

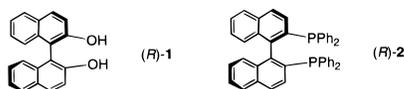
## The First Optically Active BINOL–BINAP Copolymer Catalyst: Highly Stereoselective Tandem Asymmetric Reactions

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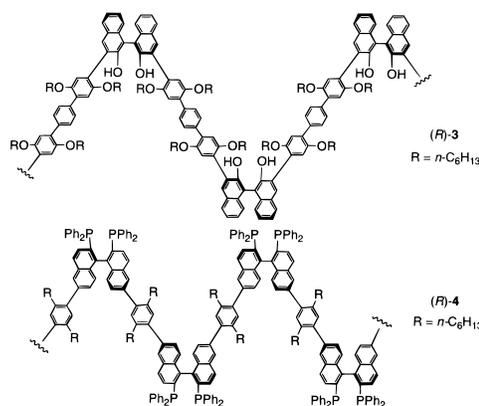
Received March 3, 2000

Optically active 1,1'-bi-2-naphthol [BINOL, (*R*)-**1**] and 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl [BINAP, (*R*)-**2**] represent two most important classes of chiral biaryl ligands and have found very extensive applications in asymmetric catalysis.<sup>1–9</sup> BINOL ligands contain hard oxygen atoms and are used to coordinate with hard metal centers such as Al(III), Ti(IV), Zn(II), and Ln(III) to generate highly enantioselective Lewis acid catalysts for many asymmetric organic transformations such as Diels–Alder reactions, Michael additions, ene reactions, and organometal additions to carbonyls.<sup>5–7</sup> BINAP ligands contain soft phosphorus atoms and are used to coordinate with soft late transition metals such as Rh and Ru to carry out asymmetric hydrogenations, olefin isomerizations and others.<sup>8,9</sup> The distinctively different coordinative ability of BINOL versus BINAP provides an excellent opportunity to design novel multifunctional catalysts for tandem asymmetric reactions by joining these two types of ligands.

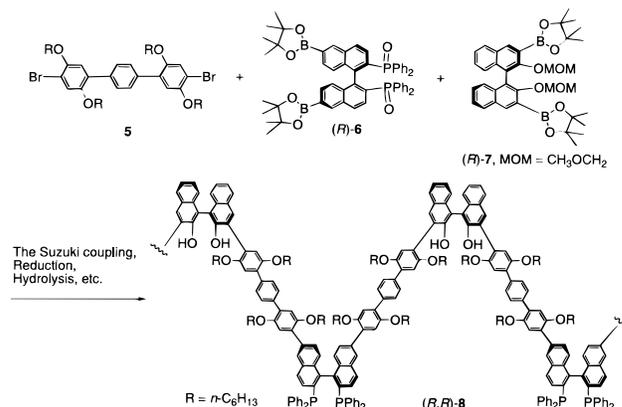


Recently, we have discovered that an optically active BINOL polymer (*R*)-**3** can catalyze highly enantioselective diethylzinc addition to a broad range of aldehydes including aryl, alkyl, and  $\alpha,\beta$ -unsaturated aldehydes.<sup>10</sup> We have also found that an optically active BINAP polymer (*R*)-**4** after treated with [RuCl<sub>2</sub>(C<sub>6</sub>H<sub>6</sub>)<sub>2</sub>] and (*R,R*)-1,2-diphenylethylenediamine (DPEN) can catalyze highly enantioselective hydrogenation of ketones.<sup>11</sup> These discoveries demonstrate that the rigid and sterically regular polybinaphthyl structure can preserve the stereoselectivity of monomer catalysts. This has encouraged us to synthesize the copolymers of BINOL and BINAP ligands for tandem asymmetric reactions. Herein, our synthesis and study of the first optically active BINOL and BINAP copolymer ligand is communicated.

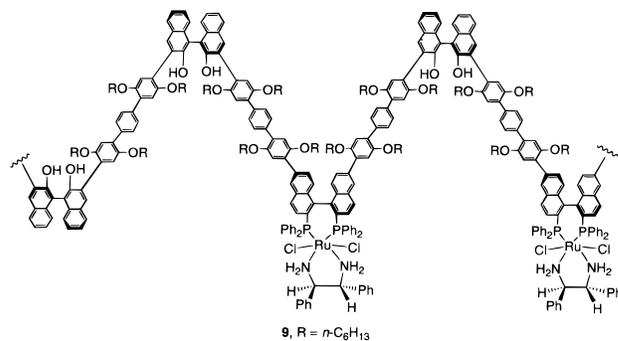
We have used a triphenylene dibromide linker molecule **5** to copolymerize with the optically active monomers (*R*)-**6** and (*R*)-**7** in a 2:1:1 ratio. After several steps including the Suzuki coupling, reduction of the phosphoryl groups and hydrolysis of the BINOL-protecting groups, a copolymer (*R,R*)-**8** was obtained (see Scheme 1 and details in the Supporting Information). In this polymer, the BINOL and BINAP units are expected to be distributed randomly along the polymer chain. This polymer is a yellow solid and can



Scheme 1. Synthesis of the First BINOL–BINAP Copolymer



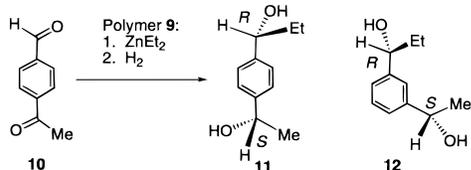
be dissolved in common organic solvents such as CH<sub>2</sub>Cl<sub>2</sub>, THF, toluene, and DMF. Its molecular weight is  $M_w = 11\,600$  and  $M_n = 7500$  (PDI = 1.55) as measured by gel permeation chromatography relative to polystyrene standards. The specific optical rotation of (*R,R*)-**8** is  $[\alpha]_D = -75$  ( $c = 0.14$ , CH<sub>2</sub>Cl<sub>2</sub>). The <sup>1</sup>H NMR spectrum of this polymer is well resolved, indicating a well-defined structure. The <sup>31</sup>P NMR spectrum of the polymer displays a predominate singlet at  $\delta = -14.77$ , consistent with the BINAP units.<sup>11</sup> Polymer (*R,R*)-**8** was then converted to a polymeric ruthenium(II) complex **9** by reacting with [RuCl<sub>2</sub>(C<sub>6</sub>H<sub>6</sub>)<sub>2</sub>] and (*R,R*)-DPEN. The <sup>31</sup>P NMR spectrum of polymer **9** shows a singlet at  $\delta 46.33$ , the same as the monomeric BINAP ruthenium complex reported by Noyori and co-workers.<sup>13</sup>



We have studied the use of the poly(BINOL–BINAP)–ruthenium complex **9** in a tandem catalytic asymmetric diethylzinc

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**Scheme 2.** Tandem Asymmetric Reaction Involving Diethylzinc Addition and Hydrogenation

**Table 1.** Tandem Asymmetric Reactions of Acetyl Benzaldehydes in the Presence of the Multifunctional Chiral Polymer Catalyst

entry	substrate	solvent		conv. (%) <sup>a</sup>	ee (%) <sup>b,c</sup>	de (%) <sup>b,d</sup>
		Et <sub>2</sub> Zn addition	H <sub>2</sub> addition			
1	<i>p</i> -acetyl benzaldehyde	toluene	<sup>i</sup> PrOH	>99%	92	86
2	<i>p</i> -acetyl benzaldehyde	toluene	toluene + <sup>i</sup> PrOH <sup>e</sup>	>99%	94	87
3 <sup>f</sup>	<i>p</i> -acetyl benzaldehyde	toluene	<sup>i</sup> PrOH	>99%	93	78
4	<i>m</i> -acetyl benzaldehyde	toluene	<sup>i</sup> PrOH	>99%	94	75

<sup>a</sup> Determined by <sup>1</sup>H NMR. <sup>b</sup> Determined by GC-chiral β-Dex 120 column after converted to the diacetate. <sup>c</sup> For the diethylzinc addition. <sup>d</sup> For the hydrogenation. <sup>e</sup> Toluene:<sup>i</sup>PrOH = 1:1. Toluene in the ZnEt<sub>2</sub> addition step is not removed. <sup>f</sup> The recovered catalyst was used.

addition and asymmetric hydrogenation of *p*-acetylbenzaldehyde (**10**)<sup>14a,b</sup> to generate chiral diol **11** (Scheme 2). The experimental results are summarized in Table 1. In the presence of 4 mol % (based on the repeating unit of the copolymer) of the BINOL–BINAP copolymer catalyst **9**, the two asymmetric reactions proceeded efficiently to generate chiral diol **11**. We found that the ee for the diethylzinc addition was 92%, and the de for the hydrogenation step was 86% (entry 1, Table 1). The configurations for the two chiral centers in **11** are assigned to be R and S as shown in Scheme 2 on the basis of the previous studies on the polymer and monomer catalysts.<sup>10–13,15</sup> The stereoselectivities of the copolymer catalyst are similar to those of the corresponding monomer catalysts when used independently.<sup>12,13,15</sup> We have also carried out the tandem asymmetric diethylzinc addition and hydrogenation of *m*-acetylbenzaldehyde<sup>14c,d</sup> using copolymer catalyst **9** and have observed good stereoselectivity for the formation of chiral diol **12** (entry 4, Table 1). The copolymer catalyst can be easily recovered by simple precipitation and filtration. The recovered copolymer showed almost the same enantioselectivity for the diethylzinc addition step and a slightly lower diastereoselectivity for the hydrogenation step (entry 3, Table 1).

A typical experimental procedure for the tandem asymmetric reactions is given here. Under nitrogen, Et<sub>2</sub>Zn (0.049 g, 0.40 mmol) was added to a toluene (2 mL) solution of polymer **9** (0.020 g, 0.0080 mmol, based on the polymer repeating unit) in a 10 mL flask. The mixture was stirred at room temperature for 15 min, and then **10** (0.030 g, 0.20 mmol) was added. The reaction mixture was stirred at 0 °C for 5 h and was quenched by addition of <sup>i</sup>PrOH (0.5 mL). After removal of the solvent under vacuum, <sup>t</sup>BuOK (0.010 g, 0.090 mmol) and <sup>i</sup>PrOH (1.5 mL) were added. The reaction flask was then placed inside a 125 mL stainless steel

pressure reactor and was degassed by two freeze–pump–thaw cycles. Hydrogen pressure (150 psi) was applied to the reactor which was stirred at room temperature for 2 d. After release of the hydrogen pressure, CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added, and the organic solution was washed with 1 N HCl (5 mL × 2) and brine (5 mL × 3). After concentration under vacuum, polymer complex **9** was recovered from the organic solution by precipitation with MeOH. Removal of the solvents from the organic solution followed by purification with column chromatography on silica gel (hexane:EtOAc = 3:1) gave **11** in 99% yield. The ee (92%) and de (86%) of the product were determined by GC-chiral column after converted to the corresponding diacetate.

In addition to the uses in the tandem asymmetric reactions, the bifunctional poly(BINOL–BINAP) catalyst can be also used as either BINOL or BINAP catalyst for individual asymmetric reactions. For example, we have used polymer **9** to catalyze the asymmetric hydrogenation of acetophenone to (*S*)-1-phenylethanol. We found that polymer **9** not only showed high enantioselectivity similar to the monomeric BINAP–Ru catalysts, but also gave high catalytic turn-overs. In the presence of polymer **9** with a BINAP unit to substrate ratio of 1:4900, the hydrogenation was completed with >99% conversion and 84% ee. The reaction was conducted under H<sub>2</sub> (175 psi) in toluene/<sup>i</sup>PrOH (1:1) in the presence of <sup>t</sup>BuOK at room temperature. Polymer **9** catalyzed the diethylzinc addition to **10** to generate (*R*)-1-(*p*-acetylphenyl)-propanol with 95% ee and complete conversion at 0 °C in 5.5 h at a BINOL unit:substrate ratio of 1:50.

In summary, the first optically active BINOL–BINAP copolymer catalyst has been designed and synthesized. This novel multifunctional polymer catalyst has shown excellent stereoselectivity in tandem asymmetric reactions involving diethylzinc addition to aldehydes and hydrogenation of ketones. It demonstrates that the rigid polybinaphthyl structure not only can preserve the catalytic properties of a monomer catalyst but can also allow distinctively different catalytic sites to function independently in the polymer chain to conduct different asymmetric reactions. The use of the copolymer catalyst rather than a mixture of monomer catalysts greatly simplifies the recovery of the catalysts as well as the purification of the products in the tandem asymmetric reaction. In addition, the rigid polymer structure prevents possible interferences between the monomer catalysts. Using copolymer catalysts is also potentially more advantageous than using polymer mixtures since it can avoid the inhomogeneity problems such as phase-separation and solubility difference associated with the use and recovery of the polymer mixtures. Besides the uses in tandem asymmetric catalysis, the distinctive catalytic functions of the BINOL and BINAP units also allows the copolymer to be used in individual reactions that require either BINOL- or BINAP-based catalysts. Therefore, the work reported here points a new direction to design chiral polymer catalysts<sup>16,17</sup> for asymmetric synthesis.

**Acknowledgment.** This research was supported by the department of chemistry at University of Virginia. We also thank the partial support of this research by the U.S. National Science Foundation (DMR-9529805) and the National Institute of Health (1R01GM58454).

**Supporting Information Available:** Detailed experimental procedures and characterizations involving all of the monomers and polymers and the GC analysis results of the chiral alcohol products (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA000778K

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