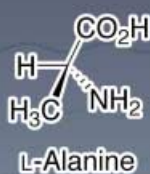
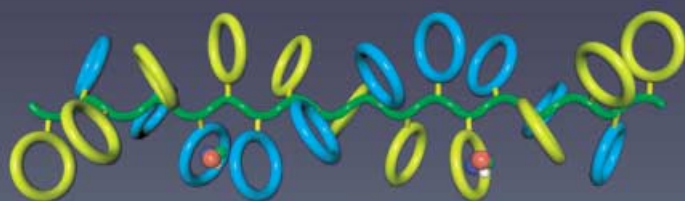
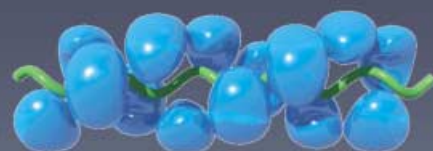


Detection and Amplification of Chirality by Helical Polymers

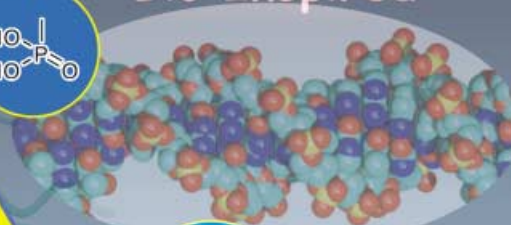
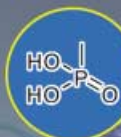
Chiral Amplification



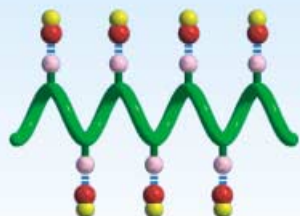
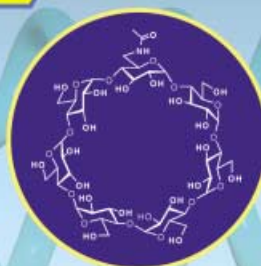
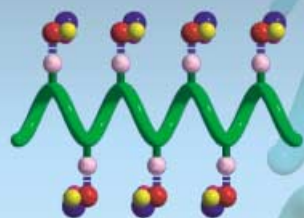
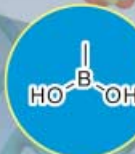
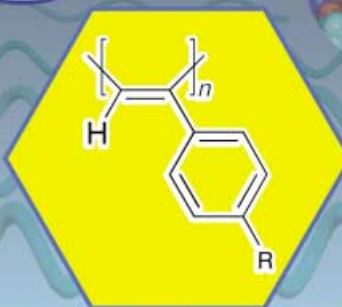
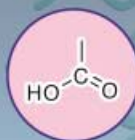
Chirality Sensing



Bio Inspired



Helicity Induction



Detection by a Color Change



Helix Inversion



Memory of Macromolecular Helicity

Detection and Amplification of Chirality by Helical Polymers

Eiji Yashima,^{*,[a, b, c]} Katsuhiro Maeda,^[a] and Tatsuya Nishimura^[a]

Dedicated to Professor Yoshio Okamoto on the occasion of his 63rd birthday

Abstract: A unique feature of synthetic helical polymers for the detection and amplification of chirality is briefly described in this article. In sharp contrast to host–guest and supramolecular systems that use small synthetic receptor molecules, chirality can be significantly amplified in a helical polymer, such as poly(phenylacetylene)s with functional pendants, which enable the detection of a tiny imbalance in biologically important chiral molecules through a noncovalent bonding interaction with high cooperativity. The rational design of polymeric receptors can be possible by using chromophoric helical polymers combined with functional groups as the pendants, which target particular chiral guest molecules for developing a highly efficient chirality-sensing system. The chirality sensing of other small molecular and supramolecular systems is also briefly described for comparison.

Keywords: chiral amplification • chirality • circular dichroism • helical structures • host–guest systems

Introduction

The transfer of chiral information to achiral or dynamically racemic supramolecules and macromolecular helical systems from nonracemic guest molecules through noncovalent

bonding interactions has attracted great interest in recent years.^[1] This is because chirality-transfer phenomenon can be used for sensing chirality for a wide range of chiral molecules, as well as for developing novel chiroptical devices and chiral materials as enantioselective adsorbents and catalysts.^[2] In particular, when a receptor molecule is achiral, but chromophoric, the noncovalent bonding to a chiral, non-racemic guest may provide a characteristic induced circular dichroism (ICD) in the absorption region of the receptor; the Cotton effect sign can be used to determine the absolute configuration of the guest.^[1] Alternative methods for sensing chirality have also been developed by means of designer chiral receptors with a rigid concave cavity and/or functional groups capable of interacting with a target chiral guest through inclusion complexation by hydrogen bonding and/or π – π and electrostatic interactions. Optically active cyclic compounds, such as modified cyclodextrins, cyclophanes, and crown ethers, are among the most extensively studied host molecules.^[3] Due to their rigidity and distinct conformational scaffold, these chiral receptors usually exhibit a high specificity and enantioselectivity for the target guests in chiral recognition events like enzymes. However, sensing chirality by using CD seems to be laborious because of their high specificity and the chiral nature of the receptor themselves.

Recently, we found a similar, but conceptually different phenomenon for the complexes of optically inactive, but dynamic helical chromophoric polymers with chiral guests; stereoregular, optically inactive poly(phenylacetylene)s bearing various functional groups can change their structures into the prevailing, dynamic one-handed helices upon complexation with specific chiral guests.^[4] The complexes showed characteristic ICDs in the UV-visible region of the polymer backbone. The Cotton effect signs corresponding to the helical sense can be used as a novel probe for the chirality assignments of the guest molecules.^[5] Helical polymers, in sharp contrast to the above-mentioned small receptor molecules, are very sensitive to a chiral environment and exhibit optical activity due to a one-handed helical chirality of the polymer main chain through a significant cooperative interaction with a considerable amplification of chirality.^[6]

The nonempirical exciton-coupled CD method developed by Nakanishi, Harada, and Berova has proved to be practi-

[a] Prof. Dr. E. Yashima, Dr. K. Maeda, T. Nishimura
Department of Molecular Design and Engineering
Graduate School of Engineering
Nagoya University
Chikusa-ku, Nagoya 464–8603 (Japan)
Fax: (+81)52-789-3185
E-mail: yashima@apchem.nagoya-u.ac.jp

[b] Prof. Dr. E. Yashima
Institute for Advanced Research, Nagoya University
Chikusa-ku, Nagoya 464–8601 (Japan)
E-mail: yashima@apchem.nagoya-u.ac.jp

[c] Prof. Dr. E. Yashima
Yashima Super-structured Helix Project
ERATO, JST, Moriyama-ku, Nagoya 464–0003 (Japan)
E-mail: yashima@apchem.nagoya-u.ac.jp

cally useful for determining the absolute configuration of a variety of chiral molecules,^[7] but this method usually requires the introduction of chromophores through covalent bonding suitable for the exciton coupling at particular functional groups and is beyond the subject of this Concept article. Here, we emphasize the helical polymers induced by noncovalent bonding interactions as a powerful chirality-sensing probe. Other noncovalent chirality-sensing molecular and supramolecular systems are also briefly described.

Chirality Sensing by Supramolecular Systems

Recently developed, novel chirality-sensing small molecules are shown in Figures 1 and 2. These receptors may be classified into two types with respect to the mechanism or origin of the chirality induced in the receptors from the chiral guests; one is induced-fit type receptors (**1–4**) and the other is inherently chiral receptors (**5–8**). The resocinol cyclotramer, (**1**),^[8] calixarenes (**2**),^[9] and bis(zincporphyrin) dimers (porphyrin tweezers) (**3**)^[10] and **4**^[11] belong to the former type. These molecules are flexible and achiral, but upon the binding of specific chiral guests, such as chiral glycols, sugars, ammonium groups, amino acid esters, and diamines, the chirality transforms to the receptors, resulting in the induced-fit generation of an enantiomeric C_2 twisted conformation at the diphenylmethane units in **1** and **2** and porphyrin helicity in **3** and **4**; therefore, the complexes exhibited exciton-coupled ICDs whose sign can be used to detect the chirality of the guest molecules. Particularly, the porphyrin tweezer **4** with a powerful porphyrin chromo-

phore is useful for the microgram-scale chirality discrimination of diamines, amino acids, and amino alcohols.^[11]

On the other hand, the receptors **5–8**^[12–15] exist as an equal mixture of enantiomeric twisted or helical conformers, which are in rapid equilibrium as shown in Figure 2. In the presence of chiral guests, however, the equilibrium shifts to one of the enantiomeric conformers (so-called asymmetric transformation or enantiomerization takes place^[16]) as a result of the diastereoselective complexation with chiral guests, thus leading to ICDs in the receptors' chromophore regions. Therefore, these receptors are regarded as inherently chiral molecules, but they cannot be resolved into the enantiomers, at least not at room temperature.^[17]

π -Conjugated achiral oligomers of *m*-phenylene ethynylene (**8**) solvophobically fold into right- and left-handed helical conformations in polar solvents, such as acetonitrile, and in aqueous solution, which creates a specific tubular cavity for hydrophobic guests. Both helices are at equilibrium, but in the presence of chiral monoterpenes, such as α -pinene, one of helices predominantly forms and the complex exhibits a characteristic ICD.^[15]

These approaches are very interesting and promising for the detection or sensing of the chirality of target chiral molecules. The key point is how to design and synthesize chromophoric achiral or dynamically racemic receptors whose conformations change to chiral or nonracemic ones as a result of binding to nonracemic guests. However, due to the stoichiometric complexation mode in their host-guest binding systems (**1–8**), chiral information of a guest transfers to a complexed receptor and, therefore, further chirality amplification appears to be, so far, not possible.^[18] Nevertheless, a very interesting chirality "memory" effect was observed for the saddle-shaped porphyrin **6**^[13] and the cerium double decker porphyrin **7**,^[14] after removal of the chiral guests followed by replacement with achiral molecules, the complexes still retained the chiral information and the memory persisted for hours. This chirality memory effect has now been observed in other supramolecular systems^[19] and is particularly interesting because of its versatility for novel molecular memory device systems as well as a chirality-sensing probe. This process can be considered as a typical example of chiral amplification of the supramolecular level.^[20]

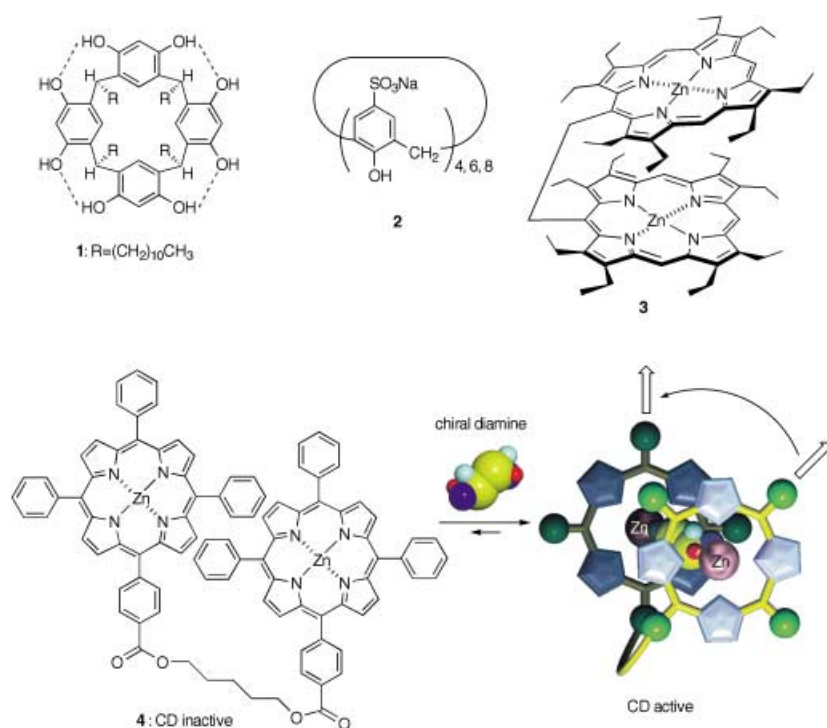


Figure 1. Structures of achiral receptor molecules **1–4** and induced-fit generation of an enantiomeric twisted porphyrin helicity in **4**.

Chirality Sensing by Helical Polymers

In 1995, we reported that macromolecular helicity with an

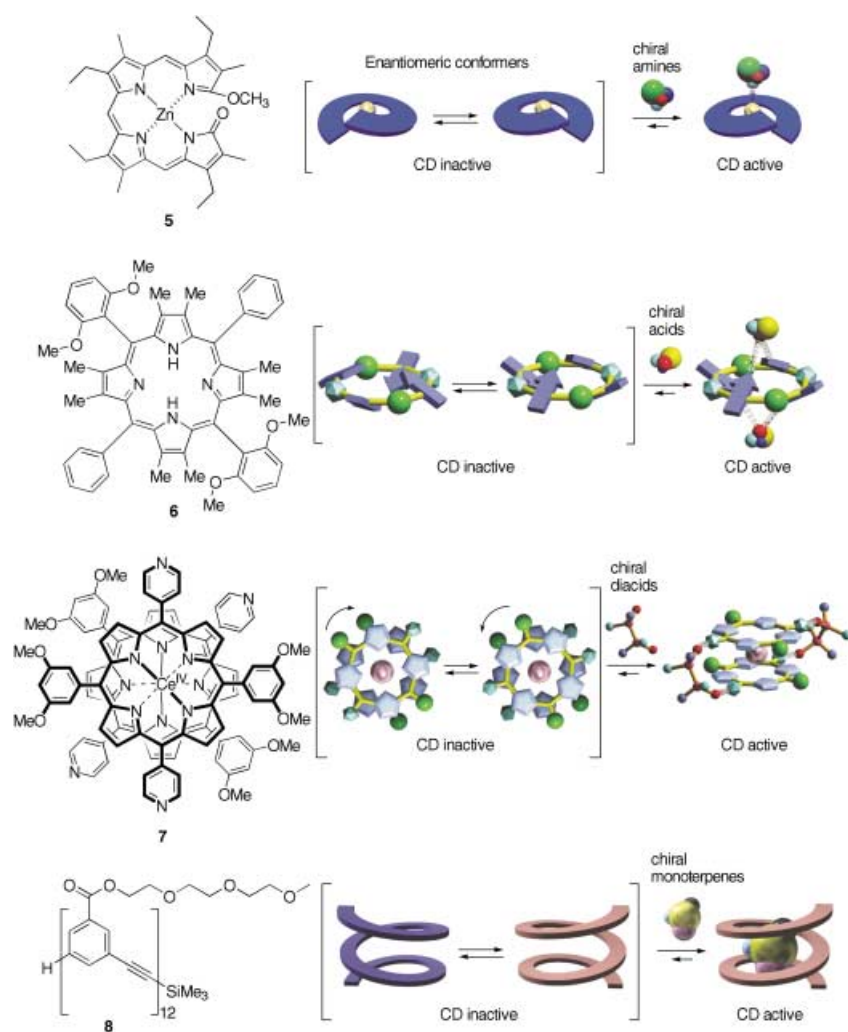


Figure 2. Structures of chiral receptor molecules **5–8** and possible enantiomerization mechanisms upon binding to chiral guests.

excess helical sense could be induced in an optically inactive, dynamic helical polymer by an optically active small molecule.^[4] A *cis-transoidal* stereoregular poly[(4-carboxyphenyl)acetylene] (**9a** in Figure 3) prepared by the polymerization of the corresponding phenylacetylene monomer with a rhodium catalyst was the first example of such a noncovalent, one-handed-helicity induction phenomenon using chiral acid–base interactions. Upon acid–base complexation with chiral amines in DMSO, a dynamic one-handed macromolecular helicity is induced in the polymer, resulting in characteristic ICDs in the long wavelength region of the π -conjugated polymer backbone (300–500 nm). The induced Cotton effect signs corresponding to the helix-sense of **9a** can be used for the chirality assignment of the amines. Primary amines and amino alcohols of the same configuration yield the same sign of the ICDs.^[4,5] Before this finding, helical polymers with optical activity due to macromolecular helicity have usually been prepared either by the polymerization of optically active monomers or by the asymmetric polymerization of achiral or prochiral monomers with chiral catalysts or initiators. In these cases, the helical structures and their helix senses are controlled by chiral pendants co-

valently bonded to the polymer backbone or kinetically during the polymerization.^[6] The advantages of the present system with the π -conjugated polyacetylene are its long-wavelength absorption, high sensitivity without derivatization, and easy preparation into a film. The concept of this helicity induction through noncovalent chiral molecular interactions is widely applicable to the design and synthesis of related chirality-responsive poly(phenylacetylene)s bearing various functional groups as the pendant. For instance, the introduction of amino (**9b**),^[21] boronate (**9c**),^[22] phosphonate (**9d**, **9e**),^[23] and sulfonate (**9f**)^[24] groups as the pendant produced poly(phenylacetylene)s that can respond to the chirality of chiral acids, sugars, amines, and ammonium groups, respectively, and their complexes show a characteristic ICD depending on the stereochemistry including the absolute configurations of the guest molecules.

This one-handed helicity induction concept allows polymer chemists to use dynamic helical, chromophoric polymers or oligomers as templates for macromolecular helicity induction

systems. In fact, similar helicity induction in the presence of chiral molecules capable of noncovalently interacting with the polymer's functional groups was achieved for aliphatic polyacetylenes (**10**, **11**),^[25] polyphosphazene (**12**),^[26] polyisocyanate (**13**),^[27] polyguanidine (**14**),^[28] and polyisocyanide (**15**)^[29] by our group or others.^[33] Inai et al. took advantage of the helicity induction concept combined with the structural feature of an achiral oligopeptide (**16**) as a template to induce a predominantly one-handed helix by chiral carboxylic acids.^[31] The binding of chiral carboxylic acids to the N-terminal amino group of the peptide produced an ICD derived from the one-handed helical conformation of the entire peptide chain. This phenomenon was called the “non-covalent domino effect”.^[32]

Chiral solvation, while its chiral bias seems to be very weak, can also be used to induce a helical conformation with a preferential screw-sense in the achiral poly(*n*-hexyl isocyanate) (**17**)^[33] and a polysilane (**18**).^[34] The helicity induction was detected by the appearance of CD in the UV-visible region of the polymer backbone. Due to the complexity of the interaction mechanism and practical unfeasibility, this method may not be applicable for general use as

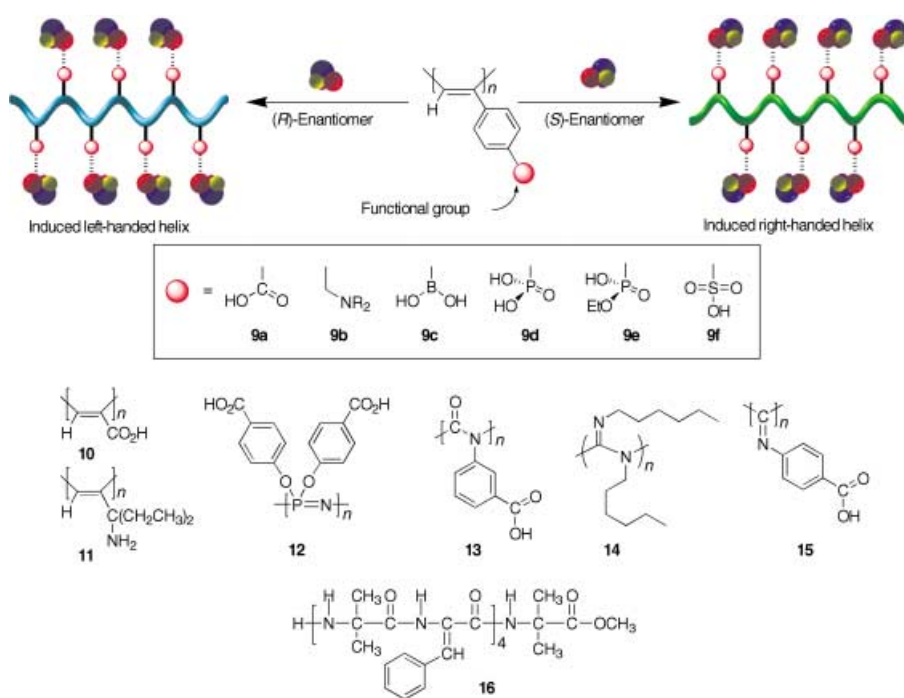
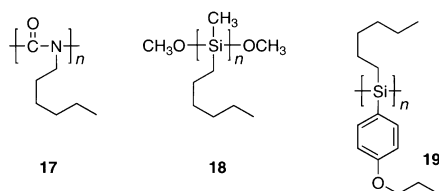


Figure 3. Schematic illustrations of the formation of a one-handed helical structure of achiral poly(phenylacetylene)s upon complexation with chiral compounds (9) and structures of induced helical polymers (10–15) and an oligopeptide (16).



a chirality-sensing probe of chiral solvents. A similar achiral stiff polysilane (19) also exhibited an ICD when the polymer formed supramolecular aggregates with helical chirality in solution that contained chiral alcohols as the co-solvent.^[35] The ICD signs reflect the position of the OH group and their absolute configurations of the alcohols. The underlying principle is conceptually interesting and may have great potential to be of general use for the chirality sensing of chiral alcohols.

Chiral Amplification by Helical Polymers

Starting with the pioneering work by Green and co-workers on the structural and chiroptical investigation of polyisocyanates, a typical stiff, rigid rodlike polymer with a long persistent length, the substantial nature of

the dynamic macromolecular helicity of polyisocyanates has been experimentally and theoretically revealed.^[6b,36] Green discovered that the copolymerization of an achiral isocyanate with a small amount of optically active isocyanate (less than 1 mol%) produced an almost perfect one-handed helical polyisocyanate.^[37,38] This is a typical and excellent example of the chiral amplification of covalent systems in a polymer and is called the “sergeants and soldiers effect”. The underlying principle for this phenomenon, based on theoretical calculations, is considered to be that even optically inactive, but dynamically racemic polyisocyanates such as poly(*n*-hexyl isocyanate) (17) and poly(2-butylhexyl isocyanate) (20), which are devoid of stereogenic centers, are an equal mixture of right- and left-handed helical

conformations separated by the helix reversal points that readily move along the polymer backbone (Figure 4).^[38] Therefore, helical polyisocyanates at dynamic equilibrium can be considered as an inherently chiral (or racemic) macromolecule like 5–8. Green further demonstrated that copolymers composed of a mixture of (*R*)- and (*S*)-enantiomers with a small enantiomeric excess (*ee*) also form a predominantly one-handed helical conformation, and only 12% *ee* was sufficient to give a single-handed helical polymer for poly(2,6-dimethylheptylisocyanate).^[39] The minority units obey the helical sense of the majority units in order to avoid introducing energetic helical reversals. This phenomenon (positive nonlinear effect in asymmetric synthesis) is

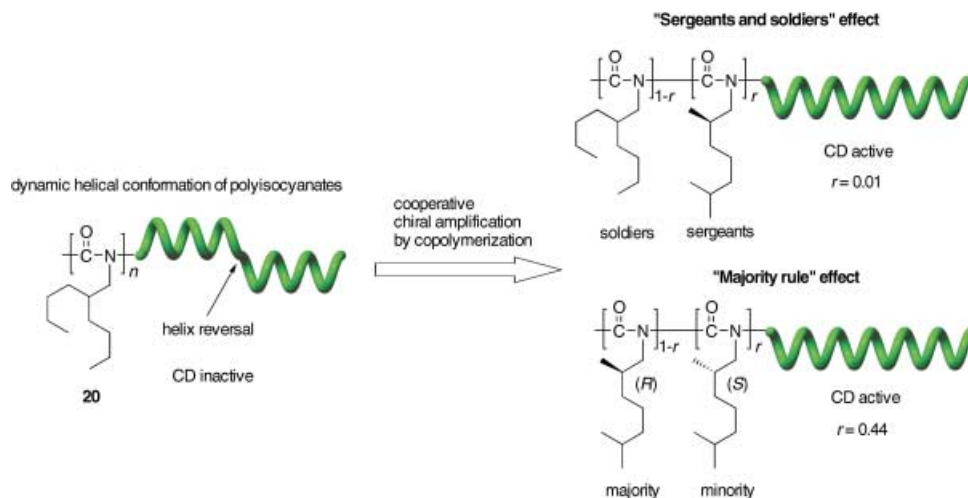


Figure 4. Characteristics of dynamic helical polyisocyanates.

called the “majority rule”.^[39] Consequently, chiral information of a tiny amount of a pendant covalently bonded to the polymer backbone is significantly amplified and transformed into an entire polymer chain through a significant cooperative manner, resulting in a higher optical activity than that expected from the monomer unit components (chiral–achiral or chiral–chiral (*R/S*) combination). This is the most important feature of dynamic helical polymers and is completely different from the above-mentioned small molecular and supramolecular systems (**1–8**). Helical polyisocyanates are very sensitive to a chiral environment, therefore, the helical dynamically racemic polyisocyanate (**17**) exhibited optical activity due to a helicity in nonracemic solvents as described above.^[33]

On the basis of these observations, the chirality-responsive polyacetylenes (**9**) described above may be regarded as an analogue of the dynamic helical polyisocyanates, although these polymers are not stiff, but rather flexible because of their short persistent length.^[40] In fact, noncovalent “sergeants and soldiers” and “majority rule” effects were observed in the poly(phenylacetylene) **9a**. Typically, when **9a** was mixed with 50% *ee* of 2-amino-1-propanol in DMSO, the complex showed an intense CD as that of 100% *ee*.^[5a] The noncovalent chirality amplification was also observed in the complexation of **9a** in the presence of a small amount of (*S*)-2-amino-1-propanol (0.3 equiv to the monomer units of **9a**) and excess achiral 2-aminoethanol. The polymer complexed with the chiral amino alcohol exhibited a weak ICD, because of the lack of one-handedness in the helical conformation of the polymer. However, the addition of an increasing amount of the achiral 2-aminoethanol caused a dramatic increase in the ICD intensity, which was ten times higher than that of the complex of **9a** with 0.3 equivalents of (*S*)-2-amino-1-propanol.^[5a] Upon complexation of **9a** with the achiral amino alcohol, the population of the right- and left-handed helices may be remarkably altered and induce a more intense ICD.^[40]

During the intensive exploration of the chirality amplification mechanism, we observed an unusual, but interesting macromolecular helicity memory in this dynamic helical polymer system; the macromolecular helicity of **9a** induced by optically active amines, such as (*R*)-1-(1-naphthyl)ethylamine (**21**), can be memorized even after complete removal and replacement of the amines with achiral ones (for instance, 2-aminoethanol (**22**) or *n*-butylamine (**23**)) (Figure 5).^[41] The macromolecular helicity memory was quite stable and lasted for a long time (over two years). The chirality memory effect has been observed for supramolecular systems (**6**, **7** and see ref. [19]), but never previously observed in helical polymers. The chiral amplification combined with the macromolecular helicity memory with achiral amines

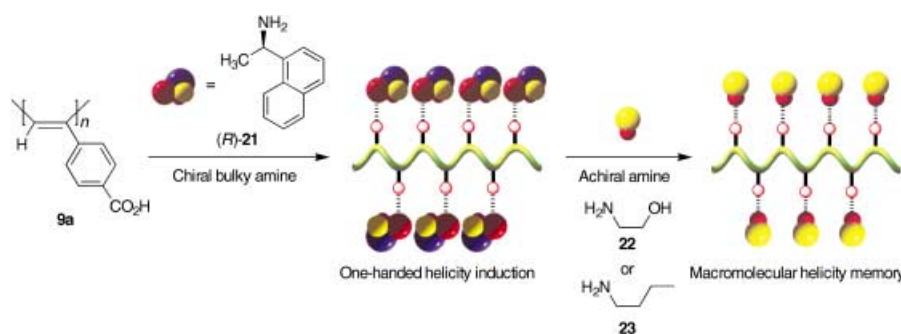


Figure 5. Schematic illustration of memory of macromolecular helicity concept. The macromolecular helicity induced on **9a** by a chiral amine (*R*)-**21** is memorized after complete removal of the amine and replacement with achiral amines (**22**, **23**).

will offer a highly sensitive, chirality detection method for chiral molecules whose optical activity is too small to detect by conventional spectroscopic means.

More recently, we have succeeded in the detection of an extremely small enantiomeric imbalance in α -amino acids by a poly(phenylacetylene) bearing the bulky crown ether as the pendant for the amino acid binding site (**24** in Figure 6).^[42] The polymer was designed and synthesized on the basis of an idea that the introduction of an achiral bulky host group such as crown ether units as the pendant may improve the rigidity of the polymer backbone, so as to act analogously to the polyisocyanates in their stiff helical char-

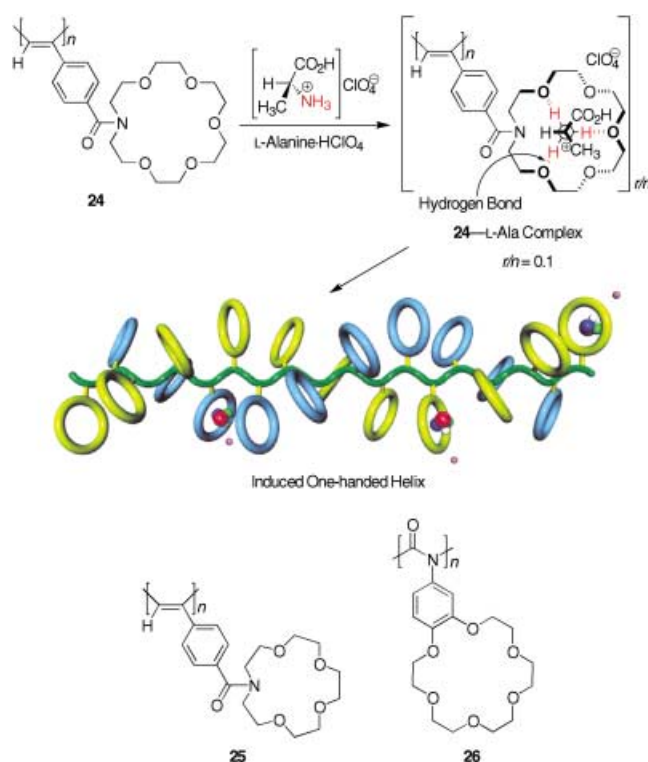


Figure 6. Structures of conjugated polymers bearing crown-ether pendants (**24–26**), and a possible model for the induced helical **24** complexed with L-alanine. The crown ether units are represented by yellow and blue rings for clarity and arrange in a helical array with a predominant screw-sense along the polymer backbone.

acter with alternating left- and right-handed helical segments separated by rarely occurring helix reversals. In fact, 0.1 equivalents of L-alanine (L-Ala) induced an almost one-handed helix on **24** in acetonitrile. Moreover, **24** exhibited an apparent ICD even with 0.01 equivalents of L-Ala, indicating a strong chiral amplification with cooperative interaction in the pendants through noncovalent interactions. The lower limit of detection of L-Ala was 70 ng for the appearance of the ICD on **24**. This means that a very small chiral bias in the pendant crown units complexed with L-Ala is significantly amplified to induce the same helix on the major free crown ether units. The significant advantage of this polymer is that all the common 19 L-amino acids as well as some amino alcohols derived from the amino acids produced the same Cotton effect signs. This indicates that for detecting amino acid chirality, **24** is indeed among the most sensitive and practically useful synthetic receptors.

An extremely strong chiral amplification was also observed in this system despite the noncovalent bonding interaction (Figure 7). Even a 5% *ee* of Ala brought about the

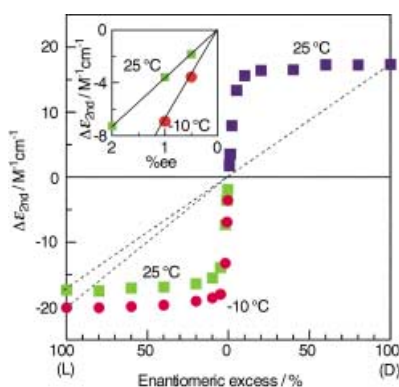


Figure 7. Changes in ICD intensity of the second Cotton ($\Delta\epsilon_{2nd}$) of **24** versus the % *ee* of alanine during the complexation with **24** in acetonitrile at 25 and -10°C .^[42a]

full ICD as induced by 100% *ee* of L-Ala.^[42] Complexation of a slight excess of one enantiomeric Ala with the pendant crown ether units gave rise to an excess of the helical sense preferred by the majority enantiomer. Similar strong chiral amplifications were also observed for leucine and tryptophan. This striking chiral amplification of **24** enabled detection of the chirality of Ala with a very small *ee* of less than 0.005% with good accuracy and reproducibility. A good linear relationship between the *ee* (from 0.1 to 0.005%) and the ICD intensities of the polymer was found.^[42] It is interesting to note that Ala is a typical amino acid frequently found in several meteorites including the Murchison meteorite, which will make it possible to detect very small enantiomeric imbalances in a wide variety of amino acids and related molecules of interest in studies of meteorites and other objects.^[43]

We expected that analogous dynamic helical polymers, including poly(phenylacetylene)s bearing other achiral crown ethers with different ring sizes or macrocyclic host pendants, could also form a dynamically induced helix in the presence

of chiral compounds capable of interacting with the pendants. In fact, a stereoregular poly(phenylacetylene) bearing the aza[15]crown-5 ether as the pendant (**25**)^[44] was found to form a predominantly one-handed helix in the presence of amino acids, amines, and amino alcohols in organic solvents, thus leading to ICDs, although the sensitivity of **25** to the amino acids chirality was not as high as that of **24**. However, **25** showed a higher sensitivity to the chirality of secondary amines and L-proline than **24**. These polymers were soluble in water and exhibited ICDs with amino acids, and chiral aromatic amines and alcohols. Currently, we speculate that the hydrophobic interaction between the polymers and guests functions as a chiral bias for inducing an excess one-handed helicity in water.

Subsequent to our reports of **24** and **25**, Kakuchi and co-workers utilized the helicity induction concept and synthesized a polyisocyanate with benzo[18]crown-6 pendants (**26**).^[45] A similar one-handed helicity induction on **25**, as revealed by an appearance of the ICD in the polymer backbone region, was observed in organic solvents upon complexation with amino acids. The chiral amplification effect was, however, smaller than those for the crown-ether-bound poly(phenylacetylene)s (**24**, **25**).

Chiral Amplification by Supramolecular Assembly

Other examples of the chiral amplification phenomenon have been reported for supramolecular assembly systems that involve self-assemblies composed of achiral–chiral or chiral–chiral (*R/S*) components in which the chiral units are covalently bonded to the components.^[3d,20,46] Supramolecular assemblies occur through intermolecular, noncovalent π – π stacking and/or hydrogen-bonded network between the components and exhibit an optical activity derived from supramolecular chirality. The chiroptical properties obey the sergeants and soldiers principle or majority rule. The recently reported self-assembled helical rosette nanotubes by Feniri et al. are one of the most interesting approaches for chirality sensing (Figure 8).^[47] They found that the heterocyclic base with the benzo[18]crown-6 unit (**27**) underwent a

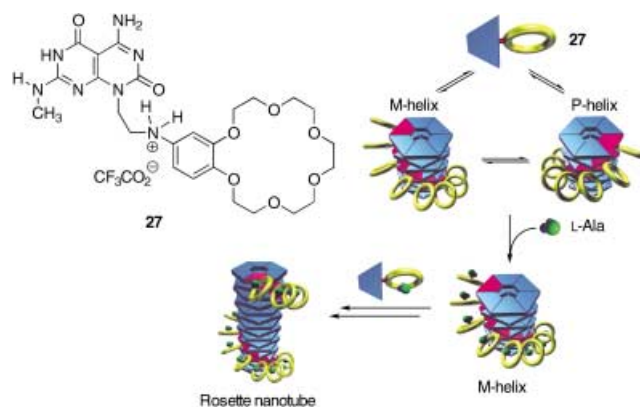


Figure 8. Schematic representations of supramolecular self-assembly of **27** to form a left-handed rosette nanotube with L-alanine.^[47]

hierarchical self-assembly to generate equal amounts of right- and left-handed helical rosette nanotubes. The further addition of *L*-Ala, however, spontaneously promoted the change of the racemic nanotubes to the one-handed helical ones as indicated by the appearance of the ICD. The majority rule effect was also observed in this system, which will offer a useful probe for sensing the amino acid chirality through a significant chiral amplification by a supramolecular assembly.

Chirality Sensing in Water by Helical Polyelectrolytes

Although a number of chiral receptor molecules have been prepared for chiral or chirality recognition in organic media,^[3,19] chiral recognition of charged biomolecules in water with charged, water soluble chiral receptors remains very difficult.^[1c,9,48] This is because small electrolytes predominantly dissociate into free ions in water by hydration, so that attractive interactions such as hydrogen bonding and electrostatic interactions may not be anticipated in water. In sharp contrast, polyelectrolytes such as nucleic acids are completely different from small electrolytes; that is, a portion of the counterions are bound to polyelectrolytes of a sufficiently high charge density, and, therefore, polyelectrolytes can effectively interact with small charged biomolecules even in water.^[49] On the basis of these considerations, we prepared a chromophoric polyelectrolyte bearing a phosphonate group as the pendant (**9d**, **9e**), bioinspired by the interaction motifs of nucleic acids, and found that these polyelectrolytes could interact with a variety of charged and noncharged biomolecules, including amino acids, aminosugars, carbohydrates, and peptides, in water. The complexes form supramolecular assemblies with controlled helicity through electrostatic and hydrogen-bonding interactions in water.^[23,50] For instance, the assay of 19 of the common free *L*-amino acids produced the ICDs of **9e** with the same Cotton effect signs, demonstrating that the polyelectrolyte functions as the first powerful chirality-sensing probe in water. This concept, that is, the use of a chromophoric dynamic helical polyelectrolyte, is promising for the construction of a specific sensory system for a target biomolecule by tuning the functional group of the polyelectrolyte.

Chirality Sensing by Helix Inversion of Helical Polymers

Several synthetic, optically active polymers and biopolymers are known to exhibit helix inversion (helix–helix transition) between right- and left-

handed helical conformations by changing the external conditions, such as solvent, temperature, or by the irradiation of light.^[6d,51] On the other hand, switching of the macromolecular helicity by chiral stimuli is quite rare, but can be used to sense the chirality of chiral guests. We previously reported the first example of such a helix inversion induced by external chiral stimuli through diastereomeric, noncovalent acid–base interactions. A poly(phenylacetylene) bearing an optically active functional group such as a (1*R*,2*S*)-norephedrin residue (**28** in Figure 9)^[52] is an optically active polymer and exhibited an ICD in the long-wavelength region due to a predominantly one-handed helical conformation. However, it underwent a transition from one helix to another in the presence of (*R*)-mandelic acid (**29**) in DMSO, which induced an inversion of the Cotton effect signs, whereas the ICD of **28** hardly changed even in the presence of (*S*)-**29**. These results suggest that the difference in the free energy between the right- and left-handed helices of the polyacetylene is relatively small and highly sensitive to the chirality of the acids, and that there is a delicate balance between the helices, which may lead to such a helix inversion by responding to the chirality of the acids. In this particular system, the chirality can be determined by CD.

Taking advantage of a chromophoric, dynamic helical polyacetylene backbone, we quite recently prepared a unique polyacetylene (**30**) bearing an optically active bulky β -cyclodextrin as the side group that exhibited the inversion of helicity induced by inclusion complexation with chiral guest molecules into the chiral cyclodextrin cavity as well as by solvent and temperature.^[53] The helicity inversion was accompanied by a color change due to a change in the twist angle of the conjugated double bonds (tunable helical pitch) that was readily visible with the naked eye and could be quantified by absorption and CD spectroscopies. (*R*)-1-Phenylethylamine (**31**) induced a negligible color change in the DMSO-alkaline water mixture of **30**. However, the polymer exhibited a color change (from yellow to red) in the presence of (*S*)-**31** accompanied by an inversion of the Cotton effect sign. This system seems to be a conceptually new chirality-sensing method using a helical polymer.

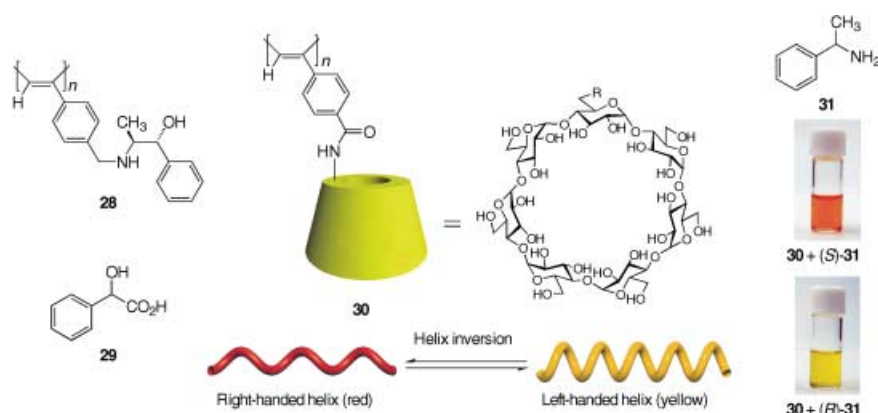


Figure 9. Structures of optically active poly(phenylacetylene) derivatives (**28**, **30**) and schematic illustration of interconvertible right- (red) and left-handed (yellow) helices of **30**. The solution colors of **30** in the presence of (*S*)- (red) and (*R*)-**31** (yellow) are also shown.

Conclusion

The most important feature of dynamic helical polymers is high sensitivity to a chiral environment and, therefore, a small chiral bias that occurred in the remote side chain through chiral molecular interactions can be transformed into a main-chain conformational change with a large amplification. Such systems might provide the basis to construct a novel chirality-sensing probe. Moreover, if the main chain is also chromophoric, as in conjugated polymers, the output signal transmitted by the chirality of the guests may be significantly enhanced when chiral conjugated polymers have a dynamic helical structure. Furthermore, when chromophoric, dynamic helical polymers are further functionalized with a conformationally labile, inherently chiral supramolecular receptor as the pendant, it may exhibit an ideal sensing system for the chirality of the desired guest molecules, whereby the chiral information of the guest first transfers to the pendant through noncovalent interactions. Subsequently, the induced supramolecular chirality can be further amplified in the polymer backbone as an excess of a single-handed helix.

Acknowledgement

The authors' work reported herein were partially supported by a Grant-in-Aid for Scientific Research from Japan Society for the Promotion of Science and the Ministry of Education, Culture, Sports, Science, and Technology, Japan and the 21st Century COE Program "Nature-Guided Materials Processing" of the Ministry of Education, Culture, Sports, Science and Technology.

- [1] a) E. Yashima, Y. Okamoto, *Circular Dichroism: Principles and Applications* (Eds.: N. Berova, K. Nakanishi, R. W. Woody), 2nd ed., Wiley-VCH, New York, **2000**, Chapter 18, pp. 521–546; b) J. W. Canary, A. E. Holmes, J. Liu, *Enantiomer* **2001**, *6*, 181–188; c) H. Tsukube, S. Shinoda, *Chem. Rev.* **2002**, *102*, 2389–2403; d) S. Allenmark, *Chirality* **2003**, *15*, 409–422.
- [2] a) Y. Okamoto, T. Nakano, *Chem. Rev.* **1994**, *94*, 349–372; b) Y. Okamoto, E. Yashima, *Angew. Chem.* **1998**, *110*, 1072–1095; *Angew. Chem. Int. Ed.* **1998**, *37*, 1020–1043.
- [3] a) T. H. Webb, C. S. Wilcox, *Chem. Soc. Rev.* **1993**, *22*, 383–395; b) X. X. Zhang, J. S. Bradshaw, R. M. Izatt, *Chem. Rev.* **1997**, *97*, 3313–3361; c) J. H. Hartley, T. D. James, C. J. Ward, *J. Chem. Soc. Perkin Trans. 1* **2000**, 3155–3184; d) L. J. Prins, D. N. Reinhoudt, P. Timmerman, *Angew. Chem.* **2001**, *113*, 2446–2492; *Angew. Chem. Int. Ed.* **2001**, *40*, 2382–2426.
- [4] E. Yashima, T. Matsushima, Y. Okamoto, *J. Am. Chem. Soc.* **1995**, *117*, 11596–11597.
- [5] a) E. Yashima, T. Matsushima, Y. Okamoto, *J. Am. Chem. Soc.* **1997**, *119*, 6345–6359; b) E. Yashima, *Anal. Sci.* **2002**, *18*, 3–6.
- [6] a) A. E. Rowan, R. J. M. Nolte, *Angew. Chem.* **1998**, *110*, 65–71; *Angew. Chem. Int. Ed.* **1998**, *37*, 63–68; b) M. M. Green, J.-W. Park, T. Sato, A. Teramoto, S. Lifson, R. L. B. Selinger, J. V. Selinger, *Angew. Chem.* **1999**, *111*, 3329–3345; *Angew. Chem. Int. Ed.* **1999**, *38*, 3138–3154; c) T. Nakano, Y. Okamoto, *Chem. Rev.* **2001**, *101*, 4013–4038; d) M. Fujiki, J. R. Koe, K. Terao, T. Sato, A. Teramoto, J. Watanabe, *Polym. J.* **2003**, *35*, 297–344.
- [7] a) N. Berova, K. Nakanishi, *Circular Dichroism: Principles and Applications* (Eds.: N. Berova, K. Nakanishi, R. W. Woody), 2nd ed., Wiley-VCH, New York, **2000**, Chapter 12, pp. 337–382. Since CD measures the difference in absorption of left- and right-handed circularly polarized light, more sensitive fluorescence-detected CD has been developed. b) T. Nehira, C. A. Parish, S. Jockusch, J. Turro, K. Nakanishi, N. Berova, *J. Am. Chem. Soc.* **1999**, *121*, 8681–8691.
- [8] Y. Kikuchi, K. Kobayashi, Y. Aoyama, *J. Am. Chem. Soc.* **1992**, *114*, 1351–1358.
- [9] a) T. Morozumi, S. Shinkai, *J. Chem. Soc. Chem. Commun.* **1994**, 1219–1220; b) T. Morozumi, S. Shinkai, *Chem. Lett.* **1994**, 1515–1518.
- [10] V. V. Borovkov, J. M. Lintuluoto, M. Fujiki, Y. Inoue, *J. Am. Chem. Soc.* **2000**, *122*, 4403–4407.
- [11] X. Huang, B. H. Rickman, B. Borhan, N. Berova, K. Nakanishi, *J. Am. Chem. Soc.* **1998**, *120*, 6185–6186.
- [12] T. Mizutani, S. Yagi, A. Honmaru, H. Ogoshi, *J. Am. Chem. Soc.* **1996**, *118*, 5318–5319.
- [13] Y. Furusho, T. Kimura, Y. Mizuno, T. Aida, *J. Am. Chem. Soc.* **1997**, *119*, 5267–5268.
- [14] A. Sugasaki, M. Ikeda, M. Takeuchi, A. Robertson, S. Shinkai, *J. Chem. Soc. Perkin Trans. 1* **1999**, 3259–3264.
- [15] R. B. Prince, S. A. Barnes, J. S. Moore, *J. Am. Chem. Soc.* **2000**, *122*, 2758–2762.
- [16] E. L. Eliel, S. H. Wilen, *Stereochemistry of Organic Compounds*, Wiley-Interscience, New York, **1994**, pp. 315–316.
- [17] Analogous double-decker porphyrins to **7** with bulky substituents were successfully resolved into the enantiomers by Aida. K. Tashiro, K. Konishi, T. Aida, *Angew. Chem.* **1997**, *109*, 882–884; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 856–858.
- [18] Recently, chiral amplification was realized for a linear dimer of zinc bilinone (**5**) and a cyclic dimer of **6** linked with achiral spacers. Binding of a chiral guest induced the chirality of one porphyrin subunit in the receptors, which further controlled the chirality of the other porphyrin subunit through intramolecular interactions of the subunits. See, a) T. Mizutani, N. Sakai, S. Yagi, T. Takagishi, S. Kitagawa, H. Ogoshi, *J. Am. Chem. Soc.* **2000**, *122*, 748–749; b) Y. Mizuno, T. Aida, *Chem. Commun.* **2003**, 20–21.
- [19] a) E. Bellacchio, R. Lauceri, S. Gurrieri, L. M. Scolaro, A. Romeo, R. Purrello, *J. Am. Chem. Soc.* **1998**, *120*, 12353–12354; b) L. J. Prins, F. D. Jong, P. Timmerman, D. N. Reinhoudt, *Nature* **2000**, *408*, 181–184; c) J. M. Rivera, S. L. Craig, T. Martín, J. Rebek, Jr., *Angew. Chem.* **2000**, *112*, 2214–2216; *Angew. Chem. Int. Ed.* **2000**, *39*, 2130–2132; d) Y. Kubo, T. Ohno, J.-I. Yamanaka, S. Tokita, T. Iida, Y. Ishimaru, *J. Am. Chem. Soc.* **2001**, *123*, 12700–12701; e) M. Ziegler, A. V. Davis, D. W. Johnson, K. N. Raymond, *Angew. Chem.* **2003**, *115*, 689–692; *Angew. Chem. Int. Ed.* **2003**, *42*, 665–668; f) R. Purrello, *Nat. Mater.* **2003**, *2*, 216–217.
- [20] T. Ishi-i, M. Crego-Calama, P. Timmerman, D. N. Reinhoudt, S. Shinkai, *J. Am. Chem. Soc.* **2002**, *124*, 14631–14641.
- [21] a) E. Yashima, Y. Maeda, Y. Okamoto, *Chem. Lett.* **1996**, 955–956; b) K. Maeda, S. Okada, E. Yashima, Y. Okamoto, *J. Polym. Sci., Part A* **2001**, *39*, 3180–3189.
- [22] E. Yashima, T. Nimura, T. Matsushima, Y. Okamoto, *J. Am. Chem. Soc.* **1996**, *118*, 9800–9801.
- [23] H. Onouchi, K. Maeda, E. Yashima, *J. Am. Chem. Soc.* **2001**, *123*, 7441–7442.
- [24] K. Maeda, H. Ishiguro, T. Hasegawa, E. Yashima, unpublished results.
- [25] a) E. Yashima, H. Goto, Y. Okamoto, *Polym. J.* **1998**, *30*, 69–71; b) K. Maeda, H. Goto, E. Yashima, *Macromolecules* **2001**, *34*, 1160–1164.
- [26] E. Yashima, K. Maeda, T. Yamanaka, *J. Am. Chem. Soc.* **2000**, *122*, 7813–7814.
- [27] K. Maeda, N. Yamamoto, Y. Okamoto, *Macromolecules* **1998**, *31*, 5924–5926.
- [28] D. S. Schlitzer, B. M. Novak, *J. Am. Chem. Soc.* **1998**, *120*, 2196–2197.
- [29] M. Ishikawa, K. Maeda, E. Yashima, *J. Am. Chem. Soc.* **2002**, *124*, 7448–7458.
- [30] π -Conjugated polymers, such as polyaniline showed an ICD in the presence of chiral dopants in solution, which was thought to be due to a helix formation of the main chain through a chiral acid-base interaction. M. R. Majidi, L. A. P. Kane-Maguire, G. G. Wallace, *Polymer* **1995**, *36*, 3597–3599.
- [31] Y. Inai, K. Tagawa, A. Takasu, T. Hirabayashi, T. Oshikawa, M. Yamashita, *J. Am. Chem. Soc.* **2000**, *122*, 11731–11732.
- [32] Covalent domino effect was reported for oligo(phenyl isocyanate) derivatives: K. Maeda, Y. Okamoto, *Polym. J.* **1998**, *30*, 100–105.

- [33] M. M. Green, C. Khatri, N. C. Peterson, *J. Am. Chem. Soc.* **1993**, *115*, 4941–4942.
- [34] P. Dellaportas, R. G. Jones, S. J. Holder, *Macromol. Rapid Commun.* **2002**, *23*, 99–103.
- [35] H. Nakashima, J. R. Koe, K. Torimitsu, M. Fujiki, *J. Am. Chem. Soc.* **2001**, *123*, 4847–4848.
- [36] M. M. Green, N. C. Peterson, T. Sato, A. Teramoto, R. Cook, S. Lifson, *Science* **1995**, *268*, 1860–1866.
- [37] M. M. Green, M. P. Reidy, R. J. Johnson, G. Darling, D. J. O'Leary, G. Willson, *J. Am. Chem. Soc.* **1989**, *111*, 6452–6454.
- [38] S. K. Jha, K.-S. Cheon, M. M. Green, J. V. Selinger, *J. Am. Chem. Soc.* **1999**, *121*, 1665–1673.
- [39] M. M. Green, B. A. Garetz, B. Munoz, H. Chang, S. Hoke, R. G. Cooks, *J. Am. Chem. Soc.* **1995**, *117*, 4181–4182.
- [40] a) K. Morino, K. Maeda, Y. Okamoto, E. Yashima, T. Sato, *Chem. Eur. J.* **2002**, *8*, 5112–5120; b) Y. Ashida, T. Sato, K. Morino, K. Maeda, Y. Okamoto, E. Yashima, *Macromolecules* **2003**, *36*, 3345–3350.
- [41] E. Yashima, K. Maeda, Y. Okamoto, *Nature* **1999**, *399*, 449–451.
- [42] a) R. Nonokawa, E. Yashima, *J. Am. Chem. Soc.* **2003**, *125*, 1278–1283; b) R. Nonokawa, E. Yashima, *J. Polym. Sci. Part A* **2003**, *41*, 1004–1013.
- [43] a) J. L. Bada, D. P. Glavin, G. D. McDonald, L. Becker, *Science* **1998**, *279*, 362–365; b) J. Podlech, *Angew. Chem.* **1999**, *111*, 501–502; *Angew. Chem. Int. Ed.* **1999**, *38*, 477–478.
- [44] R. Nonokawa, M. Oobo, E. Yashima, *Macromolecules* **2003**, *36*, 6599–6606.
- [45] R. Sakai, T. Satoh, R. Kakuchi, H. Kaga, T. Kakuchi, *Macromolecules* **2003**, *36*, 3709–3713.
- [46] a) A. R. A. Palmans, J. A. J. M. Vekemans, E. E. Havinga, E. W. Meijer, *Angew. Chem.* **1997**, *109*, 2763–2765; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2648–2651; b) L. Brunsveld, E. W. Meijer, R. B. Prince, J. S. Moore, *J. Am. Chem. Soc.* **2001**, *123*, 7978–7984; the formation of chiral liquid crystalline phases of helical polymers also leads to an amplification of the solid state supramolecular chiroptical properties; c) M. Oda, H.-G. Nothofer, G. Lieser, U. Scherf, S. C. J. Meskers, D. Neher, *Adv. Mater.* **2000**, *12*, 362–365.
- [47] H. Fenniri, B.-L. Deng, A. E. Ribbe, *J. Am. Chem. Soc.* **2002**, *124*, 11064–11072.
- [48] a) M. Alamgir, H.-J. Schneider, *J. Am. Chem. Soc.* **1998**, *120*, 11208–11209; b) K. Wada, T. Mizutani, H. Matsuoka, S. Kitagawa, *Chem. Eur. J.* **2003**, *9*, 2368–2380, and references therein.
- [49] G. S. Manning, *Acc. Chem. Res.* **1979**, *12*, 443–449.
- [50] M. A. Saito, K. Maeda, H. Onouchi, E. Yashima, *Macromolecules* **2000**, *33*, 4616–4618.
- [51] a) G. Maxein, R. Zentel, *Macromolecules* **1995**, *28*, 8438–8440; b) M. Fujiki, *J. Am. Chem. Soc.* **2000**, *122*, 3336–3343, and references therein.
- [52] E. Yashima, Y. Maeda, Y. Okamoto, *J. Am. Chem. Soc.* **1998**, *120*, 8895–8896.
- [53] E. Yashima, K. Maeda, O. Sato, *J. Am. Chem. Soc.* **2001**, *123*, 8159–8160.