

## Development of Highly Enantioselective Polymeric Catalysts Using Rigid and Sterically Regular Chiral Polybinaphthols

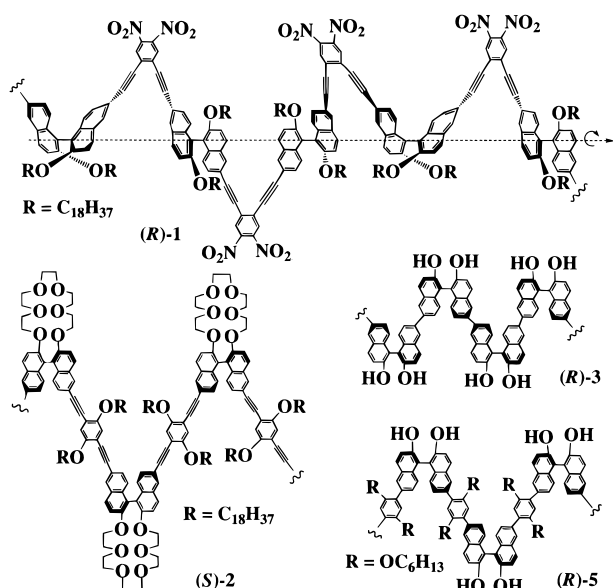
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The application of polymeric chiral catalysts in asymmetric catalysis has a number of advantages such as easy recovery of the normally quite expensive chiral catalysts, simplified product purification, and possibility to carry out flow reactor or flow membrane reactor syntheses. The traditional approach to prepare a polymeric chiral catalyst involves the development of a monomeric chiral catalyst first which is then anchored to an achiral and sterically irregular polymer backbone.<sup>1,2</sup> However, this strategy often suffers from a significant drop of enantioselectivity when a chiral metal complex is attached to a polymer support. In these polymeric chiral catalysts, their catalytic sites are randomly oriented, and the microenvironment of the catalytic centers cannot be systematically modified to achieve the desired stereoselectivity. As a result, the number of polymeric catalysts with good enantioselectivity is far less than the number of enantioselective monomeric catalysts.<sup>2</sup>

Recently, our laboratory has been working on the synthesis of binaphthyl-based chiral conjugated polymers for materials application as well as for catalysis.<sup>3–8</sup> For example, we have



discovered that the polymeric Lewis acid complex prepared from the reaction of (R)-3 with diethyl aluminum chloride shows greatly enhanced catalytic activity over the monomeric binaphthyl aluminum complex.<sup>5</sup> This polymer-based metal complex represents a new generation of polymeric chiral catalysts where the catalytic sites are highly organized in a sterically regular and inherently chiral polymer chain. Unlike the traditional polymeric chiral catalysts, these binaphthyl-based rigid chiral polymers will have a well-defined microenvironment around the catalytic centers. It is therefore possible to systematically adjust

the microenvironment of the catalytic sites in these polymers to tune both of their catalytic activity and stereoselectivity. Herein, we report the construction of a highly enantioselective polymeric catalyst by using this systematic approach.

The asymmetric reaction of aldehydes with alkylzinc complexes in the presence of either chiral amino alcohols or chiral titanium complexes has been demonstrated as a very useful method to synthesize optically active alcohols.<sup>9–11</sup> Attachment of these chiral catalysts to polymer supports has also been examined, and, in some cases, high enantioselectivity has been observed.<sup>9–11</sup> We have studied the use of the optically active polybinaphthols to carry out the asymmetric reaction of aldehydes with diethylzinc as an example to explore the potential of these new materials in asymmetric catalysis. When (R)-3 was used to catalyze the reaction of benzaldehyde with diethylzinc at room temperature, a mixture of compounds including the desired chiral alcohol, 1-phenylpropanol (4), and the side product benzyl alcohol were obtained. The ratio of 4 versus benzyl alcohol was 53:47, and the *ee* of 4 was 13%. To improve both the chemoselectivity and the stereoselectivity of this reaction, we have studied another chiral polybinaphthol (R)-5 [*M<sub>w</sub>* = 15 600 and *M<sub>n</sub>* = 8900 (PDI = 1.75)].<sup>12</sup> Unlike (R)-3 which is insoluble in common organic solvents, (R)-5 can be dissolved in methylene chloride, chloroform, and THF due to the flexible hexyloxy groups on the phenylene spacers. When (R)-5 was used to catalyze the reaction of benzaldehyde with diethylzinc, only ca. 33% conversion of benzaldehyde was observed in 20 h at room temperature. A mixture of 4 and benzyl alcohol was generated in a 71:29 ratio. The *ee* of 4 was 40%.

Both (R)-3 and (R)-5 are the major-groove polymers of 1,1'-binaphthol where the polymerization occurs at the 6,6'-positions. It has been shown that introduction of substituents to the 3,3'-positions of binaphthyl catalysts can lead to better steric control and better enantioselectivity.<sup>13</sup> To further modify the microenvironment of the metal centers in the polymer, we have carried out the Suzuki coupling of a binaphthyl monomer (R)-6<sup>14</sup> (MOM = CH<sub>2</sub>OCH<sub>3</sub>) with a diboronic acid 7<sup>15</sup> (R = OC<sub>6</sub>H<sub>13</sub>) followed by hydrolysis to prepare a minor-groove binaphthol polymer (R)-8 (Scheme 1). (R)-8 has two important features: 1. It is produced by polymerization at the minor-groove of the binaphthyl monomer, i.e., at the 3,3'-positions, and thus both phenylene spacers as well as the adjacent naphthyl units can provide steric control around the binaphthyl units. 2. The two hexyloxy groups in the *p*-phenylene linkers not only make this polymer soluble in organic solvent but also can act as ligands to bind the metal centers. (R)-8a that has a molecular weight of *M<sub>w</sub>* = 6700 and *M<sub>n</sub>* = 4600 (PDI = 1.45) is used to catalyze the

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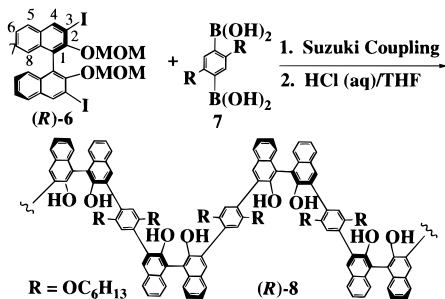
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**Scheme 1.** Preparation of the Chiral Polymer (*R*)-8**Table 1.** The Asymmetric Reaction of Aldehydes with Diethylzinc in the Presence of Chiral Catalysts

Chiral Catalyst	Aldehyde	Isolated Yield <sup>a</sup> (%)	<i>ee</i> (%) <sup>d</sup>	Product Configuration <sup>h</sup>
<i>(R)</i> -8a		89	92.2	R
		91	92.0 <sup>e</sup>	R
		70 <sup>b</sup>	84.7	R
		92 <sup>c</sup>	91.7	R
		90	92.5 <sup>e</sup>	R
		94	93.4 <sup>e</sup>	R
		84	88.3 <sup>e,f</sup>	R
		86	89.7 <sup>e,g</sup>	R
		67	82.8 <sup>e,g</sup>	[ $\alpha$ ] <sub>D</sub> = -13.25 (c = 1.95, THF)
		89	73.5 <sup>g</sup>	R
<i>(R)</i> -8b		90	92.7	R
		95	93.8	R
 (1 <i>S</i> ,2 <i>R</i> )-9 <sup>16</sup>		75	69	S
		91	82	S
 (1 <i>S</i> ,2 <i>R</i> )-10 <sup>18</sup>		95	87	S
		100	90	S

<sup>a</sup> All of the reactions using (*R*)-8 were carried out in toluene solution unless indicated otherwise. <sup>b</sup> THF was used as the solvent. <sup>c</sup> A mixed solvent (2:1 mixture of hexane/toluene) was used. <sup>d</sup> All of the *ee* values were determined by GC with a chiral column ( $\beta$ -Dex capillary column, Supelco Company) unless indicated otherwise. <sup>e</sup> The recycled polymer was used. <sup>f</sup> The *ee* was measured by HPLC-Chiracel OD column. <sup>g</sup> The *ee* was measured by analyzing the acetate derivative of the product on the GC- $\beta$ -Dex capillary column. <sup>h</sup> The absolute configurations were assigned by comparing the optical rotations with the reported data.<sup>9-11</sup>

reaction of diethylzinc with benzaldehyde. We found that in toluene solution at 0 °C, (*R*)-8a catalyzed a 100% conversion of benzaldehyde to **4** in 12 h without formation of the side product. The *ee* of **4** was 92.2%. (*R*)-8a has been used for the asymmetric reaction of different aldehydes with diethylzinc, and the results are summarized in Table 1. All of these reactions were carried out at 0 °C in the presence of 5 mol % (based on the binaphthyl unit) of (*R*)-8a. This polymer was easily recovered from the reaction mixture by simply adding methanol to precipitate. The reactions of the aromatic aldehydes were completed in 12–26 h, but the reactions of the aliphatic

aldehydes took 3–4 days. As shown in the table, excellent enantioselectivity for the para substituted benzaldehydes as well as the  $\alpha,\beta$ -unsaturated aldehyde are achieved. Good enantioselectivity is also observed for the addition to aliphatic aldehydes. This is very remarkable since most of the polymer-supported chiral amino alcohol catalysts can only give 8–65% *ee* for the reaction of aliphatic aldehydes with diethyl zinc.<sup>9a,10</sup> The best polymeric amino alcohol catalyst for aliphatic aldehydes was (1*S*,2*R*)-9 which gave 69% *ee* for the reaction of diethylzinc with nonyl aldehyde.<sup>16,17</sup> This polymer however gave much lower *ee* for benzaldehyde than other polymer-supported catalysts. The enantioselectivity of (1*S*,2*R*)-9 is also significantly reduced from that of its monomer (1*S*,2*R*)-10.<sup>18</sup>

The general procedure for the reactions catalyzed by (*R*)-8a is described in the following example. To a Schlenk flask containing toluene (10 mL, dried with Na) was added the polymer (*R*)-8a (28 mg, 0.05 mmol, based on the repeat unit) and diethylzinc (0.14 mL, 1.3 mmol) under N<sub>2</sub> at room temperature. After ca. 15 min, the flask was cooled to 0 °C, and benzaldehyde (0.1 mL, 1 mmol) was added dropwisely. After the mixture was stirred for 12 h, the <sup>1</sup>H 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. After extraction with diethyl ether, the polymer was precipitated out with methanol. The product **4** was isolated in 89% yield by column chromatography on silica gel. The *ee* was determined to be 92.2% on GC with a chiral column. The recycled polymer showed the same *ee* for the product. We have also used (*R*)-8b that was prepared under different conditions with a much higher molecular weight [ $M_w$  = 24 300 and  $M_n$  = 9900 (PDI = 2.45)] for this reaction. The observed *ee* for the reaction of benzaldehyde is 92.7% and for the reaction of *p*-chlorobenzaldehyde is 93.8%.

In summary, the first highly enantioselective polymeric catalyst based on the rigid and sterically regular chiral polymers has been developed. We have shown that the high enantioselectivity is reproducible even when the polymers prepared under different conditions and having different molecular weights are used. These polymers can be easily separated from the reaction mixture by simple precipitation, and the recycled polymer gives the same enantioselectivity as the original polymer. These excellent properties of the new polymers and their easy preparation demonstrate the great potentials of the rigid and sterically regular chiral materials in asymmetric synthesis. This study provides a new direction to design and synthesize enantioselective polymeric catalysts.

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**Supporting Information Available:** Detailed experimental procedures and characterizations involving (*R*)-5, (*R*)-8, and the use of (*R*)-8 in the catalytic reaction (4 pages). See any current masthead page for ordering and Internet access instructions.

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