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Highly *anti*-Selective Asymmetric Aldol Reactions Using Chiral Zirconium Catalysts. Improvement of Activities, Structure of the Novel Zirconium Complexes, and Effect of a Small Amount of Water for the Preparation of the Catalysts

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Abstract: Catalytic asymmetric aldol reactions of silyl enol ethers with aldehydes (Mukaiyama aldol reactions) have been performed using novel chiral zirconium catalysts. The reactions proceeded in high yields under mild conditions, and *anti*-adducts were obtained in high diastereo- and enantioselectivities. The catalysts were first prepared from zirconium(IV) *tert*-butoxide ($Zr(O^tBu)_4$), (*R*)-3,3′-diiodo-1,1′-binaphthalene-2,2′-diol ((*R*)-3,3′-I_2BINOL), a primary alcohol, and a small amount of water. It was revealed that the primary alcohol played an important role in completing the catalytic cycle and that a small amount of water was essential for obtaining high selectivities. Moreover, activities of the chiral zirconium catalysts were enhanced by using new ligands, (*R*)-3,3′-I_2-6,6′-X_2BINOL (X = Br, I, C_2F_5), and it has been shown that even aldol reactions of less reactive substrates proceeded smoothly using the novel zirconium catalysts. Finally, NMR studies of these catalysts were performed, which suggested that the catalyst would form a dimeric structure and that the water affected the catalyst formation.

Introduction

Asymmetric aldol reactions provide one of the most powerful tools for constructing chiral β-hydroxy carbonyl compounds. In the past 2 decades, several diastereoselective aldol reactions were developed to obtain these chiral compounds, and some of them were successfully applied to the synthesis of biologically important compounds.[1] Furthermore, catalytic enantioselective versions of these reactions, especially catalytic asymmetric aldol reactions of silyl enol ethers with aldehydes (the Mukaiyama aldol reaction) mediated by chiral Lewis acids, were elaborated into the most powerful and efficient asymmetric aldol methodology. Recently, several chiral Lewis acids for this reaction based on Sn, B, Cu, Ti, etc. were developed to achieve high reactivities and selectivities.[2−4] In most systems, however, the reactions were performed under strictly anhydrous conditions, and lower temperatures were needed to obtain higher selectivities. Furthermore, in the reactions of the silyl enol ethers derived from propionate derivatives, most chiral Lewis acids showed *syn*-diastereoselectivity, and few catalyst systems to give *anti*-aldol adducts with high selectivity are known.[5] Therefore, development of *anti*-selective catalytic asymmetric aldol reactions is an important target in organic chemistry.

Recently, we have shown that chiral zirconium complexes prepared from zirconium alkoxide and chiral 1,1′-binaphthalene-2,2′-diol (BINOL) derivatives activate azomethine compounds

(1) Review: *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, Chapter 1.

(2) Reviews of catalytic asymmetric aldol reactions: (a) Carreira, E. M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, Y., Eds.; Springer: Heidelberg, 1999; Vol. 3, p 998. (b) Mahrwald, R. *Chem. Rev.* **1999**, *99*, 1095. (c) Groger, H.; Vogel, E. M.; Shibasaki, M. *Chem. Eur. J.* **1998**, *4*, 1137. (d) Nelson, S. G. *Tetrahedron: Asymmetry* **1998**, *9*, 357. (e) Bach, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 417.

(3) Recent examples of catalytic asymmetric Mukaiyama aldol reactions: (a) Kobayashi, S.; Mukaiyama, T. *Chem. Lett.* **1989**, 297. (b) Kobayashi, S.; Uchiro, H.; Fujishita, Y.; Shiina, I.; Mukaiyama, T. *J. Am. Chem. Soc.* **1991**, *113*, 4247. (c) Mukaiyama, T.; Kobayashi, S.; Uchiro, H.; Shiina, I. *Chem. Lett.* **1990**, 129. (d) Kobayashi, S.; Fujishita, Y.; Mukaiyama, T. *Chem. Lett.* **1990**, 1455. (e) Kobayashi, S.; Uchiro, H.; Shiina, I.; Mukaiyama, T. *Tetrahedron* **1993**, *49*, 1761. (f) Kobayashi, S.; Kawasuji, T.; Mori, N. *Chem. Lett.* **1994**, 217. (g) Furuta, K.; Maruyama, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1991**, *113*, 1041. (h) Ishihara, K.; Maruyama, T.; Mouri, M.; Gao, Q.; Furuta, K.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3483. (i) Parmee, R. M.; Tempkin, O.; Masamune, S. *J. Am. Chem. Soc.* **1991**, *113*, 9365. (j) Corey, E. J.; Cywin, C. L.; Roper, T. D. *Tetrahedron Lett.* **1992**, *33*, 6907. (k) Kiyooka, S.; Kaneko, Y.; Kume, K. *Tetrahedron Lett.* **1992**, *33*, 4927. (l) Evans, D. A.; Kozlowski, M. C.; Murry, J. A.; Burgey, C. S.; Campos, K. R.; Connel, B. T.; Staples, R. J. *J. Am. Chem. Soc.* **1999**, *121*, 669. (m) Evans, D. A.; Burgey, C. S.; Kozlowski, M. C.; Tregay, S. W. *J. Am. Chem. Soc.* **1999**, *121*, 686. (n) Mikami, K.; Matsukawa, S. *J. Am. Chem. Soc.* **1993**, *115*, 7039. (o) Keck, G. E.; Krishnamurthy, D. *J. Am. Chem. Soc.* **1995**, *117*, 2363. (p) Carreira, E. M.; Singer, R. A.; Lee, W. *J. Am. Chem. Soc.* **1994**, *116*, 8837. (q) Sodeoka, M.; Ohrai, K.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 2648. (r) Denmark, S. E.; Stavenger, R. A.; Wong, K.-T.; Su, X. *J. Am. Chem. Soc.* **1999**, *121*, 4982. (s) Krüger, J.; Carreira, E. M. *J. Am. Chem. Soc.* **1998**, *120*, 837.

(4) Direct asymmetric aldol reactions were reported: (a) Yamada, Y. M. A.; Yoshikawa, N.; Sasai, H.; Shibasaki, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1871. (b) Yoshikawa, N.; Yamada, Y. M. A.; Das, J.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1999**, *121*, 4168. (c) Yamada, Y. M. A.; Shibasaki, M. *Tetrahedron Lett.* **1998**, *39*, 5561. (d) List, B.; Lerner, R. A.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2000**, *122*, 2395. (e) Notz, W.; List, B. *J. Am. Chem. Soc.* **2001**, *123*, 7386. (f) List, B.; Pojarliev, P.; Castello, C. *Org. Lett.* **2001**, *3*, 573. (g) Trost, B. M.; Ito, H. *J. Am. Chem. Soc.* **2000**, *122*, 12003. (h) Trost, B. M.; Ito, H.; Silcoff, E. R. *J. Am. Chem. Soc.* **2001**, *123*, 3367. (i) Yoshikawa, N.; Kumagai, N.; Matsunaga, S.; Moll, G.; Ohshima, T.; Suzuki, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2001**, *123*, 2466. (j) Yoshikawa, N.; Shibasaki, M. *Tetrahedron*, **2001**, *57*, 2569. (k) Kumagai, N.; Matsunaga, S.; Yoshikawa, N.; Ohshima, T.; Shibasaki, M. *Org. Lett.* **2001**, *3*, 1539.

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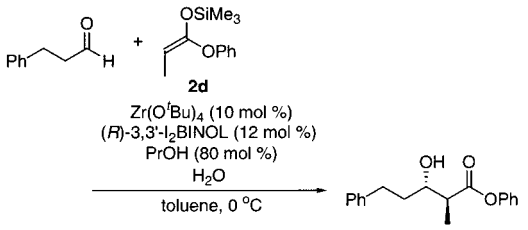
effectively to perform catalytic asymmetric Mannich-type reactions,[6] aza Diels−Alder reactions,[7] and Strecker reactions[8] in high yields with high selectivities.[9] It was shown in our studies that these chiral zirconium catalysts formed an excellent asymmetric environment close to the zirconium catalysts. Similarly, these catalysts were expected to activate aldehydes effectively. We then undertook a project to develop a new catalyst system in the Mukaiyama aldol reaction by using a novel chiral zirconium complex. After several trials, we found an effective catalyst system that mediated the aldol reactions efficiently under mild conditions.[10] In this article, we describe full details of this study.

Results and Discussion

In our initial investigations, a zirconium complex prepared from zirconium tetra-*tert*-butoxide ($Zr(O^tBu)_4$), (*R*)-3,3′-diiodo-1,1′-binaphthalene-2,2′-diol ((*R*)-3,3′-I_2BINOL), and a primary alcohol was shown to be an excellent Lewis acid catalyst for aldol reactions of silyl enol ethers with aldehydes. In most cases, the desired *anti*-aldol adducts were obtained in high yields with high diastereo- and enantioselectivities under mild conditions. However, in the course of our studies on reactions with aliphatic aldehydes, it was found that yields were lower than those of reactions with other aldehydes. In addition, it was revealed that some reactions were not reproducible. We carefully reexamined the reaction conditions and finally found that a small amount of water was essential for this catalyst system.[11] In the reaction of 3-phenylpropionealdehyde with the ketene silyl acetal derived from phenyl propionate (**2d**), the addition of a small amount of water improved yields and selectivities (Table 1, Chart 1). While the addition of 5−20 mol % of water gave the best results, the reaction did not proceed when 40 mol % of water was added.

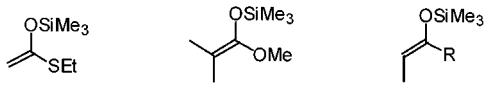
Table 1. Effect of Water



Entry	H_2O (mol %)	Yield/%	*syn*/*anti*	ee/%[a]
1[b]	——	38	12/88	85
2	H_2O (2)	37	16/84	79
3	H_2O (5)	62	14/86	89
4	H_2O (10)	65	15/85	88
5	H_2O (20)	61	14/86	89
6	H_2O (40)	trace	—	—

[a]Ee of *anti*-adducts. [b]Ref. 10.

Chart 1



2a **2b** **2c:** R = OMe **2d:** R = OPh **2e:** R = SEt

Since it was suggested that a small amount of water played an important role in the catalyst system, we decided to reinvestigate the effect of alcohols in the model aldol reaction of benzaldehyde with the silyl enol ether derived from *S*-ethyl ethanethioate (**2a**) (Table 2). It was revealed that the effect of water was significant in these substrates and that only 42% yield and 3% ee were obtained without water (Table 2, entry 1). In the presence of water, the reactions using normal primary alcohols such as ethanol, propanol, and butanol gave high yields and high enantioselectivities (entries 2−4). Other primary alcohols such as benzyl alcohol and 2,2,2-trifluoroethanol gave lower yields and selectivities (entries 5 and 6).[12] Secondary and tertiary alcohols such as 2-propanol and *tert*-butyl alcohol decreased the yields and selectivities (entries 7 and 8). Phenol also gave lower yield and selectivity (entry 9). When 80−120 mol % of propanol was used, the best yields and enantioselectivities were obtained (entries 11−13). On the other hand, the same levels of the yield and selectivity were obtained when zirconium tetrapropoxide−propanol complex ($Zr(OPr)_4$−PrOH) was employed instead of $Zr(O^tBu)_4$ (entry 15). The use of $Zr(OPr)_4$−PrOH is desirable from an economical point of view.

Other substrates were then examined, and the results are shown in Table 3. The ketene silyl acetal derived from methyl isobutyrate (**2b**) also worked well. For aldehydes, while aromatic and α,β-unsaturated aldehydes gave excellent yields and selectivities, aliphatic aldehydes showed high yields but somewhat lower selectivities. It should be noted that yields and enantioselectivities were improved by using a new catalyst system containing water.[10]

We then examined diastereoselective aldol reactions using this chiral zirconium catalyst. First, the ketene silyl acetal

(5) Recent examples of *anti*-selective aldol reactions: (a) Mikami, K.; Matsukawa, S. *J. Am. Chem. Soc.* **1994**, *116*, 4077. (b) Evans, D. A.; MacMillan, W. C.; Campos, K. R. *J. Am. Chem. Soc.* **1997**, *119*, 10859. (c) Yanagisawa, A.; Matsumoto, Y.; Nakashima, H.; Asakawa, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1997**, *119*, 9319. (d) Denmark, S. E.; Wong, K.-T.; Stavenger, R. A. *J. Am. Chem. Soc.* **1997**, *119*, 2333. (e) Parmee, E. R.; Hong, Y.; Tempkin, O.; Masamune, S. *Tetrahedron Lett.* **1992**, *33*, 1729.

(6) (a) Ishitani, H.; Ueno, M.; Kobayashi, S. *J. Am. Chem. Soc.* **1997**, *119*, 7153. (b) Kobayashi, S.; Ueno, M.; Ishitani, H. *J. Am. Chem. Soc.* **1998**, *120*, 431. (c) Ishitani, H.; Ueno, M.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 8180. (d) Kobayashi, S.; Hasegawa, Y.; Ishitani, H. *Chem. Lett.* **1998**, 1131. (e) Ishitani, H.; Kitazawa, H.; Kobayashi, S. *Tetrahedron Lett.* **1999**, *40*, 2161.

(7) (a) Kobayashi, S.; Komiyama, S.; Ishitani, H. *Angew. Chem., Int. Ed.* **1998**, *37*, 979. (b) Kobayashi, S.; Kusakabe, K.; Komiyama, S.; Ishitani, H. *J. Org. Chem.* **1999**, *64*, 4220. (c) Kobayashi, S.; Kusakabe, K.; Ishitani, H. *Org. Lett.* **2000**, *2*, 1225.

(8) (a) Ishitani, H.; Komiyama, S.; Kobayashi, S. *Angew. Chem., Int. Ed.* **1998**, *37*, 3186. (b) Ishitani, H.; Komiyama, S.; Hasegawa, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 762.

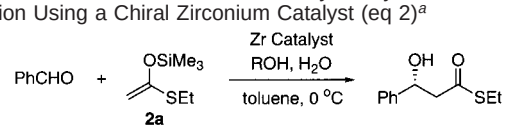
(9) For other examples of catalytic asymmetic reactions based on zirconium−BINOL complexes: (a) Bedeschi, P.; Casolari, S.; Costa, A. L.; Tagliavini, E.; Umani-Ronchi, A. *Tetrahedron Lett.* **1995**, *36*, 7897. (b) Casolari, S.; Cozzi, P. G.; Orioli, P.; Tagliavini, E.; Umani-Ronchi, A. *Chem. Commun.* **1997**, 2123. (c) Yu, C.-M.; Yoon, S.-K.; Choi, H.-S.; Baek, K. *Chem. Commun.* **1997**, 763. (d) Volk, T.; Korenaga, T.; Matsukawa, S.; Terada, M.; Mikami, K. *Chirality* **1998**, *10*. 717. (e) Ringwald, M.; Stürmer, R.; Brintzinger, H. H. *J. Am. Chem. Soc.* **1999**, *121*, 1524. (f) Bolm, C.; Beckmann, O. *Chirality* **2000**, *12*, 523. (g) Hanawa, H.; Kii, S.; Asao, N.; Maruoka, K. *Tetrahedron Lett.* **2000**, *41*, 5543.

(10) For a preliminary communication, see: Ishitani, H.; Yamashita, Y.; Shimizu, H.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 5403.

(11) In some metal-catalyzed asymmetric reactions, water affected the yields and selectivities: Ribe, S.; Wipf, P. *Chem. Commun.* **2001**, 299. Mikami, K. et al. also reported that a small amount of water affected catalytic enantioselective ene reactions using a Ti−BINOL complex; see: (a) Terada, M.; Matsumoto, Y.; Nakamura, Y.; Mikami, K. *Chem. Commun.* **1997**, 281. (b) Terada, M.; Matsumoto, Y.; Nakamura, Y.; Mikami, K. *J. Mol. Catal. A* **1998**, *132*, 165. (c) Mikami, K.; Terada, M.; Matsumoto, Y.; Tanaka, M.; Nakamura, Y. *Microporous Mesoporous Mater.* **1998**, *21*, 461. (d) Terada, M.; Matsumoto, Y.; Nakamura, Y.; Mikami, K. *Inorg. Chim. Acta* **1999**, *296*, 267.

(12) Katsuki and Evans reported independently that a fluorinated alcohol accelerated catalytic asymmetric reactions; see: (a) Kitajima, H.; Katsuki, T. *Synlett* **1997**, 568. (b) Evans, D. A.; Johnson, D. S. *Org. Lett.* **1999**, *1*, 595.

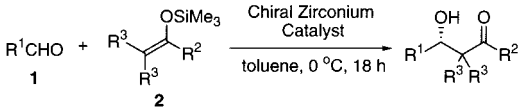
Table 2. Effect of Alcohols in the Catalytic Asymmetric Aldol Reaction Using a Chiral Zirconium Catalyst (eq 2)[a]



Entry	ROH (mol%)	Yield/%	ee/%
1[b]	PrOH (50)	42	3
2	EtOH (50)	85	87
3	PrOH (50)	94	88
4	BuOH (50)	92	86
5	BnOH (50)	76	76
6	CF_3CH_2OH (50)	47	62
7	^{i}PrOH (50)	87	85
8	^{t}BuOH (50)	39	44
9	PhOH (50)	36	54
10	PrOH (30)	68	74
11	PrOH (80)	91	95
12	PrOH (100)	95	95
13	PrOH (120)	94	95
14	PrOH (160)	95	91
15[c]	PrOH (60)	98	92

[a]All reactions were performed at 0 °C for 14 h in the presence of a zirconium catalyst prepared from $Zr(O^tBu)_4$ (10 mol %), (*R*)-3,3′-I_2BINOL (12 mol %), ROH (x mol %), and H_2O (20 mol %). [b] Without H_2O. [c] $Zr(OPr)_4$-PrOH was used instead of $Zr(O^tBu)_4$.

Table 3. Catalytic Asymmetric Aldol Reactions Using the Chiral Zirconium Catalyst[a]

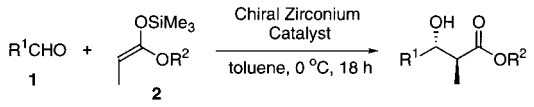


Entry	Aldehyde **1**; R^1	Silyl enolate **2**	Yield/%	ee/%
1	Ph	**2b**	95	98
2	Ph	**2a**	91	95
3	*p*-MeOPh	**2a**	92	96
4	CH_3CH=CH	**2a**	76	97
5	PhCH=CH	**2a**	94	95
6	$PhCH_2CH_2$	**2b**	92	80
7	C_5H_{11}	**2b**	93 (93)[b]	84 (87)[b]

[a]The catalyst was prepared from $Zr(O^tBu)_4$ (10 mol %), (*R*)-3,3′-I_2BINOL (12 mol %), PrOH (80 mol %) and H_2O (20 mol %). [b]The reaction was performed at –20 °C.

derived from methyl propionate (**2c**) was employed in the reaction with benzaldehyde. The reaction proceeded smoothly to afford the desired *anti*-aldol adduct in high yield with high diastereo- and enantioselectivities when ethanol was used as a primary alcohol. The selectivities were further improved using the ketene silyl acetal derived from phenyl propionate (**2d**). We tested other aldehydes such as anisaldehyde, *p*-chlorobenzaldehyde, cinnamaldehyde, and 3-phenylpropionealdehyde, etc., and in all cases the reactions proceeded smoothly and the desired *anti*-aldol adducts were obtained in high yields with high diastereo- and enantioselectivities.[13]

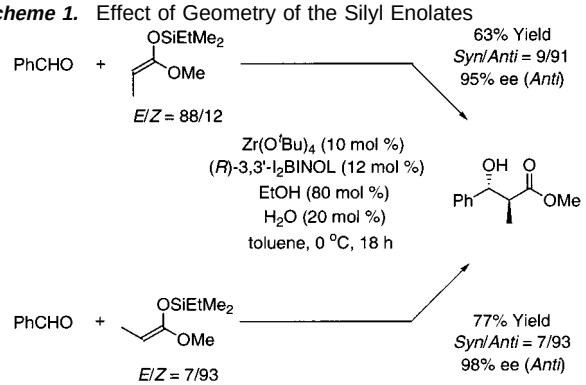
Table 4. Diastereoselective Aldol Reactions[a]



Entry	Aldehyde **1**; R^1	Silyl enolate **2**	ROH	Yield /%	*syn*/*anti*	ee /%
1	Ph	**2c**	PrOH	79	7/93	96
2	Ph	**2c**	EtOH	87	7/93	97
3	Ph	**2d**	PrOH	94	5/95	99
4	Ph	**2d**	EtOH	90	4/96	99
5	*p*-MeOPh	**2d**	PrOH	89	7/93	98
6	*p*-ClPh	**2d**	PrOH	96	9/91	96
7	CH_3CH=CH	**2d**	PrOH	65	11/89	92
8	PhCH=CH	**2d**	PrOH	92	15/85	98
9	$PhCH_2CH_2$	**2d**	PrOH	61	14/86	89

[a]The catalyst was prepared from $Zr(O^tBu)_4$ (10 mol %), (*R*)-3,3′-I_2BINOL (12 mol %), ROH (80 mol %), and H_2O (20 mol %).

Scheme 1. Effect of Geometry of the Silyl Enolates



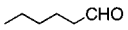
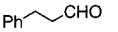
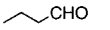
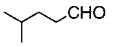
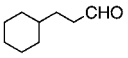
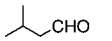
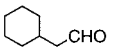
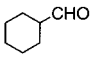
Although the high *anti*-selectivities observed in these reactions are remarkable, examination of the effect of the geometry of the ketene silyl acetals revealed further important information on the selectivity. Namely, when the (*E*)- and (*Z*)-ketene silyl acetals derived from methyl propionate were employed in the reactions with benzaldehyde, high *anti*-selectivities were obtained in both cases, and it was confirmed that the selectivities were independent of the geometry of the ketene silyl acetals.[14] For the transition states of these reactions, acyclic pathways are assumed (details are discussed in the following paragraphs).

Further investigations on the effect of the aldehyde structures were performed. Reactions of other aliphatic aldehydes were examined using a chiral zirconium catalyst consisting of Zr-(O^tBu)$_4$, (*R*)-3,3′-I_2BINOL, propanol, and water. In the cases of employing normal linear aliphatic aldehydes such as hexanal and butanal, the reactions proceeded in high selectivities. γ-Branched aldehydes also reacted smoothly to afford the desired *anti*-adducts in good yields with high diastereo- and enantioselectivities. On the other hand, the catalyst did not work

(13) The results shown in Table 4 were obtained in 0.4-mmol-scale experiments. The reaction of benzaldehyde with **2d** was carried out in a 10-mmol-scale experiment, and the same level of yield and selectivities was obtained (99% yield, *syn*/*anti* = 7/93, 99% ee (*anti*). See Table 4, entry 3). In addition, the present catalytic asymmetric aldol reaction was successfully used in an initial stage of the total synthesis of Khafrefungin; see: Kobayashi, S.; Mori, K.; Wakabayashi, T.; Yasuda, S.; Hanada, K. *J. Org. Chem.* **2001**, *66*, 5580.

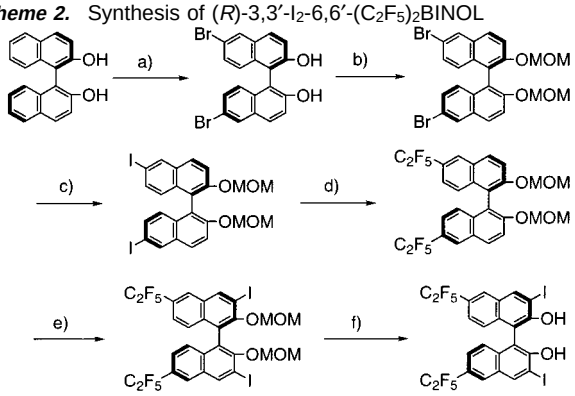
(14) Evans et al. reported chiral tin-catalyzed *anti*-selective aldol-type reactions of pyruvate esters with silyl thioketene acetals.[5b] In these reactions, both (*E*)- and (*Z*)-silyl thioketene acetals gave *anti*-adducts.

Table 5. Effect of Structures of Aliphatic Aldehydes in Reactions with **2d**[a]

Entry	Aldehyde **1**	Yield/%	*syn*/*anti*	ee/%
1		64	12/88	85
2		71	10/90	82
3		71	15/85	81
4		56	12/88	89
5		52	14/86	78
6		16	17/83	28
7		14	21/79	31
8		trace	—	—

[a] The catalyst was prepared from $Zr(O^tBu)_4$ (20 mol %), (*R*)-3,3′-I_2BINOL (24 mol %), ROH (160 mol %), and H_2O (20 mol %).

Scheme 2. Synthesis of (*R*)-3,3′-I_2-6,6′-$(C_2F_5)_2$BINOL



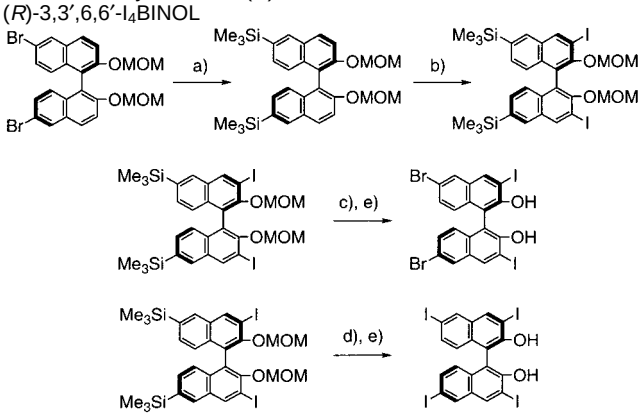
a) Br_2/CH_2Cl_2, b) NaH, MOMCl/THF, c) ^nBuLi, I_2/THF, d) $Me_3SiC_2F_5$, KF, CuI/DMF, e) ^sBuLi, I_2/THF, f) HCl/MeOH

well in the reactions of α- and *β*-branched aliphatic aldehydes. These effects seemed to be caused by steric interaction between the BINOL parts (especially large diiodo atoms at the 3,3′-positions) of the catalysts and the alkyl moieties of the aldehydes. From these results, it was indicated that the environment around the zirconium of the catalyst was crowded and that the catalyst recognized the structure of the aldehydes strictly.

Improvement of the Catalyst Activity. To create more effective catalyst systems, improvement of the catalyst activity is an important subject. In our laboratory, it was recently revealed that introduction of stronger electron-withdrawing groups at the 6,6′-positions of the binaphthyl rings was effective to improve Lewis acidity of the catalyst system.[6c] We then examined the effect of stronger electron-withdrawing groups at the 6,6′-positions of (*R*)-3,3′-I_2BINOL in this aldol system. We chose bromo, iodo, and pentafluoroethyl groups as the electron-withdrawing groups. These BINOL derivatives were literature-unknown compounds, and we first started to synthesize (*R*)-3,3′-diiodo-6,6′-bis(pentafluoroethyl)-1,1′-binaphthyl-2,2′-diol ((*R*)-3,3′-I_2-6,6′-$(C_2F_5)_2$BINOL) according to Scheme 2.

(*R*)-6,6′-Br_2BINOL was converted to its methoxymethyl (MOM) ether, whose bromine groups at the 6,6′-positions were first converted to iodo groups using I_2 [6c] and then pentafluoroethyl groups using CuC_2F_5 in DMF,[15] to afford (*R*)-2,2′-bis(methoxymethyloxy)-6,6′-bis(pentafluoroethyl)-1,1′-binaphthyl. After lithiation and iodonation at the 3,3′-positions and deprotection of the MOM groups, (*R*)-3,3′-I_2-6,6′-$(C_2F_5)_2$BINOL was isolated as colorless needles. On the other hand, (*R*)-6,6′-dibromo-3,3′-diiodo-1,1′-binaphthyl-2,2′-diol ((*R*)-6,6′-Br_2-3,3′-I_2BINOL) and (*R*)-3,3′,6,6′-tetraiodo-1,1′-binaphthyl-2,2′-diol ((*R*)-3,3′,6,6′-I_4BINOL) were synthesized according to Scheme 3. In a way similar to that shown in Scheme 2, (*R*)-6,6′-Br_2-BINOL was converted to its methoxymethyl (MOM) ether. The bromo groups at the 6,6′-positions were lithiated and trimethylsilylated, and then the 3,3′-positions were lithiated and iodonated. Finally, treatment with bromine or iodinemonochloride(ICl) afforded (*R*)-3,3′-I_2-6,6′-Br_2BINOL or (*R*)-3,3′,6,6′-I_4BINOL, respectively.[16]

Scheme 3. Synthesis of (*R*)-3,3′-I_2-6,6′-Br_2BINOL and (*R*)-3,3′,6,6′-I_4BINOL



a) ^nBuLi, Me_3SiCl/THF, b) ^sBuLi, I_2/THF, c) Br_2/CCl_4, d) ICl/CCl_4, e) HCl/MeOH

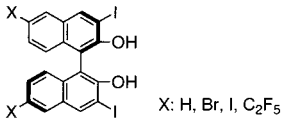
We then evaluated the catalyst activities of the zirconium complexes prepared from new BINOL derivatives in the aldol reaction of benzaldehyde with the silyl enol ether derived from *S*-ethyl propanethioate (**2e**). Compared with the catalyst prepared from 3,3′-I_2BINOL, the new catalysts prepared from 6,6′-disubstituted-3,3′-I_2BINOL showed higher activities and the reaction proceeded much faster. In particular, the iodo and pentafluoroethyl groups at the 6,6′-positions showed better results to give the desired *anti*-adducts in high yields with high diastereo- and enantioselectivities (Table 6). The new catalyst system was successfully applied to the reactions of aliphatic aldehydes. In the reactions of hexanealdehyde with the silyl enol ether derived from phenyl propionate (**2d**) and *S*-ethyl propanethioate (**2e**), the best results were obtained when (*R*)-3,3′,6,6′-I_4BINOL was employed (Table 7). The electron-withdrawing substituents at the 3,3′- and 6,6′-positions of the BINOL derivatives were assumed to increase Lewis acidities of the zirconium catalysts. By changing the chiral ligands, chemical yields were much more improved (38% to 71% in Table 6, entries 1 and 4; 9% to 92% in Table 7, entries 4 and 6) than enantioselectivity (80% ee to 87% ee in Table 7, entries 1 and 3). We calculated charges on the oxygen atoms of the BINOL derivatives, and the calculated charges were shown in Table 8. It was revealed that the order of the catalyst activities

(15) Urata, H.; Fuchikami, T. *Tetrahedron Lett.* **1991**, *32*, 91.
(16) (a) Felix, G.; Dunogues, J.; Pisciotti, F.; Calas, R. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 488. (b) Felix, G.; Dunogues, J.; Calas, R. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 402.

Table 6. Improvement of Catalyst Reactivity in the Aldol Reaction of Benzaldehyde and Silyl Enolate **2e**[a]

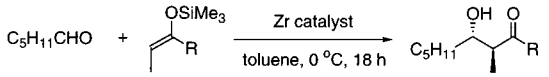
Entry	BINOL derivatives	Yield/%	*syn*/*anti*	ee/%[b]
1	(*R*)-3,3'-I_2BINOL (6 mol%)	38	5/95	96
2	(*R*)-3,3'-I_2-6,6'-Br_2BINOL (7.5 mol%)	61	4/96	98
3	(*R*)-3,3',6,6'-I_4BINOL (7.5 mol%)	70	4/96	98
4	(*R*)-3,3'-I_2-6,6'-$(C_2F_5)_2$BINOL (7.5 mol%)	71	7/93	96

[a] $Zr(O^tBu)_4$ (5 mol %) and PrOH (50 mol %), H_2O (10 mol %) were used. The reactions were performed at 0 °C for 3 h. [b] Ee of *anti*-adduct.



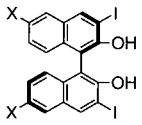
(*R*)-3,3'-I_2-6,6'-X_2BINOL

Table 7. Effect of New BINOLs in the Reactions of Hexanaldehyde[a]



Entry	X	Silyl enolate	Yield/%	*syn*/*anti*	ee/% (*anti*)
1	H	**2d**	53	16/84	80
2	C_2F_5	**2d**	39	11/89	84
3	I	**2d**	66	12/88	87
4	H	**2e**	9	12/88	93
5	C_2F_5	**2e**	80	17/83	93
6	I	**2e**	92	11/89	93

[a] The catalyst was prepared from $Zr(O^tBu)_4$ (10 mol %), (*R*)-3,3'-I_2-6,6'-X_2BINOL (12-15 mol %), PrOH (80 mol %), H_2O (20 mol %).



(*R*)-3,3'-I_2-6,6'-X_2BINOL

Table 8. Calculated Charges on the Oxygen Atoms of the BINOL Derivatives

BINOL derivatives	charge
BINOL	−0.227
3,3′-I_2BINOL	−0.204
3,3′-I_2-6,6′-Br_2BINOL	−0.201
3,3′,6,6′-I_4BINOL	−0.202
3,3′-I_2-6,6′-$(C_2F_5)_2$BINOL	−0.197

was almost corresponding to that of the electron density of the BINOL derivatives.[17]

Structure of the Chiral Catalyst. NMR experiments were performed to clarify the structure of the chiral zirconium catalyst. The catalyst was prepared from 1 equiv of zirconium tetrapropoxide−propanol complex ($Zr(OPr)_4$−PrOH), 1 equiv of 3,3′-I_2BINOL, and 1 equiv of H_2O in toluene-d_8.[18] ^1H and ^{13}C NMR were measured at room temperature, and clear and simple signals were observed (Figure 1). It was revealed that this catalyst was stable in the presence of excess propanol at room temperature and that almost the same spectra were obtained after 1 day. On the ^{13}C NMR spectrum, new two kinds of signals that corresponded to the naphthyl rings and two kinds of signals that corresponded to the propoxide groups were observed besides the signals that corresponded to the free BINOL. The existence of these two kinds of sharp signals suggested that the catalyst would form a dimeric structure. We also observed characteristic signals of the propoxide protons that were directly connected to the carbon atoms attached to the oxygen atoms at 3.8, 4.0, 4.8, and 5.2 ppm in the ^1H NMR spectrum. The integration of the proton signals indicated the existence of two kinds of propoxide moieties (one pair was observed at 3.8 and 4.0 ppm; another was at 4.8 and 5.2 ppm) in the catalyst and that the ratio was 2:1.

The role of a small amount of water in this catalyst system was also revealed by NMR analyses.[19] In the absence of PrOH and water, a clear ^{13}C NMR spectrum was obtained by the combination of $Zr(O^tBu)_4$ and 3,3′-I_2BINOL (Figure 2a). When PrOH was added to this system, rather complicated signals were observed (Figure 2b). On the other hand, clear signals appeared once again when water was added to the catalyst system consisting of $Zr(O^tBu)_4$, 3,3′-I_2BINOL, and PrOH (Figure 2c). From these results, it was assumed that the role of water in this catalyst system was to put the catalyst structure in order. Namely, the desired structure was formed from the oligomeric structure by adding water. This assumption was also supported by the following experiment: we prepared the catalyst from $Zr(O^tBu)_4$, 3,3′-I_2BINOL, and PrOH in the presence of water and performed the aldol reaction in the presence of 4Å molecular sieves by using this catalyst.[20] It was revealed that the desired aldol adduct was obtained with high selectivity. This result also strongly supported that the water did not influence the aldol reaction but affected the formation of the catalyst.

In view of the dimeric structure of the catalyst, we examined the possibility of a nonlinear effect in the asymmetric aldol reaction.[21] The reaction of benzaldehyde with the silyl enol ether derived from *S*-ethyl ethanethioate (**2a**) was chosen as a model, and the chiral Zr catalysts prepared from 3,3′-I_2BINOLs with lower enantiomeric excesses were employed. It was found that a remarkable level of positive nonlinear effect was observed as illustrated in Figure 3. On the other hand, after the chiral Zr catalysts were prepared from (*R*)-3,3′-I_2BINOL and (*S*)-3,3′-I_2-BINOL, respectively, they were combined and correlation between the ee of the zirconium catalyst and the ee of the product was investigated. In this case, a linear correlation between them was obtained (Figure 4).[22] These results might also support the dimeric structure of the catalyst, and on the basis of these experiments, we assumed the catalyst structure was as shown in Figure 5.[23]

(17) All charges shown in Table 8 were evaluated by the natural population analysis (NPA). NBO 4.0: Glendening, E. D.; Badenhoop, J. K.; Reed, A. E.; Carpenter, J. E.; Weinhold, F.; Theoretical Chemistry Institute, University of Wisconsin, Madison, 1996.

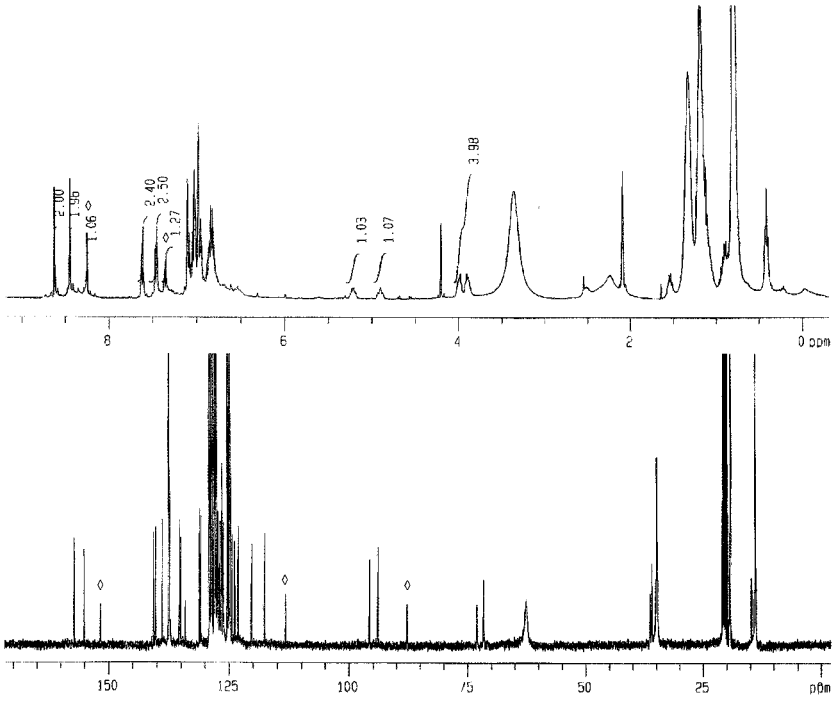
(18) Almost similar spectra were obtained in the catalyst prepared from $Zr(O^tBu)_4$, (*R*)-3,3′-I_2BINOL, PrOH, and H_2O.

(19) Mikami et al. speculated that a small amount of water composed an active Ti−BINOL catalyst by forming μ_3-oxo complex. See ref 11a−d.

(20) The reaction of benzaldehyde with the silyl thioketene acetal derived from *S*-ethyl ethanethioate (**2a**) was performed in the presence of 4Å MS at 0 °C for 18 h using a chiral zirconium catalyst prepared from from $Zr(O^tBu)_4$ (10 mol %), (*R*)-3,3′-I_2BINOL (12 mol %), PrOH (50 mol %), and H_2O (20 mol %). The desired product was obtained in 83% yield with 88% ee.

(21) Girard, C.; Kagan, H. B. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2922.

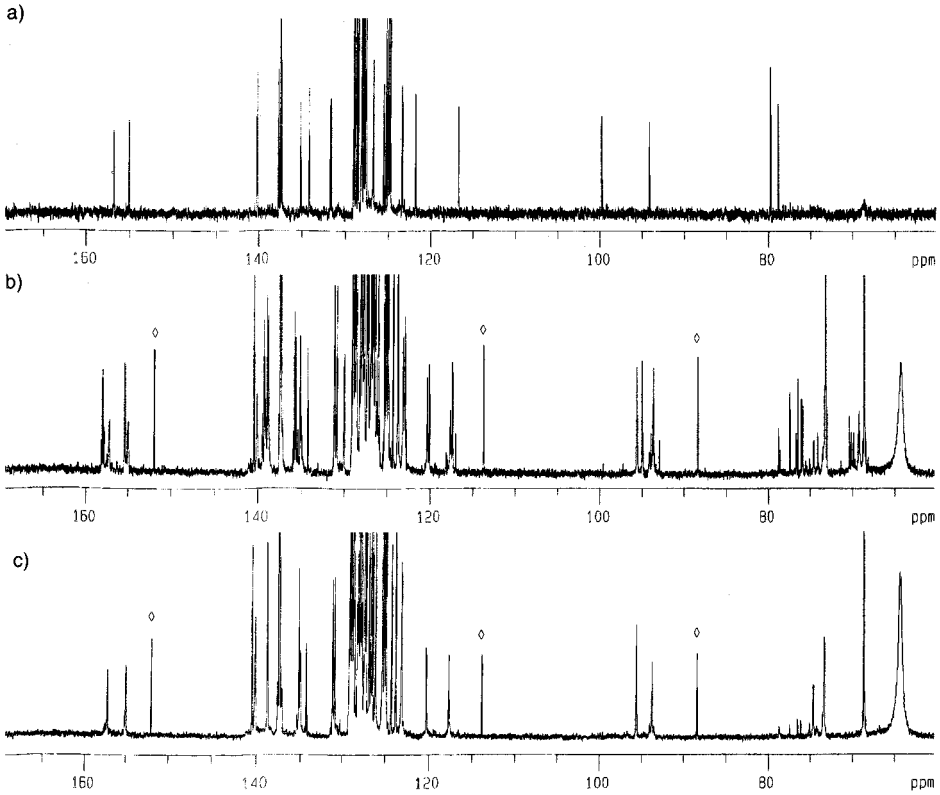
(22) Mikami, K.; Motoyama, T.; Terada, M. *J. Am. Chem. Soc.* **1994**, *116*, 2812.



[a] The complex was prepared from $Zr(OPr)_4$-PrOH (1.0 equiv.), (*R*)-3,3'-I_2BINOL (1.0 equiv.), and H_2O (1.0 equiv.).

◊: free 3,3'-I_2BINOL

Figure 1. ^1H and ^{13}C NMR spectra of the zirconium complex.[a]



a) $Zr(O^tBu)_4$ (1.0 equiv.) + (*R*)-3,3'-I_2BINOL (1.0 equiv.)

b) $Zr(O^tBu)_4$ (1.0 equiv.) + (*R*)-3,3'-I_2BINOL (1.0 equiv.) + PrOH (5.0 equiv.)

c) Sample b) +PrOH (2.0 equiv.) + H_2O (1.0 equiv.)

◊: free 3,3'-I_2BINOL

Figure 2. Effect of water.

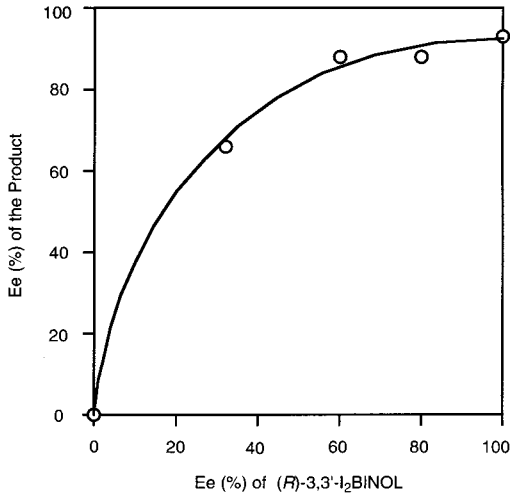


Figure 3. Correlation between the ee of the product and the ee of (*R*)-3,3′-I_2BINOL in the aldol reaction using the catalyst prepared from (*R*)-3,3′-I_2BINOLs with low ee's.

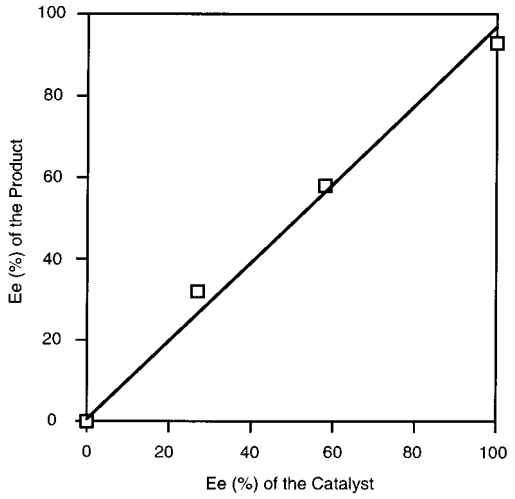
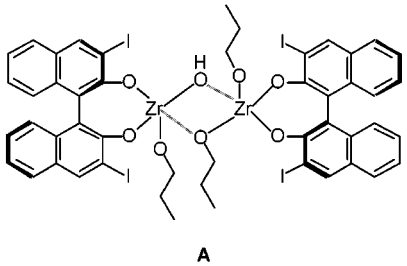


Figure 4. Correlation between the ee of the product and the ee of the catalyst in the aldol reaction using the catalyst prepared by mixing (*R*)- and (*S*)-catalyst.



A

Figure 5. Assumed catalyst structure.

The zirconium catalyst showed *anti*-selectivity independent of enolate geometry. This remarkable feature was in contrast to most *syn*-selective aldol reactions mediated by chiral Lewis acids.[3] In the usual cases affording *syn*-aldol adducts, the selectivity was explained by steric repulsion between the alkyl groups of aldehydes and the α-methyl groups of enolates in acyclic transition state models.[2a,b] In the present reactions, *anti*-aldol adducts were obtained from both (*E*)- and (*Z*)-enolates, showing that acyclic transition states were most likely. We speculated that the origin of the *anti*-selectivity was ascribed to steric interaction between the alkyl groups of aldehydes and not the α-methyl groups of enolates but chiral Lewis acids coordinated to carbonyl oxygens (Figure 6).[24] The asymmetric environment around the zirconium center seemed to be very crowded because of the existence of the bulky iodo groups at the 3,3′-positions of BINOL derivatives. Moreover, the experiments wherein this zirconium complex strictly recognized the structures of aliphatic aldehydes also seemed to indicate the highly steric hindrance around the active site of the catalyst.

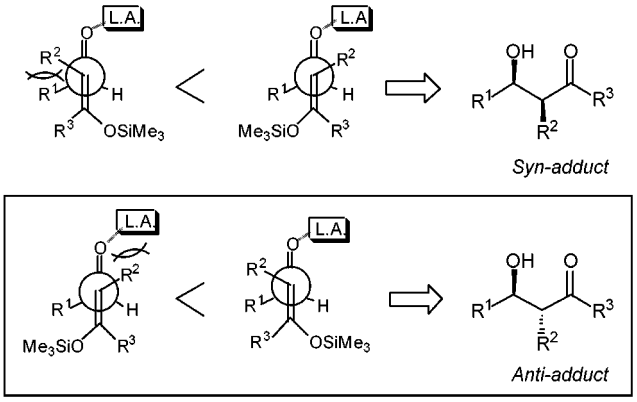
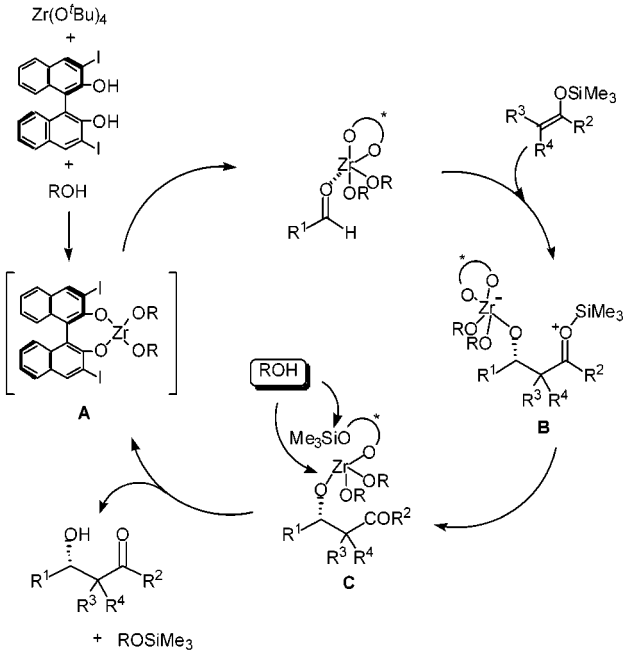


Figure 6. Assumed transition states for the *anti*-selectivity.

Scheme 4. Assumed Catalytic Cycle of the Aldol Reaction



Catalytic Cycle. An assumed catalytic cycle of this aldol reaction is shown in Scheme 4. First, the zirconium catalyst **A** is produced by mixing $Zr(O^tBu)_4$, (*R*)-3,3′-I_2BINOL, a primary alcohol, and H_2O. At this stage, the remaining *tert*-butoxide groups are exchanged for the primary alcohols or H_2O. An aldehyde coordinated to this catalyst, and a silyl enol ether attacks the carbonyl carbon of the aldehyde to generate

(23) One of reviewers pointed out that the structure might be symmetrical oligomers.

(24) (a) Mukaiyama, T.; Kobayashi, S.; Murakami, M. *Chem. Lett.* **1985**, 447. (b) Gennari, C.; Beretta, M., G.; Bernardi, A.; Moro, G.; Scolastico, C.; Todeschini, R. *Tetrahedron* **1986**, *42*, 893.

intermediate **B**. Then, the silyl group on the carbonyl oxygen moves to the most anionic atom in the same complex, the oxygen of the binaphthol, to form intermediate **C**. Finally, the primary alcohol reacts with this intermediate **C**, and the Si−O bond or the Zr−O bond is cleaved. In the case of the cleavage of the Si−O bond, the produced anionic oxygen attacks Zr and the aldol product is obtained along with regeneration of the original complex. On the other hand, when the Zr−O bond is cleaved, another alcohol cleaves the Si−O bond. This mechanism is supported by the fact that aldol adducts are obtained with free hydroxyl groups and that trimethyl silyl ethers of alcohols are observed by GC−MS analysis.[25]

Conclusion

We have developed *anti*-selective asymmetric aldol reactions that proceeded at 0 °C under mild protic conditions to afford the desired adducts in high yields with high diastereo- and enantioselectivities, using a novel chiral zirconium catalyst prepared from $Zr(O^tBu)_4$, (*R*)-3,3′-I_2BINOL, an alcohol, and water. The alcohol played an important role in the catalyst turnover, and water affected the formation of the catalyst. Furthermore, catalysts with high activities were prepared by using the BINOLs substituted by stronger electron-withdrawing groups. By NMR studies, it was assumed that the catalyst formed a dimeric structure tightly in toluene. Use of the protic additives is a unique feature of this reaction compared to other traditional catalytic asymmetric aldol reactions, and it is expected that this catalyst system is effective for other asymmetric reactions of aldehydes.

Experimental Section

Typical Experimental Procedure for Asymmetric Aldol Reactions Using Chiral Zirconium Catalyst. A typical experimental procedure is described for the reaction of benzaldehyde with silyl enol ether **2a**. To a suspension of (*R*)-3,3′-diiodo-1,1′-binaphthalene-2,2′-diol (0.048 mmol) in toluene (1.0 mL) was added $Zr(O^tBu)_4$ (0.040 mmol) in toluene (1.0 mL) at room temperature, and the solution was stirred for 30 min. Then propanol (0.32 mmol) and H_2O (0.080 mmol) in toluene (0.5 mL) were added, and the whole was stirred for 3 h at room temperature.[26] After cooling at 0 °C, benzaldehyde (0.40 mmol) in toluene (0.75 mL) and silyl enol ether **2a** (0.48 mmol) in toluene (0.75 mL) were successively added. The mixture was stirred for 18 h, and saturated aqueous $NaHCO_3$ (10 mL) was added to quench the reaction. After added dichloromethane (10 mL), the organic layer was separated and the aqueous layer was extracted twice with dichloromethane (10 mL × 2). The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the residue was treated with THF−1 N HCl (20:1) for 1 h at 0 °C. Then the solution was basicified with saturated aqueous $NaHCO_3$ and extracted with dichloromethane. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by preparative thin-layer chromatography (benzene−ethyl acetate 20:1) to afford the desired aldol adduct. The optical purity was determined by HPLC analysis using a chiral column (see below). In some compounds, the optical purity was determined after acetylation or benzoylation of the hydroxy group.

Phenyl 3-Hydroxy-2-methyl-3-(4-methoxyphenyl)propanoate. IR [cm^{-1}] (neat) 3491, 1756, 1611, 1592, 1514, 1493, 1457, 1375, 1304, 1250. ^1H NMR ($CDCl_3$) *anti* isomer δ 1.14 (d, 3H, J = 7.0 Hz), 2.74 (br, 1H), 3.03 (dq, 1H, J = 8.8, 7.3 Hz), 3.81 (s, 3H), 4.82 (d, 1H, J = 8.6 Hz), 6.91 (d, 2H, J = 8.8 Hz), 7.08 (m, 2H), 7.21−7.40 (m, 5H); detectable peaks of *syn* isomer δ 1.34 (d, 3H, J = 7.1 Hz), 5.07 (d, 1H, J = 5.6 Hz). ^{13}C NMR ($CDCl_3$) *anti* isomer δ 14.3, 47.5, 55.2, 76.0, 113.8, 121.5, 125.8, 127.9, 129.3, 133.5, 150.5, 159.4, 174.4; detectable peaks of *syn* isomer δ 11.9, 47.1, 55.2, 74.0, 113.7, 121.3, 127.4, 129.3, 129.4, 133.6, 150.3, 159.1, 173.8. HRMS (*m*/*z*) calcd for $C_{17}H_{18}O_4$ (M^+) 286.1205, found 286.1202. HPLC (after acetylation), Daicel Chiralcel OD, hexane/^{i}PrOH = 30/1, flow rate = 0.5 mL/min: *syn* isomer t_R = 17.8 min (major), t_R = 22.5 min (minor); *anti* isomer t_R = 19.7 min (major), t_R = 24.3 min (minor).

Phenyl 3-Hydroxy-2-methyl-3-(4-chlorophenyl)propanoate. IR [cm^{-1}] (neat) 3480, 1754, 1594, 1491, 1457, 1412, 1376, 1309, 1227. ^1H NMR ($CDCl_3$) *anti* isomer δ 1.17 (d, 3H, J = 7.1 Hz), 2.91 (br, 1H), 3.01 (dq, 1H, J = 8.2, 7.1 Hz), 4.83 (d, 1H, J = 8.2 Hz), 7.02−7.05 (m, 2H), 7.20−7.40 (m, 7H); detectable peaks of *syn* isomer δ 1.29 (d, 3H, J = 7.1 Hz), 5.15 (d, 1H, J = 4.8 Hz), 6.94 (d, 2H, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$) *anti* isomer δ 14.2, 47.3, 75.5, 121.4, 125.9, 128.0, 128.6, 129.4, 133.8, 139.8, 150.4, 174.1; detectable peaks of *syn* isomer δ 11.2, 47.0, 73.2, 121.3, 127.5, 128.4, 133.3, 139.9, 150.2, 173.7. HRMS (*m*/*z*) calcd for $C_{16}H_{15}O_3Cl$ (M^+) 290.0710, found 290.0706. HPLC (after acetylation), Daicel Chiralcel OD, hexane/^{i}PrOH = 60/1, flow rate = 0.5 mL/min: *syn* isomer t_R = 21.5 min (major), t_R = 31.1 min (minor); *anti* isomer t_R = 23.6 min (major), t_R = 33.6 min (minor).

Phenyl (*E*)-3-Hydroxy-2-methyl-4-hexenoate. IR [cm^{-1}] (neat) 3442, 1757, 1673, 1593, 1493, 1457, 1377, 1233. ^1H NMR ($CDCl_3$) *anti* isomer δ 1.28 (d, 3H, J = 7.1 Hz), 1.74 (dd, J = 6.4, 1.5 Hz), 2.79 (dq, 1H, J = 7.6, 7.3 Hz), 4.28 (dd, 1H, J = 7.6, 7.6 Hz), 5.53 (ddq, 1H, J = 15.4, 7.6, 1.7 Hz), 5.79 (dq, 1H, J = 15.4, 6.3 Hz), 7.08 (m, 2H), 7.22 (m, 1H), 7.37 (m, 2H); detectable peaks of *syn* isomer δ 1.33 (d, 3H, J = 7.1 Hz), 2.85 (dq, 1H, J = 7.3, 2.2 Hz), 4.42 (dd, 1H, J = 5.9, 5.9 Hz), 5.60 (ddq, 1H, J = 15, 6.8, 1.5 Hz). ^{13}C NMR ($CDCl_3$); *anti* isomer δ 13.9, 17.7, 45.8, 74.9, 121.5, 125.9, 129.4, 129.5, 130.8, 150.5, 174.2; detectable peaks of *syn* isomer δ 11.9, 45.4, 73.5, 121.4, 125.9, 128.9, 130.2, 173.7. HRMS (*m*/*z*) calcd for $C_{13}H_{16}O_3$ (M^+) 220.1099, found 220.1073. HPLC (after acetylation), Daicel Chiralcel OJ, hexane/^{i}PrOH = 9/1, flow rate = 0.5 mL/min: *syn* isomer t_R = 48 min (minor), t_R = 64 min (major); *anti* isomer t_R = 21.1 min (minor), t_R = 22.5 min (major).

Phenyl (*E*)-3-Hydroxy-2-methyl-5-phenyl-4-pentenoate. IR [cm^{-1}] (neat) 3446, 1756, 1653, 1593, 1493, 1455, 1376, 1241. ^1H NMR ($CDCl_3$) *anti* isomer δ 1.36 (d, 3H, J = 7.1 Hz), 2.59 (br, 1H), 2.92 (dq, 1H, J = 7.3 Hz, 7.1 Hz), 4.51 (dd, 1H, J = 7.3 Hz, 7.0 Hz), 6.25 (dd, 1H, J = 16 Hz, 7.0 Hz), 6.69 (d, 1H, J = 16 Hz), 7.07 (d, 2H, J = 7.7 Hz), 7.17−7.41 (m, 8H); detectable peaks of *syn* isomer δ 1.38 (d, 3H, J = 7.3 Hz), 2.92−3.02 (m, 1H), 4.69 (ddd, 1H, J = 7.7, 4.6, 1.3 Hz), 6.29 (dd, 1H, J = 16, 6.2 Hz), 6.71 (d, 1H, J = 16 Hz). ^{13}C NMR ($CDCl_3$) *anti* isomer δ 14.0, 45.9, 74.8, 121.5, 125.9, 126.6, 128.0, 128.6, 128.9, 129.4, 132.6, 136.2, 150.5, 173.9; detectable peaks of *syn* isomer δ 11.7, 45.4, 73.3, 121.4, 126.6, 127.9, 128.4, 129.5, 132.0, 136.3, 150.4, 173.7. HRMS (*m*/*z*) calcd for $C_{18}H_{18}O_3$ (M^+) 282.1256, found 282.1260. HPLC, Daicel Chiralcel OJ, hexane/^{i}PrOH = 4/1, flow rate = 0.8 mL/min: *syn* isomer t_R = 25.3 min (major), t_R = 35.1 min (minor); *anti* isomer t_R = 41.1 min (minor), t_R = 68.8 min (major).

Phenyl 3-Hydroxy-2-methyloctanoate. IR [cm^{-1}] (neat) 3465, 1754, 1593, 1493, 1458, 1378. ^1H NMR ($CDCl_3$) *anti* isomer δ 0.91 (t, 3H, J = 6.6), 1.36 (d, 3H, J = 7.1 Hz) 1.3−1.7 (m, 8H), 2.44 (br, 1H), 2.78 (dq, 1H, J = 7.1 Hz, 7.0 Hz), 3.80 (br, 1H), 7.08 (m, 2H), 7.24 (m, 1H), 7.39 (m, 2H); detectable peaks of *syn* isomer δ 1.34 (d, 3H, J = 7.1 Hz), 4.05 (br, 1H). ^{13}C NMR ($CDCl_3$) *anti* isomer δ 14.0,

(25) The trimethylsilyl ether of the alcohol was detected by direct analysis of the reaction mixture using GC−MS.

(26) In the reactions using (*R*)-3,3′-I_2-6,6′-X_2BINOL (X = Br, I, C_2F_5), the catalyst preparation was performed according to the following procedure: To a suspension of (*R*)-3,3′-I_2-6,6′-X_2BINOL (0.060 mmol) in toluene (1.0 mL) was added $Zr(O^tBu)_4$ (0.040 mmol) in toluene (1.0 mL) at room temperature, and the solution was stirred for 3 h. Propanol (0.32 mmol) and H_2O (0.080 mmol) in toluene (0.5 mL) were then added, and the whole was stirred for 30 min at room temperature.

14.3, 22.6, 25.2, 31.8, 34.7, 45.5, 73.4, 121.5, 125.9, 129.4, 150.4, 174.5; detectable peaks of *syn* isomer δ 10.7, 25.7, 34.0, 44.5, 71.8, 121.4, 174.7. HRMS (*m*/*z*) calcd for $C_{15}H_{22}O_3$ (M^+) 250.1569, found 250.1581. HPLC, Daicel Chiralpak AD, hexane/^{i}PrOH = 100/1, flow rate = 1.0 mL/min: *syn* isomer t_R = 26.3 min (major), t_R = 29.3 min (minor); *anti* isomer t_R = 32.0 min (minor), t_R = 42.1 min (major).

Phenyl 3-Hydroxy-2,6-dimethylheptanoate. IR [cm^{-1}] (neat) 3467, 1756, 1594, 1494, 1459, 1384, 1366. ^{1}H NMR ($CDCl_3$) *anti* isomer δ 0.91 (d, 3H, J = 6.6 Hz), 0.92 (d, 3H, J = 6.6 Hz), 1.36 (d, 3H, J = 7.1 Hz), 1.2−1.8 (m, 5H), 2.51 (br, 1H), 2.79 (dq, 1H, J = 7.1, 7.1 Hz), 3.77 (br, 1H), 7.08 (m, 2H), 7.23 (m, 1H), 7.38 (m, 2H); detectable peaks of *syn* isomer δ 4.02 (br, 1H). ^{13}C NMR ($CDCl_3$) *anti* isomer δ 14.2, 22.4, 22.7, 28.0, 32.5, 34.6, 45.5, 73.2, 121.5, 125.9, 129.4, 150.5, 174.5; detectable peaks of *syn* isomer δ 10.7, 22.5, 22.6, 31.8, 35.1, 44.5, 72.1, 121.4, 174.6. HRMS (*m*/*z*) calcd for $C_{15}H_{22}O_3$ (M^+) 250.1569, found 250.1567. HPLC, Daicel Chiralcel OJ, hexane/^{i}PrOH = 40/1, flow rate = 0.8 mL/min: *syn* isomer t_R = 26.8 min (major), t_R = 42.4 min (minor); *anti* isomer t_R = 38.4 min (minor), t_R = 60.4 min (major).

Phenyl 5-Cyclohexyl-3-hydroxy-2-methylpentanoate. IR [cm^{-1}] (neat) 3435, 1757, 1593, 1493, 1448, 1381, 1338, 1301, 1274. ^{1}H NMR ($CDCl_3$) *anti* isomer δ 0.8−2.0 (m, 2H), 1.1−1.8 (m, 13H), 1.36 (d, 3H, J = 7.1 Hz), 2.43 (br, 1H), 2.78 (dq, 1H, J = 7.1, 7.1 Hz), 3.76 (br, 1H), 7.07 (m, 2H), 7.23 (m, 1H), 7.38 (m, 2H); detectable peaks of *syn* isomer δ 4.01 (br, 1H). ^{13}C NMR ($CDCl_3$) *anti* isomer δ 14.2, 26.3, 26.3, 26.6, 32.0, 33.1, 33.2, 33.5, 37.6, 45.5, 73.8, 121.5, 125.9, 129.4, 150.5, 174.4; detectable peaks of *syn* isomer δ 10.7, 31.4, 33.3, 33.4, 33.6, 44.5, 72.1, 121.4, 174.6. HRMS (*m*/*z*) calcd for $C_{18}H_{26}O_3$ (M^+) 290.1882, found 290.1882. HPLC, Daicel Chiralpak AD (double), hexane/^{i}PrOH = 19/1, flow rate = 0.5 mL/min: *syn* isomer t_R = 37.3 min (major), t_R = 40.1 min (minor); *anti* isomer t_R = 42.8 min (minor), t_R = 46.8 min (major).

Phenyl 3-Hydroxy-2,5-dimethylhexanoate. IR [cm^{-1}] (neat) 3432, 1752, 1593, 1493, 1459, 1367. ^{1}H NMR ($CDCl_3$) *anti* isomer δ 0.95 (d, 3H, J = 6.6 Hz), 0.97 (d, 2H, J = 6.6 Hz), 1.37 (d, 3H, J = 7.3 Hz), 1.4−1.6 (m, 1H), 1.6−1.7 (m, 1H), 2.38 (br, 1H), 2.75 (dq, 1H, J = 7.3, 6.4 Hz), 3.87 (m, 1H), 7.08 (m, 2H), 7.24 (m, 1H), 7.39 (m, 2H); detectable peaks of *syn* isomer δ 1.34 (d, 3H, J = 7.3 Hz), 4.14 (m, 1H). ^{13}C NMR ($CDCl_3$) *anti* isomer δ 14.2, 21.6, 23.7, 24.5, 44.0, 46.1, 71.6, 121.5, 126.0, 129.4, 150.5, 174.5; detectable peaks of *syn* isomer δ 10.8, 21.9, 23.5, 24.5, 44.0, 44.9, 121.4, 174.7. HRMS (*m*/*z*) calcd for $C_{14}H_{20}O_3$ (M^+) 236.1412, found 236.1402. HPLC, Daicel Chiralpak AD (double), hexane/^{i}PrOH = 40/1, flow rate = 0.5 mL/min: *syn* isomer t_R = 51.9 min (major), t_R = 53.6 min (minor); *anti* isomer t_R = 59.8 min (minor), t_R = 68.9 min (major).

Phenyl 4-Cyclohexyl-3-hydroxy-2-methylbutanoate. IR [cm^{-1}] (neat) 3469, 1757, 1593, 1493, 1449, 1348. ^{1}H NMR ($CDCl_3$) *anti* isomer δ 0.8−1.1 (m, 2H), 1.1−1.8 (m, 10 H), 1.33 (d, 3H, J = 7.1 Hz), 1.85 (br, 2H), 2.53 (br, 1H), 2.73 (dq, 1H, J = 7.0, 7.0 Hz), 3.90 (br, 1H), 7.07 (m, 2H), 7.22 (m, 1H), 7.37 (m, 2H); detectable peaks of *syn* isomer δ 1.32 (d, 3H, J = 7.1 Hz), 4.14 (m, 1H). ^{13}C NMR ($CDCl_3$); *anti* isomer δ 13.9, 26.0, 26.3, 26.5, 32.5, 33.8, 34.4, 42.2, 46.1, 70.9, 121.4, 125.8, 129.3, 150.4, 174.4; detectable peaks of *syn* isomer δ 10.8, 26.1, 32.7, 34.0, 34.1, 41.8, 45.0, 69.2, 121.4, 174.5. HRMS (*m*/*z*) calcd for $C_{17}H_{24}O_3$ (M^+) 276.1725, found 276.1727. HPLC Daicel Chiralpak AD (double), hexane/^{i}PrOH = 19/1, flow rate = 0.8 mL/min: *syn* isomer t_R = 23.3 min (minor), t_R = 25.5 min (major); *anti* isomer t_R = 28.8 min (minor), t_R = 35.5 min (major).

***S*-Ethyl 3-Hydroxy-2-methyloctanthioate.** IR [cm^{-1}] (neat) 3456, 1679, 1454, 1413, 1376, 1266. ^{1}H NMR ($CDCl_3$) *anti* isomer δ 0.88 (t, 3H, J = 6.8 Hz), 1.23 (d, 3H, J = 7.1 Hz), 1.25 (t, 3H, J = 7.5 Hz), 1.2−1.6 (m, 8H), 2.30 (br, 1H), 2.72 (dq, 1H, J = 7.0, 5.6 Hz), 2.88 (q, 2H, J = 7.5 Hz), 3.68 (m, 1H); detectable peaks of *syn* isomer δ 2.66 (dq, 1H, J = 7.1, 4.0 Hz), 2.87 (q, 2H, J = 7.5 Hz), 3.89 (m, 1H). ^{13}C NMR ($CDCl_3$) *anti* isomer δ 14.0, 14.6, 15.2, 22.6, 23.2, 25.2, 31.7, 34.9, 53.5, 73.9, 204.3; detectable peaks of *syn* isomer δ 11.3, 23.2, 25.6, 34.0, 52.9, 71.9, 204.3. HRMS (*m*/*z*) calcd for $C_{11}H_{22}O_2S$ (M^+) 218.1341, found 218.1343. HPLC, Daicel Chiralpak AS, hexane/^{i}PrOH = 1000/1, flow rate = 1.0 mL/min: *syn* isomer t_R = 16.5 min (major), t_R = 19.2 min (minor); *anti* isomer t_R = 22.3 min (minor), t_R = 25.4 min (major).

NMR Experiments of the Chiral Zirconium Catalyst. To a suspension of (*R*)-3,3′-diiodo-1,1′-binaphthalene-2,2′-diol (0.10 mmol) in toluene-d_8 (0.2 mL) was added Zr(O^{t}Bu)$_4$ (0.10 mmol) in toluene-d_8 (0.4 mL) at room temperature, and the solution was stirred for 30 min. After a mixture of propanol (0.50 mmol) and H_2O (0.10 mmol) in toluene (0.2 mL) was added, the whole was stirred for additional 3 h at room temperature. ^{1}H and ^{13}C NMR experiments were then performed.

Experiments of Nonlinear Effects. Experiments Using BINOL with Low ee. To a suspension of 3,3′-diiodo-1,1′-binaphthalene-2,2′-diol (0.040 mmol, low ee, already prepared) in toluene (1.0 mL) was added Zr(O^{t}Bu)$_4$ (0.040 mmol) in toluene (1.0 mL) at room temperature, and the solution was stirred for an additional 30 min. Then propanol (0.32 mmol) and H_2O (0.080 mmol) in toluene (0.5 mL) were added, and the whole was stirred for 3 h at room temperature. After cooling at 0 °C, benzaldehyde (0.40 mmol) in toluene (0.75 mL) and silyl enol ether **2a** (0.48 mmol) in toluene (0.75 mL) were successively added. The mixture was stirred for 18 h, and saturated aqueous $NaHCO_3$ was added to quench the reaction. The desired product was obtained by following the usual workup procedure.

Experiments Using the Catalyst Prepared by Mixing the (*R*)- and (*S*)- Catalyst. The (*R*)-catalyst was prepared from Zr(O^{t}Bu)$_4$ (0.040 mmol), (*R*)-3,3′-diiodo-1,1′-binaphthalene-2,2′-diol (0.10 mmol), propanol (0.32 mmol), and H_2O (0.080 mmol) in toluene (2.5 mL). Then the (*R*)-catalyst and the (*S*)-catalyst, which was prepared from (*S*)-3,3′-diiodo-1,1′-binaphthalene-2,2′-diol, were mixed in desired ratio, and the mixture was used as a catalyst immediately in the reactions of benzaldehyde and silyl enol ether **2a**.

Synthesis of Chiral Ligands (*R*)-2,2′-Bis(methoxymethyloxy)-6,6′-bis(pentafluoroethyl)-1,1′-binaphthyl. Under argon atmosphere, (*R*)-6,6′-diiodo-2,2′-bis(methoxymethyloxy)-1,1′-binaphthyl (4.00 g, 6.39 mmol),[6c] trimethylpentafluoroethylsilane[27] ($TMSC_2F_5$, 4.90 g, 25.6 mmol), copper iodide (CuI, 3.65 g, 19.2 mmol), potassium fluoride (14.8 g, 25.5 mmol), and dimethylformamide (16 mL) were added in a shield tube, and the whole was heated at 100 °C for 24 h.[15] After cooling to room temperature, the reaction mixture was poured into a mixture of ethyl acetate and water. The mixture was filtered and separated, and the aqueous layer was extracted with ethyl acetate. The organic layers were combined and washed with water and brine and dried over Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by silica gel column chromatography (hexane/methylenechloride) to afford (*R*)-2,2′-bis(methoxymethyloxy)-6,6′-bis(pentafluoroethyl)-1,1′-binaphthyl (3.21 g, yield 82%) as an amorphous oil. $[\alpha]^{24}_D$ +78.5 (*c* 1.02, $CHCl_3$). IR [cm^{-1}] (KBr) 1631, 1600, 1484, 1444, 1407, 1385, 1360, 1334, 1283, 1248. ^{1}H NMR ($CDCl_3$) δ 3.18 (s, 6H), 5.05 (d, 2H, J = 6.8 Hz), 5.13 (d, 2H, J = 6.9 Hz), 7.22 (d, 2H, J = 9.0 Hz), 7.36 (d, 2H, J = 9.0 Hz), 7.71 (d, 2H, J = 9.2 Hz), 8.08 (d, 2H, J = 9.2 Hz), 8.17 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 56.0, 94.8, 113.7 (tq, J = 253, 38 Hz), 117.8, 119.2 (qt, J = 286, 39 Hz), 120.1, 122.8 (t, J = 5.1 Hz), 124.2 (t, J = 24 Hz), 126.1, 127.5 (t, J = 7.1 Hz), 128.5, 130.8, 135.3, 154.4. ^{19}F NMR (283 MHz, $CDCl_3$, CF_3COOH: −76.5 ppm) δ −84.8 (3F), −114.5 (2F). MS (*m*/*z*) 610 (M^+). HRMS (*m*/*z*) calcd for $C_{28}H_{20}F_{10}O_4$ (M^+) 610.1202, found 610.1202.

(*R*)-3,3′-Diiodo-2,2′-bis(methoxymethyloxy)-6,6′-bis(pentafluoroethyl)-1,1′-binaphthyl. To a solution of (*R*)-2,2′-bis(methoxymethyloxy)-6,6′-bis(pentafluoroethyl)-1,1′-binaphthyl (3.17 g, 5.19 mmol) in tetrahydrofuran (60 mL) was added a hexane−cyclohexane solution

(27) (a) Krishnamurti, R.; Bellew, D. R.; Prakash, G. K. S. *J. Org. Chem.* **1991**, *56*, 984. (b) Pawelke, G. *J. Fluorine Chem.* **1989**, *42*, 429.

of *s*-butyllithium (1.02 M, 20.8 mL, 21.2 mmol) at −78 °C, and the whole was stirred for 1 h at the same temperature. Iodine (7.92 g, 31.2 mmol) in tetrahydrofuran (25 mL) was then added, and the reaction mixture was stirred for an additional 3 h. After quenching with methanol, water and ethyl acetate were added. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The organic layers were combined and treated with aqueous 10% $NaHSO_3$ to destroy excess iodine; washed with water, saturated aqueous $NaHCO_3$, and brine successively; and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by silica gel column chromatography (hexane/ethyl acetate) to afford (*R*)-3,3′-diiodo-2,2′-bis(methoxymethyloxy)-6,6′-bis(pentafluoroethyl)-1,1′-binaphthyl (3.19 g, yield 71%) as an amorphous oil. $[\alpha]^{23}_D$ +3.11 (*c* 1.11, $CHCl_3$). IR [cm^{-1}] (KBr) 1629, 1561, 1467, 1447, 1430, 1371, 1351, 1331, 1317, 1263, 1207. ^1H NMR ($CDCl_3$) δ 2.55 (s, 6H), 4.83 (d, 2H, J = 5.8 Hz), 4.84 (d, 2H, J = 6.1 Hz), 7.29 (d, 2H, J = 9.1 Hz), 7.47 (d, 2H, J = 8.8 Hz), 8.09 (s, 2H), 8.69 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 56.4, 94.2, 99.8, 113.3 (tq, J = 254, 38 Hz), 119.1 (qt, J = 286, 39 Hz), 123.6 (t, J = 5.3 Hz), 125.7, 126.1 (t, J = 7.3 Hz), 126.2 (t, J = 24 Hz), 127.4, 130.9, 135.0, 141.2, 154.7. ^{19}F NMR (283 MHz, $CDCl_3$, CF_3COOH: −76.5 ppm) δ −84.7 (3F), −114.8 (2F). MS (*m*/*z*) 863 ($M^+ + 1$). Anal. Calcd for $C_{28}H_{18}F_{10}I_2O_4$: C, 39.00; H, 2.10. Found: C, 38.79; H, 2.22.

(*R*)-3,3′-Diiodo-6,6′-bis(pentafluoroethyl)-1,1′-binaphthalene-2,2′-diol. To a solution of (*R*)-3,3′-diiodo-2,2′-bis(methoxymethyloxy)-6,6′-bis(pentafluoroethyl)-1,1′-binaphthyl (3.54 g, 4.11 mmol) in dichloromethane (20 mL) was added saturated methanolic HCl at 0 °C, and the mixture was stirred for 1 h. After addition of excess water, the organic layer was separated, washed with water and brine, and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by silica gel column chromatography (hexane/ethyl aceate) to afford (*R*)-3,3′-diiodo-6,6′-bis(pentafluoroethyl)-1,1′-binaphthalene-2,2′-diol (2.81 g, yield 88%). Recrystalized product (hexane/methylene chloride) was used in the asymmetric reactions. Mp 204 °C. $[\alpha]^{23}_D$ +51.2 (*c* 1.01, $CHCl_3$). IR [cm^{-1}] (KBr) 3467, 1628, 1443, 1379, 1329, 1265, 1209, 1190. ^1H NMR ($CDCl_3$) δ 5.63 (s, 2H), 7.17 (d, J = 9.2 Hz), 7.46 (d, 2H, J = 8.9 Hz), 8.10 (s, 2H), 8.63 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 88.9, 112.7, 113.4 (tq, J = 253, 38 Hz), 116.9 (qt, J = 286, 39 Hz), 124.4 (t, J = 5.1 Hz), 125.1 (t, J = 24 Hz), 125.3, 126.7 (t, J = 7.3 Hz), 129.4, 134.8, 141.2, 151.9. ^{19}F NMR (283 MHz, $CDCl_3$, CF_3COOH: −76.5 ppm) δ −84.7 (3F), −114.8 (2F). MS (*m*/*z*) 774 (M^+). Anal. Calcd for $C_{24}H_{10}F_{10}I_2O_2$: C, 37.24; H, 1.30. Found: C, 37.00; H, 1.46.

(*R*)-2,2′-Bis(methoxymethyloxy)-6,6′-bistrimethylsilyl-1,1′-binaphthyl. To a solution of (*R*)-6,6′-dibromo-2,2′-bis(methoxymethyloxy)-1,1′-binaphthyl (5.00 g, 9.39 mmol) in tetrahydrofuran (80 mL) was added a hexane solution of *n*-butyllithium (1.60 M, 14.7 mL, 23.5 mmol) at −78 °C. The reaction mixture was stirred for 1 h, then chlorotrimethylsilane (3.06 g, 28.2 mmol) in terahydrofuran (20 mL) was added, and the mixture was stirred for additional 3 h. After quenching with water, diethyl ether was added. The organic layer was separated, and the aqueous layer was extracted with diethyl ether. The organic layers were combined, washed with water and brine, and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by silica gel column chromatography (hexane/ethyl acetate) to afford (*R*)-2,2′-bis(methoxymethyloxy)-6,6′-bistrimethylsilyl-1,1′-binaphthyl (3.84 g, yield 79%). Mp 144 °C. $[\alpha]^{23}_D$ −7.60 (*c* 1.00, $CHCl_3$). IR [cm^{-1}] (KBr) 1615, 1580, 1472, 1440, 1403, 1368, 1329, 1266, 1247, 1200. ^1H NMR ($CDCl_3$) δ 0.29 (s, 18H), 3.16 (s, 6H), 4.98 (d, 2H, J = 6.8 Hz), 5.05 (d, 2H, J = 6.6 Hz), 7.12 (d, 2H, J = 8.3 Hz), 7.32 (d, 2H, J = 8.4 Hz), 7.56 (d, 2H, J = 9.0 Hz), 7.94 (d, 2H, J = 9.0 Hz), 8.02 (s, 2H). ^{13}C NMR ($CDCl_3$) δ −1.1, 55.8, 95.3, 117.3, 121.1, 124.5, 129.4, 129.5, 130.3, 133.8, 134.2, 135.5, 153.0. MS (*m*/*z*) 518 (M^+). Anal. Calcd for $C_{30}H_{38}O_4Si_2$: C, 69.45; H, 7.38. Found: C, 69.64; H, 7.45.

(*R*)-3,3′-Diiodo-2,2′-bis(methoxymethyloxy)-6,6′-bistrimethylsilyl-1,1′-binaphthyl. To a solution of (*R*)-2,2′-bis(methoxymethyloxy)-6,6′-bistrimethylsilyl-1,1′-binaphthyl (3.07 g, 5.92 mmol) in tetrahydrofuran (30 mL) was added a solution of *s*-butyllithium (1.02 M, 23.2 mL, 23.7 mmol) at −78 °C. The reaction mixture was stirred for 1.5 h, and iodine (9.01 g, 35.4 mmol) in tetrahydrofuran (15 mL) was added. The whole was stirred for 2 h at the same temperature and quenched with methanol. After ethyl acetate and water were added to the mixture, the organic layer was separated and the aqueous layer was extracted with ethyl acetate. The organic layers were combined and treated with aqueous 10% $NaHSO_3$ to destroy excess iodine; washed with water, saturated aqueous $NaHCO_3$, and brine successively; and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by silica gel column chromatography (hexane/ethyl acetate) to afford (*R*)-3,3′-diiodo-2,2′-bis(methoxymethyloxy)-6,6′-bistrimethylsilyl-1,1′-binaphthyl (4.30 g, yield 93%). $[\alpha]^{17}_D$ −33.0 (*c* 1.02, $CHCl_3$). IR [cm^{-1}] (KBr) 1422, 1391, 1249, 1200. ^1H NMR ($CDCl_3$) δ 0.30 (s, 18H), 2.65 (s, 6H), 4.68 (d, 2H, J = 5.5 Hz), 4.79 (d, 2H, J = 5.7 Hz), 7.14 (d, 2H, J = 8.4 Hz), 7.41 (d, 2H, J = 8.4 Hz), 7.91 (s, 2H), 8.55 (s, 2H). ^{13}C NMR ($CDCl_3$) δ −1.2, 56.6, 92.2, 99.3, 125.3, 125.9, 131.1, 131.7, 132.5, 133.9, 138.1, 140.2, 152.3. MS (*m*/*z*) 770 (M^+). Anal. Calcd for $C_{30}H_{36}I_2O_4Si_2$: C, 46.76; H, 4.71; found: C, 46.67; H, 4.62.

(*R*)-6,6′-Dibromo-3,3′-diiodo-1,1′-binaphthalene-2,2′-diol. To a solution of (*R*)-3,3′-diiodo-2,2′-bis(methoxymethyloxy)-6,6′-bistrimethylsilyl-1,1′-binaphthyl (2.50 g, 3.24 mmol) in carbon tetrachloride (25 mL) was added bromine (1.53 g, 9.57 mmol) at 0 °C.[16] The whole was stirred overnight at the same temperature. The reaction mixture was quenched with aqueous 10% $NaHSO_3$ to destroy excess bromine. After ethyl acetate was added, the organic layer was separated; washed with water, saturated aqueous $NaHCO_3$, and brine successively; and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was dissolved in dichloromethane (10 mL). To the solution was added saturated methanolic HCl (15 mL) at 0 °C, and the mixture was stirred for 1 h. After addition of excess water and ethyl acetate, the organic layer was separated; washed with water, saturated aqueous $NaHCO_3$, and brine; and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by silica gel column chromatography (hexane/ethyl aceate) to afford (*R*)-6,6′-dibromo-3,3′-diiodo-1,1′-binaphthalene-2,2′-diol (2.08 g, yield 94%). Recrystalized product (hexane/ethyl acetate) was used in the asymmetric reactions. Mp 277 °C. $[\alpha]^{18}_D$ +74.3 (*c* 0.55, THF). IR [cm^{-1}] (KBr) 3521, 3503, 1567, 1484, 1432, 1377, 1352, 1290, 1261, 1218. ^1H NMR ($CDCl_3$) δ 5.44 (s, 2H), 6.89 (d, 2H, J = 9.0 Hz), 7.37 (dd, 2H, J = 9.0, 2.0 Hz), 7.94 (d, 2H, J = 2.0 Hz), 8.40 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 88.5, 112.8, 118.6, 126.1, 129.1, 131.3, 131.5, 131.8, 139.2, 150.3. MS (*m*/*z*) 694 ($M^+ - 1$), 695 (M^+), 696 ($M^+ + 1$), 697 ($M^+ + 2$), 698 ($M^+ + 3$). Anal. Calcd for $C_{20}H_{10}Br_2I_2O_2$: C, 34.52; H, 1.45; found: C, 34.75; H, 1.60.

(*R*)-3,3′,6,6′-Tetraiodo-1,1′-binaphthalene-2,2′-diol. To a solution of (*R*)-3,3′-diiodo-2,2′-bis(methoxymethyloxy)-6,6′-bistrimethylsilyl-1,1′-binaphthyl (3.30 g, 4.28 mmol) in carbon tetrachloride (50 mL) was added iodine chloride (2.76 g, 17.0 mmol) at −15 °C.[16] The whole was stirred for 10 min at the same temperature. The reaction mixture was quenched with aqueous 10% $NaHSO_3$ to destroy excess iodine chloride. After ethyl acetate was added, the organic layer was separated; washed with water, saturated aqueous $NaHCO_3$, and brine successively; and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was dissolved in dichloromethane (30 mL). To the solution was added saturated methanolic HCl (20 mL) at 0 °C, and the mixture was stirred for 1 h. After addition of excess water and ethyl acetate, the organic layer was separated; washed with water, saturated aqueous $NaHCO_3$, and brine; and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by silica gel column chroma-

tography (benzene) to (*R*)-3,3′,6,6′-tetraiodo-1,1′-binaphthalene-2,2′-diol (2.49 g, yield 75%). Recrystalized product (hexane/ethyl acetate) was used in the asymmetric reactions. Mp 299 °C. $[\alpha]^{18}_{D}$ +54.9 (*c* 0.61, THF). IR [cm^{-1}] (KBr) 3521, 3496, 1561, 1479, 1429, 1377, 1346, 1290, 1261, 1217. ^{1}H NMR ($CDCl_3$) δ 5.42 (s, 2H), 6.76 (d, 2H, J = 8.8 Hz), 7.53 (dd, 2H, J = 9.0, 1.7 Hz), 8.16 (d, 2H, J = 1.4 Hz), 8.37 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 88.1, 89.8, 112.7, 126.1, 131.9, 132.1, 135.8, 136.4, 139.1, 150.4. MS (*m*/*z*) 789 (M^+), 790 ($M^+ + 1$). Anal. Calcd for $C_{20}H_{10}I_4O_2$: C, 30.41; H, 1.28; found: C, 30.39; H, 1.47.

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Supporting Information Available: Experimental details and spectra (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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