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Counterintuitive influence of microscopic chirality on helical order in polymers

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ABSTRACT: Studies of copolymers of chiral and achiral units forming a helical array correlate to statistical physical predictions of the influence of the chiral units on the helical sense taken by the array. In the absence of conflict among the chiral units for helical sense control, the sergeants and soldiers experiment, a larger chiral bias leads to increased control. However, when conflict exists among the chiral units for helical sense control, the majority rule experiment, a larger chiral bias leads to decreased control of the helical sense and therefore a smaller optical activity. Changing the achiral units in the majority rule experiment can change the nature of the statistical physics between statistical and thermal randomness. In general, the experiments quantitatively demonstrate that the effect of chirality is not an intrinsic property of the chiral moiety but rather depends on the molecular environment. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: helical order; polymers; chirality

INTRODUCTION

There is a great deal of interest in helical conformations, which are synthetic and therefore without the intrinsic chiral bias toward helical sense inherent in biological systems (for leading references on synthetic helical structures subject to adjustable helical sense control see Ref. 1). In experiments on a model helical polymer[2] described below, we investigate predictions of a statistical physical theory[3,4] concerning how the effect of the extent of chirality in choosing helical sense can lead to more, or less, helical sense excess. The two experiments fall under the rubric of 'sergeants and soldiers' and the 'majority rule' system. As encountered experimentally below and precisely in line with the theoretical predictions,[3,4] while application of more force by sergeants increases their control, application of more force in the majority rule system leads to less control. While the result with the sergeants is intuitively reasonable, the result in the majority rule system appears counterintuitive.

RESULTS AND DISCUSSION

The experimental results shown in Fig. 1(A) describe the optical activities of two random copolymers synthesized from the monomer units shown. In both copolymers the chain is predominately formed from the achiral *n*-hexyl isocyanate, the 'soldier,' with a far smaller proportion of the chiral unit, the 'sergeant.'[2] The compared chiral units in Fig. 1(A), the citronellic group (*R*)-**1** and the extended citronellic group (*R*)-**2**, differ by a single methylene unit, which acts to distinguish the two chiral entities in the separation of the stereocenter from the polymer backbone. As is reasonable, the polymer synthesized from (*R*)-**1**, with the closer relationship between the stereocenter and the backbone, yields the polymer with the higher optical activity. The chiral influence for (*R*)-**1** on the helical sense of the polymer is greater, leading to a larger excess of the left-handed helix in this situation,[1,2] which is demonstrated by the larger negative circular dichroism band at the chromophore of the helix at 254 nm.

For the sergeants-and-soldiers experiment in Fig. 1(A), the effect of the chiral pendants on the helical sense can be described by the one-dimensional Ising model.[3] This model predicts the chiral order parameter *M* of the polymer, which is the ratio of the observed molar ellipticity to the maximum molar ellipticity of a pure chiral polymer. [The maximum molar ellipticity of the two copolymers in Fig. 1(A) is nearly the same, so a larger order parameter *M* corresponds to a larger observed molar ellipticity.] The approximate analytic prediction is

$$M = \tanh\left(\frac{\Delta G_h L r}{RT}\right) \qquad (1)$$

where ΔG_h is the chiral bias, i.e. the energetic preference of a chiral pendant for one helical sense, *r* is the fraction of chiral units in the copolymer and *L* is the cooperative

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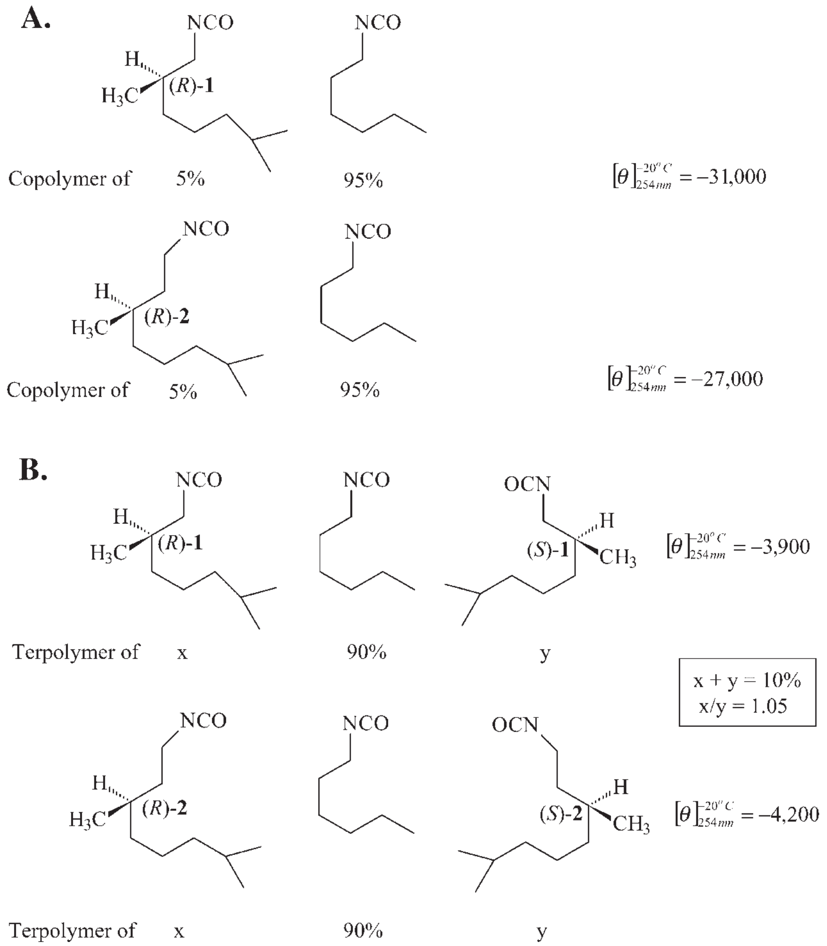

Figure 1. (A) Circular dichroism determined molar ellipticity measured in hexane at −20 °C for the two copolymers shown (with **1**: $M_w = 3\,000\,000$, ρ (polydispersity) = 1.3; with **2**: $M_w = 4\,000\,000$, $\rho = 1.3$); (B) Circular dichroism determined molar ellipticity measured in hexane at −20 °C for the two terpolymers shown (with **1**: $M_w = 2\,700\,000$, $\rho = 1.4$; with **2**: $M_w = 2\,400\,000$, $\rho = 1.3$); x/y is identical in both terpolymers and as well in the two terpolymers in Figure 2[5,6]

domain size, i.e. the number of contiguous units along the chain with a single helical sense. This domain size is determined by the equation

$$\frac{1}{L} = \frac{1}{L_{\text{th}}} + \frac{1}{N} \tag{2}$$

where $L_{\text{th}} = e^{\Delta G_r/RT}$ is the characteristic distance between thermally activated helical reversals, with energy ΔG_r, and N is the chain length.

In the experiment described in Fig. 1(A), because of the high degree of polymerization [large N in Eqn (2)] L is determined by the number of units between thermally generated helical reversals L_{th}, which will be large because of the large excess energies of such reversals (ΔG_r) and the low temperature. The circular dichroism intensities show that the insertion of a single extra methylene unit between the helical backbone and the stereogenic carbon causes a change in how the helix perceives the chirality and the closer stereocenter, reasonably with the higher chiral bias, ΔG_h, yields the higher molar ellipticity. There is no surprise here.

We can now consider more complex polymers composed of R, S and achiral units. In a manner of speaking, the chiral ‘sergeants’ are conflicted, with some favoring a right-handed helix and others favoring a left-handed helix. This conflict for helical control is described by the term ‘majority rule.’[5]

Like the sergeants-and-soldiers system, the majority-rule system can be described by a one-dimensional Ising model.[4] This model predicts the chiral order parameter of a terpolymer. The approximate analytic form of this prediction has two distinct limiting cases (the theoretical discussion of statistical and thermal randomness is in the Appendix of Ref. 6). In the limit of ‘statistical randomness,’ we have $\Delta G_h (Lr)^{1/2} \gg RT$, where ΔG_h is the chiral bias energy, L is the cooperative domain size and r is the fraction of chiral units. In this limit, the main source of randomness in the polymer is the random sequence of monomers, rather than thermal fluctuations in response to the random sequence. In this case, the prediction for the chiral order parameter is

$$M = \operatorname{erf}\left[\sqrt{2Lr}\left(p - \frac{1}{2}\right)\right] \tag{3}$$

where $\left(p - \frac{1}{2}\right)$ is the enantiomeric excess of the chiral units. In the opposite limit of 'thermal randomness,' we have $\Delta G_h (Lr)^{1/2} \ll RT$. In that limit, the main source of randomness in the polymer is thermal fluctuations rather than the random sequence of monomers. The prediction for the chiral order parameter then becomes

$$M = \tanh\left[\frac{2\Delta G_h Lr\left(p - \frac{1}{2}\right)}{RT}\right] \tag{4}$$

Both of these limits involve the cooperative domain size L. In the limit of statistical randomness, the prediction for this cooperative domain size is

$$\frac{1}{L} = \frac{1}{L_{\mathrm{rf}}} + \frac{1}{L_{\mathrm{th}}} + \frac{1}{N} \tag{5}$$

This prediction depends not only on the chain length N and the thermal domain size $L_{\mathrm{th}} = \mathrm{e}^{\Delta G_r/RT}$, but also on the random-field domain size L_{rf} arising from the random sequence of conflicting pendant groups. This random-field domain size is determined by

$$L_{\mathrm{rf}} = \frac{1}{r}\left(\frac{\Delta G_r}{2\Delta G_h}\right)^2 \tag{6}$$

where ΔG_r is the energy cost of a helical reversal, ΔG_h is the chiral bias energy and r is the fraction of chiral units along the chain. In the limit of thermal randomness, there is no such simple expression for L, but Eqn (2) provides an upper limit for L.

One experimentally observable distinction between the limits of statistical and thermal randomness is the scaling of the optical activity with chain length for short chains. In general, the optical activity is proportional to the chiral order parameter M. In the limit of statistical randomness, M scales as $\sqrt{L}$, and hence as $\sqrt{N}$ for short chains. By contrast, in the limit of thermal randomness, M scales linearly with L, and hence with N for short chains. Both of these dependences have been observed experimentally.[6]

An even more striking distinction between statistical and thermal randomness is the dependence of optical activity on the chiral bias ΔG_h. In the limit of statistical randomness, increasing ΔG_h gives a smaller random-field domain size L_{rf} in Eqn (6), hence a smaller L in Eqn (5) and a smaller chiral order parameter M in Eqn (3).[4] In other words, increasing the chiral bias energy of the pendant groups should *reduce* the chiral optical properties of the polymers! This dependence may seem counter-intuitive, but it is actually reasonable. Increase of chiral bias enhances the conflict in the system, which in line with human experience acts to undermine the cooperativity, the latter expressed as a reduction in L. By contrast, in the limit of thermal randomness, increasing ΔG_h gives a larger chiral order parameter M in Eqn (4). This is the conventional scenario, in which a larger chiral bias energy gives larger chiral optical properties, as in the sergeants-and-soldiers copolymers discussed earlier.

We investigate the dependence of optical activity on chiral bias ΔG_h through the experiments shown in Figs 1(B) and 2. These experiments use the same two types of chiral units as the sergeants-and-soldiers copolymers presented in Fig. 1(A). The sergeants-and-soldiers

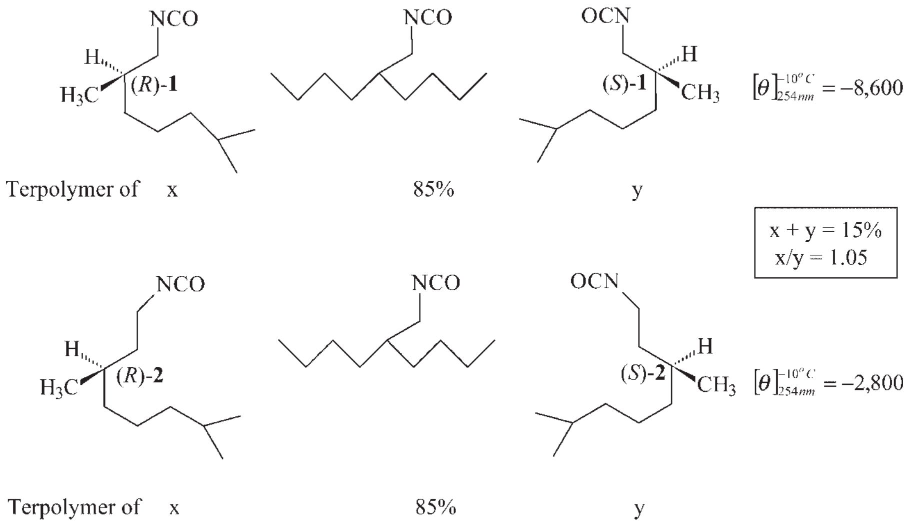

Figure 2. Circular dichroism determined molar ellipticity measured in hexane at −10 °C for the two terpolymers shown (with **1**: $M_w = 300\,000$, $\rho = 1.1$; with **2**: $M_w = 350\,000$, $\rho = 1.1$). See caption for Figure 1[5,6]

experiment demonstrates that the citronellic group (*R*)-**1** has a higher chiral bias than the extended citronellic group (*R*)-**2**. We can now see how those chiral units affect the optical activity of majority-rule terpolymers.

Figure 1(B) shows terpolymers composed of (*R*)-**1**, (*S*)-**1** and the same *n*-hexyl soldiers as in Fig. 1(A). The essential difference between polymers in Fig. 1(B) and 1(A) is that the chiral units are near to the racemic state in Fig. 1(B) rather than highly enantiomerically enriched. The experimentally observed optical activity agrees with the counterintuitive prediction for statistical randomness. The terpolymer with the extended citronellic chiral units (*R*)-**2** and (*S*)-**2** has a higher optical activity compared with the terpolymer with the citronellic chiral units (*R*)-**1** and (*S*)-**1**. [To obtain identical enantiomeric excess for both **1** and **2** the monomers were prepared by routine functional-group transformations from the same starting 2.4% *ee* (*R*)-citronellic acid that was made by mixing racemic citronellic acid (purchased from Aldrich; note that its *ee* was found to be 12% *R*-form) and pure (*S*)-citronellic acid: $[\alpha]_D = +0.25$ (*c* 5.0, 25 °C, $CHCl_3$); maximum literature (for leading references see Ref. 5a) value $[\alpha]_D = +10.3$ (*c* 5.0, 25 °C, $CHCl_3$)].[7] [Polymerizations of the copolymers and the terpolymers were carried out by the NaCN–DMF method.[8] Weight-averaged molecular masses M_w and polydispersities ρ of the polymers were determined by gel-permeation chromatography using poly(hexyl isocyanate) standards.]

Since branching of the achiral units, the soldiers,[1,2] acts to increase substantially the helical reversal energy ΔG_r[9] (see also Ref. 5), we reproduce the enantiomeric competition exhibited in Fig. 1(B) but substitute the previously studied 2-butylhexyl units[9] for the linear *n*-hexyl group. The expectation is that the helical sense excess would increase since ΔG_r appears in the numerator of L_{rf} in Eqn (6). As seen in Fig. 2, this experiment leads to the expected result for the citronellic chiral units **1**. However, it acts in the opposite direction for the extended citronellic chiral units **2**.

To understand the behavior of the terpolymers in Fig. 2, we fractionate them and measure the optical activity as a function of chain length (see Ref. 6 for details of how the fractionation is conducted on a related system). In this experiment, the citronellic terpolymers follow the prediction for statistical randomness, with optical activity scaling as $\sqrt{N}$, but the extended citronellic terpolymers follow the prediction for thermal randomness, with the optical activity scaling linearly with chain length N. Furthermore, the optical activity of the citronellic terpolymers depends only weakly on temperature, but the optical activity of the extended citronellic terpolymers is sensitive to temperature. These observations show that the environment of surrounding 2-butylhexyl units shifts the extended citronellic terpolymer into the regime of thermal randomness, presumably by reducing the chiral bias energy. However, this environment leaves the citronellic terpolymer in the regime of statistical randomness. Hence the 2-butylhexyl environment reduces the optical activity of the extended citronellic terpolymer but increases the optical activity of the citronellic terpolymer.

There are many examples in the literature of chiral optical changes associated with changes of molecular environment including concentration, temperature and solvent and with many varied causes (for an introduction to these effects in polymers and an interesting example, see Ref. 10, and for a comprehensive overview of these effects, see Ref. 11). The results above, however, offer a new kind of view in that the environment of the chiral entity affects its bias toward helical sense in a polymer that is otherwise structurally invariant. In this manner, the polymer helix acts to report on the changes occurring in the affecting chiral force, which is amplified by the cooperativity inherent in this experimental system. The results act as an experimental demonstration that chirality measures and chiral properties are decoupled from each other, as has been emphasized recently based on theoretical considerations.[12] In other words intrinsic chiral characteristics are not a dependable basis on which to choose chiral effect in helical sense control and reasonably in other regards as well.[12] For one example, the conversion of nematic to cholesteric liquid crystals, is known to depend strongly on chiral context, that is, on the relationship of the structure of the chiral dopant to the liquid crystal structure.[13]

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