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Hydrogen bonding-driven elastic bis(zinc)porphyrin receptors for neutral and cationic electron-deficient guests with a sandwich-styled complexing pattern

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Abstract—This Letter reports the design and synthesis of a new type of hydrogen bonding-mediated foldamer-derived tweezer receptors that are incorporated with two peripheral (zinc)porphyrin units. Due to the existence of four intramolecular hydrogen bonds, the (zinc)porphyrin units are forced to approach and stack with each other. ^{1}H NMR and fluorescent studies revealed that the new receptors could form 1:1 complexes with planar electron-deficient molecules such as naphthalene and benzene diimides and paraquat through a unique sandwich-styled binding pattern. The association constants of the new complexes have been evaluated by the ^{1}H NMR or fluorescent titration methods.

Molecular tweezers are a family of synthetic receptors, which are composed with two binding units and a linker to adopt a convergent conformation.[1] Typically, the linkers are constructed with rigid polycyclic skeletons, which enable the tweezers to hold size- and binding sites-matched guests.[2] However, the structural rigidity also reduces their binding ability for mismatched guests because such kind of tweezers lack the ability of adjusting the relative orientation of their binding units to achieve better complexation. Moreover, their syntheses are usually of low efficiency or time-consuming. With the advent of foldamer chemistry,[3] we have recently initiated a project to develop new generation of acyclic receptors for molecular recognition by making use of hydrogen bonding-induced aromatic oligoamide-derived foldamers as frameworks.[4,5] By incorporating zinc porphyrins to well-designed rigidified aromatic amide back-bones, we have constructed two series of non-covalently driven tweezers that strongly complex large spheric fullerenes and their derivatives.[6] We herein report the design and synthesis of two new elastic bisporphyrin receptors **1a** and **1b** and their binding properties toward planar guests **2**–**5**.

Receptors **1a** and **1b** consist of two electron-rich porphyrin units and an aromatic tetraamide linker. Dynamic modeling suggested that, due to the existence of the continuous intramolecular three-center hydrogen bonding[7,8] and the inherent planarity of the aromatic amide unit, the peripheral electron-rich (zinc)porphyrins could be forced to approach and stack with each other, giving rise to two low-energy structures (Fig. 1). Planar electron-deficient guests might be driven by the donor–acceptor interaction to insert between the two porphyrin units, leading to new complexes of sandwich-styled binding pattern.[9]

The synthetic routes for **1a** and **1b** are shown in Scheme 1. Thus, amine **6**[10] was first treated with **7**[11] in dichloromethane in the presence of triethylamine to afford **8** in 80% yield. Raney Ni-catalyzed hydrogenation of **8** in THF gave **9** in 90% yield. Compound **9** was then coupled with **10**[12] in dichloromethane to produce **11** in 60% yield. Treatment of **11** with concd sulfuric acid in dichloromethane gave metal-free **1a** in 54% yield.[13] The latter was then reacted with zinc acetate in hot dichloromethane and methanol to afford **1b** in 90% yield.[13] For comparison, **12a** and **12b** were also prepared

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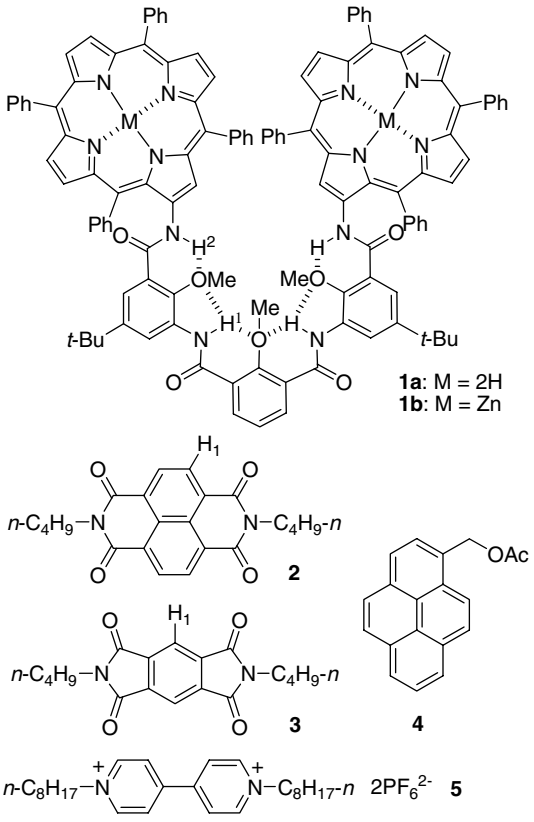


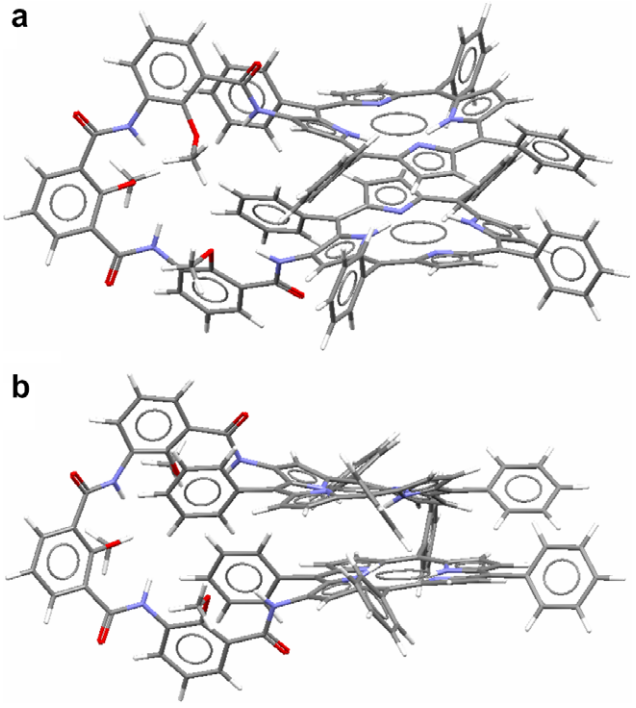
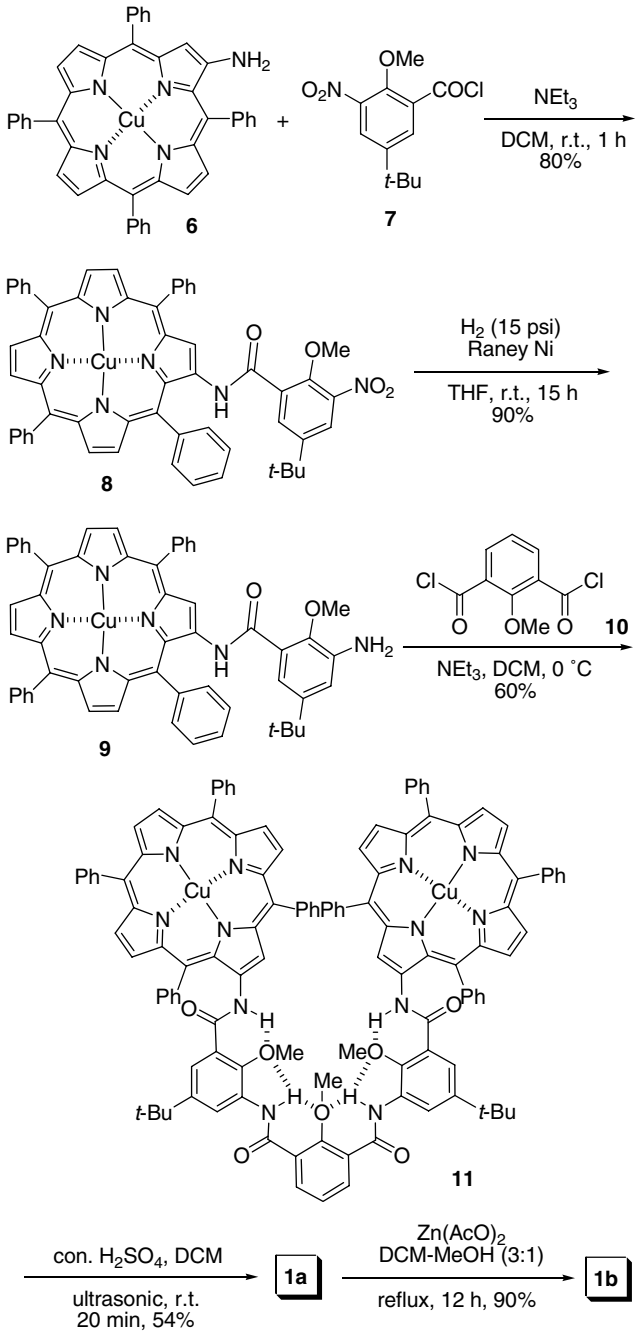


Figure 1. Two low-energy conformations **1a**: (a) with a mirror plane symmetry and (b) with a C_2 symmetry. The former is more stable than the latter with a 6 kcal/mol energy difference.

from **8** under similar conditions. All the new porphyrin compounds were soluble in organic solvents such as chloroform and acetone.

The ^{1}H NMR spectra of compounds **1a**, **1b**, and **12b** in chloroform-*d* (4 mM) was of high resolution and exhibited one set of signals (see Figs. 2 and 3, vide infra), indicating that the possible conformational isomers of **1a** and **1b**, which might be formed as a result of the different orientation of the two porphyrin units relative to each other, exchanged quickly on the ^{1}H NMR time scale. The signals in the downfield area have been assigned by the NOESY and COSY experiments. The signals of the three-center hydrogen bonded H-1 (see the structure in the text for numbering) of **1a** and **1b** appeared at the downfield area, clearly showing their involvement of the intramolecular hydrogen bonding.[7,8] Their chemical shifts were very close (9.99 and 10.04 ppm, respectively). In contrast, compared to that of H-2 of **1a** (9.16 ppm), the signal (9.31 ppm) of H-2 of **1b** shifted to the downfield area notably, which may be attributed to the increased deshielding effect produced by the stacked zinc porphyrin units in **1b**.[6a,14] Reducing the concentration of **1a** and **1b** from 5 mM to 0.2 mM did not cause salient shifting ($\leqslant$0.04 ppm) for the peaks of their aromatic protons. Within the concentration range of less than 1.5 μM, their UV–vis absorbance (the Soret band at 428 nm) observed Beer's law. These results supported that no important intermolecular stacking took place for both compounds. Within the concentration range of 0.2–2.0 μM in chloroform, the emission intensity (at 605 nm) of the fluorescent spectra of **1b** was always approximately 12% lower than that of **12b** of the identical concentration of the porphyrin units. This result indicates that there existed intramolecular stacking of the porphyrin units in **1b**, which was obviously driven by the intramolecular hydrogen bonding and caused the fluorescent self-quenching.[15] Compared to those of **12b**, the ^{1}H NMR signals of the aromatic protons of **1b** of the identical porphyrin concentration in chloroform-*d* also notably shifted upfield, further supporting intramolecular stacking of the porphyrin units of **1b**.

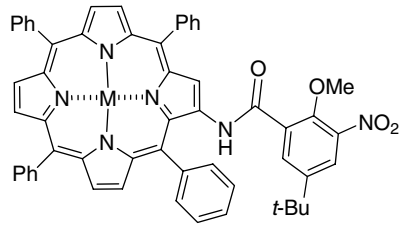
Adding **1b** to the solution of naphthalene diimide **2**[16] in chloroform-*d* caused remarkable upfield shifting of the singlet of H-1 of **2** ($\Delta\delta \geqslant 1.41$ ppm). The typical ^{1}H NMR spectra of their mixture solutions are presented in Figure 2. Similar upfield shifting was also observed for the mixture solution of **2** and **12b** (Fig. 3). Nevertheless, the changing value of the chemical shifting of H-1 of **2** under the identical conditions was remarkably smaller ($\Delta\delta \approx 0.33$ ppm). Intermolecular NOE connections were observed between the pyrrole protons of **1b** and H-1 of **2** for their 1:1 solution (5 mM) (Fig. 4). In contrast, no similar connection was exhibited by the 1:1 solution of **2** and **12b** even at the higher concentration of 8 mM. These results show that intermolecular donor–acceptor interaction occurred between the electron-rich porphyrin units of **1b** and **12b** and the electron-deficient naphthalene diimide of **2**,[17] but the interaction of **1b** was substantially stronger than that of **12b**. This difference can be explained by the formation of a sandwich-styled complex between **1b** and **2**, in which the porphyrin units of **1b** cooperatively interacted with **2** as shown in Figure 4. ^{1}H NMR titration experi-



Scheme 1. Synthesis of receptors **1a** and **1b**.

ments were then performed in chloroform-*d*. By fitting the change values of the chemical shifting of the H-1 signal of **2** with the concentration of **1b** and **12b**, the association constants (K_{assoc}) of complexes **1b**·**2** and **2**·**12b** were evaluated to be 850 (±100) and 90 (±10) M^{-1}, respectively.[18,19]

Mixing **1b** with **2** did not cause salient change of the chemical shift of the H-1 signal of **1b** (Fig. 2). However, its H-2 signal shifted upfield significantly (up to 0.20 ppm). No similar shifting was displayed for the NH signal of **12b** (Fig. 3). This difference may be explained by considering that the insertion of **2** between the stacking porphyrin units of **1b** increased the distance



12a: M = 2H
12b: M = Zn

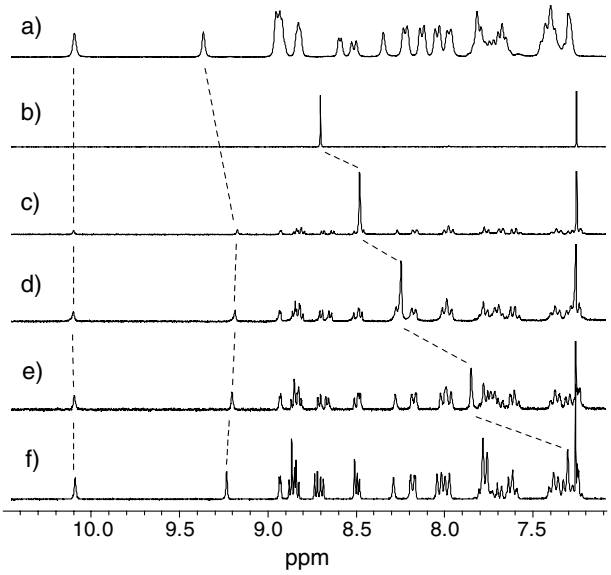


Figure 2. ^{1}H NMR spectrum (400 MHz) of (a) **1b** (5.0 mM), (b) **2**, (c) **1b** + **2** (0.5:1), (d) **1b** + **2** (1:1), (e) **1b** + **2** (2:1) and (f) **1b** + **2** (8:1) in chloroform-*d* at 25 °C ([**2**] = 5 mM).

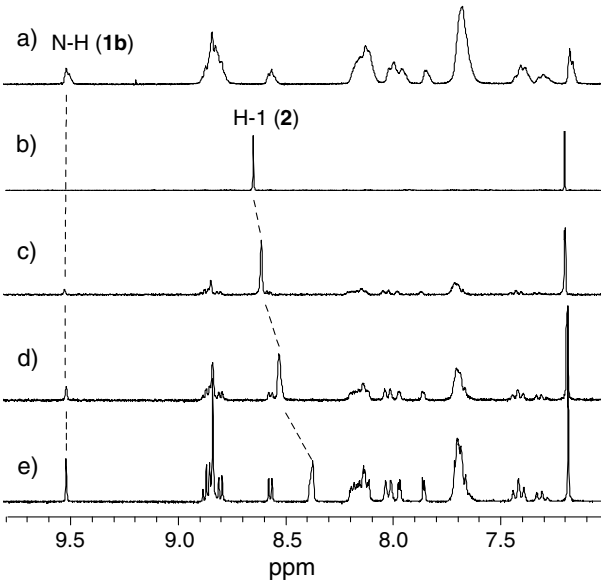


Figure 3. ^{1}H NMR spectrum (400 MHz) of (a) **11b** (5.0 mM), (b) **2**, (c) **11b** + **2** (0.5:1), (d) **11b** + **2** (1:1) and (e) **11b** + **2** (8:1) in chloroform-*d* at 25 °C ([**2**] = 5 mM).

of the two porphyrin units and consequently weakened the shielding effect of the porphyrin unit on the proton

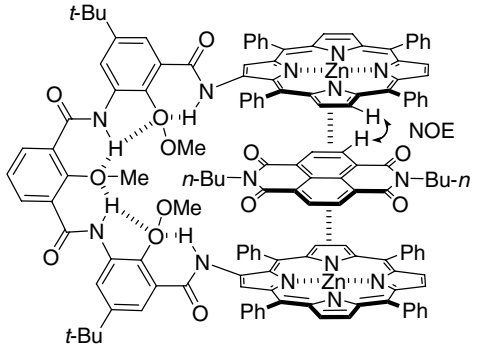


Figure 4. Sandwich-styled complex between **1b** and **2**. An intermolecular NOE connection is shown.

of the amide attached to another one. Another possibility is that the insertion would weaken the strength of the intramolecular hydrogen bonding of H-2. The result also implies that intramolecular hydrogen bonding still existed in **1b** after the binding, showing an elastic feature of its amide linker.

Similar complexing behavior was also observed for **1b** and electron-deficient benzene diimide **3**.[20] Adding **1b** (40 mM) to the solution of **3** (5 mM) caused an upfield shifting of 0.26 ppm for the H-1 signal of **3**. This value is substantially smaller than that observed for **2** in the above system, reflecting the lower electron accepting ability of **3** compared to **2**.[16] In the presence of **12b** (40 mM), the H-1 signal of **3** (5 mM) in chloroform-*d* did not move saliently ($\Delta\delta < 0.04$ ppm), suggesting that complex of **1b** and **3** also adopted a sandwich-styled binding pattern. By using the ^{1}H NMR titration method, we determined the K_{assoc} of complex **1b**·**3** in chloroform to be 120 ($\pm$15) M^{-1}.

Adding 1 equiv of **1b** to the solution of **4** (5 mM) in chloroform-*d* induced the signal of the methylene signal of **4** to shift upfield 0.12 ppm in the ^{1}H NMR spectrum. The aromatic signals did not provide useful information due to important overlapping and coupling. Similar result was not observed for the mixture solution of **4** and **12b** under the identical condition, therefore the change should be attributed to the insertion of **4** between the porphyrin units of **1b**. It has been established that pyrene is not electron-deficient,[21] so the driving force for the insertion may be efficient intermolecular π–π stacking between the porphyrin and pyrene units.[22]

The interaction of **1b** with ionic electron acceptor **5**[23] in polar acetone-d_6 was also investigated with the ^{1}H NMR spectroscopy. In the presence of 3 equiv of **1b** (4 mM), the signals of the α- and β-protons of **5** shifted upfield ca. 0.10 ppm. This value is smaller than those observed above for **2** or **3**, but notably larger than the corresponding value (<0.03 ppm) of **5** caused by **12b**, showing a weak cooperation of the zinc porphyrin units of **1b** in binding **5**. This might reflect the competitive effect of the polar solvent that weakened the intramolecular hydrogen bonding in **1b**. The fluorescent emission of **1b** was pronouncedly lower (ca. 15%) than that of **12b** in acetone when their porphyrin concentrations were kept constant, suggesting a folded conformation for **1b**, which facilitated the self-quenching of the porphyrin emission. Quantitative ^{1}H NMR titration experiments could not be performed due to the decrease of the spectral resolution at high concentration. However, incremental addition of **5** to the solution of **1b** in acetone caused the emission of **1b** to increase pronouncedly. Based on the titration results, the K_{assoc} of complex **1b**·**5** was determined to be 600 ($\pm$70) M^{-1} in acetone.

In conclusion, we have reported the synthesis of a new intramolecular hydrogen bonding-induced bisporphyrin-based molecular tweezer that complexes planar electron-deficient guests. The complexes adopt a sandwich-styled binding pattern and the hydrogen bonded linker exhibits an elastic feature upon binding. The result demonstrates the feasibility of utilizing intramolecular hydrogen bonding to modulate the shape of synthetic receptors for molecular recognition. In principle, discrete interacting functional units, such as porphyrin and C_{60}, can be simultaneously introduced to acid–base-regulated hydrogen bonded back-bones,[24] which may lead to the construction of a new single molecular device.

Acknowledgments

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13. Compound **1a**: A solution of **11** (0.20 g, 0.10 mmol) in dichloromethane (10 mL) and concentrated sulfate acid (1.0 mL) was sonicated at room temperature for 15 min and then pooled into ice-water (30 mL). The organic phase was successively washed with saturated sodium bicarbonate solution, water, brine and dried over sodium sulfate. After the solvent was removed in vacuo, the crude product was purified by column chromatography (DCM/petroleum ether 1:2) to afford **1a** as purple solid (99 mg, 54%). ^{1}H NMR ($CDCl_3$): δ 9.99 (s, 2H), 9.16 (s, 2H), 8.90 (s, 2H), 8.81–8.70 (m, 8H), 8.46 (s, 4H), 8.18 (d, $J = 6.6$ Hz, 4H), 8.09 (d, $J = 6.6$ Hz, 4H), 8.02 (d, $J = 6.6$ Hz, 4H), 7.94 (d, $J = 6.6$ Hz, 4H), 7.78–7.59 (m, 14H), 7.40–7.35 (m, 17H), 4.23 (s, 3H), 3.78 (s, 6H), 1.42 (s,18H), −3.00 (s, 4H). ^{13}C NMR ($CDCl_3$): δ 162.1, 147.8, 144.2, 142.0, 141.9, 141.8, 140.3, 135.6, 134.6, 134.4, 134.2, 133.0, 131.1, 129.6, 128.4, 127.8, 127.7, 127.6, 126.8, 126.6, 125.3, 121.3, 121.2, 121.1, 121.0, 120.9, 120.4, 120.1, 116.4, 112.2, 110.2, 71.5, 64.7, 62.8, 40.6, 35.0, 31.4, 30.1, 29.5, 29.0. MS (MALDI-TOF): *m*/*z* 1829 $[M+H]^+$. HRMS (MALDI-TOF): $[M+H]^+$ calcd for $C_{121}H_{97}N_{12}O_7$, 1829.7600; found, 1829.7600.
Compound **1b**: ^{1}H NMR ($CDCl_3$): δ 10.04 (s), 9.31 (s, 2H), 8.93 (s, 2H), 8.89–8.85 (m, 6H), 8.78–8.75 (m, 4H), 8.53 (d, $J = 4$ Hz, 2H), 8.45 (d, $J = 4.0$ Hz, 2H), 8.29 (s, 2H), 8.20 (d, $J = 7.0$ Hz, 4H), 8.17 (d, 2H), 8.08 (d, $J = 7.0$ Hz, 2H), 7.99–7.90 (m, 6H), 7.77–7.60 (m, 14H), 7.39–7.35 (m, 15H), 6.75 (d, $J = 7.0$ Hz, 2H), 4.23 (s, 3H), 3.82 (s, 6H), 1.44 (s, 18H). ^{13}C NMR ($CDCl_3$): δ 150.7, 150.4, 150.3, 150.2, 149.9, 149.5, 149.2, 149.0, 147.7, 144.2, 142.6, 142.5, 142.4, 141.2, 140.1, 139.8, 138.7, 135.7, 134.4, 134.3, 134.1, 133.6, 132.7, 132.2, 132.1, 132.0, 131.8, 131.6, 131.2, 131.1, 128.3, 128.3, 128.1, 128.0, 127.8, 127.7, 127.5, 127.4, 126.8, 126.6, 126.5, 126.4, 126.0, 121.9, 121.5, 121.3, 120.7, 120.3, 117.5, 64.7, 62.7, 35.0, 31.4. MS (MALDI-TOF): *m*/*z* 1952 $[M]^+$. HRMS (MALDI-TOF): calcd for $C_{121}H_{92}N_{12}O_7Zn_2$, 1952.5795; found, 1952.5789.
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