Biomimetic Stabilization of Helical Structure in a Synthetic Polymer by Means of Intramolecular Hydrogen Bonds

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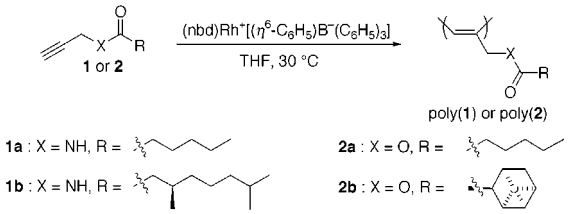
The studies on synthetic helical polymers[1−6] were initiated by the discovery of helical structures in naturally occurring macromolecules. Natural macromolecules form three-dimensionally ordered supramolecules by self-organization processes. The design strategy of nature to form helical polymers results from the appropriate arrangement of intermolecular and intramolecular noncovalent interactions, which enhances their main-chain rigidity. α-Helical polypeptides are representative examples, in which intramolecular hydrogen bonds stabilize their helical conformation.[7] Unfortunately, apart from elegantly designed oligomers,[2,8,9] this strategy has not been applicable to artificial polymers except for synthetic polypeptides and nucleic acids because of the difficulty in arranging the noncovalent interactions in macromolecules. Therefore, for flexible synthetic polymers, stabilization of the helical conformation relies upon the bulkiness of pendant groups. In this work, we report an artificial reproduction of the natural design strategy to form helical conformation in a synthetic polymer. Specifically, we synthesized a new acetylene-based polymer, poly(*N*-propargylamide) [poly(**1**)], where the helical conformation, like α-helical polypeptides, is stabilized by intramolecular hydrogen bonds between pendant groups.

Poly(**1a**) was prepared using a Rh catalyst, (nbd)$Rh^+[(\eta^6\text{-}C_6H_5)\text{-}B^-(C_6H_5)_3]$,[10] which efficiently catalyzes the polymerization of monosubstituted acetylenes (Scheme 1).[11] The unique ability of Rh catalysts to tolerate various functional groups[12−14] allowed the formation of poly(**1a**) (M_n = 18 000, M_w = 40 000 by GPC, polystyrene calibration) as a methanol-insoluble product in good yield (77%). Figure 1 illustrates the ^{1}H NMR spectra of poly(**1a**) in $CDCl_3$. At a low temperature (19 °C), poly(**1a**) exhibited very broad signals at 7.6, 6.1, and 3.9 ppm (Figure 1a). This result is not due to lower stereoregularity, because the NMR spectrum at a high temperature (55 °C) gave well-resolved signals for all protons (Figure 1b). Typically, Rh catalysts produce stereoregular cis−transoidal polyacetylenes.[12−14] Thus, the signals are assigned as shown in Figure 1. The N−H proton appears at 7.6 ppm, and the peak at 6.1 ppm corresponds to the olefinic proton in the main chain with geometrical cis-structure. The sharp resonance attributed to the vinyl proton at 55 °C indicates a highly stereoregular structure of the main chain. Furthermore, integration of the signals showed that the cis content of poly(**1a**) was quantitative. Hence, the broadening of the NMR peaks of poly(**1a**) demonstrates the limited mobility of the main chain. This result is in contrast to previous observations in which the main chains of polymers from monosubstituted aliphatic acetylenes were reported to be very flexible.[14] For example, the ester version of poly(**1a**), the Rh-based poly(**2a**) (88% cis content), which has no hydrogen-bonding donor group, displayed clear ^{1}H NMR signals even at 22 °C. Although poly(**2a**) has a relatively high molecular weight [M_n = 25 000 (GPC)], it was only a viscous yellow oil, whereas poly(**1a**) was a solid, yellow powder. Furthermore, the rigidity of poly(**1a**) was clearly evidenced by its high viscosity index (α) of $[\eta] = \kappa \cdot M^\alpha$ in the Mark−Houwink−Sakurada plot, where $[\eta]$ is the intrinsic viscosity and M is the absolute molecular weight, based on the universal calibration curve.[15] The α value of poly(**1a**) (0.98, in THF at 30 °C) verifies its stiff or semiflexible main chain, whereas that of poly(**2a**) (0.63) was close to the value for glassy polystyrene (0.68).

Scheme 1



N-Propargylalkylamide having a chiral substituent, (*R*)-*N*-propargyl-3,7-dimethyloctanamide (**1b**), was polymerized with (nbd)$Rh^+[(\eta^6\text{-}C_6H_5)B^-(C_6H_5)_3]$, giving a polymer ($M_n$ = 8100, M_w = 13 600) with 100% cis content in 62% yield. The α value of poly(**1b**) (0.91 in THF at 40 °C)[16] reveals its enhanced main-chain rigidity. Interestingly, this semiflexible polymer displayed an extremely large optical rotation, (−1470° in $CHCl_3$, c = 0.1 g/dL), which was opposite in sign to the corresponding monomer **1b** ($[\alpha]_D$ = +0.25° in $CHCl_3$, c = 0.41 g/dL). The CD spectrum of poly(**1b**) showed intense CD effects in the absorption region of the main-chain chromophore (Figure 2), indicating that the polymer backbone is chiral. Because the Cotton effect of poly(**1b**) did not depend on the polymer concentration between 0.3 and 0.005 mM (monomer unit), the chiral effect results from the individual polymer chain. In other words, the main chain of poly(**1b**) twists from coplanarity and, eventually, exists in a helical conformation. On the other hand, the ester version of poly(**1b**), poly(**2b**) (M_n = 9200, M_w = 195 000, 92% cis content), having no hydrogen-bonding donor possesses a flexible main chain (α = 0.52 in THF at 30 °C). This polymer showed very weak CD effects and poor optical rotation (+50° in $CHCl_3$, c = 0.075 g/dL), even though very bulky chiral groups that generally stabilize the helical conformation of polyacetylenes[17−19] were incorporated. Thus, the main chain of polymers from monosubstituted aliphatic acetylenes, such as poly(propargyl esters), are originally too

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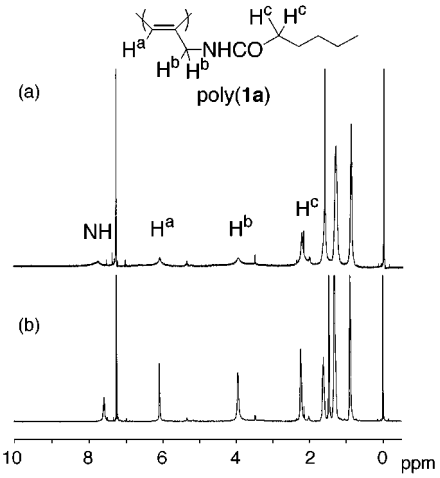

Figure 1. ^{1}H NMR spectra of poly(**1a**) in $CDCl_3$ at (a) 19 °C and (b) 55 °C.

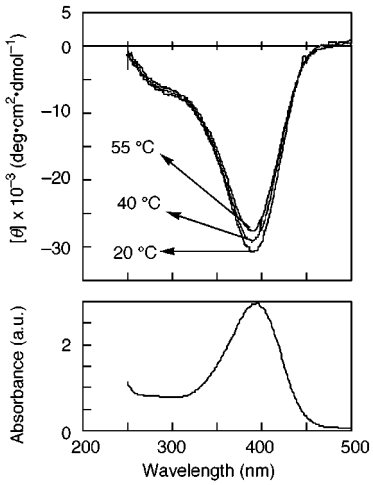

Figure 2. (Top) Temperature variable CD spectra of poly(**1b**) in $CHCl_3$ and (bottom) UV−visible spectrum of poly(**1b**) in $CHCl_3$ at 20 °C.

flexible to adopt an ordered helical conformation and essentially exist in a randomly coiled state.

These contrastive results are apparently due to the difference in the main-chain rigidigy between poly(**1**) and poly(**2**), and the semiflexibility of poly(*N*-propargylamides) undoubtedly originates from the hydrogen bonds of the amide groups. The following results evidenced that intramolecular hydrogen bonds between the pendant groups induce and stabilize the helical structure. The amide I absorption of monomer **1b** was observed at 1670 cm^{-1} in $CHCl_3$, which shifted by more than 30 cm^{-1} compared with that in the solid state (1638 cm^{-1}). The wavenumber of this IR band was independent of concentrations between 48 and 0.05 mM. Consequently, the monomer **1b** exists in a nonaggregated state in solution in the concentration range studied. The absence of a hydrogen bond between the monomers is also supported by the isolated N−H stretching vibration of **1b** at 3455 cm^{-1} in this concentration range. In contrast, under similar conditions, the wavenumber of the amide I absorption of poly(**1b**) in $CHCl_3$ (1636 cm^{-1}) was almost identical to that in the solid state (1638 cm^{-1}). Similarly, there was no significant difference in wavenumber of the stretching vibration of the N−H bond of poly(**1b**) between that in solution (3304 cm^{-1}) and in the solid state (3300 cm^{-1}). These results clearly indicate that the pendant amide groups of poly(**1b**) aggregate even at a very low concentration. It was also confirmed that the change in concentration from 0.05 to 48 mM had no effect on the frequency of the amide I absorption of poly(**1b**). These data led to a reasonable conclusion that the intramolecular hydrogen bonds are constructed between pendant amide groups in poly(**1b**) even in very diluted solution, in which the corresponding monomer cannot form aggregates.

The α value of poly(**1a**) at 40 °C (0.76) was quite small compared with that at 30 °C. This drastic change in the α value over such a small temperature variation is an indication that hydrogen bonds in poly(**1a**) are readily broken by thermal stimuli. The temperature dependence of the ^{1}H NMR spectrum of poly(**1a**) (Figure 1) also supports this assumption. On the other hand, under the same conditions (in THF at 40 °C), the α value of poly(**1b**) was much larger than that of poly(**1a**). Hence, poly(**1b**) is stiffer than poly(**1a**), which was also supported by NMR spectroscopy. The ^{1}H NMR spectrum of poly(**1b**) displayed broader resonance even at elevated temperature (55 °C).[20] These observations reveal the enhanced thermal stability of the hydrogen bonds in poly(**1b**), which contributed to the thermal stability of the helical conformation of poly(**1b**). In this regard, heating a chloroform solution of poly(**1b**) led to only a slight decrease in the intensity of the Cotton effect as shown in the temperature-variable CD spectrum (Figure 2). This enhanced thermal stability is in contrast with the instability of the helical conformation of polymers from monosubstituted acetylenes; that is, the chiroptical properties of helical polyacetylenes drastically decrease with increasing temperature unless they possess bulky substituents.[17−19]

Because the absolute secondary conformation of poly(*N*-propargylamide) is currently unknown, it is not possible to discuss the precise structure of the hydrogen bonds constructed in the polymer backbone. However, we can conclude that the present strategy allows originally very flexible, randomly coiled polymers to spontaneously organize into a helical structure utilizing intramolecular hydrogen bonds of the side chains. This phenomenon is identical to the folding transition process of polypeptides into a three-dimensionally ordered α-helix. To the best of our knowledge, this is the first example of reproducing the design strategy of the α-helix of a protein by artificial, non-peptide-based polymers.

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Supporting Information Available: The ^{1}H NMR spectra (expanded) of poly(**1b**) in $CDCl_3$ at 20 and 55 °C. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) See the Supporting Information.