Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 17 (2006) 1424–1429

Enantiodifferentiation of acyclic phosphonium salts in chiral liquid crystalline solutions

Abdelkrim Meddour,[a,*] Jacques Uziel,[b] Jacques Courtieu[a] and Sylvain Jugé[c,*]

[a]*Laboratoire de Chimie Structurale Organique, ICMMO, UMR 8074, Bât. 410, Université Paris Sud, 91405 Orsay Cedex, France*
[b]*Université de Cergy Pontoise, UMR CNRS 8123, 5 mail Gay Lussac 95031 Cergy Pontoise, France*
[c]*Université de Bourgogne, LSEO UMR CNRS 5188, 9 Av. A. Savary, 21078 Dijon, France*

Received 10 April 2006; accepted 18 April 2006

Abstract—The enantiodifferentiation of acyclic phosphonium salts bearing a stereogenic centre, whether on the phosphorus atom or on one of its substituents, was investigated by ^{2}H–$\{^{1}H\}$, ^{13}C–$\{^{1}H\}$ and ^{31}P–$\{^{1}H\}$ NMR in chiral liquid crystals composed of a polypeptide dissolved in an organic solvent. For the first time, the enantiomers of P-chirogenic phosphorus compounds were discriminated in these anisotropic media, affording good to excellent separation of the signals, allowing the determination of their proportion. While ^{31}P–$\{^{1}H\}$ NMR spectra showed no chiral separation, ^{2}H–$\{^{1}H\}$ NMR was efficient in the enantiodifferentiation of an isotopically labelled compound. Better still, ^{31}C–$\{^{1}H\}$ NMR in chiral liquid crystal appears as a powerful method for the enantiodifferentiation of this class of compounds, since separations of the signal up to 0.8 ppm were observed. In this commercially available anisotropic medium, ^{2}H and ^{13}C NMR offers a new promising alternative method for the enantiodifferentiation of chiral phosphonium salts.

1. Introduction

Considerable progress has recently been made in the asymmetric synthesis of P-chirogenic organophosphorus compounds, owing to the use of borane protecting groups.[1–4] The organophosphorus borane complexes are versatile reagents which allow either nucleophilic[2] or electrophilic attack[3] on the phosphorus atom, or alkylation at the α-position,[4] giving products that can be easily purified and handled. The borane complexes can be easily decomplexed to afford the corresponding tricoordinate phosphorus derivatives, or directly used for the preparation of phosphoryl compounds[5] and phosphonium salts,[6] or used in coordination chemistry.[7] This efficient chemistry opens up new fields for the use of chiral organophosphorus compounds, but that also raises the problem of the determination of their enantiomeric purity. Today, the enantiomeric purity of tricoordinate organophosphorus compounds is often determined by liquid chromatography on commercially available polysaccharide-based chiral columns of their borane complexes,[2–4,8] or by ^{31}P NMR of their adducts with the *ortho*-palladated dimethyl(α-methylbenzyl)amine complex.[9] Few chromatographic[10] or NMR methods have been described to date for phosphoryl compounds,[11] only the use of the TRISPHAT anion has been demonstrated by Lacour and by us to be a powerful chiral ^{1}H and ^{31}P NMR shift agent in the case of the phosphonium salts.[12] However, this reagent is not commercially available and not very soluble or stable in $CDCl_3$ solution.[13]

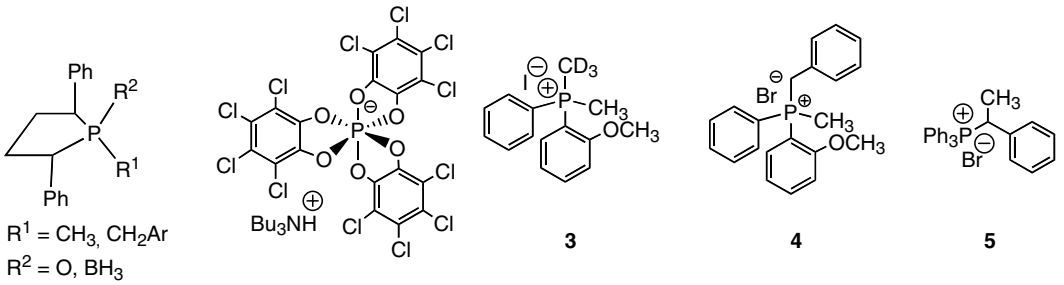
Recently, NMR spectroscopy in chiral liquid crystalline (CLC) solvents emerged as a powerful technique for the measurement of enantiomeric purity of a large variety of molecules. The best results were obtained through deuterium[14] or ^{13}C NMR[15] using concentrated solutions of commercially available polypeptides, such as poly-γ-benzyl-L-glutamate (PBLG) or poly-ε-carbobenzyloxy-L-lysine (PCBLL) in various organic solvents. In these media, enantiomers are oriented differently. This difference in orientation can be observed in the NMR spectra through dipolar couplings, D_{ij}, chemical shift anisotropies, $\Delta\sigma_i$, or quadrupolar splittings, $\Delta\nu_Q^i$, for spins $> 1/2$. It should be noted that dipolar couplings cannot be obtained directly from NMR spectra. For two non-equivalent nuclei, such as ^{31}P and ^{13}C, one observes the absolute value of the total spin-spin coupling $|T_{^{13}C-^{31}P}| = |2D_{^{13}C-^{31}P} + J_{^{13}C-^{31}P} + \Delta J_{^{13}C-^{31}P}|$ where $D_{^{13}C-^{31}P}$ is the dipolar coupling whereas

* Corresponding authors. Tel.: +33 3 80 39 61 13; fax: +33 3 80 39 60 98; e-mail: Sylvain.Juge@u-Bourgogne.fr

0957-4166/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2006.04.020

$J_{^{13}C-^{31}P}$ and $\Delta J_{^{13}C-^{31}P}$ are the isotropic and the anisotropic parts of the phosphorus–carbon-13 scalar coupling, respectively.[16] Accordingly, the enantiodifferentiation of several phosphine oxides and one phosphine borane derived from 2,5-diphenylphospholane **1** has been reported using $^{13}C-\{^1H\}$ NMR in CLC solutions.[17]

In continuation of our work on P-chirogenic phosphonium salts,[6,12] we herein report the enantiomeric discrimination of the acyclic compounds **3**–**5**, through ^2H or ^{13}C NMR spectroscopy in liquid crystalline solutions of commercially available polypeptides in DMF. The experimental conditions to observe such compounds are also outlined.



2. Results and discussion

Phosphonium salts **3**, **4** and **5** were obtained according to described procedures, either by quaternisation of the enantiomerically enriched phosphine borane with the corresponding alkyl halide,[6] or by heating triphenylphosphine with 1-phenylethylbromide.[12b]

The first step of this work was to establish the experimental conditions in which the polypeptidic liquid crystalline phase is stable in the presence of phosphonium salts. It appeared that the addition of small amounts (5–10 mg) of phosphonium salts to PBLG/chloroform liquid crystal (13–20 wt % PBLG, with PBLG Mol. Wt.: 70.000–150.000) resulted in the onset of an isotropic phase, coexisting with the liquid crystalline one.

A similar instability of PBLG mesophases was observed towards the addition of dichloroacetic acid[18] or trifluoroacetic acid,[19] two denaturant solvents. Onsager's[20] and Flory's[21] theoretical approaches of liquid crystal formation account for this behaviour. Both theories, emphasize the role of the L/d axial ratio (L is polymer length and d its diameter) in the anisotropic–isotropic transition. The critical concentration of the polymer necessary to form the liquid crystalline phase is expected to shift to a higher value when the L/d axial ratio of the polymer is decreased or flexibility is increased. Thus observation of the phase separation of small portions of isotropic phase from the liquid crystalline phase can be ascribed to an increase in the flexibility of PBLG α-helix induced by interactions between phosphonium halide ions and the polar amide groups of the polymer backbone.

In order to overcome this problem of phase stability, we used polypeptides with the largest molecular weight commercially available (Mol. Wt.: 150.000–300.000 for PBLG and 200.000–500.000 for PCBLL from Sigma), that is, polymers having the largest L. DMF was used as a co-solvent. The choice of this polar solvent was so as to minimise polymer-ions interactions. Under such conditions, stable liquid crystalline phases were obtained, which were compatible with the addition of at least 50 mg of phosphonium salts.

Once the stability of the liquid crystalline phase was realised, we undertook the chiral analysis of phosphonium halides; the first substrate studied was phosphonium iodide **3**. This compound is chiral due to isotopic substitution. We have already shown that deuterium NMR in PBLG liquid crystals was a powerful technique to observe the enantiomers of compounds bearing such chirality.[22] Here, the enantiomers of **3** were discriminated both in PBLG/DMF and in PCBLL/DMF mesophases. The $^2H-\{^1H\}$ NMR spectrum of **3** measured on a 400 MHz apparatus in PCBLL/DMF is shown in Figure 1. It exhibits quadrupolar splittings, $\Delta\nu_Q$, of 29 and 11 Hz for (*S*)- and (*R*)-enantiomers, respectively. In this spectrum, the phosphorus–deuterium spin–spin coupling was not observed. It was however revealed (and its value equals 2 Hz) when a strong filtering of the signal, using a Gaussian multiplication, was applied. The enantiomeric excess calculated from the integration of these signals is 53%. This value is in good agreement with the 54% ee, previously determined on a 600 MHz apparatus for this sample, using the TRISPHAT anion **2**.[12]

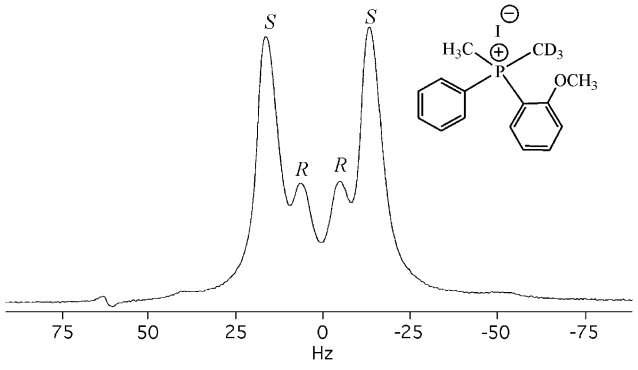


Figure 1. $^2H-\{^1H\}$ NMR spectrum of (*S*)-enriched phosphonium iodide **3** in PCBLL/DMF (22.9 wt % PCBLL) at $T = 305$ K.

Nevertheless, deuterated organophosphorus substrates are rather rare and consequently $^2H-\{^1H\}$ NMR spectroscopy cannot be used as a general method for the analysis of such

compounds. As no enantiomeric separation was observed in the ^{31}P–{^{1}H} NMR spectra for phosphonium salts **4** and **5**, we investigated these compounds by proton decoupled ^{13}C NMR spectroscopy.

For a given type of carbon in a molecule, enantiodifferentiation may be obtained on the basis of a difference in the chemical shift anisotropy, $\Delta\sigma$ [$\Delta\sigma(R) \neq \Delta\sigma(S)$], a difference in the ^{13}C–^{31}P total spin–spin coupling ($T_{^{13}C-^{31}P}(R) \neq T_{^{13}C-^{31}P}(S)$) or both. A formal description of spectral patterns associated with enantiodiscrimination through ^{13}C–{^{1}H} NMR in molecules bearing a 100% abundant magnetically active nucleus with spin $I = 1/2$, such as phosphorus or fluorine, is presented in Ref. 17. In order to test the efficiency of this approach, the ^{13}C–{^{1}H} NMR spectrum of racemic phosphonium bromide **4** was measured at 100.61 MHz in PBLG/DMF-d_7. Selected parts of this spectrum are presented in Figure 2a. As the analysis of this spectrum remains ambiguous, the ^{13}C–{^{1}H} NMR spectrum of pure (*S*)-**4** was also measured in the PBLG mesophase and is partially presented in Figure 2b. It confirms that enantiodifferentiation is achieved. Although the spectral separations are quite modest, the deconvolution of signals enables the determination of ee for an enriched sample with a quite good degree of accuracy. A complete assignment of the NMR resonances was performed and the data related to all the carbons, which exhibit enantiomeric discrimination, are reported in Table 1. For a given type of carbon (see Fig. 2 for carbon atoms numbering), (1) and (2) are related to the most and the less deshielded signals, respectively. Here, it should be pointed out that there is no direct relationship between the absolute configuration and the chemical shift anisotropy. Consequently, the NMR signals of one enantiomer should not be all shifted upfield (or downfield) relative to the signals of the other one. In other words, all the signals labelled (1) do not correspond to the same enantiomer. $|\Delta\Delta\sigma|$ is the absolute value of the difference in chemical shift anisotropy and $|\Delta T_{^{13}C-^{31}P}|$ is the absolute value of the difference in the total spin–spin coupling expressed in hertz. Isotropic chemical shifts and ^{13}C–^{31}P scalar couplings measured in DMF-d_7 are also included in this table. Enantiomeric discrimination is achieved on eight over the 14 types of aromatic carbons of the molecule. The fact that separations were obtained only with aromatic carbons is not surprising. The magnitude of the chemical shift anisotropy depends on the hybridization of the carbon atom as follows: $\Delta\sigma(sp) > \Delta\sigma(sp^2) > \Delta\sigma(sp^3)$. Therefore, the aromatic carbons are more likely to show spectral separation than aliphatic ones.[15b,16] However, spectral separations have already been reported for sp^3 carbons on the basis of chemical shift anisotropy, even though these differences are usually smaller than those observed for sp^2 or sp carbons.[15b]

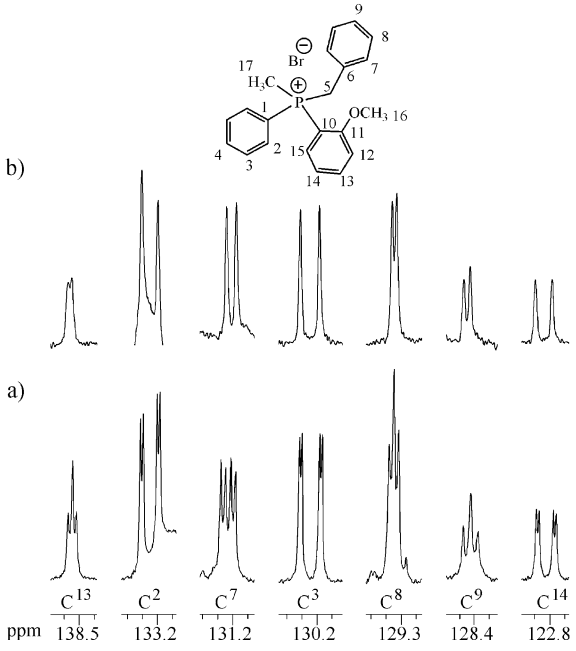


Figure 2. Selected parts of the ^{13}C–{^{1}H} NMR spectrum of (a) racemic and (b) enantiopure phosphonium bromide **4** in PBLG/DMF (30.1 wt % PBLG) at $T = 330$ K.

All carbons presented in Figure 2 are doublets due to ^{13}C–^{31}P coupling. For C(2), C(3), C(7) and C(14), ^{13}C–^{31}P coupling is larger than the difference in the chemical shift anisotropy. This leads to four lines in the ^{13}C NMR spectrum, where the first and the third peaks correspond to one enantiomer, while the second and the fourth belong to the second enantiomer. In the case of C(8), C(9) and C(13), the difference in the chemical shift anisotropy is equal to the ^{13}C–^{31}P coupling, which results in the superposition of the low-field resonance of the doublet of one

Table 1. ^{13}C NMR data at 100.6 MHz for (±) phosphonium bromide **4** in isotropic and chiral liquid crystalline solvents[a]

Solvent	Carbon atoms[b]	C2	C3	C7	C8	C9	C10	C13	C14
DMF-d_7[c]	δ (ppm)	132.95	130.00	131.13	129.27	128.54	107.04	138.07	122.37
	$\lvert J_{^{13}C-^{31}P}\rvert$ (Hz)	10.5	12.6	5.7	3.3	4.1	87.4	2.0	12.3
PBLG/DMF-d_7[e]	δ (1)[d] (ppm)	133.24	130.35	131.24	129.37	128.46	107.78	138.56	122.83
	δ (2)[d] (ppm)	133.22	130.33	131.21	129.34	128.41	107.77	138.53	122.81
	$\lvert\Delta\Delta\sigma_{^{13}C}\rvert$ (Hz)	1.8	1.6	3.1	3.1	4.7	1.1	2.6	1.7
	$\lvert T_{^{13}C-^{31}P}\rvert$ (1)[d] (Hz)	11.4	13.5	7.1	2.9	4.7	74.2	2.6	11.5
	$\lvert T_{^{13}C-^{31}P}\rvert$ (2)[d] (Hz)	11.4	13.2	6.8	3.2	4.7	76.6	2.6	11.5
	$\lvert\Delta T_{^{13}C-^{31}P}\rvert$ (Hz)	0.0	0.3	0.3	0.3	0.0	2.4	0.0	0.0

[a] Only carbons showing enantiomeric separations are depicted.
[b] Carbon atoms numbering is given in Figure 2.
[c] Spectrum measured at room temperature.
[d] (1) and (2) are related to the most and the least deshielded signals, respectively.
[e] PBLG/DMF (30.1 wt % PBLG) at $T = 330$ K.

enantiomer with the high-field resonance of the doublet of its mirror image. The resulting patterns are the triplets observed for these carbons.

For this example, enantiomeric discrimination is mainly observed through a difference in the chemical shift anisotropies. Differences in ^{13}C–^{31}P couplings are only observed for four carbon atoms over the 16 where D_{ij} is not null. This weak ratio of discrimination through ^{13}C–^{31}P dipolar coupling probably originates from the too small values of residual D_{ij} (a few hertz) due to the small order parameters of compounds embedded in PBLG liquid crystal.[23]

Chiral analysis of phosphonium bromide **5** was also investigated. The ^{13}C–{^{1}H} NMR spectrum of a racemic mixture of **5** was measured in PBLG/DMF-d_7 liquid crystal. It presents a splitting into two of the resonances associated with almost all carbons, if compared to the isotropic one (see Table 2 and Fig. 3). NMR data for C(5) are not reported, as the signals of the latter are hidden by the resonances of a methyl group from DMF-d_7. Here, enantiomeric discrimination originates both from dipolar coupling and chemical shift anisotropy. The differences in ^{13}C–^{31}P total couplings ($|\Delta T_{^{13}C-^{31}P}|$) are typically about 1 Hz, except for C(1) and C(10) where differences of 5 and 7 Hz were measured, respectively. However, the striking features of this spectrum are the uncommonly large differences in chemical shift anisotropies (67–80 Hz, i.e., 0.67–0.80 ppm) observed for all the carbons of the aromatic ring of the benzyl group. These discriminations are among the largest ever reported through ^{13}C NMR in PBLG mesophase, and no pertinent explanation can be given to

Table 2. ^{13}C NMR data at 100.6 MHz for (±)-phosphonium bromide **5** in isotropic, achiral and chiral liquid crystalline solvents[a]

Solvent	Carbon atoms[b]	C1	C2	C3	C4	C6	C7	C8	C9	C10
DMF-d_7[c]	δ (ppm)	118.52	135.40	130.82	135.66	134.89	130.85	129.45	129.50	17.26
	$\lvert J_{^{13}C-^{31}P}\rvert$ (Hz)	82.7	9.4	12.3	3.0	5.2	5.8	2.5	3.3	1.4
PBG/DMF-d_7[d]	δ (ppm)	118.81	135.80	131.19	135.94	135.11	131.27	129.66	129.83	17.37
	$\lvert T_{^{13}C-^{31}P}\rvert$ (Hz)	80.2	8.4	11.9	2.6	<2	/[e]	3.5	≈0	3.3
PBLG/DMF-d_7[g]	δ (1)[f] (ppm)	118.90	135.88	131.26	136.05	135.51	131.60	130.05	130.17	17.40
	δ (2)[f] (ppm)	118.73	135.73	131.12	135.83	134.72	130.92	129.26	129.47	17.36
	$\lvert \Delta\Delta\sigma_{^{13}C}\rvert$ (Hz)	16.8	15.0	14.5	21.6	80.0	67.6	80.2	70.7	3.7
	$\lvert T_{^{13}C-^{31}P}\rvert$ (1)[f] (Hz)	77.5	7.7	11.9	3.2	1.9	6.6	2.6	2.0	7.4
	$\lvert T_{^{13}C-^{31}P}\rvert$ (2)[f] (Hz)	82.8	8.9	12.3	/[h]	2.0	7.5	3.9	1.0	0.0
	$\lvert \Delta T_{^{13}C-^{31}P}\rvert$ (Hz)	5.3	1.2	0.4	/	0.1	0.9	1.3	1.0	7.4

[a] Only carbons showing enantiomeric separations are depicted.
[b] Carbon atoms numbering is given in Figure 3.
[c] Spectrum measured at $T = 310$ K.
[d] PBG/DMF (33.1 wt % PBG) at $T = 320$ K.
[e] Signal of C(7) overlaps with C(3).
[f] (1) and (2) are related to the most and the least deshielded signals, respectively.
[g] PBLG/DMF (32.6 wt % PBLG) at $T = 320$ K.
[h] Signal of C(4) overlaps with C(2).

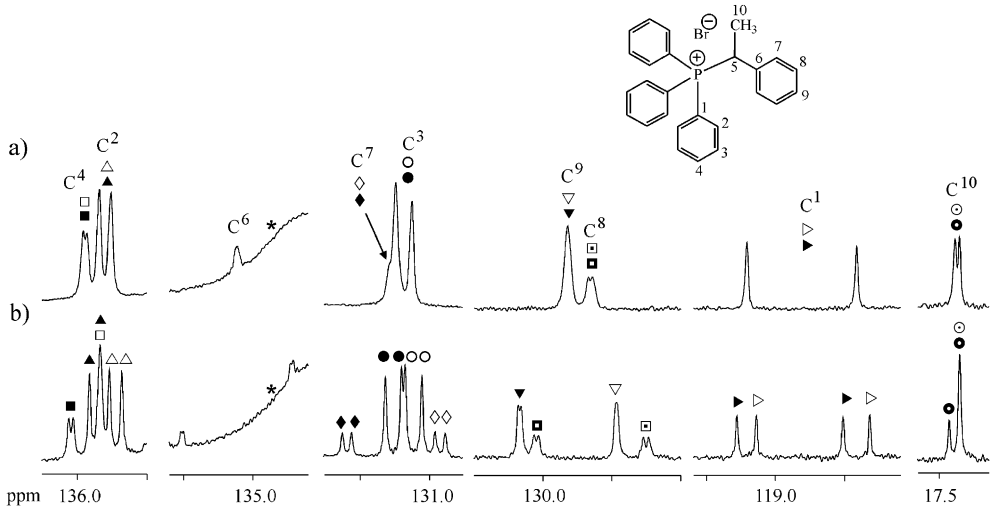


Figure 3. Part of the ^{13}C–{^{1}H} NMR spectrum of racemic phosphonium bromide **5** in (a) PBG/DMF (33.1 wt % polymer) and (b) PBLG/DMF (32.6 wt % PBLG) at $T = 320$ K. The broad signal marked with * belongs to the aromatic carbons of the polymer. Each type of carbon is labelled with a pattern. For a given carbon, signals of the enantiomers are represented with a full and open pattern.

account for such differences.[24] The signal of the methyl group (C10) is composed of two dissymmetric peaks in a 1:3 ratio. This pattern can be explained by the absence of ^{13}C–^{31}P dipolar couplings for one enantiomer, affording a singlet, which is superposed to one resonance of the doublet corresponding to the other enantiomer.

In order to confirm that these peaks doublings originate from enantiodiscrimination, and to exclude any misinterpretation of this spectrum, we measured the ^{13}C–{^1H} NMR spectrum of racemic **5** in a racemic liquid crystalline phase, obtained with a mixture of PBLG and its enantiomer PBDG in DMF-d_7 (see Table 2 and Fig. 3). In such a PBG mixture, it was shown that a rapid exchange of the chiral solute between PBLG and PBDG exists and that the enantiomeric discrimination cancels out.[25] The spectrum obtained in the PBG mesophase confirms that the signal doublings observed in PBLG mesophase stem from enantiomeric discrimination. Indeed, the spectrum in PBG is very similar to that recorded in isotropic solvents. Only slight variations in the chemical shifts and the ^{13}C–^{31}P couplings were observed, due to chemical shift anisotropy and dipolar coupling which are expressed in PBG oriented phase. Interestingly, the chemical shifts (and coupling constants) measured in PBG achiral mesophase are the exact average of the ones measured for enantiomers in PBLG (see Table 2). This feature demonstrates, once again, that chiral molecules in PBLG undergo rapid motion and that we observe an average of multiple situations. In other words, there is no stable complex formation between PBLG fibres and chiral molecules, but instead entities in rapid motion in a chiral environment.

3. Conclusion

Herein, we have investigated the enantiodifferentiation of acyclic chiral phosphonium salts bearing a stereogenic centre whether on the phosphorus atom, or on one of its substituents in polypeptidic liquid crystalline phases. The experimental conditions allowing the stability of PBLG liquid crystalline phases in the presence of phosphonium salts have been established. The enantiodiscrimination was then explored using ^2H–{^1H}, ^{13}C–{^1H} and ^{31}P–{^1H} NMR. For the first time, enantiomers of P-chirogenic phosphorus compounds were discriminated in these polypeptidic liquid crystals allowing the determination of their proportion. While ^{31}P–{^1H} NMR spectra showed no chiral separation, ^2H–{^1H} NMR appeared efficient in the case of an isotopically labelled compound. Using ^{13}C–{^1H} NMR, good to excellent separations were observed, and uncommonly large differences in the chemical shift anisotropies (up to 0.8 ppm) were observed.

The general mechanism of enantiodifferentiation in chiral liquid crystals has not been fully established. Therefore, it is not possible to predict whether enantiomers of a solute will be discriminated or not, neither the site nor the magnitude of such discrimination. Still, synergies can arise from chemical shift anisotropy and ^{13}C–^{31}P total coupling resulting in good spectral separations. Therefore, ^2H–{^1H} and especially ^{13}C–{^1H} NMR in liquid crystalline solutions of commercially available polypeptides emerge as interesting alternatives for the enantiodifferentiation of chiral phosphonium salts.

4. Experimental

4.1. Sample preparation and NMR measurements

The CLC NMR samples were prepared as follows: PBLG (about 150 mg, Mol. Wt.: 150.000–300.000 purchased from Sigma–Aldrich) was weighted into a 5 mm o.d. NMR tube. 280 μl of DMF-d_7 was added and the mixture heated to 80–100 °C, until complete dissolution of the polymer. Chiral phosphonium halide and DMF-d_7 (the adequate amount to reach the desired polymer weight fraction) were then introduced in the NMR tube. In order to homogenize the viscous mixture, the NMR tube was repeatedly centrifuged (20 times) on a low speed (600 rpm) bench top centrifuge, turning the tube upside-down between each centrifugation. ^2H–{^1H}, and ^{13}C–{^1H} and ^{31}P–{^1H} NMR spectra were recorded at 61.4, 100.6 and 162.0 MHz, respectively, on a Bruker DRX-400 spectrometer equipped with a selective deuterium, a Dual $^1H/^{13}C$ or a BBI-probe. Temperature was held constant using a BVT3000 variable temperature unit. Proton broad-band decoupling was achieved using the WALTZ-16 composite pulse sequence.

Acknowledgements

We thank Dr. J. Salaün, for a helpful discussion and the Ministry of research, the CNRS and the Sté SYNTHELOR, for financial support.

References

1. (a) Ohff, M.; Holz, J.; Quirmbach, M.; Börner, A. *Synthesis* **1998**, 1391–1415; (b) Brunel, J. M.; Faure, B.; Maffei, M. *Coord. Chem. Rev.* **1998**, *178–180*, 665–698; (c) Carboni, B.; Monnier, L. *Tetrahedron* **1999**, *55*, 1197–1248.
2. (a) Jugé, S.; Stephan, M.; Laffitte, J. A.; Genêt, J. P. *Tetrahedron Lett.* **1990**, *31*, 6357–6360; (b) Bauduin, C.; Moulin, D.; Kaloun, E. B.; Darcel, C.; Jugé, S. *J. Org. Chem.* **2003**, *11*, 4293–4301.
3. (a) Oshiki, T.; Imamoto, T. *J. Am. Chem. Soc.* **1992**, *114*, 3975–3977; (b) Wolfe, B.; Livinghouse, T. *J. Am. Chem. Soc.* **1998**, *120*, 5116–5117; (c) Miura, T.; Yamada, H.; Kikuchi, S.; Imamoto, T. *J. Org. Chem.* **2000**, *65*, 1877–1880; (d) Al-Masum, M.; Kumaraswamy, G.; Livinghouse, T. *J. Org. Chem.* **2000**, *65*, 4776–4778.
4. (a) Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.* **1990**, *112*, 5244–5252; (b) Muci, A. R.; Campos, K. R.; Evans, D. A. *J. Am. Chem. Soc.* **1995**, *117*, 9075–9076; (c) Yamanoi, Y.; Imamoto, T. *J. Org. Chem.* **1999**, *64*, 2988–2989.
5. (a) Imamoto, T.; Hirose, K.; Amano, H. *Main Group Chem.* **1996**, *1*, 331–338; (b) Uziel, J.; Darcel, C.; Moulin, D.; Bauduin, C.; Jugé, S. *Tetrahedron: Asymmetry* **2001**, *12*, 1441–1449.
6. Uziel, J.; Riegel, N.; Aka, B.; Figuière, P.; Jugé, S. *Tetrahedron Lett.* **1997**, *38*, 3405–3408.

7. (a) Brodie, N.; Jugé, S. *Inorg. Chem.* **1998**, *37*, 2438–2442; (b) Darcel, C.; Kaloun, E. B.; Merdès, R.; Moulin, D.; Riegel, N.; Thorimbert, S.; Genêt, J. P.; Jugé, S. *J. Organomet. Chem.* **2001**, *624*, 333–343.
8. Yashima, E.; Yamamoto, C.; Okamoto, Y. *Synlett* **1998**, 344–360.
9. Dunina, V. V.; Kuz'mina, L. G.; Kazakova, M. Y.; Grishin, Y. K.; Veits, Y. A.; Kazakova, E. I. *Tetrahedron: Asymmetry* **1997**, *8*, 2537–2545.
10. (a) Oliveros, L.; Cazau, M. *J. Chromatogr.* **1987**, *409*, 183–192; (b) Brandi, A.; Cicchi, S.; Gasparrini, F.; Maggio, F.; Villani, C.; Koprowski, M.; Pietrusiewicz, K. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2017–2022.
11. Dunach, E.; Kagan, H. B. *Tetrahedron Lett.* **1985**, *26*, 2649–2652.
12. (a) Ginglinger, C.; Jeannerat, D.; Lacour, J.; Jugé, S.; Uziel, J. *Tetrahedron Lett.* **1998**, *39*, 7495–7498; (b) Hebbe, V.; Londez, A.; Goujon-Ginglinger, C.; Meyer, F.; Uziel, J.; Jugé, S.; Lacour, J. *Tetrahedron Lett.* **2003**, *44*, 2467–2471.
13. A simple heating of TRISPHAT in toluene-d_8 or $CDCl_3$ leads to the formation of a major by-product at +11.7 ppm in ^{31}P NMR, when the signal must be at −68.2 ppm.
14. (a) Canet, I.; Meddour, A.; Courtieu, J.; Canet, J. L.; Salaün, J. *J. Am. Chem. Soc.* **1994**, *116*, 2155–2156; (b) Canet, I.; Courtieu, J.; Loewenstein, A.; Meddour, A.; Péchiné, J. M. *J. Am. Chem. Soc.* **1995**, *117*, 6520–6526.
15. (a) Lesot, P.; Merlet, D.; Meddour, A.; Courtieu, J.; Loewenstein, A. *J. Chem. Soc., Faraday Trans.* **1995**, *91*, 1371–1375; (b) Meddour, A.; Berdagué, P.; Hedli, A.; Courtieu, J.; Lesot, P. *J. Am. Chem. Soc.* **1997**, *11*, 4502–4508.
16. Emsley, J. W.; Lindon, J. C. *NMR Spectroscopy Using Liquid Crystal Solvents*; Pergamon Press: Oxford, 1975.
17. Rivard, M.; Guillen, F.; Fiaud, J. C.; Aroulanda, C.; Lesot, P. *Tetrahedron: Asymmetry* **2003**, *14*, 1141–1152.
18. (a) Subramanian, R.; Wittebort, R. J.; DuPré, D. B. *J. Chem. Phys.* **1982**, *77*, 4694–4697; (b) Subramanian, R.; DuPré, D. B. *J. Chem. Phys.* **1984**, *81*, 4626–4629.
19. (a) Laszlo, P.; Paris, A.; Marchal, E. *J. Phys. Chem.* **1973**, *77*, 2925–2927; (b) Uematsu, I.; Uematsu, Y. *Adv. Polym. Sci.* **1984**, *59*, 37–73.
20. Onsager, L. *Ann. N.Y. Acad. Sci.* **1949**, *56*, 627–659.
21. (a) Flory, P. J. *Proc. Roy. Soc. A* **1956**, *243*, 73–89; (b) Flory, P. J. *Adv. Polym. Sci.* **1984**, *59*, 1–36.
22. Meddour, A.; Canet, I.; Loewenstein, A.; Péchiné, J. M.; Courtieu, J. *J. Am. Chem. Soc.* **1994**, *116*, 9652–9656.
23. Lesot, P.; Merlet, D.; Courtieu, J.; Emsley, J. W.; Rantala, T. T.; Jokisaari, J. *J. Phys. Chem. A* **1997**, *101*, 5719–5724.
24. Here, the spectral separations of enantiomers can be obtained through a difference in the chemical shift anisotropy of ^{13}C. Chemical shift anisotropy results from the contribution of the non spherical distribution of electrons modulated by the Saupe order matrix elements. In polypeptidic CLC, the order parameters of a guest compound depend on its molecular geometry, the organic co-solvent, the temperature and the nature of the polymer and its concentration. Therefore, connecting a spectral separation obtained for a given carbon to molecular structure is a priori extremely complex and absolutely not intuitive.
25. Canlet, C.; Merlet, D.; Lesot, P.; Meddour, A.; Loewenstein, A.; Courtieu, J. *Tetrahedron: Asymmetry* **2000**, *11*, 1911–1918.