Asymmetric Cyclopropanation by Reaction of a γ-Chloromethylated Chiral Vinylic Sulfoxide with Allylmagnesium Bromide

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An optically active vinylic sulfoxide bearing a leaving group at the γ-position was stereoselectively transformed into a chiral cyclopropane by means of a Michael addition with an allylmagnesium bromide. The Michael induced ring-closure reaction requires both allylmagnesium bromide as a nucleophile and chloride as a leaving group for high diastereoselectivity. The absolute stereochemistry of the cycloadduct was confirmed by X-ray analysis.

Key words asymmetric cyclopropanation; vinylic sulfoxide; sulfinyl chirality; Michael addition; Grignard reagent; X-ray analysis

Stereoselective construction of functionalized cyclopropanes with high optical purity is of great importance, since these cyclopropanes can be found in a number of natural and unnatural substances of biological interest[1] and moreover they can be utilized as chiral building blocks[2] for other complex chiral molecules due to the availability of many cyclopropane ring-opening reactions.[3] In particular, the cyclopropanes bearing a sulfur atom on the ring (**1**) have potential as chiral building blocks, because many sulfur atom-directed cyclopropane ring-opening reactions have been developed.[4] Thus far, two types of elegant diastereoselective cyclopropanations employing Michael induced ring-closure (MIRC) reactions[5] have been developed to construct optically active **1** using sulfinyl chirality.[6,7] One involves initial Michael addition of malonate anions to the chiral vinylic sulfoxide (A) followed by intramolecular alkylations (Chart 1, type I),[4e,8] and the other involves that of dimethyl sulfoxonium ylide to the vinylic sulfoxide (B) activated by another electron-withdrawing group, followed by intramolecular alkylation (Chart 1, type II).[9] However, the reported diastereomeric excess of the products obtained by these reactions might be satisfactory for the practical synthesis, but is not perfect. In the expectation that employment of stronger nucleophiles possessing chelation ability would suppress the reversibility of the initial Michael addition to the vinylic sulfoxide and give predominantly the kinetically controlled product, we investigated the novel cyclopropanation of optically active vinylic sulfoxide with a Grignard reagent. In the course of our studies on asymmetric construction of a quaternary carbon center using sulfinyl chirality,[10] we discovered that the additive Pummerer reaction of the vinylic sulfoxide (**2**) with allylmagnesium bromide afforded the monoallylated product (**3**) with almost 100% enantiomeric excess, along with the diallylated compound (**4**) (Chart 2).[11] Taking this into account, we designed the following novel MIRC cyclopropanation (Chart 3).[12] Namely, treatment of the chiral vinylic sulfoxide (**5a, b**) bearing a leaving group (X=OMs, Cl) at the γ-position with an appropriate nucleophile (Nu) would give the α-sulfinyl carbanion (**6**) *via* diastereoselective Michael addition of a nucleophile from the *re* face, and then **6** should undergo intramolecular alkylation, giving rise to the desired cyclopropane (**7**) with stereocontrol of the

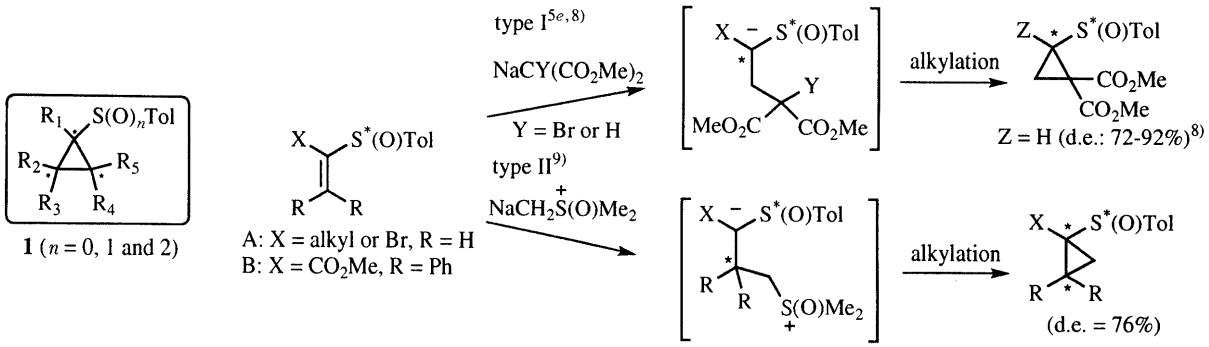

Chart 1

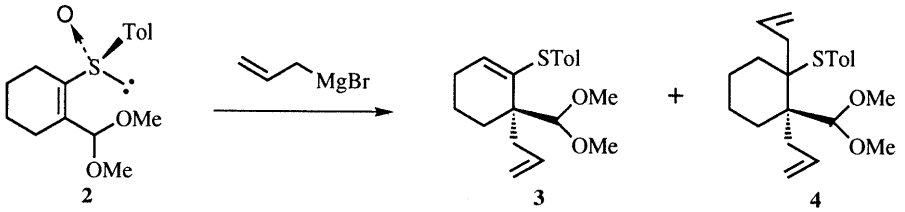

Chart 2

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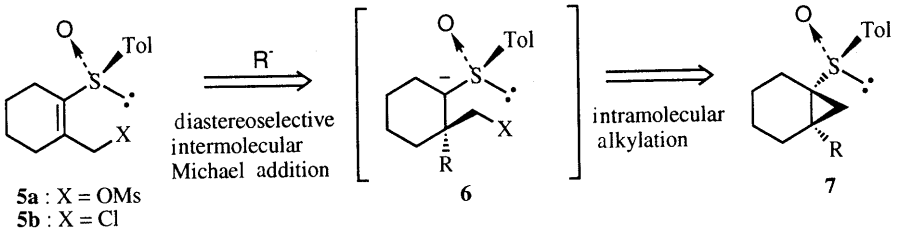
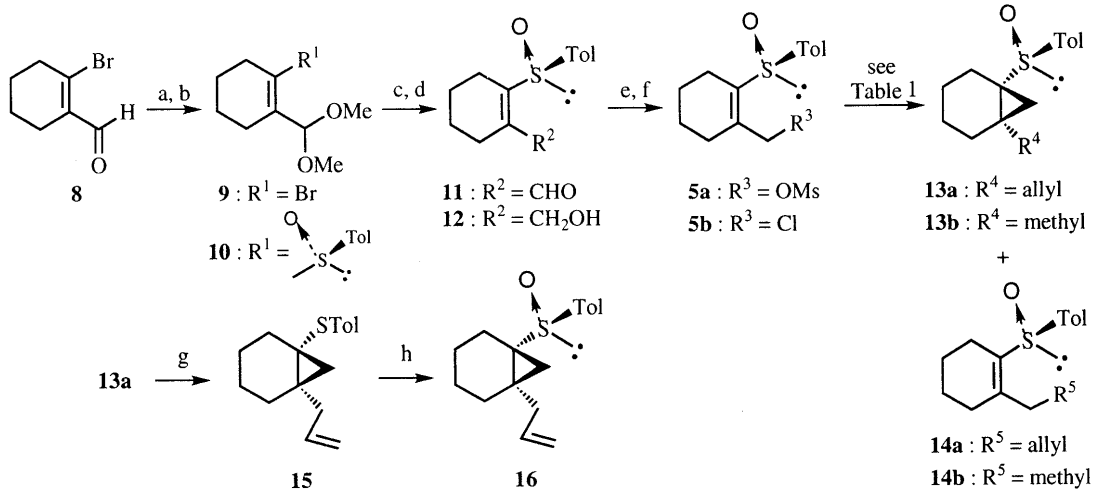


Chart 3



a : $CH(OMe)_3$, p-$CH_3C_6H_4SO_3H$, r.t. (86%) b : n-BuLi; (−)-menthyl (*S*)-p-toluenesulfinate, THF, −78°C (72%)
c : p-$CH_3C_6H_4SO_3H$, acetone, H_2O, r.t. (97%) d : $NaBH_4$, MeOH, 0°C (100%)
e : CH_3SO_2Cl, Et_3N, CH_2Cl_2, 0°C (95%) f : LiCl, THF, r.t. (95%) g : $(CF_3CO)_2O$, NaI,acetone, r.t. (100%)
h : MCPBA, CH_2Cl_2, 0°C (61%)

Chart 4

Table 1. Reaction of **5a** and **5b** with Carbon Nucleophiles

Entry	Substrate	Reaction conditions[a]	Product (% yield[b])	
1	**5a**	$(allyl)_2CuCNLi_2$ (4 eq), −78°C	**13a** (12)	**14a** (34)
2	**5a**	allylMgBr (3 eq), −78°C	**13a** (34)	**14a** (0)
3	**5b**	$(allyl)_2CuCNLi_2$ (4 eq), −78°C	**13a** (52)	**14a** (48)
4	**5b**	allylMgBr (3 eq), −78°C	**13a** (84)	**14a** (11)
5	**5b**	allylMgBr (3 eq), Li_2CuCl_4 (0.1 eq), −78°C	**13a** (70)	**14a** (21)
6	**5b**	MeMgBr (12 eq), −78°C→r.t.	**13b** (0)	**14b** (32)
7	**5b**	$Me_2CuCNLi_2$ (4 eq), −78°C→r.t.	**13b** (0)	**14b** (32)

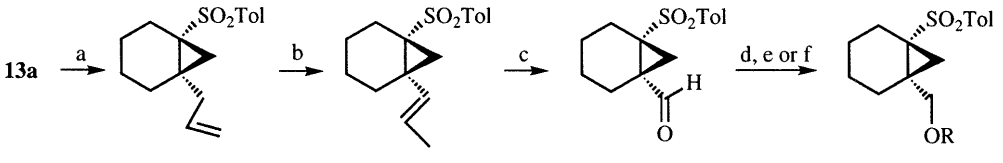
a) All reactions were carried out in tetrahydrofuran (THF). *b*) Isolated yield. r.t. = room temperature.

contiguous two asymmetric centers.

In the present paper, we present details of the diastereocontrolled synthesis of the bicyclo[4.1.0]heptane derivative (**7**, R = allyl) *via* the Michael addition of the chiral vinylic sulfoxide (**5b**) with allylmagnesium bromide, and the stereochemistry of **7**.[13]

Results and Discussion

The chiral sulfoxides (**5a, b**) were synthesized from the known compound (**8**)[14] (Chart 4). The reaction of **8** with p-toluenesulfonic acid (p-TsOH) and trimethyl orthoformate gave the dimethyl acetal (**9**) in 86% yield. Lithiation of **9** with n-butyllithium (n-BuLi) in tetrahydrofuran (THF) at −78 °C and subsequent treatment of the resulting anion with (−)-menthyl (*S*)-p-toluenesulfinate[15] at the same temperature furnished the chiral vinylic sulfoxide (**10**) in 72% yield. Hydrolysis of **10** with p-TsOH in aqueous acetone afforded the aldehyde (**11**), which was reduced with sodium borohydride ($NaBH_4$) in MeOH to give the desired alcohol (**12**) in 97% yield from **10**. The mesylate (**5a**) was obtained in 95% yield by the reaction of **12** with methanesulfonyl chloride (MsCl) in dichloromethane (CH_2Cl_2). In addition, the desired chloride (**5b**) was prepared in 95% yield by the treatment of **5a** with lithium chloride in THF. We initially investigated the diastereoselective cyclopropanation of **5a** under the two different nucleophilic conditions (Table 1, entries 1 and 2). The treatment of **5a** with $(allyl)_2CuCNLi_2$[16] gave the desired cyclopropane (**13a**) in only 12% yield along with the coupling by-product (**14a**) as a major product. On the other hand, the reaction of **5a** with allylmagnesium bromide gave only **13a** without the coupling product (**14a**), but the yield of **13a** was still low. After many experiments, the difficulty was overcome by the employment of the

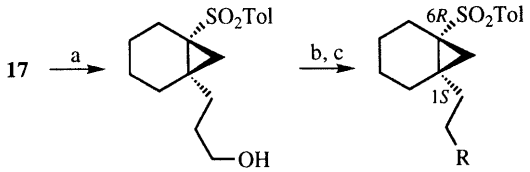


17 18 19

20 : R = H
21 : R = (+)-MTPA
22 : R = (−)-MTPA

a : H_2O_2, AcOH, r.t. (93%) b: $RhCl_3 \cdot 3H_2O$, EtOH, reflux (46%) c : OsO_4, $NaIO_4$, THF, H_2O, r.t. (79%)
d : $NaBH_4$, MeOH, 0°C (89%) e : (+)-MTPACl, Et_3N, DMAP, CH_2Cl_2, 0°C (94%)
f : (−)-MTPACl, Et_3N, DMAP, CH_2Cl_2, 0°C (100%)

Chart 5



23

24 : R = CO_2H
25 : R = $CONH_2$

a : $BH_3 \cdot Me_2S$, THF, 0°C; 3M NaOH, 30% H_2O_2, r.t. (84%)
b : Jones oxidation (91%)
c : $ClCO_2Et$, Et_3N, CH_2Cl_2, 0°C; NH_3(gas), 0°C (86%)

Chart 6

chloride (**5b**) as a substrate (Table 1, entries 3 and 4). Reaction of **5b** with $(allyl)_2CuCNLi_2$ or allylmagnesium bromide suppressed the formation of **14a**, leading to improved yields of **13a** (52% and 84%) in comparison with that of the mesylate (**5a**). Addition of a catalytic amount of dilithium tetrachlorocuprate (Li_2CuCl_4)[17] to the allylmagnesium bromide (Table 1, entry 5), however, resulted in promotion of the coupling reaction. It is clear from Table 1 that the reaction of **5b** with allylmagnesium bromide without any additive (Table 1, entry 4) gave the best yield of the desired product (**13a**).

We next examined the diastereo- and enantioselectivity of the cyclopropanation. In order to determine the diastereoselectivity reliably, an authentic standard (**16**) for HPLC analysis was synthesized from **13a** as follows. The sulfoxide (**13a**) was reduced with trifluoroacetic anhydride (TFAA) and sodium iodide (NaI) in acetone to give the sulfide (**15**), which was oxidized with *m*-chloroperoxybenzoic acid (MCPBA) in CH_2Cl_2 to afford the sulfoxide (**13a**) and the diastereomer (**16**) in 28% and 61% yields from **13a**, respectively. The HPLC analysis of the crude product obtained from the operation in entry 4 revealed that **13a** was produced with high diastereoselectivity (de ≥99%). Furthermore, in order to exclude ambiguity concerning the enantiomeric purity of **13a**, we determined the precise value as follows (Chart 5). The allyl sulfone (**17**), which was obtained by hydrogen peroxide (H_2O_2) oxidation of the allyl sulfoxide (**13a**) in acetic acid, was isomerized with rhodium(III) chloride trihydrate ($RhCl_3 \cdot 3H_2O$)[18] in refluxing EtOH over 36 h to give the (*E*)-olefin (**18**) in 43% yield from **13a** along with the starting material (**17**). Then osmium tetroxide (OsO_4)-catalyzed sodium periodate ($NaIO_4$) oxidation of **18** in aqueous THF provided the aldehyde (**19**), which was subjected to $NaBH_4$ reduction in MeOH to afford the alcohol **20** in 70% yield from **18**. Each of (+)- and (−)-α-methoxy-α-(trifluoromethyl)phenylacetic chloride (MTPACl)[19] was reacted with **20** in the usual manner to give the (+)- and (−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) ester (**21** and **22**) in 94% and 100% yields, respectively. HPLC analyses of **21** and **22** showed the high enantiomeric purity of the alcohol **20** (ee ≥99%). In addition, we confirmed the absolute configuration of **13a** by X-ray crystallographic analysis of the amide (**25**) which was obtained from **17** through the following sequences (Chart 6). Namely, hydroboration–oxidation of **17** afforded the primary alcohol **23**, which was subjected to Jones oxidation to give the carboxylic acid (**24**) in 76% yield from **17**. Compound **24** was treated with ethyl chloroformate, and subsequently with ammonia gas in CH_2Cl_2 to afford the amide (**25**) in 86% yield as white crystals. The absolute stereochemistry of **25** obtained from X-ray analysis is depicted in Fig. 1, which shows that the cyclopropane derivative (**13a**) has 1*S*,6*R* configuration. The 1*S*,6*R* configuration was significantly selected by comparing the *R*-values of Friedel pairs including the abnormal scattering effect of the sulfur atom.

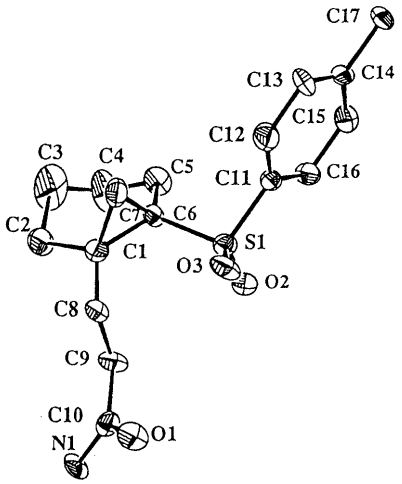


Fig. 1. ORTEP Drawing of (1*S*,6*R*)-**25** with the Atomic Numbering System

Finally, we examined the generality of the diastereoselective cyclopropanation of **5b** with other nucleophiles such as methylmagnesium bromide and higher order methyl cuprate. In both cases (Table 1, entries 6 and 7), unfortunately, only the coupling product (**14b**) was obtained

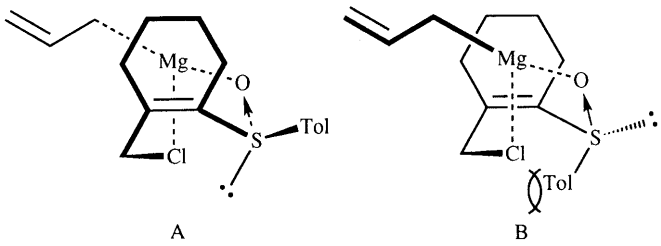


Fig. 2

and the desired cyclopropane (**13b**) could not be detected. The result indicates that the combination of allylmagnesium bromide and chloride as a leaving group is essential for the tandem Michael addition–cyclopropanation reaction. The extremely high diastereoselectivity in this cyclopropanation can be explained as follows. The magnesium center of allylmagnesium bromide should coordinate both to the oxygen atom of the sulfinyl group and to the chloride atom, as depicted in Fig. 2. Transition structure A, therefore, seems to be more favorable than B, owing to the $A^{(1,3)}$-strain[20] between the tolyl and chloromethyl groups. Consequently, the allyl anion will approach exclusively from the *re* face through the more energetically favorable transition structure A, giving rise to (1*S*,6*R*)-**13a** as a sole product.

Experimental

Melting points and boiling points are uncorrected. Optical rotations were measured using a JASCO DIP-360 digital polarimeter. IR spectra were measured with a Hitachi 260-10 IR spectrometer or a Horiba FT-210 IR spectrometer. ^{1}H-NMR spectra were measured with a Hitachi R-22 spectrometer (90 MHz), a Varian VXR-200 spectrometer (200 MHz) or a JEOL JNM-GX500 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), multiplet (m), broad (br). Mass spectra were taken with a Shimadzu QP-1000 mass spectrometer and a JEOL JMS-D300 mass spectrometer. HPLC analyses were performed using a Waters 6000A pump, a Waters μ-PORASIL (3.9 mm × 30 cm) column, and a Soma S-310 UV detector (at 254 nm). Unless otherwise noted, all reactions were performed in anhydrous solvents. Merck Kieselgel 60 was used as an adsorbent for column chromatography. All extracts were dried over anhydrous $MgSO_4$.

2-Bromocyclohexenecarbaldehyde Dimethyl Acetal (9) A mixture of the aldehyde (**8**) (21.4 g, 133 mmol), *p*-TsOH monohydrate (500 mg, 2.63 mmol) and trimethyl orthoformate (50 ml, 457 mmol) was stirred at room temperature for 12 h, then concentrated *in vacuo*. The residue was diluted with ether, washed with saturated $NaHCO_3$ solution, water, and brine, dried, and then concentrated *in vacuo*. The residue was distilled to give the dimethyl acetal (**9**) (22.9 g, 86%) as a colorless oil, bp 75—82 °C (2 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 1.58—1.78 (4H, m, C4-H and C5-H), 2.02—2.67 (4H, m, C3-H and C6-H), 3.38 (6H, s, 2 × OCH_3), 5.13 (1H, s, anomeric-H). IR ($CHCl_3$): 2950, 2845, 1652 (C=C), 1456, 1368, 1186, 1116, 1072, 978 cm^{-1}.

(*S*)-2-(*p*-Tolylsulfinyl)cyclohexenecarbaldehyde Dimethyl Acetal (10) A 1.6 M solution of *n*-BuLi (35.3 ml) in hexane was added to THF (200 ml) at −78 °C under a nitrogen atmosphere, then the bromide (**9**) (11.3 g, 48.1 mmol) was added to this solution at the same temperature. After being stirred at −78 °C for 1.5 h, the mixture was added to a solution of (−)-menthyl (*S*)-*p*-toluenesulfinate (12.7 g, 43.2 mmol) in THF (80 ml) under a nitrogen atmosphere and the whole was stirred at the same temperature for 15 min. The reaction was quenched with saturated NH_4Cl solution, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 2 : 1) to give the sulfoxide (**10**) (10.2 g, 72%) as colorless crystals, mp 49.0 °C (hexane), $[\alpha]_D^{26}$ −202° (c = 0.90, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.18—2.00 (4H, m, C4-H and C5-H), 2.17—2.61 (4H, m, C3-H and C6-H), 2.38 (3H, s, Ar-CH_3), 3.44 (3H, s, OCH_3), 3.47 (3H, s, OCH_3), 5.62 (1H, s, anomeric-H), 7.24 (2H, d, J = 7.5 Hz, Ar-H), 7.44 (2H, d, J = 7.5 Hz, Ar-H). IR ($CHCl_3$): 2945, 1676, 1604 (aromatic), 1498 (aromatic), 1452, 1366, 1184, 1082, 1036 (sulfoxide) cm^{-1}. MS m/z (%): 294 (M^+, 0.2), 277 (100), 91 (100). *Anal.* Calcd for $C_{16}H_{22}O_3S$: C, 65.29; H, 7.53; S, 10.87. Found: C, 65.24; H, 7.55; S, 10.79.

(*S*)-2-(*p*-Tolylsulfinyl)cyclohexenecarbaldehyde (11) A mixture of dimethyl acetal (**10**) (5.37 g, 18.2 mmol), *p*-TsOH monohydrate (346 mg, 1.82 mmol), H_2O (15 ml) and acetone (50 ml) was stirred at room temperature for 12 h, then the acetone was removed *in vacuo*. Saturated $NaHCO_3$ solution was added to the mixture and the resulting mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 2 : 1) to give the aldehyde (**11**) (4.41 g, 97%) as colorless crystals, mp 114—116 °C (hexane : AcOEt = 2 : 1), $[\alpha]_D^{26}$ +306° (c = 1.01, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.44—1.96 (5H, m), 2.40—2.65 (2H, m), 2.42 (3H, s, Ar-CH_3), 2.74—2.95 (1H, m), 7.33 (2H, d, J = 8.4 Hz, Ar-H), 7.44 (2H, d, J = 8.4 Hz, Ar-H), 10.72 (1H, s, CHO). IR ($CHCl_3$): 2985, 2935, 2855, 1676 (C=O), 1606 (aromatic), 1488 (aromatic), 1444, 1080, 1038 (sulfoxide) cm^{-1}. MS m/z (%): 248 (M^+, 4), 231 (100), 140 (35). *Anal.* Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49; S, 12.91. Found: C, 67.49; H, 6.47; S, 12.72.

(*S*)-2-(*p*-Tolylsulfinyl)cyclohexen-1-ylmethanol (12) $NaBH_4$ (450 mg, 11.9 mmol) was added to a solution of the aldehyde **11** (2.48 g, 10.0 mmol) in MeOH (20 ml) at 0 °C for 15 min, and then the reaction was quenched with water. After removal of MeOH, the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by recrystallization to give the alcohol (**12**) (2.50 g, 100%) as colorless crystals, mp 151—155 °C (AcOEt), $[\alpha]_D^{22}$ −106° (c = 1.00, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.36—1.82 (5H, m, C3-H_a, C4-H and C5-H), 2.24—2.64 (3H, m, C3-H_b, C6-H), 2.49 (3H, s, Ar-CH_3), 2.80—3.14 (1H, br s, OH), 4.53 (1H, d, J = 12.2 Hz, CH_a-O), 4.64 (1H, d, J = 12.2 Hz, CH_b-O), 7.27 (2H, d, J = 8.0 Hz, Ar-H), 7.45 (2H, d, J = 8.0 Hz, Ar-H). IR ($CHCl_3$): 3590 (OH), 3350, 2985, 2935, 2855, 1490 (aromatic), 1446, 1080, 1010 (sulfoxide) cm^{-1}. MS m/z (%): 251 (M^+ + 1, 25), 233 (34), 140 (100). *Anal.* Calcd for $C_{14}H_{18}O_2S$: C, 67.16; H, 7.25; S, 12.81. Found: C, 66.95; H, 7.23; S, 12.70.

(*S*)-2-(*p*-Tolylsulfinyl)cyclohexen-1-ylmethyl Methanesulfonate (5a) MsCl (0.37 ml, 4.8 mmol) was added to a mixture of the alcohol (**12**) (1.00 g, 4.00 mmol), Et_3N (0.84 ml, 6.0 mmol) and CH_2Cl_2 (10 ml) at 0 °C, and the whole was stirred for 10 min. The reaction was quenched with saturated $NaHCO_3$ solution, and the resulting mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 1 : 2) to give the sulfonate (**5a**) (1.24 g, 95%) as a colorless oil, $[\alpha]_D^{23}$ −60.3° (c = 1.04, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.24—1.84 (5H, m, C3-H_a, C4-H and C5-H), 2.14—2.72 (3H, m, C3-H_b, C6-H), 2.39 (3H, s, Ar-CH_3), 3.08 (3H, s, OSO_2-CH_3), 5.02 (1H, d, J = 11.2 Hz, CH_a-O), 5.37 (1H, d, J = 11.2 Hz, CH_b-O), 7.27 (2H, d, J = 8.0 Hz, Ar-H), 7.45 (2H, d, J = 8.0 Hz, Ar-H). IR ($CHCl_3$): 2990, 2945, 2870, 1494 (aromatic), 1362 (sulfonate), 1176 (sulfonate), 1084, 1038 (sulfoxide), 934 cm^{-1}. MS m/z (%): 328 (M^+, 0.3), 249 (100), 140 (20). High MS Calcd for $C_{15}H_{20}O_4S_2$: 328.0802. Found: 328.0797.

(*S*)-2-(*p*-Tolylsulfinyl)cyclohexen-1-ylmethyl Chloride (5b) A mixture of the mesylate (**5a**) (100 mg, 0.304 mmol), lithium chloride (38.9 mg, 0.918 mmol), and THF (1 ml) was stirred at room temperature for 3 h, then concentrated *in vacuo*. Water was added to the residue and the resulting mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : $CHCl_3$ = 1 : 3) to give the chloride (**5b**) (78 mg, 95%) as colorless crystals, mp 106—108 °C (AcOEt), $[\alpha]_D^{27}$ −129° (c = 1.08, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.33—1.88 (5H, m, C3-H_a, C4-H and C5-H), 2.00—2.70 (3H, m, C3-H_b, C6-H), 2.41 (3H, s, Ar-CH_3), 4.17 (1H, d, J = 11.2 Hz, CH_a-Cl), 5.00 (1H, d, J = 11.2 Hz, CH_b-Cl), 7.30 (2H, d, J = 8.0 Hz, Ar-H), 7.50 (2H, d, J = 8.0 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 17.88 (C3), 21.03 (Ar-CH_3), 21.39 (C4 or C5), 21.53 (C4 or C5), 28.66 (C6), 42.86 (CH_2-Cl), 123.95 (Ar-CH), 129.43 (Ar-CH), 138.27 (quaternary carbon), 140.36 (quaternary carbon), 141.26 (quaternary carbon), 142.84 (quaternary carbon). IR ($CHCl_3$): 2950, 2930, 2850, 1486 (aromatic), 1440, 1274, 1080, 1030 (sulfoxide), 800 cm^{-1}. MS m/z (%): 270 (4) and 268 (10) (M^+), 253 (13) and 251 (35), 215 (100), 140 (53). *Anal.* Calcd for $C_{14}H_{17}ClOS$: C, 62.56; H, 6.37. Found: C, 62.85; H, 6.45.

3-[(1*S*,6*R*)-6-((*S*)-*p*-Tolylsulfinyl)bicyclo[4.1.0]hept-1-yl]prop-1-ene (13a) and 4-[(*S*)-2-(*p*-Tolylsulfinyl)cyclohexen-1-yl]but-1-ene (14a) A solution of allylmagnesium bromide (10.4 ml, 1.75 M) in ether was added to a solution of the chloride (**5b**) (1.63 g, 6.06 mmol) in THF (20 ml) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 10 min, then the reaction was quenched with NH_4Cl solution. After removal of THF, the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 5 : 1) to give the cyclopropylsulfoxide (**13a**) (1.40 g, 84%) and the vinylic sulfoxide (**14a**) (0.19 g, 11%). **13a**: a colorless oil, $[\alpha]_D^{24}$ +20.7° (c = 0.97, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.80—1.56 (5H, m, C3′-H, C4′-H, C5′-H_a), 0.84 (1H, d, J = 5.8 Hz, C7′-H_a), 1.13 (1H, d, J = 5.8 Hz, C7′-H_b), 1.68—2.00 (2H, m, C2′-H), 2.26—2.52 (1H, m, C5′-H_b), 2.40 (3H, s, Ar-CH_3), 2.65 (2H, d, J = 9.0 Hz, C3-H), 5.10—5.24 (2H, m, Cl-H), 5.89—6.13 (1H, m, C2-H), 7.28 (2H, d, J = 8.0 Hz, Ar-H), 7.50 (2H, d, J = 8.0 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 19.21 (C5′), 20.45 (C7′), 20.56 (C3′ or C4′), 21.26 (Ar-CH_3), 22.48 (C3′ or C4′), 28.54 (C2′), 28.84 (C6′), 40.66 (C3), 45.32 (C1′), 117.16 (C1), 124.78 (Ar-CH), 129.29 (Ar-CH), 135.51 (C2), 138.54 (Ar-quaternary carbon), 140.43 (Ar-quaternary carbon). IR ($CHCl_3$): 2990, 2935, 2865, 1640 (C=C), 1492 (aromatic), 1448, 1080, 1032 (sulfoxide), 912 cm^{-1}. MS m/z (%): 274 (M^+, 2), 140 (36), 135 (100). High MS Calcd for $C_{17}H_{22}OS$: 274.1392. Found: 274.1395. HPLC analysis: hexane : AcOEt = 10 : 1, flow rate = 2.0 ml/min, t_R = 12.8 min. **14a**: a colorless oil, $[\alpha]_D^{26}$ −181° (c = 1.67, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.32—1.90 (5H, m), 2.14—2.62 (5H, m), 2.40 (3H, s, Ar-CH_3), 2.71 (2H, t, J = 7.6 Hz, C4-H), 5.00—5.20 (2H, m, C1-H), 5.74—6.02 (1H, m, C2-H), 7.28 (2H, d, J = 7.8 Hz, Ar-H), 7.43 (2H, d, J = 7.8 Hz, Ar-H). IR ($CHCl_3$): 2985, 2940, 2860, 1640 (C=C), 1598 (aromatic), 1494 (aromatic), 1448, 1082, 1026 (sulfoxide), 916 cm^{-1}. MS m/z (%): 274 (M^+, 3), 257 (100), 135 (62). High MS Calcd for $C_{17}H_{22}OS$: 274.1392. Found: 274.1392. HPLC analysis: hexane : AcOEt = 10 : 1, flow rate = 2.0 ml/min, t_R = 25.8 min.

3-[(1*S*,6*R*)-6-(*p*-Tolylthio)bicyclo[4.1.0]hept-1-yl]prop-1-ene (15) Trifluoroacetic anhydride (1.42 ml, 10.0 mmol) was added to a mixture of the sulfoxide (**13a**) (1.00 g, 3.65 mmol), NaI (1.65 g, 11.0 mmol), and acetone (10 ml) at 0 °C under an nitrogen atmosphere. The whole was stirred for 5 min, then the reaction was quenched with sodium thiosulfate solution. After removal of acetone, the mixture was extracted with ether. The ethereal layer was washed with water and brine, dried, then concentrated *in vacuo*. The residue was purified by column chromatography (hexane) to give the sulfide (**15**) (940 mg, 100%) as a colorless oil, $[\alpha]_D^{25}$ +65.6° (c = 1.11, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.76 (1H, d, J = 5.4 Hz, C7′-H_a), 0.86 (1H, d, J = 5.4 Hz, C7′-H_b), 1.14—2.25 (8H, m), 2.31 (3H, s, Ar-CH_3), 2.40 (1H, dd, J = 14.6, 6.4 Hz, C3-H_a), 2.55 (1H, dd, J = 14.6, 6.4 Hz, C3-H_b), 4.98—5.14 (2H, m, C1-H), 5.73—5.96 (1H, m, C2-H), 7.09 (2H, d, J = 8.2 Hz, Ar-H), 7.19 (2H, d, J = 8.2 Hz, Ar-H). IR ($CHCl_3$): 2935, 2860, 1642 (C=C), 1498 (aromatic), 1458, 1096, 918, 804 cm^{-1}. MS m/z (%): 258 (M^+, 9), 217 (100), 93 (32). *Anal.* Calcd for $C_{17}H_{22}S$: C, 79.01; H, 8.58; S, 12.41. Found: C, 79.08; H, 8.49; S. 12.33.

3-[(1*S*,6*R*)-6-((*S*)-*p*-Tolylsulfinyl)bicyclo[4.1.0]hept-1-yl]prop-1-ene (16) MCPBA (12.8 mg, 0.074 mmol) was added to a solution of the sulfide (**15**) (19.0 mg, 0.074 mmol) in CH_2Cl_2 (1.0 ml) at 0 °C. The mixture was stirred at the same temperature for 5 min, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 5 : 1) to give the allyl sulfoxide (**13a**) (5.8 mg, 28%) and the diastereomer (**16**) (12.3 mg, 61%) as a colorless oil, $[\alpha]_D^{24}$ +95.4° (c = 1.23, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.74—1.96 (8H, m), 1.02 (1H, dd, J = 5.8, 1.0 Hz, C7′-H_a), 1.63 (1H, d, J = 5.8 Hz, C7′-H_b), 2.40—2.68 (2H, m, C3-H), 2.42 (3H, s, Ar-CH_3), 5.08—5.24 (2H, m, C1-H), 5.80—6.03 (1H, m, C2-H), 7.32 (2H, d, J = 8.2 Hz, Ar-H), 7.52 (2H, d, J = 8.2 Hz, Ar-H). IR ($CHCl_3$): 2995, 2940, 2860, 1648 (C=C), 1500, 1456 (aromatic), 1086, 1042 (sulfoxide), 1028, 1016, 922, 804 cm^{-1}. MS m/z (%): 274 (M^+, 3), 257 (20), 140 (36), 135 (80), 67 (100). High MS Calcd for $C_{17}H_{22}OS$: 274.1392. Found: 274.1399. HPLC analysis: hexane : AcOEt = 10 : 1, flow rate = 2.0 ml/min, t_R = 34.3 min.

3-[(1*S*,6*R*)-6-(*p*-Tolylsulfonyl)bicyclo[4.1.0]hept-1-yl]prop-1-ene (17) A mixture of the sulfoxide (**13a**) (137 mg, 0.50 mmol), 30% H_2O_2 (567 mg, 5.00 mmol) and acetic acid (1 ml) was stirred at room temperature for 12 h. The reaction was quenched with sodium thiosulfate solution and the resulting mixture was extracted with ether. The ethereal layer was washed successively with saturated $NaHCO_3$ solution, water, brine, dried, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 4 : 1) to give the sulfone (**17**) (135 mg, 93%) as a colorless oil, $[\alpha]_D^{24}$ −39.0° (c = 0.98, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.97 (1H, d, J = 5.2 Hz, C7′-H_a), 1.00—1.44 (5H, m, C3′-H, C4′-H, C5′-H_a), 1.68—1.84 (2H, m, C2′-H), 1.79 (1H, d, J = 5.2 Hz, C7′-H_b), 2.11—2.27 (1H, m, C5′-H_b), 2.45 (3H, s, Ar-CH_3), 2.73 (1H, dd, J = 14.4, 6.6 Hz, C3-H_a), 2.90 (1H, dd, J = 14.4, 7.4 Hz, C3-H_b), 5.05—5.22 (2H, m, C1-H), 5.85—6.09 (1H, m, C2-H), 7.33 (2H, d, J = 7.2 Hz, Ar-H), 7.50 (2H, d, J = 7.2 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 20.31 (C3′ or C4′), 21.51 (Ar-CH_3), 21.56 (C3′ or C4′), 22.52 (C7′), 26.45 (C5′), 29.60 (C2′), 30.62 (C6′), 39.18 (C3), 45.79 (C1′), 116.82 (C2), 128.23 (Ar-CH), 129.47 (Ar-CH), 136.28 (C1), 137.20 (Ar-quaternary carbon), 143.72 (Ar-quaternary carbon). IR ($CHCl_3$): 3010, 2945, 2870, 1644 (C=C), 1600 (aromatic), 1500 (aromatic), 1456, 1302 (sulfone), 1142 (sulfone), 1082, 916 cm^{-1}. MS m/z (%): 290 (M^+, 5), 135 (100). 93 (38). *Anal.* Calcd for $C_{17}H_{22}S$: C, 70.31; H, 7.63; S, 11.04. Found: C, 70.11; H, 7.57; S, 11.06.

(*E*)-1-[(1*R*,6*R*)-6-(*p*-Tolylsulfonyl)bicyclo[4.1.0]hept-1-yl]prop-1-ene (18) A mixture of the olefin (**17**) (65.4 mg, 0.226 mmol), rhodium(III) chloride trihydrate (4.1 mg, 0.016 mmol) and EtOH was refluxed for 24 h under a nitrogen atmosphere, then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 20 : 1) to give the *E*-olefin (**18**) (30.2 mg, 46%) and **17** (18.3 mg, 28%). **18**: a colorless oil, $[\alpha]_D^{26}$ +66.1° (c = 1.51, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.90—2.50 (8H, m), 1.15 (1H, d, J = 5.6 Hz, C7′-H_a), 1.78 (3H, dd, J = 6.4, 1.4 Hz, C3-H), 2.00 (1H, d, J = 5.6 Hz, C7′-H_b), 2.43 (3H, s, Ar-CH_3), 5.63 (1H, dq, J = 15.4, 6.4 Hz, C2-H), 6.05 (1H, d, J = 15.4 Hz, C1-H), 7.30 (2H, d, J = 8.0 Hz, Ar-H), 7.72 (2H, d, J = 8.0 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 18.17 (C3), 19.84 (C3′ or C4′), 21.49 (Ar-CH_3), 21.56 (C3′ or C4′), 22.34 (C7′), 26.27 (C5′), 28.50 (C2′), 31.32 (C6′), 47.03 (C1′), 125.85 (C2), 128.23 (Ar-CH), 129.33 (Ar-CH), 132.45 (C1), 137.00 (Ar-quaternary carbon), 143.61 (Ar-quaternary carbon). IR (KBr): 2935, 2860, 1597 (aromatic), 1495 (aromatic), 1450, 1300 (sulfone), 1145 (sulfone), 976, 814, 677, 590 cm^{-1}. MS m/z (%): 290 (M^+,2), 135 (100), 93 (25).

(1*R*,6*R*)-6-(*p*-Tolylsulfonyl)bicyclo[4.1.0]heptanecarbaldehyde (19) OsO_4 (2.7 mg, 0.010 mmol) was added to a mixture of the olefin (**18**) (30.2 mg, 0.104 mmol), water (0.5 ml), and THF (1.5 ml) at 0 °C, and stirring was continued at the same temperature for 15 min. $NaIO_4$ (66.7 mg, 0.312 mmol) was added to the mixture at 0 °C, and then the cooling bath was removed. The whole was stirred for 3 h at room temperature, then extracted with AcOEt. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 2 : 1) to give the aldehyde (**19**) (23.0 mg, 79%) as a colorless oil, $[\alpha]_D^{24}$ +15.9° (c = 1.08, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.10—2.70 (8H, m), 1.46 (1H, d, J = 6.2 Hz, C7′-H_a), 2.46 (3H, s, Ar-CH_3), 2.60 (1H, d, J = 6.2 Hz, C7′-H_b), 7.36 (2H, d, J = 8.2 Hz, Ar-H), 7.69 (2H, d, J = 8.2 Hz, Ar-H), 9.87 (1H, s, CHO). IR (KBr): 2943, 2866, 1705 (C=O), 1597 (aromatic), 1495 (aromatic), 1450, 1302 (sulfone), 1147 (sulfone), 816, 677 cm^{-1}. MS m/z (%): 279 (M^+ + 1, 0.5), 250 (16), 157 (20), 95 (100). *Anal.* Calcd for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.52; S, 11.52. Found: C, 64.58; H, 6.53; S, 11.29.

(1*R*,6*R*)-6-(*p*-Tolylsulfonyl)bicyclo[4.1.0]hept-1-ylmethanol (20) $NaBH_4$ (3.1 mg, 0.083 mmol) was added to a solution of the aldehyde (**19**) (23.0 mg, 0.0827 mmol) in MeOH (2.0 ml) at 0 °C, and the mixture was stirred at the same temperature for 15 min. After removal of MeOH, the residue was diluted with AcOEt. The organic layer was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 2 : 1) to give the alcohol (**20**) (20.5 mg, 89%) as a colorless oil, $[\alpha]_D^{27}$ −41.8° (c = 1.03, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.06—2.44 (8H, m), 1.00 (1H, d, J = 5.6 Hz, C7-H_a), 1.85 (1H, d, J = 5.6 Hz, C7-H_b), 2.46 (3H, s, Ar-CH_3). 3.93 (1H, d, J = 12.4 Hz, CH_a-O), 4.23 (1H, d, J = 12.4 Hz, CH_b-O), 7.36 (2H, d, J = 8.2 Hz, Ar-H), 7.77 (2H, d, J = 8.2 Hz, Ar-H). IR (KBr): 3531 (OH), 2935, 2858, 1597 (aromatic), 1495 (aromatic), 1450, 1400, 1282 (sulfone), 1140 (sulfone), 814 cm^{-1}. MS m/z (%): 280 (M^+, 1.3), 157 (100), 125 (37), 107 (57), 95 (39). *Anal.* Calcd for $C_{15}H_{20}O_3S$: C, 64.26; H, 7.19; S, 11.43. Found: C, 64.14; H, 7.12; S, 11.47.

(1*R*,6*R*)-6-(*p*-Tolylsulfonyl)bicyclo[4.1.0]hept-1-ylmethyl (2*R*)-2-Methoxy-2-phenyl-2-trifluoromethylacetate (21) (+)-MTPACl (10 μl, 55 μmol) was added to a mixture of the alcohol (**20**) (10.3 mg, 36.8 μmol), Et_3N (6.9 μl, 74 μmol), 4-dimethylaminopyridine (1.0 mg, 8.2 μmol), and CH_2Cl_2 (1.0 ml) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 15 min. The reaction was quenched with saturated $NaHCO_3$ solution, and the resulting mixture was extracted with AcOEt.

The extract was washed with water and brine, dried, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane: AcOEt = 5 : 1) to give the (+)-MTPA ester (**21**) (17.1 mg, 94%) as a colorless oil, $[\alpha]_D^{20}$ +19.9° (c = 0.86, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.00—1.93 (7H, m), 1.04 (1H, d, J = 6.0 Hz, C7-H_a), 1.89 (1H, d, J = 6.0 Hz, C7-H_b), 2.11 (1H, dt, J = 13.8, 6.3 Hz), 2.43 (3H, s, Ar-CH_3), 3.58 (3H, d, J = 1.2 Hz, CH_3-O), 4.84 (1H, d, J = 11.4 Hz, CH_a-OMTPA), 5.07 (1H, d, J = 11.4 Hz, CH_b-OMTPA), 7.28 (2H, d, J = 8.4 Hz, Ar-H), 7.34—7.45 (3H, m, Ar-H), 7.55—7.65 (2H, m, Ar-H), 7.68 (2H, d, J = 8.4 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 20.06, 21.01, 21.08, 21.58, 25.97, 27.82, 29.76, 45.77, 55.60, 69.22, 121.28, 125.52, 127.57, 128.36, 128.41, 129.56, 129.61, 132.18, 136.28, 144.18, 166.59. IR (KBr): 2934, 2864, 1749 (C=O), 1597 (aromatic), 1495 (aromatic), 1452, 1302 (sulfone), 1146 (sulfone), 1018, 814, 717 cm^{-1}. MS m/z (%): 497 (M^+, 0.8), 189 (28), 107 (100). *Anal.* Calcd for $C_{25}H_{27}F_3O_5S$: C, 60.47; H, 5.48. Found: C, 60.76; H, 5.55. HPLC analysis: hexane : AcOEt = 15 : 1, flow rate = 1.5 ml/min t_R = 22.7 min.

(1*R*,6*R*)-6-(*p*-Tolylsulfonyl)bicyclo[4.1.0]hept-1-ylmethyl (2*S*)-2-Methoxy-2-phenyl-2-trifluoromethylacetate (22) By a similar procedure to that described for the preparation of the (+)-MTPA ester (**21**) from the alcohol (**20**), **20** (10.3 mg, 36.8 μmol) was converted into the (−)-MTPA ester (**22**) (18.1 mg, 100%) by treatment with (−)-MTPACl (10 μl, 53 μmol), Et_3N (6.9 μl, 74 μmol), 4-dimethylaminopyridine (1.0 mg, 8.2 μmol). **22**: a colorless oil, $[\alpha]_D^{20}$ −20.6° (c = 0.91, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.02—1.96 (7H, m), 1.07 (1H, d, J = 6.0 Hz, C7-H_a), 1.93 (1H, d, J = 6.0 Hz, C7-H_b), 2.16 (1H, dt, J = 14.8, 5.2 Hz), 2.44 (3H, s, Ar-CH_3), 3.56 (3H, d, J = 1.2 Hz, CH_3-O), 4.87 (1H, d, J = 11.4 Hz, CH_a-OMTPA), 5.07 (1H, d, J = 11.4 Hz, CH_b-OMTPA), 7.23 (2H, d, J = 8.4 Hz, Ar-H), 7.36—7.45 (3H, m, Ar-H), 7.52—7.62 (2H, m, Ar-H), 7.74 (2H, d, J = 8.4 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 20.00, 21.10, 21.57, 25.97, 27.85, 29.54, 45.95, 55.47, 69.36, 121.17, 125.41, 127.67, 128.37, 128.43, 129.60, 129.67, 131.95, 136.19, 144.24, 166.49. IR (KBr): 2945, 2864, 1747 (C=O), 1597 (aromatic), 1495 (aromatic), 1452, 1302 (sulfone), 1146 (sulfone), 1018, 814, 712 cm^{-1}. MS m/z (%): 497 (M^+, 0.4), 189 (25), 107 (100). *Anal.* Calcd for $C_{25}H_{27}F_3O_5S$: C, 60.47; H, 5.48. Found: C, 60.67; H, 5.61. HPLC analysis: hexane : AcOEt = 15 : 1, flow rate = 1.5 ml/min, t_R = 25.2 min.

3-[(1*S*,6*R*)-6-(*p*-Tolylsulfonyl)bicyclo[4.1.0]hept-1-yl]propanol (23) Borane–dimethylsulfide complex (0.570 ml, 10 M solution) was added to a solution of the olefin (**17**) (832 mg, 2.87 mmol) in THF (10 ml) at 0 °C under a nitrogen atmosphere. After being stirred at the same temperature for 1 h, the mixture was treated successively with ice, 3 N NaOH solution (0.40 ml), and 30% H_2O_2 solution (0.44 ml) and then stirring was continued for another 12 h at room temperature. The reaction was quenched with water, and the mixture was extracted with AcOEt. The extract was washed with saturated sodium thiosulfate solution, water and brine, dried, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 4 : 1) to give the alcohol (**23**) (746 mg, 84%) as a colorless oil, $[\alpha]_D^{22}$ −27.4° (c = 0.68, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.95 (1H, d, J = 5.2 Hz, C7′-H_a), 1.00—2.28 (13H, m), 1.73 (1H, d, J = 5.2 Hz, C7′-H_b), 2.44 (3H, s, Ar-CH_3), 3.71 (2H, t, J = 6.4 Hz, C1-H), 7.33 (2H, d, J = 8.4 Hz, Ar-H), 7.74 (2H, d, J = 8.4 Hz, Ar-H). IR ($CHCl_3$): 3525 (OH), 3000, 2945, 2865, 1602 (aromatic), 1500 (aromatic), 1454, 1302 (sulfone), 1142 (sulfone), 1090 cm^{-1}. MS m/z (%): 308 (M^+, 6), 153 (17), 139 (11), 135 (100). High MS Calcd for $C_{17}H_{24}O_3S$: 308.1443. Found: 308.1437.

3-[(1*S*,6*R*)-6-(*p*-Tolylsulfonyl)bicyclo[4.1.0]hept-1-yl]propionic Acid (24) A solution of the alcohol (**23**) (474 mg, 1.54 mmol) in acetone (20 ml) was treated with Jones reagent (2.28 ml, 2.7 M solution) at 0 °C, and the mixture was stirred at room temperature for 15 min. The reaction was quenched with isopropanol and the resulting mixture was concentrated *in vacuo* to give the carboxylic acid (**24**) (451 mg, 91%) as colorless crystals, mp 162—163 °C (benzene), $[\alpha]_D^{26}$ −26.6° (c = 1.17, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.96 (1H, d, J = 5.6 Hz, C7′-H_a), 1.07—1.19 (1H, m, C3′-H_a), 1.20—1.44 (4H, m, C3′-H_b, C4′-H, C5′-H_a), 1.70—1.82 (3H, m, C2′-H, C7′-H_b), 2.14—2.23 (1H, m, C5′-H_b), 2.24—2.40 (1H, m, C3-H_a), 2.44 (3H, s, Ar-CH_3), 2.48—2.62 (2H, m, C3-H_b, C2-H_a), 2.68—2.80 (1H, m, C2-H_b), 7.33 (2H, d, J = 8.1 Hz, Ar-H), 7.74 (2H, d, J = 8.1 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 20.34 (C3′), 21.46 (Ar-CH_3), 21.51 (C4′), 22.77 (C7′), 26.31 (C5′), 29.63 (C2′ and C3), 30.68 (C6′), 31.77 (C2), 46.20 (C1′), 128.28 (Ar-CH), 129.52 (Ar-CH), 136.95 (Ar-quaternary carbon), 143.86 (Ar-quaternary carbon), 179.59 (C=O). IR ($CHCl_3$): 3025, 2950, 2880, 1710 (C=O), 1600 (aromatic), 1498 (aromatic), 1418, 1302 (sulfone), 1104 (sulfone), 1088 cm^{-1}. MS m/z (%): 322 (M^+, 2), 167 (26), 149 (100). High MS Calcd for $C_{17}H_{22}O_4S$: 322.1236. Found: 322.1233.

3-[(1*S*,6*R*)-6-(*p*-Tolylsulfonyl)bicyclo[4.1.0]hept-1-yl]propionamide (25) Ethyl chloroformate (0.16 ml, 1.67 mmol) was added to a mixture of the carboxylic acid (**24**) (451 mg, 1.40 mmol), Et_3N (0.320 ml, 2.30 mmol), and CH_2Cl_2 (20 ml) at 0 °C, and stirring was continued at the same temperature for 30 min. Anhydrous NH_3 gas was bubbled through the mixture at 0 °C for 15 min. The reaction was quenched with water and the mixture was extracted with $CHCl_3$. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by recrystallization to give the amide (**25**) (423 mg, 86%) as colorless crystals, mp 146—147 °C (ether), $[\alpha]_D^{27}$ −26.6° (c = 1.17, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.99 (1H, d, J = 5.1 Hz, C7′-H_a), 1.08—1.18 (1H, m, C3′-H_a), 1.20—1.42 (4H, m, C3′-H_b, C4′-H, C5′-H_a), 1.69—1.77 (1H, ddd, J = 13.7, 9.4, 6.0 Hz, C2′-H_a), 1.75 (1H, d, J = 5.1 Hz,

Table 2. Crystal Data for **25**

Crystal dimensions (mm)	0.35 × 0.15 × 0.05
No. of molecules in an asymmetrical unit	1
Formula	$C_{17}H_{23}NO_3S$
Formula weight	321.43
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
a (Å)	11.306 (2)
b (Å)	15.907 (1)
c (Å)	9.594 (1)
α (°)	90
β (°)	90
γ (°)	90
Vol (Å^3)	1725.4 (3)
Z	4
ρ(calcd) (g/cm^3)	1.238
ρ(obsd) (g/cm^3)	1.200
Linear absorption coefficient (cm^{-1}) Cu-$K\alpha$: λ = 1.5418 Å	17.2
$(\sin\theta/\lambda)_{max}$ (Å)	0.58
Independent reflection $F_O > 3.0\,\sigma(F_O)$	1239
Absorption correction	No
No. of variables	292
Final R and (R_w)	0.0664 (0.0888)
Final R and (R_w) for the mirror image	0.0707 (0.0943)

Table 3. Atomic Coordinates and Equivalent Isotopic Thermal Parameters for Non-Hydrogen Atoms of **25** with Their Estimated Standard Deviations in Parentheses

Atom	x	y	z	B_{eq} (Å^2)
S1	0.8581 (2)	0.7391 (1)	0.9135 (2)	3.9 (1)
O1	0.7877 (6)	1.0338 (4)	0.7958 (5)	5.6 (2)
O2	0.7423 (5)	0.7322 (4)	0.8568 (6)	5.3 (2)
O3	0.8829 (6)	0.8111 (3)	0.9995 (6)	5.5 (2)
N1	0.7484 (7)	1.0359 (4)	0.5654 (7)	5.8 (2)
C1	1.0082 (8)	0.8108 (5)	0.7056 (9)	5.2 (3)
C2	1.0451 (10)	0.7969 (7)	0.5496 (10)	7.2 (3)
C3	1.0741 (17)	0.7080 (8)	0.5129 (12)	12.0 (6)
C4	0.9719 (14)	0.6492 (7)	0.5465 (10)	8.9 (4)
C5	0.9536 (10)	0.6476 (5)	0.7075 (9)	5.9 (3)
C6	0.9641 (7)	0.7318 (5)	0.7797 (8)	3.8 (2)
C7	1.0833 (8)	0.7696 (7)	0.8131 (10)	6.1 (3)
C8	0.9591 (7)	0.8976 (5)	0.7295 (9)	4.5 (2)
C9	0.8362 (9)	0.9093 (5)	0.6629 (9)	5.5 (3)
C10	0.7909 (7)	0.9990 (5)	0.6834 (8)	4.1 (2)
C11	0.8858 (7)	0.6497 (5)	1.0162 (7)	3.9 (2)
C12	0.9857 (8)	0.6463 (5)	1.0978 (9)	5.2 (3)
C13	1.0093 (8)	0.5765 (6)	1.1782 (9)	5.0 (2)
C14	0.9337 (7)	0.5085 (5)	1.1780 (8)	4.3 (2)
C15	0.8338 (8)	0.5119 (5)	1.0940 (10)	5.7 (3)
C16	0.8093 (8)	0.5820 (6)	1.0107 (9)	5.2 (3)
C17	0.9609 (8)	0.4309 (5)	1.2643 (9)	5.2 (3)

Table 4. Bond Distances (Å) of **25** for Non-Hydrogen Atoms with Their Estimated Standard Deviations in Parentheses

S1–O2	1.421 (6)	C4–C5	1.559 (15)
S1–O3	1.440 (6)	C5–C6	1.513 (12)
S1–C6	1.760 (8)	C6–C7	1.511 (12)
S1–C11	1.758 (8)	C8–C9	1.540 (12)
O1–C10	1.212 (10)	C9–C10	1.528 (12)
N1–C10	1.363 (11)	C11–C12	1.375 (11)
C1–C2	1.569 (14)	C11–C16	1.383 (11)
C1–C6	1.527 (12)	C12–C13	1.378 (12)
C1–C7	1.488 (13)	C13–C14	1.379 (12)
C1–C8	1.506 (12)	C14–C15	1.388 (12)
C2–C3	1.494 (18)	C14–C17	1.518 (12)
C3–C4	1.520 (19)	C15–C16	1.400 (13)

Table 5. Bond Angles (°) of **25** for Non-Hydrogen Atoms with Their Estimated Standard Deviations in Parentheses

O2–S1–O3	117.4 (3)	C1–C6–C5	122.7 (7)
O2–S1–C6	110.1 (4)	C1–C6–C7	58.7 (6)
O2–S1–C11	108.5 (3)	C5–C6–C7	121.3 (7)
O3–S1–C6	109.7 (3)	C1–C7–C6	61.2 (6)
O3–S1–C11	106.7 (3)	C1–C8–C9	112.3 (7)
C6–S1–C11	103.6 (4)	C8–C9–C10	111.2 (7)
C2–C1–C6	114.6 (7)	O1–C10–N1	122.1 (7)
C2–C1–C7	116.6 (8)	O1–C10–C9	123.4 (7)
C2–C1–C8	111.8 (7)	N1–C10–C9	114.4 (7)
C6–C1–C7	60.1 (6)	S1–C11–C12	119.8 (6)
C6–C1–C8	124.3 (7)	S1–C11–C16	119.8 (6)
C7–C1–C8	120.6 (8)	C12–C11–C16	120.3 (7)
C1–C2–C3	114.5 (9)	C11–C12–C13	120.6 (8)
C2–C3–C4	111.4 (11)	C12–C13–C14	120.8 (8)
C3–C4–C5	108.7 (10)	C13–C14–C15	118.3 (8)
C4–C5–C6	115.4 (8)	C13–C14–C17	120.8 (7)
S1–C6–C1	120.5 (6)	C15–C14–C17	120.9 (7)
S1–C6–C5	109.8 (6)	C14–C15–C16	121.6 (8)
S1–C6–C7	115.3 (6)	C11–C16–C15	118.4 (8)

C7′-H_b), 1.78—1.87 (1H, m, C2′-H_b), 2.13—2.23 (1H, m, C5′-H_b), 2.34—2.52 (3H, m, C2-H_a, C3-H), 2.44 (3H, s, Ar-CH_3), 2.59—2.68 (1H, m, C2-H_b), 5.71 (1H, br s, NH_a), 6.08 (1H, br s, NH_b), 7.34 (2H, d, J=8.5 Hz, Ar-H), 7.74 (2H, d, J=8.5 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 20.36 (C3′), 21.49 (Ar-CH_3 and C4′), 23.87 (C7′), 26.22 (C5′), 29.72 (C2′), 31.63 (C3), 32.08 (C6′), 34.34 (C2), 45.97 (C1′), 128.23 (Ar-CH), 129.54 (Ar-CH), 136.77 (Ar-quaternary carbon), 143.99 (Ar-quaternary carbon), 175.72 (C=O). IR ($CHCl_3$): 3515 (NH), 3420 (NH), 3010, 2955, 2880, 1680 (C=O), 1600 (aromatic), 1458 (aromatic), 1292 (sulfone), 1148 (sulfone), 1094 cm^{-1}. MS m/z (%): 321 (M^+, 2), 166 (100), 149 (56). *Anal.* Calcd for $C_{17}H_{23}NO_3$: C, 63.53; H, 7.21; N, 4.36; S, 9.96. Found: C, 63.34; H, 7.26; N, 4.41; S, 9.96.

X-Ray Crystallographic Analysis The amide (**25**) was crystallized from ether, and a suitable crystal was subjected to X-ray analysis. Intensity data were collected on a Rigaku AFC-5R diffractometer. The crystal structure was solved by the direct method using the MULTAN program, and all hydrogen atoms were found in difference Fourier calculation. Block-diagonal least-squares refinement of positional and thermal parameters, including anomalous scattering factors, led to the final convergence with R=0.0664 for the (1*S*,6*R*) absolute configuration, while R=0.0707 for the mirror image structure. The crystal data are collected in Table 2. Final atomic coordinates and equivalent isotopic thermal parameters for non-hydrogen atoms are listed in Table 3. Bond distances and bond angles are given in Tables 4 and 5, respectively. The atomic scattering factors and terms of anomalous dispersion corrections were taken from reference 21.

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