

Tetrahedron: Asymmetry 11 (2000) 2449-2454

TETRAHEDRON: ASYMMETRY

# Heterogeneous asymmetric addition of diethylzinc to aromatic aldehydes catalyzed by Ti(IV)/imine bridgedpoly(R)-binaphthol

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Received 3 April 2000; accepted 10 May 2000

## Abstract

Heterogeneous asymmetric addition of diethylzinc to aldehydes catalyzed by chiral polymer catalysts has been achieved. The conjugated polymers based on a BINOL skeleton were synthesized in five steps and applied to this reaction with yield and e.e. up to 95 and 84.5%, respectively. These chiral polymers can be easily quantitatively recovered and reused without decreasing the e.e. or catalytic activity. © 2000 Elsevier Science Ltd. All rights reserved.

# 1. Introduction

The asymmetric addition of diethylzinc to aldehydes has become a useful method for the preparation of a wide variety of chiral secondary alcohols. Many types of chiral ligands were applied to this reaction.<sup>1</sup> Recently, Chan et al.<sup>2</sup> discovered that (R)- or (S)-binaphthol was an excellent chiral ligand for alkylations of aldehydes catalyzed by titanium catalysts to give alcohols with e.e. up to 95.6%.

The study of chiral polymer catalysts has attracted very extensive attention in recent years.<sup>3</sup> These catalysts have intrinsic advantages in that they can be separated from the products by simple filtration and reused without loss of catalytic activity or enantioselectivity. Several asymmetric syntheses using chiral polymer catalysts have been reported in the literature. Traditionally, chiral polymer catalysts were prepared by attaching the chiral ligand to a sterically irregular polymer backbone.<sup>4</sup> In this system, owing to the catalytic active sites being randomly oriented along the polymer chain, it was difficult to optimize the microenvironment of the catalytic center

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to obtain a highly active and stereoselective catalyst. Therefore, preparation of chiral polymers where the catalytic centers are highly organized is necessary. Pu et al.<sup>5–7</sup> have been working on the synthesis of chiral binaphthyl-based conjugated polymers using Suzuki-coupling reactions for material applications as well as for catalysis. Because of imine ligands attracting much attention in asymmetric catalytic reactions, in this paper, we report the synthesis of chiral binaphthyl polymers coupling with an imine bond<sup>8</sup> and their application in heterogeneous asymmetric addition of diethylzinc to aldehydes.

# 2. Results and discussion

The synthetic route to chiral polymers I and II is outlined in Scheme 1. Firstly, the commercially available (R)-1,1'-bi-2,2'-naphthol 1 was reacted with bromoethane to give 2. Selective bromination of 2 gave 3 in good yield. Lithiated 3 was reacted with DMF to give 4. Finally, the title chiral polymers were obtained by condensing the corresponding diamine with 5, which was obtained by deprotection of 4.



Scheme 1. Reagents and conditions: (a) bromoethane, acetone, 95%; (b)  $Br_2$ ,  $CH_2Cl_2$ , 92%; (c) *n*-BuLi, DMF, 88%; (d)  $BBr_3$ ,  $CH_2Cl_2$ , 93%; (e) diamine, THF:acetic acid = 1:4, 56%, 68%

Both I and II were the major groove polymers of 1,1'-binaphthol where the polymerization occurred at 6,6'-position. Unlike traditional polymeric chiral catalysts, their active centers were highly organized in a regular chiral polymer chain. It was possible to systematically adjust the microenvironment of the catalytic sites to tune both catalytic activity and stereoselectivity.

The effectiveness of the two chiral polymer ligands was assessed in the enantioselective addition of diethylzinc to aldehydes (Fig. 1).

Table 1 shows the results. The active catalyst was formed in situ by mixing the polymer with titanium tetraisopropoxide in  $CH_2Cl_2$ . In this reaction, the molar ratio of substrate, titanium tetraisopropoxide, polymer ligand and diethylzinc was the same as in the homogeneous reaction. The result indicated that the polymer took 15 h to form a complex with titanium. From Table 1 it



Figure 1.

can be observed that the two polymer ligands showed different catalytic activities. The Ti(IV)/polymer II catalyst was more enantioselective than Ti(IV)/polymer I, to give 1-phenyl-2-propanol in 80.0% e.e (entry 6) while the latter gave the corresponding alcohol in 63.9% e.e (entry 1). The electronic property of substituents in substrates was an important factor influencing the enantioselectivity under the homogeneous catalytic conditions. Aldehydes with electron-donating substituents such as methyl or methoxy groups gave higher e.e. values than substrates with electron-withdrawing substituents (entries 2, 3, 7 and 8). At the same time *ortho*-substituted benzaldehydes (entries 3, 4, 8 and 9). The polymer can be recovered by simple filtration and reused under the same conditions to give almost the same result, as shown in entries 11 and 12.

entry	polymer	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	conv.(%)	e.e (%)	Config.
1	I	н	н	Н	91.0 <sup>ª</sup>	63.9 <sup>d</sup>	R
2	I	Н	Н	CH <sub>3</sub>	82.1 <sup>a</sup>	80.5 <sup>d</sup>	R
3	I	н	н	Cl	78.0 <sup>a</sup>	70.8 <sup>d</sup>	R
4	I	Cl	Н	Н	94.0 <sup>a</sup>	30.9 <sup>d</sup>	R
5	I	н	OCH <sub>3</sub>	OCH <sub>3</sub>	88.4 <sup>b</sup>	81.9 <sup>e</sup>	R
6	П	н	Н	Н	92.5 ª	80.0 <sup>d</sup>	R
7	II	н	Н	CH <sub>3</sub>	83.5 <sup>a</sup>	82.1 <sup>d</sup>	R
8	II	Н	Н	Cl	85.0 <sup>a</sup>	78.1 <sup>d</sup>	R
9	II	Cl	н	Н	95.0 <sup>a</sup>	53.6 <sup>d</sup>	R
10	II	н	OCH <sub>3</sub>	OCH <sub>3</sub>	87.5 <sup>b</sup>	84.5 <sup>e</sup>	R
11 <sup>c</sup>	I	Н	Н	Н	89.5 <sup>a</sup>	63.5 <sup>d</sup>	R
12 <sup>c</sup>	II	Н	Н	Н	91.0 <sup>a</sup>	79.5 <sup>d</sup>	R

 Table 1

 Asymmetric addition of diethylzinc to aldehydes catalyzed by chiral polymer/Ti(IV) catalysts

Conditions: aldehyde : polymer :  $Ti(O-i-Pr)_4=1:0.2:1.4$ . a: determined by GC. b: calculated. c: polymer reused. d: measured by capillary GC analyses using CP-Cyclodex-236m (0.25mmx25m) chiral column. e: determined by HPLC through chiracel OB(0.46cm×25m) column.

# 3. Conclusion

In summary, two chiral heterogeneous catalysts were prepared through a practical route and used in asymmetric additions of diethylzinc to aldehydes to give alcohols in high yields and good e.e. values. These catalysts can be recovered and reused for the same reaction without reducing catalytic activities or enantioselectivities. The use of these catalysts in other transformations is in progress.

# 4. Experimental

#### 4.1. Materials

(*R*)-1,1'-Bi-2-naphthol  $[\alpha]_D^{25} = +34.4$  (*c* = 1, THF) was obtained according to the literature.<sup>9</sup> All aromatic aldehydes were purified before use. THF was distilled under N<sub>2</sub> from Na/benzophenone and DMF was distilled from CaH<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub> was redistilled before use.

### 4.2. Measurements

Melting points were obtained on a Buchi-510 melting point apparatus. IR was recorded on a Nicolet MX-1E spectrophotometer. The <sup>1</sup>H NMR was recorded on a Varian Bruker-200A spectrometer in CDCl<sub>3</sub> or DMSO with TMS as internal standard. Elemental analyses were obtained on a Carlo Erba-1106 apparatus. Optical rotations were measured with a Perkin–Elmer 341 polarimeter in a 1 cm cell. The e.e. values were determined by GC using a CP-CYDEX-236 (0.25 mm×25 m) chiral column, or by HPLC using a Chiracel OB (0.46 cm×25 m) column.

## 4.3. (R)-2,2'-Diethoxy-1,1'-binaphthyl 2

A mixture of 3.0 g of (*R*)-2,2'-dihydroxy-1,1'-binaphthyl **1** (10.5 mmol), 6.8 g of bromoethane (62.8 mmol), 5.9 g of dry potassium carbonate and a catalytic amount of NaI in 16.0 mL of dry acetone was stirred magnetically and refluxed under anhydrous conditions for two days. After cooling the reaction mixture was poured into water, extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic phases were dried over MgSO<sub>4</sub>. The solvent was removed in vacuo after filtration. The remaining oil was recrystallized from benzene/petroleum ether (60–90°C) to give 3.4 g (95.0%) of white needles. Mp: 132–134°C,  $[\alpha]_D^{10} = +82.0$  (*c*=0.2, CHCl<sub>3</sub>); MS (m/z): 343 (MH<sup>+</sup>); IR (KBr): 2955 (-CH<sub>2</sub>CH<sub>3</sub>), 1582–1610 (-Ar), 1223 (-C–O), 825 (C–O–C); <sup>1</sup>H NMR (CDCl<sub>3</sub>): 1.03 (t, 6H, -CH<sub>3</sub>), 4.05 (m, 4H, -CH<sub>2</sub>), 7.11 (d, 2H, J=8 Hz, -ArH), 7.23–7.30 (dd, 4H, J=7.8 Hz, -ArH), 7.46 (d, 2H, J=8.8 Hz, -ArH), 7.85–7.94 (m, 4H, -ArH). Anal. calcd for C<sub>24</sub>H<sub>22</sub>O<sub>2</sub>: C, 84.21; H, 6.43. Found: C, 83.98; H, 6.38.

## 4.4. (R)-6,6'-Dibromo-2,2'-diethoxy-1,1'-binaphthyl 3

A 2.0 g of (*R*)-2,2'-diethoxy-1,1'-binaphthyl **2** (5.8 mmol) was dissolved in 20 mL of CH<sub>2</sub>Cl<sub>2</sub> and stirred at 0°C. 0.66 mL of bromine (12.8 mmol) was added in one portion with stirring and a stream of nitrogen bubbling through the solution to remove the evolving HBr. The reaction mixture was stirred for 5 h while the flask was allowed to warm to rt. The yellow solution was allowed to stand overnight. 10 mL of a 10% NaHSO<sub>3</sub> solution was added with vigorous stirring to destroy excess bromine. The organic layer was separated, washed with water and dried over MgSO<sub>4</sub> and the solvent removed in vacuo after filtration. The residue was recrystallized from benzene/petroleum ether (60–90°C) to give 2.67 g (92.0%) of a white solid after washing with petroleum ether. Mp: 159–160°C,  $[\alpha]_{D}^{12} = +15.1$  (*c*=0.2, CHCl<sub>3</sub>); MS (m/z) 501 (MH<sup>+</sup>); IR (KBr): 2925 (-CH<sub>2</sub>CH<sub>3</sub>), 1518–1605 (-ArH), 1236 (-C–O), 1070 (C–Br); <sup>1</sup>H NMR (CDCl<sub>3</sub>): 1.12 (t, 6H, -CH<sub>3</sub>), 4.05 (m, 4H, -CH<sub>2</sub>), 6.98 (d, 2H, -ArH), 7.24 (dd, 4H, J=2 Hz, J=9 Hz, -ArH), 7.84 (d, 2H, J=8.6 Hz, -ArH), 7.96 (d, 2H, -ArH). Anal. calcd for C<sub>24</sub>H<sub>20</sub>Br<sub>2</sub>O<sub>2</sub>: C, 57.60; Br, 32.00. Found: C, 57.58; Br, 31.85.

#### 4.5. (R)-2,2'-Diethoxy-6,6'-dicarbaldehyde-1,1'-binaphthyl 4

A sample of 0.5 g (*R*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthyl **3** (1.0 mmol) was dissolved in 15 mL dry THF under N<sub>2</sub> atmosphere. The stirred solution was cooled to  $-78^{\circ}$ C and 11 mL ether solution of 0.4 M *n*-BuLi was added at such a rate as not to allow the temperature to exceed  $-70^{\circ}$ C. After 5 h of stirring at this temperature 0.51 mL of dry *N*,*N*-dimethylformamide (6.6 mmol) was added slowly so that the temperature remained below  $-50^{\circ}$ C. After stirring for 45 min at this temperature, the reaction mixture was poured into HCl/ice under vigorous stirring. It was allowed to reach rt overnight and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was washed twice with water and dried over MgSO<sub>4</sub> and the solvent was removed to give an oil. The oil was submitted to chromatography on silica using CH<sub>2</sub>Cl<sub>2</sub>/AcOEt as eluting agent to give a white solid 0.35 g (80.0%). Mp: 148°C,  $[\alpha]_D^{10} = -95.8$  (*c* = 0.01, CHCl<sub>3</sub>); MS (m/z): 398 (M<sup>+</sup>); IR (KBr): 2992 (-CH<sub>2</sub>CH<sub>3</sub>), 1698 (-CHO), 1215 (-C–O); <sup>1</sup>H NMR (CDCl<sub>3</sub>): 1.05 (t, 6H, -CH<sub>3</sub>), 4.11 (m, 4H, -CH<sub>2</sub>), 7.16–7.72 (m, 6H -ArH), 8.11 (d, 2H, J = 9 Hz, -ArH), 8.42 (d, 2H, -ArH), 9.94 (s, 1H, -CHO). Anal. calcd for C<sub>26</sub>H<sub>22</sub>O<sub>4</sub>: C, 78.39; H, 5.53. Found: C, 79.12; H, 5.50.

# 4.6. (R)-6,6'-Dicarbaldehyde-1,1'-bi-2-naphthol 5

The solution of 398.0 mg (*R*)-6,6'-dicarbaldehyde-2,2'-diethoxy-1,1'-binaphthyl **4** (1 mmol) in 5.0 mL CH<sub>2</sub>Cl<sub>2</sub> was added dropwise to a 1.0 M methylene chloride solution of boron tribromide at rt. The mixture was stirred overnight, treated with water for 0.5 h and the layers were separated. The aqueous layer was extracted with methylene chloride and the combined organic layes were treated with sodium sulfate, filtered and concentrated to yield a yellow solid 0.32 g (93.0%). Mp: 180°C,  $[\alpha]_D^8 = -87.6 \ (c = 0.2, C_2H_5OH)$ ; MS (m/z): 342 (M<sup>+</sup>); IR (KBr): 3369 (-OH), 1675 (-CHO); <sup>1</sup>H NMR (CDCl<sub>3</sub>): 5.27 (s, 2H, -OH), 6.86–7.74 (m, 6H, -ArH), 7.82 (d, 2H, J = 2.0 Hz, -CHO), 8.00 (d, 2H, -ArH), 10.0 (s, 2H, -CHO). Anal. calcd for C<sub>22</sub>H<sub>14</sub>O<sub>4</sub>: C, 77.19; H, 4.09. Found: C, 77.23; H, 3.95.

#### 4.7. Synthesis of chiral polymers

To a solution of 129.0 mg of (*R*)-6,6'-dicarbaldehyde-1,1'-bi-2-naphthol **5** (0.39 mmol) in 5 mL of tetrahydrofuran and 20 mL of glacial acetic acid was added a warm solution of 40.5 mg (0.39 mmol) *o*-phenylenediamine (twice recrystallized) in 10 mL of glacial acetic acid. Then the temperature was slowly raised on a water bath, the reaction mixture was stirred for 5 min, a yellow precipitate was formed, and the mixture was allowed to reach rt. The precipitate was filtered, washed with water, alcohol, tetrahydrofuran and ether and dried to give chiral polymer I 95.0 mg (56%). [ $\alpha$ ]<sup>8</sup><sub>D</sub> = -240 (*c* = 0.2, CH<sub>3</sub>OH); IR (KBr): 3360 (-OH), 1620 (-C=N), 1280, 818, 751; <sup>1</sup>H NMR (DMSO): 5.32 (s, -OH), 6.56–7.08 (m, -PhH), 7.13–7.98 (m, -ArH), 8.87 (s, -CH=N). UV-vis (CH<sub>3</sub>OH), nm: 242, 333, 420; inherent viscosity [ $\eta$ ] = 2.64.

Polymer II was prepared through the same method, the yield was 68%. IR (KBr): 3368 (-OH), 1634 (-C=N), 1465–1598 (-Ph), 816. Because of its poor solubility, other spectra were not obtained.

#### 4.8. General procedure for asymmetric addition of diethylzinc to aldehyde

The literature procedure for the asymmetric addition of diethylzinc to aldehydes was followed with modification.

Under nitrogen, a Schlenck equipped with a magnetic stirring bar was charged with polymer I (50.0 mg, 0.125 mmol, based on the repeat unit) and 0.3 mL Ti(O-*i*-Pr)<sub>4</sub> (0.875 mmol) and 5 mL CH<sub>2</sub>Cl<sub>2</sub>. The mixture was stirred at ambient temperature for 15 h, then into this solution was added 1.875 mL of 1 M solution of diethylzinc in hexane (1.875 mmol) and the mixture was stirred for another 10 min. The solution was cooled to 0°C and 0.065 mL of benzaldehyde (0.625 mmol) was added to the solution and the final mixture was allowed to stir at 0°C for 5 h. The reaction was stopped by addition of 3 mL 1.0 M hydrochloric acid and the polymer was filtrated and washed. The ethyl acetate extract was dried over MgSO<sub>4</sub> and the yield was determined by GC; the e.e. value was analyzed by CP-Cyclodex-236 m (0.25 mm×25 m) chiral column.

#### Acknowledgements

We thank Hong Kong Polytechnic University for financial support of this study.

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