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Switching of a Macromolecular Helicity for Visual Distinction of Molecular Recognition Events

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Much attention has been recently focused on controlling and switching the helicity of (macro)molecules.[1] Such switchable materials have potential applications in data storage, optical devices, and liquid crystals for display, but still remain rare. Only a few synthetic polymers as well as biopolymers can be reversibly switched between right- and left-handed helical conformations by changing the external conditions,[2] such as solvent or temperature, or by the irradiation of light. Here we report a unique macromolecular helicity inversion accompanied by a color change responding to molecular and chiral recognition events that occurred at the remote side chain.

We designed and synthesized a stereoregular (*cis*−*transoidal*), chromophoric polyphenylacetylene having an optically active, bulky β-cyclodextrin (β-CyD) residue as the side group (poly-**1**; Figure 1A).[3] Poly-**1** appears to have a predominantly one-handed helical conformation induced by the β-CyD units so that it exhibits an intense circular dichroism (CD) in the long absorption region of the conjugated polyene backbone in dimethyl sulfoxide (DMSO) at 25 °C.[4] However, the CD pattern dramatically and sharply changed at high temperatures, and the sign inverted at 80 °C through a transition temperature ($[\theta]$ of the first Cotton effect ≈ 0 at $T_m = 70$ °C) (Figure 2A). These ICD changes were accompanied by remarkable changes in the absorption spectra; the absorbance maxima (λ_{max}) at 516 nm shifted to a shorter wavelength by 33 nm with a clear isosbestic point at 487 nm and the solution color changed from red to bright yellow (Figure 2C). These CD and absorption spectral changes are reversible and independent of the poly-**1** concentration (0.05−4.0 mg/mL) and time, indicating that the formation of aggregates depending on the temperature could be excluded.[5] These results suggest that poly-**1** may undergo a helix−helix transition from one helix to another with a different helical pitch by changing the temperature, and this conformational change leads to the thermochromism (Figure 1B).

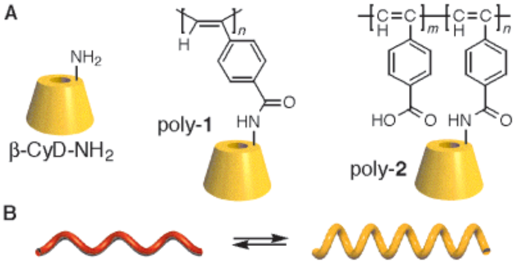

Figure 1. Structures of β-CyD-NH$_2$, poly-**1**, and poly-**2** (A) and schematic illustration of interconvertible right- (red) and left-handed (yellow) helices of poly-**1** (B).

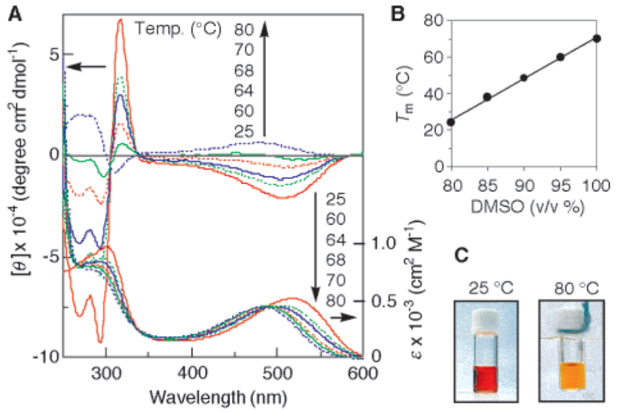

Figure 2. CD (upper) and absorption (lower) spectral changes of poly-**1** in DMSO (1 mg/mL) with temperature (the sample was kept for 5 min at the desired temperature before measurement) (A), plots of the helicity inversion temperature (T_m) of poly-**1** versus DMSO contents (%, v/v) in mixtures of DMSO and H_2O (B), and visible difference of poly-**1** in DMSO at 25 and 80 °C (C).

The right- and left-handed helices of poly-**1** are not exactly enantiomers. They are diastereomers because of the presence of chiral CyD residues of poly-**1**; therefore, their CD spectra differ from one another. Although these CD changes together with the calculation results (see below) strongly indicate the inversion of helicity of the poly-**1** backbone, there may be another possibility to explain the changes in the CD patterns; that is a change in the helical pitch of poly-**1** with the same-handedness rather than the helix inversion, and this possibility could not be thoroughly ruled out.[6]

On the other hand, the CD and absorption spectra of a DMSO solution of the poly-**2** bearing 91 mol % β-CyD residues (Figure 1A) hardly changed upon heating (no thermochromism); the solution remains yellow with a weak positive Cotton ($[\theta] = 4 \times 10^3$) at 440 nm. The cooperative interaction between the β-CyD residues at the side chains might be essential for the dramatic conformational change as observed for the poly-**1**.

The color changes of poly-**1** can be ascribed to a change in the twist angle of the conjugated double bonds. The blue-shift of the absorption spectra of poly-**1** in the high-temperature ranges

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[3] Poly-**1** was prepared by the polymerization of [(6-β-CyD)]carbamoylphenyl]acetylene (**1**) with $[Rh(nbd)Cl]_2$ (nbd = norbornadiene) in DMF at 30 °C; the number average molecular weight (M_n) was 1.63×10^5 as determined by size exclusion chromatography (SEC). Poly-**2** was prepared by the macromolecular reaction of *cis*−*transoidal* poly((4-carboxyphenyl)-acetylene) (its M_n is 1.8×10^4 as its methyl ester) with β-CyD-NH$_2$ (Figure 1A). The content of the β-CyD residue in poly-**2** was estimated to be 91 mol % by the anthrone reagent method.

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[5] SEC and static light-scattering analyses of the poly-**1** in solution also support this conclusion (see Supporting Information).

[6] Direct measurement of both helices of poly-**1** by scanning tunneling microscopy may be useful. Shinohara, K.; Yasuda, S.; Kato, G.; Fujita, M.; Shigekawa, H. *J. Am. Chem. Soc.* **2001**, *123*, 3619.

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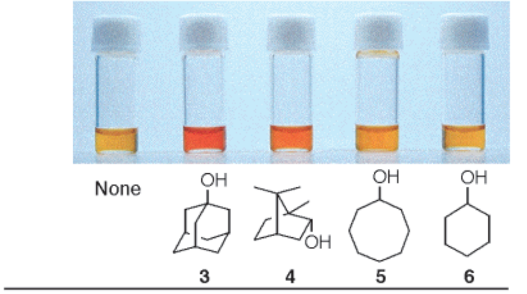

	None	**3**	**4**	**5**	**6**
λ_{max}	479	504	489	481	480
$[\theta]_{max}$	+ 0.47	- 1.76	- 1.29	+ 0.28	+ 0.43
K	—	247	67	17	3

Figure 3. Visible color changes in poly-**1** in DMSO$-$H$_2$O (8/2, v/v) at 25 °C induced by the addition of guest molecules (**3**-**6**) (20 equiv to monomer units of poly-**1**) and structures of the guests. λ_{max} (nm), $[\theta]_{max}$ of the first Cotton (10^4 degree cm^2 dmol^{-1}), and K (M^{-1}) are also shown.

suggests that the poly-**1** has a more tightly twisted helical conformation at the high temperatures in DMSO, while the red-colored poly-**1** has an extended π-conjugation (Figure 1B). Molecular mechanics calculations with the Dreiding force field for the model polymer (20-mer) reveal that the averaged dihedral angles of adjacent double bonds from planarity (ϕ) for the favorable conformations in the right- and left-handed helices are $10 \pm 4°$ and $-31 \pm 5°$, respectively (see Supporting Information). It thus seems plausible that the red-colored poly-**1** may have a right-handed helix and the yellow-colored poly-**1**, a left-handed helix.

The poly-**1** also exhibits a similar color change (from red to yellow) in the presence of an increasing amount of water (0$-$30% v/v) and alcohols accompanied by inversion of the Cotton effects at 25 °C. Moreover, we could control the T_m values by tuning the solvent compositions. For example, the T_m linearly decreased with an increase in the content of water (Figure 2B). This unique solvatochromism makes this system an effective discriminator of structurally similar alcohols with the naked eye. The DMSO solutions of poly-**1** containing simple primary alcohols such as methanol, ethanol, *n*-propanol, and *n*-butanol (DMSO/alcohol = 8/2, v/v) showed a color change, depending on the compositions and temperatures as reflected by their difference in hydrophobicity. The T_ms increased in the order of 29 (methanol), 43 (ethanol), 50 (*n*-propanol), and 55 °C (*n*-butanol), and we were able to distinguish the alcohols with the naked eye at 40 °C. On the other hand, the poly-**2** showed no solvatochromism in the presence of water and the alcohols.

It is well-known that β-CyD possesses a chiral hydrophobic cavity to form inclusion complexes with a variety of organic molecules that fit to the cavity size.[7] It then became of interest to investigate whether the poly-**1** could show a color change by formation of such inclusion complexes. When 1-adamantanol (**3**) or (−)-borneol (**4**) was added to the poly-**1** solution in DMSO$-$H$_2$O (8/2, v/v) at 25 °C, the solution color immediately changed from yellow-orange to red accompanied by the inversion of the Cotton effects (from $[\theta] = +0.47 \times 10^4$ to -1.76×10^4 for **3**) and a large red-shift of λ_{max} by 25 nm (Figure 3). In contrast, cyclooctanol (**5**) and cyclohexanol (**6**) did not bring about such a dramatic color change in the solution. The inclusion complex formation should occur between the β-CyD residues of poly-**1** and **3** and **4** as evidenced by the large association constants (Ks), obtained by the Hill plot analysis[8] of the titration data in DMSO$-$H$_2$O (8/2, v/v) at 25 °C (Figure 3). The changes in the absorbance intensity at 479 nm of poly-**1** versus the concentration of the guest showed a sigmoidal curvature, indicating that the guest cooperatively enters in the β-CyD cavity of poly-**1** to induce a conformational change.

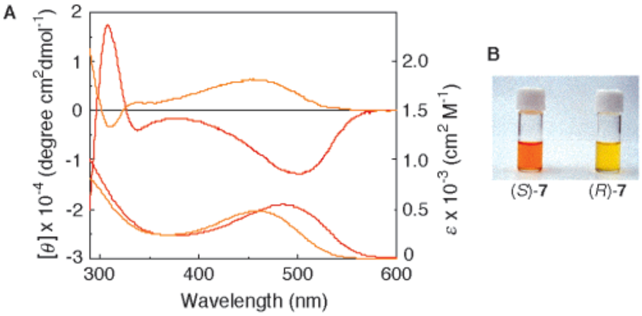

Figure 4. CD and absorption spectra of poly-**1** (1 mg/mL, 7.9×10^{-4} M monomer units) in an alkaline water (pH 11.7)-DMSO (7/3, v/v) in the presence of (*R*)-**7** (7.8×10^{-1} M) (orange lines) and (*S*)-**7** (7.8×10^{-1} M) (red lines) (A) and visible difference of the poly-**1**$-$(*R*)-**7** and the poly-**1**$-$(*S*)-**7** solutions at 25 °C (B).

The helicity of poly-**1** can also be switched by complexation with chiral guest molecules. The enantiomers of **4** induced a negligible color change in DMSO$-$water mixtures of poly-**1**. However, in a mixture of DMSO and alkaline water (pH 11.7) (3/7, v/v) the poly-**1** exhibited a color change (from yellow-orange to red) with a negative first Cotton in the presence of excess (*S*)-1-phenylethylamine ((*S*)-**7**), whereas the poly-**1**$-$(*R*)-**7** solution remained yellow with a positive first Cotton (see Figure 4). The chirality induced change in the sign of the CD spectra may result from inversion of the helicity of poly-**1**, which can be observed by the naked eye.[9] Under the same conditions, the poly-**2** did not show any spectroscopic and color change. Although a number of molecular sensors for the direct colorimetric detection of chemical species[10] including the enantiomers[11] have been developed, they have employed dyes or chromophoric macrocycles as color indicators. The present system is conceptually new and based on a change in the tunable helical pitch ("helical spring")[12] probably with the helicity inversion which may provide new approaches not only for the construction of new chiral materials as chiral sensors[11] and chiral selectors[13] but also for the rational design of novel switchable helical architectures.

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Supporting Information Available: Experimental procedures, CD data, calculated helical conformations of poly-**1**, and the Hill plots (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[9] In this case, chiral solvation effect should be also taken into consideration for the observed color change.

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