Probing peristatic chirality of alkaline cations: NMR study of alkaline borocryptates

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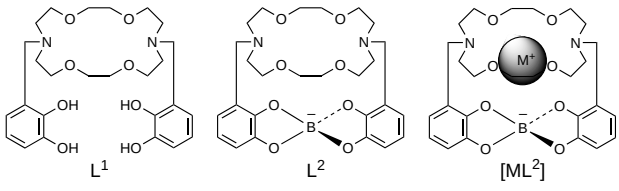
Enantiomeric differentiation of chiral borocryptates using NMR spectroscopy in a chiral liquid crystalline medium is achieved using different NMR probes localised both on the receptor and on the substrate; the observed chirality at the substrate is described as being induced by the spiroborate junction and mediated by the peristatic chirality of the cavity.

For more than a century, chemists have been dealing with chirality which appears to be one of the most subtle aspects of chemistry.[1] On one hand, synthetic chemists use their skill to prepare compounds presenting either established[2] or new types of chirality.[3] On the other hand, physical chemists develop methods allowing measurement of chirality. Amongst such methods, NMR appears to be one of the most useful techniques.[4] In particular, NMR spectroscopy in oriented nematic phases has been shown to be a powerful method for the differentiation of enantiomers.[5]

Recently, inspired by naturally occurring antibiotics such as boromycin[6a] and aplasmomycin[6b] as well as by cryptands such as [222],[7] compound L^1 was designed.[8a] In the presence of a equimolar mixture of $B(OH)_3$ and MOH (M = alkali metal) in EtOH–H_2O, L^1 affords neutral binuclear complexes of the type $[ML^2]$ (Scheme 1). The binding ability of L^2 towards alkali-metal cations has been studied both in solution by NMR spectroscopy[8b] and in the solid state by X-ray analysis.[8c]

In dealing with chirality, the binding of boron by L^1 with a tetrahedral coordination geometry, affords the chiral cryptand L^2 (Fig. 1). The latter upon complexation with alkali-metal cations leads to chiral cryptates $[ML^2]$. The X-ray analysis of complexes with M^+ = K^+, Rb^+ or Cs^+ revealed the presence of both (*R*) and (*S*) enantiomers as a racemic mixture in the solid state.[8c] Whereas the free cryptand L^2 possesses an inherent chirality of the enantiomorphic type (*R* and *S*), for the labile and exchangeable complexed alkali-metal cation, the chirality is being imposed by the chiral cavity of the receptor through non-covalent interactions, and is therefore not inherent, and may be described as peristatic chirality[9] (peristasis = environment).† This type of chirality has been also recognised in a compound in which polyethyleneglycol was used to connect two catechol units.[10]



Scheme 1

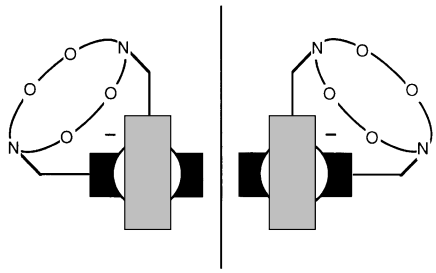


Fig. 1 Schematic representation of chirality arising from the spiroborate junction in the borocryptand L^2

Enantiomeric differentiation of chiral molecules has been demonstrated using NMR spectroscopy in oriented chiral liquid crystals[5a] in particular in a poly(γ-benzyl L-glutamate) (PBLG)–CH_2Cl_2 (11–12% m/m) mixture[5b] forming cholesteric lyotropic mesophases.[5c]

Here, we report the extension of this method to the enantiomeric differentiation of complex molecules formed by non-covalent interactions between a receptor and a substrate.

For the chiral borocryptate $[ML^2]$, the receptor L^2 contains, in addition to classical ^1H and ^{13}C NMR active nuclei, both ^{10}B (I = 3) and ^{11}B (I = 3/2) possessing quadrupolar moments. On the other hand, the alkali-metal cations, being also NMR active, and possessing a quadrupolar moment, can also be studied by the same technique. Thus, enantiomeric differentiation in the $[ML^2]$ complexes can be studied in PBLG–CH_2Cl_2 (11–12% m/m), both at the level of the receptor L^2 and the substrate by combining the NMR data collected for the receptor part (^{10}B, ^{11}B) and for the cationic substrates (^{133}Cs and ^{14}N).‡

The ^{10}B NMR spectrum of $[CsL^2]$ [Fig. 2(*a*)] can be deconvoluted into two sets of signals [Fig. 2(*b*), (*c*)] in 1 : 1 ratio as expected for a racemic mixture. The two distinct signals arise from each enantiomer. Whereas for one of the enantiomers [Fig. 2(*b*)], the signal was a broad singlet with a linewidth ($\Delta\nu_{1/2}$) of 51.9 Hz, the signal for the other enantiomer appeared as a sextet (^{10}B, I = 3) with values of 221.6 and 73.3 Hz for the quadrupolar splitting (ν_Q) and $\Delta n_{1/2}$, respectively [Fig. 2(*c*)].

$[CsL^2]$ was also studied by ^{11}B NMR. Again, the observed spectrum [Fig. 2(*d*)] could be deconvoluted into a broad signal ($\Delta\nu_{1/2}$ = 48.1) [Fig. 2(*e*)] and a triplet (^{11}B, I = 3/2) with ν_Q = 503.2 Hz and $\Delta\nu_{1/2}$ = 48.7 Hz [Fig. 2(*f*)]. For both ^{10}B and ^{11}B, the non-observation of a quadrupolar splitting for one of the enantiomers remains to be explained.

Interestingly, when investigating $[CsL^2]$ by ^{133}Cs NMR, the observed spectrum [Fig. 2(*g*)] was also composed of two sets of signals corresponding to two enantiomers. The spectrum could be deconvoluted into two septets (^{133}Cs, I = 7/2), one with a small quadrupolar splitting constant (ν_{Q1} = 73.0 Hz, $\Delta\nu_{1/2}$ = 25.0 Hz) [Fig. 2(*h*)] and the other with a larger quadrupolar splitting constant (ν_{Q2} = 188.2 Hz, $\Delta\nu_{1/2}$ = 28.7 Hz) [Fig. 2(*i*)].

The binding ability of L^2 towards cations such as NH_4^+ has been previously established by an X-ray study,[11] and NH_4L^2 has been investigated by ^{10}B, ^{11}B and ^{14}N NMR.

^{10}B NMR observations [Fig. 3(*a*–*c*)] were similar to those obtained for $[CsL^2]$ (ν_{Q1} = 120.0 Hz, $\Delta\nu_{1/2}$ = 55.1 Hz). However, for ^{11}B the observed spectrum [Fig. 3(*d*)] appeared to be a superimposition of two triplets of the same intensity with

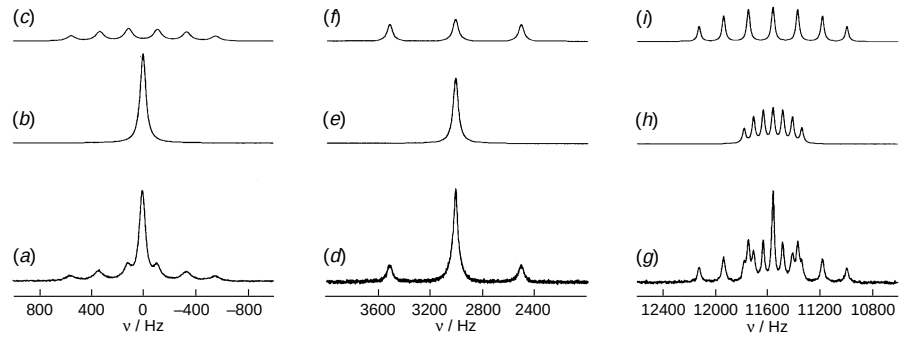


Fig. 2 NMR spectra of [CsL²] in a chiral liquid-crystalline solvent : ^{10}B (53.73 MHz) observed (*a*) and deconvoluted signals for both enantiomers (*b*), (*c*); ^{11}B (160.42 MHz) observed (*d*) and deconvoluted signals for both enantiomers (*e*), (*f*); ^{133}Cs (65.58 MHz) observed (*g*) and deconvoluted signals for both enantiomers (*h*), (*i*). ^{10}B, ^{11}B and ^{133}Cs chemical shifts were referenced to $BF_3{\cdot}Et_2O$ and aqueous saturated $CsNO_3$, respectively as external references.

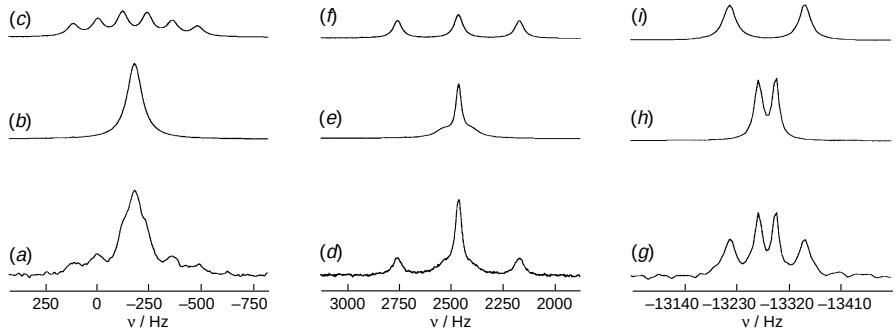


Fig. 3 NMR spectra of [NH_4L^2] in chiral liquid-crystalline solvent: ^{10}B (53.73 MHz) observed (*a*) and deconvoluted signals for both enantiomers (*b*), (*c*); ^{11}B (160.42 MHz) observed (*d*) and deconvoluted signals for both enantiomers (*e*), (*f*); ^{14}N (36.12 MHz) observed (*g*) and deconvoluted signals for both enantiomers (*h*), (*i*). ^{14}N chemical shifts were referenced to neat $MeNO_2$ as external reference.

ν_{Q1} = 66.7 Hz [Fig. 3(*e*)] and ν_{Q2} = 293.2 Hz [Fig. 3(*f*)] corresponding to both enantiomers.

In ^{14}N NMR studies, probably owing to the unsymmetrical environment around the two bridgehead nitrogen atoms leading to large quadrupolar interactions, the amino groups could not be observed. Nevertheless, the signal for the symmetrical NH_4^+ substrate was observed [Fig. 3(*f*)] as a superimposition of two doublets (^{14}N, I = 1) in 1 : 1 ratio [Fig. 3(*h*), (*i*)]. Again, the two enantiomers were differentiated by large (ν_{Q1} = 128.7 Hz, $\Delta\nu_{1/2}$ = 18.0 Hz) and small (ν_{Q2} = 30.7 Hz, $\Delta\nu_{1/2}$ = 6.0 Hz) quadrupolar splitting constants.

Although not reported here, complexes formed between the cryptand L² and other cations such as Rb^+ and K^+ behaved similarly.

Enantiomeric differentiation of chiral molecules based on NMR studies in liquid-crystalline media was elegantly demonstrated by Courtieu and coworkers.[5a,b] Using different NMR probes on both the receptor and the substrate, we were able to detect, for the first time, the chirality of the ensemble, on different locations of the complex molecule. Based on our observations, we can describe the observed chirality at the cation site as induced by the spiroborate junction and mediated by the peristatic chirality of the cavity.

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Footnotes

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† The adjective 'peristatic' (peristasis = environment) has been suggested at the EUCHEM Conference on Stereochemistry (Bürgenstock, May, 1966) by Professor S. D. Atkins (see ref. 11).

‡ The experiments were performed on dissolved single racemate crystals (the racemic nature was established by X-ray analysis). The deconvolution of the observed signal as two sets of signals was based on the observation of the quadrupolar splitting for one of the enantiomers which allowed abstraction of its contribution from the observed signal. The remaining signal was assigned to the other enantiomer. The ratio of the two signals was found to be 1 : 1 (±2%), as expected for a racemic mixture.

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