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Supramolecular Chirogenesis in Bis(zinc porphyrin): An Absolute Configuration Probe Highly Sensitive to Guest Structure

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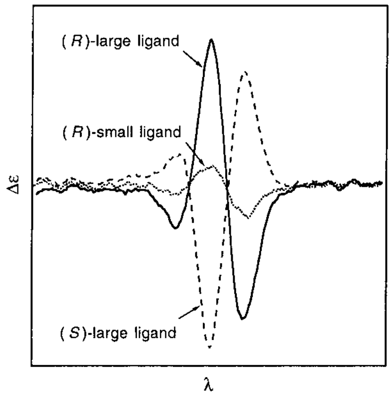
ABSTRACT



The role of the ligand's structure and absolute configuration in the supramolecular chirality induction in achiral bis(zinc porphyrin) has been studied. The amines with bulkier substituents resulted in stronger CD signals due to increased helical displacement in the *anti* conformer. All the amines with an *R* absolute configuration gave a negative first Cotton effect and positive second Cotton effect, while the ligands with an *S* absolute configuration produced CD signals with opposite signs due to formation of the left- and right-handed screw diastereomers, respectively.

Supramolecular chirality induction is "symmetry breaking" in achiral multi- or unimolecular systems upon noncovalent interactions with chiral environments, via a chirality transfer mechanism. Although this phenomenon is widely observed and obviously plays an important role in the functioning of many natural systems such as the DNA double helix, the secondary α-helical structure of proteins, heme proteins, and artificial systems,[1−6] the detailed mechanisms, and the different effects controlling the induction processes have not been well studied. Since noncovalent interactions are the key elements in chirality induction, there are several internal (steric and electronic) and external (temperature, pH, polarity, viscosity) factors which may affect these supramolecular

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interactions and as a result the chirality induction in these systems. Recently we have discovered that temperature may serve as an effective tool to control supramolecular chirality induction through enhancement of ligand binding properties at low temperature.[7] In this Letter, we report the roles of ligand structure and absolute configuration in the chirality induction process.

Bis(zinc porphyrin)[8] (**ZnD**, Figure 1) has been chosen as an achiral host molecule. This compound is well suited for a study of the supramolecular chirality induction process because of its well-resolved spectral differences between the initial noninteracting form (*syn*-**ZnD**) and the ligand-bonded species (*anti*-**ZnD**·L$_2$).[9] This is owing to the unique property of **ZnD** to switch conformation from a *syn* (face-to-face) structure in nonpolar solvents to an extended *anti* form upon complexation with the external ligands. The commercially available amines listed in Table 1 were used as the external ligands in this study.

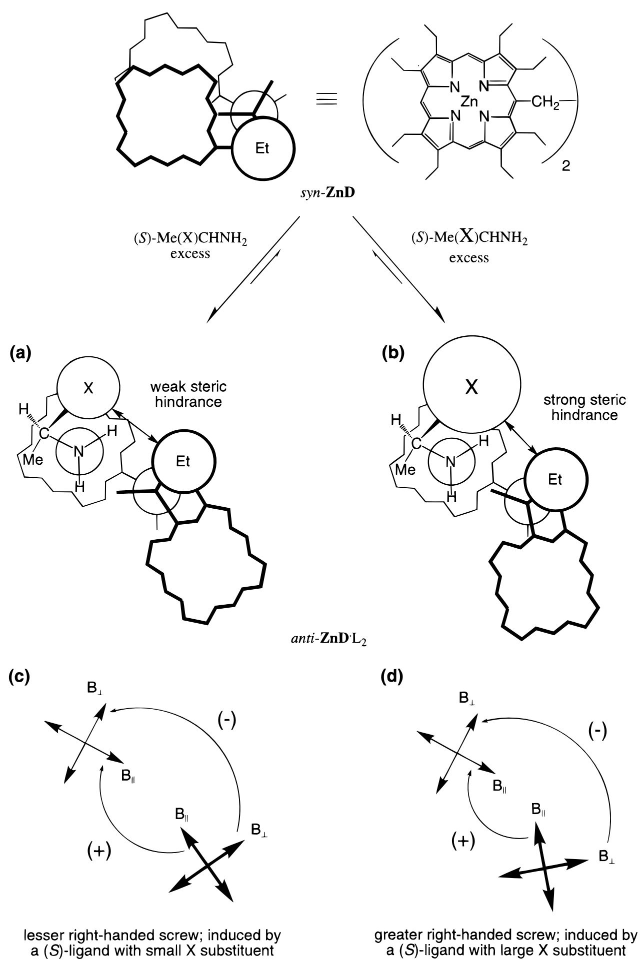

Figure 1. Size effect of the chiral amines on the mechanism of supramolecular chirality induction in *anti*-**ZnD**·L$_2$.

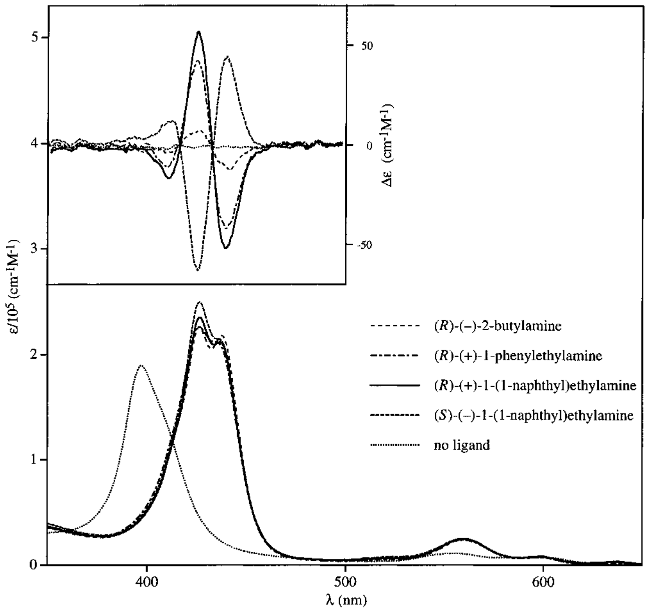

Figure 2. UV–vis and CD (inset) spectra of **ZnD** in CH$_2$Cl$_2$ (without ligands and in the presence of different chiral amines).

Ligand complexation and chiral induction in **ZnD** have been monitored by UV–vis and CD spectroscopy at saturated amine concentrations. This is the amine concentration where the UV–vis and CD changes are at their maximum and further increase of the amine concentration has no effect on the signal intensities (for the value range, see footnote a in Table 1). In the UV–vis spectra of all the systems studied, there is a common special feature attributable to the *anti*-**ZnD**·L$_2$ species. This is a Soret band consisting of two bathochromically shifted and well-resolved B$_\perp$ and B$_{||}$ transitions (Figure 2, Table 1) due to a nonequivalent excitonic coupling of these two electronic transitions.[10] The shape, positions, and intensities of these bands are almost the same regardless of the amines used. In the CD spectra bisignate Cotton effects are observed (Figure 2, inset). The positions of the first and second Cotton effects coincide very closely with the B$_\perp$ and B$_{||}$ electronic transitions seen in UV–vis spectra (Table 1). Interestingly, there is the same good match between the observed CD splitting and the sharply

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Table 1. UV−Vis and CD Spectral Data of the Resulting Supramolecular System *anti*-**ZnD**·L_2 with Different Chiral Amines[a]

	UV−vis data λ_{max} (nm) [$\epsilon/10^5$ (M^{-1} cm^{-1})]		CD data λ_{max} (nm) [$\Delta\epsilon_n$ (M^{-1} cm^{-1})]			
chiral guest, L	$B_{\parallel}$ transition	$B_{\perp}$ transition	first Cotton ($n = 1$)	second Cotton ($n = 2$)	third Cotton ($n = 3$)[b]	A[c]
(*R*)-(−)-2-butylamine	437 [2.18]	426 [2.26]	440 [−12.9]	426 [+7.6]		−20.5
(*S*)-(+)-2-butylamine	437 [2.17]	426 [2.32]	438 [+4.5]	425 [−13.5]		+18.0
(*R*)-(−)-1-cyclohexylethylamine	438 [2.53]	427 [2.52]	439 [−33.1]	425 [+39.6]	411 [−5.6]	−72.7
(*S*)-(+)-1-cyclohexylethylamine	438 [2.46]	427 [2.46]	439 [+31.7]	425 [−36.1]	411 [+6.7]	+67.8
(*R*)-(+)-1-phenylethylamine	436 [2.11]	426 [2.26]	439 [−42.0]	425 [+42.1]	410 [−11.2]	−84.1
(*S*)-(−)-1-phenylethylamine	436 [2.12]	426 [2.35]	439 [+33.7]	425 [−44.7]	410 [+8.2]	+78.4
(*R*)-(+)-1-(1-naphthyl)ethylamine	436 [2.12]	426 [2.35]	439 [−51.2]	426 [+56.7]	411 [−16.3]	−107.9
(*S*)-(−)-1-(1-naphthyl)ethylamine	436 [2.14]	426 [2.50]	439 [+44.5]	426 [−63.2]	412 [+12.2]	+107.7
(*R*)-(+)-*N*-methyl-1-phenylethylamine	437 [2.61]	426 [2.74]	438 [−46.8]	425 [+59.4]	411 [−9.7]	−106.2
(*S*)-(−)-*N*-methyl-1-phenylethylamine	437 [2.49]	426 [2.69]	438 [+50.0]	425 [−57.7]	410 [+9.0]	+107.7
(*S*)-(−)-2-methyl-1-butylamine	437 [2.41]	426 [2.63]	438 [+4.0]	426 [−7.9]		+11.9
(*R*)-(+)-bornylamine[d]	437 [2.54]	427 [2.81]	439 [+54.8]	425 [−74.9]	410 [+12.6]	+129.7

[a] $C_{ZnD} = 2.9{-}3.8 \times 10^{-6}$ M, $C_{amine} = 3.5{-}5.5 \times 10^{-2}$ M in CH_2Cl_2. [b] The third relatively small Cotton effect is likely to result from a point chirality phenomenon that may include a conformational distortion of the porphyrin plane due to ligation process and/or excitonic coupling between porphyrin B and the ligand's aromatic dipoles (in the case of aromatic amines). [c] $A = \Delta\epsilon_1 - \Delta\epsilon_2$. This value represents the total amplitude of the CD couplets. [d] *endo*-(1*R*)-2-Amino-1,7,7-trimethylbicyclo[2.2.1]heptane.

defined Davydov splitting of the Soret band for the different *anti*-**ZnD**·L_2 systems at low temperature that was reported previously.[7] However, in contrast to the almost invariant absorption bands, the intensity of CD couplets is strongly dependent on the ligand's structure. Thus, amines with bulkier substituents (X) on the asymmetric carbon result in Cotton effects with greater intensities. This is demonstrated most clearly by the linear dependence of the values of the total CD signal amplitudes on the effective size of the amines in the structurally homologous series shown in Figure 3. Since two porphyrin planes are parallel in *anti*-**ZnD**·L_2, the strongest steric interactions between the X substituents on the asymmetric carbons of the chiral amines and the ethyl group of the neighboring porphyrin ring are in the plane parallel to the porphyrin ring. Therefore, the effective size was determined as follows (Scheme 1). The N−C* bond of the MM2 optimized amine was placed perpendicular to the projection plane (bold line). The effective size value (in Å) is the horizontal distance between the N atom and the most distant atom of the X substituent. Additional steric hindrance on the amine group as in the case of *N*-methyl-1-phenylethylamine, or on the asymmetric carbon in the case of bornylamine, also leads to appreciable enhancement of the chiral induction effect. Conversely, reduction of the steric bulk around the amino group by moving the asymmetric carbon away from the binding amino site as in the case of 2-methyl-1-butylamine results in considerable decrease of the CD intensity, by approximately a factor of 2.

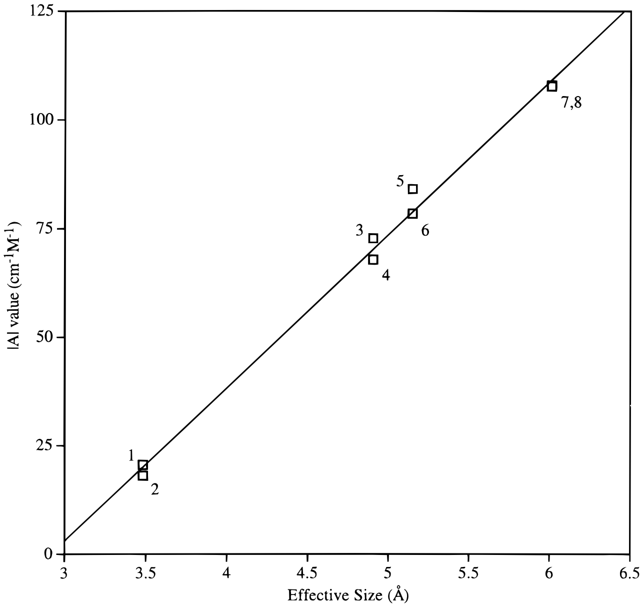
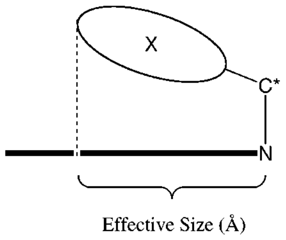


Figure 3. Dependence of the value of the CD total amplitude on the effective size of the amines: (*R*)-(−)-2-butylamine (**1**), (*S*)-(+)-2-butylamine (**2**), (*R*)-(−)-1-cyclohexylethylamine (**3**), (*S*)-(+)-1-cyclohexylethylamine (**4**), (*R*)-(+)-1-phenylethylamine (**5**), (*S*)-(−)-1-phenylethylamine (**6**), (*R*)-(+)-1-(1-naphthyl)ethylamine (**7**), (*S*)-(−)-1-(1-naphthyl)ethylamine (**8**). The linear plot is the best fit obtained for the experimental points.

Scheme 1



These observations are in good agreement with the chirality induction mechanism at low temperature reported recently.[7] This includes formation of the corresponding right- or left-handed screw (depending on the absolute configuration of the ligand used) in *anti*-**ZnD**·L_2. On the basis of CPK models, these conformations[11] are optimal for reducing the steric repulsion between the X substituent on the asymmetric carbon of the chiral amine and the ethyl group at either the 3- or 7-position of the neighboring porphyrin ring (Figure 1a,b). Because of the screw structure, the corresponding pairs of the coupled $B_{||}$ and $B_{\perp}$ electronic transitions (which are in parallel and perpendicular orientations to the axis connecting the two porphyrin rings[9]) are optically active and thus exhibit exciton split CD signals. It is therefore reasonable that the bulkier X substituents produce stronger steric repulsions and subsequently a larger screw in *anti*-**ZnD**·L_2 and in turn a greater deviation from parallel orientation of the interacting $B_{||}$ and $B_{\perp}$ dipoles (Figure 1c,d). According to CD exciton chirality theory,[12] the amplitude of the Cotton effects has a parabolic-like dependence on the dihedral angle between the coupling transitions, with zero values at 0° and 180° and a maximum value at around 70°. Indeed, in the case of the bulkier X substituents, the angle between the $B_{\perp}$ transitions becomes larger following the curve from 0° to the maximum, while the angle between the $B_{||}$ transitions becomes smaller following the curve from 180° to the maximum, resulting in an increase of the intensities of both CD signals.

A reviewer suggested that an additional factor which may play an important role in the size effect is a shifting of the overall equilibria between the right-handed, left-handed, and non screw linear structures in *anti*-**ZnD**·L_2 toward the least sterically hindered conformation (which has a greater degree of screw) upon increasing ligand bulkiness. This possibility was examined by comparison of the dissymmetry factors ($g = \Delta\epsilon/\epsilon$) at low temperatures[13] and at room temperature. The g values, which are presumably independent of the concentration change upon lowering the temperature, were found to be 2−4 times larger at low temperatures due to this enthalpically driven equilibrium shift. Therefore, it is reasonable to conclude that both steric and equilibrium factors contribute to the supramolecular chirogenesis in *anti*-**ZnD**·L_2 simultaneously.

The signs of the induced CD couplets are determined by the absolute configuration of the closest asymmetric carbon to the binding amino group of the external ligand. Thus, all the (*S*)-enantiomers of the amines studied give a positive first Cotton effect and negative second Cotton effect, while the ligands with the *R* absolute configuration produce the CD signals with opposite signs (Table 1). The signs of the Cotton effects observed for the **ZnD**/(*R*)-(+)-bornylamine system with three chiral centers are determined by the asymmetric carbon at the 2-position which has an (*S*)-configuration. This regularity is best explained also in terms of the CD exciton chirality theory.[12] This states that a clockwise orientation of two interacting electronic transition dipoles produces positive chirality, while a counterclockwise orientation leads to negative chirality. Ligands with *S* absolute configuration induce a right-handed screw in the *anti* conformer forming a clockwise twist of the coupling $B_{||}$ transitions and a counterclockwise twist of the coupling $B_{\perp}$ transitions. This results in the observed positive first Cotton effect and negative second Cotton effect (Figure 1c,d). In the case of the (*R*)-enantiomer, the dipole's directions are exactly opposite and produce inversion of the signs of the CD couplets.

In conclusion, this work demonstrates that the bulkiness of chiral ligands plays an important role in supramolecular chirality induction by controlling conformational changes in achiral host systems via a steric repulsion mechanism, with larger ligands inducing more intense CD signals. Also, this system possesses a high chiroptical sensitivity to the external guest molecules and thus is well suited for determining the absolute configuration of chiral compounds even when the asymmetry at the chiral carbon is low, as in the cases of 2-butylamine and 2-methyl-1-butylamine.

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(11) During the second ligation process there is a possibility of formation of another conformation, where the two chiral ligands are on opposite sides of *anti*-**ZnD**·L_2. The detailed conformational analysis and contribution of other conformations to the chirality induction process will be reported elsewhere. However, preliminary results obtained for monomeric zinc octaethylporphyrin binding with chiral ligands show that the total intensity of the CD signals may contain a minor contribution (up to 10%) from the point chirality due to the direct zinc porphyrin−ligand interactions.

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