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Strapped porphyrin rosettes based on the melamine–cyanuric acid motif. Self-assembly and supramolecular recognition

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Abstract—This paper describes studies on the synthesis, self-assembly behavior, and complexing properties of several strapped porphyrin-incorporated melamine–cyanuric or melamine-barbiturate-based rosette supramolecules in chloroform-*d*. Strapped porpyrin cyanuric acid $\mathbf{H_2}$**1** and its Zn (II) complex **Zn1** were designed and synthesized. Both $\mathbf{H_2}$**1** and **Zn1** could combine melamine derivatives **11** or **12** to afford porphyrin rosettes, which are more stable than the model rosette initially reported by Whitesides due to the larger size of the porphyrin unit. The new porphyrin rosettes could efficiently complex tripyridyl derivative **13** through intermolecular, cooperative coordination between Zn (II) and pyridine. Two new pyridine-bearing barbiturates **18a** and **18b** were also synthesized. Mixing the identical amount of **18a** or **18b** with **11** or **12** in chloroform-*d* led to the formation of new isomeric rosettes as a result of different orientation of the pyridine unit of **18a** or **18b** in the rosettes. ^{1}H NMR study also revealed that porpyrin-bearing rosette $\mathbf{Zn1}_3\cdot\mathbf{11}_3$ could complex pyridine-bearing rosette $\mathbf{11}_3\cdot\mathbf{18a}_3$, leading to the formation of new two-layer-typed supramolecular architectures.

1. Introduction

In recent years, the self-assembly of small molecular units into larger, ordered architectures has been intensively investigated for the design of artificial receptors and novel materials.[1–16] Because of its unique feature of directionality, specificity, and stability, hydrogen bonding has been one of the most versatile non-covalent forces for the self-assembly of well-defined supramolecular systems.[17–21] Over the years, a number of efficient triple and quadruple hydrogen bonding modes have been developed.[17–19] The triply hydrogen bonded melamine–cyanuric acid motif has been extensively studied for the formation of the so-called 'rosette' supramolecuar structures.[22] Especially, a number of elegant double rosettes have been assembled based on calix[4]arene scaffolds bearing two melamine moieties.[23] In principle, introduction of additional binding or recognizing units into this relatively stable and highly symmetric supramolecular architectures might produce new generation of artificial multi-component receptors or assemblies of higher order. However, examples of this kind of rosette receptors are very limited.[24–26]

We have recently developed an efficient method to synthesize strapped tetraphenylporphyrin derivatives.[27] The additional aliphatic strap, which connects two oppositely located phenyl groups, not only completely prevents the atropisomerization of the corresponding porphyrins,[28,29] but also ensures that any ligand can approach the porphyrin metal ion only from the strap-free side, and consequently can improves the selectivity of multi-component recognition.[30] In search for new generation of multi-component porphyrin receptors, we had introduced a cyanuric acid moiety to the strapped porphyrin skeleton. In this paper, we report the self-assembly of a new series of hydrogen bonded rosettes based on this strapped porphyrin-connected cyanuric acid and its recognition for tripyridyl and rosette guests.

2. Results and discussion

Compounds $\mathbf{H_2}$**1** and **Zn1** have been used for the self-assembly of the new porphyrin rosettes. The syntheses of $\mathbf{H_2}$**1** and **Zn1** are provided in Scheme 1. Thus, compound **2** was first treated with excessive dibromide **3** in hot DMF in the presence of potassium carbonate to produce **4** in 65% yield. Bromide **4** then reacted with phenol **5** under similar conditions to afford compound **6** in 72% yield. A Mitsunobu reaction of **6** with cyanuric acid in DMF gave precursor **7** in 36% yield. Compound **9** was then prepared in 90% yield from the reaction of **8** and iso-pentyl bromide under the conditions for preparation of **4**. Treatment of **9** with pyrrole in refluxing toluene under the catalysis of tosyl acid produced **10** in 76% yield. Dipyrrole **10** was then reacted with **7** in trifluoroacetic acid, followed by oxidation with

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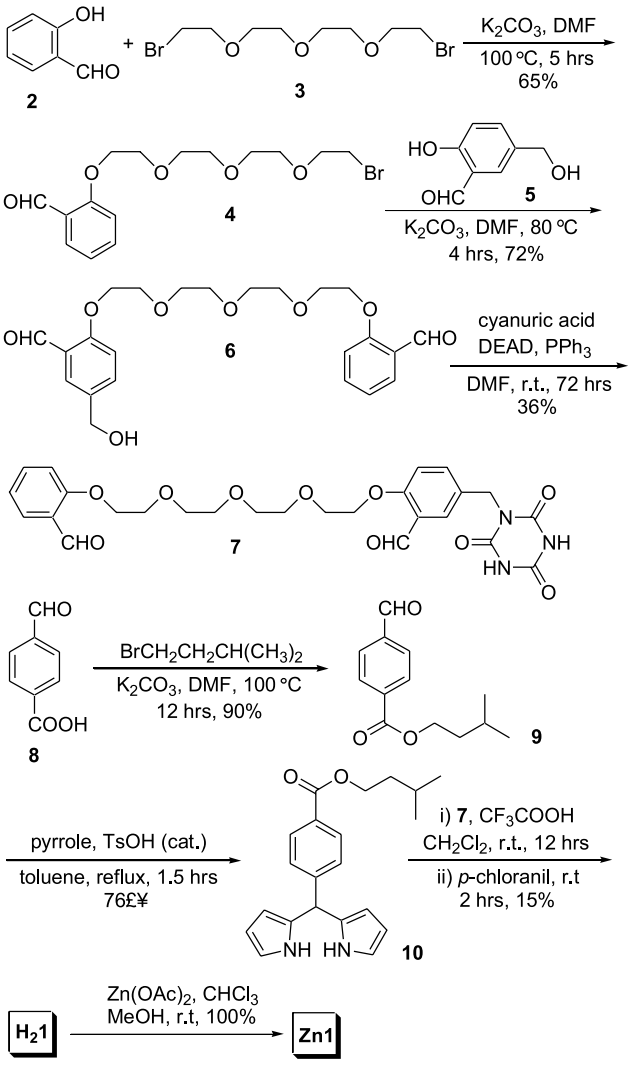
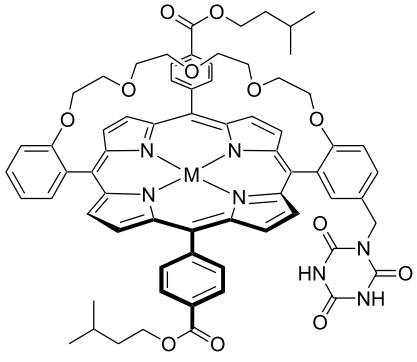


Scheme 1.

p-chloranil, to produce **1** in 15% yield. Treatment of porphyrin **1** with zinc acetate in mixture of chloroform and methanol afford **Zn1** quantitatively. Compounds $\mathbf{H_21}$ and **Zn1** are highly soluble in common organic solvents such as chloroform and dichloromethane. With porphyrins $\mathbf{H_21}$ and **Zn1** in hand, melamine derivatives **11** and **12** were prepared according to the reported method.[31]



Although both **11** and **12** are insoluble in chloroform, adding 1 equiv of **1** to the suspension of **11** or **12** in chloroform-*d* led to the melamines to dissolve completely. ^{1}H NMR spectrum displayed a singlet at $\delta=14.86$ and 14.79 ppm, respectively, for the H-1 of $\mathbf{H_21}$ (Fig. 1, the numbering of the signals are shown in Fig. 2), clearly showing that rosette structures $(\mathbf{H_21})_3\cdot\mathbf{11}_3$ and $(\mathbf{H_21})_3\cdot\mathbf{12}_3$ (Fig. 2), were generated.[31,32] It had been reported that melamines with substituents of smaller size, like **12**, and simple alkylated cyanuric acids could only generate infinite tapes but not cyclic rosette motif.[31] The formation of rosette $(\mathbf{H_21})_3\cdot\mathbf{12}_3$ might be ascribed to the introduction of the large porphyrin unit in $\mathbf{H_21}$, which prevents the formation of tape structures due to enlarged steric hindrance.

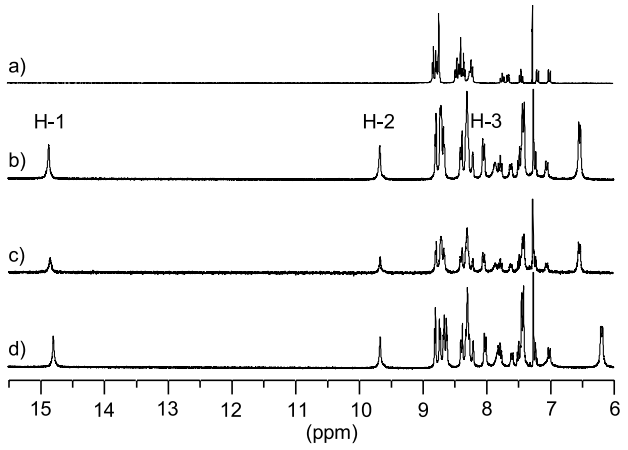


Figure 1. Partial ^{1}H NMR spectrum (400 MHz) in chloroform-*d* at 25 °C: (a) $\mathbf{H_21}$ (10 mM), (b) $\mathbf{H_21}+\mathbf{11}$ (1:1, 10 mM), (c) $\mathbf{H_21}+\mathbf{11}$ (1:1, 1 mM), and (d) $\mathbf{H_21}+\mathbf{12}$ (1:1, 10 mM).

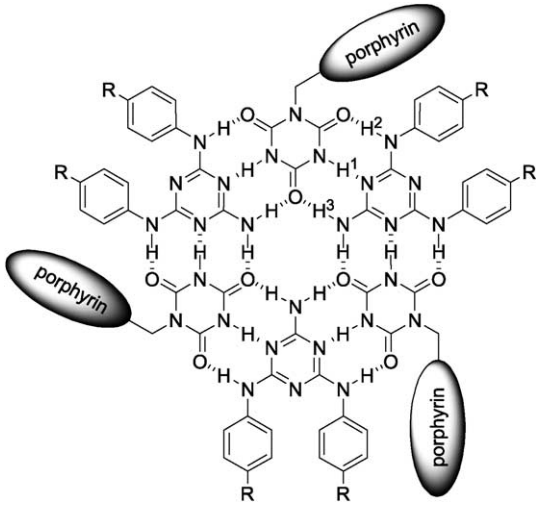


Figure 2. Porphyrin rosettes $(\mathbf{H_21})_3\cdot\mathbf{11}_3$ (R=*t*-Bu) and $(\mathbf{H_21})_3\cdot\mathbf{12}_3$ (R=*n*-Bu) formed in chloroform-*d*.

Upon reducing the concentration to 1.0 mM, the signals of the H-1 and H-2 of the 1:1 mixture of $\mathbf{H_21}$ with **11** or **12** in chloroform-*d* showed very small upfield shifts ($\leq$0.031 ppm) (Fig. 3), indicating that the rosette structures were stable within the concentration range studied. Previous study by Whitesides et al. had shown that the model rosette motif formed from **11** and alkylated cyanuric acid became unstable at the concentration of less than 4.0 mM in chloroform.[31] The present dilution experiments revealed that the new rosettes assembled from $\mathbf{H_21}$ and **11** or **12** are

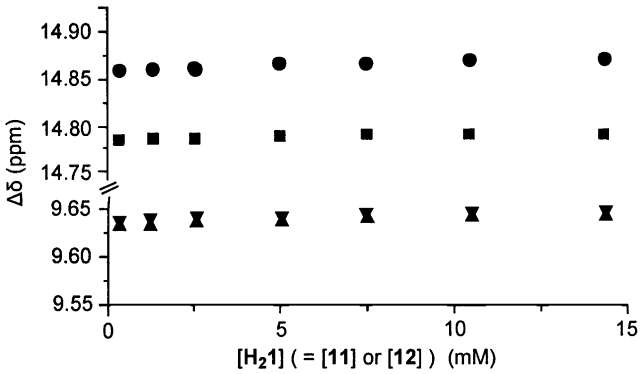
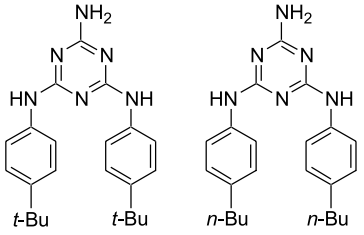


Figure 3. Concentration-dependent changes of the chemical shifts of H-1 (●) and H-2 (▼) of rosette $(\mathbf{H_2 1})_3 \cdot \mathbf{11}_3$ and H-1 (■) and H-2 (▲) of rosette $(\mathbf{H_2 1})_3 \cdot \mathbf{12}_3$ in chloroform-*d* at 25 °C.

obviously more stable than the model systems and indicated that the large porphyrin moiety in $\mathbf{H_2 1}$ facilitated the formation of the rosette motif. ^{1}H NMR experiments revealed that similar rosettes $(\mathbf{Zn1})_3 \cdot \mathbf{11}_3$ and $(\mathbf{Zn1})_3 \cdot \mathbf{12}_3$ were also formed when the identical amount of **Zn1** and **11** or **12** were mixed in chloroform-*d*. The H-1 signals of both rosettes moved upfield slightly (−0.040 and −0.058 ppm) compared with the corresponding Zn (II)-free rosettes. Lowering the concentration of the 1:1 mixtures in chloroform-*d* to 1.0 ppm did not cause the H-1 signal to shift pronouncedly (≤ -0.033 ppm). The results showed that these two rosettes are also very stable and there is no important coordination between the zinc ion of **Zn1** and the amino groups of **11** or **12**.



The complexation of rosette $(\mathbf{Zn1})_3 \cdot \mathbf{11}_3$ towards **13** was then investigated in chloroform-*d*. Compound **13** was prepared in 73% yield from **14** and cyanuric acid, as shown in Scheme 2. Addition of 1 equiv of **13** to the solution of rosette $(\mathbf{Zn1})_3 \cdot \mathbf{11}_3$ in chloroform-*d* caused the purplish red color of the rosette solution to change to dark purple. ^{1}H NMR spectrum revealed remarkable upfield shifts for all the signals of **13** (−6.73, −1.96, and ca. −1.3 ppm for the α-H, β-H, and CH_2, respectively) (Fig. 4). These results clearly indicated that the supramolecular complex $(\mathbf{Zn1}_3 \cdot \mathbf{11}_3) \cdot \mathbf{13}$ was formed.[33] The signals of **13** in the mixture solution had been assigned by changing the ratio of **13** and the rosette. The H-1 and H-2 signals of the rosette was also shifted upfield slightly upon complexation with **13**. Reducing the concentration of the 1:1 mixture of $(\mathbf{Zn1})_3 \cdot \mathbf{11}_3$ with **13** in chloroform-*d* from 10 to 0.8 mM did not cause notable change of the chemical shifts of the signals of **13**, indicating that no important dissociation occurred. Attempt to quantitatively study the binding stability of tri-component complex $[(\mathbf{Zn1})_3 \cdot \mathbf{11}_3] \cdot \mathbf{13}$ with the UV–vis titration method did not succeed since such titration needs the concentration of the porphyrin receptor to be on the scale of ca. 10^{-5}–10^{-6} M. At such low concentration, rosette $\mathbf{Zn1}_3 \cdot \mathbf{11}_3$ would dissociate partially and could not be treated as a single species. As expected, similar supramolecular complex $(\mathbf{Zn1}_3 \cdot \mathbf{12}_3) \cdot \mathbf{13}$ was also formed when the identical molar amount of rosette $(\mathbf{Zn1}_3 \cdot \mathbf{11}_3)$ and **13** was mixed in chloroform-*d*, which had also been supported by the ^{1}H NMR results.

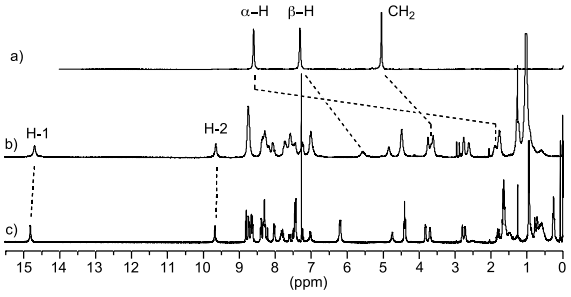
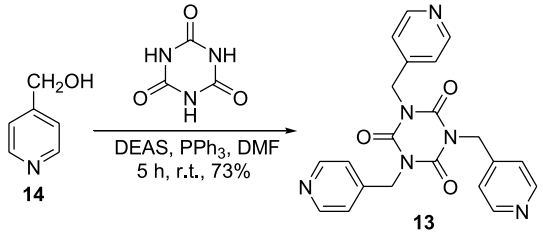
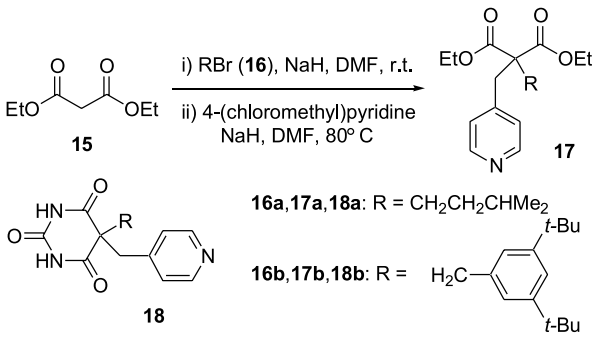


Figure 4. Partial ^{1}H NMR spectrum (400 MHz) of: (a) **13** (3.3 mM), (b) **13** (3.3 mM) + $(\mathbf{Zn1})_3 \cdot \mathbf{11}_3$ (3.3 mM) and (c) $(\mathbf{Zn1})_3 \cdot \mathbf{11}_3$ (3.3 mM) in chloroform-*d* at 25 °C.

The binding between different rosettes were also investigated. Initially, we tried to prepare mono-(4-pyridyl)methylated cyanuric acid as our precursor to assemble pyridine-bearing rosette guest. Unfortunately, the product was insoluble in chloroform even in the presence of **11** or **12**. We then prepared compounds **18a** and **18b** as our assembling building blocks, as shown in Scheme 3.



Scheme 2.



Scheme 3.

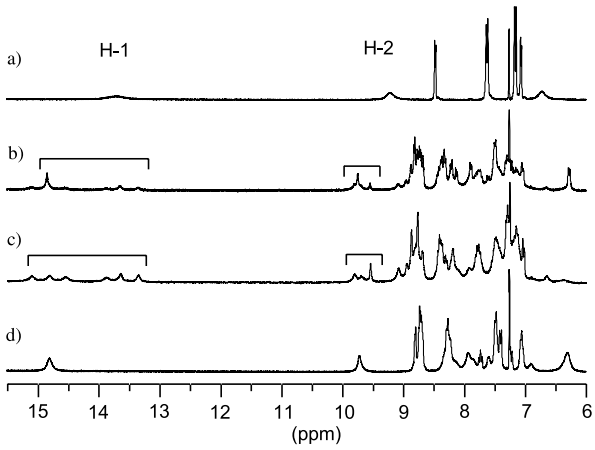
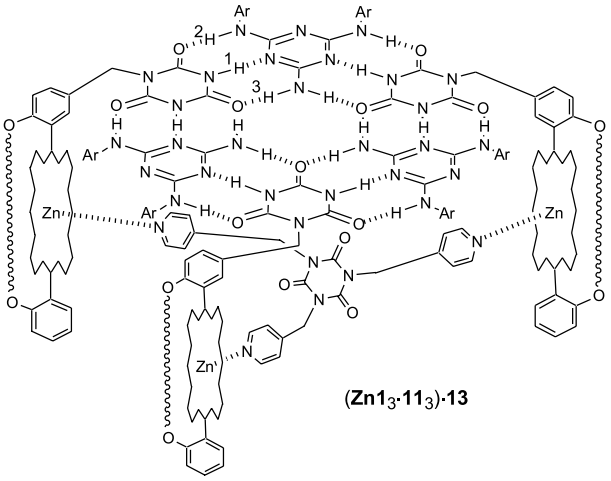
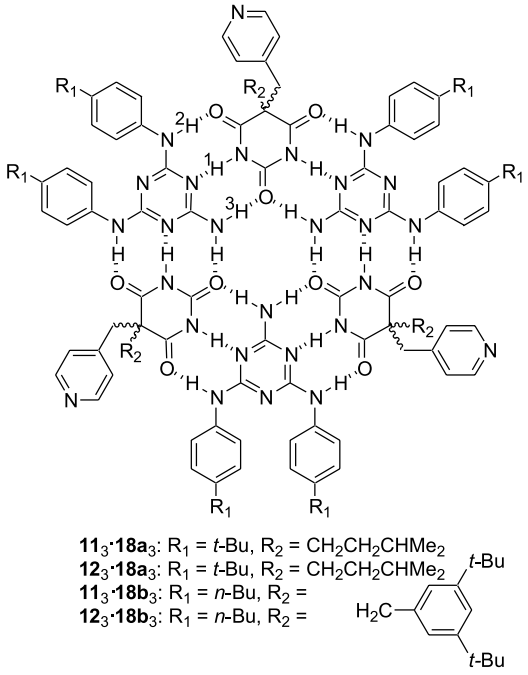


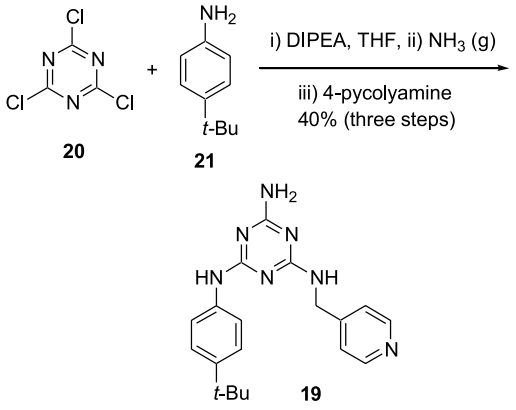
Figure 5. ^{1}H NMR spectrum (400 MHz) in chloroform-*d* at 25 °C. (a) $\mathbf{11}_3\cdot\mathbf{18a}_3$ (1:1, 3.4 mM), (b) $(\mathbf{Zn1}_3\cdot\mathbf{11}_3)$ (1.7 mM)+$\mathbf{11}_3\cdot\mathbf{18a}_3$ (1:1, 3.4 mM), (c) $(\mathbf{Zn1}_3\cdot\mathbf{11}_3)$ (3.4 mM)+$\mathbf{11}_3\cdot\mathbf{18a}_3$ (1:1, 3.4 mM), and (d) $(\mathbf{Zn1}_3\cdot\mathbf{11}_3)$ (3.4 mM).

^{1}H NMR spectrum in chloroform-*d* revealed that rosette $\mathbf{11}_3\cdot\mathbf{18a}_3$ was also formed when the identical molar amount of **11** and **18a** was mixed (Fig. 5a). In principle, there were two possible isomers depending on the relative orientation of **18a** in the rosette structure. The fact that the NH of **18a** displayed a broadened signal indicates that the two isomers exchange slowly on the ^{1}H NMR time scale. Similar results were also observed when mixing **11** with **18b** or **12** with **18a** or **18b** in chloroform-*d*, suggesting that isomeric rosettes were also formed in these mixtures. Mixing a solution of $\mathbf{11}_3\cdot\mathbf{18a}_3$ with a solution of $\mathbf{Zn1}_3\cdot\mathbf{11}_3$ caused the NH signals of both supramolecules to split into three sets of signals of comparable integrated strength in the ^{1}H NMR spectrum in chloroform-*d* (Fig. 5b and c). The prunosus color of the solution of rosette $(\mathbf{Zn1})_3\cdot\mathbf{11}_3$ also turned to dark purple after addition of $\mathbf{11}_3\cdot\mathbf{18a}_3$. These results clearly indicated that the two rosettes bound each other to afford the new supramolecular complex $[(\mathbf{Zn1})_3\cdot\mathbf{11}_3]\cdot[\mathbf{11}_3\cdot\mathbf{18a}_3]$. The splitting in the ^{1}H NMR spectrum can be attributed to different orientation of **18a** in the two-layer supramolecular complex. In principle, there were at most four isomeric complexes formed between the rosettes because the pyridine units of the three **18a** molecules could have four different patterns of arrangement in the supramolecular complex: all-up, up–up–down, up–down–down, and all-down. Unfortunately, at the present stage, we could establish the relative yields of the isomers. Similar result was also obtained when rosettes $\mathbf{11}_3\cdot\mathbf{18b}_3$ and $\mathbf{Zn1}_3\cdot\mathbf{11}_3$ was mixed, which afforded three sets of signals of the hydrogen bonded NHs. This observation indicated that the larger 3,5-di-*tert*-butylphenyl group did not function to improve the selectivity of the self-assembly of supramolecular complex $[\mathbf{11}_3\cdot\mathbf{18b}_3]\cdot[\mathbf{Zn1}_3\cdot\mathbf{11}_3]$. The fact that stable complex $[\mathbf{11}_3\cdot\mathbf{18b}_3]\cdot[\mathbf{Zn1}_3\cdot\mathbf{11}_3]$ could be formed between two giant rosette assemblies indicates that the complexation is a dynamic process and both assemblies can adapt their conformation to produce a supramolecular complex as stable as possible.

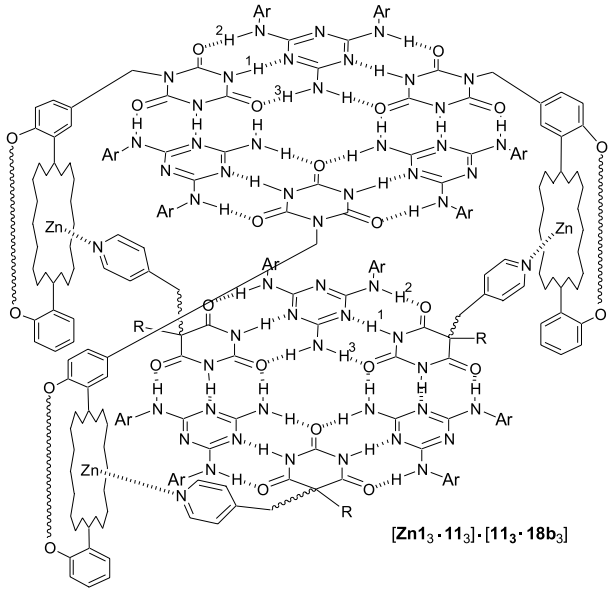




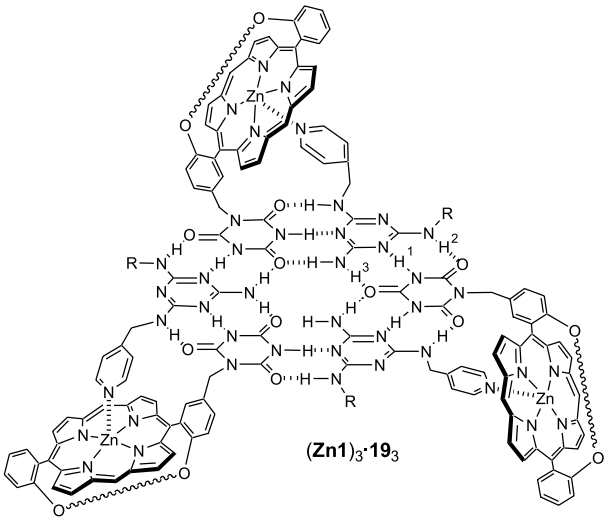
In principle, introducing pyridine unit to melamine might lead to its corresponding rosette with **Zn1** to be more stable as a result of additional intermolecular coordination. To detect this possibility, compound **19** was prepared from the reaction of compound **20** and **21**, followed by treatment of the intermediates with ammonia gas and 4-pycolyl amine, consecutively, as shown in Scheme 4. As expected, mixing the identical molar amount of **Zn1** and **19** in chloroform-*d* generated rosette $(\mathbf{Zn1})_3\cdot\mathbf{19}_3$, as indicated by the ^{1}H NMR spectrum (Fig. 6), which displayed the characteristic hydrogen bonded NH signals in the downfield area. Due to the unsymmetrical feature of the melamine skeleton, the ^{1}H NMR spectrum displayed multiple sets of signals for the hydrogen bonded NH of the rosette. This result indicated that the rosette, in which the three **19** molecules were arranged completely in one-direction pattern, was not generated exclusively, although such an arrangement should facilitate the formation of three intermolecular coordinations between the Zn (II) of **Zn1** and the pyridine of **19** and in principle the corresponding rosette should be more stable than other rosette isomers.[34,35]



Scheme 4.



Adding **19** to the solution of rosette $(\mathbf{Zn1})_3\cdot\mathbf{11}_3$ in chloroform-*d* forced **11** to release from the rosette, obviously due to the formation of more stable complexes between **Zn1** and **19**. The release of **11** as insoluble solid was completed when 1 equiv of **19** was added, as evidenced by the ^{1}H NMR spectrum (Fig. 6c), which was actually very close to that of the 1:1 mixture of **Zn1** and **19** (Fig. 6d) of the identical concentration. This observation showed that rosette $(\mathbf{Zn1})_3\cdot\mathbf{19}_3$ was remarkably more stable than $(\mathbf{Zn1})_3\cdot\mathbf{11}_3$ as a result of the additional inter-component coordination in the former assembly.



3. Conclusion

We have demonstrated that, by introducing additional strapped porphyrin unit to the cyanuric acid moiety, the hydrogen bonded melamine–cyanuric acid-motif-based rosette assemblies could be utilized as new generation of supramolecular receptors for binding relatively larger

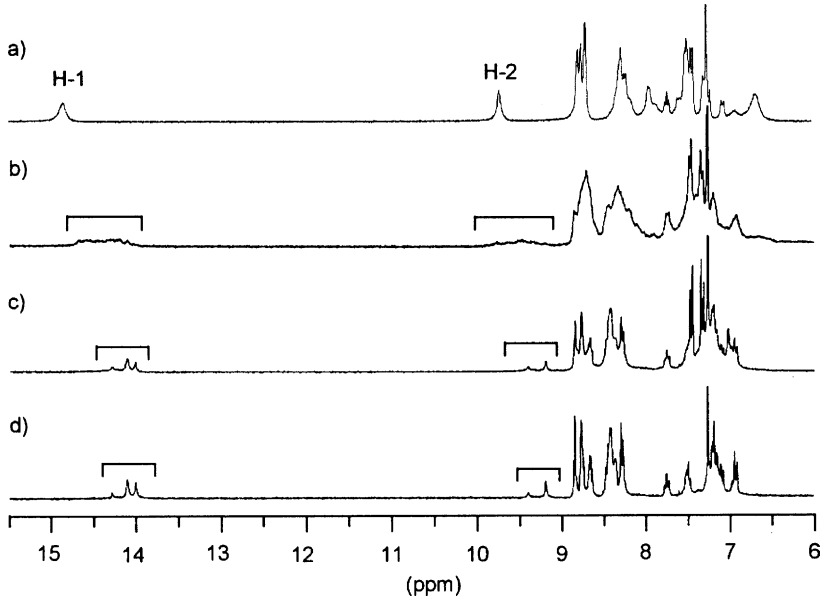


Figure 6. Partial ^{1}H NMR spectrum (400 MHz) in chloroform-*d* at 25 °C: (a) $\mathbf{Zn1}_3\cdot\mathbf{11}_3$ (1:1, 3.3 mM), (b) **Zn1** (10 mM)+**11** (10 mM)+**19** (5 mM), (c) **Zn1** (10 mM)+**11** (10 mM)+**19** (10 mM), and (d) $\mathbf{Zn1}_3\cdot\mathbf{19}_3$ (3.3 mM).

molecular or supramolecular guests. Although the binding selectivity needs to be improved further, the interaction between two discrete rosettes represents a new approach to the construction of new two-layer-typed supramolecular architectures. The next step will be introducing two cyanuric acid units to the opposite phenyl groups of the porphyrin moiety, which would produce new building block for assembling two-layer-typed porphyrin boxes for new molecular or supramolecular encapsulation.

4. Experimental

4.1. General methods

The ^{1}H NMR spectra were recorded on 400 or 300 MHz spectrometers in the indicated solvents. Chemical shifts are expressed in parts per million (δ) using residual solvent protons as internal standards. Chloroform (δ 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.

4.1.1. 2-(2-[2-[2-(2-Bromeothoxy)-ethoxy]-ethoxy]-ethoxy)-benzaldehyde (4). To a mixture of salicaldehyde **2** (8.50 mL, 80.0 mmol) and potassium carbonate (20.0 g, 0.15 mol) in DMF (100 mL) was added dibromide **3** (60.0 g, 0.19 mol). The mixture was stirred at 100 °C for 5 h and then concentrated under reduced pressure. The resulting residue was triturated with ether (500 mL) and the organic layer washed with diluted sodium hydroxide solution, water, brine, and dried over sodium sulfate. After evaporation of the solution in vacuo, the crude product was purified by column chromatography (petroleum ether/EtOAc, 2.5:1) to afford the title compound as colorless oil (18.8 g, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.47 (5, J=6.3 Hz, 2H), 3.68–3.76 (m, 8H), 3.81 (t, J=6.3 Hz, 2H), 3.93 (t, J=5.0 Hz, 2H), 4.26 (t, J=4.7 Hz, 2H), 6.89–7.06 (m, 2H), 7.54 (d, d, J_1=1.8 Hz, J_2=8.0 Hz, 1H), 7.84 (d, d, J_1=1.8 Hz, J_2=7.7 Hz, 1H), 10.49 (s, 1H). MS (EI): m/z 281 $[M-Br]^+$. Anal. Calcd for $C_{15}H_{21}Bro_5$: C, 49.88; Br, 22.12; H, 5.86. Found: C, 49.71; Br, 22.29; H, 5.86.

4.1.2. 2-[2-(2-[2-[2-(2-Formyl-phenoxy)-ethoxy]-ethoxy)-ethoxy]-5-hydroxymethyl-benzaldehyde (6). A mixture of **3** (7.60 g, 50.0 mmol), **4** (15.6 g, 43.4 mmol), potassium carbonate (13.0 g, 94.0 mmol) and tetrabutylammonium iodide (0.74 g, 2.00 mmol) in DMF (100 mL) was stirred at 80 °C for 4 h. The solvent was removed under reduced pressure and the resulting residue was triturated with dichloromethane (300 mL). The organic phase was washed with diluted sodium hydroxide solution, water, brine, and dried over sodium sulfate. After evaporation under reduced pressure, the residue was subjected to column chromatography (CH_2Cl_2/EtOAc, 80:1) to afford **6** as oily solid (13.6 g, 72). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.68–3.75 (m, 8H), 3.91–3.94 (m, 4H), 4.23–4.27 (m, 4H), 4.65 (s, 2H), 6.97–7.05 (m, 3H), 7.51–7.59 (m, 2H), 7.79–7.84 (m, 2H), 10.49 (s, 1H), 10.50 (s, 1H). MS (EI): m/z 432 $[M]^+$. Anal. Calcd for $C_{23}H_{28}O_8$: C, 63.88; H, 6.53. Found: C, 64.07; H, 6.57.

4.1.3. 2-[2-(2-{2-[2-(2-Formyl-phenoxy)-ethoxy]-ethoxy}-ethoxy)-ethoxy]-5-(2,4,6-trioxo-[1,3,5]triazinan-1-ylmethyl)-benzaldehyde (7). To a stirred solution of **6** (2.16 g, 5.00 mmol), triphenylphosphine (1.97 g, 7.50 mmol), and cyanuric acid (1.94 g, 15.0 mmol) in DMF (80 mL) was added dropwise a solution of DEAD (1.5 equiv, 40% in toluene) in DMF (10 mL) at room temperature. The solution was stirred for 60 h and the solvent was evaporated in vacuo. The resulting residue was washed with water thoroughly and dried to give a crude product, which was purified by column chromatography (CH_2Cl_2/EtOAc/MeOH, 3:3:0.3) to afford **7** as a white solid (1.02 g, 36%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67–3.73 (m, 8H), 3.89 (t, J=4.5 Hz, 4H), 4.20 (q, J=4.7 Hz, 4H), 4.80 (s, 2H), 6.85–6.99 (m, 3H), 7.49–7.55 (m, 2H), 7.77–7.83 (m, 2H), 9.69 (br, 2H), 10.38 (s, 1H), 10.46 (s, 1H). MS (EI): m/z 427 $[M-C_3H_4N_2O_3]^+$. Anal. Calcd for $C_{26}H_{29}N_3O_{10}$: C, 57.45; H, 5.38; N, 7.73. Found: C, 57.29; H, 5.21; N, 7.52.

4.1.4. 4-Formyl-benzoic acid 3-methyl-butyl ester (9). This compound was synthesized in 90% yield as colorless oil by using the procedure described for preparation of compound **4**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.99 (d, d, J_1=1.8 Hz, J_2=6.1 Hz, 6H), 1.66–1.86 (m, 3H), 4.40 (t, J=6.6 Hz, 2H), 7.96 (d, J=7.8 Hz, 2H), 8.20 (d, J=7.8 Hz, 2H), 10.11 (s, 1H). MS (EI): m/z 220 $[M]^+$. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.92; H, 7.51.

4.1.5. 4-[Bis-(1*H*-pyrrol-2-yl)-methyl]-benzoic acid 3-methyl-butyl ester (10). A solution of **9** (14.1 g, 64.0 mmol) and pyrrole (43.0 g, 0.64 mol) in toluene (250 mL) was degassed by a stream of nitrogen for 30 min. Then, hot saturated tosyl acid solution in toluene (1 mL) was added in one portion. The solution was heated under reflux for 1.5 h and then cooled to room temperature. The solution was washed with potassium carbonate solution (2 N, 50 mL), water (50 mL), brine (50 mL), and dried over potassium carbonate. After the solvent was evaporated under reduced pressure, the resulting oily residue was purified by column chromatography (chloroform) to afford compound **10** as a white solid (16.5 g, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (d, J=6.6 Hz, 6H), 1.64–1.83 (m, 3H), 4.34 (t, J=6.5 Hz, 3H), 5.52 (s, 1H), 5.89 (s, 2H), 6.16 (q, J=3.0 Hz, 2H), 6.71 (s, 2H), 7.28 (d, J=8.1 Hz, 2H), 7.97 (d, J=8.1 Hz, 4H). MS (EI): m/z 336 $[M]^+$. Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 74.76; H, 7.32; N, 8.08.

4.1.6. Porphyrin $H_2$1. Compounds **7** (2.17 g, 4.00 mmol) and **10** (2.69 g, 8.00 mmol) were dissolved in dichloromethane (850 mL). The solution was degassed with nitrogen for 30 min and then trifluoroacetic acid (1 mL) was added in one portion. The solution was stirred at room temperature for 12 h and a solution of 4-chloranil (2.00 g) in THF (50 mL) was added. The mixture was stirred at room temperature for another 2 h and then concentrated in vacuo to afford a solid residue, which was purified by column chromatography (CH_2Cl_2/AcOEt/MeOH, 15:10:1). The desired compound was obtained as a purple solid (0.68 g, 15%). Mp 182–182.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ

−2.79 (s, 2H), −0.47- −0.42 (m, 4H), 0.78–0.83 (m, 4H), 1.05 (d, J=6.3 Hz, 12H), 1.80 (q, J=6.7 Hz, 4H), 1.88–1.97 (m, 2H), 2.73–2.79 (m, 2H), 3.71 (t, J=3.5 Hz, 2H), 3.78 (t, J=3.5 Hz, 2H), 4.53 (t, J=6.7 Hz, 4H), 4.95 (s, 2H), 6.99 (d, J=8.0 Hz, 1H), 7.18 (d, J=7.5 Hz, 1H), 7.45 (t, J=7.5 Hz, 1H), 7.64 (d, d J_1=8.0 Hz, J_2=1.5 Hz, 1H), 7.73 (d, d, J_1=8.0 Hz, J_2=1.5 Hz, 1H), 8.19–8.47 (m, 12H), 8.73–8.93 (m, 8H). MS (ESI): m/z 1174 $[M+H_2O]^+$. Anal. Calcd for $C_{68}H_{67}N_7O_{12}\cdot H_2O$: C, 68.50; H, 5.84; N, 8.23. Found: C, 68.67; H, 5.84; N, 8.05.

4.1.7. Porphyrin Zn1. This compound was prepared quantitatively form $\mathbf{H_2 1}$ after stirring with zinc acetate (2 equiv) in chloroform and THF at room temperature for 12 h. Mp >200 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.47 to −0.42 (m, 4H), 0.78–0.83 (m, 4H), 1.05 (d, J=6.3 Hz, 12H), 1.80 (q, J=6.7 Hz, 4H), 1.88–1.97 (m, 2H), 2.73–2.79 (m, 2H), 3.71 (t, J=3.5 Hz, 2H), 3.78 (t, J=3.5 Hz, 2H), 4.53 (t, J=6.7 Hz, 4H), 4.95 (s, 2H), 6.99 (d, J=8.0 Hz, 1H), 7.18 (d, J=7.5 Hz, 1H), 7.44 (t, J=7.5 Hz, 1H), 7.64 (d, d, J_1=8.0 Hz, J_2=1.5 Hz, 1H), 7.73 (d, d, J_1=8.0 Hz, J_2=1.5 Hz, 1H), 8.19–8.47 (m, 12H), 8.73–8.93 (m, 8H). MS (ESI): m/z 1237 $[M+H]^+$. Anal. Calcd for $C_{68}H_{65}N_7O_{12}Zn$: C, 65.99;, 5.29; N, 7.92. Found: C, 65.69; H, 5.14; N, 7.81.

4.1.8. 1,3,5-Tris-pyridin-4-ylmethyl-[1,3,5]triazinane-2,4,6-trione (13). To a stirred solution of cyanuric acid (0.13 g, 1.00 mmol), triphenylphosphine (1.30 g, 5.00 mmol) and **14** (0.55 g, 5.00 mmol) in DMF was added DEAD (5.00 mmol, 40% in toluene) at room temperature. Stirring was continued at room temperature for another 5 h, and then the solvent was removed under reduced pressure. The resulting residue was triturated with chloroform (100 mL), and the organic phase was washed with water, brine, and dried over sodium sulfate. After evaporation of the solvent in vacuo, the residue was purified by column chromatography to afford **13** as a white solid (0.29 g, 73%). Mp 198–200 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.05 (s, 6H), 7.31 (s, 6H), 8.60 (s, 6H). MS (EI): m/z 402 $[M]^+$. Anal. Calcd for $C_{21}H_{18}N_6O_3\cdot 0.5H_2O$: C, 61.30; H, 4.66; N, 20.43. Found: C, 61.44; H, 4.51; N, 20.58.

4.1.9. 5-(3-Methyl-butyl)-5-pyridin-4-ylmethyl-pyrimidine-2,4,6-trione (18a). To a stirred solution of diethyl malonate (8.00 g. 50.0 mmol) in dry DMF (200 mL) was added sodium hydride (60%, 1.60 g, 40.0 mmol). After stirring for 30 min, iso-pentyl bromide (5.65 g, 40.0 mmol) was added in one portion and the reaction mixture was stirred at room temperature for 3 h. The mixture was concentrated in vacuo to afford a oily residue which was triturated with ether (200 mL). The organic phase was washed with diluted hydrochloric acid, water, brine, and dried with sodium sulfate. After evaporation of the solvent, the residue was purified by column chromatography ($CHCl_3$/MeOH, 20:1) to give the desired intermediate in ca. 80% yield. To a solution of this product (ca. 33 mmol) in dry DMF (100 mL) was added sodium hydride (60%, 2.80 g, 70.0 mmol) in portions. After stirring at room temperature for 30 min, 4-(chloromethyl)pyridine (4.17 g, 35.0 mmol) in DMF (50 mL) was added. The mixture was stirred at 80 °C for 3 h and then concentrated in vacuo. The residue was triturated with ether (300 mL) and the organic phase was washed with water, brine, and dried over sodium sulfate. After evaporation of the solvent and column chromatography (CH_2Cl_2/EtOAc, 15:1), the crude product **17a** was obtained as oil (3.71 g, 35%). To a solution of sodium ethoxide (3.40 g, 50.0 mmol) in ethanol (50 mL) was added urea (0.63 g, 10.5 mmol). Then, the above **17a** was added one portion. The reaction mixture was heated under reflux for 12 h and then concentrated in vacuo. The resulting residue was subjected to column chromatography (CH_2Cl_2/MeOH, 15:1) to give a crude product. After recrystallization from ethanol, pure **18a** was obtained as a white solid (1.03 g, 33%). Mp 244–246 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.83 (d, J=6.5 Hz, 6H), 0.96–1.03 (m, 2H), 1.44–1.48 (m, 1H), 1.94–1.20 (m, 2H), 3.14 (s, 2H), 6.70 (d, J=5.4 Hz, 2H), 8.47 (d, J=5.4 Hz, 2H), 11.50 (s, 1H). MS (EI): m/z 289 $[M]^+$. Anal. Calcd for $C_{15}H_{19}N_3O_3$: C, 62.27; H, 6.62; N, 14.52. Found: C, 62.20; H, 6.54; N, 14.56.

4.1.10. 5-(3,5-Di-*tert*-butyl-benzyl)-5-pyridin-4-ylmethyl-pyrimidine-2,4,6-trione (18b). This compound was prepared as a white solid following the procedures described for **18a**. Mp 266 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.22 (s, 9H), 3.27–3.33 (m, 4H), 6.86 (d, J=1.8 Hz, 2H), 7.03 (d, J=5.9 Hz, 2H), 7.23 (s, 1H), 8.47 (d, J=5.9 Hz, 2H). MS (EI): m/z 421 $[M]^+$. Anal. Calcd for $C_{25}H_{31}N_3O_3$: C, 71.23; H, 7.41; N, 9.97. Found: C, 71.35; H, 7.54; N, 9.65.

4.1.11. *N*-(4-Butyl-phenyl)-*N′*-pyridin-4-ylmethyl-[1,3,5]triazine-2,4,6-triamineA (19). A solution of 4-*tert*-butylaniline **21** (0.50 g, 3.30 mmol) in THF (5 mL) was added dropwise over 5 min to an ice-cooled solution of cyanuric chloride (0.62 g, 3.30 mmol) and DIPEA (2 mL) in THF (10 mL). The reaction mixture was stirred for 2 h, and then allowed to warm to room temperature. Ammonia gas was then bubbled to the solution for 3 h and then hexane (40 mL) was added. The precipitate resulted was filtered and washed with hexane to yield a crude product which was used for next step directly: A suspension of this precipitate, DIPEA (3 mL) and 4-picolyamine (2 mL) in chloroform and THF (10 mL, 1:1) was refluxed for 15 h and then concentrated in vacuo. The resulting residue was triturated with chloroform (50 mL) and the organic phase washed with water, brine, and dried over sodium sulfate. After removal of solvent, the residue was purified by column chromatography ($CHCl_2$/MeOH 20:1) to give **19** as a yellow solid (0.46 g, 40%). Mp 113–114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (s, 9H), 4.61 (d, J=6.0 Hz, 2H), 4.95 (s, 2H), 5.59 (br, 1H), 7.02 (s, 1H), 7.23–7.41 (br, m, 8H), 8.56 (d, J=6.0 Hz, 2H). MS (EI): m/z 349 $[M]^+$. Anal. Calcd for $C_{19}H_{23}N_7$: C, 65.31; H, 6.63; N, 28.06. Found: C, 65.19; H, 6.69; N, 28.14.

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