Diastereo- and Enantioselective Synthesis of *syn*- and *anti*-1,2-Diol Units by Asymmetric Aldol Reactions

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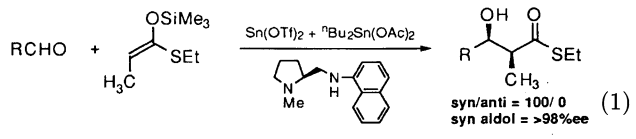
syn- and *anti*-1,2-Diol units were prepared by using asymmetric aldol reactions of the silyl enol ethers derived from α-alkoxythioacetic *S*-esters with aldehydes. In the presence of tin(II) triflate, a chiral diamine, and dibutyltin diacetate, (*Z*)-2-benzyloxy-1-ethylthino-1-(trimethylsiloxy)ethene reacted with aldehydes to afford the corresponding *anti*-aldol adducts in high yields with excellent diastereo- and enantioselectivities, while *syn*-adducts were obtained from (*Z*)-2-(*t*-butyldimethylsiloxy)-1-ethylthio-1-(trimethylsiloxy)ethene and aldehydes under the same reaction conditions. Thus, both diastereomers can be synthesized in excellent enantiomeric excesses by simply choosing the protective groups of the alkoxyl parts of the silyl enol ethers.

Optically active 1,2-diol units are widely distributed in nature as compounds such as macrolides, polyether antibiotics and carbohydrates, etc.[1] Recently, several asymmetric oxidation reactions of olefins using osmium tetraoxide with a chiral ligand have been developed and some optically active *syn*-1,2-diols have been prepared in high enantiomeric excesses.[2] However, in these syntheses, basis carbon skeletons must be constructed before the asymmetric oxidations, and preparation of optically active *anti*-1,2-diols still remains as a challenging topic.[3]

In this paper, we disclose the full details of an alternative approach to the synthesis of *syn*- and *anti*-1,2-diol units by using the aymmetric aldol reactions of the silyl enol ether of α-alkoxyacetic acid thioesters with aldehydes.[4]

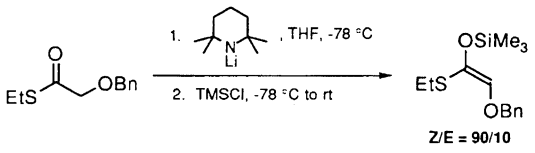
We have recently shown that the asymmetric aldol reactions between both achiral silyl enol ethers of thioesters and aldehydes are performed with almost perfect diastereo- and enantioselectivities by using a novel chiral promoter consisting of tin(II) triflate, a chiral diamine, and tributyltin fluoride or dibutyltin diacetate (Eq. 1).[5—9]



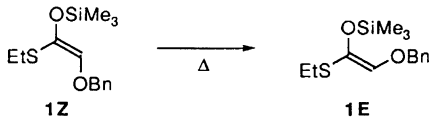
(1)

This asymmetric reaction was applied to the reaction of the silyl enol ether derived from α-benzyloxy thioester with aldehydes in order to introduce two hydroxyl groups simultaneously accompanied by stereoselective carbon–carbon bond formation.[10]

Synthesis of *anti*-α,β-Dihydroxy Thioester Derivatives. 2-Benzyloxy-1-ethylthio-1-(trimethylsiloxy)ethene (**1**) was prepared from *S*-ethyl 2-benzyloxyethanethioate by using lithium 2,2,6,6-tetramethylpiperidide followed by trapping with trimethylsilyl chloride (TMSCl) (Eq. 2). (*Z*)-Enol ether **1Z** was predominantly formed under kinetic conditions, and **1Z** was found to be isomerized rapidly to (*E*)-enol ether **1E** under thermal conditions (Eq. 3).



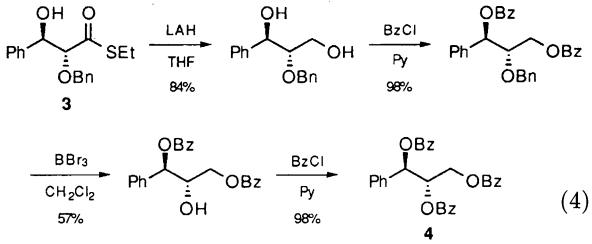
(2)



(3)

The reaction of benzaldehyde with **1** was carried out in dichloromethane by using a chiral promoter consisting of tin(II) triflate, (*S*)-1-methyl-2-[(1-naphthylamino)methyl]pyrrolidine (**2**), and tributyltin fluoride. While **1E** sluggishly reacted with benzaldehyde, the reaction of **1Z** proceeded smoothly at −78 °C to afford the corresponding aldol adduct (**3**) in a 69% yield with *anti* preference (*syn*/*anti*=26/74). The enantiomeric excesses of the *syn*- and *anti*-adducts proved to be 30 and 97%, respectively. It is noteworthy that the *anti*-aldol adduct was predominantly obtained with excellent ee in this case, while *syn*-aldol adducts were obtained (*syn*/*anti*=100/0, *syn* aldol=>98%ee) in the case of asymmetric aldol reactions of the silyl enol ether of *S*-ethyl propanethioate with aldehydes (Eq. 1).[6—9]

Relative and absolute configurations were assigned by comparison of the optical rotation of benzoate **4** with that of the literature[11] after the following derivations (Eq. 4).



(4)

Next, several chiral diamined were examined in order to improve the diastereoselectivity. When (*S*)-1-methyl-2-[(1-piperidinyl)methyl]pyrrolidine (**5**) was employed, aldol adduct **3** was obtained in a 70% chemical yield with excellent diastereo- and enantioselectivity (*syn*/*anti*= 1/99, *anti*-aldol=97%ee). Furthermore, the chemical yield was improved without loosing the diastereoselectivities when dibutyltin diacetate was combined with tin(II) triflate and (*S*)-1-ethyl-2-[(1-piperidinyl)methyl]pyrrolidine (**6**) (Table 1).

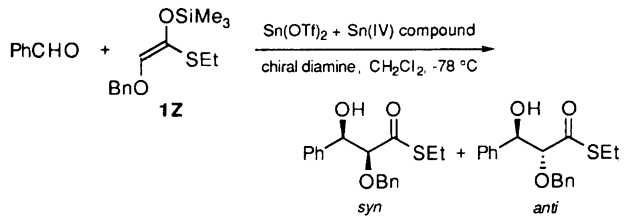
The results of the present asymmetric aldol reaction by using several aldehydes such as aromatic, aliphatic, α,β-unsaturated aldehydes, and a dienal, are shown in Table 2. In every case, *anti*-α,β-dihydroxy thioester derivatives were obtained in high yields with excellent diastereo- and enantioselectivities.

It is noted that the aldol adducts thus obtained, optically active *anti*-α,β-dihydroxy thioester derivatives, are generally difficult to prepare by conventional asymmetric oxidation,[3] and that the present asymmetric aldol reaction makes it possible to introduce two hydroxyl groups stereoselectively during new carbon–carbon bond formation.

Synthesis of *syn*-α,β-Dihydroxy Thioester Derivatives. The high *anti* selectivities attained in the reaction shown in the previous section were unexpected, because the *syn* selective aldol reactions of (*Z*)-1-ethylthio-1-(trimethylsiloxy)propene with aldehydes using the above chiral promoter had already been developed with almost perfect diastereo- and enantioselectivities (Eq. 1).[6–9] Consideration of the transition states of these enantioselective aldol reactions led us to assume that (i) the coordination of the oxygen atom of the α-benzyloxy group of silyl enol ether **1Z** to the tin(II) of tin(II) triflate was essential in the *anti*-selective transition state leading to the different course of the diastereofacial selectivily compared with that shown in Eq. 1, and (ii) thus the *syn*-α,β-dihydroxy thioester derivatives would be obtained when this coordination was restrained.

In order to prevent the coodination of the oxygen atom of the α-alkoxyl group in the silyl enol ether to tin(II), we prepared 2-(*t*-butyldimethylsiloxy)-1-ethylthio-1-(trimethylsiloxy)ethene (**17**), which has a *t*-butyldimethylsiloxy group instead of a benzyloxy group at the α-position (Eq. 5). In this case, (*Z*)-ethol ether **17Z** was also obtained under kinetic conditions. The isomerization of **17Z** to (*E*)-enol ether **17E** also occurred under thermal conditions, but was much slower than that of **1Z** to **1E** (Eq. 6).

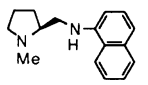
Table 1. Effect of Chiral Diamines



Chiral diamine	Sn(IV)	Yield/%	*syn*/*anti*	ee/%(*anti*)
2	F	69	26/74	97
5	F	70	1/99	97
6	F	54	1/99	99
7	F	54	1/99	99
8	F	38	1/99	97
2	OAc	80	21/79	91
5	OAc	74	1/99	96
6	OAc	96	1/99	96
7	OAc	91	1/99	97

Sn(IV) compound: F = ^{n}Bu$_3$SnF; OAc = ^{n}Bu$_2$Sn(OAc)$_2$

chiral diamine:



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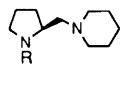
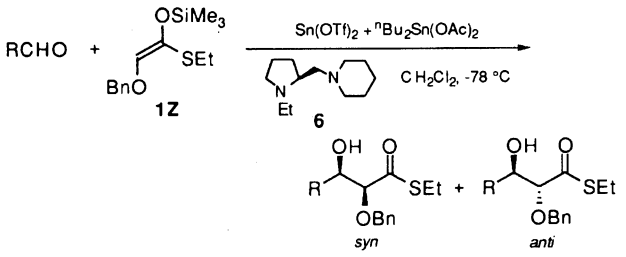
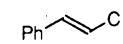
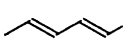


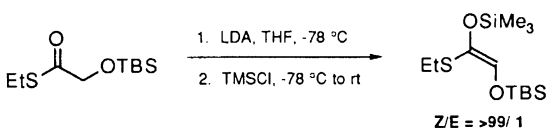
5 R = Me **7** R = Pr
6 R = Et **8** R = Pent

Table 2. Synthesis of *anti*-α,β-Dihydroxy Thioesters

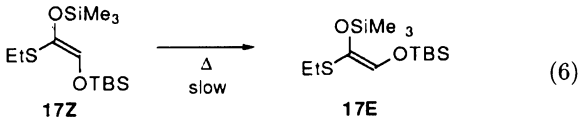


Aldehyde	Product	Yield/%	*syn*/*anti*	ee/%(*anti*)
PhCHO	**3**	96	1/99	96
	**9**	83	2/98	96
C_2H_5CHO	**10**	72	2/98	97
c-$C_6H_{11}CHO$ [a]	**11**	59	9/91	96
 [a]	**12**	67	1/99	97
 [a]	**13**	71	9/91	95
	**14**	85	2/98	97
	**15**	88	2/98	98
	**16**	90	2/98	95

a) Chiral diamine **5** was used instead of **6**.



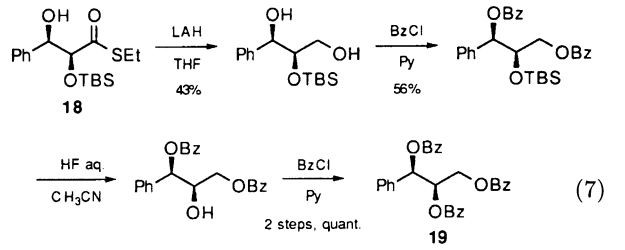
(5)



(6)

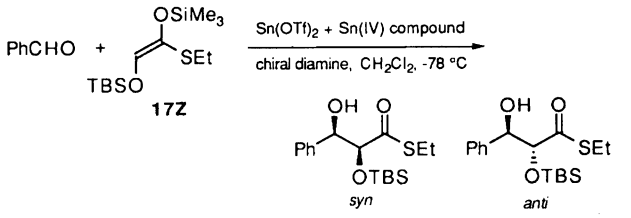
It was then found that **17Z** smoothly reacted with benzaldehyde in dichloromethane at −78 °C, in a mixture of tin(II) triflate, (*S*)-1-methyl-2-[(1-napthylamino)methyl]pyrrolidine (**2**), and dibutyltin diacetate, to afford the corresponding aldol adduct (**18**) in a 73% yield with *syn* preference (*syn*/*anti*=73/27). The enantiomeric excesses of the *syn*- and *anti*-aldol adducts were shown to be 94 and 83%, respectively. It is noteworthy that the *syn*-aldol adduct was preferentially produced as expected by using **17Z**. The diastereoselectivity was improved after examination of the effects of chiral diamines and tin(IV) compounds (Table 3). The best result was obtained (86% yield, *syn*/*anti*=88/12, *syn*-aldol=90%ee) when (*S*)-1-propyl-2-[(1-piperidinyl)-methyl]pyrrolidine (**7**) and dibutyltin diacetate were employed.

Relative and absolute configuration assignments were made by comparison of the optical rotation of benzoate **19** with that of the literature[11] after the following derivations.



(7)

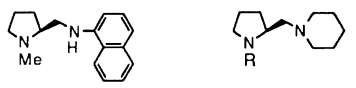
Table 3. Effect of Chiral Diamines



Chiral diamine	Sn(IV)	Yield/%	*syn*/*anti*	ee/%(*syn*)
2	F	56	70/30	90
5	F	81	86/14	49
2	OAc	73	73/27	94
5	OAc	83	91/9	49
6	OAc	83	86/14	90
7	OAc	86	88/12	90
8	OAc	63	83/17	89

Sn(IV) compound: F = $^{n}Bu_3SnF$; OAc = $^{n}Bu_2Sn(OAc)_2$

chiral diamine:



2 **5** R = Me **7** R = n-Pr
6 R = Et **8** R = n-C_5H_{11}

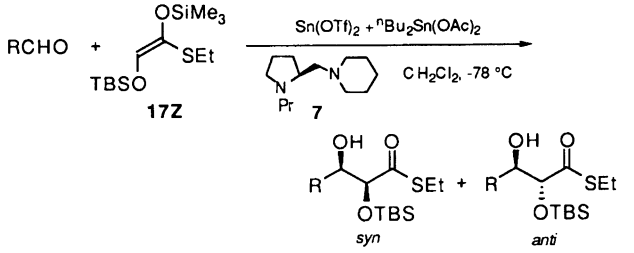
Other example are shown in Table 4, and in every case the *syn*-aldol adducts were obtained in good yields with high diastereo- and enantioselectivities.

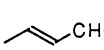
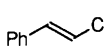
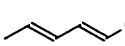
Transition States. The high selectivities attained in these aldol reactions can be explained by assuming the transition states shown in Fig. 1. In the reaction of (*Z*)-2-(*t*-butyldimethylsiloxy)-1-ethylthio-1-(trimethylsiloxy)ethene (**17Z**), the chiral tin(II) Lewis acid has a rigid bicycle structure and its conformation is highly controlled by mutual interaction between the pyrrolidinyl, piperidinyl, and trifluoromethanesulfonyl groups.[12] Thus, the *re* face of an approaching aldehyde is almost completely shielded and silyl enol ether **17Z** attacks this aldehyde via an acyclic transition state.[13] On the other hand, in the reaction of (*Z*)-2-benzyloxy-1-ethylthio-1-(trimethylsiloxy)ethene (**1Z**), preference is given to the coordination of the oxygen of the benzyloxy group to tin(II). The reaction would proceed via a five-membered cyclic transition state to give the *anti*-aldol adducts in high enantioselectivities.

In these reactions, the diastereoselectivities are controlled by the coordination ability of the oxygen of the α-alkoxyl parts of the silyl enol ethers to tin(II). When the oxygen can easily coordinate to tin(II), *anti*-aldols are obtained. On the other hand, when this coordination is sterically forbidden, *syn*-aldols are produced. These phenomena are useful in predicting the stereochemical course of the present asymmetric aldol reactions.

As expected, the *anti*-adduct was obtained with high selectivities in the reaction of 1-ethylthio-1-trimethyl-

Table 4. Synthesis of *syn*-α,β-Dihydroxy Thioesters



Aldehyde	Product	Yield/%	*syn*/*anti*	ee/%(*anti*)
PhCHO	**18**	86	88/12	90
	**20**	93	94/6	93
C_2H_5CHO	**21**	46	92/8	82
	**22**	75	97/3	94
	**23**	76	90/10	92
	**24**	73	93/7	94

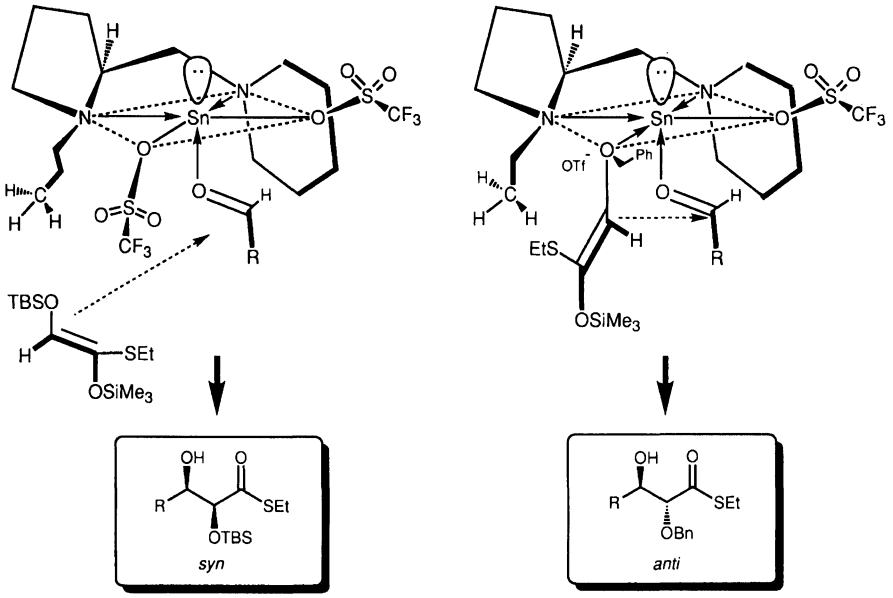
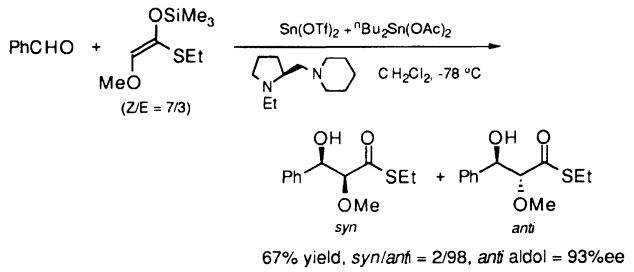


Fig. 1. Assumed transition states of the *syn*- and *anti*-selective asymmetric aldol reactions.

siloxy-2-methoxyethene with benzaldehyde (Eq. 8).



(8)

Conclusions. Both diastereomers of optically active α,β-dihydroxy thioester derivatives can be synthesized via the asymmetric aldol reactions of the silyl enol ethers derived from the α-alkoxyacetic acid thioesters with aldehydes by simply choosing the protective groups of the alkoxyl parts of the silyl enol ethers. Since D-proline is available, four possible stereoisomers of α,β-dihydroxy thioester derivatives would be prepared. Yields and selectivities in both *syn*- and *anti*-selective aldol reactions are very high in almost every case. According to these reactions, optically active 1,2-diol units can be prepared during construction of the desired carbon skeltons (carbon–carbon bond formation).

Experimental

General. IR spectra were recorded on a Horiba FT-300 infrared spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on 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_2O_5, then CaH_2, and dried over MS4A.

Tin(II) trifluoromethanesulfonate (tin(II) triflate)[15,16] and chiral diamines[9,16,17] were prepared according to the literatures. All handlings of tin(II) triflate were carried out under argon atmosphere. Benzyloxyacetyl chloride was purchased from Aldrich Chemical Co., Inc., and used without further purification.

***S*-Ethyl Benzyloxyethanethioate.** To a mixture of benzyloxyacetyl chloride (5.0 g, 27 mmol) and ethanethiol (2.2 mL, 30 mmol) in dichloromethane (14 mL) was added pyridine (7.0 mL, 32 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 10 h, and then concentrated in vacuo. Water was added to the residue, and the aqueous layer was extracted with diethyl ether. The combined organic layer was washed with brine, and dried over $MgSO_4$. After evaporation of the solvents, the crude product was purified by distillation (110 °C/0.8 mmHg) (1 mmHg=133.322 Pa) to afford 4.3 g (76%) of *S*-ethyl benzyloxyethanethioate as a colorless oil: IR (neat) 1750 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.25 (t, 3H, J=7.0 Hz), 2.85 (q, 2H, J=7.0 Hz), 4.05 (s, 2H), 4.55 (s, 2H), 7.30 (m, 5H).

(*Z*-2-Benzyloxy-1-ethylthio-1-(trimethylsiloxy)-ethene (1Z). To diisopropylamine (557 mg, 5.50 mmol) in tetrahydrofuran (THF, 20 mL) was added 1.65 M hexane solution (1 M=1 mol dm^{-3}) of butyllithium (3.33 ml, 5.50 mmol) at 0 °C. The reaction mixture was stirred for 10 min at 0 °C, and then cooled to −78 °C. To this LDA (lithium diisopropylamide) solution were added *S*-ethyl benzyloxyethanethioate (1.06 g, 5 mmol) in THF (10 mL) and chlorotrimethylsilane (598 mg, 5.50 mmol) in THF (5 mL), respectively. The reaction mixture was warmed to room temperature, and then was concentrated in vacuo. Petroleum ether (20 mL) was added to the residue, and the suspension was filtered through a celite pad under argon atmosphere. The

filtrate was then concentrated in vacuo to afford 1.33 g (94%) of a geometrical isomeric mixture of 2-benzyloxy-1-ethylthio-1-(trimethylsiloxy)ethene (**1Z/1E**=90/10). The crude product was used without further purification, because the (*E*)-isomer has no reactivity in the present asymmetric aldol reaction. The silyl enol ether was stored in refrigerator (see, text). (*Z*)-2-Benzyloxy-1-ethylthio-1-(trimethylsiloxy)ethene: ^{1}H NMR ($CDCl_3$) δ=0.16 (s, 9H), 1.24 (t, 3H, J=7.3 Hz), 2.69 (q, 2H, J=7.3 Hz), 4.78 (s, 2H), 6.25 (s, 1H), 7.26—7.53 (m, 5H); ^{13}C NMR ($CDCl_3$) δ=−0.12, 14.94, 25.06, 73.84, 127.53, 127.66, 127.84, 128.18, 128.32, 132.85, 136.84, 137.09. (*E*)-2-Benzyloxy-1-ethylthio-1-(trimethylsiloxy)ethene: ^{1}H NMR ($CDCl_3$) δ=0.22 (d, 9H), 1.20 (t, 3H, J=7.4 Hz), 2.57 (q, 2H, J=7.4 Hz), 4.78 (s, 2H), 6.04 (s, 1H), 7.26—7.53 (m, 5H); ^{13}C NMR ($CDCl_3$) δ=0.30, 14.33, 25.90, 73.77, 127.53, 127.66, 127.84, 128.18, 128.32, 132.85, 135.24, 137.11.

A Typical Procedure of the *anti*-Selective Asymmetric Aldol Reaction. A typical experimental procedure is described for the reaction of **1Z** with benzaldehyde: To a solution of tin(II) triflate (0.4 mmol) and (*S*)-1-ethyl-2-[(1-piperidinyl)methyl]pyrrolidine (**6**, 0.48 mmol) in dichloromethane (1 mL) was added dibutyltin diacetate (0.44 mmol) at room temperature. The mixture was stirred for 30 min and then cooled to −78 °C. Dichloromethane solutions (0.5 mL each) of **1Z** (0.4 mmol) and benzaldehyde (0.27 mmol) were successively added. The reaction mixture was stirred for an additional 20 h, and then quenched with saturated $NaHCO_3$. After a usual work up, *S*-ethyl 2,3-dihydroxy-3-pheylpropanethioate (**3**) was obtained in an 96% yield (*syn*/*anti*=1/99, *anti*-aldol=96%ee). The diastereomer ratio was determined by ^{1}H NMR and the optical purity was determined by HPLC analysis using a chiral column.

***S*-Ethyl (2*R*,3*R*-2-Benzyloxy-3-hydroxy-3-phenylpropanethioate (3):** (96%ee) The diastereomers were not separated in the aldol form. IR (neat) 3450, 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.22 (d, 3H, J=7.6 Hz), 2.85 (q, 2H, J=7.6 Hz), 3.19 (d, 1H, J=3.6 Hz), 4.02 (d, 1H, J=6.9 Hz), 4.20 (d, 1H, J=11.2 Hz), 4.59 (d, 1H, J=11.2 Hz), 4.87 (dd, 1H, J=3.6, 6.9 Hz), 7.11—7.42 (m, 5H); ^{13}C NMR ($CDCl_3$) δ=14.41, 22.66, 74.23, 74.93, 87.17, 127.24, 128.03, 128.27, 128.30, 128.36, 128.43, 136.53, 139.32, 203.00. Anal. Calcd for $C_{18}H_{20}O_3S$: C, 68.33; H, 6.37; S, 10.13. Found: C, 67.84; H, 6.37; S, 10.07. Optical purity was determined after derivation to the corresponding acetate. *S*-Ethyl (2*R*,3*R*)-3-acetoxy-2-benzyloxy-3-phenylpropanethioate: $[\alpha]_D^{31}$ +44.13° (*c* 1.88, PhH); ^{1}H NMR ($CDCl_3$) δ=1.22 (t, 3H, J=7.3 Hz), 1.54 (s, 3H), 2.82 (q, 2H, J=7.3 Hz), 4.25 (d, 1H, J=5.8 Hz), 4.42 (d, 1H, J=11.9 Hz), 4.76 (d, 1H, J=11.9 Hz), 6.02 (d, 1H, J=5.8 Hz), 7.17—7.36 (m, 5H); HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 19/1, flow rate = 0.8 mL min^{-1}): t_R=8.5 min (minor enantiomer), t_R=11.0 min (major enantiomer).

***S*-Ethyl (2*R*,3*S*)-2-Benzyloxy-(2-furyl)-3-hydroxypropanethioate (9):** (96%ee) $[\alpha]_D^{26}$ +79.2° (*c* 2.35, PhH); IR (neat) 3475, 1680 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.20 (t, 3H, J=7 Hz), 2.75 (q, 2H, J=7 Hz), 2.80 (br s, 1H), 4.10 (d, 1H, J=6 Hz), 4.30 (d, 1H, J=11 Hz), 4.65 (d, 1H, J=11 Hz), 4.80 (d, 1H, J=6 Hz), 6.20 (m, 1H), 7.20 (m, 2H). Anal. Calcd for $C_{16}H_{18}O_4S$: C, 62.72; H, 5.92; S, 10.47%. Found: C, 62.56; H, 6.04; S, 10.28%. HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH=19/1, flow rate=0.8 mL min^{-1}): t_R=20.0 min (minor enantiomer), t_R=31.5 min (major enantiomer).

***S*-Ethyl (2*R*,3*R*)-2-Benzyloxy-3-hydroxypentanethioate (10):** (97%ee) $[\alpha]_D^{27}$ +89.4° (*c* 2.51, PhH); IR (neat) 3450, 1675 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.70—1.70 (m, 5H), 1.25 (t, 3H, J=7 Hz), 2.15 (br s, 1H), 2.85 (q, 2H, J=7 Hz), 3.45—3.80 (m, 1H), 3.80 (d, 1H, J=5 Hz), 4.40 (d, 1H, J=11 Hz), 4.80 (d, 1H, J=11 Hz), 7.25 (m, 5H). Anal. Calcd for $C_{14}H_{20}O_3S$: C, 62.66; H, 7.51; S, 11.95%. Found: C, 62.52; H, 7.63; S, 11.95%. HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH=200/1, flow rate=1.0 mL min^{-1}): t_R=46.9 min (minor enatiomer), t_R=52.4 min (major enantiomer).

***S*-Ethyl (2*R*,3*R*)-2-Benzyloxy-3-cyclohexyl-3-hydroxypropanethioate (11):** (96%ee) The diastereomers were not separated in the aldol form. IR (neat) 3480, 1680 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.65—2.00 (m, 11H), 1.25 (t, 3H, J=7 Hz), 2.20 (br s, 1H), 2.85 (q, 2H, J=7 Hz), 3.30—3.65 (m, 1H), 3.80 (d, 1H, J=6 Hz), 4.35 (d, 1H, J=11 Hz), 4.75 (d, 1H, J=11 Hz), 7.25 (m, 5H). Anal. Calcd for $C_{18}H_{26}O_3S$: C, 67.04; H, 8.13; S, 9.94%. Found: C, 66.99; H, 8.28; S, 9.99%. Optical purity was determined after derivation to the corresponding acetate. *S*-Ethyl (2*R*,3*R*)-3-acetoxy-2-benzyloxy-3-cyclohexylpropanethioate: $[\alpha]_D^{25}$ +69.8° (*c* 2.17, PhH); ^{1}H NMR (CCl_4) δ=0.65—2.00 (m, 11H), 1.25 (t, 3H, J=7 Hz), 1.90 (s, 3H), 2.80 (q, 2H, J=7 Hz), 3.90 (q, 2H, J=6 Hz), 4.35 (d, 1H, J=11 Hz), 4.75 (d, 1H, J=11 Hz), 4.95 (d, 1H, J=6 Hz), 7.25 (m, 5H); HPLC (Daicel Chiralcel OJ, hexane/*i*-PrOH=200/1, flow rate=1.0 mL min^{-1}): t_R=12.9 min (major enantiomer), t_R=17.6 min (minor enantiomer).

***S*-Ethyl (2*R*,3*R*)-2-Benzyloxy-3-hydroxy-4-pentenethioate (12):** (97%ee) $[\alpha]_D^{27}$ +86.3° (*c* 1.44, PhH); IR (neat) 3450, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.24 (t, 3H, J=7.5 Hz), 1.70 (dd, 3H, J=1.6, 6.2 Hz), 2.45 (br s, 1H), 2.87 (q, 2H, J=7.5 Hz), 4.00 (d, 1H, J=5.0 Hz), 4.32 (m, 1H), 4.53 (d, 1H, J=11.6 Hz), 4.84 (d, 1H, J=11.6 Hz), 5.24 (ddq, 1H, J=1.6, 5.3, 15.8 Hz), 5.72 (dq, 1H, J=6.2, 15.8 Hz), 7.26—7.47 (m, 5H). Anal. Calcd for $C_{14}H_{18}O_3S$: C, 63.13; H, 6.81; S, 12.04%. Found: C, 62.94; H, 6.85; S, 11.96%. HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH=19/1, flow rate=0.8 mL min^{-1}): t_R=13.2 min (minor enantiomer), t_R=16.6 min (major enantiomer).

***S*-Ethyl (2*R*,3*R*)-2-Benzyloxy-3-hydroxy-4-methyl-4-pentenethioate (13):** (95%ee) $[\alpha]_D^{29}$ +71.2° (*c* 1.07, PhH); IR (neat) 3400, 1675 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.20 (t, 3H, J=7 Hz), 1.75 (d, 3H, J=5 Hz), 2.45 (br s, 1H), 2.80 (q, 2H, J=7 Hz), 3.85 (d, 1H, J=5 Hz), 4.25 (m, 1H), 4.45 (d, 1H, J=11 Hz), 4.75 (d, 1H, J=11 Hz), 7.25 (m, 5H). Anal. Calcd for $C_{15}H_{20}O_3S$: C, 64.26; H, 7.19; S, 11.44%. Found: C, 64.01; H, 7.34; S, 11.21%. HPLC (Daicel Chiralcel OJ, hexane/*i*-PrOH=40/1, flow rate=1.0 mL min^{-1}): t_R=21.4 min (minor enantiomer), t_R=23.9 min (major enantiomer).

***S*-Ethyl (2*R*,3*R*,4*E*)-2-Benzyloxy-3-hydroxy-4-hexenethioate (14):** (97%ee) $[\alpha]_D^{27}$ +73.1° (*c* 1.07, PhH); IR (neat) 3400, 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.24 (t, 3H, J=7.5 Hz), 1.70 (dd, 3H, J=1.6, 6.2 Hz), 2.45 (br s, 1H), 2.87 (q, 2H, J=7.5 Hz), 4.00 (d, 1H, J=5.0 Hz), 4.32 (m, 1H), 4.53 (d, 1H, J=11.6 Hz), 4.84 (d, 1H, J=11.6 Hz), 5.24 (ddq, 1H, J=1.6, 5.3, 15.8 Hz), 5.72 (dq, 1H, J=6.2, 15.8 Hz), 7.26—7.47 (m, 5H). Calcd for $C_{15}H_{20}O_3S$; C, 64.26; H, 7.19; S, 11.44%. Found: C, 64.23; H, 7.40; S, 11.43%. HPLC

(Daicel Chiralcel OD, hexane/*i*-PrOH=19/1, flow rate=0.8 mL min^{-1}): t_R=13.3 min (minor enantiomer), t_R=17.8 min (major enantiomer).

***S*-Ethyl (2*R*,3*R*,4*E*)-2-Benzyloxy-3-hydroxy-5-phenyl-4-pentenethioate (15):** (98%ee) $[\alpha]_D^{27}$ +107.6° (*c* 1.80, PhH); IR (neat) 3425, 1680 cm^{-1}; ^1H NMR (CCl_4) δ=1.15 (t, 3H, *J*=7 Hz), 2.30 (br s, 1H), 2.75 (q, 2H, *J*=7 Hz), 3.90 (d, 1H, *J*=5 Hz), 4.20—4.50 (m, 1H), 4.40 (d, 1H, *J*=11 Hz), 4.75 (d, 1H, *J*=11 Hz), 6.00 (dd, 1H, *J*=6, 16 Hz), 6.50 (d, 1H, *J*=16 Hz), 7.00—7.40 (m, 10H). Anal. Calcd for $C_{20}H_{22}O_3S$; C, 70.15; H, 6.48; S, 9.36%. Found: C, 70.13; H, 6.51; S, 9.31%. HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH=19/1, flow rate=0.8 mL min^{-1}): t_R=26.4 min (minor enantiomer), t_R=39.3 min (major enantiomer).

***S*-Ethyl (2*R*,3*R*,4*E*,6*E*)-2-Benzyloxy-3-hydroxy-4,6-octadienethioate (16):** (95%ee) A small amount of regioisomer derived from the starting aldehyde was not separated. IR (neat) 3400, 1675 cm^{-1}; ^1H NMR (CCl_4) δ=1.20 (t, 3H, *J*=7 Hz), 1.75 (d, 3H, *J*=5 Hz), 2.45 (br s, 1H), 2.80 (q, 2H, *J*=7 Hz), 3.85 (d, 1H, *J*=5 Hz), 4.25 (m, 1H), 4.45 (d, 1H, *J*=11 Hz), 4.75 (d, 1H, *J*=11 Hz), 7.25 (m, 5H). Anal Calcd for $C_{17}H_{22}O_3S$: C, 66.64; H, 7.24; S, 10.46%. Found: C, 66.35; H, 7.31; S, 10.20%. HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH=19/1, flow rate=0.8 mL min^{-1}): t_R=10.4 min (minor enantiomer of regioisomer), t_R=11.4 min (minor enantiomer), t_R=12.2 min (major enantiomer of regioisomer), t_R=14.6 min (major enantiomer).

(1*R*,2*S*)-1-Phenyl-1,2,3-tris(benzoyloxy)propane (4). To a suspension of $LiAlH_4$ (109.4 mg, 2.88 mmol) in THF (5 mL) was slowly added *S*-ethyl (2*R*,3*R*)-2-benzyloxy-3-hydroxy-3-phenylpropanethioate (**3**) (338.7 mg, 1.07 mmol) in THF (2 mL) at 0 °C, and the reaction mixture was refluxed for 3 h. Saturated Na_2SO_4 was then added to the reaction mixture at 0 °C, and the organic materials were separated by filtration. After the organic layer was dried over Na_2SO_4, the solvents were removed in vacuo to afford 231.1 mg (84%) of (1*R*,2*S*)-2-benzyloxy-1-phenyl-1,3-propanediol. To (1*R*,2*S*)-2-benzyloxy-1-phenyl-1,3-propanediol (231.1 mg, 0.895 mmol) in pyridine (6.75 mL) was added benzoyl chloride (396.0 mg, 2.82 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 12 h. The reaction mixture was quenched with cold water and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with cold 1 M HCl, saturated $CuSO_4$, saturated $NaHCO_3$, and brine successively, and dried over Na_2SO_4. After evaporation of the solvents, the crude product was purified by silica-gel column chromatography to afford 409.2 mg (98%) of (1*R*,2*S*)-2-benzyloxy-1,3-bis(benzoyloxy)-1-phenylpropane as a solid: Mp 59—61 °C; $[\alpha]_D^{26}$ +33.6° (*c* 0.91, PhH); IR (KBr) 1720, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.22 (ddd, 1H, *J*=4.0, 5.6, 6.3 Hz), 4.49 (dd, 1H, *J*=6.3, 11.5 Hz), 4.59 (d, 1H, *J*=11.7 Hz), 4.61 (dd, 1H, *J*=4.0, 11.5 Hz), 4.66 (d, 1H, *J*=11.7 Hz), 6.29 (d, 1H, *J*=5.6 Hz), 7.16—7.60 (m, 16H), 7.95—8.00 (m, 2H), 8.08—8.12 (m, 2H). To (1*R*,2*S*)-2-benzyloxy-1,3-bis (benzoyloxy)-1-phenylpropane (45.9 mg, 0.098 mmol) in dichloromethane (1 mL) was added BBr_3 (0.01 mL, 0.106 mmol) at 0 °C. The reaction mixture was quenched with saturated $NaHCO_3$, and the aqueous layer was extracted with diethyl ether. The combined organic layer was washed with brine, dried over Na_2SO_4. After evaporation of the solvents, the residue was chromatographed on silica gel to afford 21.2 mg (57%) of (1*R*,2*S*)-1,3-bis(benzoyloxy)-2-hydroxy-1-phenylpropane. To (1*R*,2*S*)-1,3-bis(benzoyloxy)-1-phenyl-2-propanol (21.2 mg, 0.056 mmol) in pyridine (0.45 mL) was added benzoyl chloride (24.9 mg, 0.18 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 10 h. The reaction was quenched with cold water and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with cold 1 M HCl, saturated $CuSO_4$, saturated $NaHCO_3$, and brine successively, and dried over Na_2SO_4. After evaporation of the solvents, the crude product was purified by preparative TLC on silica gel to afford 26.5 mg (98%) of (1*R*,2*S*)-1-phenyl-1,2,3-tris(benzoyloxy)propane as a solid: Mp 145—146 °C; $[\alpha]_{546}^{25}$ +82.5° (*c* 0.89, PhH) (lit,[11] ((1*S*,2*R*-form) $[\alpha]_{546}$ −81° (*c* 2.00, PhH)); IR (KBr) 1715 cm^{-1}; ^1H NMR (CCl_4) δ=4.70 (d, 2H, *J*=5.0 Hz), 6.00 (t, 1H, *J*=5.0 Hz), 7.10—7.75 (m, 14H), 7.80—8.25 (m, 6H).

***S*-Ethyl (*t*-Butyldimethylsiloxy)ethanethioate: Method A:** To a mixture of hydroxyacetic acid (2.82 g, 37.1 mmol) and imidazole (12.6 g, 185 mmol) in *N*,*N*-dimethylformamide (DMF, 200 mL) was added *t*-butyldimethylchlorosilane (13.4 g, 88.8 mmol) at 0 °C. The mixture was warmed to room temperature and stirred for 10 h. The reaction was quenched with water, and the aqueous layer was extracted with diethyl ether. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo to afford 11.0 g (97%) of *t*-butyldimethylsilyl (*t*-butyldimethylsiloxy)acetate: ^1H NMR ($CDCl_3$) δ=0.09 (s, 6H), 0.27 (s, 6H), 0.91 (s, 9H), 0.92 (s, 9H), 4.14 (s, 2H). To a mixture of methanol (300 mL) and THF (100 mL) was added *t*-butyldimethylsilyl (*t*-butyldimethylsiloxy)acetate (11.0 g, 36.1 mmol), and the mixture was then treated with a solution of K_2CO_3 (10 g) in water (100 mL). The reaction mixture was stirred for 1 h at room temperature, and then concentrated in vacuo to one-quater volume. The resulting aqueous mixture was cooled to 0 °C and adjusted to pH 4—5 with 1.0 M solution of aqueous HCl. After the aqueous layer was extracted with diethyl ether, the combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo to afford 4.91 g (71%) of (*t*-butyldimethylsiloxy)acetic acid: ^1H NMR ($CDCl_3$) δ=0.13 (s, 6H), 0.92 (s, 9H), 4.24 (s, 2H), 8.45 (br s, 1H). To (*t*-butyldimethylsiloxy)acetic acid (3.00 g, 15.8 mmol) in dichloromethane (200 mL) was added thionyl chloride (11.5 mL, 158 mmol) at 0 °C. The mixture was gently refluxed for 10 min, and was stirred for 10 h at room temperature. The reaction mixture was evaporated to afford 3.30 g (100%) of (*t*-butyldimethylsiloxy)acetyl chloride. To a mixture of *t*-butyldimethylsiloxyacethylchloride (3.3 g, 15.8 mmol) and ethanethiol (1.29 mL, 19 mmol) in dichloromethane (90 mL) was added pyridine (1.5 g, 19 mmol) in dichloromethane (20 mL) at 0 °C. After stirred for 10 h at room temperature, the reaction was quenched with water, and then the aqueous layer was extracted with dichloromethane. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by distillation (80 °C/2 mmHg) to afford 2.91 g (78%) of *S*-ethyl 2-(*t*-butyldimethylsiloxy)ethanethioate as a colorless oil: IR (neat) 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.11 (s, 6H), 0.94 (s, 9H), 1.25 (t, 3H, *J*=7.3 Hz), 1.85 (q, 2H, *J*=7.3 Hz), 4.24 (s, 2H); ^{13}C NMR ($CDCl_3$) δ=−5.0, 14.5, 8.3, 22.1, 25.7, 68.9, 203.2.

Method B: To a mixture of ethyl hydroxyacetate (1.04 g, 10 mmol) and imidazole (0.82 g, 12 mmol) in DMF (10 mL) was added *t*-butyldimethylchlorosilane (1.81 g, 12 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 1 h. The reaction was then quenched with water, and the aqueous layer was extracted with diethyl ether. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo to afford 2.18 g (quant.) of ethyl *t*-butyldimethylsiloxyacetate. To ethyl (*t*-butyldimethylsiloxy)acetate (2.18 g, 10 mmol) in dichloromethane (10 mL) at −78 °C was added dimethylaluminum ethanethioate, which was prepared from 1 M hexane solution of trimethylaluminum (20 mL, 20 mmol) and ethanethiol (1.48 mL, 20 mmol) (−78 °C, and then 0 °C, 1 h).[18] The reaction mixture was warmed to room temperature and stirred for 1 h. The reaction mixture was quenched with phosphate buffer (pH=7) at 0 °C, and the mixture was filtered through a celite pad. After the aqueous layer was extracted with dichloromethane, the combined organic layer was washed with brine and dried over Na_2SO_4. After evaporation of the solvents, the crude product was purified by distillation to afford 1.92 g (82%) of *S*-ethyl (*t*-butyldimethylsioxy)ethanethioate.

(*Z*)-2-(*t*-Butyldimethylsiloxy)-1-ethylthio-1-(trimethylsiloxy)ethene (17Z). To diisopropylamine (600 mg, 5.93 mmol) in THF (20 mL) was added 1.65 M hexane solution of butyllithium in THF (3.59 mL, 5.93 mmol) at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and cooled to −78 °C. To this LDA solution, were added *S*-ethyl (*t*-butyldimethylsiloxy)ethanethioate (1.26 g, 5.38 mmol) in THF (10 mL) and chlorotrimethylsilane (644 mg, 5.93 mmol) in THF (5 mL), respectively. The reaction mixture was warmed to room temperature, and then was concentrated in vacuo. Petroleum ether (20 mL) was added to the residue, and the suspension was filtered through a celite pad under argon atmosphere. After the filtrate was then concentrated in vacuo, the residue was purified by bulb to bulb distillation (100 °C/0.2 mmHg) to give 1.32 g (80%) of pure (*Z*)-2-(*t*-butyldimethylsiloxy)-1-ethylthio-1-(trimethylsiloxy)ethene as a colorless oil (*Z*/*E*=100/0): ^{1}H NMR ($CDCl_3$) δ=0.13 (s, 6H), 0.21 (s, 9H), 0.93 (s, 9H), 1.24 (t, 3H, *J*=7.2 Hz), 2.69 (q, 2H, *J*=7.2 Hz), 6.42 (s, 1H); ^{13}C NMR ($CDCl_3$) δ=0.07, 15.15, 18.33, 25.00, 25.69, 131.44, 133.94.

A Typical Procedure of the *syn*-Selective Asymmetric Aldol Reaction. A typical experimental procedure is described for the reaction of **17Z** with benzaldehyde: To a suspension of tin(II) triflate (0.4 mmol) in dichloromethane (0.5 mL) were added (*S*)-1-propyl-2-[(1-piperidinyl)methyl]pyrrolidine (**7**, 0.48 mmol) in dichloromethane (0.5 mL) and dibutyltin diacetate (0.44 mmol) successively at room temperature. The mixture was stirred for 30 min at r.t. and then cooled to −78 °C. Dichloromethane solutions (0.5 mL each) of **17Z** (0.4 mol) and benzaldehyde (0.27 mmol) were successively added and the mixture was stirred for 20 h. Saturated $NaHCO_3$ was added to quench the reaction, and after a usual work up, *S*-ethyl 2-(*t*-butyldimethylsiloxy)-3-hydroxy-3-phenylpropanethioate (**18**) was obtained in an 86% yield (*syn*/*anti*=88/12, *syn* aldol=90%ee). The diastereomer ratio was determine by ^{1}H NMR and the optical purity was determined by HPLC using a chiral column.

***S*-Ethyl (2*S*,3*R*)-2-(*t*-Butyldimethylsiloxy)-3-hydroxy-3-phenylpropanethioate (18):** (90%ee) $[\alpha]_D^{27}$ −104.4 ° (*c* 1.78, PhH); IR (neat) 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 (major enantiomer), t_R=9.4 min (minor enantiomer).

***S*-Ethyl (2*S*,3*S*)-2-(*t*-Butyldimethylsiloxy)-3-(2-furyl)-3-hydroxypropanethioate (20):** (93%ee) $[\alpha]_D^{27}$ −120.8° (*c* 2.29, PhH); IR (neat) 3490, 1680 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.00 (s, 3H), 0.30 (s, 3H), 1.15 (s, 9H), 1.50 (t, 3H, *J*=7 Hz), 2.85 (br s, 1H), 3.05 (q, 2H, *J*=7 Hz), 4.65 (d, 1H, *J*=3 Hz), 4.90—5.30 (m, 1H), 6.45 (m, 2H), 7.50 (m, 1H). 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 Chiralpak AD, hexane/*i*-PrOH=100/1, flow rate=1.0 mL min^{-1}): t_R=9.6 min (major enantiomer), t_R=11.0 min (minor enantiomer).

***S*-Ethyl (2*S*,3*R*)-2-(*t*-Butyldimethylsiloxy)-3-hydroxypentanethioate (21):** (82%ee) $[\alpha]_D^{27}$ −64.8° (*c* 1.21, PhH); IR (neat) 3510, 1680 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.10 (s, 3H), 0.15 (s, 3H), 0.80—1.70 (m, 5H), 0.90 (s, 9H), 1.25 (t, 3H, *J*=7 Hz), 2.10 (d, 1H, *J*=9 Hz), 2.85 (q, 2H, *J*=9 Hz), 3.20—3.75 (m, 1H), 4.00 (d, 1H, *J*=4 Hz). 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 (minor enantiomer), t_R=4.8 min (major enantiomer).

***S*-Ethyl (2*S*,3*R*,4*E*)-2-(*t*-Butyldimethylsiloxy)-3-hydroxy-4-hexenethioate (22):** (94%ee) $[\alpha]_D^{27}$ −72.1° (*c* 1.65, PhH); IR (neat) 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, *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). 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 (minor enantiomer), t_R=8.3 min (major enantiomer).

***S*-Ethyl (2*S*,3*R*,4*E*)-2-(*t*-Butyldimethylsiloxy)-3-hydroxy-5-phenyl-4-pentenethioate (23):** (92%ee) $[\alpha]_D^{24}$ −148.9° (*c* 2.21, PhH); IR (neat) 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). 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 Chiralpak AD, hexane/*i*-PrOH=100/1, flow rate=1.0 mL min^{-1}): t_R=15.0 min (minor enantiomer), t_R=22.1 min (major enantiomer).

***S*-Ethyl (2*S*,3*R*,4*E*,6*E*)-2-(*t*-Butyldimethylsiloxy)-3-hydroxy-4,6-octadienethioate (24):** (94% ee) A small amount of regioisomer derived from the starting aldehyde was not separated. IR (neat) 3400, 1675 cm^{-1};

^{1}H NMR (CCl_4) δ=0.10 (s, 3H), 0.15 (s, 3H), 0.90 (s, 9H), 1.20 (t, 3H, J=7 Hz), 1.75 (d, 3H, J=6 Hz), 2.35 (br s, 1H), 2.80 (q, 2H, J=7 Hz), 4.05 (m, 2H), 5.15—6.35 (m, 4H). Anal. Calcd for $C_{16}H_{30}O_3SSi$: C, 58.14; H, 9.15; S, 9.70%. Found: C, 57.50; H, 9.17; S, 9.88%. HPLC (Daicel Chiralpak AD, hexane/i-PrOH=100/1, flow rate=1.0 mL min^{-1}): t_R=6.9 min (minor enantiomer of regioisomer), t_R=7.8 min (minor enantiomer), t_R=19.5 min (major enantiomer of regioisomer), t_R=24.6 min (major enantiomer).

(1*R*,2*R*)-1-Phenyl-1,2,3-tris(benzoyloxy)propane (19). To a suspension of $LiAlH_4$ (12.9 mg, 0.340 mmol) in diethyl ether (2 mL) was slowly added a solution of *S*-ethyl (2*S*,3*R*)-2-(*t*-butyldimethylsiloxy)-3-hydroxy-3-phenylpropanethioate (**18**) (54.4 mg, 0.160 mmol) in diethyl ether (1 mL) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 1 h. Saturated Na_2SO_4 was then added to the reaction mixture at 0 °C, and the organic materials were separated by filtration. The organic layer was dried over Na_2SO_4. After evaporation of the solvents, the crude product was purified by preparative TLC on silica gel to afford 19.5 mg (43%) of (1*R*,2*R*)-2-(*t*-butyldimethylsiloxy)-1-phenyl-1,3-propanediol: ^{1}H NMR ($CDCl_3$) δ=0.04 (s, 6H), 0.90 (s, 9H), 1.86 (br s, 1H), 2.80 (d, 1H, J=4.9 Hz), 3.51—3.57 (m, 1H), 3.60—3.67 (m, 1H), 3.80 (dt, 1H, J=4.5, 5.0 Hz), 4.80 (dd, 1H, J=4.9, 5.0 Hz), 7.28—7.38 (m, 5H). To (1*R*,2*R*)-2-(*t*-butyldimethylsiloxy)-1-phenyl-1,3-propanediol (19.5 mg, 0.069 mmol) in pyridine (0.55 mL) was added benzoyl chloride (30.5 mg, 0.217 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 10 h. The reaction mixture was quenched with cold water and extracted with ethyl acetate. The organic layer was washed with cold 1 M HCl, saturated $CuSO_4$, saturated $NaHCO_3$, and brine successively, and dried over Na_2SO_4. After evaporation of the solvents, the crude product was purified by preparative TLC on silica gel to afford 18.5 mg (56%) of (1*R*,2*R*)-2-(*t*-butyldimethylsiloxy)-1,3-bis(benzoyloxy)-1-phenylpropane: ^{1}H NMR ($CDCl_3$) δ=−0.09 (s, 3H), 0.07 (s, 3H), 4.15—4.23 (m, 1H), 4.35—4.44 (m, 2H), 7.28—7.60 (m, 11H), 7.99—8.02 (m, 2H), 8.10—8.13 (m, 2H). To (1*R*,2*R*)-2-(*t*-butyldimethylsiloxy)-1,3-bis(benzoyloxy)-1-phenylpropane (18.5 mg, 0.039 mmol) in acetonitrile (1 mL) was added 47% aqueous HF (2 drops) at 0 °C. The reaction mixture was quenched with saturated $NaHCO_3$, and the aqueous layer was extracted with diethyl ether. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo to afford crude (1*R*,2*R*)-1,3-bis(benzoyloxy)-1-phenyl-2-propanol. To (1*R*,2*R*)-1,3-bis(benzoyloxy)-2-hydroxy-1-phenylpropance in pyridine (0.30 mL) was added benzoyl chloride (15.8 mg, 0.11 mmol) at 0 °C. The reaction mixture was warmed up to room temperature and stirred for 10 h. The reaction mixture was quenched with cold water and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with cold 1 mol dm^{-3} HCl, saturated $CuSO_4$, saturated $NaHCO_3$, and brine successively, and dried over Na_2SO_4. After evaporation of the solvents, the crude product was purified by preparative TLC on silica gel to afford 18.5 mg (quantitative from (1*R*,2*R*)-2-(*t*-butyldimethylsiloxy)-1-3-bis(benzoyloxy)-1-phenylpropane) of (1*R*,2*R*)-1-phenyl-1,2,3-tris(benzoyloxy)propane (90% ee) as a solid. First recrystallization of the above tribenzoate in benzene/hexane system gave optically pure (1*R*,2*R*)-1-phenyl-1,2,3-tris(benzoyloxy)propane (80%, >99% ee): Mp 139—140 °C; $[\alpha]_D^{26}$ +11.6° (*c* 0.49, $CHCl_3$) (lit,[12] $[\alpha]_D^{23}$ +12.2° (*c* 4.42, $CHCl_3$)); IR (KBr) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.32 (dd, 1H, J=5.6, 12.2 Hz), 4.63 (dd, 1H, J=3.3, 12.2 Hz), 6.03 (ddd, 1H, J=3.3, 5.6, 7.9 Hz), 6.46 (d, 1H, J=7.9 Hz), 7.28—7.66 (m, 14H), 7.96—8.05 (m, 3H), 8.07—8.16 (m, 3H). The optical purity was confirmed by using HPLC analysis: HPLC (Daicel Chiralcel OD, hexane/i-PrOH=19/1, flow rate=0.8 mL min^{-1}): t_R=10.0 min (minor enantiomer), t_R=35.9 min (major enantiomer).

(*Z*)-1-Ethylthio-2-methoxy-1-(trimethylsiloxy)-ethene: ^{1}H NMR ($CDCl_3$) δ=0.20 (s, 9H), 1.24 (t, 3H, J=7.3 Hz), 2.68 (q, 2H, J=7.3 Hz), 3.55 (s, 3H), 6.19 (s, 1H); ^{13}C NMR ($CDCl_3$) δ=0.00, 14.85, 25.20, 60.02, 131.5, 139.1. The crude mixture of 1-ethylthio-2-methoxy-1-(trimethylsiloxy)ethene (Z/E=70/30) was used in the asymmetric aldol reaction. (*E*)-1-Ethylthio-2-methoxoy-1-(trimethylsiloxy)ethene: ^{1}H NMR ($CDCl_3$) δ=0.20 (s, 9H), 1.20 (t, 3H, J=7.2 Hz), 2.54 (q, 2H, J=7.2 Hz), 3.56 (s, 3H), 5.88 (s, 1H); ^{13}C NMR ($CDCl_3$) δ=0.27, 14.31, 26.02, 59.52, 127.3, 137.0.

***S*-Ethyl (2*R*,3*R*)-3-Hydroxy-2-methoxy-3-phenylpropanethioate:** (93% ee) The diastereomer was not separated in the aldol from. ^{1}H NMR (CCl_4) δ=1.20 (d, 3H, J=7.0 Hz), 2.75 (q, 2H, J=7.0 Hz), 3.05 (s, 1H), 3.30 (s, 3H), 3.65 (d, 1H, J=4.0 Hz), 4.65—4.95 (m, 1H), 7.25 (m, 5H). Optical purity was determined after derivation to the corresponding acetate. *S*-Ethyl (2*R*,3*R*)-3-acetoxy-2-benzyloxy-3-phenylpropanethioate: ^{1}H NMR (CCl_4) δ=1.20 (t, 3H, J=7.0 Hz), 2.00 (s, 3H), 2.75 (q, 2H, J=7.0 Hz), 3.90 (d, 1H, J=6.0 Hz), 5.75 (d, 1H, J=6.0 Hz), 7.25 (m, 5H); HPLC (Daicel Chiralcel OD, hexane/i-PrOH=200/1, flow rate=1.0 mL min^{-1}): t_R=13.0 min (minor enantiomer), t_R=18.6 min (major enantiomer).

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