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Theoretical Study of Helix Induction on a Polymer Chain by Hydrogen-Bonding Chiral Molecules

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ABSTRACT: Fundamental properties of the helices induced on a polymer chain due to hydrogen bonding of chiral and achiral molecules on the chain side are studied by a new statistical-mechanical theory. Unlike optically active random copolymers, the selection process of the helical sequences on a polymer chain is thermoreversible because of the reversible nature of association. The molecular origin for nonlinear amplification of chiral order by small enantiomer excess (majority rule) in such annealed randomness is clarified. Enhancement of the chirality by added achiral molecules (sergeants-and-soldiers rule) is also derived. Theoretical calculations of the helix content θ and the helical order parameter ψ are compared with recent experimental measurements of circular dichroism in solutions of poly((4-carboxyphenyl)-acetylene) bearing optically active amino groups that are hydrogen-bonded to carboxylic groups on the polymer chain.

1. Introduction

Chiral centers, either in the main chain or in side groups, often induce helical structures along the polymer chain, whose helicity, or handedness, is determined by the chirality of the centers. For instance, random copolymers bearing pendant groups of opposite enantiomers reveal unusual sensitivity to chiral effects that arises from the long sequential helical blocks with alternating handedness separated by infrequent and mobile helical reversals. Such cooperativity in chiral ordering of random copolymers has extensively been studied in a series of experiments on polyisocyanates.[1,2] It was found that, in polyisocyanates with a random sequence of (R) and (S) pendant groups, the optical activity measured by circular dichroism (CD) responds sharply to a slight excess of (R) over (S) groups (majority effect). It was also found that, in polyisocyanates with a random sequence of (R) pendant groups and achiral pendant groups, the optical activity sharply responds to small concentrations of chiral groups. Chiral groups are therefore called “sergeants” and achiral groups “soldiers” (sergents-and-soldiers effect). Such effects were theoretically studied by mathematically mapping the polymer chain onto a one-dimensional Ising model with random external magnetic field.[3,4] Conformation fluctuation and helix reversal were recently studied by Sato et al.[5,6] in terms of the free energy difference between conformational local minima. The randomness in the sequence of pendant groups in statistical copolymers is a fixed variable that is frozen in when copolymers are polymerized (quenched randomness). Optical activity appears as a result of averaging over such a quenched randomness.

Similar cooperative chiral order in polymers with hydrogen-bonding side groups was reported by Yashima et al.[8] In a series of experiments,[8−11] poly((4-carboxyphenyl)acetylene) revealed the above two nonlinear optical effects under the presence of chiral and achiral amines and amino alcohols in a solvent of dimethyl sulfoxide (DMSO). In contrast to random copolymers, pendant groups are hydrogen-bonded onto the polymer chain in these experiments, so that the distribution of pendant groups along the polymer chain is not a frozen variable but is thermally controllable (annealed randomness). They are thermoreversibly attached onto and removed from the polymer chain. Optical activity in such hydrogen-bonding polymers therefore appears as a result of averaging over annealed randomness. In this respect, it is not entirely surprising that similar nonlinear chirality amplification is observed in self-assembled hydrogen-bonding supramolecules, i.e., polymer-like aggregates formed by linear assembly of chiral units.[12−14] Synthesis, conformation, and function of helical polymers are reviewed by Okamoto.[15]

In this paper, we attempt to theoretically describe cooperative chiral ordering in polymers carrying hydrogen-bonded pendant groups. We derive two major effects described above by directly analyzing the sequence selection process when the chiral molecules are attached onto the polymer backbone. We treat a single polymer chain dissolved in a solution of chiral (and achiral) molecules; thereby, the solution is regarded as a particle reservoir at constant chemical potentials. The grand-canonical ensemble method is applied for the particle reservoir. The mapping to the Ising model is avoided because the method is purely mathematical and it is difficult to see the physical meaning of the parameters. Attempts to extend the present theory to polymer solutions at finite concentrations in which helices interact with each other will be reported in a forthcoming paper.

2. Distribution Function of the Helices on a Polymer Chain

We first study adsorption of chiral molecules by polymer chains in a solution. In the present study, the polymer concentration is assumed to be sufficiently low so that the solution serves as a particle reservoir of chiral molecules. Let us consider a single polymer chain (poly((4-carboxyphenyl)acetylene) in ref 8) made up of

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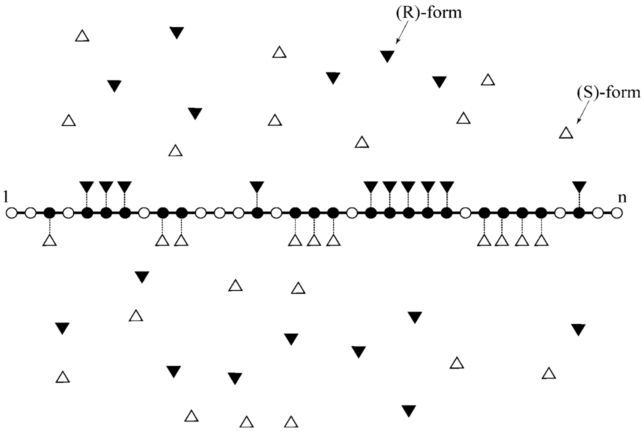

Figure 1. A single polymer chain adsorbing chiral molecules at its chain side in a solution of enantiomer mixture. Molecules of the same chirality are sequentially adsorbed onto the polymer chain. An adsorbed sequence induces a helix of fixed handedness according to the chirality of adsorbed molecules.

n monomeric units (carboxyphenyl acetylene), each carrying a hydrogen-bonding site (carboxylic group), in a solvent (DMSO) under the presence of chiral molecules (amines and amino alcohols). In the experiment,[8] it was found that the chiral molecules in the (S)-form induce left-handed helices on a polymer chain when attached onto it by hydrogen bonds, and those in the (R)-form induce right-handed helices, or vice versa. In this section, we consider a mixture of enantiomers, (S)-form and (R)-form, to study their competition in adsorption. Let their molar concentrations be given by $c^{(S)}$ and $c^{(R)}$. We first find the number and length distribution of helices along the chain in adsorption equilibrium as functions of the temperature and concentrations of the chiral molecules.

Let $j_\zeta^{(\alpha)}$ be the number of helical sequences of the length ζ (in terms of the number of monomeric units) occupied by the attached chiral molecules of the type α = S, R (see Figure 1). These sequences are randomly selected from the finite total length, or degree of polymerization (DP) n, during the thermal adsorption process of the chiral molecules. A molecule gains additional energy and is stabilized when it is adsorbed onto the position next to the already bonded molecule of the same chirality, but it cannot be adsorbed to the nearest-neighboring position of the already bonded molecule of the opposite chirality because of the strong steric hindrance. We therefore have to introduce at least one nonbonded site between the helical sequences of the different handedness. Similarly, there should be at least one nonbonded site between the helical sequences of the same handedness to distinguish the two helices (see Figure 1). The number of different ways to choose such sequences from the finite total length n is then given by

$$\omega(\{j\}) = [n - \sum \zeta (j_\zeta^{(S)} + j_\zeta^{(R)})]!/ \\ \{\prod_\zeta (j_\zeta^{(S)}!\, j_\zeta^{(R)}!)[n - \sum(\zeta+1)(j_\zeta^{(S)} + j_\zeta^{(R)})]!\} \quad (2.1)$$

We assume that the remaining parts take a random-coil conformation because the local minima in the potential of internal rotation are symmetrically located and separated by the energy barrier that can easily overcome by thermal activation. By using this combinatorial factor in sequence selection process, we find that the canonical partition function of a chain is given by

$$Z_n(n^{(S)}, n^{(R)}) = \sum_{\{j\}} \omega(\{j\}) \prod_\zeta [(\eta_\zeta^{(S)})^{j_\zeta^{(S)}} (\eta_\zeta^{(R)})^{j_\zeta^{(R)}}] \quad (2.2)$$

where $\eta_\zeta^{(\alpha)}$ is the statistical weight for a type α helix of the length ζ and

$$n^{(\alpha)} \equiv \sum_{\zeta \geq 1} \zeta j_\zeta^{(\alpha)} \quad (2.3)$$

is the total number of adsorbed molecules of type α. Such a combinatorial counting method in sequence selection process was first introduced by Gornick and Jackson[16] to study segment crystallization of polymers. We have recently applied the method to the problem of thermoreversible gelation induced by the coil-to-helix transition of polymers.[17] To find the equilibrium distribution function, we maximize this partition function by changing $\{j\}$ under the given concentration of chiral molecules. Since the solution is a particle reservoir, we introduce the activity λ_α of the molecules of type α as independent variables (functions of the concentration) and move to the grand partition function

$$\Xi_n(\{\lambda\}) \equiv \sum_{n^{(S)}, n^{(R)}=0}^{n} \lambda_S^{\,n^{(S)}} \lambda_R^{\,n^{(R)}} Z_n(n^{(S)}, n^{(R)}) \quad (2.4)$$

The most probable distribution function of helices that maximizes this grand partition function is then found to be

$$j_\zeta^{(\alpha)}/n = (1 - \theta - \nu)\eta_\zeta^{(\alpha)}(\lambda_\alpha t)^\zeta \quad (2.5)$$

by variational calculation. Here

$$\theta = \theta^{(S)} + \theta^{(R)} \quad (2.6)$$

is the total helix content (number of monomers in the helical state relative to the total DP) with

$$\theta^{(\alpha)} \equiv \sum_{\zeta \geq 1} \zeta j_\zeta^{(\alpha)}/n \quad \text{for } \alpha = \text{S, R} \quad (2.7)$$

being the helix content of each handedness. Similarly

$$\nu = \nu^{(S)} + \nu^{(R)} \quad (2.8)$$

is the total number of helices (relative to the total DP) with

$$\nu^{(\alpha)} \equiv \sum_{\zeta \geq 1} j_\zeta^{(\alpha)}/n \quad \text{for } \alpha = \text{S, R} \quad (2.9)$$

being the number of helices of each handedness. The parameter t is defined by

$$t \equiv (1 - \theta - \nu)/(1 - \theta) \quad (2.10)$$

and has the physical meaning of the probability such that an arbitrarily chosen monomer belongs to the random coil part. To see this, we substitute the equilibrium distribution (2.5) into the grand partition function and find that it is given by

$$\Xi_n(\{\lambda\}) = t^{-n} \quad (2.11)$$

Since the probability $p(n^{(S)} = 0, n^{(R)} = 0)$ for finding a completely random coil is given by $1/\Xi_n(\{\lambda\})$, we find

$$p(n^{(S)} = 0, n^{(R)} = 0) = t^n \tag{2.12}$$

and hence the physical interpretation of the parameter t is apparent. To find t as a function of the activities, we now substitute the equilibrium distribution (2.5) into the definitions of θ and ν and find

$$\theta^{(\alpha)} = (1 - \theta)tV_1^{(\alpha)}(\lambda_\alpha t) \tag{2.13}$$

and

$$\nu^{(\alpha)} = (1 - \theta)tV_0^{(\alpha)}(\lambda_\alpha t) \tag{2.14}$$

for each handedness, where functions V_0 and V_1 are defined by

$$V_0^{(\alpha)}(x) \equiv \sum_{\zeta=1}^{n} \eta_\zeta^{(\alpha)} x^\zeta \tag{2.15a}$$

$$V_1^{(\alpha)}(x) \equiv \sum_{\zeta=1}^{n} \zeta\eta_\zeta^{(\alpha)} x^\zeta \tag{2.15a}$$

By defining eq 2.10 for t, we find that it should satisfy the condition

$$\frac{t}{1 - t}\{V_0^{(S)}(\lambda_S t) + V_0^{(R)}(\lambda_R t)\} = 1 \tag{2.16}$$

This is basically the same equation found by Zimm and Bragg[18,19] (referred to as ZB) and also by Lifson and Roig,[18,20] but here properly extended to suit for helix formation induced by chiral molecules attached on the chain side. The solution of this equation gives the probability t as a function of the temperature and activities (and hence concentrations) of the chiral molecules. Upon substitution of the result into eq 2.6, together with eq 2.13, we find the helix content θ is given by

$$1 - \theta = 1/\{1 + t[V_1^{(S)}(\lambda_S t) + V_1^{(R)}(\lambda_R t)]\} \tag{2.17}$$

The helix content and the number of helices for each component of chiral molecules are then calculated from eqs 2.13 and 2.14.

3. Statistical Weight of Helices

We now proceed to employ specific form for the statistical weight of helices. ZB proposed the simple form

$$\eta_\zeta = \sigma s(T)^\zeta \tag{3.1}$$

where σ comes from a boundary between a random coil part and a helical part (the helix initiation factor), and $s(T)$ comes from the interaction between the neigboring side groups (amino acid residues in proteins). The temperature dependence of $s(T)$ is given by $\ln s(T) = \text{const} - \epsilon_H/k_BT$ with ϵ_H (<0) being the hydrogen-bonding energy between the side groups. Lifson and Roig proposed a slightly different statistical weight, but the nature of coil-to-helix transition is essentially the same, so that we do not discuss it here.

In the present study of chain-side adsorption, an adsorbed chiral molecule is bound to the main chain through hydrogen bond and interacts with the molecules that are adsorbed in the nearest-neighboring sites along the chain. Let $-\epsilon_H$ be the hydrogen-bonding energy between a monomer unit on the polymer chain and a chiral molecule adsorbed onto it, and let $-\Delta\epsilon_\alpha$ be the stabilization energy gained through the interaction with the neighboring chiral molecule of the same species that is already adsorbed on the chain. We assume that repulsive interaction between the molecules of different chirality is so large due to the steric hindrance that no nearest-neighboring pairs of different chirality appear. Then, the statistical weight of helices of each handedness is described by the factor

$$\eta_\zeta^{(\alpha)} = \sigma_\alpha u_\alpha(T)^\zeta, \quad \text{for } \alpha = \text{S, R} \tag{3.2}$$

where the factor $u_\alpha(T) \equiv \exp[(\epsilon_H + \Delta\epsilon_\alpha)/k_BT]$ now includes the hydrogen-bonding energy gain as well as the stabilization energy, and the helix initiation parameters are given by $\sigma_\alpha \equiv \exp(-\Delta\epsilon_\alpha/k_BT)$.

The V functions now take the form

$$V_0^{(\alpha)}(x) = \sigma_\alpha u_\alpha x w_0(u_\alpha x) \tag{3.3a}$$

$$V_1^{(\alpha)}(x) = \sigma_\alpha u_\alpha x w_1(u_\alpha x) \tag{3.3b}$$

where functions w are defined by

$$w_0(x) \equiv \sum_{\zeta=1}^{n} x^{\zeta-1} \tag{3.4a}$$

$$w_1(x) \equiv \sum_{\zeta=1}^{n} \zeta x^{\zeta-1} \tag{3.4b}$$

Now, the equation to determine t takes the form

$$\frac{t^2}{1 - t}\{\sigma_S\gamma_S w_0(\gamma_S t) + \sigma_R\gamma_R w_0(\gamma_R t)\} = 1 \tag{3.5}$$

where

$$\gamma_\alpha \equiv \lambda_\alpha u_\alpha(T) \quad \text{for } \alpha = \text{S, R} \tag{3.6}$$

are the statistical weight of a chiral molecule multiplied by its activity. If the concentrations of chiral molecules are small, we can assume that the activity is proportional to the molar concentration of the species. Hence, for dilute solution, we have the form

$$\gamma_\alpha = k_\alpha(T)c^{(\alpha)} \quad \text{for } \alpha = \text{S, R} \tag{3.7}$$

where $k_\alpha(T)$ is the adsorption equilibrium constant of the molecules of type α. It is proportional to the statistical weight $u_\alpha(T)$ of an adsorbed molecule and is given by $\ln k_\alpha(T) = -\Delta f_\alpha/k_BT$ in terms of the free energy change Δf_α on binding a molecule of type α. The concentrations of chiral molecules are always accompanied by the adsorption constant and appear as a set $\gamma = k(T)c$. In what follows we assume that these adsorption constants, and hence ϵ_H and $\Delta\epsilon$, are the same for both components since molecules are chemically the same except for their stereosymmetry.

4. Chirality Order Parameter

In the experiments,[8−10] optical activity (CD intensity and specific rotation) is measured as functions of the temperature and enantiomer concentrations. To compare the experimental data with the present theory, we first calculate the chiral order parameter ψ defined by the difference

$$\psi \equiv \theta^{(S)} - \theta^{(R)} \tag{4.1}$$

This order parameter is proportional to the rotation angle of an incident polarized light beam and also to the intensity of CD induced in the UV−vis region.

From the equations obtained in the preceding section, we find

$$\psi = \frac{t^2[\sigma_S\gamma_S w_1(\gamma_S t) - \sigma_R\gamma_R w_1(\gamma_R t)]}{1 + t^2[\sigma_S\gamma_S w_1(\gamma_S t) + \sigma_R\gamma_R w_1(\gamma_R t)]} \tag{4.2}$$

where parameter t is the solution of eq 3.5. For a racemic mixture where $c^{(S)} = c^{(R)}$ holds, the order parameter vanishes because $\gamma_S = \gamma_R$ and $\sigma_S = \sigma_R$ by symmetry.

We first study simple limiting cases where there is only one form of chiral molecules. The solution medium is completely polarized. Figure 2 plots theoretical calculation of the probability t and the helix content θ as functions of the reduced concentration $\gamma = k(T)c$ of the chiral molecules. The result is the same irrespective of the chirality, so that we omit the super- and subscripts. The DP of a polymer chain is fixed at $n = 1000$, while the helix initiation parameter σ is changed from curve to curve. The transition from random coil state to helical state takes place at around $\gamma = 1.0$ and becomes sharper for smaller values of σ. The transition becomes sharper also with increase in DP, and in the limit of infinite DP, the coil-to-helix transition becomes discontinuous, and hence it is a real thermodynamic phase transition.[18] Figure 3 compares the intensity of induced circular dichroism (ICD) (white circles) with the theoretically calculated chiral order parameter (solid lines). ICD is measured[8] at wavelength 374 nm for the solution of poly((4-carboxyphenyl)acetylene) in DMSO under the presence of the (R)-form of amino alcohol (more precisely (R)-(−)-2-amino-1-propanol, referred to as (R)-18 in the literature[8]) and plotted against the renormalized concentration $\gamma \equiv k(T)c$ of amino alcohols. The intensity of ICD is normalized so that the asymptotic value at the high concentration limit approaches unity. In the study,[8] polymers with molecular weight 46 000 were used, but in the recent new experiment,[21] longer chains with the molecular weight estimated to be 130 000 were used to see the effect of the molecular weight, so that we have fixed at $n = 1000$ (molecular weight of a monomer is 144) in the theoretical calculation. There are two theoretical parameters: the helix initiation probability σ and the adsorption constant $k(T)$. To find the optimal value of σ, five theoretical lines for different σ are drawn. As for the association constant $k(T)$, we have horizontally shifted (on a logarithmic scale) the original experimental data (broken line) to fit the theoretical curves. We find that the value $\sigma = 0.01$ with the shift factor $k(T) = 1.7$ gives a very good fit as shown in the figure.

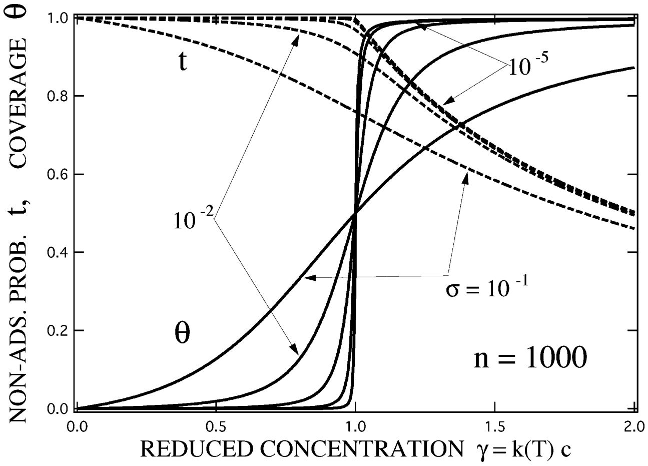

Figure 2. Helix formation by hydrogen-bonded chiral molecules of pure chirality. The coverage θ (the number of adsorbed site relative to the total DP n) and the probability t for a monomer to be in the random coil state are plotted against the reduced concentration γ (molar concentration c of chiral molecules multiplied by the adsorption constant $k(T)$). DP of the polymer chain is fixed at 1000, while the helix initiation factor σ is changed from curve to curve.

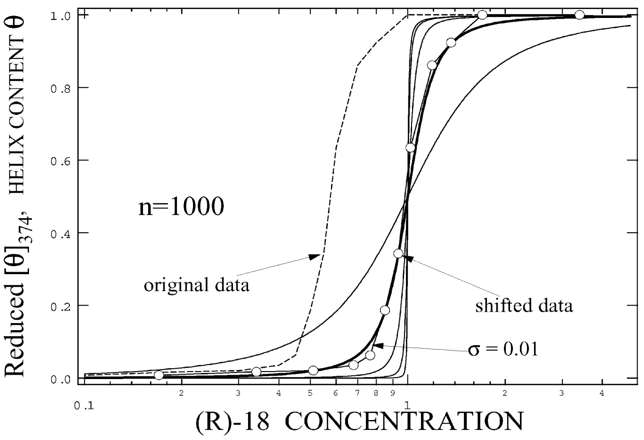

Figure 3. Helix formation by (R)-form amino alcohols. ICD intensities measured in the experiment (circles) and theoretical calculation (solid lines) of the helix content are plotted against the reduced concentration of the chiral molecules (R)-18 (amino alcohol). DP of the polymer is $n = 1000$. The helix initiation parameter is varied from curve to curve. The best fit is obtained by $\sigma = 0.01$.

Smallness of the helix initiation parameter σ leads to a very sharp increase in the chiral order at around the critical values of amino alcohol concentration ($\gamma = 1.0$ in this case). Such a nonlinear change is one of the common characteristic features of the coil-to-helix transition.[18]

Figure 4 shows the same but under the presence of the (S)-form of naphthylamine (more precisely (S)-(−)-1-(1-naphthyl)ethylamine, referred to as (S)-2 in the literature[8]). The polymer is the same. Similarly to amino alcohols, we find that the value $\sigma = 0.01$ gives a good fit to the observed sigmoidal curve, but the shift factor is found to be $k(T) = 1.4$, i.e., smaller than the case of amino alcohols. The gradual rise of ICD at low concentrations ($\gamma \simeq 0.5$) of amine is not reproduced by the theoretical curve with $\sigma = 0.01$, but the data lie in between $\sigma = 0.01$ and 0.05.

The difference in the association constant $k(T)$ can be attributed to the bulkiness of the adsorbed molecules. Since the strength of the hydrogen bond onto the

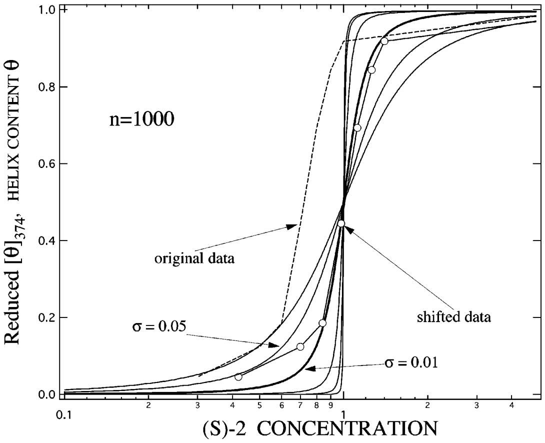

Figure 4. Same plot as in Figure 3 for the chiral molecule (S)-2-(naphthylamine).

polymer main chain is expected to be of the same order, the difference comes from the excluded-volume interaction between the neigboring molecules. Because the larger molecules (naphthylethylamine) suffer stronger steric repulsion, it is natural that their association constant is smaller than that of the smaller molecules (amino alcohol). From the above theoretical fit, we find $k(R18)/k(S2) = 1.7/1.2 = 1.42$. Recent direct experimental measurement,[22] however, gives $k(R18)/k(S2) = 1074/35 = 30.7$. The large discrepancy between these estimated ratios remains unresolved.

5. Majority Rule

We now proceed to the more interesting case of enantiomer mixtures. We first introduce the total concentration $c \equiv c^{(S)} + c^{(R)}$ of enantiomers. The enantiomer excess (referred to as e.e.), or chiral polarization of the media, is then defined by

$$e \equiv (c^{(S)} - c^{(R)})/(c^{(S)} + c^{(R)}) \tag{5.1}$$

The renormalized concentration of each species can be written as

$$\gamma_S = (1 + e)\gamma/2 \quad \text{and} \quad \gamma_R = (1 - e)\gamma/2 \tag{5.2}$$

where

$$\gamma \equiv k(T)c \tag{5.3}$$

is for the total concentration. The equation to find the probability t now takes the form

$$\frac{\gamma t^2}{2(1-t)}\{\sigma_S(1+e)w_0((1+e)\gamma t/2) + \sigma_R(1-e)w_0((1-e)\gamma t/2)\} = 1 \tag{5.4}$$

The order parameter can be calculated by eq 4.2 as before.

Figure 5 shows theoretical calculation of the order parameter as a function of the e.e. for a polymer with $n = 1000$ and for the case of $\sigma_S = \sigma_R = 0.01$. The total concentration γ is changed from curve to curve. When the total concentration exceeds a critical value γ_c, the chiral order on a chain becomes very sensitive to a slight polarization of the media from a racemic mixture. The critical value in this figure is around $\gamma_c \simeq 2.0$. Such a sharp amplification of the order parameter to the direction of an excess enantiomer is called the majority rule in the literature.[1,2] It is caused by the sequential interaction between the neighboring chiral molecules that are adsorbed onto the polymer under the constant chemical potential. As a result, the ratio $\theta^{(S)}/\theta^{(R)}$ takes a largely different value from that of the concentration $c^{(S)}/c^{(R)}$ in the bulk. At finite polymer concentration, the chemical potential of the majority component decreases with increase in the number of adsorbed molecules due to depletion, and hence the nonlinear amplification eventually saturates.

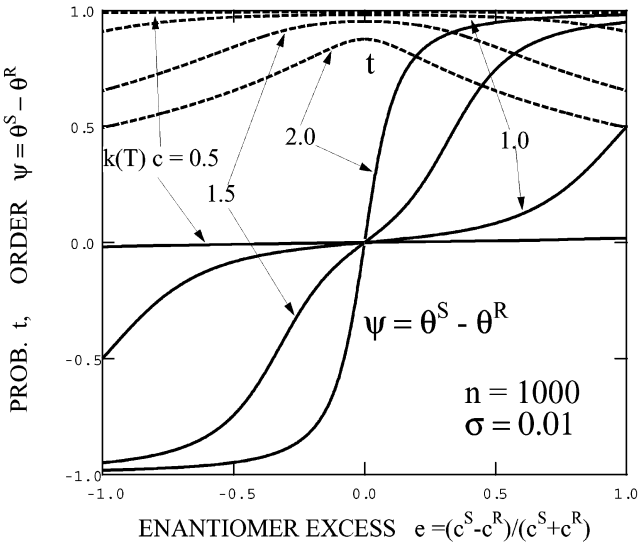

Figure 5. Chiral order parameter ψ and the probability t plotted against enantiomer excess e for $n = 1000$ and $\sigma_S = \sigma_R = 0.01$. For large total concentration (larger than 2.0), there is a sharp rise in the order papameter at small values of the enantiomer excess, and the majority rule becomes evident.

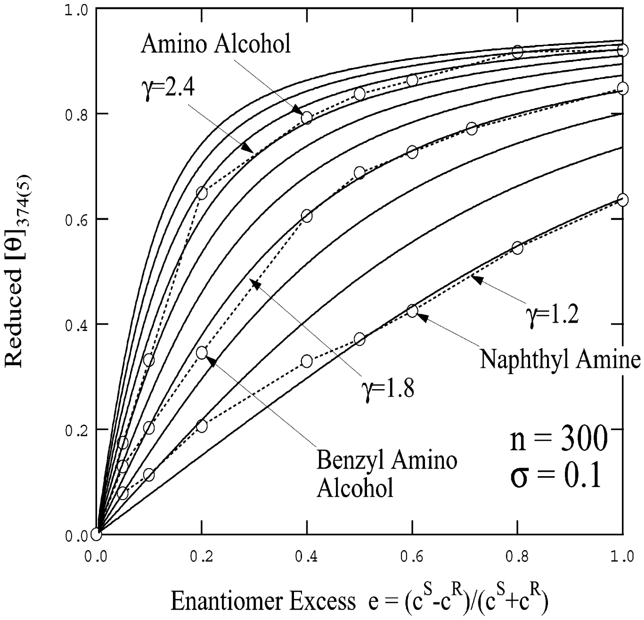

Figure 6. Theoretical fit of the observed ICD in the enantiomer mixtures. DP of the polymer and the helix initiation factors are fixed at $n = 300$ and $\sigma_S = \sigma_R = 0.1$, while the reduced total concentration of the chiral molecules is varied from curve to curve. Experimental data (circles) on three species of chiral molecules are fitted by theoretical curves (solid lines).

Figure 6 compares observed ICD intensity for three species of chiral molecules[8] with theoretical calculations of the order parameter. The molecular weight of polymer in this experiment is 46 000, so that we have fixed at $n = 300$. To get a good fit, the helix initiation factor must be $\sigma_S = \sigma_R = 0.1$, i.e., 1 order of magnitude larger than in the previous figures. Although σ is expected to be a local parameter by its original definition, this fact suggests that helices are more easily nucleated in shorter chains. In this paper, however, we sacrifice consideration of the explicit dependence of σ on the molecular weight in favor of simplicity of the theoretical model and treat σ as a fitting parameter as in the literature. The total concentration is varied from curve to curve. We have chosen the proportionality constant between ICD intensity and the order parameter by shifting the data at the highest e.e. value $e = 1.0$ (i.e., (S)-form only) to find the best fit for each species. This shift factor (proportionality constant) turned out to be 0.29 for amino alcohol (Figure 9B in the literature[8]), 0.26 for benzylamino alcohol (Figure 9C), and 0.22 for naphthylamine (Figure 9A). The difference in these proportionality constants suggests that the helical pitch depends on the shape of the side groups. The corresponding values of the total concentration is $\gamma = 2.4$, 1.8, and 1.2, respectively. The bare concentration actually measured in the experiment is $c = 0.024$, 0.24, and 0.24 mol/L. Hence, we can find the relative strength of the association constant $k(T)$ for these three species of molecules from the ratio of γ to c.

6. Sergeants-and-Soldiers Rule

We next study helix induction in mixtures of chiral and achiral molecules. In the experiments,[8] ICD was observed to be sharply amplified when achiral aminoethanol is added to the poly((4-carboxyphenyl)acetylene) solution under the presence of a small amount of (S)-form 2-aminoethanol (more precisely (S)-(+)-2-amino-1-propanol, referred to as (S)-18). Such amplification is caused by the strong enhancement of helix formation along the polymer chain by added achiral molecules. Although achiral molecules cannot induce helices by themselves, they largely contribute to the helix formation if there are chiral counterparts, just like the soldiers working under the orders of few sergeants. To study such a sergeants-and-soldiers effect, let us consider sequence selection process when the chiral and achiral molecules are hydrogen-bonded onto the polymer chain (Figure 7). The hydrogen-bonded sequences are separated into two main categories: the one consisting only of achiral molecules (pure sequence) and the one consisting of the mixture of chiral and achiral molecules (mixed sequence). Since the potential minima in the internal rotation of achiral side groups are symmetrically located, pure sequences do not induce helices. If chiral side groups are included in the sequence, however, such symmetry is broken and helices of fixed handedness are induced.

To specify a sequence, let us introduce two integers ζ_1 and ζ_2. A sequence of adsorbed molecules is specified by the set (ζ_1,ζ_2) if it carries the number ζ_1 of chiral molecule and ζ_2 of achiral molecules. Let us assume for simplicity that the chiral molecule is the (S)-form as in the experiments. Let j_{ζ_1,ζ_2} be the number of sequences specified by (ζ_1,ζ_2) on a polymer chain. An achiral molecule in a mixed sequence interacts with the neighboring (S)-form molecule and takes the position preferable in forming left-handed helix due to steric repulsion. Therefore, a sequence with $\zeta_1 \geq 1$ is assumed to become helical. The total helix content θ_h and the number ν_h of helices are given by

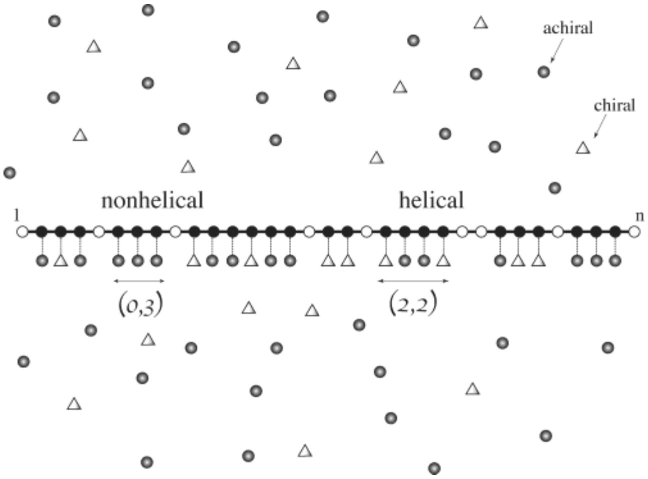

Figure 7. A single polymer chain adsorbing chiral (triangles) and achiral (spheres) molecules at its chain side in a solution of chiral/achiral mixture. They are adsorbed onto the polymer chain in pure and mixed sequences. An adsorbed sequence including chiral molecules induces a helix of definite handedness according to their chirality. The type of a sequence is indicated by an integer set (ζ_1,ζ_2).

$$\theta_h = \sum_{\zeta_1\geq 1,\zeta_2\geq 0} (\zeta_1 + \zeta_2) j_{\zeta_1,\zeta_2}/n \tag{6.1}$$

and

$$\nu_h = \sum_{\zeta_1\geq 1,\zeta_2\geq 0} j_{\zeta_1,\zeta_2}/n \tag{6.2}$$

Similarly, for the nonhelical sequence of purely achiral molecules, they are given by

$$\theta_0 = \sum_{\zeta_2\geq 1} \zeta_2 j_{0,\zeta_2}/n \tag{6.3}$$

and

$$\nu_0 = \sum_{\zeta_2\geq 1} j_{0,\zeta_2}/n \tag{6.4}$$

The total coverage of the polymer chain by the molecules is given by the sum $\theta = \theta_h + \theta_0$ and the total number of sequences by $\nu = \nu_h + \nu_0$. The numbers of (S)-form molecules and of achiral molecules on a chain are given by

$$n^{(S)} = \sum_{\zeta_1\geq 1,\zeta_2\geq 0} \zeta_1 j_{\zeta_1\zeta_2} \quad \text{((S)-form)} \tag{6.5a}$$

$$n^{(0)} = \sum_{\zeta_1\geq 0,\zeta_2\geq 1} \zeta_2 j_{\zeta_1\zeta_2} \quad \text{(achiral)} \tag{6.5b}$$

6.1. Helix Distribution Function. We now follow the same procedure as before and find the most probable distribution function j_{ζ_1,ζ_2} for the mixture of chiral/achiral molecules. The partition function now takes the form

$$Z_n(n^{(S)},n^{(0)}) = \sum_{\{j\}} \omega(\{j\}) \prod_{\zeta_1,\zeta_2} (\eta_{\zeta_1,\zeta_2})^{j_{\zeta_1,\zeta_2}} \tag{6.6}$$

where the combinatorial factor ω, now the number of different ways to select achiral and mixed sequences from the total n, is given by

$$\omega(\{j\}) = \left\{ \frac{[n - \sum(\zeta_1 + \zeta_2)j_{\zeta_1,\zeta_2}]!}{(\prod j_{\zeta_1,\zeta_2}!)[n - \sum(\zeta_1 + \zeta_2 + 1)j_{\zeta_1,\zeta_2}]!} \right\} \times \prod \left(\frac{(\zeta_1 + \zeta_2)!}{\zeta_1!\, \zeta_2!} \right)^{j_{\zeta_1,\zeta_2}} \tag{6.7}$$

The last factor comes from the number of different placement of chiral molecules inside a given sequence. We next move to the grand-canonical ensemble to remove the constraint of fixed total numbers of adsorbed molecules and maximize the grand partition function just as before. We find that the most probable distribution function is given by

$$j_{\zeta_1,\zeta_2}/n = (1 - \theta)t\tilde{\eta}_{\zeta_1,\zeta_2} x^{\zeta_1} y^{\zeta_2} \tag{6.8}$$

where

$$x \equiv \lambda_S t \quad \text{and} \quad y \equiv \lambda_0 t \tag{6.9}$$

in terms of the activity λ_S for (S)-molecules and λ_0 for achiral molecules and

$$t \equiv 1 - \nu/(1 - \theta) \tag{6.10}$$

is the probability for a randomly chosen monomer on a chain to remain unbonded. The statistical weight $\tilde{\eta}_{\zeta_1,\zeta_2}$ here includes the number of different placements of chiral molecules inside a given sequence:

$$\tilde{\eta}_{\zeta_1,\zeta_2} \equiv \frac{(\zeta_1 + \zeta_2)!}{\zeta_1!\, \zeta_2!} \eta_{\zeta_1,\zeta_2} \tag{6.11}$$

To decide the parameter t, we calculate the total adsorbance and the total number of sequences on a chain. They now take the form

$$\theta = (1 - \theta)tV_1(x,y) \tag{6.12}$$

and

$$\nu = (1 - \theta)tV_0(x,y) \tag{6.13}$$

where V functions are defined by

$$V_0(x,y) \equiv \sum \tilde{\eta}_{\zeta_1,\zeta_2} x^{\zeta_1} y^{\zeta_2} \tag{6.14a}$$

$$V_1(x,y) = \sum (\zeta_1 + \zeta_2)\tilde{\eta}_{\zeta_1,\zeta_2} x^{\zeta_1} y^{\zeta_2} \tag{6.14b}$$

These functions can be decomposed into helical part and nonhelical part as in eqs 6.1−6.4:

$$V_0(x,y) \equiv V_0^{(0)}(y) + V_0^{(h)}(x,y) \tag{6.15a}$$

$$V_1(x,y) \equiv V_1^{(0)}(y) + V_1^{(h)}(x,y) \tag{6.15b}$$

From the definition of the probability t, we find that t satisfies the relation

$$\frac{t}{1 - t} V_0(x, y) = 1 \tag{6.16}$$

This equation finds the unique value of t for given activities, and hence concentrations, of chiral and achiral molecules.

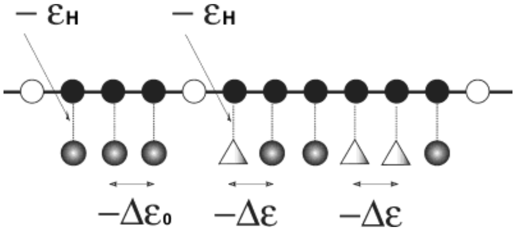

Figure 8. Energy gain by bonding molecules onto the chain is assumed to be $-\epsilon_H$ irrespective of their chirality. The stabilization energy between the neighboring molecules along the chain is given by $-\Delta\epsilon_0$ if they are both achiral and $-\Delta\epsilon$ if they are a chiral−achiral pair or chiral−chiral pair.

6.2. Models of the Statistical Weight for Helical and Nonhelical Sequences. To calculate the helical order parameter, we introduce model statistical weight on the basis of physical pictures on adsorption. We first consider a sequence consisting only of achiral molecules. When an achiral molecule is bound onto the polymer chain by hydrogen bond, it gains energy ϵ_H. It also interacts with the achiral molecule in the neighboring site by steric repulsion and takes a winding position (left or right) with equal probability (see Figure 8) because symmetry in the potential of internal rotation is preserved. With adsorbed chiral side groups, however, the symmetry in the minima is broken. The minima become deeper, and the barrier become higher, so that one-handed helical structure is preferred.

Let this stabilization energy be $\Delta\epsilon_0$. Then, the statistical weight for a nonhelical sequence is given by

$$\tilde{\eta}_{0,\zeta_2} = \sigma_0 u_0(T)^{\zeta_2} \tag{6.17}$$

where

$$u_0(T) \equiv \mathrm{e}^{(\epsilon_H + \Delta\epsilon_0)/k_B T} \tag{6.18}$$

is the weight for a molecule inside the sequence and

$$\sigma_0 \equiv \mathrm{e}^{-\Delta\epsilon_0/k_B T} \tag{6.19}$$

is the initiation factor for a nonhelical sequence.

The V functions then take the form

$$V_0^{(0)}(y) = \sigma_0 \gamma_0 t w_0(\gamma_0 t) \tag{6.20}$$

and

$$V_1^{(0)}(y) = \sigma_0 \gamma_0 t w_1(\gamma_0 t) \tag{6.21}$$

where w functions are defined by (3.4). Here, $\gamma_0 \equiv u_0(T)\lambda_0$ is proportional to the concentration $c^{(0)}$ of achiral molecules in the surrounding medium. It can be written as $\gamma_0 = k_0(T)c^{(0)}$ for a dilute solution, where $k_0(T)$ is proportional to $u_0(T)$.

As for a mixed sequence, the symmetry in the internal rotation is broken by the chiral molecules it includes, and hence a helix of fixed handedness is induced along it. The statistical weight of the mixed sequences is given by

$$\tilde{\eta}_{\zeta_1,\zeta_2} = \sigma \frac{(\zeta_1 + \zeta_2)!}{\zeta_1!\, \zeta_2!} u(T)^{\zeta_1 + \zeta_2} \tag{6.22}$$

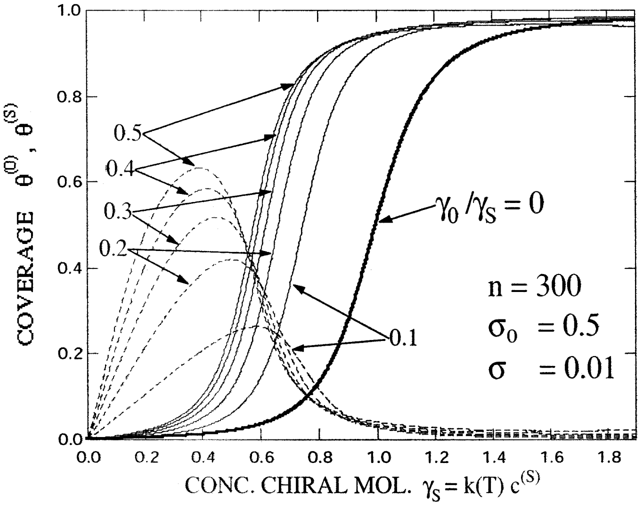

Figure 9. Model calculation of the amount of adsorption. The coverage $\theta^{(0)}$ (broken lines) by the sequences with purely achiral molecules and $\theta^{(S)}$ (solid lines) by the mixed sequences are plotted against the effective concentration of chiral molecules. Concentration of achiral molecules is varied from curve to curve. The thick solid line shows $\theta^{(S)}$ in the absence of achiral molecules. There is a large peak in $\theta^{(0)}$ before helices are induced for all concentrations of achiral molecules.

where

$$u(T) \equiv e^{(\epsilon_H+\Delta\epsilon)/k_BT} \qquad (6.23)$$

is the statistical weight for either a chiral or an achiral molecule inside the sequence and

$$\sigma \equiv e^{-\Delta\epsilon/k_BT} \qquad (6.24)$$

is the helix initiation factor. We have assumed that a molecule takes a widing position in accordance with the definite handedness when it is bound to the position next to a molecule and gains stabilization energy $\Delta\epsilon$ that might be different from $\Delta\epsilon_0$. The concentration of chiral molecules is measured by $\gamma_S \equiv k(T)c^{(S)}$ as before. The V functions then take the form

$$V_0^{(h)}(x,y) = \sigma(\gamma_0 + \gamma_S)tw_0((\gamma_0 + \gamma_S)t) \qquad (6.25)$$

and

$$V_1^{(h)}(x,y) = \sigma(\gamma_0 + \gamma_S)tw_1((\gamma_0 + \gamma_S)t) \qquad (6.26)$$

Figure 9 shows a model calculation of the nonhelical coverage $\theta^{(0)}$ by sequantial adsorption of achiral molecules (broken lines) and of the helical coverage $\theta^{(S)}$ formed by adsorption of chiral and achiral molecules in mixed sequenses (solid lines). They are plotted against the effective concentration $\gamma_S \equiv k(T)c^{(S)}$ of chiral molecules. The concentration ratio γ_0/γ_S is varied from curve to curve. DP of the polymer chain is fixed at $n = 300$. The thick solid line shows helix formation in the absence of achiral molecules ($\gamma_0 = 0$). It sharply grows around a certain concentration as before. But, under the presence of achiral molecules (thin solid lines), such a critical concentration shifts to lower value with the concentration of achiral molecules. Helix formation takes place at lower concentrations; more helices are produced by added achiral molecules (sergeants-and-soldiers effect). The sequence initiation factors are arbitrarily fixed at $\sigma_0 = 0.5$ and $\sigma = 0.01$, so that calculation is suited for the case where nucleation of achiral sequences is easier than that of mixed sequences. The coverage by pure achiral sequence (broken lines) first increases, shows a maximum, and then disappears. Mixed sequences become dominant above the critical concentration.

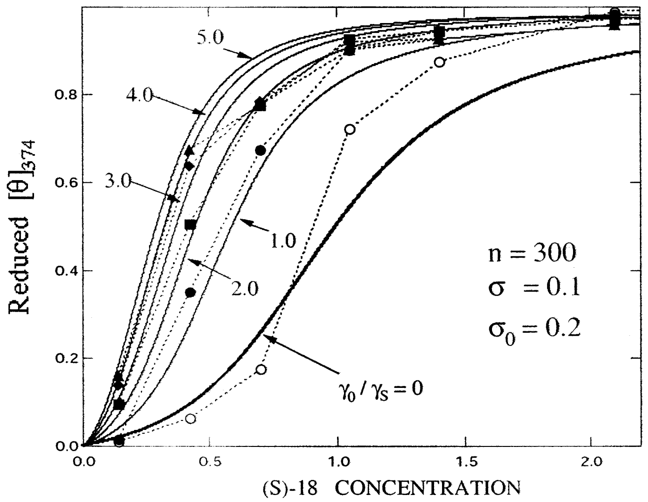

Figure 10. Observed ICD intensity (symbols) is compared with theoretical calculation (solid lines) of the total helix content. They are plotted against the concentration of chiral molecules. Concentration of achiral molecules is varied from curve to curve. $c^{(0)}/c^{(S)} = 0$ (white circles), 1.0 (black circles), 2.0 (black squares), 3.0 (black diamonds), and 5.0 (black triangles). Polymer chain has $n = 300$ statistical units, and the statistical weight for the sequence boundary is fixed at $\sigma_0 = 0.2$, $\sigma = 0.1$.

Figure 10 shows the experimentally measured ICD compared with theoretical calculation of the helical coverage $\theta^{(S)}$. Chains of $M = 46\,000$ ($n = 300$) are used in the experiment.[8] Enhancement of helix formation by added achiral molecules is clearly seen. ICD data (points and dotted lines) are fitted to the theoretical helix content (solid lines) by shifting the data point at the highest concentration to the position of the corresponding theoretical curve. To get a good fit for the curve under no achiral molecules (thick solid line), we fixed the helix initiation factor at $\sigma = 0.1$. Experimental data at finite concentrations of achiral molecules (thin solid lines) then suggest $\sigma_0 = 0.2$. The agreement is satisfactory.

7. Conclusions and Discussion

We have studied the molecular origin of two major principles (majority rule and sergeants-and-soldiers rule) governing the process of helix formation in a polymer chain to which chiral and achiral molecules are hydrogen bonded. It was found that the fundamental principles found for helix formation in random copolymers equally hold for helices induced by hydrogen bonds. As far as these fundamental two rules are concerned, the nature of randomness, whether quenched or annealed, seems to be irrelevant. The analytical method of counting the total number of sequence selections from the finite polymer chain length, combined with the standard statistical-mechanical ensemble method, turned out to be efficient in studying the induced coil-to-helix transition.

On the contrary, the interaction energy $\Delta\epsilon$ (and $\Delta\epsilon_0$) between the neighboring chiral (and achiral) molecules attached on the polymer chain needs further consideration. In the case of amines and amino alcohols that are hydrogen-bonded to poly(4-carboxyphenyl)acetylene, the relations between the structure of complexes and configurations of primary molecules with chiral centers are studied by Yashima et al.[8] A qualitative comparison between the energy due to steric repulsion followed by geometrical stabilization through twisted positioning and the value we found from the fitting of optical data may in principle be possible.

We have confined infinitely dilute polymer solution in this paper, but at finite concentration, interaction among induced helices plays an important role. Separation of enantiomers from almost racemic mixtures by using hydrogen bonds with polymers at finite concentrations can be an efficient method for optical purification. Thereby, the interaction between left-handed and right-handed helices may be different from those between helices with the same handedness. New phase transitions such as phase separation, liquid crystallization, and gelation triggered by such a helix interaction provide new important research topics to be studied.

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References and Notes

(1) Green, M. M.; Khatri, C. A.; Reidy, M. P.; Levon, K. *Macromolecules* **1993**, *26*, 4723.
(2) Green, M. M.; Peterson, N. C.; Sato, T.; Teramoto, A.; Cook, R.; Lifson, S. *Science* **1995**, *268*, 1860.
(3) Selinger, J. V.; Selinger, R. L. B. *Phys. Rev. Lett.* **1996**, *76*, 58.
(4) Selinger, J. V.; Selinger, R. L. B. *Macromolecules* **1998**, *31*, 2488.
(5) Sato, T.; Terao, K.; Teramoto, A.; Fujiki, M. *Macromolecules* **2002**, *35*, 2141.
(6) Sato, T.; Terao, K.; Teramoto, A.; Fujiki, M. *Macromolecules* **2002**, *35*, 5355.
(7) Mruk, R.; Zentel, R. *Macromolecules* **2002**, *35*, 185.
(8) Yashima, E.; Matsushima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6345.
(9) Yashima, E.; Maeda, K.; Okamoto, Y. *Nature (London)* **1999**, *399*, 449.
(10) Maeda, K.; Okada, S.; Yashima, E.; Okamoto, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 3180.
(11) Morino, K.; Maeda, K.; Okamoto, Y.; Yashima, E.; Sato, T. *Chem. Eur. J.* **2002**, *8*, 5112.
(12) Hirschberg, J. H. K. K.; Brunsveld, L.; Ramzi, A.; Vekemans, J. A. J. M.; Sijbesma, R. P.; Meijer, E. M. *Nature (London)* **2000**, *407*, 167.
(13) Brunsveld, L.; Lohmeijer, B. G. G.; Vekemans, J. A. J. M.; Meijer, E. W. *Chem. Commun.* **2000**, 2305.
(14) Cornelissen, J. J.; Rowan, A. E.; Nolte, R. J. M.; Sommerdijk, N. A. J. *Chem. Rev.* **2001**, *101*, 4039.
(15) Okamoto, Y. *Prog. Polym. Sci.* **2000**, *25*, 159.
(16) Gornick, F.; Jackson, J. L. *J. Chem. Phys.* **1963**, *38*, 1150.
(17) Tanaka, F. *Macromolecules* **2003**, *36*, 5392.
(18) Poland, D.; Scheraga, H. A. *Theory of Helix−Coil Transitions in Biopolymers*; Academic Press: New York, 1970.
(19) Zimm, B. H.; Bragg, J. K. *J. Chem. Phys.* **1959**, *31*, 526.
(20) Lifson, S.; Roig, A. *J. Chem. Phys.* **1961**, *34*, 1963.
(21) Yashima, E., private communication.
(22) Yashima, E., private communication.

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