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Synthesis of Optically Active Helical Poly(phenylacetylene)s Bearing Oligopeptide Pendants and Their Use as Polymeric Organocatalysts for Asymmetric Epoxidation

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Bioinspired by the exquisite helical structures of the biological macromolecules, chemists have been challenged to construct artificial helical polymers[1] and oligomers (foldamers)[2] with controlled helicity that not only to mimic the structures of biological helices, but also to develop chiral materials with functionality. One possible application of helical polymers involves the enantiomer separation of racemic compounds by high-performance liquid chromatography (HPLC) where optically active helical polymers have been used as chiral stationary phases.[3] Another attractive application for helical polymers is use as an asymmetric catalysis, but successful examples are quite rare.[4−7] Reggelin et al., recently reported the first catalytic asymmetric allylic alkylation reaction using fully one-handed helical polymethacrylates[1a,d,8] complexed with palladium as the catalyst.[7] They also utilized a dynamic helical polyisocyanate composed of chiral and achiral isocyanates bearing an achiral phosphine pendant complexed with rhodium for an asymmetric hydrogenation reaction as catalysts.[7b] These static and dynamic helical polymeric catalysts showed enantioselectivity mainly based on their helical chirality, thus producing optically active products with a modest enantiomeric excess (ee).

On the other hand, the polypeptide and oligopeptide are known to be versatile organocatalysts for the asymmetric epoxidation of α,β-unsaturated ketones, such as chalcone, with hydrogen peroxide in alkaline water.[9] The α-helical structures seem to be essential for their high enantioselectivities.[10] In the present study, we synthesized a series of optically active, dynamic helical poly(phenylacetylene)s bearing oligopeptide pendants (from monomer to trimer) consisting of a combination of L-alanine (L-Ala) and achiral glycine (Gly) residues[11] and investigated their abilities as asymmetric polymeric organocatalysts[12] for the epoxidation of chalcone derivatives with hydrogen peroxide in alkaline water.

Six optically active phenylacetylenes bearing oligopeptide pendants (**1**-H−**6**-H) were synthesized and polymerized with a water-soluble rhodium catalyst, $[Rh(cod)_2]BF_4$ (cod: cyclooctadiene), in water in the presence of sodium hydroxide as a base according to the previously reported method (Scheme 1).[13] The results of the polymerization of **1**-H−**6**-H are summarized in Table 1.[14] All the polymerization reactions proceeded homogeneously and afforded high-molecular-weight stereoregular (cis-transoidal) polymers (poly-**1**-Na−poly-**6**-Na) in high yield.[14]

In order to characterize the chiroptical properties of the optically active poly(phenylacetylene)s, the circular dichroism (CD) and absorption spectra of poly-**1**-Na−poly-**6**-Na in water were measured. Figure 1 shows the CD spectra of poly-**1**-Na−poly-**6**-Na together with the typical absorption spectrum (poly-**6**-Na) in water. All the polymers exhibited similar induced CDs in their patterns and intensities in the conjugated polyene chromophore regions irrespective of the differences in the size of the oligopeptides and their sequences, indicating that these polymers possess a predominantly one-handed helical conformation with the same helical sense biased by the inner L-Ala residue incorporated in the pendant oligopeptides. We anticipated that the pendant oligopeptide residues may arrange in a helical array with a predominant screw-sense along the polymer backbones, and the polypeptides were then used as optically active organocatalysts for the asymmetric epoxidation reaction of chalcone (**7**-H) (Table 2).

Table 2 shows the results of the asymmetric epoxidation of **7**-H with hydrogen peroxide in alkaline water using poly-**1**-Na−poly-**6**-Na as well as the corresponding monomers, **1**-H−

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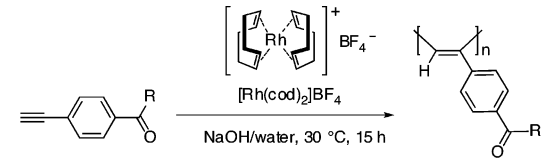
Scheme 1. Synthesis and Structures of Poly(phenylacetylene)s Bearing Oligopeptide Pendants



R = L-Ala-OH : **1**-H
L-Ala-Gly-OH : **2**-H
L-Ala-L-Ala-OH : **3**-H
L-Ala-Gly-Gly-OH : **4**-H
L-Ala-L-Ala-Gly-OH : **5**-H
L-Ala-L-Ala-L-Ala-OH : **6**-H

R = L-Ala-ONa : poly-**1**-Na
L-Ala-Gly-ONa : poly-**2**-Na
L-Ala-L-Ala-ONa : poly-**3**-Na
L-Ala-Gly-Gly-ONa : poly-**4**-Na
L-Ala-L-Ala-Gly-ONa : poly-**5**-Na
L-Ala-L-Ala-L-Ala-ONa : poly-**6**-Na

Table 1. Polymerization of Phenylacetylenes Bearing Oligopeptide Pendants (1-H−6-H) with $[Rh(cod)_2]BF_4$ in Water at 30 °C for 15 h[a]

run	monomer	yield (%)[b]	$M_n \times 10^{-5}$ [c]	M_w/M_n [c]	$[\theta]_{second} \times 10^{-4}$ (λ, nm)[d]
1	**1**-H	97	1.8	1.8	1.63 (373)
2	**2**-H	100	2.1	2.4	1.67 (377)
3	**3**-H	99	1.8	1.9	1.56 (374)
4	**4**-H	86	2.2	2.1	1.32 (377)
5	**5**-H	97	1.8	2.2	1.58 (374)
6	**6**-H	97	1.4	1.7	1.12 (375)

[a] Polymerized under nitrogen; [monomer] = 0.43 M (runs 1−3, 6) or 0.29 M (runs 4, 5), [monomer]/[Rh] = 200, [NaOH]/[monomer] = 1.5. [b] Ethanol-insoluble part. [c] Determined by SEC using DMF containing 10 mM LiCl as the eluent at 40 °C (PEO and PEG standards) as its methyl ester. [d] Second Cotton intensity of the polymers measured in water at 25 °C.

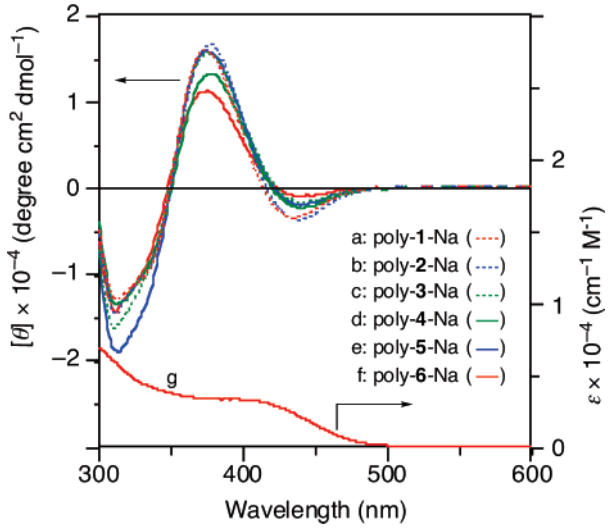
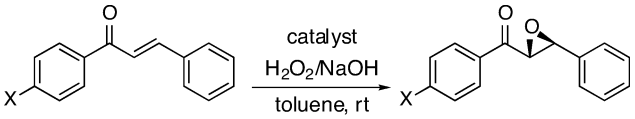


Figure 1. CD spectra of poly-**1**-Na−poly-**6**-Na ([polymer] = 1.0 mg/mL) (a−f) in water at 25 °C (pH 8). Absorption spectrum of poly-**6**-Na is also shown in part g.

6-H, as the catalysts.[15] The epoxidation reaction proceeded in the presence of poly-**1**-Na−poly-**6**-Na, giving the desired epoxide (**8**-H) in different yields (8−82%) depending on the structures of the pendant oligopeptides. Among the polymers, poly-**4**-Na and poly-**4**-H showed a remarkably high catalytic activity (runs 8−14 in Table 2), while no reaction occurred in the absence of the catalyst (run 1 in Table 2). The enantioselectivity of the helical polymers tended to increase with an increase in the length of the pendant oligopeptides even though some helical polymers possessed one (poly-**2**-Na and poly-**5**-Na) or two (poly-**4**-Na) achiral Gly residues as the component in the pendant oligopeptides. Among the helical polymers, poly-**6**-Na gave the highest enantioselectivity in the asymmetric epoxidation of **7**-H (34% ee).[16] In sharp contrast, the corresponding monomers (**1**-H−**6**-H) showed almost no enantioselectivity (<2% ee) (runs 2−7 in Table 2). These results clearly

Table 2. Results of Asymmetric Epoxidation of Chalcone Derivatives (7) at Room Temperature (ca. 22−25 °C)[a]



7-H	X = H	**8**-H
7-Cl	X = Cl	**8**-Cl
7-OMe	X = OMe	**8**-OMe
7-Me	X = Me	**8**-Me
7-Nap	X = β-Naphthyl	**8**-Nap

run	catalyst	chalcone	solvent	time (day)	yield (%)	ee (%)[b]
1	none	**7**-H	toluene	3	*c*	
2	**1**-H	**7**-H	toluene	3	26	ca. 0
3	**2**-H	**7**-H	toluene	3	42	ca. 0
4	**3**-H	**7**-H	toluene	3	39	ca. 0
5	**4**-H	**7**-H	toluene	3	44	ca. 0
6	**5**-H	**7**-H	toluene	3	69	<2
7	**6**-H	**7**-H	toluene	3	55	<2
8	poly-**1**-Na	**7**-H	toluene	3	8	5
9	poly-**2**-Na	**7**-H	toluene	1	30	21
10	poly-**3**-Na	**7**-H	toluene	3	17	25
11	poly-**4**-Na	**7**-H	toluene	1	81	24
12	poly-**4**-H	**7**-H	toluene	1	82	25
13	poly-**5**-Na	**7**-H	toluene	1	27	30
14	poly-**6**-Na	**7**-H	toluene	3	36	34
15[d]	poly-**6**-Na	**7**-H	toluene	6	60	38
16[d]	poly-**6**-Na	**7**-H	Et_2O	1	40	32
17[d]	poly-**6**-Na	**7**-H	hexane	1	52	2
18[d]	poly-**6**-Na	**7**-H	$CHCl_3$	4	72	31
19	poly-**6**-Na	**7**-Cl	toluene	3	42	12
20	poly-**6**-Na	**7**-OMe	toluene	3	69	2
21	poly-**6**-Na	**7**-Me	toluene	3	51	10
22	poly-**6**-Na	**7**-Nap	toluene	3	56	7

[a] Reactions were carried out in aqueous H_2O_2 (35%) containing NaOH (2 M)−solvent (1/1, v/v) in the presence of chiral catalysts ([monomer unit]/[chalcone] = 1.2). [b] Determined by chiral HPLC analysis using a chiral column (CHIRALPAK AD) with hexane/ethanol (9/1, v/v) as the eluent at the flow rate of 1.0 mL/min. [c] No reaction. [d] At 0 °C.

demonstrate that the helical structures of the poly(phenylacetylene)s in which the pendant oligopeptide residue are aligned in a one-handed helical array are indispensable for the effective asymmetric epoxidation of **7**-H. This speculation is supported by the previously reported facts that alanine dimer (Ala_2) and pentamer (Ala_5) with no secondary structure produced **8**-H with quite a low ee (2 and 11% ee, respectively), whereas the α-helical alanine decamer (Ala_{10}) gave 93% ee of **8**-H in the asymmetric epoxidation reaction of **7**-H.[10a,b]

We further investigated the effects of temperature and organic solvents on the enantioselectivity of the asymmetric epoxidation of **7**-H in the presence of poly-**6**-Na as the catalyst (runs 15−18 in Table 2). The enantioselectivity slightly increased at 0 °C (38% ee, run 15 in Table 2) compared to that at room temperature (ca. 22−25 °C) (34% ee, run 14 in Table 2) when toluene was used as a cosolvent. But, the enantioselectivity became quite low in hexane (run 17 in Table 2). The reason is unclear at the present stage, but a similar organic solvent effect was reported for the asymmetric epoxidation of **7**-H with poly(L-alanine) as the catalyst.[10a] The effect of substituents on the phenyl group of chalcone (**7**-Cl, **7**-OMe, **7**-Me, and **7**-Nap in Table 2) on the enantioselectivity was also investigated with poly-**6**-Na as the catalyst (runs 19−22 in Table 2). Introducing either electron donating or withdrawing substituents significantly reduced the enantioselectivity, and the highest enantioselectivity was observed for **7**-H.

In summary, we have found that optically active, dynamic helical poly(phenylacetylene)s bearing optically active oligopep-

tide pendants are effective for the asymmetric epoxidation of chalcone as polymeric organocatalysts. The one-handed helical array of the pendant oligopeptide residues along the polymer backbones seems to be essential, since the corresponding monomers showed almost no enantioselectivity. To the best of our knowledge, this may be the first example of asymmetric polymeric organocatalysts based on dynamic helical polymers. The most striking feature of dynamic helical polymers is their high sensitivity to a chiral environment, and therefore, a predominantly one-handed helical conformation can be induced in the presence of a small amount of covalently bonded chiral residue as the pendants or terminal ends.[1] We anticipate that a more efficient asymmetric polymeric catalyst may be created based on a dynamic helical polyacetylene prepared by the copolymerization of a small amount of chiral monomer and achiral one bearing achiral oligoglycines as the pendants, which may be arranged in a one-handed helical array along the polymer backbone. The work along this line is now in progress.

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Supporting Information Available: Text giving experimental details of the synthesis (including reaction schemes) and characterization of **1**-H−**6**-H and poly-**1**-Na−**6**-Na and epoxidation of chalcone derivatives, and a figure showing the ^{1}H NMR spectrum of poly-**4**-Na. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) For details of the synthesis and characterization of **1**-H−**6**-H and poly-**1**-Na−poly-**6**-Na, see the Supporting Information.

(15) For details of the reaction procedure, see the Supporting Information.

(16) When poly-**4**-Na was used as the catalyst for the epoxidation of **7**-H at 0 °C for 48 h, the polymer could be recovered in 80% yield after acidification of the polymer. The recovered polymer exhibited as an intense induced CD as that of the original polymer. These results indicate that the polymer is stable during the epoxidation reaction and can be recycled.

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