Helicity Induction in Charged Poly(phenylacetylene)s Bearing Various Acidic Functional Groups in Water and Its Mechanism

Hisanari Onouchi, Takashi Hasegawa, Daisuke Kashiwagi, Hiroyuki Ishiguro, Katsuhiro Maeda, and Eiji Yashima*

Department of Molecular Design and Engineering, Graduate School of Engineering, Nagoya University, Chikusa-ku, Nagoya 464-8603, Japan

Received July 6, 2005

ABSTRACT: We investigated the helicity induction in a series of stereoregular cis−transoidal poly(phenylacetylene)s bearing various acidic functional groups, such as a phosphonic acid and its monoethyl ester (poly-**1**−H and poly-**2**−H, respectively), a carboxylic acid (poly-**3**−H), and a sulfonic acid (poly-**4**−H) as the pendants with optically active small molecules with opposite charges, such as amino acids and amines in water. Poly-**1**−H, poly-**2**−H, and poly-**4**−H have a more acidic phosphonic or a sulfonic group than the carboxy group of poly-**3**−H as the pendant, and they could form complexes with the 19 common free L-amino acids as well as optically active amines. The complexes showed characteristic induced circular dichroisms (ICDs) in the polymer backbone regions, due to the prevailing one-handed helix formations on the polymers. On the other hand, poly-**3**−H, which was insoluble in water, but became soluble as the sodium salt (poly-**3**−Na), exhibited ICDs in the presence of only several common free L-amino acids and optically active amines. The interactions of these polyelectrolytes with selected optically active amino acids and amines in water depending on the pH were studied in detail by means of CD spectroscopy together with the potentiometric pH titrations, and the mechanism of the helicity induction in the polyelectrolytes was discussed.

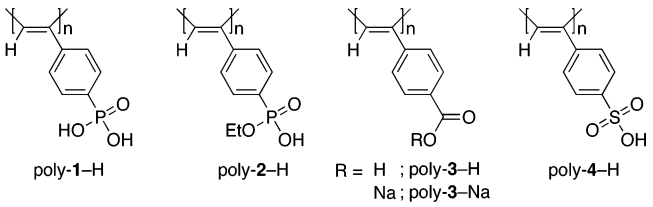
Introduction

Biological macromolecules, such as proteins and nucleic acids, are typical polyelectrolytes with optical activity, and they bind to a variety of biomolecules and drugs with opposite charges through specific interactions, such as electrostatic, directed hydrogen bonding, and van der Waals interactions in water.[1] To mimic such specific interactions occurring in biological events, a number of synthetic receptor molecules have been prepared with great interest, but they usually show chiral or molecular recognition abilities in organic media. The rationale design of charged synthetic receptors for biomolecular recognition through polar interactions in water still remains very difficult.[2] This is because small electrolytes predominantly dissociate into free ions in water by hydration, and therefore attractive interactions including hydrogen bonding and electrostatic interactions cannot be anticipated in water.[3]

However, polyelectrolytes are completely different from small electrolytes; that is, a portion of the counterions are bound to polyelectrolytes of a sufficiently high charge density, resulting in the lower ionic activity of the counterions than that expected from small electrolytes.[4,5] Therefore, polyelectrolytes can efficiently interact with small charged molecules even in water. This effect is called counterion condensation.[4] This characteristic feature of polyelectrolytes may give an important clue for the design of charged synthetic receptors for biomolecular recognition in water.

In a series of our studies, we reported the helicity induction in optically inactive poly((4-carboxyphenyl)acetylene) and its sodium salt (poly-**3**−H and poly-**3**−Na, respectively) (Chart 1) with chiral amines in DMSO[6] and some amino acids in water.[7] The complexes showed an induced circular dichroism (ICD) in the UV−visible region of the polymer backbone due to the predominantly one-handed helical structure. However, the polymer was not highly sensitive to amino acids and other biologically important chiral molecules.[7]

Chart 1. Structures of Poly(phenylacetylene)-Based Polyelectrolytes



Recently, we found that a rationally designed polyelectrolyte, cis−transoidal poly((4-phosphonophenyl)acetylene) (poly-**1**−H) (Chart 1), bioinspired by the interaction motifs of nucleic acids, interacted with a variety of biomolecules including free L-amino acids, peptides, proteins, aminoglycosides, and carbohydrates, and formed a one-handed helical conformation in water.[8] The complexes formed supramolecular assemblies through electrostatic and hydrogen bonding interactions, and exhibited an ICD in the UV−visible region of the polymer backbone in water. We anticipated that other chromophoric polyelectrolytes bearing more acidic functional groups as the pendants might be more sensitive to the chirality of biomolecules, resulting in more intense ICDs in their polymer backbone regions.

In this study, we systematically investigated the helicity induction in a series of cis−transoidal poly(phenylacetylene)s bearing various acidic functional groups as the pendants (poly-**1**−H, poly-**2**−H, poly-**3**−H, and poly-**4**−H) (Chart 1) in the presence of optically active amino acids and amines in water by means of CD spectroscopy and potentiometric pH titrations in

* To whom correspondence should be addressed. E-mail: yashima@apchem.nagoya-u.ac.jp.

10.1021/ma051617+ CCC: $30.25
Published on Web 09/17/2005

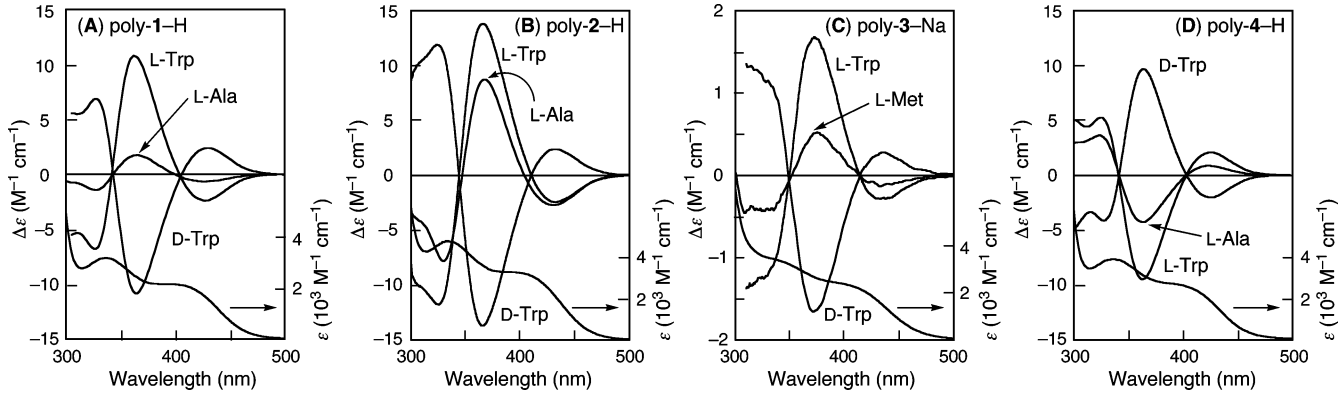


Figure 1. CD and absorption spectra of polymers with amino acids in water at 25 °C. Shown are the CD spectra of the poly-**1**−H with D- and L-Trp at pH 4.5, poly-**1**−H with L-Ala at pH 4.3 (A), poly-**2**−H with D- and L-Trp at pH 3.8, poly-**2**−H with L-Ala at pH 3.8 (B), poly-**3**−Na with D- and L-Trp at pH 7.9, poly-**3**−Na with L-Met at pH 7.7 (C), and poly-**4**−H with D- and L-Trp at pH 5.4, and poly-**4**−H with L-Ala at pH 2.3 (D). The concentration of polymers is 1.0 mg/mL and the molar ratio to polymers is 5 for L-Trp, 10 for L-Ala and L-Met. The absorption spectra of polymers in the presence of L-Trp are also shown.

order to propose the mechanism of the helicity induction in the polyelectrolytes in water. Poly-**4**−H was a new poly(phenylacetylene)-based polyelectrolyte. Poly(ethyl (4-ethynylphenyl)phosphonate) (poly-**2**−H) (Chart 1) was already reported to form a predominantly one-handed helix upon complexation with various chiral amines in DMSO, and was more sensitive to the chirality of amines than poly-**1**−H and poly-**3**−H,[9] but the helicity induction on poly-**2**−H in water has not yet been reported. These results will contribute not only to constructing novel helical polyelectrolytes as a sensitive probe for the chirality assignments of chiral biomolecules in water, but also to understanding the mechanism of specific bimolecular interactions of biological polymers with biomolecules and drugs in water.[10]

Results and Discussion

Synthesis and Helicity Induction of Polyelectrolytes with Free Amino Acids and Chiral Amino Alcohols. Cis−transoidal poly-**1**−H,[8,9] poly-**2**−H,[9] and poly-**3**−H[6,7] were prepared according to previously reported methods. A novel cis−transoidal stereoregular polymer, poly-**4**−H, was prepared by the polymerization of the ammonium salt of the corresponding monomer with a rhodium (Rh) complex in water in a method similar to that previously reported,[7,9] followed by acidification of the pendants with aqueous 2 N HCl. The number-average molecular weight (M_n) and its distribution (M_w/M_n) were estimated to be 1.48×10^5 and 1.9 (poly-**1**−H), 1.9×10^4 and 3.5 (poly-**2**−H), 5.8×10^4 and 2.5 (poly-**3**−H), and 9.5×10^4 and 5.6 (poly-**4**−H), respectively, as determined by size exclusion chromatography (SEC) (see Experimental Section in the Supporting Information). The ^{1}H NMR spectra of these polymers showed sharp singlets centered at around 5.8 ppm, due to the main chain protons, indicating that these polymers possess a highly cis−transoidal, stereoregular structure.[11]

The typical CD and absorption spectra of the polymers in the presence of free amino acids, L- and D-tryptophan (Trp) ([Trp]/[polymer] = 5) and L-alanine (L-Ala) or L-methionine (L-Met) ([Ala or Met]/[polymer] = 10) in water at 25 °C are shown in Figure 1. The complexes showed split-type similar ICDs in their patterns and the ICDs with L- and D-Trp were mirror images of each other. The assay of 19 common free L-amino acids (Ala, Arg, Asn, Asp, Cys, Gln, Glu, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Tyr, Trp, and Val) produced ICDs for poly-**1**−H, poly-**2**−H, and poly-**4**−H, while the sodium salt of poly-**3**−H (poly-**3**−Na) exhibited ICDs with only 8 of them (Gln, Ile, Leu, Met, Phe, Trp, Arg, and Lys) (Table 1). The ICD magnitudes, in most cases, increased with the decreasing temperature. The complexes with L-Trp having a bulky aromatic side group and basic amino acids, such as L-Lys and L-Arg, tend to show more intense ICDs than those with other L-amino acids. Concerning the relationship between the Cotton effect signs of poly-**1**−H and the absolute configurations of the L-amino acids, 12 neutral and 2 acidic L-amino acids gave the same ICD signs, while the secondary amino acid, L-Pro, and the three basic amino acids, L-Arg, L-His, and L-Lys, gave the opposite ICD sign (negative second Cotton) at 25 °C. In contrast, all of the primary L-amino acids gave the same ICD sign (positive second Cotton) for poly-**2**−H and poly-**3**−Na at 25 °C, but the complexes of poly-**2**−H with L-Pro at 0 and 25 °C and poly-**3**−Na with L-Phe at 0 °C exhibited the opposite ICD sign. On the other hand, there is no general relation between the ICD signs and the absolute configurations of the amino acids for poly-**4**−H. Among the four different poly(phenylacetylene)s, poly-**2**−H appeared to be the most sensitive to the chirality of the L-amino acids and exhibited the more intense ICDs in the presence of the L-amino acids, except for L-Asn, L-Asp, L-Arg, and L-His. The CD titrations using some amino acids showed that the ICD intensities increased with the increasing concentration of the amino acids (Supporting Information). Interestingly, the CD intensity of the complex of poly-**2**−H with L-Trp reached an almost constant value in the presence of ca. 1 equiv of L-Trp at 25 °C (Figure S-2B in the Supporting Information). Plots of the CD intensities of the second Cotton ($\Delta\epsilon_{second}$) of poly-**2**−H as a function of the concentration of L-Trp gave a saturated binding isotherm. The Hill plot analyses of the data for the polymers with L-Trp resulted in the apparent binding constants (Ks) of 137, 1310, 19.6, and 244 for poly-**1**−H, poly-**2**−H, poly-**3**−Na, and poly-**4**−H, respectively.[6k,12] The K value for the complexation of L-Trp with poly-**2**−H was the highest among these polymers, and more than 100 times greater than those of L-Ala with these polymers (9.8, 11.8, and 3.3 for poly-**1**−H, poly-**2**−H, and poly-**4**−H, respectively; see Figure S-1−S-4 in the Supporting Information).

To obtain information regarding the interactions between the polymers and amino acids in water, the effects of the pH and salt concentration in solution on

Table 1. Signs and Difference in Exciton Coefficient of the Second Cotton ($\Delta\epsilon_{second}$) for the Complexes of Poly-1−H, Poly-2−H, Poly-3−Na, and Poly-4−H with Amino Acids in Water[a]

	second Cotton [λ (nm) and $\Delta\epsilon_{second}$ ($M^{-1}\,cm^{-1}$)]											
	poly-**1**−H			poly-**2**−H			poly-**3**−Na			poly-**4**−H		
		λ ($\Delta\epsilon$)			λ ($\Delta\epsilon$)			λ ($\Delta\epsilon$)			λ ($\Delta\epsilon$)	
amino acid	pH	25 °C[b]	0 °C	pH	25 °C	0 °C	pH	25 °C[b]	0 °C	pH	25 °C	0 °C
L-Ala	4.3	365 (+1.8)	365 (+8.0)	3.8	368 (+9.0)	368 (+14.1)		*c*	*c*	2.3	363 (−3.6)	367 (−4.3)
N-Ac-L-Ala-OMe	3.6	*c*	*c*	4.4	367 (+3.5)	368 (+6.1)		*c*	*c*	2.8	364 (+0.8)	365 (+2.2)
L-Asn	4.3	*c*	363 (+1.2)	3.8	367 (+0.8)	369 (+2.1)		*c*	*c*	2.1	363 (+2.7)	363 (+5.3)
L-Cys	4.2	364 (+4.0)	365 (+9.2)	3.7	368 (+9.0)	369 (+14.1)		*c*	*c*	2.1	365 (−3.3)	363 (−4.0)
L-Gln	4.2	363 (−0.9)	365 (+1.8)[b]	3.8	368 (+1.7)	369 (+9.2)	7.5	388 (+0.1)	380 (+0.1)	2.0	363 (−1.0)	364 (+1.5)
L-Ile	4.3	364 (+3.3)	364 (+7.2)	3.9	367 (+9.9)	368 (+13.5)	7.5	381 (+0.3)	373 (+0.6)	2.0	367 (+6.9)	364 (+9.2)
L-Leu	4.2	364 (+3.3)	365 (+6.7)	3.9	367 (+12.2)	368 (+15.4)	7.8	372 (+0.3)	373 (+0.6)	1.9	363 (+3.1)	361 (+4.0)
L-Met	4.4	364 (+2.2)	366 (+4.8)	3.8	368 (+9.0)	369 (+12.7)	7.7	375 (+0.5)	374 (+1.5)[d]	1.5	365 (+3.6)	365 (+5.6)
L-Phe	4.4	368 (+0.8)	365 (+4.0)	3.8	368 (+6.6)	368 (+11.8)	7.6	*c*	383 (−0.4)	4.7	364 (−3.8)	364 (−6.1)
L-Pro	4.0	364 (−4.0)	365 (−7.1)	3.7	368 (−7.4)	369 (−11.6)		*c*	*c*	1.9	357 (−1.0)	363 (−2.4)
L-Ser	4.3	363 (+1.9)	365 (+6.0)	3.8	368 (+4.3)	369 (+11.1)		*c*	*c*	2.0	363 (−0.1)	364 (+0.5)
L-Thr	4.2	364 (+2.0)	365 (+5.5)	3.8	367 (+5.7)	369 (+11.5)		*c*	*c*	2.1	363 (+1.5)	364 (+2.6)
L-Trp[e]	4.5	362 (+10.8)	364 (+13.3)	3.8	366 (+13.8)	366 (+14.4)	7.9	373 (+1.7)	372 (+3.9)	5.4	363 (−9.3)	363 (−11.0)
L-Tyr[f,g]	5.3	367 (+0.1)	367 (+1.1)	6.1	367 (+1.1)	368 (+4.3)		*c*	*c*	2.1	361 (−1.6)	361 (−2.1)
L-Val	4.3	361 (+0.8)	365 (+3.6)	3.9	367 (+2.5)	368 (+8.2)		*c*	*c*	2.1	363 (+0.5)	365 (+1.8)
L-Asp[e,h]	3.1	364 (+1.4)	366 (+7.4)	3.8	368 (+1.1)	369 (+7.0)		*c*	*c*	3.1	365 (+3.1)	365 (+8.4)
L-Glu[e,h]	3.4	360 (+0.3)	365 (+3.3)	3.8	368 (+0.3)	368 (+4.6)		*c*	*c*	3.0	365 (+1.4)	365 (+3.7)
L-Arg	3.6	365 (−6.5)	365 (−4.8)	3.2	368 (+1.9)	367 (+6.1)	6.9	371 (+2.7)	371 (+3.8)	4.2	363 (+7.4)	363 (+8.1)
L-His[e,h]	3.6	364 (−3.0)	364 (−11.2)	3.1	368 (+3.6)	367 (+5.2)		*c*	*c*	2.1	362 (+6.9)	394 (+7.0)
L-Lys	3.7	365 (−3.0)	358 (+1.5)	3.3	367 (+14.1)	368 (+16.1)	6.9	371 (+2.3)	373 (+2.9)	2.5	365 (+7.5)	363 (+10.7)

[a] [polymer] = 1.0 mg/mL, [amino acid]/[polymer] = 10. [b] Taken from ref 8. [c] Not detected. [d] Taken from ref 7a. [e] [amino acid]/[polymer] = 5. [f] [amino acid]/[polymer] = 2. [g] [polymer] = 0.1 mg/mL. [h] [polymer] = 0.5 mg/mL.

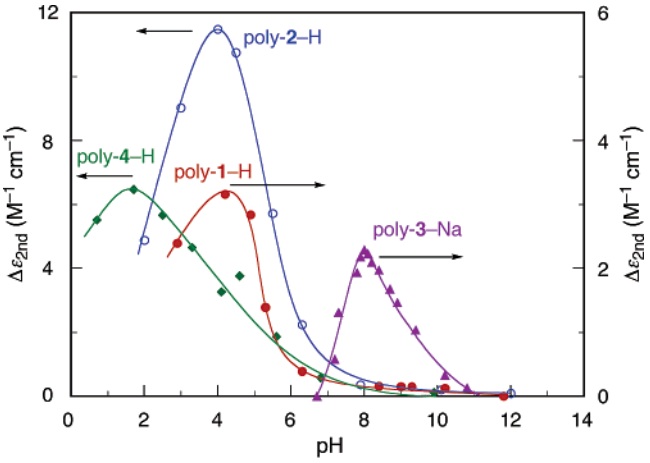
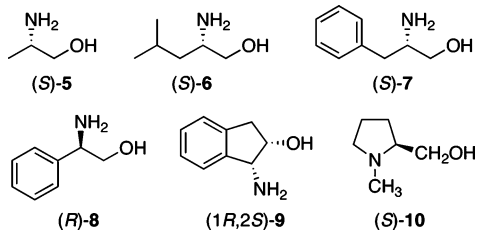


Figure 2. pH dependence of ICD (second Cotton effect) during the complexation of poly-**1**−H (●) and poly-**2**−H (○) with L-Leu at 25 °C, poly-**3**−Na with L-Met at −10 °C (▲), and poly-**4**−H with L-Ile at 25 °C (◆) in the absence of salt in water. The concentration of polymers is 1.0 mg/mL and the molar ratio of amino acids to polymers is 10. The pH was adjusted with HCl and NaOH at room temperature.

the ICDs were investigated. The ICD magnitudes of these polymers with L-amino acids were significantly influenced by the solution pH, and showed maximum values at around pH = 4, 8, and 2 for poly-**1**−H and poly-**2**−H, poly-**3**−Na, and poly-**4**−H, respectively (Figure 2). These pH-dependent ICD changes must be correlated to the degrees of dissociation of the polymer's pendants and the amino acids, which will be discussed later in detail. The ICD intensities were also strongly influenced by the salt (NaCl) concentration and decreased with the increasing concentration (see Figure S-5 in the Supporting Information). The presence of a salt is expected to attenuate the electrostatic interactions because of the charge-shielding effect of the salt,[1,4,5] so that the atropisomerization of the polymer backbones might occur more occasionally, resulting in the decreased ICD intensities. These strong dependences of the ICD intensities on the pH and salt concentration are consistent with the ionic nature of the interactions in water, which will be discussed later in detail.

Chart 2. Structures of Chiral Amino Alcohols



These polymers also exhibited ICDs in the presence of water-soluble amino alcohols (Chart 2) in water, and these results are summarized in Table 2. All the polyelectrolytes formed an induced helix with an excess one-handedness upon complexation with these amino alcohols. In particular, poly-**2**−H was highly sensitive to the chirality of the amino alcohols and exhibited relatively intense ICDs. Poly-**3**−Na responded to the chirality of (*S*)-**5** derived from the L-amino acid, L-Ala, which exhibited no ICD for poly-**3**−Na in water (Table 1), indicating that the electrostatic repulsion between the pendants of poly-**3**−Na and the carboxy group of the amino acid prevents their effective interactions. In the previous study, we reported that the amino alcohols (**5**−**10**) of the same configuration gave the same Cotton effect sign for poly-**2**−H in DMSO,[9] but a similar tendency could not be observed in water for poly-**2**−H and the other polymers. The CD titrations using (*S*)-**7**, which exhibited relatively intense ICDs upon the complexation with these polymers, were also carried out in order to estimate the *K*s for the complexation of (*S*)-**7** with the polymers. The Hill plot analyses of the data resulted in the *K*s of 174, 532, 115, and 986 for poly-**1**−H, poly-**2**−H, poly-**3**−Na, and poly-**4**−H, respectively.[6k,12] Poly-**4**−H bearing strong sulfonic acid residues showed the highest affinity to the amino alcohol (*S*)-**7** among these polymers and the CD intensity reached an

Table 2. Signs and Difference in Exciton Coefficient of the Second Cotton ($\Delta\epsilon_{second}$) for the Complexes of Poly-1−H, Poly-2−H, Poly-3−Na, and Poly-4−H with Amino Alcohols in Water at Room Temperature[a]

	second Cotton [λ (nm) and $\Delta\epsilon_{second}$ (M^{-1} cm^{-1})]							
	poly-**1**−H		poly-**2**−H		poly-**3**−Na		poly-**4**−H	
amino alcohols	pH	λ ($\Delta\epsilon$)	pH	λ ($\Delta\epsilon$)	pH	λ ($\Delta\epsilon$)	pH	λ ($\Delta\epsilon$)
(*S*)-**5**	11.0	365 (+0.2)	11.1	367 (−1.9)	11.0	369 (−1.2)	11.2	364 (−1.5)
(*S*)-**6**	10.6	360 (+0.4)	10.7	367 (+6.7)	10.7	369 (−0.6)	10.9	359 (+0.2)
(*S*)-**7**	10.3	364 (−8.6)	10.5	366 (−15.2)	10.6	366 (−5.7)	10.2	364 (+5.9)
(*R*)-**8**	9.6	367 (−0.9)	10.0	367 (−2.2)	10.2	366 (+0.9)	9.8	363 (+1.6)
(1*R*,2*S*)-**9**	10.3	363 (−10.4)	10.2	368 (−14.1)	10.0	366 (−3.0)	10.0	363 (−7.0)
(*S*)-**10**	11.0	363 (+0.6)	10.9	368 (+2.6)	11.0	363 (−2.0)	10.9	361 (+0.5)

[a] [polymer] = 1.0 mg/mL, [amino alcohol]/[polymer] = 10.

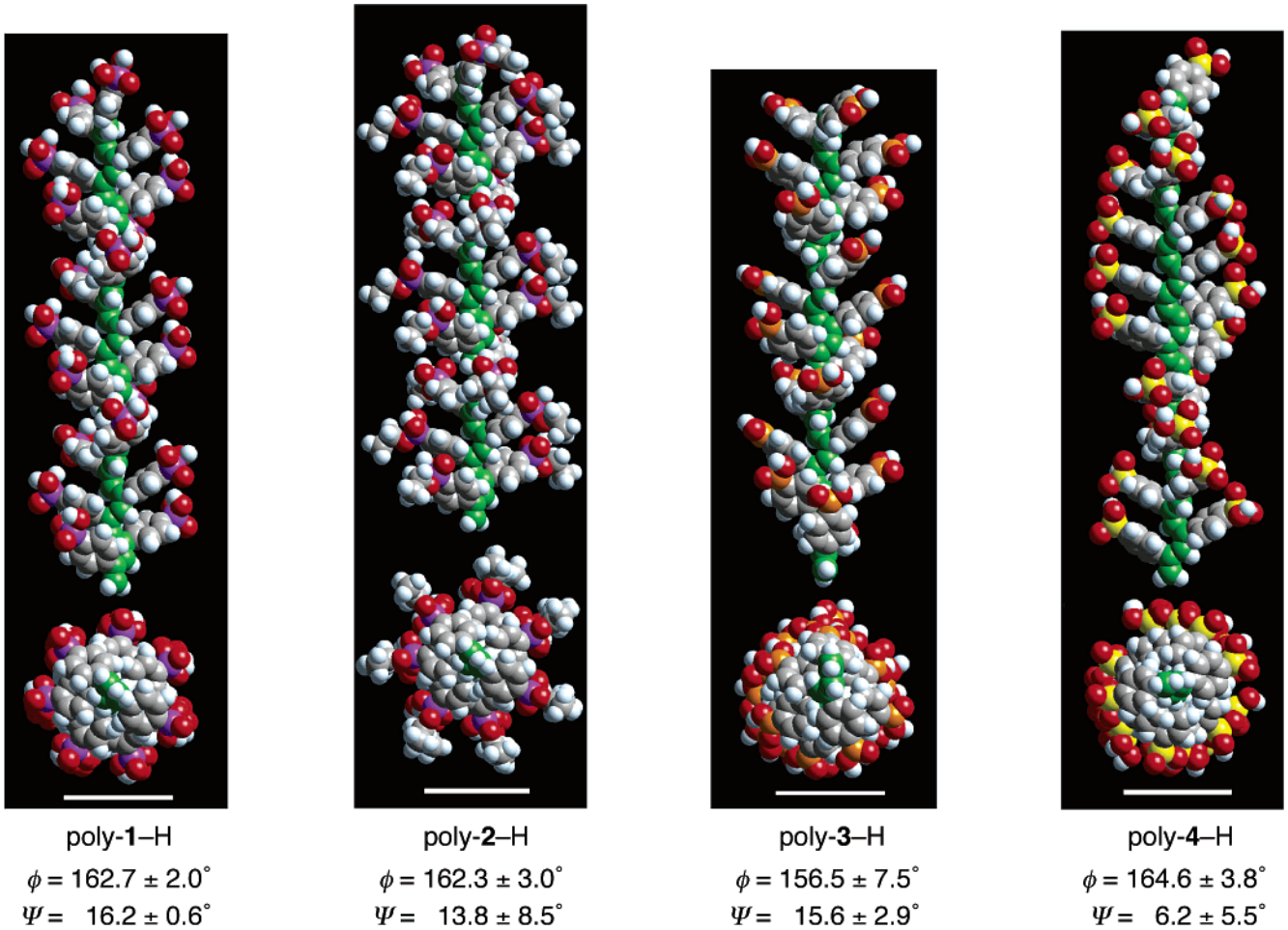


Figure 3. Optimized structures of poly-**1**−H, poly-**2**−H, poly-**3**−H,[6b] and poly-**4**−H (20-mer). Shown are space-filling models in side view (top) and top view (bottom): scale bar, 1.0 nm. The average dihedral angles of the double and single bonds (ϕ and Ψ, respectively) from planarity are also shown.

plateau value in the presence of ca. 1 equiv of (*S*)-**7** (Figure S-4C in the Supporting Information).

Molecular mechanics calculations with the Dreiding force field[13] were then carried out for the model polymers (20-mer) of poly-**1**−H, poly-**2**−H, poly-**3**−H, and poly-**4**−H in order to obtain information regarding the conformations of the polymers used in this study. The ^{1}H NMR studies revealed that these polymers possess a highly cis−transoidal, stereoregular structure. Therefore, we constructed cis−transoidal poly(phenylacetylene)s bearing a phosphonic acid and its monoethyl ester (for poly-**1**−H and poly-**2**−H, respectively) and a sulfonic acid residue (for poly-**4**−H) as model polymers for the calculations according to the previously reported method for a model polymer (20-mer) of poly-**3**−H.[6b] The calculated structures of the model polymers including the previously reported poly-**3**−H structure are shown in Figure 3. The average dihedral angles of the double and single bonds (ϕ and Ψ, respectively) from planarity for these model polymers are also shown in Figure 3. The poly-**1**−H and poly-**2**−H adopt an approximately 7/3 helical conformation similar to that of poly-**3**−H,[6b] while the model polymer of poly-**4**−H had a slightly loose helical conformation compared with the other polymers. Among the poly(phenylacetylene)s, poly-**2**−H has the most bulky side groups, which may be closely correlated to its high sensitivity to the chirality of the chiral biomolecules in water as well as in DMSO. Because the steric hindrance between the neighboring pendants of poly-**2**−H may create a steeper internal-rotation energy

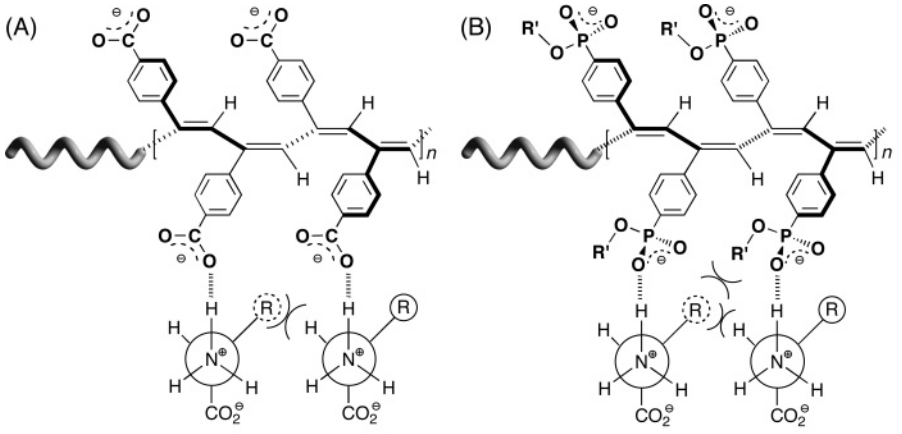


Figure 4. Possible structures for the poly-**3**−Na−L-amino acid (A) and poly-**1**−H or poly-**2**−H−L-amino acid complexes in water (B).

for the polymer main chain,[14] poly-**2**−H may be more rigid with a longer persistent length than those of the other poly(phenylacetylene)s.

Previously, the interactions of poly-**1**−H,[9] poly-**2**−H,[9] and poly-**3**−H[6b,6c,15] with optically active amines and amino alcohols in DMSO (poly-**1**−H, poly-**2**−H, and poly-**3**−H) or water (poly-**3**−H) were systematically studied using NMR and CD spectroscopies, and rational models were proposed to explain the relationships between the Cotton effect signs of the polymers reflecting the helix-sense and the absolute configurations of the chiral primary amines and amino alcohols. On the basis of these models together with the present ICD results of poly-**1**−H, poly-**2**−H, and poly-**3**−Na with L-amino acids in water, a possible mechanism for the helicity induction during the complexation of poly-**1**−H, poly-**2**−H, and poly-**3**−Na with L-amino acids in water can be proposed as follows (Figure 4). In water, L-amino acids may be favorably complexed with the poly-**3**−Na to form ion pairs as shown in Figure 4A, where the conformation of the ammonium group is closer to being anti-staggered and the carboxylate group is located outside and remote from poly-**3**−Na because of electrostatic repulsion by the negatively charged carboxylate groups in the polymer's pendants. Therefore, the predominant helix-sense may be determined by the steric difference in the bulkiness of the substituents of the amino acids (R) and the hydrogen (H) of the neighboring monomer units. The presumed molecular model of the poly-**3**−Na−L-amino acids complexes suggests that the right-handed side monomer unit in Figure 4A is favorably positioned on the front side, while the left-handed side monomer unit is on backside, so that the poly-**3**−Na backbone will possess a right-handed helix. We noted that the pendant groups of the poly-**3**−Na in Figure 4A appear to arrange in a left-handed screw-sense from the side view, but the main chain folds into a right-handed screw-sense.[15]

A similar model can be possible for the complexes of poly-**1**−H and poly-**2**−H with L-amino acids (Figure 4B). In addition to the steric difference in the R and H substituents of the neighboring monomer units, the steric repulsion between the R and the OH or OEt group (R′) of the neighboring phosphonate monomer units should be taken into consideration, resulting in a similar right-handed helical conformation of the polymer backbone as poly-**3**−Na. Therefore, poly-**1**−H, poly-**2**−H, and poly-**3**−Na take the same right-handed helix with L-amino acids, thus showing the same Cotton effect signs. As mentioned above, the complexes of poly-**1**−H with basic L-amino acids exhibited the opposite Cotton effect signs as those with neutral and acidic L-amino acids, whereas poly-**2**−H showed the same Cotton effect signs in the presence of the primary L-amino acids in water irrespective of the kinds of amino acid substituents (Table 1). The reason is not clear at present, but the fact that poly-**1**−H has two acid OH groups with different pK_a values should be an important factor.

Mechanism of the Helicity Induction on Various Polyelectrolytes Based on Poly(phenylacetylene)s with Chiral Amines and Free L-Amino Acids in Water. As described above, the electrostatic ionic interactions between the acidic pendants of the chromophoric poly(phenylacetylene)s and small electrolytes, such as amino acids and amines with the opposite charges in water appear to be the main driving force for the helicity induction in the polymer backbones in water because the ICD intensities are strongly dependent on the pH and NaCl concentration of the solutions. We then initially investigated the dissociation behaviors of the four polyelectrolytes by potentiometric pH titrations in 0.05 M aqueous NaCl. The titration experiments were performed according to reported methods[16] (the detailed procedures are described in the Experimental Section in the Supporting Information). On the basis of the potentiometric titration results of the polymers with NaOH and HCl, the relations between the degree of dissociation of the polymers (α), the solution pH and the apparent dissociation constant (pK_a) of the polymers defined by pH − log(α/(1 − α)) were obtained, and the plots are depicted in Figure 5, parts A and B, respectively. Apparently, poly-**1**−H showed a two-step dissociation process because poly-**1**−H has the two acidic OH groups with different pK_a values; the first step ended at around pH 6 and the second one started at around pH 7.5. The second dissociation was much steeper than the first one. In general, a plot of pK_a vs α shows a monotonic increase in its pK_a with α if a polyelectrolyte has no dramatic conformational change depending on the pH, and the apparent acidity decreases with the progressive dissociation of the polymer.[4,16] In fact, strong polyacid polyelectrolytes, i.e., poly-**1**−H, poly-**2**−H, and poly-**4**−H, displayed almost linear relationships between the pK_a and α values, while a weak polyacid, poly-**3**−H, showed a discontinuous increase in the pK_a vs the α value (Figure 5B). Similar

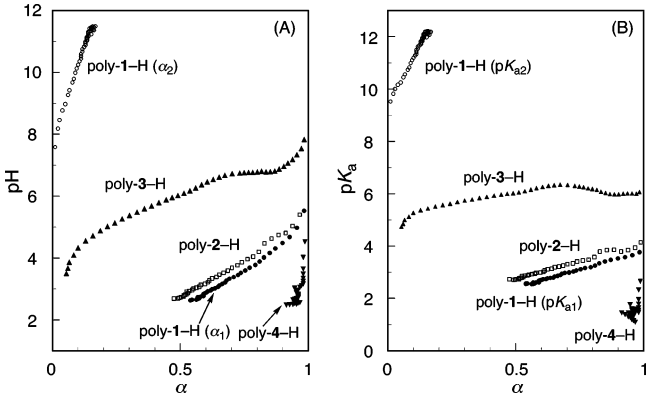


Figure 5. (A) Normalized titration curves of poly-**1**−H (●, α_1; ○, α_2), poly-**2**−H (□), poly-**3**−H (▲), and poly-**4**−H (▼) in 0.05 M NaCl. The concentrations of the polymers are 4.75, 4.83, 4.65, and 4.13 mM for poly-**1**−H, poly-**2**−H, poly-**3**−H, and poly-**4**−H, respectively. (B) Plots of pK_a values of poly-**1**−H (●, pK_{a1}; ○, pK_{a2}), poly-**2**−H (□), poly-**3**−H (▲), and poly-**4**−H (▼) against α in 0.05 M NaCl.

nonlinear changes in the potentiometric pH titration curves were reported for isotactic poly(methacrylic acid)[17] and hydrophobically modified polyelectrolytes,[18] and these nonlinear changes were considered to be due to a conformational transition from a compact form to an extended one including helix−coil transitions.[17,18] Poly-**4**−H is a very strong polyacid and dissociates into anions under acidic conditions at pH 2.5. The intrinsic dissociation constant (pK_0) can be obtained, in principle, by back-extrapolation of the titration curve to $\alpha = 0$. However, the pK_a values are dependent on the salt and polymer concentrations, and the extrapolation requires a theoretically based curve fitting, and therefore, the extrapolated values for pK_0 may be ambiguous, in particular, when the titration could not be possible at low ionization regions. In the present study, the pK_0 value could be obtained for the second dissociation of poly-**1**−H (pK_{02}) at ca. 9.4 by the linear extrapolation of the titration curve in Figure 5B. The pK_{02} value was greater than that of phenylphosphonic acid, a model compound of poly-**1**−H (7.07). This result suggests that it becomes more difficult for protons of acidic polyelectrolytes to dissociate against the attractive force from the dissociated groups in the neighboring pendants.[4] The reported pK_a values of phenylphosphonic acid and its monomethyl ester, benzoic acid, and phenylsulfonic acid as model compounds of these polymers are 1.83 and 7.07 (pK_{a1} and pK_{a2}, respectively)[19] and 2.97,[20] 4.2,[21] and 0.7,[21] respectively.

We then investigated the relationships between the ICD intensities of the polymers in the presence of chiral amines ((*S*)-**6** for poly-**1**−H, poly-**2**−H, and poly-**3**−Na and (*S*)-**5** for poly-**4**−H) and L-amino acid (L-Met) and the ionic species of the polymers and the amines and amino acid in water depending on the pH (Figure 6). The CD spectra were measured in 0.05 M NaCl under the same experimental conditions for the potentiometric pH titrations, so that the pH-dependent CD intensity changes were more or less different from those in Figure 2. In the case of poly-**2**−H with (*S*)-**6** (Figure 6B), the ICD intensity of poly-**2**−H increased with the increasing ammonium ion concentration of (*S*)-**6** at $7 < \text{pH} < 11$, and reached a maximum value when both the poly-**2**−H and (*S*)-**6** dissociated completely into the negative and positive ions, respectively. However, at $\text{pH} < 5$, the dissociation of poly-**2**−H is suppressed and the ICD intensity decreased even though the (*S*)-**6** completely ionized. These results clearly indicate that sufficiently dissociated polymer pendants are favorable for interacting with the positively charged chiral ammonium ions in order to exhibit a strong ICD in water. A similar tendency was observed for other polymers in the presence of chiral amines (Figure 6, parts A, C, and D). We note that poly-**4**−H bearing strong sulfonic acid residues exists as a dissociated form over a wide pH range even at $\text{pH} < 2$, so that the polymer can complex with (*S*)-**5** through electrostatic interactions under the basic, neutral, and acidic conditions, resulting in the ICD at pH ∼ 1 (Figure 6D).

Next we focused on the interactions of the polymers with an L-amino acid (L-Met) in water. Amino acids exist as zwitterions in aqueous solution over a large pH range, and the interaction between the negatively charged polymers and amino acids was anticipated to be complicated depending on the pH because a repulsive ionic interaction between the negatively charged polymers and amino acids should occur as well as an attractive ionic interaction between the polyelectrolytes and amino acids with opposite charges from each other. Poly-**2**−H exhibited almost no ICD in the presence of L-Met which exists as a negatively charged carboxylate or a zwitterion form under the basic and neutral conditions ($6 < \text{pH} < 12$) (Figure 6B). However, the ICD intensity of poly-**2**−H sharply increased at $\text{pH} < 6$ and reached a maximum value at around $\text{pH} = 3$, where the polymer partially protonates and the L-Met mainly exists as the zwitterion, but transforms into the positively charged form at around $\text{pH} = 2.5$. Under a more acidic condition ($\text{pH} < 3$), poly-**2**−H could not sufficiently dissociate in order to interact with the cationic L-Met, so that the ICD intensity slightly decreased. These ICD changes are quite different from those with the chiral amine ((*S*)-**6**). These results indicate that the interaction of poly-**2**−H with amino acids for the helicity induction strongly depends on the ionization state of the amino acids, and the anionic and zwitterionic amino acids cannot efficiently interact with the completely dissociated anionic poly-**2**−H because of the electrostatic repulsion between the negatively charged pendants of poly-**2**−H and the anionic carboxylates of the amino acids. Once the poly-**2**−H partially protonates, an attractive ionic interaction thus predominantly occurred with the amino acids, resulting in the appearance of the ICD. Poly-**1**−H and poly-**4**−H showed similar behaviors in their pH-dependent ICD changes as poly-**2**−H, though poly-**1**−H showed a weak, but apparent ICD at the weak alkaline and neutral pH regions probably because poly-**1**−H has the two acidic OH groups with different pK_a values. Poly-**4**−H also exhibited ICDs which gradually increased with the decreasing pH, and reached a maximum value at pH ca. 1; at around this pH, the amino acid carboxylate protonates and exists in a favorable cationic form for the complexation with the anionic poly-**4**−H. On the other hand, the pH-dependent ICD intensity changes of poly-**3**−Na with L-Met, as depicted in Figure 6C, were similar to those with (*S*)-**6**; the ICD intensities monotonically increased with an increase in the amino acid or (*S*)-**6** ammonium concentrations and showed a maximal response at pH 8, even in the presence of the zwitterions of L-Met. The reason for this is not clear at present, but electrostatic repulsion between the carboxylate anions may be weaker than

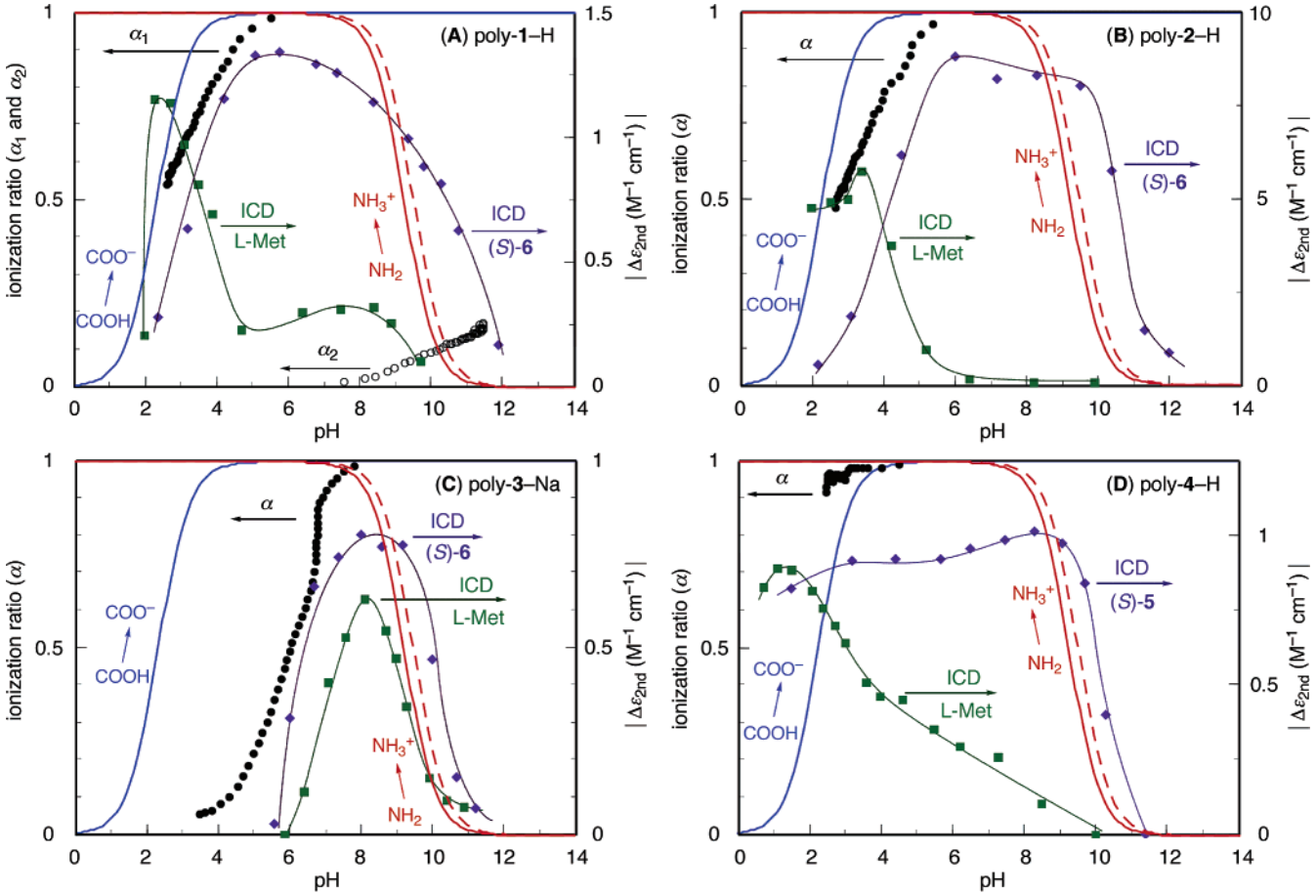


Figure 6. pH dependence of ICD intensities (the absolute value of the second Cotton effect) during the complexation with L-Met (■) and (*S*)-**6** ((*S*)-**5** for poly-**4**−H) (0.05 M, ◆) and the degree of dissociation (●, α_1; ○, α_2) of poly-**1**−H (A), poly-**2**−H (B), poly-**3**−Na (C), and poly-**4**−H (D) (0.005 M) as a function of pH in 0.05 M NaCl solution at 25 °C. The red and blue solid lines and red broken line illustrate the ionization ratios of the amino and carboxy groups of L-Met and amino group of ethanolamine as a model compound of (*S*)-**5** and (*S*)-**6**, respectively. The CD spectra of poly-**1**−H with (*S*)-**6** in A were measured at 0 °C.

those between the carboxylate and phosphonate or sulfonate anions.

Chiral Amplification (Nonlinear Effect) in Water. In our previous studies, we reported that the complex formations of poly-**1**−H, poly-**2**−H, and poly-**3**−H with partially resolved amines, such as 1-(1-naphthyl)ethylamine, displayed a unique, positive nonlinear relationship (chiral amplification or "majority rule")[6b,9,22] between the enantiomeric excess (ee) of amines and the observed molar ellipticity of the Cotton effects; that is, the ICD intensities of the polymers, corresponding to the helical sense excesses, were out of proportion to the ee's of the amines, showing a convex deviation from linearity through a wide range of ee values of the chiral amines in DMSO.

The changes in the ICD intensities of the polymers vs the ee values of amino acids, such as Ala for poly-**1**−H, poly-**2**−H, and poly-**4**−H and Met for poly-**3**−Na and a chiral amine, phenylglycinol (**8**), were then measured in water (Figure S-6 in the Supporting Information). The ICD intensities of poly-**1**−H, poly-**3**−Na, and poly-**4**−H in the presence of Ala with different ee values showed a linear effect at 25 °C and lower temperatures, while a positive nonlinear effect was observed for poly-**2**−H in water at 0 °C (see Figure S-6A in the Supporting Information). The bulky, aromatic amino acid such as Trp also showed nonlinear effects for poly-**1**−H, poly-**2**−H, and poly-**4**−H even at 25 °C (see Figure S-6B in the Supporting Information), and the nonlinearities became stronger at 0 °C; even at 40% ee of Trp gave rise to almost full ICDs as induced by the pure L-Trp for poly-**1**−H, poly-**2**−H, and poly-**4**−H at 0 °C. A similar positive, but weak nonlinear effect was observed for poly-**3**−Na at 0 °C. As mentioned above, the complexes of the polymers with L-Trp showed stronger ICDs than those with other, less bulky L-amino acids, such as L-Ala and L-Met (Figure 1 and Table 1), and this strong helicity inducing ability of Trp might be closely correlated with the chiral amplification phenomena of these polymers with Trp. The chiral amine (**8**) was not sensitive and exhibited a weak nonlinear effect for poly-**2**−H at 0 °C (Figure S-6C in the Supporting Information).

Conclusions

In summary, we found that novel polyelectrolytes based on chromophoric poly(phenylacetylene)s bearing various acidic functional groups, such as a phosphonic acid residue and its monoethyl ester, a carboxy acid, and a sulfonic acid as the pendants, can interact with L-amino acids and optically active amines in water, and the mechanism of the helicity induction in these polyelectrolytes in water was investigated by means of CD spectroscopy together with the potentiometric pH titrations. In particular, the polymer having the bulky phosphonic acid monoethyl ester as the pendant is the most sensitive induced helical polymer as a novel probe for sensing the chirality of free amino acids and amines,

without derivatization in water.[23] The complexations between the polyelectrolytes and small electrolytes are highly dependent on the ionic species of the polymers and biomolecules in water, which can be controlled by changing the pH. The polyelectrolytes have optimum pHs for their helicity induction with biomolecules in water. Sufficiently dissociated anionic polyelectrolytes interact with the positively charged ammonium groups of amines through electrostatic attractive interactions in water, whereas the electrostatic repulsions between the anionic polyelectrolytes and the carboxylate groups of amino acids disturb the effective complexation. The counterion condensation effect, which is a characteristic feature of polyelectrolytes, appears to play an important role to generate the polar ionic interactions between the synthetic receptors consisting of a polyelectrolyte and oppositely charged small molecules even in water. These findings will contribute to the development of more sensitive and selective synthetic polyelectrolytes for the detection of chirality of target biomolecules in water.

Experimental Section

Full experimental details are available in the Supporting Information.

Acknowledgment. We thank Prof. S. Kawaguchi (Yamagata University) for valuable discussions. This work was partially supported by a Grant-in-Aid for Scientific Research from Japan Society for the Promotion of Science. H.O. expresses thanks for a JSPS Research Fellowship (No.05704) for Young Scientists.

Supporting Information Available: Text giving the experimental details, including reaction schemes, and figures showing plots of the CD data and the Hill plots. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Saenger, W. *Principles of Nucleic Acid Structure;* Springer-Verlag: New York, 1984; Chapter 18. (b) Bloomfield, V.; Carpenter, I. L. *Polyelectrolytes; Science and Technology;* Hara, M., Ed.; M. Dekker Inc.: New York, Basel, 1993; pp 77−125. (c) Patel, J. D.; Suri, A. K.; Jiang, F.; Jiang, L.; Fan, P.; Kumar, R. A.; Nonin, S. *J. Mol. Biol.* **1997**, *272,* 645−664. (d) Chow, C. C.; Bogdan, F. M. *Chem. Rev.* **1997**, *97*, 1489−1513. (e) Hermann, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 1890−1905. (f) Houk, K. N.; Leach, A. G.; Kim, S. P.; Zhang, X. *Angew. Chem., Int. Ed.* **2003**, *42*, 4872−4897.

(2) For reviews of molecular recognition in water, see: (a) Murakami, Y.; Kikuchi, J.; Hisaeda, Y.; Hayashida, O. *Chem. Rev.* **1996**, *96*, 721−758. (b) Lemieux, R. U. *Acc. Chem. Res.* **1996**, *29*, 373−380. (c) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609−1646. (d) Schug, K. A.; Lindner, W. *Chem. Rev.* **2005**, *105*, 67−103.

(3) For recent examples of chiral and/or molecular recognition of free amino acids or peptides based on electrostatic interactions in water, see: (a) Hossain, M. A.; Schneider, H.-J. *J. Am. Chem. Soc.* **1998**, *120*, 11208−11209. (b) Bell, T. W.; Khasanov, A. B.; Drew, M. G. B.; Filikov, A.; James, T. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 2543−2547. (c) Herm, M.; Molt, O.; Schrader, T. *Chem.—Eur. J.* **2002**, *8*, 1485−1499. (d) Wada, K.; Mizutani, T.; Matsuoka, H.; Kitagawa, S. *Chem.—Eur. J.* **2003**, *9*, 2368−2380. (e) Imai, H.; Munakata, H.; Uemori, Y.; Sakura, N. *Inorg. Chem.* **2004**, *43*, 1211−1213. (f) Schmuck, C.; Geiger, L. *J. Am. Chem. Soc.* **2004**, *126*, 8898−8899.

(4) (a) Oosawa, F. *Polyelectrolytes*; Dekker: New York, 1971. (b) Manning, G. S. *Acc. Chem. Res.* **1979**, *12*, 443−449. (c) *Molecular Conformation and Dynamics of Macromolecules in Condensed System*, Nagasawa, M., Ed.; Elsevier: New York, 1988. (d) Manning, G. S.; Ray, J. *J. Biomol. Struct. Dyn.* **1998**, *16*, 461−476.

(5) For poly(acrylic acid) as a typical polyelectrolyte, see: (a) Huizenga, J. R.; Grieger, P. F.; Wall, F. T. *J. Am. Chem. Soc.* **1950**, *72*, 4228−4232. (b) Gregor, H. P.; Frederick, M. *J. Polym. Sci.* **1957**, *23*, 451−465. (c) Nagasawa, M.; Kagawa, I. *J. Polym. Sci.* **1957**, *25*, 61−76. (d) Nagasawa, M.; Murase, T.; Kondo, K. *J. Phys. Chem.* **1965**, *69*, 4005−4012. (e) Noda, I.; Tsuge, T.; Nagasawa, M. *J. Phys. Chem.* **1970**, *74*, 710−719.

(6) (a) Yashima, E.; Matsushima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1995**, *117*, 11596−11597. (b) Yashima, E.; Matsushima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6345−6359. (c) Maeda, K.; Morino, K.; Okamoto, Y.; Sato, T.; Yashima, E. *J. Am. Chem. Soc.* **2004**, *126*, 4329−4342. (d) Morino, K.; Watase, N.; Maeda, K.; Yashima, E. *Chem.—Eur. J.* **2004**, *10*, 4703−4707. For other optically active polyacetylenes, see: (e) Ciardelli, F.; Lanzillo, S.; Pieroni, O. *Macromolecules* **1974**, *7*, 174−179. (f) Tang, B. Z.; Kotera, N. *Macromolecules* **1989**, *22*, 4388−4390. (g) Moore, J. S.; Gorman, C. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1991**, *113*, 1704−1712. (h) Yamaguchi, M.; Omata, K.; Hirama, M. *Chem. Lett.* **1992**, 2261−2262. (i) Aoki, T.; Kokai, M.; Shinohara, K.; Oikawa, E. *Chem. Lett.* **1993**, 2009−2012. (j) Nomura, R.; Fukushima, Y.; Nakako, H.; Masuda, T. *J. Am. Chem. Soc.* **2000**, *122*, 8830−8836. (k) Yashima, E.; Maeda, K.; Sato, O. *J. Am. Chem. Soc.* **2001**, *123*, 8159−8160. (l) Schenning, A. P. H. J.; Fransen, M.; Meijer, E. W. *Macromol. Rapid Commun.* **2002**, *23*, 265−270. (m) Percec, V.; Obata, M.; Rudick, J. G.; De, B. B.; Glodde, M.; Bera, T. K.; Magonov, S. N.; Balagurusamy, V. S. K.; Heiney, P. A. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 3509−3533. (n) Nishimura, T.; Tsuchiya, K.; Ohsawa, S.; Maeda, K.; Yashima, E.; Nakamura, Y.; Nishimura, J. *J. Am. Chem. Soc.* **2004**, *126*, 11711−11717. For reviews of dynamic helical polymers, see: (o) Nakano, T.; Okamoto, Y. *Chem. Rev.* **2001**, *101*, 4013−4038. (p) Green, M. M.; Park, J.-W.; Sato, T.; Teramoto, A.; Lifson, S.; Selinger, R. L. B.; Selinger, J. V. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 3138−3154. (q) Fujiki, M. *Macromol. Rapid Commun.* **2001**, *22*, 539−563. (r) Nomura, R.; Nakako, H.; Masuda, T. *J. Mol. Catal. A* **2002**, *190*, 197−205.

(7) (a) Saito, M. A.; Maeda, K.; Onouchi, H.; Yashima, E. *Macromolecules* **2000**, *33,* 4616−4618. For other induced helical polymers and oligomers, see: (b) Schlitzer, D. S.; Novak, B. M. *J. Am. Chem. Soc.* **1998**, *120*, 2196−2197. (c) Norris, I. D.; Kane-Maguire, L. A. P.; Wallace, G. G. *Macromolecules* **1998**, *31*, 6529−6533. (d) Maeda, K.; Yamamoto, N.; Okamoto, Y. *Macromolecules* **1998**, *31*, 5924−5926. (e) Yashima, E.; Maeda, K.; Yamanaka, T. *J. Am. Chem. Soc.* **2000**, *122*, 7813−7814. (f) Prince, R. B.; Barnes, S. A.; Moore, J. S. *J. Am. Chem. Soc.* **2000**, *122,* 2758−2762. (g) Inai, Y.; Ishida, Y.; Tagawa, K.; Takasu, A.; Hirabayashi, T. *J. Am. Chem. Soc.* **2002**, *124,* 2466−2473. (h) Ishikawa, M.; Maeda, K.; Yashima, E. *J. Am. Chem. Soc.* **2002**, *124,* 7448−7458. (i) Tabei, J.; Nomura, R.; Sanda, F.; Masuda, T. *Macromolecules* **2003**, *36*, 8603−8608. (j) Nilsson, K. P. R.; Rydberg, J.; Baltzer, L.; Inganäs, O. *Proc. Nat. Acad. Sci., U.S.A.* **2004**, *101*, 11197−11202. (k) Arnt, L.; Tew, G. N. *Macromolecules* **2004**, *37*, 1283−1288. (l) Sakai, R.; Satoh, T.; Kakuchi, R.; Kaga, H.; Kakuchi, T. *Macromolecules* **2004**, *37*, 3996−4003. (m) Sannigrahi, B.; McGeady, P.; Khan, I. M. *Macromol. Biosci.* **2004**, *4*, 999−1007. (n) Guo, Y.-M.; Oike, H.; Aida, T. *J. Am. Chem. Soc.* **2004**, *126,* 716−717. (o) Mazaleyrat, J.-P.; Wright, K.; Gaucher, A.; Toulemonde, N.; Wakselman, M.; Oancea, S.; Peggion, C.; Formaggio, F.; Setnicka, V.; Keiderling, T. A.; Toniolo, C. *J. Am. Chem. Soc.* **2004**, *126,* 12874−12879. (p) Maeda, K.; Ishikawa, M.; Yashima, E. *J. Am. Chem. Soc.* **2004**, *126,* 15161−15166. (q) Maeda, K.; Takeyama, Y.; Sakajiri, K.; Yashima, E. *J. Am. Chem. Soc.* **2004**, *126,* 16284−16285. (r) Ikeda, C.; Yoon, Z. S.; Park, M.; Inoue, H.; Kim, D.; Osuka, A. *J. Am. Chem. Soc.* **2005**, *127,* 534−535. (s) Onouchi, H.; Miyagawa, T.; Furuko, A.; Maeda, K.; Yashima, E. *J. Am. Chem. Soc.* **2005**, *127,* 2960−2965. (t) Miyagawa, T.; Furuko, A.; Maeda, K.; Katagiri, H.; Furusho, Y.; Yashima, E. *J. Am. Chem. Soc.* **2005**, *127,* 5018−5019.

(8) Onouchi, H.; Maeda, K.; Yashima, E. *J. Am. Chem. Soc.* **2001**, *123*, 7441−7442.

(9) Onouchi, H.; Kashiwagi, D.; Hayashi, K.; Maeda, K.; Yashima, E. *Macromolecules* **2004**, *37*, 5495−5503.

(10) For recent reviews for chirality sensing, see: (a) Canary, J. W.; Holmes, A. E.; Liu, J. *Enantiomer* **2001**, *6*, 181−188. (b) Tsukube, H.; Shinoda, S. *Chem. Rev.* **2002**, *102*, 2389−2403. (c) Allenmark, S. *Chirality* **2003**, *15*, 409−422. (d) Borovkov,

V. V.; Hembury, G. A.; Inoue, Y. *Acc. Chem. Res.* **2004**, *37*, 449−459.
(11) (a) Simionescu, C. I.; Percec, V.; Dumitrescu, S. *J. Polym. Sci.: Polym. Chem. Ed.* **1977**, *15*, 2497−2509. (b) Simionescu, C. I.; Percec, V. *Prog. Polym. Sci.* **1982**, *8*, 133-214. (c) Furlani, A.; Napoletano, C.; Russo, M. V.; Feast, W. J. *Polym. Bull. (Berlin)* **1986**, *16*, 311−317. (d) Matsunami, S.; Kakuchi, T.; Ishii, F. *Macromolecules* **1997**, *30,* 1074−1078. (e) Kishimoto, Y.; Eckerle, P.; Miyatake, T.; Kainosho, M.; Ono, A.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1999**, *121*, 12035−12044.
(12) The CD titration results using L-amino acids and an optically active amino alcohol and the Hill plots are summarized in Figures S-1−S-4. Connors, K. A. *Binding Constants*; John Wiley: New York, 1987.
(13) (a) Mayo, S. L.; Olafson, B. D.; Goddard, W. A., III. *J. Phys. Chem.* **1990**, *94*, 8897−8909. (b) Rappé, A. K.; Goddard, W. A., III. *J. Phys. Chem.* **1991**, *95*, 3358−3363.
(14) Ashida, Y.; Sato, T.; Morino, K.; Maeda, K.; Okamoto, Y.; Yashima, E. *Macromolecules* **2003**, *36*, 3345−3350.
(15) Maeda, K.; Morino, K.; Yashima, E. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3625−3631.
(16) (a) Kitano, T.; Ishigaki, A.; Uematsu, G.; Kawaguchi, S.; Ito, K. *J. Polym. Sci., Polym. Chem. Ed.* **1987**, *25*, 979−986. (b) Kitano, T.; Kawaguchi, S.; Ito, K.; Minakata, A. *Macromolecules* **1987**, *20*, 1598−1606.
(17) Nagasawa, M.; Murase, T.; Kondo, K. *J. Phys. Chem.* **1965**, *7*, 4005−4012.
(18) (a) Dubin, P. L.; Streuss, U. P. *J. Phys. Chem.* **1967**, *71*, 2757−2759. (b) Sugai, S.; Ohno, T. *Macromolecules* **1974**, *7*, 961−963.
(19) Jaffé, H. H.; Freedman, L. D.; Doak, G. O. *J. Am. Chem. Soc.* **1953**, *75*, 2209−2211.
(20) Christol, H.; Levy, M.; Marty, C. *J. Organomet. Chem.* **1968**, *12*, 459−470.
(21) Pine, S. H. *Organic Chemistry;* 5th ed.; McGraw-Hill: New York, 1987; pp 99−102.
(22) (a) Green, M. M.; Peterson, N. C.; Sato, T.; Teramoto, A.; Cook, R.; Lifson, S. *Science* **1995**, *268,* 1860−1866. (b) Green, M. M.; Garetz, B. A.; Munoz, B.; Chang, H.; Hoke, S.; Cooks, R. G. *J. Am. Chem. Soc.* **1995**, *117*, 4181−4182.
(23) The results of chirality sensing of various biomolecules will be published elsewhere.

MA051617+