Electronic Supplementary Material (ESI) for Polymer Chemistry.


**Supporting information**

# Synthesis and Visualization of bottlebrush-shaped segmented hyperbranched polymers

*Mengjie Zhang*, *Jiasheng Wu, Zheqi Li*, *Wangmeng Hou, Yuanchao Li*, *Yi Shi** and *Yongming Chen**

School of Materials Science and Engineering, Key Laboratory for Polymeric Composite and Functional Materials of Ministry of Education, Sun Yat-Sen University, Guangzhou 510275, China

## Experimental

**Materials**：2-Hydroxyethyl methacrylate (HEMA, 99%, Aladdin) was purified by distillation under reduced pressure. Cuprous bromide (CuBr, 99.9%, Aladdin) was purified by washing with acetic acid and acetone. 2-Hydroxyrthyl acrylate (HEA, 96%, Aladdin), 2-bromoisobutyryl bromide (98%, Aladdin), triethylamine ( TEA, 99.5%, Aladdin), succinic anhydride (≥99%, Aldrich), sodium azide ($NaN_3$, >99.5%, Sigma-Aldrich), trisbromoneopentyl alcohol (>98%, Aladdin ), 2-2-bipyridine crystalline (bpy, 98%, Alfa Aesar), 4-dimethylaminopyridine (DMAP, ≥98%, Aldrich), 1-ethyl-3-(3-dimethyllaminopropyl) carbodiimide hydrochloride (EDC·HCl, 98%, Aladdin), poly (ethylene glycol) monomethyl ether (*m*PEG-OH, $M_n$ = 2 kDa, Aladdin), 4-pentynoic acid (97%, Aladdin), 4-pentyn-1-ol (99.9%, Aladdin), copper sulfate pentahydrate ($CuSO_4 \cdot 5H_2O$, 99.9%, Aladdin), ascorbic acid (99%, Aladdin), Aluminum oxide were used as received. All the solvents were dried and distilled before use.

## Instrumental methods

Proton nuclear magnetic resonance ($^1$H NMR) spectroscopy was acquired on a Bruker AVANCE III 400 MHz spectrometer at 25 $^o$C using DMSO-*d*6 or CDCl3 as the solvents. The size exclusion chromatography (SEC) was equipped with an Agilent 1260 Iso pump, PLgel columns (10 μm MIXED-B, 20 μm MIXED-A, 20 μm MIXED-A) at 50 °C with DMF flow rate = 1.00 mL $min^{-1}$, an Agilent 1260 refractive-index (RI) detector, linear polystyrene (PMMA) standards were used for calibration.

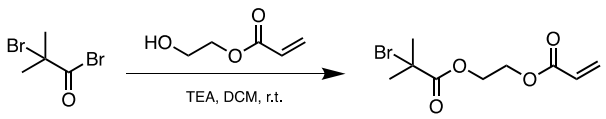
Fourier-transform infrared (FT-IR) spectroscopy was performed on a Thermo Nicolet Nexus 6700 spectrometer and the samples were dissolved in DCM and casted on a KBr plate.

The dynamic scatting (DLS) measurements were performed using a Malvern ZetaSizer and repeated three times at 25 $^{O}$C with a scattering angle (θ) of 173°.

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) measurement was performed on a Ultraflextreme MALDI-TOF/TOF instrument (Bruker Daltonics, Germany) equipped with a 355 nm Nd: YAG laser in positive reflection or liner mode. Matrix: DCTB (trans-2-[3-(4-tert-butylphenyl)2-methyl-2-propenylidene] malononitrile).

Atomic force microscopy (AFM, Bruker Multimode 8 AFM (Bruker Nano Inc.)) was used to characterize the morphological structure of molecular brushes in the tapping mode with a silicon probe. Samples were prepared by spin-coating 10 μL of dilute solutions (0.05 mg/mL in $H_2O$) on freshly cleaved mica.

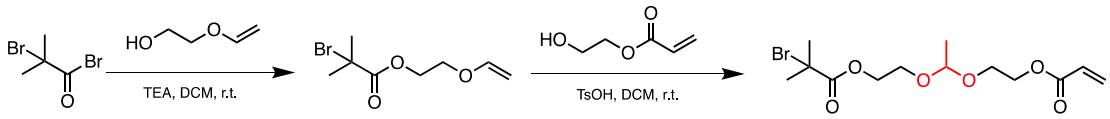
**Synthesis of 2-((2-bromo-2- methylpropannoyl)oxy)ethyl acrylate (inimer 1)[1]**




Hydroxyethyl acrylate (4.99 g, 43.0 mmol), TEA (8.70 g, 86.0 mmol) and 20 mL of dichloromethane (DCM) was mixed to a 50 mL round-bottom flask with a magnetic bar before being cooled to 0 $^{O}$C in an ice bath. 2-bromoisobutyryl bromide (11.9 g, 51.6 mmol)

was dissolved in 10 mL DCM and added to the reaction mixture *via* an addition funnel over 30 min. The reaction was kept cold for an additional 30 min before being warmed up to room temperature for 3 h. After the reaction finished, the solvent was removed under reduced pressure and the product was purified by a column chromatography (hexane: ethyl acetate = 4:1) to give 8.44 g colorless liquid (74% yield).

**Synthesis of 2-(1-(2-bromo-2-methylpropanoyl)oxy)ethoxy)ethyl acrylate (inimer 2)**




**synthesis of 2-(vinyloxy)ethyl 2-bromo-2-methylpropanoate**

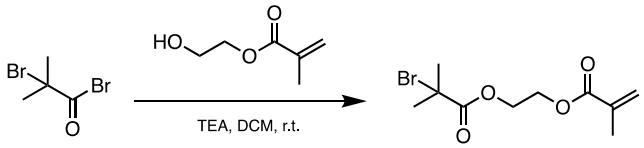
A 100 mL round-bottom flask was loaded with magnetic stir bar, 2-vinyloxyethanol (4.93g, 0.056mol), triethylamine (11.14g, 0.112mol), and 20mL of DCM before being cooled to 0 $^{o}$C in an ice bath. A mixture of 2-bromoisobutyryl bromide (15.45g, 0.067mol) was dissolved in 5mL DCM and added to the reaction mixture via an addition funnel over 30 min. The reaction was then warmed up to room temperature and reacted overnight before filtration of the solid and removal of solvent under reduced pressure. The product was purified via column chromatography (hexane: dichloromethane = 2:3), obtaining 9.70g of colorless liquid (73% yield).

**Synthesis of 2-(1-(2-bromo-2-methylpropanoyl)oxy)ethoxy)ethyl acrylate**

2-(vinyloxy) ethyl 2-bromo-2-methylpropanoate (3.80 g, 0.016 mol) and hydroxyethyl acrylate (2.20 g, 0.019 mol) were dissolved in 50 mL of DCM. A catalytic amount of p-

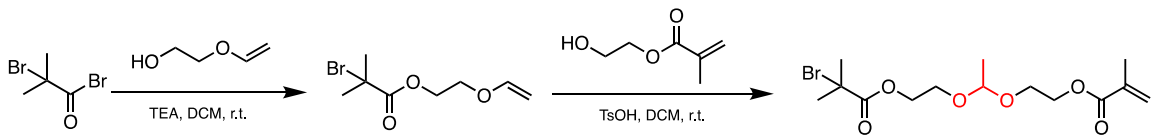
toluenesulfonic acid (30.5 mg, 0.16 mmol) was added to start the reaction. The reaction was allowed to stir for 1h and then neutralized with a few drops of TEA. The solvent was removed under reduced pressure, and the product was purified via column chromatography (hexane: ethyl acetate = 2:1 (3% TEA), obtaining 4.29g colorless liquid (75% yield).

**Synthesis of 2-((2-bromo-2- methylpropannoyl)oxy)ethyl methacrylate (inimer 3)**



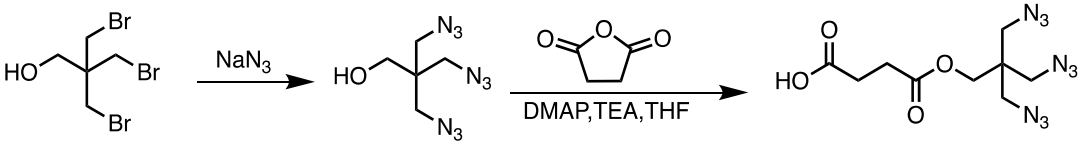

2-Hydroxyethyl methacrylate (5.59 g, 43.0 mmol), TEA (8.70 g, 86.0 mmol) and 20 mL of dichloromethane (DCM) was mixed to a 50 mL round-bottom flask with a magnetic bar before being cooled to 0 $^{o}$C in an ice bath. 2-bromoisobutyryl bromide (11.9 g, 51.6 mmol) was dissolved in 10 mL DCM and added to the reaction mixture *via* an addition funnel over 30 min. The reaction was kept cold for an additional 30 min before being warmed up to room temperature for 3 h. After the reaction finished, the solvent was removed under reduced pressure and the product was purified by a column chromatography (hexane: ethyl acetate = 4:1) to give 9.36 g colorless liquid (78% yield).

**Synthesis of 2-(1-(2-bromo-2-methylpropanoyl)oxy)ethoxy)ethyl methacrylate (inimer 4)**



2-(vinyloxy) ethyl 2-bromo-2-methylpropanoate (3.80 g, 0.016 mol) and 2-hydroxyethyl methacrylate (2.50 g, 0.019 mol) were dissolved in 50 mL of DCM. A catalytic amount of p-toluenesulfonic acid (30.5 mg, 0.16 mmol) was added to start the reaction. The reaction was allowed to stir for 1h and then neutralized with a few drops of TEA. The solvent was removed under reduced pressure, and the product was purified via column chromatography (hexane: ethyl acetate = 2:1 (3% TEA), obtaining 4.29g colorless liquid (73% yield).

**Synthesis of 4-(3-azido-2,2-bis(azidomethyl)propoxy)-4-oxobutanoic acid ($3N_3$-COOH)[2]**




Tribromo neopentyl alcohol (47.0 mmol, 15.3 g), sodium azide (169 mmol, 11.0 g) and DMSO (200 mL) were mixed in 500mL round- bottom flask, and stirred in 110 $^{o}$C for 16 h. Then 200 mL DI water was added to the reaction solution and the system was stirred for 1 h. Then the mixture was extracted with ethyl acetate for three times, and the obtained product was purified *via* distillation under reduced pressure to give light yellow liquid (90% yield).

3-azido-2,2-bis(azidomethyl)propan-1-ol (9.40 mmol, 2.00 g), succinic anhydride (14.0 mmol, 1.40 g) and DMAP (14.0 mmol, 1.71 g) were dissolved in dried THF (18 mL), then TEA (14.0 mmol, 1.42 g) was added dropwise. After the mixture reacted in room temperature for 12 h, the solvent was removed under reduced pressure, the residue was

then dissolved in 100 mL of DCM and washed with brine (3*100 mL). The organic phase was dried over anhydrous $MgSO_4$ before the solvent was evaporated. The crude product was purified by column chromatography (hexane: ethyl acetate = 1:1) to give clear liquid (81% yield).

**Synthesis of branched-PHEMA polymers by ATRP[3]**

A dried 10 mL Schlenk flask was charged with hydroxyethyl acrylate (30.0 mmol, 3.91 g), 2-bipyridine (1.2 mmol, 188 mg), inimer 1 (0.6 mmol, 210 mg) and methanol (3.9 g). The mixture was degassed by three freeze-evacuate-thaw cycles. During the final cycle, the flask was filled with nitrogen, and CuBr (0.6 mmol, 86.1 mg) was quickly added to the frozen reaction mixture. The flask was finally sealed under vacuum. The polymerization was carried out in an oil bath at 40 $^{O}$C for 2 h, and was terminated *via* exposure to air. The resulting polymer solution was purified by passing through a column of neutral $Al_2O_3$. Then, the polymer was precipitated in diethyl ether for three times. The final product was then dissolved in DMF at the concentration of 0.5 g/mL.

**Synthesis of triazido-functionlized branched-PHEMA (PHEMA-3$N_3$)**

The triazido-functionlized branched-PHEMA backbone was synthesized by esterification reaction. Branched-PHEMA (3.85 mmol, 501 mg), 3$N_3$-COOH (7.70 mmol, 2.40 g), EDC·HCl (7.7 mmol, 1.48 g), dry DMF (5 mL) and DMAP (0.77 mmol, 94.0 mg) were added sequentially. The reaction mixture was allowed to be stirred at 40 ℃ for 24 h. The

final product was precipitated in methanol three times to remove the unreacted acid and re-dissolved in DMF at the concentration of 100 mg/mL.

**Synthesis of alkynyl-terminated PEG (ay-$PEG_{45}$)**

The alkynyl-terminated PEG was synthesized by esterification reaction. Firstly, the $PEG_{2000}$ (1.5 mmol, 3.00 g) was dried by azeotropic distillation with methylbenzene (100 mL). Then, pentynonic acid (4.50 mmol, 441 mg), EDC·HCL (3.0 mmol, 0.575g), DMAP (0.60 mmol, 73.2 mg), and 30 mL DCM was added to the round-bottom flask sequentially. The reaction mixture was stirred at 40 ℃ for 24 h. The final product was recrystallized in ethyl alcohol for three times and dried under vacuum to give colorless solid (89% yield).

**Synthesis of branched molecular bottlebrushes [4]**

A dried 10 mL Schlenk flask was charged with PHEMA-$3N_3$ (0.026mmol, 10.9 mg), ay-PEG (0.078mmol, 166.8mg), $CuSO_4 \cdot 5H_2O$ ($7.8\times10^{-3}$ mmol, 1.94 mg), DMF (2 mL), and 40 μL toluene as an internal standard. The solution was degassed by three freeze-evacuate-thaw cycles. During the final cycle, the flask was filled with nitrogen and the ascorbic acid (0.039 mmol, 6.67 mg) was added to the frozen reaction mixture quickly. The flask was finally sealed under vacuum. The polymerization was carried out in an oil bath at 45 $^{O}$C for 8 h, and was terminated *via* exposure to air. The resulting polymer solution was purified by passing through a column of neutral $Al_2O_3$. At last, the polymer was precipitated in diethyl ether for three times to give colorless solid (70% yield).

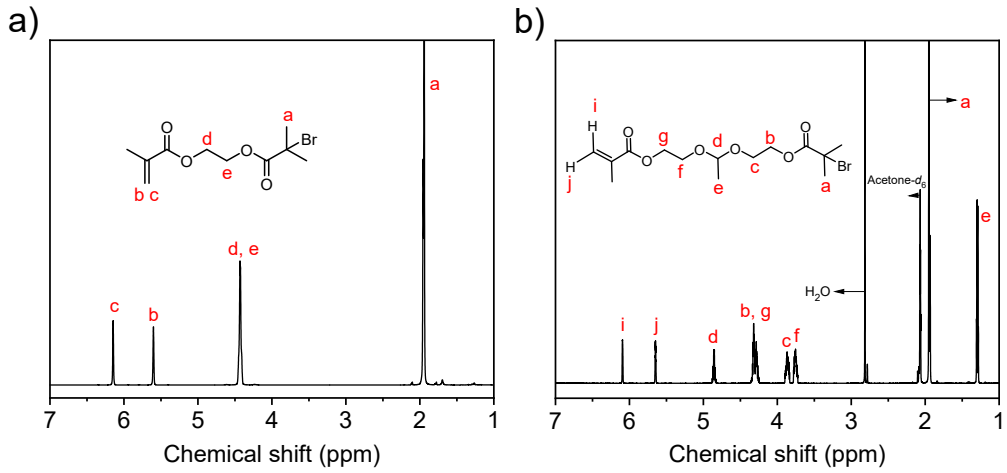



**Figure S1.** a) $^1$H NMR spectrum of inimer 1 and b) inimer 2.

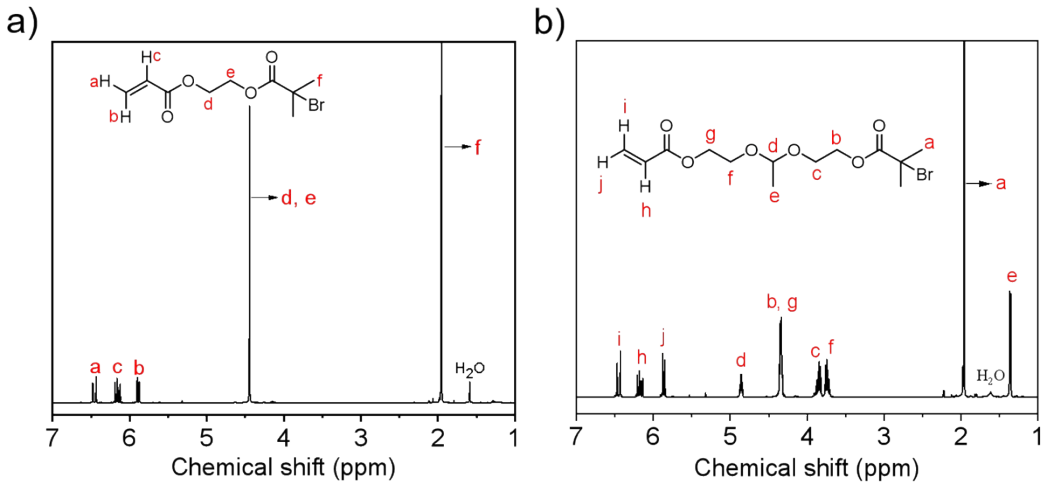



**Figure S2.** a) $^1$H NMR spectrum of inimer 3 and b) inimer 4.

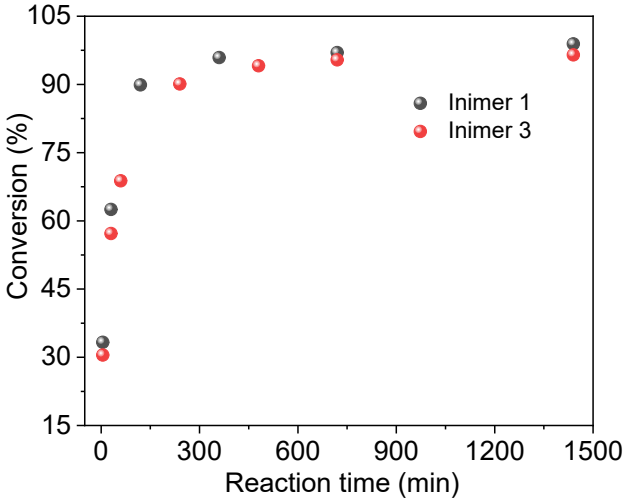



**Figure S3**. Kinetic analysis of segmented hyperbranched polymers synthesized by SCVP-ATRP of HEMA with inimer 1 and inimer 3 at feed ratios of [HEMA]:[inimer]:[Bpy]:[CuBr] = 15:1:1:0.5 at 40 ℃ in 70 wt% methanol at 40 ℃.

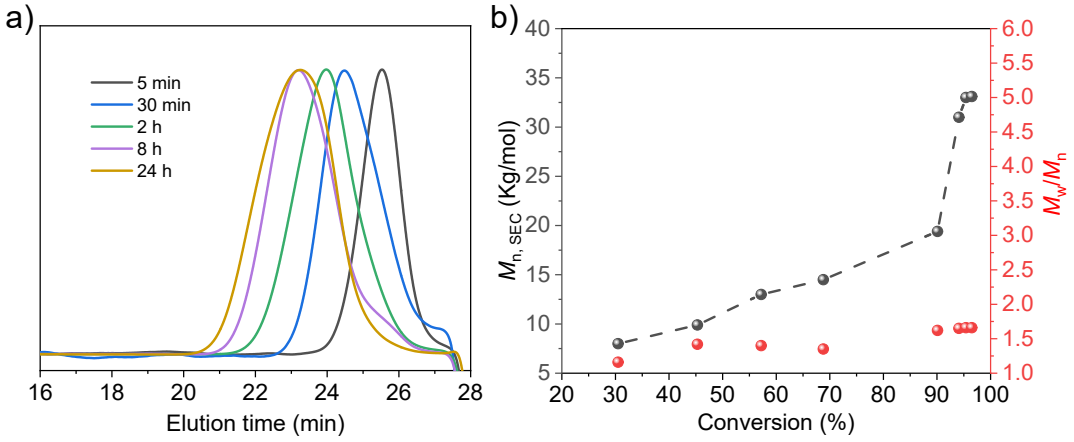



**Figure S4.** a) SEC traces, and b) evolution of the number-average molecular weight and dispersity ($M_w/M_n$) of segmented hyperbranched polymers synthesized by SCVP-ATRP of

HEMA with inimer 1 at feed ratios of [HEMA]:[inimer 3]:[Bpy]:[CuBr] = 15:1:1:0.5 in 70 wt% methanol at 40 °C.

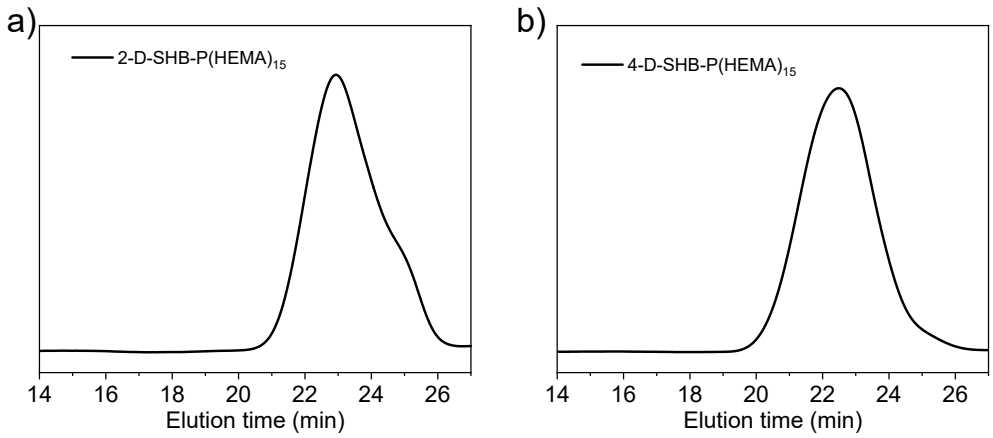



**Figure S5.** DMF SEC traces of 2-D-SHB-P(PHEMA)$_{15}$ and the 4-D-SHB-P(PHEMA)$_{15}$

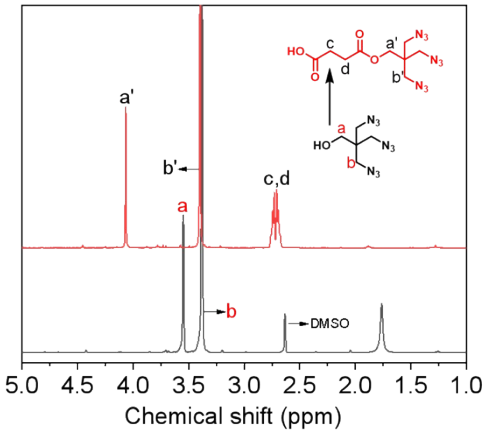



**Figure S6.** $^{1}$H NMR spectra of 4-(3-azido-2,2-bis(azidomethyl)propoxy)-4-oxobutanoic acid.

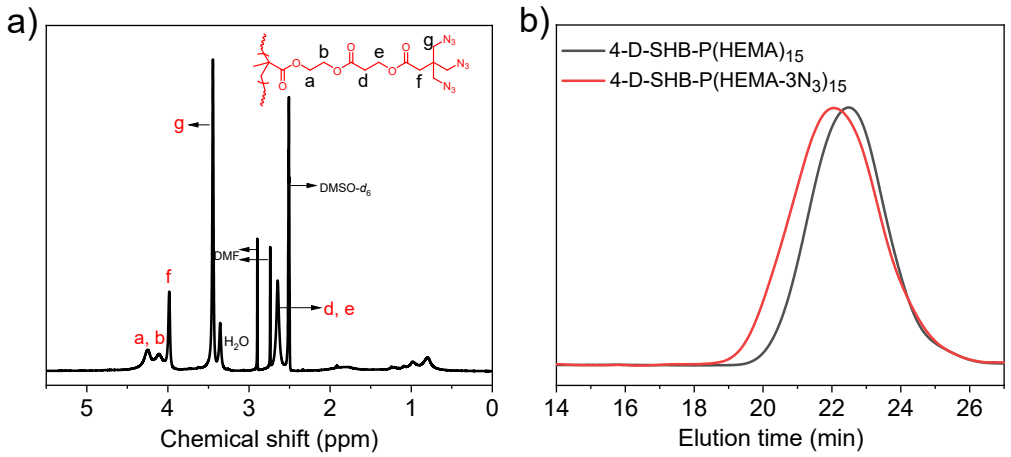



**Figure S7.** a) $^1$H NMR spectrum of 4-D-SHB-P(PHEMA-3N$_3$)$_{15}$, and b) DMF SEC traces of 4-D-SHB-P(PHEMA)$_{15}$ and the corresponding 4-D-SHB-P(PHEMA-3N$_3$)$_{15}$.

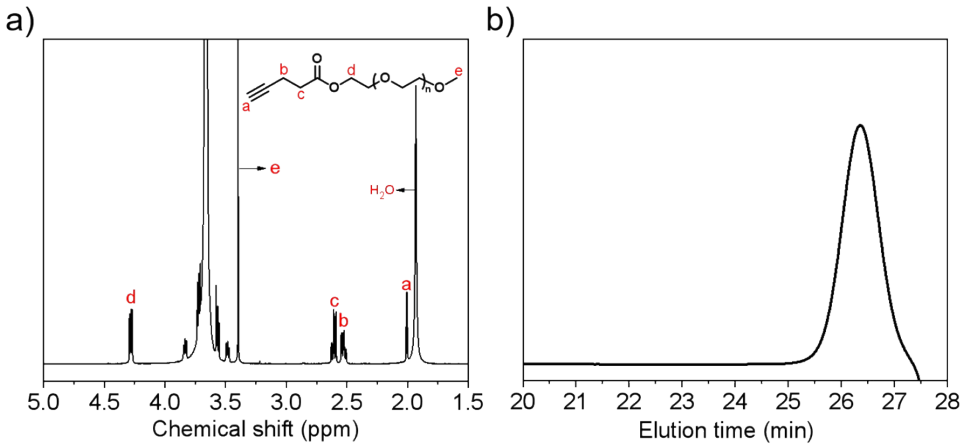



**Figure S8.** a) $^1$H NMR spectra and b) DMF SEC traces of ay-PEO$_{45}$.

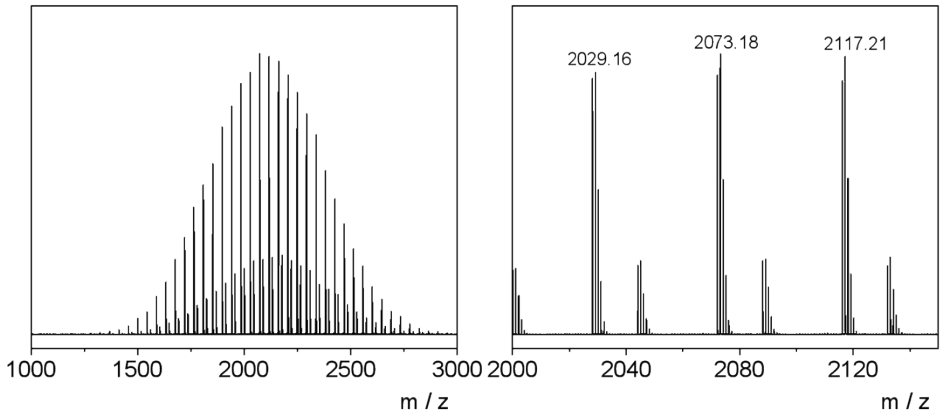



**Figure S9.** MALDI-TOF mass spectrum of ay-$PEO_{45}$.

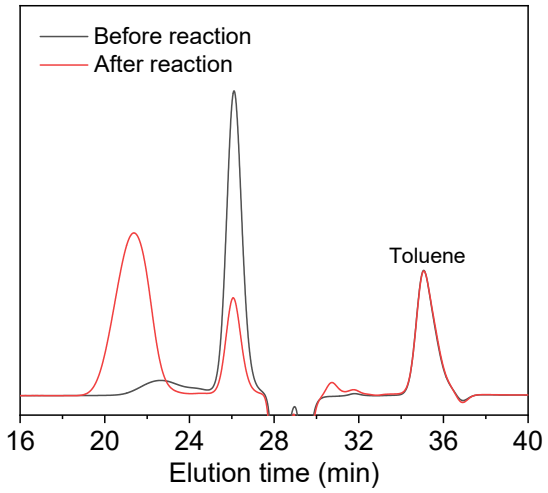



**Figure S10.** SEC traces of the accelerated CuAAC click reaction between 2-D-SHB-P(PHEMA-$3N_3$)$_{15}$ and ay-$PEO_{45}$ at the feed ratio of $[ay]_0$:$[N_3]_0$:$[CuSO_4 \cdot 5H_2O]$:[ascorbic acid] = 1.2 : 1 : 0.1 : 0.5 and fixed concentration of [ay-$PEO_{45}$]$_0$ = 0.04 M.

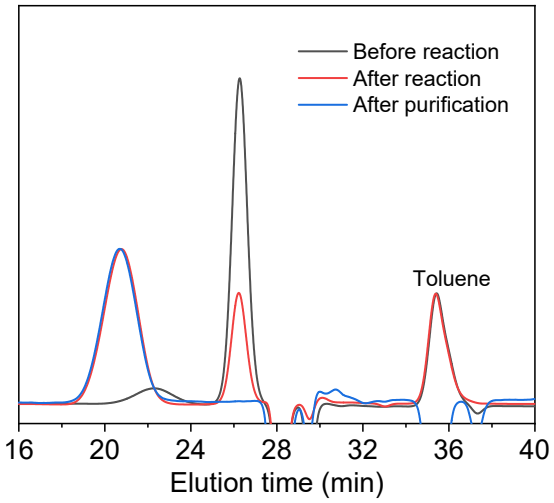



**Figure S11.** SEC traces of reaction mixture of 4-D-SHB-P(HEMA-3$N_3$)$_{15}$ and ay-PEO$_{45}$ before and after CuAAC click reaction and the purified 4-D-B-SHB-P(HEMA-*g*-PEO$_{45}$)$_{15}$. Experimental conditions: [ay]$_0$:[$N_3$]$_0$:[$CuSO_4 \cdot 5H_2O$]:[ascorbic acid] = 1.2:1:0.1:0.5 in DMF, 45 °C, [ay-PEO$_{45}$]$_0$ = 0.04 M.

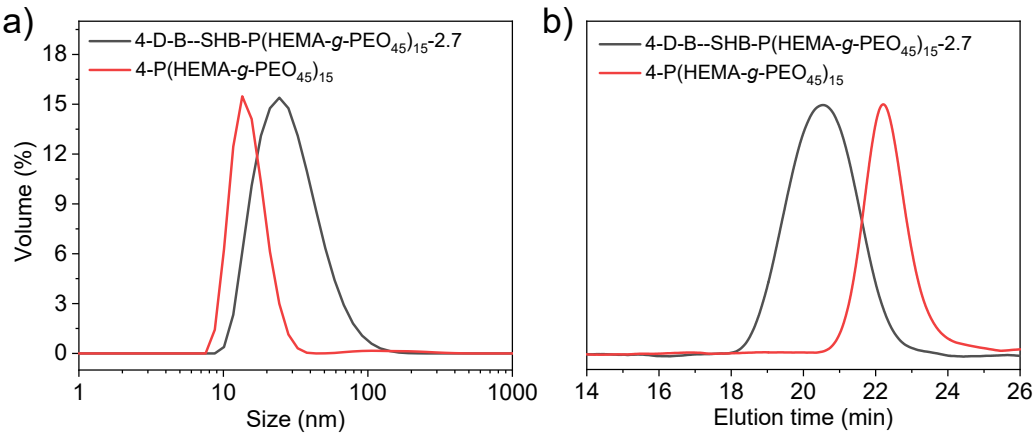



**Figure S12.** (a) hydrodynamic diameters ($D_h$) and (b) DMF SEC traces of 4-D-B-SHB-P(HEMA-*g*-PEO$_{45}$)$_{15}$-2.7 and its degradation product 4-P(HEMA-*g*-PEO$_{45}$)$_{15}$-2.7.

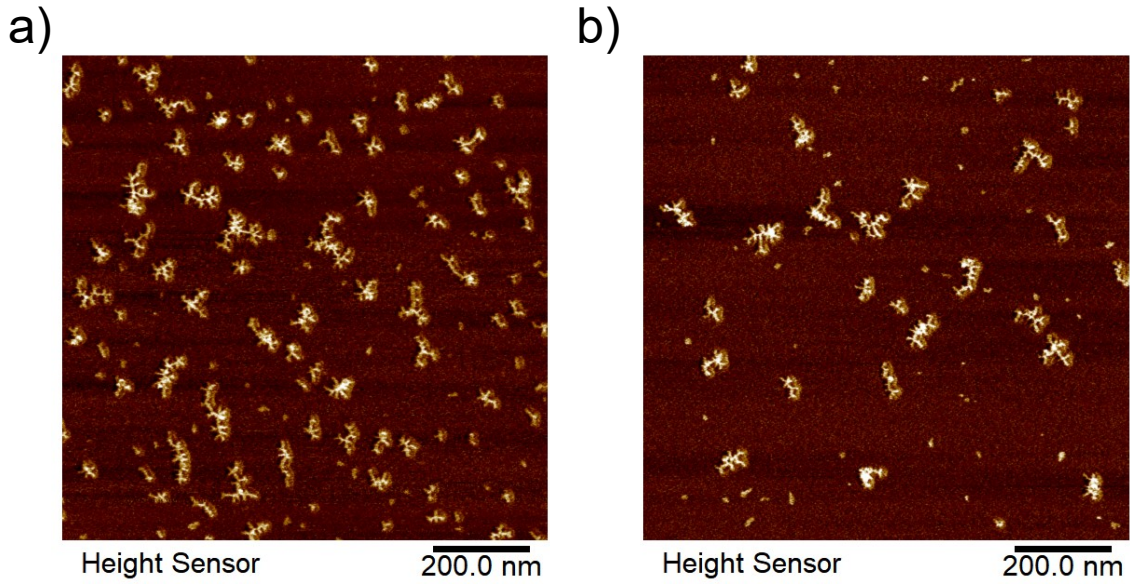



**Figure S13**. AFM height images of 2-D-B-SBH-P(HEMA-*g*-PEO)$_{15}$-2.5 in different regions on mica substrates.

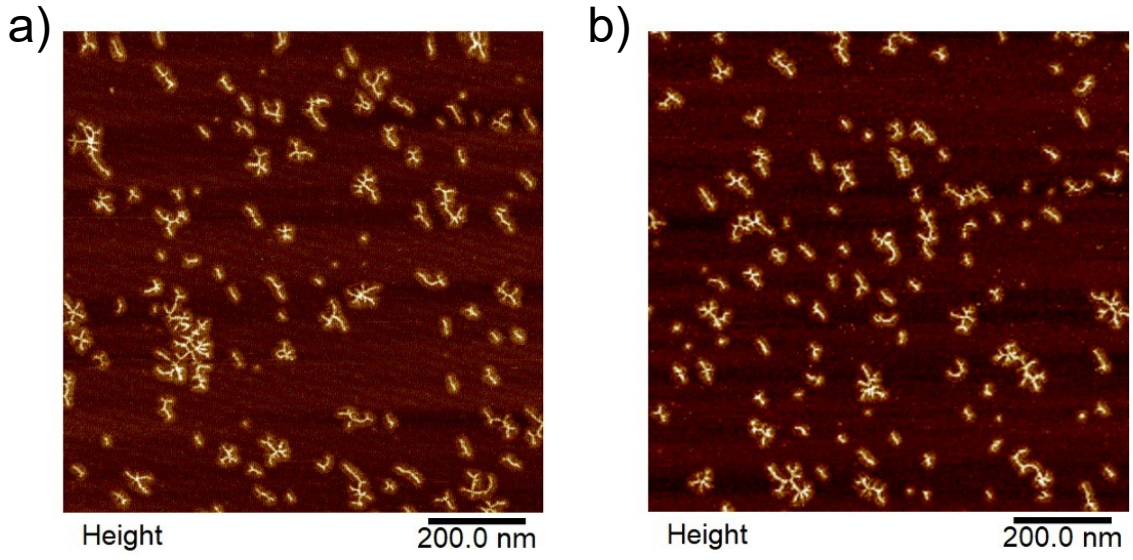



**Figure S14**. AFM height images of 4-D-B-SBH-P(HEMA-*g*-PEO$_{45}$)$_{15}$-2.7 in different regions on mica substrates.

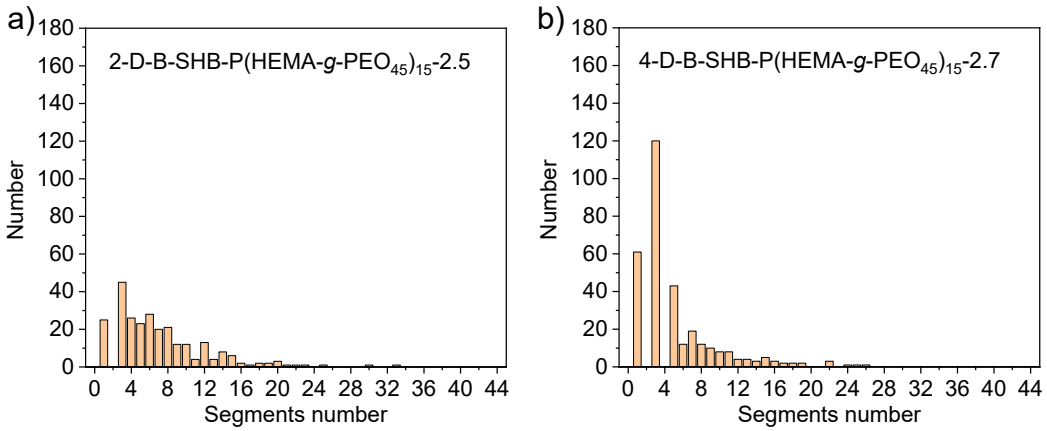



**Figure S15**. The statistics analysis of 2-D-B-SBH-P(HEMA-*g*-PEO)$_{15}$-2.5 and 4-D-B-SBH-P(HEMA-*g*-PEO$_{45}$)$_{15}$-2.7 by taking more than 300 molecules.

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