Mechanism of Helix Induction on a Stereoregular Poly((4-carboxyphenyl)acetylene) with Chiral Amines and Memory of the Macromolecular Helicity Assisted by Interaction with Achiral Amines

Katsuhiro Maeda,[†] Kazuhide Morino,[†] Yoshio Okamoto,[‡] Takahiro Sato,[§] and Eiji Yashima*,[†]

Contribution from the Department of Molecular Design and Engineering and Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Chikusa-ku, Nagoya 464-8603, Japan, and Department of Macromolecular Science, Osaka University, Machikaneyama-cho 1-1, Toyonaka, Osaka 560-0043, Japan

Received December 19, 2003; E-mail: yashima@apchem.nagoya-u.ac.jp

Abstract: Cis−transoidal poly((4-carboxyphenyl)acetylene) (poly-**1**) is an optically inactive polymer but forms an induced one-handed helical structure upon complexation with optically active amines such as (*R*)-(1-(1-naphthyl)ethyl)amine ((*R*)-**2**) in DMSO. The complexes show a characteristic induced circular dichroism (ICD) in the UV−visible region of the polymer backbone. Moreover, the macromolecular helicity of poly-**1** induced by (*R*)-**2** can be "memorized" even after complete replacement of (*R*)-**2** by various achiral amines. We now report fully detailed studies on the mechanism of the helicity induction and memory of the helical chirality of poly-**1** by means of UV−visible, CD, and infrared spectroscopies. We have found that a one-handed helix is cooperatively induced on poly-**1** upon the ion pair formation of the carboxy groups of poly-**1** with optically active amines and that the bulkiness of the chiral amines plays a crucial role for inducing an excess of a single-handed helix. On the other hand, the free ion formation was found to be essential for the macromolecular helicity memory of poly-**1** after the replacement of the chiral amine by achiral amines, since the intramolecular electrostatic repulsion between the neighboring carboxylate ions of poly-**1** significantly contributes to reduce the atropisomerization process of poly-**1**. On the basis of the mechanism of helicity induction and the memory of the helical chirality drawn from the present studies, we succeeded in creating an almost perfect memory of the induced macromolecular helicity of poly-**1** with (*R*)-**2** by using 2-aminoethanol as an achiral chaperoning molecule to assist in maintaining the memory of helical chirality.

Introduction

Proteins and nucleic acids are typical optically active, biological polymers with a one-handed helicity.[1] Their helical structures seem to be essential for their sophisticated and fundamental functions in nature. After discovery of the helical structures in these biopolymers, significant attention has been paid to developing artificial helical polymers[2] and oligomers (foldamers)[3] with a controlled helix-sense. Such studies are

interesting and valuable not only to mimic biopolymers but also to develop novel chiral materials in areas such as liquid crystals, membranes, and chiral selectors.[2,3] To date, a large number of optically active polymers have been prepared, but optically active polymers, whose optical activity is largely governed by the helical chirality of the polymer backbone, are still limited.[2] Fully synthetic helical polymers prepared so far can be classified into two types on the basis of the nature of their helical conformations; one is a stable (or static) helical polymer even in solution, and the other is a dynamic helical polymer. Poly-(triphenylmethyl methacrylate),[2b,4] polychloral,[5] polyiso-cyanides,[2c,2i,6] and poly(2,3-quinoxalines)[7] belong to the former category. The one-handed helical polymers have been prepared by the screw-sense selective polymerization of achiral or

[†] Department of Molecular Design and Engineering, Nagoya University.
[‡] Department of Applied Chemistry, Nagoya University.
[§] Osaka University.

(1) (a) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984. (b) Schulz, G. E.; Schirmer, R. H. *Principles of Protein Structure*; Springer-Verlag: New York, 1979.

(2) Reviews: (a) Farina, M. In *Topics in Stereochemistry*; Ernest, L. E., Samuel, H. W., Eds.; John Wiley & Sons: New York, 1987; Vol. 17. (b) Okamoto, Y.; Nakano, T. *Chem. Rev.* **1994**, *94*, 349−372. (c) Nolte, R. J. M. *Chem. Soc. Rev.* **1994**, *23*, 11−19. (d) Green, M. M.; Peterson, N. C.; Sato, T.; Teramoto, A.; Cook, R.; Lifson, S. *Science* **1995**, *268*, 1860−1866. (e) Pu, L. *Acta Polym.* **1997**, *48*, 116−141. (f) Rowan, A. E.; Nolte, R. J. M. *Angew. Chem., Int. Ed.* **1998**, *37*, 63−68. (g) Green, M. M.; Park, J.-W.; Sato, T.; Teramoto, A.; Lifson, S.; Selinger, R. L. B.; Selinger, J. V. *Angew. Chem., Int. Ed.* **1999**, *38*, 3138−3154. (h) Nakano, T.; Okamoto, Y. *Chem. Rev.* **2001**, *101*, 4013−4038. (i) Cornelissen, J. J. L. M.; Rowan, A. E.; Nolte, R. J. M.; Sommerdijk, N. A. J. M. *Chem. Rev.* **2001**, *101*, 4039−4070. (j) Fujiki, M. *Macromol. Rapid Commun.* **2001**, *22*, 539−563.

(3) Reviews: (a) Gellman, S. H. *Acc. Chem. Res.* **1998**, *31*, 173−180. (b) Hill, D. J.; Mio, M. J.; Prince, R. B.; Hughes, T. S.; Moore, J. S. *Chem. Rev.* **2001**, *101*, 3893−4011. (c) Cheng, R. P.; Gellman, S. H.; DeGrado, W. F. *Chem. Rev.* **2001**, *101*, 3219−3232.

(4) (a) Okamoto, Y.; Suzuki, K.; Ohta, K.; Hatada, K.; Yuki, H. *J. Am. Chem. Soc.* **1979**, *101*, 4763−4765. (b) Okamoto, Y.; Yashima, E. *Prog. Polym. Sci.* **1990**, *15*, 263−298. (c) Nakano, T.; Okamoto, Y.; Hatada, K. *J. Am. Chem. Soc.* **1992**, *114*, 1318−1329.

(5) (a) Corley, L. S.; Vogl, O. *Polym. Bull.* **1980**, *3*, 211−217. (b) Ute, K.; Hirose, K.; Kashimoto, H.; Nakayama, H.; Hatada, K.; Vogl, O. *Polym. J.* **1993**, *25*, 1175−1186.

prochiral monomers with chiral catalysts or initiators. These polymers have bulky substituents at the side chains, so that a one-handed helical conformation is formed and stabilized by steric hindrance during the polymerization under kinetic control.

On the other hand, polyisocyanates[2d,g,8] and polysilanes[2j,9] are typical helical polymers belonging to the latter category; they have long, alternate sequences of left- and right-handed helices. An equilibrium exists in solution between the helices separated by the helix reversal points that move along the polymer backbone; therefore, they are called dynamic helical polymers. However, in these polymers the helix reversals occur infrequently so that they have a long persistence length. Due to this remarkable feature, optically active polyisocyanates and polysilanes with a predominantly one-handed helix-sense have been successfully prepared by introducing a tiny amount of a chiral factor to the polymers, such as the copolymerization of achiral monomers with a small amount of optically active monomers. The helix-sense is determined under thermodynamic control.[8,9]

Poly(phenylacetylene)s bearing an optically active substituent are also considered to take a helical conformation with a predominant one-handedness in solution, because they show a characteristic induced circular dichroism (ICD) in the $\pi-\pi^*$ electronic transition region due to the conjugated double bonds in the polymer main chain.[10,11] Recently, we investigated the

Chart 1
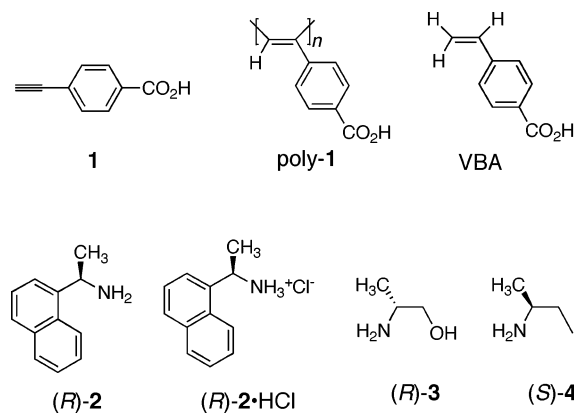
temperature dependence of the CD spectra for the homopolymers of optically active phenylacetylenes and their copolymers with achiral phenylacetylenes in detail and found that the helical conformations are dynamic in nature like polyisocyanates because the ICD magnitudes of several optically active poly(phenylacetylene)s composed of chiral and achiral phenylacetylenes significantly increased with decreasing temperature. On the basis of the theoretical analysis of the CD data, we succeeded in estimating the thermodynamic stability parameters for the helical conformations.[12]

Optically active helical polymers described above can be prepared either by polymerization of optically active monomers or by screw-sense selective polymerization; their helical structures and helix-senses are determined by chiral or bulky substituents covalently bonded to the polymer main chains, thermodynamically or kinetically, during the polymerization process.

Besides these helical polymers, we recently succeeded in inducing a predominantly one-handed helical conformation in optically inactive polymers bearing functional groups upon noncovalent complexation with optically active small molecules capable of interacting with the functional groups of the polymers. Cis–transoidal poly((4-carboxyphenyl)acetylene) (poly-**1**, Chart 1) is the first example of such a noncovalent, one-handed helicity induction.[13] In the presence of optically active amines, poly-**1** forms complexes with the amines through noncovalent, chiral acid–base interaction;[14] a one-handed helical structure can be induced on poly-**1**, resulting in a characteristic ICD in the UV–visible region of the polymer backbone (Figure

(6) (a) Nolte, R. J. M.; van Beijnen, A. J. M.; Drenth, W. *J. Am. Chem. Soc.* **1974**, *96*, 5932−5933. (b) Kamer, P. C. J.; Nolte, R. J. M.; Drenth, W. *J. Am. Chem. Soc.* **1988**, *110*, 6818−6825. (c) Deming, T. J.; Novak, B. M. *J. Am. Chem. Soc.* **1992**, *114*, 7926−7927. (d) Takei, F.; Yanai, K.; Onitsuka, K.; Takahashi, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1554−1556. (e) Cornelissen, J. J. L. M.; Fischer, M.; Sommerdijk, N. A. J. M.; Nolte, R. J. M. *Science* **1998**, *280*, 1427−1430. (f) Amabilino, D. B.; Ramos, E.; Serrano, J.-L.; Sierra, T.; Veciana, J. *J. Am. Chem. Soc.* **1998**, *120*, 9126−9134. (g) Takei, F.; Yanai, K.; Onitsuka, K.; Takahashi, S. *Chem.−Eur. J.* **2000**, *6*, 983−993. (h) Cornelissen, J. J. L. M.; Donners, J. J. J. M.; de Gelder, R.; Graswinckel, W. S.; Metselaar, G. A.; Rowan, A. E.; Sommerdijk, N. A. J. M.; Nolte, R. J. M. *Science* **2001**, *293*, 676−680.

(7) (a) Ito, Y.; Ihara, E.; Murakami, M. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1509−1510. (b) Ito, Y.; Miyake, T.; Hatano, S.; Shima, R.; Ohara, T.; Suginome, M. *J. Am. Chem. Soc.* **1998**, *120*, 11880−11893.

(8) (a) Green, M. M.; Andreola, C.; Muñoz, B.; Reidy, M. P.; Zelo, K. *J. Am. Chem. Soc.* **1988**, *110*, 4063−4065. (b) Green, M. M.; Reidy, M. P.; Johnson, R. J.; Darling, G.; O'Leary, D. J.; Willson, G. *J. Am. Chem. Soc.* **1989**, *111*, 6452−6454. (c) Lifson, S.; Andreola, C.; Peterson, N. C.; Green, M. M. *J. Am. Chem. Soc.* **1989**, *111*, 8850−8858. (d) Okamoto, Y.; Matsuda, M.; Nakano, T.; Yashima, E. *J. Polym. Sci., Part A: Polym. Chem.* **1994**, *32*, 309−315. (e) Maeda, K.; Matsuda, M.; Nakano, T.; Okamoto, Y. *Polym. J.* **1995**, *27*, 141−146. (f) Müller, M.; Zentel, R. *Macromolecules* **1996**, *29*, 1609−1617. (g) Maeda, K.; Okamoto, Y. *Macromolecules* **1998**, *31*, 1046−1052. (h) Li, J.; Schuster G. B.; Cheon, K.-S.; Green, M. M.; Selinger, J. V. *J. Am. Chem. Soc.* **2000**, *122*, 2603−2612.

(9) (a) Fujiki, M. *J. Am. Chem. Soc.* **1994**, *116*, 6017−6018. (b) Fujiki, M. *J. Am. Chem. Soc.* **1994**, *116*, 11976−11981. (c) Fujiki, M. *J. Am. Chem. Soc.* **2000**, *122*, 3336−3343.

(10) (a) Yamaguchi, M.; Omata, K.; Hirama, M. *Chem. Lett.* **1992**, 2261−2262. (b) Aoki, T.; Kokai, M.; Shinohara, K.; Oikawa, E.; *Chem. Lett.* **1993**, 2009−2012. (c) Matsuura, K.; Furuno, S.; Kobayashi, K. *Chem. Lett.* **1998**, 847−848. (d) Kwak, G.; Masuda, T. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 71−77. (e) Li, B. S.; Cheuk, K. K. L.; Salhi, F.; Lam, J. W. Y.; Cha, J. A. K.; Xiao, X.; Bai, C.; Tang, B. Z. *Nano Lett.* **2001**, *1*, 323−328. For screw-sense selective polymerization, see: (f) Aoki, T.; Kaneko, T.; Maruyama, N.; Sumi, A.; Takahashi, M.; Sato, T.; Teraguchi, M. *J. Am. Chem. Soc.* **2003**, *125*, 6346−6347. For optically active aliphatic polyacetylenes, see: (g) Ciardelli, F.; Benedetti, E.; Pieroni, O. *Makromol. Chem.* **1967**, *103*, 1−18. (h) Ciardelli, F.; Lanzillo, S.; Pieroni, O. *Macromolecules* **1974**, *7*, 174−179. (i) Moore, J. S.; Gorman, C. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1991**, *113*, 1704−1712. (j) Kishimoto, Y.; Itou, M.; Miyatake, T.; Ikariya, T.; Noyori, R. *Macromolecules* **1995**, *28*, 6662−6666. (k) Aoki, T.; Shinohara, K.; Kaneko, T.; Oikawa, E. *Macromolecules* **1996**, *29*, 4192−4198. (l) Akagi, K.; Piao, G.; Kaneko, S.; Sakamaki, K.; Shirakawa, H.; Kyotani, M. *Science* **1998**, *282*, 1683−1686. (m) Nakako, H.; Nomura, R.; Tabata, M.; Masuda, T. *Macromolecules* **1999**, *32*, 2861−2864. (n) Nomura, R.; Fukushima, Y.; Nakako, H.; Masuda, T. *J. Am. Chem. Soc.* **2000**, *122*, 8830−8836. (o) Mitsuyama, M.; Kondo, K. *Macromol. Chem. Phys.* **2000**, *201*, 1613−1618. (p) Tabei, J.; Nomura, R.; Masuda, T. *J. Am. Chem. Soc.* **2002**, *124*, 5405−5409.

(11) (a) Yashima, E.; Huang, S.; Okamoto, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 1811−1812. (b) Yashima, E.; Matsushima, T.; Okamoto, Y. *Macromolecules* **1995**, *28*, 4184−4193. (c) Yashima, E.; Matsushima, T.; Nimura, T.; Okamoto, Y. *Korean Polym. J.* **1996**, *4*, 139−146. (d) Yashima, E.; Maeda, Y.; Okamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 8895−8896. (e) Yashima, E.; Maeda, Y.; Okamoto, Y. *Polym. J.* **1999**, *31*, 1033−1036. (f) Yashima, E.; Maeda, K.; Sato, O. *J. Am. Chem. Soc.* **2001**, *123*, 8159−8160. (g) Nishimura, T.; Takatani, K.; Sakurai, S.; Maeda, K.; Yashima, E. *Angew. Chem., Int. Ed.* **2002**, *41*, 3602−3604. (h) Morino, K.; Maeda, K.; Yashima, E. *Macromolecules* **2003**, *36*, 1480−1486.

(12) Morino, K.; Maeda, K.; Okamoto, Y.; Yashima, E.; Sato, T. *Chem.−Eur. J.* **2002**, *8*, 5112−5120.

(13) (a) Yashima, E.; Matsushima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1995**, *117*, 11596−11597. (b) Yashima, E.; Matsushima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6345−6359. (c) Yashima, E. *Anal. Sci.* **2002**, *18*, 3−6. (d) Maeda, K.; Morino, K.; Yashima, E. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3625−3631. (e) Yashima, E.; Maeda, K.; Nishimura, T. *Chem.−Eur. J.* **2004**, *10*, 42−51.

(14) For related counterion induction of supramolecular chirality, see: (a) Oda, R.; Huc, I.; Candau, S. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 2689−2691. (b) Oda, R.; Huc, I.; Schmutz, M.; Candau, S. J. *Nature* **1999**, *399*, 566−569. (c) Berthier, D.; Buffeteau, T.; Léger, J.-M.; Oda, R.; Huc, I. *J. Am. Chem. Soc.* **2002**, *124*, 13486−13494 and references therein.
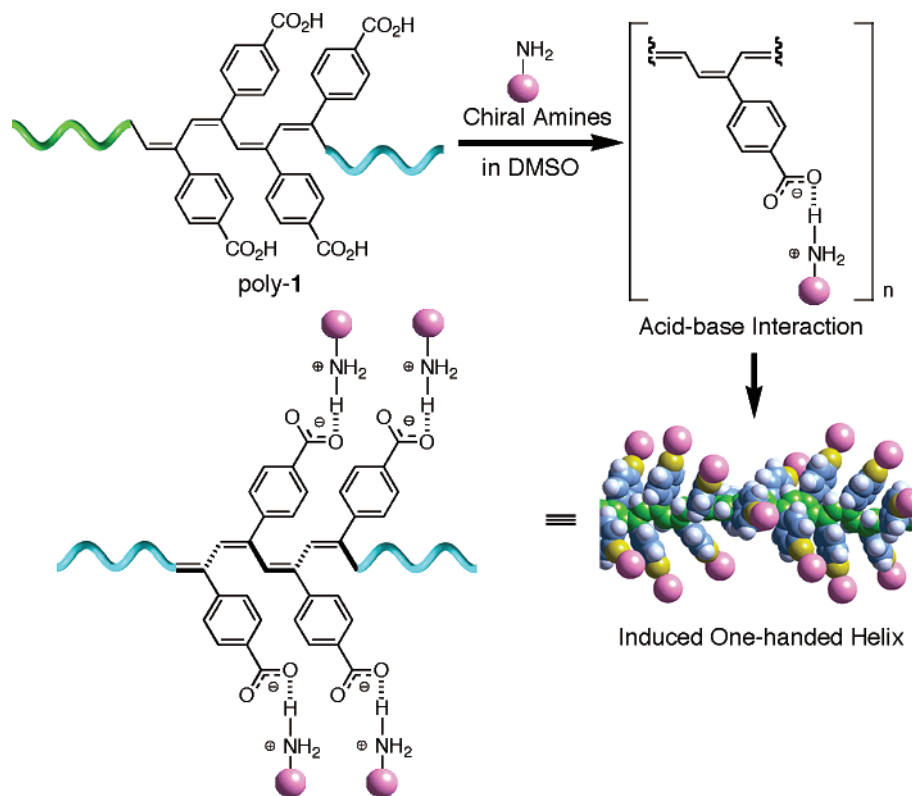
Figure 1. Schematic illustration of one-handed helicity induction on poly-**1** upon complexation with chiral amines. The original poly-**1** is drawn as a mixture of right- and left-handed helices (top), which change to a predominantly one-handed helix with chiral amines (bottom), thus exhibiting an ICD in the π-conjugated polymer backbone region.

1).[13] The split type of Cotton effect reflects the absolute configuration of the chiral amines; all primary amines of the same configuration gave the same Cotton effect signs. Therefore, the Cotton effect signs can be used as a novel probe for the assignments of the absolute configuration of the chiral amines.[13b,15] Poly-**1** is not a stiff but a flexible polymer because of its short persistent length (4.2 nm in dimethyl sulfoxide (DMSO)),[16] and therefore, a one-handed helicity induction may occur if the twist of adjacent double bonds around a single bond takes place favorably.[13b] However, our recent viscometric studies on the solution structure of poly-**1** in DMSO combined with theoretical analysis indicated that poly-**1** can be regarded as an analogue of a dynamic helical polymer of which right- and left-handed helical conformations are rapidly interconvertible.[16] Therefore, the appearance of ICDs of poly-**1** in the presence of chiral amines is considered to be due to a change in population of the dynamic helices (Figure 1).

Related stereoregular poly(phenylacetylene)s bearing other functional groups, such as a boronic acid residue,[17] an amino group,[18] a phosphonate group,[19] and a crown ether pendant[20] as well as aliphatic functional polyacetylenes,[21] also respond to the chirality of optically active compounds and form an induced one-handed helical structure, thus exhibiting a similar ICD in the UV−visible region in organic solvents.[13,18,20] Similar helicity induction can be possible in water through electrostatic interactions with a variety of biomolecules including amino acids, amino sugars, and peptides on water-soluble poly-(phenylacetylene)s including poly-**1**.[19,22]

Besides polyacetylene derivatives, similar helicity induction on an optically inactive polymer through noncovalent bonding interaction with chiral compounds has been reported for polyphosphazene,[23] polyisocyanide,[24] polyisocyanate,[25] polyguanidine,[26] polyaniline,[27] and polypyrrole.[28]

The macromolecular helicity induced on these polymers might be dynamic in nature. However, interestingly, we recently found that such induced helical chirality of poly-**1** by an optically

(15) For recent reviews of chirality recognition of chiral amines based on ICDs: see: (a) Canary, J. W.; Holmes, A. E.; Liu, J. *Enantiomer* **2001**, *6*, 181−188. (b) Borovkov, V. V.; Lintoluoto, J. M.; Inoue, Y. *J. Am. Chem. Soc.* **2001**, *123*, 2979−2989. (c) Kurtán, T.; Nesnas, N.; Li, Y.-Q.; Huang, X.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2001**, *123*, 5962−5973. (d) Tsukube, H.; Shinoda, S. *Chem. Rev.* **2002**, *102*, 2389−2403. (e) Allenmark, S. *Chirality* **2003**, *15*, 409−422.

(16) Ashida, Y.; Sato, T.; Morino, K.; Maeda, K.; Okamoto, Y.; Yashima, E. *Macromolecules* **2003**, *36*, 3345−3350.

(17) (a) Yashima, E.; Nimura, T.; Matsushima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9800−9801. (b) Kawamura, H.; Maeda, K.; Okamoto, Y.; Yashima, E. *Chem. Lett.* **2001**, 58−59.

(18) (a) Yashima, E.; Maeda, Y.; Okamoto, Y. *Chem. Lett.* **1996**, 955−956. (b) Yashima, E.; Maeda, Y.; Matsushima, T.; Okamoto, Y. *Chirality* **1997**, *9*, 593−600. (c) Maeda, K.; Okada, S.; Yashima, E.; Okamoto, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 3180−3189.

(19) Onouchi, H.; Maeda, K.; Yashima, E. *J. Am. Chem. Soc.* **2001**, *123*, 7441−7442.

(20) (a) Nonokawa, R.; Yashima, E. *J. Am. Chem. Soc.* **2003**, *125*, 1278−1283. (b) Nonokawa, R.; Yashima, E. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 1004−1013. (c) Nonokawa, R.; Oobo, M.; Yashima, E. *Macromolecules* **2003**, *36*, 6599−6606.

(21) (a) Yashima, E.; Goto, H.; Okamoto, Y. *Polym. J.* **1998**, *30*, 69−71. (b) Maeda, K.; Goto, H.; Yashima, E. *Macromolecules* **2001**, *34*, 1160−1164.

(22) Saito, M. A.; Maeda, K.; Onouchi, H.; Yashima, E. *Macromolecules* **2000**, *33*, 4616−4618.

(23) Yashima, E.; Maeda, K.; Yamanaka, T. *J. Am. Chem. Soc.* **2000**, *122*, 7813−7814.

(24) (a) Ishikawa, M.; Maeda, K.; Yashima, E. *J. Am. Chem. Soc.* **2002**, *124*, 7448−7458. (b) Ishikawa, M.; Maeda, K.; Mitsutsuji, Y.; Yashima, E. *J. Am. Chem. Soc.* **2004**, *126*, 732−733.

(25) (a) Green, M. M.; Kartri, C.; Peterson, N. C. *J. Am. Chem. Soc.* **1993**, *115*, 4941−4942. (b) Maeda, K.; Yamamoto, N.; Okamoto, Y. *Macromolecules* **1998**, *31*, 5924−5926.

(26) Schlitzer, D. S.; Novak, B. M. *J. Am. Chem. Soc.* **1998**, *120*, 2196−2197.

(27) Majidi, M. R.; Kane-Maguire, L. A. P.; Wallace, G. G. *Polymer* **1995**, *36*, 3597−3599.

(28) Zhou, Y.; Yu, B.; Zhu, G. *Polymer* **1997**, *38*, 5493−5495.

Table 1. Molecular Weight Effect of Poly-**1** on Helicity Induction with Chiral Amines in DMSO

poly-**1**	$10^{-4}M_n$ $(M_w/M_n)^a$	DP[b]	ϵ_{400}	second Cotton $(10^{-4}[\theta]\ (\lambda))^c$		
				(R)-**2**[d]	(R)-**3**[e]	(S)-**4**[f]
poly-**1a**	1.7 (2.1)	106	2840	−2.82 (376)	−2.88 (374)	0.89 (376)
poly-**1b**	3.3 (2.8)	206	3130	−2.95 (377)	−3.53 (374)	1.37 (377)
poly-**1c**	13 (4.3)[g]	812	3180	−3.08 (376)	−3.61 (373)	1.41 (377)[h]

[a] Determined by SEC as its methyl ester using polystyrene standards with THF (poly-**1a** and poly-**1b**) or chloroform (poly-**1c**) as the eluent. [b] Degree of polymerization of poly-**1**. [c] The molar ratio of (R)-**2**, (R)-**3**, and (S)-**4** to monomer units of poly-**1** was 10. The concentrations of poly-**1** were 3 ((R)-**2**) and 1 mg/mL ((R)-**3** and (S)-**4**), respectively; $[\theta]$ in deg cm^2 dmol^{-1} and λ in nm. [d] Measured just after the preparation of samples. [e] Measured after the samples had been allowed to stand at ambient temperature for 24 (poly-**1a**), 30 (poly-**1b**), and 45 h (poly-**1c**). [f] Measured after the samples had been allowed to stand at 80 °C for 5 (poly-**1a**), 6 (poly-**1b**), and 20 h (poly-**1c**). [g] Chloroform-soluble part. [h] The molar ratio of (S)-**4** to monomer units of poly-**1c** was 3. The concentration of poly-**1c** was 5 mg/mL.

active amine could be maintained, namely "memorized", when the chiral amine was replaced by various achiral amines in DMSO.[29,30] The memory of macromolecular helicity was not transient but lasted for an extremely long time. The memory efficiency was influenced by small structural changes in the achiral amines.[29]

This work is concerned with the mechanism of helix formation of poly-**1** in the presence of chiral amines and the memory of the helicity process with achiral amines by means of CD and IR spectroscopies. The results will contribute to the construction of novel helical polymeric architectures with a desired helix-sense and supramolecular helical assemblies with desired achiral molecules in a one-handed helical array.

Results and Discussion

Molecular Weight Effect of Poly-1 on Helicity Induction. In the previous studies, we used rather low molecular weight poly-**1**s (M_n = 17 000 and 46 000) prepared by the polymerization of (4-((triphenylmethoxy)carbonyl)phenyl)acetylene with [Rh(nbd)Cl]$_2$ (nbd = norbornadiene), followed by hydrolysis of the ester group, for the ICD experiments.[13a,b,29] Our recent finding of the direct polymerization of (4-carboxyphenyl)-acetylene (**1**) in water with a water-soluble rhodium catalyst in the presence of bases, such as diethylamine, made it possible to prepare a higher molecular weight poly-**1**.[22] Therefore, we first investigated the effect of molecular weights of poly-**1** on ICD with chiral amines ((R)-**2** and (S)-**4**) and an amino alcohol ((R)-**3**) in DMSO (Chart 1). The molecular weights of cis−transoidal poly-**1** (poly-**1a**−**c**) prepared with rhodium catalysts are summarized in Table 1 together with the ICD results with (R)-**2**, (R)-**3**, and (S)-**4** and molar absorptivities (ϵ_{400}) of poly-**1**s in DMSO at ambient temperature (23−25 °C).[13b,22,29] These amines were selected as a chiral bulky ((R)-**2**) and a less bulky amine ((S)-**4**) and as a chiral amino alcohol ((R)-**3**), since we

know that the magnitude of the ICD of poly-**1** corresponding to an excess of a single-handed helix (right- and left-handed helices) increases with an increase in the bulkiness of the chiral amines, whereas chiral amino alcohols generate a very intense ICD irrespective of the bulkiness.[13b] Although the assignments of the splitting Cotton effects in the ICD of poly-**1** with chiral amines have not yet been done, the presumed molecular model of the poly-**1**−(R)-primary amines or -amino alcohols suggests that the poly-**1** may have a left-handed helix in the presence of (R)-amines.[13d]

The ICD intensities tended to increase with an increase in the molecular weight of poly-**1**; especially for the poly-**1**−(R)-**3** complexes, the tendency was remarkable. The ICD intensity of poly-**1** with the less bulky amino alcohol (R)-**3** increased slowly with time, while the complex with the bulky amine (R)-**2** showed almost no change in the ICD intensity with time regardless of the molecular weight of poly-**1** (see Figure S-1A in the Supporting Information). We also followed the changes in the ICD of poly-**1** with different molecular weights using the less bulky chiral amine ((S)-**4**) and found a similar tendency but with an unusually slow increase in the ICD intensity. The ICD intensity increased very slowly with time at ambient temperature and continued to increase even after 50 days (see Figure S-1B in the Supporting Information). The increase in the ICD remarkably accelerated at 80 °C and reached an almost constant value after 5−20 h (see Table 1). However, poly-**1** showed a slight decrease in the absorption intensity, probably due to decomposition or isomerization of poly-**1** at 80 °C.

The molar absorptivities of poly-**1** in DMSO also increased with increasing the molecular weight. Judging from the ratio of the CD intensity (exactly, the molar ellipticity, $\Delta\epsilon$) and molar absorptivity (ϵ), which corresponds to the Kuhn dissymmetric ratio (g-factor = $\Delta\epsilon/\epsilon$),[31] the molecular weight of poly-**1** seems to have almost no effect on the ICD upon complexation with (R)-**2**; the g-factor values of poly-**1a**−poly-**1c** complexed with (R)-**2** are 2.69 × 10^{-3}, 2.65 × 10^{-3}, and 2.76 × 10^{-3}, respectively. On the other hand, the dissymmetric ratio for the poly-**1**−(R)-**3** and poly-**1**−(S)-**4** complexes was dependent on the molecular weight and increased with increasing the molecular weight; the g-factors of poly-**1a**−poly-**1c** complexed with (R)-**3** are 2.68 × 10^{-3}, 3.24 × 10^{-3}, and 3.37 × 10^{-3}, and those complexed with (S)-**4** are 0.82 × 10^{-3}, 1.17 × 10^{-3}, and 1.17 × 10^{-3}, respectively. Similar effect of molecular weight on the optical activity was also observed for rodlike helical polymers,

(29) Yashima, E.; Maeda, K.; Okamoto, Y. *Nature* **1999**, *399*, 449−451.

(30) For chirality memory effect in the fields of host−guest and supramolecular chemistry, see: (a) Furusho, Y.; Kimura, T.; Mizuno, Y.; Aida, T. *J. Am. Chem. Soc.* **1997**, *119*, 5267−5268. (b) Mizuno, T.; Takeuchi, M.; Hamachi, I.; Nakashima, K.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2281−2288. (c) Sugasaki, A.; Ikeda, M.; Takeuchi, M.; Robertson, A.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3259−3264. (d) Rivera, J. M.; Craig, S. L.; Martin, T.; Rebek, J., Jr. *Angew. Chem., Int. Ed.* **2000**, *39*, 2130−2132. (e) Prins, L. J.; de Jong, F.; Timmerman, P.; Reinhoudt, D. N. *Nature* **2000**, *408*, 181−184. (f) Mizuno, Y.; Aida, T.; Yamaguchi, K. *J. Am. Chem. Soc.* **2000**, *122*, 5278−5285. (g) Kubo, Y.; Ohno, T.; Yamanaka, J.; Tokita, T.; Iida, T.; Ishimaru, Y. *J. Am. Chem. Soc.* **2001**, *123*, 12700−12701. (h) Lauceri, R.; Raudino, A.; Scolaro, L. M.; Micali, N.; Purrello, R. *J. Am. Chem. Soc.* **2002**, *124*, 894−895. (i) Prins, L. J.; Verhage, J. J.; de Jong, F.; Timmerman, P.; Reinhoudt, D. N. *Chem.−Eur. J.* **2002**, *8*, 2302−2313. (j) Ishi-i, T.; Crego-Calama, M.; Timmerman, P.; Reinhoudt, D. N.; Shinkai, S. *J. Am. Chem. Soc.* **2002**, *124*, 14631−14641. (k) Ziegler, M.; Davis, A. V.; Johnson, D. W.; Raymond, K. N. *Angew. Chem., Int. Ed.* **2003**, *42*, 665−668. (l) Purrello, R. *Nat. Mater.* **2003**, *2*, 216−217.

(31) (a) Kuhn, W. *Trans. Faraday Soc.* **1930**, *46*, 293−308. (b) Dekkers, H. P. J. M. In *Circular Dichroism: Principles and Applications*; Nakanishi, K., Berova, N., Woody, R. W., Eds.; VCH: New York, 1994; Chapter 6.

Scheme 1. Series of Acid−Base Equilibria for the Complexation of Poly-**1** with Chiral Amines in DMSO

free acid and base   ion pair   free ions
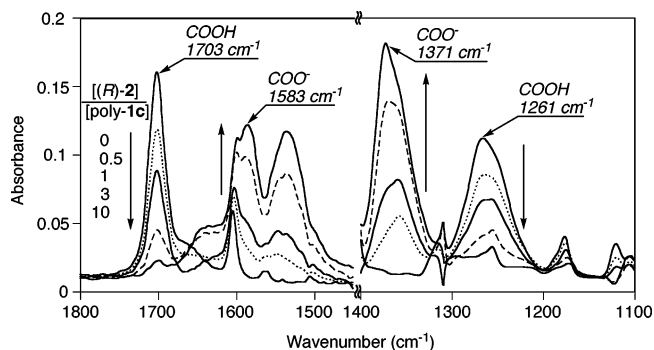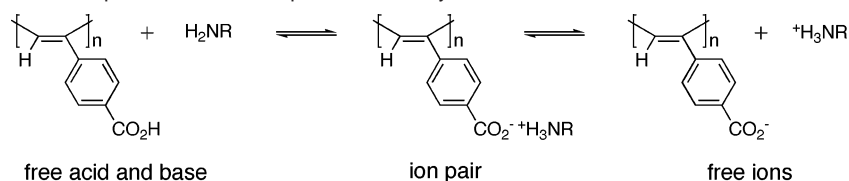
Figure 2. IR spectral changes of the poly-**1c**−(*R*)-**2** complex in DMSO. The IR spectra were measured in a 0.01 cm CaF$_2$ cell at ambient temperature with a poly-**1c** concentration of 5 mg/mL.

Table 2. Binding Constants (*K*s) for the Complexation of Amines with Poly-**1c** and VBA in DMSO

amines	*K* (M^{-1})[a]	
	VBA	poly-**1c**
(*R*)-**2**	95 (57 ± 2[b])	48
(*R*)-**3**	974 (509 ± 30[b])	2003
(*S*)-**4**	949 (671 ± 57[b,c])	1723

[a] Estimated by IR titrations (see the Supporting Information). [b] Cited from ref 13b, and these values were estimated by ^{1}H NMR titrations in DMSO-d_6. [c] Revised value in this work.

polyisocyanates[32] and polysilanes;[33] this was explained theoretically by using the Ising model. A similar model may be applicable to explain the molecular weight effect on the ICD of poly-**1** depending on the structure of chiral amines on the assumption that poly-**1**−amine complexes are dynamic helical polymers consisting of right- and left-handed helices separated by the helix reversal points.[16] However, such a theoretical analysis has not yet been done because of a limited number of data. We then used the high molecular weight poly-**1c** throughout for all the experiments of this study except for the "memory" experiments unless otherwise noted.

Complexation Behavior of Poly-1 with Chiral Amines in DMSO through Acid−base Interaction. In the acid−base complexation of poly-**1** with chiral amines in DMSO, there exist equilibria between the free acid and base, the ion pair, and the free ions as shown in Scheme 1.[13b,34] Among these three species, the ion pairs have been shown to be predominant in DMSO[35] and should be important for the helicity induction on poly-**1**, resulting in the appearance of an ICD in the polymer backbone. The IR spectral changes of poly-**1** in DMSO with an increasing amount of (*R*)-**2** support this ion pair formation. Figure 2 shows the changes in the IR spectra of poly-**1c** upon complexation with (*R*)-**2** in DMSO. Poly-**1c** showed absorptions at 1703 and 1261 cm^{-1} corresponding to the free carboxylic acid bands (COOH),[36] whose intensities decreased with increasing the concentration of (*R*)-**2** and almost completely disappeared at [(*R*)-**2**]/[poly-**1c**] = 20, and new bands at 1583 and 1371 cm^{-1} assigned to the ion-paired and/or dissociated acid band (COO$^-$)

appeared; their intensities increased with increasing the concentration of (*R*)-**2** (Figure 2). These IR spectral changes indicate that the poly-**1c** forms a complex with (*R*)-**2** through acid−base interaction and the carboxy groups of poly-**1c** change to carboxylate ions in DMSO in the presence of (*R*)-**2**.

Previously, we tried to estimate the binding constants (*K*s) of poly-**1** to chiral amines using ^{1}H NMR titrations, but it was difficult because of the broadening of the peaks of chiral amines and amino alcohols.[13b] Therefore, 4-vinylbenzoic acid (VBA) (Chart 1) was used as a model compound of poly-**1** to estimate *K* values for chiral amines by using ^{1}H NMR titrations. However, we can now follow the complexation of poly-**1** with amines in DMSO by means of IR spectroscopy, so that their *K* values upon complexation with poly-**1** could be determined (Table 2).

The *K* values of (*R*)-**2**, (*R*)-**3**, and (*S*)-**4** upon complexation with poly-**1c**, determined by the IR titration experiments, are listed in Table 2 together with those with VBA. IR titrations were performed under the conditions of constant poly-**1c** or VBA concentration (5 mg/mL) with varying amine or amino alcohol concentration at ambient temperature (ca. 25 °C), and the changes in absorbance at 1703 cm^{-1} were followed. The titration curves were analyzed by a nonlinear least-squares method by using a binding model with a 1:1 stoichiometry[37,38] and are in agreement with 1:1 complexation (see Figure S-2 in the Supporting Information). We observed no time-dependent IR spectral changes. Comparison of the *K* values indicates a higher affinity of the amine ((*S*)-**4**) and amino alcohol ((*R*)-**3**) to poly-**1c** and VBA than that of the bulky amine ((*R*)-**2**). We

(32) (a) Gu, H.; Nakamura, Y.; Sato, T.; Teramoto, A.; Green, M. M.; Andeola, C.; Peerson, N. C.; Lifson, S. *Macromolecules* **1995**, *28*, 1016−1024. (b) Okamoto, N.; Mukaida, F.; Gu, H.; Nakamura, Y.; Sato, T.; Teramoto, A.; Green, M. M.; Andeola, C.; Peerson, N. C.; Lifson, S. *Macromolecules* **1996**, *29*, 2878−2884. (c) Gu, H.; Sato, T.; Teramoto, A.; Varichon, L.; Green, M. M. *Polym. J.* **1997**, *29*, 77−84. (d) Jha, S. K.; Cheon, K.-S.; Green, M. M.; Selinger, J. V. *J. Am. Chem. Soc.* **1999**, *121*, 1665−1673.

(33) Teremoto, A.; Terao, K.; Terao, Y.; Nakamura, N.; Sato, T.; Fujuki, M. *J. Am. Chem. Soc.* **2001**, *123*, 12303−12310.

(34) (a) Izutsu, K. *Acid−Base Dissociation Constants in Dipolar Aprotic Solvents;* Blackewll: Oxford, U.K., 1990. (b) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH: Weinheim, Germany, 1990.

(35) Zingg, S. P.; Arnett, E. M.; Mcphail, A. T.; Bothner-By, A. A.; Gilkerson, W. R. *J. Am. Chem. Soc.* **1988**, *110*, 1565−1580.

(36) In nonpolar solvents such as benzene and the solid state, benzoic acid is known to exist as an intermolecular hydrogen-bonded dimer which shows a peak due to the dimeric COOH band at 1688 cm^{-1}, while in the gaseous state it exists as a monomer, showing a peak due to the free COOH band at 1762 cm^{-1}. On the other hand, in polar DMSO, benzoic acid exists as a monomer because of solvation with DMSO through hydrogen bonding, and therefore, it shows a peak due to the COOH band at 1704 cm^{-1}. See: Novak, P.; Vikic-Topic, D.; Meic, Z.; Sekusak, S.; Sabljic, A. *J. Mol. Struct.* **1995**, *356*, 131−141. In the solid state, the COOH group of benzoic acid hydrogen bonded with amines also exhibits a vibration at ca. 1720 cm^{-1}. Nemák, K.; Acs, M.; Jászay, Z. M.; Kozma, D.; Fogassy, E. *Tetrahedron* **1996**, *52*, 1637−1642.

(37) (a) Yashima, E.; Yamamoto, C.; Okamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 4036−4048. (b) Yamamoto, C.; Yashima, E.; Okamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12583−12589.

(38) (a) Sawada, M.; Okumura, Y.; Shizuma, M.; Takai, Y.; Hidaka, Y.; Yamada, H.; Tanaka, T.; Kaneda, T.; Hirose, K.; Misumi, S.; Takahashi, S. *J. Am. Chem. Soc.* **1993**, *115*, 7381−7388. (b) Albert, J. S.; Goodman, M. S.; Hamilton, A. D. *J. Am. Chem. Soc.* **1995**, *117*, 1143−1144.
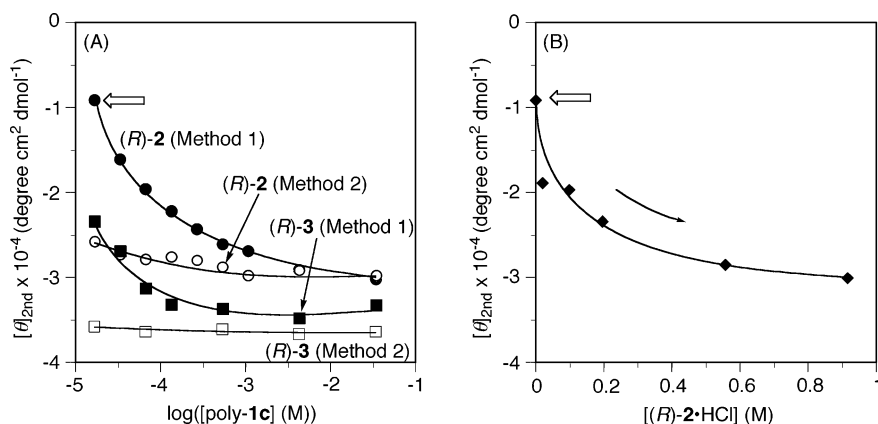
Figure 3. (A) ICD ($[\theta]_{2nd}$) intensity changes of poly-**1c** with (R)-**2** (●, method 1; ○, method 2) and (R)-**3** (■, method 1; □, method 2) versus poly-**1c** concentration in DMSO at 25 °C. The ICD ($[\theta]_{2nd}$) intensities of the poly-**1c**−(R)-**3** complexes were measured after the sample had been allowed to stand for 10 h. The concentrations of (R)-**2** and (R)-**3** were kept constant at 0.34 M and 68 mM, respectively. (B) ICD ($[\theta]_{2nd}$) intensity changes of poly-**1c** with (R)-**2** versus (R)-**2**·HCl concentration in DMSO. The initial dilute poly-**1c** solution with (R)-**2** (0.34 M) in DMSO was indicated by an arrow in part A.

note that there seems to be a macromolecular effect in the acid−base complexation depending on the structure of the chiral amines; the carboxy group of poly-**1c** has a higher binding affinity to the less bulky chiral amines ((R)-**3** and (S)-**4**) than that of its polymer model, VBA, although the K value of the bulky amine (R)-**2** upon complexation with poly-**1c** is lower than that with VBA. The decrease in binding affinity of (R)-**2** to poly-**1c** may be due to the bulkiness of (R)-**2**, which might prevent further binding of (R)-**2** to poly-**1c**.

Although acid−base complexations in organic solvents have been studied extensively,[39] a complete structural interpretation of the equilibrium species in solution is still not completely solved.[35] Particularly, it is difficult to distinguish between ion pairs and free ions and to determine the equilibrium constant between them by means of IR and ^{1}H NMR spectroscopies.[35,39a] However, we have recently confirmed the existence of the free ions by measuring viscosity of a poly-**1c** solution with or without (R)-**2** in DMSO,[16] since viscosity is very sensitive to a change in global conformation of polymers, particularly polyelectrolytes. The reduced viscosity ($[\eta]_{sp}/c$) value of poly-**1c** in the presence of (R)-**2** in DMSO increased monotonically with the decrease in the polymer concentration, while the poly-**1c** in the absence of (R)-**2** in DMSO showed a linear relationship in the Huggins plot. The dependence of the $[\eta]_{sp}/c$ on the concentration of poly-**1c** for the poly-**1c**−(R)-**2** complex in DMSO became normal after the addition of the hydrochloride of (R)-**2** ((R)-**2**·HCl) (0.02 M) into the solution. These viscosity changes are a characteristic feature of polyelectrolytes, suggesting that the ion pair complex of poly-**1c** with (R)-**2** is at least partly dissociated into the free ions (carboxylate and ammonium ions) in DMSO and the dissociation into the free ions can be suppressed in the presence

of a common salt, (R)-**2**·HCl.[16] This implies that poly-**1c** and (R)-**2** can be complexed more tightly through ion pairing in the presence of a small amount of (R)-**2**·HCl, resulting in a full ICD with a small amount of (R)-**2** with (R)-**2**·HCl (see below).

Mechanism of Helicity Induction on Poly-1 with Chiral Amines. As described above, the ion pairing is considered to be important for the helicity induction on poly-**1** with chiral amines in DMSO. To further elucidate the effect of the ion pair and the free ions on the helicity induction on poly-**1**, dilution experiments of poly-**1c** in DMSO containing a large excess of (R)-**2** or (R)-**3** to poly-**1c** were performed to correlate the concentration of poly-**1c** and the ICD intensity (Figure 3). During the dilution experiments, the concentrations of (R)-**2** and (R)-**3** in DMSO were kept constant (0.34 M and 68 mM, respectively) and these DMSO solutions were used as diluents to avoid a shift of the complexation to the free acid and base from the ion pair in the first equilibrium in Scheme 1. In the course of the dilution experiments, we found that the ICD intensities of the poly-**1c** solutions were highly dependent on the dilution methods (methods 1 and 2).

In method 1, a series of dilute poly-**1c** solutions in DMSO (0.005−10 mg/mL) and a stock solution of (R)-**2** in DMSO (0.68 M) were prepared and equal volumes of the solutions were mixed at once to give the desired concentrations of poly-**1c** complexed with (R)-**2** in DMSO. As shown in Figure 3A, the ICD intensity of the poly-**1c**−(R)-**2** complex decreased as the dilution was increased and became less than one-third the original maximum value at log([poly-**1c**]) = −4.8 as marked by an arrow in Figure 3A. A similar decrease in the ICD intensity was also observed for the poly-**1c**−(R)-**3** complex in method 1.[40] Since the degree of dissociation of the ion pair into the free ions increases with decreasing the poly-**1c** concentration, the observed decrease in the ICD intensity of poly-**1c** under the dilute conditions indicates that the ion pairing with chiral amines rather than the free ion plays a central role for the helicity induction on poly-**1c**.

As described in the previous section, the addition of the (R)-**2**·HCl is expected to suppress the degree of the dissociation of the ion pair into the free ions. The (R)-**2**·HCl was then added to the diluted poly-**1c** solution showing a weak ICD, marked

(39) (a) Wilcox, C. S. In *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H.-J., Dürr, H., Lehn, J.-M., Ed.; VCH: Weinheim, Germany, 1988; pp 123−143. (b) Rebek, J., Jr. *Acc. Chem. Res.* **1990**, *23*, 399−404. (c) Zimmerman, S. C. *Top. Curr. Chem.* **1993**, *165*, 71−101. (d) MacDonald, J. C.; Whitesides, G. M. *Chem. Rev.* **1994**, *94*, 2383−2420. (e) Kato, T.; Fréchet, J. M. J. *Macromol. Symp.* **1995**, *98*, 311−326. (f) Paleos, C. M.; Tsiouvas, D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1696−1711. (g) Desiraju, G. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311−2327. (h) Seel, C.; Galán, A.; Mendoza, J. *Top. Curr. Chem.* **1995**, *175*, 101−132. (i) Schmidtchen, F. P.; Berger, M.; Metzger, A.; Gloe, K.; Stephan, H. In *Molecular Design and Bioorganic Catalysis*; Wilcox, C. S., Hamilton, A. D., Ed.; Kluwer: Dordrecht, The Netherlands, 1996; pp 191−210. (j) Collet, A.; Ziminski, L.; Garcia, C.; Vigné-Maeder, F. In *Supramolecular Stereochemistry*; Siegel, J. S., Ed.; Kluwer: Dordrecht, The Netherlands, 1995; pp 90−110. (k) Hirose, T.; Naito, K.; Shitara, H.; Nohira, H.; Baldwin, B. W. *Tetrahedron: Asymmetry* **2001**, *12*, 375−380.

(40) The ICD intensity of the poly-**1c** with (R)-**2** in the dilute concentration region of poly-**1c** gradually decreased with time, while that with (R)-**3** hardly changed.

by an arrow in Figure 3A. As expected the ICD intensity of the diluted poly-**1c** solution gradually increased by the addition of an increasing amount of the (R)-**2**·HCl and recovered to the original maximum value at [(R)-**2**·HCl] = 0.92 M (Figure 3B). It should be noted that poly-**1c** showed no ICD in the same absorption region in the presence of excess (R)-**2**·HCl alone. These results indicate that the ion pair formation between the carboxy groups of poly-**1** and chiral amines is essential for the helicity induction in one-handedness excess.

Contrary to the results in method 1, the ICD intensities of poly-**1c** in DMSO solutions of (R)-**2** and (R)-**3** remained almost constant over the concentration range examined when the samples were prepared by method 2; the concentrated poly-**1c** samples in DMSO solutions of (R)-**2** (0.34 M) and (R)-**3** (68 mM) were initially prepared separately and then diluted with increasing volumes of the DMSO solutions of (R)-**2** (0.34 M) and (R)-**3** (68 mM), respectively; CD spectra were measured for each dilution (Figure 3A). These unusual results suggest that the induced helical chirality of poly-**1c** is maintained regardless of the increase in the amount of the free ions[41] under dilution once a one-handed helix is induced on poly-**1c** assisted by interaction with (R)-**2** and (R)-**3**. This phenomenon is closely correlated to the memory of macromolecular helicity of poly-**1c**, which will be discussed later in detail.

To correlate the ICD intensity and the amount of the chiral amine interacting with poly-**1c**, CD titration experiments were conducted under the same conditions as the IR titrations (Figure 2) because the complexation of poly-**1c** with amines in DMSO can be followed by IR as described above. In Figure 4, the ratios ($[\theta]/[\theta]_{max}$) of the observed ICD intensity of the second Cotton ($[\theta]$) during the titrations to the maximum ICD values ($[\theta]_{max}$) for the poly-**1c**−(R)-**2** (-3.06×10^4), poly-**1c**−(R)-**3** (-3.53×10^4), and poly-**1c**−(S)-**4** (1.41×10^4) were plotted against the content of the carboxylate ion ($[COO^-]$) in the poly-**1c** determined by the IR titrations.

The ICD intensity of the poly-**1c**−(R)-**2** complex dramatically increased with an increase in the amount of the carboxylate ion generated by the complexation with (R)-**2** at around the region where the $[COO^-]$ was from 20 to 50% and reached an almost maximum value at $[COO^-]$ = ca. 50%. This sudden onset and rapid increase in the optical activity of poly-**1c** with a sigmoidal fashion suggest that the polymer forms a slight excess of one-handed helical structure at around this region ($[COO^-] \cong 20\%$) and further change in the population of the right- and left-handed helices of the polymer main chain into a one-handedness takes place cooperatively on poly-**1c** upon the ion pair formation with (R)-**2**. We note that poly-**1c** can form an almost one-handed helix when half the carboxy groups of poly-**1c** complex with (R)-**2** form the ion pair, and the remaining half of carboxy groups are not necessary to form the ion pairs.[43]
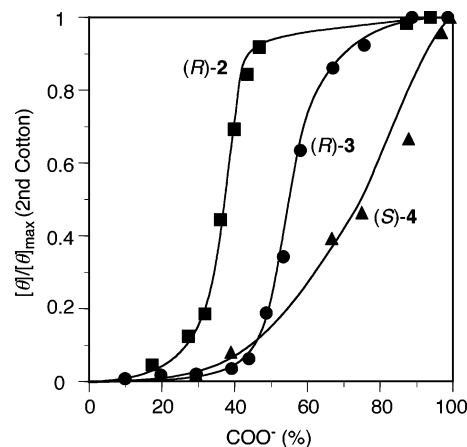

Figure 4. Plots of $[\theta]/[\theta]_{max}$ (second Cotton) for poly-**1c** complexed with (R)-**2** (■), (R)-**3** (●), and (S)-**4** (▲) against the content of the carboxylate ion (COO^-) of poly-**1c** in DMSO at ambient temperature (ca. 24−26 °C), where $[\theta]$ and $[\theta]_{max}$ represent the observed and the maximum second Cotton values for the poly-**1c**−(R)-**2** (-3.06×10^4), poly-**1c**−(R)-**3** (-3.53×10^4), and poly-**1c**−(S)-**4** (1.41×10^4) complexes, respectively, with [poly-**1c**] = 5 mg/mL. The ICD intensities ($[\theta]$) of the poly-**1c**−(R)-**2** and poly-**1c**−(R)-**3** were measured after the samples had been allowed to stand for 42 and 47 h at ambient temperature, respectively. The $[\theta]$ values of the poly-**1c**−(S)-**4** were the maximum values at 80 °C.

On the other hand, the complex with the less bulky amino alcohol (R)-**3** showed almost no ICD in the region of $[COO^-]$ < 40%. However, the ICD intensity of the poly-**1c**−(R)-**3** complex started to increase in a sigmoidal fashion at $[COO^-]$ = ca. 40% and reached a maximum value at $[COO^-]$ = ca. 80%. The less bulky (R)-**3** can also induce a one-handed helix on poly-**1** cooperatively, but which requires almost complete ion pair formation of the carboxy groups of poly-**1** with the chiral amino alcohol. The poly-**1c**−(S)-**4** complex also showed an increase in the ICD intensity with weak cooperativity. In this less bulky amine, most of the carboxy groups of poly-**1c** should be complexed with (S)-**4** to saturate the ICD; nevertheless, the complex could not exhibit a full ICD under the present conditions.

These results together with the CD titration results clearly indicate that both basicity and bulkiness of the chiral amines are important factors for the helicity induction and its excess of a single-handed helix (the ICD intensity). The importance of bulkiness for the helicity induction was already demonstrated[13b] and in good agreement with the previous results for poly-(phenylacetylene)s bearing an optically active substituent.[11b,12]

Dynamic Nature of Induced Helical Conformation of Poly-1 with Chiral Amines. The stability and dynamic nature of the helical poly-**1** induced by chiral amines were investigated by means of CD spectroscopy. The ICD of the poly-**1**−(R)-**2** complex instantly disappeared when the complex was exposed to a stronger acid such as trifluoroacetic acid, which liberates the poly-**1** so it reverts to the original, optically inactive polymer.[13,29] This suggests that the original poly-**1** with free carboxylic acid residues cannot maintain the helical conformation in DMSO.

(41) The amounts of the free ions could not be determined quantitatively using spectroscopies, but they can be calculated by considering the effect of ion condensation according to Manning[42] by using the IR titration data and the dissociation constant for the corresponding low-molar-mass salts such as a VBA−amine complex. The dissociation constant (0.0125 M^{-1}) for mandelic acid with amines in DMSO, which was determined by means of conductance measurements, is reported by Zingg et al.[35] By using this dissociation constant (0.0125 M^{-1}) on assumption that the dissociation constant is almost constant regardless of the amines used, we can estimate the amounts of the ion pair and free ions. The degrees of the ion pair and free ions (carboxylate of poly-**1**) in DMSO at 25 °C were estimated to be 0.743 and 0.196, respectively, at the infinite dilution condition of poly-**1** in the presence of (R)-**2**·HCl (0.02 M) at [(R)-**2**] = 0.35 M.[16]
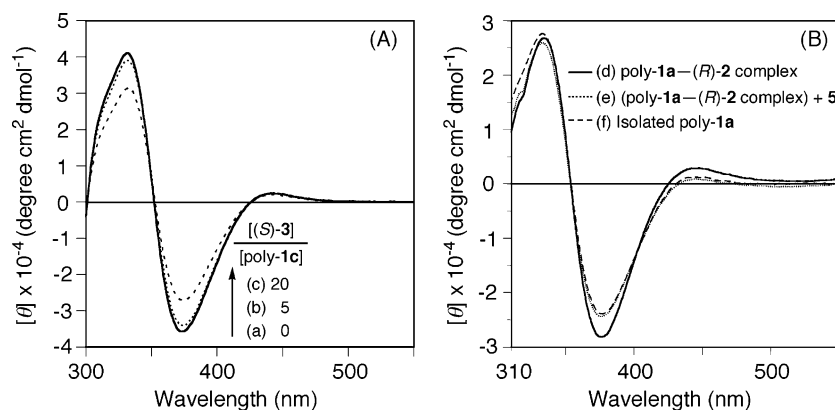
(42) Manning, G. S. *J. Chem. Phys.* **1969**, *51*, 924−933.

(43) The ion pairs of poly-**1** with amines partly dissociate into the free ions in DMSO, so the obtained $[COO^-]$ value is the sum of the ion pair and the free ions. Therefore, a practical amount of the ion pair to induce an almost one-handed helix on poly-**1** with (R)-**2** must be less than 50%. The amounts of the ion pair and free ions can be estimated by the method described in ref 41. These results together with the theoretical analyses by the Ising model will be published elsewhere.

Figure 5. (A) CD spectral changes of the poly-**1c**−(*R*)-**3** complex ((*R*)-**3**; 5 equiv of monomer units of poly-**1c**) by the addition of (*S*)-**3** (method B). Molar ratio of (*S*)-**3** to monomer units of poly-**1c** is 0 (a), 5 (b), and 20 (c). The CD spectra were measured in DMSO in a 0.01 cm quartz cell at ambient temperature (ca. 24−26 °C) with a poly-**1c** concentration of 3 mg/mL. (B) CD spectra of the poly-**1a**−(*R*)-**2** complex ([(*R*)-**2**]/[poly-**1a**] = 10) (d), the mixture of the poly-**1a**−(*R*)-**2** complex with **5** ([**5**]/[poly-**1**] = 50) (e), and the isolated poly-**1a** (f) by SEC using a DMSO solution of **5** (0.8 M) as the mobile phase, in DMSO at ambient temperature (20−25 °C). The concentration of poly-**1a** is 3.0 mg/mL for (d) and (e) and 0.13 mg/mL for (f).

The ICD intensity of the poly-**1c**−(*R*)-**2** complex in DMSO ([(*R*)-**2**]/[poly-**1c**] = 10) decreased by the addition of increasing amount of (*S*)-**2**, and the ICD completely disappeared at [(*R*)-**2**]/[(*S*)-**2**] = 1. Further addition of (*S*)-**2** induced the ICD with an opposite Cotton effect sign, whose ICD magnitude almost corresponded to the enantiomeric excess (ee) of the amine (see Figure S-3A in the Supporting Information). This indicates that the induced helix of the poly-**1c** is dynamic in nature, the (*R*)-**2** complexed with poly-**1** can exchange rapidly with (*S*)-**2**, and the helix-sense is controlled by chirality of **2**. However, upon the addition of a small amount of the chiral amino alcohol (*S*)-**3** ([(*S*)-**3**]/[(*R*)-**2**] = 0.2 ([(*S*)-**3**]/[poly-**1c**] = 2)) to the poly-**1c**−(*R*)-**2** solution ([(*R*)-**2**]/[poly-**1c**] = 10), the ICD spontaneously changed and the signs inverted to give mirror images (see Figure S-3B in the Supporting Information). In this case, the helix-sense was determined by a rather small amount of (*S*)-**3** with the opposite configuration. Since an acid−base binding constant (K (M^{-1})) of (*S*)-**3** with poly-**1c** in DMSO obtained by the IR titration experiments is much larger than that of (*R*)-**2** (see Table 2), the (*R*)-**2** is considered to be completely replaced by the (*S*)-**3** during the titration.

In the previous study, we found that the complex formation of poly-**1** with partially resolved amines including **2** and **3** displayed a unique, positive nonlinear relationship (chiral amplification or "majority rule")[2d,g,32d,44] between the ee of amines and the observed ellipticity of the Cotton effects; ICD intensities of poly-**1**, corresponding to the helical sense excesses, are out of proportion to the ee's of amines, showing a convex deviation from linearity through a wide range of ee values of the chiral amines in DMSO.[13b] For example, when poly-**1** (M_n = 4.6 × 10^4) was dissolved in DMSO with a 5-fold excess **3** of 60% ee (*R* rich) (method A), the complex showed as intense an ICD as that of 100% ee. The excess enantiomer bound to the polymer may induce an excess of a single-handed helix (right- or left-handed helix) despite its proportion, which may result in a more intense ICD than that expected from the ee of **3**. However, the departure from linearity was found to be sensitive to the mixing manner of the (*R*)- and (*S*)-amines with poly-**1**; the addition order of (*S*)- and (*R*)-**3** to the poly-**1** solution

determined the Cotton effect sign of the poly-**1** solution irrespective of the ee of **3**.[13b]

Figure 5A shows the changes of CD spectra of the poly-**1c**−(*R*)-**3** complex in DMSO ([(*R*)-**3**]/[poly-**1c**] = 5) after addition of 5 and 20 equiv of (*S*)-**3** (method B). Interestingly, even though an excess amount of (*S*)-**3** ([(*S*)-**3**]/[(*R*)-**3**] = 4; ee = 60% (*S* rich)) was present in the solution, the Cotton effect sign did not change and the ICD intensity only slightly decreased just after the addition of excess (*S*)-**3**. The ICD intensity decreased very slowly with time at ambient temperature; even after 2 months poly-**1c** still exhibited the same Cotton effect sign. At higher temperature (80 °C), however, the ICD intensity decreased rapidly and the sign inverted after 13 h at 80 °C (see Figure S-4 in the Supporting Information). These results suggest that the exchange rate between the amino alcohol enantiomers may be very slow or the inversion of helicity of poly-**1c** may be occurring very slowly after the fast exchange reaction; the latter was found to be the case on the basis of the ee determination results of the bound **3** to poly-**1c** (see the Experimental Section (Enantiomeric Excess Determination of Bound **3** to Poly-**1c**), Figure S-5, and Table S-1 in the Supporting Information). That is, once one of the helicities is induced on poly-**1c** with the chiral amino alcohol, the polymer maintains its helical conformation even after the bound amino alcohol could be randomly replaced by the opposite antipode.

We then added an excess amount of an achiral amino alcohol, 2-aminoethanol (**5** in Chart 2) ([**5**]/[poly-**1**] = 50), instead of racemic or nonracemic **3** to the poly-**1**−(*R*)-**2** complex ([(*R*)-**2**]/[poly-**1**] = 50) in DMSO (Figure 5B); in this experiment, we used poly-**1a** instead of poly-**1c**. As described below, poly-**1b** and poly-**1c** also showed almost the same results. The achiral amino alcohol **5** is a strong base similar to (*S*)-**3** (K = 2003 (M^{-1})), so that the (*R*)-**2** (K = 48 (M^{-1})) complexed with poly-**1a** will be completely replaced by an excess of **5**. However, quite interestingly, the ICD signal was still observed as such with only a slight decrease in the CD intensity (trace e in Figure 5B). This clearly indicates that the one-handed helical conformation of the poly-**1a** induced by (*R*)-**2** can be retained even after the (*R*)-**2** is replaced by achiral **5**.

Memory of the Macromolecular Helicity of Poly-1. As described above, the one-handed helicity of the poly-**1** induced

(44) Green, M. M.; Garetz, B. A.; Chang, H. *J. Am. Chem. Soc.* **1995**, *117*, 4181−4182.

Chart 2

Amino Alcohols

Amines
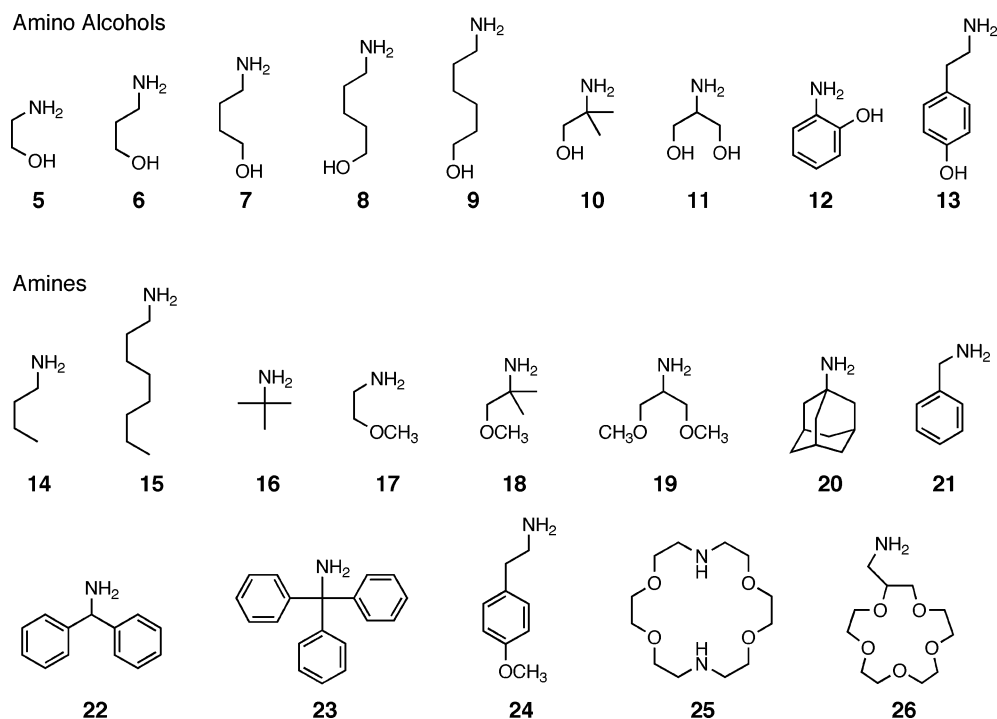
by (*R*)-**2** is considered to be maintained after removal and replacement of (*R*)-**2** by achiral **5**. To gain further concrete evidence, we isolated the poly-**1a** from the poly-**1a**−(*R*)-**2** complex with excess **5** by size exclusion chromatography (SEC) using a DMSO solution of **5** (0.8 M) as the mobile phase (Figure 6). The poly-**1a** eluted first, followed by the (*R*)-**2**. Each fraction was collected and subjected to CD and absorption measurements. On the basis of the UV spectrum of the (*R*)-**2** fraction, more than 99% of the (*R*)-**2** was recovered. Nevertheless, the poly-**1a** fraction (0.13 mg/mL) containing a large excess of achiral **5** ([**5**]/[poly-**1a**] = ca. 900) showed an intense ICD comparable to that measured before the SEC fractionation (trace f in Figure 5B), which indicates the memory of the induced helicity of poly-**1a**. To check if a small amount of (*R*)-**2** is still present in the poly-**1a** fraction after the SEC purification,[45] the fractionated, optically active poly-**1a** was injected again into the SEC system using the same mobile phase. But we could not detect any trace amounts of (*R*)-**2**, and the refractionated poly-**1a** exhibited ICD without any loss of the macromolecular
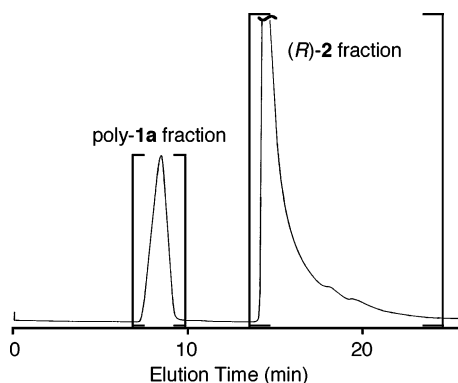

Figure 6. SEC chromatogram of the separation of the poly-**1a**−(*R*)-**2** complex with DMSO containing **5** (0.8 M) as the mobile phase. Each fraction marked by brackets was collected to measure CD and UV−visible spectra.

helicity. This procedure was further repeated, but no change in the CD spectrum of the poly-**1a** was observed.

A standard solution of poly-**1a**−(*R*)-**2** complex (the amount of (*R*)-**2** is 0.01 equiv of monomer units of poly-**1a** which corresponds to 0.1% (*R*)-**2** based on the initial amount of the (*R*)-**2**) was then prepared, and the solution was also injected into the same SEC system using the same mobile phase. The peak due to 0.1% (*R*)-**2** was clearly detected, whereas, in the chromatogram of the fractionated poly-**1a** solution, the peak due to (*R*)-**2** was hardly detected (see Figure S-6 in the Supporting Information). These results indicate that the fractionated poly-**1a** solution exhibiting the intense ICD scarcely contains (*R*)-**2** (less than 0.01% based on the detection limit). Moreover, we found that the addition of (*R*)-**2** ([(*R*)-**2**]/[poly-**1a**] = 1) to a solution of poly-**1a**−**5** complex ([**5**]/[poly-**1a**] = 50) did not induce any CD at all at ambient temperature (ca. 20−22 °C) even after 9 days and at 50 °C for 14 h. We further added 100 equiv of (*R*)-**2** to the solution, but no CD was observed. These results strongly support that the macromolecular helicity of the poly-**1a** induced by the (*R*)-**2** is undoubtedly retained by the replacement with achiral **5**. On the basis of the ratio of the ICD intensity of the second Cotton ($[\theta]_{2nd}$) just after the SEC fractionation to the original ICD intensity of the poly-**1a**−(*R*)-**2** complex, the memory efficiency with achiral **5** was estimated to be 87%. When (*S*)-**2** was used for the induction of a one-handed helix on poly-**1a**, poly-**1a** of the opposite macromolecular helicity was obtained.

We further investigated the macromolecular helicity memory of the poly-**1** induced by (*R*)-**2** using a series of achiral amino alcohols (**6**−**13**) and amines (**14**−**25**) and chiral amines **4** and

(45) It should be noted that the poly-**1a** fraction separated from the poly-**1a**−(*R*)-**2** complex using pure DMSO as the mobile phase showed no ICD, indicating that the (*R*)-**2** complexed with poly-**1a** was completely removed during the SEC fractionation, and free poly-**1a** cannot maintain the induced helical conformation.
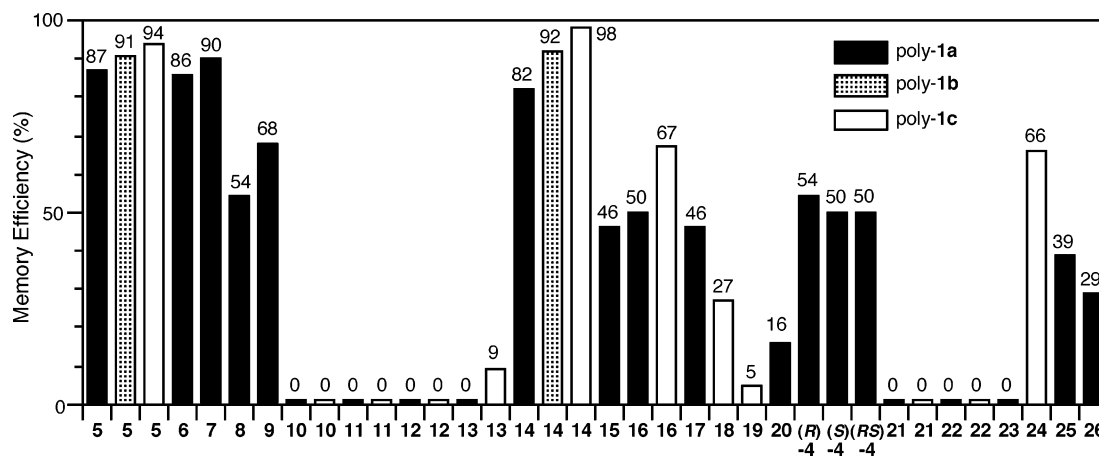
Figure 7. Memory efficiencies of the macromolecular helicity of poly-**1** induced by (*R*)-**2** using a series of achiral amino alcohols (**5**−**13**) and chiral and achiral amines (**4**, **14**−**26**). Memory efficiencies (%) were estimated on the basis of the ICD values of the second Cotton effect ($[\theta]_{2nd}$), just after the SEC fractionation of the poly-**1**−(*R*)-**2** complex solution ([poly-**1**] = 3 mg/mL, [(*R*)-**2**]/[poly-**1**] = 10) in the presence of excess amino alcohols (**5**−**12**) and amines (**17**, **19**) ([**5**−**12**, **17**, **19**]/[poly-**1**] = 50) or in the absence of an amino alcohol (**13**) and amines (**4**, **14**−**16**, **18**, **20**−**26**) using 0.8 (**5**−**8**, **10**, **11**, **17**, **19**), 0.4 (**9**), 0.2 (**12**), or 0.008 M (**4**, **13**−**16**, **18**, **20**−**26**) amines in DMSO as the mobile phase.

26 (Chart 2). Higher molecular weight poly-**1b** and poly-**1c** were also used for comparison (see below).

The results of the memory efficiency experiments are summarized in Figure 7. The magnitude of the ICD of the memorized poly-**1a** is highly dependent on the structures of the amines and amino alcohols used. As for a series of achiral amino alcohols (**5**−**9**), the memory efficiency was dependent on the number of methylene groups of the amino alcohols and the longer amino alcohols (**8** and **9**) showed relatively low memory efficiencies, although their binding affinities (*K*s) to a carboxy group estimated by the ^{1}H NMR titrations with VBA in DMSO-d_6 were not significantly different from each other (K (M^{-1}) = 1522 ± 90 (**6**), 867 ± 113 (**7**), and 1241 ± 112 (**8**)).[29] However, rather surprisingly, upon complexation with analogous amino alcohols **10** and **11**, poly-**1a** lost its chiral memory completely despite their high affinities to poly-**1a** (K (M^{-1}) = 470 ± 10 (**10**) and 774 ± 129 (**11**)). An aniline analogue **12** and a phenol derivative **13** also resulted in no memory effect for the low molecular weight poly-**1a**. A possible explanation for these no memory effects will be described later.

Besides the amino alcohols, various primary amines also work as small, achiral chaperoning molecules to assist in the memory of the macromolecular helicity of poly-**1**, although the memory efficiency is also dependent on the structure of amines used. Less bulky chiral amines such as (*S*)-, (*R*)-, and (*RS*)-**4** also showed an apparent macromolecular helicity memory with similar memory efficiencies (50−54%) independent of the absolute configuration of **4**. This clearly indicates that the memory effect is controlled kinetically, since the (*S*)- and (*R*)-**4** can induce opposite helices on the original poly-**1** depending on the configuration of **4**. Nevertheless, the macromolecular helicity of poly-**1** can be memorized by the (*S*)- and (*R*)-**4**. As described above, less bulky (*S*)- or (*R*)-**4** could not induce a single handed helix on the whole poly-**1** chain and required a long time for helicity induction with a one-handedness excess (see Figure S-1B in the Supporting Information). This is completely different from (*R*)-**2** and (*R*)-**3**; helicity induction power (or chiral twisting power for poly-**1**) of **4** is weaker than that of **2** and **3**, so that (*S*)- and (*R*)-**4** just work to maintain the helical conformation like achiral amines in this particular memory experiment. A simple *n*-butylamine (**14**) exhibited

rather high memory efficiency for poly-**1a** (82%), and other primary (**15**−**17**, **20**, **26**) and secondary (**25**) amines also showed moderate helicity memory effects on poly-**1a**. We anticipate that this helicity memory process can be used to construct new supramolecular assemblies with macromolecular helicity, for instance the crown ethers (**25**, **26**), which may exist in a helical array along the poly-**1** strand.

Effects of Molecular Weight of Poly-1 and Concentration of Achiral Amines on Macromolecular Helicity Memory. The molecular weight of poly-**1** also affects the memory efficiency as well as the helicity induction on poly-**1**. As shown in Figure 7, the memory efficiencies using the achiral amino alcohol **5** and amines **14** and **16** increased with an increase in the molecular weight of poly-**1** in the order poly-**1a** < poly-**1b** < poly-**1c**. It is worth noting that as for the memory using the amino alcohol **13**, high molecular weight poly-**1c** showed only an apparent memory effect (9%), although low molecular weight poly-**1a** lost its chiral memory.

We also investigated the concentration effect of achiral amines in the mobile phase on the memory efficiency, but we found no significant changes in the memory efficiency in the concentration ranges of 0.8−0.008 M for **5**, **14**, and **16** (see Figure S-7 in the Supporting Information). On the other hand, a remarkable concentration effect was observed for **21**; in a dilute concentration of **21** (0.008 M), **21** could not assist in the macromolecular helicity memory at all, but at higher concentrations the macromolecular helicity was memorized and its efficiency increased with an increase in the concentration of **21** in the mobile phase (from 0 to 38%) (Figure S-7). These results might be closely related to the difference in the affinity, that is, the basicity of amines to poly-**1**. The acid−base binding constant for benzylamine **21** with poly-**1** (K = 151 M^{-1}) was much smaller than those of **5** and **14**. In a lower concentration (less than 0.008 M) of weak bases such as **21**, the acid−base equilibria may shift to the free acid and base (see Scheme 1). Once free carboxy groups (COOH) of poly-**1** are generated after the SEC fractionation of the helical poly-**1** induced by (*R*)-**2**, poly-**1** could not maintain the induced helical conformation, resulting in the decrease in the memory efficiency or complete loss of the memory. However, at higher concentrations of the weak achiral amines, the macromolecular helicity memory can
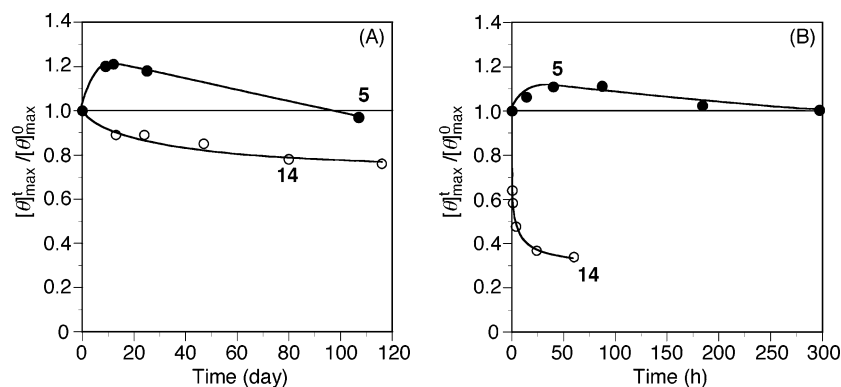
Figure 8. Stability of the macromolecular helicity memory. ICD intensity changes (second Cotton) of the poly-**1a** isolated by SEC using DMSO containing **5** (●) and **14** (○) as the mobile phase component, in DMSO at ambient temperature (A) and 50 °C (B) with time. $[\theta]^0_{max}$ represents the ICD intensity (second Cotton) of the fractionated poly-**1a** with **5** and **14** just after the SEC separation.

be attained, since the equilibria move to the ion pair and free ions formations.

Weak bases such as **12**, **22**, and **23** showed no memory effect in low and high (0.8 M for **22** and **23**, 0.2 M for **12**) concentrations in DMSO as the mobile phase for the SEC separation. This is because even at these amine concentrations, a large amounts of the free carboxy groups (COOH) of poly-**1** are generated after the SEC separation due to their quite low basicity ($K < 2$ M^{-1}). The phenol derivative **13** was also a poor achiral amine for the macromolecular helicity memory of poly-**1**. **13** has an acidic phenol OH group as well as a basic amino group, so that **13** interacts from each other through an intermolecular acid−base reaction, which must disturb the interaction of **13** with poly-**1**, resulting in no memory effect for poly-**1a** or a very low memory efficiency for poly-**1c**. This speculation was supported by the fact that **24** derived from **13** in which the acidic phenol OH group was replaced by the methoxy group showed relatively high memory efficiency (66%) for poly-**1c** using a dilute DMSO solution of **24** (0.008 M) as the mobile phase.

Repair and Stability of the Macromolecular Helicity Memory. Although the memory of the macromolecular helicity of poly-**1** assisted by **5** is not perfect just after the SEC fractionation (87−94%), we found that it was automatically amplified ("*repaired*") with time in the presence of achiral **5**. The ICD intensity of the poly-**1** increased and recovered to the original maximum values (for poly-**1a**, see Figure 8A). Similar macromolecular helicity amplification (repair) of the memorized poly-**1a** was also observed for the achiral amino alcohols **6**−**9** but not observed for the other achiral amines (for **14**, see Figure 8A).

The memory with **5** lasted for an extremely long time over 2 years at ambient temperature (20−25 °C). At higher temperatures (50−80 °C), the poly-**1a** also kept its memory for at least 300 h at 50 °C and for 10 h at 80 °C, although, at higher temperatures, poly-**1a** gradually decomposes or isomerizes accompanied by a decrease in the UV−visible intensity.

n-Butylamine (**14**) also showed a high memory efficiency (82−98%), but the memory steadily declined at ambient temperature (20−25 °C) and the CD intensity showed a decrease with time as shown in Figure 8A. At 50−80 °C, the memory was lost rapidly with nonlinearity during the initial stage. The initial half-lives were roughly estimated to be about 30 h, 2 h, 4 min, and 1 min at 50, 60, 70, and 80 °C, respectively. This may be due to the fast exchange between the free and bound

14 at the high temperatures; therefore, the memory may rapidly fade (see Figure 8B and Figure S-8 in the Supporting Information). The achiral amine **14** is good for the short-term memory of the macromolecular helicity, but for long-term memory, the amino alcohols **5**−**9** may be better.

To investigate the difference in the stability of the macromolecular helicity memory of poly-**1** with **5** and **14**, the hydroxy group of **5** was converted to the methoxy group (**17**) and its stability of the memorized poly-**1a** was examined. As shown in Figure 7, the memory efficiency significantly decreased with **17** and the memory was lost rapidly at higher temperature (50 °C) in a way similar to that for the amine **14** (see Figure S-9 in the Supporting Information). The cooperative hydrogen bond formation of the hydroxy group of **5** to a carboxy residue of poly-**1** as well as the acid−base interaction[46] must contribute to the good memory of the one-handed helical conformation of poly-**1** with respect to efficiency and stability. We postulate that during the exchange reaction between the bound (*R*)-**2** and **5**, **5** comes into a chiral binding site (carboxy groups of poly-**1**) with a chiral *gauche-staggered* conformation so as to keep the helical conformation with the same helix-sense induced by the (*R*)-**2**. The bound **5** might have a chiral conformation similar to that of the bound (*R*)-**3** which can induce the same helix-sense of poly-**1** (Figure 9A,B). Amino alcohols might have a strong ability to maintain the helical conformation after the exchange reaction (strong memory effect or holding power), and therefore, the memory lasted for an extremely long time even at higher temperatures.

The memory of macromolecular helicity should be governed kinetically, and therefore, the helical conformation induced by (*R*)-**2** may be changed to some extent through the exchange process with **5**. The conformation formed immediately after the exchange reaction between the (*R*)-**2** and **5** may be conformationally unstable. However, if the bound **5** could have a chiral conformation, which could act as an optically active amino alcohol like (*R*)- or (*S*)-**3**, the kinetically formed unstable helical poly-**1** will be repaired to a stable one with an increase in the CD intensity. The primary amine **14** may not be able to have such a chiral conformation as **5**, and helicity repair cannot be possible.

In connection with the chiral conformation of **5** described above, the reason an achiral amino alcohol **11** did not show

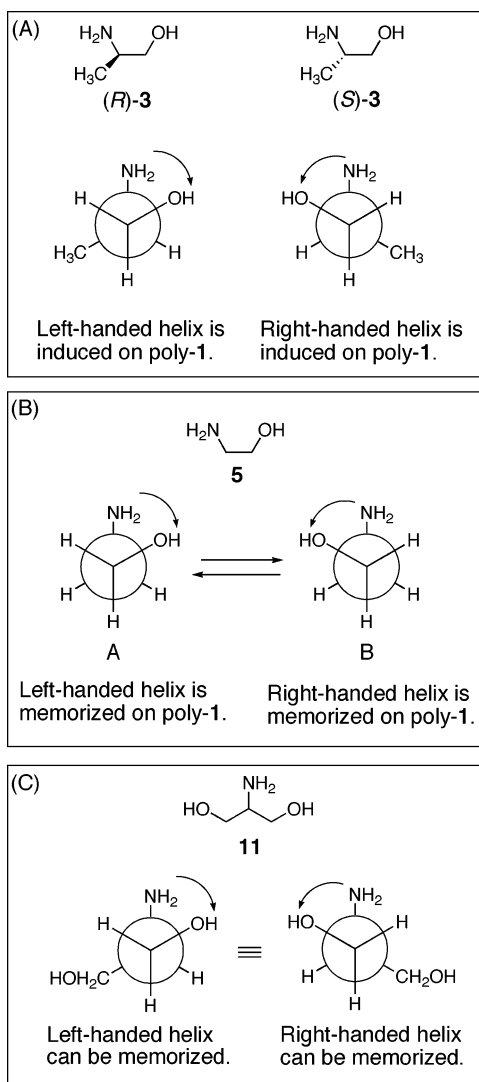(46) Manabe, K.; Okamura, K.; Date, T.; Koga, K. *J. Am. Chem. Soc.* **1993**, *115*, 5324−5325.

Figure 9. Possible chiral conformations of chiral **3** (A) and achiral **5** (B) and **11** (C).

any memory effect can be explained as follows (Figure 9C); the amine has two enantiotopic hydroxy groups and may have two chiral conformations such as (*S*)-**3** and (*R*)-**3**. When binding with poly-**1**, each enantiomeric conformer can interact with poly-**1** like chiral amino alcohols such as (*S*)- and (*R*)-**3**; therefore, the helical chirality of poly-**1** induced by (*R*)-**2** could not be memorized, since each conformer of **11** might show a strong chiral twisting power to force the poly-**1** into a racemic helical conformation. The two hydroxy groups of **11** were then converted to the methoxy group (**19**), which, however, showed a weak memory effect (5%) (Figure 7). The methoxy groups may also participate in the formation of hydrogen bonding with the carboxy groups of poly-**1**.

In the same way, chiral *gauche-staggered* conformers may be possible for achiral **10**. If this is the case, the helical conformation with the same helix-sense induced by the (*R*)-**2** may be able to be memorized when **10** forms such a chiral conformation during the exchange reaction with (*R*)-**2**. However, **10** did not show any memory effect at all. The reason seems to be difficult to explain at the present stage, but the fact that the methoxy derivative **18** exhibited moderate memory efficiency (27%) indicates that the hydroxy group of **10** makes a negative

contribution to helicity memory, since **16** with similar bulkiness showed high memory efficiency (67%).

Achiral amines having no hydroxy group cannot exist as such a chiral conformation as proposed for the achiral amino alcohol **5** (Figure 9B); the conformation of the amines bound to poly-**1** may be close to the *anti-staggered* form rather than to the *gauche-staggered* one. However, achiral amines such as **14** also nicely work as small, achiral chaperoning molecules to assist in the memory of the macromolecular helicity, which indicates that such a chiral conformation, like the amino alcohol **5**, is not necessarily required for a good-memory effect but may be essential for long-term memory and repair.

Mechanism of the Macromolecular Helicity Memory. The question is raised regarding what the main driving force is for the memory of the helical chirality of poly-**1** in DMSO despite the absence of chiral amines. The steric effect of the chaperoning molecules (amines and amino alcohols) appears not to be the central factor for the memory effect because the helical chirality of poly-**1** can be maintained independent of the bulkiness of the achiral amines. As described above, in the presence of amines poly-**1** forms an ion pair complex, which at least partly dissociates into the free ions (carboxylate and ammonium ions) in DMSO; therefore, the intramolecular electrostatic repulsions between the carboxylate groups of poly-**1** might play an important role for the maintenance of the helical chirality of poly-**1**. To confirm if the electrostatic repulsive interactions could really contribute to the macromolecular helicity memory, a common salt (hydrochloride of achiral amines), which is expected to suppress the dissociation of the ion pair to the free ions, was added to the memorized poly-**1**−achiral amine solutions after fractionation by SEC. The stabilities of the induced memory were followed by CD, and the results were compared with that in the absence of the common salts (Figure 10).

The ICD intensity of the poly-**1c**−**5** solution fractionated by SEC increased with time at the initial stage and did not change for a long time as demonstrated above. However, upon the addition of the hydrochloride of **5** (**5**·HCl) to the same solution, the ICD intensity significantly decreased with time and the decreasing rate was accelerated with increasing the amount of **5**·HCl, although the changes in the ICD intensity after the addition of **5**·HCl could not be followed completely because of precipitation of the polymer (Figure 10A). The remarkable repair of macromolecular helicity was not observed in the presence of the salt. Similar rapid decrease in the ICD intensity was also observed for the fractionated poly-**1c**−**14** solution by the addition of **14**·HCl, and the decreasing rate was much faster as compared with that for the poly-**1c**−**5** solution under the same concentrations of the salts (Figure 10B). In the presence of salts, the intramolecular electrostatic repulsion between the carboxylate ions of poly-**1** is weakened so that the atropisomerization of poly-**1** easily proceeds when the dissociation of the ion pairs into the free ions is suppressed by the common salt. The importance of the intramolecular electrostatic repulsions for the memory effect is also evidenced by the results of the dilution experiments of poly-**1** by method 2 as described above (see Figure 3); once a one-handed helix was induced on poly-**1** with chiral amines, the induced helical chirality of poly-**1** was maintained in a highly dilute solution in which the amount of the free ions increases. Consequently, the intramolecular
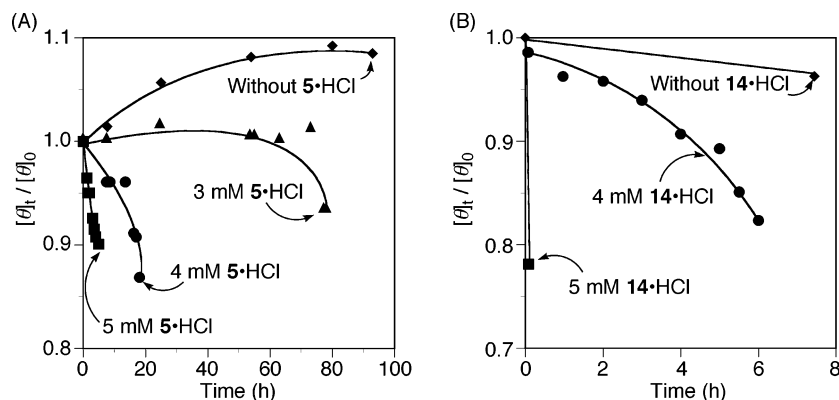
Figure 10. Changes in the ICD intensities (second Cotton) of the isolated poly-**1c** having macromolecular helicity memory assisted by **5** and **14** upon addition of **5**·HCl (A) and **14**·HCl (B), respectively, in DMSO at ambient temperature. The concentrations of **5**·HCl and **14**·HCl were 0 (◆), 3 (▲), 4 (●), and 5 (■) mM.
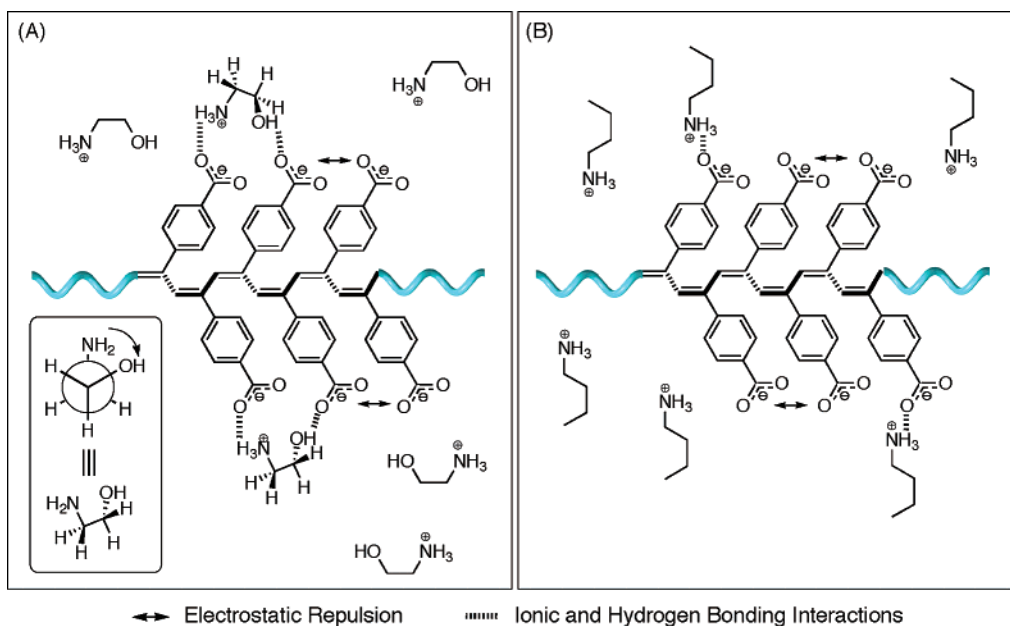

◀▶ Electrostatic Repulsion ⅲⅲ Ionic and Hydrogen Bonding Interactions

Figure 11. Schematic illustration of the mechanism of macromolecular helicity memory of poly-**1** with **5** (A) and **14** (B).

electrostatic repulsions between the carboxylate groups play the central role for the maintenance of the helical chirality of poly-**1** to prevent the atropisomerization of poly-**1** as illustrated in Figure 11. Upon complexation with amines in DMSO, poly-**1** becomes more stiff with a longer persistent length (from 4.2 to 8.6 nm),[16] which results in the difficulty of the helix reversal in the poly-**1** chains. This structural change observed in poly-**1** also contributes more or less to the memory effect. In the case of amino alcohols (Figure 11A, **5** for example), the hydrogen bond formation of the hydroxy group to a carboxy residue of poly-**1** must contribute to the maintenance of the helical chirality of poly-**1** and also for the fixation of the chiral conformation of the bound amino alcohols at the same time. These cooperative functions of the achiral amino alcohols lead to the good long-term memory of the one-handed helical conformation of poly-**1** and also to the repair of helical chirality. The longer amino alcohols (**8** and **9**) may not be able to interact cooperatively and showed relatively low memory efficiency compared to that of **5**−**7** (Figure 7). A similar model can be possible for primary amines (Figure 11B, **14** for example), and again the electrostatic repulsion between the neighboring carboxylate groups can be ascribed to the memory effect. Since the amines have no

hydroxy groups and exist as achiral conformations, their complexes with the isolated poly-**1** may not be able to be repaired but can keep the helical chirality for a rather short time as compared with amino alcohols.

The most important conclusions drawn from the present studies are (1) the ion pairing of poly-**1** with chiral amines is essential for the helicity induction and (2) the electrostatic repulsion between the carboxylate groups of poly-**1** derived from the dissociation of the ion pairs plays a central role for the macromolecular helicity memory of poly-**1** in DMSO. The memory of helicity process must be governed kinetically; the relative rate of the exchange reaction of the bound (*R*)-**2** with achiral amines and the atropisomerization process of poly-**1** might be responsible for the memory efficiency. Since poly-**1** and chiral amines can be complexed more efficiently through ion pairing in the presence of the common salt of the chiral amines, memory efficiency may be expected to improve when the replacement of the chiral amine with achiral amines is performed in the presence of the hydrochloride of the chiral amine. However, after the exchange reaction, the coexistence of the common salt prevents the maintenance of the helical chirality of poly-**1** as shown in Figure 10, and therefore, the

common salt should be removed by SEC as soon as possible just after the exchange reaction to attain high memory efficiency.

To examine this possibility, we carried out the following experiments. The poly-**1c**−(*R*)-**2** complexes containing various amount of (*R*)-**2**·HCl in DMSO were prepared, all of which showed a full ICD ([θ]$_{2nd}$ = ca. -3.1×10^4) regardless of the amount of (*R*)-**2**·HCl. Each sample was then injected into the SEC system using a DMSO solution containing **5** (0.008 M) or **16** (0.008 M) as the mobile phase to remove (*R*)-**2** and (*R*)-**2**· HCl simultaneously. The poly-**1c** was isolated in the same way as described above. After the SEC fractionation, CD spectra of the fractionated poly-**1c** were taken and the memory efficiencies were calculated. By this method, the (*R*)-**2** complexed with poly-**1c** can be completely replaced with the achiral amines in the presence of (*R*)-**2**·HCl, and the common salt as well as the (*R*)-**2** can also be removed at once during the SEC fractionation. The memory efficiency markedly increased with increasing (*R*)-**2**· HCl concentration. The maximum memory efficiencies improved from 68 to 99% for **5** and from 57 to 79% for **16** under the present conditions (see Figure S-10 in the Supporting Information). These values were higher than those in the absence of (*R*)-**2**·HCl by a factor of ca. 1.5 and 1.4, respectively. Especially, in the case of **5**, almost perfect memory could be achieved at [(*R*)-**2**·HCl] = 10 mM.

The remarkable procedure developed in this study will be useful to attain similar macromolecular helicity memory with perfect memory efficiency in other induced helical polymers.

Experimental Section

Full experimental details are available in the Supporting Information.

Materials. Three cis−transoidal poly-**1**s with different molecular weights were synthesized according to the previously reported method.[13b,22,29] The molecular weights (*M*$_n$) of poly-**1**s were estimated as its methyl ester by SEC with polystyrene standards using tetrahydrofuran (THF) or chloroform as the eluent; *M*$_n$ and *M*$_w$/*M*$_n$ = 1.7 × 10^4 and 2.1 (poly-**1a**), 3.3 × 10^4 and 2.8 (poly-**1b**), and 13.0 × 10^4 and 4.3 (poly-**1c**), respectively. Conversion of poly-**1**s into the methyl esters was carried out using diazomethane in ether solution or (trimethylsilyl)diazomethane in hexane solution according to the method reported previously.[13b,22]

Memory of Macromolecular Helicity: SEC Fractionation of Poly-1. Stock solutions of poly-**1** (6 mg/mL, 41 mM) and (*R*)-**2** (0.41 M) were prepared. A 400-μL aliquot of the stock solution of poly-**1** was transferred to a vessel equipped with a screwcap using a Hamilton microsyringe, and to this was added 400 μL of the stock solution of (*R*)-**2**; the initial CD spectrum was taken using a 0.01-cm quartz cell. SEC fractionation was performed using a Jasco PU-980 liquid chromatograph equipped with a UV (300 nm; Jasco UV-970) detector. A Shodex KF-806L SEC column was connected, and DMSO solutions containing appropriate amounts of amines were used as the mobile phase at a flow rate of 1.0 mL/min. A 100 μL of the solution of the poly-**1**−(*R*)-**2** complex was injected to the SEC system, and the poly-**1** and

(*R*)-**2** fractions were collected. The amount of the recovered (*R*)-**2** was estimated on the basis of the UV spectrum of the (*R*)-**2** fraction using the ϵ of (*R*)-**2** (ϵ_{284} = 6150 or ϵ_{300} = 2520 cm^{-1} M^{-1}). The excess amino alcohols ([amino alcohol]/[poly-**1**] = 50) were added to the solution of poly-**1**−(*R*)-**2** complex before the SEC fractionation unless otherwise stated. The CD spectra of the fractionated poly-**1**s were measured in 2-, 4-, or 5-mm quartz cell. The addition of excess amines or amino alcohols to the poly-**1a**−(*R*)-**2** complex before the SEC fractionation is not necessary for the macromolecular helicity memory, but it affects the memory efficiency depending on the structures of the amines and amino alcohols. For instance, the addition of excess amino alcohols **5**−**9** ([**5**−**9**]/[poly-**1a**] = 50) before the SEC fractionation tended to increase the memory efficiency, while the achiral amine **14** caused a slight decrease in the memory efficiency (from 82 to 68%). Therefore, achiral amino alcohols (**5**−**12**) ([**5**−**12**]/[poly-**1a**] = 50) except for **13** were added before the SEC fractionation, but an achiral amino alcohol **13** and other achiral and chiral amines except for **17** and **19** were not added to the solution of the poly-**1a**−(*R*)-**2** complex prior to SEC fractionation; the amine **17** was added before the SEC fractionation to compare its memory efficiency with an analogous amino alcohol **5**. The concentration of achiral amines and amino alcohols in the mobile phase influences the memory efficiency, but we found no significant changes in the memory efficiency for a typical amino alcohol (**5**) and amine (**14**) in the concentration ranges of 0.8−0.016 M for **5** and 0.8−0.008 M for **14**.

Supporting Information Available: Full experimental details, time-dependent ICD changes of poly-**1** with (*R*)-**3** and (*S*)-**4**, plots of IR titration data of poly-**1** and VBA with (*R*)-**2**, (*R*)-**3**, and (*S*)-**4**, CD spectral changes of poly-**1**−(*R*)-**2** complex with (*S*)-**2** and (*S*)-**3**, ICD intensity changes of poly-**1**−(*R*)-**3** complex with (*S*)-**3** with time and their CD spectral changes, CD spectral changes of poly-**1**−(*R*)-**2** complex by the addition of (*RS*)-**3**, SEC chromatograms of the refractionated poly-**1** and the poly-**1** solution containing 0.01 equiv of (*R*)-**2**, concentration effects of achiral amines on memory efficiency, CD intensity changes of the fractionated poly-**1**−**14** complex at various temperatures and the fractionated poly-**1**−**5**, −**14**, and −**17** complexes at 50 °C, and effect of (*R*)-**2**·HCl concentration on memory efficiency of the macromolecular helicity of poly-**1c** induced by (*R*)-**2** in the presence of (*R*)-**2**·HCl (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA0318378