

Supporting Information

Synthesis and properties of a dually cleavable graft copolymer comprising pendant acetal linkages

Ke Miao, Wei Shao, Huanhuan Liu and Youliang Zhao*

Jiangsu Key Laboratory of Advanced Functional Polymer Design and Application, Department of Polymer Science and Engineering, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, China

Table S1. Results for synthesis of normal (PHP, run 1) and disulfide-linked (SPHP, run 2) poly(HEMA-*co*-PEGMEMA) copolymers by RAFT copolymerization of HEMA (M_1) and PEGMEMA (M_2) and normal (CP, runs 3) and disulfide-linked (SCP, run 4) poly(PEG-*co*-PCL) comblike copolymers by CL polymerization using various macroinitiators (MI)^a

run	sample	CTA / MI	T (°C)	t (h)	C% ^b	M_n^c	PDI ^c	$M_{n,NMR}^d$	DP ₁ ^d	DP ₂ ^d	DP _{PCL} ^d	$f_{w,PCL}^e$
1	PHP	4-CPDB	60	8	39.4	5500	1.11	5050	8.2	7.8	—	—
2	SPHP	S-CPDB	60	5	33.8	7460	1.10	7730	12.2	11.5	—	—
3	CP	PHP	90	20	93.6	27100	1.12	26900	8.2	7.8	23.4	0.813
4	SCP	SPHP	90	20	96.0	49900	1.12	48900	12.2	11.5	29.6	0.842

^a Reaction conditions: $[M_1]_0:[M_2]_0:(f[CTA]_0):[AIBN]_0 = x:x:1:0.2$, $f = 1$ (4-CPDB) or 2 (S-CPDB), $x = 20$ (run 1) or 30 (run 2), $[M_1]_0 = 1.0 \text{ mol L}^{-1}$, in DMF (runs 1 and 2); $[CL]_0:[OH]_0:[Sn(Oct)_2]_0 = y:1:0.2$, $y = 25$ (run 3) or 30 (run 4), $[CL]_0 = 2.0 \text{ mol L}^{-1}$, in toluene (runs 3 and 4). ^b Total monomer conversion determined by ¹H NMR analysis. ^c Number-average molecular weight (g mol^{-1}) and polydispersity estimated by GPC ($M_{n,GPC}$, runs 1 and 2) or determined by GPC-MALLS ($M_{n,LS}$, runs 3 and 4). ^d Number-average molecular weight ($M_{n,NMR}$, g mol^{-1}) and degree of polymerization (DP) determined by ¹H NMR analysis. ^e Weight percent of PCL in copolymer determined by ¹H NMR analysis, $f_{w,PCL} = DP_1 \times DP_{PCL} / M_{n,NMR}$.

Table S2. Results for synthesis of acid-cleavable (ACG) and disulfide-linked acid-cleavable (SACG) poly(PEG-co-PCL)-*graft*-MVPEG graft copolymers via adductive reaction between poly(PEG-co-PCL) and MVPEG^a

run	sample	precursor	yield	$M_{n,th}^b$	$M_{n,LS}^c$	PDI ^c	$M_{n,NMR}^d$	DP ₁ ^e	DP ₂ ^e	DP _{PCL} ^e	$f_{w,PCL}^e$
1	ACG	CP	0.96	33600	34200	1.14	33600	8.2	7.8	23.4	0.647
2	SACG	SCP	0.98	58900	59600	1.08	58800	12.2	11.5	29.6	0.700

^a Reaction conditions: [MVPEG]₀: [OH]₀: [PPTS]₀ = 2:1:0.2, $W_{polymer} \cdot V_{DMF} = 0.30 \text{ g mL}^{-1}$, in DMF at 30 °C for 60 h. ^b Theoretical molecular weight (g mol^{-1}), $M_{n,th} = M_{n,NMR}(\text{precursor}) + DP_1 \times M_n(\text{MVPEG})$. ^c Determined by GPC-MALLS. ^d Determined by ¹H NMR analysis. ^e Polymerization degree of HEMA (DP₁), PEGMEMA (DP₂), PCL (DP_{PCL}) and weight percent of PCL in copolymer ($f_{w,PCL}$) determined by ¹H NMR analysis.

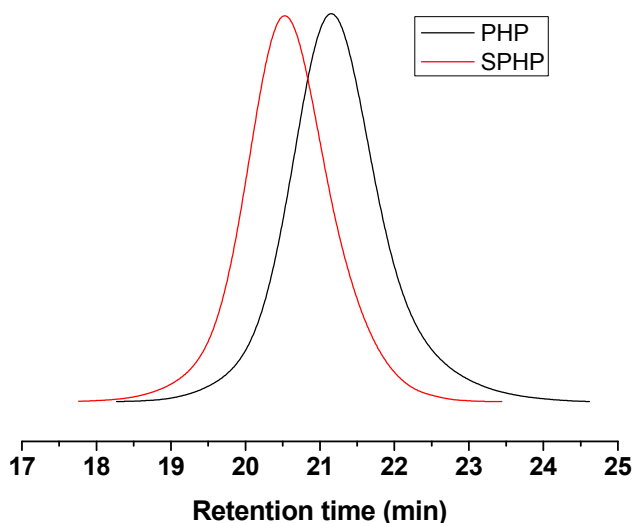


Fig. S1 GPC traces of PHP and SPHP.

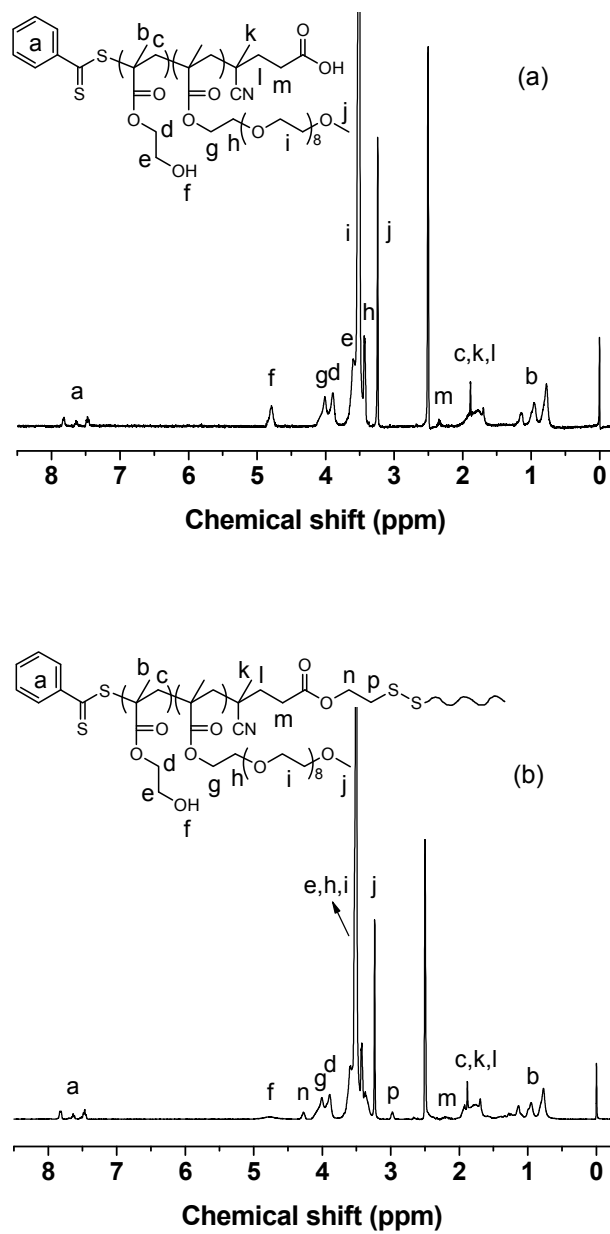


Fig. S2 ^1H NMR spectra of PHP (a) and SPHP (b) in $\text{DMSO-}d_6$.

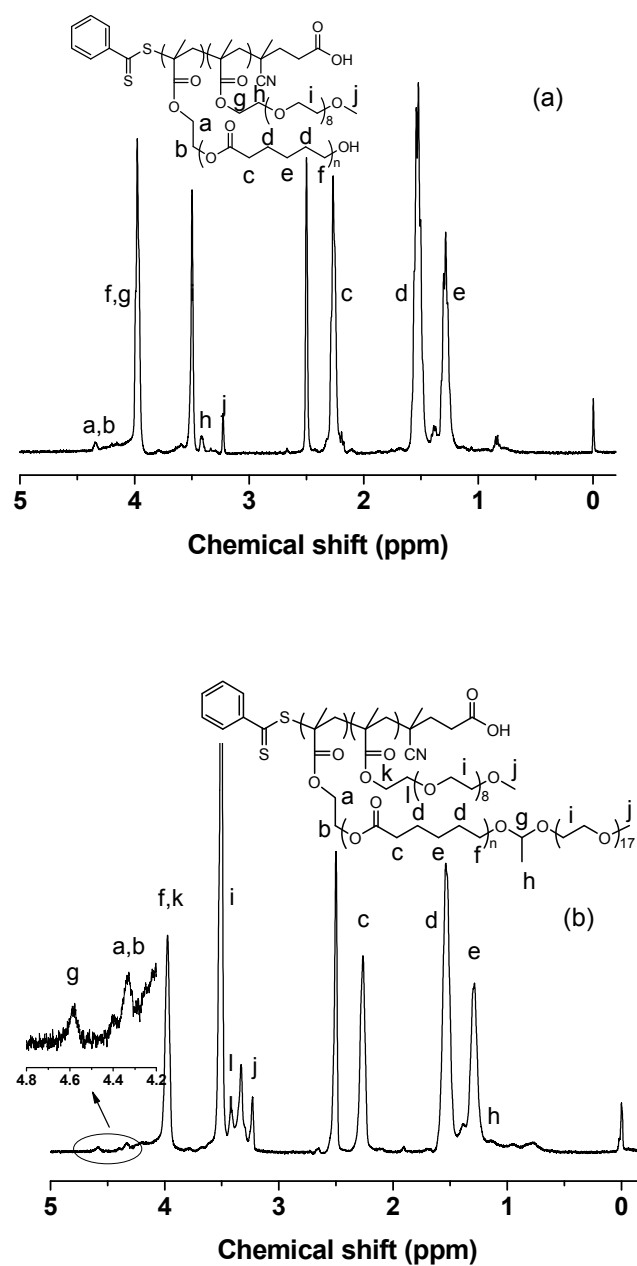


Fig. S3 ^1H NMR spectra of CP (a) and ACG (b) in $\text{DMSO-}d_6$.

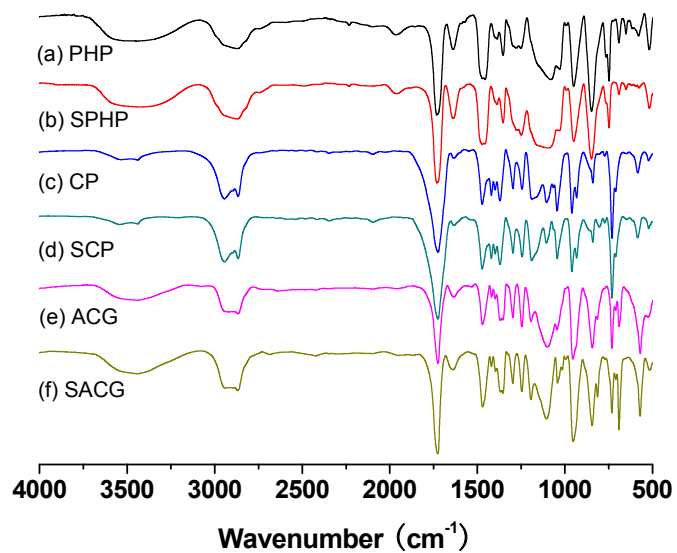


Fig. S4 IR spectra of various copolymers.

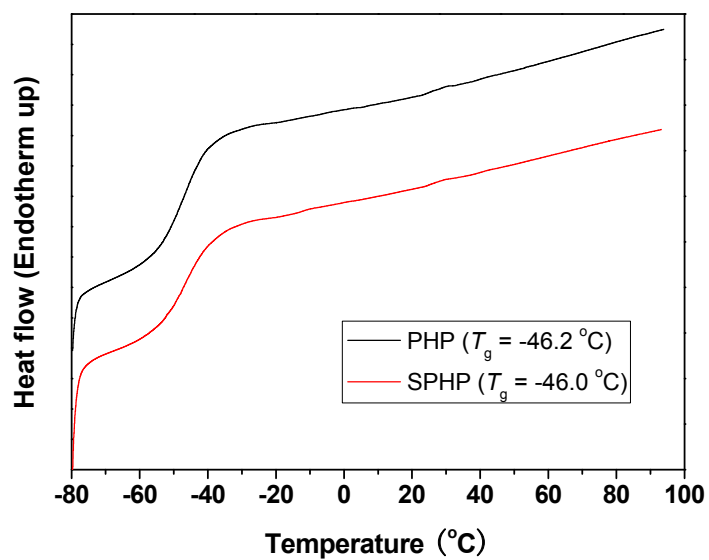


Fig. S5 DSC curves of PHP and SPHP.

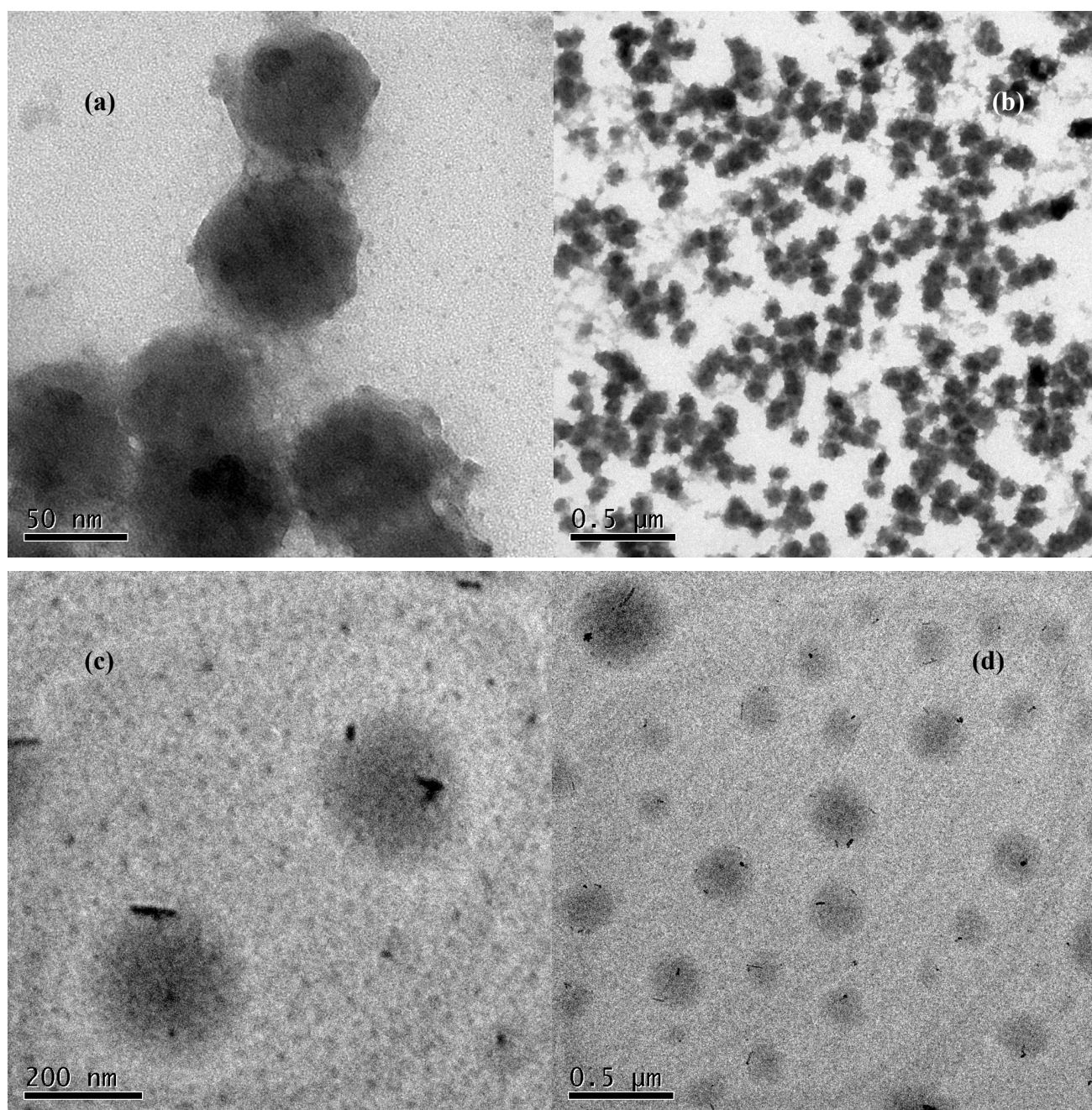


Fig. S6 Typical TEM images of copolymer micelles formed by SCP (a, b) and aggregates involving large compound micelles formed by SACG (c, d) in aqueous solution ($c = 0.50 \text{ mg mL}^{-1}$).

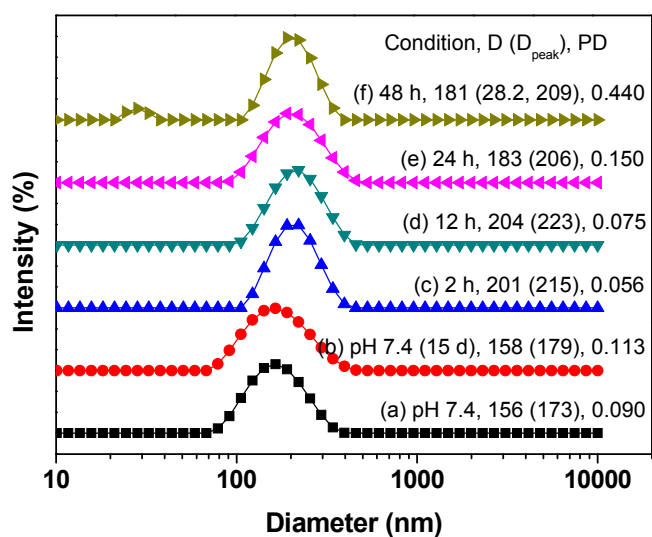


Fig. S7 DLS plots of SACG aggregates ($c = 0.50 \text{ mg mL}^{-1}$) in PBS solution (50 mM) at 37 °C: a and b, pH 7.4; c-f, pH 5.0.

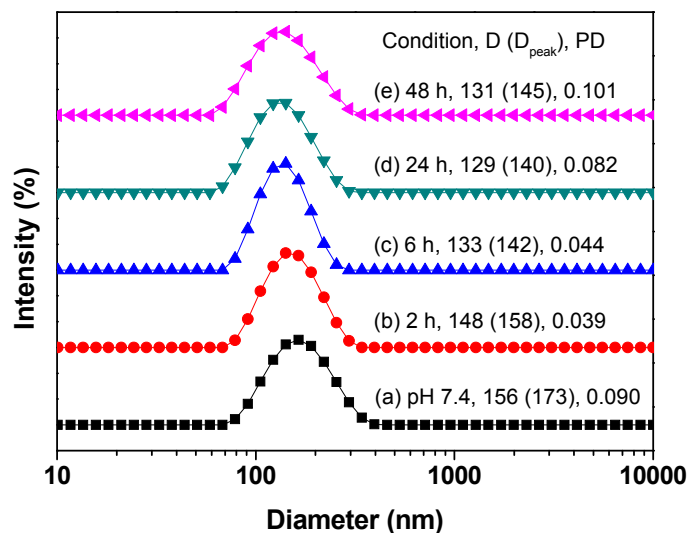


Fig. S8 DLS plots of SACG aggregates ($c = 0.50 \text{ mg mL}^{-1}$) in PBS solution (pH 7.4, 50 mM) at 37 °C: a, no DTT; b-e, 10 mM DTT.

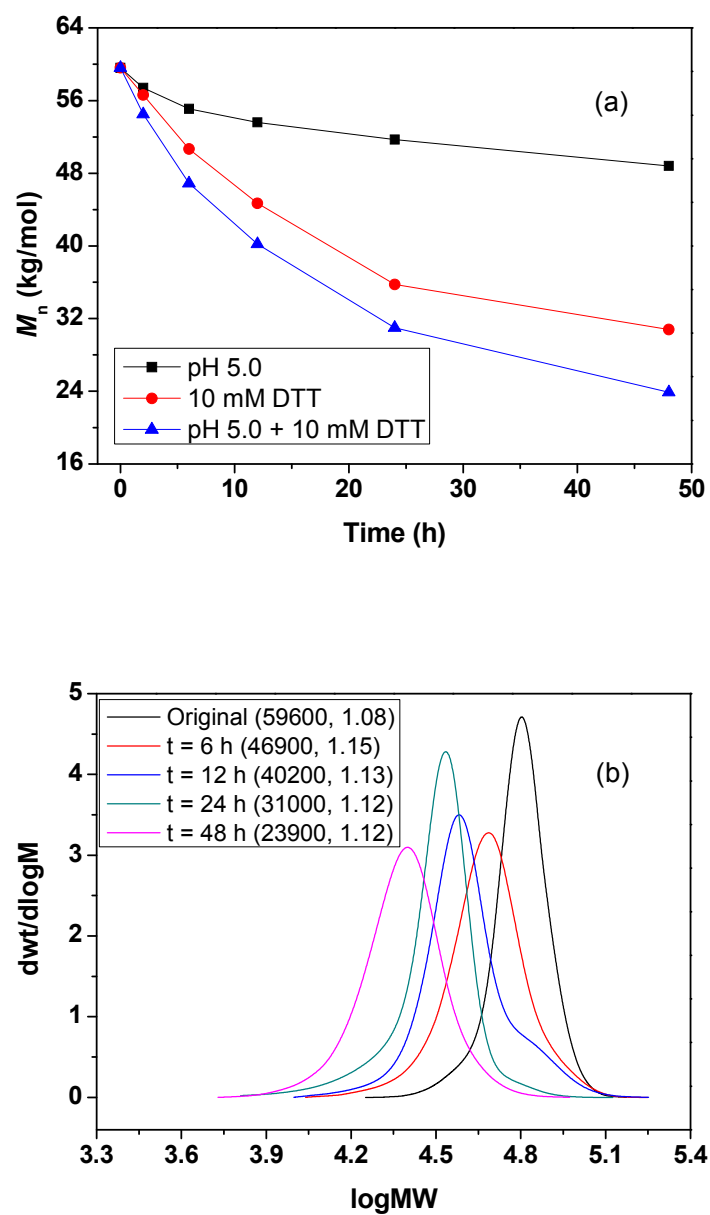


Fig. S9 Dependence of molecular weight of cleaved SACG copolymer upon external stimuli in PBS solution (50 mM) at 37 °C on time (a) and typical GPC traces of cleaved copolymers obtained at different times (b).