Chiral Auxiliaries for Asymmetric Synthesis: Enantioselective Addition of Dialkylzincs to Aldehydes Catalyzed by Chiral 1,2-Disubstituted Ferrocenyl Amino Alcohols

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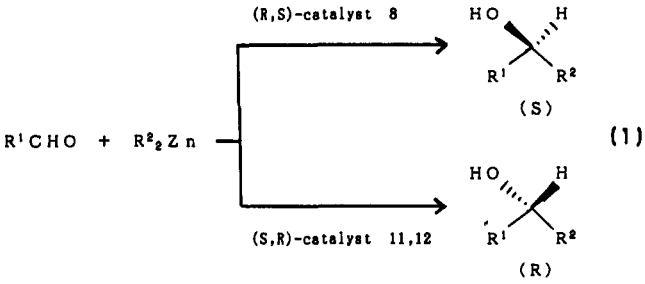
Chiral 1,2-disubstituted ferrocenyl amino alcohols derived from (*R*)- and (*S*)-*N*,*N*-dimethyl-1-ferrocenylethylamines **1** and **9** catalyze the enantioselective addition of dialkylzincs to aldehydes to afford optically active *S* and *R* secondary alcohols. The degree of enantioselectivity increases with increased bulk of substituents near the C–O and C–N bonds of the catalyst. Catalysts with *R* chirality at the carbon bearing the amino group and planar *S* chirality at the ferrocene nucleus afford *S* alcohols, regardless of the chirality of the carbon bearing the hydroxy group. Catalyst **8o** is the most effective in ethylating benzaldehyde, and it alkylates aromatic and highly branched aliphatic aldehydes in ≥90% ee. Only moderate selectivities are obtained in the ethylation of aliphatic aldehydes without an α substituent.

Asymmetric addition of dialkylzincs (R_2Zn) to aldehydes catalyzed by chiral β-amino alcohols is a convenient method for the preparation of optically active secondary alcohols. The catalytic asymmetric addition of dialkylzincs to various aldehydes has been investigated by a number of research groups.[1,2] Moreover, the mechanism of asymmetric amplification has been elucidated.[3] Although several efficient catalysts that can convert aromatic aldehydes to the corresponding alcohols in high optical purities have been discovered,[2] asymmetric addition of dialkylzincs to aliphatic aldehydes has remained a challenge.[4] This paper reports the synthesis of a series of new chiral 1,2-disubstituted ferrocenyl catalysts, their use as chiral catalysts in the asymmetric alkylation of aldehydes (eq 1), and the steric course of the asymmetric induction.



Results and Discussion

Synthesis of Chiral 1,2-Disubstituted Ferrocenyl Amino Alcohols. Chiral 1,2-disubstituted ferrocenyl amino alcohols **8** were synthesized as shown in Scheme I. Lithiation of readily accessible (*R*)-*N*,*N*-dimethyl-1-ferrocenylethylamine (**1**) with *sec*-butyllithium and subsequent iodination with iodine gave (*R*)-*N*,*N*-dimethyl-1-((*S*)-2-iodoferrocenyl)ethylamine (**2**)[5] (82% yield, 97% de[6]). Optically pure **2** could be obtained by recrystallization from acetonitrile. Chiral ferrocenylethyl derivatives with a trimethylammonium group in the α position are known to undergo nucleophilic substitution with retention of configuration.[7] Quaternization of **2** with methyl iodide followed by reaction with piperidine, diisopropylamine, diethylamine, or *N*,*N*-dimethylethylenediamine gave the respective (*R*,*S*)[8]-2-iodoferrocenes **3**–**6** in 80–100% yields with complete retention of configuration.

(*R*,*S*)-1,2-Disubstituted ferrocenyl amino alcohols **8a**–**u** were derived from **2**–**5** and **7**[9] by treatment with *n*-butyllithium followed by a carbonyl compound. When aldehydes were used as carbonyl components, two chromatographically separable diastereomers (**8a**–**b**, **8c**–**d**, **8i**–**j**, **8l**–**m**, **8q**–**r**) were obtained. In the cases of **8h**, **8k**, and **8u**, the diastereomeric mixtures were isomerized to single diastereomers without separation by treatment with aqueous phosphoric acid.[10] The absolute configuration of the two diastereomers was tentatively assigned on the basis of their ^1H NMR spectra, the stability to aqueous phosphoric acid, and spectral comparison with **8n** whose absolute configuration was confirmed by single-crystal X-ray analysis.[10]

The enantiomeric (*S*,*R*)-1,2-disubstituted ferrocenyl amino alcohols **11** and **12**[11] were similarly prepared from **9** and **10**,[12] respectively.

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(2) (a) Kitamura, M.; Suga, S.; Kawai, K.; Noyori, R. *J. Am. Chem. Soc.* **1986**, *108*, 6071. (b) Soai, K.; Ookawa, A.; Kaba, T.; Ogawa, K. *J. Am. Chem. Soc.* **1987**, *109*, 7111. (c) Corey, E. J.; Hannon, F. J. *Tetrahedron Lett.* **1987**, *28*, 5233; **1987**, *28*, 5237. (d) Yoshioka, M.; Kawakita, T.; Ohno, M. *Tetrahedron Lett.* **1989**, *30*, 1657.

(3) Oguni, N.; Matsuda, Y.; Kaneko, T. *J. Am. Chem. Soc.* **1988**, *110*, 7877. Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028.

(4) Significant developments in enantioselective alkylation of straight-chain aliphatic aldehydes have been reported: Soai, K.; Yokoyama, S.; Ebihara, K.; Hayasaka, T. *J. Chem. Soc. Chem. Commun.* **1987**, 1690. Takahashi, H.; Kawakita, T.; Yoshioka, M.; Kobayashi, S.; Ohno, M. *Tetrahedron Lett.* **1989**, *30*, 7095.

(5) Watanabe, M.; Araki, S.; Butsugan, Y.; Uemura, M. *Chem. Express* **1989**, *4*, 825.

(6) The diastereoselectivity was determined by ^1H NMR analysis of the corresponding trimethylsilyl derivative obtained by lithiation of **2** with butyllithium followed by treatment with trimethylchlorosilane: see ref 7b.

(7) (a) Gokel, G.; Hoffmann, P.; Klusacek, H.; Marquarding, D.; Ruch, E.; Ugi, I. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 64. (b) Marquarding, D.; Klusacek, H.; Gokel, G.; Hoffmann, P.; Ugi, I. *J. Am. Chem. Soc.* **1970**, *92*, 5389. (c) Gokel, G.; Marquarding, D.; Ugi, I. *J. Org. Chem.* **1972**, *37*, 3052.

(8) In *R*,*S*, the *R* refers to the configuration of the central chirality of the 1-aminoethyl group and the *S* refers to the planar chirality due to the arrangement of the substituents on the ferrocene nucleus: see ref 7b.

(9) Reaction of **6** with formaldehyde and $NaBH_4$ in methanol gave **7**.

(10) Battele, L. F.; Bau, R.; Gokel, G.; Oyakawa, R. T.; Ugi, I. *J. Am. Chem. Soc.* **1973**, *95*, 482.

(11) 1-Ferrocenylisobutylamine derivative **12** was synthesized by lithiation of **10** with *n*-butyllithium and subsequent treatment with benzaldehyde: see ref 12 for the diastereoselectivity of the lithiation.

(12) Marquarding, D.; Burghard, H.; Ugi, I.; Urban, R.; Klusacek, H. *J. Chem. Res., Synop.* **1977**, 82; *J. Chem. Res., Miniprint* **1977**, 0915.

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Table I. Asymmetric Addition of Diethylzinc to Benzaldehyde in the Presence of *R,S* Catalysts 8[a]

entry	catalyst	temp, °C	time, h	yield,[b] %	$[\alpha]^{22}_D$, deg (c, $CHCl_3$)[c]	% ee[d]
1	**8a**	rt[e]	3	95	−44.4 (5.28)	91
2	**8a**	0	6	80	−43.7 (4.19)	90
3	**8b**	rt	2	96	−45.3 (4.34)	93
4	**8c**	rt	2	95	−45.6 (4.09)	94
5	**8d**	rt	1	95	−45.7 (3.90)	94
6	**8e**	rt	2	92	−46.5 (4.08)	94
7	**8f**	rt	2	99	−47.0 (4.15)	97
8	**8o**	rt	1	99	−48.5 (3.94)	99
9	**8p**	rt	2	92	−47.5 (3.21)	98
10	**8s**	rt	22	51	−18.4 (3.97)	36
11[f]	**8o**	rt	3	95	−48.3 (3.28)	98
12[g]	**8o**	rt	22	72	−41.8 (2.90)	86
13[g]	**8o**	40	8	88	−43.1 (3.49)	89
14[g]	**8o**	60	5	78	−39.9 (3.09)	82

[a] Unless otherwise noted, the reaction was carried out in hexane with 5 mol % of catalyst and 1.6 equiv of diethylzinc to benzaldehyde. [b] Isolated yield. [c] Reported value for (*S*)-1-phenylpropanol in 98% ee is $[\alpha]^{22}_D$ −47.6° (c 6.11, $CHCl_3$).[2a] [d] Determined by HPLC using Chiralcel OB. [e] Room temperature. [f] 2 mol % of catalyst to benzaldehyde was used. [g] 0.5 mol % of catalyst to benzaldehyde was used.

Table II. Asymmetric Addition of Diethylzinc to Heptanal in the Presence of Chiral, 1,2-Disubstituted Ferrocenyl Amino Alcohols[a]

entry	catalyst	temp, °C	time, h	yield,[b] %	$[\alpha]^{22}_D$, deg (c, $CHCl_3$)	% ee[c]	confign
1	**8a**	rt[d]	3	86	+5.39 (7.84)	56	*S*
2[e]	**8a**	rt	28	69	+5.09 (3.86)	53	*S*
3	**8c**	rt	2	87	+5.32 (8.15)	55	*S*
4[f]	**8c**	rt	2	84	+5.28 (6.36)	55	*S*
5	**8c**	0	6	80	+5.41 (7.44)	56	*S*
6	**8f**	rt	2	87	+4.80 (7.08)	50	*S*
7	**8g**	rt	2	76	+3.26 (6.44)	34	*S*
8	**8h**	rt	2	86	+5.79 (7.21)	60	*S*
9	**8i**	rt	5	77	+4.67 (6.11)	49	*S*
10	**8j**	rt	7	50	+5.04 (3.83)	53	*S*
11	**8k**	rt	6	60	+3.72 (3.77)	39	*S*
12	**8m**	rt	3	70	+5.42 (5.87)	56	*S*
13	**8o**	rt	3	93	+5.63 (7.64)	59	*S*
14	**8q**	rt	2	72	+5.55 (5.60)	58	*S*
15	**8s**	rt	20	55	0 (2.54)	0	
16	**8t**	rt	3	62	+4.63 (4.08)	48	*S*
17	**8u**	rt	26	8[g]			
18	**12**	rt	2	94	−5.46 (7.98)	57	*R*

[a] See footnote *a*, Table I. Heptanal was used in place of benzaldehyde. [b] Isolated yield unless otherwise noted. [c] Based on the reported value of $[\alpha]^{24}_D$ +9.6° (c 8.3, $CHCl_3$) for (*S*)-3-nonanol.[19] [d] Room temperature. [e] Toluene was used as solvent. [f] 7 mol % of catalyst to heptanal was used. [g] Determined by GC analysis of the reaction mixture.

Enantioselective Addition of Dialkylzincs to Aldehydes in the Presence of Chiral 1,2-Disubstituted Ferrocenyl Amino Alcohols. The reaction of diethylzinc with benzaldehyde was carried out in the presence of several (*R,S*)-1,2-disubstituted ferrocenyl amino alcohols **8** in order to examine the effect of the structure of **8** upon enantioselectivity. The reaction conditions and results are summarized in Table I.

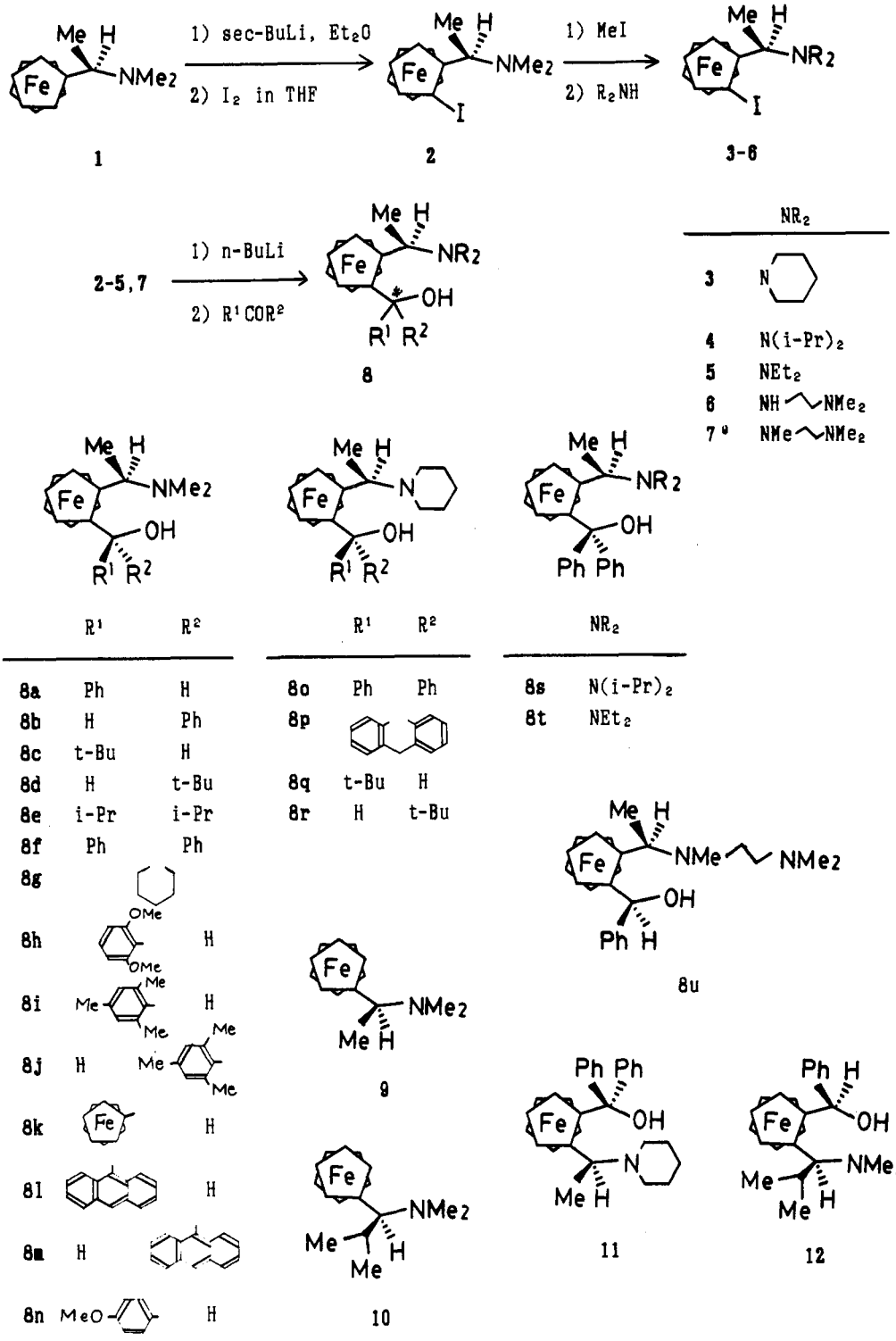
At room temperature, all *R,S* catalysts **8** (5 mol %) bearing a dimethylamino or piperidinyl group afforded (*S*)-1-phenylpropanol in high yields in ≥91% ee, regardless of the stereochemistry of the asymmetric carbon bearing the hydroxyl group. Among catalysts **8a–f** bearing a dimethylamino group, the benzhydrol derivative **8f** gave the highest ee (entry 7, 97% ee). The piperidinyl group (**8o**, entry 8, 99% ee) was superior to the dimethylamino group. The 9-hydroxyanthracene derivative **8p**, a rigid analogue of **8o**, was almost as effective (entry 9) as **8o**. On the other hand, catalysts **8s**, bearing a diisopropylamino group, had low catalytic and stereoselective activity (entry 10), probably owing to the bulky substituents that interfere with coordination of the nitrogen to zinc alkoxide.

Reducing the catalyst to benzaldehyde ratio from 5% to 2% had no effect (entry 11), but reducing the ratio to 0.5% reduced both yield and % ee (entry 12). The influence of reaction temperature on enantioselectivity was investigated with 0.5 mol % of **8o** (entries 12–14). Both chemical and optical yields reached maxima at 40 °C, although the reaction ran well at 60 °C.

The asymmetric addition of diethylzinc to heptanal, a straight-chain aliphatic aldehyde, was catalyzed by compounds **8** (Table II). All *R,S* catalysts **8** except **8s** and **8u** afforded (*S*)-3-nonanol in moderate enantiomeric excess, regardless of the stereochemistry of the asymmetric carbon bearing the hydroxy group. Cyclohexanol derivative **8g**, which has less bulk around the carbinol center than catalysts with an aryl or *tert*-butyl group, gave low selectivity (entry 7). Diferrocenylcarbinol **8k** also gave poor selectivity (entry 11), and diamine **8u**, which has a second amino group on the side chain, gave a complex mixture (entry 17). On the other hand, **12**, which has an isopropyl group on the asymmetric carbon bearing the amino group, and **8o** were the most active catalysts and had good stereoselectivity (entries 18 and 13). 2,6-Dimethoxybenzenemethanol **8h** and *tert*-butyl derivative **8q** had comparable selectivities (entries 8 and 14). We conclude that the enantioselective ethylation of heptanal with **8** as catalysts is unsatisfactory.

The effective catalyst **8o** was examined for the ethylation of other aldehydes (Table III). Para-substituted benzaldehydes, (*E*)-cinnamaldehyde, 2-furaldehyde, and 2-naphthaldehyde, which possess π electrons adjacent to the carbonyl group, afforded the corresponding secondary alcohols in high enantiomeric purity (entries 1–5). In

Scheme I



addition, cyclohexanecarboxaldehyde, 2-ethylbutyraldehyde, and pivalaldehyde, which are branched α to the carbonyl group, were ethylated in >98% ee (entries 6–11). On the other hand, ethylation of isovaleraldehyde and 3-phenylpropionaldehyde, which lack a substituent α to the carbonyl group, proceeded with low selectivity (entries 12 and 13).

We examined the reaction of di-*n*-butylzinc with aldehydes in the presence of **8o** (5 mol %) in hexane at room temperature. Benzaldehyde afforded (*S*)-1-phenylpentanol in 92% yield and 99% ee, and isobutryaldehyde gave (*S*)-2-methyl-3-heptanol in 66% yield and >98% ee. Catalysts **8** recognize the substructure adjacent to the carbonyl group and can distinguish between the prochiral faces of an aldehyde.

All chiral catalysts except **8b** and **8m** were recovered unchanged in >90% yield after the reactions. Catalysts **8b** and **8m**, with an *R* carbinol configuration, were partially isomerized (<20%) to **8a** and **8l**, respectively, with total recovery >90%. In contrast, catalysts **8d** and **8j**, also with the *R* carbinol configuration, were recovered without isomerization.

The catalytic reaction with **8** is completely different from our previously reported system with ferrocenylzinc catalysts **13**.[5] In the ethylation of aldehydes with **13**, only hydrolyzed ferrocenes **14** were recovered after aqueous

Table III. Asymmetric Addition of Diethylzinc to Aldehydes in the Presence of the Catalyst 8o[a]

entry	aldehyde	temp, °C	time, h	yield,[b] %	$[\alpha]^{22}_D$, deg (c, solvent)	% ee	confign
1	p-ClC_6H_4CHO	rt[c]	1	100	−28.2 (5.01, C_6H_6)[d]	100[e]	S
2	p-$MeOC_6H_4CHO$	rt	4	97	−32.8 (4.14, C_6H_6)[d]	90[e]	S
3	(E)-C_6H_5CH=$CHCHO$	rt	3	90	−6.30 (2.70, $CHCl_3$)[f]	100[g] (72)[h]	S
4	2-furaldehyde	rt	1	87	−16.2 (1.06, $CHCl_3$)[i]	87[j]	S
5	2-naphthaldehyde	rt	3	91	−26.6 (3.35, C_6H_6)[k]	97[e]	S
6	c-$C_6H_{11}CHO$	0	3	92	−8.02 (6.82, Et_2O)[l]	>98[m]	S[n]
7	c-$C_6H_{11}CHO$	rt	2	92	−7.96 (6.64, Et_2O)[l]	>98[m]	S[n]
8[o]	c-$C_6H_{11}CHO$	rt	4	92	−7.76 (6.64, Et_2O)[l]	97[p]	S[n]
9[q,r]	c-$C_6H_{11}CHO$	rt	3	91	+7.95 (7.11, Et_2O)[l]	>98[m]	R[n]
10	$(CH_3CH_2)_2CHCHO$	rt	3	83	−0.45 (4.00, $CHCl_3$)	>98[m]	S[s]
11	$(CH_3)_3CCHO$	rt	3	93[t]	−32.6 (2.38, $CHCl_3$)[u]	98[m]	S
12	$(CH_3)_2CHCH_2CHO$	rt	2	70	+12.6 (3.70, EtOH)[v]	62[g]	S
13[q]	$PhCH_2CH_2CHO$	rt	4	88	−16.8 (4.96, EtOH)[w]	63[g]	R

[a] See footnote *a*, Table I. Unless otherwise noted, catalyst 8o was used. [b] Isolated yield. [c] Room temperature. [d] Reported values for (S)-1-(p-chlorophenyl)propanol in 43% ee and (S)-1-(p-methoxyphenyl)propanol in 51% ee are $[\alpha]^{22}_D$ −10.4° (c 5, C_6H_6) and $[\alpha]^{22}_D$ −17.2° (c 5, C_6H_6), respectively.[20] [e] Determined by HPLC analysis using Chiralcel OB. [f] $[\alpha]^{22}_D$ −5.7° ($CHCl_3$) for (S)-1-phenylpent-1-en-3-ol in 96% ee determined by HPLC using a chiral column: see ref 2a. [g] Based on the reported values. [h] The % ee in parentheses is based on $[\alpha]^{23}_D$ −6.6° (c 3.2, $CHCl_3$) in 75% ee.[21] [i] $[\alpha]^{22}_{578}$ −17.9° (c 1.75, $CHCl_3$) for (S)-1-(2-furyl)propanol in 91% ee.[22] [j] Determined by HPLC analysis using Chiralcel OB of the corresponding (S)-MTPA ester. [k] $[\alpha]^{20}_D$ −18.81° (C_6H_6) for (S)-1-(2-naphthyl)propanol in 44.7% ee: see ref 1b. [l] $[\alpha]^{20}_D$ −9.60° (c 12.3, Et_2O) for (−)-1-cyclohexylpropanol.[23] [m] Determined by GC analysis (OV-1, nonpolar 50-m capillary column, flame ionization detector) of the corresponding (S)-MTPA ester. [n] Assigned by that (−)-1-cyclohexylpropanol was obtained by reduction of (−)-(S)-1-phenylpropanol.[24] [o] Catalyst 8a was used. [p] Based on the rotation value obtained in entry 6. [q] Catalyst 11, representing the enantiomer of 8o, was used. [r] Aldehyde was added to a mixture of 11, Et_2Zn, and hexane. [s] Tentatively assigned by analogy to the other compounds. [t] Determined by GC analysis of the reaction mixture. [u] $[\alpha]^{23}_D$ +27.4° (neat) for (R)-2,2-dimethyl-3-pentanol.[25] [v] $[\alpha]^{21}_D$ −20.3° (c 5.25, EtOH) for (R)-5-methyl-3-hexanol.[26] [w] $[\alpha]_D$ + 26.8° (c 5.0, EtOH) for (S)-1-phenyl-3-pentanol: see ref in footnote *h*.

workup, which rules out the possibility that the intermediates in the reaction are compounds akin to 8.

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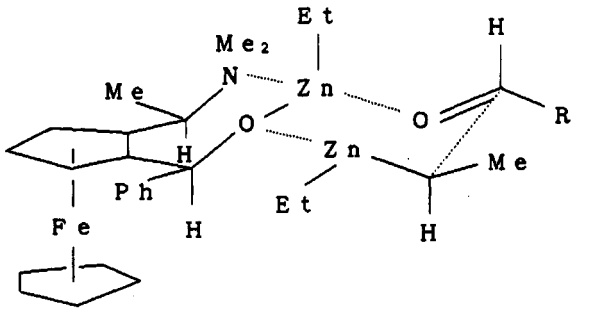
Other investigations[2,3] on β-amino alcohols as catalysts have shown that the degree of enantioselectivity depends on the bulk of substituents on the hydroxy-bearing carbon and that the chirality of the alcohol moiety of the catalyst determines the chirality of the predominant enantiomer of the product. On the other hand, our work with catalysts 8 shows that the bulk around the alcohol moiety also contributes to asymmetric induction, but the sense of induction is independent of the chirality of the alcohol moiety.

A proposed mechanism for the enantioselective addition of diethylzinc to an aldehyde on the zinc alkoxides of 8a and 8b is shown in Figure 1. Molecular models suggest that the zinc alkoxide forms a seven-membered ring with a chair conformation, regardless of the chirality of the alcohol moiety in the catalyst (15, 16). The alkylation reaction can be interpreted in terms of a six-membered cyclic transition state. Nucleophilic attack of the ethyl group from the *si* face of the aldehyde leads to the S isomer. The high enantioselectivity in the ethylation of α-branched aldehydes results from repulsion between the α substituent of the aldehyde and the ethyl group on the bridging zinc alkoxide.

The ethylation of benzaldehyde with 50% ee of 11 at 0 °C gave no asymmetric amplification. It thus appears that a single monomeric zinc alkoxide species is involved in the catalysis with 8.



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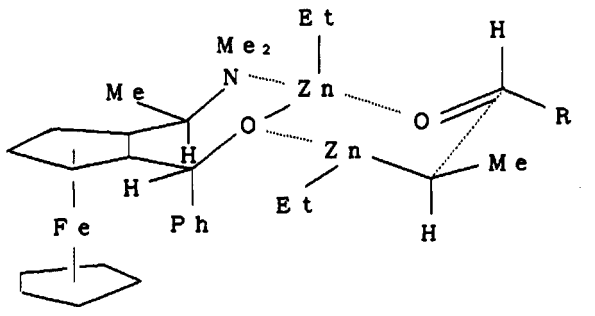

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Figure 1. Proposed mechanism for addition of chiral ligand complexed diethylzinc to aldehydes.

Experimental Section

General Procedures. ^1H NMR spectra were measured on a 90-MHz spectrometer in $CDCl_3$. Elemental analyses were performed by the Elemental Analysis Center in the Faculty of Pharmacy, Kyoto University. High-resolution mass spectra (HRMS) were measured at 70 eV. HPLC analyses were carried out on an instrument equipped with a chiral column (Chiralcel OB, Daicel Chemical Industries) and a UV detector for determining the optical purity of the products or the corresponding (S)-MTPA esters. GC analyses, including the determination of percent enantiomeric excess via the separation of diastereomeric (S)-MTPA esters, were carried out with use of a capillary gas chromatograph equipped with OV-1 nonpolar 50-m or PEG 20M polar 50-m capillary column. Optical rotations were measured on materials isolated by bulb-to-bulb distillation or chromatography, using a digital polarimeter with a 1.0-dm path length cell.

Materials. Oxygen- and water-sensitive reactions were carried out under an argon atmosphere. For TLC purifications, Merck precoated TLC plates (silica gel 60 GF_{254}, 2 mm; alumina 150 F_{254}, 1.5 mm) were used. Hexane, ether, and THF were freshly distilled from lithium aluminum hydride. Diethylzinc in hexane and

sec-butyllithium in cyclohexane were obtained from Kanto Chemical Co. Di-*n*-butylzinc was prepared from 2 equiv of *n*-butyllithium and zinc chloride in ether and purified by distillation. *n*-Butyllithium in hexane was obtained from Nakarai Chemical Co. (*R*)- and (*S*)-*N*,*N*-Dimethyl-1-ferrocenylethylamine (**1** and **9**) were obtained from Kanto Chemical or by optical resolution of the racemate[13] according to the reported procedure.[7b] (*S*)-*N*,*N*-Dimethyl-1-ferrocenyl-2-methylpropylamine (**10**) was obtained by optical resolution of the racemate[13] according to the reported procedure.[12] (*S*)-(−)-MTPA was obtained from Nakarai Chemical and converted to the acid chloride by the literature procedure.[14] Optical purities were determined by converting secondary alcoholic products into MTPA esters with MTPA-Cl.[15]

(*R*)-*N*,*N*-Dimethyl-1-((*S*)-2-iodoferrocenyl)ethylamine (2). To a solution of (*R*)-*N*,*N*-dimethyl-1-ferrocenylethylamine (**1**) (2.65 g, 10.3 mmol) in ether (25 mL) was added dropwise *sec*-butyllithium (12.4 mL, 11.7 mmol, as a 0.94 M cyclohexane solution) at 0 °C, and the resulting solution was stirred for 1 h. After the solution was cooled to −78 °C, iodine (3.00 g, 11.8 mmol) in THF (25 mL) was added dropwise and the mixture was stirred for 1 h, quenched with water, and extracted with ether. The extract was dried and evaporated under reduced pressure. The residue was purified by column chromatography on alumina (hexane–AcOEt as eluent). 2-Iodoferrocene derivative **2** was obtained in 82% yield (3.24 g) and was recrystallized from acetonitrile: mp 78–9 °C; $[\alpha]^{22}_D$ −9.32° (*c* 1.01, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.47 (d, *J* = 6.3 Hz, 3 H), 2.13 (s, 6 H), 3.60 (q, *J* = 7.5 Hz, 1 H), 4.10 (s, 5 H), 4.11–4.31 (m, 2 H), 4.38–4.53 (m, 1 H); IR (KBr) 3100, 2970, 2940, 2802, 2760, 1370, 1185, 1102, 1085, 1000, 918, 820 cm^{-1}. Anal. Calcd for $C_{14}H_{18}FeIN$: C, 43.90; H, 4.74; N, 3.66. Found: C, 43.78; H, 4.61; N, 3.70.

(*R*,*S*)-1-(2-Iodoferrocenyl)ethylamines 3–6. Reaction of **2** with methyl iodide in acetone afforded a yellow solid (100% yield, mp 133–136 °C, dec), which on reaction with an excess of the corresponding amine in acetonitrile at 30 °C for 12–60 h afforded **3**–**6**.[7c]

3: from **2** and piperidine (100% yield), recrystallized from ethanol–methanol; mp 67–8 °C; $[\alpha]^{22}_D$ −21.9° (*c* 0.960, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.16–1.75 (m, 6 H), 1.50 (d, *J* = 6.3 Hz, 3 H), 2.36 (t, *J* = 5.1 Hz, 4 H), 3.70 (q, *J* = 6.6 Hz, 1 H), 4.10 (s, 5 H), 4.11–4.28 (m, 2 H), 4.35–4.49 (m, 1 H); IR (KBr) 3100, 2998, 2950, 2860, 2805, 2760, 1377, 1108, 1002, 917, 820 cm^{-1}. Anal. Calcd for $C_{17}H_{22}FeIN$: C, 48.26; H, 5.24; N, 3.31. Found: C, 48.25; H, 5.24; N, 3.40.

4: from **2** and diisopropylamine (80% yield), recrystallized from ethanol–hexane; mp 58–60 °C; $[\alpha]^{22}_D$ −77.6° (*c* 1.08, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.96 (d, *J* = 6.0 Hz, 6 H), 1.06 (d, *J* = 6.0 Hz, 6 H), 1.49 (d, *J* = 6.3 Hz, 3 H), 2.89–3.37 (m, 2 H), 3.89–4.28 (m, 3 H), 4.06 (s, 5 H), 4.36–4.45 (m, 1 H); IR (KBr) 3105, 2995, 2950, 2898, 1365, 1195, 1109, 1002, 919, 820 cm^{-1}. Anal. Calcd for $C_{18}H_{26}FeIN$: C, 49.22; H, 5.97; N, 3.19. Found: C, 49.22; H, 6.05; N, 3.21.

5: from **2** and diethylamine (99% yield), recrystallized from ethanol; mp 49 °C; $[\alpha]^{22}_D$ −58.6° (*c* 0.596, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.98 (t, *J* = 7.2 Hz, 6 H), 1.39 (d, *J* = 6.6 Hz, 3 H), 2.39 (q, *J* = 6.9 Hz, 2 H), 2.42 (q, *J* = 6.9 Hz, 2 H), 3.90 (q, *J* = 6.6 Hz, 1 H), 4.09 (s, 5 H), 4.15–4.25 (m, 2 H), 4.38–4.44 (m, 1 H); IR (KBr) 3100, 2980, 2947, 2820, 1380, 1198, 1104, 1001, 904, 820, 813 cm^{-1}. Anal. Calcd for $C_{16}H_{22}FeIN$: C, 46.75; H, 5.39; N, 3.41. Found: C, 46.75; H, 5.51; N, 3.31.

6: from **2** and *N*,*N*-dimethylethylenediamine (95% yield), recrystallized from acetonitrile; mp 83–4 °C; $[\alpha]^{22}_D$ −35.5° (*c* 0.740, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.54 (d, *J* = 6.3 Hz, 3 H), 1.75 (br s, 1 H), 2.10 (s, 6 H), 2.15–2.23 (m, 2 H), 2.25–2.69 (m, 2 H), 3.72 (q, *J* = 6.3 Hz, 1 H), 4.10 (s, 5 H), 4.18–4.27 (m, 2 H), 4.32–4.50 (m, 1 H); IR (KBr) 3450, 3100, 3070, 2970, 2820, 2780, 1425, 1370, 1294, 1103, 1038, 1000, 960, 833, 763 cm^{-1}. Anal. Calcd for $C_{16}H_{23}FeIN_2$: C, 45.10; H, 5.44; N, 6.57. Found: C, 45.29; H, 5.47; N, 6.64.

7: To a solution of **6** (177 mg, 0.42 mmol) in methanol (5 mL) was added 37% aqueous formaldehyde (1.5 mL). At 0 °C sodium borohydride (407 mg) was added portionwise, and the mixture was stirred at room temperature for 1 h. After the usual workup and purification by TLC on alumina (hexane:ether = 1:1), **7** was obtained (167 mg, 91%) as a red-brown oil: $[\alpha]^{22}_D$ −27.6° (*c* 0.456, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.45 (d, *J* = 6.6 Hz, 3 H), 2.10 (s, 3 H), 2.19 (s, 6 H), 2.25–2.60 (m, 4 H), 3.77 (q, *J* = 6.9 Hz, 1 H), 4.10 (s, 5 H), 4.12–4.28 (m, 2 H), 4.34–4.51 (m, 1 H); IR (neat) 3100, 2980, 2950, 2820, 2770, 1460, 1373, 1109, 1023, 1002, 922, 821 cm^{-1}.

(*R*,*S*)-1,2-Disubstituted Ferrocenyl Amino Alcohols 8. The following procedure for the preparation of **8o** ((−)-DFPE) is typical: To a solution of (*R*,*S*)-1-(2-iodoferrocenyl)-1-piperidinoethane (**3**) (229 mg, 0.540 mmol) in ether (2 mL) was added *n*-butyllithium (0.38 mL, 0.62 mmol, as a 1.63 M hexane solution) at 0 °C. After 10 min, benzophenone (119 mg, 0.65 mmol) in ether (2 mL) was added at 0 °C and the mixture was stirred at room temperature for 2 h and quenched with 8% aqueous phosphoric acid. The resulting mixture was washed with ether. The aqueous acid solution was made alkaline with concentrated aqueous sodium hydroxide and was extracted with ether. The extract was dried and evaporated under reduced pressure. The residue was purified by TLC on alumina (hexane:ether = 4:1) to give **8o** (214 mg, 83%): R_f = 0.65; mp 65–9 °C; $[\alpha]^{22}_D$ −209.9° (*c* 0.486, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.29–1.40 (m, 6 H), 1.24 (d, *J* = 6.3 Hz, 3 H), 2.25 (t, *J* = 5.7 Hz, 4 H), 3.82 (s, 5 H), 3.89–4.01 (m, 1 H), 4.03–4.16 (m, 1 H), 4.20–4.30 (m, 1 H), 4.40 (q, *J* = 6.9 Hz, 1 H), 6.98–7.45 (m, 8 H), 7.50–7.75 (m, 2 H), 8.72 (br s, 1 H); IR (KBr) 3460, 3100, 3070, 3050, 2998, 2950, 2840, 1600, 1444, 1248, 1104, 1068, 1036, 1002, 820, 762, 753, 703 cm^{-1}. Anal. Calcd for $C_{30}H_{33}FeNO$: C, 75.16; H, 6.94; N, 2.92. Found: C, 74.82; H, 7.15; N, 3.04.

8a,b: from **2** and benzaldehyde (the reaction of the 2-lithioferrocene derivative derived from **2** and the carbonyl compound was conducted at −40 °C), purified by column chromatography on silica gel [hexane:acetone = 10:1–1:1 (v/v)]. The products were eluted into three bands; **8a** and **8b** were isomeric amino alcohols, and **1** was the deiodinated compound.

8a: 37% yield; $[\alpha]^{22}_D$ −120.6° (*c* 1.04, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.35 (d, *J* = 6.6 Hz, 3 H), 2.21 (s, 6 H), 3.38–3.58 (m, 1 H), 3.80–4.40 (m, 3 H), 4.03 (s, 5 H), 5.93 (s, 1 H), 7.12–7.46 (m, 3 H), 7.46–7.69 (m, 2 H), 7.92 (br s, 1 H); IR (neat) 3102, 3049, 2998, 2955, 2849, 2800, 1605, 1450, 1369, 1270, 1180, 1105, 1042, 1019, 1000, 938, 819, 770, 738, 700 cm^{-1}; HRMS M^+ calcd for $C_{21}H_{25}FeNO$ 363.1285, found 363.1311.

8b: 24% yield; $[\alpha]^{22}_D$ −92.0° (*c* 0.766, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.23 (d, *J* = 6.0 Hz, 3 H), 2.19 (s, 6 H), 3.80 (s, 5 H), 3.90–4.35 (m, 4 H), 5.47 (s, 1 H), 6.30 (br s, 1 H), 7.09–7.68 (m, 5 H); IR (neat) 3370, 3100, 3040, 2998, 2950, 2870, 2798, 1600, 1450, 1367, 1255, 1180, 1104, 1070, 1042, 1000, 937, 818, 719, 700 cm^{-1}.

8c,d: by reaction of **2** and pivalaldehyde followed by treatment of the reaction mixture with water, the usual workup, and purification by TLC on alumina (hexane:ether = 1:1).

8c: 64% yield; R_f = 0.60; mp 91 °C; $[\alpha]^{22}_D$ +130.2° (*c* 0.765, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.18 (s, 9 H), 1.29 (d, *J* = 6.0 Hz, 3 H), 2.15 (s, 6 H), 4.01 (s, 5 H), 4.05–4.18 (m, 3 H), 4.19–4.34 (m, 1 H), 4.54 (s, 1 H), 7.60 (br s, 1 H); IR (KBr) 3450, 3102, 2998, 2960, 2875, 2850, 2800, 1460, 1367, 1180, 1108, 1045, 1005, 940, 820 cm^{-1}. Anal. Calcd for $C_{19}H_{29}FeNO$: C, 66.48; H, 8.51; N, 4.08. Found: C, 66.43; H, 8.70; N, 4.08.

8d: 9% yield; R_f = 0.75; mp 121–4 °C; $[\alpha]^{22}_D$ −44.2° (*c* 0.606, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.94 (s, 9 H), 1.29 (d, *J* = 6.6 Hz, 3 H), 2.07 (s, 6 H), 2.62 (br s, 1 H), 3.80 (q, *J* = 7.5 Hz, 1 H), 3.97–4.25 (m, 3 H), 4.16 (s, 5 H), 4.25–4.35 (m, 1 H); IR (KBr) 3480, 3105, 2999, 2970, 2840, 2800, 1480, 1453, 1362, 1263, 1190, 1106, 1050, 1002, 939, 818 cm^{-1}. Anal. Calcd for $C_{19}H_{29}FeNO$: C, 66.48; H, 8.51; N, 4.08. Found: C, 66.52; H, 8.76; N, 4.04.

8e: from **2** and diisopropyl ketone, purified by TLC on alumina (hexane:ether = 1:1, R_f = 0.70); 27% yield; mp 60–1 °C; $[\alpha]^{22}_D$ +50.8° (*c* 0.634, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.37 (d, *J* = 6.6 Hz, 3 H), 0.85 (d, *J* = 6.3 Hz, 3 H), 1.26 (d, *J* = 6.6 Hz, 6 H), 1.45 (d, *J* = 6.6 Hz, 3 H), 1.60–1.97 (m, 1 H), 2.12 (s, 6 H), 2.30–2.68 (m, 1 H), 3.78–3.95 (m, 1 H), 4.09 (s, 5 H), 4.11–4.27 (m, 3 H), 7.69 (br s, 1 H); IR (KBr) 3420, 3100, 2998, 2960, 2898, 2800, 1460, 1250, 1108, 1015, 1004, 941, 828, 820 cm^{-1}. Anal. Calcd for $C_{21}H_{33}FeNO$: C, 67.92; H, 8.96; N, 3.77. Found: C, 67.65; H, 8.82; N, 3.76.

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8f:[16] from **2** and benzophenone, purified by TLC on alumina (hexane:AcOEt = 13:1, R_f = 0.50); 72% yield; mp 44–54 °C; $[\alpha]^{22}_D$ −182.8° (*c* 0.488, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.20 (d, *J* = 6.3 Hz, 3 H), 1.83 (s, 6 H), 3.83 (s, 5 H), 3.90–3.99 (m, 1 H), 4.05–4.50 (m, 3 H), 7.00–7.49 (m, 8 H), 7.55–7.77 (m, 2 H), 8.71 (br s, 1 H); IR (KBr) 3460, 3100, 3070, 3040, 2999, 2960, 2840, 2800, 1600, 1448, 1260, 1178, 1108, 1047, 1002, 943, 820, 753, 702 cm^{-1}.

8g: from **2** and cyclohexanone, purified by TLC on alumina (hexane:ether = 3:2, R_f = 0.50); 43% yield; mp 108 °C; $[\alpha]^{22}_D$ −17.3° (*c* 0.550, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.05–2.42 (m, 10 H), 1.21 (d, *J* = 6.3 Hz, 3 H), 2.09 (s, 6 H), 3.90–4.09 (m, 3 H), 4.12 (s, 5 H), 4.29 (q, *J* = 6.3 Hz, 1 H), 7.18 (br s, 1 H); IR (KBr) 3450, 3100, 2998, 2950, 2860, 2800, 1445, 1370, 1268, 1142, 1105, 989, 947, 822 cm^{-1}. Anal. Calcd for $C_{20}H_{29}FeNO$: C, 67.61; H, 8.23; N, 3.94. Found: C, 67.62; H, 8.37; N, 3.88.

8h: by reaction of **2** and 2,6-dimethoxybenzaldehyde followed by treatment of the reaction mixture with 8% aqueous phosphoric acid solution for 5 h at room temperature and usual workup and purification by TLC on alumina (Et_2O, R_f = 0.30); 48% yield; mp 45–9 °C; $[\alpha]^{22}_D$ −51.7° (*c* 0.704, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.35 (d, *J* = 6.6 Hz, 3 H), 2.20 (s, 6 H), 3.63–4.00 (m, 2 H), 3.82 (s, 6 H), 3.97 (s, 5 H), 4.02–4.20 (m, 1 H), 4.30 (q, *J* = 6.9 Hz, 1 H), 6.58 (s, 1 H), 6.68 (d, *J* = 3.3 Hz, 2 H), 7.23 (dd, *J* = 6.9, 8.4 Hz, 1 H); IR (KBr) 3450, 3100, 2998, 2950, 2848, 2800, 1595, 1475, 1245, 1180, 1100, 1072, 1004, 920, 808, 730 cm^{-1}. Anal. Calcd for $C_{23}H_{29}FeNO_3$: C, 65.26; H, 6.90; N, 3.31. Found: C, 65.12; H, 7.04; N, 3.31.

8i,j. Reaction of **2** and mesitaldehyde gave a mixture of **8i**, **8j**, and **1**, which was purified by TLC on alumina (hexane:ether = 1:1). The products separated into two bands: **8j** and the mixture of **8i** and **1**. The latter was further purified by TLC on silica gel (acetone).

8i: 28% yield; R_f = 0.60 (silica gel, acetone); mp 53–8 °C; $[\alpha]^{22}_D$ −135.2° (*c* 0.398, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.39 (d, *J* = 6.6 Hz, 3 H), 2.21 (s, 6 H), 2.27 (s, 3 H), 2.38 (s, 6 H), 3.57–3.75 (m, 1 H), 3.83–3.97 (m, 1 H), 4.03 (s, 5 H), 4.10–4.23 (m, 1 H), 4.31 (q, *J* = 6.9 Hz, 1 H), 6.53 (s, 1 H), 6.82 (s, 2 H), 8.28 (br s, 1 H); IR (KBr) 3450, 3100, 2999, 2950, 2850, 2800, 1610, 1460, 1370, 1182, 1109, 1072, 1043, 1003, 938, 850, 818, 770, 735, 680 cm^{-1}. Anal. Calcd for $C_{24}H_{31}FeNO$: C, 71.11; H, 7.71; N, 3.46. Found: C, 70.81; H, 7.67; N, 3.49.

8j: 39% yield; R_f = 0.60 (alumina, hexane:ether = 1:1); mp 136–9° C; $[\alpha]^{22}_D$ +109.6° (*c* 0.356, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.30 (d, *J* = 6.3 Hz, 3 H), 2.07 (s, 6 H), 2.24 (s, 3 H), 2.43 (s, 6 H), 3.78–3.95 (m, 1 H), 3.95–4.30 (m, 3 H), 4.15 (s, 5 H), 6.06 (s, 1 H), 6.77 (s, 2 H); IR (KBr) 3450, 3100, 3000, 2980, 2840, 2800, 1610, 1464, 1319, 1163, 1107, 1050, 1031, 1000, 950, 850, 812, 785, 737, 709 cm^{-1}. Anal. Calcd for $C_{24}H_{31}FeNO$: C, 71.11; H, 7.71; N, 3.46. Found: C, 71.24; H, 7.82; N, 3.50.

8k: from **2** and ferrocenecarboxaldehyde, purified by TLC on alumina (hexane:ether = 1:1, R_f = 0.60); 32% yield; mp 65–8 °C; $[\alpha]^{22}_D$ +45.2° (*c* 0.354, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.30 (d, *J* = 6.3 Hz, 3 H), 2.19 (s, 6 H), 3.58–3.73 (m, 1 H), 3.83–3.97 (m, 1 H), 4.03 (s, 5 H), 4.04–4.22 (m, 4 H), 4.27 (s, 5 H), 4.28–4.45 (m, 2 H), 5.67 (s, 1 H), 7.40 (br s, 1 H); IR (KBr) 3450, 3100, 2995, 2950, 2840, 2800, 1500, 1460, 1368, 1290, 1180, 1103, 1042, 1013, 1000, 935, 815, 770, 740 cm^{-1}. Anal. Calcd for $C_{25}H_{29}Fe_2NO$: C, 63.73; H, 6.20; N, 2.97. Found: C, 63.81; H, 6.33; N, 3.01.

8l,m: from **2** and 9-anthraldehyde, purified by TLC on alumina (hexane:ether = 1:1).

8l: 27% yield; R_f = 0.30; mp 97–106 °C; $[\alpha]^{22}_D$ +64.9° (*c* 0.276, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.47 (d, *J* = 6.6 Hz, 3 H), 2.34 (s, 6 H), 3.30–3.42 (m, 1 H), 3.83 (s, 5 H), 4.01–4.13 (m, 1 H), 4.14–4.30 (m, 1 H), 4.51 (q, *J* = 6.9 Hz, 1 H), 7.25–7.53 (m, 4 H), 7.55 (s, 1 H), 7.89–8.10 (m, 2 H), 8.44 (s, 1 H), 8.60–8.90 (m, 2 H); IR (KBr) 3420, 3080, 2980, 2950, 2860, 2830, 2780, 1620, 1443, 1364, 1258, 1180, 1104, 1042, 1018, 1001, 934, 883, 818, 730 cm^{-1}. Anal. Calcd for $C_{29}H_{29}FeNO$: C, 75.17; H, 6.31; N, 3.02. Found: C, 74.80; H, 6.24; N, 3.00.

8m: 28% yield; R_f = 0.60; mp 57–65 °C; $[\alpha]^{22}_D$ −51.3° (*c* 0.372, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.35 (d, *J* = 6.6 Hz, 3 H), 2.27 (s, 6 H), 3.52–3.65 (m, 1 H), 3.87–3.99 (m, 1 H), 3.97 (s, 5 H), 4.11–4.24 (m, 1 H), 4.50 (q, *J* = 6.9 Hz, 1 H), 6.05 (br s, 1 H), 7.17 (s, 1 H), 7.30–7.60 (m, 4 H), 7.88–8.10 (m, 2 H), 8.40 (s, 1 H), 8.85–9.10 (m, 2 H); IR (KBr) 3440, 3100, 3050, 2970, 2940, 2815, 2775, 1620, 1520, 1365, 1260, 1178, 1104, 1040, 1000, 880, 818, 732 cm^{-1}. Anal. Calcd for $C_{29}H_{29}FeNO$: C, 75.17; H, 6.31; N, 3.02. Found: C, 74.68; H, 6.26; N, 3.01.

8p: from **3** and anthrone, purified by TLC on alumina (hexane:AcOEt = 11:1, R_f = 0.45); 28% yield; mp 93–8 °C; $[\alpha]^{22}_D$ −190.6° (*c* 0.770, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.34 (d, *J* = 6.0 Hz, 3 H), 1.35–1.95 (m, 6 H), 2.64 (t, *J* = 5.4 Hz, 4 H), 3.20–3.39 (m, 1 H), 3.50 (s, 5 H), 3.70–3.90 (m, 1 H), 3.90–4.02 (m, 1 H), 4.02–4.18 (m, 1 H), 4.20–4.60 (m, 2 H), 7.06–7.50 (m, 6 H), 7.60–7.83 (m, 1 H), 7.89–8.09 (m, 1 H); IR (KBr) 3460, 3100, 3070, 3040, 2995, 2950, 2830, 2760, 1450, 1372, 1210, 1180, 1160, 1108, 1100, 1063, 1035, 1001, 922, 820, 760, 747 cm^{-1}. Anal. Calcd for $C_{31}H_{33}FeNO$: C, 75.76; H, 6.77; N, 2.85. Found: C, 75.20; H, 6.58; N, 2.72.

8q,r: from **3** and pivalaldehyde, purified by TLC on silica gel (hexane:acetone = 3:1).

8q: 48% yield; R_f = 0.50; $[\alpha]^{22}_D$ +131.3° (*c* 0.128, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 9 H), 1.22–1.65 (m, 6 H), 1.33 (d, *J* = 6.3 Hz, 3 H), 2.46 (t, *J* = 5.1 Hz, 4 H), 4.02 (s, 5 H), 4.04–4.20 (m, 3 H), 4.20–4.37 (m, 1 H), 4.50 (s, 1 H); IR (neat) 3250, 3105, 3000, 2960, 2840, 1454, 1365, 1277, 1215, 1162, 1121, 1112, 1069, 1009, 935, 907, 822, 762 cm^{-1}; HRMS M^+ calcd for $C_{22}H_{33}NOFe$ 383.1912, found 383.1919.

8r: 6% yield; R_f = 0.55; $[\alpha]^{22}_D$ −30.8° (*c* 0.120, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.99 (s, 9 H), 1.18–1.55 (m, 6 H), 1.27 (d, *J* = 6.0 Hz, 3 H), 2.37 (t, *J* = 5.1 Hz, 4 H), 3.79 (q, *J* = 6.9 Hz, 1 H), 4.03 (s, 1 H), 4.11 (s, 5 H), 4.15–4.24 (m, 2 H), 4.24–4.35 (m, 1 H); IR (neat) 3450, 3100, 3000, 2950, 2820, 1460, 1372, 1120, 1105, 1058, 1000, 941, 910, 820, 770 cm^{-1}.

8s: from **4** and benzophenone, purified by TLC on alumina (hexane:ether = 8:1, R_f = 0.60); 52% yield; mp 50–5 °C; $[\alpha]^{22}_D$ −192.0° (*c* 0.762, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.69 (d, *J* = 6.3 Hz, 6 H), 1.09 (d, *J* = 6.0 Hz, 6 H), 1.38 (d, *J* = 6.6 Hz, 3 H), 2.85–3.22 (m, 2 H), 3.70 (s, 5 H), 3.90–4.10 (m, 1 H), 4.12–4.23 (m, 1 H), 4.23–4.37 (m, 1 H), 4.82 (q, *J* = 6.9 Hz, 1 H), 6.98–7.47 (m, 8 H), 7.60–7.83 (m, 2 H), 8.45 (br s, 1 H); IR (KBr) 3450, 3100, 3070, 2990, 2950, 2890, 1600, 1487, 1444, 1370, 1243, 1183, 1165, 1105, 1090, 1045, 1000, 879, 819, 750, 700 cm^{-1}. Anal. Calcd for $C_{31}H_{37}FeNO$: C, 75.15; H, 7.53; N, 2.83. Found: C, 75.19; H, 7.67; N, 2.68.

8t: from **5** and benzophenone, purified by TLC on alumina (hexane:ether = 3:1, R_f = 0.75); 56% yield; mp °C; $[\alpha]^{22}_D$ −229.5° (*c* 0.346, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.63 (t, *J* = 7.2 Hz, 6 H), 1.20 (d, *J* = 6.6 Hz, 3 H), 1.89–2.58 (m, 4 H), 3.78 (s, 5 H), 3.89–4.03 (m, 1 H), 4.07–4.20 (m, 1 H), 4.20–4.31 (m, 1 H), 4.65 (q, *J* = 6.9 Hz, 1 H), 6.98–7.48 (m, 8 H), 7.53–7.76 (m, 2 H), 8.70 (br s, 1 H); IR (KBr) 3450, 3100, 3060, 2995, 2950, 2840, 1598, 1445, 1390, 1248, 1193, 1177, 1109, 1076, 1034, 1003, 871, 820, 755, 702 cm^{-1}. Anal. Calcd for $C_{29}H_{33}FeNO$: C, 74.52; H, 7.12; N, 3.00. Found: C, 74.40; H, 7.27; N, 3.04.

8u: from **7** and benzaldehyde, purified by TLC on alumina (hexane:AcOEt = 3:5, R_f = 0.75); 53% yield; $[\alpha]^{22}_D$ −125.5° (*c* 0.494, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.36 (d, *J* = 6.6 Hz, 3 H), 2.17 (s, 9 H), 2.26–2.73 (m, 4 H), 3.43–3.60 (m, 1 H), 3.86–3.98 (m, 1 H), 4.00 (s, 5 H), 4.06–4.20 (m, 2 H), 5.90 (s, 1 H), 7.20–7.48 (m, 3 H), 7.48–7.69 (m, 2 H); IR (neat) 3180, 3100, 3040, 2990, 2950, 2830, 2770, 1603, 1452, 1370, 1273, 1200, 1130, 1107, 1069, 1021, 1001, 938, 819, 743, 700 cm^{-1}.

(*S*,*R*)-1,2-Disubstituted Ferrocenyl Amino Alcohols 11 and 12. The procedure for the preparation of (*R*,*S*)-1,2-disubstituted ferrocenyl amino alcohols **8** was used.

11 ((+)-DPFE): from (*S*)-1-((*R*)-2-iodoferrocenyl)-1-piperidinoethane [mp 67–8 °C; $[\alpha]^{22}_D$ +21.9° (*c* 0.844, EtOH)] (from **9**) and benzophenone, purified by TLC on alumina (hexane:ether = 4:1, R_f = 0.65); 76% yield; mp 68–72 °C; $[\alpha]^{22}_D$ +206.0° (*c* 0.386, EtOH).

12. To a solution of **10** (159 mg, 0.56 mmol) in ether (2 mL) was added *n*-butyllithium (0.39 mL, 0.64 mmol, 1.63 M hexane solution) at room temperature. After 1 h, benzaldehyde (69 mg, 0.65 mmol) in ether (2 mL) was added at 0 °C and the whole was stirred at room temperature for 3 h and quenched by adding 8% aqueous phosphoric acid solution. The resulting mixture was washed with ether. The aqueous acid solution was separated, stirred for 2 h at room temperature, made alkaline with concentrated aqueous sodium hydroxide solution, and extracted with

(16) A known compound: see ref 7b.

ether. The extract was dried and evaporated. The residue was purified by TLC on alumina (hexane:AcOEt = 8:1, R_f = 0.40) to give 46 mg (21% yield) of 12: $[\alpha]^{22}_D$ +142.4° (c 0.644, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.25 (d, J = 6.6 Hz, 3 H), 1.46 (d, J = 6.6 Hz, 3 H), 2.45 (s, 6 H), 2.46–2.80 (m, 1 H), 3.45–3.62 (m, 1 H), 3.82–4.29 (m, 3 H), 4.01 (s, 5 H), 5.87 (s, 1 H), 7.17–7.48 (m, 3 H), 7.48–7.69 (m, 2 H), 7.75 (br s, 1 H); IR (neat) 3100, 3040, 2960, 2940, 2880, 2800, 1600, 1446, 1382, 1363, 1262, 1197, 1181, 1104, 1078, 1041, 1018, 1000, 942, 840, 816, 740, 700 cm^{-1}; HRMS M$^+$ calcd for $C_{23}H_{29}NOFe$ 391.1599, found 391.1560.

General Procedure for the Enantioselective Addition of Diethylzinc to Aldehydes Using Chiral 1,2-Disubstituted Ferrocenyl Amino Alcohols as Catalyst. The aldehyde (2 mmol) in hexane (2 mL) was added to a solution of chiral 1,2-disubstituted ferrocenyl amino alcohol (0.1 mmol) in hexane (2 mL) at room temperature. After 15 min, Et_2Zn (3.2 mL, 3.2 mmol, 1 M hexane solution) was added and the whole was stirred at room temperature for 1–4 h. Aqueous hydrochloric acid (1 N) was added to quench the reaction under cooling with ice–water. The resulting mixture was extracted with ether, and the extract was washed with brine, dried, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane–AcOEt or pentane–ether for low-boiling products) and then bulb-to-bulb distillation. The product was identified by comparing the ^{1}H NMR and IR spectra with those of authentic samples, and the optical rotation was measured. Experimental results are summarized in Tables I–III. The chiral 1,2-disubstituted ferrocenyl amino alcohol was recovered in over 90% yield after usual workup of the dilute aqueous acid solution. Optical purities (% ee) were determined by HPLC analyses of the resulting secondary alcohols or the corresponding (*S*)-MTPA esters on a chiral column, by GC analyses of the corresponding (*S*)-MTPA esters on a capillary column, or by optical rotation. Conditions of HPLC analyses: chiral column, Chiralcel OB, 4.6 × 250 mm; detection, 254-nm light. For 1-phenylpropanol: eluent, 4% 2-propanol in hexane; flow rate, 0.15 mL/min; retention time (min), *S* isomer 48.1, *R* isomer 56.5. For 1-(*p*-chlorophenyl)-propanol: 5% 2-propanol in hexane; 0.15 mL/min; *S* isomer 39.6, *R* isomer 42.4. For 1-(*p*-methoxyphenyl)propanol: 10% 2-propanol in hexane; 0.15 mL/min; *S* isomer 58.1, *R* isomer 72.4. For 1-(2-naphthyl)propanol: 7% 2-propanol in hexane; 0.15 mL/min; *S* isomer 63.3, *R* isomer 71.1. For the (*S*)-MTPA ester of 1-(2-furyl)propanol: 1% 2-propanol in hexane; 0.15 mL/min; retention time (min), 29.7 and 36.4 for the diastereomeric esters. Conditions of GC analyses: column, OV-1, nonpolar capillary column, 0.25 mm × 50 m; detection, flame ionization detector; carrier gas, N_2 (1.5 kg/cm^2). For the (*S*)-MTPA ester of 1-cyclohexylpropanol: column temperature, 170 °C; retention time (min), 58.4 and 60.2 for the diastereomeric esters. For the (*S*)-MTPA ester of 4-ethyl-3-hexanol: column temperature, 150 °C; retention time (min), 54.7 and 56.1. For the (*S*)-MTPA ester of 2,2-dimethyl-3-pentanol: column temperature, 140 °C; retention time (min), 50.2 and 51.7.

Enantioselective Addition of Di-*n*-butylzinc to Aldehydes with 8o as Catalyst. Butylation was carried out for 5 h in a manner similar to the procedure for ethylation.

(*S*)-1-Phenylpentanol: mp 31–2 °C; $[\alpha]^{22}_D$ −39.9° (c 3.08, C_6H_6) [lit.[17] $[\alpha]^{25}_D$ +35.7° (c 3.00, C_6H_6) for *R* isomer] in 99% ee, which was determined by HPLC analysis: chiral column, Chiralcel OB; eluent, 4% 2-propanol in hexane; flow rate, 0.15 mL/min; retention time (min), *S* isomer 49.5, *R* isomer 57.5.

(*S*)-2-Methyl-3-heptanol: $[\alpha]^{22}_D$ −27.1° (c 2.95, EtOH) [lit.[18] $[\alpha]_D$ +27.67° (c 10, EtOH)] in >98% ee, determined by GC analysis of the corresponding (*S*)-MTPA ester: column, PEG-20M, polar capillary column, 0.25 mm × 50 m; carrier gas, N_2 (1.5 kg/cm^2); column temperature, 145 °C; retention time (min), 63.5 and 64.5.

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