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Foldamer-based pyridine–fullerene tweezer receptors for enhanced binding of zinc porphyrin

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Abstract—This paper reports the design and synthesis of a new series of hydrogen bonding-mediated foldamer-derived tweezer receptors that are used for efficient complexation of zinc porphyrin guest. One end of the rigidified aromatic amide backbone is incorporated with one fullerene unit, while another end is connected to one pyridine or imidazole unit. The ^{1}H NMR, UV–vis, and fluorescent investigations in chloroform revealed that, due to the intramolecular hydrogen bonding-driven preorganized folded conformation, the fullerene and pyridine units of the receptors are located with suitable spatial separation and consequently able to co-complex zinc porphyrin with remarkably increased stability. In contrast, the imidazole-incorporated receptor displays a weakened binding affinity possibly due to structural mismatching and large steric hindrance. The association constants of the complexes of the new receptors with zinc porphyrin have been determined.

1. Introduction

Development of synthetic receptors for efficient recognition of special molecule or ion requires high structural and binding-site complementarity between the receptor and guest.[1] In order to achieve high binding stability and selectivity, more than one binding site is usually needed to be introduced in the receptors and the binding sites should also be located with suitable distance and orientation. Covalently bonded molecular tweezers represent one class of structurally unique receptors for many site-matching guests.[2] Nevertheless, the synthesis of these receptors is usually of low efficiency or is time-consuming, and in many cases their structural modifications are also difficult.[3] Therefore, it is of importance to develop new, simple approaches for designing tweezer-styled receptors.

We recently reported a new strategy for developing a new generation of assembling tweezers by making use of hydrogen bonding-induced aromatic amide oligomers as backbones.[4,5] Two or more zinc porphyrin or pyridine units have been introduced to rationally designed folded backbones for efficient complexation of fullerene or porphyrin guests by cooperative two-point interaction.[6] In this paper, we report the synthesis of a new series of foldamer-derived fullerene and pyridine-incorporated tweezer receptors that can efficiently complex zinc porphyrin in chloroform.[7]

Keywords: Molecular recognition; Foldamer; Hydrogen bonding; Fullerene; Porphyrin.
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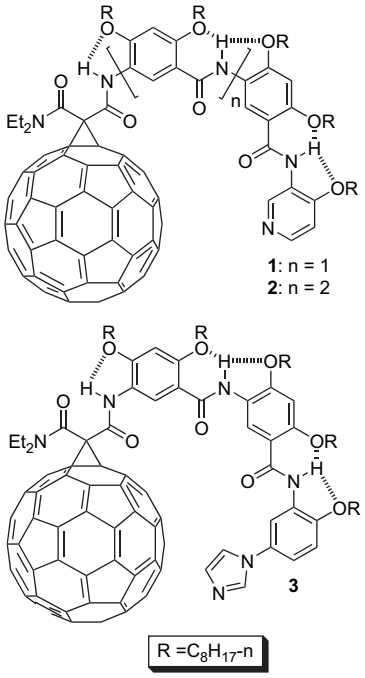
2. Results and discussion

Three foldamer-based receptors **1**–**3** have been synthesized, which were designed on the basis of recent reports that intramolecular three-centered hydrogen bonding can induce linear aromatic amide oligomers to adopt folded or other rigidified conformation.[5,8] The pyridine or imidazole unit was incorporated because they are good nitrogen ligands for coordination with metallated porphyrins,[9] and fullerene was introduced to the receptors because important π–π stacking has been revealed between fullerene and metallated porphyrin.[10]

The synthetic route for compound **1** is shown in Scheme 1. Thus, compound **4** was first nitrated in concentrated sulfuric acid to give **5**[11] in 72% yield. The latter was converted into **6** in 70% yield (two steps) by reacting with phosphorus pentachloride in 1,2-dichloroethane, followed by treatment of the chloride intermediate with *n*-octanol. Palladium-catalyzed hydrogenation of compound **6** in methanol generated amine **7** in 90% yield. With **7** available, the coupling reaction of aniline **8**[12] with acyl chloride **9**[13] in dichloromethane was performed, which produced compound **10** in 80% yield. The intermediate was again hydrogenated to give **11** in 96% yield. Aniline **11** was then reacted with 3-(diethylamino)-3-oxopropanoic acid[14] in dichloromethane in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC) to afford intermediate **12** in 80% yield. Compound **12** was then hydrolyzed with LiOH in aqueous methanol and THF to afford **13** in 90% yield. The acid was reacted with **7** in chloroform also with DCC as coupling reagent to produce **14** in 78% yield. Finally, treatment of intermediate **14** with fullerene in

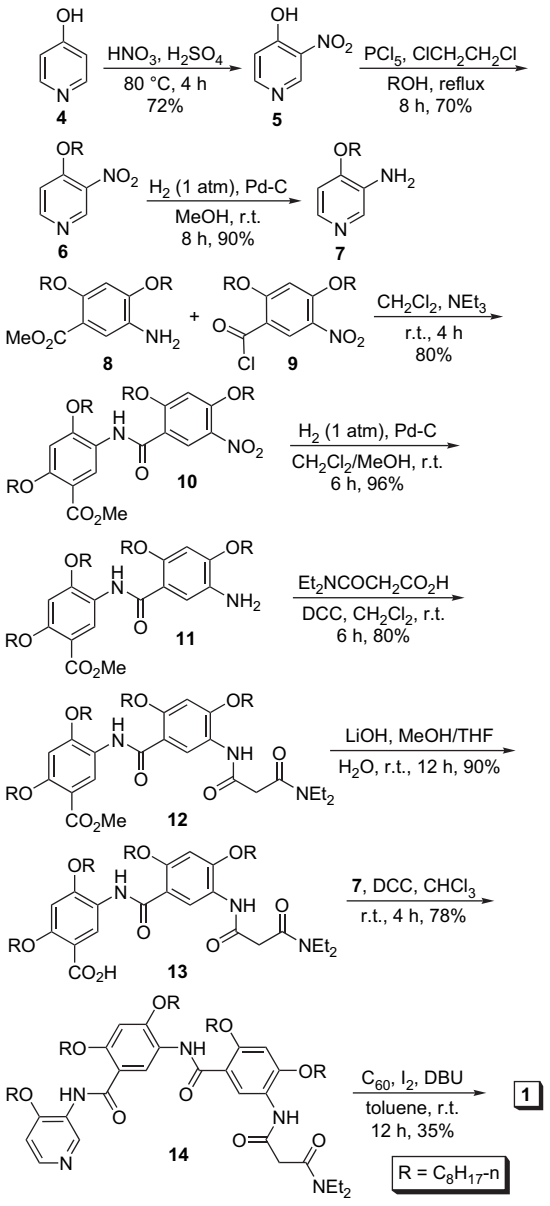


toluene at room temperature in the presence of iodine and 7,11-diazabicyclo[5.4.0]undec-11-ene (DBU) afforded **1** in 35% yield.

For the synthesis of compound **2** (Scheme 2), compound **15** was first prepared in 85% yield from the reaction of **7** with **9** in refluxing chloroform and triethylamine. The intermediate then underwent palladium-catalyzed hydrogenation in dichloromethane and methanol to afford **16** in 96% yield. Compound **16** was reacted with **13** in chloroform in the presence of DCC to afford **17** in 78% yield. Finally, compound **17** was treated with fullerene in the presence of iodine and DBU in toluene to give **2** in 20% yield.

The synthetic route for compound **3** is provided in Scheme 3. Compound **18**[15] was first treated with iodine and silver sulfate in methanol to give **19** in 90% yield. The iodide was then coupled with imidazole in hot DMF in the presence of potassium carbonate, cupric iodide, and proline to afford **20** in 70% yield. Palladium-catalyzed hydrogenation of compound **20** in methanol and dichloromethane produced **21** in 96% yield. The aniline derivative was then coupled with **13** in chloroform in the presence of DCC to afford **22** in 70% yield. Finally, the intermediate was reacted with fullerene and iodine in toluene in the presence of DBU to give **3** in 18% yield.

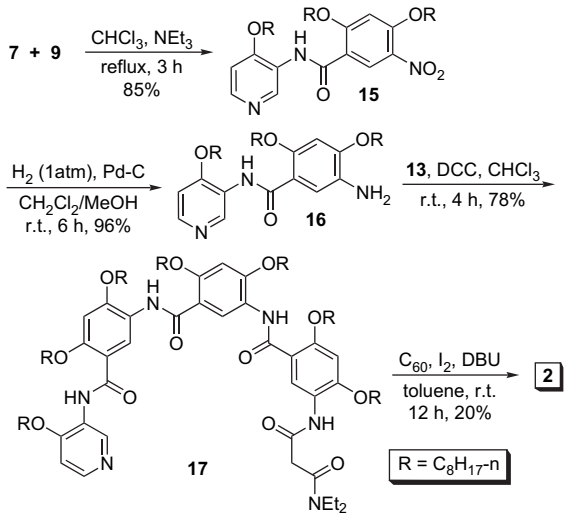
The ^{1}H NMR spectra of compounds **1**–**3** and their precursors **14**, **17**, and **22** in $CDCl_3$ are provided in Figure 1. The signals of the NH protons have been assigned by the D_2O exchange experiments. The great difference between the chemical shifts of the signals of the receptors and their precursors may be attributed to the large shielding effect of the fullerene unit in the receptors. Because the rigidified crescent secondary structure of the aromatic amide backbones in the receptors has been previously established,[16] it is reasonable to



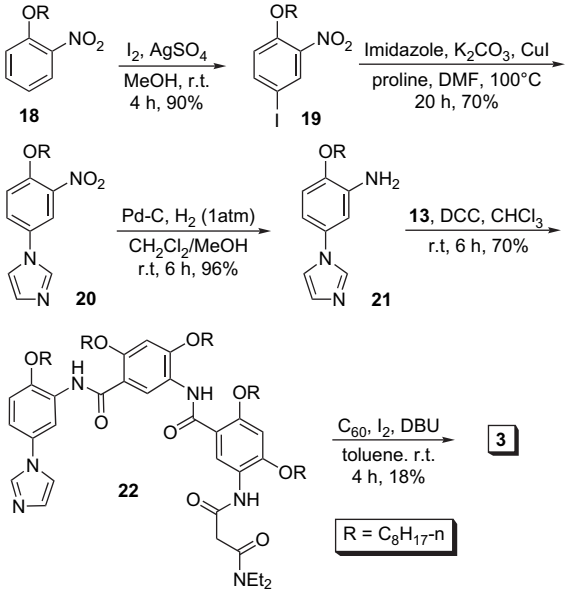
Scheme 1.

assume that the present fullerene- and nitrogen ligand-appended compounds also adopt folded conformation.

Adding zinc porphyrin **23** to the solution of **1** in $CDCl_3$ caused important shifting of several signals of both compounds (Figs. 1b–e), suggesting that important complexation occurs between them. Similar results were also observed for the solution of **2** and **23** in $CDCl_3$. Quantitative complexing behaviors of **1** and **2** with zinc porphyrin **23** in chloroform were then investigated by the UV–vis spectroscopy. The plots of the change of the UV–vis absorbance of **23** with the incremental addition of **1** and **2** are shown in Figures 2 and 3. Remarkable hypochromic effect was exhibited for the Soret band of **23**, which also supports strong intermolecular coordination. The UV–vis titration spectra of both systems displayed a clear isosbestic point for the Soret band and the Q-band, suggesting a 1:1 binding mode.[9] The association



Scheme 2.



Scheme 3.

constants (K_{assoc}) of complexes **1**·**23** and **2**·**23** in chloroform were determined by fitting their UV–vis titration data to a 1:1 binding mode,[6,17] which gave a value of approximately 7.6×10^3 and 1.2×10^4 M^{-1}, respectively. On the basis of the identical titration method, the K_{assoc} values of complexes **14**·**23** and **17**·**23** in chloroform have been determined to be ca. 1.0×10^3 and 1.4×10^3 M^{-1}, respectively. The UV–vis titration spectra of **23** with **17** are shown in Figure 4 as an example. These values are pronouncedly lowered than those of the corresponding complexes of the fullerene-appended foldamers. Considering the remarkably large size of the fullerene unit, the increase in the stability of the complexes of **1** and **2**, relative to that of the corresponding fullerene-free ligands, suggests that important π–π stacking interaction forms between **23** and the fullerene units in **1** and **2**. The increased binding stability reflects that this stacking and the intermolecular zinc–pyridine coordination join together to promote the formation of a 'two-point'-bound

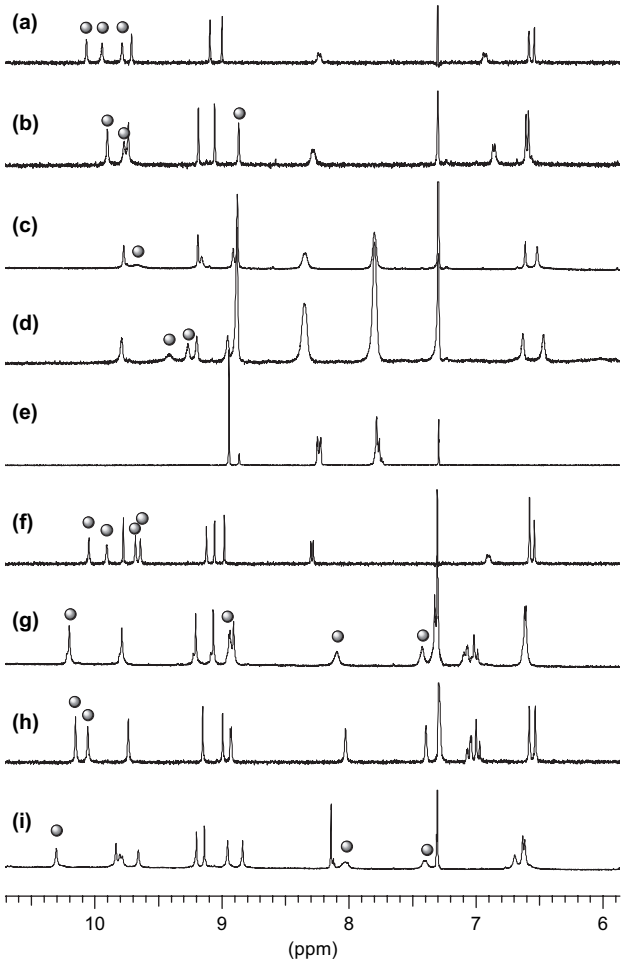


Figure 1. Partial ^{1}H NMR spectrum of (a) **14**, (b) **1**, (c) **1**+**23** (1:0.5), (d) **1**+**23** (1:1), (e) **23**, (f) **17**, (g) **2**, (h) **22**, and (i) **3** in $CDCl_3$ at 25 °C (6 mM). The labeled peaks are those of the amide protons.

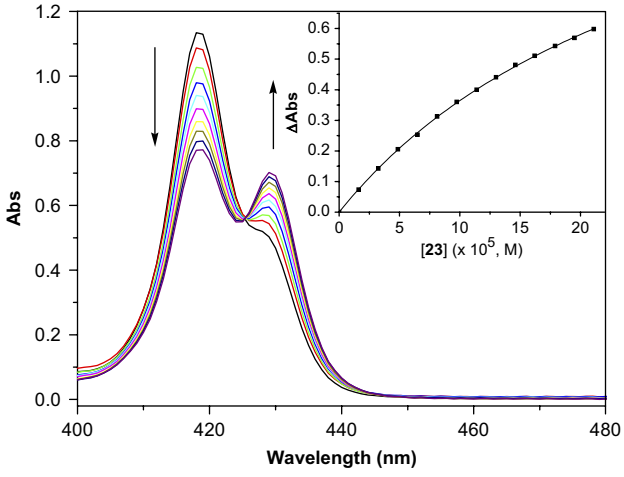


Figure 2. The change of the absorption spectra of **23** (2.8×10^{-6} M) with the addition of **1** (0–70 equiv) in chloroform at 25 °C (inset: plot of the absorption of **23** at 422 nm vs [**1**]).

complex, as shown in Figure 5. The higher binding stability of complex **2**·**23** might reflect a better spatial orientation of the pyridine and fullerene units of **2** for cooperative binding of zinc porphyrin **23**.

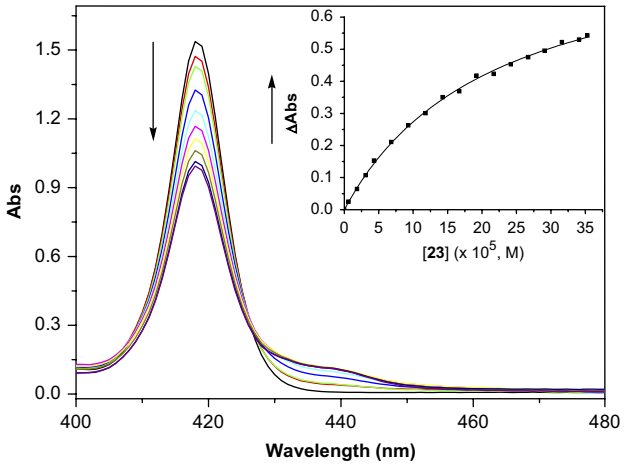


Figure 3. The change of the absorption spectra of **23** (2.8×10^{-6} M) with the addition of **2** (0–130 equiv) in chloroform at 25 °C (inset: plot of the absorption of **23** at 422 nm vs [**2**]).

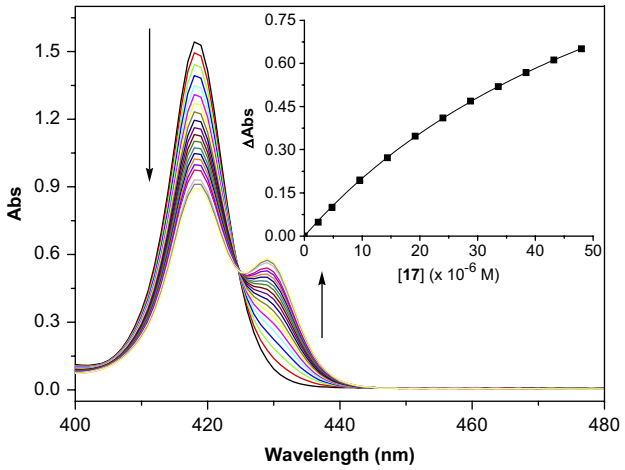
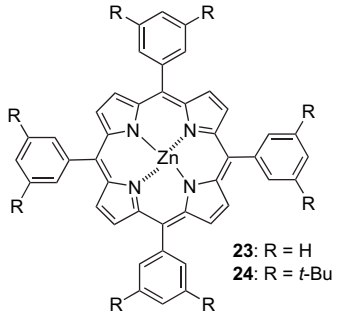


Figure 4. The change of the absorption spectra of **17** (2.8×10^{-6} M) with the addition of **23** (0–65 equiv) in chloroform at 25 °C (inset: plot of the absorption of **23** at 422 nm vs [**17**]).



The strong binding affinity of **1** and **2** toward **23** also caused efficient quenching of the emission of **23**. Fluorescent titration experiments were therefore also carried out in chloroform, which gave rise to a K_{assoc} of ca. 7.8×10^3 and 1.3×10^4 M^{-1} for complexes **1**·**23** and **2**·**23**, respectively. These values are consistent with the results obtained by the UV–vis experiments. As an example, the fluorescent titration results for compound **2** are shown in Figure 6.

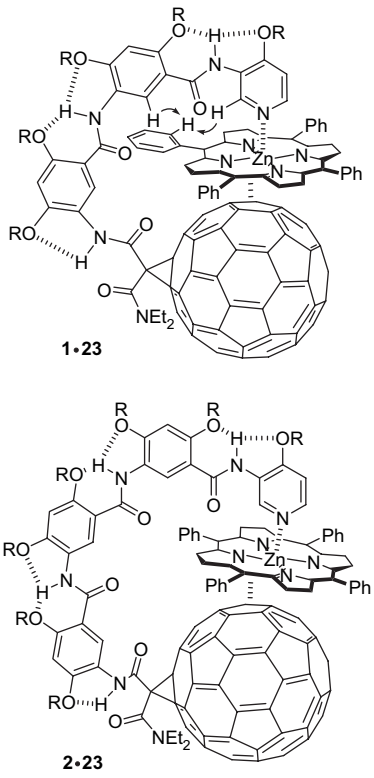


Figure 5. Proposed structures for 'two-point'-bound complexes **1**·**23** (the observed intermolecular NOE connections are shown) and **2**·**23**.

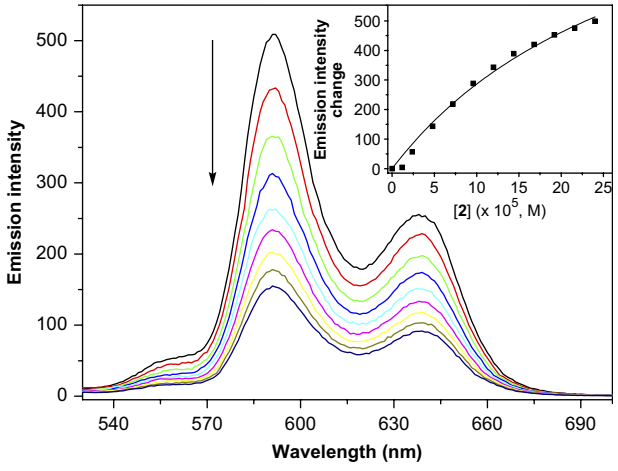


Figure 6. The change of the fluorescent spectra of **23** (1.2×10^{-6} M) with the addition of **2** (0–17 equiv) in chloroform at 25 °C (inset: plot of the emission change of **23** at 422 nm vs [**2**]).

Under similar experimental conditions, addition of **1** or **2** to the solution of **24** of larger size in chloroform did not cause obvious change of the UV–vis spectrum of **24**, implying that there is no important interaction. In contrast, UV–vis titration experiments performed in chloroform revealed important interaction between **24** and **17**, which corresponded to a K_{assoc} of ca. 1.2×10^3 M^{-1}. These results can be explained by considering the increased steric repulsion between **24** and the large fullerene units in **1** and **2**,

which retards the possible intermolecular π–π stacking and coordination interaction.

It has been established that imidazole is stronger than pyridine as ligand for zinc porphyrin.[9] Surprisingly, adding **3** to the solution of **23** in chloroform only led to slight hypochromism of the Soret band of the latter in the UV–vis spectrum (Fig. 7), which corresponded to a K_{assoc} of ca. $1.4\times10^2\ M^{-1}$ for complex **3·23**. In contrast, the K_{assoc} of complex **22·23** in the same solvent was determined by UV–vis titration experiments (Fig. 8) to be ca. $6.0\times10^3\ M^{-1}$. This value is comparable to that of many of the imidazole–zinc porphyrin complexes[9] but is remarkably higher than that of complex **3·23**. These observations may also be attributed to the great spatial hindrance of the fullerene unit in **3**, which obstructs the approach of **23** to the imidazole unit of **3** as shown in Figure 9. In contrast, the imidazole of fullerene-free **22** could efficiently coordinate to **23** of smaller size by adopting the separated conformation as shown in Figure 9 to form stable complex.

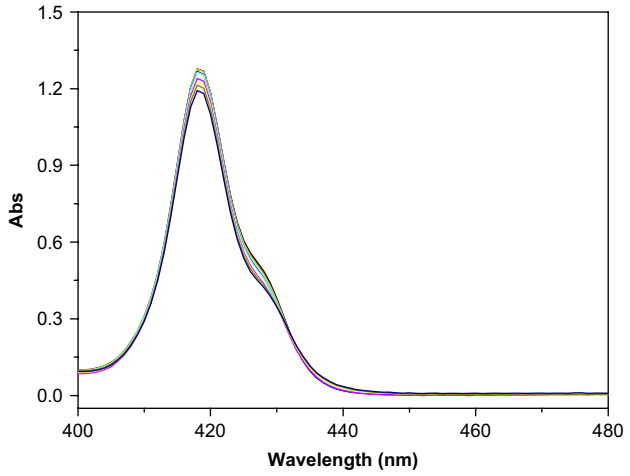


Figure 7. The change of the absorption spectra of **23** (2.8×10^{-6} M) with the addition of **3** (0–100 equiv) in $CDCl_3$ at 25 °C.

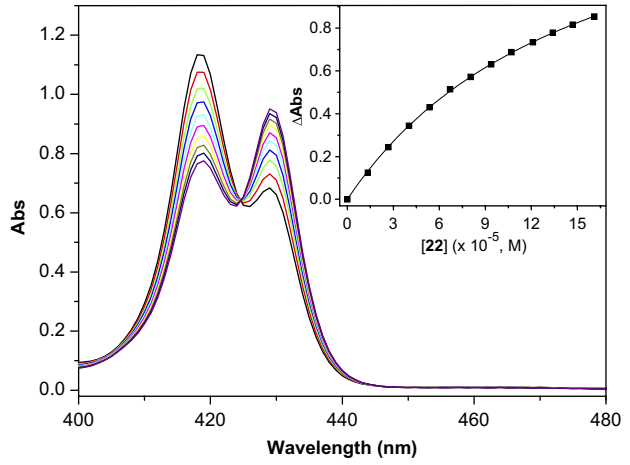


Figure 8. The change of the absorption spectra of **23** (2.8×10^{-6} M) with the addition of **22** (0–65 equiv) in chloroform at 25 °C (inset: plot of the absorption of **23** at 422 nm vs [**22**]).

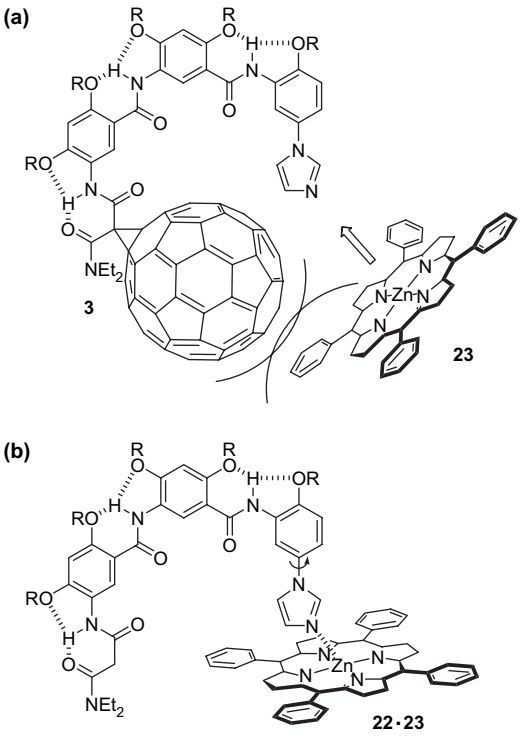


Figure 9. (a) Proposed repulsion of the fullerene unit in **3** toward zinc porphyrin **23**. (b) The structure of complex **22·23**.

3. Conclusion

In summary, we have reported the synthesis of a new series of foldamers, which are incorporated with one fullerene and one pyridine unit, at the two ends of their aromatic amide backbone. The ^{1}H NMR, UV–vis, and fluorescent investigations in chloroform have revealed that the new rigidified molecules are able to efficiently complex zinc porphyrin as a result of cooperative coordination and π–π stacking interactions. A 'two-point' binding mode has been proposed for the new complexes. The stability of the new series of complexes is sensitive to the steric effect and, as a result, very weak complexation has been revealed for zinc porphyrin and imidazole-incorporated receptor of similar structure. The result demonstrates that hydrogen bonding-induced artificial secondary structures are new versatile assembling building blocks for molecular recognition and supramolecular chemistry.

4. Experimental section

4.1. General methods

The ^{1}H NMR spectra were recorded on 500, 400 or 300 MHz spectrometer in the indicated solvents. Chemical shifts are expressed in parts per million using residual solvent protons as internal standards. Chloroform (7.26 ppm) was used as an internal standard for chloroform-*d*. Elemental analysis was carried out at the SIOC analytical center. Unless otherwise indicated, all commercially available materials were used as received. All solvents were dried before use following standard procedures. All reactions were carried out under

an atmosphere of nitrogen. Silica gel (1–4 μm) was used for column chromatography.

4.1.1. Compound 6. A suspension of compound **5**[11] (5.00 g, 35.7 mmol) and phosphorus pentachloride (7.90 g, 42.6 mmol) in 1,2-dichloroethane (35 mL) was heated under reflux until a clear solution was formed. The solution was cooled to 35 °C and *n*-octanol (55 mL) was added dropwise. The mixture was heated again under reflux for 1 h and then cooled to room temperature. The precipitate formed was filtered and washed with cold water and ethanol. The crude product was purified by recrystallization from acetonitrile to give **6** as a white solid (6.30 g, 70%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.01 (s, 1H), 8.61 (d, J=5.7 Hz, 1H), 7.02 (d, J=5.7 Hz, 1H), 4.20 (t, J=5.7 Hz, 2H), 1.86 (t, J=5.7 Hz, 2H), 1.52–1.29 (m, 10H), 0.90 (t, J=6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 158.5, 154.3, 146.8, 136.8, 109.1, 70.1, 31.7, 29.1, 29.0, 28.5, 25.6, 22.5, 14.0. MS (EI): *m*/*z* 253 $[M+H]^+$. HRMS (EI): calcd for $C_{13}H_{20}N_2O_3$ $[M-NH_2]^+$: 235.1447. Found: 235.1455.

4.1.2. Compound 7. A suspension of **6** (5.06 g, 20.0 mmol) and Pd–C (5%, 0.26 g) in methanol (200 mL) was stirred under the atmosphere of hydrogen gas (1 atm) at room temperature for 8 h. The solid was filtered off and the filtrate concentrated in vacuo. The resulting residue was subjected to flash chromatography (CH_2Cl_2/AcOEt 20:1) to give compound **7** as a pale yellow solid (4.00 g, 90%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00 (s, 1H), 7.95 (d, J=5.7 Hz, 1H), 6.68 (d, J=5.4 Hz, 1H), 4.04 (t, J=6.3 Hz, 2H), 3.74 (br, 2H), 1.87–1.83 (m, 2H), 1.47–1.25 (m, 10H), 0.89 (t, J=7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 157.0, 137.6, 130.4, 124.1, 106.6, 70.3, 31.6, 29.1, 29.0, 28.5, 25.7, 22.5, 14.0. MS (EI): *m*/*z* 222 $[M]^+$. HRMS (EI): calcd for $C_{13}H_{22}N_2O$: 222.1732. Found: 222.1742.

4.1.3. Compound 10. To a stirred solution of compound **8**[12] (3.26 g, 8.00 mmol) and triethylamine (1.00 g, 10.0 mmol) in dichloromethane (50 mL) was added a solution of **9** (3.52 g, 8.00 mmol) in dichloromethane (25 mL). The solution was stirred at room temperature for 4 h and then washed with diluted hydrochloric acid (20 mL), water (2×30 mL), brine (30 mL) and dried over sodium sulfate. Upon removal of the solvent under reduced pressure, the resulting residue was purified by column chromatography (dichloromethane/methanol 30:1) to give **10** as a yellow solid (6.50 g, 80%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.63 (s, 1H), 8.94 (s, 1H), 8.92 (s, 1H), 6.54 (s, 1H), 6.49 (s, 1H), 4.26 (t, J=7.2 Hz, 2H), 4.13–4.08 (m, 4H), 4.01 (t, J=6.6 Hz, 2H), 3.86 (s, 3H), 1.97–1.81 (m, 6H), 1.48–1.25 (m, 30H), 0.89–0.83 (m, 9H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 165.7, 160.8, 160.5, 157.0, 156.5, 152.3, 141.6, 133.6, 131.2, 124.9, 120.8, 114.8, 98.3, 97.9, 70.4, 70.1, 70.0, 69.0, 51.6, 31.9, 31.8, 31.7, 31.6, 29.6, 29.3, 29.2, 29.1, 29.07, 28.8, 28.2, 25.9, 25.8, 25.7, 22.6, 22.6, 22.5, 14.0. MS (MALDI): *m*/*z* 813.6 $[M+H]^+$, 835.5 $[M+Na]^+$. HRMS (MALDI): calcd for $C_{47}H_{76}N_2O_9Na$ $[M+Na]^+$: 835.5449. Found: 835.5443.

4.1.4. Compound 11. A suspension of compound **10** (4.07 g, 5.00 mmol) and Pd–C (5%, 0.25 g) in dichloromethane and methanol (50 mL, 1:1) was stirred under the atmosphere of hydrogen gas (1 atm) at room temperature for 6 h. The solid was filtered and the filtrate concentrated under reduced pressure. The crude product was subjected to flash chromatography (dichloromethane/methanol 30:1 v/v) to give **11** as a pale yellow solid (3.76 g, 96%). The compound was unstable in air and used for the next step without further characterization.

4.1.5. Compound 12. To a solution of compound **11** (2.35 g, 3.00 mmol) and 3-(diethylamino)-3-oxopropanoic acid (0.48 g, 3.00 mmol) in dichloromethane (50 mL) was added DCC (0.68 g, 3.3 mmol). The solution was stirred at room temperature for 6 h and the solid formed was filtrated. The solvent was then removed under reduced pressure and the resulting residue was purified by column chromatography (dichloromethane/methanol 20:1 v/v) to give **12** as a white solid (2.22 g, 80%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.99 (s, 1H), 9.76 (s, 1H), 8.95 (s, 1H), 8.90 (s, 1H), 6.43 (s, 2H), 4.10–3.92 (m, 8H), 3.78 (s, 3H), 3.43–3.33 (m, 4H), 1.85–1.78 (m, 8H), 1.50–1.09 (m, 46H), 0.82–0.76 (m, 12H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 167.9, 163.9, 156.6, 154.0, 152.6, 152.4, 124.7, 121.8, 112.3, 98.5, 97.4, 70.4, 70.1, 51.5, 42.7, 40.8, 40.7, 31.7, 29.3, 29.2, 25.9, 22.6, 14.4, 14.0, 12.9. MS (MALDI-TOF): *m*/*z* 924 $[M+H]^+$, 946 $[M+Na]^+$, 962 $[M+K]^+$. HRMS (MALDI-TOF): calcd for $C_{54}H_{90}N_3O_9$ $[M+H]^+$: 924.6677. Found: 924.6671.

4.1.6. Compound 13. To a solution of compound **12** (2.00 g, 2.02 mmol) in THF (40 mL), methanol (10 mL), and water (10 mL) was added lithium hydroxide monohydrate (1.00 g, 40 mmol). The mixture was stirred at room temperature for 12 h and then acidified with dilute hydrochloric acid to pH=3. The mixture was concentrated under reduced pressure to ca. 10 mL and then stayed until no precipitate was formed. The solid was filtered, washed with cold water thoroughly, and then dried in vacuo. The crude product obtained was purified by recrystallization from ethyl acetate to give **13** as a white solid (1.76 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.06 (s, 1H), 9.75 (s, 1H), 9.13 (s, 1H), 8.94 (s, 1H), 6.51 (s, 1H), 6.45 (s, 1H), 4.21–4.03 (m, 8H), 3.49 (s, 2H), 3.45–3.40 (m, 4H), 1.89–1.87 (m, 8H), 1.57–1.13 (m, 46H), 0.89–0.82 (m, 12H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 164.9, 164.8, 162.8, 154.7, 153.6, 153.2, 126.7, 114.4, 97.3, 96.7, 70.7, 70.3, 69.4, 69.2, 43.6, 31.7, 31.7, 31.6, 29.4, 29.3, 29.2, 29.1, 29.0, 25.9, 25.8, 22.7, 22.6, 14.1, 14.0. MS (MALDI-TOF): *m*/*z* 910 $[M+H]^+$, 932 $[M+Na]^+$, 948 $[M+K]^+$. HRMS (MALDI-TOF): calcd for $C_{53}H_{88}N_3O_9$ $[M+H]^+$: 910.6521. Found: 910.6515.

4.1.7. Compound 14. A suspension of compound **13** (0.91 g, 1.00 mmol), **7** (0.22 g, 1.00 mmol), and DCC (0.23 g, 1.10 mmol) in chloroform (25 mL) was stirred at room temperature for 4 h. The solid formed was removed by filtration and the filtrate concentrated under reduced pressure. The resulting residue was subjected to column chromatography (dichloromethane/methanol 15:1 v/v) to afford **14** as a white solid (0.85 g, 78%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.09 (s, 1H), 9.99 (s, 1H), 9.79 (s, 1H), 9.70 (s, 1H), 9.03 (s, 1H), 8.99 (s, 1H), 8.18 (d, J=6.0 Hz, 1H), 6.98 (br s, 1H), 6.56 (s, 1H), 6.50 (s, 1H), 4.32–4.03 (m, 10H), 3.47 (s, 2H), 3.45–3.36 (m, 4H), 1.92–1.85 (m, 10H), 1.56–1.13 (m, 56H), 0.87–0.82 (m, 15H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 169.8, 163.0, 162.8, 162.3, 155.2, 154.3, 153.9, 152.9, 152.4, 144.8, 126.3, 125.2, 122.6, 121.4, 115.3, 114.9,

109.9, 106.3, 97.7, 97.4, 70.5, 69.1, 69.0, 68.8, 61.5, 41.8, 31.9, 31.8, 29.4, 29.3, 29.2, 28.9, 25.9, 25.8, 25.7, 22.6, 21.6, 14.1. MS (MALDI-TOF): *m/z* 1148 $[M+H]^+$, 1136 $[M+Na]^+$. HRMS (MALDI-TOF): calcd for $C_{66}H_{108}N_5O_9$ $[M+H]^+$: 1114.8147. Found: 1114.8142.

4.1.8. Compound 1. A solution of compound **14** (0.22 g, 0.20 mmol), fullerene (0.14 g, 0.20 mmol), and iodine (50 mg, 0.20 mmol) in dry toluene was heated under reflux for 10 min and then cooled to room temperature. DBU (0.034 mL) was added with a syringe and the mixture stirred for 12 h. Upon removal of the solvent in vacuo, the resulting residue was subjected to column chromatography (toluene/dichloromethane 20:1) to give compound **1** as a purple solid (0.11 g, 35%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.93 (s, 1H), 9.78 (s, 1H), 9.72 (s, 1H), 9.15 (s, 1H), 9.04 (s, 1H), 8.85 (s, 1H), 8.25 (t, J=2.4 Hz, 1H), 6.88 (dd, J_1=1.2 Hz, J_2=6.3 Hz, 1H), 6.57 (s, 1H), 6.55 (s, 1H), 4.22–4.06 (m, 12H), 3.78 (br s, 2H), 2.02–1.86 (m, 12H), 1.46–1.30 (m, 54H), 0.89–0.84 (m, 15H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 162.6, 159.3, 158.8, 158.7, 154.9, 154.5, 145.3, 145.2, 145.1, 144.8, 144.7, 144.6, 143.8, 143.0, 142.9, 142.8, 142.3, 142.1, 141.1, 76.7, 76.6, 76.5, 31.8, 31.7, 29.6, 29.4, 29.3, 29.2, 29.1, 25.9, 22.6, 22.5, 14.1, 14.0. MS (MALDI-TOF): *m/z* 1854 $[M+Na]^+$. HRMS (MALDI-TOF): calcd for $C_{126}H_{105}N_5O_9Na$ $[M+Na]^+$: 1854.7310. Found: 1854.7805.

4.1.9. Compound 15. To a solution of compound **7** (1.11 g, 5.00 mmol) and triethylamine (0.8 mL, 8.00 mmol) in chloroform (80 mL) was added a solution of compound **9** (2.20 g, 5.00 mmol) in chloroform (20 mL). The mixture was heated under reflux for 3 h and then cooled to room temperature. After workup, the crude product was purified by column chromatography (dichloromethane/AcOEt 10:1) to afford **15** as a white solid (2.51 g, 80%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.73 (s, 1H), 9.65 (s, 1H), 8.91 (s, 1H), 8.28 (d, J=5.4 Hz, 1H), 6.86 (d, J=5.4 Hz, 1H), 6.54 (s, 1H), 4.29 (t, J=6.9 Hz, 2H), 4.21–4.12 (m, 4H), 2.00–1.84 (m, 6H), 1.49–1.29 (m, 30H), 0.89–0.86 (m, 9H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 160.9, 160.6, 156.8, 153.7, 145.9, 142.5, 133.6, 131.4, 125.3, 114.2, 106.4, 97.9, 70.5, 70.2, 68.9, 31.7, 31.6, 31.7, 29.3, 29.2, 29.1, 29.0, 28.8, 25.8, 25.7, 22.6, 22.5, 14.7, 14.4, 14.0. MS (ESI): *m/z* 628 $[M+H]^+$. HRMS (ESI): calcd for $C_{36}H_{58}N_3O_6$ $[M+H]^+$: 628.4300. Found: 628.4320.

4.1.10. Compound 16. It was prepared as a white solid in 96% yield by the palladium-catalyzed hydrogenation of **15** according to the procedure described above for **11**. ^{1}H NMR (CD_3OD, 400 MHz): δ 9.81 (s, 1H), 8.55 (d, J=6.9 Hz, 1H), 8.24 (s, 1H), 7.78 (d, J=6.9 Hz, 1H), 7.02 (s, 1H), 4.60 (t, J=6.9 Hz, 2H), 4.51 (t, J=6.9 Hz, 2H), 4.31 (t, J=6.6 Hz, 2H), 2.02–1.90 (m, 6H), 1.56–1.27 (m, 30H), 0.93–0.85 (m, 9H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 164.7, 162.1, 160.8, 159.0, 140.1, 132.9, 130.0, 128.9, 115.3, 114.4, 111.2, 100.5, 73.9, 72.6, 71.9, 33.4, 33.4, 31.0, 30.9, 30.8, 30.9, 30.8, 30.8, 30.5, 30.1, 27.3, 27.1, 24.2, 24.1, 14.8. MS (ESI): *m/z* 598 $[M+H]^+$, 638 $[M+K]^+$. HRMS (ESI): calcd for $C_{36}H_{60}N_3O_4$ $[M+H]^+$: 598.4507. Found: 598.4578.

4.1.11. Compound 17. It was prepared as a white solid (78%) from the reaction of compounds **13** and **16** according to the procedure described above for **12**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.04 (s, 1H), 10.02 (s, 1H), 9.88 (s, 1H), 9.75 (s, 1H), 9.65 (s, 1H), 9.61 (s, 1H), 9.09 (s, 1H), 9.02 (s, 1H), 8.95 (s, 1H), 8.25 (d, J=5.4 Hz, 1H), 6.87 (d, J=5.4 Hz, 1H), 6.53 (s, 2H), 6.49 (s, 1H), 4.20–4.03 (m, 14H), 3.46 (s, 2H), 3.43–3.35 (m, 4H), 1.91–1.80 (m, 20H), 1.45–1.12 (m, 70H), 0.88–0.82 (m, 21H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 167.8, 163.8, 163.0, 162.9, 154.1, 153.9, 153.7, 153.6, 152.8, 152.7, 152.5, 145.0, 142.4, 142.3, 126.3, 126.1, 126.0, 125.1, 122.6, 122.3, 121.6, 115.5, 115.1, 114.9, 106.1, 97.9, 97.6, 97.4, 70.4, 70.3, 69.1, 69.0, 68.7, 42.8, 40.8, 31.8, 31.7, 29.6, 29.4, 29.3, 29.2, 29.1, 29.0, 28.8, 25.8, 25.7, 22.6, 14.4, 14.0, 12.9. MS (MALDI-TOF): *m/z* 1490 $[M+H]^+$, 1513 $[M+Na]^+$, 1529 $[M+K]^+$. HRMS (MALDI-TOF): calcd for $C_{89}H_{145}N_6O_{12}$ $[M+H]^+$: 1490.0921. Found: 1490.0915.

4.1.12. Compound 2. It was prepared as a purple solid (20%) from the reaction of compound **17** with fullerene according to the procedure described above for the preparation of **1**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.27 (s, 1H), 9.80 (s, 1H), 9.75 (s, 1H), 9.62 (s, 1H), 9.17 (s, 1H), 9.10 (s, 1H), 8.92 (s, 1H), 8.80 (s, 1H), 8.10 (s, 1H), 7.97 (br, 1H), 7.36 (br s, 1H), 6.64 (s, 1H), 6.58 (s, 1H), 6.54 (s, 1H), 4.61 (br, 2H), 4.64 (br, 2H), 4.23–4.11 (m, 14H), 1.86–1.90 (m, 20H), 1.47–1.26 (m, 6H), 0.86–0.77 (m, 21H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 158.6, 154.3, 148.5, 145.2, 145.1, 144.7, 144.6, 144.5, 143.8, 143.1, 143.0, 142.9, 142.2, 142.0, 140.9, 138.4, 128.5, 126.9, 125.0, 121.2, 120.5, 110.4, 97.6, 70.6, 70.4, 69.5, 69.2, 63.9, 56.0, 43.1, 31.8, 31.8, 31.7, 29.6, 29.5, 29.4, 29.3, 29.2, 25.9, 25.7, 25.5, 22.7, 22.6, 14.2, 14.0. MS (MALDI-TOF): *m/z* 2208 $[M+H]^+$, 2230 $[M+Na]^+$, 2246 $[M+K]^+$. HRMS (MALDI-TOF): calcd for $C_{149}H_{144}N_6O_{12}$ $[M+H]^+$: 2208.0764. Found: 2208.0759.

4.1.13. Compound 19. To a stirred solution of compound **18** (5.00 g, 20.0 mmol) in methanol (100 mL) were added iodine (5.12 g, 20.0 mmol) and silver sulfate (6.26 g, 20.0 mmol). The suspension was stirred for 1 h and then the solid was filtered off. The filtrate was concentrated under reduced pressure and the resulting residue triturated in ethyl acetate (100 mL). The organic phase was washed with water (50 mL×2), brine (50 mL) and dried over sodium sulfate. Upon removal of the solvent under reduced pressure, the resulting residue was recrystallized from ethyl acetate to give **19** as a dark brown solid (6.79 g, 90%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08 (d, J=2.1 Hz, 1H), 7.76 (dd, J_1=2.4 Hz, J_2=8.7 Hz, 1H), 6.83 (d, J=8.7 Hz, 1H), 4.06 (t, J=6.6 Hz, 2H), 1.83–1.76 (m, 2H), 1.59–1.27 (m, 10H), 0.87 (t, J=6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 152.3, 142.4, 133.7, 116.5, 80.2, 69.9, 31.7, 29.2, 29.1, 28.8, 25.8, 25.7, 22.6, 14.0. MS (EI): *m/z* 377 $[M]^+$. HRMS (EI): calcd for $C_{14}H_{20}NO_3I$: 377.0488. Found: 377.0488.

4.1.14. Compound 20. A suspension of compound **19** (3.75 g, 10.0 mmol), imidazole (0.80 g, 12.0 mmol), pottasium carbonate (3.45 g, 25.0 mmol), cupric iodide (0.10 g, 0.50 mmol), and proline (0.10 g, 1.00 mmol) in DMF (20 mL) was stirred at 100 °C for 40 h and then concentrated under reduced pressure. The residue was washed with water and the solid filtered. The solid was triturated in ethyl acetate (100 mL). The organic phase was washed with water

(50 mL), brine (50 mL) and dried over sodium sulfate. After the solvent was removed under reduced pressure, the crude product was purified by column chromatography (dichloromethane/methanol 100:1) to give **20** as a yellow solid (2.20 g, 70%). ^{1}H NMR (CD_3COCD_3, 400 MHz): δ 8.10 (s, 1H), 8.09 (s, 1H), 7.90 (dd, J_1=3.3 Hz, J_2=9.0 Hz, 1H), 7.63 (d, J=1.5 Hz, 1H), 7.52 (d, J=9.0 Hz, 1H), 7.13 (s, 1H), 4.28 (t, J=6.6 Hz, 2H), 1.52 (m, 2H), 1.37–1.31 (m, 10H), 0.89 (t, J=6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 151.7, 139.8, 135.7, 130.8, 129.7, 127.1, 119.1, 118.5, 115.7, 70.2, 70.0, 31.7, 29.1, 29.1, 28.8, 26.0, 25.7, 22.6, 14.1. MS (EI): *m/z* 317 $[M]^+$. HRMS (EI): calcd for $C_{17}H_{24}N_3O_3$ $[M+H]^+$: 318.1818. Found: 318.1822.

4.1.15. Compound 21. It was prepared as a pale yellow solid (96%) from the palladium-catalyzed hydrogenation of **20** following the procedure described above for **11**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.63 (br, 1H), 7.29 (br, 2H), 6.88 (br, 1H), 6.73 (d, J=8.1 Hz, 2H), 6.66 (d, J=8.1 Hz, 1H), 6.11 (br, 2H), 3.93 (t, J=6.3 Hz, 2H), 1.77–1.70 (m, 2H), 1.39–1.14 (m, 10H), 0.82 (t, J=6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 146.8, 138.2, 129.1, 119.9, 111.4, 110.7, 107.9, 68.8, 31.7, 29.2, 26.0, 22.6, 14.1. MS (EI): *m/z* 287 $[M]^+$. HRMS (EI): calcd for $C_{17}H_{25}N_3O$: 287.1998. Found: 287.2004.

4.1.16. Compound 22. It was prepared as a pale yellow solid (70%) from the reaction of compounds **13** and **21** according to the procedure described above for **14**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.14 (s, 1H), 10.04 (s, 1H), 9.72 (s, 1H), 9.13 (s, 1H), 8.97 (s, 1H), 8.91 (d, J=3.0 Hz, 1H), 7.99 (s, 1H), 7.36 (s, 1H), 7.26 (s, 1H), 7.00 (dd, J_1=3.0 Hz, J_2=11.4 Hz, 1H), 6.95 (d, J=11.4 Hz, 1H), 6.54 (s, 1H), 6.49 (s, 1H), 4.21–4.03 (m, 10H), 3.46 (s, 2H), 3.44–3.34 (m, 4H), 1.93–1.84 (m, 10H), 1.58–1.12 (m, 50H), 0.89–0.82 (m, 15H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 167.8, 164.0, 163.6, 162.9, 154.0, 153.7, 152.7, 152.6, 147.3, 130.3, 125.7, 124.9, 122.7, 121.7, 115.7, 114.9, 114.8, 114.4, 111.7, 97.6, 97.2, 77.7, 76.6, 76.3, 70.5, 70.3, 69.3, 69.1, 69.0, 53.4, 42.8, 40.8, 40.6, 31.9, 31.7, 29.7, 29.3, 29.2, 29.1, 25.8, 22.6, 14.4, 14.0, 12.9. MS (MALDI-TOF): *m/z* 1179 $[M+H]^+$, 1201 $[M+Na]^+$. HRMS (MALDI-TOF): calcd for $C_{70}H_{111}N_6O_9$ $[M+H]^+$: 1179.8335. Found: 1179.8407.

4.1.17. Compound 3. It was prepared as a purple solid (18%) from the reaction of **22** with fullerene according to the procedure described above for the preparation of **1**. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 10.19 (s, 1H), 9.77 (s, 1H), 9.20 (s, 1H), 9.05 (s, 1H), 8.92 (s, 1H), 8.88 (s, 1H), 8.06 (br, 1H), 7.39 (s, 1H), 7.29 (s, 1H), 7.05 (d, J=11 Hz, 1H), 6.96 (d, J=8.7 Hz, 1H), 6.58 (s, 1H), 6.57 (s, 1H), 4.23–4.08 (m, 12H), 3.68 (br, 2H), 1.93–1.85 (m, 10H), 1.46–1.27 (m, 50H), 0.86 (t, J=3 Hz, 15H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 158.6, 148.5, 145.6, 145.5, 145.3, 145.2, 144.8, 144.7, 144.6, 143.8, 143.1, 143.0, 142.9, 142.2, 142.1, 140.9, 138.5, 126.9, 125.0, 121.2, 120.9, 120.5, 114.4, 110.4, 69.6, 63.9, 56.0, 31.8, 31.7, 31.5, 29.6, 29.5, 29.4, 29.2, 29.1, 29.0, 25.9, 25.8, 22.6, 14.3, 14.0. MS (MALDI-TOF): *m/z* 1898 $[M+H]^+$, 1920 $[M+Na]^+$, 1936 $[M+K]^+$. HRMS (MALDI-TOF): calcd for $C_{130}H_{109}N_6O_9$ $[M+H]^+$: 1897.8256. Found: 1897.8250.

The method for the determination of association constants has been reported in previous papers.[6]

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