Electronic Supplementary Information

Preparation of Stimuli Responsive Polycaprolactone Membrane of Controllable Porous Morphology via Combined Atom Transfer Radical Polymerization, Ring-Opening Polymerization and Thiol-yne Click Chemistry

Tao Cai,[a] Min Li,[b] Koon-Gee Neoh[a,b] and En-Tang Kang[*,a,b]

[a]NUS Graduate School for Integrative Science and Engineering
National University of Singapore
Kent Ridge, Singapore 117576

[b]Department of Chemical & Biomolecular Engineering
National University of Singapore
Kent Ridge, Singapore 119260

*To whom correspondence should be addressed
Tel.: +65-65162189; Fax: +65-67791936.
Email address: cheket@nus.edu.sg

Experiment Section

Materials

Bis(2-hydroxyethyl)disulfide (BHEDS, 98%), dicyclohexylcarbodiimide (DCC, 98%), 4-(*N,N*-dimethylamino)pyridine (DMAP, ≥99%), DL-1,4-dithiothreitol (DTT, 98%) and 2-bromoisobutyric acid (98%) were obtained from Sigma-Aldrich Chem. Co. and used as received without further purification. *N*-isopropylacrylamide (NIPAM, 97%) was purchased from Sigma-Aldrich Chemical Co., Ltd., St. Louis, MO. The NIPAM monomer was recrystallized twice from toluene/hexane (7:3, v/v) and stored at -10 ºC. Copper(I) bromide (CuBr, Sigma-Aldrich, 99%) was purified by stirring in acetic acid for 4 h, followed by washing thoroughly with ethanol and diethyl ether before being stored under an argon atmosphere. Isopropyl alcohol (IPA, reagent grade) and tetrahydrofuran (THF, reagent grade) were obtained from Merck Chem. Co. and used as received without further purification. Tris[2-(dimethylamino)ethyl]amine (Me_6TREN) was prepared according to procedures described in the literature.[1]

Synthesis of Disulfide Initiator Bis[2-(2-bromoisobutyryloxy)ethyl] Disulfide (BiBOEDS)

Bis[2-(2-bromoisobutyryloxy)ethyl] disulfide (BiBOEDS) was prepared according to the method reported in literature with slight modification.[2-4] BHEDS (0.50 g, 3.25 mmol), DCC (1.34 g, 6.5 mmol), DMAP (0.16 g, 1.3 mmol) and anhydrous THF (10 ml) were introduced into a 25 ml single-necked round bottom flask. The flask was immersed in an ice bath, and 2-bromoisobutyric acid (1.08 g, 6.5 mmol) in 5 ml of dry THF was added dropwise. Upon completion of the addition, the reaction mixture was kept in the ice-water bath for 1 h and then at room temperature for 24 h. The precipitated 1,3-dicyclohexylurea was filter off and washed with 50 ml of THF on the filter. The solvent was evaporated,

and the formed suspension was kept in refrigerator for several hours and then at room temperature for 3 days. The impurities crystallized and were removed by filtration. A viscous oil was obtained (yield ~81%). ^{1}H NMR ($CDCl_3$, δ, ppm, TMS): 1.93 (12H, -C$\underline{H}_3$), 2.97 (4H, -C$\underline{H}_2$S-), 4.44 (4H, -COOC$\underline{H}_2$-).

Synthesis of Thiol-terminated PNIPAM Polymers

Thiol-terminated poly(*N*-isopropylacrylamide) (PNIPAM-SH) was obtained by atom transfer radical polymerization (ATRP) of the NIPAM monomers using disulfide-based BiBOEDS as the initiator, followed by cleaved of the disulfide bond using excess DL-1,4-dithiothreitol (DTT) as the reducing agent.[5-6] In a typical reaction, BiBOEDS (100 mg, 0.22 mmol), Me_6TREN (51 mg, 0.22 mmol), NIPAM (2.5 g, 22.1 mmol) and isopropyl alcohol (5.6 ml) were introduced into a reaction flask. The reaction mixture was purged with argon for 30 min. After equilibration at 25 ºC, CuBr (32 mg, 0.22 mmol) was introduced into the reaction flask to start the polymerization. The mixture was stirred under the protection of an argon stream for 6 h at 25 ºC. The reaction mixture was diluted with THF, and then exposed to air. After passing through a column of neutral alumina to remove the copper catalysts, the solvent was removed in a rotary evaporator. The residues were redissolved in THF and precipitated into cold diethyl ether to remove the residual monomers. The above dissolution-precipitation cycle was repeated twice. After drying in a vacuum oven overnight at room temperature, the PNIPAM-S-S-PNIPAM polymer was obtained as a white solid (yield ~80%). ^{1}H NMR ($CDCl_3$, δ, ppm, TMS): 1.05-1.2 (6H×*n*, -CH(C$\underline{H}_3$)$_2$), 1.93 (12H, -C(C$\underline{H}_3$)$_2$), 1.5-2.5 (3H×*n*, -C$\underline{H}_2$C$\underline{H}$-CONH-), 2.97 (4H, -C$\underline{H}_2$S-), 3.95-4.05 (1H×*n*, -C$\underline{H}$(CH$_3$)$_2$), 4.44 (4H, -COOC$\underline{H}_2$-). 6.0-6.8 (1H×*n*, -CON$\underline{H}$-). The

molecular weight ($M_{n,NMR}$) was determined to be about 8100 g/mol from the ^{1}H NMR spectroscopy data.

The PNIPAM-S-S-PNIPAM ($M_{n,NMR}$ = 8100 g/mol, 0.95 g, 0.1 mmol) polymer was dissolved in 20 ml of THF. The reaction mixture was purged with argon for 30 min. DTT (0.77 g, 5 mmol) was then introduced into the reaction flask. The mixture was stirred under the protection of an argon stream for 24 h at 50 ºC. The resultant PNIPAM-SH was dialyzed against deionized water for 3 days and the deionized water was changed twice daily. The product was isolated via lyophilization (yield, 95%).

Table S1. Monomer Conversion, Molar Mass (M_n) and Polydispersity (PDI) Data for Atom Transfer Radical Polymerization (ATRP) of *N*-Isopropylacrylamide (NIPAM)[a] and Subsequent Cleavage of Disulfide Groups by DL-1,4-dithiothreitol (DTT)

Before Cleavage									After Cleavage			
Sample	[NIPAM]/[BiBOEDS]	Time (h)	Conv. (%)	$M_{n,th}$[b]	$M_{n,GPC}$[c]	PDI[c]	$M_{n,NMR}$[d]	DP[d,e]	Sample	$M_{n,GPC}$[c]	PDI[c]	DP[d,e]
PNIPAM-S-S-PNIPAM1	50	6	84	5200	7600	1.18	5000	40	PNIPAM-SH1	4100	1.22	20
PNIPAM-S-S-PNIPAM2	100	6	80	9500	16900	1.16	8100	68	PNIPAM-SH2	8800	1.18	34
PNIPAM-S-S-PNIPAM3	150	6	78	13700	22500	1.21	11500	98	PNIPAM-SH3	11600	1.24	49
PNIPAM-S-S-PNIPAM4	200	6	75	17400	30200	1.24	15100	130	PNIPAM-SH4	16000	1.28	65

[a] Experimental conditions: typically 2.5 g of NIPAM, 5 g of IPA; [BiBOEDS]:[CuBr]:[Me_6TREN] = 1:1:1; 25 ºC.
[b] $M_{n,th} = M_{NIPAM} \times$ Conv. $\times$ [NIPAM]/[BiBOEDS] + $M_{BiBOEDS}$, M_{NIPAM} = 113 g/mol, $M_{BiBOEDS}$ = 452 g/mol.
[c] Determined from GPC results in THF, calibration with polystyrene standards.
[d] Determined from ^{1}H NMR spectroscopy results, calculated from the ratio of methylene protons adjacent to the disulfide groups of BiBOEDS initiator to protons of the methyl group in the PNIPAM chains.
[e] Degree of Polymerization (DP).

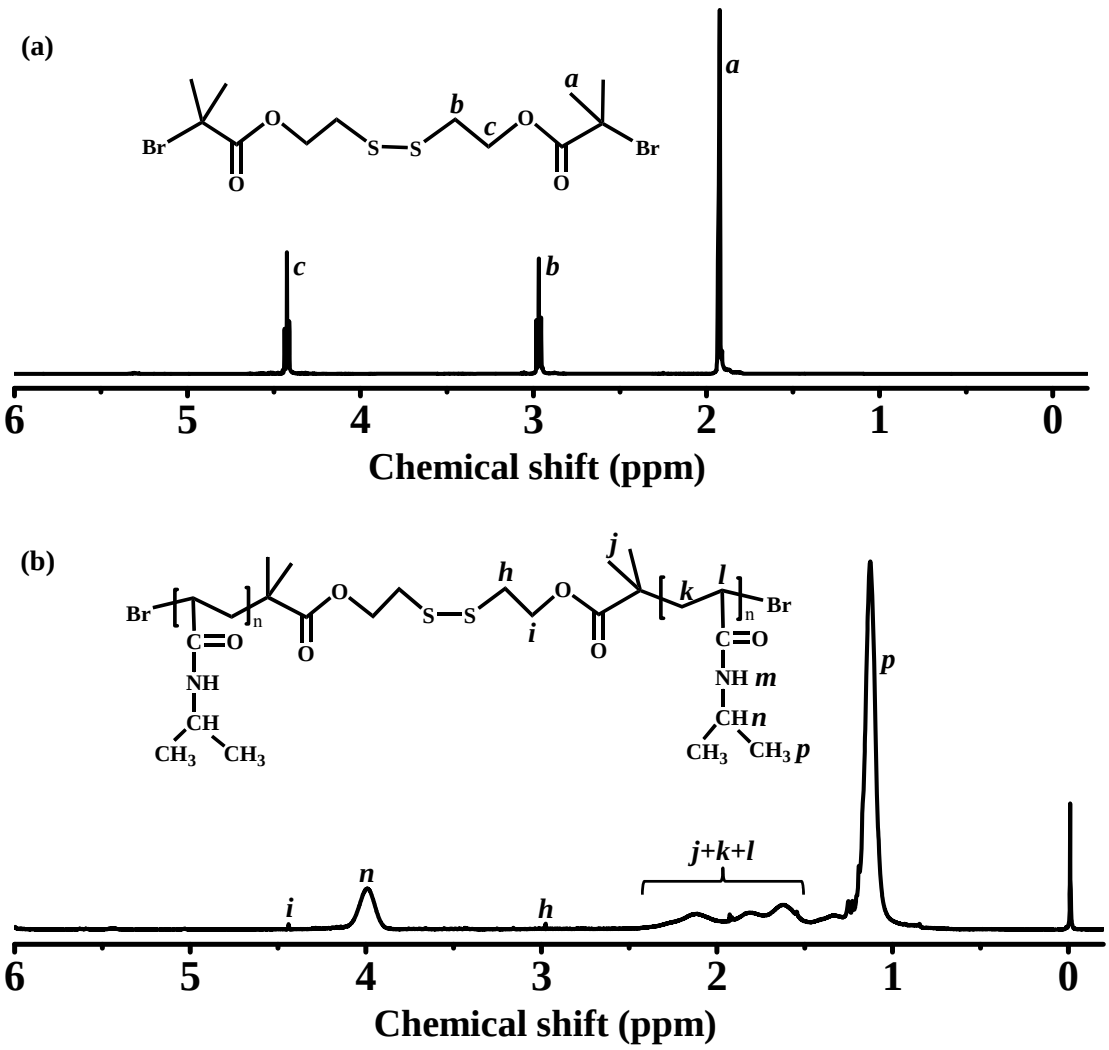

Figure S1. ^{1}H NMR spectrum of (a) bis[2-(2-bromoisobutyryloxy)ethyl] disulfide (BiBOEDS) and (b) PNIPAM-S-S-PNIPAM2 polymer.

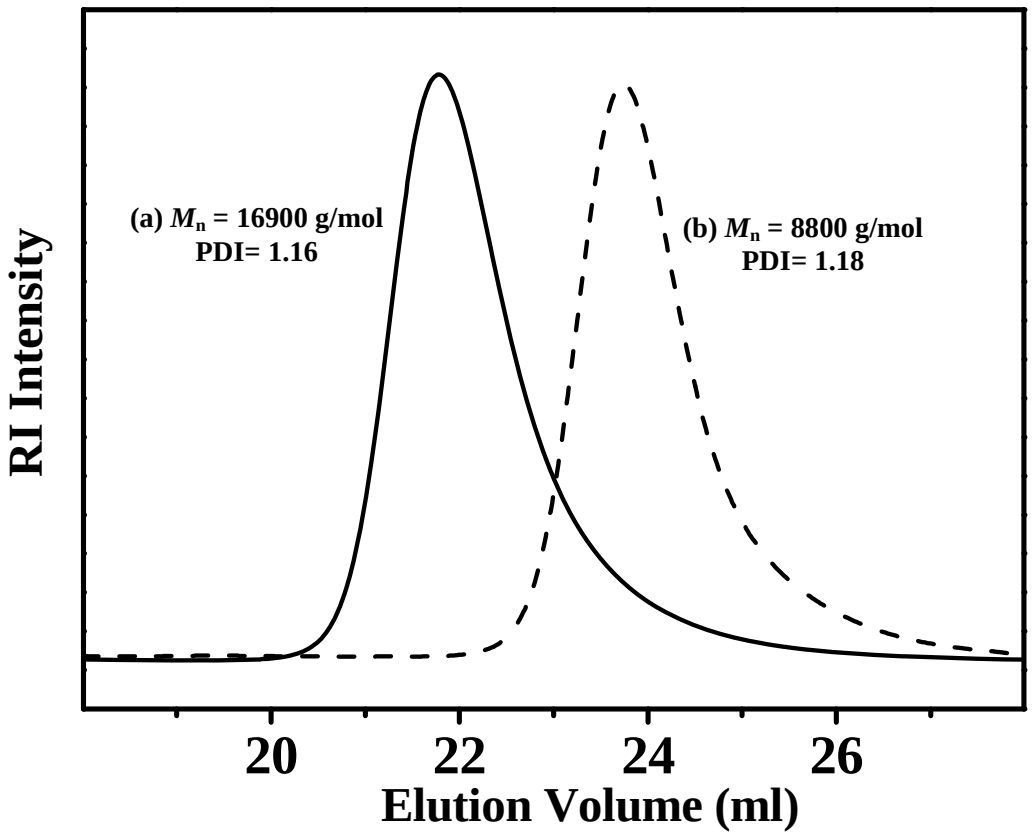

Figure S2. Gel permeation chromatography (GPC) elution curves of the (a) PNIPAM-S-S-PNIPAM2 polymer precursor and (b) the corresponding PNIPAM-SH2 formed after treatment with excess DTT.

References

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