Chiral Lewis Acid Controlled Synthesis (CLAC Synthesis): Chiral Lewis Acids Influence the Reaction Course in Asymmetric Aldol Reactions for the Synthesis of Enantiomeric Dihydroxythioester Derivatives in the Presence of Chiral Diamines Derived from L-Proline

Shū Kobayashi* and Mineko Horibe

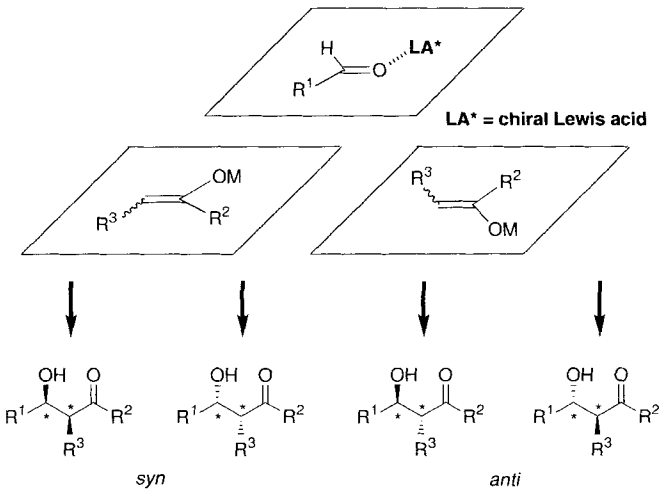
Abstract: Both enantiomers of 2,3-dihydroxythioester derivatives were prepared with almost perfect stereochemical control by chiral Lewis acid controlled synthesis (CLAC synthesis). CLAC synthesis means synthesis of all individual diastereomers or enantiomers from the same starting materials by designing chiral Lewis acids. For example, (*Z*)-1-ethylthio-1-(trimethylsiloxy)-2-(*tert*-butyldimethylsiloxy)ethene (**1**) reacted with aldehydes in the presence of chiral tin(II) Lewis acids using (*S*)-1-methyl-2-[(isoindolinyl)methyl]pyrrolidine (**4**) and (*S*)-1-methyl-2-[(indolinyl)methyl]pyrrolidine (**5**) to afford enantiomeric dihydroxythioester derivatives. Chiral diamines **4** and **5**, which were readily prepared from L-proline, differ only in the fusion point of the benzene ring connected to the pyrrolidine moiety. The unique selectivities were ascribed to the conformational difference between the chiral tin(II) Lewis acids of chiral diamines **4** and **5**, and the function of chiral sources for obtaining high selectivities has also been clarified.

Keywords
aldol reactions · asymmetric synthesis · diamines · enantioselective synthesis · Lewis acids

Introduction

The development of highly selective reactions is one of the most important tasks in modern organic synthesis. Great advances have been made in this field during the last decade, and many chemo-, regio-, diastereo- and enantioselective reactions have been reported.[1] In spite of the high selectivities attained in these reactions, however, changing the reaction courses and obtaining all diastereomers or enantiomers is difficult. For example, there are many highly *endo*-selective Diels–Alder reactions,[2] while few examples of *exo*-selective Diels–Alder reactions are known.[3] As for aldol reactions, enolate geometry is known to change the diastereoselectivity in some reactions.[4] However, in most cases these reactions do not deal with enantioselective synthesis, and therefore there is no control of enantiofacial selectivity.[5]

Our goals are to control the course of reactions and to obtain all diastereomers or enantiomers from the same starting materials. In order to attain these goals, we have focused on asymmetric reactions based on chiral Lewis acids. Recently, due to the increasing importance of asymmetric synthesis, development of new methods for the preparation of chiral compounds has become an important research topic. Thus, asymmetric reactions based on chiral Lewis acids are of great current interest as one of the most efficient asymmetric synthetic methods carried out under mild reaction conditions.[6] Asymmetric reactions with chiral Lewis acids have been carried out, for example, by coordination of the Lewis acid to achiral aldehydes. On the basis of the chirality of the Lewis acid, one face (prochiral enantioface) of an aldehyde is shielded sterically or electronically, and a nucleophile attacks the aldehyde from one open side to attain a high selectivity. We surmised that a higher level of stereocontrol could be achieved by designing chiral Lewis acids. For example, in the aldol reactions shown in Scheme 1, all individual



Scheme 1. Chiral Lewis acid controlled synthesis.

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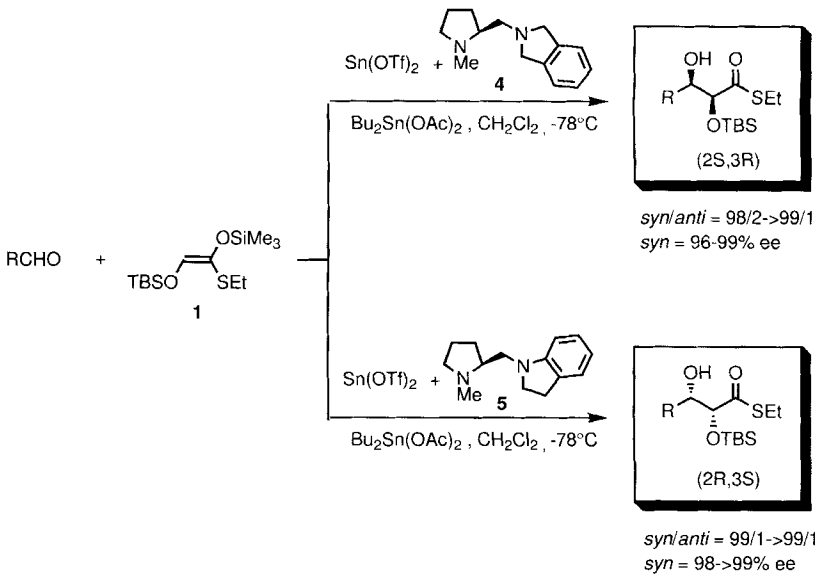
diastereomers or enantiomers would be synthesized from the same starting materials using designed chiral Lewis acids (chiral Lewis acid controlled synthesis, CLAC synthesis).

Based on this idea, we have developed a new method for the preparation of both enantiomers of a chiral compound.[7] Synthesis of both enantiomers is a very important task in asymmetric synthesis, and traditional methods have required sources of enantiomeric precursors, auxiliaries, or catalysts.[8] However, it is often hard to obtain both enantiomers of the sources (for example, alkaloids, amino acids, sugars, etc.). We now report the preparation of both enantiomers including 1,2-diol units with almost perfect selectivities by using similar types of chiral sources derived from L-proline.[9] The origin of the unique selectivities and function of the chiral sources for obtaining the selectivities are also discussed.

Results and Discussion

Synthesis of Both Enantiomers: We have already reported the asymmetric aldol reactions of silyl enol ethers with aldehydes using chiral tin(II) Lewis acids consisting of tin(II) triflate and a chiral diamine,[10, 11] and that optically active 2,3-dihydroxythioesters can be prepared from silyl enol ethers derived from α-alkoxy thioesters (or esters) and aldehydes by these reactions.[12] In the course of our investigations to examine asymmetric aldol reactions of (*Z*)-1-ethylthio-1-(trimethylsiloxy)-2-(*tert*-butyldimethylsiloxy)ethene (**1**) with α-ketoesters for constructing α-alkoxy-β-hydroxy-β-methyl units, we developed a new type of chiral diamine, **2**, which was prepared from L-proline and tetrahydroisoquinoline.[13] PM 3 calculations indicated that the benzene ring connected to the piperidine moiety had an important effect on the selectivities,[14] and that $Sn(OTf)_2$–**2** and $Sn(OTf)_2$–**3** complexes had different conformations (see the following section). Bearing this information in mind, we performed synthetic experiments. When the reaction of **1** with benzaldehyde was carried out in the presence of tin(II) triflate, chiral diamine **2**, and dibutyltin diacetate ($Bu_2Sn(OAc)_2$) in dichloromethane at −78 °C, the aldol adduct with a (2*S*,3*R*) configuration was obtained in an 85% yield with a *syn*/*anti* ratio of 95/5, and the enantiomeric excess of the *syn* adduct was 80%.[15] On the other hand, when chiral diamine **3** (prepared from L-proline and tetrahydroisoquinoline) was used, the reaction also proceeded smoothly to afford the aldol adduct in a high yield with high *syn* selectivity. The enantiomeric excess of the *syn*-aldol was also high (92% *ee*), *but the absolute configuration of the adduct was reversed (2R,3S)*. While diamines **2** and **3** were both prepared from L-proline and the absolute configurations of the 2-position are *S* in both cases, the difference is the fusion point of the benzene ring connected to the piperidine moiety. It was exciting that the slight difference in the structure of the chiral sources completely reversed the enantiofacial selectivity.[16] We further examined the effect of chiral diamines and found that almost perfect diastereo- and enantioselectivities with reverse absolute configurations were obtained when chiral diamines **4** and **5** were employed (Table 1, Scheme 2). We then tested several aldehydes; the results are summarized in Table 2. While adducts with the (2*S*,3*R*) configuration were obtained from chiral diamine **4**, adducts with the (2*R*,3*S*) configuration were produced from chiral diamine **5** for all eight typical aldehydes including aromatic, aliphatic, unsaturated, heterocyclic, and diene aldehydes. In every case, the selectivities were very high; almost perfect *syn* selectivities and more



Scheme 2. Diastereo- and enantioselectivities of reactions in the presence of chiral diamines **4** and **5**.

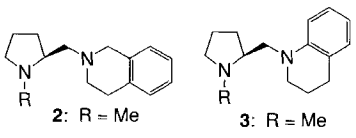
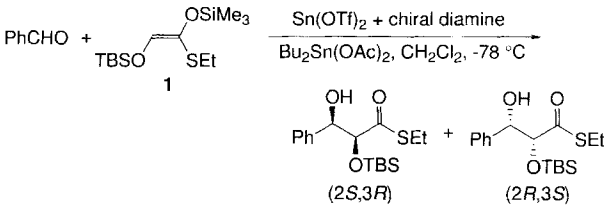
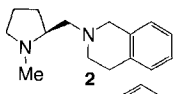
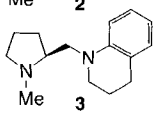
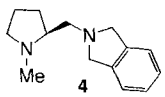
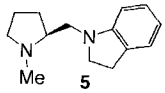


Table 1. Effect of chiral diamines.



Chiral diamine	Yield (%)	*syn*/*anti*	2*S*,3*R*/2*R*,3*S*	ee (%)[a]
 **2**	85	95/5	90.0/10.0	80
 **3**	71	94/6	4.0/96.0	92
 **4**	86	98/2	99.0/1.0	98
 **5**	82	99/1	1.0/99.0	98

[a] Enantiomeric excesses of *syn* adducts.

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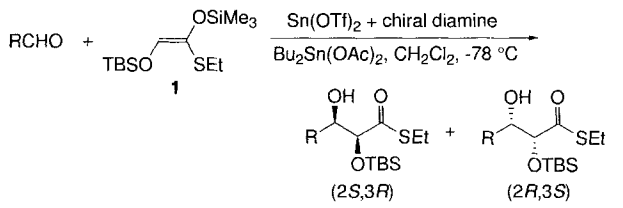
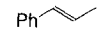
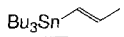
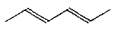
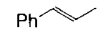
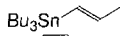
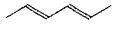
Table 2. Synthesis of both enantiomers.



R	Chiral diamine	Yield (%)	*syn*/*anti*	2*S*,3*R*/2*R*,3*S*	ee (%)[a]
Ph	**4**	86	98/2	99.0/1.0	98
C_2H_5	**4**	61	>99/1	99.0/1.0	98
C_7H_{15}	**4**	83	98/2	98.5/1.5	97
	**4**	86	>99/1	99.0/1.0	98
	**4**	84	>99/1	99.5/0.5	99
	**4**	91	>99/1	99.5/0.5	99
	**4**	94	>99/1	98.5/1.5[b]	97
	**4**	86	98/2	98.0/2.0	96
Ph	**5**	82	99/1	1.0/99.0	98
C_2H_5	**5**	63	>99/1	1.0/99.0	98
C_7H_{15}	**5**	66	97/3	1.5/98.5	97
	**5**	81	>99/1	1.0/99.0	98
	**5**	80	99/1	1.0/99.0	98
	**5**	83	>99/1	1.0/99.0	98
	**5**	86	>99/1	<0.5/>99.5[b]	>99
	**5**	78	>99/1	<0.5/>99.5	>99

[a] Enantiomeric excesses of *syn* adducts. [b] (2*S*,3*S*)/(2*R*,3*R*).

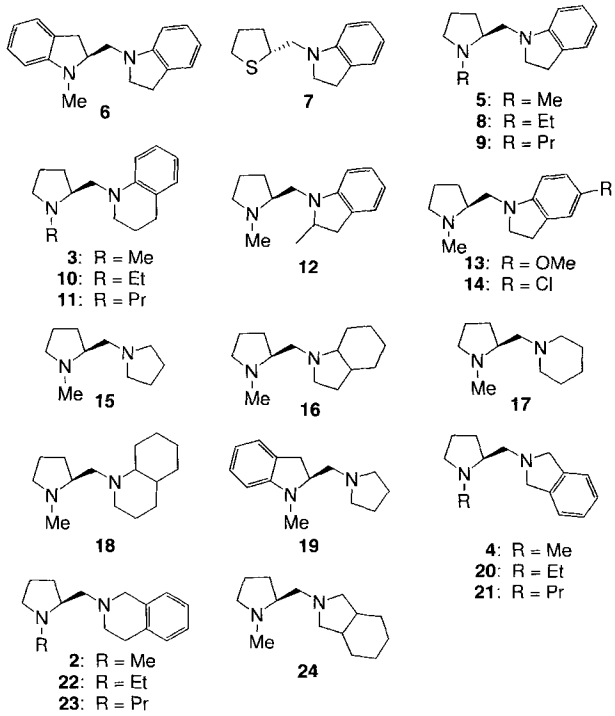
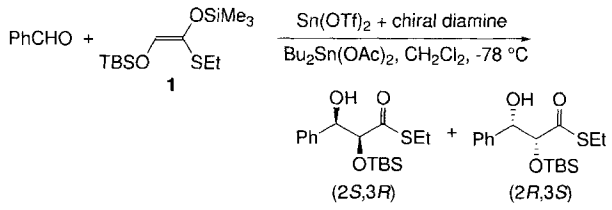


Table 3. Effect of chiral diamines.



Chiral diamine	Yield (%)	*syn*/*anti*	(2*S*,3*R*)/(2*R*,3*S*)	*ee* (%) [a]
6	89	17/83	51.0/49.0	2
7	94	66/34	11.0/89.0	78
5	82	99/1	1.0/99.0	98
8	86	96/4	7.0/93.0	86
9	90	97/3	8.0/92.0	84
3	71	94/6	4.0/96.0	92
10	78	85/15	12.0/88.0	76
11	90	94/6	6.5/93.5	87
12	77	91/9	4.5/95.5	91
13	90	97/3	1.0/99.0	98
14	81	>99/1	1.5/98.5	97
15	86	97/3	90.5/9.5	81
16	89	96/4	94.0/6.0	88
17	83	91/9	74.5/25.5	49
18	92	86/14	61.0/39.0	22
19	80	94/6	82.5/17.5	65
4	86	98/2	99.0/1.0	98
20	82	>99/1	97.5/2.5	95
21	73	>99/1	99.0/1.0	98
2	68	96/4	90.0/10.0	80 [b]
22	69	97/3	97.0/3.0	94
23	88	97/3	98.0/2.0	96
24	80	95/5	97.0/3.0	94

[a] Enantiomeric excesses of *syn* adducts. [b] Tributyltin fluoride (Bu_3SnF) was used instead of $Bu_2Sn(OAc)_2$.

than 96% enantiomeric excesses of the *syn* adducts were obtained. (*E*)-3-(Tributylstannyl)-2-propanal[17] also worked well to afford synthetically useful enantiomers in high yields with excellent selectivities. It should be noted that the benzene ring connected to the pyrrolidine moiety in the chiral diamines controlled the enantiofacial selectivities with high generality. In addition to the unique selectivities, the present reaction provides convenient methods for the preparation of both enantiomers of *syn*-2,3-dihydroxythioesters,[18] not using enantiomeric chiral sources but using similar chiral sources derived from L-proline.

Function of Chiral Diamines: In order to clarify the function of the chiral diamine ligands in the chiral tin(II) Lewis acids, we carefully screened chiral diamines in a model reaction of benzaldehyde with **1**; the results are summarized in Table 3. The excellent *syn* and (2*R*,3*S*) selectivities obtained with chiral diamine **5** decreased when diamine **6** or **7** was used. The *N*-alkyl groups also influenced the selectivity: larger groups (Et, Pr) decreased the selectivities (chiral diamines **8** and **9**). Of the larger heterocyclic segments in the chiral diamines, a pyrrolidine ring gave the best (2*R*,3*S*) selectivity and substituents on the pyrrolidine ring decreased the selectivity. A benzene ring connected to the pyrrolidine ring was found to be essential for (2*R*,3*S*) selectivity. High diastereo- and enantioselectivities were obtained by introducing electron-donating and electron-withdrawing substituents on the benzene rings, respectively (chiral diamines **13** and **14**). Reverse enantioselectivities were obtained when chiral diamine **16**, with a cyclohexane ring instead of the benzene ring, was used. Unlike the case for **5**, **8**, and **9**, the excellent *syn* and

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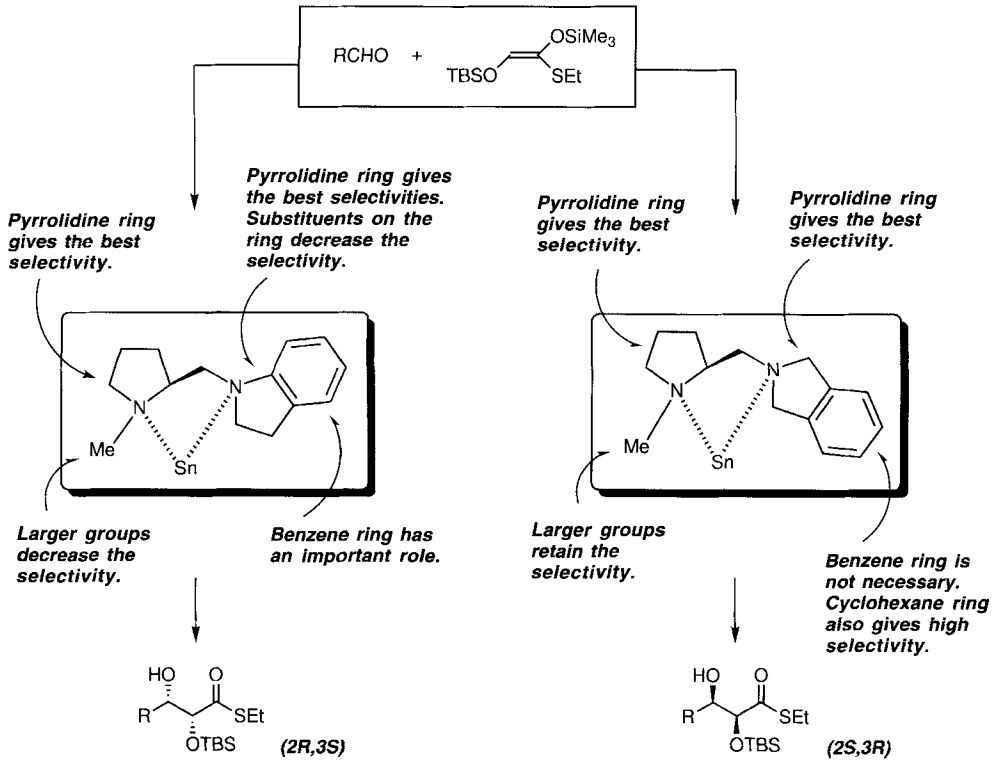
(2*S*,3*R*) selectivities obtained with chiral diamine **4** were also achieved when chiral diamines with larger *N*-alkyl groups (Et, Pr) were used (chiral diamines **20** and **21**; diastereoselectivity was slightly improved). In contrast was the fact that the high selectivities (90% *de*, 94% *ee*) were still obtained when chiral diamine **24**, having a cyclohexane ring instead of a benzene ring, was used.

The functions of the chiral diamines in these reactions are summarized in Scheme 3.



Scheme 3. Functions of chiral diamines.

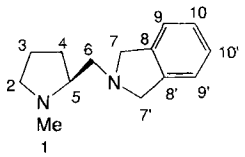
Structure of Chiral Lewis Acids: The ^{13}C NMR chemical shifts of the amine parts in the $Sn(OTf)_2$–**4** and $Sn(OTf)_2$–**5** complexes (two-component complexes), and the $Sn(OTf)_2$–**4**–$Bu_2Sn(OAc)_2$ and $Sn(OTf)_2$–**5**–$Bu_2Sn(OAc)_2$ complexes (three-component complexes) are shown in Tables 4 and 5, respectively. There are slight differences between the two- and three-component complexes. Differences in asymmetric fields created by the two- and three-component complexes have already been demonstrated.[19] Both ^{19}F NMR spectra of $Sn(OTf)_2$–**5** and $Sn(OTf)_2$–**5**–$Bu_2Sn(OAc)_2$ showed only one sharp signal, and the chemical shifts of $Sn(OTf)_2$–**5** and $Sn(OTf)_2$–**5**–$Bu_2Sn(OAc)_2$ were $\delta = -83.9$ and -79.1, respectively. These results indicated that triflate anions dissociated on coordination with the two nitrogens of the chiral diamine, and that a fast equilibrium would exist. $Bu_2Sn(OAc)_2$ interacted with triflate anion in the $Sn(OTf)_2$–**5**–$Bu_2Sn(OAc)_2$ complex to induce the lower field shift. The proposed structures of $Sn(OTf)_2$–**5** and $Sn(OTf)_2$–**5**–$Bu_2Sn(OAc)_2$ are shown in Scheme 4.

The existence of monomeric structures of the above complexes in 0.2 M CH_2Cl_2 solution was also supported by experiments that used chiral diamines **4** and **5** in lower enantiomeric excesses in the aldol reaction of **1** with benzaldehyde.[20] As shown in Figures 1 and 2, complete linear correlation was observed between the *ee* of the aldol adduct and the *ee* of the chiral diamine in each case.

Possible Mechanism and Transition States: It was confirmed from the ^1H NMR spectra of a [D_2]dichloromethane solution of tin(II) triflate, chiral diamine **4** or **5**, $Bu_2Sn(OAc)_2$, and silyl enol ether **1** at $-78\,^\circ C$ that there was no metal exchange from silicon to tin(II) in the silyl enol ether. This means that the asymmetric aldol reaction did not proceed via a tin(II) enolate,[21] but that the silyl enol ether directly attacked the aldehyde, which was activated by the chiral tin(II) Lewis acid.

The origin of the unique selectivities observed in the asymmetric reactions can be ascribed to conformational differences between the tin(II)–diamine complexes.[22] When the chiral diamines coordinate tin(II), bicyclo[3.3.0]octane-like structures form.[23] Conformational analysis by semiempirical molecular orbital calculations (PM3)[14] proved that conformation 1 had the lowest energy in the case of the $Sn(OTf)_2$–**4** complex (Figure 3). On the other hand, conformation 2 had the lowest energy in the $Sn(OTf)_2$–**5** complex. These conformations were corrobo-

Table 4. ^{13}C NMR chemical shifts of **4** (CD_3CN, $-30\,^\circ C$).



	5	$Sn(OTf)_2$ + **5**	$Sn(OTf)_2$ + **5** + $Bu_2Sn(OAc)_2$
C-1	41.6	44.2	44.7
C-2	58.4	54.8	55.0
C-3	23.2	21.5	22.0
C-4	31.0	24.9	25.5
C-5	65.4	69.3	68.8
C-6	61.3	60.9	60.4
C-7	60.3	59.7	59.0
C-7′	–	61.6	60.5
C-8	141.5	137.0	137.2
C-8′	–	137.4	138.0
C-9	123.0	123.7	123.7
C-9′	–	124.3	124.3
C-10	127.4	129.0	129.1
C-10′	–	129.1	129.2

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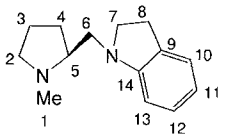
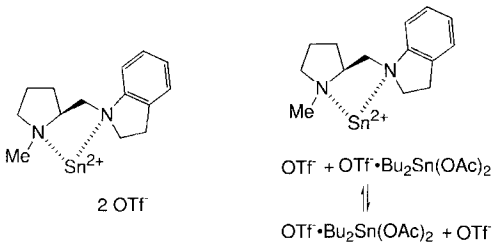
Table 5. ^{13}C NMR chemical shifts of **5** (CD_3CN, $-30\,^{\circ}C$)



	5	$Sn(OTf)_2$ + **5**	$Sn(OTf)_2$ + **5** + $Bu_2Sn(OAc)_2$
C-1	41.6	45.2	44.7
C-2	58.3	59.0	59.2
C-3	23.2	22.3	22.2
C-4	30.8	26.1	25.9
C-5	65.2	68.8	68.3
C-6	54.9	55.1	55.3
C-7	55.1	55.6	57.0
C-8	29.2	29.1	29.2
C-9	130.5	134.9	134.4
C-10	125.1	126.9	126.3
C-11	117.9	126.4	126.3
C-12	128.0	124.5	128.3
C-13	107.3	116.4	116.0
C-14	154.1	146.7	147.7



Scheme 4. Structures of $Sn(OTf)_2$–**5** and $Sn(OTf)_2$–**5**–$Bu_2Sn(OAc)_2$

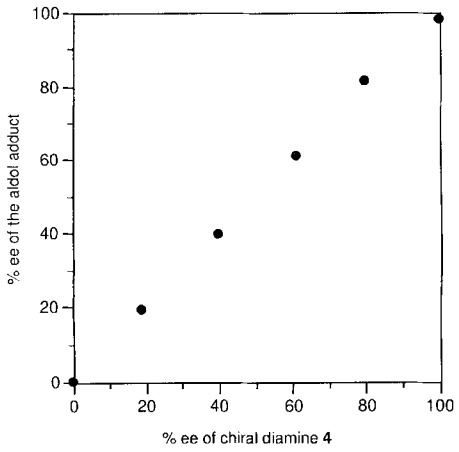


Figure 1. Correlation between the *ee* of the aldol adducts and the *ee* of chiral diamine **4**.

rated by NOE experiments.[24] We note that the benzene ring connected to the pyrrolidine part of chiral diamine **5** is located on the top side of conformation 2, and that conformations of bicyclo[3.3.0]octane-like structures in conformations 1 and 2 are quite different. We also calculated the minimized energies of the $Sn(OTf)_2$–**24** and $Sn(OTf)_2$–**16** complexes (conformations 3 and 4). Almost the same conformation as that of $Sn(OTf)_2$–**4** was indicated in the $Sn(OTf)_2$–**24** complex (conformations 1

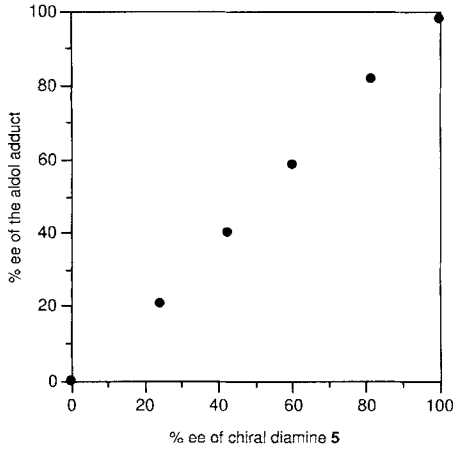


Figure 2. Correlation between the *ee* of the aldol adducts and the *ee* of chiral diamine **5**.

and 3). On the other hand, in the $Sn(OTf)_2$–**16** complex, the cyclohexane ring connected to the pyrrolidine part of chiral diamine **16** is located on the bottom side (conformation 4). The difference in selectivity between the $Sn(OTf)_2$–**5** and $Sn(OTf)_2$–**16** complexes is thus explained.

Although these considerations and explanations concerning the unique selectivities would be acceptable, we carried out investigations to confirm them. We prepared (*S*)-1-methyl-2-[(1-benz[*cd*]indolinyl)methyl]pyrrolidine (**25**),[25] a "mixed-type" chiral diamine, which means **25** was designed by combination of **4** and **5** (Scheme 5). In the $Sn(OTf)_2$–**25** complex the lowest energy was calculated for conformation 5 (PM3),[14] which is similar to conformation 2. We evaluated chiral diamine **25** in the reaction of **1** with benzaldehyde under standard conditions (CH_2Cl_2, $-78\,^{\circ}C$, 21 h), and found that the corresponding aldol adduct was obtained in an 81% yield with good diastereoselectivity (*syn*/*anti* = 80/20). The enantiomeric excess of the *syn* adduct was 81% with a (2*R*,3*S*) absolute configuration. The sense of the asymmetric induction was the same as that of the reaction using chiral diamine **5**, and these results also supported the conformational analyses.

From these experiments, the unique selectivities would be explained by assuming the existence of the transition states shown in Scheme 6. In chiral diamine **4**-coordinated tin(II) (conformation 1), an aldehyde approaches from the bottom side. The *re* face of the aldehyde is shielded by the amine part and silyl enol ether **1** attacks the aldehyde from the *si* face via an acyclic transition state[26] to form the *syn*-(2*S*,3*R*)-aldol adduct. On the other hand, in chiral diamine **5**-coordinated tin(II) (conformation 2), the bottom side of the complex is crowded with nitrogen substituents and an aldehyde coordinated at the top side of the complex. At this time, the *si* face of the aldehyde is shielded and silyl enol ether **1** attacks this aldehyde from the *re* face via an acyclic transition state to form the *syn*-(2*R*,3*S*)-aldol adduct.

We also found that the α-substituents of the silyl enol ethers influenced the selectivities.[25] (*Z*)-1-Ethylthio-1-trimethylsiloxypropene reacted with benzaldehyde in the presence of tin(II) triflate, chiral diamine **4**, and $Bu_2Sn(OAc)_2$, to afford the corresponding aldol adduct in a 98% yield with an excellent *syn* selectivity (*syn*/*anti* = 99/1). The enantiomeric excess of the *syn*

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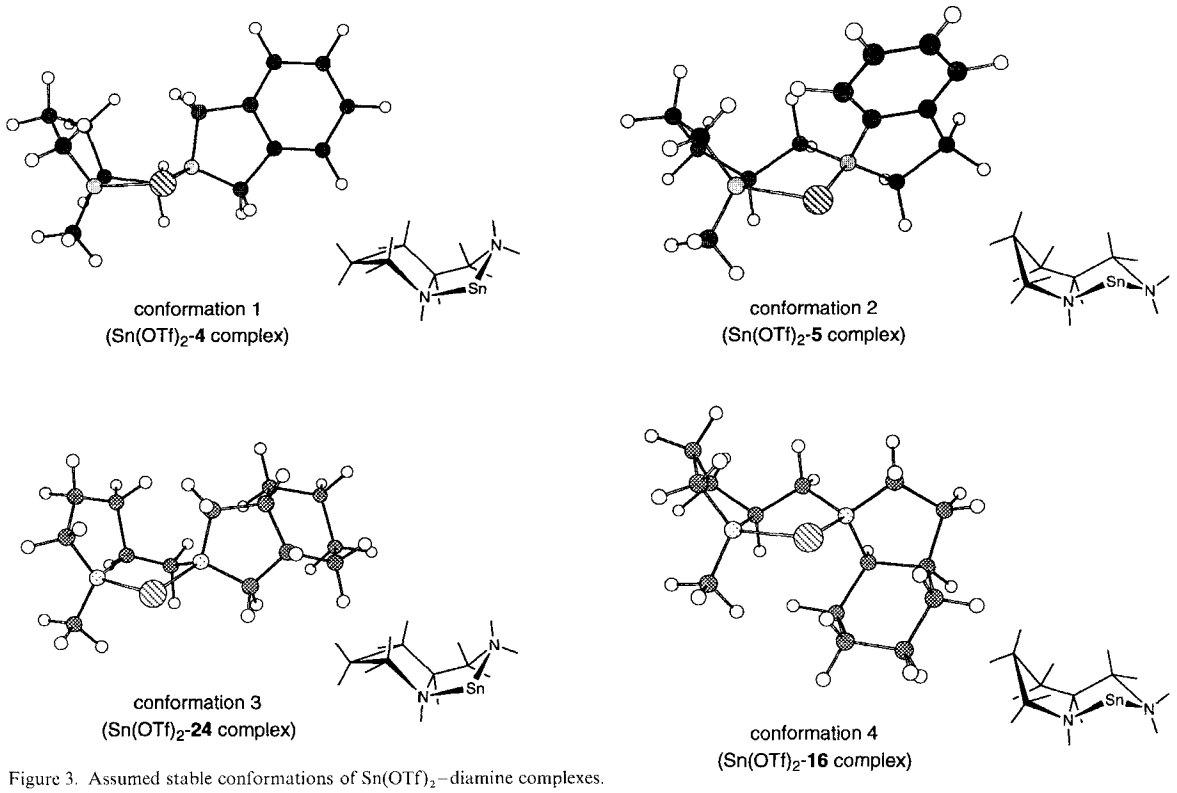
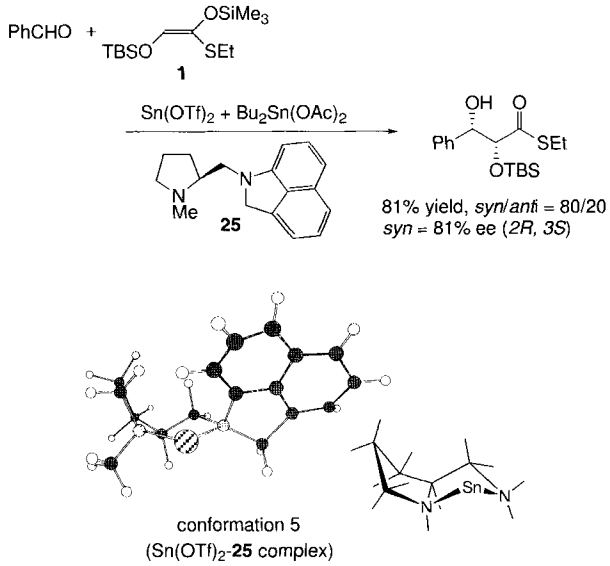


Figure 3. Assumed stable conformations of $Sn(OTf)_2$–diamine complexes.

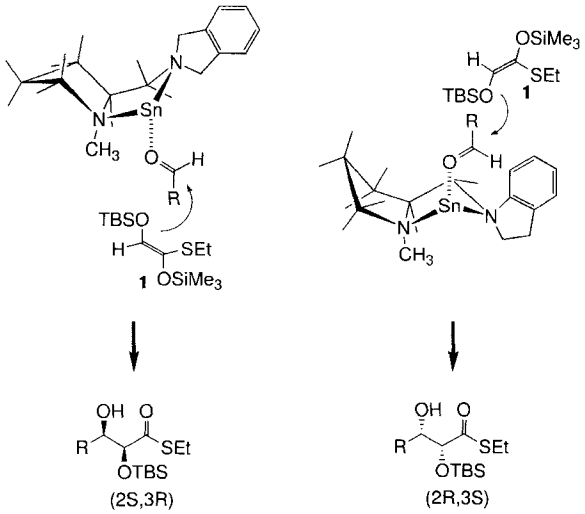
adduct was 66% with a (2*S*,3*S*) absolute configuration. On the other hand, when the same reaction was carried out in the presence of chiral diamine **5**, the reaction also proceeded smoothly to give the adduct in a high yield with a high diastereoselectivity (90% yield, *syn*/*anti* = 93/7). Although reverse (2*R*,3*R*) selectivities were observed in this case, the enantiomeric excess was only 30%. It is assumed from these results that the steric bulkiness of the *tert*-butyldimethylsilyoxy group of silyl enol ether **1** plays an important role in generating the unique high selectivities.[27]



Scheme 5. Asymmetric aldol reaction between **25** and posited stable conformation of $Sn(OTf)_2$–**25** complex.Scheme 6. Postulated transition states.

Conclusion

Synthesis of both enantiomers including 1,2-diol units has been achieved with almost perfect stereochemical control by chiral tin(II) Lewis acid mediated asymmetric aldol reactions. The chiral Lewis acids could change the reaction course (CLAC synthesis), and control of the enantiofaces in the reactions has been attained not by using enantiomers from chiral sources, but by using similar chiral diamines (**4** and **5**). Diamines **4** and **5** were readily prepared from L-proline, the only difference between them being the fusion point of the benzene ring connected to the pyrrolidine moiety. The unique selectivities were assumed to be due to conformational differences between the chiral tin(II)



Scheme 6.

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Lewis acids derived from **4** and **5**, and the means by which the chiral compounds ensure high selectivities has also been clarified.

Although this report has shown an example of the synthesis of enantiomers including 1,2-diol units, synthesis of all individual diastercomers or enantiomers from the same starting materials by chiral Lewis acids (CLAC synthesis) should also be possible. Further studies along these lines are now in progress.

Experimental Section

General: IR spectra were recorded on a Horiba FT-300 infrared spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Hitachi R-1100 or JEOL JNR-EX 270 L spectrometer, and tetramethylsilane (TMS) served as internal standard. HPLC was carried out with 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 B 5 F. All reactions were carried out under argon in dried glassware.
Dichloromethane was distilled from P_2O_5, then CaH_2, and dried over MS 4A. Tin(II) trifluoromethanesulfonate (tin(II) triflate) was prepared according to the literature,[28, 29] and always handled under argon.

(*S*)-1-methyl-2-[(isoindolinyl)methyl]pyrrolidine (4): This diamine was prepared by the literature method.[10a, 29, 30] $[\alpha]_D^{28} = -76.5°$ (*c* 1.3, EtOH); b.p. 98–99 °C/0.08 mm Hg; ^{1}H NMR ($CDCl_3$): δ = 1.62–1.85 (m, 3H), 1.99–2.38 (m, 3H), 2.44 (s, 3H), 2.65 (dd, 1H, *J* = 8.1, 11.7 Hz), 2.93 (dd, 1H, *J* = 4.6, 11.9 Hz), 3.04–3.11 (m, 1H), 3.95 (s, 4H), 7.18 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 22.5, 30.5, 41.3, 57.7, 59.6, 61.1, 64.7, 122.1, 126.5, 140.1; HRMS calcd for $C_{14}H_{20}N_2$ [M^+] 216.1628, found 216.1632.

(*S*)-1-methyl-2-[(indolinyl)methyl]pyrrolidine (5): To a dichloromethane (30 mL) solution of dicyclohexylcarbodiimide (7.10g, 34.0 mmol) was added Boc-(*S*)-proline (7.30 g, 34.0 mmol) at 0 °C. After this had been stirred for 15 min, a dichloromethane solution of indoline (4.53 g, 38.0 mmol) was slowly added to the mixture at 0 °C. The mixture was slowly warmed up to room temperature and stirred for 10 h. The solvent was evaporated in vacuo, ethyl acetate (100 mL) was added, and the precipitate was removed by filtration. The organic layer was washed with 10% citric acid solution, 4% sodium hydrogencarbonate solution and brine, and dried (Na_2SO_4). After removal of the solvents, the crude product was chromatographed on silica gel to give (*S*)-1-(*N*-*tert*-butoxycarbonylprolyl)indoline (10.21 g, 95%). A THF (20 mL) solution of this amide (6.32 g, 20.0 mmol) was added slowly to borane/THF complex (1.0 M THF solution, 34 mL) at 0 °C, and the mixture was refluxed for 2 h. 1 N HCl was added carefully at 0 °C to quench the reaction. Water was then added and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, saturated sodium hydrogencarbonate, and brine, and dried (Na_2SO_4). After removal of the solvents, the crude product was chromatographed on silica gel to give (*S*)-1-*tert*-butoxycarbonyl-2-[(indolinyl)methyl]pyrrolidine (5.18 g, 86%). A THF (20 mL) solution of this Boc-protected amine (5.18 g, 17.2 mmol) was slowly added to a THF suspension (20 mL) of $LiAlH_4$ (9.78 g, 20.5 mmol) at 0 °C, and the mixture was stirred for 2 h. Then saturated sodium sulfate solution was added carefully to the mixture at 0 °C, and the organic materials were collected by decantation. The organic layer was dried (Na_2SO_4/K_2CO_3) and the solvent was removed under reduced pressure. The crude product was chromatographed on alumina and then distilled to give **5** (2.80 g, 75%): $[\alpha]_D^{28} = -82.5°$ (*c* 1.6, EtOH); b.p. 102–104 °C/0.7 mm Hg; ^{1}H NMR ($CDCl_3$): δ = 1.57–1.86 (m, 3H), 1.94–2.08 (m, 1H), 2.21 (q, 1H, *J* = 9.1 Hz), 2.37–2.47 (m, 4H), 2.92–3.00 (m, 3H), 3.08 (t, 1H, *J* = 8.3 Hz), 3.20 (dd, 1H, *J* = 4.5, 13.4 Hz), 3.39 (t, 2H, *J* = 8.4 Hz), 6.47 (d, 1H, *J* = 7.9 Hz), 6.62 (t, 1H, *J* = 7.3 Hz), 6.97–7.23 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 22.8, 28.6, 30.3, 41.3, 54.4, 54.5, 57.7, 64.4, 106.4, 117.2, 124.2, 127.2, 129.5, 152.9; HRMS calcd for $C_{14}H_{20}N_2$ [M^+] 216.1628, found 216.1619.

Other chiral diamines were prepared from L-proline according to the literature methods.[10a, 29, 30]

(*S*)-1-methyl-2-[(1,2,3,4-tetrahydroisoquinolinyl)methyl]pyrrolidine (2): $[\alpha]_D^{28} = -53.6°$ (*c* 1.5, EtOH); ^{1}H NMR ($CDCl_3$): δ = 1.55–1.87 (m, 3H), 1.95–2.08 (m, 1H), 2.17 (dd, 1H, *J* = 7.6, 9.2 Hz), 2.35–2.47 (m, 5H), 2.64–2.79 (m, 3H), 2.87 (t, 2H, *J* = 5.6 Hz), 3.02–3.08 (m, 1H), 3.63 (s, 2H), 6.98–7.12 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 22.5, 29.0, 30.8, 41.4, 51.5, 56.8, 57.7, 63.0, 63.5, 125.4, 125.9, 126.4, 128.5, 134.3, 134.9; HRMS calcd for $C_{15}H_{22}N_2$ [M^+] 230.1785, found 230.1781.

(*S*)-1-methyl-2-[(1,2,3,4-tetrahydroquinolinyl)methyl]pyrrolidine (3): $[\alpha]_D^{27} = -90.7°$ (*c* 1.4, EtOH); b.p. 119–126 °C/0.1 mm Hg; ^{1}H NMR ($CDCl_3$): δ = 1.41–1.85 (m, 3H), 1.87–2.02 (m, 3H), 2.12–2.26 (m, 1H), 2.42 (d, 3H, *J* = 2.3 Hz), 2.47–2.53 (m, 1H), 2.73 (t, 2H, *J* = 6.1 Hz), 2.99–3.01 (m, 2H), 3.27–3.37 (m, 2H), 3.49–3.57 (m, 1H), 6.50–6.61 (m, 2H), 6.90–7.05 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 22.1, 22.2, 28.1, 30.3, 41.3, 50.7, 56.3, 57.3, 63.4, 110.4, 115.3, 121.9, 126.9, 129.1, 145.5; HRMS calcd for $C_{15}H_{22}N_2$ [M^+] 230.1785, found 230.1788.

(*S*)-1-methyl-2-[(indolinyl)methyl]indoline (6): $[\alpha]_D^{25} = -93.4°$ (*c* 1.6, EtOH); b.p. 260 °C/0.07 mm Hg (bath temp): ^{1}H NMR ($CDCl_3$): δ = 1.42 (s, 2H), 2.82 (s, 3H), 2.96 (t, 2H, *J* = 8.3 Hz), 3.10–3.22 (m, 2H), 3.30–3.40 (m, 1H), 3.43–3.52 (m, 1H), 3.61–3.64 (m, 1H), 6.45–6.49 (m, 2H), 6.61–6.69 (m, 2H), 7.02–7.11 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 28.7, 30.3, 33.9, 35.1, 54.5, 66.0, 106.4, 107.2, 117.5, 117.9, 124.2, 124.4, 125.5, 127.3, 127.4, 128.6, 129.4, 153.4; HRMS calcd for $C_{18}H_{20}N_2$ [M^+] 264.1628, found 264.1631.

(*R*)-2-[(indolinyl)methyl]tetrahydrothiophene (7): $[\alpha]_D^{26} = -76.6°$ (*c* 2.6, $CHCl_3$); b.p. 197 °C/0.02 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 1.62–1.79 (m, 3H), 1.80–2.03 (m, 3H), 2.69–2.88 (m, 2H), 2.98 (dd, 1H, *J* = 7.3, 13.5 Hz), 3.10 (dd, 1H, *J* = 7.6, 13.5 Hz), 3.22–3.33 (m, 2H), 3.36–3.59 (m, 1H), 6.36 (d, 1H, *J* = 7.6 Hz), 6.50–6.55 (m, 1H), 6.91–6.96 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 28.4, 29.7, 32.0, 34.7, 47.2, 53.7, 56.0, 106.3, 117.2, 124.2, 127.0, 129.2, 152.2; HRMS calcd for $C_{13}H_{17}NS$ [M^+] 219.1083, found 219.1091.

(*S*)-1-Ethyl-2-[(indolinyl)methyl]pyrrolidine (8): $[\alpha]_D^{25} = -86.1°$ (*c* 0.9, EtOH); b.p. 200 °C/0.05 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 1.13 (t, 3H, *J* = 7.3 Hz), 1.60–2.00 (m, 4H), 2.09–2.19 (m, 1H), 2.21–2.34 (m, 1H), 2.56–2.66 (m, 1H), 2.91–3.02 (m, 4H), 3.11–3.24 (m, 2H), 3.30–3.45 (m, 2H), 6.46 (d, 1H, *J* = 7.9 Hz), 6.61 (t, 1H, *J* = 7.4 Hz), 7.00–7.06 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.9, 22.4, 28.5, 29.8, 49.1, 53.9, 54.3, 54.8, 62.9, 106.3, 117.0, 124.1, 127.1, 129.3, 152.8; HRMS calcd for $C_{15}H_{22}N_2$ [M^+] 230.1785, found 230.1779.

(*S*)-1-Propyl-2-[(indolinyl)methyl]pyrrolidine (9): $[\alpha]_D^{25} = -91.3°$ (*c* 0.9, EtOH); b.p. 185–205 °C/0.1 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 0.92 (t, 3H, *J* = 7.4 Hz), 1.46–1.81 (m, 5H), 1.83–1.99 (m, 1H), 2.11–2.27 (m, 2H), 2.59–2.63 (m, 1H), 2.77–2.87 (m, 1H), 2.92–3.00 (m, 3H), 3.10–3.18 (m, 2H), 3.35–3.43 (m, 2H), 6.46 (d, 1H, *J* = 8.2 Hz), 6.61 (t, 1H, *J* = 7.4 Hz), 7.01–7.06 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 12.1, 22.0, 22.7, 28.6, 29.8, 54.4, 54.5, 54.8, 57.8, 106.4, 117.1, 124.2, 129.4, 153.0; HRMS calcd for $C_{16}H_{24}N_2$ [M^+] 244.1941, found 244.1946.

(*S*)-1-Ethyl-2-[(isoindolinyl)methyl]pyrrolidine (10): $[\alpha]_D^{22} = -79.1°$ (*c* 2.4, EtOH); b.p. 195 °C/0.02 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 1.12 (t, 3H, *J* = 7.2 Hz), 1.55–2.00 (m, 6H), 2.12 (dd, 1H, *J* = 8.7, 17.0 Hz), 2.20–2.33 (m, 1H), 2.66–2.75 (m, 3H), 2.93–3.11 (m, 2H), 3.16–3.27 (m, 1H), 3.30–3.35 (m, 1H), 3.48 (dd, 1H, *J* = 4.8, 14.7 Hz), 6.50–6.61 (m, 2H), 6.90 (m, 1H), 6.97–7.04 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.0, 22.4, 28.1, 29.8, 49.2, 50.8, 53.8, 56.6, 61.9, 110.3, 115.2, 121.8, 126.8, 129.0, 145.5; HRMS calcd for $C_{16}H_{24}N_2$ [M^+] 244.1941, found 244.1942.

(*S*)-1-Propyl-2-[(isoindolinyl)methyl]pyrrolidine (11): $[\alpha]_D^{28} = -83.2°$ (*c* 1.2, EtOH); b.p. 200–215 °C/0.08 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 0.84 (t, 3H, *J* = 7.3 Hz), 1.37–1.76 (m, 6H), 1.78–1.90 (m, 3H), 2.01–2.19 (m, 2H), 2.61–2.81 (m, 4H), 2.95–3.13 (m, 2H), 3.28 (t, 2H, *J* = 5.6 Hz), 3.38 (dd, 1H, *J* = 5.0, 14.5 Hz), 6.43–6.53 (m, 2H), 6.82–6.97 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 12.1, 22.1, 22.3, 22.6, 28.1, 29.7, 50.8, 54.3, 56.6, 57.6, 62.3, 110.3, 115.2, 121.8, 126.9, 129.0, 145.6; HRMS calcd for $C_{17}H_{26}N_2$ [M^+] 258.2098, found 258.2091.

(*S*)-1-Methyl-2-[(2′-methylindolinyl)methyl]pyrrolidine (12): $[\alpha]_D^{25} = -88.6°$ (*c* 0.9, EtOH); b.p. 112–113 °C/0.5 mm Hg; ^{1}H NMR ($CDCl_3$): δ = 1.26–1.29 (m, 3H), 1.56–1.84 (m, 3H), 1.92–2.04 (m, 1H), 2.14–2.28 (m, 1H), 2.39–2.61 (m, 5H), 2.87 (dd, 1H, *J* = 8.7, 13.7 Hz), 3.00–3.13 (m, 2H),

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3.19–3.27 (m, 1H), 3.57–3.76 (m, 1H), 6.45 (dd, 1H, J = 7.9, 13.9 Hz), 6.60 (dd, 1H, J = 7.1, 14.0 Hz), 6.99–7.06 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 19.4, 19.5, 22.1, 22.2, 30.4, 30.7, 37.2, 41.2, 41.4, 51.4, 52.6, 57.4, 57.7, 61.1, 61.2, 64.1, 64.8, 105.6, 106.2, 116.6, 117.0, 123.8, 124.0, 125.3, 127.1, 128.3, 128.6, 152.3, 153.0; HRMS calcd for $C_{15}H_{22}N_2$ [M^+] 230.1785, found 230.1792.

(*S*)-1-Methyl-2-[(5′-methoxyindolinyl)methyl]pyrrolidine (13): $[\alpha]_D^{26}$ = −83.0° (*c* 1.1, EtOH); b.p. 180 °C/0.02 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 1.57–1.86 (m, 3H), 1.95–2.09 (m, 1H), 2.16–2.37 (m, 1H), 2.38–2.46 (m, 4H), 2.86–2.94 (m, 3H), 3.05–3.15 (m, 2H), 3.28–3.35 (m, 2H), 3.72 (s, 3H), 6.41 (d, 1H, J = 8.3 Hz), 6.99–7.06 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 22.3, 28.9, 30.3, 41.2, 55.1, 55.8, 55.9, 57.6, 64.3, 106.9, 111.5, 111.9, 131.0, 147.3, 152.5; HRMS calcd for $C_{15}H_{22}N_2O$ [M^+] 246.1734, found 246.1730.

(*S*)-1-Methyl-2-[(5′-chloroindolinyl)methyl]pyrrolidine (14): $[\alpha]_D^{27}$ = −77.3° (*c* 1.4, EtOH); b.p. 210 °C/0.15 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 1.53–1.85 (m, 3H), 1.88–2.05 (m, 1H), 2.16–2.27 (m, 1H), 2.35–2.45 (m, 4H), 2.88–2.94 (m, 3H), 2.96–3.19 (m, 2H), 3.30–3.43 (m, 2H), 6.33 (d, 1H, J = 8.9 Hz), 6.94–6.97 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 22.3, 28.3, 30.1, 41.2, 54.25, 54.34, 57.6, 64.1, 106.8, 121.4, 124.3, 126.7, 131.2, 151.5; HRMS calcd for $C_{14}H_{19}N_2Cl$ [M^+] 250.1239, found 250.1239.

(*S*)-1-Methyl-2-[(perhydroindolinyl)methyl]pyrrolidine (16): $[\alpha]_D^{26}$ = −50.2° (*c* 1.3, EtOH); b.p. 141 °C/0.15 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 1.13–1.55 (m, 10H), 1.56–1.84 (m, 4H), 1.84–1.95 (m, 2H), 2.02–2.23 (m, 4H), 2.26–2.36 (m, 2H), 2.40–2.44 (m, 2H), 2.80–3.12 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 20.6, 21.1, 22.1, 22.3, 24.8, 24.9, 25.7, 25.9, 28.95, 29.04, 30.3, 30.6, 30.8, 38.06, 38.10, 41.3, 52.3, 52.6, 57.8, 58.2, 58.4, 59.6, 63.0, 63.5, 64.5, 64.9; HRMS calcd for $C_{14}H_{26}N_2$ [M^+] 222.2098, found 222.2091.

(*S*)-1-Methyl-2-[(perhydroisoindolinyl)methyl]pyrrolidine (18): $[\alpha]_D^{26}$ = −55.1° (*c* 1.8, EtOH); b.p. 119 °C/2.0 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 1.17–2.08 (m, 17H), 2.10–2.67 (m, 10H), 3.01–3.06 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 22.4, 24.9, 25.5, 30.2, 30.5, 30.9, 41.2, 41.5, 57.7, 57.8, 59.7, 60.7, 61.2, 63.5, 63.9; HRMS calcd for $C_{15}H_{28}N_2$ [M^+] 236.2254, found 236.2255.

(*S*)-1-Methyl-2-[(pyrrolidine)methyl]indoline (19): $[\alpha]_D^{26}$ = −71.5° (*c* 1.9, EtOH); b.p. 173 °C/0.4 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 1.65–1.85 (m, 6H), 2.48–2.57 (m, 5H), 2.72 (s, 3H), 3.04–3.13 (m, 1H), 3.35–3.43 (m, 1H), 6.37 (d, 1H, J = 7.6 Hz), 6.57 (t, 1H, J = 7.3 Hz), 6.90–7.01 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 23.5, 35.0, 35.2, 54.8, 60.4, 66.3, 107.2, 117.8, 124.0, 127.2, 129.1, 153.5; HRMS calcd for $C_{14}H_{20}N_2$ [M^+] 216.1628, found 216.1624.

(*S*)-1-Ethyl-2-[(1,2,3,4-tetrahydroquinolinyl)methyl]pyrrolidine (20): $[\alpha]_D^{24}$ = −81.8° (*c* 2.4, EtOH); b.p. 108–110 °C/1.5 mm Hg; ^{1}H NMR ($CDCl_3$): δ = 1.13 (t, 3H, J = 7.1 Hz), 1.66–1.85 (m, 3H), 1.96–2.32 (m, 3H), 2.50–2.57 (m, 1H), 2.66 (dd, 1H, J = 8.6, 11.5 Hz), 2.91 (dd, 1H, J = 4.0, 11.6 Hz), 2.96–3.08 (m, 1H), 3.16–3.23 (m, 1H), 3.94 (m, 4H), 7.16 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 13.9, 22.5, 30.1, 49.2, 53.9, 59.7, 61.4, 63.2, 122.1, 126.5, 140.0; HRMS calcd for $C_{15}H_{22}N_2$ [M^+] 230.1785, found 230.1779.

(*S*)-1-Propyl-2-[(1,2,3,4-tetrahydroquinolinyl)methyl]pyrrolidine (21): $[\alpha]_D^{24}$ = −90.0° (*c* 0.8, EtOH); b.p. 185 °C/0.05 mm Hg; ^{1}H NMR ($CDCl_3$): δ = 0.92 (t, 3H, J = 7.4 Hz), 1.49–1.62 (m, 3H), 1.67–1.80 (m, 2H), 1.96–2.06 (m, 1H), 2.12–2.27 (m, 2H), 2.43–2.56 (m, 1H), 2.65 (dd, 1H, J = 8.9, 11.9 Hz), 2.78–2.92 (m, 2H), 3.13–3.20 (m, 1H), 3.94 (m, 4H), 7.16 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 12.1, 22.1, 22.6, 30.0, 54.4, 57.7, 59.8, 61.3, 63.6, 122.1, 126.5, 140.1; HRMS calcd for $C_{16}H_{24}N_2$ [M^+] 244.1941, found 244.1940.

(*S*)-1-Ethyl-2-[(1,2,3,4-tetrahydroisoquinolinyl)methyl]pyrrolidine (22): $[\alpha]_D^{25}$ = −76.1° (*c* 1.4, EtOH); b.p. 181 °C/0.75 mm Hg; ^{1}H NMR ($CDCl_3$): δ = 1.03 (t, 3H, J = 7.3 Hz), 1.52–1.79 (m, 3H), 1.85–2.21 (m, 3H), 2.36 (dd, 1H, J = 7.6, 11.5 Hz), 2.45–2.69 (m, 4H), 2.71–2.87 (m, 2H), 2.90–3.00 (m, 1H), 3.07–3.13 (m, 1H), 3.55 (m, 2H), 6.90–7.04 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 13.8, 22.5, 29.0, 30.5, 49.1, 51.5, 53.9, 56.8, 61.8, 63.8, 125.4, 125.9, 126.4, 128.5, 134.3, 134.9; HRMS calcd for $C_{16}H_{24}N_2$ [M^+] 244.1941, found 244.1946.

(*S*)-1-Propyl-2-[(1,2,3,4-tetrahydroisoquinolinyl)methyl]pyrrolidine (23): $[\alpha]_D^{25}$ = −86.2° (*c* 2.1, EtOH); b.p. 190 °C/0.02 mm Hg; ^{1}H NMR ($CDCl_3$): δ = 0.91 (t, 3H, J = 7.3 Hz), 1.44–1.60 (m, 3H), 1.61–1.86 (m, 3H), 1.92–2.04 (m, 1H), 2.08–2.27 (m, 2H), 2.43 (dd, 1H, J = 7.9, 11.6 Hz), 2.52–2.90 (m, 6H), 3.13–3.19 (m, 1H), 3.64 (m, 2H), 6.99–7.14 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 12.1, 22.2, 22.7, 29.1, 30.5, 51.6, 54.5, 56.9, 57.8, 62.3, 63.8, 125.4, 125.9, 126.5, 128.6, 134.4, 135.1; HRMS calcd for $C_{17}H_{26}N_2$ [M^+] 258.2094, found 258.2091.

(*S*)-1-Methyl-2-[(perhydroisoindolinyl)methyl]pyrrolidine (24): $[\alpha]_D^{26}$ = −61.3° (*c* 1.1, EtOH); b.p. 155 °C/0.6 mm Hg; ^{1}H NMR ($CDCl_3$): δ = 1.30–1.37 (m, 1H), 1.43–1.61 (m, 8H), 1.63–1.84 (m, 2H), 1.90–2.08 (m, 1H), 2.10–2.27 (m, 4H), 2.38–2.42 (m, 3H), 2.43–2.53 (m, 3H), 2.70–2.77 (m, 3H), 3.00–3.07 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 22.4, 22.7, 22.9, 26.85, 26.92, 30.6, 37.0, 41.4, 57.7, 58.9, 59.3, 62.6, 64.8; HRMS calcd for $C_{14}H_{26}N_2$ [M^+] 222.2098, found 222.2103.

(*S*)-1-Methyl-2-[(1-benz[*cd*]indolinyl)methyl]pyrrolidine (25): $[\alpha]_D^{28}$ = −59.6 (*c* 3.0, EtOH); b.p. 236 °C/0.1 mm Hg (bath temp); ^{1}H NMR ($CDCl_3$): δ = 1.60–1.87 (m, 3H), 1.89–2.02 (m, 1H), 2.15–2.26 (m, 1H), 2.41–2.54 (m, 4H), 3.07 (dd, 1H, J = 6.8, 8.4 Hz), 3.27 (dd, 1H, J = 6.9, 14.1 Hz), 3.53 (dd, 1H, J = 4.6, 14.2 Hz), 4.80 (m, 2H), 6.15 (d, 1H, J = 7.3 Hz), 6.85 (d, 1H, J = 8.3 Hz), 7.08 (d, 1H, J = 6.9 Hz), 7.19–7.24 (m, 1H), 7.32–7.37 (m, 1H), 7.45 (d, 1H, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$): δ = 22.3, 29.9, 41.2, 51.4, 57.6, 58.6, 64.8, 95.7, 110.9, 115.4, 122.1, 127.7, 129.8, 130.8, 132.0, 139.1, 152.8; HRMS calcd for $C_{17}H_{20}N_2$ [M^+] 252.1628, found 252.1631.

General Procedure for the Asymmetric Aldol Reaction: A typical experimental procedure is described for the reaction of **1** with benzaldehyde. Chiral diamine **6** or **10** (0.48 mmol) in dichloromethane (0.5 mL) and dibutyltin diacetate (0.44 mmol) were added successively at room temperature to a suspension of tin(II) triflate (0.4 mmol) in dichloromethane (0.5 mL). The mixture was then cooled to −78 °C and dichloromethane solutions (0.5 mL each) of **1** (0.4 mmol) and benzaldehyde (0.27 mmol) were successively added. The mixture was stirred for 21 h, and saturated $NaHCO_3$ was added to quench the reaction. After the standard workup, the crude product was chromatographed on silica gel to give *S*-ethyl 2-(*tert*-butyldimethylsiloxy)-3-hydroxy-3-phenylpropanethioate. The diastereomers were separated and the optical purity was determined by HPLC using a chiral column.

***S*-Ethyl (2*S*,3*R*)-2-(*tert*-butyldimethylsiloxy)-3-hydroxy-3-phenylpropanethioate:** IR (neat): $\tilde{\nu}$ = 3490, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = −0.42 (s, 3H), 0.03 (s, 3H), 0.95 (s, 9H), 1.29 (t, 3H, J = 7.4 Hz), 2.93 (q, 2H, J = 7.4 Hz), 3.08 (d, 1H, J = 8.6 Hz), 4.34 (d, 1H, J = 2.7 Hz), 5.16 (dd, 1H, J = 2.7, 8.6 Hz), 7.28–7.43 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = −5.68, 14.41, 18.06, 22.79, 25.73, 75.26, 82.34, 126.11, 127.67, 128.14, 140.45, 203.38; anal. calcd for $C_{17}H_{28}O_3SSi$: C 59.96, H 8.29, S 9.42; found: C 59.89, H 8.36, S 9.73; HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 50/1, flow rate = 1.0 mL min^{-1}): t_R = 7.6 min (2*S*,3*R*), t_R = 9.4 min (2*R*,3*S*).

***S*-Ethyl (2*S*,3*R*)-2-(*tert*-butyldimethylsiloxy)-3-hydroxypentanethioate**: IR (neat): $\tilde{\nu}$ = 3510, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.10 (s, 3H), 0.14 (s, 3H), 0.97 (s, 9H), 0.99 (t, 3H, J = 7.3 Hz), 1.24 (t, 3H, J = 7.4 Hz), 1.29–1.64 (m, 2H), 2.23 (d, 1H, J = 9.2 Hz), 2.85 (q, 2H, J = 7.4 Hz), 3.48–3.66 (m, 1H), 4.12 (d, 1H, J = 3.6 Hz); ^{13}C NMR ($CDCl_3$): δ = −5.01, −4.82, 10.28, 14.46, 18.12, 22.60, 25.81, 26.23, 75.48, 80.31, 204.82; anal. calcd for $C_{13}H_{28}O_3SSi$: C 53.38, H 9.65, S 10.96; found: C 53.12, H 9.73, S 10.81; HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL min^{-1}): t_R = 4.4 min (2*R*,3*S*), t_R = 4.8 min (2*S*,3*R*).

***S*-Ethyl (2*S*,3*R*)-2-(*tert*-butyldimethylsiloxy)-3-hydroxydecanethioate**: IR (neat): $\tilde{\nu}$ = 3500, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.08 (s, 3H), 0.13 (s, 3H), 0.85 (t, 3H, J = 7.3 Hz), 0.96 (s, 9H), 1.19–1.40 (m, 13H), 1.40–1.48 (m, 2H), 2.31 (brs, 1H), 2.83 (q, 2H, J = 7.4 Hz), 3.48–3.84 (m, 1H), 4.10 (d, 1H, J = 3.2 Hz); ^{13}C NMR ($CDCl_3$): δ = −4.90, 14.04, 14.43, 18.08, 22.57, 25.72, 29.15, 29.33, 31.72, 32.98, 73.87, 80.45, 204.74; anal. calcd for $C_{18}H_{38}O_3SSi$: C 59.62, H 10.56, S 8.84; found: C 59.45, H 10.61, S 8.68; HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 200/1, flow rate = 1.0 mL min^{-1}): t_R = 8.1 min (2*R*,3*S*), t_R = 28.6 min (2*S*,3*R*).

(*S*)-Ethyl (2*S*,3*R*,4*E*)-2-(*tert*-butyldimethylsiloxy)-3-hydroxy-4-hexenethioate: IR (neat): $\tilde{\nu}$ = 3500, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.08 (s, 3H), 0.13 (s, 3H), 0.96 (s, 9H), 1.23 (t, 3H, J = 7.4 Hz), 1.70 (ddd, 3H,

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J = 1.7, 2.3, 6.6 Hz), 2.55 (d, 1H, J = 9.3 Hz), 2.84 (q, 2H, J = 7.4 Hz), 4.13 (d, 1H, J = 3.5 Hz), 4.26–4.32 (m, 1H), 5.47 (ddd, 1H, J = 1.7, 5.6, 15.2 Hz), 5.74 (ddq, 1H, J = 1.3, 6.6, 15.2 Hz); ^{13}C NMR ($CDCl_3$): δ = −4.90, 14.45, 17.68, 18.17, 22.64, 25.72, 74.23, 80.77, 128.05, 129.52, 204.15; anal. calcd for $C_{14}H_{28}O_3SSi$: C 55.22, H 9.27, S 10.53; found: C 55.47, H 9.20, S 10.52; HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 50/1, flow rate = 1.0 mL min^{-1}): t_R = 5.8 min (2*R*,3*S*), t_R = 8.3 min (2*S*,3*R*).

(*S*)-Ethyl (2*S*,3*R*,4*E*)-2-(*tert*-butyldimethylsiloxy)-3-hydroxy-5-phenyl-4-pentenethioate: IR (neat): $\tilde{\nu}$ = 3480, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.04 (s, 3H), 0.11 (s, 3H), 0.93 (s, 9H), 1.17 (t, 3H, J = 7.4 Hz), 2.76 (d, 1H, J = 9.2 Hz), 2.81 (q, 2H, J = 7.4 Hz), 4.23 (d, 1H, J = 3.3 Hz), 4.47 (ddd, 1H, J = 1.3, 5.1, 9.2 Hz), 6.17 (dd, 1H, J = 5.1, 15.8 Hz), 6.62 (dd, 1H, J = 1.3, 15.8 Hz), 7.16–7.55 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = −4.94, −4.83, 14.41, 18.13, 22.68, 25.70, 25.79, 74.22, 80.45, 126.45, 127.62, 127.85, 128.50, 131.36, 136.44, 204.25; anal. calcd for $C_{19}H_{30}O_3SSi$: C 62.25, H 8.25, S 8.75; found: C 61.98, H 8.39, S 8.94; HPLC (Daicel Chiralcel AD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL min^{-1}): t_R = 15.0 min (2*R*,3*S*), t_R = 22.1 min (2*S*,3*R*).

(*S*)-Ethyl (2*S*,3*R*,4*E*)-2-(*tert*-butyldimethylsiloxy)-3-hydroxy-5-tributylstannyl-4-pentenethioate: IR (neat): $\tilde{\nu}$ = 3500, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.08 (s, 3H), 0.14 (s, 3H), 0.84–0.90 (m, 12H), 0.96 (s, 9H), 1.20–1.36 (m, 12H), 1.42–1.53 (m, 6H), 2.74 (d, 1H, J = 9.8 Hz), 1.25 (t, 3H, J = 7.4 Hz), 2.83 (q, 2H, J = 7.4 Hz), 4.22 (d, 1H, J = 3.0 Hz), 4.27 (ddd, 1H, J = 3.0, 4.3, 9.8 Hz), 6.02 (dd, 1H, J = 4.3, 11.3 Hz), 6.28 (d, 1H, J = 11.3 Hz); anal. calcd for $C_{25}H_{52}O_3SSiSn$: C 51.81, H 9.04, S 5.53; found: C 52.07, H 9.30, S 5.38; HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 300/1, flow rate = 1.0 mL min^{-1}): t_R = 4.5 min (2*R*,3*S*), t_R = 5.8 min (2*S*,3*R*).

(*S*)-Ethyl (2*S*,3*S*)-2-(*tert*-butyldimethylsiloxy)-3-(2-furyl)-3-hydroxypropanethioate: IR (neat): $\tilde{\nu}$ = 3490, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = −0.20 (s, 3H), 0.10 (s, 3H), 0.91 (s, 9H), 1.25 (t, 3H, J = 7.4 Hz), 2.88 (q, 2H, J = 7.4 Hz), 3.01 (d, 1H, J = 10.2 Hz), 4.49 (d, 1H, J = 2.6 Hz), 4.91 (d, 1H, J = 10.2 Hz), 6.30–6.35 (m, 2H), 7.36 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = −5.65, 14.36, 18.03, 22.81, 25.63, 70.64, 79.52, 107.44, 110.42, 141.80, 153.23, 203.18; anal. calcd for $C_{15}H_{26}O_4SSi$: C 54.51, H 7.93, S 9.70; found: C 54.38, H 8.01, S 9.96; HPLC (Daicel Chiralcel AD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL min^{-1}): t_R = 9.6 min (2*S*,3*S*), t_R = 11.0 min (2*R*,3*R*).

(*S*)-Ethyl (2*S*,3*R*,4*E*,6*E*)-2-(*tert*-butyldimethylsiloxy)-3-hydroxy-4,6-octadienethioate:[13b] A small amount of geometrical isomer derived from the starting aldehyde was not separated. IR (neat): $\tilde{\nu}$ = 3400, 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.06 (s, 3H), 0.12 (s, 3H), 0.95 (s, 9H), 1.21 (t, 3H, J = 7.4 Hz), 1.73 (d, 3H, J = 6.3 Hz), 2.63 (brs, 1H), 2.83 (q, 2H, J = 7.4 Hz), 4.14 (d, 1H, J = 3.6 Hz), 4.33 (brs, 1H), 5.51–6.23 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = −4.87, 14.40, 18.10, 22.61, 25.68, 74.00, 80.56, 128.30, 130.28, 130.50, 132.00, 204.13; HPLC (Daicel Chiralcel AD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL min^{-1}): t_R = 6.9 min (minor enantiomer (2*R*,3*S*) of geometrical isomer), t_R = 7.8 min (2*R*,3*S*), t_R = 19.5 min (major enantiomer (2*S*,3*R*) of geometrical isomer), t_R = 24.6 min (2*S*,3*R*).

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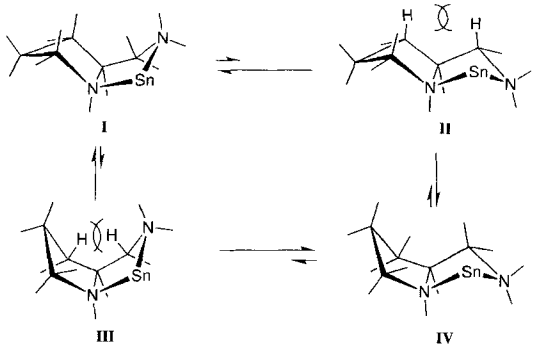
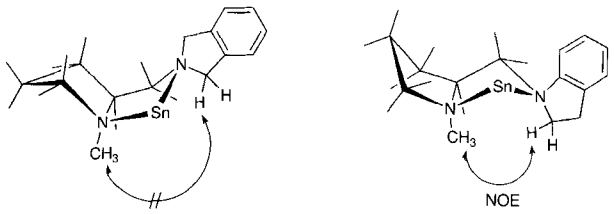


[24] We carried out NOE experiments on the chiral tin(II) Lewis acids. NOE between the *N*-methyl protons and the methylene protons of the right part of the chiral diamine was observed in the $Sn(OTf)_2$–**5**–$Bu_2Sn(OAc)_2$ complex, while no obvious NOE data was obtained in the $Sn(OTf)_2$–**4**–$Bu_2Sn(OAc)_2$ complex after several trials at various temperatures and in various solvents. (The NOE experiments were carried out in CD_3CN at 20 °C. In CD_2Cl_2 sufficient well-resolved NMR spectra were not obtained, probably due to the insolubility of the tin(II) complex and fast equilibrium. We confirmed that similar high selectivities were obtained in CH_3CN at −40 °C or in C_2H_5CN at −78 °C.)



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