Helix−Helix Transition of Optically Active Poly((1*R*,2*S*)-*N*-(4-ethynylbenzyl)norephedrine) Induced by Diastereomeric Acid−Base Complexation Using Chiral Stimuli

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Recently, much attention has been paid to controlling the helix-sense of macromolecules.[1] Helical structures are often observed in biopolymers and appear to play a dominant role in living systems as exemplified by proteins[2] and DNA[3] which adopt a right-handed α-helix and a double-helix, respectively. However, as seen in artificial polypeptides[4] and polynucleotides[5] with specific sequences, the right-handed helical structures are not universal and can be transformed into a left-handed helix, regulated by external, achiral stimuli such as pH, solvent, temperature, light, and salt concentration. Fully synthetic optically active polymers such as poly[(*S*)-diphenyl(1-methyl-pyrrolidin-2-yl)methyl methacrylate][6] and polyisocyanates bearing a photoresponsive azobenzene residue[7] also undergo a helix−helix transition in solution by the addition of an achiral acid or by irradiation of light, respectively.

We report here a unique helix−helix transition of optically active poly[(1*R*,2*S*)-*N*-(4-ethynylbenzyl)norephedrine] (poly-**1**) (Chart 1) induced by diastereomeric complexation with chiral acids. Poly-**1** is an optically active polymer with a complete cis−transoidal, regular structure[8] and exhibits an induced circular dichroism (ICD) in the UV−visible region in solution (Figure 1a) probably due to a predominantly one-handed helical conformation of the polymer.[9] The ICD is similar in pattern to those

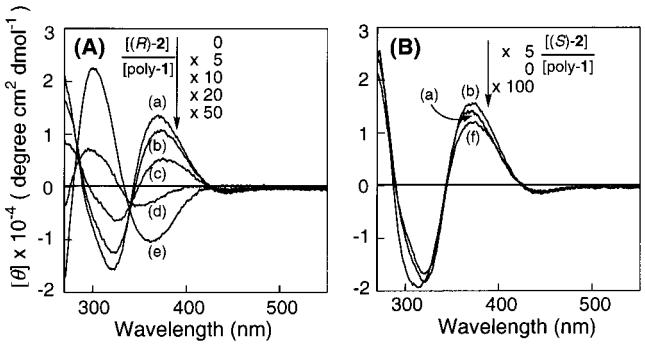
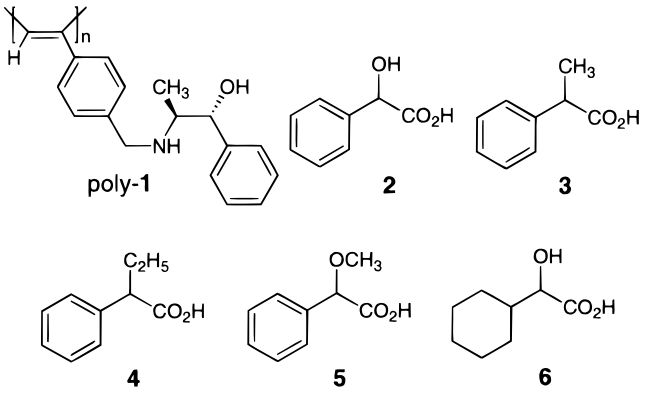


Figure 1. CD spectral changes of poly-**1** with (*R*)-**2** (A) and (*S*)-**2** (B) in DMSO; the molar ratio of **2** to monomer units of poly-**1** is 0 (a), 5 (b), 10 (c), 20 (d), 50 (e), and 100 (f). The CD spectra were measured in DMSO solutions in a 0.05-cm quartz cell at ambient temperature (*ca*, 20−22 °C) with a poly-**1** concentration of 1.0 mg (3.9 mmol monomer units)/mL.

Chart 1



of the acid−base complexes of the cis−transoidal poly((4-carboxyphenyl)acetylene) with optically active amines[10] and poly(phenylacetylenes) bearing a chiral substituent at the para position.[9,11] However, the poly-**1** undergoes a transition from one helix to another in the presence of chiral acids with an *R* configuration, which induces a dramatic change in the ICD of poly-**1**.

Figure 1 shows the drastic changes in the ICD of poly-**1** in the presence of (*R*)- or (*S*)-mandelic acid (**2**) in dimethyl sulfoxide (DMSO). The ICD significantly changed with an increase in the concentration of (*R*)-**2**; the CD intensities at ca. 370 nm decreased, and the signs inverted with isosbestic-like points to give an almost mirror image at [**2**]/[poly-**1**] = 50 (e in Figure 1A).[13] These significant changes in the ICDs were accompanied by only minor changes in the UV−visible absorption spectra; a peak around 400

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(8) Poly-**1** was obtained by the polymerization of (1*R*,2*S*)-*N*-(4-ethynylbenzyl)norephedrine with $[Rh(nbd)Cl]_2$ (nbd = norbornadiene) in THF at 30 °C. The resulting yellow polymer was soluble in dimethyl sulfoxide (DMSO) and chloroform. The molecular weight (M_n) of poly-**1** was estimated to be 4.8×10^4 as determined by gel permeation chromatography (GPC) using DMSO as the eluent. The ^1H NMR spectrum of poly-**1** in $CDCl_3$ showed a sharp singlet centered at 5.87 ppm, due to the main chain proton, indicating that the polymer possesses a highly cis−transoidal, stereoregular structure.

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(11) There exist at least three Cotton effects with the exciton-type splittings[12] in the ICD. However, the assignments of the Cotton effects and the relationship with the helix-sense of poly-**1** are not clear at present.

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(13) The right- and left-handed helices of pure poly-**1** and the (*R*)-**2**-poly-**1** complex (50/1) are not exactly enantiomers. They are diastereomers because of the presence of chiral norephedrine residues of poly-**1** and (*R*)-**2**; therefore, their CD spectra slightly differ from one another, and a set of CD curves did not cross at the tight isosbestic points ([θ] = 0). Moreover, the differences in the ICD patterns indicate that both helices may have a helical conformation with a different pitch.

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nm in the UV−visible spectrum of poly-**1** slightly shifted to a longer wavelength by ca. 5 nm in the presence of 50-fold **2**. On the other hand, the ICD of poly-**1** hardly changed even in the presence of excess (*S*)-**2** (Figure 1B).[14] Thus, mandelic acid can be used to regulate the helicity of poly-**1**.

In DMSO, the CD spectrum of poly-**1** hardly changed even in the presence of 50-fold chiral carboxylic acids such as (*R*)- or (*S*)-1-phenylpropionic acid (**3**). The hydroxy group of mandelic acid may participate in the intermolecular hydrogen bonding with the amino or hydroxy group of poly-**1** together with the acid−base ion pairing of the carboxy group. These cooperative interactions probably enhance the complexation between poly-**1** and mandelic acid in DMSO to induce a dramatic change in the ICD of poly-**1**.[10]

In chloroform, however, poly-**1** can efficiently respond to chiral carboxylic acids having an *R* configuration, such as **3**−**5**, and a hydroxy acid (**6**) (Chart 1) and exhibits a helix−helix transition upon complexation with a relatively small amount of the carboxylic acids; an equimolar amount of the (*R*)-carboxylic acids to poly-**1** is enough for an almost complete helix−helix transition in chloroform.[15] Typical changes in the ICD of poly-**1** in the presence of (*R*)- or (*S*)-**4** are shown in Figure 2 (see the Supporting Information). Similarly, (*R*)-**3**, (*R*)-**5**, and (*R*)-**6** brought about a helix−helix transition of poly-**1**, whereas the corresponding (*S*)-isomers did not cause such a dramatic conformational change. These results suggest that the helix−helix transition behaviors may be applicable to predict the absolute configuration of chiral acids. Only acids with an *R* configuration may give rise to a helix−helix transition of poly-**1**.

The mechanism of the interaction of poly-**1** with chiral acids and the reasons why only (*R*)-acids bring about the helix−helix transition of poly-**1** are not clear at present, but they may be correlated with the binding affinity of the enantiomeric acids to poly-**1**. The binding constants of the (*R*)- and (*S*)-**3** to poly-**1** and the conformational change of poly-**1** during the complexation with an increasing amount of the enantiomeric acids were investigated using ^{1}H NMR titration experiments. However, the differences between the complexation-induced shifts of poly-**1** with (*R*)- and (*S*)-**3** in $CDCl_3$ were very small, and the peaks of poly-**1** were quite broadened although the ^{1}H NMR spectra of the complexes in $CDCl_3$ are not exactly the same and there are some differences in their chemical shifts and the half-line width ($\Delta\nu_{1/2}$). The ^{1}H NMR spectrum of the poly-**1**-(±)-**3** complex (1:1) showed no signal splittings due to the enantiomers of **3**. Moreover, during the complexations of poly-**1** with nonracemic **2** and **3** (enantiomeric excess = 20, 40, 60, and 80%) in DMSO and chloroform, respectively, the complexes displayed a linear relationship between the ee of the acids and the observed ellipticity of the Cotton effects (see Figure 3 in the Supporting Information). The excess enantiomer bound to the polymer may not induce a global conformational change of poly-**1**. This linear relationship between the ee of the chiral acids and the intensity of the Cotton effects is completely different from the previously observed positive nonlinear relationship between the ee of chiral amines and the observed ellipticity of the Cotton effects in the helix formation of an optically inactive poly((4-carboxyphenyl)acetylene) in the presence of chiral amines.[10b] These results indicate that the poly-**1** may have a similar affinity to the (*R*)- and (*S*)-acids. The complexation with the (*S*)-acids may have no influence, or it may stabilize the original helical structure of poly-**1**; the complexation with the (*R*)-acids may destabilize the structure to induce the conformational change to an opposite helical structure (substrate-induced organization of the binding site, that is, *induced fit*).[18] Further experiments including low-temperature NMR measurements and computer modeling of the complexes are required.

We conclude that an optically active polyacetylene, poly-**1**, exhibits a helix−helix transition upon complexation with chiral acids and that its transition is sensitive to the chirality of the acids. We expect that related optically active polyacetylenes bearing other functional groups such as a carboxy group or a boronic acid residue[19] will also respond, for example, to chiral amines or sugars, respectively, showing a characteristic helix−helix transition depending on the chirality of the molecules. This work is now in progress.

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Supporting Information Available: Experimental procedures and CD spectral changes of the complexes of poly-**1** with **4** and nonracemic **3** in chloroform (4 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(14) The CD spectra of the (*R*)-**2**- and (*S*)-**2**-poly-**1** complexes in Figure 1 ([**2**]/[poly-**1**] = 50 (e) and 100 (f), respectively) did not change after the samples had been allowed to stand for one month at room temperature.

(15) In polar DMSO (the dielectric constant $\epsilon_r = 46.45$), ion association between poly-**1** and carboxylic acids is weak, and a hydrogen bonded ion-pair is predominant.[16a] A large excess of acid may be necessary to bring about the helix−helix transition of poly-**1**, while in less polar chloroform ($\epsilon_r = 4.8$), ion association might be strong enough[17] to give rise to the helix−helix transition with a small amount of acid. Because of the poor solubility of mandelic acid in chloroform, we could not follow the changes in the CD spectra of poly-**1** with mandelic acid. However, the complex of poly-**1** with (*R*)-mandelic acid saturated in chloroform exhibited a helix−helix transition.

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