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Supramolecular Chirogenesis in Bis-porphyrins: Interaction with Chiral Acids and Application for the Absolute Configuration Assignment

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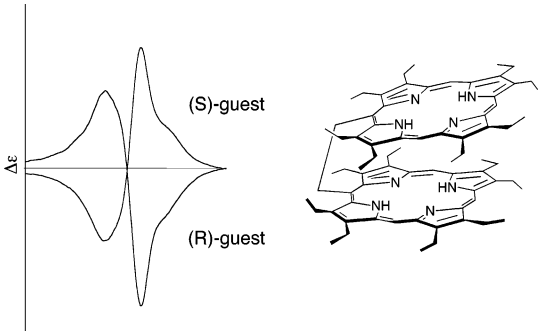
ABSTRACT



A new supramolecular chirogenic system on the basis of bis(free base porphyrin) and various enantiopure acids, which can be effectively applied for the chirality sensing purposes, is reported. The temperature and solvent are found to be key factors controlling the chirality transfer process in these assemblies.

Supramolecular chirogenesis in various systems and especially in porphyrinoids plays a decisive role in effective functioning of living organisms and has important practical implications for various fields of science and technology including molecular and supramolecular chirality sensing.[1] We have previously demonstrated that metallocomplexes of 5,5′-(ethane-1,2-diyl)bis[[2,3,7,8,12,13,17,18-octaethyl-21*H*,-23*H*-porphyrin] (**1**) (particularly Zn and Mg complexes) can be effectively used for the stereochemistry assignment of enantiomeric amines, diamines, alcohols, amino alcohols, and C-protected amino acids in solution and in solid state.[2] The general principle of enantiodifferentiation has been well established and is based on two major events: the guest binding and the subsequent host−guest steric interactions. Consequently, the guest's chirality can be read out from the CD sign induced in the region of porphyrin transitions. The straightforwardness and effectiveness of this sensing protocol combined with its simplicity offer an attractive promise to this approach as a universal tool for determining the absolute configuration of different chiral molecules using the same structural motif of host and the same methodology. As a further development of this research, here we report a new

(1) (a) Borovkov, V. V.; Inoue, Y. *Top. Curr. Chem.* **2006**, *265*, 89. (b) Lintuluoto, J. M.; Nakayama, K.; Setsune, J.-i. *Chem. Commun.* **2006**, 3492. (c) Balaban, T. S. *Acc. Chem. Res.* **2005**, *38*, 612. (d) Marchon, J.-C.; Ramasseul, R. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard R., Eds.; Academic Press: San Diego, 2003; Vol. 11, pp 75. (e) Tsukube, H.; Shinoda, S. *Chem. Rev.* **2002**, *102*, 2389. (f) Onouchi, H.; Miyagawa, T.; Morino, K.; Yashima, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 2381. (g) Lauceri, R.; Purrello, R. *Supramol. Chem.* **2005**, *17*, 61. (h) Li, W.-S.; Jiang, D.-L.; Suna, Y.; Aida, T. *J. Am. Chem. Soc.* **2005**, *127*, 7700. (i) Muranaka, A.; Okuda, M.; Kobayashi, N.; Somers, K.; Ceulemans, A. *J. Am. Chem. Soc.* **2004**, *126*, 4596. (j) Ribó, J. M.; Crusats, J.; Sagués, F.; Claret, J.; Rubires, R. *Science* **2001**, *292*, 2063. (k) Kubo, Y.; Ohno, T.; Yamanaka, J.-i.; Tokita, S.; Iida, T.; Ishimaru, Y. *J. Am. Chem. Soc.* **2001**, *123*, 12700. (l) Kurtan, T.; Nesnas, N.; Li, Y.-Q.; Huang, X.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2001**, *123*, 5962. (m) Crossley, M. J.; Mackay, L. G.; Try, A. C. *J. Chem. Soc., Chem. Commun.* **1995**, 1925.

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application of bis(free-base porphyrin) (*syn*-**1**) as a chirality sensor for various enantiopure acids (Figure 1).[3] While the

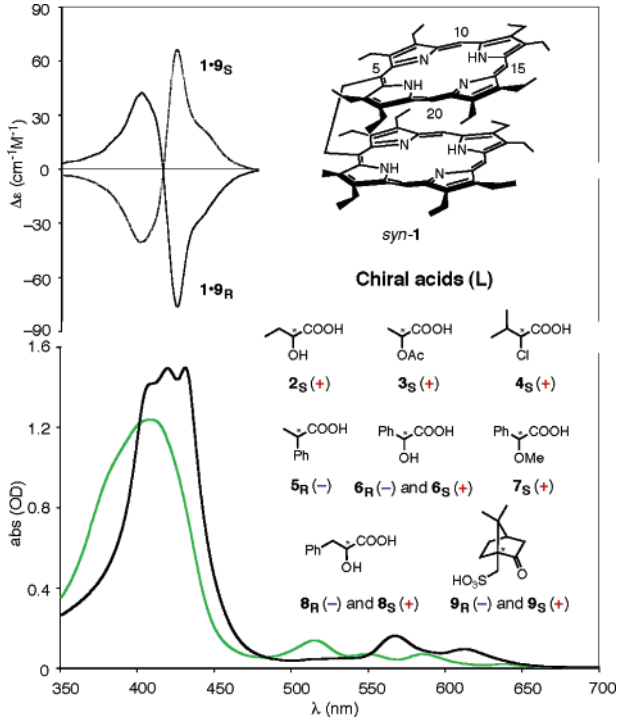

Figure 1. Structures of **1** and **L** (**2**−**9**); UV−vis (bottom) and CD (top) spectra of **1** (green line) and **1·9**$_R$ and **1·9**$_S$ (black line) in CH_2Cl_2. The subscript (R or S) indicates the absolute configuration of the carbon marked by asterisk, while the induced chirality sign is shown in parentheses.

basic chirogenic mechanism in *syn*-**1** upon interaction with chiral guests is essentially the same as in the case of corresponding metallocomplexes, the host−guest binding is significantly different. Hence, in contrast to the metallocomplexes of **1**, which bind the proper guests via the extra coordination mode, *syn*-**1** interacts with acids via the protonation mechanism.

The interaction process between *syn*-**1** as an achiral host and different acids as chiral guests has been monitored by UV−vis and CD spectroscopy at the 1000−10000 molar excess of guest. Spectral responses of the resulting complexes **1·9**$_R$ and **1·9**$_S$ are shown in Figure 1 as an example of the corresponding antipodal pair. The UV−vis spectral profile is greatly affected by the host−guest interaction resulting in red-shifted and split B (Soret) electronic transitions. Even more prominent change of the conventional four-band pattern to the two-band is observed in the Q transition region, which is a typical indication of the full protonation of free base porphyrin to yield the corresponding dicationic species.[4] In the case of **1**, this gives the respective tetracationic species. In the CD spectra, while the parent *syn*-**1** is optically inactive, **1·9**$_R$ and **1·9**$_S$ exhibit significant CD response in the region of the porphyrin's Soret band, giving the two bisignate Cotton effects of asymmetrical shape. As expected, complexation with the antipodal guests produces mirror-image CD spectra. Particularly, the (*R*)-enantiomer yields a negative first and positive second Cotton effects, while the (*S*)-guest gives the opposite signs. This is in full agreement with the data reported previously for the metallocomplexes of **1** upon interaction with monodentate chiral ligands,[2a,c] indicating the same mechanism of chirality induction. This includes the initial *syn*-to-*anti* conformational switching followed by the subsequent formation of the corresponding right- or left-handed screw in **1**, the direction of which is dictated by the stereochemistry of the guest as schematically shown in Figure 2. Specifically, the steric repulsive interactions between the

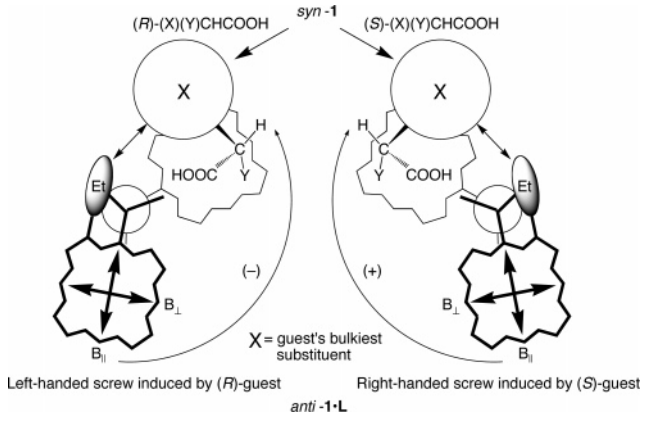

Figure 2. Supramolecular chirogenesis in **1** upon interaction with chiral acids. Only one interacting guest is shown for clarity.

3- or 7-ethyl group of one porphyrin moiety and the most bulky substituent of the chiral acid bound to the adjacent porphyrin macrocycle induce unidirectional screw formation. With the knowledge of the substituent's bulkiness at the stereogenic center, one can readily predict the helicity of the resulting *anti*-**1·L**. For example, when the bulkiness order of the guest substituents around the chiral center coincides with the substituents' priority rule, which determines the absolute configuration, the bulkiest substituents are on the left and right sides of the resulting complexes for the (*R*)- and (*S*)-guests, respectively, thus inducing the corresponding twists in *anti*-**1·L**. As this takes place, the two lowest energy $B_{||}$ electronic transitions, the orientation of which determines the sign of the induced chirality,[2] are coupled intramolecularly in an anticlockwise or clockwise fashion, which corresponds to negative or positive chirality, according to

(2) (a) Borovkov, V. V.; Hembury, G. A.; Inoue, Y. *Acc. Chem. Res.* **2004**, *37*, 449 and references therein. (b) Borovkov, V. V.; Fujii, I.; Muranaka, A.; Hembury, G. A.; Tanaka, T.; Ceulemans, A.; Kobayashi, N.; Inoue, Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 5481. (c) Borovkov, V. V.; Lintuluoto, J. M.; Inoue, Y. *J. Am. Chem. Soc.* **2001**, *123*, 2979.

(3) The *syn* conformer of **1** was synthesized according to Borovkov et al. (Borovkov, V. V.; Lintuluoto, J. M.; Inoue, Y. *Helv. Chim. Acta* **1999**, *82*, 919), and its purity was documented by its ^{1}H NMR spectrum (see the Supporting Information). Chiral acids **2**−**9** were purchased from Aldrich Chemical Co. and used as received.

(4) Smith, K. M. *Porphyrins and Metalloporphyrins*; Elsevier: Amsterdam, 1975.

the CD exciton chirality method.[5] It is of note that the electronic transitions in the fully protonated *anti*-**1·L** are orientated in the same way as the previously studied metallocomplex cases because of the increased symmetry in the porphyrin core.

In order to confirm the validity of this chirogenic rationale, a series of enantiopure acids meeting the same bulkiness criteria for external guests were tested (Figure 1 and Supporting Information). All of the guests studied (**2**−**9**) exhibit the same sign of induced chirality, as described above. However, it was found that the temperature plays an important role in controlling the host−guest interactions and subsequently induced optical activity in these supramolecular systems. Thus, while the CD couplet induced by **4**, **6**, **8**, and **9** can be easily detected at room temperature, lower temperatures are needed for **2**, **3**, **5**, and **7**. This apparently correlates with the acidity of guest and hence its capacity to bind the porphyrin's inner-core imino nitrogens to form the corresponding supramolecular complex via the simultaneous protonation followed by the ion pair interaction. The observed solvent and temperature dependences are fully consistent with this scenario (Supporting Information). Specifically, the amplitude of the induced CD signal (*A*) considerably decreases as the solvent polarity increases, due to the well-known ability of polar solvents to destabilize electrostatic interactions. In contrast, lowering the temperature enhances the host−guest interactions, thus resulting in remarkable magnification of the optical activity. For example in the case of **1·8**$_S$, reducing the temperature by 42 °C enlarges the *A* value by 38.6 times.

In addition, there is another distinctive feature of these supramolecular systems differing from the previously studied metallocomplexes of **1**;[2a,c] that is the number of the interacting steps. Thus, upon a stepwise addition of **4**$_S$ to *syn*-**1** it was clearly shown that there are four major equilibrium steps in the host−guest binding, which are best demonstrated by optical spectroscopy (Supporting Information). Initially, the maximum of Soret band (414 nm) of *syn*-**1** in the UV−vis spectra was blue-shifted yielding a new band (398 nm) at the 1:50 host/guest molar ratio. Further increase of the acid concentration up to 1:400 resulted in appearance of the absorption at even higher energy region (386 nm). At the same time, four Q bands of the acid free *syn*-**1** are considerably diminished to form a broad structureless absorption (from 500 to 650 nm). These two processes are essentially CD silent and apparently correspond to the formation of the free base-mono- and bis-monoprotonated species of **1**, both possessing the *syn* conformation.[6] This CD silence can be easily predicted upon considering the above-described chirogenic mechanism in **1**: in the *syn* conformation stereospecific host−guest interactions between the substituents at the chiral center of the guest and the neighboring porphyrin ring do not exist.

The next two steps are characterized by the opposite spectral tendency, which includes the subsequent bathochromic shifts of the Soret band to 399 nm at first and then further to 410 nm at the 1:20000 and 1:53350 molar ratios, respectively (Supporting Information). In the Q transition region a two-band spectral pattern is gradually developed due to the enhancement of molecular symmetry owing to the full protonation of porphyrin ring. These changes in absorption arise from formation of the corresponding monoprotonated−diprotonated and bis-diprotonated species of **1**, both being in the *anti*-conformations. These in turn induce the bisignate CD signal, which is further enhanced upon increasing the acid concentration, as a result of the interporphyrin excitonic interactions in the *anti*-**1·L** according to the above-discussed chirogenic mechanism. While the host−guest interaction mechanism is common for this type of supramolecular systems, guests such as **9**$_S$, which bind to the corresponding host more strongly, can reach the chirality induction steps at the lower host−guest molar ratios (Supporting Information).

The VT ^{1}H NMR spectral changes of **1** in the presence of **9**$_S$ are in full corroboration with the proposed mechanism of this host−guest equilibrium (Supporting Information). However, in contrast to the UV−vis data, which exhibited a fair indication of the existence of each equilibrium species, the chemical shifts represent just an average value of all individual components of the supramolecular system. Hence, addition of **9**$_S$ to **1** results in noticeable downfield shifts of the porphyrin *meso*, CH_2CH_2 bridge, and pyrrolic NH protons due to the protonation and subsequent *syn*-to-*anti* conformational switching. Remarkably, the singlet of bridge protons was split into two broad signals, as a clear indication of the chiral screw formation that was previously reported for the bis(Zn porphyrin).[2c] This split is further enhanced upon lowering the temperature. Similar behavior is also observed for the *meso* and NH protons.

In summary, this work demonstrates that the previously designed and thus easily accessible bis-porphyrin motif can be used as an universal tool for the chirality sensing of different classes of optically active compounds simply by varying the porphyrin inner core. Hence, application of the corresponding free-base bis-porphyrin allows facile and straightforward determination of the absolute configuration of chiral acids on the basis of induced CD couplet sign. Further studies to enhance the applicability and sensitivity of this system to this and other types of chiral compounds are currently in progress and will be reported in due course.

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Supporting Information Available: Various spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) Harada, N.; Nakanishi, K. *Circular Dichroic Spectroscopy. Exciton Coupling in Organic Stereochemistry*; University Science Books: Mill Valley, CA, 1983.

(6) A UV−vis Job plot confirms the 1:2 host−guest stoichiometry of this process (Supporting Information). The existence of the 1:2 species was additionally supported by ESI MS experiments, the results of which will be reported elsewhere.