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Helical Folding of Poly(naphthalenecarboxamide) Prompted by Solvophobic Effect

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Much attention has been paid to controlling the helical structure of polymers, oligomers, and supramolecules by utilizing solvophobic effect, hydrogen bonding, and other noncovalent interactions[1] because the one-handed helical conformations of biological macromolecules, such as DNA and proteins, which are stabilized by these interactions, are crucial for molecular recognition and information storage.[2] For instance, oligo(*m*-phenylene ethynylene)s with oligo(ethylene glycol) side chains recognize chiral small molecules on the basis of a folded helical structure induced by a solvophobic effect; in polar solvents, the polar side chain of the oligomers is solvated, but the hydrophobic main chain is intramolecularly self-associated.[3] This amphiphilic type of heterogeneity is crucial for induction of helical folded structure. On the other hand, helical poly(phenylacetylene) bearing an alanine residue with a long alkyl chain adopts a helical structure stabilized by hydrogen bonding.[4] Furthermore, hydrogen-bond-assisted helical folded structures of aromatic oligoamides have been reported.[5] However, solvophobic effect-induced helical folding of aromatic oligoamide and polyamide has not been reported yet.

We have demonstrated that poly(*p*-benzamide)s with a chiral tri(ethylene glycol) side chain adopt a thermodynamically controlled one-handed helical conformation in solution.[6] The helical structure was confirmed by X-ray crystallographic analysis of oligo(*N*-methyl-*p*-benzamide)s, which adopt a helical conformation with three monomer units per turn in the crystal, and by exciton model analysis of the CD spectra induced by the secondary structure of the polyamide. As for the effect of solvents, we have shown that the polyamide adopts the helical conformation in common organic solvents, such as chloroform, acetonitrile, and methanol, and clear solvent dependency has not been observed. However, the effects of more polar solvents, such as mixtures of water and methanol, have not been clarified. On the other hand, the CD spectra of poly(*m*-benzamide)s having chiral side chains suggest that these meta-type polyamides adopt different conformations in water from those in organic solvents,[7] but unambiguous evidence for the helical structure of the polyamides has not been obtained due to the difficulties of exciton model analysis of the CD spectra.

Azumaya and co-workers reported that the self-condensation reaction of 6-allylamino-2-naphthoic acid readily afforded a cyclic trimer.[8] Inspired by this work, we anticipated that N-substituted poly(2,6-naphthalenecarboxamide)s would adopt a helical conformation.[9] Since the naphthalene ring is more hydrophobic than the benzene ring, the helical folding of the naphthalene polyamide is expected to be prompted by the solvophobic effect more efficiently than in the case of N-substituted poly(*p*-benzamide)s. Furthermore, we expected that it would be easy to identify the helical structure by measuring CD spectra because the direction of the electric transition dipole moments of 6-acylamino-2-naphthalenecarboxamide derivatives is thought to be similar to that of 6-methoxy-2-naphthoic acid esters, which have used as CD chromophores for the exciton chirality method.[10] In this Communication, we report the folding of poly(naphthalenecarboxamide)s bearing a chiral side chain in solution and the effects of temperature and solvent on the folded structure. The UV and CD spectra in solution indicated that the polyamide preferentially adopts a one-handed helical conformation. The CD spectra in water−methanol mixed solvents indicated that, whereas the helical conformation of poly(*p*-benzamide) with the same side chain remains unchanged as the water ratio is increased, the folding of the naphthalene polyamide is enhanced by the solvophobic effect.

We attempted to synthesize poly(naphthalenecarboxamide) having a chiral tri(ethylene glycol) side chain using a similar approach to that reported for the synthesis of poly(*N*-alkyl-*p*-benzamide)s[11] by the polymerization of the phenyl ester monomer **1** with 1.0 equiv of LiHMDS in the presence of 10.5 mol % of initiator **2** in THF at −30 °C (Scheme 1). However, unreacted **1** remained in the reaction mixture even after polymerization for 6 h. Although the polymerization at higher temperature (−20 °C) for 20 h also resulted in incomplete consumption of **1**, we isolated poly$\mathbf{1}_l$ (M_n = 3150, M_w/M_n = 1.14) by preparative HPLC purification of the crude product. We thought that the incomplete conversion of the monomer might have arisen from deactivation of LiHMDS by water which could not be removed from the monomer by usual vacuum drying due to the hydrophilic nature of the side chain. Therefore, monomer **1** was dried azeotropically from toluene and used for the polymerization with a higher feed ratio ($[\mathbf{1}]_0/[\mathbf{2}]_0$ = 24) at −30 °C. In this case, the polymerization proceeded with almost complete conversion of **1**, and preparative HPLC purification gave poly$\mathbf{1}_h$ with M_n = 6070 and M_w/M_n = 1.09.

The secondary structure of the isolated poly**1** was investigated by means of UV and CD spectroscopy in chloroform, THF, and methanol (Figure 1a). The UV spectra of poly$\mathbf{1}_h$ showed a blue shift compared to naphthalene due to the amide linkages at the 2- and 6-positions, and a shoulder appeared at 260−280 nm.[12] Although the monomer **1** was almost CD-silent (Figure S1), the polyamide exhibited large CD signals induced by the backbone chromophore at 200−360 nm, and the intensity increased with decrease of the temperature (Figure 1b and Figure S2). These results indicate that the induced CD arises from a temperature-dependent chiral conformation of the polyamide. The CD spectra showed a plus-to-minus pattern, viewed from longer wavelength, at 220−300 nm, arising from transition along the long axis of the naphthalene ring.[12] According to exciton model analysis of N-substituted poly(*p*-benzamide),[6] the naphthalene polyamide is thought to prefer a right-handed helical conformation in these solvents. On the other hand, the CD signals of poly$\mathbf{1}_h$ at 300−360 nm depended on the nature of the organic solvent: the CD sign of the polyamide in THF changed from minus to plus, viewed from longer wavelength, but positive CD signals were observed in chloroform and methanol (Figure 1a). Because the CD signals at the longer wavelength region arise from transition

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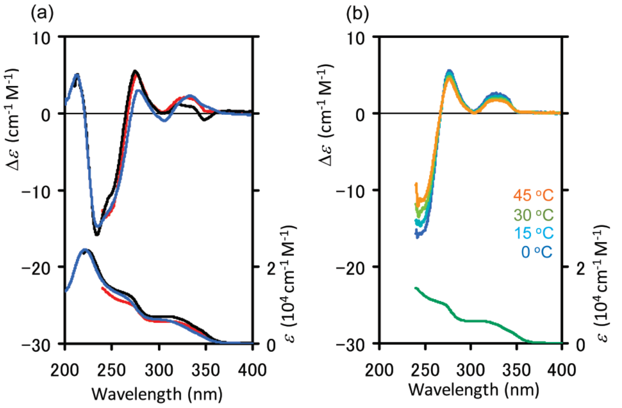
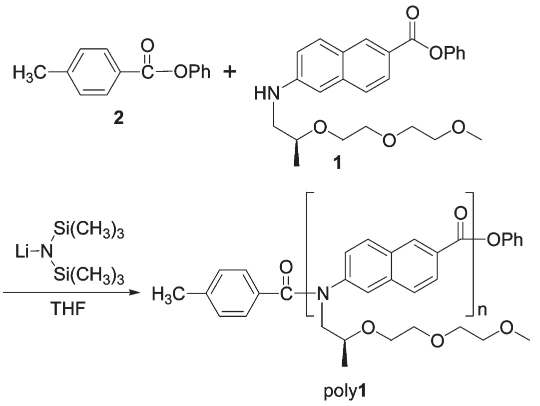


Figure 1. (a) UV and CD spectra of poly$\mathbf{1}_h$ in chloroform (red line), THF (black line), and methanol (blue line) at 25 °C. (b) UV spectra at 25 °C and temperature-dependent CD spectra of poly$\mathbf{1}_h$ in chloroform.

Scheme 1



along the short axis of the naphthalene ring,[12] this CD behavior can be attributed to solvent-dependent change of the *syn−anti* ratio of two successive naphthalene rings in poly$\mathbf{1}_h$.[8] The polyamide with lower molecular weight, poly$\mathbf{1}_l$, exhibited similarly shaped CD spectra, but the intensity was lower compared to that of poly$\mathbf{1}_h$ (Figure S3). Molecular-weight-dependent CD intensity is often observed in helical polymers.[13] In methanol, the molecular weight dependence of the CD spectra appeared not only in the intensity but also in the shape and sign at 280−360 nm (Figure S3c).

To compare the effects of polar solvents on the helical conformation of poly**1** and poly(*p*-benzamide) **3** bearing the same side chain, the UV and CD spectra of these polymers in a mixture of water and methanol with various ratios of water were examined (Figure 2). As the ratio of water was increased, the UV spectra of poly**1** did not change up to 60% water ratio, but the absorbance was slightly decreased at 70% water−methanol.[14] On the other hand, the intensity of the CD signal was dramatically increased with increasing ratio of water and reached a maximum at 50−60% water−methanol (Figure 2a). This result indicates that the helical folding of poly**1** was prompted by the increase of water ratio due to a solvophobic effect, as we had expected. However, further increase of water ratio to 70% resulted in a decrease of the CD intensity. The possibility of aggregation or partial insolubilization of poly$\mathbf{1}_h$ in 70% water−methanol can be ruled out because almost the same CD spectra were observed irrespective of the concentration of poly**1** in 70% water−methanol (Figure S4). The reason for the decrease of the UV absorption and CD intensity at 70% water−methanol was unclear at this point. On the other hand, the CD intensity of **3** in the aqueous solvent increased with increasing water ratio up to 20%, but further increase of the water content did not increase the CD intensity, indicating that the increase of water ratio from 20% to 80% did not cause the change of helical conformation of **3** (Figure 2b). The different behavior between poly**1** and **3** also supports the enhancement of helical folding of the naphthalene polyamide owing to a solvophobic effect: the hydrophobicity of the naphthalene ring of poly**1** is enough to cause intramolecular self-association of the main chain in polar solvents, but the hydrophobicity of the benzene ring of **3** is insufficient to cause this.

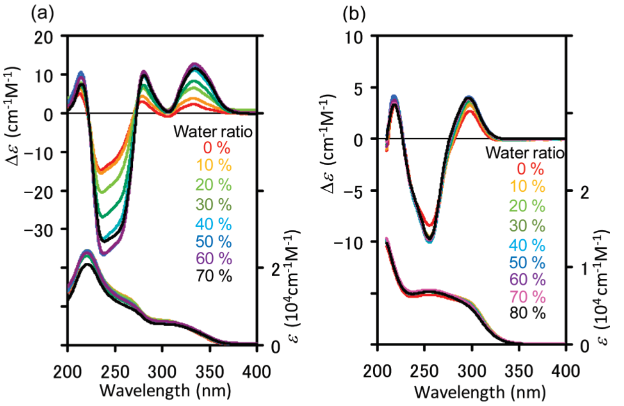


Figure 2. CD spectra of (a) poly$\mathbf{1}_h$ and (b) **3** in methanol−water of various ratios at 25 °C.

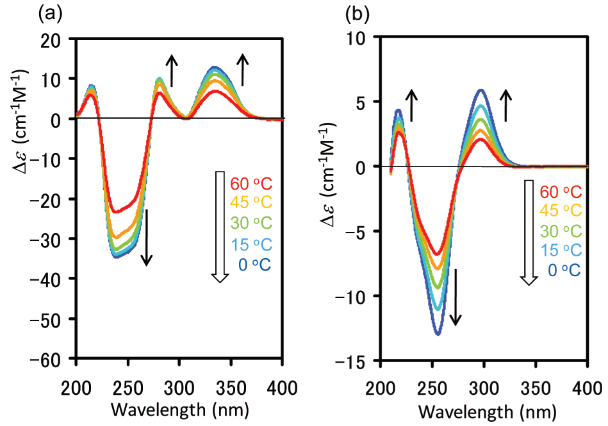
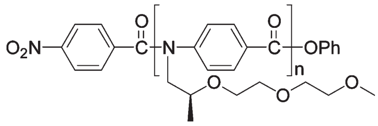


Figure 3. Temperature-dependent CD spectra of (a) poly$\mathbf{1}_h$ and (b) **3** in water/methanol = 70/30.



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We next investigated the effect of temperature on the helical conformation in aqueous solvent. Temperature-dependent CD spectra of poly$\mathbf{1}_h$ (Figure 3a) and **3** (Figure 3b) in 70% water−methanol showed that the CD intensities of these polyamides increased with decreasing temperature from 60 to 15 °C, as in the case in organic solvents, indicating that the folding of the polyamides into the right-handed helical conformation was enhanced with lowering of the temperature. However, contrary to the case of the poly(*p*-benzamide), the CD spectra of the poly(naphthalenecarboxamide) at 0−15 °C were independent of temperature. A possible explanation of this is that the strong solvophobic effect exerted in 70% water−methanol at 0−15 °C causes complete folding of the naphthalene polyamide.

In conclusion, we synthesized poly(naphthalenecarboxamide)s with a chiral tri(ethylene glycol) side chain and examined their secondary structure in solution. According to exciton model analysis, the UV and CD spectra indicated that poly(naphthalenecarboxamide)s with the chiral tri(ethylene glycol) side chain adopted a thermodynamically controlled right-handed helical conformation in organic solvents. In contrast to N-substituted poly(*p*-benzamide), the folding of the naphthalene polyamide was enhanced by a solvophobic effect and seemed to be completed at 0−15 °C in 70% water−methanol. Further investigation of the folded helical structure of the naphthalene polyamide is in progress.

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Supporting Information Available: Text and schemes dealing with synthesis and polymerization of the monomer and figures showing GPC profiles, UV, CD, and NMR spectra of **1** and poly**1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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