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Synthesis and Biological Activity of Enantiomeric Pairs of 5-(Alk-2-enyl)thiolactomycin and 5-[(*E*)-Cycloalk-2-enylidenemethyl]thiolactomycin Congeners[1,2)]

Kohei OHATA*,[a] and Shiro TERASHIMA[b]

[a] *Discovery Research Laboratories, Kyorin Pharmaceutical Co., Ltd.; 2399–1 Nogi, Nogi-machi, Shimotsuga, Tochigi 329–0114, Japan: and* [b] *Sagami Chemical Research Center; 2743–1 Hayakawa, Ayase, Kanagawa 252–1193, Japan.*

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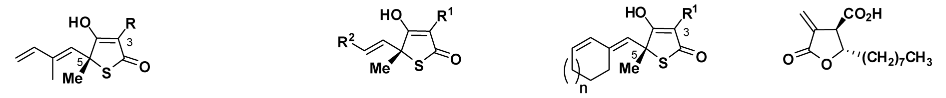
The title compounds were synthesized by the efficient route previously explored for the synthesis of enantiomeric pairs of thiolactomycin and its 3-demethyl derivative. These studies were carried out to prove the flexibility of the previously explored synthetic route to natural thiolactomycin (TLM) 1 and to examine the structure–activity relationship on the 5-position of 1. While all of the synthesized congeners lacked *in vitro* antibacterial activity, these studies led us to find 5-(alk-2-enyl)-TLM (*ent*-4d) which exhibits mammalian type I fatty acid synthase (FAS) inhibitory activity equal to that of C75, a potent inhibitor reported previously. It was also found that 5-[(*E*)-cycloalk-2-enylidenemethyl]-TLM (*ent*-5c) exhibited slightly less potent mammalian type I FAS inhibitory activity than C75.

Key words thiolactomycin; type I fatty acid synthase inhibitor; 5-(alk-2-enyl)thiolactomycin; 5-[(*E*)-cycloalk-2-enylidenemethyl]thiolactomycin

(*R*)-(+)-Thiolactomycin (TLM, **1**), a thiolactone antibiotic isolated from a soil bacterium, *Nocardia* sp.,[3)] shows moderate *in vitro* activity against a number of pathogens, including Gram-positive and Gram-negative bacteria,[4,5)] *Mycobacterium tuberculosis*[6,7)] and malaria parasites[8,9)] (Fig. 1). According to published reports,[10—13)] **1** exhibits inhibitory activity against bacterial and plant type II fatty acid synthase (FAS) but not mammalian type I FAS. In studies done in greater detail, **1** appeared to act by inhibiting β-ketoacyl-acyl carrier protein synthases.[6,11,14)] These inhibitory activities are thought to explain the antibacterial and antiparasitical properties observed for **1**. Interestingly, Townsend and colleagues recently disclosed that **1** and its derivatives also show inhibitory activity against mammalian type I FAS.[15)] Syntheses and screenings of various structural types of TLM congeners have been reported [6—9,15—21)] because these compounds seem to constitute promising drug candidates, with hitherto unexplored modes of action, for the treatment of cancer, obesity, and infectious diseases. However, probably due to the lack of an efficient synthetic route,[22—25)] very few studies have examined biological activity by utilizing optically active compounds.[16)]

We recently reported an efficient total synthesis of **1** and its 3-demethyl congener (3-demethyl-TLM, **2**) by employing a novel deconjugative asymmetric α-sulfenylation of the chiral 3-($\alpha,\beta,\gamma,\delta$-unsaturated-acyl)oxazolidin-2-one with a methanethiosulfonate as a key step.[26,27)] The flexibility of the explored synthetic route has been realized by the expeditious synthesis of (*S*)-TLM (*ent*-**1**) and (*S*)-3-demethyl-TLM (*ent*-**2**) in addition to that of **1** and **2**. From the biological activity assay carried out using **1**, *ent*-**1**, **2** and *ent*-**2**, it was evident that the *in vitro* antibacterial and type I FAS inhibitory activity of TLM congeners can be cleanly separated by changing not only the structure at the C_3-position but also the absolute configuration of the side chain at the C_5-position.[1,27)] In the course of our continuing studies on the synthesis and biological activity of **1** and its congeners from the viewpoint of medicinal chemistry, we paid attention to the effects of the structure and absolute configuration of the side chain at the C_5-position of **1** on *in vitro* antibacterial and mammalian type I FAS inhibitory activity. Therefore, enantiomeric pairs of 5-(alk-2-enyl)thiolactomycins [5-(alk-2-enyl)-TLMs] and their 3-demethyl congeners [3-demethyl-5-(alk-2-enyl)-TLMs] (**3**, *ent*-**3**, **4**, *ent*-**4**) were designed so that we could learn extensively about the structure–activity relationships of the C_5-position of **1**. We also focused our attention on the conformational effects of the isoprenoid 1,3-diene moiety at the C_5-position of **1** on *in vitro* antibacterial and mammalian type I FAS inhibitory activity. Accordingly, we next targeted the synthesis of enantiomeric pairs of 5-[(*E*)-cycloalk-2-enylidenemethyl]thiolactomycins {5-[(*E*)-cycloalk-2-enylidenemethyl]-TLMs} and their 3-demethyl congeners {5-[(*E*)-cycloalk-2-enylidenemethyl]-3-demethyl-TLMs} (**5**, *ent*-**5**, **6**, *ent*-**6**) bearing six- to eight-membered rings.[28)] In these compounds, the isoprenoid 1,3-diene moiety present in **1** is clearly locked into an *s-trans* configuration as a consequence of their involvement in a ring system. We also expected that the successful synthesis of enantiomeric pairs of **3**, **4**, **5** and **6**



(*R*)-(+)-thiolactomycin (**1**): R = Me
(*R*)-(+)-3-demethylthiolactomycin (**2**): R = H

3: R^1 = Me; **4**: R^1 = H
a: R^2 = H; **b**: R^2 = Me; **c**: R^2 = Et;
d: R^2 = *n*Pr; **e**: R^2 = *n*Bu; **f**: R^2 = *n*Hex

5: R^1 = Me; **6**: R^1 = H
a: n = 1; **b**: n = 2; **c**: n = 3.

C75

Fig. 1. Structures of (*R*)-(+)-Thiolactomycin (**1**) and Its 3-Demethyl Congener (**2**), 5-(Alk-2-enyl)thiolactomycins and Their 3-Demethyl Congeners (**3**, **4**), 5-[(*E*)-Cycloalk-2-enylidenemethyl]thiolactomycins and Their 3-Demethyl Congeners (**5**, **6**) and C75

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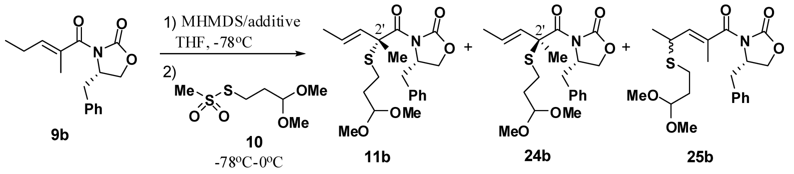
* To whom correspondence should be addressed. e-mail: kouhei.oohata@mb.kyorin-pharm.co.jp

Table 1. Deconjugative Asymmetric α-Sulfenylation of the (*S*)-*N*-Acyloxazolidin-2-one **9b** with *S*-3,3-Dimethoxypropyl Thiosulfonate **10**



Run	Base	Additive (eq)	Yield of the α-sulfenylated products		Yield of **25b** (%)[a]
			11b (%)	**24b** (%)	
1	NaHMDS	HMPA (4)	24	19	25
2	NaHMDS	None	61	5	13
3	KHMDS	None	74	6	8

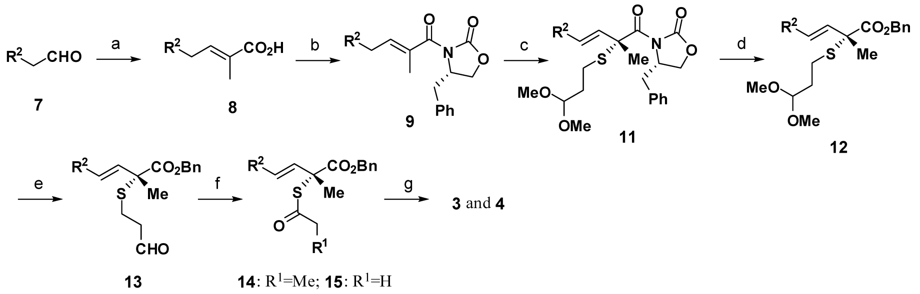
a) These samples were mixures of the two diastereoisomers. The ratio of the diastereomers was *ca.* 6 : 1—1 : 1 by ^{1}H-NMR analysis.

might further substantiate the flexibility and efficiency of our synthetic scheme previously developed for **1** and its congener. We wish to report here the details of synthesis of enantiomeric pairs of **3**, **4**, **5** and **6** and the *in vitro* antibacterial and mammalian type I FAS inhibitory activity of these pairs. The results clearly disclosed novel aspects of the structure–activity relationships of the C_5-position of TLM and led us to explore *ent*-3-demethyl-5-(alk-2-enyl)-TLM (*ent*-**4d**) and *ent*-5-[(*E*)-cycloalk-2-enylidenemethyl]-TLM (*ent*-**5c**). The former congener *ent*-**4d** exhibited mammalian type I FAS inhibitory activity equal to that of C75, a potent inhibitor previously revealed,[15,29] and twice that of *ent*-**2** previously reported.[26,27] The latter congener *ent*-**5c** showed type I FAS inhibitory activity that was a little less potent than that of C75 and a little more potent than that of *ent*-**2**. All the congeners synthesized in these studies were found to completely lack *in vitro* antibacterial activity.

Results and Discussion

Synthesis of 5-Vinylthiolactomycins [5-(Alk-2-enyl)-TLMs], Their 3-Demethyl Congeners [3-Demethyl-5-(alk-2-enyl)-TLMs] and Their Enantiomers Following the synthetic scheme previously established,[26] we commenced the synthesis of (*R*)-5-(alk-2-enyl)-TLMs and (*R*)-3-demethyl-5-(alk-2-enyl)-TLMs (**3a**—**f**, **4a**—**f**) (Chart 1). Among α,β-unsaturated carboxylic acids **8a**—**f** used as the starting materials for the synthesis of **3a**—**f** and **4a**—**f**, **8a**—**c** were commercially available while **8d**—**f** were prepared from the corresponding aldehydes **7d**—**f** by a sequential Horner–Wadsworth–Emmons reaction and alkaline hydrolysis in a method similar to that previously reported.[26,27] **8a**—**f** were transformed into (*S*)-*N*-acyloxazolidin-2-ones **9a**—**f** by first treating them with pivaloyl chloride, and the resulting mixed anhydrides were allowed to react with (*S*)-4-benzyloxazolidin-2-one.[30] The preliminarily successful synthesis of known *ent*-**3b**[22] by the use of (*R*)-4-benzyloxazolidin-2-one as a chiral source allowed us to select (*S*)-4-benzyloxazolidin-2-one as a chiral auxiliary for the synthesis of **3a**—**f** and **4a**—**f** (*vide infra*).

With **9a**—**f** in hand, we next examined the electrophilic deconjugative asymmetric α-sulfenylation using *S*-3,3-dimethoxypropyl thiosulfonate **10** as a sulfenylating agent, which constitutes the key synthetic step. Based on our previous results,[26,27] we expected **10** to be as an excellent electrophilic agent with the functional group readily transformable into a thiol. **10** was prepared starting with 3-bromopropionaldehyde dimethylacetal according to our previously reported procedure.[26,27] First, to secure the deconjugative asymmetric α-sulfenylation of **9** with **10**, the sulfenylation was examined by using **9b** as a model substrate and by employing various disilazide bases in a manner similar to that for the synthesis of **1** (Table 1). We found that the deconjugative asymmetric α-sulfenylation of **9b** took place smoothly by making use of potassium bis(trimethylsilyl)amide (KHMDS) as a base in the absence of hexamethylphosphoramide (HMPA), providing the α-sulfenylated compound **11b** in a stereoselective and regioselective manner along with the other α-sulfenylated product, **24b** diastereomeric to **11b**, and the γ-sulfenylated product, **25b** (Table 1, run 3). In our previous synthesis of **1**,[26,27] the deconjugative asymmetric α-sulfenylation was effected using sodium bis(trimethylsilyl)amide (NaHMDS) in the presence of HMPA. However, unexpectedly, when **9b** was treated under the same conditions (Table 1, run 1), the sulfenylation was found to occur in a lower yield along with a lower diastereo- and regioselectivity. The sulfenylation of **9a**, **c**—**f** also showed a low selectivity similar to that of **9b**. It was anticipated that the stereo and/or electronic difference between the dienolate derived from **9b** and the trienolate **I** (Fig. 2) presumed to be involved in the synthesis of **1** might make the transition state of sulfenylation different even under the same condition (Table 1, run 1). Thus it was presumed that the reaction condition used for the synthesis of **1** would not be directly applied to the sulfenylation of **9b**. Therefore, the sulfenylation of **9b** was next examined in the absence of HMPA in order to improve the diastereo- and regioselectivity (Table 1, run 2). Gratifyingly, both diastereoselectivity of **11b** against **24b** and the regioselectivity of **11b** against **25b** were dramatically improved. Moreover, KHMDS was more effective than NaHMDS to further increase the chemical yield and regioselectivity, affording **11b**, **24b** and **25b** in 74%, 6% and 8% yields, respectively (Table 1, run 3). Separation of **11b**, **24b** and **25b** was accomplished by flash column chromatography. While **25b** was always obtained as a mixture of the two diastereomers, their separation was not attempted. The other (*S*)-*N*-acyloxazolidin-2-one **9a**, **c**—**f** were subjected to the same conditions as those optimized using **9b**, producing the α-sulfenylated compounds **11a**, **c**—**f** in the yields shown in Chart 1 along



a: R^2=H; **b**: R^2=Me; **c**: R^2=Et; **d**: R^2=*n*Pr; **e**: R^2=*n*Bu; **f**: R^2=*n*Hex

(a) $(EtO)_2P(O)CHMeCO_2Et$, *t*BuOLi, hexane, rt, then 10% NaOH aq., EtOH, 50 °C, 92% for **8d**, 100% for **8e**, 100% for **8f**; (b) *t*BuCOCl, Et_3N, THF, −15 °C, then LiCl, (*S*)-4-benzyoxazolidin-2-one, rt 83% for **9a**, 96% for **9b**, 90% for **9c**, 87% for **9d**, 96% for **9e**, 93% for **9f**; (c) KHMDS, THF, −78 °C, then *S*-3,3-dimethoxypropyl methanethiosulfonate (**10**), −78 to 0 °C, 18% for **11a**, 74% for **11b** (see Table 1), 60% for **11c**, 50% for **11d**, 61% for **11e**, 51% for **11f**; (d) $Ti(OiPr)_4$, BnOH, 70 °C, 82% for **12a**, 88% for **12b**, 95% for **12c**, 96% for **12d**, 89% for **12e**, 85% for **12f**; (e) 6% HCl aq., THF, rt, 98% for **13a**, 98% for **13b**, 98% for **13c**, 93% for **13d**, 66% for **13e**, 76% for **13f**; (f) Cs_2CO_3, EtOH, 4 °C, then CH_3CH_2COCl or CH_3COCl, Et_3N, CH_2Cl_2, 4 °C, 81% for **14a**, 74% for **14b**, 50% for **14c**, 61% for **14d**, 62% for **14e**, 50% for **14f**, 69% for **15a**, 68% for **15b**, 52% for **15c**, 73% for **15d**, 48% for **15e**, 36% for **15f**; (g) LiHMDS, THF, −78 °C-rt, 70% for **3a**, 74% for **3b**, 65% for **3c**, 64% for **3d**, 64% for **3e**, 33% for **3f**, 86% for **4a**, 89% for **4b**, 89% for **4c**,77% for **4d**, 87% for **4e**, 76% for **4f**.

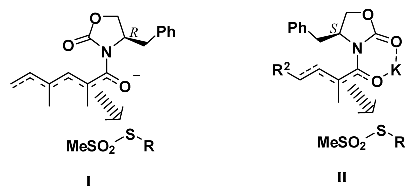
Chart 1. Synthesis of 5-(Alk-2-enyl)thiolactomycins and Their 3-Demethyl Congeners (**3**, **4**)

with the corresponding diastereomers **24a**, **c**—**f**.

The absolute stereochemistry of the 2′-position of **11b** was rigorously assigned to have the (*R*)-configuration based on the preliminarily successful synthesis of known *ent*-**3b**[22] from *ent*-**11b**. The ^{1}H-NMR spectra of **11a**, **c**—**f** which were quite similar to that of **11b**, clearly supported that **11a**, **c**—**f** bear the same (*R*)-configuration as that of **11b**.[31] Based on these preliminary results, (*S*)-4-benzyloxazolidin-2-one was employed as a chiral auxiliary for preparing **3** and **4** instead of its (*R*)-enantiomer (*vide supra*).

Unlike the previous case, in which (*R*)-*N*-acyloxazolidin-2-one derived from (*R*)-4-benzyloxazolidin-2-one provided the (*R*)-α-sulfenylated product by way of the non-chelated (*E*)-trienolate (**I**),[26,27] the deconjugative asymmetric α-sulfenylation of (*S*)-*N*-acyloxazolidin-2-one **9a**—**f** prepared from (*S*)-4-benzyloxazolidin-2-one gave the (*R*)-sulfenylated products **11a**—**f**. The latter reaction, carried out in the absence of HMPA, was expected to proceed through the chelated (*E*)-dienolate (**II**) due to the absence of HMPA with the sterically less hindered a face approach of **10** (Fig. 2).

As shown in Chart 1, the α-sulfenylated products **11a**—**f** were transformed into benzyl esters **12a**—**f** by imide-ester exchange using titanium benzyloxide $[Ti(OBn)_4]$.[32,33] Acidic hydrolysis of the dimethyl acetal moieties in **12a**—**f** produced aldehydes **13a**—**f**. The retro-Michael reaction of **13a**—**f** using cesium carbonate (Cs_2CO_3) as a base and subsequent treatments of the resulting cesium thiolates with propionyl or acetyl chloride, provided α-acylthio esters **14a**—**f** or **15a**—**f**. According to the reported protocol,[23] the Dieckmann condensation of **14a**—**f** and **15a**—**f** using lithium bis(trimethylsilyl)amide (LiHMDS) as a base furnished (*R*)-5-(alk-2-enyl)-TLM and their 3-demethyl congeners **3a**—**f** and **4a**—**f**. Using the identical synthetic scheme as described above, the enantiomers of **3a**—**f** and **4a**—**f** (*ent*-**3a**—**f**, *ent*-**4a**—**f**) were synthesized from *ent*-**9a**—**f** prepared from **8a**—**f** and (*R*)-4-benzyloxazolidin-2-one.

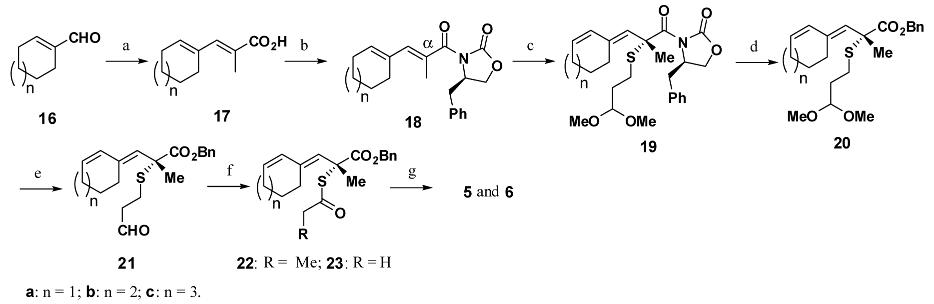


R = $(MeO)_2CHCH_2CH_2$-

Fig. 2. Plausible Transition State (II) of Deconjugative Asymmetric α-Sulfenylation of **9** in the Absence of HMPA Compared with That (I) of Corresponding Intermediate to **1** in the Presence of HMPA

Synthesis of 5-[(*E*)-Cycloalk-2-enylidenemethyl] Thiolactomycins {5-[(*E*)-Cycloalk-2-enylidenemethyl]-TLMs}, Their 3-Demethyl Congeners {5-[(*E*)-Cycloalk-2-enylidenemethyl]-3-demethyl-TLMs} and Their Enantiomers Next, in order to elucidate the relationship between the flexibility of the C5-isoprenoid 1,3-diene moiety and biological activity, the synthesis of enantiomeric pairs of 5-[(*E*)-cycloalk-2-enylidenemethyl]-TLMs **5a**—**c** and their 3-demethyl congeners **6a**—**c** was examined by employing α,β-unsaturated carboxylic acids **17a**—**c** as starting materials in a method similar to that for the synthesis of **3** and **4** described in **2.2**. Compounds **17a**—**c** were prepared from α,β-unsaturated aldehydes **16a**—**c** by a sequential Horner–Wadsworth–Emmons reaction and alkaline hydrolysis (Chart 2). **16a** was commercially available, and **16b**, **c** were prepared from 1-nitromethylcycloheptene[34] and *N*′-cyclooctylidene-4-methylbenzenesulfonohydrazide,[35] respectively, according to the reported procedures.[34,35] Activation of **17a**—**c** with pivaloyl chloride followed by treatment of the formed mixed anhydrides with (*R*)-4-benzyloxazolidin-2-one afforded (*R*)-*N*-acyloxazolidin-2-ones **18a**—**c**. In this case, (*R*)-4-benzyloxazolidin-2-one was selected as a chiral source by taking account not only of the reaction conditions for deconjugative asymmetric α-sulfenylation but also the absolute configuration of the α-sulfenylated product (*vide infra*).

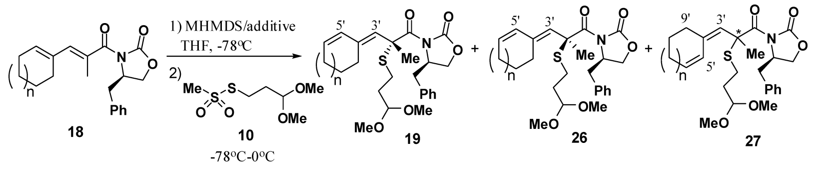
With **18a**—**c** in hand, we attempted the key deconjugative asymmetric α-sulfenylation by employing the conditions used for the sulfenylation reaction of the corresponding synthetic intermediate of **1**.[26,27] Thus, treatments of **18a** with 3,3-dimethoxypropyl methanethiosulfonate **10** using NaHMDS as a base in the presence of HMPA led to the deconjugative asymmetric α-sulfenylation, giving rise to the α-sulfenylated product **19a** highly diastereoselectively and in excellent yield (Table 2, run 1).[36] However, efficient sulfenylation reactions of **18b**, **c** were not effective under the same conditions as those for **18a** (Table 2, run 2, 4). It was antici-



(a) $(EtO)_2P(O)CHMeCO_2Et$, *t*BuOLi, hexane, rt, then 10% NaOH aq., EtOH, 50 °C, 88% for **17a**, 59% for **17b**, 81% for **17c**; (b) *t*BuCOCl, Et_3N, THF, −15 °C, then LiCl, (*R*)-4-benzyloxazolidin-2-one, rt, 81% for **18a**, 78% for **18b**, 71% for **18c**; (c) see Table 2; (d) $Ti(OiPr)_4$, BnOH, 70 °C, 76% for **20a**, 69% for **20b**, 87% for **20c**; (e) 6% HCl aq., THF, rt, 87% for **21a**, 92% for **21b**, 96% for **21c**; (f) Cs_2CO_3, EtOH, 4 °C, then CH_3CH_2COCl or CH_3COCl, Et_3N, CH_2Cl_2, 4 °C, 66% for **22a**, 68% for **22b**, 73% for **22c**, 68% for **23a**, 63% for **23b**, 67% for **23c**; (g) LiHMDS, THF, −78 °C-rt, 84% for **5a**, 89% for **5b**, 66% for **5c**, 99% for **6a**, 64% for **6b**, 46% for **6c**.

Chart 2. Synthesis of 5-[(*E*)-Cycloalk-2-enylidenemethyl]thiolactomycins and Their 3-Demethyl Congeners (**5**, **6**)

Table 2. Deconjugative Asymmetric α-Sulfenylation of the *N*-Acyloxazolidin-2-one **18a**—**c** with *S*-3,3-Dimethoxypropyl Thiosulfonate **10**



Run	Substrate	Base (eq)	Additive (eq)	Yield of the α-sulfenylated products	
				19+**26**+**27** (%)	Ratio of **19** : **26** : **27**a)a
1	**18a** (*n*=1)	NaHMDS (1.1)	HMPA (4)	92	12 : 2 : 1
2	**18b** (*n*=2)	NaHMDS (1.1)	HMPA (4)	35	11 : 1 : 4
3	**18b** (*n*=2)	NaHMDS (2)	HMPA (8)	64	14 : 1 : 4
4	**18c** (*n*=3)	NaHMDS (1.1)	HMPA (4)	<13	—b)
5	**18c** (*n*=3)	KHMDS (1.0)	18-Crown-6 (1.0)	68	12 : 1 : 1

a) Isomer ratio of **19**, **26** to **27** was determined by the ^{1}H-NMR spectrum and/or HPLC of the mixture. *b*) Isomer ratio of **19**, **26** to **27** was not determined because this sample contained several impurities.

pated that the abstraction of the ε-protons of **18b** and **18c** might be more difficult than that of **18a** because of steric and/or electronic differences between **18b**, **c** and **18a**, and that the trienolates derived from **18b**, **c** were more unstable than that produced from **18a**. Accordingly, the amount of base and the use of other additive were next examined. Thus, the sulfenylation of **18b** produced the α-sulfenylated compound **19b** in 64% yield even if the increased amounts of base and HMPA were used (Table 2, run 3). As for the sulfenylating reaction of **18c**, it was found to give a lower yield of **19c** under conditions similar to those for **18a**, **b**. Experimentation revealed that the use of KHMDS (1.0 eq) as a base in the presence of 18-crown-6 was more effective, giving rise to **19c** in a highly diastereoselective manner in a 68% yield (Table 2, run 5). In the deconjugative asymmetric α-sulfenylation of **18a**—**c**, we always observed the formation of small amounts of the α-sulfenylated products **26a**—**c** diastereomeric to **19a**—**c** and the α-sulfenylated products **27a**—**c** bearing a (*Z*)-configuration. The formation ratios of **19a**—**c**, **26a**—**c** to **27a**—**c** estimated by the ^{1}H-NMR spectra and/or HPLC analyses are summarized in Table 2.[37)] Pure samples of **19a**—**c** were obtained by sequential separation with column chromatography and HPLC.

The structures of **19a**—**c**, **26a**—**c**, and **27a**—**c** were rigorously determined by their ^{1}H-NMR spectra. Thus, the nuclear Overhauser effect spectroscopy (NOESY) spectra of **19a**—**c** and **26a**—**c** were observed between olefinic C-3′H and C-5′H. On the other hand, the structures of the **27a**—**c** were assigned by the NOESY spectra observed between C-3′H and C-9′H, and not between C-3′H and C-5′H. The absolute stereochemistries of newly created asymmetric centers for **19a**—**c** were assigned to have an (*R*)-configuration by comparing their ^{1}H-NMR spectra with that of the corresponding α-sulfenylated product for the synthesis of **1** (*vide supra*).[26,38)] A plausible mechanism of deconjugative asymmetric α-sulfenylation of **18** was anticipated to be very similar to that proposed for the synthesis of **1** because HMPA or 18-crown-6 was used as an additive in these reactions (see, Fig. 2, **I**).

Following the same synthetic scheme as previously described for the preparation of **3a**—**f** and **4a**—**f**, (*R*)-5-[(*E*)-cycloalk-2-enylidenemethyl]-TLMs **5a**—**c** and their 3-demethyl congeners **6a**—**c** were readily prepared from the α-sulfenylated products **19a**—**c** isolated in pure states by HPLC separation. Thus, as shown in Chart 2, the sequential imide-ester exchange of **19a**—**c**, acidic hydrolysis of **20a**—**c**, retro-Michael reaction of **21a**—**c**, acylation with propionyl or acetyl chloride and Dieckmann condensation of **22a**—**c** and **23a**—**c** furnished **5a**—**c** and **6a**—**c**, respectively. By the same synthetic scheme, the enantiomers of **5a**—**c** and **6a**—**c** (*ent*-**5a**—**c**, *ent*-**6a**—**c**) were prepared from *ent*-**19a**—**c** obtained from **17a**—**c** and (*S*)-4-benzyloxazolidin-2-one.

Table 3. *In Vitro* Mammalian Type I FAS Inhibitory Activity of Enantiomeric Pairs of TLM and Its Congeners (**1**, *ent*-**1**, **2**, *ent*-**2**, **3a**—**f**, *ent*-**3a**—**f**, **4a**—**f**, *ent*-**4a**—**f**, **5a**—**c**, *ent*-**5a**—**c**, **6a**—**c**, *ent*-**6a**—**c**).

Compound		Mammalian type I FAS inhibitory activity, IC_{50} (μg/ml) HepG2 ^{14}C	Compound		Mammalian type I FAS inhibitory activity, IC_{50} (μg/ml) HepG2 ^{14}C
	TLM (**1**)	>80	R^2=*n*Bu	**3e** (91% ee)	33.7
	ent-**1**	43.7		*ent*-**3e** (89% ee)	19.9
	2	>80		**4e** (91% ee)	18.6
	ent-**2**	19.0		*ent*-**4e** (88% ee)	21.0
R^2=H	**3a** (>90% ee)	>80	R^2=*n*Hex	**3f** (94% ee)	57.0
	ent-**3a** (>90% ee)	>80		*ent*-**3f** (84% ee)	34.8
	4a (>90% ee)	>80		**4f** (91% ee)	20.1
	ent-**4a** (>90% ee)	70.1		*ent*-**4f** (87% ee)	38.7
R^2=Me	**3b** (>99% ee)	72.3	*n*=1	**5a** (>99% ee)	>80
	ent-**3b** (>99% ee)	37.1		*ent*-**5a** (>99% ee)	>80
	4b (>99% ee)	72.1		**6a** (>99% ee)	57.0
	ent-**4b** (>99% ee)	>80		*ent*-**6a** (>99% ee)	18.9
R^2=Et	**3c** (>90% ee)	57.5	*n*=2	**5b** (>99% ee)	25.4
	ent-**3c** (>90% ee)	47.0		*ent*-**5b** (>99% ee)	14.9
	4c (>99% ee)	40.3		**6b** (>99% ee)	13.3
	ent-**4c** (>99% ee)	18.9		*ent*-**6b** (>99% ee)	22.6
R^2=*n*Pr	**3d** (>90% ee)	41.5	*n*=3	**5c** (>99% ee)	41.8
	ent-**3d** (>90% ee)	20.0		*ent*-**5c** (>99% ee)	11.6
	4d (>99% ee)	41.6		**6c** (>99% ee)	19.5
	ent-**4d** (>99% ee)	8.8		*ent*-**6c** (>99% ee)	24.6
	C75[a]	7.4			

[a] See Fig. 1.

Antibacterial Activity and Type I FAS Inhibitory Activity of Enantiomeric Pairs of TLM Congeners After **3a**—**f**, *ent*-**3a**—**f**, **4a**—**f**, *ent*-**4a**—**f**, **5a**—**c**, *ent*-**5a**—**c**, **6a**—**c** and *ent*-**6a**—**c** were synthesized,[39] their *in vitro* antibacterial activities against various strains of bacteria[40] and their inhibitory activities against mammalian type I FAS[41] were evaluated similarly to those for **1**, **2** and their enantiomers *ent*-**1** and *ent*-**2**.[1,27] Unlike the case in previous reports,[1,25] all the tested compounds lacked *in vitro* antibacterial activity against all the tested strains of bacteria even though **3a**—**f**, **4a**—**f**, **5a**—**c** and **6a**—**c** bear the same (*R*)-configurations as **1** and **2**. Therefore, the results on the inhibitory activity against only mammalian type I FAS are summarized in Table 3 along with those for **1**, *ent*-**1**, **2**, *ent*-**2** and C75, a potent inhibitor against type I FAS so far reported.[15,29]

As for mammalian type I FAS inhibitory activity, 14 compounds—*ent*-**4c**, *ent*-**3d**, *ent*-**4d**, *ent*-**3e**, **4e**, *ent*-**4e** and **4f**, each of which has a vinyl moiety at the C_5-position, and *ent*-**6a**, *ent*-**5b**, **6b**, *ent*-**6b**, *ent*-**5c**, **6c** and *ent*-**6c**, whose isoprenoid 1,3-diene moieties are involved in a ring system—were found to exhibit mammalian type I FAS inhibitory activity at levels equal to or more potent than that recorded for *ent*-**2**. Especially, the inhibitory activity of *ent*-**4d** was almost equal to that of C75 and more than twice that of previously synthesized *ent*-**2**.[26,27] Summing up the results for 5-(alk-2-enyl)-TLMs and their 3-demethyl congeners shown in Table 3, it might be concluded that, in general, the (*S*)-enantiomers show more potent type I FAS inhibitory activity than the corresponding (*R*)-enantiomers (see the cases for R^2=Et and *n*Pr) and that the activity of C_3-demethyl congeners is higher than that of the corresponding C_3-methyl compounds (see the cases for R^2=Et, *n*Pr and *n*Bu). As for the length of the C_5-alkenyl moiety, type I FAS inhibitory activity seems to gradually increase until the number of carbon atoms reaches 5, above which it slightly decreases. This tendency was most apparent for *ent*-**4a**—**f**. In addition, it was found that, as the C_5-alkenyl side chain becomes longer, the absolute configuration renders less effect on type I FAS inhibitory activity (see the cases for R^2=*n*Pr, *n*Bu and *n*Hex). More potent type I FAS inhibitory activity was clearly shown by *ent*-**5b**, **6b** and *ent*-**5c**. The activity of the most potent *ent*-**5c** was a little less than that of C75 and almost twice that of *ent*-**2**.[26,27] However, it appeared that locking the *s-trans* configuration of isoprenoid the 1,3-diene moiety as a consequence of the involvement in a ring system obviously decreased the tendency to separate the biological activity due to the difference in the absolute configuration at the C_5-position as previously shown for **1**, *ent*-**1**, **2** and *ent*-**2**.[1,27]

Conclusion

In summary, we have succeeded in synthesizing 12 enantiomeric pairs of 5-(alk-2-enyl)-TLMs (**3a**—**f**, *ent*-**3a**—**f**, **4a**—**f**, *ent*-**4a**—**f**) and six enantiomeric pairs of 5-[(*E*)-cycloalk-2-enylidenemethyl]-TLMs (**5**, *ent*-**5**, **6**, *ent*-**6**) by employing our efficient synthetic route previously explored for the total synthesis of TLM (**1**), 3-demethyl congener (**2**), and their enantiomers (*ent*-**1**, *ent*-**2**).The examination of *in vitro* antibacterial activity revealed that the free-rotational isoprenoid 1,3-diene moiety and the (*R*)-configuration at the C_5-position are essential for **1** and its congeners to exhibit *in vitro* antibacterial activity. As for mammalian type I FAS inhibitory activity, (*S*)-3-demethyl-TLM (*ent*-**4d**) exhibited a level of inhibitory activity against mammalian type I FAS that was almost equal to that of C75, a potent inhibitor previously reported and more than twice that of previously synthesized *ent*-**2**.[11,12] 5-[(*E*)-Cycloalk-2-enylidenemethyl]-TLM (*ent*-**5c**), in which the isoprenoid 1,3-diene moiety is locked into an *s-trans* configuration as a consequence of its involvement in a ring system, was found to exhibit slightly less inhibitory activity than C75 and almost twice that of the previously reported *ent*-**2**. Results of the biological activity collected in these studies should be useful for future attempts to design novel thiolactomycin congeners that might show more prominent and clinically useful activity than **1**.

Experimental

General All melting points were determined with a Yanaco MP-500 melting point apparatus and are uncorrected. Measurements of optical rotations were carried out using a JASCO P-1020 automatic digital polarimeter. Infrared spectra were recorded with a JASCO FT/IR-5300 spectrometer or a Perkin-Elmer spectrum 100 spectrometer. ^{1}H-NMR spectra were measured with a JEOL JNM-ECA-400 (400 MHz) spectrometer. Measurements of ^{13}C-NMR spectra were carried out using a JEOL JNM-ECA-400 (100 MHz) spectrometer. The chemical shifts are expressed in parts per million (δ value) downfield from tetramethylsilane, using tetramethylsilane (δ=0) and/or residual solvents such as chloroform (δ=7.26) as an internal standard. Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. Measurements of mass spectra were performed with a JEOL JMS-SX102X mass spectrometer. Data for elemental analyses are within ±0.3% of the theoretical values, and were determined by a Yanaco CHN-corder MT-6. Unless otherwise noted, all the experiments were carried out using anhydrous solvents under an atmosphere of argon. Throughout this study, Merck precoated TLC plates (Silica gel 60 F_{254}, 0.25 mm) were used for thin layer chromatographic (TLC) analysis, and all the spots were visualized using UV light followed by coloring with phosphomolybdic acid or anisaldehyde. Silica gel 60N (40—50 μm, neutral; Kanto Chemical Co., Inc., Tokyo, Japan) or Chromatorex® NH DM2035 (200—350 mesh; Fuji Silysia Chemical, Ltd., Aichi, Japan) was used for the flash column chromatography. Analytical and preparative HPLC was carried out using an apparatus equipped with a Hitachi L-7405 UV–vis detector, a Hitachi L-7100 HPLC pump, a Hitachi D-7500 chromato integrator, a GL Sciences UV702 UV–vis detector, a GL Sciences PU716 HPLC pump, and a CO705 column oven. The following abbreviations are used for solvents and reagents: ethanol (EtOH), methanol (MeOH), sodium sulfate (Na_2SO_4), ethyl acetate (AcOEt), dichloromethane (CH_2Cl_2), chloroform ($CHCl_3$), *t*-butyl methyl ether (MTBE), tetrahydrofuran (THF), triethylamine (Et_3N).

(*E*)-2-Methylhept-2-enoic Acid (8d) To a solution of triethyl 2-phosphonopropionate (5.5 ml, 24.8 mmol) in hexane (50 ml), lithium *tert*-butoxide (1.0 mol/l solution in hexane, 27.0 ml, 27.0 mmol) was added dropwise at room temperature, and the resulting mixture was stirred at the same temperature for 30 min. Pentanal (2.6 ml, 24.2 mmol) was added dropwise to the mixture at 0 °C, and the resulting mixture was stirred at room temperature for 30 min. After quenching the reaction by adding water (100 ml), the mixture was extracted with hexane (100 ml×3). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. The residue was dissolved in ethanol (50 ml), and 10% sodium hydroxide (40 ml) was added to the ethanolic solution. The resulting mixture was heated at 50 °C for 18 h with stirring. After cooling, the reaction mixture was washed with hexane (50 ml×3). The aqueous layer was made acidic (pH 1) by adding 2 mol/l HCl and extracted with AcOEt (50 ml×2). The organic extracts were combined, washed with brine (30 ml), dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. Flash column chromatography (hexane/AcOEt=4 : 1) of the residue gave oily **8d** (3.16 g, 92%) as a mixture of (*E*,*Z*) isomer (*E*/*Z*=8 : 1). This sample was directly used for the next acylation without separation of (*E*)- and (*Z*)-isomer. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.92 (3H, t, *J*=7.3 Hz), 1.25—1.49 (4H, m), 1.84 (24/9H, d, *J*=1.2 Hz), 1.92 (3/9H, d, *J*=1.2 Hz), 2.20 (16/9H, q, *J*=7.3 Hz), 2.52 (2/9H, q, *J*=7.3 Hz), 6.09 (1/9H, td, *J*=7.3, 1.2 Hz), 6.91 (8/9H, td, *J*=7.3, 1.2 Hz). IR (neat) cm^{-1}: 1688, 1644. MS (EI$^+$) *m*/*z*: 142 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 142.0957 (Calcd for $C_8H_{14}O_2$ (M$^+$): 142.0994).

(*E*)-2-Methyloct-2-enoic Acid (8e) Treatments of *n*-hexanal (5.8 ml, 45.1 mmol) with triethyl 2-phosphonopropionate (12.0 g, 49.4 mmol) in a manner similar to that described for the preparation of **8d**, afforded **8e** (6.48 g, 92%) as a mixture of (*E*,*Z*) isomer (*E*/*Z*=8 : 1). This sample was directly used for the next acylation without separation of (*E*)- and (*Z*)-isomer. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.86—0.91 (3H, m), 1.26—1.50 (6H, m), 1.84 (24/9H, d, *J*=1.2 Hz), 1.92 (3/9H, q, *J*=1.2 Hz), 2.20 (16/9H, q, *J*=7.3 Hz), 2.51 (2/9H, qd, *J*=7.3, 1.2 Hz), 6.09 (1/9H, td, *J*=7.3, 1.2 Hz), 6.91 (8/9H, td, *J*=7.3, 1.2 Hz). IR (neat) cm^{-1}: 1688, 1644. MS (EI$^+$) *m*/*z*: 156 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 156.1144 (Calcd for $C_9H_{16}O_2$ (M$^+$): 156.1150).

(*E*)-2-Methyldec-2-enoic Acid (8f) Treatments of *n*-octanal (9.0 ml, 54.7 mmol) with triethyl 2-phosphonopropionate (14.0 g, 57.6 mmol) in the same manner as described for the preparation of **8d**, afforded **8f** (10.75 g, 100%) as a mixture of (*E*,*Z*) isomer (*E*/*Z*=8 : 1). This sample was directly used for the next acylation without separation of (*E*)- and (*Z*)-isomer. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.89 (3H, t, *J*=7.3 Hz), 1.20—1.49 (10H, m), 1.84 (24/9H, d, *J*=1.2 Hz), 1.91 (3/9H, d, *J*=1.2 Hz), 2.20 (16/9H, q, *J*=7.3 Hz), 2.51 (2/9H, qd, *J*=7.3, 1.2 Hz), 6.09 (1/9H, td, *J*=7.3, 1.2 Hz), 6.92 (8/9H, td, *J*=7.3, 1.2 Hz). IR (neat) cm^{-1}: 1688, 1644. MS (EI$^+$) *m*/*z*: 184 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 184.1489 (Calcd for $C_{11}H_{20}O_2$ (M$^+$): 184.1463).

(*S*,*E*)-4-Benzyl-3-(2-methylpent-2-enoyl)oxazolidin-2-one (9b) and Its Enantiomer (*ent*-9b) (a) Preparation of **9b**: To a solution of (*E*)-2-methylpent-2-enoic acid (1.14 g, 9.79 mmol) and Et_3N (3.0 ml, 21.5 mmol) in THF (50 ml), pivaloyl chloride (1.65 ml, 9.98 mmol) was added dropwise at −15 °C, and the resulting mixture was stirred at the same temperature for 15 min. Lithium chloride (500 mg, 11.8 mmol) and (*S*)-4-benzyloxazolidin-2-one (2.10 g, 11.6 mmol) were added to the mixture at the same temperature, and the stirring was continued for 13 h at room temperature. After quenching the reaction by adding saturated aqueous ammonium chloride solution (30 ml), the mixture was extracted with AcOEt (30 ml×3). The organic extracts were combined, washed with saturated aqueous sodium hydrogen carbonate solution (50 ml) and brine (50 ml), dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. Flash column chromatography (hexane/AcOEt=5 : 1) of the residue gave **9b** (2.56 g, 96%) as a colorless oil. $[\alpha]_D^{26}$ +94.7 (*c*=1.0, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.06 (3H, t, *J*=7.3 Hz), 1.90 (3H, s), 2.22 (2H, quintet, *J*=7.3 Hz), 2.83 (1H, dd, *J*=13.4, 9.2 Hz), 3.35 (1H, dd, *J*=13.4, 3.7 Hz), 4.15 (1H, dd, *J*=9.2, 3.7 Hz), 4.25 (1H, t, *J*=9.2 Hz), 4.67—4.75 (1H, m), 6.08 (1H, td, *J*=7.3, 1.2 Hz), 7.19—7.35 (5H, m). IR (neat) cm^{-1}: 1788, 1680. MS (EI$^+$) *m*/*z*: 273 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 273.1354 (Calcd for $C_{16}H_{19}NO_3$ (M$^+$): 273.1365).

(b) Preparation of *ent*-**9b**: Compound *ent*-**9b** (2.61 g, 96%) was prepared as a colorless oil from (*E*)-2-methylpent-2-enoic acid (1.14 g, 9.99 mmol) and (*R*)-4-benzyloxazolidin-2-one (2.10 g, 11.6 mmol) in the same manner as described in (a). $[\alpha]_D^{25}$ −94.1 (*c*=1.0, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 273.1388 (Calcd for $C_{16}H_{19}NO_3$ (M$^+$): 273.1365).

(*S*,*E*)-4-Benzyl-3-(2-methylbut-2-enoyl)oxazolidin-2-one (9a) and Its Enantiomer (*ent*-9a) (a) Preparation of **9a**: Treatments of tiglic acid (2.00 g, 19.6 mmol) in a manner similar to that described for the preparation of **9b**, afforded **9a** (4.23 g, 83%) as a colorless crystals. mp 84.7—85.2 °C (diisopropyl ether). $[\alpha]_D^{23}$ +106 (*c*=1.0, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.81 (3H, d, *J*=7.9 Hz), 1.91 (3H, s), 2.81 (1H, dd, *J*=13.4, 9.2 Hz), 3.35 (1H, dd, *J*=13.4, 3.1 Hz), 4.15 (1H, dd, *J*=9.2, 5.5 Hz), 4.24 (1H, t, *J*=9.2 Hz), 4.67—4.75 (1H, m), 6.21 (1H, qd, *J*=7.9, 1.2 Hz), 7.19—7.36 (5H, m). IR (KBr) cm^{-1}: 1788, 1682. MS (EI$^+$) *m*/*z*: 259 (M$^+$). *Anal.* Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.36; H, 6.60; N, 5.39.

(b) Preparation of *ent*-**9a**: Compound *ent*-**9a** (2.39 g, 94%) was prepared as a colorless crystals from tiglic acid (1.00 g, 9.79 mmol) and (*R*)-4-benzyloxazolidin-2-one (2.10 g, 11.9 mmol) in the same manner as described in (a). mp 85.0—86.0 °C (diisopropyl ether). $[\alpha]_D^{24}$ −102 (*c*=1.1, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). *Anal.* Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.44; H, 6.66; N, 5.30.

(*S*,*E*)-4-Benzyl-3-(2-methylhex-2-enoyl)oxazolidin-2-one (9c) and Its Enantiomer (*ent*-9c) (a) Preparation of **9c**: Treatments of (*E*)-2-methylhex-2-enoic acid (1.5 ml, 11.9 mmol) in a manner similar to that described for the preparation of **9b**, afforded **9c** (3.08 g, 90%) as a colorless crystals. mp 42.2—42.7 °C (diisopropyl ether–hexane). $[\alpha]_D^{23}$ +94.1 (*c*=1.0, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.96 (3H, t, *J*=7.3 Hz), 1.49 (2H, q, *J*=7.3 Hz), 1.91 (3H, s), 2.18 (2H, q, *J*=7.3 Hz), 2.83 (1H, dd, *J*=13.5, 9.8 Hz), 3.35 (1H, dd, *J*=13.5, 3.1 Hz), 4.15 (1H, dd, *J*=8.6, 5.5 Hz), 4.25 (1H, t, *J*=8.6 Hz), 4.66—4.76 (1H, m), 6.10 (1H, t, *J*=7.3 Hz), 7.19—7.35 (5H, m). IR (KBr) cm^{-1}: 1790, 1680. MS (EI$^+$) *m*/*z*: 287 (M$^+$). *Anal.* Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found: C, 70.98; H, 7.37; N, 4.85.

(b) Preparation of *ent*-**9c**: Compound *ent*-**9c** (2.28 g, 100%) was prepared as a colorless crystals from (*E*)-2-methylhex-2-enoic acid (1.1 ml, 7.84 mmol) and (*R*)-4-benzyloxazolidin-2-one (1.68 g, 9.48 mmol) in the same manner as described in (a). mp 42.0—42.5 °C (diisopropyl ether–hexane). $[\alpha]_D^{24}$ −91.8 (*c*=0.9, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). *Anal.* Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found: C, 70.81; H, 7.31; N, 4.83.

(*S*,*E*)-4-Benzyl-3-(2-methylhept-2-enoyl)oxazolidin-2-one (9d) and Its

Enantiomer (*ent*-9d) (a) Preparation of **9d**: Treatments of **8d** [an 8 : 1 mixture of the (*E*)- and (*Z*)-isomer] (1.20 g, 8.44 mmol) in a manner similar to that described for the preparation of **9b**, afforded oily **9d** (2.21 g, 87%) as a mixture of (*E*,*Z*) isomer (*E*/*Z*=16 : 1). $[\alpha]_D^{28}$ +80.9 (*c*=1.1, MeOH). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 0.92 (3H, t, *J*=7.3 Hz), 1.32—1.50 (4H, m), 1.91 (3H, d, *J*=1.2 Hz), 2.20 (2H, q, *J*=7.3 Hz), 2.83 (1H, dd, *J*=13.4, 9.2 Hz), 3.35 (15/16H, dd, *J*=13.4, 3.7 Hz), 3.41 (1/16H, dd, *J*=13.4, 3.7 Hz), 4.05—4.18 (1H, m), 4.25 (1H, t, *J*=8.6 Hz), 4.67—4.75 (1H, m), 5.55 (1/16H, td, *J*=7.3, 1.2 Hz), 6.10 (15/16H, td, *J*=7.3, 1.2 Hz), 7.19—7.36 (5H, m). IR (neat) cm^{-1}: 1788, 1682. MS (EI$^+$) *m*/*z*: 301 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 301.1661 (Calcd for $C_{18}H_{23}NO_3$ (M$^+$): 301.1678).

(b) Preparation of *ent*-**9d**: Compound *ent*-**9d** (1.00 g, 89%, colorless oil) was prepared as a mixture of (*E*,*Z*) isomer (*E*/*Z*=19 : 1) from **8d** [an 8 : 1 mixture of the (*E*)- and (*Z*)-isomer] (530 mg, 3.73 mmol) and (*R*)-4-benzyloxazolidin-2-one (745 mg, 4.12 mmol) in the same manner as described in (a). $[\alpha]_D^{24}$ −82.0 (*c*=1.0, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 301.1698 (Calcd for $C_{18}H_{23}NO_3$ (M$^+$): 301.1678).

(*S*,*E*)-4-Benzyl-3-(2-methyloct-2-enoyl)oxazolidin-2-one (9e) and Its Enantiomer (*ent*-9e) (a) Preparation of **9e**: Treatments of **8e** [a 8 : 1 mixture of the (*E*)- and (*Z*)-isomer] (9.70 g, 62.1 mmol) in a manner similar to that described for the preparation of **9b**, afforded oily **9e** (18.7 g, 96%) as a mixture of (*E*,*Z*) isomer (*E*/*Z*=8 : 1). $[\alpha]_D^{18}$ +80.9 (*c*=0.5, MeOH). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 0.90 (3H, t, *J*=7.3 Hz), 1.24—1.50 (6H, m), 1.90 (3H, d, *J*=1.2 Hz), 2.19 (16/9H, q, *J*=7.3 Hz), 2.50 (2/9H, q, *J*=7.3 Hz), 2.83 (1H, dd, *J*=13.5, 9.2 Hz), 3.35 (8/9H, dd, *J*=13.5, 3.7 Hz), 3.41 (1/9H, dd, *J*=13.5, 3.7 Hz), 4.08—4.18 (1H, m), 4.24 (1H, t, *J*=8.6 Hz), 4.67—4.75 (1H, m), 5.55 (1/9H, td, *J*=7.3, 1.2 Hz), 6.10 (8/9H, td, *J*=7.3, 1.2 Hz), 7.19—7.36 (5H, m). IR (neat) cm^{-1}: 1790, 1682. MS (EI$^+$) *m*/*z*: 315 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 315.1830 (Calcd for $C_{19}H_{25}NO_3$ (M$^+$): 315.1834).

(b) Preparation of *ent*-**9e**: Compound *ent*-**9e** (10.5 g, 81%, colorless oil) was prepared as a mixture of (*E*,*Z*) isomer (*E*/*Z*=16 : 1) from **8e** [a 8 : 1 mixture of the (*E*)- and (*Z*)-isomer] (6.48 g, 41.5 mmol) and (*R*)-4-benzyloxazolidin-2-one (8.26 g, 45.7 mmol) in the same manner as described in (a). $[\alpha]_D^{18}$ −84.6 (*c*=0.5, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 315.1816 (Calcd for $C_{19}H_{25}NO_3$ (M$^+$): 315.1834).

(*S*,*E*)-4-Benzyl-3-(2-methyldec-2-enoyl)oxazolidin-2-one (9f) and Its Enantiomer (*ent*-9f) (a) Preparation of **9f**: Treatments of **8f** [an 8 : 1 mixture of the (*E*)- and (*Z*)-isomer] (10.7 g, 58.1 mmol) in a manner similar to that described for the preparation of **9b**, afforded oily **9f** (18.6 g, 93%) as a mixture of (*E*,*Z*) isomer (*E*/*Z*=18 : 1). $[\alpha]_D^{19}$ +69.3 (*c*=0.9, MeOH). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 0.89 (3H, t, *J*=7.3 Hz), 1.23—1.50 (10H, m), 1.90 (3H, s), 2.19 (36/19H, q, *J*=7.3 Hz), 2.50 (2/19H, q, *J*=7.3 Hz), 2.82 (1H, dd, *J*=13.5, 9.2 Hz), 3.35 (1H, dd, *J*=13.5, 3.7 Hz, 18/19H), 3.45 (dd, *J*=13.5, 3.7 Hz, 1/19H), 4.08—4.18 (m, 1H), 4.24 (t, *J*=8.6 Hz), 4.67—4.75 (1H, m), 5.55 (1/19H, td, *J*=7.3, 1.2 Hz), 6.10 (18/19H, td, *J*=7.3, 1.2 Hz), 7.19—7.36 (1H, m). IR (neat) cm^{-1}: 1790, 1682. MS (EI$^+$) *m*/*z*: 343 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 343.2172 (Calcd for $C_{21}H_{29}NO_3$ (M$^+$): 343.2147).

(b) Preparation of *ent*-**9f**: Compound *ent*-**9f** (12.2 g, 85% colorless oil) was prepared as a mixture of (*E*,*Z*) isomer (*E*/*Z*=16 : 1) from **8f** [an 8 : 1 mixture of the (*E*)- and (*Z*)-isomer] (7.72 g, 41.9 mmol) and (*R*)-4-benzyloxazolidin-2-one (8.33 g, 48.0 mmol) in the same manner as described in (a). $[\alpha]_D^{18}$ −75.3 (*c*=1.1, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 343.2147 (Calcd for $C_{21}H_{29}NO_3$ (M$^+$): 343.2147).

Deconjugative Asymmetric α-Sulfenylation of (*S*,*E*)- and (*R*,*E*)-4-Benzyl-3-(2-methylpent-2-enoyl)oxazolidin-2-one (9b, *ent*-9b). (*S*)-4-Benzyl-3-[(*R*,*E*)-2-(3,3-dimethoxypropylthio)-2-methylpent-3-enoyl]oxazolidin-2-one (11b), Its (*S*,*E*)-Diastereomer (24b), (*S*)-4-Benzyl-3-[(*RS*,*E*)-4-(3,3-dimethoxypropylthio)-2-methylpent-2-enoyl]oxazolidin-2-one (25b) and Their Enantiomers (*ent*-11b, *ent*-24b, *ent*-25b) (a) Preparation of **11b**, **24b** and **25b**: To a solution of **9b** (110 mg, 0.402 mmol) in THF (2.0 ml), KHMDS (0.5 mol/l solution in toluene, 0.96 ml, 0.48 mmol) was added dropwise at −78 °C, and the resulting mixture was stirred at the same temperature for 30 min. A solution of **10** (130 mg, 0.607 mmol) in THF (0.4 ml) was added to the reaction mixture at the same temperature, and the resulting mixture was allowed to slowly warm to 0 °C. After quenching the reaction by adding saturated aqueous ammonium chloride solution (10 ml), the mixture was extracted with AcOEt (10 ml×3). The organic extracts were combined, washed with brine (10 ml), dried over anhydrous Na$_2$SO$_4$, filtered, and then concentrated *in vacuo*. Flash column chromatography (hexane/AcOEt=4 : 1) of the residue gave **11b** (121 mg, 74%), its (2′*S*)-diastereomer **24b** (10 mg, 6%) and the γ-sulfenylated product **25b** (13 mg, 8%), all as an oil.

Compound **11b**: $[\alpha]_D^{27}$ +54.8 (*c*=0.6, MeOH). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.74 (3H, dd, *J*=6.1, 1.8 Hz), 1.79 (3H, s), 1.82—1.90 (2H, m), 2.50—2.64 (2H, m), 2.72 (1H, dd, *J*=13.4, 10.4 Hz), 3.315 (3H, s), 3.318 (3H, s), 3.30—3.36 (1H, m), 4.09—4.20 (2H, m), 4.47 (1H, t, *J*=6.1 Hz), 4.66—4.72 (1H, m), 5.53 (1H, qd, *J*=6.1, 15.9 Hz), 5.83 (1H, qd, *J*=1.8, 15.9 Hz), 7.23—7.36 (5H, m). IR (neat) cm^{-1}: 1790, 1680. MS (CI$^+$) *m*/*z*: 376 {[(M−CH$_3$O)+H]$^+$}. HR-MS (CI$^+$) *m*/*z*: 376.1551 (Calcd for $C_{20}H_{26}NO_4S$ {[(M−CH$_3$O)+H]$^+$}: 376.1583).

Compound **24b**: $[\alpha]_D^{25}$ +146 (*c*=0.3, MeOH). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.73 (3H, dd, *J*=6.1, 1.2 Hz), 1.79—1.87 (5H, m), 2.44—2.63 (2H, m), 2.78 (1H, dd, *J*=13.4, 9.8 Hz), 3.26—3.34 (7H, m), 4.09—4.24 (2H, m), 4.47 (1H, t, *J*=6.1 Hz), 4.66—4.76 (1H, m), 5.49 (1H, qd, *J*=6.1, 15.9 Hz), 5.82 (1H, qd, *J*=1.2, 15.9 Hz), 7.20—7.36 (5H, m). IR (ATR) cm^{-1}: 1785, 1677. MS (CI$^+$) *m*/*z*: 408 [(M+H)$^+$]. HR-MS (CI$^+$) *m*/*z*: 408.1840 (Calcd for $C_{21}H_{30}NO_5S$ [(M+H)$^+$]: 408.1845).

Compound **25b** (a Mixture of Two Diastereomers): ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.26 (3H, t, *J*=6.7 Hz), 1.51—1.58 (2H, m), 1.95 (3H, d, *J*=1.2 Hz), 2.49—2.67 (2H, m), 2.84 (1H, dd, *J*=13.4, 9.2 Hz), 3.29—3.39 (7H, m), 3.71—3.82 (1H, m), 4.08—4.20 (1H, m), 4.26 (1H, t, *J*=9.2 Hz), 4.45—4.54 (1H, m), 4.65—4.76 (1H, m), 5.83 (1H, qd, *J*=1.2, 10.4 Hz), 7.11—7.41 (5H, m). IR (ATR) cm^{-1}: 1782, 1678. MS (EI$^+$) *m*/*z*: 407 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 407.1744 (Calcd for $C_{21}H_{29}NO_5S$ (M$^+$): 407.1766). Diastereomer ratio was determined by HPLC analysis.

(b) Preparation of *ent*-**11b**: Compound *ent*-**11b** (1.67 g, 56%) was prepared as a colorless oil from *ent*-**9b** (900 mg, 3.01 mmol) in the same manner as described in (a).[42] $[\alpha]_D^{25}$ −53.6 (*c*=0.8, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 407.1722 (Calcd for $C_{21}H_{29}NO_5S$ (M$^+$): 407.1766).

Deconjugative Asymmetric α-Sulfenylation of (*S*)- and (*R*)-4-Benzyl-3-(2-methylbut-2-enoyl)oxazolidin-2-one (9a, *ent*-9a). (*S*)-4-Benzyl-3-[(*R*)-2-(3,3-dimethoxypropylthio)-2-methylbut-3-enoyl]oxazolidin-2-one (11a) and Its Enantiomer (*ent*-11a) (a) Preparation of **11a**: Treatments of **9a** (4.10 g, 15.8 mmol) in a manner similar to that described for the preparation of **11b**, afforded **11a** (1.14 g, 18%) as a colorless oil.[42] $[\alpha]_D^{27}$ +52.1 (*c*=0.5, MeOH). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.81 (3H, s), 1.82—1.90 (2H, m), 2.51—2.62 (2H, m), 2.72 (1H, dd, *J*=12.8, 11.0 Hz), 3.317 (3H, s), 3.321 (3H, s), 3.32—3.38 (1H, m), 4.09—4.21 (2H, m), 4.47 (1H, t, *J*=5.5 Hz), 4.70 (1H, m), 5.06 (1H, d, *J*=17.1 Hz), 5.18 (1H, d, *J*=11.0 Hz), 6.18 (1H, dd, *J*=17.1, 11.0 Hz), 7.23—7.37 (5H, m). IR (neat) cm^{-1}: 1790, 1680. MS (CI$^+$) *m*/*z*: 362 {[(M−CH$_3$O)+H]$^+$}. HR-MS (CI$^+$) *m*/*z*: 362.1459 (Calcd for $C_{19}H_{24}NO_4S$ {[(M−CH$_3$O)+H]$^+$}: 362.1426).

(b) Preparation of *ent*-**11a**: Compound *ent*-**11a** (1.09 g, 16%) was prepared as a colorless oil from *ent*-**9a** (4.56 g, 17.6 mmol) in the same manner as described in (a).[42] $[\alpha]_D^{27}$ −55.4 (*c*=1.1, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 393.1606 (Calcd for $C_{20}H_{27}NO_5S$ (M$^+$): 393.1610).

Deconjugative Asymmetric α-Sulfenylation of (*S*,*E*)- and (*R*,*E*)-4-Benzyl-3-(2-methylhex-2-enoyl)oxazolidin-2-one (9c, *ent*-9c). (*S*)-4-Benzyl-3-[(*R*,*E*)-2-(3,3-dimethoxypropylthio)-2-methylhex-3-enoyl]oxazolidin-2-one (11c) and Its Enantiomer (*ent*-11c) (a) Preparation of **11c**: Treatments of **9c** (2.01 g, 6.99 mmol) in a manner similar to that described for the preparation of **11b**, afforded **11c** (1.78 g, 60%) as a colorless oil.[42] $[\alpha]_D^{27}$ +54.1 (*c*=0.7, MeOH). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 0.99 (3H, t, *J*=7.9 Hz), 1.80 (3H, s), 1.82—1.90 (2H, m), 2.04—2.13 (2H, m), 2.50—2.65 (2H, m), 2.71 (1H, dd, *J*=13.4, 10.4 Hz), 3.317 (3H, s), 3.321 (3H, s), 3.30—3.37 (1H, m), 4.10—4.19 (2H, m), 4.47 (1H, t, *J*=5.5 Hz), 4.65—4.73 (1H, m), 5.52 (1H, td, *J*=6.7 15.9 Hz), 5.80 (1H, td, *J*=1.8, 15.9 Hz), 7.23—7.37 (5H, m). IR (neat) cm^{-1}: 1790, 1680. MS (CI$^+$) *m*/*z*: 390 {[(M−CH$_3$O)+H]$^+$}. HR-MS (CI$^+$) *m*/*z*: 390.1740 (Calcd for $C_{21}H_{28}NO_4S$ {[(M−CH$_3$O)+H]$^+$}: 390.1739).

(b) Preparation of *ent*-**11c**: Compound *ent*-**11c** (1.77 g, 71%) was prepared as a colorless oil from *ent*-**9c** (1.70 g, 5.92 mmol) in the same manner as described in (a).[42] $[\alpha]_D^{26}$ −55.5 (*c*=1.0, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 421.1889 (Calcd for $C_{22}H_{31}NO_5S$ (M$^+$): 421.1923).

Deconjugative Asymmetric α-Sulfenylation of (*S*,*E*)- and (*R*,*E*)-4-Benzyl-3-(2-methylhept-2-enoyl)oxazolidin-2-one (9d, *ent*-9d). (*S*)-4-Benzyl-3-[(*R*,*E*)-2-(3,3-dimethoxypropylthio)-2-methylhept-3-enoyl]oxazolidin-2-one (11d) and Its Enantiomer (*ent*-11d) (a) Preparation of **11d**: Treatments of **9d** (2.19 g, 7.27 mmol) in a manner similar to that described for the preparation of **11b**, afforded **11d** (1.59 g, 50%) as a colorless oil.[42] $[\alpha]_D^{27}$ +50.6 (*c*=1.0, MeOH). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 0.89 (3H, t, *J*=7.3 Hz), 1.39 (2H, q, *J*=7.3 Hz), 1.80 (3H, s), 1.82—1.91 (2H, m), 2.00—2.09 (2H, m), 2.50—2.65 (2H, m), 2.70 (1H, dd, J=13.4, 10.4 Hz), 3.315 (3H, s), 3.320 (3H, s), 3.30—3.37 (1H, m), 4.09—4.20 (2H, m), 4.47 (1H, t, J=5.5 Hz), 4.66—4.72 (1H, m), 5.49 (1H, td, J=7.3, 15.9 Hz), 5.80 (1H, td, J=1.2, 15.9 Hz), 7.23—7.37 (5H, m). IR (neat) cm^{-1}: 1792, 1680. MS (EI$^+$) *m/z*: 435 (M$^+$). HR-MS (EI$^+$) *m/z*: 435.2063 (Calcd for $C_{23}H_{33}NO_5S$ (M$^+$): 435.2079).

(b) Preparation of *ent*-**11d**: Compound *ent*-**11d** (659 mg, 54%) was prepared as a colorless oil from *ent*-**9d** (850 mg, 2.82 mmol) in the same manner as described in (a).[42] $[\alpha]_D^{27}$ −49.6 (c=1.1, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 404.1943 (Calcd for $C_{22}H_{30}NO_4S$ {[(M−CH_3O)+H]$^+$}: 404.1896).

Deconjugative Asymmetric α-Sulfenylation of (*S*,*E*)- and (*R*,*E*)-4-Benzyl-3-(2-methyloct-2-enoyl)oxazolidin-2-one (9e, *ent*-9e). (*S*)-4-Benzyl-3-[(*R*,*E*)-2-(3,3-dimethoxypropylthio)-2-methyloct-3-enoyl]oxazolidin-2-one (11e) and Its Enantiomer (*ent*-11e) (a) Preparation of **11e**: Treatments of **9e** (12.6 g, 40.0 mmol) in a manner similar to that described for the preparation of **11b** afforded **11e** (10.9 g, 61%) as a colorless oil.[42] $[\alpha]_D^{19}$ +46.0 (c=0.5, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.89 (3H, t, J=7.3 Hz), 1.24—1.36 (4H, m), 1.80 (3H, s), 1.81—1.92 (2H, m), 2.07 (2H, q, J=6.1 Hz), 2.54—2.65 (2H, m), 2.70 (1H, dd, J=13.4, 10.4 Hz), 3.315 (3H, s), 3.320 (3H, s), 3.32—3.37 (1H, m), 4.09—4.18 (2H, m), 4.47 (1H, t, J=6.1 Hz), 4.65—4.74 (1H, m), 5.49 (1H, td, J=6.7, 15.9 Hz), 5.80 (1H, td, J=1.2, 15.9 Hz), 7.24—7.36 (5H, m). IR (neat) cm^{-1}: 1792, 1680. MS (CI$^+$) *m/z*: 450 [(M+H)$^+$]. HR-MS (CI$^+$) *m/z*: 450.2304 (Calcd for $C_{24}H_{36}NO_5S$ [(M+H)$^+$]: 450.2314).

(b) Preparation of *ent*-**11e**: Compound *ent*-**11e** (4.57 g, 80%) was prepared as a colorless oil from *ent*-**9e** (4.00 g, 12.7 mmol) in the same manner as described in (a).[42] $[\alpha]_D^{19}$ −49.9 (c=0.6, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 450.2319 (Calcd for $C_{24}H_{36}NO_5S$ [(M+H)$^+$]: 450.2314).

Deconjugative Asymmetric α-Sulfenylation of (*S*,*E*)- and (*R*,*E*)-4-Benzyl-3-(2-methyldec-2-enoyl)oxazolidin-2-one (9f, *ent*-9f). (*S*)-4-Benzyl-3-[(*R*,*E*)-2-(3,3-dimethoxypropylthio)-2-methyldec-3-enoyl]oxazolidin-2-one (11f) and Its Enantiomer (*ent*-11f) (a) Preparation of **11f**: Treatments of **9f** (13.7 g, 40.0 mmol) in a manner similar to that described for the preparation of **11b** afforded **11f** (9.77 g, 51%) as a colorless oil.[42] $[\alpha]_D^{19}$ +41.4 (c=0.5, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.87 (3H, t, J=6.7 Hz), 1.24—1.37 (8H, m), 1.80 (3H, s), 1.80—1.90 (2H, m), 2.02—2.10 (2H, m), 2.50—2.65 (2H, m), 2.70 (1H, dd, J=13.4, 10.4 Hz), 3.315 (3H, s), 3.318 (3H, s), 3.30—3.37 (1H, m), 4.08—4.18 (2H, m), 4.47 (1H, t, J=5.5 Hz), 4.65—4.72 (1H, m), 5.48 (1H, td, J=6.7, 15.9 Hz), 5.80 (1H, td, J=1.2, 15.9 Hz), 7.23—7.36 (5H, m). IR (neat) cm^{-1}: 1792, 1680. MS (CI$^+$) *m/z*: 478 [(M+H)$^+$]. HR-MS (CI$^+$) *m/z*: 478.2617 (Calcd for $C_{26}H_{40}NO_5S$ [(M+H)$^+$]: 478.2627.

(b) Preparation of *ent*-**11f**: Compound *ent*-**11f** (3.44 g, 59%) was prepared as a colorless oil from *ent*-**9f** (4.23 g, 12.3 mmol) in the same manner as described in (a).[42] $[\alpha]_D^{19}$ −47.4 (c=0.6, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 478.2620 (Calcd for $C_{26}H_{40}NO_5S$ [(M+H)$^+$]: 478.2627).

(*R*,*E*)-Benzyl 2-(3,3-Dimethoxypropylthio)-2-methylpent-3-enoate (12b) and Its Enantiomer (*ent*-12b) (a) Preparation of **12b**: To benzyl alcohol (14.0 ml, 135 mmol), titanium isopropoxide (2.0 ml, 6.78 mmol) was added and the resulting mixture was stirred at room temperature for 5 h under a reduced pressure (0.5—1.0 mmHg). The mixture was added to **11b** (1.65 g, 4.05 mmol), and the whole was stirred at 70 °C for 16 h. After cooling, the mixture was diluted with CH_2Cl_2 (40 ml) and the reaction was quenched by adding 1 mol/l HCl (10 ml). The insoluble materials which appeared were removed by filtration through a pad of Celite and washed with CH_2Cl_2. The filtrates were combined, diluted with H_2O (20 ml) and extracted with CH_2Cl_2 (25 ml×3). The organic extracts were combined, washed with brine (25 ml), dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. Flash column chromatography (hexane/AcOEt=10 : 1) of the residue gave **12b** (1.21 g, 88%) as a colorless oil. $[\alpha]_D^{26}$ +6.1 (c=1.1, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.61 (3H, s), 1.72—1.80 (5H, m), 2.48—2.62 (2H, m), 3.29 (6H, s), 4.37 (1H, t, J=6.1 Hz), 5.16 (1H, d, J=12.8 Hz), 5.20 (1H, d, J=12.8 Hz), 5.65—5.82 (2H, m), 7.30—7.38 (5H, m). IR (neat) cm^{-1}: 1728. MS (EI$^+$) *m/z*: 338 (M$^+$). HR-MS (EI$^+$) *m/z*: 338.1542 (Calcd for $C_{18}H_{26}O_4S$ (M$^+$): 338.1552).

(b) Preparation of *ent*-**12b**: Compound *ent*-**12b** (780 mg, 94%) was prepared as a colorless oil from *ent*-**11b** (1.00 g, 2.45 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −6.5 (c=1.1, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m/z*: 338.1573 (Calcd for $C_{18}H_{26}O_4S$ (M$^+$): 338.1552).

(*R*)-Benzyl 2-(3,3-Dimethoxypropylthio)-2-methylbut-3-enoate (12a) and Its Enantiomer (*ent*-12a) (a) Preparation of **12a**: Treatments of **11a** (1.13 g, 2.87 mmol) in a manner similar to that described for the preparation of **12b**, afforded **12a** (766 mg, 82%) as a colorless oil. $[\alpha]_D^{28}$ +3.3 (c=0.8, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.62 (3H, s), 1.75—1.82 (2H, m), 2.50—2.63 (2H, m), 3.29 (6H, s), 4.38 (1H, t, J=6.1 Hz), 5.19 (2H, s), 5.23 (1H, d, J=11.1 Hz), 5.27 (1H, d, J=17.7 Hz), 6.14 (1H, dd, J=17.7, 11.1 Hz), 7.30—7.38 (5H, m). IR (neat) cm^{-1}: 1728. MS (EI$^+$) *m/z*: 324 (M$^+$). HR-MS (EI$^+$) *m/z*: 324.1424 (Calcd for $C_{17}H_{24}O_4S$ (M$^+$): 324.1395).

(b) Preparation of *ent*-**12a**: Compound *ent*-**12a** (794 mg, 92%) was prepared as a colorless oil from *ent*-**11a** (1.05 g, 2.67 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −3.9 (c=0.7, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 293.1241 (Calcd for $C_{16}H_{21}O_3S$ {[(M−CH_3O)+H]$^+$}: 293.1211).

(*R*,*E*)-Benzyl 2-(3,3-Dimethoxypropylthio)-2-methylhex-3-enoate (12c) and Its Enantiomer (*ent*-12c) (a) Preparation of **12c**: Treatments of **11c** (1.77 g, 4.20 mmol) in a manner similar to that described for the preparation of **12b**, afforded **12c** (1.40 g, 95%) as a colorless oil. $[\alpha]_D^{26}$ +3.6 (c=1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.99 (3H, t, J=7.9 Hz), 1.61 (3H, s), 1.76—1.82 (2H, m), 2.07—2.13 (2H, m), 2.48—2.62 (2H, m), 3.29 (6H, s), 4.38 (1H, t, J=5.5 Hz), 5.18 (2H, s), 5.68—5.79 (2H, m), 7.30—7.38 (5H, m). IR (neat) cm^{-1}: 1728. MS (EI$^+$) *m/z*: 352 (M$^+$). HR-MS (EI$^+$) *m/z*: 352.1727 (Calcd for $C_{19}H_{28}O_4S$ (M$^+$): 352.1708).

(b) Preparation of *ent*-**12c**: Compound *ent*-**12c** (1.42 g, 97%) was prepared as a colorless oil from *ent*-**11c** (1.75 g, 4.15 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −2.9 (c=1.0, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 321.1513 (Calcd for $C_{18}H_{25}O_3S$ {[(M−CH_3O)+H]$^+$}: 321.1524).

(*R*,*E*)-Benzyl 2-(3,3-Dimethoxypropylthio)-2-methylhept-3-enoate (12d) and Its Enantiomer (*ent*-12d) (a) Preparation of **12d**: Treatments of **11d** (1.35 g, 3.11 mmol) in a manner similar to that described for the preparation of **12b**, afforded **12d** (1.10 g, 96%) as a colorless oil. $[\alpha]_D^{28}$ +3.1 (c=0.8, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=7.3 Hz), 1.39 (2H, q, J=7.3 Hz), 1.61 (3H, s), 1.74—1.81 (2H, m), 2.01—2.08 (2H, m), 2.49—2.62 (2H, m), 3.29 (6H, s), 4.37 (1H, t, J=5.5 Hz), 5.18 (2H, s), 5.66 (1H, td, J=15.9, 6.7 Hz), 5.76 (1H, d, J=15.3 Hz), 7.30—7.39 (5H, m). IR (neat) cm^{-1}: 1728. MS (CI$^+$) *m/z*: 335 {[(M−CH_3O)+H]$^+$}. HR-MS (EI$^+$) *m/z*: 335.1695 (Calcd for $C_{19}H_{27}O_3S$ {[(M−CH_3O)+H]$^+$}: 335.1681).

(b) Preparation of *ent*-**12d**: Compound *ent*-**12d** (498 mg, 95%) was prepared as a colorless oil from *ent*-**11d** (625 mg, 1.43 mmol) in the same manner as described in (a). $[\alpha]_D^{28}$ −2.5 (c=0.8, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 335.1678 (Calcd for $C_{19}H_{27}O_3S$ {[(M−CH_3O)+H]$^+$}: 335.1681).

(*R*,*E*)-Benzyl 2-(3,3-Dimethoxypropylthio)-2-methyloct-3-enoate (12e) and Its Enantiomer (*ent*-12e) (a) Preparation of **12e**: Treatments of **11e** (10.7 g, 23.8 mmol) in a manner similar to that described for the preparation of **12b**, afforded **12e** (8.03 g, 89%) as a colorless oil. $[\alpha]_D^{21}$ +1.9 (c=1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=7.3 Hz), 1.24—1.37 (4H, m), 1.60 (3H, s), 1.78 (2H, td, J=7.3, 6.1 Hz), 2.07 (2H, q, J=6.1 Hz), 2.49—2.62 (2H, m), 3.29 (6H, s), 4.37 (1H, t, J=6.1 Hz), 5.18 (2H, s), 5.66 (1H, td, J=6.7, 15.9 Hz), 5.75 (1H, d, J=15.9 Hz), 7.30—7.39 (5H, m). IR (neat) cm^{-1}: 1728. MS (CI$^+$) *m/z*: 381 [(M+H)$^+$]. HR-MS (CI$^+$) *m/z*: 381.2067 (Calcd for $C_{21}H_{33}O_4S$ [(M+H)$^+$]: 381.2100).

(b) Preparation of *ent*-**12e**: Compound *ent*-**12e** (3.11 g, 92%) was prepared as a colorless oil from *ent*-**11e** (4.00 g, 8.90 mmol) in the same manner as described in (a). $[\alpha]_D^{21}$ −2.8 (c=1.0, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 381.2059 (Calcd for $C_{21}H_{33}O_4S$ [(M+H)$^+$]: 381.2100).

(*R*,*E*)-Benzyl 2-(3,3-Dimethoxypropylthio)-2-methyldec-3-enoate (12f) and Its Enantiomer (*ent*-12f) (a) Preparation of **12f**: Treatments of **11f** (9.60 g, 20.1 mmol) in a manner similar to that described for the preparation of **12b**, afforded **12f** (7.00 g, 85%) as a colorless oil. $[\alpha]_D^{21}$ +2.0 (c=1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=6.7 Hz), 1.24—1.37 (8H, m), 1.61 (3H, s), 1.78 (2H, td, J=7.3, 6.7 Hz), 2.06 (2H, q, J=6.7 Hz), 2.48—2.62 (2H, m), 3.29 (6H, s), 4.37 (1H, t, J=5.5 Hz), 5.18 (2H, s), 5.63 (1H, td, J=6.7, 15.3 Hz), 5.75 (1H, d, J=15.3 Hz), 7.31—7.39 (5H, m). IR (neat) cm^{-1}: 1728. MS (CI$^+$) *m/z*: 409 [(M+H)$^+$]. HR-MS (CI$^+$) *m/z*: 409.2408 (Calcd for $C_{23}H_{37}O_4S$ [(M+H)$^+$]: 409.2413).

(b) Preparation of *ent*-**12f**: Compound *ent*-**12f** (2.69 g, 98%) was prepared as a colorless oil from *ent*-**11f** (3.20 g, 6.70 mmol) in the same manner as described in (a). $[\alpha]_D^{26}$ −2.5 (c=1.1, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 409.2403 (Calcd for $C_{23}H_{37}O_4S$ [(M+H)$^+$]: 409.2413).

(*R*,*E*)-Benzyl 2-Methyl-2-(3-oxopropylthio)pent-3-enoate (13b) and Its

Enantiomer (*ent*-13b) (a) Preparation of **13b**: To a solution of **12b** (1.19 g, 3.52 mmol) in THF (18 ml), 6% HCl (6.0 ml) was added at room temperature, and the resulting mixture was stirred at the same temperature for 6 h. After quenching the reaction by adding saturated aqueous sodium hydrogen carbonate (30 ml) under cooling in an ice bath, the mixture was extracted with AcOEt (15 ml×3). The organic extracts were combined, washed with brine (20 ml), dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. Flash column chromatography (hexane/AcOEt=7 : 1) of the residue gave **13b** (1.01 g, 98%) as a colorless oil. $[\alpha]_D^{27}$ +1.2 (*c*=0.9, THF). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.61 (3H, s), 1.74 (3H, d, *J*=5.5 Hz), 2.57 (2H, t, *J*=7.3 Hz), 2.71—2.85 (2H, m), 5.16 (1H, d, *J*=12.8 Hz), 5.21 (1H, d, *J*=12.8 Hz), 5.66—5.80 (2H, m), 7.31—7.39 (5H, m), 9.62 (1H, s). IR (neat) cm^{-1}: 1726. MS (CI$^+$) *m*/*z*: 293 [(M+H)$^+$]. HR-MS (CI$^+$) *m*/*z*: 293.1210 (Calcd for $C_{16}H_{21}O_3S$ [(M+H)$^+$]: 293.1211).

(b) Preparation of *ent*-**13b**: Compound *ent*-**13b** (630 mg, 98%) was prepared as a colorless oil from *ent*-**12b** (743 mg, 2.20 mmol) in the same manner as described in (a). $[\alpha]_D^{26}$ −4.7 (*c*=0.9, THF). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 292.1122 (Calcd for $C_{16}H_{20}O_3S$ (M$^+$): 292.1133).

(*R*)-Benzyl 2-Methyl-2-(3-oxopropylthio)but-3-enoate (13a) and Its Enantiomer (*ent*-13a) (a) Preparation of **13a**: Treatments of **12a** (750 mg, 2.31 mmol) in a manner similar to those described for the preparation of **13b** afforded **13a** (631 mg, 98%) as a colorless oil. $[\alpha]_D^{21}$ −2.0 (*c*=0.8, toluene). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.62 (3H, s), 2.58 (2H, td, *J*=6.7, 1.2 Hz), 2.74—2.86 (2H, m), 5.19 (1H, d, *J*=12.8 Hz), 5.22 (1H, d, *J*=12.8 Hz), 5.25 (1H, d, *J*=10.4 Hz), 5.28 (1H, d, *J*=17.1 Hz,), 6.11 (1H, dd, *J*=17.1, 10.4 Hz), 7.31—7.40 (5H, m), 9.63 (1H, s). IR (neat) cm^{-1}: 1724. MS (CI$^+$) *m*/*z*: 279 [(M+H)$^+$]. HR-MS (CI$^+$) *m*/*z*: 279.1021 (Calcd for $C_{15}H_{19}O_3S$ [(M+H)$^+$]: 279.1055).

(b) Preparation of *ent*-**13a**: Compound *ent*-**13a** (621 mg, 93%) was prepared as a colorless oil from *ent*-**12a** (780 mg, 2.40 mmol) in the same manner as described in (a). $[\alpha]_D^{26}$ +2.2 (*c*=0.5, toluene). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m*/*z*: 279.1046 (Calcd for $C_{15}H_{19}O_3S$ [(M+H)$^+$]: 279.1055).

(*R*,*E*)-Benzyl 2-Methyl-2-(3-oxopropylthio)hex-3-enoate (13c) and Its Enantiomer (*ent*-13c) (a) Preparation of **13c**: Treatments of **12c** (1.34 g, 3.80 mmol) in a manner similar to that described for the preparation of **13b**, afforded **13c** (1.14 g, 98%) as a colorless oil.[43] ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.00 (3H, t, *J*=7.3 Hz), 1.61 (3H, s), 2.06—2.14 (2H, m), 2.58 (2H, td, *J*=7.3, 1.2 Hz), 2.71—2.85 (2H, m), 5.17 (1H, d, *J*=12.2 Hz), 5.21 (1H, d, *J*=12.2 Hz), 5.71—5.74 (2H, m), 7.30—7.40 (5H, m,), 9.63 (1H, s). IR (neat) cm^{-1}: 1726. MS (CI$^+$) *m*/*z*: 307 [(M+H)$^+$]. HR-MS (CI$^+$) *m*/*z*: 307.1325 (Calcd for $C_{17}H_{23}O_3S$ [(M+H)$^+$]: 307.1368).

(b) Preparation of *ent*-**13c**: Compound *ent*-**13c** (1.01 g, 97%) was prepared as a colorless oil from *ent*-**12c** (1.20 g, 3.41 mmol) in the same manner as described in (a).[43] ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m*/*z*: 307.1334 (Calcd for $C_{17}H_{23}O_3S$ [(M+H)$^+$]: 307.1368).

(*R*,*E*)-Benzyl 2-Methyl-2-(3-oxopropylthio)hept-3-enoate (13d) and Its Enantiomer (*ent*-13d) (a) Preparation of **13d**: Treatments of **12d** (992 mg, 2.71 mmol) in a manner similar to that described for the preparation of **13b**, afforded **13d** (811 mg, 93%) as a colorless oil. $[\alpha]_D^{28}$ +2.4 (*c*=0.6, toluene). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.88 (3H, t, *J*=7.3 Hz), 1.39 (2H, d, *J*=7.3 Hz), 1.61 (3H, s), 2.05 (2H, q, *J*=6.7 Hz), 2.57 (2H, td, *J*=6.7, 1.2 Hz), 2.71—2.85 (2H, m), 5.17 (1H, d, *J*=12.2 Hz), 5.20 (1H, d, *J*=12.2 Hz), 5.64—5.76 (2H, m), 7.32—7.38 (5H, m), 9.62 (1H, d, *J*=1.2 Hz). IR (neat) cm^{-1}: 1726. MS (CI$^+$) *m*/*z*: 321 [(M+H)$^+$]. HR-MS (CI$^+$) *m*/*z*: 321.1498 (Calcd for $C_{18}H_{25}O_3S$ [(M+H)$^+$]: 321.1524).

(b) Preparation of *ent*-**13d**: Compound *ent*-**13d** (389 mg, 92%) was prepared as a colorless oil from *ent*-**12d** (485 mg, 1.32 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −2.6 (*c*=0.6, toluene). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m*/*z*: 321.1552 (Calcd for $C_{18}H_{25}O_3S$ [(M+H)$^+$]: 321.1524).

(*R*,*E*)-Benzyl 2-Methyl-2-(3-oxopropylthio)oct-3-enoate (13e) and Its Enantiomer (*ent*-13e) (a) Preparation of **13e**: Treatments of **12e** (7.67 g, 20.2 mmol) in a manner similar to that described for the preparation of **13b**, afforded **13e** (4.43 g, 66%) as a colorless oil.[43] ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.89 (3H, t, *J*=7.3 Hz), 1.24—1.40 (4H, m), 1.61 (3H, s), 2.07 (2H, q, *J*=6.7 Hz), 2.58 (2H, td, *J*=7.3, 1.2 Hz), 2.72—2.85 (2H, m), 5.17 (1H, d, *J*=12.2 Hz), 5.21 (1H, d, *J*=12.2 Hz), 5.67 (1H, td, *J*=6.1, 15.9 Hz), 5.73 (1H, d, *J*=15.9 Hz), 7.32—7.38 (5H, m), 9.63 (1H, d, *J*=1.2 Hz). IR (neat) cm^{-1}: 1715. MS (EI$^+$) *m*/*z*: 334 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 334.1593 (Calcd for $C_{19}H_{26}O_3S$ (M$^+$): 334.1603.

(b) Preparation of *ent*-**13e**: Compound *ent*-**13e** (2.55 g, 100%) was prepared as a colorless oil from *ent*-**12e** (2.90 g, 7.62 mmol) in the same manner as described in (a).[43] ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 334.1634 (Calcd for $C_{19}H_{26}O_3S$ (M$^+$): 334.1603).

(*R*,*E*)-Benzyl 2-Methyl-2-(3-oxopropylthio)dec-3-enoate (13f) and Its Enantiomer (*ent*-13f) (a) Preparation of **13f**: Treatments of **12f** (6.85 g, 16.8 mmol) in a manner similar to that described for the preparation of **13b**, afforded **13f** (4.62 g, 76%) as a colorless oil.[43] ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.88 (3H, t, *J*=7.3 Hz), 1.25—1.55 (8H, m,), 1.61 (3H, s), 2.03—2.09 (2H, m), 2.57 (2H, td, *J*=7.3, 1.2 Hz), 2.71—2.85 (2H, m), 5.18 (1H, d, *J*=12.2 Hz), 5.21 (1H, d, *J*=12.2 Hz), 5.63—5.75 (2H, m), 7.30—7.39 (5H, m), 9.62 (1H, d, *J*=1.2 Hz). IR (neat) cm^{-1}: 1713. MS (EI$^+$) *m*/*z*: 362 (M$^+$). HR-MS (EI$^+$) *m*/*z*: 362.1891 (Calcd for $C_{21}H_{30}O_3S$ (M$^+$): 362.1916).

(b) Preparation of *ent*-**13f**: Compound *ent*-**13f** (2.01 g, 88%) was prepared as a colorless oil from *ent*-**12f** (2.57 g, 6.29 mmol) in the same manner as described in (a).[43] ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m*/*z*: 362.1887 (Calcd for $C_{21}H_{30}O_3S$ (M$^+$): 362.1916).

(*R*,*E*)-Benzyl 2-Methyl-2-(propionylthio)pent-3-enoate (14b) and Its Enantiomer (*ent*-14b) (a) Preparation of **14b**: To a suspension of Cs_2CO_3 (2.30 g, 7.06 mmol) in EtOH (105 ml), a solution of **13b** (400 mg, 1.37 mmol) in EtOH (34 ml) was added dropwise at 4 °C, and the resulting mixture was stirred at the same temperature for 20 min. The reaction mixture was poured into a mixture of saturated aqueous ammonium chloride solution and 1 mol/l HCl (3 : 1, 120 ml), and the aqueous mixture was extracted with Et_2O (20 ml×3). The organic extracts were combined, dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. The residue was diluted with CH_2Cl_2 (7 ml). Et_3N (0.3 ml, 2.15 mmol) and propionyl chloride (0.13 ml, 1.46 mmol) were added dropwise to the resulting CH_2Cl_2 solution at 4 °C, and the mixture was stirred at the same temperature for 30 min. After quenching the reaction by adding saturated aqueous ammonium chloride solution (30 ml), the mixture was extracted with CH_2Cl_2 (20 ml×3). The organic extracts were combined, washed with brine (20 ml), dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. Flash column chromatography (hexane/AcOEt=20 : 1) of the residue gave **14b** (295 mg, 74%) as a colorless oil. $[\alpha]_D^{26}$ +38.0 (*c*=0.4, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.10 (3H, t, *J*=7.3 Hz), 1.70 (3H, d, *J*=5.5 Hz), 1.75 (3H, s), 2.48 (2H, q, *J*=7.3 Hz), 5.15 (1H, d, *J*=12.2 Hz), 5.19 (1H, d, *J*=12.2 Hz), 5.60—5.80 (2H, m), 7.30—7.36 (5H, m). IR (neat) cm^{-1}: 1738, 1691. MS (CI$^+$) *m*/*z*: 293 [(M+H)$^+$]. HR-MS (CI$^+$) *m*/*z*: 293.1201 (Calcd for $C_{16}H_{21}O_3S$ [(M+H)$^+$]: 293.1211).

(b) Preparation of *ent*-**14b**: Compound *ent*-**14b** (241 mg, 86%) was prepared as a colorless oil from *ent*-**13b** (281 mg, 0.961 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −30.3 (*c*=0.4, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m*/*z*: 293.1249 (Calcd for $C_{16}H_{21}O_3S$ [(M+H)$^+$]: 293.1211).

(*R*)-Benzyl 2-Methyl-2-(propionylthio)but-3-enoate (14a) and Its Enantiomer (*ent*-14a) (a) Preparation of **14a**: Treatments of **13a** (240 mg, 1.06 mmol) in a manner similar to that described for the preparation of **14b**, afforded **14a** (240 mg, 81%) as a colorless oil. $[\alpha]_D^{30}$ +39.3 (*c*=0.5, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.11 (3H, t, *J*=7.3 Hz), 1.75 (3H, s), 2.49 (2H, q, *J*=7.3 Hz), 5.18 (2H, s), 5.25 (1H, d, *J*=11.0 Hz), 5.32 (1H, d, *J*=17.1 Hz), 6.13 (1H, dd, *J*=17.1, 11.0 Hz), 7.28—7.38 (5H, m). IR (neat) cm^{-1}: 1738, 1693. MS (CI$^+$) *m*/*z*: 279 [(M+H)$^+$]. HR-MS (CI$^+$) *m*/*z*: 279.1065 (Calcd for $C_{15}H_{19}O_3S$ [(M+H)$^+$]: 279.1055).

(b) Preparation of *ent*-**14a**: Compound *ent*-**14a** (227 mg, 73%) was prepared as a colorless oil from *ent*-**13a** (310 mg, 1.11 mmol) in the same manner as described in (a). $[\alpha]_D^{30}$ −34.7 (*c*=0.5, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m*/*z*: 279.1065 (Calcd for $C_{15}H_{19}O_3S$ [(M+H)$^+$]: 279.1055).

(*R*,*E*)-Benzyl 2-Methyl-2-(propionylthio)hex-3-enoate (14c) and Its Enantiomer (*ent*-14c) (a) Preparation of **14c**: Treatments of **13c** (468 mg, 1.53 mmol) in a manner similar to that described for the preparation of **14b**, afforded **14c** (232 mg, 50%) as a colorless oil. $[\alpha]_D^{27}$ +33.1 (*c*=0.6, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.96 (3H, t, *J*=7.3 Hz), 1.11 (3H, t, *J*=7.3 Hz), 1.76 (3H, s), 2.00—2.10 (2H, m), 2.50 (2H, q, *J*=7.3 Hz), 5.17 (2H, s), 5.62 (1H, td, *J*=1.2, 15.9 Hz), 5.77 (1H, td, *J*=6.1, 15.9 Hz), 7.29—7.36 (5H, m). IR (neat) cm^{-1}: 1738, 1692. MS (CI$^+$) *m*/*z*: 307 [(M+H)$^+$]. HR-MS (CI$^+$) *m*/*z*: 307.1328 (Calcd for $C_{17}H_{23}O_3S$ [(M+H)$^+$]: 307.1368).

(b) Preparation of *ent*-**14c**: Compound *ent*-**14c** (209 mg, 60%) was prepared as a colorless oil from *ent*-**13c** (349 mg, 1.14 mmol) in the same manner as described in (a). $[\alpha]_D^{28}$ −25.1 (*c*=0.6, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m*/*z*: 307.1354 (Calcd for $C_{17}H_{23}O_3S$ [(M+H)$^+$]: 307.1368).

(*R*,*E*)-Benzyl 2-Methyl-2-(propionylthio)hept-3-enoate (14d) and Its Enantiomer (*ent*-14d) (a) Preparation of **14d**: Treatments of **13d** (400 mg, 1.25 mmol) in a manner similar to that described for the preparation of **14b**, afforded **14d** (244 mg, 61%) as a colorless oil. $[\alpha]_D^{27}$ +28.2 (c=0.5, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.85 (3H, t, J=7.9 Hz), 1.11 (3H, t, J=7.3 Hz), 1.36 (2H, d, J=7.3 Hz), 1.76 (3H, s), 1.96—2.06 (2H, m), 2.48 (2H, q, J=7.9 Hz), 5.17 (2H, s), 5.63 (1H, d, J=15.9 Hz), 5.72 (1H, td, J=6.1, 15.9 Hz), 7.30—7.36 (5H, m). IR (neat) cm^{-1}: 1738, 1694. MS (CI$^+$) m/z: 321 $[(M+H)^+]$. HR-MS (CI$^+$) m/z: 321.1518 (Calcd for $C_{18}H_{25}O_3S$ $[(M+H)^+]$: 321.1524).

(b) Preparation of *ent*-**14d**: Compound *ent*-**14d** (240 mg, 60%) was prepared as a colorless oil from *ent*-**13d** (400 mg, 1.25 mmol) in the same manner as described in (a). $[\alpha]_D^{26}$ −29.5 (c=0.5, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 321.1491 (Calcd for $C_{18}H_{25}O_3S$ $[(M+H)^+]$: 321.1524).

(*R*,*E*)-Benzyl 2-Methyl-2-(propionylthio)oct-3-enoate (14e) and Its Enantiomer (*ent*-14e) (a) Preparation of **14e**: Treatments of **13e** (1.40 g, 4.19 mmol) in a manner similar to that described for the preparation of **14b**, afforded **14e** (875 mg, 62%) as a colorless oil. $[\alpha]_D^{27}$ +34.5 (c=1.1, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=7.3 Hz), 1.11 (3H, t, J=7.3 Hz), 1.20—1.36 (4H, m), 1.76 (3H, s), 1.97—2.07 (2H, m), 2.50 (2H, q, J=7.3 Hz), 5.17 (2H, s), 5.63 (1H, d, J=15.9 Hz), 5.72 (1H, td, J=6.7, 15.9 Hz), 7.29—7.38 (5H, m). IR (neat) cm^{-1}: 1738, 1694. MS (EI$^+$) m/z: 334 (M^+). HR-MS (EI$^+$) m/z: 334.1580 (Calcd for $C_{19}H_{26}O_3S$ (M^+): 334.1603).

(b) Preparation of *ent*-**14e**: Compound *ent*-**14e** (759 mg, 76%) was prepared as a colorless oil from *ent*-**13e** (1.00 g, 2.99 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −33.9 (c=1.1, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 334.1572 (Calcd for $C_{19}H_{26}O_3S$ (M^+): 334.1603.

(*R*,*E*)-Benzyl 2-Methyl-2-(propionylthio)dec-3-enoate (14f) and Its Enantiomer (*ent*-14f) (a) Preparation of **14f**: Treatments of **13f** (1.40 g, 3.86 mmol) in a manner similar to that described for the preparation of **14b**, afforded **14f** (697 mg, 50%) as a colorless oil. $[\alpha]_D^{27}$ +38.9 (c=0.5, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.87 (3H, t, J=7.3 Hz), 1.11 (3H, t, J=7.3 Hz), 1.20—1.40 (8H, m), 1.76 (3H, s), 1.97—2.06 (2H, m), 2.48 (2H, q, J=7.3 Hz), 5.17 (2H, s), 5.63 (1H, d, J=15.3 Hz), 5.73 (1H, td, J=6.1, 15.3 Hz), 7.30—7.37 (5H, m). IR (neat) cm^{-1}: 1740, 1694. MS (EI$^+$) m/z: 362 (M^+). HR-MS (EI$^+$) m/z: 362.1895 (Calcd for $C_{21}H_{30}O_3S$ (M^+): 362.1916).

(b) Preparation of *ent*-**14f**: Compound *ent*-**14f** (806 mg, 90%) was prepared as a colorless oil from *ent*-**13f** (900 mg, 2.48 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −35.6 (c=1.0, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 362.1887 (Calcd for $C_{21}H_{30}O_3S$ (M^+): 362.1916).

(*R*,*E*)-Benzyl 2-Methyl-2-(acetylthio)pent-3-enoate (15b) and Its Enantiomer (*ent*-15b) (a) Preparation of **15b**: Treatments of **13b** (448 mg, 1.53 mmol) in a manner similar to that described for the preparation of **14b** from **13b** using acetyl chloride (0.11 ml, 1.52 mmol) in place of propionyl chloride, afforded **15b** (288 mg, 68%) as a colorless oil. $[\alpha]_D^{27}$ +25.9 (c=1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.70 (3H, d, J=5.5 Hz), 1.75 (3H, s), 2.25 (3H, s), 5.15 (1H, d, J=12.2 Hz), 5.20 (1H, d, J=12.2 Hz), 5.65—5.80 (2H, m), 7.31—7.37 (5H, m). IR (neat) cm^{-1}: 1738, 1692. MS (CI$^+$) m/z: 279 $[(M+H)^+]$. HR-MS (CI$^+$) m/z: 279.1035 (Calcd for $C_{15}H_{19}O_3S$ $[(M+H)^+]$: 279.1055).

(b) Preparation of *ent*-**15b**: Compound *ent*-**15b** (165 mg, 52%) was prepared as a colorless oil from *ent*-**13b** (330 mg, 1.13 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −20.1 (c=1.0, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 279.1052 (Calcd for $C_{15}H_{19}O_3S$ $[(M+H)^+]$: 279.1055).

(*R*)-Benzyl 2-Methyl-2-(acethylthio)but-3-enoate (15a) and Its Enantiomer (*ent*-15a) (a) Preparation of **15a**: Treatments of **13a** (310 mg, 1.11 mmol) in a manner similar to that described for the preparation of **15b**, afforded **15a** (203 mg, 69%) as a colorless oil. $[\alpha]_D^{29}$ +32.5 (c=0.6, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.75 (3H, s), 2.26 (3H, s), 5.18 (2H, s), 5.24 (1H, d, J=10.4 Hz), 5.32 (1H, d, J=17.1 Hz), 6.13 (1H, dd, J=17.1, 10.4 Hz), 7.29—7.39 (5H, m). IR (neat) cm^{-1}: 1738, 1693. MS (CI$^+$) m/z: 265 $[(M+H)^+]$. HR-MS (CI$^+$) m/z: 265.0935 (Calcd for $C_{14}H_{17}O_3S$ $[(M+H)^+]$: 265.0898).

(b) Preparation of *ent*-**15a**: Compound *ent*-**15a** (215 mg, 75%) was prepared as a colorless oil from *ent*-**13a** (300 mg, 1.08 mmol) in the same manner as described in (a). $[\alpha]_D^{30}$ −32.7 (c=0.6, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 265.0934 (Calcd for $C_{14}H_{17}O_3S$ $[(M+H)^+]$: 265.0898).

(*R*,*E*)-Benzyl 2-Methyl-2-(acetylthio)hex-3-enoate (15c) and Its Enantiomer (*ent*-15c) (a) Preparation of **15c**: Treatments of **13c** (468 mg, 1.53 mmol) in a manner similar to that described for the preparation of **15b**, afforded **15c** (234 mg, 52%) as a colorless oil. $[\alpha]_D^{28}$ +20.7 (c=0.6, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.95 (3H, t, J=7.3 Hz), 1.76 (3H, s), 2.00—2.10 (2H, m), 2.25 (3H, s), 5.15 (1H, d, J=12.2 Hz), 5.19 (1H, d, J=12.2 Hz), 5.61 (1H, td, J=1.2, 15.3 Hz), 5.77 (1H, td, J=6.1, 15.3 Hz), 7.28—7.36 (5H, m). IR (neat) cm^{-1}: 1738, 1692. MS (CI$^+$) m/z: 293 $[(M+H)^+]$. HR-MS (CI$^+$) m/z: 293.1172 (Calcd for $C_{16}H_{21}O_3S$ $[(M+H)^+]$: 293.1211).

(b) Preparation of *ent*-**15c**: Compound *ent*-**15c** (289 mg, 75%) was prepared as a colorless oil from *ent*-**13c** (401 mg, 1.31 mmol) in the same manner as described in (a). $[\alpha]_D^{28}$ −21.4 (c=0.6, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 293.1212 (Calcd for $C_{16}H_{21}O_3S$ $[(M+H)^+]$: 293.1211).

(*R*,*E*)-Benzyl 2-Methyl-2-(acetylthio)hept-3-enoate (15d) and Its Enantiomer (*ent*-15d) (a) Preparation of **15d**: Treatments of **13d** (390 mg, 1.22 mmol) in a manner similar to that described for the preparation of **15b**, afforded **15d** (274 mg, 73%) as a colorless oil. $[\alpha]_D^{21}$ +19.2 (c=0.7, $CHCl_3$). ^{1}H-NMR($CDCl_3$) δ: 0.85 (3H, t, J=7.3 Hz), 1.36 (2H, d, J=7.3 Hz), 1.76 (3H, s), 1.96—2.06 (2H, m), 2.25 (3H, s), 5.15 (1H, d, J=12.2 Hz), 5.20 (1H, d, J=12.2 Hz), 5.63 (1H, d, J=15.3 Hz), 5.72 (1H, td, J=15.3, 6.7 Hz), 7.29—7.36 (5H, m). IR (neat) cm^{-1}: 1738, 1692. MS (CI$^+$) m/z: 307 $[(M+H)^+]$. HR-MS (CI$^+$) m/z: 307.1344 (Calcd for $C_{17}H_{23}O_3S$ $[(M+H)^+]$: 307.1368).

(b) Preparation of *ent*-**15d**: Compound *ent*-**15d** (252 mg, 66%) was prepared as a colorless oil from *ent*-**13d** (400 mg, 1.25 mmol) in the same manner as described in (a). $[\alpha]_D^{21}$ −16.2 (c=0.7, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 307.1338 (Calcd for $C_{17}H_{23}O_3S$ $[(M+H)^+]$: 307.1368).

(*R*,*E*)-Benzyl 2-Methyl-2-(acetylthio)oct-3-enoate (15e) and Its Enantiomer (*ent*-15e) (a) Preparation of **15e**: Treatments of **13e** (2.94 g, 8.79 mmol) in a manner similar to that described for the preparation of **15b**, afforded **15e** (1.35 g, 48%) as a colorless oil. $[\alpha]_D^{27}$ +24.6 (c=1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=6.7 Hz), 1.22—1.36 (4H, m), 1.76 (3H, s), 2.04 (2H, q, J=6.7 Hz), 2.25 (3H, s), 5.15 (1H, d, J=12.2 Hz), 5.20 (1H, d, J=12.2 Hz), 5.62 (1H, d, J=15.9 Hz), 5.72 (1H, td, J=15.9, 6.7 Hz), 7.29—7.37 (5H, m). IR (neat) cm^{-1}: 1738, 1694. MS (EI$^+$) m/z: 320 (M^+). HR-MS (EI$^+$) m/z: 320.1479 (Calcd for $C_{18}H_{24}O_3S$ (M^+): 320.1446).

(b) Preparation of *ent*-**15e**: Compound *ent*-**15e** (359 mg, 37%) was prepared as a colorless oil from *ent*-**13e** (1.00 g, 2.99 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −25.9 (c=1.0, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 320.1480 (Calcd for $C_{18}H_{24}O_3S$ (M^+): 320.1446).

(*R*,*E*)-Benzyl 2-Methyl-2-(acetylthio)dec-3-enoate (15f) and Its Enantiomer (*ent*-15f) (a) Preparation of **15f**: Treatments of **13f** (3.05 g, 8.41 mmol) in a manner similar to that described for the preparation of **15b**, afforded **15f** (1.06 g, 36%) as a colorless oil. $[\alpha]_D^{27}$ +21.2 (c=1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.87 (3H, t, J=6.7 Hz), 1.20—1.38 (8H, m), 1.76 (3H, s), 1.97—2.05 (2H, m), 2.24 (3H, s), 5.15 (1H, d, J=12.2 Hz), 5.20 (1H, d, J=12.2 Hz), 5.62 (1H, d, J=15.3 Hz), 5.73 (1H, td, J=15.3, 6.7 Hz), 7.29—7.40 (5H, m). IR (neat) cm^{-1}: 1740, 1694. MS (EI$^+$) m/z: 348 (M^+). HR-MS (EI$^+$) m/z: 348.1745 (Calcd for $C_{20}H_{28}O_3S$ (M^+): 348.1759).

(b) Preparation of *ent*-**15f**: Compound *ent*-**15f** (803 mg, 83%) was prepared as a colorless oil from *ent*-**13f** (1.00 g, 2.76 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ −29.5 (c=1.0, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 348.1715 (Calcd for $C_{20}H_{28}O_3S$ (M^+): 348.1759).

(*R*,*E*)-4-Hydroxy-3,5-dimethyl-5-(prop-1-enyl)thiophen-2(5*H*)-one (3b) and Its Enantiomer (*ent*-3b) (a) Preparation of **3b**: To a solution of **14b** (289 mg, 0.988 mmol) in THF (49 ml), LiHMDS (1.0 mol/l solution in THF, 2.5 ml, 2.5 mmol) was added dropwise at −78 °C, and the resulting mixture was allowed to slowly warm to room temperature over 3.5 h. The mixture was poured into a solution of 1 mol/l HCl (40 ml), and the aqueous mixture was extracted with Et_2O (40 ml×3). The organic extracts were combined, dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. The residue was added to a saturated aqueous sodium hydrogen carbonate solution (20 ml). The aqueous mixture was washed with Et_2O (20 ml×2), then made acidic (pH1) by adding 1 mol/l HCl. The resulting aqueous mixture was extracted with Et_2O (20 ml×2) and AcOEt (20 ml×2). The organic extracts were combined, dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo* to give **3b** (134 mg, 74%) as a colorless powder. mp 128—131 °C (diisopropyl ether–cyclohexane). $[\alpha]_D^{26}$ +55.1 (c=0.3, MeOH) [ref. 22, $[\alpha]_D$ +44 (c=0.7, MeOH)]. The optical purity of **3b** obtained here was determined to be >99% ee by HPLC analysis with a chiral column [Daicel Chiralpak AS ϕ0.46 cm×25 cm, hexane/2-propanol/TFA=90 : 10 : 0.1, flow rate 1.0 ml/min; t_R 10.5 min (**3b**), 14.4 min (*ent*-**3b**)]. ^{1}H-NMR (400 MHz, CD$_3$OD) δ: 1.63 (3H, s), 1.72 (3H, s), 1.74 (3H, d, J=1.8 Hz), 5.57 (1H, dd, J=15.3, 1.8 Hz), 5.78 (1H, qd, J=6.6, 15.3 Hz). ^{13}C-NMR (100 MHz, CD$_3$OD) δ: 7.7, 17.9, 24.4, 58.4, 109.9, 127.9, 132.6, 182.6, 197.4. IR (KBr) cm^{-1}: 1605. MS (EI$^+$) m/z: 184 (M$^+$). HR-MS (EI$^+$) m/z: 184.0539 (Calcd for $C_9H_{12}O_2S$ (M$^+$): 184.0558).

(b) Preparation of *ent*-**3b**: Compound *ent*-**3b** (57 mg, 39%) was prepared as a colorless powder from *ent*-**14b** (230 mg, 0.787 mmol) in the same manner as described in (a). mp 130—134.5 °C (diisopropyl ether–cyclohexane). $[\alpha]_D^{26}$ −53.8 (c=0.3, MeOH) [ref. 22, $[\alpha]_D$ −53.7 (c=0.7, MeOH)]. The optical purity of *ent*-**3b** prepared here was estimated to be >99% ee using a method similar to that described in (a). ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 184.0597 (Calcd for $C_9H_{12}O_2S$ (M$^+$): 184.0558).

(*R*)-4-Hydroxy-3,5-dimethyl-5-vinylthiophen-2(5*H*)-one (3a) and Its Enantiomer (*ent*-3a) (a) Preparation of **3a**: Treatments of **14a** (231 mg, 0.830 mmol) in a manner similar to that described for the preparation of **3b**, afforded **3a** (99 mg, 70%) as a colorless powder. mp 114—116 °C (diisopropyl ether). $[\alpha]_D^{25}$ +42.1 (c=0.3, MeOH). While the optical purity of **3a** could not be determined by HPLC analysis, it was calculated to be >90% ee based on the diastereomeric excess of the corresponding **11a** which had been determined as >90% de by the ^{1}H-NMR spectra of **11a** and its (2′*S*)-diastereomer. ^{1}H-NMR (400 MHz, CD$_3$OD) δ: 1.68 (3H, s), 1.75 (3H, s), 5.22 (1H, d, J=10.4 Hz), 5.34 (1H, d, J=17.1 Hz), 5.95 (1H, dd, J=17.1, 10.4 Hz). ^{13}C-NMR (100 MHz, CD$_3$OD) δ: 7.7, 23.6, 58.5, 110.3, 116.0, 139.8, 181.6, 197.0. IR (KBr) cm^{-1}: 1597. MS (EI$^+$) m/z: 170 (M$^+$). HR-MS (EI$^+$) m/z: 170.0384 (Calcd for $C_8H_{10}O_2S$ (M$^+$): 170.0402).

(b) Preparation of *ent*-**3a**: Compound *ent*-**3a** (89 mg, 67%) was prepared as a colorless powder from *ent*-**14a** (218 mg, 0.783 mmol) in the same manner as described in (a). mp 111—114 °C (diisopropyl ether). $[\alpha]_D^{25}$ −38.2 (c=0.3, MeOH). The optical purity of *ent*-**3a** was calculated to be >90% ee similar to that for **3a**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 170.0384 (Calcd for $C_8H_{10}O_2S$ (M$^+$): 170.0402).

(*R*,*E*)-5-(But-1-enyl)-4-hydroxy-3,5-dimethylthiophen-2(5*H*)-one (3c) and Its Enantiomer (*ent*-3c) (a) Preparation of **3c**: Treatments of **14c** (222 mg, 0.724 mmol) in a manner similar to that described for the preparation of **3b**, afforded **3c** (94 mg, 65%) as a colorless powder. mp 103.5—105 °C (cyclohexane). $[\alpha]_D^{23}$ +52.1 (c=0.3, MeOH). While the optical purity of **3c** could not be determined by HPLC analysis, it was calculated to be >90% ee based on the diastereomeric excess of the corresponding **11c** which had been determined as >90% de by the ^{1}H-NMR spectra of **11c** and its (2′*S*)-diastereomer. ^{1}H-NMR (400 MHz, CD$_3$OD) δ: 1.01 (3H, t, J=7.3 Hz), 1.67 (3H, s), 1.73 (3H, s), 2.04—2.14 (2H, m), 5.55 (1H, td, J=1.2, 15.3 Hz), 5.81 (1H, td, J=6.1, 15.3 Hz). ^{13}C-NMR (100 MHz, CD$_3$OD) δ: 7.7, 13.7, 24.5, 26.4, 58.3, 109.9, 130.6, 134.6, 182.5, 197.4. IR (KBr) cm^{-1}: 1616. MS (EI$^+$) m/z: 198 (M$^+$). HR-MS (EI$^+$) m/z: 198.0681 (Calcd for $C_{10}H_{14}O_2S$ (M$^+$): 198.0715).

(b) Preparation of *ent*-**3c**: Compound *ent*-**3c** (90 mg, 70%) was prepared as a colorless powder from *ent*-**14c** (200 mg, 0.653 mmol) in the same manner as described in (a). mp 104—105.5 °C (cyclohexane). $[\alpha]_D^{22}$ −48.6 (c=0.3, MeOH). The optical purity of *ent*-**3c** was calculated to be >90% ee similar to that for **3c**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 198.0681 (Calcd for $C_{10}H_{14}O_2S$ (M$^+$): 198.0715).

(*R*,*E*)-4-Hydroxy-3,5-dimethyl-5-(pent-1-enyl)thiophen-2(5*H*)-one (3d) and Its Enantiomer (*ent*-3d) (a) Preparation of **3d**: Treatments of **14d** (234 mg, 0.730 mmol) in a manner similar to that described for the preparation of **3b**, afforded **3d** (99 mg, 64%) as a colorless crystals. mp 71—73 °C (heptane–diisopropyl ether). $[\alpha]_D^{25}$ +48.0 (c=0.3, MeOH). While the optical purity of **3d** could not be determined by HPLC analysis, it was calculated to be >90% ee based on the diastereomeric excess of the corresponding **11d** which had been determined as >90% de by the ^{1}H-NMR spectra of **11d** and its (2′*S*)-diastereomer. ^{1}H-NMR (400 MHz, CD$_3$OD) δ: 0.91 (3H, t, J=7.3 Hz), 1.42 (2H, q, J=7.3 Hz), 1.67 (3H, s), 1.73 (3H, s), 2.06 (2H, q, J=7.3 Hz), 5.56 (1H, d, J=15.9 Hz,), 5.76 (1H, td, J=7.3, 15.9 Hz). ^{13}C-NMR (100 MHz, CD$_3$OD) δ: 7.7, 13.9, 23.3, 24.5, 35.4, 58.4, 109.8, 131.8, 132.9, 182.7, 197.4. IR (KBr) cm^{-1}: 1618. MS (EI$^+$) m/z: 212 (M$^+$). HR-MS (EI$^+$) m/z: 212.0875 (Calcd for $C_{11}H_{16}O_2S$ (M$^+$): 212.0871).

(b) Preparation of *ent*-**3d**: Compound *ent*-**3d** (115 mg, 75%) was prepared as a colorless crystals from *ent*-**14d** (230 mg, 0.718 mmol) in the same manner as described in (a). mp 70—73 °C (heptane–diisopropyl ether). $[\alpha]_D^{25}$ −43.1 (c=0.3, MeOH). The optical purity of *ent*-**3d** was calculated to be >90% ee similar to that for **3d**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 212.0883 (Calcd for $C_{11}H_{16}O_2S$ (M$^+$): 212.0871).

(*R*,*E*)-5-(Hex-1-enyl)-4-hydroxy-3,5-dimethylthiophen-2(5*H*)-one (3e) and Its Enantiomer (*ent*-3e) (a) Preparation of **3e**: Treatments of **14e** (800 mg, 2.39 mmol) in a manner similar to that described for the preparation of **3b**, afforded **3e** (346 mg, 64%) as a colorless oil. $[\alpha]_D^{25}$ +69.1 (c=0.9, MeOH). The optical purity of **3e** obtained here was determined to be 91% ee by HPLC analysis with a chiral column [Daicel Chiralcel OD-H ϕ0.46 cm×25 cm, hexane/2-propanol/TFA=98 : 2 : 0.1, flow rate 0.35 ml/min; t_R 23.0 min (**3e**), 25.8 min (*ent*-**3e**)]. ^{1}H-NMR (400 MHz, CD$_3$OD) δ: 0.91 (3H, t, J=7.3 Hz), 1.26—1.42 (4H, m), 1.68 (3H, s), 1.73 (3H, s), 2.05—2.12 (2H, m), 5.55 (1H, td, J=1.2, 15.9 Hz), 5.76 (1H, td, J=6.7, 15.9 Hz). ^{13}C-NMR (100 MHz, CD$_3$OD) δ: 7.7, 14.2, 23.2, 24.5, 32.4, 33.0, 58.3, 110.1, 131.4, 131.8, 181.9, 197.4. IR (neat) cm^{-1}: 1705, 1616. MS (EI$^+$) m/z: 226 (M$^+$). HR-MS (EI$^+$) m/z: 226.1070 (Calcd for $C_{12}H_{18}O_2S$ (M$^+$): 226.1028).

(b) Preparation of *ent*-**3e**: Compound *ent*-**3e** (165 mg, 49%) was prepared as a colorless oil from *ent*-**14e** (500 mg, 1.50 mmol) in the same manner as described in (a). $[\alpha]_D^{19}$ −66.9 (c=0.8, MeOH). The optical purity of *ent*-**3e** prepared here was estimated to be 89% ee using a method similar to that described in (a). ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 226.0986 (Calcd for $C_{12}H_{18}O_2S$ (M$^+$): 226.1028).

(*R*,*E*)-4-Hydroxy-3,5-dimethyl-5-(oct-1-enyl)thiophen-2(5*H*)-one (3f) and Its Enantiomer (*ent*-3f) (a) Preparation of **3f**: Treatments of **14f** (670 mg, 1.85 mmol) in a manner similar to that described for the preparation of **3b**, afforded **3f** (155 mg, 33%) as a colorless oil. $[\alpha]_D^{21}$ +57.2 (c=1.1, MeOH). The optical purity of **3f** obtained here was determined to be 94% ee by HPLC analysis with a chiral column [Daicel Chiralpak AS-H ϕ0.46 cm×25 cm, hexane/2-propanol/TFA=95 : 5 : 0.1, flow rate 0.45 ml/min; t_R 12.1 min (**3f**), 16.1 min (*ent*-**3f**)]. ^{1}H-NMR (400 MHz, CD$_3$OD) δ: 0.90 (3H, t, J=7.3 Hz), 1.22—1.42 (8H, m), 1.68 (3H, s), 1.73 (3H, s), 2.05—2.12 (2H, m), 5.55 (1H, td, J=1.2, 15.3 Hz), 5.76 (1H, td, J=7.3, 15.3 Hz). ^{13}C-NMR (100 MHz, CD$_3$OD) δ: 7.7, 14.4, 23.7, 24.5, 29.8, 30.1, 32.8, 58.3, 110.1, 131.5, 133.2, 181.9, 197.4. IR (neat) cm^{-1}: 1707, 1615. MS (EI$^+$) m/z: 254 (M$^+$). HR-MS (EI$^+$) m/z: 254.1329 (Calcd for $C_{14}H_{22}O_2S$ (M$^+$): 254.1341).

(b) Preparation of *ent*-**3f**: Compound *ent*-**3f** (92 mg, 26%) was prepared as a colorless oil from *ent*-**14f** (500 mg, 1.38 mmol) in the same manner as described in (a). $[\alpha]_D^{20}$ −54.5 (c=0.9, MeOH). The optical purity of *ent*-**3f** prepared here was estimated to be 84% ee using a method similar to that described in (a). ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 254.1383 (Calcd for $C_{14}H_{22}O_2S$ (M$^+$): 254.1341).

(*R*,*E*)-4-Hydroxy-5-methyl-5-(prop-1-enyl)thiophen-2(5*H*)-one (4b) and Its Enantiomer (*ent*-4b) (a) Preparation of **4b**: Treatments of **15b** (273 mg, 0.981 mmol) in a similar manner to that described for the preparation of **3b**, gave **4b** (148 mg, 89%) as a colorless powder. mp 97—98.5 °C (hexane–AcOEt). $[\alpha]_D^{25}$ +10.1 (c=0.3, MeOH). The optical purity of **4b** prepared here was determined to be >99% ee by HPLC analysis with a chiral column [Daicel Chiralcel IA ϕ0.46 cm×25 cm, hexane/2-propanol/TFA=98 : 2 : 0.1, flow rate 0.7 ml/min; t_R 18.0 min (**4b**) and 19.5 min (*ent*-**4b**)]. ^{1}H-NMR (400 MHz, CD$_3$OD) δ: 1.72 (3H, d, J=1.2 Hz), 1.74 (3H, s), 5.63 (1H, dd, J=15.3, 1.2 Hz), 5.76—5.86 (1H, m). ^{13}C-NMR (400 MHz, CD$_3$OD) δ: 17.9, 24.9, 60.8, 127.7, 132.5, 189.6, 197.1. IR (KBr) cm^{-1}: 1607. MS (EI$^+$) m/z: 170(M$^+$). HR-MS (EI$^+$) m/z: 170.0380 (Calcd for $C_8H_{10}O_2S$ (M$^+$): 170.0402).

(b) Preparation of *ent*-**4b**: Compound *ent*-**4b** (54 mg, 88%) was prepared as a colorless powder from *ent*-**15b** (100 mg, 0.359 mmol) in the same manner as described in (a). mp 96—98.5 °C (hexane–AcOEt). $[\alpha]_D^{25}$ −8.4 (c=0.3, MeOH). The optical purity of *ent*-**4b** prepared here was estimated to be >99% ee using a method similar to that described in (a). ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 170.0377 (Calcd for $C_8H_{10}O_2S$ (M$^+$): 170.0402).

(*R*)-4-Hydroxy-5-methyl-5-vinylthiophen-2(5*H*)-one (4a) and Its Enantiomer (*ent*-4a) (a) Preparation of **4a**: Treatments of **15a** (192 mg, 0.726 mmol) in a manner similar to that described for the preparation of **3b**, afforded **4a** (98 mg, 86%) as a colorless powder. mp 73—75 °C (cyclohexane–diisopropyl ether). $[\alpha]_D^{25}$ +23.3 (c=0.3, MeOH). While the optical purity of **4a** could not be determined by HPLC analysis, it was calculated to be >90% ee based on the diastereomeric excess of the corresponding **11a** which had been determined as >90% de by the ^{1}H-NMR spectra of **11a** and its (2′*S*)-diastereomer. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.77 (3H, s), 5.22 (1H, d, *J*=11.0 Hz), 5.37 (1H, d, *J*=17.1 Hz), 6.02 (1H, dd, *J*=17.1, 11.0 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 24.2, 60.0, 115.9, 139.7, 189.1, 196.6. IR (KBr) cm^{-1}: 1605. MS (EI$^+$) *m/z*: 156 (M$^+$). HR-MS (EI$^+$) *m/z*: 156.0242 (Calcd for $C_7H_8O_2S$ (M$^+$): 156.0245.

(b) Preparation of *ent*-**4a**: Compound *ent*-**4a** (110 mg, 91%) was prepared as a colorless powder from *ent*-**15a** (205 mg, 0.776 mmol) in the same manner as described in (a). mp 73—75 °C (cyclohexane–diisopropyl ether). $[\alpha]_D^{25}$ −18.9 (*c*=0.3, MeOH). The optical purity of *ent*-**4a** was calculated to be >90% ee similar to the case for **4a**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m/z*: 156.0240 (Calcd for $C_7H_8O_2S$ (M$^+$): 156.0245).

(*R*,*E*)-5-(But-1-enyl)-4-hydroxy-5-methylthiophen-2(5*H*)-one (4c) and Its Enantiomer (*ent*-4c) (a) Preparation of **4c**: Treatments of **15c** (224 mg, 0.766 mmol) in a manner similar to that described for the preparation of **3b**, afforded **4c** (126 mg, 89%) as a colorless powder. mp 102—104 °C (cyclohexane–diisopropyl ether). $[\alpha]_D^{25}$ +9.2 (*c*=0.3, MeOH). The optical purity of **4c** prepared here was determined to be >99% ee by HPLC analysis with a chiral column [Daicel Chiralcel IA ϕ0.46 cm×25 cm, hexane/2-propanol/TFA=98 : 2 : 0.1, flow rate 0.5 ml/min; t_R 21.1 min (**4c**), 23.3 min (*ent*-**4c**)]. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.01 (3H, t, *J*=7.3 Hz), 1.74 (3H, s), 2.05—2.14 (2H, m), 5.61 (1H, td, *J*=1.2, 15.9 Hz), 5.88 (1H, td, *J*=6.1, 15.9 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 13.8, 25.0, 26.4, 60.7, 130.5, 134.5, 189.7, 197.1. IR (KBr) cm^{-1}: 1605. MS (EI$^+$) *m/z*: 210 (M$^+$). HR-MS (EI$^+$) *m/z*: 184.0553 (Calcd for $C_9H_{12}O_2S$ (M$^+$): 184.0558).

(b) Preparation of *ent*-**4c**: Compound *ent*-**4c** (126 mg, 73%) was prepared as a colorless powder from *ent*-**15c** (205 mg, 0.776 mmol) in the same manner as described in (a). mp 105—107 °C (cyclohexane–diisopropyl ether). $[\alpha]_D^{25}$ −8.8 (*c*=0.3, MeOH). The optical purity of *ent*-**4c** prepared here was estimated to be >99% ee using a method similar to that described in (a). ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m/z*: 184.0521 (Calcd for $C_9H_{12}O_2S$ (M$^+$): 184.0558).

(*R*,*E*)-4-Hydroxy-5-methyl-5-(pent-1-enyl)thiophen-2(5*H*)-one (4d) and Its Enantiomer (*ent*-4d) (a) Preparation of **4d**: Treatments of **15d** (260 mg, 0.849 mmol) in a manner similar to that described for the preparation of **3b**, afforded **4d** (129 mg, 77%) as a colorless powder. mp 90—92 °C (cyclohexane–diisopropyl ether). $[\alpha]_D^{25}$ +112 (*c*=0.3, $CHCl_3$). The optical purity of **4d** prepared here was determined to be >99% ee by HPLC analysis with a chiral column [Daicel Chiralpak IA ϕ0.46 cm×25 cm, hexane/2-propanol/TFA=98 : 2 : 0.1, flow rate 0.5 ml/min; t_R 19.6 min (**4d**), 21.2 min (*ent*-**4d**)]. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.01 (3H, t, *J*=7.3 Hz), 1.14—1.27 (2H, m), 1.74 (3H, s), 1.82—1.90 (2H, m), 5.61 (1H, td, *J*=1.2, 15.9 Hz), 5.88 (1H, td, *J*=6.1, 15.9 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 13.8, 23.3, 25.0, 35.4, 60.7, 131.7, 132.9, 189.4, 197.1. IR (KBr) cm^{-1}: 1615. MS (CI$^+$) *m/z*: 199 [(M+H)$^+$]. HR-MS (CI$^+$) *m/z*: 199.0820 (Calcd for $C_{10}H_{15}O_2S$ [(M+H)$^+$]: 199.0793).

(b) Preparation of *ent*-**4d**: Compound *ent*-**4d** (114 mg, 73%) was prepared as a colorless powder from *ent*-**15d** (243 mg, 0.793 mmol) in the same manner as described in (a). mp 90—92.5 °C (cyclohexane–diisopropyl ether). $[\alpha]_D^{21}$ −103 (*c*=0.3, $CHCl_3$). The optical purity of *ent*-**4d** prepared here was estimated to be >99% ee using a method similar to that described in (a). ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 199.0766 (Calcd for $C_{10}H_{15}O_2S$ [(M+H)$^+$]: 199.0793).

(*R*,*E*)-5-(Hex-1-enyl)-4-hydroxy-5-methylthiophen-2(5*H*)-one (4e) and Its Enantiomer (*ent*-4e) (a) Preparation of **4e**: Treatments of **15e** (1.30 g, 4.06 mmol) in a manner similar to that described for the preparation of **3b**, afforded **4e** (752 mg, 87%) as a colorless oil. $[\alpha]_D^{22}$ +85.7 (*c*=0.9, $CHCl_3$). The optical purity of **4e** prepared here was determined to be 91% ee by HPLC analysis with a chiral column [Daicel Chiralcel OD-H ϕ0.46 cm×25 cm, hexane/2-propanol/TFA=98 : 2 : 0.1, flow rate 0.35 ml/min, t_R 23.0 min (**4e**), 25.8 min (*ent*-**4e**)]. ^{1}H-NMR (400 MHz, CD_3OD) δ: 0.91 (3H, t, *J*=7.3 Hz), 1.26—1.42 (4H, m), 1.75 (3H, s), 2.09 (2H, qd, *J*=7.3, 1.2 Hz), 5.61 (1H, td, *J*=1.2, 15.3 Hz), 5.79 (1H, td, *J*=6.7, 15.3 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 14.2, 23.1, 25.0, 32.4, 33.0, 60.7, 131.4, 133.1, 189.1, 197.0. IR (neat) cm^{-1}: 1624, 1586. MS (CI$^+$) *m/z*: 213 [(M+H)$^+$]. HR-MS (CI$^+$) *m/z*: 213.0945 (Calcd for $C_{11}H_{17}O_2S$ [(M+H)$^+$]: 213.0949).

(b) Preparation of *ent*-**4e**: Compound *ent*-**4e** (138 mg, 83%) was prepared as a colorless oil from *ent*-**15e** (250 mg, 0.780 mmol) in the same manner as described in (a). $[\alpha]_D^{21}$ −85.5 (*c*=0.7, $CHCl_3$). The optical purity of *ent*-**4e** prepared here was estimated to be 88% ee using a method similar to that described in (a). ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) *m/z*: 213.0948 (Calcd for $C_{11}H_{17}O_2S$ [(M+H)$^+$]: 213.0949).

(*R*,*E*)-4-Hydroxy-5-methyl-5-(oct-1-enyl)thiophen-2(5*H*)-one (4f) and Its Enantiomer (*ent*-4f) (a) Preparation of **4f**: Treatments of **15f** (1.00 g, 2.87 mmol) in a manner similar to those described for the preparation of **3b**, afforded **4f** (526 mg, 76%) as a colorless oil. $[\alpha]_D^{22}$ +78.7 (*c*=0.8, $CHCl_3$). The optical purity of **4f** prepared here was determined to be 91% ee by HPLC analysis with a chiral column [Daicel Chiralcel OD-H ϕ0.46 cm×25 cm, hexane/2-propanol/TFA=98 : 2 : 0.1, flow rate 0.35 ml/min, t_R 21.3 min (**4f**), 24.5 min (*ent*-**4f**)]. ^{1}H-NMR (400 MHz, CD_3OD) δ: 0.90 (3H, t, *J*=6.7 Hz), 1.22—1.42 (8H, m), 1.75 (3H, s), 2.08 (2H, qd, *J*=6.7, 1.2 Hz), 5.61 (1H, td, *J*=1.2, 15.3 Hz), 5.80 (1H, td, *J*=6.7, 15.3 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 14.4, 23.7, 24.9, 29.8, 30.1, 32.8, 33.3, 60.7, 131.4, 133.2, 189.1, 197.0. IR (neat) cm^{-1}: 1630, 1586. MS (EI$^+$) *m/z*: 240 (M$^+$). HR-MS (EI$^+$) *m/z*: 240.1155 (Calcd for $C_{13}H_{20}O_2S$ (M$^+$): 240.1184).

(b) Preparation of *ent*-**4f**: Compound *ent*-**4f** (306 mg, 89%) was prepared as a colorless oil from *ent*-**15f** (500 mg, 1.43 mmol) in the same manner as described in (a). $[\alpha]_D^{22}$ −75.8 (*c*=0.7, $CHCl_3$). The optical purity of *ent*-**4f** prepared here was estimated to be 87% ee using a method similar to that described in (a). ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m/z*: 240.1152 (Calcd for $C_{13}H_{20}O_2S$ (M$^+$): 240.1184).

Cyclohept-1-enecarbaldehyde (16b) To a solution of 1-(nitromethyl)cyclohept-1-ene[17] (1.86 g, 12.0 mmol) in MeOH (60 ml), sodium methoxide (750 mg, 13.2 mmol) was added at room temperature, and the resulting mixture was stirred at the same temperature for 30 min. Titanium(III) chloride (20% aqueous solution, 37.0 g, 48.0 mmol) was added to the mixture at the same temperature, and the stirring was continued for 3 h at room temperature. The reaction mixture was extracted with Et_2O (30 ml×5). The organic extracts were combined, dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. Flash column chromatography (hexane/AcOEt=10 : 1) of the residue gave **16b** (1.14 g, 77%) as a colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.46—1.54 (2H, m), 1.58—1.64 (2H, m), 1.76—1.84 (2H, m), 2.41—2.49 (4H, m), 6.87 (1H, t, *J*=6.4 Hz), 9.34 (1H, s). IR (ATR) cm^{-1}: 1679, 1641. MS (EI$^+$) *m/z*: 124 (M$^+$). HR-MS (EI$^+$) *m/z*: 124.0896 (Calcd for $C_8H_{12}O$ (M$^+$): 124.0888).

(*E*)-Cyclooct-1-enecarbaldehyde (16c) To a stirred suspension of 4-methylbenzenesulfonohydrazide (38.9 g, 198 mmol) and cyclooctanone (25.0 g, 0.198 mmol) in MeOH (132 ml) was added conc. HCl (0.6 ml) at room temperature and the resulting mixture was stirred at the same temperature for 2 h. The precipitates which appeared were collected by filtration and dried *in vacuo* to afford *N*′-cyclooctylidene-4-methylbenzenesulfonohydrazide as a white solid (52.7 g, 91%). To a stirred suspension of *N*′-cyclooctylidene-4-methylbenzenesulfonohydrazide (1.00 g, 3.40 mmol) in TMEDA (13.6 ml), *n*-BuLi (1.6 mol/l in hexane, 4.9 ml, 7.84 mmol) was added dropwise at −78 °C. After the resulting mixture was stirred at room temperature for 30 min, DMF (1.3 ml, 16.8 mmol) was added at 4 °C. The reaction mixture was stirred at room temperature for 2 h. After quenching the reaction by adding water, the mixture was extracted with AcOEt (20 ml×3). The organic extracts were combined, washed with brine (20 ml), dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. Flash column chromatography (hexane/AcOEt=20 : 1) of the residue gave **16c** (370 mg, 79%) as a colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.40—1.58 (6H, m), 1.65—1.74 (2H, m), 2.40—2.50 (4H, m), 6.72 (1H, t, *J*=8.3 Hz), 9.41 (1H, s). IR (ATR) cm^{-1}: 1681. MS (EI$^+$) *m/z*: 138 (M$^+$). HR-MS (EI$^+$) *m/z*: 138.1043 (Calcd for $C_9H_{14}O$ (M$^+$): 138.1045).

(*E*)-3-Cyclohexenyl-2-methylacrylic acid (17a) Treatments of **16a** (2.90 ml, 24.9 mmol) and triethyl 2-phosphonopropionate (6.40 g, 26.3 mmol) in a manner similar to that described for the preparation of **8d**, afforded **17a** (3.64 g, 88%) as a colorless crystals. mp 102—103 °C (MeOH−H_2O). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.56—1.70 (4H, m), 2.02 (3H, s), 2.16—2.30 (4H, m), 6.00 (1H, br s), 7.18 (1H, s). IR (KBr) cm^{-1}: 1661. MS (EI$^+$) *m/z*: 166 (M$^+$). HR-MS (EI$^+$) *m/z*: 166.1002 (Calcd for $C_{10}H_{14}O_2$ (M$^+$): 166.0994).

(*E*)-3-Cycloheptenyl-2-methylacrylic Acid (17b) Treatments of **16b** (17.4 g, 140 mmol) and triethyl 2-phosphonopropionate (33.4 g, 137 mmol) in a manner similar to that described for the preparation of **8d**, afforded **17b** (15.0 g, 59%) as a colorless crystals. mp 102—103 °C (MeOH−H_2O). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.50—1.59 (4H, m), 1.75—1.82 (2H, m), 1.97 (3H, d, *J*=1.2 Hz), 2.24—2.36 (4H, m), 6.06 (1H, t, *J*=6.7 Hz), 7.25 (1H, s). IR (ATR) cm^{-1}: 1670 cm^{-1}. MS (CI$^+$) *m/z*: 181 [(M+H)$^+$]. HR-MS (CI$^+$) *m/z*: 181.1241 (Calcd for $C_{11}H_{17}O_2$ [(M+H)$^+$]: 181.1229).

(*E*)-3-[(*E*)-Cyclooctenyl]-2-methylacrylic Acid (17c) Treatments of **16c** (6.91 g, 50.0 mmol) and triethyl 2-phosphonopropionate (13.4 g, 55.1 mmol) in a manner similar to that described for the preparation of **8d**, afforded **17c** (7.81 g, 81%) as a colorless crystals. mp 61—62 °C (MeOH−H_2O). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.49—1.56 (8H, m), 2.01 (3H, d, J=1.2 Hz), 2.20—2.38 (4H, m), 5.49 (1H, br s), 5.90 (1H, t, J=8.6 Hz), 7.17 (1H, s). IR (ATR) cm^{-1}: 1664. MS (CI$^+$) m/z: 195 [(M+H)$^+$]. HR-MS (CI$^+$) m/z: 195.1392 (Calcd for $C_{12}H_{19}O_2$ [(M+H)$^+$]: 195.1385).

(*R*,*E*)-4-Benzyl-3-(3-cyclohexenyl-2-methylacryloyl)oxazolidin-2-one (18a) and Its Enantiomer (*ent*-18a) (a) Preparation of **18a**: Treatments of **17a** (3.00 g, 18.0 mmol) in a manner similar to that described for the preparation of **9b**, afforded **18a** (4.73 g, 81%) as a colorless crystals. mp 95—96 °C (diisopropyl ether). $[\alpha]_D^{25}$ −75.0 (c=1.0, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.56—1.71 (4H, m), 2.08 (3H, s), 2.15—2.21 (2H, m), 2.24—2.31 (2H, m), 2.83 (1H, dd, J=13.5, 9.2 Hz), 3.35 (1H, dd, J=13.5, 3.7 Hz), 4.15 (1H, dd, J=9.2, 5.5 Hz), 4.25 (1H, t, J=9.2 Hz), 4.68—4.76 (1H, m), 5.95 (1H, br s), 6.38 (1H, s), 7.19—7.35 (5H, m). IR (KBr) cm^{-1}: 1792, 1663. MS (EI$^+$) m/z: 325 (M$^+$). HR-MS (EI$^+$) m/z: 325.1691 (Calcd for $C_{20}H_{23}NO_3$ (M$^+$): 325.1678).

(b) Preparation of *ent*-**18a**: Compound *ent*-**18a** (2.07 g, 79%) was prepared as a colorless crystals from **17a** (1.41 g, 8.48 mmol) and (*S*)-4-benzyloxazolidin-2-one (1.71 g, 9.46 mmol) in the same manner as described in (a). mp 95—97 °C (diisopropyl ether). $[\alpha]_D^{25}$ +81.8 (c=0.9, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 325.1697 (Calcd for $C_{20}H_{23}NO_3$ (M$^+$): 325.1678).

(*R*,*E*)-4-Benzyl-3-(3-cycloheptenyl-2-methylacryloyl)oxazolidin-2-one (18b) and Its Enantiomer (*ent*-18b) (a) Preparation of **18b**: Treatments of **17b** (2.00 g, 11.1 mmol) in a manner similar to that described for the preparation of **9b**, afforded **18b** (2.94 g, 78%) as a colorless crystals. mp 98—103 °C (diisopropyl ether). $[\alpha]_D^{23}$ −62.7 (c=0.3, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.50—1.59 (4H, m), 1.74—1.82 (2H, m), 2.04 (3H, d, J=1.8 Hz), 2.22—2.36 (4H, m), 2.82 (1H, dd, J=13.5, 9.2 Hz), 3.36 (1H, dd, J=13.5, 3.1 Hz), 4.15 (1H, dd, J=9.2, 5.5 Hz), 4.25 (1H, t, J=7.9 Hz), 4.69—4.76 (1H, m), 6.06 (1H, t, J=6.7 Hz), 6.45 (1H, s), 7.19—7.36 (5H, m). IR (KBr) cm^{-1}: 1792, 1667. MS (EI$^+$) m/z: 339 (M$^+$). HR-MS (EI$^+$) m/z: 339.1812 (Calcd for $C_{21}H_{25}NO_3$ (M$^+$): 339.1834).

(b) Preparation of *ent*-**18b**: Compound *ent*-**18b** (4.84 g, 86%) was prepared as a colorless crystals from **17b** (3.00 g, 16.6 mmol) and (*S*)-4-benzyloxazolidin-2-one (3.53 g, 19.5 mmol) in the same manner as described in (a). mp 94—96 °C (diisopropyl ether). $[\alpha]_D^{25}$ +70.5 (c=0.3, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 339.1846 (Calcd for $C_{21}H_{25}NO_3$ (M$^+$): 339.1834).

(*R*,*E*)-4-Benzyl-3-[(*E*)-3-cyclooctenyl-2-methylacryloyl]oxazolidin-2-one (18c) and Its Enantiomer (*ent*-18c) (a) Preparation of **18c**: Treatments of **17c** (2.31 g, 11.9 mmol) in a manner similar to that described for the preparation of **9b**, afforded **18c** (3.00 g, 71%) as a colorless crystals. mp 91.5—93.0 °C (diisopropyl ether). $[\alpha]_D^{28}$ −72.1 (c=0.3, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.44—1.63 (8H, m), 2.08 (3H, d, J=1.2 Hz), 2.19—2.39 (4H, m), 2.84 (1H, dd, J=13.4, 9.2 Hz), 3.35 (1H, dd, J=13.4, 3.7 Hz), 4.15 (1H, dd, J=8.6, 5.8 Hz), 4.26 (1H, t, J=8.6 Hz), 4.69—4.77 (1H, m), 5.91 (1H, t, J=8.3Hz), 6.39 (1H, s), 7.19—7.36 (5H, m). IR (ATR) cm^{-1}: 1790, 1669. MS (EI$^+$) m/z: 353 (M$^+$). HR-MS (EI$^+$) m/z: 353.2030 (Calcd for $C_{22}H_{27}NO_3$ (M$^+$): 353.1991).

(b) Preparation of ent-**18c**: Compound *ent*-**18c** (3.29 g, 65%) was prepared as a colorless crystals from **17c** (2.78 g, 14.3 mmol) and (*S*)-4-benzyloxazolidin-2-one (3.04 g, 16.8 mmol) in the same manner as described in (a). mp 93.0—94.5 °C (diisopropyl ether). $[\alpha]_D^{28}$ +70.0 (c=0.3, MeOH). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 353.2030 (Calcd for $C_{22}H_{27}NO_3$ (M$^+$): 353.1991).

Deconjugative Asymmetric α-Sulfenylation of (*R*,*E*)- and (*S*,*E*)-4-Benzyl-3-(3-cyclohexenyl-2-methylacryloyl)oxazolidin-2-one (18a, *ent*-18a). (*R*)-4-Benzyl-3-[(*R*,*E*)-3-(cyclohex-2-enylidene)-2-(3,3-dimethoxypropylthio)-2-methylpropanoyl]oxazolidin-2-one (19a), Its (*S*,*E*)-Diastereomer (26a), (*R*,*Z*)-Isomer (27a) and Their Enantiomers (*ent*-19a, *ent*-26a, *ent*-27a) (a) Preparation of **19a**, **26a** and **27a**: To a solution of **18a** (1.30 g, 4.00 mmol) and HMPA (2.8 ml, 16.1 mmol) in THF (20 ml), NaHMDS (1.0 mol/l solution in THF, 4.4 ml, 4.40 mmol) was added dropwise at −78 °C, and the resulting mixture was stirred at the same temperature for 30 min. A solution of **10** (1.14 g, 5.32 mmol) in THF (4 ml) was added to the reaction mixture at the same temperature, and the resulting mixture was allowed to slowly warm to 0 °C. After quenching the reaction by adding saturated aqueous ammonium chloride solution (40 ml), the mixture was extracted with AcOEt (40 ml×3). The organic extracts were combined, washed with brine (40 ml), dried over anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo*. Flash column chromatography (hexane/AcOEt=4 : 1) of the residue gave a mixture of **19a**, **26a** and **27a** (1.70 g, 92%) as an oil.[21] The mixture of **19a**, **26a** and **27a** (260 mg) was further separated by HPLC [Daicel Chiralpak IC ϕ2.0 cm×25 cm, hexane/2-propanol=85 : 15, flow rate 8.0 ml/min, followed by Daicel Chiralpak IA ϕ2.0 cm×25 cm, hexane/EtOH=90 : 10, flow rate 10 ml/min. HPLC analyses of **19a**, **26a** and compound **27a**: Daicel Chiralpak IC ϕ0.46 cm×25 cm, hexane/2-propanol=85 : 15, flow rate 0.5 ml/min; t_R 23.8 min (**26a**), 24.2 min (**27a**), 27.4 min (**19a**)] to give pure samples of **19a**, **26a** and **27a**, all as an oil.

Compound **19a** (209 mg): $[\alpha]_D^{27}$ −265 (c=1.0, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.62 (2H, quintet, J=6.1 Hz), 1.82—1.89 (2H, m), 1.95 (3H, s), 1.96—2.10 (3H, m), 2.40—2.49 (1H, m), 2.59—2.66 (2H, m), 2.73 (1H, dd, J=13.1, 10.1 Hz), 3.31—3.38 (7H, m), 4.10—4.15 (2H, m), 4.49 (1H, t, J=5.5 Hz), 4.63—4.71 (1H, m), 5.44 (1H, s), 5.76 (1H, td, J=10.4, 5.5 Hz), 6.03 (1H, d, J=10.4 Hz), 7.23—7.36 (5H, m). IR (ATR) cm^{-1}: 1785, 1677 cm^{-1}. MS (CI$^+$) m/z: 460 [(M+H)$^+$]. HR-MS (CI$^+$) m/z: 460.2173 (Calcd for $C_{25}H_{34}NO_5S$ [(M+H)$^+$]: 460.2158).

Compound **26a** (29 mg): $[\alpha]_D^{28}$ −11.8 (c=0.2, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.55—1.71 (2H, m), 1.79—1.93 (5H, m), 2.01—2.32 (4H, m), 2.56—2.70 (3H, m), 3.32 (3H, s), 3.34 (3H, s), 3.38—3.46 (1H, m), 4.06—4.15 (2H, m), 4.47 (1H, t, J=5.8 Hz), 4.63—4.71 (1H, m), 5.50 (1H, s), 5.71—5.81 (1H, m), 6.04 (1H, d, J=9.8 Hz), 7.24—7.38 (5H, m). IR (ATR) cm^{-1}: 1786, 1672. MS (CI$^+$) m/z: 460 [(M+H)$^+$]. HR-MS (CI$^+$) m/z: 460.2146 (Calcd for $C_{25}H_{34}NO_5S$ [(M+H)$^+$]: 460.2158).

Compound **27a** (16 mg): $[\alpha]_D^{23}$ −228 (c=0.3, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.56—1.68 (1H, m), 1.70—1.80 (1H, m), 1.82—1.90 (2H, m), 1.97 (3H, s), 2.06—2.13 (2H, m,), 2.24—2.32 (2H, m), 2.58—2.80 (3H, m), 3.30—3.38 (7H, m), 4.01 (1H, t, J=8.6 Hz), 4.19 (1H, dd, J=8.6, 1.2 Hz), 4.49 (1H, t, J=5.5 Hz), 4.58—4.63 (1H, m), 5.32 (1H, s), 5.79—5.90 (1H, m), 6.04 (1H, d, J=10.4 Hz), 7.14—7.39 (5H, m). IR (ATR) cm^{-1}: 1785, 1681. MS (CI$^+$) m/z: 460 [(M+H)$^+$]. HR-MS (CI$^+$) m/z: 460.2146 (Calcd for $C_{25}H_{34}NO_5S$ [(M+H)$^+$]: 460.2185).

(b) Preparation of *ent*-**19a**: Compound *ent*-**19a** (1.17 g, 51%) and two types of by-products enantiomeric to **26a** [*ent*-**26a**] (179 mg, 8%) and **27a** [*ent*-**27a**] (112 mg, 5%) were prepared all as a colorless oil from *ent*-**18a** (1.63 g, 5.01 mmol) in the same manner as described in (a) after separation by HPLC [Daicel Chiralpak IA ϕ2.0 cm×25 cm, hexane/EtOH=90 : 10, flow rate 20 ml/min. HPLC analyses of *ent*-**19a**, *ent*-**26a** and *ent*-**27a**: Daicel Chiralpak IA ϕ0.46 cm×25 cm, hexane/EtOH=90 : 10, flow rate 0.5 ml/min; t_R 18.4 min (*ent*-**27a**), 20.4 min (*ent*-**26a**), 25.3 min (*ent*-**19a**)]. *ent*-**19a**: $[\alpha]_D^{23}$ +298 (c=1.0, MeOH). HR-MS (ESI$^+$) m/z: 428.18955 (Calcd for $C_{24}H_{30}NO_4S$ {[(M−CH_3OH)+H]$^+$}: 428.18955). ^{1}H-NMR, IR and MS spectra of these samples were identical to those described in (a).

Deconjugative Asymmetric α-Sulfenylation of (*R*,*E*)- and (*S*,*E*)-4-Benzyl-3-(3-cycloheptenyl-2-methylacryloyl)oxazolidin-2-one (18b, *ent*-18b). (*R*)-4-Benzyl-3-[(*R*,*E*)-3-(cyclohept-2-enylidene)-2-(3,3-dimethoxypropylthio)-2-methylpropanoyl]oxazolidin-2-one (19b) and Its Enantiomer (*ent*-19b) (a) Preparation of **19b**: Treatments of **18b** (2.80 g, 8.25 mmol) in a manner similar to that described for the preparation of **19a**, afforded **19b** (1.20 g, 31%) as a colorless oil after separation by HPLC [Daicel Chiralpak IA ϕ2.0 cm×25 cm, hexane/EtOH=91 : 9, flow rate 10 ml/min. HPLC analysis of **19b**: Daicel Chiralpak IA ϕ0.46 cm×25 cm, hexane/EtOH=91 : 9, flow rate 0.5 ml/min; t_R 22.8 min]. $[\alpha]_D^{27}$ −164 (c=0.6, MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.54—1.73 (4H, m), 1.82—1.90 (2H, m), 1.96 (3H, s), 2.20 (2H, q, J=5.1 Hz), 2.28—2.42 (2H, m), 2.58—2.69 (2H, m), 2.74 (1H, dd, J=13.1, 10.1 Hz), 3.31—3.37 (7H, m), 4.10—4.17 (2H, m), 4.49 (1H, t, J=5.8 Hz), 4.62—4.68 (1H, m), 5.56 (1H, s), 5.63—5.69 (1H, m), 6.01 (1H, d, J=12.2 Hz), 7.22—7.36 (5H, m). IR(ATR) cm^{-1}: 1784, 1679. MS (CI$^+$) m/z: 474 [(M+H)$^+$]. HR-MS (CI$^+$) m/z: 474.2286 (Calcd for $C_{26}H_{36}NO_5S$ [(M+H)$^+$]: 474.2314). Although the formation of two types of the by-products **26b** and **27b** was observed similarly to the preparation of **19a**, **26a** and **27a**, their isolation was not attempted.[37]

(b) Preparation of *ent*-**19b**: Compound *ent*-**19b** (1.39 g, 36%) was prepared from *ent*-**18b** (2.80 g, 8.25 mmol) as a colorless oil in the same manner as described in (a) after separation by HPLC [Daicel Chiralpak IC ϕ2.0 cm×25 cm, hexane/MTBE/AcOEt/EtOH=88 : 7 : 3 : 2, flow rate 15 ml/min. HPLC analysis of *ent*-**19b**: Daicel Chiralpak IC ϕ0.46 cm×25 cm, hexane/MTBE/AcOEt/EtOH=88 : 7 : 3 : 2, flow rate 0.75 ml/min; t_R 13.7 min]. $[\alpha]_D^{26}$ +160 (c=0.6, MeOH). HR-MS (CI$^+$) m/z: 474.2286 (Calcd for $C_{26}H_{36}NO_5S$ [(M+H)$^+$]: 474.2314). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). Although the formation of two types of the by-products *ent*-**26b** and *ent*-**27b** was anticipated similarly to the case described in (a), their isolation was not attempted.

Deconjugative Asymmetric α-Sulfenylation of (*R*,*E*)- and (*S*,*E*)-4-Ben-

zyl-3-(3-cyclooctenyl-2-methylacryloyl)oxazolidin-2-one (18c, *ent*-18c).

(*R*)-4-Benzyl-3-[(*R*,*E*)-3-(cyclooct-2-enylidene)-2-(3,3-dimethoxypropylthio)-2-methylpropanoyl]oxazolidin-2-one (19c) and Its Enantiomer (*ent*-19c) (a) Preparation of **19c**: Treatment of **18c** (2.50 g, 7.07 mmol) in a manner similar to that described for the preparation of **19a**, afforded **19c** (1.72 g, 50%) as a colorless powder after separation by HPLC [Daicel Chiralpak IA ϕ2.0 cm×25 cm, hexane/MTBE/2-propanol=80 : 10 : 10, flow rate 18 ml/min followed by Daicel Chiralpak IC ϕ2.0 cm×25 cm, hexane/2-propanol=75 : 25, flow rate 10 ml/min. HPLC analysis of **19c**: Daicel Chiralpak IA ϕ0.46 cm×25 cm, hexane/MTBE/2-propanol=80 : 10 : 10, flow rate 0.9 ml/min; t_R 9.7 min: Daicel Chiralpak IC ϕ0.46 cm×25 cm, hexane/2-propanol=75 : 25, flow rate 0.5 ml/min; t_R 21.4 min]. mp 63—65.5 °C (cyclohexane). $[\alpha]_D^{25}$ −368 (c=0.5, MeOH). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.40—1.56 (5H, m), 1.65—1.78 (1H, m), 1.82—1.90 (2H, m), 1.98 (3H, s), 2.20—2.32 (1H, m), 2.40—2.70 (5H, m), 2.75 (1H, q, J=13.4 Hz), 3.27—3.37 (7H, m), 4.06—4.17 (2H, m), 4.48 (1H, t, J=5.5 Hz), 4.63—4.70 (1H, m), 5.46 (1H, td, J=12.2, 8.6 Hz), 5.64 (1H, s), 6.11 (1H, d, J=12.2 Hz), 7.22—7.36 (5H, m). IR (ATR) cm^{-1}: 1787, 1672. MS (EI$^+$) m/z: 487 (M$^+$). HR-MS (EI$^+$) m/z: 487.2380 (Calcd for $C_{27}H_{37}NO_5S$ (M$^+$): 487.2392). Although the formation of two types of the by-products **26c** and **27c** was observed similarly to the preparation of **19a**, **26a** and **27a**, their isolation was not attempted.[37]

(b) Preparation of *ent*-**19c**: Compound *ent*-**19c** (1.53 g, 44%) was prepared as a colorless powder from *ent*-**18c** (2.50 g, 7.07 mmol) in the same manner as described in (a) after separation by HPLC [Daicel Chiralpak IC ϕ2.0 cm×25 cm, hexane/MTBE/EtOH=85 : 10 : 5, flow rate 15 ml/min. HPLC analysis of *ent*-**19c**: Daicel Chiralpak IC ϕ0.46 cm×25 cm, hexane/MTBE/EtOH=85 : 10 : 5, flow rate 0.75 ml/min; t_R 11.5 min]. mp 63—65.5 °C (cyclohexane). $[\alpha]_D^{26}$ +349 (c=0.5, MeOH). HR-MS (EI$^+$) m/z: 487.2368 (Calcd for $C_{27}H_{37}NO_5S$ (M$^+$): 487.2392). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). Although the formation of two types of the by-products *ent*-**26c** and *ent*-**27c** was anticipated similarly to the case described in (a), their isolation was not attempted.

(*R*,*E*)-Benzyl 3-(Cyclohex-2-enylidene)-2-(3,3-dimethoxypropylthio)-2-methylpropanoate (20a) and Its Enantiomer (*ent*-20a) (a) Preparation of **20a**: Treatments of **19a** (1.30 g, 2.83 mmol) in a manner similar to that described for the preparation of **12b**, afforded **20a** (844 mg, 76%) as a colorless oil. $[\alpha]_D^{24}$ +26.1 (c=1.0, CHCl$_3$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.50—1.64 (2H, m), 1.65 (3H, s), 1.74—1.81 (2H, m), 2.02—2.10 (2H, m), 2.15—2.38 (2H, m), 2.52—2.65 (2H, m), 3.28 (6H, s), 4.37 (1H, t, J=5.5 Hz), 5.17 (1H, d, J=12.2 Hz), 5.21 (1H, d, J=12.2 Hz), 5.46 (1H, s), 5.76—5.82 (1H, m), 6.01 (1H, d, J=10.4 Hz), 7.31—7.40 (5H, m). IR (ATR) cm^{-1}: 1721. MS (EI$^+$) m/z: 390 (M$^+$). HR-MS (EI$^+$) m/z: 390.1889 (Calcd for $C_{22}H_{30}O_4S$ (M$^+$): 390.1865).

(b) Preparation of *ent*-**20a**: Compound *ent*-**20a** (713 mg, 76%) was prepared as a colorless oil from *ent*-**19a** (1.10 g, 2.39 mmol) in the same manner as described in (a). $[\alpha]_D^{26}$ −24.9 (c=1.0, CHCl$_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 390.1826 (Calcd for $C_{22}H_{30}O_4S$ (M$^+$): 390.1865).

(*R*,*E*)-Benzyl 3-(Cyclohept-2-enylidene)-2-(3,3-dimethoxypropylthio)-2-methylpropanoate (20b) and Its Enantiomer (*ent*-20b) (a) Preparation of **20b**: Treatments of **19b** (1.60 g, 3.38 mmol) in a manner similar to that described for the preparation of **12b**, afforded **20b** (936 mg, 69%) as a colorless oil. $[\alpha]_D^{25}$ +5.6 (c=0.5, CHCl$_3$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.56—1.69 (4H, m), 1.66 (3H, s), 1.76—1.80 (2H, m), 2.19—2.24 (2H, m), 2.28—2.42 (2H, m), 2.51—2.64 (2H, m), 3.30 (6H, s), 4.37 (1H, t, J=5.8 Hz), 5.16 (1H, d, J=12.2 Hz), 5.21 (1H, d, J=12.2 Hz), 5.60 (1H, s), 5.64—5.72 (1H, m), 6.00 (1H, d, J=12.8 Hz), 7.31—7.40 (5H, m). IR (ATR) cm^{-1}: 1722. MS (EI$^+$) m/z: 404 (M$^+$). HR-MS (EI$^+$) m/z: 404.2023 (Calcd for $C_{23}H_{32}O_4S$ (M$^+$): 404.2021).

(b) Preparation of *ent*-**20b**: Compound *ent*-**20b** (742 mg, 87%) was prepared as a colorless oil from *ent*-**19b** (1.00 g, 2.11 mmol) in the same manner as described in (a). $[\alpha]_D^{26}$ −5.4 (c=0.5, CHCl$_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 404.2044 (Calcd for $C_{23}H_{32}O_4S$ (M$^+$): 404.2021).

(*R*,*E*)-Benzyl 3-(Cyclooct-2-enylidene)-2-(3,3-dimethoxypropylthio)-2-methylpropanoate (20c) and Its Enantiomer (*ent*-20c) (a) Preparation of **20c**: Treatments of **19c** (1.40 g, 2.87 mmol) in a manner similar to that described for the preparation of **12b**, afforded **20c** (1.05 g, 87%) as a colorless oil. $[\alpha]_D^{24}$ +17.5 (c=0.3, CHCl$_3$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.49—1.68 (6H, m), 1.66 (3H, s), 1.73—1.80 (2H, m), 2.30—2.44 (2H, m), 2.46—2.64 (4H, m), 3.28 (6H, s), 4.37 (1H, t, J=5.8 Hz), 5.15 (1H, d, J=12.2 Hz), 5.20 (1H, d, J=12.2 Hz), 5.48 (1H, td, J=12.2, 9.6 Hz), 5.69 (1H, s), 6.09 (1H, d, J=12.2 Hz), 7.30—7.38 (5H, m). IR (ATR) cm^{-1}: 1722. MS (EI$^+$) m/z: 418 (M$^+$). HR-MS (EI$^+$) m/z: 418.2159 (Calcd for $C_{24}H_{34}O_4S$ (M$^+$): 418.2178).

(b) Preparation of *ent*-**20c**: Compound *ent*-**20c** (998 mg, 89%) was prepared as a colorless oil from *ent*-**19c** (1.30 g, 2.67 mmol) in the same manner as described in (a). $[\alpha]_D^{24}$ −15.0 (c=0.5, CHCl$_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 418.2171 (Calcd for $C_{24}H_{34}O_4S$ (M$^+$): 418.2178).

(*R*,*E*)-Benzyl 3-(Cyclohex-2-enylidene)-2-methyl-2-(3-oxopropylthio)-propanoate (21a) and Its Enantiomer (*ent*-21a) (a) Preparation of **21a**: Treatments of **20a** (730 mg, 1.87 mmol) in a manner similar to that described for the preparation of **13b**, afforded **21a** (562 mg, 87%) as a colorless oil. $[\alpha]_D^{21}$ +44.8 (c=0.6, CHCl$_3$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.50—1.65 (2H, m), 1.65 (3H, s), 2.02—2.10 (2H, m), 2.14—2.23 (1H, m), 2.28—2.37 (1H, m), 2.57 (2H, td, J=6.7, 1.2 Hz), 2.75—2.87 (2H, m), 5.16 (1H, d, J=12.2 Hz), 5.23 (1H, d, J=12.2 Hz), 5.47 (1H, s), 5.78—5.84 (1H, m), 6.01 (1H, d, J=9.8 Hz), 7.30—7.41 (5H, m), 9.62 (1H, d, J=1.2 Hz). IR (neat) cm^{-1}: 1725. MS (EI$^+$) m/z: 344 (M$^+$). HR-MS (EI$^+$) m/z: 344.1424 (Calcd for $C_{20}H_{24}O_3S$ (M$^+$): 344.1446).

(b) Preparation of *ent*-**21a**: Compound *ent*-**21a** (494 mg, 82%) was prepared as a colorless oil from *ent*-**20a** (680 mg, 1.74 mmol) in the same manner as described in (a). $[\alpha]_D^{26}$ −43.5 (c=1.0, CHCl$_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 344.1432 (Calcd for $C_{20}H_{24}O_3S$ (M$^+$): 344.1446).

(*R*,*E*)-Benzyl 3-(Cyclohept-2-enylidene)-2-methyl-2-(3-oxopropylthio)propanoate (21b) and Its Enantiomer (*ent*-21b) (a) Preparation of **21b**: Treatments of **20b** (900 mg, 2.22 mmol) in a manner similar to that described for the preparation of **13b**, afforded **21b** (733 mg, 92%) as a colorless oil.[43] ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.58—1.70 (7H, m), 2.18—2.24 (2H, m), 2.33—2.40 (2H, m), 2.56 (2H, t, J=7.0 Hz), 2.76—2.88 (2H, m), 5.16 (1H, d, J=12.2 Hz), 5.23 (1H, d, J=12.2 Hz), 5.60 (1H, s), 5.67—5.73 (1H, m), 6.00 (1H, d, J=11.6 Hz), 7.30—7.40 (5H, m), 9.62 (1H, s). IR (ATR) cm^{-1}: 1718. MS (EI$^+$) m/z: 358 (M$^+$). HR-MS (EI$^+$) m/z: 358.1635 (Calcd for $C_{21}H_{26}O_3S$ (M$^+$): 358.1603).

(b) Preparation of *ent*-**21b**: Compound *ent*-**21b** (614 mg, 98%) was prepared as a colorless oil from *ent*-**20b** (704 mg, 1.74 mmol) in the same manner as described in (a).[43] ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 359.1662 (Calcd for $C_{21}H_{27}O_3S$ [(M+H)$^+$]: 359.1681).

(*R*,*E*)-Benzyl 3-(Cyclooct-2-enylidene)-2-methyl-2-(3-oxopropylthio)-propanoate (21c) and Its Enantiomer (*ent*-21c) (a) Preparation of **21c**: Treatments of **20c** (978 mg, 2.34 mmol) in a manner similar to that described for the preparation of **13b**, afforded **21c** (838 mg, 96%) as a colorless oil. $[\alpha]_D^{28}$ +34.3 (c=0.3, CHCl$_3$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.46—1.68 (6H, m), 1.67 (3H, s), 2.30—2.46 (2H, m), 2.48—2.58 (4H, m), 2.76—2.86 (2H, m), 5.15 (1H, d, J=12.2 Hz), 5.22 (1H, d, J=12.2 Hz), 5.49 (1H, td, J=9.6, 12.2 Hz), 5.69 (1H, s), 6.09 (1H, d, J=12.2 Hz), 7.30—7.40 (5H, m), 9.62 (1H, t, J=1.2 Hz). IR (ATR) cm^{-1}: 1720. MS (EI$^+$) m/z: 372 (M$^+$). HR-MS (EI$^+$) m/z: 372.1789 (Calcd for $C_{22}H_{28}O_3S$ (M$^+$): 372.1759).

(b) Preparation of *ent*-**21c**: Compound *ent*-**21c** (776 mg, 96%) was prepared as a colorless oil from *ent*-**20c** (913 mg, 2.18 mmol) in the same manner as described in (a). $[\alpha]_D^{28}$ −25.1 (c=0.3, CHCl$_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 372.1754 (Calcd for $C_{22}H_{28}O_3S$ (M$^+$): 372.1759).

(*R*,*E*)-Benzyl 3-(Cyclohex-2-enylidene)-2-methyl-2-(propionylthio)-propanoate (22a) and Its Enantiomer (*ent*-22a) (a) Preparation of **22a**: Treatments of **21a** (240 mg, 1.06 mmol) in a manner similar to that described for the preparation of **14b**, afforded **22a** (172 mg, 66%) as a colorless oil. $[\alpha]_D^{23}$ +24.9 (c=0.1, CHCl$_3$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.10 (3H, t, J=7.4 Hz), 1.50—1.61 (2H, m), 1.90 (3H, s), 2.01—2.06 (2H, m), 2.24—2.34 (1H, m), 2.35—2.44 (1H, m), 2.49 (2H, q, J=7.4 Hz), 5.16 (1H, d, J=12.8 Hz), 5.19 (1H, d, J=12.8 Hz), 5.41 (1H, s), 5.81 (1H, td, J=3.7, 9.8 Hz), 5.95 (1H, td, J=3.0, 9.8 Hz), 7.28—7.38 (5H, m). IR (neat) cm^{-1}: 1738, 1694. MS (EI$^+$) m/z: 344 (M$^+$). HR-MS (EI$^+$) m/z: 344.1427 (Calcd for $C_{20}H_{24}O_3S$ (M$^+$): 344.1446).

(b) Preparation of *ent*-**22a**: Compound *ent*-**22a** (163 mg, 68%) was prepared as a colorless oil from *ent*-**21a** (240 mg, 0.697 mmol) in the same manner as described in (a). $[\alpha]_D^{23}$ −23.7 (c=0.4, CHCl$_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 344.1451 (Calcd for $C_{20}H_{24}O_3S$ (M$^+$): 344.1446).

(*R*,*E*)-Benzyl 3-(Cyclohept-2-enylidene)-2-methyl-2-(propionylthio)-propanoate (22b) and Its Enantiomer (*ent*-22b) (a) Preparation of **22b**: Treatments of **21b** (251 mg, 0.700 mmol) in a manner similar to that described for the preparation of **14b** afforded **22b** (170 mg, 68%) as a colorless oil. $[\alpha]_D^{25}$ +14.5 (c=0.6, CHCl$_3$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.11 (3H, t, J=7.3 Hz), 1.59—1.70 (4H, m), 1.89 (3H, s), 2.13—2.24 (2H, m), 2.35—2.57 (4H, m), 5.17 (2H, s), 5.56 (1H, s), 5.68—5.73 (1H, m), 5.96 (1H, d, J=11.6 Hz), 7.30—7.38 (5H, m). IR (ATR) cm^{-1}: 1734, 1690. MS (EI$^+$) m/z: 358 (M^+). HR-MS (EI$^+$) m/z: 358.1605 (Calcd for $C_{21}H_{26}O_3S$ (M^+): 358.1603).

(b) Preparation of *ent*-**22b**: Compound *ent*-**22b** (158 mg, 53%) was prepared as a colorless oil from *ent*-**21b** (300 mg, 0.837 mmol) in the same manner as described in (a). $[\alpha]_D^{25}$ -19.4 (c=0.6, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (CI$^+$) m/z: 359.1671 (Calcd for $C_{21}H_{27}O_3S$ [$(M+H)^+$]: 359.1681).

***(R,E)*-Benzyl 3-(Cyclooct-2-enylidene)-2-methyl-2-(propionylthio)-propanoate (22c) and Its Enantiomer (*ent*-22c)** (a) Preparation of **22c**: Treatments of **21c** (335 mg, 0.899 mmol) in a manner similar to that described for the preparation of **14b**, afforded **22c** (245 mg, 73%) as a colorless oil. $[\alpha]_D^{22}$ $+11.0$ (c=0.3, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.10 (3H, t, J=7.6 Hz), 1.44—1.70 (6H, m), 1.90 (3H, s), 2.35—2.40 (2H, m), 2.46—2.52 (2H, m), 2.56—2.64 (2H, m), 5.17 (2H, s), 5.49 (1H, td, J=9.6, 12.2 Hz), 5.66 (1H, s), 6.05 (1H, d, J=12.2 Hz), 7.29—7.37 (5H, m). IR (ATR) cm^{-1}: 1734, 1690. MS (EI$^+$) m/z: 372 (M^+). HR-MS (EI$^+$) m/z: 372.1791 (Calcd for $C_{22}H_{28}O_3S$ (M^+): 372.1759).

(b) Preparation of *ent*-**22c**: Compound *ent*-**22c** (162 mg, 54%) was prepared as a colorless oil from *ent*-**21c** (300 mg, 0.805 mmol) in the same manner as described in (a). $[\alpha]_D^{22}$ -7.9 (c=0.1, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 372.1791 (Calcd for $C_{22}H_{28}O_3S$ (M^+): 372.1759).

***(R,E)*-Benzyl 2-Acetylthio-3-(cyclohex-2-enylidene)-2-methypropanoate (23a) and Its Enantiomer (*ent*-23a)** (a) Preparation of **23a**: Treatments of **21a** (290 mg, 0.842 mmol) in a manner similar to that described for the preparation of **15b**, afforded **23a** (188 mg, 68%) as a colorless oil. $[\alpha]_D^{28}$ $+20.4$ (c=1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.50—1.61 (2H, m), 1.90 (3H, s), 2.01—2.06 (2H, m), 2.24 (3H, s), 2.24—2.34 (1H, m), 2.37—2.45 (1H, m), 5.18 (2H, s), 5.40 (1H, s), 5.82 (1H, td, J=4.3, 9.8 Hz), 5.95 (1H, td, J=1.3, 9.8 Hz), 7.28—7.38 (5H, m). IR (neat) cm^{-1}: 1738, 1692. MS (EI$^+$) m/z: 330 (M^+). HR-MS (EI$^+$) m/z: 330.1251 (Calcd for $C_{19}H_{22}O_3S$ (M^+): 330.1290).

(b) Preparation of *ent*-**23a**: Compound *ent*-**23a** (148 mg, 65%) was prepared as a colorless oil from *ent*-**21a** (238 mg, 0.691 mmol) in the same manner as described in (a). $[\alpha]_D^{25}$ -19.2 (c=0.3, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 330.1310 (Calcd for $C_{19}H_{22}O_3S$ (M^+): 330.1290).

***(R,E)*-Benzyl 2-Acetylthio-3-(cyclohept-2-enylidene)-2-methypropanoate (23b) and Its Enantiomer (*ent*-23b)** (a) Preparation of **23b**: Treatments of **21b** (251 mg, 0.700 mmol) in a manner similar to that described for the preparation of **15b**, afforded **23b** (152 mg, 63%) as a colorless oil. $[\alpha]_D^{29}$ $+4.7$ (c=0.1, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.59—1.68 (4H, m), 1.89 (3H, s), 2.17—2.24 (2H, m), 2.25 (3H, s), 2.39—2.56 (2H, m), 5.16 (1H, d, J=12.2 Hz), 5.19 (1H, d, J=12.2 Hz), 5.54 (1H, s), 5.68—5.74 (1H, m), 5.96 (1H, d, J=11.6 Hz), 7.30—7.36 (5H, m). IR (neat) cm^{-1}: 1738, 1692 MS (CI$^+$) m/z: 345 [$(M+H)^+$]. HR-MS (CI$^+$) m/z: 345.15688 (Calcd for $C_{20}H_{25}O_3S$ [$(M+H)^+$]: 345.15245).

(b) Preparation of *ent*-**23b**: Compound *ent*-**23b** (143 mg, 36%) was prepared as a colorless oil from *ent*-**21b** (415 mg, 1.16 mmol) in the same manner as described in (a). $[\alpha]_D^{25}$ -3.7 (c=0.3, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 344.1430 (Calcd for $C_{20}H_{24}O_3S$ (M^+): 344.1446).

***(R,E)*-Benzyl 2-Acetylthio-3-(cyclooct-2-enylidene)-2-methypropanoate (23c) and Its Enantiomer (*ent*-23c)** (a) Preparation of **23c**: Treatments of **21c** (335 mg, 0.899 mmol) in a manner similar to that described for the preparation of **15b**, afforded **23c** (217 mg, 67%) as a colorless oil. $[\alpha]_D^{21}$ $+7.3$ (c=0.3, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.43—1.64 (6H, m), 1.90 (3H, s), 2.24 (3H, s), 2.38 (2H, q, J=7.1 Hz), 2.54—2.68 (2H, m), 5.15 (1H, d, J=12.2 Hz), 5.20 (1H, d, J=12.2 Hz), 5.49 (1H, td, J=8.6, 12.2 Hz), 5.65 (1H, s), 6.05 (1H, d, J=12.2 Hz), 7.29—7.37 (5H, m). IR (ATR) cm^{-1}: 1735, 1689. MS (EI$^+$) m/z: 358 (M^+). HR-MS (EI$^+$) m/z: 358.1624 (Calcd for $C_{21}H_{26}O_3S$ (M^+): 358.1603).

(b) Preparation of *ent*-**23c**: Compound *ent*-**23c** (191 mg, 66%) was prepared as a colorless oil from *ent*-**21c** (300 mg, 0.805 mmol) in the same manner as described in (a). $[\alpha]_D^{28}$ -4.8 (c=0.3, $CHCl_3$). ^{1}H-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 358.1623 (Calcd for $C_{21}H_{26}O_3S$ (M^+): 358.1603).

***(R,E)*-5-(Cyclohex-2-enylidenemethyl)-4-hydroxy-3,5-dimethylthiophen-2(5*H*)-one (5a) and Its Enantiomer (*ent*-5a)** (a) Preparation of **5a**: Treatments of **22a** (222 mg, 0.724 mmol) in a manner similar to that described for the preparation of **3b**, afforded **5a** (85 mg, 84%) as a colorless powder. mp 111—113 °C (cyclohexane). $[\alpha]_D^{27}$ $+128$ (c=0.3, MeOH). The optical purity of **5a** was calculated to be >99% ee based on the diastereomeric excess of the corresponding **19a** which had been determined as >99% de by HPLC analysis. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.56—1.68 (2H, m), 1.68 (3H, s), 1.77 (3H, s), 2.05—2.12 (2H, m), 2.12—2.22 (1H, m), 2.26—2.35 (1H, m), 5.33 (1H, s), 5.85 (1H, td, J=4.3, 9.8 Hz), 6.02 (1H, td, J=1.8, 9.8 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 7.7, 23.0, 26.1, 26.2, 30.3, 56.5, 109.9, 125.6, 131.5, 131.8, 141.8, 183.4, 197.8. IR (KBr) cm^{-1}: 1609. MS (EI$^+$) m/z: 236 (M^+). HR-MS (EI$^+$) m/z: 236.0869 (Calcd for $C_{13}H_{16}O_2S$ (M^+): 236.0871).

(b) Preparation of *ent*-**5a**: Compound *ent*-**5a** (99 mg, 91%) was prepared as a colorless powder from *ent*-**22a** (158 mg, 0.459 mmol) in the same manner as described in (a). mp 107—112 °C (cyclohexane). $[\alpha]_D^{25}$ -133 (c=0.6, MeOH). The optical purity of *ent*-**5a** was estimated to be >99% ee similarly to case for **5a**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 236.0876 (Calcd for $C_{13}H_{16}O_2S$ (M^+): 236.0871).

***(R,E)*-5-(Cyclohept-2-enylidenemethyl)-4-hydroxy-3,5-dimethylthiophen-2(5*H*)-one (5b) and Its Enantiomer (*ent*-5b)** (a) Preparation of **5b**: Treatments of **22b** (139 mg, 0.391 mmol) in a manner similar to that described for the preparation of **3b**, afforded **5b** (81 mg, 89%) as a colorless oil. $[\alpha]_D^{27}$ $+86.4$ (c=0.2, MeOH). The optical purity of **5b** was calculated to be >99% ee based on the diastereomeric excess of the corresponding **19b** which had been determined as >99% de by HPLC analysis. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.66—1.75 (7H, m), 1.80 (3H, s), 2.20—2.28 (2H, m), 2.40—2.50 (2H, m), 5.51 (1H, s), 5.70—5.78 (1H, m), 6.02 (1H, d, J=11.6 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 7.7, 25.2, 26.5, 28.2, 29.0, 30.6, 56.4, 110.0, 128.9, 134.1, 135.6, 146.1, 197.9. IR (ATR) cm^{-1}: 1603. MS (EI$^+$) m/z: 250 (M^+). HR-MS (EI$^+$) m/z: 250.1065 (Calcd for $C_{14}H_{18}O_2S$ (M^+): 250.1028).

(b) Preparation of *ent*-**5b**: Compound *ent*-**5b** (97 mg, 96%) was prepared as a colorless oil from *ent*-**22b** (145 mg, 0.404 mmol) in the same manner as described in (a). $[\alpha]_D^{27}$ -92.9 (c=0.2, MeOH). The optical purity of *ent*-**5b** was estimated to be >99% ee similarly to case for **5b**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 250.0998 (Calcd for $C_{14}H_{18}O_2S$ (M^+): 250.1028).

***(R,E)*-5-(Cyclooct-2-enylidenemethyl)-4-hydroxy-3,5-dimethylthiophen-2(5*H*)-one (5c) and Its Enantiomer (*ent*-5c)** (a) Preparation of **5c**: Treatments of **22c** (187 mg, 0.502 mmol) in a manner similar to that described for the preparation of **3b**, afforded **5c** (88 mg, 66%) as a colorless powder. mp 112—116 °C (cyclohexane). $[\alpha]_D^{27}$ $+77.3$ (c=0.3, MeOH). The optical purity of **5c** was calculated to be >99% ee based on the diastereomeric excess of the corresponding **19c** which had been determined as >99% de by HPLC analysis. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.50—1.70 (6H, m), 1.68 (3H, s), 1.77 (3H, s), 2.30—2.40 (1H, m), 2.46—2.58 (3H, m), 5.48—5.57 (2H, m), 6.11 (1H, d, J=11.6 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 7.8, 23.8, 26.9, 27.1, 27.9, 28.6, 30.8, 56.3, 109.8, 129.1, 131.4, 137.8, 146.2, 183.7, 197.7. IR (ATR) cm^{-1}: 1608. MS (EI$^+$) m/z: 264 (M^+). HR-MS (EI$^+$) m/z: 264.1173 (Calcd for $C_{15}H_{20}O_2S$ (M^+): 264.1184.

(b) Preparation of *ent*-**5c**: Compound *ent*-**5c** (67 mg, 71%) was prepared as a colorless powder from *ent*-**22c** (128 mg, 0.357 mmol) in the same manner as described in (a). mp 113—115 °C (cyclohexane). $[\alpha]_D^{27}$ -79.8 (c=0.3, MeOH). The optical purity of *ent*-**5c** was estimated to be >99% ee similarly to case for **5c**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) m/z: 264.1173 (Calcd for $C_{15}H_{20}O_2S$ (M^+): 264.1184).

***(R,E)*-5-(Cyclohex-2-enylidenemethyl)-4-hydroxy-5-methylthiophen-2(5*H*)-one (6a) and Its Enantiomer (*ent*-6a)** (a) Preparation of **6a**: Treatments of **23a** (171 mg, 0.726 mmol) in a manner similar to that described for the preparation of **3b**, afforded **6a** (114 mg, 99%) as a colorless powder. mp 106—110 °C (cyclohexane). $[\alpha]_D^{27}$ $+138$ (c=0.2, MeOH). The optical purity of **6a** was calculated to be >99% ee based on the diastereomeric excess of the corresponding **19a** which had been determined as >99% de by HPLC analysis. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.60—1.72 (2H, m), 1.80 (3H, s), 2.06—2.13 (2H, m), 2.23—2.32 (1H, m), 2.36—2.46 (1H, m), 5.37 (1H, s), 5.84 (1H, td, J=4.3, 9.8 Hz), 6.01 (1H, td, J=1.8, 9.8 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 23.0, 26.1, 26.6, 30.4, 58.9, 125.6, 131.4, 131.7, 141.7, 190.3, 197.5. IR (KBr) cm^{-1}: 1603. MS (EI$^+$) m/z: 222 (M^+). HR-MS (EI$^+$) m/z: 222.0728 (Calcd for $C_{12}H_{14}O_2S$ (M^+): 222.0715).

(b) Preparation of *ent*-**6a**: Compound *ent*-**6a** (61 mg, 63%) was prepared as a colorless powder from *ent*-**23a** (205 mg, 0.776 mmol) in the same manner as described in (a). mp 105—107 °C (cyclohexane). $[\alpha]_D^{27}$ -133 (c=0.6, MeOH). The optical purity of *ent*-**6a** was estimated to be >99% ee similarly to the case for **6a**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m/z*: 222.0742 (Calcd for $C_{12}H_{14}O_2S$ (M$^+$): 222.0715).

(*R*,*E*)-5-(Cyclohept-2-enylidenemethyl)-4-hydroxy-5-methylthiophen-2(5*H*)-one (6b) and Its Enantiomer (*ent*-6b) (a) Preparation of **6b**: Treatments of **23b** (144 mg, 0.418 mmol) in a manner similar to that described for the preparation of **3b**, afforded **6b** (63 mg, 64%) as a colorless powder. mp 85—89 °C (cyclohexane). $[\alpha]_D^{27}$ +137 (c=0.2, MeOH). The optical purity of **6b** was calculated to be >99% ee based on the diastereomeric excess of the corresponding **19b** which had been determined as >99% de by HPLC analysis. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.66—1.75 (4H, m), 1.80 (3H, s), 2.20—2.28 (2H, m), 2.40—2.50 (2H, m), 5.50 (1H, s), 5.70—5.78 (1H, m), 6.02 (1H, d, J=11.6 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 26.7, 28.3, 29.0, 29.8, 30.8, 59.0, 116.8, 129.0, 134.0, 135.6, 145.9, 190.7, 197.6. IR (ATR) cm^{-1}: 1600. MS (EI$^+$) *m/z*: 236 (M$^+$). HR-MS (EI$^+$) *m/z*: 236.0918 (Calcd for $C_{13}H_{16}O_2S$ (M$^+$): 236.0871).

(b) Preparation of *ent*-**6b**: Compound *ent*-**6b** (73 mg, 74%) was prepared as a colorless powder from *ent*-**23b** (205 mg, 0.776 mmol) in the same manner as described in (a). mp 88—91 °C (cyclohexane). $[\alpha]_D^{27}$ −128 (c=0.2, MeOH). The optical purity of *ent*-**6b** was estimated to be >99% ee similarly to the case for **6b**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m/z*: 236.0893 (Calcd for $C_{13}H_{16}O_2S$ (M$^+$): 236.0871).

(*R*,*E*)-5-(Cyclooct-2-enylidenemethyl)-4-hydroxy-5-methylthiophen-2(5*H*)-one (6c) and Its Enantiomer (*ent*-6c) (a) Preparation of **6c**: Treatments of **23c** (162 mg, 0.452 mmol) in a manner similar to that described for the preparation of **3b**, afforded **6c** (52 mg, 46%) as a colorless powder. mp 132—135 °C (cyclohexane). $[\alpha]_D^{24}$ +75.3 (c=0.3, MeOH). The optical purity of **6c** was calculated to be >99% ee based on the diastereomeric excess of the corresponding **19c** which had been determined as >99% de by HPLC analysis. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.50—1.62 (4H, m), 1.64—1.74 (2H, m), 1.81 (3H, s), 2.30—2.40 (1H, m), 2.46—2.64 (3H, m), 5.48—5.56 (1H, m), 5.60 (1H, s), 6.11 (1H, d, J=11.6 Hz). ^{13}C-NMR (100 MHz, CD_3OD) δ: 23.9, 27.0, 27.3, 27.9, 28.8, 31.0, 58.9, 129.1, 131.3, 137.7, 145.9, 190.6, 197.5. IR (ATR) cm^{-1}: 1593. MS (EI$^+$) *m/z*: 250 (M$^+$). HR-MS (EI$^+$) *m/z*: 250.1007 (Calcd for $C_{14}H_{18}O_2S$ (M$^+$): 250.1028).

(b) Preparation of *ent*-**6c**: Compound *ent*-**6c** (50 mg, 45%) was prepared as a colorless powder from *ent*-**23c** (159 mg, 0.444 mmol) in the same manner as described in (a). mp 134—136 °C (cyclohexane). $[\alpha]_D^{23}$ −76.5 (c=0.3, MeOH). The optical purity of *ent*-**6c** was estimated to be >99% ee similarly to the case for **6c**. ^{1}H-NMR, ^{13}C-NMR, IR and MS spectra of this sample were identical to those described in (a). HR-MS (EI$^+$) *m/z*: 250.1000 (Calcd for $C_{14}H_{18}O_2S$ (M$^+$): 250.1028).

Biological Assay *In vitro* antibacterial activity assay: The minimum inhibitory concentration (MIC) (μg/ml) was determined by the ager dilution method[22] with Muller-Hinton agar (Difco Laboratories, Detroit, MI, U.S.A.). The MIC was defined as the lowest concentration of an antibacterial agent that inhibited visible growth after incubation at 35 °C for 18 h.

In vitro inhibitory activity assay for mammalian type I fatty acid synthase: Fatty acid synthesis was evaluated by measuring the incorporation of [1-^{14}C] acetate into cellular fatty acid as previously described[23] with some modification. Human HepG2 cells were seeded in a 12-well plate and cultured in Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal calf serum supplemented with 100 U/ml penicillin and 100 μg/ml streptomycin in a 5% CO_2 atmosphere at 37 °C for 24 h. The medium was removed and replaced with serum-free DMEM. After 24 h incubation, the cells were treated with various concentrations of the test compound for 4 h in Krebs-Ringer phosphate HEPES buffer (pH 7.4). [1-^{14}C] acetate (0.4 uCi/ml; 56.5 mCi/mmol; Perkin-Elmer Inc., Norwalk, CT, U.S.A.) was added to the medium, which was then incubated at 37 °C for 2 h. The metabolic reaction was stopped by the addition of ethanolic KOH, and the samples were left at 80 °C for 2 h. After extracting nonsaponifiable lipids with petroleum ether, the water-soluble residual layer was acidified to pH <1 by the addition of HCl. Total fatty acids were extracted with petroleum ether, and the combined organic extracts were dried and concentrated *in vacuo*. The residue was dissolved with methanol and was transferred into a scintillaton vial. Radioactivity of total fatty acids was counted by a liquid scintillation counter (Perkin-Elmer Inc.). IC_{50} values were calculated by the auto-analysis program GraphPad Prism, version 4.00 (GraphPad Software Inc., La Jolla, CA, U.S.A.).

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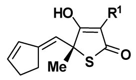
28) In addition to **5a**—**c**, **6a**—**c** and their enantiomers (*ent*-**5a**—**c**, *ent*-**6a**—**c**), 5-[(*E*)-cyclopent-2-enylidenemethyl]-TLM, its 3-demethyl congener and their enantiomers (**5d**, **6d**, *ent*-**5d**, *ent*-**6d**) were designed and their synthesis was attempted following the same synthetic scheme shown in Chart 2. Although the scheme proceeded smoothly to the stage of **20** (n=0), aldehyde **21** (n=0) derived from **20** (n=0) was found to be very unstable, probably due to facile isomerization to the cyclopentadiene derivative and the subsequent intramolecular Diels–Alder reaction (Ohata K. and Terashima S., unpublished re-

sults).



5d: R^1 = Me; **6d**: R^1 = H

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31) In ^{1}H-NMR spectrum, the two olefinic protons of **11b** showed larger chemical shifts than **24b**. The same relationships were also observed for the chemical shift values of **11a**, **c**—**f** and **24a**, **c**—**f**.

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36) In the absence of HMPA, the deconjugative asymmetric α-sulfenylation of **19a** did not take place at all.

37) Formation ratios of **19**, **26** to **27** estimated by the ^{1}H-NMR spectrum and/or HPLC analysis are as follows: **19**/**26**/**27**; 12 : 2 : 1 for **19a**/**26a**/**27a**; 14 : 1 : 4 for **19b**/**26b**/**27b**; 12 : 1 : 1 for **19c**/**26c**/**27c**.

38) Some representative data are as follows: ^{1}H-NMR ($CDCl_3$): 5.44 ppm [(Me)(SR)C–C$\underline{\text{H}}$=C] for **19a**; 5.50 ppm [(Me)(SR)C–C$\underline{\text{H}}$=C] for the (*S*)-diastereomer of **19a** (**26a**); 5.56 ppm [(Me)(SR)C–C$\underline{\text{H}}$=C] for **19b**; 5.62 ppm [(Me)(SR)C–C$\underline{\text{H}}$=C] for the (*S*)-diastereomer of **19b** (**26b**); 5.64 ppm [(Me)(SR)C–C$\underline{\text{H}}$=C] for **19c**; 5.72 ppm [(Me)(SR)C–C$\underline{\text{H}}$=C] for the (*S*)-diastereomer of **19c** (**26c**); 5.72 ppm [(Me)(SR)C–C$\underline{\text{H}}$=C] for the synthetic intermediate of **1**; 5.77 ppm [(Me)(SR)C–C$\underline{\text{H}}$=C] for the (*S*)-diastereomer of the synthetic intermediate of **1**.

39) The enantiomeric exesses of **3a**—**f**, *ent*-**3a**—**f**, **4a**—**f**, *ent*-**4a**—**f**, **5a**—**c**, *ent*-**5a**—**c**, **6a**—**c** and *ent*-**6a**—**c** were shown in Table 3 and in Experimental.

40) Determination of MICs by agar dilution methods was performed according to the guideline M7-A6 of the Clinical and Laboratory Standards Institute (2003).

41) Fatty acid synthesis was evaluated by measuring the incorporation of [1-^{14}C] acetate into cellular fatty acid as previously described with some modifications. See, Murakami K., Tobe K., Ide T., Mochizuki T., Ohashi M., Akanuma Y., Yazaki Y., Kadowaki T., *Diabetes*, **47**, 1841—1847 (1998).

42) Formation of two types of the by-products corresponding to **24b** and **25b** was observed, similar to the case described for the preparation of **11b**, **24b** and **25b** from **9b**.

43) Since the absolute optical rotation values for the enantiomeric pairs of the oily compounds bearing an 3-oxopropylthio group were occasionally found to be inconsistent, the $[\alpha]_D$ α values for those compounds were not included in this report. At present, the reason for the observed inconsistency is unclear.