Pergamon

Tetrahedron: Asymmetry Vol. 5, No. 3, pp. 411-424, 1994
Elsevier Science Ltd
Printed in Great Britain
0957-4166/94 $6.00+0.00

0957-4166(94)E0052-C

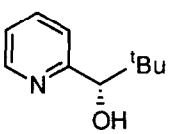
Catalysed Asymmetric Reaction of Aldehydes with Dialkylzinc in the Presence of Chiral Pyridyl Alcohols as Ligands[1]

Miyuki Ishizaki, Ko-ichi Fujita, Mahoko Shimamoto, and Osamu Hoshino*

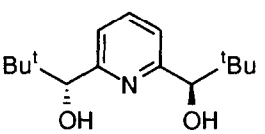
Faculty of Pharmaceutical Sciences, Science University of Tokyo, Shinjuku-ku, Tokyo 162, Japan

Abstract: The synthesis of homochiral pyridyl alcohols (**1**,**2**,**3a-c**) and a catalytic asymmetric addition of dialkylzinc to various aldehydes using **1-3** as ligands are described. Although the reaction of benzaldehyde with Et_2Zn in the presence of (S)-**1** and (R,R)-**2** gave (S)- and (R)-1-phenyl-1-propanol, respectively, in moderate enantiomeric excess (e.e.), tridentate ligands (**3a-c**) accelerated the reaction to produce the corresponding alcohols in high e.e. Particularly, (S)-**3b** was found to be the most efficient catalyst, for which asymmetric reactions of various aldehydes with dialkylzinc gave the corresponding alcohols in good to high e.es. (up to 95% e.e.).

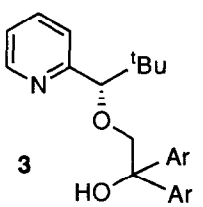
A catalytic method for asymmetric reactions has been a challenging subject in organic synthesis during this decade.[2] For example, asymmetric addition[3] of dialkylzinc to aldehydes in the presence of catalytic amounts of chiral ligands is one of the reactions. Since a first report on the reaction using a catalytic amount of certain β-amino alcohols by Oguni and Omi[4] in 1984, numerous efforts have been made to search for new effective ligands in the reaction and to prove the reaction mechanism by many organic chemists.[3a,5] In the reaction, chiral β-amino alcohols have been used as effective ligands. Recently, however, the employment of some pyridyl alcohols[6a-c] and amines[6d,e] as ligands has been reported by Bolm and Chelucci. These reports prompted us to publish our results on the present reaction by use of a catalytic amount of new pyridyl alcohols. The present



1

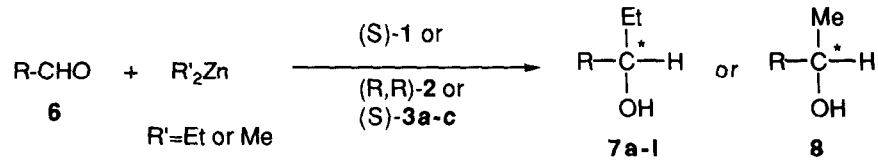


2



3

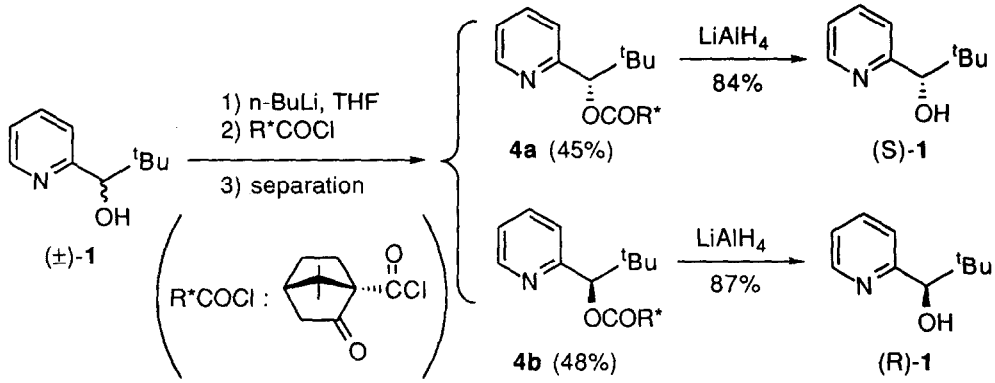
a: Ar = Ph
b: Ar = α-Naphthyl
c: Ar = β-Naphthyl



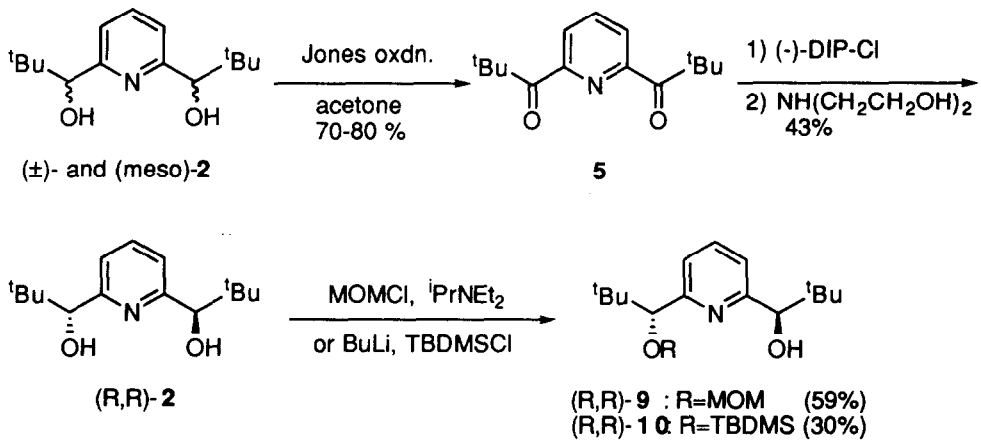
a: R=Ph
b: R=p-MeC_6H_4
c: R=p-MeC_6H_4
d: R=p-BrC_6H_4
e: R=p-ClC_6H_4
f: R=p-FC_6H_4
g: R=o-FC_6H_4
h: R=p-$CF_3C_6H_4$
i: R=(E)-PhCH=CH
j: R=$PhCH_2CH_2$
k: R=c-C_6H_{11}
l: R=$CH_3(CH_2)_7$

paper deals with synthesis of novel homochiral pyridyl alcohols (**1**-**3**) as ligands and with their utility in the addition of dialkylzinc to various aldehydes.

Chiral pyridyl alcohols (**1**,**2**) were synthesized as follows. Although **1**[6a,b] has been prepared by reduction of the corresponding ketone with (+)-diisopinocamphenylborane chloride (DIP-Cl),[7] its e.e. was only 90%. Therefore, we planned the separation of diastereomeric esters of **1**. Esterification of racemic alcohol (**1**), derived from 2-lithiopyridine and pivalaldehyde, with D-ketopinyl chloride[8] afforded a diastereomeric mixture of esters (**4a**,**b**), which was separated by medium-pressure liquid chromatography to give **4a** and **4b** in 45 and 48% yields, respectively. Treatment of **4a** and **4b** with $LiAlH_4$ led to (S)- and (R)-pyridyl alcohols (**1**) in 84 and 87% yields, respectively. E.es. of (S)- and (R)-**1** were determined to be 100% by HPLC analysis of the corresponding acetates using chiral column .



Although pyridyl diol (**2**) has been synthesized previously by a resolution procedure,[9] the procedure seems to be unsuitable for a large scale preparation of **2**. Hence, the asymmetric synthesis of **2** was examined. Oxidation of racemic and meso-**2**[9] gave ketone **5** in 80 and 70% yields, respectively. Reduction of **5** with (+)- or (-)-DIP-Cl[7] gave (R,R)- and (S,S)-**2**, e.es. of which were estimated to be both 100% by HPLC analysis



using a chiral column. These findings are different from those reported for **1** but might be due to stereoselective reduction of keto alcohols, which would be formed by a first reduction of **5** with (+)- or (-)-DIP-Cl. Thus, we could prepare both enantiomers of **2** in homochiral form.

At first, the reaction of benzaldehyde (**6a**) with Et_2Zn in the presence of 2-15mol% (S)-**1** in hexane for 15-18 h was performed. Despite of employment of (S)-**1** of 100% e.e., the e.e. of (S)-1-phenyl-1-propanol (**7a**) was not more than 66%. The best result was obtained in the reaction using 4 eq. of Et_2Zn with 10 mol% of (S)-**1** in 0.128M solution (70% yield, 66% e.e.); it might be dependent on concentration of the reactants and molar ratio of Et_2Zn to aldehydes in the reaction.[10]

Next, we examined the reaction using (R,R)-**2**. Ligand **2** was expected to enhance the enantioselectivity by interaction between the aldehyde and a chiral alcohol moiety at the C_6 position of the pyridine ring. The reaction of various aromatic (**6b-g**) and aliphatic aldehydes (**6i,j**) with Et_2Zn was carried out in hexane containing 5 mol% of (R,R)-**2** at room temperature. The results are shown in Table 1. Contrary to expectation, however, the reaction of benzaldehyde gave results similar to that in the reaction using (S)-**1** (Table 1, entries 1,2). The reaction of benzaldehyde using lithium or titanium alkoxides of (R,R)-**2** decreased remarkably the enantioselectivity (Table 1, entry 3-5). The reaction of aromatic aldehydes (**6c-f**) expect **6b,g** gave the corresponding alcohols (**7c-f**) in fair e.es. and yields, whereas that of aliphatic aldehydes (**6i,j**) did not afford satisfactory results.[11]

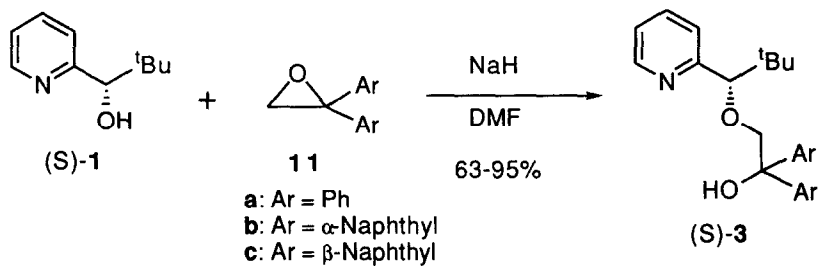
In order to examine the influence of the C_6 substituent on the pyridine ring, (R,R)-**2** was converted to the methoxymethyl ether (**9**) and t-butyldimethylsilyl ether (**10**) in the usual manner. Thus, asymmetric ethylation of benzaldehyde in the presence of 5 mol% of (R,R)-**9** or -**10** afforded (R)-1-phenyl-1-propanol in 71 (51% e.e.) or 79% (67% e.e.) yield. The findings suggested that a chiral C_6-alcohol or ether moiety in the pyridine ring did not play an important role in the reaction.[12]

Table 1. Catalysed asymmetric addition of diethylzinc to various aldehydes in the presence of (R,R)-**2**.

Entry[a]	**7** R	Time(h)	Yield(%)	E.e.(%)[b]	Config.
1	Ph	16	70	68	R
2[c]	Ph	25	77	65	S
3[d]	Ph	25	54	57	R
4[e]	Ph	28	51	55	R
5[f]	Ph	28	69	31	R
6	p-MeO-C_6H_4	21	58	46	R
7	p-Me-C_6H_4	17	64	64	R
8	p-Br-C_6H_4	14	76	71[g]	R
9	p-Cl-C_6H_4	14	81	72[h]	R
10	p-F-C_6H_4	14	63	75	-
11	o-F-C_6H_4	15	80	39[g]	-
12	(E)-PhCH=CH	17	66	20	R
13	$PhCH_2CH_2$	17	32	44[h]	R

a) All reactions were carried out at room temperature using 5 mol% of (R,R)-**2** in hexane, unless otherwise noted. b) Determined by HPLC analyses using DAICEL chiral cel OB or OD, unless otherwise noted. c) 5 mol% of (S,S)-**2** was used. d) 1 eq. of BuLi to (R,R)-**2** was added. e) 2 eq. of BuLi to (R,R)-**2** was added. f) 1 eq. of $Ti(O^iPr)_4$ to (R,R)-**2** was added. g) Determined by ^{1}H-NMR analysis of the corresponding (-)-MTPA esters. h) Based on the reported value of optical rotation.

Next, we turned our attention to tridentate ligand,[13] because such ligands[5,14] are known to accelerate more effectively the reaction than bidentate ligands. For this purpose, we designed tridentate ligands bearing aryl groups. Thus, tridentate ligands (**3a-c**) were synthesized in 63 to 95% yield by the reaction of (S)-**1** with epoxides (**11a-c**)[15] in the presence of NaH in DMF.



Using the homochiral tridentate ligands (**3a-c**), the reaction of benzaldehyde with Et_2Zn was performed at room temperature. E.es. of the products were determined by HPLC analyses using DAICEL chiral cel OB or OD. The results are shown in Table 2. In general, it is known that addition of Et_2Zn to benzaldehyde using β-amino alcohol required a prolonged reaction time (more than ten hours).[3] Surprisingly, the reaction using **3a-c**

Table 2. Catalysed asymmetric addition of dialkylzinc to benzaldehyde in the presence of (S)-**3a-c**.

Entry	Ligand	mol%	Solvent[a]	Alcohol	Time(min)	Yield(%)	E.e.(%)[b]
1	**3a**	5	H	**7a**	25	79	83
2	**3a**	5	H-T	**7a**	60	81	86
3	**3a**	5	H	**8**	43x60	21	37
4	**3b**	5	H	**7a**	10	97	91
5	**3b**	2	H	**7a**	20	92	91
6	**3b**	5	H-T	**7a**	20	94	93
7	**3b**	2	H-T	**7a**	70	96	93
8[c]	**3b**	2	H-T	**7a**	70	97	91
9	**3b**	2	Et_2O	**7a**	20	88	90
10	**3b**	2	THF	**7a**	180	91	86
11	**3b**	0.5	H-T	**7a**	270	90	89
12	**3b**	0.1	H-T	**7a**	24x60	70	80
13	**3b**	0.01	H-T	**7a**	72x60	46	53
14	**3b**	5	H	**8**	240	93	92
15	**3c**	5	H	**7a**	20	97	93
16	**3c**	2	H	**7a**	60	94	87
17	**3c**	5	H-T	**7a**	50	94	93
18	**3c**	2	H-T	**7a**	140	85	91
19	**3c**	5	H	**8**	24x60	84	88

a) H = hexane, H-T = hexane : toluene (1 : 1). b) Determined by HPLC analyses using DAICEL chiral cel OB. Absolute configuration of the alcohols was (S), unless otherwise noted. c) (R)-**3b** was used. The absolute configuration of the alcohol was (R).

was completed smoothly in a short reaction time to give the product in high chemical and optical yields. Particularly, the reaction using (S)-**3b** (5 mol%) proceeded completely within 20 min (entries 4, 6).[16] Longer reaction time was required in polar solvents such as THF (entry 10). After careful examination of the reaction, we found that a mixture of toluene and hexane was the best solvent in the reaction. Moreover, the amount of catalyst could be decreased from 5 to 2 mol% without loss of enantioselectivity. Favourable enantioselectivity was obtained even with 0.1 mol% of (S)-**3b**, though the reaction was slow (entry 12). Furthermore, addition of Me_2Zn to benzaldehyde in the presence of (S)-**3b** gave (S)-alcohol (**8**) in 92% e.e. for 4 h (entry 14).[17] To our knowledge, this is the shortest time in the reaction of benzaldehyde with Me_2Zn.

In order to examine the utility of the catalyst, the catalysed reaction of Et_2Zn with various aldehydes (**6b-l**) using 2 mol% of (S)-**3b** was carried out (Table 3). The reaction of Et_2Zn with aromatic aldehydes (**6b-h**) in a mixture of toluene and hexane afforded the corresponding alcohols with high enantioselectivity and chemical yields (entries 1-7). In particular, p-fluorobenzaldehyde (**6f**) gave the corresponding alcohol (**7f**)[18] in 95%

Table 3. Catalysed asymmetric addition of diethylzinc to various aldehydes in the presence of (S)-**3b**.

Entry[a]	7 R	Solvent[b]	Time(min)	Yield(%)	E.e.(%)[c]	Config.
1	p-MeO-C_6H_4	H-T	120	96	90	S
2	p-Me-C_6H_4	H-T	70	96	91	S
3	p-Br-C_6H_4	H-T	60	97	93	S
4	p-Cl-C_6H_4	H-T	60	92	91	S
5	p-F-C_6H_4	H-T	40	96	95[d]	-
6	o-F-C_6H_4	H-T	40	97	89[d]	-
7	p-CF_3-C_6H_4	H-T	30	97	89[d]	S
8	(E)-PhCH=CH	H-T	120	93	70	S
9	(E)-PhCH=CH	H	20	95	71	S
10[e]	(E)-PhCH=CH	H	5	99	71	S
11[f]	(E)-PhCH=CH	H	30	91	64	S
12	$PhCH_2CH_2$	H-T	120	56	88	S
13	$PhCH_2CH_2$	H	10	83	84	S
14	$CH_3(CH_2)_7$	H	30	84	80	S
15	c-C_6H_{11}	H	30	88	86[d]	S

a) All reactions were carried out at room temperature using 2 mol% of (S)-**3b**, unless otherwise noted. b) H = hexane, H-T = hexane : toluene = 1 : 1. c) Determined by HPLC analyses using DAICEL chiral cel OB or OD, unless otherwise noted. d) Determined by ^{1}H- or ^{13}C-NMR analysis of the corresponding (-)-MTPA esters. e) 5 mol% of (S)-**3b** was used. f) The reaction was carried out at 0°C.

e.e., though the absolute configuration was uncertain (entry 5). Other fluorine containing alcohols were also synthesized in high e.es.. Hence, the present reaction seems to be an effective method to obtain optically active fluorine containing alcohols.[19]

On the other hand, the reaction of aliphatic aldehyde (**6i,j**) in a mixture of toluene and hexane was 6-12 times slower than that in hexane. However, enantioselectivity was almost the same in each solvent (entries 8 vs 9 and 12 vs 13). With cinnamaldehyde (**6i**), an increase of catalyst did not improve the enantioselectivity, although the reaction was accelerated (entry 10). Furthermore, the reaction at low temperature resulted in low enantioselectivity (entry 11).[20] On the whole, the asymmetric addition of Et_2Zn to aliphatic aldehydes (**6i-l**) furnished the alcohols in good e.e. (71-88%).

The observed stereochemical outcome in the reaction of Et_2Zn with benzaldehyde using **3** could be explained by the mechanistic pathway as depicted in Fig. 1. First, the reaction of tridentate ligand **3a-c** with Et_2Zn could generate adduct (**12**). Coordination of the aldehyde oxygen with **12** gave pentacoordinated Zn intermediate **13**[14] rather than **14** owing to steric repulsion between aromatic group of aldehyde and the pyridine moiety of the catalysts. Consequently, (S)-alcohol was produced predominantly.

It is noteworthy that in the reaction using **3**, the reaction rate was significantly enhanced. Namely, considering the fact that zinc is coordinated with bidentate ligands to form dimeric compound,[2a] which has no catalytic activity, rapid formation of monomeric species would be interpreted by the assumption that tridentate ligand (**3**) would prevent formation of dimeric compound because of saturated coordination on the zinc atom (*cf.* **1 2**) and sterical crowded by two aryl groups. Furthermore, an intermediate (**1 3**) is preferable to **1 4**, because of steric repulsion between the pyridine moiety of the catalyst and aromatic group of benzaldehyde. Thus, steric factors[21] owing to the bulky aryl groups might rapidly detach the ethylzinc alkoxide formed from coordinated chiral catalyst (**1 3**).

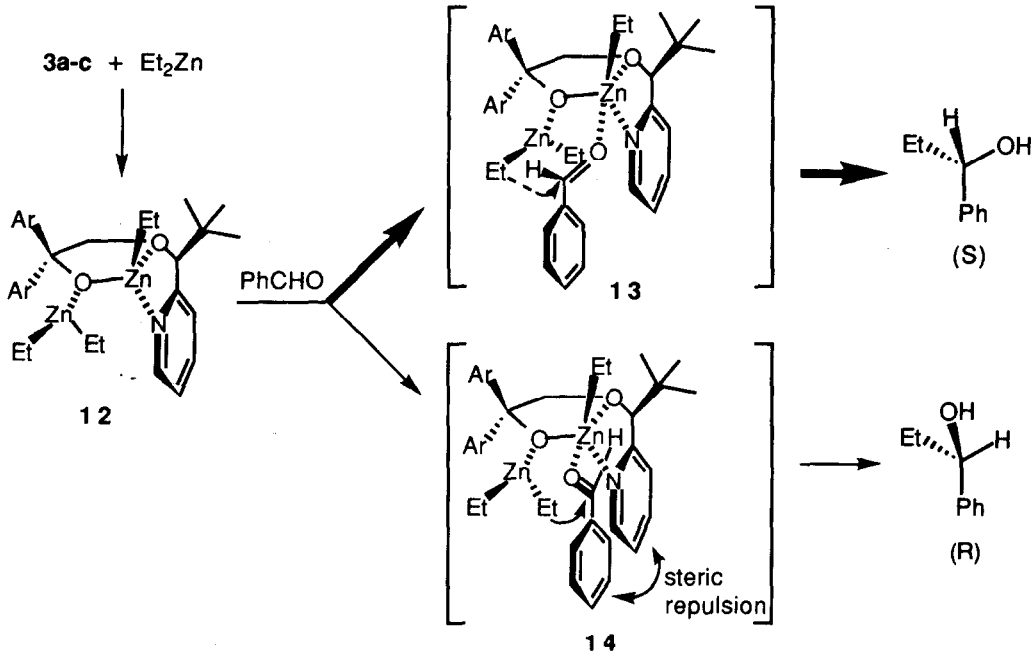


Fig. 1

In the summary, novel tridentate pyridyl alcohols (**3a-c**) were found to be effective catalysts for the enantioselective addition of dialkylzinc to various aldehydes. It is noteworthy that **3 b** considerably accelerates the reaction. Application of these ligands (**3a-c**) to further asymmetric syntheses is now under way.

Acknowledgment: We are thankful to Miss N. Sawabe, Mrs. F. Hasegawa, and Mr. H. Igarashi of this faculty for ^{1}H-NMR and mass spectral measurements and elementary analyses.

Experimental Section

General. All melting points were measured on a Büchi melting point apparatus and are uncorrected. Unless otherwise noted, IR spectra were performed with a Hitachi 260-10 spectrometer in $CHCl_3$ solution, and ^{1}H-

NMR spectra were taken with a JEOL JMX-FX100 (100 MHz) spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal standard. Mass spectra were measured on a Hitachi M-80 or a JEOL JMS D-300 spectrometer. HPLC analysis was performed with SSC flow system 3100 and SSC UV detector 3000A-II using Daicel Chiral Cel OB or OD (0.46ϕ x 25cm). Preparative TLCs were run on Merck 7730 plates.

Materials. Tetrahydrofuran (THF), ether, hexane, and toluene were distilled from $LiAlH_4$ prior to use. Aldehydes were distilled prior to use. Diethylzinc (1M in hexane solution) was purchased from Kanto Chemical Co., Ltd. Dimethylzinc (1M in hexane solution) was purchased from Trichemical Co., Ltd. (-)- and (+)-DIP-Cl were purchased from Aldrich Co., Ltd.

(±)-2,2-Dimethyl-1-(2'-pyridyl)propanol (1). To a solution of 2-bromopyridine (15 g, 95 mmol) in THF (300 ml) at -78 °C under argon atmosphere was added BuLi (65 ml, 101 mmol, 1.55 M in hexane) over a period of 5 min. After being stirred for 1 h, pivalaldehyde (8.7 g, 101 mmol) was added to the mixture over 10 min and the mixture was stirred for additional 1.5 h. The reaction was quenched with water. The solvent was removed under reduced pressure and the residue was taken up in ether. The organic layer was washed with brine, dried (K_2CO_3) and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 8 : 1) and subsequent distillation under reduced pressure (100-110 °C/13 mmHg) to give (±)-**1** (11.1 g, 71%) as colorless crystals. Mp 53-54 °C; ^{1}H-NMR δ: 0.91 (9H, s, ^{t}Bu), 4.32 (2H, s, H-2, OH), 7.06-7.24 (2H, m, H-3', H-5'), 7.60 (1H, dt, J = 2, 7.5 Hz, H-4'), 8.50 (1H, ddd, J = 1, 2, 5 Hz, H-6'); IR 3425 cm^{-1}; MS *m/z* 165 (M^+); High-resolution mass *m/z* calcd for $C_{10}H_{15}NO$ (M^+) 165.1152. Found: 165.1150. HPLC analysis of (±)-**1** using DAICEL chiral cel OD with 1% 2-propanol in hexane (flow; 1.0 ml/min) gave two peaks at 6.5 and 9.3 mins.

(S)-(-)-(4a) and (R)-(+)-2,2-Dimethyl-1-(2'-pyridyl)propyl D-Ketopinate (4b). To a solution of (±)-**1** (3.62 g, 21.9 mmol) in THF (75 ml) at -78 °C under argon atmosphere was added BuLi (15 ml, 24.8 mmol, 1.65 M in hexane). After being stirred for 0.5 h, a solution of D-ketopinyl chloride (5.27 g, 26.3 mmol) in THF (25 ml) was added and the mixture was stirred for additional 0.5 h. The reaction was quenched with water. The aqueous layer was extracted with ether. The extract was washed with brine, dried (K_2CO_3) and evaporated under reduced pressure. The residue was purified by medium-pressure silica gel column chromatography (hexane : AcOEt = 9 : 1) to give **4a** (3.26 g, 45.2%) and **4b** (3.48 g, 48.1%) as each colorless crystals. **4a**: Mp 120-120.5 °C (hexane); $[\alpha]_D^{24}$ -14.2 (c=1, $CHCl_3$); ^{1}H-NMR δ: 0.98 (9H, s, ^{t}Bu), 1.06, 1.26 (each 3H, s, Mex2), 1.68-2.72 (7H, m, $CH_2CH_2CH_2$, CH), 5.53 (1H, s, H-2), 7.12 (1H, ddd, J = 1.2, 5.0, 7.5 Hz, H-5'), 7.36 (1H, dt, J = 1.2, 7.5 Hz, H-3'), 7.62 (1H, dt, J = 2, 7.5 Hz, H-4'), 8.51 (1H, ddd, J = 1.2, 2, 5.0 Hz, H-6'); IR 1730, 1760 cm^{-1}; MS *m/z* 329 (M^+); Anal. Calcd for $C_{20}H_{27}NO_3$: C, 72.92; H, 8.26; N, 4.25. Found: C, 73.24; H, 8.01; N, 4.30. **4b**: Mp 106-107 °C (hexane); $[\alpha]_D^{26}$ +60.6 (c=1, $CHCl_3$); ^{1}H-NMR δ: 0.98 (9H, s, ^{t}Bu), 1.09, 1.24 (each 3H, s, Mex2), 1.66-2.72 (7H, m, $CH_2CH_2CH_2$, CH), 5.60 (1H, s, H-2), 7.13 (1H, ddd, J = 1.2, 5, 8 Hz, H-5'), 7.36 (1H, dt, J = 1.2, 8 Hz, H-3'), 7.63 (1H, dt, J = 2, 8 Hz, H-4'), 8.51 (1H, ddd, J = 1.2, 2, 5 Hz, H-6'); IR 1730, 1760 cm^{-1}; MS *m/z* 329 (M^+); Anal. Calcd for $C_{20}H_{27}NO_3$: C, 72.92; H, 8.26; N, 4.25. Found: C, 73.27; H, 7.92; N, 4.35.

(S)-(-)-2,2-Dimethyl-1-(2'-pyridyl)propanol (1). To a solution of **4a** (2.966 g, 9.0 mmol) in THF (90 ml) at room temperature under argon atmosphere was added $LiAlH_4$ (0.511 g, 13.5 mmol) in small portions. After the mixture was stirred for 0.5 h, the reaction was quenched with saturated aq. Na_2SO_4. The

precipitate was filtered off and the filtrate was dried (K_2CO_3) and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 4 : 1) to give (S)-**1** (1.251 g, 84.1%, 100% e.e.) as colorless crystals. The HPLC analysis in a similar way to that noted for (±)-**1** gave only one peak at 9.3 min. Mp 36.5-37.5 °C; $[\alpha]_D^{28}$ -47.8 (c=1, EtOH); ^{1}H-NMR δ: 0.91 (9H, s, ^{t}Bu), 4.32 (2H, s, H-2, OH), 7.06-7.24 (2H, m, H-3', H-5'), 7.60 (1H, dt, J = 2, 7.5 Hz, H-4'), 8.50 (1H, ddd, J = 1, 2, 5 Hz, H-6'); IR 3425 cm^{-1}; MS *m/z* 166 (M^++1); High-resolution mass *m/z* calcd for $C_{10}H_{16}NO$ (M^++1) 166.1231. Found: 166.1239.

(R)-(+)-2,2-Dimethyl-1-(2'-pyridyl)propanol (1). Reaction of **4b** (3.296 g, 10 mmol) with $LiAlH_4$ (0.571 g, 15.1 mmol) in a similar manner to that described for **4a**, (R)-**1** (1.440 g, 87.1%, 100% e.e.) was obtained. HPLC analysis as described above gave only one peak at 6.5 min. Mp 37-37.5 °C; $[\alpha]_D^{28}$ +47.1 (c=1, EtOH); ^{1}H-NMR δ: 0.91 (9H, s, ^{t}Bu), 4.32 (2H, s, H-2, OH), 7.06-7.24 (2H, m, H-3', H-5'), 7.60 (1H, dt, J = 2, 7.5 Hz, H-4'), 8.50 (1H, ddd, J = 1, 2, 5 Hz, H-6'); IR 3425 cm^{-1}; MS *m/z* 166 (M^++1); High-resolution mass *m/z* calcd for $C_{10}H_{16}NO$ (M^++1) 166.1231. Found: 166.1232.

2,6-Bis(2',2'-dimethylpropionyl)pyridine (5). a) From (±)-**2**; A mixture of (±)-**2**[9] (2.0 g, 8.0 mmol) and 8N Jones reagent (30 ml, 240 mmol) in acetone (100 ml) at 0 °C was stirred for 1.5 h. Then, 2-propanol (6 ml) was added to the mixture. The mixture was made alkaline with 3N NaOH, and the precipitate was filtered through Celite 545 short pad. The filtrate was extracted with CH_2Cl_2 and the extract was washed with brine, dried (K_2CO_3), and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 16 : 1) to give **5** (1.57 g, 80 %). oil; ^{1}H-NMR δ: 1.56 (18H, s, ^{t}Bux2), 7.58-8.00(3H, m, arom. Hx3); IR 1680 cm^{-1}; MS *m/z* 247 (M^+); High-resolution mass *m/z* calcd for $C_{15}H_{21}NO_2$ (M^+) 247.1571. Found: 247.1574. b) From (meso)-**2**; Reaction of (meso)-**2**[9] (2.0 g, 8.0 mmol) and 8N Jones reagent (30 ml, 240 mmol) in acetone (100 ml) in a similar manner to that described in a) gave **5** (1.37g, 70 %).

(R,R)-(+)-2,6-Bis(1'-hydroxy-2',2'-dimethylpropyl)pyridine (2). A mixture of **5** (2.4 g, 9.7 mmol) and (-)-DIP-Cl (13.2 g, 41.2 mmol) was stirred at room temperature for 9 days. Then, pinene was removed under reduced pressure (0.5 mmHg). The residue was treated with diethanolamine (4.6 g, 44 mmol) in ether (40 ml). The precipitate was filtered off and the filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 5 : 1) followed by Kugelrohr distillation (150 °C/5 mmHg) to give (R,R)-**2** (1.0 g, 43 %, 100% e.e.). E.e. was determined by HPLC analysis using DAICEL chiral cel OD with 10% 2-propanol in hexane (flow; 1.0 ml/min). Retention time; 7.8 min. Racemic **2** showed two peaks at 5.6 and 7.8 mins. Mp 87-87.5 °C; $[\alpha]_D^{25}$ 40.3 (c=1.0, EtOH); ^{1}H-NMR δ: 0.92 (18H, s, ^{t}Bux2), 3.74 (2H, d, J=6.3Hz, OHx2), 4.34 (2H, d, J=6.3Hz, CHOHx2), 7.10 (2H, d, J=7.7Hz, arom. Hx2), 7.58 (1H, t, J=7.7Hz, arom. H); IR 3450 cm^{-1}; MS *m/z* 251 (M^+); Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.03; N, 5.57. Found: C, 71.70; H, 9.93; N, 5.20.

(S,S)-(-)-2,6-Bis(1'-hydroxy-2',2'-dimethylpropyl)pyridine (2). Reaction of **5** (2.5 g, 10.1 mmol) with (+)-DIP-Cl (13.0 g, 51.4 mmol) for 5 days in a manner similar to that described for (-)-**2** gave (S,S)-**2** (1.1 g, 42 %, 100% e.e.). E.e. was determined by HPLC analysis using DAICEL chiral cel OD with 10% 2-propanol in hexane (flow; 1.0 ml/min). Retention time; 5.8 min. Mp 87-88 °C; $[\alpha]_D^{27}$ -40.5 (c=1.0,

EtOH); ^{1}H-NMR δ: 0.92 (18H, s, ^{t}Bux2), 3.74 (2H, d, J=6.3Hz, OHx2), 4.34 (2H, d, J=6.3Hz, CHOHx2), 7.10 (2H, d, J=7.7Hz, arom. Hx2), 7.58 (1H, t, J=7.7Hz, arom. H); IR 3470 cm^{-1}; MS *m/z* 251 (M^+); Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.03; N, 5.57. Found: C, 71.50; H, 10.06; N, 5.68.

(R,R)-(+)-2-(1'-Hydroxy-2',2'-dimethylpropyl)-6-(1''-methoxymethyloxy-2'',2''-dimethylpropyl)pyridine (9). A mixture of (R,R)-(+)-**2** (0.02 g, 0.08 mmol), methoxymethyl chloride (0.117 g, 1.44 mmol) and diisopropylamine (0.156 g, 1.38 mmol) in CH_2Cl_2 (4 ml) was stirred at room temperature for 2 days. The mixture was washed with brine and dried (K_2CO_3). Evaporation of the solvent under reduced pressure gave an oily residue, which was purified by preparative TLC (hexane : AcOEt = 5 : 1) to afford **9** (0.014 g, 59%). Mp 65-66 °C; $[\alpha]_D^{26}$ 111.4 (c=0.97, $CHCl_3$); ^{1}H-NMR δ: 0.90, 0.95 (each 9H, s, ^{t}Bux2), 3.35 (3H, s, OMe), 4.30 (1H, d, J=7.1Hz, OH), 4.41, 4.53 (each 1H, d, J=5.7Hz, CHOCH$_3$x2), 4.42 (1H, s, CHOMOM), 4.72 (1H, s, CHOH), 7.03, 7.25 (each 1H, d, J=7.7Hz, arom. Hx2), 7.59 (1H, t, J=7.7Hz, arom. H); IR 3420 cm^{-1}; MS *m/z* 296 (M^++1); High-resolution mass *m/z* calcd for $C_{17}H_{30}NO_3$ (M^++1) 296.2223. Found: 296.2221.

(R,R)-(+)-2-(1'-Hydroxy-2',2'-dimethylpropyl)-6-(1''-t-butyldimethylsilyloxy-2'',2''-dimethylpropyl)pyridine (10). To a solution of (R,R)-(+)-**2** (0.038 g, 0.15 mmol) in THF (3 ml) at 0 °C under argon atmosphere was added BuLi (0.2 ml, 0.32 mmol, 1.6 M in hexane). After being stirred for 0.5 h, a solution of t-butyldimethylsilyl chloride (0.05 g, 0.33 mmol) in THF (1.5 ml) was added to the mixture and the mixture was warmed up to room temperature for 16 h. The reaction was quenched with water. The solvent was removed under reduced pressure and the residue was taken up in ether. The organic layer was washed with brine, dried (K_2CO_3) and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 10 : 1) to give **10** (0.017 g, 30%) as colorless oil. $[\alpha]_D^{26}$ 27.9 (c=0.56, $CHCl_3$); ^{1}H-NMR δ: -0.39, 0.01 (each 3H, s, $SiMe_2$), 0.86 (27H, s, ^{t}Bux3), 4.27 (1H, d, J=6.9Hz, OH), 4.39 (1H, s, CHOTBS), 4.77 (1H, d, J=6.9Hz, CHOH), 6.97, 7.26 (each 1H, d, J=7.4Hz, arom. Hx2), 7.54 (1H, t, J=7.4Hz, arom. H); IR 3380 cm^{-1}; MS *m/z* 366 (M^+); High-resolution mass *m/z* calcd for $C_{21}H_{40}NO_2Si$ (M^+) 366.2801. Found: 366.2825.

(S)-(-)-2-[2',2'-Dimethyl-1'-(2''-pyridyl)propoxy]-1,1-diphenylethanol (3a). To a suspension of NaH (0.189 g, 4.73 mmol, 60% in oil dispersion, washed with hexane prior to use) in DMF under argon atmosphere was added (S)-**1** (0.267 g, 1.62 mmol) in DMF (20 ml) at room temperature. After the mixture was stirred for 25 min, a solution of 1,1-diphenylethylene oxide (**11a**) (0.784 g, 3.99 mmol) in DMF was added. Then, the mixture was heated at 100 °C for 2 h. After cooling, the reaction was quenched with water and the mixture was extracted with ether. The extract was washed with brine and dried (K_2CO_3). Evaporation of the solvent under reduced pressure gave an oily residue, which was purified by column chromatography (hexane : AcOEt = 5 : 1) to afford **3a** (0.555 g, 95.1%). Mp 94-95 °C; $[\alpha]_D^{28}$ -58.8 (c=0.88, EtOH); ^{1}H-NMR δ: 0.84 (9H, s, ^{t}Bu), 3.74, 3.93 (each 1H, d, J=10Hz, H-2x2), 3.88 (1H, s, OH), 4.19 (1H, s, H-1'), 7.00-7.70 (13H, arom. Hx13), 8.42-8.56 (1H, m, arom. H); IR 3350 cm^{-1}; MS *m/z* 362 (M^++1); Anal. Calcd for $C_{24}H_{27}NO_2$: C, 79.74; H, 7.53; N, 3.88. Found: C, 79.49; H, 7.47; N, 4.00.

(S)-(-)-2-[2',2'-Dimethyl-1'-(2''-pyridyl)propoxy]-1,1-di-(α-naphthyl)ethanol (3b). (S)-(-)-**3b** (0.868 g, 62.7%) was obtained by using NaH (0.240 g, 6.0 mmol, 60% in oil dispersion, washed with hexane prior to use), (S)-**1** (0.495 g, 3.0 mmol), and 1,1-di(α-naphthyl)ethylene oxide (**11b**) (1.779 g, 6.0

mmol) in a similar manner to that described for (S)-**3a**. Mp 142-144 °C; $[\alpha]_D^{28}$ -48.0 (c=0.8, EtOH); ^{1}H-NMR δ: 0.92 (9H, s, ^{t}Bu), 4.09, 4.32 (each 1H, d, J=10Hz, H-2x2), 4.28 (1H, s, OH), 4.43 (1H, s, H-1'), 6.88-7.88 (15H, m, arom. Hx15), 8.16-8.60 (3H, m, arom. Hx3); IR 3575 cm^{-1}; MS *m/z* 461 (M^+); High-resolution mass *m/z* calcd for $C_{32}H_{31}NO_2$ (M^+) 461.2352. Found: 461.2340.

(S)-(-)-2-[2',2'-Dimethyl-1'-(2''-pyridyl)propoxy]-1,1-di-(β-naphthyl)ethanol (3c). (S)-(-)-**3c** (0.615 g, 66.7%) was obtained by using NaH (0.160 g, 4.0 mmol, 60% in oil dispersion, washed with hexane prior to use), (S)-**1** (0.300 g, 2.0 mmol), and 1,1-di(β-naphthyl)ethylene oxide (**11c**) (1.184 g, 4.0 mmol) in a similar manner to that described for (S)-**3a**. Mp 75-77 °C; $[\alpha]_D^{29}$ -5.36 (c=0.8, EtOH); ^{1}H-NMR δ: 0.88 (9H, s, ^{t}Bu), 3.94, 4.17 (each 1H, d, J=9.1Hz, H-2x2), 4.12 (1H, s, OH), 4.29 (1H, s, H-1'), 7.02-8.02 (17H, arom. Hx17), 8.48-8.60 (1H, m, arom.c H); IR 3550 cm^{-1}; MS *m/z* 461 (M^+); High-resolution mass *m/z* calcd for $C_{32}H_{31}NO_2$ (M^+) 461.2352. Found: 461.2339.

(R)-(+)-2-[2',2'-Dimethyl-1'-(2''-pyridyl)propoxy]-1,1-di-(α-naphthyl)ethanol (3b). (R)-(+)-**3b** (0.615 g, 66.7%) was obtained by using NaH (0.160 g, 4.0 mmol, 60% in oil dispersion, washed with hexane prior to use), (R)-**1** (0.300 g, 2.0 mmol), and 1,1-di(α-naphthyl)ethylene oxide (**11b**) (1.184 g, 4.0 mmol) in a similar manner to that described for (S)-**3a**. Mp 140-142 °C; $[\alpha]_D^{28}$ 48.3 (c=0.81, EtOH); ^{1}H-NMR δ: 0.92 (9H, s, ^{t}Bu), 4.09, 4.32 (each 1H, d, J=10Hz, H-2x2), 4.28 (1H, s, OH), 4.43 (1H, s, H-1'), 6.88-7.88 (15H, m, arom. Hx15), 8.16-8.60 (3H, m, arom. Hx3); IR 3575 cm^{-1}; MS *m/z* 461 (M^+); High-resolution mass *m/z* calcd for $C_{32}H_{31}NO_2$ (M^+) 461.2352, Found: 461.2358.

General Procedure for Catalytic Asymmetric Addition of Various Aldehydes with Dialkylzinc in the Presence of Chiral Pyridyl Alcohols. To a suspension of **1-3** (0.00008-0.04 mmol, 0.01-5 mol%) in toluene (2.5 ml) was added Et_2Zn or Me_2Zn (2.4 ml, 2.4 mmol, 1M in hexane) followed by aldehyde (0.8 mmol) at room temperature under argon atmosphere. After being stirred for appropriate time, the reaction was quenched with 3N HCl. The mixture was extracted with ether. The organic extract was washed with brine, dried (K_2CO_3), and evaporated under reduced pressure to give an oily residue. Purification of the residue by preparative TLC gave optically active alcohol.

(R)-(+)-1-Phenyl-1-propanol (7a) (Table 2, entry 5): $[\alpha]_D^{25}$ -42.0 (c=5.0, $CHCl_3$) {lit.[23] $[\alpha]_D^{25}$ -45.45 (c=5.15, $CHCl_3$) for 100% e.e.(R)}; ^{1}H-NMR δ: 0.88 (3H, t, J=6.8Hz, $CH_2\underline{CH_3}$), 1.68 (2H, q, J=6.8Hz, $\underline{CH_2}CH_3$), 2.35 (1H, s, OH), 4.48 (1H, t, J=6.8Hz, $\underline{CH}OH$), 7.25 (5H, s, arom. Hx5); IR 3450 cm^{-1}; MS *m/z* 136 (M^+). E.e. (91%) was determined by HPLC analysis using DAICEL chiral cel OB with 10% 2-propanol in hexane (flow; 0.2 ml/min). Retention time: 16.4 min for a major peak and 18.4 min for a minor peak.

(S)-(-)-1-Phenyl-1-ethanol (8) (Table 2, entry 14): $[\alpha]_D^{25}$ -49.2 (c=3.3, cyclopentane) {lit.[24] $[\alpha]_D^{20}$ -43.1 (c=7.9, cyclopentane) for (R)}; ^{1}H-NMR δ: 1.50 (3H, d, J=6.4Hz, CH_3), 1.75 (1H, s, OH), 4.85 (1H, q, J=6.4Hz, $\underline{CH}OH$), 7.30 (5H, s, arom. Hx5); IR 3400 cm^{-1}; MS *m/z* 122 (M^+). E.e. (92%) was determined by HPLC analysis using DAICEL chiral cel OB with 10% 2-propanol in hexane (flow; 1.0 ml/min). Retention time: 6.1 min for a major peak and 8.0 min for a minor peak.

(S)-(-)-1-(4'-Methoxyphenyl)-1-propanol (7b) (Table 3, entry 1): $[\alpha]_D^{25}$ -34.6 (c=5.0, C_6H_6) {lit.[21]

$[\alpha]_D^{22}$ -17.2 (c=5, C_6H_6) for 51% e.e.(S)}; ^{1}H-NMR δ: 0.90 (3H, t, J=6.8Hz, $CH_2\underline{CH_3}$), 1.68 (2H, q, J= 6.8Hz, $\underline{CH_2}CH_3$), 2.19 (1H, s, OH), 3.78 (3H, s, OMe), 4.47 (1H, t, J=6.8Hz, C<u>H</u>OH), 6.82, 7.22 (each 2H, d, J=8.6Hz, arom. Hx2); IR 3450 cm^{-1}; MS *m/z* 166 (M^+). E.e. (90%) was determined by HPLC analysis using DAICEL chiral cel OB with 10% 2-propanol in hexane (flow; 1.0 ml/min). Retention time: 9.3 min for a major peak and 13 min for a minor peak.

(S)-(-)-1-(4'-Methylphenyl)-1-propanol (7c) (Table 3, entry 2): $[\alpha]_D^{25}$ -39.3 (c=5.0, C_6H_6) {lit.[21] $[\alpha]_D^{26}$ -20.4 (c=5, C_6H_6) for 52% e.e.(S)}; ^{1}H-NMR δ: 0.89 (3H, t, J=6.8Hz, $CH_2\underline{CH_3}$), 1.68 (2H, q, J=6.8Hz, $\underline{CH_2}CH_3$), 2.10 (1H, s, OH), 2.32 (3H, s, ArMe), 4.47 (1H, t, J=6.8Hz, C<u>H</u>OH), 7.11 (4H, s, arom. Hx4); IR 3450 cm^{-1}; MS *m/z* 150 (M^+). E.e. (91%) was determined by HPLC analysis using DAICEL chiral cel OB with 10% 2-propanol in hexane (flow; 1.0ml/min). Retention time: 5.5min for a major peak and 6.8min for a minor peak.

(S)-(-)-1-(4'-Bromophenyl)-1-propanol (7d) (Table 3, entry 3): $[\alpha]_D^{27}$ -16.6 (c=2.0, C_6H_6) {lit.[25] $[\alpha]_D^{20}$ 13.33 (c=1.0, C_6H_6) for 76% e.e.(R)}; ^{1}H-NMR δ: 0.89 (3H, t, J=6.8Hz, $CH_2\underline{CH_3}$), 1.65 (2H, q, J=6.8Hz, $\underline{CH_2}CH_3$), 2.40 (1H, s, OH), 4.45 (1H, t, J=6.8Hz, C<u>H</u>OH), 7.11, 7.42 (each 2H, d, J=8Hz, arom. Hx2); IR 3440 cm^{-1}; MS *m/z* 214 (M^+-1). E.e. (93%) was determined by calculation of peaks (δ 3.44 and 3.54) due to methoxyl group in ^{1}H-NMR spectrum of the corresponding (-)-MTPA ester.

(S)-(-)-1-(4'-Chlorophenyl)-1-propanol (7e) (Table 3, entry 4): $[\alpha]_D^{25}$ -25.8 (c=5.0, C_6H_6) {lit.[21] $[\alpha]_D^{22}$ -10.4 (c=5, C_6H_6) for 43% e.e.(S)}; ^{1}H-NMR δ: 0.87 (3H, t, J=6.8Hz, $CH_2\underline{CH_3}$), 1.64 (2H, q, J=6.8Hz, $\underline{CH_2}CH_3$), 2.40 (1H, s, OH),4.46 (1H, t, J=6.8Hz, C<u>H</u>OH), 7.22 (4H, s, arom. Hx4); IR 3450 cm^{-1}; MS *m/z* 170 (M^+). E.e. (91%) was determined by calculation of peaks (δ 3.42 and 3.52) due to methoxyl group in ^{1}H-NMR spectrum of the corresponding (-)-MTPA ester.

(-)-1-(4'-Fluorophenyl)-1-propanol (7f) (Table 3, entry 5): $[\alpha]_D^{25}$ -39.1 (c=3.0, $CHCl_3$) {lit.[18] $[\alpha]_D$ -36.6 (c=5.0, $CHCl_3$) for 93% e.e.}; ^{1}H-NMR δ: 0.85 (3H, t, J=7.1Hz, $CH_2\underline{CH_3}$), 1.70 (2H, q, J=7.1Hz, $\underline{CH_2}CH_3$), 2.20 (1H, s, OH), 4.52 (1H, t, J=7.1Hz, C<u>H</u>OH), 6.76-7.68 (4H, m, arom. Hx4); IR 3450 cm^{-1}; MS *m/z* 154 (M^+). E.e. (95%) was determined by calculation of peaks (δ 3.42 and 3.52) due to methoxyl group in ^{1}H-NMR spectrum of the corresponding (-)-MTPA ester.

(-)-1-(2'-Fluorophenyl)-1-propanol (7g) (Table 3, entry 6): $[\alpha]_D^{30}$ -30.7 (c=4.8, $CHCl_3$) {lit.[18] $[\alpha]_D$ -24.0 (c=5.0, $CHCl_3$) for 85% e.e.}; ^{1}H-NMR δ: 0.94 (3H, t, J=7.1Hz, $CH_2\underline{CH_3}$), 1.77 (2H, q, J=7.1Hz, $\underline{CH_2}CH_3$), 1.99 (1H, brs, $W_{1/2}$=7.7Hz, OH), 4.76-5.02 (1H, m, C<u>H</u>OH), 6.84-7.52 (4H, m, arom. Hx4); IR 3450 cm^{-1}; MS *m/z* 154 (M^+). E.e. (89%) was determined by calculation of peaks (δ 3.47 and 3.53) due to methoxyl group in ^{1}H-NMR spectrum of the corresponding (-)-MTPA ester.

(S)-(-)-1-(4'-Trifluoromethylphenyl)-1-propanol (7h) (Table 3, entry 7): $[\alpha]_D^{25}$ -19.7 (c=5.0, C_6H_6) {lit.[18] $[\alpha]_D$ -36.6 (c=5.0, C_6H_6) for 93% e.e.}; ^{1}H-NMR δ: 0.92 (3H, t, J=8Hz, $CH_2\underline{CH_3}$), 1.73 (2H, q, J= 8Hz, $\underline{CH_2}CH_3$), 2.08 (1H, d, J=2Hz, OH), 4.64 (1H, dt, J=2, 6Hz, C<u>H</u>OH), 7.42, 7.56 (each 2H, d, J=

8.6Hz, arom. Hx2); IR 3450 cm^{-1}; MS *m/z* (M^+). E.e. (93%) was determined by calculation of peaks (δ 3.44 and 3.55) due to methoxyl group in ^{1}H-NMR spectrum of the corresponding (-)-MTPA ester.

(S)-(-)-1-Phenyl-1-penten-3-ol (7i) (Table 3, entry 8): $[\alpha]_D^{27}$ -6.3 (c=5.0, $CHCl_3$) {lit.[26] $[\alpha]_D^{22}$ -6.6 (c=3.2, $CHCl_3$) for 75% e.e.(S)}; ^{1}H-NMR δ: 0.97 (3H, t, J=7Hz, $CH_2\underline{CH_3}$), 1.69 (2H, q, J=7Hz, $\underline{CH_2}CH_3$), 2.00 (1H, s, OH), 3.84-4.46 (1H, m, $\underline{CH}OH$), 5.89-6.76 (2H, m, olefinic Hx2), 7.30 (5H, s, arom. Hx5); IR 3450 cm^{-1}; MS *m/z* 162 (M^+). E.e. (70%) was determined by HPLC analysis using DAICEL chiral cel OD with 10% 2-propanol in hexane (flow; 0.4 ml/min). Retention time: 14.3 min for a minor peak and 19.2 min for a major peak.

(S)-(+)-1-Phenyl-3-pentanol (7j) (Table 3, entry 13): $[\alpha]_D^{27}$ 20.7 (c=2.3, EtOH) {lit.[26] $[\alpha]_D$ 26.8 (c=5.0, EtOH) for 100% e.e.(S)}; ^{1}H-NMR δ: 0.93 (3H, t, J=7.1Hz, $CH_2\underline{CH_3}$), 1.32-1.88(5H, m, $\underline{CH_2}\underline{CH}(OH)\underline{CH_2}$), 2.58-2.85 (2H, m, $PhCH_2$), 3.30-3.75 (1H, m, OH), 6.96-7.38 (5H, m, arom. Hx5); IR 3450 cm^{-1}; MS *m/z* 164 (M^+). E.e. (88%) was determined by HPLC analysis of the corresponding benzoate ester using DAICEL chiral cel OD with 0.1% 2-propanol in hexane (flow; 1.0 ml/min). Retention time: 19.2 min for a major peak and 23.1 min for a minor peak.

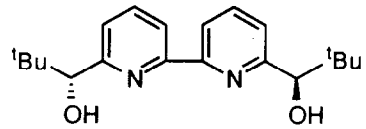
(S)-(-)-1-Cyclohexyl-1-propanol (7k) (Table 3, entry 14): $[\alpha]_D^{24}$ -6.3 (c=5.4, $CHCl_3$) {lit.[27] $[\alpha]_D^{20}$ 8.1 ($CHCl_3$) for 100% e.e.(R)}; ^{1}H-NMR δ: 0.72-2.00 (14H, m), 0.96 (3H, t, J=7Hz, $CH_2\underline{CH_3}$), 3.28 (3H, dt, J=4, 8Hz, $\underline{CH}OH$); IR 3450 cm-1; MS *m/z* 142 (M^+). E.e. (86%) was determined by calculation of peaks (δ 40.24 and 40.54) in ^{13}C-NMR spectrum of the corresponding (-)-MTPA ester.

(S)-(+)-3-Undecanol (7l) (Table 3, entry 15): $[\alpha]_D^{24}$ 6.1 (c=4.8, EtOH) {lit.[28] $[\alpha]_D^{20}$ -6.25 (EtOH) for (R)}; ^{1}H-NMR δ: 0.56-1.06 (3H, m), 0.94 (3H, t, J=6.4Hz, $CH_2\underline{CH_3}$), 1.06-1.76 (8H, m), 3.50 (1H, brs, W1/2=14Hz, $\underline{CH}OH$); IR 3450 cm-1; MS *m/z* 172 (M^+). E.e. (80%) was determined by HPLC analysis of the corresponding benzoate ester using DAICEL chiral cel OD with 0.1% 2-propanol in hexane (flow; 0.1 ml/min). Retention time: 32.3 min for a major peak and 34.4 min for a minor peak.

References and Notes

1. Part of this work was presented at a)113rd Meeting of Pharmaceutical Society of Japan (Osaka), March, 1993, Abstracts *2*, p60. b)7th IUPAC Symposium on Organo-Metallic Chemistry directed towards Organic Synthesis (OMCOS-7, Kobe), September, 1993, Abstracts, p147.
2. For reviews; a)Narasaka, K. *Synthesis* **1991**, 1. b)Tomioka, K. *Synthesis* **1990**, 541. c)Bosnich, B. *Asymmetric Catalyst*; Martinus Nijhoff Publishers, Dordrecht, The Netherlands, 1986.
3. For reviews: a)Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49. b)Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833.
4. Oguni, N.; Omi, T. *Tetrahedron Lett.* **1984**, *25*, 2823.
5. Corey, E. J.; Yuen, P-W.; Hammon, F. J.; Wierda, D. A. *J. Org. Chem.* **1990**, *55*, 784.
6. a)Bolm, C.; Zehnder, M.; Bur, D. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 205. b)Bolm, C.; Ewald, M.; Felder, M.; Schlingloff, G. *Chem. Ber.* **1992**, *125*, 1169. c)Falorni, M.; Giacomelli, G. *Gazz. Chim. Itall.* **1992**, *122*, 339. d)Chelucci, G.; Conti, S.; Falorni, M.; Giacomelli, G. *Tetrahedron* **1991**, *47*, 8251. e)Chelucci, G.; Falorni, M.; Giacomelli, G.; Soccolini, F. *Tetrahedron* **1992**, *48*, 8993.
7. Brown, H. C.; Park, W. W.; Cho, B. T.; Ramachoandran, P. V. *J. Org. Chem.* **1987**, *52*, 5406

8. Bartlett, P. D.; Knox, L. H. *Org. Synth. Coll. Vol. 5* **1973**, 689.
9. a)Hawkins, J. M.; Sharpless, K. B. *Tetrahedron Lett.* **1987**, *28*, 2825. b)Hawkins, J. M.; Dewan, J. C.; Sharpless, K. B. *Inorg. Chem.* **1986**, *25*, 1501.
10. The reaction of benzaldehyde with 2.5 eq. or 4 eq. of Et_2Zn using 5mol% of (S)-**1** gave (S)-1-phenyl-1-propanol in 22% or 41% e.e. On the other hand, reaction using 4 eq. of Et_2Zn and 5mol% of (S)-**1** in 0.128M or 0.064M solution gave the alcohol in 41 or 55% e.e.
11. The similar tendency to ours is found in the reaction using bipyridyl alcohol (**15**).[6b]



(R,R)-**15**

12. Bolm et al[6b] have reported that enantioselectivity in the reaction increases by introduction of aromatic substituents at 6-position of **1**. Mechanistic pathway on ethylation using **2** would be similar to that reported on the reaction using **15**.[6b]
13. (R,R)-**2** may not serve as tridentate ligand in this reaction. Because inspection of Dreiding model showed distance of five membered-coordinated zinc and another hydroxyl oxygen is longer than that of Zn-O bond length.
14. Oppolzer, W.; Radinov, R. N. *Tetrahedron Lett.* **1988**, *29*, 5645 and references cited therein.
15. Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.
16. When aldehyde was added to a mixture of (S)-**3b** and Et_2Zn, the reaction mixture became yellow, which may be due to coordination of aldehyde oxygen to zinc atom. In the reaction in hexane, yellow color of the reaction mixture disappeared after 2 min. Although at this time spot of benzaldehyde on TLC (Table 2, entry 4) was not observed, work-up was performed after 10 min.
17. Alkylation of benzaldehyde with Me_2Zn in the presence of (-)-3-exo-(dimethylamino)isoborneol (DAIB) has been reported to proceed 21 times[3a] slower than that with Et_2Zn; reaction of benzaldehyde with Me_2Zn in the presence of (-)-DAIB requires for 70 h to give the (S)-alcohol in 91% e.e.; Kitamura, M.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1986**, *108*, 6071.
18. Soai, K.; Hirose, W.; Niwa, S. *J. Fluorine Chem.* **1993**, *59*.
19. *cf.* Brano, P.; Resnati, G. *Tetrahedron Asymm.* **1990**, *1*, 661.
20. Similar temperature effect has been reported; a)Ref. 6d. b)Niwa, S.; Soai, K. *J. Chem. Soc. Perkin Trans 1*, **1990**, 937.
21. Efficiency of diarylmethanol moiety on the α,α,α',α'-tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs) was reported; Seebach, D.; Plattner, D. A.; Beck, A. K.; Wang, Y. M.; Hunziker, D.; Petter, W. *Helv. Chim. Acta* **1992**, *75*, 2171 and references cited therein.
22. Capillon, J.; Guette, J. P. *Tetrahedron* **1979**, *35*, 1817.
23. Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1914**, 1115.
24. Yamaguchi, S.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 1870.
25. Chaloner, P. A.; Perena, S. A. R. *J. Chem. Soc. Perkin Trans. 1* **1991**, 2731.
26. Sato, T.; Gotoh, Y.; Wakabayashi, Y.; Fujisawa, T. *Tetrahedron Lett.* **1983**, *24*, 4123.
27. Burrows, E. P.; Welch, F. J.; Mosher, H. S. *J. Am. Chem. Soc.*, **1960**, *82*, 880.
28. Pickard, R. H.; Blackburn, J. K. *J. Chem. Soc.* **1913**, 1923.

(*Received in Japan* 12 *January* 1994)