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Enantiodiscrimination in Deuterium NMR Spectra of Flexible Chiral Molecules with Average Axial Symmetry Dissolved in Chiral Liquid Crystals: The Case of Tridioxyethylenetriphenylene

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Abstract: Flexible chiral molecules undergoing fast interconversion (on the NMR time scale) between different conformational enantiomers may yield "average" axial species with enantiotopically related sites. Contrary to the situation observed for rigid axial molecules, signals from these enantiotopic sites in NMR spectra recorded in chiral liquid-crystalline solvents can be resolved. In the present work, we studied the deuterium NMR spectra of tridioxyethylenetriphenylene (compound **4**) statistically deuterated to 10% in the flexible side chains and dissolved in chiral and achiral lyotropic liquid crystals based on poly(γ-benzylglutamate). The fast chair−chair flipping of the side chains in **4** on average renders the molecule axially symmetric (D_{3h}) with pairs of enantiotopic ethylene deuterons. These deuterons exhibit unusually large enantiodiscrimination. To explain this observation, we first describe how the average symmetry of flexible molecules can be derived from the symmetry of the "frozen" conformers and the nature of the averaging process. The procedure is then applied to **4** and used to analyze the NMR results. It is shown that the large enantiodiscrimination in the present case reflects a large difference in the orientational ordering of the conformational enantiomers participating in the interconversion processes as well as a large geometrical factor due to the special shape of the dioxyethylene side groups. ^{1}H and ^{13}C NMR spectra of **4** in the same lyotropic liquid crystalline solvent are analyzed to determine its ordering characteristics. Several related cases are also discussed.

Introduction

It is well-known that enantiodiscrimination in the NMR spectra of chiral or prochiral solutes is observed more often and is much more pronounced in chiral liquid-crystalline (CLC) solvents[1,2] than in chiral isotropic solvents, in which such discrimination is relatively rare.[3] By the general term spectral enantiodiscrimination we mean the doubling of the NMR spectra of racemic mixtures (*enantiomeric* discrimination) or the splitting of signals corresponding to enantiotopic sites in prochiral molecules (*enantiotopic* discrimination). In chiral isotropic solvents, enantiomeric discrimination usually results from differences in the isotropic NMR observables of the enantiomers. In the absence of very specific forces, solute−solvent interactions are too weak to significantly affect chemical shifts and J couplings, so spectral enantiodiscrimination is very small or absent. For the same reasons, only a few examples of enantiotopic discrimination in isotropic NMR have been reported in the literature.[3] In a CLC solvent, an additional factor affects the discrimination, namely, the different orientational orderings of the different enantiomers of the solute. This ordering modifies the NMR spectrum of the solute by affecting anisotropic terms in the spin Hamiltonian, such as chemical-shift anisotropy (CSA), quadrupolar interactions (for nuclei with $I \geq 1$), and intramolecular dipole−dipole interactions.[4] In practice, the numerous dipolar interactions of protons with other protons or with carbon-13 nuclei often result in spectra that are too complex to analyze, even if simplifying two-dimensional (2D) NMR methods are used.[5] For this reason, one commonly uses ^{2}H-{^{1}H} and ^{13}C-{^{1}H} NMR techniques, which exhibit simple spectra with discrimination due to dispersion in the quadrupolar interaction ($I = 1$ for ^{2}H) and the CSA, respectively. Likewise, the reduction of the effective symmetries of prochiral solutes

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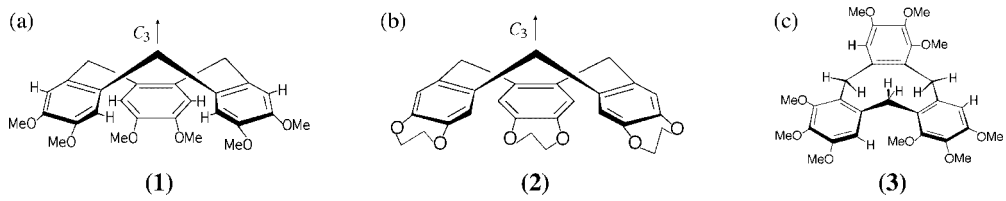

Figure 1. Structural formulas of (a) hexamethoxytribenzocyclononatriene (**1**), commonly called cyclotriveratrylene (CTV), which is the parent compound of the CTV series; (b) the tridioxyethylene derivative of CTV (**2**), in which the flexible dioxyethylene groups undergo fast chair−chair switches (see Figure 2b); and (c) the saddle isomer of nonamethoxy-CTV (**3**), which is a flexible molecule that undergoes rapid pseudorotation involving six isodynamic conformers.

when they are dissolved in CLC solvents renders the enantiotopically related sites nonequivalent.[6–8] Both types of spectral discrimination have been amply studied, particularly in lyotropic liquid crystals based on solutions of poly(γ-benzyl-L-glutamate) (PBLG) in suitable organic cosolvents (chloroform, DMF, etc.).[1] These chiral nematic-phase solvents proved extremely useful in studying enantiodiscrimination of a large range of chiral solutes, including chiral hydrocarbons.[9]

A common feature of these studies is that rigid prochiral compounds having a C_n symmetry axis with $n \geq 3$ do not exhibit enantiotopic discrimination, even though such discrimination is consistent with the general principles of chirality.[6] For example, in CLC solutions of the rigid-crown isomer of cyclotriveratrylene (CTV, compound **1** in Figure 1a), no splittings are observed in the ^{13}C-{^{1}H} or ^{2}H-{^{1}H} NMR spectra for nuclei which are related by the molecular vertical symmetry planes.[10] When such axial molecules are dissolved in achiral nematic liquid crystals, their ordering is characterized by a single independent order parameter, S_{zz}, which corresponds to the degree of alignment of the molecular C_n axis in the mesophase. This situation remains unchanged when such a solute is dissolved in a CLC solvent, since C_n (a symmetry element of the first kind) remains a symmetry axis in a chiral environment.[6] Consequently, sites that are enantiotopically related remain degenerate in CLC solution unless the chiral environment exerts forces that are sufficiently strong to twist the solute's geometrical or electronic structure, thereby selectively modifying the magnetic parameters of the enantiotopic sites. As indicated above, such effects have not been observed experimentally to date.

The situation is different for flexible molecules that on average possess axial symmetry (C_n with $n \geq 3$). By "flexible" we mean that the molecule rapidly (on the NMR time scale) interconverts between two or more conformations having similar energies. Below we shall define in a precise way what we mean by "average" symmetry, but for now we will simply say that this term refers to the symmetry of the spin Hamiltonian that describes the NMR spectrum in the fast-exchange regime. In contrast to rigid axial molecules, there are several known examples of flexible molecules having average axial symmetry that exhibit enantiodiscrimination of sites that on average are enantiotopically related. Two such previously studied examples

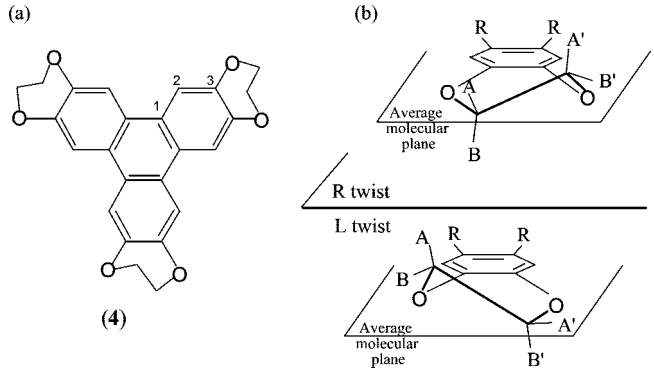

Figure 2. (a) Structural formula of tridioxyethylenetriphenylene (**4**), showing the numbering used for the aromatic carbon atoms. (b) The two interconverting chair conformations of the dioxyethylene side groups and the labeling of their hydrogens. The "average molecular plane" is the plane of the triphenylene core.

are compounds **2** and **3**, whose structures are shown in panels b and c, respectively, of Figure 1. In tridioxyethylene-CTV (**2**), the rapid flipping of the dioxyethylene groups results in an average C_{3v} symmetry for the molecule and renders the ethylene hydrogens pairwise-enantiotopic, as explained in the section entitled Comparison with Related Systems (see below) and in ref 10. In the ^{2}H-{^{1}H} NMR spectra of **2**, these ethylene deuterons indeed exhibit two doublets in achiral liquid-crystalline solutions but four doublets in CLC solutions.[10] Similarly, the saddle form of nonamethoxy-CTV (**3**) undergoes rapid pseudorotation, resulting in an average C_{3h} symmetry with the methylene hydrogens related pairwise-enantiotopically. In the deuterium NMR spectra of **3** in achiral liquid crystals, the methylene deuterons exhibit a single doublet, while two doublets are observed in CLC solutions.[11] The origin of the enantioseparation in these compounds stems from the fact that the interconverting species comprises different enantiomeric conformers that experience different orientational orderings in the chiral mesophases. As a result, sites that in the average molecule are enantiotopically related actually experience different "histories", and when the bookkeeping is complete, they yield different average quadrupolar interactions.

In this paper, we generalize the discussion of the origin of enantiotopic discrimination in flexible molecules with average axial symmetry. We first discuss how the average symmetry can be derived from the symmetry of the individual conformers and the nature of the dynamic process. New experimental results for tridioxyethylenetriphenylene (**4**) (see Figure 2a) are then presented and analyzed in terms of these symmetry considerations. In this example, the spectral discrimination of the

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enantiotopic sites of the average molecule is exceptionally large. This apparently results from the relatively large difference in the ordering characteristics of interchanging enantiomers as well as from the special chair geometry of their side groups.

Symmetry of Chiral Flexible Molecules

To identify the symmetry of the spin Hamiltonian of a rapidly interconverting molecular species, or more generally, the average symmetry of such a flexible molecule, it is usually sufficient to use intuition or apply simple inspection methods. However, it is useful to support such assignments by means of a more formal procedure. The symmetry of flexible molecules was extensively discussed in the 1960s,[12] mainly in connection with vibrational−rotational spectroscopy but also for NMR.[13,14] To date, however, no special attention has been paid to the family of processes in which rapidly interconverting chiral conformers yield on-average achiral (but possibly prochiral) species. Here we are particularly interested in processes where the average structures have axial symmetry. In such cases, the symmetries of the fixed (frozen) conformers are limited to (proper) point groups lacking symmetry elements of the second kind, while some of the dynamic processes are isomorphic with just such operations. For our present discussion, it is convenient to use the formalism developed by Altmann.[15] Although this formalism met with some criticism, it is still adequate (and useful) for the specific examples treated here.[16–18]

We consider a set of two or more equivalent chiral conformers that are rapidly interconverting on the NMR time scale. The symmetry group of the frozen conformers, G, is called the Schrödinger group. Since we are interested in chiral molecules, G is a proper group in all of our cases. By "equivalent conformers" we mean conformers having identical structures, namely, identical numbers of A−B-type bonds with the same lengths (where A and B represent atoms). In an achiral environment, all of the conformers therefore have identical energies and are termed isodynamic. For reasons discussed in the Introduction, we shall assume that this equivalence also holds for enantiomers in chiral environments, even though in principle they may have slightly different geometries and energies in such solvents. The operations that permute one isodynamic conformer into another are called isodynamic operations. The set of all such permutations form a group that is called the isodynamic group, I. Except for the identity element, this group has no elements in common with G. In simple cases, isodynamic groups are often isomorphic with symmetry point groups. Altmann's method is particularly convenient to apply in such cases. For chiral molecules undergoing racemization, these groups clearly contain elements that are isomorphic with improper symmetry operations, since they represent interconversions between enantiomers.

To discuss the situation in the fast-exchange regime, it is convenient to introduce the Schrödinger supergroup, S. According to Altmann,[15] S is the semidirect product of I and G:

$$S = I \wedge G \tag{1}$$

If the isodynamic operations are feasible, as is clearly the case in the fast-NMR regime, then S reflects the effective symmetry of the average molecule. In particular, it is isomorphic with the symmetry of the spin Hamiltonian of the rapidly interconverting molecule. In all of the examples discussed below, I and G commute, so instead of the semidirect product, we can in fact define S using the direct product:

$$S = I \otimes \mathrm{G} \tag{2}$$

Finally, in a chiral environment such as a CLC solution, the effective symmetry of the average molecule is reduced to S', the proper subgroup of S, since the improper operations are eliminated in a chiral environment. Enantiotopically related sites in S become inequivalent in S' and may exhibit enantiodiscrimination in their NMR spectra.

Experimental Section

Compound **4** was prepared by one-step oxidative trimerization of benzo-1,2-dioxyethylene.[19] To a stirred solution of $MoCl_5$ (2.8 g) in 10 mL of dry CH_2Cl_2, 1.36 g of benzo-1,2-dioxyethylene was added slowly (over 30 min) at room temperature. The dark-green reaction product was poured into 40 mL of a 1/1 water/methanol mixture. The yellow precipitate was treated with 150 mL of *n*-hexane and stirred for 30 min. The desired crystalline product was filtered, washed with water, methanol, and *n*-hexane, and dried. Yield: 720 mg (5%). TLC (silica/CH_2Cl_2): one spot, $M = 402$. For the deuterium NMR measurements, an isotopologue of **4** that was statistically enriched to 10% deuterium in the ethylene groups was prepared by trimerization of the correspondingly deuterated benzo-1,2-dioxyethylene. The latter was prepared by alkylation of benzocatechin with 10% statistically deuterated 1,2-dibromoethylene, which in turn was prepared as described in ref 10.

Two types of lyotropic oriented solvents based on poly(γ-benzylglutamate) were employed: chiral solvents consisting of PBLG dissolved in CH_2Cl_2 and achiral solvents (denoted PBG) consisting of mixtures of equal masses of PBLG and poly(γ-benzyl-D-glutamate) (PBDG) dissolved in CH_2Cl_2. The samples were prepared as described previously.[10,11] A typical solution consisted of 15 wt % PBLG (or PBLG + PBDG) and ~0.3 wt % solute in CH_2Cl_2. More information on sample preparation can be found in ref 1. Detailed compositions of the solutions used in the present work are given in the figure captions of the relevant spectra.

The ^{2}H-{^{1}H} NMR spectra shown here were recorded near room temperature (302 K) at 92.1 MHz using a 14.1 T Bruker Avance II spectrometer equipped with a selective ^{2}H cryoprobe. ^{2}H−^{1}H scalar and dipolar couplings were removed using the WALTZ-16 decoupling sequence. The ^{1}H and ^{13}C spectra were recorded at 9.4 T. Additional experimental details are given in the figure captions.

Results and Discussion

^{1}H and ^{13}C NMR Spectra of 4 in Achiral Isotropic Solutions. The proton NMR spectrum of **4** in CD_2Cl_2 is a simple two-line spectrum due to the aromatic (δ_{ar}) and oxyethylene aliphatic (δ_{al}) hydrogens, while the ^{13}C-{^{1}H} spectrum consists of a single aliphatic resonance and three aromatic peaks. In the absence of proton decoupling, the ^{13}C signals of the aromatic C2−H and aliphatic CH_2 carbons exhibit splittings due to $^1J_{C-H}$ couplings. The data derived from these spectra are summarized in Table 1.

Analysis of Deuterium NMR Spectra of 4 in Liquid-Crystalline Solutions. The structure of **4** is shown in Figure 2a. There are three half-chair dioxyethylene groups bonded at the periphery of the triphenylene plane; at room temperature, these groups undergo fast chair−chair interconversions between the

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Table 1. Chemical Shifts and *J* Couplings for a Solution of **4** in CD_2Cl_2[a]

parameter	^{1}H spectrum		^{13}C spectrum			
	aromatic	aliphatic	Ar-1	Ar-2	Ar-3	aliphatic
δ (ppm)[b]	7.87	4.46	123.1	109.4	142.7	64.0
$^2J_{H-H}$ (Hz)	–	−11.1[c]	–	–	–	–
$^1J_{C-H}$ (Hz)	–	–	–	+155.4[c]	–	+148.5[c]

[a] A $^1J_{C-D}$ value of 27.0 Hz was measured for the solvent. [b] The carbon and proton chemical shifts were measured relative to the natural-abundance ^{13}C and residual ^{1}H signals in the CD_2Cl_2 solvent, respectively, for which the respective values on the δ scale were 5.32 and 53.8 ppm. [c] The signs of the *J* couplings are based on data in ref 8.

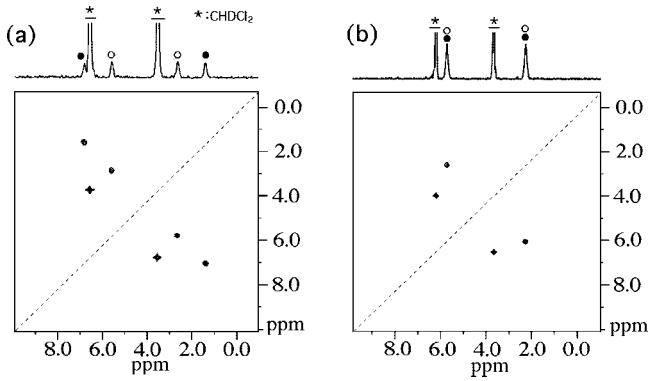

Figure 3. Deuterium *Q*-COSY Fz 2D spectra (at 92.1 MHz with proton decoupling) of solutions of compound **4** (statistically deuterated to 10% in the dioxyethylene side chains) in (a) the chiral solvent PBLG/CH_2Cl_2 and (b) the achiral solvent PBG/CH_2Cl_2 at 302 K. 1D projection spectra are shown at the top of each 2D map. The truncated doublet (∗) is due to natural-abundance deuterium in the CH_2Cl_2 solvent. Experimental details: 1024 (t_2) × 400 (t_1) data points with 8 scans per FID, LB = 0. Sample compositions: (a) PBLG (100 mg), CH_2Cl_2 (560 mg), **4** (1.7 mg); (b) PBLG (51 mg), PBDG (50 mg), CH_2Cl_2 (562 mg), **4** (1.5 mg).

left (L) and right (R) conformations shown in Figure 2b. The fast flipping is clearly demonstrated by the single aliphatic proton signal of **4** observed in isotropic liquids. The ^{2}H-{^{1}H} *Q*-COSY Fz 2D spectra of **4** dissolved in chiral and achiral polypeptide liquid-crystalline solutions are shown in Figure 3a,b, respectively. The compound was 10% statistically deuterated in the ethylene hydrogens, and the spectra were recorded under broadband proton decoupling. Both spectra exhibit a strong (truncated) doublet due to natural-abundance deuterons in the CH_2Cl_2 cosolvent. In addition, one or two doublets due to the dioxyethylene deuterons of the solute molecules are observed in the achiral or chiral solvent, respectively. The measured quadrupolar splittings in the two mesophases are summarized in Table 2.

The single doublet observed for the ethylene deuterons in the achiral solvent is consistent with fast flipping of the dioxyethylene groups that renders all of the ethylene hydrogens equivalent. On the other hand, the doubling of the spectrum in the chiral solvent reflects the enantiotopic relation within the various oxyethylene groups in the average molecule. In order to determine the symmetry of the average molecule and trace the origin of this chiral splitting, we need to consider the nature of the averaging process and the symmetries of the frozen conformers. Actually, as shown in Figure 4, there are two types of frozen conformers associated with compound **4**. The first consists of two enantiomers in which the twists of the three dioxyethylene groups are cyclic, i.e., either anticlockwise (RRR) or clockwise (LLL), where the R and L twists are defined in

Table 2. Absolute Values of Quadrupolar Splittings ($\Delta\nu_Q$) Observed in Solutions of **4** in Poly(γ-benzylglutamate)-Based Liquid-Crystalline Solvents

solvent[a]	$\lvert\Delta\nu_Q\rvert$ (Hz)	
	$CHDCl_2$[b]	**4**
PBG/CH_2Cl_2	232 ± 2	318 ± 8
PBLG/CH_2Cl_2	278 ± 2	271 ± 8 / 499 ± 8[c]
ratio[d]	1.20	1.21

[a] The compositions of the solutions are given in the caption of Figure 3. [b] Splitting observed for the natural-abundance deuterons in the cosolvent. [c] Splittings observed for the inner/outer doublets of the ethylene deuterons in **4**. [d] Ratio of the average splitting in the PBLG solvent to the splitting in the PBG solvent.

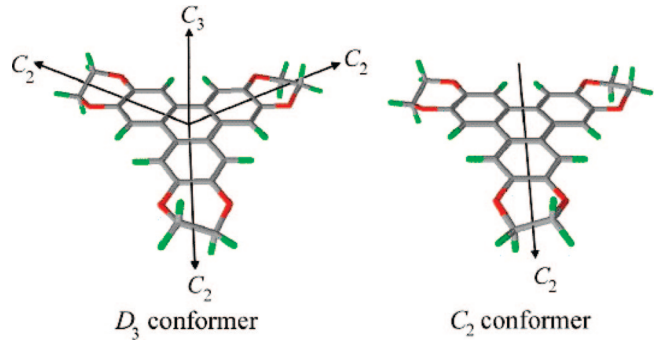

Figure 4. Structures of the conformers of compound **4**: (a) the LLL conformer with D_3 symmetry; (b) the LRR conformer with C_2 symmetry. Carbon, hydrogen, and oxygen atoms are shown in gray, lime, and red respectively. The elements of the associated symmetry point groups are displayed.

Figure 2b. The point group symmetry of these conformers (their Schrödinger group) is $G = D_3$, with the C_3 axis perpendicular to the triphenylene plane and the three C_2 axes lying within this plane (Figure 4a). If the chair−chair switching proceeds in concert, the isodynamic group, *I*, is isomorphous with $C_s = \{E, \sigma_h\}$, where σ_h corresponds to reflection with respect to the triphenylene plane. Consequently, the average symmetry of the molecule (the Schrödinger supergroup) becomes $S = C_s \otimes D_3 \approx D_{3h}$. A similar result is obtained for the second conformer, which consists of a set of six isodynamic conformations. In this set, the twists of the dioxyethylene groups result in three homomers of the form RLL, LLR, and LRL and their corresponding antipodes, in which R and L are interchanged. The symmetry group of these frozen conformers is $C_2 = \{E, C_2\}$, where the C_2 axis lies in the molecular plane (Figure 4b). The isodynamic group of this set of conformers consists of two types of operations: interchanges between homomers, which correspond to C_3 operations, and interchanges between enantiomers, which correspond to σ_h (reflection in the triphenylene plane). Hence, the isodynamic group is $I = C_3 \otimes C_s \approx C_{3h}$, and the symmetry in the fast-exchange limit becomes $S = C_{3h} \otimes C_2 \approx D_{3h}$, which is identical to that for the cyclically twisted set of conformers. Clearly, exchange between the two sets of conformers leads to the same average symmetry.

The symmetry operations in the D_{3h} group consist of all of the proper rotations of the D_3 subgroup plus three vertical and one horizontal reflection as well as a pair of improper rotations. Thus, in a chiral environment where the latter operations are eliminated, the effective symmetry of the average molecule is reduced to $S' = D_3$. Referring to Figure 2b, we note that atoms in the pairs AB′ and BA′ are related by C_2 rotations and are

thus completely equivalent, while those in the AA′ and BB′ pairs and the AB and A′B′ pairs in the average molecule are related by vertical and horizontal reflections, respectively, and therefore are enantiotopically related. These relations are reflected in the NMR results shown in Figure 3. In the achiral solvent (Figure 3b), a single doublet due to all of ethylene deuterons is observed, while in the CLC solvent (Figure 3a), there are two doublets, one for the AB′ pair and one for the BA′ pair.

Origin of the Enantiodiscrimination in Compound 4. In this section we analyze the spectral enantiodiscrimination described in the previous paragraph. We first consider only the conformers with D_3 symmetry. Qualitatively similar results are expected if the other conformers are included in the analysis. We label the two enantiomers R and L, as shown in Figure 2b. In these conformers, the three dioxyethylene groups are equivalent, and within each group in the fast exchange limit, sites A and B′ as well as sites B and A′ are related by C_2 symmetry; hence, $\langle\Delta\nu_Q{}^{A}\rangle = \langle\Delta\nu_Q{}^{B'}\rangle$ and $\langle\Delta\nu_Q{}^{A'}\rangle = \langle\Delta\nu_Q{}^{B}\rangle$. It is therefore sufficient to consider one deuterium of type A and one of type B. Their average quadrupolar splittings are given by eqs 3 and 4, respectively:

$$\langle\Delta\nu_Q{}^{A}\rangle = P^R S_{zz}{}^R(\Delta\nu_Q{}^A)^R + P^L S_{zz}{}^L(\Delta\nu_Q{}^A)^L \quad (3)$$

$$\langle\Delta\nu_Q{}^{B}\rangle = P^R S_{zz}{}^R(\Delta\nu_Q{}^B)^R + P^L S_{zz}{}^L(\Delta\nu_Q{}^B)^L \quad (4)$$

where P^J and $S_{zz}{}^J$ are the relative population and axial order parameter of enantiomer J, respectively, and $(\Delta\nu_Q{}^N)^J$ is the quadrupole splitting of a deuteron at site N in enantiomer J:

$$(\Delta\nu_Q{}^N)^J = \frac{3}{4}Q_{C-D}(3\cos^2\beta^{NJ} - 1) \quad (5)$$

In eq 5, Q_{C-D} is the deuterium quadrupolar interaction constant of the C−D bond (∼170 kHz for aliphatic deuterons) and β^{NJ} is the angle between the molecular C_3 axis and the C−D bond of site N in enantiomer J. From the structure of the oxyethylene group, it follows that $\beta^{AR} = \pi - \beta^{BL}$ and $\beta^{BR} = \pi - \beta^{AL}$, so $(\Delta\nu_Q{}^A)^R = (\Delta\nu_Q{}^B)^L$ and $(\Delta\nu_Q{}^B)^R = (\Delta\nu_Q{}^A)^L$.

In an achiral solvent, $P^R = P^L = {}^1/_2$ and $S_{zz}{}^R = S_{zz}{}^L \equiv S_{zz}$, resulting in identical splittings for the two deuterons:

$$\begin{aligned}\langle\Delta\nu_Q{}^{A}\rangle &= \langle\Delta\nu_Q{}^{B}\rangle \equiv \langle\Delta\nu_Q\rangle \\ &= \frac{S_{zz}}{2}[(\Delta\nu_Q{}^A)^R + (\Delta\nu_Q{}^B)^R] \\ &= \frac{S_{zz}}{2}[(\Delta\nu_Q{}^A)^L + (\Delta\nu_Q{}^B)^L] \quad (6)\end{aligned}$$

The geometry of the dioxyethylenebenzene moiety was calculated previously using DFT,[10] and values of 8.6 and 105.0° for β^{AL} and β^{BL}, respectively, were obtained. Thus, from eq 5, we obtain $(\Delta\nu_Q{}^A)^L = 246.4$ kHz and $(\Delta\nu_Q{}^B)^L = -101.9$ kHz; use of these values and $|\langle\Delta\nu_Q\rangle| = 318$ Hz (from Table 2) in eq 6 yields an estimate of 4.4×10^{-3} for the order parameter $|S_{zz}|$. It is shown below that the sign of S_{zz} is in fact negative, indicating that the solute molecules are oriented with their C_3 axes perpendicular to the director. This is common for disklike molecules in nematic solvents.

The situation is different in CLC solutions. In this case, the values of the order parameters $S_{zz}{}^L$ and $S_{zz}{}^R$ will in general be different, resulting in different average splittings of the A and B deuterons. However, we expect the average of the splittings observed in the chiral solvent to be similar to the splitting in the achiral one. Assuming that the splittings of the enantiomers in the chiral solvent have identical signs gives an average value of 384 Hz, which is a factor of 1.21 larger than the value of 318 Hz measured in the achiral solvent (see Table 2). The difference is most likely due to the different composition of the two solutions. This is supported by the observation that the same ratio is observed for the splittings of the solvent deuterons in the two solutions: 278/232 = 1.20 (Table 2). The similarity of the two ratios also provides support for the assumption of identical signs (negative) for the splittings observed for the two enantiotopic deuterons. The enantiodiscrimination, $\Delta(\Delta\nu_Q) \equiv \langle\Delta\nu_Q{}^A\rangle - \langle\Delta\nu_Q{}^B\rangle$, can now be calculated from the structure of the oxyethylene chains in the enantiomers. Neglecting any effects of the chiral environment on their geometries and using the equalities indicated after eq 5, we obtain:

$$\begin{aligned}\Delta(\Delta\nu_Q) &\equiv \langle\Delta\nu_Q{}^A\rangle - \langle\Delta\nu_Q{}^B\rangle \\ &= (P^L S_{zz}{}^L - P^R S_{zz}{}^R)[(\Delta\nu_Q{}^A)^L - (\Delta\nu_Q{}^B)^L] \quad (7)\end{aligned}$$

The discussion of the conformers with C_2 symmetry is more involved; since these conformers are not axial, several order parameters are required for calculating the enantiodiscrimination. Although the relevant equations can in principle be written down, they cannot be solved because the number of required parameters exceeds the number of NMR observables.[11] Also, the relative abundance of the C_2 and D_3 conformers, which is required for the calculation of the overall enantiodiscrimination, is not known. On the basis of the overall shape of the molecule (Figure 2a), however, it is safe to assume that the dominant ordering parameter for all of the conformers is S_{zz}, where the z axis is perpendicular to the triphenylene plane. In order to make the calculations tractable and obtain an estimate for the overall enantiodiscrimination, we shall assume that the flipping processes of the R and L dioxyethylene groups (Figure 2b) are uncorrelated[20] and that associated with each conformer is a single order parameter ($S_{zz}{}^R$ or $S_{zz}{}^L$, respectively) that reflects the net effect of all of the side groups. We shall also assume that the probabilities for R and L twists are equal ($P^R = P^L = {}^1/_2$). A significant population preference is energetically highly unlikely. In fact, no such preferences have been experimentally observed to date in case of mixtures of interconverting enantiomers dissolved in polypeptide CLC solvents.[21,22] When this assumption is made, an equation similar to eq 7 is obtained, in which the $S_{zz}{}^J$ parameters reflect some kind of average ordering for enantiomers which are predominantly R or L twisted:

$$\begin{aligned}\Delta(\Delta\nu_Q) &= \frac{1}{2}(S_{zz}{}^L - S_{zz}{}^R)[(\Delta\nu_Q{}^A)^L - (\Delta\nu_Q{}^B)^L] \\ &= (174.2\ \text{kHz})\Delta S_{zz} \quad (8)\end{aligned}$$

where $\Delta S_{zz} = S_{zz}{}^L - S_{zz}{}^R$ and we have used the quadrupolar splitting values given after eq 6. Likewise, the average splitting of the two doublets is:

$$\begin{aligned}\langle\Delta\nu_Q\rangle &= \frac{1}{2}[\langle\Delta\nu_Q{}^A\rangle + \langle\Delta\nu_Q{}^B\rangle] \\ &= \frac{1}{4}(S_{zz}{}^L + S_{zz}{}^R)[(\Delta\nu_Q{}^A)^L + (\Delta\nu_Q{}^B)^L] \\ &= (72.2\ \text{kHz})\langle S_{zz}\rangle \quad (9)\end{aligned}$$

(20) This assumption is equivalent to neglecting intramolecular interactions between side groups, which is amply justified in view of the large (>10 Å) distance between them.

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where $\langle S_{zz}\rangle = (S_{zz}^{L} + S_{zz}^{R})/2$. Thus, from Table 2, an average value of $|\langle S_{zz}\rangle| = 5.3 \times 10^{-3}$ is estimated in the CLC solution. Moreover, the ratio of the enantiodiscrimination to the average splitting of the enantiotopic deuterons is given by:

$$\frac{\Delta(\Delta\nu_Q)}{\langle\Delta\nu_Q\rangle} = 2.4\frac{\Delta S_{zz}}{\langle S_{zz}\rangle} \tag{10}$$

From Table 2, we obtain $|\Delta(\Delta\nu_Q)/\langle\Delta\nu_Q\rangle| = 0.6$, so from eq 10, $|\Delta S_{zz}/\langle S_{zz}\rangle| = 0.25$. Only the magnitudes of these ratios can be given, since we have no way to correlate the two deuterium doublets observed in the CLC solution with the AB′ and BA′ pairs in **4**. The spectral discrimination of the enantiotopic sites in this compound is especially large. This is mainly due to a large intrinsic discrimination in the ordering of the two enantiomers induced by interaction with the chiral solvent, which is augmented by the relatively large geometrical coefficient (2.4) in eq 10. This coefficient reflects the difference in the splittings of a particular deuteron in the two enantiomers or of the two exchanging deuterons in the same enantiomer, i.e., $[(\Delta\nu_Q^{A})^{L} - (\Delta\nu_Q^{B})^{L}] = [(\Delta\nu_Q^{B})^{R} - (\Delta\nu_Q^{A})^{R}]$. The value of the coefficient is particularly large in the present case because one of the exchanging C−D bonds is nearly parallel to the molecular C_3 axis whereas the other is nearly perpendicular to it. From the results following eq 10, a value of 1.29 or 0.78 (depending on the sign of $\Delta S_{zz}/\langle S_{zz}\rangle$) is calculated for the ratio S_{zz}^{L}/S_{zz}^{R}. This corresponds to a very effective discrimination, probably reflecting the screw shape of the half-chair dioxyethylene groups at the periphery of the triphenylene plane.

Ordering of 4 in the PBLG-Based Liquid Crystals. In the above discussion, it was indicated that S_{zz} of **4** in the PBG solutions is negative, i.e., that the solute molecules have a preference for being aligned with their z axes perpendicular to the director. Here we briefly provide experimental evidence for this statement obtained from analysis of additional ^{1}H and ^{13}C spectra (with and without proton decoupling) of isotopically normal **4** in PBLG/CD_2Cl_2 solution at 302 K. The composition of this sample was similar to that given in the caption of Figure 3a.

The ^{1}H spectrum of **4** exhibits two doublets with broad components associated with the aromatic (with a splitting of ∼130 Hz) and aliphatic (∼105 Hz) hydrogens, respectively. The splitting of the aromatic signal reflects the through-space dipolar coupling between nearby hydrogens on adjacent benzene rings of the triphenylene core. Assuming threefold symmetry for the latter yields a calculated interhydrogen distance of ∼1.72 Å. We recall that the dipolar splitting for a pair of equivalent hydrogens is $T_{H-H} = 3D_{H-H}$,[23] where for an axially symmetric molecule, D_{H-H} is given by the general formula:

$$D_{X-Y} = -S_{zz}[K_{X-Y}/(r_{X-Y})^3][(3\cos^2\beta_{X-Y} - 1)/2] \tag{11}$$

where β_{X-Y} is the angle between the r_{X-Y} direction and the molecular symmetry axis and K_{X-Y} is a constant proportional to the magnetic moments of the X and Y nuclei ($K_{H-H} = 1.20 \times 10^5$ Hz/Å^3 and $K_{C-H} = 3.02 \times 10^4$ Hz/Å^3). Inserting the measured splitting ($|T_{H-H}| = 3|D_{H-H}| = 130$ Hz) in eq 11 yields $|S_{zz}| \approx 3.7 \times 10^{-3}$. This result is similar to that derived above for the quadrupole splitting of the methylene deuterons (5.3×10^{-3}), but the sign of S_{zz} remains undetermined.

The doublet due to the aliphatic protons predominantly reflects the dipolar interaction between hydrogens belonging to the same methylene group (A and B or A′ and B′). The components of this doublet exhibit some unresolved structure that is partly attributable to their (slight) enantiotopic nonequivalence and perhaps also due to dipolar interactions with hydrogens of nearby methylene groups. The measured splitting, $T_{H-H'}$, can nevertheless provide a rough estimate for the magnitude of the intramethylene dipolar interaction ($|D_{H-H'}| \approx |T_{H-H'}|/3 = 35$ Hz) and will be used below in the analysis of the ^{13}C methylene spectrum.

The proton-coupled ^{13}C spectrum of **4** in the PBLG/CH_2Cl_2 solution (not shown) exhibits a single peak for the aromatic C−H carbon and a symmetric five-line pattern for the oxyethylene carbons. The ^{13}C spectrum of a C−H pair is expected to yield a doublet with a total splitting, T_{C-H}, equal to $^{1}J_{C-H} + 2D_{C-H}$. The lack of such a splitting for the aromatic carbon indicates that the scalar and dipolar couplings fortuitously cancel each other. Hence, $D_{C-H} \approx -^{1}J_{C-H}/2 = -78$ Hz, and use of eq 11 with $\beta_{C-H} = \pi/2$ and $r_{C-H} = 1.09$ Å yields $S_{zz} = -6.7 \times 10^{-3}$. The result is somewhat larger in magnitude than the previous values, but now the sign of the order parameter is clearly determined.

Finally, we confirm the above conclusion by analyzing the ^{13}C spectrum of the oxyethylene group. Its symmetric five-line pattern consists of a strong central peak, a weak doublet with components at ±42 Hz relative to the central peak, and an outer doublet with components at ±208 Hz that are about half as intense as the central line. Schematic examples of such as spectral pattern are reported in ref 8. The spectrum corresponds to AA′X spin, where A and A′ represent the nonequivalent enantiotopic hydrogens and X the ^{13}C nucleus. If differences in the chemical shifts of A and A′ and any interactions between hydrogens on neighboring methylene groups are neglected, the spin Hamiltonian for this system becomes:

$$\begin{aligned}\hat{H} = &-\nu_0^{C}\hat{S}_z - \nu_0^{H}(\hat{I}_z^{H} + \hat{I}_z^{H'}) + ({}^{1}J_{C-H} + 2D_{C-H})\hat{S}_z\hat{I}_z^{H} + \\ &({}^{1}J_{C-H'} + 2D_{C-H'})\hat{S}_z\hat{I}_z^{H'} + ({}^{2}J_{H-H'} + 2D_{H-H'})\hat{I}_z^{H}\hat{I}_z^{H'} + \\ &\tfrac{1}{2}({}^{2}J_{H-H'} - D_{H-H'})(\hat{I}_+^{H}\hat{I}_-^{H'} + \hat{I}_-^{H}\hat{I}_+^{H'})\end{aligned} \tag{12}$$

where the first two terms are the Zeeman energies of the ^{13}C and ^{1}H nuclei, respectively, the third and fourth terms correspond to the ^{13}C−^{1}H scalar and dipolar couplings, respectively (with the latter assumed to be different for the two hydrogens), and the last two terms correspond to the scalar and dipolar interactions, respectively, between the methylene hydrogens. A straightforward exact solution of eq 12 indeed yields a symmetric five-line spectrum with peak positions and relative intensities given by the formulas in Table 3.

The formulas in Table 3 show that the combined relative intensity of the central line and the two components of the inner doublet is exactly equal to 2, as is the combined intensity of the two outer-doublet components. Hence, the latter could readily be identified by comparison with the peak intensities in the spectrum. The signs and magnitudes of D_{C-H} and $D_{C-H'}$ could then be determined from the measured splitting of this doublet and the corresponding deuterium quadrupole interactions given in Table 2. Recalling that $|\Delta\nu_Q|/|D_{C-H}| \approx 12$,[10] we expect the dipolar interactions to have magnitudes of $|D_{C-H}| \approx 22.6$ Hz and $|D_{C-H'}| \approx 41.6$ Hz and identical signs (since the $\Delta\nu_Q$'s have identical signs). Since $^{1}J_{C-H} = +148.5$ Hz (Table 1), it follows from the formula for the outer-doublet positions in Table 3 that only a positive sign for the D_{C-H} values is consistent with the measured positions of the outer-doublet components

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Table 3. Peak Positions and Relative Intensities of the Five-Line Pattern in the ^{13}C Spectrum of a Methylene Group Calculated Using the Hamiltonian of eq 12

spectral feature	position	relative intensity[a]
central peak	ν_o	$2(^2J_{H-H'} - D_{H-H'})^2[(D_{C-H} - D_{C-H'})^2 + (^2J_{H-H'} - D_{H-H'})^2]^{-1}$
inner doublet (weak)	$\nu_o \pm [(D_{C-H} - D_{C-H'})^2 + (^2J_{H-H'} - D_{H-H'})^2]^{1/2}$	$(D_{C-H} - D_{C-H'})^2[(D_{C-H} - D_{C-H'})^2 + (^2J_{H-H'} - D_{H-H'})^2]^{-1}$
outer doublet (strong)	$\nu_o \pm [^1J_{C-H} + D_{C-H} + D_{C-H'}]$	1

[a] For the inner and outer doublets, the entries give the relative intensity of each doublet component.

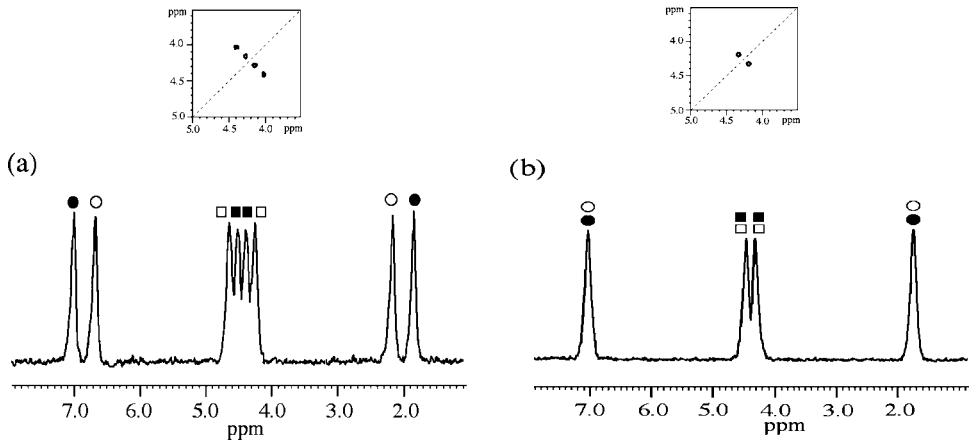

Figure 5. Columns extracted from the 92.1 MHz tilted deuterium *Q*-COSY Fz 2D spectra (with proton decoupling) of **2** (statistically deuterated to 10% in the dioxyethylene side chains) at 302 K in (a) the chiral solvent PBLG/CH_2Cl_2 and (b) the achiral solvent PBG/CH_2Cl_2. The central parts of the respective *Q*-COSY maps are shown as insets. Experimental details: 1500 (t_2) × 512 (t_1) data points with 16 scans per FID, LB = 1 Hz. Sample compositions: (a) PBLG (101 mg), CH_2Cl_2 (581 mg), **2** (2 mg); (b) PBLG (51 mg), PBDG (50 mg), CH_2Cl_2 (584 mg), **2** (1.5 mg).

(±208 Hz). An exact calculation assuming $D_{C-H}/D_{C-H'} = \Delta\nu_Q(H)/\Delta\nu_Q(H')$ yields $D_{C-H} = +20.9$ Hz and $D_{C-H'} = +38.6$ Hz. All of the parameters in Eq. 12, are now determined except for the sign of $D_{H-H'}$. To determine this sign, we can calculate $D_{H-H'}$ from the outer-doublet position formula in Table 3 using the just-derived D_{C-H} values, $^2J_{H-H} = -10$ Hz (see Table 1), and the observed positions of the inner-doublet components (±42 Hz). The calculation yields two values for $D_{H-H'}$, +28 and −48 Hz. These values must be compared with the approximate result obtained above from the proton spectrum ($|D_{H-H'}| \approx 35$ Hz). Neither of the ^{13}C results fits exactly with the latter one, but the positive one is somewhat closer, so we tentatively assign the value of +28 Hz to $D_{H-H'}$ and explore the validity of the chosen sign in the next paragraph.

We first note that the $D_{H-H'}$ interaction is not modulated by the chair−chair flipping of the oxyethylene groups. This follows from the symmetry of the two conformations in Figure 2b; the polar angle $\beta_{H-H'}$ between the vector $r_{H-H'}$ and the symmetry axis of the triphenylene core in the R-twist conformation (upper diagram) becomes $\pi - \beta_{H-H'}$ in the L-twist conformation (lower diagram). Hence, the $D_{H-H'}$ value is identical in the two conformations and of course identical to that in the dynamically averaged molecule. The value of $\beta_{H-H'}$ can be estimated from the geometrical parameters of the frozen oxyethylene group (given in Table 3 of ref 10) to be 40°. Substituting this value into eq 11 along with $D_{H-H'} = +28$ Hz yields $S_{zz} = -3.4 \times 10^{-3}$, thus confirming the positive sign for $D_{H-H'}$. We note that whenever the sign of S_{zz} could be determined, it consistently came out negative, but the estimates of the magnitude of S_{zz} (5.3, 3.7, 6.7, and 3.4 in units of 10^{-3}) varied by almost a factor of 2. The large dispersion in these values is partly due to uncertainty in the measurements (broad doublets in the ^1H spectra) and partly due to lack of exact knowledge of the molecular geometry.

Comparison with Related Systems. It is interesting to compare the above results with those for the cone-shaped molecule **2** (Figure 1b).[10] Here too, flexible dioxyethylene groups are linked to the periphery of a rigid axial moiety, but in the frozen state of **2**, unlike the case in **4**, all four hydrogens in an oxyethylene group are nonequivalent, with the A (B) hydrogens pointing outward from (inward to) the CTV core (see Figure 2b). This compound, like **4**, exhibits two types of frozen conformers having different symmetries. One of these conformers consists of the two isodynamic enantiomers RRR and LLL having symmetry $G = C_3$. A correlated chair−chair interconversion corresponds to a vertical reflection; thus, the isodynamic group is $I = \{E, \sigma_v\} = C_s$, and the average symmetry in the fast-exchange regime becomes $S = C_s \otimes C_3 = C_{3v}$. A similar result is obtained for the second type of conformer, which consists of the three isodynamic homomers RLL, LRL, and LLR and their corresponding antipodes, with $G = C_1$. In this case, there are two types of chair−chair flips: those interchanging between enantiomers ($C_s = \{E, \sigma_v\}$) and those interchanging between homomers ($C_3 = \{E, C_3\}$). Hence, the isodynamic group is $I = C_3 \otimes C_s = C_{3v}$, and the Schrödinger supergroup is again $S = C_1 \otimes C_{3v} = C_{3v}$. Exchange between the two types of conformers clearly retains the C_{3v} symmetry. In achiral media, hydrogens A and A′ (Figure 2b) are equivalent but enantiotopically related, and so are B and B′. However, A and B (A′ and B′) remain nonequivalent. In CLC media, the effective symmetry of the average molecule reduces to $S' = C_3$, and enantiodiscrimination of the A and A′ as well as the B and B′ sites is expected. These relations were well-demonstrated in the deuterium spectrum of compound **2** (10% statistically deuterated in the dioxyethylene side chains) dissolved in PBLG/$CHCl_3$.[10] We have now obtained somewhat better resolved spectra of this compound using CH_2Cl_2 as cosolvent. The spectra are shown in Figure 5, and the measured splittings are summarized in Table 4.

Table 4. Absolute Values of Quadrupolar Splittings ($\Delta\nu_Q$) Observed in Oriented Solutions of **2**

	$\lvert\Delta\nu_Q\rvert$ (Hz)		
solvent[a]	$CHDCl_2$[b]	**2**A	**2**B
PBG/CH_2Cl_2	236 ± 3	16 ± 7	500 ± 8
PBLG/CH_2Cl_2	213 ± 3	34 ± 6 / 12 ± 6[c]	472 ± 7 / 416 ± 7[c]
ratio[d]	1.11	1.45[e]	1.13

[a] The compositions of the solutions are given in the caption of Figure 5. [b] Splitting observed for the natural-abundance deuterons in the cosolvent. [c] Splittings observed for the inner/outer doublets. [d] Ratio of the splitting in the PBG solvent to the average splitting in the PBLG solvent. [e] This value is obtained if opposite signs for the two splittings in the chiral solvent are assumed.

In the achiral solvent, two doublets are observed for the oxyethylene deuterons, which split into pairs of doublets in the chiral solvent. A geometrical analysis shows that the outer one corresponds to the BB′ pair and the inner one to the AA′ pair.[11] An analysis similar to the one described above for **4** applied to the outer pairs of doublets (**2**B in Table 4) yields the following results for the order parameters in the chiral solvent: $|\langle S_{zz}\rangle| \approx 5.7 \times 10^{-3}$, $|\Delta S_{zz}/\langle S_{zz}\rangle| \approx 0.13$, and $S_{zz}^{L}/S_{zz}^{R} \approx 1.13$ or 0.89. Apparently the dominant factor in the alignment of compound **2** is the cone-shaped structure of the rigid part of the molecule. Consequently, the value of the order parameter is somewhat larger than for compound **4**, but the enantioseparation is smaller. It is difficult to make a similar analysis on the inner doublets due to the A deuterons, for which the splittings are very small as a result of almost complete cancellation of large geometrical factors. The remaining splittings are then very sensitive to the approximations made in deriving the equations relating the splittings and the axial order parameter. In particular, neglect of small distortions of the chiral solutes and of even minor nonaxial order parameters for the nonaxial conformers have a relatively strong effect on the final results. The data in Table 4 even suggest that the two doublets arising from the A deuterons in the chiral solvent may have opposite signs. This follows from the comparison of the splittings in the chiral and achiral oriented solvents. In order for the average splitting ratio of the A deuterons to be similar to that of the natural-abundance deuterons in the solvent (as is that for the B deuterons), such an assumption must be made.

The saddle form of nonamethoxy-CTV, compound **3**, is another example of a flexible molecule that averages to an axial species with enantiotopically related sites. As in the above examples, enantiodiscrimination was observed in the deuterium NMR spectra of these sites. However, the symmetry of the six interconverting chiral conformers is far from axial, allowing only qualitative analysis of the results.[11] Another case worth mentioning in this connection is the ring inversion of *cis*-decalin.[24,25] However, the symmetry of the average molecule is not axial in that case, so the above considerations do not apply.

Conclusions

Rigid axial molecules with a C_n ($n \geq 3$) symmetry axis possessing enantiotopically related sites do usually not exhibit NMR spectral enantiotopic discrimination when dissolved in CLC solvents. Exhibition of such discrimination would require significant distortions[26–28] of the geometrical and/or electronic structure that renders the enantiotopic sites nonequivalent. The solute−solvent interactions in PBG-based lyotropic solvents are apparently not strong enough to cause such distortions. In contrast, chiral flexible molecules with average axial symmetries do exhibit such spectral enantiodiscrimination. The discrimination could stem from selective preferences in the population and/or ordering of one of the interconverting enantiomers. We have argued that the dominant discrimination originates from the latter effect. Discrimination in the ordering of conformational enantiomers is associated with only weak solute−solvent interactions and is commonly observed for racemic mixtures dissolved in CLC solvents. Furthermore, deviation from the equilibrium population of racemic mixtures is neither observed nor energetically expected in the case of interconverting enantiomers. Here we have demonstrated such an effect on the deuterium NMR spectra of partially deuterated tridioxyethylenetriphenylene (**4**). In its frozen state, this molecule is chiral and axially symmetric (or nearly so). Fast chair−chair flipping of the dioxyethylene side chains renders the molecule fully axial with pairs of enantiotopic sites. These sites exhibit large enantiodiscrimination in the deuterium NMR spectrum of **4** in a CLC solvent, which could be explained in terms of large selective ordering of the different conformational enantiomers.

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