ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2018, **54**, 13821

Received 14th October 2018,
Accepted 13th November 2018

DOI: 10.1039/c8cc08226j

rsc.li/chemcomm

A dual-responsive hyperbranched supramolecular polymer constructed by cooperative host–guest recognition and hydrogen-bond interactions†

Yu-Qin Jiang, Kai Wu, Qian Zhang, * Ke-Qing Li, Yan-Yan Li, Peng-Yang Xin, Wei-Wei Zhang and Hai-Ming Guo*

A homotritopic pillar[5]arene (H_3) containing adenine units was synthesized and employed to interact with a uracil derivative (6-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)hexanenitrile, G) to form a hyperbranched supramolecular polymer. The hyperbranched supramolecular polymer showed a dual stimulus response both to heat and acid/base. The cooperative host–guest binding and hydrogen-bond interactions play a key role in the supramolecular polymerization.

Supramolecular polymers,[1] the combination of supramolecular chemistry and polymer science, have aroused considerable research interest and have shown a broad range of potential applications in many fields.[2] Various non-covalent interactions, such as host–guest binding,[3,4] multiple hydrogen bonds,[5] π-stacking interactions,[6] and metal–ligand coordination,[4,7] have been used for the construction of supramolecular polymers. Because of the reversibility and adjustability of these weak interactions, supramolecular polymers show special functions such as degradability, self-healing properties and stimuli-responsiveness.[8]

Pillararenes (PAs), which are made up of (substituted) hydroquinone units linked by methylene bridges, possess rigid and π-rich cavities and could bind guests to construct various novel supramolecular systems. Among them, supramolecular polymers based on pillararenes are a popular research topic and many scientists have conducted a variety of studies in this field.[3,4,9] To the best of our knowledge, all pillararene-based supramolecular polymers have been constructed through single or orthogonal non-covalent interactions[1g,3,4,9] but cooperative supramolecular polymerization based on pillararenes has not been reported. Cooperative non-covalent interactions are very important in biosystems[10] and functional supramolecular systems.[11,12]

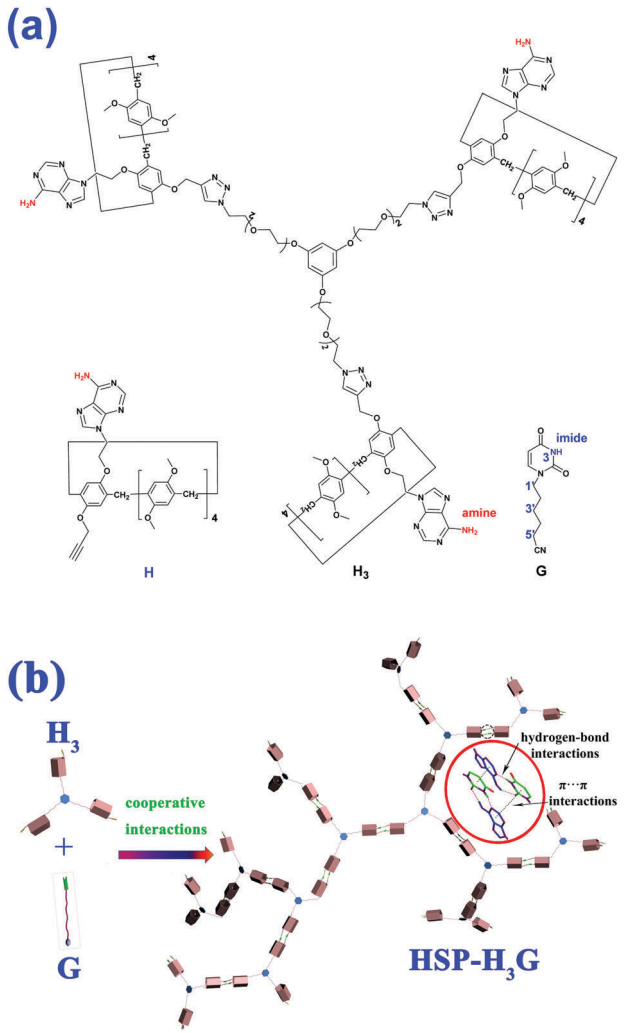
Henan Key Laboratory of Organic Functional Molecule and Drug Innovation, Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang, Henan 453007, China. E-mail: zhangqian1980@163.com, guohm518@hotmail.com; Tel: +86 373 3329276

† Electronic supplementary information (ESI) available: Experimental details, ^{1}H NMR, ^{13}C NMR and DOSY analysis. See DOI: 10.1039/c8cc08226j

Nucleobases are important supramolecular motifs because of their famous base-pair interactions including hydrogen bondings, π–π stacking and the hydrophobic effect.[13] Several supramolecular polymers have been constructed through base-pair interactions and have shown excellent stimulus responsiveness or efficient drug delivery ability.[14] Furthermore, nitrile guests have been excellent motifs for the development of supramolecular systems based on pillar[5]arenes.[15] We have reported a four-unit [c2] daisy chain constructed using an adenine monofunctionalized pillar[5]arene and a nitrile guest **G** through cooperative host–guest binding and hydrogen-bond interactions.[16] Here, we report the formation of a hyperbranched supramolecular polymer based on a homotritopic pillar[5]arene $\mathbf{H_3}$ constructed by cooperative host–guest binding and hydrogen-bond interactions (Scheme 1). To the best of our knowledge, this is the first report of pillararene-based supramolecular polymerization through cooperative non-covalent interactions.

$\mathbf{H_3}$, which is composed of three adenine mono-functionalized pillar[5]arene (**H**) groups, was synthesized (Scheme S1, ESI†) and its structure was characterized by ^{1}H NMR, ^{13}C NMR and MALDI-TOF MS (see the ESI†). Guest **G**, which contains both a uracil group and a nitrile binding site, was also synthesized and carefully characterized.

The binding stoichiometry of **H** and **G** in $CDCl_3$ was first determined to be 1 : 1 (Fig. S19, ESI†). Then, the host–guest complexation was investigated by ^{1}H NMR spectroscopy (Fig. 1). As shown in Fig. 1, the addition of **H** resulted in a significant upfield shift and broadening of the methylene protons ($H_{1'-5'}$) on the guest, suggesting that **G** entered into the cavity of **H** to form [2]pseudorotaxane as a result of a slow exchange process on the NMR spectroscopy time scale.[16,17] According to the reports by Li and co-workers,[18] dipole–dipole, C–H···π and C–H···O interactions usually exist between pillar[5]arenes and nitrile guests. Therefore, similar interactions between **H** and **G** were probably present. A DFT study showed that π···π interactions between A–U base pairs were present in every [2]pseudorotaxane.[19] Further investigation showed that the signal of imide N–H (3-position) shifted downfield and split into a doublet



Scheme 1 (a) Chemical structures of **H**, $\mathbf{H_3}$ and **G**. (b) The illustration of the construction of hyperbranched supramolecular polymer **HSP-$\mathbf{H_3}$G** from $\mathbf{H_3}$ and **G** through cooperative host–guest recognition and hydrogen-bond interactions.

with the addition of **H**, indicating that hydrogen-bond interactions formed between the A–U base pairs of the neighboring [2]pseudorotaxanes in a rapid association–dissociation process on the NMR time scale. Such hydrogen-bond interactions can make two adjacent [2]pseudorotaxanes dimerize together.[16] The association constant between **H** and **G** was determined to be as high as $(7.2 \pm 0.2) \times 10^4$ M^{-1} in $CDCl_3$. The high binding ability resulted from the cooperative hydrogen-bond interactions and host–guest binding, which involved dipole–dipole, C–H···π, C–H···O and π···π interactions.

Then, the aggregation behavior of $\mathbf{H_3}$ and **G** to form hyperbranched supramolecular polymer **HSP-$\mathbf{H_3}$G** was investigated by ^{1}H NMR spectroscopy. In $CDCl_3$, three equivalents of **G** were mixed with one equivalent of $\mathbf{H_3}$ to form some pseudorotaxanes. When the concentration of $\mathbf{H_3}$ was 3.3 mM (Fig. 2c), proton signals $H_{5'}^{uc}$ for uncomplexed **G** could be observed. When the concentration of $\mathbf{H_3}$ increased from 3.3 mM to 20.0 mM (Fig. 2d–g), the NMR peak of $H_{5'}^{uc}$ disappeared. At the same time, the signals of the imide N–H on **G** (3-position) shifted downfield from 11.39/10.20 ppm to 12.37/11.67 ppm. The chemical shift of the amide N–H on $\mathbf{H_3}$ also shifted from 1.77 to 2.77/1.65 ppm, accompanied with the broadening of the peaks. These significant shifts and broadening indicated the formation of hydrogen-bond interactions and the formation of a hyperbranched supramolecular polymer. According to the well-defined method of Gibson and Li,[20] the maximum possible polymerization degree (n_{max}) was calculated (Table S1, ESI†). With the increase of the concentrations of $\mathbf{H_3}$ and **G**, the calculated sizes of the aggregate increased to large values.

The formation of supramolecular polymers is often accompanied by a sharp decrease of the diffusion coefficient. Therefore, two dimensional diffusion-ordered NMR spectroscopy (DOSY) experiments were performed to study the aggregation of $\mathbf{H_3}$ and **G**. As shown in Fig. S21–S27 (ESI†) and Fig. 3, as the concentrations of $\mathbf{H_3}$ increased from 1.7 mM to 20.0 mM (the concentrations of the P5A cavity increased from 5.1 mM to 60.0 mM), the value of the weight

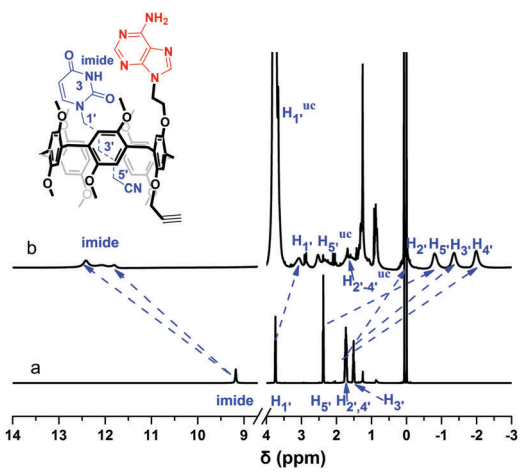


Fig. 1 Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of **G** (a) at a concentration of 10.0 mM upon addition of equimolar **H** (b). uc: peaks of uncomplexed guests.

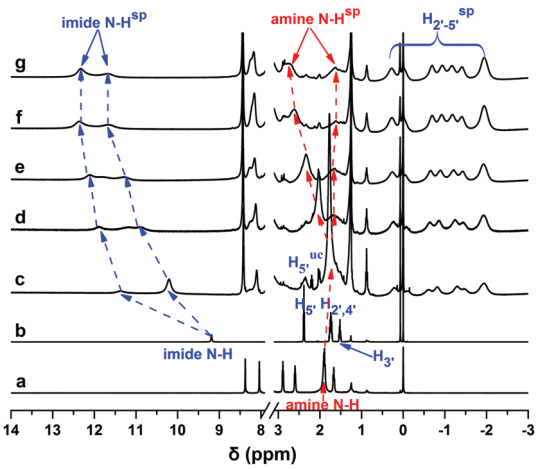


Fig. 2 Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of $\mathbf{H_3}$ ((a), 3.3 mM), **G** ((b), 3.3 mM) and $\mathbf{H_3}$ upon addition of three equivalents of **G** at various concentrations: (c) 3.3 mM, (d) 8.3 mM, (e) 11.6 mM, (f) 16.7 mM, and (g) 20.0 mM. uc: peaks of uncomplexed guests; sp: peaks of the supramolecular polymer (for proton designations, see Scheme 1a).

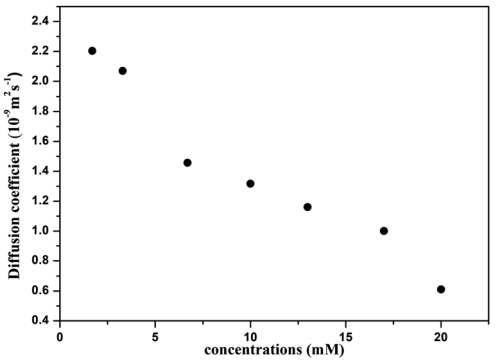


Fig. 3 2D DOSY (600 MHz, 298 K) plot of solutions of $\mathbf{H_3}$ with three equivalents of **G** in $CDCl_3$.

average diffusion coefficients (D) decreased from 2.2×10^{-9} to 6.1×10^{-10} m^2 s^{-1} ($D_{1.7}/D_{20}$ = 3.6), revealing the concentration dependence of the supramolecular polymerization of the $\mathbf{H_3}$ and **G** mixture.

The concentration-dependent viscosity changes provided further convincing evidence of the self-assembly behaviors of the components. As shown in Fig. 4, the supramolecular polymer **HSP-H$_3$G** that aggregated from $\mathbf{H_3}$ and **G** showed a viscosity transition that was described by a change in the slope in the double logarithmic plots of the specific viscosity *versus* concentration. In the low concentration range, the slope of the curve was 0.7, which suggested a linear relationship between the specific viscosity and the concentration, which is one of the characteristics of non-interacting assemblies of a constant size and this demonstrated the predominance of the oligomers in dilute solutions. When the concentration increased above 7.8 mM, a slope of 1.6 was observed, indicating a transition from the oligomer to a hyperbranched supramolecular polymer with increasing size.

Interestingly, the reversible aggregation and disaggregation of **HSP-H$_3$** could be realized by stimulation with aspirin and heat, respectively. Upon addition of 60.0 mM aspirin to the 20.0 mM solution of **HSP-H$_3$G**, the value of D increased from 6.1×10^{-10} (Fig. S27, ESI†) to 1.2×10^{-9} m^2 s^{-1} (Fig. S28, ESI†). This was because aspirin destroyed the hydrogen-bond interactions between the base pairs. Afterwards, upon addition of 63.0 mM **Et$_3$N** to the above solution, the value of D decreased to

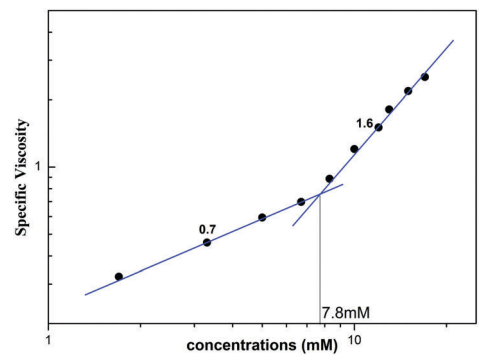


Fig. 4 Specific viscosity of **HSP-H$_3$G** (298 K) in a $CHCl_3$ solution *versus* the concentration of $\mathbf{H_3}$.

6.0×10^{-10} m^2 s^{-1} (Fig. S29, ESI†), indicating that the aggregate reassembled through the removal of acid by the addition of excess **Et$_3$N**. In addition, upon increasing the temperature of the 20.0 mM **HSP-H$_3$G** solution to 323 K, the value of D increased obviously from 6.1×10^{-10} to 1.0×10^{-8} m^2 s^{-1} (Fig. S30, ESI†), indicating the disaggregation of the supramolecular polymers. This could be explained by the fact that heating could result in the decomplexation of the host–guest complexes and the dissociation of the hydrogen-bond interactions, which results in the destruction of the supramolecular polymer network. After the mixed solution was cooled to room temperature, the value of D decreased to 5.8×10^{-10} m^2 s^{-1} (Fig. S31, ESI†), suggesting the reassembly of the supramolecular polymers.

As shown in Fig. S33 (ESI†), as the concentrations of the mixed solution of $\mathbf{H_3}$ and three equivalents of **G** increased from 1.7 mM to 17.0 mM (the concentration of $\mathbf{H_3}$), the specific viscosity increased dramatically from 0.3 to 2.5 mPa S (red dots). As the concentrations of $\mathbf{H_3}$ increased from 1.7 mM to 17.0 mM, the specific viscosity increased from 8.6×10^{-3} to 2.4×10^{-1} mPa S (blue dots in Fig. S33, ESI†). The completely different phenomena of the viscosity change showed that $\mathbf{H_3}$ did not aggregate to form a supramolecular polymer.[21] DOSY experiments also supported such a conclusion. The value of D of 20.0 mM $\mathbf{H_3}$ was 1.2×10^{-9} m^2 s^{-1} (Fig. S32, ESI†), which was significantly bigger than that of 20.0 mM **HSP-H$_3$G** ($D = 6.1 \times 10^{-10}$ m^2 s^{-1}, Fig. S27, ESI†). The possible reason was that only hydrogen-bond interactions existed between the adenines in the $\mathbf{H_3}$ solution, which were too weak to form supramolecular polymers. The cooperative non-covalent interactions between $\mathbf{H_3}$ and **G** were strong enough to make them assemble.

We synthesized a homotritopic pillar[5]arene $\mathbf{H_3}$ containing three adenine units. $\mathbf{H_3}$ interacted with (6-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)hexanenitrile (**G**)) through cooperative hydrogen-bond interactions and host–guest binding, which involved dipole–dipole, C–H$\cdots\pi$, C–H$\cdots$O and $\pi\cdots\pi$ interactions. Thanks to the strong cooperative interactions, $\mathbf{H_3}$ and **G** formed a hyperbranched supramolecular polymer at a low concentration. ^{1}H NMR, viscosity measurements and DOSY experiments at various concentrations confirmed the cooperative hyperbranched supramolecular polymerization. The supramolecular polymer showed dual-responsiveness to heating and cooling, or the addition of aspirin and a base. This was the first report of a supramolecular polymer based on a pillar[5]arene constructed through cooperative non-covalent interactions. The present research provides a new method for the construction of smart supramolecular polymer materials.

This work was supported financially by the Innovative Talents Programme of Henan Province (174100510025), the Henan Science and Technology Program (162300410204, 18A150030), and the Scientific Research Foundation for Doctors (qd16106 and 2016QK09) of Henan Normal University.

Conflicts of interest

There are no conflicts to declare.

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