



## New soluble bifunctional polymeric chiral ligands for enantioselectively catalytic reactions

Qing-Hua Fan,<sup>a,\*</sup> Guo-Hua Liu,<sup>a</sup> Guo-Jun Deng,<sup>a</sup> Xiao-Min Chen<sup>a</sup> and Albert S. C. Chan<sup>b,\*</sup>

<sup>a</sup>LMRSS, Center for Molecular Science, Institute of Chemistry, The Chinese Academy of Sciences, Beijing 100080, PR China

<sup>b</sup>Open Laboratory of Chirotechnology and Department of Applied Biology and Chemical Technology,  
The Hong Kong Polytechnic University, Hong Kong, PR China

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**Abstract**—Two new soluble bifunctional polymeric ligands (*R,R*)-**4** and (*R,R*)-**5** have been prepared via the direct condensation reaction of (*R*)-3,3'-diformyl-1,1'-bi-2-naphthol (*R*)-**1** with (*R*)-5,5'-diamino BINAP (*R*)-**2** and with (*R*)-5,5'-diamino BINAPO (*R*)-**3**, respectively. The different types of catalytic centers, BINOL and BINAP or BINAPO, were alternatively organized in a regular chiral polymer chain. Both polymeric ligands were found to be effective in the addition of diethylzinc to benzaldehyde either in the presence or in the absence of Ti(OPr)<sub>4</sub> with different enantioselectivities. (*R,R*)-**4**/Ti(IV) catalyst, which showed similar efficiency to the parent catalyst BINOL/Ti(IV), was more enantioselective than (*R,R*)-**5**/Ti(IV). (*R,R*)-**4** was also found to be highly effective in the Ru(II)-catalyzed asymmetric hydrogenation of 2-arylacrylic acids. The results demonstrated that the use of the co-polymer catalyst rather than a mixture of monomer catalysts not only simplified the recycling of the catalyst, but also improved the enantioselectivity and/or the activity in some cases. © 2001 Elsevier Science Ltd. All rights reserved.

Bifunctional ligands and multifunctional asymmetric catalysis have been attracting much attention in recent years.<sup>1,2</sup> The joining of two different types of catalytic centers together provides some unique advantages over their mono functional counterparts. Recently, Pu and co-workers extended this approach to bifunctional polymeric catalysts.<sup>3</sup> They reported the first optically active bifunctional BINOL–BINAP copolymer catalyst, in which the two catalytically different units, BINOL and BINAP, were distributed randomly along the polymer chain. This finding was highly interesting because it not only demonstrated two different asymmetric transformations in a one-pot protocol, but also established the combination of two concepts of ‘bifunctional catalysis’ and ‘soluble polymer-supported ligand for catalysis’.<sup>4</sup> Because of the possible facilitation of and the potential positive influence of the polymer support on the rate and/or stereoselectivity of the bifunctional catalyst, the successful use of soluble bifunctional polymeric ligands for asymmetric catalysis may open a new front for active research.

The development of soluble polymer-supported chiral ligands for asymmetric catalysis combines the advantages of homogeneous and heterogeneous catalysis.<sup>5</sup> Recently, we have developed several kinds of soluble polymer or dendrimer-supported chiral ligands.<sup>6</sup> Herein, we report the synthesis and applications of two new soluble polymer-supported bifunctional chiral catalysts based on the BINOL and BINAP ligands. The key feature of this kind of bifunctional ligand is that two different types of chiral ligands, BINOL and BINAP or BINAPO, were alternatively organized in a regular chiral polymer chain, which provided an opportunity for the study of interactions between the two types of catalytic centers. Furthermore, the two chiral binaphthyl moieties were linked together with an imine bond. Recently, imine and other nitrogen-containing ligands have attracted much attention in asymmetric catalytic reactions.<sup>7</sup>

The commercially available (*R*)-BINOL and (*R*)-BINAP were chosen as model ligands for this study due to their very extensive applications in asymmetric catalysis.<sup>8,9</sup> (*R*)-3,3'-Diformyl-1,1'-bi-2-naphthol (*R*)-**1**<sup>10</sup> was synthesized and used as a monomer for this study. (*R*)-5,5'-Diamino BINAP (*R*)-**2** and its phosphine oxide, (*R*)-5,5'-Diamino BINAPO (*R*)-**3**, were used as the co-monomer. In contrast to BINAP, its phosphine oxide may be used to coordinate with a hard metal

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\* Corresponding authors. Tel.: +86-10-62554472; fax: +86-10-62559373; e-mail: fanqh@infoc3.icas.ac.cn

center to generate a Lewis acid catalyst.<sup>11</sup> Both (*R*)-**2** and (*R*)-**3** were synthesized directly from (*R*)-BINAP according to published methods.<sup>12</sup> With these monomers in hand, two optically active bifunctional polymeric ligands, BINOL–BINAP copolymer (*R,R*)-**4** and BINOL–BINAPO copolymer (*R,R*)-**5**, were prepared by direct condensation reactions using glacial acetic acid as solvent.<sup>13</sup> The synthetic routes to chiral polymer (*R,R*)-**4** and (*R,R*)-**5** are outlined in Scheme 1. Since the two types of catalytic centers were linked together at the 3,3'-positions of (*R*)-**1** and 5,5'-positions of (*R*)-**2** or (*R*)-**3** via an imine bond, alternative major groove and minor groove structures along the chiral polymer chain were expected to be formed.

Both polymer (*R,R*)-**4** and (*R,R*)-**5** can be dissolved in common organic solvents such as CH<sub>2</sub>Cl<sub>2</sub>, THF and toluene, but quantitatively precipitated upon the addition of methanol. This different solubility provided a convenient and reliable method for the characterization and recycling of these polymeric ligands. The molecular weights of (*R,R*)-**4** and (*R,R*)-**5** were *M<sub>w</sub>* = 4251 (PDI = 2.7) and 5083 (PDI = 3.7), respectively, which were measured by gel permeation chromatography relative to polystyrene standards. The specific optical rotation of (*R,R*)-**4** and (*R,R*)-**5** were found to be [ $\alpha$ ]<sub>D</sub> = -14 (*c* = 0.1, CHCl<sub>3</sub>) and [ $\alpha$ ]<sub>D</sub> = 138 (*c* = 1.0, CHCl<sub>3</sub>), respectively. The <sup>31</sup>P NMR spectra of (*R,R*)-**4** and (*R,R*)-**5** displayed singlet signals at  $\delta$  -14.2 and 30.0, respectively, which were consistent with the BINAP and BINAPO ligands. A singlet at  $\delta$  8.93 in the <sup>1</sup>H NMR spectra and a strong absorption at 1612  $\nu$ /cm<sup>-1</sup> in the IR spectra of these copolymers indicated the existence of the C=N bond.

In order to evaluate the efficiency of these soluble bifunctional polymeric chiral ligands, the enantioselective

addition of diethylzinc to benzaldehyde was chosen as a model reaction.<sup>14</sup> Our previous study showed that toluene was a suitable solvent for this type of reaction. We also found that toluene dissolved these polymeric ligands and thus used it as a solvent for this study. The preliminary results are summarized in Table 1. Both polymeric ligands were found to be active in the addition of diethylzinc to benzaldehyde **6** in the presence of Ti(OPr<sup>*i*</sup>)<sub>4</sub>, while they showed notably different enantioselectivities. The (*R,R*)-**4**/Ti(IV) catalyst was found to have similar efficiency to the parent catalyst (entries 1 and 2),<sup>15</sup> which gave 1-phenyl-2-propanol **7** in 84%

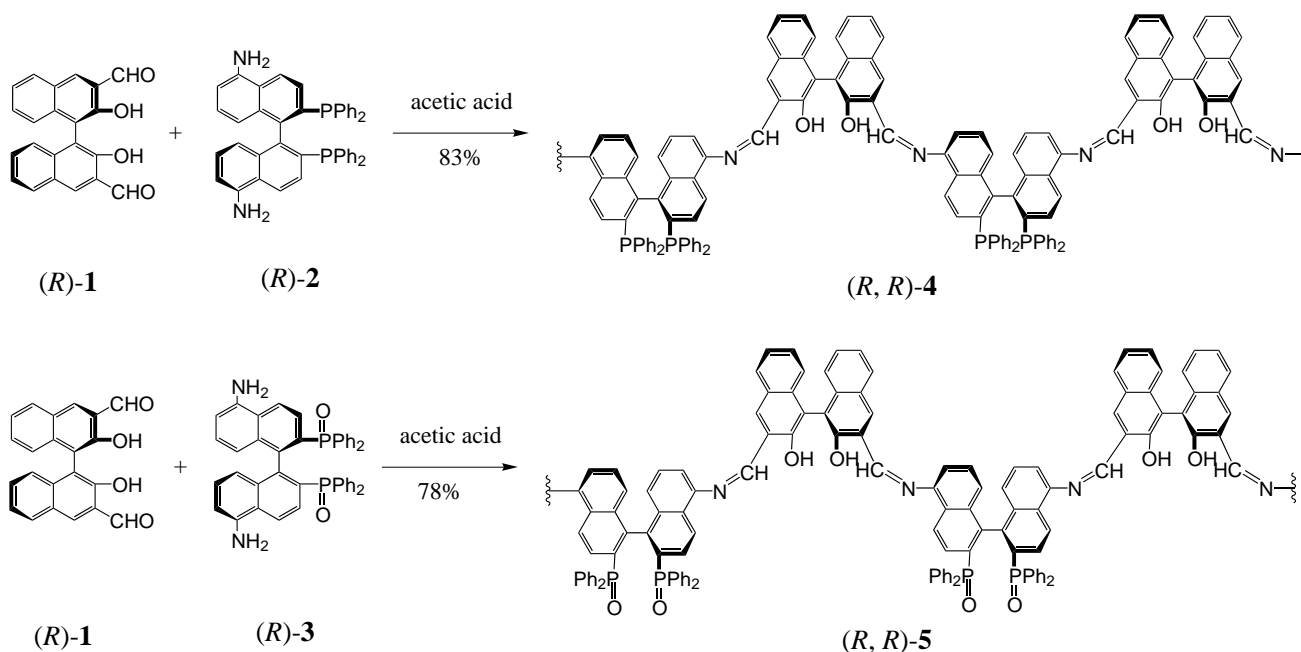
**Table 1.** Asymmetric addition of diethylzinc to **6** catalyzed by (*R*)-BINOL and the bifunctional polymeric ligands in the presence or absence of Ti(OPr<sup>*i*</sup>)<sub>4</sub><sup>a</sup>

Entry	Catalyst	E.e. (%) <sup>b</sup>	Conv. (%) <sup>b</sup>
1	( <i>R</i> )-BINOL + Ti(OPr <sup><i>i</i></sup> ) <sub>4</sub>	85	98
2	( <i>R,R</i> )- <b>4</b> + Ti(OPr <sup><i>i</i></sup> ) <sub>4</sub>	84	95
3 <sup>c</sup>	( <i>R,R</i> )- <b>4</b> + Ti(OPr <sup><i>i</i></sup> ) <sub>4</sub>	84	99
4	( <i>R,R</i> )- <b>5</b> + Ti(OPr <sup><i>i</i></sup> ) <sub>4</sub>	48	100
5	BINAPO + Ti(OPr <sup><i>i</i></sup> ) <sub>4</sub>	5	86
6	BINOL + BINAPO + Ti(OPr <sup><i>i</i></sup> ) <sub>4</sub>	14	99
7	( <i>R</i> )-BINOL	5	19
8	( <i>R,R</i> )- <b>4</b>	38	100
9	( <i>R,R</i> )- <b>5</b>	16	98

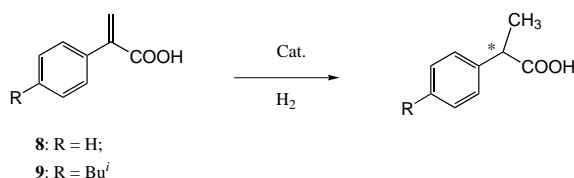
<sup>a</sup> **6**:ligand:Ti(OPr<sup>*i*</sup>)<sub>4</sub>:ZnEt<sub>2</sub> = 1.0:0.2:0.8:3 (molar ratio); reaction temperature = 0°C; solvent = toluene; reaction time = 24 h.

<sup>b</sup> Determined by chiral GLC analyses. The absolute configuration of the product is *R*.

<sup>c</sup> Recovered ligand of entry 2 was used.



**Scheme 1.** The synthesis of bifunctional BINOL–BINAP and BINOL–BINAPO copolymers.

**Table 2.** Asymmetric hydrogenation of **8** and **9** catalyzed by Ru[(*R,R*)-**4**] and Ru(BINAP)<sup>a</sup>

Entry	Ligand	Sub.	Solvent	Time (h)	Conv. (%) <sup>b</sup>	E.e. (%) <sup>b</sup>
1	( <i>R,R</i> )- <b>4</b>	8	Toluene/MeOH (1:1)	16	70	88
2	( <i>R,R</i> )- <b>4</b>	8	CH <sub>2</sub> Cl <sub>2</sub> /MeOH (1:1)	16	100	84
3	( <i>R,R</i> )- <b>4</b>	9	Toluene/MeOH (1:1)	14	76	84
4	( <i>R,R</i> )- <b>4</b>	9	CH <sub>2</sub> Cl <sub>2</sub> /MeOH (1:1)	14	58	85
5	BINAP	8	Toluene/MeOH (1:1)	18	99	92
6	BINAP	9	Toluene/MeOH (1:1)	18	100	88
7	BINAP	9	CH <sub>2</sub> Cl <sub>2</sub> /MeOH (1:1)	18	100	87

<sup>a</sup> The hydrogenation was carried out in 0.032 M of **8** and **9** under the following conditions: H<sub>2</sub> pressure = 50 atm; substrate/ruthenium (molar ratio) = 100:1; substrate/NEt<sub>3</sub> (molar ratio) = 1.5:1.

<sup>b</sup> Based on GLC analysis with a Chrompack Chirasil-dex (25 m×0.25 mm). The absolute configuration of the product is *R*.

ee (entry 2) while (*R,R*)-**5**/Ti(IV) gave the corresponding alcohol in 48% ee only (entry 4). This was probably due to the different enantioselectivity of the two types of catalytically active centers on (*R,R*)-**5**. In order to further explain this phenomenon, two control experiments were carried out under similar reaction conditions using (*R*)-BINAPO and the 1:1 (mole ratio) mixture of (*R*)-BINOL and (*R*)-BINAPO as ligands, respectively. The results showed that much lower ee's were obtained (entries 5 and 6). Most interestingly, however, enhancement of the enantioselectivity (14 to 48% ee) was achieved by organizing these two types of catalytically active units in a regular polymer chain (entries 4 and 6). We also investigated this addition reaction under the same conditions in the absence of Ti(OPr<sup>i</sup>)<sub>4</sub>. It was found that the polymeric ligands performed very differently from BINOL. Polymer (*R,R*)-**4** gave **7** in 100% conversion and 38% ee, while BINOL gave the corresponding alcohol only in 19% conversion and 5% ee (entries 7 and 8). The higher efficiency of polymer (*R,R*)-**4** might be due to the existence of the imine groups at the 3,3'-position of BINOL. Demonstration of the role of the imine groups on the catalytic reaction required further experimental evidence. Polymer (*R,R*)-**5** also showed lower enantioselectivity than polymer (*R,R*)-**4**, which was probably due to the different enantioselectivity of the catalytically active centers, BINOL and BINAPO, on the polymer chain, as described above (entries 8 and 9). An important feature of the design of soluble polymeric catalyst is the easy and reliable separation of the chiral ligand based on its different solubilities in various organic solvents. For example, upon completion of the reaction, polymer (*R,R*)-**4** was quantitatively precipitated by the addition of methanol and was recovered via filtration. The recovered ligand showed similar enantioselectivity and reactivity (entry 3).

In addition to the use in the asymmetric addition of diethylzinc to benzaldehyde, the bifunctional polymer (*R,R*)-**4** can also be used as a ligand for asymmetric hydrogenation. In order to test the asymmetric induction of (*R,R*)-**4**, we chose the asymmetric hydrogenation of 2-arylacrylic acid as a model reaction. The catalyst, which was conveniently prepared in situ from (*R,R*)-**4** and [RuCl<sub>2</sub>(cymene)]<sub>2</sub> in a methanol–toluene (3:2, v/v) mixed solvent system, was completely homogeneous. The preliminary results are summarized in Table 2. It was seen that the Ru[(*R,R*)-**4**] catalyst gave high enantioselectivity and high catalytic activity. In comparison with the parent Ru(BINAP) catalyst, only slight decreases in enantioselectivity and activity were observed.

In summary, two new soluble bifunctional polymeric ligands were prepared via the direct condensation reaction of (*R*)-3,3'-diformyl-1,1'-bi-2-naphthol (*R*)-**1** with (*R*)-5,5'-diamino BINAP (*R*)-**2** and with (*R*)-5,5'-diamino BINAPO (*R*)-**3**, respectively. The different types of catalytic centers, BINOL/BINAP or BINOL/BINAPO, were alternatively organized in a regular chiral polymer chain. Both polymer ligands were found to be active in the addition of diethylzinc to benzaldehyde in the presence or absence of Ti(OPr<sup>i</sup>)<sub>4</sub> with different enantioselectivities. The polymer (*R,R*)-**4**/Ti(IV) catalyst, which showed similar efficiency to the parent catalyst BINOL/Ti(IV), was more enantioselective than (*R,R*)-**5**/Ti(IV). (*R,R*)-**4** was also found to be effective in the Ru(II)-catalyzed asymmetric hydrogenation of 2-arylacrylic acid. The results demonstrated that the use of the copolymer catalyst rather than a mixture of monomer catalysts not only simplified the recycling of the catalyst, but also improved the enantioselectivity and/or the activity in some cases. The use of these bifunctional polymeric ligands in other transformations is in progress.

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