Chiral Lewis Acid-Controlled Synthesis of Both Diastereomers. Enantioselective Synthesis of Both *syn*- and *anti*-2,3-Dihydroxy Ester Derivatives from the Same Starting Materials via Asymmetric Aldol Reactions by Choice of Chiral Ligands

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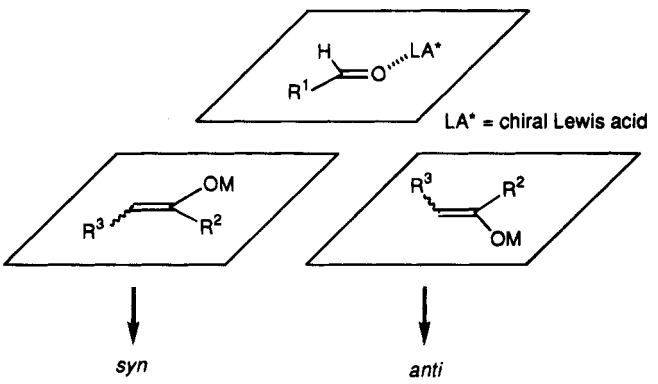
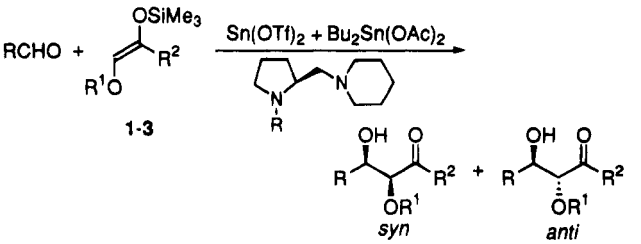
Asymmetric reactions based on chiral Lewis acids are of great current interest.[1] Although some successful examples of the asymmetric version of the Mukaiyama aldol reaction[2] (Lewis acid-mediated reactions of silyl enol ethers with aldehydes) have been reported,[3] there are no examples of chiral Lewis acid-controlled syntheses of both individual diastereomers (synthesis of both diastereomers in high enantiomeric excesses from the same starting material) as a function of choice of chiral Lewis acids. This may be due to difficulty in achieving control by chiral Lewis acids, since the enolate components controlled are not connected to the chiral Lewis acids, which coordinate aldehydes (Scheme 1). We now wish to report that both diastereomers of optically active 2,3-dihydroxy ester derivatives can be prepared from the same starting materials via chiral Lewis acid-mediated asymmetric aldol reactions by choosing different chiral ligands.

In organic synthesis, optically active 1,2-diol derivatives are useful chiral building blocks, and development of efficient methods for the preparation of these compounds is strongly desired. Recently, several asymmetric oxidations of olefins using osmium tetraoxide and chiral ligands have been reported, and practical preparations of some optically active 1,2-diols, especially *syn*-1,2-diol derivatives, have been realized.[4] Alternatively, we have shown that optically active 1,2-diol derivatives can be prepared by asymmetric aldol reactions of the silyl enol ethers derived from α-alkoxy ester derivatives with aldehydes using a chiral tin(II) Lewis acid.[5] Following this method, both diastereomers of 2,3-dihydroxy ester derivatives can be prepared with high diastereo- and enantioselectivities by simply choosing the appropriate protective groups for the alkoxy moieties of the silyl enol ethers or the ester groups. Namely, while *syn*-2,3-dihydroxy thioesters are obtained in the reactions of (*Z*)-2-(*tert*-butyldimethylsiloxy)-1-(ethylthio)-1-(trimethylsiloxy)ethene (**1**) with aldehydes,[5a,c] *anti*-2,3-dihydroxy thioesters are prepared from (*Z*)-2-(benzyloxy)-1-(ethylthio)-1-(trimethylsiloxy)ethene (**2**).[5b,c] On the other hand, *anti*-2,3-dihydroxy ester derivatives are synthesized from (*E*)-2-(*tert*-butyldimethylsiloxy)-1-(trimethylsiloxy)-1-phenoxyethene (**3**) and aldehydes (Scheme 2).[5d]

Scheme 1



Scheme 2



R^1	R^2		yield(%)	*syn*/*anti*	ee (%)
TBS	SEt	(1)	46-93	88/12-97/3	82-94 (*syn*)
Bn	SEt	(2)	59-88	9/91-1/99	95-98 (*anti*)
TBS	OPh	(3)	31-93	69/31-98/2	84-95 (*syn*)

We recently found in asymmetric aldol reactions using chiral tin(II) Lewis acids (prepared from tin(II) triflate and chiral ligands) that the reaction course could be controlled by the chiral ligands employed.[6] On the basis of this finding, we planned to prepare both diastereomers of aldols in high enantiomeric excesses from the same starting material by choosing different chiral ligands. After testing several silyl enol ethers and chiral ligands, (*Z*)-1-(benzyloxy)-1-(trimethylsiloxy)-1-phenoxyethene (**4**)[7] was found to be a good substrate for our purpose.

The effect of chiral diamines[8] on the reaction of **4** with benzaldehyde is shown in Table 1. When (*S*)-1-alkyl-2-[(1-piperidin-1-yl)methyl]pyrrolidines **5-7** or (*S*)-1-alkyl-2-[(1-pyrrolidin-1-yl)methyl]pyrrolidines **8-10** were used, the reactions proceeded with *anti*-preferences in high yields with good to high diastereo- and enantioselectivities. The best results were obtained when (*S*)-1-ethyl-2-[(1-pyrrolidin-1-yl)methyl]pyrrolidine (**9**) was used as a chiral ligand. On the other hand, the reactions proceeded with *syn*-preferences when chiral diamines **11-15** were used,[9] and in particular, 90% diastereomeric and

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(2) (a) Mukaiyama, T.; Banno, K.; Narasaka, K. *Chem. Lett.* **1973**, 1011. (b) Mukaiyama, T.; Narasaka, K.; Banno, *J. Am. Chem. Soc.* **1974**, *96*, 7503.

(3) (a) Mukaiyama, T.; Kobayashi, S. *Stereocontrolled Organic Synthesis*; Trost, B. M., Ed.; Blackwell Scientific Publication, Boston, 1994; p 37. (b) Bach, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 417 and references cited therein. See also: (c) Carreira E. M.; Singer, R. A.; Lee, W. *J. Am. Chem. Soc.* **1994**, *116*, 8837.

(4) Johnson, R. A.; Sharpless, K. B. Catalytic Asymmetric Dihydroxylation. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: Weinheim, Germany, 1993; pp 227–272.

(5) (a) Mukaiyama, T.; Uchiro, H.; Shiina, I.; Kobayashi, S. *Chem. Lett.* **1990**, 1019. (b) Mukaiyama, T.; Shiina, I.; Uchiro, H.; Kobayashi, S. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1708. (c) Mukaiyama, T.; Shiina, I.; Kobayashi, S. *Chem. Lett.* **1991**, 1901. (d) Kobayashi, S.; Kawasuji, T. *Tetrahedron Lett.* **1994**, *35*, 3329.

(6) Kobayashi, S.; Horibe, M. *J. Am. Chem. Soc.* **1994**, *106*, 9805.

(7) For the preparation of **4**, see: (a) Kobayashi, S.; Kawasuji, T. *Synlett* **1993**, 911. Cf. (b) Wissner, A. *J. Org. Chem.* **1979**, *44*, 4617. Yamamoto et al. reported catalytic asymmetric aldol reactions of silyl enolates derived from phenyl esters. (c) Furuta, K.; Maruyama, T.; Yamamoto, H. *Synlett* **1991**, 439.

(8) Mukaiyama, T.; Asami, M. *Top. Curr. Chem.* **1985**, *127*, 133.

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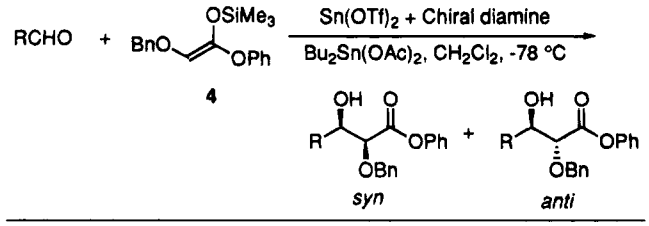
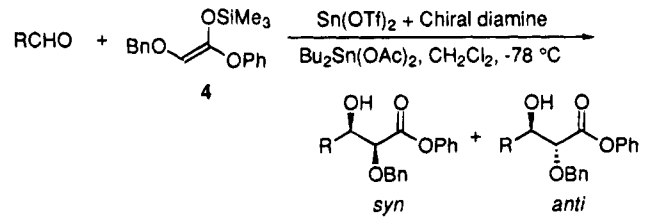
Table 1. Effect of Chiral Diamines[a]



chiral diamine	yield (%)	*syn/anti*	ee (%)[b]
5	90	29/71	78
6	84	25/75	73
7	79	27/73	73
8	73	9/91	75
9	80	9/91	90
10	80	10/90	90
11	85	95/5	91
12	77	93/7	92
13	60	88/12	72
14	78	79/21	78
15	92	93/7	85
16	85	68/32	20[c]
17	83	40/60	34
18	75	35/65	43

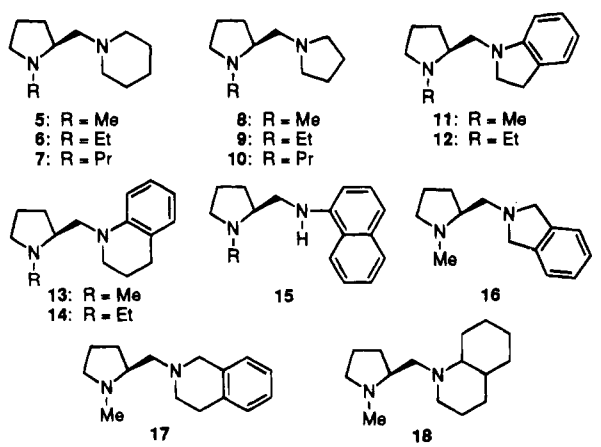
[a] R = Ph. [b] Enantiomeric excesses of the major isomers. [c] Major enantiomer, 2*R*,3*S*.

Table 2. Synthesis of Both Diastereomers



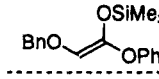
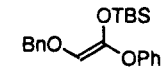
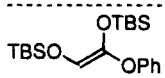
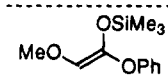
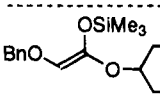
R	chiral diamine	yield (%)	*syn/anti*	ee (%)[a]
Ph	**11**	85	95/5	91
C_5H_{11}	**11**	90	94/6	94
$CH_3CH{=}CH$	**11**	89	>99/1	98
$PhCH{=}CH$	**11**	89	>99/1	98
2-furyl	**11**	88	>99/1	94
Ph	**9**	80	9/91	90
C_5H_{11}[b]	**10**	88	8/92	92
$CH_3CH{=}CH$	**9**	51	7/93	92
$PhCH{=}CH$[b]	**9**	63	12/88	94
2-furyl	**10**	77	12/88	91

[a] Enantiomeric excesses of the major isomers. [b] Bu_3SnF was used instead of $Bu_2Sn(OAc)_2$.



91% enantiomeric excesses were obtained when chiral diamine **11** was used. It is exciting that the slight difference in the structure of the chiral diamines completely reverses the diastereofacial selectivities. Moreover, the high *syn*-selectivity was found to disappear when chiral diamines **16-18** were used. The benzene ring connected to the pyrrolidine or piperidine moiety at the 2′ and 3′ positions of the chiral diamines plays an important role in the unique selectivities.

Table 3. Effect of Silyl Enolates in the Reactions with Benzaldehyde

silyl enolate		chiral diamine	yield (%)	*syn/anti*	ee (%)[a]
	**4**	**11**	85	95/5	91
		9	80	9/91	90
	**19**	**11**	82	95/5	89
		9	73	25/75	84
	**20**	**11**	13	77/23	6[b]
		9	53	82/18	3
	**21**	**11**	66	94/6	90
		9	56	19/81	60
	**22**	**11**	94	57/43	30
		9	90	67/33	30

[a] Enantiomeric excesses of the major isomers. [b] Major enantiomer, 2*R*,3*S*.

Finally, in order to clarify the origin of the unique selectivities, we carefully examined the reactions using several silyl enolates, and the results are shown in Table 3. When (*Z*)-1,2-bis(*tert*-butyldimethylsiloxy)-1-phenoxyethene (**20**) or (*Z*)-2-(benzyloxy)-1-cyclohexyl-1-(trimethylsiloxy)ethene (**22**) was reacted with benzaldehyde in the presence of tin(II) triflate, chiral diamine **9** or **11**, and $Bu_2Sn(OAc)_2$, lower selectivities were observed. On the other hand, 90% ee (*syn*) and 60% ee (*anti*) were obtained when (*Z*)-2-methoxy-1-(trimethylsiloxy)-1-phenoxyethene (**21**) was used. From these results, although the precise transition states remain unclear, we believe that the coordination of the alkoxy oxygen to tin(II) and the presence of the ester phenyl ring are essential for the unique selectivities.

In summary, we have achieved chiral Lewis acid-controlled syntheses of each diastereomer of several 2,3-dihydroxy ester derivatives. The key step is an asymmetric aldol reaction using a chiral tin(II) Lewis acid. High enantiomeric excesses were attained by judicious choice of the chiral source in the chiral Lewis acid. We can now obtain both *syn*- and *anti*-2,3-dihydroxy ester derivatives with high diastereo- and enantioselectivities from the same starting materials, silyl enol ether **4** and aldehydes.

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Supplementary Material Available: General procedures and characterization data (7 pages).

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(9) Recently, we found that the truly catalytic asymmetric aldol reactions of **4** with aldehydes could be carried out by using tin(II) triflate–chiral diamine **15** complex to afford *syn*-adducts.[7a] As for the synthesis of *anti*-adducts, we have tried the truly catalytic version[11] by using chiral diamine **9** or **10**, but have not yet succeeded.

(10) For experimental procedures, see the supplementary material.

(11) Kobayashi, S.; Fujishita, Y.; Mukaiyama, T. *Chem. Lett.* **1990**, 1455.