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The synthesis of dendritic BINOL ligands and their applications in the enantioselective Lewis acid catalyzed addition of diethylzinc to aldehydes

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Abstract—Novel dendritic chiral BINOL ligands have been synthesized through coupling of MOM-protected 3,3′-dihydroxymethyl-binaphthol with Fréchet-type polyether benzyl bromide dendrons followed by deprotection of the MOM groups using TsOH. These dendritic chiral BINOL ligands were found to be effective in the enantioselective addition of diethylzinc to benzaldehyde both in the presence and absence of Ti(O-*iso*-Pr)$_4$. The enantioselectivity decreased with increasing generation in both cases. In the latter case, the dendritic chiral BINOL ligands showed much higher catalytic activity and enantioselectivity than BINOL. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Homogeneous asymmetric catalysis is one of the most important developments in modern chemistry over the past several decades. Many Chiral catalysts are known to exhibit high activities and enantioselectivities.[1] As the synthesis of these chiral catalysts is often expensive, it is highly desirable to re-use them as often as possible. A practical approach is to 'heterogenize' a homogeneous catalyst onto a polymer support. Over the past two decades, the studies of insoluble polymer-supported chiral catalysts have attracted much attention.[2] However, this kind of polymer-supported catalyst often suffer from lowered catalytic activity and enantioselectivity. Their catalytic sites are randomly oriented among the support and the microenvironment around the active sites is usually not clear. It is thus, difficult, even impossible to fine-tune both the catalytic activity and enantioselectivity of the polymer-supported catalyst through systematically adjusting the microstructure of the catalytic sites in the polymer supports. A possible solution to this problem is to use soluble linear polymer as supports for chiral catalysts.[3] Recently, we have developed a soluble chiral polyester-supported Ru(BINAP) catalyst which offered a higher rate of reaction than the parent homogeneous catalyst while maintaining high enantioselectivity.[4] Most recently, dendritic organometallic catalysts have become a very active field of research.[5] The dendrimer architecture offers a means of better controlling the disposition of the catalytic species in soluble polymer-based catalysts. Several chiral dendritic catalysts for asymmetric catalysis have been described.[6] We recently reported the use of chiral diphosphine BINAP ligands bearing dendritic wedges (the dendritic BINAP **1**) as catalysts for asymmetric hydrogenation.[7] It was found that the size of the dendritic wedges influenced the reactivity of the catalysts. The rate of the reaction increased using higher generation catalysts. Herein, we report the synthesis of another novel dendritic binaphthyl-containing chiral ligand (the dendritic BINOL **2**) by using a similar strategy and applications in asymmetric addition of diethylzinc to aldehydes. Optically active BINAP and BINOL represent two most important classes of chiral biaryl ligands reported in the literature and have found very extensive applications in asymmetric catalysis.[1c,8] In contrast to the dendritic BINAP **1**, the 3,3′-position on the naphthyl backbone of BINOL was chosen for the attachment of dendritic wedges. The proximity of the dendritic wedges to the catalytic center provided a unique opportunity to study the influence of the shape and architecture of the dendritic wedges on the chiral

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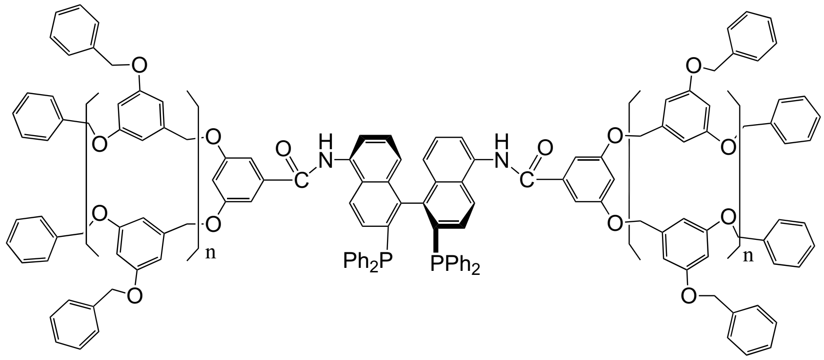
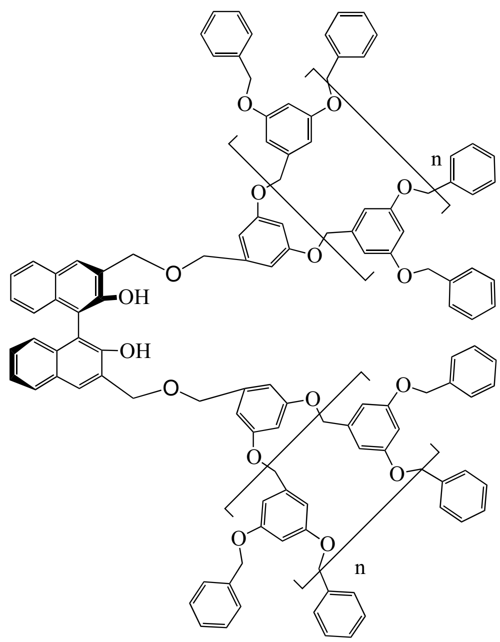
microenvironment built around the catalytic active site through systematically adjusting the generation of the dendrimer. Most recently, optically active dendritic BINOL ligands bearing dendrimer wedges on the 6,6′-positons were reported by Seebach et al. and Yosida et al., respectively.[6a,9]



1 Dendritic BINAP Ligands: n=0, 1, 2.



2 Dendritic BINOL Ligands: n=0, 1, 2.

2. Results and discussion

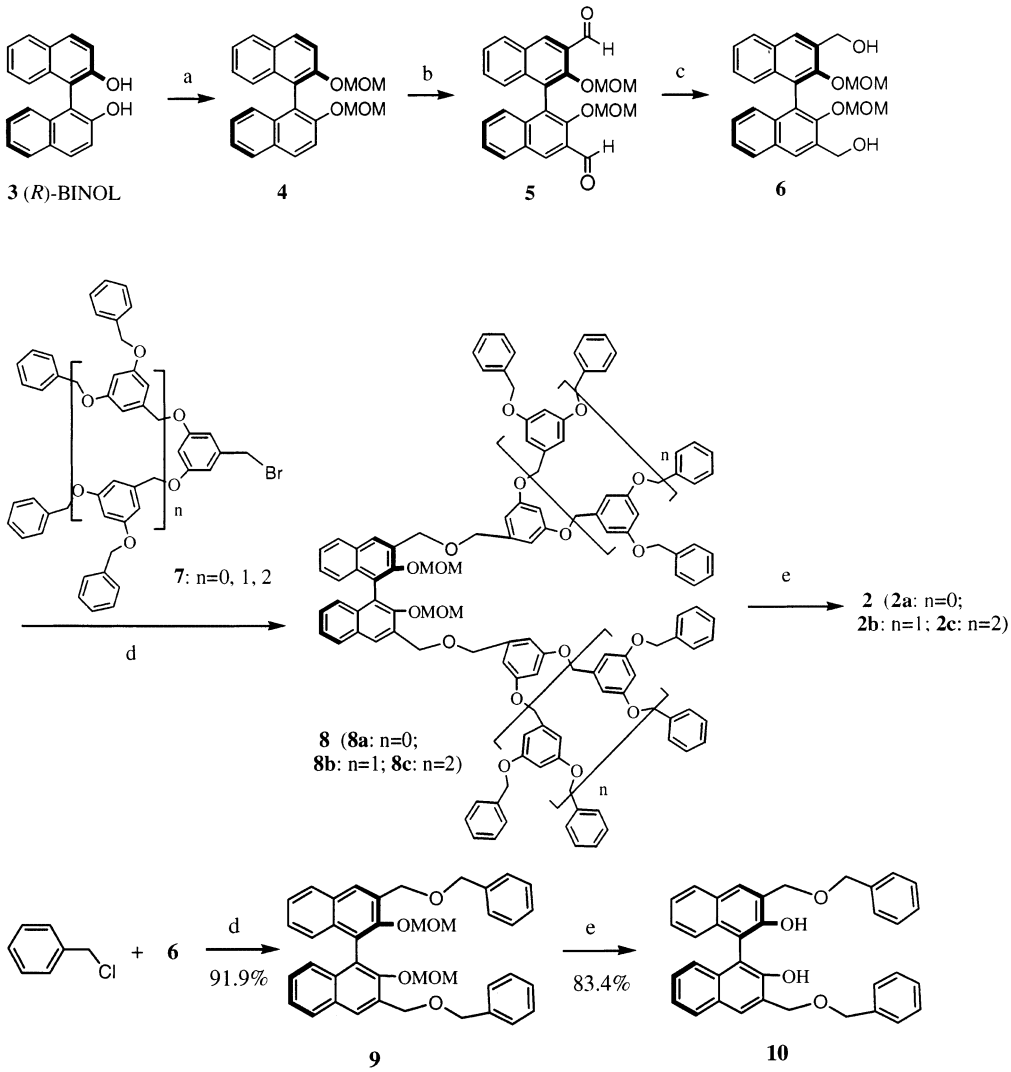
2.1. Synthesis of dendritic BINOL ligands 2a–2c

A number of BINOL derivatives with substituents at 3,3′-positions have been reported,[10] which thus provided a synthetic accessibility of these positions for the attachment of dendritic wedges. The synthetic route is outlined in Scheme 1. The key BINOL derivative, 3,3′-dihydroxymethyl-2, 2′-methoxymethyl-1, 1′-binaphthol **6** for the coupling reaction of dendrimer was synthesized by using the method reported by Shibasaki.[11] The commercially available (*R*)-BINOL **3** was used as starting material. The hydroxyl group of **3** was protected with the methoxyl methyl (MOM) group, and the resulting protected BINOL **4** was lithiated with *n*-BuLi followed by carbonylation to give MOM-protected 3,3′-bis(formyl)-BINOL **5**. Reduction of **5** with $NaBH_4$ in MeOH/THF at 0°C produced **6**. We have chosen Fréchet's polyether dendrimer as the building blocks due to their inertness to catalytic reaction. Dendrons **7** with benzyl bromide groups located at the focal point were synthesized by the convergent-group approach introduced by Hawker and Fréchet.[12] The coupling of dendritic benzyl bromide **7** with **6** was successfully carried out using NaH as deprotonation reagent to afford **8a** ($n=0$), **8b** ($n=1$) and **8c** ($n=2$) in 80%, 74 and 72% yields, respectively. After removal of the MOM protecting group, dendritic BINOL 2**a** ($n=0$), **2b** ($n=1$) and **2c** ($n=2$) were obtained in 43, 37 and 36% yields from (*R*)-BINOL, respectively. For comparison, a model compound of small molecule **10** was also synthesized using the same method (as shown in Scheme 1.)

All of these dendritic BINOL ligands give well-resolved ^1H NMR spectra consistent with their structures. The ^1H NMR spectra also indicate that these dendritic BINOL maintain a C_2 symmetry in solution. As shown in Table 1, the results of MALDI mass spectra and elemental analysis of these dendritic ligands match the calculated values. The MALDI mass spectra of **2a**, **2b** and **2c** showed the $(M+Na)^+$ ions at m/z 973.26, 1821.33 and 3517.77, respectively, confirming the formation of monodisperse BINOL containing dendrimers. The optical rotation and molar rotation data are also collected in Table 1. The specific optical rotation $[\alpha]_D$ decreased with the increase in the dendritic generation from 1 to 3. However, the molar rotation was almost identical regardless of the generation, which showed that the dendritic wedges attached to the binaphthyl core do not lead to major chiral amplification.

2.2. Asymmetric induction of the dendritic BINOL ligands in the enantioselective addition of $ZnEt_2$ to benzaldehyde in the presence or absence of Ti(O-*iso*-Pr)$_4$

In recent years the catalytic enantioselective addition of organozinc reagents to aldehydes has attracted much attention because of its potential in the preparation of



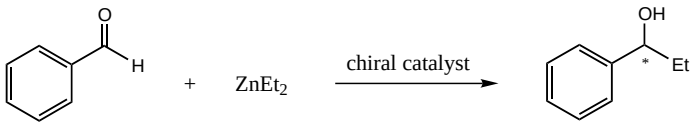
Scheme 1. Synthesis of dendritic BINOL. *Reagents and conditions*: (a) NaH, MOMCl, THF, DMF, 98%; (b) *n*-BuLi, DMF, 76%; (c) $NaBH_4$, THF, 93%; (d) NaH, THF, DMF; (e) $TsOH.H_2O$, CH_3OH, CH_2Cl_2.

a variety of high value non-racemic chiral alcohols.[13] Most recently titanium complexes of BINOL and H_8-BINOL were reported to be effective catalysts for the asymmetric addition of diethylzinc to aldehydes by Chan et al. and Nakai et al., respectively.[14–16] Pu et al. also reported the synthesis and application of polymer-bounding BINOL ligands and its monomeric BINOL derivative.[17] It was found that these ligands were highly effective auxiliaries in the enantioselective addition of diethylzinc to aldehydes in the absence of Ti(O-*iso*-Pr)$_4$. With the dendritic BINOL ligands in hand, we then examined their asymmetric induction in the Lewis acid-catalyzed enantioselective addition of diethylzinc to aldehydes. Benzadehyde was chosen as the model sub-

Table 1. Characterization of dendritic BINOL ligands

Dendritic BINOL	MALDI-MS $(M+Na)^+$ data (calcd)[a]	Elemental analysis (calcd value)	Specific rotation $[\alpha]_D^{25}$ ($c=1$, $CHCl_3$)	Molar rotation [M]
(*R*)-**10**	549.09 (M 526.21)	C 80.93, H 5.78 (C 80.73, H 5.65)[b]	+36.0	189
(*R*)-**2a**	973.26 (M 950.38)	C 80.84, H 5.37 (C 80.82, H 5.72)	+18.0	171
(*R*)-**2b**	1821.33 (M 1798.72)	C 79.76, H 5.89 (C 80.07, H 5.71)	+6.0	107
(*R*)-**2c**	3517.77 (M 3495.39)	C 79.79, H 6.04 (C 79.66, H 5.71)	+3.3[c]	115

[a] Data in brackets denote the exact mass.
[b] Calcd value for (*R*)-**10**+1/2 H_2O.
[c] Specific rotation measured with $c=4.8$ in $CHCl_3$.



Scheme 2. The catalytic asymmetric reaction of benzaldehyde with diethylzinc.

strate for comparing the asymmetric induction of BINOL ligands with different generation dendritic wedges (Scheme 2). Firstly, we used the model compound of small molecule (*R*)-**10** to optimize the reaction conditions. Because excess titanium tetra-*iso*-propoxide was required to render the reaction efficiently catalytic in such a system,[15] we thus first investigated the effect of the molar ratio of (*R*)-**10**/Ti(O-*iso*-Pr)$_4$ on the enantioselectivity and reactivity of the reaction. The experimental results are summarized in Table 2. It was found that the molar ratio of (*R*)-**10**/Ti(O-*iso*-Pr)$_4$ influenced significantly both the enantioselectivity and catalytic activity (entries1-4). In contrast to the BINOL-Ti system,[14] only one equivalent amount of Ti(O-*iso*-Pr)$_4$ was required to afford the better catalytic enantioselectivity. A large excess of Ti(O-*iso*-Pr)$_4$ led to high activity but gave significantly decreased enantioselectivity. For example, e.e. values of 89.3% (L/Ti=1/14)[14] and 13.6% (L/Ti=1/12) were obtained for (*S*)-BINOL-Ti and (*R*)-**10**-Ti catalysts, respectively. As shown in Table 2, the reaction solvent also played an important role on the enantioselectivity and catalytic activity, which showed very differently from the BINOL-Ti system.[14] Much lower enantioselectivity and catalytic activity were obtained when using THF or diethyl ether as solvent (entry 6 and entry 7). The use of toluene or dichloromethane as solvent gave better enantioselectivity and reactivity. The difference in performance between (*R*)-**10**-Ti complex and (*S*)-BINOL-Ti complex may be attributed to the presence of an oxygen on the 3,3′-position substituents which may possibly coordinate to titanium or zinc atoms.

Based on the optimized reaction conditions obtained above, we then tested the asymmetric induction of the dendritic BINOL ligands in the same reaction. As shown in Table 3, the catalysts derived from all three dendritic BINOL ligands were found to be effective. In general, high conversion and no side products, and moderate to good enantioselectivities were observed. It was found that the dendritic wedges decreased the enantioselectivity with the increase of generation. This effect is most pronounced when going from (*R*)-**10** to generation 1 ((*R*)-**2a)** and to generation 2 (*R*)-**2b**) (Table 2, entries 2–4). The size effect is probably due to the steric bulk of the dendritic wedges. This steric effect may influence the formation of the monomeric or dimeric Ti(IV) complexes which are proposed as the possible catalytically active species.[16,18] The importance of the attachment of dendritic wedges, on the other hand, is the easy and reliable separation of the chiral BINOL ligands due to their different solubilities in various organic solvents. For example, upon completion of the reaction, chiral BINOL ligand was quantitatively precipitated by the addition of methanol and recovered via filtration. The recovered ligands showed the same enantioselectivity and reactivity (Table 3, entries 5 and 7).

Table 3. Asymmetric addition of diethylzinc to benzaldehyde catalyzed by (*R*)-BINOL-Ti and dendritic BINOL-Ti catalysts[a]

Entry	Ligand	Conv.(%)[b]	E.e (%)[b]
1	(*R*)-BINOL	98	85.1
2	(*R*)-**10**	99	84.1
3	(*R*)-**2a**	94	73.7
4	(*R*)-**2b**	94	53.8
5[c]	(*R*)-**2b**	81	53.3
6	(*R*)-**2c**	79	52.2
7[c]	(*R*)-**2c**	94	51.5

[a] Benzaldehyde:ligand:Ti(O-*iso*-Pr)$_4$:ZnEt$_2$=1.0:0.2:0.8:3 (molar ratio), reaction temperature=0°C; solvent=toluene; reaction time=7 h.
[b] Determined by chiral GLC analyses. The absolute configuration of product is (*R*).
[c] Recycle chiral dendritic BINOL ligand was used.

Table 2. Optimization of reaction conditions for asymmetric addition of diethylzinc to benzaldehyde catalyzed by titanium complex of (*R*)-**10**[a]

Entry	Solvent	Time (h)	L/Ti(M/M)	Conv.(%)[b]	E.e. (%)[b]
1	Toluene	7	1:2	66	79.7
2	Toluene	7	1:4	99	84.1
3	Toluene	7	1:6	96	64.7
4	Toluene	7	1:12	97	13.6
5	Toluene	9	1:4	99	83.8
6	Ether	5	1:4	64	61.5
7	THF	5	1:4	30	25.1
8	CH_2Cl_2	5	1:4	94	84.1

[a] Benzaldehyde:ligand:ZnEt$_2$=1.0:0.2:3 (molar ratio), reaction temperature=0°C.
[b] Determined by chiral GLC analyses. The absolute configuration of product is (*R*).

We also studied the use of these dendritic BINOL ligands to catalyze the enantioselective reaction of benzaldehyde with diethylzinc in the absence of Ti(O-*iso*-Pr)$_4$. It was found that the chiral dendritic ligands performed very differently from the BINOL. The experimental results are summarized in Table 4. All the dendritic BINOL ligands showed higher catalytic activity and enantioselectivity than BINOL. For example, in the presence of 20 mol% of (*R*)-**2a** in toluene, 98% conversion with e.e. of 62% was observed after a reaction of 7 h at 0°C. However, a conversion of only 19% and 4.6% e.e. was seen under the same conditions when BINOL was used in place of (*R*)-**2a**.

The effect of the dendritic wedges was also observed. In the case of dendritic BINOL-Ti complex, the enantioselectivity decreased with the increase of the generation (Table 4, entries 2–5), while a slight negative effect was observed in the absence of Ti(O-*iso*-Pr)$_4$. The high efficiency of the dendritic BINOL ligands is probably due to the following two factors: (1) the existence of oxygen on the linkage between the dendritic wedges and the binaphthyl core; (2) the bulk of the substituents in the 3,3′-positions of BINOL. The reaction of BINOL with diethylzinc provides the zinc phenoxide and aggregates through intermolecular Zn–O–Zn bonds. These complexes, in which the zinc ions are coordinatively saturated, are considered to be catalytically inactive.[19] The attachment of bulky dendritic wedges onto the 3,3′-positions of binaphthyl backbone may hinder the formation of aggregates of zinc species in comparison to BINOL. Furthermore, the oxygen on the linkage of the dendritic BINOL may possibly coordinate to, or interact with the zinc species, which may serve to generate more active catalytic zinc species.[20] Pu et al. also observed similar enhancement of catalytic activity and enantioselectivity when they used the BINOL derivative, 3,3′-bis(2″,4″-dihexyloxyphenyl)-1,1′-binaphthol as chiral ligand in the addition reaction of diethylzinc to aldehydes in the absence of Ti(O-*iso*-Pr)$_4$.[17] With increasing dendrimer generation, steric effects may become more significant, which may possibly influence the interaction between the oxygen atom on the linkage and the zinc atom or the structure of the zinc complex. Thus, the decrease in enantioselectivity with increasing dendrimer generation may be due to steric effects within the dendrimer structure, although this is not completely clear at this time.

Table 4. Asymmetric addition of diethylzinc to benzaldehyde catalyzed by (*R*)-BINOL and dendritic BINOL ligands in the absence of Ti(O-*iso*-Pr)$_4$[a]

Entry	Ligand	Conv. (%)[b]	E.e (%)[b]
1	(*R*)-BINOL	19.0	4.6
2	(*R*)-**10**	97.9	66.0
3	(*R*)-**2a**	97.5	61.9
4	(*R*)-**2b**	77.7	49.5
5	(*R*)-**2c**	79.8	48.6

[a] Benzaldehyde:ligand:$ZnEt_2$ = 1.0:0.2:3 (molar ratio), reaction temperature = 0°C; solvent = toluene; reaction time = 7 h.

[b] Determined by chiral GLC analyses. The absolute configuration of product is (*R*).

In summary, novel recyclable dendritic chiral BINOL ligands have been synthesized through coupling of MOM-protected 3,3′-dihydroxymethyl-binaphthol and Fréchet-type polyether dendritic benzyl bromides followed by deprotection of the MOM protecting groups with TsOH. These dendritic chiral BINOL ligands were found to be effective in the enantioselective addition of diethylzinc to benzaldehyde both in the present and absence of Ti(O^{i}Pr)$_4$. The enantioselectivity decreased with the increase of generation in both cases. In the latter case, the dendritic chiral BINOL ligands showed much higher catalytic activity and enantioselectivity than BINOL.

3. Experimental

3.1. Materials

All moisture or air sensitive experiments were carried out under a nitrogen atmosphere using standard Schlenk techniques. Commercial reagents were used as received without further purification unless otherwise noted. Toluene, diethyl ether and THF were distilled from sodium benzophenone ketyl, and dichloromethane from calcium hydride. Benzaldehyde was distilled from calcium hydride before use. Compounds **4**–**6** were prepared according to the reported procedures.[11]

3.2. Measurements

Melting points were measured with a X-4 digital melting point apparatus. IR was recorded on a Bruker IFS 25 spectrophotometer. The ^{1}H NMR was recorded on a Bruk DM 300 spectrometer in $CDCl_3$ with TMS as internal standard. MALDI-TOF mass spectra were obtained on an Instrum III spectrometer with α-cyano-4-hydroxycinnamic acid (CCA) as a matrix. Elemental analysis was performed with a Carlo Erba 1106 Elemental Analyzer. Optical rotations were measured with AA-10R automatic polarimeter. The e.e. values were determined by GLC using a Supelco β-Dex 120 chiral column (30 m×0.25 mm (i.d.), 0.25 μm film).

3.3. General procedure for the synthesis of MOM-protected dendritic BINOL ligands (*R*)-9 and (*R*)-8a-(*R*)-8c

Typical procedure: To a suspension of sodium hydride (52% dispersion in mineral oil; 0.22 g, 4.77 mmol,) in a mixture of THF (15 mL) and DMF (5 mL) under nitrogen was slowly added a solution of (*R*)-**6** (0.5 g, 1.15 mmol) in THF (3 mL) over 15 min at 0°C. The mixture was allowed to warm to room temperature and stirred for 1 h. Benzyl chloride (0.29 mL, 2.53 mmol) was then added dropwise over 10 min at 0°C. The mixture was then allowed to warm to room temperature and stirred for 4 h. The mixture was cooled to 0°C and water (5 mL) was added to quench the reaction. The solution was extracted with CH_2Cl_2 several times. The combined organic layer was washed with water and brine, and then dried over Na_2SO_4. After evaporation of solvent, the residue was purified by column chro-

matography on silica gel (hexane:ethyl acetate = 4:1) to give (*R*)-**9** as a colorless oil (0.54 g, 92%). $[\alpha]_D^{20} = -128.0$ (*c* 1, $CHCl_3$); IR (KBr): 1619, 1292, 1052 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.92–7.17 (m, 20H, Ar-H), 4.90 (m, 4H, BINOL-CH_2), 4.73 (s, 4H, Ph-CH_2), 4.58–4.45 (dd, 4H, -OCH_2O-), 2.77 (s, 6H, -OCH_3); MS(EI): *m*/*z* (%): 615 (0.3) $[M+1]^+$, 614 (0.6) $[M]^+$, 462 (13.8), 432 (10.8), 400 (14.7), 340 (100), 311 (23.8), 310 (24.4), 309 (13.9), 283 (16.6), 282 (24.9), 281 (23.7), 254 (12.7), 253 (23.7), 252 (14.9), 91 (99.9), 77 (13.4), 45 (57.7), 32 (31.7). Anal. calcd for $C_{40}H_{38}O_6$: C, 78.15; H, 6.23. Found: C, 78.31; H, 6.05%.

Compound (*R*)-**8a**: Prepared according to the above general procedure, the resulting residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2 = 1:2) to give (*R*)-**8a** as a white foam. Yield: 80%; mp: 38–39°C; $[\alpha]_D^{20} = -64.0$ (*c* 1, $CHCl_3$); IR (KBr): 1590, 1445, 1148, 1053 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.18–6.65 (m, 36H, Ar-H), 5.11 (s, 8H, Ph-CH_2), 4.99–4.94 (m, 4H, BINOL-CH_2), 4.74 (s, 4H, Ph-CH_2), 4.66–4.51 (dd, 4H, -OCH_2O-), 2.83 (s, 6H, -OCH_3); MALDI-TOF-MS: *m*/*z*: 1061.49 $[M+Na]^+$, 1077.46 $[M+K]^+$. Anal. calcd for $C_{68}H_{62}O_{10}$: C, 78.59; H, 6.01. Found: C, 78.33; H, 6.00%.

Compound (*R*)-**8b**: Prepared according to the above general procedure, the resulting residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2 = 1:3) to give (*R*)-**8b** as a white foam. Yield: 74%; mp: 52–54°C; $[\alpha]_D^{20} = -36.0$ (*c* 1,$CHCl_3$); IR (KBr): 1590, 1452, 1155, 1053 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.13–6.57 (m, 68H, Ar-H), 5.04 (s, 16H, Ph-CH_2), 5.00 (s, 8H, Ph-CH_2), 4.9–4.90 (m, 4H, BINOL-CH_2), 4.68 (s, 4H, Ph-CH_2), 4.60–4.45 (dd, 4H, -OCH_2O-), 2.79 (s, 6H, -OCH_3); MALDI-TOF-MS: *m*/*z*: 1909.79 $[M+Na]^+$, 1925.74 $[M+K]^+$. Anal. calcd for $C_{124}H_{110}O_{18}$: C, 78.88; H, 5.87. Found: C, 79.04; H, 6.00%.

Compound (*R*)-**8c**: Prepared according to the above general procedure, the resulting residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2 = 1:4) to give (*R*)-**8c** as a white foam. Yield: 72%; mp: 54–56°C; $[\alpha]_D^{20} = -16.0$ (*c* 1, $CHCl_3$); IR (KBr): 1598, 1452, 1148, 1046 cm^{--}; ^1H NMR ($CDCl_3$): δ 8.17–6.51 (m, 132H, Ar-H), 5.03–4.79 (m, 64H, BINOL-CH_2, Ph-CH_2), 4.50–4.48 (dd, 4H, -OCH_2O-), 2.79 (s, 6H, -OCH_3); LALDI-TOF-MS: *m*/*z*: 3517.77 $[(M-2MOM)+Na]^+$. Anal. calcd for $C_{236}H_{206}O_{34}$: C, 79.04; H, 5.79. Found: C, 78.96; H, 5.83%.

3.4. General procedure for the synthesis of dendritic BINOL ligands (*R*)-10 and (*R*)-2a-(*R*)-2c

Typical procedure: To a stirred solution of (*R*)-**9** (0.5 g, 0.81 mmol) in 1:1 ethanol/CH_2Cl_2 (10 mL/10 mL) was added a catalytic amount of TsOH (monohydrate) at 40°C. The solution was stirred overnight. After evaporation of most of the solvent, the residue was diluted with ethyl acetate, washed with water and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over Na_2SO_4. After removing the solvent under reduced pressure the residue was further purified by column chromatography on silica gel (hexane:ethyl acetate = 4:1) to give (*R*)-**10** (0.36 g, yield 83%) as a white crystal. mp: 128–129°C; $[\alpha]_D^{20} = +36.0$ (*c* 1,$CHCl_3$); IR (KBr): 3426 (-OH), 1619, 1292, 1052 cm^{-1}; ^{1} H NMR ($CDCl_3$): δ 7.92–7.17 (m, 20H, Ar-H), 6.68 (s, 2H, -OH), 5.02–4.92 (m, 4H, BINOL-CH_2), 4.74 (s, 4H, Ph-CH_2); MALDI-TOF-MS: *m*/*z*: 549.09 $[M+Na]^+$, 564.12 $[M+K]^+$, 526.21 $[M]^+$. Anal. calcd for $C_{36}H_{30}O_4 \cdot 0.5\ H_2O$: C, 80.73; H, 5.65. Found: C, 80.93; H, 5.78%.

Compound (*R*)-**2a**: Prepared according to the above general procedure, the resulting residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2 = 1:2) to give (*R*)-**2a** as a white foam. Yield: 79%; mp: 39–40°C; $[\alpha]_D^{20} = +18$ (*c* 1,$CHCl_3$); IR (KBr): 3442 (-OH), 1590, 1445, 1148, 1053 cm^{-1}; ^{1} H NMR ($CDCl_3$): δ 7.87–6.49 (m, 38H, Ar-H, -OH), 4.99 (s, 8H, Ph-CH_2), 4.93–4.83 (m, 4H, BINOL-CH_2), 4.61 (s, 4H, Ph-CH_2); MALDI-TOF-MS: *m*/*z*: 973.26 $[M+Na]^+$, 989.24 $[M+K]^+$, 950.38 $[M]^+$. Anal. calcd for $C_{64}H_{54}O_8$: C, 80.82; H, 5.72. Found: C, 80.84; H, 5.37%.

Compound (*R*)-**2b**: Prepared according to the above general procedure, the resulting residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2 = 1:3) to give (*R*)-**2b** as a white foam. Yield: 73%; mp: 63–65°C; $[\alpha]_D^{20} = +6.0$ (*c* 1, $CHCl_3$); IR (KBr): 3441 (-OH), 1590, 1452, 1155, 1053 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.79–6.46 (m, 70H, Ar-H, -OH), 4.95–4.53 (m, 32H, Ph-CH_2, BINOL-CH_2); MALDI-TOF-MS: *m*/*z*: 1821.33 $[M+Na]^+$, 1837.30 $[M+K]^+$, 1798.72 $[M]^+$. Anal. calcd for $C_{120}H_{102}O_{16}$: C, 80.07; H, 5.71. Found: C, 79.76; H, 5.89%.

Compound (*R*)-**2c**: Prepared according to the above general procedure, the resulting residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2 = 1:4) to give (*R*)-**2c** as a white foam. Yield: 72%; mp: 58–60°C; $[\alpha]_D^{20} = +3.3$ (*c* 4.8,$CHCl_3$); IR (KBr): 3434 (-OH), 1598, 1452, 1148, 1046 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.85–6.54 (m, 134H, Ar-H, -OH), 5.08–4.17 (m, 64H, BINOL-CH_2, Ph-CH_2); MALDI-TOF-MS: m/z: 3517.77 $[M+Na]^+$, 3533.73 $[M+K]^+$, 3495.39 $[M]^+$. Anal. calcd for $C_{232}H_{198}O_{32}$: C, 79.66; H, 5.71. Found: C, 79.79; H, 6.04%.

3.5. General procedure for asymmetric addition of diethylzinc to benzaldehyde

Under nitrogen, Ti(O-*iso*-Pr)$_4$ (34 μL, 0.10 mmol) was added to a solution of (*R*)-**10** (13.2 mg, 0.025 mmol) in toluene (1 mL) at room temperature and the mixture was stirred at ambient temperature for 10 min followed by the addition of diethylzinc (1.0 M, 0.375 mL) in hexane with continued stirring for 10 min. Benzaldehyde (13 μL, 0.125 mmol) was added via syringe at 0°C and the mixture was allowed to stir at 0°C for a given time. The reaction was quenched with aqueous hydrochloric acid solution (1.0N, 2.0 mL), the mixture was then filtered through a short pad of Celite to remove the insoluble material and the filtrate was extracted with ethyl acetate (2×1.0 mL). The combined organic

layers were dried over Na_2SO_4 and concentrated to solvent free. The residue was purified by column chromatography on silica gel to afford 1-phenyl-1-propanol as a colorless liquid. The conversion and enantioselectivity of the product were determined by GLC using a Supelco β-Dex 120 chiral column (30 m×0.25 mm (i.d.), 0.25 μm film) and absolution configuration was based on the comparison with the GLC trace of 1-phenyl-1-propanol of known configuration.

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