Synthesis and Macromolecular Helicity Induction of a Stereoregular Polyacetylene Bearing a Carboxy Group with Natural Amino Acids in Water

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Since most important biological events occur in aqueous solution where biopolymers such as proteins and DNA form a characteristic helical conformation, significant attention has recently been paid to developing artificial polymers and oligomers that adopt a one-handed helical conformation in aqueous solution, particularly in light of emerging applications in the biomedical and materials science fields and also for mimicking protein folding.[1] However, most synthetic helical polymers and oligomers prepared so far are optically active due to their helicity in organic solvents.[2]

We recently reported that macromolecular helicity can be induced on a stereoregular, *cis-transoidal* poly((4-carboxyphenyl)acetylene) (poly-**1**-H) by an optically active amine,[3] and this helicity can be "*memorized*" when the amine is replaced by various achiral amines in organic solvents.[4] The poly-**1**-H was prepared by the polymerization of (4-(triphenylmethoxycarbonyl)phenyl)acetylene with a rhodium (Rh) complex, ([Rh(nbd)Cl]$_2$: nbd = norbornadiene), in tetrahydrofuran (THF), followed by hydrolysis of the ester groups.[3] We now show that this polymer can be directly prepared by the homogeneous, stereospecific polymerization of (4-carboxyphenyl)acetylene (**1**-H) in water in the absence of surfactants and any organic solvents, using water-soluble rhodium complexes, such as [Rh(cod)$_2$]BF$_4$ (cod = cyclooctadiene), [Rh(nbd)$_2$]ClO$_4$, and [Rh(nbd)(tos)(H$_2$O)] (tos = *p*-toluenesulfonate)[5] in the presence of bases such as alkaline hydroxides and amines (Scheme 1). Furthermore, the macromolecular helicity can be induced on the polymer in water as a result of noncovalent, electrostatic interactions with natural, free amino acids; the complexes showed a characteristic induced circular dichroism (ICD) in the UV−vis region. Accordingly, the sequence of events including the synthesis of a polymer and the helicity induction on the polymer is entirely possible in water, which is an extremely important medium for organic reactions, polymerizations, and processes, because water is cost-effective, safe, and environment-friendly; the use of wet-organic solvents or aqueous biphasic systems is still considered ecologically harmful.[6,7]

Table 1 summarizes the polymerization results of **1**-H with water-soluble Rh complexes. The Rh-based complexes effectively polymerize phenylacetylenes to afford high molecular weight, *cis-transoidal* polymers, and well-defined Rh-based initiators can induce living polymerization in organic solvents.[8,9] For these polymerizations, acetic acid is used to remove the active Rh moiety from the propagating polymer end to terminate the polymerization.[8,9] This indicates that acetylenes bearing a carboxy group may not be directly polymerized by the Rh-based complexes.[10,11] However, the use of bases brought about the stereospecific polymerization of **1**-H in water. The polymerization was rapid and homogeneous in the presence of bases, producing yellow-orange fibrous, high molecular weight polymers in high yields (Table 1), although the molecular weight distributions (M_w/M_n) of the polymers were rather broad (>2). The ^{1}H NMR spectra of the sodium salt of poly-**1**-H (poly-**1**-Na) and poly-**1**-H derived from the poly-**1**-Na or poly-**1**-Et$_2$NH$_2$ through acidification with 1 N HCl(aq) showed sharp singlets centered at 5.89 (D$_2$O) and 5.83 ppm (DMSO-d_6), respectively, due to the main chain protons, indicating that these polymers possess a highly *cis-transoidal*, stereoregular structure (see Supporting Information).[8,12] Other bases such as LiOH, KOH, RbOH, and CsOH can be used to obtain stereoregular poly-**1**'s in high yields (>88%) under the same conditions shown in Table 1 (run 1). The polymerization reaction also proceeded in air and water to yield a stereoregular poly-**1**-Na (run 3).[13]

The monomer **1**-H is insoluble in pure water but soluble in dimethyl sulfoxide (DMSO). The polymerization did not occur in the absence of amines in DMSO with [Rh(nbd)Cl]$_2$ and [Rh(cod)$_2$]BF$_4$, but a small amount of polymer was obtained in DMSO in the presence of diethylamine (yield < ca. 10%). The neutralization reaction of **1**-H with bases resulting in the dissociation into a carboxylate ion may be necessary for an effective polymerization. In water **1**-H reacts with a base to give a free carboxylate ion. However, in polar organic solvents, such as DMSO, ion pairing predominates, and the dissociation of the ion pair may be restricted.[14] Therefore, water is a much better solvent than DMSO.

Scheme 1

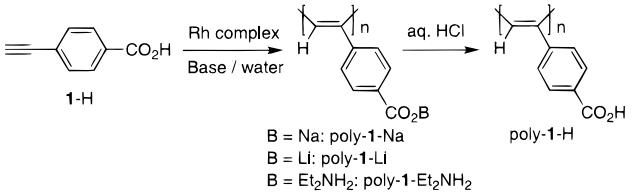

Table 1. Polymerization of 1-H with Water-Soluble Rh Complexes in Water in the Presence of Base at 30 °C for 3 h[a]

run	Rh catalyst	base	yield (%)[b]	$M_n \times 10^{-4}$ [c]	M_w/M_n[c]
1	[Rh(cod)$_2$]BF$_4$	NaOH	100	5.8	2.5
2	[Rh(cod)$_2$]BF$_4$	NaOH	97	5.5	2.9
3[d]	[Rh(cod)$_2$]BF$_4$	NaOH	90	2.9	3.0
4	[Rh(nbd)$_2$]ClO$_4$	NaOH	100	6.4	4.2
5	[Rh(cod)(tos)(H$_2$O]	NaOH	90	8.5	2.1
6	[Rh(cod)$_2$]BF$_4$	diethylamine	85	4.0	3.4
7	[Rh(nbd)$_2$]ClO$_4$	diethylamine	88	16	4.9

[a] Polymerized under nitrogen; [**1**-H] = 0.5 M, [**1**-H]/[Rh] = 200, [base]/[**1**-H] = 1.05 (run 2), 1.5 (runs 1, 3−7). [b] Ethanol insoluble part (runs 1−5) and H$_2$O insoluble part after acidification with HCl (runs 6, 7). [c] Determined by SEC (polystyrene standards) as its methyl ester. [d] Polymerized in air for 48 h.

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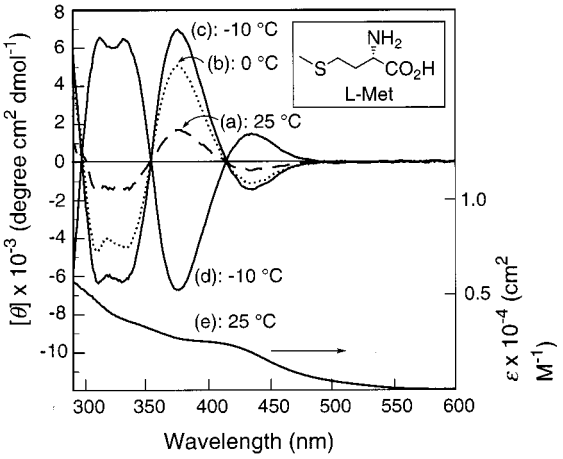

Figure 1. CD spectra of poly-**1**-Na (1.0 mg/mL) with L-Met (a, b, c) and D-Met (d) in H_2O (pH = 7.7) at 25 (a), 0 (b), and −10 °C (c, d). Absorption spectrum of poly-**1**-Na with L-Met at 25 °C is also shown in (e); the molar ratio of Met to monomer units of poly-**1**-Na is 10. The CD spectra were measured on a Jasco J-725 spectropolarimeter with a temperature controller in a 0.10 cm quartz cell.

Figure 1 shows typical CD and absorption spectra of poly-**1**-Na in the presence of a free amino acid, D- and L-methionine (D- and L-Met), in water. The complexes showed split-type ICDs of mirror images even in water. The ICD intensity increased with decreasing temperature and also increased with increasing concentration of L-Met and reached a value ($[\theta] = 16\,500$ deg cm^2 dmol^{-1} at 375 nm at [L-Met]/[poly-**1**-Na] = 30 (−10 °C)). These results clearly indicate that the complexation involves an equilibrium in the ion-exchange reactions[15] between bound sodium ions of poly-**1**-Na and amino acid zwitterions, and the polymer may be transformed into the helical conformation with a predominant screw sense by interacting with the bound amino acids in water. The absorption spectra showed a blue shift with decreasing temperature, indicating that the polymer may have a rather tight helical conformation at lower temperatures.

Poly-**1**-Na formed a complex with other natural amino acids including the L-isomers of glutamine, leucine, isoleucine, phenylalanine, tryptophan, arginine, and lysine through noncovalent interactions to exhibit ICDs (see Table S-1 in Supporting Information).[16] The complexes with the tested L-amino acids exhibited the same Cotton effect signs except for L-phenylalanine.[17]

Although a number of receptor molecules for protected amino acids have been prepared for chiral or chirality recognition or enantioselective transport through liquid membranes, these results have been obtained in organic media, where attractive interactions such as hydrogen-bond and electrostatic interactions can predominate.[18] The design of a model receptor for natural amino acids in water is still difficult.[19] However, the present results significantly indicate that polyelectrolytes may be a promising candidate for this purpose, because polyelectrolytes including DNA, RNA, and proteins are completely different from small electrolytes; that is, a portion of the counterions are bound to polyelectrolytes of sufficiently high charge density even in water, whereas small electrolytes exhibit only the dissociated free ions.[20] This substantial effect of polyelectrolytes must be responsible for the unprecedented helicity induction on poly-**1**-Na with natural amino acids in water. To the best of our knowledge, the present study is the first example of the prevailing helix formation of an achiral (macro)molecule induced by natural amino acids in water.[21]

In summary, we have developed a very simple and easy method for preparing *cis-transoidal* polyacetylene bearing a carboxy group and helicity induction of the polymer in water. This simple methodology may be applicable to the polymerization and helicity induction of other variety of acetylenes bearing a functional group in water. The use of chiral chromophoric polyelectrolytes may provide a novel approach for the development of new chiral sensory systems in water. We are now trying to lower the polydispersities in the present polymerization systems, as well as to elucidate the mechanism of helicity induction on poly-**1**-Na assisted by interaction with free amino acids.

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Supporting Information Available: Experimental procedures, NMR spectra of polymers, CD results of the complexes of poly-**1**-Na with other natural amino acids in water, and ICD intensity changes in the pH and salt concentration for the complex of poly-**1**-Na with L-methionine. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) The magnitude of the ICDs was significantly influenced by the pH and salt (NaCl) concentration, which is consistent with the ionic nature of the interaction. ICD intensity changes in the pH and salt concentration for the complex of poly-**1**-Na with L-methionine are available in the Supporting Information. ICD intensities decreased slowly with time probably because the polymer gradually decomposed or isomerized accompanied by a decrease in the UV−vis intensity.

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