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Synthesis of polystyrene living nanoparticles (LNPs) in water *via* nano-confined free radical polymerization†

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Living nanoparticles (LNPs), analogs of living polymers, are particles that contain active species for further polymerization. We created these novel nanoparticles *via* free radical polymerization of styrene encapsulated within the hydrophobic interior of a unimolecular micelle (UM) in water. The resultant particles contain mono-disperse polystyrenes with active free radicals. The livingness of the particles was verified by the reaction with radical scavengers and their capability to initiate further polymerization of either water-insoluble or water-soluble monomers. This creation of LNPs is unprecedented and opens a new technique for polymer synthesis using particle initiators.

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Introduction

The unpaired electron of free radicals makes them highly chemically reactive, and they usually undergoes radical coupling,¹ once generated, to terminate the reactivity. The creation of polymers with active radical species is challenging,² but desirable for living polymerization, a technique for the defined synthesis of polymers. Alternatively, the concept of dormant radicals was introduced, which are able to reversibly generate less concentrated active radicals for polymerization under designed conditions. The low concentration of active radicals suppresses the termination reaction leading to the development of a number of living/controlled free radical polymerizations,^{3–8} such as nitroxide-mediated radical polymerization (NMP), atom-transfer radical polymerization (ATRP) and reversible addition–fragmentation chain-transfer polymerization (RAFT). Macromolecules with dormant species have been used as initiators for polymerization-induced self-assembly (PISA). The resultant assembled nanoparticles contain the dormant species, which can be used for further chain extension.^{9–11}

On the other hand, long-lived free radical species, particularly small molecules,¹² have been created by introducing electron resonance and steric hindrance.^{13–15} Emulsion polymerization was initially explored to confine free radicals for possible living radical polymerization by Bianchi *et al.* in 1957 and Horie *et al.* in 1974.^{16,17} The technique has led to the production of mono-disperse styrene polymers and copolymers, but the molecular weight distribution is broad and polystyrene (PSt) homopolymers are present in the block copolymers. These results indicate that emulsion polymerization based on micelles assembled from surfactants did not guarantee the livingness of the polymer chains and was not able to create living nanoparticles. We, therefore, speculate that nano-confinement by single-molecule micelles may create a sufficient steric hindrance for long-lived free radicals. With this idea, we were prompted to examine the possibility to create polymers with active free radicals. A unimolecular micelle (UM) of a star molecule with a hydrophobic interior and hydrophilic periphery in water will be used to host hydrophobic styrene monomers.^{18–20} A conventional free radical polymerization of nano-confined styrene is expected to produce PSt nanoparticles.²¹ The steric hindrance between the particles may allow the active free radicals to stay alive after the polymerization and be available for further chain extension.

Herein, we report that nanoconfinement is an effective approach to create living polymer particles, analogs of living polymers.²² The livingness is proved by their capability for the initiation of the polymerization of the second batch of monomers and the production of block copolymers. In our previous study,²³ we demonstrated the nano-confined polymerization of 2-hydroxyethyl methacrylate in an oil-soluble amphiphilic den-

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drimer, but were not able to harvest living nanoparticles. Studies showed that tethered nano-building blocks lead to richer self-assembled structures than those found in conventional self-assembled units.^{24,25} The ability to produce nanoparticles that contain living polymer radicals is expected to extend both the host-guest and polymerization chemistry for nanomaterial innovation.^{23,26,27}

Results and discussion

Synthesis of unimolecular micelles (UMs) as a host for styrene

The star-shaped amphiphilic macromolecule with a hydrophobic interior and hydrophilic periphery, as shown in Fig. 1a, was synthesized *via* hydrosilylation of octasilane-POSS (polyoctahedral oligomeric silsesquioxane) with amphiphilic dendrons. The detailed synthesis (Scheme S1†) and characterization (Fig. S1–S4†) are described in the Experimental section and the ESI.† The resultant molecules are soluble in water forming UMs with a hydrodynamic diameter (D_h) of *ca.* 10.10 nm (Fig. 1b). The small angle X-ray scattering (SAXS) profile of the UM solution can be fitted by a monodisperse spherical model (Fig. 1c). The diameter for the domain with electron density contrast with D₂O, namely the core of the UM, is *ca.* 8.60 nm consisting of POSS (*ca.* 0.8 nm) and hydrophobic segments (*ca.* 8 nm).

Various amounts of styrene (0.11–0.50 mL, 0.32–1.45 mol L⁻¹) were added to the aqueous solution of the UMs (5.5 × 10⁻⁵ mol L⁻¹ in 3 mL D₂O) to examine the loading capability of the UM. The mixture is a two-phase solution because styrene is hydrophobic and scarcely soluble in water (1.54 × 10⁻⁶ mmol L⁻¹). After stirring for 24 hours, the solution was

left quiescently which allowed the separation of the two phases. The water phase, which contains the UMs with styrene monomers encapsulated (denoted as St/UM), was isolated and analyzed using DLS, SAXS, and UV-Vis spectroscopy. The D_h as revealed by the DLS experiment is *ca.* 12.30 nm (Fig. 1b) for the St/UMs which is slightly larger than that for the UMs in water (*ca.* 10.10 nm) due to the swelling of the hydrophobic domain; the core diameter as indicated by SAXS experiments also increased from 8.6 nm to *ca.* 9.4 nm for all the solutions (Fig. 1c and Fig. S5†), and the intensities of the absorption peaks at 245 nm due to styrene are similar as indicated by the UV-Vis spectra for these solutions (Fig. S6†). So, the uptake of styrene by the UMs is saturated. In Fig. S7,† the integration ratio of the ¹H-NMR peaks due to styrene (4.90, 5.44, 6.38 ppm) to that due to the UMs (−0.19 ppm) indicates that each UM takes up *ca.* 107 styrene molecules.

Nano-confined synthesis of PSt nanoparticles

The aqueous solution of the St/UMs with a mole ratio of 107/1 was heated at 40 °C in the presence of a redox initiating system (cumene hydroperoxide (CHP) with fructose (reducing agent) and activators of Fe₂(SO₄)₃ and Na₄P₂O₇·10H₂O).²⁸ The initiating system generates water-insoluble radical species at a fast rate, which can effectively initiate the polymerization within the hydrophobic domain of the UMs. The cartoon illustration for this nano-confined synthesis is shown in Fig. 2a. Fig. 2b shows the ¹H-NMR spectra of the solution at various polymerization times (2, 3, 6, and 12 hours). The ¹H NMR signals due to the liquid styrene monomers within the hydrophobic domains are visible initially and disappear upon the initiation of the polymerization (Fig. 2b). Nevertheless, the blown up spectra between 6.63–7.06 ppm show weak peaks

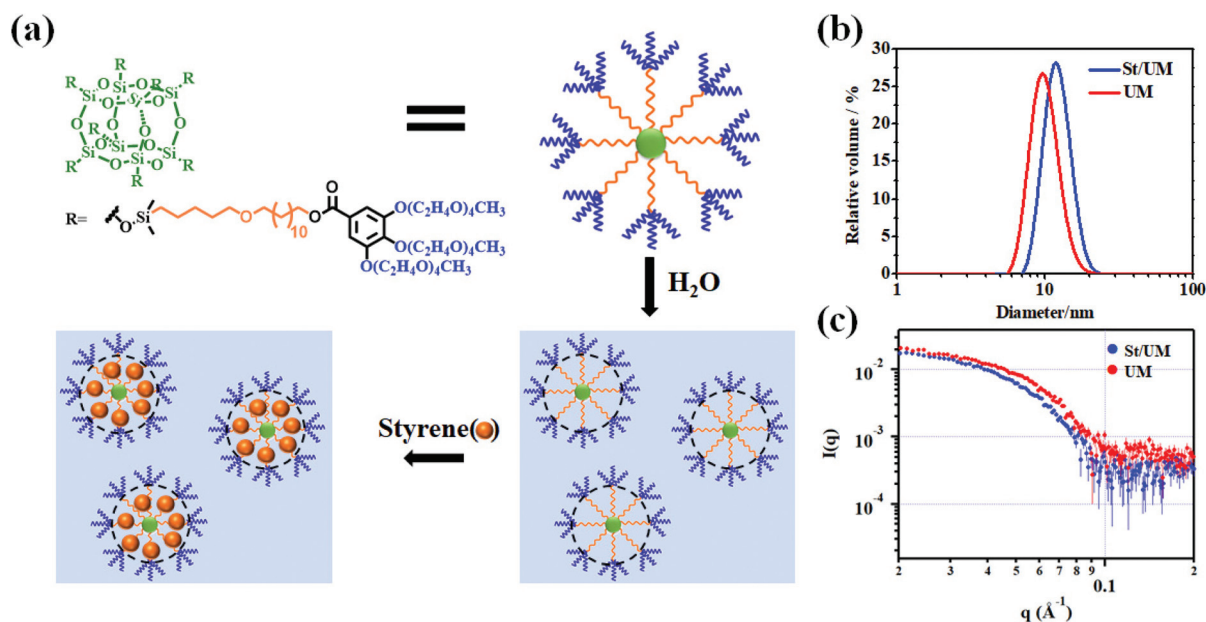


Fig. 1 The unimolecular micelles (UMs) as a host for styrene. (a) Chemical structure and cartoon illustration of the UM. (b) DLS and (c) SAXS profiles of the UMs and St/UMs in D₂O.

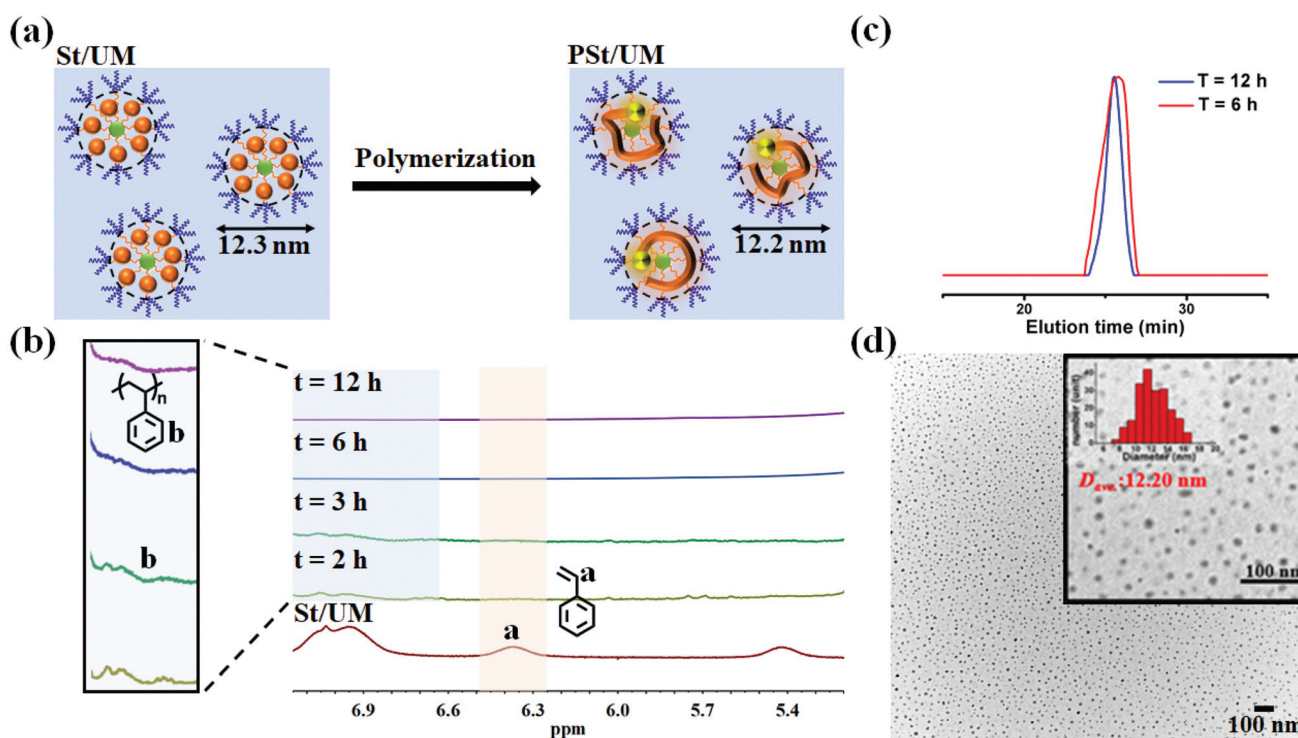


Fig. 2 Nano-confined synthesis of PSt living particles. (a) Cartoon illustration and (b) $^1\text{H-NMR}$ (300 MHz) spectra of the solution of the St/UMs in D_2O after polymerization at $40\text{ }^\circ\text{C}$ for various times (0, 2, 3, 6, 12 hours). (c) GPC traces of the products isolated after polymerization for 6 hours (red) and 12 hours (blue) (d) TEM images of the products after polymerization for 6 hours. The St/UM molar ratio is 107/1 in the presence of a redox initiating system of $\text{CHP} : \text{Fe}_2(\text{SO}_4)_3 : \text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O} : \text{fructose}$ with a molar ratio of 1 : 0.1 : 8.82 : 2.94.

due to the phenyl groups for styrene-swelled PSt at the early stage of the polymerization (2 hours). These peaks are weakened as the polymerization further progresses vitrifying the core. After 6 hours, these peaks are not detectable, suggesting that most styrene monomers are consumed. The GPC analysis of the isolated PSt after polymerization for 6 hours (Fig. 2c) reveals an M_n of 11 300 Da corresponding to the degree of polymerization (DP) of 108. This DP is close to the number of styrene molecules (107) within the UM host, suggesting that all guest monomers are consumed. No obvious increase in M_n was observed when the polymerization time was prolonged to 12 hours (Fig. 2c). It is also noticed that the molecular weight distributions as indicated by PDI for both polymers are very low (<1.13). This low PDI, plus the similarity of the DP with the number of guest styrene molecules, suggests that the radical termination reactions are suppressed. This suppression is rationalized by the confinement effect of the hydrophobic interior of the UM, which sterically prevents the termination reactions *via* the encounter of the PSt chains with active free radicals. This nano-confinement effect is verified by TEM experiments. A solution after polymerization for 6 hours was dried on a carbon-coated TEM grid for the experiment, which shows spherical particles with an average diameter of *ca.* 12.20 nm (Fig. 2d). This size is close to the D_h of the St/UM host-guest colloids (12.30 nm), indicating that the polymerization is confined within the UMs. Both oleophilic and hydrophilic thermal initiators, azobisisobu-

tyronitrile (AIBN) and 2,2'-azobis(2-methylpropionamide) dihydrochloride (V50), also initiated the nano-confined polymerization (Table 1 and Fig. S8[†]). Since the molecular weight of resultant PSt is close to the weight of encapsulated St monomers in each UM, it can be concluded that in each UM, only one PSt chain is produced, so the nano-confined polymerization resulted in a low PDI (Table 1).

Livingness of the nanoparticles

As the confinement suppressed the radical termination, we tested the livingness of the resultant nanoparticles by adding a

Table 1 The conditions of the nano-confined synthesis and the yield, PDI, and MW of the obtained PSt^a

Initiator	Temp. ($^\circ\text{C}$)	Reaction time (h)	M_n (Da)/PDI
Redox ^b	40	6	11 300/1.13
Redox ^b	40	12	11 600/1.06
V-50	70 ^c	3	10 200/1.06
AIBN	70 ^c	3	10 400/1.08

^a In all nano-confined synthesis, the concentration of the UMs in the solution is 0.5 mg mL^{-1} and 3 mL of the UM solution was used in each reaction. ^b The redox initiator includes chemicals with the ratio of the parts of $\text{CHP} : \text{Fe}_2(\text{SO}_4)_3 : \text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O} : \text{fructose}$ being 1 : 0.1 : 8.82 : 2.94. ^c The higher reaction temperature ($70\text{ }^\circ\text{C}$) was applied for the azo initiators because they have lower rate constants for dissociation.

new batch of styrene (200 μL) to the solution. Although the added styrene is immiscible with water, the monomer can diffuse through the water for the polymerization. This polymerization lasted for a few days and produced increased amounts of PSt as the polymerization time was prolonged. The initiation of the new batch of styrene for the further growth of PSt chains (Fig. 3a) suggests that the nanoparticles possess living free radicals. The polymerization of the second batch of St increases the volume of the resulting PSt chains beyond the host capacity of the UMs. Consequently, the nano-confinement was removed resulting in a broad PDI (Fig. 3a). Nevertheless, as shown in Fig. 3a, the GPC curves for the polymers isolated after polymerization for 3 and 5 days shift to the lower retention times, corresponding to M_n values of 28 900 and 42 700 Da, respectively.

We have made an effort to characterize the living particles by electron paramagnetic resonance (EPR) spectroscopy. To avoid the interference caused by the metal ions in the redox initiator, the PSt/UM nanoparticles were prepared by using the hydrophilic initiator V50. However, the EPR spectra show no signals due to free radicals (Fig. S9[†]). Ballard *et al.* have reported that the low radical concentration, the broadness of the EPR signal, and the ease of power saturation of the polystyryl-propagating radicals in emulsion polymerization caused the EPR silence of the PSt radicals in water.^{29,30} Thus, the low concentration of PSt/UM particles and the confinement of the radicals within nanoparticles that lowers the mobility may impede EPR detection. Alternatively, we used a radical scavenger, 1,1-diphenyl-2-picrylhydrazyl (DPPH), for the characterization. As shown in Fig. 3b, the UV-Vis absorbance due to DPPH decreases proportionally with the amount of added

living particles. It indicates the presence of active radicals in the particles that consume DPPH, because DPPH is well known for its high reactivity to radicals.³¹

The livingness is further confirmed by their capability to initiate the polymerization of 2-dimethylaminoethyl methacrylate (DMA) for the synthesis of PSt-*b*-PDMA block copolymers. We found that the solution of PSt/UM particles (3 mL, 5.5×10^{-5} mol L⁻¹) in the presence of DMA (280 μL , 1.65 mmol) becomes viscous after a few hours at room temperature. The resultant polymers were precipitated by adding NaOH_(aq) to the aqueous solution.

The GPC analysis of the isolated polymers reveals the chain extension from the PSt within the particles (M_n of 11 300 Da) to the PSt-*b*-PDMA with M_n of 33 200 Da and PDI of 1.38 (Fig. 4a). The block copolymer undergoes assembly in methanol which is a selective solvent for PDMA. NMR analysis indicates that the PDMA blocks form the corona of the micelles as expected

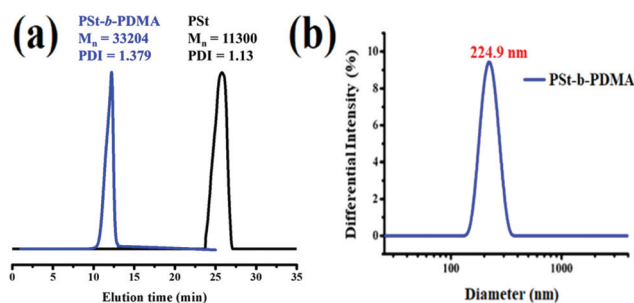


Fig. 4 (a) GPC traces of PSt ($M_n = 11\,300$, PDI = 1.13) and PSt-*b*-PDMA ($M_n = 33\,200$, PDI = 1.38) and (b) DLS profiles for PSt-*b*-PDMA.

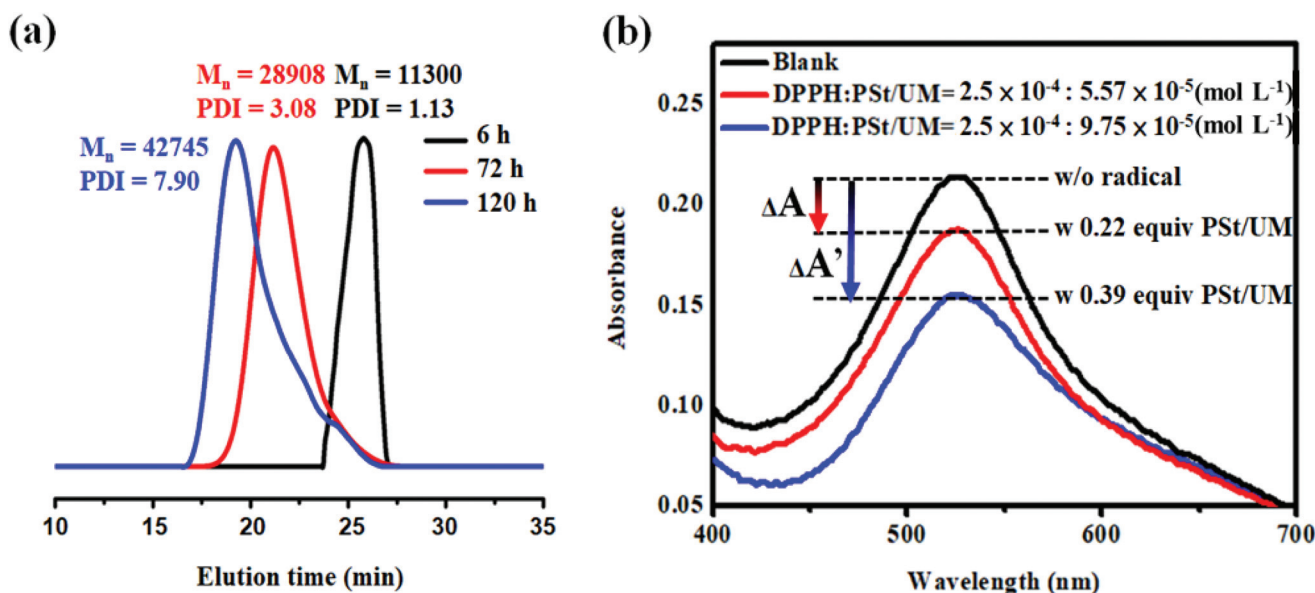


Fig. 3 (a) GPC traces of the nano-confined polymerization at a reaction time of 6 hours (black), 72 hours (red), and 120 hours (blue). (b) The UV-Vis absorption spectra of the radical scavenger, DPPH (2.5×10^{-4} mol L⁻¹ in MeOH), and the DPPH solution with 5.57×10^{-5} mol L⁻¹ (red curve) and 9.75×10^{-5} mol L⁻¹ of PSt/UMs (blue curve). The decreases in the absorbance of DPPH (ΔA and $\Delta A'$) were caused by the added LNP that consumed DPPH molecules.

(Fig. S10†). The D_h for the resultant micelles is 224.9 nm as indicated by DLS analysis (Fig. 4b). This micellization behavior confirms the production of PSt-*b*-PDMA block copolymers.

Conclusions

To sum up, LNPs containing an active polymer radical were created. The UMs with a hydrophobic interior were used to host styrene monomers and confined a free radical polymerization, generating one PSt chain per UM. The single PSt chain formed particles with active free radicals, which is attributed to the steric hindrance. The resulting living particles can initiate polymerization of a second batch of monomers for the synthesis of block copolymers. The creation of LNPs is unprecedented and opens a new technique for polymer synthesis using particle initiators.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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