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COMMUNICATIONS

Published on Web 12/31/2003

Chiroptical Transcription of Helical Information through Supramolecular Harmonization with Dynamic Helices

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Helices are indispensable structural elements in biological systems, and molecular design to sense helical structures is an interesting subject for better understanding of the stereochemical aspects of biological events.[1] Transcription of helical information may also be an important step to realize molecular informatics with biological macromolecules. Here we report a novel bioinspired approach to the transcription of helical information, using "bundling of peptide helices" as a motif for molecular design. Thus, we synthesized a chromophoric cyclic host (**1**, Chart 1; see also Figure 1a) consisting of two zinc porphyrin units that are connected by oligo(aminoisobutyric acid) (Aib) posts.[2] Although poly(Aib) is devoid of any chiral centers, it adopts a helical conformation due to a steric requirement of the $C(CH_3)_2$ unit.[3] It is also noted that the helical chain of poly(Aib) is dynamic, i.e., an equilibrium mixture of thermodynamically interconverting right- and left-handed helices.[3−5] We found that **1** can develop intense chiroptical signals upon inclusion of helical guests via stereochemical harmonization with the dynamic helical chains used for the post component.

Cyclic host **1** was obtained by metalation with $Zn(OAc)_2$ of a precursor free-base porphyrin, synthesized by coupling of an Aib nonamer with 5,15-bis(3-aminophenyl)-10,20-dimesitylporphyrin, followed by macrocyclization with 5,15-bis(3-carboxyphenyl)-10,20-dimesitylporphyrin.[6] On the basis of spectroscopic titration and Job's plots,[6] host **1** in $CHCl_3$ was found to form a stable 1:1 inclusion complex with guest molecule *L*-**2** (Figure 1b), a pyridine-anchored helical guest containing a (*L*)-leucine residue at its center (Chart 1). The association constant K_{assoc} was evaluated to be 1.7×10^6 M^{-1}. Although **1** is CD-silent, inclusion complex **1**⊃*L*-**2** displayed an intense exciton-coupled CD signal at the Soret absorption band of the zinc porphyrin moieties (410−450 nm) (Figure 2a, red solid curve), while **1**⊃*D*-**2** showed a mirror-image CD spectrum (red broken curve) of **1**⊃*L*-**2**. The inclusion complexes also showed CD bands in a short wavelength region, which most likely originate from the *meso*-aryl groups of the zinc porphyrin units, since the guest molecules themselves exhibit only negligibly weak CD bands at 250−350 nm.[6] These observations suggest that the two zinc porphyrin units of **1**, upon inclusion with helical **2**, adopt a twisted geometry in either clockwise or anticlockwise manner, depending on the helical sense of the guest.[2b] In sharp contrast, when a nonhelical guest such as *L*-**3** was used for the complexation with **1**, a CD-silent inclusion complex with a much smaller association constant ($K_{assoc} = 0.04 \times 10^6$ M^{-1}) resulted.[6] Host **1** remained CD-silent even upon addition of a large excess of *L*-**3** (e.g., 60-fold) with respect to **1**. Likewise, helical guest *L*-**2** (mono) carrying only a single pyridyl terminal (Chart 1) showed a poor binding affinity and did not gave a CD-active complex.[6] Therefore, it is most likely that inclusion of the guest with a helical conformation plays an essential role in generating a twisted geometry of the two facing zinc porphyrin units.

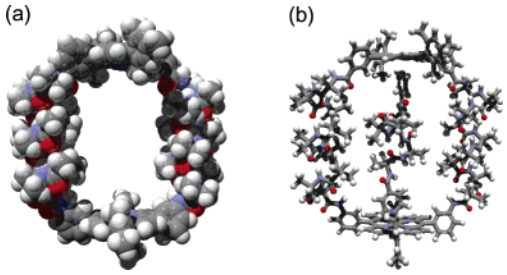
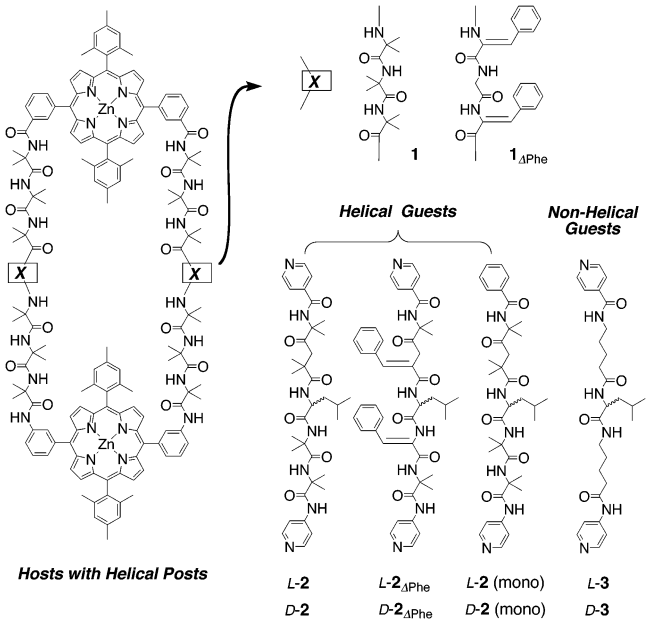


Figure 1. Molecular models of (a) **1** and (b) inclusion complex of **1** with *L*-**2**. The structures were created by combining a MM2-optimized structure of the zinc porphyrin unit and a crystallographically defined 3_{10}-helical structure of oligo(Aib).[3]

Chart 1. Schematic Structures of Hosts **1** and Guests **2** and **3**



We also synthesized host molecule $\mathbf{1}_{\Delta Phe}$ having, at the post parts, chromophoric dehydrophenylalanine (ΔPhe) units, since ΔPhe-containing single-handed peptides display enhanced CD bands centered at 280 nm, whose signs have been correlated with the helical senses.[4] Similar to the case with **1**, new host $\mathbf{1}_{\Delta Phe}$ was found to form CD-active inclusion complexes with helical guest **2** ($\mathbf{1}_{\Delta Phe}$⊃**2**; $K_{assoc} = 1.5 \times 10^6$ M^{-1}).[6] As shown in Figure 2a (blue curves), the exciton-coupled CD signals at the Soret absorption band of $\mathbf{1}_{\Delta Phe}$⊃**2** are less intensified than those observed for **1**⊃**2**. On the other hand, the CD spectral pattern in the short wavelength region is different from that of **1**⊃**2**, because of a possible overlap

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10.1021/ja039369p CCC: $27.50

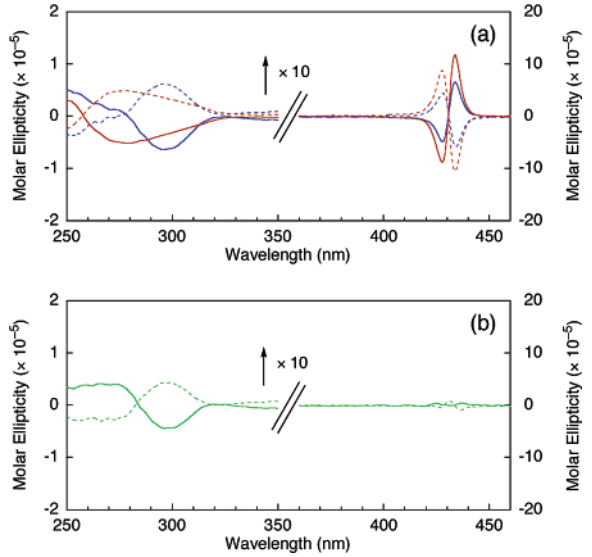

Figure 2. (a) CD spectra of **1** (red) and $\mathbf{1}_{\Delta Phe}$ (blue) in the presence of *L*-**2** (solid curves) and *D*-**2** (broken curves) ([guest]/[host] = 1.0) in $CHCl_3$ at 25 °C. (b) Differential spectra by subtraction of the CD spectrum of $\mathbf{1}\supset$*L*-**2** from that of $\mathbf{1}_{\Delta Phe}\supset$*L*-**2** (solid curve), and subtraction of the CD spectrum of $\mathbf{1}\supset$*D*-**2** from that of $\mathbf{1}_{\Delta Phe}\supset$*D*-**2** (broken curve).

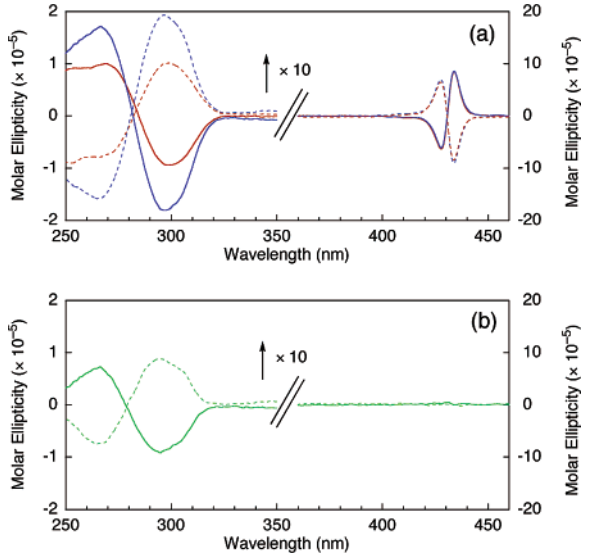

Figure 3. (a) CD spectra of **1** (red) and $\mathbf{1}_{\Delta Phe}$ (blue) in the presence of *L*-$\mathbf{2}_{\Delta Phe}$ (solid curves) and *D*-$\mathbf{2}_{\Delta Phe}$ (broken curves) ([guest]/[host] = 1.0) in $CHCl_3$ at 25 °C. (b) Differential spectra by subtraction of the CD spectrum of $\mathbf{1}\supset$*L*-$\mathbf{2}_{\Delta Phe}$ from that of $\mathbf{1}_{\Delta Phe}\supset$*L*-$\mathbf{2}_{\Delta Phe}$ (solid curve), and subtraction of the CD spectrum of $\mathbf{1}\supset$*D*-$\mathbf{2}_{\Delta Phe}$ from that of $\mathbf{1}_{\Delta Phe}\supset$*D*-$\mathbf{2}_{\Delta Phe}$ (broken curve).

of the CD band originating from the *meso*-aryl groups of the zinc porphyrin units with that of the ΔPhe-containing oligopeptides posts. In fact, when the CD spectra of $\mathbf{1}\supset\mathbf{2}$ (red curves) were subtracted from those of $\mathbf{1}_{\Delta Phe}\supset\mathbf{2}$ (blue curves) in Figure 2a, in a way that the CD signals at the Soret band region were canceled, green curves in Figure 2b were obtained as differential spectra, which are virtually identical to the CD spectral profiles of ΔPhe-containing single-handed oligopeptides.[4] This observation gave an insight that the dynamic helices in the post parts of **1**, upon inclusion of *L*-**2** and *D*-**2**, adopt, as judged from the CD signs,[4] right- and left-handed helical conformations (solid and broken curves in Figure 2b), respectively.

Since the helical conformations of *L*-**2** and *D*-**2** are not established, we utilized conformationally defined *L*-$\mathbf{2}_{\Delta Phe}$ (right-handed) and *D*-$\mathbf{2}_{\Delta Phe}$ (left-handed) as the helical guests for the inclusion with **1** and $\mathbf{1}_{\Delta Phe}$ (Chart 1).[4,6] The K_{assoc} values of $\mathbf{1}\supset\mathbf{2}_{\Delta Phe}$ and $\mathbf{1}_{\Delta Phe}\supset\mathbf{2}_{\Delta Phe}$ were 2.1×10^6 and 2.3×10^6 M^{-1}, respectively,[6] which are close to those for the inclusion complexes with **2**. On the other hand, the CD spectra of $\mathbf{1}\supset\mathbf{2}_{\Delta Phe}$ and $\mathbf{1}_{\Delta Phe}\supset\mathbf{2}_{\Delta Phe}$ (Figure 3a), though significantly enhanced in the short wavelength region due to the ΔPhe units, were similar in shape to those of $\mathbf{1}_{\Delta Phe}\supset\mathbf{2}$. Subtraction of the observed CD spectra in a way analogous to that in Figure 2b gave green curves in Figure 3b as differential spectra, which are again identical to those of ΔPhe-containing right- and left-handed oligopeptides. Judging from the signs of the split cotton effects centered at 280 nm,[4] it is clear that the oligopeptide posts in inclusion complex $\mathbf{1}_{\Delta Phe}\supset\mathbf{2}_{\Delta Phe}$ adopt the same helical conformation as that of the guest.

In conclusion, by using the biologically important "peptide bundling" as the motif, in conjunction with coordination chemistry of metalloporphyrins, we have demonstrated a novel method to sense helical conformations of oligopeptides. The results clearly indicate that dynamic helical peptides are stereochemically harmonized with right- or left-handed peptide helices in a confined nanospace, leading to a chiroptical output from the connecting zinc porphyrin chromophores. Stereochemical selection of helices through elaboration of the host structures is one of the subjects worthy of further investigation.

Acknowledgment. We thank N. Saeki and G. Ogawa for experimental assistance.

Supporting Information Available: Details for synthesis and characterization of **1**, $\mathbf{1}_{\Delta Phe}$, **2**, $\mathbf{2}_{\Delta Phe}$, **2** (mono), and **3**, and results of UV−vis and CD titration experiments and Job's plots (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) See Supporting Information.

JA039369P