Novel Amphiphilic Multi-Arm, Star-Like Block Copolymers as Unimolecular Micelles

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Ⓢ *Supporting Information*

ABSTRACT: A series of novel amphiphilic multiarm, star-like block copolymers, poly(acrylic acid)-*b*-polystyrene (PAA-*b*-PS) based on β-cyclodextrin (β-CD) with well-defined molecular architectures, molecular weight, and ratio of two dissimilar blocks were prepared by sequential atom transfer radical polymerization (ATRP). β-CD with 21 hydroxyl groups was esterified by the reaction of its hydroxyl end groups with 2-bromoisobutyryl bromide, producing star-like heptakis[2,3,6-tri-*O*-(2-bromo-2-methylpropionyl]-β-cyclodextrin) (denoted 21-Br-β-CD). Subsequently, 21-Br-β-CD was utilized to initiate sequential ATRP of *tert*-butyl acrylate (*t*BA) and styrene (St). A series of 21-arm, star-like diblock copolymers, poly(*tert*-butyl acrylate)-*b*-polystyrene (P*t*BA-*b*-PS) were thus obtained. Finally, the ester groups of *t*BA in star-like P*t*BA-*b*-PS were selectively hydrolyzed by trifluoroacetic acid (TFA), thereby yielding amphiphilic 21-arm, star-like diblock copolymer PAA-*b*-PS with narrow molecular weight distribution (polydispersity index, PDI < 1.2). The intermediate and final products were systematically characterized and confirmed by GPC, ^{1}H NMR and FT-IR. The *unimolecular micelles* (i.e., composed of single copolymer molecule) formed from amphiphilic star-like PAA-*b*-PS were analyzed by dynamic light scattering, TEM, and AFM.
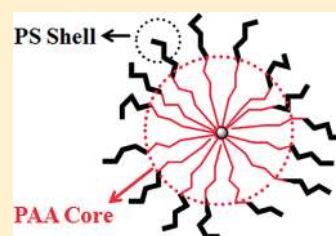
INTRODUCTION

Star-like polymers have attracted considerable attention over the past decade due to their unique solution and solid-state properties. The main feature of star-shaped polymers, differing from the linear analogues of identical molar mass, is their compact structure (i.e., smaller hydrodynamic volume and radius of gyration) and high concentration of functional terminal groups, which enable them with higher solubility in common solvents, lower solution and melt viscosities, and modified thermal properties.[1−5] As such, star-like polymers provide most of the properties of high molecular weight materials without the solution viscosity penalty of linear materials of similar molecular weight for potential applications in coatings, additives, drug and gene delivery, and supramolecular science.[6−10]

Living polymerization, atom transfer radical polymerization (ATRP) and reversible addition−fragmentation chain-transfer (RAFT) polymerization in particular,[4,11,12] has been extensively used for synthesis of star-like polymers through either a core-first method or an arm-first approach.[13−19] In the arm-first method, a living linear monofunctional macromolecule is initially synthesized. The star is then prepared either through the cross-linking by a difunctional comonomer during propagation[20] or by connecting a number of arms with a multifunctional terminating agent.[21] However, the number of arms in these star-like polymers cannot be precisely controlled. The resulting structures are not well-defined, and certain stringent experimental conditions may

be required.[20,21] In stark contrast, in the core-first method, star-like polymers are produced with a multifunctional initiator to induce the growth of arms. It has been successfully implemented to achieve well-defined stars with a discrete number of arms. For example, several styrenic and (meth)acrylic star-like polymers have been prepared by living radical polymerization using the multifunctional core of initiators, such as cyclotriphosphazenes, cyclosiloxanes, and organic polyols.[22] The synthesis of star-like polystyrene by RAFT polymerization[23] and (tetramethylpiperidine-1-oxyl) (TEMPO)-mediated living radical polymerization have also been demonstrated.[24] However, it is noteworthy that these multiarm polymers were only star-like *homopolymers*, and the number of arms were rarely greater than four.[20] More importantly, *limited* work was reported on the preparation of star-like block copolymers[17] because it is difficult to purify star-like macroinitiators and grow the second block at the end of star-like first block.

Amphiphilic linear block copolymers are well-known to self-assemble into micelles composed of hydrophobic core and hydrophilic shell in aqueous solutions.[25] These micelles known as "polymeric micelles" are expected to play an important role in the drug delivery, analytical chemistry, etc.[26,27] Self-assembled

micellar structures have also been employed as multifunctional cross-linkers for the preparation of elastomeric hydrogels.[28] However, these conventional linear block polymer micelles represent thermodynamic aggregates of amphiphilic molecules above their critical micelle concentration. As a result, they are dynamically stable and their characteristics for a given system depend heavily on temperature and the properties of solvent. The shape of micelles may change upon varying the experimental conditions, such as concentration, solvent, temperature, and pH. In sharp contrast to these conventional micellar systems, dendritic macromolecules can readily form unimolecular micelles in which the hydrophilic and hydrophobic segments are covalently linked to the dendritic core.[29] These unimolecular micellar structures are static rather than dynamic, thereby leading to the formation of monodisperse and structurally stable spherical macromolecules.[30−32] To date, no transmission electron microscopy (TEM) and/or atomic force microscopy (AFM) measurements have been performed to support the formation of unimolecular micelles and the dynamic light scattering (DLS) results. Similar to dendritic macromolecules, amphiphilic multiarm, star-like block copolymers composed of hydrophilic and hydrophobic blocks that are covalently connected to a small core can also form unimolecular micelles. This has yet to be explored.

Herein, we report on a simple yet robust approach to synthesize a series of novel amphiphilic 21-arm, star-like block copolymers, poly(acrylic acid)-*b*-polystyrene (PAA-*b*-PS) based on β-cyclodextrin (β-CD) with well-defined molecular architectures, molecular weight, and ratio of two dissimilar blocks by sequential ATRPs. β-CD is a cyclic oligosaccharide consisting of seven glucose units linked by α-1,4-glucosidic bonds.[33−35] The 21 substitutable hydroxyl groups on the outer surface of β-CD provide the capability of making a core with 21 initiation sites to form 21-arm, star-like block copolymers. The star-like PAA-*b*-PS diblock copolymers were composed of hydrophilic PAA block as the core and hydrophobic PS block as the shell with narrow molecular weight distribution and well controlled molecular weight of each block. The unimolecular micelles formed from star-like PAA-*b*-PS were analyzed by dynamic light scattering, TEM and AFM. This new class of star-like block copolymers promises opportunities for studying the fundamental relationship between the star-like nanostructures and their properties.

■ EXPERIMENTAL METHODS

Materials. 2-Bromoisobutyryl bromide (98%), *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylene triamine (PMDETA, 99%), and anhydrous 1-methyl-2-pyrrolidinone (99.5%) were purchased from Sigma-Aldrich, and used as received. CuBr (98%, Sigma-Aldrich) was stirred overnight in acetic acid, filtrated, washed with ethanol and diethyl ether successively, and dried in vacuum. β-cyclodextrin (β-CD, Sigma-Aldrich) was used as received. *tert*-Butyl acrylate (*t*BA, Sigma-Aldrich 98%) and methyl ethyl ketone (Fisher Scientific, 99.9%) were distilled over CaH$_2$ under reduced pressure prior to use. Styrene (St, Sigma-Aldrich ≥99%) was washed with 10% NaOH aqueous solution and water successively, dried over anhydrous MgSO$_4$ and CaH$_2$ sequentially, and distilled under reduced pressure. All other reagents were purified by common purification procedures.

Characterizations. The molecular weight of polymers was measured by GPC, equipped with an Agilent1100 with a G1310A pump, a G1362A refractive detector, and a G1314A variable wavelength detector. THF used as eluent at 35 °C at 1.0 mL/min. One 5 μm LP gel column (500 Å, molecular range: 500−2 × 10^4 g/mol) and two 5 μm LP gel

mixed bed columns (molecular range: 200−3 × 10^6 g/mol) were calibrated with PS standard samples. ^{1}H NMR spectra were performed using Varian VXR-300 spectroscopy. CDCl$_3$ and DMF-*d*$_7$ were used as solvents. FTIR spectra were recorded by a Magna-550 Fourier transform infrared spectrometer. Morphology of amphiphilic 21-arm, star-like PAA-*b*-PS unimolecular micelles were imaged by TEM (JEOL 1200EX scanning/transmission electron microscope (STEM); operated at 80 kV). TEM samples were prepared by applying a drop of star-like PAA-*b*-PS DMF solution (∼4 μL at *c* = 1 mg/mL) onto a carbon coated copper TEM grid (300 mesh) and allowing DMF to evaporate under ambient condition. Subsequently, the samples were stained with uranyl acetate. A droplet of freshly prepared saturated uranyl acetate aqueous solution (∼10 μL) was deposited onto dried samples. After 2 min, the excess solution was removed with a filter paper. The samples were then allowed to dry for TEM imaging. Morphologies of amphiphilic 21-arm, star-like PAA-*b*-PS unimolecular micelles were examined by atomic force microscopy (AFM, Dimension 3000) in the tapping mode. The scanning rate was 2 Hz. Each sample was imaged at more than five locations to ensure the reproducibility of features observed. AFM samples were prepared by spin-coating the 1 mg/mL DMF solution on a Si substrate at the spin speed of 2000 rpm for 1 min (Headway PWM32 spin coater under ambient conditions). Dynamic light scattering (DLS) data was acquired using laser light scattering spectrometer (Malvern Autosizer 4700) at 25 °C.

Synthesis of Heptakis[2,3,6-tri-*O*-(2-bromo-2-methylpropionyl]-β-cyclodextrin) (Denoted 21Br-β-CD). β-CD (6.82 g, 6 mmol, vacuum-dried at 80 °C over calcium oxide overnight immediately prior to use) was dissolved in 60 mL anhydrous 1-methyl-2-pyrrolidione (NMP) and cooled to 0 °C. 2-Bromoisobutyryl bromide (58.0 mL, 252 mmol) was then added dropwise to the β-CD solution with magnetic stirring. The reaction temperature was maintained at 0 °C for 2 h and then slowly increased to ambient temperature, after which the reaction was allowed to continue for 22 h. The brown solution obtained was concentrated in a vacuum oven for 12 h. The resulting syrup-like product was diluted with 100 mL dichloromethane, and then washed sequentially with saturated NaHCO$_3$ aqueous solution (3 × 200 mL) and DI water (3 × 200 mL). The organic layer obtained was concentrated in a vacuum oven, and then crystallized in cold *n*-hexane to produce a white precipitate (18.21 g, yield =71.2%). The chemical compositions of 21Br-β-CD were confirmed by FTIR: 2931 cm^{-1} (ν_{C-H}), 1737 cm^{-1} ($\nu_{C=O}$), 1158 cm^{-1} (ν_{C-O-C}), 1039 and 1105 cm^{-1} (coupled ν_{C-C} and ν_{C-O}).

Synthesis of 21-Arm, Star-Like P*t*BA by ATRP Using 21Br-β-CD as Macroinitiator. Polymerization of *tert*-butyl acrylate (*t*BA) was performed using 21Br-β-CD as a macroinitiator possessing 21 ATRP initiation sites. An ampule charged with CuBr (0.0707 g), PMDETA (0.1707 g), 21Br-β-CD (0.1 g), *t*BA (42.9 mL), and 43 mL methyl ethyl ketone was degassed by three freeze−thaw cycles in liquid N$_2$, then sealed and placed in an oil bath at 60 °C. The ampule was taken out from the oil bath and dipped in liquid N$_2$ at different desired times to terminate the polymerization. The solution was then diluted with acetone and passed through a neutral alumina column to remove the catalyst, and precipitated in the mixed solvents of methanol/water (v/v = 1/1). After filtration, the final product was purified by dissolution−precipitation twice with acetone and methanol/water and dried at 40 °C in vacuum for 2 days.

Synthesis of 21-Arm, Star-Like P*t*BA-*b*-PS by ATRP Using 21-Arm, Star-Like P*t*BA as Macroinitiator. All polymerizations were performed in an ampule. The reaction mixtures (styrene:star-like P*t*BA (i.e., Br in P*t*BA macroinitiator):copper bromide:PMDETA = 800:1:1:2; molar ratio) in anisole (1 g St in 1 mL solvent) were degassed by three freeze−pump−thaw cycle in liquid N$_2$ and then placed in a thermostated oil bath maintained at 90 °C prior to polymerization. After a desired polymerization time, the mixture was dipped in liquid N$_2$ to terminate the reaction. The mixture was then diluted with THF and passed through a column of neutral alumina to remove the copper salt.

Scheme 1. Schematic Representation of the Synthetic Route to a Novel Amphiphilic 21-Arm, Star-Like Diblock Copolymer, PAA-*b*-PS, by Sequential ATRP

Figure 1. ^{1}H NMR spectrum of the macroinitiator, 21Br-β-CD.
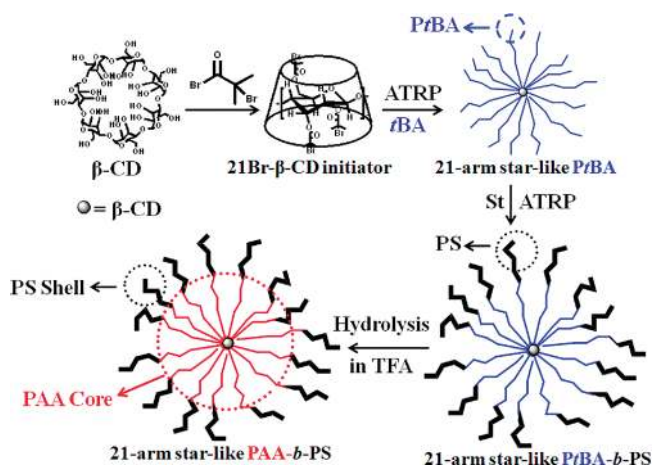
The polymers were precipitated with an excess of methanol, filtered, and dried under vacuum to yield 21-arm, star-like diblock copolymer, P*t*BA-*b*-PS.

Synthesis of Amphiphilic 21-Arm, Star-Like PAA-*b*-PS by Hydrolysis of *tert*-Butyl Ester Groups of P*t*BA Block in P*t*BA-*b*-PS. In a typical process, star-like diblock copolymer, P*t*BA-*b*-PS (0.3 g) was dissolved in 30 mL CH$_2$Cl$_2$, and then 10 mL trifluoroacetic acid was added. The reaction mixture was stirred at room temperature for 24 h. After the hydrolysis, the resulting star-like diblock copolymer, PAA-*b*-PS was gradually precipitated in CH$_2$Cl$_2$. The final product was purified, washed with CH$_2$Cl$_2$, and thoroughly dried under vacuum at 40 °C overnight.

Preparation of Unimolecular Micelles via Amphiphilic 21-Arm, Star-Like PAA-*b*-PS. A small amount of the amphiphilic star-like PAA-*b*-PS diblock copolymers (i.e., ∼10 mg; four samples in Table 3) were dissolved in anhydrous dimethylformamide (DMF, ∼10 mL), a good solvent for both PAA and PS blocks, at a concentration, $c = 1$ mg/mL, at room temperature. The resulting solution was stirred for 2 days.

■ RESULTS AND DISCUSSION

Synthesis of Heptakis[2,3,6-tri-*O*-(2-bromo-2-methyl-propionyl]-β-cyclodextrin) (21Br-β-CD). In light of recent reports on multifunctional initiators that were produced by using 2-bromoisobutyl bromide to directly modify the compounds containing hydroxyl groups,[34,35] in this work, a simple route was utilized to synthesize the heptakis[2,3,6-tri-*O*-(2-bromo-2-methylpropionyl]-β-cyclodextrin) (i.e., 21Br-β-CD) initiator by directly reacting 2-bromoisobutyric bromide with β-CD as the latter possesses 21 substitutable hydroxyl groups on its outer surface[33−35] (Scheme 1). However, a challenge remained in that anhydrous pyridine, which is a commonly used good solvent for β-CD, was immiscible with 2-bromoisobutyl bromide, leading to the precipitation. As a result, the reaction yield was significantly reduced. Notably, similar precipitation was reported when 2-bromopropionyl bromide was used and the precipitate was pyridine salt.[34] To overcome this problem, an appropriate solvent for β-CD needed to be identified, which is compatible with both 2-bromoisobutyl bromide and small amounts of HBr. In this context, 1-methyl-2-pyrrolidone (NMP) was employed as solvent for the reaction of 2-bromoisobutyl bromide with β-CD, yielding 21Br-β-CD with high yield of 71.2% (Scheme 1). The resulting
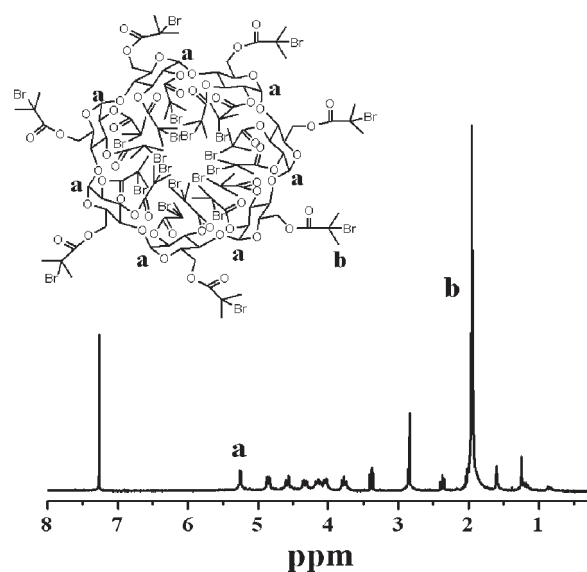
21Br-β-CD is a white powder that is moderately soluble in aqueous solution and highly soluble in most organic solvents, including chloroform, ether, toluene, and dichloromethane.

The hydroxyl groups on β-CD were esterified with 2-bromoisobutyryl bromide to yield the ATRP macroinitiator, 21Br-β-CD. The complete esterification of 21 hydroxyl groups was confirmed by ^{1}H NMR as shown in Figure 1, in which $\delta = 1.8−2.2$ (126 H) can be assigned to the methyl protons of 21Br-β-CD, and $\delta = 3.5−5.5$ (49H) were attributed to residues of β-CD. The hydroxyl group conversion can be calculated based on the following equation.

$$E_T = \frac{A_b}{18 A_a} \times 100\% \qquad (1)$$

where E_T is the conversion efficiency of hydroxyl groups on β-CD; A_b and A_a are the integral area of the methyl protons of 21Br-β-CD and the integral area of the protons (H$_a$) (the peaks at $\delta = 5.2−5.3$), respectively. An E_T value of 100% was obtained, suggesting that hydroxyl groups were completely converted to bromoisobutyryl units.

Synthesis of 21-Arm, Star-Like P*t*BA by ATRP Using 21Br-β-CD as Macroinitiator. ATRP of *t*BA was performed in methyl ethyl ketone at 60 °C using 21Br-β-CD as the macroinitiator and PMDETA/CuBr as the cocatalyst (Scheme 1). Four star-like P*t*BA homopolymers with different molecular weight were synthesized as summarized in Table 1. The obtained star-like P*t*BA showed the monomodal GPC traces (Figure 2). The molecular weight of P*t*BA increased with the polymerization time, and the molecular weight distributions of all polymers were low (PDI = $M_w/M_n < 1.1$). Notably, in all GPC measurements, symmetric peaks were observed, indicating that there were no intermacromolecular coupling reactions (i.e., coupling of two P*t*BA chains to produce a larger macromolecule of twice molecular weight) and no homopolymerization of *t*BA occurred. We note that the molecular weight of star-like P*t*BA derived from ^{1}H NMR was close to the theoretical values, but significantly different from those obtained from GPC; this was due to different hydrodynamic volume of star-like polymers compared to the linear PS standard used in GPC columns.

Table 1. Summary of 21-Arm, Star-Like PtBA Homopolymer

	time (h)	conversion (%)[a]	$M_{n,GPC}$[b]	M_w/M_n[c]	$M_{n,NMR}$[d]	$M_{n,theory}$[e]	$M_{n,PtBA}$[f]	E_T (%)[g]
sample-1	3	10.5	88 200	1.09	172 200	168 760	8100	99.2
sample-2	8	19.4	120 600	1.07	317 940	307 210	14 940	97.5
sample-3	18	38.9	256 000	1.10	631 680	626 580	29 880	98.3
sample-4	36	64.9	312 600	1.08	1053 780	1036 290	49 980	96.8

[a] Determined by gravimetric method. [b] Number-average molecular weight, $M_{n, GPC}$ determined by GPC, calibrated by PS standard. [c] Polydispersity index, PDI, determined by GPC. [d] Number-average molecular weight, $M_{n, NMR}$ calculated from ^1H NMR data. [e] The theoretical values of M_n calculated from the monomer conversion and the concentration of initiators. [f] M_n of each PtBA arm calculated from ^1H NMR data (Figure S1, Supporting Information) based on the following equation:

$$M_{n, PtBA} = \frac{A_b/9}{A_a/6} \times 128.17$$

Here A_b and A_a are the integral area of the methyl protons in *tert*-butyl group of PtBA chains and the integral area of methyl protons at the α-end of PtBA chains, respectively, and 128.17 is the molecular weight of the tBA monomer. [g] The initiation efficiency of bromoisobutyryl for ATRP can be estimated from the ^1H NMR spectrum shown in Figure S1,

$$E_T = \frac{M_{n, theory}}{21 \mathrm{x} M_{n, PtBA}} \times 100\%$$

where E_T is the reaction efficiency of bromoisobutyryl for ATRP, $M_{n,theory}$ is the theoretical value of M_n of star-like PtBA calculated from the monomer conversion and the concentration of ATRP macroinitiator, 21Br-β-CD. $M_{n,PtBA}$ is the M_n of each PtBA arm calculated from the ^1H NMR spectrum (Figure S1, Supporting Information).
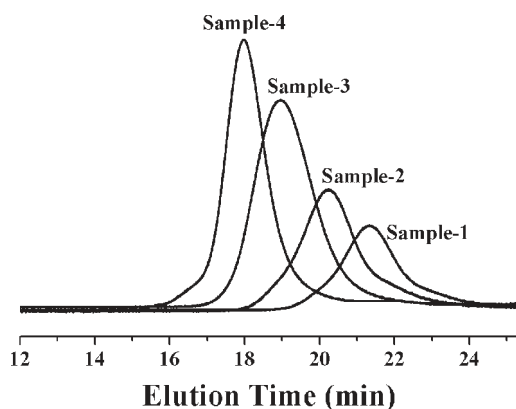

Figure 2. GPC traces of four star-like PtBA homopolymers. Their molecular weights are summarized in Table 1.

Figure S1, Supporting Information, shows the ^1H NMR spectrum of sample-1 of star-like PtBA obtained after the reaction for 3 h (Table 1). An intense characteristic peak at $\delta = 1.45$ ppm (peak b) corresponded to the methyl protons in *tert*-butyl group ($-C(CH_3)_3$). The chemical shift at $\delta =1.21$ ppm represented the methyl protons at the α-end of PtBA chain.

The initiation efficiency in the synthesis of copolymers by ATRP has been widely studied. It was demonstrated that not every initiating site generated polymer chain and incomplete initiation was attributed to the steric hindrance due to high density of initiating centers.[36,37] In this work, however, the density of initiating centers in 21Br-β-CD was lower than that reported in literature[38−40] (i.e., 21 sites in 21Br-β-CD as compared to 60−70 reported), so higher initiation efficiency is expected. The initiation efficiency of bromoisobutyryl for ATRP can be estimated from the ^1H NMR spectrum shown in Figure S1, Supporting Information. The initiation efficiency of all the samples were nearly 100% (in Table 1), suggesting that nearly all bromoisobutyryl groups were involved in the polymerization of tBA, and 21-arm, star-like PtBA homopolymers were successfully produced.

Preparation of 21-Arm, Star-Like PtBA-*b*-PS Diblock Copolymer by ATRP Using a 21-Arm, Star-Like PtBA Homopolymer as Macroinitiator. A series of star-like diblock copolymer PtBA-*b*-PS with different molecular weight were yielded via ATRP using the star-like PtBA homopolymer synthesized above as a 21-site macroinitiator (Scheme 1; i.e., second ATRP). The ATRP of styrene was performed in anisole at 90 °C using PMDETA/CuBr as the cocatalyst. The resulting four star-like PtBA-*b*-PS diblock copolymers of different molecular weight with PtBA cores and PS shells were summarized in Table 2.

The GPC traces of star-like PtBA-*b*-PS diblock copolymer exhibited the monomodal characteristic (Figure 3). The molecular weight of diblock copolymers increased as a function of the polymerization time, and all PDIs were low (PDI < 1.2), which was indicative of the absence of intermacromolecular coupling (i.e., the coupling of two diblock copolymer chains to produce a larger macromolecule with higher molecular weight) and no degradation of PtBA during the polymerization, as well as no homopolymerization of St.

Figure S2 (Supporting Information) shows a representative ^1H NMR spectrum of star-like PtBA-*b*-PS diblock copolymer (i.e., sample-a in Table 2). The chemical shift at $\delta = 6.33−7.31$ ppm can be assigned to the protons on phenyl ring of PS chain. A characteristic peak at $\delta = 1.45$ ppm (peak d) was associated with the methyl protons in *tert*-butyl group ($-C(CH_3)_3$). The $\delta =1.21$ ppm (peak a) represented the methyl protons at the α-end of diblock copolymer. The initiation efficiency of 21-arm, star-like PtBA macroinitiator can be calculated based on the equation (Table 2), the calculated E_T values of all the samples were nearly 100%, suggesting that almost all initiation sites of 21-arm, star-like PtBA participated in the initiation.

Formation of Amphiphilic 21-Arm, Star-Like PAA-*b*-PS by Hydrolysis of the *tert*-Butyl Ester Groups of PtBA Block in PtBA-*b*-PS. Hydrophilic poly(acrylic acid) (PAA) is a weak polyelectrolyte, in which the degree of ionization is governed by pH and ionic strength of aqueous solution.[41] PAA possesses many unique properties, including the transformation of polarity as a function of pH, and the interaction with metal ions, colloidal particles and biomolecules.[42−45] These properties make block

Table 2. Summary of 21-Arm, Star-Like Diblock Copolymer, PtBA-b-PS

entry[a]	time (h)	conversion (%)[b]	$M_{n,GPC}$[c]	M_w/M_n[d]	$M_{n,NMR}$[e]	$M_{n,theory}$[f]	$M_{n,PS}$[g]	E_T (%)[h]
sample-a	2	4.9	138 300	1.13	258 300	255 450	4100	98.9
sample-b	6	6.2	178 500	1.10	427 140	422 400	5200	96.5
sample-c	12	18.2	306 200	1.16	950 460	938 200	15 180	95.1
sample-d	24	35.6	428 900	1.18	1677 060	1650 890	29 680	93.6

[a] Four samples (i.e., a, b, c, and d) were prepared by utilizing sample-1, sample-2, sample-3, and sample-4 in Table 1 as the ATRP macroinitiators, respectively. [b] Determined by gravimetric method. [c] Number-average molecular weight, $M_{n,GPC}$ determined by GPC, calibrated by PS standard. [d] Polydispersity index, PDI determined by GPC. [e] Number-average molecular weight, $M_{n,NMR}$ calculated from ^{1}H NMR data. [f] The theoretical values of M_n calculated from the monomer conversion and the concentration of initiators. [g] M_n of each PS arm calculated from ^{1}H NMR data (Figure S2, Supporting Information) based on the equation:

$$M_{n,PS} = \frac{A_g/5}{A_a/6} \times 104.15$$

where $M_{n,PS}$ is the M_n of each PS arm, A_g and A_a are the integral area of phenyl protons on the PS block and the integral area of methyl protons at the α-end of the diblock arm, respectively, and 104.15 is the molecular weight of St monomer. [h] The initiation efficiency of star-like PtBA macroinitiator can be calculated based on the following equation:

$$E_T = \frac{M_{n,theory} - 21xM_{n,PtBA}}{21xM_{n,PS}} \times 100\%$$

where $M_{n,PS}$ is the M_n of each PS arm, E_T is the reaction efficiency of bromoisobutyryl for ATRP, $M_{n,theory}$ is the theoretical value of M_n of star-like PtBA-b-PS calculated from the monomer conversion and the concentration of ATRP macroinitiator. $M_{n,PtBA}$ is the M_n of each PtBA arm (Table 1) calculated from the ^{1}H NMR spectrum (Figure S1, Supporting Information).
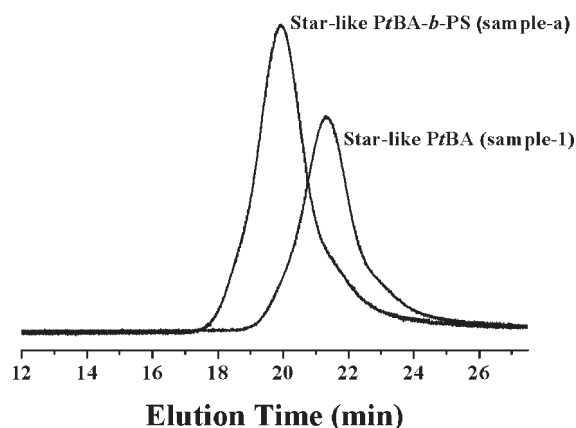

Figure 3. GPC traces of 21-arm, star-like PtBA-b-PS (i.e., sample-a in Table 2) and the corresponding star-like PtBA macroinitiator (i.e., sample-1 in Table 1).

Table 3. Molecular Weights of Amphiphilic 21-Arm, Star-Like Diblock Copolymer, PAA-b-PS

entry[a]	$M_{n,PAA}$[b]	$M_{n,PS}$[c]
sample-A	4500	4100
sample-B	8400	5200
sample-C	16 800	15 180
sample-D	28 100	29 680

[a] Four samples (i.e., A, B, C, and D) were prepared by hydrolysis of PtBA block in sample-a, sample-b, sample-c, and sample-d in Table 2, respectively. [b] Number average molecular weight, M_n of each PAA block calculated from the molecular weight difference between PtBA block (before hydrolysis) and PAA block (after hydrolysis). [c] M_n of each PS arm calculated from ^{1}H NMR data (Table 2).

copolymers containing PAA block very attractive for many applications, such as reverse-assembly,[43,46] stabilization of inorganic particles,[47] crystal growth modifiers,[44] drug carriers,[42] and gene therapy.[45,48] In this work, $tert$-butyl substituent of star-like PtBA-b-PS diblock copolymer can be readily hydrolyzed by trifluoroacetic acid, a process which is highly selective and efficient,[49,50] yielding the final amphiphilic 21-arm, star-like PAA-b-PS. The ^{1}H NMR spectra of a representative star-like PtBA-b-PS before and after hydrolysis are shown in Figure S3, Supporting Information. Four amphiphilic star-like PAA-b-PS diblock copolymers were prepared, and the molecular weights of PAA cores and PS shells are summarized in Table 3.

The complete disappearance of the intense characteristic peak at δ =1.45 ppm, corresponding to the methyl protons of the $tert$-butyl group, reflected that PtBA blocks were totally hydrolyzed into PAA. To further confirm the success of hydrolysis, FT-IR measurements were performed by identifying the presence of

carboxylic acid functional group in PAA. As evidenced in Figure 4, a broad absorbance was seen at 2500—3600 cm^{-1}, signifying the formation of carboxylic acid group. Additionally, the carbonyl stretching shifted from 1726 cm^{-1} in PtBA to 1700 cm^{-1} in PAA.

Amphiphilic 21-Arm, Star-Like PAA-b-PS Unimolecular Micelles. In stark contrast to conventional micellar systems produced using linear amphiphilic block copolymers, the unimolecular micellar structures yielded from amphiphilic star-like PAA-b-PS diblock copolymers are static rather than dynamic. These unimolecular micelles are monodisperse and structurally stable spherical macromolecules.[30−32] The amphiphilic star-like PAA-b-PS (i.e., sample-A in Table 3) was completely dissolved in DMF, a good solvent for both PAA and PS blocks, thereby leading to the formation of a unimolecular micelle (c = 1 mg/mL). The hydrodynamic diameter, D_h, of unimolecular micelles was 22 nm. They possessed monodisperse size distribution as evidenced by the DLS measurement, in which a narrow peak was observed (Figure S4). AFM measurements were also performed to quantify the structures of unimolecular micelles (see Experimental Methods). A DMF solution of amphiphilic 21-arm, star-like PAA-b-PS (i.e., sample-A in Table 3) was spin-coated on a Si substrate. Clearly, the amphiphilic star-like PAA-b-PS formed
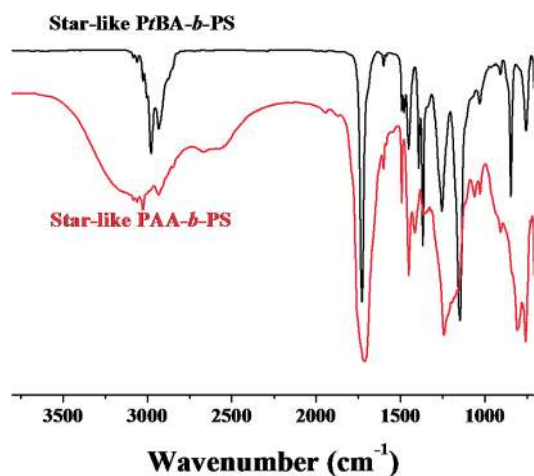
Figure 4. FTIR spectra of 21-arm, star-like diblock copolymers. Star-like P*t*BA-*b*-PS (i.e., sample-a in Table 2; top black curve), and the resulting amphiphilic star-like PAA-*b*-PS (sample-A in Table 3; bottom red curve).
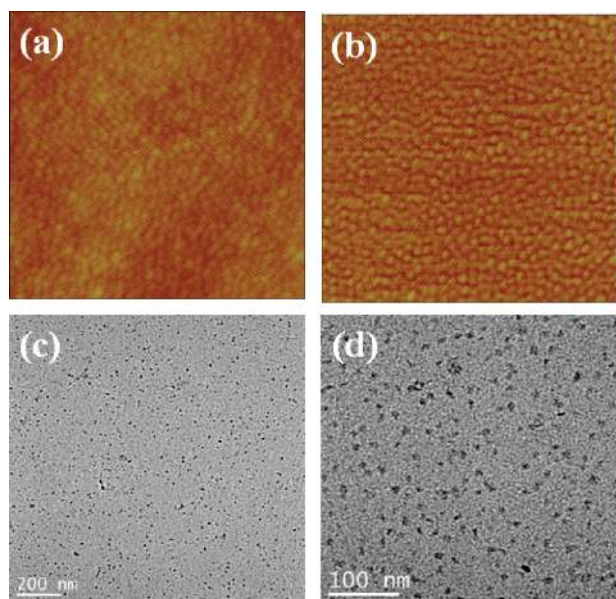

Figure 5. (a, b) AFM height and phase images of amphiphilic star-like PAA-*b*-PS (i.e., sample-A in Table 3), respectively. Scan size =0.7 μm × 0.7 μm, z scale =15 nm in part a, and phase scale =30° in part b. (c, d) TEM images of amphiphilic star-like PAA-*b*-PS (i.e., sample-A in Table 3): (c) scale bar =200 nm and (d) scale bar = 100 nm. The samples were treated with uranyl acetate before imaging to selectively stain the hydrophilic PAA blocks.

spherical unimolecular micelles with an average diameter of 19 ± 2.6 nm (Figure 5, parts a and b), correlating well with D_h = 22 nm in the DLS measurement. With the increased molecular weight of PAA-*b*-PS, the average diameter of unimolecular micelles increased from ∼19 nm (i.e., sample-A in Table 3), to ∼29 nm (i.e., sample-B in Table 3), to ∼41 nm (i.e., sample-C in Table 3), and to ∼65 nm (i.e., sample-D in Table 3) according to the AFM studies (data not shown). To further explore the structures of amphiphilic star-like PAA-*b*-PS unimolecular micelles, TEM imaging was conducted (see Experimental Methods). The dark dots in the TEM micrographs corresponded to the hydrophilic

PAA core as uranyl acetate preferentially stained the PAA block of unimolecular micelles (Figure 5, parts c and d).[51,52] The average diameter of dots was 10 ± 1.6 nm; the size of PAA core was approximately half of that of unimolecular micelle measured by DLS and AFM.

CONCLUSIONS

Functionalized β-CD was exploited as a useful initiator for synthesis of well-defined multiarm, star-like diblock copolymers with copper(I)-mediated living radical polymerization. As such, a series of amphiphilic 21-arm, star-like PAA-*b*-PS diblock copolymers with precisely tailorable molecular architectures, different molecular weight, and varied ratio of two dissimilar blocks were successfully synthesized by sequential atom transfer radical polymerization (ATRP). They possessed narrow molecular weight distribution with the molecular weight of each arm being well controlled by changing the reaction time during ATRP. The amphiphilic star-like PAA-*b*-PS diblock copolymers were composed of hydrophilic PAA cores and hydrophobic PS shells. The unimolecular micelles produced from star-like PAA-*b*-PS were analyzed by dynamic light scattering, TEM and AFM. We envision that, by judicious choice of inorganic precursors, a family of intriguing functional nanocrystals capped with PS shells can be produced via the reaction between carboxyl acid groups of inner PAA blocks with the precursors; this study is currently underway.

ASSOCIATED CONTENT

ⓢ Supporting Information. ¹H NMR spectra of star-like P*t*BA, P*t*BA-*b*-PS and PAA-*b*-PS and DLS measurement on unimolecular micelles of PAA-*b*-PS in DMF. This material is available free of charge via the Internet at http://pubs.acs.org.

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