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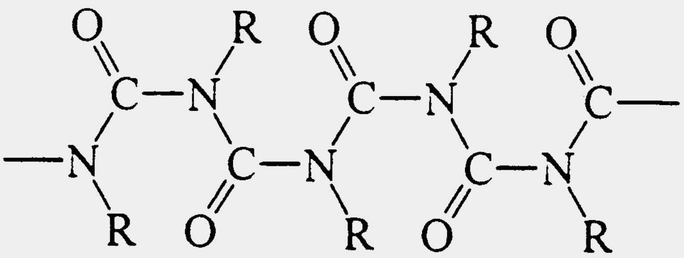

In the Chinese language a large number of small forces making a large force expresses the connection between cooperation and amplification. This finds parallel in the chiral properties of the polyisocyanates, a model helical system.

The Macromolecular Route to Chiral Amplification

Mark M. Green,* Ji-Woong Park, Takahiro Sato, Akio Teramoto, Shneior Lifson, Robin L. B. Selinger, and Jonathan V. Selinger

Dedicated to Professors Kurt Mislow and Herbert Morawetz

Polymers show cooperative phenomena for almost all of their properties, and this is no less true for the optical activity of chiral polymers. This phenomena was first observed by the "Italian School" in their early work following the discovery of stereoregular polymerization, and led to observations of nonlinear relationships between enantiomeric characteristics of monomeric materials used in polymerizations and the polymers produced. These observations confirmed the hypothesis that the conformations of these polymers in the melt and dissolved states resembled those found in the solid crystal. In recent years a version of the Nylons, which failed to make the grade as a fiber, turned out to carry these cooperative properties of chirality to an extreme. Minute chiral forces control the chain properties, allowing experiments in which chirality arising from isotopic substitution, or solvation effects, or even nearly racemic states can be studied. Statistical physics and the one-dimensional Ising model describe the properties of these polymers in quantitative perfection and yield insight into how to manipulate the chirality and the polymer properties to gain even higher amplification of the chiral forces. Through work on such disparate materials as vinyl polymers and polyisocyanates, we discover the structural boundaries for these observations and therefore which other polymeric and supramolecular systems may behave similarly. This is already being seen. However, these studies also demonstrate that structural theory appears inadequate to interpret the small energies driving these chiral effects, and this has parallels in other areas where equilibrium states are balanced on cooperatively driven forces.

Keywords: asymmetric amplification · chirality · helical structures · polymers

1. Introduction

A large number of small forces adding up to a large force expresses the mutually intertwined ideas of cooperation and amplification (Figure 1). Since polymers are an ideal molecular form for cooperative phenomena, and this manifests itself across the spectrum of polymer science, it is not surprising that early observations of optical activity in polymers revealed the signature characteristics of chiral amplification. These early observations derived from the possibility of producing stereoregular polymers by the methods of Ziegler and Natta. In these polymers, such as isotactic polypropylene, the pendant groups are connected to the chain through centers of identical configuration, and this uniformity leads to helical conformations for these materials in the crystalline regions of their solid state. It was quickly understood, as most elegantly explained by Mario Farina in Milan,[1] that although a nearly perfect asymmetric synthesis was necessary to produce identical configurations for these pendant groups, the fact that the chain ends in a very long polymer are indistinguishable led to what Mislow[2] has termed a cryptochiral state. The


Figure 1. Chinese character for cooperation–amplification.

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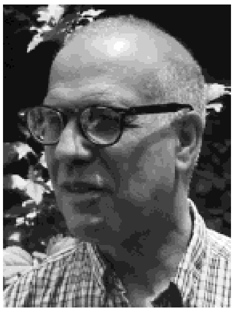
M. M. Green

Ji-Woong Park, born in 1965 in Korea, graduated from Seoul National University in 1989. He studied polymer chemistry for an M.S. at the Korea Advanced Institute of Science and Technology (KAIST) under the supervision of Professor Iwhan Cho, and worked in the Korea Research Institute of Chemical Technology (1991–1995) with Dr. Suh Bong Rhee on the development of new polyimides. Since 1995 he has been studying the molecular dynamics of optically active polymers and their small molecule analogues in viscous liquids and polymer glasses as part of his doctoral thesis with Professor Green.


J.-W. Park


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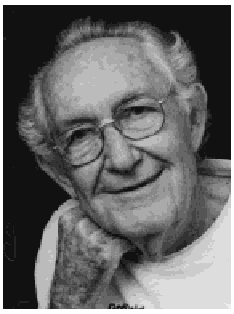
Takahiro Sato, born in 1957 in Osaka (Japan), studied macromolecular science and received his D.Sci. in 1985 from Professor H. Fujita at Osaka University. After working with Dr. C. C. Han at NBS, Gaithersberg, MD (USA), as a guest scientist, he was appointed to a position at Osaka University in 1988, where he is now associate professor. His resarch interests include the physical chemistry of macromolecular solutions.

Akio Teramoto, born in 1933, received his B.S. in 1956 and his Ph.D. in 1961 from Kyoto University. He worked at Osaka University from 1961 to 1997, where he is Professor Emeritus, and is currently Chair Professor at Ritsumeikan University. His research interests include chain conformations and conformational transitions in dilute solution, thermodynamics, and dynamics of polymers solutions, including polymer liquid crystals.


A. Teramoto


S. Lifson

Shneior Lifson, born in 1914 in Tel-Aviv, obtained his M.Sc. degree in physics from the Hebrew University of Jerusalem in 1949. That year he joined the Weizmann Institute of Science, where he has stayed since, receiving his Ph.D. in 1954 and becoming Professor of Chemical Physics at the Weizmann Institute of Science in 1961 and Head of the Department of Chemical Physics in 1963. His long list of research interests includes light scattering of polyelectrolytes, conformations and vibrations of large molecules, and statistical mechanics and conformation analysis of rigid polymers.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Jonathan V. Selinger, born in 1961, received his doctorate in Physics from Harvard University in 1989. He then did postdoctoral research with a joint appointment at UCLA Department of Physics and Caltech Department of Chemical Engineering. In 1992 he came to the Naval Research Laboratory in Washington, D.C. His research focuses on the statistical mechanics of complex fluids, including polymers, liquid crystals, Langmuir monolayers, and self-assembled lipid microstructures.

isotactic polymer chain is chiral only by virtue of the different chain ends. However, these chain ends in a high molecular weight polymer are an unimportant part of the structure, therefore precluding any manifestation of chirality such as optical activity. The isotactic polymer belongs to a class of molecules in which chirality is buried, that is, resides in a crypt. Optical activity could though be produced in these polymers in another manner.

Italian researchers under the direction of Piero Pino in Pisa in the 1960s began to prepare stereoregular vinyl polymers with chiral, nonracemic pendant groups (for example, from (*R*)- or (*S*)-3-methyl-1-pentene) and discovered that the optical activities of such materials in solution showed nonlinear relationships between the configurational enantiomeric characteristics of the monomer units and the optical activity of the derived polymer. This nonlinear optical activity was difficult to understand except as arising from the chiral units affecting some aspect of the chain conformation. Although the measurements were made in solution rather than with the crystal the results pointed to the presence of a helical conformation. A full understanding was impeded though by the absence of an accessible chromophore, blocking therefore direct observation by circular dichroism of the source of the chiral optical observations. In addition, the magnitude of the effects was limited by the flexibility of the polymers since helical reversal states were relatively easily accessible. Such defects in the helical structure, as we shall see, limited the cooperativity responsible for the nonlinear effects.

In the early 1960s chemists at DuPont had found a route to the simplest Nylon, the addition polymer of organic isocyanates. These different types of Nylon-1, or poly(isocyanates), show unusual dimensional properties which arise from a strongly preferred local helical conformation of the chain. This is consistent with a high persistence in the chain directionality. In other words, if tangents are drawn to the chain at any two points the angle with which they meet, for the same distance along the chain, will be much smaller than for a random coil polymer. The polyisocyanates became an excellent system for testing theories in the area of stiff wormlike polymers and lyotropic liquid crystals.[3] In addition, these polymers, though helical, were synthesized from achiral monomers, which led to the property that their mirror helical senses were of equal probability. This fact in combination with the expected low population of conformations that reversed the helical sense, consistent with their stiff structure, suggested that a more extreme manifestation of the chiral amplification properties encountered by the group of Pino with the isotactic vinyl polymers would be found in the polyisocyanates. Furthermore, the chromophore of the polymers absorbs light in an accessible region of the spectrum, suggesting that circular dichroism measurements might allow direct observation of the helices whenever the balance between the mirror helical senses is upset. The magnitude of the amplification of chirality of the polyisocyanates has lived up to the expectation and has allowed precise correlations with cooperative models of statistical physics based on one-dimensional Ising models (see Section 3.2), which in turn has offered insight into how to manipulate the chiral amplification. In this review we trace the path of this macromolecular chiral amplification from its origins in Italy to the present day. Through this work we show the principles involved to be independent of the precise structure of the polymer, and in this way these observations may stimulate similar experiments in other systems which may have their own unique advantages.

2. Stereoregular Vinyl Polymers Synthesized from Chiral Monomers

Driven by questions concerning the conformational properties of isotactic vinyl polymers in solution and the melt, Pino and co-workers used the Ziegler–Natta organometallic methods to polymerize chiral molecules containing 1-alkene moieties.[4] Highly stereoregular polymers were produced. It was known from earlier studies that increasing isotacticity is correlated to increased crystallinity and therefore to lower solubility, so that samples could be fractionated according to their tacticity by dissolution in increasingly high boiling solvents at higher temperatures. All fractions of the optically active polymers produced in this manner showed increased optical activity compared to the monomer units from which they were made. However, as the isotacticity increased, as evidenced by decreasing solubility, so did the optical activity and its temperature dependence. The original data from this classic work, showing these effects, are presented in Table 1.[4]

If the isotactic polymer chain exists as a series of blocks of left- and right-handed regions separated by helical reversals, sense can be made of the data in Table 1. In such a model the bias per unit from the chiral side group casting the left- and right-handed helical senses into a diastereomeric relationship must be multiplied by the number of units which take the same helical sense. This is the ultimate source of the amplification and the central idea of all the discussions to follow. This amplified chiral bias will determine the excess of one helical sense over the other and therefore the optical activity, but any factor that interrupts the continuity of the helix will limit this amplification. What can be the nature of these interruptions? Accumulation of energy in the chain can allow the conformation to defect from the helical state and attain higher energy states, which can act to reverse the helical sense. The population of such helical reversals would depend exponentially on the temperature, following Boltzmann statistics, and this could be the source of the strong temperature dependence of the optical activity seen in Table 1. Another source of interruptions in the helical conformation could arise from mistakes in the polymerization mechanism, allowing defects in the stereoregular configurations along the chain. This would be the reason why higher optical activities are observed in the samples which dissolve only in higher boiling solvents and for which the isotactic content is higher (Table 1).

A helical conformation in solution was the central tenet of the interpretation of the data in Table 1.[4] Although such conformations could be demonstrated in crystals of isotactic vinyl polymers, there was no experimental way to directly address the question in the isotropic state of the melt or in solution. Guiseppe Allegra in Milan took up the question with force field calculations which clearly showed that helical

Table 1. Original table reprinted with permission from reference [4a].

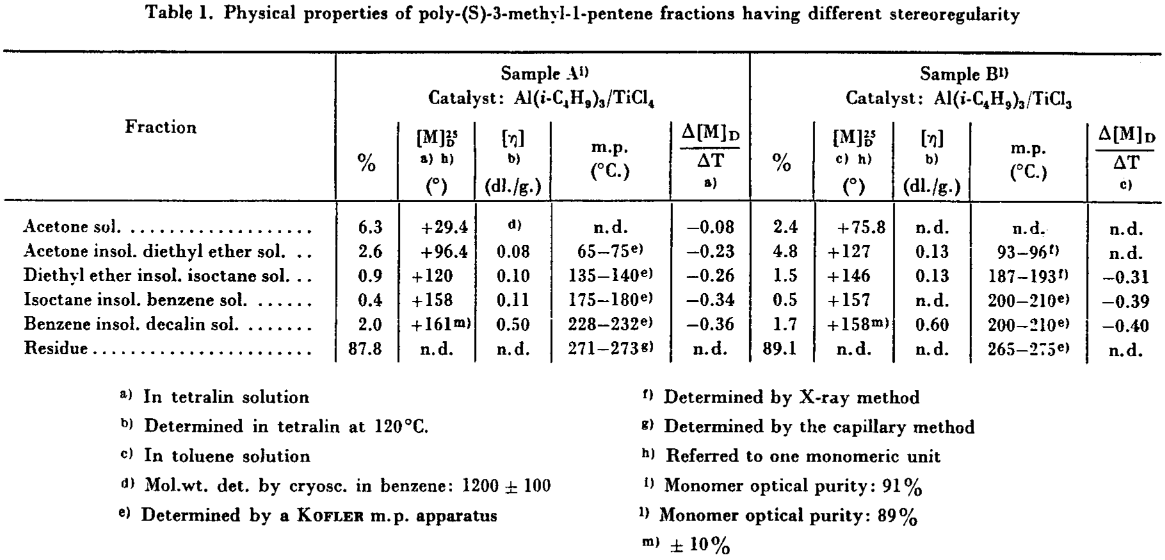


Table 1. Physical properties of poly-(S)-3-methyl-1-pentene fractions having different stereoregularity

Fraction	Sample A[i] Catalyst: $Al(i\text{-}C_4H_9)_3/TiCl_4$					Sample B[l] Catalyst: $Al(i\text{-}C_4H_9)_3/TiCl_3$				
	%	$[M]_D^{25}$ [a) h)] (°)	$[\eta]$ [b)] (dl./g.)	m.p. (°C.)	$\frac{\Delta[M]_D}{\Delta T}$ [a)]	%	$[M]_D^{25}$ [c) h)] (°)	$[\eta]$ [b)] (dl./g.)	m.p. (°C.)	$\frac{\Delta[M]_D}{\Delta T}$ [c)]
Acetone sol.	6.3	+29.4	d)	n.d.	−0.08	2.4	+75.8	n.d.	n.d.	n.d.
Acetone insol. diethyl ether sol. ..	2.6	+96.4	0.08	65–75[e)]	−0.23	4.8	+127	0.13	93–96[f)]	n.d.
Diethyl ether insol. isoctane sol. ..	0.9	+120	0.10	135–140[e)]	−0.26	1.5	+146	0.13	187–193[f)]	−0.31
Isoctane insol. benzene sol.	0.4	+158	0.11	175–180[e)]	−0.34	0.5	+157	n.d.	200–210[e)]	−0.39
Benzene insol. decalin sol.	2.0	+161[m)]	0.50	228–232[e)]	−0.36	1.7	+158[m)]	0.60	200–210[e)]	−0.40
Residue	87.8	n.d.	n.d.	271–273[g)]	n.d.	89.1	n.d.	n.d.	265–275[e)]	n.d.

a) In tetralin solution
b) Determined in tetralin at 120°C.
c) In toluene solution
d) Mol.wt. det. by cryosc. in benzene: 1200 ± 100
e) Determined by a KOFLER m.p. apparatus
f) Determined by X-ray method
g) Determined by the capillary method
h) Referred to one monomeric unit
i) Monomer optical purity: 91%
l) Monomer optical purity: 89%
m) ± 10%

conformations were important in isolated chains,[5] offering strong support for Pino's hypothesis. Later work was to extend this and suggested the ability to roughly estimate the population of the proposed helical reversals and even their possible effect on the overall chain dimensions.[6] At the time of the initial work though direct experimental evidence was sought through observation by circular dichroism of the helical chromophore, but this could not be probed directly because of its inaccessible wavelength. Seeking other ways to support their hypothesis, Pino and co-workers took the approach[7] of synthesizing an isotactic copolymer of styrene with a large excess of (*R*)-3,7-dimethyl-1-octene. The large increase in the molar ellipticity of the aromatic chromophore in the polymer compared to the model (Figure 2) was suggested as arising from an extended conformation of the polymer, which they considered to be helical.

The experiments were extended further to isotactic copolymers derived from units offering conflicting information to the helical sense of the chain. In these seminal stereochemisty experiments, a series of copolymers of enantiomers were prepared from three structurally different molecules, namely, (*S*)-5-methyl-1-heptene, (*S*)-4-methyl-1-hexene, and (*R*)-3,7-dimethyl-1-octene. The results are shown in Figure 3.[8]

When the stereocenter of the chiral side chain is far removed from the backbone we could expect its influence on the helical conformation to be small, so that changes in the enantiomeric excess of the monomer units should scale linearly with optical activity. In this case the optical activity of the polymer would be derived from the chiral side chains and the backbone would be unaffected; that is, there would be equal proportions of left- and right-handed helical segments. Moving the stereocenter closer to the backbone should give an entirely different result though since the asymmetry of the side chains will be coupled to the helical backbone, favoring one sense of the helix. If the minor enantiomer takes part in the helical sense dictated by the major enantiomer, so as to avoid placing many helical reversals along the backbone in response to the changing information from the side groups, we would expect to see a nonlinear response of the optical activity of the polymer to the enantiomeric excess of the side chain groups. This would arise from the strong contribution of the helix to the optical activity. As seen in Figure 3 this is precisely what is found.[8]

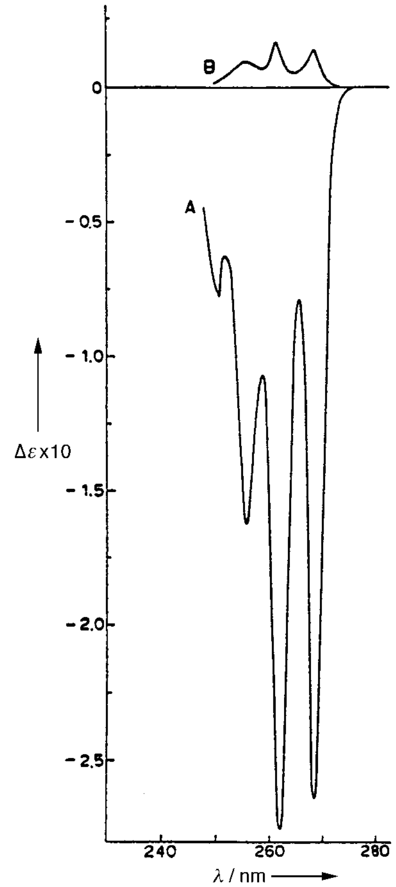


Figure 2. Circular dichroism in chloroform at 25 °C of (3*S*,9*S*)-3,9-dimethyl-6-phenylundecane (B) and of the diethyl ether extractable fraction of the styrene – (*R*)-3,7-dimethyl-1-octene copolymer (A); Δε is based on one unit of styrene. Reprinted with permission from reference [7a].

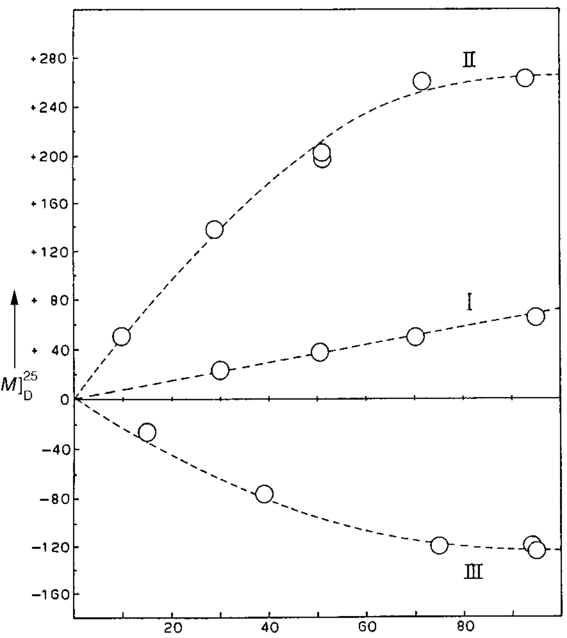


Figure 3. Molar rotatory power ($[M]^{25}_{D}$), referred to one monomeric unit, in hydrocarbon solution for the unfractionated methanol-insoluble polymers obtained from samples having different optical purity (P_i) of (*S*)-5-methyl-1-heptene (I), (*S*)-4-methyl-1-hexene (II), and (*R*)-3,7-dimethyl-1-octene (III). Reprinted with permission from reference [8].

Alternatively in another kind of experiment, the Italian chemists considered copolymerization of enantiomerically pure chiral units randomly dispersed among achiral units. The constraint of several units taking the same helical sense would require that the chiral units impose their bias on the helical conformations in the region of the chain where the achiral units were pendant. As a control experiment, isotactic homopolymers from two related monomers—one achiral, 4-methyl-1-pentene, and the other chiral, (*S*)-4-methyl-1-hexene—were prepared. Copolymers from the same two monomer units were also synthesized. Figure 4 shows a linear response of the optical activity to the proportion of the chiral molecules only in the mixture of the homopolymers. In the copolymer of the chiral and achiral units 50% of the chiral comonomer is enough to yield the full optical activity, and this effect is more extreme in the higher boiling solvent, which favors, as discussed above, polymers with higher isotactic content.[9]

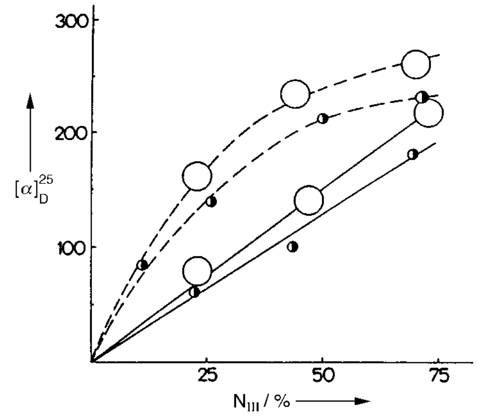


Figure 4. Rotatory power in methylcyclohexane versus mole fraction in units derived from (*S*)-4-methyl-1-hexene (N_{III}) for copolymers of (*S*)-4-methyl-1-hexene with 4-methyl-1-pentene (dashed line) and for mixtures of the two homopolymers (solid line). ◑ fraction extracted with cyclohexane. Reprinted with permission from reference [9].

In this beautifully designed early work in Italy the effects were limited by the random coil nature of the isotactic vinyl polymers. Clearly these chiral, nonlinear relationships could be further amplified in a helical polymer with fewer interruptions in the helical conformation—that is, in a stiffer polymer—and this is the subject of Section 3.

3. Chiral Properties of the Polyisocyanates

3.1. Structural Considerations

Shashoua, working at Dupont in the 1950s, realized that addition polymerization of the isocyanates could produce a material at one extreme of the Nylon structure, the Nylon-1. In this material the amide groups follow each other without interruption (Figure 5), in contrast to the higher Nylons where aliphatic groups intervene.[10]

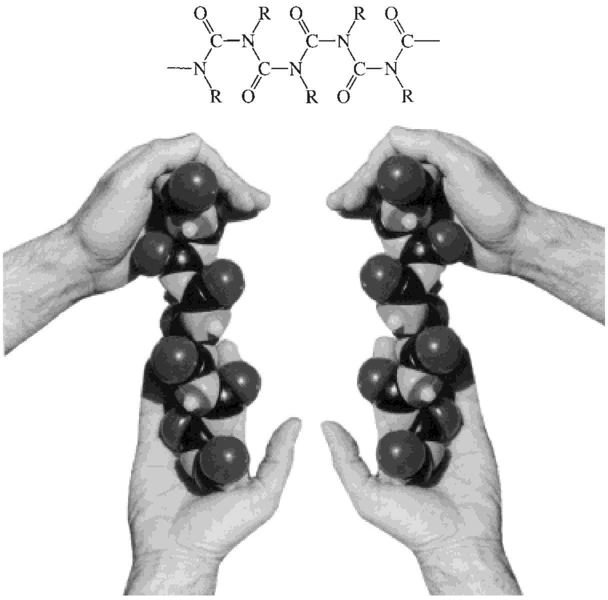


Figure 5. Top: *cis–trans* alternating structure of the polyisocyanate backbone. Bottom: left- and right-handed 8/3 helix constructed of CPK models; only the backbone atoms are shown.

In Figure 5 the chain is first drawn in two dimensions as an extended crankshaft to represent what is now known to be the basic conformation. Reducing steric interactions from the proximity of the carbonyl oxygen atom to the alkyl group on nitrogen requires turning of the structure out of the plane so as to form a helix. In the case of the *n*-butyl side chain X-ray work in Israel on stretched, oriented films showed this helix to take eight units for three turns.[11] The conjugative requirements between the recurring amide groups combined with this steric effect forces all nonhelical conformations to occupy far higher energy states, with the consequence that the overall or global dimension of the chain is very large for the molecular weight. Conformations which would change the direction of the chain are low in population and segmental motions are restricted, leading to a stiffening of the chain. Therefore, for the same contour length along the chain backbone the distance between the ends of the chain is far larger than for a random coil polymer. This leads to extremely viscous solutions even at low concentrations, while at high enough concentrations in the dissolved state, lyotropic liquid crystals are formed.[12] These characteristics, discovered over the years since the first synthesis[13] have fostered a continuing interest in these polymers.

As in the isotactic vinyl polymers discussed above, polyisocyanates constructed of achiral units allow both helical senses with equal probability intervened by helical reversals. These helical reversals are likely to cause a change in the chain direction. Are the chains long enough so that these changes can be found? What is their nature? Do they contribute to the dimensions of the chain?[14]

In the first experiments the above questions were studied by light scattering experiments, which showed the chain dimensions of certain optically active polyisocyanates[15, 16] to be greatly increased over that, for example, in poly(*n*-hexyl isocyanate), where there can be no preference for one helical sense. Unfortunately the chiral pendant naively first investigated[16] was sterically bulky, so that in addition to excluding the helical reversals by exclusively favoring one helical sense, it forced restrictions on the local segmental motions of the chain. This latter parameter, revealed by NMR line width measurements,[17] rather than the absence of the helical reversals was responsible for the increased chain dimensions.[17, 18] A way had to be found to favor one helical sense without changing the segmental characteristics of the chain.

3.2. The Uniform Chiral Field

The concept of a uniform chiral field in a polyisocyanate—namely, of introducing a single stereospecific deuterium substituent in the side chain of every unit—arose from the desire to cast the mirror helical states into a diastereomeric relationship without changing the torsional characteristics of the backbone.[19] Samples of 1- and 2-deuterio-*n*-hexyl isocyanate (see Figure 6) were synthesized by the key step of yeast-mediated reduction of 1-deuterio-hexanal and 1-deuterio-pentanal. The resulting alcohols, which were chiral only by virtue of the deuterium substitution, were produced in the *S* configuration, as is known for the biochemical reducing agent associated with the yeast. This was followed by routine functional group transformations that inverted the configuration at the stereocenter and produced the (*R*)-deuterated isocyanates.[19] While the optical activity at the sodium D line, $[\alpha]_D$, was so small as to be almost unmeasureable—a characteristic of this kind of chirality which impeded its acceptance for many years[20]—the polyisocyanates produced had very large $[\alpha]_D$ values in the hundreds of degrees and also of opposite sign from the precursor monomers. Clearly the optical activity of the polymer could not be arising simply from the deuterated stereocenter.

The large circular dichroism signal for the helical chromophores of poly(1-deuterio-*n*-hexyl isocyanate) and poly(2-deuterio-*n*-hexyl isocyanate) in Figure 6 is direct evidence for an excess of one helical sense in these polymers and demonstrates a large chiral amplification, since the per unit bias favoring one helical sense arising from the deuterium substitution must be very small, while the intensity of the CD band is consistent with a large, although not complete, excess

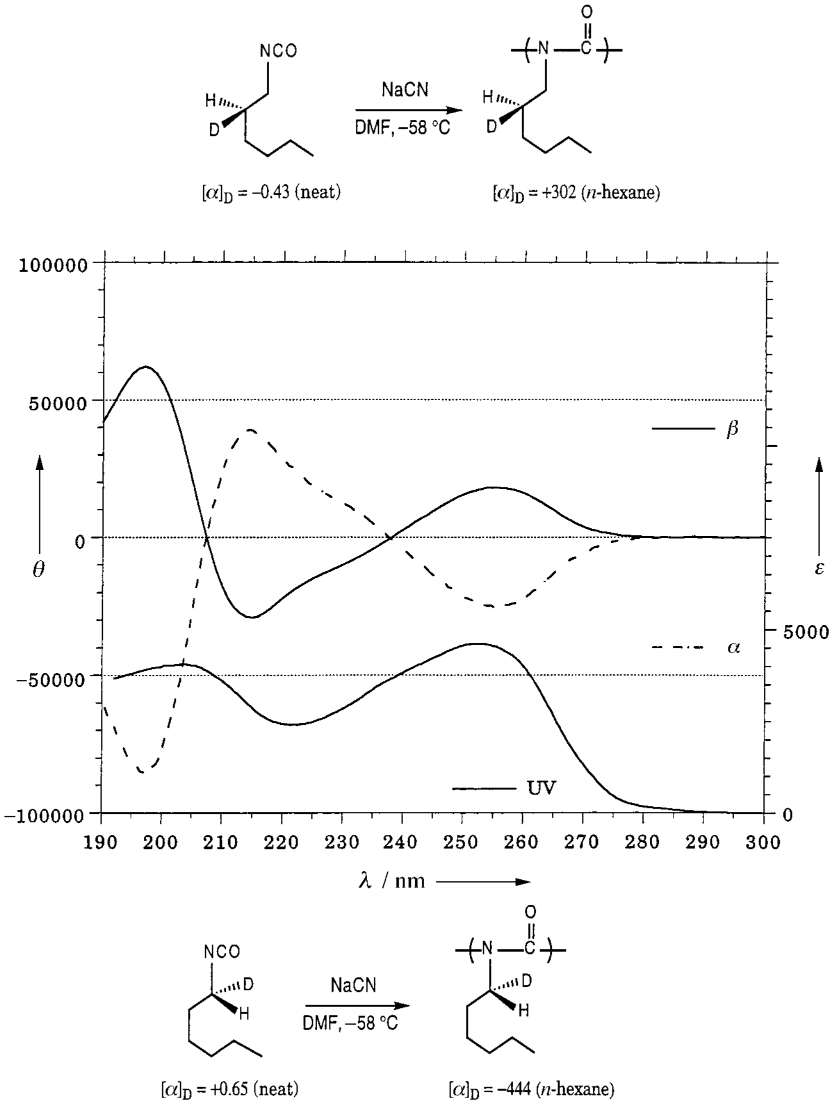


Figure 6. Graph showing the CD and UV spectra of poly(1-deuterio-*n*-hexyl isocyanate) and poly(2-deuterio-*n*-hexyl isocyanate) (reprinted with permission from reference [3]). Also shown are the structures and changes in optical activities in the conversion of the monomers into these polymers. θ = molar ellipticity; ε = molar extinction coefficient.

of the preferred helical sense. What is the structural basis of this isotope effect?[21] Any hope to answer this question must come from knowledge of the energy parameter associated with the preference for one helical sense for the configuration of the deuterated stereocenter. As we shall see statistical physics can be very helpful in this regard.

The polyisocyanate chain with its long blocks of left- and right-handed helical states, interrupted occasionally by helical reversals, provides a model allowing understanding of the amplification factor that can be clearly seen from the effect of the stereospecific placement of the deuterium on the helical sense ratio. Since many units are forced by the low population of helical reversals to take one helical sense, any chiral perturbation favoring one helical sense must be multiplied by the number of these cooperating units. In this way a small effect per unit, which is certainly the situation for the deuterium placement, will be amplified.

In chains that are long enough to contain helical reversals, the amplification will be limited by the number of units between reversals. In chains so short that reversals rarely occur, the number of cooperating units will be the number of units in each chain, that is, the degree of polymerization. In this way the relative lengths of left- and right-handed blocks will reflect the amplified energy. In long chains the number of units of the favored helical sense will be larger than of the unfavored sense, with this ratio depending on the energy difference and the temperature in the usual manner. The helical reversals will interrupt the higher energy helical sense more often. However, the the population of reversals depends exponentially on temperature, and therefore the amplification controlling the energy difference between the left- and right-handed helical states will depend strongly on temperature. In short chains though, as defined above, temperature will play its conventional role in moderating the equilibrium between left- and right-handed helical states since there is no role for the reversal. The degree of polymerization is the amplification factor, and it is fixed.

These qualitative considerations can be expressed in quantitative form, as explained in detail below, by a one-dimensional Ising model for which a partition function can be written and specifically evaluated.[22] The controlling parameters are temperature, T; the degree of polymerization, N; the excess energy of the helical reversal state, ΔG_r; and the per unit energy favoring one helical state over the other, $2\Delta G_h$. The qualitative picture discussed above is expressed in quantitative terms for the limit of short and long chains by Equations (1) and (2) derived from the partition function.[22] These equations are valuable in demonstrating in quantitative terms the picture of the amplification mechanism drawn above, although they are simplifications of a more complex equation which was actually used to fit the experimental data.

$$[\alpha] = [\alpha]_m \tanh(\Delta G_h N/RT) \quad (1)$$

$$[\alpha] = [\alpha]_m (L\Delta G_h/RT)/((L\Delta G_h/RT)^2+1)^{1/2} \quad (2)$$

In Equation (1) the optical activity term on the left does not depend on the helical reversal energy ΔG_r. These are short chains and the optical activity will grow in proportion to N and to ΔG_h, the "chiral bias". On the contrary, in Equation (2) for long chains, N does not appear as a variable, while the term $L = \exp(\Delta G_r/RT)$ appears, designating the length of the helical sense blocks. As Equation (2) shows, as L becomes very large the observed optical activity $[\alpha]$ will approach the optical activity of a chain of a single helical sense, $[\alpha]_m$.

An intensive research effort produced samples of variable N of the two deuterated polyisocyanate; each sample had a narrow range of molecular weights around N for that sample. This was accomplished by synthesis of highly polydisperse polymers followed by fractionation by gel permeation chromatography These materials were studied in great detail for the relationships between N, $[\alpha]$, and temperature T, and experiment and theory were shown to be in perfect agreement. The qualitative picture drawn for the polyisocyanates and the understanding of the source of the chiral amplification are supported quantitatively.[23] The key energy parameters defining the excess energy of the helical reversal and the energetic bias favoring one helical sense arising from the deuterium substitution were revealed.[23] These results took the work in two unrelated directions based on these different energy terms.

3.3. Chiral Bias

Only a tiny amount of energy, on the order of a single calorie per mole per unit[23] (approximately $^1/_{600}$ of the ambient energy), distinguishes the left- and right-handed helices in the deuterated polyisocyanates, where the R configuration at the α- and β-carbon atoms favors opposing helical senses (Figure 6). In general terms, substitution of deuterium for hydrogen leads to a lower zero-point energy, and the stronger the carbon–hydrogen bond is, the greater is the decrease in the zero-point energy.[21] The two hydrogens atoms of any methylene unit in the side chain of poly(n-hexyl isocyanate) are diastereotopic and therefore different to some extent in their bond strength. They exchange this difference as the local helix changes from one handedness to the other. If one hydrogen atom of one of the methylene groups is substituted for deuterium, this will favor the helical sense which confers a higher bond frequency on the substituted hydrogen. This is the basis of the approximately one calorie per mole difference we are measuring from the cooperative properties of the polyisocyanates, an energy so small as to be virtually invisible in the absence of the chiral amplification. Understanding the structural basis of the isotope effect, beyond the general considerations outlined above, is far more difficult because of its magnitude. Normally, in chemical phenomena, given the kind of information available to us on the polyisocyanates, we could point to the structural source of observed effects. However, in ths case such a small amount of energy is so far within the noise level of any structural theory there is no hope at this time of pointing to the responsible structural features of the polymer. This interesting difficulty can be seen in even more extreme terms for the experiment described below.

When poly(n-hexyl isocyanate) is dissolved in a series of optically active solvents of similar structure, the circular

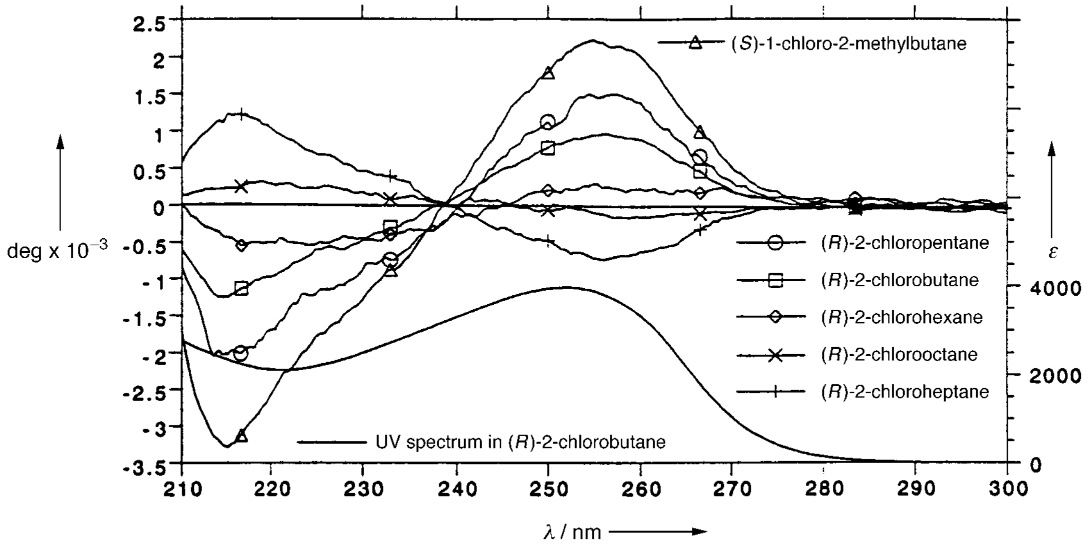


Figure 7. Circular dichroism spectra of poly(*n*-hexyl isocyanate) dissolved in optically active solvents at 20°C. UV spectrum shown only for (*R*)-2-chlorobutane. Continuous lines represent the experimental data; all concentrations of polymer are 1.9 mg mL^{-1}. Reprinted with permission from reference [24].

dichroism spectra (Figure 7) demonstrate that one of the dynamically interconverting helical senses is preferred by each solvent. Fitting this "chiral solvation" in the identical manner to the theory discussed above for the deuterated polyisocyanates[23] for one of the chiral solvents, 2-chlorobutane, yields a remarkably minute energy. The chiral bias for the units is 0.04 cal mol^{-1}.[24] Again, as with the isotope effect, we have no structural interpretation of the chiral solvation, and cannot test our speculations of what aspect of the relationship between the polymer chain and the solvent is responsible for the intriguing fact that a change in the length of the alkyl group results in a change in the preference for the helical sense for an otherwise identical stereocenter (Figure 7). As noted above, structural hypotheses are tested by predictions of energy and in this case the magnitude of the energy is beyond our predictive ability. However, there is a way for the experiment to be turned in a manner to allow a correlation with structural theory.

Chiral solvation[24] opens a new way to look at an interesting phenomenon in the solution properties of both polymers and small molecules. Mixing achiral or racemic solvents with the nonracemic solvents described in Figure 7 allows determination of the contact of the "competing" solvents with the polymer backbone by measuring how the overall solvent composition scales with the chiral optical signal. This solvent–polymer contact is an interesting aspect of this first use of chiral solvation to measure preferential solvation, and differs from other preferential solvation experiments in polymers where, for example, index of refraction increments place ill-defined boundaries on the nature of the solvent surrounding the polymeric solute. Actual contact with the chiral solvent is necessary to cause a discrimination between the helical senses, and this is directly responsible for the magnitude of the circular dichroism signal.[25] Treatment of the circular dichroism data obtained on mixing various proportions of (*S*)-1-chloro-2-methylbutane with 13 achiral or racemic solvents allowed determination of a series of equilibrium constants *K* defining the preferential solvation (Table 2).[25]

Why should the two isomeric alcohols 1- and 2-butanol and 1- and 2-octanol, which are nonsolvents for the polymer and act to precipitate the polymer on addition to a solution in (*S*)-1-chloro-2-methylbutane, preferentially solvate the polymer up to the point of precipitation? In fact the alcohol isomers which are the stronger precipitants are more attracted to the polymer! Why should the highly branched hydrocarbon 2,2,4,4,6,8,8-heptamethylnonane, also a precipitant for the polymer, be strongly attracted to it? Fortunately, in contrast to the isotope and solvation effects on chirality discussed above, these preferential solvation effects are likely associated with solvation energies of a magnitude which can be subjected to theoretical analysis, although this possibly valuable effort has yet to be undertaken.[26]

Table 2. Preferential solvation of poly(*n*-hexyl isocyanate) by 1-chloro-2-methylbutane in solutions of this solvent with an achiral or racemic cosolvent.

Cosolvent	*K*[a]	Vol. % cosolvent at polymer precipitation
2,2-dimethylbutane	2.90	
octane	2.40	
hexane	2.11	
2,2-dimethylhexane	1.40	
2-chlorobutane	0.99	
2-butanol	0.86	55
tetrahydrofuran	0.84	
1-bromobutane	0.75	
1-butanol	0.75	40
chloroform	0.63	
2-octanol	0.57	50
1-octanol	0.36	25
2,2,4,4,6,8,8-heptamethylnonane	0.27	60

[a] $K = ([PA][I])/([PI][A])$, where [PA] and [PI] are the concentrations of optically active and inactive solvents in contact with the polyisocyanate backbone. [A] and [I] are the concentrations of optically active solvent and inactive solvent.

3.4. Helical Reversal

In hydrocarbon solvents the value of ΔG_r[22–24] is about 3.8 kcal mol^{-1} for poly(*n*-hexyl isocyanate), which translates to the low population expected (see Section 3.2), that is, about one helical reversal per about 600 units at 20 °C. This energy could be used in concert with an empirical force field to determine the torsional potential along the backbone and to describe the conformational properties of the reversal.[27]

These insights arising from the empirical force field show that the low number of helical reversals along the chain, about one every 120 nm, and the 50° angular change in the chain direction cannot contribute significantly to the overall chain dimension. This agrees with light scattering and viscosity measurements comparing poly(*n*-hexyl isocyanate) with the deuterated, optically active polyisocyanates described in Figure 6.[18] The answer to the longstanding question concerning the dimensions of the polyisocyanates, the question which initially drove the inquiry leading to the experiments discussed here, is that this property is controlled by local segmental motions. As predicted originally by Cook,[17a] small dynamic variations in torsion and bond angle have a far larger effect on the global dimensions and the persistence length than the kinks in the chain associated with the rarely occurring helical reversals.[17, 18]

The kink in the chain caused by a helical reversal has interesting consequences in situations where the chains are not isolated from each other. This was seen first in aggregates formed by optically active variations of poly(*n*-hexyl isocyanate) in hydrocarbon solvents at low temperature. These aggregates can be detected in dilute solution by light scattering methods[28] and are revealed in macroscopic dimensions when the aggregates lead to gels which form and unform as a function of temperature, that is, they are thermally reversible. In such gels chain enlargements rather than cross-links maintain the gel structure. When the polyisocyanate chains forming these aggregates consist of unequal populations of left- and right-handed helical blocks separated necessarily by helical reversals, entering the aggregate phase was associated with a strong increase in the optical activity (Figure 8). This must mean a decrease in the number of helical reversals, which makes sense considering that electron microscopy[28] of the gel state arising from the aggregate shows parallel packing of the chains in fibrous bundles. In such a packing arrangement the kinked helical reversals would interfere, and since they are an equilibrium state their population would be reduced. In chains in which there was an excess of one helical state, the population of the preferred helix would increase, giving rise to an increase in optical activity, as we observe.[28, 29]

The parallel packing seen in the aggregates of the polyisocyanates has similarities to the parallel arrangements of the mesogenic molecules in liquid crystals,[31] and in fact the polyisocyanates form lyotropic liquid crystals. What would be the fate of helical reversals in a liquid crystal phase? To address this question, a subject of theoretical interest,[12, 32–34] a series of copolymers of *n*-hexyl isocyanate with varying proportions of one or the other of the enantiomers of 2,6-dimethylheptyl isocyanate was prepared. In this way we obtained chains of a single helical sense as well as chains with blocks of opposite sense. Only the latter would contain helical reversals.

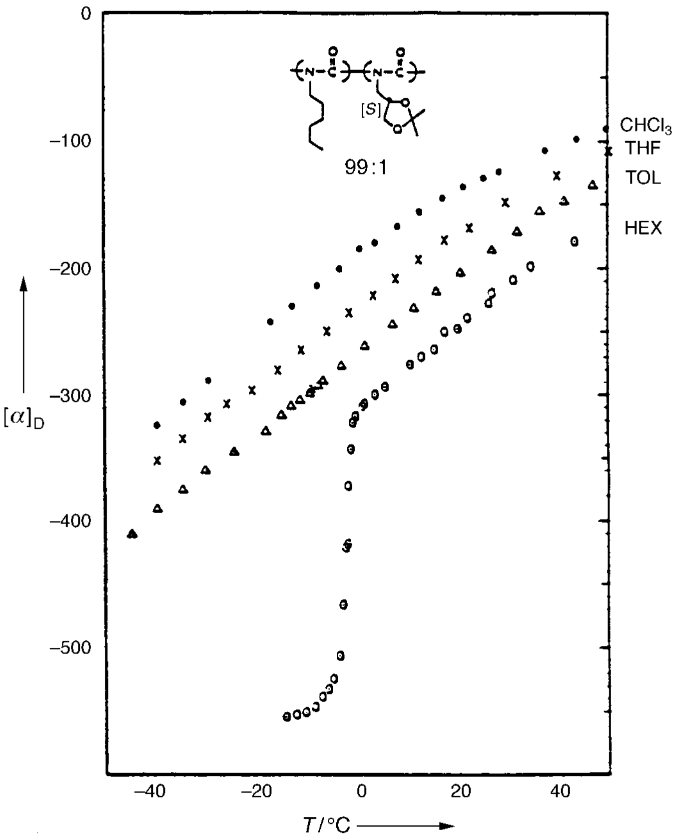


Figure 8. The temperature dependence of the D-line optical activity for a random copolymer of *n*-hexyl isocyanate and a chiral nonracemic isocyanate in chloroform (0.54 mg mL^{-1}), tetrahydrofuran (0.60 mg mL^{-1}), toluene (TOL, 0.82 mg mL^{-1}), and hexane (HEX, 0.54 mg mL^{-1}) in descending order. Reprinted with permission from reference [35].

Figure 9[36] is a plot of *Xr*, a parameter designating the optical rotation in dilute solution at a constant dopant concentration, against a term 2π/pitch, defining the pitch property of the continuously twisting cholesteric arrangement

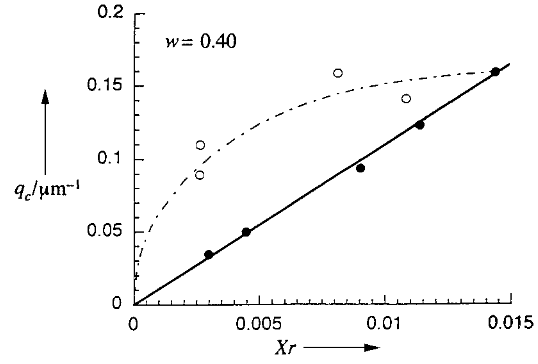


Figure 9. Plot of 2π/pitch versus *Xr*, a parameter related to the ratio of left- and right-handed units in the samples for optically active polyisocyanates used as dopants for the lyotropic liquid crystal formed from poly(*n*-hexyl isocyanate). Open circles are data for polymers with left- and right-handed blocks within each chain, while closed circles are for mixtures of fully left- and fully right-handed chains. The total polymer concentration in toluene is 40%. Reprinted with permission from reference [36].

ment. The plot presents data for the cholesteric liquid crystals formed by doping a nematic phase of poly(*n*-hexyl isocyanate) in toluene with the various polyisocyanates designated. Two variations of the dopants were used for the data in Figure 9. The filled circles represent the results for mixtures of mirror-image chains of a single helical sense with different compositions, while the unfilled circles represent the results for polyisocyanate chains with blocks of helical senses along a single chain. The data clearly show that the cholesteric liquid crystal property (ordinate) scales linearly with the dilute solution property (abscissa) for the dopants which are mixtures of fully left- and fully right-helical chains, whereas identical ratios of left- and right-handed helices within single chains scale nonlinearly with this cholesteric pitch property.

The nonlinearity in the data shown in Figure 9 for polyisocyanates with alternating helical blocks can reasonably arise from the fact that the ratio of left- and right-handed helical units determined from the optical activity of the dilute solution does not represent the ratio in the liquid crystal state. In fact, the data showing tighter twisting (smaller pitch) for the helical block dopants, the open circles in Figure 9, inform us that the enantiomeric excesses in these dopants are higher in the liquid crystal than in dilute solution. The proportion of the favored helical sense is expanding at the expense of the other helical sense, which is expected if the helical reversal population is reduced in the liquid crystal compared to isotropic solution yielding an example of this sought-after phenomenon.[32, 33, 37]

The details of the helical reversal conformation, as described by the force field calculation,[27] are shown in Figure 10. The kink in combination with the stiffness of the polyisocyanate chain indicates that movement of the reversal would force many units of the chain on either side of the reversal to move along with it. This would sweep out a large volume, which suggests that in a glassy state, where many entanglements offer impediment to motion, the movement of the reversal would be severely impeded or even stopped. Consider spin coating a sample of an optically active polyisocyanate with helical reversals between blocks of left- and right-handed units at a temperature far below the glass transition temperature. On raising the temperature the polyisocyanate would be frustrated in its ability to respond to the increase in thermal energy and, as the glass around it, would fall out of equilibrium. The temperature would be too high for the low population of helical reversals. On reaching the melt state the system would equilibrate and the population of the helical reversals would be suddenly diminished, causing a large reduction in the optical activity.

Successful blending[38] of certain functionalized polyisocyanates with copolymers of styrene and vinyl phenol allowed this experiment to be carried out. A material was formed without birefringence, allowing measurement of the optical activity properties of the polyisocyanate in the solid state. The results, along with the variation of optical activity with temperature in solution as a comparison,[39a] are shown in Figure 11. The strong change in optical activity on reaching the glass transition temperature confirms the theoretical picture drawn above and is therefore consistent with the kinked nature of the reversal determined from the force field calculation (Figure 10). We have extended this idea to the motions associated with the racemization of 1,1′-binaphthyls with oligophenyl "paddles" of various lengths attached to

Figure 10. Molecular mechanics generated helical reversal in a polyisocyanate. Reprinted with permission from reference [3].

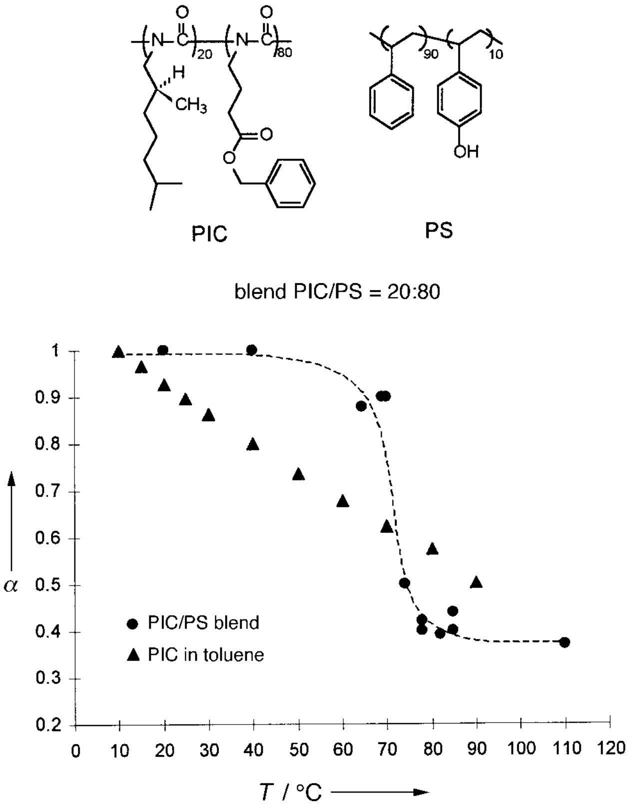


Figure 11. The temperature dependence of the optical properties of a polyisocyanate with unequal proportions of left- and right-handed blocks in dilute solution in toluene and in an amorphous blend with a glass transition temperature near 70 °C. PIC = polyisocyanate; PS = polystyrene.

each ring at the 6- and 6′-positions. We measured the effect of the length of the paddle (number of phenyl units) on the restriction to motion at the glass transition temperature in several polymers; this led to a new way to judge the correlation between length scale and motion in polymeric glassy and melt states.[39b]

3.5. The Quenched Random Field

When the chiral information distinguishing the helical senses of the polyisocyanate are not distributed uniformly along the chain, as in the case of the deuterium substitution or the chiral solvation discussed in Section 3.3, the Ising model describing the situation is slightly altered, leading to an important change in the partition function derived from it. For this partition function to be evaluated and lead to algebraic expressions such as Equations (1) and (2), every unit of the chain must be identically affected by the chiral information. The Ising model for the uniform chiral influence is seen in Equation (3), while that for a random input of this chiral information is seen in Equation (4).

$$H = -\tfrac{1}{2}\Delta G_{\mathrm{r}} \sum_{i=1}^{N-1} \sigma_i \sigma_{i+1} - \Delta G_{\mathrm{h}} \sum_{i=1}^{N} \sigma_i \qquad (3)$$

$$H = -\tfrac{1}{2}\Delta G_{\mathrm{r}} \sum_{i=1}^{N-1} \sigma_i \sigma_{i+1} - \sum_{i=1}^{N} \Delta G_{\mathrm{h},i} \sigma_i \qquad (4)$$

The Ising models described by Equations (3) and (4) are widely used in statistical physics to describe the cooperative properties of one-dimensional magnetic materials. In magnetic systems, σ_i is the spin state representing the localized magnetic moment, which can be $+1$ or -1. The first term in the Hamiltonian H represents the energy cost of a boundary between domains of opposite spin, and the second term represents the energy of a single spin interacting with the local magnetic field. For polyisocyanates, the spin σ_i corresponds to the local helical sense, the first term in the Hamiltonian represents the energy cost of a helical reversal, and the second term represents the local chiral bias. In the standard Ising notation, the first term in the Hamiltonian has the coefficient J and the second term has the coefficient h. Here, we replace these coefficients by $\tfrac{1}{2}\Delta G_{\mathrm{r}}$ and ΔG_{h}, respectively, in order to emphasize the interpretation of these coefficients for polyisocyanates.

The movement of the ΔG_{h} term from outside the summation term to inside the summation in Equations (3) and (4) represents the nature of the chiral information. In Equation (3), which describes a uniform chiral field, all units of the chain are subjected to an identical influence. In the case of Equation (4) though each unit of the chain may be subject to differing chiral influences, therefore the use of $\Delta G_{h,i}$, which must appear within the summation to allow this higher level of information. Unfortunately, evaluation of the partition function derived from Equation (4) requires specifying the precise input of the chiral information, a factor that will differ according to how the chiral information is arranged along the chain. This is termed a "quenched random field". In a random copolymer of, for example, chiral and achiral units, each differing chain would require a different partition function. We cannot therefore for any random system apply the theory developed for the uniform chiral field [Eqs. (1)–(3)]. How can such random systems, which can certainly be synthesized (see below), be theoretically dealt with?

In analogy to the experiments of the Italian researchers where copolymers of enantiomers and of chiral and achiral monomers were synthesized (Figures 3 and 4),[1, 4, 7–9] polyisocyanates were prepared with different units along the chains. The experimental results for these copolymers in which the chiral information is fixed by the details of the mechanisms of the copolymerizations—that is, in which there is a quenched random chiral field—are found in Figure 12[35] and Table 3.[40, 41] As in the Italian work we see the signature characteristics of cooperativity in the nonlinear relationships between the enantiomeric content of the units used in the synthesis and the chiral optical propertiesof the polymer.

In qualitative terms the data in Table 3 demonstrate that a small proportion of chiral units, shown to be randomly distributed in the chain among achiral units, causes an excess

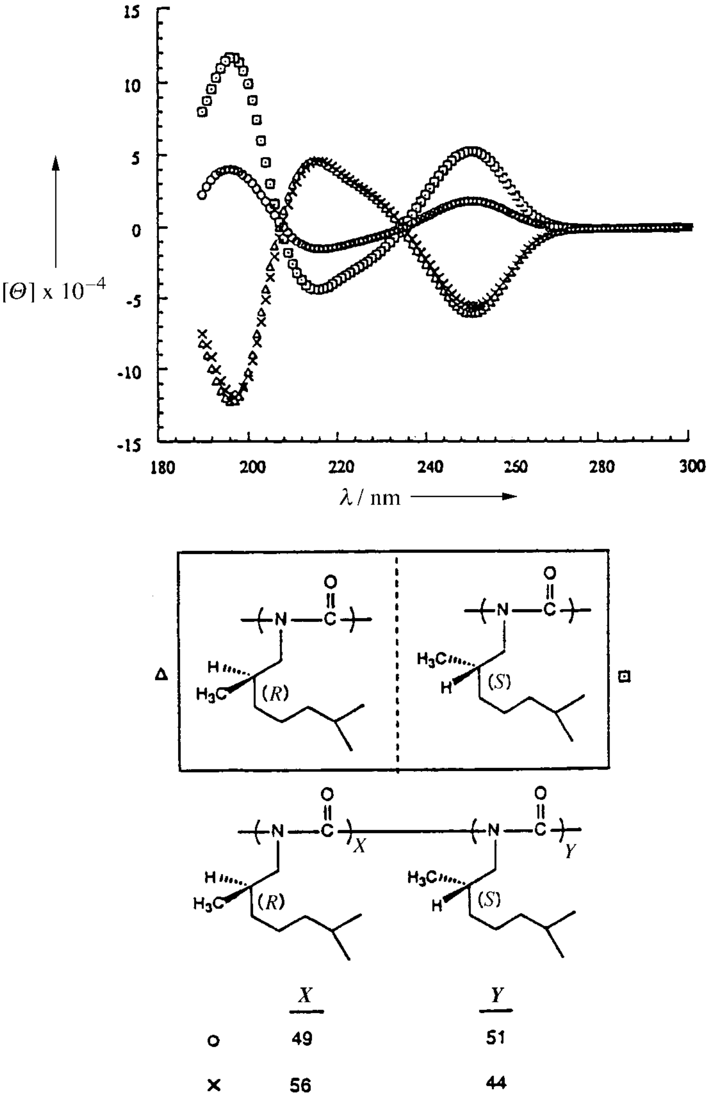
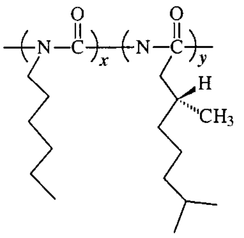


Figure 12. Circular dichromism data for random copolymers of enantiomers. Reprinted with permission from reference [40].

Table 3. Specific rotation of polyisocyanate coploymers.[a,b] [35]



x	y	$[\alpha]_D^{-20}$	$[\alpha]_D^{+20}$
100	0	0	0
99.5	0.5	− 140	− 66
97.7	2.3	− 379	− 231
85	15	− 532	− 480
0	100	− 514	− 500

[a] Measured in $CHCl_3$ ($c = 0.5$ mg mL^{-1}). [b] x = mole percent of *n*-hexyl isocyanate, y = mole percent of 2,6-dimethylheptylisocyanate.

of one helical sense far out of proportion to their population. A chain with 15% of the chiral units gives essentially the same optical activity as a chain made entirely of the chiral units, while even the presence of 0.5% of the chiral units provides a large optical activity. In addition the strong temperature dependence of the optical activity for a chain with less than a full preference for one helical sense is consistent with the exponential relationship of the helical reversal population with temperature. That population is reduced at lower temperature, as discussed above for the uniform chiral field work, as a result therefore increasing the domain sizes and the cooperativity and the effect of the chiral units. These experiments have been called the "sergeants-and-soldiers" experiments, the chiral units being sergeants and the achiral units soldiers.[35]

The results in Figure 12 are also startling. Here a polyisocyanate made up of an isocyanate synthesized from a citronellic acid (3,7-dimethyl-6-octenoic acid) which is considered essentially racemic by Aldrich Chemical Company yields a polymer whose circular dichroism spectrum is identical to that of a polymer synthesized from nearly enantiomerically pure monomers. The enantiomeric excess in the "racemic" monomer turns out to be 12%. Even a 2% enantiomeric excess in the monomer units is enough to produce one-third of the circular dichroism signal of the polymer of a single helical sense. This phenomenon has been termed "majority rule" and arises from the minority units taking part in the helical sense of the majority units, presumably to avoid introducing increased numbers of helical reversals.[40]

These experiments are subject to analysis using the Ising model expressed in Equation (4), and therefore special procedures are necessary to apply the cooperative theory. The effort, as seen below, offers insights into the nature of the cooperativity that are entirely contrary to one's intuition.

One approach to evaluating the Ising model for the quenched random field is a numerical transfer-matrix calculation,[42, 43] where one specifies specific arrangements of the groups along the backbone within the random constraint. Each specific realization can then be theoretically evaluated since the detailed characteristics of the chiral field are specified. If one then averages over all these specific realizations, given that one has chosen enough of them to describe the system realistically, something which is only limited by computer time, the optical activity can be predicted as a function of the energetic parameters and the degree of polymerization. This approach involves a great deal of computation, but correlations with experimental measurements of the relationship between N and $[\alpha]$ yield precise results for the energetic parameters ΔG_r and ΔG_h. Although this information has great value in continuing work in the area, it does not yield qualitative insight into how the various parameters interact with each other to control the properties of the cooperative system.

In an approximate analytical approach developed for the specific situation of a copolymer of achiral and chiral units with proportions r and $1 - r$, respectively (Table 3), the chiral and achiral units have $\Delta G_{h,i} = \Delta G_h$ and $\Delta G_{h,i} = 0$. In this case the characteristic domain size L is determined precisely in the same way as for the uniform chiral field discussed in the analysis of the deuterated polyisocyanates (see Section 3.2)—that is, with $L = \exp(\Delta G_r/RT)$—except in the situation of small chains, where N may limit the domain size. If we define the chiral order parameter M as the fraction of the optical activity of a chain of a single helical sense, under certain approximations, M for the random copolymer of chiral and achiral units can be expressed by the total chiral field acting on a domain of size L as given by Equation (5).[42]

$$M = \tanh(rL\Delta G_h/RT) \qquad (5)$$

All the energy terms in Equation (5) can be expressed, as discussed above, in terms of ΔG_r and ΔG_h, and so estimation of these values allows predictions of the optical activity as a function of the proportion r of chiral units. In the nature of the hyperbolic tangent the optical activity will scale linearly with low values of r and show saturation at a value of r that depends on the energetic parameters. Saturation at low values of r is seen in the experimental data in Table 3, and a numerical analytical procedure allows fitting of Equation (5) to these data. By this procedure a plot can be constructed which defines a locus of points in the $(\Delta G_h, \Delta G_r)$ plane which fit the experimental findings. By assigning the value of ΔG_r as that obtained from the uniform chiral field, one can determine ΔG_h.[42] Although Equation (5) offers an accurate view of the cooperative factors in the copolymers of chiral and achiral units, the analysis provides no further insight beyond our qualitative understanding that increase of L and/or ΔG_h and reduction of T must increase the excess of one helical sense and therefore M and the optical activity.

This sergeants-and-soldiers system[35] has in addition been treated by the numerical transfer-matrix calculation discussed above, and this approach in combination with a large range of samples with molecular weights of narrow dispersity yields accurate values for the two energetic parameters.[43] The theoretical work leaves little question of the accuracy of the conformational model proposed for this polymer.

Analysis of the quenched random field of the copolymer of enantiomeric units (Figure 12) using the approximate analytical approach offers two surprises into how the cooperativity works in these copolymers, which has an important impact on how to vary the experimental approach. In the copolymer of enantiomeric units we define proportions of p and $1-p$ for the randomly placed enantiomeric units. If the right-handed units have $\Delta G_{h,i} = +\Delta G_h$ and the left-handed units $\Delta G_{h,i} = -\Delta G_h$, and ΔG_r, as usual, is the energy of the helical reversal, an approximate analytical analysis shows that the domain size L of a single helical sense is determined not only by ΔG_r and the temperature, but as well by ΔG_h in an interesting manner. This is seen in quantitative form in Equations (6)–(8).[44] As expected, the chiral order parameter M—that is, the excess of one helical sense and therefore the optical activity—will increase as the domain size L increases and as the enantiomeric excess $p - ½$ increases.

$$L_{rf} = (\Delta G_r/2\,\Delta G_h)^2 \tag{6}$$

$$1/L = 1/L_{rf} + 1/L_{th} + 1/N \tag{7}$$

$$M = \mathrm{erf}[(2\,L)^{1/2}(p - ½)] \tag{8}$$

The error function, erf, can be described in the following manner: If one were to draw a Gaussian function around zero, movement along the abscissa is determined by the right-hand side of Equation (8). From the nature of the Gaussian, small deviations from zero subsect a far larger volume under the curve than further away from zero. The volume under the curve subsected determines the value of M, and the sharper the Gaussian, the faster M rises for small increases in enantiomeric excess. The error function therefore causes small increases in enantiomeric excess close to the racemic state to result in far larger changes in optical activity than equivalent changes at higher enantiomeric excesses. The optical activity is predicted to change steeply only near to the racemic state and to reach a value corresponding to a single helical sense far from the enantiomerically pure state.

The term L_{rf} designates the random field domain size that is influenced by the competition among the enantiomeric units for the helical sense of the backbone. This competition, not seen in the uniform field systems or in the quenched random field of chiral and achiral units, is one of the fascinating aspects of the enantiomeric copolymers. Before going into this let us see how the domain that ultimately determines the cooperativity is determined itself. In the sergeants-and-soldiers copolymers or in the deuterated polyisocyanates or in the chiral solvation the cooperative domain, as discussed above, is determined by ΔG_r and T, unless it is limited by N. The cooperative domain though in the copolymers of enantiomers is determined in a far more complex and interesting manner [Eq. (7)].

Under conditions where the degree of polymerization and the thermal domain are large, Equation (7) informs us that the domain size L in Equation (8) will be dominated by the random field domain size. This turns out to be the experimental situation for all of the data in Figure 12.[44] Under these conditions L in Equation (8) can be replaced by the right-hand side of Equation (6). Since ΔG_r is divided by ΔG_h, and squared, the algebra remarkably predicts that, within certain limits, *increasing* the chiral bias will *decrease* the influence of the majority enantiomer, giving therefore lower optical activities. This can be understood from the symmetry properties of the system. Any change in ΔG_h will effect the majority and minority units with equal and opposite effects, so that the minority objection will rise in concert with the majority force for its favored helical sense. The physics predicts that the minority objection will override the majority force by limiting the cooperativity. In this most unhuman situation of cooperativity along a one-dimensional polymer chain we encounter a familiar human behavior.

The theory has been applied to the optical activities of polymers obtained from the copolymerization of enantiomers for several enantiomeric excesses, including those in Figure 12. Using the value of ΔG_r obtained from the uniform chiral field work on deuterated polyisocyanates and the value of ΔG_h for the chiral group shown in Figure 12, estimated from a force field calculation,[27] one can predict the change of optical activity with enantiomeric excess. The prediction fits the experimental data with no adjustable parameters (Figure 13).[44]

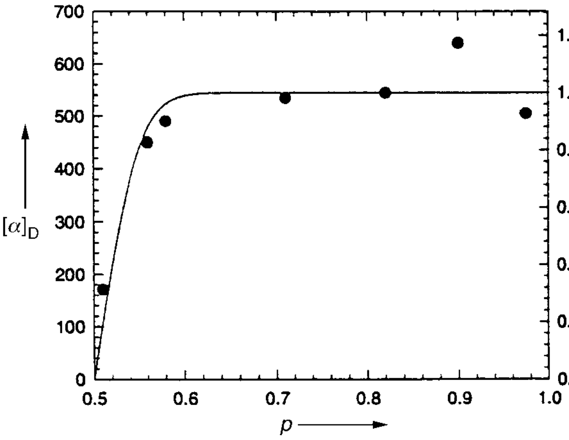


Figure 13. Fit of the theory from the random field Ising model to the data points for the optical activity versus the enantiomeric excess for random copolymers of enantiomers. $[\alpha]_D$ is the optical activity fo the random copolymer at the sodium D line as a function of enantiomer concentration p. Solid line: theoretical prediction for the chiral order parameter M from Equation (8), with the domain size $L = 164$. The prediction agrees with the data with no adjustable parameters, other than the relative scale of the vertical axes. Reprinted with permission from reference [44].

Although experiments are in progress to test the prediction about the effect of the magnitude of the chiral bias ΔG_h, the prediction that reduction of the minority objection to the helical sense of the majority units increases the domain size and therefore the optical activity is made in another way. Terpolymerization of mirror-image enantiomers near to the racemic state with an achiral monomer could be used to modify the theory[45] to produce Equations (9) and (10), which are directly analogous to Equations (6) and (8). Here r is the fraction of the chiral comonomers in the terpolymer. If the

$$L_{rf} = 1/r(\Delta G_r/2\,\Delta G_h)^2 \tag{9}$$

$$M = \mathrm{erf}[(2rL)^{1/2}(p - ½)] \tag{10}$$

random field domain dominates the term L, it follows that the right-hand side of Equation (9) can be substituted in Equation (10), and that r cancels out! In other words, if N and the thermal domain size L_{th} are large enough that L_{rf} can be used in the error function equation, dilution of the competing chiral units with achiral units will make no difference to the optical activity. The critical cancellation of r in this case arises qualitatively from the fact that this dilution does not change the number of chiral units within a single cooperative domain. This effect of the dilution of the chiral units with achiral units has now been observed experimentally, with the details in line with the predictions of the theory.[46]

The possibilities for experiment and the development of new materials are extended also by random copolymerization of enantiomerically pure isocyanates of different structure, where each structure favors the opposite helical sense. Since the chiral biases of each of the competing units differ, in contrast to enantiomers, the helical senses of the polymer will be equally populated at a ratio, a pseudoracemic state, other than when the proportion of the competing chiral units is 50:50. In addition since the temperature dependencies of these chiral biases will differ, again in contrast to enantiomers, this pseudoracemic ratio will depend on temperature. It follows that the proportion of the chiral comonomers, which can be easily varied, determines the temperature at which the optical activity is zero, but below and above that temperature the optical activity increases with opposite sign. This unusual effect, which can also be described by the statistical physical theory discussed above, has been recently observed.[47]

4. Summary and Outlook

For the phenomena described here, the helical systems associated with biological origins have the disadvantage of a given nonracemic chirality. In this way nature blocks our observations of certain fascinating aspects of the cooperativity of helical arrays, although when it serves a specific purpose "wrong" enantiomers may be inserted in specific places.[48] In synthetic systems, on the contrary, incorporation of nonracemic chirality is an additional burden, and the work presented here shows that this burden may be considerably alleviated by taking advantage of the amplification of chirality inherent in helical systems. Could it be possible to design a catalytic helical polymer directed to asymmetric synthesis in which the enantiomeric excess of the products were independent, over a wide range, of the enantiomeric excess of the units making up the polymer?[49] Analogously, could the chromatographic properties of a chiral polymer allow the same separation of enantiomers independent, over a wide range, of the enantiomeric excess of the units making up the polymer?[50]

Helical arrays are of considerable interest[51] and several show parallels to the findings discussed here. Hopefully the intense effort we have taken to understand the limits and theoretical basis of these effects may help others to evaluate the limits and opportunities in other materials. The fact that these effects find parallels in materials as disparate as vinyl polymers and an analogue of the Nylons is encouraging, as is the fact that polypeptides synthesized from mixtures of enantiomers also show a majority rule effect.[52] In another direction, could the lamella boundaries of helical polymer crystals play the role of the helical reversals, so that annealing could determine the amplification resulting from stereospecific placement of deuterium at, for example, the 3-position of poly(1-butene) and produce excesses of a single helical sense in the crystal?[53]

The amplification characteristics studied here spotlight the inability of structural theory to deal with the very small energies that entirely control the chiral properties of these helical polymers. Certainly such small forces are widely present in all of chemistry, and likely amplified in many cases,[54] but their understanding is less critical in systems in which they play a minor role because larger forces are also at work in controlling the equilibrium properties, for example in crystals or in the folding of proteins. This point goes beyond stereochemistry. Such structurally incomprehensible small forces can yield complete control over miscibility in polymer blends such as that between poly(styrene) and poly(vinyl methyl ether). Here deuterium substitution of all the aryl hydrogen atoms considerably helps the miscibility.[55] Is this due to C–H··O–R hydrogen bonds[56, 57] between these hydrogen atoms and the ether oxygen atoms, attractive interactions that could have only minor effects in the absence of the amplification associated with large numbers of polymer units in contact?

The work presented here might be relevant to proposals that the circularly polarized light discovered in outer space was responsible for small enantiomeric excesses produced by photoresolution processes that then lead to the origin of homochirality in life. The prerequisite must be chiral amplification, which as shown here requires a stable helix, a conformational state which is common in biological systems.[58].

This kind of idea has an evolutionary aspect since in such a polymer the minority units residing in the helix sense of the majority, and vice versa, would be of higher energy, as quantitatively discussed in this review. Even a small excess of majority units could therefore lead to a preference for epimerization of the minority units to the configuration of the majority units, which would lead to a fuller excess of the majority helical sense and thus to a cycle of increasing enantiomeric excess of the units making up the chain. The outcome of this cycle, and as well the minimum excess of majority units to initiate the evolutionary process, would depend on the same parameters controlling the one-dimensional cooperativity discussed in this review and could also be described theoretically by a statistical physical model. The decreased entropy of the enantiomerically enriched system opposes the process and enforces the limitations. Within these limits, even in an ensemble of chains with an overall exactly equal proportion of the competing enantiomers, there could be an excess of one or the other mirror-related units in the single chains so that an epimerization mechanism could allow the ensemble to evolve toward a true racemic mixture of chains. The observation of majority rule in certain DL-polypeptides[52] and the variety of mechanisms for epimerization of the amino acid constituents suggests that these ideas may apply to a biologically relevant system.[59,60]

The interplay of classic stereochemical ideas with cooperativity, a characteristic of large molecular organizations, continues to be rich with research potential.

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