

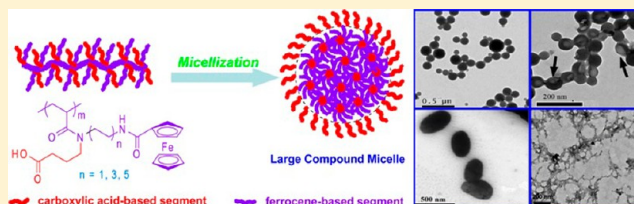
Self-Assembly of Amphiphilic Homopolymers Bearing Ferrocene and Carboxyl Functionalities: Effect of Polymer Concentration, β -Cyclodextrin, and Length of Alkyl Linker

Chun Feng, Guolin Lu, Yongjun Li, and Xiaoyu Huang*

Key Laboratory of Organofluorine Chemistry and Laboratory of Polymer Materials, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, P. R. China

S Supporting Information

ABSTRACT: Three new acrylamide monomers containing ferrocene and *tert*-butyl ester groups were first synthesized via multistep nucleophilic substitution reaction under mild conditions followed by reversible addition–fragmentation chain transfer (RAFT) homopolymerization to give well-defined homopolymers with narrow molecular weight distributions ($M_w/M_n \leq 1.36$). The target amphiphilic homopolymers were obtained by the acidic hydrolysis of *tert*-butoxycarbonyls to carboxyls in every repeating unit using CF_3COOH . The self-assembly behaviors of these amphiphilic homopolymers bearing both ferrocene and carboxyl moieties in each repeating unit in aqueous media were investigated by transmission emission microscopy (TEM), dynamic light scattering (DLS), and atomic force microscopy (AFM). Large compound micelles with different morphologies were formed by these amphiphilic homopolymers, which consist of the corona formed by hydrophilic carboxyls and the core containing numerous reverse micelles with hydrophilic islands of carboxyls in continuous hydrophobic phase of ferrocene-based segments. The morphologies of the formed micelles could be tuned by the concentration of amphiphilic homopolymers, pH value of the solution, the length of $-\text{CH}_2$ linker between ferrocene group and carboxyl, and the amount of β -cyclodextrin (β -CD).



INTRODUCTION

Amphiphilic copolymers can self-assemble into a variety of aggregates, such as spheres, rods, tubes, vesicles, helical superstructures, bowl-shaped micelles, onion-like micelles, disclike micelles, multicompartment micelles, and so on, in which the fundamental driving force involves the mutual immiscibility of the blocks and/or the immiscibility of one segment in certain solvent.^{1–12} These nanometer to micrometer structures have many potential important applications from material science to biology, which leads to ever-increasing interest in this field over the past few decades.^{13–18} Previous studies on the self-assembly of linear block, graft, starlike, hyperbranched copolymers, and dendrimers indicate that the architecture and composition of the copolymers play an extremely critical role in determining micellar morphology, since they affect the conformational packing geometry of micellar structure.^{19–22} In order to deepen the understanding of structure–property correlation and explore novel self-assembled structures, considerable attention has been paid to the copolymers with novel chemical structure and topological architecture.^{1–12}

In 2004, Thayumanavan et al. reported a new class of amphiphilic polymer, in which a hydrophilic carboxyl and a hydrophobic benzyl moieties were incorporated into the same repeating unit of a homopolymer,²³ and they demonstrated that this amphiphilic homopolymer could self-assemble into spherical micelles in aqueous solution. In 2006, the same

group reported that the amphiphilic homopolymer also could form vesicles in aqueous media, in which two hydrophilic carboxyls linked by a long hydrophobic alkyl spacer were introduced into the same repeating unit of a homopolymer.²⁴ In 2010, Lee et al. reported that poly(2-(4-vinylphenyl)-pyridine) could form vesicles in the mixture of tetrahydrofuran (THF)/water, in which the 2-phenylpyridine moiety in each monomer unit acted as a hydrophilic headgroup and vinyl backbone collectively behaved as a hydrophobic moiety.²⁵ These results indicated that amphiphilic homopolymers could assemble into spheres and vesicles same as amphiphilic block copolymers did. However, the primary driving force for the formation of micelles by amphiphilic homopolymer originated from the intramolecular phase separation, which was much different from that of the block copolymer.²³

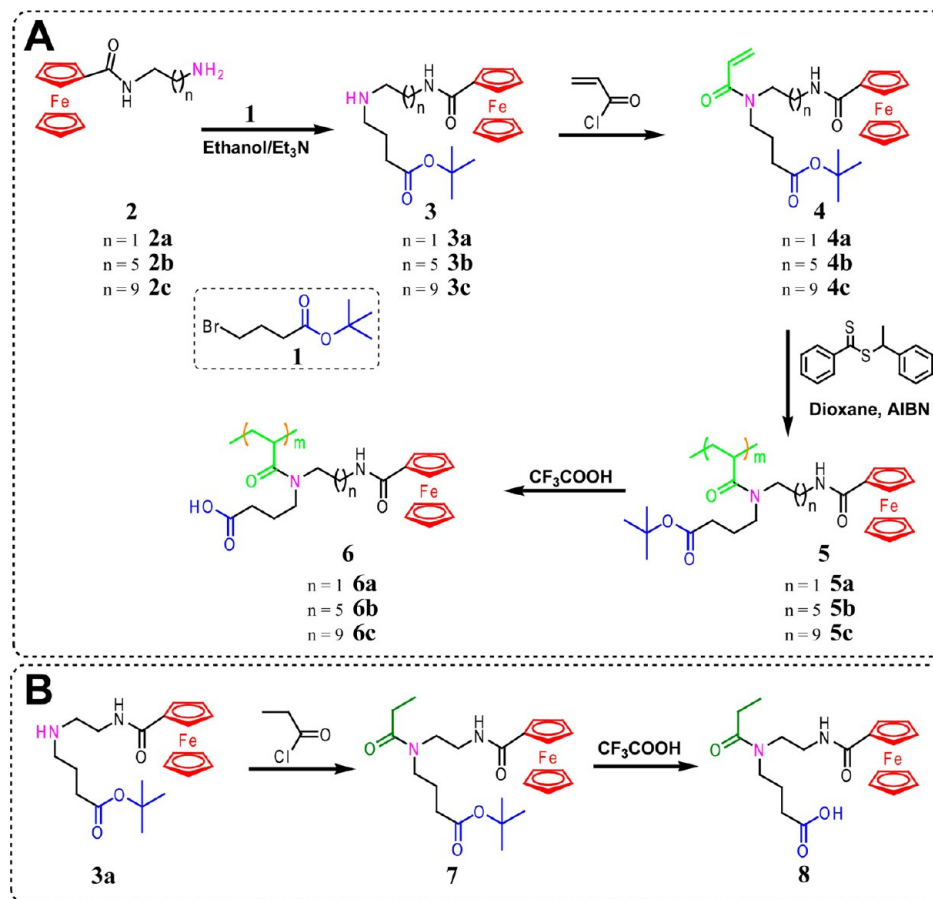
Ramamurthy and Thayumanavan et al. also demonstrated that the environment of the core of micelles formed by an amphiphilic homopolymer was more rigid and confined than that of the micelles formed from diblock amphiphilic copolymers and small molecular surfactants, which resulted in a higher selectivity of micelles using as a microreactor in aqueous media.¹⁸ They also found that the unique property of the aggregates formed by amphiphilic homopolymers provided

Received: June 20, 2013

Revised: July 25, 2013

Published: July 29, 2013

Scheme 1. (A) Synthesis of Ferrocene-Containing Amphiphilic Homopolymers; (B) Small Molecular Model Reaction



them with the ability to recognize proteins by their commensurate size and capacity to adapt their conformations upon reversibly binding to the surface of proteins without denaturing the protein.²⁶ On the basis of these observations, the same group constructed a new protein sensor array of the amphiphilic homopolymer aggregates²⁷ and demonstrated the utility of the amphiphilic homopolymer aggregates in applications of dye separation, peptide extraction, and protein function modulation.^{26,28} These observations could lead to a conclusion that the novel structure of amphiphilic homopolymers could bring about some certain attractive properties and applications.²⁹ However, the studies on the synthesis and self-assembly of amphiphilic homopolymers are still largely unexplored.^{22–31}

In order to enhance our understanding on the self-assembly of amphiphilic homopolymers and exploring their applications, it is of great importance to synthesize amphiphilic homopolymer with functional building blocks and investigate their self-assembly behaviors. Organometallic polymers are considered as interesting building blocks for novel materials due to some unusual and attractive characteristics including electrical, magnetic, catalytic, and nonlinear optical properties.³² Among organometallic materials, ferrocene-containing polymers have received increasing consideration in light of their applications in semiconductors, sensors, photonic crystals, etching resists, redox-responsive gels, and so on.³³ Winnik and Manner have prepared a variety of well-defined cylinder micelles and comicelles through the “crystalline-driven self-assembly” of polyferrocenylsilane-based copolymers, in which the excellent crystallization property of ferrocene-based repeating unit was a

crucial parameter for micellar morphologies.^{34–36} In addition, the ferrocene group can form a 1:1 stable adduct with β -CD in aqueous solution, which are oligosaccharides composed of seven D-glucopyranose residues attached by α -1,4-linkages in a cyclic array.^{37,38} The fundamental driving force of inclusion complexation of β -CD with ferrocene group is the hydrophobic interaction, which pushes the hydrophobic ferrocene group into the hydrophobic internal cavity of β -CD.^{37,38} Because the exterior of β -CD is highly polar due to the presence of hydroxyls, the complex of β -CD with ferrocene group is hydrophilic. Thus, the incorporation of β -CD into a ferrocene-containing polymer will significantly change the “water solubility” of the polymer, which could be employed to tune the solubility and self-assembly of ferrocene-containing polymers.^{39–43} Given these aforementioned attractive properties of ferrocene group, the ferrocene group is chosen as a hydrophobic building block for constructing amphiphilic homopolymer in the current work. Moreover, carboxyl is chosen as the hydrophilic building block since it render the formed aggregates able to introduce biomacromolecules, fluorescent label molecules, drugs, or inorganic nanoparticles via electrostatic interaction or 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide hydrochloride (EDC) chemistry.^{29,44,45}

In this work, we first synthesized a series of ferrocene-containing amphiphilic homopolymers through RAFT homopolymerization of acrylamide monomers consisting of both ferrocene and *tert*-butyl ester groups, a potential carboxyl, and the sequential acidic hydrolysis of *tert*-butoxycarbonyl into carboxyl as shown in Scheme 1A. We examined the influence of polymer concentration, pH, the amount of β -CD, and the

length of linker between ferrocene group and carboxyl on the self-assembly behaviors of amphiphilic homopolymers by transmission emission microscopy (TEM), dynamic light scattering (DLS), and atomic force microscopy (AFM). Large compound micelles with different morphologies were formed by these amphiphilic copolymers, which consist of the corona formed by hydrophilic carboxyls and the core containing numerous reverse micelles with hydrophilic islands of carboxyls in continuous hydrophobic phase of ferrocene-based segments. A variety of micellar morphologies were observed including sphere, bowl shape, fiber, spindle, and connected-spindle, which could be tuned by the concentration of amphiphilic homopolymers, pH value of the solution, the length of $-CH_2-$ linker between ferrocene group and carboxyl, and the amount of β -cyclodextrin (β -CD).

EXPERIMENTAL SECTION

Materials. Details of synthesis of amphiphilic homopolymers **6** and model organic compound **8** (Scheme 1) are all presented in the Supporting Information.

Measurements. FT-IR spectra were recorded on a Nicolet AVATAR-360 FT-IR spectrophotometer with a resolution of 4 cm^{-1} . All ^1H (500 MHz) and ^{13}C (125 MHz) NMR analyses were performed on a Bruker Avance 500 spectrometer; tetramethylsilane (^1H NMR) and CDCl_3 (^{13}C NMR) were used as internal standards. Electron ionization mass spectrometry (EI-MS) was measured by an Agilent 5937N system. Absolute molecular weights were determined by GPC equipped with a multiangle light scattering detector (GPC/MALS). DMF was used as solvent with a flow rate of 1.0 mL/min ; detectors: Wyatt Optilab rEX refractive index detector and Wyatt DAWN HELEOS 18-angle light scattering detector. Hydrodynamic diameter (D_h) was measured by DLS with a Malvern Nano-ZS90 Zetasizer. AFM image was performed by a Veeco Nanoscope IV-MultiMode microscope. TEM images were obtained by a JEOL JEM-1230 instrument operated at 80 kV .

TEM Image. 2.0 mL of redistilled water was added slowly (0.8 mL/h) to 1.0 mL of DMSO solution of amphiphilic homopolymer (0.4 mg/mL), and DMSO was removed by dialysis. When the influence of β -CD on self-assembly behaviors was studied, β -CD was added into the solution followed by stirring at $25\text{ }^\circ\text{C}$ for 12 h . When the influence of pH on self-assembly behaviors was studied, basic aqueous solution ($\text{pH} = 10$) was added instead of redistilled water. For TEM measurement, $10\text{ }\mu\text{L}$ of micellar solution was deposited on an electron microscopy copper grid coated with carbon film and the water evaporated at room temperature.

AFM Image. For AFM measurement, $10\text{ }\mu\text{L}$ of micellar solution was deposited on a piece of freshly cleaved mica, water evaporated at room temperature. AFM image was obtained with tapping mode using standard Si probe.

RESULTS AND DISCUSSION

Monomer Synthesis. The key in the preparation of amphiphilic homopolymer is to incorporate a polymerizable group, hydrophilic functionality, and hydrophobic moiety within a monomer. In 2004, Thayumanavan et al. employed a styrene-based strategy, where hydrophilic carboxyl and hydrophobic benzyl functionalities were substituted at the 3- and 5-positions of benzene ring of a styryl group.²³ In 2006, the same group developed an acrylamide strategy to expand the scope of amphiphilic homopolymer, where the secondary amine of glycines derivatized with alkyl chains with different lengths was reacted with an acryloyl chloride, followed by the hydrolysis of ester group of the glycine.²⁴ Inspired by these results, we developed a similar acrylamide strategy to prepare ferrocene-based amphiphilic homopolymers as shown in Scheme 1A. The monomer containing a ferrocene group and *tert*-butyl ester

group (a precursor of carboxyl) was synthesized by three steps using commercially available ferrocenecarboxylic acid as starting material. A key feature of this synthesis was that amino group was employed as a bridge to connect ferrocene group, *tert*-butyl ester group, and acrylamide group together.

In order to study the influence of the length of linker between carboxyl and ferrocene group on the self-assembly of ferrocene-based amphiphilic homopolymers, three different molecules (1,2-diaminoethane, 1,6-diaminohexane, and 1,10-diaminodecane) were incorporated into the monomer. The chemical structures of these three monomers were confirmed on the basis of ^1H NMR, ^{13}C NMR, FT-IR, and EI-MS. Figure 1A shows ^1H NMR spectrum of monomer **4b**, which exhibits

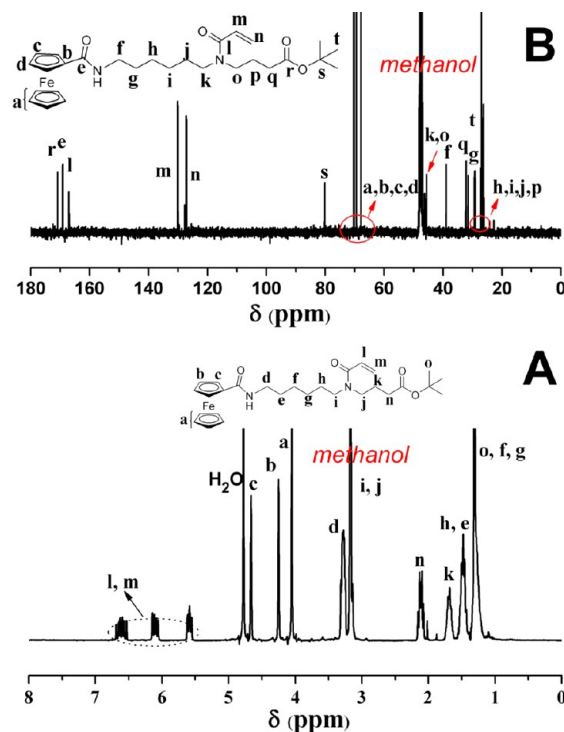


Figure 1. ^1H (A) and ^{13}C (B) NMR spectra of acrylamide **4b** in CD_3OD .

the typical proton resonance signals of double bond at 5.69, 6.36, and 6.57 ppm (peaks "l" and "m"), ferrocene moiety at 4.22, 4.37, and 4.68 ppm (peaks "a", "b", and "c"), and *tert*-butyl at 1.44 ppm (peak "o"). The existence of characteristic peaks of a double bond at 127.7 and 130.5 ppm, a ferrocene group at 67.9, 69.4, and 70.3 ppm, and *tert*-butyl at 26.9 and 80.3 ppm in the ^{13}C NMR spectrum (Figure 1B) also verified the structure of **4b**. Similar results were also obtained for **4a** and **4c**.

Synthesis of Ferrocene-Based Homopolymers via RAFT. RAFT polymerization is a versatile process in terms of reaction conditions, variety of monomers, and tolerance of monomer functionalities.^{46,47} Previous results have shown that cumyl dithiobenzoate (CDB) is one of the effective chain transfer agents (CTA) for RAFT of acrylamide.⁴⁷ Lu and co-workers reported the preparation of polymers containing both an aldehyde and a ferrocene group with a narrow molecular weight distribution by RAFT polymerization.⁴⁸ Zhu et al. reported the preparation of well-defined polystyrene using a ferrocene-based CTA.⁴⁹ These results demonstrated that ferrocene group would not affect RAFT polymerization. In

the present work, monomers **4** were homopolymerized via RAFT polymerization in dioxane at 90 °C using AIBN as initiator and CDB as CTA, and the results are summarized in Table 1.

Table 1. Synthesis of Ferrocene-Based Homopolymer **5 by RAFT Polymerization^a**

sample	$M_{n, \text{GPC/MALS}}^b$ (g/mol)	M_w/M_n^b	dn/dc^b (mL/g)
5a	15 200	1.24	0.117
5b	34 600	1.30	0.104
5c	39 600	1.36	0.119

^a[**4**] = 1.0 M, [**4**]:[CDB]:[AIBN] = 100:3:1, polymerization temperature: 90 °C. ^bMeasured by GPC/MALS in DMF.

After RAFT homopolymerization, the disappearance of the resonance signals of double bond in the ¹H NMR spectrum (Figure 2A) showed the performance of the polymerization of

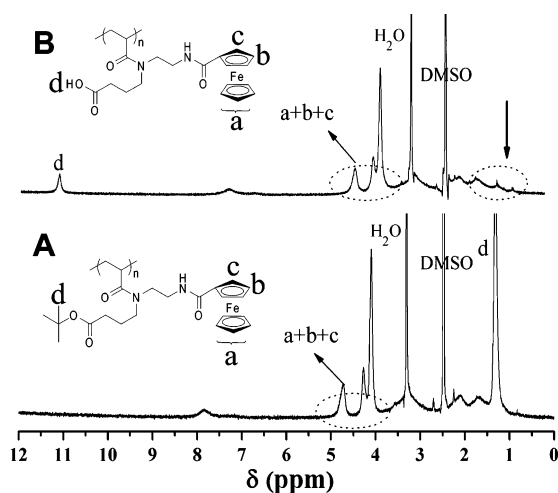


Figure 2. ¹H NMR spectra of homopolymers of **5a** (A) and **6a** (B) in DMSO-*d*₆.

monomer **4**. The resonance signals of a ferrocene group at 4.09, 4.28, and 4.72 ppm (peaks “a”, “b”, and “c”) and a *tert*-butyl at 1.37 ppm (peak “d”) still appeared in Figure 2A. Moreover, every GPC curve of homopolymer **5** showed a unimodal and symmetrical peak with narrow molecular weight distribution ($M_w/M_n \leq 1.36$) as shown in Figure 3, which is the characteristic of RAFT polymerization and confirmed the formation of well-defined ferrocene-containing polymers.

Preparation of Ferrocene-Based Amphiphilic Homopolymer. Previous studies have showed that *tert*-butoxycarbonyl could be efficiently hydrolyzed by trifluoroacetic acid in CH₂Cl₂.^{50–52} In order to make sure whether trifluoroacetic acid would break the chemical structure of the polymer, a small molecular model reaction was conducted. First, a small molecule possessing the same chemical structure as that of the repeating unit of homopolymer **5a** was synthesized as shown in Scheme 1B. As shown in Figure S1A, the typical proton resonance signals of ferrocene group at 4.18, 4.32, and 4.70 ppm (peaks “a”, “b”, and “c”) and *tert*-butyl at 1.45 ppm (peak “k”) of compound **7** could be found. After the reaction with trifluoroacetic acid, the signal for nine protons of *tert*-butyl (1.45 ppm) of compound **7** completely disappeared (Figure S1B), while the characteristic peaks of other groups of the molecule still remained after the hydrolysis reaction (Figure

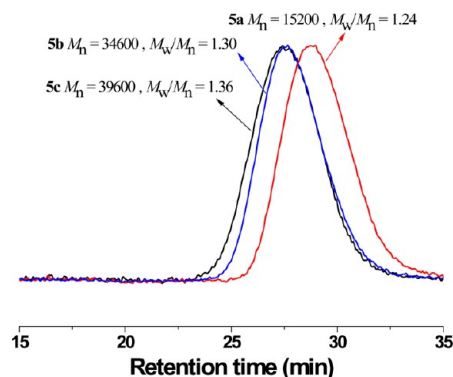


Figure 3. GPC traces of homopolymer **5**.

S1B), which was further confirmed by ¹³C NMR, FT-IR, and EI-MS. The almost quantitative yield of 96.2% for the hydrolysis reaction, which was measured after the purification by silica chromatography, illustrated that under this condition *tert*-butoxycarbonyl could be completely hydrolyzed to carboxyl without affecting other groups of the molecule.

Therefore, the ferrocene-based homopolymer **5** was treated with trifluoroacetic acid in CH₂Cl₂ for transforming *tert*-butoxycarbonyl into carboxyl. Figure 2B shows ¹H NMR spectrum of the hydrolyzed products **6a** from **5a** and the signal of nine protons of *tert*-butyl at 1.37 ppm entirely completed. Besides, a new peak located at 12.0 ppm appeared in Figure 2B, which corresponded to the proton of –COOH. Figure 4 show

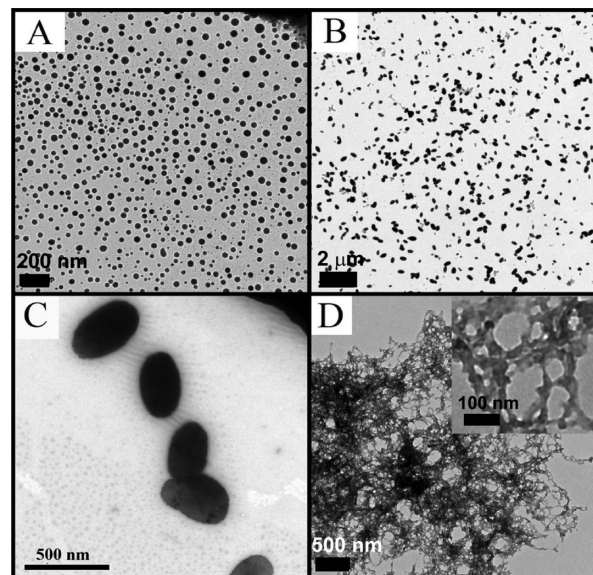


Figure 4. TEM images of micelles formed by **6b** with different initial concentrations of 0.2 (A), 0.4 (B, C), and 0.8 (D) mg/mL. Inset of (D) is a TEM image with a higher magnification of the micelles.

FT-IR spectra before and after the hydrolysis. We can notice that a much stronger peak at 3360 cm^{–1} and a weaker peak at 1156 cm^{–1} appeared in the FT-IR spectrum after the hydrolysis (Figure S2B) in comparison with that before the hydrolysis (Figure S2A), which was attributed to the newly formed carboxyl and disappeared *tert*-butyl after the hydrolysis. These observations further indicated the presence of the –COOH group and the hydrolysis of *tert*-butoxycarbonyl. It should be noted that typical signals of other groups in the homopolymer

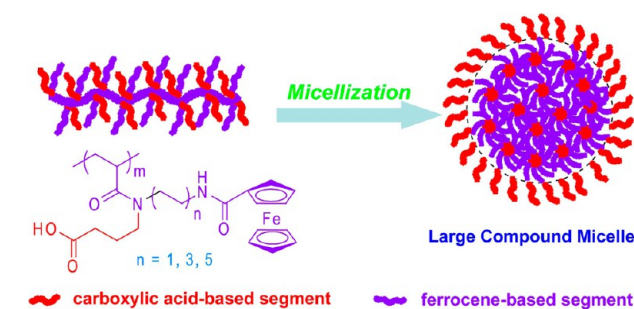
were found to remain in the ^1H NMR spectrum after the hydrolysis, which suggested that other groups in the homopolymer kept inert during the hydrolysis, consistent with the results obtained from the small molecular model reaction. Thus, all above-mentioned results evidenced the completely hydrolysis of *tert*-butoxycarbonyl in homopolymer 5 so that homopolymer 5 was converted to homopolymer 6 containing hydrophilic carboxyl in every repeating unit.

Self-Assembly Behavior of Ferrocene-Based Amphiphilic Homopolymer. Block copolymers consisting of both a hydrophilic segment and a hydrophobic segment are often the choice for the preparation of nano- or microsupramolecular assemblies.^{1–12} The driving force for the self-assembly is the immiscibility of the segments and/or the immiscibility of one of the segments in certain solvent. Significant attention has been paid to the self-assembly of amphiphilic block copolymers due to the fact that a variety of interesting nanostructures with different morphologies, including sphere, tube, vesicle, cylinder, and so on, could be formed.^{1–12} Recently, Thayumanavan and co-workers reported that micelle could also be formed through the intramolecular phase separation of amphiphilic homopolymers, in which hydrophilic carboxyl functionality and hydrophobic benzyl or alkyl moiety were incorporated into the same repeated unit.²³ In the current case, the ferrocene group and carboxyl were introduced into the same repeating unit, and self-assembly behavior of this new amphiphilic homopolymer was investigated in detail.

Influence of Concentration of Amphiphilic Homopolymer 6 on Self-Assembly. We first examined the influence of concentration of homopolymer 6b on its self-assembly behavior. Different amounts of amphiphilic homopolymer 6b (0.2, 0.4, or 0.8 mg) were dissolved in 1.0 mL of DMSO. Redistilled H_2O (2.0 mL) was added into the solution slowly (0.8 mL/h) by a syringe pump. DMSO was removed by dialysis with water for 5 days, and the final volumes of solutions were adjusted to 4.0 mL by adding another certain amount of water.

Aliquots with an initial concentration of 0.2 mg/mL examined by TEM showed the presence of spherical micelles with a diameter of 85 nm obtained by DLS as shown in Figure 4A. It should be noted that the maximum length of the repeating unit of homopolymer 6b is around 2.7 nm estimated by ChemOffice software. Therefore, the largest diameter of spherical micelles formed from homopolymer 6b should be smaller than 5.4 nm supposing that hydrophobic segment is located in the core of the micelle and hydrophilic segment covers the core to stabilize the micelle in a typical fashion. Here, the size of spherical micelles (85 nm) was much larger than 5.4 nm. A similar phenomenon was encountered during the investigation of self-assembly of PS_{200} -*b*- PAA_4 diblock copolymer, in which large micelles with a diameter of $\sim 1\ \mu\text{m}$ were observed, much larger than the length of the diblock copolymer.⁵³ The authors examined the internal structure of these micelles and found that reverse micelles with PAA as core and PS as corona constituted the core of the micelles and the outer surface of the large micelles were the short PAA chains. This kind of micelle was named as a large compound micelle. In the current work, large compound micelles were supposed to be formed by homopolymer 6b, in which hydrophilic carboxyls formed the corona of micelles and the core consisted of numerous reverse micelles with hydrophilic islands of carboxyls in continuous hydrophobic phase of ferrocene-based segments as shown in Scheme 2.

Scheme 2. Formation of Large Compound Micelles by Homopolymer 6



When the initial concentration of homopolymer 6b was increased to 0.4 mg/mL, spindle-like micelles were observed with a length of about 350 nm and a width of about 200 nm as shown in Figures 4B and 4C. Lin et al. found that poly(γ -benzyl-L-glutamate)-*graft*-poly(ethylene glycol) (PBLG-*g*-PEG) rod-coil graft copolymers could form spindle-like micelles in ethanol and water under some certain conditions.^{54,55} For these spindle-like micelles, PBLG blocks within the aggregate cores took rigid helix conformation and aligned with each other adopting a side-by-side packing fashion with their direction paralleled with the axial direction of the micelle, and protruded PEG chains were excluded out of PBLG aggregate core to form a shell, stabilizing the formed micelle. Such a kind of packing model is also revealed by a Brownian dynamic stimulation on the investigation of micellar structure of amphiphilic T-shaped graft copolymer consisting of a rigid backbone and flexible side chains in a selective solvent for the side chain by Jo et al.⁵⁶ In addition, Lin et al. found that spindle-like micelles formed by PBLG-*g*-PEG diblock copolymer transformed into spherical large compound micelle as the conformation of PBLG block changed from rigid helix to random coil by adding denaturant trifluoroacetic acid.⁵⁵ These results indicated that the ability of the segment within the core of a micelle to form a rigid and ordered packing conformation was one of the most important factors in the formation of spindle-like micelles. Considering the rigidity and crystalline of ferrocene group,^{34–36} ordered packing of ferrocene-based segments of homopolymer 6b might exist within the core of spindle-like micelles.

As the initial concentration of homopolymer 6b was increased to 0.8 mg/mL, connected-spindle micelles with a width of around 40 nm were observed in Figure 4D. These observations indicated that the initial concentration of homopolymer 6 played an important role in determining the final micellar morphology. Eisenberg et al. examined the self-assembly of PS_{190} -*b*- PAA_{20} with different initial polymer concentrations in the mixture of DMF/water.⁵⁷ They found that with the increasing of the polymer concentration the morphology of the aggregates changed in the direction from spheres to rod-like micelles, to interconnected rods, and then to bilayers. In the current case, as the initial concentration increased, micelles transformed in the direction from spherical micelles with a diameter of around 80 nm, to spindle-like micelles with a length of about 350 nm and a width of about 200 nm, and then to connected-spindle-like micelles, this indicating the enlargement of aggregation number of the micelles. In order to reduce the entropic penalty resulting from the increasing in the degree of stretching of ferrocene-based hydrophobic segment as the polymer concentration increased,

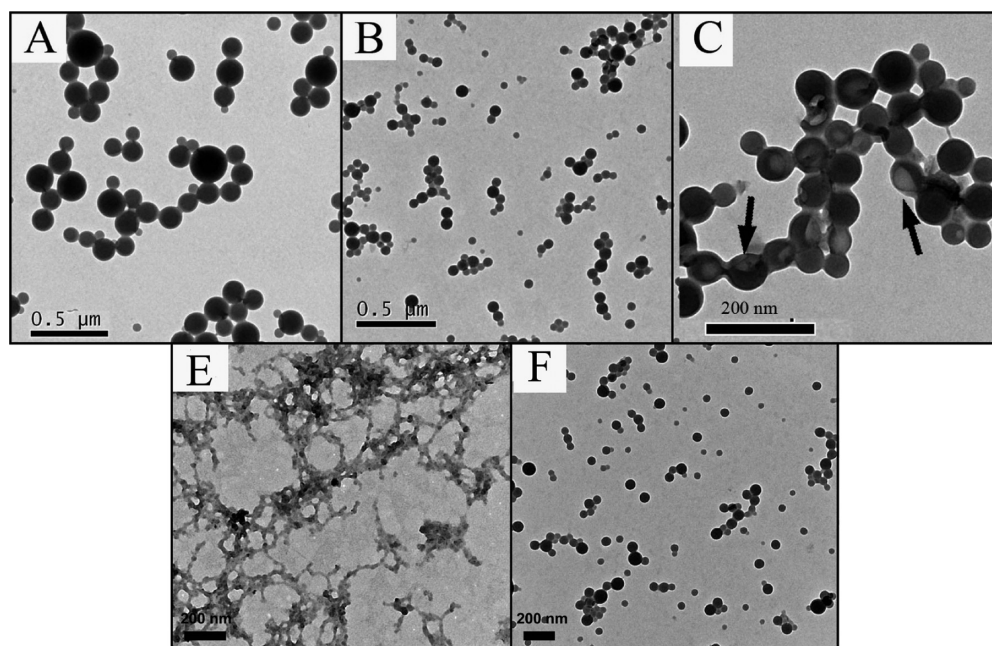


Figure 5. TEM images of micelles formed by **6b** with 0.25 (A), 0.50 (B), and 1.0 equiv (C) of β -CD based on ferrocene groups; **6a** (D) and **6c** (E) with 1.0 equiv of β -CD based on ferrocene groups. The initial concentration of amphiphilic homopolymer **6b** was 0.4 mg/mL.

micellar morphology changed from sphere to spindle-like correspondingly.⁵⁷

Influence of Amount of β -CD on Self-Assembly of Amphiphilic Homopolymer 6. β -CD, containing seven D-glucopyranose residues attached by α -1,4-linkages in a cyclic array, has a rigid conical molecular structure with a hollow interior of a specific volume. The exterior of β -CD with hydroxyls is sufficiently hydrophilic to impact its water solubility. In contrast, the internal cavity of β -CD is highly hydrophobic, which can host a variety of guest molecules, including aliphatic, aromatic hydrocarbons, and organometallic complex driven by van der Waals forces, hydrophobic interactions, electronic effects, and steric factors.^{37,38} Previous studies showed that the ferrocene group could form a 1:1 adduct with β -CD in DMSO with an association constant of 60 M^{-1} , 20% aqueous DMSO with an association constant of 320 M^{-1} , or water with an association constant of $1.65 \times 10^4 M^{-1}$,^{58,59} which indicated all of ferrocene groups would be hosted in the cavity of β -CD when the molar ratio of ferrocene to β -CD is 1:1 in water. Moreover, the complex of β -CD with ferrocene group is thermally stable and do not liberate ferrocene group even on heating at 100 $^{\circ}C$ *in vacuo*.⁶⁰

Ferrocene group is hydrophobic, while the complex of ferrocene group with β -CD is hydrophilic. The addition of β -CD into amphiphilic homopolymer solution would make the “ferrocene part” hydrophilic since the ferrocene group would be hosted into the hydrophobic cavity of hydrophilic β -CD, which would change the ratio of hydrophilic segment to hydrophobic segment in the amphiphilic homopolymer. The studies on the influence of addition of β -CD on the self-assembly of amphiphilic homopolymer will deepen our understanding about self-assembled behaviors of this kind of amphiphilic homopolymer. Furthermore, after the incorporation of β -CD into the corona of micelles, lots of free hydroxyls located on the exterior of β -CD will provide more reactive sites for the modification of obtained micelles for further applications.

In order to study the influence of the amount of β -CD on the self-assembly of ferrocene-based amphiphilic homopolymers, different amounts of β -CD ($[\beta\text{-CD}]:[\text{ferrocene groups}] = 0.25:1, 0.50:1, \text{ and } 1:1$) were added into 1 mL of DMSO solution of **6b** (0.4 mg/mL), respectively. The solutions were stirred for 24 h at room temperature, and 2.0 mL of redistilled water was added into the solution with a rate of 0.8 mL/h. Subsequently, DMSO was removed from the solutions by dialysis in water, and the final volumes of solutions were tuned to 4.0 mL by adding a certain amount of water.

Because the ferrocene group could form a 1:1 adduct with β -CD in DMSO with an association constant of 60 M^{-1} , 88.6% of β -CD was associated with ferrocene groups in DMSO solution while 99.4% and 98.4% of β -CD were associated with ferrocene groups in DMSO solution with the molar ratio of β -CD to ferrocene groups of 0.25:1 and 0.5:1, respectively. The increase in the content of water would not only facilitate the formation of micelles but also facilitate the association of ferrocene groups with β -CD. Therefore, almost all of β -CD already formed the complex with ferrocene before the micellization.

Changes in the morphology of the self-assembly of amphiphilic homopolymers after the addition of different amounts of β -CD were examined by TEM and AFM. Aliquots from these micelle solutions were taken after the dialysis, followed by TEM and AFM analysis. Without the addition of β -CD, homopolymer **6b** with an initial concentration of 0.4 mg/mL self-assembled into spindle-like micelles with a length of around 350 nm and a width of around 200 nm in water as shown in Figures 4B and 4C. The morphology turned into spheres with a diameter of 235 nm determined by DLS after 0.25 equiv of β -CD based on ferrocene groups was added as shown in Figure 5A. The diameter of spherical micelles decreased to 155 nm (Figure 5B) after 0.50 equiv of β -CD was added. After β -CD was added into the solution before the formation of micelles, ferrocene groups would be adducted into the cavity of β -CD and hydrophobic ferrocene groups would be covered by hydrophilic β -CD. The content of hydrophobic

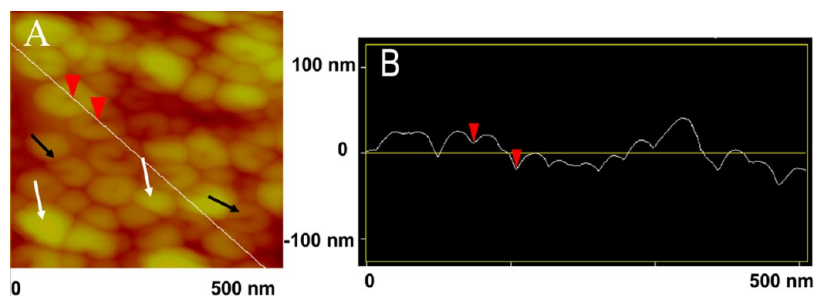


Figure 6. Tapping mode AFM image of bowl-shaped micelles self-assembled from homopolymer **6b** with 1.0 equiv of β -CD based on ferrocene groups: (A) height image and (B) section analysis of the micelles.

segments would decrease and hydrophilic segments would increase correspondingly, which would lead to the increase of repulsion in the corona.^{1,2,57} The increase in steric repulsion resulted in the change of morphology from spindles to spheres after the addition of 0.25 equiv of β -CD because spherical morphology possesses a larger interfacial area, which could release the repulsion between the corona chains.^{1,2,57} As more β -CD was added, the content of hydrophobic segments decreased further and hydrophilic segments increased correspondingly, this resulting in further increase in the steric repulsion between the corona segments, which would facilitate the formation of smaller spherical micelles with a much larger interfacial area.⁵⁷

Interestingly, after the molar ratio of β -CD to ferrocene groups was increased to 1:1, bowl-shaped micelles with a size of around 90 nm were found in Figure 5C. Bowl-shaped micelle is a kind of large compound micelle with a cavity in each aggregate.^{60–63} The structure of bowl-shaped micelle is similar to that of vesicle. However, the difference between vesicle and bowl-like micelle in TEM image is the location of “hollow”. For vesicle, the location of “hollow” is in the center of the micelle since vesicle is symmetrical structure and only the wall of vesicle could be observed in bright field TEM; on the contrary, bowl-shaped micelle is unsymmetrical structure, and “hollow” could locate in the edge of the micelle. Thus, the “hollow” could be observed in the center or edge of the micelle in bright field TEM. From the image shown in Figure 5C, we could find that most of “hollows” were in the edge of the micelles, which suggested that these were bowl-shaped micelles, not vesicles.

Tapping mode AFM test was conducted, and the image is shown in Figure 6. A brightness difference was observed in AFM height image (Figure 6A). One can notice that some “shadow” areas were located in the center or edge of the micelles as highlighted by the black arrows. It can be seen from Figure 6B that the “shadow” areas indicated lower domains in the micelles, indicative of the “hollow” of the micelles. We could also note that there was not “hollow” in part of micelles as highlighted by the white arrows. This phenomenon was reasonable. If the hollow of the micelles in the bottom of the micelles, they could not be detected by AFM since AFM just could provide information about the surfaces of the structures. On the contrary, if the hollows in the top or side of the micelles, they could be detected as depression in the image. This observation further proved the bowl-shaped morphology of micelles.

In 2002, Eisenberg and co-workers reported the formation of bowl-shaped micelles from poly[5-(*N,N,N*-diethylmethylammonium)isoprene]-*b*-polystyrene-*b*-poly[5-(*N,N,N*-diethylmethylammonium)isoprene], and a possible

mechanism for the formation of this aggregate was proposed.⁶¹ When water was added into DMF solution of the triblock copolymer, large compound micelles were formed, in which DMF and water were trapped inside the micelles. Because of the relatively high content of DMF in the micelles at the beginning, the viscosity of the core of micelles was low and the chain mobility was high. Therefore, the diffusion of solvent including water and DMF out and into micelles was rapid. In this stage, liquid–liquid phase separation occurred inside the core of micelles, and bubbles filled with solvent formed in the interior of the micelles. Upon further addition of water, the viscosity of the core became higher and mobility of the chains became lower due to the extraction of DMF from the micelles. At this stage, the interior viscosity was not so high for the solvent bubbles inside the core to coalesce and broke through the surface of the micelles, but it was high enough to restrict the mobility of the chains and the shrinkage of micelles could not occurred after the breakthrough of solvent bubbles. Then, bowl-shaped micelles formed. Thus, the internal viscosity of micelles played an important role in the formation of bowl-shaped micelles, and the viscosity window for the formation of bowl-shaped micelles must be very narrow. Except for the solvent, the initial concentration of copolymer, the composition of copolymer, and the molecular weight of copolymer, some other viscosity-controlled factors were essential.^{61–63} The authors speculated that the aminoisoprene blocks in the triblock copolymer might provide extra physical cross-linking, which would increase the interior viscosity of the micelles during the formation of bowl-shaped micelles. The same group also observed bowl-shaped aggregates during the investigation of the self-assembly of poly(styrene-*co*-methacrylate acid) random copolymer, in which hydrogen bonding between methacrylic acid units was likely to provide extra viscosity control.⁶² Jiang et al. also prepared bowl-shaped micelles from polyimide with two carboxyl ends. It was assumed that the rigidity of the backbone and carboxyl ends provided extra viscosity control mechanism.⁶³

In the current work, the mechanism for the formation of bowl-shaped micelle was similar to that proposed by Eisenberg et al. The complex of β -CD with ferrocene group was relatively rigid, and the possibility of the formation of hydrogen bonding between hydroxyls in β -CD and carboxyls in backbone increased after the introduction of β -CD. Previous studies indicated that the internal viscosity of micelles must be in very narrow range for the formation of bowl-shaped micelles. When 1 equiv of β -CD was incorporated into the homopolymer through the association of β -CD with ferrocene groups, the rigidity of the homopolymers and possibility of formation of hydrogen bonding increased, which might provide appropriate

viscosity control for the formation of bowl-shaped micelles. Interestingly, for homopolymers **6a** and **6c**, which had shorter and longer carbon chain between ferrocene group and carbonyl respectively, the addition of 1 equiv of β -CD did not yield the bowl-shaped aggregates under the same preparative conditions. Instead, fibers with a width of 20 nm and spheres with a diameter of 95 nm were observed for **6a** (Figure 5E) and **6c** (Figure 5F), respectively. Thus, while the addition of 1 equiv of β -CD benefited the formation of bowl-shaped aggregates, the bowl-shaped aggregates formed by homopolymer **6b** apparently reflected that the viscosity control mechanism for the formation of bowl-shaped aggregates was very sensitive to the structure of the homopolymers. On the other hand, the results indicated that micellar morphologies of these amphiphilic homopolymers could be tuned through the adjusting the length of linker between ferrocene group and carbonyl.

Influence of pH on Self-Assembly of Amphiphilic Homopolymer 6. The protonation–deprotonation of carboxyls in the amphiphilic homopolymer is highly affected by pH of the solution because carboxyl is a kind of weak acid and its pK_a is around 4.25, which means that only around 10–13% of carboxyls are in the state of deprotonation in pure water.⁶⁴ When pH of the solution is increased to 10.0, carboxyls would almost completely be in the state of deprotonation. In pure water, diverse micellar morphologies formed by homopolymer **6b** were observed. We were curious about whether the diverse nano- or microstructures could be formed in alkaline environment as the concentration of amphiphilic homopolymers and the amount of β -CD changed. Therefore, we examined the influence of the concentration of homopolymer **6b** and the amount of β -CD on the self-assembly of **6b** in alkaline solution (pH = 10.0). The aqueous alkaline solution (pH = 10.0) was used to prepare micelle solution instead of pure water, and the other procedures were the same as before.

Figure 7 show TEM images of the micelles formed in alkaline solution (pH = 10.0). Micellar morphologies formed by homopolymer **6b** at three different initial concentrations of 0.2, 0.4, and 0.8 mg/mL were all spheres as shown in Figures 7A, 7B, and 7C, respectively, and the diameters of spheres were 137, 287, and 316 nm determined by DLS (Figure 7F) for the micelles formed at the initial concentrations of 0.2, 0.4, and 0.8 mg/mL, which indicated that the size of spherical micelles raised as the concentration of **6b** increased. The influence of β -CD was checked with an initial concentration of 0.4 mg/mL. When 0.5 equiv of β -CD based on the ferrocene groups was added, spherical micelles with an average diameter of 169 nm was observed in Figure 7D, which was smaller compared to the micelles formed without β -CD in Figure 7B. The size of spherical micelles became smaller to 90 nm (Figure 7E) as more β -CD (1.0 equiv) was added. It should be noted that as water was replaced by alkaline aqueous solution with a pH value of 10.0, the morphology transformed from bowl shape (Figure 5C) to sphere (Figure 7E), which indicated that pH of the solution was also one of important viscosity controlling factors during the micellization process of homopolymer **6b**. Furthermore, these observations suggested that the size of spherical micelles formed by homopolymer **6b** could be adjusted through the changing of the concentration of amphiphilic homopolymers and the amount of β -CD under alkaline conditions.

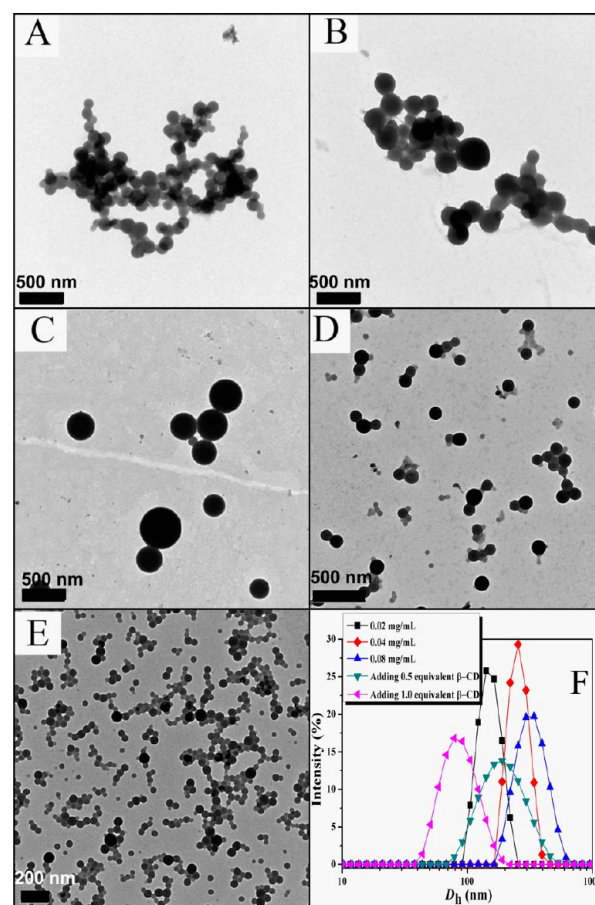


Figure 7. TEM images of the micelles formed by **6b** in alkaline aqueous solution (pH = 10.0) with different initial concentrations and amounts of β -CD, (A) 0.2, (B) 0.4, and (C) 0.8 mg/mL; 0.4 mg/mL with 0.5 (D) and 1.0 equiv (E) of β -CD based on ferrocene group; (F) D_h distributions of micelles prepared under different conditions.

CONCLUSIONS

Through RAFT homopolymerization and the sequential selective hydrolysis, a series of amphiphilic ferrocene-containing homopolymers were prepared. These amphiphilic homopolymers could self-assemble into diverse nano- or microstructures, including spheres, fibers, bowl-shaped micelles, spindle-like, and connected-spindle-like micelles, in water upon changing the concentration of amphiphilic homopolymers, pH value, the amount of β -CD, and the length of linker between ferrocene group and carbonyl. In particular, to our best knowledge, although a variety of micellar morphologies have been observed in self-assembly of amphiphilic copolymers to date, this is the first time that new spindle-like and bowl-shaped micelles were formed via the self-assembly of amphiphilic homopolymers.

Given the fact that β -CD could be incorporated into the corona of micelles through its complexation with ferrocene group, a large amount of hydroxyls of β -CD would be available for the further functionalization of the formed micelles; on the other hand, the complex of β -CD with ferrocene group could be adjusted through the reversible redox reaction of ferrocene group to construct a redox-responsive micellization system. In addition, these large compound micelles containing both hydrophobic and hydrophilic domains within the core could be loaded both hydrophilic and hydrophobic moieties, while

the common micelle just could be loaded with hydrophobic matters. Thus, this kind of micelle should have broader applications in controllable release and extraction.

■ ASSOCIATED CONTENT

■ Supporting Information

Materials employed for, and details of, the synthesis of amphiphilic homopolymers **6** and compound **8**, ^1H NMR spectra of compounds **7** and **8**, and FT-IR spectra of **5a** and **6a**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail xyhuang@mail.sioc.ac.cn; Tel +86-21-54925310; Fax +86-21-64166128 (X.H.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the financial support from National Natural Science Foundation of China (21174158 and 21274162) and Shanghai Scientific and Technological Innovation Project (12JC1410500).

■ REFERENCES

- (1) Zhang, L. F.; Eisenberg, A. Multiple morphologies of "crew-cut" aggregates of polystyrene-*b*-poly(acrylic acid) block copolymers. *Science* **1995**, *268*, 1728–1731.
- (2) Zhang, L. F.; Yu, K.; Eisenberg, A. Ion-induced morphological changes in "crew-cut" aggregates of amphiphilic block copolymers. *Science* **1996**, *272*, 1777–1779.
- (3) Van Hest, J. C. M.; Delnoye, D. A. P.; Baars, M. W. P. L.; Van Genderen, M. H. P.; Meijer, E. W. Polystyrene-dendrimer amphiphilic block copolymers with a generation-dependent aggregation. *Science* **1995**, *268*, 1592–1595.
- (4) Discher, D. E.; Eisenberg, A. Polymer vesicles. *Science* **2002**, *297*, 967–973.
- (5) Jia, L.; Liu, M.; Di Cicco, A.; Albouy, P. A.; Brissault, B.; Penelle, J.; Boileau, S.; Barbier, V.; Li, M. H. Self-assembly of amphiphilic liquid crystal polymers obtained from a cyclopropane-1,1-dicarboxylate bearing a cholesteryl mesogen. *Langmuir* **2012**, *28*, 11215–11224.
- (6) Adams, D. J.; Holtzmann, K.; Schneider, C.; Butler, M. F. Self-assembly of surfactant-like peptides. *Langmuir* **2007**, *23*, 12729–12736.
- (7) Yin, L. G.; Hillmyer, M. A. Disklike micelles in water from polyethylene-containing diblock copolymers. *Macromolecules* **2011**, *44*, 3021–3028.
- (8) Edmonds, W. F.; Li, Z. B.; Hillmyer, M. A.; Lodge, T. P. Disk micelles from nonionic coil-coil diblock copolymers. *Macromolecules* **2006**, *39*, 4526–4530.
- (9) Liu, C.; Hillmyer, M. A.; Lodge, T. P. Evolution of multicompartment micelles to mixed corona micelles using solvent mixtures. *Langmuir* **2008**, *24*, 12001–12009.
- (10) Li, Z. B.; Hillmyer, M. A.; Lodge, T. P. Laterally nanostructured vesicles, polygonal bilayersheets, and segmented wormlike micelles. *Nano Lett.* **2006**, *6*, 1245–1249.
- (11) Pochan, D. J.; Zhu, J.; Zhang, K.; Wooley, K. L.; Miesch, C.; Emrick, T. Multicompartment and multigeometry nanoparticle assembly. *Soft Matter* **2011**, *7*, 2500–2506.
- (12) Cui, H.; Chen, Z.; Zhong, S.; Wooley, K. L.; Pochan, D. J. Block copolymer assembly via kinetic control. *Science* **2007**, *317*, 647–650.
- (13) Sebakhy, K. O.; Kessel, S.; Monteiro, M. J. Nanoreactors to synthesize well-defined polymer nanoparticles: decoupling particle size from molecular weight. *Macromolecules* **2010**, *43*, 9598–9600.
- (14) Nystrom, A. M.; Xu, Z.; Xu, J.; Taylor, S.; Nittis, T.; Stewart, S. A.; Leonard, J.; Wooley, K. L. SCKs as nanoparticle carriers of doxorubicin investigation of core composition on the loading, release and cytotoxicity profiles. *Chem. Commun.* **2008**, 3579–3581.
- (15) Lee, N. S.; Sun, G.; Neumann, W. L.; Freskos, J. N.; Shieh, J. J.; Dorshow, R. B.; Wooley, K. L. Photonic shell-crosslinked nanoparticle probes for optical imaging and monitoring. *Adv. Mater.* **2009**, *20*, 1344–1348.
- (16) González-Toro, D.; Savariar, E. N.; Thayumanavan, S. Fluorescence patterns from supramolecular polymer assembly and disassembly for sensing metallo- and nonmetalloproteins. *J. Am. Chem. Soc.* **2009**, *131*, 7708–7716.
- (17) Zhang, Y.; Kuang, Y.; Gao, Y.; Xu, B. Versatile small-molecule motifs for self-assembly in water and the formation of biofunctional supramolecular hydrogels. *Langmuir* **2011**, *27*, 529–537.
- (18) Arumugam, S.; Vutukuri, D. R.; Thayumanavan, S.; Ramamurthy, V. Amphiphilic homopolymer as a reaction medium in water: product selectivity within polymeric nanopockets. *J. Am. Chem. Soc.* **2005**, *127*, 13200–13206.
- (19) Feng, C.; Li, Y. J.; Yang, D.; Hu, J. H.; Zhang, X. H.; Huang, X. Y. Well-defined graft copolymers: from controlled synthesis to multipurpose applications. *Chem. Soc. Rev.* **2011**, *40*, 1282–1295.
- (20) Forster, S.; Plantenberg, T. From self-organizing polymers to nanohybrid and biomaterials. *Angew. Chem., Int. Ed.* **2002**, *41*, 688–714.
- (21) Riess, G. Micellization of block copolymers. *Prog. Polym. Sci.* **2003**, *28*, 1107–1170.
- (22) Gao, C.; Yan, D. Y. Hyperbranched polymers: from synthesis to applications. *Prog. Polym. Sci.* **2004**, *29*, 183–275.
- (23) Basu, S.; Vutukuri, D.; Shyamroy, S.; Sandanaraj, B. S.; Thayumanavan, S. Invertible amphiphilic homopolymers. *J. Am. Chem. Soc.* **2004**, *126*, 9890–9891.
- (24) Savariar, E. N.; Aathimankandan, S. V.; Thayumanavan, S. Supramolecular assemblies from amphiphilic homopolymers: testing the scope. *J. Am. Chem. Soc.* **2006**, *128*, 16224–16230.
- (25) Changez, M.; Kang, N. M.; Lee, C. H.; Lee, J. S. Reversible and pH-sensitive vesicles from amphiphilic homopolymer poly(2-(4-vinylphenyl)pyridine). *Small* **2010**, *6*, 63–68.
- (26) Sandanaraj, B. S.; Vutukuri, D. R.; Simard, J. M.; Klaikherd, A.; Hong, R.; Rotello, V. M.; Thayumanavan, S. Noncovalent modification of chymotrypsin surface using an amphiphilic polymer scaffold: implications in modulating protein function. *J. Am. Chem. Soc.* **2005**, *127*, 10693–10698.
- (27) Sandanaraj, S. B.; Demont, R.; Thayumanavan, S. Generating patterns for sensing using a single receptor scaffold. *J. Am. Chem. Soc.* **2007**, *129*, 3506–3507.
- (28) Combariza, Y.; Savariar, E. N.; Vutukuri, D. R.; Thayumanavan, S.; Vachet, R. W. Polymeric inverse micelles as selective peptide extraction agents for MALDI-MS analysis. *Anal. Chem.* **2007**, *79*, 7124–7130.
- (29) Kale, T. S.; Klaikherd, A.; Popere, B.; Thayumanavan, S. Supramolecular assemblies of amphiphilic homopolymers. *Langmuir* **2009**, *25*, 9660–9670.
- (30) Jin, Y.; Song, L.; Wang, D. L.; Qiu, F.; Yan, D. Y.; Zhang, B. S.; Zhu, X. Y. Synthesis and self-assembly of nonamphiphilic hyperbranched polyoximes. *Soft Matter* **2012**, *8*, 10017–10025.
- (31) Liu, J. Y.; Huang, W.; Pang, Y.; Huang, P.; Zhu, X. Y.; Zhou, Y. F.; Yan, D. Y. Molecular self-assembly of a homopolymer: an alternative to fabricate drug-delivery platforms for cancer therapy. *Angew. Chem., Int. Ed.* **2011**, *50*, 9162–9166.
- (32) Laine, R. M. *Inorganic and Organometallic Polymers with Special Properties*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1992.
- (33) Nguyen, P.; Gomez-Elipe, P.; Manners, I. Organometallic polymers with transition metals in the main chain. *Chem. Rev.* **1999**, *99*, 1515–1548.
- (34) Qian, J. S.; Gurald, G.; Lu, Y. J.; Cambridge, G.; Manners, I.; Winnik, M. A. Self-seeding in one dimension: an approach to control

the length of fiberlike polyisoprene–polyferrocenylsilane block copolymer micelles. *Angew. Chem., Int. Ed.* **2011**, *50*, 1622–1625.

(35) Qian, J. S.; Zhang, M.; Manners, I.; Winnik, M. A. Nanofiber micelles from the self-assembly of block copolymers. *Trends Biotechnol.* **2010**, *28*, 84–92.

(36) Wang, H.; Patil, A. J.; Liu, K.; Petrov, S.; Mann, S.; Winnik, M. A.; Manners, I. Polymer/metal oxide nanowires using cylindrical micelles and block comicelles as templates. *Adv. Mater.* **2009**, *21*, 1805–1809.

(37) Hapiot, F.; Tilloy, S.; Monflier, E. Cyclodextrins as supramolecular hosts for organometallic complexes. *Chem. Rev.* **2006**, *106*, 767–781.

(38) Chen, G. S.; Jiang, M. Cyclodextrin-based inclusion complexation bridging supramolecular chemistry and macromolecular self-assembly. *Chem. Soc. Rev.* **2011**, *40*, 2254–2266.

(39) Ritter, H.; Mondrzyk, B. E.; Rehahn, M.; Gallei, M. Free radical homopolymerization of a vinylferrocene/cyclodextrin complex in water. *Beilstein J. Org. Chem.* **2010**, *6*, 60.

(40) Mondrzyk, A.; Mondrzyk, B.; Gingter, S.; Ritter, H. New enzymatically polymerized copolymers from 4-*tert*-butylphenol and 4-ferrocenylphenol and their modification and inclusion complexes with β -cyclodextrin. *Beilstein J. Org. Chem.* **2012**, *8*, 2118–2123.

(41) Munteanu, M.; Kolb, U.; Ritter, H. Supramolecular nanocycles comprising β -cyclodextrin-click-ferrocene units: rings of rings of rings. *Macromol. Rapid Commun.* **2010**, *31*, 616–618.

(42) Nnakahata, M.; Takashima, Y.; Yamaguchi, H.; Harada, A. Redox-responsive self-healing materials formed from host–guest polymers. *Nat. Commun.* **2011**, *2*, 511–516.

(43) Nakahata, M.; Takashima, Y.; Hashidzume, A.; Harada, A. Redox-generated mechanical motion of a supramolecular polymeric actuator based on host–guest interactions. *Angew. Chem., Int. Ed.* **2013**, *52*, 5731–5735.

(44) Zhang, M. F.; Muller, A. H. E. Cylindrical polymer brushes. *J. Polym. Sci., Polym. Chem.* **2005**, *43*, 3461–3481.

(45) Staros, J. V.; Wright, R. W.; Swingle, D. M. Enhancement by *N*-hydroxysulfosuccinimide of water-soluble carbodiimide-mediated coupling reactions. *Anal. Biochem.* **1986**, *156*, 220–222.

(46) Chiefari, J.; Chong, Y. K.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P. T.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H. Living free-radical polymerization by reversible addition-fragmentation chain transfer: The RAFT process. *Macromolecules* **1998**, *31*, 5559–5562.

(47) Moad, G.; Rizzardo, E.; Thang, S. H. Radical addition–fragmentation chemistry in polymer synthesis. *Polymer* **2008**, *49*, 1079–1131.

(48) Shi, M.; Li, A. L.; Liang, H.; Lu, J. Reversible addition-fragmentation transfer polymerization of a novel monomer containing both aldehyde and ferrocene functional groups. *Macromolecules* **2007**, *40*, 1891–1896.

(49) Zhou, N. C.; Zhang, Z. B.; Zhu, J.; Cheng, Z. P.; Zhu, X. L. RAFT polymerization of styrene mediated by ferrocenyl-containing RAFT agent and properties of the polymer derived from ferrocene. *Macromolecules* **2009**, *42*, 3898–3905.

(50) O'Reilly, R. K.; Joralemon, M. J.; Wooley, K. L.; Hawker, C. J. Functionalization of micelles and shell cross-linked nanoparticles using click chemistry. *Chem. Mater.* **2005**, *17*, 5976–5988.

(51) Ruehl, J.; Nilsen, A.; Born, S.; Thoniyot, P.; Xu, L. P.; Chen, S. W.; Braslau, R. Nitroxide-mediated polymerization to form symmetrical ABA triblock copolymers from a bidirectional alkoxyamine initiator. *Polymer* **2007**, *48*, 2564–2571.

(52) Li, P. P.; Li, Z. Y.; Huang, J. L. Water-soluble star brush copolymer with four arms composed of poly(ethylene oxide) as backbone and poly(acrylic acid) as side chains. *Macromolecules* **2007**, *40*, 491–498.

(53) Zhang, L. F.; Eisenberg, A. Multiple morphologies and characteristics of “crew-cut” micelle-like aggregates of polystyrene-*b*-poly(acrylic acid) diblock copolymers in aqueous solutions. *J. Am. Chem. Soc.* **1996**, *118*, 3168–3181.

(54) Cai, C. H.; Lin, J. P.; Chen, T.; Tian, X. H. The self-assembly behavior of poly(γ -benzyl-L-glutamate)-*graft*-poly(ethylene glycol) rod-coil graft copolymers in aqueous solution was investigated. *Langmuir* **2010**, *26*, 2791–2797.

(55) Lin, J. P.; Zhu, G. Q.; Zhu, X. M.; Lin, S. L.; Nose, T.; Ding, W. W. Aggregate structure change induced by intramolecular helix–coil transition. *Polymer* **2008**, *49*, 1132–1136.

(56) Kim, K. H.; Huh, J.; Jo, W. H. Wirelike micelle formed by a T-shaped graft copolymer with a rigid backbone. *Macromolecules* **2004**, *37*, 676–679.

(57) Zhang, L. F.; Eisenberg, A. Thermodynamic vs kinetic aspects in the formation and morphological transitions of crew-cut aggregates produced by self-assembly of polystyrene-*b*-poly(acrylic acid) block copolymers in dilute solution. *Macromolecules* **1999**, *32*, 2239–2249.

(58) Matsue, T.; Akiba, U.; Suzufuji, K.; Osa, T. Cyclic voltammetric determination of formation constant of ferrocene- β -cyclodextrin in dimethyl sulfoxide by using digital simulation. *Denki Kagaku* **1985**, *53*, 508–509.

(59) Wu, J. S.; Toda, K.; Tanaka, A.; Sanemasa, I. Association constants of ferrocene with cyclodextrins in aqueous medium determined by solubility measurements of ferrocene. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1615–1624.

(60) Harada, A.; Hu, Y.; Yamamoto, S.; Takahashi, S. Preparation and properties of inclusion compounds of ferrocene and its derivatives with cyclodextrins. *J. Chem. Soc., Dalton Trans.* **1988**, 729–732.

(61) Riegel, I. C.; Eisenberg, A.; Petzhold, C. L.; Samios, D. Novel bowl-shaped morphology of crew-cut aggregates from amphiphilic block copolymers of styrene and 5-(*N,N*-diethylamino)isoprene. *Langmuir* **2002**, *18*, 3358–3363.

(62) Liu, X. Y.; Kim, J. S.; Wu, J.; Eisenberg, A. Bowl-shaped aggregates from the self-assembly of an amphiphilic random copolymer of poly(styrene-*co*-methacrylic acid). *Macromolecules* **2005**, *38*, 6749–6751.

(63) Wang, J.; Kuang, M.; Duan, H. W.; Chen, D. Y.; Jiang, M. pH-dependent multiple morphologies of novel aggregates of carboxyl-terminated polyimide in water. *Eur. Phys. J. E* **2004**, *15*, 211–215.

(64) Zhang, L. F.; Eisenberg, A. Morphogenic effect of added ions on crew-cut aggregates of polystyrene-*b*-poly(acrylic acid) block copolymers in solutions. *Macromolecules* **1996**, *29*, 8805–8815.