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TETRAHEDRON

Stereoselective Synthesis of a 2,2,5-Trisubstituted Tetrahydropyran Chiron *via* 1,3- and 1,6-Asymmetric Induction: A Total Synthesis of (–)-Malyngolide

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Abstract: A new mode of synthesizing chiral 2,2,5-trisubstituted tetrahydropyran is described, in which two chiral centers are simultaneously introduced *via* facial and group selective nucleophilic acetal cleavage reaction of a bicyclic acetal **1**, thereby accomplishing 1,3- and 1,6-asymmetric induction. It is revealed that acetal cleavage of the pro-*R* C–O bond and nucleophilic attack opposite the cleaved bond proceed preferentially. With $TiCl_4$ and allyltrimetylsilane at –100 °C, the selectivity of acetal fission is 10 :1 and that of nucleophilic attack is 12 : 1. This reaction is successfully applied to a total synthesis of marine antibiotics, (–)-malyngolide.

Keywords Asymmetric induction; Sulfoxides; Acetals; Cleavage reaction

INTRODUCTION

Long-range asymmetric induction has been a challenging issue in asymmetric synthesis. Generally, asymmetric induction to the prochiral centers separated by more than two carbons is considerably inefficient. Recently, various intriguing strategies have been developed to improve selectivity.[1] However, there exist few examples of simultaneous asymmetric induction involving long-range asymmetric induction.[2] We previously reported a novel asymmetric desymmetrization of prochiral 1,3-diols *via* intramolecular acetalization followed by diastereoselective acetal fission, affording a chiral 3-substituted dihydropyran derivative (Scheme 1).[3] This process is 1,6-asymmetric induction from the sulfinyl chirality to a prochiral center. If a nucleophile can be introduced in accompaniment with an acetal cleavage reaction, two stereogenic centers would be installed simultaneously, enabling 1,3- and 1,6-asymmetric induction.[4] The selectivity of the C–O bond cleavage (diastereotopic group selectivity) and nucleophilic attack (diastereofacial selectivity) are required to realize high selectivity. We have already reported that the nucleophilic acetal cleavage of **1** with $TiCl_4$ and Et_3SiH (Nu = H) proceeded with high diastereotopic group selectivity but poor diastereofacial selectivity.[5] In the course of this research, we investigated the nucleophilic acetal fission of **1** with carbon nucleophiles, such as allyltrimethylsilane and propargyl-

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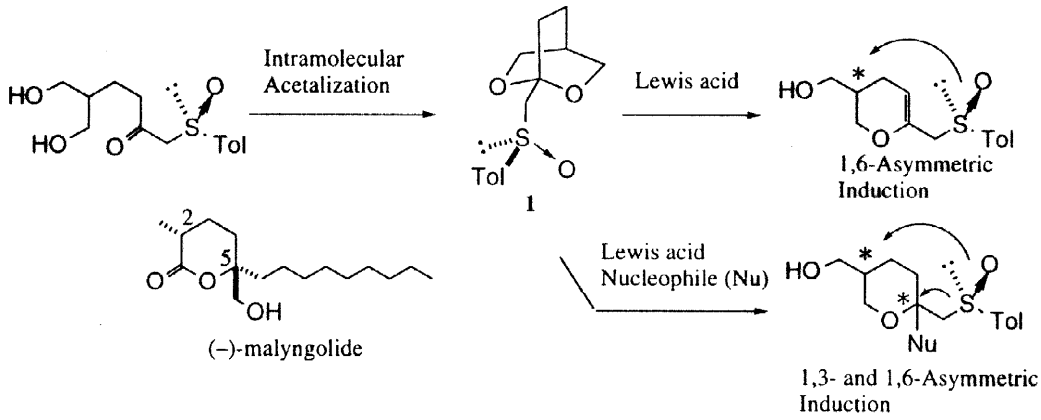
trimethylsilane, since the resulting 2,2,5-trisubstituted tetrahydropyran skeleton is considered a useful chiral synthon for the syntheses of diverse biologically active natural products with 2,2,5-trisubstituted tetrahydropyran skeletons, *i.e.* (–)-dactyloxene A[6] and (–)-malyngolide[7]. In this paper, we describe the full details of the asymmetric nucleophilic acetal cleavage reaction of **1** with carbon nucleophiles, which proceeds with high diastereofacial and diastereotopic group selectivity in contrast to its reaction with hydride. We also describe its application towards a total synthesis of (–)-malyngolide.



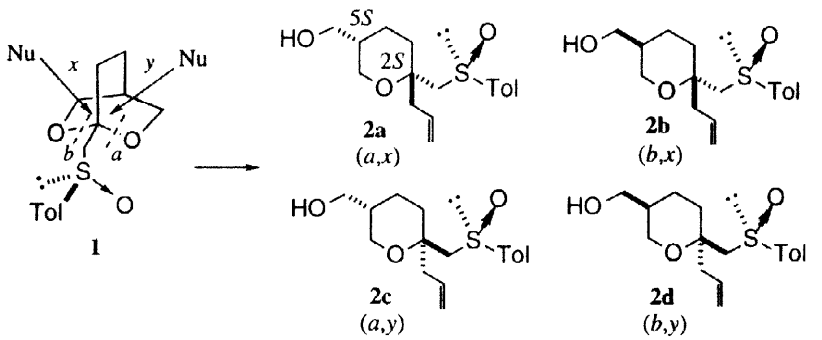
Scheme 1

Results and Discussion

Nucleophilic Acetal Cleavage Reaction of Bicyclic Acetal 1

Bicyclic acetal **1**[3] was prepared according to the previously reported procedure and the enantiomeric excess was determined as >98% *e.e.* by ^{1}H-NMR spectroscopy with europium(III) tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato] [Eu(tfc)$_3$] as a chiral shift reagent. The nucleophilic acetal cleavage reaction of **1** was investigated (Scheme 2). The results are summarized in Table 1. A mixture of bicyclic acetal **1** and allyltrimethylsilane was treated with titanium tetrachloride and stirred at –78°C. Nucleophilic acetal cleavage reaction took place promptly to provide an allylated alcohol **2a** having a (2*S*,5*S*)-configuration accompanied mainly with its diastereomeric isomers **2b**–**2d** (run 2). Acetal fission of the pro-*R* C–O bond (cleavage *a*) and nucleophilic attack opposite the cleaved bond (nucleophilic attack *x*) predominated. Selectivity was affected by the reaction temperature. Selectivity increased as the reaction temperature was lowered (run 3). At the higher temperature (–20°C), selectivity decreased and (2*R*,5*S*)-isomer **2c** was the main product (run 1). The similar trend in selectivity was obtained when $TiCl_4$ was added prior to allyltrimethylsilane (run 4). A less polar solvent, toluene, afforded a poorer yield and less selectivity than CH_2Cl_2 (run 5). Etherial solvents [ether and tetrahydrofuran (THF)] did not afford the above products (runs 6, 7). The amount of reagent slightly affected the results. (run 8–11). The best results were obtained when $TiCl_4$ (5 eq.) was added to a mixture of substrate and allyltrimethylsilane (10 eq.) in CH_2Cl_2 at –100 °C (**2a** : **2b** : **2c** : **2d** = 84 : 6 : 7 : 3) (run 12). The selectivity of acetal fission was 10 : 1 (cleavage *a* : cleavage *b*) and that of nucleophilic attack was 12 : 1 (nucleophilic attack *x* : nucleophilic

attack *y* in cleavage *a*). Other Lewis acids ($SnCl_4$, BF_3•ether) afforded a complex mixture.



Scheme 2

Table 1. Nucleophilic Acetal Cleavage Reaction of the Bicyclic Acetal **1**

Run	Conditions (eq.) [a]	Yield (%)	Ratio [c]
			2a : 2b : 2c : 2d
1	$TiCl_4$ (5), Me_3Si(allyl) (5), CH_2Cl_2, –20°C	91	19 : 26 : 48 : 7
2	$TiCl_4$ (5), Me_3Si(allyl) (5), CH_2Cl_2, –78°C	93	67 : 10 : 17 : 6
3	$TiCl_4$ (5), Me_3Si(allyl) (5), CH_2Cl_2, –100°C	92	79 : 6 : 9 : 6
4	$TiCl_4$ (5), Me_3Si(allyl) (5), CH_2Cl_2, –78°C [b]	93	25 : 19 : 51 : 5
5	$TiCl_4$ (5), Me_3Si(allyl) (5), toluene, –78°C	93	66 : 10 : 16 : 8
6	$TiCl_4$ (5), Me_3Si(allyl) (5), Et_2O, –78°C	0	—
7	$TiCl_4$ (5), Me_3Si(allyl) (5), THF, –78°C	0	—
8	$TiCl_4$ (3), Me_3Si(allyl) (5), CH_2Cl_2, –78°C	87	68 : 6 : 17 : 9
9	$TiCl_4$ (10), Me_3Si(allyl) (5), CH_2Cl_2, –78°C	94	67 : 8 : 20 : 5
10	$TiCl_4$ (5), Me_3Si(allyl) (2), CH_2Cl_2, –78°C	89	66 : 8 : 18 : 8
11	$TiCl_4$ (5), Me_3Si(allyl) (10), CH_2Cl_2, –78°C	91	76 : 5 : 10 : 9
12	$TiCl_4$ (5), Me_3Si(allyl) (10), CH_2Cl_2, –100°C	90	84 : 6 : 7 : 3
13	$TiCl_4$ (5), Bu_3Sn(allyl) (5), CH_2Cl_2, –78°C	65	71 : 13 : 9 : 7

a) All reactions were performed by the addition of Lewis acid to a mixture of allyltrimethylsilane unless mentioned. *b)* Allyltrimethylsilane was added to a mixture of the bicyclic acetal and $TiCl_4$. *c)* Determined by 500 MHz ^{1}H-NMR spectroscopy.

Stereochemistry of the main product **2a** was inferred to have (2*S*,5*S*)-absolute configuration from the relative configuration, as determined by single crystal X-ray analysis of the *p*-nitrobenzoate **3**[8] and the known absolute configuration of the sulfoxide (*R*s) (Fig. 1). It was finally determined by the conversion of **2a** into (–)-malyngolide.

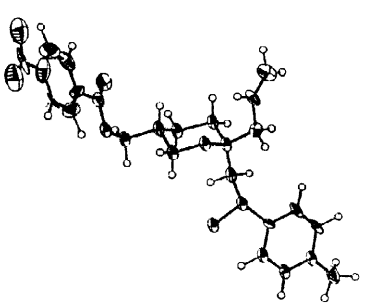
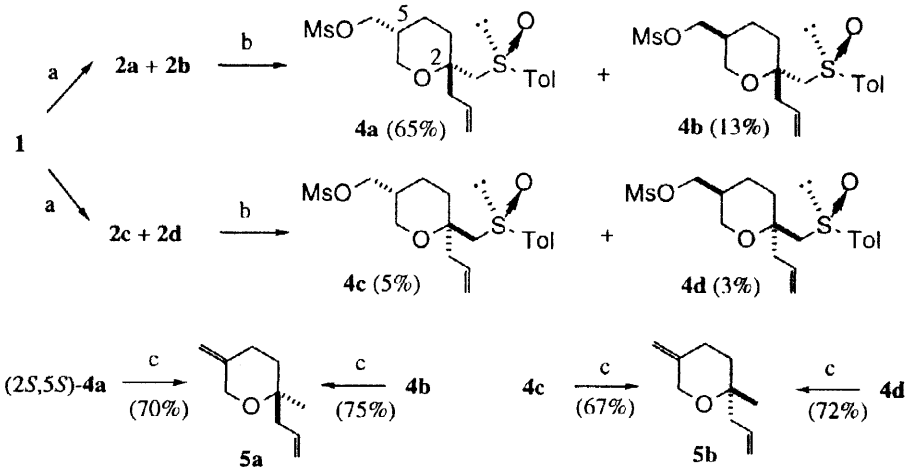


Fig. 1 ORTEP Drawing of *p*-Nitrobenzoate **3**

The absolute configurations of other diastereomeric isomers **2b–2d** were determined based on the stereochemistry of **2a**. The alcohols **2a–2d** were separated into the alcohols **2a,b** (81%) and the alcohols **2c,d** (9%) by column chromatography. The mixture of **2a** and **2b** was mesylated with methanesulfonyl chloride and DMAP to give **4a** (80%) and **4b** (16%). In a similar manner, a mixture of **2c** and **2d** was converted into **4c** (60%) and **4d** (36%). Mesylates **4a** and **4b** gave the

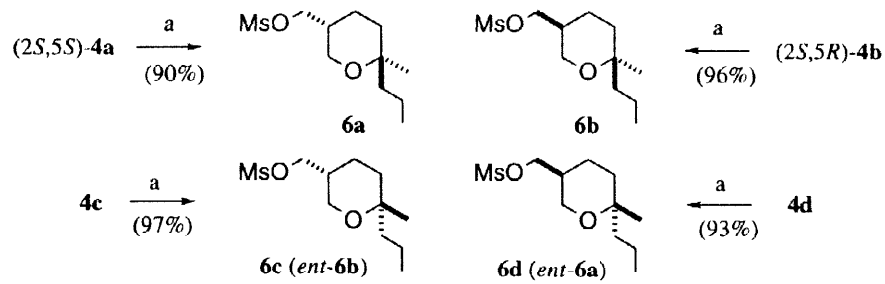
same olefin **5a** by elimination of methanesulfonic acid, indicating that the absolute configuration of **4b** is (2*S*,5*R*). Similarly, **4c** and **4d** gave the C_2-epimer **5b**, thereby confirming that they are epimers at the C_5-position (**Scheme** 3).



a: $TiCl_4$, allyltrimethylsilane, CH_2Cl_2, −100°C; b: MsCl, DMAP, CH_2Cl_2, 0°C;
c: (i) *o*-$NO_2PhSeCN$, $NaBH_4$, EtOH, room temp., (ii) H_2O_2, 0 °C.

Scheme 3

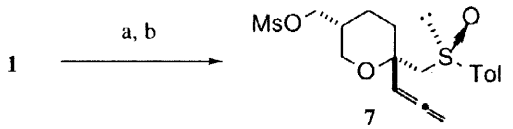
To determine the remaining absolute configurations at the C_5-position of **4c** and **4d**, the chirality of the mesylates **4a–4d**'s sulfur atom was removed by desulfurization to give each **6a–6d** (Scheme 4). The products **6a** and **6b** are enantiomeric with **6d** and **6c**, respectively. Based on the absolute configurations of **4a** and **4b**, those of **4c** and **4d** were established as (2*R*,5*S*) and (2*R*,5*R*), respectively. Thus, the stereochemistry of all diastereomeric isomers was established.



a: Raney Ni (W2), EtOH, room temp.

Scheme 4

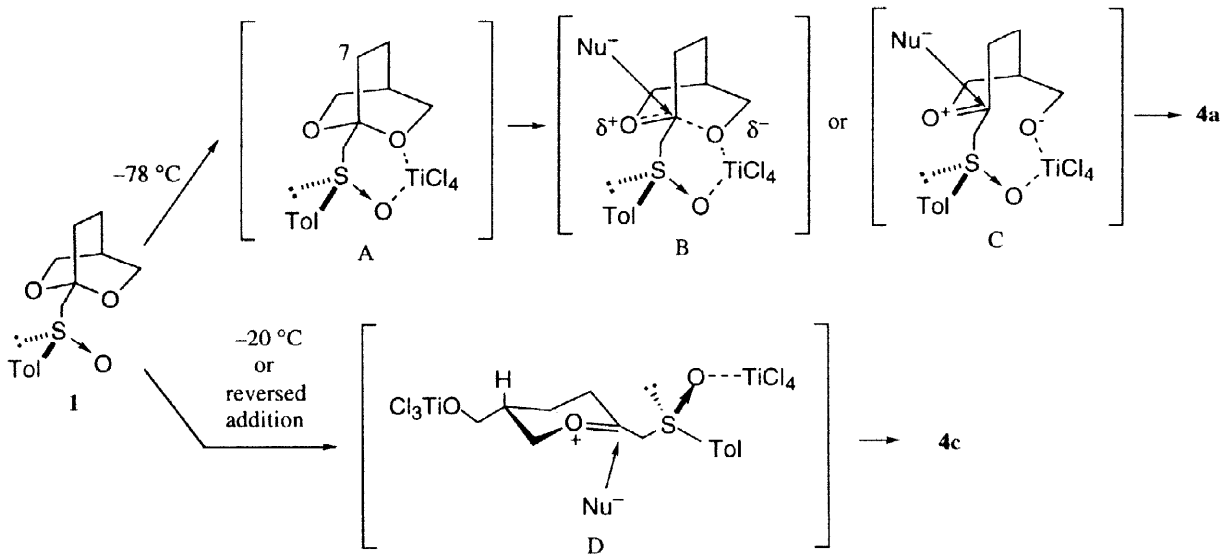
Nucleophilic acetal cleavage reaction was carried out using propargyltrimethylsilane as a nucleophile (Scheme 5). After mesylation, the main allenyl product **7** was separated from the minor isomers by column chromatography in a 57% yield from **1**. The stereochemistry of the nucleophilic acetal cleavage using propargyltrimethylsilane is the same as that with allyltrimethylsilane.[9]



a: $TiCl_4$, propargyltrimethylsilane, CH_2Cl_2, −100°C;
b: MsCl, DMAP, CH_2Cl_2, 0°C (57% from **1**).

Scheme 5

The reaction mechanism was rationalized as follows: Titanium tetrachloride would coordinate between the sulfinyl oxygen and one of the acetal oxygens to form the stable six-membered ring chelation intermediate A, in which the electron-positive sulfur atom is located between electron-negative oxygens and is *anti* to the bulky 7-methylene group in the intermediate A (Scheme 6).[10] Then, allyltrimethylsilane would attack from the backside of the cleaved C–O bond *via* concerted substitution (transition state B) or addition to a tight ion-pair (transition state C) to give the (2*S*,5*S*)-isomer **4a** as the predominate product.[11] On the other hand, raised temperature or inverse addition (addition of nucleophile to a mixture of the substrate **1** and excess $TiCl_4$) afford the opened intermediate D, which underwent stereoelectronically favorable axial attack to give **4c** as a main product.[12]



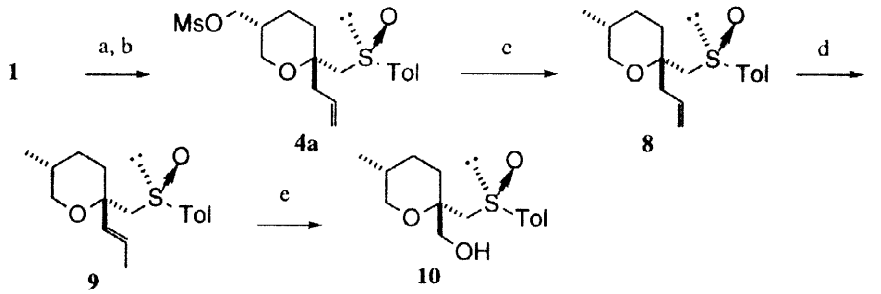
Scheme 6

Application to the Synthesis of (−)-Malyngolide

(−)-Malyngolide is the antibiotic isolated from the marine blue-green alga, *Lyngbya majuscula* GOMONT.[7] Most previous synthetic routes lack stereocontrol at the C_2 methyl group.[13,14] Although a few methods have overcome this problem, they constructed the two stereogenic centers one by one.[13c,d,k,l,q,w]

We applied the newly developed nucleophilic acetal cleavage reaction of **1** to a synthesis of (−)-malyngolide, in which the two stereogenic centers are constructed simultaneously with high

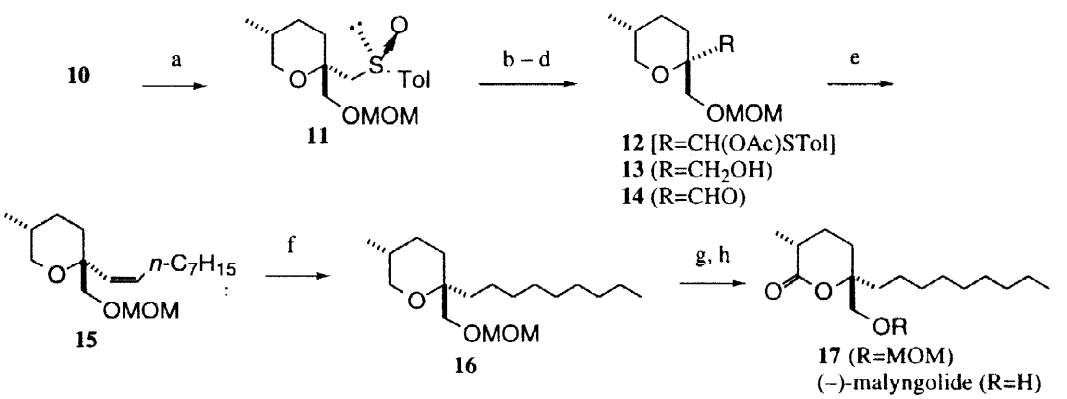
stereoselectivity. After reduction of the mesylate **3a** with Super Hydride®, the allyl group was isomerized to *trans*-1-propenyl group with a catalytic amount of $PdCl_2(PhCN)_2$ to give **9** in a 60% yield.[15] Ozonolysis of **9** followed by reduction with $NaBH_4$ yielded the alcohol **10** (Scheme 7).



a: $TiCl_4$, allyltrimethylsilane, CH_2Cl_2, −100°C; b: MsCl, DMAP, CH_2Cl_2, 0°C (65–73% from **1**); c: Super Hydride®, THF, room temp. (97%); d: $(PhCN)_2PdCl_2$, benzene, 80°C (60%, 90% based on the consumed **8**); e: O_3, MeOH, −78°C then $NaBH_4$, room temp. (93%).

Scheme 7

Next task was the introduction of the C_8-unit into the sulfinylmethyl side-chain to construct the nonyl substitutent of (−)-malyngolide. After protection as a methoxymethyl (MOM) ether, the *p*-tolylsulfinyl group was converted into the aldehyde **14** by a series of transformations featuring Pummerer rearrangement, reduction with $LiBH_4$, and Dess–Martin oxidation (Scheme 8).[16] Then, the aldehyde **14** was treated with Wittig reagent prepared from *n*-octyltriphenylphosphonium bromide with potassium hexamethyldisilazide (KHMDS) to exclusively afford the *Z*-olefin **15** in high yield. After the hydrogenation of olefin on 10% Pd–C to give the compound **16**, the tetrahydropyran ring of **16** was oxidized to the δ-lactone with RuO_4



a: MOMCl, i-Pr_2NEt, CH_2Cl_2, room temp. (77%); b: Ac_2O, AcONa, 130°C (90%);c: $LiBH_4$, THF, room temp. (97%); d:Dess–Martin reagent, CH_2Cl_2, 0°C (88%); e: $Ph_3P(n\text{-}C_8H_{17})Br$, KHMDS, THF, 0°C (94%); f: H_2, Pd–C, MeOH, room temp. (86%); g: $RuCl_3{\cdot}3H_2O$ (cat.), $NaIO_4$, CCl_4–MeCN–H_2O (1:1:1.5), room temp. (57%, 80% based on the consumed **16**); h: TMSBr, CH_2Cl_2, −30°C (85%).

Scheme 8

generated *in situ* by a catalytic amount of $RuCl_3 \cdot 3H_2O$ and $NaIO_4$ in low yield (28%),[17] and most of **16** was recovered. The acetonitrile modification developed by Sharpless and co-workers[18] improved conversion to afford **17** in a 57 % yield (80% based on the consumed **16**). Oxidation with $RuO_2 \cdot xH_2O$ and $NaIO_4$ was ineffective giving **17** at 17%. Finally, the MOM ether **17** was deprotected with TBSBr[19] to give (–)-malyngolide without epimerization at the methyl group. The spectroscopic data (^{1}H-NMR, ^{13}C-NMR, IR, and MS) was identical to the authentic data and the specific rotation [$[\alpha]_D$ –12.5 ($CHCl_3$)] was consistent with the reported value [$[\alpha]_D$ –13 ($CHCl_3$)].[7]

In summary, the nucleophilic acetal cleavage reaction of the bicyclic acetal **1** was investigated. On treatment with allyltrimethylsilane and $TiCl_4$, the acetal cleavage of the pro-*R* C–O bond and nucleophilic attack from the backside of the cleaved bond proceeded with high stereoselectivity to give the 2,2,5-trisubstituted tetrahydropyran derivative diastereoselectively. The reaction was successfully applied to a total synthesis of (–)-malyngolide.

Experimental

Melting points are uncorrected. Optical rotations were measured using a JASCO DIP-360 digital polarimeter. IR spectra were measured with a Horiba FT-210 IR spectrometer. ^{1}H-NMR spectra were measured with a JEOL JNM-GX500 spectrometer (500 MHz) or a JEOL JNM-LA-500 spectrometer (500 MHz). ^{13}C-NMR spectra were measured with a JEOL JNM-EX270 spectrometer (67.8 MHz). All signals are expressed as ppm downfield from tetramethylsilane used as an internal standard (δ value). The following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). Mass spectra were taken with a Shimadzu QP-1000 mass spectrometer and a JEOL JMS-D300 mass spectrometer. High resolution mass spectra were measured by a JEOL JMS-D300 or a JEOL JMS-600. Merck Kieselgel 60 was used as an adsorbent for column chromatography. For preparative TLC (PTLC), Kieselgel 60 F_{254} (Merck) was used. Unless stated, all solvents were used after dryness and all extracts were dried over $MgSO_4$.

(2*S*,5*S*,*Rs*)-, (2*S*,5*R*,*Rs*)-, (2*R*,5*S*,*Rs*)-, and (2*R*,5*R*,*Rs*)-2-Allyl-5-hydroxy-2-(*p*-toluenesulfinylmethyl)-tetrahydropyran (2a, 2b, 2c, and 2d) Titanium tetrachloride (52 µl, 0.47 mmol) was added to a solution of the bicyclic acetal **1** (25.0 mg, 93.9 µmol) and allyltrimethylsilane (14.9 µl, 0.939 mmol) in CH_2Cl_2 (2.5 ml) with stirring at –100 °C under N_2. After 10 min, the reaction was quenched with saturated $NaHCO_3$, and the mixture was extracted with ether. The extract was washed with 10% HCl, water, saturated $NaHCO_3$, and brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 1 : 1) to give **2a** and **2b** (23.4 mg, 81%), and **2c** and **2d** (2.6 mg, 9%) each as a colorless oil. Analytical samples of **2a–d** were purified by HPLC (for **2a,b**: hexane–AcOEt = 5 : 1, for **2c,d**: hexane–AcOEt = 3 : 1). **2a**: $[\alpha]_D^{25}$ +26.9 (c = 0.51, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.42–1.60 (m, 3H), 1.80–1.82 (m, 2H), 1.91–1.97 (m, 1H), 2.41 (s, 3H, Ar-C$\underline{H}_3$), 2.49 (dd, 1H, J = 14.6, 6.9 Hz, C$\underline{H}_2$CH=CH$_2$), 2.69 (dd, 1H, J = 14.6, 7.7 Hz, C$\underline{H}_2$CH=CH$_2$), 2.79 (d, 1H, J = 14.1 Hz, CH$_2$SO), 3.22 (d, 1H, J = 14.1 Hz, CH$_2$SO), 3.62–3.71 (m, 2H, C$\underline{H}_2$OH), 3.73 (dd, 1H, J = 12.4, 8.1 Hz, 6-H), 3.89 (dd, 1H, J = 12.4, 3.0 Hz, 6-H), 5.12–5.16 (m, 2H, CH=C$\underline{H}_2$), 5.74–5.80 (m, 1H, C$\underline{H}$=CH$_2$), 7.32 (d, 2H, J = 7.7 Hz, Ar-$\underline{H}$), 7.52 (d, 2H, J = 7.7 Hz, Ar-$\underline{H}$). IR (KBr): 3381, 2926, 2864, 1728, 1495, 1444, 1396, 1288, 1086, 1038 cm^{-1}.

MS *m/z* (%): 308 (M^+, 1.0), 267 (100). High MS Calcd for $C_{17}H_{24}O_3S$: 308.1446. Found: 308.1447. **2b**: $[\alpha]_D^{24}$ +100.2 (*c* = 0.13, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.48–1.60 (m, 3H), 1.74–1.80 (m, 2H), 1.90–1.95 (m, 1H), 2.18–2.24 (m, 1H, C<u>H</u>$_2$CH=CH$_2$), 2.41 (s, 3H, Ar-C<u>H</u>$_3$), 2.66 (1H, dd, *J* = 14.5, 6.9 Hz, C<u>H</u>$_2$CH=CH$_2$), 2.86 (d, 1H, *J* = 14.1 Hz, CH$_2$SO), 2.97 (d, 1H, *J* = 14.1 Hz, CH$_2$SO), 3.51–3.58 (m, 2H, C<u>H</u>$_2$OH), 3.60 (dd, 1H, *J* = 10.3, 5.1 Hz, 6-H), 3.97 (dd, 1H, *J* = 10.3, 3.4 Hz, 6-H), 5.08–5.14 (m, 2H, CH=C<u>H</u>$_2$), 5.65–5.72 (m, 1H, C<u>H</u>=CH$_2$), 7.32 (d, 2H, *J* = 8.1 Hz, Ar-<u>H</u>), 7.54 (d, 2H, *J* = 8.1 Hz, Ar-<u>H</u>). IR (KBr): 3396, 2927, 2856, 1495, 1456, 1441, 1084, 1063, 1038 cm^{-1}. MS *m/z* (%): 308 (M^+, 1.8), 155 (100). High MS Calcd for $C_{17}H_{24}O_3S$: 308.1446. Found: 308.1443. **2c**: $[\alpha]_D^{22}$ +66.8 (*c* = 0.50, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.50–1.88 (m, 6H), 2.41 (s, 3H, Ar-C<u>H</u>$_3$), 2.60 (dd, 1H, *J* = 14.6, 8.6 Hz, C<u>H</u>$_2$CH=CH$_2$), 2.83 (d, 1H, *J* = 13.7 Hz, CH$_2$SO), 2.86 (dd, 1H, *J* = 14.6, 6.0 Hz, C<u>H</u>$_2$CH=CH$_2$), 3.06 (d, 1H, *J* = 13.7 Hz, CH$_2$SO), 3.53–3.59 (m, 2H, C<u>H</u>$_2$OH), 3.57–3.59 (m, 1H, 6-H), 3.82 (dd, 1H, *J* = 12.0, 4.3 Hz, 6-H), 5.18–5.23 (m, 2H, CH=C<u>H</u>$_2$), 5.81–5.89 (m, 1H, C<u>H</u>=CH$_2$), 7.31 (d, 2H, *J* = 8.1 Hz, Ar-<u>H</u>), 7.53 (d, 2H, *J* = 8.1 Hz, Ar-<u>H</u>). IR (KBr): 3392, 2854, 1740, 1639, 1495, 1441, 1396, 1086, 1038, 1014 cm^{-1}. MS *m/z* (%): 308 (M^+, 1.2), 267 (100). High MS Calcd for $C_{17}H_{24}O_3S$: 308.1446. Found: 308.1448. **2d**: $[\alpha]_D^{22}$ +24.1 (*c* = 0.20, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.40-2.05 (m, 6H), 2.42 (s, 3H, Ar-C<u>H</u>$_3$), 2.66–2.74 (m, 2H, C<u>H</u>$_2$CH=CH$_2$), 2.87 (d, 1H, *J* = 13.7 Hz, CH$_2$SO), 3.16 (d, 1H, *J* = 13.7 Hz, CH$_2$SO), 3.36 (dd, 1H, *J* = 12.0, 9.4 Hz, 6-H), 3.52–3.57 (m, 2H, C<u>H</u>$_2$OH), 3.82–3.85 (m, 1H, 6-H), 5.19–5.25 (m, 2H, CH=C<u>H</u>$_2$), 5.91–5.93 (m, 1H, C<u>H</u>=CH$_2$), 7.32 (d, 2H, *J* = 7.7 Hz, Ar-<u>H</u>), 7.54 (d, 2H, *J* = 7.7 Hz, Ar-<u>H</u>). IR (KBr): 3388, 2926, 2854, 1738, 1464, 1445, 1263, 1088, 1038 cm^{-1}. MS *m/z* (%): 308 (M^+, 2.2), 127 (100). High MS Calcd for $C_{17}H_{24}O_3S$: 308.1446. Found: 308.1464.

(2*S*,5*R*,*Rs*)-2-Allyl-5-(*p*-nitrobenzoyloxymethyl)-2-(*p*-toluenesulfinylmethyl)tetrahydropyran (3) *p*-Nitrobenzoyl chloride (87.0 mg, 0.282 mmol) was added to a mixture of **2a** (77.3 mg, 0.251 mmol) and 4-*N*,*N*-dimethylaminopyridine (DMAP) (103 mg, 0.847 mmol) in CH_2Cl_2 (7 ml) with stirring at 0 °C under N_2. After 5 min, the reaction was quenched with water, and the mixture was extracted with ether. The extract was washed with saturated NH_4Cl and brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 1 : 1) to give **3** (105 mg, 82%) as colorless needles. mp 80–81 °C (Et_2O). $[\alpha]_D^{23}$ +128.6 (*c* = 0.86, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.66–1.72 (m, 1H), 1.86–1.99 (m, 3H), 2.14–2.18 (m, 1H), 2.42 (s, 3H, Ar-C<u>H</u>$_3$), 2.54 (dd, 1H, *J* = 14.1, 6.4 Hz, C<u>H</u>$_2$CH=CH$_2$), 2.72 (dd, 1H, *J* = 14.1, 8.1 Hz, C<u>H</u>$_2$CH=CH$_2$), 2.78 (d, 1H, *J* = 14.3 Hz, CH$_2$SO), 3.29 (d, 1H, *J* = 14.3 Hz, CH$_2$SO), 3.83 (dd, 1H, *J* = 12.0, 8.1 Hz, 6-H), 3.97 (dd, 1H, *J* = 12.0, 3.8 Hz, 6-H), 4.37 (dd, 1H, *J* = 11.1, 8.1 Hz, C<u>H</u>$_2$OPNB), 4.43 (dd, 1H, *J* = 11.1, 6.0 Hz, C<u>H</u>$_2$OPNB), 5.16 (d, 1H, *J* = 18.4 Hz, CH=C<u>H</u>$_2$), 5.18 (d, 1H, *J* = 9.8 Hz, CH=C<u>H</u>$_2$), 5.74–5.83 (m, 1H, C<u>H</u>=CH$_2$), 7.33 (d, 2H, *J* = 8.1 Hz, Ar-<u>H</u>), 7.53 (d, 2H, *J* = 8.1 Hz, Ar-<u>H</u>). ^{13}C-NMR ($CDCl_3$) δ: 21.3, 21.5, 30.2, 34.1, 43.1, 63.6, 64.8, 66.4, 74.2, 119.6, 123.5 (2C), 123.8 (2C), 130.0 (2C), 130.1 (2C), 132.5, 135.4, 141.3, 142.1, 150.5, 164.4. IR (KBr): 2947, 1724, 1527, 1348, 1275, 1088, 1041, 1014 cm^{-1}. MS *m/z* (%): 457 (M^+, 1.8), 139 (100). *Anal.* Calcd for $C_{24}H_{27}NO_6S$: C, 63.00; H, 5.95; N, 3.06; S, 7.01. Found : C, 62.78; H, 5.93; N, 3.07; S, 6.97.

Crystal data for 3 $C_{24}H_{27}NO_6S$, *M*=457.542; Orthorhombic *a*=15.387(2), *b*=23.920(2). *c*=6.280(4) Å, *V*=2311.4(5) Å^3; Space group $P2_12_12_1$; *Z*=4, *D*x=1.3148 gcm^{-3}; μ(Cu-Kα)=15.38cm^{-1}; Rigaku AFC-5R diffractometer graphite monochromated Cu-Kα (λ=1.5148 Å) radiation; 2023 ($2\theta_{max}$=125°) measured reflections; 1356 observed reflections with $Fo>3\sigma$ (*Fo*). Final *R* factor=0.125. Atom coordinates, bond

lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC).

(2*S*,5*R*,*Rs*)- and (2*S*,5*S*,*Rs*)-2-Allyl-5-(methanesulfonyloxymethyl)-2-(*p*-toluenesulfinylmethyl)tetrahydropyran (4a and 4b) Methanesulfonyl chloride (10 μl, 0.13 mmol) was added to a mixture of **2a** and **2b** (20.0 mg, 0.0649 mmol, **2a** : **2b** = 5 : 1) and DMAP (23.8 mg, 0.195 mmol) in CH_2Cl_2 (3 ml) with stirring at 0 °C under N_2. After 5 min, the reaction was quenched with water, and the mixture was extracted with ether. The extract was washed with saturated NH_4Cl and brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 1 : 5) to give **4a** (20.0 mg, 80%) and **4b** (4.0 mg, 16%) each as a colorless oil. **4a**: $[\alpha]_D^{22}$ +124.9 (*c* = 0.98, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.53–1.65 (m, 2H), 1.88–1.94 (m, 1H), 2.08–2.17 (m, 2H), 2.42 (s, 3H, Ar-C$\underline{H}_3$), 2.38–2.45 (m, 1H, C$\underline{H}_2$CH=CH$_2$), 2.72 (dd, 1H, *J* = 14.1, 7.3 Hz, C$\underline{H}_2$CH=CH$_2$), 2.77 (d, 1H, *J* = 13.7 Hz, CH$_2$SO), 3.07 (s, 3H, SO_2CH_3), 3.08 (d, 1H, *J* = 13.7 Hz, CH$_2$SO), 3.79 (dd, 1H, *J* = 12.8, 5.5 Hz, 6-H), 3.89 (dd, 1H, *J* = 12.8, 3.8 Hz, 6-H), 4.29 (dd, 1H, *J* = 10.3, 6.4 Hz, CH$_2$OS), 4.41 (dd, 1H, *J* = 10.3, 7.7 Hz, CH$_2$OS), 5.11–5.18 (m, 2H, CH=C$\underline{H}_2$), 5.69–5.78 (m, 1H, C$\underline{H}$=CH$_2$), 7.32 (d, 2H, *J* = 8.1 Hz, Ar-$\underline{H}$), 7.52 (d, 2H, *J* = 8.1 Hz, Ar-$\underline{H}$). ^{13}C-NMR ($CDCl_3$) δ: 20.8, 21.3, 28.9, 33.7, 36.9, 41.4, 62.4, 65.4, 70.2, 74.2, 119.6, 123.8 (2C), 130.8 (2C), 132.2, 141.3, 141.9. IR (KBr): 2929, 1354, 1174, 1088, 1039 cm^{-1}. MS *m/z* (%): 386 (M$^+$, 1.9), 139 (100). High MS Calcd for $C_{18}H_{26}O_5S_2$: 386.1222. Found : 386.1217. **4b**: $[\alpha]_D^{23}$ +74.5 (*c* = 0.28, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.53–1.64 (m, 1H), 1.75–1.84 (m, 2H), 2.16–2.23 (m, 2H), 2.41 (s, 3H, Ar-C$\underline{H}_3$), 2.38–2.44 (m, 1H, C$\underline{H}_2$CH=CH$_2$), 2.65 (dd, 1H, *J* = 14.1, 7.3 Hz, C$\underline{H}_2$CH=CH$_2$), 2.83 (d, 1H, *J* = 14.5 Hz, CH$_2$SO), 3.00 (d, 1H, *J* = 14.5 Hz, CH$_2$SO), 3.03 (s, 3H, SO_2CH_3), 3.57 (dd, 1H, *J* = 12.0, 9.4 Hz, 6-H), 3.98 (dd, 1H, *J* = 12.0, 3.9 Hz, 6-H), 4.13 (dd, 1H, *J* = 9.8, 7.3 Hz, CH$_2$OS), 4.18 (dd, 1H, *J* = 9.8, 5.6 Hz, CH$_2$OS), 5.09–5.16 (m, 2H, CH=C$\underline{H}_2$), 5.65–5.71 (m, 1H, C$\underline{H}$=CH$_2$), 7.32 (d, 2H, *J* = 7.7 Hz, Ar-$\underline{H}$), 7.52 (d, 2H, *J* = 7.7 Hz, Ar-$\underline{H}$). IR (KBr): 2927, 2854, 1354, 1174, 1088, 1039 cm^{-1}. MS *m/z* (%): 386 (M$^+$, 1.2), 233 (100). High MS Calcd for $C_{18}H_{26}O_5S_2$: 386.1222. Found : 386.1236.

(2*R*,5*R*,*Rs*)- and (2*R*,5*S*,*Rs*)-2-Allyl-5-(methanesulfonyloxymethyl)-2-(*p*-toluenesulfinylmethyl)tetrahydropyran (4c and 4d) By the same procedure for **4a** and **4b** from **2a** and **2b**, a mixture of **2c** and **2d** (20.0 mg, 0.0649 mmol, **2c** : **2d** = 5 : 3) was converted into **4c** (15.0 mg, 60%) and **4d** (9.0 mg, 36%) each as a colorless oil. **4c**: $[\alpha]_D^{26}$ +48.2 (*c* = 0.54, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.54–1.73 (m, 2H), 1.78–1.89 (m, 2H), 2.05–2.07 (m, 1H), 2.41 (s, 3H, Ar-C$\underline{H}_3$), 2.61 (dd, 1H, *J* = 14.5, 8.5 Hz, C$\underline{H}_2$CH=CH$_2$), 2.83 (d, 1H, *J* = 13.7 Hz, C$\underline{H}_2$SO), 2.84 (dd, 1H, *J* = 14.5, 4.7 Hz, C$\underline{H}_2$CH=CH$_2$), 3.03 (s, 3H, SO_2CH_2), 3.07 (d, 1H, *J* = 13.7 Hz, CH$_2$SO), 3.57 (dd, 1H, *J* = 12.0, 8.6 Hz, 6-H), 3.80 (dd, 1H, *J* = 12.0, 3.9 Hz, 6-H), 4.15–4.18 (m, 2H, CH$_2$OS), 5.20–5.24 (m, 2H, CH=C$\underline{H}_2$), 5.80–5.89 (m, 1H, C$\underline{H}$=CH$_2$), 7.32 (d, 2H, *J* = 8.1 Hz, Ar-$\underline{H}$), 7.52 (d, 2H, *J* = 8.1 Hz, Ar-$\underline{H}$). IR (KBr): 2931, 2858, 1354, 1174, 1088, 1043 cm^{-1}. MS *m/z* (%): 386 (M$^+$, 0.3), 233 (100). High MS Calcd for $C_{18}H_{26}O_5S_2$: 386.1222. Found : 386.1227. **4d**: $[\alpha]_D^{25}$ +61.2 (*c* = 0.44, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.51–1.70 (m, 2H), 1.80–1.84 (m, 1H), 1.95–2.06 (m, 2H), 2.42 (s, 3H, Ar-C$\underline{H}_3$), 2.66 (dd, 1H, *J* = 14.5, 8.6 Hz, C$\underline{H}_2$CH=CH$_2$), 2.75 (dd, 1H, *J* = 14.5, 6.4 Hz, C$\underline{H}_2$CH=CH$_2$), 2.83 (d, 1H, *J* = 13.7 Hz, CH$_2$SO), 3.03 (s, 3H, SO_2CH_3), 3.14 (d, 1H, *J* = 13.7 Hz, CH$_2$SO), 3.39 (dd, 1H, *J* = 12.0, 8.6 Hz, 6-H), 3.83 (dd, 1H, *J* = 12.0, 3.8 Hz, 6-H), 4.11 (dd, 1H, *J* = 10.0, 7.7 Hz, CH$_2$OMs), 4.16 (dd, 1H, *J* = 10.0, 5.6 Hz, CH$_2$OMs), 5.20–5.24 (m, 2H, CH=C$\underline{H}_2$), 5.84–5.92 (m, 1H, C$\underline{H}$=CH$_2$), 7.33 (d, 2H, *J* = 8.6 Hz, Ar-$\underline{H}$), 7.53 (d, 2H, *J* = 8.6 Hz, Ar-$\underline{H}$). IR (KBr): 2927, 2854, 1354, 1174, 1085, 1043 cm^{-1}. MS *m/z*

(%): 386 (M^+, 1.4), 139 (100). High MS Calcd for $C_{18}H_{26}O_5S_2$: 386.1222. Found : 386.1215.

(2*S*,*Rs*)-2-Allyl-5-methylidene-2-(*p*-toluenesulfinylmethyl)tetrahydropyran (5a) From **4a**: Sodium borohydride (2.4 mg, 0.062 mmol) was added to a suspension of 2-nitrophenyl selenocyanate (14.1 mg, 0.0622 mmol) in EtOH (0.6 ml) with stirring at 0 °C under N_2. After 5 min, a solution of **4a** (8.0 mg, 0.021 mmol) in EtOH (0.2 ml) was added to the mixture with stirring at 0 °C. The stirring was continued for 20 h at room temperature. Then, the mixture was diluted with THF (0.4 ml) and cooled with ice bath. After 30% H_2O_2 (71 μl, 0.62 mmol) was added to the mixture with stirring at 0 °C, the whole was stirred for 24 h at room temperature. The mixture was partitioned between hexane and water. The organic layer was separated and the aqueous layer was extracted with hexane. The combined organic layers were washed with brine and dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 1 : 2) to give **5a** (4.2 mg, 70%) as a colorless oil. $[\alpha]_D^{20}$ +38.1 (*c* = 0.36, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.82–1.86 (m, 1H), 2.00–2.13 (m, 2H), 2.37–2.43 (m, 1H), 2.41 (s, 3H, Ar-C$\underline{H}_3$), 2.53 (dd, 1H, *J* = 14.3, 7.5 Hz, C$\underline{H}_2$CH=CH_2), 2.72 (dd, 1H, *J* = 14.3, 7.5 Hz, C$\underline{H}_2$CH=CH_2), 2.85 (d, 1H, *J* = 14.1 Hz, CH_2SO), 3.15 (d, 1H, *J* = 14.1 Hz, CH_2SO), 4.19 (d, 1H, *J* = 13.2 Hz, 6-H), 4.24 (d, 1H, *J* = 13.2 Hz, 6-H), 4.81–4.85 (m, 2H, C=C$\underline{H}_2$), 5.13–5.17 (m, 2H, CH=C$\underline{H}_2$), 5.73–5.78 (m, 1H, C$\underline{H}$=CH_2), 7.31 (d, 2H, *J* = 8.1 Hz, Ar-$\underline{H}$), 7.54 (d, 2H, *J* = 8.1 Hz, Ar-$\underline{H}$). ^{13}C-NMR ($CDCl_3$) δ: 21.4, 27.3, 33.4, 40.6, 66.3, 66.9, 74.1, 109.5, 119.4, 124.0 (2C), 129.9 (2C), 132.6, 141.2, 142.4, 142.6. IR (KBr): 2926, 2852, 1732, 1462, 1288, 1263, 1176, 1149, 1088, 1065 cm^{-1}. MS *m/z* (%): 290 (M^+, 35.3), 161 (100). High MS Calcd for $C_{17}H_{22}O_2S$: 290.1338. Found: 290.1337.

From **4b**: By the same procedure, **4b** (3.0 mg, 0.0078 mmol) was converted into **5a** (1.7 mg, 75%).

(2*R*,*Rs*)-2-Allyl-5-methylidene-2-(*p*-toluenesulfinylmethyl)tetrahydropyran (5b) From **4c**: By the same procedure for **5a** from **4a**, **4c** (5.0 mg, 0.013 mmol) was converted into **5b** (2.5 mg, 67%) as a colorless oil. $[\alpha]_D^{22}$ +20.9 (*c* = 0.46, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.81–1.95 (m, 2H), 2.30–2.39 (m, 2H), 2.41 (s, 3H, Ar-C$\underline{H}_3$), 2.70 (dd, 1H, *J* = 14.5, 8.6 Hz, C$\underline{H}_2$CH=CH_2), 2.85 (dd, 1H, *J* = 14.5, 6.0 Hz, C$\underline{H}_2$CH=CH_2), 2.88 (d, 1H, *J* = 13.7 Hz, CH_2SO), 3.15 (d, 1H, *J* = 13.7 Hz, CH_2SO), 4.03 (d, 1H, *J* = 13.3 Hz, 6-H), 4.12 (d, 1H, *J* = 13.3 Hz, 6-H), 4.79–4.81 (m, 2H, C=CH_2), 5.22–5.26 (m, 2H, CH=C$\underline{H}_2$), 5.88–5.94 (m, 1H, C$\underline{H}$=CH_2), 7.32 (d, 2H, *J* = 8.6 Hz, Ar-$\underline{H}$), 7.54 (d, 2H, *J* = 8.6 Hz, Ar-$\underline{H}$). IR (KBr): 2926, 2854, 1736, 1458, 1379, 1261, 1244, 1151, 1122, 1065 cm^{-1}. MS *m/z* (%): 290 (M^+, 2.6), 137 (100). High MS Calcd for $C_{17}H_{22}O_2S$: 290.1338. Found: 290.1338.

From **4d**: By the same procedure, **4d** was (5.0 mg, 0.013 mmol) was converted into **5b** (2.7 mg, 72%).

(2*R*,5*R*,*Rs*)-5-(Methanesulfonyloxymethyl)-2-methyl-2-propyltetrahydropyran (6a) Raney Ni (W2) (*ca.* 30 mg) was added to a solution of **4a** (12.0 mg, 0.0311 mmol) in EtOH (3 ml) with stirring at room temperature. The stirring was continued for 30 min. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 1 : 3) to give **6a** (7.0 mg, 90%) as a colorless oil. $[\alpha]_D^{24}$ +1.7 (*c* = 0.70, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.92 (t, 3H, *J* = 7.3 Hz, $CH_2CH_2C\underline{H}_3$), 1.15 (s, 3H, CCH_3), 1.29–1.60 (m, 8H), 1.97–2.00 (m, 1H, CH), 3.01 (s, 3H, SO_2CH_3), 3.46 (dd, 1H, *J* = 12.0, 9.4 Hz, 6-H), 3.76 (ddd, 1H, *J* = 12.0, 4.3, 1.7 Hz, 6-H), 4.10 (dd, 1H, *J* = 9.4, 6.9 Hz, CH_2OMs), 4.15 (dd, 1H, *J* = 9.4,

6.0 Hz, CH_2OMs). ^{13}C-NMR ($CDCl_3$) δ: 14.7, 16.5, 21.0, 21.8, 33.1, 35.4, 37.3, 44.1, 62.5, 70.8, 73.2. IR (KBr): 2933, 2872, 1732, 1468, 1356, 1176, 1097, 1061 cm^{-1}. MS *m/z* (%): 250 (M^+, 1.8), 207 (100). High MS Calcd for $C_{11}H_{22}O_4S$: 250.1239. Found: 250.1236.

(2*R*,5*S*,*Rs*)-5-(Methanesulfonyloxymethyl)-2-methyl-2-propyltetrahydropyran (6b) By the same procedure for **6a** from **4a**, **4b** (4.0 mg, 0.010 mmol) was converted into **6b** (2.5 mg, 96%) as a colorless oil. $[\alpha]_D^{24}$ –5.4 (*c* = 0.70, $CHCl_3$). ^1H-NMR ($CDCl_3$) δ: 0.93 (t, 3H, *J* = 7.3 Hz, $CH_2CH_2CH_3$), 1.17 (s, 3H, 5-CH_3), 1.27–1.78 (m, 8H), 1.96–2.02 (m, 1H, 5-H), 3.01 (s, 3H, SO_2CH_3), 3.44 (dd, 1H, *J* = 12.0, 7.7 Hz, 6-H), 3.77 (dd, 1H, *J* = 12.0, 3.4 Hz, 6-H), 4.15 (dd, 1H, *J* = 9.4, 6.9 Hz, CH_2OMs), 4.18 (dd, 1H, *J* = 9.4, 6.0 Hz, CH_2OMs). IR (KBr): 2926, 2854, 1738, 1466, 1358, 1176, 1101, 1074 cm^{-1}. MS *m/z* (%): 250 (M^+, 0.8), 207 (100). High MS Calcd for $C_{11}H_{22}O_4S$: 250.1239. Found : 250.1217.

(2*S*,5*S*,*Rs*)-5-(Methanesulfonyloxymethyl)-2-methyl-2-propyltetrahydropyran (6c) By the same procedure for **6a** from **4a**, **4c** (3.5 mg, 0.0091 mmol) was converted into **6c** (2.2 mg, 97%) as a colorless oil. $[\alpha]_D^{24}$ +2.9 (*c* = 0.22, $CHCl_3$). ^1H-NMR ($CDCl_3$) δ: 0.93 (t, 3H, *J* = 7.3 Hz, $CH_2CH_2CH_3$), 1.17 (s, 3H, 2-CH_3), 1.28–1.78 (m, 8H), 1.97–2.02 (m, 1H, 5-H), 3.01 (s, 3H, SO_2CH_3), 3.44 (dd, 1H, *J* = 12.0, 7.7 Hz, 6-H), 3.77 (dd, 1H, *J* = 12.0, 3.4 Hz, 6-H), 4.15 (dd, 1H, *J* = 9.4, 6.9 Hz, CH_2OMs), 4.18 (dd, 1H, *J* = 9.4, 6.0 Hz, CH_2OMs). IR (KBr): 2926, 2854, 1734, 1458, 1356, 1176, 1099, 1074 cm^{-1}. MS *m/z* (%): 250 (M^+, 2.1), 235 (M^+–CH_3, 13.6), 207 (100). High MS Calcd for $C_{10}H_{19}O_4S$ (M^+–CH_3): 235.1001. Found: 235.1001.

(2*S*,5*R*,*Rs*)-5-(Methanesulfonyloxymethyl)-2-methyl-2-propyltetrahydropyran (6d) By the same procedure for **6a** from **4a**, **4d** (2.5 mg, 0.0065 mmol) was converted into **6d** (1.5 mg, 93%) as a colorless oil. $[\alpha]_D^{24}$ –0.9 (*c* = 0.23, $CHCl_3$). ^1H-NMR ($CDCl_3$) δ: 0.92 (t, 3H, *J* = 7.3 Hz, $CH_2CH_2CH_3$), 1.15 (s, 3H, 2-CH_3), 1.29–1.60 (m, 8H), 1.98–2.00 (m, 1H, 5-H), 3.01 (s, 3H, SO_2CH_3), 3.46 (dd, 1H, *J* = 12.0, 9.4 Hz, 6-H), 3.76 (ddd, 1H, *J* = 12.0, 4.3, 1.7 Hz, 6-H), 4.10 (dd, 1H, *J* = 9.4, 6.9 Hz, CH_2OMs), 4.15 (dd, 1H, *J* = 9.4, 6.0 Hz, CH_2OMs). IR (KBr): 2926, 2854, 1734, 1466, 1356, 1176, 1097, 1063 cm^{-1}. MS *m/z* (%): 250 (M^+, 1.0), 235 (M^+–CH_3, 18.2), 207 (100). High MS Calcd for $C_{10}H_{19}O_4S$ (M^+–CH_3): 235.1001. Found: 235.1000.

(2*S*,5*R*,*Rs*)-5-(Methanesulfonyloxymethyl)-2-(1,2-propadienyl)-2-(*p*-tolylsulfinylmethyl)tetrahydropyran (7) Titanium tetrachloride (0.560 ml, 3.76 mmol) was added to a mixture of **1** (100 mg, 0.376 mmol) and propargyltrimethylsilane (0.206 ml, 1.88 mmol) in CH_2Cl_2 (10 ml) with stirring at –100 °C for 10 min under N_2. After 10 min, the reaction was quenched with saturated $NaHCO_3$ aqueous solution, and the mixture was extracted with ether. The extract was washed with 10% HCl, water, saturated $NaHCO_3$ aqueous solution, and brine, and then dried. After filtration, the solvent was evaporated and the residue was passed through silica gel (hexane–AcOEt = 3 : 1) to give the crude alcohol (87.0 mg). Methanesulfonyl chloride (44 µl, 0.57 mmol) was added to a mixture of the crude alcohol (87.0 mg) and DMAP (104 mg, 0.853 mmol) in CH_2Cl_2 (5 ml) with stirring at 0 °C under N_2. The whole was stirred at 0 °C for 5 min. The reaction was quenched with water, and the mixture was extracted with ether. The extract was washed with saturated NH_4Cl aqueous solution and brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 2 : 3) to give **7** (83.0 mg, 57% in 2 steps) as a colorless oil. $[\alpha]_D^{26}$ +209.8 (*c* = 0.87, $CHCl_3$). ^1H-NMR ($CDCl_3$) δ: 1.70–1.75 (m,

2H), 1.94–2.05 (m, 2H), 2.37–2.44 (m, 1H), 2.39 (s, 3H, Ar-C$\underline{H}_3$), 2.86 (d, 1H, J = 13.7 Hz, CH_2SO), 2.98 (d, 1H, J = 13.7 Hz, CH_2SO), 3.10 (s, 3H, SO_2CH_3), 3.92 (m, 2H, C$\underline{H}_2$OMs), 4.41 (dd, 1H, J = 10.2, 7.2 Hz, 6-H), 4.62 (t, 1H, J = 10.2 Hz, 6-H), 4.89 (dd, 1H, J = 12.0, 6.9 Hz, C=CH_2), 4.93 (dd, 1H, J = 12.0, 6.9 Hz, C=CH_2), 5.13 (t, 1H, J = 6.9 Hz, CH=C), 7.31 (d, 2H, J = 8.6 Hz, Ar-$\underline{H}$), 7.53 (d, 2H, J = 8.6 Hz, Ar-$\underline{H}$). ^{13}C-NMR ($CDCl_3$) δ: 20.6, 21.4, 26.5, 32.8, 36.8, 62.8, 69.9, 69.9, 74.8, 78.5, 94.4, 123.9 (2C), 130.0 (2C), 141.3, 141.9, 207.8. IR (KBr): 2935, 2927, 2872, 1954, 1493, 1454, 1352, 1211, 1174, 1086, 1057, 1036 cm^{-1}. MS m/z (%): 384 (M^+, 23.6), 137 (100). High MS Calcd for $C_{18}H_{24}O_5S_2$: 384.1065. Found: 384.1069.

(2*S*,5*R*,*R*s)-2-Allyl-5-methyl-2-(*p*-tolylsulfinylmethyl)tetrahydropyran (8) Super Hydride® (1.0 M THF solution) (1.04 ml, 1.04 mmol) was added to a solution of **4a** (100 mg, 0.259 mmol) in THF (5 ml) with stirring at room temperature under N_2. The stirring was continued at room temperature for 1 h. Water was added to the solution. The mixture was extracted with ether, and the extract was washed with brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 3 : 1) to give **8** (74.0 mg, 98%) as a colorless oil. $[\alpha]_D^{32}$ +123.6 (c = 1.05, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.89 (d, 3H, J = 6.0 Hz, 5-CH_3), 1.60–1.77 (m, 5H), 2.41 (s, 3H, Ar-C$\underline{H}_3$), 2.53 (dd, 1H, J = 13.7, 6.4 Hz, C$\underline{H}_2$CH=CH_2), 2.65 (dd, 1H, J = 13.7, 8.5 Hz, C$\underline{H}_2$CH=CH_2), 2.78 (d, 1H, J = 14.1 Hz, CH_2SO), 3.37 (d, 1H, J = 14.1 Hz, CH_2SO), 3.47 (dd, 1H, J = 11.5, 10.3 Hz, 6-H), 3.72 (dd, 1H, J = 11.5, 3.4 Hz, 6-H), 5.14 (d, 1H, J = 16.2 Hz, CH=C$\underline{H}_2$), 5.15 (d, 1H, J = 11.1 Hz, CH=C$\underline{H}_2$), 5.76–5.82 (m, 1H, C$\underline{H}$=CH_2), 7.32 (d, 2H, J = 8.6 Hz, Ar-$\underline{H}$), 7.54 (d, 2H, J = 8.6 Hz, Ar-$\underline{H}$). ^{13}C-NMR ($CDCl_3$) δ: 17.0, 21.3, 27.3, 30.0, 31.8, 44.8, 63.8, 68.2, 73.6, 119.2, 123.8 (2C), 129.9 (2C), 133.0, 141.1, 142.4. IR (KBr): 2929, 2872, 1639, 1493, 1456, 1396, 1086, 1039 cm^{-1}. MS m/z (%): 292 (M^+, 2.4), 69 (100). *Anal.* Calcd for $C_{17}H_{24}O_2S$: C, 69.82; H, 8.27; S, 10.96. Found: C, 69.43; H, 8.10; S, 11.06.

(2*S*,5*R*,*R*s)-5-Methyl-2-[(*E*)-1-propenyl]-2-(*p*-tolylsulfinylmethyl)tetrahydropyran (9) A mixture of $(PhCN)_2PdCl_2$ (7.1 mg, 0.019 mmol) and **8** (27.0 mg, 0.0924 mmol) in benzene (2 ml) was heated to 80 °C for 54 h under N_2. After cooling, the reaction was quenched with saturated $NaHCO_3$ aqueous solution. The mixture was extracted with ether, and the extract was washed with water and brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 5 : 1) to give **9** (16.3 mg, 60%) as a colorless oil along with **8** (8.0 mg, 30%). $[\alpha]_D^{27}$ +111.2 (c = 1.73, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.02 (d, 3H, J = 6.8 Hz, 5-CH_3), 1.62–1.77 (m, 4H), 1.72 (dd, 3H, J = 6.8, 1.7 Hz, CH=CHC$\underline{H}_3$), 2.05 (m, 1H), 2.40 (s, 3H, Ar-C$\underline{H}_3$), 2.83 (d, 1H, J = 13.7 Hz, CH_2SO), 3.28 (d, 1H, J = 13.7 Hz, CH_2SO), 3.51 (dd, 1H, J = 12.0, 6.4 Hz, 6-H), 3.81 (dd, 1H, J = 12.0, 3.4 Hz, 6-H), 5.43 (dd, 1H, J = 16.2, 1.7 Hz, C$\underline{H}$=CHCH$_3$), 5.73 (qd, 1H, J = 16.2, 6.8 Hz, CH=C$\underline{H}$CH$_3$), 7.30 (d, 2H, J = 8.1 Hz, Ar-$\underline{H}$), 7.53 (d, 2H, J = 8.1 Hz, Ar-$\underline{H}$). ^{13}C-NMR ($CDCl_3$) δ: 16.9, 17.9, 21.3, 26.8, 29.1, 30.7, 68.1, 68.8, 74.2, 124.0 (2C), 126.6, 129.8 (2C), 134.6, 141.0, 142.7. IR (KBr): 2926, 2858, 1493, 1452, 1385, 1086, 1041 cm^{-1}. MS m/z (%): 292 (M^+, 1.3), 153 (100). High MS Calcd for $C_{17}H_{24}O_2S$: 292.1497. Found: 292.1485.

(2*S*,5*R*,*R*s)-2-Hydroxymethyl-5-methyl-2-(*p*-tolylsulfinylmethyl)tetrahydropyran (10) From **9**: A stream of ozone was bubbled through a solution of **9** (95.0 mg, 0.291 mmol) in dry MeOH (4 ml) at –78 °C until a pale blue color developed (5 min). Nitrogen was bubbled through the solution to remove excess ozone. Sodium borohydride (55.0 mg, 1.45 mmol) was added, the reaction mixture was allowed to warm to room temperature, and the stirring was continued for 1 h. Water was added to the mixture. The whole was

extracted with AcOEt, and the extract was washed with brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 1 : 2) to give **10** (85.0 mg, 93%) as a colorless powder. mp 92–94 °C (Et_2O). $[\alpha]_D^{24}$ +65.8 (c = 0.63, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.83 (d, 3H, J = 6.0 Hz, 5-CH_3), 1.20–1.24 (m, 1H), 1.60–1.96 (m, 4H), 2.43 (s, 3H, Ar-C$\underline{H}_3$), 3.03 (d, 1H, J = 13.7 Hz, CH_2SO), 3.17 (d, 1H, J = 12.4 Hz, C$\underline{H}_2$OH), 3.22 (d, 1H, J = 12.4 Hz, C$\underline{H}_2$OH), 3.26 (d, 1H, J = 13.7 Hz, CH_2SO), 3.64 (dd, 1H, J = 12.0, 7.7 Hz, 6-H), 3.65–3.70 (m, 1H, OH), 3.78 (dd, 1H, J = 12.0, 6.9 Hz, 6-H), 7.36 (d, 2H, J = 8.1 Hz, Ar-$\underline{H}$), 7.57 (d, 2H, J = 8.1 Hz, Ar-$\underline{H}$). ^{13}C-NMR ($CDCl_3$) δ: 17.0, 21.4, 27.3, 28.8, 30.3, 61.0, 68.2, 69.5, 74.4, 123.9 (2C), 130.1 (2C), 141.0, 141.8. IR (KBr): 3359, 2927, 2872, 1495, 1456, 1383, 1244, 1171, 1088, 1012 cm^{-1}. MS m/z (%): 282 (M^+, 0.5), 140 (100). *Anal.* Calcd for $C_{15}H_{22}O_3S$: C, 63.80; H, 7.85; S, 11.35. Found: C, 63.59; H, 7.68; S, 11.24.

(2*S*,5*R*,*Rs*)-2-Hydroxymethyl-5-methyl-2-(*p*-tolylsulfinylmethyl)tetrahydropyran (10) From **7**: Super Hydride® (1.0 M THF solution) (0.117 ml, 0.117 mmol) was added to a solution of **7** (9.0 mg, 0.023 mmol) in THF (0.8 ml) with stirring at room temperature under N_2. The stirring was continued at room temperature for 6 h. Water was added to the mixture. The mixture was extracted with ether and the organic layer was washed with brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 5 : 2) to give the methyl compound (6.0 mg, 88%) as a colorless oil. $[\alpha]_D^{24}$ +145.6 (c = 0.52, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.08 (d, 3H, J = 6.9 Hz, 5-CH_3), 1.35–1.85 (m, 4H), 2.10–2.18 (m, 1H), 2.38 (s, 3H, Ar-C$\underline{H}_3$), 2.95 (d, 1H, J = 13.7 Hz, CH_2SO), 3.24 (d, 1H, J = 13.7 Hz, CH_2SO), 3.55 (dd, 1H, J = 12.0, 5.3 Hz, 6-H), 3.86 (dd, 1H, J = 12.0, 3.4 Hz, 6-H), 4.87 (dd, 1H, J = 11.1, 6.9 Hz, C=CH_2), 4.90 (dd, 1H, J = 11.1, 6.9 Hz, C=CH_2), 5.26 (t, 1H, J = 6.9 Hz, CH=C), 7.31 (d, 2H, J = 8.6 Hz, Ar-$\underline{H}$), 7.56 (d, 2H, J = 8.6 Hz, Ar-$\underline{H}$). ^{13}C-NMR ($CDCl_3$) δ: 16.7, 21.4, 26.4, 28.5, 29.4, 68.5, 69.3, 74.1, 78.3, 96.0, 124.0 (2C), 129.8 (2C), 141.0, 142.6, 207.3. IR (KBr): 2926, 2856, 1956, 1732, 1493, 1452, 1385, 1136, 1086, 1041, 1014 cm^{-1}. MS m/z (%): 290 (M^+, 19.7), 137 (100). High MS Calcd for $C_{17}H_{22}O_2S$: 290.1340. Found: 290.1341.

A stream of ozone was bubbled through a solution of the above product (75.0 mg, 0.259 mmol) in dry MeOH (3 ml) at –78 °C until a pale blue color developed (5 min). Nitrogen was bubbled through the solution to remove excess ozone. Sodium borohydride (48.9 mg, 1.29 mmol) was added, the reaction mixture was allowed to warm to room temperature, and the stirring was continued for 1 h. Water was added to the mixture. The whole was extracted with AcOEt, washed with brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 1 : 1) to give **10** (67.0 mg, 92%).

(2*S*,5*R*,*Rs*)-2-(Methoxymethoxymethyl)-5-methyl-2-(*p*-tolylsulfinylmethyl)tetrahydropyran (11) Methoxymethyl chloride (52 μl, 0.68 mmol) was added to a mixture of **10** (64.0 mg, 0.227 mmol) and diisopropylethylamine (0.198 ml, 1.13 mmol) in CH_2Cl_2 (2.5 ml) with stirring at room temperature under N_2. The stirring was continued at room temperature for 21 h. Saturated $NaHCO_3$ aqueous solution was added to the mixture. The mixture was extracted with ether, and the extract was washed with saturated NH_4Cl aqueous solution and brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 2 : 1) to give **11** (57.0 mg, 77%) as a colorless oil. $[\alpha]_D^{21}$ +88.1 (c = 1.14, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.89 (d, 3H, J = 6.7 Hz, 5-CH_3), 1.60–1.86 (m, 5H), 2.41 (s, 3H, Ar-C$\underline{H}_3$), 2.99 (d, 1H, J = 14.3 Hz, CH_2SO), 3.37 (s, 3H, OCH_3), 3.42 (d, 1H, J = 14.3 Hz,

CH_2SO), 3.48 (dd, 1H, J = 12.2, 10.1 Hz, 6-H), 3.57 (d, 1H, J = 10.1 Hz, C$\underline{H}_2$OMOM), 3.74 (ddd, 1H, J = 12.2, 4.3, 1.8 Hz, 6-H), 3.79 (d, 1H, J = 10.1 Hz, C$\underline{H}_2$OMOM), 4.67 (s, 2H, OCH_2O), 7.32 (d, 2H, J = 8.3 Hz, Ar-$\underline{H}$), 7.55 (d, 2H, J = 8.3 Hz, Ar-$\underline{H}$). ^{13}C-NMR ($CDCl_3$) δ: 17.1, 21.3, 27.2, 30.2, 30.4, 55.5, 61.7, 68.3, 73.3, 73.6, 96.9, 124.0 (2C), 129.9 (2C), 141.1, 142.5. IR (KBr): 2929, 2857, 1495, 1456, 1151, 1113, 1088, 1043 cm^{-1}. MS m/z (%): 326 (M^+, 1.3), 111 (100). High MS Calcd for $C_{17}H_{26}O_4S$: 326.1552. Found: 326.1556.

(2*S*,5*R*,*Rs*)-2-[1-Acetoxy-1-(*p*-tolylthio)methyl]-2-(methoxymethoxymethyl)-5-methyltetrahydropyran (12) Sodium acetate (69.2 mg, 0.844 mmol) was added to a mixture of **11** (55.0 mg, 0.169 mmol) in acetic anhydride (1 ml) with stirring at room temperature under N_2. The mixture was heated at 130 °C for 2.5 h. After cooling, acetic anhydride was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 6 : 1) to give **12** (56.0 mg, 90%, 67 : 33 diastereomeric mixture) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.85 (d, 3x67/100H, J = 6.0 Hz, 5-CH_3), 0.91 (d, 3x33/100H, J = 7.0 Hz, 5-CH_3), 1.60–2.17 (m, 5H), 1.98 (s, 3x33/100H, $COCH_3$), 2.02 (s, 3x67/100H, $COCH_3$), 2.33 (s, 3H, Ar-C$\underline{H}_3$), 3.34–3.38 (m, 1H, 6-H), 3.39 (s, 3x33/100H, OCH_3), 3.40 (s, 3x67/100H, OCH_3), 3.62–3.64 (m, 67/100H, 6-H), 3.63 (d, 67/100H, J = 10.0 Hz, C$\underline{H}_2$OMOM), 3.67 (d, 3/100H, J = 10.5 Hz, C$\underline{H}_2$OMOM), 3.76–3.78 (m, 33/100H, 6-H), 3.77 (d, 67/100H, J = 10.0 Hz, C$\underline{H}_2$OMOM), 3.81 (d, 33/100H, J = 10.5 Hz, C$\underline{H}_2$OMOM), 4.68 (d, 2x33/100H, J = 1.0 Hz, OCH_2O), 4.69 (s, 2x67/100H, OCH_2O), 6.69 (s, 67/100H, CHS), 6.70 (s, 33/100H, CHS), 7.11 (d, 2x33/100H, J = 7.8 Hz, Ar-$\underline{H}$), 7.12 (d, 2x67/100H, J = 8.3 Hz, Ar-$\underline{H}$), 7.40 (d, 2x67/100H, J = 8.3 Hz, Ar-$\underline{H}$), 7.42 (d, 2x33/100H, J = 7.8 Hz, Ar-$\underline{H}$). IR (KBr): 2951, 2881, 1751, 1493, 1456, 1369, 1221, 1149, 1113, 1086, 1049 cm^{-1}. MS m/z (%): 368 (M^+, 5.9), 173 (100). High MS Calcd for $C_{19}H_{28}O_5S$: 368.1657. Found: 368.1634.

(2*R*,5*R*)-2-(Hydroxymethyl)-2-(methoxymethoxymethyl)-5-methyltetrahydropyran (13) Lithium borohydride (66.3 mg, 3.04 mmol) was added to a solution of **12** (56.0 mg, 0.152 mmol) in THF (2 ml) with stirring at room temperature under N_2. The stirring was continued for 70 h. Water was added to the mixture. The mixture was extracted with ether, and the extract was washed with brine, and dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 2 : 1) to give **13** (30.0 mg, 97%) as a colorless oil. $[\alpha]_D^{18}$ –29.9 (c = 0.64, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.85 (d, 3H, J = 6.0 Hz, 5-CH_3), 1.45–1.55 (m, 2H), 1.57–1.63 (m, 2H), 1.63–1.73 (m, 1H), 2.24–2.26 (m, 1H, OH), 3.24 (dd, 1H, J = 11.5, 9.8 Hz, 6-H), 3.38 (s, 3H, OCH_3), 3.49 (d, 1H, J = 9.8 Hz, C$\underline{H}_2$OMOM), 3.56 (d, 1H, J = 9.8 Hz, C$\underline{H}_2$OMOM), 3.55-3.59 (m, 1H, C$\underline{H}_2$OH), 3.69 (ddd, 1H, J = 11.5, 4.5, 2.3 Hz, 6-H), 3.93 (dd, 1H, J = 11.5, 4.5 Hz, C$\underline{H}_2$OH), 4.65 (s, 2H, OCH_2O). ^{13}C-NMR ($CDCl_3$) δ: 17.1, 27.1, 27.4, 30.1, 55.4, 60.8, 68.0, 73.0, 73.8, 96.9. IR (KBr): 3448, 2951, 2927, 1458, 1146, 1113, 1086, 1049 cm^{-1}. MS m/z (%): 204 (M^+, 1.4), 129 (100). High MS Calcd for $C_{10}H_{20}O_4$: 204.1361. Found: 204.1358.

(2*R*,5*R*)-2-Formyl-2-(methoxymethoxymethyl)-5-methyltetrahydropyran (14) Dess–Martin reagent (93.5 mg, 0.220 mmol) was added to a solution of **13** (15.0 mg, 0.0735 mmol) in CH_2Cl_2 (1 ml) with stirring at 0 °C under N_2. The stirring was continued for 30 min. The mixture was diluted with ether. Saturated $NaHCO_3$ aqueous solution and saturated $Na_2S_2O_3$ aqueous solution were added to the mixture with stirring at 0 °C. The stirring was continued for 30 min. The mixture was extracted with ether, and the extract was washed with brine, and dried. After filtration, the solvent was evaporated and the residue was

chromatographed on silica gel (hexane–AcOEt = 5 : 1) to give **14** (13.0 mg, 88%) as a colorless oil. $[\alpha]_D^{21}$ −140.2 (c = 0.96, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.78 (d, 3H, J = 6.7 Hz, 5-CH_3), 1.01–1.05 (m, 1H), 1.35–1.42 (m, 1H), 1.64–1.73 (m, 2H), 2.07–2.12 (m, 1H), 3.24 (t, 1H, J = 11.6 Hz, 6-H), 3.31 (s, 3H, OCH_3), 3.55 (d, 1H, J = 9.8 Hz, C$\underline{H}_2$OMOM), 3.59 (d, 1H, J = 9.8 Hz, C$\underline{H}_2$OMOM), 3.93 (ddd, 1H, J = 11.6, 3.7, 1.8 Hz, 6-H), 4.57 (d, 1H, J = 6.7 Hz, OCH_2O), 4.59 (d, 1H, J = 6.7 Hz, OCH_2O), 9.83 (d, 1H, J = 1.8 Hz, CHO). ^{13}C-NMR ($CDCl_3$) δ: 16.9, 26.8, 28.4, 30.0, 55.3, 71.5, 72.4, 81.3, 96.6, 206.5. IR (KBr): 2954, 2877, 1736, 1460, 1149, 1113, 1088, 1047 cm^{-1}. MS m/z (%): 202 (M^+, 19.8), 173 (M^+–CHO, 42.9), 111 (100). High MS Calcd for $C_9H_{17}O_3$ (M^+–CHO): 173.1178. Found: 173.1192.

(2*R*,5*R*)-2-(Methoxymethoxymethyl)-5-methyl-2-[(*Z*)-1-nonenyl]tetrahydropyran (15) Potassium hexamethyldisilazide (0.5 M toluene solution) (1.73 ml, 0.866 mmol) was added to a solution of *n*-octyltriphenylphosphonium bromide (394 mg, 0.866 mmol) in THF (10 ml) with stirring at 0 °C under N_2. After 5 min, a solution of **14** (70.0 mg, 0.346 mmol) in THF (2 ml) was added with stirring at 0 °C. The whole was stirred at room temperature for 30 min. Water was added to the mixture. The mixture was extracted with ether, and the extract was washed with brine, and dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 20 : 1) to give **15** (97.0 mg, 94%) as a colorless oil. $[\alpha]_D^{25}$ −15.1 (c = 0.59, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.77 (d, 3H, J = 6.1 Hz, 5-CH_3), 0.88 (t, 3H, J = 6.7 Hz, $CH_2C\underline{H}_3$), 1.19–1.32 (m, 11H), 1.57–1.82 (m, 4H), 2.19–2.35 (m, 2H, CH=CHC$\underline{H}_2$), 3.20 (t, 1H, J = 11.0 Hz, 6-H), 3.35 (s, 3H, OCH_3), 3.45 (d, 1H, J = 10.1 Hz, C$\underline{H}_2$OMOM), 3.49 (d, 1H, J = 10.1 Hz, C$\underline{H}_2$OMOM), 3.59 (ddd, 1H, J = 11.0, 4.3, 1.8 Hz, 6-H), 4.65 (s, 2H, OCH_2O), 5.12 (td, 1H, J = 11.6, 1.8 Hz, C$\underline{H}$=CHCH$_2$), 5.61 (td, 1H, J = 11.6, 7.3 Hz, CH=C$\underline{H}$CH$_2$). ^{13}C-NMR ($CDCl_3$) δ: 14.1, 17.2, 22.6, 27.9, 28.5, 29.2, 29.5, 29.7, 30.7, 31.8, 32.7, 55.2, 68.8, 73.8, 77.1, 96.8, 128.6, 136.5. IR (KBr): 2924, 2854, 1458, 1146, 1113, 1086, 1051 cm^{-1}. MS m/z (%): 267 (M^+– OCH_3, 0.8), 223 (100). High MS Calcd for $C_{17}H_{31}O_2$ (M^+– OCH_3): 267.2324. Found : 267.2334.

(2*S*,5*R*)-2-(Methoxymethoxymethyl)-5-methyl-2-nonyltetrahydropyran (16) A solution of **15** (97.0 mg, 0.325 mmol) in MeOH (5 ml) was hydrogenated on 10% Pd–C (19.4 mg) with stirring at room temperature. The stirring was continued for 2 h. After filtration, the filtrate was concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane–AcOEt = 20 : 1) to give **16** (84.0 mg, 86%) as a colorless oil. $[\alpha]_D^{22}$ −15.6 (c = 0.77, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.82 (d, 3H, J = 6.7 Hz, 5-CH_3), 0.88 (t, 3H, J = 6.7 Hz, $CH_2C\underline{H}_3$), 1.19–1.34 (m, 14H), 1.49–1.78 (m, 7H), 3.20 (t, 1H, J = 11.3 Hz, 6-H), 3.36 (s, 3H, OCH_3), 3.38 (d, 1H, J = 9.8 Hz, C$\underline{H}_2$OMOM), 3.41 (d, 1H, J = 9.8 Hz, C$\underline{H}_2$OMOM), 3.61 (ddd, 1H, J = 11.3, 4.3, 1.8 Hz, 6-H), 4.64 (s, 2H, OCH_2O). ^{13}C-NMR ($CDCl_3$) δ: 14.1, 17.3, 22.6, 23.1, 27.4, 29.3, 29.6 (2C), 29.6, 29.9, 30.3, 30.5, 31.9, 55.2, 67.5, 73.1, 74.3, 96.8. IR (KBr): 2947, 2924, 2854, 1458, 1149, 1115, 1088, 1049 cm^{-1}. MS m/z (%): 269 (M^+– OCH_3, 0.7), 225 (100). High MS Calcd for $C_{17}H_{33}O_2$ (M^+– OCH_3): 269.2480. Found: 269.2481.

(2*R*,5*S*)-5-(Methoxymethoxymethyl)-2-methyl-5-tetradecanolide (17) With $RuCl_3$•$3H_2O$–$NaIO_4$ in CCl_4–MeCN–water: Sodium periodate (71.2 mg, 0.333 mmol) and $RuCl_3$•$3H_2O$ (2.2 mg, 0.0083 mmol) were successively added to a solution of **16** (25.0 mg, 0.0833 mmol) in CCl_4–MeCN–water (1 : 1 : 1.5) (3.5 ml) with stirring at room temperature. The whole was vigorously stirred at room temperature for 7.5 h. The mixture was filtered through Celite, extracted with ether, and the extract was washed with saturated

$NaHCO_3$, brine, and then dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 4 : 1) to give **17** (15.0 mg, 57%) as a colorless oil along with **16** (5.8 mg, 23%). $[\alpha]_D^{22}$ –10.7 (c = 0.64, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, 3H, J = 6.7 Hz, $CH_2C\underline{H}_3$), 1.25–1.39 (m, 14H), 1.28 (d, 3H, J = 6.7 Hz, 2-CH_3), 1.53–2.04 (m, 6H), 2.43–2.49 (m, 1H, 2-H), 3.36 (s, 3H, OCH_3), 3.48 (d, 1H, J = 8.6 Hz, $C\underline{H}_2$OMOM), 3.55 (d, 1H, J = 8.6 Hz, $C\underline{H}_2$OMOM), 4.63 (s, 2H, OCH_2O). ^{13}C-NMR ($CDCl_3$) δ: 14.1, 17.2, 22.6, 23.2, 25.4, 27.2, 29.2, 29.36, 29.44, 30.0, 31.8, 35.3, 37.7, 55.4, 72.4, 84.8, 96.7, 175.0. IR (KBr): 2924, 2854, 1736, 1464, 1377, 1331, 1254, 1205, 1149, 1115, 1049 cm^{-1}. MS m/z (%): 314 (M^+, 1.8), 239 (100). High MS Calcd for $C_{18}H_{34}O_4$: 314.2457. Found: 314.2461.

With $RuCl_3 \cdot 3H_2O$– $NaIO_4$ in CCl_4–water: Sodium periodate (14.2 mg, 0.0666 mmol) and $RuCl_3 \cdot 3H_2O$ (0.4 mg, 0.0002 mmol) were successively added to a solution of **16** (5.0 mg, 0.017 mmol) in CCl_4–water (1 : 1) (1.2 ml) with stirring at room temperature. The whole was vigorously stirred at room temperature for 22 h. After work-up and purification, **17** (1.5 mg, 28%) was obtained along with **16** (2.0 mg, 40%).

With $NaIO_4$–$RuO_2 \cdot xH_2O$ in CCl_4–MeCN–water: Sodium periodate (28.5 mg, 0.133 mmol) and $RuCl_3 \cdot xH_2O$ (0.4 mg) were successively added to a solution of **16** (10.0 mg, 0.0333 mmol) in CCl_4–MeCN–water (1 : 1 : 1.5) (2.1 ml) with stirring at room temperature. The whole was vigorously stirred at room temperature for 17 h. After work-up and purification, **17** (1.8 mg, 17%) was obtained along with **16** (6.3 mg, 63%).

(–)-Malyngolide Trimethysilyl bromide (19 μl, 0.14 mmol) was added to a solution of **17** (11.0 mg, 0.0350 mmol) in CH_2Cl_2 (1.5 ml) with stirring at –30 °C under N_2. The stirring was continued for 30 min. The mixture was quenched with saturated $NaHCO_3$ aqueous solution, and extracted with ether. The extract was washed with brine, and dried. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel (hexane–AcOEt = 3 : 1) to give (–)-malyngolide (8.0 mg, 85%) as a colorless oil. The synthesized (–)-malyngolide was shown to be identical with an authentic data by comparison of the spectroscopic property (IR, ^{1}H-NMR, MS). $[\alpha]_D^{22}$ –12.5 (c = 0.80, $CHCl_3$). lit[7] $[\alpha]_D^{22}$ –13 (c = 2, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, 3H, J = 6.7 Hz, $CH_2C\underline{H}_3$), 1.26–1.29 (m, 14H), 1.28 (d, 3H, J = 6.7 Hz, 2-CH_3), 1.47–2.13 (m, 7H, OH, CH_2), 2.43 (m, 1H, 2-H), 3.49 (d, 1H, J = 12.2 Hz, $C\underline{H}_2$OH), 3.66 (d, 1H, J = 12.2 Hz, $C\underline{H}_2$OH). ^{13}C-NMR ($CDCl_3$) δ: 14.1, 17.1, 22.6, 23.7, 25.2, 26.3, 29.3, 29.4, 29.5, 30.0, 31.8, 35.6, 36.5, 67.7, 86.9, 175.0. IR (KBr): 3398, 2926, 2854, 1732, 1462, 1377, 1252, 1207, 1126, 1101, 1070 cm^{-1}. MS m/z (%): 270 (M^+, 3.6), 239 (100), 223 (11), 211 (51), 155 (32), 143 (39), 115 (10), 109 (10), 95 (12), 81 (16), 71 (27). High MS Calcd for $C_{15}H_{27}O_2$ (M^+–CH_2OH): 239.2011. Found: 239.2009.

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