

Supporting Information for

First Double Hydrophilic Graft Copolymer Bearing Poly(2-hydroxyethyl acrylate) Backbone Synthesized by Sequential RAFT Polymerization and SET-LRP

Yinan Cui,^{1,#} Xiuyu Jiang,^{1,#} Guangxin Gu,^{2,*} Jie Xu,² Chun Feng,¹ Xiaoyu Huang^{1,*}

¹ Key Laboratory of Synthetic and Self-Assembly Chemistry for Organic Functional Molecules, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, People's Republic of China

² Department of Materials Science, Fudan University, 220 Handan Road, Shanghai 200433, People's Republic of China

Experimental Section

Materials

N-isopropylacrylamide (NIPAM, 97%, Aldrich) was recrystallized from a mixture of benzene and *n*-hexane (v:v = 1:3). 2,2'-Azobis(isobutyronitrile) (AIBN, Aldrich, 98%) was recrystallized from anhydrous ethanol twice. Copper (I) chloride (CuCl, Aldrich, 98%) was purified by stirring overnight over CH₃CO₂H at room temperature, followed by washing the solid with ethanol, diethyl ether, and acetone prior to drying at 40°C *in vacuo* for one day. Dimethyl formamide (DMF, Aldrich, 99.8%) was dried over KOH and distilled from CaH₂ under N₂ prior to use. Tetrahydrofuran (THF, Aldrich, 99%) was dried over CaH₂ and distilled from sodium and benzophenone

under N₂ prior to use. 2-Hydroxyethyl 2-((2-chloropropanoyloxy)methyl)acrylate (HECPMA),¹ cumyl dithiobenzoate (CDB),² and tris(2-(di-methylamino)ethyl)amine (Me₆TREN)³ were synthesized according to previous literatures.

Measurements

FT-IR spectra were recorded on a Nicolet AVATAR-360 FT-IR spectrophotometer with a 4 cm⁻¹ resolution. All ¹H (500 MHz) and ¹³C (125 MHz) NMR analyses were performed on a Bruker Avance 500 spectrometer in DMSO-*d*₆, CD₃OD, and D₂O. Elemental analysis was carried out on a Carlo-Erba1106 system. Conversion of NIPAM monomer was determined by GC using an HP 6890 system equipped with an SE-54 column. Relative molecular weights and molecular weight distributions were measured by conventional gel permeation chromatography (GPC) system equipped with a Waters 1515 Isocratic HPLC pump, a Waters 2414 refractive index detector, and a set of Waters Styragel columns (HR3 (500-30,000), HR4 (5,000-600,000), and HR5 (50,000-4,000,000), 7.8×300 mm, particle size: 5 μm). GPC measurements were carried out at 35°C using LiBr-added DMF ([LiBr] = 15 mM) as eluent (flow rate: 1.0 mL/min). The system was calibrated with linear poly(methyl methacrylate) standards. Absolute molecular weight of the macroinitiator was determined by GPC equipped with a multiangle light scattering detector (GPC/MALS), THF was used as the eluent with a flow rate of 1.0 mL/min, detectors: Wyatt Optilab rEX refractive index detector and Wyatt DAWN HELEOS 18-angle light scattering detector with a 50 mW solid-state laser operating at 658 nm.

Hydrodynamic diameter (D_h) was measured by dynamic light scattering (DLS) with a Wyatt DynaPro laser photometer, the samples were allowed to equilibrate for 2 min at changed temperature prior to the measurement.

RAFT Homopolymerization of HECMA

AIBN (18.6 mg, 0.11 mmol) and CDB (92.5 mg, 0.34 mmol) were first added into a 10 mL Schlenk flask (flame-dried under vacuum prior to use) sealed with a rubber septum for degassing and kept under N_2 . Next, HECMA **1** (2.00 g, 8.5 mmol) and 0.43 mL of anhydrous DMF were added via a gastight syringe. The flask was degassed by three cycles of freezing-pumping-thawing followed by immersing the flask into an oil bath set at 80°C. The polymerization was terminated by immersing the flask into liquid N_2 after 10.5 h. THF was added to dilute the solution and the solution was precipitated into ether. The crude product was purified by repeated dissolution and precipitation followed by drying *in vacuo* overnight to give 1.41 g of pink powder.

To remove the dithiobenzoate end moiety, AIBN (1.23 g, 7.5 mmol) and 1.2 g of pink powder (0.375 mmol of dithiobenzoate group) were first added to a 100 mL Schlenk flask (flame-dried under vacuum prior to use) sealed with a rubber septum for degassing and kept under N_2 . Next, 50 mL of anhydrous THF was added via a gastight syringe. The flask was immersed into an oil bath set at 60°C and the reaction was quenched by liquid N_2 after 60 h. The solution turned colorless and was precipitated into ether after concentration. After repeated purification via dissolution

and precipitation, 0.72 g of white powder, poly(2-hydroxyethyl 2-((2-chloropropanoyloxy)methyl)acrylate) (PHECPMA) **2**, was obtained by drying *in vacuo* overnight. GPC: $M_n = 6,700$ g/mol, $M_w/M_n = 1.17$. GPC/MALS: $M_n = 13,460$ g/mol, $M_w/M_n = 1.08$. FT-IR: ν (cm^{-1}): 3435 ($\nu_{\text{O-H}}$), 2953 ($\nu_{\text{C-H}}$), 2876 ($\nu_{\text{C-H}}$), 1735 ($\nu_{\text{C=O}}$), 1450, 1380, 1253, 1175, 1075, 1008, 971, 912, 845, 748. ^1H NMR (DMSO- d_6): δ (ppm): 1.18 (12H, terminal $\text{C}(\text{CH}_3)_2$), 1.67 (3H, CHClCH_3), 1.97 (2H, CH_2CCO_2), 3.56 (2H, $\text{CO}_2\text{CH}_2\text{CH}_2\text{OH}$), 3.83 (2H, $\text{CO}_2\text{CH}_2\text{CH}_2\text{OH}$), 4.07 (2H, $\text{CO}_2\text{CCH}_2\text{O}$), 4.62 (1H, CHClCH_3), 4.87 (1H, CH_2OH), 7.12-7.29 (5H, terminal C_6H_5). ^{13}C NMR (DMSO- d_6): δ (ppm): 21.7 (CHClCH_3), 44.4 (CH_2CCO_2), 47.6 (CHClCH_3), 53.3 ($\text{CO}_2\text{CH}_2\text{CH}_2\text{OH}$), 58.6 ($\text{CO}_2\text{CCH}_2\text{O}$), 64.7 (CH_2CCO_2), 67.2 ($\text{CO}_2\text{CH}_2\text{CH}_2\text{OH}$), 126.1, 128.3 (C_6H_5), 169.3 (CH_2CCO_2), 172.5 (CO_2CHCl).

SET-LRP Graft Copolymerization of NIPAM

In a typical procedure, PHECPMA **2** (24.0 mg, $M_n = 13,460$ g/mol, $M_w/M_n = 1.08$, 0.1 mmol ATRP initiating group), NIPAM (1.13 g, 10 mmol), and CuCl (9.9 mg, 0.1 mmol) were first added to a 10 mL Schlenk flask (flame-dried under vacuum prior to use) sealed with a rubber septum for degassing and kept under N_2 . Next, Me_6TREN (27 μL , 0.1 mmol) and freshly-distilled DMF (2.0 mL) were added via a gastight syringe. The flask was degassed by three cycles of freezing-pumping-thawing followed by immersing the flask into an oil bath set at 25°C. The polymerization was terminated by immersing the flask into liquid N_2 after 1 h. The reaction mixture was diluted by THF and passed through an alumina column to remove the residual copper

catalyst. The solution was concentrated and precipitated into diethyl ether. After repeated purification by dissolving in THF and precipitating in diethyl ether, 425 mg of white powder, PHEA-*g*-PNIPAM **3a**, was obtained after drying *in vacuo* overnight. GPC: $M_n = 70,400$ g/mol, $M_w/M_n = 1.31$. FT-IR: ν (cm^{-1}): 3438 ($\nu_{\text{O-H}}$), 3305 ($\nu_{\text{N-H}}$), 3067, 2970 ($\nu_{\text{C-H}}$), 2932, 2874, 1739 ($\nu_{\text{O-C=O}}$), 1643 ($\nu_{\text{HN-C=O}}$), 1539, 1458, 1387, 1364, 1264, 1228, 1172, 1132, 1064, 991, 882, 805, 660. ^1H NMR (CD_3OD): δ (ppm): 1.16 (6H, $\text{NCH}(\text{CH}_3)_2$), 1.58 (2H, CH_2CH ; 2H, CH_2C), 2.09 (1H, CH_2CH), 3.49 (2H, $\text{CO}_2\text{CH}_2\text{CH}_2\text{OH}$), 3.96 (2H, $\text{CO}_2\text{CH}_2\text{CH}_2\text{OH}$; 1H, $\text{NCH}(\text{CH}_3)_2$; 2H, $\text{CO}_2\text{CCH}_2\text{O}$).

For SET-LRP kinetics investigation, the first sample taken as the time = 0 data point was obtained by withdrawing 0.20 mL of solution from the Schlenk flask using a purged syringe and it was then added to 1.00 mL of THF used as external standard. The flask was immersed into an oil bath set at 25°C. At every time interval (0.5, 1.0, and 1.5 hour), 0.20 mL of sample solution was taken using a purged syringe and added to 1.00 mL of THF. Every sample solution in THF taken at different time was injected into GC to determine the conversion of NIPAM in comparison with the time = 0 data point.

Temperature-Dependent Turbidimetry

The optical transmittance of aqueous solution of PHEA-*g*-PNIPAM **3** graft copolymers with different concentrations (0.5, 1.0, and 2.0 mg/mL) in the range of 200-600 nm was acquired on a Hitachi U-2910 spectrophotometer over a temperature range of 20°C-70°C. The temperature was controlled by using a DC-1006 variable

temperature cryostat and the data were obtained after the solution was equilibrated for 10 min at every temperature. LCST value of the copolymer was defined as the onset of the sharp decrease of the transmittance.

References and Notes

1. Jiang, X. Y.; Lu, G. L.; Feng, C.; Huang, X. Y. *Polym. Chem.* **2014**, *5*, 4915-4925.
2. Moad, G.; Chiefari, J.; Chong, Y. K.; Krstina, J.; Mayadunne, R. T. A.; Postma, A.; Rizzardo, E.; Thang, S. H. *Polym. Int.* **2000**, *49*, 993-1001.
3. Tillmanns, E. J.; Ritter, J. *J. Org. Chem.* 1957, **22**, 839-840.

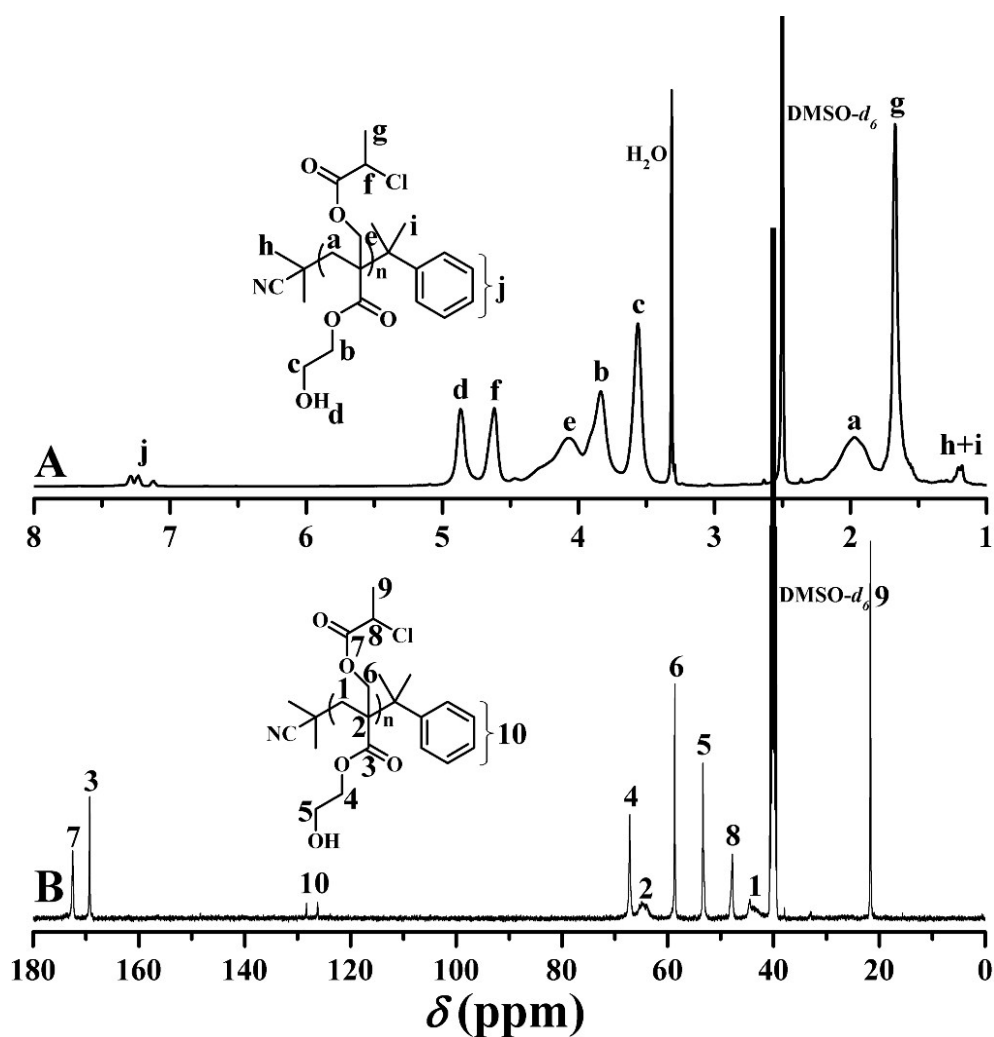


Figure S1. ^1H (A) and ^{13}C (B) NMR spectra of PHECPMA **2** in $\text{DMSO-}d_6$.