Functionalized Major-Groove and Minor-Groove Chiral Polybinaphthyls: Application in the Asymmetric Reaction of Aldehydes with Diethylzinc

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Abstract: A series of functionalized and optically active major-groove polybinaphthyls and minor-groove polybinaphthyls have been synthesized by using the Suzuki coupling reaction and have been spectroscopically characterized. The application of these chiral polymers in the asymmetric addition of diethylzinc to aldehydes has been studied. A minor-groove polybinaphthyl is found to be an excellent catalyst for the asymmetric reaction of diethylzinc with a number of aldehydes. The molecular weight and the molecular weight distribution of the polymer have little effects on the catalytic process. The chiral polymer can be easily recovered and reused without loss of catalytic activity as well as enantioselectivity. These rigid and sterically regular chiral polybinaphthyls represent a new generation of enantioselective polymeric catalysts. The reaction of the polybinaphthyls as well as certain monomeric binaphthyl molecules with diethylzinc has been investigated which has provided further information on the novel polymeric catalysts.

Introduction

The use of polymeric chiral catalysts in asymmetric synthesis has important practical advantages. Due to the solubility difference between macromolecules and small molecules, polymeric reagents or catalysts can be easily separated from the reaction mixture by simple filtration or by precipitation with the addition of a nonsolvent. The recovery of chiral catalysts is particularly important since it is often quite expensive to obtain these optically pure materials. Using polymeric catalysts also makes it possible to carry out reactions in flow reactors or in flow membrane reactors for large-scale production. Traditionally, polymeric chiral catalysts are prepared by anchoring a chiral metal complex to a flexible and sterically irregular achiral polymer backbone.[1−3] It is generally observed that the polymer-supported chiral catalysts are usually less efficient than their monomeric version. This indicates that the microenvironment of the catalytic sites in the polymers is very important for their effectiveness in steric control. The flexible and sterically irregular polymer backbone of the traditional polymeric chiral catalysts generates randomly oriented catalytic sites which cannot be systematically modified to achieve the desired catalytic activity and stereoselectivity.

Optically active binaphthyl compounds have been extensively applied in asymmetric catalysis and in molecular recognition.[4−6] We have used optically active binaphthyls to construct a family of novel chiral conjugated materials.[7−10] Figure 1 shows a few chiral polybinaphthyls prepared in our laboratory. These rigid and sterically regular chiral polymers not only are potentially useful in electrical and optical applications but also can be used to prepare a new generation of polymeric chiral catalysts when appropriate functional groups are introduced. For example, we have studied the direct polymerization of the chiral binaphthyl monomers (*R*)-**1a−c** in the presence of either Ni(0)(cyclooctadiene) or $NiCl_2$/Zn to generate polymers (*R*)-**2a−c** (Scheme 1).[11] These polymers are then converted to the optically active poly(1,1′-bi-2-naphthol) (*R*)-**3** by removal of the protecting groups. In the helical structure of an 1,1′-binaphthyl molecule, there exists a major groove and a minor groove divided by the 1,1′-bond as indicated in Scheme 1. We therefore designate the polymers obtained from the polymerization at the 6,6′-positions as “major-groove” polybinaphthyls and the polymers obtained from the polymerization at the 3,3′-positions as “minor-groove” polybinaphthyls. (*R*)-**3** is a major-groove polymer of 1,1′-bi-2-naphthol. When (*R*)-**3** is reacted with diethylaluminum chloride, a polymeric aluminum complex (*R*)-**4** is obtained. This polymer shows greatly enhanced catalytic activity over the corresponding monomeric binaphthyl aluminum complex in a Mukaiyama aldol condensation, although no enantioselectivity is observed. In (*R*)-**4**, all of the aluminum centers are expected to be highly organized in the rigid and sterically regular chiral polymer chain, leading to a well-defined microenvironment for the catalytic sites. It is therefore possible to systematically adjust the steric and electronic properties of the metal centers in the polymer to

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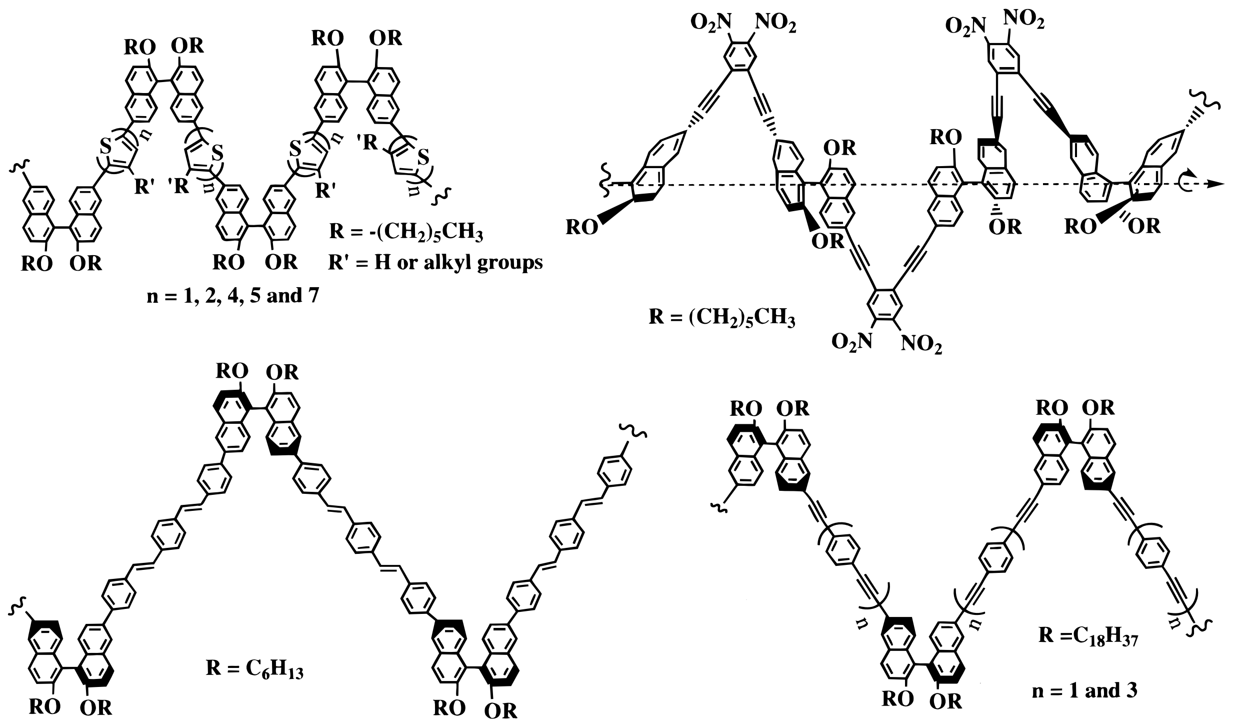
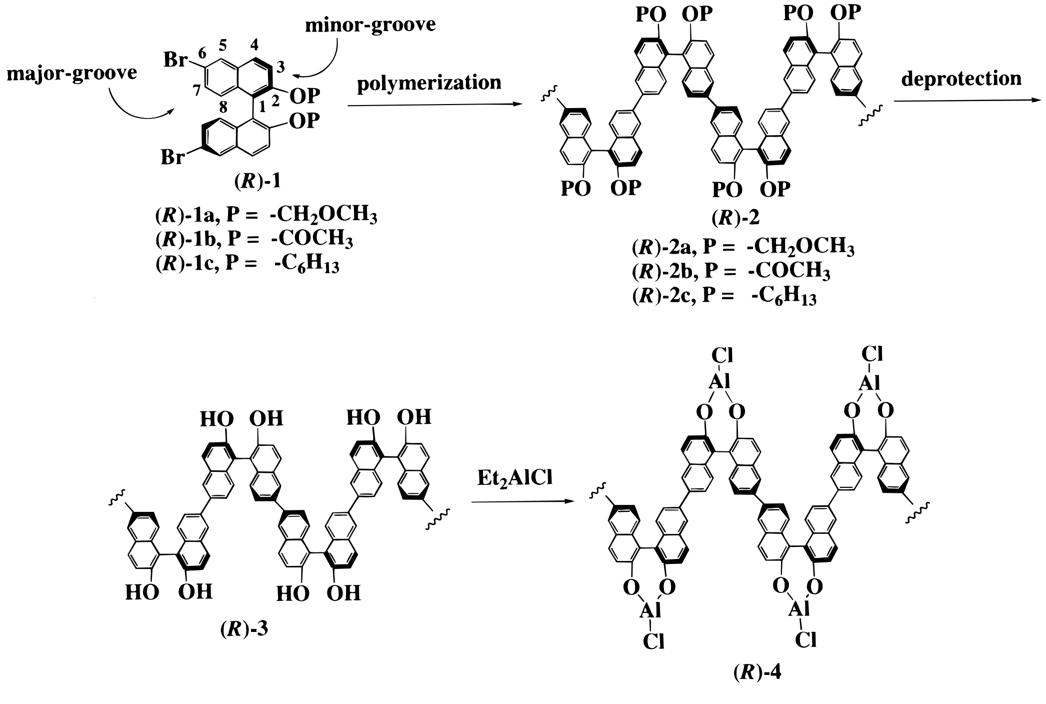


Figure 1.

Scheme 1. Preparation of a Chiral Polybinaphthyl Aluminum Complex



optimize their catalytic activity and stereoselectivity. Herein, we report the detailed synthesis and characterization of novel functionalized major-groove and minor-groove chiral polybinaphthyls. Their application in the catalysis of diethylzinc addition to aldehydes is found to be highly enantioselective.[12]

Results and Discussion

1. Synthesis and Characterization of Functionalized Major-Groove Chiral Polybinaphthyls. The major-groove polybinaphthol (*R*)-**3** can be dissolved in DMSO or basic aqueous solution, but it is not soluble in common organic solvents such as methylene chloride, toluene, and THF. In order to prepare soluble polybinaphthyls, we have synthesized the benzenediboronic acid monomers **6a,b** that contain long-chain alkyl groups (Scheme 2).[13] Hydroquinone is alkylated and then brominated to give **5** which is then reacted with *n*-butyllithium, triethyl borate, and diluted hydrochloric acid to generate **6a,b**. Compound **6a** contains two hexyloxy groups and **6b** contains two octadecyloxy groups.

The Suzuki coupling[14] of (*R*)-**1a** with **6a** produces (*R*)-**7**, which is converted to the major-groove polybinaphthol (*R*)-**8** by hydrolysis (Scheme 3). The polymerization is carried out

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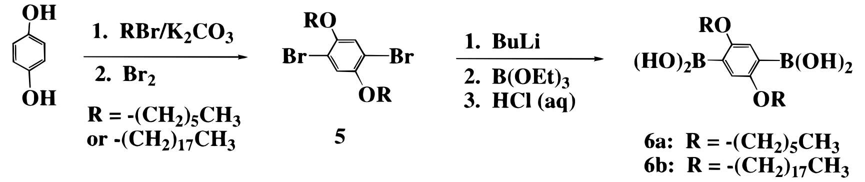
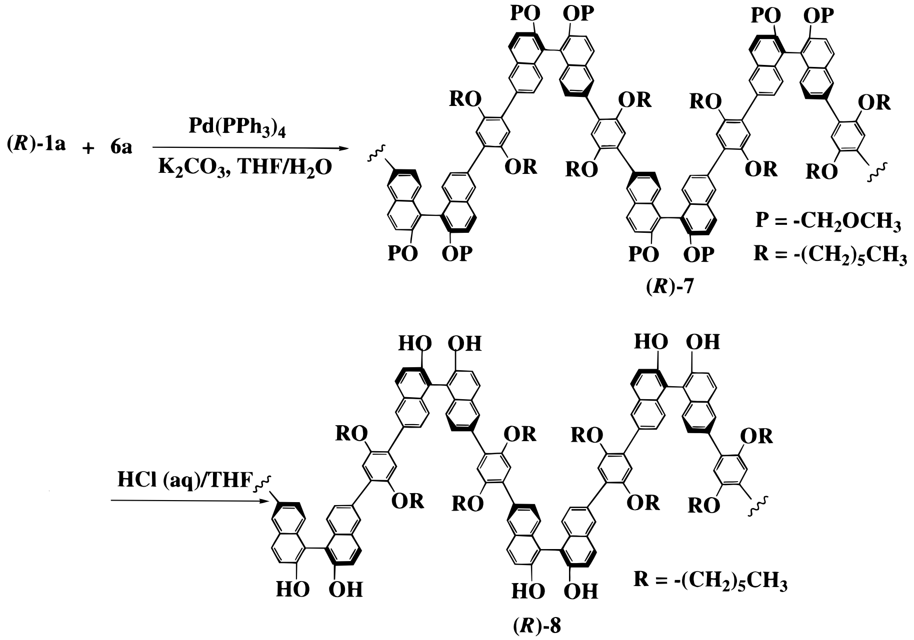
Scheme 2. Preparation of the Diboronic Acid Monomer **6a,b**



Scheme 3. Preparation of the Major-Groove Polybinaphthyl (*R*)-**8**



by heating a 1:1 mixture of (*R*)-**1a** and **6a** in THF in the presence of 5 mol % $Pd(PPh_3)_4$ and aqueous K_2CO_3 at reflux under nitrogen for 48 h. The resulting polymer (*R*)-**7** is then dissolved in THF and treated with 6 N HCl at 80 °C for 12 h to give (*R*)-**8** as a pale white solid in an overall yield of 85%. Since the chiral configuration of 1,1′-binaphthyl molecules is known to be stable at high temperature over extended periods of time,[15a] there should not be racemization during the preparation of (*R*)-**8**. We have also shown previously that the optical activity of the binaphthyl polymers is quite stable at over 100 °C in solution.[7b] Unlike (*R*)-**3**, (*R*)-**8** is soluble in organic solvents such as THF, chloroform, and methylene chloride. Gel permeation chromatography (GPC) analysis shows its molecular weight is $M_w = 18\,500$ and $M_n = 9000$ (PDI = 2.1). The specific optical rotation of (*R*)-**8** is $[\alpha]_D = -398.6$ ($c = 1.00$, CH_2Cl_2). A well-resolved ^1H NMR spectrum of (*R*)-**8** is obtained which is consistent with the polymer structure. Small peaks corresponding to the end groups are also observed.

A chiral binaphthyl polymer containing pyridine ligands is prepared. The reaction of (*R*)-6,6′-dibromo-1,1′-bi-2-naphthol, (*R*)-**9**,[15b] with 2-picolyl chloride hydrochloride salt in the presence of K_2CO_3 in refluxing acetone gives (*R*)-**10** (Scheme 4). Direct polymerization of (*R*)-**10** using $NiCl_2$/Zn catalysts produces a mostly insoluble polymer (*R*)-**11**. The Suzuki coupling of (*R*)-**10** with **6b** generates polymer (*R*)-**12**. This polymer is soluble in normal organic solvents. GPC analysis shows its molecular weight is $M_w = 9900$ and $M_n = 8100$ (PDI = 1.2). The specific optical rotation of (*R*)-**12** is $[\alpha]_D = -73.1$ ($c = 0.20$, CH_2Cl_2). The polymer with shorter alkyl groups (R = *n*-C_6H_{13}) has very poor solubility.

2. Synthesis and Characterization of Functionalized Minor-Groove Chiral Polybinaphthyls. Polymers (*R*)-**3**, (*R*)-**8**, and (*R*)-**12** are the major-groove binaphthyl polymers. We have also prepared minor-groove polybinaphthols by carrying out the polymerization at the 3,3′-positions of a binaphthyl monomer (*R*)-**15**. This compound is readily prepared following the literature procedures (Scheme 5).[16,17] Protection of the phenolic groups of (*R*)-1,1′-bi-2-naphthol, (*R*)-**13**,[16] as methoxymethyl ether gives (*R*)-**14**[17a] {$[\alpha]_D = +97.75$ ($c = 1.00$, THF)}. Reaction of (*R*)-**14** with *n*-butyllithium followed by treatment with iodine gives (*R*)-**15**.[17b] The optical purity of this molecule is over 99.9% as determined by HPLC analysis on a Chiracel OD column. The specific optical rotation of (*R*)-**15** is $[\alpha]_D = -11.05$ ($c = 1.01$, THF).

The Suzuki coupling polymerization of (*R*)-**15** with **6a** is conducted (Scheme 6). When $Pd(OAc)_2$ is used as the catalyst,[18] a low molecular weight polymer (*R*)-**16a** is obtained. This polymerization involves the reaction of a 1:1 mixture of (*R*)-**15** and **6a** in the presence of $Ba(OH)_2{\cdot}8H_2O$, $Pd(OAc)_2$, and tri-*o*-tolylphosphine in DMF and H_2O at reflux under nitrogen. After 42 h, (*R*)-**16a** is obtained as a yellow solid in 93% yield. GPC analysis of (*R*)-**16a** shows that its molecular weight is $M_w = 5900$ and $M_n = 3900$ (PDI = 1.5). The specific optical rotation of (*R*)-**16a** is $[\alpha]_D = -63.4$ ($c = 0.50$, THF).

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[14] Selected references on the Suzuki coupling: (a) Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513. (b) Wallow, T. I.; Novak, B. M. *J. Am. Chem. Soc.* **1991**, *113*, 7411. (c) Suzuki, A. *Acc. Chem. Res.* **1982**, *15*, 178.

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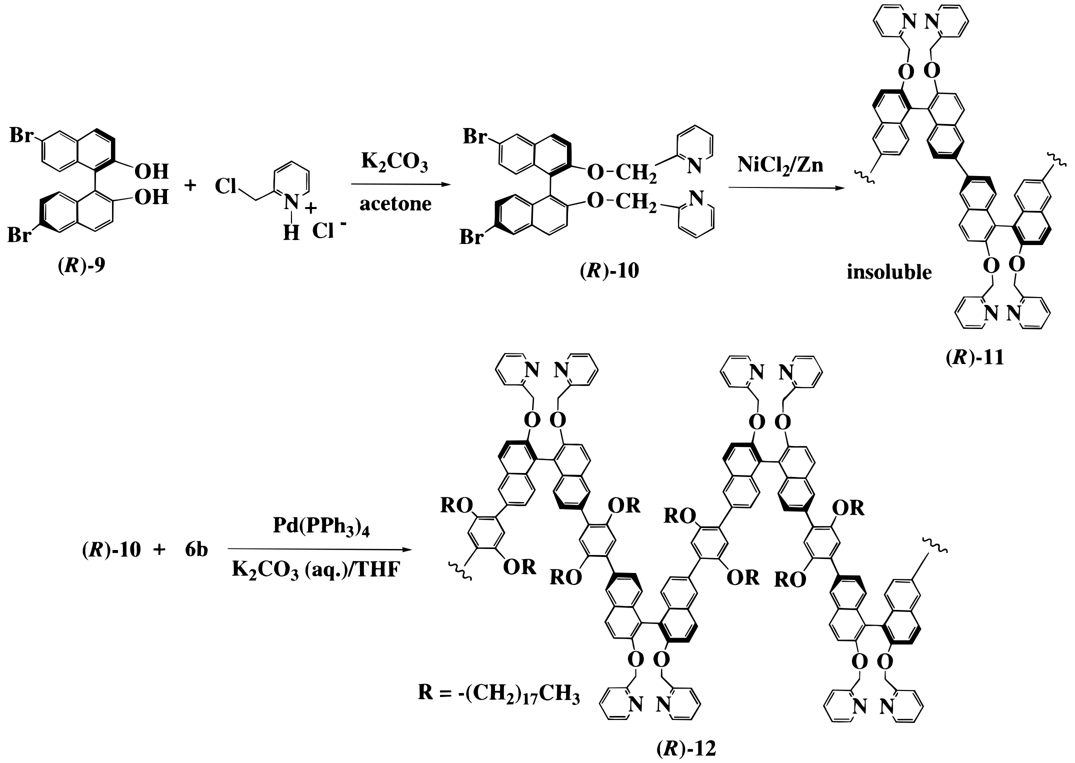
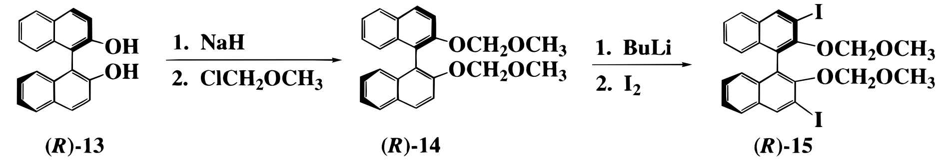
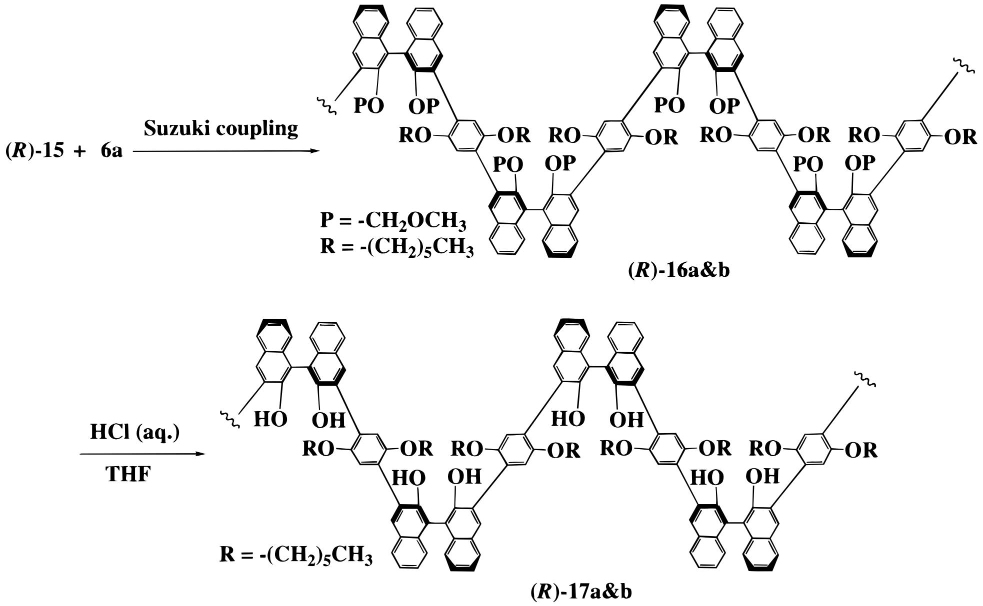
Scheme 4. Synthesis of a Pyridine Containing Chiral Polybinaphthyl (*R*)-**12**



Scheme 5. Preparation of the Monomer (*R*)-**15**

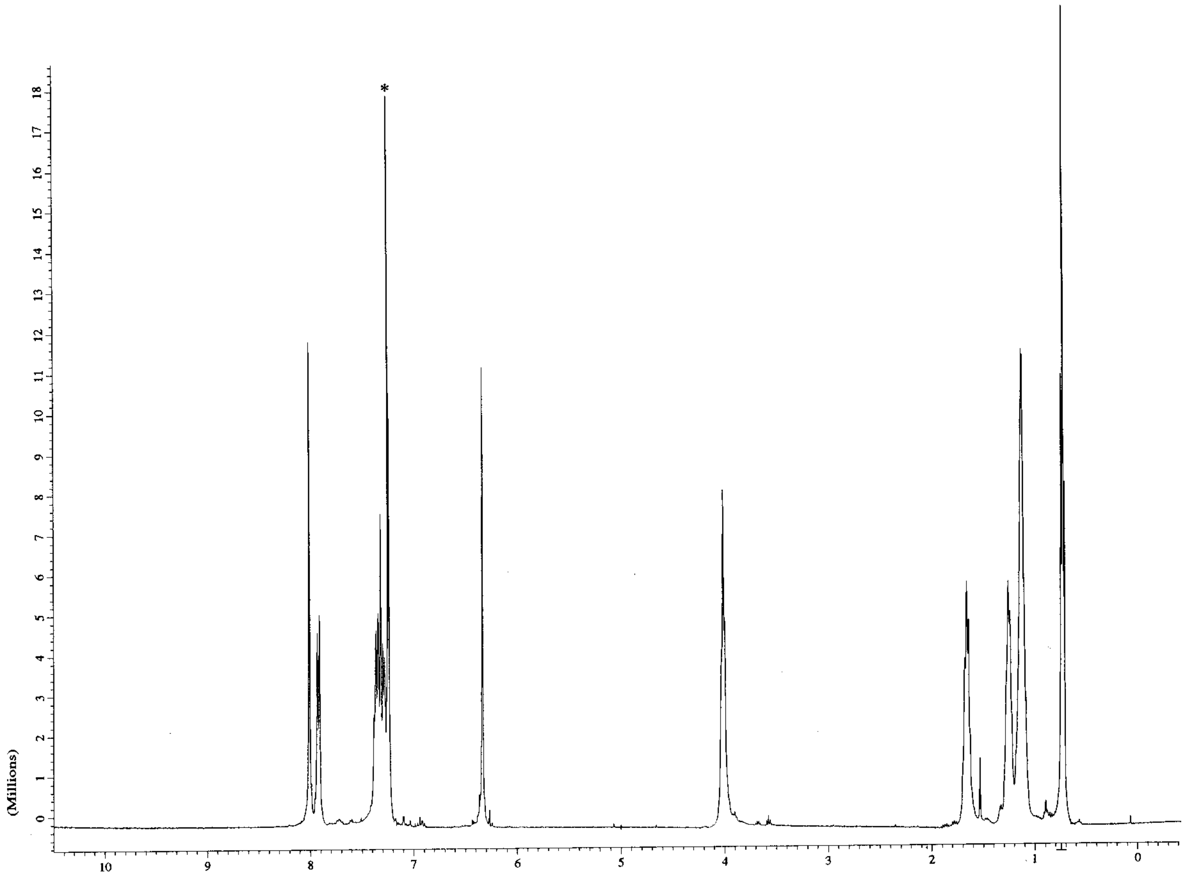


Scheme 6. Synthesis of the Minor-Groove Chiral Polybinaphthyls (*R*)-**16** and (*R*)-**17**



Because of the low molecular weight of this polymer, significant end group signals are observed in the ^{1}H NMR spectrum. Higher molecular weight polymer (*R*)-**16b** is obtained by using Pd(PPh$_3$)$_4$ as the catalyst.[14] This polymerization is carried out by heating a 1:1 mixture of (*R*)-**15** and **6a** in THF in the presence of 5 mol % Pd(PPh$_3$)$_4$ and aqueous K$_2$CO$_3$ at reflux under nitrogen. After 36 h, polymer (*R*)-**16b** is isolated in 97% yield also as a yellow solid. GPC analysis of this polymer shows $M_w = 20\,200$ and $M_n = 7300$ (PDI = 2.8). The specific optical rotation of (*R*)-**16b** is $[\alpha]_D = -90.1$ ($c = 0.51$, THF). The ^{1}H NMR spectrum of (*R*)-**16b** does not show the end group signals as observed in (*R*)-**16a**.

The methoxymethyl protecting groups of these polymers are easily hydrolyzed to generate (*R*)-**17a** and (*R*)-**17b** by refluxing



*** solvent**

Figure 2. ^{1}H NMR spectrum of (*R*)-**17b** in $CDCl_3$.

the THF solution of (*R*)-**16a** and (*R*)-**16b** in the presence of aqueous HCl.[19] GPC analysis of (*R*)-**17a** shows that its molecular weight is $M_w = 6700$ and $M_n = 4600$ (PDI = 1.5). Its specific optical rotation is $[\alpha]_D = +11.8$ ($c = 0.50$, THF). GPC analysis of (*R*)-**17b** shows that its molecular weight is $M_w = 24\,300$ and $M_n = 9900$ (PDI = 2.45). Its specific optical rotation is $[\alpha]_D = -16.6$ ($c = 0.5$, THF). Both (*R*)-**17a** and (*R*)-**17b** are soluble in common organic solvents such as THF, methylene chloride, chloroform, and toluene. Figure 2 shows the ^{1}H NMR spectrum of (*R*)-**17b** in $CDCl_3$. This very well-resolved ^{1}H NMR spectrum suggests a well-defined structure. The singlet at δ 6.34 is due to the phenolic groups of the polymer as shown by a D_2O exchange experiment. The singlet at δ 8.01 is assigned to H-4 of the binaphthyl unit.

The minor-groove polymer (*R*)-**17** has two important features that are different from the major-groove polymer (*R*)-**8**. First of all, since (*R*)-**17** is produced by polymerization at the 3,3′-positions of the binaphthyl monomer, both the phenylene spacers as well as the adjacent naphthyl groups can provide steric control around each binaphthyl unit where metal centers are introduced when used as a catalyst. Secondly, the two hexyloxy groups in the *p*-phenylene linkers of (*R*)-**17** not only make this polymer soluble in organic solvent but also act as ligands to bind the metal center.

By using the same experimental procedure as the preparation of (*R*)-**17b**, polymer (*S*)-**17** is obtained from the polymerization of (*S*)-**15** with **6a**. GPC shows its molecular weight is $M_w = 10\,000$ and $M_n = 4600$ (PDI = 2.17). Its specific optical rotation is $[\alpha]_D = -14.2$ ($c = 1.01$, CH_2Cl_2). In THF, the optical rotation of (*S*)-**17** is almost zero $\{[\alpha]_D = +0.5$ ($c = 0.51$, THF)$\}$. However, the circular dichroism (CD) spectrum of this polymer exhibits very strong Cotton effects. This indicates that the optical rotation of these polymers at $\lambda = 589$ nm (the sodium D line) is not suitable to determine their optical activity. Figure 3 shows the CD spectra of (*S*)-**17** and (*R*)-**17b**. The CD signals of these two polymers are exact mirror images of each other.

Both of the methoxymethyl protecting groups and the hexyl groups of (*R*)-**16** can be hydrolyzed simultaneously when this polymer is treated with excess BBr_3. A new polymer (*R*)-**18**, whose possible structure is shown in Scheme 7, is isolated. The structure of this polymer is interesting since it closely resembles the ligands of (*R*)-**19**[20] and (*R*)-**20**.[21] These chiral Lewis acid complexes are discovered by Yamamoto *et al.* to catalyze the highly enantioselective Diels−Alder reaction. However, (*R*)-**18** cannot be dissolved in organic solvents and basic aqueous solution which prevents the structural characterization of this polymer. We are working on the structural modification of this polymer in order to make it soluble for characterization and application purposes.

3. Comparison of the Spectroscopic Properties of the Major-Groove Polybinaphthol (*R*)-8 with the Minor-Groove Polybinaphthol (*R*)-17. The UV spectrum of (*R*)-**8** in CH_2Cl_2 displays maximum absorptions at $\lambda_{max} = 238$, 270, 336 nm and the UV spectrum of (*R*)-**17** in CH_2Cl_2 displays maximum absorptions at $\lambda_{max} = 244$, 260, 322 nm. There is ca. 14 nm blue-shift from the major-groove polymer to the minor-groove polymer, indicating a reduced effective conjugation in (*R*)-**17**. According to our earlier work on the binaphthyl-based

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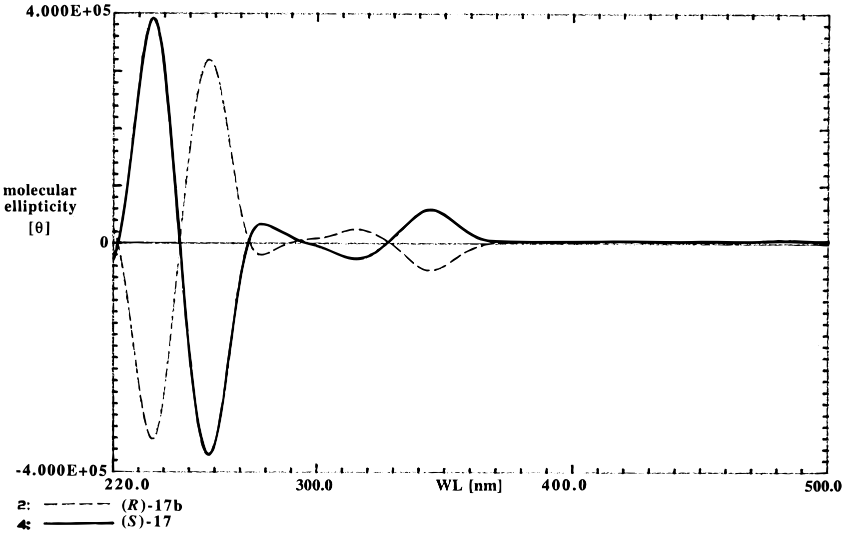
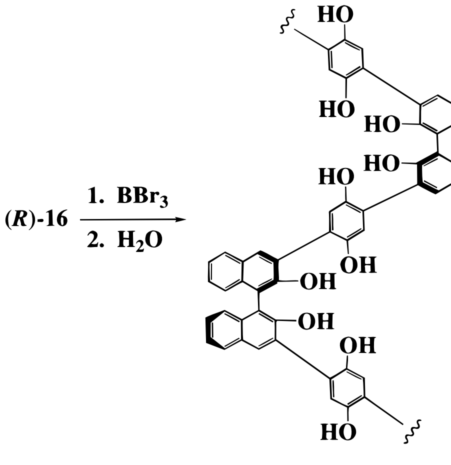
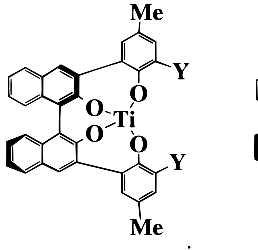


Figure 3. CD spectrum of (*S*)-**17** and (*R*)-**17b** in methylene chloride.

Scheme 7. Preparation of (*R*)-**18**

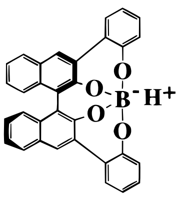


(***R***)**-18**



Y = Ph, SiPh$_3$, SiPr$^i_3$, etc.

(***R***)**-19**



(***R***)**-20**

chiral conjugated polymers, the conjugation of these materials is determined by their repeat units and there is no extended conjugation along the polymer chain.[10] Therefore, the reduced effective conjugation of (*R*)-**17** is due to a steric interaction between the alkoxy groups on the phenylene spacer and the hydroxyl groups on the binaphthyl unit which disrupts the planarity of the repeat unit. Such interaction is absent in the repeat unit of (*R*)-**8**.

There is also a very large change in optical rotation from the major-groove polymer to the minor-groove polymers. The absolute value of the optical rotation of (*R*)-**8** ($[\alpha]_D = -398.6$) is much larger than those of (*R*)-**17a** ($[\alpha]_D = +11.8$) and (*R*)-**17b** ($[\alpha]_D = -16.6$), although they all have the same functional groups. To gain more information on the structure of these polymers, their CD spectra in CH_2Cl_2 are compared (Figure 4). Although (*R*)-**17a** and (*R*)-**17b** have opposite signs for their optical rotations, their CD signals are almost identical. This indicates that these two polymers should have the same macromolecular structure and their differences in optical rotation and CD intensity are most likely due to the end groups. The ^{1}H NMR spectrum of the low molecular weight material (*R*)-**17a** shows a significant amount of unreacted binaphthyl iodide end groups for this low molecular weight material. This polymer may also have some boronic acid end groups. Both the minor-groove polymer (*R*)-**17** and the major-groove polymer (*R*)-**8** are made of optically pure (*R*)-binaphthyl monomer.

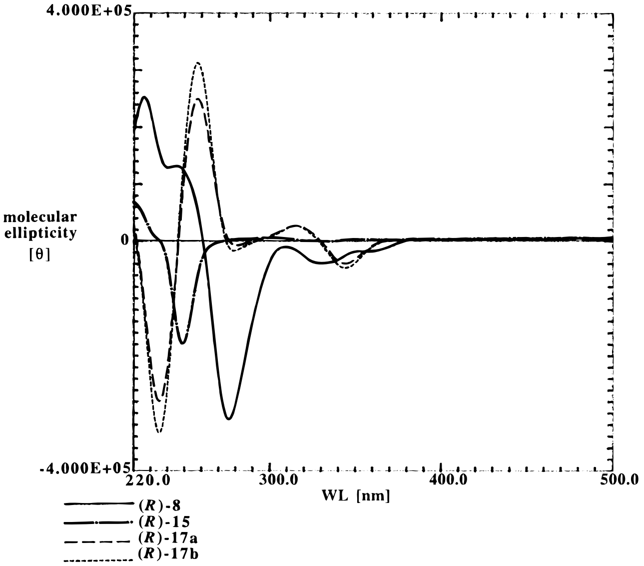
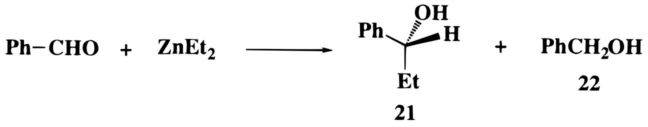


Figure 4. Comparison of the CD spectra of (*R*)-**8**, (*R*)-**15**, and (*R*)-**17a,b**.

However, their CD effects are almost mirror image of each other except that the long wavelength CD signal of (*R*)-**8** is red-shifted because of its better conjugation. Further investigation is needed in order to understand this phenomena.

Table 1. Reaction of Benzaldehyde with Diethylzinc in the Presence of Chiral Polybinaphthyls



polymer	solvent	temp[a] (°C)	time (h)	conv (%)	**21:22**	ee (%)[b]
(*R*)-**2b**	toluene	rt	24	trace		
(*R*)-**2c**	toluene	rt	48	54	19:35	8
(*R*)-**3**	CH_2Cl_2	rt	112	100	53:47	13
(*R*)-**8**	CH_2Cl_2	rt	20	33	71:29	40
(*R*)-**12**	toluene	rt	48	no reaction		
(*R*)-**16b**	toluene	rt	24	85	97.6:2.3	19
(*R*)-**17a**	CH_2Cl_2	rt	70	100	94:6	67.0
(*R*)-**17a**	toluene	rt	10	100	99.6:0.4	89.4
(*R*)-**17a**	THF	0	10	79	100:0	84.7
(*R*)-**17a**	hexane:toluene (2:1)	0	16	100	100:0	91.7
(*R*)-**17a**	toluene	0	12	100	100:0	92.2

[a] rt = room temperature. [b] All the ees were determined by GC with a chiral column (β-Dex capillary column, Supelco Co.).

4. Asymmetric Reaction of Aldehydes with Diethylzinc Catalyzed by the Functionalized Chiral Polybinaphthyls. As an example to study the applications of the chiral polybinaphthyls in asymmetric catalysis, we have used these polymers to catalyze reaction of benzaldehyde with diethylzinc.[22,23] The results are summarized in Table 1. All of the reactions are carried out under nitrogen in the presence of ca. 5 mol % (based on the binaphthyl unit) of the polymer and 1−2 equiv of diethylzinc. Formations of a chiral alcohol product 1-phenyl propanol (**21**) and a side product benzyl alcohol (**22**) are observed in many cases. As shown in the table, (*R*)-**17a** is an excellent catalyst for this reaction with high enantioselectivity and good catalytic activity. Polybinaphthyl (*R*)-**12**, which contains pyridine functional groups, has no catalytic activity at all. (*R*)-**16b**, the polymer in which the phenolic groups are protected, is a more efficient catalyst than most of other polymers, but it gives much lower enantiomeric excess (ee) for **21** compared to its unprotected version (*R*)-**17a**. From the major-groove polybinaphthols (*R*)-**3** and (*R*)-**8** to the minor-groove polybinaphthol (*R*)-**17a**, there is a dramatic increase of both the catalytic activity and enantioselectivity. The best condition for the use of (*R*)-**17a** is to carry out the reaction in toluene solution at 0 °C which produces **21** in 92.2% ee without formation of the side product **22**. Further lowering of the temperature to −40 °C shows no increase of the ee.

Polymer (*R*)-**17a** has therefore been used to catalyze the asymmetric reaction of different aldehydes with diethylzinc, and the results are listed in Table 2. The ee's are determined relative to the racemic mixture of the alcohol products. These reactions are carried out in toluene solution at 0 °C in the presence of 5 mol % (based on the binaphthyl units) of (*R*)-**17a**. All of the alcohol products except the one from the reaction of 3,3,7-trimethyl-6-octenal have the *R* configuration as determined by comparing their specific optical rotations with the reported data.[22,23] The reactions are completed in 12−26 h for aromatic aldehydes and *trans*-cinnamaldehyde. The addition to aliphatic aldehydes are much slower and take 70−100 h to go to completion. As shown in the table, excellent enantioselectivities for the para-substituted benzaldehydes as well as for *trans*-cinnamaldehyde are achieved. But much lower ee's are observed for the reaction of the *o*-substituted aromatic aldehydes. The ee's observed for the addition to the aliphatic aldehydes are also very significant since few polymeric catalysts are good for the reaction of aliphatic aldehydes.

Table 2. Asymmetric Reaction of Aldehydes with Diethylzinc in the Presence of the Polybinaphthols

polymer	aldehyde	isolated yield (%)	ee (%)[a]
(*R*)-**17a**	benzaldehyde	89	92.2
		91	92.0[b]
	p-methylbenzaldehyde	90	92.5[b]
	p-cholorobenzaldehyde	94	93.4[b]
	p-methoxybenzaldehyde	84	88.3[b,c]
	p-tert-butylbenzaldehyde	63	74.3[b,c]
	o-fluorobenzaldehyde	86	35.1[b]
	o-methoxybenzaldehyde	90	59.0[b]
	cinnamaldehyde	86	89.7[b,d]
	3,3,7-trimethyl-6-octenal	67	82.8[b,d,e]
	nonyl aldehyde	89	73.5[d]
	cyclohexanecarbaldehdye	70	83.3[b,d]
	hexaldehyde	65	74.3[b,d]
(*R*)-**17b**	benzaldehyde	90	92.7
	p-cholorobenzaldehyde	95	93.8
(*S*)-**17**	benzaldehyde	94	93.0

[a] All of the ees were determined by GC with a chiral column (β-Dex capillary column, Supelco Co.) except those specifically indicated. [b] The recycled polymer was used. [c] The ee was measured by HPLC-Chiracel OD column. [d] The ee was measured by GC analysis (β-Dex capillary column) of the corresponding acetate derivative. [e] The absolute configuration of the product was not determined. $[\alpha]_D = -13.25$ ($c = 1.95$, THF).

In these reactions, (*R*)-**17a** can be easily recovered from the reaction mixture by precipitation with methanol. The recycled polymer shows a similar enantioselectivity. When the higher molecular weight polymer (*R*)-**17b** is used, the ee for the reaction of benzaldehyde is 92.7% and for the reaction of *p*-chlorobenzaldehyde is 93.8%. Therefore, both the molecular weight of the polymer and the method of polymer preparation have little effect on the asymmetric process. This is an excellent property for practical application.

(*S*)-**17** is also used to catalyze the reaction of benzaldehyde with diethylzinc. In the presence of (*S*)-**17**, **21** is obtained in 93.0% ee, similar to that obtained from (*R*)-**17**. As expected, the configuration of the resulting chiral alcohol is opposite of that obtained with (*R*)-**17**. Thus, the *R* polybinaphthyl produces the *R* chiral alcohol and the *S* polymer generates the *S* chiral alcohol.

A number of highly enantioselective monomeric amino alcohol catalysts have been developed.[22] Polymer-supported chiral amino alcohols have also been studied, and in some cases, high enantioselectivities have been observed.[22] However, the best polymeric chiral amino alcohol catalyst gives only 69% ee for the reaction of aliphatic aldehydes, and at the same time

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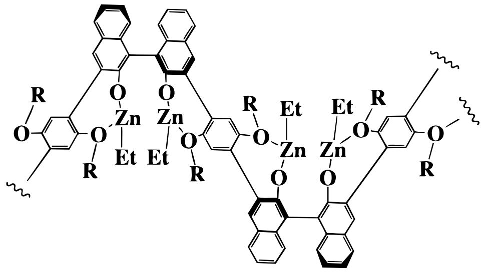
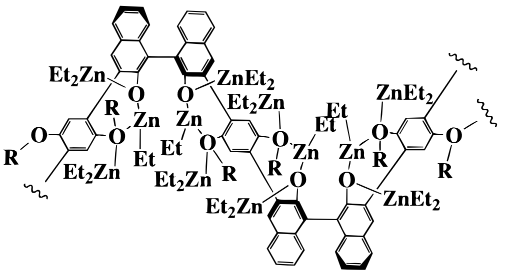
(22) Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833.
(23) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49.

it shows much lower enantioselectivity for aromatic aldehydes compared to other polymeric chiral catalysts.[24] Excellent enantioselectivity for certain aliphatic aldehydes and benzaldehyde is recently observed by Seebach *et al.* when polymer-supported chiral α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol−Ti(IV) complexes are used to carry out the diethylzinc addition, but more than 1 equiv of $Ti(O^iPr)_4$ versus the aldehydes are required in the reaction.[25]

5. Reaction of (*R*)-17 and Some Monomeric Binaphthols with Diethylzinc. We have studied the reaction of (*R*)-**17** with diethylzinc in the absence of aldehydes. We find that when 1 equiv of diethylzinc is added to a toluene solution of (*R*)-**17b** at room temperature, the solution becomes viscous. With the addition of the second equiv of $ZnEt_2$, the polymer solution is changed to an unmovable gel, suggesting the formation of a cross-linked polymer network. (*R*)-**23** is one of the possible structures proposed for the polymer generated from the reaction of (*R*)-**17** with 2 equiv of diethylzinc. The cross-linked polymer gel is probably formed through the interchain coordination of the oxygen atoms to the zinc atoms in (*R*)-**23**. After 6−16 equiv of diethylzinc is added, a viscous but clear solution is obtained. This indicates that the cross-linked polymer gel has collapsed in the presence of excess diethylzinc, probably through multiple zinc coordination to the oxygen atoms of the polymer as shown by the structure of (*R*)-**24**. Such interaction breaks the interchain coordination and destroys the cross-linked polymer gel. The coordinated diethylzinc in (*R*)-**24** should be in equilibrium with free diethylzinc in solution since free diethylzinc is observable by ^1H NMR spectroscopy when 3 equiv or more diethylzinc are added to the polymer solution. However, the ^1H NMR spectrum of the polymer in the presence of diethylzinc is too broad to give any structural information.



(***R***)**-23**



(***R***)**-24**

In order to learn more about the binaphthyl−zinc species in the polymer, we have studied the reaction of a monomeric binaphthyl compound (*R*)-**25** with diethylzinc (Scheme 8). When 1 equiv of diethylzinc is added to a chloroform-*d* solution of (*R*)-**25**, a new compound (*R*)-**27** is produced probably via (*R*)-**26**. In the ^1H NMR spectrum of (*R*)-**27**, a multiplet is observed at δ −0.88 for the methylene protons adjacent to the zinc atoms. Both the ^1H and ^{13}C NMR spectra of (*R*)-**27** show a C_2 symmetric molecular structure. Cryoscopic molecular weight determination of (*R*)-**27′** in cyclohexane confirms a bisbinaphthyl structure for this compound in solution. The measured molecular weight of (*R*)-**27′** is 964, and the calculated molecular weight for the dimer is 926. The similar dinuclear zinc complexes have been obtained and structurally characterized from the reaction of amino alcohols with diethylzinc by Noyori *et al.*[27] When more diethylzinc is added to (*R*)-**27**, the aromatic NMR signals of this compound do not show observable change but more peaks are observed at δ −0.3 to −1.15. This may be due to the reversible coordination of diethylzinc with the oxygen atoms in (*R*)-**27** in the presence of excess diethylzinc.

The reaction of diethylzinc with (*R*)-1,1′-bi-2-naphthol [(*R*)-**13**] is more complicated. When 1 equiv of diethylzinc is added into the $CDCl_3$ solution of (*R*)-**13** at room temperature, a white precipitate is formed with the release of ethane. The addition of the second equiv of diethylzinc converts the suspension to a clear solution. The precipitate is probably a polymeric binaphthyl zinc complex formed through Zn−O−Zn bridging bonds. Excess diethylzinc breaks some of these bridging bonds to form soluble complexes as observed in the reaction of (*R*)-**17** with excess diethylzinc. Earlier, Katsuki *et al.* have made a similar observation in the reaction of a binaphthyl amide derivative with diethylzinc.[26] The ^1H and ^{13}C NMR spectra of the product solution obtained from the reaction of (*R*)-**13** with 2 equiv of diethylzinc suggest the formation of two compounds. They are probably multibinaphthyl complexes with multiple zinc coordination. Their actual structures are not determined at this time due to the difficulty in their separation. Previously, Yamamoto *et al.* have used the complex made from the reaction of (*R*)-1,1′-bi-2-naphthol with dimethylzinc at low temperature to catalyze asymmetric ene reactions, and up to 90% ee is observed.[28]

Both (*R*)-**13** and (*R*)-**25** are used to catalyze the reaction of diethylzinc with benzaldehyde. (*R*)-**13** is a poor catalyst for this reaction. In toluene solution at room temperature, 37% conversion of benzaldehyde is observed over 24 h in the presence of 5 mol % of (*R*)-**13**. The formation of **21** and **22** is observed in 95.9:4.1 ratio. The ee of **21** is 32.9%. When the reaction is carried out in methylene chloride solution, after more than 5 days, 84% conversion of benzaldehyde is observed in the presence of 10 mol % of (*R*)-**13**. The ratio of **21** versus **22** is 61:39, and the ee of **21** is 15%.

(*R*)-**25** shows higher catalytic activity than (*R*)-**13**. After 24 h in toluene solution, 72% conversion of benzaldehyde is observed in the presence of 5 mol % of (*R*)-**25**. The ratio of **21** versus **22** is 90.6:9.4 and the ee of **21** is 57.0%.

Unlike (*R*)-**27** whose bridging Zn−O−Zn bonds are stable even in the presence of excess diethylzinc, the cross-linked polymer gel of (*R*)-**23** collapses when excess diethylzinc is added and a structure of (*R*)-**24** may be produced. In this polymeric zinc complex, its central zinc atoms that are responsible for the catalysis are coordinatively less saturated than those in (*R*)-**27**. This may explain the enhanced catalytic activity of (*R*)-**17** over the monomeric compounds (*R*)-**13** and (*R*)-**25**. It is our general observation that higher catalytic activity is associated with higher asymmetric induction in the chiral binaphthyl-catalyzed reaction of aldehydes with diethylzinc.

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[24] Soai, K.; Watanabe, M. *Tetrahedron: Asymmetry* **1991**, *2*, 97.

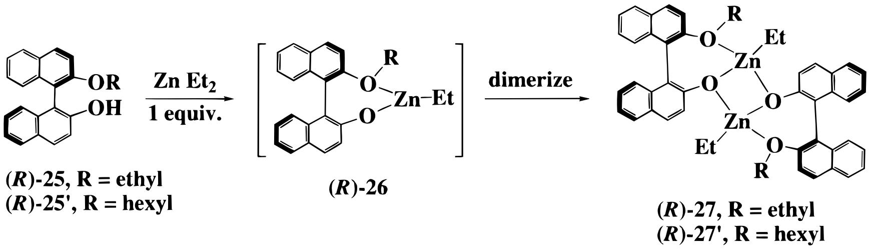
[25] Seebach, D.; Marti, R. E.; Hintermann, T. *Helv. Chim. Acta* **1996**, *79*, 1710.

[26] The reaction of diethylzinc with a binaphthol molecule containing 3,3′-bis(amide) groups has been studied. Formation of a trimeric binaphthylzinc complex is observed and its crystal structure is obtained: Kitajima, H.; Ito, K.; Aoki, Y.; Katsuki, T. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 207.

[27] Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028.

[28] Sakane, S.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1985**, *26*, 5535.

Scheme 8. Formation of a Bisbinaphthyl Dinuclear Zinc Complex



Summary

In summary, a series of soluble major-groove and minor-groove chiral polybinaphthyls with hydroxyl or pyridine functional groups have been synthesized and characterized. We find that a minor-groove polybinaphthyl has less effective conjugation than its corresponding major-groove polymer due to the steric hindrance in the repeat unit of the minor-groove polymer. The application of these chiral polymers in the asymmetric reaction of aldehydes with diethylzinc has been studied. We have discovered that the minor-groove polybinaphthols (*R*)-**17** and (*S*)-**17** are excellent enantioselective catalysts for the reaction of a number of aldehydes with diethylzinc. The molecular weight and the molecular weight distribution of these polymers have little effect on the catalytic process. They can be easily recovered and reused without loss of both catalytic activity and enantioselectivity. These rigid and sterically regular chiral polymers represent a new generation of enantioselective polymeric catalysts different from the traditionally prepared polymer-supported catalysts. The reactions of the polybinaphthol (*R*)-**17** and certain monomeric binaphthol compounds with diethylzinc in the absence of the aldehyde substrates have been studied in order to gain more understanding on the catalytically active chiral zinc species. The use of the functionalized chiral polybinaphthyls in other asymmetric organic reactions is also under investigation in our laboratory.

Experimental Sections

General Data. NMR spectra were recorded on JEOL-270 MHz and JEOL-400 MHz spectrometers. Infrared spectra were recorded on a 2020/Galaxy Series FT-IR spectrometer by preparing KBr pellets of the materials. Elemental analyses were carried out using a Perkin-Elmer 2400 Series II CHN S/O analyzer. Mass spectra were obtained using Hewlett-Packard 5890 Series II GC/DIP MS. Gel permeation chromatography (GPC) utilized a Waters 510 HPLC pump, a Waters 410 differential refractometer, and Ultrastyragel linear GPC columns. THF was used as the solvent for the GPC analysis and polystyrene standard was used. UV−vis spectra were recorded on a Hewlett-Packard 8451A diode array spectrophotometer. Circular dichroism spectra were recorded using a JASCO J-710 spectropolarimeter. Optical rotations were measured on a JASCO polarimeter at $\lambda = 589$ nm. THF and ether were dried with sodium/benzophenone. Tetrakis(triphenylphosphine)palladium(0) and palladium(II) acetate were purchased from Strem and used directly. All of the aldehydes were purchased from Aldrich.

Preparation and Characterization of 6a. To a THF (80 mL) solution of 1,4-bis(hexyloxy)-2,5-dibromobenzene (6.4 g, 14.7 mmol) at −78 °C was added *n*-BuLi (20 mL, 2.5 M in hexanes, 50 mmol). After 2 h of stirring at this temperature, the resulting solution was cannulated into a solution of $B(OEt)_3$ (15 mL) in THF (40 mL) over 30 min. The mixture was warmed to room temperature and stirred for 12 h. Excess 2 N HCl was then added. After filtration, the solid was washed with water and CH_2Cl_2 and dried under vacuum to give pure **6a** (4.05 g, 75.4% yield) as a white solid: ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.81 (s, 4H, B-OH), 7.17 (s, 2H), 3.98 (t, $J = 6.4$ Hz, 4 H), 1.72 (m, 4H), 1.41 (m, 4H), 1.31 (m, 8H), 0.87 (t, $J = 7.0$ Hz, 6H, $2CH_3$); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 157.40, 125.08, 118.45, 68.90, 31.50, 29.29, 25.69, 22.60, 14.43; FT-IR (KBr, cm^{-1}) 3353 (s), 2938 (s), 2872 (m), 2857 (m), 1495 (s), 1468 (s), 1418 (s), 1389 (s), 1300 (s), 1271 (m), 1202 (s), 1127 (m), 1084 (m), 1047 (s), 887 (w), 822 (m), 793 (m), 725 (m). Anal. Calcd for $C_{18}H_{32}O_6B_2$: C, 59.08; H, 8.81. Found: C, 58.79; H, 8.74. **6b** is prepared and characterized similarly.

Preparation and Characterization of (*R*)-8. Under N_2, a mixture of (*R*)-**1a** (1.06 g, 2.0 mmol), **6a** (0.73 g, 2.0 mmol), and $Pd(PPh_3)_4$ (116 mg, 0.10 mmol, 5 mol %) in THF (10 mL) and 1 M K_2CO_3 (10 mL) was heated at reflux for 48 h. CH_2Cl_2 (200 mL) was then added to the reaction mixture, and the organic layer was separated. The solution was washed with brine and dried over Na_2SO_4. After the solution was concentrated under vacuum, methanol was added to precipitate out the polymer. This precipitation was repeated one more time, and the resulting polymer (*R*)-**7** was dissolved in THF (10 mL) and 6 N HCl (10 mL). After the solution was degassed with nitrogen, it was heated at 80 °C for 12 h. CH_2Cl_2 (200 mL) was then added to extract the hydrolyzed polymer. The organic layer was washed with brine and dried over Na_2SO_4. After removal of the solvent, the residue was redissolved in a minimum amount of CH_2Cl_2 and precipitated with MeOH. This process was repeated three times to give (*R*)-**8** as a pale white solid in 85% yield. GPC analysis shows its molecular weight is $M_w = 18\,500$ and $M_n = 9000$ (PDI = 2.1). The specific optical rotation of (*R*)-**8** is $[\alpha]_D = -398.6$ ($c = 1.00$, CH_2Cl_2). Another batch of reaction generated (*R*)-**8** with $M_w = 15\,600$ and $M_n = 8900$ (PDI = 1.8). The UV spectrum of this polymer in CH_2Cl_2 shows maximum absorptions at $\lambda_{max} = 238, 270, 336$ nm: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.16 (s, 2H), 8.01 (d, $J = 8.3$ Hz, 2H), 7.64 (d, $J = 8.6$ Hz, 2H), 7.42 (d, $J = 8.3$ Hz, 2H), 7.27 (d, $J = 8.6$ Hz, 2H), 7.10 (s, 2H), 3.96 (m, 4H), 1.68 (m, 4H), 1.36 (m, 4H), 1.22 (m, 8H), 0.78 (s, 6H), very small peaks for the end groups were observed at δ 8.09, 7.57, 7.36, 7.01, 6.93, 3.90, 3.72, 3.57, 1.84, 1.76, 0.90; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.93, 150.51, 134.28, 132.44, 131.75 (br), 130.37, 129.66 (br), 129.50, 128.89 (br), 123.82, 117.96, 116.29, 110.87, 69.64, 31.52, 29.36, 25.87, 22.63, 14.03, very weak signals were observed at δ 132.25, 132.15, 131.53. Anal. Calcd for $C_{38}H_{40}O_4$: C, 81.40; H, 7.19. Found: C, 80.23; H, 7.26.

Preparation and Characterization of (*R*)-10. Under nitrogen, to a 50 mL Schlenk flask were added (*R*)-6,6′-dibromo-1,1′-bi-2-naphthol, (*R*)-**9** (1.0 g, 2.25 mmol), 2-picolyl chloride (1.05 g, 6.4 mmol), K_2CO_3 (4.0 g, 2.8 mmol), and acetone (30 mL). After the mixture was heated at reflux for 24 h, it was cooled to room temperature, and water (20 mL) was added. The solution was extracted with EtOAc (2 × 100 mL), and the organic layer was dried over Na_2SO_4. After filtration, the organic solution was concentrated under reduced pressure. Column chromatography (silica gel, hexane:EtOAc = 1:1) of the residue gave (*R*)-**10** as a yellow solid in 72% yield (1.01 g): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 5.20 (s, 4H), 6.70 (d, $J = 6.9$ Hz, 2H), 7.04 (tm, $J_t = 7.5$ Hz, 2H), 7.03 (dm, $J_d = 8.9$ Hz, 2H), 7.28 (dd, $J = 2.0, 9.1$ Hz, 2H), 7.26 (dd, $J = 2.2, 7.4$ Hz, 2H), 7.45 (d, $J = 9.1$ Hz, 2H), 7.85 (d, $J = 8.9$ Hz, 2H), 8.03 (d, $J = 2.0$ Hz, 2H), 8.44 (ddd, $J = 4.9, 1.8, 1.8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 71.50, 115.97, 117.82, 119.71, 120.72, 122.43, 127.14, 129.00, 130.03, 130.04, 130.46, 132.57, 136.65, 148.89, 154.00, 157.31; MS(DIP) for $C_{32}H_{22}Br_2N_2O_2$ (*m/z*) M^+ (626), $M^+ - C_6H_6N$ (534).

Preparation and Characterization of the Pyridine-Containing Polymer (*R*)-12. Under nitrogen, to a 50 mL Schlenk flask were added (*R*)-**10** (316 mg, 0.5 mmol), **6b** (315 mg, 0.5 mmol), K_2CO_3 (1 M aqueous solution, 7.2 mmol, degassed with N_2), $Pd(PPh_3)_4$ (30 mg, 0.026 mmol in 5 mL THF), and THF (15 mL). After the mixture was heated at reflux for 28 h, it was cooled to room temperature, and water (25 mL) was added. CH_2Cl_2 (20 mL) was used to extract, and the organic solution was washed five times with H_2O. The polymer was then precipitated out of the methylene chloride solution with MeOH. It was redissolved and reprecipitated for two more times. After centrifuge separation and drying under vacuum, (*R*)-**12** was isolated as a dark yellow solid in 65% yield: GPC $M_w = 9900$ and $M_n = 8100$ (PDI = 1.2); $[\alpha]_D = -73.1$ ($c = 0.20$, CH_2Cl_2); ^1H NMR ($CDCl_3$, 270 MHz) δ 0.86 (m, 6H), 1.16−1.25 (m, 60H), 1.64 (m, 4H), 3.90 (m, 4H), 5.22 (m, 4H), 6.78 (m, 2H), 7.04 (m, 2H), 7.08 (m, 2H), 7.25 (m, 4 H), 7.39 (m, 2H), 7.45 (dm, $J_d = 9.2$ Hz, 2H), 7.56 (d, $J = 9.2$ Hz, 2H), 8.01 (d, $J = 9.4$ Hz, 2H), 8.15 (br s, 2H), 8.44 (m, 2H), small peaks were observed at δ 3.09, 5.22, 6.70, 6.82, 7.16, 7.18, 7.20, 7.44, 7.47, 7.55, 7.86, 7.88, 8.05, and 8.13 due to the end groups; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.24, 22.08, 26.21, 29.39, 29.48, 29.70, 29.78, 29.83, 32.03, 69.64, 71.57, 115.02, 115.45, 116.44, 120.11, 120.97, 122.20, 122.32, 125.11, 128.41, 128.71, 128.74, 129.46, 129.84, 129.92, 130.57, 133.06, 133.28, 134.03, 136.58, 148.67, 148.84, 150.60, 153.86, 157.85, small peaks were observed at δ 68.73, 116.05, 117.74, 119.30, 120.55, 120.75, 124.68, 127.55, 128.00, 128.94, 129.63, 130.18, 130.51, 130.65, 132.78, 134.17, 154.06, 157.55, and 157.63 due to the end groups.

Preparation and Characterization of (*R*)-17a. A mixture of (*R*)-**15** (7.32 g, 11.7 mmol), **6a** (4.3 g, 11.7 mmol), $Ba(OH)_2{\cdot}8H_2O$ (6.17 g, 36.0 mmol), $Pd(OAc)_2$ (0.134 g, 0.6 mmol), tri-*o*-tolylphosphine (0.365 g, 1.2 mmol) in DMF (60 mL), and H_2O (10 mL) was heated at reflux under nitrogen for 42 h. EtOAc was then added, and the organic layer was washed with H_2O and filtered. After removal of EtOAc with rotary evaporation, the residue polymer was redissolved in CH_2Cl_2 and precipitated with MeOH. This procedure was repeated three times. The precipitate was collected and dried under vacuum to give a yellow solid polymer (*R*)-**16a** (7.0 g, 93%). (*R*)-**16a** (3.0 g) was then dissolved in THF (30 mL) to which 6 N HCl (20 mL) was added subsequently. After the mixture was heated at reflux for 16 h, CH_2Cl_2 was added. The organic layer was separated and washed with H_2O. Removal of the solvent with rotary evaporation gave a polymer residue which was redissolved in CH_2Cl_2 and precipitated with MeOH. This procedure was repeated three times. After being dried under vacuum, (*R*)-**17a** was obtained as a yellow solid in 89% yield (2.3 g). GPC analysis of (*R*)-**17a** showed its molecular weight to be $M_w = 6700$ and $M_n = 4600$ (PDI = 1.5): $[\alpha]_D = +11.8$ ($c = 0.50$, THF); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.49 (s, low intensity), 8.00 (s, 2H), 7.92 (d, $J = 8.0$ Hz, 2H), 7.77 (d, low intensity), 7.34 (m, 6H), 7.24 (m, 2H), 6.32 (s, 2H), 6.15−7.4 (low intensity) 4.01 (m, 4H), 1.66 (m, 4H), 1.26 (m, 4H), 1.13 (m, 8H), 0.73 (m, 6H). The observed lower intensity peaks are due to the end groups.

Preparation and Characterization of (*R*)-17b. To a flask containing (*R*)-**15** (13.70 g, 22 mmol), **6a** (8.0 g, 22.0 mmol), THF (75 mL), and 1 M K_2CO_3 (100 mL) was added $Pd(PPh_3)_4$ (0.5 g in 25 mL THF), and the reaction mixture was heated at reflux under nitrogen for 36 h. EtOAc was then added, and the organic layer was washed with H_2O and filtered. After removal of EtOAc with rotary evaporation, the residue polymer was redissolved in CH_2Cl_2 and precipitated with MeOH. This procedure was repeated three times. After being dried under vacuum, (*R*)-**16b** was obtained as a yellow solid polymer in 97% yield (13.90 g). (*R*)-**16b** was hydrolyzed to (*R*)-**17b** in a procedure similar to the hydrolysis of (*R*)-**16a**. GPC analysis of the resulting (*R*)-**17b** showed its molecular weight to be $M_w = 24\,300$ and $M_n = 9900$ (PDI = 2.5): $[\alpha]_D = -16.6$ ($c = 0.5$, THF); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.01 (s, 2H), 7.92 (d, $J = 8.0$ Hz, 2H), 7.32 (m, 6H), 7.24 (br s, 2H), 6.34 (s, 2H), 4.02 (m, 4H), 1.66 (m, 4H), 1.26 (m, 4H), 1.13 (m, 8H), 0.73 (t, $J = 7.0$ Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.74, 150.47, 133.83, 131.32, 129.35, 128.82, 128.76, 128.37, 126.82, 125.04, 123.96, 117.89, 116.58, 70.75, 31.55, 29.40, 25.63, 22.58, 14.10; UV−vis λ_{max} (CH_2Cl_2, nm) 244, 260, 322. FT-IR (KBr, cm^{-1}) 3530 (s), 3393 (s), 2926 (s), 2865 (s), 1622 (m), 1599 (w), 1501 (s), 1431 (s), 1383 (s), 1256 (s), 1198 (s), 1148 (s), 1128 (s), 1011 (s), 938 (m), 891 (m), 785 (w), 747 (s). Anal. Calcd for $C_{38}H_{40}O_4$: C, 81.40; H, 7.19. Found: C, 80.16; H, 7.21.

Preparation and Characterization of (*S*)-17. (*S*)-**17** was prepared and characterized in a similar way as (*R*)-**17b**. GPC $M_w = 10\,000$ and $M_n = 4600$ (PDI = 2.2). $[\alpha]_D = -14.2$ ($c = 1.01$, CH_2Cl_2). ^1H NMR and ^{13}C NMR spectra of (*S*)-**17** are similar to those of (*R*)-**17b**.

The general procedure to carry out the reaction of aldehydes with diethylzinc in the presence of (*R*)-**17** is described in the following examples.

(a) Reaction of Benzaldehyde with Diethylzinc Catalyzed by (*R*)-17a. To a Schlenk flask containing toluene (10 mL, dried with Na and degassed with N_2) were added the polymer (*R*)-**17a** (28 mg, 0.05 mmol) and diethylzinc (0.14 mL, 1.3 mmol) under N_2 at room temperature. After ca. 15 min, the flask was cooled to 0 °C, and benzaldehyde (0.1 mL, 1 mmol) was added dropwise. After 12 h of stirring, the ^1H NMR spectrum of the crude mixture showed 100% conversion of benzaldehyde with no side product. The reaction was then quenched with the addition of 1 N HCl at 0 °C, and the aqueous layer was extracted with diethyl ether. The combined organic layer was washed with brine until pH = 7 and then dried over anhydrous Na_2SO_4. Concentration of the solution in vacuum gave a pale yellow oil, which upon treatment with MeOH (20 mL) precipitated the polymer. The filtrate was concentrated and purified by column chromatography on silica gel with EtOAc/hexanes (1:4) to afford the product, (*R*)-1-phenylpropanol, as a colorless liquid (122 mg, 89%). (*R*)-1-phenylpropanol, **21**: ^1H NMR (270 MHz, $CDCl_3$) δ 0.90 (t, $J = 7.5$ Hz, 3H), 1.74 (m, 2H), 2.73 (s, 1H), 4.52 (t, $J = 6.5$ Hz, 1H), 7.23−7.38 (m, 5H); $[\alpha]_D = 42.91$ ($c = 2.44$, $CHCl_3$). The ee was determined to be 92.2% on GC with a chiral column (β-Dex capillary column, Supelco Co.). GC conditions: injection temperature, 200 °C; detector temperature, 280 °C; flow rate, 1.05 cm^3/min; increasing the oven temperature from 105 to 220 °C at the speed of 1.0 °C/min. The retention time is 22.31 min for the *R* enantiomer and 23.09 min for the *S* enantiomer. The recovery of the polymer: After the precipitation with methanol, the polymer was collected and dissolved in acetone. A very small amount of insoluble inorganic impurity was filtered off, and the solvent of the filtrate was removed under reduced pressure. The solid residue was washed with methanol and dried under vacuum prior to use.

(b) The Reaction of 3,3,7-Trimethyl-6-octenal with Diethylzinc Catalyzed by (*R*)-17a. To a Schlenk flask containing toluene (10 mL, dried with Na and degassed with N_2) were added (*R*)-**17a** (28 mg, 0.05 mmol) and diethylzinc (0.21 mL, 2 mmol) under N_2 at room temperature. After ca. 15 min, the flask was cooled to 0 °C, and 3,3,7-trimethyl-6-octenal (0.19 mL, 1 mmol) was added dropwise. After the reaction solution was stirred at this temperature for 63 h, the ^1H NMR spectrum of the crude mixture showed 79% conversion of the aldehyde. The reaction was quenched with 1 N HCl, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine until pH = 7 and then dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave a pale yellow oil, which upon treatment with MeOH precipitated the polymer. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel with EtOAc/hexanes (1:15) to afford the product as a colorless liquid (132 mg, 67%): ^1H NMR (270 MHz, $CDCl_3$) δ 0.90 (t, $J = 7.4$ Hz, 3H), 0.91 (s, 3H), 0.92 (s, 3H), 1.21−1.47 (m, $3CH_2$ and OH, 7H), 1.57 (s, 3H), 1.65 (s, 3H), 1.90 (m, 2H), 3.65 (m, 1H), 5.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.03, 17.63, 22.85, 25.78, 27.74, 32.46, 32.73, 42.89, 48.86, 70.66, 125.25, 130.98. GC showed two peaks for the two enantiomers of the product but the resolution is not good. The carbinol product was therefore converted to its acetate derivative for the determination of ee. The carbinol was dissolved in acetic anhydride (20 equiv) and triethylamine (10 equiv) was added. The resulting mixture was stirred at room temperature. The reaction was monitored by TLC. After 80 h, the reaction was complete. The volatile component was removed under reduced pressure, and the residue was subjected to column chromatography on silica gel to give the pure acetate derivative: ^1H NMR (270 MHz, $CDCl_3$) δ 0.86 (s, 6H), 0.88 (t, $J = 7.2$ Hz, 3H), 1.15−1.56 (m, 6H), 1.58 (s, 3H), 1.66 (s, 3H), 1.89 (m, 2H), 1.99 (s, 3H), 4.94 (m, 1H), 5.07 (m, 1H). GC: increasing the oven temperature from 100 to 150 °C. The retention time for the two enantiomers was 34.16 and 34.74 min, respectively.

Preparation and Characterization of (*R*)-25. Under N_2, K_2CO_3 (2.0 g, 14.5 mmol) was added to a solution of (*R*)-**13** (1.41 g, 5 mmol) and iodoethane (0.4 mL, 5 mmol) in acetone (30 mL), and the resulting mixture was heated at reflux for 5 h. After the mixture was cooled to room temperature, H_2O was added and EtOAc (2 × 50 mL) was used to extract. The combined organic layer was washed with brine and dried over Na_2SO_4. After removal of the solvent by rotary evaporation, the residue was purified with flash chromatography to give (*R*)-**25** as a white solid in 91% yield (1.43 g): mp 81.0−83.0 °C, $[\alpha]_D = -26.9$ ($c = 1.01$, CH_2Cl_2); FT-IR (KBr, cm^{-1}) 3455 (s), 3057 (w), 3000 (w), 2928 (w), 1620 (s), 1593 (s), 1508 (s), 1460 (m), 1431 (w), 1381 (s), 1329 (m), 1262 (s), 1238 (s), 1204 (s), 1175 (s), 1146 (s), 1076 (s), 1051 (s), 810 (s), 750 (s); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.11 (t, $J = 6.9$ Hz, 3H), 4.08 (m, 2H, OC*H*2), 4.99 (s, 1H, OH), 7.08 (d, $J = 8.2$ Hz, 1H), 7.19−7.40 (m, 6H), 7.45 (d, $J = 8.7$ Hz, 1H), 7.90 (m, 3H), 8.02 (d, $J = 9.2$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.96, 65.29, 115.34, 115.66, 116.41, 117.58, 123.23, 124.30, 125.06, 125.13, 126.36, 127.29, 128.16, 128.22, 129.19, 129.62, 129.77, 130.96, 133.91, 134.20, 151.34, 155.37; MS (EI) *m/z* 314 (M^+, 100), 286 ($M^+ + 1 - Et$, 38). Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.67; H, 5.66.

Preparation and Characterization of (*R*)-27. Diethylzinc (3.5 μL, 0.035 mmol) was added to a $CDCl_3$ solution (0.60 mL) of (*R*)-**25** (11.0 mg, 0.035 mmol). After the solution was shaken for 5 min, the ^1H NMR spectrum showed the quantitative formation of (*R*)-**27**: ^1H NMR ($CDCl_3$, 400 MHz) δ −0.88 (m, 2H, ZnC*H*$_2$), 0.44 (t, $J = 8.2$ Hz, 3H), 0.88 (s, ethane), 0.92 (t, $J = 6.9$ Hz, 3H), 3.94 (m, 1H), 4.02 (m, 1H), 7.02 (d, $J = 8.7$ Hz, 1H), 7.12 (d, $J = 8.7$ Hz, 1H), 7.18 (m, 3H), 7.24 (t, $J = 7.2$ Hz, 1H), 7.35 (t, $J = 7.4$ Hz, 1H), 7.39 (d, $J = 8.7$ Hz, 1H), 7.79 (d, $J = 8.7$ Hz, 1H), 7.81 (d, $J = 7.7$ Hz, 1H), 7.88 (d, $J = 8.2$ Hz, 1H), 7.98 (d, $J = 9.2$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −2.17, 6.97, 11.79, 15.00, 67.89, 118.59, 119.10, 122.53, 122.62, 123.00, 123.86, 124.86, 125.43, 125.94, 126.49, 127.12, 128.13, 128.33, 128.70, 129.58, 130.36, 134.12, 134.28, 153.33, 157.33.

Cryoscopic Molecular Weight Determination of (*R*)-27′. (*R*)-**25′** and (*R*)-**27′** were prepared because of their better solubility in cyclohexane than (*R*)-**25** and (*R*)-**27**, which is important for the molecular weight measurement. (a) Preparation of (*R*)-**25′**: (*R*)-**25′** was prepared similarly as the preparation of (*R*)-**25**; ^1H NMR ($CDCl_3$, 270 MHz) δ 0.73 (t, $J = 7.0$ Hz, 3H), 0.99 (m, 6H), 1.43 (m, 2H), 3.98 (m, 2H), 4.95 (s, 1H), 7.04 (d, $J = 8.3$ Hz, 1H), 7.16−7.39 (m, 6H), 7.45 (d, $J = 9.0$ Hz, 1H), 7.86 (m, 3H), 8.01 (d, $J = 9.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.10, 25.58, 29.31, 31.40, 69.86,-115.38, 115.75, 116.49, 117.62, 123.24, 124.32, 125.10, 125.20, 126.39, 127.35, 128.18, 128.29, 129.26, 129.63, 129.79, 130.97,134.02, 134.26, 151.43, 155.70. (b) Molecular weight measurement of (*R*)-**27′**: Diethylzinc (100 μL, 1.0 mmol) was added to a solution of (*R*)-**25′** (370 mg, 1.0 mmol) in cyclohexane (7.4 mL). After 10 min at room temperature, the produced ethane was removed by bubbling N_2 through for 5 min. The resulting solution was used for the melting point depression measurement.[29] This solution was loaded in a test tube that is equipped with a thermometer under N_2. The test tube was inserted into a saturated NaCl aqueous solution in a beaker. The beaker was then placed into an 2-propanol−dry ice bath at −15 °C. The change of temperature was recorded every 30 s. The measured frozen point is 5.0 °C. According to $\Delta T_f = k_f m$, the measured molecular weight of (*R*)-**27′** is 964 ($T_f° = 6.7$, $k_f = 20.4$). The calculated molecular weight is 926.

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