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A Macromolecular Conformational Change Driven by a Minute Chiral Solvation Energy[†]

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The equilibrium in a dynamic racemic mixture may be displaced to favor one enantiomer by a nonracemic chiral entity external to the chiral racemic structure.[1-3] We have come across this phenomenon in a stiff helical macromolecule where cooperative interactions give rise to an easily measurable excess of one helical sense even though the energetic preference per monomer unit is far smaller than has been possible to determine previously.

Figure 1 shows the solvent-subtracted circular dichroism spectra of a sample of poly(*n*-hexyl isocyanate)[4-6] (**1**) of a viscosity average degree of polymerization of about 500, dissolved in a series of optically active chlorinated hydrocarbons.

These circular dichroism spectra are identical in shape[4-6] to those obtained from optically active polyisocyanates in which an excess of one helical sense is enforced by chirotopic stereogenicity in the side chain.

In this macromolecule (**1**), the helical sections of opposite sense are both equally populated and rapidly interconverting in an achiral environment. Thus, when **1** is dissolved either in an achiral solvent or in a racemic mixture of 2-chlorobutane, no circular dichroism spectrum is seen, but in the case of 2-chloroheptane the solvent enantiomers give equal and opposite circular dichroism spectra.

In one of the solvents, (*R*)-2-chlorobutane, the intensity of the 257-nm band as a function of degree of polymerization (DP) of **1** and of temperature is shown in Figure 2. The weak dependence on temperature but stronger dependence on molecular weight at low molecular weights (low DP) and the opposite relative dependence at high molecular weights (high DP) are characteristic of the low population of helix reversals which enforce the cooperative interactions first seen in poly((*R*)-1-deuterio-1-hexyl isocyanate).[4] This has been theoretically interpreted by statistical thermodynamics.[5,6]

The mathematical description of this cooperative effect[5] allowed us to numerically fit[7] the data in Figure 2 and determine the difference in free energy per mole of monomer units for the helix to take a right- or left-handed state in the solvent (*R*)-2-chlorobutane. The best fit[7] for each temperature is shown as a continuous line in Figure 2 and corresponds at 300 K to a helix reversal energy (G_r)[7,8] of 3500 cal/mol, which matches well to the earlier independent determination,[5] and a chiral solvation energy (G_h) of 0.04×10^{-3} kcal/mol monomer residue [sic!]. The fact that we can determine G_h is remarkable and derives from the unusual linear cooperativity shown by this polymer (**1**),[4-6] which multiplies the effect of this minute energy.

The chiral optical properties of nonracemic polyisocyanates have been connected to helix sense using the cholesteric liquid crystal properties of these mesogenic macromolecules[9] and independently by empirical force field calculations.[8] Although this information allows an assignment of a right-handed helix excess to the polymers dissolved in the 2-chlorobutane, 2-chloropentane, and 2-chlorohexane and left-handed to the polymers in the longer 2-chlorooctane and 2-chloroheptane,[8,9] the extremely small energies driving these intriguing preferences are so far below the noise level of theoretical models of solvation[10] that no dependable structural model can explain these results. Only empirical structural models can be developed for such a system, and this predicament already finds parallels in other systems where minute energy differences can accumulate by cooperative interactions to control equilibria.[11]

Assuming that the optical activity of the polymer depends on the concentration of the nonracemic chiral solvent in the polymer domain, we can conclude from optical activities in solvent mixtures which of these solvents is preferentially attracted to the polymer. The data shown in Figure 3 demonstrate that the optical activity of the polymer is linear in the concentration of (*S*)-chloromethylbutane when it is diluted with the racemic chloromethylbutane, indicating that the polymer has no preference for either enantiomer. By the same reasoning the polymer is preferentially solvated by chloromethylbutane when diluted by hexane or octane, but preferentially solvated by chloroform when chloroform is the diluent. In this case, where the polymer conformation is rigidly

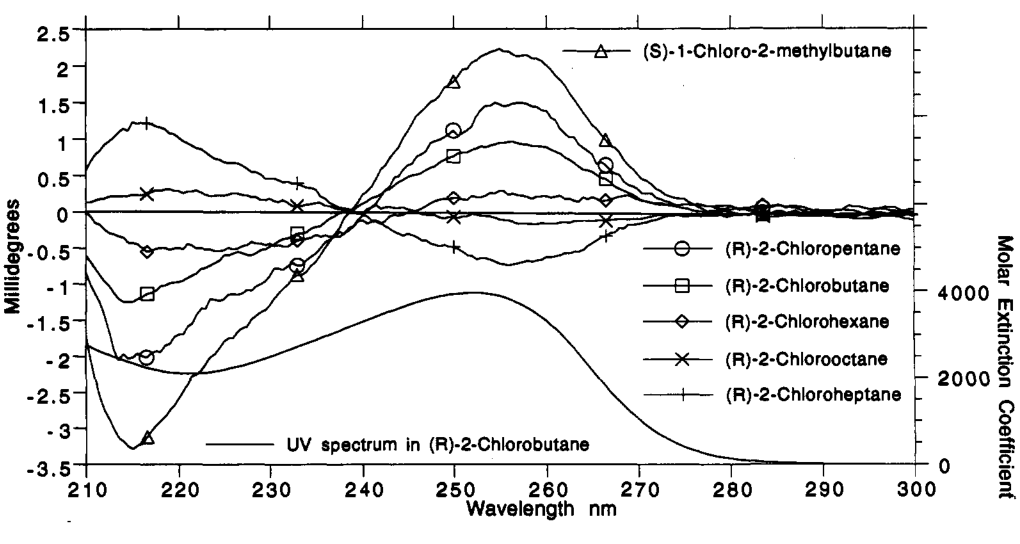

Figure 1. Circular dichroism spectra of poly(*n*-hexyl isocyanate) dissolved in optically active solvents at 20 °C. Ultraviolet spectrum (—) shown only for (*R*)-2-chlorobutane; please see the text. Continuous lines represent the experimental data; all concentrations of polymer are 1.9 mg/mL.

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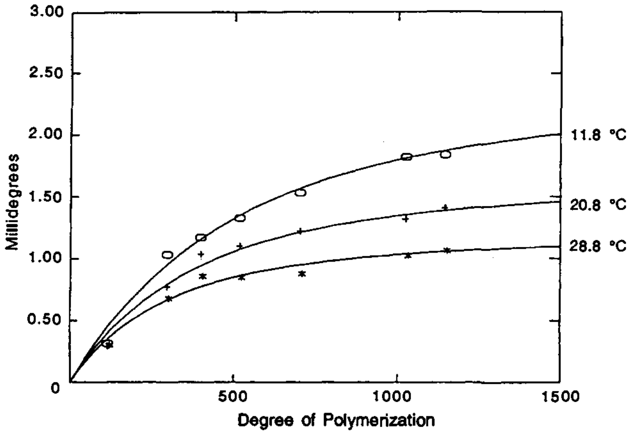

Figure 2. Experimental and theoretical dependence on degree of polymerization and temperature of the optical activity for poly(*n*-hexyl isocyanate) dissolved in (*R*)-2-chlorobutane. Continuous lines are the theoretical prediction; please see the text. For experimental data, all concentrations of polymer are 2.4 mg/mL.

defined and where subtle variations may be made in the side chains and in the solvents, a high versatility is offered to study this effect[12] and the chiral solvation.[13] Finally, related first-order asymmetric transformations[1,2] have likely applicability to other examples of the large number of dynamically racemic synthetic macromolecules in existence.

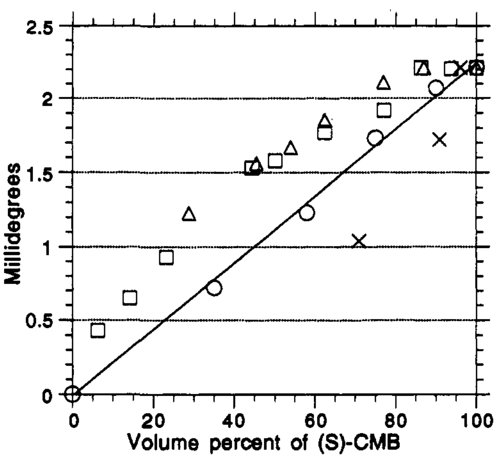

Figure 3. Circular dichroism intensity at 257 nm for poly(*n*-hexyl isocyanate) dissolved in solvents mixed with (*S*)-1-chloro-2-methylbutane ((*S*)-CMB). Symbols correspond to the various cosolvents: ○, racemic CMB; □, *n*-hexane; △, *n*-octane; ×, chloroform. All concentrations of polymer are 2.0 mg/mL.

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† This paper is dedicated to Professor Kurt Mislow on the occasion of his 70th birthday.

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(13) Nonracemic cosolutes of **1** in achiral solvents also give rise to the effects shown in Figure 1 (unpublished work of C. Khatri).