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Supramolecular Chiral Recognition by Bischlorins: A Two-Point Interaction Mode Combined with the Host's Conformational Modulation Controlled by the Guest's Stereochemistry and Bulkiness

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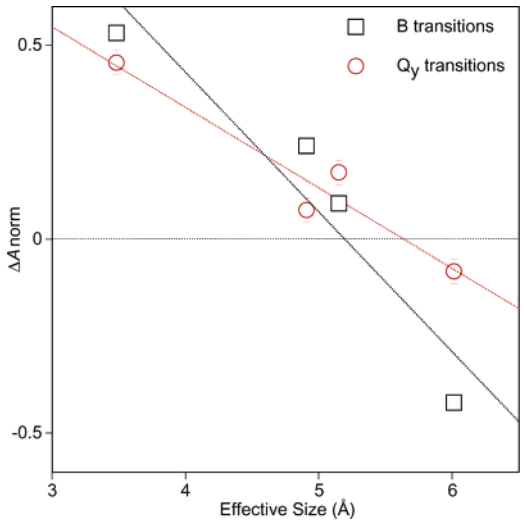
ABSTRACT



Supramolecular chiral recognition based on two-point host–guest interactions coupled with the different host's conformational response using the enantiopure bischlorin hosts and different antipodal amine guests is reported. The bulkiness at the guest's stereogenic center controls the chiral recognition properties resulting in switching of the enantioselectivity.

Chiral recognition is one of the vital fundamental processes in natural systems and plays a key role in various fields of science and technology.[1] In general, this phenomenon is based on a three-dimensional "lock-and-key" concept, which implies that the binding sites of the guest and host are fitted well to each other in size and shape usually through three-point interactions. Therefore, in principle, only one enantiomeric guest will properly bind to the complimentary host to yield a tightly bound complex, whereas the antipodal guest is bound rather weakly. This difference in binding can be detected by various conventional spectroscopic methods. In this context, porphyrinoids are particularly interesting and

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advantageous for chiral recognition, owing to their specific physicochemical and spectral properties as well as their great biological importance and wide potential applicability.[2]

Here, we propose a new approach to the chiral recognition effect, which is based on the difference in conformational response of an enantiopure host upon two-point interactions with various antipodal guests, which in turn is finely tunable through bulkiness control. To demonstrate the effectiveness of this principle, a pair of bischlorin enantiomers ($\mathbf{1_R}$ and $\mathbf{1_S}$)[3] was successfully employed (Figure 1). These host

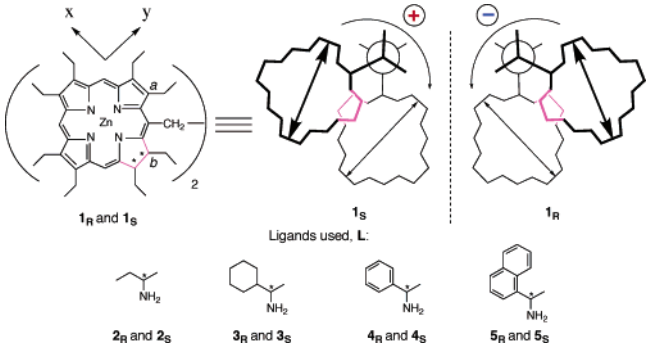

Figure 1. Structures of chiral bischlorins **1** (based on calculated $\mathbf{1_R}$, see ref 3) and amines **2**−**5**. The subscript (**R** or **S**) indicates the absolute configuration of the asymmetric carbon, which is marked by an asterisk.

molecules possess several important structural features that are most suitable for this purpose. In particular, as was previously shown with the bisporphyrin analogues, the conformation of these dimeric compounds is highly sensitive to a minute structural alteration at the stereogenic center of a chiral guest (such as **2**), which can be readily detected and characterized by various spectroscopic methods.[4] In addition, the chlorin structure offers a great advantage in the unambiguous assignment of optical activity in $\mathbf{1_R}$ and $\mathbf{1_S}$ and its corresponding supramolecular complexes owing to the energetically isolated and well-defined low-energy Q_y electronic transition that is polarized along the *y* axis (Figure 1).[3,5] Furthermore, preliminary studies revealed that the diastereomeric complexes $\mathbf{1_R{\cdot}2_R}$ and $\mathbf{1_R{\cdot}2_S}$ yielded a pronounced distinction in the chiroptical outcomes as a result of the different degrees of excitonic coupling modulation.[5] In this study, we employed a series of homologous amines **2**−**5** as chiral guests because their interactions with achiral bisporphyrins and racemic bischlorin have been well investigated to date[4,5] (Figure 1).

Ligand complexation and the resulting chiral modulation in $\mathbf{1_R}$ and $\mathbf{1_S}$ have been monitored by UV−vis and CD spectroscopy at saturated amine concentrations.[6] The UV−vis spectra of all the systems ($\mathbf{1_R}$/$\mathbf{1_S{\cdot}L}$) are essentially the same and are characterized by the intense bathochromic shifts of the B and Q_y transitions (see Supporting Information), which are associated with the ligation process and the subsequent conformational changes and are similar in general to the spectral properties of the supramolecular complexes based on racemic bischlorin.[5] However, in contrast to the almost invariant absorption bands, the corresponding chiroptical properties are strongly affected by the amine's structure and its absolute configuration. Thus, all ligands equally induced the bathochromic shifts of the corresponding CD couplets at the B and Q_y bands, along with similar low-energy shifts of the UV−vis absorption bands, which additionally resulted in reduction in the overall signal amplitudes (*A*) in comparison to the ligand-free $\mathbf{1_R}$ and $\mathbf{1_S}$ (Figure 2). The magnitude of the observed change in *A* is dependent on the substituent's relative bulkiness at the stereogenic center and the stereochemistry of the amine guest. Interestingly, homochiral host−guest complexes, i.e., $\mathbf{1_R{\cdot}L_R}$ and $\mathbf{1_S{\cdot}L_S}$, exhibited larger CD responses than the corresponding heterochiral ones, $\mathbf{1_R{\cdot}L_S}$ and $\mathbf{1_S{\cdot}L_R}$, where **L** = **2**−**4**. However, the more bulky guest **5** showed the opposite tendency. To better understand the chiral recognition properties and to get an adequate comparison, we plotted the difference between the normalized *A* values of the corresponding diastereomeric complexes ($\Delta A_{norm} = [A(\mathbf{1_R{\cdot}L_R}$ or $\mathbf{1_S{\cdot}L_S}) - A(\mathbf{1_R{\cdot}L_S}$ or $\mathbf{1_S{\cdot}L_R})]/A(\mathbf{1_R}$ or $\mathbf{1_S})$) against the previously established effective size of the bulkiest substituent at the stereogenic center.[4a,j] As can be seen from Figure 3, the ΔA_{norm} values for both the B and Q_y transitions gradually decrease with increasing size of the substituent, eventually exhibiting an inversion of the sign in the case of **5**. Deviation from the linearity (the corresponding linear

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(6) These are the ligand concentrations where the spectral changes associated with the chlorin chromophores are at their maximum, and further increase of the amine concentration has no effect on the signal intensities ($C_L = 4.1 \times 10^{-2} - 1.4 \times 10^{-1}$ M), which corresponded to the 1:2 host−guest complexes.

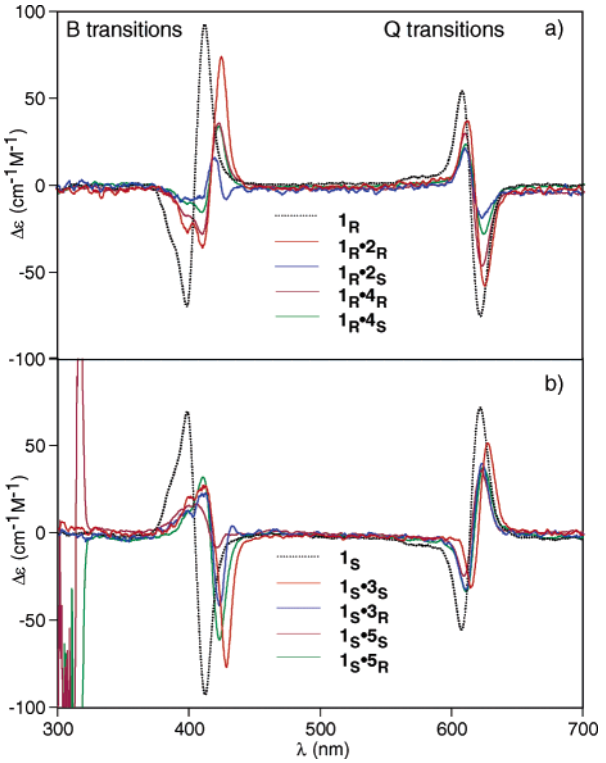

Figure 2. CD spectra of $\mathbf{1_R}$, $\mathbf{1_R{\cdot}2_R}$, $\mathbf{1_R{\cdot}2_S}$, $\mathbf{1_R{\cdot}4_R}$, and $\mathbf{1_R{\cdot}4_S}$ (a) and $\mathbf{1_S}$, $\mathbf{1_S{\cdot}3_S}$, $\mathbf{1_S{\cdot}3_R}$, $\mathbf{1_S{\cdot}5_S}$, and $\mathbf{1_S{\cdot}5_R}$ (b) in CH_2Cl_2 at room temperature ($C_1 = 4 \times 10^{-6} - 7 \times 10^{-6}$ M).

dependencies were observed previously for the analogous bisporphyrin[4a,j,k]) is apparently a result of the nonequivalence in the steric interactions between the bulkiest substituent of the chiral guest and the ethyl groups at the *a*- and *b*-positions of the neighboring chlorin ring caused by the reduced pyrrole ring (see Figure 1). The difference in ΔA_{norm} between the B and Q_y transitions appears to arise from the nonplanarity of the chlorin ring, thus producing dissimilar homocouplings of the electronic transitions polarized along the *x* and *y* axes

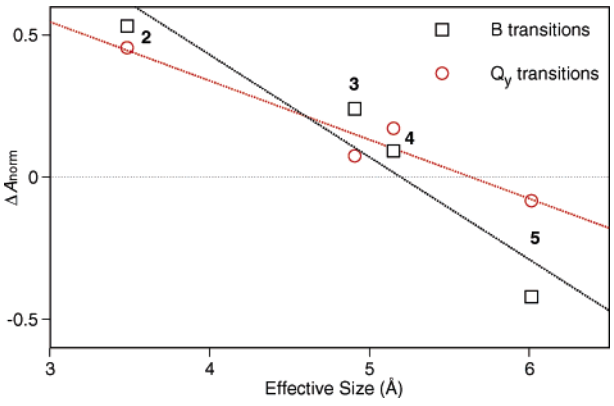

Figure 3. Dependence of ΔA_{norm} on the effective size of **2**−**5**. The linear plot is the best fit obtained for the experimental data.

(it is of note also that the Q_y couplet is a result of a sole coupling of the *y* electronic transitions, whereas the B couplet is caused by two pairs of couplings of the *x* and *y* electronic transitions as was established previously[3]).

A schematic drawing of the enantioselective recognition mechanism is depicted in Figure 4. For the sake of simplicity,

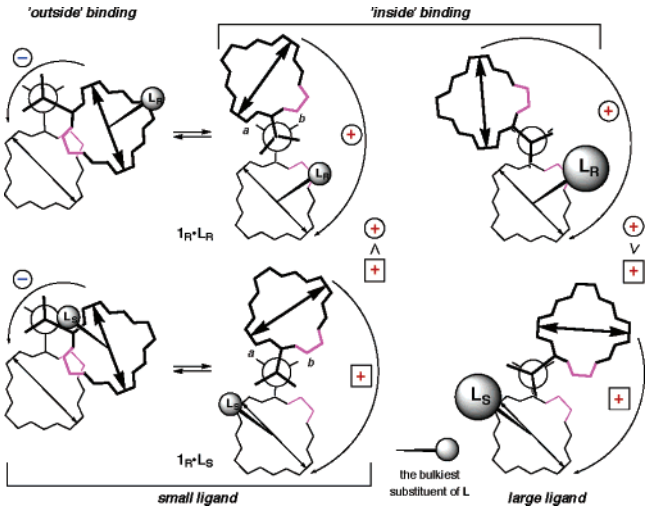

Figure 4. Schematic mechanism of the chiral recognition by $\mathbf{1_R}$ upon interaction with $\mathbf{L_R}$ and $\mathbf{L_S}$ of a different bulkiness. Only one ligand is shown, whereas the second ligand attached to the neighboring chlorin ring is omitted for clarity.

only the binding of one ligand is shown, and the second ligand has the same probability of interaction with the neighboring chlorin ring. Also, for clarity purposes, only couplings of the clearly distinctive electronic transitions polarized along the *y* axis are presented and discussed, and the effect of the interactions of the *x* transitions can readily be understood, considering their perpendicular orientation (see Figure 1). Particularly, the choice of the *y* transitions as the diagnostic tool is dictated by its energetic separation in the Q-band region, which allows unambiguous rationalization of the chiral recognition events from the viewpoint of interchromophoric excitonic couplings. As a representative example, the interactions of a single enantiomeric host $\mathbf{1_R}$ with antipodal ligands ($\mathbf{L_R}$ and $\mathbf{L_S}$) of a different bulkiness are discussed. As shown previously for various bisporphyrinoids of a similar structural type,[4] the external ligation can occur from both sides of the macrocycle to yield the "outside" and "inside" coordination species (as for $\mathbf{1_R{\cdot}L_R}$ and for $\mathbf{1_R{\cdot}L_S}$; see Figure 4), which are in a fast dynamic equilibrium. Apparently, upon the outside binding, the original conformation of bischlorin remains essentially unchanged because of the lack of direct host−guest steric interactions. Even if the outside ligation may cause a slight change in the spatial arrangement of the two chlorin rings, this should be independent of the stereochemistry or bulkiness of the outside binder, and thus, the overall conformation should be very similar to the original ligand-free geometry, in which the total dipole moment of the bischlorin chro-

mophore is minimized.[3] Hence, in the case of the outside binding, the two diastereomeric complexes, i.e., $\mathbf{1_R{\cdot}L_R}$ and $\mathbf{1_R{\cdot}L_S}$, are very alike in the chlorin spatial arrangement and preserve the right-handed helicity resulting in the anticlockwise coupling of the relevant *y* transitions and generating negative chirality. In contrast, the inside binding, as was the case with the bisporphyrin analogues,[4] induces significant conformational changes due to steric interactions between the guest and the neighboring chlorin ring of the bischlorin. This eventually leads to the conformational switching to the anti structure, in which the *y* transitions are oriented in the opposite clockwise fashion, resulting in positive chirality. However, further steric repulsive interactions between the bulkiest substituent at the stereogenic center of the guest and one of the ethyl groups of the neighboring chlorin ring (*a* and *b* in the case of $\mathbf{1_R{\cdot}L_S}$ and $\mathbf{1_R{\cdot}L_R}$, respectively) produce a unidirectional screw in the anti conformation, the handedness of which is dependent on the position of the bulkiest group. In the case of $\mathbf{L_R}$, the right position of the bulkiest substituent dictates the left-handed screw structure, and $\mathbf{L_S}$ gives the opposite turn. The dihedral angles between the coupling *y* transitions (as well as between the *x* transitions) are obviously different for these two diastereomeric $\mathbf{1_R{\cdot}L_R}$ and $\mathbf{1_R{\cdot}L_S}$ complexes, being larger or smaller than 90°, respectively. According to the exciton chirality theory,[7] this anticipates generation of a positive CD couplet of higher intensity in the case of $\mathbf{1_R{\cdot}L_S}$ in comparison to that of $\mathbf{1_R{\cdot}L_R}$. Taking into account that the resulting CD signal is a summation of the induced couplets of opposite signs (negative for the outside and positive for the inside binding modes), two different chiroptical scenarios may take place: enhancement of the positive chirality for $\mathbf{1_R{\cdot}L_S}$ in comparison to $\mathbf{1_R{\cdot}L_R}$ if the inside ligation is the major contributor or alternative reduction of the corresponding negative chirality if the outside binding dominates. Indeed, it is clear the latter situation is realized for the $\mathbf{1_R{\cdot}2}-\mathbf{1_R{\cdot}4}$ systems. Thus, it is of note that in the case of $\mathbf{1_S{\cdot}3}$ systems containing the antipodal host the overall tendency is simply opposite (see, Figure 2). However, the degree of the differences between the corresponding diastereomeric pairs ($\mathbf{1_R{\cdot}L_S}$/$\mathbf{1_R{\cdot}L_R}$ and $\mathbf{1_S{\cdot}L_R}$/$\mathbf{1_S{\cdot}L_S}$) is clearly reduced upon increasing the guest's bulkiness, and finally, the most bulky **5** exhibits the reverse behavior; that is, $\mathbf{1_S{\cdot}5_S}$ gives a less intense positive couplet in comparison to $\mathbf{1_S{\cdot}5_R}$ (Figures 2 and 3). This at first sight surprising chiral recognition switching behavior can also be readily rationalized by considering the bulkiness effect at the stereogenic center upon inside binding (Figure 4). Hence, further increasing the ligand bulkiness results in enhancement of the degree of screw sense between two chlorin moieties as in $\mathbf{1_R{\cdot}L_R}$ and $\mathbf{1_R{\cdot}L_S}$, which in turn changes the angles between the coupling electric dipoles. For example, the angle between the *y* transitions is increased in the former case or decreased in the latter case. Again, according to the exciton chirality method,[7a] upon the simultaneous angle changes, the amplitude of the positive couplet of $\mathbf{1_R{\cdot}L_S}$ is decreased faster than that of $\mathbf{1_R{\cdot}L_R}$, eventually leading to such a situation in which the positive chirality of $\mathbf{1_R{\cdot}L_R}$ becomes greater than that of $\mathbf{1_R{\cdot}L_S}$, in turn resulting in greater reduction of the overall negative chirality (or the positive chirality in the case of the antipodal host). Indeed, this situation is realized for the bulkiest ligand **5** producing the observed switching effect of chiral recognition.

Furthermore, an interesting chiroptical effect was discovered upon addition of the antipodal guest to the supramolecular complex formed by the guest of opposite chirality. The corresponding CD amplitudes exhibit pronounced nonlinear dependencies upon increasing the portion of antipodal **L** (see Supporting Information), thus indicating a significant synergetic effect. Although the origin of this phenomenon has yet to be clarified, plausible explanations include a further equilibrium shift to the anti conformation and/or geometrical changes in the anti form of the supramolecular complex containing both antipodal ligands resulting in enhancement of the induced CD couplet, thus maximizing the corresponding positive or negative chirality (in the case of *y* transitions of *anti*-$\mathbf{1_R{\cdot}L}$ and -$\mathbf{1_S{\cdot}L}$, respectively).

In summary, we demonstrated a new principle of chiral recognition based on a two-point host−guest interaction model coupled with the different host's conformational response. It was found that the bulkiness at the stereogenic center effectively controls the chiral recognition properties of supramolecular systems, which is also able to switch the enantioselectivity. These results should have important implications for designing new chiroptical devices and sensors, especially for chiral recognition purposes.

Supporting Information Available: UV−vis spectra and dependencies of the A_{norm} value upon increasing the portion of antipodal guest (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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