# Visualisation of axial chirality using $^2$H-{$^1$H} NMR in poly(γ-benzyl L-glutamate), a chiral liquid crystal solvent

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**Disubstituted, racemic, axially chiral compounds with true and isotopic chiralities have been discriminated through the differential ordering effect of enantiomers when dissolved in a chiral liquid crystal solvent made of organic solutions of poly(γ-benzyl L-glutamate).**

As a result of the widespread interest in the axial chirality found in allenes[1–4] and alkylidenecyclohexanes,[5] it is important to develop a general, reliable and precise method for the measurement of their enantiomeric excesses (ees).[1] It is already known that, for some disubstituted allenes, the use of $^1$H NMR chiral lanthanide shift reagents (CLSR)[1,6a–c] and $^{195}$Pt[1] and $^{31}$P[6d] NMR chiral derivatising agents (CDA), give good results. Recently, ees of trisubstituted allenes and bromoallenes were determined by $^1$H NMR[6e] using as a permethylated β-cyclodextrin a chiral solvating agent (CSA).

A direct and very efficient technique has been recently developed in our laboratory, using deuterium NMR in a chiral liquid crystal medium made of organic solutions of poly(γ-benzyl L-glutamate) (PBLG).[7a–c] This technique appears to be much more sensitive and more general than those previously described in which only the variation of a chemical shift is utilised. In our anisotropic environment, enantiomers have different averaged orientations towards the PBLG α-helix which results in a difference in the order-sensitive NMR interactions, noticeably the deuterium quadrupolar splitting ($\Delta\nu_Q$). Thus the proton-decoupled deuterium NMR [$^2$H-{$^1$H} NMR] spectrum of a chiral deuteriated substrate in a PBLG–organic solvent medium is evident and appears as two quadrupolar doublets, one for each enantiomer. A schematic illustration is given for a 50% ee mixture (Fig. 1).

The differential ordering effect[8] of enantiomers may be defined as the difference between the quadrupolar splittings of the *R* and *S* molecules: DOE = $|\Delta\nu_Q^R - \Delta\nu_Q^S|$. More conveniently the DOE value relative to the average splitting is used; eqn. (1). The NDOE may be seen as an enantiomeric discrimination measurement.

$$\text{NDOE} = (|\Delta\nu_Q^R - \Delta\nu_Q^S|)/[\tfrac{1}{2}(|\Delta\nu_Q^R| + |\Delta\nu_Q^S|)] \qquad (1)$$

This communication describes the application of the PBLG method to visualise axially chiral racemic compounds **1**–**4**§

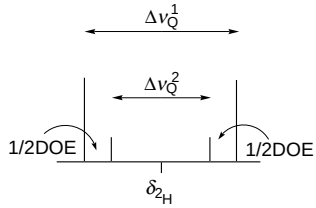
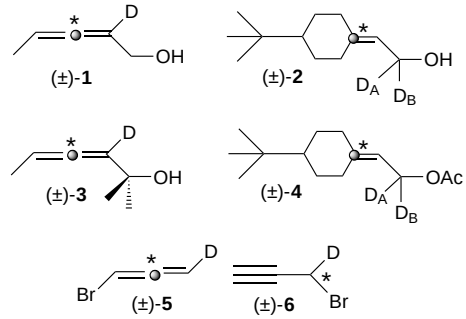



**Fig. 1** Enantiomer visualisation using $^2$H-{$^1$H} NMR in PBLG. When the enantiomers are not assigned, the superscripts *R* and *S* in eqn. (1) are replaced by 1 and 2.




bearing *polar* substituents. The $^2$H-{$^1$H} NMR spectra in PBLG–organic solvent media of products **1**–**4** have been recorded. For all of them the discrimination between enantiomers is large enough to allow an accurate ee measurement (Fig. 2). The enantiomers of primary alcohols **1** and **2** appeared as one and two pairs of doublets respectively. The deuterium of

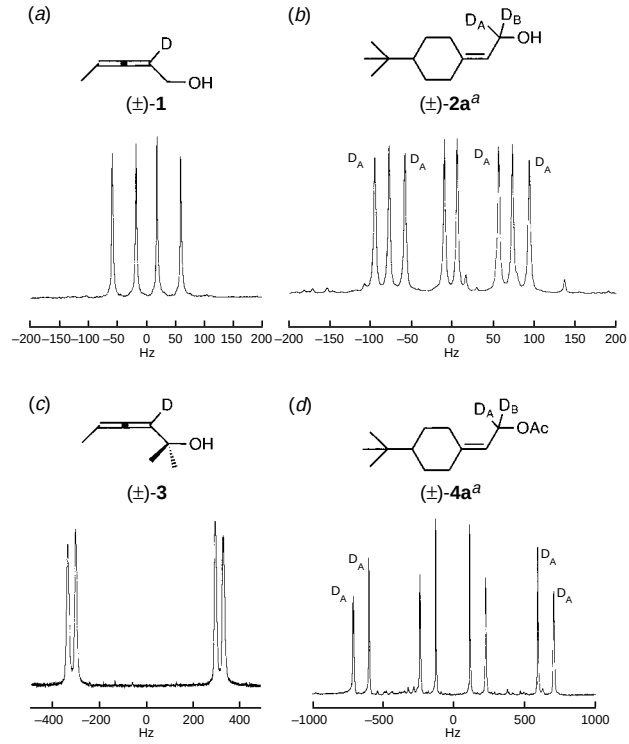



**Fig. 2** Visualisation of axial chiralities in compounds (±)-**1**–(±)-**4** using $^2$H-{$^1$H} NMR (64.1 MHz) in PBLG–organic solvent mixture. [a] For clarity, only diastereotopic deuteriums $D_A$ are quoted, the remaining signals belong to $D_B$.

**Table 1** Enantiomeric discrimination of racemic axially chiral compounds (±)-**1**–(±)-**5** using $^2$H-{$^1$H} NMR (64.1 MHz at 300 K) in PBLG–organic solvent

| Entry/ compound no. | Solvent | PBLG (%) | $\Delta\nu_Q^1$/ Hz[a] | $\Delta\nu_Q^2$/ Hz[a] | NDOE |
|---|---|---|---|---|---|
| **1** | $CH_2Cl_2$ | 14 | 118 | 36 | 1.06 |
| | | | 164 | 96 | 0.52 ($D_A$) |
| **2** | $CH_2Cl_2$ | 14 | | | |
| | | | 141 | 19 | 1.51 ($D_B$) |
| **3** | DMF | 30 | 664 | 595 | 0.11 |
| | | | 1413 | 1190 | 0.17 ($D_A$) |
| **4**[b] | DMF | 30 | | | |
| | | | 462 | 239 | 0.63 ($D_B$) |
| **5** | $CHCl_3$ | 19 | 231 | 174 | 0.28 |
| **6** | $CHCl_3$ | 19 | 951 | 631 | 0.40 |

[a] For racemic compounds (±)-**1**–(±)-**6**, quadrupolar splittings of the *R* and *S* enantiomers are not known at this stage, therefore, in the formula (see text) superscripts *R* and *S* are replaced by 1 and 2 [eqn. (1)]. [b] At 320 K.

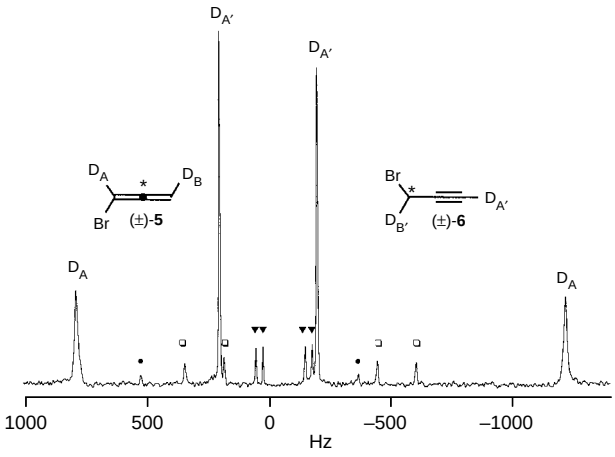



**Fig. 3** Visualisation of allenic and prop-2-ynylic isotopic chiralities in compounds (±)-**5** and (±)-**6** using $^2$H-{$^1$H} NMR (64.1 MHz) in PBLG, $CHCl_3$ at 300 K; (●) $CDCl_3$, (▼) $D_B$ in (±)-**5** and (□) $D_{B'}$ in (±)-**6**

allene **1** is split with an NDOE value of 1.06 (entry 1, Table 1) [Fig. 2(*a*)], whereas the $D_A$ and $D_B$ diastereotopic deuteriums of methylenecyclohexane **2**, are split with NDOEs of 0.52 and 1.51 respectively (entry 2, Table 1) [Fig. 2(*b*)]. The excellent visualisation of the enantiomers of alcohols **1** and **2** is probably due to a hydrogen-bond interaction between their primary hydroxy groups and the PBLG in $CH_2Cl_2$. Indeed, in this solvent, low or even no discrimination was observed with the corresponding tertiary alcohol **3** and primary acetate **4** respectively, which are known to give poor hydrogen-bonding associations. The enantiomers of **3** and **4**, are well-differentiated only when $CH_2Cl_2$ is replaced by DMF, together with a PBLG concentration increasing from 14 to 30%. Again, two and four doublets were observed for **3** and **4**, with NDOEs of 0.11, 0.17 and 0.63 respectively (entries 3 and 4, Table 1) [Fig. 2(*c*) and (*d*)]. In the methylenecyclohexanes **2** and **4**, the differentiation of diastereotopic deuteriums with no-discrimination through their chemical shifts ($\delta_A$ and $\delta_B$), mainly arises from a different orientation of the C–$D_A$ and C–$D_B$ bonds towards the magnetic field [Fig. 2(*b*) and (*d*)].

The efficiency of the PBLG technique may be emphasised by the result obtained with the allenic bromide **5**§ which is chiral only by virtue of an isotopic substitution. It is worth noting that the enantiomers of this compound, now, identically orientated but with an axis of isotopic chirality, are discriminated with an NDOE of up to 0.28 (entry 5, Table 1) (Fig. 3). Furthermore and as expected, enantiomers of an acetylenic counterpart **6**§ with a centro-symmetric isotopic chirality[7c] are also discriminated (entry 6, Table 1) (Fig. 3).

In conclusion, the $^2$H-{$^1$H} NMR spectra in PBLG successfully discriminate enantiomers with the axis of true chirality found in allenes **1**, **3** and methylenecyclohexanes **2**, **4** bearing *polar* substituents, whether or not the substituents interact strongly through hydrogen-bonding with PBLG. Whereas, enantiomers of bromoallene **5** with an axis of isotopic chirality are clearly visualised by our method.

## Footnotes and References

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§ Compounds **1**–**6** gave satisfactory mass and/or $^1$H, $^2$H and $^{13}$C NMR data. Allenols **1** and **3** were synthesised by the Landor method[2] ($LiAlD_4$ reduction of mono-THP-ether of prop-2-ynylic glycol followed by elimination of OTHP). Bromides **5** and **6** were obtained as a mixture by the Elsevier method[3] (bromination of prop-2-ynylic tosylate followed by a prop-2-ynylic–allenic rearangement). Finally, **2** and **4** were obtained by Wittig–Horner reaction of 4-*tert*-butyl cyclohexanone[5] followed by $LiAlD_4$ reduction and subsequent esterification using $Ac_2O$, DMAP and $Et_3N$.

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