

Supporting Information

Synthesis of Polystyrene Living Nanoparticles (LNP) in Water via Nano-Confined Free Radical Polymerization

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

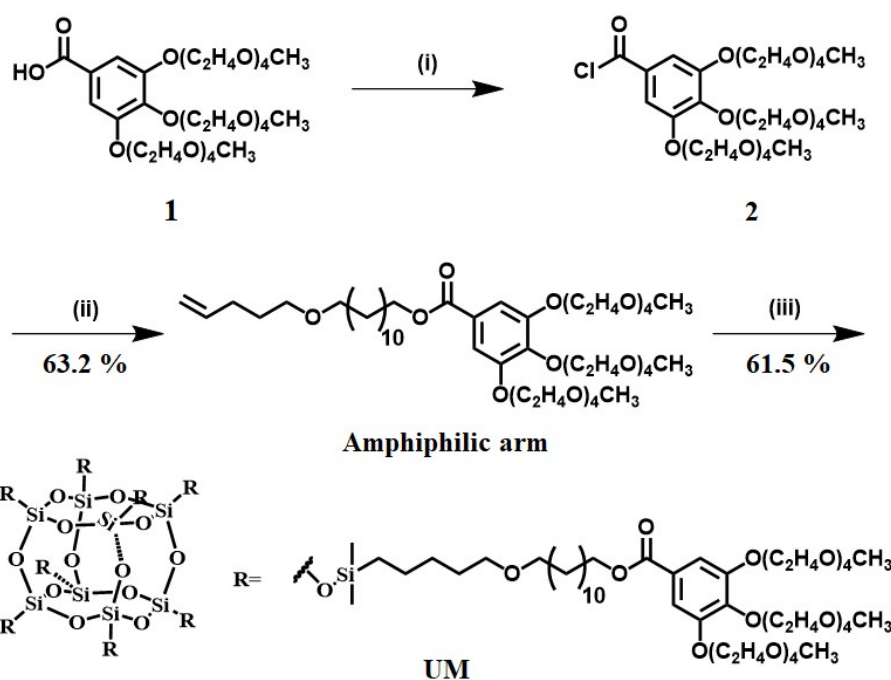
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Experimental Procedures

Materials and Instrumentation

All reagents were purchased from commercial sources and were used without purification. Solvents and reagents were degassed by purging with nitrogen. ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on an Agilent Unity-400 NMR spectrometer (400 MHz for ^1H , 101 MHz for ^{13}C), using CDCl_3 or D_2O as the D-solvent to identify the molecular structures at 25 °C. The signal of the residual protic solvent of CDCl_3 are at δ 7.26 ppm (s) in the ^1H NMR spectrum and at δ 77.0 ppm (t) in the ^{13}C NMR spectrum. The signal of the residual protic solvent of D_2O is at δ 4.65 ppm (s) in the ^1H NMR spectrum. The synthesized UM and compounds were analyzed using an NMR spectrometer. The field desorption ionization mass spectrometry (FD-mass) was recorded with the JEOL Accu TOF FCX system to record the molecular weight of UM. Electronic absorption spectra were obtained on a SHIMADZU UV-2450 spectrometer. SAXS measurements were recorded at the 23A beamline of the National Synchrotron Radiation Research Center (NSRRC) in Taiwan. The ring energy of NSRRC was operated at 15 eV with a typical current of 300 mA. The wavelength of the X-rays was 0.827 Å and the distance was 3168.67 mm between samples and detectors to give a q range of 0.006 to 0.42 Å $^{-1}$. q is the scattering vector. Related to the scattering angle (2θ) and the photon wavelength (λ) by $q = 4\pi \sin(\theta)/\lambda$. The 2D SAXS images were converted into 1D SAXS profiles $I(q)$ to q . Igor Pro 6.3 software was used to analyze all SAXS data and the models were used for fitting the form-factor from the NCNR package. The analytical solution was prepared at a concentration of 0.5 mg mL $^{-1}$ at 25 °C. All of the samples and solvents were filtered into empty vials through a 220 nm syringe filter. Pure D_2O was used as a blank. Gel permeation chromatography (GPC) equipped with Ultimate 3000 liquid chromatography associated with a 101 refractive index detector and Shodex columns (Shodex KF-802, Shodex KF-803, and Shodex KF-805) was used to analyze the polymeric products using THF as the eluent at 30 °C with 1 mL min $^{-1}$ flow rate. The M_n and polydispersity (PDI) of the polymeric products were calculated by DIONEX Chromeleon software. Dynamic light scattering (DLS) spectra were collected on Malvern, Zetasizer nano spectrometer, using D_2O as the solvent to measure the hydrodynamic diameter on molecular structures. All of the samples were filtered into empty vials through a 220 nm syringe filter. UV-visible absorption spectra were recorded with a UV-2600 spectrophotometer. The wavelength of absorption spectra was set at 300-800 nm. Electronic paramagnetic resonance (EPR) spectra were recorded with GERMANY BRUKER ELEXSYS, E-580 (The range of temperature was 4 K to 463 K) spectrometer.



General scheme and procedure for preparation of compounds 1, amphiphilic arm and UM

Scheme S1. The synthetic route of UM (i) SOCl_2 , CH_2Cl_2 , 25 °C, 6 h; (ii) 12-(pent-4-en-1-yloxy)dodecan-1-ol, pyridine, CH_2Cl_2 , 25 °C, 20 h, yield: 63.2%; (iii) Polyhedral Oligomeric Silsesquioxane (POSS), Karstedt's catalyst, ether, 20 h, yield: 61.5%.

Synthetic Procedures and Characterization Data

UM was synthesized according to the synthetic route shown in **Scheme S1**. The hydrophobic dodecyloxy group is introduced to create the hydrophobic interior, whereas the tris(tetraethylene oxide)benzoate group act as the hydrophilic shell of the dendrimer. The synthetic route was designed based on the concept of the convergent approach in dendrimer synthesis, in which the peripheral dendritic arms are prepared before connecting to core unit. The amphiphilic arms of **UM** contain three segments: the hydrophilic tris(tetraethylene oxide) benzoate segment, the hydrophobic dodecyloxy segment, and pent-4-ene segment. The hydrophilic dendron (**1**) was synthesized according to the literature.¹⁻³ The successful connection between the hydrophilic 3,4,5-tris(tetraethylene oxide)benzoic chloride (**2**), hydrophobic dodecyloxy segment and the pent-4-ene was evidenced by the correct integration numbers of the proton signals from the 3,4,5-tris(tetraethylene oxide)benzoate segment (H_a-H_i), the dodecyloxy segment (H_g-H_l) and pent-4-ene (H_j-H_k) shown in **Figure S1a**. The reaction of 12 equal of the amphiphilic arm with octasilane-POSS via a hydrosilylation reaction allows the formation of the Unimolecular micelle (**UM**) in the 61.5% yield. In **Figure S1b**, the disappearance of the vinyl proton (H_j-H_k) and the appearance of H_m and H_n confirm the success of the reaction. The formation of **UM** was further proved by the FD-mass spectra as shown in **Figure S2** and the ¹³C-NMR spectra of **UM** is shown in **Figure S3**. The observed mass-to-charge (m/z) values of 8964.74 closely match the calculated [M]⁺ value of **UM** (8964.09 Da). These results clearly indicate the success of the reaction and confirm the chemical identity and purity of **UM**.

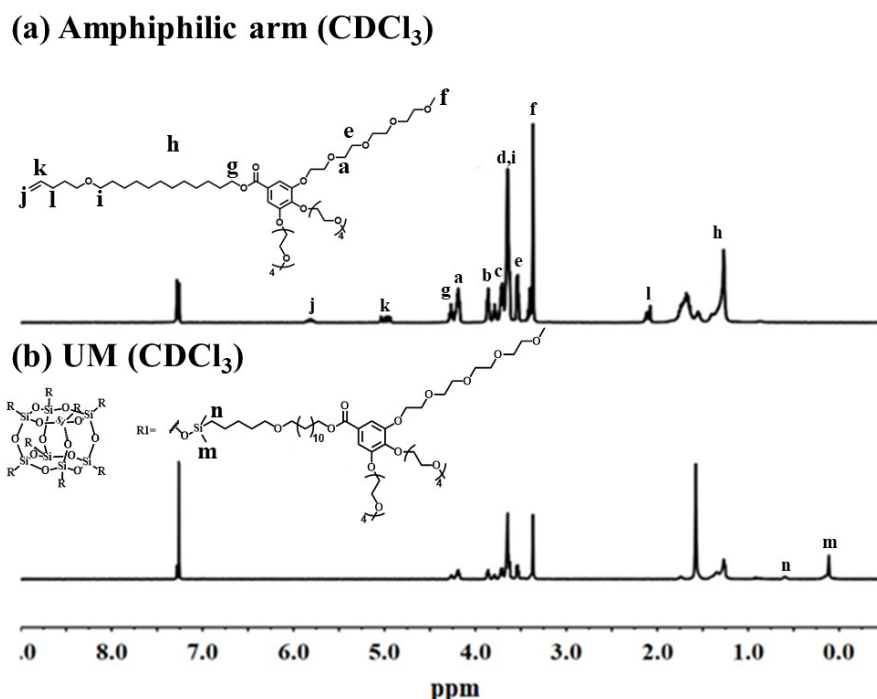


Figure S1. ¹H-NMR spectra of (a) the amphiphilic arm and (b) **UM**. (400 MHz in CDCl₃)

Amphiphilic arm. Compounds **1** (1.35 mmol, 1.00 g) was dissolved in dry dichloromethane (1.53 mL) and freshly distilled thionyl chloride (0.522 mL) was added. After the addition, the reaction mixture was stirred at 25 °C for 6 h. the reaction was stopped and excess thionyl chloride was removed by rotary evaporator under reduced pressure to achieve the crude product compounds **2**. the solution of compounds **2** (1.35 mmol) in dichloromethane (3.86 mL), cooled with an ice bath, was dropped a pyridine (0.58 mmol, 45.88 mg) and 12-(pent-4-en-1-yloxy)dodecan-1-ol (1.74 mmol, 470.00 mg). After the addition, the ice bath was removed and the mixture was stirred at room temperature for 20 h. The mixture was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The crude product was purification by column chromatography on silica gel with the eluent of EtOAc/MeOH (9/1, v/v) to give amphiphilic arm as a yellow viscous oil (860 mg, yield: 63.2%).

¹H NMR (400 MHz, CDCl₃) δ 7.26 (s, 2H), 5.80 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 5.03 – 4.91 (m, 2H), 4.25 (t, J = 6.8 Hz, 2H), 4.21 – 4.14 (m, 6H), 3.84(m, 4H), 3.77(m, 2H), 3.58 – 3.72 (m, 30H), 3.52 (m, 6H), 3.37 (m, 4H), 3.35 (s, 9H), 2.1 (m, 2H), 1.82 – 1.20 (m, 22H).

UM. Amphiphilic arm (0.629 mmol, 624.8 mg) was dissolved in diethyl ether (2.1 mL) and Karstedt's catalyst (0.022 mL, 0.375 mg) was added. The reaction mixture was stirred at 25 °C for 30 min under N_{2(g)}. Then, to the resulting reaction mixture was added octakis(dimethylsilyloxy)POSS (0.046 mmol, 50.00 mg) and refluxed at 50 °C under N_{2(g)} for 24 h. The reaction mixture was filtered through Celite, washed with diethyl ether, and then concentrated to dryness. The crude product was purified by column chromatography on silica gel with the eluent of DCM/MeOH (19/1, v/v) to give UM as a yellow viscous oil. (270 mg, yield: 61.5%).

¹H NMR (400 MHz, CDCl₃) δ 7.30 (s, 16H), 4.25 (t, J = 6.9 Hz, 16H), 4.19 (dd, J = 9.5, 4.3 Hz, 48H), 3.85 (m, 32H), 3.77 (m, 16H), 3.54 – 3.72 (m, 240H), 3.49 (m, 48H), 3.35 (m, 24H), 3.32 (s, 96H), 1.74 (m, 16H), 1.66 – 1.23 (m, 176H), 0.62 (s, 16H), 0.14 (s, 48H);

¹³C NMR (101 MHz, CDCl₃) δ 166.08, 152.18, 142.42, 125.32, 108.95, 77.42, 77.10, 76.78, 72.35, 71.85, 70.96, 70.73, 70.57, 70.51, 70.42, 69.56, 68.80, 65.22, 58.93, 29.82, 29.62, 29.46, 29.29, 28.72, 26.20, 25.95, 22.80, 17.60, -0.34 ppm; FD-MASS (m/z) calcd [M]⁺ for C₄₂₄H₇₉₂O₁₆₄Si₁₆, 8964.09, found 8964.74.

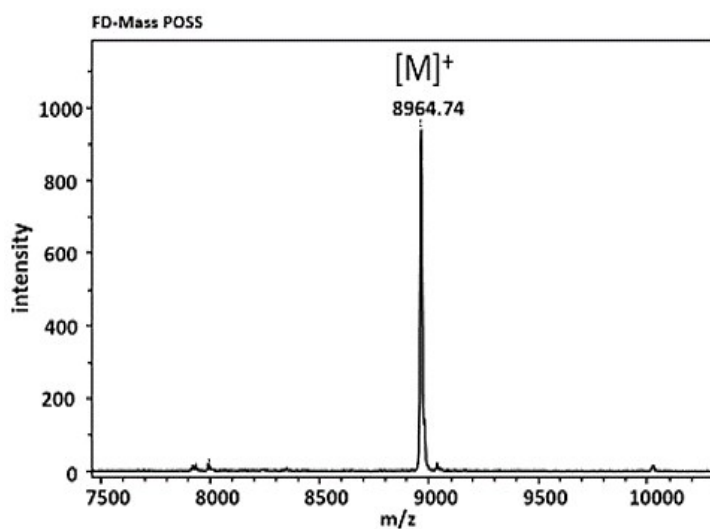


Figure S2. FD-mass spectra of UM.

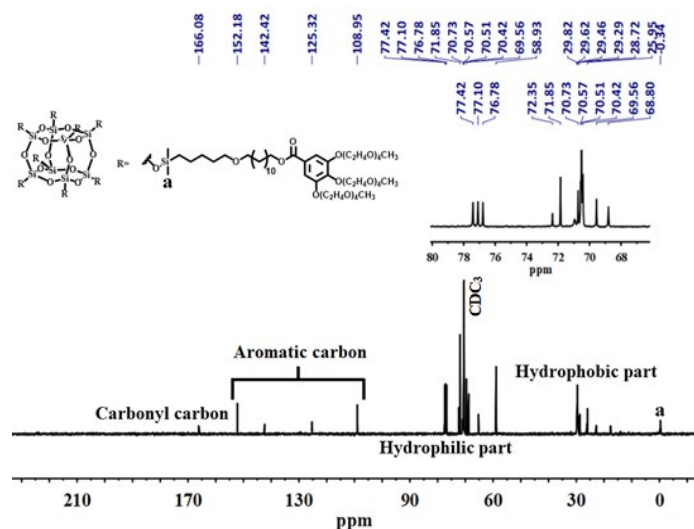


Figure S3. ¹³C-NMR spectra of UM (101 MHz in CDCl₃)

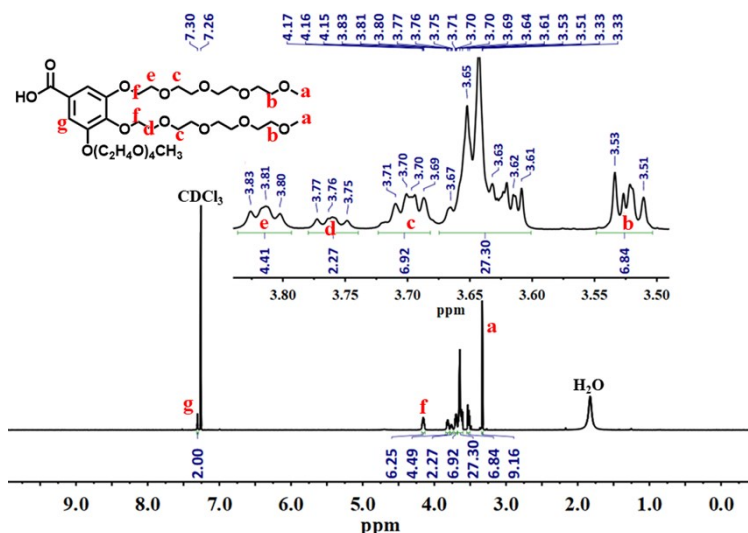


Figure S4. $^1\text{H-NMR}$ spectra of **Compound 1**. (400 MHz in CDCl_3)

Compounds 1. 3,4,5-tris(2,5,8,11-tetraoxatridecan-13-yloxy) benzoic acid were prepared according to the literature.¹⁻³ The $^1\text{H-NMR}$ spectra of compounds 1 is shown in **Figure S4**.

Preparation of the St/UM. The 1.5 mg of UM had dissolved in 3 mL D_2O ($5.5 \times 10^{-5} \text{ mol L}^{-1}$), and then 500 μL guest molecules (styrene, $4.3 \times 10^{-3} \text{ mol L}^{-1}$) were added to the solution. The mixtures were stood for 24 h and the water-layer solution was filtered with PTFE membrane filter (pore size: 220 nm). The filtered solution was then used in the SAXS, UV and NMR measurements.

Preparation of the PSt/UM. The 1.5 mg of UM had dissolved in 3 mL of D_2O or H_2O ($5.5 \times 10^{-5} \text{ mol L}^{-1}$), and then 500 μL guest molecules (styrene, $4.3 \times 10^{-3} \text{ mol L}^{-1}$) were added to the solution. The mixtures were stirred for 60 mins, stood still for 24 h and then the aqueous part of the mixture solution was filtered with PTFE membrane filter (pore size: 220 nm) to obtain the St/UM solution. Before polymerization, $\text{N}_{2(\text{g})}$ was bubble into the solution to remove $\text{O}_{2(\text{g})}$. After deoxygenation, we added 1.25 mg of cumene hydroperoxide (CHP) as initiator, 0.47 mg of $\text{Fe}_2(\text{SO}_4)_3$, 32.78 mg of $\text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O}$ as activator, and 8.64 mg of lactose as reducing agent into the St/UM solution. The reaction mixture was stirred at 40°C for 6 h to obtain the PSt/UM solutions. After polymerization, the solution was freeze dried to remove water and the polymer products were separated from the inorganic salts via dissolving in dichloromethane. The dichloromethane solution was filtered with PTFE membrane filter (pore size: 220 nm) to remove the precipitated salts. Then, the solution was concentrated and dried to obtain the PSt/UM for the subsequent characterization. For the GPC measurement, the PSt/UM was further washed by MeOH to remove the UM from the PS. When V50 and AIBN were used as the initiator, 1.13 mg of V50 or 0.69 mg of AIBN were added into the 3 mL of the deoxygenated St/UM solution. The reaction mixture was stirred at 70°C for 3 h. After polymerization, the solution was freeze dried to obtain the PSt/UM.

Preparation of the PS-b-PDMA. 280 μL of 2-dimethylaminoethyl methacrylate (DMA) was added into 3 mL of the above-mentioned PS/UM solution with syringe and then continue to reacting for 2 h. After 2 h, the reaction mixture was freeze dried to remove water and dissolved in dichloromethane. The dichloromethane solution was filtered with PTFE membrane filter (pore size: 220 nm) to remove the precipitated salts. Then, the solution was concentrated and dried to obtain PS-b-PDMA/UM. Finally, 1 mL 1M $\text{NaOH}_{(\text{aq})}$ was added into bottle to dissolve UM and precipitate PS-b-PDMA. The final product was obtained after filtration.

Small-angle X-ray scattering experiments

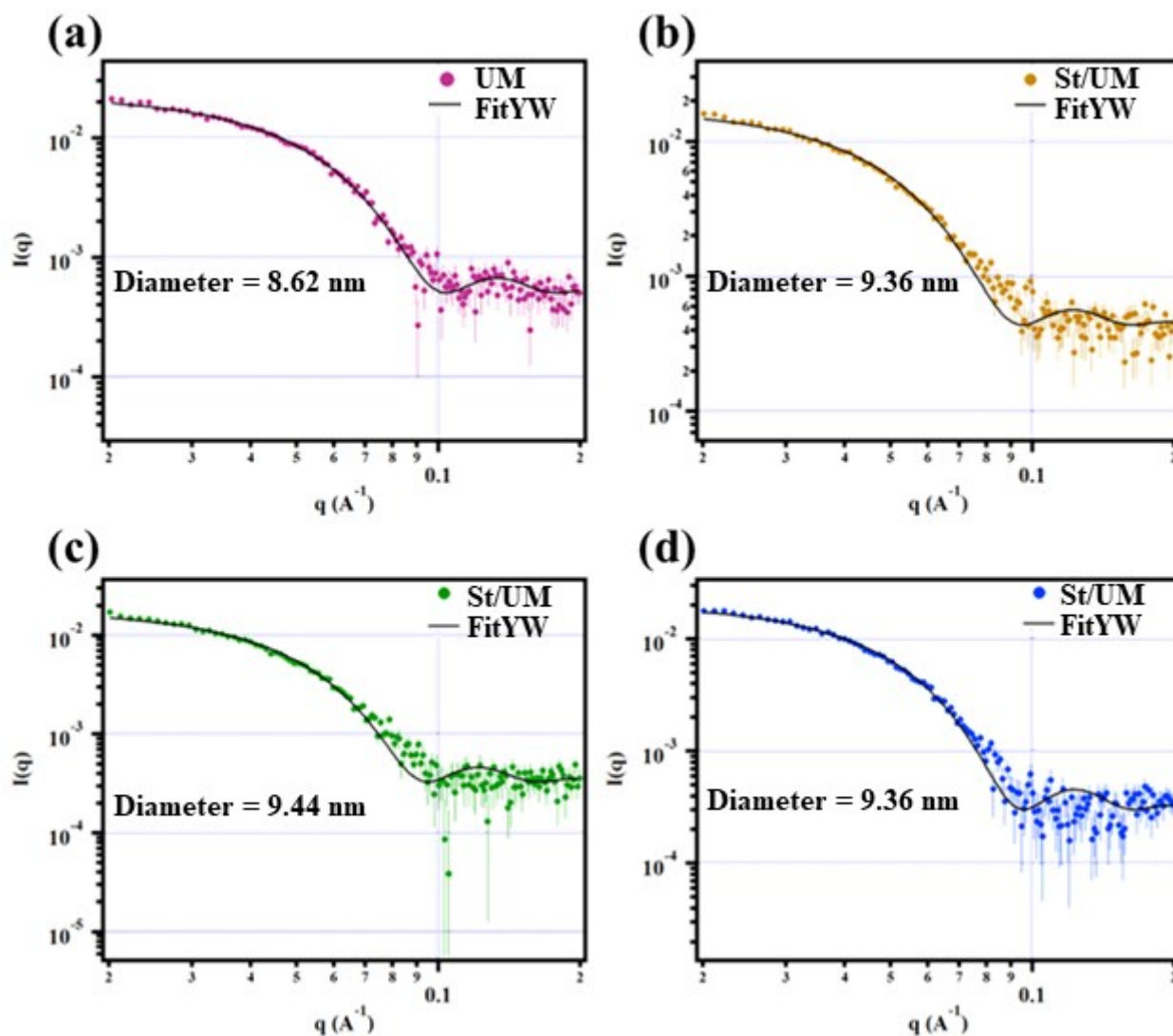


Figure S5. SAXS scattering curve $I(q)$ of the D_2O solution (a) UM ($5.5 \times 10^{-5} \text{ mol L}^{-1}$) (b) UM ($5.5 \times 10^{-5} \text{ mol L}^{-1}$) and $3.2 \times 10^{-1} \text{ mol L}^{-1}$ styrene (c) UM ($5.5 \times 10^{-5} \text{ mol L}^{-1}$) and $9.6 \times 10^{-1} \text{ mol L}^{-1}$ styrene (d) UM ($5.5 \times 10^{-5} \text{ mol L}^{-1}$) and 1.45 mol L^{-1} styrene.

Ultraviolet-Visible experiments

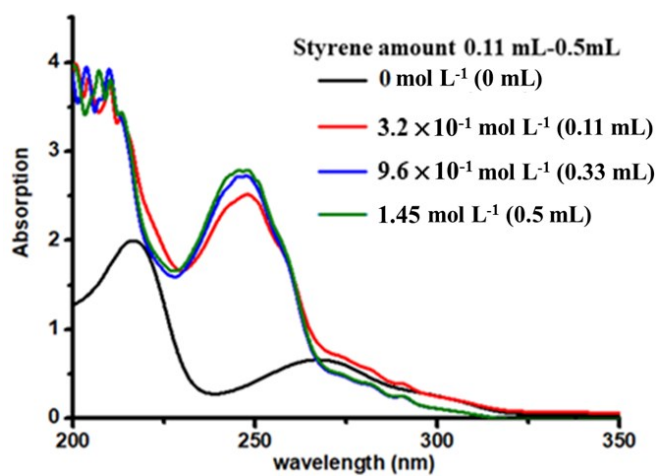


Figure S6. The UV-absorption spectra of St/UM with different amount of styrene.

Nuclear magnetic resonance experiments

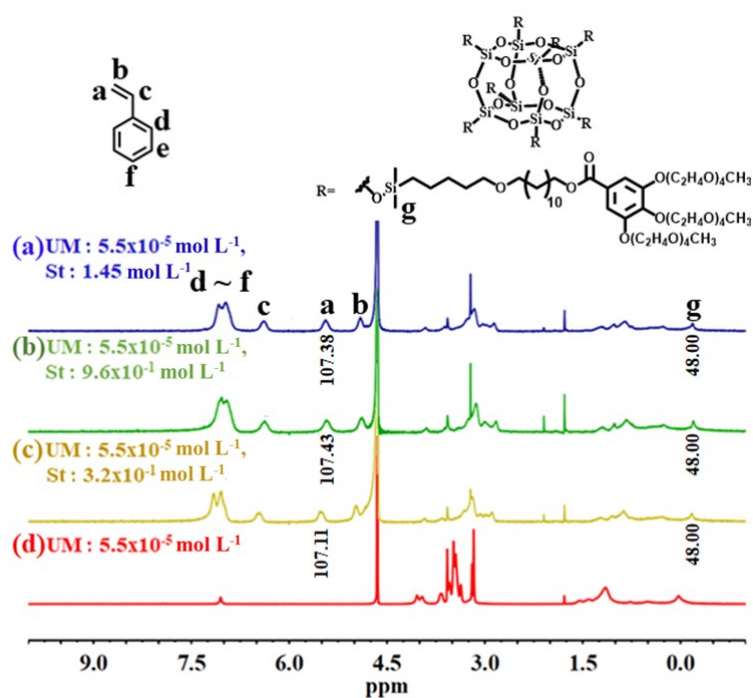


Figure S7. $^1\text{H-NMR}$ spectra of **St/UM** (a) **UM** ($5.5 \times 10^{-5} \text{ mol L}^{-1}$) and 1.45 mol L^{-1} styrene, (b) **UM** ($5.5 \times 10^{-5} \text{ mol L}^{-1}$) and $9.6 \times 10^{-1} \text{ mol L}^{-1}$ styrene, (c) **UM** ($5.5 \times 10^{-5} \text{ mol L}^{-1}$) and $3.2 \times 10^{-1} \text{ mol L}^{-1}$ styrene (d) **UM** ($5.5 \times 10^{-5} \text{ mol L}^{-1}$). (400 MHz in D_2O)

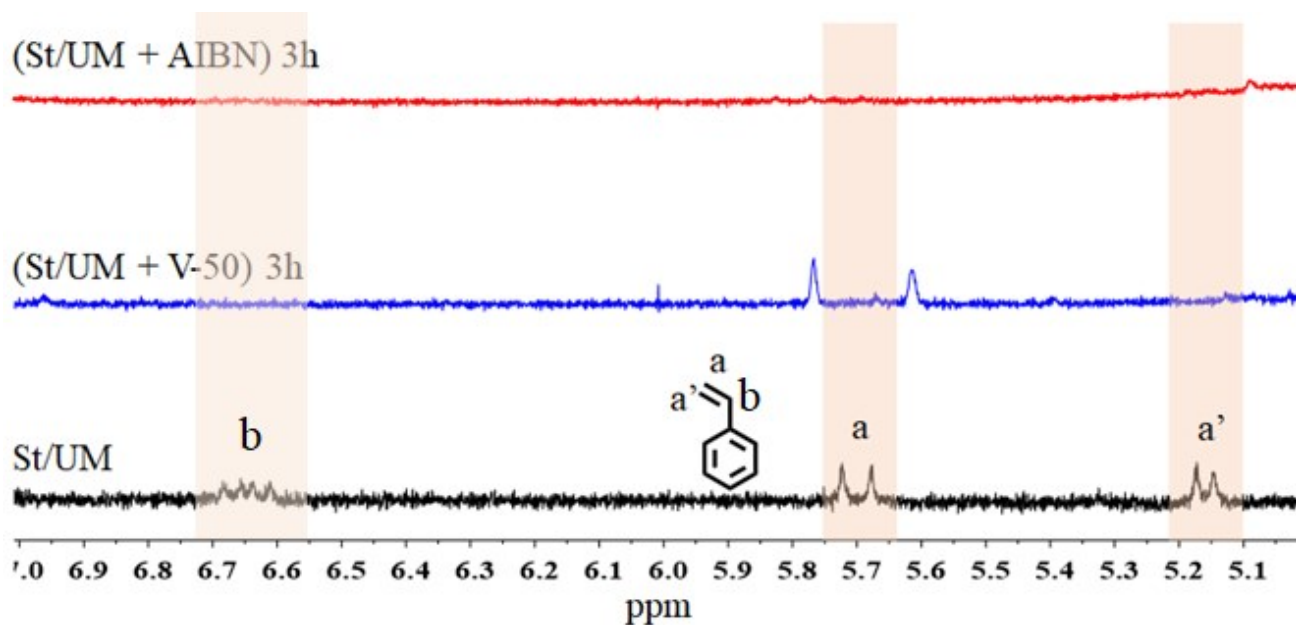


Figure S8. $^1\text{H-NMR}$ spectra for the solution of **St/UM** in D_2O after polymerization at 70°C with two kinds of initiator (water-soluble azo system and water-insoluble azo system).

Electron Paramagnetic Resonance experiments

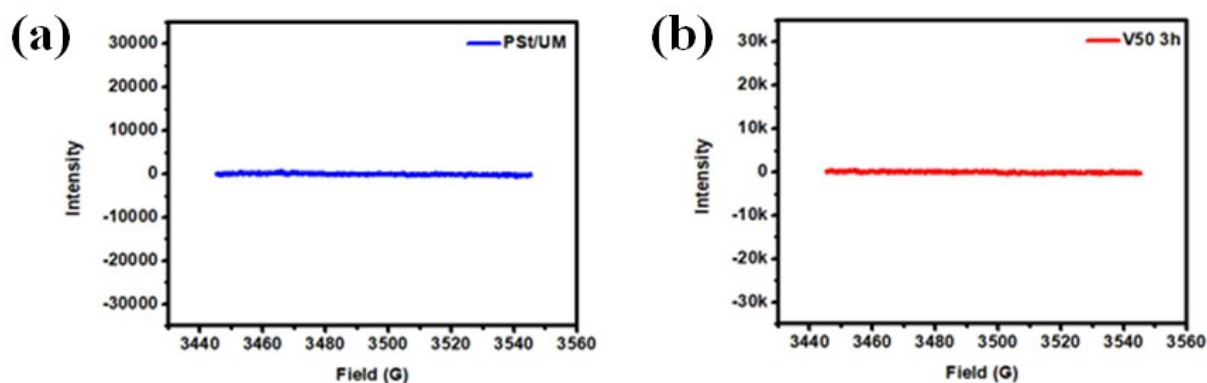


Figure S9. The EPR spectra of the aqueous solutions of (a) PSt/UM and (b) V50.

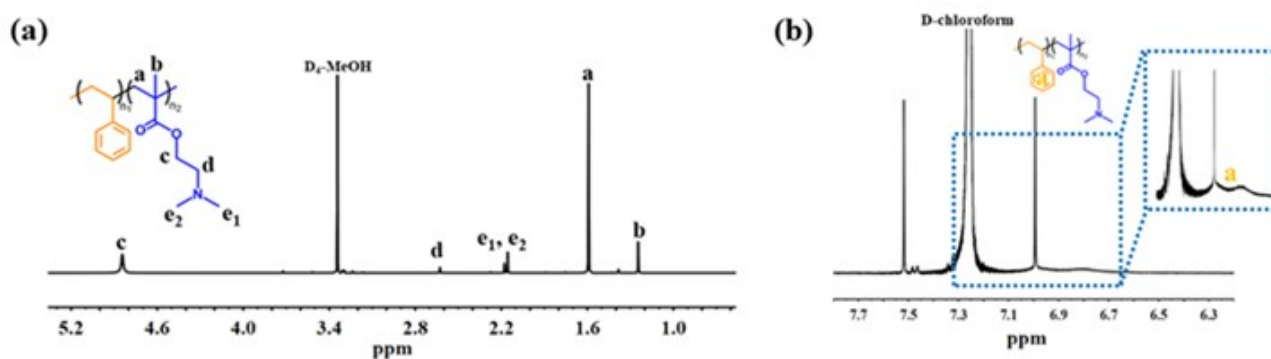


Figure S10. The $^1\text{H-NMR}$ spectra of PSt-b-PDMA (400 MHz) (a) in $d_4\text{-MeOH}$ and (b) in $d\text{-chloroform}$. The two sharp peak at 6.99 and 7.52 ppm in (b) are the spin side bands of the signal at 7.26 ppm of CDCl_3 .

Control experiments

The presence of living particles is also supported by a control experiment. A solution of the UM host and initiator in the absence of styrene monomers was heated at 40°C for 6 hours, followed by the addition of styrene or DMA. The resultant solution was continuously heated at 40°C for 120 hours, which barely produced PSt and PDMA, suggesting all initiators are terminated and generated no living free radicals in the system without the confined living polymer chains. Figure S10 show the NMR spectra of the control experiment of DMA.

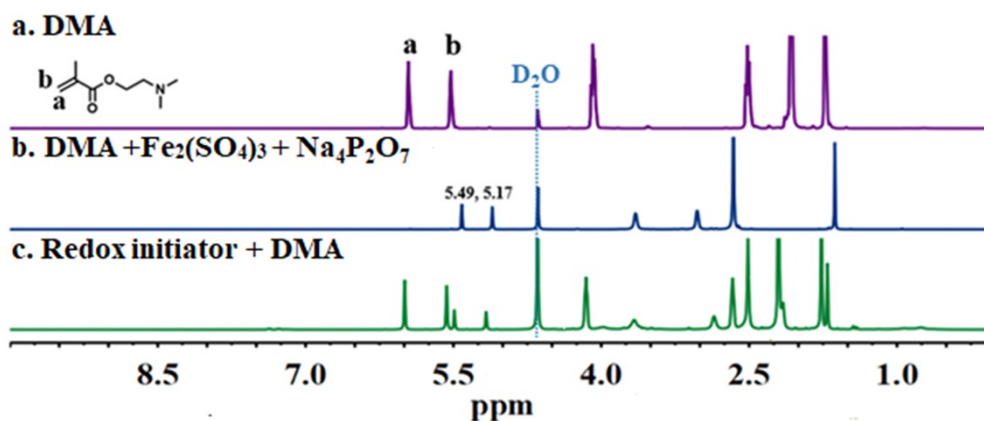


Figure S11. The $^1\text{H-NMR}$ of (a) DMA (b) DMA, $\text{Fe}_2(\text{SO}_4)_3$, and $\text{Na}_4\text{P}_2\text{O}_7$ (c) DMA add redox initiator and salts. All of these condition are polymerized for 6 h at 40°C

References

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