

Use of two-dimensional correlation between ^2H quadrupolar splittings and ^{13}C CSA's for assignment of NMR spectra in chiral nematics

Olivier Lafon, Philippe Berdagué and Philippe Lesot*

Laboratoire de Chimie Structurale Organique, CNRS UMR 8074, ICMMO, Bât. 410, Université de Paris-Sud, 91405, Orsay cedex, France. E-mail: philesot@icmo.u-psud.fr; Fax: 33 (0)1 69 15 81 05; Tel: 33 (0)1 69 15 47 59

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The possibility of correlating visible spectral enantiodiscriminations in a single 2D map using simultaneously both quadrupolar and dipolar nuclei is presented and experimentally demonstrated. The method uses deuterium-carbon-13 heteronuclear 2D experiments with ^{13}C in natural abundance applied to deuterated compounds oriented in chiral, nematic liquid crystals (PBLG/ CHCl_3). Illustrative examples involving chiral and prochiral solute molecules are analysed and discussed. We show that this approach provides an efficient and elegant way to assign deuterium resonances for each enantiomer or enantiotopic directions in prochiral molecules.

1. Introduction

Proton-decoupled deuterium (^2H - $\{^1\text{H}\}$) and proton-decoupled carbon-13 (^{13}C - $\{^1\text{H}\}$) 1D NMR spectroscopies using weakly orienting, chiral, nematic liquid crystals (CLC's), made of poly- γ -benzyl-L-glutamate (PBLG) or poly- ϵ -carbobenzyloxy-L-lysine (PCBLL), as chiral ordering agents (COA) are efficient tools for the enantiomeric and enantiotopic analysis.^{1,2} From a practical point of view, the spectral enantiodifferentiation in ^2H - $\{^1\text{H}\}$ NMR and ^{13}C - $\{^1\text{H}\}$ NMR is based on differences of quadrupolar splittings, $\Delta\nu_Q^R \neq \Delta\nu_Q^S$ (spin $I > 1$), and ^{13}C chemical shift anisotropies (^{13}C CSA's), $\Delta\sigma^R \neq \Delta\sigma^S$, respectively.

In previous works, we have reported spectral enantiodistinctions using separately ^2H - $\{^1\text{H}\}$ or ^{13}C - $\{^1\text{H}\}$ NMR but the correlation between the two sets of NMR data was only possible when enantiomerically enriched mixtures were studied.³ Furthermore, such a strategy is obviously totally precluded in case of prochiral molecules that can never present any enantiomeric enrichment, and hence only NMR approaches can be used to reach this aim. To correlate ^2H quadrupolar splittings with ^{13}C CSA's for a pair of enantiomers dissolved in chiral nematics could prove to be useful. Indeed, this possibility can be used, e.g., to facilitate the spectral assignment of ^{13}C and ^2H resonances as well as to investigate the ^{13}C nuclear shielding and ^2H quadrupolar tensors of each enantiomer.

To overcome the weak chemical shift dispersion of signals in ^2H tilted Q -COSY 2D spectra,¹ we have recently proposed an efficient deuterium-carbon 2D correlation NMR experiment, to analyse isotopically labelled solutes dissolved in weakly ordering liquid crystals.⁴ The method is based on the use of deuterium-carbon-13 correlation 2D experiments (derived from HETCOR experiments, hereafter referred to as CDCOM experiments (Carbon-Deuterium Correlation in Oriented Media) to simplify the notation. The pulse scheme can be found in ref. 4.

After a two-step phase cycle and disregarding all relaxation terms and phase factors, the simplest expression of the NMR signal, $S(t_1, t_2)$, for a coupled deuterium-carbon-

^{13}C pair is

$$S(t_1, t_2) = A \{ \sin[(2\pi\nu_D - \pi\Delta\nu_Q)(t_1 + \tau)] + \sin[(2\pi\nu_D + \pi\Delta\nu_Q)(t_1 + \tau)] \} \times \{ \sin(\pi^1 T_{CD}\tau) \times \sin(2\pi^1 T_{CD}\tau') \exp[i2\pi\nu_C(\tau' + t_2)] \} \quad (1)$$

In this equation, A is the amplitude of the signal, $\nu_{2\text{H}}$ and $\nu_{^{13}\text{C}}$ denote the ^2H and ^{13}C frequencies while $\Delta\nu_Q$ and $^1T_{CD}$ denote the ^2H quadrupolar splitting and the ^{13}C - ^2H total spin-spin couplings where $^1T_{CD} = ^1J_{CD} + 2^1D_{CD}$, respectively, each of them being expressed in Hz. The double Fourier transform of this signal allows us to correlate ^{13}C chemical shifts in the F_2 dimension to the ^2H quadrupolar splittings centred on their respective chemical shifts in the F_1 dimension. The refocussing delays, τ and τ' , are equal to $1/(2 \ ^1T_{C-D})$ and $1/(6 \ ^1T_{C-D})$, respectively.⁴

The use of HETCOR scheme with ^{13}C detection is advantageous compared with the ^2H detection because this allows shorter recycling times between subsequent scans and therefore the total time for such 2D experiments can be significantly reduced.⁴ This situation is very adapted for weakly ordered deuterated compounds because the values of the $T_{1\text{H}}$ vary generally between 0.3 and 1 s.

In a recent work,⁴ we have reported the analysis of a fully deuterated chiral acid, the 2-ethylhexanoic acid- d_{15} , dissolved in an organic solution of PBLG. However as the ^{13}C CSA for sp^3 hybridized carbon atoms is generally very small, no spectrally-resolved ^{13}C enantiodistinction was observed for this compound, thus preventing the possibility to correlate deuterium and carbon data for each optical isomer. Because ^{13}C CSA is magnetic field sensitive, NMR enantiodiscriminations involving both deuterium and carbon-13 in a single 2D map could be obtained using spectrometers operating at higher fields. However it was more pertinent (and obviously less expensive !!) to explore other examples containing sp and sp^2 carbon atoms for which the ^{13}C CSA is larger.

In the present paper, we report the possibility to experimentally correlate in a single heteronuclear 2D map the spectral enantiodiscrimination induced by a CLC using simultaneously quadrupolar and dipolar NMR nuclei. For this purpose, we

have investigated the case of selectively monodeuterated enantiomers, the 1-deutero-1-octyn-3-ol (**1**) and the case of a perdeuterated prochiral molecule with C_s symmetry, the 1-deutero-di-(2',3',4',5',6'-pentadeuterophenyl)methanol (**2**), both of them being embedded in the PBLG/chiral nematic solvent. The molecular structures of compounds and their numbering system are sketched in Fig. 1.

2. Experimental

Synthesis

Compounds **1** and **2** were synthesised following standard procedures according to the reported procedures in ref. 5 and 6, respectively. Both compounds are not labelled with carbon-13.

NMR sample preparation

The liquid-crystalline NMR samples investigated in this work were prepared using a standard procedure described elsewhere.⁴ The NMR samples of were prepared using 100 mg of PBLG (commercially available from Sigma) with a MW \sim 112 000 50 mg (**1**) or 100 mg (**2**) of solute, and around 400 mg of $CHCl_3$ directly weighed into a 5 mm od NMR tube. Note that all 5 mm od NMR tubes were sealed to avoid organic solvent evaporation and centrifuged back and forth until an optically homogeneous birefringent phase was obtained.

NMR spectroscopy

The 1D and 2D NMR experiments were performed at 9.4 T on a Bruker DRX 400 high-resolution spectrometer equipped with a direct multinuclear broadband probe (BBO) operating at 61.4 MHz for deuterium and 100.6 MHz for carbon-13. The temperature of the sample was controlled by the standard variable temperature unit (BVT 3200) and the NMR tube was not spun. All NMR experiments have been recorded at 300 K. The 2D matrices are zero-filled to $1k(t_1) \times 2k(t_2)$ data points prior to the double Fourier transformation, and the spectra are displayed in magnitude mode. For the carbon-deuterium correlation 2D experiments, the deuterium channel (lock) of the BBO probe was used. Proton broadband decoupling was achieved using the standard WALTZ-16 composite pulse sequence.⁷ Due to the small magnitude of the residual 1H - 2H , 1H - ^{13}C or 2H - ^{13}C dipolar couplings (few hertz) and the magnitude of quadrupolar splittings (<1500 Hz), the 1H and 2H decoupled ^{13}C spectra of solutes embedded in organic solutions of PBLG do not necessitate more average power than for isotropic samples. Attempts to perform deuterium

decoupling using GARP, COMARO or SPINAL pulse sequences have not improved the quality of decoupled ^{13}C spectra.⁸ For carbon-13 spectra, the chloroform signal was used as internal reference and assigned at 77.0 ppm. Other experimental NMR parameters or details are given in the figure captions.

3. Results and discussion

Binuclear NMR differentiation of enantiomers

Enantiodiscriminations based both on a difference of 2H quadrupolar splittings and ^{13}C chemical shift anisotropies can be expected for chiral, deuterated molecules having sp or sp^2 hybridized carbon atoms, such as compound **1**. Indeed, on these sites we benefit from a large shape anisotropy of the C-13 electronic cloud, and hence visible spectral discriminations can occur even if the ordering difference between the enantiomers is small.^{9,10} In contrast, no special condition is required to discriminate enantiomers using 2H quadrupolar splittings because this order-dependent interaction presents an excellent sensitivity to an orientational difference.^{1,11} As a consequence, enantiomers of almost all organosoluble chiral molecules have been discriminated using deuterium NMR in PBLG so far, including the difficult case of flexible chiral alkanes.¹²

The deuterium-coupled carbon signal associated with C-1 of **1** consists of two partially overlapped triplets of 1 : 1 : 1 relative intensity centered on two distinct chemical shifts, thus indicating a spectral enantiodistinction. The ^{13}C - $\{^1H, ^2H\}$ spectrum confirms this analysis since the spectral pattern for C-1 is reduced to two independent ^{13}C lines, one for each enantiomer. The spectral splittings between two successive components (for each triplet) allows the determination of the absolute value of deuterium-carbon total coupling $|^1T_{CD}|$ ($|^1T_{CD}| = |^1J_{CD} + 2^1D_{CD}|$) for each enantiomer.¹ The measured values for the two enantiomers are 11.8 and 28.3 Hz.

In Fig. 2a we present the CDCOM 2D contour plot of (\pm)-**1** recorded in 15 h. The delays τ and τ' of the sequence were set to 23.8 and 7.9 μ s, respectively, corresponding to the average value of $|^1T_{CD}|$ equal to 21 Hz. As expected, if one-bond magnetisation-transfer processes dominate, only the acetylenic carbon atom bearing the deuterium nucleus exhibits heteronuclear cross-correlation on the 2D map. Besides, the existence of two pairs of correlations between deuterium and carbon-13 signals located on two distinct ^{13}C chemical shifts indicates clearly that the chiral discrimination is observed on both

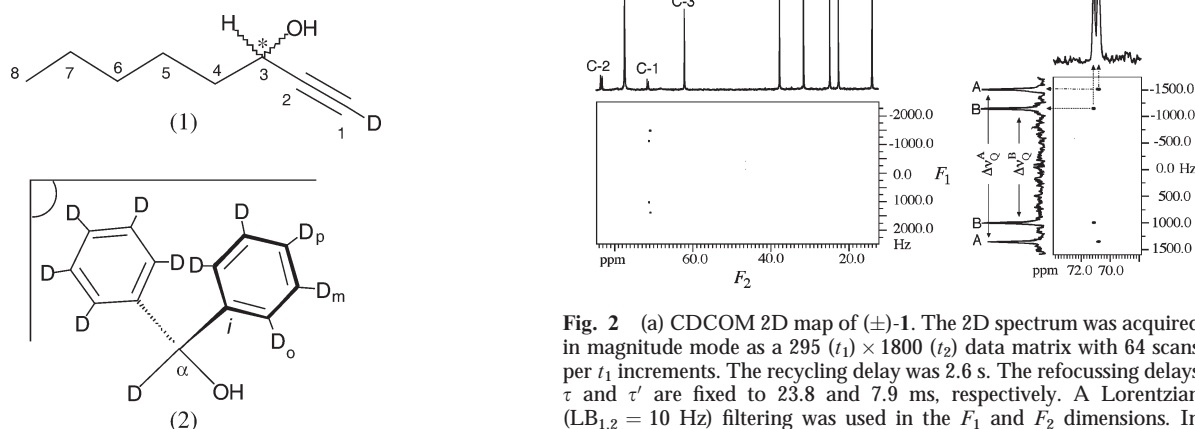


Fig. 1 Chemical structures of compounds **1** and **2** showing the numbering or the notation of the atoms used. The chemical notation (α , i , o , m , p) for **2** defines both the deuterium and the carbon atoms.

Fig. 2 (a) CDCOM 2D map of (\pm)-**1**. The 2D spectrum was acquired in magnitude mode as a $295(t_1) \times 1800(t_2)$ data matrix with 64 scans per t_1 increments. The recycling delay was 2.6 s. The refocussing delays τ and τ' are fixed to 23.8 and 7.9 ms, respectively. A Lorentzian ($LB_{1,2} = 10$ Hz) filtering was used in the F_1 and F_2 dimensions. In the F_2 projection the ^{13}C - $\{^1H, ^2H\}$ 1D spectrum is displayed. Note the total absence of C-D correlations for non-labelled carbon atoms. (b) Expansion associated with signal C-1 acetylenic carbon atom. In F_1 and F_2 dimensions are displayed the 2D projections.

nuclei. Note here that the difference in chemical shift for C-1 ($\Delta\delta = \delta^A - \delta^B = 32$ Hz) is particularly large in this example, thus indicating a large difference in the ^{13}C CSA.¹⁰ This result is, therefore, the first binuclear enantiodistinction observed simultaneously using a single heteronuclear 2D map and involving both quadrupolar and dipolar nuclei.

The analysis of the 2D map indicates that the outer ($|\Delta\nu_Q^A| = 2849$ Hz) and inner ($|\Delta\nu_Q^B| = 2139$ Hz) quadrupolar doublets correlate with the shielded carbon atom ($\delta^A = 70.92$ ppm) and deshielded carbon atom ($\delta^B = 71.24$ ppm), respectively. In this particular example, we can demonstrate that there exists a mathematical relationship between the relative position of the acetylenic ^{13}C resonances (δ^A and δ^B) and the relative magnitude of ^2H quadrupolar doublets, $\Delta\nu_Q^A$ and $\Delta\nu_Q^B$. Thus, assuming that the quadrupolar and nuclear shielding tensors are axial and colinear for the alkyne fragment, we can write that

$$\Delta\nu_Q^A - \Delta\nu_Q^B = \frac{9K_{\text{C-D}}}{4\zeta} (\delta^A - \delta^B) \quad \text{with} \quad K_{\text{C-D}} = \frac{e^2Qq_{a'a'}}{h} \quad (2)$$

where ζ and $q_{a'a'}$ are the main components of the electronic screening and electric field gradient, respectively, both along the CD bond.¹¹ In this equation, K_{CD} is positive and ζ (related to CSA) is negative for an oblate axial tensor (here, $\eta = 0$) according to the definition given in ref. 13. Because the differential ordering effect between enantiomers is rather small in organic solutions of PBLG, and disregarding quadrupolar splittings close to zero, we can confidently assume that the two quadrupolar doublets possess the same sign. This situation is advantageous because we can then determine the absolute sign of the alkyne quadrupolar splittings when spectral enantiodiscrimination is observed both on deuterium and deuterium-decoupled carbon-13 nuclei. When the outer ^2H quadrupolar doublet is correlated to the most deshielded carbon, the sign of quadrupolar splittings is negative. In contrast, when the outer doublet is correlated to the most shielded ^{13}C resonance, both quadrupolar splittings have a positive sign. Such a spectral occurrence is observed here, and implies that the order parameter for the alkyne CD internuclear axis is positive.¹ As this kind of molecules can be modelled as a crude rod, the NMR results clearly indicate that the molecular long axis of **1** is aligned parallel along the magnetic field axis on average. This orientational behaviour is consistent with previous results.^{3,9,12}

Binuclear NMR differentiation of enantiotopic C–D directions in prochiral molecules

In a second step, we have explored the case of a polydeuterated prochiral molecule. The phenomenon of enantiotopic discrimination in chiral liquid crystalline solvents is determined by a change in the orientational probability function, $P(\Omega)$, and physically relates to the change in the symmetry of the intermolecular potential experienced by the solute when the environment is chiral compared with achiral media.^{14–17} Consequently, prochirality can be *a priori* experimentally observed by NMR in chiral liquid crystals as we have shown in previous work.^{14–17}

For our purpose we have chosen the 1-deuteriodi-(2',3',4',5',6'-pentadeuterophenyl)methanol (**2**). This prochiral molecule possesses both enantiotopic directions (aromatic C–D bonds) as well as enantiotopic nuclei (aromatic carbon atoms) susceptible to be spectrally differentiated using both ^2H and ^{13}C - $\{^2\text{H}\}$ NMR.¹⁴ In this example, we benefit from aromatic sp^2 hybridised carbon atoms that can exhibit significant ^{13}C CSA.¹³ For the sake of clarity, we will use hereafter the notation *i*-X, *o*-X, *m*-X, *p*-X for nuclei X (X = C or D) in *ipso*, *ortho*, *meta* and *para* positions in the benzenic cycle, and α -X for nuclei associated with the prostereogenic methine

group. Note here that the pairs of deuterium atoms and carbon atoms in *ortho* position as well as in *meta* position are homotopic for each phenyl group, hence totally equivalent even if a chiral oriented solvent is used.

The ^2H - $\{^1\text{H}\}$ 1D spectrum of **2** is reported in Fig. 3a. This spectrum presents seven quadrupolar doublets associated with the *ortho*-, *meta*-, *para*- and α -deuterons of the molecule. The most shielded quadrupolar doublet (labelled α -D) can be easily assigned to the α -deuteron while the pair of doublet with small intensity (labelled *p*-D) corresponds to the single aromatic deuteron in *para*-position. The other doublets correspond to the *ortho*- and *meta*-deuterons, but their assignment is not straightforward.

Due to ^2H - ^2H long-distance dipolar couplings, the deuterium-coupled carbon-13 1D spectrum of the aromatic region (not presented) is a congested second order spectrum, difficult to interpret and its analysis is beyond the scope of this paper. The aromatic ^{13}C - $\{^2\text{H}\}$ spectrum (Fig. 3b) is more interesting to analyse as only independent ^{13}C resonances appear here.

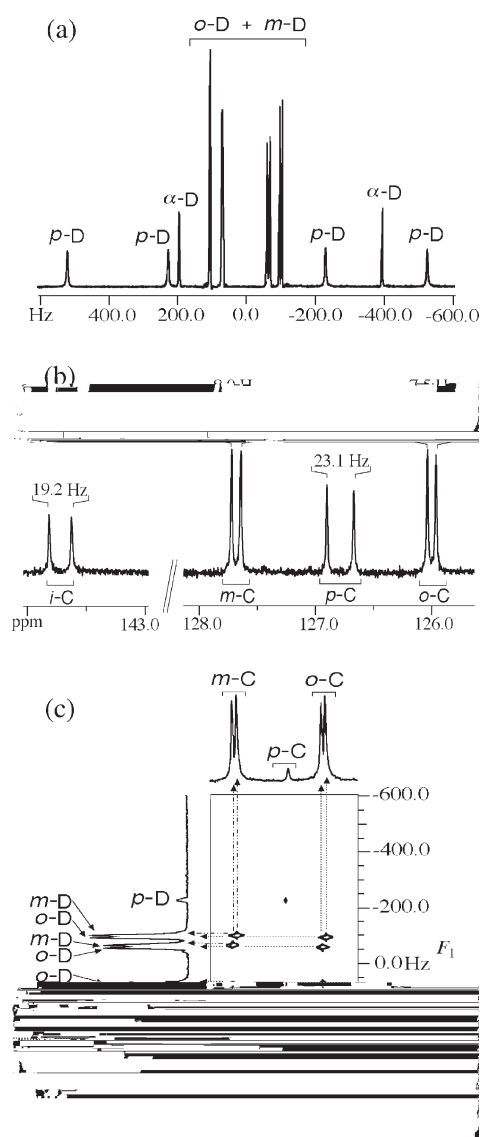


Fig. 3 (a) and (b) ^2H - $\{^1\text{H}\}$ and aromatic region of the ^{13}C - $\{^2\text{H}\}$ 1D spectra of **2** recorded with 64 and 512 scans, respectively. A Gaussian filtering (LB = -4.5 Hz, GB = 40%) is used to enhance the spectral appearance of the ^2H - $\{^1\text{H}\}$ spectrum. (c) CDCOM 2D map of **2** showing the signals of *ortho*, *meta* and *para* aromatic nuclei. The 2D spectrum was acquired in magnitude mode as a $256 (t_1) \times 1800 (t_2)$ data matrix with 32 scans per t_1 increments. The recycling delay was 2 s. A Gaussian (LB₁ = -3 Hz, GB₁ = 50%) and Lorentzian (LB₂ = 1 Hz) filtering was used in the F_1 and F_2 dimensions, respectively.

As the methine carbon atom (C-1) belongs to the molecular symmetry plane of **2**, no enantiodiscrimination can be detected. In contrast, we have experimentally detected four pairs of singlets associated with the four enantiotopic carbon atoms of the aromatic ring, thus showing the spectral enantiodiscrimination. The ^{13}C peak assignment is confidently based on additive rules for benzene substituents.¹⁸ Note that the assignment of the ^{13}C resonances can be accomplished using ^{13}C - ^{13}C INADEQUATE experiment in isotropic phase,^{4,19} because the ^{13}C chemical shifts in PBLG and in liquid are generally expected to be similar disregarding the enantiomeric or enantiotopic distinction. In this example, the difference of chemical shift anisotropies for the carbon atoms *i*-C, *o*-C, *m*-C and *p*-C are 19.2 Hz, 8.0 Hz, 7.5 Hz and 23.1 Hz, respectively. Note that the largest spectral enantiodiscrimination is obtained on the enantiotopic *para*-carbon atoms. A similar result is also observed in ^2H NMR because the *para*-deuteron also shows the largest quadrupolar difference. This spectral situation could be related to the fact that the molecular long axis is more or less aligned along the *ipso*-*para* carbon direction.

As aimed in this study, the possibility to correlate deuterium and carbon signals of **2** should provide a way to easily assign the quadrupolar doublets associated to the *ortho*- and *meta*-deuterons. Fig. 3c presents the CDCOM 2D spectrum of **2** centered on the carbon-13 aromatic region (the signal of *ipso*-carbon atom is not shown). The 2D spectrum was recorded in around 6 h using a recycling delay below 2 s and refocussing delays τ and τ' equal to 28.6 ms and 9.4 ms, respectively, corresponding approximately to the average of $|^1T_{\text{CD}}|$ values for the aromatic region (*ca.* 17.5 Hz).

Surprisingly, the intensity of the ^{13}C signal associated with the *para*-carbon atoms strongly differs from those observed on the ^{13}C - $\{^2\text{H}\}$ 1D spectrum. Thus one of resonance is not visible on the 2D map anymore while the other one shows an important loss of intensity. Theoretically, four distinct reasons can explain such an experimental result. Two of them are related to the spectral features of the solute under study, others find their origin in the principle of the CDCOM sequence. First of all, the total carbon-deuterium coupling, $^1T_{\text{CD}}$, can be averaged to zero ($^1J_{\text{CD}} = -2^1D_{\text{CD}}$), thus precluding the deuterium to carbon-13 magnetization transfers, and hence eliminating any heteronuclear correlations.⁴ Second, very small values for $^1T_{\text{CD}}$ can require unacceptably large delays for the τ and τ' periods in the CDCOM sequence with respect to deuterium T_1 relaxation times, that are generally very small in liquid crystalline solvent (<0.7 s). Third, it is impossible to optimize the refocussing delays to the $^1T_{\text{CD}}$ value for each CD pair, even using an average value of the $^1T_{\text{CD}}$. "Accordion" or tridimensional NMR sequences could be advantageously considered to limit this effect.^{19,20} Fourth, eqn. (1) points out that the signal for the CDCOM sequence depends on ^{13}C and ^2H chemical shifts as well as the quadrupolar splittings during the refocussing delays τ and τ' . Such a modulation can reduce the intensity of the observed signal. The refocalisation of these interactions using a judicious choice of ^{13}C and ^2H 180°-pulses and ^2H 90°-pulses should eliminate this dependence. This problem is currently under investigation.

In this example, the lack of signal for the enantiotopic *para*-deuterons is mainly due to extremely short deuterium T_1 relaxation times. Indeed, the measurement of T_1 relaxation times for the *para*-deuterons is *ca.* 45 ms, while the T_1 for enantiotopic deuterons in *ortho* and *meta* position is over 90 ms. These values have to be compared with delay τ equal to 28.6 ms. In addition, for the most deshielded signal associated with the *para*-carbon atom, the magnitude of $^1T_{\text{CD}}$ is below 3 Hz, thus reducing considerably the magnitude of the deuterium to carbon magnetization transfer. This value was extracted from the analysis of a carbon-deuterium "T"-resolved 2D experiment of **2** shown in Fig. 4. This 2D

experiment directly derives from the well-known proton-carbon-13 *J*-resolved applied in isotropic solvents.¹⁹⁻²¹ Similarly to the heteronuclear *J*-resolved spectrum, the deuterium-decoupled carbon signals and the deuterium-carbon coupling patterns are observed in the F_2 and F_1 dimensions, respectively. Note that the long-range C-D couplings contribute to linewidths in F_1 dimension. In case of monodeuterated carbon atoms, the spectral patterns consist of triplets with 1:1:1 relative intensity parallel to the F_1 axis, centred at 0 Hz, and located at the corresponding carbon frequency on the F_2 axis. Separations between two deuterium resonances are equal to the $|^1T_{\text{CD}}|/2$. On the 2D map of **2**, we can see a single, large correlation peak for the most deshielded *para*-carbon atom signal, instead of three if the total deuterium-carbon-13 spin-spin coupling was not null and larger than the peak linewidths. Such a situation clearly indicates that the C-D coupling is below 2-3 Hz.

Finally, the analysis of data for the deuterium and carbon atom in *para* position shows that the smallest quadrupolar splitting is correlated with the most shielded carbon signal.

Here again, the analysis of the CDCOM 2D spectrum reveals immediately the correlation between deuterium quadrupolar doublets and carbon signals, and thereby they can be easily used for assigning the aromatic quadrupolar doublets. The deuterium and carbon-13 spectral data of **2** are listed in Table 1 as well as valuable information related to the enantiodiscrimination, such as the ^2H DOE factor that provides a quantitative measurement of the differential ordering effect (DOE) between two given enantiomeric or enantiotopic directions in the CLC, and hence may be used to rationalize a series of experimental results.^{1,12} In this second example, it appears that the most shielded ^{13}C resonances correlate with the largest deuterium quadrupolar doublet for the *ortho*- and *meta*-carbon atoms, but not for the *para*-carbon atom, thus emphasizing that there is no direct correlation between the magnitude of the quadrupolar

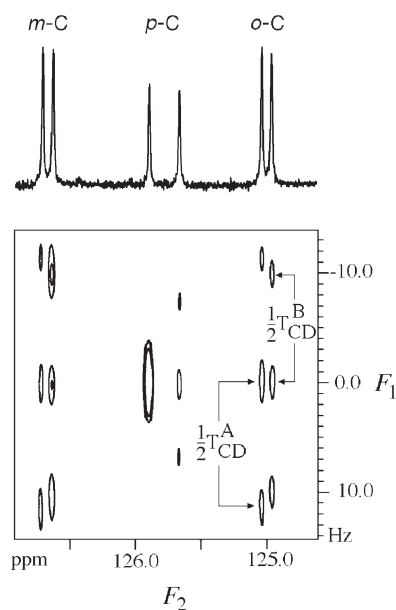


Fig. 4 ^{13}C - ^2H "T"-resolved 2D map of **2** recorded in less than 1 h and showing the signals of *ortho*, *meta* and *para* aromatic nuclei. The 2D spectrum was acquired in magnitude mode as a $100 (t_1) \times 2000 (t_2)$ data matrix with 32 scans *per* t_1 increments and a recycling delay of 2.1 s. Deuterium decoupling (CPD) is only applied during the first incremented period and the acquisition period of the sequence. In the F_2 projection the ^{13}C - $\{^1\text{H}, ^2\text{H}\}$ 1D spectrum is displayed. As the stereochemistry for the CD enantiotopic directions is not known the notations A and B are used.

Table 1 Spectral ^{13}C and ^2H data of compound **2** in the PBLG/ CHCl_3 phase at 300 K

Chem. notation	$\delta_{13\text{C}}^{\text{pro-R,S}}/\text{ppm}^a$	$ \Delta\delta_{13\text{C}} /\text{Hz}$	^{13}C DOE ^b	$ ^1\text{T}_{\text{C-D}} ^{\text{pro-R,S}}/\text{Hz}^c$	$ \Delta\nu_{\text{Q}} ^{\text{pro-R,S}}/\text{Hz}^d$	$ \Delta\Delta\nu_{\text{Q}} /\text{Hz}$	^2H DOE ^e
α	74.93	—	—	37	589	—	—
i	143.81	19.2	1.32	—	—	—	—
	143.62						
o	143.81	7.5	0.55	<3	203	73	0.44
	125.95						
m	126.03	8.0	0.63	15	129	70	0.40
	127.64						
p	127.72	23.1	1.81	24	209	70	0.40
	126.67						
	126.90			20	1045		

^a The accuracy of the δ_i is around ± 0.05 ppm. ^b $\text{DOE}(^{13}\text{C}) = \frac{|\delta^{\text{pro-R}} - \delta^{\text{pro-S}}|}{(\delta^{\text{pro-R}} + \delta^{\text{pro-S}})/2} \times 1000$. ^c The accuracy on the $^1\text{T}_{\text{C-D}}$ measured on the “T”-resolved 2D map is around ± 3 Hz. ^d The accuracy of the $\Delta\nu_{\text{Q}_i}$ values is ± 1 Hz, respectively. ^e $\text{DOE}(^2\text{H}) = \frac{|\Delta\nu_{\text{Q}}^{\text{pro-R}}| - |\Delta\nu_{\text{Q}}^{\text{pro-S}}|}{(|\Delta\nu_{\text{Q}}^{\text{pro-R}}| + |\Delta\nu_{\text{Q}}^{\text{pro-S}}|)/2}$.

doublets and ^{13}C chemical shifts associated with a pair of enantiotopic C–D directions.

4. Conclusion

In this work, we have reported the first simultaneous binuclear NMR enantiodiscriminations involving quadrupolar and dipolar nuclei in cases of deuterated chiral and prochiral materials dissolved in chiral nematic systems. The correlation of two kinds of spectral data probing enantiotopicity of molecules is important and was never obtained so far for prochiral molecules. This opportunity can provide valuable information that can be used for investigating the orientational order of two enantiomers, for instance, and therefore improve our understanding of the chiral recognition mechanisms in oriented helical polypeptides.²²

Intrinsic drawbacks of this approach include the requirement of isotopically enriched samples. Consequently, the ultimate achievement of this analytical tool would be its application for investigating natural abundance samples. This is likely to be a practical possibility shortly. Modern spectrometers operating at higher frequencies combined with double resonance, cryoprobes should answer such a challenge soon by solving the problem of sensitivity inherent to the simultaneous detection of two rare isotopic nuclei. To provide a comparison, calculations indicate that the sensitivity of a 600 MHz spectrometer equipped with a selective cryogenically cooled probe would be equivalent to a 1500 MHz spectrometer using a classical selective probe. As a second advantage, the use of very high frequency spectrometers will warrant larger spectral enantiodiscrimination on carbon-13 signals because the difference of chemical shift anisotropy is magnetic field dependent. Consequently, differentiation on sp^3 hybridized carbon atoms should be more efficient in these conditions.

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