# Communications to the Editor

## Solvent and Temperature Effect on Chiral Conformation of Poly(*m*-benzamide)s

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Helical structures of artificial polymers[1] or oligomers[2] have attracted much attention from chemists in recent years. In particular, several helical structures consisting of *meta*-substituted aromatic rings as a framework, in which helical conformation is induced and stabilized by various interactions, have been reported. For example, oligo(*meta*-phenylene ethynylene)s show a dynamic folded conformation in polar solvents owing to a solvophobic interaction.[3] Helical structures of *meta*-directed aromatic oligoamides folded by hydrogen bonds between the amide linkages and the substituents on the aromatic rings have also been reported.[4,5] In those helical structures, the aromatic rings lie almost perpendicular to the helical axis and serve as planar bending sites.

We have previously reported that the oligomers and polymers of *N*-alkyl-*p*-benzamide show a helical conformation.[6] X-ray crystallographic analysis demonstrated that *N*-methylated oligo(*p*-benzamide)s adopt a helical conformation with three monomer units per turn in the crystal. The *N*-alkylamide bonds in the helical structure are in the cis conformation and are not coplanar with the aromatic rings, while the three consecutive aromatic rings are arranged in a syn conformation. Further, exciton model analysis of the absorption and circular dichroism (CD) spectra of poly(*p*-benzamide)s with a chiral oligo(ethylene glycol) side chain as the *N*-alkyl group revealed a one-handed helical structure in solution, showing temperature- and chain-length-dependent CD signals. On the other hand, Azumaya et al. have reported that all the amide bonds of *para*- and *meta*-substituted *N*,*N*′-dimethyl-*N*,*N*′-diphenylbenzenedicarboxamides adopt the cis conformation, but the arrangement of the benzene units of the *meta* isomer is different from that of the *para* isomer in the crystal.[7] That is, the three benzene rings of the *para* isomer adopt an anti conformation, while those of the *meta* isomer adopt a syn conformation. Therefore, we were interested in the conformations of *N*-alkylated poly(*m*-benzamide)s, which are expected to be different from those of the *para*-substituted polyamides. In the present study, we synthesized poly(*m*-benzamide)s bearing hydrophobic or hydrophilic chiral side chains and examined the solvent and temperature effects by measuring the CD spectra in solution. The results indicated that *N*-alkyl poly(*m*-benzamide)s adopt chiral conformations with thermodynamic control.

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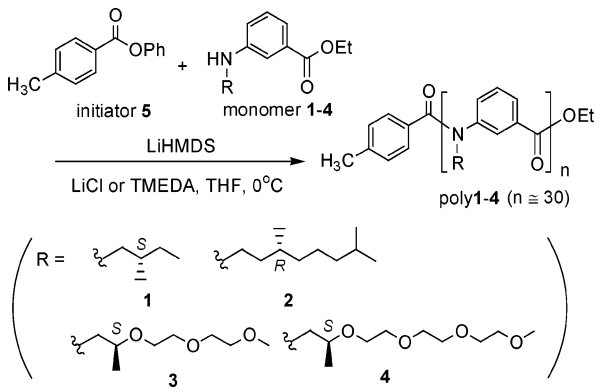
**Scheme 1. Synthesis of Poly1−4**




*N*-Alkylated poly(*m*-benzamide)s with well-defined molecular weights and low polydispersities were synthesized by means of the chain-growth polycondensation method reported recently by us.[8] We designed the monomers **1**−**4** in order to examine the influence of *N*-alkyl side chains on the conformation of poly(*m*-benzamide)s. The monomers **1** and **2** have chiral hydrophobic alkyl groups with an asymmetric carbon at the $\beta$- and $\gamma$-position from the nitrogen atom, respectively. These monomers were expected to reveal the effect of the position of the asymmetric carbon on the conformation of the polyamide. The monomers **3** and **4** possess hydrophilic chiral oligo(ethylene glycol) side chains, and the asymmetric carbons exist at the $\beta$-position. The polymerization was carried out in the presence of the initiator **5** in THF at 0 °C using lithium hexamethyldisilazide (LiHMDS) as a base (Scheme 1). We used lithium chloride (LiCl)[9] or *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA)[10] as an additive. LiCl was used to stabilize the nucleophilic aminyl anion formed by the deprotonation of **1** and **2** with the base. Polymerization of **1** and **2** in the absence of LiCl resulted in self-polycondensation of the monomers as well as chain-growth polymerization from the initiator. On the other hand, the polymerization of **3** and **4** with the oligo(ethylene glycol) side chain in the absence of the additives proceeded slowly and did not go to completion. We speculate that low reactivity of the deprotonated **3** and **4** can be attributed to coordination of the oxygen atom of the oligo(ethylene glycol) unit to the Li cation. When the polymerization was carried out in the presence of TMEDA, which can coordinate the Li cation, the polymerization proceeded in a chain-growth polymerization manner. We used 3.3 mol % of the initiator **5** in order to obtain the polyamide with the degree of polymerization (DP) of 30 because the CD intensities of poly(*p*-benzamide)s showed DP dependence and reached saturation when the DP was more than 30. The results of the polymerization are summarized in Table 1. Poly**1**−**4** with narrow polydispersities ($M_w/M_n$ = 1.05−1.07) and controlled molecular weights (DP ≈ 30) were obtained. The DPs were estimated by using the $M_n$ values determined from the $^1$H NMR spectra rather than by GPC analysis because the $M_n$ values determined from the $^1$H NMR spectra of poly(*p*-benzamide)s with the oligo(ethylene glycol) side chain were similar to those

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**Table 1. Polymerization of 1−4 with 5**[a]

| polymer | additive | $M_n$ GPC[b] | $M_n$ NMR[c] | DP[c,d] | $M_w/M_n$[b] |
|---|---|---|---|---|---|
| poly**1** | LiCl | 6200 | 6100 | 32 | 1.05 |
| poly**2** | LiCl | 7200 | 8000 | 30 | 1.07 |
| poly**3** | TMEDA | 6300 | 9200 | 33 | 1.06 |
| poly**4** | TMEDA | 6300 | 9400 | 29 | 1.06 |

[a] The polymerization of **1**−**4** was carried out with 3.3 mol % of **5** in the presence of 1.1 equiv of LiHMDS and 5 equiv of the additive in THF at 0 °C ([**1**−**4**]$_0$ = 0.2−0.3 M). [b] Determined by GPC based on polystyrene standards (eluent: THF). [c] Estimated by $^1$H NMR. [d] Degree of polymerization.

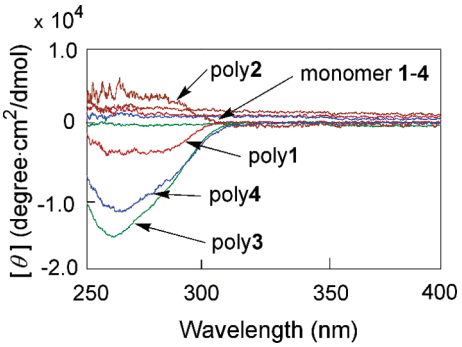


**Figure 1.** CD spectra of **1** and poly**1** (red line), **2** and poly**2** (brown line), **3** and poly**3** (green line), and **4** and poly**4** (blue line) in $CH_3OH$ at 25 °C.

determined by multiangle laser light scattering (MALLS), but GPC analysis gave smaller $M_n$ values than MALLS.[6]

Figure 1 shows CD spectra of the monomers **1**−**4** and poly**1**−**4** at 25 °C in methanol ($CH_3OH$), and those in chloroform ($CHCl_3$) are shown in Figure S2A in the Supporting Information. All the polyamides exhibited characteristic CD signals in these organic solvents, whereas the corresponding monomers showed no remarkable Cotton effect. Thus, the CD spectra of poly**1**−**4** appear to be derived not from the intrinsic chirality of the monomer unit, but from the chiral conformation of the main chain. The Cotton effect in the CD spectra of these polymers in $CHCl_3$ was similar to that in $CH_3OH$, and there was no significant solvent dependence of the chiral conformation of the polyamides. The CD signal of poly**1** was more intense than that of poly**2**, but had opposite sign. Considering the opposite configurations of the asymmetric carbons, the conformation of poly**1** is considered to be similar to that of poly**2**, and the polymer in which asymmetric carbon is closer to the nitrogen atom shows the stronger CD intensity. Therefore, the thermal stability of the conformation would depend on the distance between the nitrogen atom and the chiral carbon, as shown in CD studies of poly(propiolic ester)s[11] and poly(3,4-dialkoxythiophene)s.[12] On the other hand, the distance between the polymer main chain and the chiral carbon of **1**, **3**, and **4** is the same, but the relative spatial positions of the substituents at the asymmetric carbon in **3** and **4** are opposite to that in **1** despite the same configuration based on the CIP system. However, the sign of the CD signals derived from poly**3** and poly**4** was the same as that in the case of poly**1**, and the intensities of the CD signals of poly**3** and poly**4** with hydrophilic side chains were larger than those of poly**1** and poly**2** with hydrophobic side chains. These results indicate that the conformation of poly**3** and poly**4** is different from that of poly**1**. It is noteworthy that the sign of the CD signal of poly**3** at 250−320 nm in these solvents is minus, but the *para* counterpart showed a plus-to-minus pattern (viewed from longer wavelength) at the same region.

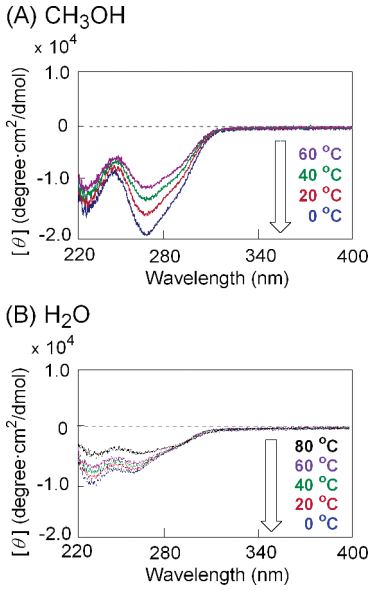


**Figure 2.** CD spectra of poly**4** in (A) $CH_3OH$ and (B) $H_2O$ at 0 °C (blue line), 20 °C (red line), 40 °C (green line), 60 °C (violet line), and 80 °C (black line).

Figures 2A and S2B show the temperature dependence of the CD spectra of $CH_3OH$ and $CHCl_3$ solutions of poly**4**, respectively, which showed the highest solubility and intense CD signal among poly**1**−**4**. The intensities of the CD signals of poly**4** depended on temperature and decreased with increasing temperature. The shapes of the CD spectra, however, did not change. Therefore, the chiral conformation of poly**4** is thermodynamically controlled and would become disordered gradually at higher temperature, as in the case of the *para* counterpart.[6]

Poly**3** was sparingly soluble in water, but poly**4** was highly soluble. A CD study of the aqueous solution of poly**4** was also carried out at various temperatures (Figure 2B). These CD spectra showed a Cotton effect, and exhibited temperature dependence, as in the cases of $CH_3OH$ and $CHCl_3$ solution. Further, the CD spectra of the aqueous solution showed the same sign as that in $CH_3OH$ or in $CHCl_3$, but the signal pattern differed between the solutions in water and in organic solvents. This result suggests that poly**4** adopts a different conformation in water from that in organic solvents. We consider that such a conformational change might be driven by solvophobic interaction, as in the case of oligo(*m*-phenylene ethynylene)s,[3] but the aggregation[13] of the polyamide in water cannot be ruled out.

A CPK model study of 3-(methylamino)benzoic acid pentamer, which was used as a model compound of the polymers, indicated possible chiral conformations of *N*-alkyl poly(*m*-benzamide)s. Because *N*-alkylated aromatic amide bonds prefer the cis conformation,[7] the structure of *N*-alkyl poly(*m*-benzamide)s depends on the dihedral angles between the amide linkages and benzene units. The anti arrangement[7] of the consecutive three benzene rings leads to two kinds of structures. When the amide bonds connect the two benzene units so that the carbons at the 2-position of the two 3-(alkylamino)benzoyl units are oriented in the opposite direction relative to the amide plane, the polymers adopt a helical conformation, as shown in Figure S3 in the Supporting Information. The same orientation of the carbons at the 2-position results in a zigzag structure (Figure S4), in which the amide bonds are located on the same side (viewed from the benzene units). In the zigzag conformation shown in Figure S4, for example, the carbons at the 2-position of the 3-(alkylamino)benzoyl units, as well as the amide linkages, are located to the front side of the paper, whereas the

carbons at the 2-position of the central benzene unit in the helical conformation in Figure S3 are directed behind the plane of the paper. On the other hand, the syn arrangement of the benzene rings and the cis conformation of the amide bonds lead to a crowded structure, resulting in limited rotational flexibility between the benzene units and the amide moieties, though a helical conformation is possible (Figure S5). It seems that the *N*-alkyl poly(*m*-benzamide)s would adopt these conformations dependently upon the conditions and *N*-alkyl side chains.

In conclusion, we have synthesized poly(*m*-benzamide)s, bearing either a hydrophobic or a hydrophilic chiral *N*-alkyl group, with well-defined polydispersities and controlled molecular weights by means of chain-growth polycondensation. The strong CD intensities of the polyamides compared with the corresponding monomers show that all the polymers adopt chiral conformations, and the temperature dependence of the CD spectra indicates thermodynamic control of the conformation. In addition, the CD spectra of poly**4** in water and organic solvents suggest that the conformation of poly**4** in water is different from that in organic solvents. Studies to determine the conformation of *N*-alkyl poly(*m*-benzamide)s are in progress.

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**Supporting Information Available:** Synthesis and polymerization of the monomers, UV and CD spectra measured in $CHCl_3$, $CH_3OH$, and $H_2O$, and stereoviews of the proposed structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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