

## Catalytic Asymmetric Aldol-type Reaction Using a Chiral Tin(II) Lewis Acid #

Shū KOBAYASHI, Hiromi UCHIRO, Isamu SHIINA, and Teruaki MUKAIYAMA

Department of Applied Chemistry, Faculty of Science,  
Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162

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**Abstract:** Highly diastereo- and enantioselective aldol-type reactions of a silyl enol ether with aldehydes including aromatic, aliphatic, and  $\alpha,\beta$ -unsaturated ones are performed in propionitrile (solvent) by the use of a catalytic amount of chiral tin(II) Lewis acid consisting of tin(II) triflate and a chiral diamine. The asymmetric environments created by the chiral catalysts in the enantioselective aldol reaction are discussed by employing five kinds of chiral diamines.

The asymmetric aldol reaction is one of the most powerful tools for the construction of carbon-carbon bonds with control of absolute configurations of new chiral centers,<sup>1</sup> and the utility of this reaction has been demonstrated by a number of applications to the synthesis of natural products such as macrolide and polyether antibiotics, carbohydrates, etc.<sup>2</sup>

Conventional asymmetric aldol reactions have been mostly performed in a diastereoselective manner by using chiral enolates and achiral carbonyl compounds as starting materials.<sup>3-8</sup> For example, the chiral boron enolate, generated in situ from the corresponding chiral oxazolidone derivative, dialkylboron triflate, and diisopropylethylamine, stereoselectively reacts with aldehydes to afford the corresponding aldol-type adducts in good yields.<sup>3b</sup> These reactions proceed in excellent diastereoselectivities; however, additional steps to first introduce a chiral function into the reactant and to remove it after the reactions are essentially required. On the other hand, there have been reported some examples of the direct preparation of chiral aldols from both achiral enolates and aldehydes.<sup>9</sup> For example, the tin(II) enolate generated from achiral 3-acetylthiazolidine-2-thione creates an asymmetric environment with the aid of a chiral amine and then reacts with achiral aldehydes to give the corresponding aldol-type adducts in high enantioselectivities.<sup>9b</sup> In these reactions, optically active aldol-type adducts can be obtained in high enantiomeric excesses by using a stoichiometric amount of chiral source.

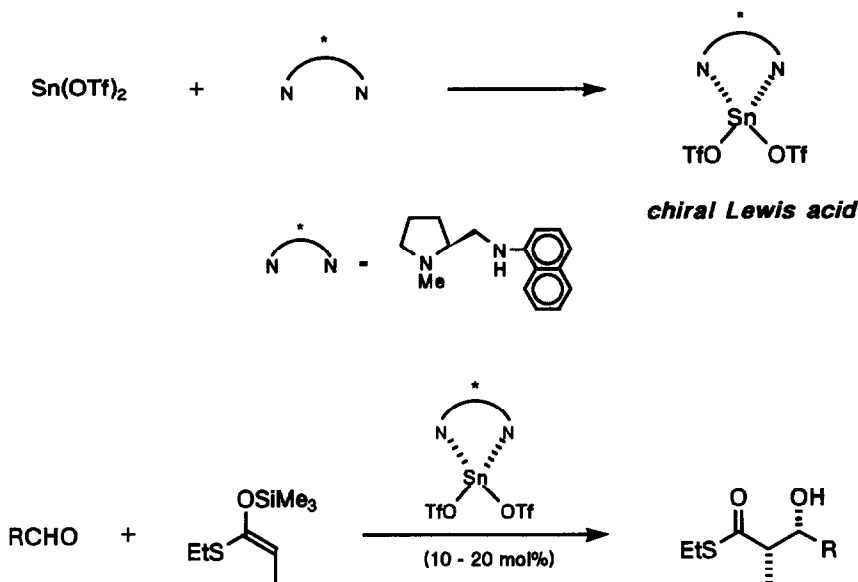
The development of the asymmetric aldol reaction which proceeds in a truly catalytic manner with high diastereo- and enantioselectivities has been a challenging task in organic synthesis.<sup>10</sup> Although use of a chiral

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# Dedicated to Professor Shun-ichi Yamada on the occasion of his 77th birthday.

Lewis acid seems to be one of the most prospective way to solve the problem, less progress has been made in this field compared with the fruitful results obtained in the chiral Lewis acid catalyzed Diels-Alder and related reactions.<sup>11</sup>

In this paper, we would like to report an efficient catalytic asymmetric aldol reaction of a silyl enol ether with aldehydes by using a chiral tin(II) Lewis acid as a catalyst.<sup>12</sup>

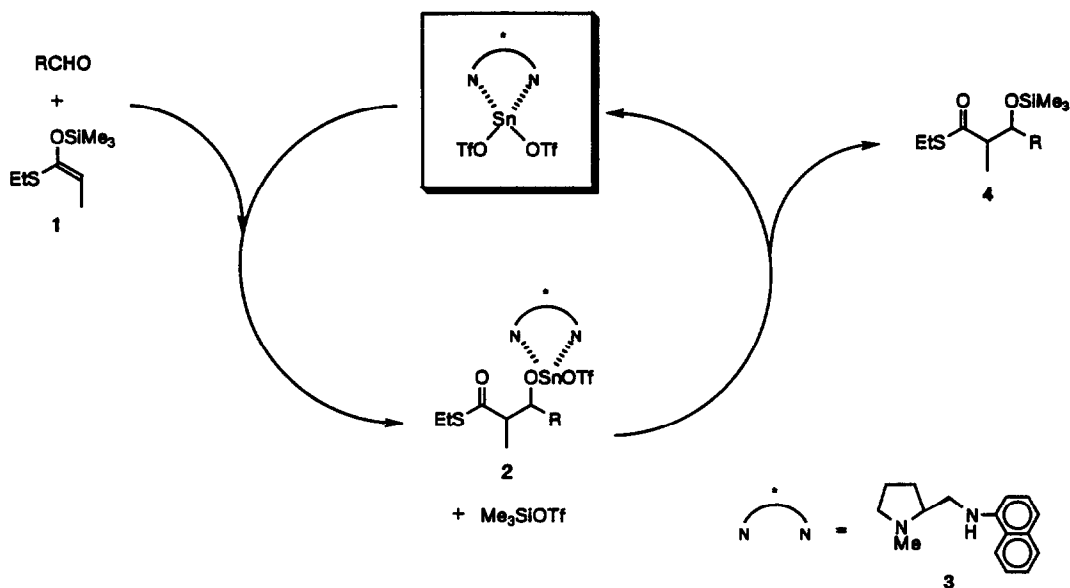


## RESULTS AND DISCUSSION

### *Catalytic Asymmetric Aldol Reaction*

In the previous papers, we reported a highly diastereo- and enantioselective aldol reaction of silyl enol ethers of thioesters with aldehydes by using a novel promoter system, combined use of stoichiometric amounts of tin(II) triflate, a chiral diamine, and a tin(IV) compound (tributyltin fluoride or dibutyltin diacetate).<sup>13</sup> According to these reactions, optically active aldol-type adducts are easily prepared starting from both achiral aldehydes and silyl enol ethers, while stoichiometric use of chiral source still remained as a problem in terms of practical use. In the course of our investigations to characterize the above promoter system as well as to clarify the mechanism of these reactions toward a truly catalytic aldol-type process, the following catalytic cycle was postulated (Scheme 1).

Tin(II) triflate coordinated with a chiral diamine (a chiral tin(II) Lewis acid) interacts with an aldehyde, and tin(II) alkoxide **2** and trimethylsilyl triflate (TMSOTf) are initially produced by the attack of silyl enol ether **1** onto the activated aldehyde. When the metal exchange between tin(II) and silicon of the above product **2** takes place smoothly, the corresponding aldol-type adduct can be obtained as its trimethylsilyl ether **4** along with the regeneration of the catalyst. If the above mentioned metal exchange step is slow, coexisted undesirable TMSOTf-promoted reaction<sup>14</sup> (to afford the achiral aldol-type adduct) proceeds to result in lowering the selectivity.



Scheme 1. The Catalytic Cycle of the Asymmetric Aldol Reaction

Table 1. Synthesis of *syn*- $\alpha$ -Methyl- $\beta$ -hydroxythioesters (solvent: CH<sub>2</sub>Cl<sub>2</sub>)<sup>a)</sup>

R	product	yield (%)	syn/anti	ee (%) <sup>b)</sup>
Ph	5	86	93/ 7	91
p-Cl Ph	6	80	93/ 7	93
p-Me Ph	7	82	78/22	80
(E)-CH <sub>3</sub> CH=CH	8	51	84/16	77
(E)-CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> CH=CH	9	62	81/19	74
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>6</sub>	10	75	100/ 0	>98
cC <sub>6</sub> H <sub>11</sub>	11	31	99/ 1	74

a) Slow addition of 1 and benzaldehyde to the catalyst over 9 h at -78°C.

b) Ee's of *syn* aldol-type adducts. Enantiomeric excesses of *anti* aldol-type adducts were not determined.

Based on these considerations, a slow addition of the substrates to the solution of the catalyst was tried in order to keep trimethylsilyl triflate in as low concentration as possible during the reaction. Namely, a

dichloromethane solution of the silyl enol ether<sup>15</sup> and an aldehyde were added for over 9 h to a dichloromethane solution of the catalyst (20 mol%). The results are shown in Table 1. As expected, aldol-type adducts were obtained in good yields with excellent enantiomeric excesses and high diastereoselectivities in some cases, but the selectivities were not so high when *p*-tolualdehyde,  $\alpha,\beta$ -unsaturated aldehydes and cyclohexanecarboxaldehyde were used.

The lower selectivities are considered to be ascribed to the incompleteness of the above catalytic cycle, especially the metal exchange reaction of the initially formed aldol-type adduct **2** with trimethylsilyl triflate (metal exchange between tin(II) and silicon). In order to accelerate this metal exchange step, various polar solvents with low melting points (under  $-78\text{ }^{\circ}\text{C}$ ) were carefully examined by taking the reaction of **1** with benzaldehyde as a model, and finally propionitrile was found to be an excellent solvent (Table 2).<sup>16</sup> The examination of the addition time (addition of the reactants to the solution of the catalyst) revealed that the rate of the metal exchange in propionitrile is faster than that in dichloromethane (Table 3). While 9 h (addition time) was necessary to attain the best result in dichloromethane, comparable selectivities were achieved when the substrates were added to the catalyst for 3 h in propionitrile. It is noted that tin(II) triflate is more soluble in propionitrile than dichloromethane<sup>17</sup> indicating that the coordination of the nitrile group to tin(II) is expected to be rather strong, but the ligand exchange of the nitrile for the diamine smoothly took place to form the desired chiral Lewis acid by the addition of the chiral diamine to this propionitrile solution of tin(II) triflate. Although tin(II) triflate is also soluble in tetrahydrofuran (THF) or 1,2-dimethoxyethane (DME), the above aldol-type reaction did not proceed at  $-78\text{ }^{\circ}\text{C}$  after the addition of chiral diamine **3** in these solvents.

Several aldehydes including aromatic, aliphatic and  $\alpha,\beta$ -unsaturated ones, were applicable to this reaction, and the desired products were obtained in good yields with high selectivities ( $>90\%$ ee, see Table 4). In particular, the lower yields or selectivities observed in the reaction of *p*-tolualdehyde, (E)-crotonaldehyde, (E)-2-hexenal, and cyclohexanecarboxaldehyde, were remarkably improved by using propionitrile as a solvent. High selectivities were also attained even when 10 mol% of the catalyst was employed.<sup>18</sup>

Table 2. Effect of solvent in the Reaction of **1** with benzaldehyde <sup>a)</sup>

solvent	yield (%)	syn/anti	ee (%) <sup>b)</sup>
$\text{CH}_2\text{Cl}_2$	86	93/ 7	91
$\text{C}_2\text{H}_5\text{CN}$	77	92/ 8	89
$\text{C}_3\text{H}_7\text{CN}$	84	93/ 7	86
$\text{C}_2\text{H}_4\text{Cl}_2\text{-CH}_2\text{Cl}_2$ (1:1)	75	49/51	0
$\text{C}_2\text{H}_5\text{NO}_2\text{-CH}_2\text{Cl}_2$ (1:1)	43	60/40	0
THF	0	—	—
DME	0	—	—

a) Slow addition of **1** and benzaldehyde to the catalyst over 9 h at  $-78\text{ }^{\circ}\text{C}$ .

b) Ee's of syn aldol-type adducts.

Table 3. Effect of Addition Time in the Reaction of 1 with Benzaldehyde

addition time (h)	solvent : CH <sub>2</sub> Cl <sub>2</sub>			solvent : C <sub>2</sub> H <sub>5</sub> CN		
	yield (%)	syn/anti	ee (%) <sup>a)</sup>	yield (%)	syn/anti	ee (%) <sup>a)</sup>
0	88	53/47	48	81	70/30	69
2	85	54/46	52	79	79/21	82
3	86	58/42	57	77	93/ 7	90
4	84	88/12	85	80	90/10	89
6	86	89/11	87	74	90/10	89
9	86	93/ 7	91	77	92/ 8	89
12	72	92/ 8	86	75	91/ 9	89

a) Ee's of syn aldol-type adducts.

Table 4. Synthesis of syn- $\alpha$ -Methyl- $\beta$ -hydroxythioesters (solvent: C<sub>2</sub>H<sub>5</sub>CN)

R	product	yield (%)	syn/anti	ee (%) <sup>a)</sup>	addition time (h)
Ph	5	77	93/ 7	90	3
p-Cl Ph	6	83	87/13	90	4.5
p-Me Ph	7	75	89/11	91	3
(E)-CH <sub>3</sub> CH=CH	8	76	96/ 4	93	3
(E)-CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> CH=CH	9	73	97/ 3	93	3
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>6</sub>	10	80	100/ 0	>98	4.5
c-C <sub>8</sub> H <sub>11</sub>	11	71	100/ 0	>98	3

a) Ee's of syn aldol-type adducts.

The assumed transition state of this asymmetric aldol reaction is shown in Fig. 1. The chiral Lewis acid with the rigid cis-fused bicyclo[3,3,0]octene structure would be produced by the coordination of the chiral diamine to tin(II) triflate. Since tin(II) can accommodate five coordination, there still remain one vacant orbital, with which an aldehyde can interact to form the five-coordinate tin(II) complex<sup>19</sup> maintaining the bicyclic excellent asymmetric environment. The conformation of this complex is highly controlled by mutual interactions between pyrrolidyl, naphthylamino and trifluoromethanesulfonyl groups, and *re* face of the aldehyde is almost completely shielded. The silyl enol ether attacks this aldehyde from *si* face via the acyclic transition state<sup>1a,14</sup> to afford the corresponding syn aldol-type adduct in excellent enantiomeric excess.

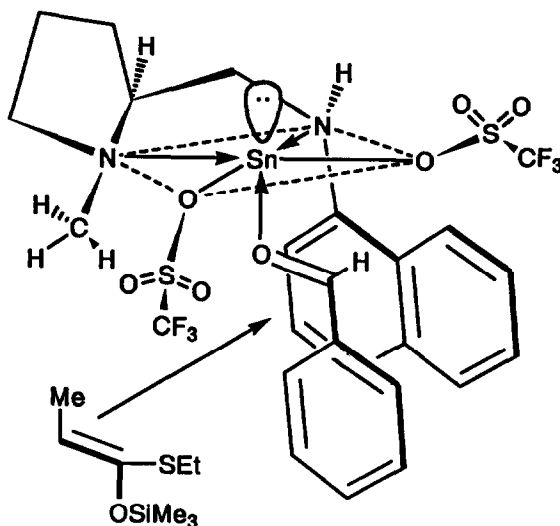


Fig. 1. The Assumed Transition State in the Asymmetric Aldol-type Reaction of 1 with Benzaldehyde

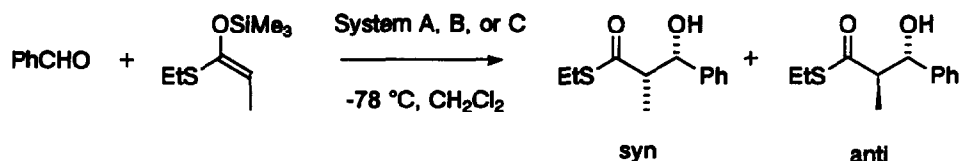
#### ***Comparison of the Asymmetric Environments***

In our previous work, it was found that a chiral promoter system consisting of tin(II) triflate, a chiral diamine and a tin(IV) compound such as tributyltin fluoride or dibutyltin diacetate (three components system), effectively promoted the asymmetric aldol reaction of silyl enol ethers of thioesters with aldehydes.<sup>13</sup> The problem of stoichiometric use of the chiral source has been overcome by the use of a catalytic amount of chiral tin(II) Lewis acid (the two components system) according to a slow addition procedure, and then our next interest is concerned to the asymmetric environments created by the above two systems.

While perfect stereochemical control was realized by using the three components system as a promoter, about 10% loss in the selectivities was observed when the two components system was employed. Though the formation of the three components complex was supported by <sup>119</sup>Sn NMR spectra of the mixture of tin(II) triflate, a chiral diamine and dibutyltin diacetate in dichloromethane,<sup>13d,h</sup> the role of the third component, the tin(IV) compound, in the transition state is not yet clear. It is quite a significant problem that the difference in the selectivity is ascribed whether to the discrimination ability of the promoter or the catalyst, or to the presence of competitive catalytic cycle promoted by trimethylsilyl triflate leading to the selective formation of the undesirable aldol-type adducts. We synthesized four chiral diamines in addition to (*S*)-1-methyl-2-(1-naphthylaminomethyl)pyrrolidine 3,<sup>9b,13g,h</sup> and compared the effectiveness of the three components and the two components systems using the above four chiral ligands in the above aldol reaction.<sup>13i</sup>

The reaction of the silyl enol ether of *S*-ethyl propanethioate 1 with benzaldehyde was carried out in the presence of the three components system (System A, B) or the two components system (System C).

The results are listed in Table 5 and the followings can be noted: 1) Different diastereo- and enantioselectivities were observed in the reactions of using System A, B and C, respectively. 2) System B gave the best diastereo- and enantioselectivities in all of the present experiments. 3) The three components systems



System A :  $\text{Sn(OTf)}_2$  + chiral diamine +  $^n\text{Bu}_3\text{SnF}$

System B :  $\text{Sn(OTf)}_2$  + chiral diamine +  $^n\text{Bu}_2\text{Sn(OAc)}_2$

System C :  $\text{Sn(OTf)}_2$  + chiral diamine (20 mol%)

Table 5. Effect of Chiral Diamines in System A, B, or C

entry	chiral diamine	System	yield (%)	syn / anti	ee (%) <sup>a)</sup>
1	 3	A	86	100 / 0	>98
		B	85	100 / 0	>98
		C	91	94 / 6	93
2		A	58	88 / 12	42
		B	89	96 / 4	67
		C	78	84 / 16	60
3		A	59	98 / 2	64
		B	84	93 / 7	80
		C	80	65 / 35	55
4		A	79	100 / 0	84
		B	85	100 / 0	93
		C	83	82 / 18	83
5		A	70	100 / 0	19 (-) <sup>b)</sup>
		B	86	100 / 0	97
		C	69	91 / 9	80

a) Ee's of syn aldol-type adducts.

b) The optical rotation was observed in the opposite sense.

(System A and B) are superior to the two components system (System C) in the diastereoselectivities (syn/anti ratio). It is noteworthy to point out that, in entries 2 and 5, the enantioselectivities in System C are better than those in System A, and in these cases, trimethylsilyl triflate-promoted achiral aldol-type reaction is not a main reason for the low selectivities. These observations indicate that the three components system and two components system form different asymmetric fields in the transition states. Furthermore, these experiments strongly support our "double activation" hypothesis in System A<sup>13a,h</sup>; namely, tin(II) triflate activates an aldehyde and, at the same time, the electronegative fluoride interacts with a silicon atom of a silyl enol ether.

The screening of the chiral diamines also revealed the influence of their structures on the diastereo- and enantioselectivities. 1-Naphthylamino group of the chiral diamine would work like a wall in the transition state to enhance the diastereoselectivities (syn/anti ratio). (S)-1-Methyl-2-(5,6,7,8-tetrahydro-1-naphthylaminomethyl)pyrrolidine also worked well (entry 4), but the selectivities were decreased in the case of using (S)-1-methyl-2-(2-isopropyl-1-anilinomethyl)pyrrolidine (entry 3) or (S)-1-methyl-2-(anilinomethyl)pyrrolidine (entry 2) as a ligand. Furthermore, 1-alkyl group of the pyrrolidine ring had strong influence on the diastereo- and enantioselectivities in the cases of System A and C. When (S)-1-ethyl-2-(1-naphthylaminomethyl)pyrrolidine was employed as a chiral diamine (entry 5), even reverse enantioselection was observed in the case of System A and lower diastereo- and enantioselectivities were found in the case of System C.

### Conclusion

The catalytic asymmetric aldol-type reaction of **1** with several aldehydes including aromatic, aliphatic, and  $\alpha,\beta$ -unsaturated ones is successfully performed by using a chiral tin(II) Lewis acid consisting of tin(II) triflate and a chiral diamine. The chiral Lewis acid is easily prepared by just mixing the above two components at room temperature, and several synthetically valuable syn- $\alpha$ -methyl- $\beta$ -hydroxythioesters are prepared in high optical purities (>90%ee) according to the present procedure. It is further noted that our result indicates the use of propionitrile as a solvent is quite effective in these types of reactions involving the metal exchange step for the regeneration of the catalyst. Moreover, the considerations of the asymmetric environments would lead us to design new catalyst systems containing such functions as to effectively control the asymmetric environments in this aldol and other carbonyl compounds related reactions. These projects are currently in progress in our laboratory.

## EXPERIMENTAL

IR spectra were recorded on a Horiba FT-300 infrared spectrometer. <sup>1</sup>H NMR spectra were recorded on a Hitachi R-1100 or JEOL JNR-EX270L spectrometer, and tetramethylsilane (TMS) served as internal standard. HPLC was carried out using a Hitachi LC-Organizer, L-4000 UV Detector, L-6200 Intelligent Pump, and D-2500 Chromato-Integrator. Optical rotations were recorded on a Jasco DIP-360 digital polarimeter. Column chromatography was performed on Silica gel 60 (Merck) or Wakogel B5F. All reactions were carried out under argon atmosphere in dried glassware.

Dichloromethane was distilled from P<sub>2</sub>O<sub>5</sub>, then CaH<sub>2</sub>, and dried over MS4A. Propionitrile was dried with CaH<sub>2</sub>, decanted and distilled from P<sub>2</sub>O<sub>5</sub>, then CaH<sub>2</sub>, and dried over MS4A.

Tin(II) trifluoromethanesulfonate (tin(II) triflate)<sup>9d</sup> and chiral diamines<sup>13g,h</sup> were prepared by the literature method. All handling of tin(II) triflate was carried out under argon atmosphere. The silyl enol ether **1** was



prepared according to the conventional method<sup>13h,20</sup> (1. LDA/THF, -78 °C; 2. TMSCl, -78 °C to rt), and the Z/E ratio was determined by <sup>1</sup>H NMR.

Optical purity of the aldol-type adducts 5-11 was determined by HPLC analysis using Daicel Chiralcel: 5 (AS, hexane/IPA=50/1); 6 (the corresponding acetyl derivative, OD, hexane/IPA=500/1); 7 (AS, hexane/IPA=30/1); 8 (OD, hexane/IPA=50/1); 9 (OD, hexane/IPA=200/1); 10 (the corresponding acetyl derivative, AD, hexane/IPA=500/1); 11 (AD, hexane/IPA=400/1). Absolute configurations of these adducts were determined by comparison with the authentic samples.<sup>13h</sup>

#### **Typical Procedure for the Catalytic Asymmetric Aldol Reaction**

To a solution of tin(II) triflate (33.4 mg, 0.080 mmol, 20 mol%) in propionitrile (1 ml) was added (S)-1-methyl-2-(1-naphthylaminomethyl)pyrrolidine (3, 21.1 mg, 0.088 mmol) in propionitrile (1 ml). The mixture was cooled to -78 °C, then a mixture of 1 (76.0 mg, 0.40 mmol) and an aldehyde (0.40 mmol) was slowly added to this solution over 3-4.5 h (see Table 4). The mixture was further stirred for 2 h, then quenched with saturated aqueous sodium hydrogen carbonate. The organic layer was separated and the aqueous layer was extracted with dichloromethane (three times). The combined organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, evaporated, and chromatographed on silica gel to afford the aldol-type adduct as the corresponding trimethylsilyl ether.

The trimethylsilyl ether was treated with THF-1N HCl (20:1) at 0 °C to give the corresponding alcohol. All the physical data of these aldol-type adducts were completely consistent with those of the authentic samples which we prepared previously.<sup>13h</sup>

**(2S,3S)-S-Ethyl 3-hydroxy-2-methyl-3-phenylpropanethioate (5):**<sup>13h</sup> [ $\alpha$ ]<sub>D</sub><sup>25</sup> +78.5 ° (c 1.12, PhH) (91% ee); IR (neat) 3450, 1675 cm<sup>-1</sup>; <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\delta$  1.10 (d, 3H, J=7.0 Hz), 1.20 (t, 3H, J=7.0 Hz), 2.65 (br s, 1H), 2.55-2.95 (m, 1H), 2.80 (q, 2H, J=7.0 Hz), 5.00 (d, 1H, J=4.0 Hz), 7.20 (m, 5H).

**(2S,3S)-S-Ethyl 3-(4-chlorophenyl)-3-hydroxy-2-methylpropanethioate (6):**<sup>13h</sup> [ $\alpha$ ]<sub>D</sub><sup>23</sup> +79.9 ° (c 0.98, PhH) (93% ee); IR (neat) 3450, 1675 cm<sup>-1</sup>; <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\delta$  1.10 (d, 3H, J=7.0 Hz), 1.20 (t, 3H, J=7.0 Hz), 2.70 (m, 1H), 2.80 (q, 2H, J=7.0 Hz), 3.00 (br s, 1H), 4.95 (d, 1H, J=4.0 Hz), 7.20 (m, 4H).

**(2S,3S)-S-Ethyl 3-hydroxy-2-methyl-3-p-tolylpropanethioate (7):**<sup>13h</sup> [ $\alpha$ ]<sub>D</sub><sup>30</sup> +83.5 ° (c 1.2, PhH) (91% ee); IR (neat) 3450, 1675 cm<sup>-1</sup>; <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\delta$  1.10 (d, 3H, J=7.0 Hz), 1.20 (t, 3H, J=7.0 Hz), 2.30 (s, 3H), 2.70 (br s, 1H), 2.70 (m, 1H), 2.80 (q, 2H, J=7.0 Hz), 4.95 (d, 1H, J=4.0 Hz), 7.10 (m, 4H).

**(2S,3R)-S-Ethyl 3-hydroxy-2-methyl-trans-4-hexenethioate (8):**<sup>13h</sup> [ $\alpha$ ]<sub>D</sub><sup>26</sup> +44.7 ° (c 1.1, PhH) (93% ee); IR (neat) 3400, 1665 cm<sup>-1</sup>; <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\delta$  1.20 (d, 3H, J=7.0 Hz), 1.25 (t, 3H, J=7.0 Hz), 1.70 (d, 3H, J=5.0 Hz), 2.35-2.75 (m, 1H), 2.55 (br s, 1H), 2.80 (q, 2H, J=7.0 Hz), 4.05-4.35 (m, 1H), 5.05-5.95 (m, 2H).

**(2S,3R)-S-Ethyl 3-hydroxy-2-methyl-trans-4-octenethioate (9):**<sup>13h</sup> [ $\alpha$ ]<sub>D</sub><sup>27</sup> +37.4 ° (c 1.1, PhH) (93% ee); IR (neat) 3400, 1665 cm<sup>-1</sup>; <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\delta$  0.60-1.70 (m, 9H), 1.80-2.45 (m, 4H), 2.30 (br s, 1H), 2.45-2.85 (m, 1H), 2.80 (q, 2H, J=7.0 Hz), 4.10-4.35 (m, 1H), 5.05-5.90 (m, 2H).

**(2S,3R)-S-Ethyl 3-hydroxy-2-methyldecanethioate (10):**<sup>13h</sup> [ $\alpha$ ]<sub>D</sub><sup>29</sup> +30.5 ° (c 2.2, PhH) (>98% ee); IR (neat) 3450, 1680 cm<sup>-1</sup>; <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\delta$  0.80-1.70 (m, 21H), 2.25 (br s, 1H), 2.35-2.65 (m, 1H), 2.85 (q, 2H, J=7.0 Hz), 3.45-3.95 (m, 1H).

**(2S,3R)-S-Ethyl 3-cyclohexyl-3-hydroxy-2-methylpentanethioate (11):**<sup>13h</sup> [ $\alpha$ ]<sub>D</sub><sup>28</sup> +33.0° (c 1.1, PhH) (>98% ee); IR (neat) 3475, 1680 cm<sup>-1</sup>; <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\delta$  0.50-2.10 (m, 11H), 1.15 (d, 3H, J=7.0 Hz), 1.25 (t, 3H, J=7.0 Hz), 2.25 (br s, 1H), 2.75 (m, 1H), 2.90 (q, 2H, J=7.0 Hz), 3.40-3.70 (m, 1H).

### **Comparison of the Asymmetric Environments**

**System A:** To a solution of tin(II) triflate (0.40 mmol) and chiral diamine (0.48 mmol) in dichloromethane (1 ml) was added tributyltin fluoride (0.44 mmol) at room temperature. After the mixture was cooled to -78 °C, the silyl enol ether (0.40 mmol) in dichloromethane (0.5 ml) and benzaldehyde (0.36 mmol) in dichloromethane (1 ml) was successively added. The mixture was further stirred for 3 h, then quenched with aqueous sodium hydrogen carbonate. The organic layer was separated and the aqueous layer was extracted with dichloromethane (three times). The combined organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, evaporated, and chromatographed on silica gel to afford the aldol-type adduct.

**System B:** The same procedure as System A except using dibutyltin diacetate instead of tributyltin fluoride.

**System C:** To a vigorously stirred suspension of tin(II) triflate (0.080 mmol, 20 mol%) in dichloromethane (1 ml) was added chiral diamine (0.088 mmol) in dichloromethane (1 ml). The mixture was cooled to -78 °C, then a mixture of the silyl enol ether (0.40 mmol) and benzaldehyde (0.40 mmol) in dichloromethane (1.5 ml) was slowly added to this solution over 9 h. The mixture was further stirred for 15 h, then quenched with saturated aqueous sodium hydrogen carbonate. After usual work up, the aldol-type adduct was isolated as the corresponding trimethylsilyl ether.

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16. After our preliminary report, a few groups reported very recently on the same type of asymmetric aldol reaction using propionitrile as a solvent. See, references 12c), 12d), and 12g).
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