Foldamers

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Helicity Induction in Hydrogen-Bonding-Driven Zinc Porphyrin Foldamers by Chiral C_{60}-Incorporating Histidines**

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Helical biomacromolecules such as DNA and polypeptides or proteins play important roles in living systems. Extensive efforts have been devoted to helicity induction in unnatural oligomers, polymers, and dendrimers to explore new properties and functions.[1–3] In many cases, chiral amplification has been observed, which has found applications in molecular recognition,[4] light harvesting,[5] and catalysis.[6] We are motivated to explore new applications of hydrogen-bonding-driven aromatic oligoamide foldamers in chiral recognition.[7–9] Herein we report a new efficient strategy for helicity induction based on porphyrin-appended hydrogen-bonded foldamers and chiral C_{60}-incorporating histidines.

It is well established that zinc porphyrin is coordinated by N ligands such as pyridine and imidazole,[10,11] and also spontaneously attracted to C_{60} by π–π interaction.[12] Since zinc porphyrin is five-coordinate, we envisioned that rationally designed zinc porphyrin-appended foldamers might complex N ligand–C_{60} adducts through cooperation of the two discrete noncovalent interactions. Therefore, receptors **1**–**4** were synthesized and characterized. Previously,[13] we demonstrated that the repeating oligoamide skeletons in **2**–**4** adopt rigid, planar folding conformations due to intramolecular three-centered hydrogen bonding.[14] Indeed, the ^{1}H NMR spectra of **2**, **3**, and **4** in $CDCl_3$ revealed that all the signals of their NH protons appear in the downfield region, indicating the existence of intramolecular hydrogen binding and folding conformation for these molecules. The appended

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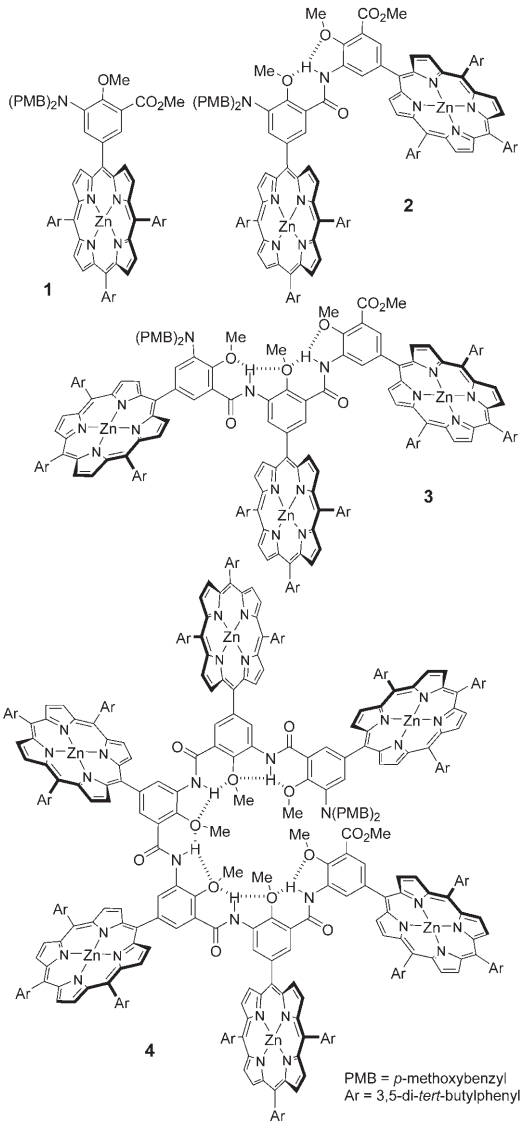

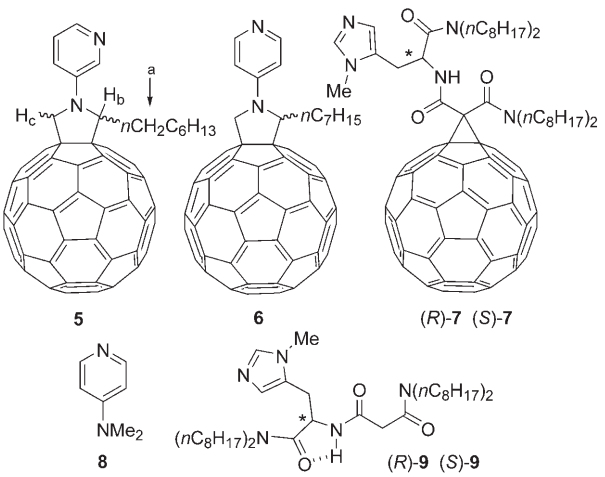

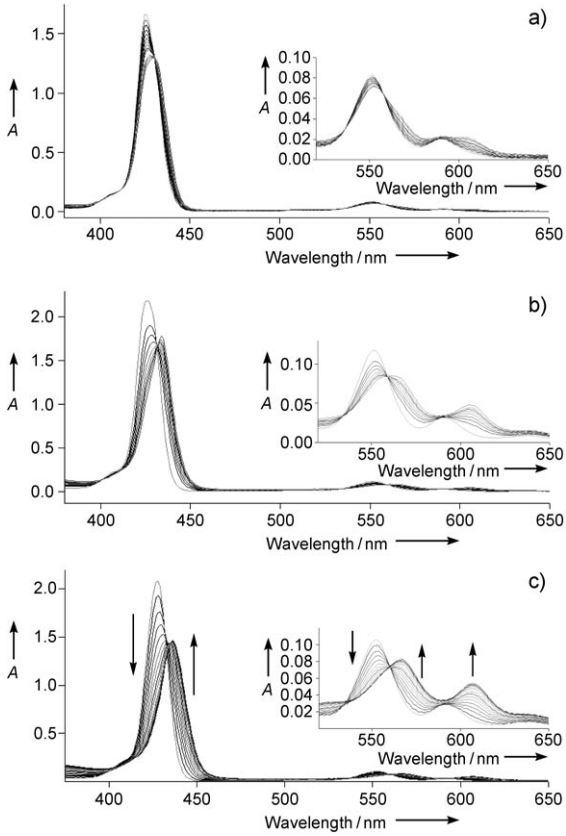

Figure 1. Absorption spectral changes of a) **2** (3.6×10^{-6} M), b) **3** (2.4×10^{-6} M), and c) **4** (1.2×10^{-6} M) on titration with (*R*)-**7** (0–7.2×10^{-4} M) in $CHCl_3$ at 25 °C.

zinc porphyrin units should adopt a conformation that is on average perpendicular to the folding skeleton.[4a] Such an arrangement would facilitate cooperative, "domino" interaction with structurally matching C_{60}–ligand adducts. Receptors **1**–**4** have good solubility in $CHCl_3$, and their absorption and ^{1}H NMR spectra in this solvent showed no evidence of intermolecular aggregation of the oligoamide skeletons or inter- or intramolecular aggregation of the porphyrin units.

With **1**–**4** in hand, guests **5**–**7** were synthesized. Upon addition of **5**–**7**, the UV/Vis spectra of **1**–**4** in $CHCl_3$ changed substantially, indicative of strong complexation. The UV/Vis titration results of **2**, **3**, and **4** with (*R*)-**7** are presented in Figure 1. The λ_{max} of the Soret and Q bands of **4** were red-shifted from 427.6 and 552.4 nm to 436.8 and 556.8 nm, respectively, with tight isosbestic points at 433.1 and 560.0 nm. In contrast, the shorter oligomers **2** and **3** exhibited smaller red shifts. Interestingly, a clear isosbestic point is observed for the Soret band in the UV/Vis spectra of all complexes. This result may reflect that the zinc porphyrin units in the foldamers have very similar binding affinities due to their ordered arrangement. The apparent association constants K_a between the zinc porphyrin unit of the receptors and **5**–**9** in $CHCl_3$ were determined on the basis of the titration experiments (Table 1).[15,16]

For a given guest, the K_a value increases pronouncedly with elongation of the foldamer. This increased binding affinity is clearly the result of increased π–π stacking between zinc porphyrin and C_{60}.[12,17] This increasing π–π interaction in the longer oligomers may be attributed to the enhanced

Table 1: Apparent association constants K_a [M^{-1}] for the complexes of the zinc porphyrin unit of receptors **1**–**4** with guests **5**–**9** in $CHCl_3$ at 25 °C, measured by UV/Vis titration.[a]

1:**5**	3.8×10^4	**1**:**6**	3.7×10^4	**1**:(*R*)-**7**	5.9×10^3				
2:**5**	1.4×10^5	**2**:**6**	1.6×10^5	**2**:(*R*)-**7**	1.1×10^4	**2**:**8**	8.7×10^3	**2**:(*R*)-**9**	9.7×10^2
3:**5**	2.8×10^5	**3**:**6**	1.6×10^5	**3**:(*R*)-**7**	2.1×10^4	**3**:**8**	8.5×10^3	**3**:(*R*)-**9**	3.4×10^3
4:**5**	2.0×10^5	**4**:**6**	1.5×10^6	**4**:(*R*)-**7**	3.5×10^4	**4**:**8**	1.1×10^4	**4**:(*R*)-**9**	5.4×10^3
4:**5**[b]	2.1×10^5	**4**:**6**[b]	1.7×10^6	**4**:(*R*)-**7**[b]	2.3×10^4			**4**:(*S*)-**7**	3.6×10^4

[a] With error of $\leq$15%. [b] Determined by fluorescence titration method (excitation wavelength 559 nm, emission wavelength 600 nm).

spatial matching between the C_{60} and porphyrin units due to warping of the porphyrin units in one direction. The larger **6** and **7** exhibit even greater binding ability than their C_{60}-free counterparts **8** and **9**, and this clearly shows the important contribution of π–π stacking to complexation. Although imidazole is a stronger ligand to zinc porphyrin than pyridine,[11] **7** has lower binding capability than both **5** and **6**, which may be rationalized by considering the greater structural flexibility of **7**.

The stoichiometry of the complexes was also estimated. For example, the ^{1}H NMR spectra for [**2**]/[**5**] ([**5**] = 11 mM) in $CDCl_3$ revealed a clear inflexion point for the change in the chemical shift of H_a of **5** at [**2**]/[**5**] = 0.5. This value indicates that these two compounds form a stable complex with 1:2 stoichiometry. Due to signal overlap, association constants could not be obtained from the ^{1}H NMR titration experiments. The Job plot for the **4**:**7** system, based on the UV/Vis experiments, revealed maximum change in absorbance at [**4**]/([**4**] + [(*R*)-**7**]) ≈ 0.17, which corresponds to 1:5 stoichiometry and is smaller than the value of 0.14 expected for 1:6 stoichiometry. This result may indicate that with both compounds being at low concentration for the UV/Vis measurement, the maximum stoichiometry was not achieved. Nevertheless, Job plots revealed a 1:6 stoichiometry for the complexes of **4** with **5** and **6** due to increased binding affinity (see Supporting Information).

Fluorescence studies revealed that the emissions of the zinc porphyrin units of **1**–**4** could be quenched significantly by the guests.[18] The quenching data for their fluorescent emission at 600 nm (excitation wavelength: 559 nm at the isosbestic point of the Q band) is presented in Table 2. Quenching efficiency increases remarkably with elongation of the oligomers. This result is consistent with the above UV/Vis study and also supports the existence of cooperativity for the complexation of the oligomers with the guests. Based on the fluorescence quenching experiments,[17a,19] the apparent association constants of the complexes of **4** with **5**–**7** were also determined (Table 1), which are quite comparable with those evaluated by UV/Vis titration. As an example, the titration spectra of **4** with (*R*)-**7** are shown in Figure 2.

Chirality amplification was then investigated for the new porphyrin-appended foldamers. When (*R*)-**7** or (*S*)-**7** was added to solutions of **2**–**4** in $CHCl_3$, mirror-image Cotton effects resulted (Figure 3, the CD spectrum of the guest has been subtracted). In contrast, **1** is completely silent under identical conditions. The second Cotton effect is noticeably stronger than the first and increased substantially with elongation of the oligomers. The maximum CD amplitude $\Delta\varepsilon$ is 162, 1098, and

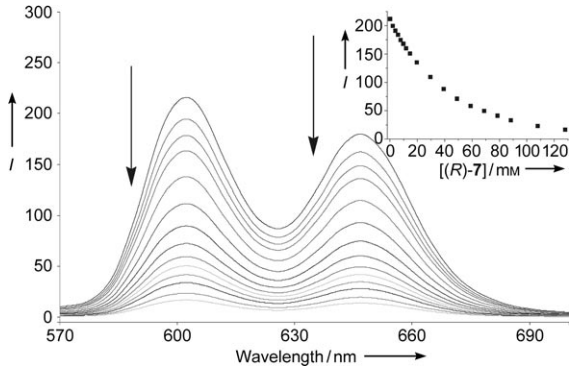

Figure 2. Fluorescence spectral changes of **4** (1.2×10^{-6} M) on addition of (*R*)-**7** (0–1.3×10^{-4} M) in $CHCl_3$ at 25 °C. Inset: plot of emission intensity of **4** at 600 nm versus [(*R*)-**7**].

2346 $M^{-1}cm^{-1}$ for **2**, **3**, and **4**, respectively, and the ability of **4** for chiral amplification is about 14.5 and 2.1 times as large as those of **2** and **3**. Because the total concentration (20 μM) of porphyrin units is identical for all oligomers, the results clearly indicate a remarkably large cooperativity in **4** for transferring the chirality of the histidine unit to the whole supramolecular architecture. In contrast, the chiral induction of C_{60}-free **9** is much smaller (Figure 4). Compared to those of **2** and **3**, the CD signal of **4** in the region of the porphyrin Soret band is also shifted remarkably on complexation with **7**. The CD band between 500 and 580 nm in Figure 3 should be produced from the chiral C_{60} unit of **7**, since similar signals were not observed when **7** was replaced by C_{60}-free **9** (Figure 4). Interestingly, another strong Cotton effect was also displayed between 580 and 640 nm in the assembly of **4** and **7**,[20] which is not observed in the assembly of **2** or **3**. The chiral amplification, signal shifting, and new additional Cotton effect in the region of long wavelength displayed by the longer foldamers on complexation with the chiral C_{60} derivatives may be explained by considering that the increased binding affinity of the chiral

Table 2: Fluorescent quenching data of receptors **1**–**4** by adducts **5**–**7** in $CHCl_3$ at 25 °C.

	I_0[a]	I[b] $[(I_0-I)/I_0]$[c]			[**5**] [M][d]	[**6**] [M][d]	[(*R*)-**7**] [M][d]
		5	**6**	(*R*)-**7**			
1	179	173 (0.04)	161 (0.10)	163 (0.09)	–[e]	–[e]	–[e]
2	213	129 (0.39)	107 (0.50)	195 (0.08)	1.2×10^{-5}	8.6×10^{-6}	–[e]
3	214	117 (0.45)	90 (0.58)	188 (0.12)	8.2×10^{-6}	5.7×10^{-6}	3.7×10^{-5}
4	210	51 (0.76)	21 (0.90)	174 (0.17)	3.6×10^{-6}	2.9×10^{-6}	3.0×10^{-5}

[a] Values of pure receptors at [porphyrin] = 7.2×10^{-6} M. [b] Values when 1 equiv of guest (7.2×10^{-6} M) was added. [c] Quenching efficiency. [d] Guest concentration at $[I_0-I]/I_0 = 0.5$. [e] $[I_0-I]/I_0 > 0.5$ in the concentration range investigated.

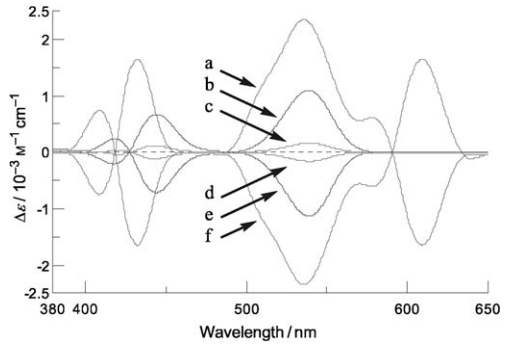

Figure 3. CD spectra of **4** (3.3×10^{-6} M) in the presence of (*R*)-**7** (a) and (*S*)-**7** (f), **3** (6.7×10^{-6} M) in the presence of (*R*)-**7** (b) and (*S*)-**7** (e), and **2** (1.0×10^{-5} M) in the presence of (*R*)-**7** (c) and (*S*)-**7** (d) in $CHCl_3$ at 25 °C ([(*R*)-**7**] = [(*S*)-**7**] = 5.0×10^{-3} M).

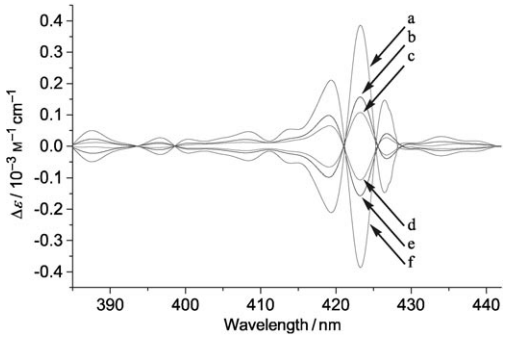

Figure 4. CD spectra of **4** (3.3 μM) in the presence of (*S*)-**9** (a) and (*R*)-**9** (f), **3** (6.6 μM) in the presence of (*S*)-**9** (b) and (*R*)-**9** (e), and **2** (10 μM) in the presence of (*S*)-**9** (c) and (*R*)-**9** (d) in $CHCl_3$ at 25 °C ([(*R*)-**9**] = [(*S*)-**9**] = 5.0×10^{-3} M).

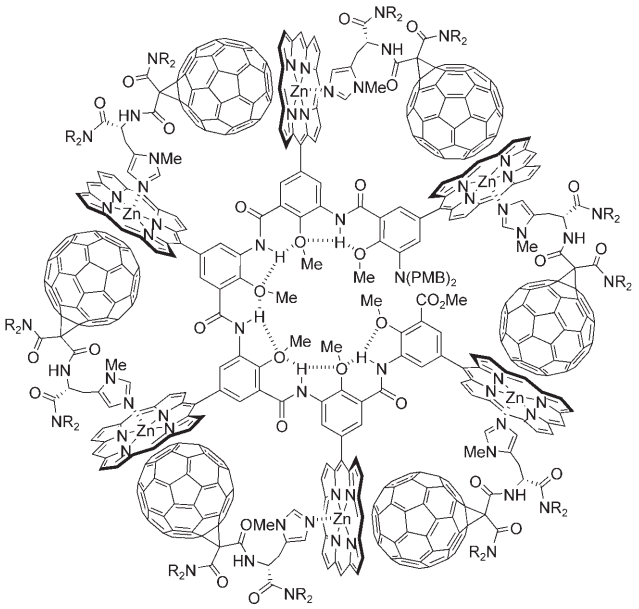

Figure 5. Proposed binding mode for the complex between **4** and (*R*)-**7**.

guest to the longer receptors would lead to more ordered chiral assembling architecture in which all the porphyrin and C_{60} units are warped in one direction. Based on these spectral investigations, we propose that for the complexation of the porphyrin-appended foldamer receptors, a clockwise or anticlockwise one-direction binding mode should be of lowest energy. Figure 5 presents a plausible binding mode for the system of **4** with (*R*)-**7**.

Chiral induction or amplification of nonnatural oligomers and polymers has been the subject of intensive research in recent years.[4,20] In this work, we demonstrated that foldamers are suitable skeletons for achieving this target. In principle, the chiral-recognition subunits can also be incorporated into one folding skeleton, which would lead to increased chiral amplification, while chiral induction based on rigid, unfolding architectures might also exhibit new interesting features.

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