convenient synthesis of **4** and **5** was completed without any difficulty. The overall yield of 18 steps from the starting ester (**7**) to **5** was 33%. Finally, the sulfoxide (**6**) was also synthesized from **16** *via* oxidation of an intermediary sulfide. Quite recently, all of **4**, **5** and **6** were actually applied to the total synthesis of lysocellin.[8)]

Experimental

(2*S*,3*S*,4*S*)-5-Benzyloxymethoxy-2,3-epoxy-4-methylpentan-1-ol (9) Titanium tetra-isopropoxide (1.68 ml, 6.1 mmol) was added to a stirred suspension of molecular sieves 3A (4.0 g) in CH_2Cl_2 (20 ml) containing diethyl (+)-tartrate (1.4 g, 6.78 mmol) at −20 °C under argon. After 10 min, a solution of **8**[4)] (4.2 g, 17.8 mmol) in CH_2Cl_2 (10 ml) was added dropwise, and the stirring was continued for 30 min, then a 3 M 2,2,4-trimethylpentane solution of *tert*-butyl hydroperoxide (8.4 ml, 25.4 mmol) was added. The whole mixture was stirred for 12 h at −20 °C, and then poured into a cold solution of $FeSO_4 \cdot 7H_2O$ (5 g) and tartaric acid (1.5 g) in H_2O (5 ml). Stirring was continued at 0 °C for 20 min, insoluble materials were filtered off, 30% aqueous NaOH (5 ml) was added to the filtrate, and stirring was continued for a further 30 min at 0 °C. The mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo* to leave an oil, which was



1



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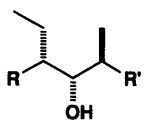

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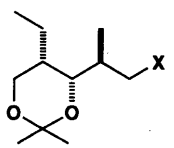
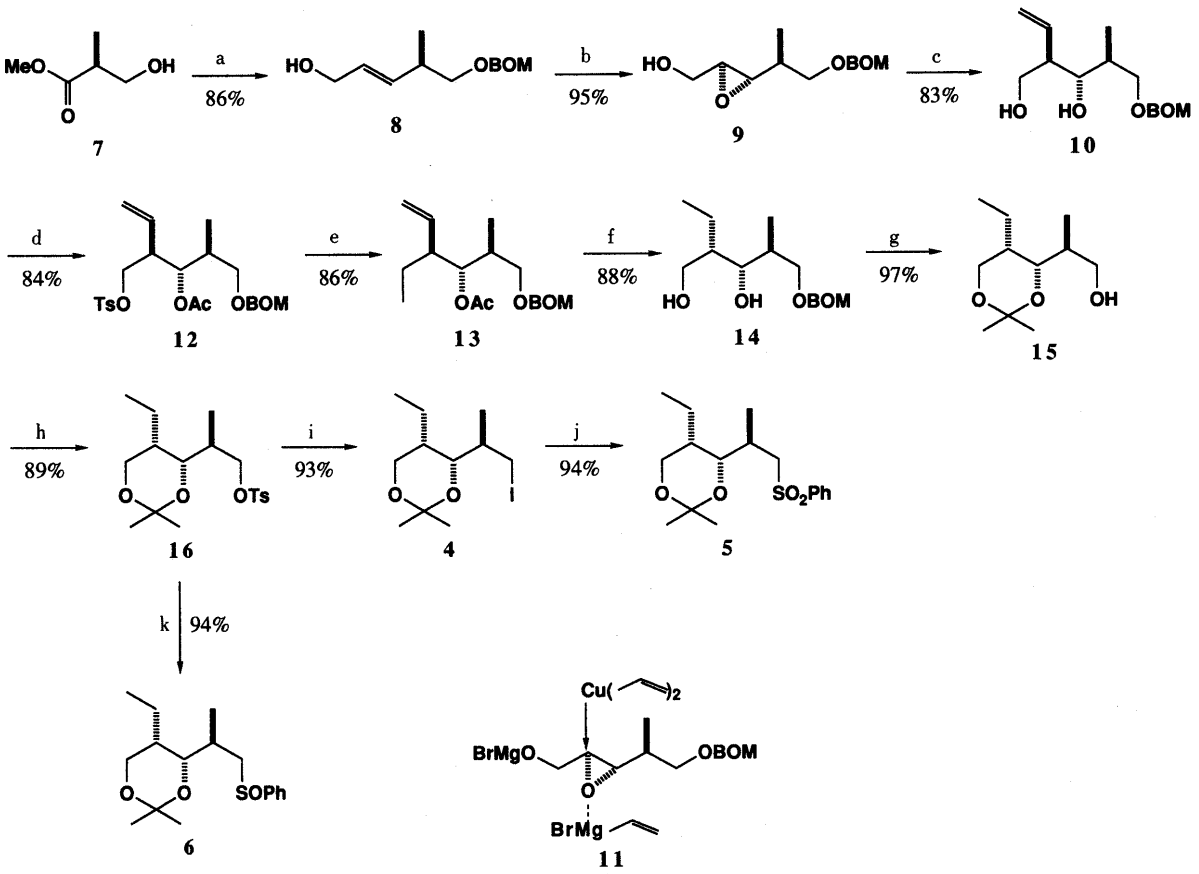


4 : X= I
5 : X= SO_2Ph
6 : X= SOPh



(a) 1) BOMCl, iso-Pr_2NEt, CH_2Cl_2; 2) $LiAlH_4$, Et_2O; 3) Swern oxid; 4) $Ph_3P{=}CHCO_2Me$, CH_2Cl_2; 5) DIBAL, CH_2Cl_2, $-78°C$ (b) (+)-DET, Ti(O iso-Pr)$_4$, *tert*-BuOOH, CH_2Cl_2, $-20°C$ (c) $CH_2{=}CHMgBr$, CuI, Et_2O, $-20°C$ (d) 1) TsCl, pyridine; 2) Ac_2O, Et_3N, DMAP, CH_2Cl_2 (e) Me_2CuLi, Et_2O, $-20°C$ (f) 1) OsO_4, NMO; 2) $NaIO_4$, MeOH-H_2O; 3) $LiAlH_4$, Et_2O (g) 1) $Me_2C(OMe)_2$, CSA, PhH; 2) liq. NH_3, Na, THF (h) TsCl, pyridine (i) NaI, MEK, $NaHCO_3$, 60°C (j) $PhSO_2Na$, DMF, 60°C (k) 1) PhSH, NaH, DMF, 70°C; 2) $NaIO_4$, MeOH-H_2O

Chart 1

chromatographed on a silica gel column (*n*-hexane–EtOAc, 3:2) to give **9** as a colorless oil (4.3 g, 95%). $[\alpha]_D^{23}$ $-16.4°$ ($c=0.97$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.02 (d, 3H, $J=7.0$ Hz), 1.72—1.82 (m, 2H), 2.95 (dd, 1H, $J=2.0$, 7.0 Hz), 3.00 (dt, 1H, $J=2.0$, 4.5 Hz), 3.61 (d, 2H, $J=5.5$ Hz), 3.63 (ddd, 1H, $J=4.5$, 7.5, 12.5 Hz), 3.92 (ddd, 1H, $J=2.5$, 5.5, 12.5 Hz), 4.61 (s, 2H), 4.78 (s, 2H), 7.27—7.36 (m, 5H). MS *m/z* (%): 221 (M^+-31, 0.1), 161 (M^+-91, 1.3), 145 (1.2), 120 (19), 107 (22), 91 (100). HR-MS Calcd for $C_{13}H_{17}O_3$: 221.1179. Found: 221.1158.

(2*R*,3*S*,4*S*)-5-Benzyloxymethoxy-4-methyl-2-vinylpentane-1,3-diol (10) A 1 M tetrahydrofuran (THF) solution of vinylmagnesium bromide (140 ml, 0.14 mol) was added dropwise to a stirred suspension of CuI (2.7 g, 14 mmol) in Et_2O (120 ml) at -30 °C under argon. After 10 min at -20 °C, a solution of **9** (4.9 g, 19 mmol) in Et_2O (30 ml) was added, and stirring was continued for 1 h. The reaction mixture was poured into cold saturated aqueous NH_4Cl, and extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and evaporated to leave an oil, which was chromatographed on a silica gel column (*n*-hexane–EtOAc, 2:3) to give **10** as a colorless oil (4.6 g, 83%). $[\alpha]_D^{21}$ $-10.2°$ ($c=0.99$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.10 (d, 3H, $J=7.5$ Hz), 1.94—2.01 (m, 1H), 2.47—2.54 (m, 1H), 3.11—3.13 (m, 1H), 3.53 (d, 1H, $J=6.0$ Hz), 3.61 (dd, 1H, $J=5.0$, 9.5 Hz), 3.65—3.69 (m, 1H), 3.75 (dd, 1H, $J=5.0$, 16.5 Hz), 3.85 (dd, 1H, $J=6.0$, 12.0 Hz), 3.88 (dd, 1H, $J=4.0$, 9.5 Hz), 4.62 (s, 2H), 4.76—4.79 (m, 2H), 5.16 (d, 1H, $J=9.0$ Hz), 5.17 (d, 1H, $J=17.0$ Hz), 5.70 (ddd, 1H, $J=9.0$, 10.5, 17.0 Hz), 7.28—7.37 (m, 5H). MS *m/z* (%): 281 (M^++1, 0.2), 249 (M^+-31, 0.1), 179 (4.3), 141 (1.2), 120 (8.8), 101 (12), 91 (100). HR-MS Calcd for $C_{15}H_{21}O_3$: 249.1492. Found: 249.1494.

(3*R*,4*S*,5*S*)-4-Acetoxy-6-benzyloxymethoxy-5-methyl-3-(4-methylphenylsulfonyloxymethyl)hex-1-ene (12) Tosyl chloride (610 mg, 3.2 mmol) was added to a stirred, ice-cold solution of **10** (690 mg, 2.46 mmol) in pyridine (15 ml) under argon. After being stirred at 10 °C for 28 h, the reaction mixture was diluted with H_2O, and extracted with CH_2Cl_2. The extract was successively washed with H_2O, 4 N HCl, H_2O, saturated aqueous $NaHCO_3$, and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (*n*-hexane–EtOAc, 3:2) to give (2*S*,3*S*,4*R*)-1-benzyloxymethoxy-2-methyl-4-(4-methylphenylsulfonyloxymethyl)hex-5-en-3-ol as a colorless oil (934 mg, 84%). $[\alpha]_D^{21}$ $-5.4°$ ($c=1.17$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.04 (d, 3H, $J=7.5$ Hz), 1.68—1.98 (m, 2H), 2.43 (s, 3H), 2.52—2.62 (m, 1H), 3.48 (dd, 1H, $J=5.0$, 7.5 Hz), 3.54 (dd, 1H, $J=5.0$, 10.0 Hz), 3.77 (dd, 1H, $J=7.5$, 9.5 Hz), 4.15 (dd, 1H, $J=7.5$, 9.5 Hz), 4.30 (dd, 1H, $J=4.0$, 10.0 Hz), 4.53—4.63 (m, 2H), 4.68—4.76 (m, 2H), 5.11 (d, 1H, $J=17.0$ Hz), 5.13 (d, 1H, $J=10.5$ Hz), 5.64 (ddd, 1H, $J=9.0$, 10.5, 17.0 Hz), 7.27—7.39 (m, 7H), 7.76—7.83 (m, 2H). MS *m/z* (%): 327 (M^+-107, 0.3), 255 (7.4), 173 (11), 155 (35), 108 (59), 91 (100), 79 (66), 54 (82). HR-MS Calcd for $C_{16}H_{23}O_5S$: 327.1268. Found: 327.1245.

Et_3N (6.2 ml, 44 mmol), 4-dimethylaminopyridine (100 mg), and Ac_2O (3.1 ml, 33 mmol) were added to a stirred solution of the above alcohol (4.8 g, 11 mmol) in CH_2Cl_2 (48 ml) at room temperature. After 10 min, MeOH (6 ml) was added to quench the reaction, and the mixture was evaporated *in vacuo*. The residue was chromatographed on a silica gel column (*n*-hexane–EtOAc, 4:1) to give **12** as a colorless oil (5.4 g, 100%). $[\alpha]_D^{22}$ $-9.2°$ ($c=1.54$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.93 (d, 3H, $J=7.0$ Hz), 1.98 (s, 3H), 2.03—2.22 (m, 1H), 2.44 (s, 3H), 2.78—2.90 (m, 1H), 3.32 (dd, 1H, $J=7.0$, 10.0 Hz), 3.60 (dd, 1H, $J=5.5$, 10.0 Hz), 3.97 (dd, 1H, $J=7.0$, 10.0 Hz), 4.06 (dd, 1H, $J=5.0$, 10.0 Hz), 4.57 (s, 2H), 4.67—4.72 (m, 2H), 4.97 (dd, 1H, $J=5.0$, 8.0 Hz), 5.16 (d, 1H, $J=17.0$ Hz), 5.17 (d, 1H, $J=11.0$ Hz), 5.56 (ddd, 1H, $J=9.0$, 11.0, 17.0 Hz), 7.28—7.39 (m, 7H), 7.65—7.81 (m, 2H). MS *m/z* (%): 339 (M^+-137, 0.4), 310 (0.6), 155 (10), 107 (26), 91 (100), 43 (44). HR-MS Calcd for $C_{17}H_{23}O_5S$: 339.1268. Found: 339.1285.

(3*S*,4*S*,5*S*)-4-Acetoxy-6-benzyloxymethoxy-3-ethyl-5-methylhex-1-ene (13) A 1.5 M Et_2O solution of MeLi (15.8 ml, 23.7 mmol) was added dropwise to a stirred suspension of CuI (2.4 g, 12.6 mmol) in Et_2O (25 ml) at −25°C under argon. After 30 min, a solution of **12** (1.0 g, 2.07 mmol) in Et_2O (10 ml) was added. The stirred reaction mixture was allowed to warm to −10 °C during 20 min, and poured into saturated aqueous NH_4Cl. After filtration to remove insoluble materials, the filtrate was extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (*n*-hexane–EtOAc, 7 : 1) to give **13** as a colorless oil (576 mg, 86%). $[\alpha]_D^{20}$ −2.0° (*c* = 0.66, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.83 (t, 3H, *J* = 7.5 Hz), 0.98 (d, 3H, *J* = 7.0 Hz), 1.13 (ddq, 1H, *J* = 7.5, 10.5, 13.5 Hz), 1.49 (ddq, 1H, *J* = 3.5, 7.5, 13.5 Hz), 2.06 (s, 3H), 2.03—2.30 (m, 2H), 3.35 (dd, 1H, *J* = 8.0, 9.5 Hz), 3.72 (dd, 1H, *J* = 4.5, 9.5 Hz), 4.59—4.62 (m, 2H), 4.70—4.78 (m, 2H), 4.89 (dd, 1H, *J* = 4.5, 8.0 Hz), 5.07 (dd, 1H, *J* = 2.0, 17.0 Hz), 5.13 (dd, 1H, *J* = 2.0, 10.5 Hz), 5.51 (ddd, 1H, *J* = 9.5, 10.5, 17.0 Hz), 7.27—7.39 (m, 5H). MS *m/z* (%): 214 (M^+ − 106, 1.0), 183 (0.4), 101 (33), 91 (100), 43 (36). HR-MS Calcd for $C_{12}H_{22}O_3$: 214.1570. Found: 214.1566.

(2*S*,3*S*,4*S*)-5-Benzyloxymethoxy-2-ethyl-4-methylpentane-1,3-diol (14) *N*-Methylmorpholine oxide (3.4 g, 25 mmol) and a 4% *tert*-BuOH solution of OsO_4 (7 ml) was added to a stirred solution of **13** (4.0 g, 12.5 mmol) in acetone (35 ml) and H_2O (6.5 ml) at room temperature. After 24 h, a solution of $Na_2S_2O_3 \cdot 5H_2O$ (4.0 g) in H_2O (20 ml) and Celite were added, and the mixture was stirred for 3 h. After filtration to remove insoluble materials, the filtrate was extracted with Et_2O. The extract was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (*n*-hexane–EtOAc, 1 : 2) to give a 3 : 1 mixture of diastereoisomer (2*RS*,3*R*,4*S*,5*S*)-4-acetoxy-6-benzyloxymethoxy-3-ethyl-5-methylhexane-1,2-diol as a colorless oil (4.1 g, 93%). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, 3H, *J* = 7.0 Hz), 0.94 (d, 3H, *J* = 7.0 Hz), 1.12—1.22 (m, 1H), 1.37—1.74 (m, 3H), 1.95 (s, 0.75H), 1.97 (s, 2.25H), 2.03—2.11 (m, 1H), 2.24—2.42 (br s, 0.75H), 2.60—2.72 (br s, 0.25H), 3.33 (dd, 0.75H, *J* = 6.0, 9.0 Hz), 3.41 (dd, 0.75H, *J* = 5.5, 11.5 Hz), 3.41—3.79 (m, 3.5H), 4.50 (s, 1.5H), 4.51 (s, 0.5H), 4.63 (s, 0.5H), 4.65 (s, 1.5H), 4.92 (dd, 0.25H, *J* = 3.5, 7.5 Hz), 5.05 (dd, 0.75H, *J* = 1.5, 10.0 Hz), 7.18—7.31 (m, 5H). MS *m/z* (%): 355 (M^+ + 1, 0.1), 248 (3.2), 157 (8.0), 125 (20), 91 (100). HR-MS Calcd for $C_{19}H_{31}O_6$: 355.2123. Found: 355.2107.

A solution of $NaIO_4$, (3.4 g, 16 mmol) in H_2O (30 ml) was added to a stirred solution of the above diol (4.0 g, 11.4 mmol) in MeOH (40 ml) and THF (40 ml) at room temperature. After 30 min, insoluble materials were filtered off, and the filtrate was extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo* to leave a crude aldehyde as a colorless oil (3.7 g), which was dissolved in Et_2O (37 ml) and added dropwise to a stirred suspension of $LiAlH_4$ (866 mg, 22.8 mmol) in Et_2O (40 ml) at 0 °C under argon. After being stirred at room temperature for 30 min, the reaction mixture was cooled to 0 °C and MeOH was added to decompose excess reagent. Then 15% aqueous NaOH (0.8 ml) and H_2O (2.4 ml) were added, the mixture was stirred for 30 min, and Na_2SO_4 was added. After 1 h, insoluble materials were filtered off with the aid of Celite, and the filtrate was evaporated *in vacuo*. The residue was chromatographed on a silica gel column (*n*-hexane–EtOAc, 1 : 2) to give **14** as a colorless oil (3.0 g, 95%). $[\alpha]_D^{21}$ +29.8° (*c* = 0.93, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.82 (d, 3H, *J* = 7.0 Hz), 0.98 (t, 3H, *J* = 7.5 Hz), 1.37—1.49 (m, 2H), 1.56—1.70 (m, 2H), 1.95—2.05 (m, 1H), 2.88 (br d, 1H, *J* = 6.5 Hz), 3.59 (dd, 1H, *J* = 8.0, 9.5 Hz), 3.70—3.91 (m, 4H), 4.61 (s, 2H), 4.76 (s, 2H), 7.27—7.40 (m, 5H). MS *m/z* (%): 283 (M^+ + 1, 0.1), 251 (M^+ − 31, 0.3), 209 (0.4), 195 (0.5), 179 (4.7), 120 (12), 108 (27), 91 (100). HR-MS Calcd for $C_{16}H_{27}O_4$: 283.1911. Found: 283.1938.

(2*S*,3*S*,4*S*)-4-Ethyl-3,5-isopropylidenedioxy-2-methylpentan-1-ol (15) 2,2-Dimethoxypropane (14.7 ml, 12 mmol) and camphorsulfonic acid (60 mg) were added to a stirred solution of **14** (3.0 g, 10.6 mmol) in benzene (15 ml) at room temperature. After 1 h, the reaction mixture was neutralized with Et_3N, and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (*n*-hexane–EtOAc, 4 : 1) to give (2*S*,3*S*,4*S*)-1-benzyloxymethoxy-4-ethyl-3,5-isopropylidenedioxy-2-methylpentane as a colorless oil (3.3 g, 97%). $[\alpha]_D^{23}$ −9.7° (*c* = 1.04, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.93 (t, 3H, *J* = 7.0 Hz), 0.97 (d, 3H, *J* = 7.0 Hz), 1.17—1.27 (m, 1H), 1.30—1.45 (m, 1H), 1.35 (s, 3H), 1.40 (s, 3H), 1.60—1.80 (m, 1H), 1.84—1.93 (m, 1H), 3.55 (dd, 1H, *J* = 6.0, 9.0 Hz), 3.66 (dd, 1H, *J* = 3.0, 9.0 Hz), 3.76 (dd, 1H, *J* = 2.0, 10.0 Hz), 3.86 (dd, 1H, *J* = 1.5, 12.0 Hz), 3.95 (ddd, 1H, *J* = 1.0, 2.5, 12.0 Hz), 4.60 (s, 2H), 4.72—4.79 (m, 2H), 7.27—7.38 (m, 5H). MS *m/z* (%): 307 (M^+ − 15, 13), 169 (2.8), 120 (15), 109 (9.4), 101 (9.7), 91 (100), 59 (40), 43 (19). HR-MS Calcd for $C_{18}H_{27}O_4$: 307.1911. Found: 307.1911.

A solution of the above oil (3.2 g, 9.94 mmol) in THF (32 ml) was added dropwise to stirred liquid NH_3 (100 ml) containing Na (2.0 g, 86.9 mmol) at −78 °C. After 10 min, NH_4Cl was added, and the reaction mixture was allowed to warm to room temperature. Insoluble materials were removed by filtration, and the filtrate was evaporated *in vacuo* to leave an oil, which was chromatographed on a silica gel column (*n*-hexane–EtOAc, 2 : 1) to give **15**[1)] as a colorless oil (2.0 g, 100%).

(2*S*,3*R*,4*R*)-2-Ethyl-1,3-isopropylidenedioxy-4-methyl-5-phenylsulfinylpentane (6) PhSH (0.86 ml, 8.4 mmol) was added to a stirred suspension of NaH [60% oil dispersion (320 mg, 8.0 mmol), washed with *n*-hexane] in 1,2-dimethoxyethane (5 ml) at room temperature. After 1 h, a solution of **16**[1)] (1.0 g, 2.8 mmol) in 1,2-dimethoxyethane (10 ml) was added dropwise. The reaction mixture was stirred at 70 °C for 1 h, then poured into H_2O, and extracted with Et_2O. The extract was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (*n*-hexane–EtOAc, 4 : 1) to give (2*S*,3*R*,4*R*)-2-ethyl-1,3-isopropylidenedioxy-4-methyl-5-phenylthiopentane as a colorless oil (809 mg, 98%). ^{1}H-NMR ($CDCl_3$) δ: 0.93 (t, 3H, *J* = 6.5 Hz), 0.95 (d, 3H, *J* = 7.5 Hz), 1.21—1.36 (m, 2H), 1.38 (s, 3H), 1.40 (s, 3H), 1.66—1.75 (m, 1H), 1.92—2.00 (m, 1H), 2.70 (dd, 1H, *J* = 8.0, 13.0 Hz), 3.39 (dd, 1H, *J* = 2.5, 13.0 Hz), 3.71 (dd, 1H, *J* = 2.0, 10.0 Hz), 3.83—3.97 (m, 2H), 7.09—7.15 (m, 1H), 7.21—7.30 (m, 2H), 7.32—7.37 (m, 2H).

A solution of $NaIO_4$ (1.7 g, 8.24 mmol) in H_2O (4 ml) was added dropwise to a stirred solution of the above sulfide (808 mg, 2.74 mmol) in MeOH (8 ml) at 0 °C. After 4 h, the reaction mixture was poured into H_2O, and extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (*n*-hexane–EtOAc, 1 : 1) to give **6** as a colorless solid (807 mg, 95%). Recrystallization from *n*-hexane gave colorless plates, mp 91—94 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.95 (t, 3H, *J* = 7.5 Hz), 1.07 (d, 3H, *J* = 7.0 Hz), 1.27—1.41 (m, 1H), 1.34 (s, 3H), 1.40 (s, 3H), 1.62—1.77 (m, 1H), 1.92—2.12 (m, 1H), 2.16—2.27 (m, 1H), 2.70 (dd, 1H, *J* = 7.5, 13.0 Hz), 2.96 (dd, 1H, *J* = 4.5, 13.0 Hz), 3.66 (dd, 1H, *J* = 2.0, 10.0 Hz), 3.86 (dd, 1H, *J* = 2.0, 11.0 Hz), 3.89 (dd, 1H, *J* = 1.0, 2.0 Hz), 7.46—7.57 (m, 3H), 7.60—7.69 (m, 2H). MS *m/z* (%): 331 (M^+ + 1, 1.3), 295 (15), 235 (34), 126 (38), 109 (44), 71 (65), 59 (100), 43 (86). HR-MS Calcd for $C_{17}H_{27}O_3S$: 311.1682. Found: 311.1691. *Anal.* Calcd for $C_{17}H_{26}O_3S$: C, 65.77; H, 8.44; S, 10.33. Found: C, 65.76; H, 8.47; S, 10.33.

References and Notes

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