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ARTICLE

Based on the host-guest chemistry to build smart Janus-like supramolecular polymer and Its Self-Assembly

Long Yang, Yinzhou Guo, Zhongli Lei*

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We report on the synthesis a double stimuli-responsive self-assembly of Janus-like supramolecular polymer based on the host-guest chemistry. It is constructed by the noncovalent coupling between a hyperbranched PMAA with an apex of an Adamantane (Ad) group and a hyperbranched PNIPAAm with an apex of a β -cyclodextrin (β -CD) group. Upon adjusting solution pH or temperature, the supramolecular polymer can reversibly self-assemble in solution.

Introduction

Since the term of "Janus grains" was coined by de Gennes in his Nobel lecture two decades ago.¹ Janus particles have attracted extensive attention owing to their unique and fascinating properties correlated to their asymmetric structure and functionalization as well as their great potentials to be used as new building blocks in self-assembly.²⁻⁸ Typical Janus particles were micro- or nano-sized particles composed of two hemispheres of distinct chemical or physical properties. Because of the different properties on the two sides of Janus particles, many unique phenomena had been observed such as self-assembly, rotation and self-propulsion.⁹⁻¹⁰

These unique properties also made Janus-type supramolecular polymers very promising in biomedical applications including mimicking primitive biological membranes, configuring into biomimetic nanocapsules, fabricating functional nanomedicines, and so on.¹¹⁻¹⁷ However, the difficulties in synthesizing Janus supramolecular polymers were enormous.¹⁸ Recently, some noncovalent interactions, such as host-guest interaction, which were strong enough between host and guest molecular to sustain the structures in aqueous solution just like the covalent bond. Therefore, host-guest interaction had been proved to be a new and powerful way to get supramolecular polymers with various architectures and functions.¹⁹⁻²⁹ Frechet et al. reported a supramolecular Janus dendrimer by multiple hydrogen bonds and electrostatic interactions between a polyester dendron having a carboxylic acid apex and a polyester dendron having a bis-adamantyl

urea apex.³⁰

Inspired by this idea, the host-guest interaction and the property of stimuli-responsive can be conjointly introduced into smart Janus-like supramolecular polymers. Very recently, we designed and fabricated a novel Janus-like supramolecular polymers via host-guest interactions between β -CD-(PNIPAAm)₄ and Ad-(PMAA)₇, as illustrated in scheme 1. Through the molecular recognition between β -CDs and Ad moieties, supramolecular polymers can reversibly self-assemble by adjusting corresponding the pH or temperature of solution.

Experimental

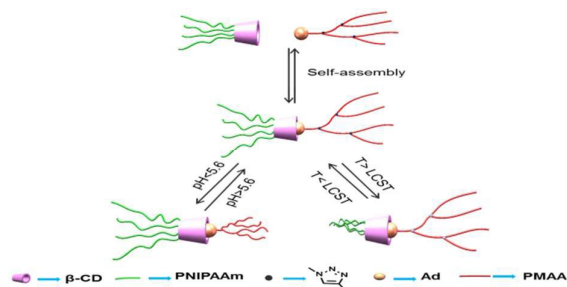
Materials

β -Cyclodextrin (β -CD) (Shanghai Sinopharm Chemical Reagent Co. Ltd.) was dried for 48 h in vacuum oven before use. Copper(I) bromide (Fluka, 98%) was washed with glacial acetic acid in order to remove any soluble oxidized species, filtered, washed with ethanol, and dried. N-isopropylacrylamide (Aldrich, 99%) was recrystallized twice from hexane before use. Tris[2-(dimethylamino)ethyl]amine (Me₆-TREN) was prepared according to literature.³¹ 1-Adamantanemethanol (Aldrich, 99%), Dichloromethane (DCM) and triethylamine (TEA) from Sinopharm were distilled over CaH₂ just prior to use. N,N''N''',N''''',N''''''-Pentamethyl-diethylenetriamine (PMDETA, Aldrich, 99%), sodium azide (NaN₃, Aldrich, 99%), 2,2-bis(hydroxymethyl) propionic acid (DMPA, Fluka, 97%), N,N-dimethyl-4-amidopyridine (DMAP, Aladdin, 99%), dicyclohexyl carbodiimide (DCC, Aladdin, 99%), 2-bromoisobutyryl bromide (Aladdin, 98%), p-toluenesulfonic acid monohydrate (PTSA, Aladdin, 99%), 2,2-dimethoxypropane (Aladdin, 99%), propargyl alcohol (Aldrich, 99%), Tetrahydrofuran (THF, Fisher, GR grade), and other

* Key Laboratory of Applied Surface and Colloid Chemistry, Ministry of Education, Shaanxi Normal University, Xi'an, 710062, China E-mail address:

zhlllei2013@163.com Tel: +86 029 81530812; fax: +86 29 85307774
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analytic grade reagents from Sinopharm were used as received.



Scheme 1 Schematic illustration of preparation of β -CD-(PNIPAAm)₄/Ad-(PMAA)₇ supramolecular.

Synthesis of initiator Ad-Br

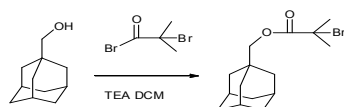


Figure 1 Synthesis route of initiator Ad-Br.

1-Adamantane methanol (0.8315 g, 5 mmol) and TEA (1.1 mL, 7.9 mmol) were dissolved in dry CH_2Cl_2 in an ice-water bath. After stirring for 0.5 h, 2-bromoisobutyryl bromide (0.93 mL, 7.5 mmol) in CH_2Cl_2 was added drop wise over 1 h. Subsequently, the reaction mixture was stirred at 0°C for another 1 h and then at room temperature for 16 h. The mixture was extracted with HCl (3 M, 3×30 mL), deionized water (3×30 mL), NaOH (3 M, 3×30 mL), deionized water (3×30 mL) in sequence. The organic phase was dried over anhydrous Na_2SO_4 . After removing the solvents by a rotary evaporator, the final product was obtained as a brown solid. ^1H NMR (CDCl_3 , 400 MHz, δ): 1.57 (s, 6H, $-\text{CH}_2-$), 1.63-1.75 (m, 6H, $-\text{CH}_2-$), 2.00 (s, 3H, $-\text{CH}-$), 1.94 (s, 6H, $-\text{CH}_3$), 3.7 (s, 2H, $-\text{OCH}_2-$) ppm; ^{13}C NMR (CDCl_3 , 400 MHz, δ) 33.62, 36.92, 30.89, 39.17, 56.17, 171.74, 27.99, 75.32 ppm. FTIR (KBr): 2910, 2852, 2655, 1728, 1456, 1273, 1168, 1053, 824 cm^{-1} .

Synthesis of polymer Ad-PtBMA-Br

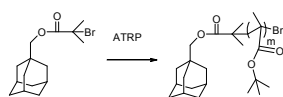


Figure 2 Synthesis route of the Ad-PtBMA-Br.

CuBr (112 mg, 0.781 mmol) and initiator Ad-Br (188 mg, 0.391 mmol) were added to a clean, dry, round-bottom flask, which was subsequently evacuated for 15 min and backfilled with argon. Freshly distilled tBMA (5.0 g, 39.0 mmol) was added via a degassed syringe followed by degassed toluene (2.5 mL) and PMDETA (130 mg, 0.781 mmol). The reaction flask was immediately submerged in liquid N_2 until frozen, evacuated for 15 min, removed from liquid N_2 , and backfilled with argon. When the mixture thawed completely, the flask was submerged in a 70°C oil bath and stirred for 5 h under an argon atmosphere. After 5 h, the reaction flask was opened to

air, and the viscous, black mixture was diluted with tetrahydrofuran (20 mL) and frozen in liquid N_2 . After thawing, the mixture was passed through a column of neutral alumina, concentrated on a rotary evaporator, precipitated in a 10:1 volume of 50-50 methanol-water three times, dissolved in diethyl ether, dried over MgSO_4 , filtered, concentrated on a rotary evaporator, and dried in vacuo for 2 days to yield Ad-PtBMA-Br as a white solid.

Synthesis of Ad-PtBMA- N_3

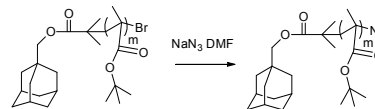


Figure 3 Synthesis route of Ad-PtBMA- N_3 .

Sodium azide (106 mg, 1.63 mmol) was added to a round-bottom flask containing Ad-PtBMA-Br (5.344 g, 0.783 mmol) dissolved in DMF (74 mL). The reaction mixture was stirred at 50°C for 1 day, after which time it was allowed to cool to room temperature, diluted with ether (50 mL), and washed four times with water (100 mL). The organics were concentrated on a rotary evaporator and precipitated into a 10:1 volume of 50-50 methanol-water. After decanting the methanol-water solution, the remaining solid was dissolved in diethyl ether, dried over MgSO_4 , filtered, concentrated on a rotary evaporator, and dried for 2 days in vacuo to yield Ad-PtBMA- N_3 as a white solid.

Synthesis of 2,2-Bis(2'-bromo-2'-methylpropionyloxymethyl) Propionic Acid (BPA)

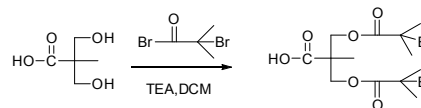


Figure 4 Synthesis route of the BPA.

2-Bromoisobutyryl bromide (44 mL, 357 mmol) was added dropwise to a solution of bis(hydroxymethyl) propionic acid (bis-MPA) (20 g, 149 mmol), and triethylamine (52 mL, 366 mmol) in 500 mL of dry dichloromethane at 0°C under argon atmosphere. After stirring at 0°C for 1 h, the reaction was completed by stirring for another 2 h at 25°C . After evaporation of the solvent, the residue was dissolved in diethyl ether, and the triethylamine hydrochloride was filtered off. The solution was then extracted with 2N hydrochloride, the ether phase dried over MgSO_4 , and the solvent evaporated to give a viscous liquid. To remove all 2-bromo-2-methylpropionic acid by product, the residue was stirred with hot water several times and again dissolved in diethyl ether. After drying and evaporation of the diethyl ether, the crude product was recrystallized from hexane to give the 2,2-Bis(2'-bromo-2'-methylpropionyloxymethyl) Propionic Acid (BPA) as a white solid. ^1H NMR (CDCl_3 , 400 MHz, δ): 1.33 (s, 3H, $-\text{CH}_3$), 1.89 (s, 12H, $-\text{C}(\text{Br})-\text{CH}_3$), 4.43-4.41 (q, 4H, $-\text{CH}_2-$) ppm. ^{13}C NMR (CDCl_3 , 400 MHz, δ): 17.78, 30.63, 46.56, 55.21, 65.97, 170.96, 178.57 ppm. FTIR (KBr): 2700-3200, 1736, 1694, 1289, 1178, 1105 cm^{-1} .

Elemental Analysis: Calcd for $C_{13}H_{2}OBr_2O_6$: C, 36.10; H, 4.64; Br, 36.90. Found: C, 36.95; H, 4.98; Br, 37.10.

Synthesis of initiator propargyl 2,2-Bis((2'-bromo-2'-methylpropionyloxy)methyl) Propionate (PBMP)

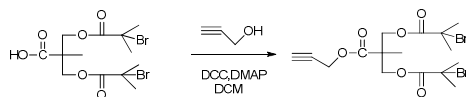


Figure. 5 Synthesis route of the PBMP.

The BPA (8.0 g, 18.5mmol), propargyl alcohol (1.5mL, 25mmol), and DCC (5.3g, 25mmol) were added to 100 mL of CH_2Cl_2 . After a small amount of DMAP was added, the suspension was stirred for 24 h and then filtered to remove insoluble solid. The target product (3.5g) was afforded through silica gel chromatography with petroleum ether and dichloromethane (V/V =10/1) mixture as eluent to give the propargyl 2,2-Bis((2'-bromo-2'-methylpropionyloxy)methyl) Propionate (PBMP). 1H NMR ($CDCl_3$, 400 MHz, δ): 4.7(s, 2H, $CH\equiv C-CH_2-$), 4.4(q, 4H, $C-CH_2-CO-$), 2.5 (s, 1H, $CH\equiv C-CH_2-$), 1.9 (s, 12H, $-CO-C(CH_3)_2-Br$) 1.4 (s, 3H, $C-CH_3$)-ppm. ^{13}C NMR($CDCl_3$, 400 MHz, δ): 171.6, 170.9, 77.4, 75.5, 66.1, 55.3, 52.8, 46.7, 30.7, 17.7ppm. Elem. Anal: Calcd for $C_{16}H_{22}Br_2O_6$: C, 40.9; H, 4.72; Br, 34.0. Found: C, 41.4; H, 4.84; Br, 33.6.

Synthesis of polymer alkyne-(PtBMA-Br)₂

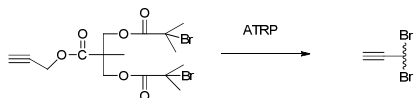


Figure. 6 Synthesis route of the alkyne-(PtBMA-Br)₂.

The PBMP (0.157 g, 0.5 mmol), tBMA (7.25 mL, 0.5 mol), PMDETA (104 μ L, 1 mmol), and toluene (2 mL) were charged into a reaction flask. After one brief freeze-thaw cycle, CuBr (71.5 mg, 0.5 mmol) was introduced under protection of N_2 flow. The reaction tube was degassed by three freeze-pump-thaw cycles, and placed in an oil bath thermo-stated at 70°C for 5 h. The reaction mixture was exposed to air, and then the mixture was evaporated to dryness, and dissolved in tetrahydrofuran (THF) and precipitated in excess of 50-50 methanol-water. The above mentioned dissolution precipitation cycle was repeated three times. After drying in a vacuum oven overnight at room temperature, alkyne-(PtBMA-bromine)₂ was obtained.

Synthesis of Hyperbranched Ad-(PtBMA)₃ by click reaction



Figure. 7 Synthesis route of the Ad-(PtBMA)₃.

The typical procedure is as follows. A three-necked flask equipped with a magnetic stirring bar and three rubber septum was charged with Ad-PtBMA- N_3 (0.648g, 0.095mmol), alkyne-(PtBMA-Br)₂ (1.325g, 0.095 mmol), PMDETA (94.5 μ L, 0.19 mmol) and DMF (5mL). The flask was degassed by three freeze-pump-thaw cycles, and then placed in a water bath

thermostated at 35°C. After 2 min, CuBr (27 mg, 0.19 mmol) was introduced to start the reaction under N_2 positive pressure. After 24 h, the reaction mixture was cooled to room temperature and diluted with THF, then passed through a short column of neutral alumina to remove the metal salt. After most of the solvents were removed by a rotary evaporator, the residue was precipitated into a mixture of cold methanol/water mixture (1/1, v/v). After drying in a vacuum oven overnight at 40 °C, the product Ad-(PtBMA)₃ was obtained.

Synthesis of hyperbranched Ad-(PtBMA)₇ by click reaction

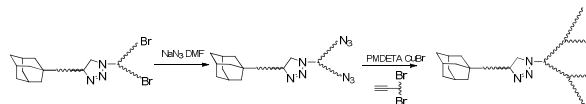


Figure. 8 Synthesis route of the Ad-(PtBMA)₇.

Then, the product Ad-(PtBMA)₇ was synthesized as the same as Ad-(PtBMA)₃.

Synthesis of guest polymer Ad-(PMAA)₇

The typical procedure is as follows. The mixture of hyperbranched PtBMA obtained in the previous step was dissolved in CH_2Cl_2 ($C \sim 100$ g·L⁻¹) and a fivefold molar excess (tBMA unit) of trifluoroacetic acid (TFA) was added under N_2 positive pressure. After 36.0 h, TFA and dichloromethane were removed by a rotary evaporator. The product was dissolved in water/THF mixture (v/v, 5/1) and transferred into dialysis tubing, and dialyzed against deionized water for 5 days. After the freeze drying, a fluffy white solid hyperbranched PMAA was obtained.

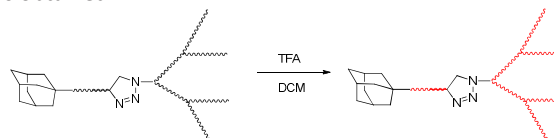


Figure. 9 Synthesis route of the Ad-(PMAA)₇.

Synthesis of initiator 4Br- β -CD

The product 4Br- β -CD was synthesized following a similar method to previous reports.³² β -CD (5.11 g, 4.5 mmol, vacuum dried at 100 °C overnight before use) was dissolved in 30 mL of anhydrous N, N-dimethylacetamide with stirring and then was cooled to 0 °C. Subsequently, a solution of 2-bromo-isobutyric bromide (4.14g, 18.0mmol) in anhydrous N, N-dimethylacetamide (10 mL) was added dropwise to the β -CD solution for a period of 1 h at 0 °C under N_2 atmosphere. After the addition, the reaction temperature was maintained at 0 °C for another 2 h and then allowed to rise slowly to r.t., after which the reaction was allowed to continue for 24 h. The final reaction mixture was precipitated with 900 mL of diethyl ether. The resulting white powder was collected by centrifugation, washed with acetone (2 \times 30 mL). In the purification process, the crude product was suspended in 100 mL of DI water, and the mixture was stirred at r.t. overnight. The purified product was collected by centrifugation, washed

with acetone (2x30 mL), dried under vacuum. ^1H NMR (400 MHz, DMSO- d_6 , δ): 1.88 (m, 24H, $-\text{OCO}-\text{C}(\text{CH}_3)_2\text{Br}$), 3.00-6.00 (m, 66H, $-\text{OH}$ and $-\text{CH}-$ of β -CD)ppm. ^{13}C NMR (400 MHz, DMSO- d_6 , δ): 170.7, 170.5 (C=O), 102.5-101.3, 81.9-80.5, 73.1, 72.8, 72.1, 72.0, 69.1, 69.0, 65.0, 64.4, 59.4, 57.1, 30.4, 30.3ppm; FTIR (KBr): 1746, 681.5 cm^{-1} ; Elem. Anal: Calcd for $\text{C}_{58}\text{H}_{90}\text{Br}_4\text{O}_{39}\cdot 2\text{H}_2\text{O}$: C, 39.42; H, 5.36; Br, 18.09; Found: C, 37.96; H, 5.46; Br, 22.39.

Synthesis of host polymer β -CD-(PNIPAAm) $_4$

Macroinitiator 4Br- β -CD (176.8 mg, 0.103mmol) and NIPAAm (1.358 g, 12.0 mmol) were added into a dry flask. The flask was sealed with a septum and subsequently purged with dry nitrogen for several minutes. Then, $\text{Me}_6\text{-TREN}$ (111.0 mg, 0.48 mmol) in 3.5 mL of thoroughly degassed methanol was added with a degassed syringe. The mixture was stirred at room temperature and purged with dry nitrogen for 10 min. Last, CuBr (57.4 mg, 0.4 mmol) was added and the mixture was purged with dry nitrogen for another 10 min at room temperature. The mixture was then heated at 70 $^\circ\text{C}$ in an oil bath. After 4h, the experiment was stopped by opening the flask and exposing the catalyst to air. The final green mixture was diluted with THF and passed through a short Al_2O_3 column to remove copper catalyst. The resulting eluate solution was concentrated to ca. 10 mL, and precipitated with 500 mL diethyl ether. The white product was collected by centrifugation, washed with diethyl ether, and dried under vacuum.

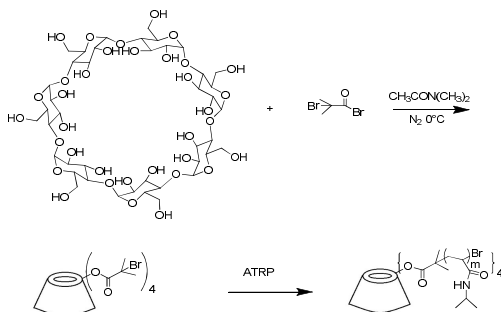


Figure. 10 Synthesis route of the β -CD-(PNIPAAm) $_4$.

Characterization

Fourier transformation infrared spectrometer (FTIR, Equinox55, Bruke, Germany) was utilized to inspect the main chemical functional group changes of the synthesized copolymer hydrogel samples by a KBr pellet method.

Nuclear magnetic resonance (NMR) spectroscopy. All ^1H NMR spectra were performed at on a Bruker AV300 NMR spectrometer (resonance frequency of 400 MHz for ^1H) operating in the Fourier transform mode.

Gel permeation chromatography (GPC). Molecular weight distributions were determined by GPC using a series of three linear Styragel columns HR2, HR4, HR5 and an oven temperature of 45 C. Waters 1515 pump and Waters 2414 differential refractive index detector (set at 30 $^\circ\text{C}$) was used. The eluent was THF at a flow rate of 1.0 mL/min. A series of six

polystyrene standards with molecular weights ranging from 800 to 400,000 g/mol were used for calibration.

Optical transmittances. The optical transmittance of the polymer solution at 500 nm was followed by using a UV-visible spectrophotometer (Shimadzu UV-2501PC).

Dynamic light scattering spectrophotometer (DLS). The hydrodynamic radius (Rh) of the micelles of copolymer micelles was investigated using DLS techniques. The experiments were performed using a Malven Autosizer 4700 DLS spectrometer. DLS was performed at a scattering angle of 90 $^\circ$.

Transmission electron microscopy (TEM). Transmission electron microscopy (TEM) measurements were conducted on a Philips CM 120 electron microscope at an acceleration voltage of 100 kV. The samples for TEM observations were prepared by placing 10 mL of solutions at a concentration of 0.5 g/L on copper grids, which were coated with thin films of Formvar and carbon successively. No staining was required.

Results and discussion

From figure 2 to 10 showed that how host/guest polymers were prepared. The characterization results of molecular parameters of prepared polymers were summarized in Table 1. (Figure S1, ESI $^+$)

Synthesis and Characterization of host polymers.

The host polymer β -CD-(NIPAAm) $_4$ was synthesized by the ATRP of NIPAAm using 4Br- β -CD as macroinitiator. The number-average molecular weight (M_n) of the final host polymer calculated based on ^1H NMR, GPC measurements were 9376 Da and 5121 Da ($M_w/M_n=1.27$), respectively. These values based on different measurements were found to correlate well with the predicted molecular weight (10350Da) calculated from the feed initiator concentration and the consumption of monomer, showing that the above-mentioned side reactions were negligible under this polymerization conditions. The ^1H NMR spectrum of β -CD-(PNIPAAm) $_4$ (Figure S2, ESI $^+$), the strong signals at $\delta = 1.04$, 1.52, 1.95 and 3.85 ppm were associated with the methyl protons (a), methylene protons (b), methine protons (c), and methine protons (d) of PNIPAAm arms, respectively; The weak signals appeared in the region of 3.40-4.00 ppm and around 5.01 ppm were attributable to the protons of the β -CD core, respectively.

Synthesis and Characterization of guest polymers.

The well-defined hyperbranched polymers Ad-(PtBMA) $_7$ was prepared via ATRP and click reaction.

First, the Ad-PtBMA polymer was synthesized through ATRP of tBMA with Ad-Br (the ^1H NMR spectrum of Ad-Br (Figure S1, ESI $^+$)) as initiator. The proton resonance signals corresponding to Ad-PtBMA were observed (Figure S4, ESI $^+$). The strong signals at $\delta = 1.14$, 1.42 and 1.89 ppm were associated with the methyl protons(a), methylene protons(b), tert-butyl protons(c) of PtBMA(the FTIR spectrum of Ad-PtBMA (Figure S9 (a), ESI $^+$)). The GPC curve of Ad-PtBMA suggests a

narrow distribution ($M_w/M_n=1.19$). Conversion of the chain ends of Ad-PtBMA to azides by treatment with sodium azide in DMF proceeded efficiently to yield Ad-ptBMA- N_3 (Figure. 2). The IR spectrum of Ad-PtBMA- N_3 possesses an absorbance at $\sim 2100\text{cm}^{-1}$, confirming the presence of azide groups (Figure S9 (b), ESI[†]).

The alkyne-(PtBMA-bromine)₂ polymer was synthesized through ATRP of tBMA using PBMP as macroinitiator. The ¹H NMR spectrum of BPA, PBMP and alkyne-(PtBMA-bromine)₂, respectively. (Figure S5, Figure S6, Figure S7, ESI[†]). Further grafting alkyne-(PtBMA)₂ chains onto the Ad-PtBMA- N_3 results in graft polymer with a hyperbranched Ad-(PtBMA)₃. To ensure 100% grafting efficiency, three fold excess of alkyne-(PtBMA)₂ was used in click reaction. The success of grafting reaction is reflected first in the absolute disappearance of N=N=N stretch in FTIR spectra (Figure S9(c), ESI[†]). The ¹H NMR spectrum of Ad-(PtBMA)₇ (Figure S8, ESI[†]). The product Ad-(PtBMA)₇ was obtained via azidation reaction in a similar way, then five folds excess of alkyne-(PtBMA)₂ was used in click reaction. It can also be confirmed by infrared spectroscopy and ¹H NMR spectra.

Synthesis of guest hyperbranched polymer Ad-(PMAA)₇ by hydrolyzing tBMA into AA Moiety.

The Hyperbranched polymers were characterized by FT-IR and ¹H NMR (Figure S9 (d), Figure S10, ESI[†]). For the hyperbranched Ad-(PMAA)₇, the absorption band at $3400\text{--}3250\text{cm}^{-1}$, 1730cm^{-1} were contributed to the carboxymethyl hydroxyl, carbonyl groups, the typical proton resonance signals at 0.5, 1.0, 1.25, 1.54, 1.84, 2.0, 2.12, 3.85, 4.75 and 7.87ppm were corresponded to the protons of Ad-(PMAA)₇, indicating that the guest polymer was synthesized successfully.

Thermo-responsive of supramolecular polymer in aqueous solution

The optical transmittance changes of the host polymer, guest polymer and host-guest mixtures in aqueous solution at 500 nm were followed by using a UV-visible spectrophotometer equipped with a circulating water bath in the temperature range of 20-40 °C (heating rate: $1.0\text{ }^\circ\text{C}\cdot\text{min}^{-1}$). In this study, the lower critical solution temperature (LCST) was also equal to the temperature exhibiting a 50% decrease in optical transmittance of the aqueous solution at 500 nm.

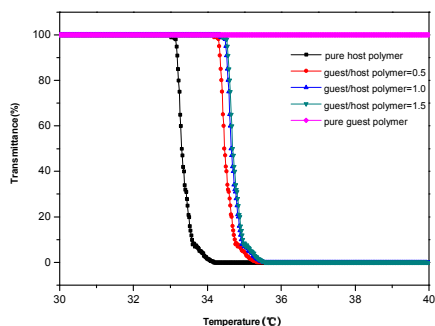


Figure 11. Transmittance of polymers in aqueous solutions. $C_{\text{host polymer}} = 1.0\text{ g}\cdot\text{L}^{-1}$

It can be seen from Figure 11, the LCST of the β -CD-(PNIPAAm)₄ (pure host polymer) was ca. $33.5\text{ }^\circ\text{C}$. The LCST of the host polymer shifted to a higher temperature upon the addition of the hyperbranched Ad-(PMAA)₇ (guest polymers). The LCST significantly changed with a LCST increase of $1.2\text{ }^\circ\text{C}$ when the adamantyl moiety/CD core molar ratio was 0.5. When the adamantyl moiety/CD core molar ratio was 1.0, the LCST was enhanced just a little compared with adamantyl moiety/CD core, whose molar ratio was 0.5. However, the LCST became almost saturated upon further increase of the host/guest ratio beyond 1.0. In order to confirm that the shift of LCST was caused by the complexation between the guest polymer and the host polymer, the transmittances of pure guest polymer were carried out at different temperature in Figure 11. The transmittances of pure guest polymer in aqueous solution kept steady state, indicating that this polymer had no thermo-responsive behaviors.

Therefore, the above experiments revealed a phenomenon that the supramolecular polymer can change the LCST of β -CD-(PNIPAAm)₄ (pure host polymer) upon the addition of Ad-(PMAA)₇ (guest polymers) in a limited range of values.

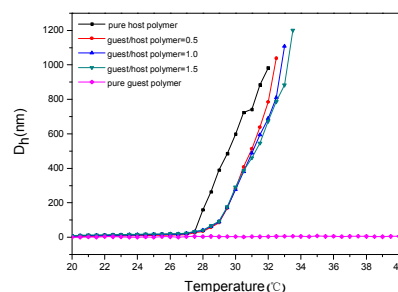


Figure 12. Average diameters obtained by DLS measurements for polymer solutions. $C_{\text{host polymer}} = 1.0\text{ g}\cdot\text{L}^{-1}$

The size distribution and morphology of the noncovalently connected micelles were investigated by DLS, DLS was proved to be a sensitive method to trace the formation of noncovalently connected micelle according to the change in particle size. The changes of micelle size at different temperature ($20\text{--}40\text{ }^\circ\text{C}$) were shown in Figure 12. For the pure guest polymer in aqueous solution, we can see that as temperature rised, the micelle sizes were almost in a very small scale. Such a phenomenon was also proved to be a similar result in Figure 11, which indicating the guest polymer was not sensitive to temperature. Due to the guest polymer was not the thermal-responsive polymer, the size will not change in any temperature. For the host polymer, the changes of micelle size of the polymers can be divided into two stages. In the first stage, the values of both micelle size were very small and kept unchanging under lower temperature ($<26\text{ }^\circ\text{C}$). When temperature reached above $26\text{ }^\circ\text{C}$, in the second stage, a rapid increase of the D_h were observed, and the pure host polymer in aqueous solution emerged turbidity

and precipitation. From this figure we can see that the aqueous solution of host-guest mixtures had an analogous phenomenon, but the mixed polymer solution had higher temperature when the polymer solution became turbidity.

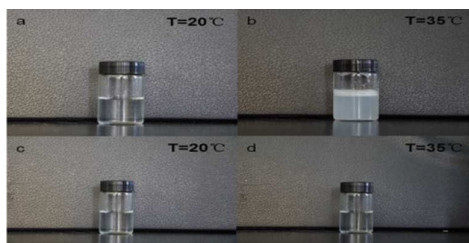


Figure 13. Representative photos of the host/guest=1.0 in aqueous solution. $C_{\text{host polymer}} = 1.0 \text{ g}\cdot\text{L}^{-1}$

As seen in Figure 13(a, b), representative photos of the host/guest=1.0 in aqueous solution at two typical temperatures (20°C, 35 °C), proving that the mixed polymer responded to temperature. Meanwhile, the photos of the pure guest polymer in aqueous solution were shown in Figure 13(c, d), we can clearly see that the pure guest polymer was no response to temperature.

pH-responsive of supramolecular polymer in buffer solution

The pH-responsive behavior of the host polymer, guest polymer and host-guest mixtures in buffer solution were estimated by the UV-Vis transmittance at wavelength of 500 nm.

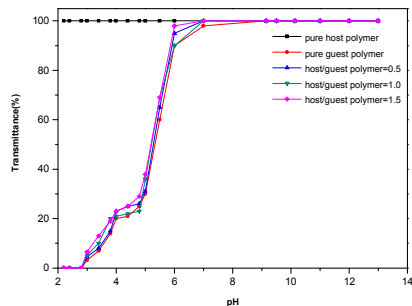


Figure 14. Transmittance of polymers in butter solutions. $C_{\text{host polymer}} = 1.0 \text{ g}\cdot\text{L}^{-1}$

In Figure 14, it can be seen that pure guest polymers showed a sharp increase of transmittance at ca. $\text{pH}=5.4$, which was very close to the pK_a (about 5.6) of PMAA blocks. Below this value of 5.4, nonionized PMAA assumed a hydrophobic conformation, and the polymer was apt to form the aggregate micelles due to the intramolecular hydrogen bonding of the MAA units resulting from protonation of PMAA moieties,³³ therefore, the transmittance had a relative lower values. When pH value of the butter solution was increased above 5.4, PMAA chains were in extended chain conformation due to the electrostatic repulsion between the PMAA segments after deprotonation of PMAA blocks. The transmittance of solution increased dramatically to ca. 100%, and the solution became transparent. It was obvious that the transmittances of pure

guest polymer in different butter solutions was consistent with the transmittance of mixture, however, the pure host polymer almost had no phase behaviours from Figure 14, which indicating that adding host polymer into the butter aqueous of guest polymer had no effect on the pK_a of guest polymer.

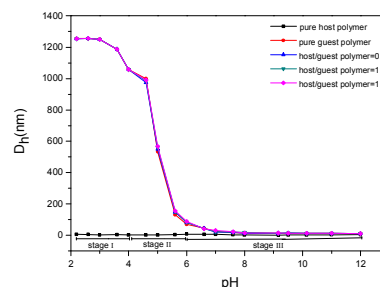


Figure 15. Average diameters obtained by DLS measurements for polymer in butter solutions at 20°C. $C_{\text{host polymer}} = 1.0 \text{ g}\cdot\text{L}^{-1}$

The changes of micelle size of the polymer in different butter solutions were shown in Figure 15. For pure guest polymer and mixed polymer system, we can see that with the increase of pH value to 4.0, micelle size slowly reduced from about 1250nm to 1000 nm at stage I. The micelle size was observed to have a sharply decrease to about 120 nm with further increase of the $\text{pH}=5.4$ at stage II. However, for the pure host polymer system, we can see its micelles size almost maintained in a very small scale, it was further indicated that the host polymer was not the pH-responsive polymer.

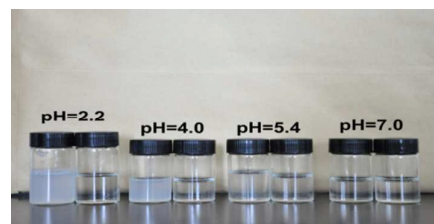


Figure 16. Representative photos of butter solutions of host/guest=1.0 mixture at 20°C. $C_{\text{host polymer}} = 1.0 \text{ g}\cdot\text{L}^{-1}$

As seen in Figure 16, representative photos of the host/guest=1.0 in butter solutions (right) and pure host polymer in butter solutions (left) at four typical pH values (2.2, 4.0, 5.6 and 7.0). For pure host polymer in butter solution, we can see obviously that it had no change with the increase of pH values. However, the mixed system gradually became clear. It was a further proof that the host polymers were not sensitive to pH.

Morphologies of supramolecular polymers at different pH and temperature

The actual self-assembled morphologies of the supramolecular polymer in different butter solution ($\text{pH}=2.2$, $\text{pH}=4.0$, $\text{pH}=5.4$, $\text{pH}=7.0$) were characterized by TEM, and representative images were shown in Figure 17(a, b, c, d).

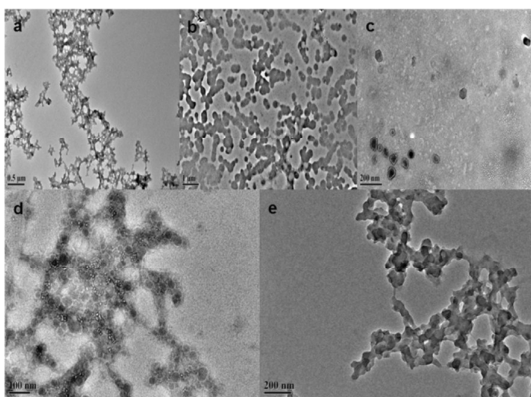


Figure 17. TEM images of host/guest polymer=1.0 mixture at different pH and temperature. (a) pH=2.2; (b) pH=4.0; (c) pH=5.4; (d) pH=7.0 at 20 °C; (e) pH=7.0 at 35 °C

As shown in Figure 17(a), because of the role of non-ionizing PMMA, we can see that the colloidal particles violently reunited so that the micellar morphology was difficult to be observed. Upon increasing the pH to 4.0 in Figure 17(b), although colloidal particles aggregated slightly to a certain extent, the micelle morphology was still observed as spherical micelles structure and the diameter of micelles varied from 100 nm to 150 nm. When the pH=5.6 in Figure 17(c), it was clear to see the spherical micelles structure and the diameters of micelles were between 80 and 120 nm. From the Figure 17(b) and 17(c), it explains exactly the PMAA blocks became hydrophobic when the pH was blow 5.6, and they should be hidden in the hydrophobic cores of the micelles during the self-assembly and form the isotropic spherical micelles. Finally, both the hosts and the supramolecular polymer of β -CD-(PNIPAAm)₄-Ad-(PMAA)₄ were totally hydrophilic at pH=7.0, so they can formed unimolecular micelles, and the diameter of spherical micelles structure should very small, however, we still faintly see the spherical micelles around 20 nm from the Figure 17(d), it may be due to the electron beam bombard sample surface lead to the sample temperature was enhanced. It indicated that this supramolecular polymer self-assembly system can form the spherical micelles structure.

Morphologies of supramolecular polymers at different temperature were shown in Figure 17(d, e). It was found by above related conclusions that the host polymer β -CD-(PNIPAAm)₄ was a kind of thermo-responsive polymer, the lower critical solution temperature (LCST) of β -CD-(PNIPAAm)₄ was about 33.5 °C in aqueous solution. When the outside temperature changed, the host polymer β -CD-(PNIPAAm)₄ showed a significant transformation by the hydration and dehydration. When the temperature was below the lower critical solution temperature (LCST), the chain structure of host polymer β -CD-(PNIPAAm)₄ in aqueous solution became expansile. On the other hand, when the temperature was higher than the lower critical solution temperature (LCST), due to dehydration, the hydrophobicity of the polymer chain was increased so that colloidal particles shrank together. We studied two typical temperature (20 °C, 35 °C) in the condition of the host/guest polymer=1.0 system. As figure 17(d), the supramolecular polymer of Ad-(PMAA)₇- β -CD-(PNIPAAm)₄ were

totally hydrophilic below LCST, and they were supposed to be kept as the unimolecular micelles. However, because of the reason of the electron beam produced spherical micelles about 20 nm. As the temperature rised to 35°C, we can see the colloidal particles emerged serious agglomeration from Figure 17(e). Thus, we can get the conclusion that the supramolecular system can change the morphologies reversibly by altering the temperature of aqueous solution.

The sizes of micelles observed from TEM measurement were not in accord with DLS measurement, which may be attributed to the different principles of DLS and TEM. The DLS data present an intensity average with a comprehensive balance result, while the TEM image was a direct picture of the polymeric micelles and only showed a localized viewing field.

Conclusions

In summary, we have reported a double stimuli-responsive supramolecular polymer through noncovalent host-guest coupling between the Ad-(PMAA)₇ and β -CD-(PNIPAAm)₄. This kind of supramolecular polymer material formed the spherical micelles structure in solution by properly tuning pH or temperature. We believed the present work will cast a new Janus-like structure on design, synthesis, and self-assembly of supramolecular polymers with more complex topologies or architectures.

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