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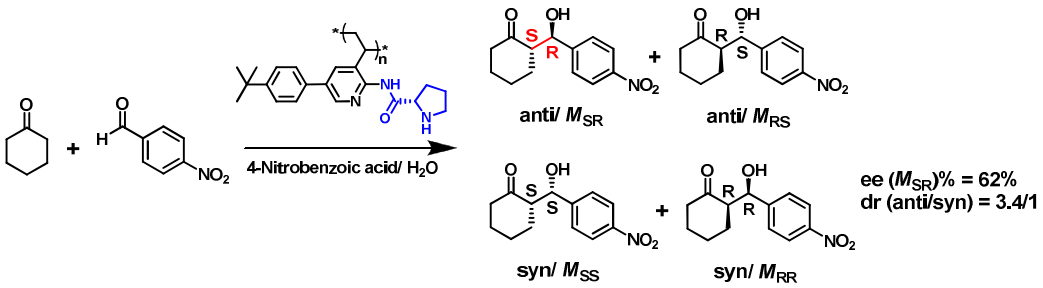

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ARTICLE TYPE

Synthesis and Property of Novel Helical 3-Vinylpyridine Polymers Containing Proline Moieties for Asymmetric Aldol Reaction

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Novel optically active polymers containing pendant proline moieties, poly{(−)-L- and (+)-D-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide}, were prepared through radical polymerization of (−)-L- and (+)-D-*N*-Boc-proline-[5-(4'-tert-phenyl)-3-vinyl- pyridin-2-yl]amide, followed by de-protection of Boc group. Polarimetry and circular dichroism spectroscopy studies indicated that these polymers took chiral secondary structures. They were employed to catalyze the homogeneous asymmetric aldol reaction of 4-nitrobenzaldehyde with cyclohexanone ~~in bulk~~. The polymeric catalysts showed obviously enhanced reaction rate but slightly shrunken enantio-selectivity compared with (−)-L- and (+)-D-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide, the low molar mass counterparts. The lowered enantio-selectivity of polymeric catalyst might be attributed to the antagonistic action of configurational chirality of side-group and conformational chirality of polymer backbone on the stereochemistry of aldol reaction.

Introduction

Asymmetric catalysis has drawn increasing attentions for its outstanding ability to produce enantiomerically rich or even pure compounds.[1, 2] As a result, it is considered as the heart part of contemporary organic chemistry and has found remarkable practical and potential applications in medicine, pesticide and perfume industry.[3] Asymmetric aldol catalysis is one of the most powerful and widely applied C–C bond forming transformation to afford β-hydroxyketones with one or two new stereocenters by combining two molecules of carbonyl compounds.[4] Among many aldolases, proline and its derivatives are the simplest but most effective, successful and commonly employed class of catalysts, that catalyze a great number of aldol reactions with excellent yield and high enantio-selectivity.[5-8] Apart from aldolization, proline and its derivatives via enamine catalysis are widely utilized in asymmetric Mannich reactions,[9-11] Michael reactions,[12-14] D–A reactions,[15-17] and α-aminations.[18, 19] Moreover, their nitrogen dioxides are used as organocatalysts or the chiral ligands of organometallic catalyst in various asymmetric transformations,[20] including α-chlorinations,[21] cycloadditions,[22] Roskamp-Feng reactions,[23] Friedel-Crafts reactions,[24] homologations of carbonyl compounds,[25] Ene[26] and Aza-Ene reactions.[27]

In order to facilitate the recyclability and reduce the cost, great efforts have been made to tether proline-based small molecule catalysts onto polymer matrix.[28] The most commonly used polymeric matrix includes commercially available polymers, such as polystyrene,[29-31] polyethylene glycol,[32] and polymethyl methacrylate.[33-37] In most cases, proline moieties are introduced to the polymer backbone through long and flexible spacers. Such a macromolecular design has the advantage to avoid or reduce the adverse influence of polymer backbone on catalytic property. Recently, the effect of the micro-environment given by polymer matrix on the reactivity and stereo-selectivity of the catalyst attracts more and more attention. Some well-defined polymer aggregates, which could be switched by solvent,[31] pH,[34] and temperature,[35, 36] were prepared to promote aldol reaction performance. Dendrimers instead of linear or cross-linked polymers were also used as the matrix to immobilize aldolases.[38, 39] Especially, some helical polymers with one-prevailing handedness are found to significantly enhance the enantio-selectivity by the resemblance to enzymes.[40-43] Sanda and co-workers bonded trans-4-hydroxy-L-proline to poly(phenylacetylene)s via ester bonds and found the resultant polymers yielded the aldol reaction adducts with opposite configurations to their lower molar mass counterparts.[44] Deng et al introduced L-proline to polyacetylenes through amide groups and achieved good enantio-selectivity.[45]

Our group developed a novel type helical vinyl polymers containing laterally attached biphenyl or p-terphenyl groups terminated by chiral alkyloxy or alkyloxycarbonyl groups, whose helical conformations are driven and stabilized by the steric repulsive interaction of bulky side chains.[46-53] These polymers display interesting "chiral memory effect",[46] "odd-even effect",[48-50] and remarkable chemical and physical stability. They can even be conveniently prepared via free radical polymerization. These characteristics enable them to act as chiral scaffolds to asymmetrically position function groups in space around polymer backbone and find wide potential applications such as asymmetric catalysis and chiral recognition.

The present work aimed to devise a novel kind of polymer catalyst consisting of proline as a "privileged framework" and conformational specific helical polymer as a linker to build a macro "chiral environment". To this end, a pair of optically active

helical polymers, poly{(−)-L- and (+)-D-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide} were synthesized and characterized by polarimetry and circular dichroism (CD) spectroscopy. They were applied as catalysts of asymmetric aldolization of cyclohexanone with 4-nitrobenzaldehyde. Various amount of water and organic acids were added to optimize reaction condition. Compared with their low molar mass counterparts, polymeric catalysts showed obviously faster reaction rate but slightly lower enantio-selectivity, implying an antagonistic effect on aldol reaction stereochemistry of configurational and conformational chirality originated from side-groups and polymer backbone, respectively.

Experimental Section

Materials.

2-Amino-3-methyl-5-bromopyridine (97%, Alfa Aesar), phthalic anhydride (AR, Beijing Chemical Co.), tetrachloromethane (CCl_4, AR, Beijing Chemical Co.), *N*-bromosuccinimide (NBS, 99%, Aldrich), triphenylphosphine (PPh_3, 99%, Acros), hydrazine hydrate (85%, Sinopharm Chemical reagent Co.), aqueous formaldehyde solution (40%, AR, Beijing Chemical Co.), 4-*tert*-butylphenylboronic acid (98%, J&K Scientific Ltd.), tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_3$, 99%, Acros), dicyclohexylcarbodiimide (DCC, Beijing Ouhe Technology Co.), N-Boc-L-proline (99%, J&K Scientific Ltd.), and N-Boc-D-proline (99%, J&K Scientific Ltd.) were used as purchased. Azobisisobutyronitrile (AIBN, AR, Wuhan Chemical Co.) was recrystallized from ethanol and dried under vacuum at room temperature. Tetrahydrofuran (THF, AR, Beijing Chemical Co.), anisole (AR, Beijing Chemical Co.), and hexane (AR, Beijing Chemical Co.) were refluxed with sodium and distilled out just before use. Benzene (AR, Beijing Chemical Co.) and toluene (AR, Beijing Chemical Co.) were washed with oil of vitriol three times, water three times, saturated brine once, dried with magnesium sulfate, and then refluxed over sodium and distilled out before use.

Measurements.

^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) spectra were recorded on a Bruker ARX400 spectrometer, and ^{1}H-NMR (300 MHz) spectra were recorded on a Varian Mercury Plus spectrometer at room temperature in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. High resolution mass spectra (HRMS) were collected on a Burker Apex IV FTMS mass spectrometer. The melting points were collected on a SGW X-4 melting point apparatus equipped with a microscope. The weight- and number-average molecular weights (M_w and M_n, respectively) were estimated by a gel permeation chromatography (GPC) apparatus equipped with a Waters 2410 refractive-index detector and a Water 515 pump. Three Waters Styragel columns with a 10 μm bead size were connected in series. Their effective molecular weight ranges were 100–10,000 Dalton for Styragel HT2, 500–30,000 Dalton for Styragel HT3, and 5000–600,000 Dalton for Styragel HT4, separately. The pore sizes were 50, 100, and 1000 nm for Styragel HT2, HT3, and HT4, respectively. THF was employed as the eluent at a flow rate of 1.0 mL min^{-1}. The temperature of column chamber was mediated at 35 ℃. All GPC curves were calibrated against a series of monodispersed polystyrene standards. Specific optical rotations were obtained on a JASCO Model P-1030 digital polarimeter using a water-jacketed 50 mm cell at 25 ℃. For Boc-protected monomers and polymers, measurements were run in THF whereas those de-protected in methanol due to the distinct solubility. UV-Vis absorption spectra were determined on a Varian Cary 1E UV-Vis spectrometer. CD spectra were recorded on a JASCO J-810 with a 10 mm quartz cell at 25 ℃. The temperature was mediated with a Julabo F25-Me controller. The enantiomer excess was estimated on a high performance liquid chromatography (HPLC) equipped with a JASCO PU-2089 pump, a AS-2055 automatic sampler, a UV-2070 UV-Vis spectrometer, a CD-2095 circular dichroism spectrometer, and a Daicel CHIRALPAK AD-H column. The eluents used were the mixtures of isopropanol and hexane with the compositions of 10/90 (v/v) at a rate of 1.0 mL/min.

Monomer Synthesis.

*2-(3-Methyl-5-bromopyridin-2-yl)-isoindole-1,3-dione (**I**).*

2-Amino-3-methyl-5-bromopyridine (93.5 g. 0.50 mol) and phthalic anhydride (74.0 g, 0.50 mol) were mixed and then heated at 190 °C for 5 h. After cooled to room temperature, the mixture was dissolved in CH_2Cl_2 (600 mL). The solution was washed with water (2 × 200 mL) and saturated brine (200 mL), dried over $MgSO_4$, filtrated, treated with activated carbon, and then concentrated under vacuum. The solid residue was triturated with ether. Solid products were collected by filtration and dried under vacuum to give 139.5 g of product as white powders. Yield: 88%. ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 8.56 (d, 1H, 6-*H* pyridinyl group), 7.93-7.99 (m, 2H, 3, 4-*H* phenyl group), 7.87 (d, 1H, 4-*H* pyridinyl group), 7.77-7.82 (m, 2H, 2, 5-*H* phenyl group), 2.28 (s, 3H, -C*H*$_3$).

*2-(3-Vinyl-5-bromopyridin-2-yl)-isoindole-1,3-dione (**II**).*

A mixture of 2-(3-methyl-5-bromopyridin-2-yl)-isoindole-1,3-dione (23.8 g, 0.10 mol), NBS (19.6 g, 0.11 mol) in CCl_4 (270 mL) was refluxed upon sun lamp (250 W each) exposure. The bromination reaction was initiated by AIBN in 50 mg portions, and 200 mg of AIBN was added in total over 3 hours. Opon cooled to room temperature, the solids suspended on the surface of the reaction mixture were filtered off. The solvent was removed under vacuum. The residue was dissolved in CH_2Cl_2 (300 mL) and washed with warm water (3 × 200 mL), saturated brine (200 mL), dried with anhydrous Na_2SO_4, filtrate and then concentrated in vacuum. The residue was mixed with PPh_3 (26.2 g, 0.10 mol) and acetone (250 mL). The mixture was refluxed for 4 hours, and a great amount of precipitates were formed. The solids were collected by filtration and washed with chilly acetone to afford {[5-bromo-2-(1,3-dioxoisoindolin-2-yl)-pyridin-3-yl]-methyl}-triphenylphosphonium bromide as white powders. The phosphonium bromide was dissolved 200 mL of CH_2Cl_2, and 250 mL aqueous formaldehyde (40%, 250 mL) was then added. The mixture was cool to 0 ℃. With a rapid stirring, 2 mol/L K_2CO_3 aqueous solution (90 mL) was dropped slowly over 1 hour. The mixture was stirred for another 2 hours at room temperature. When the reaction was completed, organic layer was separated. The aqueous layer was extracted with 2 × 200 mL portions of CH_2Cl_2. The organic layers were combined and dried over anhydrous Na_2SO_4. The solvent was taken away under reduced pressure and the residue was purified by silica gel column (CH_2Cl_2 as eluent) to give 14.80 g of product as white powders.

The total yield of the three steps is 45%.

^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 5.48 (d, 1H, =CH_2), 5.85 (d, 1H, =CH_2), 6.54 (dd, 1H, -CH=), 7.81-7.85 (m, 2H, phenyl rings), 7.96-7.99 (m, 2H, phenyl rings), 8.17 (dd, 1H, 4-H pyridinyl group), 8.61 (dd, 1H, 6-H pyridinyl group).

*3-Vinyl-2-amino-5-bromopyridine (**III**).*

A hot solution of 2-(3-vinyl-5-bromopyridin-2-yl)-isoindole-1,3-dione (16.45 g, 0.05 mol) in 600 mL ethanol was added into hydrazine hydrate (80%, 1.8 mL). The mixture was stirred at room temperature over night and white solids formed gradually. The precipitates were filtered off and the filtrate was concentrated under vacuum. The semisolid residue was extracted with CH_2Cl_2 (3 × 150 mL). The CH_2Cl_2 solution was extracted by 5% HCl aqueous solution (3 × 75 mL). The collected water phase was neutralized by 2 mol/L NaOH aqueous solution, and extracted by CH_2Cl_2 (3 × 150 mL). The combined organic layers were washed with saturated brine (3 × 200 mL), dried over anhydrous Na_2SO_4. The evaporation of solvent under vacuum gave 9.15 g of light yellow oil (92% yield), which was directly used for the next reaction without further purification.

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 4.33~5.05 (br, 2H, -NH_2), 5.43 (d, 1H, -CH=CH_2), 5.67 (d, 1H, -CH=CH_2), 6.56 (dd, 1H, -CH=CH_2), 7.59 (dd, 1H, 4-*H* pyridinyl ring), 8.04 (dd, 1H, 6-*H* pyridinyl ring). ^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 108.86, 118.54, 120.18, 130.63, 137.00, 147.76, 154.35. HRMS (m/z): 198.9864 (MH+), 200.9843 (MH+), $C_7H_8N_2Br$ required 198.9865, 200.9850.

*3-Vinyl-5-(4'-tert-phenyl)-2-amino-pyridine (**IV**).*

To a degassed mixture of 3-vinyl-2-amino-5-bromopyridine (2.78 g, 13.9 mmol), 4-*tert*-butylphenylboronic acid (3.60 g, 20.2 mmol), 2,6-di-tert-butyl-4-methylphenol (25 mg, 0.1 mmol), LiCl (1.85 g, 43.6 mol), and $Pd(PPh_3)_4$ (0.73 g, 0.07 mmol), were added into benzene (60 mL), ethanol (60 mL) and aqueous Na_2CO_3 solution (1 mol/L, 30 mL) under a continuous stream of nitrogen. The mixture was vigorously stirred and refluxed for 4 hours. Afterwards, the organic layer was separated, and the aqueous layer was extracted by CH_2Cl_2 (3 × 30 mL). The separated organic layers were combined and washed with water (3 × 50 mL), saturated brine (50 mL), and dried over anhydrous Na_2SO_4. After evaporation of solvent under reduced pressure, the residue was purified by silica gel column (CH_2Cl_2/acetone: 3/1 (v/v) as eluent) to give 2.88 g of product as yellow solids. Yield: 82%.

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.36 (s, 9H, -C(CH_3)$_3$), 4.36-4.98 (s, 2H, -NH_2), 5.43 (d, 1H, -CH=CH_2), 5.75 (d, 1H, -CH=CH_2), 6.70 (dd, 1H, -CH=CH_2), 7.53 (dd, 4H, phenyl ring), 7.72 (d, 1H, 4-*H* pyridinyl ring), 8.25 (d, 1H, 6-*H* pyridinyl ring). ^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 31.32, 34.50, 117.55, 118.33, 125.84, 126.03, 128.07, 128.41, 131.72, 132.03, 133.71, 135.23, 145.35, 150.07, 154.66. HRMS (m/z): 258.1707 (MH+), $C_{17}H_{21}N_2$ required 258.1705. Melting point: 118-120 °C.

*(−)-L-N-Boc-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide (**S-BPhVPyA**).*

A mixture of 3-vinyl-5-(4'-tert-phenyl)-2-amino-pyridine (2.58 g, 0.010 mol), L-*N*-Boc-proline (2.34 g, 0.011 mol) and anhydrous CH_2Cl_2 was cooled to 0 °C. DCC (4.12 g, 0.020 mol) was added into the mixture and the obtained solution was stirred vigorously first at 0 °C for 2 hours and then at room temperature overnight. After the reaction was stopped, the mixture was filtered. The filtrate was concentrated under vacuum. The residue was purified by silica gel column (CH_2Cl_2/acetone: 10/1 (v/v) as eluent) twice to afford 2.38 g of product as foamy solids. Yield: 53%.

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.37 (s, 9H, -Ph-C(CH_3)$_3$), 1.52 (s, 9H, -O-C(CH_3)$_3$), 1.80-2.70 (m, 4H, -CH_2-CH_2-CH_2N-), 5.30-5.70 (m, br, 2H, -CH-CH_2-N-), 5.35-5.65 (m, br, 1H, -CO-CH-CH_2-), 3.34-3.62 (br, 2H, -CH_2N-), 4.33-4.62(br, 1H, -COCH-), 5.39-5.50 (d, 1H, =CH_2), 5.73-5.90 (d, 1H, =CH_2), 6.65-6.95 (br, 1H, =CH-), 7.48-7.55 (m, 4H, *H* phenyl ring), 8.02 (s, 1H, 4-*H* pyridinyl ring), 8.18 (s, 0.3 H, -CONH-), 8.59 (s, 1H, 6-*H* pyridinyl ring), 9.36 (s, 0.7H, -CONH-). ^{13}C-NMR (100 MHz, CDCl3, δ ppm): 170.3, 156.3, 151.2, 146.8, 146.1, 134.5, 134.2, 133.1, 131.6, 126.7, 126.4, 126.0, 117.6, 80.9, 61.7, 60.6, 47.4, 34.6, 31.3, 28.4, 24.7. HRMS (m/z): 450.2756 (MH+), $C_{27}H_{36}N_3O_3$ required 450.2757. Optical rotation: $[\alpha]_{365}^{25}$ = −399° (c 0.1 g/dL, THF). Melting point: 83-89 °C.

*(+)-D-N-Boc-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide (**R-BPhVPyA**).*

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.37 (s, 9H, -Ph-C(CH_3)$_3$), 1.52 (s, 9H, -O-C(CH_3)$_3$), 1.80-2.70 (m, 4H, -CH_2-CH_2-CH_2N-), 5.30-5.70 (m, br, 2H, -CH-CH_2-N-), 5.35-5.65 (m, br, 1H, -CO-CH-CH_2-), 3.34-3.62 (br, 2H, -CH_2N-), 4.33-4.62(br, 1H, -COCH-), 5.40-5.50 (d, 1H, =CH_2), 5.74-5.91 (d, 1H, =CH_2), 6.66-6.96 (br, 1H, =CH-), 7.48-7.55 (m, 4H, *H* phenyl ring), 8.02 (s, 1H, 4-*H* pyridinyl ring), 8.18 (s, 0.3 H, -CONH-), 8.59 (s, 1H, 6-*H* pyridinyl ring), 9.36 (s, 0.7H, -CONH-). ^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 170.3, 156.3, 151.2, 146.8, 146.1, 134.5, 134.2, 133.1, 131.6, 126.7, 126.4, 126.0, 117.6, 80.9, 61.7, 60.6, 47.4, 34.6, 31.3, 28.4, 24.7. HRMS (m/z): 450.2752 (MH+), $C_{27}H_{36}N_3O_3$ required 450.2757. Optical rotation: $[\alpha]_{365}^{25}$ = +430° (c 0.1 g/dL, THF). Melting point: 78-82 °C.

*(−)-L-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide (**S-PhVPyA**).*

To a mixture of **S-BPhVPyA** (0.45 g, 1.0 mmol) and CH_2Cl_2 (2 mL) was added TFA (2 mL) dropwise at 0 °C. The solution was vigorously stirred for 3 hours at room temperature. Afterwards, the solvent was taken away under reduced pressure and the residue was dissolved in another 10 mL of CH_2Cl_2. The obtained solution was washed by 1 mol/L NaOH aqueous solution (3 × 5 mL), saturated brine (2 × 5 mL), and dried over anhydrous Na_2SO_4. The solution was concentrated under vacuum and the residue was purified by silica gel column (CH_2Cl_2/methanol: 20/1 (v/v) as eluent) to give 0.30 g of product as colorless oil. Yield: 86%.

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.36 (s, 9H, -C(CH_3)$_3$), 1.83 (m, 2H, -CH_2-CH_2N-), 2.10-2.25 (m, 2H, -CH-CH_2-), 2.30-2.90 (br, 1H, -NH), 2.95 (m, 2H, -CH_2N-), 3.75 (dd, 1H, -COCH-), 5.22 (d, 1H, =CH_2), 5.63(d, 1H, =CH_2), 6.64(dd, 1H, =CH-), 7.38(m, 4H, *H* phenyl ring), 8.12(dd, 1H, 6-*H* pyridinyl ring), 8.58 (dd, 1H, 4-*H* pyridinyl ring), 8.5-11.0 (br, 1H, -CONH-). ^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 25.84, 30.40, 31.38, 34.25, 46.91, 60.62, 116.86, 120.74, 125.33, 126.39, 127.81, 131.19, 133.35, 134.51, 147.40, 147.44, 156.35, 173.39. MS (m/z): 350.22344 (MH+), $C_{22}H_{28}N_3O$ required 350.2332. Optical rotation: $[\alpha]_{365}^{25}$ = −122° (c 0.1 g/dL, methanol).

*(+)-D-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide (**R-***

PhVPyA).

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.37 (s, 9H, -C(CH_3)$_3$), 1.81 (m, 2H, -CH_2-CH_2N-), 2.10-2.28 (m, 2H, -CH-CH_2-), 1.90-2.60 (br, 1H, -N*H*), 2.97 (m, 2H, -CH_2N-), 3.75 (m, 1H, -COC*H*-), 5.22 (d, 1H, =CH_2), 5.63 (d, 1H, =CH_2), 6.68 (dd, 1H, =C*H*-), 7.40 (m, 4H, *H* phenyl ring), 8.10 (dd, 1H, 6-*H* pyridinyl ring), 8.60 (dd, 1H, 4-*H* pyridinyl ring), 9.0-11.0 (br, 1H, -CON*H*-). ^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 25.84, 30.42, 31.32, 34.33, 47.03, 60.65, 116.88, 120.74, 125.33, 126.39, 127.81, 131.22, 133.38, 134.49, 147.40, 147.44, 156.35, 173.42. Optical rotation: $[\alpha]_{365}^{25}$ = +127° (c 0.1 g/dL, methanol).

Radical polymerization.

Take **S-BPhVPyA** as an example. **S-BPhVPyA** (0.200 g, 0.44 mmol), AIBN (0.7 mg, 0.004 mmol), and benzene (1.0 mL) were added into a reaction tube. After three freeze-pump-thaw cycles, the tube was sealed under vacuum and put into an oil bath thermostated at 60 °C for 24 hours. After being cooled to room temperature, the tube was opened and the solution was diluted with 10 mL of THF. The solution was dropped into hexane (200 mL). The precipitates were collected by filtration and washed by fresh hexane. After drying under vacuum at 50 °C for 48 hours, 0.17 g of poly{(−)-L-*N*-Boc-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide} (**P(S)-BPhVPyA**) as white solids was obtained. Yield: 81%.

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 0.2-2.8 (broad peaks, -COCHCH_2CH_2CH$_2$N-, -C*H*-CH_2-, Ph-C(CH_3)$_3$, -COC(CH_3)$_3$), 2.8-5.2 (broad peaks, -COCHCH$_2$CH$_2$CH_2N-), 5.5-9.0 (broad peaks, *H* pyridine ring and phenyl rings). M_n= 3.2 ×10^5 Da, *PDI* = 1.76. Optical rotation: $[\alpha]_{365}^{25}$ = −264° (c 0.1 g/dL , THF).

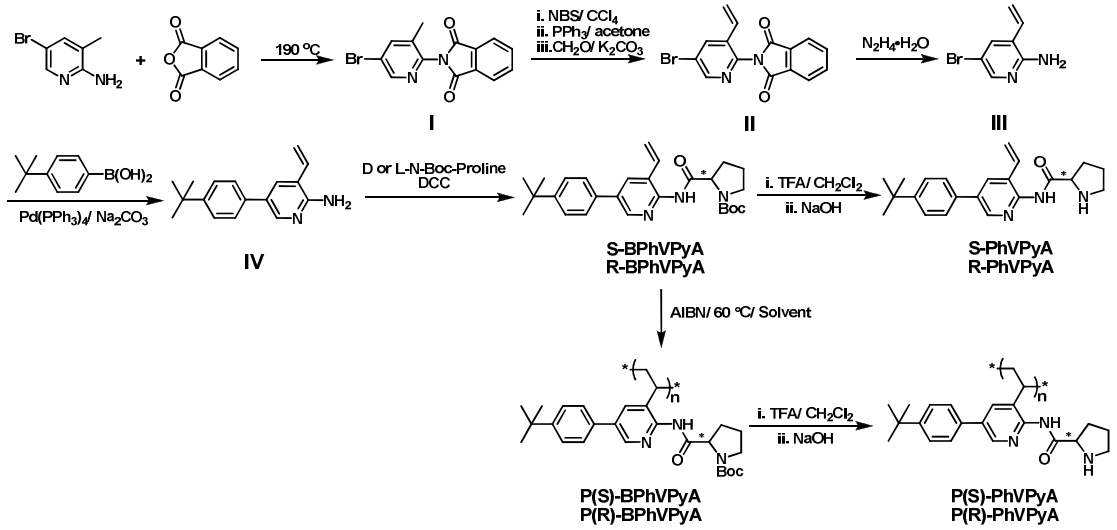
De-protection of Boc group

Take **P(S)-BPhVPyA** as an example. **P(S)-BPhVPyA** (0.15 g, 0.33 mmol) was dissolved in 5 mL of chloroform. To this solution cooled to 0 °C was added dropwise 3 mL of TFA. Afterwards, the mixture was stirred at room temperature for 6 hours, and was concentrated under reduced pressure. The residue was dissolved in 10 mL of methanol and dropped into 200 mL of 1 mol/L NaOH aqueous solution. The solids were collected by filtration and dried under vacuum at 50 °C for 48 hours, which gave 0.11 g of poly{(−)-L-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide} (**P(S)-PhVPyA**) as white solids. Yield: 91%. ^{1}H-NMR (400 MHz, CD_3OD, δ (ppm)): 0.0-2.5 (broad peaks, -COCHCH_2CH_2CH$_2$N-, -C*H*-CH_2-, C(CH$_3$)$_3$), 2.5-4.8 (broad peaks, -COC*H*CH$_2$CH$_2$CH_2N-), 6.0-8.8 (broad peaks, *H* pyridine ring, *H* phenyl ring). Optical rotation: $[\alpha]_{365}^{25}$ = +136° (c 0.1 g/dL, methanol).

Procedure of aldol catalysis by polymeric catalysts

Take **P(S)-PhVPyA** as an example. **P(S)-PhVPyA** (17.5 mg, 0.05 mmol) was dissolved in 2 mL of cyclohexanone. To the solution were added water (90 mg, 5 mmol), 4-nitrobenzoic acid (16.7 mg, 0.10 mmol), and 4-nitrobenzaldehyde (38.0 mg, 0.25 mmol) consequently. The mixture was stirred vigorously at a water bath thermostated at 25 °C until the full conversion of 4-nitrobenzaldehyde monitored by TLC. The mixture was poured into 25 mL of acetate ester and filtered. The precipitate was collected, washed by fresh ethyl acetate three times and dried under vacuum at 50 °C for 48 hours. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel column (estate ester/petroleum: 1/3 (v/v) as eluent) to give 60 mg of product as white solids. Yield: 97%, dr (endo/exo): 2.8/1, ee%: 62%.

^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 1.00-1.65 (m, 4H, -COCH$_2$CH_2CH_2CH$_2$CH-), 1.65-2.20 (m, 2H, -COCH$_2$CH$_2$CH$_2$CH_2CH-), 2.20-2.65 (m, 3H, -COCH_2CH$_2$CH$_2$CH$_2$C*H*-), 3.20 (s, br, 1H, -O*H* of syn product), 4.09 (s, br, 1H, -O*H* of anti product), 4.90 (d, 1H, -C*H*(OH)- of anti product), 5.50 (d, 1H, -C*H*(OH)- of syn product), 7.50 (dd, 2H, 2, 6 *H* in the phenyl group), 8.21 (dd, 2H, 3, 5 *H* in the phenyl group). Chiral HPLC analysis (Daicel CHIRALPAK AD-H, isopropanol/hexane = 10/90, 1.0 mL/min, 25°C, UV detector 240 nm, CD detector 240 nm). t_{R1}(syn) = 11.4 min，t_{R2}(syn) = 12.3 min，t_{R1}(anti) = 13.4 min，t_{R2}(anti) = 17.1 min.



Scheme 1 Syntheses of the monomers **S-BPhVPyA**, **R-BPhVPyA**, **S-PhVPyA**, **R-PhVPyA** and their corresponding polymers **P(S)-BPhVPyA**, **P(R)-BPhVPyA**, **P(S)-PhVPyA**, **P(R)-PhVPyA**.

Results and Discussion

Synthesis

The synthetic routes of **S-BPhVPyA** and **R-BPhVPyA** were illuminated in Scheme 1. Phthalic anhydride was used to protect the amine group of the starting reagent, 2-amino-5-bromopyridine. Bromination of the phthalic anhydride protected compound with NBS, followed by the reaction with triphenylphosphine, yielded [5-bromo-2-(1,3-dioxoisoindolin-2-yl)-pyridin-3-yl]-ethyl-triphenylphosphonium bromide. The Wittig reaction of phosphonium bromide with formaldehyde in aqueous solution under alkaline condition produced 2-(3-vinyl-5-bromopyridin-2-yl)-isoindole-1,3-dione (**II**). It was treated with hydrazine hydrate to produce 3-vinyl-2-amino-5-bromopyridine (**III**). The Suzuki coupling reaction of vinylpyridine bromide with 4-*tert*-butylbenzeneboronic acid catalyzed by $Pd(PPh_3)_4$ produced the key intermediate, 3-vinyl-5-(4'-*tert*-phenyl)-2-aminopyridine (**IV**), which was condensed with L- or D-*N*-Boc-proline using DCC as the activator to yield the target monomers, (−)-L-N-Boc-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide (**S-BPhVPyA**) and (+)-L-N-Boc-proline-[5-(4'-tert-phenyl)-3-vinyl-pyridin-2-yl]amide (**R-BPhVPyA**), respectively. **S-PhVPyA** and **R-PhVPyA**, employed as the low molar mass model compounds, were obtained from **S-BPhVPyA** and **R-BPhVPyA** via de-protection of Boc groups.

Probably owing to the electron deficiency of **II**, the bromination of methyl group by NBS could not take place just through heating, one commonly used method. To efficiently induce the reaction, sunshine or sun lamp was applied. In addition, it is necessary to run Suzuki coupling reaction after hydrazinolysis because the intermediate **II** may complex with pd(0) and poison the catalyst. The chemical structures of all the key intermediates, model compounds, and monomers were confirmed by $^1H/^{13}C$-NMR, and HRMS.

Polymerization

Free radical polymerizations of **S-BPhVPyA** and **R-BPhVPyA** were carried out at 60 °C with AIBN as the initiator. For **S-BPhVPyA**, various solvents were utilized to investigate their effects on the chiroptical property of the resultant polymers. The results are summarized in Table 1 (Entries 1~5). Under all conditions, the obtained polymers had high molar masses (M_n = 15~32 × 10^4 Da), moderate polydispersities (*PDI* = 1.2~1.8), and good solubilities in various solvents (chloroform, THF, anisole, methanol, etc). The polymer prepared in benzene had the highest molar mass and lowest polydispersity. Therefore, benzene was selected as the radical polymerization solvent of **R-BPhVPyA** (Entry 6, Table 1).

Table 1 Summary of radical polymerization results of **S-BPhVPyA** and **R-BPhVPyA** and chiroptical properties of **P(S)-PhVPyA** and **P(R)-PhVPyA** [a]

Entry	Polymer	Sol.	Yield (%)	M_n [b] ($\times 10^4$)	M_w/M_n [b]	Polymer [c]	$[\alpha]_{365}^{25}$ [d] (°)
1	**P(S)-BPhVPyA**	Anisole	89	28	1.2	**P(S)-PhVPyA**	+86
2	**P(S)-BPhVPyA**	THF	82	26	1.3	**P(S)-PhVPyA**	+113
3	**P(S)-BPhVPyA**	Toluene	90	23	1.4	**P(S)-PhVPyA**	+122
4	**P(S)-BPhVPyA**	Heptane	93	15	1.8	**P(S)-PhVPyA**	+132
5	**P(S)-BPhVPyA**	Benzene	89	32	1.2	**P(S)-PhVPyA**	+136
6	**P(R)-BPhVPyA**	Benzene	90	28	1.2	**P(R)-PhVPyA**	-130

[a] Polymerization conditions: monomer concentration [M], 0.2 g/mL; initiator, AIBN; [M]/[I] =100:1; temperature 60 °C. [b] Number-average molecular weight (M_n), weight-average molecular weight (M_w) and polydispersity (M_w/M_n) were determined by GPC. [c] **P(S)-PhVPyA** and **P(R)-PhVPyA** were prepared from their corresponding polymeric precursors via de-protection of Boc group by TFA. [d] Specific optical rotations of de-protected polymers measured in methanol solution (c = 0.1 g/dL).

Fig. 1 displays the ^{1}H-NMR spectra of **S-BPhVPyA** and **P(S)-BPhVPyA**. The peaks at 5.39–5.50, 5.73–5.90 and 6.65–6.95 ppm were attributed to the proton resonances of vinyl group (Fig. 1a). They vanished after polymerization, accompanied by the appearance of broad peaks in the region of 0–1.50 ppm (Fig. 1b), implying the formation of polymer backbone. In addition, the proton resonance peaks became obviously dispersed after the polymerization, owing to the limited mobility of protons in the polymer chain.

Catalytically active polymers, **P(S)-PhVPyA** and **P(R)-PhVPyA** were derived from **P(S)-BPhVPyA** and **P(R)-BPhVPyA** through the decomposition of Boc group under acidic condition. They had poor solubilities in less polar solvents (chloroform, THF, anisole, etc), but good solubilities in polar solvents (methanol, ethanol, DMF, DMSO, etc).

Fig. 2 shows the FT-IR spectra of **P(S)-PhVPyA** and **P(S)-BPhVPyA**. The vibration of C=O stretching, symmetric in-plane

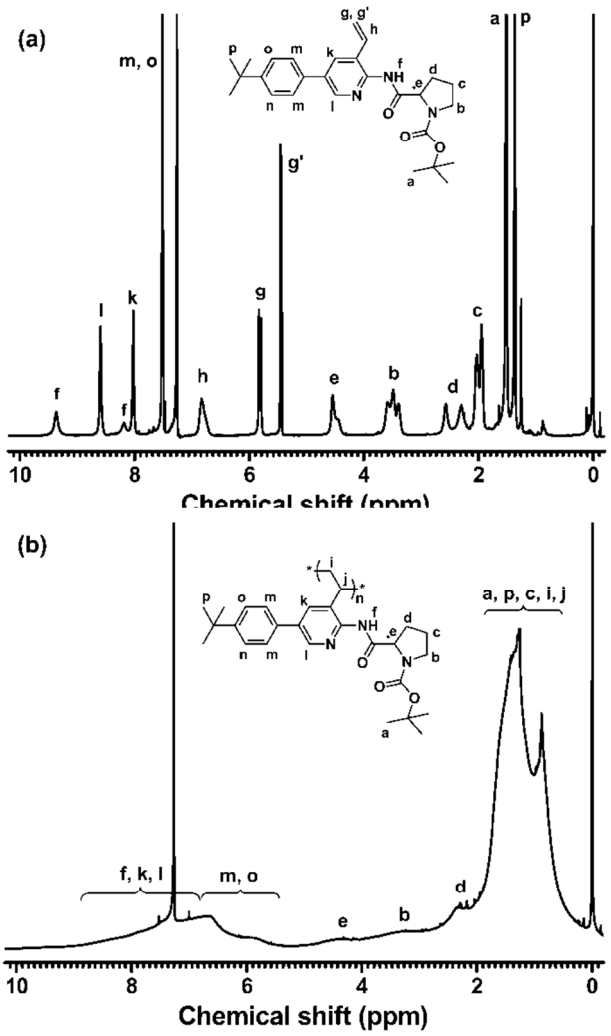


Fig. 1 1H-NMR spectra of **S-BPhVPyA** (a) and **P(S)-BPhVPyA** (b) in $CDCl_3$ solution with TMS as an internal standard.

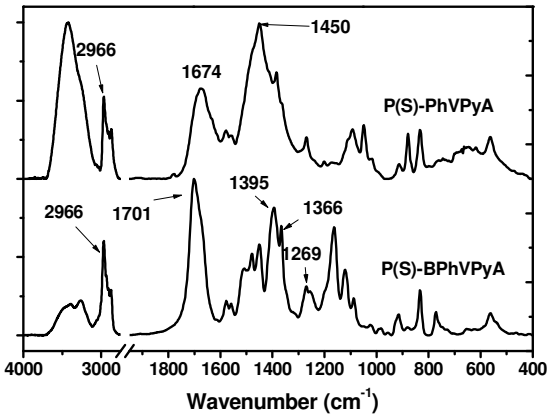


Fig. 2 FT-IR spectra of **P(S)-BPhVPyA** and **P(S)-PhVPyA**

H–C–H bending, and out-of-plane H–C–H bending of Boc group are observed at 1701, 1395 and 1366, and 1269 cm^{-1}, respectively. They are absent in the spectrum of **P(S)-PhVPyA**, suggesting the complete removal of Boc groups.

Chiroptical properties.

The specific optical rotation $[\alpha]_{365}^{25}$ of **S-PhVPyA** is −122° (c: 1 mg/mL, methanol). The corresponding polymer, **P(S)-PhVPyA**, shows an $[\alpha]_{365}^{25}$ value of +132°. This distinct variation indicated that the optical activity of **P(S)-PhVPyA** did not solely arise from the configurational chirality of the side group, but a higher chiral structure, most likely helical conformation of the main chain was formed. Changing the configuration of stereocenter from S to R, as in **R-PhVPyA** and **P(R)-PhVPyA**, led to an inversion of the sign of specific optical rotations for both monomer and polymer, suggesting that the stereocenter in the side group played a dominant role in the induction of a prevailing twist sense. It should be noted that **P(S)-BPhVPyA** displayed an $[\alpha]_{365}^{25}$ value of -264°. The optical rotation sign alternation before and after de-protection might be attributed to the change in the orientation of proline pendants. Boc groups are bulky and have strong steric conflicts with polymer backbone. As a result, the carboxyamide groups tend to be away from polymer backbone. Whereas, the amine groups of proline moieties in **P(S)-PhVPyA** are smaller and may orient in a different way, which caused conformational variation of side-groups. Another possible explanation is the difference of solvents in which optical rotations were measured, THF for of **P(S)-BPhVPyA** and methanol for **P(S)-PhVPyA**.

Circular dichroism (CD) spectrometry was applied to further characterize the secondary structures of polymers. Fig. 3 shows the CD and UV-Vis spectra of **S-PhVPyA**, **P(S)-PhVPyA** and **P(R)-PhVPyA**. The UV-Vis spectrum of monomer **S-PhVPyA** presents four obvious absorption bands centered at 213 nm, 240 nm, 266 nm, 310 nm, which may be assigned as the electronic transitions of side carbonyl, vinyl, phenylpyridinyl and phenylpyridinyl amide groups, respectively.[54, 55] The CD spectrum of **S-PhVPyA** only shows very week negative Cotton effects around 210 nm. The corresponding polymer, **P(S)-PhVPyA** exhibits three obvious absorption bands in the UV-Vis spectrum centered at 210 nm, 265 nm and 285 nm, separately. The CD spectrum of **P(S)-PhVPyA** presents one intensive and two weak negative peaks at 220 nm, 250 nm and 315 nm, and an intensive positive peak at 285 nm, suggesting the side groups were arranged in a skewed way. By analogous to the previously reported polymers,[46, 51] the formation of chiral secondary structure was proposed for **P(S)-PhVPyA.** The CD curve of **P(S)-PhVPyA** had mirror symmetry with that of **P(R)-PhVPy**, indicating again that the prevailing twist sense of polymer backbone was determined by the configuration of stereocenter.

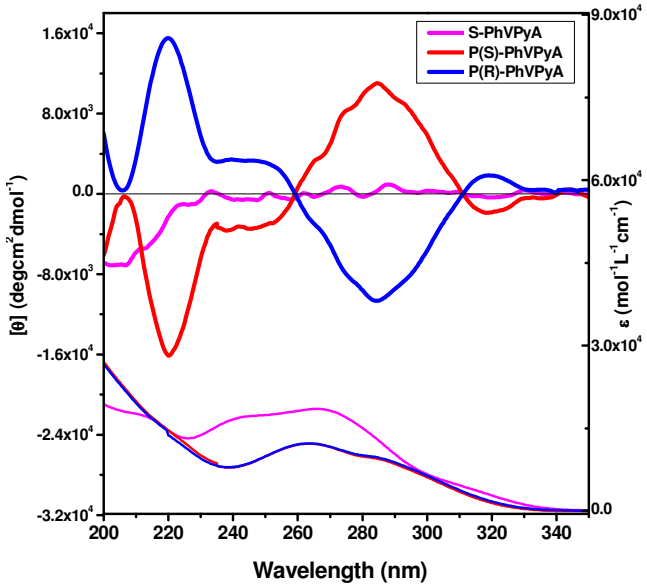
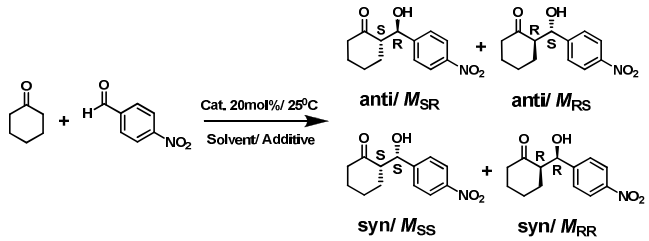


Fig. 3 CD and UV-Vis spectra of **S-PhVPyA**, **P(S)-PhVPyA** and **P(R)-PhVPyA** in THF at 25 °C with a concentration of 5×10^{-5} mol/L

The polymers resulted from the polymerization of **S-BPhVPyA** in polar solvent such as anisole and THF displayed lower optical rotations than those obtained from apolar solvents. It might be rationalized by the lack of hydrogen bonding between amide groups during polymerization in polar sovent. [51]

Asymmetric aldol catalysis



Scheme 2. Asymmetric aldol catalysis of cyclohexanone with p-nitrobenzaldehyde.

The helical polymers, **P(S)-PhVPyA** and **P(R)-PhVPyA**, and their corresponding low molar mass counterparts, **S-PhVPyA** and **R-PhVPyA**, were separately applied in the asymmetric aldol reaction of cyclohexanone with 4-nitrobenzaldehyde (Scheme 2). Four stereoisomers of 2-[hydroxyl-(4-nitrophenyl)-methyl]cyclohexanone, defined as M_{SR}, M_{RS}, M_{SS}, and M_{RR}, respectively, could be obtained according to the configuration of newly formed stereocenters. Among these isomers, M_{SR} and M_{RS} are a pair of enantiomers with anti-configuration, while M_{SS} and M_{RR} are the syn-configuration enantiomers. The diastereomer ratio of aldol transformation was defined as dr = anti/syn, and the enantiomer excess of the anti-configuration products was defined as ee% (anti) = $(M_{SR}-M_{RS})/(M_{SR}+M_{RS})\times100\%$ (M_{SR} as the major product) or ee% (anti) = $(M_{RS}-M_{SR})/(M_{SR}+M_{RS})\times100\%$ (M_{RS} as the major product).

Table 2 summaries the results of catalytic reactions in cyclohexanone bulk solution with water and 4-nitrobenzoic acid as the additives. It was evident that the polymeric aldolases promoted the reaction between 4-nitrobenzaldehyde and cyclohexanone to proceed much faster than low molar mass ones. For example, it took only 10 h for 4-nitrobenzaldehyde to be fully converted in the presence of **P(S)-PhVPyA** (Entry 3, Table 2). Whereas, 24 h was needed when **S-PhVPyA** was employed (Entry 2, Table 2). All the reactions yielded cis-isomers as the major products with dr around 3.0 (Entry 2~5). Besides the reaction activity and diastereo-selectivity, the next and most important parameter of asymmetric catalysis is its enantio-selectivity. When **S-PhVPyA** acted as the catalyst, the reaction afforded M_{SR} as the major isomer with the enantio-selectivity as high as 87% ee, which was comparable to the catalytic results of most reported L-proline derivative organocatalysts.[6, 7] The transformation catalyzed by **P(S)-PhVPyA** also mainly yielded M_{SR} but with slightly lower enantio-selectivity, i.e. 62% ee. Changing the configuration of catalyst led to the configuration inversion of product, indicating that the chirality of side groups dominated the stereoselection of the aldol reaction. Furthermore, it seemed that the configurational chirality of side groups and the conformational chirality of polymer main chain exerted competitive influence.

Table 2 Results of asymmetric aldol reactions between cyclohexanone and 4-nitrobenzaldehyde catalyzed by **P(S)-PhVPyA**, **P(R)-PhVPyA** and their low molecular mass counterparts[a]

Entry	Cat.	Time (h)	Yield (%)[b]	ee% (anti)[c]	dr (anti/syn)[d]
1	**None**	24	NULL	–[e]	–[e]
2	**S-PhVPyA**	24	93	87 (M_{SR})	3.0/1
3	**P(S)-PhVPyA**	10	>95	62 (M_{SR})	3.4/1
4	**R-PhVPyA**	24	91	86 (M_{RS})	3.0/1
5	**P(R)-PhVPyA**	10	>95	62 (M_{RS})	3.2/1

[a.] Reaction temperature: 25 °C; 4-nitrobenzaldehyde: 0.25 mmol; cyclohexanone: 2 mL; catalyst: 0.05 mmol; 4-nitrobenzoic acid: 0.10 mmol; H_2O: 5.0 mmol. The time for full conversion was monitored by TLC. [b.] Isolated product after column separation. [c.] Determined by HPLC using a Daicel CHIRALPAK AD-H column. [d.] Determined by ^{1}H-NMR. [e.] Not determined.

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Table 3 Results of asymmetric aldol catalysis between cyclohexanone and 4-nitrobenzaldehyde by **P(S)-PhVPyA** and **S-PhVPyA** in the presence of various additive[a]

Entry	Cat.	Additive	Time	Conv.(%)[b]	ee% (anti)[c]	dr (anti/syn)[b]
1	**S-PhVPyA**	–	72	trace	–	–
2	**P(S)-PhVPyA**	–	72	73	28	1.9/1
3	**S-PhVPyA**	H_2O (20 eq.)	72	trace	–	–
4	**P(S)-PhVPyA**	H_2O (20 eq.)	24	92	20	2.2/1
5	**S-PhVPyA**	p-NO_2PhCOOH (0.2 eq.)	72	48	28	2.1/1
6	**P(S)-PhVPyA**	p-NO_2PhCOOH (0.2 eq.)	24	>95	32	2.1/1
7	**S-PhVPyA**	p-NO_2PhCOOH (0.2 eq.) H_2O (20 eq.)	24	80	79	2.3/1
8	**P(S)-PhVPyA**	p-NO_2PhCOOH (0.2 eq.) H_2O (20 eq.)	10	94	50	2.9/1
9	**S-PhVPyA**	p-NO_2PhCOOH (0.4 eq.) H_2O (20 eq.)	24	93	87	3.0/1
10	**P(S)-PhVPyA**	p-NO_2PhCOOH (0.4 eq.) H_2O (20 eq.)	10	>95	62	3.4/1
11	**P(S)-PhVPyA**	p-NO_2PhCOOH (1 eq.) H_2O (20 eq.)	10	>95	50	2.0/1
12	**P(S)-PhVPyA**	TFA (0.4 eq.) H_2O (20 eq.)	10	91	26	1.7/1
13	**P(S)-PhVPyA**	PhCOOH (0.4 eq.) H_2O (20 eq.)	24	89	24	1.8
14	**P(S)-PhVPyA**	p-CH_3OPhCOOH (0.4 eq.) H_2O (20 eq.)	24	88	19	1.7/1
15[d]	**P(S)-PhVPyA**	TFA (0.4 eq.) H_2O (20 eq.)	24	78	39	3.0/1
16[e]	**P(S)-PhVPyA**	p-NO_2PhCOOH (0.4 eq.) H_2O (20 eq.)	24	80	37	2.5/1
17[f]	**P(S)-PhVPyA**	p-NO_2PhCOOH (0.4 eq.) H_2O (20 eq.)	24	38	34	1.5/1

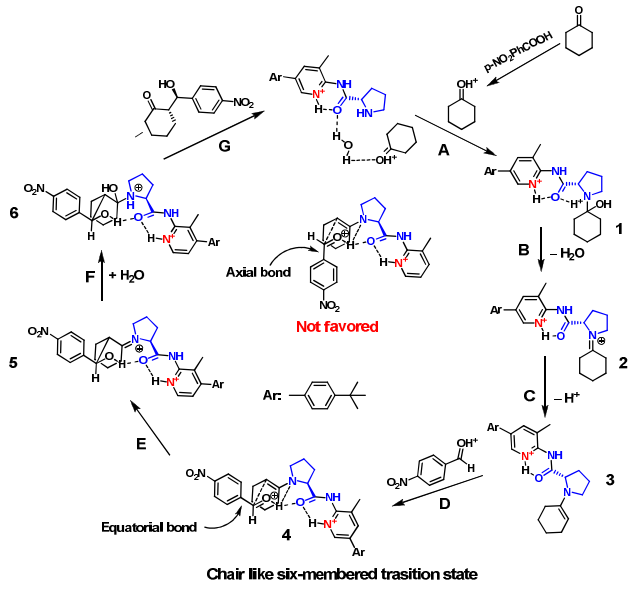
[a] All experiments were carried out under 25°C water bath, 4-nitrobenzaldehyde (0.25 mmol), cyclohexanone (2 mL), catalyst (0.05 mmol); the time for full conversion in all cases monitored by TLC. [b] Determined by ^{1}H-NMR. [c] Determined by HPLC using a Daicel CHIRALPAK AD-H. [d] 2 mL of chloroform was used as solvent. [e] 2 mL of DMSO was used as solvent. [f] 2 mL of methanol was used as solvent.

Water and Brønsted acid are known to enhance the catalytic performance of proline amide based aldolases.[56-58] In order to optimize the catalytic condition, the aforementioned reaction was carried out in the presence of various additives. The results are summarized in Table 3. Without any additive, **S-PhVPyA** yielded only trace products over 72 h (Entry 1, Table 3). By contrast, the reaction catalyzed by **P(S)-PhVPyA** presented a moderate yield (73%) under otherwise identical condition, although ee% and dr were low (Entry 2, Table 3). When 20 eq. of water was added, the reaction rate catalyzed by **P(S)-PhVPyA** was dramatically increased with similar ee% and dr (Entry 4, Table 3)); however, **S-PhVPyA** still did not efficiently catalyze the reaction (Entry 3, Table 3). p-Nitrobenzoic acid could also promote the reaction together with **P(S)-PhVPyA** (Entry 6, Table 3). But unlike water, it was also efficient to promote **S-PhVPyA** to catalyze reaction and showed a yield of 48% with 28% ee and 2.1 dr. The addition of both water and p-nitrobenzoic acid together could further enhance the reaction rate and improve stereoselectivity. The addition of 20 eq. water and 0.4 eq. of 4-nitrobenzoic acid together resulted in the best results in terms of chemical yield and stereoselectivity (Entries 7 and 8, Table 3). When the amount of water added was fixed, more or less 4-nitrobenzoic acid led poor ee% and dr values. Other organic acid such as TFA, 4-methoxylbenzoic acid, and benzoic acid were applied as additives instead of 4-nitrobenzoic acid (Entry 11~14). Unfortunately, all the reactions gave undesired results.

In order to shed light on the effect of solvent, chloroform, DMSO, and methanol were used as the solvents of reactions catalyzed by **P(S)-PhVPyA.** In nonpolar chloroform, the polymeric catalyst was not soluble and afforded the products in relative low yield and poor stereo-selectivity (Entry 15, Table 3). The reactions in DMSO and methanol did not proceed well, too (Entries 16 and 17, Table 3) and many substrate were transformed to unidentified by-products.

Proposed Catalytic Mechanism.

The proposed catalytic cycle of the aldol reaction is presented in Scheme 3.[5, 59-61] The carbonyl groups of both substrates are protonated and activated by the additive (i.e., 4-nitro-benzoic acid). The activated cyclohexanone is attacked by the amino group of **P(S)-PhVPyA** to afford the intermediate **1**, which sets off one H_2O molecule and rearranges from iminium (**2**) to enamine (**3**). The intermediate **3** attacks the carbonyl group of 4-nitrobenzaldehyde through the transition state **4** to yield intermediate **5**. The iminium 5 is hydrolyzed and releases a molecule of product to recycle the catalyst.



Scheme 3 Proposed catalytic cycle of cyclohexanone with 4-nitro-benzaldehyde catalyzed by **P(S)-PhVPyA**

Based on this mechanism, the diastereo-selectivity and enantio-selectivity of the reaction is determined by the position and direction where the enamine **3** attacks the aldehyde. With the help of the intermolecular hydrogen bond, the aldehyde substrate tends to be arranged the same side with the amide bond of the catalyst. As a result, the enamine faces the aldehyde with its *Si* face. In addition, when nucleophilic addition reaction happens, the enamine and aldehyde are arranged in a six-membered ring transition state, in which 4-nitro-phenyl, the larger group of the aldehyde, has a higher opportunity to settle at the equatorial bond than at the axial bond. The favored equatorial arrangement of 4-nitro-phenyl group affords the M_{SR} isomer, while the not favored axial form affords the M_{RR} one. M_{SS} and M_{RS} isomers are obtained when the aldehyde steps forward **3** on the opposite side of the amide bond (*Re* face of the enamine bond). As a result, the catalytic aldol reaction afford anti adduct with enantio-selectivity.

During the catalytic cycle, the acid additive, i.e. 4-nitro-benzoic acid, plays the key roles of activating the carbonyl groups of the both substrates. Furthermore, the additional protons benefit for the formation of the six-membered ring transition state **4** through the hydrogen bond, which dramatically enhance the influence from the chiral proline moiety and increase the enantio-selectivity. On the other hand, the added water helps to accelerate the aldol reaction possibly because of the hydrogen bond bridge between the catalyst molecule with the substrate molecules.

Without the additives, **P(S)-PhVPyA** prohibit the enhancement in catalytic activity (Table 3, Entry 1, 2), probably because the amide protons of the neighbor side groups in the polymeric catalysts help to form additional hydrogen bonds with the substrate.[45]

Conclusions

In this work, a pair of L- and D-proline amide containing optically active helical polymers, **P(S)-PhVPyA** and **P(R)-PhVPyA**, were synthesized via radical polymerizations of **S-BPhVPyA** and **R-BPhVPyA** and subsequent de-protection of Boc groups. They efficiently catalyzed asymmetric aldol reactions of cyclohexanone and 4-nitrobenzaldehyde using water and 4-nitrobenzoic acid as additives. Compared to low molar mass counterparts, the polymeric catalysts afforded faster reaction rate but slightly poorer enantio-selectivity. The shrunken enantio-selectivity of polymeric catalyst suggested that the side-group and polymer backbone did not act synergically on the stereochemistry of aldol catalysis. This mismatch should be avoided in the design of helical polymeric catalysts to mimic enzymes.

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Notes and references

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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

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