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Asymmetric Cu-catalyzed Henry reaction using chiral camphor Schiff bases Immobilized on a macromolecular chain

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ABSTRACT

Immobilized catalysts have attracted chemists' attention for long time because of convenient recycling, which is very important for some special catalyst even immobilizations accompanying the decrease of catalytic activity and selectivity. Our group focused on the developing chiral catalysts with camphor framework to catalyze various asymmetric reactions for long time. For easily recycling the unique chiral catalysts, a series of polymer catalysts with chiral camphor unit were synthesized by RAFT polymerization. Herein, the performance of the synthesized polymer chiral catalysts was reported by catalyzing asymmetric Henry reaction. After optimizing the reaction conditions, the synthesized chiral polymer catalyst provides a good yield and enantioselectivity to the reaction of *p*-nitrobenzaldehyde and nitromethane. In the meantime, the recycles and reused properties of synthesized polymer catalysts were examination by the model asymmetric Henry reaction. The catalyzed activities and enantioselectivities did not show obviously decrease until recycling five times.

1. Introduction

The asymmetric Henry reaction is one of the most classical reactions in organic name reactions. The most prominent feature of asymmetric Henry reaction is the formation of asymmetric C-C bonds, which accompanied to form one or two chiral centers. Generally, Henry reaction occurs between aldehyde or ketone and nitroalkanes containing active ortho-hydrogen in presence of an organic base to produce *β*-nitroalcohol [1], which has wide range applications in synthesis of natural products and medicines. *β*-nitroalcohol is easy to convert other useful intermediate compounds, such as amino compounds by reduction, conjugated nitroalkenes by elimination, or aldehydes, ketones, carboxylic acids by oxidation. In addition, it also can be used as a nucleophile to participate an addition reaction with an electrophilic substance [2].

The key point of the asymmetric Henry reaction lies in the synthesis of chiral catalyst. Nowadays, there are many mature catalytic systems applied to the asymmetric Henry reaction. The main catalyst categories are organic small molecule catalysts [3], metal complex catalysts [4] and supported catalysts [5]. Among the metal complex catalyzes the Henry reaction, copper is most widely used coordination metals, the ligand which reported mainly include amino alcohol ligands [6], bisoxazoline ligands [7], bis-imidazoline ligands [8], bisthiazoline ligands [9], Schiff base ligands [10], Salen ligands [11] and so on. Recently years, our group focuses on the development new chiral catalyst based on the natural camphor structure [12]. However, the catalysts reuse and recycles is still a challenge for the development of the unique chiral catalyst. The immobilization is a very useful method for the catalyst recycle and reuse. In this paper, the sensitive polymer was selected as the supporter to immobilize the synthesis chiral camphor *β*-amino alcohols [13], which will take the advantage of polymer supporter for recycle and chiral catalyst for high catalytic ability. Even many polymer immobilization catalysts have been reported [14], the use of camphor-derived chiral amino alcohol ligands for immobilization into polymer chains *via* a chain transfer agent has not been reported [15]. The new immobilized catalyst easily separate and recycle from the reaction mixture. The catalyst does not need re-coordinated with metal salt after recycling and maintaining stable catalytic efficiency till to five times recycling [16].

Four different style copolymers with chiral functional group were designed and synthesized (Scheme 1). The best block copolymer catalysts was selected by comparing the effects of copolymerization and the other functional groups, in which we screened the ligand species, metal salts, solvents, monomer ratios, ligand amounts, and the ratio of metals.

2. Results and discussion

The synthetic process of L1-L4 can be found in the supporting information. Based on the paper reported the Henry reaction condition, the catalytic performance of L1-L4 to the asymmetric Henry reaction was screened by the model reaction of *p*-nitrobenzaldehyde and nitromethane using 20mol% ligand

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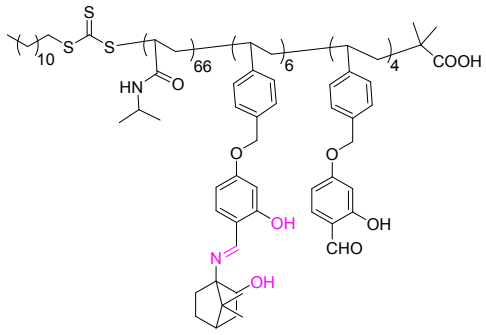
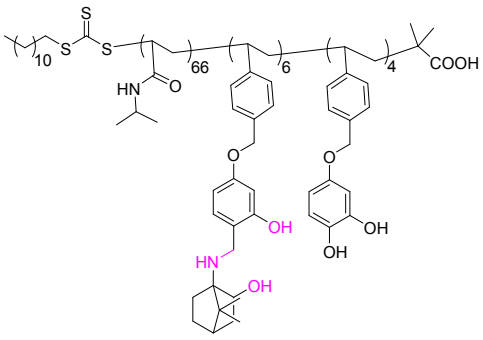
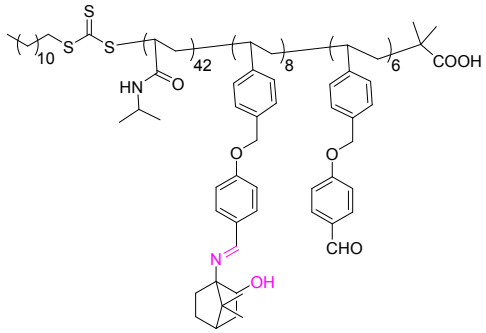


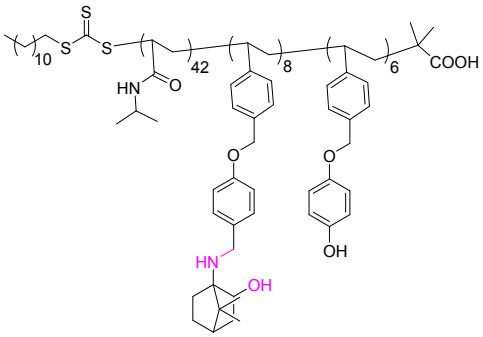
Ligand L1



Ligand L2



Ligand L3



Ligand L4

Scheme 1. The structure of **L1-L4**

and 10mol% CuCl (all the amount of the catalysts are based on the amount of camphor Schiff base unit) at room temperature in *t*-BuOH as the initial reaction condition. The results are listed in Table 1. L1 show the best results as 82% yield and 79% *e.e.* (Table 1, entry 1). Then, the L1 ligand was selected as target to check the catalytic effect of different molar ratio of copolymer block to model reaction. The best catalytic property was obtained as 80% yield and 82% *e.e.* (Table 2, entry 2) in the ratio of NIPAM to functional monomer to chain transfer agent to AIBN as 110 to 10 to 1 to 0.4. Next, different metal salts were used as the source of coordination metal species to copolymer ligand to check the catalytic effect. The results are show in Table 3 and cuprous chloride gave the best result as 80% yield and 82% *e.e.*. Other metal salts showed inferior performances than cuprous chloride. Therefore, cuprous chloride was proved to be the best source of coordination metal species and was used to investigate the further reaction condition. When the ratio of copolymer ligand and copper salt was adjusted from 1:1 to 1:2, the model reaction yield and enantioselectivity were change from 70% and 76% *e.e.* (Table 3, entry 11) to 74% and 76% *e.e.* (Table 3, entry 12). In addition, the catalyst loading also affected the reaction results, when the catalyst loading was reduced to 5mol%, the yield and enantioselectivity was increased to 85% and 84% *e.e.* (Table 3, entry 14). Thus, 5mol% ligand L1 (in definite ratio of copolymer block) /2.5mol% CuCl complex was selected as the most efficient catalyst for the model reaction.

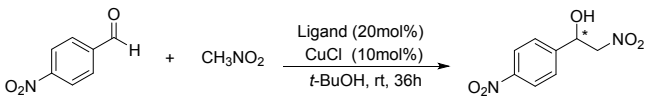
The solvent effect was examined and summarized in Table 4. Protic solvents (Table 4, entry 1–3) give higher yield and enantioselectivity than aprotic solvents (Table 4, entries 4–10).

Under the optimal reaction condition, the substrate scope of new catalytic system was investigated between nitromethane and different aldehydes in the presence of 5mol% L1/2.5mol% CuCl in *t*-butanol at room temperature. The results are presented in table 6. The electronic properties of substitution in aromatic aldehydes have a great effect on the chemical yield and enantioselectivity. In generally, an aromatic aldehyde having electron withdrawing group can produce higher selectivity and reaction rate than the case with an electron donating group. The aldehyde, not only with aromatic substitution but also with heterocyclic substitution, was suitable this new catalytic process. Unfortunately, the heterocyclic aldehydes show the lower yield and inferior enantioselectivity (Table 6, entry 18).

The recycling of new catalytic system was also examined under the optimal reaction condition by model reaction. After finished the first cycle, the reaction mixture was added to ether for separation catalyst after centrifugation. The solution part was used to separate final product by column chromatography. The precipitate was used as the second times catalyst. The results of recycling this new catalytic system were summarized in Table 5. Those results implied this new catalytic system can maintain good yields and enantioselectivities until the fifth time recycles without complement metal salt.

Table 1

Enantioselective Henry reaction of nitromethane with *p*-nitrobenzaldehyde using different ligands [a]



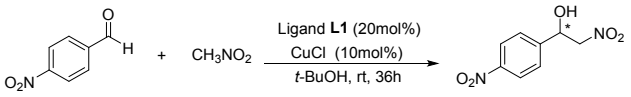
1a 2a

Entry	Ligand	%Yield [b]	%ee [c]	Config. [d]
1	L1	82	79	*R*
2	L2	61	53	*R*
3	L3	31	15	*R*
4	L4	56	65	*R*

[a] All reactions were carried out with 0.5 mmol *p*-nitrobenzaldehyde and 5 mmol nitromethane in 2 mL *t*-BuOH.
[b] Isolated yield after chromatographic purification.
[c] Determined by chiral HPLC.
[d] Absolute configuration through other articles comparison.

Table 2

Effect of the Molar ratio of two monomers in the Ligand L1 on the Asymmetric Henry reaction [a]



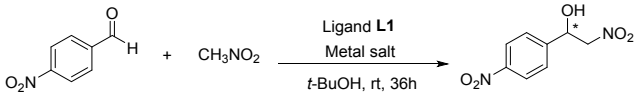
1a 2a

Entry	Molar Ratio [b]	%Yield [c]	%ee [d]	Config. [e]
1	220:10:1:0.4	82	79	*R*
2	110:10:1:0.4	80	82	*R*
3	50:10:1:0.4	65	62	*R*
4	10:10:1:0.4	71	64	*R*

[a] All reactions were carried out with 0.5 mmol *p*-nitrobenzaldehyde and 5 mmol nitromethane in 2 mL *t*-BuOH.
[b] Molar ratio was the molar ratio of NIPAM, 2-hydroxy-4-[(4-vinylbenzyl)oxy]benzaldehyde, 2-Methyl-2-[(dodecylsulfanylthiocarbonyl)sulfanyl]propanoic acid and AIBN.
[c] Isolated yield after chromatographic purification.
[d] Determined by chiral HPLC.
[e] Absolute configuration through literature comparison.

Table 3

Effect of metal salt on the asymmetric Henry reaction under the chiral ligand L1 [a]



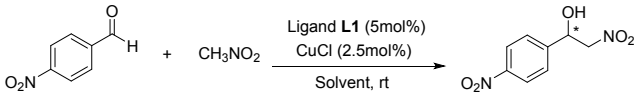
1a 2a

Entry	Metal salt	Ligand/metal	%Yield [b]	%ee [c]
1	CuCl	2:1	80	82
2	CuBr	2:1	75	70
3	$CuCl_2$	2:1	-	-
4	$CuBr_2$	2:1	7	60
5	$Cu(OAc)_2$	2:1	82	35
6	$Cu(OTf)_2$	2:1	13	73
7	$FeCl_2$	2:1	15	18
8	$FeCl_3$	2:1	8	21
9	$Ni(OTf)_2$	2:1	-	-
10	$Zn(OTf)_2$	2:1	-	-
11	CuCl	1:1	70	76
12	CuCl	1:2	74	76
13 [d]	CuCl	2:1	73	64
14 [e]	CuCl	2:1	85	84
15 [f]	CuCl	2:1	79	80
16 [g]	CuCl	2:1	74	61

[a] All reactions were carried out with 0.5 mmol p-nitrobenzaldehyde and 5 mmol nitromethane in 2 mL *t*-BuOH.
[b] Isolated yield after chromatographic purification.
[c] Determined by chiral HPLC.
[d] CuCl (1.25mol%) and ligand (2.5mol%) were used.
[e] CuCl (2.5mol%) and ligand (5mol%) were used.
[f] CuCl (5mol%) and ligand (10mol%) were used.
[g] CuCl (12.5mol%) and ligand (25mol%) were used.

Table 4

Effect of Solvents on Asymmetric Henry reaction [a]



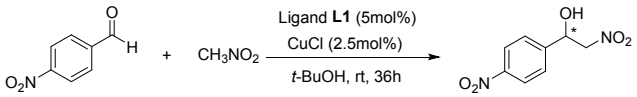
1a 2a

Entry	Solvent	Temp(℃)	Time(h)	%Yield [b]	%ee [c]
1	*i*-PrOH	rt	36	75	71
2	*t*-BuOH	rt	36	85	84
3	EtOH	rt	36	61	53
4	dioxane	rt	36	10	2
5	THF	rt	36	31	15
6	CH_2Cl_2	rt	36	25	15
7	DMSO	rt	36	74	11
8	CH_3CN	rt	36	5	15
9	Toluene	rt	36	52	44
10	CH_3NO_2	rt	48	31	17

[a] All reactions were carried out with 0.5 mmol *p*-nitrobenzaldehyde and 5 mmol nitromethane in 2 mL solvent.
[b] Isolated yield after chromatographic purification.
[c] Determined by chiral HPLC.

Table 5

Recycling of Catalysts in Asymmetric Henry reactions [a]



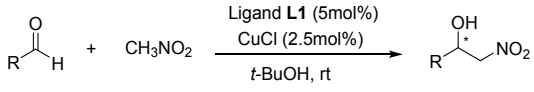
1a 2a

Recycling [b]	Temp(℃)	Time(h)	%Yield [c]	%ee [d]
1	rt	36	82	83
2	rt	36	80	80
3	rt	36	75	82
4	rt	36	73	76
5	rt	36	60	78

[a] All reactions were carried out with 0.5 mmol *p*-nitrobenzaldehyde and 5 mmol nitromethane in 2 mL *t*-BuOH.
[b] Catalyst recycling times. The catalyst is precipitated by ether and centrifuged before the next catalytic reaction.
[c] Isolated yield after chromatographic purification.
[d] Determined by chiral HPLC.

Table 6

Asymmetric Henry reaction of nitromethane with various aldehydes [a]



1 2

Entry	Aldehyde	Product	Time(h)	%Yield [b]	%ee [c]
1	$2\text{-}NO_2C_6H_4$	**2a**	36	71	66
2	$3\text{-}NO_2C_6H_4$	**2b**	36	78	78
3	$4\text{-}NO_2C_6H_4$	**2c**	36	85	84
4	$2\text{-}BrC_6H_4$	**2d**	36	51	71
5	$3\text{-}BrC_6H_4$	**2e**	36	32	63
6	$4\text{-}BrC_6H_4$	**2f**	36	43	49
7	$2\text{-}ClC_6H_4$	**2g**	36	43	61
8	$3\text{-}ClC_6H_4$	**2h**	36	36	83
9	$4\text{-}ClC_6H_4$	**2i**	36	48	69
10	$3\text{-}FC_6H_4$	**2j**	36	53	40
11	$4\text{-}FC_6H_4$	**2k**	36	83	54
12	$4\text{-}CF_3C_6H_4$	**2l**	36	35	78
13	C_6H_5	**2m**	36	30	58
14	$2\text{-}MeOC_6H_4$	**2n**	48	45	62
15	$3\text{-}MeC_6H_4$	**2o**	48	32	48
16	$4\text{-}MeC_6H_4$	**2p**	48	37	56
17	1-Naphthyl	**2q**	36	76	64
18	2-Furyl	**2r**	36	37	63

[a] All reactions were carried out with 0.5 mmol aldehydes and 5 mmol nitromethane in 2 mL *t*-BuOH.
[b] Isolated yield after chromatographic purification.
[c] Determined by chiral HPLC.

3. Conclusion

Four novel camphor chiral Schiff base block copolymer L1-L4 were synthesized by RAFT polymerization, which can used as catalyst for asymmetric Henry reaction giving good results after coordinated with CuCl. It's the first time that a polymer with chiral camphor-derived Schiff base was used as ligand for copper-catalyzed asymmetric Henry. The catalytic process is mild, operationally easy, and insensitive to air and water. The

polymer catalyst can be reused for five times with steady catalytic ability.

4. Experimental section

4.1. General

All chemical reagents were purchased from commercial suppliers and used as received, if not stated otherwise. Anhydrous solvents and reagents were absolutized as usual and distilled prior to use. The^{1}H NMR spectra were recorded on a JEOL 400 NMR spectrometer (400 MHz for ^{1}H). Chemical shifts are reported in δ ppm referenced to an internal TMS standard for ^{1}H NMR. IR spectra were recorded on a Bruker Tensor27 spectrometer. The relative molecular weights and polydispersity index (PDI) were estimated by a gel permeation chromatography (GPC, Waters Corp., Milford, MA, USA) equipped with Waters 515 pump and Waters 2410 differential refractive index detector. The apparent particle size and size distribution of polymer micelles were detected on a dynamic light scattering (DLS) instrument (BI-90Plus, Brookhaven Instruments Corp., Holtsville, NY, USA) equipped with a 15 mM argon ion laser operating at λ = 660 nm and scattering angle of 90° at room temperature. The morphology observations were performed on a transmission electron microscope (TEM, JEM-2100, Hitachi Corporation, Tokyo, Japan) and operated at an accelerating voltage of 200 kV. Before measurement, a drop of micellar solution was dipped onto carbon coated copper grids which were then dried at ambient temperature. Chemical composition and chemical state were measured by a X-ray Photoelectron Spectroscopy (XPS, AXIS ULTRA, Kratos Analytical Ltd). The reactions were monitored by thin layer chromatography (TLC)and visualized by UV light (254 nm). Flash column chromatography was carried out on silica gel (200–400 mesh).

4.2 General procedure for the asymmetric Henry reaction

A dried Schlenk tube was charged with L1 (0.025 mmol) in dry *t*-BuOH (2 mL), then CuCl (0.0125 mmol) was added. The reaction mixture was stirred at 25℃ under N_2 atmosphere for overnight. Nitromethane (0.5 mL) was added to the resulting solution by a syringe. Then the reaction mixture was stirred for an additional 30 min, and the aldehyde (0.5 mmol) was added. After that, the reaction mixture was stirred at 25°C (monitoring by TLC) for assigned time.

After the reaction completed, the catalyst was removed by using ether precipitation and centrifugation. The solvents were evaporated under reduced pressure and the residue was purified by column chromatography (PE/EA = 2:1). The e.e. values were determined by HPLC analysis with a chiral column.

4.2.1. (R)-2-Nitro-1-(2-nitrophenyl)ethanol 2a

Pale Yellow oil; 71% yield, 66% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 13.986 min, t_R(minor) = 15.617 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.0 Hz, 1H), 7.89 (d, *J* = 6.9 Hz, 1H), 7.68 (t, *J* = 7.1 Hz, 1H), 7.53 – 7.46 (m, 1H), 5.98 (d, *J* = 11.4 Hz, 1H), 4.80 (d, *J* = 15.8 Hz, 1H), 4.54 – 4.44 (m, 1H), 3.30 (s, 1H).

4.2.2. (R)-2-Nitro-1-(3-nitrophenyl)ethanol 2b

Yellow solid; 78% yield, 78% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 20.123 min, t_R(minor) = 23.550 min; ^{1}H NMR (400 MHz, CDCl3) δ 8.24 (s, 1H), 8.14 (d, J = 9.2 Hz, 1H), 7.71 (d, J = 8.3 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 5.56 (s, 1H), 4.68 – 4.41 (m, 2H), 3.39 (s, 1H).

4.2.3. (R)-2-Nitro-1-(4-nitrophenyl)ethanol 2c

Yellow solid; 85% yield, 84% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 20.467 min, t_R(minor) = 24.025 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.17 (m, 2H), 7.71 – 7.57 (m, 2H), 5.61 (dd, J = 8.0, 4.5 Hz, 1H), 4.68 – 4.54 (m, 2H), 3.71 (d, J = 2.8 Hz, 1H).

4.2.4. (R)-1-(2-Bromophenyl)-2-nitroethanol 2d

Colorless oil; 51% yield, 71% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 41.677 min, t_R(minor) = 46.028 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.50 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.36 – 7.31 (m, 1H), 5.74 (d, *J* = 9.7 Hz, 1H), 4.65 (d, *J* = 2.3 Hz, 1H), 4.41 – 4.33 (m, 1H), 3.04 (s, 1H).

4.2.5. (R)-1-(3-Bromophenyl)-2-nitroethanol 2e

Colorless oil; 32% yield, 63% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 12.824 min, t_R(minor) = 16.343 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.44 – 7.34 (m, 1H), 7.34 – 7.25 (m, 2H), 5.45 (dd, *J* = 9.3, 3.2 Hz, 1H), 4.62 – 4.49 (m, 2H), 3.08 (s, 1H).

4.2.6. (R)-1-(4-Bromophenyl)-2-nitroethanol 2f

Colorless oil; 43% yield, 49% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 12.777 min, t_R(minor) = 16.347 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 5.36 (d, *J* = 9.4 Hz, 1H), 4.54 – 4.38 (m, 2H), 2.88 (d, *J* = 3.7 Hz, 1H).

4.2.7. (R)-1-(2-Chlorophenyl)-2-nitroethanol 2g

Colorless oil; 43% yield, 61% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 95:5, 1 mL/min, 254 nm): t_R(major) = 37.927 min, t_R(minor) = 40.850 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.4 Hz, 1H), 7.46 – 7.28 (m, 2H), 7.28 – 7.22 (m, 1H), 6.11 – 5.73 (m, 1H), 4.60 (dd, *J* = 13.6, 2.4 Hz, 1H), 4.38 (dd, *J* = 13.6, 9.6 Hz, 1H), 3.02 (s, 1H).

4.2.8. (R)-1-(3-Chlorophenyl)-2-nitroethanol 2h

Colorless oil; 36% yield, 83% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 95:5, 1 mL/min, 254 nm): t_R(major) = 34.807 min, t_R(minor) = 45.022 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.30 – 7.25 (m, 2H), 7.24 – 7.20 (m, 1H), 5.53 – 5.30 (m, 1H), 4.51 (dd, *J* = 13.5, 9.3 Hz, 1H), 4.44 (dd, *J* = 13.5, 3.2 Hz, 1H), 2.91 (s, 1H).

4.2.9. (R)-1-(4-Chlorophenyl)-2-nitroethanol 2i

Colorless oil; 48% yield, 69% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 11.445 min, t_R(minor) = 14.036 min; ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.39 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 2H), 5.46 (d, *J* = 10.2 Hz, 1H), 4.62 – 4.47 (m, 2H), 2.97 (s, 1H).

4.2.10. (R)-1-(3-Fluorophenyl)-2-nitroethanol 2j

Colorless oil; 53% yield, 40% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 10.561 min, t_R(minor) = 12.081 min;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (td, *J* = 8.0, 5.7 Hz, 1H), 7.19 – 7.14 (m, 2H), 5.55 – 5.44 (m, 1H), 4.63 – 4.50 (m, 2H), 3.12 (s, 1H).

4.2.11. (R)-1-(4-Fluorophenyl)-2-nitroethanol 2k

Colorless oil; 83% yield, 54% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 10.125 min, t_R(minor) = 11.569 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 5.39 (d, *J* = 9.5 Hz, 1H), 4.56 – 4.40 (m, 2H), 2.87 (s, 1H).

4.2.12. (R)-2-Nitro-1-(4-(trifluoromethyl)phenyl)ethanol 2l

Colorless oil; 35% yield, 78% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 9.493 min, t_R(minor) = 11.604 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.2 Hz, 2H), 5.36 (d, *J* = 9.4 Hz, 1H), 4.50 (dd, *J* = 13.8, 9.0 Hz, 1H), 4.42 (dd, *J* = 13.1, 3.5 Hz, 1H), 2.89 (s, 1H).

4.2.13. (R)-2-Nitro-1-phenylethanol 2m

Colorless oil; 30% yield, 58% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 11.890 min, t_R(minor) = 14.141 min;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 13.2 Hz, 1H), 7.28 – 7.16 (m, 1H), 5.77 (dd, *J* = 10.3, 3.3 Hz, 1H), 4.60 (dd, *J* = 13.6, 2.3 Hz, 2H), 4.38 (dd, *J* = 13.6, 9.6 Hz, 2H), 2.99 (s, 1H).

4.2.14. (R)-1-(2-methoxyphenyl)-2-nitroethanol 2n

Colorless oil;45% yield, 62% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 9.897 min, t_R(minor) = 11.487 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.31 (m, 2H), 6.96 (dd, *J* = 36.3, 7.9 Hz, 2H), 5.64 (s, 1H), 4.71 – 4.53 (m, 2H), 3.17 (d, *J* = 6.0 Hz, 1H).

4.2.15. (R)-2-Nitro-1-(m-tolyl)ethanol 2o

Colorless oil; 32% yield, 48% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 9.788 min, t_R(minor) = 11.131 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 7.5 Hz, 1H), 7.13 (dd, *J* = 15.8, 7.6 Hz, 3H), 5.40 – 5.34 (m, 1H), 4.54 (dd, *J* = 13.4, 9.6 Hz, 1H), 4.44 (dd, *J* = 13.4, 3.0 Hz, 1H), 2.70 (s, 1H), 2.31 (s, 3H).

4.2.16. (R)-2-Nitro-1-(p-tolyl)ethanol 2p

Colorless oil; 37% yield, 56% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 11.262 min, t_R(minor) = 14.087 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 5.37 (d, *J* = 9.7 Hz, 1H), 4.54 (dd, *J* = 13.3, 9.6 Hz, 1H), 4.48 – 4.40 (m, 1H), 2.66 (s, 1H), 2.30 (s, 3H).

4.2.17. (R)-1-(Naphthalen-1-yl)-2-nitroethanol 2q

Colorless oil; 76% yield, 64% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 15.306 min, t_R(minor) = 22.003 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.3 Hz, 1H), 7.82 (dd, *J* = 21.8, 8.1 Hz, 2H), 7.69 (d, *J* = 7.2 Hz, 1H), 7.56 – 7.41 (m, 3H), 6.19 (d, *J* = 8.6 Hz, 1H), 4.73 – 4.48 (m, 2H), 2.84 (s, 1H).

4.2.18. (R)-1-(2-furyl)-2-nitroethanol 2r

Colorless oil; 37% yield, 63% e.e., HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 85:15, 1 mL/min, 254 nm): t_R(major) = 11.262 min, t_R(minor) = 14.087 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 1H), 6.33 (d, *J* = 2.8 Hz, 2H), 5.41 (dd, *J* = 9.1, 3.4 Hz, 1H), 4.72 (dd, *J* = 13.5, 9.1 Hz, 1H), 4.61 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.89 (s, 1H).

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at

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Highlights

- Chiral camphor unit was immobilized in polymer chain.
- Chiral polymer was synthesized by RAFT polymerization.
- The chiral polymer catalyst show high catalytic ability and recycle four times.