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Enantioselective Synthesis of Both Diastereomers, Including the α-Alkoxy-β-hydroxy-β-methyl(phenyl) Units, by Chiral Tin(II) Lewis Acid-Mediated Asymmetric Aldol Reactions

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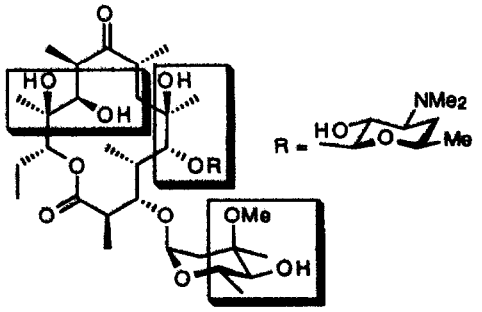
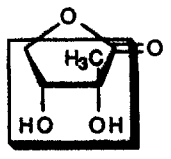
Abstract: *Diastereo- and enantioselective synthesis of both diastereomers, including the α-alkoxy-β-hydroxy-β-methyl(phenyl) units, was performed by using chiral tin(II) Lewis acid-mediated asymmetric aldol reactions of α-alkoxy silyl enol ethers with α-ketoesters. (S)-1-Propyl-2-[(1,2,3,4-tetrahydroisoquinolinyl))methyl]pyrrolidine (13), a new type of chiral diamine, was found to be effective as a chiral source in these reactions and also in the reactions of 2-(t-butyldimethylsiloxy)-1-ethylthio-1-(trimethylsiloxy)ethene (9) with aldehydes for the synthesis of optically active syn-α,β-dihydroxy thioester derivatives. (-)-2-C-Methyl-D-erythrono-1,4-lactone and (+)-2-C-methyl-L-threono-1,4-lactone were synthesized by using these reactions.*

Introduction

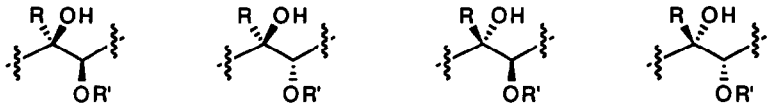
α-Alkoxy-β-hydroxy-β-methyl(phenyl) units (Scheme 1) are often observed in natural products, especially in biologically active macrolides and pyrrolizidine alkaloids, some branched sugars and their derivatives.[1] Diastereo- and enantioselective synthesis of these units, consisting of successive asymmetric centers including tertiary alcohol parts, is difficult, and development of efficient methods has been one of the most challenging tasks in organic synthesis.[2] In this paper, we disclose a new approach to this hard problem, the enantio-



erythromycin A



(-)-2-C-methyl-erythrono-1,4-lactone



Scheme 1. Stereoisomers Including the α-Alkoxy-β-hydroxy-β-methyl(aryl) Units

selective syntheses of both diastereomers including the α-alkoxy-β-hydroxy-β-methyl(phenyl) units, based on a chiral tin(II) Lewis acid-mediated asymmetric aldol methodology.[3] The enantioselective syntheses of (-)-2-C-Methyl-D-erythrono-1,4-lactone and (+)-2-C-methyl-L-threono-1,4-lactone are also described.

Synthesis of the *anti*-α-Alkoxy-β-hydroxy-β-methyl(phenyl) Units

Recently, we reported the diastereoselective synthesis of both stereoisomers including the α-alkoxy-β-hydroxy-β-methyl units by using aluminum triflate-mediated aldol reactions of silyl enol ethers with α-ketoesters.[4] Although this method is convenient for the construction of racemic α-alkoxy-β-hydroxy-β-methyl units, the asymmetric version of this reaction using chiral aluminum reagents did not succeed. Our successful method is based on the chiral tin(II) Lewis acid-mediated asymmetric aldol reaction of α-alkoxy silyl enol ethers[5] with α-ketoesters. First, the reaction of methyl pyruvate with (Z)-2-benzyloxy-1-ethylthio-1-(trimethylsiloxy)ethene (**1**) was performed in the presence of tin(II) triflate, (*S*)-1-methyl-2-[(piperidinyl)methyl]pyrrolidine (**2**), and tributyltin fluoride (Bu_3SnF).[6] The reaction proceeded smoothly to afford the desired adduct (**7**) in a 64% yield with *anti*-preference (*syn*/*anti* = 14/86), and the enantiomeric excess of the *anti* isomer was 83%. Use of dibutyltin diacetate ($Bu_2Sn(OAc)_2$) instead of Bu_3SnF gave lower selectivities (71% yield, *syn*/*anti* = 33/67, *anti* isomer = 28% ee).[7] After screening several reaction conditions, the best enantiomeric excess was attained when (*S*)-1-propyl-2-[(piperidinyl)methyl]pyrrolidine (**4**) was used as a chiral source (*syn*/*anti* = 13/87, *anti* isomer = 91% ee) (Table 1).

Methyl benzoylformate also worked well under these conditions to afford the *anti*-adduct (**8**-*anti*) in high selectivities (Table 1, entries 7-11).

Synthesis of the *syn*-α-Alkoxy-β-hydroxy-β-methyl(phenyl) Units

Next, in order to prepare optically active *syn*-α-alkoxy-β-hydroxy-β-methyl(phenyl) units, the reaction of methyl pyruvate with (Z)-2-(*t*-butyldimethylsiloxy)-1-ethylthio-1-(trimethylsiloxy)ethene (**9**) was examined in the presence of tin(II) triflate, chiral diamine **2**, and Bu_3SnF.[5] Although the reaction proceeded with high enantioselectivity (*syn* isomer = 84% ee), *syn*-selectivity was moderate (*syn*/*anti* = 70/30). Use of $Bu_2Sn(OAc)_2$ instead of Bu_3SnF gave disappointing results (*syn*/*anti* = 47/53, *syn* isomer = 54% ee).[7] Although the enantioselectivity improved (89% ee) when chiral diamine **4** was used, the *syn*/*anti* ratio remained moderate (*syn*/*anti* = 68/32). It is noted that when tin(II) triflate, the chiral diamine, and $Bu_2Sn(OAc)_2$ were combined, *anti*-adducts were preferentially obtained in good enantiomeric excesses (Table 2).

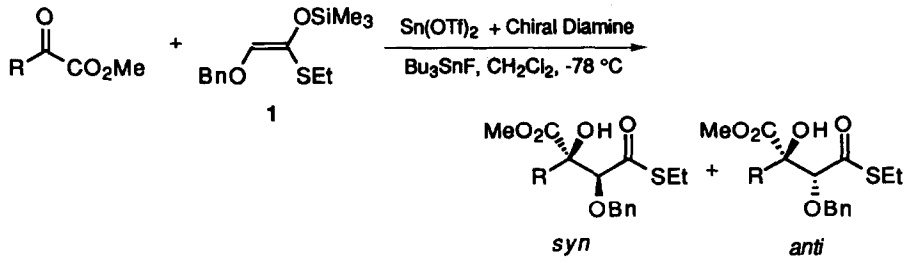
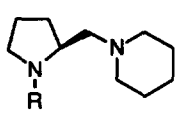


Table 1. Synthesis of the *anti*-α-Alkoxy-β-hydroxy-β-methyl(phenyl) Units[a)]

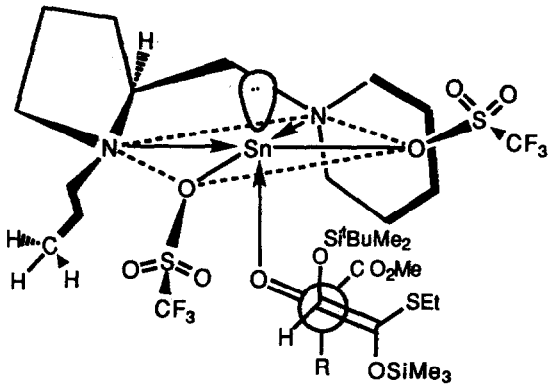
Entry	R	Chiral Diamine	Product	Yield / %	*syn* / *anti*	ee / % (*anti*)
1	Me	**2**	**7**	64	14 / 86	83
2		**3**	**7**	90	10 / 90	83
3		**4**	**7**	93	13 / 87	91
4		**5**	**7**	78	12 / 88	86
5		**6**	**7**	87	11 / 89	85
6[b)]		**2**	**7**	71	33 / 67	28
7	Ph	**2**	**8**	59	8 / 92	88
8		**3**	**8**	70	7 / 93	92
9		**4**	**8**	66	7 / 93	91
10		**5**	**8**	61	7 / 93	80
11		**6**	**8**	70	7 / 93	86

a) The reactions were carried out for 20 h (entry 3), 24 h (entries 1, 2, 4-6), or 44 h (entries 7-11).
b) $Bu_2Sn(OAc)_2$ was used instead of Bu_3SnF.



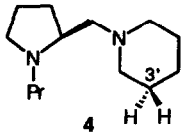
2 R = Me
3 R = Et
4 R = Pr
5 R = Bu
6 R = C_5H_{11}

At this stage, we reexamined the transition state of this reaction (Scheme 2). The chiral tin(II) Lewis acid activates an α-ketoester and silyl enol ether **9** attacks this ketoester via the acyclic transition state.[5b,c,8)] It was suggested from modeling studies that there was steric repulsion between the *t*-butyldimethylsiloxy group of silyl enolate **9** and the 3'-hydrogen of chiral diamine **4** and that this lowered the *syn*-selectivity. In fact, use of chiral diamine **10**,



Scheme 2. Assumed Transition States for the *syn*-Selective Reactions

having a 3'-methyl group instead of hydrogen, further lowered the *syn*-selectivity (*syn*/*anti* = 43/57, *syn* isomer = 57% ee).



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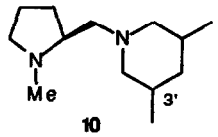

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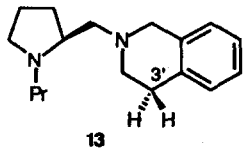
In order to decrease the steric repulsion, we designed a new chiral diamine, (*S*)-1-propyl-2-[(1,2,3,4-tetrahydroisoquinolinyl)methyl]pyrrolidine (**13**). Owing to the benzene ring, the *N*-containing six-membered ring was expected to be flatter than that of chiral diamine **4**, and the steric repulsion between the *t*-butyldimethylsiloxy group of silyl enolate **9** and the hydrogen was expected to be reduced.



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The reaction of methyl pyruvate with **9** was carried out in the presence of tin(II) triflate, chiral diamine **13**, and Bu_3SnF under standard conditions, and, as expected, the diastereomer ratio

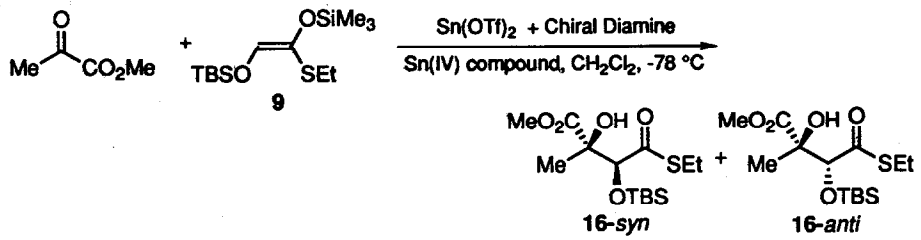
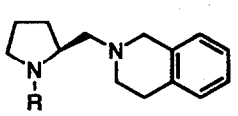


Table 2. Synthesis of the *syn*-α-Alkoxy-β-hydroxy-β-methyl Units[a)]

Entry	Chiral Diamine	Sn(IV) compound	Yield / %	*syn* / *anti*	ee / % (*syn*)
1	**2**	Bu_3SnF	81	70 / 30	84
2	**3**	Bu_3SnF	70	66 / 34	84
3	**4**	Bu_3SnF	73	68 / 32	89
4	**5**	Bu_3SnF	61	64 / 36	82
5	**6**	Bu_3SnF	66	62 / 38	82
6	**2**	$Bu_2Sn(OAc)_2$	54	47 / 53	54
7	**3**	$Bu_2Sn(OAc)_2$	86	34 / 66	54
8	**4**	$Bu_2Sn(OAc)_2$	73	18 / 82	56
9	**5**	$Bu_2Sn(OAc)_2$	86	26 / 74	56
10	**6**	$Bu_2Sn(OAc)_2$	78	25 / 75	43
11	**11**	Bu_3SnF	75	85 / 15	76
12	**12**	Bu_3SnF	88	84 / 16	76
13	**13**	Bu_3SnF	89	94 / 6	88
14	**14**	Bu_3SnF	80	85 / 15	76
15	**15**	Bu_3SnF	86	85 / 15	72
16	**11**	$Bu_2Sn(OAc)_2$	55	39 / 61	54
17	**12**	$Bu_2Sn(OAc)_2$	86	40 / 60	52
18	**13**	$Bu_2Sn(OAc)_2$	73	31 / 69	50
19	**14**	$Bu_2Sn(OAc)_2$	86	22 / 78	60
20	**15**	$Bu_2Sn(OAc)_2$	52	33 / 67	46

a) The reactions were carried out for 24 h.



11 R = Me
12 R = Et
13 R = Pr
14 R = Bu
15 R = C_5H_{11}

was rather improved (*syn*/*anti* = 94/6) and the enantiomeric excess of the *syn* isomer was 88% (Table 2).

The results of the reactions of methyl benzoylformate with **9** are summarized in Table 3. When (*S*)-1-alkyl-2-[(piperidinyl)methyl]pyrrolidine-type diamines (**2-6**) were used, very high enantiomeric excesses were obtained, but the diastereoselectivities were moderate. On the other hand, high *syn*-selectivities with high enantiomeric excesses were attained when (*S*)-1-alkyl-2-[(1,2,3,4-tetrahydroisoquinolinyl)methyl]pyrrolidine-type diamines (**11-15**) were used.

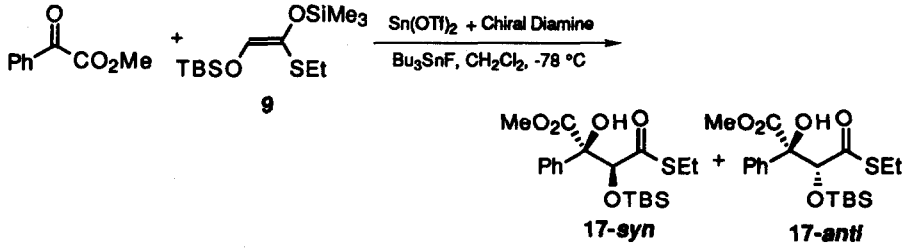


Table 3. Synthesis of the *syn*-α-Alkoxy-β-hydroxy-β-phenyl Units[a)]

Entry	Chiral Diamine	Yield / %	*syn* / *anti*	ee / % (*syn*)
1	**2**	64	59 / 41	89
2	**3**	72	64 / 36	94
3	**4**	65	67 / 33	96
4	**5**	63	67 / 33	94
5	**6**	68	72 / 28	94
6	**11**	82	83 / 17	80
7	**12**	80	75 / 25	86
8	**13**	76	84 / 16	87
9	**14**	75	82 / 18	84
10	**15**	70	82 / 18	81

a) The reactions were carried out for 44 h.

syn-Selective Aldol Reactions of 9 with Aldehydes Using Chiral Diamine 13. Enantioselective Synthesis of _syn_-α,β-Dihydroxy Thioester Derivatives

Our newly-developed chiral diamine **13** was next evaluated in the reactions of **9** with achiral aldehydes. We have already reported that the aldol reactions of **9** with aldehydes proceeded smoothly in the presence of tin(II) triflate, a chiral diamine, and $Bu_2Sn(OAc)_2$ to

afford the *syn*-aldol adducts in high yields with high diastereo- and enantioselectivities.[5b,c] For example, benzaldehyde reacted with **9** under the above conditions ((*S*)-1-propyl-2-[(piperidinyl)methyl]pyrrolidine (**4**) was used as a chiral diamine) to give the aldol adduct in an 86% yield, *syn*/*anti* = 88/12, and the enantiomeric excess of the *syn*-adduct was 90% ee. The same reaction was carried out with chiral diamine **13** instead of **4**, and it was found that the diastereo- and enantioselectivities were further improved (*syn*/*anti* = 97/3, *syn* aldol = 96% ee). Typical aldehydes, including aromatic, aliphatic, α,β-unsaturated aldehydes, and a dienal, were examined and in most cases the selectivities were improved (Table 4). Thus, chiral diamine **13** was found to be effective not only in the reaction of **9** with α-ketoesters but also in the reaction of **9** with various aldehydes. Moreover, optically active *syn*-α,β-dihydroxy thioester derivatives can be prepared in high selectivities according to these reactions.

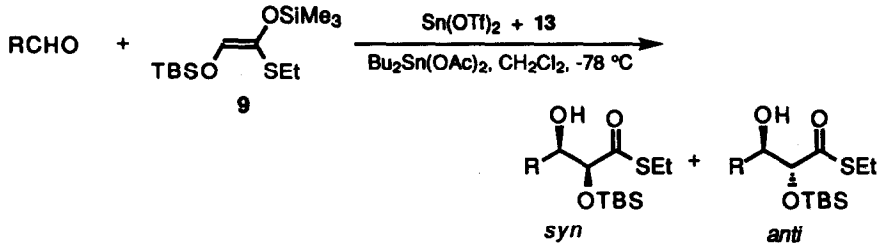
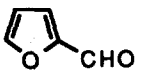
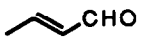
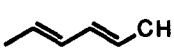


Table 4. Synthesis of *syn*-α,β-Dihydroxy Thioesters

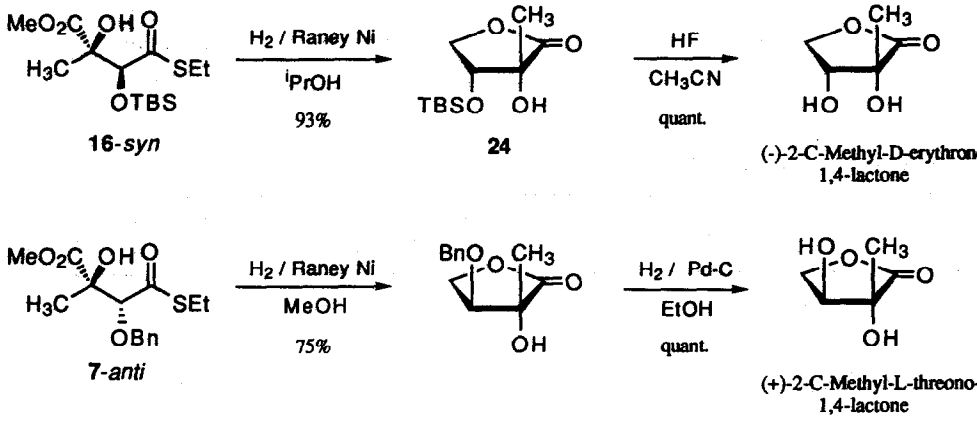
Entry	RCHO	Product	This Work			Previous Work[a]		
			Yield/%	*syn*/*anti*	ee/% (*syn*)	Yield/%	*syn*/*anti*	ee/% (*syn*)
1	PhCHO	**18**	88	97 / 3	96	86	88 / 12	90
2		**19**	88	97 / 3	94	93	94 / 6	93
3		**20**	69	95 / 5	86	46	92 / 8	82
4		**21**	77	99 / 1	94	75	97 / 3	94
5		**22**	79	94 / 6	94	76	90 / 10	92
6		**23**	89	94 / 6	96	89	93 / 7	94

a) Ref. 5b, c.

Syntheses of (-)-2-C-methyl-erythrono- and (+)-2-C-methyl-L-threono-1,4-lactones

The asymmetric aldol reactions developed here provide a useful method for the preparation of both diastereomers, including the α-alkoxy-β-hydroxy-β-methyl(phenyl) units, in high enantiomeric excesses. As examples to show the utility of this methodology, we synthesized (-)-2-C-Methyl-D-erythrono-1,4-lactone[9] and (+)-2-C-methyl-L-threono-1,4-lactone[9] (Scheme 3). Aldol adduct **16-*syn*** was treated with Raney Nickel under hydrogen atmosphere to afford lactone **24** directly. The *t*-butyldimethylsilyl group of **24** was then deprotected to give (-)-2-C-Methyl-D-erythrono-1,4-lactone in a 93% yield from **16-*syn***. The optical rotation of the lactone was consistent with that of the literature.[9a] Similarly, (+)-2-C-methyl-L-threono-1,4-lactone was prepared from **7-*anti***[10] in a 75% yield. The optical purity of the lactone was confirmed by HPLC analysis after derivation to the corresponding dibenzoate (>99.5% ee).

Thus, (-)-2-C-Methyl-D-erythrono-1,4-lactone and (+)-2-C-methyl-L-threono-1,4-lactone were prepared stereoselectively from methyl pyruvate and **1** and **9** in just 3 steps.



Scheme 3. Synthesis of (-)-2-C-Methyl-D-erythrono-1,4-lactone and (+)-2-C-Methyl-L-threono-1,4-lactone

Conclusions

Both enantiomers, including the α-alkoxy-β-hydroxy-β-methyl(phenyl) units, were prepared by using chiral tin(II) Lewis acid-mediated asymmetric aldol reactions of α-alkoxy silyl enol ethers with α-ketoesters. The protective groups of the α-alkoxy silyl enol ethers were crucial in controlling the diastereoselectivities. Since D-proline is available, four possible stereoisomers of the α-alkoxy-β-hydroxy-β-methyl(phenyl) units (Scheme 1) would be prepared.[11] In the synthesis of the *syn*-α-alkoxy-β-hydroxy-β-methyl(phenyl) units, (*S*)-1-propyl-2-[(1,2,3,4-tetrahydroisoquinolinyl)methyl]pyrrolidine (**13**), a new type of chiral diamine, was found to be effective as a chiral source. Chiral diamine **13** also gave high selectivities in the reaction of **9** with aldehydes for the synthesis of *syn*-α,β-dihydroxy thioester

derivatives. Finally, the methodology developed here was applied to the synthesis of (-)-2-C-Methyl-D-erythrono-1,4-lactone and (+)-2-C-methyl-L-threono-1,4-lactone.

Experimental Section

General. IR spectra were recorded on a Horiba FT-300 infrared spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Hitachi R-1100 or JEOL JNR-EX270L spectrometer, and tetramethylsilane (TMS) served as internal standard. HPLC was carried out using a Hitachi LC-Organizer, L-4000 UV Detector, L-6200 Intelligent Pump, and D-2500 Chromato-Integrator. Optical rotations were recorded on a Jasco DIP-360 digital polarimeter. Column chromatography was performed on Silica gel 60 (Merck) or Wakogel B5F. All reactions were carried out under argon atmosphere in dried glassware.

Dichloromethane was distilled from P_2O_5, then CaH_2, and dried over MS4A.

Tin(II) trifluoromethanesulfonate (tin(II) triflate)[12,13] were prepared according to the literatures. All handlings of tin(II) triflate were carried out under argon atmosphere. Chiral diamines[13-15] were prepared from *L*-proline according to the literature methods. Similarly, (*S*)-1-propyl-2-[(1,2,3,4-tetrahydroisoquinolinyl)methyl]pyrrolidine (**13**) was prepared from *N*-(benzyloxycarbonyl)-*L*-proline (CBZ-*L*-proline) and 1,2,3,4-tetrahydroisoquinoline.

13: $[\alpha]_D^{26}$ -84.6 ° (c 2.9, EtOH); ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H, *J* = 7.3 Hz), 1.43-2.89 (m, 16H), 3.13-3.18 (m, 1H), 3.60 (d, 1H, *J* = 14.8 Hz), 3.67 (d, 1H, *J* = 14.8 Hz), 6.98-7.12 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 12.1, 22.1, 22.7, 29.0, 30.4, 51.5, 54.4, 56.8, 57.7, 62.2, 63.7, 125.4, 125.9, 126.4, 128.5, 134.3, 135.0; HRMS calcd for $C_{17}H_{26}N_2$ [M+] 258.2094, found 258.2091.

***S*-Ethyl benzyloxyethanethioate.**[5a,c] 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) to afford 4.3 g (76%) of *S*-ethyl benzyloxyethanethioate as a colorless oil: IR (neat) 1750 cm^{-1}; ^1H 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 (1).[5a,c] To 2,2,6,6-tetramethylpiperidine (777 mg, 5.5 mmol) in tetrahydrofuran (THF, 6 mL) was added 1.65 M hexane solution of butyllithium (3.33 mL, 5.5 mmol)) at 0 °C. The reaction mixture was stirred for 10 min at 0 °C, and then cooled to -78 °C. To this lithium 2,2,6,6-tetramethylpiperidide solution were added *S*-ethyl benzyloxyethanethioate (1.06 g, 5.0 mmol) in THF (3 mL) over 30 min. The mixture was stirred for 30 min and chlorotrimethylsilane (598 mg, 5.5 mmol) in THF (1 mL) was added. 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 (*Z* / *E* = 93/7). 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. While the (*Z*)-enol ether was predominantly formed under kinetic conditions, the (*Z*)-enol ether was found to be isomerized rapidly to the (*E*)-enol ether under thermal conditions. ^1H 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.[5a,c] ^{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.

***S*-Ethyl (*t*-butyldimethylsiloxy)ethanethioate.**[5b,c] **Method A:** To a mixture of hydroxyacetic acid (2.82 g, 37.1 mmol) and imidazole (12.6 g, 185.1 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 up 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: ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 6H), 0.27 (s, 6H), 0.91 (s, 9H), 0.92 (s,6H), 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 (10.0 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 N 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: ^{1}H 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 room temperature. 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 (quant.) of (*t*-butyldimethylsiloxy)acetyl chloride. To a mixture of *t*-butyldimethylsiloxyacethylchloride (3.30 g, 15.8 mmol) and ethanethiol (1.29 mL, 19.0 mmol) in dichloromethane (90 mL) was added pyridine (1.50 g, 19.0 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}; ^{1}H 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, 10.0 mmol) and imidazole (0.82 g, 12.0 mmol) in DMF (10 mL) was added *t*-butyldimethylchlorosilane (1.81 g, 12.0 mmol) at 0 °C. The reaction mixture was warmed up 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, 10.0 mmol) in dichloromethane (10 mL) at -78 °C was added dimethylaluminum ethanethiolate, which was prepared from 1 M hexane solution of trimethylaluminum (20.0 mL, 20.0 mmol) and ethanethiol (1.48 mL, 20.0 mmol) (-78 °C and then 0 °C, 1 h). 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*-butyldimethylsiloxy)ethanethioate.

(*Z*)-2-(*t*-Butyldimethylsiloxy)-1-ethylthio-1-(trimethylsiloxy)ethene (9).[5b,c] 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 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 Asymmetric Aldol Reaction. A typical experimental procedure is described for the reaction of **1** with methyl pyruvate: To a suspension of tin(II) triflate (0.40 mmol) in dichloromethane (1.0 ml) were added chiral diamine **4** (0.48 mmol) in dichloromethane (1.0 ml) and Bu_3SnF (0.44 mmol) successively at room temperature. The mixture was then cooled to -78 °C, and dichloromethane solution (0.5 ml each) of **1** (0.40 mmol) and methyl pyruvate (0.27 mmol) were successively added. The mixture was stirred for 20 h, and sat. aqueous sodium hydrogencarbonate was then added to quench the reaction. After the usual work up, *S*-ethyl 2-benzyloxy-3-hydroxy-3-methoxycarbonylbutanethioate (**7**) was obtained in a 93% yield (*syn*/*anti* = 13/87, *anti* isomer = 91% ee). The diastereomer ratio was determined by ^{1}H NMR (C-2 methine protons and $CO_2\underline{Me}$). The both diastereomers were separated by column chromatography (silica gel) and the optical purity was determined by HPLC analysis using a chiral column. **7-*Anti*** was recrystallized from *n*-hexane to give an optically pure form (>99.5% ee).

For the synthesis of the *syn* isomers, silyl enol ether **9** and chiral diamine **13** were used instead of **1** and **4**, respectively.

***S*-Ethyl (2*R*,3*R*)-2-benzyloxy-3-hydroxy-3-methoxycarbonylbutanethioate (7-*anti*).** (91% ee) Mp 80.0 °C; $[\alpha]_D^{26}$ +120.1 ° (c 1.9, PhH); IR (KBr) 3552, 1743, 1672 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (t, 3H, *J* = 7.5 Hz), 1.44 (s, 3H), 2.92 (q, 2H, *J* = 7.5 Hz), 3.47 (brs, 1H), 3.61 (s, 3H), 4.16 (s, 1H), 4.37 (d, 1H, *J* = 11.2 Hz), 4.81 (d, 1H, *J* = 11.2 Hz), 7.29-7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.3, 21.1, 22.8, 52.8, 74.1, 76.7, 87.1, 128.2, 128.3, 128.4, 136.3, 174.0, 200.2. Anal. Calcd for $C_{15}H_{20}O_5S$: C, 57.68; H, 6.45. Found: C, 57.95; H, 6.38. HPLC (Daicel Chiralpak AD, hexane/*i*-PrOH = 19/1, flow rate = 1.0 mL / min): t_R = 10.6 min (major enantiomer), t_R = 13.6 min (minor enantiomer).

***S*-Ethyl (2*R*,3*R*)-2-benzyloxy-3-hydroxy-3-methoxycarbonyl-3-phenylpropanethioate (8-*anti*).** (92% ee) Mp 84.0-85.0 °C; $[\alpha]_D^{26}$ -119.0 ° (c 3.1, PhH); IR (KBr) 3539, 1726, 1674 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.14 (t, 3H, *J* = 7.4 Hz), 2.75 (q, 2H, *J* = 7.4 Hz), 3.65 (s, 3H), 3.98 (s, 1H), 4.48 (d, 1H, *J* = 11.1 Hz), 4.76 (s, 1H), 4.83 (d, 1H, *J* = 11.1 Hz), 7.31-7.39 (m, 8H), 7.64-7.68 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.3, 22.8, 53.3, 74.4, 80.7, 87.7, 126.1, 128.0, 128.2, 128.41, 128.45, 135.8, 136.4, 172.5, 198.5. Anal. Calcd for $C_{20}H_{22}O_5S$: C, 64.15; H, 5.92. Found: C, 64.25; H, 5.89. HPLC (Daicel Chiralpak AD, hexane/*i*-PrOH = 9/1, flow rate = 1.0 mL / min): t_R = 23.2 min (major enantiomer), t_R = 27.0 min (minor enantiomer).

***S*-Ethyl (2*S*,3*R*)-2-*t*-butyldimethylsiloxy-3-hydroxy-3-methoxycarbonylbutanethioate (16-*syn*).** (88% ee) $[\alpha]_D^{26}$ -72.9 ° (c 1.47, PhH); IR (KBr) 3530, 1743, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.10 (s, 6H), 0.95 (s, 9H), 1.18 (t, 3H, *J* = 7.5 Hz), 1.42 (s, 3H), 2.79 (q, 2H, *J* = 7.5 Hz), 3.34 (brs, 1H), 3.75 (s, 3H), 4.16 (s, 1H); ^{13}C NMR ($CDCl_3$) δ -4.4, -4.3, 14.8, 18.6, 22.6, 23.1, 26.2, 53.2, 77.3, 82.9, 174.6, 203.3. Anal. Calcd for $C_{14}H_{28}O_5SSi$: C, 49.97; H, 8.38. Found: C, 50.30; H, 8.42. HPLC (Daicel Chiralpak AD, hexane/*i*-PrOH = 200/1, flow rate = 1.0 mL / min): t_R = 10.7 min (minor enantiomer), t_R = 14.2 min (major enantiomer).

***S*-Ethyl (2*S*,3*R*)-2-*t*-butyldimethylsiloxy-3-hydroxy-3-methoxycarbonyl-3-phenylpropanethioate (17-*syn*).** (87% ee) Mp 106.0-107.0 °C; $[\alpha]_D^{28}$ -139.4 ° (c 2.3, PhH); IR (KBr)

3514, 1736, 1672 cm^{-1}; ^1H NMR ($CDCl_3$) δ -0.56 (s, 3H), 0.00 (s, 3H), 0.79 (s, 9H), 1.24 (t, 3H, *J* = 7.5 Hz), 2.86 (q, 2H, *J* = 7.5 Hz), 3.81 (s, 1H), 3.90 (s, 3H), 4.88 (s, 1H), 7.31-7.35 (m, 3H), 7.70-7.73 (m, 2H); ^{13}C NMR ($CDCl_3$) δ -4.8, 14.3, 18.0, 22.9, 25.7, 53.2, 80.8, 82.5, 126.8, 128.0, 128.2, 137.8, 172.5, 203.0. Anal. Calcd for $C_{19}H_{30}O_5SSi$: C, 57.26; H, 7.58. Found: C, 57.01; H, 7.63. HPLC (Daicel Chiralpak AD, hexane/*i*-PrOH = 50/1, flow rate = 1.0 mL / min): t_R = 11.6 min (minor enantiomer), t_R = 15.4 min (major enantiomer).

***S*-Ethyl (2*S*,3*R*)-2-(*t*-butyldimethylsiloxy)-3-hydroxy-3-phenylpropanethioate (18-*syn*).**[5b,c] (96% ee) $[\alpha]_D^{27}$ -113.4 ° (c 2.2, PhH); IR (neat) 3490, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) d -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 ($CDCl_3$) d -5.68, 14.41, 18.06, 22.79, 25.73, 75.26, 82.34, 126.11, 127.67, 128.14, 140.45, 203.38. HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 50/1, flow rate = 1.0 mL / min): 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 (19-*syn*).**[5b,c] (94% ee) $[\alpha]_D^{26}$ -122.1 ° (c 3.5, PhH); IR (neat) 3490, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ -0.25 (s, 3H), 0.05 (s, 3H), 0.89 (s, 9H), 1.24 (t, 3H, *J* = 7.4 Hz), 2.87 (q, 2H, *J* = 7.4 Hz), 3.00 (d, 1H, *J* = 10.2 Hz), 4.48 (d, 1H, *J* = 2.6 Hz), 4.98 (dd, 1H, *J* = 2.3, 10.2 Hz), 6.30-6.34 (m, 2H), 7.35 (s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.9, -5.2, 14.4, 18.0, 22.8, 25.6, 70.6, 79.5, 107.4, 110.4, 141.8, 153.2, 203.1. HPLC (Daicel Chiralcel AD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL / min): 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 (20-*syn*).**[5b,c] (86% ee) $[\alpha]_D^{25}$ -67.1 ° (c 0.9, PhH); IR (neat) 3510, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.09 (s, 3H), 0.14 (s, 3H), 0.96 (s, 9H), 1.24 (t, 3H, *J* = 7.4 Hz), 1.29-1.64 (m, 5H), 2.31 (d, 1H, *J* = 9.2 Hz), 2.84 (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 -5.0, -4.8, 10.3, 14.5, 18.1, 22.6, 25.8, 26.2, 75.5, 80.3, 204.8. HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min): 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 (21-*syn*).**[5b,c] (94% ee) $[\alpha]_D^{26}$ -69.4 ° (c 2.2, PhH); IR (neat) 3500, 1680 cm^{-1}; ^1H 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); ^{13}C NMR ($CDCl_3$) δ -4.9, 14.4, 17.7, 18.2, 22.6, 25.7, 74.2, 80.8, 128.1, 129.5, 204.1. HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 50/1, flow rate = 1.0 mL / min): 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 (22-*syn*).**[5b,c] (94% ee) $[\alpha]_D^{25}$ -141.4 ° (c 2.6, PhH); IR (neat) 3480, 1680 cm^{-1}; ^1H 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 -4.5, -4.4, 14.9, 18.6, 23.1, 26.1, 77.9, 80.9, 126.9, 128.1, 128.3, 129.0, 131.8, 136.9, 204.7. HPLC (Daicel Chiralcel AD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min): 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 (23-*syn*).**[5b,c] (96% ee) A small amount of regioisomer derived from the starting aldehyde was not separated. IR (neat) 3400, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.08 (s, 3H), 0.14 (s, 3H), 0.97 (s, 9H), 1.23 (t, 3H, *J* = 7.4 Hz), 1.75 (d, 3H, *J* = 6.3 Hz), 2.66 (br s, 1H), 2.84 (q, 2H, *J* = 7.4 Hz), 4.16 (d, 1H, *J* = 3.6 Hz), 4.35 (br s, 1H), 5.50-5.57 (m, 1H), 5.66-5.74 (m, 1H), 6.00-6.09 (m, 1H), 6.20-6.26 (m, 1H); ^{13}C NMR ($CDCl_3$) δ -4.9, 14.4, 18.1, 22.6, 25.7, 74.0, 80.6, 128.3, 130.3, 130.5, 132.0, 204.1. Anal. Calcd for $C_{16}H_{30}O_3SSi$: C, 58.14; H, 9.15; S, 9.70. Found: C, 58.05; H, 9.14; S, 9.58. HPLC (Daicel Chiralcel AD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/ min): 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).

(2*R*,3*R*)-3-*t*-Buthyldimethylsiloxy-2-hydroxy-2-methyl-γ-butyrolactone (24). **16-*Syn*** (88% ee, 67.3 mg, 0.20 mmol) was treated with Raney Ni (W-2) under hydrogen atmosphere in 2-propanol (1.0 ml) for 1 h. After filtration, the filtrate was concentrated and chromatographed on silica gel to afford **24** (45.8 mg, 93%). $[\alpha]_D^{28}$ -24.7 ° (c 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.00 (s, 6H), 0.77 (s, 9H), 1.30 (s, 3H), 3.00 (s, 1H), 3.94 (dd, 1H, *J* = 1.5, 3.6 Hz), 4.00 (dd, 1H, *J* = 1.5, 10.3 Hz), 4.24 (dd, 1H, *J* = 3.6, 10.3 Hz); ^{13}C NMR ($CDCl_3$) δ -5.2, -5.0, 17.8, 20.4, 25.3, 25.4, 25.6, 71.5, 72.6, 74.3, 176.9. Anal. Calcd for $C_{11}H_{22}O_4Si$: C, 53.63; H, 9.00. Found: C, 53.35; H, 8.89.

(-)-2-C-Methyl-D-erythrono-1,4-lactone ((2*R*,3*R*)-2,3-Dihydroxy-2-methyl-γ-butyrolactone). **24** (45.8 mg, 0.19 mmol) was solved in acetonitrile (1.0 ml) at room temperature and then a few drops of HF (40% water solution) was added. The mixture was concentrated *in vacuo* and chromatographed on silica gel to give (-)-2-C-Methyl-D-erythrono-1,4-lactone (24.6 mg, quant.). $[\alpha]_D^{25}$ -61.2 ° (c 0.2, H_2O) (lit.[9a] $[\alpha]_D$ -58.6 ° (c 0.68, H_2O)); ^1H NMR (D_2O) δ 1.30 (s, 3H), 4.09 (d, 1H, *J* = 3.6 Hz), 4.15 (d, 1H, *J* = 10.9 Hz), 4.44 (dd, 1H, *J* = 3.6, 10.9 Hz); ^{13}C NMR (D_2O) δ 15.9, 70.4, 73.2, 74.6, 179.6. Anal. Calcd for $C_5H_8O_4$: C, 45.46; H, 6.10. Found: C, 44.25; H, 6.23.

(2*R*,3*S*)-3-Benzyloxy-2-hydroxy-2-methyl-γ-butyrolactone. **7-*Anti*** (62.5 mg, 0.20 mmg, >99.5% ee) was treated with Raney Ni (W-2) under hydrogen atmosphere in methanol (1.0 ml) for 1 h. After filtration, the filtrate was concentrated and chromatographed on silica gel to afford (2*R*,3*S*)-3-benzyloxy-2-hydroxy-2-methyl-γ-butyrolactone (33.3 mg, 75%). $[\alpha]_D^{25}$ -75.3 ° (c 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.48 (s, 3H), 3.08 (s, 1H), 3.93 (dd, 1H, *J* = 7.3, 8.6 Hz), 4.30 (dd, *J* = 7.3, 7.3 Hz), 4.38 (dd, *J* = 7.3, 8.9 Hz), 4.60 (d, 1H, *J* = 11.7 Hz), 4.79 (d, 1H, *J* = 11.7 Hz), 7.37-7.41 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 18.6, 67.9, 72.4, 75.1, 80.2, 127.8, 128.2, 128.6, 137.0, 178.2. Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 65.01; H, 6.40.

(+)-2-C-methyl-L-threono-1,4-lactone ((2*R*,3*S*)-2,3-Dihydroxy-2-methyl-γ-butyrolactone). (2*R*,3*S*)-3-Benzyloxy-2-hydroxy-2-methyl-γ-butyrolactone (33.3 mg, 0.15 mmol) was treated with Pd/C under hydrogen atmosphere in ethanol (1.0 ml) for 3 h. After filtration, the crude product was purified by colum chromatography on silica gel to addord (+)-2-C-methyl-L-threono-1,4-lactone (19.8 mg, quant.). $[\alpha]_D^{25}$ +20.6 ° (c 0.1, H_2O) (lit.[2] ((2*S*,3*R*) form) $[\alpha]_D^{28}$ -18 ° (c 0.4, H_2O)); ^1H NMR (D_2O) δ 1.24 (s, 3H), 3.92 (dd, 1H, *J* = 6.3, 9.6 Hz), 4.27 (t, 1H, *J* = 6.3 Hz), 4.44 (dd, 1H, *J* = 6.3, 9.6 Hz); ^{13}C NMR (D_2O) δ 15.9, 70.4, 73.2, 74.6, 179.6. Anal. Calcd for $C_5H_8O_4$: C, 45.46; H, 6.10. Found: C, 45.19; H, 6.35.

(2*R*,3*S*)-2,3-Dibenzoyloxy-2-methyl-γ-butyrolactone. (+)-2-C-methyl-L-threono-1,4-lactone (19.8 mg, 0.15 mmol) was dissolved in pyridine (1.0 ml) and benzoyl chloride (210.8 mg, 1.50 mmol) was added. The mixture was stirred at room temperature for 24 h. After a usual work up, 34.7 mg of (2*R*,3*S*)-2,3-dibenzoyloxy-2-methyl-γ-butyrolactone was obtained (68%). The enantiomeric excess was determined to be >99.5% ee by HPLC analysis. ^1H NMR ($CDCl_3$) δ 1.81 (s, 3H), 4.27 (dd, 1H, *J* = 5.8, 10.1 Hz), 5.08 (dd, 1H, *J* = 8.2, 10.1 Hz), 6.09 (dd, 1H, *J* = 5.8, 8.2 Hz), 7.44-7.52 (m, 4H), 7.58-7.67 (m, 2H), 8.03-8.09 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 18.0, 69.4, 73.6, 78.7, 128.5, 128.7, 129.8, 130.1, 133.9, 165.4, 165.9, 172.9. HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 9/1, flow rate = 1.0 mL/min): t_R = 14.7 min (minor enantiomer), t_R = 23.4 min (major enantiomer). Anal. Calcd for $C_{19}H_{16}O_6$: C, 67.05; H, 4.74. Found: C, 66.95; H, 4.74.

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