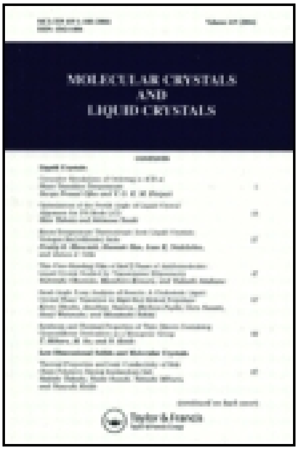

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The Effect of Trifluoroacetic Acid on the Viscoelastic Properties of a Polypeptide Liquid Crystal

Donald B. Dupré [a] , Russell W. Duke [a] , William A. Hines [b] & Edward T. Samulski [b]
[a] Department of Chemistry, University of Louisville, Louisville, Kentucky, 40208
[b] Department of Physics and Department of Chemistry, Institute of Materials Science, University of Connecticut, Storrs, Connecticut, 06268

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The Effect of Trifluoroacetic Acid on the Viscoelastic Properties of a Polypeptide Liquid Crystal

DONALD B. DUPRÉ, RUSSELL W. DUKE
Department of Chemistry, University of Louisville, Louisville, Kentucky 40208

and

WILLIAM A. HINES and EDWARD T. SAMULSKI
Department of Physics and Department of Chemistry, and
Institute of Materials Science, University of Connecticut, Storrs, Connecticut 06268

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The viscoelastic properties of a liquid crystal are characterized by a set of elastic moduli, K_{ij}, and viscosity coefficients, γ_i, that are fundamental in the establishment of the mesophase. Together with the anisotropic diamagnetic (dielectric) susceptibility, these parameters determine the response of the material to external perturbations such as applied magnetic (electric) fields. The measurement of the twist elastic modulus, K_{22}, and the rotational viscosity coefficient, γ_1, has been recently reported for lyotropic liquid crystalline solutions of the polypeptide poly-γ-benzyl-L-glutamate. This system is of particular interest in that a number of molecular parameters (e.g., supporting solvent and molecular weight, i.e.. length) can be easily varied for quantitative comparison with theory. We have examined K_{22}, γ_1 and the diamagnetic susceptibility in the presence of small amounts of a second solvent, trifluoroacetic acid (TFA), which is known to disrupt the α-helical conformation of this polypeptide in dilute solution. γ_1 changes abruptly with the additions of even small amounts ($< 1\%$) of the acid, whereas K_{22} remains insensitive to TFA concentration in the pre-helix–coil transition range. The results are discussed in terms of the effect of the acid on the molecular conformation of the polypeptide in the liquid crystal.

INTRODUCTION

The effect of halogenated organic acids on solution properties of polypeptides is both unusual and dramatic. A variety of experimental techniques have shown that in mixed solvent systems containing a helicogenic solvent and a denaturing solvent, dichloroacetic acid (DCA) and trifluoroacetic acid (TFA) will cause synthetic polypeptides, such as poly-γ-benzyl-L-glutamate

(PBLG), to undergo an intramolecular phase transition from a rigid, rodlike, α-helical polymer to a flexible, random coil.[1] TFA is more effective in that the transition occurs at 10–30% acid by volume (dependent on the nature of the helicogenic solvent and the polymer molecular weight) whereas ~75% of the weaker acid DCA is required. In addition the literature contains many reports of more subtle, gradual changes in the condition of the polypeptide macromolecule in the pretransition range (1–10% volume range for TFA). Such pretransition behavior at low acid concentrations has been accounted for with a variety of explanations and models including disruption of aggregated polymer helices,[2] gradual unfreezing of sidechains on the periphery of the macromolecule,[3] and "melting" of low molecular weight helical moieties to random coils in polydisperse samples prior to the precipitous helix–coil transition itself.[4]

It has also been noted that small amounts of TFA have remarkable effects on liquid crystal formation and response at higher concentrations of the polymer. For example, a few percent TFA added to the helicogenic solvent promotes solubilization of the polymer, and rapid formation and maturation of the cholesteric structure exhibited by this lyotropic liquid crystal. A large decrease in the response time of the mesophase to external perturbations such as electric or magnetic fields is also noted upon the addition of even 1% TFA. Indeed, the use of sparing quantities of this highly polar acid is a part of the art of handling research on these less extensively studied, macromolecular liquid crystals.

Below, we present a more quantified discussion of our recent studies of these observations on the liquid crystal state of PBLG doped with small amounts of TFA. Unless otherwise indicated, all liquid crystal samples used for experimental measurements consisted of solutions of PBLG of molecular weight 300,000 in the helicogenic solvent dioxane (24 mg polymer/cc dioxane) to which various amounts of TFA were added.

RESULTS AND DISCUSSION

1 Orientational order

Liquid crystal orientational order is most usually specified in terms of a parameter, S, which is the first nontrivial multipole average involving the cosine of the angle between the major axis of a representative molecule and the preferred direction, or director, of the medium:[5] $S = \frac{1}{2}\langle 3\cos^2\theta - 1\rangle$. S as a function of polymer concentration and temperature have recently been determined by X-ray analysis[6] on magnetically oriented liquid crystal solutions of PBLG in dioxane and by following the temperature dependence

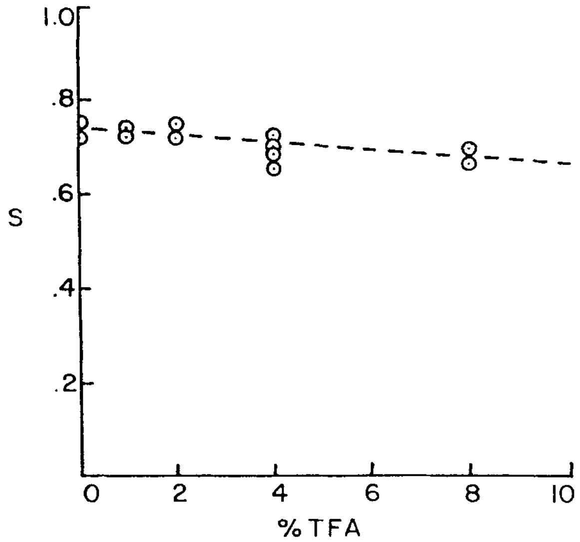

FIGURE 1 Order parameter vs %TFA in PBLG-dioxane : TFA liquid crystals Ref. 6.

of the anisotropy of the diamagnetic susceptibility[7] over the liquid crystal regime.

In PBLG-dioxane liquid crystals, S decreases linearly from an initial value of 0.73 in a liquid crystal without TFA by about 10% when TFA is added in the range 0–10% TFA (Figure 1). The initial value of S is considerably less than that of a perfectly ordered system of close-packed rigid rods ($S = 1$). This reduced value of S is thought to be due to disorder in the liquid crystal in the form of correlated flexing of neighboring helices which broadens the diffracted azimuthal X-ray intensity, i.e., the helices are not ideal *rigid* rods. In this context, addition of TFA to the liquid crystal would be expected to decrease S if the TFA perturbs the PBLG so as to increase the flexibility of the helical conformation.

2 Pitch of cholesteric supramolecular organization

The inherent asymmetry of the α-helix of PBLG results in an asymmetric intermolecular potential which produces a cholesteric structure in the polypeptide liquid crystal which is closely related to that formed in thermotropic liquid crystals. This supramolecular structure is characterized by a pitch, P_0, which is a measure of the periodicity of the helicoidal arrangement of macromolecules about an axis of torsion. (The subscript "o" indicates an absence of external fields and/or acid which perturbs the equilibrium value of the pitch.) In those macroscopic regions of the bulk sample which are viewed along a direction normal to the axis of torsion, the cholesteric texture is manifested as a series of parallel, equispaced, retardation lines of spacing $P_0/2$. In the liquid crystalline PBLG solution, P_0 is of the order of 1–100 microns, varies with temperature ($P_0 \propto T$) and with PBLG concentrations, c, is an inverse manner ($P_0 \propto 1/c^2$).[8]

The sign of the associated form optical rotation is a measure of the sense of the cholesteric twist. It is positive for cholesteric structures with a right-handed twist and negative for structures with a left-handed sense. The sense of the cholesteric twist is dependent on the chirality of the constituent macromolecules *and* the supporting solvent of the lyotropic liquid crystal. For example, in liquid crystals with dioxane as a solvent, the right-handed α-helix PBLG generates a cholesteric structure with a positive form optical rotation and the left-handed α-helix PBLG (a homopolypeptide with D-amino acids) generates a cholesteric structure with negative form optical rotation. Liquid crystals containing a racemic mixture of PBLG and PBDG exhibit no form optical rotation regardless of solvent, i.e., they form the untwisted nematic structure.

Robinson[8] noted an unusual behavior of the pitch and sense of the cholesteric structure when PBLG liquid crystals were prepared in various solvents and mixed solvents. As noted above, PBLG-dioxane liquid crystals have positive form optical rotation. However, PBLG-CH_2Cl_2 liquid crystals have negative form optical rotation. In both solvents, the PBLG α-helix is right-handed.[1,9] The situation is exactly reversed for PBDG. In Figure 2, we show the change in the form optical rotation ($2/P_0$) for liquid crystals prepared in binary solvent mixtures. P_0 increases as the fraction of *polar solvent* in dioxane : CH_2Cl_2 or dioxane : nitrobenzene mixtures is increased. At a critical ratio of solvents, $P_0 \rightarrow \infty$; the cholesteric structure is compensated (becomes a nematic structure). The form optical rotation changes sign at the critical solvent ratio.

Utilizing the polarizing microscope to observe the retardation lines, the variation of the pitch for the PBLG-dioxane : TFA liquid crystal in zero magnetic field has been determined as a function of TFA concentration (vol. %). In Figure 3, the data has been normalized to the value of the pitch in the absence of TFA, $P_0 = 47$ microns. The effect of TFA is minimal below 2%. After this initial insensitivity, the pitch decreases more rapidly with TFA concentration in the remainder of the range 1–10% TFA (the helix-coil transition, determined by changes in the chemical shift of the $^{\alpha}C$—H proton,[10] occurs at ~25% TFA (vol. %). This pitch decrease is opposite to the trend observed in other mixed solvent systems when the concentration of a more polar moiety is increased.

Recently, Samulski and Samulski[11] have developed a theory of the origin of the spontaneously twisted (cholesteric) structure which, when applied to

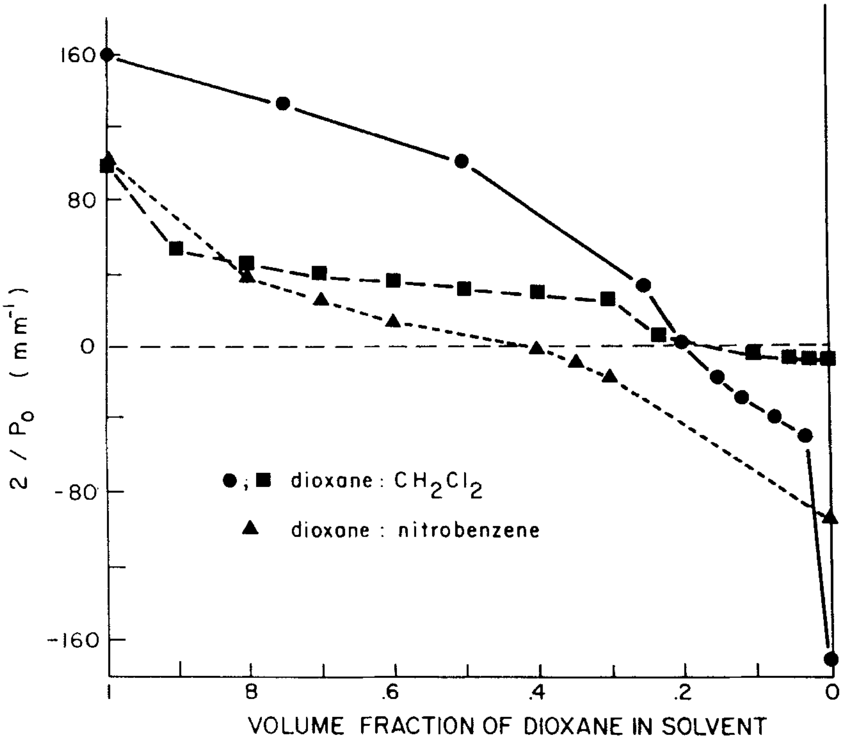

FIGURE 2 The form optical rotation, $2/P_o$, for cholesteric textures in PBLG liquid crystals with mixed solvent systems: (●) data for the binary solvent dioxane: CH_2Cl_2 (unspecified PBLG concentration)[8]; (■) dioxane: CH_2Cl_2 (PBLG concentration, 20 mg polymer/cm^3 solvent); (▲) dioxane: nitrobenzene (PBLG concentration, 20 mg polymer/cm^3 solvent).

lyotropic polymer systems, may account for the above anomaly. The development explicitly includes easily visualized parameters such as the chirality and polarizability of the macromolecule and the dielectric constant of the intervening solvent. The theory correctly predicts the increase of pitch observed when the dielectric constant of the solvent medium is increased by the addition of a polar, aprotic second solvent component. Halogenated acids, however, may do more than just increase the dielectric constant of the medium. There is evidence that small amounts of TFA protonate the N-terminal amide group of the polymer and associate with PBLG by H-bonding with the carboxyl group of the side chain ester.[12] The effect is to reduce the overall dipole moment of the polymer and modify the polarizability of local segments. These latter specific polymer-solvent associations may change the magnitude of the asymmetric term in the interhelix potential[11] and lead to a decrease of the cumulative pitch with the addition of TFA to the liquid crystal. Detailed calculations are now in progress.[13]

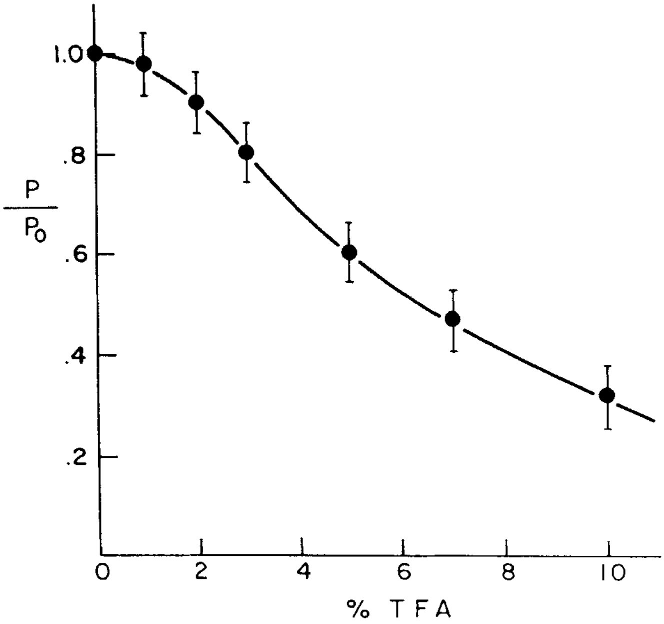

FIGURE 3 The pitch of the cholesteric structure, P, normalized by the value for 0% TFA, P_0, as a function of % TFA (vol) in PBLG-dioxane: TFA liquid crystals (24 mg polymer/cm^3 dioxane).

The temperature dependence of the pitch over a range of TFA concentrations is shown in Figure 4. Again, an anonomalous behavior is observed. In most liquid crystals an increase in temperature is accompanied by a decrease in pitch[5] of the cholesteric structures, i.e., $dP/dT < 0$. At the higher acid concentration, the pitch is noted to approach temperature independence. We know of only one other system exhibiting the latter behavior,[14] thermotropic mixtures of *dextro*-active and racemic *p*-ethoxybenzal-*p*-(β-methylbutyl)aniline.

3 Rotational viscosity coefficient

Individual PBLG macromolecules in the helical conformations have anisotropic dielectric and diamagnetic susceptibilities which are in both cases positive.[15] As a result they will tend to align themselves in an applied electric or magnetic field such that their long axes are parallel to the field direction. Liquid crystal solutions subjected to sufficiently high field strengths may therefore be made to transform to nematic order with the director of the molecular aggregates more or less parallel to the field axis. The phenomenon of this field induced transition, which is completed at a critical

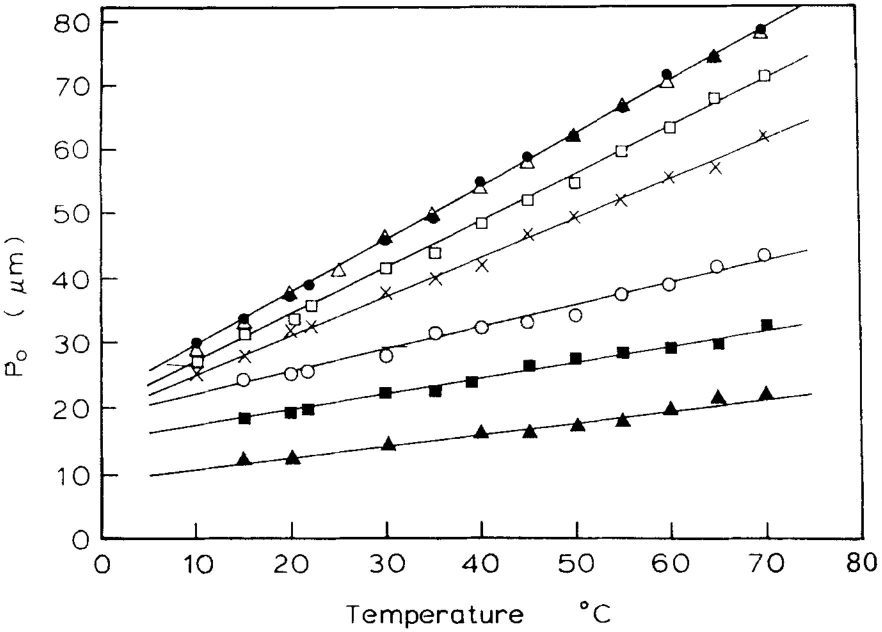

FIGURE 4 Cholesteric pitch versus temperature for various TFA concentrations in PBLG-dioxane: TFA liquid crystals. The closed circles represent the data for 0% TFA, open triangles—1% TFA, open squares—2% TFA, crosses—3% TFA, open circles—5%, closed squares—7% TFA and the closed triangles are the data points for 10% added TFA.

field value (H_c, for the magnetic case), is a result of the dilation and eventual divergence of the helical pitch of the cholesteric superstructure. The unwinding process for polymer solutions is slow in taking place, but addition of trace amounts of TFA markedly reduces the equilibration time.[15–18]

The slow reorientation rate of this polymeric liquid crystal facilitates a number of physical measurements. For example, if the material is subjected to a magnetic field, H, in excess of H_c, a measureable, time dependent anisotropy of the magnetic moment, $\Delta\mu(t)$, will develop in the liquid crystal during the course of the cholesteric–nematic transition. Also, once the cholesteric structure has been completely untwisted and the macromolecules aligned, the nematic director can be quickly rotated to any desired orientation in the field and $\Delta\mu(t)$ can be observed as a function of time as the nematic director realigns. If ϕ represents the angle the director makes with the original magnetic axis, the realignment is driven by the magnetic torque $T_{\text{mag}} = \frac{1}{2}(\Delta\chi)H^2 \sin(2\phi)$ and opposed by a viscous torque $T_{\text{vis}} = -\gamma_1(d\phi/dt)$, where $\Delta\chi$ is anisotropic diamagnetic susceptibility and γ_1 is a rotational viscosity coefficient. By equating the torques and relating $\phi(t)$ to $\Delta\mu(t)$, one can obtain[17]

$$\gamma_1 = \tau(\Delta\chi)H^2, \tag{1}$$

where τ is the characteristic time constant for reorientation and $\Delta\chi$ is given by

$$\Delta\chi = \Delta\mu(\infty)/\eta H, \tag{2}$$

η being the number of moles of peptide residues.

Figure 5 illustrates the change in $\Delta\mu$ as a function of time and the effect of TFA in PBLG-dioxane: TFA liquid crystals with 0%, 1%, and 2% TFA after setting $\phi = \phi_0 = 90°$ at $t = 0$ ($H = 18$ kOe, $H > H_c$); the values of γ_1 obtained are 2.7×10^3, 8.4×10^2, and 6.4×10^2 poise respectively. It can be seen that the rate of reorientation increases dramatically with the addition of small amounts of TFA. The calculated value of γ_1 decreases by a factor of four with addition of ~1% TFA. Reorientation rates for higher TFA concentrations (>2%) are too fast for accurate determination with the magnetometer.

NMR studies of this process yield plots of the temporal development of solvent dipolar splittings and suggest that after the abrupt increase in the reorientation rate at 1%, γ_1 does not decrease significantly at higher TFA

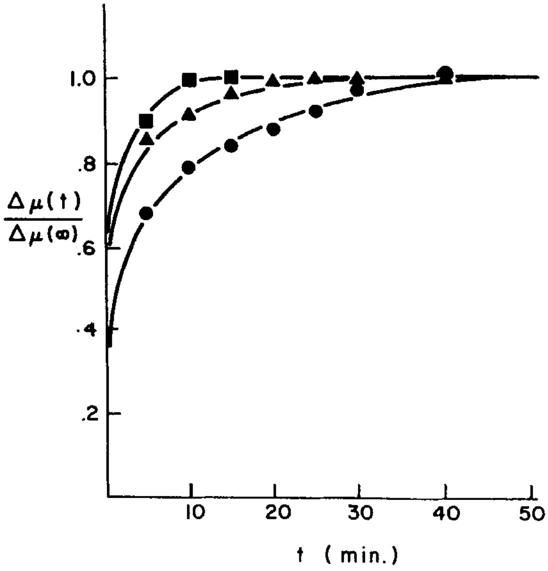

FIGURE 5 The change in the anisotropy of magnetic moment as a function of time for oriented, nematic PBLG-dioxane: TFA liquid crystals; at $t = 0$, the nematic director is aligned perpendicular to the magnetic field: (●) 0% TFA, (▲) 1% TFA, (■) 2% TFA.

concentrations.[18] The determination of γ_1 using solvent NMR spectra has also been reported for PBLG liquid crystals.[19]

The abrupt change in the rotational viscosity coefficient, γ_1 with the addition of small amounts of TFA to the liquid crystal is reminiscent of the behavior of dilute, isotropic solutions of PBLG. In such isotropic solutions, PBLG molecules aggregate in certain solvents, e.g. dioxane, benzene, ethylene dichloride.[20] Various modes of aggregation have been proposed: end-to-end, parallel and antiparallel lateral associations.[2,20] Although the nature of the intermolecular interactions responsible for aggregation are uncertain, there is general agreement that the addition to the solution of very small amounts of certain agents: dimethylformamide, foramide, dichloroacetic acid, and TFA, will breakdown the aggregates; the solution then acquires the properties of a dispersion of descrete PBLG helices.[2,20] In the liquid crystal, aggregation of the PBLG would result in an intermittant and tenuous 3-dimensional gel-like network with viscoelastic properties characteristic of melts of ordinary random coil polymers. Destruction of the aggregated network would be accompanied by an increase in fluidity of the liquid crystal. The decrease in γ_1 at 1–2% TFA and the apparent insensitivity of γ_1 at higher acid concentrations[18] strongly suggest that PBLG aggregates in the liquid crystal in the manner observed in dilute solutions.

Figure 6 is a plot of $\Delta\chi$ as a function of TFA content obtained from Eq. (2). It should be noted that the measured value of $\Delta\chi$ in the PBLG-dioxane : TFA liquid crystal reflects the anisotropy of the polypeptide only. This is so because the solvent molecules are only slightly oriented and therefore contribute negligibly to $\Delta\chi$ (solvent order parameters in these liquid crystals determined with NMR, even in the case of specific solvent–polymer binding, are of the order of 0.001).[21] Hence, changes in $\Delta\chi$ or PBLG liquid crystals in binary solvent systems which occur on changing the relative amounts of the two solvents reflect changes in the susceptibility of the macromolecule and/or changes in the order parameter. Information about the side chain organization itself can be obtained from such experiments by, for example, subtracting out the magnetic anisotropy of the helical backbone core of PBLG.[22]

4 Twist elastic modulus

Polypeptide liquid crystals, as all mesophases, are characterized by a set of five viscoelastic constants, K_{ij}, that are fundamental in the establishment of the phase and determine its extraordinary sensitivity to external perturbations. In liquid crystals three of these moduli, $K_{ij} = \{K_{11}, K_{22}, K_{33}\}$, pertain to the description of bulk properties. These moduli correspond to

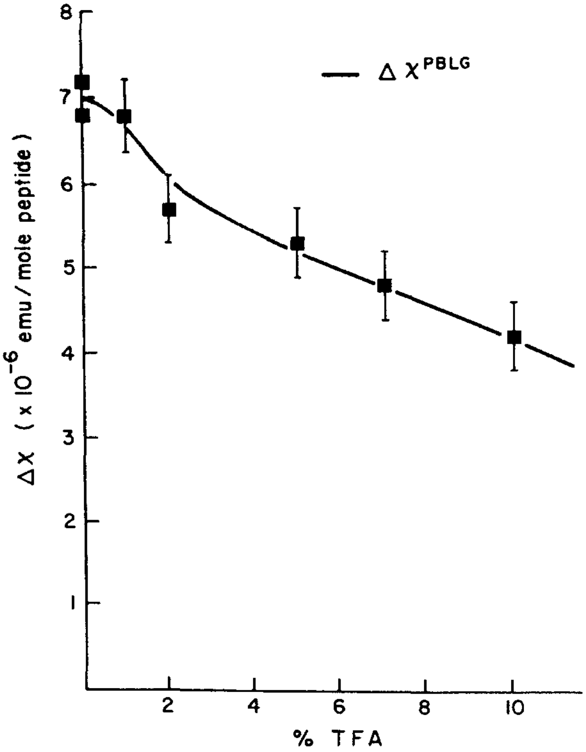

FIGURE 6 The anisotropy of the diamagnetic susceptibility of PBLG-dioxane: TFA liquid crystals as a function of % TFA (vol).

the forces necessary to induce in the director field of the material deformations of splay, twist, and bend, respectively.[5] Extensive measurements of the K_{ij} have been made on a number of thermotropic liquid crystals.[5] As yet only the twist modulus, K_{22}, has been examined in polymer systems.[16,17,22,23,24]

Meyer[24] and deGennes[25,26] have derived theoretical expressions connecting the pitch of the cholesteric structure and an applied magnetic field which involves K_{22}. They predict an increase in the pitch as the applied field is increased with a logarithmic divergence when the field strength approaches the critical value. This behavior has been verified for lyotropic polypeptide liquid crystals by the authors.[16,17] Theory relates the critical field, H_c, the initial (zero field) pitch, P_0, to K_{22} and $\Delta\chi$ through:

$$H_c = \pi^2(K_{22}/\Delta\chi)^{1/2}2P_0, \tag{3}$$

and provides a nonmechanical way to measure K_{22}.

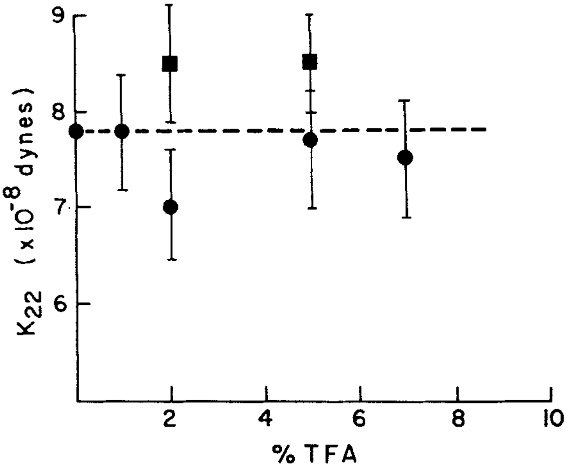

FIGURE 7 The twist elastic constant, K_{22}, as a function of % TFA (vol) in PBLG-dioxane: TFA liquid crystals: (●) PBLG mol wt = 300,000; (■) PBLG mol wt = 310,000.

The variation of H_c with increasing TFA concentration has been determined.[23] This, along with the acid dependence of P_0 (Figure 3) and $\Delta\chi$ (Figure 6), is sufficient to determine the behavior of the modulus K_{22} in the presence of TFA. Figure 7 is a plot of the trend which, within experimental error, is surprisingly constant. In view of the results above (pitch and γ_1 dependence on TFA), this insensitivity of the modulus to TFA appears to be an anomaly among the anomalies. For a possible origin of the effect (or absence thereof) we return to theory.

The formation of the spontaneously twisted liquid crystal is apparently due to asymmetric terms that arise from molecular chirality in the angular dependent part of the potential of interaction between molecules.

Goossens has presented a general theory relating the origin of cholesteric twist to molecular chirality.[27] He derives an angular dependent intermolecular potential for planar molecules whose long axes lie in adjacent "twist planes" separated by a distance r_{ab}:

$$-V_{ab} = \left(\frac{A}{r_{ab}^4}\cos 2\theta_{ab} + \frac{B}{r_{ab}^5}\sin 2\theta_{ab}\right) \tag{4}$$

The planes are perpendicular to the cholesteric axis; θ_{ab} is the angle between the directions of the long axis alignment in respective planes a and b. The coefficient of the symmetric part of this potential, A, is related to the anisotropy of the molecular polarizability. The cholesteric twist occurs because of the asymmetric part of the potential; B is related to the dispersion energy determined by electric dipole–electric quadrupole interactions. The magnitude of the twist, θ_{ab}, is proportional to the ratio $B/r_{ab}A$.[27] Physically, the twist elastic constant, K_{22}, describes the force necessary to induce a twist deformation in the cholesteric structure, either mechanically, through an external field, or by natural thermal excitations. The twist elastic constant is dependent both on short range and long range order in the liquid crystal. In principle, K_{22} can be related to the intermolecular potential through the appropriate derivatives of a partition function. Although TFA changes the equilibrium angular orientation of one PBLG molecule relative to its neighbor (θ_{ab}), K_{22} is not changed in the range 1–10% TFA (Figure 7). P_0 is related to the ratio of the coefficients in Eq. (4) and K_{22}, presumably, is a function of the total V_{ab}. However, since $B \ll A$, a sizable change in P_0 is not necessarily accompanied by a comparable change in K_{22}. Polypeptide concentration, molecular weight, and solvent in the liquid crystal do influence K_{22}.[17,23]

Acknowledgements

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