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Synthesis and asymmetric catalytic performance of one-handed helical poly (phenylacetylene)s bearing proline dipeptide pendants

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ABSTRACT

One-handed helical substituted polyacetylene has received extensive attention due to its potential in chiral stationary phases and molecular recognition. Here, three one-handed helical poly(phenylacetylene)s bearing proline or proline dipeptide as the pendants (**PPA-Pro, PPA-Pro-Pro and PPA-Pro-Hyp**) were synthesized. As the catalyst, the three helical polymers separately catalyzed the asymmetric aldol reaction of acetone with *p*-nitrobenzaldehyde in a various media. The results indicate that **PPA-Pro-Pro and PPA-Pro-Hyp** bearing dipeptide pendants showed the higher catalytic activity and enantioselectivity than the **PPA-Pro** bearing proline pendants and the corresponding monomer catalysts. This indicates the synergistic effect of the dipeptide pendants with the one-handed helical mainchain of the polymer catalyst. The polymer catalysts can be recycled and maintain the catalytic performance after four circles. When imidazole was added to the reaction system, the reaction yield could be efficiently improved without affecting the enantioselectivity.

1. Introduction

Chirality is an asymmetric property of matter and one of the basic properties in nature. Both macroscopic substances and microscopic biological molecules are generally chiral, and the study on the natural properties of biological chiral molecules is conducive to the artificial synthesis of chiral drugs [1]. Although the pairs of enantiomeric compounds have very similar physical and chemical properties to each other, they behave differently in biology, because the function of biomolecules such as nucleic acids and proteins is determined by their helical structure, which is an important factor to show biological activity [2,3]. Inspired by the exquisite helical structures of the biomacromolecules, wide studies have been conducted on the synthesis of non-biological helical polymers [4–9], such as polymethyl methacrylate and polymethylacrylamide [10,11], polyisocyanate [12,13], polysilane [14], polyolefin [15], polyacetylene and its derivatives [16]. Among these helical polymers, as a typical dynamic helical polymer, poly (substituted acetylene)s attract broad attention due to its potential in the fields such as chiral recognition [17], chiral separation [18], and catalytic asymmetric reactions [19]. Deng synthesized a series of optically active poly(substituted acetylene)s bearing different chiral pendants, which are utilized to catalyze asymmetric Michael reaction and aldol reaction and show considerable enantioselectivity [20–23]. Yashima reported one-handed helical poly(substituted acetylene)s bearing cinchona alkaloid pendants, the asymmetric aldol reactions are catalyzed by the helical poly(substituted acetylene)s and shows the higher ee values than the corresponding monomer catalysts [19]. The one-handed helical main chain in these helical polymers is thought to form synergistic effect with the chiral pendants, which plays important roles in the improvement on enantioselectivity of these asymmetric reactions. Therefore, developing polymer catalyst having one-handed helical structure is one of important fields for asymmetric synthesis.

The formation of the carbon-carbon bonds occupies an important position in the field of asymmetric catalytic. Aldol reaction is one of simple methods in producing carbon - carbon bonds. Generally, reaction conditions for the asymmetric catalytic reaction are very sensitive, some minor structural differences can lead to unexpected changes. Therefore, the research of the relationship between the structure and the catalytic performance of the catalysts is of great importance for constructing chiral compounds. Proline, as a kind of natural small molecule, is widely used in asymmetric catalysis. However, proline-derivative catalyst has the common short comings as many small molecular catalysts, it is difficult to recover and reuse. In order to solve these problems, immobilized or polymer-supported catalyst is a general

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method. However, in these polymer-supported catalysts, the polymer merely as a carrier, and cannot improve the catalytic performance. Further research was reported that the polymer catalyst was designed as a helical conformation to simulate the structure of the enzyme [24], and then synergistic effect of the helical conformation with the small chiral ligand improved the catalytic efficiency and enantioselectivity.

Dipeptides are the simplest peptides that consist of two identical or different amino acids. Compared with a single amino acid, dipeptides can form a large number of hydrogen bonds when forming a helical polymer, which is conducive to the stability of the polymer. At the same time, dipeptides have two chiral centers, which can increase the selectivity of asymmetric reactions [25]. Therefore, in this study, proline or its dipeptide derivatives were introduced into the side chains of the helical poly(phenylacetylene)s to produce the helical polymeric catalysts, catalytic properties of the helical polymeric catalysts on the aldol reaction of acetone with 4-nitrobenzaldehyde were systematically investigated.

2. Experimental

2.1. Materials

Fmoc-L-proline (purity 99%), Fmoc-L-hydroxyproline (purity 99%), Fmoc-L-Proline dipeptide (purity 99%), cyclohexanone (purity99%) and *p*-nitrobenzaldehyde (purity 98%) were purchased from Aladdin Chemical Co., Ltd. (Shanghai, China). Morpholine (purity 99%) and 4-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMT-MM) (purity 98%) was purchased from Sahn Chemical Technology Co., Ltd. (Shanghai, China). Triphenylphosphine (purity 99%) was purchased from J&K Chemical Co., Ltd. (Beijing, China). Rh(nbd)BPh_4 was prepared based on a previous report [26]. All solvents used in the reactions were of analytical grade, carefully dried, and distilled before use. Silica gel with a mean particle size of 37–56 μm for column chromatography was purchased from Qingdao Haiyang Chemical Co., Ltd. (Qingdao, China).

2.2. Instruments

The ^{1}H NMR spectra (500 MHz) were recorded using a Bruker AVANCE III-500 instrument at room temperature. IR spectra were obtained with a Perkin-Elmer FTIR-100 spectrophotometer. The circular dichroism (CD) and ultraviolet visible (UV − vis) spectra were measured in a 1-mm path length cell using a JASCO *J*-815 spectropolarimeter. The absolute configuration of aldol products was determined by JASCO PU-2089 high performance liquid chromatograph (HPLC) system equipped with UV − vis (JASCO-UV-2070), circular dichroism (JASCO-CD-2095) detectors and a column of DAICEL CHIRALCEL AS-1 using a solution of hexane/2-propanol as eluent at a flow rate of 1.0 mL min^{-1} according to the literature [27]. A solution of aldol product (3.00 mg mL^{-1}) was injected into the chromatographic system through an intelligent sampler (JASCO AS-2055).

2.3. Synthesis of the polymer catalysts

The polymer catalysts were synthesized according to the route shown in Scheme 1 and S1 in the supporting information. The precursor polymers were deprotected to produce the corresponding polymer catalysts. The typical deprotection procedure is described as below. **PPA-Pro**, for example. Morpholine (6.00 mL) was added to a solution of precursor polymer (1.33 mmol) in DCM (6.00 mL), and the resulting mixture was stirred at room temperature for 10 h. Then, the mixture was precipitated in methanol, after filtration and dried in vacuo at room temperature overnight, the polymer catalyst was obtained.

(1) **PPA-Pro** is a yellow powder. (0.18 g, 71.20%) ^{1}H NMR (500 MHz, DMSO-d_6, δ): 1.98–2.22and 2.89–3.31 (m, 4H, CH_2), 4.17–5.25 (m, 4H, CO-CH, CH_2, NH), 5.58 (s, 1H, H-C ≡ C), 7.12–7.78 (m, 4H, Ar—H), 9.98 (s, 1H, NH-CO). IR (KBr): ν = 3346 (w), 3103 (w), 3099 (w), 3039 (w), 1705 cm^{-1} (s).

(2) **PPA-Pro-Pro** is a yellow solid. (0.29 g, 89.30%) [1]HNMR (500 MHz, DMSO-d_6, δ): 1.67–2.37 (m, 9H, CH_2, NH), 2.86–3.12 (m, 2H, CH_2), 4.07–4.51 (m, 4H, CH-CO, CH_2), 5.80 (s, 1H, H-C ≡ C), 6.62–7.35 (m, 4H, Ar—H), 10.20 (s, 1H, NH-CO). IR (KBr): ν = 3335 (w), 3104 (w), 3048 (w), 3036 (w), 1705 cm^{-1} (s).

(3) **PPA-Pro-Hyp** is a yellow solid. (0.27 g, 87.40%) ^{1}H NMR (500 MHz, DMSO-d_6, δ): 1.84–2.14 (m, 6H, CH_2), 3.60–4.50 (m, 9H, CH-CO, CH_2, OH, NH), 5.73 (s, 1H, H-C ≡ C), 6.56–7.65 (m, 4H, Ar—H), 9.99 (s, 1H, NH-CO). IR (KBr): ν = 3303 (w), 3295 (w), 3183 (w), 3104 (w), 3064 (w), 1697 cm^{-1} (s).

2.4. Aldol reaction of acetone with p-nitrobenzaldehyde

Acetone and a solvent were added to a flusk containing *p*-nitrobenzaldehyde and the catalyst, and then the mixture was stirred at a set temperature. The reaction was quenched with brine, and the product was extracted with dichloromethane and saturated ammonium chloride solution. The organic extract was dried over anhydrous Na_2SO_4 and then concentrated by evaporation. The residue was purified by column chromatography (SiO_2, petroleum ether/ethyl acetate = 2/3 *v*/v) to give product as a yellow solid. The *ee* was determined by chiral HPLC analysis (Chiralpak AS-1 column, hexane/isopropanol 95/5, v/v, 1.0 mL min^{-1}, λ = 254 nm), tR = 50.19 min, tS = 76.26 min.

3. Results and discussion

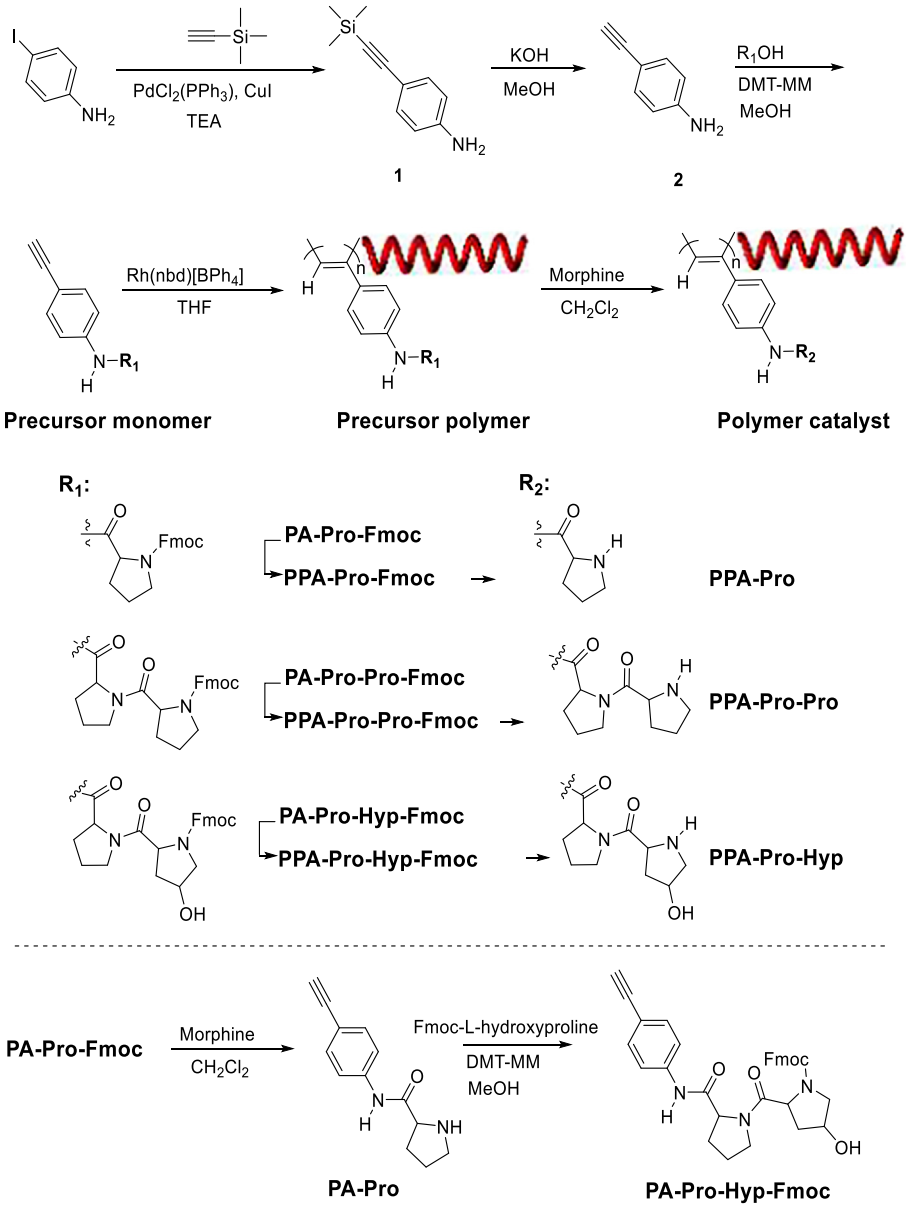
3.1. Synthesis of one-handed helical poly(phenylacetylene) catalyst

Three phenylacetylene precursor monomers having a protected proline or proline dipeptide group were synthesized and then polymerized by a Rh catalyst (Rh(nbd)BPh_4) to produce the corresponding polymer precursors. (Scheme 1, **PPA-Pro**-Fmoc, **PPA-Pro-Pro**-Fmoc and **PPA-Pro-Hyp**-Fmoc) Then, the deprotection reaction of the precursors produced the corresponding polymer catalysts, **PPA-Pro** having proline as pendants, **PPA-Pro-Pro** having proline dipeptide as the pendants and **PPA-Pro-Hyp** having proline-hydroxyproline dipeptide as the pendants (Scheme 1) [28–31].

Solubility of the polymers and their precursors was tested at room temperature (Table 1). Although the precursors showed good solubilities in most organic solvents, the resulting polymeric catalysts showed poor solubility in organic solvent and were merely soluble in high polar solvent, such as DMSO, DMAc and methanol. It was thought to be due to that after removing the protective groups, the steric resistance of the polymer side chains is reduced, and the exposed amino group form the intramolecular hydrogen bonds which reduced the solubility of the polymer.

3.2. Chiroptical properties of the synthesized poly(phenylacetylene) derivatives

The specific optical rotation ($[\alpha]_D^{20}$) of the polymer catalysts (**PPA-Pro**, **PPA-Pro-Pro** and **PPA-Pro-Hyp**) and their monomers (PA-Pro, PA-Pro-Pro and PA-Pro-Hyp) were separately measured at room temperature. The$[\alpha]_D^{20}$ values of the polymer catalysts are very different from those of the corresponding monomers. The sign of **PPA-Pro**'s optical rotation is opposite to its monomer PA-Pro $[\alpha]_D^{20} = -42$ (c = 1 mg mL^{-1} in DMSO), **PPA-Pro**$[\alpha]_D^{20} = +4$ (c = 1 mg mL^{-1} in DMSO); and **PPA-Pro-Pro** and **PPA-Pro-Hyp** show the larger absolute $[\alpha]_D^{20}$ values than their monomers, for instance, PA-Pro-Pro $[\alpha]_D^{20} = -143$(c = 1 mg mL^{-1} in MeOH) and **PPA-Pro-Pro** $[\alpha]_D^{20} = -176$(c = 1 mg mL^{-1} in MeOH); PA-Pro-Hyp $[\alpha]_D^{20} = -70$ (c = 1 mg mL^{-1} in DMSO) and **PPA-Pro-Hyp** $[\alpha]_D^{20} = -234$ (c = 1 mg mL^{-1} in DMSO). The difference in $[\alpha]_D^{20}$ value of the



Scheme 1. Synthesis of poly(phenylacetylene) bearing L-proline or proline dipeptide pendants

Table 1
Solubility of the synthesized polymers in different solvents.

Polymer	Solvent							
	$CHCl_3$	DCM	THF	DMF	DMSO	DMAc	MeOH	H_2O
PPA-Pro-Fmoc	+ +	+ +	+ +	+ +	+	+ +	−	−
PPA-Pro	−	−	−	+	+ +	+	−	−
PPA-Pro-Pro-Fmoc	+ +	+ +	+ +	+	+	+	−	−
PPA-Pro-Pro	−	−	−	−	−	−	+ +	−
PPA-Pro-Hyp-Fmoc	+ +	+ +	+ +	+ +	+	+ +	−	−
PPA-Pro-Hyp	−	−	−	−	+	−	+ +	−

Note: + +: soluble(completely soluble under 1 mg mL^{-1}); +: slightly soluble (partly soluble under 1 mg mL^{-1});-: insoluble.

polymer catalyst from the corresponding monomer might due to some reasons, such as the structure change from a monomer to a polymer; the formed helical main chain; and the chiral spatial position of the chiral pendants aggregated along with the main chain.

CD spectra of the polymer catalysts were measured together with their precursors. (Fig. 1 and FIG. S19) Both the polymer catalysts and the precursor polymers showed the clear the split-type Cotton effects in the range from 300 to 500 nm, which indicates that all the polymers take one-handed helical structure in the main chain. **PPA-Pro** showed the similar CD signals in DMSO, DMF and DMAc, (Fig. 1A) the first positive Cotton effect at 380 nm and the second negative Cotton effect at 335 nm. The methanol solution of **PPA-Pro-Pro** showed the first negative Coton effect at 430 nm and the second positive Coton effect at 360 nm. (Fig. 1B) **PPA-Pro-Hyp** showed the first negative Cotton effect at 380 nm and the second positive Cotton effect at 335 nm in DMSO, (Fig. 1C) it is interesting that the CD profile of **PPA-Pro-Hyp** in methanol was nearly mirror image of that found in DMSO, which indicates the opposite helix sense of **PPA-Pro-Hyp** in DMSO and methanol. Compare to the CD signal of the corresponding precursor polymers, (FIG. S19) after removing the protective Fmoc groups in the precursors, the CD signals of the resulting polymer catalysts weakened, which might be due to the removal of the protective groups caused the hydrogen bonding between the adjacent side chains.

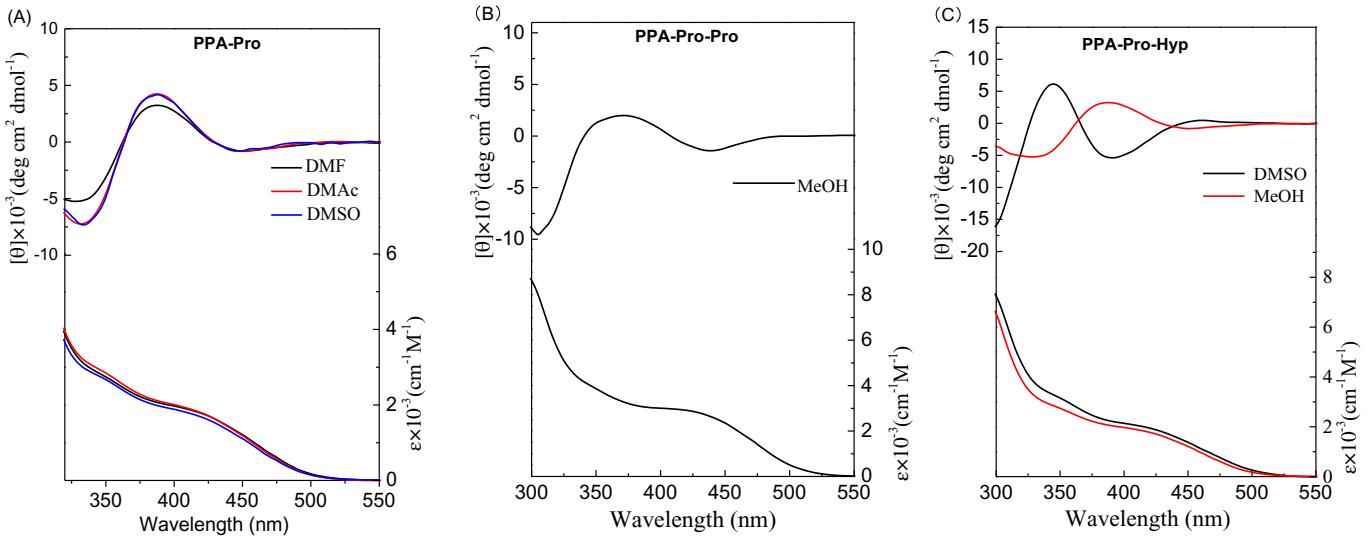


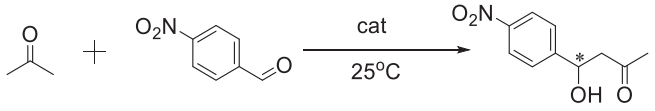
Fig. 1. CD (up) and UV–vis (down) spectra of the polymer catalysts at different solvents. (c = 1 mg mL^{-1}).

3.3. Asymmetric catalytic performance of the helical poly(phenylacetylene) catalyst

Asymmetric aldol reactions of acetone with *p*-nitrobenzaldehyde were separately catalyzed by the helical polymer catalysts, the results were compared to those catalyzed by the monomer catalyst (Table 2). The influences of the solvent on the reaction were investigated by conducting the reaction in different solvents (H_2O, DMF, DMSO, methanol and Toluene). The results show that all the catalysts successfully catalyzed the reaction and showed the certain enantioselectivity in H_2O, DMF, DMSO, MeOH and Toluene, (Table 2) the maximum enantioselectivity (*ee* = 34%) was realized in DMF and DMSO (Table 2, entry 7–8). It was found that the polymer having the dipeptide pendants (**PPA-Pro-Pro** and **PPA-Pro-Hyp**) showed the higher enantioselectivity and yield than the corresponding monomer catalysts, however, the enantioselectivity and yield of **PPA-Pro** having proline as the pendants are lower than those of the monomer catalyst and the polymer having the dipeptide pendants (**PPA-Pro-Pro** and **PPA-Pro-Hyp**). (Table 2) These indicate that the dipeptide pendants and the helical mainchain induced by the dipeptide pendants in **PPA-Pro-Pro** and **PPA-Pro-Hyp** could form the synergistic effect to improve the catalytic efficiency and enantioselectivity. However, compare to the corresponding monomer catalyst, the enantioselectivity and yield of **PPA-Pro** are similar or lower, which suggested that the proline pendants in **PPA-Pro** could not form the synergistic effect with the its helical mainchain.

The influence of solvent on the enantioselectivity and yield were summarized in Table 2 and Fig. 2. It was found that the polymer catalysts had the better enantioselectivity and acceptable yield in high polar aprotic solvents, such as DMF and DMSO. It might be due to that the high polar aprotic solvent could relax the intramolecular hydrogen bonds between the side chains in the polymer and improve the synergistic effect between the pendants and the helical mainchain. The

Table 2
The aldol reaction of acetone with *p*-nitrobenzaldehyde catalyzed by the monomer catalyst and helical polymer catalysts in different solvents[a].



Entry	Time (d)	Solvent	Monomer catalyst			Polymer catalyst		
			Catalyst	Yield[b] (%)	*ee* [c] (%)	Catalyst	Yield[b] (%)	*ee* [c] (%)
1	3	H_2O	PA-Pro	56	13	PPA-Pro	69	7
2	7	DMF		25	19		13	17
3	7	DMSO		13	32		13	15
4	7	MeOH		25	12		35	14
5	7	Toluene		18	11		24	9
6	3	H_2O	PA-Pro-Pro	40	3	PPA-Pro-Pro	75	3
7	7	DMF		27	17		52	34
8	7	DMSO		23	19		52	34
9	7	MeOH		20	7		33	17
10	7	Toluene		21	9		23	10
11	3	H_2O	PA-Pro-Hyp	45	6	PPA-Pro-Hyp	67	6
12	7	DMF		28	25		48	27
13	7	DMSO		20	28		47	33
14	7	MeOH		22	11		38	12
15	7	Toluene		17	13		55	13

[a] The reaction was performed with *p*-nitrobenzaldehyde (0.3 mmol), acetone (3.0 mmol), catalyst (0.09 mmol) and DMSO (1.0 mL) at 25 °C.
[b] Isolated yields.
[c] For R enantiomer, determined by chiral HPLC analysis (Chiralpak AS-1) with hexane/isopropanol (95/5, v/v) as the eluent.

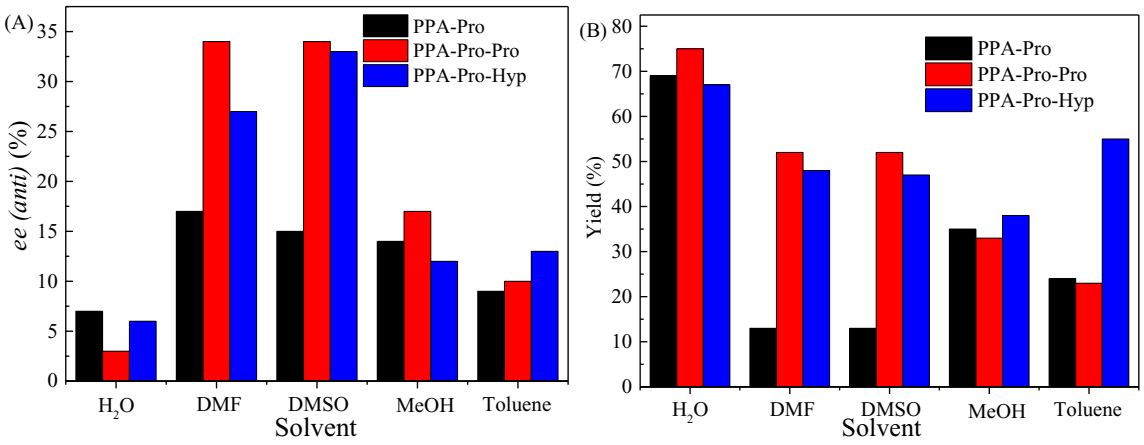


Fig. 2. The *ee* value (A) and yield (B) of the aldol reactions of acetone with *p*-nitrobenzaldehyde catalyzed by the helical polymer catalyst in different solven.

protic solvent can form strong intermolecular hydrogen bonds with the polymer and it might disturb the synergistic effect between the pendants and the helical mainchain. For instance, **PPA-Pro-Hyp** showed the opposite helical sense in aprotic DMSO and protic methanol (Fig. 1C), the enantioselectivity in methanol was much lower than that in DMSO (Table 2). It was thought that methanol form strong intermolecular hydrogen bonds with **PPA-Pro-Hyp** and make **PPA-Pro-Hyp** take an opposite helical sense to that in DMSO, and the opposite helical sense of the mainchain could not form synergistic effect with the dipeptide pendants. As a result, the synergistic effect between the chiral pendants and the helical mainchain on the asymmetric aldol reaction was found in the polymer catalyst having proline dipeptide pendants; the aprotic high polar solvent could improve the enantioselectivity and catalytic efficiency of the helical polymer catalyst. Therefore, DMSO was selected as the solvent for the reaction.

The reaction in H_2O showed the highest yield, however, the enantioselectivity in H_2O is very poor. This was thought to be due to the water-accelerating effect in the proline-catalyzed aldol reaction according to the reports by Pihko [32,33] and Amstrong [34]. The generally accepted enamine mechanism of the reaction is shown in Fig. 3. In which, the ketone forms iminium intermediate with proline residue, then the iminium converts to enamine to proceed the catalytic cycle. However, in the absence of water, the aldehyde can also reacted with proline to produce an off-cycle iminium ions (FIG. S22) [34], which

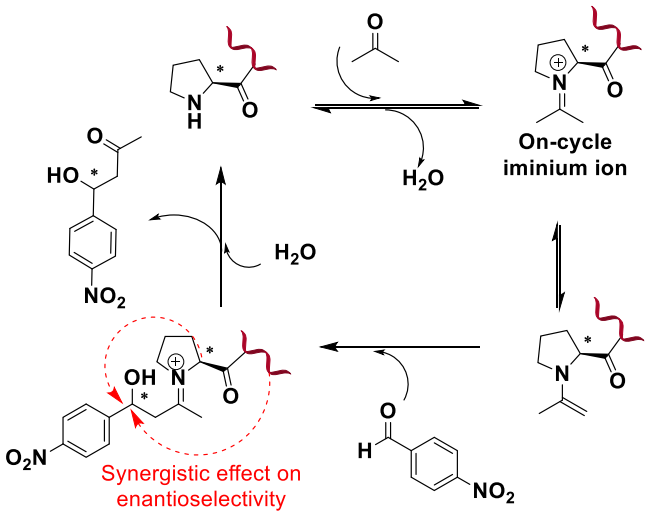


Fig. 3. Proposed catalytic cycle for aldol reaction catalyzed by poly(phenylacetylene)s bearing proline residues.

decreases the total catalyst concentration. Addition of water suppresses formation of off-cycle iminium ions, and increases the total catalyst concentration within the cycle, therefore, water accelerate the reaction and give the higher yields.

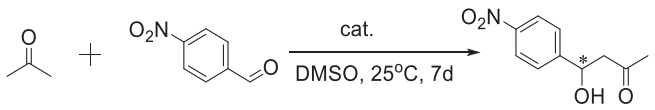
In addition, the CD spectra of PPA-Pro-Pro in methanol/water were measured as shown in FIG. S23, the CD intensity shows a downward trend along with the increase of the water content in the system, which indicate addition of water caused the decrease in helical preference of the polymer. This is consistence with the trend that the ee values of the reactions decreased with the increase of water content in methanol/water system (TABLE S1). The monomer-catalyzed reactions were conducted in water as the control, the obtained ee values are very poor and similar to those of the reactions catalyzed by polymer catalysts in high water content system (TABLEs S1 and 2). These indicate that the water molecules disturb the helical structure of the polymers and decrease the synergistic effect between the pendants and the helical mainchain so as to cause the low ee values of the reactions in water.

Then the effects of the amount of the polymer catalyst on the aldol reaction was investigated in DMSO. (Table 3) For **PPA-Pro**, increasing the catalyst amount in the reaction clearly improved the reaction yield and enantioselectivity, although the maximum values are not high (Table 3). Increasing the catalyst amount also improved the yields of reactions catalyzed by **PPA-Pro-Pro** or **PPA-Pro-Hyp**, and slightly increased the enantioselectivity of the reactions. In the case of **PPA-Pro-Pro**, when the catalyst amount ([catalyst]/[*p*-nitrobenzaldehyde] × 100%) was 25 mol%, both the enantioselectivity and the yield the reaction reached the highest value (58% and 38%, respectively, Table 3, Entry 4). In the case of **PPA-Pro-Hyp**, the suitable catalyst amount is 20 mol%, the yield and enantioselectivity reached 58% and 39%, respectively.

Additives have a certain impact on asymmetric catalytic effect, and some additives can form a co-catalytic effect with the catalyst. As a cocatalyst, imidazole can be combined with a variety of catalysts to achieve high yield and *ee* value. For instance, without imidazole, the **PPA-Pro-Hyp** catalyzed reaction needs 7 days and afforded the yield of 47% and the ee of 33% (Table 4, Entry 7); adding 10 mol% of imidazole in the system shortened the reaction time to 3 days and afforded the higher yield of 69%. Meanwhile, the enantioselectivity of the reaction was well maintained, *ee* values before and after adding imidazole in the reaction were 33% and 34%. In the cases of the other two polymer catalysts, adding imidazole showed the similar acceleration effects on the reaction. These results indicate that imidazole is an efficient cocatalyst for this asymmetric reaction.

The acceleration by imidazole might due to that imidazole affects the outcome of the enamine-forming step. The imidazole was thought to interact with the α-proton in the iminium intermediate and make the equilibrium shift to forming enamine (Fig. 4). As reported by Houk, the

Table 3
Effect of the amount of the polymer catalysts on the aldol reaction of acetone with *p*-nitrobenzaldehyde[a].



Entry	Catalyst (mol%)[d]	PPA-Pro		PPA-Pro-Pro		PPA-Pro-Hyp	
		Yield (%)[b]	*ee*[c] (%)	Yield(%)[b]	*ee*[c] (%)	Yield(%)[b]	*ee*[c] (%)
1	10	13	15	52	34	47	33
2	15	14	14	58	34	44	35
3	20	18	17	57	37	58	39
4	25	21	20	58	38	46	35
5	30	27	17	54	33	48	35

[a] The reaction was performed with *p*-nitrobenzaldehyde (0.3 mmol), acetone (3.0 mmol), catalyst and DMSO (1.0 mL) at 25 °C. Reaction time was 7 days.
[b] Isolated yields.
[c] For *R* enantiomer, determined by chiral HPLC analysis (Chiralpak AS-1) with hexane/isopropanol (95/5, *v*/v) as the eluent.
[d] [Catalyst]/[*p*-nitrobenzaldehyde] × 100.

transition state leading to the enamine is approximately equal in energy to the aldol addition step. [35] Therefore, adding imidazole in the proline-catalyzedaldol reaction was thought to be favorable for enamine formation so as to accelerate the reaction.

As mentioned above, the solubility of the helical polymer catalysts is poor in most organic solvents; therefore, these polymer catalysts may be easily recovered from the reaction mixture by filtration or centrifuge. Hence, the recyclability of the polymer catalysts was investigated and the results were summarized in Table 5. It was found that for all the polymer catalysts, the yield and the enantioselectivity of reaction did not show clear change even after four cycles, which indicate the polymer catalysts well maintained their reactivity and selectivity after recycle, i.e., the polymer catalysts have the good recyclability.

4. Conclusions

Three one-handed helical poly (phenylacetylene)s separately bearing proline (**PPA-Pro**), proline-proline dipeptide (**PPA-Pro-Pro**) and proline-hydroxyproline dipeptide (**PPA-Pro-Hyp**) as the pendants were successfully synthesized. The Cotton effect patterns of the polymer significantly affected by the solvent. The resulting three polymers were separately utilized as the catalyst to catalyze the asymmetric aldol reaction of acetone with *p*-nitrobenzaldehyde in a various media. **PPA-Pro-Pro** and **PPA-Pro-Hyp** bearing dipeptide pendants showed the higher catalytic activity and enantioselectivity than the **PPA-Pro** bearing proline pendants. The catalytic activity and enantioselectivity of **PPA-Pro-Pro** and **PPA-Pro-Hyp** were also higher than the corresponding monomer catalysts at the same condition indicating the synergistic catalyze effect of the dipeptide pendants with the one-handed helical mainchain of the polymers for the reaction. Adding imidazole could efficiently accelerate the aldol reaction and afford the higher yields without the decrease in enantioselectivity. All the polymer catalysts showed good recyclability, the catalytic activity and enantioselectivity of the catalysts were well maintained even after 4 cycles.

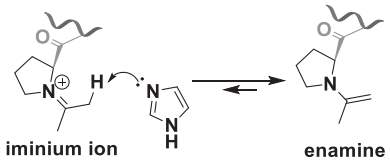
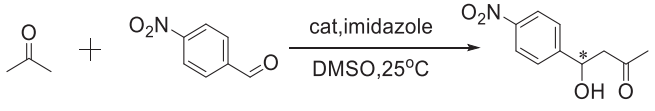


Fig. 4. Possible effect of imidazole on the enamine forming step of the proline-catalyzed aldol reaction.

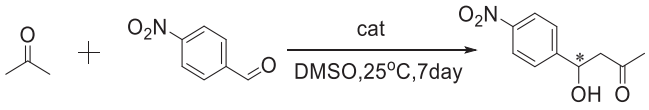
Table 4
The aldol reaction of acetone with *p*-nitrobenzaldehyde catalyzed by the helical polymer catalyst with the assistance of imidazole[a].



Entry	Catalyst	Imidazole (mol %)[d]	Time (d)	Yield (%)[b]	*ee*[c] (%)
1	PPA-Pro	0	7	33	15
2		5%	4	41	15
3		10%	3	64	15
4	PPA-Pro-Pro	0	7	52	34
5		5%	4	64	33
6		10%	3	77	31
7	PPA-Pro-Hyp	0	7	47	33
8		5%	4	58	33
9		10%	3	69	34

[a] The reaction was performed with *p*-nitrobenzaldehyde (0.3 mmol), acetone (3.0 mmol), catalyst (0.075 mmol) imidazole and DMSO (1.0 mL) at 25 °C.
[b] Isolated yields.
[c] For R enantiomer, determined by chiral HPLC analysis (Chiralpak AS-1) with hexane/isopropanol (95/5, *v*/v) as the eluent.
[d] [IMIDAZOLE]/[*p*-nitrobenzaldehyde] × 100%.

Table 5
Recyclability of the helical polymer catalysts for the aldol reaction of acetone with *p*-nitrobenzaldehyde[a].



Entry	Catalyst	Yield (%)[b]	*ee*[c] (%)
1	PPA-Pro	13[c]	15
2	(cycle 1)	10	16
3	(cycle 2)	12	15
4	(cycle 3)	17	15
5	(cycle 4)	13	14
6	PPA-Pro-Pro	52	34
7	(cycle 1)	49	33
8	(cycle 2)	51	34
9	(cycle 3)	54	34
10	(cycle 4)	52	34
11	PPA-Pro-Hyp	47	33
12	(cycle 1)	43	33
13	(cycle 2)	46	31
14	(cycle 3)	47	30
15	(cycle 4)	44	33

[a] The reaction was performed with p-nitrobenzaldehyde (0.3 mmol), acetone (3.0 mmol), catalyst (0.075 mmol) and DMSO (1.0 mL) at 25 °C. Reaction time was 7 days.
[b] Isolated yields.
[c] For R enantiomer, determined by chiral HPLC analysis (Chiralpak AS-1) with hexane/isopropanol (95/5, v/v) as the eluent.

Data availability

The raw/processed data required to reproduce these findings cannot be shared at this time due to legal reasons.

Declaration of Competing Interest

The authors have no competing interests to declare

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.reactfunctpolym.2019.104392.

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