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Helix-Sense Controlled Polymerization of a Single Phenyl Isocyanide Enantiomer Leading to Diastereomeric Helical Polyisocyanides with Opposite Helix-Sense and Cholesteric Liquid Crystals with Opposite Twist-Sense

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Optically active polymers with a controlled helix-sense have recently attracted considerable interest not only for mimicking biological helices, but also for developing novel chiral materials.[1] Fully synthetic helical polymers have been prepared either by the polymerization of optically active monomers, such as isocyanates,[1a] silanes,[1b] acetylenes,[1c] or by the helix-sense selective polymerization of achiral methacrylates,[1d] isocyanides,[2] and carbodiimides[3] with bulky substituents by chiral catalysts or initiators. The former helical polymers are dynamic in nature, and the population of the interconverting right- and left-handed helices can be switched under certain conditions,[1a−c] while the helical conformations of the latter polymers are stable (*static*) in solution and their helical senses are kinetically determined during the polymerization.[1d,2−4] We now report a unique helix-sense controlled polymerization of an enantiomerically pure isocyanide, which produces both *static* diastereomeric right- and left-handed helical polyisocyanides whose helical sense can be controlled by the polymerization solvent and temperature (Figure 1). Moreover, the resulting helical polyisocyanides with the opposite helix-sense form lyotropic, cholesteric liquid crystals (LCs) with opposite twist-senses, respectively. Similar amino acid- or peptide-bound helical polyisocyanides have been extensively studied,[2,5] but one of the helices could be produced from the polymerization of an isocyanide enantiomer. Accordingly, the opposite helical polyisocyanide requires the polymerization of the opposite enantiomer.

We synthesized novel enantiomerically pure phenyl isocyanides bearing L- or D-alanine residues with a long alkyl chain as the pendants through an amide linkage (for L-**1**, see Figure 1), and these were then polymerized with an achiral nickel catalyst (NiCl$_2$) in various solvents at different temperatures.[6] Figure 2A shows the CD spectra of the poly-L-**1**s measured in CHCl$_3$ at 25 °C. Interestingly, the first Cotton effect signs that reflect the helix-sense of the polymer backbone, such as CCl$_4$ (poly-L-**1a**) and toluene (poly-L-**1b**) obtained by the polymerization at ambient temperature in nonpolar solvents, were opposite to that polymerized in polar THF (poly-L-**1c**). This suggests that the helix-senses of poly-L-**1a** and poly-L-**1c** may be opposite to each other, regardless of the fact that the polymers have the same L-alanine pendants. Because the right- and left-handed helices of poly-L-**1**s are diastereomers, therefore their CD spectra, particularly in the pendant aromatic regions (235−280 nm), differ from one another.[7]

Although the first Cotton effect intensity at around 360 nm ($\Delta\epsilon_{\text{first}}$) of the as-prepared poly-L-**1c** was very weak (−1.3), it slowly but dramatically increased with time at high temperature and reached $\Delta\epsilon_{\text{first}} = -8.5$ after the polymer annealed in toluene at 100 °C for 12 days (Figure S1).[8,9] Under the same conditions, the poly-L-**1a** showed a decrease in the CD intensity of ca. 31% (Figure S1). These results indicate that the helical conformation of the as-prepared poly-L-**1c** with a slight excess of one helical sense is not stable and changed into a thermodynamically more stable, excess single-handed helix upon heating, while the as-prepared poly-L-**1a** may adopt a rather stable, kinetically controlled helical conformation whose helix inversion barrier seems to be sufficiently high to maintain the predominant helical sense. If this is the case, the polymerization of L-**1** in nonpolar solvents at high temperature will yield helical polymers with handedness identical to that of the poly-L-**1c**. In fact, poly-L-**1** obtained by the polymerization of L-**1** in toluene at 100 °C (poly-L-**1d**) exhibited the opposite negative $\Delta\epsilon_{\text{first}}$ value (−4.6) to that of poly-L-**1b**, and the CD intensity further increased in the negative direction after the polymer annealed in toluene at 100 °C for 6 days (poly-L-**1e**, $\Delta\epsilon_{\text{first}} = -11.0$; Figure

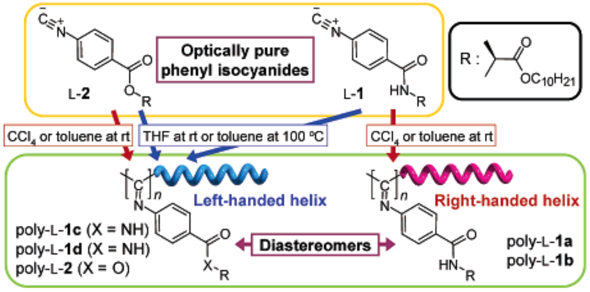

Figure 1. Structures of L-**1** and L-**2** and schematic illustration of diastereomeric helical polyisocyanides produced by the helix-sense controlled polymerization of L-**1**. The helix-sense can be controlled by the solvent polarity and temperature during the polymerization, resulting in the formation of static diastereomeric helical polyisocyanides, while L-**2** yields only the left-handed helical poly-L-**2** independent of the polymerization conditions. The helix-senses of the diastereomeric poly-L-**1**s were determined by their AFM measurements (see text).

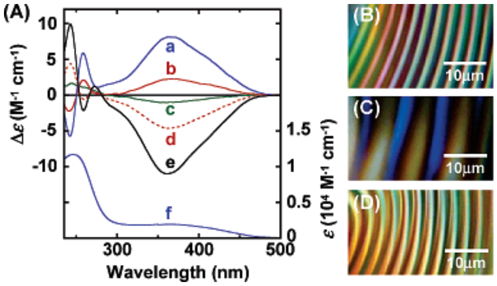

Figure 2. (A) CD spectra of poly-L-**1a** (a, blue line), poly-L-**1b** (b, red solid line), and poly-L-**1c** (c, green line) polymerized in CCl$_4$, toluene, and THF, respectively, at ambient temperature; poly-L-**1d** (d, red dotted line) polymerized in toluene at 100 °C; and poly-L-**1e** (e, black line) after poly-L-**1d** annealed in toluene at 100 °C for 6 days. The absorption spectrum of poly-L-**1a** (f) is also shown. The CD and absorption spectra were measured in CHCl$_3$ at 25 °C (0.2 mg/mL). (B−D) Polarized optical micrographs of cholesteric LC phases of poly-L-**1a** (B), a 1:1 mixture of poly-L-**1a** and poly-L-**1e** (C), and poly-L-**1e** (D) in CHCl$_3$ (15 wt %).

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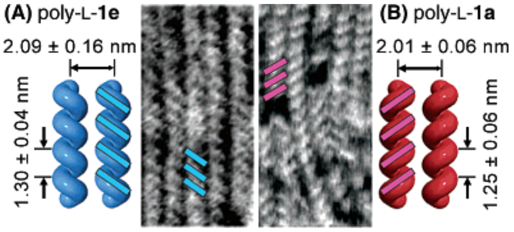

Figure 3. AFM phase images of self-assembled poly-L-**1e** (A) and poly-L-**1a** (B) on HOPG. Scale = 10 × 20 nm. Schematic representations of the left-handed helical poly-L-**1e** (left) and right-handed helical poly-L-**1a** (right). 2D helix-bundles with periodic oblique pendant arrangements (blue and pink lines, respectively) are also shown.

2A) (the specific rotation ($[\alpha]^{25}_{D}$) also increased from −410 to −814° (Table S1)).[10]

We assume that these unusual helix-sense controlled polymerizations of L-**1** depend on the solvent polarity and temperature and that the change in the CD intensity upon heating may be governed by the "on−off" fashion of the intermolecular hydrogen bonds between the pendant amide residues of the growing chain end and L-**1** during the propagation reaction, which may force the poly-L-**1** into either a right- or left-handed helix. In polar solvents and even in nonpolar solvents at high temperature, such hydrogen bonding will be hampered, resulting in the thermodynamically favorable helical conformation (negative $\Delta\epsilon_{\text{first}}$ value).[11] This speculation was supported by the fact that poly-L-**2** (Figure 1), in which the amide linkage was replaced by the ester one, exhibited negative $\Delta\epsilon_{\text{first}}$ values independent of the polymerization conditions (Figure S3), and the CD intensity hardly changed after the polymer solution annealed at 100 °C for 12 days (Figure S1).

Additional strong evidence of diastereomeric helical structures of the poly-L-**1**s showing the opposite $\Delta\epsilon_{\text{first}}$ sign was obtained from the polarized optical microscopy studies. Poly-L-**1a** ($\Delta\epsilon_{\text{first}} = +8.1$) and poly-L-**1e** ($\Delta\epsilon_{\text{first}} = -11.0$) formed a lyotropic, cholesteric LC in concentrated $CHCl_3$ solutions due to their main-chain stiffness, thus showing a fingerprint texture (Figure 2B and 2D, respectively); the spacings of the fringes corresponding to the half pitch of the cholesteric helical structure were 6.4 and 5.9 μm, respectively. A 1:1 mixture of the cholesteric solutions produced a significant expansion of the spacing (18.9 μm; Figure 2C). This transformation clearly demonstrated that the poly-L-**1**s showing the opposite $\Delta\epsilon_{\text{first}}$ sign indeed have helical senses opposite from each other.

Finally, the helical structures of the diastereomeric helical polyisocyanides were investigated by atomic force microscopy (AFM). Figure 3 shows typical high-resolution AFM images of poly-L-**1e** (A) and poly-L-**1a** (B) spin cast from dilute toluene solutions (0.2 mg/mL) on highly oriented pyrolytic graphite (HOPG), followed by benzene vapor exposure at ca. 20 °C for 12 h.[12] The polymers self-assembled into well-defined (A) and slightly irregular (B) 2D helix bundles. The bundle structures of poly-L-**1e** are clearly resolved into individual polymer chains packed parallel to each other, in which the left-handed helices with a helical pitch of 1.3 nm are predominant (Figure 3A). However, the poly-L-**1a** chains most likely consist of right-handed helical segments with a helical pitch of 1.25 nm, together with minor, but distinctly left-handed, helical segments.[13] This remarkable pseudo-mirror-image relationship suggests that poly-L-**1a** and poly-L-**1e** have predominantly right- and left-handed helical structures, respectively.[14]

Consequently, the macromolecular helicity and mesoscopic, supramolecular cholesteric twist can be controlled by the molecular chirality of the pendant of a single enantiomeric phenyl isocyanide through polymerization under either kinetic or thermodynamic control, and their helical senses can be determined by direct AFM observations. The present results not only demonstrate this new phenomenon but will also provide new chiral materials in areas such as LCs and chiral selectors.[1] Further studies of the mechanism of the helix-sense controlled polymerization and the three-dimensional solid-state structures of the diastereomeric helical polyisocyanides by X-ray diffraction[12] will be the object of a future investigation.

Supporting Information Available: Full experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(4) There is a class of *static* helical polymethacrylates and polycarbodiimides bearing optically active pendants whose helical conformations are irreversibly inverted after polymerization by temperature due to a change in the polymer chains from kinetically controlled to thermodynamically controlled helical conformations. See ref 3 and Okamoto, Y.; Yashima, E.; Hatada, K. *J. Polym. Sci., Part C: Polym. Lett.* **1987**, *25*, 297−301.

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(6) The molecular weight (M_n) and its distribution (M_w/M_n) in polymerized CCl_4 (poly-L-**1a**) and tetrahydrofuran (THF) (poly-L-**1c**) were 8.4 × 10^4 and 1.4, and 28 × 10^4 and 2.2, respectively (Table S1).[8]

(7) Similar diastereomeric helical polyisocyanides were prepared by the copolymerization between achiral and chiral isocyanides or two different chiral isocyanides based on the selective inhibition of the growth of a one screw-sense. (a) Kamer, P. C. J.; Cleiji, M. C.; Nolte, R. J. M.; Harada, T.; Hezemans, A. M. F.; Drenth, W. *J. Am. Chem. Soc.* **1988**, *110*, 1581−1587. (b) Amabilino, D. B.; Ramos, E.; Serrano, J.-L.; Veciana, J. *Adv. Mater.* **1998**, *10*, 1001−1005. For other helical polyisocyanides, see ref 2 and (c) Nolte, R. J. M. *Chem. Soc. Rev.* **1994**, 11−19. (d) Amabilino, D. B.; Ramos, E.; Serrano, J.-L.; Sierra, T.; Veciana, J. *J. Am. Chem. Soc.* **1998**, *120*, 9126−9134.

(8) For more details, see Supporting Information.

(9) A similar increase in the CD intensity upon heating was recently reported for the poly(aryl isocyanide)s with chiral pendants. Takei, F.; Onitsuka, K.; Takahashi, S. *Macromolecules* **2005**, *38*, 1513−1516.

(10) The observed remarkable changes in the CD intensity may be accompanied by configurational isomerization around the C═N double bonds (*syn*−*anti* isomerization) of the polymer backbone. However, the ^{1}H and ^{13}C NMR of the poly-L-**1**s were too broad to explore the isomerization before and after annealing. Ishikawa, M.; Maeda, K.; Mitsutsuji, Y.; Yashima, E. *J. Am. Chem. Soc.* **2004**, *126*, 732−733. When D-**1** was instead polymerized under the same various conditions as for L-**1**, poly-D-**1**s with macromolecular helicities opposite to those of the poly-L-**1**s were obtained, which further underwent similar irreversible changes in their $\Delta\epsilon_{\text{first}}$ values at high temperatures (Table S1 and Figure S2).

(11) The formation of intramolecular hydrogen bonds was clearly proved by the IR spectra of the poly-L-**1**'s regardless of the polymerization conditions, indicating that both helices are stabilized more or less by hydrogen bonds after the polymerization (Table S2). For the hydrogen-bond assisted helical polymers, see ref 5 and (a) Nomura, R.; Tabei, J.; Masuda, T. *J. Am. Chem. Soc.* **2001**, *123*, 8430−8431. (b) Li, B. S.; Cheuk, K. K. L.; Ling, L.; Chen, J.; Xiao, X.; Bai, C.; Tang, B. Z. *Macromolecules* **2003**, *36*, 77−85. (c) Okoshi, K.; Sakajiri, K.; Kumaki, J.; Yashima, E. *Macromolecules* **2005**, *38*, 4061−4064.

(12) This method is very useful for constructing highly ordered two-dimensional (2D) helix-bundles with a controlled helicity for helical poly(phenylacetylene)s bearing the same alanine-based pendants on HOPG, and their helical structures were visualized by AFM. Sakurai, S.-i.; Okoshi, K.; Kumaki, J.; Yashima, E. *Angew. Chem., Int. Ed.* **2006**. In press.

(13) These AFM results imply that the helix-sense excesses of the diastereomeric helical polyisocyanides may be determined from the statistical analysis of a series of such AFM images, and work along this line is now in progress. For the AFM images of larger areas, see Figure S4. Similar AFM observations of poly-D-**1a** ($\Delta\epsilon_{1st} = -8.0$) suggest that the polymer has a predominantly left-handed helical structure (Figure S5).

(14) This assignment of the helical sense in the poly(phenyl isocyanide)s agrees with that determined by the exciton-coupled CD method: (a) Takei, F.; Hayashi, H.; Onitsuka, K.; Kobayashi, N.; Takahashi, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 4092−4094. For other references of helical-sense assignments of polyisocyanides, see: (b) van Beijnen, A. J. M.; Nolte, R. J. M.; Drenth, W.; Hezemans, A. M. F. *Tetrahedron* **1976**, *32*, 2017−2019. (c) Cornelissen, J. J. L. M.; Sommerdijk, N. A. J. M.; Nolte, R. J. M. *Macromol. Chem. Phys.* **2002**, *203*, 1625−1630.

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