

## An Unprecedented Memory of Macromolecular Helicity Induced in an Achiral Polyisocyanide in Water

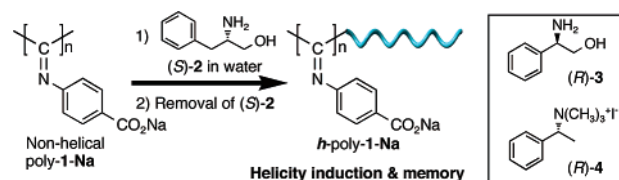
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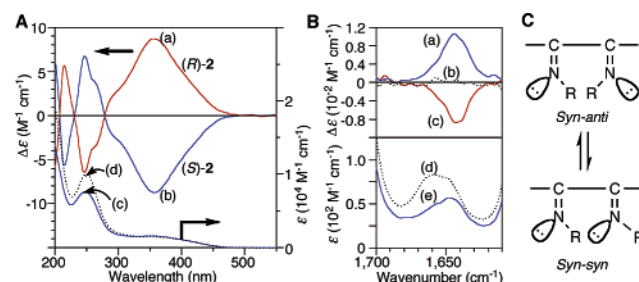
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The helix is an essential structural motif for biological macromolecules such as DNA and proteins, which further self-assemble into supramolecular structures, responsible for their sophisticated functions involving molecular recognition, self-replication, and catalytic activity.<sup>1</sup> Hence, the design and synthesis of artificial helical polymers and supramolecular polymers has become an attractive challenge with implications for biological helicity, superstructures, and functions.<sup>2</sup> In earlier studies, we reported that macromolecular helicity induced in an achiral poly((4-carboxyphenyl)acetylene) by an optically active amine can be *memorized* when the amine is removed and replaced by achiral amines in dimethyl sulfoxide (DMSO).<sup>3</sup> Here we show that macromolecular helicity in an achiral polyisocyanide (poly-1-Na) (Figure 1)<sup>4</sup> is induced by optically active amines (2–4) in water and this helicity is automatically memorized even after complete removal of the amines. Although the chirality memory has been observed in a variety of supramolecular systems, the present memory is an unprecedented example that has never been considered thus far.<sup>5</sup>

The achiral poly-1-Na was first complexed with (*S*)- or (*R*)-2 (10 equiv to monomer units of poly-1-Na) in water, but the complex exhibited almost no induced circular dichroism (ICD) in the imino chromophore region of the polymer backbone during the initial stage. However, the ICD intensity (the molar ellipticity at 360 nm,  $\Delta\epsilon_{360}$ ) slowly but dramatically increased with time at 50 °C and reached  $\Delta\epsilon_{360} = -9.31$  (poly-1-Na-(*S*)-2) and 9.74 (poly-1-Na-(*R*)-2) after 29 days (Supporting Information). At lower temperatures, the complexes exhibited weaker ICDs after the same time period. We then isolated the helical poly-1-Na (*h*-poly-1-Na) by precipitation of the polymers into tetrahydrofuran to measure the CD and absorption spectra (Figure 2A). Surprisingly, after complete removal of the (*S*)- and (*R*)-2, the isolated polymers maintained the helicity with the memory efficiency of 89 and 92% based on the ICD values of the poly-1-Na-(*S*)-2 or -(*R*)-2 complex after 29 days, respectively, and exhibit mirror images of the ICDs in the polymer backbone (280–450 nm) as well as in the pendant aromatic regions (200–280 nm) (Figure 2A, a and b). Similar macromolecular helicity memory is possible for poly-((4-carboxyphenyl)acetylene), but the use of achiral amines is essential for the memory.<sup>3b</sup> The observed exciton-coupled ICDs<sup>6</sup> in the aromatic region suggest that the pendant phenyl groups are aligned in a one-handed helical array. This is proved by the reduction in the absorption intensity of 25% (hypochromic effect) in the aromatic region ( $\lambda_{\max} = 251$  nm) of *h*-poly-1-Na (Figure 2A, c), as compared with the non-helical poly-1-Na (Figure 2A, d). We also observed significant upfield shifts of the aromatic proton resonances (0.2–0.3 ppm) of *h*-poly-1-Na in the <sup>1</sup>H NMR spectrum. These results provide strong evidence of intramolecular stacking of the aromatic



**Figure 1.** Schematic illustration of one-handed helicity induction and memory in poly-1-Na. A one-handed helix is induced in poly-1-Na with (*S*)-2 in water, and the induced helicity is memorized after complete removal of (*S*)-2. The helix-sense of *h*-poly-1-Na prepared by (*S*)-2 is tentative.



**Figure 2.** Helicity induction in poly-1-Na and the memory. (A) CD spectra of isolated *h*-poly-1-Na prepared by (a) (*R*)-2 or (b) (*S*)-2 and absorption spectra of *h*-poly-1-Na prepared by (c) (*S*)-2 and (d) original poly-1-Na in water are shown. (B) VCD spectra of enantiomeric *h*-poly-1-Me ( $\Delta\epsilon_{360} = -9.43$  and 9.26, traces a and c, respectively) and (b) non-helical poly-1-Me and IR spectra of (d) poly-1-Me and (e) *h*-poly-1-Me in chloroform at ca. 25 °C with a concentration of 100 mg/mL. (C) *Syn-anti* configurational isomerization of the C=N double bond of polyisocyanide backbone.

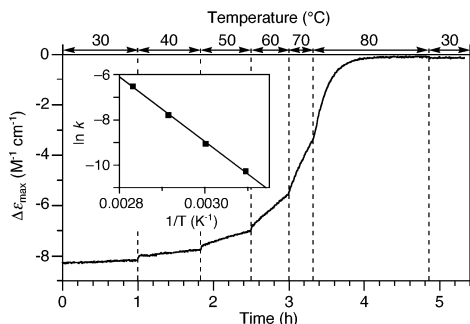
pendants, which are favored in water.<sup>7</sup> We note that the isolated *h*-poly-1-Nas prepared by (*S*)- and (*R*)-2 show a very large specific rotation ( $[\alpha]_{20}^{20} = -1380^\circ$  and  $1480^\circ$ , respectively), despite the fact that they no longer have any chiral components. As well as 2, various chiral amines such as (*R*)-3 and (*R*)-4 (Figure 1) can be used. In particular, *h*-poly-1-Na prepared by (*R*)-3 shows higher optical activity; the  $\Delta\epsilon_{360}$  and  $[\alpha]_{20}^{20}$  values in water are  $-10.73$  and  $-1790^\circ$ , respectively.

*h*-Poly-1-Na can be converted to the corresponding carboxylic acid (*h*-poly-1-H) ( $\Delta\epsilon_{360} = -10.06$ ,  $[\alpha]_{20}^{20} = -1930^\circ$ ) and methyl esters (*h*-poly-1-Me) ( $\Delta\epsilon_{360} = -9.48$ ,  $[\alpha]_{20}^{20} = -1560^\circ$ ) without the loss of the macromolecular helicity, although their optical activities depend on the structures and solvent.

Additional strong evidence of a one-handed helical structure of the polyisocyanides was obtained from the vibrational CD (VCD) spectra.<sup>8</sup> The VCD spectra of the enantiomeric *h*-poly-1-Mes obtained from the corresponding *h*-poly-1-Nas induced by (*S*)- and (*R*)-2 (Figure 2B, a and c) show Cotton effects in the C=N stretching bands, reflecting the helical structure of the polymer backbone. Moreover, the fact that the C=N stretching frequency of *h*-poly-1-Me in the IR spectrum is significantly different from that of the non-helical poly-1-Me (Figure 2B, d and e) indicates

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**Figure 3.** Stability of the macromolecular helicity memory of *h*-poly-1-**Na** obtained by (*S*)-**2** studied by CD in water following temperature jumps. Shown is the change in CD intensity at 360 nm of *h*-poly-1-**Na** in water. (Inset) Arrhenius plot of the temperature dependence of the first-order rate constants obtained at 50–80 °C for *h*-poly-1-**Na** in water.

that configurational isomerization around the C=N double bonds (*syn*–*anti* isomerization)<sup>9</sup> may take place during the helix formation (Figure 2C), that is, an imino configurational mixture of *syn* and *anti* of non-helical poly-1-**Na** is transformed to one of a single configuration<sup>10</sup> upon complexation with chiral amines, and this configurational homogeneity then forces a helical conformation on the polymer backbone, which is influenced by the chiral amines to take an excess helical sense.<sup>11</sup> Such *syn*–*anti* isomerism readily occurs for *N*-aromatic isocyanides, while it slowly occurs for *N*-alkyl isocyanides.<sup>12</sup> This isomerization must be accelerated at high temperature, so that it is reasonable to understand that the helix formation of poly-1-**Na** needs a long time at high temperature.

Although polyisocyanides are believed to adopt a 4<sub>1</sub> helical conformation when they have a bulky side group,<sup>2d,13</sup> aromatic polyisocyanides are reported to have a non-helical conformation.<sup>14</sup> The present results, however, clearly indicate that a similar helical polyisocyanide that is stable in solution can be synthesized from a non-helical polyisocyanide by non-covalently interacting chiral molecules through configurational isomerization. We postulate that hydrophobic and chiral ionic interactions in water might be necessary for the selective configurational isomerism, followed by the helix formation and memory, because helical poly(4-carboxyphenyl isocyanide) induced by chiral amines in DMSO<sup>15</sup> cannot maintain the helicity after removal of the chiral amines.

The thermal stability of *h*-poly-1-**Na** was then measured by monitoring the decrease in the CD intensity with time at different temperatures (Figure 3). The CD intensity of *h*-poly-1-**Na** gradually decreased at 30 °C, and the polymer lost its helical memory at 80 °C. The activation energy and half-life period at 30 °C estimated by the Arrhenius analysis are 28.5 kcal/mol and 3 days, respectively. When the recovered optically inactive *h*-poly-1-**Na** is annealed again with (*S*)- or (*R*)-**2** in water, an *h*-poly-1-**Na** with the same optical activity can be obtained. The <sup>1</sup>H and <sup>13</sup>C NMR spectra of the optically inactive *h*-poly-1-**Na** were completely different from those of the *h*-poly-1-**Na** but were similar to the original poly-1-**Na** (Supporting Information), indicating that this process is not racemization (helix-to-helix transition) but probably a helix-to-coil transition through the *syn*–*anti* isomerization. Moreover, the fact that *h*-poly-1-**Na** prepared by (*R*)-**3** exhibited an inversion of the CD upon heating with (*S*)-**3** in water also supports a helix-to-coil transition. *h*-Poly-1-**H** and *h*-poly-1-**Me** showed similar thermal stabilities comparable to that of *h*-poly-1-**Na**.

In summary, we have found an unprecedented memory of macromolecular helicity induced in an achiral polyelectrolyte, poly-1-**Na**, which folds into a one-handed helix through configurational isomerization around the C=N backbones by interactions with optically active amines in water. The helix remains when the

optically active amines are completely removed, so that further modifications of the side groups with a variety of functional groups can be possible with maintaining the macromolecular helicity memory. Furthermore, due to the supramolecular helical array of the pendant functional groups, the helical polyisocyanides will provide new chiral materials for chiral recognition and enantioselective catalysis.<sup>16</sup> The work is now in progress.

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**Supporting Information Available:** Experimental procedures and CD and NMR data (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (10) The assignments of *syn* and *anti* configurations have not yet been done but may be possible by comparison of the observed IR and VCD spectra of the helical and non-helical poly-1-**Me**s with the calculated ones.
- (11) Similar *syn*–*anti* isomerization did not take place upon heating the nonhelical poly-1-**Na** alone in water. However, the <sup>1</sup>H NMR spectrum of poly-1-**Na** significantly changed with time at 50 °C in the presence of achiral 2-aminoethanol. This indicates that *syn*–*anti* isomerization can occur for poly-1-**Na** with achiral amines, which may result in the formation of an equal mixture of right- and left-handed helical segments in part. The same helicity induction and memory of the helical chirality is possible for the poly-1-**H**-(*S*)-**2** system in water.
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- (16) Preliminary experiments revealed that *h*-poly-1-**Na** could discriminate the enantiomers of amines such as **4** based on NMR (see Supporting Information).

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