

Supporting Information

Facile synthesis of monocyclic, dumbbell-shaped and jellyfish-like copolymers using a telechelic multisite hexablock copolymer

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Experimental

Materials

Styrene (St, 99%, TCI) was consecutively washed with 5% NaOH aqueous solution and water, followed by drying over MgSO₄ and distillation under reduced pressure. Poly(ethylene glycol) methyl ether acrylate (PEGA, $M_n \approx 480$ Da, 98%, Sigma-Aldrich) and *tert*-butyl acrylate (*t*BA, 99%, Alfa-Aesar) were passed through a basic alumina column to remove the inhibitor, and ϵ -caprolactone (CL, 99%, Sigma-Aldrich) was distilled from CaH₂ under reduced pressure. CuBr (98%, Aladdin) was purified by stirring in acetic acid and washing with ethanol before vacuum drying. 2,2'-Azobis(isobutyronitrile) (AIBN, 98%, Macklin) was recrystallized twice from ethanol. 2-Bromoisobutyryl bromide (97%, Macklin), *N,N,N',N'',N''*'-pentamethyldiethylenetriamine (PMDETA, 99%, Aladdin), stannous octoate (Sn(Oct)₂, 97%, Sigma-Aldrich), and other reagents with analytical grade were used directly. The organic solvents were dried and distilled according to standard procedures. 3-(2-Formyl-3-methylphenoxy)propyl 4-(benzodithioyl)-4-cyanopentanoate (FBCP),¹ 2-maleimidyl-4-thiobutyrolactone (MTL),² *N*-(2-hydroxyethyl) maleimide (HEMI),³ and *N*-(2-(2-

bromoisobutyroxy))ethyl maleimide (BEMI)⁴ were synthesized and purified according to literature procedures.

Synthesis of *l*-PSM

FBCP (68 mg, 0.15 mmol), MTL (0.177 g, 0.90 mmol), St (6.25 g, 60 mmol), AIBN (2.5 mg, 0.015 mmol) and dioxane were successively added to a Schlenk tube, and the total volume was 15 mL. After degassing via bubbling nitrogen for 30 min, RAFT copolymerization was initially conducted at 70 °C for 4 h. Under nitrogen, 0.5 mL of polymer solution was carefully drawn, and 0.5 mL of degassed dioxane solution comprising HEMI (0.123 g, 0.87 mmol) was added to the Schlenk tube, followed by polymerization for another 6 h. Similarly, 0.5 mL of polymer solution was drawn under nitrogen, and then 0.5 mL of degassed dioxane solution comprising BEMI (0.244 g, 0.84 mmol) was carefully injected into the Schlenk tube. The resultant solution was subjected to polymerization for another 10 h. The polymer solution was cooled down and precipitated into excess methanol. After vacuum drying at 40 °C, 3.25 g (50% conversion) of *l*-PSM ($t = 20$ h) was obtained as red powders. Similarly, linear P(St-*co*-MTL)-*b*-PSt (denoted as *l*-PSM-a, $t = 4$ h) and linear P(St-*co*-MTL)-*b*-PSt-*b*-P(St-*co*-HEMI)-*b*-PSt' (denoted as *l*-PSM-b, $t = 10$ h) were purified for further characterization.

l-PSM-a: GPC and ¹H NMR analyses: $M_{n, \text{GPC}} = 5.50$ kDa, $D_M = 1.12$, and $M_{n, \text{NMR}} = 5.80$ kDa. ¹H NMR (CDCl₃): δ 10.66 (s, CHO), 5.8-8.1 (m, terminal PhH and ArH, and PhH of St unit), 4.49 (m, CHN of MTL unit), 4.24 (m, ArOCH₂), 4.10 (m, ArOCH₂CH₂CH₂O), 3.20 (m, CH₂S and CHCON of MTL unit), 0.5-2.9 (m, other CH, CH₂ and CH₃ originating from end group and monomer units).

l-PSM-b: GPC and ¹H NMR analyses: $M_{n, \text{GPC}} = 12.1$ kDa, $D_M = 1.09$, and $M_{n, \text{NMR}} = 12.5$ kDa. ¹H NMR (CDCl₃): δ 10.66 (s, CHO), 5.8-8.1 (m, terminal PhH and ArH, and PhH of St unit), 4.49 (m, CHN of MTL unit), 3.9-4.2 (m, ArOCH₂CH₂CH₂O), 3.22 (m, CH₂S of MTL unit, NCH₂CH₂OH of HEMI unit, and CHCON of maleimide units), 0.5-2.9 (m, other CH, CH₂ and CH₃ originating from end group and monomer units).

l-PSM: GPC and ¹H NMR analyses: $M_{n, \text{GPC}} = 21.4$ kDa, $D_M = 1.07$, and $M_{n, \text{NMR}} = 22.8$ kDa. ¹H NMR (CDCl₃): δ 10.66 (s, CHO), 5.8-8.1 (m, terminal PhH and ArH, and PhH of St unit), 4.49 (m, CHN of MTL unit), 4.24 (m, ArOCH₂), 4.09 (m, CH₂O of BEMI unit and ArOCH₂CH₂CH₂O), 2.9-3.7 (m, CH₂S of MTL unit, NCH₂CH₂OH of HEMI unit, NCH₂ of BEMI unit, and CHCON of various maleimide units), 0.5-2.8 (m, other CH, CH₂ and CH₃ originating from end group and monomer units).

Synthesis of *c*-PSM

UV-induced Diels-Alder ring-closure reaction was adopted to synthesize the cyclic copolymer. A low-pressure mercury lamp (120 W, with an irradiation dosage of 0.10 mW cm⁻²) was chosen as the UV light source. In a typical run, *l*-PSM (30 mg) and mixed solvents (50 mL of THF and 450 mL of

CH₃CN) were added to a round-bottom flask, and the solution was subjected to UV irradiation at 25 °C for 20 h. After evaporation of the solvents, *c*-PSM was isolated as yellow solid powders. Ring-closure reaction using recycled solvents and fresh *l*-PSM was repeatedly conducted to enhance the amount of cyclic copolymer. GPC analysis: $M_{n, \text{GPC}} = 17.3$ kDa, and $D_M = 1.06$. ¹H NMR (CDCl₃): δ 5.8-7.7 (m, PhH and ArH of linking group, and PhH of St unit), 5.66 (m, ArCHOH), 4.48 (m, CHN of MTL unit), 4.30 (m, ArOCH₂), 4.09 (m, CH₂O of BEMI unit and ArOCH₂CH₂CH₂O), 2.9-3.7 (m, CH₂S of MTL unit, NCH₂CH₂OH of HEMI unit, NCH₂ of BEMI unit, and CHCON of various maleimide units), 0.5-2.8 (m, other CH, CH₂ and CH₃ originating from linking group and monomer units).

Synthesis of F1 and F2

Tandem amine-thio-bromo click reactions were initially conducted to prepare intracyclic folding copolymer F1. Under nitrogen, *c*-PSM (0.114 g, 0.030 mmol of BEMI unit, 0.030 mmol of MTL unit), triethylamine (0.303 g, 3.0 mmol), THF (11 mL), and acetonitrile (99 mL) were added to a round flask. After bubbling nitrogen for 30 min, the acetonitrile solution comprising *n*-propylamine (0.178 g, 3.0 mmol) was slowly added to the polymer solution. The mixture was subjected to reaction at room temperature for 48 h. Afterwards, the polymer solution was concentrated and precipitated into excess methanol. Intracyclic folding dumbbell-shaped copolymer F1 (0.111 g, 98% yield) was isolated after purification. GPC and ¹H NMR analyses: $M_{n, \text{GPC}} = 15.4$ kDa, $D_M = 1.07$, and $M_{n, \text{NMR}} = 22.7$ kDa. ¹H NMR (CDCl₃): δ 5.8-7.8 (m, PhH and ArH of linking group, and PhH of St unit), 5.54 (m, ArCHOH), 4.51 (m, CHN connecting with maleimide unit), 4.31 (m, ArOCH₂), 4.08 (m, ArOCH₂CH₂CH₂O and CH₂OCO of maleimide unit), 2.9-3.8 (m, CH₃CH₂CH₂NHCO, NCH₂ and CHCON of various maleimide units, and CH₂OH of HEMI unit), 0.5-2.8 (m, other CH, CH₂ and CH₃ originating from linking group, side group and monomer units).

On this basis, ring-opening polymerization of CL using F1 as a macroinitiator was performed to generate F1-g-PCL (abbreviated as F2). Under nitrogen, F1 (76 mg, 0.020 mmol of OH), Sn(Oct)₂ (4.1 mg, 0.010 mmol) and CL (57 mg, 0.50 mmol) were successively added to a Schlenk tube, and anhydrous toluene was added to reach a total volume of 0.50 mL. After three freeze-pump-thaw degassing cycles, the mixture was subjected to polymerization at 100 °C for 24 h. The polymer solution was cooled down and precipitated into excess hexane, and F2 (0.123 g, 82% conversion) was obtained after purification. GPC and ¹H NMR analyses: $M_{n, \text{GPC}} = 25.0$ kDa, $D_M = 1.08$, and $M_{n, \text{NMR}} = 37.1$ kDa. ¹H NMR (CDCl₃): δ 5.8-7.5 (m, PhH and ArH of linking group, and PhH of St unit), 5.58 (m, ArCHOH), 4.26-4.80 (m, CHN connecting with maleimide unit and ArOCH₂), 3.8-4.2 (m, ArOCH₂CH₂CH₂O, CH₂OCO of maleimide unit, CH₂O of PCL, and NCH₂CH₂O connecting with

PCL), 2.7-3.7 (m, $\text{CH}_3\text{CH}_2\text{CH}_2\text{NHCO}$, NCH_2 and CHCON of various maleimide units, and terminal CH_2OH of PCL), 0.5-2.5 (m, other CH , CH_2 and CH_3 originating from linking group, side group and monomer units).

Synthesis of jellyfish-like copolymers with a cyclic backbone

First, (*c*-PSM)-*g*-PtBA (G1) was synthesized by ATRP of *t*BA using *c*-PSM as the macroinitiator. Under nitrogen, *c*-PSM (0.114 g, 0.030 mmol of Br), CuBr (4.3 mg, 0.030 mmol) and *t*BA (0.461 g, 3.6 mmol) were successively added to a Schlenk tube, and anhydrous acetone was added to reach a total volume of 1.8 mL. After two freeze-pump-thaw degassing cycles, PMDETA (5.2 mg, 0.030 mmol) was added to the polymerization tube in nitrogen atmosphere. The polymerization was conducted at 60 °C for 16 h. The polymer solution was diluted with excess THF and passed through neutral alumina column to remove the metal salt. After concentration, the crude product was precipitated into excess hexane, and G1 (0.340 g, 49% conversion) was obtained after vacuum drying. GPC and ^1H NMR analyses: $M_{n,\text{GPC}} = 52.6$ kDa, $D_M = 1.12$, and $M_{n,\text{NMR}} = 67.4$ kDa. ^1H NMR (CDCl_3): δ 5.8-7.7 (m, PhH and ArH of linking group, and PhH of St unit), 5.59 (m, ArCHOH), 4.48 (m, CHN of MTL unit), 4.28 (m, ArOCH₂), 4.13 (m, ArOCH₂CH₂CH₂O and CH₂O of maleimide unit), 2.8-4.0 (m, CH₂S of MTL unit, CH₂OH of HEMI unit, and NCH₂ and CHCON of various maleimide units), 0.6-2.8 (m, other CH, CH₂ and CH₃ originating from linking group, St and maleimide units, and PtBA).

Second, (*c*-PSM)-*g*-PtBA/PEG (G2) was prepared by consecutive thio-bromo and amine-thiol-ene reactions. Under nitrogen, G1 (0.225 g, 0.020 mmol of MTL unit), butylmercaptan (18 mg, 0.20 mmol), triethylamine (20 mg, 0.20 mmol) and THF were successively added to a Schlenk tube, and the total volume was 2.2 mL. After stirring at 25 °C for 24 h, *n*-propylamine (12 mg, 0.20 mmol) was added in nitrogen atmosphere, and aminolysis of thiolactone unit was conducted at 40 °C for 24 h. Afterwards, PEGA (0.288 g, 0.60 mmol) was added under nitrogen, and thiol-acrylate Michael addition was performed at 40 °C for 24 h. After precipitation into hexane, dialysis against deionized water and freeze drying, G2 (0.232 g, 99% yield) polymer was obtained. GPC and ^1H NMR analyses: $M_{n,\text{GPC}} = 55.0$ kDa, $D_M = 1.15$, and $M_{n,\text{NMR}} = 70.3$ kDa. ^1H NMR (CDCl_3): δ 5.8-7.7 (m, PhH and ArH of linking group, and PhH of St unit), 5.56 (m, ArCHOH), 4.66 (m, CHN of MTL unit), 4.17 (m, ArOCH₂CH₂CH₂O and CH₂O of maleimide unit), 3.0-4.0 (m, $\text{CH}_3\text{CH}_2\text{CH}_2\text{NHCO}$, CH₂OH of HEMI unit, NCH₂ and CHCON of various maleimide units, CH₂O of PEG, and terminal CH₃O), 0.6-2.9 (m, other CH, CH₂ and CH₃ originating from linking group, side group, St and maleimide units, and PtBA).

Third, (*c*-PSM)-*g*-PtBA/PEG/PCL (G3) was prepared by ROP of CL using G2 as a macroinitiator. Under nitrogen, G2 (0.117 g, 0.010 mmol of OH), Sn(Oct)₂ (2.1 mg, 0.005 mmol) and CL (91 mg, 0.80 mmol) were successively added to a Schlenk tube, and anhydrous toluene was added to reach a

total volume of 1.0 mL. After three freeze-pump-thaw degassing cycles, the mixture was subjected to polymerization at 100 °C for 24 h. The polymer solution was cooled down and precipitated into excess hexane, and G3 (0.199 g, 90% conversion) was obtained after purification. GPC and ¹H NMR analyses: $M_{n, \text{GPC}} = 85.2$ kDa, $D_M = 1.17$, and $M_{n, \text{NMR}} = 118$ kDa. ¹H NMR (CDCl₃): δ 5.8-7.6 (m, PhH and ArH of linking group, and PhH of St unit), 5.70 (m, ArCHOH), 4.66 (m, CHN of MTL unit), 3.8-4.4 (m, ArOCH₂CH₂CH₂O, CH₂O of maleimide unit, and CH₂O of PCL), 2.9-3.8 (m, CH₃CH₂CH₂NHCO, NCH₂ and CHCON of various maleimide units, CH₂O of PEG, terminal CH₃O, and terminal CH₂OH), 0.6-2.9 (m, other CH, CH₂ and CH₃ originating from linking group, side group, St and maleimide units, PtBA, and PCL).

Finally, the PtBA side chains of JFPs (G_x, $x = 1-3$) were converted into PAA segments via hydrolysis using five-fold excess trifluoroacetic acid. The polymer concentration was fixed at about 0.10 g mL⁻¹, and the reaction was conducted in dichloromethane at ambient temperature for 24 h. After evaporating the solvent, the resultant copolymer was dissolved in THF, followed by precipitation into excess hexane. The isolated solid samples were subjected to vacuum drying, and PAA-bearing JFPs (G_x') were obtained.

Self-assembly of F2 in organic solvents

F2 (16 mg) and THF (4.0 mL) were added to a vial, followed by stirring in a closed system for 2 h to form clear solution. Afterwards, methanol was carefully added to the copolymer solution via a metering pump (with addition rate of 1.0 mL h⁻¹) under vigorous stirring. At a fixed volume ratio of methanol to THF (i.e., $v(\text{CH}_3\text{OH})/v(\text{THF}) = 1, 2, 3, 5, 8, 10, 12$ and 14), about 1.0 mL of copolymer solution was drawn, followed by stirring overnight to reach an equilibrium. On this basis, the resultant copolymer assemblies were subjected to DLS and TEM analyses.

Self-assembly of G1'-G3' in aqueous solutions

The solvent switch method was used to prepare copolymer assemblies formed in aqueous solutions. Copolymer (5.0 mg) was initially dissolved in DMF (2.0 mL). Under vigorous stirring, deionized water (7.0 mL) was slowly added to the copolymer solution via metering pump (with addition rate of 1.0 mL h⁻¹). After further stirring for 8 h, the resultant solution was transferred into a dialysis membrane tubing (MWCO 3000) and subjected to dialysis against deionized water for 48 h. Afterwards, deionized water was carefully added to obtain copolymer assemblies with a c_p of 0.5 mg mL⁻¹. The solution pH of initial copolymer solutions was 5.7 (for G1' assemblies), 5.9 (for G2' assemblies) and 6.2 (for G3' assemblies), respectively. Dilute HCl and NaOH aqueous solution were carefully added to copolymer solutions to reach pH 3.0 or 10, followed by stirring to reach an equilibrium. On this basis, the copolymer assemblies formed at distinct pH values were subjected to DLS and TEM analyses.

Characterization

^1H NMR spectra were recorded in CDCl_3 on a Varian Unity Inova 400 MHz spectrometer at 25 °C, and ^1H DOSY NMR spectra were recorded in CD_2Cl_2 on an Agilent ProPulse 600 MHz spectrometer at 25 °C. Apparent molar mass ($M_{n,\text{GPC}}$) and dispersity (D_M) of various polymers were measured on a TOSOH HLC-8320 gel permeation chromatography (GPC) using three TSKgel SuperMultipore HZ-M columns at 40 °C. THF was used as an eluent at a flow rate of 0.35 mL min^{-1} , and the samples were calibrated with PSt standard samples. Differential scanning calorimetry (DSC) was measured on Q200 DSC from TA Instruments using a heating/cooling rate of 10 K min^{-1} . To determine apparent hydrodynamic diameter (D_h), peak hydrodynamic diameter (D_{peak}) and particle size distribution (PD) of copolymer assemblies formed in organic solvents or aqueous solutions, dynamic light scattering (DLS) analysis was performed using Zetasizer Nano-ZS from Malvern Instruments ($T = 25 \text{ }^\circ\text{C}$) or BI200-SM from Brookhaven Instruments (for temperature-variable DLS measurement) equipped with a 633 nm He-Ne laser using back-scattering detection. To check the morphology of nano-objects, transmission electron microscopy (TEM) images were measured using a Hitachi HT7700 electron microscope with an acceleration voltage of 120 kV. A drop of copolymer aqueous solution was casted on a carbon-coated copper grid at a fixed temperature, immediately quenched with liquid nitrogen, followed by freeze-drying to prepare the sample for TEM measurement.

References

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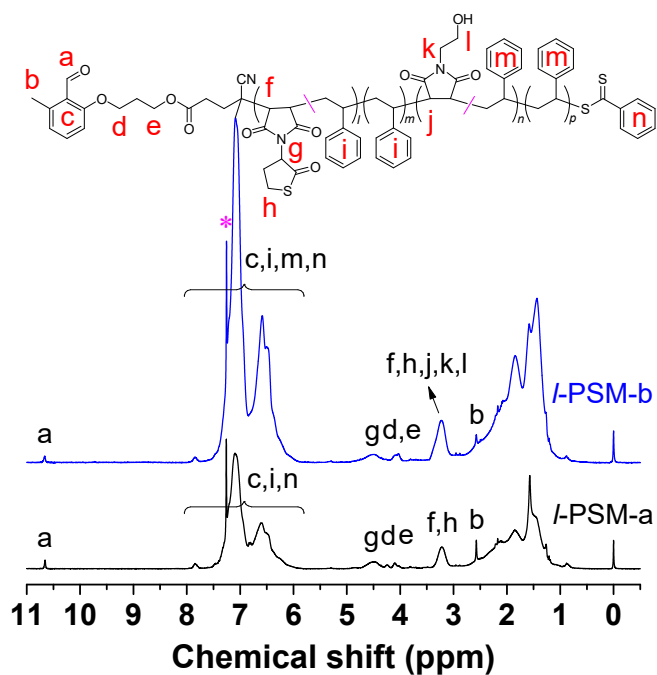


Fig. S1 ^1H NMR spectra of linear P(St-co-MTL)-*b*-PSt (*l*-PSM-a) and P(St-co-MTL)-*b*-PSt-*b*-P(St-co-HEMI)-*b*-PSt' (*l*-PSM-b) recorded in CDCl_3 (*).

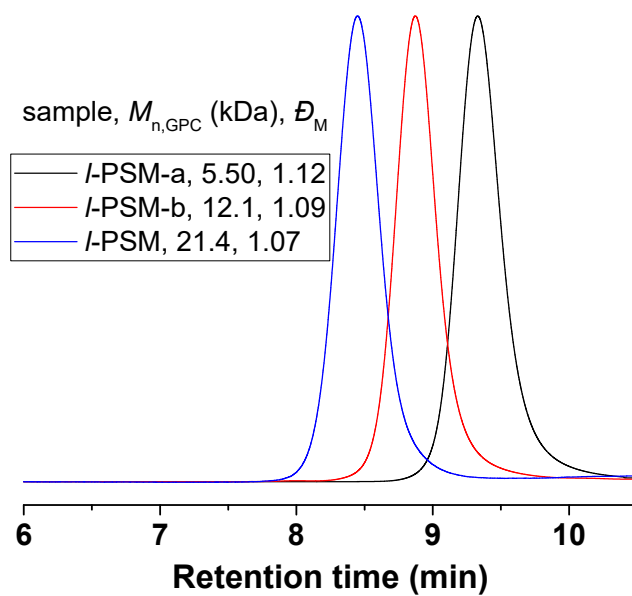


Fig. S2 GPC traces of *l*-PSM and its precursors.

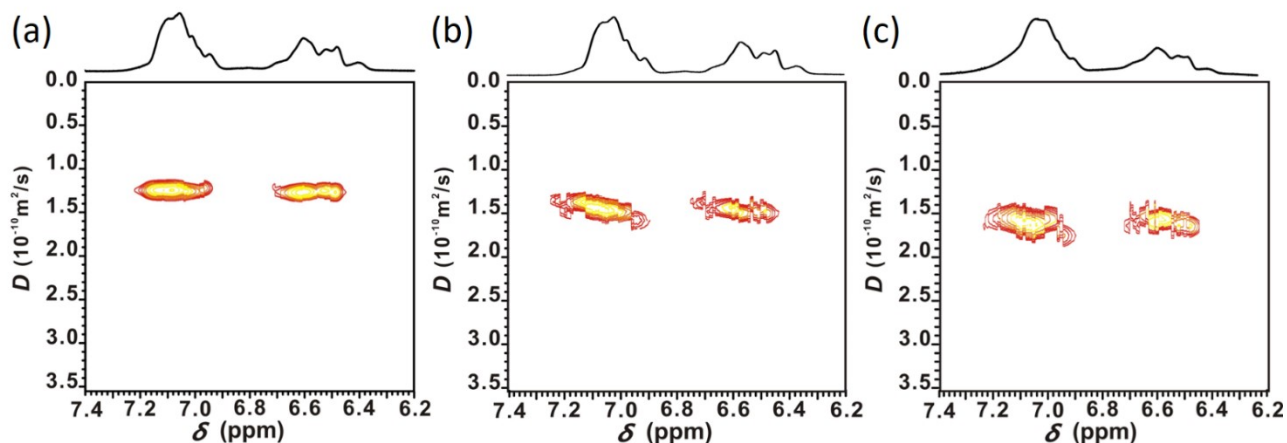


Fig. S3 DOSY spectra of linear (*l*-PSM, a), cyclic (*c*-PSM, b) and intrachain folding dumbbell-shaped (F1, c) copolymers comprising St and MI units recorded in CD_2Cl_2 ($c_p = 2.0 \text{ mg mL}^{-1}$), in which *x*-axis denoted the ^1H resonance and *y*-axis denoted the diffusion coefficient.

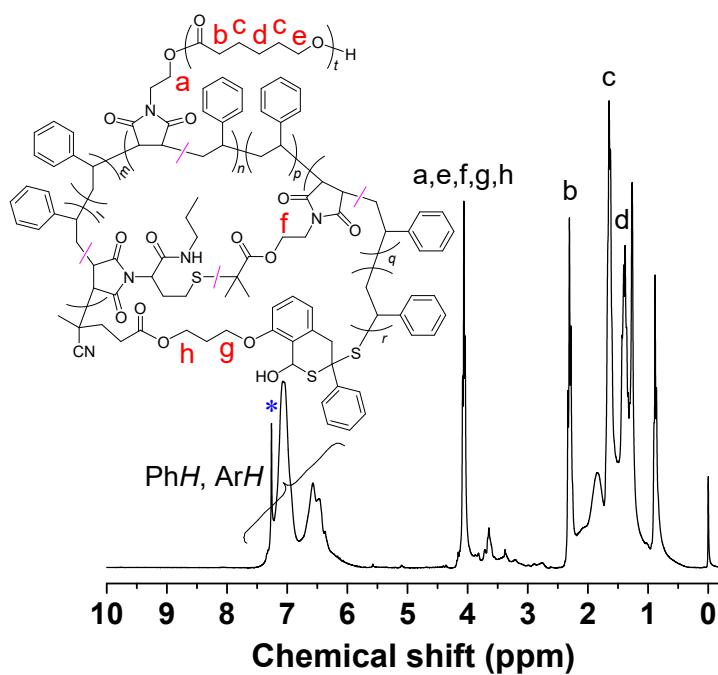


Fig. S4 ^1H NMR spectrum of F2 recorded in CDCl_3 (*).

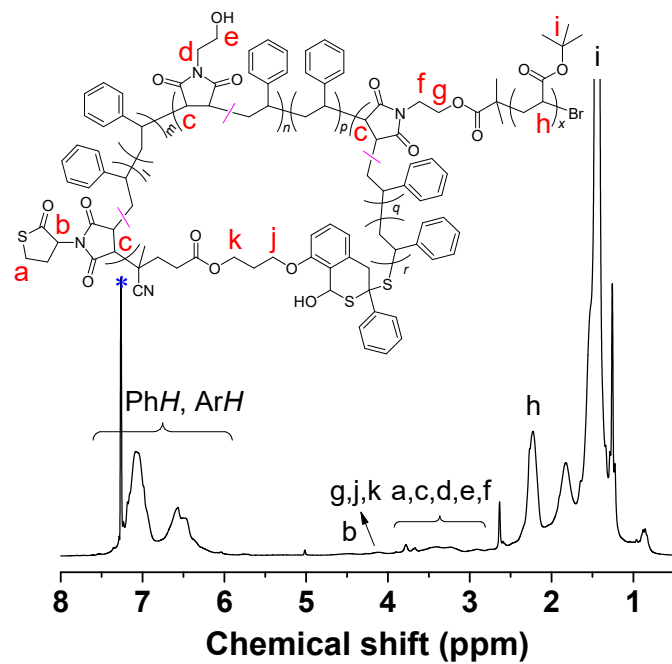


Fig. S5 ¹H NMR spectrum of G1 recorded in CDCl₃ (*).

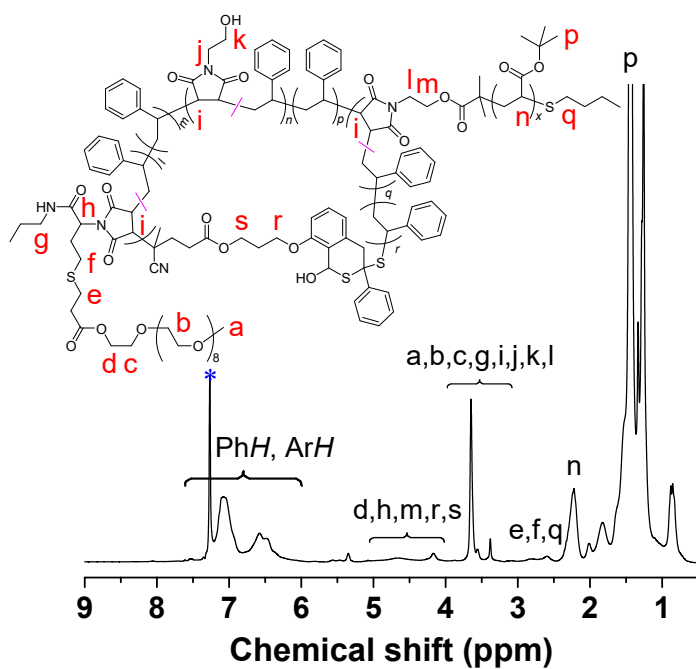


Fig. S6 ¹H NMR spectrum of G2 recorded in CDCl₃ (*).

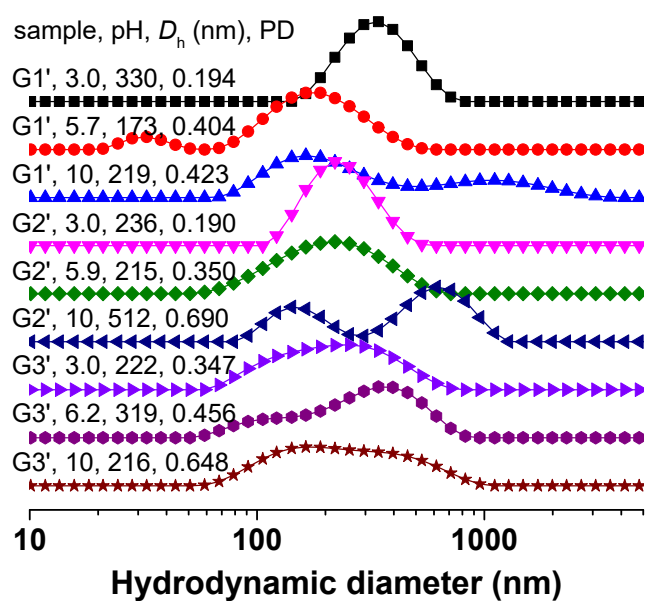


Fig. S7 DLS plots of copolymer assemblies ($c_p = 0.5 \text{ mg mL}^{-1}$) formed from G1'-G3' in aqueous solutions at different pH values.