Observation of Enantiomers, Chiral by Virtue of Isotopic Substitution, through Deuterium NMR in a Polypeptide Liquid Crystal

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Received March 7, 1994®

Abstract: The use of poly (γ-benzyl L-glutamate) (PBLG), as an orientation matrix, for the observation of enantiomers through proton-decoupled deuterium NMR is reported. The work is focused on the compounds which are chiral due to H/D isotopic substitution. The effect, unlike that which was observed in regular enantiomers, does not originate mainly from asymmetric molecular ordering. Rather, it is shown that the origin of the phenomenon is the same that allowed observation of enantiotopic nuclei of the nonchiral perdeuterated benzyl alcohol few years ago (Czarniecka, K.; Samulski, E. T. *Mol. Cryst. Liq. Cryst.* **1981**, *63*, 205-214). Only in a few cases is it demonstrated that a very small difference in the molecular ordering of such enantiomers can be detected, due to the geometrical differences between protonated and deuterated molecules. Furthermore, the results obtained with CHD_2–OH, where both enantiotopic deuterons show separate NMR signals, permit the anticipation that the technique will work for the direct NMR observation of the enantiomers in CHDT–OH.

The enantiomeric analysis of compounds that owe their chirality to isotopic substitution is of particular interest for the determination of the stereochemical course of microbiological and enzymatic catalytic conversions. This problem is not amenable to chromatographic methods of analysis. Classical approaches using chiroptical methods are difficult owing to the weak circular dichroism involved, as pointed out in a recent review by Parker.[1] Chiral shift reagents are generally not applicable except in the case of some α-deuterated benzylic alcohols.[2] The use of time-consuming, chiral, derivatizing agents has proved to be much more useful.

On the other hand, as has been shown recently in our laboratory, the use of a chiral lyotropic liquid crystal as an orientational matrix for proton-decoupled deuteron NMR is a very powerful and general technique for the observation of enantiomers.[3] This effect has been shown to originate from the difference in the molecular ordering of the optical isomers dissolved in chiral nematic liquid crystals such as solutions of PBLG [poly (γ-benzyl L-glutamate)] in organic solvents. The purpose of this paper is to show that such chiral nematic solvents provide a general technique for the visualization of isotopic enantiomers. The origin of the enantiomeric separation will be shown to originate from a different mechanism as compared to that for normal enantiomers.

In the following only isotopic chirality will be addressed. A general review dealing with chiral recognition through NMR in polypeptidic liquid crystal solvents will be published elsewhere.

Experimental Section

In order to obtain good ^2H high resolution spectra in such liquid crystal solvents the sample preparation is very important.

A total of 120 mg of PBLG (DP 1183, MW 259 000 from Sigma) was weighed directly into a 5 mm NMR tube. A solution of about 30 mg of the isotopic enantiomer mixture dissolved in 600 mg of CH_2Cl_2 was then added. The NMR tube, after being carefully plugged or sealed, was centrifuged back and forth until an optically homogeneous mixture was obtained. After a few minutes in the field a deuterium spectrum was measured with proton broad-band decoupling. If the observed ^2H NMR line width were greater than 1–3 Hz the sample had to be rehomogenized through centrifugation. Under such conditions only 32 transients or less were necessary to obtain a spectrum with a good signal to noise ratio. When a precise enantiomeric excess is to be measured it may be needed to acquire more transients.

In most of this work a Bruker AM-250 spectrometer was used, equipped with a selective 5 mm deuterium probe working at 38.37 MHz. The broad-band proton decoupling was achieved, using the WALTZ composite pulse scheme, using 1 W of RF power. A good temperature controller is highly recommended, because the spectra are very sensitive to temperature fluctuations and it is sometime useful to make variable-temperature measurements. The temperature was controlled by the Bruker BVT 1000 system (±0.2 °C regulation). Interferograms (8K) were collected using 90° pulses, 3000 Hz spectrum width, and a short relaxation delay. No apodisation was applied in the spectra shown in this paper. Samples were spun in the magnetic field.

Experimental Results

The proton-decoupled spectrum of a deuterium in an isotropic solvent consists of a single line. When the molecules are partially oriented in a nematic liquid crystal the average of the quadrupolar coupling becomes nonzero, which splits the line into two. The separation of each doublet is the quadrupolar splitting $\Delta\nu_Q$. In the high-field approximation and assuming a negligible asymmetry parameter, this splitting is proportional to the order parameter of the principal component of the electric field gradient at the deuterium site with respect to the magnetic field:[4]

$$\Delta\nu_Q = \frac{3}{2}\frac{Q_D V_{CD}}{h}\left(\frac{1}{2}\langle 3\cos^2\theta^z_{CD} - 1\rangle\right)$$

where Q_D is the deuterium quadrupole moment, V_{CD} is the electric field gradient along the C–D bond and θ^z_{CD} is the angle between the electric field gradient and the external magnetic field. The $\langle\ \rangle$ brackets denotes the average value over the anisotropic molecular reorientations.

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® Abstract published in *Advance ACS Abstracts*, September 1, 1994.

(1) Parker, D. *Chem. Rev.* **1991**, *91*, 1441-1457.
(2) Fraser, R. R.; Petit, M. A.; Miskow, M. *J. Am. Chem. Soc.* **1972**, *94*, 3253-3254.
(3) Bayle, J. P.; Courtieu, J.; Gabetti, E.; Loewenstein, A.; Péchiné, J. M. *New. J. Chem.* **1992**, *16*, 837-838.
(4) Emsley, J. W.; Lindon, J. C. *NMR Spectroscopy Using Liquid Crystal Solvents*; Pergamon Press: Oxford, 1975; pp 221-257.

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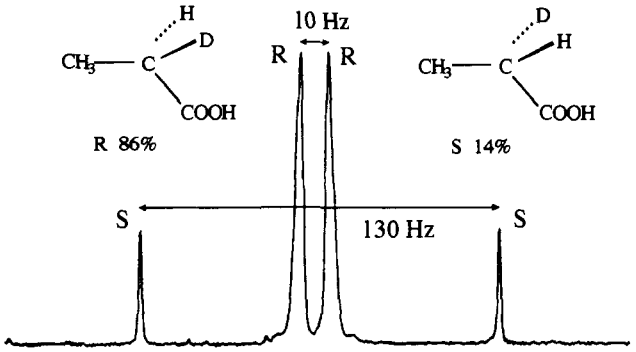


Figure 1. Proton-decoupled deuterium NMR spectrum of an *R*-enriched mixture of CH_3–CHD–COOH enantiomers (ee 72%) dissolved in PBLG/CH_2Cl_2 liquid crystal at T = 300 K.

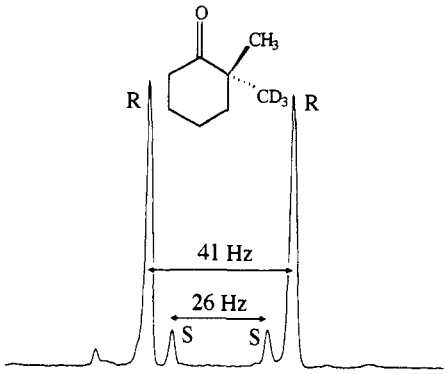


Figure 2. Proton-decoupled ^2H NMR spectrum of *R*-enriched 2-(methyl-d_3)-2-methylcyclohexanone (ee 80%) dissolved in PBLG/CH_2Cl_2 liquid crystal at T = 300 K.

If, for any reason, there is a difference in the molecular ordering between the *R* and *S* enantiomers four lines should be observed in a singly labeled molecule, i.e. a doublet for each enantiomer, and this indeed was observed experimentally. Figures 1 and 2 illustrate two typical examples, for *R*-enriched CH_3–*CHD–COOH (ee 72%) and *R*-enriched 2-(methyl-d_3)-2 methylcyclohexanone (ee 80%) which were synthesized following standard procedures.[5,14] Obviously, the enantiomers have different quadrupolar splittings, and the enantiomeric excesses can be measured very easily through line integration.

In order to illustrate the generality of the method, the results for several isotopically substituted chiral molecules are reported in Table 1, together with the temperature dependence of the quadrupolar splittings for each enantiomer. The technique worked very well for all the samples, and the effect appears much stronger than was expected. To date, we did not fail with any compound prepared in this laboratory, and this method appears to be quite general.

Temperature Dependence. In Table 1, it can be seen that the spectra of the enantiomers are very sensitive to the temperature. In the case of C_6H_5–CDH–OH, for instance, it must be noted that $\Delta\nu_Q^S < \Delta\nu_Q^R$ at 300 K, is the inverse of that at 320 K, where $\Delta\nu_Q^S > \Delta\nu_Q^R$. At 310 K only one doublet is observed. Hence at this temperature both enantiomers exhibit the same quadrupolar splitting. This effect has already been described for normal enantiomers.[3] It might be related to the temperature dependence of the helix pitch in the PBLG.[7,8] Thus in a given experiment it is sometimes important to do systematic temperature studies, since the difference between the NMR quadrupolar splittings of the enantiomers is strongly dependent upon temperature.

Visualization of Isotopic Chirality and Molecular Ordering. The early work of enantiomeric observation through NMR in homogeneously aligned cholesterics showed that the difference between enantiomers, in such a medium, arises from a difference in the molecular ordering.[9] This differential ordering effect of enantiomers is clearly evident, when using polydeuterated molecules, because *all* the deuterium NMR signals are split into two, i.e. a doublet is observed for each deuteron in each enantiomer. Such an example can be seen in Figure 3 for *R*-enriched C_6D_5–$CD(CH_3)$–OH. From this result, it must be concluded that the average molecular ordering matrix is different for each enantiomer.

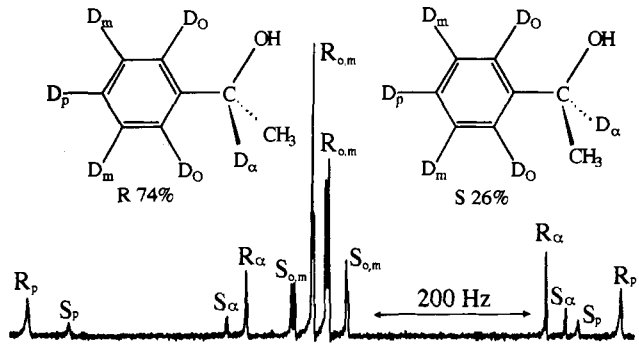
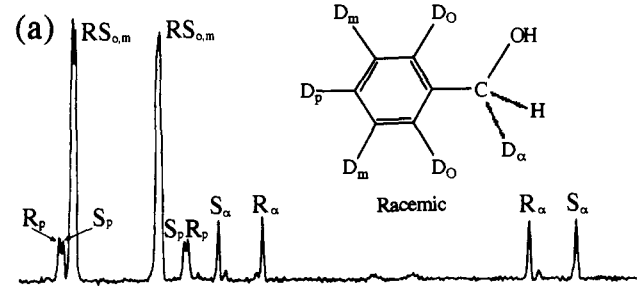


Figure 3. Proton-decoupled ^2H NMR spectrum of C_6D_5–$CD(CH3)$–OH enriched in the *R* enantiomer (ee 48%) dissolve in PBLG/CH_2Cl_2 liquid crystal at T = 303 K.



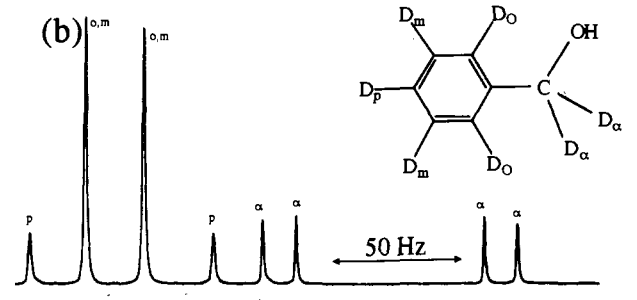
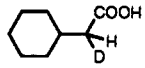
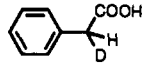
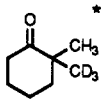
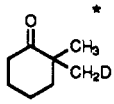
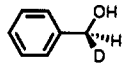
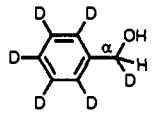
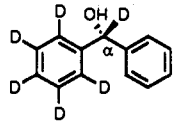


Figure 4. Proton-decoupled ^2H NMR spectra in PBLG/CH_2Cl_2 solvent of (a) racemic C_6D_5–CHD–OH at T = 300 K, and (b) nonchiral C_6D_5–CD_2–OH at T = 306 K.

For the case of isotopic (H/D substitution) chirality, it can hardly be assumed that the small differences between the hydrogen and the deuterium atoms can give rise to large differences in molecular ordering, such as those observed and illustrated in Figure 1 and Table 1. In order to understand the origin of the effect in the case of isotopic chirality it was decided to compare the spectrum of C_6D_5–$CD(CH_3)$–OH with the spectrum of racemic C_6D_5–CDH–OH depicted in Figure 4a. It can be seen that the deuterons of the –CDH– group were split, while all the other deuterons were not split, and showed a single doublet (except for a very small splitting of the para deuterons that we will neglect for now but will analyze later). This result implies that both the

(5) Sood, G. R.; Ashworth, D. M.; Ajaz, A. A.; Robinson, J. A. *J. Chem. Soc., Perkin Trans.* **1988**, *1*, 3183–3193.
(6) Yamaguchi, S.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 1870–1877.
(7) Toruimi, H.; Yamasaki, T.; Abe, A.; Samulski, E. T. *Liq. Cryst.* **1986**, *1*, 87–96.
(8) Abe, A.; Yamasaki, T. *Macromolecules* **1989**, *22*, 2138–2145; 2145–2149.
(9) Lafontaine, E.; Péchiné, J. M.; Courtieu, J.; Mayne, C. L. *Liq. Cryst.* **1990**, *2*, 293–298.

Table 1. Experimental Quadrupolar Splittings Measured on the Proton Decoupled Deuterium NMR Spectra for Various Compounds[a]

compound	ref	D	T (K)	$\lvert\Delta\nu_{Q1}\rvert$ (Hz)	$\lvert\Delta\nu_{Q2}\rvert$ (Hz)	PBLG/CH_2Cl_2/compound (mg)
CH_3–CHD–COOH 72% ee	5		300	10 (*R*)	130 (*S*)	100/780/70
			305	259	174	81/606/27
			310	237	154	
			315	216	135	
			305	90	57	83/612/33
			310	68	74	
			315	47	89	
CH_3–CHD–COO–CH_3 76% ee (*R*)	5		304	161 (*S*)	149 (*S*)	103/754/40
			305	158 (*R*)	147 (*S*)	
			311	155 (*R*)	145 (*S*)	
			291	541	517	110/600/32
			302	507	496	
			306	495	495	
	14		300	41 (*R*)	26 (*S*)	108/688/12
	14		300	35 (*R*)	22 (*S*)	124/703/15
CH_3–CHD–OH			240	75	46	118/712/28
			260	75	40	
			280	61	45	
			300	55	47	
			320	41	50	
 36% ee (*S*)	6		300	118 (*R*)	104 (*S*)	113/673/42
			310	102 (*R*)	102 (*S*)	
			320	93 (*R*)	100 (*S*)	
	6	α	300	134	99	120/725/20
			310	130	93	
			320	122	81	
 20% ee (*R*)	15	*p*	297	602 (*R*)	253 (*S*)	85/700/20
			305	545 (*R*)	249 (*S*)	
			314	498 (*R*)	241 (*S*)	
		o, *m*	297	115 (*R*)	174 (*S*)	
			305	93 (*R*)	144 (*S*)	
			314	77 (*R*)	121 (*S*)	
		m, *o*	297	110 (*R*)	169 (*S*)	
			305	88 (*R*)	139 (*S*)	
			314	72 (*R*)	117 (*S*)	
		α	294	246 (*R*)	246 (*S*)	
			305	229 (*R*)	229 (*S*)	
			314	215 (*R*)	215 (*S*)	

[a] $\lvert\Delta\nu_{Q1}\rvert$ and $\lvert\Delta\nu_{Q2}\rvert$ refer to each enantiomer. *R* and *S* specify the absolute configuration when it was known. Column D describes the type of the deuterium in polydeuterated molecules, column *T* gives the temperature of the NMR experiment (in K), and the last column gives the composition of the sample with the following order: mass of PBLG/mass of CH_2Cl_2/mass of the solute (all in mg).

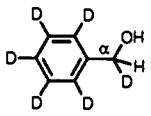
R and the *S* enantiomers must have roughly the same molecular ordering matrices. Why then is the deuterium NMR spectra of the chiral carbon split into two doublets? This may be explained using arguments presented by Czarniecka and Samulski.[10] They showed that, when perdeuterated benzyl alcohol was dissolved in the PBLG liquid crystal, the enantiotopic deuterons of the $-CD_2-$OH group behave diastereotopically and consequently show a quadrupolar doublet for each deuteron as can be seen in Figure 4b. This is indeed the same effect, due to a binding of the enantiomers to the polypeptide, which we observe here in the case of the isotopic chirality. One remaining point that must be made clear is how to explain this effect with respect to isotopic enantiomers. In Figure 4b we note that separate signals for the pro-*R* and pro-*S* deuterium were observed. If some of the pro-*R* nuclei, for instance, are exchanged by protons the signal intensity of the pro-*R* signal will become smaller. It is obvious that the ratio of the number of pro-*R* to the number of pro-*S* deuteriums is the mass ratio of the *R* and *S* isotopic enantiomers.

It should be emphasized that the effect of the PBLG solution transforming enantiotopic nuclei into diastereotopic nuclei, as first observed by Samulski et al. for benzyl alcohol, is a very general effect as may be seen on different examples reported in Table 2. To illustrate this phenomenon, the deuterium NMR spectra of perdeuterated octanol is interesting. In these spectra we notice that all the $-CD_2-$ groups show four lines, i.e. one doublet for each enantiotopic deuterium, where the effect propagates all along the entire chain (Table 2).

Another interesting example confirms this proposed explanation: The NMR spectrum of *R*-enriched C_6H_5–CDOH–C_6D_5 (ee 20%), whose chirality stems from the difference between a hydrogenated and a deuterated benzene rings,[15] has been measured. The spectrum is easily assigned as illustrated in Figure 5. Contrary to the C_6H_5–CDH–OH case, all the ring deuterons, ortho, meta, and para, are split into two doublets, i.e. one for each

(10) Czarniecka, K; Samulski, E. T. *Mol. Cryst. Liq. Cryst.* **1981**, *63*, 205–214.

Table 2. Experimental Quadrupole Splittings of Some Enantiotopic Deuterium Nuclei in Liquid Crystal PBLG Solvent

compound	ref	D	T (K)	$\lvert\Delta\nu_{Q1}\rvert$ (Hz)	$\lvert\Delta\nu_{Q2}\rvert$ (Hz)	PBLG/CH_2Cl_2/compound (mg)
CD_3–$^{\alpha}CD_2$–OH		α	220	51	30	120/650/20
			260	50	32	
			290	47	33	
			310	45	33	
	6	α	306	99	73	83/610/19
			314	85	72	
			322	74	70	
C_6D_5–$^{\alpha}$CDOH–C_6D_5	15	*p*	300	825	395	101/656/60
		o, m		182	112	
		α		406	406	
CD_3–$^{\gamma}CD_2$–$^{\beta}CD_2$–$^{\alpha}CD_2$–OD[a]		α	295	106	81	113/719/17
		β		68	59	
		γ		137	126	
CD_3–$(CD_2)_6$–$^{\alpha}CD_2$–OD[b]		α	295	320	206	109/640/38
		β		118	105	
		γ		17	6	
		δ		34	28	
		ϵ		155	153	
		ζ		117	95	
		η		124	115	
CHD_2–OH			271	72	69	102/612/16
			280	69	66	
			296	61	58	
			300	58	55	
			310	50	47	

[a] Spectrum taken at 61.4 MHz. [b] Spectrum taken at 76.75 MHz. The assignment is based on the assumption that the chemical shifts change sequentially from α to η. δ and ϵ show the same shift and consequently the assignment for these two is ambiguous.

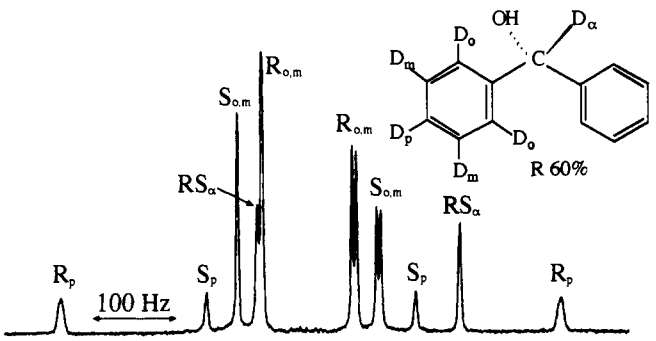


Figure 5. Proton-decoupled ^2H NMR spectra of *R*-enriched C_6D_5–CDOH–C_6H_5 (ee 20%) in PBLG/CH_2Cl_2 liquid crystal at $T = 297$ K. The enantiotopic benzenic deuterium are all giving two doublets, but the deuterium on the central carbon shows one doublet.

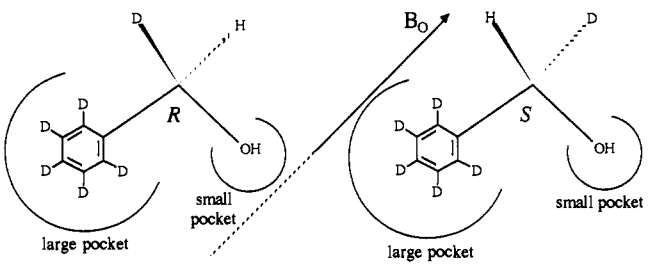


Figure 6. Schematic representation of the binding of *R* and *S* isotopic enantiomers of C_6H_5–CHD–OH to a binding site of PBLG showing that the local order parameters of the C–D bonds, relative to B_o in each enantiomers, may be different even if the molecular ordering parameters are the same for both molecules.

enantiomer but not the central CD! It would be expected, as was explained above, that the benzene rings become diastereotopic when this molecule is dissolved in the PBLG liquid crystal. On the other hand, the deuterium on the central carbon gives one doublet, since this nucleus is enantiotopic to nothing and since both enantiomers have the same molecular ordering parameters.

Thus it appears that this kind of weak chirality, due to isotopic substitution, is observed by NMR through a mechanism which originates from a strong assymmetrical molecular interaction between the enantiomer molecules and the PBLG helical polymer. This intermolecular process transforms enantiotopic nuclei into diastereotopic nuclei, that are distinguishable because they are nonequivalent. The intensity ratio of these NMR signals is the mass ratio of the enantiomers.

Why $|\Delta\nu_Q^S - \Delta\nu_Q^R|$ Is So Large? The above deductive scheme raises new questions concerning the large difference of the quadrupolar interactions and conversely why no corresponding effects of chemical shifts are observed. In order to reach an understanding of this experimental observation it is interesting to notice that the chiral solvent PBLG/CH_2Cl_2, being used as the NMR orientation matrix, might be seen as acting as a biopolymer. The observed phenomenon might be rationalized in terms of the classical mechanism involved for enzyme enantioselectivity[11] as depicted in Figure 6. This model predicts that the order parameter of the electric field gradient along each C–D bond, $^1/_2\langle 3\cos^2\theta_{CD}^z - 1\rangle$, would be quite different for both enantiomers, even if the molecular ordering matrix is the same. This is derived from the fact that in a molecular fixed-axis system the CD bonds for the *R* and the *S* configurations are not oriented in the same directions. It is well known[4] that the order parameter of the CD bonds is related to the molecular order matrix elements through:

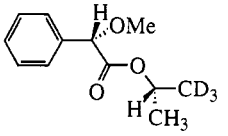
$$S_{CD} = \sum_{pq}^{c}{}_{a}(\cos\varphi_{CD}^{p}\cos\varphi_{CD}^{q}S_{pq})$$

where the φ_{CD}^p's are the angles between a CD bond and the molecular fixed-axis system (a, b, c), and the S_{pq} are the elements of the molecular ordering matrix. In other words it appears that $\Delta\nu_Q^R$ is different from $\Delta\nu_Q^S$ essentially because the ordering parameters S_{CD}^S and S_{CD}^R are different. This situation is illustrated in Figure 6 and is not incompatible with a unique molecular ordering matrix. This model may best be conceived in terms of a rapid dynamic equilibrium, on the NMR time scale, between free and bound molecules. In spite of its crudeness this model provides a simple understanding of the phenomenon. It also predicts that the chemical shift of the deuterons in the

(11) Fitzpatrick, A.; Klibanov, A. M. *J. Am. Chem. Soc.* **1991**, *113*, 3166–3171.

enantiomers should be different for two reasons. First because the deuterons become diastereotopic in the presence of the PBLG, and secondly because if the ordering parameters of the CD bonds are different, the chemical shift anisotropy, which is sensitive to order, should also be different for both enantiomer. Nevertheless we have never been able to observe any significant chemical shift difference in the deuterium spectra of enantiomers. The reason is due to the order of magnitude of the expected effects.

Primarily it is well established that the proton NMR chemical shift anisotropy should be very small and that, for deuterium nuclei, the NMR chemical shift anisotropy effect will be more than six times smaller than that expected for protons because of the difference in magnetogyric ratios. Furthermore, the ordering parameters of molecules dissolved in the PBLG/CH_2Cl_2 are very small (generally $S_{CD} \leq 0.001$). These factors do not leave much hope for the detection of the deuterium NMR chemical shift anisotropy effects in the present experiments. As to the magnitude of the expected isotropic chemical shift difference we may consider an example demonstrated by Mislow[12] in the proton NMR spectrum of



where the *R* and *S* methyl groups are shifted by 0.08 ppm. If a somewhat comparable situation is assumed to exist in the present study for the deuterated molecules bound to the PBLG, then a difference in the deuterium NMR chemical shift of the order of about 3 Hz at 38.4 MHz might be expected. This value, scaled by the rapid binding equilibrium, appears too small to be measurable on our samples.

The conclusion here is that although there must be a chemical shift difference, it will usually be very small. The quadrupolar splitting are several orders of magnitude more sensitive than the chemical shifts for the measurements of enantiomers.

The -CHDT Chiral Methyl Problem. From the results given above we conclude that the molecular ordering parameters of isotopic enantiomers are essentially identical and that this visualization of enantiomers by NMR becomes possible only if there are enantiotopic nuclei that turn diastereotopic when partially oriented in the polypeptidic liquid crystal. Hence we could deduce that the NMR method should not operate for the interesting case of chiral methyl[13]

because there are no enantiotopic nuclei in such a molecule. Actually the matter does not seem to be so simple because in a single case a very small isotopic effect on the molecular ordering between two isotopic enantiomers was detected. In Figure 4a the spectrum obtained at 300 K for racemic C_6D_5–CHD–OH is illustrated. As usual a very large difference between the enantiotopic nuclei attached to the chiral carbon was observed. No effect was seen for the ortho and meta deuterons, but a very small effect, that at first we had neglected, was seen for the para deuterium. The NMR resonances are separated by only 2 Hz. This result shows that in this case, at this temperature, we observe a very small difference in the molecular ordering which must be due to the small difference in the geometry between a deuterium and a proton. Consequently, there may be a slight chance to see a difference in the deuterium quadrupolar splittings in molecules such as CHDT–OH for instance.

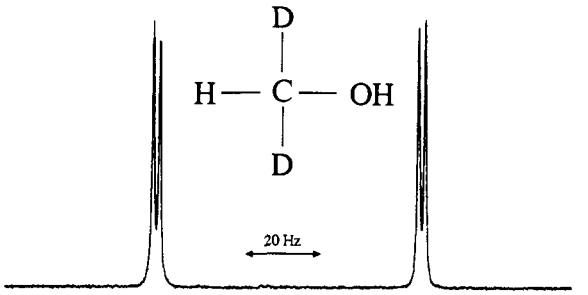


Figure 7. Proton-decoupled ^2H NMR spectrum of CHD_2–OH in PBLG/CH_2Cl_2 liquid crystal at T = 271 K. Note that the pro-*R* and pro-*S* deuterium give separate signals. If one of them is replaced by a tritium, the corresponding signal will be smaller. This experiment is used to demonstrate that the technique will work for a direct visualization of CHDT–OH enantiomers.

Although we have not performed such an experiment, prediction can be made. Let it be supposed the molecule CHD_2–OH where there are two enantiotopic deuterons, which are enantiotopic only through the difference between a deuterium and a proton (we could call it an isotopic enantiotopy). Now if in the polypeptic liquid crystal solvent we are able to observe different quadrupolar splittings for these two deuterons, then it must be concluded that the solvent will recognize a difference between a proton and a deuterium and consequently separate signals for both enantiomers of the CHDT–OH case will be observed.

The proton-decoupled spectrum of the commercially available CHD_2–OH is presented in Figure 7 and its temperature dependance reported in Table 2. It is clear that there are four lines, one quadrupolar splitting for each of the pro-*R* and pro-*S* deuteriums. The effect is small as the difference was only 3 Hz at 271 K, which is only a 4% relative difference in the two quadrupolar splittings of the deuterons. Still the effect is observed and following the same arguments as above, if one of the deuterons is exchanged by a tritium the corresponding deuterium signal intensity will be lowered. It is concluded that this polypeptide liquid crystal will be able to give separate deuterium NMR signals for the CHDT–OH enantiomers. We are currently working on this problem.

Conclusion

In the present study it has been shown that the polypeptide liquid crystal PBLG used as a molecular orientation matrix allows the observation of separate ^2H NMR signals from the isotopic enantiomers, which owe their chirality to isotopic substitution of one or several protons by deuterons. This effect appears to be general as shown through several examples. Working with polydeuterated compounds it was shown that the molecular ordering parameters appear to be essentially identical for isotopic enantiomers and that the origin of the effect lies in the fact that, in the presence of the PBLG, the enantiotopic nuclei become diastereotopic. In this situation the local order parameters of the CD bonds in each enantiomer are different and this explanation is not in contradiction with a unique molecular ordering matrix as can be seen using a crude enzyme-like model. This effect is actually the same that enabled Samulski et al. to see the enantiotopic deuterons of the benzylic alcohol-α-α'-d_2.[10]

Finally, it is sometime possible to observe very small differential molecular ordering effects between isotopic enantiomers. The result on CHD_2–OH, where it was shown that it is possible to distinguish the enantiotopic deuterons, allowed for the hope that this chiral solvent would enabled us to visualize the enantiomers of the chiral methanol CHDT–OH.

Acknowledgment. The authors thank Dr. Barnier and Dr. Blanco[14] for samples of deuterated dimethylcyclohexanone derivatives. A.L. acknowledges support by the Fund for the Promotion of Research at the Technion and by Technion V.P.R. Fund.

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