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# Synthesis of Helical Poly(phenylacetylene)s with Amide Linkage Bearing L-Phenylalanine and L-Phenylglycine Ethyl Ester Pendants and Their Applications as Chiral Stationary Phases for HPLC

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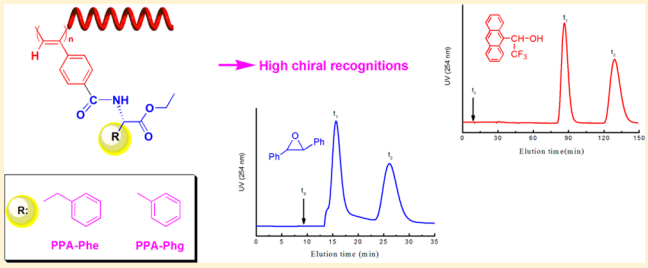
Supporting Information

**ABSTRACT:** Novel stereoregular helical poly(phenylacetylene) derivatives (**PPA-Phe** and **PPA-Phg**) with an amide linkage bearing L-phenylalanine and L-phenylglycine ethyl ester pendants were synthesized for use as chiral stationary phases (CSPs) in HPLC. The polymers showed different chiral recognition abilities depending on the coating solvents. Both **PPA-Phe** and **PPA-Phg** exhibited higher chiral recognitions when coated with $CHCl_3$ by having preferable conformations. Their chiral recognition abilities depended on their molecular weight and optical rotations which were influenced by the polymerization solvents and monomer concentration. **PPA-Phe** and **PPA-Phg** showed rather different chiral recognitions, indicating that the benzyl group of the former and the phenyl group of the latter also play important roles in the chiral recognition. A few racemates were completely separated on **PPA-Phe** or **PPA-Phg** with separation factors comparable or higher than those obtained on the popular polysaccharide-based CSPs.




## INTRODUCTION

In recent years, considering the different pharmacokinetics, physiological, toxicological, and metabolic activities of a pair of enantiomers of chiral compounds, more and more scientists are paying much more attention to the preparation and application of the single-isomer forms of chiral pharmaceuticals, agrochemicals, and food additives, etc.[1,2] Chiral separation, especially by high-performance liquid chromatography (HPLC), which can easily provide a pair of enantiomers with a high enantiomeric excess, is recognized as a reliable tool to obtain pure enantiomers on analytical and industrial scales.[3−5] The chiral recognition ability of chiral stationary phases (CSPs) is the key point of this separation technique. Although polysaccharide derivatives with high chiral recognition abilities have been widely developed as popular CSPs, optically active synthetic polymers as CSPs have also attracted significant interest by researchers around the world.[6−12] Many optically active synthetic polymers have been prepared and some of them show chiral recognition abilities as CSPs for HPLC.[13−19] A few optically active synthetic polymers with a stereoregular structure, such as the one-handed helical poly(triphenylmethyl methacrylate), have been commercialized. Several stereoregular helical poly(phenylacetylene) derivatives bearing chiral pendants, which are synthesized using a rhodium catalyst, have proved to be prospective CSPs for the HPLC separation of enantiomers.[20−25] However, the effect of the chiral pendant groups and chiral recognition mechanism as CSPs are still not well-known and have been attractive research areas.

Previously, we reported that the regular structure of the poly(phenylacetylene) main chains is essential for the high chiral recognition of poly(phenylacetylene)-based CSPs for HPLC, and an amide linkage group between the poly(phenylacetylene) main chains and chiral pendants showed a higher chiral recognition than the urea or sulfonamide linkage groups. We also reported that the coating solvents on silica gel also played an important role in the chiral recognition because

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**Scheme 1. Synthesis of Poly(phenylacetylene) Derivatives PPA-Phe and PPA-Phg**

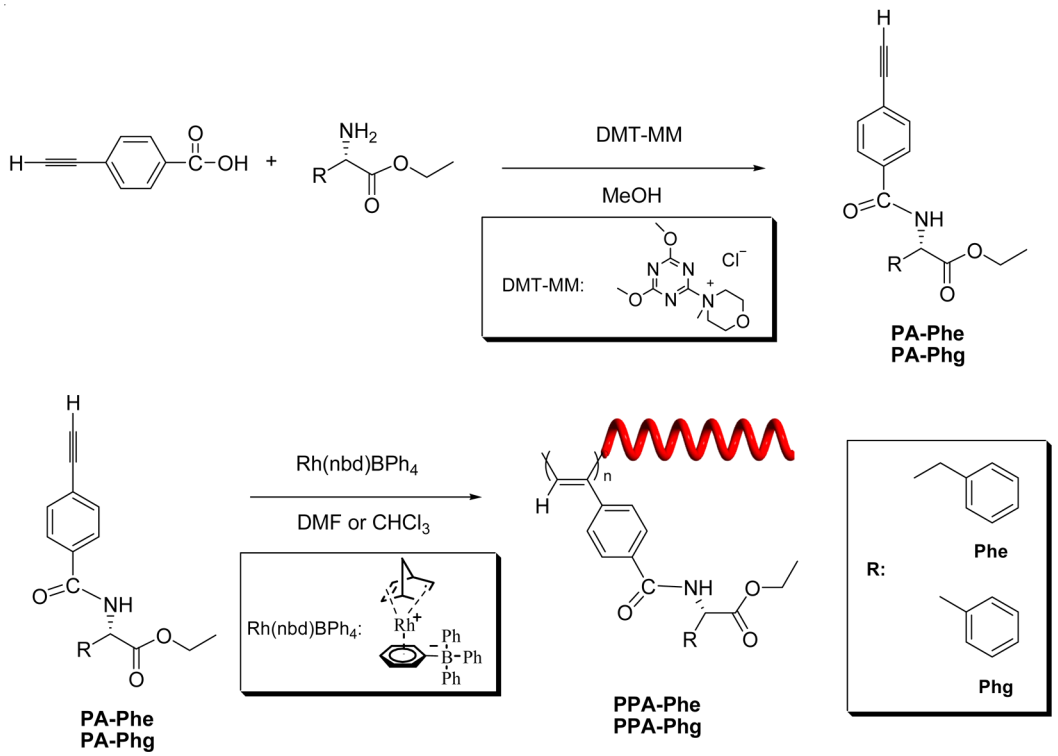


**Table 1. Polymerization Results of PA-Phe and PA-Phg**

| polymer[a] | monomer | yield[b]/% | solvent | [monomer]/M | $M_n$[c] | PDI[c] | $[\alpha]_D^{20}$[d]/deg |
|---|---|---|---|---|---|---|---|
| **PPA-Phe-1a** | **PA-Phe** | 99.3 | $CHCl_3$ | 0.03 | $3.90 \times 10^4$ | 2.7 | −714 |
| **PPA-Phe-1b** | **PA-Phe** | 98.6 | $CHCl_3$ | 0.06 | $5.09 \times 10^4$ | 2.3 | −749 |
| **PPA-Phe-1c** | **PA-Phe** | 99.1 | $CHCl_3$ | 0.10 | $1.14 \times 10^5$ | 3.6 | −754 |
| **PPA-Phe-2a** | **PA-Phe** | 97.8 | DMF | 0.03 | $1.40 \times 10^5$ | 5.9 | −718 |
| **PPA-Phe-2b** | **PA-Phe** | 98.3 | DMF | 0.06 | $1.61 \times 10^5$ | 6.0 | −707 |
| **PPA-Phe-2c** | **PA-Phe** | 97.2 | DMF | 0.10 | $2.57 \times 10^5$ | 5.6 | −667 |
| **PPA-Phg-1a** | **PA-Phg** | 96.7 | $CHCl_3$ | 0.03 | $4.50 \times 10^3$ | 3.3 | −573 |
| **PPA-Phg-1b** | **PA-Phg** | 97.6 | $CHCl_3$ | 0.06 | $1.38 \times 10^5$ | 4.4 | −787 |
| **PPA-Phg-1c** | **PA-Phg** | 98.1 | $CHCl_3$ | 0.10 | $2.07 \times 10^5$ | 5.6 | −805 |
| **PPA-Phg-2a** | **PA-Phg** | 97.7 | DMF | 0.03 | $1.69 \times 10^5$ | 5.5 | −756 |
| **PPA-Phg-2b** | **PA-Phg** | 98.4 | DMF | 0.06 | $1.75 \times 10^5$ | 6.2 | −738 |
| **PPA-Phg-2c** | **PA-Phg** | 98.2 | DMF | 0.10 | $2.19 \times 10^5$ | 6.0 | −695 |

[a]Polymerization condition: catalyst, $Rh(nbd)BPh_4$; [Monomer]/[$Rh(nbd)BPh_4$] = 45/1; temperature, 28 °C; time, 24 h. [b]Hexane insoluble part, determined via gravimetry. [c]Determined by SEC in DMF containing LiCl (0.01 M) using polystyrene standards. [d]In $CHCl_3$, specific rotations of the monomers in $CHCl_3$: $[\alpha]_D^{20}$(**PA-Pha**) = +123°, $[\alpha]_D^{20}$(**PA-Phg**) = +58.5°.

different conformations of the helical poly(phenylacetylene) derivatives were induced by changing the coating solvents.[25,26] In this study, we designed and synthesized novel stereoregular one-handed helical poly(phenylacetylene) derivatives (**PPA-Phe** and **PPA-Phg**) with an amide linkage bearing L-phenylalanine and L-phenylglycine ethyl ester pendants in order to develop effective CSPs for HPLC. The influence of the molecular weight and optical activity of the polymers on the chiral recognition abilities, and the influence of the structure of the pendant groups on the chiral recognition abilities will be mainly discussed.

## EXPERIMENTAL SECTION

**Materials.** L-Phenylalanine (purity 99%) and L-phenylglycine (purity 98%) were purchased from Shanghai Jingchun Reagent Co., Ltd. (Shanghai, China). Hydrochloride in ethanol (30−40%) was purchased from Chengdu Xiya Chemistry Technology Co., Ltd. (Chengdu, China). 4-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-4-methyl morpholinium 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). 4-Ethynylbenzoic acid was synthesized according to a previously reported method.[27] $Rh^+$(2,5-norbornadiene)$[(\eta^6\text{-}C_6H_5)B(C_6H_5)_3]$ ($Rh(nbd)BPh_4$) was prepared based on a previous report.[28] 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). The porous spherical silica gel with a mean particle size of 7 μm and a mean pore diameter of 100 nm (Daiso gel SP-1000−7) for HPLC was kindly supplied by Daiso Chemicals (Osaka, Japan), then silanized with (3-aminopropyl)triethoxysilane in toluene at 80 °C before use. All solvents used in the preparation of the chiral stationary phases were of analytical grade. Hexane and 2-propanol used in chromatographic


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experiments were of HPLC grade. The racemates were commercially available or were prepared by the usual methods.

**Instrumentation.** The $^1$H NMR spectra (500 MHz) were recorded using a Bruker AVANCE III-500 instrument at room temperature. The number-average molecular weight ($M_n$), the weight-average molecular weight ($M_w$), and the polydispersity ($M_w/M_n$) of the polymers were determined by size exclusion chromatography (SEC) calibrated with standard polystyrenes at 40 °C using a JASCO SEC system (PU-980 Intelligent pump, CO-965 column oven, RI-930 Intelligent RI detector, and Shodex DEGAS KT-16) equipped with a Shodex Asahipak GF-310 HQ column (linear, 7.6 mm ×300 mm; pore size, 20 nm; bead size, 5 μm; exclusion limit, 4 × 104) and a Shodex Asahipak GF-7 M HQ column (linear, 7.6 mm ×300 mm; pore size, 20 nm; bead size, 9 μm; exclusion limit, 4 × $10^7$) in DMF containing lithium chloride (0.01 M) at the flow rate of 0.4 mL· $min^{-1}$. The optical rotation was measured in $CHCl_3$ at room temperature using a Perkin-Elmer Model 341 polarimeter. 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. All the enantioseparation experiments were performed using a JASCO PU-2089 high performance liquid chromatograph (HPLC) system equipped with UV−vis (JASCO-UV-2070) and circular dichroism (JASCO-CD-2095) detectors. A solution of a racemate (3 mg/mL) was injected into the chromatographic system through an intelligent sampler (JASCO AS-2055). The thermogravimetric analyses (TGA) were performed using a TGA Q 50 (TA) instrument.

**Synthesis of L-Phenylalanine Ethyl Ester and L-Phenylglycine Ethyl Ester.** L-Phenylalanine ethyl ester and L-phenylglycine ethyl ester were synthesized via the esterification reaction of the corresponding L-amino acid in a hydrochloride ethanol solution. A typical procedure is described as follows. L-Phenylalanine (8.00 g, 48.0 mmol) and hydrochloride in ethanol (1.50M, 160 mL) were added to a 500 mL round-bottomed flask. The mixture was refluxed with stirring for 15 h and turned yellow. It was then cooled to room temperature, and extracted in a saturated $NaHCO_3$ aqueous solution and $CH_2Cl_2$. The organic layer was dried using $MgSO_4$ and filtered. The filtrate was evaporated to remove the $CH_2Cl_2$ to give the L-phenylalanine ethyl ester as a brown-yellow liquid. Yield: 7.63g (82.2%). $^1$H NMR (500 MHz, $CDCl_3$, TMS, ppm): $\delta$ = 7.33−7.20 (m, 5H, Ar−***H***), 4.20−4.15 (q, 2H, −O−C***H***$_2$−), 3.77−3.74 (t, 1H, −C***H***−), 3.13−2.88 (d, 2HAr−C***H***$_2$−), 2.13 (s, 2H, −N***H***$_2$), 1.27−1.23 (t, 3H, −C***H***$_3$).

According to the above procedure, the L-phenylglycine ethyl ester was synthesized as a pale yellow liquid. Yield: 76.4%. $^1$H NMR (500 MHz, $CDCl_3$, TMS, ppm): $\delta$ = 7.39−7.28 (m, 5H, Ar−***H***), 4.59 (s, 1H, −C***H***−), 4.24−4.09 (q, 2H, −C***H***$_2$−), 1.86 (s, 2H, −N***H***$_2$), 1.25−1.19 (t, 3H, −C***H***$_3$).

**Synthesis of *N*-(4-Ethynylbenzoyl)-L-phenylalanine Ethyl Ester (PA-Phe) and *N*-(4-Ethynylbenzoyl)-L-phenylglycine Ethyl Ester (PA-Phg).** The *N*-(4-ethynylbenzoyl)-L-phenylalanine ethyl ester (**PA-Phe**) and *N*-(4-ethynylbenzoyl)-L-phenylglycine ethyl ester (**PA-Phg**) were synthesized via the amidation reaction between 4-ethynylbenzoic acid and L-phenylalanine ethyl ester or L-phenylglycine ethyl ester. A typical procedure is described as follows. To a solution of the 4-ethynylbenzoic acid (4.30 g, 29.4 mmol) and DMT-MM (8.93 g, 32.3 mmol) in MeOH (150 mL) was added the L-phenylalanine ethyl ester (5.68 g, 29.4 mmol). After stirring at room temperature for 18 h, the reaction mixture was purified by column chromatography on silica gel with hexane/ethyl acetate (3/1, v/v) to give **PA-Phe** as pale yellow crystals. Yield: 7.36 g (78.0%). $^1$H NMR (500 MHz, $CDCl_3$, TMS, ppm): $\delta$ = 7.68−7.66 (d, 2H, Ar−***H***), 7.54−7.52 (d, 2H, Ar−***H***), 7.30−7.26 (t, 1H, Ar−***H***), 7.26−7.23 (t, 2H, Ar−***H***), 7.14−7.12 (d, 2H, Ar−***H***), 6.57−6.54 (d, 1H, −N***H***−), 5.07−5.02 (q, 1H, NH−C***H***−), 4.24−4.19 (q, 2H, −O−C***H***$_2$−), 3.31−3.21(m, 2H, Ar−C***H***$_2$−), 3.20 (s, 1H, ≡C***H***), 1.30−1.26 (t, 3H, −C***H***$_3$). $^{13}$C NMR (125 MHz, $CDCl_3$, TMS, ppm): $\delta$ = 171.5 (−***C***O−(ester)), 166.0 (−***CO***− (amino)), 153.8 (aromatic), 134.0 (aromatic), 132.3 (aromatic), 129.4 (aromatic), 128.6 (aromatic), 127.2 (aromatic), 127.0 (aromatic), 125.7 (aromatic), 82.7 (−***C***≡CH), 79.6 (−C≡***C***H), 61.7(−***C***H$_2$−CH$_3$), 53.6 (−***C***H−NH), 37.9 (−***C***H$_2$−CH), 14.2 (−CH$_2$−***C***H$_3$). Anal. Calcd for $C_{20}H_{19}O_3N$ (321): C, 74.77; H, 5.92; N, 4.36. Found: C, 74.75; H, 5.95; N, 4.40.

According to the procedure, **PA-Phg** was synthesized as pale yellow crystals. Yield: 7.28 g (75.5%). $^1$H NMR (500 MHz, $CDCl_3$, TMS, ppm): $\delta$ = 7.80−7.75 (d, 2H, Ar−***H***), 7.57−7.54 (d, 2H, Ar−***H***), 7.45−7.43 (t, 2H, Ar−***H***), 7.40−7.36 (t, 1H, Ar−***H***), 7.36−7.32 (d, 2H, Ar−***H***), 7.17−1.15 (d, 1H, −N***H***−), 5.76−5.74 (d, 1H, NH−C***H***−), 4.32−4.15 (mm, 2H, −O−C***H***$_2$−), 3.21 (s, 1H, ≡C***H***), 1.26−1.23 (t, 3H, −C***H***$_3$). $^{13}$C NMR (125 MHz, $CDCl_3$, TMS, ppm): 171.0 (−***C***O−(ester)), 165.7 (−***CO***− (amino)), 136.6 (aromatic), 133.6 (aromatic), 132.3 (aromatic), 129.0 (aromatic), 128.6 (aromatic), 127.3 (aromatic), 127.1 (aromatic), 125.7 (aromatic), 82.7 (−***C***≡CH), 79.7 (−C≡***C***H), 62.1(−***C***H$_2$−CH$_3$), 56.9 (−***C***H−NH), 14.0 (−CH$_2$−***C***H$_3$). Anal. Calcd for $C_{19}H_{17}O_3N$ (321): C, 74.27; H, 5.54; N, 4.56. Found: C, 74.62; H, 5.62; N, 4.56.

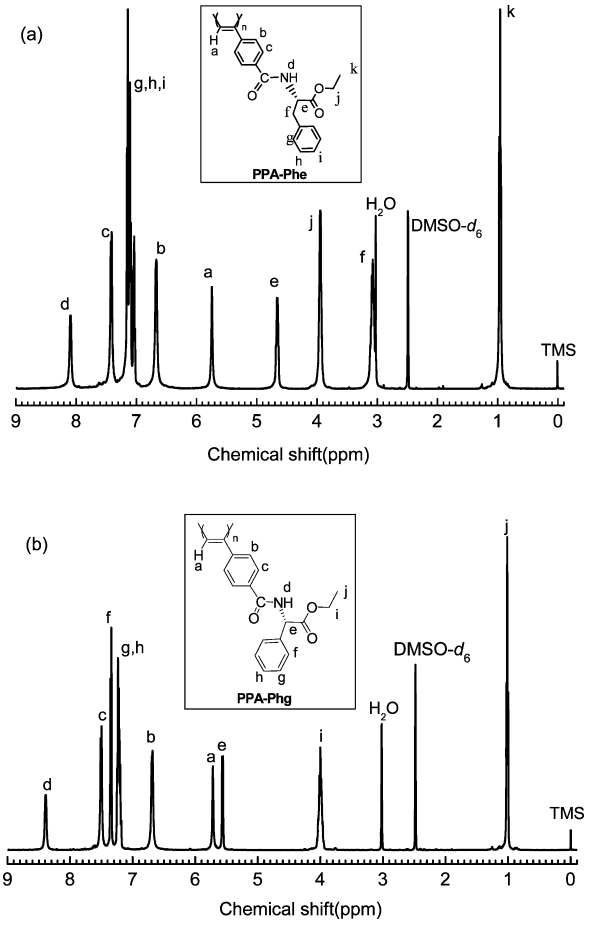


**Figure 1.** $^1$H NMR spectra of (a) **PPA-Phe-1a** and (b) **PPA-Phg-1a** in DMSO-$d_6$ at 80 °C.

**Table 2. Specific Rotations of PPA-Phe-1a and PPA-Phg-1a in Different Solvents**

| | $[\alpha]_D^{20}$/deg | | | | | |
|---|---|---|---|---|---|---|
| polymers[a] | $CHCl_3$ | $CH_2Cl_2$ | DMF | acetone | DMSO | DMAc |
| **PPA-Phe-1a** | −714 | −159 | +418 | +378 | +288 | +261 |
| **PPA-Phg-1a** | −573 | −381 | +259 | +271 | +331 | +221 |

[a]Specific rotations of the monomers in $CHCl_3$: $[\alpha]_D^{20}$ (**PA-Phe**) = +123°, $[\alpha]_D^{20}$(**PA-Phg**) = +58.5°.

**Polymerization.** The polymerization of **PA-Phe** and **PA-Phg** was carried out in dry $CHCl_3$ or DMF using Rh(nbd)$BPh_4$ as a catalyst under a nitrogen atmosphere for 24 h at 28 °C with $[monomer]_0$ = 0.03, 0.06, 0.10 M, and $[monomer]_0/[Rh(nbd)BPh_4]_0$ = 44.5. A typical procedure is described as follows. **PA-Phe** (1.40 g, 4.36 mmol)


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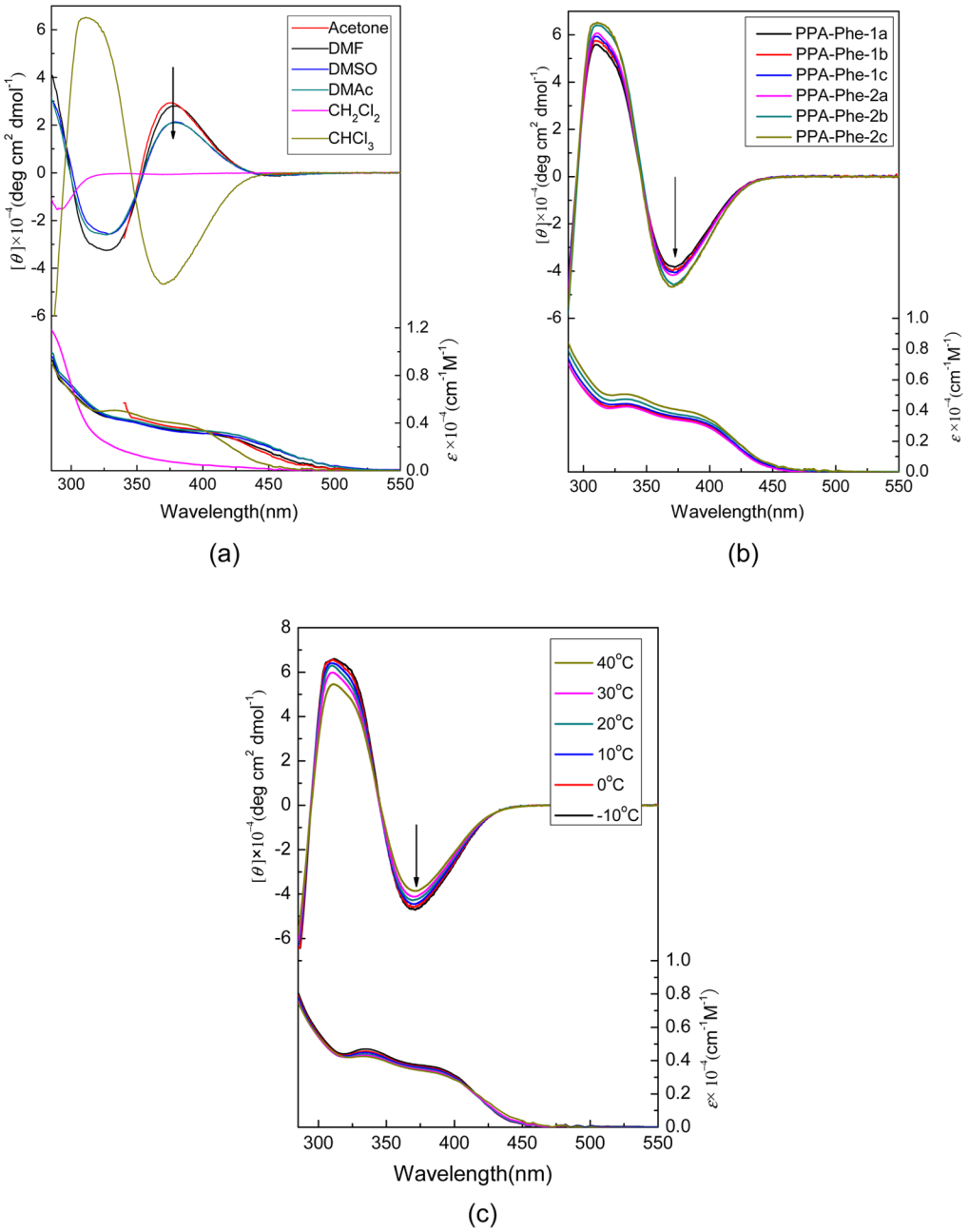


**Figure 2.** CD (upper) and UV–vis (lower) spectra of (a) **PPA-Phe-2c** in variable solvents at 25 °C, (b) **PPA-Phe-1a–c** and **PPA-Phe2a–c** in $CHCl_3$ at 25 °C, and (c) **PPA-Phe-1a** in $CHCl_3$ at different temperature ($c$ = 1 mg/mL).

was weighed into a flask and dissolved in dry $CHCl_3$ (132.8 mL) before a solution of Rh(nbd)$BPh_4$ (50.4 mg, 98 $\mu$mol) in dry $CHCl_3$ (12.5 mL) was added. After stirring at room temperature for 24 h, triphenylphosphine (214.0 mg, 0.82 mmol) was added to the reaction mixture. The solution was concentrated and then poured into a large amount of hexane (1000 mL). The precipitates were purified by reprecipitation using hexane and then dried under reduced pressure to give **PPA-Phe** as a yellow solid (1.39 g, 99.3%). $M_n$ = 3.90 × 10$^4$; $M_w/M_n$ = 2.7. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS, ppm): $\delta$ = 8.15–8.04 (d, 1H, –N***H***–), 7.50–7.35 (d, 2H, Ar–***H***), 7.22–7.00 (m, 5H, Ar–***H***), 6.76–7.58 (d, 2H, Ar–***H***), 5.75 (s, 1H, main chain), 4.72–4.60 (q, 1H, NH–C***H***–), 4.03–3.88 (q, 2H, –O–C***H***$_2$–), 3.16–3.01 (m, 2H, Ar–C***H***$_2$–), 1.04–0.88 (t, 3H, –C***H***$_3$).

According to the above procedure, **PA-Phg** was polymerized to give **PPA-Phg** as a yellow solid. Yield = 96.7–98.4%. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS, ppm): $\delta$ = 8.45–8.32 (d, 1H, –N***H***–), 7.54–7.46 (d, 2H, Ar–***H***), 7.37–7.32 (d, 2H, Ar–***H***), 7.26–7.17 (m, 3H, Ar–***H***), 6.73–7.65 (d, 2H, Ar–***H***), 5.72 (s, 1H, main chain), 5.58–5.54 (d, 1H, NH–C***H***–), 4.05–3.94 (m, 2H, –O–C***H***$_2$–), 1.05–0.98 (t, 3H, –C***H***$_3$).

**Preparation of Chiral Stationary Phases (CSPs).** The poly(phenylacetylene) derivatives (**PPA-Phe** and **PPA-Phg**) (0.2 g each) were first dissolved in a coating solvent (5 mL) and then coated on aminopropyl silanized silica gel (0.8 g) according to a previous method.[29] The polymer-coated silica gels were then packed in a stainless-steel tube (25 cm ×0.20 cm i.d.) by a slurry method. The plate numbers of the packed columns were 1600–3100 for benzene using a hexane/2-propanol (95/5, v/v) mixture as the eluent at the flow rate of 0.1 mL/min at 25 °C. The dead time ($t_0$) of the columns was estimated using 1,3,5-tritert-butylbenzene as the nonretained compound.[30] The theoretical plate number ($N$) and $t_0$ of each column are summarized in Table S1 (see the Supporting Information). In order to tell variability from column preparation, an assessment of repeatability has been carried out. We repeated coating and packing processes three times to prepare three columns on one polymer as a


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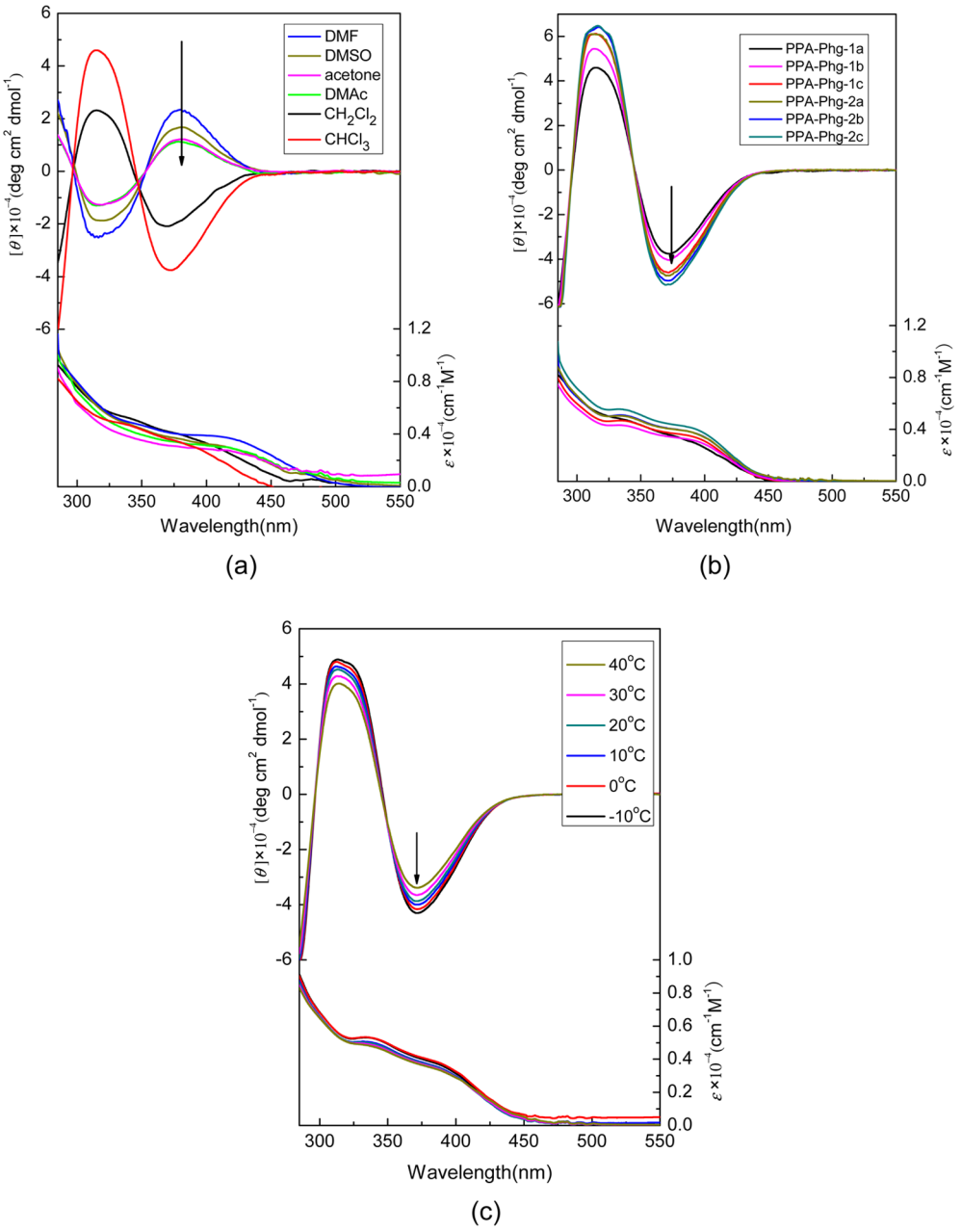


**Figure 3.** CD (upper) and UV−vis (lower) spectra of (a) **PPA-Phg-1a** in variable solvents at 25 °C, (b) **PPA-Phg-1a−c** and **PPA-Phg-2a−c** in $CHCl_3$ at 25 °C, and (c) **PPA-Phg-1a** in $CHCl_3$ at different temperature ($c$ = 1 mg/mL).

representative example, **PPA-Phe-1a**, which was synthesized in $CHCl_3$ with monomer concentration of 0.03 M. The comparison of resolution results on the three columns are summarized in Table S2 (see the Supporting Information). Thus, it has been confirmed that the inherent variability of $\alpha$ is quite small.

## RESULTS AND DISCUSSION

**Synthesis of Polymers PPA-Phe and PPA-Phg.** The monomers and polymers were synthesized via the route illustrated in Scheme 1. The amidation reaction of 4-ethynylbenzoic acid with the L-phenylalanine ethyl ester and L-phenylglycine ethyl ester proceeded using 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methyl morpholinium chloride (DMT-MM) as a catalyst in good yields to produce two novel monomers, *N*-(4-ethynylbenzoyl)-L-phenylalanine ethyl ester (**PA-Phe**) and *N*-(4-ethynylbenzoyl)-L-phenylglycine ethyl ester (**PA-Phg**), respectively. Comparing the structures of the two monomers, the benzyl group is adjacent to the chiral carbon atom of **PA-Phe**, while the phenyl group is adjacent to the chiral carbon atom of **PA-Phg**. The acetylenyl protons of **PA-Phe** and **PA-Phg** appeared at 3.20 and 3.21 ppm, respectively.

To obtain the stereoregular polymers for chiral separation, the monomers were polymerized using $Rh(nbd)BPh_4$ as a catalyst (Table 1). **PPA-Phe-1a−c** and **PPA-Phg-1a−c** were synthesized in $CHCl_3$ with the monomer concentrations of 0.03M, 0.06 M, and 0.10M, while **PPA-Phe-2a−c** and **PPA-Phg-2a−c** were obtained in *N,N*-dimethylformamide (DMF) with the monomer concentrations of 0.03M, 0.06 M, and 0.10 M. In all cases, the SEC profiles of the polymers were monomodal with high molecular weights. As shown in Table 1, the polymerization solvents and monomer concentration had effects on the molecular weight of the resultant polymers. **PPA-**


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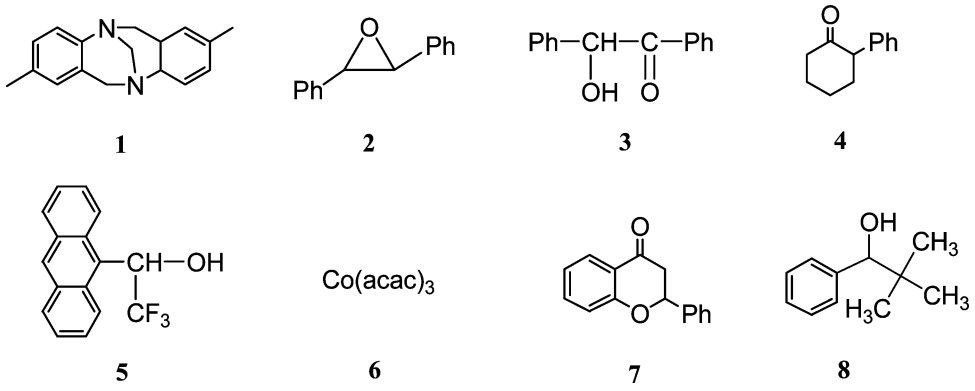


**Figure 4.** Structures of racemates.

**Table 3. Influence of Coating Solvents on Resolution of Racemates on PPA-Phe-2c**[a]

| | $CHCl_3$ | | $CH_2Cl_2$ | | acetone | | DMF | |
|---|---|---|---|---|---|---|---|---|
| racemates | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ |
| **1** | 0.36 | ~1(+) | 0.53 | 1.00 | 0.23 | 1.00 | 0.35 | 1.00 |
| **2** | 0.37 | 3.50(+) | 0.77 | 1.00 | 0.31 | 1.00 | 0.37 | 1.00 |
| **3** | 3.36 | 1.00 | 3.44 | 1.00 | 2.64 | 1.00 | 3.36 | 1.00 |
| **4** | 0.92 | ~1(−) | 0.97 | 1.00 | 0.67 | 1.00 | 0.90 | 1.00 |
| **5**[b] | 9.45 | 1.33(+) | 10.13 | 1.00 | 7.97 | 1.00 | 9.97 | 1.00 |
| **6** | 1.36 | ~1(+) | 1.04 | ~1(+) | 0.87 | ~1(+) | 1.46 | ~1(+) |
| **7** | 1.37 | 1.00 | 1.52 | 1.00 | 0.88 | 1.00 | 1.18 | 1.00 |
| **8** | 0.48 | 1.00 | 0.57 | 1.00 | 0.28 | 1.00 | 0.35 | 1.00 |

**Phe-1a−c** and **PPA-Phg-1a−c** synthesized in $CHCl_3$ showed lower molecular weights than **PPA-Phe-2a−c** and **PPA-Phg-2a−c** synthesized in DMF. In addition, the molecular weight of the polymers increased with the increasing monomer concentration in both solvents. All of the obtained polymers were soluble in $CHCl_3$, $CH_2Cl_2$, acetone, DMF, *N*,*N*-dimethylacetamide (DMAc), and dimethyl sulfoxide (DMSO), but only partially soluble in tetrahydrofuran (THF), and insoluble in hexane and 2-propanol. Figure 1 depicts the assigned $^1$H NMR spectra of **PPA-Phe-1a** and **PPA-Phg-1a** in DMSO-$d_6$ at 80 °C as representative examples. The $^1$H NMR spectra showed the characteristic signals due to the main chain proton at 5.75 and 5.72 ppm, respectively, indicating the stereoregular *cis*-configuration in the polyacetylene main chain.

**Chiroptical Properties of PPA-Phe and PPA-Phg.** As shown in Table 1, a series of **PPA-Phe**s showed high levorotatory optical rotations ($[\alpha]_D^{20}$ = −754° to −667°) in $CHCl_3$, though the optical rotation of the corresponding monomer (**PA-Phe**) was +123° in the same solvent. These opposite optical rotations of the polymers in $CHCl_3$ suggest that a new structure, most likely a secondary helical structure, is formed after the polymerization. Moreover, the polymerization solvents and monomer concentration had influences on the optical rotations of the resultant polymers. **PPA-Phe-1a−c** synthesized in $CHCl_3$ exhibited higher optical rotations, and the optical rotations increased with the increasing concentration of **PA-Phe**. In contrast, **PPA-Phe-2a−c** synthesized in DMF showed lower optical rotations, and the optical rotations slightly decreased with the increasing concentration of **PA-Phe**.

Table 1 also shows the optical rotations of a series of **PPA-Phg**s in $CHCl_3$. Compared to the optical rotation of **PA-Phg** ($[\alpha]_D^{20}$ = +58°), high levorotatory optical activities ($[\alpha]_D^{20}$ = −805° to −573°) of the **PPA-Phg**s were obtained in $CHCl_3$. These results also suggest that the polymer main chains possess a helical conformation with a preferred screw sense. As well as **PPA-Phe**, the optical rotations of **PPA-Phg**s were also influenced by the polymerization solvents and monomer concentration. **PPA-Phg-1a−c** synthesized in $CHCl_3$ exhibited higher optical rotations than those obtained in DMF. In $CHCl_3$, the optical rotations of the obtained polymers increased with the increasing concentration of **PA-Phg**, whereas the optical rotations of **PPA-Phg-2a−c** synthesized in DMF slightly decreased with the increasing concentration of **PA-Phg**.

In addition, the optical rotations of **PPA-Phe-1a** and **PPA-Phg-1a** were also determined in various solvents (Table 2). The $[\alpha]_D^{20}$ values of **PPA-Phe-1a** and **PPA-Phg-1a** were negative in $CH_2Cl_2$ and $CHCl_3$, while these values were positive in polar solvents, such as acetone, DMF, DMAc, and DMSO. The observed significant solvent dependence of the optical activity suggests that the polymers possess dynamic helical structure highly dependent on solvent.

To confirm the helical structure of **PPA-Phe** and **PPA-Phg**, their chiroptical properties were investigated by CD spectroscopy (Figures 2 and 3). Figure 2a shows the solvent dependence on the chiroptical properties of **PPA-Phe-2c** as a representative example for a series of **PPA-Phe**s. **PPA-Phe-2c** showed distinct Cotton effects due to the absorption of the helical poly(phenylacetylene) backbone in acetone, DMF, DMSO, DMAc, and $CHCl_3$ in the range from 300 to 500 nm, indicating that **PPA-Phe-2c** main chain definitely possesses a predominantly one-handed helical conformation.[21,31] Similar to the $[\alpha]_D^{20}$ values, the chain helicity of the **PPA-Phe**s changed with the solvents. The polymer induced the same split-type Cotton effects in acetone, DMF, DMSO, and DMAc, i.e., the first positive Cotton effect at 375 nm and the second negative Cotton effect at


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320 nm. The CD profiles in $CHCl_3$ were nearly mirror images of those found in acetone, DMF, DMSO, and DMAc, showing the first negative Cotton effect at 370 nm and the second positive Cotton effect at 312 nm. In addition, weak Cotton effects and a UV−vis absorption were exhibited in $CH_2Cl_2$.[32] These results suggested that **PPA-Phe-2c** has a dynamic helical conformation in these solvents. Figure 2(b) shows the CD and UV−vis spectra of **PPA-Phe-1a−c** and **PPA-Phe-2a−c** in $CHCl_3$ at 25 °C. These polymers showed the consistent CD and UV−vis profiles in $CHCl_3$ in the range from 300 to 500 nm with similar CD intensities. Figure 2(c) shows the influence of temperature on the chiroptical property of **PPA-Phe-1a** in $CHCl_3$. **PPA-Phe-1a** showed the consistent CD and UV−vis profiles in $CHCl_3$ at the temperatures of −10 to +40 °C. The CD intensities of **PPA-Phe-1a** in $CHCl_3$ slightly decreased when the temperature was progressively increased from −10 to +40 °C. This suggests that the rigid and one-handed helical conformation of **PPA-Phe-1a** is probably stabilized by intramolecular hydrogen bonds so that the CD intensity is almost unchanging even when the solution is heated to 40 °C.[33,34]

The chiroptical properties of a series of **PPA-Phg**s are similar to those of the **PPA-Phe**s. As shown in Figure 3a, **PPA-Phg-1a**, as a representative example for a series of **PPA-Phg**s, exhibited intense CD signals at 300 nm-500 nm with high molar ellipticities in $CHCl_3$, while its monomer is completely CD-inactive in this wavelength range. Thus, the observed Cotton effects must be associated with the polymer backbone, unambiguously indicating that the polymer takes a helical structure with a predominant one-handed screw sense. Similar to the $[\alpha]_D^{20}$ values, the chain helicity of **PPA-Phg**s changed with the solvents. The polymer induced the same split-type Cotton effects in acetone, DMF, DMSO, and DMAc, showing the first positive Cotton effect at 380 nm and the second negative Cotton effect at 322 nm. The CD profiles in $CHCl_3$ and $CH_2Cl_2$ were nearly mirror images of those found in acetone, DMF, DMSO, and DMAc, showing the first negative Cotton effect at 372 nm and the second positive Cotton effect at 315 nm. As shown in Figure 3b, the CD and UV−vis profiles of **PPA-Phg-1a−c** and **PPA-Phg-2a−c** are quite similar, and from Figure 3c, the existence of the stable one-handed helical conformation of **PPA-Phg-1a** at the temperatures of −10 to +40 °C was confirmed.

**Chiral Recognition of PPA-Phe.** Because a series of **PPA-Phe**s not only have a chirality at pendants, but also possess a one-handed helical conformation at the main chains, they are expected to show a chiral recognition. Their chiral recognition abilities were evaluated as CSPs in HPLC using the eight tested racemates shown in Figure 4.

As **PPA-Phe**s showed different optical rotations and Cotton effects in $CHCl_3$, $CH_2Cl_2$, acetone, and DMF, these solvents were selected as the solvent for coating the **PPA-Phe**s on the silica gel. The influences of the coating solvents on the resolution of the racemates on **PPA-Phe-2c** were evaluated by HPLC as a representative example of a series of **PPA-Phe**s, and these results are summarized in Table 3. **PPA-Phe-2c** showed different chiral recognition abilities under the same chromatographic conditions when different coating solvents were used.[25] The retention factor, $k_1'$ [$=(t_1 - t_0)/t_0$], for the first eluted enantiomer in Table 3 is the factor indicating the interaction strength between a CSP and the corresponding enantiomer, and can be obtained from its elution time $t_1$ and the dead time $t_0$. The $k_1'$ values varied with the coating solvents of **PPA-Phe-2c**. The separation factor $\alpha$, which is directly correlated to the chiral recognition ability of a CSP, is an important factor for

**Table 4. Resolution of Racemates on PPA-Phe-1a−c and PPA-Phe-2a−c**[a]

| | PPA-Phe-1a | | PPA-Phe-1b | | PPA-Phe-1c | | PPA-Phe-2a | | PPA-Phe-2b | | PPA-Phe-2c | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| racemates | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ |
| **1** | 0.28 | 1.25(+) | 3.71 | 1.00 | 0.57 | ~1(+) | 0.49 | ~1(+) | 0.58 | ~1(+) | 0.36 | ~1(+) |
| **2** | 0.36 | ~1(−) | 0.52 | 1.69(+) | 0.69 | 2.69(+) | 0.54 | 2.60(+) | 0.67 | 2.35(+) | 0.37 | 3.50(+) |
| **3** | 2.34 | 1.00 | 3.03 | 1.00 | 3.62 | 1.08(+) | 3.02 | 1.00 | 3.56 | 1.00 | 3.36 | 1.00 |
| **4** | 0.65 | ~1(+) | 0.90 | 1.00 | 1.17 | ~1(−) | 1.01 | ~1(−) | 1.13 | ~1(−) | 0.92 | ~1(−) |
| **5** | 9.37 | 1.55(+) | 8.11 | 1.43(+) | 8.03 | 1.07(+) | 6.44[b] | 1.35(+)[b] | 6.84[b] | 1.25(+)[b] | 9.45[b] | 1.33(+)[b] |
| **6** | 0.97 | ~1(+) | 1.30 | ~1(+) | 1.18 | ~1(+) | 1.13 | ~1(+) | 1.21 | ~1(+) | 1.36 | ~1(+) |
| **7** | 1.01 | 1.00 | 1.25 | 1.00 | 1.54 | 1.00 | 1.31 | 1.00 | 1.47 | 1.00 | 1.37 | 1.00 |
| **8** | 0.34 | ~1(−) | 0.39 | 1.00 | 0.63 | ~1(+) | 0.49 | ~1(+) | 0.60 | ~1(+) | 0.48 | 1.00 |

[a]Column: 25 cm × 0.20 cm i.d. Coating solvent: $CHCl_3$. Eluent: hexane/2-propanol (95/5, v/v). Flow rate: 0.1 mL/min. The signs in parentheses represent the optical rotation of the first-eluted enantiomer. [b]Flow rate: 0.5 mL/min.


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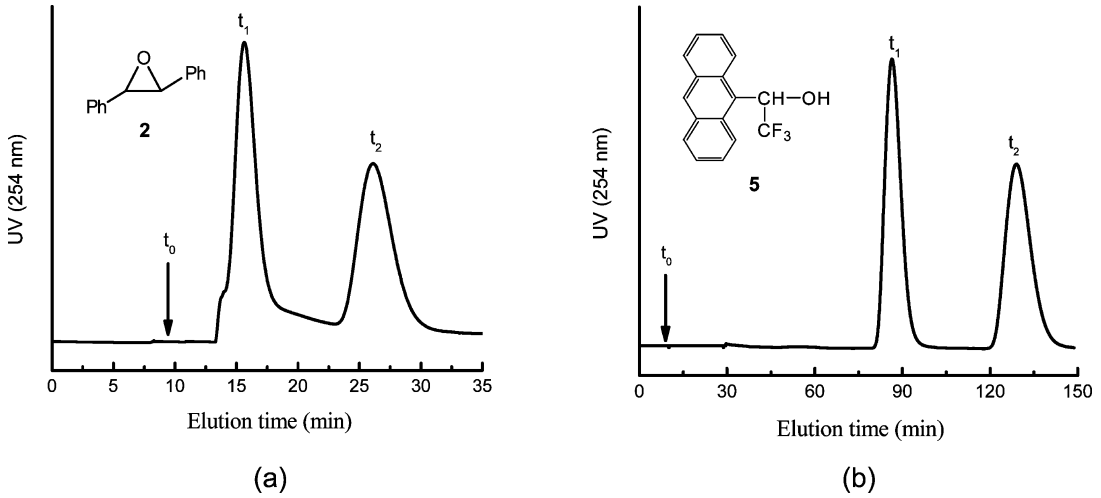


**Figure 5.** Chromatograms for the resolution of (a) *trans*-stilbene oxide (**2**) on **PPA-Phe-2c** and (b) 1-(9-anthyl)-2,2,2-trifluoroethanol (**5**) on **PPA-Phe-1a** with hexane/2-propanol (95/5) as eluent.

**Table 5. Influence of Coating Solvents on Resolution of Racemates on PPA-Phg-1a**[a]

| | $CHCl_3$ | | CH2Cl2 | | Acetone | |
|---|---|---|---|---|---|---|
| racemates | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ | $K_1'$ | $\alpha$ |
| **1** | 0.56 | 1.50(+) | 0.52 | 1.00 | 0.54 | 1.00 |
| **2** | 0.37 | 1.24(−) | 0.68 | 1.00 | 0.64 | 1.00 |
| **3** | 5.18 | 1.00 | 5.39 | 1.00 | 6.03 | 1.00 |
| **4** | 1.32 | ~1(+) | 1.25 | 1.00 | 1.33 | 1.00 |
| **5** | 20.13[b] | 1.57(+)[b] | 19.88 | 1.49(+) | 22.82 | 1.22(+) |
| **6** | 1.99 | ~1(+) | 0.79 | 1.00 | 0.49 | 1.00 |
| **7** | 2.34 | 1.00 | 2.25 | 1.00 | 2.31 | 1.00 |
| **8** | 0.55 | ~1(−) | 0.49 | ~1(−) | 0.47 | 1.00 |

[a]Column: 25 cm ×0.20 cm i.d. Eluent: hexane/2-propanol (95/5, v/v). Flow rate: 0.1 mL/min. The signs in parentheses represent the optical rotation of the first-eluted enantiomer. [b]Flow rate: 0.5 mL/min.

evaluating a CSP. If $\alpha$ is equal to 1.00, this means no chiral recognition, and the higher $\alpha$ value, the better the chiral recognition ability of a CSP. Although **PPA-Phe-2c** coated with $CH_2Cl_2$, acetone or DMF exhibited a very low chiral recognition for 6 racemates, it showed a clear enantioselectivity of *trans*-stilbene oxide (**2**) and 1-(9-anthyl)-2,2,2-trifluoroethanol (**5**) when coated with $CHCl_3$. The coating solvent dependence of **PPA-Phe-2c** is probably due to the variation in its conformation on the silica surface induced by the coating solvents. A higher chiral recognition was obtained when **PPA-Phe-2c** was coated with $CHCl_3$ in which the polymer exhibited a negative $[\alpha]_D^{20}$ value and showed the first negative Cotton effect at 370 nm and the second positive Cotton effect at 312 nm. This conformation is preferable in order to attain a higher chiral recognition. The **PPA-Phe-2c** in acetone or DMF showed nearly mirror images of that found in $CHCl_3$, and exhibited very low chiral recognition abilities. In addition, the **PPA-Phe-2c** with a weak Cotton effects below 320 nm in $CH_2Cl_2$ also exhibited very low chiral recognition abilities.

As already mentioned, the polymerization conditions, such as the polymerization solvents and monomer concentration, have effects on the molecular weight and chiroptical properties of the resultant polymers. In this study, the influences of these factors on the chiral recognition abilities of the **PPA-Phe**s were investigated for some racemates, and the results are summarized in Table 4. Most of the **PPA-Phe**s recognized the enantiomers of racemates **2** and **5**, but the retention factor and separation factor did not show a clear dependence on the molecular weight and optical rotations. **PPA-Phe-1a−c**, which were synthesized in $CHCl_3$, showed a higher chiral recognition for **2** with the increasing molecular weight. One the other hand, their chiral recognition for **5** decreased with the increasing molecular weight and the highest separation factor was 1.55, which is comparable to those obtained on the very popular polysaccharide-based CSPs, Chiracel OD ($\alpha$ = 2.59) and Chiralpak AD ($\alpha$ = 1.39).[11,29]

**PPA-Phe-2a−c**, which were synthesized in DMF, exhibited a higher chiral recognition for **2** than **PPA-Phe-1a−c** synthesized in $CHCl_3$. In addition, a higher chiral recognition of $\alpha$ = 3.50 for **2** was achieved by the higher molecular weight polymer **PPA-Phe-2c**. This high $\alpha$ value is higher than those obtained on Chiralcel OD ($\alpha$ = 1.68) and Chiralpak AD ($\alpha$ = 2.81).[11,29] Figure 5 shows the chromatograms of the resolution of **2** on **PPA-Phe-2c** and **5** on **PPA-Phe-1a**, whose enantiomers were completely separated. These results indicated that the chiral recognition abilities of the helical **PPA-Phe**s are sensitive to the polymer structures such as molecular weight and stereoregularity. Their chiral recognition abilities were maintained for at least half a year, implying the good conformational stability of the **PPA-Phe**s series.

**Chiral Recognition of PPA-Phg.** To elucidate the role of the chiral pendants on the chiral recognition of the helical poly(phenylacetylene) derivatives, another new monomer **PA-Phg** was synthesized and polymerized in $CHCl_3$ and DMF with


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Table 6. Resolution of Racemates on PPA-Phg-1a−c and PPA-Phg-2a−c[a]

| | PPA-Phg-1a | | PPA-Phg-1b | | PPA-Phg-1c | | PPA-Phg-2a | | PPA-Phg-2b | | PPA-Phg-2c | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| racemates | $k_1'$ | $\alpha$ | $k_1'$ | $\alpha$ | $k_1'$ | $\alpha$ | $k_1'$ | $\alpha$ | $k_1'$ | $\alpha$ | $k_1'$ | $\alpha$ |
| **1** | 0.56 | 1.50(+) | 0.54 | 1.71(+) | 1.56 | ~1(+) | 0.66 | ~1(+) | 0.60 | 1.59(+) | 0.50 | 1.33(+) |
| **2** | 0.37 | 1.24(−) | 0.78 | 1.36(−) | 0.70 | ~1(−) | 0.70 | 1.00 | 0.88 | 1.32(−) | 0.70 | ~1(−) |
| **3** | 5.18 | 1.00 | 5.88 | 1.00 | 5.01 | 1.00 | 5.01 | 1.00 | 5.70 | 1.00 | 4.60 | 1.00 |
| **4** | 1.32 | ~1(+) | 1.49 | ~1(+) | 1.32 | ~1(+) | 1.24 | ~1(+) | 1.49 | ~1(+) | 1.18 | ~1(+) |
| **5**[b] | 20.13 | 1.57(+) | 21.89 | 1.52(+) | 16.73 | 1.23(+) | 17.39 | 1.21(+) | 24.92 | 1.77(+) | 19.10 | 1.53(+) |
| **6** | 1.99 | ~1(+) | 2.91 | ~1(+) | 2.37 | 1.00 | 2.09 | ~1(+) | 1.94 | 1.00 | 1.63 | ~1(+) |
| **7** | 2.34 | 1.00 | 2.98 | 1.00 | 2.16 | 1.00 | 2.08 | 1.00 | 2.83 | 1.00 | 2.03 | 1.00 |
| **8** | 0.55 | ~1(−) | 0.47 | ~1(−) | 0.47 | ~1(−) | 0.47 | 1.00 | 0.70 | ~1(−) | 0.54 | ~1(−) |

[a]Column: 25 cm ×0.20 cm i.d. Coating solvent: $CHCl_3$. Eluent: hexane/2-propanol (95/5, v/v). Flow rate: 0.1 mL/min. The signs in parentheses represent the optical rotation of the first-eluted enantiomer. [b]Flow rate: 0.5 mL/min.

different monomer concentrations using $Rh(nbd)BPh_4$ as the catalyst to obtain a series of helical **PPA-Phg**s. The difference between the chemical structures of **PPA-Phg** and **PPA-Phe** is the group adjacent to the chiral carbon atom at the pendants; **PPA-Phg** has a phenyl group and **PPA-Phe** has a benzyl group.

The chiral recognition abilities of a series of **PPA-Phg**s were also evaluated as CSPs for HPLC. Similar to the **PPA-Phe**s, a series of **PPA-Phg**s also showed different optical rotations and Cotton effects in $CHCl_3$, $CH_2Cl_2$, acetone, and DMF (see Table 2 and Figure 3, respectively). $CHCl_3$, $CH_2Cl_2$, and acetone were selected as the coating solvents to prepare the **PPA-Phg** CSPs. The influences of the coating solvents on the resolution of the racemates on **PPA-Phg-1a** as a representative example were evaluated by HPLC, and the results are summarized in Table 5. As shown in Table 5, the retention factor $k_1'$ and separation factor $\alpha$ varied depending on the coating solvents of **PPA-Phg-1a** on silica gel. The **PPA-Phg-1a** coated with $CHCl_3$ showed a higher chiral recognition than that coated with $CH_2Cl_2$ and acetone. The high negative $[\alpha]_D^{20}$ value and the stronger first negative Cotton effect at 372 nm and second positive Cotton effect at 315 nm in $CHCl_3$ suggested that the polymer has a higher one-handedness in this solvent, which seems to be related to the higher chiral recognition.

Table 6 shows the resolution results of the racemates on a series of **PPA-Phg**s under the same chromatographic conditions. Most of the **PPA-Phg**s showed a chiral recognition for the Tröger base (**1**) in addition to **2** and **5**, which were well resolved on the **PPA-Phe**s. In addition, the retention factor of racemate **5** on the **PPA-Phg**s was much greater than that on **PPA-Phe**s, indicating the stronger interaction between the **PPA-Phg**s and racemate **5**. These results imply that the absence of the $-CH_2-$ group between the chiral carbon atom and phenyl group at the pendants improved the chiral recognition for racemate **1** and increased the interaction with racemate **5**. This means that the group adjacent to the chiral carbon atom at the pendants also plays an important role in the chiral recognition.

## CONCLUSION

A series of novel dynamic helical poly(phenylacetylene) derivatives, **PPA-Phe** and **PPA-Phg**, with an amide linkage bearing L-phenylalanine and L-phenylglycine ethyl ester pendants, respectively, were synthesized to evaluate their chiral recognition as CSPs in HPLC using 8 racemates. The polymers changed their conformation in different solvents, which resulted in different chiral recognition abilities depending on the coating solvents on silica gel. Both **PPA-Phe** and **PPA-Phg** showed higher chiral recognitions when $CHCl_3$ was used as the coating solvent. In this solvent, the polymers showed a high negative $[\alpha]_D^{20}$ value and high first negative Cotton effect at 370−372 nm with the second positive Cotton effect at 312−315 nm. The chiral recognition abilities of the helical **PPA-Phe** and **PPA-Phg** probably depended on their molecular weight and optical rotations. The phenyl and benzyl groups adjacent to the chiral carbon atom at the pendants also play an important role in the chiral recognition. A few racemates were completely separated on **PPA-Phe** or **PPA-Phg** with high separation factors comparable or even higher than those obtained on the very popular CSPs derived from the phenylcarbamate derivatives of cellulose and amylose.

## ASSOCIATED CONTENT

### Supporting Information

Theoretical plate number ($N$) and dead time ($t_0$) of each column and comparison of resolution results on the three


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columns. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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