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Synthetic Studies on Spiroketal Natural Products. II.[1] An Enantioselective Synthesis of (*R*)- and (*S*)-1,7-Dioxaspiro[5.5]undecane[2]

CHUZO IWATA,* MASAHIRO FUJITA, TOSHIO KUROKI, KOHJI HATTORI, SHUJI UCHIDA, and TAKESHI IMANISHI

Faculty of Pharmaceutical Sciences, Osaka University,
1-6 Yamadaoka, Suita, Osaka 565, Japan

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Both enantiomers of 1,7-dioxaspiro[5.5]undecane, a chiral compound with C_2 symmetry, were stereoselectively synthesized from an (*R*)-sulfoxide compound **8**. The reaction of menthyl (*S*)-*p*-toluenesulfinate with a Grignard reagent gave the chiral sulfoxide (**8**), which was derived to a dihydropyran (**12**) by a several-step sequence. The base-catalyzed intramolecular Michael reaction of **12** exclusively afforded a dioxaspiro product (**13**) as a single stereoisomer. An acidic treatment of **13** resulted in isomerization of the spiro center to give **14**. Desulfurization of **13** and **14** over Raney nickel in the presence of sodium hydroxide gave (*R*)- and (*S*)-1,7-dioxaspiro[5.5]undecane (*R*-**1** and *S*-**1**), respectively.

Keywords——asymmetric synthesis; chiral sulfoxide; insect pheromone; C_2-symmetry; spiroketal; intramolecular Michael addition; 1,7-dioxaspiro[5.5]undecane

In the preceding paper,[1] we reported that a base-catalyzed intramolecular Michael addition reaction of 2,3-dihydro-6-(4-hydroxybutyl)-2-methyl-5-phenylsulfinyl-4*H*-pyrans afforded 1,6-dioxaspiro compounds with extremely high stereocontrol at the spiro center. In this novel method for construction of the spiroketal framework, the crucial point is that appearance of the stereocontrol was found to be attributable to the sulfinyl stereochemistry rather than other chiralities. This observation prompted us to investigate asymmetric synthesis of other spiroketal natural products using a chiral sulfinyl group as the only chiral source.

(*R*)- and (*S*)-1,7-dioxaspiro[5.5]undecane (*R*-**1** and *S*-**1**) is a very interesting compound from the viewpoint of its axial chirality (a chiral compound with C_2-symmetry). This simple spiroketal was first isolated from the olive fruit fly, *Dacus oleae*, and characterized as a major component of sex pheromones of the fly.[3,4] Although the absolute configuration of the pheromone is still unknown at present, it may occur as a single enantiomer because studies of other bridged-ring acetal pheromones such as *exo*-brevicomin and frontalin suggested a strong correlation between chirality and pheromone activity.[5] Therefore, development of an efficient synthetic route to chiral spiroketal compounds is quite important. Concerning

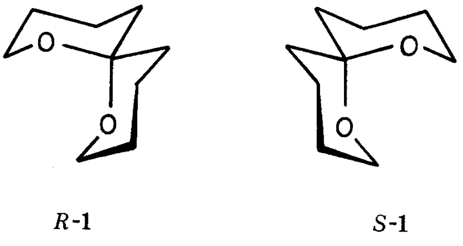

Chart 1

synthesis of **1**, there have been many reports of racemate synthesis,[6] while only two groups have succeeded in the chiral synthesis to date. Mori *et al.*[7] utilized (−)-malic acid as a chiral source and the synthesis by Redlich and Francke[8] was achieved by starting from D-glucose. In this paper, we wish to report a facile and useful stereoselective synthesis of both enantiomers (*R*-**1** and *S*-**1**) of 1,7-dioxaspiro[5.5]undecane by asymmetric induction from a single enantiomeric sulfinyl chiral source.

In general, there are two methods to obtain chiral sulfoxide compounds: one is asymmetric oxidations of sulfides[9] and the other is transformation from readily available chiral sulfinates.[10] The former seems to be inappropriate for preparation of enantiomerically pure sulfoxides because of difficulty in separating the enantiomers. Therefore, we adopted the latter for the present investigations. According to the known procedure,[11] (−)-menthyl (*S*)-*p*-toluenesulfinate (**2**), $[\alpha]_D$ −200°, was prepared by the reaction of *p*-toluenesulfinyl chloride and (−)-menthol, followed by repeated fractional recrystallizations. The chiral sulfoxide (**3**), prepared from **2** and methylmagnesium iodide by the literature method,[12] was allowed to react with lithium diisopropylamide (LDA) followed by treatment with the ester (**4**) which was obtained from δ-valerolactone. The keto sulfoxide (**5**) was isolated in 79% yield. In order to transform **5** into the alkylated product (**6**), the alkylation with **7** was tried under various conditions, but all the efforts failed. Thus, an alternative route to get **6** was examined. Namely, the route involves initial alkylation followed by acylation. The reaction of **2** with the Grignard reagent derived from 4-(tetrahydropyran-2-yl)oxybutyl chloride[13] in tetrahydrofuran (THF) at −10 °C gave the sulfoxide (**8**) in quantitative yield. The protecting group in **8**

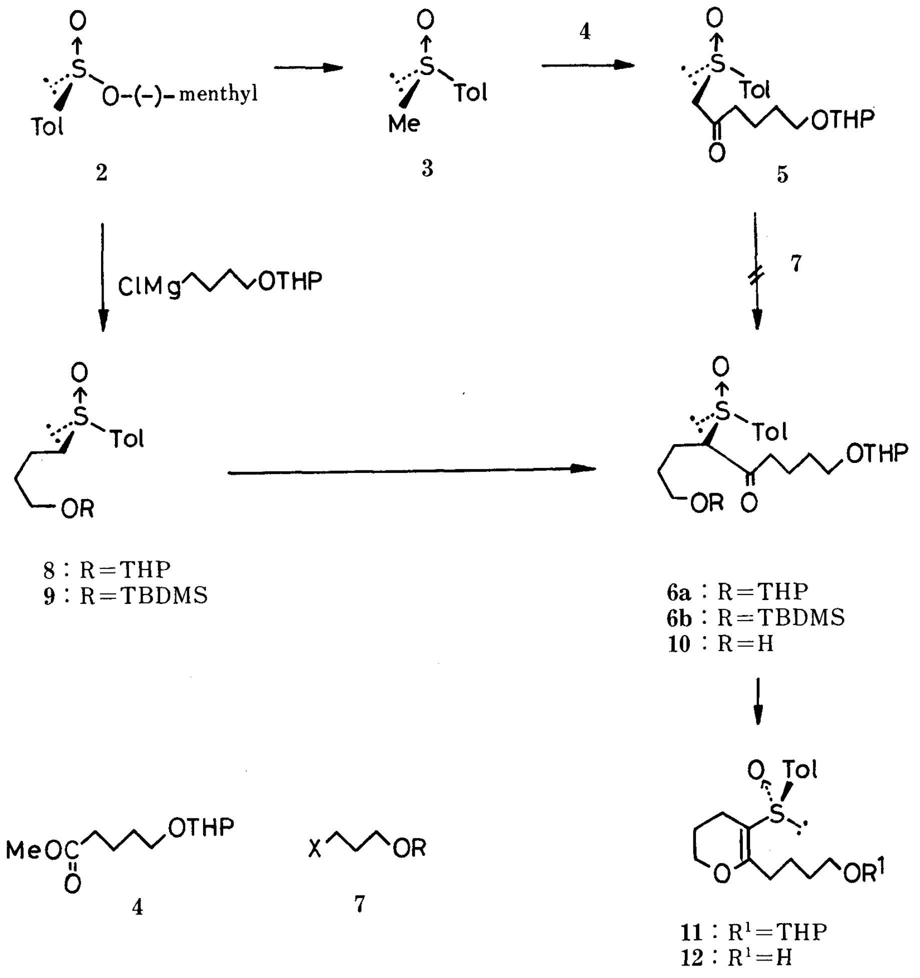

Chart 2

was exchanged from the tetrahydropyranyl group to *tert*-butyldimethylsilyl in the usual manner, and the formed **9** (86% yield), $[\alpha]_D^{27}$ +99.2° ($c=1.00$, $CHCl_3$), was subjected to condensation with **4**. The lithio salt of **9** was reacted with 1.5eq of **4** in THF–hexamethylphosphoramide (HMPA) at 0 °C to afford the desired product (**6b**) in 56% yield together with the unchanged starting material (39%). Treatment of **6b** with tetra-*n*-butylammonium fluoride in THF resulted in chemoselective deprotection to afford the mono alcohol (**10**) in 94% yield. On reaction with *p*-toluenesulfonic acid (TSA) and anhydrous magnesium sulfate in methylene chloride, **10** easily gave the dihydropyran (**11**; 72%), which was converted into the alcohol (**12**), $[\alpha]_D^{19}$ −37.2° ($c=0.87$, $CHCl_3$), in 79% yield.

Under the same conditions (potassium hydride in THF at room temperature) as those previously reported,[1] the hydroxyalkylated dihydropyran (**12**) easily underwent a spiroketal

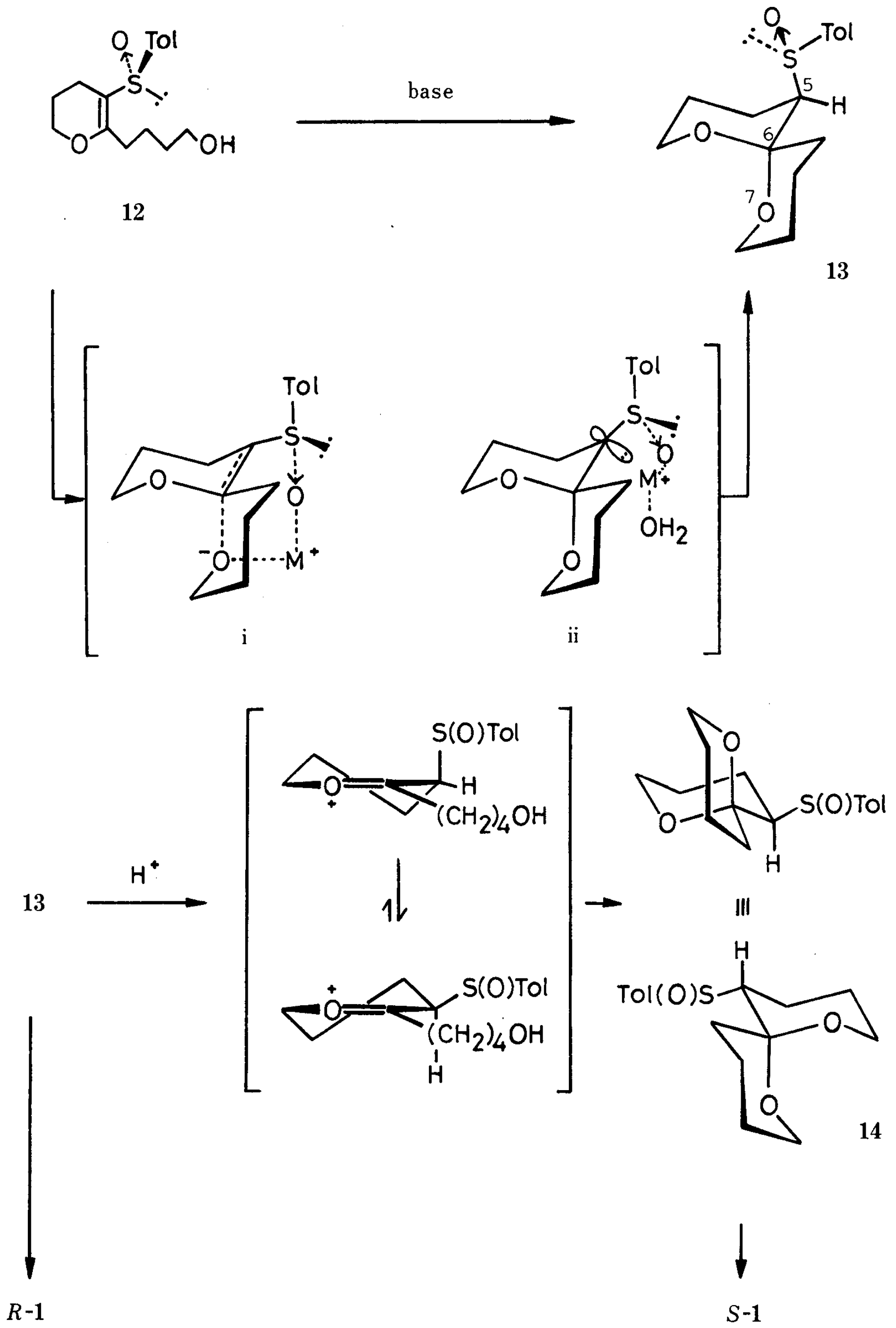

Chart 3

formation reaction, affording the spiroketal product (**13**), mp 108—109 °C; $[\alpha]_D^{16}$ +7.0° (c= 0.80, $CHCl_3$), in 66% yield as a single stereoisomer. A similar treatment of **12** with sodium hydride instead of potassium hydride resulted in a somewhat improved yield of **13** (77%). As discussed in the preceding paper, the observed high stereocontrol at the C-5 and C-6 centers can be well interpreted in terms of possible intermediates (i and ii) of this reaction. In the intermediate i, chelation between the side-chain oxido anion and the sulfinyl oxygen should strictly control the direction of the newly formed C–O bond. In the next step, the α-sulfinyl carbanion would be protonated kinetically from the same side of the sulfinyl oxygen *via* intermediate ii. The expected stereochemistry of **13** was consisted with the proton nuclear magnetic resonance (^{1}H-NMR) spectrum, which exhibited the C-5 proton signal at 2.51 ppm as a doublet of doublets (J=2, 5 Hz). The signal pattern with the same coupling constants indicates that the proton is situated equatorially on the tetrahydropyran ring and therefore the sulfinyl group occupies an axial position. From the consideration that a strong anomeric effect fixes the preferred conformation of a 1,7-dioxaspiro[5.5]undecane ring system to one of two possible twin-chair conformations, the sulfinyl group must be *trans* to the C_6–O_7 bond.

Thus, the stereoselectively obtained spiroketal (**13**), possessing the axially orientated sulfinyl group, seems to be a thermodynamically less-stable isomer. In fact, on treatment with 1 eq of TSA in methanol at room temperature, isomerization at the spiro center in **13** took place and the other isomer (**14**), mp 113—114 °C; $[\alpha]_D^{16}$ +92.6° (c=0.83, $CHCl_3$), was isolated in 69% yield.

Finally, by removal of the sulfinyl group by treatment with Raney nickel (W-2) in methanol in the presence of sodium hydroxide, **13** and **14** were converted into (*R*)- and (*S*)-1,7-dioxaspiro[5.5]undecane (*R*-**1** and *S*-**1**), respectively, in good yields. The spectral properties of the synthetic products coincided with those reported in the literature.[7] Mori *et al.* reported specific optical rotations of $[\alpha]_D^{21}$ −121° (c=1.84, pentane) and $[\alpha]_D^{21}$ +119° (c=1.41, pentane) for >99.5% optical purity of *R*-**1** and 92% purity of *S*-**1**, respectively.[7] The observed specific optical rotations of the present products, $[\alpha]_D^{25}$ −128° (c=0.503, pentane) for *R*-**1** and $[\alpha]_D^{24}$ +123° (c=0.234, pentane) for *S*-**1**, indicate that their enantiomeric purities are extremely high.

In conclusion, using only the single chirality of the sulfinyl group both enantiomers of 1,7-dioxaspiro[5.5]undecane were efficiently synthesized in highly pure forms.

Experimental

All melting and boiling points are uncorrected. Infrared (IR) spectra were recorded with a Hitachi 260-10 spectrometer. ^{1}H-NMR spectra were measured with a Hitachi R-60 (60 MHz), a Hitachi R-22 (90 MHz), a JEOL JNM-FX-90Q (90 MHz), or a JEOL JNM-GX-500 instrument. ^{13}C-Nuclear magnetic resonance (^{13}C-NMR) spectra were measured with a JEOL JNM-FX-90Q (22.5 MHz). The chemical shifts are given as δ values with tetramethylsilane as an internal standard. Optical rotations were recorded with a JASCO DIP-360 polarimeter. Electron impact, chemical impact, and high-resolution mass spectra (EI-MS, CI-MS, and high MS) were obtained with a Shimadzu QP-1000 or a JEOL NMS D-300 mass spectrometer. For column chromatography, Aluminiumoxid 90 or Kieselgel 60 (E. Merck) was used. After drying over anhydrous sodium sulfate or magnesium sulfate, all organic extracts were concentrated under reduced pressure.

Methyl 4-[(Tetrahydropyran-2-yl)oxy]valerate (4)——Methyl 4-hydroxyvalerate was prepared from Mg (290 mg, 12 mmol) and δ-valerolactone (15 g, 0.15 mol) according to the known method.[14] A mixture of the crude ester, 2,3-dihydro-4*H*-pyran (42 ml, 0.46 mol), TSA (10 mg), and dry CH_2Cl_2 (100 ml) was stirred at room temperature for 1.5 h. The reaction mixture was treated with 1 drop of saturated $NaHCO_3$, washed with brine, and dried. Evaporation of the solvent left an oil, which was distilled under reduced pressure to give **4** (27 g, 83%) as a colorless oil, bp 103 °C (3.5 mmHg). *Anal.* Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 61.31; H, 9.40. IR ($CHCl_3$) cm^{-1}: 1730, 1440, 1355, 1170. ^{1}H-NMR ($CDCl_3$) δ: 1.3—1.9 (10H, m), 2.26 (2H, t, J=7 Hz, CH_2COO), 3.1—3.9 (4H, m, $OCH_2 \times 2$), 3.60 (1H, br s, anomeric H). EI-MS m/z (%): 131 (M^+−85, 4.8), 115 (68), 85 (100).

(R_S)-6-(Tetrahydropyran-2-yl)oxy-1-(*p*-tolyl)sulfinyl-2-hexanone (5)——A solution of *n*-BuLi in hexane (1.6 M, 4.5 ml, 7.2 mmol) was added dropwise to a stirred solution of Et_2NH (0.67 ml, 6.5 mmol) in dry THF (16 ml) at

−40 °C and the mixture was stirred at 0 °C for 1.5 h. A solution of (*R*)-methyl *p*-tolyl sulfoxide (**3**; 0.50 g, 3.2 mmol) in dry THF (16 ml) was added to the above mixture at −40 °C and the resulting mixture was further stirred at 0 °C for 30 min. A solution of the ester (**4**; 1.1 g, 4.9 mmol) in dry THF (8 ml) was added to the mixture at −40 °C and the whole was stirred at 0 °C for 30 min and then under reflux for 1 h. The reaction mixture was neutralized with saturated NH_4Cl and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$. The combined organic layers were washed with brine, dried, and concentrated. The oily residue was chromatographed on silica gel with AcOEt–hexane (4 : 1) to give **5** (860 mg, 79%) as a colorless oil and the unchanged starting material (0.10 g). $[\alpha]_D^{25}$ +124.3° (c=3.0, $CHCl_3$). IR ($CHCl_3$) cm^{-1}: 1710, 1600, 1500, 1030. ^{1}H-NMR ($CDCl_3$) δ: 1.0—2.0 (10H, m), 2.42 (3H, s, Ar-CH_3), 2.52 (2H, t, J=6 Hz, C_3-H × 2), 3.2—4.0 (4H, m, OCH_2 × 2), 3.79 and 3.86 (2H, ABq, J=13 Hz, C_1-H × 2), 4.53 (1H, br s, anomeric H), 7.28 (2H, d, J=8 Hz, Ar-H × 2), 7.51 (2H, d, J=8 Hz, Ar-H × 2). EI-MS m/z (%): 253 (M^+ −85, 1.5), 237 (15), 199 (1.5), 139 (100).

(R_S)-1-(Tetrahydropyran-2-yl)oxy-4-[(*p*-tolyl)sulfinyl]butane (8)——A solution of 4-[(tetrahydropyran-2-yl)-oxy]butylmagnesium chloride, prepared from Mg (215 mg, 8.83 mmol) and 4-[(tetrahydropyran-2-yl)oxy]butyl chloride[13) (1.70 g, 8.8 mmol), in dry THF (*ca.* 10 ml) was added dropwise to a stirred solution of **2** (866 mg, 2.9 mmol) in dry THF (20 ml) at −10 °C over 30 min, and the resulting mixture was further stirred at the same temperature for 2 h. Saturated NH_4Cl was added and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$. The combined organic layers were washed with brine, dried, and concentrated. The oily residue was chromatographed on silica gel with hexane–AcOEt (2 : 1) to give **8** (872 mg, 100%) as a colorless oil. $[\alpha]_D^{22}$ +111.0° (c=1.02, $CHCl_3$). *Anal.* Calcd for $C_{16}H_{24}O_3S$: C, 64.83; H, 8.16; S, 10.82. Found: 64.43; H, 8.60; S, 11.02. IR ($CHCl_3$) cm^{-1}: 1600, 1030. ^{1}H-NMR ($CDCl_3$) δ: 1.4—2.0 (10H, m), 2.38 (3H, s, Ar-CH_3), 2.82 (2H, t, J=7.5 Hz, C_4-H × 2), 3.2—4.0 (4H, m, OCH_2 × 2), 4.52 (1H, br s, anomeric H), 7.24 (2H, d, J=8.5 Hz, Ar-H × 2), 7.45 (2H, d, J=8.5 Hz, Ar-H × 2).

(R_S)-1-(*tert*-Butyldimethylsilyl)oxy-4-[(*p*-tolyl)sulfinyl]butane (9)——A solution of **8** (872 mg, 2.9 mmol) in MeOH (10 ml) was adjusted to pH 4 by addition of TSA and the mixture was stirred at room temperature for 4.5 h. After neutralization of the mixture with saturated $NaHCO_3$, MeOH was evaporated off and the residue was extracted with $CHCl_3$. The extract was washed with brine, dried, and concentrated. The oily residue was chromatographed on silica gel with AcOEt–EtOH (4 : 1) to give (R_S)-4-[(*p*-tolyl)sulfinyl]butan-1-ol (579 mg, 93%) as a colorless oil. $[\alpha]_D^{20}$ +189° (c=0.95, $CHCl_3$). IR ($CHCl_3$) cm^{-1}: 3380, 1600, 1495, 1015. ^{1}H-NMR ($CDCl_3$) δ: 1.4—1.9 (4H, m), 2.40 (3H, s, Ar-CH_3), 2.80 (1H, br s, OH), 2.83 (2H, t, J=7.5 Hz, C_4-H × 2), 3.63 (2H, t, J=6 Hz, C_1-H × 2), 7.26 (2H, d, J=8.5 Hz, Ar-H × 2), 7.47 (2H, d, J=8. 5Hz, Ar-H × 2). EI-MS m/z (%): 194 (M^+ −18, 1.3), 140 (100).

A mixture of the above alcohol (8.20 g, 39 mmol), imidazole (6.5 g, 95 mmol), TBDMSCl (7.2 g, 48 mmol), and dry DMF (30 ml) was stirred at room temperature for 4 h. The solvent was evaporated off at 40—50 °C and the residue was diluted with water. The resulting mixture was extracted with $CHCl_3$. The extract was washed with brine, dried, and concentrated. The oily residue was chromatographed on silica gel with AcOEt–hexane (2 : 3) to give **9** (11.6 g, 92%) as a colorless oil. $[\alpha]_D^{27}$ +99.2° (c=1.00, $CHCl_3$). *Anal.* Calcd for $C_{17}H_{30}O_2SSi$: C, 62.53; H, 9.26. Found: C, 62.31; H, 9.54. IR ($CHCl_3$) cm^{-1}: 1600, 1495, 1255, 1030. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (6H, s, $SiCH_3$ × 2), 0.82 (9H, s, $C(CH_3)_3$), 1.4—1.9 (4H, m), 2.37 (3H, s, Ar-CH_3), 2.74 (2H, t, J=7 Hz, C_4-H × 2), 3.56 (2H, t, J=5.5 Hz, C_1-H × 2), 7.21 (2H, d, J=8.5 Hz, Ar-H × 2), 7.42 (2H, d, J=8.5 Hz, Ar-H × 2). EI-MS m/z (%): 311 (M^+ −15, 4.0), 73 (100).

(R_S)-1-[*tert*-Butyldimethylsilyl)oxy-9-(tetrahydropyran-2-yl)oxy-4-[(*p*-tolyl)sulfinyl]nonan-5-one (6b)——A solution of **9** (2.00 g, 6.1 mmol) in dry THF (20 ml) was added dropwise to a stirred solution of $LiNEt_2$ in THF [prepared from Et_2NH (1.3 ml, 13 mmol) and BuLi (1.6 M in hexane, 7.9 ml, 13 mmol) in dry THF (20 ml)] at −40 °C over 10 min. Stirring was continued at the same temperature for 30 min. HMPA (2.1 ml, 12 mmol) and then a dry THF (10 ml) solution of **4** (4.1 g, 19 mmol) were added to the above solution at −70 °C and the reaction mixture was gradually warmed to 0 °C. After being stirred overnight at 0 °C, the reaction mixture was treated with saturated NH_4Cl (*ca.* 5 ml) and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ and the combined organic layers were washed with brine. The dried solvent was evaporated off to leave an oil, which was chromatographed on silica gel with hexane–AcOEt (1 : 1) to give a mixture of **6b** and the starting material (4.8 g). Chromatography of the mixture by the use of a Lobar column (LiChroprep Si 60) with hexane–AcOEt (5 : 4) afforded **6b** (1.75 g, 56%) as a colorless oil from the foregoing fraction and the starting material (0.79 g) from the second fraction. Based on the consumed starting material, the yield of **6b** was 92%. $[\alpha]_D^{28}$ +37.4° (c=1.00, $CHCl_3$). *Anal.* Calcd for $C_{27}H_{46}O_5SSi$: C, 63.49; H, 9.08. Found: C, 63.46; H, 9.22. IR ($CHCl_3$) cm^{-1}: 1707, 1600, 1255, 1025. ^{1}H-NMR ($CDCl_3$) δ: 0.00 and 0.04 (total 6H, each s, $SiCH_3$ × 2), 0.87 and 0.90 (total 9H, each s, $C(CH_3)_3$), 1.4—2.1 (14H, m), 2.42 (3H, s, Ar-CH_3), 2.53 (2H, br t, J=6 Hz, C_6-H × 2), 3.2—4.0 (7H, m), 4.54 (1H, br s, anomeric H), 7.2—7.5 (4H, m, Ar-H × 4). EI-MS m/z (%): 453 (M^+ −57, 0.2), 85 (100).

(R_S)-1-Hydroxy-9-(tetrahydropyran-2-yl)oxy-4-[(*p*-tolyl)sulfinyl]nonan-5-one (10)——A THF solution of Bu_4NF (1 M; 0.85 ml, 0.85 mmol) was added to a stirred solution of **6b** (218 mg, 0.43 mmol) in dry THF (1.2 ml) at 0 °C. The mixture was allowed to stand at room temperature for 1 h and then poured into ice water. The resulting mixture was extracted with $CHCl_3$ and the extract was washed with brine. The dried organic layer was concentrated to leave an oil, which was chromatographed on silica gel with AcOEt–EtOH (6 : 1) to give **10** (160 mg, 94%) as a colorless oil. $[\alpha]_D^{27}$ +45.8° (c=1.01, $CHCl_3$). *Anal.* Calcd for $C_{21}H_{32}O_5S$: C, 63.61; H, 8.13; S, 8.08. Found: C, 63.44; H, 8.34; S, 8.34. IR ($CHCl_3$) cm^{-1}: 3420, 1708, 1600, 1495, 1030. ^1H-NMR ($CDCl_3$) δ: 1.2—2.1 (14H, m), 2.40 (3H, s, Ar-CH_3), 2.48 (2H, t, $J=8$ Hz, C_6-H $\times$ 2), 2.76 (1H, br s, OH), 3.2—4.1 (7H, m), 4.52 (1H, br s, anomeric H), 7.26 (2H, br d, $J=8.5$ Hz, Ar-H $\times$ 2), 7.42 (2H, br d, $J=8.5$ Hz, Ar-H $\times$ 2). EI-MS m/z (%): 295 (M^+-101, 1.9), 85 (100).

(R_S)-3,4-Dihydro-6-[4-(tetrahydropyran-2-yl)oxybutyl]-5-(*p*-tolyl)sulfinyl-2*H*-pyran (11)——A mixture of **10** (1.23 g, 3.1 mmol), anhydrous $MgSO_4$ (740 mg, 6.2 mmol), TSA (10 mg), and dry CH_2Cl_2 (60 ml) was stirred at room temperature for 1 h and then neutralized with saturated $NaHCO_3$. The CH_2Cl_2 layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined extracts were washed with brine, dried, and concentrated. The oily residue was chromatographed on silica gel to give **11** (840 mg, 72%) from the fraction eluted with AcOEt–hexane (2 : 1) and the starting material (265 mg) from the fraction eluted with AcOEt–EtOH (6 : 1). Based on the consumed starting material, the yield of **11** was 92%. $[\alpha]_D^{20}$ $-29.1°$ ($c=1.56$, $CHCl_3$). IR ($CHCl_3$) cm^{-1}: 1627, 1600, 1240, 1030. ^1H-NMR ($CDCl_3$) δ: 1.2—2.1 (12H, m), 2.2—2.9 (4H, m), 2.38 (3H, s, Ar-CH_3), 3.2—4.3 (6H, m), 4.56 (1H, br s, anomeric H), 7.22 (2H, d, $J=9$ Hz, Ar-H $\times$ 2), 7.40 (2H, d, $J=9$ Hz, Ar-H $\times$ 2). EI-MS m/z (%): 294 (M^+-84, 4.2), 85 (100). CI-MS m/z (%): 379 (M^++1, 3.1), 58 (100).

(R_S)-3,4-Dihydro-6-(4-hydroxybutyl)-5-(*p*-tolyl)sulfinyl-2*H*-pyran (12)——A solution of **11** (1.67 g, 4.4 mmol) in MeOH (70 ml) was adjusted to pH 4 by addition of TSA (*ca.* 10 mg) and the mixture was stirred at room temperature until the starting material had disappeared on TLC (40 min). After neutralization with saturated $NaHCO_3$, MeOH was evaporated off and the residue was diluted with water (10 ml). The resulting mixture was extracted with $CHCl_3$ and the extract was washed with brine. The dried extract was concentrated to leave an oil, which was chromatographed on silica gel with AcOEt–EtOH (10 : 1) to give **12** (1.03 g, 79%) as a colorless oil. $[\alpha]_D^{19}$ $-37.2°$ ($c=0.87$, $CHCl_3$). IR ($CHCl_3$) cm^{-1}: 3380, 1628, 1597, 1022. ^1H-NMR ($CDCl_3$) δ: 1.2—2.0 (6H, m), 2.1—2.5 (2H, m, C_4-H $\times$ 2), 2.36 (3H, s, Ar-CH_3), 2.65 (2H, t, $J=7$ Hz, 6-CH_2), 2.96 (1H, br s, OH), 3.63 (2H, t, $J=6$ Hz, $C\underline{H}_2OH$), 3.7—4.2 (2H, m, C_2-H $\times$ 2), 7.18 (2H, d, $J=9$ Hz, Ar-H $\times$ 2), 7.34 (2H, d, $J=9$ Hz, Ar-H $\times$ 2). EI-MS m/z (%): 294 (M^+, 26), 277 (100). High MS Calcd for $C_{16}H_{22}O_3S$: 294.129. Found: 294.129.

(5*R*,6*R*,S_S)-5-(*p*-Tolyl)sulfinyl-1,7-dioxaspiro[5.5]undecane (13)——a) By the Use of KH: A solution of **12** (87.2 mg, 0.30 mmol) in dry THF (2.5 ml) was added to a stirred suspension of KH (86 mg, 2.1 mmol) in dry THF (5.5 ml) at 0 °C and the mixture was further stirred at room temperature for 1 h. After careful addition of wet ether (3 ml), the reaction mixture was diluted with $CHCl_3$. The organic layer was washed with brine, dried, and concentrated. The residue was chromatographed on alumina with ether–EtOH (20 : 1) to give **13** (57 mg, 66%) as colorless needles, mp 108—109 °C (from benzene–hexane). $[\alpha]_D^{16}$ $+7.0°$ ($c=0.80$, $CHCl_3$). *Anal.* Calcd for $C_{16}H_{22}O_3S$: C, 65.28; H, 7.53; S, 10.89. Found: C, 65.16; H, 7.58; S, 10.66. IR (CCl_4) cm^{-1}: 1600, 1495, 1160, 1090, 1060, 1040, 1035. ^1H-NMR (CCl_4) δ: 0.9—2.3 (10H, m), 2.40 (3H, s, Ar-CH_3), 2.51 (1H, dd, $J=2$, 5 Hz, 5-H), 3.4—3.9 (4H, m), 7.21 (2H, d, $J=8.5$ Hz, Ar-H), 7.51 (2H, d, $J=8.5$ Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 17.67 (t), 20.25 (t), 20.54 (t), 20.69 (q), 24.35 (t), 33.80 (t), 59.16 (t), 60.33 (t), 70.08 (d), 95.38 (s), 125.17 (d), 129.12 (d), 139.07 (s), 141.26 (s). EI-MS m/z (%): 279 (M^+-15, 1.1), 140 (100). CI-MS m/z (%): 295 (M^++1, 2.8), 155 (100).

b) By the Use of NaH: A solution of **12** (50.0 mg, 0.17 mmol) in dry THF (2 ml) was added to a stirred suspension of NaH (60% in mineral oil; 34 mg, 0.85 mmol) [prewashed with dry hexane] in dry THF (3 ml) at 0 °C and the mixture was further stirred at room temperature for 40 min. Work-up as described above gave **13** (38.3 mg, 77%), which was identical with the sample obtained in a).

(5*R*,6*S*,S_S)-5-(*p*-Tolyl)sulfinyl-1,7-dioxaspiro[5.5]undecane (14)——A mixture of **13** (85.6 mg, 0.291 mmol), TSA (55.0 mg, 0.289 mmol), and MeOH (4 ml) was stirred at room temperature for 24 h. After neutralization with saturated $NaHCO_3$, the solvent was evaporated off and the residue was taken up in $CHCl_3$. The $CHCl_3$ layer was washed with brine, dried, and concentrated to leave an oil, which was passed through a short silica gel column with AcOEt–hexane (1 : 1). The crude crystalline product (85.4 mg), which contained **14** and **13** in 96 : 4 ratio, was recrystallized from benzene–hexane (1 : 5) to afford **14** (59.2 mg, 69%) as colorless needles, mp 113—114 °C. $[\alpha]_D^{16}$ $+92.6°$ ($c=0.83$, $CHCl_3$). *Anal.* Calcd for $C_{16}H_{22}O_3S$: C, 64.28; H, 7.53; S, 10.89. Found: C, 64.91; H, 7.55; S, 11.40. IR ($CHCl_3$) cm^{-1}: 1596, 1495, 1197, 1144, 1090, 1065, 1039. ^1H-NMR (CCl_4) δ: 0.9—2.0 (9H, m), 2.0—2.8 (1H, m, C_7-H), 2.35 (3H, s, Ar-CH_3), 2.49 (1H, dd, $J=4.5$, 9.5 Hz, C_5-H), 3.3—3.7 (4H, m), 7.11 (2H, d, $J=8$ Hz, Ar-H $\times$ 2), 7.38 (2H, d, $J=8$ Hz, Ar-H $\times$ 2). ^{13}C-NMR ($CDCl_3$) δ: 18.33 (t), 19.55 (t), 21.21 (q), 24.77 (t), 25.16 (t), 33.35 (t), 58.75 (t), 60.70 (t), 69.38 (d), 95.37 (s), 126.13 (d), 129.16 (d), 139.30 (s), 141.15 (s). EI-MS m/z (%): 294 (M^+, 0.2), 155 (100).

(*R*)-1,7-Dioxaspiro[4.5]undecane (*R*-1)——A mixture of **13** (90.0 mg, 0.306 mmol), NaOH (24.5 mg, 0.613 mmol), Raney Ni (W-2, *ca.* 1.0 g), and dry MeOH (9 ml) was stirred at 50 °C for 3 h. The catalyst was filtered off and washed thoroughly with ether. The filtrate was concentrated carefully and the residue was passed through a short alumina column with pentane to give *R*-**1** (37.4 mg, 78%) as a colorless oil, bp 68—70 °C (bath temperature) (25 mmHg). $[\alpha]_D^{25}$ $-128°$ ($c=0.503$, pentane) [lit.[7] $[\alpha]_D^{19}$ $-122.8°$ ($c=3.2$, pentane)]. IR (CCl_4) cm^{-1}: 1193, 1099, 1067, 1042. ^1H-NMR (C_6D_6) δ: 1.0—2.2 (12H, m), 3.2—3.8 (4H, m, OCH_2 $\times$ 2). ^{13}C-NMR (C_6D_6) δ: 19.03 (t), 25.79 (t), 36.19 (t), 60.16 (t), 94.87 (s). EI-MS m/z (%): 156 (M^+, 17), 128 (13), 101 (100). High MS Calcd for $C_9H_{16}O_2$: 156.1151. Found: 156.1154.

(*S*)-1,7-Dioxaspiro[5.5]undecane (*S*-1)——A mixture of **14** (59.2 mg, 0.201 mmol), NaOH (16.0 mg, 0.400 mmol), Raney Ni (W-2, *ca.* 0.7 g), and dry MeOH (6 ml) was stirred at 50 °C for 2 h. Work-up as described for

R-**1** gave *S*-**1** (26.1 mg, 83%) as a colorless oil, bp 73 °C (bath temperature) (39 mmHg). $[\alpha]_D^{24}$ +123° (c=0.234, pentane). All spectral data (IR, ^{1}H-NMR, ^{13}C-NMR, MS) were identical with those of *R*-**1**. High MS Calcd for $C_9H_{16}O_2$: 156.1151. Found: 156.1165.

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References and Notes

1) Part I: C. Iwata, K. Hattori, T. Kuroki, S. Uchida, and T. Imanishi, *Chem. Pharm. Bull.*, **36**, 2909 (1988).
2) A part of this work appeared in a preliminary communication: C. Iwata, M. Fujita, K. Hattori, S. Uchida, and T. Imanishi, *Tetrahedron Lett.*, **26**, 2221 (1985).
3) R. Baker, R. Herbert, P. E. Howse, and O. T. Jones, *J. Chem. Soc., Chem. Commun.*, **1980**, 52.
4) P. Gariboldi, L. Verotta, and R. Fanelli, *Experientia*, **39**, 502 (1983).
5) D. L. Wood, L. E. Browne, B. Ewing, K. Lindahl, W. D. Bedard, P. E. Tilden, K. Mori, G. B. Pitman, and P. R. Hughes, *Science*, **192**, 896 (1976).
6) R. Amouroux, *Heterocycles*, **22**, 1489 (1984); S. V. Ley and B. Lygo, *Tetrahedron Lett.*, **25**, 113 (1984) and references cited therein.
7) K. Mori, T. Uematsu, H. Watanabe, K. Yanagi, and M. Minobe, *Tetrahedron Lett.*, **25**, 3875 (1984); K. Mori, H. Watanabe, K. Yanagi, and M. Minobe, *Tetrahedron*, **41**, 3663 (1985).
8) H. Redlich and W. Francke, *Angew. Chem. Int. Ed. Engl.*, **23**, 519 (1984).
9) Cf. P. Pitchen and H. B. Kagan, *Tetrahedron Lett.*, **25**, 1049 (1984); F. Di Furia, G. Moden, and R. Seraglia, *Synthesis*, **1984**, 325; T. Komori and T. Nonaka, *J. Am. Chem. Soc.*, **106**, 2656 (1984).
10) Cf. K. K. Andersen, *Tetrahedron Lett.*, **1962**, 93; C. Mioskowski and G. Solladie, *Tetrahedron*, **36**, 227 (1980).
11) G. Solladie, J. Hutt, and A. Girardin, *Synthesis*, **1987**, 173.
12) G. Solladie, *Synthesis*, **1981**, 185.
13) D. Starr and R. M. Hixon, "Organic Syntheses," Coll. Vol. II, ed. by A. H. Blatt, John Wiley, and Sons, Inc., New York, 1943, p. 571.
14) Y. Muramoto, I. Ichimoto, and H. Ueda, *Nippon Nogeikagaku Kaishi*, **48**, 525 (1974).