Recyclable Polyvinyl Chloride-Supported Pyrrolidine-Thiourea as a Bifunctional Organocatalyst for Direct Asymmetric Aldol Reaction in Aqueous Medium

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ABSTRACT: Novel polyvinyl chloride (PVC)-supported pyrrolidine-thiourea has been first synthesized in a simple route. The target product was used as a bifunctional organocatalyst for the direct asymmetric aldol reaction between cyclohexanone and arylaldehydes. Effects of solvent and catalyst loading on reaction have been explored. It was found that even at a small dosage of 2.5 mol %, the catalyst exhibited high catalytic activity and stereoselectivities at room temperature in aqueous medium. Additionally, the catalyst can be reused at least for three times. The PVC resin can provide hydrophobic microenvironment for the substrates and catalytic center (pyrrolidine and thiourea moiety) to contact closely. The aldol reaction may take place at the interface between the polymer and aqueous phase. And the results indicated that the thiourea moiety of catalyst had an important effect on the activity and selectivity of the aldol reaction. © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 121: 1506–1511, 2011

Key words: polyvinyl chloride-supported; pyrrolidine-thiourea; bifunctional organocatalyst; aldol reaction; aqueous medium

INTRODUCTION

Much attention has been paid to enantioselective organocatalysis in recent years.[1–4] Of various "metal-free" organic molecules, proline and its derivatives[5–8] have proven to be useful and applied to highly stereoselective transformation like direct aldol reaction, one of the most powerful carbon–carbon bond-forming reactions.[9] And many proline-based organocatalysts have been designed for obtaining higher stereoselectivities. For example, a range of proline mimetics containing structural groups or additional hydrogen-bonding donors such as diamines,[10] small amino acids,[11] triazole,[12] tetrazole,[13] large apolar groups,[14] amide phenols,[15] sulfamido,[16] camphor[17] etc., has been successfully synthesized and found to have increased stereoselectivities in aldol reaction.

Thanks to the ability of thiourea group as a weak Brønsted acid to stabilize the transition state via forming double-hydrogen-bonding, thiourea-based organocatalysts were able to promote the highly enantioselective Strecker reaction of *N*-allyl imines[18] and have been widely used in various asymmetric reactions such as Michael addition,[19,20] Mannich reaction,[21,22] Baylis-Hillman reaction,[23] as well as Henry reaction.[24,25] However, little is currently available about the direct aldol reaction catalyzed by thiourea organocatalysts, and previous researches in this aspect are usually limited by additives which are indispensable for achieving satisfactory catalytic performance. For example, Chen and coworkers[17] found that the catalytic properties of synthetic bifunctional thiourea-amine organocatalysts bearing a chiral camphor scaffolding for direct aldol reaction were closely dependent on dodecylbenzenesulfonic acid (DBSA). Recently, Demir and coworkers[26] found that (3,5-bistrifluoromethylphenyl) thiourea as an additive was critical to the catalytic properties of proline for direct aldol reactions in nonpolar solvents. Needless to say, proline-thiourea as a host–guest complex should have higher stereoselectivities than proline for aldol reactions. Unfortunately, the coexistence of two organic molecules in the complex catalyst means a higher loading of catalyst, not to mention that the reactions are closely dependent on organic solvents and the recovery of the catalyst yet has not been dealt with.

With those perspectives in mind, we are particularly interested in polymer-supported catalysts[27–29] which can be easily separated and recovered and can provide microenvironment for asymmetric reactions as

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well. We have found in previous researches that the natural polymer chitosan supported L-proline as recyclable catalyst has high activity and stereoselectivities for asymmetric aldol reaction in aqueous medium.[30] Encouraged by those findings, we anticipate that new recyclable and bifunctional organocatalysts similar to natural enzymes may be first synthesized by coupling thiourea group with L-proline in the presence of insoluble PVC resin as the supporter. The resulting as-synthesized catalyst should have improved performance due to the synergistic activation of the nucleophilic and electrophilic substrate through enamine-iminium formation and hydrogen bond formation as well.

Therefore, in this article we first report that the synthesis of PVC-supported pyrrolidine-thiourea organocatalyst and its performance in the aldol reaction between cyclohexanone and arylaldehydes at room temperature, highlighting the effect of thiourea moiety on the reactivity and selectivity of the aldol reaction.

EXPERIMENTAL

General

All the reagents and solvents were purchased from commercial suppliers and used without further purification. Analytical thin layer chromatography (TLC) was performed on GF254 silica gel plates. Infrared (IR) spectra were recorded with an Avatar360 Fourier transformation infrared spectrometer (Nicolet Company, USA). Nuclear magnetic resonance (NMR) spectra were obtained from Bruker Avance 400*M* system, and the chemical shifts of ^{1}H NMR spectra were reported in relation to tetramethyl silane ($\delta = 0$). Melting points were measured with an X-6 melting point apparatus. Analytical high performance liquid chromatography (HPLC) was performed on Agilent 1100 equipped with a diode array ultraviolet (UV) detector, and Daicel Chiralpak AD or AS columns were used for the HPLC analysis.

Synthesis of *N*-Fmoc-L-proline

About 1.5 g L-proline was dissolved in 30 mL aqueous Na_2CO_3 (mass fraction 10%) and mixed with 4.3 g *N*-(9-Fluorenylmethoxycarbonyloxy)succinimide (Fmoc-Osu) dissolved in 30 mL tetrahydrofuran (THF), followed by stirring for 48 h. The mixture was added with water (50 mL) and extracted with aether (3×50 mL). The aqueous phase was adjusted to a pH value of 2–3 with aqueous HCl and extracted with ethyl acetate (3×50 mL), while the organic layer was dried by Na_2SO_4 and evaporated to remove solvent generating 4.0 g white solid product with a yield of 91%. The resultant product was directly used in the next step. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.7 ("protuberance" s, 1H), 7.78–7.76 (m, 1H), 7.62–7.58 (m, 1H), 7.43–7.38 (m, 1H), 7.36–7.27 (m, 1H), 4.49–4.39(m, 1H), 4.27–4.29 (d, 1H), 3.60 (s, 1H), 3.49 (m, 2H), 2.0–1.97 (m, 2H), 1.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.13, 176.5, 155.72, 154.43, 143.83, 141.2, 127.62, 127.03, 124.99, 119.9, 67.80, 67.46, 59.23, 58.47, 47.1, 46.74, 30.94, 29.28, 24.30, 23.27. Mass spectrometry (MS) (EI, *m/z*): $C_{20}H_{19}NO_4$ $[M + Na]^+$ calculated 360.36, found 360.2.

Modification of polymer

Into a round-bottomed flask filled with 20 mL tetraethylenepentamine was added 2.0 g polyvinyl chloride (PVC). After being stirred at 80°C for 2 h, the reaction mixture was cooled to room temperature, filtered, and fully washed with H_2O, followed by drying in vacuum for 12 h allowing generation of brown polyvinyl chloride-tetraethylenepentamine (abbreviated as PVC-TEPA).

Synthesis of compound 2

Fmoc-L-proline (1.687 g, 5 mmol) was dissolved in CH_2Cl_2 (20 mL) and mixed with dripping $SOCl_2$ (1 mL, 3 equiv). The mixture was stirred at room temperature for 30 min and decompressed at 40°C to remove HCl formed during the reaction as well as solvent and superfluous $SOCl_2$, generating a yellow oil product. Into the as-synthesized yellow oil were added NH_4SCN (0.570 g, 7.5 mmol), polyethylene glycol (PEG)-400 (0.053 mL, 0.15 mmol) and CH_2Cl_2 (25 mL) at room temperature within 1 h to give isothiocyanate. Then PVC-TEPA (0.86 g) was added to mix with isothiocyanate and stirred at room temperature. After being stirred for 24 h, water was added to dissolve salt formed during the reaction, and ethanol was used to deposit the product. Compound **2**, a red-brown solid, was obtained after filtering, washing with water, CH_2Cl_2, and acetone, and drying in vacuum. Proline loading was determined by weight gain as ~ 0.69 mmol g^{-1}.

Synthesis of catalyst 1

Compound **2** (1 g) was added into a 50-mL round-bottomed flask filled with saturated aqueous NH_3 (25 mL) and stirred at room temperature for 24 h. Then ethanol was added to deposit the product. After being filtered, washed with water and acetone, and dried in vacuum, Catalyst **1** was obtained as a red-brown solid. The product was characterized by means of Fourier transformation infrared (FTIR) spectrometry. The final target product, PVC-supported pyrrolidine-thiourea, was used as a novel catalyst for direct asymmetric aldol reaction.

The recyclability of the PVC-supported pyrrolidine-thiourea catalyst

At the end of the aldol reaction between cyclohexanone and *p*-nitrobenzaldehyde, the catalyst was filtered in vacuum and washed with C_2H_5OH and CH_2Cl_2. After drying in an oven for 24 h, the PVC resin-supported catalyst can be reused directly without further purification.

General procedure of direct aldol reaction

Substituted benzaldehyde (0.5 mmol) was added into the mixture of cyclohexanone, a certain amount of Catalyst **1** and solvent (3 mL). And then the mixture was stirred at room temperature, while the reaction system was detected by TLC (ethyl acetate/petroleum ether = 1 : 2.5). Upon completion of the reaction, the products were filtered and extracted with ethyl acetate; then the organic layer was dried over Na_2SO_4, filtered, concentrated, and purified by thin layer chromatography on a silica gel (ethyl acetate/petroleum ether) giving pure aldol products. Finally, pure products were weighed to calculate yield as well as e.e. and d.r. values of HPLC.

2-[hydroxy(4-nitrophenyl)methyl]cyclohexanone

White powder; mp 129–130°C; [Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 92 : 8, flow rate 1.0 mL min^{-1}, λ = 268 nm; t_R (anti) = 40.25 min (major) and 29.86 min, t_R (syn) = 22.99 min and 26.25 min (major)]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.20–8.24 (m, 2H), 7.48–7.54 (m, 2H), 4.90 (d, J = 8.1 Hz, 1H), 4.09 (s, 1H), 2.32–2.64 (m, 3H), 2.08–2.16 (m, 1H), 1.82–1.86 (m, 1H), 1.35–1.73 (m, 4H).

2-[hydroxy(2-nitrophenyl)methyl]cyclohexanone

Yellow powder; mp 116–118°C; [Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 92 : 8, flow rate 1.0 mL min^{-1}, λ = 209 nm; t_R (anti) = 24.05 min and 22.53 min (major)]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.84 (d, J = 7.8 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.64 (t, J = 7.2 Hz, 1H), 7.40–7.46 (m, 1H), 5.44 (d, J = 7.2 Hz, 1H), 4.11 (br, 1H), 2.73–2.81 (m, 1H), 2.29–2.48 (m, 2H), 2.04–2.14 (m, 1H), 1.55–1.86 (m, 5H).

2-[hydroxy(3-nitrophenyl)methyl]cyclohexanone

White powder; mp 69–71°C; [Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 92 : 8, flow rate 1.2 mL min^{-1}, λ = 263 nm; t_R (anti) = 31.32 min and 24.48 min (major), t_R (syn) = 21.56 min (major) and 20.52 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.15–8.22 (m, 2H), 7.67 (d, J = 7.5 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 4.90 (d, J = 8.4 Hz, 1H), 4.14 (d, J = 2.4, 1H), 2.58–2.67 (m, 1H), 2.32–2.54 (m, 2H), 2.09–2.16 (m, 1H), 1.82–1.86 (m, 1H), 1.36–1.71 (m, 4H).

2-[hydroxy(2,4-nitrophenyl)methyl]cyclohexanone

[Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 92 : 8, flow rate 1.2 mL min^{-1}, λ = 254 nm; t_R (anti) = 40.73 min and 36.67 min (major), t_R (syn) = 23.23 min and 28.61 min (major)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.74–8.75 (d, 1H, J = 2.3), 8.45–8.49 (d, 1H, J = 8.7, J = 2.4), 8.06–8.08 (d, 1H, J = 8.7), 6.05–6.06 (d, 1H, J = 1.9), 5.51–5.53 (brs, 1H), 2.73–2.77 (m, 1H), 2.44–2.47 (m, 1H), 2.11–2.33 (m, 1H), 2.04–2.14 (m, 1H), 1.82–1.88 (m, 1H), 1.79–1.82 (m, 1H), 1.69–1.79 (m, 1H), 1.61–1.68 (m, 1H).

2-[hydroxy(4-cyanophenyl)methyl]cyclohexanone

White powder; mp 82–83°C; [Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 92 : 8, flow rate 1.2 mL min^{-1}, λ = 267 nm; t_R (anti) = 40.26 min (major) and 37.35 min, t_R (syn) = 25.21 min and 29.52 min (major)]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.65 (d, J = 8.1 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 4.84 (d, J = 8.4 Hz, 1H), 4.07 (s, 1H), 2.47–2.62 (m, 2H), 2.31–2.41 (m, 1H), 2.08–2.15 (m, 1H), 1.81–1.83 (m, 1H), 1.49–1.73 (m, 3H), 1.32–1.41 (m, 1H).

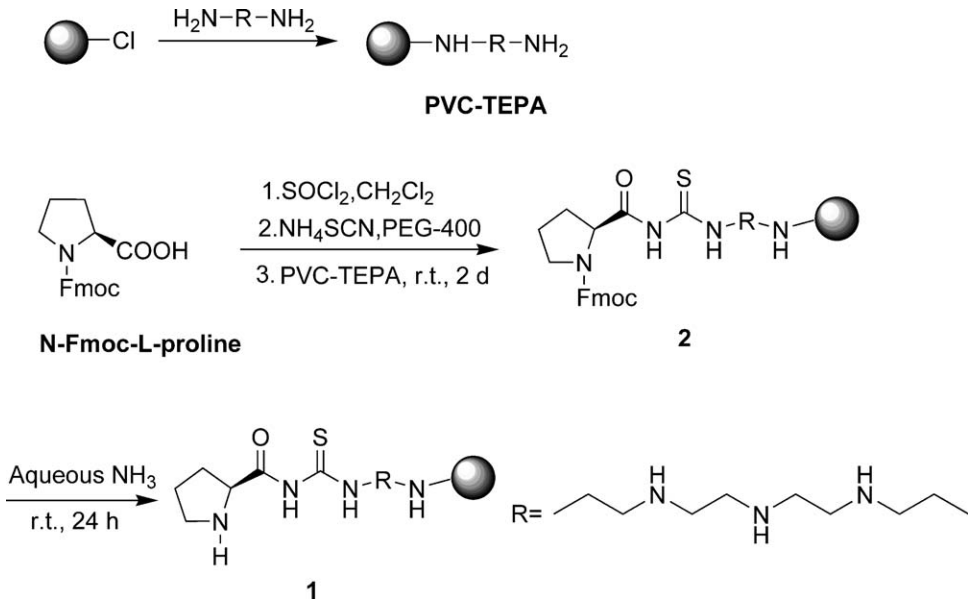
4-hydroxy-4-(4-nitrophenyl) butan-2-one

[Daicel Chiralpak AS-H column, *n*-hexane/isopropanol = 70 : 30, flow rate 1.0 mL min^{-1}, λ = 254 nm; t_R (major) = 9.90 min, t_R (minor) = 12.02 min); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.23 (s, 3H, CH_3), 2.84–2.87 (m, 2H, CH_2), 3.57 (s, 1H, OH), 5.26–5.28 (m, 1H, CH), 7.55 (d, J = 8.1 Hz, 2H, ArH), 8.22 (d, J = 8.1 Hz, 2H, ArH).

RESULTS AND DISCUSSION

The preparation of the supported catalyst is outlined in Scheme 1. First, commercially available PVC resin was modified by tetraethylenepentamine (TEPA) as the linker between polymer backbone and organic molecule generating functionalized PVC-TEPA. Then, PVC-TEPA was allowed to react with *N*-9-fluorenylmethyloxy-carbonyl (Fmoc)-L-proline derived isothiocyanate ($SOCl_2$ and NH_4SCN) in CH_2Cl_2 giving Fmoc-protected thiourea derivative. Finally, desired PVC-supported pyrrolidine-thiourea, i.e., Catalyst **1**, was obtained after removing protecting group *N*-Fmoc using aqueous NH_3.

The catalytic performance of Catalyst **1** was evaluated by carrying out the aldol reaction between cyclohexanone and *p*-nitrobenzaldehyde at room temperature. During screening solvents for the reaction (Table I), it was found that the catalyzed aldol



Scheme 1 Synthesis of PVC-supported pyrrolidine-thiourea **1**.

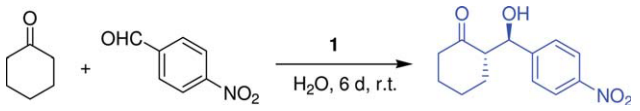
reaction proceeded efficiently in both organic solvents and aqueous media. Particularly, high enantioselectivity and good yield along with a fair diastereoselectivity were obtained in petroleum ether (Table I, Entry 1). Similar stereoselectivity along with a low yield was obtained in hexane (Table I, Entry 2). At the same time, the e.e. value gradually increased (from 37 to 90%) with decreasing polarity of the organic solvents (Table I, Entries 5 down to 1), and slightly increased diastereoselectivity was obtained in ethyl acetate and isopropanol (Table I, Entries 3 and 4). Moreover, anti diastereomers of a lowered e.e. value was observed when dimethylfomamide (DMF) and tetrahydrofuran (THF) with good resin-swelling capability were used as the solvents (Table I, Entries 5 and 6). And both the yield and enantioselectivity were increased and reaction time was shortened when mixed solvents were employed at the expense of decreasing diastereoselectivity (Table I, Entries 7 and 8). In addition, brine

TABLE I
Effect of Solvent on the Aldol Reaction Between Cyclohexanone and *p*-Nitrobenzaldehyde Catalyzed by 1[a]

Entry	Solvent	Time (d)	Yield[b] (%)	d.r.[c] (syn/anti)	e.e.[c] (%) (anti)
1	Petroleum ether	10	70	52 : 48	90
2	*n*-hexane	10	58	46 : 54	89
3	Ethyl acetate	10	48	42 : 58	79
4	Isopropanol	10	40	45 : 55	76
5	DMF	10	46	59 : 41	37
6	THF	10	34	45 : 55	28
7	H_2O + DMSO	6	63	50 : 50	69
8	H_2O + DMF	6	50	47 : 53	75
9	Brine	6	34	39 : 61	67
10	H_2O (cycle 1)	6	58	31 : 69	94
11	Cycle 2	6	43	46 : 53	96
12	Cycle 3	6	58	38 : 62	93

[a] Reaction was performed at 0.5 mmol scale of aldehyde and 6 equiv of ketone in the presence of 2.5 mol % of catalyst **1** in 3 mL of solvent.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis (Chiralpak AD-H).

TABLE II
Effect of the Amount of Catalyst on the Aldol Reaction Between Cyclohexanone and *p*-Nitrobenzaldehyde Catalyzed by 1[a]



Entry	Loading of catalyst (mol %)	Yield[b] (%)	d.r.[c] (syn/anti)	e.e.[c] (%) (anti)
1	2.5	58	31 : 69	94
2	5	82	27 : 73	94
3	8	81	32 : 68	95
4	10	83	47 : 53	95
5	15	74	51 : 49	95

[a] Reaction was performed at 0.5 mmol scale of aldehyde and 6 equiv of ketone in 3 mL of water.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis (Chiralpak AD-H).

had similar function as mixed solvents (Table I, Entry 9), while water seemed to be the optimal medium for the reaction (Table I, Entry 10; in this case aldol anti product was harvested with a high diastereoselectivity and enantiselectivity as well). This implies that the reaction may take place at the interface between the polymer and aqueous phase. In terms of the recycle of the catalysts, Catalyst **1** maintained high stereoselectivities after three cycles (Table I, Entries 10–12).

Next, the aldol reaction between cyclohexanone and *p*-nitrobenzaldehyde catalyzed by Catalyst **1** with various dosages was investigated at room temperature in the presence of water as a solvent (Table II). A lower yield was observed when only 2.5 mol % of catalyst was employed, but the e.e. and d.r. values in this case remained high (Table II, Entry 1). When the dosage of catalyst was increased to 5–15 mol %, high yields and excellent enantioselectivities were obtained (Table II, Entries 2–5); and in particular, the best enantioselectivity along with a high yield of as much as 81% was reached when 8 mol % of catalyst was used (Table II, Entry 3). This

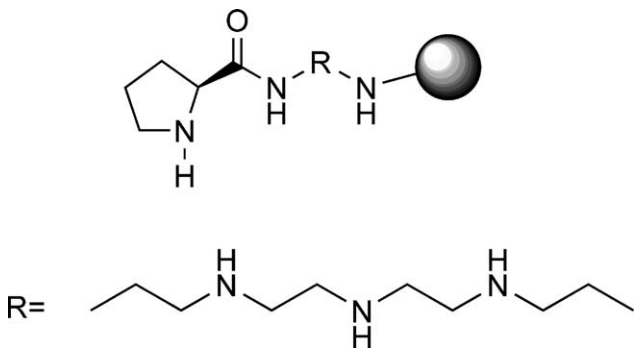
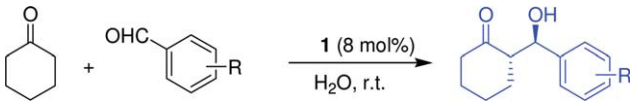


Figure 1 PVC-TEPA-supported proline-based catalyst.

TABLE III
Asymmetric Aldol Reaction Between Cyclohexanone and Various Arylbenzaldehydes Catalyzed by Catalyst 1 Under the Optimal Conditions[a]



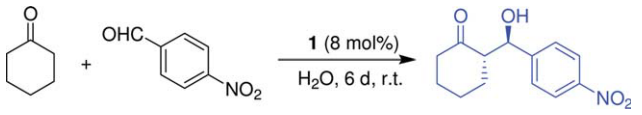
Entry	*R*	Time (d)	Yield[b] (%)	d.r.[c] (syn/anti)	e.e.[c] (%) (anti)
1	*p*-NO_2	6	81	32 : 68	95
2	*o*- NO_2	6	17	52 : 48	39
3[d]	*o*- NO_2	10	14	28 : 72	67
4[e]	*o*- NO_2	10	17	25 : 75	73
5	*m*- NO_2	10	49	45 : 55	31
6	2,4-dinitro	10	48	50 : 50	53
7	*p*-CN	15	62	43 : 57	89
8[f]	*p*-NO_2	10	17	–	15

[a] Reaction was performed at 0.5 mmol scale of aldehyde and 6 equiv of ketone in the presence of 8 mol % of catalyst in 3 mL of water.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis (Chiralpak AD-H or AS-H).
[d] Reaction was carried out at 10°C.
[e] Reaction was carried out at 0°C.
[f] Acetone instead of cyclohexanone was used.

differs from our previous research on the asymmetric aldol reaction of cyclohexanone with *p*-nitrobenzaldehyde catalyzed by PVC-TEPA-supported proline derivative (Fig. 1). Namely, a yield of 71% and an e.e. value of 84% were obtained in water for the aldol reaction catalyzed by PVC-TEPA-supported proline derivative (5 mol %), much lower than 82 and 94% in the present research (Table II, Entry 2). Therefore, it can be rationally inferred that the thiourea moiety in Catalyst **1** has an important effect on the activity and selectivity of the aldol reaction.

Further, cyclohexanone and a representative set of arylaldehydes were examined under optimal reaction conditions (8 mol % of Catalyst **1**, water solvent, room temperature). Poor results were obtained when *o*-nitrobenzaldehyde was employed as the acceptor at room temperature (Table III, Entry 2), while quite good e.e. and d.r. values were obtained at low temperature (Table III, Entries 3 and 4). At the same time, *m*-nitrobenzaldehyde was similar to *o*-nitrobenzaldehyde in terms of the selectivities (Table III, Entry 5). Moderate yield and enantioselectivity were obtained with 2,4-dinitrobenzaldehyde, but the diastereoselectivity was lowered (Table III, Entry 6). When *p*-cyanobenzaldehyde was employed, a dramatically increased enantioselectivity was recorded together with a good yield (Table III, Entry 7). Thus, *p*-nitrobenzaldehyde can be regarded as the optimal acceptor. Hydrophilic acetone was further observed as a nucleophilic ketone, but low enantioselectivity was recorded (Table III, Entry

TABLE IV
The Reusability of Catalyst 1 Under the Optimal Conditions[a]



Entry (cycle number)	Yield[b] (%)	d.r.[c] (syn/anti)	e.e.[c] (%) (anti)
1	81	32 : 68	95
2	71	50 : 50	91
3	82	38 : 62	93

[a] Reaction was performed at 0.5 mmol scale of aldehyde and 6 equiv of ketone in the presence of 8 mol % of catalyst in 3 mL of water.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis (Chiralpak AD-H).

8). Besides, the reusability of Catalyst **1** was investigated under the optimal reaction conditions (Table IV). The research showed that good yield and high stereoselectivities were retained even after three cycles of the catalyst (Table IV, Entry 5).

At this stage, the stereochemical procedures of the aldol reaction catalyzed by Catalyst **1** remain unknown. Nevertheless, it is obvious that water plays an important role in facilitating the reaction,[31] and so does insolvable polymer resin in providing hydrophobic microenvironment for the substrates and catalytic center (pyrrolidine and thiourea moiety) to contact closely. The aldol reaction may take place at the interface between the polymer and aqueous phase,[12] and Catalyst **1** can be thought of as a bifunctional organocatalyst. Namely, the double-hydrogen-bonding between thiourea and aldehyde acceptor should be favorable to activate the aldehyde and facilitate the aldol reaction, while enamine formed from pyrrolidine and cyclohexanone in the transition state would mainly attack the aldehyde.[17]

CONCLUSIONS

To sum up, we have first developed PVC-supported pyrrolidine-thiourea under mild conditions via a simple route. The product was tested as a novel bifunctional organocatalyst for the direct asymmetric aldol reaction between ketone and aromatic aldehydes. High yield and enantioselectivity were obtained in water at room temperature and a catalyst dosage of only 2.5 mol %. And the catalyst exhibited good reusability under optimal reaction conditions. In general, the introduction of thiourea moiety in L-proline endows it with significantly increased activity and selectivity, making it feasible to efficiently manipulate direct asymmetric aldol reaction between ketone and aromatic aldehydes without using additives. Further study on similar types of polymer-supported pyrrolidine-thiourea organocatalysts and reaction mechanism is being underway.

References

1. Werner, T. Adv Synth Catal 2009, 351, 1469.
2. Guillena, G.; Nájera, C.; Ramón, D. J Tetrahedron 2007, 18, 2249.
3. Guillena, G.; Ramón, D. J Tetrahedron 2006, 17, 1465.
4. Doyle, A. G.; Jacobsen, E. N. Chem Rev 2007, 107, 5713.
5. Notz, W.; Tanaka, F.; Barbas, C. F. Acc Chem Res 2004, 37, 580.
6. Sato, K.; Kuriyama, M.; Shimazawa, R.; Morimoto, T.; Kakiuchi, K.; Shirai, R. Tetrahedron Lett 2008, 49, 2402.
7. Chandrasekhar, S.; Johny, K.; Reddy, C. R. Tetrahedron: Asymmetry 2009, 20, 1742.
8. Kantam, M. L.; Rajasekhar, C. V.; Gopikrishna, G.; Rajender Reddy, K.; Choudary, B. M. Tetrahedron Lett 2006, 47, 5965.
9. Mahrwald, R. Modern Aldol Reaction; Wiley-VCH: Weinheim, 2004; Vol. 1–2.
10. Samanta, S.; Liu, J. Y.; Dodda, R.; Zhao, C. G. Org Lett 2005, 7, 5321.
11. Shi, L. X.; Sun, Q.; Ge, Z. M.; Zhu, Y. Q.; Cheng, T. M.; Li, R. T. Synlett 2004, 2215.
12. Font, D.; Jimeno, C.; Pericàs, M. A. Org Lett 2006, 8, 4653.
13. Torii, H.; Nakadai, M.; Ishihara, K.; Saito, S.; Yamamoto, H. Angew Chem Int Ed 2004, 43, 1983.
14. Fu, Y. Q.; An, Y. J.; Liu, W. M.; Li, Z. C.; Zhang, G.; Tao, J. C. Catal Lett 2008, 124, 397.
15. Zhang, S. P.; Fu, X. K.; Fu, S. D.; Tetrahedron Lett 2009, 50, 1173.
16. Wu, Y. Y.; Zhang, Y. Z.; Yu, M. L.; Zhao, G.; Wang, S. W. Org Lett 2006, 8, 4417.
17. Tzeng, Z. H.; Chen, H. Y.; Huang, C. T.; Chen, K. Tetrahedron Lett 2008, 49, 4134.
18. Sigman, M. S.; Jacobsen, E. N. J Am Chem Soc 1998, 120, 4901.
19. Inokuma, T.; Takasu, K.; Sakaeda, T.; Takemoto, Y. Org Lett 2009, 11, 2425.
20. Okino, T.; Hoashi, Y.; Takemoto, Y. J Am Chem Soc 2003, 125, 12672.
21. Tian, X.; Jiang, K.; Peng, J.; Du, W.; Chen, Y. C. Org Lett 2008, 10, 3583.
22. Song, J.; Wang, Y.; Deng, L. J Am Chem Soc 2006, 128, 6048.
23. Wang, J.; Li, H.; Yu, X. H.; Zu, L. S.; Wang, W. Org Lett 2005, 7, 4293.
24. Sohtome, Y.; Hashimoto, Y.; Nagasawa, K. Eur J Org Chem 2006, 2894.
25. Sohtome, Y.; Hashimoto, Y.; Nagasawa, K. Adv Synth Catal 2005, 347, 1643.
26. Reis, O.; Eymur, S.; Reis, B.; Demir, A. S. Chem Commun 2009, 1088.
27. Trindade, A. F. P.; Gois, M. P. C.; Afonso, A. M. Chem Rev 2009, 109, 418.
28. Benaglia, M.; Puglisi, A.; Cozzi, F. Chem Rev 2003, 103, 3401.
29. Gruttadauria, M.; Giacalone, F.; Noto, R. Chem Soc Rev 2008, 37, 1666.
30. Zhang, H. F.; Zhao, W. S.; Zou, J.; Liu, Y.; Li, R. T.; Cui, Y. C. Chirality 2009, 21, 492.
31. Giacalone, F.; Gruttadauria, M.; Meo, P. L.; Riela, S.; Noto, R. Adv Synth Catal 2008, 350, 2747.