Amphiphilic Nano-Capsules Entangled with Organometallic Coordination Polymers for Controlled Cargo Release.

ARTICLE *in* LANGMUIR · MAY 2014

Impact Factor: 4.46 · DOI: 10.1021/la501442g · Source: PubMed

7 AUTHORS, INCLUDING:

Guodong Liang
Sun Yat-Sen University
75 PUBLICATIONS **1,164** CITATIONS
SEE PROFILE

Qing wu
Sun Yat-Sen University
197 PUBLICATIONS **3,172** CITATIONS
SEE PROFILE

Ben Zhong Tang
The Hong Kong University of Science and Tec…
785 PUBLICATIONS **29,069** CITATIONS
SEE PROFILE

Langmuir

Article

pubs.acs.org/Langmuir

Amphiphilic Nanocapsules Entangled with Organometallic Coordination Polymers for Controlled Cargo Release

Guodong Liang,*[,†] Huan Ni,[†] Suping Bao,[†] Fangming Zhu,[†] Haiyang Gao,[†] Qing Wu,[†] and Ben Zhong Tang*[,‡,§,∥]

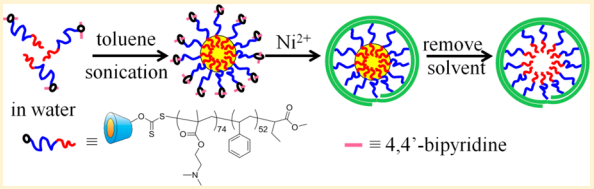
[†]DSAP Lab, PCFM Lab, School of Chemistry and Chemical Engineering, Sun Yat-Sen University, Guangzhou 510275, China

[‡]HKUST-Shenzhen Research Institute, No. 9 Yuexing 1st RD, South Area, Hi-tech Park, Nanshan, Shenzhen, China 518057

[§]Department of Chemistry, Institute for Advanced Study, Division of Biomedical Engineering, Institute of Molecular Functional Materials, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China

[∥]Guangdong Innovative Research Team, SCUT-HKUST Joint Research Laboratory, State Key Laboratory of Luminescent Materials and Devices, South China University of Technology, Guangzhou 510640, China

ABSTRACT: A class of new amphiphilic nanocapsules entangled with organometallic coordination polymers has been developed for the first time. Poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene capped with *β*-cyclodextrin (*β*-CD) (CD-PDMAEMA-*b*-PS) is first synthesized using sequent RAFT polymerization of styrene and 2-(*N*,*N*-dimethyl amino)ethyl methacrylate with xanthate modified *β*-CD as chain transfer agent. The end group of *β*-CD is allowed to include 4,4′-bipyridine through host−guest inclusion to yield PDMAEMA-*b*-PS terminated with an inclusion complex of *β*-CD and bipyridine (bpy-PDMAEMA-*b*-PS), which is then used as surfactant to prepare emulsion droplets in toluene/water mixture. Upon addition of Ni(II), bipyridine coordinates with Ni(II) to form coordination polymers in the periphery of emulsion droplets, affording amphiphilic capsules entangled with organometallic coordination polymers, as confirmed by GPC, ^{1}H NMR, SEM, TEM, DLS, and so on. The organometallic coordination polymer capsules are capable of encapsulating organic cargoes. Interestingly, encapsulated cargoes can be extracted from the capsules without damaging the capsules. Such capsules are potential candidates for encapsulating and controlled release of organic cargoes.



1. INTRODUCTION

Capsules featuring a vast volume of internal cavity represent a class of promising materials with broad range of applications in cargo encapsulation, controlled drug delivery, and so on.[1−3] While a number of techniques such as template[4] and microfluidic[5] approaches have been developed, self-assembly of amphiphilic block copolymers has emerged as a promising approach for the preparation of nanocapsules due to ease of synthesis, mass-production, controllable size, and amphiphilic nature.[6,7] The nature of nanocapsules is dictated by the composition of block copolymers and self-assembly conditions.[8−13]

To date, self-assembled nanocapsules of block copolymers with various hydrophilic and hydrophobic components have been widely reported.[14−25] Zhao and co-workers synthesized PS tethered PDMAEMA single-chain nanoparticles (PDMAEMA-*b*-PS) by sequent RAFT polymerization followed by intramolecular cross-linking of PDMAEMA block (PS, polystyrene; PDMAEMA, poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate; RAFT, reversible addition−fragmentation chain transfer). The polymers self-assembled into vesicles in aqueous media depending on their compositions.[26] Armes and co-workers in situ synthesized amphiphilic PHPMA-*b*-PBzMA vesicles via RAFT alcoholic dispersion polymerization (PHPMA, poly(2-hydroxypropyl methacrylate; PBzMA, poly(benzyl methacrylate)), which depended on chain length of hydrophobic segments.[27] Du and co-workers prepared genus vesicles through self-assembly of $PMEO_2MA$-*b*-PTA block copolymers ($PMEO_2MA$, poly(2-(2-methoxyethoxy)ethyl methacrylate), PTA, poly(2-(*tert*-butylaminoethyl)methacrylate)) in DMF/water mixture. The genus vesicles showed enhanced blood compatibility and retarded release rate of drugs.[28]

Although amphiphilic capsules of block copolymers have been proved to be efficient in encapsulating cargoes, they are metastable in aqueous media. When conditions change such as decreasing concentration, pH changes, and temperature fluctuations, the capsules dissemble, leading to encapsulated cargoes precipitating out from aqueous solution. This limits the application of block copolymer capsules in engineering sectors. Thus, exploring new capsules is highly desirable for development of drug delivery system with enhanced stability. Herein, we reported a class of new hybrid amphiphilic capsules entangled with coordination polymers. Poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene capped with *β*-cyclodextrin (*β*-CD) (CD-PDMAEMA-*b*-PS) was first synthesized using sequent RAFT polymerization of styrene and 2-(*N*,*N*-dimethylamino)-ethyl methacrylate with xanthate modified *β*-CD as chain

Received: April 14, 2014
Revised: May 13, 2014
Published: May 14, 2014

   dx.doi.org/10.1021/la501442g | *Langmuir* 2014, 30, 6294−6301

transfer agent. The end group of β-CD was allowed to include 4,4′-bipyridine through host−guest inclusion to yield PDMAEMA-*b*-PS terminated with inclusion complex of β-CD and bipyridine (bpy-PDMAEMA-*b*-PS), which was then used as surfactant to prepare emulsion droplets in toluene/water mixture. Upon addition of Ni(II), bipyridine coordinates with Ni(II) to form coordination polymers in the periphery of emulsion droplets, affording coordination polymer capsules. The coordination polymer capsules were capable of encapsulating organic cargoes. We demonstrated that encapsulated cargoes could be extracted from the capsules without damaging the capsules. Such capsules are potential candidates for encapsulating and controlled release of organic cargoes.

2. EXPERIMENTAL SECTION

2.1. Materials. β-Cyclodextrin (β-CD), butyl 2-bromobutyrate, styrene, 2-(*N*,*N*-dimethyl amino)ethyl methacrylate, 4,4′-bipyridine (bpy), Nile Red, and toluene were purchased from Sigma-Aldrich (China) and used without further purification unless otherwise indicated.

2.2. Characterization. Molecular weight and molecular weight distribution of polymers synthesized were determined using gel permeation chromatography (GPC) (Waters Breeze 2417) calibrated with PS standard and with tetrahydrofuran (THF) as eluent. ^{1}H NMR spectra of polymers were carried out using a Mercury-Plus 300 instrument (VARIAN). UV−vis spectroscopy data were obtained by use of a Hitachi U3500 instrument at room temperature. Fourier transform infrared (FT-IR) spectra were recorded using a Nicolet/Nexus 670 FT-IR spectrophotometer. Powder samples were mixed with KBr and then pressed into pellets for FT-IR measurements. A field-emission scanning electron microscope (Hitachi S4800) was used to examine the morphologies of nanocapsules. The samples were mounted on freshly polished copper stoppers and rinsed with distilled water to remove excess Ni^{2+}. The specimens were coated with a gold/platinum alloy thin film prior to observation. A field emission gun transmission electron microscope (JEM2010HR) equipped with an Oxford instrument UTW ISIS EDX system was used to characterize the microstructure of nanocapsules. The acceleration voltage was 200 kV. The sample was prepared by adding a drop of capsule suspension on a carbon-coated copper grid and then rinsing with distilled water to remove excess Ni^{2+}. Solvents were allowed to evaporate at room temperature. The specimen was directly observed without staining due to the presence of iron elements. Dynamic light scattering (DLS) measurements were performed using a Brookhaven instrument. Scattering angle was fixed at 90°.

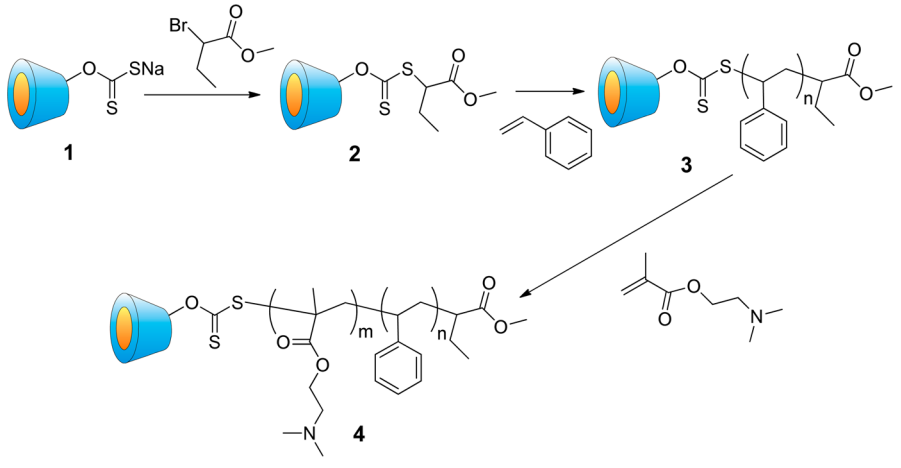
2.3. Synthesis. *Synthesis of β-CD Modified with Xanthate (CD-X).* Synthesis of β-CD modified with xanthate was adapted from a literature protocol.[29] A typical run was as follows: 6 g (5.29 mmol) of β-cyclodextrin (β-CD) was dissolved in 100 mL of 20 wt % sodium hydroxide aqueous solution. To the solution was added dropwise 0.6 mL of CS_2 (10 mmol) at 0 °C under stirring. The resulting solution was allowed to restore to room temperature and then was stirred for 4 h. The crude product was precipitated by adding it dropwise into 200 mL of ethanol. The crude product was solved in 20 mL of distilled water, and the solution was added into 200 mL of ethanol. The solid was collected by filtration and dried in vacuum at 40 °C overnight to get compound **1** (yield: 42%).

An amount of 4 g of compound **1** (3.52 mmol) was dissolved in 20 mL of distilled water. To the solution was added dropwise 0.85 mL (7.4 mmol) of butyl 2-bromobutyrate. The mixture was stirred at 35 °C overnight. The solid was collected by filtration, rinsed with distilled water and ethanol, and dried in vacuum at 40 °C overnight to yield xanthate modified β-CD (CD-X, **2**) (yield: 93%). ^{1}H NMR (300 MHz, DMSO-d_6) δ (TMS, ppm): 0.92 (t, 3H, CH_3CH_2), 3.36 (m, 15H, H_2, H_4 and SC*H*), 3.62 (m, 24H, H_3, H_5, H_6, and OCH_3), 4.43 (t, 6H, O_6H), 4.82 (d, 7H, H_1), 5.70 (m, 14H, O_2H and O_3H). FT-IR (KBr): υ (cm^{-1}) 3353 (O—H stretching), 2924 (CH_2 stretching), 1735 (C═O stretching), 1157 (C═S stretching).

Synthesis of β-CD Terminated Polystyrene (CD-PS, 3). β-CD terminated polystyrene was synthesized using RAFT polymerization technique with CD-X as chain transfer agent. In a typical run, azobisisobutyronitrile (AIBN), compound **2**, and freshly distilled styrene were dissolved in 10 mL of anhydrous dimethylformamide (DMF) under N_2. Polymerization was carried out at 70 °C for 24 h. Upon cooling to room temperature, the mixture was added dropwise to 200 mL of cold ethanol under stirring. The solid was isolated by filtration and then dried in vacuum at 40 °C overnight to get β-CD terminated polystyrene (CD-PS, **3**) (monomer conversion: 62%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (TMS, ppm): 0.80 (t, 3H, CH_2CH_3 from chain transfer agent), 1.42 (br, 104H, $ArCHCH_2$), 1.85 (br, 52H, $ArCHCH_2$), 3.51 (s, 3H, OCH_3 from chain transfer agent), 6.55−7.08 (br, 260H, Ar−*H*). Degree of polymerization of polystyrene was determined to be 52. Number-average molecular weight of CD-PS was determined using M_n = 104 × 52 + 1135 = 6.5 kg/mol. FT-IR (KBr): υ (cm^{-1}) 3082, 3059, 3025 (CH stretching of phenyl ring), 2922, 2848 (CH_2 stretching of phenyl ring), 1943, 1870, 1800 (CH bending of phenyl ring),1735 (C═O stretching), 1157 (C═S stretching).

Synthesis of β-CD Terminated Poly(2-(N,N-dimethyl amino)ethyl methacrylate)-b-polystyrene (CD-PDMAEMA-b-PS, 4). β-CD terminated poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene (CD-PDMAEMA-*b*-PS) was synthesized using **3** as chain transfer agent. In a typical run, AIBN, **3**, and freshly distilled 2-(*N*,*N*-dimethyl amino)ethyl methacrylate were dissolved in 10 mL of anhydrous DMF under N_2. Polymerization was carried out at 70 °C for 24 h. Upon cooling to room temperature, the mixture was added dropwise into

Scheme 1. Synthetic Route for β-CD Terminated Poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene (CD-PDMAEMA-*b*-PS)



dx.doi.org/10.1021/la501442g | *Langmuir* 2014, 30, 6294−6301

200 mL cold NaOH aqueous solution (10 wt %) with stirring. The solid was isolated by filtration and then dried in vacuum at 40 °C overnight (monomer conversion: 41%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (TMS, ppm): 0.86−1.10 (d, 222H, CCH_3 from PDMAEMA), 1.45 (d, 104H, CH_2CH from PS), 1.84 (m, 200H, CH_2CH from PS and CCH_3CH_2 from PDMAEMA), 2.26 (s, 444H, $N(CH_3)_2$ from PDMAEMA), 2.53 (t, 144H, NCH_2CH_2O from PDMAEMA), 3.50 (s, 3H, OCH_3 from chain transfer agent), 4.05 (t, 144H, NCH_2CH_2O from PDMAEMA), 6.55−7.06 (d, 260H, Ar−*H* from PS). The ^{1}H NMR spectrum agreed with literature data.[26,30] Polymerization degree of PDMAEMA was determined to be 74. Number-average molecular weight of CD-PDMAEMA-*b*-PS was determined to be 157 g/mol × 74 + 104 g/mol × 52 + 1135 g/mol = 18.2 kg/mol. FT-IR (KBr): υ (cm^{-1}) 2940 (CH_3 stretching), 2820 (CH_2 stretching of phenyl ring), 1735 (C═O stretching), 1150 (C—N stretching).

Synthesis of Poly(2-(N,N-dimethyl amino)ethyl methacrylate)-b-polystyrene Terminated with Inclusion Complex of β-CD and Bipyridine (bpy-PDMAEMA-b-PS). An amount of 0.86 g (0.05 mmol) CD-PDMAEMA-*b*-PS in 5 mL of THF was added dropwise to 20 mL of distilled water under stirring. To the mixture was added 62 mg (0.4 mmol) of 4,4′-bipyridine (bpy). The mixture was stirred overnight at room temperature. The resulting mixture was extracted with dichloromethane (DCM) (20 mL × 3). The combined organic phase was dried with anhydrous magnesium sulfate. The solution was concentrated and added into cold ethyl ether with stirring. The solid was isolated by filtration and then dried in vacuum at 40 °C overnight to give bpy-PDMAEMA-*b*-PS with yield of 90%. ^{1}H NMR (300 MHz, $CDCl_3$) δ (TMS, ppm): 0.86−1.15 (d, 252H, CCH_3 from PDMAEMA), 1.45 (d, 116H, CH_2CH from PS), 1.84 (m, 226H, CH_2CH from PS and CCH_3CH_2 from PDMAEMA), 2.26 (s, 504H, $N(CH_3)_2$), 2.53 (t, 168H, NCH_2CH_2O from PDMAEMA), 3.51 (br, 3H, OCH_3 from chain transfer agent), 4.05 (t, 168H, NCH_2CH_2O from PDMAEMA), 6.55−7.06 (d, 290H, Ar−*H* from PS). ^{1}H NMR (300 MHz, DMSO-d_6) δ (TMS, ppm): 3.28−3.34 (m, 14H, H_2 and H_4), 3.56 (d, 7H, H_5), 3.60−3.64 (br, 14H, H_3 and H_6), 4.45 (t, 6H, O_6H), 4.80 (d, 7H, H_1), 5.65−5.70 (m, 14H, O_2H and O_3H), 7.80 (d, 4H, Py−*H*), 8. 70 (d, 4H, Py−*H*). FT-IR (KBr): υ (cm^{-1}) 2940 (CH_3 stretching), 2820 (CH_2 stretching of phenyl ring), 1735 (C═O stretching), 1594 (C═N stretching), 1150 (C—N stretching).

For the purpose of comparison, the inclusion complex of β-CD and 4,4′-bipyridine was also prepared according to reference protocol.[31,32] In a typical run, a mixture of β-CD (1 mmol) and 4,4′-bipyridine (1 mmol) was allowed to react in distilled water (60 mL) with stirring for 5 h at 30 °C. The precipitate was isolated by filtration to give white powders. Yield: 56%. ^{1}H NMR (300 MHz, DMSO-d_6), δ (TMS, ppm): 3.28−3.33 (m, 14H, H_2 and H_4), 3.55 (d, 7H, H_5), 3.60−3.64 (br, 14H, H_3 and H_6), 4.44 (t, 7H, O_6H), 4.80 (d, 7H, H_1), 5.65−5.70 (m, 14H, O_2H and O_3H), 7.80 (m, 4H, pyridine ring), 8.70 (m, 4H, pyridine ring). ^{1}H NMR (300 MHz, D_2O), δ (TMS, ppm): 3.35−3.72 (m, 42H, H_2−H_6 of β-CD), 4.90 (d, 7H, H_1 of β-CD), 7.52 (d, 4H, pyridine ring), 8.50 (d, 4H, pyridine ring). ^{1}H NMR spectra of the inclusion complex of β-CD and 4,4′-bipyridine agreed with literature data.[31−33]

Synthesis of Coordination Polymer Capsules. To 51 mg of bpy-PDMAEMA-*b*-PS in 5 mL of distilled water was added 0.25 g of toluene. The mixture was homogenerized with a homogenerizer for 10 min in an ice−water bath. To the resulting mixture was added an equivalent molar amount of $NiCl_2$ in 0.1 mL of distilled water. The reaction mixture was stirred at room temperature overnight. The resulting mixture was centrifuged and then rinsed with distilled water until the top layer solution became clear. The solid was dried in vacuum at 40 °C overnight to yield capsules of organometallic coordination polymers (yield: 70%). ^{1}H NMR (300 MHz, D_2O), δ (TMS, ppm): 3.35−3.78 (m, 42H, H_2−H_6 of β-CD), 7.68 (d, 4H, pyridine ring), 8.50 (d, 4H, pyridine ring). ^{1}H NMR spectra of the coordination polymers agreed with literature data.[31,32] FT-IR (KBr): υ (cm^{-1}) 2940 (CH_3 stretching), 2820 (CH_2 stretching of phenyl ring), 1735 (C═O stretching), 1609 (C═N stretching), 1150 (C—N stretching).

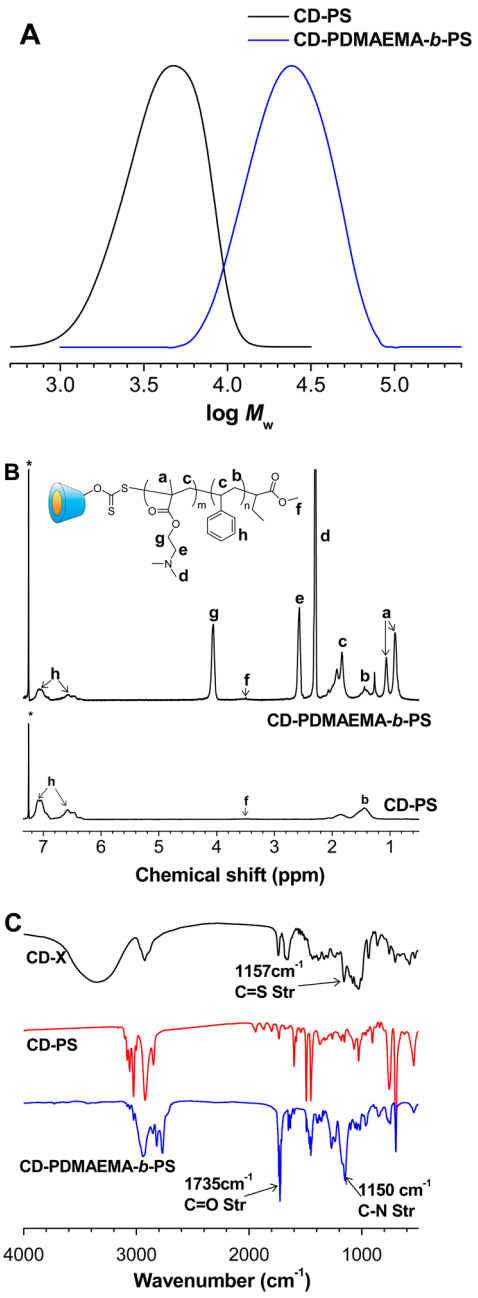


Figure 1. (A) GPC traces, (B) ^{1}H NMR spectra, and (C) FT-IR spectra of β-CD terminated polystyrene (CD-PS) and poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene (CD-PDMAEMA-*b*-PS). Solvent peaks are marked with asterisks in the ^{1}H NMR spectra.

Encapsulation of Nile Red in Capsules. The procedure for synthesis of Nile Red loaded capsules was similar to that for unloaded capsules, except that Nile Red/toluene solution (Nile Red weight percentage was 0.3 wt %) was used instead of toluene.

3. RESULTS AND DISCUSSION

3.1. Synthesis of Poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene (CD-PDMAEMA-*b*-PS) Terminated with Inclusion Complex of β-CD and Bipyridine (bpy-PDMAEMA-*b*-PS). β-Cyclodextrin (β-CD) terminated poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene (CD-PDMAEMA-*b*-PS) was synthesized using sequent RAFT polymerization of styrene and 2-(*N*,*N*-dimethyl amino)ethyl methacrylate with xanthate modified β-CD as chain transfer

dx.doi.org/10.1021/la501442g | Langmuir 2014, 30, 6294−6301

Table 1. Number-Average Molecular Weight, Polydispersity Index, and Polymerization Degree of β-CD Terminated Polymers

sample	M_n (kg/mol)[a]	M_n (kg/mol)[b]	M_n (kg/mol)[c]	PDI[c]	m[d]	n[d]
CD-PS	7.0	6.5	6.8	1.33		52
CD-PDMAEMA-*b*-PS	18.8	18.2	18.4	1.23	74	52

[a]Designed. [b]Determined by ^{1}H NMR spectra. [c]Determined by GPC calibrated with PS standard. [d]m and n denote polymerization degree of PDMAEMA and PS blocks, respectively. m was calculated from ^{1}H NMR using $m = 1.5I_{4.05}/I_{3.51}$, where $I_{4.05}$ and $I_{3.51}$ are the integration of peaks at 4.05 and 3.51 ppm, respectively. n was calculated from ^{1}H NMR using $n = 0.6I_{6.55-7.06}/I_{3.51}$, where $I_{6.55-7.06}$ and $I_{3.51}$ are the integration of peaks from 6.55 to 7.06 ppm and at 3.51 ppm, respectively.

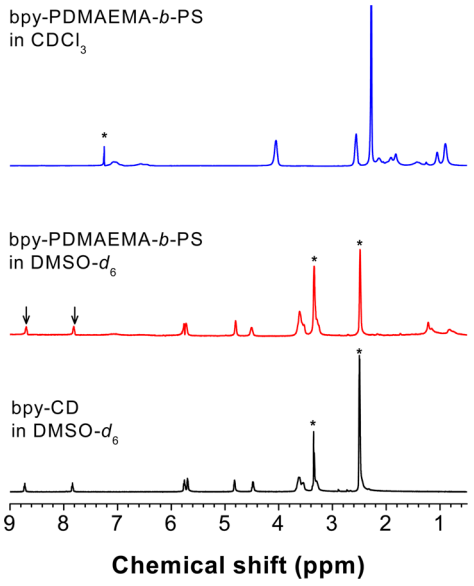
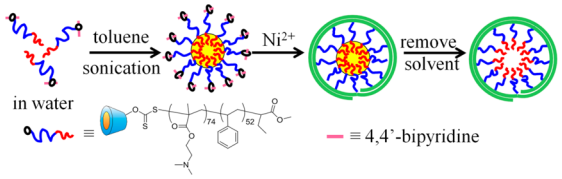


Figure 2. ^{1}H NMR spectra of the inclusion complex of β-CD and 4,4′-bipyridine as well as the inclusion complex terminated poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene (bpy-PDMAEMA-*b*-PS). Solvent peaks are marked with asterisks.

Scheme 2. Schematic Illustration of the Synthesis of Coordination Polymer Capsules



agent, as schematically illustrated in Scheme 1. GPC traces of β-CD terminated polystyrene (CD-PS) and poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene (CD-PDMAEMA-*b*-PS) are shown in Figure 1A. Both polymers showed a single peak. The molecular weight of polymers increased significantly after incorporation of the second monomer of 2-(*N*,*N*-dimethyl amino)ethyl methacrylate, implying the formation of CD-PDMAEMA-*b*-PS. The composition of polymers was confirmed using ^{1}H NMR (Figure 1B) and FT-IR (Figure 1C), respectively. The detailed assignments of peaks are shown in the Experimental Section. Polymerization degree of polystyrene (n) and PDMAEMA (m) was determined to be 52 and 74 respectively, and the data are summarized in Table 1.

The end group of β-CD of CD-PDMAEMA-*b*-PS was allowed to include 4,4′-bipyridine through host−guest inclusion to yield poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene terminated with inclusion complex of β-CD and bipyridine (bpy-PDMAEMA-*b*-PS). The ^{1}H NMR spectrum of bpy-PDMAEMA-*b*-PS is shown in Figure 2. Both $CDCl_3$ and

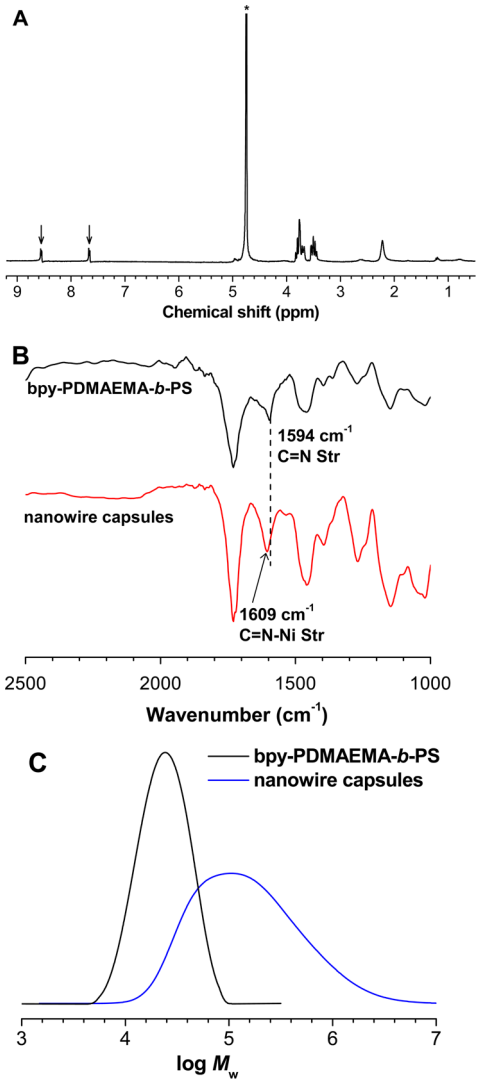


Figure 3. (A) ^{1}H NMR spectra of the capsules in D_2O. Solvent peaks are marked with asterisks. (B) FT-IR spectra and (C) GPC traces of bpy-PDMAEMA-*b*-PS and capsules.

DMSO-d_6 were used as solvents, which were selective solvents for PDMAEMA-*b*-PS and the inclusion complex, respectively. The resonance peaks from the inclusion complex of β-CD and bipyridine were absent in the ^{1}H NMR spectrum of bpy-PDMAEMA-*b*-PS using $CDCl_3$ as solvent due to its poor solubility. For the purpose of comparison, the inclusion complex of β-CD and 4,4′-bipyridine was synthesized according to a literature protocol, and its ^{1}H NMR spectrum in DMSO-d_6 was also recorded.[31,32] The signals attributed to the resonances of pyridine rings of inclusion complex were observed at δ 7.80 and 8.70 in the ^{1}H NMR spectrum of bpy-PDMAEMA-*b*-PS in DMSO-d_6, confirming the formation of bpy-PDMAEMA-*b*-PS.

dx.doi.org/10.1021/la501442g | *Langmuir* 2014, 30, 6294−6301

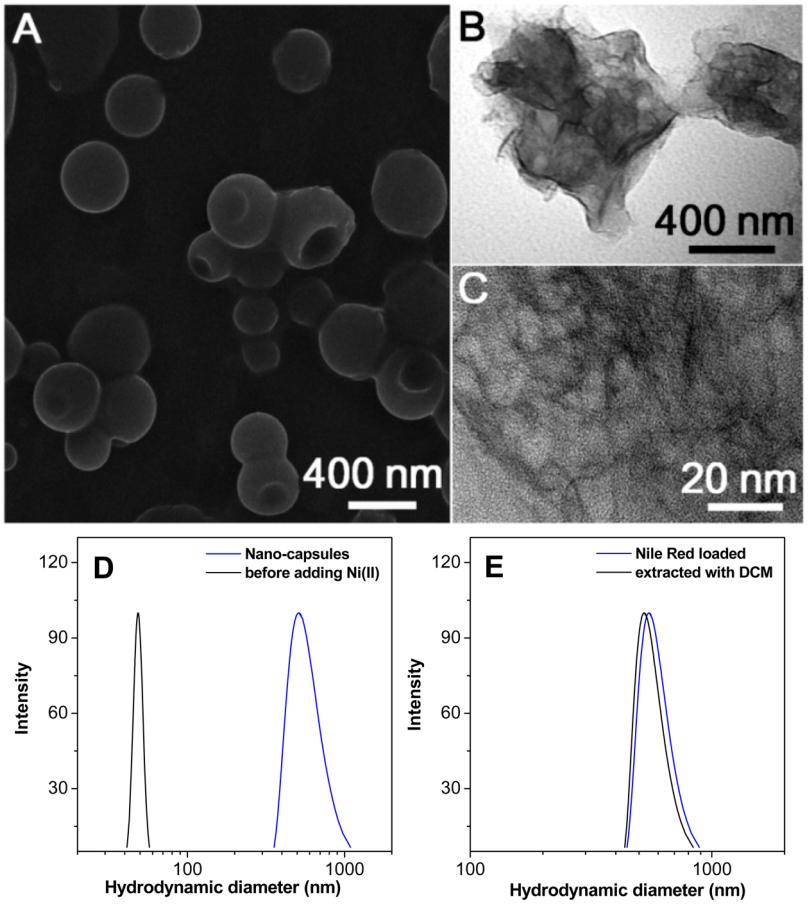


Figure 4. Typical SEM image (A). TEM images at low magnification (B) and at high magnification (C) of the coordination polymer capsules. Particle size distributions of (D) nanocapsules after and before adding Ni(II) and (E) nanocapsules loaded with Nile Red and extracted with DCM.

3.2. Synthesis of Coordination Polymer Capsules. We next prepared amphiphilic capsules through self-assembly of bpy-PDMAEMA-*b*-PS in toluene/water mixture. bpy-PDMAEMA-*b*-PS was used as surfactant to stabilize oil-in-water emulsion droplets. The water-soluble inclusion complex of β-CD and 4,4′-bipyridine as well as PDMAEMA block were located in the periphery of the emulsion droplets. Upon addition of Ni(II), bipyridine coordinated alternatively with Ni(II) to form coordination polymer capsules. Synthesis of coordination polymer capsules is schematically illustrated in Scheme 2.

The coordination polymers were analyzed by using ^{1}H NMR, FT-IR, and GPC. The signals attributed to the resonances of bipyridine−Ni(II) bridging were observed at δ 7.68 and 8.50 in the ^{1}H NMR spectrum of capsules (Figure 3A), confirming the formation of bipyridine−Ni(II) bonding.[31,32] In the FT-IR spectra (Figure 3B), the C═N stretching vibration band of bipyridine shifted from 1594 to 1609 cm^{-1} after coordination with Ni(II).[31,32] The molecular weight of the coordination polymer was measured using GPC, as shown in Figure 3C. The coordination polymer showed a broader peak as compared to parent polymer of bpy-PDMAEMA-*b*-PS. The number-average molecular weight of the coordination polymer was 109.6 × 10^3 g/mol with a distribution of 3.76, much higher than that of its parent polymer of bpy-PDMAEMA-*b*-PS (18.8 × 10^3 g/mol with distribution of 1.25). This suggested that the bipyridine−Ni(II) coordination polymer stringed up PDMAEMA-*b*-PS polymers to form supramacromolecules, as schematically illustrated in Scheme 2.

3.3. Morphology of Capsules. The morphology of the particles was characterized using field emission scanning electron microscopy (SEM) and transmission electron microscopy (TEM), as shown in Figure 4. The SEM image showed spherical particles with diameter of approximately 400 nm. The broken particles showed a hollow structure of capsules. TEM images of deformed capsules (Figure 4B) showed that the capsules were composed of randomly aligned wires. We failed to recognize the wires from intact spherical capsules likely due to sterical stacking of the wires. Indeed, individual wires were observed at the rim of deformed capsules in TEM images at high magnitudes (Figure 4C). The nanowires had a diameter of 2 nm and a length of tens of nanometers. The particle size of the nanocapsules was also measured by using DLS (Figure 4D). The nanocapsule suspension was diluted by 100 times and was subjected to sonication for 2 min prior to DLS measurements. The nanocapsules had a hydrodynamic diameter of 508 nm, larger than that shown by SEM possibly due to swelling of PDMAEMA block in aqueous media. In contrast, unstabilized capsules before adding Ni(II) had by far a smaller hydrodynamic diameter of 48 nm. A possible reason is that unstabilized capsules disassemble during dilution and sonication.

3.4. Thermostability of the Capsules. The thermostability of the capsules was evaluated using thermogravitic analysis (TGA) (Figure 5). The parent polymer began to lose its mass at 142 °C. The capsules started to decompose at 261 °C, 119 °C higher than their parent PDMAEMA-*b*-PS, showing that the capsules possessed improved thermal

dx.doi.org/10.1021/la501442g | *Langmuir* 2014, 30, 6294−6301

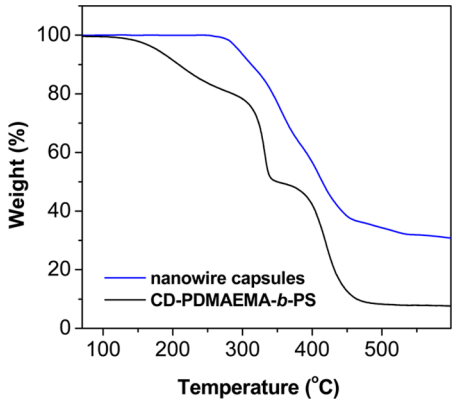


Figure 5. TGA traces of the capsules and bpy-PDMAEMA-*b*-PS.

stability contrasting with its parent polymers. A possible reason is that the rigid coordination polymers restrict mobility of macromolecules, which prevents the radicals produced during thermal decomposition from propagating. This results were consistent with those of the hybrid nanomaterials such as polymer/Prussian blue nanoshells,[34] tiny flowers,[35] and nanoribbons.[36]

3.5. Encapsulating Cargoes. The capsules possess a hydrophobic cavity and hydrophilic periphery enwound with coordination polymers, which offers them as good candidates for encapsulating organic cargoes.[37,38] Thus, we tested the possibility of the capsules to encapsulate organic cargoes using Nile Red as a model cargo. Loading Nile Red in the capsules led to a pink emulsion, which was stable over 3 days without obvious Nile Red aggregates. When adding hexane into the Nile Red loaded emulsion without stirring and letting it stand, the top hexane layer remained clear over 2 days (Figure 6A).

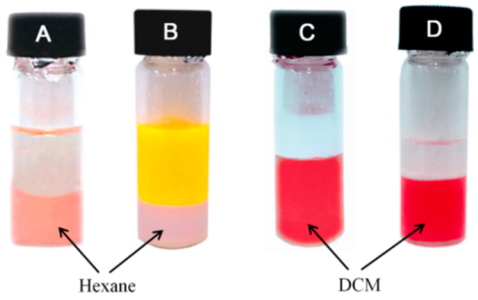


Figure 6. Selective extraction of Nile Red encapsulated inside the capsules: (A) mixing Nile Red loaded capsules with hexane without stirring; (B) extracting Nile Red with hexane; (C) extracting Nile Red with DCM; and (D) extracting Nile Red stabilized by bpy-PDMAEMA-*b*-PS with DCM.

This implied that Nile Red molecules were encapsulated by the capsules because unencapsulated Nile Red molecules dispersed in aqueous media are not stable. After stirring vigorously and then letting it stand for 1 h, the pink emulsion layer turned to milky because of the extraction of Nile Red from the capsules by hexane (Figure 6B). The milky aqueous layer implied that polymer capsules are still retained in the aqueous phase after extraction. This is rationalized by the fact that PDMAEMA-*b*-PS is not soluble in hexane. We therefore used the common solvent DCM to extract Nile Red from the emulsion. Nile Red was exacted from the capsules by using DCM (Figure 6C), as expected. Interestingly, the aqueous phase still remained milky after extraction, showing that the capsules were retained in aqueous phase. The milky aqueous suspension was centrifuged and rinsed with distilled water. The morphology of the solids was checked using SEM. Again, spherical particles were observed (Figure 7), verifying that capsules remained after

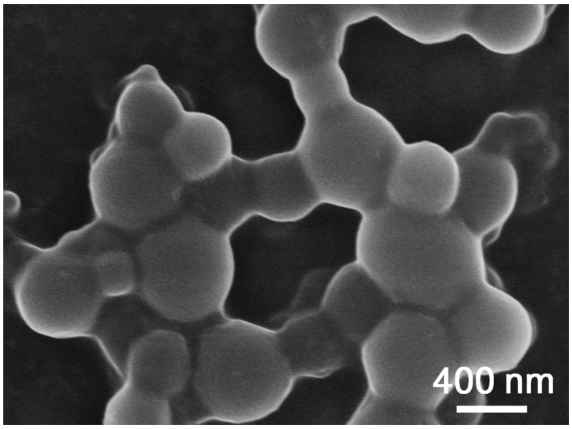


Figure 7. Typical SEM image of the coordination polymer capsules after extracting with DCM.

extraction. In contrast, after extracting Nile Red stabilized by bpy-PDMAEMA-*b*-PS with DCM, the aqueous layer became clear (Figure 6D), showing that PDMAEMA-*b*-PS capsules were destroyed during extraction. Such selective extraction of cargoes of the coordination polymer capsules is likely due to the formation of rigid coordination polymers, which prevents capsules from disassembling during extraction, but allows solvents to penetrate through. The particle size of the nanocapsules loaded with Nile Red was measured using DLS (Figure 4E). Nile Red loaded nanocapsules had a hydrodynamic diameter of 553 nm, slightly larger than that of unloaded capsules (508 nm). After extraction with DCM, particles with a hydrodynamic diameter of 527 nm were still detected using DLS, verifying that the capsules still remained in aqueous phase after extraction.

4. CONCLUSION

In summary, β-cyclodextrin (β-CD) terminated poly(2-(*N*,*N*-dimethyl amino)ethyl methacrylate)-*b*-polystyrene (CD-PDMAEMA-*b*-PS) was successfully synthesized using sequent RAFT polymerization of styrene and 2-(*N*,*N*-dimethyl amino)-ethyl methacrylate with xanthate modified β-CD as chain transfer agent. The end group of β-CD of CD-PDMAEMA-*b*-PS was allowed to include 4,4′-bipyridine through host−guest inclusion to yield PDMAEMA-*b*-PS terminated with inclusion complex of β-CD and bipyridine (bpy-PDMAEMA-*b*-PS). bpy-PDMAEMA-*b*-PS was then used as surfactant to prepare emulsion droplets in toluene/water mixture. Upon addition of Ni(II), bipyridine coordinated with Ni(II) to form coordination polymers in the periphery of emulsion droplets, affording amphiphilic capsules entangled with organometallic coordination polymers. The capsules were capable of encapsulating organic cargoes. Interestingly, encapsulated cargoes could be extracted from the capsules without damaging the capsules. Such capsules are potential candidates for encapsulation and controlled release of organic cargoes.

dx.doi.org/10.1021/la501442g | *Langmuir* 2014, 30, 6294−6301

AUTHOR INFORMATION

Corresponding Authors

*E-mail: lgdong@mail.sysu.edu.cn (G.D.L.).
*E-mail: tangbenz@ust.hk (B. Z. T.).

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The financial support is partially from NSFC (21074151 and 21374136), The Fundamental Research Funds for the Central Universities (13lgzd04), the SRF for ROCS and SEM (2011-1568), and the Hong Kong Scholar Program (XJ2011047). S.P.B. is thankful for financial support from the China Postdoctoral Science Foundation (2012M510206 and 2013T60822).

REFERENCES

(1) De Koker, S.; Hoogenboom, R.; De Geest, B. G. Polymeric Multilayer Capsules for Drug Delivery. *Chem. Soc. Rev.* **2012**, *41*, 2867−2884.

(2) De Cock, L. J.; De Koker, S.; De Geest, B. G.; Grooten, J.; Vervaet, C.; Remon, J. P.; Sukhorukov, G. B.; Antipina, M. N. Polymeric Multilayer Capsules in Drug Delivery. *Angew. Chem., Int. Ed.* **2010**, *49*, 6954−6973.

(3) Brinkhuis, R. P.; Rutjes, F. P. J. T.; van Hest, J. C. M. Polymeric Vesicles in Biomedical Applications. *Polym. Chem.* **2011**, *2*, 1449−1462.

(4) Tong, W. J.; Song, X. X.; Gao, C. Y. Layer-by-Layer Assembly of Microcapsules and Their Biomedical Applications. *Chem. Soc. Rev.* **2012**, *41*, 6103−6124.

(5) Zhang, J.; Coulston, R. J.; Jones, S. T.; Geng, J.; Scherman, O. A.; Abell, C. One-Step Fabrication of Supramolecular Microcapsules from Microfluidic Droplets. *Science* **2012**, *335*, 690−694.

(6) Mai, Y. Y.; Eisenberg, A. Self-Assembly of Block Copolymers. *Chem. Soc. Rev.* **2012**, *41*, 5969−5985.

(7) Rodriguez-Hernandez, J.; Checot, F.; Gnanou, Y.; Lecommandoux, S. Toward 'Smart' Nano-Objects by Self-Assembly of Block Copolymers in Solution. *Prog. Polym. Sci.* **2005**, *30*, 691−724.

(8) He, J.; Zhang, P.; Babu, T.; Liu, Y. J.; Gong, J. L.; Nie, Z. H. Near-Infrared Light-Responsive Vesicles of Au Nanoflowers. *Chem. Commun.* **2013**, *49*, 576−578.

(9) Wang, S. H.; Shen, Q. X.; Nawaz, M. H.; Zhang, W. A. Photocontrolled Reversible Supramolecular Assemblies of a Diblock Azo-Copolymer Based on Beta-Cyclodextrin-Azo Host-Guest Inclusion Complexation. *Polym. Chem.* **2013**, *4*, 2151−2157.

(10) Lu, H.; Yu, L.; Liu, Q. M.; Du, J. Z. Ultrafine Silver Nanoparticles with Excellent Antibacterial Efficacy Prepared by a Handover of Vesicle Templating to Micelle Stabilization. *Polym. Chem.* **2013**, *4*, 3448−3452.

(11) Lu, H.; Fan, L.; Liu, Q. M.; Wei, J. R.; Ren, T. B.; Du, J. Z. Preparation of Water-Dispersible Silver-Decorated Polymer Vesicles and Micelles with Excellent Antibacterial Efficacy. *Polym. Chem.* **2012**, *3*, 2217−2227.

(12) Ray, J. G.; Ly, J. T.; Savin, D. A. Peptide-Based Lipid Mimetics with Tunable Core Properties via Thiol-Alkyne Chemistry. *Polym. Chem.* **2011**, *2*, 1536−1541.

(13) Yan, Q.; Yuan, J. Y.; Kang, Y.; Yin, Y. W. Dynamic Supramacromolecular Self-Assembly: Deformable Polymer Fabricated Nanostructures through a Host-Controlled Approach. *Polym. Chem.* **2010**, *1*, 423−425.

(14) Sun, J. T.; Hong, C. Y.; Pan, C. Y. Recent Advances in RAFT Dispersion Polymerization for Preparation of Block Copolymer Aggregates. *Polym. Chem.* **2013**, *4*, 873−881.

(15) Xiao, X.; He, S. J.; Dan, M. H.; Su, Y.; Huo, F.; Zhang, W. Q. Brush Macro-RAFT Agent Mediated Dispersion Polymerization of Styrene in the Alcohol/Water Mixture. *J. Polym. Sci., Polym. Chem.* **2013**, *51*, 3177−3190.

(16) Qi, W.; Ghoroghchian, P. P.; Li, G. Z.; Hammer, D. A.; Therien, M. J. Aqueous Self-Assembly of Poly(ethylene oxide)-*block*-Poly-(epsilon-caprolactone) (PEO-*b*-PCL) Copolymers: Disparate Diblock Copolymer Compositions Give Rise to Nano- and Meso-Scale Bilayered Vesicles. *Nanoscale* **2013**, *5*, 10908−10915.

(17) Praveen, L.; Saha, S.; Jewrajka, S. K.; Das, A. Self-Assembly of Modified Rhodamine-6G with Tri-block Copolymer: Unusual Vesicle Formation, pH Sensing and Dye Release Properties. *J. Mater. Chem. B* **2013**, *1*, 1150−1155.

(18) Plamper, F. A.; Gelissen, A. P.; Timper, J.; Wolf, A.; Zezin, A. B.; Richtering, W.; Tenhu, H.; Simon, U.; Mayer, J.; Borisov, O. V.; Pergushov, D. V. Spontaneous Assembly of Miktoarm Stars into Vesicular Interpolyelectrolyte Complexes. *Macromol. Rapid Commun.* **2013**, *34*, 855−860.

(19) Pearson, R. T.; Warren, N. J.; Lewis, A. L.; Armes, S. P.; Battaglia, G. Effect of pH and Temperature on PMPC-PDPA Copolymer Self-Assembly. *Macromolecules* **2013**, *46*, 1400−1407.

(20) Madsen, J.; Canton, I.; Warren, N. J.; Themistou, E.; Blanazs, A.; Ustbas, B.; Tian, X. H.; Pearson, R.; Battaglia, G.; Lewis, A. L.; Armes, S. P. Nile Blue-Based Nanosized pH Sensors for Simultaneous Far-Red and Near-Infrared Live Bioimaging. *J. Am. Chem. Soc.* **2013**, *135*, 14863−14870.

(21) He, J.; Huang, X. L.; Li, Y. C.; Liu, Y. J.; Babu, T.; Aronova, M. A.; Wang, S. J.; Lu, Z. Y.; Chen, X. Y.; Nie, Z. H. Self-Assembly of Amphiphilic Plasmonic Micelle-Like Nanoparticles in Selective Solvents. *J. Am. Chem. Soc.* **2013**, *135*, 7974−7984.

(22) Chen, L. L.; Chen, T.; Fang, W. X.; Wen, Y.; Lin, S. L.; Lin, J. P.; Cai, C. H. Synthesis and pH-Responsive "Schizophrenic" Aggregation of a Linear-Dendron-Like Polyampholyte Based on Oppositely Charged Polypeptides. *Biomacromolecules* **2013**, *14*, 4320−4330.

(23) Doncom, K. E. B.; Hansell, C. F.; Theato, P.; O'Reilly, R. K. pH-Switchable Polymer Nanostructures for Controlled Release. *Polym. Chem.* **2012**, *3*, 3007−3015.

(24) Meeuwissen, S. A.; Debets, M. F.; van Hest, J. C. M. Copper-Free Click Chemistry on Polymersomes: Pre- vs. Post-Self-Assembly Functionalisation. *Polym. Chem.* **2012**, *3*, 1783−1795.

(25) Li, B.; Chen, G.; Meng, F. B.; Li, T. H.; Yue, J.; Jing, X. B.; Huang, Y. B. A Novel Amphiphilic Copolymer Poly(ethylene oxide-*co*-allyl glycidyl ether)-*graft*-Poly(ε-caprolactone): Synthesis, Self-Assembly, and Protein Encapsulation Behavior. *Polym. Chem.* **2012**, *3*, 2421−2429.

(26) Wen, J. G.; Yuan, L.; Yang, Y. F.; Liu, L.; Zhao, H. Y. Self-Assembly of Monotethered Single-Chain Nanoparticle Shape Amphiphiles. *ACS Macro Lett.* **2013**, *2*, 100−106.

(27) Zehm, D.; Ratcliffe, L. P. D.; Armes, S. P. Synthesis of Diblock Copolymer Nanoparticles via RAFT Alcoholic Dispersion Polymerization: Effect of Block Copolymer Composition, Molecular Weight, Copolymer Concentration, and Solvent Type on the Final Particle Morphology. *Macromolecules* **2013**, *46*, 128−139.

(28) Zhu, H. S.; Geng, Q. R.; Chen, W. Q.; Zhu, Y. Q.; Chen, J.; Du, J. Z. Antibacterial High-Genus Polymer Vesicle as an "Armed" Drug Carrier. *J. Mater. Chem. B* **2013**, *1*, 5496−5504.

(29) Humeres, E.; Geronimo, V. F.; Zwirtes, I. R.; Mazera, E.; Aliev, A. E. Supramolecular Catalysis Induced by Polysaccharides. Homogeneous Hydrolysis of p-nitrobenzyl Amylose Xanthate. *J. Phys. Org. Chem.* **2003**, *16*, 513−518.

(30) Jiang, G. H.; Wang, Y.; Zhang, R.; Wang, R. J.; Wang, X. H.; Zhang, M.; Sun, X. K.; Bao, S. Y.; Wang, T.; Wang, S. Preparation of Redox-Sensitive Shell Cross-Linked Nanoparticles for Controlled Release of Bioactive Agents. *ACS Macro Lett.* **2012**, *1*, 489−493.

(31) Zhao, Y. L.; Zhang, H. Y.; Guo, D. S.; Liu, Y. Nanoarchitectures Constructed from Resulting Polypseudorotaxanes of the β-Cyclodextrin/4,4′-Dipyridine Inclusion Complex with Co^{2+} and Zn^{2+} Coordination Centers. *Chem. Mater.* **2006**, *18*, 4423−4429.

(32) Liu, Y.; Zhao, Y. L.; Zhang, H. Y.; Song, H. B. Polymeric Rotaxane Constructed from the Inclusion Complex of β-Cyclodextrin and 4,4′-Dipyridine by Coordination with Nickel(II) Ions. *Angew. Chem., Int. Ed.* **2003**, *42*, 3260−3263.

(33) Liang, G. D.; Lam, J. W. Y.; Qin, W.; Li, J.; Xie, N.; Tang, B. Z. Molecular Luminogens Based on Restriction of Intramolecular Motions through Host-Guest Inclusion for Cell Imaging. *Chem. Commun.* **2014**, *50*, 1725−1727.
(34) Liang, G. D.; Xu, J. T.; Wang, X. S. Synthesis and Characterization of Organometallic Coordination Polymer Nanoshells of Prussian Blue Using Miniemulsion Periphery Polymerization (MEPP). *J. Am. Chem. Soc.* **2009**, *131*, 5378−5379.
(35) Bao, S. P.; Liu, T. T.; Liang, G. D.; Gao, H. Y.; Zhu, F. M.; Wu, Q. The Synthesis of Organometallic Coordination Polymer Flowers of Prussian Blue with Ultrathin Petals by Using Crystallization-Assisted Interface Coordination Polymerization (CAICP). *Chem.—Eur. J.* **2012**, *18*, 15272−15276.
(36) Bao, S. P.; Qin, W. P.; Wu, Q. H.; Liang, G. D.; Zhu, F. M.; Q, W. Synthesis and Characterization of Ultrathin Metal Coordination Prussian Blue Nanoribbons. *Dalton Trans.* **2013**, *42*, 5242−5246.
(37) Hu, J. M.; Zhang, G. Y.; Ge, Z. S.; Liu, S. Y. Stimuli-Responsive Tertiary Amine Methacrylate-Based Block Copolymers: Synthesis, Supramolecular Self-Assembly and Functional Applications. *Prog. Polym. Sci.* **2013**, DOI: 10.1016/j.progpolymsci.2013.10.006.
(38) Ge, Z. S.; Hu, J. M.; Huang, F. H.; Liu, S. Y. Responsive Supramolecular Gels Constructed by Crown Ether Based Molecular Recognition. *Angew. Chem., Int. Ed.* **2009**, *48*, 1798−1802.