# Synthetic Studies on Spiroketal Natural Products. IV.[1] A Stereoselective Synthesis of (3*S*,5*S*,6*R*,9*R*,$R_S$)-3-Benzyloxymethyl-9-hydroxymethyl-5-(*p*-tolyl)sulfinyl-1,7-dioxaspiro[5.5]undecane, a Key Intermediate for Talaromycins[2]

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**A dioxaspiro compound (4), a common intermediate for the synthesis of talaromycin A (1) and (−)-talaromycin B (2), was synthesized by two routes utilizing two kinds of asymmetric recognition of prochiral 1,3-diols controlled by sulfinyl chirality, that is, firstly by acid promoted diastereoselective C–O bond fission of the bicyclic acetal (7) to give the dihydropyran derivative (6), which has an *S*-hydroxymethyl group at the C3-position (7→6), and secondly by diastereoselective intramolecular Michael addition of the diol (5), in which the three chiral centers at C5, C6, C9 were constructed in one step (5→4).**

**Keywords** asymmetric recognition; prochiral 1,3-diol; sulfinyl chirality; Michael addition; talaromycin

In the course of our synthetic studies of natural products prossessing a dioxaspiro skeleton, we directed our attention to the relatively complex compounds, talaromycins A and B, as synthetic targets.[3] They have four asymmetric carbon centers and exhibit potassium current blocking activity, leading to muscle dysfunction. Our synthetic analysis is outlined in Chart 1.

We assumed that compound **4** would be an important common intermediate for the synthesis of (+)-talaromycin A (**1**) and (−)-talaromycin B (**2**). Compound **4** is thermodynamically unstable, furnishing its stable isomer (**3**) by acid-catalyzed isomerization. Although this approach appears to be thermodynamically difficult, it was accomplished by the diastereoselective spiroannulation of **5** controlled by a sulfinyl chirality.[2] This transformation (**5**→**4**) can be performed by two routes, *i.e.*, by remote-controlled asymmetric differentiation of the prochiral 1,3-diol (direct differentiation) and by diastereoselective Michael addition to the vinylic sulfoxide from the *si*-face of the dihydropyran ring.

Asymmetric induction at the C3-position of **6** would be accomplished by diastereoselective cleavage of the bicyclic acetal (**7**). This transformation is also formally equivalent to the asymmetric differentiation of a 1,3-prochiral diol (indirect differentiation). Although these differentiations represented by Eq. 1 in Chart 1 are undoubtedly synthetically valuable, there are few chemical methods available, in contrast to the enzymatic technique.[4]

We herein report a synthetic approach to (+)-talaromycin A (**1**) and (−)-talaromycin B (**2**) involving two kinds of novel asymmetric recognition of prochiral 1,3-diols using a sulfinyl chirality.

**Model Study of Diastereoselective Acetal Fissions for the Synthesis of Talaromycins** Initially, we examined the diastereoselectivity of acetal fissions using the simple acetal (**15**) as a model compound.

Compound **15** was prepared as follows. The diol (**8**)[5] was protected as an acetonide followed by decarboxylation by treatment with sodium chloride in an aqueous solution of dimethylsulfoxide (DMSO). The resulting ester (**9**) was reduced with lithium aluminum hydride, followed by tosylation to afford **10** by treatment with NaI in acetone, as shown in Chart 2.

The lithium salt of (*R*)-methyl tolyl sulfoxide (**11**)[6] was allowed to react with ethyl acetate at −78 °C and then alkylated with **10** in the presence of 18-crown-6 to give the

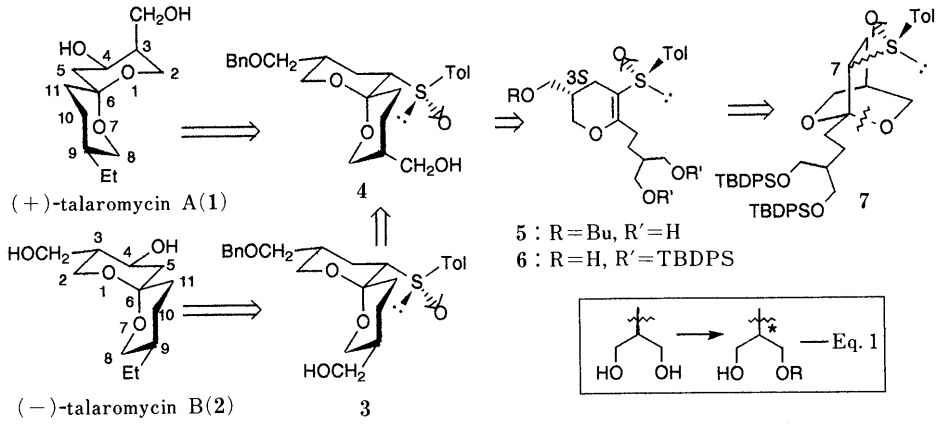



Chart 1

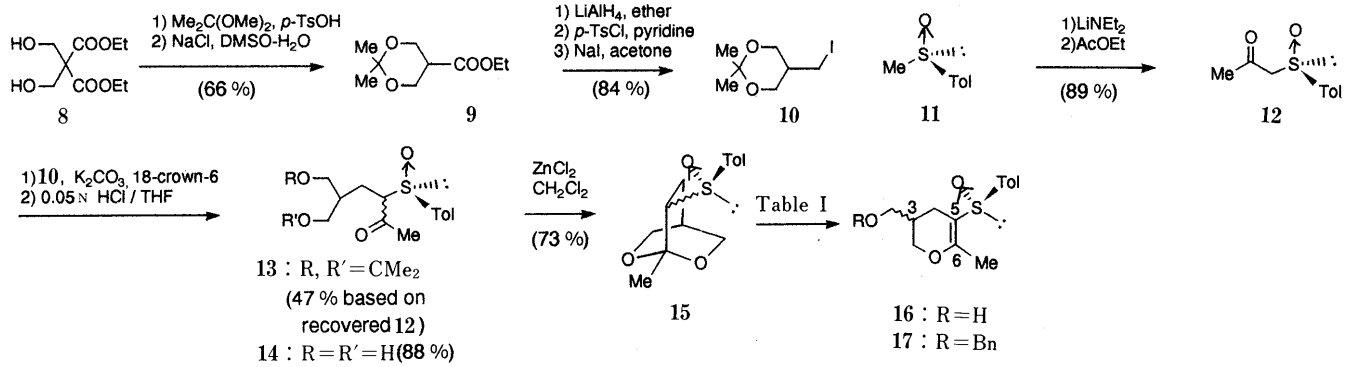
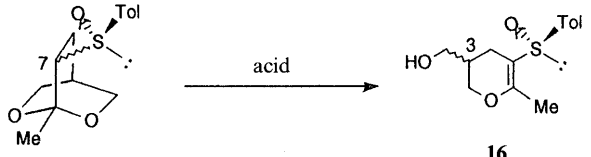



Chart 2

TABLE I. Diastereoselective Acetal Cleavage of the Bicyclic Acetal (**15**)




**15** **16**

| Substrate | $CF_3COOH$[a] | | $AlCl_3$ | |
|---|---|---|---|---|
| | Yield (%) | Ratio (3*S*:3*R*)[b] | Yield (%) | Ratio (3*S*:3*R*)[b] |
| **15**[c] | 78 | 2.7:1 | 90 | 1:2.5 |
| (7*S*)-**15** | 79 | 2.4:1 | 90 | 1:2.9 |
| (7*R*)-**15** | 76 | 3.7:1 | 84 | 1.2:1 |

*a*) The trifluoroacetate formed was hydrolyzed, and the yield and the ratio were calculated. *b*) The diastereomeric ratio was determined by HPLC as the benzyl ether (**17**). *c*) The diastereomeric mixture (7*S*/7*R*=3.6/1).

ketosulfoxide (**13**) in 47% yield on the basis of the recovered **12**.[7] After deprotection (88%), the resulting diol (**14**) was treated with zinc chloride in methylene chloride to give the bicyclic acetal (**15**) (73%; 7*S*/7*R*=3.6/1).[8] On treatment with trifluoroacetic acid, the diastereomeric mixture of **15** was cleaved with moderate diastereoselectivity to give predominantly (3*S*)-**16** (78%; 3*S*/3*R*=2.7/1). Interestingly, the diastereoselectivity was reversed when aluminum chloride was used (89%; 3*S*/3*R*=1/2.5). The results are shown in Table I.

The stereochemistry of a hydroxymethyl group at the C3-position in **16** was confirmed by the proton nuclear magnetic resonance ($^1$H-NMR) analysis of the benzyl ether (**17**). That is, considering the $A^{(1,3)}$-strain between the C5-sulfinyl group and the C6-methyl group, the most stable conformation is expected to be that in which the lone pair electrons of the sulfur atom are situated in the same plane as the C5–C6 double bond, as shown in Chart 2. In this conformation, the C3-methine proton on the same side as the tolyl group would be shielded. In fact, the signal due to the C3-methine proton of (3*S*)-**17** ($\delta$ 1.86—2.22) appeared at a high field compared with that of (3*R*)-**17** ($\delta$ 2.13—2.60).

The diastereomeric isomers [(7*S*)- and (7*R*)-**15**] were separated[9] and treated with trifluoroacetic acid or aluminum chloride, but the diastereoselectivity did not improve much (Table I). The reason for the diastereoselectivity is not clear, but the chirality of the sulfinyl group is important.

Thus, we succeeded in the asymmetric recognition of *gem*-bis(1,3-hydroxymethyl) groups, thereby constructing an asymmetric center at the C3-position in the dihydropyran derivative (**16**).

**Construction of the C3 Asymmetric Center by Diastereoselective Cleavage of the Bicyclic Acetal (7)** As described above, we found reaction conditions for the preferential formation of the (3*S*)-epimer. Next, we applied the method to the intermediate (**7**) for the synthesis of talaromycins with a more functionalized side chain.

The bicyclic acetal (**7**) was synthesized as follows. The known aldehyde (**18**)[10] was protected as an ethylene acetal (92%), which was then reduced with lithium aluminum hydride (80%). Protection of the resulting diol as *tert*-butyldiphenylsilyl (TBDPS) ethers (96%) followed by acid-catalyzed deacetalization (62%) converted **20** to the aldehyde (**22**). The aldehyde (**22**) was allowed to react with the lithium salt of the sulfoxide (**11**) to give the alcohol (**23**) (84%), which was oxidized with pyridinium chlorochromate (PCC) to **24** (87%). The $\beta$-ketosulfoxide (**24**) was alkylated with the iodide (**10**) using potassium carbonate in the presence of 18-crown-6 (32%, 46% based on the recovered **24**).[7] The acetonide (**25**) was hydrolyzed with 0.05 N HCl to provide the diol (**26**) in 93% yield, and this was converted by using zinc chloride to the bicyclic compound (**7**) in 91% yield (7*S*/7*R*=2/9), along with a small amount of **6** (9%).[11]

As in the preliminary examination, the bicyclic acetal (**7**) was treated with trifluoroacetic acid and the resulting trifluoroacetate was hydrolyzed with potassium carbonate followed by benzylation to give the desired (3*S*)-**27** as a major product (66%) together with a small amount of the (3*R*)-epimer (16%).[12]

**Construction of Three Chiral Centers (C5, C6, and C9) by Diastereoselective Intramolecular Michael Addition** Three chiral centers (C5, C6, and C9) were constructed in one step by the intramolecular Michael addition[1,13] of the alkoxide to the chiral vinylic sulfoxide moiety.

After deprotection of the silyl group of (3*S*)-**27** with tetra-*n*-butylammonium fluoride, the resulting diol (**5**) was treated with potassium hydride in tetrahydrofuran (THF) at room temperature to provide the dioxaspiro compound (**4**) as a single stereoisomer in 87% yield from (3*S*)-**27**. The stereochemistry of the product was assigned as the represented structure **4** on the basis of the $^1$H-NMR spectrum [$\delta$ 2.33 (1H, dd, *J*=12.5, 5.2 Hz, 5-H)] and the

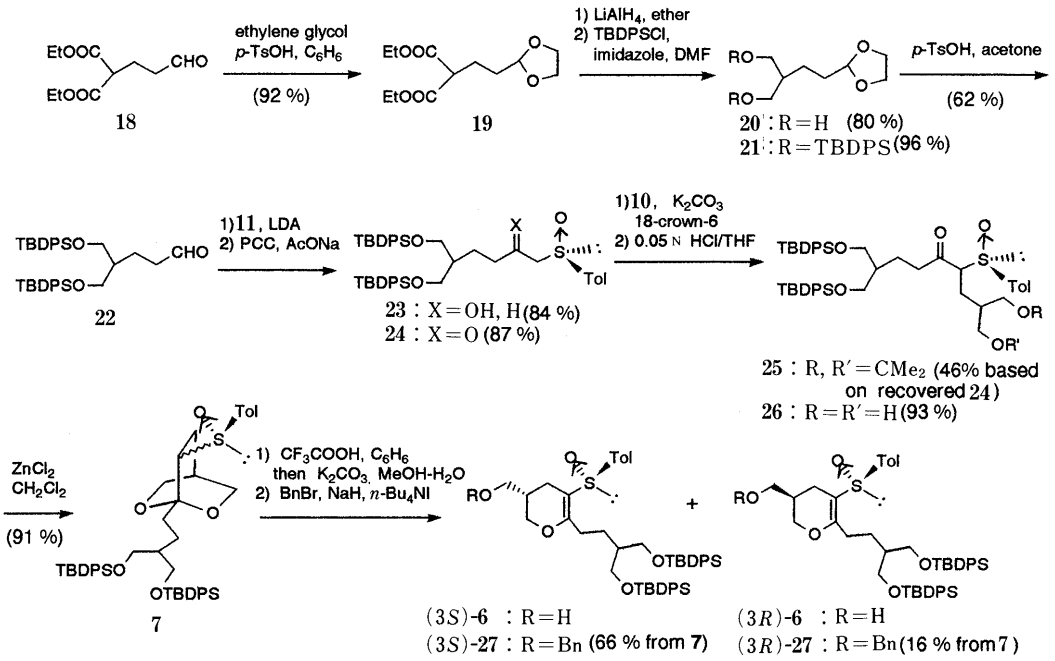



Chart 3

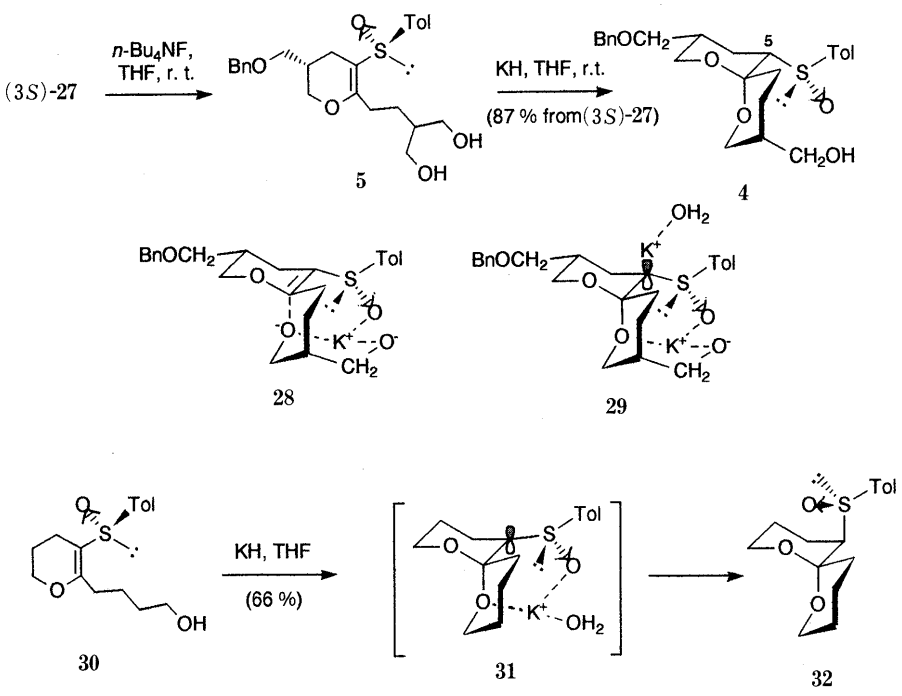



Chart 4

mechanism of spiroannulation illustrated in Chart 4. That is, attack of the hydroxy group would occur from the *si*-face by analogy with the result previously observed in the more simple compound (**30**).[13c,e] The pro-*R* hydroxymethyl group in the diol (**5**) would be exclusively cyclized *via* the most stable chelation intermediate (**28**) to form **4**. In this cyclization, the chiral sulfinyl group would not only control the stereochemistry of Michael addition, but also differentiate the prochiral hydroxymethyl group to afford the thermodynamically less stable isomer (**4**) with high diastereoselectivity. Interestingly, the stereochemistry of the sulfinyl group at the C5 position in **4** was different from the result previously obtained in **30**. In that case, a spiro compound (**32**) with an axially oriented sulfinyl group was formed exclusively. Therefore, it is considered that protonation to the intermediate (**31**) would have occurred from the same side as the sulfinyl oxygen, since a water molecule may coordinate with the potassium cation. On the other hand, the intermediate (**29**) was protonated from the less hindered side to give **4** since the vacant orbital of the potassium cation was occupied by the alkoxy group.

Thus, we succeeded in the stereoselective synthesis of the common intermediate (**4**) for talaromycins. The two strategies for the differentiation of prochiral 1,3-diols, that is, diastereoselective acetal fission and diastereoselective

acetal formation, are likely to be useful for the synthesis of other natural products.

## Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded with a Hitachi 260-10 spectrometer. $^1$H-NMR spectra were measured with a Hitachi R-22 (90 MHz), a JEOL FX-99Q (90 MHz), or a JEOL JNM-GX-500 (500 MHz) instrument. The chemical shifts are given as $\delta$ (ppm) values with tetramethylsilane (TMS) as an internal standard. Optical rotations were recorded with a Yanagimoto OR-20 or a JASCO DIP-360 polarimeter. Mass spectra (MS) and high-resolution MS (High-MS) were obtained with a Shimadzu QP-1000 or a JEOL JMS D-300 mass spectrometer. Analytical HPLC was performed by using a Shimadzu LC-5A equipped with a Soma S-310A ultraviolet detector. A Sumipax OA-2000A optically active column was used for analysis. For column chromatography, Aluminiumoxide 90 or Kieselgel 60 (E. Merck) was used.

**5-Ethoxycarbonyl-2,2-dimethyl-1,3-dioxane (9)** A mixture of the diol (**8**)[5] (15.0 g, 68.1 mmol) and a catalytic amount of *p*-toluenesulfonic acid monohydrate (10 mg, 0.053 mmol) in 2,2-dimethoxypropane (50.0 ml, 0.41 mol) was stirred at room temperature for 5 h. The methanol formed was evaporated off, then the residue was diluted with ether, washed with saturated $NaHCO_3$ and brine, dried over $Na_2SO_4$, and evaporated to dryness. The residue was distilled to give the acetonide (15.7 g, 89%) as a colorless oil, bp 98—105 °C (4 mmHg). *Anal.* Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.75. Found: C, 55.17; H, 7.88. IR ($CCl_4$): 1730 cm$^{-1}$. $^1$H-NMR ($CCl_4$) $\delta$: 1.30 (6H, t, $J$=7.0 Hz, $CH_2C\underline{H}_3$), 1.36 (6H, s, $CCH_3$), 4.17 (4H, q, $J$=7.0 Hz, $C\underline{H}_2CH_3$), 4.11 (4H, s, 4 and 6-H). CI-MS $m/z$ (%): 261 ($M^+$+1, 100).

A mixture of the acetonide (8.00 g, 30.7 mmol), water (1.1 ml, 61.0 mmol), and NaCl (1.80 g, 31.0 mmol) in dry DMSO (60 ml) was heated at 180 °C for 24 h. Brine (100 ml) was added to the cooled mixture and the whole was extracted with ether. The ether layer was washed 5 times with brine, dried over $Na_2SO_4$, and evaporated to dryness. The residue was distilled to give **9** (4.29 g, 74%) as a colorless oil, bp 88 °C (6 mmHg). *Anal.* Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.19; H, 8.69. IR ($CCl_4$): 1740 cm$^{-1}$. $^1$H-NMR ($CCl_4$) $\delta$: 1.27 (3H, t, $J$=7.0 Hz, $CH_2C\underline{H}_3$), 1.31 (3H, s, $CCH_3$), 1.41 (3H, s, $CCH_3$), 2.70 (1H, m, 5-H), 3.91 (4H, d, $J$=7.0 Hz, 4 and 6-H), 4.70 (2H, q, $C\underline{H}_2CH_3$). CI-MS $m/z$ (%): 189 ($M^+$+1, 100).

**5-Iodomethyl-2,2-dimethyl-1,3-dioxane (10)** A solution of **9** (4.00 g, 21.3 mmol) in dry ether (50 ml) was added to a suspension of lithium aluminum hydride (0.80 g, 21.0 mmol) in dry ether (100 ml) with stirring at 0 °C. Stirring was continued at room temperature for 5 h, then saturated potassium sodium tartrate was added and the mixture was stirred at room temperature overnight. The mixture was filtered, the filtrate was dried over $Na_2SO_4$, and the solvent was evaporated off. The residue was used in the next step without further purification. An analytical sample was distilled as a colorless oil, bp 105 °C (4 mmHg). *Anal.* Calcd for $C_7H_{14}O_3$: C, 57.51; H, 9.65. Found: C, 57.30; H, 9.88. IR ($CCl_4$): 3640, 3460 cm$^{-1}$. $^1$H-NMR ($CCl_4$) $\delta$: 1.33 (3H, s, $C\underline{H}_3$), 1.38 (3H, s, $C\underline{H}_3$), 1.60—1.85 (1H, m, 5-H), 3.50 (2H, d, $J$=7.5 Hz, $C\underline{H}_2OH$), 3.62 (2H, dd, $J$=11.0, 5.0 Hz, 4 and 6-$H_{ax}$), 3.89 (2H, dd, $J$=11.0, 4.0 Hz, 4 and 6-$H_{eq}$). CI-MS $m/z$ (%): 147 ($M^+$+1, 100).

*p*-Toluenesulfonyl chloride (3.99 g, 21.0 mmol) was added to a solution of the crude alcohol in dry pyridine (5 ml) with stirring at 0 °C. And the mixture was stirred at room temperature for 3 h. Saturated $NaHCO_3$ was added to the mixture at 0 °C. The mixture was extracted with ether, and the extract was washed with water, saturated $CuSO_4$, water, and brine, dried over $Na_2SO_4$, and evaporated to dryness. The residue was used in the next step without further purification. An analytical sample was recrystallized from ethanol as colorless needles, mp 57—58 °C. *Anal.* Calcd for $C_{14}H_{20}O_5S$: C, 55.98; H, 6.71; S, 10.68. Found: C, 55.95; H, 6.72; S, 10.64. IR ($CCl_4$): 1600, 1360, 1175 cm$^{-1}$. $^1$H-NMR ($CCl_4$) $\delta$: 1.22 (3H, s, $C\underline{H}_3$), 1.32 (3H, s, $C\underline{H}_3$), 1.87 (1H, ddd, $J$=7.0, 4.5, 3.5 Hz, 5-H), 2.44 (3H, s, $ArCH_3$), 3.57 (2H, dd, $J$=12.0, 4.5 Hz, 4 and 6-$H_{ax}$), 3.89 (2H, dd, $J$=12.0, 3.5 Hz, 4 and 6-$H_{eq}$), 4.08 (2H, d, $J$=7.0 Hz, $C\underline{H}_2OTs$), 7.25 (2H, d, $J$=8.0 Hz, Ar), 7.68 (2H, d, $J$=8.0 Hz, Ar). CI-MS $m/z$ (%): 301 ($M^+$+1, 100).

A solution of the crude tosylate and NaI (6.3 g, 42.0 mmol) in dry acetone (50 ml) was heated at 50 °C for 12 h. The solvent was evaporated off and the residue was partitioned between ether and water. The ether layer was washed with water, saturated $Na_2S_2O_3$, water, and brine, and then dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with $C_6H_6$ to give **10** (4.56 g, 84%) as a colorless oil. An analytical sample was distilled, bp 98—100 °C (10 mmHg). *Anal.* Calcd for $C_7H_{13}IO_2$: C, 32.83; H, 5.12. Found: C, 32.52; H, 5.07. IR ($CCl_4$): 1200, 1130, 1080, 1050 cm$^{-1}$. $^1$H-NMR ($CCl_4$) $\delta$: 1.33 (6H, s, $C\underline{H}_3$), 1.80—2.20 (1H, m, 5-H), 3.17 (2H, d, $J$=7.0 Hz, $CH_2I$), 3.59 (2H, dd, $J$=12.0, 6.0 Hz, 4 and 6-$H_{ax}$), 3.89 (2H, dd, $J$=12.0, 4.0 Hz, 4 and 6-$H_{eq}$). MS $m/z$ (%): 241 ($M^+$−Me, 55), 141 ($^+CH_2I$, 8.3).

**($R_S$)-1-Methyl-2-*p*-tolylsulfinyl-1-ethanone (12)** *n*-Butyllithium (1.6 M *n*-hexane solution) (8.87 ml, 13.2 mmol) was added to a solution of diethylamine (1.33 ml, 13.2 mmol) in dry THF (30 ml) with stirring at −78 °C under $N_2$. The mixture was stirred at 0 °C for 30 min, and a solution of ($R_S$)-methyl tolyl sulfoxide (**11**)[6] (1.02 g, 6.60 mmol) in THF (15 ml) was added dropwise with stirring at −78 °C. The mixture was stirred at −40 °C for 40 min, then a solution of ethyl acetate (1.33 ml, 13.2 mmol) in THF (15 ml) was added dropwise. The mixture was stirred for 1 h, then the reaction was quenched with saturated $NH_4Cl$, and the whole was extracted with $CHCl_3$. The extract was washed with brine and dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with hexane–AcOEt (1:2) to give **12** (1.15 g, 89%) as a colorless oil. $[\alpha]_D^{26}$ +216.70° ($c$=2.00, $CHCl_3$). IR ($CHCl_3$): 1715, 1600, 1500, 1050 cm$^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 2.19 (3H, s), 2.38 (3H, s), 3.82 (2H, s), 7.26 (2H, d, $J$=8 Hz), 7.48 (2H, d, $J$=8 Hz). MS $m/z$ (%): 196 ($M^+$, 18.0), 139 (100), 91 (25.9). High MS Calcd for $C_{10}H_{12}O_2S$: 196.0556. Found: 196.0543.

**($R_S$)-1-Methyl-2-(2,2-dimethyl-1,3-dioxolanyl)-2-*p*-tolylsulfinyl-1-ethanone (13)** A solution of the iodide (**10**) (2.00 g, 8.20 mmol) in dry MeCN (5 ml) was added to a mixture of **12** (804 mg, 4.10 mmol), $K_2CO_3$ (1.70 g, 12.3 mmol) and 18-crown-6 (528 mg, 2.05 mmol) in dry MeCN (15 ml) with stirring at 35—40 °C for 12 h. After cooling, the mixture was diluted with ether. The reaction was quenched with saturated $NH_4Cl$, and the whole was washed with brine and dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with hexane–AcOEt (1:2) to give **13** (343 mg, 47% based on the recovered **12**) as a colorless oil accompanied with **12** (365 mg, 1.86 mmol). $[\alpha]_D^{29}$ +45.42° ($c$=1.10, $CHCl_3$). IR ($CHCl_3$): 1715, 1600, 1500, 1050 cm$^{-1}$ $^1$H-NMR ($CDCl_3$) $\delta$: 1.35 (6H, s), 1.54—1.98 (3H, m), 2.06, 2.14 (total 3H, s), 2.38 (3H, s), 3.35—3.97 (5H, m), 7.15—7.48 (4H, m). MS $m/z$ (%): 309 ($M^+$−Me, 0.33), 139 (S(O)Tol, 61.1).

**($R_S$)-1-Methyl-7-*p*-tolylsulfinyl-2,6-dioxabicyclo[2.2.2]octane (15)** Hydrochloric acid (0.05 N, 2.00 ml, 0.10 mmol) was added to a solution of **13** (421 mg, 1.30 mmol) in dry THF (10 ml) with stirring at room temperature. Stirring was continued at room temperature for 6 h, then saturated $NaHCO_3$ was added to the mixture. Most of the THF was evaporated off and then the residual aqueous layer was extracted with $CHCl_3$, and the extract was washed with brine and dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with AcOEt to give **14** (325 mg, 88%) as a colorless oil. $[\alpha]_D^{22}$ +103.13° ($c$=2.23, $CHCl_3$). IR ($CHCl_3$): 3380, 1730, 1600, 1500, 1040 cm$^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.24—2.40 (3H, m), 1.74 (3H, s), 2.40 (3H, s), 3.30—4.10 (5H, m), 4.08 (1H, br s), 4.80 (1H, br s), 7.20—7.57 (4H, m).

Zinc chloride (491 mg, 3.60 mmol) was added to a solution of **14** (51 mg, 0.18 mmol) in dry $CH_2Cl_2$ (2 ml) with stirring at 0 °C. Stirring was continued at room temperature for 8 h, then the mixture was poured into ice-water, and extracted with $CHCl_3$. The extract was washed with brine and dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with hexane–AcOEt (1:2) to give (7*R*)-**15** (10 mg, 21%) and (7*S*)-**15** (35 mg, 73%). (7*R*)-**15**: mp 99—100 °C from hexane–benzene. $[\alpha]_D^{23}$ +31.24° ($c$=0.83, $CHCl_3$). IR ($CHCl_3$): 1600, 1500, 1060 cm$^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.39—1.45 (1H, m), 1.66 (3H, s), 1.75—1.95 (2H, m), 2.42 (3H, s), 3.36 (1H, dd, $J$=4.9, 11.0 Hz), 3.72—4.27 (4H, m), 7.28 (2H, d, $J$=8.0 Hz), 7.65 (2H, d, $J$=8.0 Hz). MS $m/z$ (%): 267 ($M^+$+1, 0.17), 127 (100). High MS Calcd for $C_{14}H_{18}O_3S$: 266.0975. Found: 266.0955. (7*S*)-**15**: mp 116—117 °C from hexane–benzene. $[\alpha]_D^{23}$ +246.40° ($c$=0.63, $CHCl_3$). IR ($CHCl_3$): 1600, 1500, 1040 cm$^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.85—2.08 (2H, m), 1.63 (3H, s), 2.40 (3H, s), 2.56—2.62 (1H, m), 2.98 (1H, dd, $J$=4.9, 11.6 Hz), 3.78—4.28 (4H, m), 7.25 (2H, d, $J$=8.5 Hz), 7.40 (2H, d, $J$=8.5 Hz). MS $m/z$ (%): 267 ($M^+$+1, 0.12), 127 (100). High MS Calcd for $C_{14}H_{18}O_3S$: 266.0975. Found: 266.0974.

**($R_S$)-3-Benzyloxymethyl-3,4-dihydro-6-methyl-5-*p*-tolylsulfinyl-2*H*-pyran (17). Procedure A** Trifluoroacetic acid (0.075 ml, 1.00 mmol) was added to a solution of **15** (27 mg, 0.10 mmol) in dry benzene (2 ml) with stirring at 0 °C. Stirring was continued at room temperature for 3 h, then the mixture was poured into ice-saturated $NaHCO_3$. The organic solution

was washed with brine and dried over $Na_2SO_4$. The solvent was evaporated off. The residue was taken up in a 1:1 mixture of MeOH–water (2 ml), and $K_2CO_3$ (14 mg, 0.10 mmol) was added with stirring at 0 °C. The mixture was stirred at room temperature for 1 h. After most of the MeOH had evaporated, the residue was extracted with $CHCl_3$. The extract was washed with brine, and then dried over $Na_2SO_4$. The solvent was evaporated off and the residue was purified by preparative TLC (PTLC) (hexane : AcOEt = 1 : 2) to give **16** (21 mg, 78%, 3*S*/3*R* = 2.7/1) as a colorless oil. The diastereomeric mixture was used in the next step without further purification.

**Procedure B** Aluminum chloride (85 ml, 0.64 mmol) was added to a solution of **15** (17 mg, 0.06 mmol) in dry THF (2 ml) with stirring at 0 °C. Stirring was continued at room temperature for 3 h, then the mixture was poured into ice-saturated $NaHCO_3$. The organic solution was washed with brine and dried over $Na_2SO_4$. The solvent was evaporated off and the residue was purified by PTLC (hexane : AcOEt = 1 : 2) to give **16** (15 mg, 90%, 3*S*/3*R* = 1/2.5) as a colorless oil. The diastereomeric mixture was used in the next step without further purification. IR ($CHCl_3$): 3360, 1640, 1600, 1500, 1030 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.40—1.82 (2H, m), 1.63 (1H, m), 1.87—2.17 (2H, m), 2.25 (3H, s), 2.40 (3H, s), 3.23—3.66 (2H, m), 3.88—4.40 (2H, m), 7.22 (2H, d, $J$ = 8.0 Hz), 7.35 (2H, d, $J$ = 8.0 Hz).

Compound **16** (37.9 mg, 0.14 mmol, 3*S*/3*R* = 2.7/1) was added to a suspension of 60% NaH (8.5 mg, 0.21 mmol) in dry THF (5 ml) with stirring at 0 °C under $N_2$. The mixture was stirred for 1 h, then benzyl bromide (0.033 ml, 0.28 mmol) was added and the reaction mixture was stirred at room temperature for 12 h. The excess NaH was destroyed by the addition of wet ether. The organic layer was separated, washed with brine, and dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with hexane–AcOEt (2 : 1) to give (3*R*)-**17** (14.2 mg, 28%) as a colorless oil and (3*S*)-**17** (31.1 mg, 61%) as a colorless oil. (3*R*)-**17**: $[\alpha]_D^{25}$ +11.51° ($c$ = 0.30, $CHCl_3$). IR ($CHCl_3$): 1635, 1600, 1500, 1030 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 2.13—2.60 (3H, m), 2.29 (3H, s), 2.42 (3H, s), 2.13—2.49 (2H, m), 3.58—3.80 (1H, m), 4.24—4.62 (1H, m), 4.66 (2H, s), 7.24—7.57 (9H, m). MS $m/z$ (%): 339 ($M^+ - 17$, 0.04), 91 ($C_7H_7$, 100). (3*S*)-**17**: $[\alpha]_D^{25}$ +41.15° ($c$ = 0.62, $CHCl_3$). IR ($CHCl_3$): 1640, 1600, 1500, 1030 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.86—2.22 (3H, m), 2.27 (3H, s), 2.38 (3H, s), 3.29—3.88 (2H, m), 3.61—3.64 (2H, m), 4.45 (2H, s), 7.07—7.50 (9H, m). MS $m/z$ (%): 356 ($M^+$, 0.04), 91 ($C_7H_7$, 100).

**4,4-Bis(ethoxycarbonyl)butanal Ethylene Acetal (19)** A mixture of the aldehyde (**18**)[10] (57.5 g, 0.22 mol), ethylene glycol (24.7 ml, 0.44 mol), and a catalytic amount of *p*-toluenesulfonic acid monohydrate (10 mg, 0.053 mmol) in benzene (150 ml) was refluxed for 24 h. The resulting water was collected in a Dean-Stark trap. After cooling, the mixture was washed with saturated $NaHCO_3$ and brine, and dried over $Na_2SO_4$, and the solvent was evaporated off. The residue was distilled to give **19** (63.7 g, 92%) as a colorless oil, bp 144 °C (5 mmHg). *Anal.* Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.75. Found: C, 55.07; H, 7.85. IR ($CCl_4$): 1755, 1735, 1370 $cm^{-1}$. $^1$H-NMR ($CCl_4$) $\delta$: 1.24 (6H, d, $J$ = 7.0 Hz, $CH_3$), 1.40—1.75 (2H, m), 1.75—2.05 (2H, m), 3.26 (1H, t, $J$ = 7.0 Hz), 3.70—3.95 (4H, m), 4.14 (4H, q, $J$ = 7.0 Hz), 4.74 (1H, t, $J$ = 4.0 Hz). CI-MS $m/z$ (%): 261 ($M^+ + 1$, 100).

**4,4-Bis(hydroxymethyl)butanal Ethylene Acetal (20)** Lithium aluminum hydride (1.50 g, 39.0 mmol) was added to a solution of **19** (7.00 g, 26.9 mmol) in dry ether (200 ml) with stirring at 0 °C. The mixture was stirred for 15 h at room temperature. After addition of saturated potassium sodium tartrate, the mixture was stirred at room temperature overnight, then filtered. The filtrate was dried over $Na_2SO_4$. The solvent was evaporated off and the residue was distilled to give **20** (3.80 g, 80%) as a colorless oil, bp 178 °C (0.08 mmHg). IR ($CHCl_3$): 3600, 3450 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.16—2.07 (5H, m), 3.59—3.77 (4H, m, $CH_2OH$), 3.77—3.99 (4H, m), 4.81 (1H, t, $J$ = 4.5 Hz).

**4,4-Bis(*tert*-butyldiphenylsiloxymethyl)butanal Ethylene Acetate (21)** TBDPS chloride (5.20 g, 20.0 mmol) was added to a mixture of **20** (1.75 g, 9.93 mmol) and imidazole (2.90 g, 42.0 mmol) in dry DMF (6 ml) with stirring at 0 °C. The reaction mixture was stirred for 4.5 h at room temperature, then partitioned between ether and water and the organic layer was separated. The aqueous layer was extracted with ether. The combined organic layer was washed with water and brine, and then dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with benzene to give **21** (6.20 g, 96%) as a powder, mp 67.5—69.0 °C from EtOH–acetone (5 : 1). *Anal.* Calcd for $C_{40}H_{52}O_4Si_2$: C, 73.57; H, 8.03. Found: C, 73.37; H, 8.08. IR ($CCl_4$): 1590, 1480, 1115 $cm^{-1}$. $^1$H-NMR ($CCl_4$) $\delta$: 1.03 (18H, s, Si-*tert*-Bu), 1.40—1.60 (4H, m, 2-H and 3-H), 1.60—1.80 (1H, m), 3.60—3.90 (8H, m, $CH_2O$), 4.68 (1H, br t, $J$ = 4.0 Hz), 7.10—7.40 (12H, m, Ph), 7.40—7.70 (8H, m, Ph). MS $m/z$ (%): 595 ($M^+$ – *tert*-Bu, 4.8).

**4,4-Bis(*tert*-butyldiphenylsiloxymethyl)butanal (22)** *p*-Toluenesulfonic acid monohydrate (200 mg, 1.05 mmol) was added to a solution of **21** (1.98 g, 3.03 mmol) in acetone (200 ml) with stirring at 0°C. Stirring was continued at 50 °C for 8 h, then the mixture was cooled and neutralized with saturated $NaHCO_3$. Most of the acetone was evaporated off, and the residue was extracted with ether. The extract was washed with water and brine, and then dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with hexane–benzene (1 : 1) to afford **22** (1.14 g, 62%, 92% based on the recovered **21**) as a colorless oil along with **21** (0.71 g, 36%). IR ($CCl_4$): 1730, 1480, 1120 $cm^{-1}$. $^1$H-NMR ($CCl_4$) $\delta$: 1.05 (18H, s, Si-*tert*-Bu), 1.50—1.80 (3H, m, 3-H and 4-H), 2.16 (2H, dt, $J$ = 6.0, 2.0 Hz, 2-H), 3.69 (4H, d, $J$ = 5.0 Hz, $CH_2O$), 7.10—7.40 (12H, m, Ph), 7.40—7.70 (8H, m, Ph). MS $m/z$ (%): 593 ($M^+$ – Me, 0.8).

**($R_S$)-5,5-Bis(*tert*-butyldiphenylsiloxymethyl)-2-hydroxy-1-(*p*-tolyl)sulfinylpentane (23)** A solution of **11**[6] (241 mg, 0.82 mmol) in THF (7 ml) was added to a stirred diisopropylamide (LDA) solution [prepared from *n*-BuLi (1.55 M in hexane; 1.10 ml, 1.70 mmol) and diisopropylamine (0.24 ml, 1.70 mmol) in THF (7 ml)] at −40 °C under $N_2$, and the mixture was stirred at −20 °C for 30 min. A solution of **22** (500 mg, 8.21 mmol) in THF (7 ml) was added to the stirred mixture at −78 °C and stirring was continued at the same temperature for 2 h. The reaction was quenched with saturated $NH_4Cl$ aqueous solution, and the reaction mixture was extracted with $CHCl_3$. The extract was washed with brine, dried over $Na_2SO_4$, and concentrated *in vacuo*. The residue was chromatographed on silica gel with hexane–AcOEt (3 : 2) to afford **23** (527 mg, 84%) as a colorless oil. $[\alpha]_D^{10}$ +33.8° ($c$ = 3.29, $CHCl_3$). *Anal.* Calcd for $C_{46}H_{58}O_4SSi_2$: C, 72.40; H, 7.66. Found: C, 72.49; H, 7.71. IR ($CHCl_3$): 3400, 1600, 1480, 1130, 1040 $cm^{-1}$. $^1$H-NMR ($CDCl_3$ $\delta$: 1.01 (18H, s), 1.22—1.47 (4H, m), 1.60—1.80 (1H, m), 2.40 (3H, s, $ArCH_3$), 2.50—2.90 (2H, m), 3.60—3.79 (5H, m), 3.91—4.21 (1H, m), 7.50—7.68 (24H, m, Ar-H). CI-MS $m/z$ (%): 763 ($M^+ + 1$, 0.6).

**($R_S$)-5,5-Bis(*tert*-butyldiphenylsiloxymethyl)-1-(*p*-tolyl)sulfinyl-2-pentanone (24)** AcONa (379 mg, 4.62 mmol) and PCC (994 mg, 4.61 mmol) were added to a solution of **23** (2.35 g, 3.08 mmol) in $CH_2Cl_2$ (100 ml) with stirring at room temperature. Stirring was continued for 12 h, then the mixture was diluted with ether (200 ml) and passed through Florisil. The filtrate was concentrated *in vacuo*. The residue was chromatographed on silica gel with hexane–AcOEt (2 : 1 to 1 : 1) to afford **24** (2.05 g, 87%) as a colorless oil. $[\alpha]_D^{10}$ +47.3° ($c$ = 3.29, $CHCl_3$). IR ($CHCl_3$): 1710, 1600, 1480, 1110 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.08 (18H, s), 1.45—1.76 (3H, m), 2.28 (2H, t, $J$ = 7.0 Hz), 2.38 (3H, s, $ArCH_3$), 3.55 (1H, d, $J$ = 15.0 Hz), 3.76 (1H, d, $J$ = 15.0 Hz), 3.69 (4H, d, $J$ = 6.0 Hz), 7.11—7.73 (24H, m, Ar-H). MS $m/z$ (%): 745 ($M^+$ – Me, 0.7), 703 ($M^+$ – *tert*-Bu, 0.5), 135 (100).

**($R_S$)-1,1-Bis(*tert*-butyldiphenylsiloxymethyl)-7,7-bis(hydroxymethyl)-5-(*p*-tolyl)sulfinyl-4-heptanone (26)** $K_2CO_3$ (550 mg, 3.98 mmol) and 18-crown-6 (174 mg, 0.66 mmol) were added to a solution of **24** (865 mg, 1.14 mmol) in dry MeCN (15 ml), and then a solution of **10** (1.50 g, 5.90 mmol) in dry MeCN (5 ml) was added with stirring at room temperature. The mixture was vigorously stirred at 35 °C for 12 h, then diluted with ether, washed with water and brine, dried over $Na_2SO_4$, and evaporated to dryness. The residue was roughly chromatographed on silica gel with hexane–AcOEt (2 : 1) to give a mixture of **25** and **24**. The mixture was subjected to medium-pressure chromatography (a Lobar column: Merck LiChroprep Si 60) with hexane–AcOEt (3 : 1) to afford **25** (324 mg, 32%, 46% based on the recovered **24**) as a colorless oil along with **24** (264 mg, 31%). $[\alpha]_D^{10}$ +16.3° ($c$ = 2.39, $CHCl_3$). IR ($CHCl_3$): 1730, 1600, 1480, 1115, 1040 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.01 (18H, s), 1.33 (6H, s), 1.28—1.88 (6H, m), 2.22 and 2.31 (total 3H, each s, $ArCH_3$), 2.20—2.40 (2H, m, $COCH_2$), 3.15—4.10 (9H, m), 7.00—7.70 (24H, m, Ar-H).

Compound **25** (280 mg, 0.32 mmol) was added to a mixture of THF (8 ml) and 0.05 N HCl (2 ml) with stirring at 50 °C for 5 h. After cooling, the mixture was neutralized with saturated $NaHCO_3$, and concentrated *in vacuo*. The residue was extracted with $CHCl_3$, then the extract was washed with brine, dried over $Na_2SO_4$, and evaporated to dryness. The residue was chromatographed on silica gel with hexane–AcOEt (1 : 1 to AcOEt) to afford **26** (250 mg, 93%) as a colorless oil. $[\alpha]_D^{10}$ +26.0° ($c$ = 0.96, $CHCl_3$). IR ($CHCl_3$): 3400, 1725, 1585, 1470, 1110, 1040 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.01 (18H, s), 1.40—2.12 (6H, m), 2.30 (2H, t, $J$ = 6.5 Hz, $COCH_2$), 2.36 (3H, s, $ArCH_3$), 3.30—3.80 (11H, m),

7.00—7.70 (24H, m, Ar-H). MS *m/z* (%): 734 ($M^+ - tert\text{-}Bu \times 2$, 1.7), 91 (Tol, 30).

**(3*S*,$R_S$)-3-Benzyloxymethyl-6-[3,3-bis(hydroxymethyl)propyl]-3,4-dihydro-3-hydroxymethyl-5-(*p*-tolyl)sulfinyl-2*H*-pyran (5)** Zinc chloride (400 mg, 76 mmol) was added to a solution of **26** (2.60 g, 3.07 mmol) in $CH_2Cl_2$ (52 ml) with stirring at room temperature and the mixture was stirred for 6 h, then partitioned between $CHCl_3$ and water. The aqueous layer was extracted with $CHCl_3$, and the combined organic solution washed with saturated $NaHCO_3$ and brine, and then dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with hexane–AcOEt (1 : 1) to afford a mixture of (7*S*)-**7** and (7*R*)-**7** (2.23 g, 91%, 7*S*/7*R*=2/9) as a colorless oil along with a mixture of (3*S*)-**6** and (3*R*)-**6** (220 mg, 9%, 3*S*/3*R*=9/1) as a colorless oil. The diastereomeric mixture was used in the next step without further purification. (7*S*)-**7**: IR ($CHCl_3$): 1600, 1480, 1120, 1080, 1060 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.02 (18H, s), 1.33—2.14 (8H, m), 2.36 (3H, s, $ArCH_3$), 2.61 (1H, m, CHS(O)), 3.23—4.18 (8H, m), 7.10—7.78 (24H, m, Ar-H). (7*R*)-**7**: IR ($CHCl_3$): 1600, 1480, 1120, 1080, 1040 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.02 (9H, s), 1.33—2.14 (8H, m), 2.32 (3H, s, $ArC\underline{H}_3$), 2.89 (1H, dd, $J$=4.0, 11.0 Hz, CHS(O)), 3.23—4.18 (8H, m), 7.10—7.78 (24H, m, Ar-H).

Trifluoroacetic acid (2.10 ml, 27 mmol) was added to a solution of **7** (2.17 g, 2.61 mmol, 7*S*/7*R*=2/9) in dry benzene (108 ml) with stirring at room temperature for 1.5 h. The mixture was washed with saturated $NaHCO_3$, then diluted with ether, and brine, and the organic layer was dried over $Na_2SO_4$. The solvent was evaporated off and the residue was dissolved in a 1 : 1 mixture of MeOH and water (216 ml). $K_2CO_3$ (2.17 g, 15.7 mmol) was added to the mixture with stirring at 0 °C for 30 min. After almost of the MeOH had evaporated off, the residue was extracted with $CHCl_3$. The extract was washed with brine, and dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with AcOEt to afford **6** (2.01 g, 93%, 3*S*/3*R*=17/4) as a colorless oil. The diastereomeric mixture was used in the next step without further purification. IR ($CHCl_3$): 3400, 1630, 1475, 1115 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.09 (18H, s), 1.50—2.10 (6H, m), 2.10—2.60 (2H, m), 2.34 (3H, s, $ArC\underline{H}_3$), 3.20—4.00 (9H, m), 7.10—7.70 (24H, m, Ar-H). MS *m/z* (%): 814 ($M^+ - H_2O$, 0.6), 91 ($C_7H_7$, 100).

Sodium hydride (60% in oil) (973 mg, 40.5 mmol) was washed three times with hexane under $N_2$ and suspended in dry THF (36 ml). A solution of **6** (2.01 g, 2.42 mmol, 3*S*/3*R*=17/4) in dry THF (10 ml) was added to the mixture, followed by the addition of benzyl bromide (1.64 ml, 13.8 mmol) and tetra-*n*-butylammonium iodide (437 mg, 1.18 mmol). The mixture was stirred for 12 h, then the reaction was quenched with wet ether. The solution was washed with brine, and dried over $Na_2SO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel with hexane–AcOEt (1 : 2) to give a mixture of (3*S*)-**27** and (3*R*)-**27**. The mixture was subjected to medium-pressure chromatography (a Lobar column: Merck LiChroprep Si 60) with hexane–AcOEt (1 : 1) to afford (3*S*)-**27** (less polar) (1.58 g, 71%) and (3*R*)-**27** (polar) (369 mg, 17%), each as a colorless oil. (3*S*)-**27**: $[\alpha]_D^{10}$ −4.1° ($c$=2.18, $CHCl_3$). IR ($CHCl_3$): 1635, 1600, 1495, 1025 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.01 (18H, s), 1.40—1.95 (4H, m), 1.95—2.20 (2H, m), 2.34 (3H, s, $ArC\underline{H}_3$), 2.40—2.70 (2H, m), 3.10—3.40 (2H, m), 3.65—3.85 (4H, br s), 3.92 (2H, d, $J$=4.0 Hz, $C\underline{H}_2OBn$), 4.40 (2H, s, $C\underline{H}_2OPh$), 7.00—7.70 (29H, m, Ar-H). MS *m/z* (%): 426 ($M^+ - H_2O$, 0.3), 91 ($C_7H_7^+$, 100). (3*R*)-**27**: $[\alpha]_D^{10}$ −20.6° ($c$=1.46, $CHCl_3$). IR ($CHCl_3$): 1630, 1590, 1115, 1025 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.01 (18H, s), 1.40—2.70 (8H, m), 2.35 (3H, s, $ArC\underline{H}_3$), 3.00—3.40 (2H, m), 3.53 (1H, dd, $J$=9.0, 11.0 Hz, $C\underline{H}_2OBn$), 3.60—3.85 (4H, br s), 4.17 (1H, br d, $J$=11.0 Hz, $C\underline{H}_2OBn$), 4.35 (2H, s, $OC\underline{H}_2Ph$), 7.00—7.70 (29H, m, Ar-H).

A 1 M solution of tetra-*n*-butylammonium fluoride in THF (0.3 ml, 0.30 mmol) was added to a solution of (3*S*)-**27** (65 mg, 0.07 mmol) in dry THF (1.5 ml) with stirring at 0 °C. The mixture was stirred for 7 h at room temperature. The solvent was evaporated off and the residue was chromatographed on silica gel with AcOEt–MeOH (4 : 1) to afford **5** (31 mg, quant.) as a colorless oil. $[\alpha]_D^{15}$ +10.2° ($c$=2.44, $CHCl_3$). IR ($CHCl_3$): 3400, 1630, 1080, 1025 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.30—1.90 (4H, m), 1.90—2.20 (2H, m), 2.36 (3H, s, $ArC\underline{H}_3$), 2.50—3.00 (2H, m), 3.10—3.85 (8H, m), 3.97 (2H, d, $J$=4.0 Hz, $C\underline{H}_2OBn$), 4.36 (2H, s, $OC\underline{H}_2Ph$), 6.90—7.50 (9H, m, Ar-H). MS *m/z* (%): 444 ($M^+$, 0.7), 426 ($M^+ - H_2O$, 0.3), 91 ($C_7H_7^+$, 100). High MS Calcd for $C_{25}H_{32}O_5S$: 444.1969. Found: 444.1969.

**(3*S*,5*S*,6*R*,9*R*,$R_S$)-3-Benzyloxymethyl-9-hydroxymethyl-5-(*p*-tolyl)sulfinyl-1,7-dioxaspiro[5.5]undecane (4)** A solution of **5** (31 mg, 0.07 mmol) in dry THF (3 ml) was added to a stirred suspension of KH (*ca.* 28 mg, 0.7 mmol) in dry THF (5 ml) at 0 °C under $N_2$. The mixture was further stirred at room temperature for 2 h and treated with wet ether to decompose the excess KH. The resulting mixture was washed with brine, and dried over $Na_2SO_4$. The solvent was evaporated off and the residue was purified by PTLC with ether to afford **4** (27 mg, 87%) as a colorless oil. $[\alpha]_D^{15}$ +96.9° ($c$=1.65, $CHCl_3$). IR ($CHCl_3$): 3400, 1496, 1453, 1082, 1038 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 1.10—2.30 (9H, m), 2.37 (3H, s, $ArCH_3$), 3.27 (2H, d, $J$=6.0 Hz, $C\underline{H}_2OH$), 3.30—4.10 (7H, m), 4.40 (2H, s, $OCH_2Ph$), 7.10—7.50 (9H, m, Ar-H). MS *m/z* (%): 444 ($M^+$, 0.6), 426 ($M^+ - H_2O$, 0.2), 305 ($M^+ -$ TolS(O), 100). High MS Calcd for $C_{25}H_{32}O_5S$: 444.1967. Found: 444.1956.

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7) Alkylations of β-ketosulfoxide proceed only with difficulty. See, for example, P. A. Bartlett, *J. Am. Chem. Soc.*, **98**, 3305 (1976).
8) On treatment with *p*-toluenesulfonic acid, **14** afforded the dihydropyran derivative (**16**) directly, but no stereoselectivity was observed at the C3-position, presumably due to the long distance between the chiral auxiliary and the prochiral center.
9) (7*S*)-**15**: mp 116—117 °C, $[\alpha]_D^{23}$ +246.4° ($c$=0.63, $CHCl_3$) and (7*R*)-**15**: mp 99—100 °C, $[\alpha]_D^{23}$ +31.24° ($c$=0.83, $CHCl_3$). Stereochemistry of (7*S*)- and (7*R*)-**15** was deduced as follows. Figure 1 shows the most stable conformation of (7*S*)- and (7*R*)-**15** calculated by modified neglect of diatomic overlap, parametric method 3 (MNDOPM3).[14] According to the result, it was expected that the C7-methine proton is shielded by the aromatic ring and 8α-H is deshielded by the sulfinyl oxygen in (7*S*)-**15**, whereas the C7-methine proton is deshielded by the sulfinyl oxygen and 8β-H is shielded by the tolyl group in the (7*R*)-epimer. The observed chemical shift of major and minor products showed good accordance with the results of conformational analysis of (7*S*)- and (7*R*)-**15**, respectively (Fig. 1).

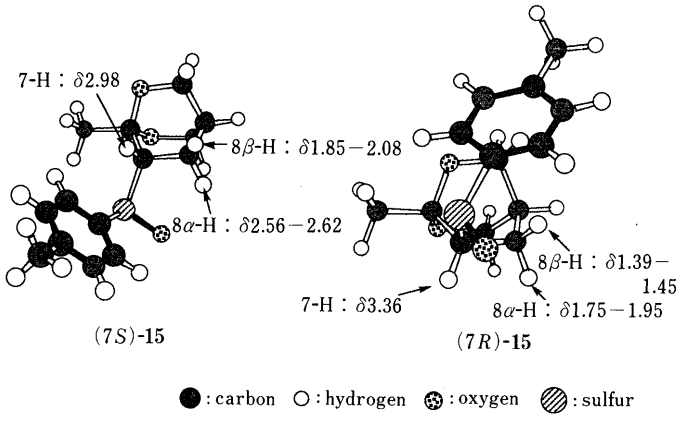


Fig. 1

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11) The intramolecular acetalization in the presence of *p*-toluenesulfonic acid and Dowex 50W-X12 proceeded in 65% and 52% yields, respectively. The dihydropyran derivative **6** was produced in 25% and 48% yields, respectively.
12) The ratio of (3*S*)-**27** and (3*R*)-**27** was found to be almost independent of the ratio of the two diastereomeric isomers in **7**.
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14) J. J. P. Stewart, *J. Comput. Chem.*, **10**, 209 (1989); *ibid.*, **10**, 221 (1989).