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Enantioselective Lewis Acid-Catalyzed Mukaiyama−Michael Reactions of Acyclic Enones. Catalysis by *allo*-Threonine-Derived Oxazaborolidinones

Xiaowei Wang, Shinya Adachi, Hiroyoshi Iwai, Hiroshi Takatsuki, Katsuhiro Fujita, Mikako Kubo, Akira Oku, and Toshiro Harada*

Department of Chemistry and Materials Technology, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606-8585, Japan

harada@chem.kit.ac.jp

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allo-Threonine-derived *O*-aroyl-*B*-phenyl-*N*-tosyl-1,3,2-oxazaborolidin-5-ones **1g**,**n** catalyze the asymmetric Mukaiyama−Michael reaction of acyclic enones with a trimethylsilyl ketene *S*,*O*-acetal in high enantioselectivity. A range of alkenyl methyl ketones is successfully employed as Michael acceptors affording ee values of 85−90% by using 10 mol % of the catalyst. The use of 2,6-diisopropylphenol and *tert*-butyl methyl ether as additives is found to be essential to achieve high enantioselectivity in these reactions. The effects of the additives are discussed in terms of the retardation of an Si^+-catalyzed racemic pathway, which seriously deteriorates the enantioselectivity of asymmetric Mukaiyama−Michael reactions. A working model for asymmetric induction is proposed based on correlation between catalyst structures and enantioselectivities.

The Michael addition reaction stands for the most straightforward methods for constructing 1,5-dicarbonyl skeletons and is regarded as a fundamental method in organic synthesis.[1] Recently, much attention has been focused on the enantioselective version of this reaction.[2] Significant advances have been made in direct Michael reactions involving in situ generation of enolate anions.[3,4] To this approach, however, nucleophilic partners of the reaction are limited to readily enolizable carbonyl compounds such as active methylene compounds.

The Mukaiyama−Michael reaction in which silyl ketene acetals and enolsilanes are used as nucleophiles is well recognized to be a powerful and reliable method for the preparation of various types of 1,5-dicarbonyl compounds.[5] In comparison with the great success of the chiral Lewis acid catalysis in mechanistically related asymmetric Mukaiyama aldol reactions, only limited advances have been made toward the enantioselective version of the Mukaiyama−Michael reaction.[6,7] Kobayashi et al. have reported the highly enantioselective reaction for cyclopent-2-enone by using a BINOLate titanium(IV) complex.[6a] Recently, Evans et al. demonstrated the utility of chiral bis(oxazoline) copper(II) catalysts for the reaction of bidentate Michael acceptors such as alkylidene malonates and alkenoyl oxazolidinones.[6g−k] Most recently, the enantioselective organocatalytic reaction of enals with siloxy furans has been developed by MacMillan et al.[7] Despite these advances, the asymmetric Michael reaction to simple acyclic enones leading directly to enantiopure 1,5-dicarbonyl compounds remains a challenging issue in this field.[6l]

* Corresponding author.

(1) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon Press: Oxford, UK, 1992.

(2) Review: (a) Tomioka, K.; Nagaoka, Y. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, Germany, 1999; Vol. 3, Chapter 31.1. (b) Kanai, M.; Shibasaki, M. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley: New York, 2000; p 569. (c) Sibi, M.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033. (d) Krause, N.; Hoffmann-Röder, A. *Synthesis* **2001**, 171.

(3) For leading references, see; (a) Yamaguchi, M.; Shiraishi, T.; Hirama, M. *J. Org. Chem*. **1996**, *61*, 3520. (b) Harada, S.; Kumagai, N.; Kinoshita, T.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 2582. (c) Itoh, K.; Kanemasa, S. *J. Am. Chem. Soc.* **2002**, *124*, 13394.

(4) (a) Colonna, S.; Hiemstra, H.; Wynberg, H. *J. Chem. Soc., Chem. Commun*. **1978**, 238. (b) Sawamura, H.; Hamashima, H.; Ito, Y. *J. Am. Chem. Soc*. **1992**, *114*, 8295. (c) Yamaguchi, M.; Shiraishi, T.; Hirama, M. *Angew. Chem., Int. Ed. Engl*. **1993**, *32*, 1176. (d) Sasai, H.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1994**, *116*, 1571.

(5) (a) Narasaka, T.; Soai, K.; Mukaiyama, T. *Chem. Lett.* **1974**, 1223. (b) For leading references, see: Otera, J.; Fujita, Y.; Sakuta, N.; Fujita, M.; Fukuzumi, S. *J. Org. Chem*. **1996**, *61*, 2951.

(6) (a) Kobayashi, S.; Suda, S.; Yamada, M.; Mukaiyama, T. *Chem. Lett*. **1994**, 97. (b) Bernardi, A.; Colombo, G.; Scolastico, C. *Tetrahedron Lett.* **1996**, *37*, 8921. (c) Bernardi, A.; Karamfilova, K.; Sanguinetti, S.; Scolastico, C. *Tetrahedron* **1997**, *53*, 13009. (d) Kitajima, H.; Ito, K.; Katsuki, T. *Tetrahedron* **1997**, *53*, 17015. (e) Kitajima, H.; Katsuki, T. *Synlett* **1997**, 568. (f) Nishikori, H.; Ito, K.; Katsuki, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1165. (g) Evans, D. A.; Rovis, T.; Kozlowski, M. C.; Tedrow, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 1994. (h) Evans, D. A.; Willis, M. C.; Johnston, J. N. *Org. Lett*. **1999**, *1*, 865. (i) Evans, D. A.; Johnston, J. S.; Olhava, E. J. *J. Am. Chem. Soc.* **2000**, 122, 1635. (j) Evans, D. A.; Rovis, T.; Kozlowski, M. C.; Downey, C. W.; Tedrow, J. S. *J. Am. Chem. Soc.* **2000**, *122*, 9134. (k) Evans, D. A.; Scheidt, K. A.; Johnston, J. N.; Willis, M. C. *J. Am. Chem. Soc.* **2001**, *123*, 4480. (l) Zhang, F.-Y.; Corey, E. J. *Org. Lett*. **2001**, *3*, 639. (m) Desimoni, G.; Faita, G.; Filippone, S.; Mella, M.; Zampori, M. G.; Zema, M. *Tetrahedron* **2001**, *57*, 10203−10212.

(7) (a) Paras, N. A.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2001**, *123*, 4370. (b) Austin, J. F.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 1172. (c) Paras, N. A.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 7894. (d) Brown, S. P.; Goodwin N. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 1192.

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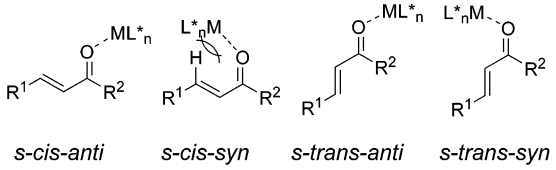
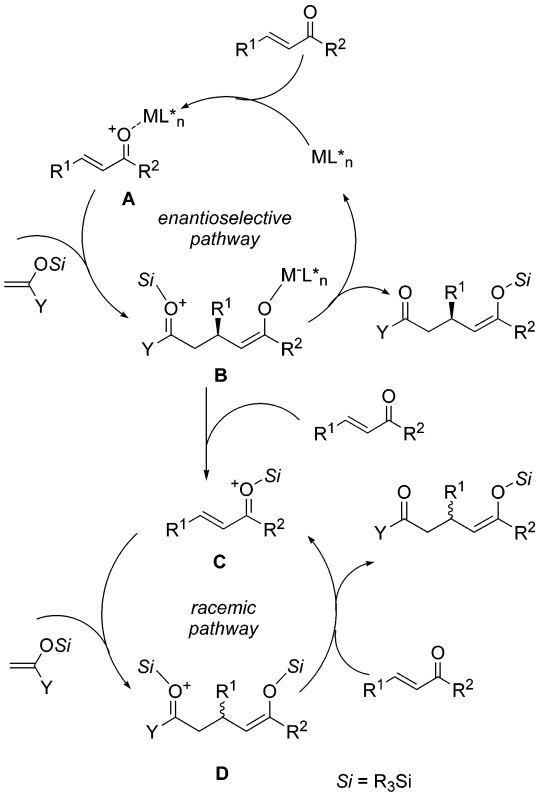
SCHEME 1



SCHEME 2



Two major difficulties to be overcome are conceivable in the asymmetric Mukaiyama−Michael reaction of acyclic enones. There are four possible coordination modes of an acyclic enone to a chiral Lewis acid (ML*$_n$) (Scheme 1). Except for the sterically congested s-cis-syn isomer, three other isomers are all feasible structures for activated complexes. Since the enantiotopic faces of the coordinating enone at the olefinic carbons are opposite between the s-cis and s-trans isomers, the reaction is required to proceed selectively through one of these activated complexes. The second problem is a competing silyl cation-catalyzed racemic pathway that may cause reduction in enantioselectivity (Scheme 2). Coordination of an enone by a chiral Lewis acid to form activated complex **A** followed by addition of a silyl ketene acetal gives rise to intermediate **B**. For the regeneration of the Lewis acid catalyst ML*$_n$, the silyl group attached to a carbonyl oxygen atom needs to migrate to a remote enolate oxygen atom. Alternatively, the silyl group of **B** could be transferred to the starting enone to form another activated complex **C**, leading to the silyl cation catalyzed racemic pathway through intermediate **D**. The pathway may cause a severe decrease in overall enantioselectivity. A similar problem has been reported for the mechanistically related Mukaiyama−aldol reaction.[8] It may be more serious in the asymmetric Michael reaction.

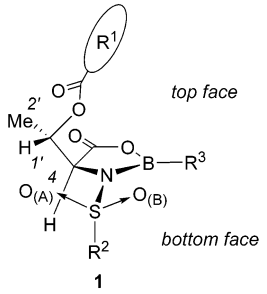


FIGURE 1.

Herein we wish to report that (L)-*allo*-threonine derived oxazaborolidinones **1g** and **1n** are efficient catalysts for the asymmetric Mukaiyama−Michael reaction of *simple acyclic enones*. The use of 2,6-diisopropylphenol and *tert*-butyl methyl ether as additives is found to retard the undesirable Si^+-catalyzed racemic pathway efficiently, leading to enantioselective formation of various γ-ketoacid thiol esters.[9]

Results and Discussion

Molecular Design and Synthesis of *allo*-Threonine-Derived OXB. In the present study, we focused on a new *N*-sulfonyl-1,3,2-oxazaborolidin-5-one (OXB) catalyst[10] **1** derived from *allo*-threonine (Figure 1). Previously reported X-ray[11] and calculated[12] structures of related OXBs show that the heterocyclic ring is almost planar and the SO_2-R^2 bond is nearly perpendicular to this plane at the bottom face.[13] The rotation around the C(4)−C(1′) bond is expected to be fixed as depicted in Figure 1 by the methyl group (C(2′)H_3) because of unfavorable interaction between the sulfonyl oxygen atom, O(A), and the methyl (or *O*-acyl) group in an alternative conformer. Accordingly, the acyloxy group is anticipated to reside at the top face of the ring. If we assume a top-face coordination of enones, the chiral environment around the enones could be optimized by modifying the structure of the acyl group in OXBs. It is also anticipated that slight deviation from the planarity for the bond rotation around the C(1′)−O and the adjacent O−COR^1 bonds would make the acyloxy moiety

(8) (a) Carreira, E. M.; Singer, R. A. *Tetrahedron Lett.* **1994**, *35*, 4323−4326. (b) Carreira, E. M.; Singer, R. A.; Lee, W. *J. Am. Chem. Soc.* **1994**, *116*, 8837−8838. (c) Hollis, T. K.; Bosnich, B. *J. Am. Chem. Soc.* **1995**, *117*, 4570−4581.

(9) For a preliminary report of the work described here, see: (a) Harada, T.; Iwai, H.; Takatsuki, H.; Fujita, K.; Kubo, M.; Oku, A. *Org. Lett.* **2001**, *3*, 2101. (b) Wang, X.; Harada, T.; Iwai, H.; Oku, A. *Chirality* **2003**, *15*, 28.

(10) (a) Takasu, M.; Yamamoto, H. *Synlett* **1990**, 194. (b) Sartor, D.; Saffrich, J.; Helmchen, G. *Synlett* **1990**, 197. (c) Kiyooka, S.-i.; Kaneko, Y.; Komura, M.; Matsuo, H.; Nakano, M. *J. Org. Chem.* **1991**, *56*, 2276. (d) Corey, E. J.; Loh, T.-P. *J. Am. Chem. Soc.* **1991**, *113*, 8966. (e) Kinugasa, M.; Harada, T.; Oku, A. *J. Org. Chem.* **1996**, *61*, 6772. (f) For leading references, see: Ishihara, K.; Kondo, S.; Yamamoto, H. *J. Org. Chem.* **2000**, *65*, 9125.

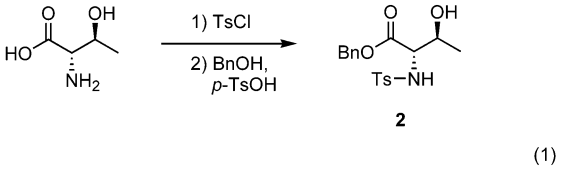
(11) Vedejs, E.; Chapman, R. W.; Lin, S.; Muller, M.; Powell, D. R. *J. Am. Chem. Soc.* **2000**, *122*, 3047.

(12) Salvatella, L.; Ruiz-López, F. *J. Am. Chem. Soc.* **1999**, *121*, 10772 and references therein.

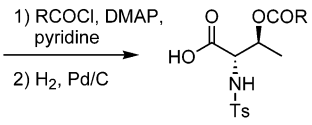
(13) For a nomenclature of top and bottom faces of OXB, see: Kaneko, Y.; Kiyooka, S. *Kochi Daigaku Rigakubu Kiyo, Kagaku* **1994**, *15*, 9.

flexible, allowing the space for the structural change in the transition state of the Michael reaction.

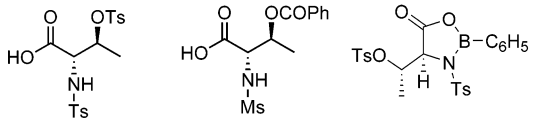
A variety of *O*-acyl-*N*-sulfonyl-(L)-*allo*-threonines **3a**−**k** were prepared starting from (L)-*allo*-threonine. Except for **3d**,**j**,**k**,[14] these ligands were synthesized by *N*-tosylation of the amino acid under Schotten−Baumann conditions and esterification with benzyl alcohol followed by *O*-acylation of the resulting monoesters **2** and hydrogenolysis of the benzyl ester moiety (eq 1). Treatment of

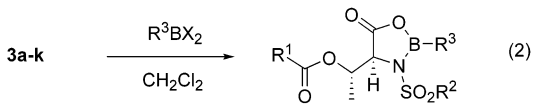


(1)



3a Ph
3b 1-naphthyl
3c 2-naphthyl
3d 2-anthracenyl
3e 4-$MeOC_6H_4$
3f 4-$CF_3C_6H_4$
3g biphenyl
3h 3,5-$(MeO)_2C_6H_3$
3i CH_3





(2)

	R^1	R^2SO_2	R^3
1a	C_6H_5	Ts	C_6H_5
1b	C_6H_5	Ts	*p*-ClC_6H_4
1c	C_6H_5	Ts	*m*-ClC_6H_4
1d	C_6H_5	Ts	3,4-$Cl_2C_6H_3$
1e	C_6H_5	Ms	C_6H_5
1f	1-Naphthyl	Ts	C_6H_5
1g	2-Naphthyl	Ts	C_6H_5
1h	2-Naphthyl	Ts	*p*-ClC_6H_4
1i	2-Naphthyl	Ts	*m*-ClC_6H_4
1j	2-Naphthyl	Ts	3,4-$Cl_2C_6H_3$
1k	Anthracenyl	Ts	C_6H_5
1l	*p*-$MeOC_6H_4$	Ts	C_6H_5
1m	*p*-$CF_3C_6H_4$	Ts	C_6H_5
1n	biphenyl	Ts	C_6H_5
1o	3,5-$(MeO)_2C_6H_3$	Ts	C_6H_5
1p	CH_3	Ts	C_6H_5

ligands **3** with aryldihaloboranes in CH_2Cl_2 followed by removal of HX (X = Cl, Br) and the solvent in vacuo gave the corresponding OXB **1a**−**q** (eq 2).[15] In several cases, clean formation of the complexes was ascertained by ^1H NMR analysis. A relatively small coupling constant (J = ca. 2 Hz) observed between H(4) and H(1′) is consistent with the anticipated structure in Figure 1.

Optimization of Reaction Conditions. In the presence of *O*-benzoyl-OXB **1a** (20 mol %), the reaction of

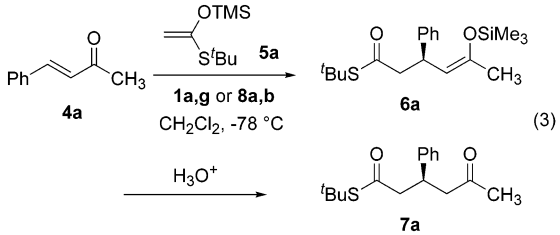
(14) For the preparation of **3d**,**j**,**k**, see the Experimental Section.

TABLE 1. OXB-Catalyzed Michael Reaction of Benzalacetone (4a) with Silyl Ketene Acetal 5a

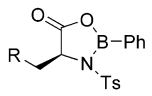
entry	OXB	mol %	method[a]	yield (%)	ee (%)
1	**1a**	20	A	94	7
2	**1a**	10	A	97	18
3	**1a**	20	B	79	14
4	**1a**	40	B	76	32
5	**1a**	100	B	85	53
6	**1g**	20	A	88	10
7	**8a**	20	A	86	8
8	**8b**	20	A	90	<5

[a] Method A: a mixture of **4a** (0.5 M), **5a** (1.5 equiv), and **1a**,**g** in CH_2Cl_2 was stirred for 1 h at −78 °C. Method B: To a solution of **5a** (1.5 equiv, 0.75 M) and **1a** in CH_2Cl_2 at −78 °C was added a CH_2Cl_2 solution of **4a** (0.25 M) over 4 h.

benzalacetone (**4a**) with trimethylsilyl ketene *S*,*O*-acetal **5a** proceeded smoothly at −78 °C to give enolsilane **6a** as an initial product, which was hydrolyzed under acidic conditions to give Michael adduct **7a** in high yield without enantioselectivity (eq 3, entry 1 in Table 1). OXB **1a**, as



(3)



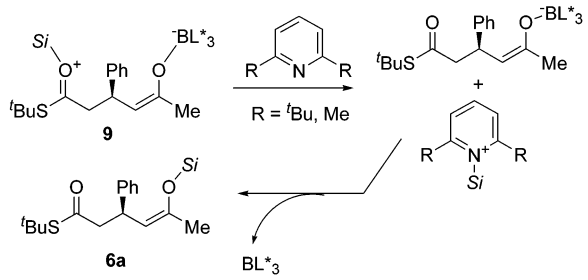
8a; R = Ph
8b; R = 2-indolyl

well as *O*-(2-naphthoyl) derivative **1g**, did not give advantageous results over other conventional OXBs **8a**,**b**[10,15] (entries 7 and 8 vs 1 and 6). Slight improvement of the enantioselectivity was observed when the reaction was carried out by slowly adding enone **4a** to a mixture of **5a** and **1a** (entries 3−5). The observed effect of slow addition suggests intervention of a Si^+-catalyzed racemic pathway (Scheme 2), which was retarded to some extent by transformation of enolborate intermediate **B** (ML^*_n = OXB) to the product during slow addition of the enone.

With anticipation that a sterically hindered Lewis base could act as a silicon shuttle[8b] to retard the Si^+-pathway (Scheme 3), reactions were carried out in the presence of pyridine derivatives. In the presence of 2,6-di-*tert*-butylpyridine (0.2 equiv), the reaction of **1a** and **4a**, under the conditions similar to those of entry 4 (Table 1), gave **7a** of 48% ee in 39% yield. The use of less bulky 2,6-lutidine (0.2 equiv) as an additive, on the other hand, exhibited higher ee of 69% albeit with lower product yield (20%). When a similar reaction was carried out for 15 h after accomplishment of the slow addition, **7a** was obtained in higher yield (58%) but with lower enantioselectivity (50% ee). More hindered 2,6-di-*tert*-butylpyridine seems to be less efficient in capturing the Si^+ species in comparison with 2,6-lutidine, which, however, may also

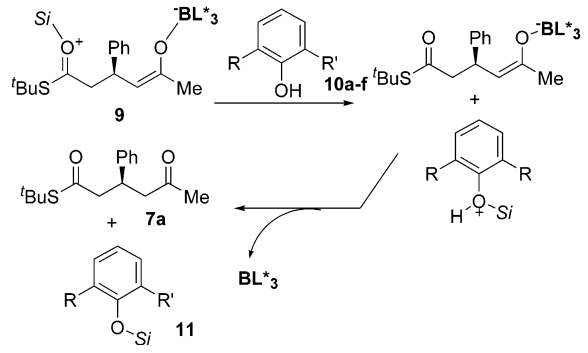
(15) Kinugasa, M.; Harada, T.; Egusa, T.; Fujita, K.; Oku, A. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 3639.

SCHEME 3[a]



[a] BL^*_3 = OXB **1**, *Si* = TMS.

SCHEME 4[a]



[a] BL^*_3 = OXB **1**, *Si* = TMS.

act as a catalyst poison through complexation at the boron atom. The use of diethyl ether as an additive did not cause any effect on either the enantioselectivity or the product yield.

An alternative approach to the retardation of the Si^+ pathway may involve the use of a hydroxyl compound as an additive (Scheme 4).[16] Thus, a phenol as an additive would react with intermediate **9** to give adduct **7a** and the corresponding silyl phenol **11** with simultaneous regeneration of catalyst **1**. Reactions were carried out by adding a solution of enone **4a** and several phenols (**10a**–**f**) to a solution of OXB catalyst **1a** (40 mol %) and **5a** (Table 2, entries 2–7). Of the 2,6-disubstituted phenols examined, *sec*-alkyl derivatives **10c**,**d** and phenyl derivative **10e** exhibited improved enantioselectivity of ca. 50% ee without lowering the product yield. For these reactions, GC analysis of the crude reaction mixture before acid treatment showed the formation of Michael adduct **7a** and the corresponding silyl phenol **11** together with enolsilane **6a** and the starting phenol. Both the sterically less demanding phenols **10a**,**b** and the more hindered phenol **10f**, on the other hand, showed reduced enantioselectivity. In the later reaction, no silylation of the phenol was observed in the GC analysis of the crude reaction mixture, suggesting that Si^+-trap was sterically hampered. Lower enantioselectivity observed for **10a**,**b** can be understood if we assume that these phenols react with OXB **1a** competitively to reduce the amount of active catalyst. No reaction was observed when **4a** was added to a solution of OXB **1a**, **5a**, and 2,6-diisopropylphenol (**10c**). The observation implies that even sterically more encumbered **10c** reacts with the catalyst in the absence of enone **4a**.

(16) Hexafluoro-2-propanol, which has been reported to be an effective additive for a similar purpose,[6d,h] did not give us improved enantioselectivity.

TABLE 2. Effect of Phenolic Additives in the OXB-Catalyzed Reaction of 4a with 5a

entry	OXB	phenolic additive	equiv	yield (%)	ee (%)
1	**1a**			76	32
2	**1a**	**10a**: R = ^{i}Pr, R′ = H	1.0	52	5
3	**1a**	**10b**: R, R′ = Me	1.0	76	21
4	**1a**	**10c**: R, R′ = ^{i}Pr	1.0	80	50
5	**1a**	**10d**: R, R′ = ^{s}Bu	1.0	61	45
6	**1a**	**10e**: R, R′ = Ph	1.0	74	48
7	**1a**	**10f**: R = ^{t}Bu, R′ = Me	1.0	76	24
8	**1g**	**10c**	1.0	89	64
9	**1g**	**10c**	3.0	43	81
10[b]	**1g**	**10c**	3.0	81	74
11[b,c]	**1g**	**10c**	3.0	77	81
12[b,d]	**1g**	**10c**	3.0	88	79

[a] Unless otherwise noted, reactions were carried out at −78 °C by adding a CH_2Cl_2 solution of **4a** (0.5 M) and **10** to a CH_2Cl_2 solution of OXB **1a**,**g** (40 mol %, 0.1 M) and **5a** (1.5 equiv) over 4 h. [b] 3 equiv of **5a** were used. [c] Reaction was carried out at 0.2 M of **1g**. [d] OXB **1g** (20 mol %) was used.

In the presence of diisopropylphenol **10c** (1 equiv), 2-naphthoyl OXB **1g** exhibited a higher ee of 65% (entry 8). Increasing the amount of the phenol brought about a further improvement in enantioselectivity albeit with a significant lowering of the product yield (entry 9). The GC analysis of the aliquots from the reaction mixture of this reaction showed consumption of the nucleophile **5a** before the completion of slow addition. A separate experiment in which phenol **10c** was treated with **5a** (1.5 equiv) in the presence of **1g** (20 mol %) at −78 °C gave trimethylsilyl phenol **11** (R, R′ = ^{i}Pr) quantitatively, indicating that the OXB also catalyzes silylation of the phenol with the silyl ketene acetal. The lower conversion observed in entry 9 is most probably due to the competing consumption of **5a** by this reaction. Indeed, full conversion of the enone while keeping the level of enantioselectivity was achieved by using 3 equiv each of **5a** and the phenol (entry 10). The better result of 81% ee was obtained when the reaction was conducted at higher concentration (0.2 M) of the catalyst (entry 11). The reaction with 20 mol % of the catalyst afforded the comparable ee as well as the high chemical yield (entry 12).

Effect of Ethereal Additive. Although diethyl ether alone was not effective in retarding the undesirable Si^+-catalyzed racemic pathway (vide supra), the additive was found to be advantageously used in combination with phenol **10c** especially in the reaction without an excess amount of the phenol (Table 3). Even 0.4 equiv of diethyl ether exhibited improved enantioselectivity in the reaction, using OXB-catalyst **1g** (20 mol %) with 1.0 equiv of **10c** (entry 2 vs 1). The enantioselectivity was improved by the increase of the amount of the additive, reaching almost plateau values in the presence of >1.6 equiv of diethyl ether (entries 2–6). When diethyl ether was used as a solvent, the reaction became heterogeneous, resulting in lower ee and product yield (entry 7).

Reactions with several ethereal additives (2 equiv) and the addition time of 6 h revealed that the effect is sensitive to their structures (entries 8 and 10–13). Anisole as an additive gave lower enantioselectivity. Nonselective reaction was observed when relatively more basic THF was used (entry 10). Of ethers examined, ^{t}BuOMe exhibited the highest ee of 83% (entry 13). It

TABLE 3. Effect of Ethereal Additive in the Asymmetric Michael Reaction of 4a Catalyzed by OXB 1b[a]

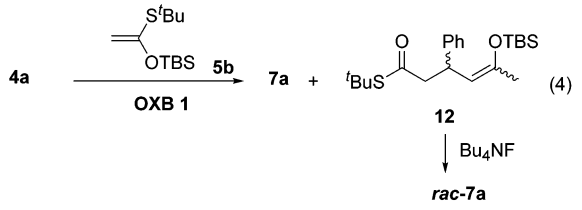
entry	**1b** (mol %)	additive (equiv)	time[b] (h)	yield (%)	ee (%)
1	20		4	64	63
2	20	Et_2O (0.4)	4	71	69
3	20	Et_2O (0.8)	4	53	72
4	20	Et_2O (1.6)	4	84	74
5	20	Et_2O (2.0)	4	86	77
6	20	Et_2O (3.2)	4	82	74
7	20	Et_2O[c]	4	45	64
8	20	Et_2O (2.0)	6	87	81
9[d]	10	Et_2O (1.0)	6	79	76
10	20	THF (2.0)	6	71	2
11	20	PhOMe (2.0)	6	73	70
12	20	$^iPr_2O$ (2.0)	6	84	77
13	20	^{t}BuOMe (2.0)	6	84	83
14[d]	10	^{t}BuOMe (1.0)	6	91	80

[a] Unless otherwise noted, the reactions were carried out at −78 °C by adding a CH_2Cl_2 solution of **4a** (0.5 M) and **10c** (1.0 equiv) to a CH_2Cl_2 solution of **1b** (0.1 M), **5a** (1.5 equiv), and an ethereal additive. [b] Time for slow addition. [c] The reaction was carried out in diethyl ether. [d] A CH_2Cl_2 solution of **4a** (1 M) and **10c** was added.

should be noted that, even with a 10 mol % catalyst load, the reaction in the presence of ^{t}BuOMe afforded adduct **7a** of 80% ee in 91% yield (entry 14). On the other hand, the use of diethyl ether under similar conditions resulted in lowering of the ee (entry 9).

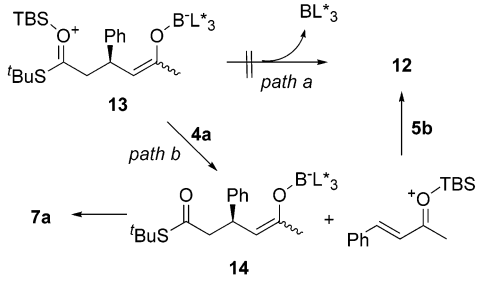
The way an ethereal additive works is uncertain at this time. The ineffectiveness of the additive in the absence of the phenol implies that it is not a simple silicon shuttle[8b] but plays a role in the trapping reaction of Me_3Si^+ species by the phenol. Nonselective reaction in the presence of THF can be rationalized by its coordination to the catalyst, reducing its effective concentration.

Enantioselectivity of OXB Catalysts 1 in the Reaction of TBS Ketene Acetal 5b. In the present OXB-catalyzed Michael reaction, enantioselectivity is determined both by the intrinsic selectivity of the catalyst and by the extent of competing Si^+-catalyzed racemic pathway. This makes it difficult to optimize OXB structures especially with respect to their enantioselectivities. The reaction with TBS ketene acetal **5b** as a nucleophile (eq 4) turned out to be very informative for the evaluation of the intrinsic selectivity.



The reaction of enone **4a** with TBS ketene acetal **5b** catalyzed by *O*-benzoyl OXB derivative **1a** (40 mol %) gave adduct **7a** of 83% ee and racemic enolsilane **12** (2% ee) in 6% and 71% yield, respectively. In this reaction, intermediate **13** might undergo intermolecular TBS group transfer to **4a** to catalyze a nonselective reaction (path b) rather than undergoing intramolecular transfer to the enolate oxygen atom to give **12** (path a, Scheme 5). Therefore, the adduct **7a** of high ee might be derived from boron enolate **14** thus formed, therefore showing the intrinsic enantioselectivity of OXB **1a**.

SCHEME 5[a]



[a] BL*$_3$ = OXB **1**.

TABLE 4. Asymmetric Michael Reaction of 4a and TBS Ketene Acetal 5b with OXB 1a−q[a]

entry	OXB	yield (%)	ee (%)	entry	OXB	yield (%)	ee (%)
1	**1a**	6	83	10	**1j**	27	88
2	**1b**	13	83	11	**1k**	17	77
3	**1c**	36	82	12	**1*l***	2	92
4	**1d**	30	81	13	**1m**	19	93
5	**1e**	10	82	14	**1n**	20	94
6	**1f**	23	83	15	**1o**	28	87
7	**1g**	15	88	16	**1p**	19	67
8	**1h**	21	88	17	**1q**	28	51
9	**1i**	20	89				

[a] Reactions were carried out at −78 °C by adding a CH_2Cl_2 solution of **4a** (0.25 M) and **10c** (1.0 equiv) over 4 h to a CH_2Cl_2 solution of **5b** (1.5 equiv) and **1a**−**q** (40 mol %, 0.2 M).

Taking advantage of the above observation, the enantioselectivity of various OXBs (**1a**−**q**) was evaluated by the reaction with TBS ketene acetal **5b** as a nucleophile (Table 4). The modification of the aryl group attached to the boron atom of an OXB did not affect the enantioselectivity (entries 1−4 and 7−10). *N*-Mesyl derivative **1e** exhibited an ee similar to that for the corresponding tosyl derivative **1a** (entry 5 vs 1). On the other hand, the structure of the *O*-acyl group (R^1CO) was found to be influential. Thus, in comparison with *O*-benzoyl OXB **1a**, *O*-(2-naphthoyl) OXB **1g** of the more extended π-system exhibited higher enantioselectivity (entry 7 vs 1). 1-Naphthoyl and 2-anthracenoly derivatives **1f**,**k**, however, did not give better results (entries 6 and 11). Introduction of a substituent at the para position of the benzoyl group significantly improved the enantioselectivity of the resulting OXB-catalysts **1*l***−**n** (entries 12−14). Both electron-donating (MeO) and electron-withdrawing (CF_3) substituents are effective. Of these, *p*-biphenoyl OXB **1n** showed the highest ee value of 94% ee. 3,5-Dimethoxybenzoyl OXB **1o** also exhibited selectivity higher than that of **1a** (entry 15) but not better than para substituted **1*l***−**n**. The low selectivity observed for *O*-acetyl OXB **1p** and *O*-tosyl OXB **1q** indicates that planar aroyloxy groups attached at the 2′ position are essential to the high enantioselectivity of the OXB catalysts.

Enantioselectivity of OXB Catalysts 1 in the Reaction of TMS Ketene Acetal 5a. Results obtained in the reaction of **4a** with TMS ketene acetal **5a** by using selected OXB catalysts (10−20 mol %) in the presence of diisopropylphenol and ^{t}BuOMe are summarized in Table 5. *O*-Biphenoyl OXB **1n** showed the highest ee value of 89% also in the reaction with **5a** (entries 6 and 7). If we assume that the degree of enantioselectivity of the catalyst is similar to that for the reaction with TBS

TABLE 5. Asymmetric Michael Reaction of 4a and TMS Ketene Acetal 5a with Selected OXB[a]

entry	OXB	mol %	yield (%)	ee (%)	% OXB[b]
1	**1a**	20	71	79	95
2	**1g**	20	84	83	94
3[c]	**1g**	10	90	80	91
4	**1*l***	20	87	82	89
5	**1m**	20	60	72	77
6	**1n**	20	88	89	95
7[c]	**1n**	10	88	89	95
8	**1o**	20	60	51	59

[a] Unless otherwise noted, reactions were carried out at −78 °C by adding a CH_2Cl_2 solution of **4a** (0.5 M) and **10c** (1.0 equiv) over 6 h to a CH_2Cl_2 solution of OXB **1** (0.1M), **5a** (1.5 equiv), and ^{t}BuOMe (2.0 equiv). [b] For definition, see text. [c] A CH_2Cl_2 solution of **4a** (1.0 M) and **10c** was added. 1.0 Equiv of ^{t}BuOMe was used.

ketene acetals **5b**, the fraction of the chiral Lewis acid-catalyzed pathway (% OXB) is assessed to be 95% in these reactions. While % OXB values are not much influenced by a catalyst load (entry 2 vs 3 and entry 6 vs 7), they are sensitive to the catalyst structure. For 4-methoxy OXB **1m** and 3,5-dimethoxy OXB **1o**, the Si^+-catalyzed pathway concurrently took place to a significant degree resulting in low enantioselectivity (entries 4, 5, and 8).

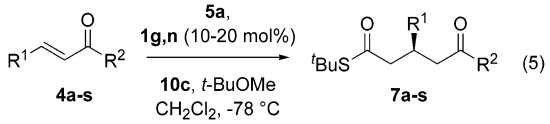
Scope and Limitation. Asymmetric Michael reaction of a variety of enones **4a**−**s** with **5a** was examined by using *O*-(2-naphthoyl)-OXB **1g** and *O*-(biphenoyl)-OXB **1n** as catalysts (Table 6). Reaction of benzalacetone derivatives **4a**−**i** with substituents on the benzene ring gave the corresponding products **7a**−**i** with high enantioselectivity (entries 1−11). Ee values of 85−90% could be achieved by using 10 mol % of **1g** or **1n** except for *m*-fluoro derivative **4e** (entry 6). When *O*-(2-naphthoyl)-OXB **1g** was employed, benzalacetone derivatives **4h**,**i** with electron-donating substituents attached on the benzene ring showed relatively low enantioselectivity (entries 9 and 11). However, a satisfactory level of the selectivity could be attained by using *O*-(biphenoyl)-OXB **1n**. For enones **4b**−**g** with electron-withdrawing substituents, on the other hand, both **1g** and **1n** exhibited a high enantioselectivity (entries 2−8). Enantioselectivity comparable to benzalacetone **4a** was obtained in the reaction of 2-naphthyl and 2-furyl derivatives **4j**,***l*** (entries 12 and 14).

The reaction of aliphatic enone **4m** was also enantioselective (entry 15). Low yield in the reaction of homologous enone **4n** represents one of the limitations of the present reaction (entry 16). More hindered 5-methylhex-3-en-2-one did not react under these reaction conditions.

The structure of the alkyl group attached to the carbonyl group is influential to the enantioselectivity (entries 17−21). Although the reaction of the *tert*-butyl and phenyl derivatives **4q**,**r** was nonselective, modest enantioselectivity was obtained for ethyl and isopropyl derivatives **4o**,**p** (entry 6). Finally, in sharp contrast to the high enantioselectivity observed for various acyclic enones, OXB **1g**,**n** did not show selectivity in the reaction of cyclic enones such as **4s** (entry 22).

The absolute structures of Michael adducts **7a** and **7o** were determined after conversion to the known methyl

TABLE 6. Asymmetric Michael Reaction of Enones 4a−s and TMS Ketene Acetal 5a Catalyzed by OXB 1g and 1n



	enone			mol % of	reaction with **1g**		reaction with **1n**	
entry	enone	R^1	R^2	catalyst	yield (%)	ee (%)	yield (%)	ee (%)
1	**4a**	Ph	Me	10	90	80	88	89
2	**4b**	*p*-ClC_6H_4	Me	10	83	86	91	85
3[b]	**4b**			20	94	85	86	89
4	**4c**	*m*-ClC_6H_4	Me	10	82	86	80	83
5	**4d**	*p*-FC_6H_4	Me	10	78	86	76	90
6	**4e**	*m*-FC_6H_4	Me	10	75	74	67	73
7	**4f**	*p*-$CF_3C_6H_4$	Me	10	77	90	70	80
8	**4g**	*m*-$CF_3C_6H_4$	Me	10	71	90	71	89
9	**4h**	*p*-MeC_6H_4	Me	10	78	74	75	86
10[b]	**4h**			20	*c*		74	89
11	**4i**	*p*-$MeOC_6H_4$	Me	10	50	60	78	85
12	**4j**	2-Naph	Me	10	76	81	59	75
13[b]	**4k**	1-Naph	Me	20	90	41	c	
14	**4*l***	2-furyl	Me	10	48	81	44	75
15	**4m**	Me	Me	10	28	86	75	89
16[b]	**4n**	*n*-C_5H_{11}	Me	20	34	64	*c*	
17	**4*o***	Ph	Et	10	53	61	63	59
18	**4p**	Ph	^{i}Pr	10	74	66	52	72
19[d]	**4p**			40	71	81	*c*	
20[d]	**4q**	Ph	^{t}Bu	40	72	16	*c*	
21[d]	**4r**	Ph	Ph	40	90	14	*c*	
22[d]	**4s**	2-cyclohexenone		40	74	9	*c*	22[d]

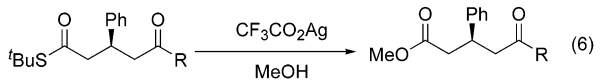
[a] Unless otherwise note, reactions were carried out at −78 °C by adding a CH_2Cl_2 solution of an enone **4** (1 M) and **10c** (1.0 equiv) over 6 h to a CH_2Cl_2 solution of OXB **1g**,**n** (0.1M), **5a** (1.5 equiv), and ^{t}BuOMe (1.0 equiv). [b] A CH_2Cl_2 solution of **4a** (0.5 M) and **10c** was added. 2.0 equiv of ^{t}BuOMe was used. [c] The reaction was not examined. [d] The reaction was carried out by adding a CH_2Cl_2 solution of an enone **4** (0.5 M) and **10c** (3.0 equiv) over 4 h to a CH_2Cl_2 solution of OXB **1g** (0.2 M) and **5a** (3.0 equiv).

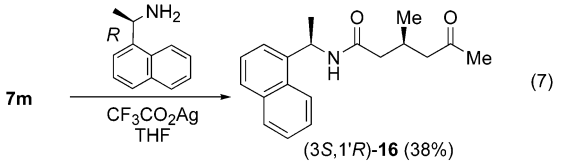
TABLE 7. Asymmetric Michael Reaction of Selected Benzalacetone Derivatives with TBS Ketene Acetal 5b Catalyzed by OXB 1g and 1n[a]

		reaction with **1g**			reaction with **1n**		
entry	enone	yield (%)	ee (%)	% OXB	yield (%)	ee (%)	% OXB
1	**4a**	15	88	91	20	94	95
2	**4b**	7	96	90	20	92	92
3	**4c**	7	95	91	12	86	97
4	**4h**	13	89	83	18	95	91
5	**4i**	3	90	67	5	95	89

[a] Reactions were carried out under the conditions similar to those described in footnote a of Table 5.

esters (*S*)-**15a**,**b**[17] by their treatment with silver trifluoroacetate in methanol (eq 6).[18] A method based on ^{1}H NMR





chemical shift differences developed by Hoye et al.[19] was applied to the absolute structure determination of adduct **7m**. Treatment of **7m** with (*R*)-1-(α-naphthyl)ethylamine and silver trifluoroacetate in THF gave amide **16** (eq 7).[18] The 3-methyl protons and CH_3CO protons of major diastereomer (3*S*,1′*R*)-**16** resonated in the lower and upper fields, respectively, relative to those of the minor diastereomer.

The origin of the lower enantioselectivity observed for **4h**,**i** with electron-rich aryl groups in the reaction employing *O*-(2-naphthoyl)-OXB **1g** is of interest in connection with a model catalyst−substrate complex of the present reaction (vide infra). To gain information on this issue, reactions of selected benzalacetone derivatives were carried out with TBS ketene acetal **5b**. Results summarized in Table 7 reveal a high intrinsic enantioselectivity of **1g** (88−96% ee) and **1n** (86−95% ee) irrespective of the electronic nature of enones. Specifically, for the reactions of **4h**,**i**, selectivity comparable to that for the parent benzalacetone **1a** was obtained irrespective of the use of **1g** or **1n** (entries 4 and 5). The result implies that the lower selectivity observed in the reaction with **1g** (Table 6, entries 9 and 11) is the result of the competing Si^+-catalyzed racemic pathway as suggested by the corresponding % OXB values: 83% for **1h** and 67% for **1i**. These relatively electron-rich enones might be less reactive toward the attack of nucleophile **5a**,**b**. This might be influential to the lowering of % OXB in the reaction with use of sterically more demanding catalyst **1g**. Similar trends of a smaller % OXB value for **1g** than that for **1n** were also observed in the reaction of enones **4a**−**c**, although to a lesser extent (e.g., entries 1−3).

Working Model. Our working model for the mode of enantioface selection is shown in Figure 2. The enantioselectivity of OXB catalysts **1** is not sensitive to the

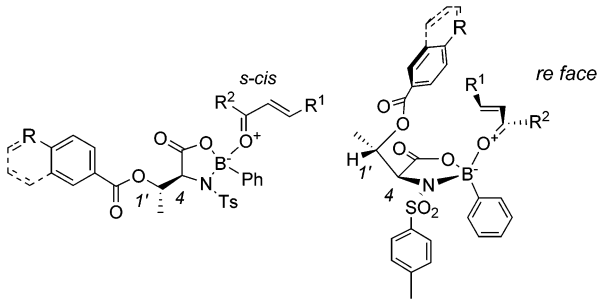


FIGURE 2.

modification of the *B*-aryl group and the *N*-sulfonyl group but it is affected by the structure of the *O*-acyl group (Table 4). The observation is consistent with the coordination of enone **4** to the top face of OXB **1** in which the *B*-phenyl and *N*-tosyl group locate at the bottom face. The boron atom is coordinated by enone **4** in a s-cis-anti fashion. The C(4)−C(1′) bond rotation might be fixed by the methyl group (C(2′)H_3) such that the *O*-aroyl moiety shields the *si* face of the enone, leading to a selective attack of the nucleophile on the *re* face. Nonselective reactions observed for *tert*-butyl and phenyl ketones **4q**,**r** as well as cyclic enones **4s** can be understood as a consequence of low selectivity with respect to the syn and anti coordination mode. The enantioselectivity of OXB is determined mainly by the shape of *O*-acyl groups rather than their electronic nature (Table 4). Introduction of either an electron-donating or -withdrawing substituent to the benzene ring of benzalacetone also does not affect the intrinsic enantioselectivity of OXB **1g**,**n** (Table 7). These observations suggest that $\pi-\pi$ interaction[20] between an electron-deficient coordinating enone and the aromatic ring of the acyl group is not a major factor in the present reaction.[21]

Conclusion. New OXB catalysts derived from *O*-acyl-*N*-sulfonyl-(L)-*allo*-threonines have been developed for enantioselective activation of acyclic enones. The asymmetric Mukaiyama−Michael reaction of acyclic enones with a trimethylsilyl ketene *S*,*O*-acetal catalyzed by thus developed *O*-(2-naphthoyl)- and *O*-biphenoyl-*N*-tosyl OXB **1g**,**n** provides an expedient entry into enantioenriched γ-ketoacid thiol esters. A number of alkenyl methyl ketones are successfully employed as Michael acceptors affording ee values of 85−90% by using 10 mol % of the catalyst. The use of 2,6-diisopropylphenol and ^{t}BuOMe as additives is essential to achieve high enantioselectivity in these reactions. A Si^+-catalyzed racemic pathway that seriously deteriorates the enantioselectivity of the asymmetric Mukaiyama−Michael reaction could be retarded for the most part (<10%) by the use of these additives. The structure model for the activated complex (Figure 2), in which the *O*-aroyl group and the enone moiety face

(17) Enders, D.; Papadopoulos, K. *Tetrahedron Lett.* **1983**, *24*, 4967.
(18) (a) Masamune, S.; Kamata, S.; Schilling, W. *J. Am. Chem. Soc.* **1975**, *97*, 3515. (b) Booth, P. M.; Fox, C. M. J.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1987**, 121.
(19) Hoye, T. R.; Koltun, D. O. *J. Am. Chem. Soc.* **1998**, *120*, 4638.
(20) Kim, K. S.; Tarakeshwar, P.; Lee, J. Y. *Chem. Rev.* **2000**, *100*, 4145.
(21) Corey, E. J.; Loh, T.-P.; Roper, T. D.; Azimioara, M. D.; Noe, M. C. *J. Am. Chem. Soc.* **1992**, *114*, 8290.

each other in a parallel arrangement on the top face of OXB, has been proposed based on the correlation between catalyst structures and enantioselectivities. The present investigation demonstrates a potential of (L)-*allo*-threonine-derived OXB catalysts whose chiral environment can be readily optimized for specific reactions by the modification of the *O*-acyl group.

Experimental Section

The following compounds were prepared according to a literature procedure: (L)-*allo*-threonine,[22] $ArBBr_3$ (Ar = *p*-chlorophenyl, *m*-chlorophenyl, 3,4-dichlorophenyl),[23] silyl ketene *S*,*O*-acetal **5a**,**b**,[24] and enones **4c**−**k**,**o**−**q**.[25]

***N*-Tosyl-(L)-*allo*-threonine.** To a solution of (L)-*allo*-threonine[22] (10.0 g, 83.9 mmol) in 1 N NaOH (150 mL) at room temperature was added an ether (150 mL) solution of *p*-toluenesulfonyl chloride (17.6 g, 92.3 mmol). The mixture was stirred vigorously at room temperature overnight. The aqueous layer was separated, washed twice with ether, and acidified with conc HCl. This was extracted three times with ethyl acetate. The combined organic layers were dried and concentrated in vacuo to give 17.0 g (74%) of the tosyl amide: ^{1}H NMR (300 MHz, d_6-aceteone) δ 1.18 (3H, d, J = 7.0 Hz), 2.37 (3H, s), 3.83 (1H, dd, J = 7.0 and 12.8 Hz), 3.96 (1H, quintet, J = 7.0 Hz), 6.56 (1H, br d, J = 13 Hz), 7.41 (2H, m), 7.71 (2H, m).

***N*-Tosyl-(L)-*allo*-threonine Benzyl Ester (2).** A solution of *N*-tosyl-(L)-*allo*-threonine (5.10 g, 18.7 mmol), benzyl alcohol (4.04 g, 37.4 mmol), and *p*-toluenesulfonic acid monohydrate (356 mg, 1.87 mmol) in toluene (340 mL) was refluxed with a Dean−Stark trap for 12 h. The mixture was poured into aqueous $NaHCO_3$ and extracted three times with ether. The organic layers were dried and concentrated in vacuo. Purification of the residue by flash chromatography (20−40% ethyl acetate in hexane) gave 5.71 g (84%) of **2**: mp 95−98 °C (recrystallized from ethyl acetate and hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (3H, d, J = 6.4 Hz), 2.30 (1H, br d, J = 8.5 Hz), 2.40 (3H, s), 3.97 (1H, dd, J = 3.9 and 8.8 Hz), 4.06 (1H, m), 4.95 (2H, m), 5.49 (1H, br d, J = ca. 9 Hz), 7.17−7.35 (7H, m), 7.71 (2H, m).

***O*-(2-Naphthoyl)-*N*-tosyl-(L)-*allo*-threonine Benzyl Ester.** To a solution of the benzyl ester **2** (1.00 g, 2.75 mmol) in pyridine (5 mL) at 0 °C was added dropwise a solution of 2-naphthoyl chloride (587 mg, 3.08 mmol) in CH_2Cl_2 (5 mL). After being stirred at room temperature for 26 h, the mixture was poured into water and extracted three times with ethyl acetate. The organic layers were washed successively with 1 N HCl water and aq $NaHCO_3$, dried, and concentrated in vacuo. Purification of the residue by flash chromatography (10−20% ethyl acetate in hexane) and recrystallization from ethyl acetate and hexane gave 1.39 g (96%) of the *O*-(2-naphthoyl) derivative: mp 106−107 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (3H, d, J = 6.5 Hz), 2.31 (3H, s), 4.39 (1H, dd, J = 4.8 and 9.8 Hz), 4.98 (2H, s), 5.36 (1H, dq, J = 4.8 and 6.4 Hz), 5.53 (1H, br d, J = ca. 10 Hz), 7.18 (4H, m), 7.27 (3H, m), 7.56 (1H, br t, J = ca. 8 Hz), 7.62 (1H, br t, J = ca. 8 Hz), 7.72 (2H, m), 7.85 (1H, br d, J = ca. 8.5 Hz), 7.90 (2H, m), 7.95 (1H, br d, J = ca. 8.5 Hz), 8.51 (1H, br s).

***O*-(2-Naphthoyl)-*N*-tosyl-(L)-*allo*-threonine (3c).** A mixture of the *O*-(2-naphthoyl) derivative (500 mg, 0.970 mmol) and Pd/C (10%) (80 mg) in ethyl acetate (20 mL) was vigorously stirred under hydrogen atmosphere at room temperature for 16 h. The mixture was filtered through a pad of cellulose powder and the filtrate was concentrated in vacuo to give pure **3c** (428 mg, 100% yield): mp 135−136 °C (recrystallized from ether); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 (3H, d, J = 6.5 Hz), 2.23 (3H, s), 4.45 (1H, dd, J = 4.6 and 9.2 Hz), 4.5 (1H, br), 5.42 (1H, dq, J = 3.9 and 6.5 Hz), 5.69 (1H, br d, J = ca. 9 Hz), 7.15 (2H, m), 7.57 (1H, br t, J = ca. 7 Hz), 7.62 (1H, br t, J = ca. 7 Hz), 7.72 (2H, m), 7.85 (1H, br d, J = ca. 8 Hz), 7.88 (1H, br d, J = ca. 8 Hz), 7.96 (2H, m), 8.52 (1H, br s); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 15.7, 21.4, 58.5, 70.9, 125.2, 125.9, 126.7, 127.1, 127.7, 128.1, 128.5, 129.5, 129.7, 131.5, 132.3, 135.7, 136.4, 143.9, 165.9, 171.6; IR (KBr disk) 3200 (br), 1740, 1700, 1275, 660 cm^{-1}. Anal. Calcd for $C_{22}H_{21}NO_6S$: C, 61.82; H, 4.95. Found: C, 61.63; H, 4.91.

***O*-Benzoyl-*N*-tosyl-(L)-*allo*-threonine benzyl ester:** 74% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (3H, d, J = 6.5 Hz), 2.36 (3H, s), 4.29 (1H, dd, J = 4.5 and 6.5 Hz), 4.92 (1H, d, J = 12.0 Hz), 4.95 (1H, d, J = 12.0 Hz), 5.45 (1H, dq, J = 4.5 and 6.5 Hz), 5.45 (1H, d, J = 9.7 Hz), 7.15−7.2 (4H, m), 7.25−7.35 (3H, m), 7.37 (2H, m), 7.54 (1H, m), 7.68 (2H, m), 7.90 (2H, m); IR (KBr disk) 3280, 1715, 1280, 1165, 715 cm^{-1}.

***O*-Benzoyl-*N*-tosyl-(L)-*allo*-threonine (3a):** 100% yield; mp 193−202 °C (recrystallized from CH_3OH-H_2O); ^{1}H NMR (500 MHz, acetone-d_6) δ 1.42 (3H, d, J = 6.5 Hz), 2.37 (3H, s), 2.5 (1H, br), 4.42 (1H, dd, J = 4.6 and 9.4 Hz), 5.39 (1H, dq, J = 4.6 and 6.5 Hz), 7.05 (1H, br d, J = 9.4 Hz), 7.3 (2H, m), 7.5 (2H, m), 7.65 (1H, m), 7.74 (2H, m), 7.97 (2H, m); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 15.1, 20.5, 58.8, 70.7, 126.9, 128.3, 129.4, 129.5, 130.1, 133.0, 138.4, 143.0, 165.0, 169.4; IR (KBr) 3300, 3000 (br), 1720, 1275, 710, 670 cm^{-1}.

***O*-(1-Naphthoyl)-*N*-tosyl-(L)-*allo*-threonine benzyl ester:** 79% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (3H, d, J = 6.5 Hz), 2.30 (3H, s), 4.42 (1H, dd, J = 4.6 and 9.6 Hz), 4.96 (2H, s), 5.39 (1H, dq, J = 4.7 and 6.5 Hz), 5.49 (1H, br d, J = 9.6 Hz), 7.1−7.2 (6H, m), 7.2−7.3 (3H, m), 7.40 (1H, t, J = 7.7 Hz), 7.5−7.65 (2H, m), 7.7 (2H, m), 7.88 (1H, br d, J = 7.9 Hz), 8.01 (1H, d, J = 8.1 Hz), 8.07 (1H, d, J = 6.5 Hz), 8.91 (1H, d, J = 8.4 Hz).

***O*-(1-Naphthoyl)-*N*-tosyl-(L)-*allo*-threonine (3b):** 100% yield; mp 63−64 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (3H, d, J = 6.5 Hz), 2.21 (3H, s), 4.45 (1H, dd, J = 4.8 and 9.8 Hz), 5.41 (1H, dq, J = 4.2 and 6.6 Hz), 5.63 (1H, br d, J = 9.3 Hz), 7.06 (2H, m), 7.44 (1H, t, J = 7.6 Hz), 7.5−7.7 (6H, m), 7.87 (1H, br d, J = 7.8 Hz), 8.01 (1H, d, J = 8.1 Hz), 8.09 (1H, dd, J = 1.0 and 7.3 Hz), 8.87 (1H, d, J = 8.4 Hz); IR (KBr disk) 3560, 3480, 3300, 1735, 1710, 785, 675 cm^{-1}.

***O*-(4-Methoxybenzoyl)-*N*-tosyl-(L)-*allo*-threonine benzyl ester:** 77% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (3H, d, J = 6.4 Hz), 2.37 (3H, s), 3.85 (3H, s), 4.29 (1H, dd, J = 4.5 and 9.8 Hz), 4.93 (2H, m), 5.25 (1H, dq, J = 4.5 and 6.4 Hz), 5.52 (1H, d, J = 9.7 Hz), 6.85 (2H, m), 7.15−7.35 (7H, m), 7.68 (2H, m), 7.5 (2H, m).

***O*-(4-Methoxybenzoyl)-*N*-tosyl-(L)-*allo*-threonine (3e):** 100% yield; mp 132−133 °C (recrystallized from ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (3H, d, J = 6.5 Hz), 2.85 (3H, s), 3.85 (3H, s), 4.32 (2H, m, including dd (1H, J = 3.4 and 8.9 Hz)), 5.82 (1H, dq, J = 3.4 and 6.5 Hz), 5.63 (1H, br, J = 9.3 Hz), 6.85 (2H, m), 7.19 (2H, m), 7.69 (2H, m), 7.88 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 16.0, 21.7, 55.6, 58.9, 70.7, 113.8, 121.9, 127.3, 129.9, 132.0, 136.7, 144.1, 163.4, 165.7, 172.4; IR (KBr) 3250, 3000 (br), 1705, 1605, 1255, 770 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_7S$: C, 56.01; H, 5.20; N, 3.44. Found: C, 55.89; H, 5.21; N, 3.67.

***O*-(4-Trifluoromethylbenzoyl)-*N*-tosyl-(L)-*allo*-threonine benzyl ester:** 70% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (3H, d, J = 6.6 Hz), 2.38 (3H, s), 4.33 (1H, dd, J = 4.5 and 9.5 Hz), 4.96 (2H, s), 5.31 (1H, m), 5.41 (1H, d, J = 9.5 Hz), 7.18 (2H, m), 7.21 (2H, m), 7.30 (3H, m), 7.63 (2H, d, J = 8.3 Hz), 7.68 (2H, d, J = 8.3 Hz), 8.01 (2H, d, J = 8.1 Hz).

***O*-(4-Trifluoromethylbenzoyl)-*N*-tosyl-(L)-*allo*-threonine (3f):** 99% yield; mp 159−160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (3H, d, J = 6.6 Hz), 2.38 (3H, s), 4.45 (1H, dd, J = 3.9 and 9.4 Hz), 5.38 (1H, dq, J = 3.9 and 6.5 Hz), 5.56 (1H, d, J = 9.4 Hz), 6.0 (1H, br), 7.25 (2H, m), 7.71 (4H, m),

(22) Elliot, D. F. *J. Chem. Soc.* **1950**, 62−68.
(23) Haubold, W.; Herdtle, J.; Gollinger, W.; Einholz, W. *J. Organomet. Chem.* **1986**, *315*, 1.
(24) Kita, Y.; Segawa, J.; Haruta, J.; Yasuda, H.; Tamura, Y. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1099.
(25) Hill, G. A.; Bramann, G. M. *Org. Synth.* **1941**, *1*, 77 and 81.

8.08 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 8, 15.3, 21.5, 58.2, 71.0, 123.5 (q, J = 273 Hz), 125.4, 127.1, 129.8, 130.2, 132.6, 134.7 (q, J = 32.8 Hz), 136.3, 144.1, 164.5, 172.4; IR (KBr) 3275 (br), 3180 (br), 1730, 1710, 1315, 660 cm^{-1}.

***O*-(4-Biphenoyl)-*N*-tosyl-(L)-*allo*-threonine benzyl ester:** 63% yield; ^{1}H NMR (500 MHz, C_6D_6) δ 1.41 (3H, d, J = 7.0 Hz), 2.41 (3H, s), 4.28 (1H, dd, J = 4.5 and 5.0 Hz), 5.33−5.38 (1H, m), 5.48 (1H, d, J = 10 Hz), 7.22−7.27 (4H, m), 7.52−7.53 (2H, m), 7.64−7.67 (4H, m), 7.74−7.76 (2H, m), 8.01−8.03 (2H, m), 7.81−7.88 (2H, m).

***O*-(4-Biphenoyl)-*N*-tosyl-(L)-*allo*-threonine (3 g):** 99% yield; mp 153−154 °C (recrystallized from benzene); ^{1}H NMR (500 MHz, acetone-d_6) δ 1.46 (3H, d, J = 6.4 Hz), 2.35 (3H, s), 4.45 (1H, dd, J = 5.4 and 9.4 Hz), 5.44 (1H, dq, J = 5.4 and 6.4 Hz), 7.07 (1H, br d, J = 9.4 Hz), 7.31 (2H, m), 7.45 (1H, m), 7.50 (2H, m), 7.75−7.8 (6H, m), 8.05 (2H, m); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 15.0, 20.5, 58.7, 59.8, 70.7, 126.8, 129.0, 129.1, 130.2, 131.0, 131.4, 132.2, 140.5, 141.7, 145.0, 147.5, 166.9, 171.4; IR (KBr) 3300, 3000 (br), 1715, 1695, 1280, 810, 740 cm^{-1}. Anal. Calcd for $C_{24}H_{23}NO_6S$: C, 63.56; H, 5.11; N, 3.09. Found: C, 63.37; H, 5.27; N, 3.03.

***O*-(3,5-Dimethoxybenzoyl)-*N*-tosyl-(L)-*allo*-threonine benzyl ester:** 87% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (3H, d, J = 6.5 Hz), 2.37 (3H, m), 4.30 (1H, dd, J = 4.5 and 9.6 Hz), 5.27 (1H, dq, J = 4.5 and 6.5 Hz), 5.44 (1H, br d, J = 9.6 Hz), 6.64 (1H, t, J = 2.4 Hz), 7.1−7.2 (6H, m, including d (2H, J = 2.4 Hz)), 7.25−7.35 (3H, m), 7.67 (2H, m).

***O*-(3,5-Dimethoxybenzoyl)-*N*-tosyl-(L)-*allo*-threonine (3h):** 100% yield; mp 166−167 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (3H, d, J = 6.5 Hz), 2.34 (3H, s), 3.81 (6H, s), 4.33 (1H, dd, J = 4.0 and 9.3 Hz), 5.29 (1H, dq, J = 4.0 and 6.5 Hz), 5.40 (1H, br), 5.68 (1H, br d, J = 9.3 Hz), 6.63 (1H, t, J = 2.3 Hz), 7.12 (2H, d, J = 2.3 Hz), 7.18 (2H, m), 7.68 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 15.7, 21.4, 55.5, 58.6, 71.0, 106.0, 107.4, 127.1, 129.7, 131.2, 136.4, 145.0, 160.5, 165.4, 172.1; IR (KBr disk) 3275, 3200 (br), 1750, 1695, 1595, 1050, 675 cm^{-1}. Anal. Calcd for $C_{20}H_{23}NO_8S$: C, 54.91; H, 5.30; N, 3.20. Found: C, 54.75; H, 5.40; N, 3.39.

***O*-(Acetyl)-*N*-tosyl-(L)-*allo*-threonine benzyl ester:** 100% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (3H, d, J = 6.5 Hz), 1.93 (3H, s), 2.40 (3H, s), 4.22 (1H, dd, J = 4.4 and 9.3 Hz), 4.96 (2H, m), 5.03 (1H, dq, J = 4.4 and 6.5 Hz), 5.36 (1H, br d, J = 9.3 Hz), 7.15−7.3 (4H, m), 7.3−7.4 (3H, m), 7.69 (2H, m).

***O*-(Acetyl)-*N*-tosyl-(L)-*allo*-threonine (3i):** 100% yield; mp 119−120 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (3H, d, J = 6.5 Hz), 1.96 (3H, s), 2.40 (3H, s), 4.27 (1H, dd, J = 4.0 and 9.1 Hz), 5.08 (1H, dq, J = 4.0 and 6.6 Hz), 5.73 (1H, br d, J = 9.1 Hz), 7.28 (2H, m), 7.74 (2H, m); IR (KBr disk) 3525, 3300, 1725, 1165, 820 cm^{-1}.

***N*,*O*-Ditosyl-(L)-*allo*-threonine Benzyl Ester.** Treatment of *N*-tosyl-(L)-*allo*-threonine benzyl ester with *p*-toluenesulfonyl chloride (1.1 equiv) in pyridine in the presence of a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine gave the ditosylate in 72% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (3H, d, J = 6.6 Hz), 2.39 (3H, s), 2.44 (3H, s), 4.02 (1H, dd, J = 4.0 and 9.4 Hz), 4.77 (1H, dq, J = 4.1 and 6.5 Hz), 4.89 (1H, d, J = 12.2 Hz), 4.95 (1H, d, J = 12.2 Hz), 5.24 (1H, br d, J = 9.4 Hz), 7.15−7.25 (4H, m), 7.3−7.4 (5H, m), 7.63 (2H, m), 7.72 (2H, m).

***N*,*O*-Ditosyl-(L)-*allo*-threonine (3j):** 100% yield; mp 99−100 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 1.29 (3H, d, J = 6.5 Hz), 2.42 (3H, s), 2.49 (3H, s), 4.17 (1H, dd, J = 4.1 and 9.4 Hz), 4.89 (1H, dq, J = 4.1 and 6.5 Hz), 6.76 (1H, br d, J = 9.5 Hz), 7.36 (2H, m), 7.49 (2H, m), 7.72 (2H, m), 7.80 (2H, m); IR (KBr disk) 3280 (br), 1750, 900, 680 cm^{-1}.

***O*-(2-Anthracenoyl)-*N*-tosyl-(L)-*allo*-threonine Methyl Ester.** Thionyl chloride (9.2 mL, 126 mmol) and *N*-tosyl-(L)-*allo*-threonine (2.0 g, 7.3 mmol) were added successively to methanol (10 mL) at 0 °C. After being stirred for 40 h at room temperature, the mixture was concentrated in vacuo to give crude *N*-tosyl-(L)-*allo*-threonine methyl ester: ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.03 (3H, d, J = 6.2 Hz), 2.30 (3H, s), 3.30 (3H, s), 3.51 (1H, dd, J = 8.2 and 9.3 Hz), 3.70 (2H, m), 7.38 (2H, m), 7.62 (2H, m), 8.24 (1H, d, J = 9.4 Hz). Esterification of the crude *N*-tosyl-(L)-*allo*-threonine methyl ester with 2-anthracenoyl chloride by a procedure similar to that described above gave the ester in 30% overall yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (3H, d, J = 6.5 Hz), 2.27 (3H, s), 3.63 (3H, s), 4.43 (1H, dd, J = 4.3 and 9.6 Hz), 5.42 (1H, dq, J = 4.3 and 6.5 Hz), 5.56 (1H, br d, J = 9.6 Hz), 7.20 (2H, m), 7.65−7.75 (5H, m), 8.04 (1H, dd, J = 1.6 and 9.2 Hz), 8.5−8.6 (4H, m), 9.20−9.24 (1H, br s).

***O*-(2-Anthracenoyl)-*N*-tosyl-(L)-*allo*-threonine (3d).** A solution of *O*-(2-anthracenoyl)-*N*-tosyl-(L)-*allo*-threonine methyl ester (500 mg, 1.00 mmol) and iodotrimethylsilane (0.8 mL, 5.6 mmol) in $CHCl_3$ (1 mL) was heated at 70 °C for 6 h. Concentration of the mixture followed by flash chromatography (SiO_2, $CHCl_3$:methanol:acetic acid; 25:1:1) gave 373 mg (78% yield) of **3d**: mp 142−143 °C ^{1}H NMR (300 MHz, acetone-d_6) δ 1.54 (3H, d, J = 6.6 Hz), 2.18 (3H, s), 4.58 (1H, dd, J = 4.4 and 9.5 Hz), 5.52 (1H, dq, J = 4.4 and 6.6 Hz), 7.17 (1H, d, J = 9.5 Hz), 7.27 (2H, m), 7.79 (2H, m), 7.85−7.95 (3H, m), 8.12 (1H, dd, J = 1.5 and 9.2 Hz), 8.55−8.65 (4H, m), 9.19 (1H, br s); IR (KBr disk) 3200 (br), 1720, 1230, 815, 760, 670 cm^{-1}.

***O*-Benzoyl-*N*-methanesulfonyl-(L)-*allo*-threonine Methyl Ester.** Thionyl chloride (1.6 mL, 22 mmol) and (L)-*allo*-threonine (5 g, 42 mmol) were added successively to methanol (42 mL) at 0 °C. After being stirred for 19 h at room temperature, the mixture was concentrated in vacuo to give crude (L)-*allo*-threonine methyl ester hydrochloride (7.1 g). Triethylamine (17.6 mL, 126 mmol) and methanesulfonyl chloride (3.6 mL, 46.2 mmol) were added successively to a suspension of the crude methyl ester hydrochloride in CH_2Cl_2 (100 mL) at 0 °C. After being stirred for 4 h at room temperature, the mixture was poured into brine and extracted with ethyl acetate. Concentration of the dried organic layers gave 4.39 g (50% yield) of the crude *N*-methanesulfonyl-*allo*-threonine methyl ester: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (3H, d, J = 6.6 Hz), 3.0 (1H, br), 3.00 (3H, s), 3.79 (3H, s), 4.20 (2H, m), 5.76 (1H, d, J = 10.8 Hz). Esterification of the *N*-methanesulfonyl-(L)-*allo*-threonine methyl ester with benzoyl chloride by a procedure similar to that described above gave the benzoate in 59% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (3H, d, J = 6.6 Hz), 2.97 (3H, s), 3.84 (3H, s), 4.55 (1H, dd, J = 3.6 and 8.7 Hz), 5.39 (1H, br d, J = 8.4 Hz), 5.43 (1H, dq, J = 3.6 and 6.6 Hz), 7.44 (2H, m), 7.57 (1H, m), 8.02 (2H, m).

***O*-Benzoyl-*N*-methanesulfonyl-(L)-*allo*-threonine (3k).** A solution of *O*-benzoyl-*N*-methanesulfonyl-(L)-*allo*-threonine methyl ester (1.46 g, 4.64 mmol) and iodotrimethylsilane (1.06 mL, 7.42 mmol) in $CHCl_3$ (1.2 mL) was heated at 50 °C for 10 h. Concentration of the mixture followed by flash chromatography (SiO_2, $CHCl_3$−MeOH−acetic acid; 25:1:1) gave 424 mg (30% yield) of **3k**: mp 142−143 °C (recrystallized from $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (3H, d, J = 6.6 Hz), 2.98 (3H, s), 4.60 (1H, dd, J = 3.6 and 9.0 Hz), 5.48 (1H, dq, J = 3.9 and 6.6 Hz), 5.58 (1H, d, J = 9.0 Hz), 6.2 (1H, br), 7.44 (2H, m), 7.57 (1H, m), 8.02 (2H, m); IR (KBr disk) 3400 (br), 1755, 1720, 1270, 715 cm^{-1}.

***S*-*tert*-Butyl (*S*)-5-Oxo-3-phenylhexanethioate (7a) (Typical Procedure for Asymmetric Michael Reaction, Table 5, entry 7).** To a solution of *allo*-threonine derivative **3g** (45.4 mg, 0.10 mmol) in CH_2Cl_2 (1 mL) under nitrogen atmosphere at room temperature was added dichlorophenylborane (13 μL, 0.10 mmol). After being stirred for 1 h, the mixture was concentrated in vacuo. To a solution of the resulting OXB **1n** and silyl ketene acetal **5a** (306 mg, 1.5 mmol) in CH_2Cl_2 (1 mL) at −78 °C were added a CH_2Cl_2 (1 mL) solution of enone **4a** (146 mg, 1.0 mmol) and 2,6-diisopropylphenol (178 mg, 1.0 mmol) over 6 h with use of a syringe pump. After completion of the addition, the mixture was quenched by the addition of saturated aqueous $NaHCO_3$

and filtered.[26] The filtrate was extracted three times with hexane, dried (Na_2SO_4), and concentrated in vacuo. The residue was dissolved in 1 N HCl (4 mL)−THF (20 mL) and the resulting solution was stirred at room temperature for 30 min. The mixture was poured into aqueous $NaHCO_3$ extracted three times with ether. The organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification of the residue by flash chromatography (SiO_2, 5% ethyl acetate in hexane) gave 245 mg, (88%) of adduct (*S*)-**7a** (89% ee): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (9H, s), 2.04 (3H, s), 2.25 (1H, dd, J = 7.3 and 15.0 Hz), 2.76 (1H, dd, J = 6.6 and 15.0 Hz), 2.79 (1H, dd, J = 7.8 and 16.8 Hz), 2.83 (1H, dd, J = 6.6 and 16.6 Hz), 3.69 (1H, quintet, J = 7.2 Hz), 7.16−7.30 (5H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.6, 30.3, 37.9, 48.0, 48.9, 50.3, 126.7, 127.3, 128.5, 142.6, 198.4, 206.6; IR (liquid film) 1725, 1675, 790, 705 cm^{-1}; MS *m*/*z* (rel intensity) 278 (M^+, 2), 189 (100), 131 (88); HRMS calcd for $C_{16}H_{22}O_2S$ 278.1342, found 278.1346. Anal. Calcd for $C_{16}H_{22}O_2S$: C, 69.03; H, 7.96. Found: C, 68.78; H, 7.97. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 16.8 min, (*R*) t_2 = 14.1 min.

Oxazaborolidinone 1g: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.73 (3H, d, J = 6.6 Hz), 2.31 (3H, s), 4.64 (1H, d, J = 1.9 Hz), 5.72 (1H, br q, J = ca. 6.5 Hz), 7.07 (2H, br d, J = ca. 8 Hz), 7.41 (2H, m), 7.50 (1H, m), 7.55−7.6 (3H, m), 7.72 (1H, d, J = 8.2 Hz), 7.78 (1H, d, J = 8.3 Hz), 7.8−7.85 (2H, m), 8.11 (2H, br d, J = ca. 8 Hz), 8.33 (1H, s).

***S-tert*-Butyl (*S*)-3-(4-chlorophenyl)-5-oxohexanethioate (7b):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (9H, s), 2.05 (3H, s), 2.66 (1H, dd, J = 7.6 and 14.8 Hz), 2.75 (1H, dd, J = 7.2 and 14.8 Hz), 2.74 (1H, dd, J = 8.2 and 17.2 Hz), 2.83 (1H, dd, J = 6.4 and 17.2 Hz), 3.68 (1H, quintet, J = 7.2 Hz), 7.13 (2H, m), 7.25 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.6, 30.3, 37.2, 48.2, 48.8, 50.0, 128.6, 128.8, 132.4, 141.1, 198.2, 206.1; IR (liquid film) 1725, 1680, 730 cm^{-1}; MS *m*/*z* (rel intensity) 312 (M^+, 6), 223 (100), 194 (63), 166 (100), 138 (60), 51(47); HRMS calcd for $C_{16}H_{21}O_2SCl$ 312.0952, found 312.0957. Anal. Calcd for $C_{16}H_{21}O_2SCl$: C, 61.43; H, 6.76. Found: C, 61.18; H, 6.60. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 2% 2-PrOH in hexane) (*S*) t_1 = 14.1 min, (*R*) t_2 = 13.2 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-(3-chlorophenyl)-5-oxohexanethioate (7c):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (9H, s), 2.07 (3H, s), 2.66 (1H, dd, J = 7.4 and 14.8 Hz), 2.75 (1H, dd, J = 7.2 and 14.7 Hz), 2.78 (1H, dd, J = 7.7 and 17.1 Hz), 2.85 (1H, dd, J = 6.6 and 17.1 Hz), 3.68 (1H, quintet, J = 7.0 Hz), 7.09 (1H, m), 7.17 (3H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.6, 30.3, 37.4, 48.2, 48.5, 49.9, 125.7, 126.9, 127.5, 129.7, 134.2, 144.7, 198.1, 206.0; IR (liquid film) 1725, 1680, 735, 690 cm^{-1}; MS *m*/*z* (rel intensity) 312 (M^+, 5), 223 (100), 166 (77), 138 (15), 51(12); HRMS calcd for $C_{16}H_{21}O_2SCl$ 312.0952, found 312.0957. Anal. Calcd for $C_{16}H_{21}O_2SCl$: C, 61.43; H, 6.77. Found: C, 60.98; H, 6.74. Ee determination (HPLC, Daicel Chiralpak ADH, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 15.7 min, (*R*) t_2 = 16.8 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-(4-fluorophenyl)-5-oxohexanethioate (7d):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36 (9H, s), 2.04 (3H, s), 2.66 (1H, dd, J = 7.5 and 14.5 Hz), 2.70−2.85 (3H, m), 3.69 (1H, quintet, J = 7.5 Hz), 6.95 (2H, m), 7.16 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.6, 30.3, 37.2, 48.1, 49.0, 50.3, 115.3 (d, J = 21.4 Hz), 128.9 (d, J = 7.5 Hz), 138.3 (d, J = 3.8 Hz), 161.5 (d, J = 244 Hz), 198.3, 206.4; IR (liquid film) 1720, 1685, 835 cm^{-1}; MS *m*/*z* (rel intensity) 296 (M^+, 4), 207 (100), 150 (58), 122 (28), 51(11); HRMS calcd for $C_{16}H_{21}O_2SF$ 296.1247, found 296.1241. Anal. Calcd for $C_{16}H_{21}O_2SF$: C, 64.83; H, 7.14. Found: C, 64.41; H, 6.84. Ee determination (HPLC, Daicel Chiralpak OJ, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 19.7 min, (*R*) t_2 = 26.4 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-(3-fluorophenyl)-5-oxohexanethioate (7e):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (9H, s), 2.09 (3H, s), 2.71 (1H, dd, J = 7.5 and 14.5 Hz), 2.75−2.85 (2H, m), 2.87 (1H, dd, J = 6.5 and 16.5 Hz), 3.73 (1H, quintet, J = 7.0 Hz), 6.91 (2H, m), 7.0 (1H, d, J = 7.5 Hz), 7.26 (1H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.6, 30.3, 37.6, 48.2, 48.7, 50.0, 113.7 (d, J = 21.4 Hz), 114.3 (d, J = 21.4 Hz), 123.1, 130.0 (d, J = 7.5 Hz), 145.3 (d, J = 6.3 Hz), 162.8 (d, J = 245 Hz), 198.2, 206.1; IR (liquid film) 1710, 1685, 785, 700 cm^{-1}; MS *m*/*z* (rel intensity) 296 (M^+, 2), 207 (100), 150 (72); HRMS calcd for $C_{16}H_{21}O_2SF$ 296.1247, found 296.1245. Anal. Calcd for $C_{16}H_{21}O_2SF$: C, 64.84; H, 7.14. Found: C, 64.65; H, 7.19. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 16.3 min, (*R*) t_2 = 24.2 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-(4-trifluoromethylphenyl)-5-oxohexanethioate (7f):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (9H, s), 2.07 (3H, s), 2.73 (1H, dd, J = 7.6 and 15.0 Hz), 2.75−2.85 (2H, m), 2.88 (1H, dd, J = 6.3 and 17.1 Hz), 3.78 (1H, quintet, J = 7.3 Hz), 7.33 (2H, m), 7.54 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.6, 30.3, 37.5, 48.3, 48.6, 49.8, 124.1 (q, J = 273 Hz), 125.4 (q, J = 3.8 Hz), 127.9, 129.0 (q, J = 32.7 Hz), 146.8, 198.0, 205.9; IR (liquid film) 1720, 1680, 730 cm^{-1}; MS *m*/*z* (rel intensity) 346 (M^+, 3), 257 (100), 199 (60); HRMS calcd for $C_{17}H_{21}O_2F_3S$ 346.1215, found 346.1220. Anal. Calcd for $C_{17}H_{21}O_2F_3S$: C, 58.94; H, 6.11. Found: C, 59.00; H, 6.08. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 19.9 min, (*R*) t_2 = 27.8 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-(3-trifluoromethylphenyl)-5-oxohexanethioate (7g):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (9H, s), 2.11 (3H, s), 2.73 (1H, dd, J = 7.5 and 15.0 Hz), 2.8−2.9 (2H, m), 2.93 (1H, dd, J = 6.5 and 17.5 Hz), 3.80 (1H, quintet, J = 7.0 Hz), 7.43 (2H, m), 7.45−7.5 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.6, 30.3, 37.6, 48.3, 48.6, 49.9, 123.67, 123.70, 124.2, 129.0, 131.1, 143.7, 198.1, 205.9; IR (liquid film) 1720, 1675, 800, 705 cm^{-1}; MS *m*/*z* (rel intensity) 346 (M^+, 2), 257 (100), 199 (71); HRMS calcd for $C_{17}H_{21}O_2F_3S$ 346.1215, found 346.1220. Anal. Calcd for $C_{17}H_{21}O_2F_3S$: C, 58.94; H, 6.11. Found: C, 58.50; H, 6.09. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 10.7 min, (*R*) t_2 = 11.7 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-(4-Methylphenyl)-5-oxohexanethioate (7h):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (9H, s), 2.03 (3H, s), 2.29 (3H, s), 2.64−2.87 (4H, m), 3.66 (1H, quintet, J = 7.5 Hz), 7.07 (4H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 21.0, 29.6, 30.3, 37.6, 48.0, 49.0, 50.5, 127.1, 129.2, 136.2, 139.6, 199.5, 206.7; IR (liquid film) 2960, 2920, 1725, 1675, 725, 700 cm^{-1}; MS *m*/*z* (rel intensity) 292 (M^+, 1), 203 (99), 145 (100), 118 (12), 57 (11); HRMS calcd for $C_{17}H_{24}O_2S$ 292.1498, found 292.1497. Anal. Calcd for $C_{17}H_{24}O_2S$: C, 69.82; H, 8.27. Found: C, 69.51; H, 8.42. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 16.7 min, (*R*) t_2 = 14.4 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-(4-methoxyphenyl)-5-oxohexanethioate (7i):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (9H, s), 2.04 (3H, s), 2.65−2.85 (4H, m), 3.65 (1H, quintet, J = 7.3 Hz), 3.77 (3H, s), 6.82 (2H, m), 7.11 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.6, 30.4, 37.3, 48.0, 49.2, 50.6, 55.2, 113.9, 128.3, 134.6, 158.3, 198.6, 206.9; IR (liquid film) 1720, 1675, 870, 760 cm^{-1}; MS *m*/*z* (rel intensity) 308 (M^+, 14), 190 (100), 177 (56); HRMS calcd for $C_{17}H_{24}O_3S$ 308.1447, found 308.1442. Anal. Calcd for $C_{17}H_{24}O_3S$: C, 66.20; H, 7.84. Found: C, 65.84; H, 7.56. Ee determination (HPLC, Daicel Chiralcel OJ, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 28.1 min, (*R*) t_2 = 31.8 min. The absolute stereochemistry was assumed by analogy.

(26) *allo*-Threonine derivative **3g** was separated by filtration as its sodium salt. The sodium salts of **3g** obtained from several runs were combined and extracted with ethyl acetate after acidification with 1 N HCl. A pure ligand could be recovered by concentration of the dried organic extracts and recrystallization from benzene.

***S-tert*-Butyl (*S*)-3-(2-naphthyl)-5-oxohexanethioate (7j):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (9H, s), 1.91 (3H, s), 2.65−2.8 (4H, m), 3.75 (1H, quintet, J = 7.1 Hz), 7.20 (1H, dd, J = 1.7 and 7.6 Hz), 7.25−7.35 (2H, m), 7.50 (1H, br s), 7.6−7.7 (3H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.7, 30.4, 38.1, 48.2, 49.0, 50.4, 125.6 (2c), 126.1 (2c), 127.6, 127.7, 128.4, 132.4, 133.4, 140.1, 198.3, 206.7; IR (liquid film) 1720, 1680, 745 cm^{-1}; MS *m*/*z* (rel intensity) 328 (M^+, 27), 272 (2), 210 (89), 181 (100), 156 (24), 128(8), 51(7); HRMS calcd for $C_{20}H_{24}O_2S$ 328.1498, found 328.1500. Anal. Calcd for $C_{20}H_{24}O_2S$: C, 73.13; H, 7.36. Found: C, 72.92; H, 7.21. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 21.2 min, (*R*) t_2 = 27.4 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-(1-naphthyl)-5-oxohexanethioate (7k):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (9H, s), 2.10 (3H, s), 2.85−3.1 (4H, m), 4.65 (1H, quintet, J = 7.0 Hz), 7.35 (1H, br d, J = ca. 7 Hz), 7.45 (1H, t, J = ca. 9 Hz), 7.51 (1H, t, J = ca. 8 Hz), 7.59 (1H, t, J = ca. 7.5 Hz), 7.75 (1H, br d, J = ca. 8.5 Hz), 7.87 (1H, br d, J = ca. 8 Hz), 8.24 (1H, br d, J = ca. 8.5 Hz); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.6 (2c), 30.2, 48.2, 48.6, 50.0, 123.0, 124.4, 125.3, 125.6, 126.3, 127.4, 128.9, 131.1, 134.0, 138.9, 198.7, 206.6; IR (liquid film) 1715, 1680, 795, 780 cm^{-1}; MS *m*/*z* (rel intensity) 328 (M^+, 13), 239 (14), 181 (100), 153 (76); HRMS calcd for $C_{20}H_{24}O_2S$ 328.1498, found 328.1495. Anal. Calcd for $C_{20}H_{24}O_2S$: C, 73.13; H, 7.36. Found: C, 72.92; H, 7.25. Ee determination (HPLC, Daicel Chiralcel OD, 1 mL/min, 0.4% 2-PrOH in hexane) (*S*) t_1 = 40.5 min, (*R*) t_2 = 46.6 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-(2-furanyl)-5-oxohexanethioate (7*l*):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (9H, s), 2.12 (3H, s), 2.75−2.85 (4H, m), 3.82 (1H, quintet, J = 7.0 Hz), 6.05 (1H, d, J = 3.5 Hz), 6.27 (1H, dd, J = 2.0 and 3.5 Hz), 7.31 (1H, d, J = 2.0 Hz); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 29.7, 30.1, 31.4, 46.3, 47.5, 48.2, 105.5, 110.1, 141.3, 155.4, 198.2, 206.4; IR (liquid film) 1720, 1680, 730 cm^{-1}; MS *m*/*z* (rel intensity) 268 (M^+, 13), 179 (49), 152 (100); HRMS calcd for $C_{14}H_{20}O_3S$ 268.1134, found 268.1136. Anal. Calcd for $C_{14}H_{20}O_3S$: C, 62.66; H, 7.51. Found: C, 61.93; H, 7.50. Ee determination (HPLC, Daicel Chiralpak OD, 1 mL/min, 0.7% 2-PrOH in hexane) (*S*) t_1 = 12.1 min, (*R*) t_2 = 13.0 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-3-methyl-5-oxohexanethioate (7m):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (3H, d, J = 6.5 Hz), 1.44 (9H, s), 2.13 (3H, s), 2.25−2.56 (5H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 19.6, 27.0, 29.6, 30.21, 47.9, 49.7, 50.5, 199.3, 207.0; IR (liquid film) 2960, 2925, 1725, 1675, 730 cm^{-1}; MS *m*/*z* (rel intensity) 217 (M^+, 13), 169 (6), 127 (100), 99 (4), 69(2); HRMS calcd for $C_{11}H_{20}O_2S$ 217.1263, found 217.1268. Anal. Calcd for $C_{11}H_{20}O_2S$: C, 61.07; H, 9.32. Found: C, 60.73; H, 8.96. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 2% 2-PrOH in hexane) (*S*) t_1 = 6.2 min, (*R*) t_2 = 6.0 min.

***S-tert*-Butyl (*S*)- 5-oxo-3-pentylhexanethioate (7n):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (3H, t, J = 7.2 Hz), 1.2−1.35 (8H, m), 1.45 (9H, s), 2.14 (3H, s), 2.35−2.55 (5H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.0, 22.5, 26.3, 29.7, 30.3, 31.78, 31.81, 33.9, 47.7, 48.0, 48.2, 199.8, 208.1; IR (liquid film) 2940, 1720, 1680; MS (CI) *m*/*z* (rel intensity) 273 (MH^+, 100), 255 (42), 183 (42); HRMS (CI) calcd for $C_{15}H_{29}O_2S$ (MH^+) 273.1888, found 273.1887. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 6.4 min, (*R*) t_2 = 7.0 min.

***S-tert*-Butyl (*S*)-5-oxo-3-phenylheptanethioate (7o):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (3H, t, J = 7.3 Hz), 1.37 (9H, s), 2.22−2,42 (2H, m), 2.67−2.86 (4H, m), 3.71 (1H, quintet, J = 7.2 Hz), 7.15−7.31 (4H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 7.5, 29.6, 36.3, 38.0, 47.7, 48.0, 50.3, 126.7, 127.3, 128.4, 142.7, 198.5, 209.2; IR (liquid film) 2950, 2920, 1710, 1675, 780, 700 cm^{-1}; MS *m*/*z* (rel intensity) 292 (M^+), 236, 203 (100), 131 (5), 104 (15), 57; HRMS calcd for $C_{17}H_{24}O_2S$ 292.1498, found 292.1491. Anal. Calcd for $C_{17}H_{24}O_2S$: C, 69.82; H, 8.27. Found: C, 69.53; H, 7.93. Ee determination (HPLC, Daicel Chiralpak AD, 0.5 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 29.1 min, (*R*) t_2 = 24.3 min.

***S-tert*-Butyl (*S*)-6-methyl-5-oxo-3-phenylheptanethioate (7p):** ^{1}H NMR (300 MHz, CDCl3) δ 0.94 (3H, d, J = 6.9 Hz), 1.00 (3H, d, J = 6.9 Hz), 1.36 (9H, s), 2.46 (1H, septet, J = 6.9 Hz), 2.69 (1H, dd, J = 7.4 and 14.7 Hz), 2.80 (1H, dd, J = 7.4 and 14.7 Hz), 2.82 (2H, m), 3.71 (1H, quintet, J = 7.0 Hz), 7.14−7.29 (4H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 17.8, 29.6, 37.8, 41.0, 45.8, 47.9, 50.1, 126.6, 127.3, 128.4, 142.8, 198.4, 212.2; IR (liquid film) 2970, 2925, 1720, 1680, 735, 700 cm^{-1}; MS *m*/*z* (rel intensity) 306 (M^+), 217 (100), 188, 131 (49), 71(17); HRMS calcd for $C_{18}H_{26}O_2S$ 306.1655, found 306.1656. Anal. Calcd for $C_{18}H_{26}O_2S$: C, 70.54; H, 8.55. Found: C, 70.18; H, 8.51. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 11.4 min, (*R*) t_2 = 10.4 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl (*S*)-6,6′-dimethyl-5-oxo-3-phenylheptanethioate (7q):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (9H, s), 1.38 (9H, s), 2.68−2.98 (4H, m), 3.74 (1H, quintet, J = 7.2 Hz), 7.16−7.32 (5H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 26.0, 29.6, 37.7, 45.3, 44.0, 47.9, 50.0, 126.5, 127.5, 128.3, 143.1, 198.5, 213.3. Ee determination (HPLC, Daicel Chiralpak AD, 1 mL/min, 1% 2-PrOH in hexane) (*S*) t_1 = 8.3 min, (*R*) t_2 = 9.0 min. The absolute stereochemistry was assumed by analogy.

***S-tert*-Butyl 5-oxo-3,5-diphenylpentanethioate (7r):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (9H, s), 2.80 (1H, dd, J = 7.4 and 14.8 Hz), 2.90 (1H, dd, J = 7.4 and 14.8 Hz), 3.34 (1H, dd, J = 7.4 and 16.8 Hz), 3.39 (1H, dd, J = 6.7 and 16.8 Hz), 3.90 (1H, quintet, J = 7.2 Hz), 7.35−7.5 (5H, m), 7.4−7.6 (3H, m), 7.90 (2H, m).

***S-tert*-Butyl 2-(3-oxocyclohexyl)ethanethioate (7s):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.3−1.5 (10H, including s (9H) at 1.44), 1.68 (1H, m), 1.93 (1H, m), 2.0−2,1 (2H, m), 2.2−2.5 (6H, m).

***S-tert*-Butyl 5-(*tert*-butyldimethylsiloxy)-3-phenyl-4−2-(3-oxocyclohexyl)ethanethioate (12):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.10 (3H, s), 0.16 (3H, s), 0.97 (9H, s), 1.37 (9H, s), 1.78 (3H, s), 2.65−2.85 (2H, m), 4.28 (br q, J = ca. 8 Hz), 4.6 (1H, br d, J = ca. 9 Hz), 7.1−7.3 (5H, m) [a minor geometric isomer resonated at 3.93 (1H, m) and 4.78 (1H, br d, J = ca. 10 Hz)].

Methyl (*S*)-5-Oxo-3-phenylhexanethioate (15a). To a solution of **7a** (61.6 mg, 0.220 mmol, 79% ee) in ether (1 mL) at room temperature was added silver trifluoroacetate (88.0 mg, 0.40 mmol). The resulting suspension was stirred at room temperature for 4 h. Methanol (40 μL, 1.0 mmol) was added to this mixture. After being stirred for 36 h at room temperature, the mixture was filtered through a pad of cellulose powder and the filtrate was concentrated in vacuo. Purification of the residue by flash chromatography (5% ethyl acetate in hexane) gave 24.4 mg (55% yield) of **13a**: $[\alpha]^{24}_D$ −16.9 (*c* 1.22, benzene) [lit.[17] (for *R*-enantiomer) $[\alpha]^{24}_D$ 22.4 (benzene)]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.06 (3H, s), 2.60 (1H, dd, J = 7.6 and 15.3 Hz), 2.69 (1H, dd, J = 7.2 and 15.3 Hz), 2.79 (1H, dd, J = 7.4 and 16.7 Hz), 2.86 (1H, dd, J = 7.0 and 16.7 Hz), 3.58 (3H, s), 3.68 (1H, quintet, J = ca. 7.5 Hz), 7.17−7.24 (3H, m), 7.26−7.33 (2H, m).

Methyl (*S*)-5-Oxo-3-phenylheptanethioate (15b). The compound was obtained in 47% yield from **7o** (61% ee) by a procedure similar to that described above; $[\alpha]^{24}_D$ −24.1 (*c* 0.150, benzene) [lit.[17] (for *R*-enantiomer) $[\alpha]^{24}_D$ 35.3 (benzene)]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (3H, t, J = 7.3 Hz), 2.32 (2H, m), 2.69 (1H, dd, J = 7.7 and 15.3 Hz), 2.69 (1H, dd, J = 7.2 and 15.3 Hz), 2.76 (1H, dd, J = 7.3 and 16.5 Hz), 2.82 (1H, dd, J = 7.0 and 16.5 Hz), 3.58 (3H, s), 3.69 (1H, quintet, J = ca. 7.5 Hz), 7.16−7.32 (5H, m).

(3*S*,1′*R*)-*N*-(1′-(α-Naphthyl)ethyl)-3-methyl-5-oxohexaneamide (16). To a solution of **7m** (46.5 mg, 0.22 mmol) and (*R*)-(+)-α-naphthylethylamine (71 μL, 0.44 mmol) in THF (2.2 mL) at room temperature was added the silver trifluoroacetate (97 mg, 0.44 mmol). After being stirred for 1 day at room temperature, the mixture was quenched by the addition of 1

N HCl and extracted twice with ethyl acetate. The organic layers were washed successively with $NaHCO_3$ and water, dried, and concentrated in vacuo. Purification of the residue by flash chromatography (20−50% ethyl acetate in hexane) gave 24.4 mg (38% yield) of **14**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99 (3H, d, J = 6.6 Hz), 1.69 (3H, d, J = 6.5 Hz), 2.08 (3H, s), 2.12 (1H, dd, J = 7.0 and 13.8 Hz), 2.20 (1H, dd, J = 6.8 and 13.8 Hz), 2.30 (1H, dd, J = 6.8 and 16.3 Hz), 2.45 (1H, sextet, J = 6.6 Hz), 2.54 (1H, dd, J = 6.1 and 16.3 Hz), 5.95−6.0 (2H, m), 7.45−7.6 (4H, m), 7.82 (1H, d, J = ca. 8 Hz), 7.89 (1H, d, J = ca. 8 Hz), 8.12 (1H, d, J = ca. 8 Hz) [a minor diastereomer resonated at δ 0.98 (3H, d, J = 6.6 Hz) and 2.09 (3H, s)].

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Supporting Information Available: ^{1}H NMR spectra of **1g**, **2**, **3a**,**b**,**d**,**f**,**i**−**k**, **7n**,**q**−**s**, **12**, and **16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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