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Polyvinylidene Chloride Supported L-Prolineamide as Recoverable Catalyst for Asymmetric Aldol Reaction Between Ketone and Aromatic Aldehyde

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ABSTRACT: A series of prolineamide modified by polyvinylidene chloride (PVDC) was synthesized and used as green recoverable organocatalysts for the asymmetric Aldol reactions between various ketones and aromatic aldehydes. The effects of solvent and catalyst dosage on the catalytic performances of as-synthesized organocatalysts were investigated. It was found that as-synthesized PVDC-supported L-prolineamides possessed good catalytic performance for the asymmetric Aldol reactions between cyclohexanone and a variety of aromatic aldehydes, affording high yields of up to 99%, excellent diastereoselectivities of up to above 8 : 92 d.r. value, and high enantioselectivities of up to above 92.3% e.e. value. In general, the catalytic performance of as-synthesized organocatalysts closely depended on the catalyst dosage and solvent type as well. Particularly, as-synthesized organocatalyst **1c**, at a dosage of 5 mol % in 10 μL of water, exhibited high catalytic activity and stereoselectivity for the asymmetric Aldol reaction between cyclohexanone and *p*-nitrobenzaldehyde at room temperature. In the meantime, it could be easily recovered and recycled, while the activity and enantioselectivity were nearly completely retained even after five cycles of recovery, showing promising application as an efficient green organocatalyst for the aforementioned asymmetric Aldol reactions. © 2012 Wiley Periodicals, Inc. J. Appl. Polym. Sci. 000: 000–000, 2012

KEYWORDS: polyvinylidene chloride; proline; catalyst; supported; aldol reaction

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INTRODUCTION

Organocatalytic synthesis has emerged as a powerful methodology in the past decades.[1–4] Particularly, the development of metal-free small organic molecules as useful catalysts for enantioselective reactions has been attracting much interest. Resultant metal-free small organic molecules as organocatalysts may have extraordinary advantages under the condition that they can be efficiently recovered and recycled.[5–7] Naturally, the efficient recovery and recycling of organocatalysts are of considerable significance in terms of cost-effectiveness and environmental acceptance of synthetic processes, because organocatalysts are often used up to a dosage of 30 mol %.[8] This is why water, with reliable safety, low cost and good environmental acceptance, is desirable and important as a solvent for organocatalytic asymmetric reactions.[9–13]

Of various recyclable catalysts, polymer-supported proline,[14] prolineamides,[15] diarylprolinols,[16] MacMillan imidazolidinones,[17] and cinchona-derivatives,[18] as well as ionic liquid supported organic catalysts[19] and inorganic material supported organocatalysts[20] have been extensively researched. We previously focused on the immobilization of chiral ligands on polymeric supports including natural polymers[21] and synthetic polymers[22] for the purpose of developing recyclable organocatalysts that can be applied to asymmetric reactions under mild and convenient conditions. Our attempts in those respects, with the aim of facilitating catalyst recovery and recycling, may help to establish powerful synthetic tools readily available to the chemical community in organic synthesis.[23] Recently, Benaglia et al.[24] developed a poly(ethylene-glycol)-supported proline for the enantioselective Aldol and imino Aldol reactions in good yields and high enantiomeric excess. Gruttadauria et al.,[9,15] developed polystyrene supported prolineamide for asymmetric reactions. Nevertheless, further work is urgently needed to search for more efficient polymer-supported catalysts with a higher enantioselectivity and a broader substrate scope.

Bearing those perspectives in mind, we have prepared a new class of prolineamides (PROA) supported by polyvinylidene

Additional Supporting Information may be found in the online version of this article.

chloride (PVDC) in the present research. As-synthesized PVDC-supported PROA can be used for the asymmetric Aldol reactions of ketones yielding aromatic aldehydes under mild and green conditions.

EXPERIMENTAL

PVDC powder (type #2051-2) was purchased from Kureha Corporation, Japan; aromatic aldehydes and L-proline were purchased from commercial supplier Alfa Aesar, China; ketones and polyethylene polyamine were purchased from Sinopharm Chemical Reagent Co. Ltd, China; and other common solvents and reagents were bought from common suppliers. All the reagents and solvents were used without further purification. Thin layer chromatography analysis was carried out with GF_{254} silica gel plates. Infrared spectra were recorded with an Avatar 360 Fourier transform infrared spectrometer (Nicolet Company, USA). Nuclear magnetic resonance (NMR) spectra were obtained from Bruker Avance 300M system (Bruker, German), 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. Ultimate analysis was measured with PE 2400-II. CHNS/O elemental analyzer (PE Company, USA). High-performance liquid chromatography (HPLC) analysis was performed on Agilent 1100 (Bruker, German; Daicel Chiralpak AD-H or AS-H columns, Daicel, Japan) equipped with a diode array ultraviolet (UV) detector, and isopropanol and *n*-hexane as the eluents.

Synthesis of *N*-(9-Fluorenylmethoxycarbonyl)-L-proline

A total of 1.5 g (0.013 mol) of L-proline was dissolved in 30 mL of aqueous solution of Na_2CO_3 (mass fraction 10%), then mixed with 4.4 g (0.013 mol) of *N*-(9-fluorenylmethoxycarbonyloxy)succinimide (Fmoc-Osu) dissolved in 30 mL of tetrahydrofuran (THF), and stirred at room temperature for 24 h. Into resultant mixture was added 50 mL of water, extracted with ethyl acetate (3 × 25 mL). The aqueous phase was treated with dilute hydrochloric acid to pH 2–3 and extracted with ethyl acetate (3 × 50 mL). Organic extracts were combined and washed with water (2 × 25 mL), dried, concentrated, and crystallized from petroleum ether, producing 4.2 g of white solid in a yield of 97%. (See supporting information). ^{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): $C_{20}H_{19}O_4N$ $[M + Na]^+$: calculated 360.36, found 360.2.

Synthesis of *N*-Fmoc-L-Pro-Cl

A total of 1.5 g (4.45 mmol) of Fmoc-L-proline was dissolved in 20 mL of CH_2Cl_2. Into resultant mixture was dripped 2 mL of $SOCl_2$ (7 equiv.) during reflux. The reaction system was stirred at room temperature for 2 h, after that solvent and superfluous thionyl chloride were distilled under reduced pressure, yielding product N-Fmoc-L-Pro-Cl as a yellow solid.

Modification of Polymer

Into a round-bottomed flask filled with 5 mL of tetraethylenepentamine was added 1.0 g of PVDC. After being stirred at room temperature for 4 h, 10 mL of water was injected to the reaction mixture, then filtered and thoroughly washed with water and ethanol, and dried in vacuum for 12 h to generate black powder polyvinylidene chloride-tetraethylenepentamine (PVDC-TEPA, compound 3c). Ultimate analysis shows that compound **1c** has nitrogen loading of 14.86% and the TEPA loading of 2.12 mmol/g.

Synthesis of *N*-Fmoc-L-PROA-PVDC-TEPA (Compound 2c)

A total of 1.5 g (4.2 mmol) of *N*-Fmoc-L-Pro-Cl and 0.5 mL of pyridine were dissolved in 25 mL of CH_2Cl_2. Into resultant mixture was added 1.0 g of PVDC-TEPA. The mixture was stirred at room temperature for 24 h and ethanol was added to deposit crude product. The crude product was filtered, washed with water and ethanol, and dried in vacuum. The black powder product *N*-Fmoc-L-PROA-PVDC-TEPA (Compound 2c) was obtained.

Synthesis of Catalyst 1c

One gram of compound 2c was added into a 50 mL round-bottomed flask filled with ammonia solution (25 mL) and stirred at room temperature for 24 h, after that ethanol was added to deposit the crude product. Resultant crude product was filtered, washed with water and ethanol, and dried in vacuum generating catalyst IR spectrum of catalyst **1c** (see supporting information) as a black solid. Ultimate analysis shows that catalyst **1c** has a proline unit loading of 1.03 mmol/g. As-synthesized catalyst **1c** was used as a novel catalyst for direct asymmetric Aldol reaction.

General Procedure for Aldol Reactions

Into the solution of aldehyde acceptor (0.25 mmol) and ketone donor (2.5 mmol) in 10 μL of water was added desired catalyst at a pre-set dosage (5 mol %). Resultant reaction system was stirred at room temperature for a period of pre-set time. At the end of reaction, ethyl acetate was added into the reaction system, and then filtered, washed with ethyl acetate, dried over anhydrous Na_2SO_4, and concentrated. As-obtained crude products were then separated and purified using a silica gel chromatographic column using of petroleum ether-ethyl acetate (2.5 : 1) as the eluent, affording corresponding pure Aldol adducts. (See supporting information).

Recyclability of PVDC Resin Supported L-Prolineamide

After carrying out the asymmetric reaction, the mixture was vacuum-filtered using a sintered glass funnel and washed with ethyl acetate (4 × 2.0 mL). As-recovered catalyst can be reused directly without further purification.

2-[Hydroxyl(4-nitrophenyl)methyl]cyclohexan-1-one[22,25]

White powder; mp 129–130°C; [Daicel Chiralpak AD-H column, *n*-hexane/ isopropanol = 92 : 8; flow rate in first 10 min is 1.0 mL/min, then it is gradually increased to 1.5 mL/min in another ten minutes. $\lambda = 268$ nm; t_R (anti) = 32.05 min (major) and 25.04 min, t_R (syn) = 22.49 min and 20.58 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.36–1.75 (m, 4H), 1.81–1.88 (m, 1H), 2.06–2.17 (m, 1H), 2.32–2.67 (m, 3H), 4.09 (s, 1H),

4.93 (d, J = 8.1 Hz, 1H), 7.47–7.54 (m, 2H), 8.20–8.26 (m, 2H).

2-[Hydroxyl(3-nitrophenyl)methyl]cyclohexan-1-one[22,25]
White powder; mp 69–71°C; [Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 92 : 8, flow rate 1.2 mL/min, λ = 268 nm; t_R (anti) = 30.90 min and 24.56 min (major), t_R (syn) = 21.41 min (major) and 20.20 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 136–1.71 (m, 4H), 1.82–1.86 (m, 1H), 2.09–2.16 (m, 1H), 2.32–2.54 (m, 2H), 2.58–2.67 (m, 1H), 4.14 (d, J = 2.4 Hz, 1H), 4.90 (d, J = 8.4 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.67 (d, J = 7.5 Hz, 1H), 8.15–8.22 (m, 2H).

2-[Hydroxyl(2,4-dinitrophenyl)methyl]cyclohexan-1-one[22]
Yellow oil; [Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 92 : 8, flow rate 1.2 mL/min, λ = 254 nm; t_R (anti) = 40.51 (major) min and 36.63 min, t_R (syn) = 26.97 min and 23.57 min (major)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.61–1.68 (m, 1H), 1.69–1.79 (m, 1H), 1.79–1.82 (m, 1H), 1.82–1.88 (m, 1H), 2.04–2.14 (m, 1H), 2.11–2.33 (m, 1H), 2.44–2.47 (m, 1H), 2.73–2.77 (m, 1H), 5.51–5.53 (brs, 1H), 6.05–6.06 (d, J = 1.9 Hz, 1H), 8.06–8.08 (d, J = 8.7 Hz, 1H), 8.45–8.49 (d, J = 2.4, 8.7 Hz, 1H), 8.74–8.75 (d, J = 2.3 Hz, 1H).

2-[Hydroxyl(4-cyanophenyl)methyl]cyclohexan-1-one[22,25]
White powder; mp 82–83°C; [Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 92 : 8, flow rate 1.0 mL/min, λ = 268 nm; t_R (anti) = 30.82 min (major) and 24.69 min, t_R (syn) = 20.98 and 17.85 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.32–1.41 (m, 1H), 1.49–1.73 (m, 3H), 1.81–1.83 (m, 1H), 2.08–2.15 (m, 1H), 2.31–2.41 (m, 1H), 2.47–2.62 (m, 2H), 4.07 (s, 1H), 4.84 (d, J = 8.4 Hz, 1H), 7.43 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 8.1 Hz, 2H).

2-[Hydroxyl(4-fluorophenyl)methyl]cyclohexan-1-one[26]
[Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 90 : 10, flow rate 0.3 mL/min; λ = 208 nm; t_R (anti) = 46.55 min (major) and 42.58 min, t_R (syn) = 32.09 and 28.24 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.41–1.87 (m, 5H), 1.91–2.21 (m, 1H), 2.26–2.49 (m, 3H), 3.01–3.20 (br s, 1H), 3.88–3.92 (br s, 1H), 4.70–4.73 (d, J = 9.0 Hz, 1H), 5.29 (s, 1H), 6.96–7.00 (m, 2H), 7.20–7.23 (br s, 2H).

2-[Hydroxyl(4-chlorophenyl)methyl]cyclohexan-1-one[26]
[Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 90 : 10, flow rate 0.3 mL/min; λ = 224 nm; t_R (anti) = 50.60 (major) min and 44.72 min, t_R (syn) = 33.78 min and 29.16 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.55–1.87 (m, 5H), 1.98–2.09 (m, 1H), 2.33–2.55 (m, 3H), 3.00 (br s, 1H), 3.91 (br s, 1H), 4.71–4.74 (d, J = 9.0 Hz, 1H), 5.33 (s, 1H), 7.20–7.30 (m, 4H).

2-[Hydroxyl(4-bromophenyl)methyl]cyclohexan-1-one[26]
[Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 90 : 10, flow rate 0.3 mL/min; λ = 222 nm; t_R (anti) = 54.74 min (major) and 47.82 min, t_R (syn) = 35.56 min and 30.25 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.50–1.87 (m, 5H), 2.05–2.11 (m, 1H), 2.33–2.57 (m, 3H), 3.05 (br s, 1H), 3.93 (br s, 1H), 4.70–4.73 (d, J = 9.0 Hz, 1H), 5.30 (br s, 1H), 7.14–7.18 (m, 2H), 7.42–7.46 (m, 2H).

2-[Hydroxyl(4-methoxyphenyl)-methyl]cyclohexan-1-one[25]
White powder; mp 74–76°C; [Daicel Chiralpak AD-H column, *n*-hexane/isopropanol = 92 : 8, flow rate 1.0 mL/min, λ = 218 nm; t_R (anti) = 36.54 min and 29.20 min, t_R (syn) = 25.25 min (major) and 21.15 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.19–1.33 (m, 1H), 1.48–1.81 (m, 4H), 2.05–2.13 (m, 1H), 2.31–2.64 (m, 3H), 3.80 (s, 3H), 3.92 (s, 1H), 4.74 (d, J = 8.7 Hz, 1H), 6.86–6.90 (m, 2H), 7.22–7.26 (m, 2H).

4-Hydroxyl-4-(4′-nitrophenyl)-butan-2-one[27]
Pale brown viscous oil; [Daicel Chiralpak AS-H column, *n*-hexane/isopropanol = 70 : 30, flow rate 1.0 mL/min, λ = 254 nm; t_R = 15.21 min and 12.05 min (major)]; ^{1}H NMR (300MHz, $CDCl_3$) δ: 2.21 (s, 3H), 2.85–2.80 (m, 2H), 3.56 (br s, 1H), 5.30–5.20 (m, 1H), 7.52 (d, J = 7.0 Hz, 2H), 8.20 (d, J = 7.0 Hz, 2H).

4-Hydroxyl-4-(2′-nitrophenyl)-butan-2-one[27]
Pale brown viscous oil, [Daicel Chiralpak AS-H column, *n*-hexane/isopropanol = 70 : 30, flow rate 1.0 mL/min, λ = 254 nm; t_R = 11.32 min (major) and 8.24 min]; ^{1}H NMR (300MHz, $CDCl_3$), δ: 2.24 (s, 3H), 2.70–2.85 (m, 2H), 3.76–3.70 (br s, 1H), 5.70 (dd, J = 9.3 Hz, 1H), 7.71 (dt, J = 1.2, 8.1 Hz, 1H), 7.44 (dt, J = 1.2, 8.1 Hz, 1H), 7.91 (dd, J = 1.2 Hz, 8.1 Hz, 1H), 7.96 (dd, J = 1.2 Hz, 8.1 Hz, 1H).

4-(2′,4′-dinitrophenyl)-4-hydroxybutan-2-one
Brown viscous oil; [Daicel Chiralpak AS-H column, *n*-hexane/isopropanol = 70 : 30, flow rate 1.0 mL/min, λ = 254 nm; t_R = 16.72 min (major) and 11.46 min]; ^{1}H NMR (300MHz, $CDCl_3$) δ: 2.13 (s, 3H), 3.06–2.79 (m, 2H), 3.65 (br s, 1H), 4.73 (dd, J = 9.3 Hz, 1H), 7.88 (dt, J = 1.2, 8.1 Hz, 1H), 8.53 (dd, J = 1.2, 8.1 Hz, 1H), 8.84 (dd, J = 1.2, 1H).

RESULTS AND DISCUSSION

The preparation of PVDC supported catalysts **1a–c** is outlined in Scheme 1, and **1c**'s exhaustive preparation is explained in the Experimental section.

Screening Catalysts and Solvents for the Asymmetric Aldol Reaction

The catalytic performance of PVDC-supported L-prolineamide derivatives **1a–c** for the direct asymmetric Aldol reaction between cyclohexanone and *p*-nitrobenzaldehyde was examined at a catalyst dosage of 20 mol % and room temperature. Corresponding results are listed in Table I. It can be seen that PVDC-supported L-prolineamide derivatives provide good enantioselectivity but low activity for the Aldol reactions in neat environment (Table I, entries 1, 3, and 9); and they possess high activity but low enantioselectivity in water (Table I, entries 2, 4, and 10). In general, catalyst **1c** in neat environment (Table I, entry 9) shows a much higher activity and a slightly higher selectivity then catalysts **1a** and **1b** therein, but they have similar activity in water. When organic solvents are used, moderate activity is reached, but the selectivity is still low (Table I, entries 5–8). Although L-proline was used as catalyst and water as solvent, the reaction doesn't take place (Table I, entry 11). **1c** shows a little higher enantioselectivity than **1a** and **1b**, maybe the long arm between polymer and L-prolineamide could improve the flexibility of the catalyst chain and the catalyst would integrate

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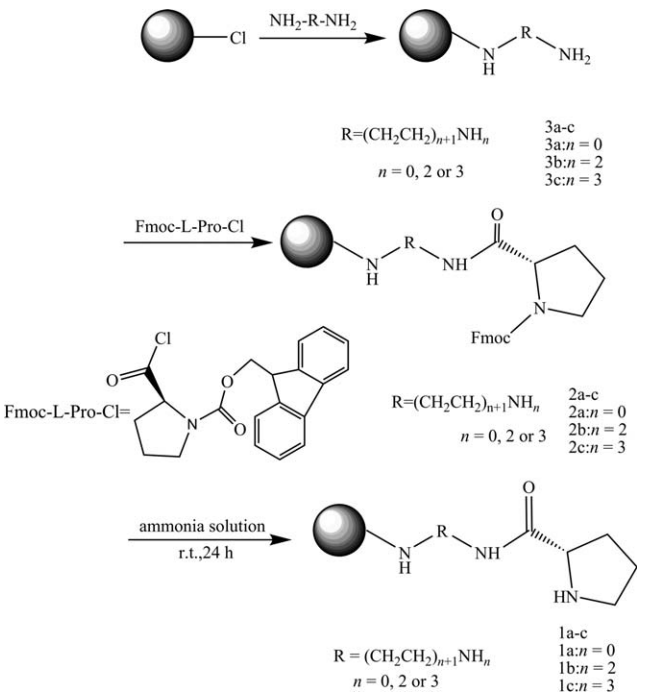


Scheme 1. Synthetic route of the PVDC-supported L-prolineamide catalysts **1a–c**.

the substrates. Therefore, it can be concluded that catalyst **1c** is the most efficient catalyst for the aforementioned asymmetric Aldol reaction.

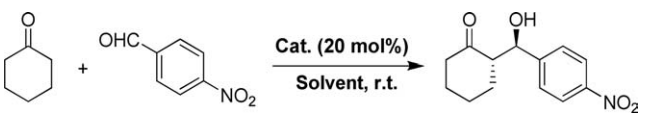
To balance the activity and selectivity, we mixed different amount of catalyst **1c** with different amount of water and examined the catalytic performance of resultant mixtures for the above-mentioned asymmetric Aldol reaction. Corresponding results are shown in Table II. As it can be seen in Table II, the activity keeps almost unchanged but the selectivity significantly rises with decreasing amount of the catalyst and water. Particularly, when 5 mol % catalyst and 10 μL of water are used, the enantioselectivity rises to be nearly the same as that under neat condition, and the activity remains high up to a reaction time of 3 days (Table II, entry 6; yield 99%, d.r. 16 : 84, e.e. 92.3%). This indicates that the enantioselectivity and activity of the catalysts highly depend on the amount of both the catalyst and water. It seems that a larger amount of catalyst lead to a stronger alkalinity as well as a lower selectivity, meanwhile, a larger amount of water result in a stronger activity as well as a lower selectivity. In forthcoming section, the substrate generality was investigated with 5 mol% catalyst **1c** and 10 μL of water was adopted.

Substrate Generality

Under the optimized reaction conditions, the application of polymer-supported L-prolineamide in direct asymmetric intermolecular Aldol reaction between different acceptors and donors was further explored, where a series of aromatic aldehyde acceptors and several ketone donors were examined. Due to the advantages of water as a reaction solvent over organic solvents, such as safety, convenience, economy, and environmental acceptance, it was adopted as the reaction solvent to investigate the substrate generality. Relevant results are summarized in Table III.

As it can be seen in Table III, most of the studied Aldol reactions catalyzed by 5 mol % **1c** in the presence of 10 μL of water afford high yields and good selectivities. When different Aldol donors (cyclohexanone, and acetone) are used, the best result (Table III, entry 1; e.e. 91.6%) is obtained with cyclohexanone as the donor and 3-nitrobenzaldehyde as the acceptor. Particularly, when cyclohexanone is used as the donor, the reactions

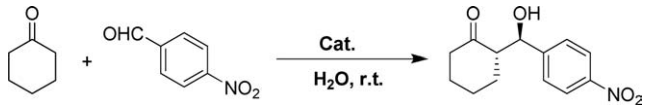
Table I. Screening Catalysts and Solvents for the Asymmetric Aldol Reaction Between Cyclohexanone and *p*-Nitrobenzaldehyde[a]



Entry	Catalyst	Solvent	Time (d)	Yield[b] (%)	d.r.[c] (syn/anti)	e.e.[c] (%) (anti)
1	**1a**	Neat	7	19	25 : 75	89.1
2	**1a**	H_2O	1	98	46 : 54	54.2
3	**1b**	Neat	6	18	31 : 69	89.3
4	**1b**	H_2O	1	99	33 : 67	56.7
5	**1b**	Hexane	7	60	40 : 60	53.9
6	**1b**	Isopropanol	7	44	61 : 39	67.8
7	**1b**	Ethyl acetate	7	40	45 : 55	73.2
8	**1b**	Petroleum ether	7	29	37 : 63	78.5
9	**1c**	Neat	7	31	19 : 81	91.2
10	**1c**	H_2O	1	99	59 : 41	58.7
11	L-Proline	H_2O 100 µL	7	Trace	-	-

[a]Reaction was performed at 0.25 mmol scale of aldehyde, 10 equiv of ketone and 1 mL of solvent in the presence of 20 mol % catalyst, [b]Isolated yield, [c]Determined by chiral HPLC analysis (Chiralpak AD-H).

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



Entry	Amount of catalyst (mmol %)	Amount of water (μL)	Time (d)	Yield[b] (%)	d.r.[c] (syn/anti)	e.e.[c] (%) (anti)
1	20	1000	1	99	59 : 41	58.7
2	10	1000	1	99	47 : 53	61.2
3	10	100	2	99	33 : 67	78.2
4	5	100	2	97	34 : 67	83.8
5	5	50	2	96	27 : 73	89.4
6	5	10	3	99	16 : 84	92.3

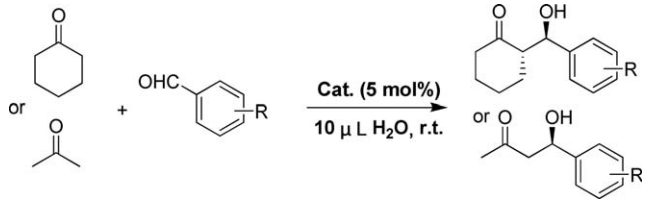
[a]Reaction was performed at 0.25 mmol scale of aldehyde and 10 equiv of ketone in the presence different amount of water and catalyst, [b]Isolated yield, [c]Determined by chiral HPLC analysis (Chiralpak AD-H).

with a series of aldehydes proceed well (Table III, entries 1–7 and entry 11). Thus, it can be concluded that aromatic aldehydes containing electron-withdrawing groups usually afford higher enantioselectivities and yields of the aforementioned asymmetric Aldol reaction, while moderate e.e. is obtained when acetone is used as the donor (Table III, entries 8–10).

Recyclability of Catalyst 1c

The recyclability of catalyst **1c** for the reaction between 4-nitrobenzaldehyde and cyclohexanone was also investigated, where the organic reaction solution was vacuum-filtered through a sintered glass funnel after the reaction was completed, followed by washing successively with ethyl acetate. Recovered catalyst was reused directly without further purification. Relevant recyclability of catalyst **1c** is presented in Table IV. Encouragingly, catalyst **1c** retains good activity and enantioselectivity even after being recycled for five times, showing promising application as an efficient green organocatalyst for the asymmetric Aldol reaction between ketones and aromatic aldehydes.

Table III. Asymmetric Aldol Reaction Between Various Ketones and Various Benzaldehydes Catalyzed by Catalyst **1c**[a]



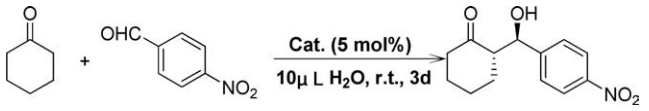
Entry	R	Time (d)	Yield[b] (%)	d.r.[c] (syn/anti)	e.e.[c] (%) (anti)
1	3-NO_2	3	93	8 : 92	91.6
2	2,4-Dinitro	3	97	43 : 57	83.4
3	4-CN	5	78	22 : 78	83.1
4	4-F	7	47	30 : 70	47.9
5	4-Cl	7	45	27 : 73	79.1
6	4-Br	7	36	27 : 73	83.9
7	4-CH_3O	7	18	72 : 28	78.5[d]
8[e]	4-NO_2	3	87	-	63.4
9[e]	2-NO_2	3	86	-	76.5
10[e]	2,4-Dinitro	3	91	-	71.0
11	4-NO_2	3	99	16 : 84	92.3

[a]Reaction was performed at 0.25 mmol scale of aldehyde and 10 equiv of ketone in the presence of 5 mol % catalyst and 10 μL of water, [b]Isolated yield, [c]Determined by chiral HPLC analysis (Chiralpak AD-H or ASH), [d]The value is the e.e. of syn isomerism, [e]0.3 mL acetone was used.

CONCLUSIONS

To sum up, we have developed a series of PVDC-immobilized polyamines, L-prolineamides, as novel highly stereoselective and recyclable organocatalysts for the asymmetric Aldol reaction of ketones to aromatic aldehydes by making use of simple synthetic procedures. As-synthesized PVDC-supported L-prolineamide **1c** is able to catalyze the asymmetric Aldol reaction between cyclohexanone and a variety of aromatic aldehydes with high yields (up to 99%) as well as excellent diastereoselectivities (up to >8 : 92 d.r. value) and enantioselectivities (up to >92.3% e.e. value). Furthermore, catalyst **1c** can be readily recovered and recycled, and it retains good activity and

Table IV. Recyclability of Catalyst **1c** Under the Optimized Conditions[a]



Cycle	Yield[b] (%)	d.r.[c] (syn/anti)	e.e.[c] (%; anti)
1	99	17 : 83	92.3
2	99	16 : 84	91.9
3	97	17 : 83	93.4
4	96	17 : 83	93.1
5[d]	98	16 : 84	92.8

[a]Reaction was performed at 0.25 mmol scale of aldehyde and 10 equiv of ketone in the presence of 5 mol % catalyst and 10 μL of water, [b]Isolated yield, [c]Determined by chiral HPLC analysis (Chiralpak AD-H), [d] Reacted for 5 days.

enantioselectivity even after five cycles of recovery, showing promising application as an efficient green organocatalyst for the asymmetric Aldol reaction between ketones and aromatic aldehydes.

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