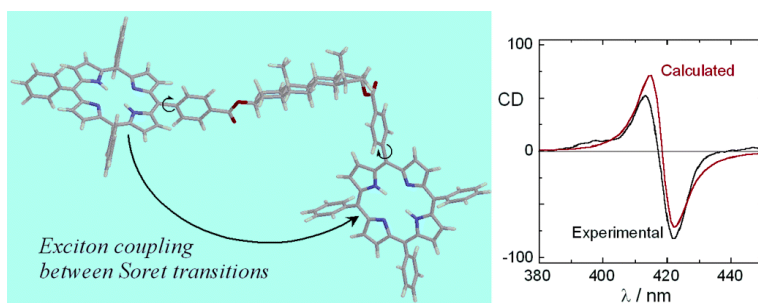


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Theoretical Analysis of the Porphyrin–Porphyrin Exciton Interaction in Circular Dichroism Spectra of Dimeric Tetraarylporphyrins

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Abstract: Chiral bis-porphyrins are currently the subject of intense interest as chiral receptors and as probes in the determination of structure and stereochemistry. To provide an improved framework for interpreting the circular dichroism (CD) spectra of bis-porphyrins, we have calculated the CD spectra of chiral bis-porphyrins from three classes: I, where porphyrins can adopt a relatively wide range of orientations relative to each other; II, porphyrins have a fixed relative orientation; III, porphyrins undergo π -stacking. The calculations primarily utilized the classical polarizability theory of DeVoe, but were supplemented by the quantum mechanical matrix method. Class I was represented by three isomers of the diester of 5 α -cholestane-3,17-diol with 5-(4'-carboxyphenyl)-10,15,20-triphenylporphyrin (2- $\alpha\beta$, 2- $\beta\alpha$, 2- $\beta\beta$). Careful analysis of the torsional degrees of freedom led to two to four minimum-energy conformers for each isomer, in each of which the phenyl–porphyrin bonds had torsional angles near 90°. Libration about these bonds is relatively unrestricted over a range of $\pm 45^\circ$. CD spectra in the Soret region were calculated as Boltzmann-weighted averages over the low-energy conformers for each isomer. Three models were used: the effective transition moment model, in which only one of the degenerate Soret components is considered, along the 5-15 direction; the circular oscillator model, in which both Soret components are given equal weight; and the hybrid model, in which the 10-20 oscillator is given half the weight of the 5-15 oscillator, to mimic the effect of extensive librational averaging about the 5-15 direction. All three models predict Soret exciton couplets with signs in agreement with experiment. Quantitatively, the best results are given by the hybrid and circular oscillator models. These results validate the widely used effective transition moment model for qualitative assignments of bis-porphyrin chirality and thus permit application of the exciton chirality model. However, for quantitative studies, the circular oscillator or hybrid models should be used. The simplified effective transition moment and hybrid models are justified by the librational averaging in the class I bis-porphyrins and should only be used with such systems. Two class II bis-porphyrins were also studied by DeVoe method calculations in the circular oscillator model, which yielded good agreement with experiment. Class III bis-porphyrins were represented by 2- $\alpha\alpha$, for which the calculations gave qualitative agreement. However, limitations in the conformational analysis with the close contacts and dynamic effects in these π -stacked systems preclude quantitative results.

Introduction

The tremendous interest in porphyrin–porphyrin interactions, witnessed by the literature of the past four decades, has a twofold reason.¹ First, many of the biologically relevant processes involving porphyrins, such as photosynthesis, and most por-

phyrin-based electronic and optical devices are known to depend on interacting porphyrin units. Second, since such interactions give rise to distinctive spectroscopic features, their monitoring is of crucial interest in any application of multi-porphyrin compounds as molecular receptors.

We are especially interested in employing porphyrin derivatives as chiral receptors and circular dichroism (CD) reporter groups for the structural determination of organic compounds.^{2,3}

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In fact, a combination of geometric and electronic properties renders these compounds ideal structural probes: (a) the approximately planar geometry, minimizing the conformational freedom; (b) the ease of incorporation of a wide variety of metal ions, as well as peripheral functional groups, allowing for a tuning of the chemical recognition, solubility, and aggregation properties; (c) a unique electronic structure, giving rise to diagnostic absorption and emission bands and to intense ring current effects, both useful for the ultra-sensitive monitoring of recognition processes.

In the present paper we focus on the absorption and CD spectra of bis-porphyrin derivatives in the Soret region. Absorption and emission spectra of regular porphyrins are dominated by the electronic π - π^* transitions associated with the aromatic chromophore.⁴ The most intense band in the UV-vis range, known as the Soret band, appears around 400 nm with an extinction coefficient over $10^5 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$, and it is allied to two quasidegenerate transitions, oriented perpendicularly to each other. Both the wavelength and the intensity of this band are essential for its sensitive and selective detection at low concentration in the presence of other organic chromophores, which represents the main advantage of using porphyrins as CD probes.³

The theoretical basis for our analysis lies in considering the two porphyrins, which constitute the bis-derivatives under investigation, as independent units from an electronic point of view. The independent system approximation (ISA) simplifies the optical properties of polychromophoric molecules, oligomers, or aggregates, whose interpretation may be complicated by the molecular complexity, as a combination of the corresponding properties of the isolated chromophores, constituting units or monomers.^{5,6} In particular, in the presence of intense electric dipole-allowed transitions, the coupled-dipole mechanism⁷ holds, which leads to unique tools for predicting absorption and CD spectra on a nonempirical basis and relating them to the molecular geometry in a quantitative way.^{8,9} When two degenerate or quasidegenerate transition dipole moments lie close to each other, their through-space interaction gives rise to distinctive spectral features: in the CD spectrum, a bisignate couplet is obtained whose sign is determined by the absolute

sense of twist defined by the two dipoles. When the direction of the transition moments within the chromophores is known, the absolute configuration of the substrate may be derived by the exciton chirality method: in the paradigmatic case of *para*-substituted benzoates of 1,2-diols, the 1L_a transition is polarized parallel to the $C_{Ar}-C(=O)$ and then to the alcohol C^*-O bonds (due to the preferred $C=O/C^*-H$ *syn* and ester $C(=O)-O$ *s-trans* orientation); thus, a positive CD couplet always corresponds to a positive chirality defined by the two $C-O$ bonds and vice versa.^{8,9} A full quantitative prediction of exciton-coupled UV-vis and CD spectra is also possible by means of coupled-oscillator calculations, for which different methods are available;¹⁰ in particular, DeVoe's polarizability theory¹¹ is used here.

Tetraarylporphyrins have been extensively employed as chromophoric probes for structural analysis and determination of chirality. In recent years, three main approaches have been followed.

(a) 5-(4'-Carboxyphenyl)-10,15,20-triphenylporphyrin (TPP-COOH) has been used as an alternative to benzoate-like CD reporter groups for exciton analysis of chiral diols with a rigid skeleton. In fact, the enhanced sensitivity allows observation of exciton coupling over very large distances.^{12,13}

(b) For OH- and NH-containing chiral compounds with an acyclic and flexible skeleton, bis-derivatives of Zn(TPP-COOH) may be formed that undergo stereoselective intramolecular π - π stacking. The absolute sense of twist between stacked porphyrins, revealed by CD, is dictated by the configuration of the chiral substrate. This approach has been applied to chiral diols, including ceramides, amino alcohols, amino acids and α -hydroxy acids.¹⁴

(c) For mono- and bis-functionalized chiral compounds, an alternative approach requiring no porphyrin derivatization is possible. The chiral substrate or a suitable bis-functional conjugate containing two amino groups forms a host/guest complex with an achiral bis(Zn-porphyrin) host (tweezer), in a stereocontrolled manner, through double N/Zn ligation. The absolute sense of twist between the two porphyrins in the complex, revealed by CD, is dictated by the configuration of the chiral substrate. This approach has been applied to α,ω -diamines, primary and secondary amines, and secondary alcohols, including many natural products.¹⁵⁻¹⁷ Recently, a combined O/Zn and N/Zn ligation has been used for determining the absolute configuration of chiral carboxylic acids deriva-

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- (7) The term *coupled-dipole* or *exciton model* refers to a theoretical mechanism of optical activity that involves the Coulombic coupling between electric transition dipoles. This dipole-dipole coupling is often referred to as *exciton coupling* or *interaction*. UV-vis and CD spectra dominated by the coupled-dipole mechanism are often called *exciton-coupled*. The analysis of optical spectra according to the coupled-dipole mechanism (also referred to as *exciton analysis* or *approach*) may be qualitative or quantitative. In a qualitative way, the *exciton chirality method* (or simply *exciton method*) relates the sign of CD spectrum with the absolute configuration. In a quantitative way, full CD spectra may be evaluated through *coupled-dipole* calculations; these can be accomplished within a quantum-mechanics (*exciton*) or classical physics (*coupled-oscillator*) frame. One example of a coupled-oscillator method is DeVoe's *polarizability theory*.
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tized as *N*- γ -aminopropyl amides,¹⁸ as an alternative to the standard approach.¹⁹

In all the methods above, CD spectroscopy affords crucial information, as the sign of the CD couplet in the Soret region is taken as proof of the absolute configuration of the chiral substrate. Understanding the nature of the porphyrin–porphyrin interactions responsible for this diagnostic spectral feature remains an intriguing task, mainly due to the pivotal role played by conformational factors and to the structural and electronic complexity introduced by the porphyrins. As a matter of fact, while the exciton model has been extensively used for the interpretation of UV–vis spectra of porphyrin oligomers and aggregates,^{20–23} no comprehensive review is available describing a general approach for quantitative prediction of CD spectra of this important class of compounds. In particular, the use of porphyrins as chirality probes has so far relied on a simplified presentation of the porphyrin electronic properties: in order to apply the exciton chirality method, the Soret band has been described in terms of a single transition dipole (effective transition moment approximation).¹³

The aim of the present paper is to analyze theoretically the nature and origin of porphyrin–porphyrin CD exciton coupling and its dependence on structural and conformational factors. The scope and limitations in applicability of coupled-oscillator formalism to tetraarylporphyrin dimers are tested. Only covalently linked derivatives are taken into account, to minimize the uncertainty relative to the molecular structure; for each compound, the geometry is calculated by molecular modeling and the CD spectrum is calculated by the DeVoe method¹¹ (point-dipole approximation) and the matrix method²⁴ (monopole or distributed dipole approximation). In particular, we focus on three model categories which are schematically represented in Figure 1: class I, compounds with porphyrin rings with largely unrestricted rotation (about one or more preferential axes); class II, compounds with two porphyrin rings with fixed spatial orientation; class III, compounds with porphyrins undergoing π – π stacking.

The comparison between classes I and II allows us to stress the impact on CD spectra of the conformational key factor of porphyrin ring rotation and to discuss the limitations and theoretical justification of the effective transition moment approximation. Class III represents a challenge for CD calculations based on the ISA, because of the short interchromophoric distance.

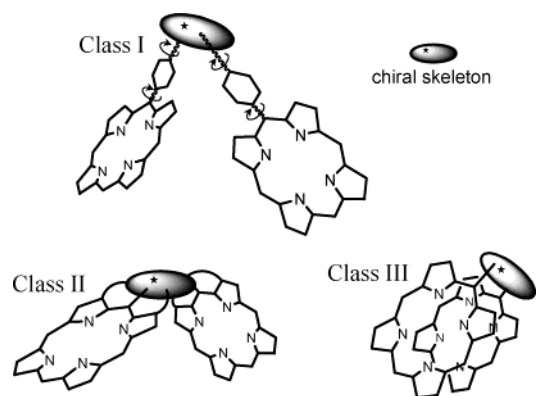


Figure 1. Schematic representation of the three classes of bis-porphyrin compounds investigated. Class I: compounds with porphyrin rings with unrestricted rotation (about one or more axes). Class II: compounds with two porphyrin rings with fixed spatial orientation. Class III: compounds with π – π stacked porphyrins.

Finally, the results and conclusions of calculations on model compounds are extended to many CD exciton-coupled spectra of chiral bis-porphyrin derivatives reported earlier.

Electronic Structure of the Porphyrin Chromophore and Exciton Analysis of UV–Vis Absorption Spectra of Multi-porphyrin Compounds

The electronic structure of porphyrin-like compounds has been the subject of thorough investigations, and many calculation methods have been applied ranging from Hückel-type to ab initio.^{4,25} At lower energies, two bands (often with pronounced vibrational structure) appear between 500 and 600 nm with extinction coefficients around 10^4 $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$, referred to as Q bands in Platt's nomenclature.²⁶ The Soret or B bands are usually found as a single absorption band between 380 and 420 nm, with an extinction coefficient of the order of 10^5 $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$, with position and intensity perturbed to varying extents by substituents and the metal ion. The system of Q and B bands arises from the combination of the four excitations from the two HOMOs to the two LUMOs of the 18-electron π ring (Gouterman's four-orbital model).⁴ A shoulder sometimes appears on the high-energy side of the B band, attributed to one mode of vibrational excitation B(1–0) with $\sim 1250 \text{ cm}^{-1}$ spacing. At higher energies, other bands with much smaller intensities (N, L, and M bands) are present.

The intensity and position of B bands justify employing the exciton model to interpret UV–vis and CD spectra of multi-porphyrin derivatives. For this method to be valid, in fact, intense electric dipole-allowed transitions must be responsible for the spectral features considered, interacting through space via an electric dipole–dipole mechanism.^{6,8} In the presence of two or more porphyrin chromophores located nearby in space, the spectral region around 400 nm will be largely determined by the exciton coupling between B transitions.

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The nondegenerate coupling with Q and other transitions will be negligible in most cases, as will the coupling with many organic chromophores absorbing below 300 nm (the extent of any kind of interaction between electronic transitions is directly proportional to their intensity and inversely proportional to the energy difference). This situation is almost ideal for treatment within a degenerate exciton coupling framework. Since the vibrational spacing associated with B bands may be of the same order of magnitude as the exciton coupling potential, the B–B coupling may fall in the range of so-called weak coupling, for which the interaction between individual vibronic bands should be considered.^{27,28} However, given the much smaller intensity of the B(1–0) component, its effect on the coupling between B(0–0) components is minor and may be neglected.²⁰

The main feature of the exciton model is the straightforward mathematical relationship between spectroscopic properties and molecular geometry.^{6,8} Given two degenerate electronic transitions at energy $E_0 = hc\tilde{\nu}_0$ ($\tilde{\nu}_0$ in wavenumbers), the transition dipole moments $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ interact through the potential V_{12} , which can be approximated with the dipole–dipole term:

$$V_{12} = \frac{\boldsymbol{\mu}_1 \cdot \boldsymbol{\mu}_2}{R_{12}^3} - 3 \frac{(\boldsymbol{\mu}_1 \cdot \mathbf{R}_{12})(\boldsymbol{\mu}_2 \cdot \mathbf{R}_{12})}{R_{12}^5} = \frac{\mu_1 \mu_2}{R_{12}^3} G_{12}$$

where \mathbf{R}_{12} is the interchromophoric vector between the two point dipoles, G_{12} is a geometrical factor depending on their orientation, $R_{12} = |\mathbf{R}_{12}|$, $\mu_i = |\boldsymbol{\mu}_i|$. The dipole–dipole term is the leading term in the multipole expansion of the interaction between two transition charge densities. Higher order terms are important for interporphyrin distances comparable to or smaller than the dimensions of the chromophores. For such systems, the monopole (distributed dipole)²⁹ approximation is preferable²² to the point-dipole approximation. In the monopole approximation, the transition charge density is represented by a set of point charges, the first moment of which is the transition dipole moment:

$$\boldsymbol{\mu}_i = \sum_s q_{is} \mathbf{r}_s$$

where q_{is} is the charge of monopole s for transition i and \mathbf{r}_s is the position of the monopole. The interaction between the two transition charge densities, V_{12} , is obtained from Coulomb's law:

$$V_{12} = \sum_s \sum_t (q_{1s} q_{2t}) / r_{1s2t}$$

where $r_{1s2t} = |\mathbf{r}_{2t} - \mathbf{r}_{1s}|$ is the distance between monopole s of transition 1 and monopole t of transition 2.

This exciton interaction will give rise to the distinctive UV–vis absorption (either split, or more often appearing as a single band with increased broadening, or with a shoulder) and bisignate CD feature (exciton couplet), with in-phase (+) and out-of-phase (–) components at energies $E_{\pm} = E_0 \pm V_{12}$ and dipolar and rotational strengths as follows:

$$D_{\pm} = \frac{1}{2}(\boldsymbol{\mu}_1 \pm \boldsymbol{\mu}_2)^2 \therefore R_{\pm} = \mp \frac{\pi}{2} \tilde{\nu}_0 \mathbf{R}_{12} \cdot \boldsymbol{\mu}_1 \times \boldsymbol{\mu}_2$$

It is generally accepted that the porphyrin B band is due to two quasidegenerate transitions with perpendicular polarization (referred to as B_x and B_y).⁴ In metal porphyrins with D_{4h} symmetry, the two B transitions are exactly degenerate; for free-base porphyrins with D_{2h} symmetry, the degeneracy is theoretically removed, but the absorption is still not detectably split, and only an increased bandwidth is apparent. Therefore, the B band cannot be described in terms of a single transition dipole or linear oscillator but as a combination of two mutually perpendicular oscillators. If they are considered degenerate, that is with the same energy and intensity, any linear combination of the two will provide the same overall result^{30,31} and a better description of the B transitions will then involve a so-called circular oscillator.^{13,30,32} Any simplification of this picture in terms of a single linear oscillator in each porphyrin is theoretically not justified but, as discussed below, may hold in some cases, depending on the structural features. It is still possible to use the above equations for a circular oscillator, as the principle of pairwise additivity states that the overall effect of exciton coupling between three or more transitions is equivalent to the summation of all possible pairwise terms.^{9,33} Even though this principle is only approximated in the general case, it is exact when the coupling between the two components (arbitrarily chosen) of a circular oscillator and a third oscillator is considered.^{30,31} In practice, all-order matrix-based methods exist, such as those of Schellman²⁴ and DeVoe/Applequist,^{11,34} which can be profitably employed for the calculations of optical properties of systems composed of any number of chromophores, within the ISA and/or the exciton model, if the spectroscopic properties of the single chromophores are known.

After Kasha first described the exciton model for molecular aggregates,³⁵ a large number of papers followed concerning the application to bis- and oligo-porphyrin derivatives.^{20–23} In many reports, the exciton analysis of UV–vis absorption spectra has been qualitative but still extremely useful. For instance, it correctly predicts the well-known red- and blue-shifting of B bands in respectively head-to-tail and face-to-face porphyrin aggregates. However, the exciton model can also serve as a tool for full quantitative prediction of spectra and detailed structural analysis. To extract the structural information, experimental spectra are usually compared with those calculated for a set of geometries. More simply, but less accurately, the experimentally estimated and calculated values for two parameters are compared: (a) the bandwidth, often expressed as full width at half-maximum (FWHM), which is connected to the wavelength separation (Davydov splitting) between the exciton components but is always dominated by the inherent bandwidth of the Soret band; (b) the intensities of the two split components, which requires an accurate deconvolution of the experimental band into two Gaussian or Lorentzian curves.

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Several reports have demonstrated the usefulness of this approach for assessing structural parameters such as porphyrin–porphyrin distances or offsets in π – π dimers, torsional angles, and even conformational dynamics properties, in covalently linked porphyrin derivatives.^{20–23,36} The main obstacle to this approach is the extended dimension of the porphyrin chromophore (~ 7 Å) which in some cases (especially for π – π stacked aggregates) may be comparable with the interchromophoric distances, thus making the point-dipole approximation poor and leading to over- or underestimates of the coupling potential (vide infra).²²

It is well accepted that CD spectroscopy has enhanced structural sensitivity with respect to UV–vis absorption spectroscopy; also, due to the nature of CD spectra, the two exciton-coupled components always appear as bands with opposite signs, which in turn makes the extraction of relevant parameters (Davydov splitting and couplet intensity) easier and less prone to errors.³⁷ Despite this clear advantage, only a few examples exist of full calculations of CD spectra of multi-porphyrin compounds with the exciton model. The power of this approach was demonstrated years ago by Woody and co-workers on biologically crucial systems such as hemoglobins and chlorophylls.^{32,38,39} More recently, CD spectroscopy has been widely employed as a detection tool in the emerging field of porphyrin-mediated chiral recognition.^{2,3,14–19,40,41} In these studies, the application of the exciton chirality method has relied on a simplified view of the complex electronic structure of porphyrins, namely, the approximation of a circular oscillator by a linear dipole. Matile et al. in fact demonstrated that in most cases bis-porphyrin derivatives of chiral diols give exciton-coupled CD spectra consistent with those of the bis(*p*-dimethylaminobenzoates) analogues, thus supporting the view that the B transition may be described by means of an effective transition dipole moment.¹³ Even if this model has never been justified on a theoretical basis, which is one of the aims of the present paper, it has been generally accepted in recent studies. In most reports the sign of the exciton-coupled CD has been taken into account as a proof of the interchromophoric absolute sense of twist.^{12–14,41–45} Determining interporphyrin helicity from the CD

is especially important when dealing with complexes between chiral guests and achiral bis-porphyrin hosts,^{15–17,40} as it turns out that this helicity reveals the absolute configuration of the chiral substrate. In some cases the couplet intensity has been considered too, to draw qualitative or semiquantitative structural conclusions.^{13,46,47} All these reports will be further analyzed in the Results and Discussion section IV below.

Computational Methods

Coupled-Oscillator CD Calculations. Coupled-oscillator CD calculations were accomplished within the classical model known as DeVoe's polarizability theory.¹¹ This method is an all-order treatment widely employed for configurational and conformational investigations of organic⁴⁸ and biomolecules.^{49,50} In the case of the bis-porphyrin compounds currently investigated, as well in many similar biologically relevant examples,³⁸ DeVoe's method is especially useful because the observed exciton coupling is extended over large distances, which makes the effective value of the interaction potential V_{12} quite low and much smaller than the inherent bandwidth of the Soret band. In this situation, known as weak coupling,²⁷ it has been demonstrated that the polarizability theory may substantially differ from and give better results than the standard strong-coupling exciton approach.^{11,38,49} This is because in most exciton calculations, the monomer bandwidth is neglected and the intensity is treated as a Dirac δ function in the calculation of the oligomer or polymer dipole and rotational strengths, equivalent to the strong-coupling limit.⁵¹ Band shapes and bandwidths are then rather arbitrarily assigned to the oligomer or polymer transitions. In the DeVoe method, the monomer band shape is explicitly taken into account in calculating the monomer oscillator polarizability and their coupling, which is consistent with weak coupling.

DeVoe's method requires that the chromophore electronic transitions be described in terms of transition multipoles (in the current case, point dipoles),⁵² characterized by position, direction of polarization, frequency, dipolar strength, and band shape (which can be approximated by a Lorentzian curve with defined bandwidth).

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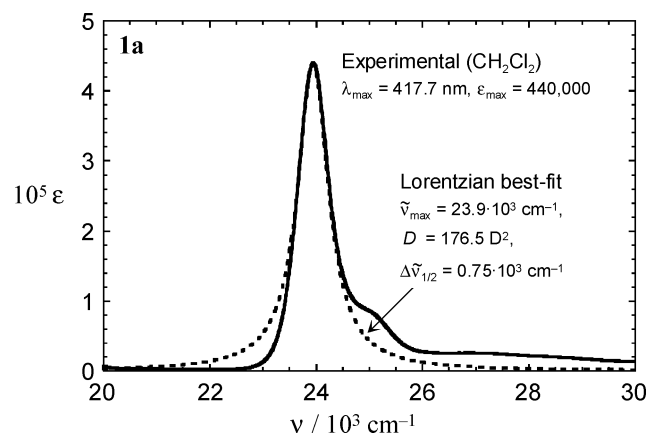


Figure 2. UV-vis spectrum of TPP-COOMe (**1a**) 2.34 μM in CH_2Cl_2 (solid line) and best-fitting Lorentzian curve (dotted line) with relevant parameters.

In the following calculations, the Soret absorption band has been approximated with a best-fit Lorentzian curve (see Figure 2), which for 5-(4'-carboxymethylphenyl)-10,15,20-triphenylporphyrin (TPP-COOMe, **1a**) free base in CH_2Cl_2 ($\lambda_{\text{max}} = 417.7 \text{ nm}$, $\epsilon_{\text{max}} = 440\,000 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) has the following parameters: frequency maximum $\tilde{\nu}_{\text{max}} = 23.9 \times 10^3 \text{ cm}^{-1}$, dipole strength $D = 176.5 \text{ D}^2$ (square Debye), FWHM $\Delta\tilde{\nu}_{1/2} = 0.75 \times 10^3 \text{ cm}^{-1}$. For describing the B transition of each porphyrin, two mutually perpendicular dipoles have been used in the DeVoe calculations,^{13,30,32} placed in the center of the porphyrin ring (between opposite C_{meso} atoms), directed for convenience along $C_{\text{meso}} - C_{\text{meso}}$ (5–15 and 10–20) directions (any other orientation did not affect the result),^{30,31} each with dipole strength $D = 88.3 \text{ D}^2$. Since we assumed the two Soret components are exactly degenerate, our results are strictly valid for those bis-porphyrin derivatives where this degeneracy is not apparently removed, i.e., the Soret band is not detectably split; in fact, this is the case for most of the tetraporphyrin compounds used as molecular receptors.^{2,3,12–18} For the calculations, a Fortran program developed by Hug was employed.^{49,53}

To test the point-dipole approximation, calculations were also performed with the same geometries using the monopole approximation.⁵² These calculations used the matrix method of Schellman and co-workers,²⁴ as implemented in the program MATMAC.⁵⁴ Monopoles were centered at the heavy atoms of the porphyrin ring. The monopole charges were calculated from π -MO wave functions in Gouterman's four-orbital model,⁴ using Hsu's porphyrin geometry³⁰ and the standard parameters of Weiss et al.⁵⁵ The porphyrin geometry⁵⁶ is given in Table

- (52) The point-dipole approximation is used here with the DeVoe method, and the monopole approximation with the matrix method, as is commonly the case. It should be noted, however, that the monopole approximation can be used in the DeVoe method⁴⁹ and the point-dipole approximation can be used with the matrix method.³⁸
- (53) No solvent dielectric constant was used in the calculations; although some impact of solvent on the exciton interaction is conceivable,^{21f} the question of the propriety of including a dielectric constant in coupled-dipole calculations is still not clear. In some reports, a value $\epsilon_{\text{eff}} \approx n^2 \approx 2$, has been employed, since the square of refractive index n can be taken as an estimate of the effective dielectric constant at optical frequencies.^{23,38} This would require the medium around and between the two chromophores to be describable as a continuum, which for the covalently linked bis-porphyrins considered, even separated by distances around 20 Å, is still questionable. Introducing the value $\epsilon_{\text{eff}} = 2$ would scale down all our calculated spectra by a factor of about 2. Recently, Hsu et al. (Hsu, C.-P.; Fleming, G. R.; Head-Gordon, M.; Head-Gordon, T. *J. Chem. Phys.* **2001**, *114*, 3065–3072) pointed out that a screening factor of $(2\epsilon_{\text{eff}} + 1)/3$ is more rigorously correct for two dipoles included in distinct cavities separated by the solvent. Moreover, when the two dipoles lie so close to each other as to be included in a single cavity, the effect of the solvent may suppress (up to 25%) or enhance (up to 10%) the interaction, depending on the geometry. The authors conclude that this “enhancement/suppression effect [...] may explain the excellent agreement of some quantum chemistry calculations [of excitation energy transfer] to experimental results without considering the effects of the medium”.
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S1 and the monopole charges for the Soret transitions are given in Table S2 (Supporting Information). The MO-derived charges were scaled to reproduce the experimental transition dipole moment magnitude of the monomeric model, 9.40 D. Lorentzian band shapes were assumed in calculating the CD spectrum with the same bandwidth used in the DeVoe calculations.

Molecular Modeling. In addition to the spectral parameters, the CD calculations require the molecular structure to be known. Many easily accessible and computationally nondemanding Molecular Mechanics (MM) methods have been applied to porphyrin-derived compounds.⁵⁷ In this study we use the Merck Molecular Force Field (MMFF94) developed by Halgren,⁵⁸ in its “static” version MMFFs (which ensures the planarity of sp^2 nitrogen atoms), which is the default in MacroModel 7.1.⁵⁹ The efficiency of MMFFs in modeling bis-porphyrin systems has already been tested by us, as reported elsewhere.¹⁷ The conformation of all compounds was investigated through Monte Carlo (MC) conformational searches and combined Monte Carlo/Stochastic Dynamics (MC/SD) simulations; both methods are implemented in MacroModel 7.1.^{59,60,61}

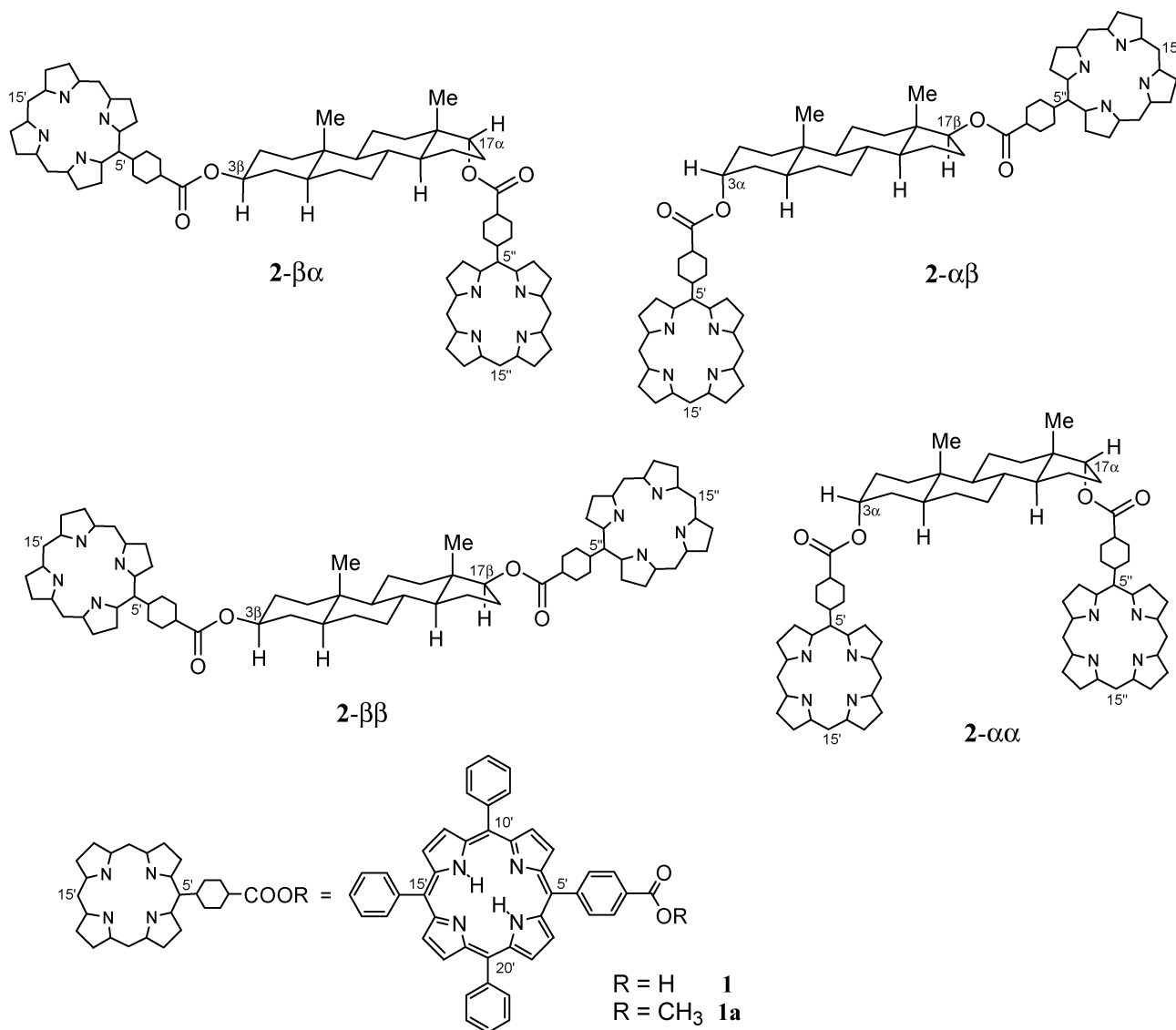
Experimental Section

Solvents employed were reagent grade and dried before use. Deuterated solvents were purchased from CIL, Inc. 5 α -Cholestan-17 β -ol was purchased from Steraloids, Inc. TPP-COOMe (**1a**) was purchased from TCI (Japan). UV-vis spectra were recorded on a Perkin-Elmer Lambda 40 spectrophotometer in a 1-cm quartz cell. CD spectra were recorded on a Jasco-810 spectropolarimeter in a 1-cm quartz cell. For variable-temperature CD spectra, a Jasco Crys-415 cryostat and a TC-22HK thermo controller were used with a 0.5-cm quartz cell. ¹H NMR spectra were measured with a Bruker DMX 400 or 500 MHz spectrometer and are reported in parts per million (ppm) relative to TMS. ¹H–¹³C HSQC spectra were recorded with a Bruker DMX 500 MHz spectrometer, with 512 points in f1 and f2, digital resolution 40 Hz in f1 and 4 Hz in f2, spectral widths 160 ppm in f1 and 8 ppm in f2, and 4 scans per increment. Low- and high-resolution FAB mass spectra were measured on a JEOL JMS-DX303 HF mass spectrometer using a glycerol matrix and Xe ionizing gas.

Synthesis and characterization of compounds **1**, **2**, and **3** have been reported elsewhere.^{13,62}

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- (59) Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440–467. Molecular modeling calculations were executed with the MacroModel 7.1 package (Schrödinger, Inc., Portland, OR) including Maestro 3.0 as GUI, on a Dell Precision 330 workstation. Molecular mechanics calculations were run using the native MMFFs in vacuo or in CHCl_3 (GB/SA solvation model), with default parameters and convergence criteria, except that the maximum number of minimization steps was set to 50 000, and the convergence threshold was set to 0.005 kJ/mol. MC conformational searches were run with default parameters and convergence criteria, sampling all the structures within 10 kJ/mol over 1000 fully optimized steps. MC/SD simulations were run with default parameters and convergence criteria, and the following conditions: temperature 300 K, time step 1.0 or 1.5 ps, equilibration time 2 ps, simulation time 1 ns, 1:1 ratio between MC and SD steps; bond-length constraints were not used. DFT B3LYP/6-31G** calculations were run with Jaguar 4.1 (Schrödinger, Inc., Portland, OR).
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- (61) Guarnieri, F.; Still, W. C. *J. Comput. Chem.* **1994**, *15*, 1302–1310.
- (62) Jiang, H. Structural Studies of Biologically Active Natural Products; Ph.D. Thesis, Columbia University New York, 1998; pp 68–107.

Chart 1



5 α -Cholestan-17 β -ol *p*-[10',15',20'-triphenyl-5'-porphyrinyl]benzoate was prepared according to the standard procedure from 2.5 mg of 5 α -cholestan-17 β -ol (9.0 μ mol), TPP-COOH (**1**, 1.5 equiv), EDC (2 equiv), and DMAP (2 equiv) in refluxing CHCl₃ for 36 h and purified by column chromatography (silica gel, CH₂Cl₂, *R_f* = 0.9). UV-vis (CH₂Cl₂) 417.6 nm (ϵ = 440 000), 514.7 (18 400), 549.9 (8300), 589.3 (5600), 646.9 (4900). CD (CH₂Cl₂) 417.1 nm ($\Delta\epsilon$ = +4.3). ¹H NMR (400 MHz, CDCl₃) δ -2.77 (s, 2H), 0.8–2.5 (several m, 45H), 5.03 (t, 1H, *J* = 9.0 Hz), 7.75–7.80 (m, 9H), 8.20–8.22 (m, 6H), 8.29 (d, 2H, *J* = 8.0 Hz), 8.43 (d, 2H, *J* = 8.0 Hz), 8.79–8.86 (m, 8H). FAB-MS *m/z* 917 (*M* + 1⁺). FAB-HRMS *m/z* calcd for C₆₄H₆₁N₄O₂ 917.4795, found 917.4818.

Results and Discussion

I. Bis-porphyrin Derivatives with Unrestricted Porphyrin Rotation (Class I).

I.1. Experimental CD Spectra of Bis-porphyrin Derivatives of 5 α -androstane-3,17-diol (2- $\alpha\beta$, 2- $\beta\beta$, 2- $\beta\alpha$). The rigid chiral scaffold derived from functionalized steroids is ideal for testing the properties of chromophores as circular dichroism reporter groups. The CD spectra of diesters (**2**) of 5-(4'-carboxyphenyl)-10,15,20-triphenylporphyrin (TPP-COOH, **1**) and

Table 1. Experimental CD Data for Compounds **2** (Soret Band, in CH₂Cl₂) and **3** (¹B₀ Band, in CH₃CN)^a

steroid	porphyrinates 2		anthroates 3	
	$\lambda_{\text{ext}}/\text{nm}$ ($\Delta\epsilon$)	<i>A</i>	$\lambda_{\text{ext}}/\text{nm}$ ($\Delta\epsilon$)	<i>A</i>
3 α ,17 β	423 (+122)	+193	271 (+59)	+88
	414 (-71)		253 (-29)	
3 β ,17 β	423 (-17)	-32	272 (-18)	-57
	415 (+15)		254 (+39)	
3 β ,17 α	423 (-83)	-135	272 (-15)	-29
	414 (+52)		253 (+13)	
3 α ,17 α	420 (-67)	-97	272 (+88)	+157
	411 (+30)		253 (-69)	

^a λ_{ext} peak or trough wavelength, *A* couplet amplitude.

5 α -androstane-3,17-diols have been reported earlier.^{12,13} In this section we discuss 3 α ,17 β (**2- $\alpha\beta$**), 3 β ,17 β (**2- $\beta\beta$**), and 3 β ,17 α (**2- $\beta\alpha$**) isomers (Chart 1). The 3 α ,17 α isomer (**2- $\alpha\alpha$**) will be discussed in section III.

Table 1 and Figure 3 (solid lines) show the CD spectra of **2- $\alpha\beta$** , **2- $\beta\beta$** , and **2- $\beta\alpha$** in CH₂Cl₂; the spectra in all other solvents (methylcyclohexane MCH, hexane, benzene, toluene, CHCl₃, and CH₃CN) are consistent in sign and shape, with some

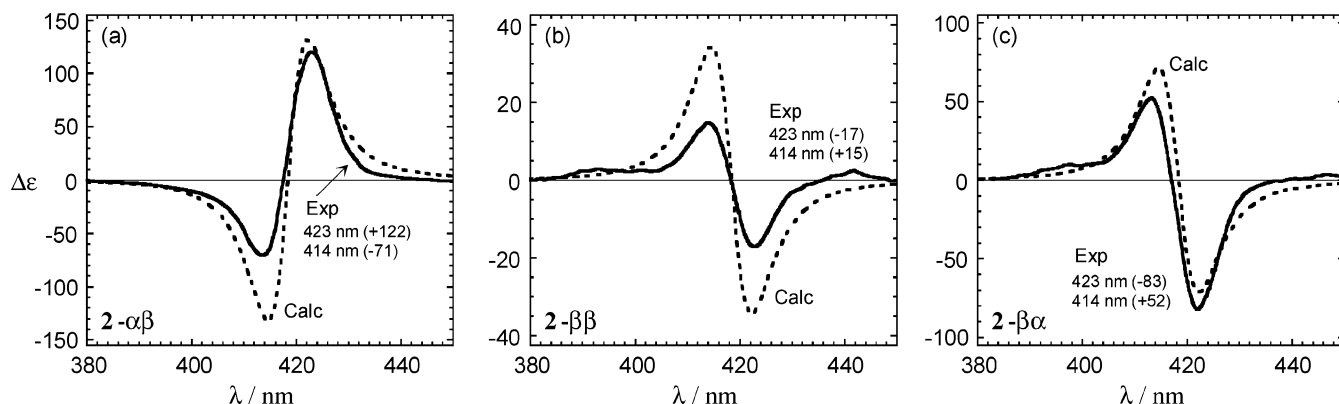
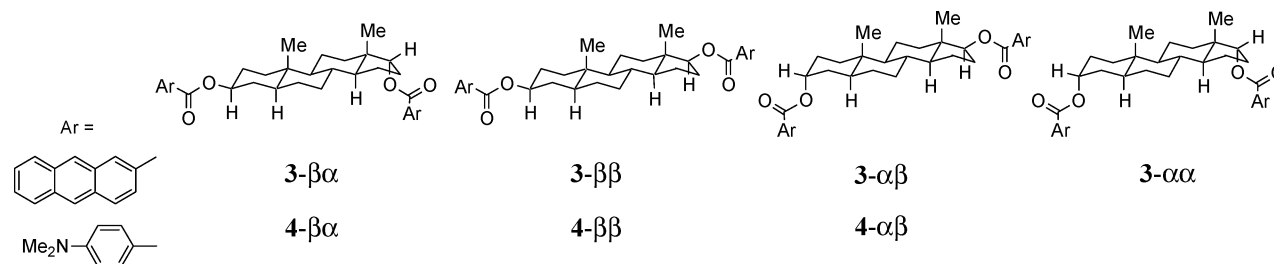


Figure 3. CD spectra of compounds (a) **2- $\alpha\beta$** , (b) **2- $\beta\beta$** , and (c) **2- $\beta\alpha$** . Solid lines: experimental $\approx 1 \mu\text{M}$ in CH_2Cl_2 . Dotted lines: calculated Boltzmann-weighted (at 298 K) average with DeVoe's method and hybrid approach on lowest energy MC/MMFFs structures (Table 2).

Chart 2



variation observed for the intensity (usually weaker in MCH and hexane).^{3,9,62} The spectra of Zn^{2+} complexes are very similar in shape to those of the free bases, but about 50% more intense, as expected considering the increased absorption for ZnTPP-COOMe ($\lambda_{\text{max}} = 419 \text{ nm}$, $\epsilon_{\text{max}} = 550\,000 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) with respect to TPP-COOMe , largely due to a narrower band. Although the intense CD spectra of Zn complexes seem more favorable for analysis, we have focused on the free bases that are more convenient for structure calculations; however, our results are general and can be extended to metal complexes provided that an accurate structure is available.

Table 1 also contains, for comparison, the CD data of bis(2-anthroate) esters **3- $\alpha\beta$** , **3- $\beta\beta$** , and **3- $\alpha\alpha$** (Chart 2) of the same steroidal diols in CH_3CN .⁶² The anthroate chromophore has a strong electric dipole-allowed transition around 260 nm (methyl 2-anthroate in CH_3CN has $\lambda_{\text{max}} = 258.4 \text{ nm}$, $\epsilon_{\text{max}} = 93\,000 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$). This transition, named ${}^1\text{B}_b$ in Platt's nomenclature, is described with a single dipole ($\tilde{\nu}_{\text{max}} = 38.7 \times 10^3 \text{ cm}^{-1}$, $D = 90 \text{ D}^2$, $\Delta\tilde{\nu}_{1/2} = 3.7 \times 10^3 \text{ cm}^{-1}$) polarized approximately along the aromatic ring long axis;⁶³ therefore, the chirality defined by the two dipoles is expected to reflect the twist between the alcohol C3–O and C17–O bonds. Previously, the CD of the bis(*p*-dimethylaminobenzoate) esters **4** (Chart 2) have also been reported;¹³ the bisanthroates, with moderately intense CD spectra, allow for a better comparison than the *p*-dimethylaminobenzoates, with only modest CD intensities. In the cases of compounds **2- $\alpha\beta$** , **2- $\beta\beta$** , and **2- $\beta\alpha$** ,

the sign of the couplets obtained for the corresponding isomers of **2**, **3**, and **4** are consistent; this observation supports phenomenologically the description of the porphyrin B band in compounds **2** in terms of an effective transition dipole moment directed along the 5–15 axis, that is, parallel to the alcohol C–O bonds.¹³ In the following, we discuss the scope, the validity, and the theoretical foundation of this widely applied approximation.

1.2. Molecular Modeling of Compounds 2- $\alpha\beta$, 2- $\beta\beta$, and 2- $\beta\alpha$. The molecular structure of compounds **2- $\alpha\beta$** , **2- $\beta\beta$** , and **2- $\beta\alpha$** was investigated by a combination of the following methods: selective energy surface scans with molecular mechanics (MM) and DFT calculations on model compounds; solid-state structure searches in the Cambridge Structural Database (CSD);⁶⁴ NMR experiments; Monte Carlo and Molecular Dynamics calculations on the full structures.

From inspection of the molecular models (Figure 4), it is clear that these compounds possess five main degrees of conformational freedom: (1) the torsional modes around the alcohol C3–O and C17–O bonds (θ_A and θ_D); (2) the torsional modes around the 5'/5''-phenyl–porphyrin bonds⁶⁵ (π_A and π_D); (3) the conformation of the five-membered D ring (ϕ_{1D}). As for the remaining structural features, the *s*-trans (or *Z*) conformation of the ester C(=O)–O bonds is strongly preferred over the *s*-cis (or *E*) one.⁶⁶ Both the steroidal fused six-membered rings system and the porphyrin cores should ensure a relatively rigid conformation; the rotation of 10'/10'', 15'/15'', and 20'/20''-phenyl–porphyrin bonds⁶⁵ does not affect the porphyrin–

(63) With a CNDO method, we calculated for methyl 2-anthroate (with C2–COOMe bond in *s*-cis and *s*-trans conformation) an angle of 4.2–5.0° between the polarization of ${}^1\text{B}_b$ transition and the aromatic long axis. CNDO-S/CI calculations were carried out with a CNDO/M program, according to Del Bene and Jaffé's formulation (Del Bene, J.; Jaffé, H. H. *J. Chem. Phys.* **1968**, *49*, 1221–1229), with Mataga approximation of two-electron repulsion integrals. One hundred singly excited states, with maximum energy values of 7.0 eV, were included in the CI. DFT (B3LYP/6-31G**) optimized structures⁵⁹ were used as the input geometries.

(64) Allen, F. H. *Acta Crystallogr., Sect. B: Struct. Sci.* **2002**, *B58*, 380–388.

(65) Numbers 5', 10', 15', and 20' refer to the *meso* positions of the porphyrin at position C-3 and 5'', 10'', 15'', and 20'' to the porphyrin at C-17. When referring to transition dipole directions, with 5-15 (or 10-20) both 5'-15' and 5''-15'' (or 10'-20' and 10''-20'') are intended.

(66) (a) Jones, G. I. L.; Owen, N. L. *J. Mol. Struct.* **1973**, *18*, 1–32. (b) Exner, O. In *The Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; Wiley: London, 1977; Vol. 1, pp 1–92.

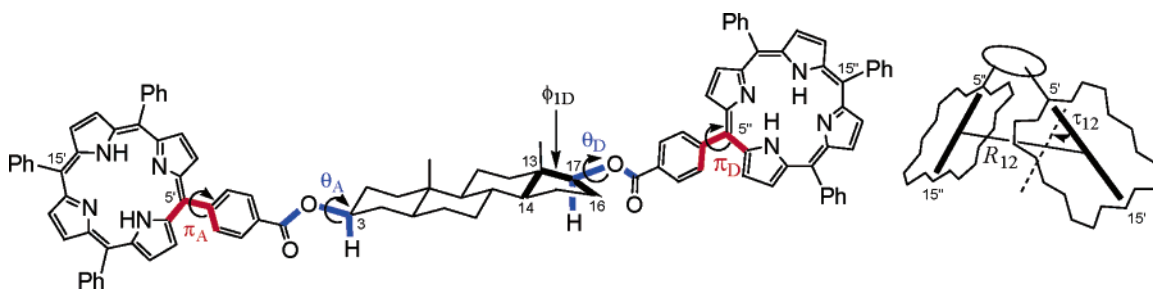


Figure 4. Left: main conformational parameters for compounds **2**; θ_A and θ_D , C(=O)–O–C3–H3 and C(=O)–O–C17–H17 dihedrals; π_A and π_D , 5'/5''-phenylporphyrin dihedrals; ϕ_{1D} , D ring C14–C13–C17–C16 dihedral. Right: relevant geometrical parameters for the porphyrin–porphyrin exciton interaction: R_{12} , interporphyrin center-to-center distance; τ_{12} , projection angle between 5'–15' and 5''–15'' directions.

porphyrin arrangement and may be overlooked. On the contrary, the five torsions described above, which are analyzed in detail in the following, must be taken explicitly into account as they directly affect the interchromophoric distance and orientation.

1.2.1. Investigation of Model Compounds. 1.2.1.a. Torsional Modes θ_A and θ_D around C3–O and C17–O Bonds.

These torsions may be described in terms of angles C(=O)–O–C3–H3 and C(=O)–O–C17–H17, referred to as θ_A and θ_D (Figure 4). In many practical applications concerning benzoate-like compounds, this angle has been considered equal to zero, that is, with a *syn* disposition between ester C(=O)–O and aliphatic C–H bonds.⁹ A careful inspection of solid-state structures found in the CSD for cyclohexyl and cyclopentyl benzoates, however, reveals a dispersion of values between -60 and $+60^\circ$, with actually a minimum number of structures at 0° , and the maximum number around ± 30 – 40° for the six- and ± 40 – 50° for the five-membered ring benzoates (Figure S1c–d, Supporting Information). This is accurately reproduced by torsional angle MMFFs energy scans for cyclohexyl and cyclopentyl benzoates (Figure S1a–b, Supporting Information), for which we found a shallow well with a flat maximum at 0° and minima near $\pm 30^\circ$ (six-membered ring) and $\pm 40^\circ$ (five-membered ring).⁶⁷ Incidentally, the ester C(=O)–O *s-cis* (or *E*) conformers have calculated energies much higher than those of the most stable *s-trans* (or *Z*) ones ($\Delta E \sim 50$ kJ/mol for both equatorial and axial cyclohexyl benzoate); the common *s-trans* conformational preference of the ester linkage⁶⁶ is apparently further enhanced^{68,69} by unfavorable steric interactions between *ortho* phenyl protons and the aliphatic C(–O)–H proton in the *s-cis* conformation.

1.2.1.b. Torsional Modes π_A and π_D around Phenyl–Porphyrin Bonds.

The conformational dynamics around the phenyl–*meso* porphyrin junction (referred to as π_A and π_D in our compounds, Figure 4) has been widely discussed in the literature.^{70,71} In the absence of substituents on the porphyrin β carbons and the phenyl *ortho* position, it has been determined

that the rotation around the C–C bond is largely unrestricted and is better described in terms of an almost free libration between dihedral angles of $+45$ and $+135^\circ$.^{70,71} This is confirmed by CSD data and by an MMFFs energy scan for *meso*-phenyl porphine, which show a flat-bottomed well with a distinctive minimum at 90° (Figure S2a–b, Supporting Information). Although the 90° value represents the average and the most probable value, the librational motion can have a marked effect on the CD spectra, as discussed in the following.

1.2.1.c. Conformation of the Five-Membered Steroidal D Ring (ϕ_{1D}).

The conformation of the five-membered steroidal D ring is known to vary widely depending on numerous factors, such as the presence of unsaturation (also on the C ring) and the nature and the position of substituents.⁷² Due to the ring closure and the almost fixed value of the C13–C14 dihedral imposed by the C-ring conformation, the conformation of the D ring may be described in terms of one degree of freedom; here, we choose the dihedral C14–C13–C17–C16 (referred to as ϕ_{1D} , Figure 4). When only 5 α -steroids with no unsaturation in the C and D rings and one oxygen substituent at C17 (alkoxy, aryloxy, or acyloxy groups) are considered, the conformational situation is very homogeneous as demonstrated by CSD data (Figure S3, Supporting Information),⁷² showing for ϕ_{1D} a clear-cut preference for values between -39 and -45° . Both MMFFs and DFT B3LYP/6-31G** calculations on the benzoate of 5 α -androstan-17-ol lead to -39° for 17 α and -41 to -42° for 17 β , in agreement with CSD data.⁷³

1.2.2. NMR and Molecular Dynamics Studies.

In pursuit of information about the solution dynamics of *meso*-aryl porphyrin derivatives employing some standard NMR methods,^{71,74} we measured ¹H NMR spectra of 2- $\alpha\beta$, 2- $\beta\beta$, and 2- $\beta\alpha$ at 27 and -58 °C in CDCl₃ (data not shown; the NMR characterization of compounds **2** has been reported elsewhere).^{13,62} The low temperature was expected to slow the librational motion and allow for resolution of the complicated spectral patterns. However, it was observed that at both temperatures all 18 10'/10'', 15'/15'', and 20'/20''-phenyl *para*

(67) In the two model compounds **S1** and **S2** (Figure S1, Supporting Information), a portion of the steroidal skeleton was included in order to keep the aliphatic ring rigid and assess the effect of the close stereogenic centers. Thus, the torsional energy curves are not symmetrical around 0° . For **S2** (including C/D rings), actual minima are at $-30/+40^\circ$ and $-45/+35^\circ$, as a consequence of the steric hindrance provided by the methyl group.

(68) In the over 2650 entries for benzoate esters in the CSD,⁶⁴ the *s-trans* conformation of the ester linkage is ubiquitous. Only 4 structures are exceptional, all of which are *ansa* compounds, where the *s-cis* conformation is locked by the *para* bridging chain.

(69) (a) Le Fevre, R. J. W.; Sundaram, A. *J. Chem. Soc.* **1962**, 3904–3915. (b) Pinkus, A. G.; Lin, E. Y. *J. Mol. Struct.* **1975**, *24*, 9–26.

(70) (a) Wolberg, A. *J. Mol. Struct.* **1974**, *21*, 61–66. (b) Chachaty, C.; Gust, D.; Moore, T. A.; Nemeth, G. A.; Liddell, P. A.; Moore, A. L. *Org. Magn. Reson.* **1984**, *22*, 39–46. (c) Anderson, H. L. *Chem. Commun.* **1999**, 2323–2330.

(71) (a) Eaton, S. S.; Eaton, G. R. *J. Am. Chem. Soc.* **1975**, *97*, 3660–3666. (b) Schrijvers, R.; van Dijk, M.; Sanders, G. M.; Sudholter, E. J. R. *Recl. Trav. Chim. Pays-Bas* **1994**, *113*, 351–354. (c) Noss, L.; Liddell, P. A.; Moore, A. L.; Moore, T. A.; Gust, D. *J. Phys. Chem. B* **1997**, *101*, 458–465.

(72) (a) Altona, C.; Geise, H. J.; Romers, C. *Tetrahedron* **1968**, *24*, 13–32. (b) Duax, W. L.; Weeks, C. M.; Rohrer, D. C. *Top. Stereochem.* **1976**, *9*, 271–383.

(73) The impact of the ϕ_{1D} oscillation on the projection angle τ_{12} between 5'–15' and 5''–15'' directions (Scheme 2), which may be taken as a main parameter of the exciton coupling, is insignificant for 2- $\alpha\beta$, 2- $\beta\beta$, and 2- $\beta\alpha$. For example, with ϕ_{1D} varying between -37 and -45° , τ_{12} varies only slightly ($+58.1$ – 59.4°) for compound 2- $\alpha\beta$ in the lowest energy conformation.

(74) Crossley, M. J.; Field, L. D.; Forster, A. J.; Harding, M. M.; Sternhell, S. *J. Am. Chem. Soc.* **1987**, *109*, 341–348.

and *meta* protons resonate at similar frequencies (around 7.8 ppm) and are indistinguishable; also, in the HSQC spectrum we measured for **2-β α** , the six 10'/10'', 15'/15'', and 20'/20''-phenyl *para* carbon resonances are not resolved and are superimposed on the four *ortho* and *meta* carbon resonances of the 5'/5''-phenyls (around 128.5 ppm). Thus, our attempt to measure the relaxation times for phenyl *para* carbons^{71,74} was unsuccessful. Moreover, in the ¹H NMR spectra at both temperatures, the *ortho* and *meta* protons on the 5'/5''-phenyls give rise to four doublets between 8.30 and 8.53, which do not decoalesce or show increased line width at -58 °C. Thus, we could not employ NMR spectroscopy for studying the dynamics relative to the phenyl–porphyrin libration and the rotation around the ester bond.

Some insight into the molecular dynamics was gained through combined Stochastic Dynamics/Monte Carlo (MC/SD) calculations⁶¹ run on compound **2-β α** in CHCl₃ at 300 K with MMFFs. The data corroborate the picture described above: the main torsional motions for **2-β α** are in fact the ones relative to ester and aryl–porphyrin bonds, with occurrence profiles as a function of the dihedral values (θ_A , θ_D , π_A , and π_D , Figure 4) similar to those of the energy scans reported above (sections I.2.1.a–b and Figures S1–2, Supporting Information).

I.2.3. Monte Carlo Conformational Searches. In light of the results discussed above (section I.2.1), it can be concluded that MMFFs is able to reproduce with good accuracy the conformations of the steroidal D ring and around the ester bonds for compounds **2-αβ**, **2-ββ**, and **2-β α** ; as for the phenyl–porphyrin torsion, MMFFs can reproduce the librational motion, although it is likely biased toward the minimum energy point at 90°. Because these five quantities represent the main degrees of conformational freedom (Figure 4), as argued above, it may be expected that MMFFs will be able to predict the reciprocal porphyrin–porphyrin arrangement with good accuracy for compounds **2-αβ**, **2-ββ**, and **2-β α** , which is relevant for the subsequent CD calculations.

MC/MMFFs conformational searches of compounds **2-αβ**, **2-ββ**, and **2-β α** were executed by including as “torsion rotations” only C(=O)–O–C3–H3 (θ_A) and C(=O)–O–C17–H17 (θ_D) angles. In each step (1000–5000 overall), the torsion rotations are randomly varied, the obtained structure is fully optimized (with MMFFs in CHCl₃), and the minimum is stored after checking the energy threshold and duplicate structures. In all cases, we obtained as a result a limited number (two to four) of sets of minima within 15 kJ/mol (referred to as I–IV), with each set found about 100 times over 1000 steps. Geometrical parameters and relative energies are shown in Table 2. In particular, π_A and π_D of 90° were found for all cases.

I.3. CD Coupled-Oscillator Calculation of Compounds 2-αβ, 2-ββ, and 2-β α . The CD spectra of **2-αβ**, **2-ββ**, and **2-β α** were calculated with DeVoe’s method (point-dipole approximation) and the matrix method (monopole approximation with MATMAC), using the spectral parameters for TPP-COOMe in CH₂Cl₂ and MC/MMFFs-derived structures within 15 kJ/mol, weighted with Boltzmann factors; the calculated *A* values with the two methods are reported in Table 3. We used three different models in both the DeVoe and the matrix method calculations. (1) Effective moment model: only the 5-15 moment was included with dipolar strength $D = 88.3 D^2$. (2) Circular

Table 2. Geometrical Parameters of Calculated MC/MMFFs Structures (Lowest Energy Conformations I–IV) for Compounds **2 α** ^a

structure ^b	<i>E</i> /kJ·mol ⁻¹	<i>R</i> ₁₂ /Å	τ_{12} /deg	π_A, π_D /deg	θ_A, θ_D /deg	ϕ_{1D} /deg
2-αβ I	0	23.9	+59	90	-38, -46	-42
2-αβ II	0.53	24.0	+66	90	+37, -46	-42
2-ββ I	0	29.0	-20	90	-39, -45	-42
2-ββ II	0.13	29.0	-6	90	+38, -45	-41
2-βα I	0	24.6	-13	90	-38, -28	-39
2-βα II	0.13	24.6	-30	90	+38, -28	-39
2-βα III	1.24	24.6	-23	90	-38, +40	-40
2-βα IV	1.26	24.6	-6	90	+38, +40	-40
2-α I	0	7.2	+1	110, 96	+45, -30	-37
2-α II	0.35	8.1	+10	94, 104	+37, +44	-40

^a *E* is the energy relative to the absolute minimum (conformation I); *R*₁₂ the interporphyrin center-to-center distance; τ_{12} the projection angle between 5-15 directions; π_A, π_D the porphyrin-phenyl torsions; θ_A, θ_D the ester bond torsions; ϕ_{1D} the ring D torsion (Figure 4). ^b Lowest energy conformations (I–IV) within 15 kJ/mol.

Table 3. Experimental (in CH₂Cl₂) and Calculated Couplet Intensities (*A*) of Soret Bands of Compounds **2-αβ**, **2-ββ**, and **2-β α** (Chart 1)

compd	exptl <i>A</i>	calcd <i>A</i> ^a (dipole)			calcd <i>A</i> ^a (monopole)		
		5-15 ^b	circular ^c	hybrid ^d	5-15 ^b	circular ^c	hybrid ^d
2-αβ	+193	+434	+90	+262	+438	+145	+315
2-ββ	-32	-105	-111	-68	-108	-59	-44
2-βα	-135	-145	-138	-142	-148	-161	-139
RMSD ^e		145	75	45	148	35	71

^a Boltzmann-weighted (at 298 K) average of spectra for lowest energy MC/MMFFs structures (Table 2) and spectral parameters: $D = 176.5 D^2$, $\tilde{\nu}_{\max} = 23.9 \times 10^3 \text{ cm}^{-1}$, Lorentzian band with $\Delta\tilde{\nu}_{1/2} = 0.75 \cdot 10^3 \text{ cm}^{-1}$ width. Columns 3–5 calculated with DeVoe’s method in point-dipole approximation; columns 6–8 calculated with matrix method in monopole approximation. See text for details. ^b 5-15 (or effective moment) approach: only 5-15 dipoles included. ^c Circular oscillator approach: all dipoles (5-15 and 10-20) included. ^d Hybrid approach: 5-15 dipoles included with full *D*; 10-20 dipoles included with half *D*. ^e Root-mean-square deviation of calculated *A* values with respect to experimental values.

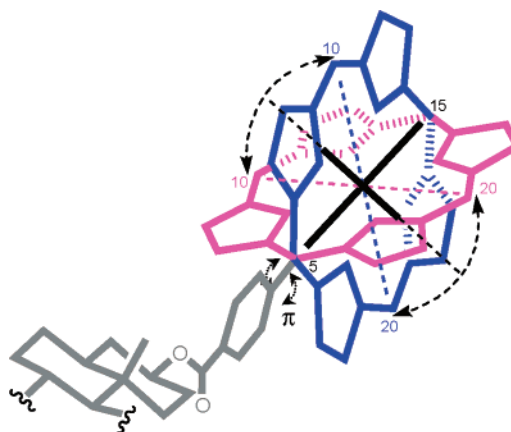


Figure 5. Schematic representation of the structural basis for the hybrid approach. Following the $\pm 45^\circ$ libration around the meso porphyrin–phenyl bond (torsional angle π), the 10-20 moment rotates around the 5-15 direction and its effective magnitude is reduced by $\sqrt{2}$, while the 5-15 moment is unaltered.

oscillator model: the 5-15 and 10-20 dipoles were used with the same $D = 88.3 D^2$ each. (3) Hybrid model: the 10-20 dipole was given half the dipolar strength $D = 44.1 D^2$ of the 5-15 dipole. This value is heuristically justified as follows (Figure 5): an unrestricted libration of π_A and π_D angles between the values $45\text{--}135^\circ$, with ideally constant potential, would preserve the whole transition moment intensity along the 5-15 direction, but would reduce the effective 10-20 moment by a factor of $\sqrt{2}$ and its dipole strength by a factor of 2. Thus, this hybrid

model takes into account both the presence of the 10-20 component (which is overlooked in the effective moment model) and the libration around π_A and π_D (which is neglected in the circular oscillator model). Since, in the MC/MMFFs structures used, these two dihedrals are 90° , corresponding to the average and most probable values (see Section 1.2.1.b), this treatment aims at reproducing the effect of the librational averaging.⁷⁵

The results shown in Table 3 lead to the following interpretation: (a) for all three compounds, the CD signs for the average rotational strengths calculated with all three models and by both methods are consistent with those from experiment in CH_2Cl_2 ; (b) the CD couplet sign coincides with the absolute sense of twist defined by 5-15 transitions (projection angle τ_{12} in Figure 4 and Table 2), and with the absolute sense of twist between C3–O and C17–O bonds, in the MC/MMFFs-derived structures; hence the exciton chirality method, applied to these bisporphyrin derivatives with effective transition moments in the 5–15 direction, does lead to the correct assignment of absolute configuration of C3 and C17 stereogenic centers; (c) however, the best agreement with the experimental couplet intensity is achieved with calculations using the hybrid model in the DeVoe method and the circular oscillator model in the matrix method;⁷⁶ (d) the point-dipole results from DeVoe's method and the monopole results from MATMAC agree very well for the effective transition moment model. This demonstrates that the point-dipole approximation of the transition density is fully satisfactory for the interporphyrin distances in the three isomers ($> \sim 24 \text{ \AA}$), as expected. However, discrepancies as large as $\sim 50\%$ are found between point-dipole and monopole calculations in the circular oscillator and hybrid models. These differences cannot be due to errors caused by the point-dipole approximation, and their origin must be sought instead in the overlapping between multiple interactions. If only two transition moments interact, as in the effective transition moment model, the DeVoe and matrix methods give essentially identical results for small coupling energies,⁷⁷ as in the present case. When more than two transition moments interact, as in the circular oscillator and hybrid models, the band shapes and hence the amplitudes obtained from the DeVoe and matrix methods can deviate significantly. These differences are primarily due to the different ways in which the two methods treat band shape (vibronic structure), as discussed in the Methods section.

(75) The introduction of a weighting factor for the intensity of the 10-20 component corresponds to a conformational averaging of this component preceding the exciton interaction. A more rigorous approach would be represented by a spectral averaging following the interaction between dipoles with full intensity. This requires a lengthier procedure consisting of fractionating such motion into several steps for each porphyrin, and calculating the Boltzmann-weighted average of all possible combinations.

(76) The major source of the remaining differences between experimental and calculated spectra is probably represented by our conformational, rather than spectral, averaging.⁷⁵ Other factors conceivably playing minor roles are (a) the point-dipole approximation (the shortest interchromophoric distances are around 24 Å); (b) the solvent effect (see note 53); (c) the presence of other mechanisms contributing to the optical activity. It is reasonable to rule out porphyrin ring distortions for compounds 2- $\alpha\beta$, 2- $\beta\beta$, and 2- $\beta\alpha$. The chiral perturbation exerted by the steroidal skeleton on the B transition is also negligible: the monoester formed by 5 α -androstano-17 β -ol and TPP-COOH shows only a weak positive Cotton effect at 417 nm, $\Delta\epsilon = +4.3$. This 17 β isomer has the most intense CD spectrum among mono-porphyrin derivatives of steroids (because of the proximity to the stereogenic center and the rigid environment of the chromophore, cis to the 13 β methyl group). The intensity is still too low to interfere with the more intense exciton-coupled spectra, although it may account for bisporphyrin derivatives with long-distance coupling.¹³

(77) Cech, C. M. Polynucleotide Circular Dichroism Calculations: Use of All Order Polarizability Theory; Ph.D. Thesis, University of California Berkeley, 1975.

The results from the three models and the two calculation methods for individual conformers are compared in Table S3 (Supporting Information). It will be noted that the effective transition moment and hybrid models each give Soret couplets of sign opposite to that for the circular oscillator model for three conformers. For a specific conformer, the circular oscillator model is definitive, so the incorrect signs predicted by the simpler models is disconcerting at first sight. However, it must be realized that the individual conformers treated here are average structures in which libration over a wide angular range around the 5,15-direction has been frozen. When the librational motion about the 5,15-direction is considered, the circular oscillator model is no longer definitive and the cruder but simpler models are viable.

On the basis of this comparison between the three different models in the DeVoe and matrix methods and the experimental spectra, *the present study provides a new interpretation of the widely employed effective transition moment approximation for bis-porphyrin derivatives.*¹³ From our results it is clear that *this approximation represents a simple way of considering the impact of conformational factors, namely, the porphyrin ring libration, on CD spectra.* This libration reduces significantly the weight of the 10-20 component of the interacting B transitions and makes the 5-15 component dominant. On the other hand, a better way of depicting the exciton coupling in this kind of compounds is constituted by the hybrid approach, in which the 10-20 component is scaled down in intensity but not entirely neglected. This amounts to saying that, *while the 5-15 approximation is sufficient for a qualitative assignment of absolute configuration, a more complicated approach (such as the hybrid or circular oscillator) must necessarily be employed for a quantitative prediction of CD spectra.*⁷⁵

In conclusion, the theoretical basis of the effective transition moment approximation is of a purely structural, and not spectroscopic, nature; it can be therefore employed only in such cases where a more or less unrestricted rotation of porphyrin rings is conceivable.

II. Bis-porphyrin Derivatives with Spatially Fixed Porphyrins (Class II). Two examples of covalently linked and conformationally rigid bis-porphyrin derivatives (**5** and **6**) are described in the literature. These molecules, in which the arrangement between the two chromophores is fixed due to a multi-point anchoring to the chiral skeleton, show intense exciton-coupled CD spectra. These compounds are very useful for stressing the inadequacy of the effective transition moment model when the structural requisite of unrestricted porphyrin ring libration is missing.

II.1. Tröger Base Derivative 5. The chiral Zn^{2+} complex **5** (Figure 6a) has been described by Crossley et al. as a chiral receptor for a number of diamines.^{42,78} We calculated the structure starting from the X-ray structure of a Pd analogue;⁷⁹ only one minimum is found by MMFFs. The spectral parameters for the B transition were extracted from the UV–vis spectrum of **5** in CHCl_3 (Figure 6b) as follows: $\lambda_{\text{max}} = 424 \text{ nm}$, $\tilde{\nu}_{\text{max}} = 23.5 \times 10^3 \text{ cm}^{-1}$, $D = 150 \text{ D}^2$, $\Delta\tilde{\nu}_{1/2} = 1.0 \times 10^3 \text{ cm}^{-1}$ (from the best fit of the calculated UV–vis spectrum).

(78) Allen, P. R.; Reek, J. N. H.; Try, A. C.; Crossley, M. J. *Tetrahedron: Asymmetry* **1997**, 8, 1161–1164.

(79) Crossley, M. J.; Hambley, T. W.; Mackay, L. G.; Try, A. C.; Walton, R. *J. Chem. Soc., Chem. Commun.* **1995**, 1077–1079.

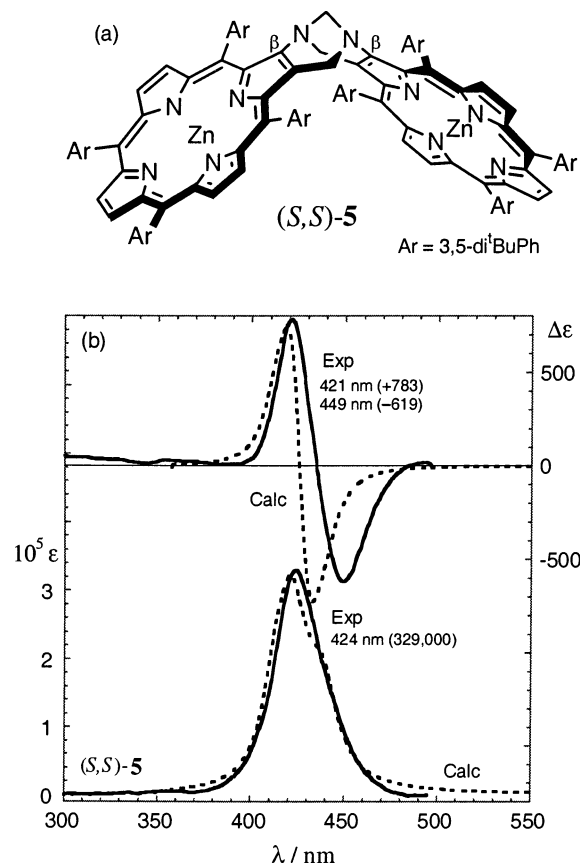


Figure 6. (a) Structure of compound (S,S) -**5**. (b) UV-vis and CD spectrum. Solid lines: experimental in CHCl_3 (adapted from ref 42, with permission from The Royal Society of Chemistry). Dotted lines: calculated with DeVoe's method and circular oscillator approach on lowest energy MC/MMFFs structure.

The CD was calculated with DeVoe's method within the circular oscillator approach and is in excellent agreement with the experimental spectrum (Figure 6b); in fact, the couplet intensity is very well reproduced (experimental $A = -1400$, calculated -1450). This is especially remarkable in view of the short interchromophoric distance (9.7 \AA between Zn atoms, but around 3.1 \AA between the closest points on the aromatic rings), which should in principle reduce the accuracy of the point-dipole approximation.⁸⁰

Compound **5** may be taken as a paradigm of any derivative where the two porphyrins lie in a close, spatially fixed position; in these cases, the choice of any effective transition moment for porphyrin B transition is arbitrary.⁸¹ Thus, compound **5** exemplifies the situation in which the exciton chirality method, requiring that the electronic transitions be characterized by a single dipole, is not applicable; on the contrary, coupled-dipole calculations with the circular oscillator approach are able to reproduce the observed CD spectral features with very good accuracy.

(80) Probably due to the very intense coupling, the through-space exciton interaction is dominant for **5** even if other mechanisms of optical activity may contribute, such as: (a) the inherent chirality of porphyrin rings distorted by the presence of *tert*-butyl groups; (b) the through-bond porphyrin-porphyrin conjugation (Piet, J. J.; Taylor, P. N.; Anderson, H. L.; Osuka, A.; Warman, J. M. *J. Am. Chem. Soc.* **2000**, *122*, 1749–1757).

(81) From a spectroscopic point of view, one could take the auxochromic nitrogen substituents at the β positions as the major symmetry-breaking effectors. However, the $C_{\beta N}$ -Zn directions define for the (S,S) -(-) enantiomer a positive chirality, in disagreement with the observed negative couplet.^{78,79} Moreover, just a slight rotation of the dipole toward the N-N directions is sufficient to reverse the defined chirality.

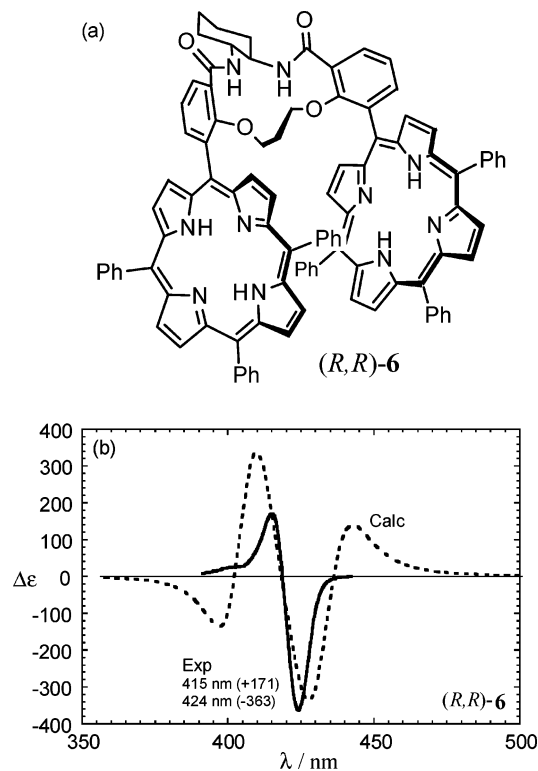


Figure 7. (a) Structure of compound (R,R) -**6**. (b) UV-vis and CD spectrum. Solid line: experimental in CH_2Cl_2 (adapted from ref 82, with permission from The Chemical Society of Japan). Dotted line: calculated with DeVoe's method and circular oscillator approach on lowest energy MC/MMFFs structure.

II.2. 1,2-Cyclohexanediamine Derivative 6. The Zn^{2+} complex of the bis-porphyrin derivative **6** (Figure 7a), with a chiral cyclophane as spacer, has been reported by Ema et al. as a chiral receptor for linear alkyl diamines.⁸² For free base **6**, we found by MC/MMFFs only one minimum energy structure within 10 kJ/mol , consistent with the one reported (also calculated by an MM method).

The CD spectrum was calculated with DeVoe's method and the circular oscillator approach, using the spectral parameters for TPP-COOME. It shows good agreement with the experimental one (Figure 7b), except for some overestimation of the coupling potential as seen from the couplet wavelength splitting (experimental $\Delta\lambda_{\text{max}} = 9 \text{ nm}$, calculated 15 nm) and the presence of the two extra bands flanking the stronger couplet (sidebands). Such a characteristic pattern is typical of calculated CD spectra when the two porphyrins lie at very short distance (5 \AA on the average in our structure for **6**), but it is not observed in the experimental spectrum, probably due to the molecular dynamics in solution (see paragraph III.3 below). In fact, both NMR data and MD simulations suggest that compounds **6** undergoes considerable structural fluctuations in solution.⁸² This is also confirmed by our MD trajectories at 300 K (not shown). Although the overall porphyrin-porphyrin arrangement is maintained during the simulation (for example, the chirality defined by $5'-15'$ and $5''-15''$ directions remains negative), the face-to-face stacking is easily relieved.⁸³

It is worth mentioning that the point-dipole approximation, which is supposed to be largely inaccurate in this condition,

(82) Ema, T.; Misawa, S.; Nemugaki, S.; Sakai, T.; Utaka, M. *Chem. Lett.* **1997**, 487–488.

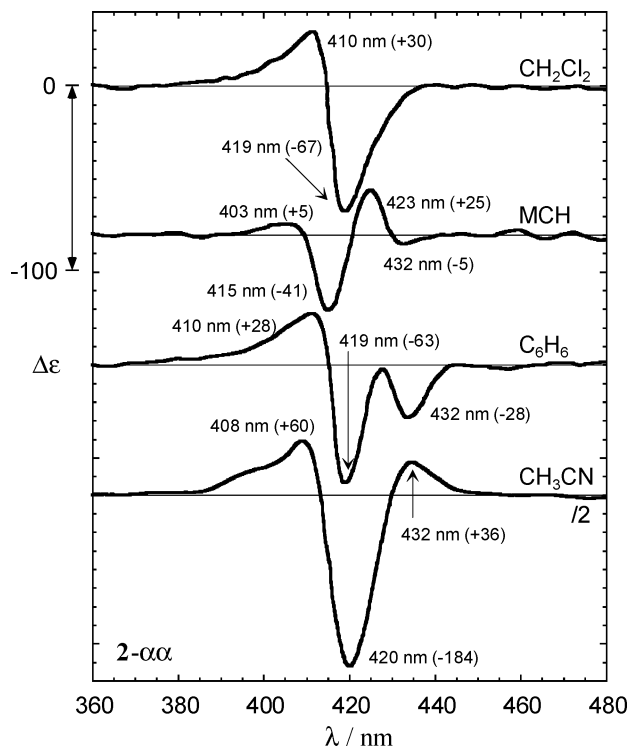


Figure 8. CD spectra of $2-\alpha\alpha \approx 1 \mu\text{M}$ in various solvents.

can not only reproduce the sign but even predicts the spectral intensity well, provided that the circular oscillator approach is used.⁸⁴

III. Bis-porphyrin Derivatives with $\pi-\pi$ Stacked Porphyrins (Class III). The coupled-oscillator method is expected to lose accuracy for strongly interacting chromophores, especially as a consequence of the possibility of conjugation,⁸⁵ electron exchange, and resonance phenomena which make the overlap between chromophore wave functions non-negligible. Moreover, the smaller the interchromophoric distance, the less accurate is the ISA, and the poorer is the point-dipole approximation for the coupling potential. It was therefore stimulating to test the limits and applicability of DeVoe calculations for compounds with two closely interacting porphyrin chromophores; moreover, structures with $\pi-\pi$ stacked porphyrin are of great interest in the field of molecular recognition.¹⁴ To this category might also be assigned the cyclophane derivative **6** just described; in this section, we report the $3\alpha,17\alpha$ isomer of bis-porphyrin derivatives of 5α -androstane-3,17-diol ($2-\alpha\alpha$, Chart 1).

III.1. Experimental CD Spectrum of Bis-porphyrin Derivative of 5α -Androstane- $3\alpha,17\alpha$ -diol ($2-\alpha\alpha$). The spectral properties of compound $2-\alpha\alpha$ are exceptional in comparison with other isomers $2-\alpha\beta$, $2-\beta\beta$, and $2-\beta\alpha$ in many respects (Figure 8, Tables 1 and S4, Supporting Information). The sign,

shape, and intensity of the CD spectrum is strongly dependent on the solvent.⁶² A clear-cut negative couplet is found only in CH_2Cl_2 ; in most other solvents three bands are detected, with either alternating $+/-/+$ (hexane, CH_3CN) or $-/-/+$ (benzene and toluene, from long to short wavelength) signs, and the middle Cotton effect always stronger; in MCH, a positive couplet with small sidebands is detected. The spectra of the Zn^{2+} complex are consistent with those of the free base, except in aromatic solvents where a sequence $+/-/+$ is found (data not shown). The corresponding bis-anthraoate compound $3-\alpha\alpha$ (Chart 2) shows a positive couplet centered at 262 nm with $A = +157$ in CH_3CN (Table 1).⁶² While the presence of multiple conformations whose equilibrium is solvent-dependent may explain the sign discrepancy, the unique appearance of the spectra must have a more complex origin.

III.2. Molecular Modeling of Compound $2-\alpha\alpha$. MC/MMFFs calculations of $2-\alpha\alpha$, in vacuo or in CHCl_3 , resulted in two minima ($2-\alpha\alpha$ I and $2-\alpha\alpha$ II, Table 2 and Figure 9a) very close in energy with quasimirrored image arrangement of the two porphyrins. In both structures, the two rings lie almost parallel to each other, with an average plane-plane distance less than 4 Å.⁸⁶ The structures exhibit $\pi-\pi$ stacking^{22,87} with an offset of ~ 6.3 Å, allowing for a favorable interaction between *ortho* and *meta* 10,20 phenyl protons and electron-rich pyrrole rings. In the ^1H NMR spectrum of $2-\alpha\alpha$ in CDCl_3 , these protons experience an upfield ring current shift⁸⁸ around 0.5 ppm when compared to the monomer TPP-COOMe and to the other isomers of **2**; these are by far the largest observed shifts for the whole compound, which supports the calculated MMFFs structures in Figure 9a. The shift magnitude, though much smaller than the one found for face-to-face stacked and spatially fixed bis-porphyrins linked through a double bridge,⁸⁹ is still indicative of a stacking interaction; in fact, values comparable to those above have been taken as evidence of stacking for bis-porphyrin derivatives linked through a single bridge allowing for structure fluctuations.¹⁴ MC/SD calculations on $2-\alpha\alpha$ in CHCl_3 also reveal a very dynamic situation with nonstacked conformations prevailing. It must be stressed that, apart from the experimental evidence given above, it is difficult to check further the accuracy of MMFFs calculated structures for compound $2-\alpha\alpha$, dominated by π -stacking interactions. As a matter of fact, even more sophisticated semiempirical calculation methods are unsuited for predicting the geometry of π -stacked porphyrin aggregates,⁹⁰ while higher level DFT methods are prohibitive for complicated molecular systems such as compounds **2**.

(83) A simulated annealing procedure (heating from 0 to 300 K in 1 ps, 50–100 ps at 300 K, cooling from 300 to 0 K in 5 ps, simulation step 1 fs) run on **6** systematically converged to a set of edge-to-face stacked structures, with center-to-center distance around 8.5 Å. Minimized energies are above the 10 kJ/mol threshold from the minimum found by MC simulations. The calculated CD for these structures (DeVoe method, circular oscillator model) shows a negative couplet with $A \approx -780$ and no flanking bands.

(84) Employing the effective dipole approximation in the DeVoe calculation (directed along $5'-15'$ and $5''-15''$ directions), we obtained a couplet with the correct negative sign, but the amplitude and splitting ($A = -1090$, $\Delta\lambda_{\text{max}} = 32$ nm) were substantially overestimated.

(85) Yoshida, N.; Ishizuka, T.; Osuka, A.; Jeong, D. H.; Cho, H. S.; Kim, D.; Matsuzaki, Y.; Nogami, A.; Tanaka, K. *Chem. Eur. J.* **2003**, *9*, 58–75.

(86) In the minimized MMFFs structures for $2-\alpha\alpha$, the porphyrin rings show distortions from planarity of the saddling type (Jentzen, W.; Song, X. Z.; Shelmutt, J. A. *J. Phys. Chem. B* **1997**, *101*, 1684–1699). Alternate pyrrole rings are tilted above and below the mean plane; the average RMS deviations from planarity are about 0.38 Å. This nonplanar distortion is a mechanism for relieving steric crowding in the α isomer. Both the DeVoe and the MATMAC calculations use transition parameters developed for planar porphyrins, so the use of these parameters in calculations with nonplanar porphyrins inevitably introduces some errors. However, the results are expected to be qualitatively correct.

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(88) (a) Abraham, R. J.; Bedford, G. R.; McNeillie, D.; Wright, B. *Org. Magn. Reson.* **1980**, *14*, 418–425. (b) Abraham, R. J.; Marsden, I. *Tetrahedron* **1992**, *48*, 7489–7504. (c) Abraham, R. J.; Medforth, C. J. *Magn. Reson. Chem.* **1990**, *28*, 343–347.

(89) Leighton, P.; Cowan, J. A.; Abraham, R. J.; Sanders, J. K. M. *J. Org. Chem.* **1988**, *53*, 733–740.

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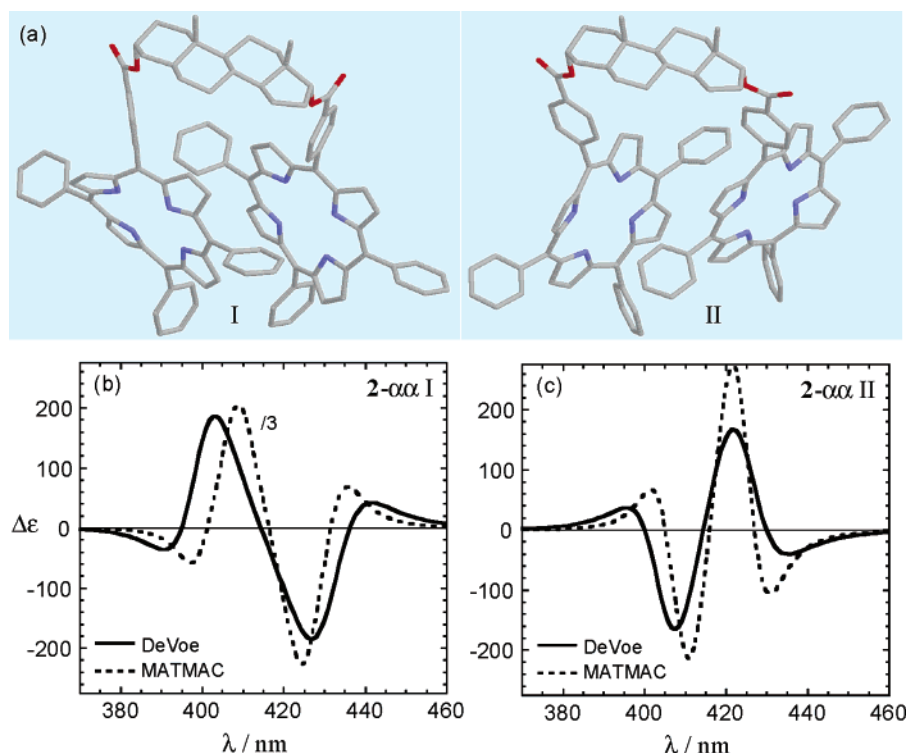


Figure 9. (a) Lowest energy MC/MMFFs structures of 2- $\alpha\alpha$. (b–c) Calculated CD spectra for conformers 2- $\alpha\alpha$ I (b) and 2- $\alpha\alpha$ II (c), with DeVoe's method and circular oscillator approach (solid lines), and with MATMAC (dotted lines).

III.3. CD Coupled-Oscillator Calculation of Compound

2- $\alpha\alpha$. The CD spectra of the two lowest energy structures 2- $\alpha\alpha$ I and 2- $\alpha\alpha$ II (Table 2) were calculated with the DeVoe and matrix methods and the circular oscillator model. The spectra calculated with the DeVoe method (Figure 9b–c, solid lines) are quasimirror images and show a very intense middle couplet with distinctive sidebands. The matrix method using the monopole approximation gives a spectrum for the higher energy conformer 2- $\alpha\alpha$ II (Figure 9c, dotted line) that is similar to that from the DeVoe method. However, this similarity is probably fortuitous because the spectrum for the lower energy conformer 2- $\alpha\alpha$ I is about 3-fold more intense in the monopole-based calculations (Figure 9b, dotted line) relative to the dipole-based results. This large discrepancy is not unexpected for such extended chromophores at these short distances.

The most intriguing spectral features in these predicted spectra are the intense sidebands, whose large Davydov splitting arises from a very strong coupling between some components of the coupled circular oscillators. Although the experimental spectra in most solvents exhibit multiple bands (Figure 8), in no case do they appear similar to the calculated ones in the position and intensity of the sidebands.

It is possible that MMFFs overestimates the porphyrin–porphyrin interaction, thus providing structures biased toward a short interchromophoric distance. On the other hand, it is also likely that molecular motions in solution tend to diminish the stacking as suggested by MC/SD results. In fact, cooling the ^1H NMR sample to $-58\text{ }^\circ\text{C}$ shifts the *ortho* and *meta* 10,20-phenyl protons a further 0.1–0.3 ppm upfield, consistent with the calculated absolute minima (Figure 9a). More interestingly, variable-temperature CD spectra in MCH (Figure 10) show, upon cooling, a progressive increase in couplet intensity and especially of the sidebands, reaching at the lowest temperature

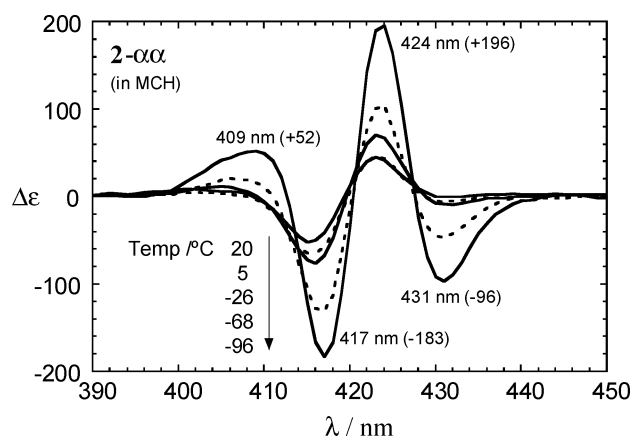


Figure 10. Variable-temperature CD spectra of 2- $\alpha\alpha$ 1.15 μM in MCH. Data shown refer to the spectrum at $-96\text{ }^\circ\text{C}$.

half of the intensity of the middle bands. It is noteworthy that the spectrum at $-96\text{ }^\circ\text{C}$ strongly resembles the calculated one for 2- $\alpha\alpha$ II (Figure 9c), with the only significant difference in the exciton splitting (experimental $\Delta\lambda_{\text{max}} = 7\text{ nm}$, calculated 14.5 nm, for the inner couplet). To our knowledge, the low-temperature spectra of 2- $\alpha\alpha$ are the first reported CD for a bis-porphyrin derivative with such distinctive sidebands,⁹¹ which are correctly predicted by circular oscillator calculations.

(91) The experimental CD spectra of 2- $\alpha\alpha$ in different solvents at room temperature (Figure 8 and Table S4, Supporting Information) are uniquely characterized by multiple bands, with one strongly red-shifted band of unpredictable sign that breaks down spectral symmetry and conservation. This band might result from the presence of other sources of optical activity than the coupled-oscillator mechanism, notably: (a) inherent chirality of distorted porphyrin rings (as found in the calculated structure);⁸⁶ (b) chirality of aromatic π – π conjugated system; (c) in the case of aromatic solvents (benzene and toluene), contribution from solvent molecules strongly interacting with the chromophores (see for example: Arai, T.; Takei, K.; Nishino, N.; Fujimoto, T. *Chem. Commun.* **1996**, 2133–2134).

In conclusion, in coupled-oscillator calculations of bis-porphyrin derivatives undergoing π - π stacking, two elements are critical: (a) the short interchromophoric distance makes the point-dipole approximation poor; (b) conformational and dynamic factors may play a key role that is difficult to predict and evaluate by means of MM-based geometry calculations. Still, when a coherent structural picture is available, the circular oscillator approach should lead to satisfactory results as in the case of the cyclophane derivative **6** above, while the effective transition moment approximation is inadequate.

IV. Overview of Other Porphyrin Dimers. In the previous sections, we illustrated the scope of DeVoe calculations on several examples of derivatives containing two covalently linked porphyrin chromophores. In this section, we briefly review some other chiral bis-porphyrin derivatives whose exciton-coupled CD spectra have been reported in the literature. Most of these derivatives can be assigned to one of the three classes I–III introduced before (Figure 1).

IV.1. Class I Analogues. Many reports deal with compounds derived from a more or less rigid chiral skeleton to which two porphyrins are linked through a single point of attachment (Class I, Figure 1). This situation is well exemplified by the class I of steroid derivatives described above, since porphyrin rings are allowed to freely rotate around one or more single bonds, one of which is a porphyrin–phenyl or other porphyrin–aromatic. For these compounds, plain symmetric couplets are usually observed in the Soret region with moderate to strong intensity depending on the interchromophoric distance. In most cases CD spectra have been discussed only qualitatively.^{92,93} When used for determining the absolute sense of chromophoric twist, or for semiquantitative structural inferences, the effective moment approximation has been implicitly^{41,43,47} or explicitly^{12,13} adopted. In a few cases a circular oscillator-like model has been qualitatively considered,^{44,46} without discussing the consequences of ring rotations.

As already stressed by Stomphorst et al.²³ and substantiated by the current study, the conformational flexibility may play a determining role in the exciton interaction that cannot be overlooked. Even if the effective transition moment approximation may be sufficient for qualitative analysis, its application should rely on the awareness of conformational factors. When one or more librations around single porphyrin–aryl bond are especially important,^{13,41,43,46,47,93} an approach similar to our hybrid one would be beneficial for quantitative CD calculations; this amounts to finding, for each case, a suitable weighting factor to be used for the librating component (corresponding to the value 0.5 used for the 10–20 component in compounds **2**), depending on the geometrical requisites.

IV.2. Class II Analogues. In a few examples reported concerning rigid derivatives, such as the ones belonging to class II above (Figure 1, Class II), the reported CD spectra have been analyzed only qualitatively;^{42,45,82,94} they are characterized by very intense couplets in the Soret region. It must be stressed that in these situations the conventional exciton chirality method cannot be applied, and even defining the absolute sense of twist

between the two chromophores, only on the basis of the molecular geometry, may be questionable. Only circular oscillator calculations can provide (as previously pointed out^{30,32,38} and confirmed by our results) a faithful picture of the exciton coupling.

A comprehensive study of *meso-meso* rigidly linked porphyrin dimers, with emphasis on the effects of conjugation on UV–vis and CD spectra, has recently appeared.⁸⁵

IV.3. Class III Analogues. Some CD spectra of covalently linked porphyrins undergoing π - π stacking (Figure 1, Class III) have been reported and analyzed only qualitatively.⁹⁵ As discussed for compounds **6** and **2- α** (class III) above, a coupled-oscillator calculation, necessarily with the circular oscillator approach, may provide a satisfactory prediction of CD spectra. For this category of compounds, however, the structure calculation may represent the difficult step and seriously hamper any quantitative application.

This is especially true for a very interesting series of derivatives of TPP-COOH (**1**) and chiral diols, diamines, amino alcohols, and α -hydroxy acids used for configurational assignment. The two porphyrin rings, linked through a flexible alkyl chain, undergo a π - π stacking interaction with a preferred twist governed by the absolute configuration at the stereogenic center, determined by the sign of the couplet in the Soret region.¹⁴ In these cases the conformational flexibility renders the exact determination of structure impracticable.

IV.4. Complexes between Achiral Bis(Zn-porphyrin) Host and a Chiral Guest. One of the most recent applications of multi-porphyrin derivatives as CD reporters concerns 1:1 host–guest complexes formed between an achiral bis(Zn-porphyrin) host and a chiral bisfunctional derivative carrying nitrogen or oxygen atoms. The molecular recognition occurs through a double host/guest Zn/N or Zn/O ligation, and the two porphyrins adopt a defined twist depending on the absolute configuration of the guest. The bis-ester of Zn-TPP-COOH and pentanediol linker (porphyrin tweezer) has been employed by some of us for α,ω -diamines, primary and secondary amines, alcohols, and carboxylic acids.^{15–18} An ethane-bridged bis(Zn-octaethylporphyrin) has been employed by Borovkov, Inoue, and co-workers for amines, alcohols, and amino acids.⁴⁰

In these approaches, the sign of the CD couplet observed in the Soret region has been taken as proof of the absolute configuration of the substrate. In the tweezer case, the 5–15 effective transition moment approximation has proven to afford a practical model for predicting the sign of interporphyrin twist and the observed couplet sign has been consistently related to the sign of the projection angle defined by 5–15 directions (5-phenyl is the one attached to the linker).^{15–17} Borovkov et al. have used a peculiar model where the $B_{\parallel}/B_{\parallel}$ and B_{\perp}/B_{\perp} Soret component couplings have been considered (B_{\parallel} is the component passing through the *meso* carbon attached to the ethane linker), but not the B_{\parallel}/B_{\perp} ones; no theoretical basis has been given for such a model.⁴⁰

Due to difficulties in obtaining crystals suitable for X-ray analysis, the exact structure of these host/guest complexes still remains unknown. Moreover, the structural complexity and the

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(94) Fan, J.; Whiteford, J. A.; Olenyuk, B.; Levin, M. D.; Stang, P. J.; Fleischer, E. B. *J. Am. Chem. Soc.* **1999**, *121*, 2741–2752.

(95) (a) Arai, T.; Takei, K.; Nishino, N.; Fujimoto, T. *Chem. Commun.* **1996**, 2133–2134. (b) Liu, H.-Y.; Huang, J.-W.; Tian, X.; Jiao, X.-D.; Luo, G.-T.; Ji, L.-N. *Chem. Commun.* **1997**, 1575–1576. (c) Liu, H.-Y.; Huang, J.-W.; Tian, X.; Jiao, X.-D.; Luo, G.-T.; Ji, L.-N. *Inorg. Chim. Acta* **1998**, *272*, 295–299.

presence of metal ions constitute a challenge for structure optimization methods.¹⁷ However, experimental and computational results on these complexes indicate a close proximity between the two porphyrin rings, favoring strong porphyrin/porphyrin interactions. For the case of bis-porphyrin tweezers, we believe that the observed CD, and the effectiveness of the 5-15 moment model, may be again justified on a structural basis. At the interchromophoric distances reported (about 9 Å for the center-to-center, but much less for the closest points on porphyrin rings),^{16,17} the circular oscillator approach not surprisingly leads to calculated spectra (not shown) with very intense couplets, very large wavelength splittings, and pronounced sidebands, which are not experimentally observed even in low-temperature spectra. However, NMR spectra indicate a very fluxional situation in solution.^{16,17} Our MC/SD calculations on the complexes between the pentanediol bis-porphyrin tweezer and some conjugates of secondary amines¹⁷ confirm that porphyrin rings rotation is largely allowed around the 5-15 directions, which reduces the effective contribution due to the 10-20 component of the circular oscillator.

Thus, the complexes between bis-porphyrin tweezer host and bifunctional guests can be considered as intermediate between classes I and III presented above, with strongly interacting and fluctuating porphyrin rings making the coupling between 5-15 directions largely prevalent. A similar picture may possibly hold for intramolecularly stacked porphyrins linked through a flexible chiral bridge (section IV.3 above).¹⁴

Conclusions

We have demonstrated how coupled-oscillator DeVoe calculations can afford quite an accurate picture of the exciton interaction between Soret transitions of porphyrin chromophores that are involved in crucial biological systems and widely employed as molecular receptors and chirality probes.

When the arrangement between the two chromophores is fixed, the circular oscillator approach represents the only reasonable way of calculating CD spectra of bis-porphyrin compounds. Very good agreement is found between experimental and calculated CD spectra for this class of compounds. In these cases, the application of the exciton chirality method is unjustified, because the Soret transition cannot be depicted in terms of a single linear dipole.

When unrestricted libration of the porphyrin ring is possible around one preferential axis (corresponding to the linkage to

the rest of molecule), an effective transition dipole moment directed along that axis (5-15 moment in TPP-COOH derivatives) can efficiently describe the coupling between B transitions. This is because the contribution to the exciton interaction coming from the component of the circular oscillator perpendicular to the axis (10-20 moment) is partially canceled, as a consequence of the librational averaging. The use of the porphyrin chromophore as a very sensitive benzoate-like CD probe is then theoretically justified, which allows for employing the straightforward exciton chirality method for qualitative applications of these kind of compounds. On the other hand, the presence of the 10-20 component cannot be entirely neglected in quantitative calculations. We demonstrated how a partial inclusion of this component, within a so-called hybrid approach, may lead to calculated spectra in good agreement with experimental ones.

Coupled-oscillator calculations can still be used for strongly interacting, and even stacked, porphyrins, although an overestimation of coupling potential and spectral intensities is conceivable in this case.

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Note Added after ASAP Publication: Concentrations in the captions of Figures 2, 3, 8, and 10 were incorrect in the version published on the Web 5/31/2003. The final Web version published 6/3/2003 and the print version are correct.

Supporting Information Available: Porphyrin geometry (Table S1) and monopole charges for the Soret transition (Table S2) used for MATMAC calculations; calculated Soret couplet intensities for individual conformers of compounds **2** (Table S3); experimental CD data of **2- $\alpha\alpha$** in various solvents (Table S4); MM energy scans and CSD data for model compounds used for MMFFs calculations (Figures S1–S3). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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