Solvent-Induced Chirality Switching

The Origin of Solvent-Controlled Supramolecular Chirality Switching in a Bis(Zinc Porphyrin) System

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Chirogenic processes induced by means of supramolecular interactions have been one of the major focuses of research interest for chemists and material scientists in recent years due to their direct relation to many natural and artificial systems and potential applicability.[1] The understanding of chirality induction in supramolecular systems, including the detailed mechanisms and various driving forces, is of particular importance and allows rational control of these phenomena. Owing to the noncovalent nature of supramolecular interactions, the medium effect and solvent interactions with

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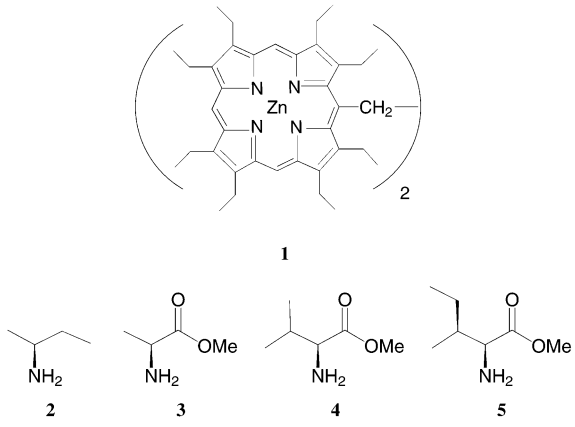
the molecular components of whole systems can play a key role in such association processes, thus influencing all aspects of the assembly, in particular the stereochemistry, and consequently the degree of induced chirality. Although a vast number of examples of the solvent effect on asymmetry transfer were reported,[1a,i–m,2] to our knowledge this important factor and its origin have not yet been well-investigated and rationalized, with consideration only going as far the observation of the results of these phenomena and the qualitative investigation into the influence of the bulk solvent properties. Herein, we describe a remarkable phenomenon that leads to the origin, and consequently a molecular-level understanding, of how the solvent may control and even switch the induced chirality in a supramolecular system that consists of an achiral host and a chiral guest.

To investigate the influence of the solvent on supramolecular chirality, a host–guest system on the basis of ethane-bridged bis(zinc porphyrin) host[3] (**1**) was chosen as the most suitable because the corresponding spectral changes upon the interaction of **1** with chiral guests (L) can be easily monitored.[4] Essentially, this host undergoes *syn*-to-*anti* conformational switching upon complexation with external ligands and unidirectional screw formation based on the stereochemistry of the chiral guests. To date the detailed mechanism, driving forces, and various external and internal controlling factors of this phenomenon have been thoroughly investigated and well-characterized. The choice of chiral guests was particularly important and dictated by a relatively small difference in the bulkiness between two of the largest substituents (excluding the binding amine) as it is the distinction between the competing steric interactions of these ligand substituents and the neighboring porphyrin that are responsible for the induced helical sense in **1**.[4] Another major factor is the considerable difference in the ability of the substituents of the ligand to interact with solvent molecules, which can be roughly represented by their polarity. Thus, with the aim of achieving a molecular-level understanding of the solvent effect, four enantiopure compounds **2**–**5** of *S* configuration were chosen as the corresponding chiral guests with comparably sized substituents as judged from the relatively modest amplitudes (*A*) of the induced circular dichroism (ICD)[5] observed with **1** in CH_2Cl_2.[4d,e] In addition, the amino acid derivatives **3**–**5** are expected to exhibit drastic distinctions in the polarity of their substituents, that is, between the carboxy ester *C*-terminus and the alkyl side chain, whilst **2** has only two nonpolar competing substituents (methyl and ethyl) and is an ideal "solvent-inert" reference compound.



As in the case of previously studied systems,[4] the UV/Vis spectra of **1**·L_2 in different solvents[6] show that the Soret (B) band is significantly bathochromically shifted (compared to initial **1**) and exhibits a well-resolved split into two major transitions arising from the through-space interactions of the corresponding pairs of porphyrin B electric dipoles of the two porphyrin rings in the *anti* conformation (see Figure 1 and Supporting Information), which is in full agreement with the exciton coupling theory of Kasha et al.[4j,7] The maxima positions and magnitude of their split (Davydov splitting) are essentially independent of the solvent. However, the relative ratio between the intensities of the high (B_1) and low(B_2) energy components of the Soret band are noticeably affected by the solvent. Generally, in more polar solvents the intensity of B_1 transition is enhanced in comparison to that of the B_2 transition, whilst in nonpolar solvents the opposite tendency was observed.[8] This reflects the ability of polar and nonpolar solvents to form an overall solvation shell around the **1**·L_2 system, thus affecting the relative probability of light-absorption pathways to certain levels of the split S_2 excited states arising from the bisporphyrin coupling, whilst having little or no effect on its energy levels.

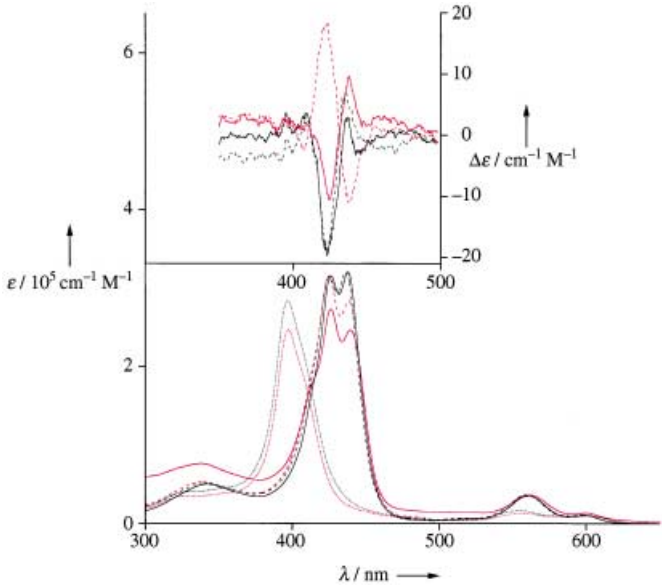


Figure 1. UV/Vis and CD (inset) spectra of **1** without ligand (dotted lines) and in the presence of **2** (solid lines) and **3** (dashed lines) in CH_2Cl_2 (black lines) and in cyclohexane (red lines).

The CD spectra of **1**·L_2 in various solvents show similar features as reported previously for these systems in CH_2Cl_2,[4] including a bisignate CD signal comprising of two Cotton effects, the positions of which coincide very closely with the maxima of the split Soret band in UV/Vis spectra, thus indicating the same origin (see Figure 1, inset, and Supporting Information); these properties are also independent of the

solvent used. However, there was a dramatic difference in the spectral behavior between the amino acid-based systems $\mathbf{1}\cdot\mathbf{3}_2$–$\mathbf{1}\cdot\mathbf{5}_2$ that contain the polar ester group and the reference system $\mathbf{1}\cdot\mathbf{2}_2$ that contains only alkyl substituents. As can be seen, the intensity and sign of the CD couplets of $\mathbf{1}\cdot\mathbf{3}_2$–$\mathbf{1}\cdot\mathbf{5}_2$ are strongly affected by the surrounding medium, whilst $\mathbf{1}\cdot\mathbf{2}_2$ is largely unaffected by the solvent. Although in recent reports there were several examples of solvent-induced chirality switching, none of them give a rational or detailed insight at the molecular level into this remarkable and important phenomenon of solvent–solute interactions.[1i,2c,2e–2g] To highlight and understand the role of the solvent, the *A* values were plotted versus the dielectric constants (ε_s) of the solvents as a parameter of its polarity and thus its ability to interact with the ligands (Figure 2). As mentioned above, the *A* values of $\mathbf{1}\cdot\mathbf{2}_2$ are essentially independent of ε_s, whilst the chirality of $\mathbf{1}\cdot\mathbf{3}_2$–$\mathbf{1}\cdot\mathbf{5}_2$ correlates well with the solvent polarity, essentially, exhibiting positive ICD sign in polar media and negative ICD sign in nonpolar media.

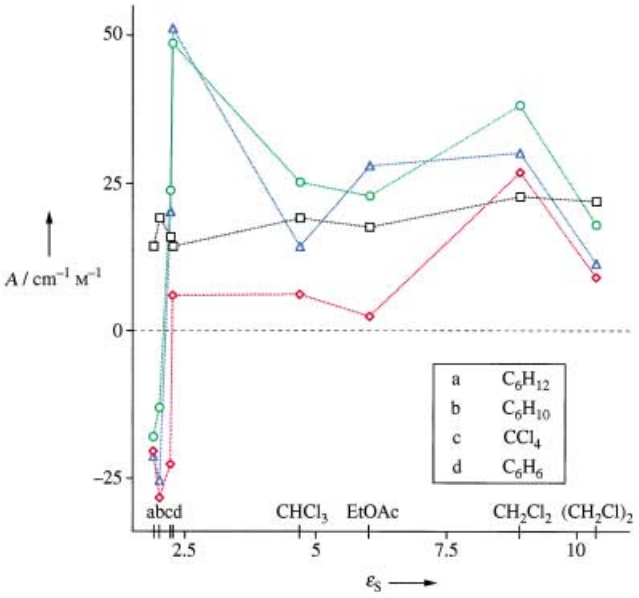


Figure 2. The dependence of the ICD amplitudes of $\mathbf{1}\cdot L_2$, black L = **2**, red L = **3**, green L = **4**, and blue L = **5**, upon the dielectric constant of the solvent used.

In consideration of the main tendency of the experimentally observed solvent–ICD relationship, a general mechanism of the effect of the medium on supramolecular chirality induction at the molecular level of solvent–solute interactions can be schematically described (Figure 3).

In polar media the solvent molecules are able to interact electrostatically (through dipole–dipole, dipole–quadrupole interactions, etc.) with the ester group of the amino acid derivatives. Arising from such specific interactions with the solvent, a fairly well structurally organized solvent shell surrounding the polar substituent is formed. This is in sharp contrast to the nonpolar alkyl substituents that are unable to

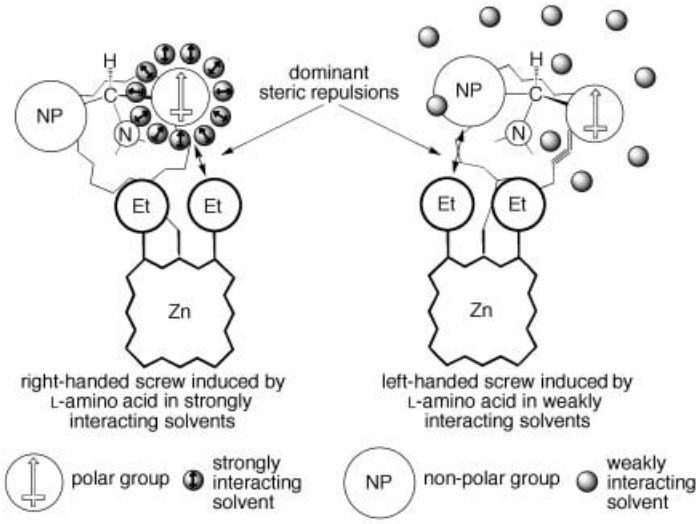


Figure 3. Solvent effect on the mechanism of supramolecular chirality induction in $\mathbf{1}\cdot L_2$, in strongly and weakly interacting solvents (the ligand coordinated to the upper porphyrin has been omitted for clarity).

interact in such a manner, as they do not have such strong and defined permanent electrostatic distributions. As a result of the selective polar solvent–polar substituent interactions the relative "effective sizes" of the competing ligand substituents can be changed and even inverted. Thus, when both the *C*-terminus ester and the side-chain groups are comparable in size, or even if the nonpolar side-chain substituent is slightly larger than the polar *C*-terminus ester group (as in the present case), a "small" increase in the size of the polar group as a result of specific solvent–substituent interactions can cause a subsequent total equilibrium shift towards the formation of the right-handed screw structure in $\mathbf{1}\cdot L_2$ (when L has *S* configuration) (Figure 3). This helical orientation corresponds to positive-induced chirality, and is in accordance with the exciton chirality method[9] and also reported previously.[4] In contrast, in nonpolar solvents, because of the negligible solvent–solute electrostatic interactions there is no observable formation of any selective solvent–solute interaction around the polar group, and as a result, the dominant steric repulsion takes place between the larger side chain and ethyl group of the neighboring porphyrin ring. This interaction induces a corresponding equilibrium shift towards the formation of the left-handed screw structure in $\mathbf{1}\cdot L_2$, which corresponds to negative chirality. In the case of reference $\mathbf{1}\cdot\mathbf{2}_2$ it is obvious that both the methyl and ethyl nonpolar groups will interact to almost the same extent, thus preserving the right-handed screw owing to the larger size of ethyl substituent of **2** regardless of the medium used.

However, at first glance there is an apparent deviation of the proposed mechanism. This is the unexpected enhancement of the positive *A* values of $\mathbf{1}\cdot\mathbf{4}_2$ and $\mathbf{1}\cdot\mathbf{5}_2$ in benzene, whereas for the other solvents of corresponding low dielectric constant, small positive or highly negative *A* values are observed (Figure 2 and Supporting Information). This can occur either through the enhancement of the effective size of the ester group or reduction of the effective size of the alkyl side chain. Although benzene has a low ε_s value, because of its

pronounced quadrupolar electrostatic distribution it is still able, in principle, to have significant electrostatic interaction with the polar ester group, which will consequently increase its effective size and thus result in the observed increase in positive chirality. Another possibility, although less probable, is a reduction in the effective size of the branched alkyl side-chain groups in **4** and **5** due to a conformational change that reduces their effective size as a result of CH-π interactions with benzene.[10]

To investigate the remarkable effect of high solvent sensitivity on supramolecular chirogenesis and particularly the chirality switching in a narrow polarity range,[11] the chirality induction processes in **1** were studied in mixed solvents. Thus, the CD and UV/Vis spectra of $\mathbf{1}\cdot\mathbf{3}_2$ were taken at different ratios by volume of CH_2Cl_2 (a strongly interacting solvent) to cyclohexane (a weakly interacting solvent) and the corresponding spectral data (A values for CD and B_1/B_2 relative intensities ratio for UV/Vis) were plotted against the solvent content (Figure 4).

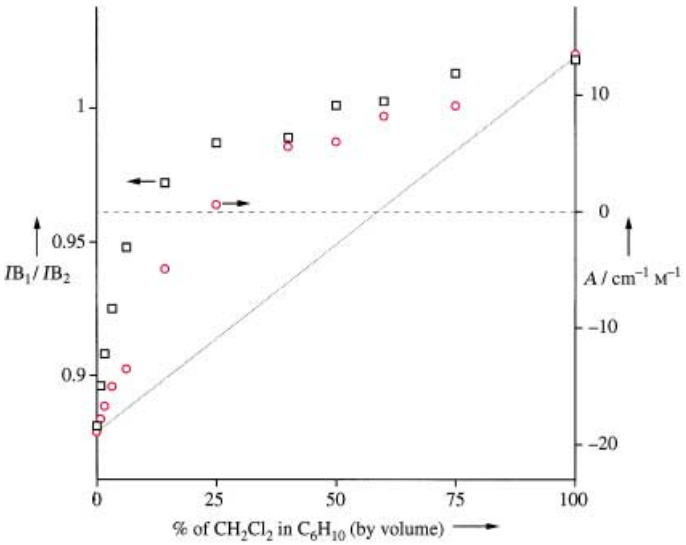


Figure 4. Dependences of the ratio of the intensities of B_1 and B_2 transitions (IB_1 and IB_2) from UV/Vis data and ICD amplitude from CD data of $\mathbf{1}\cdot\mathbf{3}_2$ versus the percentage of CH_2Cl_2 in cyclohexane by volume.

The UV/Vis changes are associated with the overall solvation effect of the mixed solvents on the supramolecular system and essentially its chromophoric, that is, porphyrin, moiety. As expected from the above results, CH_2Cl_2 more strongly interacts with the zinc porphyrins that results in a considerable nonlinear increase in the probability of the B_1 transition on increasing CH_2Cl_2 content. In contrast, the CD dependence reflects specific solvent interactions with a certain part of the supramolecular system (particularly the polar group of L), thus resulting in a dramatic nonlinear dependence upon increasing the CH_2Cl_2 component. These significant deviations from linearity clearly indicate that the CH_2Cl_2 molecules much more strongly interact with the ester moiety than cyclohexane. Indeed, even at only 25% CH_2Cl_2 the sign of the chirality of the supramolecular system is switched from negative to positive as a result of the formation of a structurally organized solvent shell surrounding the polar substituent, which increases its effective size. Thus the behavior of the chiral supramolecular system is dictated not by the properties of the bulk solvent, but by the specific molecular solvent–solute interactions.

In summary, this work shows that through judicious control of the medium, the properties of supramolecular chirogenesis, including chirality switching phenomenon, may be controlled through specific solvent–solute interactions. Furthermore, as such interactions are common to all solution based supramolecular systems, and not just chiral ones, the realization and application of this approach to molecular control may have important implications for understanding the mechanisms and driving forces of numerous artificial and natural assemblies.

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[11] In the case of **1**·(**3**)$_2$ the extremely narrow ε_s gap of chirality switching is apparently because benzene also enhances a positive component of chirality induction for the same reasons as in the case of **1**·**4**$_2$ and **1**·**5**$_2$ but to a lesser extent.

