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Cooperative Complexation of Amino Acid Derivatives to Platinum Acetylide-Based Bolaamphiphile

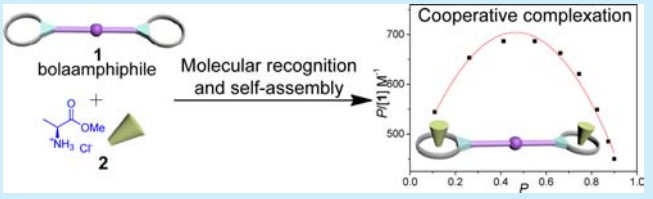
Yu-Jing Tian,[†,‡] En-Tai Shi,[‡] Yu-Kui Tian,[‡] Ri-Sheng Yao,*[,†] and Feng Wang*[,‡]

[†]School of Medical Engineering, Hefei University of Technology, Hefei, Anhui 230009, P. R. China

[‡]Key Laboratory of Soft Matter Chemistry, Department of Polymer Science and Engineering, University of Science and Technology of China, Hefei, Anhui 230026, P. R. China

Supporting Information

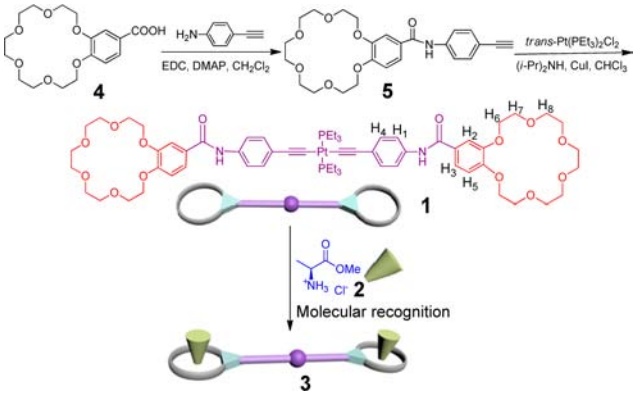
ABSTRACT: A platinum(II) acetylide-based bolaamphiphile equipped with two peripheral B18C6 moieties has been successfully prepared, which demonstrates cooperative recognition behavior toward L-alanine ester salt in chloroform. In a polar methanol/chloroform (3/1, v/v) medium, the amino acid additives influence the aggregation of the bolaamphiphile significantly, leading to the morphological transition from nanospherical to disordered structures. The adaptive properties of the current host–guest binary system will benefit the development of stimuli-responsive supramolecular materials.



Integration of biomolecules such as amino acids and peptides into π-conjugated chromophores represents an efficient strategy to realize biological–synthetic hybrid materials with tailored chemical and physical properties.[1] Much effort has been devoted to the covalent linkage of amino acid derivatives to the π-conjugated molecules.[2] In contrast, incorporation of these bioactive ligands to the π-conjugated assemblies via a molecular recognition process has been far less exploited. Such a noncovalent strategy could realize the fine-tuning of solubility as well as electrical and optical properties for the resulting supramolecular assemblies.[3] More importantly, it commonly involves complex recognition events, serving as a feasible platform to mimic biological systems which take advantage of multivalency and cooperativity principles to achieve enhanced binding efficiency.[4]

We endeavor to construct platinum(II)-containing π-conjugated supramolecular assemblies and examine their recognition properties toward amino acid additives. Due to the presence of d^8 transition metal ion Pt^{2+} with square planar geometry, platinum(II) acetylide complexes have exhibited interesting self-assembly properties.[5,6] For example, we have recently demonstrated that rod-like platinum(II) acetylide complexes show the propensity to undergo cooperative supramolecular polymerization in apolar methylcyclohexane solution.[5d] Herein, bolaamphiphilic monomer **1** is designed which bears two benzo-18-crown-6-ether (B18C6) moieties on both sides of the rod-like platinum(II) acetylide core (Scheme 1). Considering that the appending B18C6 units act as solvophilic groups and provide appreciable solubility, bolaamphiphile **1** is expected to assemble spontaneously in polar environments. Meanwhile, since B18C6 is a versatile receptor for a variety of ammonium cations,[7] the homoditopic monomer **1** could associate with amino acid derivatives such as L-alanine ester salt **2** to achieve host–guest paired structure **3** (Scheme 1). When combining the above two self-assembly processes together, noncovalent decoration of L-alanine ester salt **2** to the multivalent self-assembling nanostructures would be realized, which is advantageous for the development of supramolecular sensing and chiroptical materials.[8]

Scheme 1. Synthetic Route to the Platinum(II) Acetylide-Based Bolaamphiphile 1 and Schematic Representation for the Complexation of L-Alanine Ester Salt 2 with 1 To Afford the Host–Guest Paired Structure 3



The synthetic route toward the targeted monomer **1** is quite straightforward (Scheme 1). Reaction of B18C6 acid **4** with 4-ethynylaniline in the presence of EDC·HCl and DMAP yielded the amide **5**. Further treatment of **5** with *trans*-$[Pt(PEt_3)_2Cl_2]$ in the presence of diisopropylamine and copper(I) iodide afforded bolaamphiphile **1**, which was characterized by multinuclear NMR (^1H, ^{13}C, ^{31}P) and ESI-MS spectroscopies

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(Figures S4–S7). The ^{31}P NMR spectrum of **1** displays one signal at 7.22 ppm in *d*-chloroform (Figure S6), suggesting the equivalence of the two phosphorus atoms and validating the *trans* configuration for the two triethylphosphine units.

Since chloroform is a solvent that limits aggregation of chromophores, the maxima UV–Vis absorption band of **1** located at 354 nm in chloroform is assigned to the long-axis polarized π–π^* and Pt–π^* transitions from the molecularly dissolved platinum(II) acetylide unit (Figure 1a, black line).

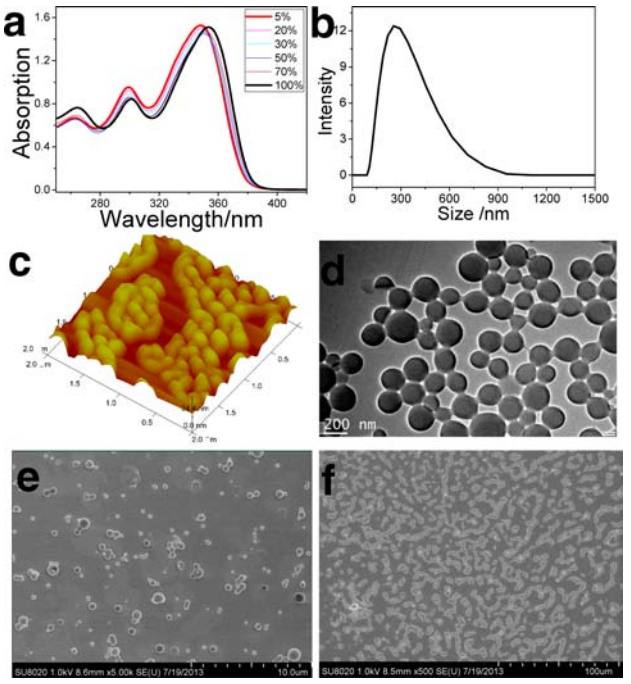

Figure 1. (a) Changes in absorption spectra of **1** in $CHCl_3$/MeOH solutions of different solvent compositions (from 100% $CHCl_3$ (black line) to 5% chloroform in methanol (red line)); (b) hydrodynamic size distributions of a 10^{-4} M solution of **1** in MeOH/$CHCl_3$ (3/1, v/v) measured by DLS at 25 °C; (c) spherical aggregates prepared by drop-casting a 10^{-4} M solution of **1** in MeOH/$CHCl_3$ (3/1, v/v) on mica substrate, as imaged by tapping mode AFM; (d) TEM images of **1** recorded on a copper grid; (e) FE-SEM images of **1** recorded on silicon wafer; (f) FE-SEM images of a 1:2 mixture of **1** and **2** recorded by drop-casting of the MeOH/$CHCl_3$ (3/1, v/v) solution on silicon wafer.

The evolution from the monomeric to self-assembled state of bolaamphiphile **1** is probed by varying the chloroform–methanol compositions, while keeping the concentration of **1** at 10^{-4} M. Specifically, increasing the amount of methanol in a molecularly dissolved solution of **1** in chloroform leads to a remarkable blue shift of the maxima absorption spectra (348 nm for **1** in methanol/chloroform (19/1, v/v), Figure 1a, red line), indicating the overlapping of platinum(II) acetylide chromophores to form H-type aggregates.

For a deeper understanding of the noncovalent forces driving the self-assembly process, ^{1}H NMR measurements were investigated for bolaamphiphile **1** in deuterated solvents of different polarities (*d*-chloroform and d_4-methanol/*d*-chloroform (3/1, v/v)) (Figures S8–S9). For both experiments, the aromatic protons shield slightly upfield at high monomer concentration, thus suggesting the involvement of weak aromatic π–π stacking interactions for the aggregation process. In *d*-chloroform, upon increasing the concentration of bolaamphiphile **1**, significant downfield shifts are observed for the amide protons, indicating the formation of intermolecular hydrogen bonding arrays between the amide groups (Figure S8). It should be noted that the resonance of the amide protons disappears in d_4-methanol/*d*-chloroform (3/1, v/v) (Figure S9), as a consequence of the H/D exchange with the solvent. In the meantime, no obvious changes occur for the ethyleneoxy protons on the B18C6 moiety, reflecting the negligible hydrogen bonding interaction between the ethyleneoxy oxygen atoms on the B18C6 unit and the amide groups. Therefore, such phenomena suggest that, in a polar medium, hydrogen bonding is still maintained between the intermolecular amide groups, which results in the tight packing of the solvophobic segments, thereby making significant contributions for the self-assembly process.[9]

Detailed microscopic measurements were then performed to investigate the morphology of the resulting assemblies derived from **1**. Atomic force microscopy (AFM) reveals the presence of spherical structures for a 10^{-4} M solution of **1** in methanol/chloroform (3/1, v/v) (Figure 1c), for which the horizontal distances of the individual spheres have an average diameter of 220 nm. The size is similar to the hydrodynamic diameter of the aggregates measured by dynamic light scattering (DLS) (248 nm, Figure 1b), indicating that the nanospheres do not spread in the AFM sample preparation. In contrast, based on DLS measurement, very small aggregates (hydrodynamic diameter ≈ 5 nm) are detected for a 10^{-4} M solution of **1** in chloroform (Figure S13), highlighting the effect of solvent polarity on the assembling size of the platinum acetylide-based oligomers. It should be noted that the resulting spherical structures in polar solvent tend to aggregate together on the surface, which is supported by transmission electron microscopy (TEM) (Figure 1d) and field emission scanning electron microscopy (FE-SEM) (Figure 1e) measurements. Such phenomena could be ascribed to the existence of molecule–surface interactions when depositing the aggregates on the solid support.[10]

Next, host–guest paired structure **3** resulting from the association between bolaamphiphile **1** and L-alanine methyl ester salt **2** was examined in chloroform, which remains the monomeric state for the platinum(II) acetylide chromophore. The spectrum of a 1:2 mixture of **1** and **2** displays only one set of peaks (Figure 2), suggesting fast-exchange complexation between B18C6 and ammonium cations on the ^{1}H NMR time scale. After complexation, a significant downfield shift is observed for the amide protons NH on **1** from 7.69 to 9.42 ppm. Moreover, peaks corresponding to H_1, H_3, H_5, and H_6 of **1** move downfield, while CH and CH_3 protons of **2** exhibit upfield shifts due to the shielding effect of the electron-rich B18C6 macrocyclic ring. In addition, protons H_6 of **1** are split into two signals locating at 4.48 and 4.22 ppm, respectively, attributing to the different chemical environments. The apparent proton shifting and splitting phenomena illustrate that the NH_3^+ recognition site forms an edge-to-face orientation with B18C6 cavities.[7c]

Further experiments were carried out to determine the complexation stoichiometry between **1** and **2**. Electrospray ionization mass spectrometry characterization (ESI-MS) was performed for a mixture solution of **1** and **2** under mild conditions, which displays two intense peaks locating at m/z 722.7 (100%) and 774.2 (76%), corresponding to $[\mathbf{1}\cdot\mathbf{2} - \mathrm{Cl} - \mathrm{H}]^{2+}$ and $[\mathbf{1}\cdot\mathbf{2}_2 - 2\mathrm{Cl}]^{2+}$, respectively (Figure S10). Proton NMR titration experiments were also performed, for which the

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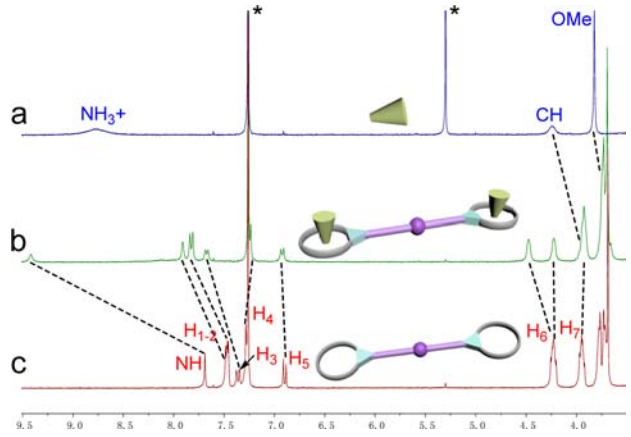


Figure 2. (a) Partial ^{1}H NMR spectra (300 MHz, *d*-chloroform, 25 °C): (a) 4.00 mM **2**; (b) a 1:2 mixture of **1** and **2** ([**1**] = 2 mM, [**2**] = 4 mM); (c) 2.00 mM **1**. Signals affiliated with solvents are denoted by star symbols.

initial concentration of **1** was kept constant at 2.00 mM while the concentration of **2** was systematically varied (Figure S11). Based on the molar ratio plot, the complexation stoichiometry between **1** and **2** is determined to be 1:2 at room temperature (Figure 3a).

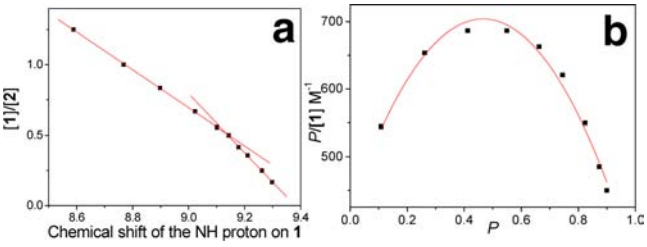
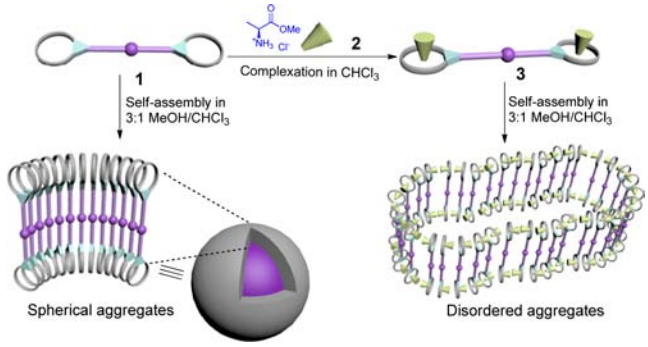


Figure 3. (a) Mole ratio plot for **1** and **2**; (b) Scatchard plot for the complexation between **1** and **2**. *P* = fraction of L-alanine ester salt **2** units complexed. The titration experiments were performed in *d*-chloroform at 25 °C.

The Δ_0 value of amide protons NH on **1**, representing the chemical shift difference between the uncomplexed and fully complexed species, was determined to be 1.58 ppm (Figure S12). The extent of complexation, *p*, of the B18C6 unit can be subsequently calculated from $p = \Delta/\Delta_0$ (Δ: chemical shift difference for NH between the uncomplexed and partially complexed species). The Scatchard plot (Figure 3b) is nonlinear and exhibits a maximum value, indicating that the two B18C6 units of **1** associate with **2** in a cooperative manner. From the slope and the intercept of the Scatchard plot, K_1 was estimated to be 382 M^{-1} and K_2 was determined to be 549 M^{-1}. The cooperative complexation between **1** and **2** is confirmed by the K_2/K_1 ratio (1.4), which is higher than the value of 0.25 expected for statistical complexation.[11] The arising cooperative complexation could be mainly attributed to the electrostatic repulsion effect.[12] Briefly, the 1:1 complex **1**·**2** leads to the redistribution of the electron density along the π-conjugated platinum(II) acetylide rod, which facilitates complexation for the second L-alanine ester salt to form the **1**·$\mathbf{2}_2$ structure. Meanwhile, allosteric changes could also be involved after formation of the 1:1 complex **1**·**2**.

Finally, we turned to investigate the complexation behavior between **1** and **2** in polar solvent. Although the noncovalent B18C6/NH_3^+ recognition motif exhibits weaker binding affinity in methanol/chloroform (3/1, v/v) than that in pure chloroform (manifested by the slight upfield shifts for protons H_{1-5} in ^{1}H NMR spectra, Figure S14), the amino acid additive exerts a significant influence on the morphology of the resulting supramolecular assemblies. Specifically, upon adding 2 equiv of **2** to **1** in methanol/chloroform (3/1, v/v), FE-SEM reveals the transition from the original spherical structures (Figure 1e) to disordered and coagulated aggregates (Figure 1f). We speculated that, to form the desired edge-to-face host–guest complexes between B18C6 and NH_3^+ units, more steric hindrance and electrostatic repulsion could be imparted to the periphery of bolaamphiphile **1** (Scheme 2). As a result, the

Scheme 2. Schematic Representation for the Morphological Transition of Bolaamphiphile 1 in Response to L-Alanine Ester Salt Additives 2



original particle's radius of curvature increases to accommodate additional strain, resulting in the coacervate of the nanospheres to form disordered aggregates.[13]

In summary, we have demonstrated that platinum(II) acetylide bolaamphiphile **1**, equipped with two solvophilic B18C6 moieties on the periphery, exhibits a strong tendency to form spherical aggregates in a polar methanol/chloroform (3/1, v/v) solution. High-affinity host–guest molecular recognition leads to the cooperative complexation behaviors between L-alanine ester salt **2** and the homoditopic platinum(II) acetylide bolaamphiphile **1**. Notably, upon addition of **2** to **1**, the disappearance of nanospheres derived from bolaamphiphile **1** could be visualized, accompanied by the formation of disordered coagulated assemblies. Therefore, the current study provides an example for morphological transition in response to amino acid additives, which serves as a potential candidate for the development of intelligent materials for controlled release, biosensing, and optical resolution.

■ ASSOCIATED CONTENT

Supporting Information

Synthetic route to the bolaamphiphile **1**, characterizations, ^{1}H NMR titration between **1** and **2**, and the corresponding Benesi–Hildebrand plot. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: Rishengyao@163.com.
*E-mail: drfwang@ustc.edu.cn.

Notes

The authors declare no competing financial interest.

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