Anti-Selective Reaction of α-Sulfenyl Acetals with Silylated Carbon Nucleophiles. Scope, Limitation, and Mechanism[1]

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Received June 24, 1992

In the presence of a Lewis acid, α-sulfenyl acetals **1** reacted with various silylated carbon nucleophiles **2** to give anti adducts (*anti*-**3**) with high diastereoselectivity. The stereochemistry was only slightly affected by the reaction conditions, such as temperature, solvent, and Lewis acid. However, the structure of substrate **1** and the kind of nucleophile **2** had considerable effect on the stereochemical course of the reaction. Almost exclusive anti selectivity was attained when 1,1-dimethoxy-2-(*tert*-butylthio)propane (**1b**) was used as a substrate or when ketene silyl acetal **2c** was employed as a nucleophile. The mechanism of this reaction is essentially S_N2, although the S_N1 process participates to a various extent, depending on the structure of substrate **1**. The usefulness of this anti-selective reaction was exemplified by the easy transformation of *anti*-**3o** to synthetically valuable allylic alcohol *anti*-**6** without any loss of stereochemical information. The reaction of α-(benzyloxy)acetal **4** with **2** was also investigated. It gave a syn-rich mixture of diastereomers with lower selectivity.

Introduction

The Lewis acid-promoted reaction of acetals with nucleophiles is now one of the most common strategies for C–C bond formation; it has been widely investigated by using various types of nucleophiles and activators.[2] Concerning the stereochemical aspect, the reaction of acyclic acetals with silyl enol ethers proceeds syn-selectively, irrespective of the nucleophile geometry. This selectivity is rationalized by assuming an antiperiplanar orientation of the nucleophile and an intermediate oxocarbenium ion.[3] For such an aldol-type reaction there is another interest regarding acyclic stereoselection, i.e., asymmetric induction. From this point of view, the reaction of α-chiral *aldehydes* has been intensively studied both experimentally[4] and theoretically.[5] In contrast, the corresponding *acetals* have not been much explored. Regarding this matter, Heathcock and co-workers elegantly pointed out that the Cram-selectivity of the reaction of α-chiral thioacetals increases proportionally with increasing the steric bulkiness of the alkylthio group.[6] More recently, they systematically investigated the stereochemical course of the reaction of α-chiral oxoacetals and arrived at the same conclusion concerning the size of the alkoxy group.[7]

On the other hand, for the reaction of aldehydes, it is well-known that a heteroatom attached to the α-chiral position affects the stereochemistry of the product (chelation/nonchelation control) and that in many cases the selectivity is very high.[8] Taking into account the above-mentioned fact, the reaction of α-heteroatom-substituted α-chiral acetals is of great interest. Although there have been several studies concerning the reaction of such a substrate, only a few refer to the stereochemical course of the reaction. The reactions of 1,1-dimethoxy-2-siloxypropane with a silyl enol ether[9] or a lithium allylborate[10] have been reported by two groups; in both cases, 1/1 mixtures of diastereomers are obtained. The reaction of α-(Boc-amino)acetals with allylsilane gives the corresponding adducts with very low selectivity (anti/syn ≈ 2/1); when the acetal moiety is changed to a chiral one, the template effect of the chiral acetal moiety overrides the 1,2-asymmetric induction, indicating that the 1,2-asymmetric induction is scarcely realized in the reaction.[11] In contrast, excellent stereoselectivity is attained in the reaction of α-siloxy diselenoacetals. However, the substrate acts as a nucleophilic species in this case; this reaction proceeds through a lithium–selenium exchange and subsequent C–C bond formation.[12] Thus, there is no example of highly efficient 1,2-asymmetric induction for the nucleophilic displacement of α-heteroatom-substituted α-chiral acetals.

In this paper we report on the electrophilic, stereoselective reaction of α-sulfenyl acetals and discuss the mechanistic aspects.

Results and Discussion

At first, the reaction of **1a** with pinacolone-derived silyl enol ether **2a** was carried out in dichloromethane at −78 °C in the presence of tin(IV) chloride. The adduct was obtained in 87% yield with a ratio of anti/syn = 87/13; good anti selectivity was observed. Encouraged by this finding, we optimized the reaction conditions by using **1a** and **2a**. The results are given in Table I.

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(1) Saigo, K.; Kudo, K.; Hashimoto, Y.; Kimoto, H.; Hasegawa, M. *Chem. Lett.* **1990**, 941.

(2) Mukaiyama, T.; Murakami, M. *Synthesis* **1987**, 1043 and references cited therein.

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(6) Mori, I.; Bartlett, P. A.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 7199.

(7) Mori, I.; Ishihara, K.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 6107.

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(9) Sato, S.; Matsuda, I.; Izumi, Y. *Tetrahedron Lett.* **1987**, *28*, 6657.

(10) Hunter, R.; Tomlinson, G. D. *Tetrahedron Lett.* **1989**, *30*, 2013.

(11) Kano, S.; Yokomatsu, T.; Iwasawa, H.; Shibuya, S. *Chem. Lett.* **1987**, 1531. Andrew, R. G.; Conron, R. E.; Elliott, J. D.; Johnson, W. S.; Ramezani, S. *Tetrahedron Lett.* **1987**, *28*, 6535.

(12) Hoffmann, R. W.; Bewersdorf, M. *Tetrahedron Lett.* **1990**, *31*, 67.

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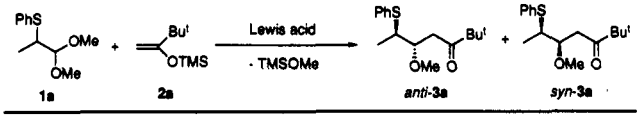
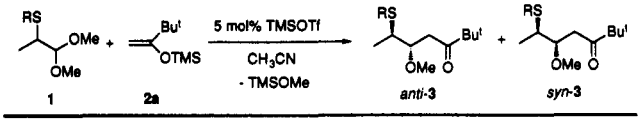
Table I. Reaction of 1a and 2a under Various Conditions[a]



entry	Lewis acid	solvent	temp/°C	yield/%	anti/syn
1	$SnCl_4$	CH_2Cl_2	−95	84	78/22
2			−78	87	87/13
3			−45	82	85/15
4			−20	82	88/12
5			0	71	86/14
6		Toluene	−78	61	89/11
7		Et_2O	−78 to rt	0	
8		CH_3CN	−40	87	93/7
9	$TiCl_4$			88	92/8
10	$BF_3{\cdot}OEt_2$			80	92/8
11	TMSOTf[b]			85	91/9
12	cat. TMSOTf[b,c]			92	92/8

[a] 1.1 equiv of Lewis acid was added to a mixture of **1a** (1.0 equiv) and **2a** (2.0 equiv). [b] 1.2 equiv of **2a** was used. [c] 5 mol % TMSOTf was used.

Table II. Effect of Sulfenyl Group



entry	substrate	R	product	yield/%	anti/syn
1	**1a**	Ph	**3a**	92	92/8
2	**1b**	^{t}Bu	**3b**	81[a]	>99/1
3	**1c**	Et	**3c**	88	92/8
4	**1d**	Me	**3d**	83	95/5

[a] 1.1 equiv of TMSOTf was used.

The reaction was carried out at various temperatures (Table I, entries 1–5). The reaction proceeded very smoothly, even at −78 °C; a TLC check after 5 min upon the addition of an activator indicated completion of the reaction. The yield was somewhat lower at 0 °C because of a partial decomposition of the substrates. An unusual temperature effect for a 1,2-asymmetric induction was observed; the anti selectivity was almost identical between −78 and 0 °C and slightly lowered at −95 °C.

The solvent effect was also subtle (Table I, entries 2, 6–8). The anti selectivity was slightly better in acetonitrile than in the other solvents. When ether was used as a solvent, the reaction did not proceed; the coordination of the solvent might be so strong that the Lewis acid could not activate the substrate.

It is noteworthy that the nature of the Lewis acid (acidity, chelation ability) scarcely affected the stereoselectivity (Table I, entries 8–12).[13] However, among the Lewis acids examined, TMSOTf was practically advantageous for this reaction because (1) the handling was easy in acetonitrile (no complex formation), (2) only a catalytic amount was sufficient,[3a] and (3) both the yield and selectivity were slightly better.

On the basis of these observations we concluded that the optimum reaction conditions were those of entry 12 in Table I; afterwards the reaction was conducted under such conditions.

The sulfenyl moiety exhibited some influence upon the diastereoselectivity (Table II). A very high anti selectivity was attained for the reaction of substrate **1b** having a *tert*-butylthio group; only one isomer could be detected by GC and ^{1}H NMR. With this substrate, however, an equimolar amount of TMSOTf was required, indicating that α-(*tert*-butylthio) acetal is disadvantageous from the viewpoint of a catalytic reaction.

In the next stage, the reactions of several substrates and nucleophiles were carried out in order to elucidate the generality of this reaction (Table III). In most cases, the reaction proceeded with high anti selectivity, although the selectivity was dependent on the kind of nucleophile (Table III, entries 1–4). Nucleophile **2c** showed excellent diastereoselectivity (Table I, entries 3, 9); even with substrate **1h**, which gave very low anti selectivity in the reaction of **2a**, only one diastereomer was detectable (compare entries 8 and 9, Table III). Moreover, for the reaction of α-(methylthio) acetals, the stereoselectivity was markedly dependent on the carbon framework of the acetals; the reaction of substrates without a branch at the β position proceeded with high anti selectivity (anti/syn ≥ 9/1; Table III, entries 1, 5, 6), whereas the selectivity for substrates having a branch at that position was much lower (anti/syn = 6/4; Table III, entries 7, 8).[14]

In order to clarify the effect of the α-sulfenyl group on simple diastereoselection in the aldol reaction of the acetals, we carried out the reaction of **1a** with **2e** (entry 14 and footnote b in Table III). As a result, the simple diastereoselection was 3/1 for syn/anti, which is much lower than that of the TMSOTf-promoted reaction of 1,1-dimethoxy-2-methylpropane, an α-branched achiral acetal, with **2e** (6/1 for syn/anti).[3a] This result indicates that α-sulfenyl acetals are less favorable for simple diastereoselection than are achiral acetals.

Heathcock's group[7] and Denmark's group[13] have independently reported that when methoxy groups of acetals are changed to bulkier isopropoxy groups the stereochemical result of the reaction changes dramatically. In contrast, the reaction of 1,1-diisopropoxy-2-(phenylthio)-propane (**1k**), an isopropoxy analog of **1a**, with **2a** gave the corresponding adduct with a ratio of anti/syn = 93/7, which is almost the same as that for the reaction of **1a** with **2a** (anti/syn = 92/8).

For the present reaction, several reaction paths are considered to be possible, as depicted in Scheme I.

The Lewis acid can coordinate to either of the two alkoxy groups of the acetal moiety. However, the dissociation of C–O bond would take place more easily when the Lewis acid coordinates to the alkoxy group antiperiplanar to the C–S bond because of the hyperconjugative effect of the C–S bond.[15] Among the conformers of the complex, conformer **A** is more favorable, taking into account the steric repulsion. As a result, the nucleophilic attack occurs toward the acetal center (path A) to lead the preferential formation of the anti isomer.

On the other hand, the episulfonium ion **B** can be formed by a neighboring group participation of the sulfenyl group.[16] When a nucleophilic attack occurs on **B** directly, the syn isomer is obtained (path B). Moreover, oxocar-

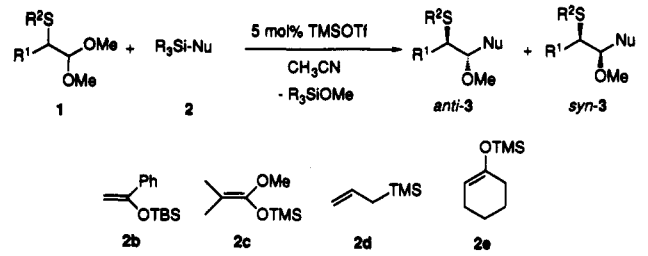
(13) In the intramolecular allylation of acetals, the stereochemistry of the product showed a marked dependence on the kind of Lewis acid: Denmark, S. E.; Willson, T. M. *J. Am. Chem. Soc.* **1989**, *111*, 3475.

(14) Similar alkyl-group-dependence of diastereoselectivity was observed in the BF_3-promoted reaction of α-(methylthio) aldehydes with an allylstannane: Shimagaki, M.; Takubo, H.; Oishi, T. *Tetrahedron Lett.* **1985**, *26*, 6235.

(15) The electron-donating character of σ_{CS} bond is stronger than those of σ_{CC} and σ_{CH}: Cieplak, A. S. *J. Am. Chem. Soc.* **1981** *103*, 4540.

(16) A neighboring-group participation has been reported for the reaction of the chromium(0) complex of benzaldehyde-derived acetal: Davies, S. G.; Newton, R. F.; Williams, M. J. *Tetrahedron Lett.* **1989**, *30*, 2967.

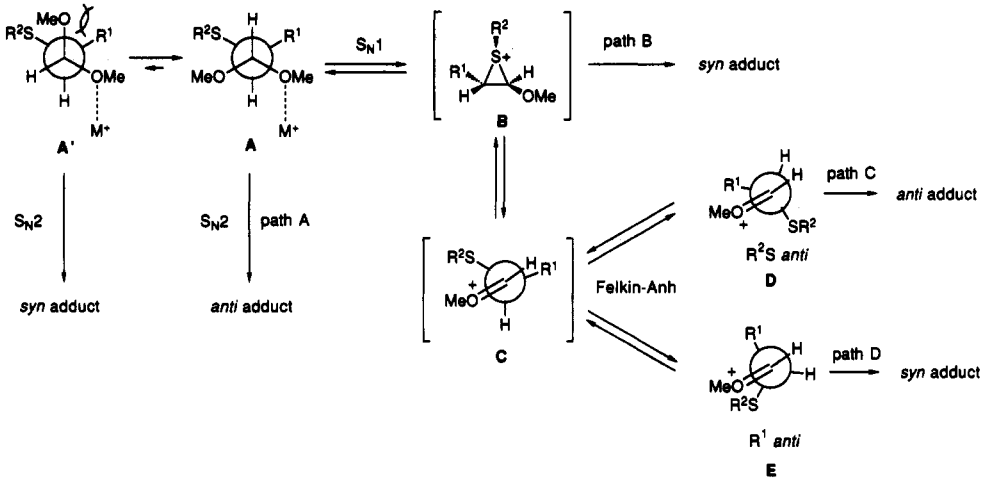
Table III. Reaction of Various α-Sulfenyl Acetals with Silylated Carbon Nucleophiles



entry	substrate	R^1	R^2	nucleophile	product	yield/%	anti/syn
1	**1d**	Me	Me	**2a**	**3d**	83	95/5
2				**2b**	**3e**	87	94/6
3				**2c**	**3f**	88	>99/1
4				**2d**	**3g**	57	75/25
5	**1e**	Et		**2a**	**3h**	78	98/2
6	**1f**	Bn			**3i**	86	90/10
7	**1g**	Ph			**3j**	80	59/41
8	**1h**	^{i}Pr			**3k**	58	59/41
9				**2c**	**3l**	83	>99/1
10	**1b**	Me	^{t}Bu	**2a**	**3b**	81[a]	>99/1
11				**2d**	**3m**	35[a]	97/3
12	**1i**	Bu	Me		**3n**	66	88/12
13	**1j**	(*E*)-MeCH=CH-	Ph	**2a**	**3o**	89	87/13
14	**1a**	Me	Ph	**2e**	**3p**	93	78/22[b]

[a] 1.1 equiv of TMSOTf was used. [b] Four diastereomers were obtained in a ratio of 57:17:21:5. On the basis of the diastereomer ratio, simple diastereoselection was estimated to be syn/anti = 74/26. The main product was (2*R**,1′*R**,2′*S**)-2-[1-methoxy-2-(phenylthio)propyl]cyclohexanone.

Scheme I



benium ion **C** can possibly be formed by a further transformation of **B**; the stereochemistry is determined by the Felkin–Anh model of two possible conformers, **D** and **E**, which give the anti and syn adducts, respectively. Due to the electronic effect of the sulfenyl group, conformer **D** is considered to be preferable; the anti isomer becomes the main product (path C).

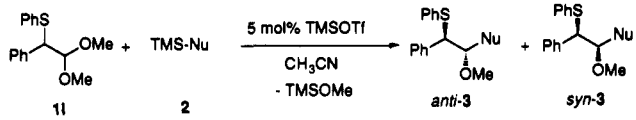
Thus, the observed anti selectivity would be explained by either path A (S_N2 mechanism) or path C (S_N1 mechanism).

As described above, the stereoselectivity of the reaction of **1a** with **2a** was hardly affected by the reaction conditions such as the temperature and the solvent. This fact is in sharp contrast with the result concerning the reaction of α-chiral 1,1-dimethoxy-2-phenylpropane with **2a** (higher selectivity is achieved at a lower temperature in a more polar solvent), which proceeds through S_N1 in acetonitrile.[7] Moreover, another feature of the reaction of **1a** with **2a** is that the stereochemical result of the reaction promoted by a weak Lewis acid, TMSOTf, was almost identical with those promoted by stronger Lewis acids, such as BF_3·OEt_2 and $SnCl_4$, indicating that the C–C bond formation occurs as soon as a complex is formed between **1a** and the Lewis acid.[17] These remarkable features of the reaction of **1a** with **2a** strongly indicate that the present reaction proceeds through essentially S_N2.

The result concerning substrate **1b**, having a *tert*-butylthio group, supports this S_N2 mechanism, since its very high selectivity can be consistently explained as follows: There is a severe steric repulsion between *tert*-butylthio and the methoxy group in the episulfonium ion **B** to seriously depress the formation of such an ion; the reaction proceeds through only path A to give the anti isomer selectively.

(17) In acetonitrile–deuteriochloroform at −40 °C, ^{13}C NMR signals of **1a** exhibited no significant change (<1 ppm) upon mixing with an equimolar amount of TMSOTf; there was no sign for ionization or complexation. This result is in good agreement with the NMR study concerning the interaction between an achiral acetal and TMSOTf reported by Denmark's group and can be rationalized by assuming that the coordination of silyl cation is very slow: Denmark, S. E.; Willson, T. M. *Selectivities in Lewis Acid Promoted Reactions*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1989; p 247–263.

Table IV. Reaction of α-Sulfenyl Acetal 1l with Silylated Carbon Nucleophiles



1l 2

entry	nucleophile	product	yield/%	anti/syn
1	**2a**	**3r**	80	21/79
2[a]			93	42/58
3	**2c**	**3s**	92	65/35
4	**2d**	**3t**	83	14/86

[a] The reaction was performed with 1.1 equiv of $TiCl_4$ in CH_2Cl_2 at −78 °C.

The low diastereoselectivity for the reaction of substrates having a β-branched alkyl group, **1g** and **1h**, is, however, unable to be explained by the S_N2 mechanism. For these substrates, the contribution of path B and/or path D must be considered; the steric interaction between branched R^1 and a methoxy group becomes larger in conformation **A**, thus prompting the formation of the episulfonium ion **B** in order to release such an interaction.

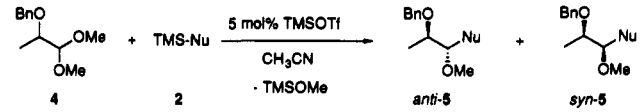
The rather abnormal temperature effect in this reaction can also be consistently explained by this reaction scheme. The intramolecular formation of the episulfonium ion would be faster than an intermolecular substitution reaction at a lower temperature due to a favorable entropy factor. Since the ionic species reacts more easily than does the nonionic one, the contribution of path B might become larger at −95 °C.

Concerning the quite high anti selectivity observed for the reaction of nucleophile **2c**, even with a β-branched α-sulfenyl acetal, the steric repulsion between the nucleophile and electrophile may play an important role. A molecular model study revealed that there is a substantial repulsive interaction between **2c** and the episulfonium ion **B**; the contribution of path B might be repressed. Subsequently, the reaction occurs via path A and/or path C to give the anti adducts selectively.[18]

Substrate **1l** behaved in an entirely different manner compared to the other substrates (Table IV); the reason for the exceptional behavior is not clear. However, in the case of **1l**, the reaction may proceed via path D; the contribution of the path is consistent with the result reported by Otera and co-workers, in which the formation of the same oxocarbenium ion is proposed.[19]

There have been only a few reports concerning the reaction of acyclic α-oxygenated acetals.[9,10,12] However, the stereocontrol of the vicinal dioxy function is very important in synthetic organic chemistry. From this point of view, the reaction of α-benzyloxy acetal **4** was carried out in order to compare it with that of the α-sulfenyl series (Table V). In this case, a syn preference was observed, irrespective of the kind of nucleophile, though the selectivity was not as satisfactory as in the α-sulfenyl case.[20] In addition, when **4** was allowed to react with **2a** in CH_2Cl_2, a complex mixture was obtained. These facts indicate that the reaction involves a labile ionic intermediate, namely, an oxocarbenium ion. The observed syn preference, however, is quite different from the stereochemical course of the reaction of the corresponding aldehyde under nonchelation control. Although we did not investigate this reaction in detail, the counter anion might play an important role.[21]

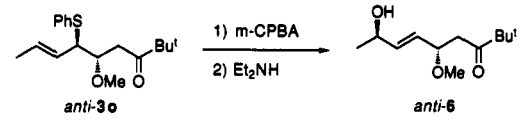
Table V. Reaction of α-(Benzyloxy) Acetal 4



4 2

entry	nucleophile	temp/°C	product	yield/%	anti/syn
1	**2a**	−40 to −15	**5a**	86	23/77
2	**2c**	−40 to rt	**5b**	56	40/60
3	**2d**	−40 to rt	**5c**	55	37/63

Scheme II



The above-mentioned fact manifests the unique electronic effect of the sulfur atom on the stereoselective aldol reaction of α-sulfenyl acetals. From a synthetic point of view it is important to remove the sulfenyl group without any loss of stereochemical information, since most of the synthetically interesting targets do not contain such a functional group. Concerning this matter, *anti*-**3o** was successfully converted via a sulfoxide–sulfenate rearrangement to *anti*-**6**, which should be a valuable precursor for a stereocontrolled, highly oxygenated carbon chain (Scheme II).[22] This example emphasizes the synthetic usefulness of this diastereoselective reaction of α-sulfenyl acetals.

Determination of Relative Stereochemistry of Products

X-ray crystallographic analyses were performed in order to establish the structures of the following compounds: the major isomer of **3o**, the main isomer of **3p**, sulfone **7** derived from **3f**, sulfone **8** derived from major isomer of **3r**, and ester **10** derived from the major isomer of **9** (Scheme III).[18] Compound **9** was methylated (NaH/MeI) to give **3s** as a 9/1 mixture of diastereomers. The major isomer of the thus-obtained **3s** was proved to be the same as the major isomer of **1l**-derived **3s**.

The stereochemistry of **3n** was assured by a comparison of its ^1H NMR spectrum with that of the authentic anti-rich mixture (97/3), which was obtained by methylation (NaH/MeI) of the corresponding alcohol.[14] Compounds **5a–c** were analyzed in the same way using authentic syn-rich isomers. To obtain authentic **5a**, a careful methylation procedure was carried out through a reduction (BH_3)–monomethylation–oxidation (PCC) sequence.[7]

(18) The reaction via path C is closely related to the reaction of α-sulfenyl aldehydes under nonchelation control: Annunziata, R.; Cinquini, M.; Cozzi, F.; Cozzi, P. G.; Consolandi, E. *J. Org. Chem.* **1992**, *57*, 456.

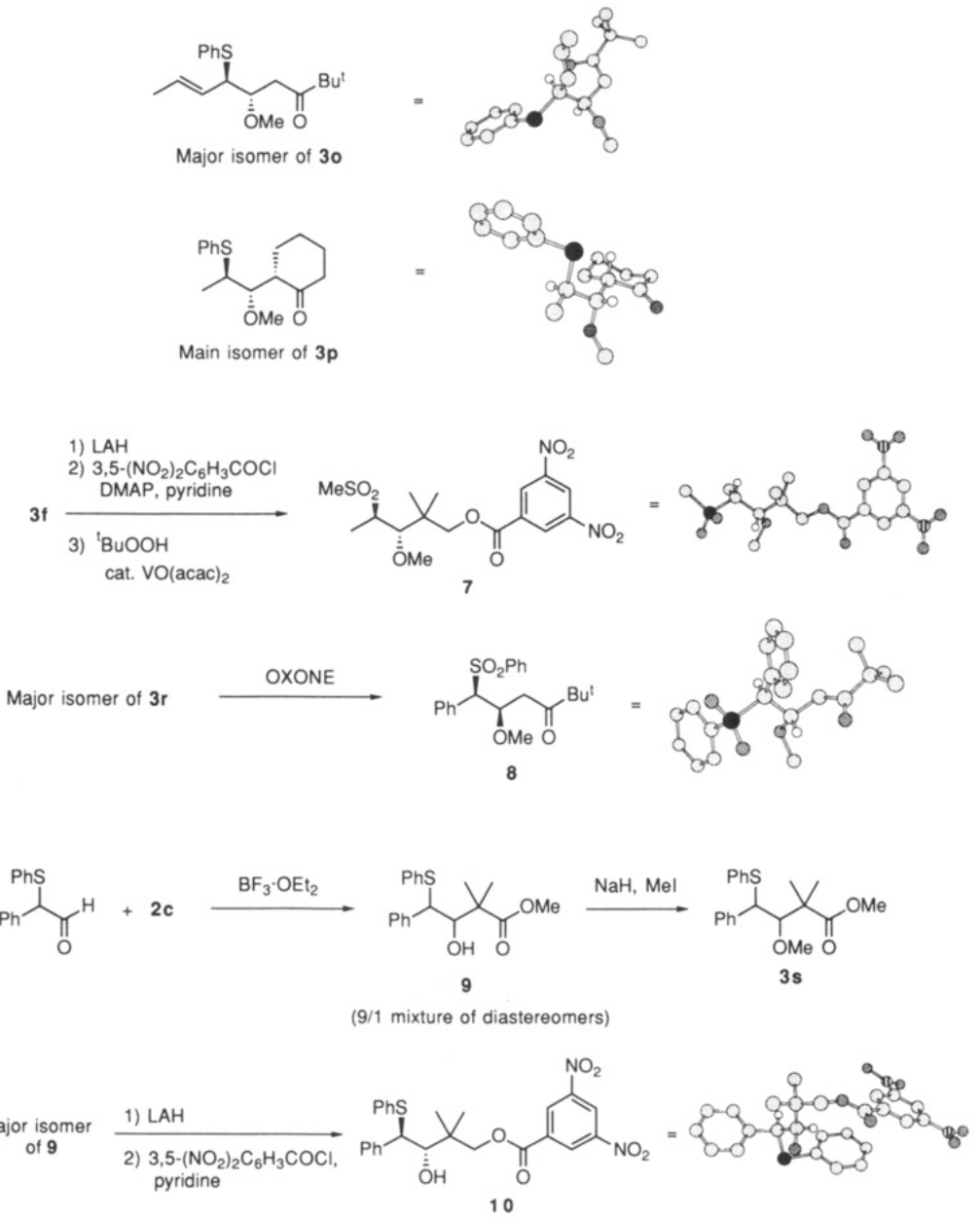
(19) They pointed out that the selectivity was more reasonably explicable by considering the electrostatic interaction between the sulfur lone pair and the oxonium ion than by a usual Felkin–Anh model: Sato, T.; Otera, J.; Nozaki, H. *J. Org. Chem.* **1990**, *55*, 6116.

(20) Lower stereoselectivities were observed for the reactions of **2a** with *tert*-butyldimethylsiloxy (68/32) and benzoyloxy (64/36) counterparts of **4**.

(21) When the reaction of **2a** with **4** was carried out in the presence of 2 equiv of $EtOSiMe_3$, there was no observed incorporation of an EtO group in the product, and the diastereomer ratio was not changed. This result may rule out the existence of a free oxocarbenium ion intermediate.

(22) Although the relative configuration of **6** was not confirmed, it is most likely that **6** has an anti configuration, judging from the known stereochemical course of this type of [2,3] sigmatropy: Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 563.

Scheme III



Product **3t** is a known compound;[19] its stereochemistry is determined by the ^{1}H NMR spectrum.

The stereochemistries of the other compounds having a sulfenyl group were confirmed on the basis of a correlation of the ^{1}H NMR chemical shifts of selected peaks (*t*-Bu, MeO, MeS); in the case that such a comparison was not available, it was assumed that the reaction proceeded through an analogous mechanism.

Experimental Section

General. A GC analysis was performed with a 25-m fused-silica capillary column using cyanopropyl silicone as a stationary phase. The melting points were determined using a metal block apparatus and an open capillary tube and were uncorrected. NMR spectra were measured on a FT spectrometer operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C, or on a continuous-wave instrument (60 MHz for ^{1}H). For ^{1}H NMR, the δ values are given in ppm with TMS as an internal standard, and the coupling constants are recorded in Hz. For ^{13}C NMR, the chemical shifts are reported in ppm relative to TMS or $CDCl_3$ (δ 77.0). The unit for the values of IR spectra is cm^{-1}. The mass spectra were recorded with the EI method (70 eV); the relative intensity is given in parentheses after the corresponding *m*/*z* value. Silica gel was used for column chromatography (particle size: 63–200 μm) and preparative TLC (<46 μm).

Nucleophiles **2a**, **2b**, **2c**, and **2e** were synthesized according to a method described in the literature.[23] Allylsilane **2d** was purchased from Shin-etsu Silicone.

1,1-Dimethoxy-2-(phenylthio)propane (1a), 1,1-Dimethoxy-2-(*tert*-butylthio)propane (1b), and 1,1-Dimethoxy-2-(ethylthio)propane (1c). To a flask containing 53.27 g (0.45 mol) of pyruvaldehyde dimethyl acetal (available from Aldrich) in EtOH (200 mL) was added 8.53 g (0.23 mol) of $NaBH_4$ by portions over a period of 15 min at 0 °C. The reaction mixture was allowed to warm to rt and was then stirred for 6 h. Acetone was added by portions until no more exothermic reaction occurred. The mixture was concentrated by a rotary evaporator, and a 3 M HCl solution was carefully added to the white syrupy residue until the solution became homogeneous. The water solution was extracted thoroughly with EtOAc (5 × 50 mL), and the combined organic layers were dried over $MgSO_4$. Concentration followed by distillation gave 30.09 g (56%) of 1,1-dimethoxy-2-propanol:

(23) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: New York, 1988; p 99.

bp 64–66 °C/35 mmHg [lit.[24] bp 62–67 °C/30 mmHg]. The ^{1}H NMR spectrum was identical with that reported in literature.[24]

The alcohol thus obtained was mesylated according to the method in literature:[25] 91% yield; bp 105–111 °C/1 mmHg; ^{1}H NMR (CCl_4, 60 MHz) 1.4 (d, 3 H, J = 6, CH_3CH), 2.9 (s, 3 H, CH_3SO_2), 3.4 (s, 6 H, CH_3O), 4.3 (d, 1 H, J = 6, $(MeO)_2CH$), 4.3–4.9 (m, 1 H, MeCH).

To a stirred solution of sodium thiolate (15 mmol) in EtOH (10 mL) was added an EtOH (2 mL) solution of the mesylate (15 mmol), and the mixture was refluxed for 10 h. Upon progressing the reaction, dense white masses precipitated. To the reaction mixture were added hexane (30 mL) and water (30 mL), and the two layers were separated. The organic layer was washed with 1 M NaOH solution (2 × 10 mL), dried over Na_2SO_4, and concentrated to give the crude material. Purification as described below afforded the α-sulfenyl acetal.

1a: 81% yield; column chromatography (EtOAc/hexane = 1/30); ^{1}H NMR (CCl_4, 60 MHz) 1.2 (d, 3 H, J = 7, CH_3CH), 3.2–3.3 (m, 1 H, MeCH), 3.3 (s, 3 H, CH_3O), 3.4 (s, 3 H, CH_3O), 4.6 (d, 1 H, J = 6, $(MeO)_2CH$), 7.1–7.6 (m, 5 H, phenyl); ^{13}C-NMR ($CDCl_3$–CH_3CN) 15.9, 45.9, 55.1, 55.5, 107.3, 127.0, 129.0, 132.1, 135.0; IR (neat) 1585, 1480, 1440, 1140, 1070, 750, 695; MS 212 (M^+, 48), 181 (17), 149 (37), 137 (11), 109 (26), 75 (100), 47 (23); HRMS calcd for $C_{11}H_{16}O_2S$ 212.0871, found 212.0849.

1b: 40% yield; Kugelrohr distillation; bp 110 °C (ot)/1 mmHg; purity >99% by GC analysis; ^{1}H NMR (CCl_4, 60 MHz) 1.2 (d, 3 H, J = 7, CH_3CH), 1.3 (s, 9 H, $(CH_3)_3C$), 2.5–3.0 (m, 1 H, MeCH), 3.4 (s, 6 H, CH_3O), 4.2 (d, 1 H, J = 5, $(MeO)_2CH$); HRMS calcd for $C_9H_{20}O_2S$ 192.1184, found 192.1159.

1c: 36% yield; bp 43 °C/1 mmHg; purity >99% by GC analysis; ^{1}H NMR (CCl_4, 60 MHz) 1.2 (t, 6 H, J = 7, CH_3CH_2 overlapping CH_3CH), 2.7 (pseudo quintet, 3 H, J = 8, $MeCH_2$ overlapping MeCH), 3.3 (s, 3 H, CH_3O), 3.4 (s, 3 H, CH_3O), 4.2 (d, 1 H, J = 6, $(MeO)_2CH$); HRMS calcd for $C_7H_{16}O_2S$ 164.0871, found 164.0864.

1,1-Dimethoxy-2-(methylthio)propane (1d). The α-sulfenyl acetal was prepared under the phase-transfer conditions[26] by using the above-mentioned mesylate and commercially available 15% aqueous solution of sodium methanethiolate in the presence of 10 mol % tributylhexadecylphosphonium bromide: 31% yield; bp 46–47 °C/6 mmHg; purity >99% by GC analysis; ^{1}H NMR (CCl_4, 60 MHz) 1.2 (d, 3 H, J = 7, CH_3CH), 2.1 (s, 3 H, CH_3S), 2.7 (quintet, 1 H, J = 7, MeCH), 3.3 (s, 3 H, CH_3O), 3.4 (s, 3 H, CH_3O), 4.2 (d, 1 H, J = 7, $(MeO)_2CH$); HRMS calcd for $C_6H_{14}O_2S$ 150.0715, found 150.0697.

1,1-Dimethoxy-2-(methylthio)butane (1e), 1,1-Dimethoxy-3-methyl-2-(methylthio)butane (1h), and 1,1-Dimethoxy-2-(methylthio)hexane (1i). The α-sulfenyl acetals were obtained by the same procedure as that for **1a** by using α-bromo acetals[27] instead of the mesylate. Since it was difficult to isolate the products from unreacted starting materials, the yields were rather low.

1e: 19% yield; bp 57 °C/9 mmHg; purity 96% by GC analysis; ^{1}H NMR (CCl_4, 60 MHz) 1.0 (d, 3 H, J = 7, CH_3CH_2), 1.2–1.8 (m, 2 H, $MeCH_2$), 2.1 (s, 3 H, CH_3S), 2.2–2.6 (m, 1 H, MeSCH), 3.3 (s, 3 H, CH_3O), 3.4 (s, 3 H, CH_3O), 4.3 (d, 1 H, J = 6, $(MeO)_2CH$).

1h: 6% yield; bp 73–76 °C/9 mmHg; purity 99% by GC analysis; ^{1}H NMR (CCl_4, 60 MHz) 0.8 (d, 3 H, J = 7, CH_3CHCH_3), 1.0 (d, 3 H, J = 7, CH_3CHCH_3), 1.9–2.3 (m, 1 H, Me_2CH), 2.1 (s, 3 H, CH_3S), 2.4 (dd, 1 H, J = 3, 8, MeSCH), 3.3 (s, 3 H, CH_3O), 3.4 (s, 3 H, CH_3O), 4.3 (d, 1 H, J = 8, $(MeO)_2CH$); HRMS calcd for $C_8H_{18}O_2S$ 178.1027, found 178.1004.

1i: 38% yield; bp 97 °C/3 mmHg; purity >99% by GC analysis; ^{1}H NMR (CCl_4, 60 MHz) 0.7–1.9 (m, 9 H, butyl), 2.1 (s, 3 H, CH_3S), 2.3–2.7 (m, 1 H, MeSCH), 3.4 (s, 3 H, CH_3O), 3.4 (s, 3 H, CH_3O), 4.3 (d, 1 H, J = 7, $(MeO)_2CH$).

1,1-Dimethoxy-2-(methylthio)-3-phenylpropane (1f). 2-(Methylthio)-3-phenylpropanal (2.00 g, 11 mmol)[28] was dissolved in $HC(OMe)_3$ (30 mL). To this solution was added *p*-TsOH (0.5 g, 3.2 mmol), and the mixture was stirred for 2 h at rt. After aqueous alkaline workup, the crude material was purified by column chromatography (EtOAc/benzene/hexane = 1/1/20): 34% yield; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.02 (s, 3 H, CH_3S), 2.74 (dd, 1 H, J = 9, 14, PhCHH), 2.89 (pseudo quintet, 1 H, J = 5, MeSCH), 3.13 (dd, 1 H, J = 5, 14, PhCHH), 3.44 (s, 3 H, CH_3O), 3.47 (s, 3 H, CH_3O), 4.32 (d, 1 H, J = 5, $(MeO)_2CH$), 7.18–7.33 (m, 5 H, phenyl); ^{13}C-NMR ($CDCl_3$) 15.3, 35.9, 51.3, 55.3, 55.8, 107.7, 126.3, 128.2, 129.3, 139.4; HRMS calcd for $C_{12}H_{18}O_2S$ 226.1028, found 226.1028.

1,1-Dimethoxy-2-(methylthio)-2-phenylethane (1g). To a solution of 1-methoxy-2-phenylethylene[29] (1.48 g, 11 mmol) in CH_2Cl_2 (15 mL) was added MeSCl[30] (50 mmol) drop by drop at 0 °C. The reaction mixture was allowed to warm to rt, and MeOH (5 mL) was added to the mixture. After being stirred for 8 h, the mixture was concentrated and purified by column chromatography (EtOAc/hexane = 1/20): 54% yield; ^{1}H NMR (CCl_4, 60 MHz) 1.8 (s, 3 H, CH_3S), 3.2 (s, 3 H, CH_3O), 3.4 (s, 3 H, CH_3O), 3.9 (d, 1 H, J = 8, MeSCH), 4.6 (d, 1 H, J = 8, $(MeO)_2CH$), 7.3 (s, 5 H, phenyl); ^{13}C-NMR ($CDCl_3$) 14.6, 54.2, 54.4, 54.5, 106.9, 127.3, 128.3, 128.7, 138.3.

(*E*)-1,1-Dimethoxy-2-(phenylthio)-3-pentene (1j) and 1,1-Dimethoxy-2-(phenylthio)-2-phenylethane (1l). The α-sulfenyl acetals were synthesized according to the procedure described by Mandai et al.[31]

1j: ^{1}H NMR ($CDCl_3$, 400 MHz) 1.60 (dd, 3 H, J = 1, 6, CH_3), 3.42 (s, 3 H, CH_3O), 3.43 (s, 3 H, CH_3O), 3.78 (dd, 1 H, J = 5, 9, PhSCH), 4.41 (d, 1 H, J = 5, $(MeO)_2CH$), 5.29–5.49 (m, 2 H, CH=CH), 7.20–7.30 (m, 3 H, phenyl), 7.38–7.42 (m, 2 H, phenyl). Anal. Calcd for $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61. Found: C, 65.23; H, 7.53.

1l: ^{1}H NMR (CCl_4, 60 MHz) 3.2 (s, 3 H, CH_3O), 3.4 (s, 3 H, CH_3O), 4.3 (d, 1 H, J = 6, PhSCH), 4.6 (d, 1 H, J = 6, $(MeO)_2CH$), 6.8–7.6 (m, 10 H, phenyl); ^{13}C-NMR ($CDCl_3$) 54.8, 55.1, 56.5, 106.5, 127.1, 127.3, 128.2, 128.6, 128.9, 132.5, 134.5, 138.4.

1,1-Diisopropoxy-2-(phenylthio)propane (1k). In 2-propanol (30 mL) was dissolved **1a** (2.53 g, 11.9 mmol), and the solution was refluxed for 8 h in the presence of *p*-TsOH (0.1 g). After aqueous alkaline workup, the reaction mixture was purified by column chromatography (EtOAc/hexanes = 1/50) to give 0.45 g (14% yield) of **1k**: ^{1}H NMR ($CDCl_3$, 400 MHz) 1.14 (d, 3 H, J = 6, isopropyl), 1.19 (d, 3 H, J = 6, isopropyl), 1.19 (d, 3 H, J = 6, isopropyl), 1.22 (d, 3 H, J = 6, isopropyl), 1.33 (d, 3 H, J = 7, $PhSCHCH_3$), 3.32 (dq, 1 H, J = 4, 7, $PhSCHCH_3$), 3.79 (septet, 1 H, J = 6, isopropyl), 3.88 (septet, 1 H, J = 6, isopropyl), 4.61 (d, 1 H, J = 4, $(i\text{-}PrO)_2CH$), 7.18–7.45 (m, 5 H, phenyl); ^{13}C-NMR ($CDCl_3$) 15.0, 22.2, 22.6, 23.0, 23.3, 47.5, 69.2, 69.5, 101.0, 126.5, 128.8, 131.2, 136.0; IR (neat) 1380, 1125, 1025, 745, 695; MS 209 (3), 137 (17), 131 (29), 109 (9), 89 (100), 59 (11).

2-(Benzyloxy)-1,1-dimethoxypropane (4). To a DMF (50 mL) dispersion of NaH (55% in mineral oil; 1.10 g, 25 mmol), which was washed twice with hexane, was added a DMF (6 mL) solution of 1,1-dimethoxy-2-propanol (3.00 g, 25 mmol). After the exothermic reaction ceased, a DMF (6 mL) solution of BnBr (4.24 g, 25 mmol) was added. The mixture was warmed to 100 °C and stirred for 3 h. Usual aqueous workup followed by column chromatography (EtOAc/hexane = 1/20–1/10) gave 1.82 g (35% yield) of **4**: ^{1}H NMR (CCl_4, 60 MHz) 1.1 (d, 3 H, J = 6, CH_3CH), 3.2–3.6 (m, 1 H, MeCH), 3.4 (s, 6 H, CH_3O), 4.1 (d, 1 H, J = 6, $(MeO)_2CH$), 4.6 (s, 2 H, $PhCH_2$), 7.3 (s, 5 H, phenyl). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.41; H, 8.53.

General Procedure for the Reaction of the Acetals. To a stirred solution of the acetal (0.5 mmol) and nucleophile (0.6 mmol) in CH_3CN (4 mL) was added TMSOTf (0.1 M solution in CH_3CN, 0.25 mL, 0.025 mmol) at −40 °C under an argon atmosphere. The reaction mixture was stirred for 30 min at the temperature and quenched by adding saturated aqueous $NaHCO_3$ solution (3 mL). The organic materials were extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4. After evaporation of the solvents, the residue was

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purified by silica gel column chromatography (ether/hexane = 1/30) or preparative TLC (EtOAc/hexanes = 1/10) to give the corresponding adduct as an inseparable mixture of the diastereomers. The diastereomer ratio was determined by GC or ^{1}H-NMR.

When **2d** was used as a nucleophile, the acetal was added to a mixture of nucleophile and TMSOTf.

5-Methoxy-2,2-dimethyl-6-(phenylthio)-3-heptanone (3a): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.13 (s, 9 × 0.08 H, $(CH_3)_3C$), 1.15 (s, 9 × 0.92 H, $(CH_3)_3C$), 1.28 (d, 3 × 0.92 H, J = 7, CH_3CH), 1.33 (d, 3 × 0.08 H, J = 7, CH_3CH), 2.66 (dd, 1 H, J = 4, 17, CHHCO), 2.94 (dd, 1 H, J = 7, 17, CHHCO), 3.19 (td, 1 H, J = 4, 7, MeOCH), 3.30 (s, 3 × 0.08 H, CH_3O), 3.36 (s, 3 × 0.92 H, CH_3O), 3.40 (dq, 1 H, J = 4, 7, MeCH), 7.21–7.33 (m, 3 H, phenyl), 7.39–7.49 (m, 2 H, phenyl); IR (neat) 1710, 1585, 1480, 1370, 1095, 1070, 750, 695; MS 280 (M^+, 1), 248 (M^+ – MeOH, 13), 180 (9), 163 (29), 137 (31), 85 (31), 57 (100), 41 (57); HRMS calcd for $C_{16}H_{24}O_2S$ 280.1497, found 280.1495.

6-(*tert*-Butylthio)-5-methoxy-2,2-dimethyl-3-heptanone (3b): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.15 (s, 9 H, $(CH_3)_3C$), 1.30 (d, 3 H, J = 7, CH_3CH), 1.35 (s, 9 H, $(CH_3)_3CS$), 2.64 (dd, 1 H, J = 4, 17, CHHCO), 2.84–2.92 (m, 2 H, CHHCO overlapping MeCH), 3.39 (s, 3 H, CH_3O), 3.80 (td, 1 H, J = 4, 8, MeOCH); IR (neat) 1710, 1365, 1090; MS 228 (M^+ – MeOH, 25), 172 (19), 143 (17), 117 (35), 85 (44), 61 (19), 57 (100); HRMS calcd for $C_{13}H_{24}OS$ (M – MeOH) 228.1548, found 228.1540.

6-(Ethylthio)-5-methoxy-2,2-dimethyl-3-heptanone (3c): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.16 (s, 9 × 0.92 H, $(CH_3)_3C$), 1.17 (s, 9 × 0.08 H, $(CH_3)_3C$), 1.26 (m, 6 H), 2.62 (dd, 1 H, J = 4, 17, CHHCO), 2.63 (m, 1 H), 2.92 (dd, 1 H, J = 8, 17, CHHCO), 2.99 (dq, 1 H, J = 4, 7, MeCH), 3.34 (s, 3 × 0.08 H, CH_3O), 3.38 (s, 3 × 0.92 H, CH_3O), 3.86 (td, 0.92 H, J = 4, 8, MeOCH), 3.90 (m, 0.08 H, MeOCH); IR (neat) 1705, 1620, 1480, 1365, 1095; MS 200 (M^+ – MeOH, 9), 143 (29), 89 (27), 85 (18), 57 (100); HRMS calcd for $C_{11}H_{20}OS$ (M – MeOH) 200.1235, found 200.1235.

5-Methoxy-2,2-dimethyl-6-(methylthio)-3-heptanone (3d): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.16 (s, 9 × 0.95 H, $(CH_3)_3C$), 1.20 (s, 9 × 0.05 H, $(CH_3)_3C$), 1.26 (d, 3 × 0.95 H, J = 7, CH_3CH), 1.31 (d, 3 × 0.05 H, J = 8, CH_3CH), 2.12 (s, 3 × 0.05 H, CH_3S), 2.14 (s, 3 × 0.95 H, CH_3S), 2.65 (dd, 0.95 H, J = 4, 17, CHHCO), 2.77 (m, 0.05 H, CHHCO), 2.86 (m, 0.05 H, CHHCO), 2.91 (dd, 0.95 H, J = 8, 17, CHHCO), 3.34 (s, 3 × 0.05 H, CH_3O), 3.38 (s, 3 × 0.95 H, CH_3O), 3.87 (ddd, 0.95 H, J = 4, 7, 8, MeOCH), 3.92 (m, 0.05 H, MeOCH); ^{13}C-NMR ($CDCl_3$) for the anti isomer, 14.1, 16.7, 26.4, 39.2, 44.7, 58.7, 80.4, 213.6; for the syn isomer (identifiable peaks only), 15.7, 37.1, 43.1, 79.0; IR (neat) 1710, 1480, 1460, 1365, 1100; MS 186 (M^+ – MeOH, 40), 118 (10), 101 (25), 85 (35), 75 (25), 57 (100), 41 (10); HRMS calcd for $C_{10}H_{18}OS$ (M – MeOH) 186.1078, found 186.1098.

3-Methoxy-4-(methylthio)-1-phenyl-1-pentanone (3e): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.32 (d, 3 × 0.94 H, J = 7, CH_3CH), 1.44 (d, 3 × 0.06 H, J = 7, CH_3CH), 2.03 (s, 3 × 0.06 H, CH_3S), 2.17 (s, 3 × 0.94 H, CH_3S), 2.96 (dq, 0.94 H, J = 4, 7, MeSCH), 3.02 (m, 0.06 H, CHHCO), 3.16 (dd, 0.94 H, J = 4, 17, CHHCO), 3.23 (m, 0.06 H, MeSCH), 3.37 (s, 3 × 0.06 H, CH_3O), 3.39 (dd, 1 H, J = 7, 17, CHHCO), 3.42 (s, 3 × 0.94 H, CH_3O), 4.03 (td, 0.94 H, J = 4, 7, MeOCH), 4.08 (m, 0.06 H, MeOCH), 7.44–7.60 (m, 3 H, phenyl), 7.93 (dm, 2 × 0.06 H, phenyl), 7.99 (dm, 2 × 0.94 H, phenyl); IR (neat) 1690, 1600, 1455, 1115, 760, 710; MS 206 (M^+ – MeOH, 24), 118 (24), 105 (100), 77 (33), 75 (12); HRMS calcd for $C_{12}H_{14}OS$ (M – MeOH) 206.0765, found 206.0764. Anal. Calcd for $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61. Found: C, 65.24; H, 7.62.

Methyl 3-methoxy-2,2-dimethyl-4-(methylthio)pentanoate (3f): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.15 (s, 3 H, CH_3CCH_3), 1.22 (s, 3 H, CH_3CCH_3), 1.33 (d, 3 H, J = 7, CH_3CH), 2.07 (s, 3 H, CH_3S), 2.71 (qd, 1 H, J = 5, 7, MeCH), 3.52 (s, 3 H, CH_3O), 3.55 (d, 1 H, J = 5, MeOCH), 3.67 (s, 3 H, $COOCH_3$); IR (neat) 1735, 1270, 1140, 1095, 665; MS 188 (M^+ – MeOH, 25), 149 (54), 145 (25), 119 (29), 75 (79), 73 (29), 59 (54), 51 (100); HRMS calcd for $C_9H_{16}O_2S$ (M – MeOH) 188.0872, found 188.0903.

4-Methoxy-5-(methylthio)-1-hexene (3g): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.27 (d, 3 × 0.25 H, J = 7, CH_3CH), 1.28 (d, 3 × 0.75 H, J = 7, CH_3CH), 2.13 (s, 3 × 0.75 H, CH_3S), 2.14 (s, 3 × 0.25 H, CH_3S), 2.22–2.35 (m, 1 H, CH_2=CHCHH), 2.41–2.51 (m, 1 H, CH_2=CHCHH), 2.78–2.85 (m, 0.75 H, MeSCH), 2.85–2.92 (m, 0.25 H, MeSCH), 3.24–3.32 (m, 1 H, MeOCH), 3.39 (s, 3 × 0.25 H, CH_3O), 3.42 (s, 3 × 0.75 H, CH_3O), 5.03–5.17 (m, 2 H, CH_2=CH), 5.78–5.92 (m, 1 H, CH_2=CH); IR (neat) 1640, 1455, 1195, 915; MS 160 (M^+, 8), 128 (M^+ – MeOH, 40), 119 (53), 85 (100), 75 (20), 71 (15), 55 (27), 41 (16); HRMS calcd for $C_8H_{16}OS$ 160.0922, found 160.0927.

5-Methoxy-2,2-dimethyl-6-(methylthio)-3-octanone (3h): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.07 (t, 3 H, J = 7, CH_3CH_2), 1.16 (s, 9 × 0.98 H, $(CH_3)_3C$), 1.17 (s, 9 × 0.02 H, $(CH_3)_3C$), 1.43 (qdd, 1 H, J = 7, 9, 15, MeCHH), 1.65 (dqd, 1 H, J = 5, 7, 15, MeCHH), 2.11 (s, 3 H, CH_3S), 2.59 (td, 1 H, J = 5, 9, MeSCH), 2.65 (dd, 1 H, J = 4, 17, CHHCO), 2.95 (dd, 1 H, J = 8, 17, CHHCO), 3.33 (s, 3 × 0.02 H, CH_3O), 3.35 (s, 3 × 0.98 H, CH_3O), 3.91 (ddd, 1 H, J = 4, 5, 8, MeOCH); ^{13}C-NMR ($CDCl_3$) for the anti isomer, 12.3, 14.5, 23.8, 26.3, 39.4, 44.4, 52.7, 58.3, 80.0, 214.1; IR (neat) 1710, 1480, 1465, 1370, 1100; MS 200 (M^+ – MeOH, 27), 115 (21), 89 (33), 85 (39), 57 (100), 41 (28); HRMS calcd for $C_{11}H_{20}OS$ (M – MeOH) 200.1235, found 200.1237.

5-Methoxy-2,2-dimethyl-6-(methylthio)-7-phenyl-3-heptanone (3i): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.13 (s, 9 × 0.1 H, $(CH_3)_3C$), 1.15 (s, 9 × 0.9 H, $(CH_3)_3C$), 1.96 (s, 3 × 0.1 H, CH_3S), 2.00 (s, 3 × 0.9 H, CH_3S), 2.63–2.74 (m, 2 H, $PhCH_2$), 2.93–3.01 (m, 3 H, CH_2CO and MeSCH), 3.34 (s, 3 × 0.1 H, CH_3O), 3.34 (s, 3 × 0.9 H, CH_3O), 3.78 (td, 0.1 H, J = 6, 12, MeOCH), 3.97 (td, 0.9 H, J = 4, 8, MeOCH), 7.16–7.32 (m, 5 H, phenyl); IR (neat) 1710, 1480, 1460, 1370, 1110, 1090, 755, 705, 670; MS 262 (M^+ – MeOH, 65), 177 (27), 151 (61), 91 (32), 85 (50), 57 (100); HRMS calcd for $C_{16}H_{22}OS$ (M – MeOH) 262.1392, found 262.1422. Anal. Calcd for $C_{18}H_{26}O_2S$: C, 69.34; H, 8.90. Found: C, 69.63; H, 8.85.

5-Methoxy-2,2-dimethyl-6-(methylthio)-6-phenyl-3-hexanone (3j): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.07 (s, 9 × 0.59 H, $(CH_3)_3C$), 1.15 (s, 9 × 0.41 H, $(CH_3)_3C$), 1.91 (s, 3 × 0.59 H, CH_3S), 1.92 (s, 3 × 0.41 H, CH_3S), 2.60 (dd, 0.41 H, J = 5, 10, CHHCO), 2.65 (dd, 0.41 H, J = 5, 10, CHHCO), 2.74 (dd, 0.59 H, J = 7, 17, CHHCO), 2.87 (dd, 0.59 H, J = 7, 17, CHHCO), 3.25 (s, 3 × 0.41 H, CH_3O), 3.39 (s, 3 × 0.59 H, CH_3O), 3.89 (m, 1 H, MeSCH), 4.11 (m, 1 H, MeOCH), 7.20–7.40 (m, 5 H, phenyl); IR (neat) 1710, 1370, 1110, 1090, 705; MS 248 (M^+ – MeOH, 11), 163 (13), 137 (22), 115 (33), 57 (100), 41 (35); HRMS calcd for $C_{15}H_{20}OS$ (M – MeOH) 248.1235, found 248.1197. Anal. Calcd for $C_{16}H_{24}O_2S$: C, 68.53; H, 8.63. Found: C, 68.56; H, 8.75.

5-Methoxy-2,2,7-trimethyl-6-(methylthio)-3-octanone (3k): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.03 (d, 3 × 0.59 H, J = 7, CH_3CHCH_3), 1.04 (d, 3 × 0.59 H, J = 6, CH_3CHCH_3), 1.08 (d, 3 × 0.41 H, J = 7, CH_3CHCH_3), 1.09 (d, 3 × 0.41 H, J = 7, CH_3CHCH_3), 1.16 (s, 9 × 0.59 H, $(CH_3)_3C$), 1.17 (s, 9 × 0.41 H, $(CH_3)_3C$), 1.96 (m, 0.59 H, Me_2CH), 2.06 (m, 0.41 H, Me_2CH), 2.09 (s, 3 × 0.41 H, CH_3S), 2.16 (s, 3 × 0.59 H, CH_3S), 2.28 (dd, 0.41 H, J = 3, 7, MeSCH), 2.47 (t, 0.59 H, J = 6, MeSCH), 2.69 (dd, 0.59 H, J = 3, 17, CHHCO), 2.89 (dd, 0.41 H, J = 8, 17, CHHCO), 2.99 (dd, 0.59 H, J = 8, 17, CHHCO), 3.08 (dd, 0.41 H, J = 7, 17, CHHCO), 3.31 (s, 3 × 0.41 H, CH_3O), 3.34 (s, 3 × 0.59 H, CH_3O), 3.98 (ddd, 0.59 H, J = 3, 6, 8, MeOCH), 4.03 (ddd, 0.41 H, J = 3, 7, 8, MeOCH); IR (neat) 1710, 1365, 1100; MS 214 (M^+ – MeOH, 38), 129 (26), 103 (69), 85 (63), 57 (100), 55 (20); HRMS calcd for $C_{11}H_{22}OS$ (M – MeOH) 214.1391, found 214.1389.

Methyl 3-methoxy-2,2,5-trimethyl-4-(methylthio)hexanoate (3l): ^{1}H NMR ($CDCl_3$, 400 MHz) 0.96 (d, 3 H, J = 7, CH_3CHCH_3), 1.06 (d, 3 H, J = 7, CH_3CHCH_3), 1.15 (s, 3 H, CH_3CCH_3), 1.26 (s, 3 H, CH_3CCH_3), 2.09 (s, 3 H, CH_3S), 2.25–2.33 (m, 2 H, Me_2CH overlapping MeSCH), 3.53 (s, 3 H, CH_3O), 3.60 (d, 1 H, J = 8, MeOCH), 3.65 (s, 3 H, $COOCH_3$); IR (neat) 1730, 1275, 1140, 1095; MS 248 (M^+, 17), 216 (M^+ – MeOH, 15), 149 (76), 145 (73), 138 (54), 103 (24), 75 (59), 55 (100); HRMS calcd for $C_{12}H_{24}O_3S$ 248.1446, found 248.1435.

5-(*tert*-Butylthio)-4-methoxy-1-hexene (3m): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.32 (d, 3 H, J = 7, CH_3CH), 1.33 (s, 9 × 0.97 H, $(CH_3)_3C$), 1.36 (s, 9 × 0.03 H, $(CH_3)_3C$), 2.28 (pseudo td, 1 H, J = 7, 14, CH_2=CHCHH), 2.41 (pseudo td, 1 H, J = 7, 14, CH_2=CHCHH), 2.83 (dq, 1 H, J = 4, 7, MeCH), 3.28 (dt, 1 H, J = 4, 7, MeOCH), 3.41 (s, 3 × 0.03 H, CH_3O), 3.43 (s, 3 × 0.97 H, CH_3O), 5.06–5.16 (m, 2 H, CH_2=CH), 5.78–5.89 (m, 1 H, CH_2=CH); IR (neat) 1640, 1460, 1365, 1090, 915; MS 202 (M^+, 3), 170 (M^+ – MeOH, 14), 145 (34), 117 (28), 114 (45), 105 (63), 85 (91), 57 (100); HRMS calcd for $C_{11}H_{22}OS$ 202.1391, found 202.1367.

4-Methoxy-5-(methylthio)-1-nonene (3n): ^{1}H NMR ($CDCl_3$, 400 MHz) 0.92 (t, 3 H, J = 7, CH_3CH_2), 1.26–1.70 (m, 6 H, $-(CH_2)_3-$), 2.11 (s, 3 × 0.88 H, CH_3S), 2.12 (s, 3 × 0.12 H, CH_3S), 2.36 (pseudo quintet, 1 H, J = 7, CH_2=CHC*H*H), 2.50 (pseudo quintet, 1 H, J = 7, CH_2=CHCH*H*), 2.62 (pseudo quintet, 1 H, J = 4, MeSC*H*), 3.33 (dt, 1 H, J = 4, 7, MeOC*H*), 3.38 (s, 3 × 0.12 H, CH_3O), 3.40 (s, 3 × 0.88 H, CH_3O), 5.08 (dm, 1 H, J = 10, C*H*H=CH), 5.12 (dm, 1 H, J = 17, CH*H*=CH), 5.86 (tdd, 1 H, J = 7, 10, 17, CH_2=C*H*); IR (neat) 1640, 1460, 1435, 1095, 910; MS 202 (M^+, 14), 161 (22), 123 (17), 117 (26), 85 (100), 81 (26), 71 (15), 61 (18); HRMS calcd for $C_{11}H_{22}OS$ 202.1392, found 202.1383.

5-Methoxy-2,2-dimethyl-6-(phenylthio)-7-nonen-3-one (3o): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.13 (s, 9 × 0.87 H, $(CH_3)_3C$), 1.14 (s, 9 × 0.13 H, $(CH_3)_3C$), 1.62 (dd, 3 H, J = 1, 6, CH_3CH=CH), 2.64 (dd, 0.87 H, J = 6, 18, C*H*HCO), 2.82 (dd, 0.13 H, J = 5, 17, C*H*HCO), 2.88 (dd, 0.13 H, J = 8, 17, CH*H*CO), 2.89 (dd, 0.87 H, J = 7, 18, CH*H*CO), 3.35 (s, 3 × 0.13 H, CH_3O), 3.39 (s, 3 × 0.87 H, CH_3O), 3.77 (dd, 0.87 H, J = 4, 10, PhSC*H*), 3.81 (dd, 0.13 H, J = 4, 8, PhSC*H*), 3.97 (ddd, 0.13 H, J = 4, 5, 8, MeOC*H*), 4.00 (ddd, 0.87 H, J = 4, 6, 7, MeOC*H*), 5.33 (qd, 0.87 H, J = 6, 15, MeC*H*=CH), 5.39–5.53 (m, 0.87 + 2 × 0.13 H, olefin), 7.20–7.52 (m, 5 H, phenyl); IR (neat) 1705, 1580, 1480, 1370, 1090, 970, 740, 690.

(5*R,6*S**)-5-Methoxy-2,2-dimethyl-6-(phenylthio)-7-nonen-3-one (*anti*-3o)**: colorless prisms (EtOH); mp 76 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 1.13 (s, 9 H, $(CH_3)_3C$), 1.62 (dd, 3 H, J = 1, 6, CH_3CH=CH), 2.64 (dd, 1 H, J = 6, 18, C*H*HCO), 2.89 (dd, 1 H, J = 7, 18, CH*H*CO), 3.39 (s, 3 H, CH_3O), 3.77 (dd, 1 H, J = 4, 10, PhSC*H*), 4.00 (ddd, 1 H, J = 4, 6, 7, MeOC*H*), 5.33 (qd, 1 H, J = 6, 15, MeC*H*=CH), 5.47 (ddd, 1 H, J = 1, 10, 15, MeCH=C*H*), 7.20–7.32 (m, 3 H, phenyl), 7.38–7.43 (m, 2 H, phenyl). Anal. Calcd for $C_{18}H_{26}O_2S$: C, 70.40; H, 8.52. Found: C, 70.55; H, 8.55.

2-[1-Methoxy-2-(phenylthio)propyl]cyclohexanone (3p). The reaction mixture of **1a** (261 mg, 1.23 mmol) and **2e** (245 mg, 1.44 mmol) was purified by preparative TLC (eluent: EtOAc/hexane = 1/10) to give two fractions, A (R_f = 0.5, 237 mg) and B (R_f = 0.4, 81 mg). GC analysis indicated each fraction consists of two components; relative abundance was 77:23 for fraction A, and 81:19 for B. We assigned the fraction A as the 2,3-syn isomer and B as the 2,3-anti isomer on the basis of known chromatographic tendency for 1-methoxyalkylcyclohexanones.[3a]

Anal. Calcd for $C_{16}H_{22}O_2S$: C, 69.02; H, 7.96. Found: C, 68.84; H, 7.97 for fraction A; C, 69.30; H, 8.05 for fraction B.

(2*R,1′*R**,2′*S**)-2-[1-Methoxy-2-(phenylthio)propyl]cyclohexanone (2,3-*syn*-3,4-*anti*-3p)**. The major isomer of fraction A, obtained as mentioned above, slowly crystallized upon standing. Then, it was recrystallized from EtOH: colorless hexagonal plates; mp 73 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 1.30 (d, 3 H, J = 7, CH_3CH), 1.50–1.74 (m, 3 H), 1.84–2.42 (m, 5 H), 2.81 (pseudo td, 1 H, J = 5, 10, COC*H*), 3.36 (quintet, 1 H, J = 7, PhSC*H*), 3.48 (s, 3 H, CH_3O), 3.79 (dd, 1 H, J = 5, 6, MeOC*H*), 7.21–7.33 (m, 3 H, phenyl), 7.42–7.45 (m, 2 H, phenyl); IR (KBr) 1705, 1090, 1085, 750; MS 278 (M^+, 2), 246 (M^+ – MeOH, 12), 180 (22), 141 (33), 137 (85), 109 (51), 81 (100), 67 (42); HRMS calcd for $C_{16}H_{22}O_2S$ 278.1340, found 278.1362.

Assignable ^{1}H-NMR peaks for other isomers of **3p** ($CDCl_3$, 400 MHz): fraction A(minor), 1.39 (d, J = 6, CH_3), 3.90–3.98 (m, MeOC*H*); fraction B(major), 1.34 (d, J = 7, CH_3), 3.52 (dq, J = 4.9, 7.0, PhSC*H*), 3.55 (s, CH_3O), 3.60 (dd, J = 5, 6, MeOC*H*); fraction B(minor) 1.31 (d, J = 7, CH_3).

5-Isopropoxy-2,2-dimethyl-6-(phenylthio)-3-heptanone (3q): 63% yield; ^{1}H NMR (CCl_4, 60 MHz) 0.9–1.5 (m, 9 H), 1.1 (s, 9 H, $(CH_3)_3C$), 2.6–2.9 (m, 2 H, CH_2CO), 3.1–4.3 (m, 3 H), 7.2–7.6 (m, 5 H); MS 308 (M^+, 1), 248 (M^+ – *i*-PrOH, 8), 208 (3), 163 (7), 137 (17), 129 (21), 85 (45), 57 (100).

5-Methoxy-2,2-dimethyl-6-phenyl-6-(phenylthio)-3-hexanone (3r): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.06 (s, 9 × 0.21 H, $(CH_3)_3C$), 1.07 (s, 9 × 0.79 H, $(CH_3)_3C$), 2.56 (dd, 0.21 H, J = 5, 17, C*H*HCO), 2.81 (d, 2 × 0.79 H, J = 6, CH_2CO), 2.87 (dd, 0.21 H, J = 7, 17, CH*H*CO), 3.31 (s, 3 × 0.21 H, CH_3O), 3.31 (s, 3 × 0.79 H, CH_3O), 4.14–4.20 (m, 1 H, MeOC*H*), 4.37 (d, 0.79 H, J = 5, PhSC*H*), 4.42 (d, 0.21 H, J = 6, PhSC*H*), 7.09–7.40 (m, 10 H, phenyl); IR (neat) 1705, 1480, 1110, 1090, 740, 700; MS 310 (M^+ – MeOH, 9), 225 (21), 199 (31), 115 (16), 91 (12), 85 (32), 57 (100); HRMS calcd for $C_{20}H_{22}OS$ (M – MeOH) 310.1392, found 310.1377.

Methyl 3-methoxy-2,2-dimethyl-4-phenyl-4-(phenylthio)-butanoate (3s): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.19 (s, 3 × 0.65 H, CH_3CCH_3), 1.20 (s, 3 × 0.35 H, CH_3CCH_3), 1.22 (s, 3 × 0.65 H, CH_3CCH_3), 1.33 (s, 3 × 0.35 H, CH_3CCH_3), 3.20 (s, 3 × 0.65 H, CH_3O), 3.39 (s, 3 × 0.35 H, CH_3O), 3.64 (s, 3 × 0.35 H, CH_3O), 3.74 (s, 3 × 0.65 H, CH_3O), 3.96 (d, 1 H, J = 7, MeOC*H*), 4.10 (d, 0.65 H, J = 7, PhSC*H*), 4.39 (d, 0.35 H, J = 7, PhSC*H*), 7.11–7.31 (m, 8 H, phenyl), 7.38–7.41 (m, 2 H, phenyl); IR (neat) 1740, 1270, 1100, 745, 700; MS 344 (M^+, 5), 312 (M^+ – MeOH, 44), 235 (15), 199 (72), 175 (33), 145 (100), 91 (28), 75 (67); HRMS calcd for $C_{19}H_{20}O_2S$ (M – MeOH) 312.1184, found 312.1162.

6-(Benzyloxy)-5-methoxy-2,2-dimethyl-3-heptanone (5a): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.12 (s, 9 × 0.77 H, $(CH_3)_3C$), 1.13 (s, 9 × 0.23 H, $(CH_3)_3C$), 1.16 (d, 3 × 0.23 H, J = 6, CH_3(BnO)CH), 1.18 (d, 3 × 0.77 H, J = 6, CH_3(BnO)CH), 2.52–2.60 (m, 1 H, C*H*HCO), 2.74–2.86 (m, 1 H, CH*H*CO), 3.36 (s, 3 × 0.77 H, CH_3O), 3.38 (s, 3 × 0.23 H, CH_3O), 3.62–3.75 (m, 1 H, BnOC*H*), 3.79–3.85 (m, 0.23 H, MeOC*H*), 3.90 (pseudo quintet, 0.77 H, J = 4, MeOC*H*), 4.48 (d, 1 H, J = 12, PhC*H*H), 4.60 (d, 1 H, J = 12, PhCH*H*), 7.23–7.38 (m, 5 H, phenyl); IR (neat) 1710, 1455, 1365, 1100, 1070, 740, 700, 665. Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.41. Found: C, 73.19; H, 9.22.

Methyl 4-(benzyloxy)-3-methoxy-2,2-dimethylpentanoate (5b): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.10 (s, 3 × 0.4 H, CH_3CCH_3), 1.14 (s, 3 × 0.6 H, CH_3CCH_3), 1.16 (d, 3 × 0.6 H, J = 6, CH_3CH), 1.21 (s, 3 × 0.4 H, CH_3CCH_3), 1.28 (s, 3 × 0.6 H, CH_3CCH_3), 1.29 (d, 3 × 0.4 H, J = 7, CH_3CH), 3.36 (s, 3 × 0.4 H, CH_3O), 3.41 (d, 0.6 H, J = 6, MeOC*H*), 3.43 (d, 0.4 H, J = 9, MeOC*H*), 3.52 (s, 3 × 0.4 H, $COOCH_3$), 3.55 (s, 3 × 0.6 H, $COOCH_3$), 3.61 (s, 3 × 0.6 H, CH_3O, overlapping m, 1 H, MeC*H*), 4.32 (d, 0.4 H, J = 11, PhC*H*H), 4.49 (pseudo d, 1 H, J = 11, PhCH*H*), 4.58 (d, 0.6 H, J = 11, PhC*H*H), 7.23–7.38 (m, 5 H, phenyl); IR (neat) 1740, 1145, 1100, 740, 700. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63. Found: C, 68.42; H, 8.62.

5-(Benzyloxy)-4-methoxy-1-hexene (5c): ^{1}H NMR ($CDCl_3$, 400 MHz) 1.17 (d, 3 × 0.63 H, J = 6, CH_3CH), 1.21 (d, 3 × 0.37 H, J = 6, CH_3CH), 2.19–2.42 (m, 2 H, CH_2=CHC*H*$_2$), 3.22 (td, 0.63 H, J = 5, 8, MeOC*H*), 3.26 (td, 0.37 H, J = 5, 7, MeOC*H*), 3.41 (s, 3 × 0.63 H, CH_3O), 3.42 (s, 3 × 0.37 H, CH_3O), 3.55 (dq, 0.37 H, J = 5, 6, BnOC*H*), 3.62 (dq, 0.63 H, J = 5, 6, BnOC*H*), 4.50 (d, 0.37 H, J = 12, PhC*H*H), 4.51 (d, 0.63 H, J = 12, PhC*H*H), 4.60 (d, 0.37 H, J = 12, PhCH*H*), 4.62 (d, 0.63 H, J = 12, PhCH*H*), 5.01–5.12 (m, 2 H, CH_2=CH), 5.77–5.90 (m, 1 H, CH_2=C*H*), 7.22–7.40 (m, 5 H, phenyl); IR (neat) 1645, 1460, 1100, 920, 740, 700. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.04; H, 9.01.

(5*R,8*S**,6*E*)-8-Hydroxy-5-methoxy-2,2-dimethyl-6-nonen-3-one (*anti*-6)**. To a solution of *anti*-**3o** (92.8 mg, 0.30 mmol) in CH_2Cl_2 (2 mL) was added drop by drop a CH_2Cl_2 (2 mL) solution of *m*-CPBA (80% purity, 69.6 mg, 0.32 mmol) at 0 °C. The mixture was stirred for 15 min at the temperature and then poured into saturated aqueous $NaHCO_3$ solution (10 mL). The organic materials were extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4. After evaporation, the residue was dissolved in MeOH (5 mL), and Et_2NH (0.2 mL, 1.9 mmol) was added. The mixture was stirred for 12 h and concentrated. Purification by preparative TLC (EtOAc/hexane = 1/3; repeated three times) gave 30.5 mg (47% yield) of allyl alcohol *anti*-6: ^{1}H NMR ($CDCl_3$, 400 MHz) 1.12 (s, 9 H, $(CH_3)_3C$), 1.28 (d, 3 H, J = 6, CH_3CHOH), 2.17 (br s, 1 H, O*H*), 2.49 (dd, 1 H, J = 5, 17, C*H*H), 2.89 (dd, 1 H, J = 7, 17, CH*H*), 3.25 (s, 3 H, CH_3O), 4.13 (pseudo dt, 1 H, J = 5, 7, MeOC*H*), 4.33 (pseudo quintet, J = 6, C*H*OH), 5.54 (ddd, 1 H, J = 1, 7, 16, C*H*=CH), 5.79 (dd, 1 H, J = 6, 16, CH=C*H*); IR (neat) 3450 (br), 1715, 1480, 1370, 1100, 975; MS 196 (23), 149 (53), 121 (23), 115 (27), 97 (40), 81 (48), 69 (92), 67 (35), 57 (100); HRMS calcd for $C_{12}H_{20}O_2$ (M – H_2O) 196.1463, found 196.1460.

(3*R,4*S**)-3-Methoxy-4-(methanesulfonyl)-2,2-dimethylpentyl 3,5-Dinitrobenzoate (7)**. To a solution of lithium aluminum hydride (0.08 g, 2.10 mmol) in ether (4 mL) was added a solution of ester **3f** (0.39 g, 1.78 mmol) in ether (3 mL). After the exothermic reaction ceased, EtOAc (10 mL) and saturated aqueous NH_4Cl solution (0.5 mL) were successively added to the

mixture. Filtration through the Celite pad followed by evaporation gave a crude oil (0.34 g, 99% yield), which was essentially pure judging from its ^{1}H NMR. The alcohol (0.31 g, 1.61 mmol) and pyridine (0.16 g, 2.05 mmol) were dissolved in benzene (4 mL). To this solution was added a benzene (4 mL) solution of 3,5-dinitrobenzoyl chloride (0.38 g, 1.65 mmol) at 0 °C. The reaction mixture was allowed to warm to rt and stirred overnight. After aqueous workup, the organic layer was dried and concentrated to give the crude material, which was in turn dissolved in benzene (10 mL). To the solution was added $VO(acac)_2$ (0.5 g, 1.89 mmol) and *t*-BuOOH (4.36 *M* solution in isooctane, 0.8 mL, 3.49 mmol), and then the mixture was stirred for 3 h at rt. Usual aqueous workup followed by recrystallization from EtOH gave 0.38 g (56% overall yield from alcohol) of **7** as yellow needles: mp 142 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 1.10 (s, 3 H, CH_3CCH_3), 1.12 (s, 3 H, CH_3CCH_3), 1.47 (d, 3 H, J = 7, $CH_3(MeSO_2)CH$), 2.94 (s, 3 H, CH_3SO_2), 3.27 (dq, 1 H, J = 2, 7, MeC*H*), 3.51 (s, 3 H, CH_3O), 3.91 (d, 1 H, J = 2, MeOC*H*), 4.32 (s, 2 H, CH_2), 9.14 (d, 2 H, J = 2, phenyl), 9.23 (t, 1 H, J = 2, phenyl); IR (KBr) 1737, 1555, 1350, 1310, 1290, 1175, 1140, 960, 725, 500; MS 418 (M^+, 1), 311 (7), 195 (19), 151 (100), 99 (11), 89 (12), 87 (16), 72 (34), 71 (15); HRMS calcd for $C_{16}H_{22}N_2O_9S$ 418.1046, found 418.1085.

(5*R,6*R**)-6-(Benzenesulfonyl)-5-methoxy-2,2-dimethyl-6-phenyl-3-hexanone (8).** The major diastereomer of **3r** (17.0 mg, 55 μmol), which was isolated by preparative TLC, was treated with $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (0.09 g, 145 μmol) according to the method in the literature[32] to give 18.0 mg (96% yield) of sulfone **8**: colorless needles (EtOH); mp 133 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 0.97 (s, 9 H, $(CH_3)_3C$), 2.62 (dd, 1 H, J = 6, 18, C*H*HCO), 2.69 (dd, 1 H, J = 4, 18, CH*H*CO), 3.36 (s, 3 H, CH_3O), 4.53 (d, 1 H, J = 8, PhSC*H*), 4.73 (ddd, 1 H, J = 4, 6, 8, MeOC*H*), 7.22–7.26 (m, 5 H, phenyl), 7.37 (tm, 2 H, J = 7, phenyl), 7.49 (tm, 1 H, J = 7, phenyl), 7.65 (dm, 2 H, J = 7, phenyl); IR (KBr) 1705, 1315, 1295, 1150, 1105, 770, 700. Anal. Calcd for $C_{21}H_{26}O_4S$: C, 67.35; H, 7.00; S, 8.56. Found: C, 67.10; H, 6.96; S, 8.34.

Methyl 3-Hydroxy-2,2-dimethyl-4-phenyl-4-(phenylthio)-butanoate (9). To a mixture of 2-phenyl-2-(phenylthio)-acetaldehyde (0.79 g, 3.5 mmol) and **2c** (0.75 g, 4.3 mmol) in CH_2Cl_2 (8 mL) was added $BF_3 \cdot OEt_2$ (0.98 g, 6.9 mmol) at −78 °C. The mixture was stirred for 1 h, and saturated aqueous $NaHCO_3$ (10 mL) was added. The organic materials were extracted by CH_2Cl_2 (2 × 10 mL) and the extracts were dried over Na_2SO_4 and concentrated. Column chromatography (EtOAc/hexane = 1/10) gave 0.91 g (80%) of **9** as a 9/1 mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 400 MHz) 1.13 (s, 3 × 0.1 H, CH_3CCH_3), 1.18 (s, 3 × 0.9 H, CH_3CCH_3), 1.23 (s, 3 × 0.9 H, CH_3CCH_3), 1.27 (s, 3 × 0.1 H, CH_3CCH_3), 3.28 (br, 1 H, O*H*), 3.29 (s, 3 × 0.9 H, CH_3O), 3.49 (s, 3 × 0.1 H, CH_3O), 4.07 (dd, 0.9 H, J = 4, 7, C*H*OH), 4.12 (t, 0.1 H, J = 6, C*H*OH), 4.22 (d, 0.1 H, J = 6, PhC*H*), 4.33 (d, 0.9 H, J = 4, PhC*H*), 7.17–7.40 (m, 10 H, phenyl).

(3*R,4*S**)-3-Hydroxy-2,2-dimethyl-4-phenyl-4-(phenylthio)butyl 3,5-Dinitrobenzoate (10).** Ester **9** (109.6 mg, 0.33 mmol) obtained above was treated with lithium aluminum hydride (0.1 g, 2.6 mmol) in ether (5 mL) to give 86.2 mg (86% yield) of 2,2-dimethyl-4-phenyl-4-(phenylthio)-1,3-butanediol as a 9/1 mixture of the diastereomers: ^{1}H NMR ($CDCl_3$, 400 MHz) 0.61 (s, 3 × 0.9 H, CH_3CCH_3), 0.70 (s, 3 × 0.1 H, CH_3CCH_3), 0.91 (s, 3 × 0.9 H, CH_3CCH_3), 0.95 (s, 3 × 0.1 H, CH_3CCH_3), 2.60 (br, 1 H, O*H*), 3.23 (ABq, 2 × 0.9 H, J = 14, CH_2OH), 3.40 (br, 1 H, O*H*), 3.44 (d, 0.1 H, J = 11, C*H*HOH), 3.58 (d, 0.1 H, J = 11, CH*H*OH), 3.91 (d, 0.9 H, J = 3, C*H*OH), 3.93 (d, 0.1 H, J = 6, C*H*OH), 4.30 (d, 0.1 H, J = 6, PhC*H*), 4.41 (d, 0.9 H, J = 3, PhC*H*), 7.71–7.48 (m, 10 H, phenyl).

The major isomer of the above diol (5.8 mg, 19 μmol) was dissolved in THF (1 mL), and to this solution were successively added pyridine (10 μL, 124 μmol) and a THF (0.5 mL) solution of 3,5-dinitrobenzoyl chloride (21 mg, 91 μmol) at rt. The mixture was stirred overnight and directly charged onto the preparative TLC (EtOAc/hexane = 1/1). Recrystallization of the main fraction from EtOH gave 6.6 mg (69% yield) of **10** as pale yellow prisms: mp 133 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 0.74 (s, 3 H, CH_3CCH_3), 1.02 (s, 3 H, CH_3CCH_3), 1.57 (br s, 1 H, O*H*), 3.83 (d, 1 H, J = 3, PhSC*H*), 4.01 (d, 1 H, J = 11, C*H*HOCO), 4.33 (d, 1 H, J = 11, CH*H*OCO), 4.43 (d, 1 H, J = 3, MeOC*H*), 7.08–7.50 (m, 10 H, phenyl), 8.98 (d, 2 H, J = 2, phenyl), 9.22 (t, 1 H, J = 2, phenyl); IR (KBr) 3450 (br), 1727, 1545, 1345, 1290, 1175, 720. Anal. Calcd for $C_{25}H_{24}N_2O_7S$: C, 60.47; H, 4.87; N, 5.64. Found: C, 60.25; H, 5.14; N, 5.58.

Acknowledgment. We thank Dr. Hiroki Kimoto for the X-ray crystal structure determination of compound *anti*-**3o**. A part of this work was financially supported by Sankyo Co., Ltd., Award in Synthetic Organic Chemistry, Japan.

Supplementary Material Available: ^{13}C NMR spectra for **1a**, **1f**, **1g**, **1k**, and **1l**; ^{1}H NMR spectra of **3a–d**, **3f–h**, **3k**, **3l**, **3n**, **3q–t**, *anti*-**6**, and **7**; full details on X-ray crystallographic analyses for compounds *anti*-**3o**, 2,3-*syn*-3,4-*anti*-**3p**, **7**, **8**, and **10** (39 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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