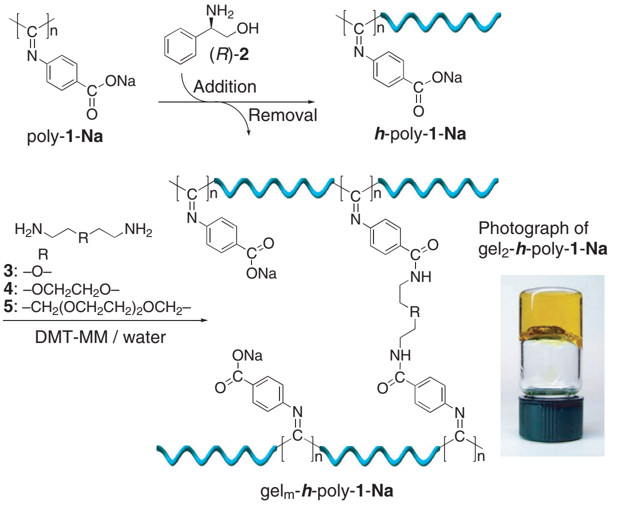
An Optically Active Hydrogel Composed of Cross-linked Poly(4-carboxyphenyl isocyanide) with a Macromolecular Helicity Memory

Masayoshi Ishikawa, Daisuke Taura, Katsuhiro Maeda, and Eiji Yashima*
Department of Molecular Design and Engineering, Graduate School of Engineering, Nagoya University,
Chikusa-ku, Nagoya 464-8603

(Received January 22, 2004; CL-040085)

Hydrogels composed of a poly(phenyl isocyanide) bearing a carboxylate group with a macromolecular helicity memory were synthesized by cross-linking with achiral diamines in water, and the obtained hydrogels were found to maintain their memory even at 90 °C in water, although the helical polymer before the cross-linking lost its memory at high temperature.

The design and synthesis of helical polymers and supramolecular helical assemblies have recently attracted significant attention because of their possible applications as novel chiral materials, such as liquid crystals and chiral selectors.[1] We previously reported that optically inactive polyacetylenes bearing various functional pendant groups such as a carboxy[2] and a phosphonate group[3] exhibited an induced circular dichroism (ICD) in the polymer backbone region because of a predominantly one-handed helix formation upon complexation with chiral amines, and the induced macromolecular helicity could be memorized when the amines were replaced by achiral amines.[4] A similar macromolecular helicity induction is possible in an achiral polyisocyanide, the sodium salt of poly(4-carboxyphenyl isocyanide) (poly-**1**-**Na**), with chiral amines in water as well as in DMSO.[5] However, in sharp contrast to the previously reported helical chirality memory of the polyacetylenes, the helicity of the polyisocyanide remains after complete removal of the chiral amines, and further modifications of the side group to carboxy and esters can be possible without loss of the macromolecular helicity memory.[5b] The memory of the helical polyisocyanide (***h***-poly-**1**-**Na**) is retained for a long time in water at room temperature, but completely disappears at high temperature.[5b] In order to improve the stability of the helical conformation of ***h***-poly-**1**-**Na** and also to develop novel optically active gels with a macromolecular helicity memory, we prepared ***h***-poly-**1**-**Na**-based hydrogels by the cross-linking (condensation) of ***h***-poly-**1**-**Na** with diamines (Scheme 1) and investigated the stability of the helical conformation of the gels using CD spectroscopy.



Scheme 1. Gel synthesis by cross-linking of ***h***-poly-**1**-**Na** with achiral diamine (**3**–**5**) in the presence of DMT-MM in water.

h-Poly-**1**-**Na** was prepared in a similar method as previously reported.[5b] Poly-**1**-**Na**, which had been prepared by polymerization of the corresponding monomer with $NiCl_2 \cdot 6H_2O$ as a catalyst in water (the number-average molecular weight was 3.3×10^4, as determined by size-exclusion chromatography with polystyrene standards in chloroform as its methyl esters), was annealed with (*R*)-phenylglycinol ((*R*)-**2**) in water at 50 °C for 44 days ([(*R*)-**2**]/[poly-**1**-**Na**] = 10). During this helicity induction process, the helical structure of the polyisocyanide was automatically memorized, probably through configurational isomerization around the C=N double bonds (*syn–anti* isomerization),[5b] so that the isolated ***h***-poly-**1**-**Na** containing no (*R*)-**2** exhibited optical activity; the molar ellipticity at 360 nm ($\Delta\varepsilon_{360}$) of the ***h***-poly-**1**-**Na** was -10.3 in water. Figure 1a shows a CD spectrum of the isolated ***h***-poly-**1**-**Na** in water. The polymer formed a predominantly one-handed helix and exhibited an ICD in the imino chromophore region of the polymer backbone (280–450 nm) as well as in the pendant aromatic regions (200–280 nm). The CD patterns and $\lambda_{\max}$ of the Cotton effects are very similar to those of the reported optically active poly(phenyl isocyanide)s bearing bulky chiral substituents on the phenyl moieties.[6]

The ***h***-poly-**1**-**Na** gels were then synthesized by the cross-linking of ***h***-poly-**1**-**Na** with diamines (**3**–**5**) in the presence of a condensation reagent, 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-

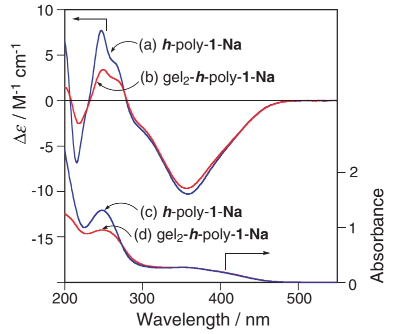


Figure 1. CD spectra of ***h***-poly-**1**-**Na** in water (a) and gel$_2$-***h***-poly-**1**-**Na** swollen in water (b) at room temperature. Absorption spectra of ***h***-poly-**1**-**Na** (c) and gel$_2$-***h***-poly-**1**-**Na** (d) are also shown. The CD intensity of gel$_2$-***h***-poly-**1**-**Na** was normalized using the molar absorptivity at 354 nm ($\varepsilon_{354} = 1590$).

methylmorpholinium chloride (DMT-MM),[7] in water, as schematically illustrated in Scheme 1.[8] The results of the cross-linking are summarized in Table 1. The cross-linking efficiency was highly dependent on the structure of the diamines, the molar ratio to the monomer units of ***h***-poly-**1**-**Na**, and the ***h***-poly-**1**-**Na** concentration. When the molar ratio of the diamines to the monomer units of ***h***-poly-**1**-**Na** in the feed and the concentration of ***h***-poly-**1**-**Na** were greater than 35 (**3** and **4**) and 60 (**5**) (mol %), and 0.16 (**3**) and 0.18 (**4** and **5**) M, respectively, yellow transparent gels insoluble in water were successfully obtained in high yields. However, for a dilute concentration of ***h***-poly-**1**-**Na** or using smaller amounts of the diamines, ***h***-poly-**1**-**Na** gels insoluble in water could not be obtained. Presumably, the intramolecular condensation reaction preferentially occurred rather than the intermolecular cross-linking.

Figure 1b shows a CD spectrum of an ***h***-poly-**1**-**Na** gel prepared with the diamine **4** (gel$_2$-***h***-poly-**1**-**Na**) swollen in water at room temperature. The CD intensity of the gel in the main chain region slightly decreased, while that in the pendant aromatic region significantly decreased accompanied with a decrease in the absorption in the same aromatic region (Figures 1c and 1d). The reason is not clear at present, but the intermolecular cross-linkings appear to disturb the pendant aromatic groups in a one-handed helical array leading to changes in the CD and absorption spectra.

The thermal stability of the gels was then measured by monitoring the decrease in the CD intensity in the polymer backbone region with time at different temperatures and the result was compared with that of the ***h***-poly-**1**-**Na**. As previously reported, the CD intensity of ***h***-poly-**1**-**Na** gradually decreased at 30 °C, and the polymer completely lost its optical activity derived from the macromolecular helicity memory at 80 °C (Figure 2a).[5b] On the contrary, the cross-linking of the polymer effectively improved the stability of the helical conformation; in particular, the gel$_2$-***h***-poly-**1**-**Na** did not lose its optical activity even upon continuous heating at 90 °C for 37 h in water.[9] The swelling ratio of the gel hardly changed with temperature. Other gels were also stable at high temperature, although their CD intensities slightly decreased after annealing at 90 °C (Table 1).

In conclusion, we have successfully prepared novel optically active poly(phenyl isocyanide)-based hydrogels that maintain their induced helical structure with excellent thermal stability. These hydrogels exhibited ICDs due to the predominantly one-handed helix in the gels. Although a large number of polymer-based, optically active hydrogels have been prepared mostly using biological polymers,[10] this is the first example of an optically active gel with a macromolecular helicity memory.[11] The present strategy can be applicable for designing and synthesizing other various optically active helical gels bearing various achiral and chiral functional pendants. We believe that these optically active gels will be used not only as chiral materials for separating and sensing enantiomers, but also as biomimetic gels. This work is now in progress.

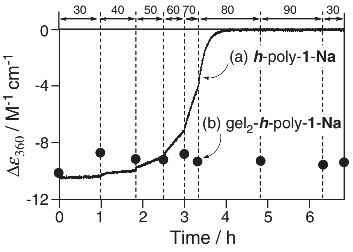


Figure 2. Stability of the macromolecular helicity memory of ***h***-poly-**1**-**Na** in water (a) and gel$_2$-***h***-poly-**1**-**Na** swollen in water (b) studied by CD following temperature jumps. The gel was allowed to stand in water at fixed temperature and its CD was then measured at room temperature.

Table 1. Cross-linking of ***h***-poly-**1**-**Na** with diamine (**3**–**5**) in the presence of condensation reagent (DMT-MM) in water[a]

Gel	Diamine in feed / mol %	DMT-MM in feed / mol %	gel-***h***-poly-**1**-**Na** $\Delta\varepsilon$[b]	$\Delta\varepsilon$ (h)[c]
gel$_1$-***h***-poly-**1**-**Na**[d]	**3** (35)	70	−8.96	−7.41 (1)
gel$_2$-***h***-poly-**1**-**Na**	**4** (35)	70	−9.73	−9.55 (37)
gel$_3$-***h***-poly-**1**-**Na**	**5** (60)	120	−9.20	−7.78 (15)

[a]Cross-linked under nitrogen at room temperature; [monomer units of ***h***-poly-**1**-**Na**] = 0.18 M. The cross-linking time was 18, 23, and 2 h for the diamines **3**–**5**, respectively. [b]CD spectra were measured at room temperature; $\Delta\varepsilon$ (M^{-1} cm^{-1}) at 360 nm. The CD intensities were normalized using the molar absorptivity at 354 nm ($\varepsilon_{354} = 1590$). [c]Measured after the gels had been allowed to stand in water at 90 °C for hours. [d][monomer units of ***h***-poly-**1**-**Na**] = 0.16 M.

This work was partially supported by Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science and the Ministry of Education, Culture, Sports, Science and Technology, Japan and ERATO, JST.

References and Notes

1 For reviews: a) M. M. Green, N. C. Peterson, T. Sato, A. Teramoto, R. Cook, and S. Lifson, *Science*, **268**, 1860 (1995). b) M. Fujiki, *Macromol. Rapid. Commun.*, **22**, 539 (2001). c) D. J. Hill, M. J. Mio, R. B. Prince, T. S. Hughes, and J. S. Moore, *Chem. Rev.*, **101**, 3893 (2001). d) Y. Okamoto and T. Nakano, *Chem. Rev.*, **101**, 4013 (2001). e) J. A. A. W. Elemans, A. E. Rowan, and R. J. M. Nolte, *J. Mater. Chem.*, **13**, 2661 (2003). f) L. Brunsveld, E. W. Meijer, A. E. Rowan, and R. J. M. Nolte, "Materials-Chirality: Volume 24 of Topics in Stereochemistry," John Wiley & Sons (2003), p 373.

2 a) E. Yashima, T. Matsushima, and Y. Okamoto, *J. Am. Chem. Soc.*, **119**, 6345 (1997). b) M. A. Saito, K. Maeda, H. Onouchi, and E. Yashima, *Macromolecules*, **33**, 4616 (2000). c) K. Maeda, H. Goto, and E. Yashima, *Macromolecules*, **34**, 1160 (2001).

3 H. Onouchi, K. Maeda, and E. Yashima, *J. Am. Chem. Soc.*, **123**, 7441 (2001).

4 E. Yashima, K. Maeda, and Y. Okamoto, *Nature*, **399**, 449 (1999).

5 a) M. Ishikawa, K. Maeda, and E. Yashima, *J. Am. Chem. Soc.*, **124**, 7448 (2002). b) M. Ishikawa, K. Maeda, Y. Mitsutsuji, and E. Yashima, *J. Am. Chem. Soc.*, **126**, 732 (2004).

6 a) F. Takei, K. Yanai, K. Onitsuka, and S. Takahashi, *Chem.—Eur. J.*, **6**, 983 (2000). b) D. B. Amabilino, E. Ramos, J.-L. Serrano, T. Sierra, and J. Veciana, *J. Am. Chem. Soc.*, **120**, 9126 (1998). c) N. Hida, F. Takei, K. Onitsuka, K. Shiga, S. Asaoka, T. Iyoda, and S. Takahashi, *Angew. Chem., Int. Ed.*, **42**, 4349 (2003).

7 M. Kunishima, C. Kawachi, K. Hioki, K. Terao, and S. Tani, *Tetrahedron*, **57**, 1551 (2001).

8 A typical experimental procedure: Stock solutions of DMT-MM (89 mg/mL) and diamine **4** (60 mg/mL) in water were prepared. ***h***-Poly-**1**-**Na** (20 mg, 0.12 mmol) was dissolved in water (0.3 mL) and to this was added the stock solutions of DMT-MM (0.26 mL) and then **4** (0.10 mL) at room temperature. The cross-linking reaction gradually occurred. After 23 h, the resulting gel was allowed to stand in water overnight to remove the remaining condensing reagent and water-soluble ***h***-poly-**1**-**Na**. The gel was sandwiched between quartz plates (2-cm diameter), and the CD and absorption spectra were measured.

9 For examples of helical polymers or peptides stabilized by intramolecular cross-linking: a) H. E. Blackwell and R. H. Grubbs, *Angew. Chem., Int. Ed.*, **37**, 3281 (1998). b) S. Hecht and A. Khan, *Angew. Chem., Int. Ed.*, **42**, 6021 (2003).

10 a) R. Kishi, M. Sisido, and S. Tazuke, *Macromolecules*, **23**, 3779 (1990). b) W. A. Petka, J. L. Harden, K. P. McGrath, D. Wirtz, and D. A. Tirrell, *Science*, **281**, 389 (1998). c) C. Wang, R. J. Stewart, and J. Kopecek, *Nature*, **397**, 417 (1999). d) A. Kikuchi and T. Okano, *Adv. Drug Delivery Rev.*, **54**, 53 (2002).

11 Chiral stimuli-responsive gels composed of an induced helical poly(4-carboxyphenylacetylene) were prepared by the cross-linking with diamines: H. Goto, H. Q. Zhang, and E. Yashima, *J. Am. Chem. Soc.*, **125**, 2516 (2003).

Published on the web (Advance View) April 12, 2004; DOI 10.1246/cl.2004.550