SUPPORTING INFORMATION

Bottlebrush Polymers with Self-Immolative Side Chains

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Experimental Section

Materials

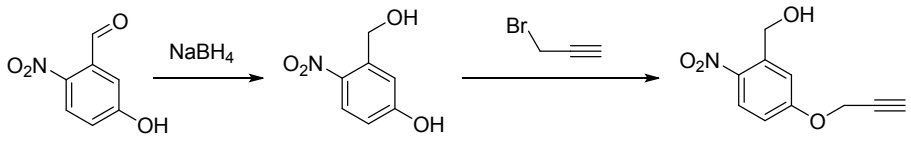
Propargyl bromide, 5-hydroxy-2-nitrobenzaldehyde, $NaBH_4$, K_2CO_3, dibutyltin dilaurate (DBTL), $CuSO_4{\cdot}5H_2O$, L-ascorbic acid, trifluoroacetic acid (TFA), NH_4Cl, anhydrous $MgSO_4$, toluene, methanol, dichloromethane (DCM), tetrahydrofuran (THF), dioxane, ethyl acetate (EA), dimethylsulfoxide (DMSO) and *N,N*-dimethylformamide (DMF) were purchased as regent grade from Alfa Aesar, Aldrich, Acros, J&K Chemical, or Beijing Chemical Reagent Co. and used as received unless otherwise noted. For making dry solvents: DMSO and DMF were refluxed over calcium hydride. Dioxane was refluxed over Na prior to use. Polystyrene (PS) gel bead (S-X1) was purchased from Bio-Rad. Dialysis bag (Spectra/Pro® 7, molecular weight cutoff = 10 kDa) was produced by SPECTRUM® LABs. Inc. Philips (/12) low-pressure fluorescent lamp (UVB, 290-320 nm) was used as the UV light source. The backbones PGA_{100} and PGA_{540}

were synthesized by the procedure similar to our previously reports.[1] Phenyl carbamate monomers (monomer **1** and **2**) were prepared according to the literature.[2]

Characterization

^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker Avance 400 spectrometer at room temperature. DMSO-d_6 was used as the solvent and TMS as the internal standard. Fourier Transform Ion Cyclotron Resonance Electrospray Ionization Mass Spectrometry was performed on a Bruker Solarix mass spectrometer equipped with a 9.4 T superconducting magnet (Bruker Daltonics) and an ESI source set to operate over m/z 57.75-400.00. Dry gas flow was set at 4.0 L/min. Dry gas temperature was set at 200℃. The capillary was 3000 V. The end plate offset was -500 V. Gel permeation chromatography (GPC) in DMF was conducted on a system comprised of a Waters 515 HPLC pump, and a Waters 2414 RI detector equipped with three Agilent mixed columns (PLgel MIXED-A and PLgel MIXED-B × 2). DMF with 0.01 M LiBr was used as the eluent at a flow rate of 1 mL/min. PS standards were used for the calibration. Preparative GPC (SHIMADZU LC-20AR) equipped with a LC-201R pump, a RID-20A refractive index detector, and an Agilent Plgel Mixed-B column. DMF was used as the eluent at a flow rate of 10 mL/min. Fourier transform infrared (FT-IR) spectroscopy was performed on a Thermo Nicolet Avatar-330 Spectrometer at room temperature. Fluorescence spectra were recorded using a Cary Eclipse fluorescence spectrophotometer. Atomic force microscopy (AFM) images were recorded under ambient conditions using a Multimode 8 (Bruker) AFM in tapping mode and silicon tips (spring constant = 20-80 N/m, resonance frequency = 304-351 kHz). Samples were prepared by spin coating 0.1 mg/mL solution onto freshly cleaved mica. Fluorescence spectra were recorded using a Cary Eclipse fluorescence spectrophotometer.

Preparation of compound 2 (end-capping reagent of the side chains)

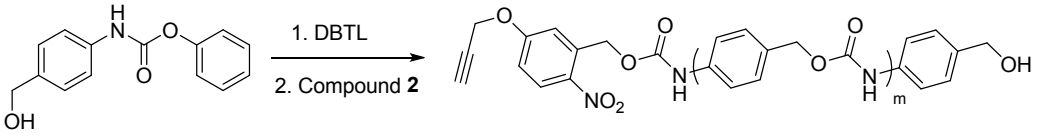


1 **2**

$NaBH_4$ (3.4 g, 90 mmol) was slowly added into the solution of 5-hydroxy-2-nitrobenzaldehyde (10 g, 60 mmol) in 50 mL methanol with stirring in an ice bath. Then the reaction solution was stirred at room temperature for 24 h. After the addition of 40 mL saturated NH_4Cl solution, the reaction mixture was extracted with EA (80 mL × 3). The organic phase was collected and dried by anhydrous $MgSO_4$, and concentrated on a rotary evaporator to afford compound **1** as a light yellow solid (8.41 g, yield 83.1%). ^{1}H-NMR (DMSO-d_6), δ (ppm): 10.89 (br, 1H), 8.06 (d, 1H), 7.25 (s, 1H), 6.81 (d, 1H), 5.50 (br, 1H), 4.82 (s, 2H). ^{13}C-NMR (DMSO), δ (ppm): 161.6, 142.4, 140.0, 127.4, 113.8, 113.2, 79.1, 78.4, 60.3, 56.2. HRMS (EI-MS) m/z calculated for $C_{10}H_9NNaO_4$ [M+Na^+] 230.04238, found 230.04250.

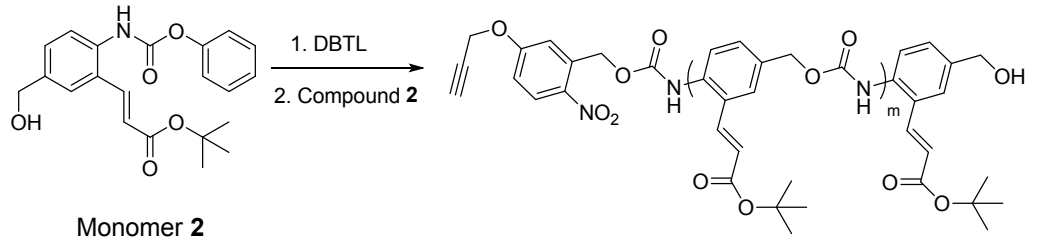
Compound **1** (5 g, 29.6 mmol) and K_2CO_3 (4.9 g, 35.5 mmol) were dissolved in 70 mL dry DMF and stirred at 60 °C for 1 h. Then propargyl bromide (5.2 g, 43.7 mmol) was added, and the reaction was kept stirring for additional 10 h. After removing the DMF under reduced pressure, the reaction mixture was dissolved in 50 mL EA and washed with distilled water (50 mL × 2). The organic phase was collected and dried by anhydrous $MgSO_4$, and concentrated on a rotary evaporator. The crude product was purified by passing through a silica column with DCM/methanol (v/v = 10/1) as eluent to afford compound **2** as a light yellow solid (4.8 g, yield 78.3%). ^{1}H-NMR (DMSO-d_6), δ (ppm): 8.16 (d, 1H), 7.41 (s, 1H), 7.10 (d, 1H), 5.61 (s, 1H), 4.97 (s, 2H), 4.86 (d, 2H), 3.67 (s, 1H). ^{13}C-NMR (DMSO), δ (ppm): 163.3, 143.1, 138.2, 128.0, 114.1, 114.0, 60.7 HRMS (EI-MS) m/z calculated for $C_7H_6NO_4$ [M-H^+] 160.03023, found 160.03027.

Preparation of the side chains (SC 1 and SC 2)



Monomer **1** Side chain: SC**1**

SC 1: Monomer **1** (1.3 g, 5.3 mmol) and DBTL (338 mg, 0.53 mmol) were dissolved in dry DMSO (3 mL) in a 25 mL Schlenk tube equipped with a stir bar. After degassing by three freeze-evacuate-thaw cycles, the solution was stirred at 110 °C for 15 min. Then a degassed solution of compound **2** (1.1 g, 5.3 mmol) in dry DMSO (3 mL) was added into the above reaction solution through a needle piercing the rubber septum. The mixture was stirred at 110 °C for additional 1 h, cooling to room temperature and precipitated into methanol for three times to afford SC **1** as a light yellow solid (500 mg, yield 50%). ^{1}H-NMR (DMSO-d_6), δ (ppm): 9.79 (s, 9H), 8.26 (d, 1H), 7.15-7.65 (m, 42H), 4.91-5.21 (m, 22H), 4.42(d, 2H), 3.66 (s, 1H). $M_{n,NMR}$ was calculated as 1700 from ^{1}H-NMR spectrum. GPC determined $M_{n,GPC}$ = 5720 Da and $Đ$ = 1.37, respectively.



Monomer **2** Side chain: SC**2**

SC 2: Monomer **2** (925 mg, 2.5 mmol) and DBTL (160 mg, 0.25 mmol) were dissolved in dry dioxane (3 mL) in a 25 mL Schlenk tube equipped with a stir bar. After degassing by three freeze-evacuate-thaw cycles, the solution was stirred at 110 °C for 30 min. Then a degassed solution of compound **2** (2.59 g, 12.5 mmol) in dry dioxane (5 mL) was added into the above reaction solution through a needle piercing the rubber septum. The mixture was stirred at 110 °C for additional 4 h, cooling to room temperature and precipitated into methanol for three times to afford SC **2** as a light yellow solid (230 mg, yield 26%). ^{1}H-NMR (DMSO-d_6), δ (ppm): 9.63 (s, 7H), 8.29 (d, 1H), 6.38-6.61 (m, 7H), 5.09-5.29 (m, 14H), 5.02(d,

2H), 4.53 (d, 2H), 3.69 (s, 1H). $M_{n,NMR}$ was calculated as 2130 from ^{1}H-NMR spectrum. GPC determined $M_{n,GPC}$ = 8420 Da and $Đ$ = 1.18, respectively.

Preparation of bottlebrush polymers

Bottlebrush 1: PGA_{100} (5.6 mg, 0.03 mmol of azide groups), SC **1** (77 mg, 0.045 mmol), L-ascorbic acid (5 mg, 0.03 mmol), DMF (6 mL) and several drops of toluene as internal standard were added into a 25 mL Schlenk tube equipped with a stir bar. After degassing by three freeze-evacuate-thaw cycles, $CuSO_4{\cdot}5H_2O$ (1.5 mg, 0.006 mmol) was added to the mixture in frozen state under N_2. After another freeze-evacuate-thaw cycle, the reaction was stirred at 50 °C for 12 h and quenched by exposure to air. The crude product was precipitated in methanol to remove copper catalyst and further purified by preparative GPC to remove the excess SC **1**. Bottlebrush **1** (ca. 40 mg) was preserved in DMF (ca. 1.2 mg/mL). GPC determined $M_{n,GPC}$ = 182.4 kDa and $Đ$ = 1.20, respectively.

Bottlebrush 2: PGA_{540} (7.4 mg, 0.04 mmol of azide groups), SC **1** (136 mg, 0.08 mmol), L-ascorbic acid (7 mg, 0.04 mmol), DMF (8 mL) and several drops of toluene as internal standard were added into a 25 mL Schlenk tube equipped with a stir bar. After degassing by three freeze-evacuate-thaw cycles, $CuSO_4{\cdot}5H_2O$ (2 mg, 0.008 mmol) was added to the mixture in frozen state under N_2. After another freeze-evacuate-thaw cycle, the reaction was stirred at 50 °C for 12 h and quenched by exposure to air. The crude product was passed through a PS gel beads column using DMF as the eluent to remove copper catalyst and further purified by preparative GPC to remove the excess SC **1**. Bottlebrush **2** (ca. 50 mg) was preserved in DMF (ca. 1.2 mg/mL). GPC determined $M_{n,GPC}$ = 634.5 kDa and $Đ$ = 1.39, respectively.

Bottlebrush 3: PGA_{100} (11.1 mg, 0.06 mmol of azide groups), SC **2** (192 mg, 0.09 mmol), L-ascorbic acid (11 mg, 0.06 mmol), DMF (12 mL) and several drops of toluene as internal standard were added into a 25 mL Schlenk tube equipped with a stir bar. After degassing by three freeze-evacuate-thaw cycles, $CuSO_4{\cdot}5H_2O$ (3 mg, 0.012 mmol) was added to the mixture in frozen state under N_2. After another freeze-

evacuate-thaw cycle, the reaction was stirred at 50 °C for 12 h and quenched by exposure to air. The crude product was precipitated in methanol to remove copper catalyst and further purified by preparative GPC to remove the excess SC **2**. Bottlebrush **3** (ca. 100 mg) was preserved in DMF (ca. 1.2 mg/mL). GPC determined $M_{n,GPC}$ = 193.8 kDa and $Đ$ = 1.27, respectively.

Bottlebrush 4: Bottlebrush **3** solution (10 mL, 5 mg/mL in DMF) was mixed with 20 mL mixture of TFA/DCM (v/v =1/1), and then was stirred at room temperature for 3 days. After removing the TFA and DCM under reduced pressure, the crude product was dialyzed against methanol and distilled water successively. Bottlebrush **4** was preserved in distilled water (ca. 1 mg/mL).

UV-triggered disassembly of bottlebrush polymers

The disassembly of the bottlebrush polymers was performed in 0.5 mg/mL solutions (DMF for Bottlebrush **1-3** and distilled water for Bottlebrush **4**, respectively) containing 5 v/v% PBS solution (0.01 mol/L). The bottlebrush polymer solutions were stirred under UV irradiation (0.5 cm from the light source) for 1.5 h and kept stirring in dark. GPC analysis (sampled directly) and fluorescence analysis (sampled and diluted eight times with THF) were performed at different time intervals.

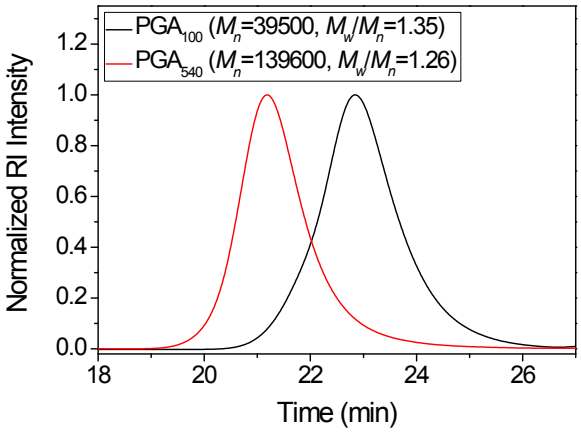


Figure S1. GPC characterization of the PGA_{100} (black) and PGA_{540} (red) backbones.

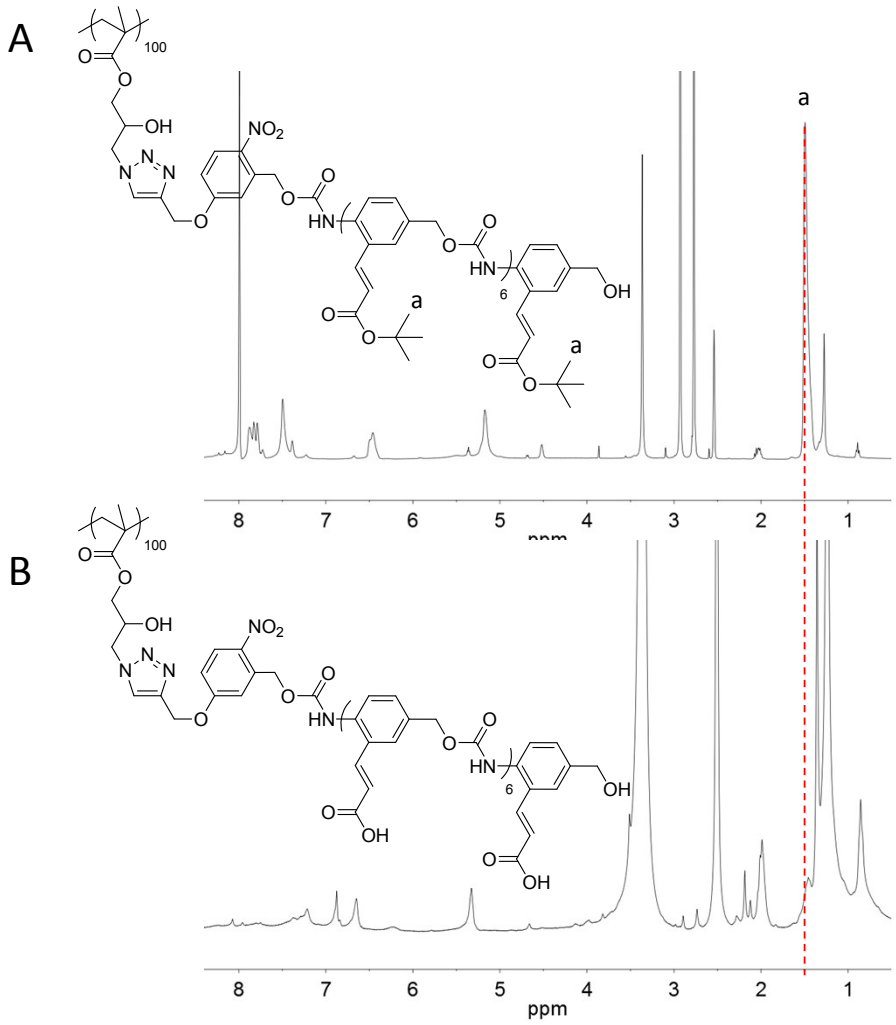


Figure S2. ^{1}H-NMR spectra of bottlebrush **3** (A) and bottlebrush **4** (B) in DMSO-d_6.

References

[1] Y. C. Yan, Y. Shi, W. Zhu, Y. M. Chen, *Polymer,* 2013, **54**, 5634.

[2] A. Sagi, R. Weinstain, N. Karton, D. Shabat, *J. Am. Chem. Soc.,* 2008, **130**, 5434.