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Helicity Induction on a Poly(phenylacetylene) Derivative Bearing Aza-15-crown-5 Ether Pendants in Organic Solvents and Water

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ABSTRACT: A novel stereoregular poly(phenylacetylene) with the bulky aza-15-crown-5 ether as the pendant was prepared by polymerization of the corresponding phenylacetylene monomer with a rhodium catalyst. The polymer was found to form a predominantly one-handed helical conformation upon complexation with various chiral compounds, such as amino acids, amines, and amino alcohols through noncovalent interaction in organic solvents and water. The complexes exhibited an induced circular dichroism (ICD) in the UV−vis region of the polymer backbone; in particular, the polymer showed high affinity to secondary amines, and the complexes exhibited relatively intense ICDs. The assay of 19 common free L-amino acids gave the same ICD sign in acetonitrile−5 N $HClO_4$ (99.88/0.12, v/v). The effects of pH, temperature, and guest concentration on the ICD during the complexation of poly-**1** with chiral compounds were also investigated.

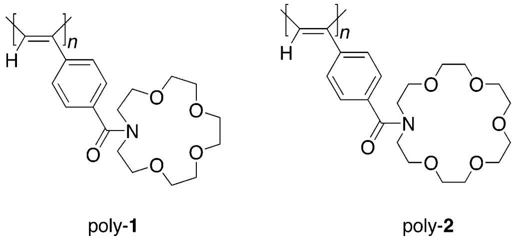
Introduction

Molecular and chiral recognition of biologically active compounds such as amino acids and amines is an attractive challenge in host−guest and supramolecular chemistry,[1] and a number of synthetic receptor molecules consisting of crown ether moieties for the amino acid and amine binding site have been prepared.[2] However, most of the crown ether-based receptors showed molecular and chiral recognition for protected amino acids, and the crown ethers that are capable of recognizing free amino acids are still rare.[3]

In earlier studies, we reported the helicity induction on optically inactive poly(phenylacetylene)s bearing functional groups, such as carboxy,[4] amino,[5] boronate,[6] and phosphonate groups.[7] These polymers formed a predominantly one-handed helical conformation upon complexation with chiral compounds capable of interacting with the functional groups of the polymers. The complexes exhibited a characteristic induced circular dichroism (ICD) in the UV−vis region.[8] Very recently, we designed and synthesized a new stereoregular poly(phenylacetylene) with aza-18-crown-6 ether pendants (poly-**2**) as the amino acid binding site (Chart 1).[9] Poly-**2** is highly sensitive to the amino acid chirality and can form an induced helix upon complexation with free L- or D-amino acids and chiral amines, thus showing ICDs in organic solvents as well as in water.[10] We also found that poly-**2** showed a very strong positive nonlinear effect (chiral amplification) between the enantiomeric excess (ee) of amino acids and the observed ICD intensity. This unusual behavior of poly-**2** can be used to detect an extremely small enantiomeric imbalance in α-amino acids, for instance, a 0.005% ee of alanine (Ala).[9a]

We expected that analogous stereoregular poly(phenylacetylene)s bearing other achiral crown ethers with different ring sizes or macrocyclic pendants could also form a dynamically induced helix in the presence of chiral compounds capable of interacting with the pendants. Here we report that a novel stereoregular poly(phenylacetylene) bearing the aza-15-crown-5 ether as the pendant (poly-**1** in Chart 1) can form a predominantly one-handed helical conformation in the presence of amino acids, amines, and amino alcohols in organic solvents and water by means of CD and UV−vis spectra.

Chart 1. Structures of Poly-1 and Poly-2



Results and Discussion

Synthesis and Helicity Induction of Poly-1 with Chiral Amino Acids, Amines, and Amino Alcohols in Organic Solvents. *Cis−transoidal* stereoregular poly-**1** was prepared by polymerization of the corresponding monomer with a rhodium catalyst in a method similar to that previously reported (see Schemes 1 and 2 in the Experimental Section).[9a] The number-average molecular weight (M_n) and its distribution (M_w/M_n) were estimated to be 13.2 × 10^4 (degree of polymerization (DP) = 380) and 4.0, respectively, as determined by size exclusion chromatography (SEC) with poly(ethylene oxide) and poly(ethylene glycol) standards in *N*,*N*-dimethylformamide (DMF) containing 10 mM lithium chloride as the eluent. Poly-**1** was soluble in common organic solvents including tetrahydrofuran (THF), chloroform, DMF, methanol, acetone, and toluene and in water. The stereoregularity of the polymer was investigated by ^1H NMR spectroscopy. The ^1H NMR spectrum of poly-**1** in $CDCl_3$ showed a sharp singlet centered at 5.86 ppm, due to the main chain protons, indicating that the polymer possesses a highly *cis−transoidal*, stereoregular structure (Supporting Information).[11] The CD spectra of poly-**1** in the presence of L- or D-amino acids and chiral amines and amino alcohols were then measured to investigate whether the polymer could respond

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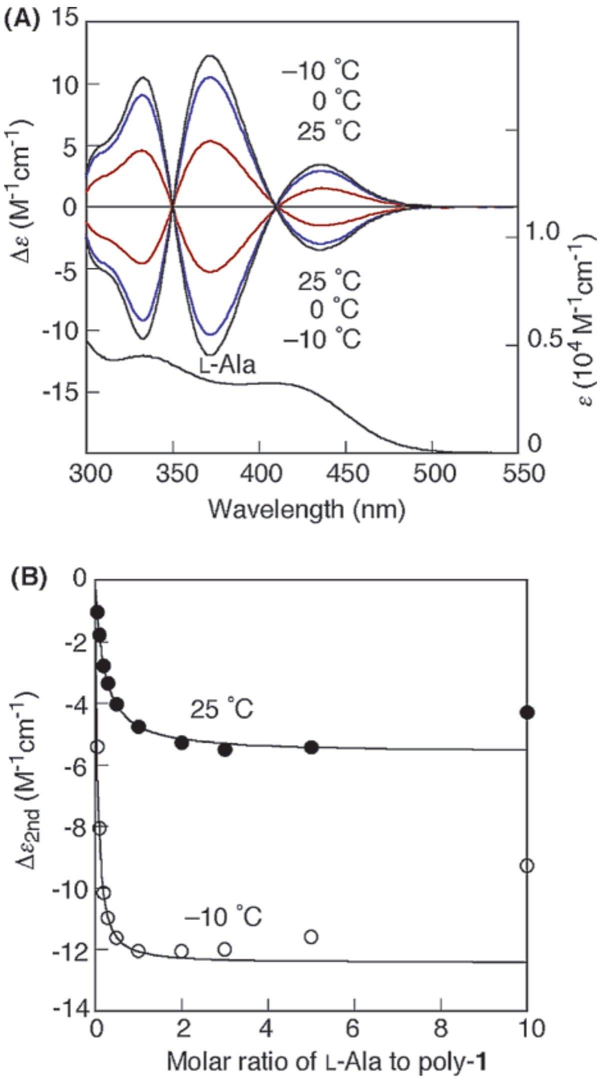
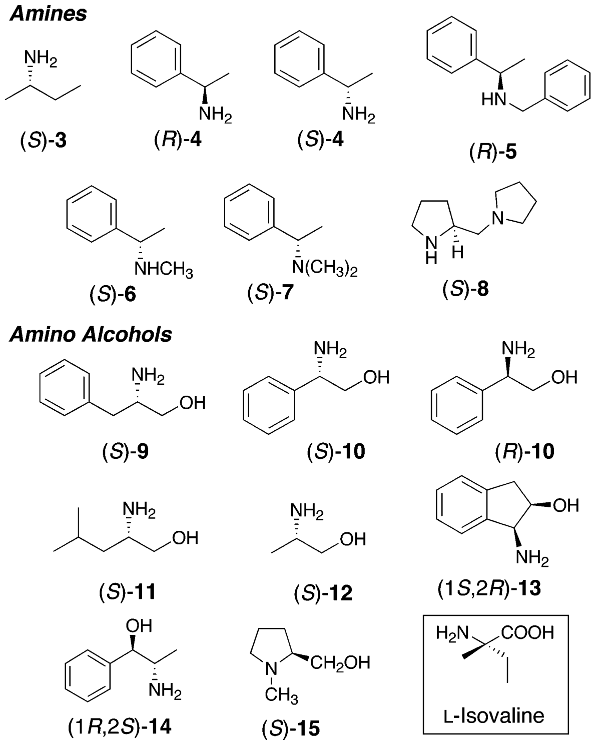


Figure 1. Helicity induction on poly-**1** with Ala. (A) CD spectra (molar ellipticity, Δε) of poly-**1** (1.0 mg/mL) with L- and D-Ala·HClO$_4$ ([Ala]/[poly-**1**] = 2) in acetonitrile at 25, 0, and −10 °C. Absorption spectrum (molar absorptivity, ε) of poly-**1** with L-Ala·HClO$_4$ at 25 °C is also shown. (B) Titration curves of poly-**1** (Δε$_{2nd}$ of 372 nm) with L-Ala·HClO$_4$ in acetonitrile at 25 and −10 °C. Curves in the plots were the calculated ones in the concentration range (0 < [L-Ala]/[poly-**1**] < 2) using K = 1.7 × 10^3 and 5.8 × 10^3 at 25 and −10 °C, respectively.

Chart 2. Structures of Isovaline, Amines, and Amino Alcohols



to the chirality of the chiral compounds to show characteristic ICDs.

The typical CD and absorption spectra of poly-**1** in the presence of L- and D-Ala (2 equiv to monomer units of poly-**1**) complexed with HClO$_4$ in pure acetonitrile are shown in Figure 1A. The poly-**1** complexed with L- and D-Ala exhibited intense, split-type ICDs in the UV−vis region of the polymer main chain, and the ICDs are mirror images of each other. The ICD magnitude increased with the decreasing temperature. The CD titrations using L-Ala showed that the CD intensity increased with the increasing concentration of L-Ala and reached an almost constant value at 2 and 1 equiv of L-Ala at 25 and −10 °C, respectively (Figure 1B). However, the CD intensity decreased with further increase in the concentration of L-Ala ([L-Ala]/[poly-**1**] ≥ 3 at −10 °C). The reason is not clear at present. The Hill plot analysis of the changes in the CD intensities of the second Cotton (Δε$_{2nd}$) of poly-**1** as a function of concentration of L-Ala (0 < [L-Ala]/[poly-**1**] < 2) resulted in the apparent binding constants (K's) of 1.7 × 10^3 and 5.8 × 10^3 at 25 and −10 °C, respectively.[12] These values were smaller than those in the complex formation of poly-**2** with L-Ala·HClO$_4$ in acetonitrile; K values were 1.8 × 10^4 and 2.6 × 10^4 at 25 and −10 °C, respectively.[9a] At −10 °C, 1 equiv of L-Ala induced an almost one-handed helix, and poly-**1** exhibited an apparent ICD even with 0.05 equiv of L-Ala, indicating a strong chiral amplification with cooperative interaction in the crown ether pendants. A similar, but stronger, chiral amplification was also observed in the complexation with L-Leu; K = 2.7 × 10^3 and 1.4 × 10^4 at 25 and −10 °C, respectively (see Supporting Information). These results indicate that a very small chiral bias in the monomeric crown ether units of poly-**1** complexed with L-Ala and L-Leu is amplified to induce the same helix on the major free monomeric crown ether units. Similar helicity induction on optically inactive polymers and oligomers through intermolecular chiral interactions has been reported.[13]

The assay of 19 of the common L-amino acids produced ICDs with the same Cotton effect signs even at 25 °C (Table 1), although the complexes of poly-**1** with basic amino acids (L-Arg, L-His, and L-Lys) showed relatively weak ICDs. An unnatural amino acid, L-isovaline (Chart 2),[14] also exhibited the same Cotton effect sign as the naturally occurring L-amino acids. This indicates that poly-**1** can be used as a probe for sensing the chirality of natural and unnatural amino acids without derivatization.[15] As recently reported, poly-**2** also exhibited ICDs with the common 19 L-amino acids in acetonitrile and the Cotton effect signs were the same, but the ICD intensities were larger than those of poly-**1** complexed with the L-amino acids.[9a]

Poly-**1** also responded to chiral amines and amino alcohols (Chart 2), and the complexes exhibited similar ICDs in their patterns. The ICD intensity increased with the decreasing temperature (Table 1). The amino

Table 1. Signs and Difference in Exciton Coefficient of the Second Cotton ($\Delta\epsilon_{2nd}$) for the Complexes of Poly-1 with Amino Acids, Amines, or Amino Alcohols in CH_3CN−5 N $HClO_4$ (99.88/0.12, v/v)[a]

		second Cotton [λ (nm) and $\Delta\epsilon_{2nd}$ (M^{-1} cm^{-1})]			
		λ ($\Delta\epsilon$)			
guest	sign	25 °C	10 °C	0 °C	−10 °C
		Amino Acid			
L-Ala	−	372 (5.40)	371 (8.47)	371 (10.40)	371 (11.96)
L-Ala[b]	−	372 (5.28)	372 (8.34)	372 (10.37)	372 (12.07)
D-Ala	+	371 (5.43)	372 (8.56)	371 (10.58)	372 (12.00)
L-Asn	−	371 (1.50)	373 (2.50)	371 (3.10)	371 (3.26)
L-Cys	−	372 (6.81)	372 (9.78)	372 (11.50)	371 (12.83)
L-Gln	−	372 (5.67)	372 (9.50)	372 (11.84)	372 (13.53)
L-Ile	−	372 (7.25)	372 (10.33)	372 (12.00)	372 (13.21)
L-Leu	−	373 (8.22)	372 (11.30)	372 (12.95)	373 (14.05)
L-Met	−	373 (7.28)	372 (10.35)	372 (11.98)	373 (13.19)
L-Phe	−	372 (9.56)	371 (12.68)	372 (14.19)	372 (15.33)
L-Pro	−	371 (2.37)	371 (4.93)	373 (7.34)	372 (9.75)
L-Ser	−	371 (2.58)	371 (4.87)	371 (6.83)	371 (8.76)
L-Thr	−	371 (7.75)	372 (12.01)	371 (14.04)	371 (15.47)
L-Trp	−	372 (7.18)	372 (10.01)	372 (11.55)	371 (12.71)
L-Tyr	−	372 (6.26)	372 (9.35)	372 (11.16)	372 (12.64)
L-Val	−	372 (8.22)	372 (11.60)	371 (13.39)	371 (14.72)
L-Asp	−	371 (1.29)	375 (2.13)	371 (2.83)	372 (3.41)
L-Glu	−	372 (5.69)	372 (8.89)	372 (10.90)	372 (12.41)
L-Arg[c]	−	372 (0.50)	375 (0.71)	*d*	*d*
L-His[e]	−	370 (0.44)	369 (0.65)	*d*	*d*
L-Lys[c]	−	377 (0.23)	*d*	*d*	*d*
L-isovaline	−	374 (0.31)	369 (0.40)	372 (0.40)	372 (0.39)
		Amine			
(*S*)-**3**	−	374 (0.07)	367 (0.20)	371 (0.38)	371 (0.68)
(*S*)-**4**	+	372 (2.94)	373 (5.07)	373 (6.91)	373 (8.99)
(*R*)-**5**	+	372 (1.71)	373 (2.63)	373 (2.85)	374 (1.94)
(*S*)-**6**	+	372 (0.97)	373 (2.59)	373 (4.73)	373 (7.82)
(*S*)-**7**	−	374 (0.22)	372 (0.31)	371 (0.43)	371 (0.57)
(*S*)-**8**[f]	−	371 (0.08)	374 (0.17)	371 (0.40)	375 (0.81)
		Amino Alcohol			
(*S*)-**9**	−	373 (1.73)	372 (3.14)	373 (4.46)	373 (6.03)
(*S*)-**10**	−	372 (2.29)	374 (3.98)	374 (5.41)	375 (6.79)
(*R*)-**10**	+	372 (2.27)	373 (3.78)	374 (5.13)	375 (6.45)
(*S*)-**11**	−	372 (1.86)	372 (3.50)	373 (5.12)	373 (6.91)
(*S*)-**12**	−	373 (1.70)	373 (3.34)	373 (4.98)	373 (6.89)
(1*S*,2*R*)-**13**	−	373 (1.54)	372 (2.27)	372 (2.78)	372 (3.13)
(1*R*,2*S*)-**14**	−	372 (1.62)	372 (2.80)	371 (3.92)	372 (5.26)
(*S*)-**15**	−	373 (0.15)	365 (0.27)	373 (0.43)	373 (0.72)

[a] The concentration of poly-**1** is 1.0 mg/mL, and the molar ratio of a guest to monomer units of poly-**1** is 2; [$HClO_4$]/[guest] = 1.03. [b] In CH_3CN. [c] In CH_3CN−5 N $HClO_4$−water (91.38/0.12/8.50, v/v). [d] It could not be measured because the solution became turbid. [e] In CH_3CN−5 N $HClO_4$−water (92.38/0.12/7.50, v/v). [f] In CH_3CN−5 N $HClO_4$ (99.76/0.24, v/v).

alcohols ((*S*)-**9**−(*S*)-**12**) derived from the L-amino acids, L-phenylalanine, L-phenylglycine, L-leucine, and L-alanine, respectively, showed the same Cotton effect signs as the L-amino acids, whereas the amines ((*S*)-**3** and (*S*)-**4**) exhibited the opposite sign from each other. Generally, crown ethers are difficult to form stable complexes with a secondary amino acid, L-Pro, and secondary and tertiary amines.[2] Nevertheless, poly-**1** and poly-**2** formed the complexes with L-Pro and secondary and tertiary amines (**5**−**8**), and the complexes exhibited apparent ICDs (see Table 1 and Supporting Information). In particular, poly-**1** showed much more intense ICDs for L-Pro and **6** than poly-**2** did, indicating that poly-**1** can be used as a probe for chirality recognition of secondary or tertiary amines, which are usually very difficult to recognize with crown ether host compounds.[16] The ICD intensities were stronger than those of poly-**2**.

The crown ether−ammonium ion complexation is known to be influenced by the solvent property, and the complex formation is generally weaker in protic solvents than in aprotic ones.[2] To investigate the solvent effect on the ICD, CD spectra of poly-**1** in the presence of L-Ala·$HClO_4$ were then measured in various organic solvents, and the results are summarized in Table 2 together with the CD data for poly-**2** for comparison. The complexes of poly-**1** and poly-**2** with L-Ala tended to show more intense ICDs in aprotic solvents than those measured in protic solvents such as methanol because protic solvents disturb hydrogen bonds between the ammonium group and the oxygen and/or nitrogen atoms in the crown ether.[2,18] But, the ICD intensities of poly-**2** were much stronger than poly-**1** in both protic and aprotic solvents.

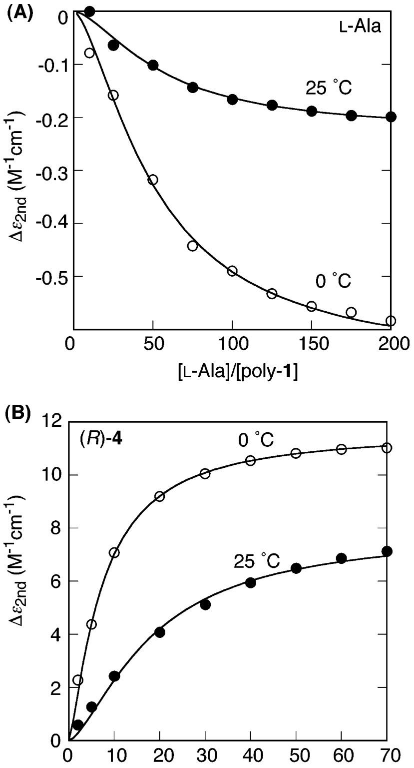


Figure 2. Titration curves of ICD intensity ($\Delta\epsilon_{2nd}$) in the complexation of poly-**1** (1.0 mg/mL) with L-Ala (pH 0.89−2.66) (A) and (*R*)-**4** (pH 0.77−1.84) (B) in water at 25 and 0 °C. Curves in the plots were the calculated ones using $K = 6.3$ and 6.8 (L-Ala) and 18.9 and 47.4 ((*R*)-**4**) at 25 and 0 °C, respectively.

Helicity Induction on Poly-1 with Amino Acids and Chiral Amines and Amino Alcohols in Water. Poly-**1** was soluble in water, and the ICD studies for the complexation with L-amino acids and chiral amines and amino alcohols were then performed in water. The results are summarized in Table 3. All the L-amino acids and chiral amines and amino alcohols produced ICDs, but the Cotton effect intensities were relatively weak except for Trp, L-Arg, and **4**, **6**, **9**, **10**, **13**, and **14** as compared with those measured in organic solvents, and their signs did not reflect the absolute configurations. In contrast, poly-**2** bearing the aza-18-crown-6 ether pendants showed almost the same Cotton effect signs for the L-amino acids independent of the solvent. This suggests that other interactions, for instance, the hydrophobic interaction as well as the crown ether−ammonium ion complexation may play a role in the helicity induction on poly-**1**.

The Hill plot analysis of the complexation of poly-**1** with L-Ala resulted in the *K* values of 6.3 and 6.8 at 25 and 0 °C, respectively (Figure 2A). These values were

Table 2. Signs and Difference in Exciton Coefficient of the Second Cotton ($\Delta\epsilon_{2nd}$) for the Complexes of Poly-1 or Poly-2 with L-Alanine Perchlorate in Various Organic Solvents[a]

		second Cotton [λ (nm) and $\Delta\epsilon_{2nd}$ (M^{-1} cm^{-1})] poly-**1**					second Cotton [λ (nm) and $\Delta\epsilon_{2nd}$ (M^{-1} cm^{-1})] poly-**2**				
solvent (v/v)	ϵ_r[b]	sign	25 °C	10 °C	0 °C	−10 °C	sign	25 °C	10 °C	0 °C	−10 °C
CH_3CN	35.94	−	372 (5.28)	371 (8.34)	371 (10.37)	371 (12.07)	−	364 (19.50)	363 (20.69)	363 (21.40)	363 (21.95)
MeOH	32.66	−	374 (0.05)	374 (0.07)	370 (0.10)	370 (0.12)	−	371 (9.13)	371 (14.58)	371 (16.69)	*c*
$CHCl_3/CH_3CN$ (1/1)	4.81/35.94	−	375 (1.33)	375 (1.92)	375 (2.37)	375 (2.81)	−	366 (18.49)	366 (19.75)	367 (20.28)	367 (20.67)
toluene/CH_3CN (1/1)[d]	2.38/35.94	−	376 (2.07)	376 (2.44)	377 (2.49)	376 (2.30)	−	365 (21.09)	365 (22.05)	365 (22.56)	365 (22.98)
$CHCl_3$/MeOH (1/1)	4.81/32.66	−	366 (0.20)	376 (0.25)	373 (0.38)	374 (0.40)	−	372 (7.22)	371 (11.70)	371 (13.71)	371 (15.06)
toluene/MeOH (1/1)	2.38/32.66	−	367 (0.17)	365 (0.26)	374 (0.38)	373 (0.46)	−	371 (12.91)	370 (16.64)	370 (18.17)	*c*

[a] The concentration of poly-**1** and poly-**2** was 1.0 mg/mL, and the molar ratios of L-Ala·$HClO_4$ to monomer units of poly-**1** and poly-**2** were 2 and 10, respectively. [b] Relative permittivity (dielectric constant) for the pure liquid at 25 °C. The values are cited from ref 17.[c] It could not be measured because the solution became turbid. [d] The molar ratio of L-Ala·$HClO_4$ to monomer units of poly-**2** was 5.

much smaller than those estimated in acetonitrile ($K = 1.7 \times 10^3$ at 25 °C) but were comparable to that in the complex formation between poly-**2** and L-Ala in water ($K = 6.2$ at 0 °C).[10] On the other hand, the K values for the complexation of poly-**1** with the primary amine (*R*)-**4** determined by the CD titration were slightly larger, 18.9 and 47.4 at 25 and 0 °C, respectively (Figure 2B). The ICD intensities in water, however, were much weaker than those measured in aprotic organic solvents because water disturbs hydrogen bonds in the crown ether−ammonium complex formation.[2,18]

Bulky aromatic amines and amino alcohols (**4**−**6**, **9**, **10**, **13**, **14**) tended to produce more intense ICDs than aliphatic ones in water. As for the relationship between the absolute configurations and the Cotton effect signs of the amines and amino alcohols, there is not a general relationship because of the limited data. However, structurally similar amino alcohols (**9**−**12**, **14**, **15**) of the same configuration showed the same ICD sign in alkaline water. The chiral amines (**3**, **4**) also gave the same ICD sign, reflecting the absolute configurations in acidic and alkaline water. Their ICD intensities were slightly stronger as compared with those of poly-**2** in water.[10]

Figure 3 shows ICD intensity changes in the pH for the complexes of poly-**1** with L-Leu and (*R*)-**4** in water at 25 and 0 °C. The CD intensity decreased with increasing in the pH for L-Leu and disappeared at pH = 4, while the poly-**1**−(*R*)-**4** complex still exhibited an intense ICD even in the neutral and alkaline pH ranges. Similar decrease and disappearance of ICDs at pH = 4 were observed for an aromatic amino acid, L-Phe. Interestingly, the ICD intensity of the poly-**1**−(*R*)-**4** complex dramatically increased at pH > 10. We recently reported a similar increase in the ICD intensity in the alkaline pH range in the complexation of poly-**2** with the bulky aromatic amine ((*R*)-**4**) and (*R*)-1-phenylethanol.[10] This indicates that the hydrophobic interaction between the poly-**1** and (*R*)-**4** functions as a chiral bias for helicity induction on poly-**1** in water.

Chiral Amplification in Acetonitrile and Water. Next, we investigated the changes in the ICD intensity of poly-**1** against the ee of Ala in acetonitrile−5 N $HClO_4$ (99.88/0.12, v/v) and water (Figure 4). The CD intensities of poly-**1**, corresponding to the helical sense excesses, were slightly out of proportion to the ee's of Ala, showing a convex deviation from the linearity in acetonitrile−5 N $HClO_4$ (99.88/0.12, v/v) at −10 °C, while Ala showed a linear effect at 25 °C. Similar positive nonlinear effects were also observed for Leu and Trp at −10 °C. However, the nonlinearities were very weak as compared with those observed for poly-**2**,[9a] indicating that a slight change in the ring size of the pendant crown ether significantly influences the substantial feature of the helical conformation of the crown ether-bound poly(phenylacetylene)s. In water, the similar convex deviation from linearity was also observed for Leu at 0 °C and Trp at 25 and 0 °C. In particular, the extent of the departure from linearity was greater for

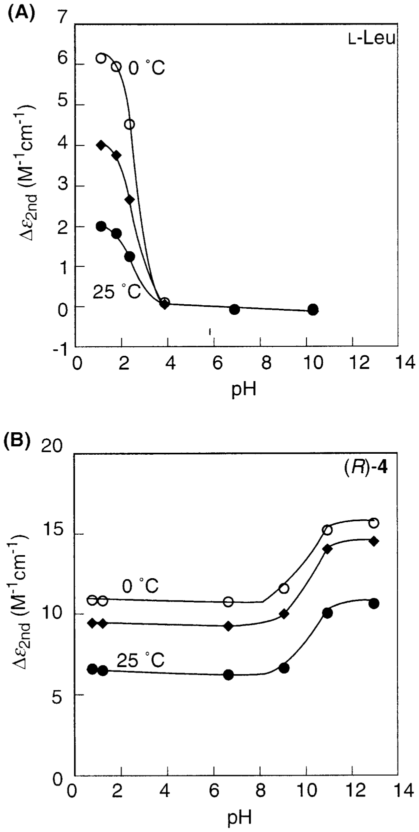


Figure 3. pH dependence of ICD intensity ($\Delta\epsilon_{2nd}$) in the complexation of poly-**1** (1.0 mg/mL) with L-Leu ([L-Leu]/[poly-**1**] = 50) (A) and (*R*)-**4** ([(*R*)-**4**]/[poly-**1**] = 50) (B) in water at 25, 10, and 0 °C. The pH was adjusted with 1 N $HClO_4$ and 1 N NaOH at room temperature.

Table 3. Signs and Difference in Exciton Coefficient of the Second Cotton ($\Delta\epsilon_{2nd}$) for the Complexes of Poly-1 with Amino Acids, Amines, and Amino Alcohols in Water[a]

			second Cotton [λ (nm) and ($\Delta\epsilon_{2nd}$ $M^{-1}cm^{-1}$)]		
			λ ($\Delta\epsilon$)		
guest	pH	sign	25 °C	10 °C	0 °C
			Amino Acid		
L-Ala	1.13	−	379 (0.10)	372 (0.18)	365 (0.32)
L-Asn	1.10	−	*b*	376 (0.07)	369 (0.17)
L-Cys	1.11	+	372 (1.77)	372 (4.18)	370 (7.36)
L-Gln	1.16	−	373 (0.08)	369 (0.10)	372 (0.13)
L-Ile	1.16	+	372 (2.25)	370 (3.89)	369 (5.56)
L-Leu	1.12	+	372 (2.01)	370 (4.01)	370 (6.15)
L-Met	1.16	+	372 (3.16)	371 (6.46)	369 (9.34)
L-Phe	1.16	+	371 (5.79)	370 (8.90)	370 (10.53)
L-Pro	1.14	−	367 (0.30)	369 (0.31)	367 (0.88)
L-Ser	1.16	−	*b*	368 (0.09)	371 (0.36)
L-Thr	1.15	+	372 (0.20)	372 (0.29)	369 (0.36)
L-Trp[c]	2.19	−	372 (9.40)	371 (12.10)	371 (12.74)
D-Trp[c]	2.20	+	371 (9.67)	371 (12.26)	371 (12.87)
L-Tyr[d]	0.80	+	370 (2.01)	370 (4.32)	370 (6.61)
L-Val	1.15	+	372 (1.05)	369 (1.90)	370 (3.01)
L-Asp	1.12	+	371 (0.65)	372 (1.48)	370 (2.74)
L-Glu	1.12	+	374 (0.16)	375 (0.51)	369 (1.19)
L-Arg	1.12	−	371 (0.84)	370 (2.42)	368 (5.34)
L-His	1.05	−	371 (0.19)	365 (0.24)	370 (0.22)
L-Lys	1.10	−	371 (0.17)	369 (0.35)	371 (0.66)
			Amine		
(*S*)-**3**	1.15	−	369 (0.24)	367 (0.47)	368 (0.70)
	11.9[e]	−	372 (0.10)	382 (0.10)	369 (0.12)
(*R*)-**4**	1.22	+	371 (6.49)	370 (9.41)	369 (10.82)
	10.9[e]	+	372 (10.03)	372 (14.03)	371 (15.22)
(*R*)-**5**	0.77[f]	−	373 (0.16)	372 (0.38)	371 (0.78)
	10.3[g]	−	373 (0.83)	374 (1.56)	374 (2.34)
(*S*)-**6**	1.23[h]	+	370 (0.84)	369 (3.82)	370 (7.76)
	11.2[i]	−	371 (4.85)	371 (8.50)	372 (10.36)
(*S*)-**7**	1.09[f]	+	381 (0.17)	372 (0.45)	369 (0.85)
	10.4[g]	+	374 (0.17)	374 (0.29)	372 (0.41)
(*S*)-**8**	0.64[j]	+	*b*	374 (0.14)	366 (0.34)
	11.6[e]	+	386 (0.12)	366 (0.10)	371 (0.10)
			Amino Alcohol		
(*S*)-**9**	1.15	+	370 (2.73)	370 (5.01)	370 (6.81)
	10.6[i]	+	372 (2.60)	372 (4.80)	372 (6.69)
(*R*)-**10**	0.90[h]	−	370 (3.51)	370 (6.72)	370 (9.02)
	10.2[i]	−	371 (0.48)	374 (1.34)	373 (2.31)
(*S*)-**11**	1.63	+	368 (1.11)	369 (2.06)	370 (3.10)
	11.4[e]	+	373 (0.62)	376 (0.94)	370 (1.14)
(*S*)-**12**	1.55	−	369 (0.05)	375 (0.08)	373 (0.09)
	11.4[e]	+	387 (0.06)	379 (0.07)	362 (0.07)
(1*S*,2*R*)-**13**	1.20	−	371 (10.05)	370 (12.42)	369 (13.33)
	10.1[e]	−	372 (5.95)	372 (9.20)	372 (11.08)
(1*R*,2*S*)-**14**	1.18	+	370 (9.45)	369 (12.63)	368 (13.79)
	10.5[e]	+	372 (10.24)	372 (12.89)	372 (13.84)
(*S*)-**15**	1.18	−	369 (0.15)	369 (0.18)	369 (0.24)
	11.3[e]	+	378 (0.18)	376 (0.18)	380 (0.14)

[a] The concentration of poly-**1** is 1.0 mg/mL, and the molar ratio of a guest to monomer units of poly-**1** is 50; [$HClO_4$] = 0.20 M. [b] No distinctive CD. [c] [Amino acid]/[poly-**1**] = 10 and [$HClO_4$] = 0.025 M. [d] [Amino acid]/[poly-**1**] = 10 and [$HClO_4$] = 0.20 M. [e] [Guest]/[poly-**1**] = 50. The samples were prepared by mixing poly-**1** with a guest in water. [f] [Guest]/[poly-**1**] = 0.5 and [$HClO_4$] = 0.20 M. [g] [Guest]/[poly-**1**] = 0.5. [h] [Guest]/[poly-**1**] = 20 and [$HClO_4$] = 0.20 M. [i] [Guest]/[poly-**1**] = 20. [j] [Guest]/[poly-**1**] = 50 and [$HClO_4$] = 0.40 M.

Trp, and the sensitivity of poly-**1** to the amino acid chirality in water was almost the same as that of poly-**2**.[10]

In summary, we found that a novel poly(phenylacetylene) with the aza-15-crown-5 ether pendants formed a predominantly one-handed helical conformation induced by a noncovalent interaction with amino acids and chiral amines and amino alcohols in organic solvents as well as in water. The complexes exhibited characteristic ICDs. In particular, the polymer showed the same Cotton effect sign if the configurations of α-amino acids were the same in acetonitrile. Although the sensitivity of poly-**1** to the chirality of amino acids and primary amines is not as high as that of poly-**2** bearing the aza-18-crown-6 ether as the pendant, poly-**1** showed higher sensitivity to the chirality of secondary amines and L-Pro than poly-**2**; this is a merit of this polymer. Consequently, the present results demonstrate that analogous stereoregular polyacetylenes and other dynamic helical polymers bearing rationally designed macrocyclic pendants will also form an induced helix in the presence of chiral compounds.

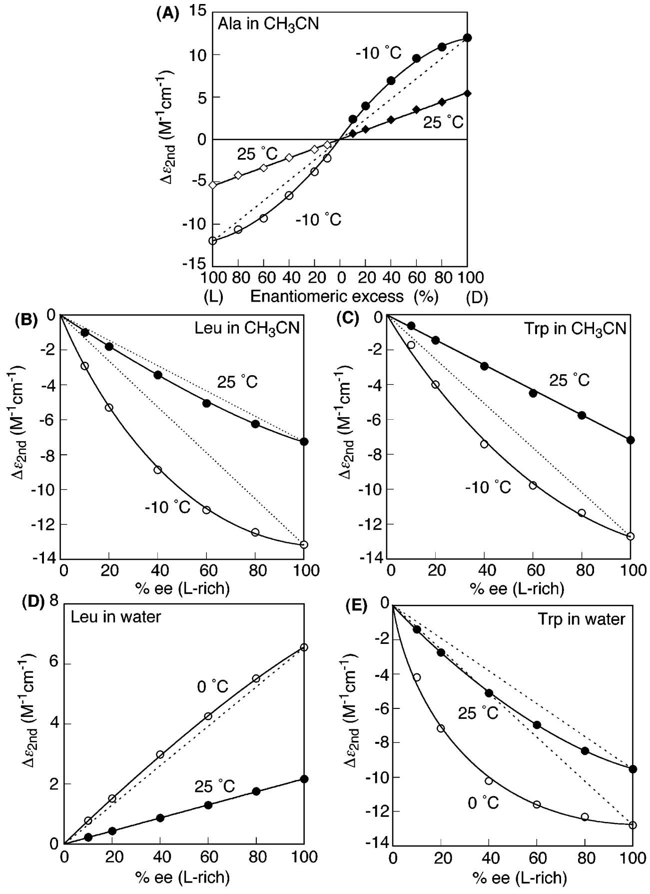
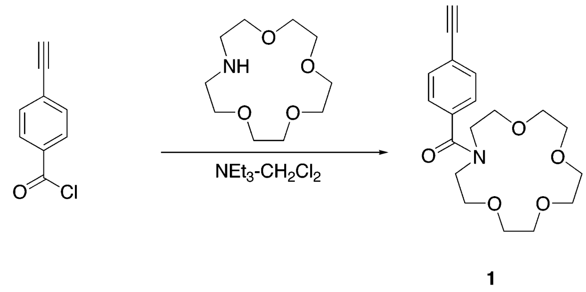


Figure 4. Changes in ICD intensity ($\Delta\epsilon_{2nd}$) of poly-**1** (1.0 mg/mL) vs the % ee of Ala (A), Leu (B), and Trp (C) ([amino acid]/[poly-**1**] = 2) in acetonitrile containing 0.12 vol % 5 N $HClO_4$ in water at 25 and −10 °C and Leu ([Leu]/[poly-**1**] = 50; pH 1.09−1.11) (D) and Trp ([Trp]/[poly-**1**] = 10; pH 2.17−2.19) (E) in acidic water with $HClO_4$ during the complexation with poly-**1**.

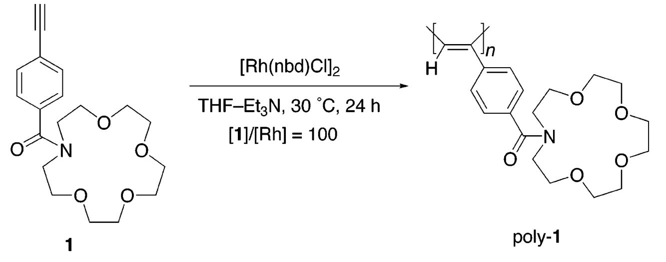
Experimental Section

Materials. All starting materials were obtained from commercial suppliers and were used as received. 1,4,7,10-Tetraoxa-13-azacyclopentadecane (1-aza-15-crown-5) was purchased from Tokyo Kasei (TCI, Tokyo, Japan). Dry acetonitrile (water content <0.005 vol %) and dichloromethane (water content <0.005 vol %) were obtained from Kanto Kagaku (Tokyo, Japan) and Aldrich (Milwaukee, WI), respectively. THF was dried over sodium benzophenone ketyl and distilled onto $LiAlH_4$ under nitrogen. Triethylamine was dried over KOH pellet and distilled under nitrogen. These solvents were distilled again under high vacuum just before use. [(Norbornadiene)rhodium(I) chloride]$_2$ ([Rh(nbd)Cl]$_2$) was obtained from Aldrich. L-Alanine and d-alanine (>99.9% ee) were purchased from Peptide Institute Inc. (Osaka, Japan). DL-Alanine and

Scheme 1



Scheme 2



aqueous perchloric acid solution (60 wt %) were from Kanto Kagaku. L-Leucine, D-leucine, dl-leucine, and tryptophan (purity >98%) were purchased from TCI. Other L-, D-, and DL-amino acids were available from Aldrich. The enantiomeric excesses of these amino acids are not determined by suppliers. (*S*)-Alaninol and (*S*)-*sec*-butylamine were purchased from Aldrich, and other amino alcohols used in this study were from TCI. (*S*)-Isovaline (99% purity and ee > 99%) was obtained from Acros Organics (Geel, Belgium). (*R*)-1-Phenylethylamine (ee > 98%) was kindly supplied from Yamakawa Chemical (Tokyo, Japan).

Synthesis of (4-Ethynylbenzoyl)-monoaza-15-crown-5 (1). This new compound was synthesized according to Scheme 1. 4-Ethynylbenzoyl chloride was prepared according to the previously reported method.[4b,9a] To a mixture of 1-aza-15-crown-5 (3.0 g, 14 mmol) in triethylamine (5.2 mL) and dichloromethane (160 mL) was added 4-ethynylbenzoyl chloride (3.2 g, 19 mmol) at 0 °C. The mixture was stirred under nitrogen at 25 °C for 7 h. After evaporating the solvent, the residue was purified by silica gel chromatography with chloroform−methanol (30/1, v/v) as the eluent to give 3.0 g of **1** as a white solid (64% yield); mp (78.2−79.1 °C). IR (KBr, cm^{-1}): 3191 ($\nu_{C\equiv C}$), 1623 ($\nu_{C=O}$), 1127 (ν_{C-O}). ^{1}H NMR (CDCl$_3$, 500 MHz, TMS): δ 7.51 (d, J = 8.5 Hz, aromatic, 2H), 7.38 (d, J = 8.5 Hz, aromatic, 2H), 3.80−3.40 (m, CH$_2$, 20H), 3.13 (s, ≡CH, 1H). ^{13}C NMR (CDCl$_3$, 125 MHz, TMS): δ 171.6, 137.2, 132.3, 126.9, 123.3, 83.1, 78.5, 71.6, 70.9, 70.5−70.3 (br), 69.8, 69.3, 51.3, 48.3. MS (FAB$^+$): Calcd for $C_{19}H_{26}NO_5$ (M + H): 348. Found: 348. Anal. Calcd for $C_{19}H_{25}NO_5 \cdot {}^1/_6H_2O$: C, 65.13; H, 7.29; N, 4.00. Found: C, 65.21; H, 7.34; N, 3.78.

Polymerization. Polymerization was carried out according to Scheme 2 in a dry glass ampule under a dry nitrogen atmosphere using [Rh(nbd)Cl]$_2$ as a catalyst. A typical polymerization procedure is described below. Monomer **1** (2.0 g, 5.8 mmol) was placed in a dry ampule, which was then evacuated on a vacuum line and flushed with dry nitrogen. After this evacuation−flush procedure was repeated three times, a three-way stopcock was attached to the ampule, and dry THF (26 mL) and triethylamine (0.8 mL) were added with a syringe. To this was added a solution of [Rh(nbd)Cl]$_2$ in THF (1.0 mL) at 30 °C. The concentrations of the monomer and the rhodium catalyst were 0.2 and 0.002 M, respectively. After 24 h, the resulting poly-**1** was precipitated into a large amount of ether, collected by centrifugation, and dried in vacuo at 50 °C for 2 h (1.9 g, 95% yield). The number-average molecular weight and molecular weight distribution were 13.2 × 10^4 and 4.0, respectively, as determined by SEC with poly(ethylene oxide) and poly(ethylene glycol) standards in DMF containing 10 mM lithium chloride as the eluent.

Spectroscopic data of poly-**1**. IR (KBr, cm^{-1}): 1637 ($\nu_{C=O}$), 1122 (ν_{C-O}). ^{1}H NMR (CDCl$_3$, 60 °C, 300 MHz, TMS): δ 7.12 (s, aromatic, 2H), 6.71 (s, aromatic, 2H), 5.86 (s, =CH, 1H), 3.59 (br, CH$_2$, 20H). Anal. Calcd for $(C_{19}H_{25}NO_5 \cdot {}^2/_3H_2O)_n$: C, 63.49; H, 7.38; N, 3.90. Found: C, 63.66; H, 7.63; N, 3.74.

Instruments. NMR spectra were taken on a Varian Mercury 300 operating at 300 MHz for ^{1}H or a Varian VXR-500S spectrometer operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C with tetramethylsilane (TMS) as the internal standard. Fast atom bombardment (FAB) mass spectra were obtained on a JEOL JMS-AX505HA spectrometer (Akishima, Japan). Elemental analyses were performed by the Nagoya University Analytical Laboratory in School of Engineering. Melting points were measured on a Büchi melting point apparatus and are uncorrected. SEC measurements were performed with a JASCO PU-980 liquid chromatograph (Hachioji, Japan) equipped with a UV (254 nm; JASCO UV-970) and an RI (JASCO RI-1530) detector and a column oven (JASCO CO-965). The molecular weight of poly-**1** was determined at 60 °C using Tosoh (Tokyo, Japan) TSKgel α-3000 (30 cm) and α-5000 (30 cm) SEC columns connected in series, and DMF containing 10 mM lithium chloride was used as the eluent at a flow rate of 0.5 mL/min. The molecular weight calibration curve was obtained with poly(ethylene oxide) and poly(ethylene glycol) standards (Tosoh). IR spectra were recorded using a JASCO Fourier transform IR-620 spectrophotometer. Absorption and CD spectra were measured in a 1.0 mm quartz cell on a JASCO V-570 spectrophotometer and a JASCO J-820 spectropolarimeter, respectively. The temperature was controlled with a JASCO PTC-423L apparatus (−10−25 °C). The solution pH was measured with a GST-5428S pH meter (DKK-TOA, Tokyo, Japan).

CD Measurements in Acetonitrile−5 N HClO$_4$ (99.88/0.12, v/v). Deionized, distilled water and dry acetonitrile were distilled again just before use and stored under nitrogen. The concentration of poly-**1** was calculated on the basis of monomer units and was 1.0 mg/mL (2.9 mM monomer units) unless otherwise stated. In the complexation of poly-**1** with D- or L-amino acids, stock solutions of poly-**1** (2.0 mg/mL (5.8 mM)) in acetonitrile and 5 N HClO$_4$ in water were prepared in 5 and 50 mL flasks equipped with a stopcock, respectively. Stock solutions of D- or L-amino acid (30.3 mM, 2 mL) containing 0.0125 mL of 5 N HClO$_4$ ([HClO$_4$]/[amino acid] = 1.03 (mol/mol)) in acetonitrile were also prepared. A 0.50 mL aliquot of the poly-**1** solution was transferred to a 1 mL flask equipped with a stopcock. To this was added a 0.19 mL aliquot of the D- or L-amino acid stock solution, and the solution was diluted with acetonitrile to keep the poly-**1** concentration at 1.0 mg/mL and the molar ratio of amino acids to monomer units of poly-**1** was 2. The solution was thoroughly mixed with a vibrator (Iuchi, Osaka, Japan) before measuring the absorption and CD spectra. The same procedure was performed for all the D- or L-amino acids, isovaline, amines, and amino alcohols to measure CD spectra. The volumetric ratio of water to acetonitrile was held constant at acetonitrile/water = 99.88/0.12 (v/v) for these ICD experiments, but water affects the amino acid−crown ether complexation in aprotic organic solvents.[2e] We found that the ICD signals of the poly-**1**−L-Ala complex decreased with an increase in the amount of water, so that we used pure acetonitrile in the CD titrations of poly-**1** with L-Ala and L-Leu. In the CD titrations in acetonitrile, the L-Ala and L-Leu complexed with HClO$_4$ were prepared according to the reported method.[19]

CD Titrations of Poly-1 with L-Ala in Acetonitrile. A stock solution of poly-**1** (2.0 mg/mL (5.8 mM)) in acetonitrile was prepared in a 10 mL flask equipped with a stopcock. Stock solutions of l-Ala·HClO$_4$ complexes (88.8 and 4.82 mM) in acetonitrile were also prepared in 2 and 25 mL flasks, respectively. The 0.50 mL aliquots of the poly-**1** solution were transferred to 10 1 mL flasks equipped with a stopcock, and increasing amounts of the stock solutions of the L-Ala·HClO$_4$ complexes were added to the flasks; the molar ratios of L-Ala·HClO$_4$ to poly-**1** were 0.05, 0.1, 0.2, 0.3, 0.5 (4.82 mM L-Ala·HClO$_4$) and 1.0, 2.0, 3.0, 5.0, 10 (88.8 mM L-Ala·HClO$_4$), and the resulting solutions were diluted with acetonitrile to keep the poly-**1** concentrations at 1.0 mg/mL (2.9 mM). The absorption and CD spectra were then taken for each flask to determine the changes in the CD spectra (Figure 1B). Plots of the CD intensities of the second Cotton ($\Delta\epsilon_{2nd}$) of poly-**1** as a function of concentration of L-Ala gave an unusual binding isotherm, so that the data ($0 < [\text{L-Ala}]/[\text{poly-}\mathbf{1}] < 2$) were used in the Hill plot analysis to obtain apparent binding constants (K's) according to the Hill equation, $\log(Y/(1 - Y)) = n \log[G] + n \log K$, where Y, n, and [G] represent the fractional saturation, the Hill coefficient, and the concentration of the guest, respectively.[12] The n values were 1.08 and 1.24 with a correlation coefficient $r > 0.999$ at 25 and −10 °C, respectively. In a similar way, a CD titration with L-Leu was performed.

Nonlinear Effects in Acetonitrile−5 N $HClO_4$ (99.88/0.12, v/v). A typical experimental procedure using Ala is described below. The molar ratios of Ala to the monomer units of poly-**1** and $HClO_4$ were held constant at 2 and 0.97, respectively, and the volumetric ratio of water to acetonitrile was held constant at acetonitrile/water = 99.88/0.12 (v/v), unless otherwise stated. Stock solutions of poly-**1** (2.0 mg/mL (5.8 mM), 5 mL) in acetonitrile and L-Ala (28.8 mM, 5 mL) and D-Ala (28.8 mM, 5 mL) containing 0.030 mL of 5 N $HClO_4$ in acetonitrile were prepared. Aliquots of the stock solutions of L- and D-Ala were added into five 1 mL flasks equipped with a stopcock using a micropipet (Sibata, Tokyo, Japan) so that the percent ee of Ala (L- or D-rich) was 10, 20, 40, 60, and 80. To the flasks was added a 0.50 mL aliquot of the stock solution of poly-**1**, and the resulting solutions were diluted with acetonitrile to keep the poly-**1** concentration at 1.0 mg/mL (2.9 mM) ([Ala]/[poly-**1**] = 2 (mol/mol)). The solutions were immediately mixed with a vibrator before the CD and absorption measurements. In the same way, nonlinear effects on ICDs of poly-**1** complexed with Leu and Trp with different ee's were investigated.

CD Measurements in Water. Deionized, distilled water was degassed with nitrogen and used throughout for all measurements. The concentration of poly-**1** was 1.0 mg/mL (2.9 mM monomer units), unless otherwise stated. In the complexation of poly-**1** with D- or L-amino acids, stock solutions of poly-**1** (4.0 mg/mL (11.5 mM)) and 1 N $HClO_4$ in water were prepared in 3 and 50 mL flasks equipped with a stopcock, respectively. 0.14 mmol of D- or L-amino acid (18.88 mg of Leu, for example) was placed in a 1 mL flask equipped with a stopcock. 0.2 mL of 1 N $HClO_4$ followed by 0.25 mL of the poly-**1** solution was transferred to the 1 mL flask, and the solution was diluted with water to keep the poly-**1** concentration at 1.0 mg/mL; the molar ratio of amino acids to monomer units of poly-**1** was 50. The same procedure was performed for all D- or L-amino acids. The solution pH (ca. 1.10) was measured with a GST-5428S pH meter.

In the same way, CD spectra of poly-**1** with various amines and amino alcohols were measured. In the pH dependence CD measurements, the solution pH was adjusted with 1 N $HClO_4$ and 1 N NaOH at room temperature.

CD Titrations in Acidic Water with $HClO_4$. A stock solution of poly-**1** (4.0 mg/mL (11.5 mM)) in water was prepared in a 3 mL flask equipped with a stopcock. A stock solution of L-Ala (1.13 M) in water was also prepared in a 3 mL flask. The 0.25 mL aliquots of the poly-**1** solution and 0.20 mL aliquots of 1 N $HClO_4$ were transferred to nine 1 mL flasks equipped with a stopcock. Increasing amounts of the stock solution of the L-Ala were added to the flasks; the molar ratios of l-Ala to poly-**1** were 10, 25, 50, 75, 100, 125, 150, 175, and 200, and the resulting solutions were diluted with water to keep the poly-**1** concentrations at 1.0 mg/mL (2.9 mM, pH 0.89−2.66). The absorption and CD spectra were then taken for each flask to determine the changes in the CD spectra (Figure 2).

In a similar way, a CD titration of poly-**1** with (R)-**4** in water was performed. The Hill plot analyses of the data were then done to estimate the apparent binding constants (K's).

Nonlinear Effects in Acidic Water with $HClO_4$. A typical experimental procedure using Trp is described below. The molar ratio of Trp to the monomer units of poly-**1** was held constant at 10. Stock solutions of poly-**1** (4.0 mg/mL (11.5 mM), 5 mL) and L-Trp (57.6 mM, 5 mL) and D-Trp (57.6 mM, 5 mL) containing 2.5 mL of 0.1 N $HClO_4$ in water were prepared. Aliquots of the stock solutions of L- and D-Trp were added into five 1 mL flasks equipped with a stopcock using a micropipet so that the percent ee of Trp (L-rich) was 10, 20, 40, 60, and 80. To the flasks was added a 0.25 mL aliquot of the stock solution of poly-**1**, and the resulting solutions were diluted with water to keep the poly-**1** concentration at 1.0 mg/mL (2.9 mM) ([Trp]/[poly-**1**] = 10 (mol/mol)). The solutions were thoroughly mixed with a vibrator before the CD and absorption measurements.

In the same way, the nonlinear effect on ICD of poly-**1** complexed with Leu with different ee was investigated.

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Supporting Information Available: ^1H NMR spectrum of poly-**1**, titration curves of ICD intensity ($\Delta\epsilon_{2nd}$) in the complexation of poly-**1** with L-Leu·$HClO_4$ in acetonitrile, and CD data of poly-**2** in acetonitrile−1 N $HClO_4$. This material is available free of charge via the Internet at http://pubs.acs.org.

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