Notes

Helix Induction in Poly(phenylacetylene)s Bearing Achiral Oligoglycine Pendants by Chiral Oligopeptides in Water

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Introduction

Most biological macromolecules adopt characteristic, one-handed helical structures, such as the α-helix in proteins and the double helix in DNA, to exert their sophisticated functions essential for the maintenance of life. In the formation of these helical structures, specific, directional and noncovalent hydrogen-bonding plays a crucial role.[1] In host−guest and supramolecular chemistry, hydrogen bonding has been widely used for molecular recognition and constructing supramolecular assemblies because of their moderate stability, directionality, and dynamic properties.[2] However, most of the studies on hydrogen bonding have been performed in organic solvents because water molecules prevent the effective hydrogen bonding formation. Recently, hydrogen bonding formation in water has been achieved by utilizing a hydrophobic environment, such as an air−water interface,[3] the interior of aqueous micelles,[4] and aromatic surfaces,[5−7] or by simultaneous formation of amphiphilic tubes and membranes assisted by stacking and hydrophobic interactions,[8] in order to exclude the influence of water molecules. Intramolecular hydrogen bonding has also been used to construct synthetic helical polymers and oligomers,[9−19] some of which were stable even in water like biological systems.[16a,17,18a,19] However, construction of helical polymers with optical activity through intermolecular hydrogen bonding in water has not yet been achieved.[20,21]

We previously reported helicity induction in dynamically racemic helical poly(phenylacetylene)s bearing functional groups through noncovalent acid−base interactions with chiral compounds in organic solvents[22] as well as through electrostatic interactions with biomolecules in water.[23] The complexes exhibited characteristic induced circular dichroisms (ICDs) in the polymer backbone regions. The Cotton effect signs, which correspond to the helical sense of the polymers can be used to predict the absolute configurations of chiral molecules. We now report that intermolecular hydrogen bonding combined with electrostatic and hydrophobic interactions can be used in water for the helicity induction with a predominant screw-sense in poly(phenylacetylene)s with achiral oligoglycine pendants for intermolecular hydrogen-bonding sites.

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Results and Discussion

Three novel poly(phenylacetylene)s bearing achiral oligoglycine residues (poly-**1**−poly-**3**) were designed and synthesized by the polymerization of the corresponding monomers (**1**−**3**) with a water-soluble rhodium complex $[Rh(cod)_2]BF_4$ (cod: cyclooctadiene) in water in the presence of NaOH as outlined in Scheme 1.[23a] All polymers soluble in water with relatively high molecular weights ($M_n = (1.3-1.5) \times 10^5$) were quantitatively obtained, and their stereoregularities were confirmed to be highly cis-transoidal on the basis of their characteristic ^{1}H NMR spectra (for a typical ^{1}H NMR spectrum, see Figure S1).

We first investigated the helicity induction of poly-**1**−poly-**3** in the presence of L-alanine (L-Ala), L-alanylalanine ((L-Ala)$_2$), and L-alanylalanylalanine ((L-Ala)$_3$) ([oligoalanine]/[poly-**3**] = 20) in water at 0 °C. L-Ala could not exhibit any ICD at all for poly-**1**−poly-**3** in water (Figure 1), probably because the carboxylate groups of the polymers are far from the main chains and the ionic interactions with L-Ala appeared not to be effective for the helicity induction. In addition, repulsive ionic interactions between the negatively charged poly-**1**−poly-**3** and the C-terminal carboxylate group of L-Ala may inhibit the attractive ionic interaction in water. However, interestingly, poly-**1**−poly-**3** showed weak, but apparent split-type ICDs in the presence of (L-Ala)$_2$ and (L-Ala)$_3$ in the long absorption regions of their polymer backbones.

The magnitude of the ICD of poly-**1**−poly-**3** was dependent on the degree of polymerization (DP) of the oligoalanines and tended to increase with an increase in the DP of the oligoalanines (Figure 2), except for the complex of poly-**1** with (L-Ala)$_2$, which showed an unexpectedly strong ICD with an opposite Cotton effect sign in water (Figure 1). The reason is not clear at the present. In the presence of glycylglycyl(L-alanine) (Gly−Gly-L-Ala) bearing a free amino group at the N-terminal achiral glycine residue, poly-**3** also showed an ICD comparable to that of the poly-**3**−(L-Ala)$_3$ complex (Figure 1). These results suggest that the ionic interactions between the N-terminal ammonium groups of the free oligoalanines and the carboxylate groups of poly-**1**−poly-**3** may not be a major driving force, but intermolecular hydrogen bonding interactions may contribute more or less to induce a preferred-handed helical structure in water, because the ICD intensity with (L-Ala)$_3$ decreased in the order of poly-**3** > poly-**2** > poly-**1**, although the difference is not significant.[24]

We further investigated the effect of the charges of the oligoalanines on the helicity induction in poly-**1**−poly-**3** in water and measured the CD spectra of poly-**1**−poly-**3** in the presence of an alanine trimer whose N- and/or C-terminal groups were protected ((L-Ala)$_3$-OMe, *N*-Ac-(L-Ala)$_3$, and *N*-Ac-(L-Ala)$_3$-OMe) (Figure 1). A dramatic increase in the ICD intensities was observed for the negatively charged poly-**1**−poly-**3** com-

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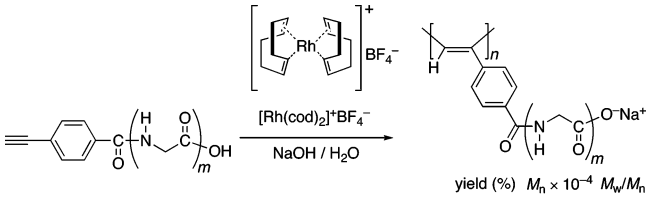
Scheme 1. Synthesis of Poly-1−poly-3



plexed with the positively charged (L-Ala)$_3$-OMe compared with those with zwitterionic (L-Ala)$_3$, whereas poly-**1**−poly-**3** exhibited very weak ICDs ($[\theta]_{2nd}$ < 400 deg cm^2 dmol^{-1}) in the presence of *N*-Ac-(L-Ala)$_3$. In fact, the binding affinity of (L-Ala)$_3$-OMe to poly-**3** (K = 149) was much larger than that of (L-Ala)$_3$ (K < 1) (Figure S2). It is worth noting that poly-**1**−poly-**3** showed intense ICDs in the presence of the neutral alanine trimer (*N*-Ac-(L-Ala)$_3$-OMe) in water, although the binding affinity of *N*-Ac-(L-Ala)$_3$-OMe (K = 5.8) to poly-**3** was smaller than that of (L-Ala)$_3$-OMe, indicating that a preferred-handed helicity can be induced in poly-**1**−poly-**3** even in the absence of attractive ionic interactions in water.

We presume that hydrophobic interactions assisted by multivalent hydrogen bonding may play an important role in the helicity induction. The regular multivalent hydrogen bondings can be possible for the poly-**3**−(L-Ala)$_3$-OMe and poly-**3**−*N*-Ac-(L-Ala)$_3$-OMe complexes as schematically illustrated in Figure 3, parts A and B, respectively.[25] However, the fact that poly-**1** and poly-**2** having a smaller size of the glycine residues also showed ICDs similar to those of poly-**3** in the presence of (L-Ala)$_3$-OMe and *N*-Ac-(L-Ala)$_3$-OMe suggests that regular hydrogen bonding arrays as shown in Figure 3, parts A and B, are not necessary, but a possible intermolecular hydrogen bonding (Figure 3C)[25] may contribute to the preferred-handed helicity induction in poly-**1** and poly-**2**.[26]

We then prepared the *N*-methylated *N*-Ac-(L-Ala)$_3$-OMe, namely *N*-Ac-(L-Ala-Me)$_3$-OMe, to explore each contribution of the hydrogen bonding and hydrophobic interactions to the helicity induction in poly-**1** and poly-**3** in water (Figure 1). As shown in Figure 1, these polymers showed ICDs with *N*-Ac-(L-Ala-Me)$_3$-OMe, but their ICD intensities significantly decreased compared with that of *N*-Ac-(L-Ala)$_3$-OMe.[27] In addition, the fact that poly-**1**−poly-**3** showed no ICD in the presence of neutral *N*-Ac-L-Ala-OMe likely supports our speculation that hydrophobic interactions assisted by multivalent hydrogen bonding interaction play a dominant role in the helicity induction in poly-**1**−poly-**3** in water.[28]

In summary, we found that a predominantly one-handed helix could be induced in optically inactive poly(phenylacetylene)s bearing achiral oligoglycine residues in water through intermolecular interactions including ionic, hydrogen bonding, and hydrophobic interactions with chiral oligopeptides. Recently, we reported that a water-soluble positively charged poly(phenylacetylene) could trap a hydrophobic chiral guest within its hydrophobic cavity in water, and the resulting helical poly(phenylacetylene) with a predominantly one-handed helical sense induced by the chiral guest could serve as a template for further supramolecular helical arrays of an achiral porphyrin with opposite charges along the helical backbone, resulting in the formation of optically active J-homo-aggregates.[21b] The present poly(phenylacetylene)s have additional amide residues as the pendants, which may be further used for selective inclusion of specific chiral guests within their cavities to produce more sophisticated supramolecular helical assemblies with achiral dyes. Work along this line is now in progress.

Experimental Section

Instruments. Melting points were measured on a Büchi melting point apparatus and are uncorrected. NMR spectra were measured on a Varian Mercury 300 (300 MHz for ^{1}H) or Varian VXR-500S (500 MHz for ^{1}H) spectrometer using acetone (2.22 ppm) for D_2O and D_2O/H_2O (1/9, v/v) or a solvent residual peak (2.50 ppm) for DMSO-d_6 as the internal standards. IR spectra were recorded using a JASCO Fourier Transform IR-620 spectrophotometer. Absorption and CD spectra were taken on a JASCO V-570 spectrophotometer and a JASCO J-725 spectropolarimeter, respectively, in a 0.1 cm quartz cell. Temperature was controlled with a JASCO PTC-348WI and a JASCO ETC-505T apparatus for CD and absorption measurements, respectively. A size exclusion chromatography (SEC) was performed using a JASCO PU-980 liquid chromatograph equipped with a RI (JASCO RI-930) detector. Tosoh TSKgel α-3000 and α-5000 SEC columns (30 cm) were connected in series, and DMF containing 10 mM LiCl was used as the eluent at a flow rate of 1.0 mL/min. The molecular weight calibration curve was obtained with poly(ethylene oxide) standards (Tosoh). Recycling preparative high-performance liquid chromatography (HPLC) was performed using an LC-918 liquid chromatograph (JAI, Tokyo) equipped with UV−visible (JAI UV 310) and RI (JAI) detectors. HPLC columns, JAIGEL-1H and JAIGEL-2H (60 × 2 cm (i.d.)) were connected in series, and chloroform was used as the solvent. The solution pH was measured with a B-211 pH meter (Horiba, Japan). FAB-MS spectra were acquired on a JEOL JMS-700 mass spectrometer using *m*-nitrobenzyl alcohol (NBA) as the matrix. Mass spectra were recorded at the Nagoya University Chemical Instrument Center. Elemental analyses were performed by the Nagoya University Analytical Laboratory in School of Engineering.

Materials. Glycine (Gly) and glycylglycine (Gly−Gly) were purchased from Tokyo Kasei (Tokyo, Japan). Glycylglycylglycine (Gly−Gly−Gly) and other optically active alanine oligomers were obtained from Sigma. $[Rh(cod)_2]BF_4$ was prepared from $[Rh(nbd)Cl]_2$ with $AgBF_4$ according to the literature.[29] $[Rh(nbd)Cl]_2$ (Azmax, Japan) and $AgBF_4$ (Sigma) were used as received. (4-Carboxyphenyl)acetylene was synthesized according to the previously reported method.[22b]

***N*-(4-Ethynylbenzoyl)glycine (1).** This new compound was prepared according to Scheme 2. (4-Carboxyphenyl)acetylene (6.0 g, 41 mmol) was dissolved in thionyl chloride (85 mL, 1.2 mol) and the solution was stirred under nitrogen at 60 °C for 6 h. Excess thionyl chloride was removed by distillation under reduced pressure, and the residue was dissolved in THF (41 mL, 1 M). The THF solution (18 mL) was added dropwise to a solution of Gly (1.5 g, 20 mmol) in water (50 mL) containing 6.4 g Na_2CO_3 (60 mmol). After the reaction mixture was stirred at room temperature for 5 h, the solution was neutralized with 1 N HCl and the precipitated solid was collected by filtration and washed with water. The crude product was purified by silica gel chromatography with ethyl acetate−methanol−acetic acid (100/10/1, v/v/v) as the eluent, followed by recrystallization from ethanol−water (1/2, v/v) to give a white solid in 46% yield. Mp: 199.8−200.7 °C. IR (KBr, cm^{-1}): 3276 ($\nu_{\equiv CH}$), 1736 ($\nu_{C=O}$ of carboxylic acid), 1631 (amide I), 1543 (amide II). ^{1}H NMR (DMSO-d_6, 300 MHz, 30 °C): δ 3.90 (d, J = 6.0 Hz, CH_2, 2H), 4.38 (s, ≡CH, 1H), 7.58 (d, J = 8.4 Hz, aromatic, 2H), 7.86 (d, J = 8.4 Hz, aromatic, 2H), 8.95 (t, J = 6.0 Hz, NH, 1H), 12.61 (s, CO_2H, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz, 30 °C): δ 41.24, 82.77, 82.88, 124.49, 127.37, 131.56, 133.68, 165.44, 170.97. FAB-MS: *m/e* 204 $(M+H)^+$. Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 64.84; H, 4.34; N, 6.81.

***N*-(4-Ethynylbenzoyl)glycylglycine (2).** This compound was prepared from Gly−Gly according to an analogous method for the synthesis of **1**. The crude product was purified by recrystallization from ethanol−water (1/5, v/v) to give a brown solid in 61% yield. Mp: 213.0−213.8 °C. IR (KBr, cm^{-1}): 3287 ($\nu_{\equiv CH}$), 1754 ($\nu_{C=O}$ of carboxylic acid), 1651 (amide I), 1553 (amide II). ^{1}H NMR

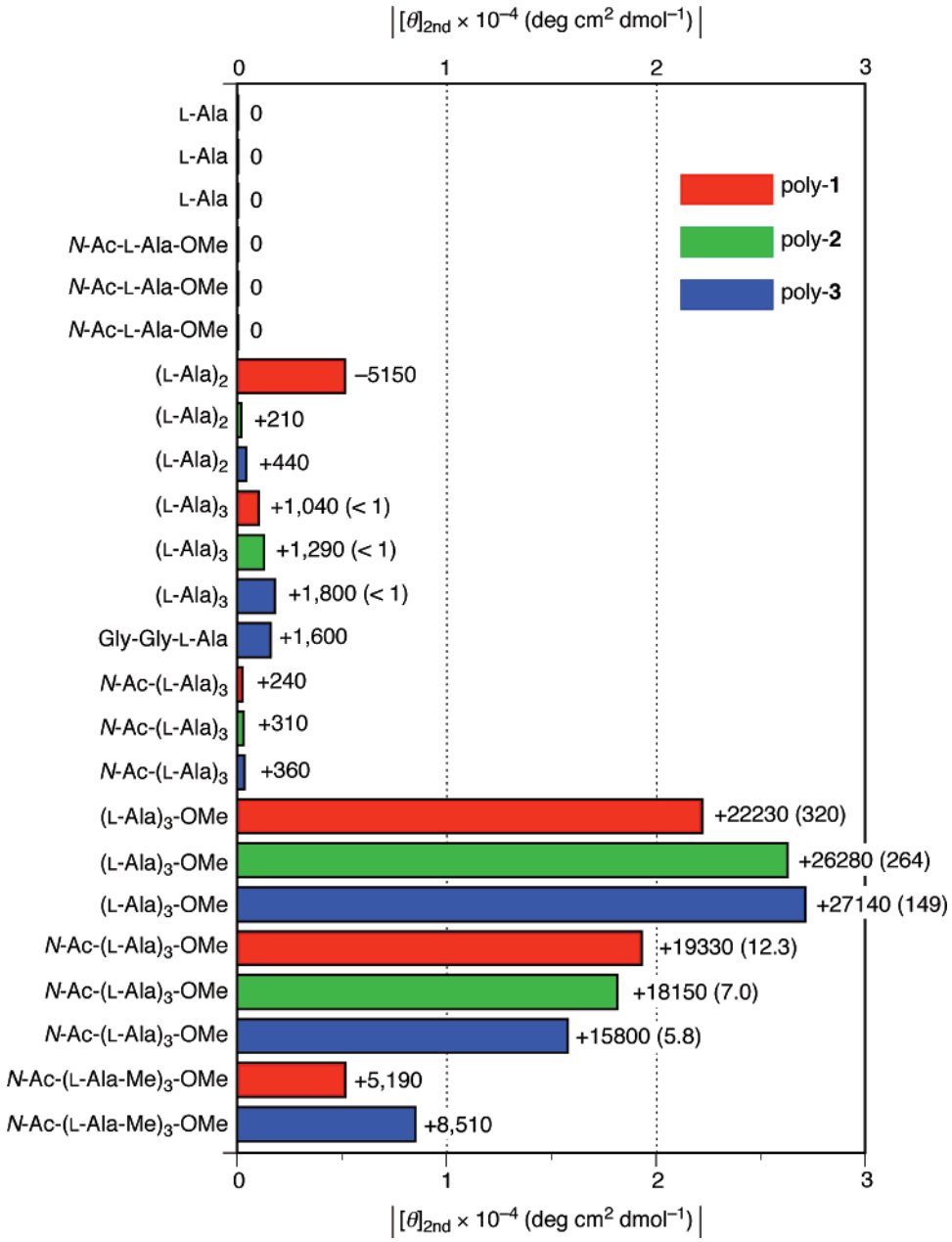


Figure 1. ICD (second Cotton) intensities of poly-**1**−poly-**3** (1 mg/mL) in the presence of L-Ala and its derivatives and oligopeptides (20 equiv. to monomer units of poly-**1**−poly-**3**) in water at 0 °C. Apparent binding constants (*K*s) estimated by the Hill plot analyses using the CD titration experiments are also shown in the parentheses. For a typical ICD spectrum, see Figure 2.

(DMSO-d_6, 300 MHz, 30 °C): δ 3.75 (d, J = 5.7 Hz, CH_2, 2H), 3.89 (d, J = 5.7 Hz, CH_2, 2H), 4.38 (s, ≡CH, 1H), 7.57 (d, J = 8.4 Hz, aromatic, 2H), 7.88 (d, J = 8.4 Hz, aromatic, 2H), 8.24 (t, J = 6.0 Hz, NH, 1H), 8.88 (t, J = 6.0 Hz, NH, 1H), 12.57 (s, CO_2H, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz, 30 °C): δ 40.64, 42.44, 82.85, 82.90, 124.42, 127.56, 131.48, 133.90, 165.44, 169.03, 170.98. FAB-MS: *m*/*e* 261 $(M+H)^+$. Anal. Calcd for $C_{13}H_{12}N_2O_4$: C, 59.05; H, 4.75; N, 10.59. Found: C, 59.31; H, 4.63; N, 10.29.

***N*-(4-Ethynylbenzoyl)glycylglycylglycine (3).** This compound was prepared from Gly−Gly-Gly according to an analogous method for the synthesis of **1**. The crude product was purified by recrystallization from ethanol−water (1/7, v/v) to give a cream-colored solid in 45% yield. Mp: >235 °C (decomposition). IR (KBr, cm^{-1}): 3270 ($\nu_{\equiv CH}$), 1741 ($\nu_{C=O}$ of carboxylic acid), 1649 (amide I), 1553 (amide II). ^{1}H NMR (DMSO-d_6, 300 MHz, 30 °C): δ 3.74 (d, J = 5.7 Hz, CH_2, 2H), 3.75 (d, J = 5.7 Hz, CH_2, 2H), 3.90 (d, J = 5.7 Hz, CH_2, 2H), 4.35 (s, ≡CH, 1H), 7.57 (d, J = 8.4 Hz, aromatic, 2H), 7.88 (d, J = 8.4 Hz, aromatic, 2H), 8.13 (t, J = 6.0 Hz, NH, 1H), 8.22 (t, J = 6.0 Hz, NH, 1H), 8.86 (t, J = 6.0 Hz, NH, 1H), 12.55 (s, CO_2H, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz, 30 °C): δ 40.57, 41.79, 42.75, 82.79, 124.40, 127.49, 131.43, 133.84, 165.57, 168.90, 168.92, 170.81. FAB-MS: *m*/*e* 318 $(M+H)^+$. Anal. Calcd for $C_{15}H_{15}N_3O_5$: C, 56.78; H, 4.76; N, 13.24. Found: C, 56.50; H, 4.72; N, 13.13.

***N*-Ac-(L-Ala-Me)$_3$-OMe.** This compound was prepared from *N*-Ac-(L-Ala)$_3$-OMe in a manner similar to the literature method.[30] To a solution of *N*-Ac-(L-Ala)$_3$-OMe (0.25 g, 0.88 mmol) in DMF (12.5 mL) were added iodomethane (1.3 mL, 21 mmol) and silver-(I) oxide (2.45 g, 10.6 mmol) at room temperature. After the mixture was stirred at room temperature for 3 days under nitrogen, the insoluble part was removed by filtration and the filtrate was diluted with chloroform (80 mL). The solution was washed with 5% potassium cyanide aqueous solution (2 × 50 mL) and water (2 × 50 mL), and then the chloroform layer was dried over $MgSO_4$. The solvent was removed under reduced pressure to give a crude product, which was then purified by recycling preparative HPLC with an eluent of chloroform to give 0.23 g of *N*-Ac-(L-Ala-Me)$_3$-OMe as colorless oil in 79% yield. IR (NaCl plate, cm^{-1}): 1744 ($\nu_{C=O}$ of ester), 1645 (amide I). ^{1}H NMR (DMSO-d_6, 300 MHz,

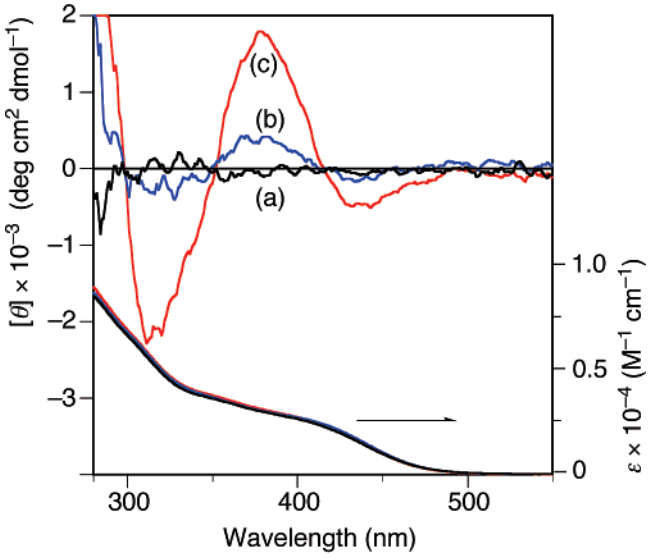


Figure 2. CD and absorption spectra of poly-**3** in the presence of (L-Ala) (pH 4.8) (a), (L-Ala)$_2$ (pH 5.3) (b), and (L-Ala)$_3$ (pH 4.8) (c) in water at 0 °C. [poly-**3**] = 1.0 mg/mL, [oligoalanine]/[poly-**3**] = 20.

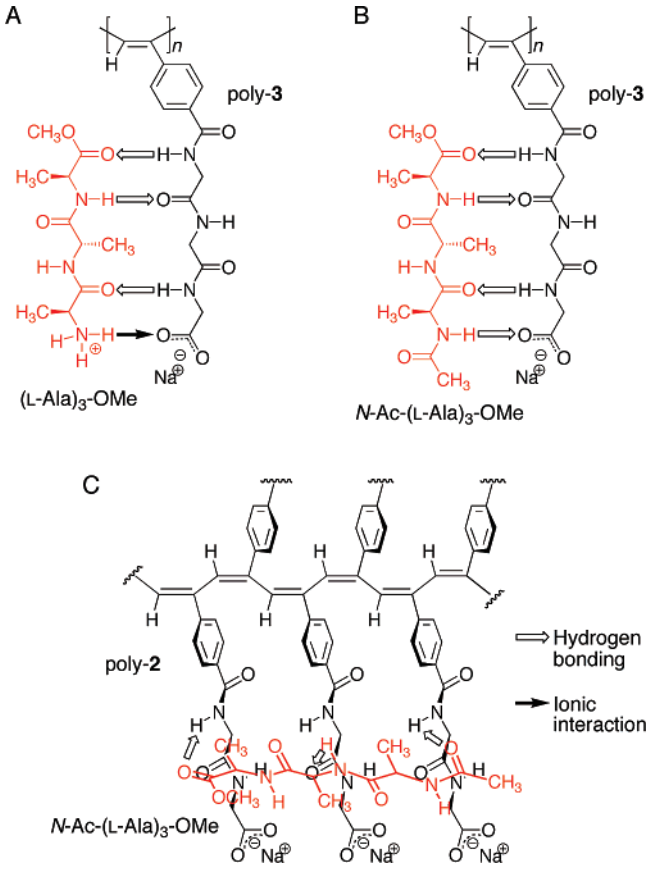
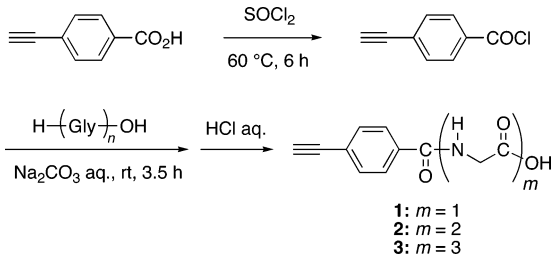


Figure 3. Possible interaction models of poly-**3** with (L-Ala)$_3$-OMe (A), *N*-Ac-(L-Ala)$_3$-OMe (B), and poly-**2** with *N*-Ac-(L-Ala)$_3$-OMe (C).

80 °C): δ 1.12 (s, 2CH$_3$, 6H), 1.34 (d, CH$_3$, 3H), 2.02 (s, CH$_3$CO, 3H), 2.78 (s, NCH$_3$, 3H), 2.83 (s, 2NCH$_3$, 6H), 3.63 (s, CH$_3$O, 3H), 4.72 (s, CH, 1H), 5.35 (s, 2CH, 2H). ^{13}C NMR (DMSO-d_6, 75 MHz, 80 °C): δ 13.5, 13.9, 15.2, 21.0, 28.9, 30.1, 31.5, 48.2, 49.1, 51.3, 53.4, 169.2, 169.4, 170.0, 171.0. FAB-MS: *m*/*e* 330 (M+H)$^+$. Anal. Calcd for $C_{15}H_{27}N_3O_5 \cdot {}^9/_{10}H_2O$: C, 52.13; H, 8.40; N, 12.16. Found: C, 52.19; H, 8.41; N, 12.01. $[\alpha]_D^{25}$ −221° (*c* 1.1, chloroform).

Polymerization. Polymerization was carried out according to Scheme 1 in a dry glass ampule under a dry nitrogen atmosphere

Scheme 2. Synthesis of 1−3



using [Rh(cod)$_2$]BF$_4$ as the catalyst. A typical polymerization procedure is described below.

Monomer **3** (1.00 g, 3.16 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 appropriate amounts of ion-exchanged, distilled water and aqueous NaOH (1 N) ([NaOH]/[**3**] = 1.5) were added with a syringe. To this was added a solution of [Rh(cod)$_2$]BF$_4$ (0.025 M) in water at 30 °C. The concentrations of **3** and the rhodium catalyst were 0.5 and 0.0025 M, respectively. After 8 h, the resulting polymer (poly-**3**) was precipitated into a large amount of ethanol, collected by centrifugation, washed with ethanol, and then dried in vacuo at room temperature over night (1.10 g, 99.8% yield). The molecular weight (M_n) of the polymer was estimated as its methyl ester by SEC with poly(ethylene oxide) standards using DMF containing 10 mM LiCl as the eluent (M_n = 13.4 × 10^4, M_w/M_n = 2.2). The ^{1}H NMR spectrum of poly-**3** in D$_2$O showed a sharp singlet centered at 5.83 ppm due to the main chain protons (see the Supporting Information), indicating that the polymer possesses a highly cis-transoidal, stereoregular structure.[31]

Spectroscopic data of poly-**3**. IR (KBr, cm^{-1}): 1655 (amide I), 1605 ($\nu_{C=O}$ of carboxylate), 1543 (amide II). ^{1}H NMR (D$_2$O, 300 MHz, 60 °C): δ 3.72 (s, CH$_2$, 2H), 3.95 (s, CH$_2$, 2H), 4.07 (s, CH$_2$, 2H), 5.83 (s, CH, 1H), 6.77 (s, aromatic, 2H), 7.50 (s, aromatic, 2H). Anal. Calcd for $(C_{15}H_{14}N_3NaO_5 \cdot {}^3/_2H_2O)_n$: C, 49.18; H, 4.68; N, 11.47. Found: C, 49.46; H, 4.47; N, 11.04.

Poly-**3** was dissolved in a small amount of distilled water. The aqueous solution was acidified with 1 N HCl aq. and the precipitated acid form polymer (poly-**3**-H) was collected by centrifugation and dried in vacuo at room temperature over night. The poly-**3**-H was quantitatively converted to its methyl ester (poly-**3**-Me) by reaction with diazomethane to obtain a sample for SEC analysis.

Spectroscopic data of poly-**3**-Me. IR (KBr, cm^{-1}): 1735 ($\nu_{C=O}$ of ester), 1654 (amide I), 1542 (amide II). ^{1}H NMR (DMSO-d_6, 300 MHz, 60 °C): δ 3.59 (s, OCH$_3$, 3H), 3.68−4.04 (broad singlet, CH$_2$, 6H), 5.83 (s, CH, 1H), 6.77 (s, aromatic, 2H), 7.50 (s, aromatic, 2H), 8.09 (s, NH, 2H), 8.31 (s, NH, 1H).

Polymerizations of **1** and **2** were performed in the same way.

Spectroscopic Data of poly-1. IR (KBr, cm^{-1}): 1644 (amide I), 1604 ($\nu_{C=O}$ of carboxylate), 1543 (amide II). ^{1}H NMR (D$_2$O, 300 MHz, 60 °C): δ 3.85 (s, CH$_2$, 2H), 5.82 (s, CH, 1H), 6.80 (s, aromatic, 2H), 7.51 (s, aromatic, 2H). Anal. Calcd for $(C_{11}H_8NNaO_3 \cdot {}^5/_3H_2O)_n$: C, 51.77; H, 4.48; N, 5.49. Found: C, 51.73; H, 4.27; N, 5.10.

Spectroscopic Data of poly-2. IR (KBr, cm^{-1}): 1643 (amide I), 1605 ($\nu_{C=O}$ of carboxylate), 1543 (amide II). ^{1}H NMR (D$_2$O, 300 MHz, 60 °C): δ 3.74 (s, CH$_2$, 2H;), 4.04 (s, CH$_2$, 2H), 5.81 (s, CH, 1H), 6.80 (s, aromatic, 2H), 7.49 (s, aromatic, 2H). Anal. Calcd for $(C_{13}H_{11}N_2NaO_4 \cdot 2H_2O)_n$: C, 49.06; H, 4.75; N, 8.80. Found: C, 48.80; H, 4.50; N, 8.25.

The molecular weights (M_n) of poly-**1** and poly-**2** were estimated as their methyl esters by SEC with poly(ethylene oxide) standards using DMF containing 10 mM LiCl as the eluent (poly-**1**: M_n = 15.0 × 10^4, M_w/M_n = 2.1; poly-**2**: M_n = 15.1 × 10^4, M_w/M_n = 2.2).

CD Measurements. Deionized, distilled water was degassed with argon and used throughout for all measurements. The concentrations of poly-**1**−poly-**3** were calculated based on the monomer units. A

typical procedure for CD measurements is described below. A stock solution of poly-**1** (2 mg/mL) in water was prepared in a 5 mL flask equipped with a stopcock. A 500 μL aliquot of the polymer solution was transferred to a 1 mL flask equipped with a stopcock using a Hamilton microsyringe. An appropriate amount of an alanine oligomer was directly added to the flask and the solution was diluted with water to keep the polymer concentration to be 1.0 mg/mL, and absorption and CD spectra were taken. The solution pH was measured with a B-211 pH meter (Horiba, Kyoto, Japan). Similar procedures were done for the CD measurements with poly-**2** and poly-**3**. The concentrations of the polymers were corrected by using the ϵ values of the polymers (ϵ_{400} (cm^{-1} M^{-1}) = 2790 (poly-**1**), 2890 (poly-**2**), and 2990 (poly-**3**)). For the ICD intensity changes in pH and salt concentrations for the complexation of poly-**3** with (L-Ala)$_3$ and/or *N*-Ac-(L-Ala)$_3$-OMe (see Figures S5 and S6 in Supporting Information, respectively).

The changes in pH resulting from the addition of excess alanine oligomers were not negligible, and therefore, the CD titrations with (L-Ala)$_n$, (L-Ala)$_3$-OMe, and *N*-Ac-(L-Ala)$_3$-OMe were performed in sodium acetate/acetic acid (pH 5.0), imidazole/HCl (pH 6.6), and tris/HCl (pH 8.4) buffers, respectively, to maintain the pH. Plots of the CD intensities of the second Cotton of the polymer as a function of concentrations of alanine oligomers gave a saturation binding isotherm at 0 °C. The Hill plot analysis of the data resulted in 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 (see Figure S2 in Supporting Information).[32]

^{1}H NMR Titration. The ^{1}H NMR titration experiment of *N*-Ac-(L-Ala)$_3$-OMe with poly-**3** were performed as follows: poly-**3** (6.5 mg) was dissolved in 800 μL of D_2O/H_2O (1/9, v/v) containing a small amount of acetone as the internal standard, the solution was transferred to a 5 mm NMR tube, and the initial ^{1}H NMR spectrum was recorded at 30 °C. To this was added increasing amount of *N*-Ac-(L-Ala)$_3$-OMe (5.5, 5.5, 11, 22, and 22 mg) and their ^{1}H NMR spectra were recorded at 30 °C for each addition of *N*-Ac-(L-Ala)$_3$-OMe. A 1331 pulse sequence was used to suppress water signal.[33] The changes in the chemical shift of the N−H_A proton resonance of poly-**3** was followed, but those of the N−H_B and N−H_C proton resonance of poly-**3** could not be followed because of overlapping of the signals due to *N*-Ac-(L-Ala)$_3$-OMe (see Figure S4 in Supporting Information).

Molecular Modeling and Calculations. Molecular modeling and molecular mechanics calculation were performed with the Dreiding force field (version 2.21)[34] as implemented in CERIUS^2 software (version 3.8; Molecular Simulations Inc., Burlington, MA) running on an Indigo^2-Extreme graphics workstation (Silicon Graphics). For the calculations, the acid form polymers, poly-**3**-H and poly-**2**-H, were used. The polymer models (20 repeating monomer units) of poly-**3**-H and poly-**2**-H were constructed using a Polymer Builder module in CERIUS^2 in a similar method reported previously.[22b] Charges on atoms of these polymers were calculated using charge equilibration (Q_{Eq}) in CERIUS;^{2} total charge of molecules was zero. The starting main-chain conformations of polymer models were defined as the double bond geometry (*cis* or *trans*) and a conformation of a rotational single bond. The double bond geometry was fixed to *cis* and the initial dihedral angle of a single bond from planarity (ϕ) could be varied. The initial dihedral angles of single and double bonds from planarity were set to 156.5° (*transoid*) and 15.6° (*cis*), respectively, and the phenyl rings were twisted out of the backbone by 57.8° on the basis of the calculated structure of poly(4-carboxyphenylacetylene).[22b] The constructed models (20-mer) were optimized by the conjugate gradient method. The energy minimization was continued until the root-mean-square (rms) values became less than 0.1 kcal mol^{-1} $Å^{-1}$. The optimized *N*-Ac-(L-Ala)$_3$-OMe was then manually placed into the interaction sites of poly-**2** and poly-**3** so that intermolecular hydrogen bonds were visually satisfied (see Figure S3 in Supporting Information).

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Supporting Information Available: Figures showing the ^{1}H NMR spectrum of poly-**3**, plots of the ICD intensities for poly-**3** vs the concentration of *N*-Ac-(L-Ala)$_3$-OMe, (L-Ala)$_3$-OMe, and (L-Ala)$_3$ and Hill plots, the computer-generated models of the complexes of poly-**2** and poly-**3** with *N*-Ac-(L-Ala)$_3$-OMe, changes of the N−H protons resonances of poly-**3** with an increasing amount of *N*-Ac-(L-Ala)$_3$-OMe in H_2O/D_2O (9/1, v/v), the pH dependence of ICD in the complexation with (L-Ala)$_3$ and *N*-Ac-(L-Ala)$_3$-OMe, and the dependence of the ICD intensity on NaCl concentration for the poly-**3**−*N*-Ac-(L-Ala)$_3$-OMe complex, and CD and absorption spectral changes of poly-**3**−*N*-Ac-(L-Ala)$_3$-OMe in water upon the addition of methanol. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Schulz, G. E.; Schirmer, R. H. *Principles of Protein Structure*; Springer-Verlag: New York, 1979; Chapter 5. (b) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984; Chapter 6.

(2) For recent reviews: (a) Archer, E. A.; Gong, H.; Krische, M. J. *Tetrahedron* **2001**, *57*, 1139−1159. (b) Prins, L. J.; Reinhoudt, D. N.; Timmerman, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 2383−2426. (c) Brunsveld, L.; Folmer, B. J. B.; Meijer, E. W.; Sijbesma, R. P. *Chem. Rev.* **2001**, *101*, 4071−4097. (d) Zimmerman, S. C.; Lawless, L. J. *Top. Curr. Chem.* **2001**, *217*, 95−120. (e) Sijbesma, R. P.; Meijer, E. W. *Chem. Commun.* **2003**, 5−16.

(3) Ariga, K.; Kunitake, T. *Acc. Chem. Res.* **1998**, *31*, 371−378.

(4) Nowick, J. S.; Chen, J. S. *J. Am. Chem. Soc.* **1992**, *114*, 1107−1108.

(5) Kato, Y.; Conn, M. M.; Rebek, J. *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 1208−1212.

(6) Asanuma, H.; Ban, T.; Gotoh, S.; Hishiya, T.; Komiyama, M. *Macromolecules* **1998**, *31*, 371−377.

(7) Hirschberg, J.; Brunsveld, L.; Ramzi, A.; Vekemans, J.; Sijbesma, R. P.; Meijer, E. W. *Nature (London)* **2000**, *407*, 167−170.

(8) (a) Gottarelli, G.; Mezzina, E.; Spada, G. P.; Carsughi, F.; DiNicola, G.; Mariani, P.; Sabatucci, A.; Bonazzi, S. *Helv. Chim. Acta* **1996**, *79*, 220−234. (b) Baumeister, B.; Matile, S. *Chem. Commun.* **2000**, 913−914. (c) Fenniri, H.; Packiarajan, M.; Vidale, K. L.; Sherman, D. M.; Hallenga, K.; Wood, K. V.; Stowell, J. G. *J. Am. Chem. Soc.* **2001**, *123*, 3854−3855. (d) Kawasaki, T.; Tokuhiro, M.; Kimizuka, N.; Kunitake, T. *J. Am. Chem. Soc.* **2001**, *123*, 6792−6800.

(9) (a) Nomura, R.; Tabei, J.; Masuda, T. *J. Am. Chem. Soc.* **2001**, *123*, 8430−8431. (b) Tabei, J.; Nomura, R.; Sanda, F.; Masuda, T. *Macromolecules* **2003**, *36*, 8603−8608. For examples of amino acid-bound helical polyacetylenes, see: (c) Cheuk, K. K. L.; Lam, J. W. Y.; Chen, J. W.; Lai, L. M.; Tang, B. Z. *Macromolecules* **2003**, *36*, 5947−5959. (d) Zhao, H. C.; Sanda, F.; Masuda, T. *Macromolecules* **2004**, *37*, 8893−8896. (e) Lam, J. W. Y.; Tang, B. Z. *Acc. Chem. Res.* **2005**, *38*, 745−754. (f) Lai, L. M.; Lam, J. W. Y.; Tang, B. Z. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 6190−6201. (g) Zhao, H. C.; Sanda, F.; Masuda, T. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 1691−1698.

(10) Okoshi, K.; Sakurai, S.-i.; Ohsawa, S.; Kumaki, J.; Yashima, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 8173−8176.

(11) Aoki, T.; Kaneko, T.; Maruyama, N.; Sumi, A.; Takahashi, M.; Sato, T.; Teraguchi, M. *J. Am. Chem. Soc.* **2003**, *125*, 6346−6347.

(12) Cary, J. M.; Moore, J. S. *Org. Lett.* **2002**, *4*, 4663−4666.

(13) Hamuro, Y.; Geib, S. J.; Hamilton, A. D. *J. Am. Chem. Soc.* **1997**, *119*, 10587−10593.

(14) Yang, X.; Yuan, L.; Yamato, K.; Brown, A. L.; Feng, W.; Furukawa, M.; Zeng, X. C.; Gong, B. *J. Am. Chem. Soc.* **2004**, *126*, 3148−3162.

(15) Odriozola, I.; Kyritsakas, N.; Lehn, J.-M. *Chem. Commun.* **2004**, 62−63.

(16) (a) Huc, I.; Maurizot, V.; Gornitzka, H.; Léger, J.-M. *Chem. Commun.* **2002**, 578−579. (b) Gillies, E. R.; Deiss, F.; Staedel, C.; Schmitter, J.-M.; Huc, I. *Angew. Chem., Int. Ed.* **2007**, *46*, 4081−4084.

(17) Sinkeldam, R. W.; Houtem, M. H. C. J.; Pieterse, K.; Vekemans, J. A. J. M.; Meijer, E. W. *Chem.—Eur. J.* **2006**, *12*, 6129−6137.

(18) (a) Cornelissen, J.; Donners, J.; de Gelder, R.; Graswinckel, W. S.; Metselaar, G. A.; Rowan, A. E.; Sommerdijk, N.; Nolte, R. J. M. *Science* **2001**, *293*, 676−680. (b) Metselaar, G. A.; Adams, P. J. H. M.; Nolte, R. J. M.; Cornrlissen, J. J. L. M.; Rowan, A. E. *Chem.*−*Eur. J.* **2007**, *13*, 950−960.

(19) (a) Cheng, R. P.; Gellman, S. H.; DeGrado, W. F. *Chem. Rev.* **2001**, *101*, 3219−3232. (b) Seebach, D.; Kimmerlin, T.; Sebesta, R.; Campo, M. A.; Beck, A. K. *Tetrahedron* **2004**, *60*, 7455−7506.

(20) For preferred-handed helicity induction through intermolecular hydrogen bonding with saccharides in water-organic solvent mixtures, see: Waki, M.; Abe, H.; Inouye, M. *Chem.*−*Eur. J.* **2006**, *12*, 7839−7847.

(21) For preferred-handed helicity induction through hydrophobic interactions with optically active guest molecules in water, see: (a) Stone, M. T.; Moore, J. S. *Org. Lett.* **2004**, *6*, 469−472. (b) Onouchi, H.; Miyagawa, T.; Morino, K.; Yashima, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 2381−2384. (c) Miyagawa, T.; Yamamoto, M.; Muraki, R.; Onouchi, H.; Yashima, E. *J. Am. Chem. Soc.* **2007**, *129*, 3676−3682.

(22) (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) Yashima, E.; Goto, H.; Okamoto, Y. *Polym. J.* **1998**, *30*, 69−71. (d) Yashima, E.; Maeda, K.; Okamoto, Y. *Nature (London)* **1999**, *399*, 449−451. (e) Maeda, K.; Okada, S.; Yashima, E.; Okamoto, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 3180−3189. (f) Nonokawa, R.; Yashima, E. *J. Am. Chem. Soc.* **2003**, *125*, 1278−1283. (g) Maeda, K.; Morino, K.; Okamoto, Y.; Sato, T.; Yashima, E. *J. Am. Chem. Soc.* **2004**, *126*, 4329−4342. (h) Onouchi, H.; Kashiwagi, D.; Hayashi, K.; Maeda, K.; Yashima, E. *Macromolecules* **2004**, *37*, 5495−5503. (i) Kamikawa, Y.; Kato, T.; Onouchi, H.; Kashiwagi, D.; Maeda, K.; Yashima, E. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 4580−4586. (j) Onouchi, H.; Miyagawa, T.; Furuko, A.; Maeda, K.; Yashima, E. *J. Am. Chem. Soc.* **2005**, *127*, 2960−2965. (k) Miyagawa, T.; Furuko, A.; Maeda, K.; Katagiri, H.; Furusho, Y.; Yashima, E. *J. Am. Chem. Soc.* **2005**, *127*, 5018−5019. (l) Hasegawa, T.; Maeda, K.; Ishiguro, H.; Yashima, E. *Polym. J.* **2006**, *38*, 912−919. For reviews on dynamic helical polymers, see: (m) Green, M. M.; Peterson, N. C.; Sato, T.; Teramoto, A.; Cook, R.; Lifson, S. *Science* **1995**, *268*, 1860−1866. (n) Nakano, T.; Okamoto, Y. *Chem. Rev.* **2001**, *101*, 4013−4038. (o) Maeda, K.; Yashima, E. *Top. Curr. Chem.* **2006**, *265*, 47−88.

(23) (a) Saito, M. A.; Maeda, K.; Onouchi, H.; Yashima, E. *Macromolecules* **2000**, *33*, 4616−4618. (b) Maeda, K.; Goto, H.; Yashima, E. *Macromolecules* **2001**, *34*, 1160−1164. (c) Onouchi, H.; Maeda, K.; Yashima, E. *J. Am. Chem. Soc.* **2001**, *123*, 7441−7442. (d) Maeda, K.; Ishikawa, M.; Yashima, E. *J. Am. Chem. Soc.* **2004**, *126*, 15161−15166. (e) Maeda, K.; Takeyama, Y.; Sakajiri, K.; Yashima, E. *J. Am. Chem. Soc.* **2004**, *126*, 16284−16285. (f) Onouchi, H.; Hasegawa, T.; Kashiwagi, D.; Ishiguro, H.; Maeda, K.; Yashima, E. *Macromolecules* **2005**, *38*, 8625−8633. (g) Nagai, K.; Sakajiri, K.; Maeda, K.; Okoshi, K.; Sato, T.; Yashima, E. *Macromolecules* **2006**, *39*, 5371−5380.

(24) Mammen, M.; Choi, S.-K.; Whitesides, G. M. *Angew. Chem., Int. Ed.* **1998**, *37*, 2754−2794.

(25) Computer-generated molecular models of poly-**3** and poly-**2** complexed with *N*-Ac-(L-Ala)$_3$-OMe are shown in Figure S3, which support the interaction models schematically illustrated in Figure 3, parts B and C, respectively.

(26) The ICD intensities of the polymers with (L-Ala)$_3$ decreased in the order of poly-**3** > poly-**2** > poly-**1** as the case with (L-Ala)$_3$-OMe, while completely opposite with *N*-Ac-(L-Ala)$_3$-OMe. This can be explained in view of the contribution of the interaction models illustrated in Figure 3. *N*-Ac-(L-Ala)$_3$-OMe may mainly interact with the polymers through the intermolecular hydrogen bonding as illustrated in Figure 3C because of the absence of attractive ionic interactions. If this is the case, the preferred-handed helicity induction may occur more efficiently in poly-**1** and poly-**2** rather than poly-**3** because the *N*-Ac-(L-Ala)$_3$-OMe can be located at position closer to the polymer backbones of poly-**1** and poly-**2** having a smaller size of the glycine residues.

(27) The hydrogen bonding between the N-H of the pendants of polymers and the carbonyl groups of the oligopeptides and/or the dipole−dipole interaction between the carbonyl groups of the pendants of polymers and oligopeptides may also contribute to the helicity induction to some extent because apparent ICDs are observed in the presence of *N*-Ac-(L-Ala-Me)$_3$-OMe.

(28) The changes in the ^{1}H NMR spectra during the complexation of poly-**3** with *N*-Ac-(L-Ala)$_3$-OMe also support the hydrogen-bond formation. In the presence of an increasing amount of *N*-Ac-(L-Ala)$_3$-OMe, the resonance of the N-H proton of poly-**3** showed a small but significant downfield shift (0.023 ppm) (Figure S4).[4,6] Moreover, the magnitude of the ICDs in the poly-**3**−*N*-Ac-(L-Ala)$_3$-OMe and poly-**3**−(L-Ala)$_3$ complexes were influenced by the pH (Figure S5) and the salt (NaCl) concentration (Figure S6), which also supports the importance of the polar interaction rather than a hydrophobic one in the helicity induction in water.[21b] However, the ICD intensity of poly-**3** with *N*-Ac-(L-Ala)$_3$-OMe ([*N*-Ac-(L-Ala)$_3$-OMe]/[poly-**3**] = 20) in water at 0 °C gradually decreased by adding increasing volumes of methanol and almost disappeared in the presence of 75 vol % of methanol (see Figure S7), suggesting that the hydrophobic interactions between the polymers and oligopeptides likely contribute to the helicity induction in the polymers.

(29) Schenck, T. G.; Downes, J. M.; Milene, C. R. C.; Mackenzie, P. B.; Boucher, H.; Whela, J.; Bosnich, B. *Inorg. Chem.* **1985**, *24*, 2334−2337.

(30) Olsen, R. K. *J. Org. Chem.* **1970**, *35*, 1912−1915.

(31) (a) Simionescu, C. I.; Percec, V.; Dumitrescu, S. *J. Polym. Sci.: Polym. Chem. Ed.* **1977**, *15*, 2497−2509. (b) Furlani, A.; Napoletano, C.; Russo, M. V.; Feast, W. J. *Polym. Bull. (Berlin)* **1986**, *16*, 311−317. (c) Matsunami, S.; Kakuchi, T.; Ishii, F. *Macromolecules* **1997**, *30*, 1074−1078. (d) Kishimoto, Y.; Eckerle, P.; Miyatake, T.; Kainosho, M.; Ono, A.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1999**, *121*, 12035−12044. (e) Percec, V.; Rudick, J. G.; Peterca, M.; Wagner, M.; Obata, M.; Mitchell, C. M.; Cho, W.-D.; Balagurusamy, V. S. K.; Heiney, P. A. *J. Am. Chem. Soc.* **2005**, *127*, 15257−15264. (f) Morino, K.; Asari, T.; Maeda, K.; Yashima, E. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 4711−4722.

(32) Connors, K. A. *Binding Constants*; John Wiley: New York, 1987.

(33) (a) Plateau, P.; Guéron, M. *J. Am. Chem. Soc.* **1982**, *104*, 7310−7311. (b) Hore, P. J. *J. Magn. Reson.* **1983**, *55*, 283−300.

(34) (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.

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