# Synthesis of 6,6′- and 6-MeO–PEG–BINOL-Ca soluble polymer bound ligands and their application in asymmetric Michael and epoxidation reactions

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## Abstract

Design and synthesis of a flexible spacer attached 6-MeO–PEG–BINOL ligand has been described. The enantioenriched Ca soluble polymer bound ligand (SPB-II) was generated utilizing easily available, eco-friendly $CaCl_2$, and applied for C—C as well as C—O bond forming reactions. The ligand was precipitated adding diethylether, and the same ligand was used with equal efficiency for two more cycles.
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## 1. Introduction

In recent years, the use of polymeric supports in organic synthesis has become common practice, especially under the aspects of green chemistry as well as the rapid development of combinatorial chemistry [1]. Although the solid-phase strategy developed by Merrifield [2] on insoluble polymers appeared to solve the problem of separation and purification, it is limited because of the drawbacks such as the possibility of lower reactivity at the polymer–solvent interface and the difficulty in characterizing the polymer attached ligand. However, the uses of soluble polymers provide an alternative platform to alleviate some of the problems associated with insoluble supports. Following the first report by Bayer et al. [3] for the asymmetric hydrogenation, Janda et al. [4] developed the first soluble polymeric support for the sharpless AD reaction. Presently, a great deal of efforts has been devoted for the immobilization of homogeneous catalysts as it couples the advantages of both solution-phase as well as solid-phase chemistry [5].

The outcome of a given asymmetric transformation depends on both steric and electronic properties of the chiral ligand. 2,2′-Substituted 1,1′-binaphthyls are particularly good examples due to their highly stable configuration, and are potential candidates for asymmetric catalysis [6]. Recovery and reusability of the chiral ligand not only offers economic efficacy of the process but also is imperative under the aspects of environmentally benign synthesis [7]. Many research groups have been investigating ways to immobilize chiral binaphthyl base catalysts on various supports [8]. Pu et al. developed optically active 1,1′-binaphthyl molecules to build novel, rigid and sterically regular chiral polymers [9] for various catalytic asymmetric transformations. Shibasaki et al. [10], reported a polymer supported multifunctional catalyst for the asymmetric Michael reaction. Recently Uozumi and coworkers [11] reported the immobilization of boxax binaphthyl moieties on various polymeric supports for the asymmetric Wacker-type reaction. Introduction of chirality in polymers is of great importance in order to develop highly efficient ligands for asymmetric catalysis. This can be accomplished by anchoring chiral fragments in the polymeric backbone via suitable

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functionality. As part of our research efforts to develop catalytic enantioselective Michael addition and epoxidation [12] reactions using enantioenriched calcium–BINOL complexes [13], using an eco-friendly metal, like calcium (CaCl$_2$), we were intrigued in developing a soluble polymer supported catalyst for the same. In this paper we disclose our results towards design and synthesis of novel MeO–PEG bound BINOL ligands and their application towards asymmetric catalysis.

## 2. Experimental

### 2.1.1. General

All manipulations were carried out in oven or flame dried glassware under nitrogen atmosphere using dry, freshly distilled solvents, unless otherwise stated. NMR spectra were recorded on Varian FT-200 MHz (Gemini), Bruker-300, Unity-400 and Inova-500 MHz spectrometers. Mass spectra were recorded on a VG Micromass 70-70H and Finnigan Mat 1020B Mass spectrometers. Optical rotations were measured with a HORIBA SEPA 300 polarimeter. Melting points were recorded on Buchi 535 melting point apparatus and are uncorrected.

### 2.1.2. (R)-2,2′-Bis(benzyloxy)-6,6′-dibromo-1,1′-binaphthyl-2,2′-diol, (R)-3

To a solution of **(R)-2** (20 g, 45 mmol) in DMF, K$_2$CO$_3$ (15.5 g, 112.6 mmol) and benzyl chloride (10.9 mL, 12.0 g, 94.8 mmol) were added sequentially. After stirring the reaction mixture for 18 h at 60 °C, the solvent was removed under reduced pressure and quenched with 3 M aq. HCl (300 mL). The contents were extracted with EtOAc (3 × 100 mL), dried over anhydrous Na$_2$SO$_4$ and evaporation under reduced pressure gave a brown colour residue, which upon recrystallization from THF/cyclohexane afforded **(R)-3** (22.4 g, 80%) as a white crystalline solid. mp: 98–100 °C; IR (KBr): 1580, 1225 cm$^{-1}$; $[\alpha]_D^{25} = +27.8$ (c 1, CHCl$_3$); $^1$H NMR (CDCl$_3$, 200 MHz) $\delta$ 5.05 (s, 4H), 6.94 (d, J = 7.1 Hz, 4H), 6.98 (d, J = 9.0 Hz, 2H), 7.09–7.15 (m, 6H), 7.25 (dd, J = 9.0, 2.5 Hz, 2H), 7.39 (d, J = 9.0 Hz, 2H), 7.81 (d, J = 9.0 Hz, 2H), 8.02 (s, 2H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 71.1, 116.7, 117.6, 120.3, 126.7, 127.2, 127.5, 128.3, 129.6, 129.8, 129.9, 130.4, 132.6, 137.1, 154.4; FAB–MS: 625 (M$^+$); Anal. calcd. for C$_{34}$H$_{24}$Br$_2$O$_2$: C, 65.41; H, 3.87; found: C, 65.32; H, 3.92.

### 2.1.3. (R)-2,2′-bis(benzyloxy)-1,1′-binaphthyl-6,6′-dicarboxylic acid, (R)-4

To a cooled (−78 °C) THF (100 mL) solution of *n*-BuLi (1.6 M in hexane, 25 mL, 40.05 mmol) was added a solution of **(R)-3** (10 g, 16.02 mmol) in dry THF (70 mL). After being stirred for 30 min, excess dry ice (400 g) was added and the resulted yellow solution was warmed to room temperature

in a period of 2 h. The solvent was evaporated followed by water (50 mL) addition. The crude residue was partitioned between EtOAc (200 mL) and water (300 mL). The aqueous layer was acidified with 2 M HCl, and the precipitated product was isolated by filtration and dried to give **(R)-4** (6.65 g, 75%) as a white solid. mp: 110–112 °C; IR (KBr): 3115, 2925, 2856, 1685, 1465, 1275, 805 cm$^{-1}$; $[\alpha]_D^{25} = +37.5$ (c 1, MeOH); $^1$H NMR (CDCl$_3$ + DMSO, 200 MHz) $\delta$ 5.12 (s, 4H), 6.92–7.05 (m, 4H) 7.08–7.19 (m, 8H), 7.51 (d, J = 8.5 Hz, 2H), 7.65 (s, 2H), 7.80 (d, J = 8.2 Hz, 2H), 8.11 (d, J = 8.5 Hz, 2H), 8.65 (s, 2H); FAB–MS: 555 (M$^+$ + 1); Anal. calcd. for C$_{36}$H$_{26}$O$_6$: C, 77.97; H, 4.73; found: C, 78.12; H, 4.65.

### 2.1.4. Preparation of soluble polymer bound BINOL ligand, (R)-5

**(R)-4** (1 g, 1.80 mmol) in benzene (50 mL) was added to SOCl$_2$ (0.40 mL, 0.642 g, 5.40 mmol), and the contents were refluxed at 90 °C for 2 h. The benzene layer was evaporated and the excess SOCl$_2$ was removed by repeated evaporation with (2 × 10 mL) benzene afforded acid chloride (1.10 g). The crude acid chloride was dissolved in 10 mL of CH$_2$Cl$_2$ and cooled to 0 °C. Then, a solution of MeO–PE–OH (n = 5000, 2.25 g, 0.45 mmol) in 10 mL of CH$_2$Cl$_2$ was added drop wise, followed by Et$_3$N (0.30 mL, 0.218 g, 2.16 mmol). The reaction mixture was allowed to warm up to room temperature and stirred for an additional 3 h. The organic layer was evaporated to a minimum amount and cooled, followed by addition of cold ether solution (40 mL), the required PEG-attached ligand was precipitated. The precipitate was filtered and washed with diethylether (2 × 20 mL), redissolved in CH$_2$Cl$_2$ (5 mL) and precipitated by adding cold ether (40 mL) to obtain **(R)-5** (2.4 g, 74%) as a white solid. mp: 51–52 °C; $^1$H NMR (CDCl$_3$, 200 MHz) $\delta$ 3.20–4.05 (protons of PEG), 4.48 (t, J = 2.5 Hz, 2H), 6.92–7.20 (m, 12H), 7.45 (d, J = 8.2 Hz, 2H), 7.79 (d, J = 8.2 Hz, 2H), 8.12 (d, J = 8.5 Hz, 2H), 8.63 (s, 2H).

### 2.1.5. Preparation of soluble polymer bound BINOL ligand, (R)-6

To a solution of **(R)-5** (5 g, 0.47 mmol) in a mixture of EtOAc:EtOH (1:2, 15 mL), 50 mg of Pd–C (10%) was added and stirred at room temperature under the hydrogen atmosphere for 18 h. Filter the Pd–C using celite, and the filtrate was evaporated. To the residue, add 5 mL of CH$_2$Cl$_2$ and cool to 0 °C. By slow addition of 40 mL of cold diethylether, a white precipitate forms. Filter the white precipitate, wash and dry to obtain **(R)-6** as a light brown colour solid (4.2 g, 85%); mp: 47–49 °C; $^1$H NMR (CDCl$_3$, 200 M Hz) $\delta$ 3.20–4.00 (protons of PEG), 4.50 (t, J = 2.5 Hz, 2H), 7.02 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 7.80 (d, J = 8.2 Hz, 2H), 8.12 (d, J = 8.5 Hz, 2H), 8.62 (s, 2H).

### 2.1.6. (R)-2,2′-Dimethoxy-1,1′-binaphthalene, (R)-7

To a well-stirred solution of **(R)-1** (20 g, 0.0698 mol) in anhydrous acetone (650 mL) were added anhydrous $K_2CO_3$ (28.9 g, 0.209 mol) and methyl iodide (29.7 g, 0.210 mol). The reaction mixture was heated at reflux under a calcium chloride guard tube for 18 h. After cooling, the volatiles were removed in vacuum and the residual solids dissolved in $CH_2Cl_2$ (700 mL) and $H_2O$ (600 mL). The layers were separated, and the aqueous phase was extracted with $CH_2Cl_2$ (3 × 300 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, and the solvent was removed under reduced pressure to leave a pale yellow solid. The solid was washed with MeOH (3 × 50 mL) and recrystallized from toluene to afford **(R)-7** (19.3 g, 88%) as a white crystalline solid. mp: 228–230 °C; IR (KBr): 2925, 1585, 1500, 1460, 1244 and 1090 $cm^{-1}$; $[\alpha]_D^{25} = +111.5$ (c 1, toluene); $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 3.78 (s, 6H), 7.12 (d, $J = 8.0$ Hz, 2H), 7.24 (dd, $J = 9.0, 12.0$ Hz, 2H), 7.32 (t, $J = 9.0$ Hz, 2H), 7.48 (d, $J = 12.0$ Hz, 2H), 7.88 (d, $J = 8.0$ Hz, 2H), 8.00 (d, $J = 9.0$ Hz, 2H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 56.9, 114.2, 119.5, 123.2, 125.2, 126.3, 127.9, 129.8, 129.9, 134.2, 155.0; EIMS: 314 ($M^+$); Anal. calcd. for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77; found: C, 83.52; H, 5.93.

### 2.1.7. (R)-Ethyl 4-(2,2′-dimethoxy-1,1′-binaphth-6-yl)-4-oxobutanoate, (R)-8

To a cooled (0 °C) solution of **(R)-7** (10 g, 0.032 mol) in $CH_2Cl_2$ (250 mL) under argon was added solid $AlCl_3$ (4.65 g, 0.035 mol). The red colored solution was stirred for 10 min, and to this ethyl succinyl chloride (5.76 g, 0.035 mol) was added dropwise. The resulting brown solution was warmed to room temperature, stirred for 18 h, and the contents were poured carefully onto $H_2O$ (300 mL). The layers were separated and the aqueous phase was extracted with $CH_2Cl_2$ (2 × 125 mL). The combined organic fractions were dried over anhydrous $Na_2SO_4$, and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography (hexane/EtOAc; 8:2) to yield **(R)-8** (8.45 g, 60%) as a white solid. mp: 123–125 °C; IR (KBr): 2935, 1725, 1689, 1480, 1240, 1150 $cm^{-1}$; $[\alpha]_D^{25} = +85.6$ (c 1, toluene); $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 1.26 (t, $J = 7.0$ Hz, 3H), 2.80 (t, $J = 8.0$ Hz, 2H), 3.40 (t, $J = 8.0$ Hz, 2H), 3.75 (s, 3H), 3.79 (s, 3H), 4.18 (q, $J = 7.0$ Hz, 2H), 7.11 (d, $J = 9.0$ Hz, 1H), 7.20 (d, $J = 9.0$ Hz, 1H), 7.24 (t, $J = 9.0$ Hz, 1H), 7.32 (t, $J = 9.0$ Hz, 1H), 7.48 (d, $J = 9.0$ Hz, 1H), 7.51 (d, $J = 9.0$ Hz, 1H), 7.80 (d, $J = 9.0$ Hz, 1H), 7.88 (d, $J = 9.0$ Hz, 1H), 8.00 (d, $J = 9.0$ Hz, 1H), 8.10 (d, $J = 9.0$ Hz, 1H), 8.55 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 14.5, 28.4, 33.6, 56.5, 56.9, 60.9, 114.0, 114.3, 118.8, 119.8, 123.8, 124.1, 125.0, 125.8, 126.5, 128.1, 128.2, 129.3, 130.0, 130.2, 131.6, 131.9, 134.0, 136.8, 155.3, 157.7, 173.2, 197.7; FAB–MS: 443 ($M^+ + 1$); Anal. calcd. for $C_{28}H_{26}O_5$: C, 76.00; H, 5.92; found: C, 75.89; H, 5.84.

### 2.1.8. (R)-Ethyl 4-(2,2′-dimethoxy-1,1′-binaphth-6-yl) butanoate, (R)-9

A round-bottomed flask containing ketone **(R)-8** (5 g, 0.0113 mol), Pd on carbon (0.69 g), trifluoromethanesulfonic acid (1.305 g, 0.0136 mol), acetic acid (2.5 mL), EtOH (85 mL) was thoroughly purged with argon and then hydrogen. The reaction mixture was stirred under an atmosphere of hydrogen for 18 h, and the contents were filtered through celite. Evaporation of the solvent was done under reduced pressure to obtain a brown color residue. The residue was dissolved in EtOAc (100 mL), and treated with saturated aqueous $NaHCO_3$ (100 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried over anhydrous $Na_2SO_4$ and the volatiles were removed in vacuo. The crude product was purified by flash column chromatography (hexane/EtOAc, 7:3) afforded **(R)-9** (3.48 g, 72%) as clear viscous oil that solidified upon standing for 3–4 days. mp: 121–122 °C; IR (KBr): 2935, 1720, 1595, 1469, 1245, 1140 $cm^{-1}$; $[\alpha]_D^{25} = +67.2$ (c 1, toluene); $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 1.23 (t, $J = 7.0$ Hz, 3H), 1.95–2.05 (m, 2H), 2.31 (t, $J = 8.0$ Hz, 2H), 2.73 (t, $J = 8.0$ Hz, 2H), 3.74 (s, 3H), 3.78 (s, 3H), 4.10 (q, $J = 7.0$ Hz, 2H), 6.98–7.03 (m, 2H), 7.07 (d, $J = 9.0$ Hz, 1H), 7.14–7.20 (m, 1H), 7.28 (t, $J = 9.0$ Hz, 1H), 7.38–7.42 (m, 2H), 7.59 (s, 1H), 7.79–7.94 (m, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 14.3, 26.4, 33.8, 35.0, 56.8, 56.9, 60.9, 114.2, 114.4, 119.0, 119.7, 125.2, 125.3, 125.4, 125.9, 126.1, 126.5, 127.0, 128.1, 128.8, 128.9, 129.1, 132.8, 134.5, 136.4, 154.7, 155.0, 173.2; FAB–MS: 429 ($M^+ + 1$); Anal. calcd. for $C_{28}H_{28}O_4$: C, 78.48; H, 6.59; found: C, 78.60; H, 6.60.

### 2.1.9. (R)-Ethyl 4-(2,2′-dihydroxy-1,1′-binaphth-6-yl) butanoate, (R)-10

At −78 °C, to a solution of **(R)-9** (1 g, 2.33 mmol) in dry $CH_2Cl_2$ was added dropwise a 1.0 M $CH_2Cl_2$ solution of $BBr_3$ (5.1 mL, 5.10 mmol). The mixture was warmed to room temperature over a period of 2 h. After stirring for an additional 2 h at ambient temperature the reaction mixture was treated with saturated aqueous $NaHCO_3$ (50 mL). The two layers were separated and the aqueous phase was extracted with $CH_2Cl_2$ (3 × 25 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$ and the volatile materials were removed under vacuo. The crude product was purified by silica gel column chromatography (hexane/acetone; 9:1) to yield **(R)-10** (0.72 g, 78%) as a white solid. mp: 138–140 °C; IR (KBr): 3330, 2935, 1725, 1595, 1245, 1140 $cm^{-1}$; $[\alpha]_D^{25} = -77.3$ (c 1, toluene); $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 1.23 (t, $J = 7.0$ Hz, 3H), 1.96–2.05 (m, 2H), 2.32 (t, $J = 8.0$ Hz, 2H), 2.73 (t, $J = 8.0$ Hz, 2H), 4.10 (q, $J = 7.0$ Hz, 2H), 5.01 (s, 1H), 5.10 (s, 1H), 6.98–7.08 (m, 3H), 7.16 (t, $J = 9.0$ Hz, 1H), 7.28 (t, $J = 9.0$ Hz, 1H), 7.35–7.42 (m, 2H), 7.59 (s, 1H), 7.79–7.94 (m, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 14.2, 26.4, 33.8, 34.9, 60.4, 111.2, 111.4, 117.8,

118.0, 124.0, 124.3, 124.4, 127.2, 127.4, 128.4, 128.8, 129.6, 130.8, 131.3, 132.2, 133.8, 137.8, 152.3, 152.8, 173.8; EIMS: 400 (M$^+$); Anal. calcd. for $C_{26}H_{24}O_4$: C, 77.98; H, 6.04; found: C, 78.20; H, 6.26.

### 2.1.10. (R)-4-(2,2′-dihydroxy-1,1′-binaphth-6-yl) butanoic acid, (R)-11

To a solution of ester **(R)-10** (1 g, 0.0025 mol) in THF (20 mL) was added 20 mL of aqueous LiOH.H$_2$O (5.25 g, 0.125 mol), and the mixture was heated at reflux for 12 h. After being cooled to room temperature, the solution was acidified to pH 3 with 2.0 M aqueous HCl and extracted with EtOAc (3 × 25 mL). The combined organic extracts were dried over anhydrous Na$_2$SO$_4$ and the solvent was removed in vacuo. The crude product was purified by column chromatography using silica gel (hexane/EtOAc, 7:3) afforded pure acid **(R)-11** (0.86 g, 92.5%) as a white solid. mp: 138–140 °C; $[\alpha]_D^{25} = -62.3$ (c 1, toluene); IR (KBr): 3055, 2930, 1711, 1413, 1285, 825 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz), δ 1.97–2.05 (m, 2H), 2.33 (t, $J = 8.0$ Hz, 2H), 2.74 (t, $J = 8.0$ Hz, 2H), 5.01 (s, 1H), 5.12 (s, 1H), 6.98–7.09 (m, 3H), 7.15 (t, $J = 9.0$ Hz, 1H), 7.23 (t, $J = 9.0$ Hz, 1H), 7.35–7.42 (m, 2H), 7.58 (s,1H), 7.79–7.94 (m, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz), δ 26.1, 33.2, 34.6, 111.1, 111.2, 117.5, 118.0, 123.8, 123.9, 124.1, 127.1, 127.8, 128.2, 128.3, 129.6, 130.6, 131.5, 132.4, 133.9, 137.8, 150.3, 150.8, 180.2; EIMS: 372 (M$^+$); Anal. calcd. for $C_{24}H_{20}O_4$: C, 77.40; H, 5.41; found: C, 78.20; H, 5.56.

### 2.1.11. Preparation of soluble polymer bound BINOL ligand, (R)-13

Thionyl chloride (0.383 g, 0.23 mL, 3.22 mmol) was added to a benzene (20 mL) solution of **(R)-11** (1 g, 2.68 mmol) and refluxed at 100 °C for 2 h. Benzene was evaporated in vacuo and high vacuum for 15 min was applied to remove the excess SOCl$_2$. The residue was dissolved in CH$_2$Cl$_2$ (3 mL), followed by addition of dichloromethane solution (5 mL) of MeO–PEG (n = 5000) (3.12 g, 0.625 mmol). The reaction mixture was cooled to 0 °C and was added to Et$_3$N (0.383 mL, 0.278 g, 2.75 mmol). The reaction mixture was allowed to warm up to room temperature and stirred further for 2 h. To this, 60 mL of cold ether solution was added to form a white precipitate. The precipitate was filtered and washed with cold ether (2 × 10 mL), and dried under vacuum to afford **(R)-13** (3.45 g, 83.5%) as white solid. mp: 56–57 °C; IR (KBr): 3300, 2900, 2350, 1675, 1110, 805 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) δ 1.98–2.08 (m, 2H), 2.37 (t, $J = 6.1$ Hz, 2H), 2.75 (t, $J = 8.32$ Hz, 2H), 3.38–3.89 (protons of PEG), 4.20 (t, $J = 4.4$ Hz, 2H), 6.98–7.08 (m, 3H), 7.18 Hz, 1H; Anal. calcd. for $(C_2H_4O)_{5000} \cdot CH_4O$ (for authentic PEG–OMe, n = 5000): C, 54.54; H, 9.09; found: C, 54.86. H, 9.04; Anal. calcd. for $(C_2H_4O)_{5000} \cdot CH_3 + C_{24}H_{19}O_4$ (for PEG–Me + BINOL, n = 5000): C, 54.58; H, 9.08; found: C, 55.09; H, 9.22.

### 2.1.12. Preparation of soluble polymer catalyst, SPB-I

To an abs. ethanol (6 mL) solution of **(R)-6** (1 g, 0.096 mmol), pot.t-butoxide (21.7 mg, 0.193 mmol) was added at room temperature under an argon atmosphere. After stirring for 1 h, ethanol was evaporated under reduced pressure and to the residue solid CaCl$_2$ (90%) (11.8 mg, 0.096 mmol) was added. Then, the solid was dried under vacuum (1 mm Hg, 15 min) followed by the addition of abs. EtOH (6 mL) resulting in the formation of white suspension, which was stirred for 5 h at ambient temperature. Subsequent evaporation of ethanol under reduced pressure gave a white solid powder. To this solid catalyst, toluene (15 mL) was added under argon atmosphere and the mixture was stirred for 12 h at ambient temperature resulted the catalyst **(R)-I**.

### 2.1.13. Procedure for the Michael addition using SPB-I

To the above cooled toluene solution of catalyst **SPB-I,** sequentially a toluene solution was added (0.5 mL) of chalcone (133.1 mg, 0.64 mmol), and dimethylmalonate (101.4 mg, 0.768 mmol) at 0 °C. The resulting reaction mixture was stirred for 12 h at the same temperature. Then, toluene was evaporated and to the residue CH$_2$Cl$_2$ (5 mL) was added and followed by cold ether solution (40 mL), resulting in a white precipitation. The precipitate was filtered, washed and dried under high vacuum for 1 h. The filtrate was evaporated and subjected to high vacuum for 30 min, which gave the pure adduct **16** (195.8 mg, 90%) as a white solid. $[\alpha]_D^{25} = +8.35$ (c 1, CHCl$_3$) (25% e.e.).

### 2.1.14. Preparation of soluble polymer catalyst, SPB-II

Abs. ethanol (6 mL) was added at room temperature under an argon atmosphere to a mixture of **(R)-13** (1 g, 0.186 mmol) and pot.t-butoxide (41.9 mg, 0.373 mmol). After stirring for 1 h, ethanol was evaporated under reduced pressure and to the residue, solid CaCl$_2$ (99%) (20.6 mg, 0.186 mmol) was added. Then, the solid was dried under vacuum (1 mmHg, 15 min) followed by the addition of abs. EtOH (6 mL) resulting in the formation of clear solution, which was stirred for 3 h at ambient temperature. Subsequent evaporation of ethanol under reduced pressure gave a white solid powder. To this solid catalyst, toluene (15 mL) was added under argon atmosphere and the mixture was stirred for 12 h at ambient temperature, which resulted the catalyst **SPB-II**.

### 2.1.15. General procedure for the Michael addition using SPB-II

To the above cooled (0 °C) toluene solution of catalyst **SPB-II**, was added a toluene solution (0.5 mL) of chalcone (257.9 mg, 1.24 mmol), followed by dimethylmalonate (196.5 mg, 1.48 mmol). After being stirred for 24 h at the same temperature, toluene evaporated and the residue was dissolved in CH$_2$Cl$_2$ (5 mL). To this, cold ether solution

(40 mL) was added and resulting white precipitate was filtered off, washed with additional cold ether and dried under high vacuum for 1 h to reuse. The filtrate was evaporated and the resulting mass subjected to high vacuum [24] for 30 min gave the pure adduct **16** as a white solid.

### 2.1.16. (S)-(+)-Methyl-3,5-diphenyl-2-methoxycarbonyl-5-oxopentanoate, **16**

Yield: 379.5 mg, 90% (white solid); mp: 77–79 °C; IR (KBr): 1730, 1682, 1235 cm$^{-1}$; $[\alpha]_D^{25}$: +10.6 (c 2, CHCl$_3$, 32% e.e.); $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 3.51 (s, 3H), 3.52 (dd, J = 5.3, 7.9 Hz, 1H), 3.61 (d, J = 5.3 Hz, 1H), 3.73 (s, 3H), 3.81 (d, J = 9.2 Hz, 1H), 4.16 (dt, J = 5.3, 9.2 Hz, 1H), 7.17–7.56 (m, 8H), 7.88–7.91 (m, 2H); $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 40.7, 42.3, 52.4, 52.7, 57.3, 125.6, 127.2, 127.9, 128.1, 128.5, 133.1, 136.8, 140.4, 168.1, 168.7, 197.5. FAB–MS: 341 (M + H). Anal. calcd. for C$_{20}$H$_{20}$O$_5$: C, 70.57; H, 5.92; found: C, 70.48; H, 6.00.

### 2.1.17. (R)-(+)-3-[Bis(methoxycarbonyl)methyl]cyclopentanone, **18**

Yield: 243 mg, 92% (colourless oil); $[\alpha]_D^{25}$: +16.5 (c 5, CHCl$_3$, 44% e.e.); IR (CCl$_4$): 1775, 1730 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 1.59–1.69 (m, 1H), 1.95–2.00 (m, 1H), 2.18–2.34 (m, 3H), 2.45 (dd, J = 7.55, 18.0 Hz, 1H), 2.75–2.90 (m, 1H), 3.32 (d, J = 9.06 Hz, 1H), 3.74 (s, 3H), 3.76 (s, 3H); EIMS: 214 (M$^+$); Anal. calcd. for C$_{10}$H$_{14}$O$_5$: C, 56.07; H, 6.59; found: C, 55.98; H, 6.61.

### 2.1.18. (R)-(+)-3-[Bis(ethoxycarbonyl)methyl]cyclopentanone, **19**

Yield: 326.5 mg, 91% (colourless oil); $[\alpha]_D^{25}$: +14.5 (c 5, CHCl$_3$, 42% e.e.); IR (CCl$_4$): 1774, 1734 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 1.20 (t, J = 7.32 Hz, 3H), 1.21 (t, J = 7.32 Hz, 3H), 1.58–1.66 (m, 1H), 1.93–2.00 (m, 1H), 2.10–2.31 (m, 3H), 2.45 (dd, J = 7.82, 18.5 Hz, 1H), 2.75–2.86 (m, 1H), 3.27 (d, J = 9.28 Hz, 1H), 4.12–4.19 (m, 4H); $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 13.93, 27.34, 36.18, 38.06, 42.77, 56.38, 61.47, 61.57, 167.95, 168.04, 217.11; EIMS: 242 (M$^+$); Anal. calcd. for C$_{12}$H$_{18}$O$_5$: C, 59.49; H, 7.49; found: C, 59.28; H, 7.52.

### 2.1.19. General procedure for the epoxidation using SPB-II

To the toluene solution of catalyst SPB-II, 4A MS powder (750 mg, activated at 260–280 °C/10 mm Hg, 3 h) was added, following the cooling of the reaction mixture to 0 °C was added TBHP (0.84 mL, 2.79 mmol, 3.32 M solution in toluene). After 15 min, a toluene solution of chalcone 14 (386.8 mg, 1.86 mmol) 1 mL was added and the reaction mixture was maintained at 0 °C. After being stirred for 24 h, the contents were treated with minimum amount of satu-

rated NH$_4$Cl solution (2 mL) and filtered. The aqueous phase was separated and the toluene layer was evaporated under reduced pressure to obtain a viscous gel. This was redissolved in CH$_2$Cl$_2$ (5 mL) and precipitated by adding cold ether solution (40 mL). The precipitate was filtered off, washed with cold ether and dried under high vacuum for 1 h to reuse. The filtrate was treated with the saturated NaHSO$_3$ solution (5 mL) to remove the traces of peroxide, followed by water (5 mL). The organic layers were dried over anhydrous Na$_2$SO$_4$, and subsequent evaporation of solvent afforded the epoxide 17.

### 2.1.20. trans-(2R,3S)-Epoxy-1,3-diphenylpropane-1-one, **20**

Yield: 383 mg, 92%; (white solid); mp: 89–90 °C; $[\alpha]_D^{25}$: +121 (c 1, CHCl$_3$, 45% e.e.); IR (neat): 1688, 1230 cm$^{-1}$; $^1$H-NMR (CDCl$_3$, 200 MHz): $\delta$ 4.09 (d, J = 1.96 Hz, 1H), 4.18 (d, J = 1.96 Hz,1H),7.22–7.52 (m, 8H), 8.01–8.03 (m, 2H). $^{13}$C-NMR (CDCl$_3$, 75 MHz): $\delta$ 59.3, 60.9, 76.5, 76.9, 77.4, 125.7, 128.3, 128.7, 128C.8, 129.0, 133.9, 135.4, 193.0. EIMS: 224 (M$^+$). Anal. calcd. for C$_{15}$H$_{12}$O$_2$: C, 80.34; H, 5.39; found: C, 80.32; H, 5.31.

### 2.1.21. trans-(2R,3S)-Epoxy-3-(4-chlorophenyl)-1-phenylpropan-1-one, **22**

Yield: 456.5 mg, 95%; (white solid) mp: 68–70 °C; $[\alpha]_D^{25}$: +95.2 (c 1, CHCl$_3$, 41% e.e.); IR (KBr): 1705, 1240, 810, 705 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 4.06 (d, J = 1.8 Hz, 1H), 4.25 (d, J = 1.8 Hz, 1H), 7.25–7.68 (m, 7H), 7.97–8.08 (m, 2H); EIMS: 258 (M$^+$). Anal. calcd. for C$_{15}$H$_{11}$ClO$_2$: C, 69.6; H, 4.30; found: C, 69.6; H, 4.3.

### 2.1.22. trans-(2R,3S)-Epoxy-3-(4-methylphenyl)-1-phenylpropan-1-one, **24**

Yield: 411.5 mg, 93%; (white solid) mp: 89–91 °C; $[\alpha]_D^{25}$: +111.5 (c 1, CHCl$_3$, 47% e.e.). IR (KBr): 1710, 1240 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 2.39 (s, 3H), 4.01 (d, J = 1.85 Hz, 1H), 4.19 (d, J = 1.85 Hz, 1H), 7.16–7.29 (m, 4H), 7.42–7.51 (m, 2H), 7.56–7.62 (m, 1H), 8.01–8.03 (m, 2H); EIMS: 238 (M$^+$); Anal. calcd. for C$_{16}$H$_{14}$O$_2$: C, 80.65; H, 5.92; found: C, 80.26; H, 5.63.

### 2.1.23. trans-(2R,3S)-Epoxy-3-phenyl-1-(4-methylphenyl)-propan-1-one, **26**

Yield: 420.5 mg, 95% (white solid); mp: 60–62 °C. $[\alpha]_D^{25}$: +91.0 (c 1, CH$_2$Cl$_2$, 40% e.e.); IR (KBr): 1705, 1240 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 2.45 (s, 3H), 4.05 (d, J = 1.9 Hz, 1H), 7.26–7.38 (m, 5H), 7.64–7.68 (m, 2H); EI MS: 238 (M$^+$); Anal. calcd. for C$_{16}$H$_{14}$O$_2$: C, 80.65; H, 5.92; found: C, 80.11; H, 5.56.
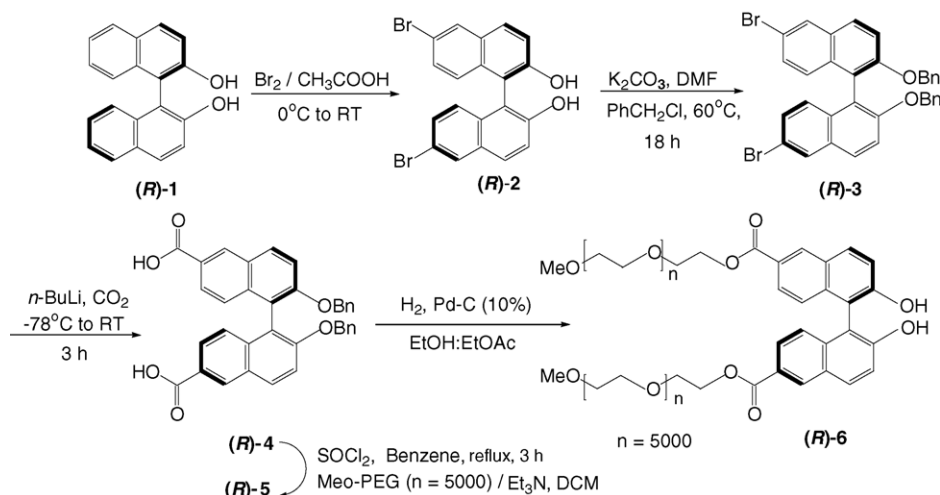
Scheme 1.

## 3. Results and discussion

BINOL is a $C_2$-symmetric axially chiral molecule in which the 6,6′-positions are equally activated towards the electrophilic aromatic substitution by the two hydroxyl groups. We have chosen to incorporate the BINOL scaffold at 6,6′-position onto a soluble polymer and thus provide a homogeneous catalyst that could be precipitated from the reaction medium towards end of the reaction and reused for subsequent cycles. In order to accomplish the immobilization, the appropriate poly (ethyleneglycol) monomethylether (MeO–PEG, $n = 5000$) as a soluble support was selected owing to the many advantages associated with it. To anchor the soluble polymer, the proposed structures should posses suitable functionality and should be away from the active catalytic reaction center. Thus, acid functionalities at 6,6′-position (i.e., BINOL-6,6′-dicarboxylic acid) was considered for the synthesis.

### 3.1. Synthesis of soluble polymer bound BINOL, (R)-6

The required ligand for attachment, benzyl protected diacid (**R**)-**4** was obtained starting from the optically active BINOL (**R**)-**1**, with an overall yield of 75% in four steps

[14]. The carboxylic acid functionalities of the ligand (**R**)-**4** were converted to acid chloride and on reaction with the MeO–PEG–OH ($n = 5000$) in the presence of base lead to (**R**)-**6** [15]. As anticipated the benzyl ether functionalities were smoothly removed by using $H_2$/Pd–C (10%) in a solvent mixture of EtOAc: EtOH to furnish the desired soluble polymer bound (**R**)-**6** in 85% yield (Scheme 1).

The calcium metal was incorporated into the PEG attached ligand (**R**)-**6** using 2 mol equiv. of KO-*t*-Bu in abs. EtOH, following evaporation and addition of 1 mol equiv. of $CaCl_2$ resulting in the formation of calcium-soluble polymer bound BINOL ligand [12] SPB-I (Scheme 2). Initially, 15 mol% of this ligand was tested for Michael reaction of chalcone 14 and dimethyl malonate 15. After stirring for 16 h at 0 °C the product was isolated (86% yield). Though the product yields were high but the enantioselectivity found to be negligible (25% e.e.).

### 3.2. Synthesis of soluble polymer bound BINOL, (R)-13

Subtle variations in the ligand framework can have profound implications in the catalytic activity as well as stereochemical course of the reaction [16]. A flexible spacer is often placed between the soluble polymer and the catalyst
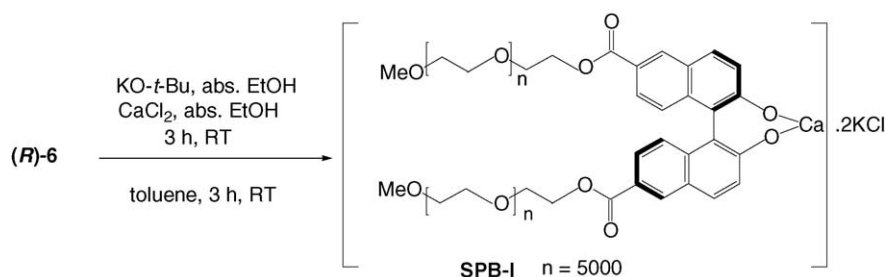


Scheme 2.
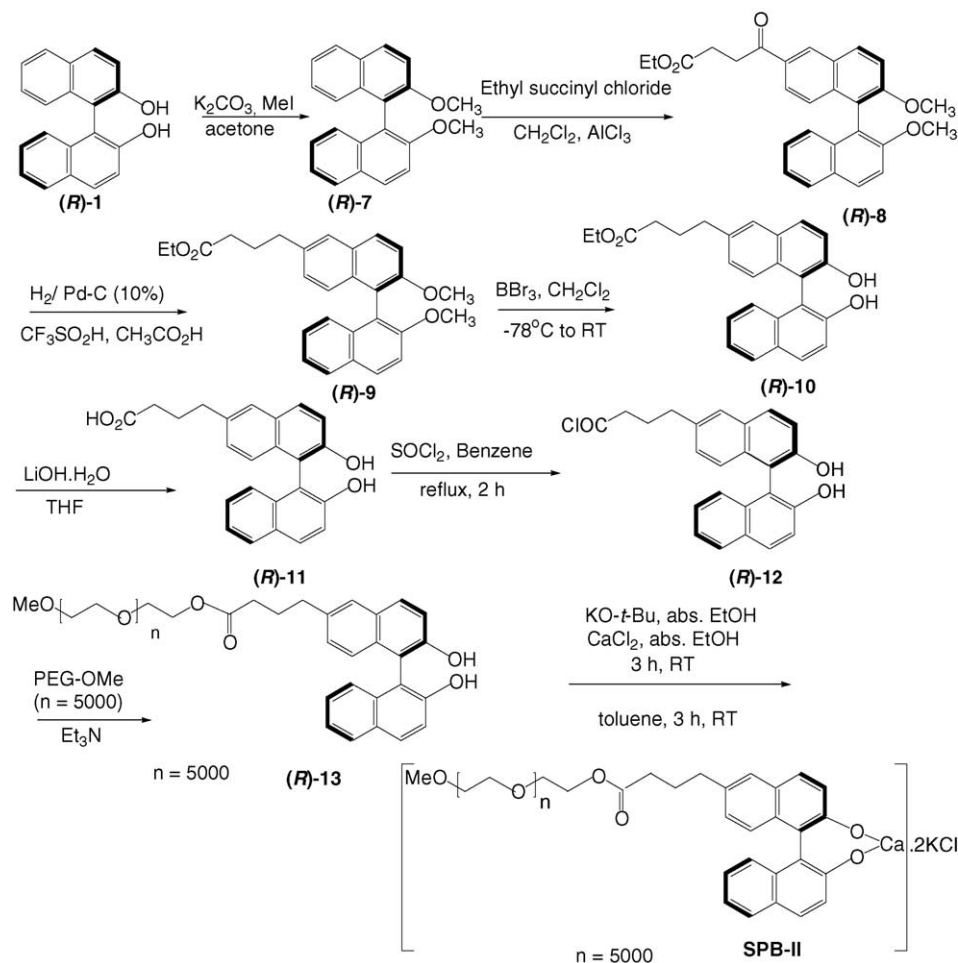
Scheme 3.

not only increases the accessibility of the catalytic sites but also generates distance between the polymer and active site, so as to avoid the adverse affects associated during the catalytic transformation [17].

To overcome the shortcomings allied with the ligand (*R*)-**6** [18], we intended to synthesize a suitably functionalized BINOL containing single alkyl carboxylic acid functionality with a spacer between the chiral BINOL and acid functionality (*R*)-**11**, which provides greatest flexibility to incorporate MeO–PEG by any of the known coupling reactions. Starting from enantiomerically pure BINOL (*R*)-**1**, the monoester (*R*)-**10** was obtained from the known steps using literature procedure [19]. Hydrolysis of the ester function using LiOH.H$_2$O afforded the corresponding acid (*R*)-**11**, which then converted into acid chloride followed by the reaction with MeO–PEG-OH ($n = 5000$), which resulted the polymer bound ligand (*R*)-**13** (Scheme 3). The loading of the ligand (*R*)-**13** on the soluble polymer was estimated on the basis of corresponding $^1$H NMR spectrum and was found to be ~98% [20]. The soluble polymer bound BINOL was made into calcium salt **SPB-II** by adopting the above procedure.

### 3.3. Asymmetric Michael addition using Ca-soluble polymer bound BINOL catalyst

The scope of the Ca-soluble polymer bound BINOL catalyst **SPB-II** was initially examined for the Michael addition reaction between chalcone and dimethyl malonate. By means of 15 mol% of **SPB-II** as a catalyst at 0 °C, the reaction proceeded smoothly to afford the Michael adduct **16** in 90% yield with 32% e.e. after 24 h (Scheme 4) [21]. The catalytic activity of **SPB-II** was also tested for the reaction between cyclopentenone **17** and different malonate esters and the e.e.'s were found to be better than the acyclic enone. The ligands were recovered by the usual precipitation method, once again were made as calcium salts, reused for two cycles and obtained almost constant results (Table 1).

### 3.4. Asymmetric epoxidation using Ca-soluble polymer bound BINOL catalyst

The enantiocontrolling capacity of the calcium-soluble polymer bound BINOL catalyst was also investigated for the epoxidation of chalcone. By means of 10 mol% of **SPB-II**
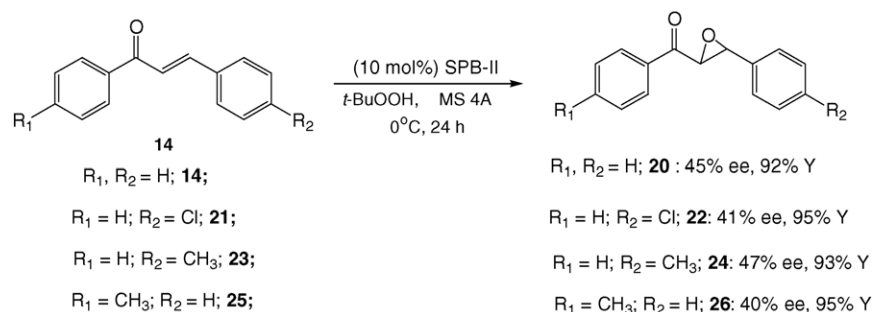
SPB-I; 25% ee, 86% Y;

SPB-II; 32% ee, 90% Y;

R = Me; **18**: 44% ee, 92% Y;

R = Et; **19**: 42% ee, 91% Y;
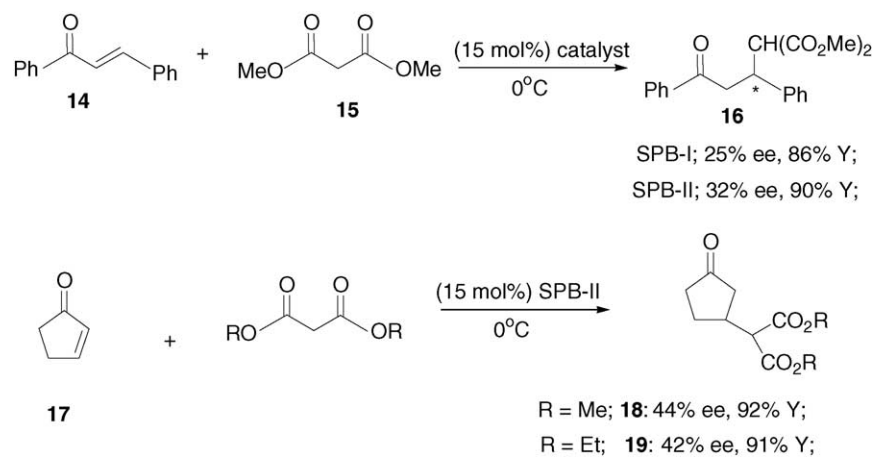
Scheme 4.

Table 1
SPB-II catalyzed asymmetric Michael and epoxidation reactions

| Michael reaction | | | | Epoxidation reaction | | | |
|---|---|---|---|---|---|---|---|
| Product[a,b] | Cycles | | | Product | Cycles | | |
| | 1st e.e. (Y) | 2nd e.e. (Y) | 3rd e.e. (Y) | | 1st e.e. (Y) | 2nd e.e. (Y) | 3rd e.e. (Y) |
| **16** | 32 (90) | 31 (90) | 31 (88) | **22** | 41 (95) | 35 (85) | 32 (82) |
| **18** | 44 (92) | 44 (90) | 42 (90) | **24** | 47 (93) | 44 (90) | 40 (84) |
| **19** | 42 (91) | 42 (88) | 40 (85) | **26** | 40 (95) | 35 (87) | 32 (80) |
| **20** | 45 (92) | 40 (90) | 38 (88) | | | | |

  [a] Precipitated yields based on the enone (isolated through small plug of silica whenever required).

  [b] Enantiomeric excess (e.e.) values were determined by optical rotation and comparison of values from known literature and the absolute configurations were assigned by comparison of specific rotation with literature value.



R₁, R₂ = H; **14**;

R₁ = H; R₂ = Cl; **21**;

R₁ = H; R₂ = CH₃; **23**;

R₁ = CH₃; R₂ = H; **25**;

R₁, R₂ = H; **20** : 45% ee, 92% Y

R₁ = H; R₂ = Cl; **22**: 41% ee, 95% Y

R₁ = H; R₂ = CH₃; **24**: 47% ee, 93% Y

R₁ = CH₃; R₂ = H; **26**: 40% ee, 95% Y

Scheme 5.

as a catalyst at −10 °C, the epoxidation of chalcone using TBHP did not proceed [22]. But raising the temperature to 0 °C the epoxidation reaction smoothly occurred. After 24 h, the epoxide was formed in 92% yield with 45% e.e. [23]. The scope and potential of the epoxidation reaction catalyzed by calcium-soluble polymer bound BINOL, SPB-II was further demonstrated with substituted chalcones. The methyl substituted chalcone **23** gave better e.e. than the rest of the substrates tested. In both reactions (Michael and epoxidation) the use of **SPB-II** as a catalyst gave the best results. The ligands were precipitated from the reaction medium and reused for three cycles. In the case of epoxidation, though the products were

obtained with constant yield the e.e.'s varied. This may be because of the deterioration of the PEG bound BINOL ligand in association with peroxides for a longer period (Scheme 5).

## 4. Conclusions

The use of soluble polymer support provides a substitute platform for organic synthesis by incorporating valuable aspects of both solution-phase and solid-phase chemistry. We have developed two new soluble polymer bound optically active BINOL ligands. These ligands were successfully utilized

in the presence of calcium metal to catalyze Michael reaction as well as epoxidation. The optically active ligands were recovered and reused successfully. These ligands have simplified the purification procedure of the product and can be precipitated easily by using their macromolecular properties. Efforts are on for improving enantioselectivity of the product by modifying the ligand motif.

## Acknowledgments

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