Pergamon

Tetrahedron 56 (2000) 3511–3516

TETRAHEDRON

# Preparation and Application of Polymer-Grafted Ti–BINOL Complexes as Chiral Catalysts in the Enantioselective Addition of Diethylzinc to Aldehydes☆

Xiaowu Yang,[a] Wu Su,[a] Daxue Liu,[a] Hengshan Wang,[a] Jianheng Shen,[a] Chaoshan Da,[a] Rui Wang[a,*] and Albert S. C. Chan[b]

[a]*Department of Biochemistry & Molecular Biology, National Laboratory of Applied Organic Chemistry, School of Life Sciences, Lanzhou University, Lanzhou 730000, People's Republic of China*

[b]*Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, People's Republic of China*

Received 11 January 2000; revised 6 March 2000; accepted 23 March 2000

**Abstract**—Enantiomeric BINOL has been anchored to aminomethylated polystyrene resin at the 3- and 3,3′-positions of BINOL respectively. The resulting functionalized polymers **4** and **7** have been used as chiral ligands in the Ti-catalytic enantioselective addition of diethylzinc to aldehydes. Compared with the homogeneous ligands **5** and **8** in the same reaction, the polymer-supported ligands **4** and **6** gave, in some cases, higher enantioselectivity. The conformational inflexibility of the ligands was analyzed to illustrate the results. 

## Introduction

Since Merrifield[1] employed a cross-linked polystyrene resin as an anchor for peptide synthesis, the idea of using polymers as supports has found many applications in organic chemistry, such as the development of polymer-supported reagents and catalysts.[2,3] The strategy of attaching a chiral ligand onto a polymer support offers several advantages in catalytic asymmetric synthesis over the use of the homogeneous ligand. These advantages include: (1) the easy separation of the catalyst from the reaction mixture which allows very efficient recovery and reuse of the catalysts; (2) the possibility of carrying out the desired transformation in continuous mode in a flow reactor; and (3) much safer and simpler handling and processing of toxic or odorous reagents when they are attached to polymer supports. Although chiral ligands attached to insoluble polymers are useful and practical, there are still some shortcomings such as lower catalytic activity and enantioselectivity compared with those recorded for their homogeneous counterparts. Thus, continuous efforts in this area aim to narrow the gap between the homogeneous and heterogeneous catalysis approaches.

Of the many chiral reagents developed for preparing chiral ligands or catalysts in asymmetric synthesis, 1,1′-bi-2-naphthol (BINOL, **1**) has proved to be one of the most useful ligands, and has made a considerable contribution to asymmetric synthesis.[4] With the aim of incorporating the advantages of heterogeneous catalysis[5] onto BINOL, we wish to anchor BINOL to aminomethylated polystyrene resin.† The first question we face is, which position of BINOL is the best one to anchor to the polymer? It is reported that the introduction of bulky substituents to the 3,3′-positions of BINOL can lead to better steric control and consequently increase enantioselectivity,[6] and the positions are closest to the chiral catalytic center, leading to better investigation of the effect of the polymer backbone on the capability of the catalyst. We considered that the polymer body would behave as a very bulky substituent, and thus anchored BINOL to the polymer at the 3,3′-positions of BINOL. In the present paper, we report the anchoring of BINOL to the polymer and the catalytic properties of the polymer-supported BINOL in the asymmetric addition of diethylzinc to aldehydes.

## Results and Discussion

Our first effort was to attach BINOL to the aminomethylated polystyrene resin at the 3-position of BINOL to observe the

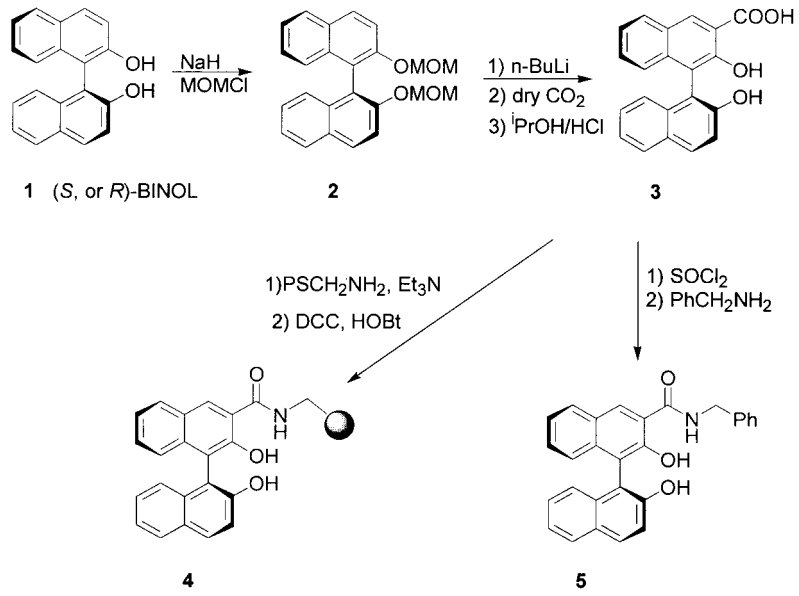
☆ The preliminary results of the research are published in *J. Org. Chem.* **2000**, *65*, 295–296.

*Keywords*: Ti-BINOL complexes; enantioselective addition; aldehydes.

* Corresponding author. Tel.: +86-931-891-2567; fax: +86-931-861-0862; e-mail: wangrui@lzu.edu.cn

† The aminomethylated polystyrene resin (poly-4-vinyl benzylamine, 1% DVB, active $-NH_2$ group: 1.0 mmol/g) with its HCl salt was purchased from Hecheng Science & Technology Development Co., Nankai University, and was treated with $Et_3N$ before use.

0040–4020/00/$ - see front matter 
PII: S0040-4020(00)00260-X




**Scheme 1.**

effect of the polymer. The linkage was carried out using commercially available enantiomeric BINOL as starting material (Scheme 1). A binaphthyl molecule **3** was prepared in two steps from BINOL by protection of hydroxyls with methoxymethyl groups[7] and then by the reaction of **2** with *n*-butyllithium followed by carboxylation to give the corresponding 3-carboxylic acid, which was hydrolyzed by treatment with hydrogen chloride in isopropyl alcohol–tetrahydrofuran (THF) to give BINOL-3-carboxylic acid **3**. The key procedure was carried out by controlling the amount of BuLi to obtain **3** bearing one carboxyl group at the 3-position of BINOL. The polymer-supported chiral ligand **4** with a polymer chain in the 3-position of BINOL was prepared by the standard procedure of solid phase peptide synthesis with solid phase peptide synthesis apparatus in the presence of DCC and 1-hydroxybenzotriazole hydrate (HOBt) and found to have a loading of 0.36 mmol/g (by mass increase). The IR spectrum (KBr) of resin-immobilized **4** revealed one new absorption at 1644 $cm^{-1}$, indicating that the desired substitution had occurred. Next, the soluble chiral ligand **5** was also synthesized easily from **3** by the reaction of the corresponding carbonyl chloride resulting from **3** and benzylamine in dichloromethane at 0°C in 46% yield.

After the synthesis of the polymer-supported chiral ligand **4**, we started a study of diethylzinc addition reaction catalyzed by a complex conveniently prepared by mixing a catalytic amount (20 mol%) of **4** with $Ti(O^iPr)_4$.[8] The catalyst was found to give moderate enantioselectivity but high chemical yields for the asymmetric addition of diethylzinc to a variety of aldehydes as indicated in Table 1. For example, it gave optically active 1-phenyl-1-propanol with 65% ee and 88% yield (run 1). When the ligand was applied to other aldehydes with the same substituents at different positions of the phenyl group, similar enantioselectivities and chemical yields were observed (runs 2–8). We also examined the catalytic ability of the homogeneous chiral ligand **5** as shown in Table 2. Compared with the results using the heterogeneous chiral ligand **4**, all the aldehydes except 3-chlorobenzaldehyde and piperonal provided higher or slightly higher enantioselectivity with **4** than its homogeneous counterpart **5**, suggesting that the polystyrene skeleton was behaving as a sufficiently bulky substituent. A 65% ee with benzaldehyde (Table 1, run 1) was achieved employing **4** compared with 61% ee for the same reaction

**Table 1.** Asymmetric addition of $Et_2Zn$ to aldehydes catalyzed by the heterogeneous catalyst **4**

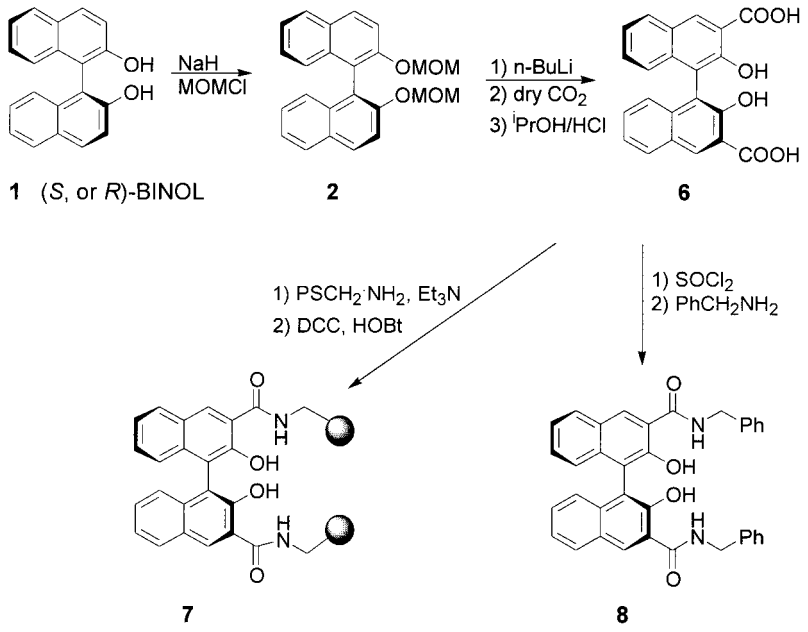
| Run | R/RCHO | Temperature (°C), Rt (h) | Yield (%)[a] | Ee (%)[b] |
|---|---|---|---|---|
| 1 | Ph | 0, 35 | 88 | 65 |
| 2 | 4-ClPh | 0, 35 | 94 | 60 |
| 3 | 3-ClPh | 0, 35 | 91 | 55 |
| 4 | 4-MeOPh | 0, 35 | 88 | 51 |
| 5 | 3-MeOPh | 0, 35 | 82 | 61 |
| 6 | 2-MeOPh | 0, 35 | 91 | 34 |
| 7 | 4-$NO_2$Ph | 0, 40 | 85 | 82 |
| 8 | 3-$NO_2$Ph | 0, 50 | 89 | 79 |
| 9 | PhCH=CH | 0, 35 | 92 | 35 |
| 10 | Piperonyl | 0, 35 | 88 | 41 |

[a] Isolated yields.
[b] Determined by HPLC with chiral OD column.

**Table 2.** Asymmetric addition of $Et_2Zn$ to aldehydes in the presence of the chiral ligand **5**

| Run | R/RCHO | Temperature (°C), Rt (h) | Yield (%)[a] | Ee (%)[b] |
|---|---|---|---|---|
| 1 | Ph | 0, 20 | 92 | 61 |
| 2 | 4-ClPh | 0, 20 | 95 | 33 |
| 3 | 3-ClPh | 0, 20 | 95 | 64 |
| 4 | 4-MeOPh | 0, 20 | 85 | 28 |
| 5 | 3-MeOPh | 0, 20 | 92 | 55 |
| 6 | 2-MeOPh | 0, 20 | 93 | 3 |
| 7 | 3-$NO_2$Ph | 0, 40 | 93 | 76 |
| 8 | PHCH=CH | 0, 20 | 90 | 32 |
| 9 | Piperonyl | 0, 20 | 95 | 67 |

[a] Isolated yields.
[b] Determined by HPLC with chiral OD column.




**Scheme 2.**

with the ligand **5** (Table 2, run 1). The gap of ee's between using **4** and **5** as chiral ligands for other aldehydes such as 4-ClPhCHO, 4-MeOPhCHO, and 2-MeOPhCHO was more obvious. For example, using **4** as a chiral ligand, 2-methoxylbenzaldehyde provided 34% ee (Table 1, run 6), the ligand **5**, however, gave an almost racemic product (Table 2, run 6).

The primary investigation showed that the heterogeneous chiral ligand **4** bearing one polymer chain promoted the enantioselective addition of diethylzinc to aldehydes, which impelled us to further improve the catalytic performance of the polymer-supported ligand. Based on the concept that $C_2$-symmetry element often serves to reduce the number of competing diastereomeric intermediates in reactions involving their use,[9] and a recent report that a $C_2$-symmetric solid-phase catalyst having two polymer chains gave higher ee than the pendant catalyst with one polymer chain in the reaction of diethylzinc with benzaldehyde,[10] our secondary effort aimed to anchor BINOL to the resin at both of the 3,3′-positions of BINOL (Scheme 2).

**Table 3.** Reaction of aldehydes with diethylzinc catalyzed by chiral polymer-supported Ti-complex of **7** (Aldehyde: $Ti(O^iPr)_4$: $Et_2Zn$: 7=1: 1.8: 4: 0.2; all the reactions were carried out at 0°C)

| Run | R/RCHO | Temperature (°C), Rt (h) | Yield (%)[a] | Ee (%)[b] |
|---|---|---|---|---|
| 1[c] | Ph | 0, 24 | 79 | 15 |
| 2[d] | Ph | 0, 24 | 90 | 31 |
| 3[e] | Ph | 0, 24 | 92 | 86 |
| 4[f] | Ph | 0, 24 | 93 | 97 (91.5) |
| 5 | 2-ClPh | 0, 25 | 92 | 91 (68.6) |
| 6 | 3-ClPh | 0, 24 | 89 | 94 (88.2) |
| 7 | 4-ClPh | 0, 30 | 88 | 92 (88.1) |
| 8 | 2-MeOPh | 0, 24 | 92 | 89 |
| 9 | 3-MeOPh | 0, 28 | 78 | 92 (94.0) |
| 10 | 4-MeOPh | 0, 48 | 90 | 83 (79.0) |
| 11 | 3-$NO_2$Ph | 0, 54 | 88 | 99 (70.0) |
| 12 | 4-$NO_2$Ph | 0, 48 | 90 | 96 |
| 13 | 4-$N(Me)_2$Ph | 0, 18 | 97 | 57 |
| 14 | 3,4-$(MeO)_2$Ph | 0, 24 | 93 | 95 |
| 15 | Piperonyl | 0, 30 | 89 | 65 |
| 16 | 1-Br-2-Nap | 0, 28 | 95 | 95 |
| 17 | (*E*)-PhCH=CH | 0, 28 | 97 | 93 |
| 18 | 2-Nap | 0, 48 | 89 | 94 |
| 19 | 2-MeO-1-Nap | 0, 24 | 87 | 99 |

[a] Isolated yields.
[b] Determined by HPLC with a Daicel Chiracel OD.
[c] 5 mol% of **7** was used.
[d] Used 10 mol% of **7**.
[e] 15 mol% of **7**.
[f] 20 mol% of **7**, the data in brackets were the results from a study using BINOL ligand. See Ref. 8.

The key procedure was achieved by controlling the amount of *n*-BuLi to obtain **6** with two carboxyl groups at the 3,3′-positions. By the same operation as ligands **4** and **5**, polymer-supported **7** and ligand **8** were prepared respectively from the diacid **6**. The presence of the expected polymeric ligand **7** bear two identical polymeric substituents, which is evidenced by the presence of –CONH– functionality at 1626 $cm^{-1}$ and the disappearance of peaks for –COOH at 1660 and 3058 $cm^{-1}$ in the FT-IR spectra (KBr).

The catalytic capability of the $C_2$-symmetric resin-supported ligand **7** was investigated in the same reaction described above. A profound solvent effect was observed in the initial study of ethylation of benzaldehyde and dichloromethane (DCM) was found to swell the polymer sufficiently and to be superior to other common organic solvents ($Et_2O$, THF, hexane, toluene, etc.). The enantioselectivity also varied significantly when different levels of ligands were used as summarized in Table 3 (runs 1–4). The optimum amount of the ligand is 20 mol%. In most cases, the Ti-**7** complex was found to be highly effective in the addition of diethylzinc to aldehydes. Interestingly, similar results were observed for the substrates with identical substituents at *ortho*-, *meta*-, or *para*- positions of the aromatic aldehydes (runs 5–12),

**Table 4.** Ethylation of aldehydes with $Et_2Zn$ in the presence of **8**

| Run | RCHO/ (R) | Temperature (°C), Time (h) | Yield (%) | Ee (%) |
|---|---|---|---|---|
| 1 | Ph | 0, 15 | 93 | 63 |
| 2 | 3-ClPh | 0, 24 | 92 | 94 |
| 3 | PhCH=CH | 0, 20 | 89 | 36 |
| 4 | Piperyl | 0, 20 | 87 | 36 |

which was also observed using chiral ligand **4** in the above reaction. The 3,4-dimethoxybenzaldehyde and the structurally similar Piperonal gave very different results (runs 14 and 15). It was reported that electronic properties had a remarkable effect on the enantioselectivity and the substituents bearing electron-withdrawing groups in the *para*-position of aryl aldehydes often afforded higher enantioselectivity than those with electron-donating groups.[11] This might explain the low enantioselectivity of the diethylzinc addition to 4-(dimethylamino)benzaldehyde (Hammett constant $\sigma_p=-0.83$ for $-N(CH_3)_2$) (run 13). Good enantioselectivity was also achieved for the α,β-unsaturated aliphatic aldehydes and naphthyl aldehydes (runs 16–19). Compared with Ti–BINOL catalyst,[8] the resin-supported ligand **7** gave higher enantioselectivity in most cases (runs 4–7, 9–11).

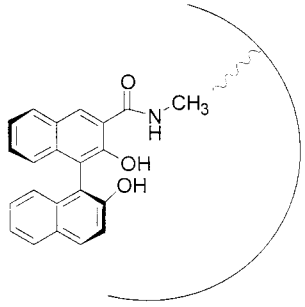
To learn more about the influence of the polymer on the enantioselectivity, we also studied the homogeneous chiral ligand **8** having $-CONHCH_2C_6H_5$ groups at the 3,3′-positions of BINOL instead of the polymer chains in the above reaction. The results are listed in Table 4. Obviously, the homogeneous ligand **8** provided much lower enantioselectivity than its polymer-supported **7**. For instance, using the heterogeneous ligand **7** for the diethylzinc addition to benzaldehyde, 97% ee was obtained (Table 3, run 4); however the homogeneous ligand **8** gave only 63% ee (Table 4, run 1). Differences in the ligand structure strongly influence the enantioselectivity of the reaction. The $C_2$-symmetric polymer-supported **7** with two polymer chains at the 3,3′-positions of BINOL gave much higher enantioselectivity (Table 3) than **4** with only one polymer chain in the asymmetric reaction of diethylzinc to aldehydes substrates (Table 1).

Recent reports suggested that increasing ligand rigidity was the key factor for the ligand to be effective in asymmetric catalytic reactions.[12] A careful comparison of the structure of the polymer-supported ligands **4** and **7** respectively with their homogeneous ligands **5** and **8** could reveal the possible reason for the difference in their catalytic effectiveness as chiral ligands in the asymmetric reaction as summarized in Fig. 1. Ligand **4** bears one polymer chain at the 3-position of BINOL, so both of the naphthyl rings are more difficult to twist due to steric hindrance from the polymer backbone than those in homogeneous **5**, resulting in the conformational inflexibility of **4**. However, since there is only one polymer chain anchored to one aromatic ring of **4**, the other aromatic ring can twist to some extent. That is to say, ligand **4** is more rigid than **5**, but the difference in conformational inflexibility is not very obvious. As a result, ligand **4** provided slightly higher enantioselectivity than **5**. In ligand **7**, with two polymer chains at the 3,3′-positions, both of the polymer chains, like two 'arms', help to lock the two naphthyl rings, greatly restricting its conformational flexibility. Compared with ligand **4** with one polymer chain and ligand **8**, both of the naphthyl rings in the chiral ligand **7** are simultaneously bound onto the polymer support and are more difficult to twist. Thus the polymer-supported ligand **7** can give the best rigidity and steric control, consequently increasing its enantioselectivity. This result was also recently observed by Kurth[10] employing a $C_2$-symmetric solid-phase catalyst in the same asymmetric addition reaction. It is important to note that although the heterogeneous ligands **4** and **7** gave slightly higher or much higher enantioselectivity than their homogeneous counterparts **5** and **8** respectively, slightly lower chemical yields and extended reaction times result because of the nature of diffusion limitation of the polymer matrix. This may be overcome by a wider investigation of the heterogeneous catalysts.

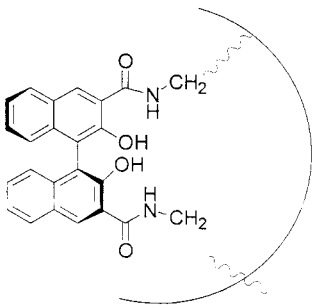
In conclusion, we have succeeded in attaching useful BINOL to the aminomethylated polystyrene resin and synthesized their homogeneous counterparts. The titanium complexes of these ligands were examined as chiral catalysts in the enantioselective addition of diethylzinc to aldehydes. In most cases, the heterogeneous chiral ligands were found to be more effective than their homogeneous counterparts.

## Experimental

All reactions were carried out under dry Ar atmosphere with dry, freshly distilled solvent unless otherwise stated and




4




7

**Figure 1.**

followed by TLC using silica gel $GF_{254}$ precoated plates with ethyl acetate and petroleum ether as eluent. Anhydrous dichloromethane (DCM) was distilled from calcium hydride. THF and $Et_2O$ were refluxed on Na prior to use. Diethylzinc was synthesized by the reaction of Zn and EtI and diluted with DCM before use. All aldehydes used were freshly distilled from $CaH_2$. Melting points (mp) were uncorrected and recorded on X-4 melting point apparatus. $^1$H NMR spectra were recorded on Bruker AM80, AM400 instruments in $CDCl_3$ with TMS as an internal standard. FT-IR spectra were recorded on a Nicolet 170SX spectrometer.

### General procedure for 3 and 6

A solution of **2**[7] (1.0 g, 2.67 mmol) in THF (10 mL) was charged with *n*-BuLi (2.4 mL, 1.11 M) in hexane at 0°C under Ar atmosphere. After stirring for 2 h at 0°C, dry $CO_2$ was carefully bubbled through, and the solution color turned red. When the reaction was complete as measured by TLC, water was introduced and the mixture was washed with $Et_2O$ (15 mL) and then acidified to pH 2 with 5% aqueous HCl. The acidic aqueous layer was extracted with ethyl acetate (3×20 mL). The combined organic phase was washed with $H_2O$, dried over $Na_2SO_4$. After removal of solvent, THF (3 mL) and saturated HCl/$^i$PrOH (10 mL) was added and stirring was continued for 2 h at room temperature. After evaporation of solvent, the residue was dissolved in ethyl acetate, which was washed with water, dried over $Na_2SO_4$, and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (PE:EE=2:1) to give (*R*)-2,2′-dihydroxy-1,1′-binaphthyl-3-carboxylic acid (**3**) as yellow solid. Yield: 56%; mp 190–191°C; $[\alpha]_D^{18}=+17.4$ (0.44, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.08–7.42 (m, 8H, Ar, ArOH), 7.87–7.98 (m, 3H, Ar), 8.81 (s, OH), 10.58 (s, 1H, COOH); IR (KBr) $\gamma$: 3329, 3056 (br), 1672, 1622, 1506, 1437, 1340, 1271, 1198, 1149, 805, 750 cm$^{-1}$. (*S*)-2,2′-dihydroxy-1,1′-binaphthyl-3,3′-dicarboxylic acid (**6**): The resulting residue was treated with $CHCl_3$ to give yellow crystalline solid collected by filtration in 68% yield; mp >290°C; $[\alpha]_D^{18}=-187$ (*c* 1.1, pyridine). Lit.,[7] (*R*)-2,2′-dihydroxy-1,1′-binaphthyl-3,3′-dicarboxylic acid: mp >290°C; $[\alpha]_D^{25}=+189$ (*c* 1.06, pyridine); $^1$H NMR ($CD_3COCD_3$, 400 MHz) $\delta$: 7.13 (m, 2H), 7.38 (m, 6H), 8.08 (m, 2H), 8.81 (s, OH), 10.99 (s, COOH); IR (KBr) $\gamma$: 3058 (br), 1659, 1625, 1503, 1454, 1338, 1277, 1206, 1151, 795, 749 cm$^{-1}$.

### General procedure for polymer-supported 4 and 7

A solid phase peptide synthesis apparatus was charged with the white aminomethylated polystyrene·HCl (2.3 g, 1.0 mmol/g) in a solution of 20% $Et_3N$ in DCM (20 mL). After stirring for 10 min, the resin was filtered under suction and washed with MeOH (1×20 mL), and then DCM (2×20 mL). A solution of **6** (0.46 g, 1.23 mmol) in DCM (5 mL) and DMF (0.2 mL) was added to the apparatus by syringe under Ar, followed by a solution of DCC (0.51 g, 2.5 mmol) and 1-hydroxybenzotriazole hydrate (HOBt, 0.31 g, 2.3 mmol) in DCM (3 mL). The mixture was again stirred for 24 h and then filtered under suction. The resulting yellow resin was washed successively with DMF (2×20 mL), MeOH (2×20 mL), and DCM (2×20 mL). A solution of acetic anhydride (5 mL) in DCM (10 mL) was added to the above apparatus and the mixture was stirred for 1 h to eliminate the 'free amino group'. After removal of the solvent, the resin was again washed with DCM (3×20 mL), and ether (3×15 mL). The yellow resin was collected and dried in vacuo for 4 h to give the desired new catalyst **7** with a loading of 0.38 mmol/g (mass increase). A sample for analysis was taken out before the washing of acetic anhydride. The sample was dried in vacuo for 12 h for elemental analysis; Found: C, 86.85, H, 6.39, N, 4.33. IR (KBr) $\gamma$: 2927, 1626, 1576, 1445, 1312, 1223, 746, 695 cm$^{-1}$. The solid phase catalyst **4**: light yellow beads, IR (KBr) $\gamma$: 2919, 1644, 1599, 1439, 1308, 1245, 741, 673 cm$^{-1}$, loading 0.36 mmol/g (mass increase).

### General procedure for 5 and 8

A solution of dicarboxylic acid **6** (0.20 g, 0.53 mmol) in thionyl chloride ($SOCl_2$, 5 mL) was refluxed for 1 h. After removal of $SOCl_2$ under reduced pressure, the resulting carbonyl chloride was dissolved in DCM (15 mL). To the mixture was added dropwise a solution of benzylamine (1.2 mL, 11 mmol) in DCM (2 mL). The reaction mixture was stirred for 0.5 h at 0°C and then was acidified to pH 2 with 5% aqueous HCl. The mixture was extracted with ethyl acetate (3×10 mL). The combined organic phase was washed with saturated brine, dried ($MgSO_4$), and concentrated to give an oil. The residue was purified by column chromatography on a silica gel to give (*S*)-*N*,*N*′-dibenzyl-2,2′-dihydroxy-1,1′-binaphthyl-3,3′-dicarboxamine (**8**) as pale yellow prisms. Yield 32%; mp 174–175°C; $[\alpha]_D^{25}=-45.5$ (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 4.59 (dd, *J*=5.1 Hz, 2H), 4.81 (dd, *J*=6.08 Hz, 2H), 7.07 (d, *J*=7.7 Hz, 2H), 7.13 (m, 2H), 7.23 (m, 2H), 7.37 (m, 10H), 7.56 (d, *J*=8.16 Hz, 2H), 8.04 (s, 1H), 12.19 (s, 1H); IR (KBr) $\gamma$: 2928, 2852, 2640, 1547, 1448, 1326, 1232, 1151, 746, 690 cm$^{-1}$. Found: C,78.05, H, 5.49, N, 5.12. Required for $C_{36}H_{28}N_2O_4$: C, 78.24, H, 5.11, N, 5.07. (*R*)-*N*-benzyl-2,2′-dihydroxy-1,1′-binaphthyl-3-carboxamine (**5**): yield 46%; mp 135–138°C; $[\alpha]_D^{20}=+24.8$ (*c* 0.7, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 4.69 (m, 2H), 7.11 (d, 1H), 7.16 (d, 1H), 7.26 (m, 1H), 7.42 (m, 10 H), 7.69 (d, 1H), 7.87 (d, 1H), 7.93 (d, 1H), 8.12 (s, 1H), 8.25 (s, 1H); IR (KBr) $\gamma$: 2859, 1645, 1580, 1209, 746, 697 cm$^{-1}$.

### General procedure for enantioselective addition of diethylzinc to aldehydes

A suspension of the polymer-supported **7** (50 mg, 0.38 mmol/g) in DCM was allowed to stir under Ar at room temperature for 12 h to swell the polymer. Ti(O$^i$Pr)$_4$ (52 μL, 0.175 mmol) was added and the mixture became red immediately. After 10 min, a solution of diethylzinc (0.38 mL of 1 M solution in DCM, 0.38 mmol) was introduced to the above reaction. The mixture was further stirred for 20 min. Benzaldehyde (10 μL, 0.1 mmol) was added dropwise at 0°C and the reaction was allowed to proceed for a period of time at the end of which the cool solution of $NH_4Cl$ was introduced to quench the reaction. The polymer was removed by filtration. The alcohol was isolated to give a colorless oil after extraction with DCM followed by column chromatography (silica gel, PE:EE=5:1), and the ee value was determined by HPLC with a Daicel chiral OD column.

## Acknowledgements

We thank the National Natural Science Foundation of China (No. 29972016), the Hong Kong Polytechnic University, Fok Ying Tung Education Foundation (Hong Kong), and the Natural Science Foundation of Gansu Province of China (No. GS992-A43-087 and No. ZS991-A23-056Y) for financial support.

## References

1. (a) Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149. (b) Merrifield, R. B. *Science* **1986**, *232*, 341.
2. (a) Hermkens, P. H. H.; Ottenheijm, H. C. J.; Rees, D. C. *Tetrahedron* **1997**, *53*, 5643. (b) Hermkens, P. H. H.; Ottenheijm, H. C. J.; Rees, D. C. *Tetrahedron* **1996**, *52*, 4527. (c) Gravert, D.; Janda, K. *Chem. Rev.* **1997**, *97*, 489. (d) Kobayashi, S. *Chem. Soc. Rev.* **1999**, *28*, 1.
3. (a) Li, T.; Janda, K. D.; Ashley, J. A.; Lerner, R. A. *Science* **1994**, *264*, 1289. (b) Vidal-Ferran, A.; Bampos, N.; Moyano, A.; Pericas, M. A.; Riera, A.; Sandera, J. K. M. *J. Org. Chem.* **1998**, *63*, 6309. (c) Seebach, D.; Marti, R. E.; Hintermann, T. *Helv. Chim. Acta.* **1996**, *79*, 1710. (d) Canali, L.; Cowan, E.; Deleuze, H.; Gibson, C. L.; Sherrington D. C. *Chem. Commun.* **1998**, 2561. (e) Altava, B.; Burguete, M. I.; Escuder, B.; Luis, S. V.; Salvador, R. V. *J. Org. Chem.* **1997**, *62*, 3126. (f) Dreisbach, C.; Wischnewski, G.; Kragl, U.; Wandrey, C. *J. Chem. Soc., Perkin. Trans. 1* **1995**, 875.
4. (a) Chan, A. S. C.; Huang, T. T.; Fan, Q. H.; Pai, C. C.; Li, Y. C. *Huaxie* **1997**, *55*, 117. (b) Pu, L. *Chem. Rev.* **1998**, *98*, 2405. (c) Kagan, H.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007. (d) Roshini, C.; Franzini, L.; Raffaelli, A.; Salladori, P. *Synthesis* **1992**, 503.
5. Bayston, D. J.; Travers, C. B.; Polywka, M. E. C. *Tetrahedron: Asymmetry* **1998**, *9*, 2015–2018.
6. (a) Huang, W. S.; Hu, Q. S.; Zhang, X. F.; Anderson, J.; Pu, L. *J. Am. Chem. Soc.* **1997**, *119*, 4313. (b) Qian, C.; Zhu, C.; Huang, T. *J. Chem. Soc., Perkin Trans. 1. 1998*, 2131. (c) Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310.
7. (a) Kitajima, H.; Ito, K.; Katsuki, T. *Chem. Lett.* **1996**, 343. (b) Kitajima, H.; Ito, K.; Aoki, Y.; Katsuki, T. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 207.
8. (a) Zhang, F. Y.; Yip, C. W.; Cao, R.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1997**, *8*, 585. (b) Zhang, F. Y.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1997**, *8*, 3651. (c) Chan, A. S. C.; Zhang, F. Y.; Yip, C. W. *J. Am. Chem. Soc.* **1997**, *119*, 4080.
9. (a) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581. (b) Whitesell, J. K. *Acc. Chem. Res.* **1985**, *18*, 280. (c) RajanBabu, T. V.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 6325.
10. Halm, C.; Kurth, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 510.
11. (a) Zhang, H.; Xue, F.; Mak, T. C. W.; Chan, K. S. *J. Org. Chem.* **1996**, *61*, 8002. (b) Yang, D.; Yip, Y. C.; Chen, J.; Cheung, K. K. *J. Am. Chem. Soc.* **1998**, *120*, 7659. (c) Corey, E. J.; Helal, C. J. *Tetrahedron: Lett.* **1995**, *36*, 9153.
12. (a) Ohta, T.; Takaya, H.; Noyori, R. *Inorg. Chem.* **1988**, *27*, 566. (b) Chan, A. S. C.; Hu, W.; Pai, C. C.; Lau, C. P.; Jiang, Y.; Mi, A.; Yan, M.; Sun, J.; Lou, R.; Deng, J. *J. Am. Chem. Soc.* **1997**, *119*, 9570. (c) Zhu, G.; Zhang, X. *J. Org. Chem.* **1998**, *63*, 3133.