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Quantitative Description of the Facial Discrimination of Molecules Containing a Prochiral Group by NMR in a Chiral Liquid Crystal

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Abstract: The quantitative description of the facial discrimination in molecules containing a prochiral group oriented in a polypeptide liquid crystalline system is reported. From the analysis of proton, carbon-13, and deuterium NMR spectra of ethanol dissolved in an organic solution of poly-γ-(benzyl-L-glutamate) (PBLG), the full molecular order matrix and the principal axis system were determined. It is shown that five nonzero independent order parameters are necessary to describe correctly the molecular ordering of ethanol in this medium, which clearly demonstrates that in this chiral liquid crystal, the symmetry of the ordering in a prochiral molecule is broken. Due to the nonequivalence in terms of the dipolar couplings of the two enantiotopic protons of ethanol, it is possible to determine the sign and the magnitude of geminal scalar couplings between them. This new approach to obtain the geminal ${}^2J_{\mathrm{HH}}$ constants is tested on a series of linear alcohols and compared to values derived from ${}^2J_{\mathrm{HD}}$ of the same molecules by the isotopic substitution method.

1. Introduction

It is now well established that the observation of enantiomers through their proton, carbon, or deuterium NMR spectra in organic solutions of poly-γ-(benzyl-L-glutamate) (PBLG) is a powerful analytical tool for the measurements of the enantiomeric excess.[1−5] This method was successfully applied to a wide range of chiral molecules, including some that are chiral due to isotopic substitution.[2]

In previous analyses and discussions of the reasons why two enantiomers are discriminated in PBLG, we pointed out that the nature of the mechanism of chiral discrimination is not quite the same for the cases of ordinary enantiomers and enantiomers which are chiral due to isotopic substitution.[2,6,7] We have shown that the former differ both in the magnitude of the elements of the orientational order matrix and in the orientation of their principal axis systems (PAS) while for the latter this is not true.[6,7] This result implies that the average orientation of two ordinary enantiomers differs in the presence of PBLG and indicates that molecular shape plays an important role in the solute−PBLG interactions which lie in the basis of the mechanism of chiral discrimination.[6,7] For isotopic enantiomers, the situation is rather different. Indeed, as we have shown, the elements of the molecular ordering matrixes appear to be essentially identical for the two enantiomers and the origin of the chiral discrimination is related to the fact that two enantiotopic nuclei (or groups) become diastereotopic in the presence of PBLG. Thus, for example, the two enantiomers are discriminated by the difference in the local order parameters of the CD bonds, S_{CD}, for each enantiomer.[2]

The general mechanism for chiral discrimination arising in an organic solution of PBLG is complex. Still, it is reasonable to draw an analogy between the PBLG liquid crystal phase and any enantioselective natural biopolymer possessing a helical structure or an enzymatic system.[8] With this assumption, we might expect that PBLG could distinguish between two magnetically equivalent nuclei (or groups of nuclei) in molecules which are prochiral, thus leading to the discrimination between the two faces of the molecule. A priori we may anticipate that the discrimination mechanisms for this class of molecules should be very similar to those which are involved in the case of molecules which are chiral due to isotopic substitution.[2]

To support this thesis, it is pertinent to explore the optically inactive molecules containing magnetically equivalent protons (or deuterons) such as in a prochiral methylene group. Indeed if these enantiotopic nuclei become diastereotopic in the PBLG liquid crystalline phase, we would expect to distinguish them through their deuterium, proton or, indirectly, carbon-13 NMR spectra. In fact, this effect was discovered long ago by Samulski et al. for the case of the prochiral deuterons of the methylene group in deuterated benzyl alcohol dissolved in PBLG and later confirmed by us for several classes of molecules such as alcohols, acid, etc.[2,9] However, no quantitative description in terms of order parameters has been reported. Indeed, deuterium spectra may be considered rather "poor" in information since quadrupolar splittings essentially depend on a single element

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of the ordering matrix because the electric field gradient (EFG) is parallel to the CD bond.[10] Consequently, limited anisotropic information can be derived to calculate the molecular order parameters, $S_{\alpha\beta}$.

In the first part of this paper, we report the deuterium, proton, and carbon-13 spectra of samples of ethanol and deuterated ethanol dissolved in the liquid crystalline phase PBLG/$CDCl_3$ and the determination of the molecular ordering tensor. The elements of the order matrix were derived from the measurements of the $^1H-^1H$ and $^{13}C-^1H$ dipolar couplings, assuming a model geometry for the ethanol.[6,7] This molecule, which possesses C_s symmetry, was chosen because it contains a prochiral methylene group and because the set of interacting nuclei is large enough to allow us to calculate all the elements of the orientational order matrix. An extensive investigation of ethanol and partially deuterated ethanol in a nematic liquid crystal has been reported by Emsley et al.[11] We shall point out that three independent order parameters, which are usually sufficient to define the ordering of a molecule of C_s symmetry, are not sufficient to describe correctly the molecular ordering of ethanol in PBLG and thereby manifest the nonequivalence of the prochiral protons.

Finally, we shall present a novel application derived from the nonequivalence of prochiral protons in PBLG: the ability to determine directly the sign and the magnitude of the scalar coupling between the two geminal protons.

2. Experimental Section

Sample Preparation. The sample containing ethanol was made from 100 mg of PBLG (DP = 393, MW ≈ 75000), 15 mg of ethanol, 15 mg of perdeuterated ethanol, and 350 mg of $CDCl_3$. The materials were weighed directly into a 5 mm o.d. NMR tube. Samples with other alcohols were prepared in a similar way. All samples were sealed to avoid the evaporation of deuteriochloroform and centrifuged back and forth until an optically homogeneous birefringent phase was obtained.

NMR Measurements. Proton, deuterium and carbon-13 spectra NMR experiments were performed on a Bruker high-resolution spectrometer equipped with a 5 mm diameter $^1H/^{13}C$ dual probe and operating at frequencies of 400.13 and 100.62 MHz, respectively. The recording of the deuterium spectrum (61.51 MHz) was performed with use of the deuterium channel (lock) of the probe. For the proton and carbon-13 spectra, the deuteriochloroform signal provided the deuterium lock signal. Proton, deuterium, and carbon-13 spectra were recorded with 90° pulses and collecting 32, 64, and 15000 transients with 8K, 4K, and 16K of data points, respectively. The deuterium spectrum was recorded applying broad-band proton decoupling by using the WALTZ composite pulse sequence. For the carbon-13 spectrum, proton irradiation was applied during the relaxation delay period (3 s) to benefit from the nuclear Overhauser effect. The temperature of the samples was maintained at 300 K by the Bruker BVT 1000 and the tubes were not spun.

3. Results and Discussions

The numbering of the nuclei in ethanol used in this study is shown in Figure 1. Note that the *pro-R* and *pro-S* protons of the molecule were denoted as H3 and H4, respectively.[12] The same notation was adopted for the perdeuterated derivative. The analyses of the deuterium, proton, and carbon-13 spectra were performed with the simulation program PANIC (supplied by Bruker).

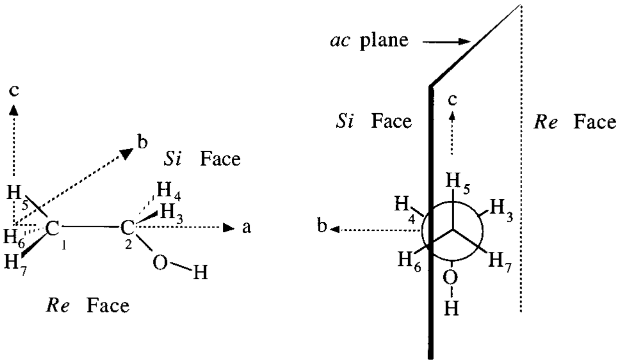

Figure 1. Definition of axes labels *(a,b,c)* of the reference molecular coordinate frame and numbering system of the atoms of ethanol.

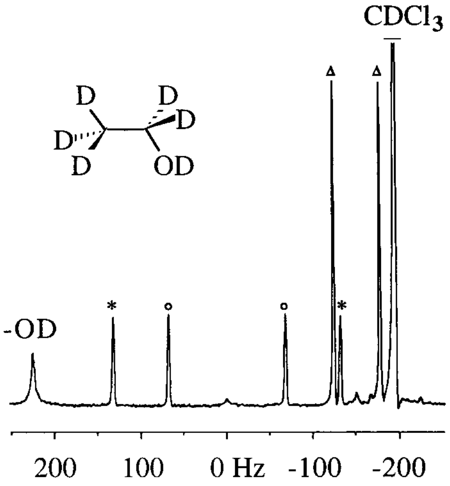

Figure 2. $^2H-\{^1H\}$ partial spectrum of perdeuterated ethanol dissolved in the PBLG/$CDCl_3$ phase. A Gaussian filtering and zero filling to 8K data points were used to improve the spectral appearance and the digital resolution. (*, o) Components of doublets belonging to the methylene group. (△) Components of the doublet belonging to the methyl group. The measured quadrupolar splittings for the −OD group and $CDCl_3$ were 765.8 and 841.3 Hz, respectively. Only the shielded component of each doublet is shown in the figure.

Analysis of the Deuterium Spectrum. The deuterium spectrum of perdeuterated ethanol is presented in Figure 2. The analysis is straightforward and the quadrupolar splittings, $\Delta\nu_Q$, were read directly from the deuterium doublets.[10] As expected, one doublet with a quadrupolar splitting of 53.3 Hz is observed for the methyl group while two quadrupolar doublets with a $\Delta\nu_Q$ equal to 136.1 and 264.2 Hz are measured for the two prochiral deuterons of the methylene group. This means that the two enantiotopic nuclei, D3 and D4, are not magnetically equivalent in the presence of PBLG, giving rise to two distinct doublets. However, as outlined in the Introduction, deuterium spectra provide little information for the calculation of the molecular order parameters, $S_{\alpha\beta}$, in an anisotropic medium. Furthermore, information on the sign of $\Delta\nu_Q$ cannot be directly derived from the analysis of the deuterium spectrum.

Description and Analysis of the Proton and Carbon Spectra. Due to fast exchange of the hydroxyl proton, on the NMR time scale, we have not observed interactions between the OH group and the other nuclei of the molecule. The proton spectrum of ethanol appears as an anisotropic A_3X_2 spin system, i.e., a triplet of triplets for CH_3 and a doublet of quartets for CH_2. No difference of chemical shifts between H3 and H4 and no additional lines were observed in the spectrum.

The carbon-13 spectrum of the CH_2 group of ethanol and the CD_2 group of the perdeuterated ethanol is shown in Figure

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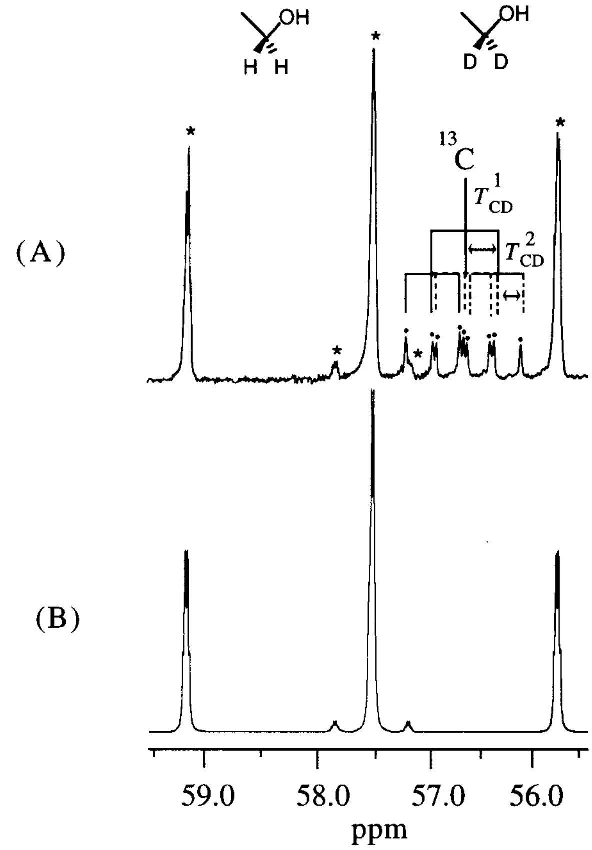

Figure 3. Carbon-13 spectrum of the C2 carbon of ethanol (*) and perdeuterated ethanol (○) dissolved in the PBLG/CDCl$_3$ system (A). Zero filling to 32K data points increased the digital resolution. The carbon-13 signal of the CDCl$_3$ was used as an internal reference and assigned to the value of 77.0 ppm. Simulated carbon-13 spectrum of the C2 carbon for the protonated ethanol (B). The simulation presented here does not include signals from the deuterated ethanol. Note the effect of the dipolar splittings with the methyl group and the large isotopic chemical shift.

3. Disregarding for the moment the part of the spectrum due to the perdeuterated ethanol, we observe that the pattern associated with the CH$_2$ group is a second order spectrum mostly manifested as a triplet of quartets with relative intensity for the triplet components which is not 1:2:1. Additionally, two small inner quartet structures, centered on δ_{C2}, are observed. All signals are reproduced in the simulated spectrum. The spectral pattern for the two prochiral protons indicates that the spin system cannot be considered as an A$_2$X spin system, but as an AA′X spin system (where A and A′ are the two protons of the methylene group). In this situation, the two nuclei are magnetically nonequivalent in terms of their dipolar couplings, and consequently, the proton−carbon couplings, D_{23} and D_{24}, are different. No differences in the D_{13} and D_{14} constants, however, were measured, meaning that these couplings are either identical or the difference between them is too small to be determined. Note that if these dipolar couplings were different, extra lines would be observed in the spectra. Simulations have shown that these extra lines appear when a difference larger than 1.2 Hz exists between them. Consequently, the absolute errors in D_{13} and D_{14} are relatively large and have been estimated to be ±0.6 Hz. Obtained from the proton spectrum, the same situation applies also for the $D_{3-(5,6,7)}$ and $D_{4-(5,6,7)}$ dipolar couplings.

The magnetic nonequivalence of the two enantiotopic nuclei is also clearly visible from the CD$_2$ part of the carbon-13 spectrum, which appears as a superimposed triplet of triplets. If the two D_{CD} were identical, then a simple quintuplet with an intensity distribution of 1:2:3:2:1 would be obtained. These results show conclusively that the transformation of two enantiotopic nuclei into diasteorotopic nuclei in the presence of the PBLG can be observed in their carbon-13 NMR. To the best of our knowledge, this effect has never been detected with nuclei other than deuterium.

The experimental residual dipolar couplings for two nonequivalent spins, D_{ij}^{exp}, which were used to calculate the molecular order parameters, were derived from the measurements of the experimental dipolar splittings, T_{ij}^{aniso}, in the spectra, as

$$D^{\text{exp}}{}_{ij} = \frac{T_{ij}^{\text{aniso}} - J_{ij}^{\text{iso}}}{2} \qquad (1)$$

where J_{ij}^{iso} are the scalar couplings measured in an isotropic solvent.[10] Since the anisotropies of J_{HH} and J_{CH} are generally assumed to be negligible, they were taken to be zero. The magnitude of all J_{ij} values obtained from measurements in a solution of ethanol in CDCl$_3$ at 300 K was kept fixed in the iterative analyses of the proton and carbon-13 spectra in the anisotropic medium. Their signs were taken from the literature.[13] Note that the ^{1}H−^{1}H dipolar couplings were also kept constant during the fitting process for the analysis of the carbon-13 spectrum. The sign of $^{1}J_{\text{CH}}$ can be safely assumed to be positive, which then allows the determination of the magnitude and sign of the $^{1}D_{\text{CH}}$.[14] The signs of the long-range ^{1}H−^{1}H and ^{13}C−^{1}H scalar and dipolar couplings are not easy to determine. Therefore, we have chosen their respective sign and magnitude by testing all possible logical combinations of their values in the calculation of the order parameters. The final set of dipolar couplings corresponds to a set for which the best fit between the experimental and calculated values was obtained.

Using these assumptions, the spectral iterative analysis of the proton spectrum gave a maximum deviation in line positions between the simulated and experimental spectra which was smaller than 0.09 Hz and the root-mean-square (rms) error of the fit was equal to 0.06 Hz.

The ^{13}C analysis of the methyl and the methylene group was performed separately. The root-mean-square (rms) errors of the fits for the methyl and methylene were equal to 0.02 and 0.115 Hz, respectively. As a direct consequence of the nonequivalence of the *pro-R* and *pro-S* protons, it is now possible to determine the sign and the magnitude of the geminal scalar coupling $^{2}J_{34}$ through the analysis of the carbon-13 spectrum. This topic will be discussed in detail later. For ethanol, this scalar coupling was found to be negative and equal to −9.40 ± 0.10 Hz. With this value the maximum deviation between the observed and calculated line positions in the methylene carbon-13 spectrum was 0.2 Hz. To illustrate this point, the calculated spectrum is shown in Figure 3. The final values for the proton−proton and proton−carbon scalar and dipolar couplings are listed in Table 1. It should be noted that the assignment of the carbon−proton dipolar couplings, D_{23} and D_{24}, was not possible, due to the impossibility to distinguish between protons 3 and 4. Consequently in the following, we have assumed that the dipolar couplings, D_{23} and D_{24}, were equal to 24.94 and 10.18 Hz, respectively. However, the interchange of the assignment (D_{23} and D_{24}) does not affect the magnitude of the S_{ab} and S_{bc} but only reversed their sign (cf. Table 3).

Finally, it should be noticed that the sign of the ^{13}C−D dipolar coupling constants then can be derived from the ^{13}C−^{1}H dipolar constants, by assuming that the molecular orientations for the

Table 1. Experimental Scalar and Dipolar Couplings Measured on the ^{1}H and ^{13}C NMR Spectra (in Hz)

type of atoms	interacting nuclei[a]	no. of bonds	$J_{ij}^{\mathrm{iso}\ b}$	$D_{ij}^{exp\ b}$
C···H	1−3	2	−2.67 ± 0.10	3.40 ± 0.60
C···H	1−4	2	−2.67 ± 0.10	3.40 ± 0.60
C···H	1-(5,6,7)	1	125.47 ± 0.10	−4.59 ± 0.10
C···H	2−3 (or 2−4)	1	141.19 ± 0.10	24.94 ± 0.10
C···H	2−4 (or 2−3)	1	141.19 ± 0.10	10.18 ± 0.10
C···H	2-(5,6,7)	2	−4.59 ± 0.10	1.12 ± 0.10
H···H	3−4	2	−9.40 ± 0.10	23.65 ± 0.10
H···H	3-(5,6,7)	3	7.09 ± 0.10	4.76 ± 0.50
H···H	4-(5,6,7)	3	7.09 ± 0.10	4.76 ± 0.50
H···H	(5,6,7)	2		−6.78 ± 0.10

[a] See Figure 1 for the atom numbering. [b] Experimental fitted values with use of the program 'PANIC'.

Table 2. Structural Parameters for Ethanol

parameters	value
$R_{13,14}/R_{12}$[a]	1.425
$R_{15,16,17}/R_{12}$	0.720
angle H5−C1−H6[b]	108.3°
angle H3−C2−H4[b]	107.2°
angle H5,6,7-C1−C2	110.6°
angle H3,4-C2−C1	110.7°

[a] R_{12} = 1.520 Å. [b] Angle (H5−C1−H6) = H6−C1−H7 = H7−C1−H5.

Table 3. Non-Zero Independent Values, $S_{\alpha\beta}$, of the Molecular Order Tensor with 3 and 5 Elements

parameters[a]	3 independent elements	5 independent elements
S_{aa}	−0.00064	−0.00064
S_{bb}	−0.00108	−0.00108
S_{cc}	0.00172	0.00172
S_{ab}		−0.00004[b]
S_{ac}	−0.00113	−0.00113
S_{bc}		0.00045[b]

[a] The $S_{\alpha\beta}$ values are reported with respect to the reference molecular axis system shown in Figure 1. [b] The sign of these elements depends on the assignment of D_{23} and D_{24} relative to H3 and H4.

Table 4. Calculated Dipolar Couplings from the Program SHAPE (in Hz)

type of atoms	interacting nuclei[a]	3 independent elements		5 independent elements	
		D_{ij}^{calc}	$\Delta D_{ij}{}^{b}$	D_{ij}^{calc}	ΔD_{ij}
C···H	1−3	3.12	0.28	3.30	0.10
C···H	1−4	3.12	0.28	2.95	0.45
C···H	1-(5,6,7)	−4.61	0.03	−4.61	0.03
C···H	2−3	17.65	−7.48	25.03	−0.09
C···H	2−4	17.65	7.29	10.28	−0.10
C···H	2-(5,6,7)	1.26	−0.14	1.26	−0.14
H···H	3−4	23.58	0.07	23.58	0.07
H···H	3-(5,6,7)	4.68	0.08	4.64	0.11
H···H	4-(5,6,7)	4.68	0.08	4.72	0.04
H···H	(5,6,7)	−6.84	0.07	−6.84	0.07
rms[c]			2.34		0.13

[a] See Figure 1 for the atom numbering. [b]Difference between the calculated and corrected values: $\Delta D_{ij} = D_{ij}^{\mathrm{exp}} - D_{ij}^{\mathrm{calc}}$. [c] Root mean square error in Hz.

protonated and deuterated compounds are essentially identical. In this way, we could also determine the sign of the quadrupolar splittings. For the deuterated methyl group, this sign was found to be positive, while for the methylene group, the two quadrupolar splittings are negative. However, the indistinguishability between nuclei 3 and 4 did not permit the individual assignment of the two deuterons.

The Model Molecular Structure of the Ethanol. The ethanol geometry was calculated with the Gaussian MP2/6-31G program.[15] The ratios between bond lengths and angles are given in Table 2. The methyl group has a 3-fold symmetry axis coincident with the C1−C2 direction.[7,16] In this model geometry the location of the methyl protons is such that the C1−H5 bond (Figure 1) lies in the *ac* plane, thus corresponding to a staggered position. The reference molecular axis system *(a,b,c)* associated with the molecule was also defined as displayed in Figure 1.

The Ordering Tensor Calculation. The general relationship between the residual dipolar couplings D_{ij}^{exp} (expressed in frequency units) and the components $S_{\alpha\beta}$ of the molecular ordering tensor is given by

$$D_{ij}^{\mathrm{exp}} = -\frac{\mathrm{h}\gamma_i\gamma_j}{8\pi^2\langle r^3{}_{ij}\rangle}[S_{\mathrm{cc}}\langle 3\cos^2\varphi_{ij}^{\mathrm{c}} - 1\rangle + \langle S_{\mathrm{aa}} - S_{\mathrm{bb}})(\cos^2\varphi_{ij}^{\mathrm{a}} - \cos^2\varphi_{ij}^{\mathrm{b}})\rangle + 4S_{\mathrm{ab}}\langle\cos\varphi_{ij}^{\mathrm{a}}\cdot\cos\varphi_{ij}^{\mathrm{b}}\rangle + 4S_{\mathrm{ac}}\langle\cos\varphi_{ij}^{\mathrm{a}}\cdot\cos\varphi_{ij}^{\mathrm{c}}\rangle + 4S_{\mathrm{bc}}\langle\cos\varphi_{ij}^{\mathrm{b}}\cdot\cos\varphi_{ij}^{\mathrm{c}}\rangle] \quad (2)$$

In this equation, *i* and *j* specify the interacting nuclear pair, γ_i is the gyromagnetic ratio for the *i*th nucleus, and φ_{ij}^{α} defines the angle between the internuclear vectors r_{ij} and any molecular reference axis system (*a*,*b*,*c*).[10,11] "⟨ ⟩" denotes an ensemble average. Vibrational corrections will not be considered in this work.

The number of nonzero independent elements of an ordering tensor depends on the point symmetry group of the molecule.[10] Thus, a molecule belonging to the *Cs* point group symmetry (one mirror plane), such as ethanol, requires only three independent nonzero elements, which are S_{cc}, $S_{aa} - S_{bb}$, and S_{ac} when the *b* axis is chosen to be perpendicular to the mirror plane.[10] The three nonzero independent order parameters, denoted as $S_{\alpha\beta}^{(3)}$, were obtained from eq 2 by a least-squares fitting method by using the SHAPE program developed by Diehl et al., but modified to take into account the averaging produced by the rotation of the methyl group.[7,17] The values obtained for the $S_{\alpha\beta}^{(3)}$ are shown in Table 3 and the calculated dipolar couplings are reported in Table 4. The values of ΔD_{23} and ΔD_{24}, corresponding to the differences between the calculated and experimental dipolar couplings for the methylene group, are unacceptably large and lead to a rms error of 2.34 Hz. The important point is that in this situation the two calculated dipolar couplings are equal, which is contradictory to reality. This situation arises because the two enantiotopic nuclei of the methylene group in the isolated ethanol become diastereotopic in PBLG. Consequently, five order parameters must be considered to compute correctly the elements of the molecular order matrix.

We therefore calculated the ordering tensor of the ethanol using 5 nonzero independent order parameters, denoted as $S_{\alpha\beta}^{(5)}$. The values obtained for $S_{\alpha\beta}^{(5)}$, are shown in Table 3 and the derived calculated dipolar couplings are reported in Table 4. The agreement between the calculated dipolar values, D_{23}^{calc} and D_{24}^{calc}, and the experimental ones is now excellent, leading to a rms error equal to 0.13 Hz. The difference between $S_{\alpha\beta}^{(3)}$ and $S_{\alpha\beta}^{(5)}$ is only shown in the new elements, S_{ab} and S_{bc}, but no differences in other order parameters are observed. We note

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Table 5. Principal Components, $S_{\alpha'\alpha'}$, of the Diagonalized Matrix, $S^{(5)}_{\alpha\beta}$, and Biaxiality Term

parameters[a]	values
$S_{a'a'}$	−0.00125
$S_{b'b'}$	−0.00098
$S_{c'c'}$	0.00223
$S_{b'b'} - S_{a'a'}$	0.00027

[a] The $S_{a'a'}$ values are reported with respect to the principal molecular axis system described in Figure 4.

that the calculated values of D_{13} and D_{14} are different, and so too are $D_{3-(5,6,7)}$ and $D_{4-(5,6,7)}$, which is because they are in reality nonequivalent. Thus, the discrepancies between their calculated and experimental values are in agreement with the errors given for the dipolar couplings in Table 4.

With the purpose of checking the precision of these calculations, we have explored two other models for the methyl group. In the first model, we assumed that the C1−H5 bond does not lie in the *ac* plane. In this case, minimum energy is for a position in which the methyl group is not in the staggered conformation, but tilted by some angle. Calculations did not produce a significant improvement on the rms error values. In the second model, we have assumed that the methyl group was freely rotating around the C1−C2 bond. Again, no significant decrease of the rms error was obtained, thus justifying the choice of the first model described above.

We have shown that 5 order parameters, and not 3 as in any achiral nematic phases, are necessary to define correctly the average molecular orientation of the ethanol in PBLG. In other words, the PBLG breaks the symmetry of ordering in prochiral groups, leading the prochiral molecule to behave as if it were a chiral molecule, for which 5 order parameters are necessary to compute the $S_{\alpha\beta}$. In this sense, PBLG is therefore able to discriminate the two faces of a prochiral molecule. This situation might be similar to that involved in asymmetric synthesis or enzymatic catalysis, where the substrate is attached to the enzyme in a specific orientation. We may therefore suggest that the two faces of a prochiral solute in PBLG are not equivalent with respect to their average orientation. We believe that the possibility of converting two enantiotopic nuclei into diastereotopic nuclei should exist in all cholesterics and chiral nematics. The second consequence of this effect, as far as the calculation of molecular orientation is concerned, is that we cannot define the group symmetry of a solute from its molecular geometry, but must also consider the nature of the liquid crystalline phase.

Determination of the Principal Order Matrix and Eigenvectors. The ordering tensor was diagonalized to give both their eigenvalues, $S_{\alpha'\alpha'}$, and their associated eigenvectors (a',b',c').[6,7] The three nonzero diagonalized order parameters are listed in Table 5 together with the biaxiality term, ($S_{b'b'} - S_{a'a'}$). To give a visual support, the orientation of the eigenvectors is presented in Figure 4, where the principal axis system was drawn in 3-dimensional space. We have chosen the direction of the three principal axes (a',b',c') in such a way as to minimize their angular differences with the reference system (a,b,c).

For C_s symmetry molecules in a nonchiral nematic, two principal axes are oriented in the molecular plane of symmetry (*ac* plane) while the third one is perpendicular to it (*b* axis). In this figure, we can observe that this is not the case in the chiral nematics since the three principal axes (a',b',c') are out of the plane of symmetry, *ac*. Mathematically, the transformation of (a,b,c) into (a',b',c') can be viewed as a rotation of the *a* and *c* axes around the *b* axis accompanied by a tilt out the *ac* plane. Consequently, we can measure the angle between the projection of the principal axes and the *ac* plane. The value of these angles could provide a measure for the magnitude of the facial discrimination in PBLG. Therefore we may quantify in angular terms the facial discrimination of a prochiral molecule. These calculations were performed for the ethanol and we found 49°, 40°, and 7° for the projection of the *a*′, *b*′, and *c*′ axes, respectively. Finally, it should be noted that by replacing H3 and H4 in the calculations, we obtain a PAS inverted relative to the *ac* plane with the same values of angles given above. In all nonchiral nematics, these angles are expected to be always 90°, 0°, and 0°.

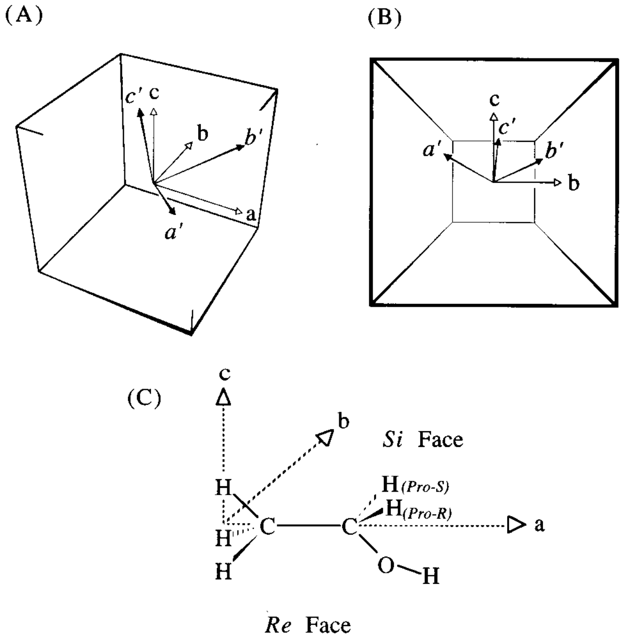

Figure 4. Representation in space (A) and view from the direction of the *bc* plane (B) of the principal axis system (a',b',c') of the ethanol derived from five-order parameters. The eigenvectors associated with the eigenvalues of the diagonal matrix are orthonormal. For the sake of clarity, we add the ethanol molecule with its reference frame (a,b,c) (C).

4. Measurement of Geminal Scalar Couplings

It is well-known that the geminal coupling constant between two magnetically equivalent hydrogen atoms does not exhibit the spin−spin scalar coupling in their NMR spectra.[18] Thus, for a methylene group, the sign and the magnitude of this constant cannot be obtained from the analysis of the proton spectrum in isotropic solutions. However, we can get this spectral parameter by replacement of one of the equivalent protons of the methylene group with deuterium. In this case, a triplet (doublet) whose components are of equal intensity is expected for the proton (deuterium) spectrum, from which the heteronuclear geminal coupling, ${}^2J_{HD}$, can be measured. A simple relationship provides the corresponding value, ${}^2J_{HH}$,

$$ {}^2J_{HH} = \left(\frac{\gamma_H}{\gamma_D}\right)^2 J_{HD} \tag{3} $$

where $(\gamma_H/\gamma_D) = 6.514$. This procedure, however, possesses

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(17) Diehl, P.; Henrichs, P. M.; Niederberger, W. *Mol. Phys.* **1971**, *20-(1)*, 139.

(18) Bhacca, N. S.; Williams, D. H. *Applications of NMR Spectroscopy in Organic Chemistry*; Holden-Day: San Francisco, 1964, p 55.

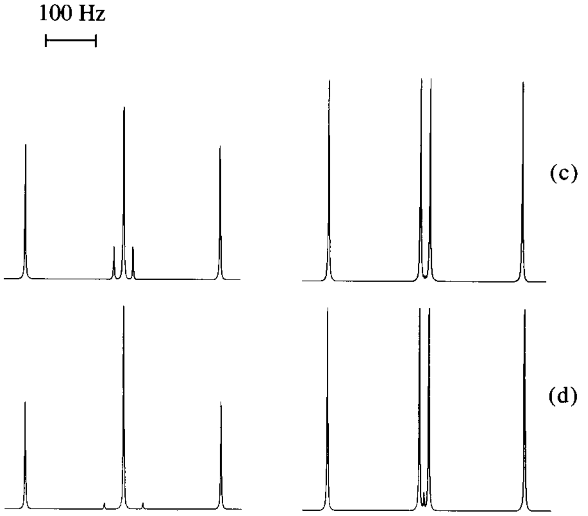

Figure 5. Simulation of spectral patterns of the X part of an AA′X versus the relative sign of the T_{AX} and $T_{A'X}$ dipolar splittings and the $D_{AA'}$ and $J_{AA'}$ couplings. The T_{AX} and $T_{A'X}$ are assumed to be larger than the $T_{AA'}$. (a) T_{AX}, $T_{A'X}$, $J_{AA'}$ and $D_{AA'}$ have an identical sign. (b) T_{AX} and $T_{A'X}$ have an identical sign, but $J_{AA'}$ and $D_{AA'}$ have an opposite sign. (c) T_{AX} and $T_{A'X}$ have an opposite sign, but $J_{AA'}$ and $D_{AA'}$ have an identical sign. (d) T_{AX} and $T_{A'X}$ have an opposite sign and $J_{AA'}$ and $D_{AA'}$ have an opposite sign. Note that the relative signs of T_{AX} ($T_{A'X}$) and $D_{AA'}$ do not produce any effect on the spectra.

some limitations. The most important is the need to perform the isotopic substitution, which is not always simple. Second, the proton−deuterium geminal coupling constants, J_{gem}, usually are of the order of 1−2 Hz or even smaller, which limits the precision of the measurements. Third, no information on the absolute sign of J_{gem} can be derived directly from the analysis of the spectra. In most cases, the sign of J_{gem} is assumed to be negative and opposite to that of the vicinal coupling constants which are mostly positive.[19]

As shown above, the NMR data for a prochiral group dissolved in the PBLG liquid crystalline system provides a novel technique that yields both the magnitude and sign of the geminal scalar couplings. In this part, we shall present the study of the measurement of J_{gem} on a series of linear aliphatic alcohols. These results will be compared with values derived from $^2J_{HD}$ by isotopic substitution.

The loss of symmetry of ordering permits the visualization of two enantiotopic nuclei through the carbon-13 NMR. A second-order carbon-13 spectrum is obtained from which the geminal scalar coupling can be determined. This situation arises because the frequencies and the amplitudes of resonances of the X (^{13}C) part in an AA′X spin system depend on the $^1J_{CH}$, D_{CH}, $D_{CH'}$, $^2J_{HH'}$, and $D_{HH'}$ values, resulting in a unique solution for the sign and the amplitude of these parameters.

In Figure 5 are summarized the different types of spectral patterns for the X part of an AA′X spin system as a function of the relative signs of T_{AX}, $T_{A'X}$, $^2J_{AA'}$, and $D_{AA'}$. These simulations were performed by the PANIC program by using values which are similar in magnitude as those reported in Table 1.

In all schemes, we have assumed that there is no chemical shift between *A* and *A′* nuclei and the dipolar splittings, T_{AX} and $T_{A'X}$ (with $^1J_{A'X} = {}^1J_{AX} > 0$), are larger than the $T_{AA'}$, which is generally the case for solutes dissolved in PBLG. We note that cases for which T_{AX} and $T_{A'X}$ have equal or opposite signs can readily be discriminated by observing the number of major components (3 or 4) in the spectrum. From the intensity of the smaller lines in the spectra, we can then determine the relative signs of $^2J_{AA'}$ and $D_{AA'}$. Since we assumed that the signs of $^1J_{AX}$ and $^1J_{A'X}$ are equal and positive, we can deduce the signs of D_{AX} and $D_{A'X}$ directly from the values of the splittings of the major components of the triplets. In all cases, the $^2J_{AA'}$ values are obtained by fitting the intensities of the smaller components in the spectra. However, this procedure cannot be performed automatically by PANIC. Consequently, the J_{gem} value was introduced in the program as input and varied until the relative intensities measured on calculated spectra were comparable to the experimental ones and the least rms error was achieved. It should be emphasized again that the values of D_{AA}' ($=T_{AA}'/3$) were calculated from the analysis of the proton spectra, while the $^2J_{AA'}$ constants can be extracted only from the carbon-13 spectrum.

Table 6. Values of the Geminal Couplings, $^2J_{HH}$, Using the PBLG and the Isotopic Substitution Methods

	in PBLG solution	isotopic substitution
ethanol	-9.4 ± 0.1	$\pm 9.5 \pm 0.1$
propanol	-10.2 ± 0.1	$\pm 10.3 \pm 0.1$
butanol	-10.3 ± 0.1	$\pm 10.3 \pm 0.1$
pentanol	-10.1 ± 0.1	

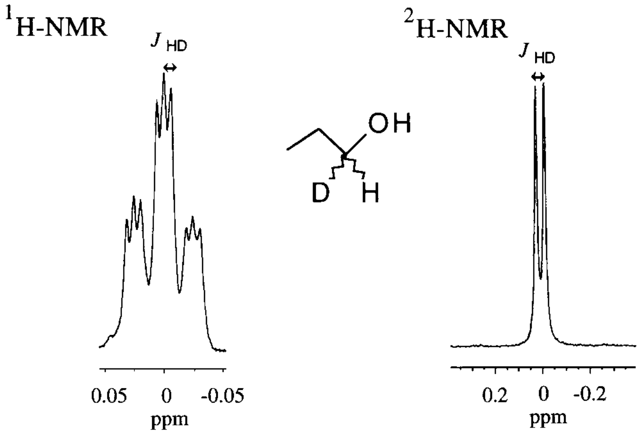

Figure 6. Proton and deuterium spectra (32 and 128 scans, respectively) of the α-methylene group of the (±)1-deuteriopropanol recorded at 250.16 and 38.39 MHz. The proton spectrum was recorded in $CDCl_3$ while the deuterium spectrum was recorded in $CHCl_3$ with selective decoupling of the β-methylene group. For each spectrum, the center of the structure was assigned as 0 ppm.

We have used this technique to measure the values of $^2J_{HH}$ in ethanol, propanol, butanol, and pentanol. The PBLG samples were prepared as described in the Experimental Section. The quantities of PBLG, $CDCl_3$, and alcohol for the different samples were 100, 370, and 30 mg, respectively. The results are presented in Table 6.

We compared our results with measurements performed on the corresponding monodeuterated materials (except for pentanol). These were prepared from the corresponding aldehydes by reduction with lithium aluminum deuteride using conventional methods. The measurements of $^2J_{HD}$ were achieved through the measurements of the proton and deuterium spectra in a solution of $CDCl_3$ and $CHCl_3$, respectively. Both deuterium and proton measurements were performed to test the precision on the values. For illustration we present in Figure 6 the proton and deuterium spectra of the (±)1-deuteriopropanol. Note that the triplet structure observed in the proton spectrum arises due to the coupling with the methylene group in the β position. We can observe the excellent agreement between the two methods. This new method appears as a useful and interesting alternative

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to the classical technique for measuring the scalar coupling constants between magnetically equivalent nuclei.

5. Conclusions

We report in this paper the first quantitative description of the facial discrimination of a prochiral molecule oriented in a organic solution of poly-γ-(benzyl-L-glutamate). From the analysis of proton and carbon-13 NMR dipolar data, we were able to calculate the full order matrix and determine its principal axis system. It is shown that five independent order parameters are necessary to describe correctly the molecular ordering of ethanol in this medium, thus demonstrating clearly the loss of symmetry of ordering in the PBLG in the case of prochiral groups. In other words, while for molecules with C_s symmetry dissolved in ordinary nematics two principal axes are in the symmetry plane and the third is perpendicular to this plane, this is not the case for the nematic cholesteric that we used.

We have shown that this facial discrimination could be quantified in terms of angles between the principal axes and their projection in the molecular plane of symmetry which exists in all prochiral molecules. This work requires further experimental studies on a series of model prochiral molecules in order to collect data and promote our understanding of the prochiral discrimination in PBLG. In the future, it would be a real challenge to be able to assign the two enantiotopic nuclei (or groups of nuclei). Such studies are presently underway.

Finally, as a consequence of the loss of magnetic equivalence of prochiral nuclei, a novel method to determine the sign and the magnitude of the geminal scalar couplings between two enantiotopic protons in a methylene group is proposed and described.

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