

Synthesis of a rigid and optically active poly(BINAP) and its application in asymmetric catalysis

Hong-Bin Yu, Qiao-Sheng Hu and Lin Pu *

Department of Chemistry, University of Virginia, Charlottesville, Virginia 22901, USA

Received 23 November 1999; accepted 3 January 2000

Abstract

The first rigid and sterically regular chiral poly[2,2'-bis(diphenylphosphino)-1,1'-binaphthyl] [poly(BINAP)] is synthesized. The application of this polymer ligand in asymmetric hydrogenations is examined. High enantioselectivity for the asymmetric hydrogenation of ketones is achieved. The catalytic properties of the poly(BINAP)-based catalysts are very similar to those of the BINAP catalysts. This study further demonstrates that rigid and sterically regular polymer structures are able to preserve the catalytic properties of monomer catalysts. © 2000 Elsevier Science Ltd. All rights reserved.

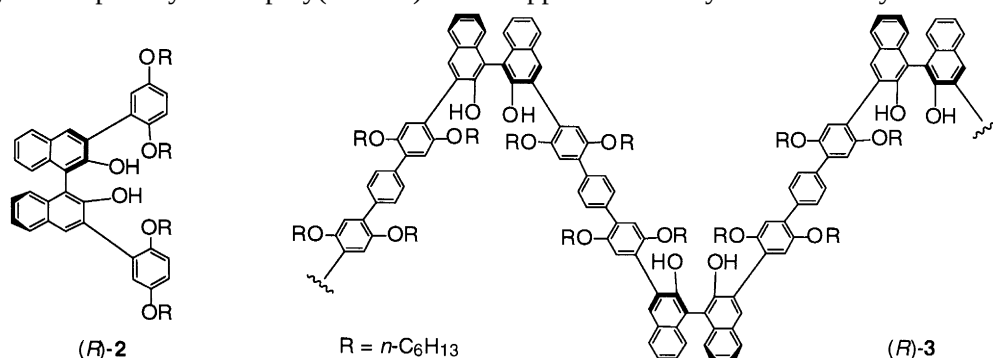
Application of chiral phosphine ligands in transition metal-catalyzed asymmetric hydrogenations has been studied extensively in the past two decades.^{1–4} This activity has led to the discovery of a number of highly enantioselective chiral phosphine-based catalysts which have been used in the pharmaceutical industry for the synthesis of chiral drug molecules. Among the successful asymmetric hydrogenation catalysts are those made of optically active 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) (*R*)- or (*S*)-**1**.^{1–3} The BINAP-based transition metal catalysts are found to catalyze the hydrogenation of compounds such as enamides and ketones with good enantioselectivity.



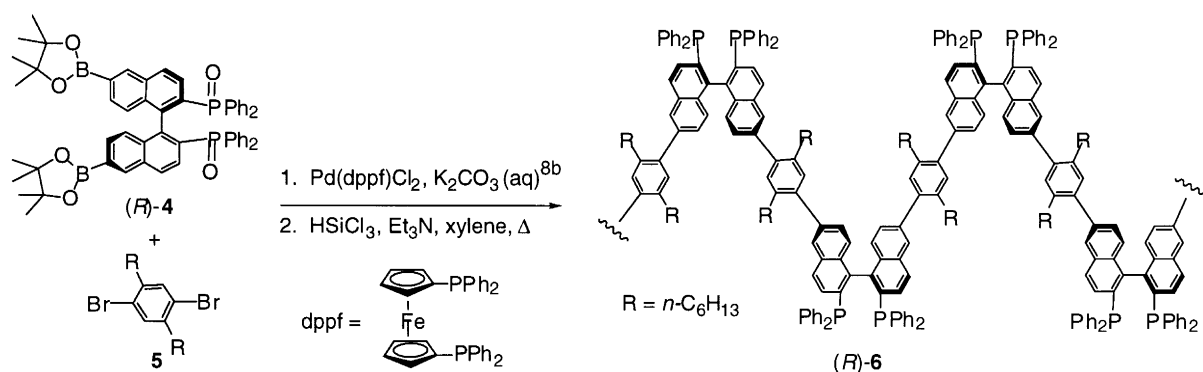
In our laboratory, we are interested in developing polymer-based chiral ligands for asymmetric catalysis because using polymers allows the easy recovery and reuse of the often quite expensive chiral ligands.⁵ We have recently demonstrated that incorporation of highly enantioselective monomer ligands into rigid and sterically regular polymer backbones can generate highly enantioselective polymeric catalysts.^{6,7} Both the steric and electronic environments of the monomer catalysts can be maintained in the rigid and sterically regular polymers. For example, we have converted a monomeric binaphthyl compound (*R*)-**2** into a polymer (*R*)-**3** and have found that both (*R*)-**2** and (*R*)-**3** are excellent catalysts

* Corresponding author. E-mail: lp6n@virginia.edu (L. Pu)

for the asymmetric reactions of organozincs with aldehydes.⁷ We have also applied the same strategy to construct an enantioselective polymeric catalyst based on the BINAP ligand. Herein, our synthesis of the novel rigid and optically active poly(BINAP) and its application in asymmetric catalysis are reported.



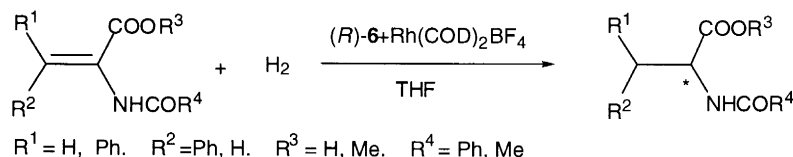
We have carried out the Suzuki coupling⁸ of a chiral binaphthyl monomer (*R*)-4⁹ with 5¹⁰ followed by reduction of the phosphinoxy groups with trichlorosilane¹¹ to prepare poly(BINAP) (*R*)-6 (Scheme 1).¹² This polymer is a yellow solid and is soluble in common organic solvents such as methylene chloride, THF, chloroform and toluene. Gel permeation chromatography analysis shows that its molecular weight is $M_w=5800$ and $M_n=4300$ (PDI=1.35) relative to polystyrene standards. The specific optical rotation of (*R*)-6 is $[\alpha]_D=36.6$ ($c=0.12$, THF). The ³¹P NMR spectrum of the polymer shows a predominate singlet at -14.8 ppm, identical to the phosphine signal of (*R*)-1 (-14.8 ppm). The ¹H NMR spectrum of this polymer is also well resolved, indicating a well-defined structure.



Scheme 1. Synthesis of a rigid and optically active poly(BINAP)

We have used (*R*)-6 to prepare a polymeric rhodium complex for the asymmetric hydrogenation of dehydroamino acid derivatives (Scheme 2).^{4,13} The catalyst was obtained in situ by treatment of (*R*)-6 with Rh(COD)₂BF₄ (COD=1,5-cyclooctadiene) in a 1.1:1 ratio in THF. The resulting catalyst suspension was tested for the hydrogenation of dehydroamino acid derivatives at room temperature. The reactions were conducted under 30 psi of hydrogen and were stopped until there was no further hydrogen uptake. The experimental results are summarized in Table 1. In the presence of this poly(BINAP) catalyst, up to 75% ee was observed for the hydrogenation of *Z*-methyl α-(benzamido) cinnamate (entry 1). This result is almost the same as the use of the rhodium complex made from the monomeric BINAP ligand (*R*)-1 (entry 2). This again demonstrates that the catalytic properties of the monomer ligand are preserved in the rigid polymer. The polymeric complex can be easily recovered by simple filtration under nitrogen

after the reaction. The recovered polymer catalyst exhibited the same enantioselectivity as the original polymer catalyst (entry 3).



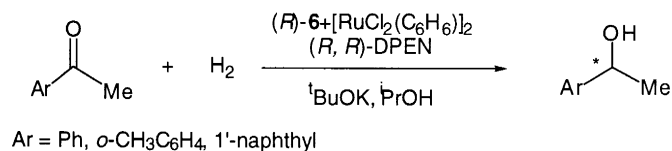
Scheme 2. Asymmetric hydrogenation of dehydroamino acid derivatives by the poly(BINAP)–Rh catalyst

Table 1
Hydrogenation of dehydroamino acid using poly(BINAP) (*R*)-**6** as the chiral ligand^a

	Substrates	Chiralligand	Conv.(%) ^b	ee (%) ^c	Conf. ^d
1	(<i>Z</i>)-methyl α -(benzamido) cinnamate	(<i>R</i>)- 6	>99	75	S
2	(<i>Z</i>)-methyl α -(benzamido) cinnamate	(<i>R</i>)- 1	>99	76	S
3	(<i>Z</i>)-methyl α -(benzamido) cinnamate	(<i>R</i>)- 6 ^g	>99	75	S
4	methyl α -(acetamido)acrylate	(<i>R</i>)- 6	>99	32	ND
5	(<i>Z</i>)- α -benzamido-cinnamic acid	(<i>R</i>)- 6	>99	59 ^e	S
6	(<i>Z</i>)- α -benzamido-cinnamic acid ^f	(<i>R</i>)- 6	>99	57 ^e	S
7	(<i>E</i>)-methyl α -(benzamido) cinnamate	(<i>R</i>)- 6	>99	40	ND

a. All the reactions were carried out at room temperature under 30 psi of H₂ in the presence of 2 mol% of Rh(COD)₂BF₄ and 2.2 mol% of (*R*)-**6** in THF. b. Determined by ¹H NMR. c. Determined by HPLC chiral OD column. d. The absolute configuration was determined by comparing the sign of the optical rotations with the literature data.¹² e. Determined by HPLC after converted to the methyl ester. f. 0.5 equiv of Et₃N was added. g. Recovered catalyst (2 mol%) was used.

We have also used poly(BINAP) (*R*)-**6** to prepare a chiral polymeric ruthenium complex for the asymmetric hydrogenation of methyl aryl ketones (Scheme 3). Recently, Noyori and co-workers reported an air-stable BINAP/diamine–Ru complex which showed high selectivity in the hydrogenation of ketones.¹⁴ Following the same procedure, a polymeric phosphine–diamine–Ru complex was prepared by treatment of (*R*)-**6** with [RuCl₂(C₆H₆)₂] in DMF followed by addition of (*R,R*)-DPEN [(*R,R*)-DPEN=(*R,R*)-1,2-diphenylethylenediamine]. The resulting catalyst showed a predominate ³¹P NMR signal at 46.3 ppm, very close to the corresponding monomeric BINAP complex (47.4 ppm).^{14b} This poly(BINAP) complex is air-stable which allows both the reaction work-up and the catalyst recovery to be conducted in air. As shown in Table 2, this polymeric catalyst exhibits very good enantioselectivity for the hydrogenation of certain ketones. The hydrogen pressure did not influence the stereoselectivity but higher hydrogen pressure accelerated the reaction. The catalyst was recovered by precipitation with methanol after work-up. The recovered polymer catalyst showed similar reactivity and selectivity to the original catalyst. The catalytic properties of this poly(BINAP)-based catalyst are also very similar to those of the monomer catalyst made from (*R*)-**1**.



Scheme 3. Asymmetric hydrogenation of ketones by a poly(BINAP)–Ru catalyst

In summary, a novel rigid and sterically regular chiral polymeric phosphine ligand has been synthesized. The catalysts based on this poly(BINAP) ligand have been used in asymmetric catalysis and have

Table 2
Asymmetric hydrogenation of ketones catalyzed by the poly(BINAP)–Ru complex^a

	Substrates	H ₂ Pressure (psi)	Time (h)	Conversion (%) ^b	ee (%) ^b
1	acetophenone	60	72	100	80
2	2'-methyl 1-acetophenone	60	100	78	91
3	2'-methyl 1-acetophenone ^c	200	24	86	90
4	2'-methyl 1-acetophenone ^c	200	44	>99	90
5	1'-acetophenone	60	96	13	nd.
6	1'-acetophenone	200	66.5	>99	92
7	1'-acetophenone ^c	200	22	33.5	87
8	1'-acetophenone ^c	200	66	>99	89

a. The reactions were carried out in 2-propanol at room temperature by using a suspension of 0.5 mol% of (*R*)-6/(*R,R*)-DPEN/Ru complex and 20 mol% of potassium *t*-butoxide. b. Determined by GC with a chiral β -Dex 120 column. c. Recovered (*R*)-6/(*R,R*)-DPEN/Ru catalyst was used.

exhibited very good enantioselectivity.¹⁵ The study of these polymer catalysts versus the monomeric BINAP catalysts demonstrates again that the catalytic properties of an enantioselective monomer catalyst can be preserved in a rigid and sterically regular polymer backbone. The use of the polymer-based materials allows the easy recovery and reuse of these catalysts.

Acknowledgements

This research was supported by the Department of Chemistry at the University of Virginia. We also thank the partial support of this research by the US National Science Foundation (DMR-9529805).

References

1. *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993.
2. Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley & Sons: New York, 1994.
3. (a) Noyori, R. *Acc. Chem. Res.* **1990**, 23, 345. (b) Noyori, R. *Tetrahedron* **1994**, 50, 4259.
4. (a) Kagan, H. B.; Dang, T.-P. *J. Am. Chem. Soc.* **1972**, 94, 642912. (b) Miyashita, A.; Yasud, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, 102, 7932. (c) Miyashita, A.; Takaya, H.; Souchi, T.; Noyori, R. *Tetrahedron* **1984**, 40, 1245. (d) Kawano, H.; Ikariya, T.; Ishii, Y.; Saburi, M.; Yoshikawa, S.; Uchida, Y.; Kumobayashi, H. *J. Chem. Soc., Perkin Trans.* **1989**, 1571. (e) Noyori, R.; Ikeda, T.; Ohkuma, T.; Widhalm, M.; Kitamura, M.; Takaya, H.; Akutagawa, S.; Sayo, N.; Saito, T.; Taketomi, T.; Kumobayashi, H. *J. Am. Chem. Soc.* **1989**, 111, 9134. (f) Burk, M. J.; Lee, J. R.; Martinez, J. P. *J. Am. Chem. Soc.* **1994**, 116, 10847. (g) Zhu, G.; Cao, P.; Jiang, Q.; Zhang, X. *J. Am. Chem. Soc.* **1997**, 119, 1799 and references cited therein.
5. Itsuno, S. In *Polymeric Materials Encyclopedia; Synthesis, Properties and Applications*; Salamone, J. C., Ed.; CRC Press: Boca Raton, FL, 1996; Vol. 10, p. 8078.
6. Pu, L. *Chem. Eur. J.* **1999**, 5, 2227.
7. (a) Hu, Q.-S.; Huang, W.-S.; Pu, L. *J. Org. Chem.* **1998**, 63, 2798. (b) Huang, W.-S.; Hu, Q.-S.; Pu, L. *J. Org. Chem.* **1999**, 64, 7940.
8. (a) Suzuki, A. *Acc. Chem. Res.* **1982**, 15, 178. (b) Giroux, A.; Han, Y.; Prasit, P. *Tetrahedron Lett.* **1997**, 38, 3841.
9. Preparation and characterization of (*R*)-**4**: To a mixture of (*R*)-6,6'-trifluoromethylsulfonyloxy-2,2'-bis(diphenylphosphinoxy)-1,1'-binaphthyl (1.650 g, 1.740 mmol, preparation to be published) and bis(pinacolato)diboron (1.770 g, 6.960 mmol) in dioxane (15 mL) was added Pd(dppf)Cl₂·CH₂Cl₂ (0.071 g, 0.087 mmol), dppf (0.048 g, 0.087 mmol) and KOAc (1.360 g, 13.920 mmol). The mixture was stirred at 85°C for 40 h and then filtered at room temperature. The solid was washed with H₂O (4×10 mL), acetone (2 mL) and EtOAc (2×5 mL) to give (*R*)-**4** as a pale grey solid 1.200 g (76%). ¹H NMR (CDCl₃, 300 MHz) δ 1.38 (s, 24H, 8 CH₃), 6.74 (d, *J*=8.7 Hz, 2H, Ar-H), 7.14–7.45 (m, 20H, Ar-H), 7.66, 7.70 (dd, *J*=8.1

- Hz, $J=12.3$ Hz, 4H, Ar-H), 7.89 (d, $J=8.1$ Hz, 2H, Ar-H), 8.34 (s, 2H, Ar-H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 24.94, 25.48, 84.07, 126.14, 127.97, 128.13, 128.30, 129.75, 130.73, 131.14, 131.37, 132.01, 132.13, 132.60, 132.73, 133.44, 133.57, 134.85, 134.99, 136.15, 142.57. ^{31}P NMR (CDCl_3 , 121 MHz, 85% phosphoric acid as the external standard) δ 28.9 (s). MS (CI) m/e 906 (M^+ , 100). Anal. calcd for $\text{C}_{56}\text{H}_{54}\text{O}_6\text{B}_2\text{P}_2$: C, 74.19; H, 6.00%. Found: C, 74.18; H, 6.76%.
10. Rehahn, M.; Schlüter, A.-D.; Feast, W. J. *Synthesis* **1988**, 386.
 11. Takaya, H.; Akutagawa, S.; Noyori, R. *Org. Synth.* **1988**, 67, 20.
 12. Preparation of polymer (*R*)-**6**: (1) Under nitrogen, to a solution of (*R*)-**4** (0.920 g, 1.020 mmol) and 2,5-dihexyl-1,4-dibromobenzene (0.404 g, 1.000 mmol) in 10 mL THF was added $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{CH}_2\text{Cl}_2$ (24 mg, 0.030 mmol) and 2 M K_2CO_3 (8 mL). The mixture was refluxed for 51 h followed by adding of 4-butyl-bromobenzene (100 μL). The resulting mixture was refluxed for another 18 h. The organic layer of the reaction mixture was separated and washed with 1N HCl (2 $\times$ 5 mL) and brine (2 $\times$ 5 mL). After concentration, methanol (20 mL) was added to precipitate out the polymer. This precipitation procedure was repeated three times to give a dark brown solid in 80.5% yield (0.720 g). (2) To a mixture of the above polymer (0.600 g, 0.670 mmol), Et_3N (7 mL) and *o*-xylene (50 mL) was added HSiCl_3 (5 mL). After the mixture was heated at reflux for 48 h under nitrogen, NaOH (30%, 30 mL) was added carefully at room temperature which was then stirred for 10 min. The resulting mixture was extracted with CH_2Cl_2 (3 $\times$ 50 mL). After filtration, methanol was then added under nitrogen to precipitate out polymer (*R*)-**6** (repeated three times) as a yellow solid in 93% yield (0.540 g).
 13. Burk, M. J.; Feaster, J. E.; Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1993**, 115, 10125.
 14. (a) Ohkuma, T.; Ooka, H.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, 117, 2675. (b) Doucet, H.; Ohkuma, T.; Murata, K.; Yokozawa, T.; Kozawa, M.; Katayama, E.; England, A. F.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed.* **1998**, 37, 1703.
 15. A chiral polymer-based BINAP catalyst was recently reported to show high enantioselectivity in asymmetric hydrogenation: Fan, Q.; Ren, C.; Yeung, C.; Hu, W.; Chan, A. S. C. *J. Am. Chem. Soc.* **1999**, 121, 7407.