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Switching of Macromolecular Helicity of Optically Active Poly(phenylacetylene)s Bearing Cyclodextrin Pendants Induced by Various External Stimuli

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Abstract: A series of novel phenylacetylenes bearing optically active cyclodextrin (CyD) residues such as α-, *β*-, and *γ*-CyD and permethylated *β*-CyD residues as the pendant groups was synthesized and polymerized with a rhodium catalyst to give highly cis−transoidal poly(phenylacetylene)s, poly-**1α**, poly-**2*β***, poly-**3*γ***, and poly-**2*β***-Me, respectively. The polymers exhibited an induced circular dichroism (CD) in the UV−visible region of the polymer backbones, resulting from the prevailing one-handed helical conformations. The Cotton effect signs were inverted in response to external chiral and achiral stimuli, such as temperature, solvent, and interactions with chiral or achiral guest molecules. The inversion of the Cotton effect signs was accompanied by a color change due to a conformational change, such as inversion of the helicity of the polymer backbones with a different twist angle of the conjugated double bonds, that was readily visible with the naked eye and could be quantified by absorption and CD spectroscopies. The dynamic helical conformations of poly-**2*β*** showing opposite Cotton effect signs in different solvents could be further fixed by intramolecular cross-linking between the hydroxy groups of the neighboring *β*-CyD units in each solvent. The cross-link between the pendant CyD units suppressed the inversion of the helicity; therefore, the cross-linked poly-**2*β***s showed no Cotton effect inversion, although the polymer backbones were still flexible enough to alter their helical pitch with the same handedness, resulting in a color change depending on the degree of intramolecular cross-linking.

Introduction

The development of molecular sensors for the direct colorimetric detection of achiral and chiral chemical species, in particular organic neutral molecules including enantiomers, as well as solvent polarity and temperature has recently been attracting significant interest with implications for their potential applications in chiral and sensing materials.[1] A number of receptor molecules and supramolecules have been developed for this purpose.[2−4] In general, they have employed dyes, transition metals, or chromophoric macrocycles as color indicators combined with selective binding components for target guests.[1−4] *π*-Conjugated polymers also exhibit a color change in response to external physical and chemical stimuli[5] such as temperature, light, pH, and solvent composition[6] or by interaction with specific guests;[7] their color changes are ascribed to a change in their effective *π*-conjugation lengths of the polymer backbones or a conformational change due to supramolecular *π*-stacked aggregations.

Recently, we reported a conceptually new colorimetric detection system based on a unique helical macromolecule consisting of a chromophoric polyacetylene backbone and a *β*-cyclodextrin (CyD) as the side group (poly-**2*β*** in Scheme 1), which exhibited a visible color change due to a change in the twist angle of the conjugated double bonds induced by inclusion

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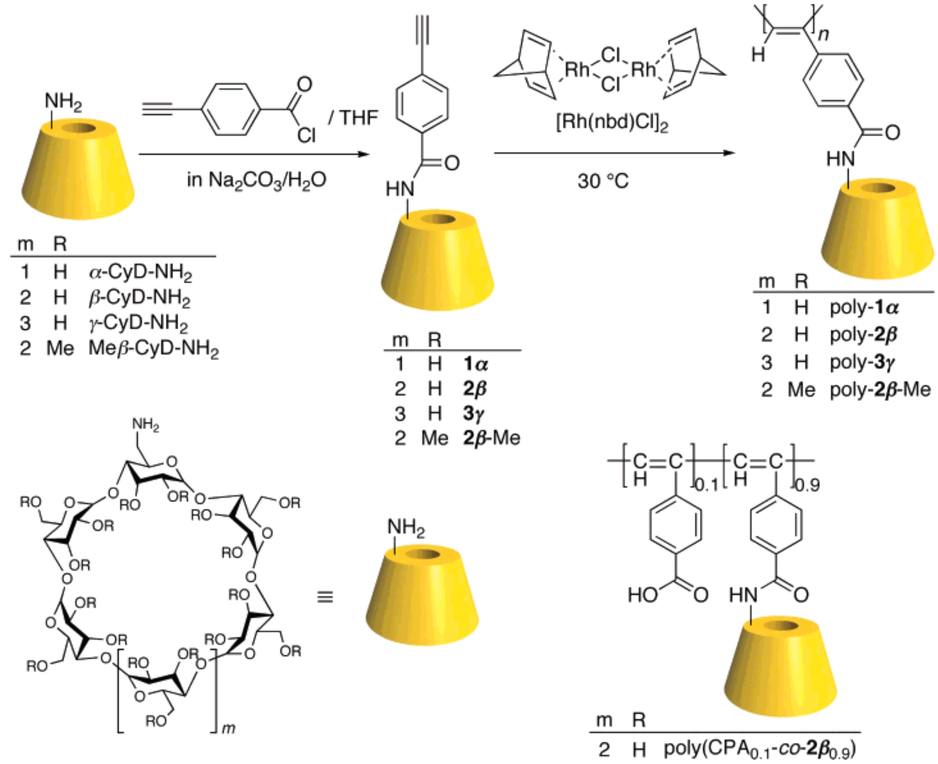
Scheme 1. Synthesis and Structures of Poly(phenylacetylene)s Bearing CyD Pendants



complexation with neutral, chiral, and achiral guest molecules into the chiral cyclodextrin cavity as well as by solvent and temperature.[8] This peculiar visual distinction of molecular recognition events that occurred at the remote side chain was accompanied by the inversion of Cotton effect signs in the long absorption region of the polymer backbone, suggesting a dramatic conformational change such as inversion of the helicity of the polymer backbone (Figure 1A).[8] Up to now, several biological[9] and synthetic polymers[10,11] and supramolecules[12] are known to exhibit the inversion of helicity (helix−helix transition) regulated by external achiral stimuli, such as a change in

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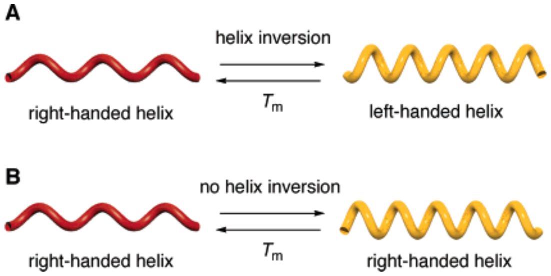

Figure 1. Schematic illustrations of a possible conformational change of poly-**1α**, -**2β**, -**3γ**, and -**2β**-Me accompanied by a visible color change and inversion of the Cotton effect sign.

pH, temperature, solvent, salt concentration, or by irradiation with light. These switchable helical materials have potential applications in data storage, optical devices, and liquid crystals for displays, but switching of the macromolecular and supramolecular helicity by chiral stimuli still remains rare,[1c,d,f,4,8,11d,*o*] although such chiral materials can be used to sense the chirality of chiral guests.

The present work is concerned with the mechanism of the visible color change of poly-**2β**, with respect to the inversion of helicity of the polymer backbone during changes in the Cotton effect signs. A series of stereoregular helical poly(phenylacetylene)s bearing α-, β-, and γ-CyD and permethylated β-CyD residues as the pendants (poly-**1α**, poly-**2β**, poly-**3γ**, and poly-**2β**-Me, respectively; Scheme 1) was synthesized. The effects of the ring size of the CyD pendants and the hydroxy groups in the β-CyD unit on their chiroptical properties including the macromolecular helicity inversion were then investigated by means of absorption and circular dichroism (CD) spectroscopies.

Although we previously proposed the inversion of helicity of the poly-**2β** backbone as a plausible conformational change for the visual color change by external stimuli based on the Cotton effect inversion together with the calculation results of a model polymer,[8] there may be another possibility to explain the changes in the CD patterns; that is a change in the helical pitch of poly-**2β** with the same-handedness rather than the helix inversion (Figure 1B). This possibility could not be ruled out.

To obtain more direct evidence for inversion of the helicity, the dynamic helical conformations of poly-**2β** showing opposite Cotton effect signs in different solvents were fixed by intramolecular cross-linking between the hydroxy groups of the neighboring β-CyD units in each solvent, and changes in their chiroptical properties after cross-linking were investigated in detail. We anticipated that the intramolecular cross-linking would suppress conformational changes in the polymer backbones to fix the helix-senses in each solvent. On the basis of these results, the origin of the inversion of the Cotton effect signs of CyD-bound helical poly(phenylacetylene)s by external stimuli accompanied by a visible color change was discussed.

Results and Discussion

Synthesis and Polymerization of Phenylacetylenes Bearing CyD Pendants and Structural Characteristics of the Polymers. Four optically active phenylacetylenes bearing CyD pendants, such as, α- (**1α**), β- (**2β**), γ-CyD (**3γ**), and permethylated β-CyD (**2β**-Me), were prepared as outlined in Scheme 1. The reaction of 4-ethynylbenzoyl chloride with the monoamino-CyD derivatives, α-CyD-NH_2, β-CyD-NH_2, γ-CyD-NH_2, and Meβ-CyD-NH_2, which had been prepared from the corresponding CyDs according to the literature method,[13] afforded **1α**, **2β**, **3γ**, and **2β**-Me in good yields, respectively. The polymerization was performed with a rhodium catalyst, $[Rh(nbd)Cl]_2$,[14] in the presence of triethylamine, giving high molecular weight, cis−transoidal poly(phenylacetylene)s. The polymerization results are summarized in Table 1.

The polymerization in DMF proceeded rapidly and homogeneously, yielding high molecular weight polymers with low molecular weight oligomers except for **2β**-Me (run 6 in Table 1), as evidenced by the size exclusion chromatography (SEC) measurements, which could be removed by reprecipitation (Table 1 and Supporting Information). On the other hand, the polymerization in DMSO and pyridine (runs 2 and 3 in Table 1, respectively) gave low molecular weight polymers and oligomers.

The stereoregularity of the polymers was investigated by ^{1}H NMR[14a,15] and Raman spectroscopies,[16,17] and all the polymers were found to possess a highly cis−transoidal structure (Figures S1 and S2 in Supporting Information). The obtained cis−

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Table 1. Polymerization of Phenylacetylenes Bearing CyD Pendants with $[Rh(nbd)Cl]_2$ at 30 °C[a]

				polymer					
								$[\alpha]_D^{25}$	
run	monomer	solvent	time (h)	sample code	yield (%)[b]	$10^{-4}M_n$[c]	M_w/M_n[c]	in DMSO	in alkaline water
1	**2β**	DMF	17	poly-**2β**[d]	60[e]	16.3	1.5	−1817	508
2	**2β**	DMSO	160	poly-**2β**	24[f]	1.9[g]	–	–	–
3	**2β**	pyridine	117	poly-**2β**	27[f]	2.3[g]	–	–	–
4	**1α**	DMF	17	poly-**1α**[h]	68[e]	16.0	1.2	−786	527
5	**3γ**	DMF	17	poly-**3γ**[h]	48[e]	11.1	1.2	−365	234
6	**2β**-Me	DMF	17	poly-**2β**-Me[i]	52	8.5[j]	1.4[j]	−414[k]	875[l]
7	–	–	–	poly($CPA_{0.1}$-*co*-$\mathbf{2\beta}_{0.9}$)[m]	–	n	n	141	147

[a] Polymerized under nitrogen: [monomer] = 0.1 M; [triethylamine]/[Rh] = 100; [monomer]/[Rh] = 10 (runs 1 and 4−6), 100 (runs 2 and 3). [b] MeOH insoluble part (runs 1−5) and EtOH insoluble part (run 6). [c] Determined by SEC using DMF containing 10 mM LiCl as the eluent (PEO and PEG standards). [d] Soluble in DMSO, DMF, and alkaline water, but insoluble in other common organic solvents and neutral and acidic water. [e] After removal of oligomers. [f] Containing oligomers. [g] Based on the peak top values of the higher molecular weight fractions in the SEC chromatogram. [h] Soluble in DMSO, DMF, and alkaline water. [i] Soluble in various solvents, such as $CHCl_3$, THF, acetone, ethyl acetate, toluene, and water, but insoluble in DMSO. [j] Determined by SEC using $CHCl_3$ as the eluent (polystyrene standards). [k] In DMSO/DMF (1:1, v/v). [l] In $CHCl_3$. [m] Prepared by the macromolecular reaction of PCPA with β-CyD-NH_2. See the Supporting Information. [n] The M_n and M_w/M_n of the original PCPA are 1.8×10^4 and 2.5, respectively.

transoidal high molecular weight polymers (runs 1, 4−6 in Table 1) were used for further chiroptical properties measurements.

Chiroptical Properties of Polymers: Conformational Changes in Poly-CyDs with Color Change by Temperature and Solvent. The chiroptical properties of the optically active poly(phenylacetylene)s bearing CyD pendants were investigated by means of absorption and CD spectroscopies. Figure 2 shows the CD and absorption spectra of poly-**1α** (A in Figure 2), -**2β** (B), and -**3γ** (C) in DMSO and poly-**2β**-Me in DMSO−DMF (1:1, v/v) (D). Poly-**2β**-Me was insoluble in pure DMSO, and a DMSO−DMF mixture was used. These polymers appear to have a predominantly one-handed helical conformation induced by the covalent-bonded chiral CyD pendants so that they exhibit an intense CD in the long absorption region of the conjugated polyene backbones at 25 °C. However, the CD patterns dramatically and sharply changed at high temperatures and the signs inverted through a transition temperature (T_m), where the $[\theta]$ values of the first Cotton effect became almost zero. These CD spectral changes were accompanied by remarkable changes in the absorption spectra; the absorbance maxima (λ_{max}) (514 nm, poly-**1α**; 516 nm, poly-**2β**; 517 nm, poly-**3γ**; 494 nm, poly-**2β**-Me) shifted to a shorter wavelength by 60 nm for poly-**1α**, 33 nm for poly-**2β**, 36 nm for poly-**3γ** , and 18 nm for poly-**2β**-Me with clear isosbestic points at 475, 487, 484, and 477 nm, respectively, and the solution color changed from red to bright yellow (poly-**1α**), red to yellow-orange (poly-**2β** and poly-**3γ**), or orange to yellow (poly-**2β**-Me) (Figure 2). Because poly-**2β**-Me was insoluble in DMSO, the CD and absorption spectral changes of poly-**1α**, -**2β**, and -**3γ** were also measured in DMSO−DMF (1:1, v/v) to investigate the effects of solvent and the size of the CyD units on the CD inversion behavior. Similar temperature-induced CD and absorption spectral changes were also observed in the solvent mixture for poly-**1α**, -**2β**, and -**3γ**, but the T_m's in DMSO−DMF (1:1, v/v) were lower than those in DMSO, as summarized in Table 2. On the basis of these results, it was found that the T_m's are remarkably influenced by the solvent composition and tend to increase with an increase in the bulkiness of the pendant CyDs in the order of poly-**1α** ≤ poly-**2β** < poly-**2β**-Me < poly-**3γ**.

The poly-**1α**, -**2β**, and -**3γ** also exhibit a similar color change (from red to yellow) in the presence of an increasing amount of water (0 to 50% v/v) accompanied by inversion of the Cotton effect signs in DMSO at 25 °C. For example, the CD and absorption spectral changes as well as the visible color changes of poly-**2β** in DMSO in the presence of an increasing amount of water are shown in Figure 3A,C, respectively. The absorbance maxima (λ_{max}) at 516 nm shifted to a shorter wavelength by 54 nm, and the solution color changed from red to yellow accompanied by the inversion of the first Cotton effect sign from the negative to positive direction at around DMSO−water = 8:2 (v/v). As shown in Figure 3B, the T_m values of poly-**1α**, -**2β**, and -**3γ** linearly decreased with an increase in the content of water, demonstrating that we could control the T_m values by adjusting the solvent compositions. In addition, the specific rotation ($[\alpha]_D$) of the polymers also changed from negative in DMSO to positive values in alkaline water as shown in Table 1.

These unique solvatochromisms of poly-**1α**, -**2β**, and -**3γ** were also observed in DMSO in the presence of an increasing amount of various alcohols instead of water. The DMSO solutions of poly-**1α**, -**2β**, and -**3γ** containing simple primary alcohols such as methanol, ethanol, *n*-propanol, and *n*-butanol showed a color change, depending on the compositions and temperatures as reflected by their difference in hydrophobicity (Figure S3 in Supporting Information). These changes were also accompanied by inversion of the Cotton effect signs. The T_m values increased in the order of methanol, ethanol, *n*-propanol, and *n*-butanol, but decreased in the order of poly-**3γ** > poly-**1α** > poly-**2β** (Table 2). These unique solvatochromisms make these systems effective discriminators of structurally similar alcohols with the naked eye on the basis of the temperature-dependent color changes.

The cooperative interaction between the adjacent CyD pendants may play an important role in these solvatochromisms with the Cotton effect inversion stimulated by temperature and solvent compositions. To explore this, a copolymer of (4-carboxyphenyl)acetylene (CPA) and **2β** (poly($CPA_{0.1}$-*co*-$\mathbf{2\beta}_{0.9}$)) bearing 91 mol % β-CyD residues was prepared from cis−

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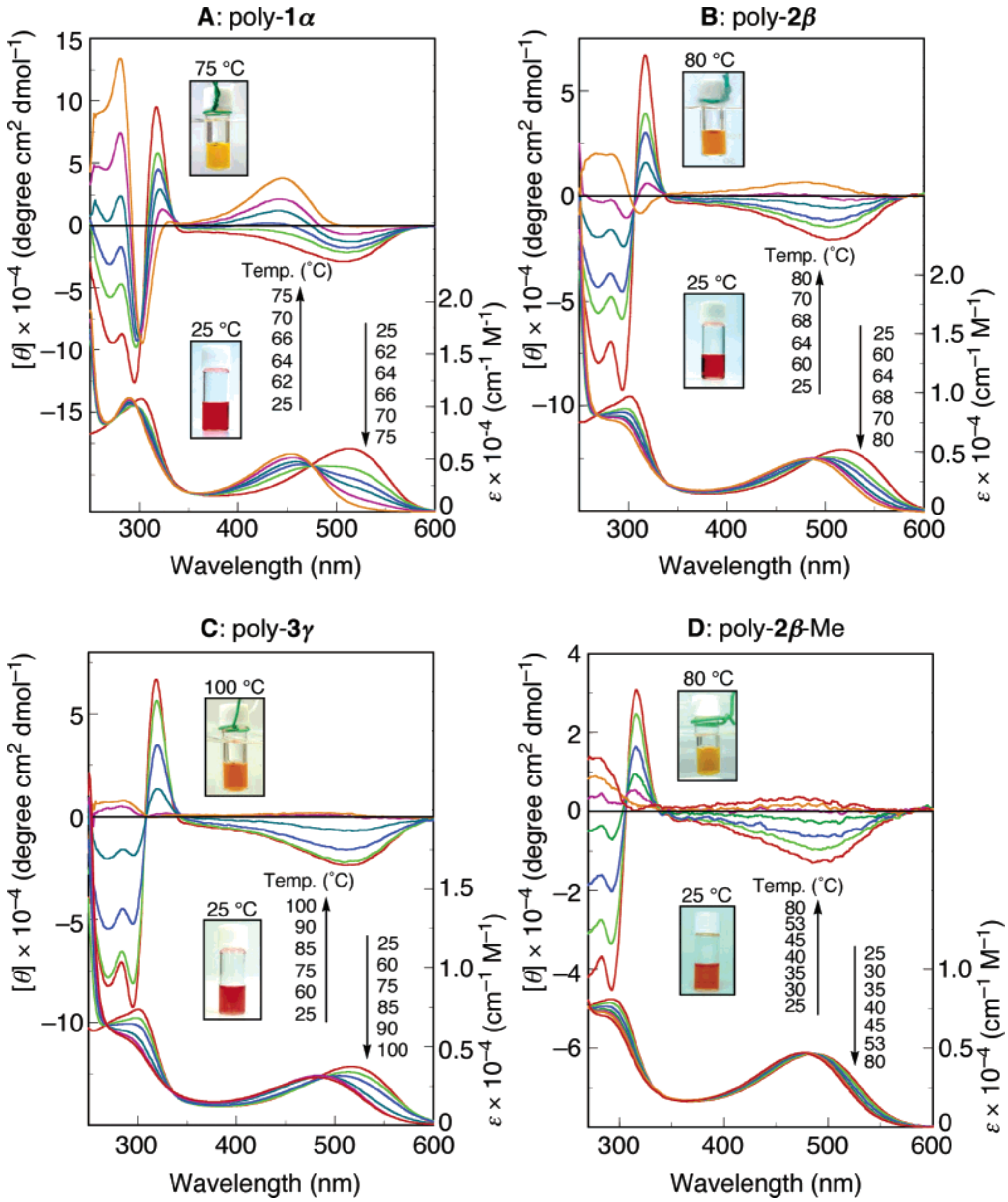

Figure 2. CD and absorption spectral changes of poly-**1α** (A), poly-**2*β*** (B), and poly-**3*γ*** (C) in DMSO and poly-**2*β***-Me (D) in DMSO/DMF (1:1, v/v) (1 mg/mL) with temperature; visible differences in color at 25 °C and higher temperatures are also shown in insets.

Table 2. CD Inversion Temperature (T_m) of Poly(phenylacetylene)s Bearing CyD Pendants in Various Solvent Mixtures[a]

	T_m (°C)			
solvent	poly-**1α**	poly-**2*β***	poly-**3*γ***	poly-**2*β***-Me
DMSO	66	70	90	*b*
DMSO−DMF[c]	35	32	53	45
DMSO−MeOH[d]	55[e]	29	56	*b*
DMSO−EtOH[d]	61[e]	43	69	*b*
DMSO−*n*PrOH[d]	64[e]	50	73	*b*
DMSO−*n*BuOH[d]	65[e]	55	77	*b*

[a] The concentration of the polymers is 1 mg/mL. [b] Insoluble in the solvent mixture. [c] DMSO/DMF = 1:1 (v/v). [d] DMSO/alcohol = 8:2 (v/v). [e] DMSO/alcohol (9:1, v/v) was used because of solubility limit.

transoidal poly((4-carboxyphenyl)acetylene) (PCPA) with *β*-CyD-NH_2 through a macromolecular substitution reaction (Scheme 1). The CD and absorption spectra of a DMSO solution of the poly($CPA_{0.1}$-*co*-$\mathbf{2}\boldsymbol{\beta}_{0.9}$) hardly changed upon heating (no thermochromism); the solution remains yellow with a weak positive Cotton ($[\theta] = 4 \times 10^3$) at 440 nm. Moreover, the DMSO solution showed no solvatochromism in the presence of water and alcohols (MeOH 30 vol %), and the specific rotation sign of the copolymer in DMSO ($[\alpha]^{25}_D$ +141) was the same as that in alkaline water ($[\alpha]^{25}_D$ +147) (Table 1), indicating that the cooperative interaction between the *β*-CyD pendants might be essential for the dramatic conformational change as observed for the poly-**2*β***. However, the intramolecular hydrogen bond interaction between the *β*-CyD units may not be the major

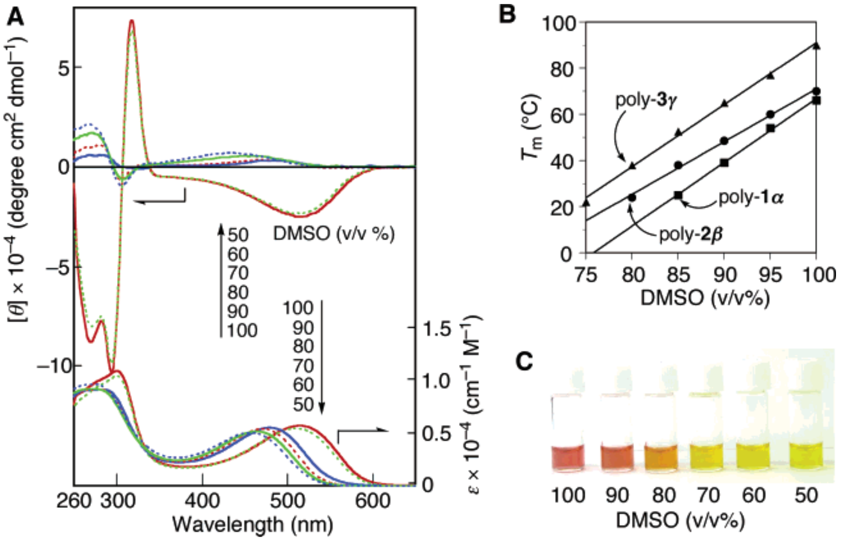

Figure 3. CD and absorption spectral changes of poly-**2β** in DMSO−water (100:0−50:50, v/v) at 25 °C (A), plots of the CD inversion temperature (T_m) of poly-**1α** (■), poly-**2β** (●), and poly-**3γ** (▲) versus DMSO contents (%, v/v) in mixtures of DMSO and water (B), and visible color changes of poly-**2β** in DMSO−water mixtures at ambient temperatures (C). The concentration of the polymers is 1 mg/mL.

driving force for the transition because the poly-**2β**-Me, where all of the hydroxy groups of β-CyD residues are replaced with methoxy groups, also exhibited a similar thermochromism in DMSO−DMF (1:1, v/v) with a higher T_m of 45 °C (Table 2).

Except for poly-**1α**, the CD and absorption spectral changes of these CyD-bound helical poly(phenylacetylene)s in DMSO, DMSO−DMF, and DMSO−alcohol mixed solvents with temperature were completely reversible and independent of the polymer concentrations (0.05−4.0 mg/mL) and time, indicating that the formation of aggregates depending on the temperature could be excluded. SEC and dynamic light scattering (DLS) analyses of the poly-**2β** in solution also support this conclusion (Supporting Information). In the SEC analysis using DMSO as the eluent at temperatures below and above T_m (70 °C) (30 and 80 °C), the elution time and peak shape of the poly-**2β** were independent of the temperatures. We then tried to measure the DLS of the poly-**2β** in DMSO, but the T_m value of poly-**2β** was too high to measure the DLS.[18] We then used a DMSO−methanol mixture (8:2, v/v) as the solvent because poly-**2β** exhibited a similar thermochromism in DMSO−methanol (8:2, v/v) with a lower T_m of 29 °C. The DLS data were analyzed by the cumulant method to give the translational diffusion coefficients (Ds). The corresponding hydrodynamic radius (R_h) was calculated using the Stokes−Einstein equation. The estimated R_h values for the poly-**2β** in DMSO−methanol (8/2) at 20 and 40 °C were almost the same, 12 and 14 nm, respectively.[19] Consequently, these polymers may undergo a conformational transition including a helix-inversion with a different helical pitch by changing the temperature and solvent compositions, and these conformational changes lead to the thermochromism and solvatochromism. We will discuss in more detail the conformational changes in these polymers later.

Among the CyD-bound helical poly(phenylacetylene)s, poly-**1α** was found to show an interesting hysteresis effect on the CD and absorption spectral changes with temperature in DMSO and DMSO−DMF (1:1, v/v) (Figure S4 in Supporting Information). Poly-**1α** also exhibited inversion of the Cotton effect sign at T_m = 66 and 35 °C in DMSO and DMSO−DMF (1:1, v/v) upon heating, accompanied by a blue-shift of their absorption maxima at high temperatures (Figure 2A and Table 2). However, the CD and absorption spectra of the poly-**1α** did not change in the cooling process even after the temperature became below the T_m during the heating process, and a further cooling was required to recover the original state before heating. These hysteresis changes occurred reversibly, indicating that poly-**1α** may form an aggregate at high temperatures. Filtration experiments support the formation of aggregates of poly-**1α** at high temperatures in DMSO and DMSO−DMF (1:1, v/v); for example, the poly-**1α** solution in DMSO−DMF (1:1, v/v) (B in Figure S4) could not pass through a membrane with a pore size of 0.2 μm at room temperature (ca. 20 °C) after heating the solution above the T_m, whereas it passed through the membrane before heating and after cooling to −10 °C, once heated above the T_m. This aggregate formation of poly-**1α** is considered to be due to the low solubility of poly-**1α** in DMSO and DMSO−DMF (1:1, v/v) compared with the other polymers. These results imply that the helix-sense of dynamic helical poly-**1α** can be "frozen" simply by heating the polymer solution above the T_m followed by cooling to an appropriate temperature.

The visible color changes in these polymers can be ascribed to a change in the twist angle of the conjugated double bonds. The blue-shifts of the absorption spectra of these polymers in the high temperature ranges suggest that the polymers may have a more tightly twisted helical conformation at high temperatures in solution, whereas the red-colored polymers may have an extended π-conjugation. Molecular mechanics calculations with the Dreiding force field for the model polymer of poly-**2β** (20-mer) were then conducted to obtain information regarding possible helical conformations of poly-**2β** (Supporting Information).[20] The optimized right- and left-handed helical structures of poly-**2β** are shown in Figure 4. The averaged dihedral angles

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(18) In the DLS measurements, we used a poly-**2β** with different molecular weight (M_n = 10.0 × 10^4 and M_w/M_n = 1.5).

(19) The DLS measurements of poly-**2β** in DMSO/H_2O (9:1, v/v) were also performed at above (60 °C) and below (25 °C) the T_m (55 °C). The estimated R_h value at 25 °C (13 nm) was almost the same as that at 60 °C (19 nm), supporting that the formation of aggregates in the DMSO/H_2O mixed solvent depending on the temperature could be also excluded.

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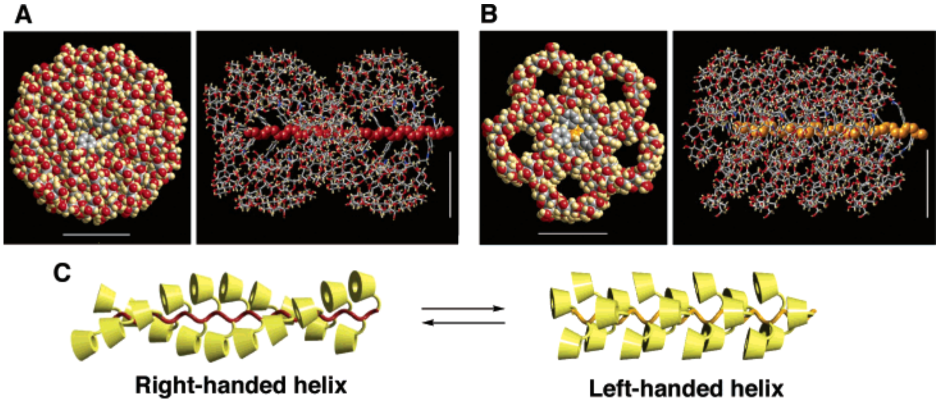
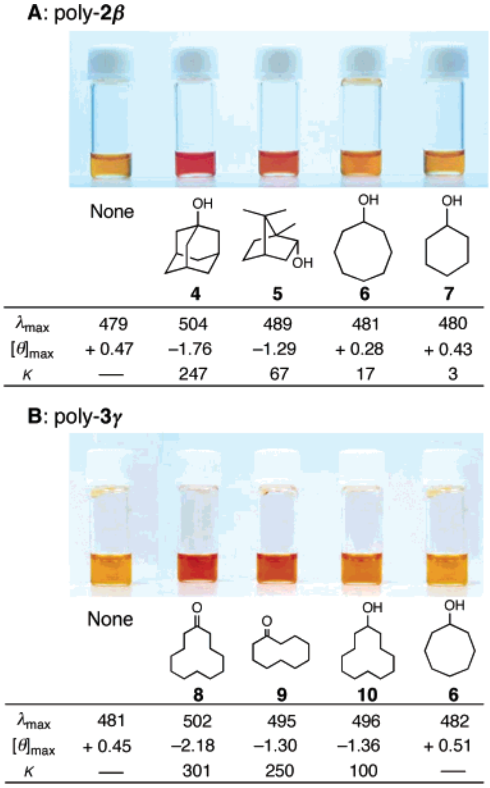


Figure 4. Calculated right- (A, $\phi = 10 \pm 4°$) and left-handed (B, $\phi = -31 \pm 5°$) helical conformations of poly-**2*β*** (20-mer). Shown are space-filling models in top view (A, B; left) and cylinder models in side view (A, B; right): scale bar, 1.5 nm. The main chain carbon atoms are shown in red (A) and yellow (B) using the space-filling model for clarity (side view). Schematic illustration of interconvertible right- and left-handed helices of poly-**2*β*** is also shown in C. The pendant CyDs arrange in left- and right-handed helical array along the right- and left-handed poly-**2*β*** backbones, respectively.

of adjacent double bonds from planarity (ϕ) for the favorable conformations in the right- and left-handed helices are 10 ± 4° (Figure 4A) and −31 ± 5° (Figure 4B), respectively. Therefore, it seems plausible that the red-colored poly-**2*β*** may have a right-handed helix and the yellow-colored poly-**2*β*** may have a left-handed helix (Figure 4C).

The right- and left-handed helices of the CyD-bound helical poly(phenylacetylene)s are not exactly enantiomers but are diastereomers because of the presence of chiral CyD pendants; therefore, their CD and absorption spectra differ from one another. The observed changes in the CD spectra (inversion of the Cotton effect signs) due to temperature and solvent compositions together with the calculation results strongly indicate the inversion of helicity of these polymers' backbones (Figure 1A). However, there may be another possibility to explain the changes in the CD patterns; that is a change in the helical pitch of these polymers with the same handedness rather than the helix inversion (Figure 1B), and this possibility could not be thoroughly ruled out. Further experimental results and discussions on the helix inversion will be described later.



A: poly-**2*β***

	None	**4**	**5**	**6**	**7**
λ_{max}	479	504	489	481	480
$[\theta]_{max}$	+0.47	−1.76	−1.29	+0.28	+0.43
K	—	247	67	17	3

B: poly-**3*γ***

	None	**8**	**9**	**10**	**6**
λ_{max}	481	502	495	496	482
$[\theta]_{max}$	+0.45	−2.18	−1.30	−1.36	+0.51
K	—	301	250	100	—

Figure 5. Visible color changes in poly-**2*β*** in DMSO−water (8:2, v/v) (A) and poly-**3*γ*** in DMSO−water (75:25, v/v) (B) at 25 °C induced by the addition of guest molecules (**4**−**7** for poly-**2*β***, **6** and **8**−**10** for poly-**3*γ***) (20 equiv to monomer units of the polymers) and structures of the guests. λ_{max} (nm), $[\theta]_{max}$ of the first Cotton effect (10^4 degree cm^2 dmol^{-1}), and K (M^{-1}) are also shown.

CD Inversion Accompanied by Color Change on Complexation with Small Molecules. CyDs possess a chiral hydrophobic cavity to form inclusion complexes with a variety of organic molecules that fit the cavity size of CyDs, and they have been widely used as building components to construct various supramolecular assemblies[21] and as chiral selectors for chromatographic enantioseparations.[22] We anticipated that the CyD-bound poly(phenylacetylene)s could also form such inclusion complexes, which might induce a change in their helical conformations in the polymer backbones, resulting in a color change. When 1-adamantanol (**4**) or (−)-borneol (**5**) was added to the poly-**2*β*** solution (20 equiv to monomer units of the polymer) in DMSO−H_2O (8:2, v/v) at 25 °C, the solution color immediately changed from yellow-orange to red accompanied by the inversion of the Cotton effect signs and a large red-shift of λ_{max} by 25 and 10 nm with clear isosbestic points at 335 and 493 nm for **4** and **5**, respectively (Figure 5A) (see also Figures S5A and S5B in Supporting Information). In contrast, cyclooctanol (**6**) and cyclohexanol (**7**) brought about neither such a dramatic color change in the solution nor the Cotton effect inversion. The changes in the absorbance intensity at 479 nm of poly-**2*β*** as a function of the concentration of the guests showed a sigmoidal curvature, indicating that the guest cooperatively entered in the β-CyD cavity of poly-**2*β*** to induce a

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conformational change (Figure S6 in Supporting Information). A Hill plot analysis[23] of the absorption titration data resulted in the apparent binding constants (*K*s) (Figure 5A and Figures S5 and S6 in Supporting Information). The increasing order of *K*s is in good agreement with that reported for the modified *β*-CyD derivative,[24] but the *K* values are smaller than those during the complexation of the modified *β*-CyD in pure water, because organic solvents such as DMSO cause a decrease in the stability of the inclusion complexes relative to water. Therefore, in pure DMSO, the poly-**2β** showed no color change with **4**−**7**. On the other hand, poly(CPA$_{0.1}$-*co*-**2β**$_{0.9}$) showed no change in the CD and absorption spectra upon the addition of **4** and **5** in DMSO−H_2O (8:2, v/v). These results suggest that the cooperative interaction between the adjacent CyD pendants may play an important role in the conformational change induced by inclusion complexation with the guest molecules. Even if the change of the interaction between the neighboring pendants upon inclusion complexation would be very small for each monomer unit, the effect can be significantly amplified by the cooperative interaction, resulting in the change in the backbone conformation.

Poly-**3γ** also showed a similar CD inversion accompanied by a color change in response to the specific guest molecules capable of interacting with *γ*-CyD[25] as evidenced by the large *K* values (Figure 5B and Figures S5 and S7 in Supporting Information). The addition of cyclododecanone (**8**), cyclodecanone (**9**), and cyclododecanol (**10**) to the poly-**3γ** solution in DMSO−H_2O (75:25, v/v) at 25 °C brought about a color change from yellow-orange to red or orange accompanied by the inversion of the Cotton effect signs (Figure 5B and Figure S5C in Supporting Information) and a large red-shift of λ_{max} (Figure S5D in Supporting Information). On the other hand, the addition of **8** and **9** to the poly-**2β** solution in DMSO−H_2O (8:2, v/v) at 25 °C did not bring about such a color change. These results indicate that poly-**2β** and poly-**3γ** can respond to molecular recognition events that occurred at the remote CyD pendants through inclusion complexation with specific organic molecules, which can be observed as a color change with the naked eye.[26]

Color Change by Complex Formation with Polymers. It is known that CyDs can selectively form inclusion complexes (rotaxanes) with polymers[27] as well as small molecules, depending on their cavity sizes. For example, *β*-CyD can be selectively threaded onto a poly(propylene glycol) (PPG) chain in water to form an insoluble, crystalline polyrotaxane, whereas it cannot form a complex with poly(ethylene glycol) (PEG) and poly(methyl vinyl ether) (PMVE). Instead, these are selectively complexed with α- and *γ*-CyDs, respectively.[27] We then investigated if poly-**2β** bearing *β*-CyD pendants could form inclusion complexes with PPG, thus showing a conformational change. PPG (20 equiv to monomer units of poly-**2β**) with different molecular weights (M_n = 400, 1000, 2000, and 4000) was then added to the alkaline solution of poly-**2β**. The absorption and CD spectral changes were highly dependent on the molecular weight of PPGs and were not dramatic for PPGs of M_n = 400 and 2000 and almost no change was observed with the addition of PPG of M_n = 4000, whereas the λ_{max} and $[\theta]_{max}$ showed a large blue-shift (44 nm) with a dramatic decrease in the absorbance intensity with the addition of PPG of M_n = 1,000 (PPG$_{1000}$) (Figure S8). The solution color changed from orange-yellow to bright yellow, but the solution was a nonviscous liquid, and neither gelation nor precipitation was observed. A similar molecular weight-dependent inclusion complexation was reported for *β*-CyD, which could most efficiently form such a complex with PPG$_{1000}$.[27d] On the other hand, the addition of PEG (M_n = 1,000) and PMVE (M_n = 60,000) did not bring about any absorption and CD spectral changes.[27d] Therefore, these observations suggest the possibility of a polyrotaxane formation between the poly-**2β** and PPG. The ^{1}H NMR spectrum of poly-**2β** with PPG$_{1000}$ ([PPG$_{1000}$]/[poly-**2β**] = 1) also supports such a polyrotaxane formation, at least in part, because the peak due to the methyl group of the PPG$_{1000}$ became considerably broadened in the presence of poly-**2β** (Figure S9 in Supporting Information).[27d]

CD Inversion Accompanied by Color Change on Complexation with Chiral Molecules. Although a number of molecular sensors for visual detection of chemical species have been developed,[1−7] the direct colorimetric detection of enantiomers remains difficult and rare.[1c,d,f,4,8] However, the visual detection of chirality is among the most powerful and convenient methods to assign the absolute configuration of chiral compounds, and such molecular sensors can also be applied to separate enantiomers as chiral stationary phases in HPLC.[28] We then investigated whether the present CyD-bound poly(phenylacetylene)s could respond to the chirality of chiral guest molecules and exhibit an enantioselective visible color change. Among the four CyD-bound helical poly(phenylacetylene)s tested, we found that poly-**2β** can discriminate the chirality of the enantiomers of 1-phenylethylamine (**11**) and exhibited a color change (Figure 6). In a mixture of DMSO and alkaline water (pH 11.7) (3:7, v/v), poly-**2β** exhibited a negative first Cotton effect in the presence of excess (*S*)-**11** ([(*S*)-**11**]/[poly-**2**] = 990), and the solution color immediately changed from red to yellow; whereas poly-**2β** and the poly-**2β**−(*R*)-**11** in the same solvent remained yellow with a positive first Cotton effect. Consequently, the chirality of **11** can be discriminated with the naked eye. However, the fact that a large amount of (*S*)-**11** was required for these changes in the CD and the solution color suggests that a chiral solvation effect rather than an enantioselective inclusion complexation in the *β*-CyD residues may be the driving force for the observed color change.[29] Poly-**1α** and poly-**3γ** did not show any difference in their solution colors in the presence of (*S*)- and (*R*)-**11** under the same experimental conditions. We then investigated the changes in the Cotton effect pattern and absorption spectra accompanied by a color change

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(26) We also investigated the inclusion complexation of poly-**1α** in DMSO−H_2O (85:15, v/v) with small guest molecules, such as indole, anthranilic acid, and 1, 10-decanediol, which are known to form inclusion complexes with α-CyD in water.[24] However, poly-**1α** showed no apparent CD and absorption spectral changes with these guests. The reason is not clear at the present time, but the poly-**1α** formed aggregates in the solvent mixture, which may prevent a further conformational change induced by the inclusion complexation with the guest molecules.

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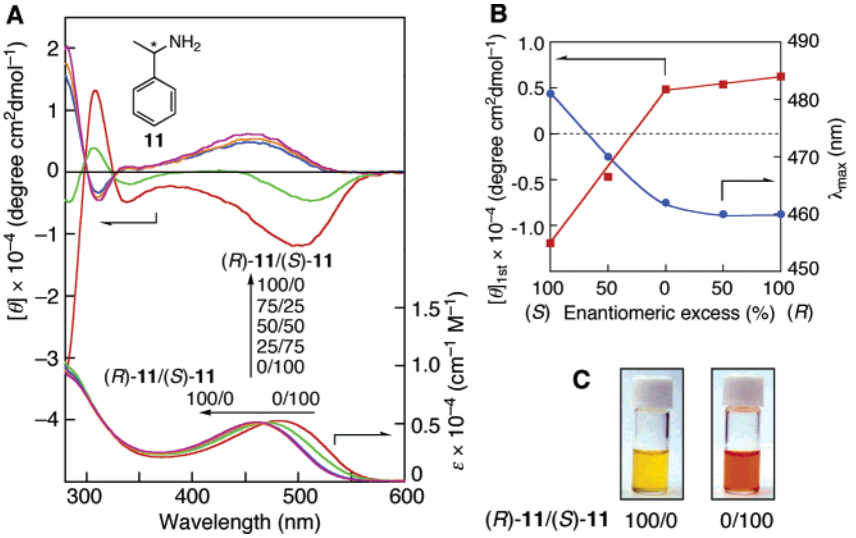

Figure 6. (A) CD and absorption spectral changes of poly-**2*β*** in alkaline water (pH 11.7)−DMSO (7:3, v/v) in the presence of 0−100% ee of **11** at 25 °C. (B) Changes in CD intensity ($[\theta]_{\text{first}}$) (red ■)and $\lambda_{\max}$ (blue ●) of poly-**2*β*** versus the % ee of **11** and (C) visible difference of the poly-**2*β*** with (*R*)- (left) and (*S*)-**11** (right).

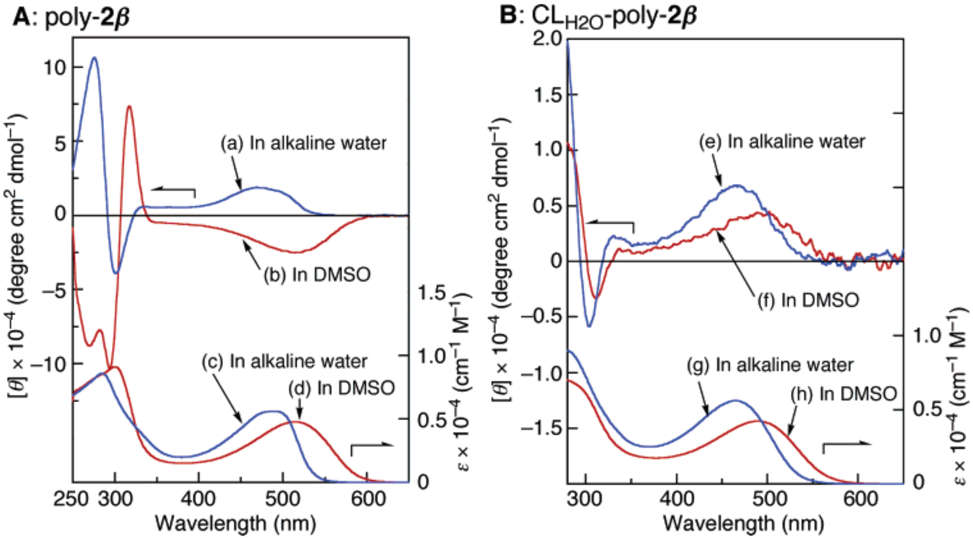

Figure 7. Effect of cross-linking of poly-**2*β*** in alkaline water. CD and absorption spectra before (A: poly-**2*β***) and after (B: CL$_{H_2O}$−poly-**2*β***) cross-linking in alkaline water (pH 11.7) (a, c, e, and g) and DMSO (b, d, f, and h) at 25 °C. The concentration of polymers is 1 mg/mL.

in the poly-**2*β*** solution in the presence of **11** with a different enantiomeric excess (ee) of **11** (0, 50, and 100% ee of **11** (*R*- or *S*-rich)) (Figure 6B). Interestingly, the racemic **11** and (*R*)-rich **11** of 50% ee could not induce a conformational change in poly-**2*β***, resulting in almost no change in their absorption and CD spectra (Figure 6A), while the poly-**2*β*** is sensitive to the chirality of (*S*)-**11**, and (*S*)-rich **11** of 50% ee showed a significant change in the CD and absorption spectra as well as 100% ee of (*S*)-**11**. The CD intensity and the $\lambda_{\max}$ of poly-**2*β*** seem to have a linear relationship with the ee of **11** ((*S*)-rich) (Figure 6B). Under the same conditions, the poly(CPA$_{0.1}$-*co*-**2*β***$_{0.9}$) did not show any spectroscopic and color change, indicating that the cooperative interaction between the fully substituted, neighboring *β*-CyD units might be indispensable for this phenomenon. Other chiral compounds such as phenylalaninol and 1-phenylethyl alcohol were also tested, but similar changes in the CD and absorption spectra depending on the difference in their configuration could not be observed.

Fixation of Interconvertible Helical Structures of Poly-2*β* by Intramolecular Cross-Linking. As described above, the CyD-bound poly(phenylacetylene)s show inversion of the Cotton effect signs accompanied by a visible color change by responding to various external stimuli, such as temperature and solvent. For example, poly-**2*β*** showed ICDs with opposite Cotton effect signs in the polymer backbone regions in DMSO and alkaline water (Figure 7A). The Cotton effect inversion, in particular, the first Cotton effect accompanied by a dramatic change in their absorption spectra, was assumed to originate from inversion of the helicity of the polymer backbone. If this is the case, poly-**2*β*** may have a helical conformation with an opposite helical sense in DMSO and in alkaline water. The molecular mechanics calculation results suggested that the predominant helix-sense

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(29) Although the enantioselective binding of **11** with *β*-CyD derivatives has been investigated, the selectivity was poor, indicating that a chiral solvation effect rather than an enantioselective inclusion complexation may be the driving force for the observed color change. (a) Keim, W.; Köhnes, A.; Meltzow, W.; Römer, H. *J. High Resol. Chromatogr.* **1991**, *14*, 507−527. (b) Nie, M. Y.; Zhou, L. M.; Wang, Q. H.; Zhu, D. Q. *Chromatographia* **2000**, *51*, 736−740. (c) Rekharsky, M.; Inoue, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4418−4435.

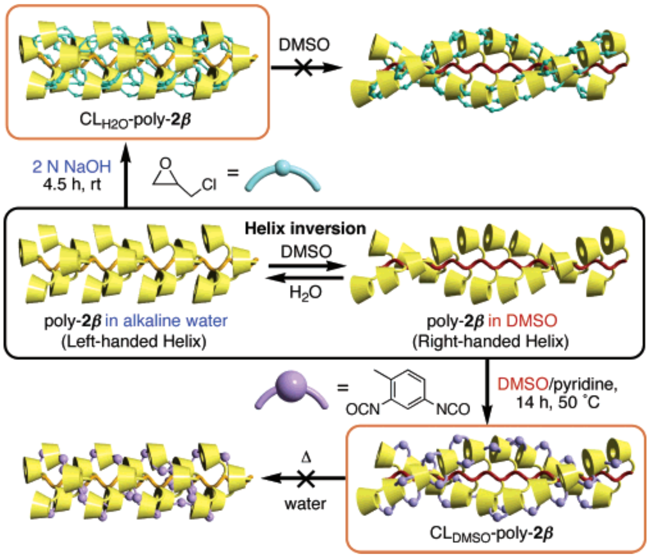

Figure 8. Schematic illustrations of intramolecular cross-linking of the *β*-CyD pendants in poly-**2β** in alkaline water and DMSO; CL$_{H_2O}$−poly-**2β** and CL$_{DMSO}$−poly-**2β** stand for the intramolecularly cross-linked poly-**2β**s in water and DMSO, respectively.

of poly-**2β** may be right-handed with an extended helical conformation in DMSO, but in alkaline water, poly-**2β** may have an opposite left-handed helix with a tight helical conformation (Figure 4). These changes in their helical senses with a different helical pitch can lead to the solvatochromism and thermochromism. However, a change in the helical pitch of poly-**2β** with the same-handedness rather than the helix inversion cannot be ruled out to explain the observed changes in their CD patterns and the solution color as shown in Figure 1. To obtain more direct evidence for inversion of the helicity of dynamic helical poly-**2β** in DMSO and alkaline water, the helical structures of poly-**2β** showing opposite Cotton effect signs were intramolecularly cross-linked between the hydroxy groups of the neighboring *β*-CyD units in each solvent. We anticipated that if the helix-sense of the poly-**2β** could be fixed by the intramolecular cross-linking reaction, the resulting cross-linked poly-**2β** could not show such changes in the Cotton effect signs and absorption spectra, resulting in no thermo- and solvatochromisms. The cross-linking reactions were performed in alkaline water and DMSO using epichlorohydrin (ECH) and 4-methyl-1,3-phenylene diisocyanate (TDI) as the cross-linking reagents, respectively (Figure 8).

In alkaline water, poly-**2β** (10 mM monomer units) was allowed to react with an excess amount of ECH ([ECH]/[poly-**2β**] = 176) at ambient temperature for 4 h.[30] Most of the obtained cross-linked polymer (CL$_{H_2O}$−poly-**2β**) was soluble in water, DMF, and DMSO but contained an insoluble part (ca. 30%) in these solvents, which was removed by filtration after dissolving the polymer in water. The soluble part (CL$_{H_2O}$−poly-**2β**) appears to consist mainly of intramolecularly cross-linked poly-**2β** as supported by SEC analysis; the elution time of the peak top of CL$_{H_2O}$−poly-**2β** was almost the same as that of poly-**2β** before cross-linking, although the polymer contained a higher molecular weight fraction in part due to the intermolecular cross-linking reaction (Figure S10 in Supporting Information). Atomic force microscopy (AFM) measurements also support the intramolecular cross-linking (see below). The ECH content introduced in the CL$_{H_2O}$−poly-**2β** was estimated to be 8.5 residues per CyD unit on the basis of the molar absorptivity at 466 nm ($\epsilon_{466} = 5475$) of the original poly-**2β** in 2 N NaOH solution. This value satisfied the elemental analysis (see Supporting Information). The cross-linked polymer maintained its cis−transoidal structure, which was confirmed by laser Raman spectroscopy. The CD and absorption spectra of CL$_{H_2O}$−poly-**2β** were then measured in DMSO and alkaline water (Figure 7B). Although the absorbance maximum of CL$_{H_2O}$−poly-**2γ** in DMSO exhibited a considerable red-shift as observed for poly-**2β** (Figure 7A), the first Cotton effect sign of the CL$_{H_2O}$−poly-**2β** corresponding to the polymer backbone region remained positive in DMSO as well as in alkaline water, although the CD intensity of the first Cotton effect ($[\theta]_{\text{first}}$) decreased from 1.88×10^4 to 0.69×10^4 in alkaline water after cross-linking.[31] In sharp contrast, poly-**2β** showed an opposite, negative first Cotton effect in DMSO in the same region. Moreover, the CL$_{H_2O}$−poly-**2β** showed almost the same CD pattern in the shorter wavelength region irrespective of the solvents. These results indicate that the cross-linking reaction between the pendant CyD residues significantly influences the dynamic nature of the helical conformation of poly-**2β**; the helix-sense of the CL$_{H_2O}$−poly-**2β** appears to be fixed to that in alkaline water before the cross-linking.

The cross-linking reaction of poly-**2β** (10 mM) was also performed in DMSO using an excess amount of TDI ([TDI]/[poly-**2β**] = 180) as a cross-linker at 50 °C for 14 h. A DMSO−soluble, intramolecularly cross-linked polymer (CL$_{DMSO}$−poly-**2β**) was obtained after removal of a DMSO insoluble part (ca. 35%) by filtration. The TDI content introduced in the CL$_{DMSO}$−poly-**2β** was estimated to be 3.5 residues per one CyD unit using the $\epsilon_{\max}$ value of poly-**2β** in DMSO ($\epsilon_{514} = 5380$). The obtained CL$_{DMSO}$−poly-**2β** was insoluble in alkaline water, and therefore, the CD and absorption spectra were measured in DMSO at various temperatures to determine if the helix-sense could be fixed by the cross-linking reaction (Figure 9A). The CD spectra of CL$_{DMSO}$−poly-**2β** hardly changed upon heating (25−90 °C) while maintaining the negative first Cotton effect and the magnitude of the CD was almost constant;[32] the results were completely different from those of poly-**2β** (see Figure 2B). Furthermore, the addition of water to the DMSO solution of CL$_{DMSO}$−poly-**2β** did not bring about an inversion of the Cotton effect sign, although a large blue-shift in the absorption spectra was observed in the presence of increasing amounts of water (Figure 9B). A similar blue-shift also occurred for poly-**2β**, but which was accompanied by inversion of the Cotton effect sign (see Figure 3A).[33] These results indicate that the right- and left-handed helical conformations of poly-**2β** in different solvents

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(31) The specific rotation $[\alpha]^{25}_{D}$ of CL$_{H_2O}$−poly-**2β** in DMSO also changed from a negative (−1817°) to a positive (+168°) value after cross-linking in alkaline water, whereas the specific rotation sign remained a positive value in alkaline water after cross-linking ($[\alpha]^{25}_{D}$ +185°).

(32) The specific rotation $[\alpha]^{25}_{D}$ of CL$_{DMSO}$−poly-**2β** in DMSO also maintained a negative value in the temperature range of 25−80 °C ($[\alpha]^{25}_{D}$ −521° and $[\alpha]^{80}_{D}$ −357°).

(33) One may think that CL$_{DMSO}$−poly-**2β** contained phenylcarbamate groups on the CyD units, which may affect the chiroptical property of the polymer. Poly-**2β** was then allowed to react with phenyl isocyanate (PI) to produce a noncross-linked model polymer, whose hydroxy groups were partially modified with phenylcarbamoyl groups. The content of the introduced PI units was 3.2 residues per CyD unit, and this value was almost the same as that of CL$_{DMSO}$−poly-**2β**. This model polymer also showed a similar inversion of the Cotton effect signs with temperature as did poly-**2β** in DMSO. Therefore, the effect of the phenylcarbamate groups on the CyD pendants on the CD spectrum can be neglected.

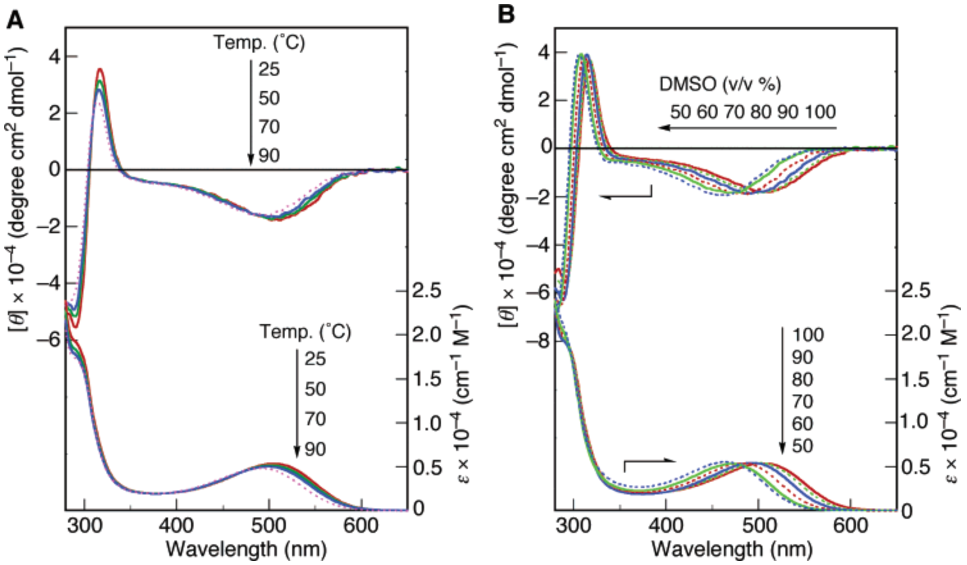

Figure 9. Effect of cross-linking of poly-**2*β*** in DMSO. CD and absorption spectral changes of CL$_{\mathrm{DMSO}}$−poly-**2*β*** (1 mg/mL) (A) in DMSO at various temperatures and (B) in DMSO−water mixtures (100:0−50:50, v/v) at 25 °C.

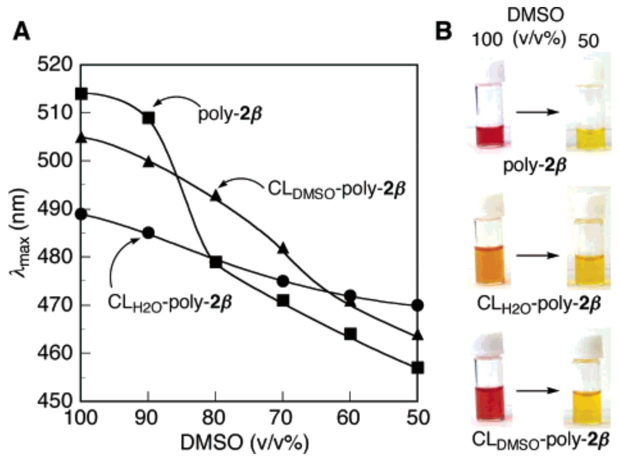

Figure 10. (A) Changes in λ_{max} of poly-**2*β***, CL$_{\mathrm{H_2O}}$−poly-**2*β***, and CL$_{\mathrm{DMSO}}$−poly-**2*β*** versus the changes in DMSO−water ratio (100:0−50:50, v/v) at 25 °C. (B) Visible color changes of the polymers in DMSO and DMSO−water (50:50, v/v) at 25 °C. The concentration of polymers is 1 mg/mL.

can be fixed at each handedness by the intramolecular cross-linking reactions in each solvent. Consequently, the inversion of the Cotton effect signs might originate not from a change in the helical pitch of poly-**2*β*** with the same-handedness but from the inversion of the helix-sense of the polymer backbones.

Figure 10 shows the changes in the absorbance maxima of poly-**2*β***, CL$_{\mathrm{H_2O}}$−poly-**2*β***, and CL$_{\mathrm{DMSO}}$−poly-**2*β*** in DMSO−water mixed solvents relative to the DMSO content (100 to 50 v/v%) of the solvents. Poly-**2*β*** exhibited a large blue-shift in the presence of an increasing amount of water, resulting in a change in the solution color from red to yellow accompanied by an inversion of the Cotton effect signs. After cross-linking, CL$_{\mathrm{H_2O}}$−poly-**2*β*** and CL$_{\mathrm{DMSO}}$−poly-**2*β*** more or less showed a similar blue-shift of the λ_{max}, leading to a visible color change. However, these cross-linked polymers maintained their Cotton effect signs in the mixed solvents. In particular, the change in the solution color of CL$_{\mathrm{DMSO}}$−poly-**2*β*** was remarkable. The difference in the absorption spectral changes and the solution color between CL$_{\mathrm{DMSO}}$−poly-**2*β*** and CL$_{\mathrm{H_2O}}$−poly-**2*β*** may arise from the difference in the degree of cross-linking; in the case of CL$_{\mathrm{DMSO}}$−poly-**2*β***, the change in the helical pitch could not be suppressed due to its low degree of cross-linking, although such a low degree of intramolecular cross-linking was sufficient to fix the helix-sense. Consequently, the cross-linking between the CyD pendants suppresses the inversion of the helicity, but the polymer backbones are still flexible and can alter their helical pitch, resulting in a color change.

AFM analyses of poly-**2*β*** before and after the cross-linking on a freshly cleaved mica surface were then conducted to observe changes in morphology and conformation of the polymer main chains (Figure S11 in Supporting Information). Individual polymer chains can be directly visualized on mica prepared from dilute solutions of the CL$_{\mathrm{DMSO}}$−poly-**2*β*** and CL$_{\mathrm{H_2O}}$−poly-**2*β*** as well as poly-**2*β*** in DMSO (0.05 mg/mL). These results also support the belief that the observed Cotton effect inversions accompanied by a color change are not due to the aggregation of the polymers. The average height of the poly-**2*β*** was determined to be 2.0 ± 0.3 from ca. 100 cross-section profiles, which was shorter than the molecular diameter of a helical poly-**2*β*** model; the computer-generated molecular diameters of helical poly-**2*β***s having left- and right-handed helical conformations are 4.1 and 4.0 nm, respectively (Figure 4). The strong interaction of the polymer chains with the mica surface and the decompression of the polymer due to solvent vaporization as well as a tip-induced deformation of the samples should be taken into consideration for the reduced heights of the poly-**2*β*** on mica.[34] The average height value of the CL$_{\mathrm{H_2O}}$-poly-**2*β*** slightly increased to 2.6 ± 0.2 nm compared with that of the poly-**2*β***, and the polymer chains appear to become thicker, although this value is still shorter than those of the computer-generated molecular diameters of the helical poly-**2*β***. Similar AFM images were also observed for CL$_{\mathrm{DMSO}}$−poly-**2*β***. These results indicate that the intramolecular cross-linking between the CyD units may contribute to retention of their cylindrical

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structure on a mica surface during the AFM observation. Although the helical structures of diastereomeric helical poly-**2*β*** could not be visualized by the AFM, a recently developed high-resolution AFM technique based on ordered two-dimensional helix-bundle formation of helical poly(phenylacetylene)s bearing a long alkyl pendant[35] may be useful for the direct visualization of the diastereomeric helical poly-**2*β*** after introducing similar long alkyl chains in the CyD pendants. The work along this line is now in progress.

Conclusions

In summary, we have demonstrated a conceptually new direct colorimetric detection system for neutral chemical species including enantiomers as well as solvent and temperature based on a change in the tunable helical pitch ("helical spring")[36] with the macromolecular helicity inversion. In addition, such a switchable dynamic helical conformation can be, for the first time, fixed in each handedness as a result of the intramolecular cross-linking,[37] which will be further used as novel chiral materials for enantiomer separations and catalysts.

Experimental Section

Full experimental details are available in Supporting Information.

Acknowledgment. We thank S. Ohsawa, Dr. S. Sakurai, and Dr. T. Nishimura for their help in the AFM measurements and computer simulations. This work was partially supported by Grant-in-Aid for Scientific Research from Japan Society for the Promotion of Science and the Ministry of Education, Culture, Sports, Science, and Technology, Japan, and the 21st Century COE Program "Nature-Guided Materials Processing" of the Ministry of Education, Culture, Sports, Science and Technology.

Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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