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Cu(II) Ion-Responsive Self-Assembly Based on a Water-Soluble Pillar[5]arene and a Rhodamine B-Containing Amphiphile in Aqueous Media

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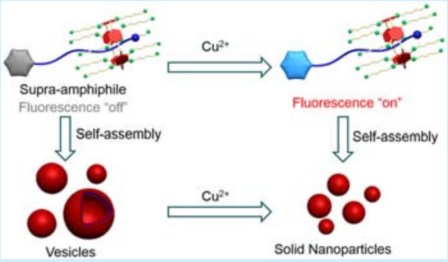
Supporting Information

ABSTRACT: Cu(II) ion-responsive self-assembly in aqueous media was achieved based on a water-soluble pillar[5]arene host and a rhodamine B-containing amphiphile guest. The host–guest complex acted as a supra-amphiphile and self-assembled into vesicles. After addition of Cu(II), vesicles turned into solid nanoparticles, accompanied by the color change of the solution from colorless to red and a fluorescence "on" phenomenon.



Stimuli-responsive self-assembly has attracted the attention of chemists from many subdisciplines due to the fact that it has applications in various fields such as sensors, controlled release, drug delivery, and diagnostic imaging.[1−7] Control of stimuli-responsive behavior displays a complementary step to increase the functionality and utility of these stimuli-responsive systems.[8−11] External stimuli including pH, temperature, ion, light, enzyme, and gas have been widely used to control the responsive self-assembly systems.[12−17] Among them, the metal ion stimulus is remarkably attractive due to its environmental and biological importance. Cu ions are particularly attractive because of copper's high natural abundance and low cost. Various convenient and practical methods have been explored for the preparation of Cu-based nanomaterials.[18] In addition, rhodamine B is a useful moiety for the design of "naked-eye" chemosensors for the Cu(II) ion because of the well-known spirolactam (fluorescence "off") to ring-opened amide (fluorescence "on") equilibrium of rhodamine derivatives.[19] Therefore, rhodamine B derivatives are very good building blocks for the construction of Cu(II) ion-responsive self-assembly systems.

Amphiphilic molecules, containing both hydrophilic and hydrophobic parts, have been widely used building blocks among the various components for self-assembly systems.[20−22] Compared to conventional amphiphiles, supra-amphiphiles are constructed by noncovalent interactions or dynamic covalent bonds, endowing them with recyclability, stimuli-responsiveness, and so on.[23,24] Host–guest interactions, a kind of important noncovalent interactions to design supra-amphiphiles, exhibit distinct properties in fabricating supra-amphiphiles by bringing macrocyclic hosts in the supramolecular systems.[25,26] Pillararenes,[27−29] a new class of macrocyclic hosts next to crown ethers,[30−35] cyclodextrins,[36,37] calixarenes,[38,39] and cucurbiturils,[40−42] can bind various guests, endowing them with the ability to fabricate various interesting supramolecular systems, for example, stimuli-responsive self-assemblies, liquid crystals, drug delivery systems, supramolecular polymers, transmembrane channels, sensors, adsorption, green catalysis, and so on.[43−59] However, copper ion-responsive self-assemblies in aqueous media based on pillararenes have rarely been reported. Herein, we fabricated a Cu(II) ion-responsive self-assembly based on a water-soluble pillar[5]arene and a rhodamine B-containing amphiphile. To the best of our knowledge, it is the first time that Cu(II)-responsive self-assembly based on a rhodamine B group using a pillararene host molecule is reported. First, a rhodamine B containing amphiphile guest (**G1**) with a triethylammonium bromide group for binding the pillar[5]arene cavity was designed and synthesized. This amphiphilic guest (**G1**) self-assembled into micelles in aqueous media. When copper(II) chloride was added into a solution of **G1**, micelles self-assembled from **G1** transformed into irregular aggregates due to the complexing between **G1** and Cu(II) ion. Meanwhile, the solution changed from colorless to red and a fluorescence "turn-on" phenomenon was observed. While an equal molar water-soluble pillar[5]arene host (**H**) was added into the solution of **G1**, these micelles turned into vesicles because of the formation of a supra-amphiphile **H**⊃**G1**. Moreover, after the addition of copper(II) chloride into the solution of **H**⊃**G1**, the vesicles were destroyed and transformed into solid nanoparticles, accompanied by the color change of the solution from colorless to red and a fluorescence "turn-on" phenomenon (Scheme 1).

First, ^{1}H NMR spectroscopy was used to study the host–guest complexation between **H** and **G1** by using **G** as the model guest to simplify the host–guest complexation studies. The ^{1}H NMR spectroscopy experiments of free **H**, free **G**, and

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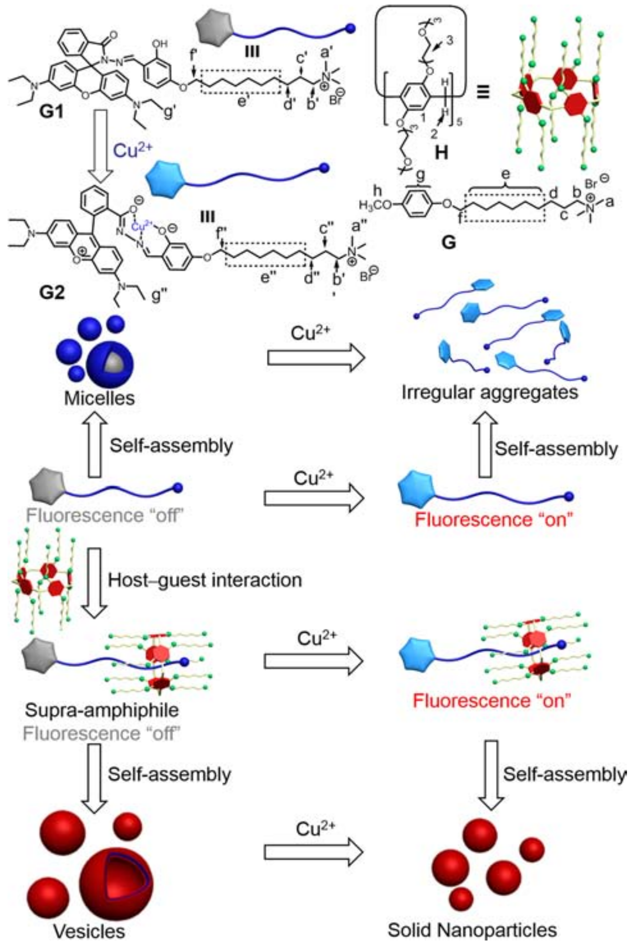
Scheme 1. Chemical Structures of H, G, G1, and G2 and Cartoon Representation of the Pillararene-Based Host−Guest Interaction and Cu(II) Ion-Responsive Self-Assembly and Morphology Transformation



an equimolarmixture of **H** and **G** were performed in a mixture of deuterated water and acetonitrile (v/v = 4:1). As shown in Figure 1, significant chemical shift changes of the signals for the protons on **G** occurred in the presence of equimolar **H** (Figure 1b) compared with free **G** (Figure 1a). The peaks related to H_a, H_b, H_d, and H_e shifted upfield and became broad. Meanwhile, the peak related to proton H_1 on **H** (Figure 1c) shifted downfield slightly. The reason for these phenomena is that protons H_a, H_b, H_d and H_e on **G** are shielded by the electron-rich cyclic structure of **H** when **G** threads into the cavity of **H** to form a threaded structure **H⊃G**. These results provided convincing evidence for the host−guest interactions between **H** and **G**.

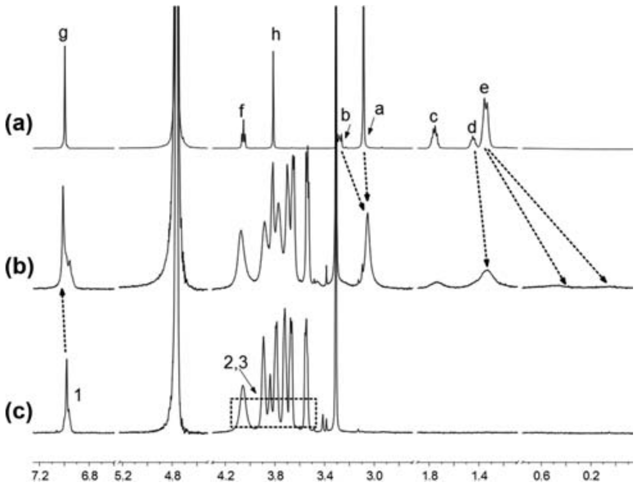


Figure 1. Partial ^{1}H NMR spectra (500 MHz, 4:1 D_2O/CD_3CN, 298 K): (a) **G** (2.50 mM); (b) **G** (2.50 mM) and **H** (2.50 mM); (c) **H** (2.50 mM).

Meanwhile, a 2D NOESY NMR experiment was performed to study the relative positions of the components in the complex **H⊃G** (Figure S4). NOE correlation signals were observed between protons H_a, H_b, H_d, and H_e of **G** and proton H_1 of **H** (Figure S4, A, B and C), between proton H_d of **G** and protons H_2 and H_3 of **H** (Figure S4, D), confirming the ^{1}H NMR results. Additionally, the isothermal titration calorimetry (ITC) experiments were used to determine the association constant (K_a) of this host−guest complex. The K_a value was estimated to be $(3.14 \pm 0.69) \times 10^4$ M^{-1} for **H⊃G** in the 1:1 complexation mode (Figure S5).

After the establishment of the **H⊃G** recognition motif, we explored whether it could be used to construct a Cu(II)-responsive system. By introducing the rhodamine B group into **G**, a rhodamine B-containing amphiphile **G1** was obtained which may complex with **H** to form a supra-amphiphile **H⊃G1**. First, ^{1}H NMR spectroscopy was used to confirm the host−guest complexation between **H** and **G1** and the existence of the complexation after addition of Cu(II). As shown in Figure S6, compared to free **G1** and **H** (Figure S6a and 6c), the peaks related to $H_{a'}$, $H_{b'}$, $H_{c'}$, $H_{d'}$, and $H_{e'}$ on **G1** shifted upfield and became broad after mixing equimolar **G1** and **H**. Meanwhile, the peak related to proton H_1 on **H** (Figure S6b) shifted downfield slightly, indicating the complexation between **G1** and **H**. In addition, after addition of 10.0 equiv of Cu(II) to the solution of **G1**, the peaks related to protons $H_{a''}$, $H_{b''}$, $H_{c''}$, $H_{d''}$, and $H_{e''}$ on **G2** and proton H_1 on **H** (Figure S6d) showed the same changes as the counterpart protons on complexed **G1** and **H**, proving the host−guest interaction between **H** and **G2**. Next, the UV−vis absorption spectroscopy experiments were carried out to confirm the Cu(II)-responsive property of **G1** and the complex **H⊃G1**. As shown in Figure 2a, the maximum absorption band of rhodamine B group in the mixture of water and acetonitrile was at ∼559 nm; upon addition of 10.0 equiv of Cu(II), the solution changed from colorless to red and the maximum absorption band increased remarkably. These phenomena indicated that the rhodamine B containing amphiphile **G1** has a beneficial Cu(II)-responsive property which was consistent with the previous report.[19] When equimolar **H** was added to the solutions of **G1** and **G1** + Cu(II), there was no obvious change regarding the maximum absorption band of **G1**, indicating that the host−guest complexation between **H** and **G1** had almost no effect on the UV−vis absorption property of **G1**. Meanwhile, the fluorescence emission spectroscopy experiments were also performed to confirm these results. As shown in Figure 2b, **G1** and **H⊃G1** exhibited a fluorescence emission peak at 577 nm, while, after the addition of 10.0 equiv of Cu(II) to the solutions, a remarkable enhancement of the fluorescence intensity and a red shift of the emission peak from 577 to 593 nm were observed,[19] confirming the Cu(II)-responsive property of **G1** and the complex **H⊃G1**.

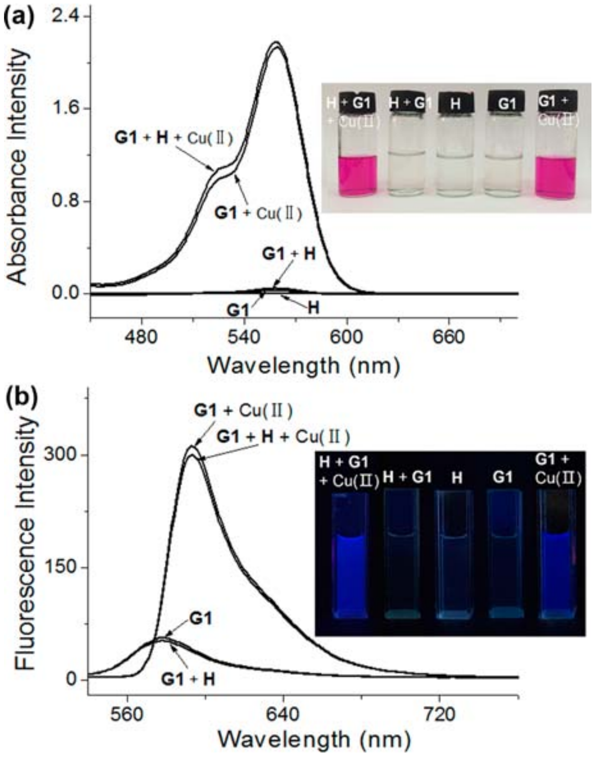


Figure 2. (a) UV−vis spectra of **H**, **G1**, **G1** + **H**, **G1** + Cu(II), and **G1**+ **H** + Cu(II). (b) Fluorescence emission spectra of **G1**, **G1** + Cu(II), **G1** + **H**, and **G1** + **H** + Cu(II). The excitation wavelength was 520 nm. Inset: (a) **H**, **G1**, **G1** + **H**, **G1** + Cu(II), and **G1**+ **H** + Cu(II); (b) **G1**, **H**, **G1** + Cu(II), **G1** + **H**, and **G1** + **H** + Cu(II) under UV light at 365 nm. The concentration of **G1** and **H** was 2.50×10^{-5} M in 4:1 (v/v) water/acetonitrile.

Considering the Cu(II)-responsive property of the amphiphile **G1** and the supra-amphiphile **H⊃G1**, we further explored whether it could be used to construct a Cu(II)-responsive self-assembly system. First, by using the concentration-dependent conductivity measurements (Figure S7), the critical aggregation concentrations were measured to be 5.06×10^{-5} M and 1.01×10^{-5} M for **G1** and **H⊃G1** in 4:1 (v/v) H_2O/CH_3CN, respectively. The self-assembly morphologies of **G1**, **H⊃G1** in 4:1 (v/v) H_2O/CH_3CN above their critical aggregation concentrations and their Cu(II)-induced morphology changes were then investigated via transmission electron microscopy (TEM) and atomic force microscopy (AFM). As shown in Figure 3a, **G1** formed micelles with an average diameter of ∼3 nm. Upon addition of Cu(II), micelles turned into irregular aggregates (Figure 3b). While upon addition of **H** to the solution of **G1**, vesicles with an average diameter of ∼300 nm were obtained (Figure 3c and 3d). AFM results confirmed the results (Figure 3e), and the wall thickness of the vesicles was measured to be about 2.46 nm (Figure S8), which was about the length of two **H⊃G1** complexes with antiparallel packing, suggesting that the vesicles had a bilayer wall. When Cu(II) was added to the solution of **H⊃G1** complex, vesicles changed into solid nanoparticles with an average diameter of ∼70 nm (Figure 3f). Dynamic light scattering (DLS) was utilized to monitor the size changes of the self-assemblies (Figure S9), which were in accordance with the TEM results.

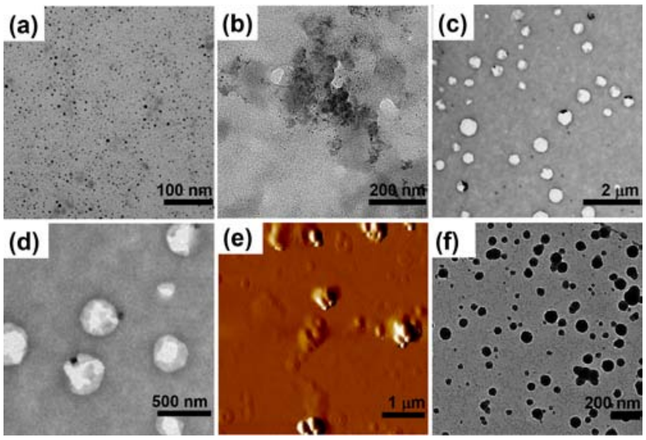


Figure 3. (a) TEM image of **G1** (2.50×10^{-4} M) aggregates in the mixture of 4:1 (v/v) water/acetonitrile; (b) TEM image of (a) after adding equimolar Cu(II); (b) TEM image of **H⊃G1** aggregates (2.50×10^{-4} M for both) in the mixture of 4:1 (v/v) water/acetonitrile; (d) enlarged image of (c); (e) AFM image of **H⊃G1** aggregates (2.50×10^{-4} M for both) in the mixture of 4:1 (v/v) water/acetonitrile; (f) TEM image of (c) after adding 10.0 equiv of Cu(II).

A possible mechanism is proposed to explain the morphological changes of the Cu(II)-responsive self-assemblies. Amphiphilic **G1** forms micelles in the aqueous media. Upon addition of Cu(II), the rhodamine B group turned into the ring-opened amide state with the change from the hydrophobic state to the hydrophilic state.[19] Therefore, the amphiphilicity of **G1** was destroyed, leading to the formation of the irregular aggregates.[60] While **H** was added to the solution of **G1**, **G1** threads into the hydrophobic cavity of **H** to form an inclusion complex **H⊃G1**, which acts as a supra-amphiphile, resulting in the formation of vesicles with lower curvature due to the steric hindrance.[44,61] After addition of Cu(II) to the solution, the rhodamine B group turns into the hydrophilic state, causing the change of the amphiphilicity of **H⊃G1**. The packing arrangement of the amphiphilic building blocks changes, resulting in the self-assembly morphology turning to solid nanoparticles.[24,62]

In conclusion, Cu(II) ion-responsive self-assembly in aqueous media was achieved based on a water-soluble pillar[5]arene **H** and a rhodamine B-containing amphiphile **G1**. Amphiphilic **G1** self-assembled into micelles in aqueous media. When copper(II) chloride was added to a solution of **G1**, **G1** complexed with the Cu(II) ion, micelles changed to irregular aggregates, and the solution changed from colorless to red. While **H** was added into the **G1** solution, the supra-amphiphile **H⊃G1** formed, and the micelles turned into vesicles. After copper(II) chloride was further added into the solution, vesicles turned into solid nanoparticles, accompanied by the color of the solution changing from colorless to red. This self-assembly system shows a Cu(II)-responsive property which can be detected by fluorescence emission spectroscopy and the naked eye, endowing them with potential applications in various fields such as sensors, controlled release, and drug delivery. Therefore, this work can enrich the fields of both pillararene chemistry and stimuli-responsive self-assembly systems.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03486.

Synthesis, characterizations, ^{1}H NMR data, 2D NOESY NMR data, ITC data, AFM result, DLS result, and other materials (PDF)

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Notes

The authors declare no competing financial interest.

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