Pergamon

Tetrahedron, Vol. 53, No. 36, pp. 12101-12114, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00545-0

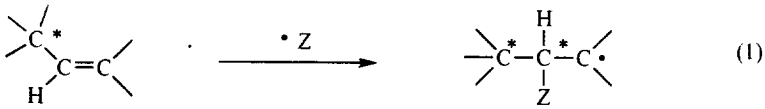
Highly Stereoselective Radical Addition to 3-Hydroxy-1-(methylthio)-1-(*p*-tolylsulfonyl)-1-alkenes and Its Application to the Preparation of Optically Active Compounds

Akio Kayano, Motohiro Akazome, Makoto Fujita, and Katsuyuki Ogura*

Department of Applied Chemistry, Faculty of Engineering, Chiba University, 1-33 Yayoicho, Inageku, Chiba 263, Japan

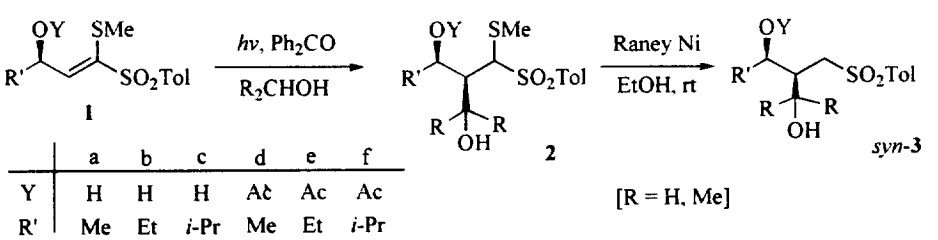
Abstract. Efficient 1,2-asymmetric induction was realized in the addition of a 1-hydroxyalkyl radical ($R_2\dot{C}$-OH) to 3-hydroxy-1-(methylthio)-1-(*p*-tolylsulfonyl)-1-alkenes and their acetates (**1**): Irradiation of **1** and benzophenone in an alcohol (R_2CHOH) gave an adduct (**2**) with a high syn selectivity. Optically active **1** is easily obtainable by means of Lipase PS-catalyzed transesterification and, therefore, the present radical asymmetric induction provides a synthetic route leading to various chiral compounds.

Free radical reactions provide an efficient method for carbon-carbon bond formation in organic synthesis.[1,2] Hitherto the radical reactions accompanied by asymmetric induction have been investigated.[3] but only a few papers appeared for 1,2-asymmetric induction in intermolecular addition of an achiral radical to an acyclic chiral C-C double bond to select a stereogenic π-face (eq 1).[4]



(1)

In general, a radical adds so exothermically to an alkene that its transition state is reactant-like (the Hammond postulate). Therefore, the following problems must be solved to attain the efficient 1,2-asymmetric induction in the above equation: i) How is a chiral center conformationally fixed? ii) How is the radical constrained to attack on the carbon adjacent to the chiral center? Hehre and his coworkers reported that the conformational preference of allylic alcohols is quite sensitive to the substitution on the alkene and, in particular, an electron-withdrawing groups favors the conformation in which the C-O linkage eclipses the double bond.[5] This would provide a clue to solve the first problem. It has also been established by us that the ability of 2-(methylthio)-2-(*p*-tolylsulfonyl)ethenyl moiety to accept various kinds of radicals, especially nucleophilic 1-hydroxyalkyl radicals, is high enough to control the regioselectivity of the radical attack.[4,7] Hence we selected 3-hydroxy-1-(methylthio)-1-(*p*-tolyl-sulfonyl)alkenes (**1**) as a radical acceptor for establishing the efficient 1,2-asymmetric induction of eq 1. We also found that an enzymatic transesterification of **1** with vinyl acetate was catalyzed by lipase PS to give optically active **1** with a high efficiency. In this paper, we report that the addition reaction of 1-hydroxyalkyl radicals to **1** takes place



	a	b	c	d	e	f
Y	H	H	H	Ac	Ac	Ac
R'	Me	Et	*i*-Pr	Me	Et	*i*-Pr

(2)

[R = H, Me]

with a highly 1,2-asymmetric induction and, in a combination with this asymmetric induction, optically active **1** can be utilized for synthesizing several types of optically active compounds.

Results and Discussion

Intermolecular Stereoselective Addition of 1-Hydroxyalkyl Radical to 1.

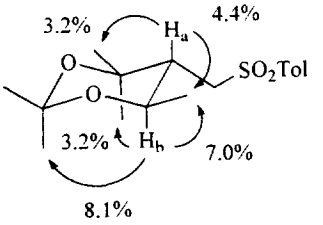
The 1-hydroxyalkyl radical ($R_2\dot{C}$-OH) was generated by α-hydrogen abstraction of an alcohol (R_2CHOH) with excited triplet benzophenone.[7] When a solution of (*E*)-**1a**[9] and benzophenone (1.0 mol equiv) in 2-propanol was irradiated with a high pressure Hg lamp through Pyrex filter, an adduct (**2a**, R=Me) was formed as a mixture of four (mainly two) diastereomers in 97% yield. Reductive desulfurization of the mixture with Raney-Ni (W2) afforded **3a** which consisted of two diastereomers in a ratio of 95:5. The major diastereomer of **3a** (R=Me) was determined to have a *syn* relationship between C_2 and C_3 chiral centers by the conversion to its acetonide (**4a**), which showed H_a-H_b coupling of 9.60 Hz in ^{1}H NMR spectrum and satisfactory NOE (Figure 1).

The ratio of 95:5 reflects the syn:anti selectivity in the addition of $Me_2\dot{C}$-OH radical to **1a**. This selectivity is extremely high as to 1,2-asymmetric induction in a simple acyclic system.[3] Similar irradiation of (*Z*)-**1a** gave **2a** (R = Me) with a comparably high *syn* selectivity (*syn*:*anti*=95:5). Monitoring of the reaction by HPLC exhibited that isomerization of (*Z*)-**1a** to (*E*)-**1a** occurred concurrently. Actually, a solution of (*Z*)-**1a** in acetonitrile or benzene containing benzophenone was irradiated to cause the *Z*-*E* isomerization which reached to a photostationary state within 2 h (*E*:*Z*=95:5 or 89:11, respectively). Therefore, it is reasonably rationalized that the geometrical isomerism of the starting **1** did not affect the selectivity. Similarly, **1b** and **1c** produced the corresponding **2** in a ratio of 96:4. Hydroxymethyl radical also added to **1** with a high *syn* selectivity as shown in Table 1. The structure of the major isomer of **3b** was confirmed by X-ray crystallography (Figure 2) and, in a similar manner to **3a**, syn configuration was assigned to the major isomer of **3c** (see Experimental Section). It is noteworthy that the protection of the hydroxyl group with acetyl group does not affect so much the stereochemical course of the radical addition. In fact, 1-methyl-1-hydroxyethyl radical added **1d-f** with high *syn* selectivity as summarized in Table 1 (entries 9-12).

Table 1. Photochemical Addition to **1**.

entry	**1**				R_2CHOH	yield /%	
		Y	R'	(*E*:*Z*)	R	**2**	**3** (*syn*:*anti*)
1	**1a**	H	Me	(100:0)	Me	97	84 (95: 5)
2			Me	(0:100)	Me	98	89 (95: 5)
3			Me	(25:75)	Me	79	100 (95: 5)
4			Me	(100:0)	H	86	72 (86:14)
5	**1b**		Et	(100:0)	Me	79	94 (96: 4)
6			Et	(100:0)	H	83	100 (94: 6)
7	**1c**		*i*-Pr	(100:0)	Me	69	96 (96: 4)
8			*i*-Pr	(100:0)	H	81	96 (94: 6)
9	**1d**	Ac	Me	(50:50)	Me	94	85 (85:15)
10	**1e**		Et	(25:75)	Me	96	84 (87:13)
11	**1f**		*i*-Pr	(18:82)	Me	48 (94)[b]	92 (89:15)

[a] The yield based on the unrecovered **1**.



4a [$J_{Ha.Hb}$ = 9.60 Hz]

Fig. 1. The NOEs of **4a**.

Since the synergistic effect of an electron-donating methylthio group and an electron-withdrawing *p*-tolylsulfonyl group makes the carbon radical very stable,[8] the radical addition to **1** is so exothermic[11] that its transition state is reactant-like (the Hammond postulate). The preferred conformation of **1a** was suggested by the crystal structure (Figure 3) of **1a** which possesses the hydroxyl group outside the double bond and the methyne proton (H_b) inside.[13] The ^1H NMR spectra of **1a-f** in $CDCl_3$ or CD_3OD exhibited large coupling constants (7.60-9.20 Hz) and no NOE between H_a and H_b was observed.[14] Therefore, the most favorable conformation about the C_2-C_3 bond of **1** in a solution seems to be similar to that in a crystalline state, in which allylic 1,3-strain[15] may play an important role in dictating the conformation. If a radical approaches from the less crowded side (Figure 3), opposite to the methyl and *p*-tolylsulfonyl groups, the adduct would have the *syn*-configuration. *In conclusion, the combination of methylthio and p-tolylsulfonyl groups at the 1-position not only controls the regioselectivity of the reaction, but also amplifies the C_3 chirality through the double bond to attain high syn selectivity.*

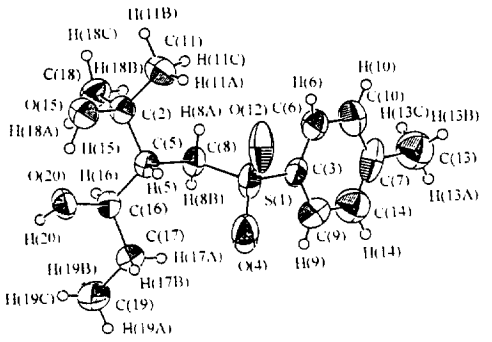


Fig. 2. ORTEP drawings of the crystal structure of **3b** (R = Me).

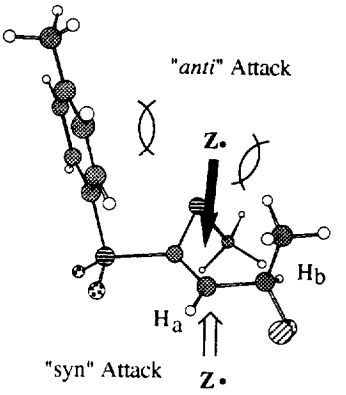


Fig. 3. Chem 3D representation of the X-ray structure of **1a**.

Application to the Synthesis of Optically Active Compounds

Recently, Carretero and Dominguez reported an efficient optical resolution of γ-hydroxy-α,β-unsaturated sulfones by transesterification using lipase PS.[16] Since their (*Z*)-isomers gave rise to an unsatisfactory result, we wondered whether our starting compounds (**1**) could be optically resolved by means of lipase. Fortunately, we found that lipase PS from *Pseuodomonas cepacia* (Amano PS)[17] catalyzes

Table 2. Lipase PS-mediated Transesterification of *Rac*emic **1**.

entry	*Rac*-**1**			time / h	the acetate			the recovered			E^b
	E / *Z*		R'			yield / %%ee[a]			yield / %	%ee[a]	
1	*E*	**1a**	Me	12	**1d**	44	99(*R*)	**1a**	46	98(*S*)	525
2		**1b**	Et	24	**1e**	49	99(*R*)	**1b**	51	98(*S*)	525
3		**1c**	*i*-Pr	168	**1f**	25	96(*R*)	**1c**	82	18(*S*)	58
4	*Z*	**1a**	Me	57	**1d**	30	95(*R*)	**1a**	70	20(*S*)	47
5		**1b**	Et	94	**1e**	29	88(*R*)	**1b**	84	16(*S*)	18
6		**1c**	*i*-Pr	168	**1f**	*c*	---	**1c**	90	2 (*S*)	---

[a] Ee was determined by analytical HPLC (CHIRALCEL OD or CHIRALPAK AS). [b] E value was obtained from conversion and the ee of the recovered substrate.[20] [c] The acetate was not isolated.

transesterification of **1** with vinyl acetate.[18] A mixture of racemic (*E*)-**1a** (0.66 mmol), lipase PS (330 mg), vinyl acetate (5.0 mol equiv), and powdered molecular sieves 4A (180 mg) in benzene was stirred at room temperature for 12 h. Chromatographic separation afforded (*R*)-(*E*)-**1d** (99% ee, 44% chemical yield) and (*S*)-(*E*)-**1a** (98% ee, 47%). On treatment of (*Z*)-**1a** under the same conditions, the reaction occurred slowly and, after stirring for 57 h, (*R*)-(*Z*)-**1d** (30% yield) was produced in an enantiomeric excess of 95%.

The absolute configurations of the obtained optically active **1a** and **1d** were determined by the following chemical correlation: Reduction of the obtained (*E*)-**1a** with sodium borohydride afforded 4-(methylthio)-4-(*p*-tolylsulfonyl)-2-butanol (**5**), which was converted to 4-(*p*-tolylsulfonyl)-2-butanol (**6**) by desulfurization with Raney-Ni (W2). This was identified as (*S*)-**6** by agreement of its physical properties with those of an authentic sample[19] which was prepared by the reaction of (*S*)-propylene oxide by the dilithio derivative of methyl *p*-tolyl sulfone. Thus, the absolute configuration of the recovered (*E*)-**1a** was determined to be *S*. Similarly, the acetylation product [(*Z*)-**1d**] from (*Z*)-**1a** was shown to have *R* configuration.

The influence of substituent bulkiness and geometrical isomerism were examined on **1**. The results are summarized in Table 2. As mentioned above, the geometrical isomerism exhibited a significant effect to give a better result in the transesterification of (*E*)-**1**. As can be seen clearly from Table 2, the larger the alkyl (R') group was, the slower the acetylation became. Especially, we observed a wide gap between R=Et (entry 2) and R=*i*-Pr (entry 3).

In recent years, a model for the active site of some lipases has been extensively discussed,[21] and the simple empirical rule shown in Figure 4 can predict which enantiomer of a secondary alcohol undergoes the lipase-mediated transesterification more preferentially.[22] If it is assumed that the alkyl (R') group is medium and 2-(methylthio)-2-(*p*-tolylsulfonyl)ethenyl moiety is the largest in size, lipase PS is anticipated to convert (*R*)-**1** to the corresponding acetate with a high enantiomer selectivity. In fact, this is the case in the reaction of (*E*)-**1a-c** and (*Z*)-**1a-c**.

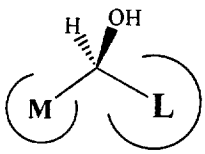
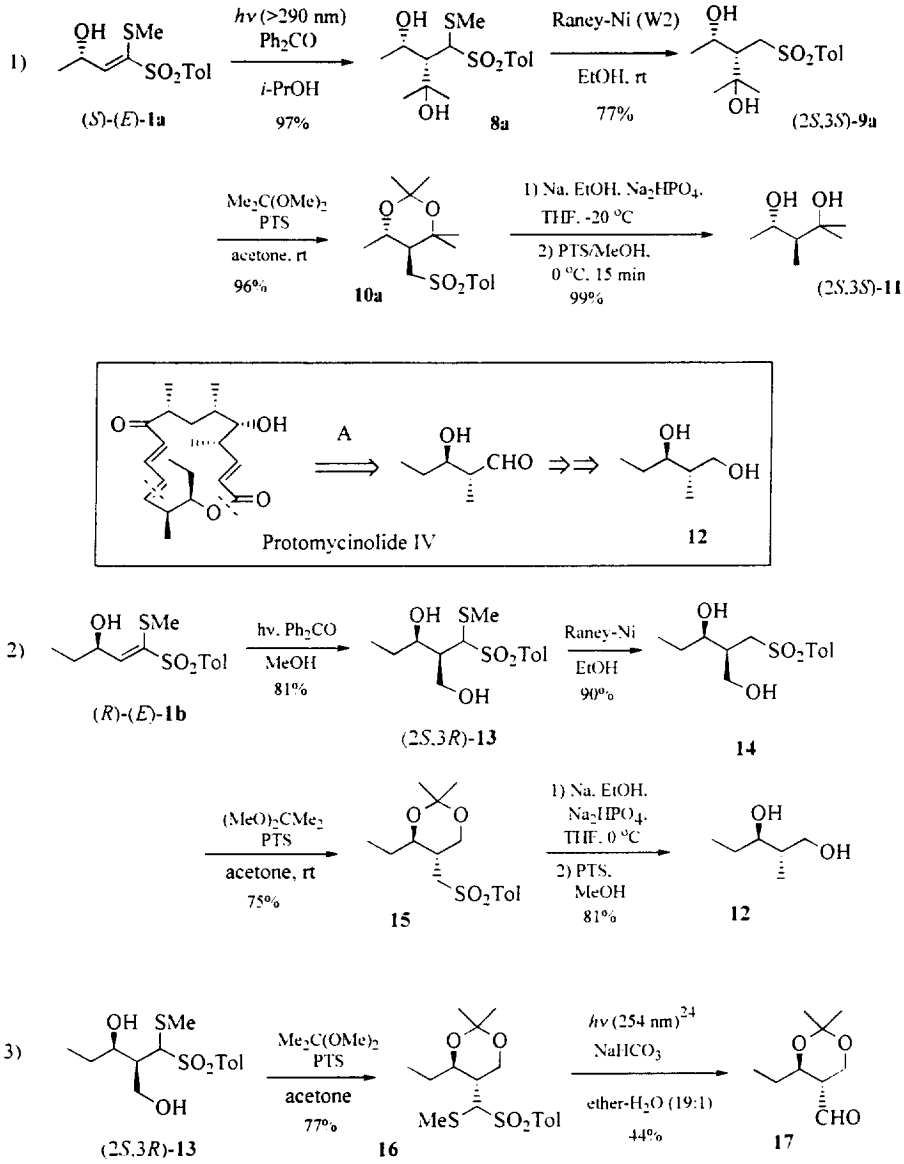


Fig. 4. The enatiomer that is predicted by an empirical rule to be faster acetylated by lipase and vinyl acetate.[22] "M" and "L" represent medium and large substituents, respectively.

With optically active **1** in hand, we attempted to synthesize some optically active compounds using the present radical 1,2-asymmetric induction. Scheme 1 summarizes the results. Efficient stereoselective addition of 1-hydroxy-1-methylethyl radical to (*S*)-(*E*)-**1a** (90% ee) gave an adduct (**8a**), subsequent desulfurization of which with Raney-Ni (W2) afforded a 1,3-diol [(2*S*,3*S*)-**9a**; $[\alpha]_D^{23}$ -16.4 (*c* 1.01, $CHCl_3$)]. Two hydroxyl groups of (2*S*,3*S*)-**9a** were protected by 2,2-dimethoxypropane and PTS to form an acetonide (**10a**). Reductive removal of *p*-tolylsulfonyl group of **10a** followed by deprotection afforded an optically active (2*S*,3*S*)-**11** ($[\alpha]_D^{23}$ -4.39 (*c* 1.00, $CHCl_3$)), the enantiomeric excess of which was 88%. Similarly, (2*S*,3*R*)-2-methyl-1,3-pentanediol (**12**), a synthetic intermediate of Protomycinolide IV,[23] was also synthesized starting from (*R*)-(*E*)-**1b**: addition of 1-hydroxymethyl radical to (*R*)-(*E*)-**1b** gave (2*S*,3*R*)-**13**, which was converted to **14** (90% ee) by reductive desulfurization with Raney-Ni. After its transformation to an acetonide (**15**), the reductive removal of the sulfonyl group followed by deprotective hydrolysis afforded **12**. (2*S*,3*R*)-**13** was shown to be a synthetic intermediate of a chiral aldehyde (**17**), which was derived by protection of the two hydroxyl groups of **13** and the subsequent photochemical hydrolysis of the 1-(methylthio)-1-(*p*-tolylsulfonyl)methyl moiety.[24]

Conclusion

High 1,2-asymmetric induction was realized in the 1-hydroxyalkyl radical addition to acyclic 3-hydroxy-1-methylthio-1-(*p*-tolylsulfonyl)-1-alkenes (**1**). The syn-selectivity of the reaction was interpreted in terms of a preferable attack of the radical from the less crowded side of the most stable conformation of **1**. We also found that optically active **1** was easily prepared by transesterification with lipase PS in an organic medium. The combination of these two findings enabled us to prepare various useful optically active compounds.



Scheme 1. Synthesis of Some Optically Active Compounds

EXPERIMENTAL

General. Melting points were determined on a hot-stage microcsope apparatus (Yanagimoto) and are uncorrected. ^{1}H NMR spectra in $CDCl_3$ were obtained on JEOL JNM-FX 270 (270 MHz) and JEOL JNM-GSX 500 (500 MHz) spectrometers. Infrared spectra were determined with a JASCO A-200. Microanalytical data were provided by the Analysis Center of Chiba University.

Photochemical Addition of 2-Propanol to 3-Hydroxy-1-methylthio-1-(*p*-tolylsulfonyl)-1-butene (1a). A Typical Procedure. A solution of **1a** (272 mg, 1.00 mmol, *E*:*Z* = 25:75) and benzophenone (182.2 mg, 1.00 mmol) in 2-propanol (70 mL) was irradiated with a 100-W high-pressure Hg lamp (Sigemi Standard) with a water-cooled Pyrex jacket under N_2 bubbling at room temperature for 80 min. Evaporation and chromatography on silica gel (hexane/ethyl acetate 2:1~1:1) gave a diastereomeric mixture (**A**:**B**:**C**:**D**= 55:40:2.5:2.5) of **2a** (R=Me) (261 mg, 79% yield) and the recovered **1a** (40 mg, 15%). An analytical sample was obtained by preparative HPLC (GPC; JAIGEL-1H and JAIGEL-2H; $CHCl_3$): a colorless viscous oil; IR (neat) 3450, 2980, 1370, 1280, 1140, 1080 cm^{-1};^1H NMR (270 MHz, $CDCl_3$): [the diastereomer **A**] δ 7.86 (d, 2H, *J*=8.24 Hz), 7.39 (d, 2H, *J*=7.91 Hz), 4.13 (dq, 1H, *J*=1.32 and 6.59 Hz), 4.12 (d, 1H, *J*=1.68 Hz), 3.65 (broad, 1H, O*H*), 2.58 (broad, 1H, O*H*), 2.47 (s, 3H), 2.44 (m, 1H), 1.68 (s, 3H, SCH_3), 1.41 (d, 3H, *J*=6.92 Hz), 1.39 (s, 3H), 1.286 (s, 3H); [the diastereomer **B**] δ 7.91 (d, 2H, *J*=8.56 Hz), 7.38 (d, 2H, *J*=8.24 Hz), 4.35 (dq, 1H, *J*=3.96 and 6.26 Hz), 3.98 (d, 1H, *J*=0.7 Hz), 2.96 (broad, 1H, O*H*), 2.74 (dd, 1H, *J*=1.49 and 3.96 Hz, $CH_3CH(OH)CH$), 2.47 (s, 3H), 2.34 (broad, 1H, O*H*), 2.00 (s, 3H), 1.44 (s, 3H), 1.38 (s, 3H, $(CH_3)_2COH$), 1.30 (s, 3H, *J*=6.59 Hz); [the diastereomers **C**] δ 2.17 (s, 3H, SCH_3); [the diastereomers **D**] δ 2.05 (s, 3H, SCH_3). Anal. Calcd for $C_{15}H_{24}O_4S_2$: C, 54.22; H, 7.23. Found: C, 54.04; H, 7.09.

Desulfurization of 2a (R=Me) with Raney-Ni. To a solution of a diastereomeric mixture of **2a** (R= Me) (116 mg, 0.36 mmol) in 99% ethanol (1.0 mL) was added Raney-Ni (W2) (1.5 cm^3), and the resulting suspension was stirred vigorously at room temperature for 25 h. After filtration, the filtrate was evaporated and the residue was purified by flash chromatography on silica gel (hexane/ethyl acetate 1:2) to give a diastereomeric mixture of **3a** (R=Me) (914 mg, 100% yield) as a colorless solid, which consisted of two diastereomers (*syn*:*anti*= 95:5): IR (KBr) 3250, 2980, 2900, 1290, 1190, 1140 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the *syn*-isomer] δ 7.82 (d, 2H, *J*=8.24 Hz), 7.37 (d, 2H, *J*=8.24 Hz), 4.14 (dq, 1H, *J*=4.90 and 6.59 Hz), 3.32 (dd, 1H, *J*=3.0 and 15.0 Hz,), 3.13 (dd, 1H, *J*=6.26 and 15.0 Hz, 1H), 2.99 (broad, 1H, O*H*), 2.61 (broad, 1H, O*H*), 2.46 (s, 3H), 2.29 (ddd, 1H, *J*=3.26, 4.92, and 6.26 Hz), 1.27 (d, 3H, *J*=6.59 Hz), 1.25 (s, 3H) 1.22 (s, 3H); [the *anti*-isomer] δ 4.44 (m, 1H, CH_3CH(OH)) and 3.88 (d-like, 2H, CH_2SO_2Tol). An analytical sample was obtained by recrystallization from hexane-CH_2Cl_2: colorless crystals; mp 115.8-116.3 °C. Anal. Calcd for $C_{14}H_{22}O_4S$: C, 58.71; H, 7.74. Found: C, 58.92; H, 7.76.

Similarly, irradiation of **1b** and benzophenone in 2-propanol (70 mL) for 6.5 h afford a mixture of three diastereomers (**A**:**B**:**C**=54:44:2) of **2b** (R=Me) (275 mg, 79% yield) after purification by column chromatography and preparative HPLC (GPC).

2b (R=Me): a colorless oil; a mixture of three diastereomers (**A**:**B**:**C**=54:44:2); IR (neat) 3450, 2950, 1590, 1285, 1140, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the diastereomer **A**] δ 7.86 (d, 2H, *J*=8.24 Hz,), 7.38 (d, 2H, *J*=7.91 Hz), 3.98 (d, 1H, *J*=0.99 Hz,), 3.75 (ddd, 1H, *J*=0.99, 4.28, and 9.62 Hz), 2.71 (dd, 1H, *J*=1.68 and 3.93 Hz), 2.47 (s, 3H), 2.01 (s, 3H), 1.52-1.61 (m, 2H), 1.41 (s, 3H), 1.40 (s, 3H), 0.93 (t, 3H, *J*=7.56 Hz); [the diastereomer **B**] δ 7.91 (d, 2H, *J*=8.24 Hz), 7.38 (d, 2H, *J*=7.91 Hz), 4.10 (d, 1H, *J*=1.68 Hz), 4.01 (ddd, 1H, *J*=2.32, 4.04, and 9.89 Hz), 2.47 (s, 3H), 2.46 (broad s, 1H), 2.01-2.40 (broad, 2H, O*H*), 1.81-1.92 (m, 2H), 1.70 (s, 3H), 1.40 (s, 3H), 1.26 (s, 3H), 1.03 (t, 3H, *J*=7.56 Hz); [the diastereomer **C**] δ 4.18 (d, 1H) and 1.63 (s, 3H). Anal. Calcd for $C_{16}H_{26}O_4S_2$•0.27$CHCl_3$: C, 51.53; H, 6.98. Found: C, 51.60; H, 6.99.

3b (R=Me): colorless crystals; IR (KBr) 3200, 2950, 1290, 1135, 1080, 960 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the *syn* isomer] δ 7.80 (d, 2H, *J*=8.57 Hz), 7.37 (d, 2H, *J*=7.91 Hz), 3.81 (ddd, 1H, *J*=3.82, 3.63, and 9.21 Hz), 3.34 (dd, 1H, *J*=2.68 and 15.0 Hz), 3.16 (dd, 1H, *J*=6.93 and 15.0 Hz), 2.30-2.70 (broad, 2H, O*H*), 2.46 (s, 3H), 2.25 (ddd, 1H, *J*=2.7, 4.0, and 6.82 Hz), 1.60-1.70 (m, 2H), 1.23 (s, 3H), 1.20 (s, 3H), 1.01 (t, 3H, *J*=7.26 Hz); [the *anti*-isomer] δ 4.00 (broad m, 1H), 2.15 (diffused m, 1H), 1.35 (s, 3H), and 1.29 (s, 3H). Recrystallization gave colorless needles: mp 125-125.5 °C (hexane-ethyl acetate). Anal. Calcd for $C_{15}H_{24}O_4S$: C, 59.97; H, 8.05. Found: C, 60.11; H, 8.11.

2c (R=Me): colorless crystals; IR (KBr) 3200, 1590, 1380, 1310, 1140, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the diastereomer **A**] δ 7.87 (d, 2H, *J*=8.57 Hz), 7.38 (d, 2H, *J*=7.91 Hz), 3.98 (d, 1H, *J*=0.66 Hz), 3.63 (broad d, 1H, *J*=9.56 Hz), 2.78 (diffused m, 1H), 2.47 (s, 3H), 2.09-2.18 (m, 1H), 1.85 (s, 3H), 1.45 (s, 3H), 1.22 (s, 3H), 1.04 (d, 3H, *J*=6.59 Hz), 1.03 (d, 3H, *J*=6.60 Hz); [the diastereomer **B**] δ 7.89 (d, 2H, *J*=8.57 Hz), 7.38 (d, 2H, *J*=7.91 Hz), 3.89 (dd, 1H, *J*=5.28 and 5.61 Hz), 3.24 (d, 1H, *J*=1.98 Hz), 2.76 (dd, 1H, *J*=1.97 and 5.94 Hz), 2.47 (s, 3H), 2.05-1.87 (m, 1H), 1.78 (s, 3H), 1.50 (s, 3H), 1.44 (s, 3H), 1.01 (d, 3H, *J*=6.92 Hz), 0.95 (d, 3H, *J*=6.59 Hz); [the diastereomer **C**] δ 1.67 (s, 3H, SCH_3), 1.56 (s, 3H, $(CH_3)_2COH$), 1.36 (s, 3H, $(CH_3)_2COH$). An analytical sample was obtained by recrystallization from benzene: colorless crystals; mp 130.5-131 and 141-142 °C (decomp.). Anal. Calcd for $C_{17}H_{28}O_4S_2$: C, 56.63; H, 7.83. Found: C, 56.92; H, 7.66.

3c (R=Me): colorless crystals; IR (KBr) 3200, 1420, 1300, 1135, 1083, 975 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the *syn* isomer] δ 7.79 (d, 2H, *J*=8.57 Hz), 7.36 (d, 2H, *J*=7.91 Hz), 3.68 (dd, 1H, *J*=4.61 and 6.92 Hz), 3.52 (broad, 1H, O*H*), 3.30 (dd, 2H, *J*=2.63 and 15.2 Hz), 3.11 (dd, 2H, *J*=6.60 and 14.4 Hz), 2.75 (broad, 1H, O*H*), 2.45 (s, 3H), 2.31 (ddd, 1H, *J*=2.63, 4.62, and 6.59 Hz), 2.05-2.16 (m, 1H), 1.31 (s, 3H), 1.10 (s, 3H), 1.00 (d, 3H, *J*=6.93 Hz), 0.98 (d, 3H, *J*=6.59 Hz); [the *anti*-isomer] δ 3.41 (dd, 1H, *J*=4.06 and 15.5 Hz), 3.33 (dd, 1H, *J*=4.06 and 15.5 Hz), and 1.34 (s, 3H). An analytical sample was obtained by recrystallization from hexane-CH_2Cl_2: colorless crystals; mp 134-136 °C (hexane-CH_2Cl_2). Anal. Calcd for $C_{16}H_{26}O_4S$: C, 61.12; H, 8.33. Found: C, 60.82; H, 8.32.

2a (R=H): a colorless oil: a diastereomeric mixture (**A**:**B**:**C**:**D**=54:36:6:4); IR (neat) 3430, 2930, 1280, 1138, 1080, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): [the diastereomer **A**] δ 7.88 (d, 2H, *J*=8.24 Hz), 7.39 (d, 2H, *J*=7.91 Hz), 4.45 (dq, 1H, *J*=4.26 and 6.59 Hz), 4.24 (d, 1H, *J*=7.00 Hz), 4.15 (dd, 1H, *J*=3.93 and 13.0 Hz), 3.91 (dd, 1H, *J*=4.03 and 12.0 Hz), 2.48 (s, 3H), 2.25 (dq-like, 1H, *J*=1.42 and 4.03 Hz) 1.87 (s, 3H), 1.36 (d, 3H, *J*=6.59 Hz); [the diastereomer **B**] δ 7.88 (d, 2H, *J*=8.24 Hz), 7.39 (d, 2H, *J*=7.91 Hz), 4.39 (dq, 1H, *J*=1.05 and 6.59 Hz), 4.27 (dd, 1H, *J*=2.82 and 13.0 Hz), 4.12 (dd, 1H, *J*=4.03 and 13.0 Hz), 4.11 (d, 1H, *J*=5.50 Hz), 2.48 (s, 3H), 2.09-2.13 (m, 1H), 1.92 (s, 3H), 1.32 (d, 3H, *J*=6.59 Hz); [the diastereomer **C**] δ 4.32 (d, 1H, *J*=1.92 Hz), 3.97 (dd, 1H, *J*=4.26 and 12.0 Hz), 3.79 (dd, 1H, *J*=3.26 and 12.0 Hz), 1.76 (s, 3H), and 1.28 (d, 3H, *J*=6.26 Hz); [the diastereomer **D**] δ 4.34 (d, 1H, *J*=3.28 Hz), 4.02 (dq, 1H, *J*=7.68 and 6.92 Hz), 3.75 (dd, 1H, *J*=7.82 and 12.0 Hz), 2.03 (s, 3H), and 1.20 (d, 3H, *J*=6.26 Hz). Anal. Calcd for $C_{13}H_{20}O_4S_2$: C, 51.32; H, 6.58. Found: C, 51.56; H, 6.46.

3a (R=H) (*syn*:*anti*=86:14): colorless crystals; IR(KBr) 3400, 2930, 1400, 1280, 1140, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the *syn* isomer] δ 7.80 (d, 2H, *J*=8.58 Hz), 7.37 (d, 2H, *J*=7.91 Hz), 4.09 (dq, 1H, *J*=4.04 and 12.0 Hz,), 4.01 (dd, 1H, *J*=3.63 and 12.0 Hz), 3.79 (dd, 1H, *J*=3.92 and 12.0 Hz), 3.39 (dd, 1H, *J*=6.92 and 14.0 Hz), 3.32 (dd, 1H, *J*=5.62 and 14.0 Hz), 2.60 (broad, 2H, O*H*), 2.45 (s, 3H), 2.14-2.20 (m, 1H), 1.24 (d, 3H, *J*=6.59 Hz)): [the *anti*-isomer] δ 3.23 (dd, 1H, *J*=2.97 and 14.5 Hz) and 1.11 (d, 3H, *J*=6.59 Hz,). Recrystallization from hexane-ethyl acetate gave colorless crystals: mp 88-90 °C. Anal. Calcd for $C_{12}H_{18}O_4S$: C, 55.79; H, 7.02. Found: 55.84; H, 6.99.

2b (R=H): colorless crystals; a diastereomeric mixture (**A**:**B**:**C**:**D**=62:32:3:3); IR (KBr) 3480, 2950,1290, 1140, 1080, 1030 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the diastereomer **A**] δ 7.89 (d, 2H, *J*=8.24 Hz), 7.39 (d, 2H, *J*=8.57 Hz), 4.32-3.90 (diffused m, 3H), and 4.26 (d, 1H, *J*=7.58 Hz), 2.48 (s, 3H), 2.20-2.10 (m, 1H), 1.86 (s, 3H), 1.92-1.44 (m, 2H), 0.986 (t, 3H, *J*=7.58 Hz); [the diastereomer **B**] δ 7.88 (d, 2H, *J*=8.24 Hz), 7.39 (d, 2H, *J*=8.57 Hz), 4.32-3.90 (diffused m, 3H), 4.13 (d, 1H, *J*=6.26 Hz), 2.48 (s, 3H), 2.27-2.20 (dq-like, 1H, *J*=3.63 and 6.26 Hz), 1.92-1.44 (m, 2H), 1.91 (s, 3H), 0.994 (t, 3H, *J*=7.25 Hz); [the diastereomer **C**] δ 2.173 (s, 3H, SCH_3); [the diastereomer **D**] δ 2.168 (s, 3H, SCH_3). An analytical sample was obtained by recrystallization from hexane-ethyl acetate: colorless crystals; mp 88-89 °C. Anal. Calcd for $C_{14}H_{22}O_4S_2$: C, 52.80; H, 6.96. Found: C, 52.85; H, 6.90.

3b (R=H) mixture: a colorless oil (*syn*:*anti*=94:6); IR (neat) 3450, 2940, 1595, 1290, 1140, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the *syn*-isomer] δ 7.80 (d, 2H, *J*=8.24 Hz), 7.37 (d, 2H, *J*=7.91 Hz), 4.00 (dd, 1H, *J*=3.30 and 12.5 Hz), 3.86-3.70 (broad m, 2H), 3.45 (dd, 1H, *J*=6.60 and 14.1 Hz), 3.35 (dd, 1H, *J*=6.60 and 14.5 Hz), 2.46 (s, 3H), 2.90-2.60 (broad, 2H, O*H*), 2.37-2.21 (m, 1H), 1.61-1.51 (m, 2H), 0.95 (t, 3H, *J*=7.59 Hz); [the *anti*-isomer] δ 0.87 (t, 3H, *J*=7.59 Hz). Anal. Calcd for $C_{13}H_{20}O_4S$: C, 57.33; H, 7.40. Found: C, 57.13; H, 7.57.

2c (R=H): a colorless oil; a diastereomeric mixture (**A**:**B**:**C**:**D**=62:32:3:3); IR (neat) 3475, 2950, 1595, 1440, 1290, 1140 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the diastereomer **A**] δ 7.88 (d, 2H, *J*=8.24 Hz), 7.38 (d, 2H, *J*=8.24 Hz), 4.40-4.30 (diffused m, 1H), 4.29 (d, 1H, *J*=8.24 Hz), 4.16-4.04 (diffused m, 1H), 3.76-3.66 (t-like, 1H), 2.48 (s, 3H), 2.40-2.26 (m, 1H), 1.81 (s, 3H), 1.94-1.81 (m, 1H), 1.10 (d, 3H, *J*=6.59 Hz), 0.86 (d, 3H, *J*=6.59 Hz); [the diastereomer **B**] δ 7.87 (d, 2H, *J*=8.24 H), 7.38 (d, 2H, *J*=8.24 Hz), 4.09 (d, 1H, *J*=6.59 Hz), 4.04-3.92 (broad-m, 1H, CH_2OH), 3.86-3.76 (broad, 1H), 2.48 (s, 3H), 2.40-2.26 (m, 1H), 1.95 (s, 3H), 1.94-1.81 (m, 1H), 0.99 (d, 3H, *J*=6.59 Hz), 0.91 (d, 3H, *J*=6.93 Hz); [the diastereomer **C**] δ 2.17 (s, 3H, SCH_3); [the diastereomer **D**] δ 1.94 (s, 3H, SCH_3). Anal. Calcd for $C_{15}H_{24}O_4S_2$: C, 54.19; H, 7.28. Found: C, 54.24; H, 7.32.

3c (R=H): colorless crystals; IR (KBr) 3450, 2950, 1300, 1135, 1080, 1050 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the *syn* isomer] δ 7.80 (d, 2H, *J*=8.24 Hz), 7.37 (d, 2H, *J*=7.91 Hz), 4.16-4.00 (broad d, 1H), 3.90-3.80 (diffused m, 1H), 3.50 (dd, 1H, *J*=6.92 and 14.5 Hz), 3.50-3.30 (diffused m, 1H), 3.33 (dd, 1H, *J*=5.93 and 14.5 Hz), 2.86-2.70 (br, 2H, O*H*), 2.46 (s, 3H), 2.44-2.36 (m, 1H), 1.90-1.75 (m , 1H), 0.99 (d, 3H, *J*=6.59 Hz), 0.97 (d, 3H, *J*=6.59 Hz); [the *anti* isomer] δ 0.78 (d, 3H, *J*=6.59 Hz). An analytical sample was obtained by recrystallization from hexane-ethyl acetate: colorless crystals; mp 74.0-75.0 °C. Anal. Calcd for $C_{14}H_{22}O_4S$: C, 58.71; H, 7.74. Found: C, 58.82; H, 7.78.

2d (R=Me): colorless crystals; a diastereomeric mixture (**A**:**B**:**C**:**D**=69:16:10:4); IR (KBr) 3500, 1723, 1365, 1280, 1140, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the diastereomer **A**] δ 7.88 (d, 2H, *J*=8.24 Hz), 7.37 (d, 2H, *J*=8.56 Hz), 5.08 (dq, 1H, *J*=2.64 and 6.60 Hz), 4.14 (d, 1H, *J*=1.31 Hz), 2.61 (dd, 1H, *J*=1.32 and 2.50 Hz), 2.32 (broad, 1H, O*H*), 2.47 (s, 3H), 2.04 (s, 3H), 1.84 (s, 3H), 1.39 (s, 3H), 1.38 (s, 3H), 1.37 (d, 3H, *J*=6.59 Hz); [the diastereomer **B**] δ 7.89 (d, 2H, *J*=8.57 Hz), 7.38 (d, 2H, *J*=8.57 Hz), 5.01 (quintet-like, 1H, *J*=6.60 Hz), 3.89 (d, 1H, *J*=0.99 Hz), 3.55 (broad, 1H, O*H*), 2.50-2.44 (m, 1H), 1.91 (s, 3H), 1.85 (s, 3H), 1.37 (s, 3H), 1.36 (d, 3H, *J*=6.26 Hz), 1.24 (s, 3H); [the diastereomer **C**] δ 7.88 (d, 2H, *J*=8.24 Hz), 7.37 (d, 2H, *J*=8.56 Hz), 5.19 (dq, 1H, *J*=3.30 and 6.59 Hz), 4.49 (d, 1H, *J*=1.98 Hz), 2.80 (diffused dd, 1H), 2.77-2.79 (broad, 1H, O*H*), 1.88 (s, 3H), 1.86 (s, 3H), 1.43 (s, 3H), 1.40 (d, 3H, *J*=6.59 Hz), 1.24 (s, 3H); [the diastereomer **D**] δ 2.00 (s, 3H, OCOCH_3), 1.68 (s, 3H, SCH_3). Recrystallization from hexane-CH_2Cl_2 gave colorless crystals for an analytical sample: mp 114.5-115.5 °C. Anal. Calcd for $C_{17}H_{26}O_5S_2$: C, 54.52; H, 7.00. Found: C, 54.74; H, 6.73.

3d (R=Me): a colorless viscous oil; a mixture of two diastereomers (*syn*:*anti*=85:15); IR (neat) 3500, 1725, 1370, 1280, 1140, 1085 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the *syn* isomer] δ 7.74 (d, 2H, *J*=8.24 Hz), 7.30 (d, 2H, *J*=7.91 Hz), 5.09 (dq, 1H, *J*=4.26 and 6.40 Hz), 3.38 (dd, 1H, *J*=4.95 and 14.6 Hz), 3.10 (dd, 1H, *J*=4.28 and 14.8 Hz), 2.49-2.44 (quintet-like, 1H, *J*=4.29 Hz), 2.39 (s, 3H), 2.18-2.16 (br, 1H, O*H*), 1.92 (s, 3H), 1.25 (s, 3H), 1.15 (s, 3H); [the *anti* isomer] δ 7.78 (d, 2H, *J*=8.24 Hz), 7.31 (d, 2H, *J*=7.91 Hz), 5.15 (dq, 1H, *J*=1.28 and 6.59 Hz), 2.40 (s, 3H), 3.40 (dd, 1H, *J*=4.95 and 14.8 Hz), 3.26 (dd, 1H, *J*=3.62 and 14.9 Hz), 2.18-2.16 (broad, 1H, O*H*), 2.17 (diffused m, 1H), 1.89 (s, 3H), 1.27 (s, 3H), 1.17 (d, 3H, *J*=6.59 Hz), 0.97 (s, 3H). Anal. Calcd for $C_{16}H_{24}O_5S$•0.06CH_2Cl_2: C, 57.84; H, 7.29. Found: C, 57.82; H, 7.29.

2e (R=Me): a mixture of four diastereomers (**A**:**B**:**C**:**D**=63:24:10:3); colorless crystals; IR (KBr) 3500, 1735, 1450, 1282, 1120, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the diastereomer **A**] δ 7.89 (d, 2H, *J*=8.57 Hz), 7.37 (d, 2H, *J*=7.91 Hz), 5.13-5.06 (m, 1H), 4.11 (d, 1H, *J*=1.32 Hz), 2.47 (s, 3H), 2.72 (diffused d, 1H), 2.30-2.10 (broad, 1H, O*H*), 2.07 (s, 3H), 1.76 (s, 3H), 1.90-1.70 (m, 2H), 1.39 (s, 3H), 1.37 (s, 3H), 0.90 (t,

3H, *J*=7.58 Hz,); [the diastereomer **B**] δ 7.86 (d, 2H, *J*= 8.57 Hz), 7.39 (d, 2H, *J*=7.91 Hz), 4.98-4.91 (m, 1H), 3.89 (d, 1H, *J*=2.00 Hz), 2.86 (diffused d, 1H), 2.47 (s, 3H), 2.30-2.10 (broad, 1H, O*H*), 1.92 (s, 3H), 1.83 (s, 3H), 1.38 (s, 6H), 1.90-1.70 (m, 2H), 0.89 (t, 3H, *J*=7.58 Hz); [the diastereomer **C**] δ 4.43 (diffused d, 1H), 1.95 (s, 3H, OCOCH_3), 1.38 (s, 3H, $(CH_3)_2$COH), 1.26 (s, 3H, $(CH_3)_2$COH); [the diastereomer **D**] δ 2.01 (s, 3H, OCOCH_3), 1.64 (s, 3H, SCH_3). An analytical sample was obtained by recrystallization from benzene-hexane (mp 147.5-147.7 °C). Anal. Calcd for $C_{18}H_{28}O_5S_2$: C, 55.64; H, 7.26. Found: C, 55.54; H, 7.22.

3e (R=Me): a colorless oil; a diastereomeric mixture (*syn*:*anti*=87:13); IR (neat) 3500, 1720, 1370, 1280, 1140, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the *syn* isomer] δ 7.80 (d, 2H, *J*=8.24 Hz), 7.37 (d, 2H, *J*=7.91 Hz), 5.10 (dt-like, 1H, *J*=3.63 and 7.25 Hz), 3.40 (dd, 1H, *J*=4.61 and 14.8 Hz), 3.21 (dd, 1H, *J*=4.62 and 14.8 Hz), 2.53 (q-like, 1H, *J*=3.95 Hz), 2.45 (s, 3H), 2.19 (br, 1H, O*H*), 2.03 (s, 3H), 1.79-1.44 (m, 2H), 1.31 (s, 3H), 1.24 (s, 3H), 0.89 (t, 3H, *J*=7.58 Hz) ; [the *anti* isomer] δ 7.84 (d, 2H, *J*=8.57 Hz), 7.38 (d, 2H, *J*=7.91 Hz), 5.02 (t-like, 1H, *J*=7.58 Hz), 3.43 (dd, 1H, *J*=4.90 and 14.8 Hz), 3.32 (dd, 1H, *J*=4.90 and 14.8 Hz), 2.47 (s, 3H), 2.38 (t-like, 1H, *J*=3.80 Hz), 2.19 (br, 1H, O*H*), 1.98 (s, 3H), 1.60-1.48 (m, 2H), 1.35 (s, 3H), 1.02 (s, 3H), 0.90 (t, 3H, *J*=7.33 Hz). The diastereomeric mixture of **3e** was deacetylated with K_2CO_3 in MeOH (0 °C, 2 h) to afford **3b** (R=Me). Its spectral data were in accordance with those of the product obtained by the reaction of **1b**.

2f (R=Me): a mixture of four diastereomers (**A**:**B**:**C**:**D**=45:44:7:4); colorless crystals (recrystallized from hexane-$CHCl_3$): mp 166.6-169.3 °C (decomp.); IR (KBr) 3480, 2970, 1734, 1282, 1230, 1121 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the diastereomer **A**] δ 7.89 (d, 2H, *J*=8.24 Hz), 7.36 (d, 2H, *J*=7.91 Hz), 5.18 (dd, 1H, *J*=4.29 and 6.92 Hz), 4.21 (d, 1H, *J*=2.31 Hz), 2.95 (dd, 1H, *J*=1.31 and 4.29 Hz), 2.46 (s, 3H), 2.09 (s, 3H), 1.57 (s, 3H), 1.41 (s, 3H), 1.32 (s, 3H), 1.27 (s, 3H,), 1.05 (d, 3H, *J*=6.59 Hz), 0.91 (d, 3H, *J*=6.60 Hz); [the diastereomer **B**] δ 7.87 (d, 2H, *J*=8.24 Hz), 7.38 (d, 2H, *J*=7.91 Hz), 4.96 (t-like, 1H, *J*=5.60 Hz), 3.99 (d, 1H, *J*=1.65 Hz), 2.99 (dd, 1H, *J*=1.31 and 5.28 Hz), 2.46 (s, 3H), 2.10 (s, 3H), 1.74 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H), 0.90 (d, 3H, *J*=6.59 Hz), 0.89 (d, 3H, *J*=6.59 Hz); [the diastereomer **C**] δ 5.03-4.99 (m, 1H), 4.40 (d, 1H, *J*=1.00 Hz,), 3.07 (diffused dd, 1H), 2.07 (s, 3H), 1.58 (s, 3H), 1.42 (s, 3H), 1.27 (s, 3H), 1.01 (d, 3H, *J*=6.59 Hz); [the diastereomer **D**] δ 2.03 (s, 3H), 1.62 (s, 3H). The diastereomeric mixture of **2f** was converted to **2c** (R=Me) by deacetylation.

3f (R=Me): a colorless oil; a diastereomeric mixture (*syn* :*anti*=89:11); IR (neat) 3520, 1730, 1370, 1285, 1140, 1085 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): [the *syn* isomer] δ 7.81 (d, 2H), 7.36 (d, 2H, *J*=7.91 Hz), 5.00 (dd, 1H, *J*=4.29 and 7.25 Hz), 3.40 (dd, 1H, *J*=2.96 and 14.5 Hz), 3.13 (dd, 1H, *J*=5.93 and 14.5 Hz), 2.64-2.59 (ddd, 1H, *J*=3.26, 5.93 and 7.86 Hz), 2.45 (s, 3H), 2.22-2.14 (m, 1H), 2.14 (broad, 1H, O*H*), 2.08 (s, 3H), 1.31 (s, 3H), 1.22, (s, 3H), 0.98 (d, 3H, *J*=6.59 Hz), 0.88 (d, 3H, *J*=6.59 Hz); [the *anti* isomer] δ 7.84 (d, 2H, *J*=8.57 Hz), 7.38 (d, 2H, *J*= 7.91 Hz), 4.83 (d-like, 1H, *J*=9.90 Hz), 2.47 (s, 3H), 1.97-1.83 (m, 1H), 1.99 (s, 3H), 1.36 (s, 3H), 1.02 (s, 3H), 1.01 (d, 3H, *J*=6.59 Hz), 0.85 (d, 3H, *J*=6.60 Hz). Anal. Calcd for $C_{18}H_{28}O_5S$: C, 60.65; H, 7.92. Found: C, 60.82; H, 7.97.

Photochemical Isomerization of (*Z*)-1a to (*E*)-1a in Benzene. A Typical Procedure. A solution of (*Z*)-**1a** (273 mg, 1.00 mmol) and benzophenone (182 mg, 1.00 mmol) in benzene (70 mL) was irradiated with a 100-W high-pressure Hg lamp at room temperature under bubbling N_2 for 2 h. Purification by column chromatography on silica gel (hexane/ethyl acetate, 6:1 to 2:1) afforded a mixture of (*E*)- **1a** and (*Z*)-**1a** (248 mg, 91% yield) in a ratio of 89:11. HPLC analysis showed that the *Z*-*E* isomerization reached to a photostationary state (*E*:*Z* = 89:11) after irradiation for 20 min.

2,2,4,4,6-Pentamethyl-5-[(*p*-tolylsulfonyl)methyl]-1,3-dioxane (4a). A Typical Procedure. A solution of **3a** (*syn*:*anti*= 95:5; 32.7 mg, 0.11 mmol) in acetone (1.0 mL) and 2,2-dimethoxypropane (1.0 mL) was stirred together with 10-camphorsulfonic acid (3.0 mg) for 17.5 h at room temperature. After the addition of powdered sodium carbonate (3.0 mg) followed by filtration, the filtrate was evaporated and chromatographed on basic aluminum oxide (hexane/ethyl acetate, 4:1) to give colorless solid (41 mg). Further purification by preparative HPLC (GPC) gave one diastereomer of **4a** (32.3 mg, 87% yield): colorless crystals;

mp 108-110 °C (hexane-CH_2Cl_2); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.81 (d, 2H, *J*=8.24 Hz), 7.38 (d, 2H, *J*=7.91 Hz), 3.84 (dq, 1H, *J*=9.60 and 6.28 Hz), 2.99 (dd, 1H, *J*=3.60 and 15.0 Hz), 2.89 (dd, 1H, *J*=5.60 and 15.0 Hz), 2.46 (s, 3H), 2.03 (ddd, 1H, *J*=5.4, 5.6, and 9.5 Hz), 1.39 (s, 3H), 1.37 (s, 3H), 1.23 (d, 3H, *J*=5.9 Hz), 1.19 (s, 3H), 1.15 (s, 3H); the following NOEs were observed: C5-*H* to 6-CH_3 (4.4%), C5-*H* to 4-CH_3 (equatorial) (3.2%), C_6-*H* to 2-CH_3 (axial) (8.1%), C_6-*H* to 4-CH_3 (axial) (3.2%), and C_6-*H* to 6-CH_3 (7.0%), C_6-*H* to CH_2SO_2Tol (4.8%); IR (KBr) 2980, 1590, 1300, 1280, 1250, 1140, 1080 cm^{-1}. Anal. Calcd for $C_{17}H_{26}O_4S$: C, 62.55; H, 8.03. Found: C, 62.50; H, 8.03.

4c: colorless crystals; mp 106-111 °C; IR (KBr) 2920, 1378, 1310, 1190, 1144, 1085, 1035 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.79 (d, 2H, *J* =8.24 Hz), 7.37 (d, 2H, *J*=8.24 Hz), 3.46 (dd, 1H, *J*=2.20 and 9.20 Hz), 3.15 (dd, 1H, *J*=4.82 and 15.0 Hz), 2.86 (dd, 1H, *J*=5.10 and 15.0 Hz), 2.46 (s, 3H), 2.24 (dt-like, 1H, *J*=4.82 and 9.20 Hz), 1.91 (d and septet, 1H, *J*=1.98 and 6.92 Hz), 1.37 (s, 3H), 1.311 (s, 2×3H), 1.305 (s, 3H), 0.99 (d, 3H, *J* =6.58 Hz), 0.90 (d, 3H, *J*=6.92 Hz); the following NOEs were observed: C5*H* to $(CH_3)_2CH$ (5.4%), C5*H* to $(CH_3)C$ (4.0%), C5*H* to 5-CH_2 (3.1%), C_6-*H* to $(CH_3)_2CH$ (4.7%), C_6-*H* to 2-CH_3(axial) (5.0%), C_6-*H* to 4-CH_3 (3.2%), C_6-*H* to 6-$(CH_3)_2CH$ (6.0%), C_6-*H* to CH_2SO_2Tol (6.5%). Anal. Calcd for $C_{17}H_{26}O_4S$: C, 64.37; H, 8.53. Found: C, 64.30; H, 8.55.

X-ray Crystallography. The single crystals of *syn*-**3b** (R=Me) and (*E*)-**1** were obtained by recrystallization from hexane-ethyl acetate. Data were collected on a Mac Science MXC18 diffractometer. All computations used "Crystan GM (ver 6.2.1) , Computer Program for the Solution and Refinement of Crystal Structure from X-ray Diffraction Data (1994)", Mac Science Co. Ltd.[25]

Table 3. Crystallographic Data for *syn*-**3b** and (*E*)-**1a**.

Compounds	*syn*-**3b**	(*E*)-**1a**		*syn*-**3b**	(*E*)-**1a**
Chemical Formula	$C_{15}H_{24}O_4S$	$C_{12}H_{16}O_3S_2$	Formula Weight	300.40	272.40
a / Å	0.627 (2)	28.062 (8)	α / °	90.000 (0)	90.000 (0)
b / Å	33.298 (8)	12.188 (3)	β / °	90.000 (0)	93.100 (3)
c / Å	9.360 (3)	8.078 (3)	γ / °	90.000 (0)	90.000 (0)
V / Å^3	3312 (1)	759 (1)	Crystal System	Orthorhombic	Monoclinic
Space Group	*P* b c a (# 61)	*P* 21/a (# 14)	*Z*	8	8
D_{calc} / g cm^{-3}	1.20	1.31	Radiation	Cu *Ka*	Mo *Ka*
Residuals. *R*	0.0887	0.0466	Residuals. R_w	0.0802	0.0406

Lipase PS-Mediated Transesterification of (*E*)-1a (R=Me). A Typical Procedure. To a solution of racemic (*E*)-**1a** (180 mg, 0.66 mmol) in benzene (1.8 mL) were added lipase PS from *pseudomonas cepacia* (Amano PS, 302 mg), vinyl acetate (0.30 mL, 3.27 mmol), and powdered molecular sieves 4A (180 mg). The resulting mixture was then stirred at room temperature for 12 h. After insoluble solids were filtered off, the filtrate was evaporated and the residue was separated by preparative TLC (SiO_2; hexane/ethyl acetate, 2:1) to afford (*R*)-(*E*)-**1d** (92 mg, 44% yield) and the recovered (*S*)-(*E*)-**1a** (83.6 mg, 47% yield). Their enantiomeric excess were determined by HPLC analysis with CHIRALCEL OD (Daicel Co., Ltd.).

(*S*)-(*E*)-**1a**: 99% ee; $[\alpha]_D^{21}$ +2.63 (*c* 1.00, $CHCl_3$). (*R*)-(*E*)-**1d**: >99% ee; $[\alpha]_D^{21}$ +22.7 (*c* 1.00, $CHCl_3$). (*R*)-(*Z*)-**1d**: 95% ee; $[\alpha]_D^{21}$ +184.6 (*c* 1.00, $CHCl_3$). (*R*)-(*E*)-**1e**: 87% ee; $[\alpha]_D^{21}$ +35.3 (*c* 1.01, $CHCl_3$). (*S*)-(*E*)-**1b**: 98.9% ee; $[\alpha]_D^{21}$ +9.06 (*c* 1.02, $CHCl_3$). (*R*)-(*E*)-**1f**: 96% ee; $[\alpha]_D^{21}$ +49.7 (*c* 0.50, acetone). (*R*)-(*Z*)-**1e**: 87.6% ee [by HPLC (Daicel CHIRALPACK AS)] $[\alpha]_D^{21}$ +163.7 (*c* 1.01, $CHCl_3$) .

(2*S*)-4-(*p*-Tolylsulfonyl)-2-butanol [(*S*)-7]. To a solution of methyl *p*-tolyl sulfone (340 mg, 2.00 mmol) in THF (10 mL), was dropwise added a 1.62 M hexane solution (2.90 mL) of n-BuLi (4.00 mmol) over

10 min at -78 °C under N_2 atmosphere. After the mixture was stirred at the same temperature for 1 h, (*S*)-(-)-propylene oxide (0.14 mL, 2.00 mmol) was dropwise added. The resulting mixture was stirred at -78 °C for 30 min, and the reaction temperature was gradually raised up to room temperature over 1 h and further stirred for 30 min. After aqueous NH_4Cl (1.0 mL) was added, the mixture was extracted with diisopropyl ether (20 mL × 3). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Column chromatography on SiO_2 (hexane/ethyl acetate, 2:1) afforded the desired (*S*)-**7** (92.7 mg, 20% yield) and methyl *p*-tolyl sulfone (256 mg, 75% yield). The enantiomeric excess of (*S*)-**7** was determined by analytical HPLC (Daicel CHIRALCEL OD) to be >99%. Its spectral data accorded with those reported in the literature.[19]

Conversion of (*S*)-(*E*)-1a to (*S*)-7. To a solution of (*S*)-(*E*)-**1a** (89 mg, 0.33 mmol) in 2-propanol (5.0 mL) was added $NaBH_4$ (27 mg, 0.72 mmol)[25] at 0 °C and then the mixture was stirred at the same temperature for 2.5 h. After the addition of water (20 mL), extraction with CH_2Cl_2 and evaporation afforded crude 4-(methylthio)-4-(*p*-tolylsulfonyl)-2-pentanol (**6**) (101 mg) as a colorless oil. This oil (101 mg) was dissolved in ethanol (4.0 mL), and Raney-Ni (W2) (1.0 cm^3) was added. After the suspension was stirred at room temperature for 18.5 h, insoluble solids were filtered off, and the filtrate was evaporated. Column chromatography on silica gel (hexane/ethyl acetate, 1:1) gave (*S*)-**7** (48.6 mg, 65% yield, >99% ee) as a colorless oil. In a similar manner, (*R*)-(*Z*)-**2a** was converted to (*R*)-**7**.

Preparation of (3*S*,4*S*)-2,3-dimethyl-2,4-pentanediol (11). To a solution of (3*S*,4*S*)-**9a** (160 mg, 0.56 mmol; 90% ee), which was prepared from (*S*)-(*E*)-**1a**, in acetone (2 mL) were added 2,2-dimethoxypropane (2 mL) and a catalytic amount of *p*-toluenesulfonic acid and the resulting mixture was stirred at room temperature for 17 h. After evaporation in the presence of powdered $NaHCO_3$, the residue (280 mg) was purified by column chromatography on silica gel [hexane/ethyl acetate 4:1 to 2:1] to give **10a** (168 mg, 92% yield) as a colorless solid: $[\alpha]_D^{23}$ -16.4 (*c* 1.01, $CHCl_3$).

To a stirring solution of **10a** (148 mg, 0.45 mmol) in THF (2.3 mL) and absolute ethanol (0.39 mL) containing Na_2HPO_4 (377 mg), sodium (101 mg) was added at -20 °C under N_2 atmosphere. After further stirring at -20 °C for 1.5 h, the reaction temperature was raised to room temperature and then the mixture was further stirred for 30 min. The reaction was quenched with methanol and acidified with *p*-toluenesulfonic acid. After insoluble solids were filtered off, the filtrate was evaporated and the residue was purified by column chromatography on silica gel (CH_2Cl_2/ether, 3:2) to give **11** (59 mg, 99% yield) as a colorless oil: IR (neat) 3330, 2980, 1460,1380,1183, 945 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 4.20-3.80 (broad, 2H, O*H*), 3.85 (dq, 1H, *J*=2.96 and 5.93 Hz), 1.54 (dq, 1H, *J*=2.30 and 6.93 Hz), 1.25 (s, 3H), 1.23 (d, 3H, *J*=6.26 Hz), 1.21 (s, 3H), 0.78 (d, 3H, *J*=6.92 Hz); $[\alpha]_D^{23}$ -4.39 (*c* 1.00, $CHCl_3$); exact mass (FAB) calcd for $C_7H_{16}O_2$ 133.1229 $[M+1]^+$, found 133.1226. Anal. Calcd for $C_7H_{16}O_2$: C, 63.60; H, 12.20. Found: C, 63.26; H, 12.35. The enantiomeric excess (88% ee) was determined by HPLC (Daicel CHIRALPAK AS) analysis of its monobenzoyl derivative.

(2*S*,3*R*)-2-Methyl-1,3-pentanediol (12). Irradiation of a solution of (*R*)-(*E*)-**1b** (510 mg, 1.78 mmol; 93.3% ee) and benzophenone (490 mg) in methanol (70 mL) for 3.5 h gave a diastereomeric mixture of **13** (458 mg, 81% yield) after column chromatography on silica gel (hexane/ethyl acetate, 4:1 to 1:1). When the above diastereomeric mixture (458 mg) was treated with Raney-Ni (W2) (1.5 cm^3) in ethanol (2.0 mL) at room temperature for 30 min, a diastereomeric mixture (*syn*:*anti*=94:6) of (2*S*,3*R*)-2-[(*p*-tolylsulfonyl)methyl]-1,3-pentanediol (**14**) (350 mg, 1.29 mmol; 90% yield) was obtained after filtration and column chromatography on silica gel (ethyl acetate). Its spectral data agreed with those of its racemate.

To a solution of the diastereomeric mixture (350 mg) of **14** in acetone (2.0 mL) and 2,2-dimethoxypropane (2.0 mL) was added a catalytic amount of *p*-toluenesulfonic acid and the resulting mixture was stirred for 24 h at room temperature. After powdered $NaHCO_3$ was added, the solvent was evaporated. The residue was chromatographed on basic alumina (hexane/ethyl acetate, 6:1) to give a single isomer of **15** (346 mg, 75% yield) as a colorless solid: IR (KBr) 2990, 2930, 1295, 1200, 1135, 1060 cm^{-1}; ^1H NMR (270

MHz, $CDCl_3$) δ 7.79 (d, 2H, *J*=7.56 Hz), 7.37 (d, 2H, *J*=7.91 Hz), 4.03 (dd, 1H, *J*=5.28 and 11.9 Hz), 3.66 (dd, 1H, *J*=8.90 and 11.9 Hz), 3.42 (ddd, 1H, *J*=2.30, 8.24, and 10.5 Hz), 3.00 (dd, 1H, *J*=2.97 and 14.5 Hz), 2.89 (dd, 1H, *J*=8.90 and 14.5 Hz), 2.46 (s, 3H), 2.07 (ddq, 1H, *J*=2.97, 5.28, and 8.90 Hz), 1.55-1.46 (m, 1H), 1.38 (s, 3H), 1.35 (s, 3H), 1.32-1.22 (m, 1H), 0.82 (t, 3H, *J*=7.25 Hz). Recrystallization from hexane-ether gave an analytical sample: mp 99.5-100 °C; $[\alpha]_D^{22}$ +59.8 (*c* 1.00, $CHCl_3$). Anal. Calcd for $C_{16}H_{24}O_4S$: C, 61.51; H, 7.74. Found: C, 61.44; H, 7.60.

To a stirring solution of **15** (311 mg, 1.00 mmol), dry ethanol (0.45 mL), and Na_2HPO_4 (710 mg, 5.00 mmol) in dry THF (5.0 mL) was added sodium (230 mg) at -20 °C and the resulting mixture was stirred at 0 °C for 3 h. After the addition of methanol, the reaction was acidified with *p*-toluenesulfonic acid. The suspension was stirred at room temperature for 10 min and then, insoluble solids were filtered off. The filtrate was evaporated and chromatographed on basic alumina (CH_2Cl_2/ether 0:1 to 2:3) to give **12** (95.4 mg, 81% yield), the enantiomeric excess of which was determined by HPLC analysis (Daicel CHIRALCEL OJ) of its monobenzoate to be 90%. **12**: a colorless oil; IR (neat) 3350, 2930, 1650, 1460, 1030, 970 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 3.76 (dd, 1H, *J*=3.95 and 10.9 Hz), 3.56 (dd, 1H, *J*=7.25 and 10.9 Hz), 3.50 (dt, 1H, *J*=3.63 and 7.58 Hz), 2.80-3.20 (broad, 2H, O*H*), 1.73 (ddq, 1H, *J*=3.63, 10.9, and 6.92 Hz), 1.62 (ddq, 1H, *J*=3.63, 10.9, and 6.92 Hz), 1.58-1.39 (m, 1H), 0.97 (t, 3H, *J*=7.25 Hz), 0.88 (d, 3H, *J*=6.92 Hz); $[\alpha]_D^{21}$ +17.7 (*c* 0.99, $CHCl_3$); EI-MS (relative intensity) *m/z* 119(3) [M+1], 101[M+1-H_2O] (6), 89[M+1-2H_2O] (6), 59[$(C_3H_7O)^+$] (100). Its spectral data agreed with those in the literature.[23]

Preparation of 4-Ethyl-5-formyl-2,2-dimethyl-1,3-dioxane (17). Irradiation of (*R*)-(*E*)-**1b** (596 mg, 2.08 mmol) and benzophenone (2.5 mol equiv) in methanol (70 mL) gave a diastereomeric mixture (62:32:3:3) of **13** (647 mg, 97% yield) which, without further purification, was used in the next reaction. A solution containing the crude **13** (647 mg, 0.71 mmol), acetone (5.0 mL), and 2,2-dimethoxypropane (5.0 mL), and *p*-toluenesulfonic acid (11 mg) was stirred at room temperature for 24 h. The usual workup and chromatography on silica gel (hexane-ethyl acetate 6:1 to 4:1) afforded a diastereomeric mixture (mainly two isomers, 65:35) of **16** (567 mg, 77% yield) as colorless crystals: IR(KBr) 2980, 2860, 1310, 1200, 1138, 1010 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of the major isomer: δ 7.85 (d, 2H, *J*=8.24 Hz), 7.37 (d, 2H, *J*=7.91 Hz), 4.11 (dt, 1H, *J*=2.31 and 8.90 Hz), 3.83 (dd, 1H, *J*=4.61 and 11.9 Hz), 3.74 (dd, 1H, *J*=1.65 and 11.9 Hz), 3.63 (d, 1H, *J*=3.63 Hz), 2.47 (s, 3H), 2.40-2.20 (m, 1H), 2.17 (s, 3H), 1.72-1.62 (m, 1H), 1.46 (s, 3H), 1.37 (s, 3H), 1.39-1.23 (m, 1H), 0.92 (t, 3H, *J*=7.25 Hz); ^1H NMR of the minor isomer: δ 7.85 (d, 2H, *J*=8.24 Hz), 7.38 (d, 2H, *J*=7.91 Hz), 4.11 (dd, 1H, *J*=9.56 and 11.5 Hz), 3.94 (dt, 1H, *J*=2.67 and 7.75 Hz), 3.88 (dd, 1H, *J*=5.60 and 11.9 Hz), 3.23 (d, 1H, *J*=5.17 Hz), 2.21 (s, 3H), 1.41 (s, 3H), 1.32 (s, 3H), 0.83 (t, 3H, *J*=7.42 Hz). The C*H*$_2$CH$_3$ and OCH$_2$C*H* protons of the minor isomer could not be assigned because their signals overlapped with those of the major isomer. Recrystallization from hexane-CH_2Cl_2 gave the major isomer as colorless crystals: mp 94-96 °C. Anal. Calcd for $C_{17}H_{26}O_4S_2$: C, 56.95; H, 7.31. Found: C, 56.92; H, 7.25.

A solution of **16** (500 mg, 1.40 mmol) in diethyl ether (76 mL)-water (4 mL) containing $NaHCO_3$ (352 mg) was irradiated by a 20-W low-pressure Hg lamp (Vycor) under bubbling N_2 at room temperature for 4 h. The reaction mixture was washed with brine, dried over anhydrous $MgSO_4$, and evaporated. Chromatography on silica gel (hexane/ethyl acetate 8:1) gave **17** (107 mg, 44% yield) as a colorless oil: IR (neat) 2950, 1723, 1380, 1200, 1170, 1110 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) d 9.76 (d, 1H, *J*=1.97 Hz), 3.93-4.01 (m, 3H), 2.69 (ddt, 1H, *J*=1.96, 6.27, and 10.3 Hz), 1.50-1.76 (m, 2H), 1.44 (s, 3H), 1.40 (s, 3H), 0.96 (t, 3H); $[\alpha]_D^{21}$ +33.1 (*c* 0.95, $CHCl_3$); exact mass (FAB) *m/z* calcd for $C_9H_{17}O_3$ 173.1178 $[M+1]^+$, found 173.1181.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research (No.07405041) from the Ministry of Education, Science and Culture of Japan and "Research for the Future" Program (JSPS-RFTF

96P00304) from The Japan Society for the Promotion of Science.

REFERENCES AND NOTES

1. Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds;* Pergamon Press: Oxford, 1986.
2. For reviews, see: (a) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (b) Curran, D. P. *Synthesis* **1988**, 417 and 489. (c) Hart, D. J. *Science* **1984**, *223*, 883. (d) Jasperse, C. D.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237.
3. For reviews, see: (a) Beckwith, A. L. *Tetrahedron* **1981**, *37*, 3073. (b) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969. (c) RajanBabu, R. V. *Acc. Chem. Res.* **1991**, *24*, 139. (d) Porter, N. A.; Giese, B.; Curran, D. P. *Acc. Chem. Res.* **1991**, *24*, 296. (e) Smadja, W. *Synlett* **1994**, 1.
4. a) Giese, B.; Witzel, T. *Tetrahedron Lett.* **1987**, *23*, 2571. b) Yamamoto, Y.; Nishii, S.; Ibuka, T. *J. Am. Chem. Soc.* **1988**, *110*, 617. c) Smadja, W.; Zahouily, M.; Journet, M.; Malacria, M. *Tetrahedron Lett.* **1991**, *32*, 3683. d) Smadja, W.; Zahouily, M.; Malacria, M. *Tetrahedron Lett.* **1992**, *33*, 5511. e) Morikawa, T.; Washio, Y.; Shiro, M.; Taguchi, T. *Chem. Lett.* **1993**, 249.
5. Kahy, S. D.; Pau, C. F.; Chamberlin, A. R.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*. 650.
6. A part of this work was preliminarily reported: Ogura, K.; Kayano, A.; Sumitani, N.; Akazome, M.; Fujita, M. *J. Org. Chem.* **1995**, *60*, 1106.
7. Ogura, K.; Yanagisawa, A.; Fujino, T.; Takahashi, K. *Tetrahedron Lett.* **1988**, *29*, 5387.
8. Ogura, K.; Sumitani, N.; Kayano, A.; Iguchi, H.; Fujita, M. *Chem. Lett.* **1992**, 1487.
9. The starting compounds (**1**) were synthesized according to the following typical procedure: Bromination of 1-(methylthio)-1-(*p*-tolylsulfonyl)-1-butene[10] with NBS (1.0 mol equiv) and benzoyl peroxide (0.1 mol equiv) in CCl_4 gave (*E*)-3-bromo-1-(methylthio)-1-(*p*-tolylsulfonyl)-1-butene in 88% yield. Subsequent hydrolysis in the presence of Ag_2O (1.2 equiv) in acetone-H_2O (2:3) at room temperature afforded **1a** as a mixture of (*E*)- and (*Z*)-geometric isomers in good yield. Treatment of the bromide with Ag_2O in acetic acid afforded the acetate (**1d**). Irradiation of the mixture in the presence of benzophenone produced mainly (*E*)-**1a** (see Experimental Section). (*E*)-**1a**: colorless crystals; mp 59.5-60.0 °C (CCl_4); IR (KBr) 3450, 1598, 1440, 1289, 1145, 1082 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.81 (d, 2H, *J*=8.24 Hz), 7.42 (d, 1H, *J*=7.58 Hz), 7.33 (d, 2H, *J*=7.91 Hz), 4.92 (dq, 1H, *J*=7.58 and 6.59 Hz), 2.44 (s, 3H), 2.34 (s, 3H), 2.25 (broad, 1H), 1.33 (d, 3H, *J*=6.59 Hz): the observed NOE ($CDCl_3$): C3-*H* to C2-*H*, 2.5%; C3-*H* to O*H*, 2.8%; C3-*H* to 4-C*H*$_3$, 6.1%. Anal. Calcd for $C_{12}H_{16}O_3S_2$: C, 52.91; H, 5.92. Found: C, 52.61; H, 5.87. (*Z*)-**1a**: colorless crystals; mp 86.0-86.5 °C (hexane-CH_2Cl_2); IR (KBr) 3320, 1598, 1305, 1280, 1150, 855 cm^{-1}; λ_{max} ($CHCl_3$) 244 nm (ε_{max} 13040) and 268 (a shoulder, 3670); ^1H NMR (270 MHz, $CDCl_3$) δ 7.86 (d, 2H, *J*=8.24 Hz), 7.36 (d, 2H, *J*=7.91 Hz), 6.16 (d, 1H, *J*=8.24 Hz), 5.36 (dq, 1H, *J*=8.24 and 6.27 Hz), 2.45 (s, 3H), 2.45-2.30 (broad 1H, O*H*), 2.30 (s, 3H), 1.34 (d, 3H, *J*=6.26 Hz); the observed NOE ($CDCl_3$): C3-*H* to Ar-ortho-*H*, 3.7%; C3-*H* to 4-C*H*$_3$, 6.3%; C2-*H* to 4-C*H*$_3$, 2.9%. Anal. Calcd for $C_{12}H_{16}O_3S_2$: C, 52.91; H, 5.92. Found: C, 52.66; H, 5.71. **1b**: an *E*-*Z* mixture (36:64): colorless crystals: IR (KBr) 3499, 2925, 1316, 1290, 1142, 1081 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of (*E*)-**1b**: δ 7.80 (d, 2H, *J*=8.24 Hz), 7.39 (d, 1H, *J*=7.91 Hz), 7.33 (d, 2H, *J*=7.91 Hz), 4.68 (quintet-like, 1H, *J*=6.60 Hz), 2.44 (s, 3H), 2.35 (s, 3H), 2.21 (broad, 1H, O*H*), 1.77-1.56 (m, 1Hr), 0.95 (t, 3H, *J*=7.25 Hz); ^1H NMR (270 MHz, $CDCl_3$) of (*Z*)-**1b**: δ 7.86 (d, 2H, *J*=8.24 Hz), 7.35 (d, 2H, *J*=7.91 Hz), 6.15 (d, 1H, *J*=8.24 Hz), 5.10 (ddd, 1H, *J*=5.60, 7.25, and 8.24 Hz,), 2.57 (broad, 1H, O*H*), 2.45 (s, 3H), 2.31 (s, 3H), 1.76-1.50 (m, 2H), 0.94 (t, 3H, *J*=7.58 Hz). Recrystallization from benzene-hexane afforded a sample for elemental analysis; colorless crystals; mp 55.0-57.0 °C. Anal. Calcd for $C_{14}H_{20}O_3S_2$: C, 54.52; H, 6.33. Found: C, 54.47; H, 6.26. **1c**: an *E*:*Z* mixture (41:59): colorless crystals; IR (KBr) 3499, 2955, 1313, 1283, 1145,

1083 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of *E*-isomer: δ 7.80 (d, 2H, *J*=8.24 Hz), 7.40 (d, 1H, *J*=8.24 Hz), 7.33 (d, 2H, *J*=7.91 Hz), 4.49 (ddd, 1H, *J*=4.94, 6.26, and 8.24 Hz), 2.44 (s, 3H), 2.37 (s, 3H), 2.18 (broad, 1H, O*H*), 1.85 (d and septet, 1H, *J*=6.59 and 6.92 Hz), 0.98 (d, 3H, *J*=6.59 Hz), 0.90 (d, 3H, *J*=6.92 Hz); ^1H NMR of *Z*-isomer: δ 7.87 (d, 2H, *J*=8.24 Hz), 7.35 (d, 2H, *J*=7.91 Hz,), 4.89 (dd, 2H, *J*=6.59 and 8.57 Hz), 2.45 (s, 3H), 2.31 (s, 3H), 1.80 (d and septet, 1H, *J*=6.59 and 6.92 Hz), 0.99 (d, 3H, *J*=6.59 Hz), 0.86 (d, 3H, *J*=6.92 Hz). A sample for elemental analysis was obtained by recrystallization from hexane-CH_2Cl_2; colorless crystals; mp 51.5-52.5 °C. Anal. Calcd for $C_{14}H_{20}O_3S_2$: C, 55.97; H, 6.71. Found: C, 55.66; H, 6.51.

10. Ogura, K.; Iihama, T.; Kiuchi, S.; Kajiki, T.; Koshikawa, O.; Takahashi, K.; Iida, H. *J. Org. Chem.* **1986**, *51*, 700.
11. Indeed, addition of a methyl radical to the energy minimized structure of **1a** is calculated by the MNDO/PM3 method[12] to be exothermic by 34.2 kcal mol^{-1}. The transition state was estimated by the use of the appropriate reaction coordinate analysis and the SADDLE routine. Further refinement of the transition state geometries was carried out by the use of the NLLSQ algorithm. The distance between the carbon of the methyl radical and the2-carbon of **1a** is 2.20 Å.
12. With MOPAC (ver. 6) molecular orbital package packed in Materia (ver. 2.1; Teijin System Technology, Ltd.): Stewart, J. J. P. *QCPE Bull.* **1989**, *9*, 10.
13. Important torsional angles: H_a-C_2-C_3-H_b = 145.3°, H_a-C_2-C_3-C_4 = -96.1°, H_a-C_2-C_3-O_3 = 21.9°, C_5-S_2-C_1-C_2 = 101.9°; O_2-S_1-C_1-C_2 = -13.4°, C_6-S_2-C_1-C_2 = 98.8°.
14. a) Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870. b) Garbisch, E. W. Jr. *J. Am. Chem. Soc.* **1964**, *86*, 5561. c) Gung, B. W.; Wolf, M. A.; Zhu, Z. *J. Org. Chem.* **1993**, *58*, 3350.
15. Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.
16. Carretero, J. C.; Domínguez, E. *J. Org. Chem.* **1992**, *57*, 3867.
17. Amano PS (from *Pseudomonas cepacia*) was provided by Amano Pharm. Co., Ltd.
18. Berger, B.; Feber, K. *J. Chem. Soc., Chem. Commun.* **1991**, 1198.
19. a) Kuhn, R.; Kum K. *Chem. Ber.* **1962**, *95*, 2009. (b) Trost, B. M.; Lynch, J.; Renaut, D.; Steiman, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 284. (c) Gopalan, A. S.; Jacobs, H. K. *Tetrahedron Lett.* **1990**, *31*, 5575. (d) Jacobs, H. K.; Mueller, B. H.; Gopalan, A. S. *Tetrahedron* **1992**, *48*, 8891. (e) Jacobs, H. K.; Gopalan, A. S. *J. Org. Chem.* **1994**, *59*, 2014.
20. Chen, C.-S.; Fujimoto, Y.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1982**, *104*, 7294.
21. a) Brady, L.; Brzozowski, A. M.; Derewenda, Z. S.; Dodson, E.; Dodson, G.; Tolley, S.; Turkenburg, J. P.; Christiansen, L.; Huge-Jensen, B.; Norskov, L.; Thim, L.; Menge, U. *Nature* **1990**, *343*, 767. b) Winkler, F. K.; D'Arcy, A.; Hunziker, W. *Nature* **1990**, *343*, 771. c) Sussman, J. L.; Harel, M.; Frolow, F.; Oefner, C.; Coldman, A.; Toker, L.; Silman, I. *Science* **1991**, *253*, 872. d) Schrag, J. D.; Li, Y.; Wu, S.; Cygler, M. *Nature* **1991**, *351*, 761. e) Grochulski, P.; Li, Y.; Schrag, J. D.; Bouthillier, F.; Smith, P.; Harrison, D.; Rubin, B.; Cygler, M. *J. Biol. Chem.* **1993**, *268*, 12843.
22. a) Kazlauskas, R. J.; Weissfloch, A. N. E.; Rappaport, A. T.; Cuccia, L. A. *J. Org. Chem.* **1991**, *56*, 2656. b) Kim, M.-J.; Choi, Y. K. *J. Org. Chem.* **1992**, *57*, 1605. c) Cygler, M.; Grochulski, P.; Kazlauskas, R. J.; Scharag, J. D.; Bouthillier, F.; Rubin, B.; Serreqi, A. N.; Gupta, A. K. *J. Am. Chem. Soc.* **1994**, *116*, 3180.
23. a) Honda, H.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1984**, *35*, 3857. b) Tamao, K.; Nakajima, T.; Sumiya, R.; Arai, H.; Higuchi, N.; Ito, Y. *J. Am. Chem. Soc.* **1986**, *108*, 6090. c) Menicagli, R.; Malanga, C.; Dell'Innocenti, M.; Lardicci, L. *J. Org. Chem.* **1987**, *52*, 5700.
24. Ogura, K.; Ohtsuki, K.; Nakamura, M.; Yahata, N.; Takahashi, K.; Iida, H. *Tetrahedron Lett.* **1985**, *26*, 2455.
25. The X-ray crystallographic data were deposited at the Cambridge Crystallographic Data Center.

(*Received* 28 *February* 1997; *accepted* 28 *April* 1997)