

Electronic Supplementary Information

Hyperbranched Polycaprolactone-*click*-Poly(*N*-vinylcaprolactam) Amphiphilic Copolymers and Their Applications as Temperature-responsive Membranes

Tao Cai,^a Min Li,^b Bin Zhang,^b Koon-Gee Neoh^{a,b} and En-Tang Kang^{*,a,b}

^aNUS Graduate School for Integrative Science and Engineering
National University of Singapore
Kent Ridge, Singapore 117576

^bDepartment 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: chet@nus.edu.sg

Experiment Section

Materials

Propargyl alcohol (PA, 99%), stannous octoate ($\text{Sn}(\text{Oct})_2$, 95%), ϵ -caprolactone (ϵ -CL, $\geq 99\%$), dicyclohexylcarbodiimide (DCC, 98%), 4-(*N,N*-dimethylamino)pyridine (DMAP, $\geq 99\%$), 3,3'-dithiobis(propionic acid) (DTPA, 99%), DL-1,4-dithiothreitol (DTT, 98%), *N*-vinylcaprolactam (VCL, 98%) and 1,4-dioxane (ACS reagent, $\geq 99\%$) were obtained from Sigma-Aldrich Chem. Co. and used as received without further purification. Reagent grade tetrahydrofuran (THF), toluene and dichloromethane (DCM) were obtained from Merck Chem. Co. and used as received without further purification. 2,2'-Azobisisobutyronitrile (AIBN, Kanto, 97%) was recrystallized from methanol. *O*-(2-azidoethyl) *S*-benzyl dithiocarbonate (AEBDC)¹ was prepared according to procedures described in the literature.

Synthesis of α -Hydroxyl- ω -alkyne-poly(ϵ -caprolactone) ($\text{CH}\equiv\text{C-PCL-OH}$) via Ring-Opening Polymerization (ROP)

In a typical polymerization process, ϵ -CL (15 ml, 0.136 mol), PA (396 μl , 6.8 mmol) and $\text{Sn}(\text{Oct})_2$ (511 mg, 1.36 mmol) in dry toluene (2 ml) were introduced into a 25 ml reaction flask. The reaction mixture was purge with argon for 30 min to remove the dissolved oxygen. Polymerization was carried out under continuous stirring at 110 °C. After 12 h, the reaction mixture turned viscous, and the reaction was stopped by diluting with THF. The PCL homopolymer was precipitated in 300 ml of hexane. The adduct was re-dissolved in 30 ml of THF and precipitated into 300 ml of hexane to remove the residual monomers. The resulting polymer was filtered and dried in a vacuum oven overnight at room temperature. About 13.8 g of a white solid was obtained (yield $\sim 89.3\%$). $M_{n,\text{NMR}} = 2,100$ g/mol; $M_{n,\text{GPC}} = 2,600$ g/mol and PDI = 1.15 (Figure S2). ¹H

NMR (CDCl_3 , δ , ppm, TMS): 1.38 ($2\text{H}\times m$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$), 1.57-1.65 ($4\text{H}\times m$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$, $-\text{OC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.31 ($2\text{H}\times m$, $-\text{OC}(=\text{O})\text{CH}_2\text{CH}_2-$), 2.5 (1H, $-\text{C}\equiv\text{CH}$), 3.65 (2H, $-\text{CH}_2\text{CH}_2\text{OH}$), 3.95-4.05 ($2\text{H}\times(m-1)$, $-\text{CH}_2\text{CH}_2\text{O}-$), 4.65 (2H, $-\text{OC}(=\text{O})\text{CH}_2\text{C}\equiv\text{CH}$). As can be seen from Scheme 1, m denotes the degree of polymerization of ϵ -CL monomers in the $\text{CH}\equiv\text{C-PCL-OH}$ homopolymer.

Synthesis of α -Thiol- ω -alkyne-poly(ϵ -caprolactone) ($\text{CH}\equiv\text{C-PCL-SH}$)^{2,3}

$\text{CH}\equiv\text{C-PCL-OH}$ (8.4 g, $M_{n,\text{NMR}} = 2,100$ g/mol, 4 mmol), DCC (824 mg, 4 mmol), DMAP (97.6 mg, 0.8 mmol) were completely dissolved in anhydrous DCM (120 ml). The flask was immersed in an ice bath and DTPA (840 mg, 4 mmol) in 20 ml of dry DCM 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 48 h. The precipitated 1,3-dicyclohexylurea was filter off and washes with 50 ml of DCM on the filter. The solution was washed consecutively with saturated NaHCO_3 solution (2×100 ml) and water (3×100 ml). The organic layer was dried over magnesium sulfate and concentrated by rotary evaporator, and then precipitated into 200 ml of hexane. The copolymer sample was re-dissolved in DCM and precipitated into 300 ml of hexane to remove the residual reactants. After drying in a vacuum oven overnight at room temperature, the $\text{CH}\equiv\text{C-PCL-DTPA}$ polymer was obtained as a solid (7.9 g, yield $\sim 85.5\%$). ^1H NMR (CDCl_3 , δ , ppm, TMS): 1.38 ($2\text{H}\times m$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$), 1.57-1.65 ($4\text{H}\times m$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$, $-\text{OC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.31 ($2\text{H}\times m$, $-\text{OC}(=\text{O})\text{CH}_2\text{CH}_2-$), 2.5 (1H, $-\text{C}\equiv\text{CH}$), 2.75 (4H, $-\text{SCH}_2\text{CH}_2\text{C}(=\text{O})\text{OH}$), 2.97 (4H, $-\text{SCH}_2\text{CH}_2\text{C}(=\text{O})\text{OH}$), 3.95-4.05 ($2\text{H}\times m$, $-\text{CH}_2\text{CH}_2\text{O}-$), 4.65 (2H, $-\text{OC}(=\text{O})\text{CH}_2\text{C}\equiv\text{CH}$).

The CH₂=C-PCL-DTPA ($M_{n,NMR} = 2,300$ g/mol, 6.9 g, 3 mmol) polymer was dissolved in 40 ml of THF. The reaction mixture was purged with argon for 30 min. DTT (1.84 g, 12 mmol) was then introduced into the reaction flask. The mixture was stirred under the protection of an argon stream at room temperature for 24 h. The solution was concentrated under reduced pressure and then precipitated into 200 ml of hexane. The copolymer sample was re-dissolved in THF and precipitated into 200 ml of hexane to remove the residual reactants. After drying in a vacuum oven overnight at room temperature, the CH₂=C-PCL-SH polymer was obtained as a white solid (6.1 g, yield ~92.4%). ¹H NMR (CDCl₃, δ , ppm, TMS): 1.38 (2H \times *m*, -CH₂CH₂CH₂-), 1.57-1.65 (4H \times *m*, -CH₂CH₂CH₂O-, -OC(=O)CH₂CH₂CH₂-), 2.31 (2H \times *m*, -OC(=O)CH₂CH₂-), 2.5 (1H, -C \equiv CH), 2.65 (2H, -OC(=O)CH₂CH₂SH), 2.77 (2H, -OC(=O)CH₂CH₂SH), 3.95-4.05 (2H \times *m*, -CH₂CH₂O-), 4.65 (2H, -OC(=O)CH₂ C \equiv CH).

Synthesis of Azide-Terminated Poly(*N*-vinylcaprolactam) (PVCL-N₃) via Xanthate-Mediated RAFT Polymerization

The azide-terminated poly(*N*-vinylcaprolactam) (PVCL-N₃) chains were prepared via xanthate-mediated reversible addition-fragmentation chain-transfer (RAFT) polymerization of the VCL monomer using *O*-(2-azidoethyl) *S*-benzyl dithiocarbonate (AEBDC) as the RAFT agent.^{1,4,5} In a typical reaction, VCL (2.5 g, 18 mmol), AIBN (11.8 mg, 0.072 mmol), AEBDC (91.1 mg, 0.36 mmol) and 1,4-dioxane (5 ml) were introduced into a 25 ml reaction flask. The light yellow homogeneous solution was purged with argon for about 20 min to remove the dissolved oxygen. The reaction flask was then sealed and placed in an oil bath at 80 °C to initiate the polymerization. At the end of the reaction (10 h), the reaction flask was quenched in cold water and opened, diluted with THF and precipitated into cold hexane to remove the residual monomers.

The dissolution-precipitation cycle was repeated twice. After drying in a vacuum oven overnight at room temperature, the PVCL-N₃ polymer was obtained as a white solid (1.66 g, yield ~64%). $M_{n,NMR} = 4,400$ g/mol; $M_{n,GPC} = 6,500$ g/mol and PDI = 1.18 (Figure S2). ¹H NMR (CDCl₃, δ, ppm, TMS): 1.0-1.8 (8H×*n*, -CHNC(=O)CH₂CH₂CH₂CH₂-, -CH₂CHNC(=O)-), 2.2-2.65 (2H×*n*, -CHNC(=O)CH₂CH₂-), 2.95-3.45 (2H×*n*, -CH₂NC(=O)CH₂-), 3.65 (2H, -CH₂N₃), 4.1-4.4 (1H×*n*, -CHNC(=O)CH₂-), 4.42 (2H, -CH₂S-), 4.76 (2H, -SC(=S)OCH₂-), 7.25-7.4 (5H, -CH-, aromatic ring). As can be seen from Scheme 1, *n* denotes the degree of polymerization of VCL monomers in the PVCL-N₃ homopolymer.

Table S1 Characteristics of the PVCL-N₃ Homopolymers

Entry	Sample ^a	[VCL]/[AEBDC]	Time (h)	Cov. (%)	$M_{n,th}$ (g/mol) ^b	$M_{n,GPC}$ (g/mol) ^c	PDI ^c	$M_{n,NMR}$ (g/mol) ^d	DP ^e	LCST (°C) ^f
1	PVCL-N ₃ -1	50:1	10	64	4700	6500	1.18	4400	30	37.4
2	PVCL-N ₃ -2	100:1	10	60	8600	12200	1.25	8000	56	35.9
3	PVCL-N ₃ -3	200:1	10	58	16400	19600	1.22	14400	102	34.6
4	PVCL-N ₃ -4	300:1	10	55	23200	28300	1.28	20800	148	33.5

^a Experimental conditions: typically 2.5 g of VCL, 5 ml of 1,4-dioxane; [AEBDC]:[AIBN] = 5:1; 80 °C. VCL = *N*-vinylcaprolactam, AEBDC = *O*-(2-azidoethyl) *S*-benzyl dithiocarbonate, AIBN = 2,2'-azobis(2-methylpropionitrile).

^b $M_{n,th} = M_{VCL} \times \text{Conv.} \times [\text{VCL}]/[\text{AEBDC}] + M_{\text{AEBDC}}$, $M_{VCL} = 139$ g/mol, $M_{\text{AEBDC}} = 253$ g/mol.

^c Determined from gel permeation chromatography (GPC) results in THF, calibrated with polystyrene (PS) molecular weight standards. $\text{PDI} = M_w/M_n$.

^d Determined from ¹H NMR spectroscopy results, calculated from the ratio of methylene protons adjacent to the azide groups of AEBDC initiator to protons of the methylene protons adjacent to the amide groups of PVCL chains.

^e Degree of Polymerization (DP).

^f Lower critical solution temperature (LCST) was denoted as the cloud point of 0.1 wt% aqueous solution of respective polymer upon heating, which can be determined from the initial transition point in the UV-visible absorption spectra.

Table S2 Elemental Analyses of CH≡C-PCL-SH, HPCL and HPCL-*click*-PVCL Polymer

Entry	Sample	C	S	N	PVCL content (mol%) ^a
1	CH≡C-PCL-SH	97.5%	2.5%	-	-
2	HPCL	97.3%	2.7%	-	-
3	HPCL- <i>click</i> -PVCL1	96.2%	2.4%	1.4%	6.8
4	HPCL- <i>click</i> -PVCL2	95.4%	2.1%	2.5%	13.4
5	HPCL- <i>click</i> -PVCL3	94.5%	2.0%	3.5%	20.2
6	HPCL- <i>click</i> -PVCL4	93.9%	1.5%	4.6%	26.9
7	HPCL- <i>click</i> -PVCL5	95.1%	2.1%	2.8%	15.1
8	HPCL- <i>click</i> -PVCL6	94.2%	1.9%	3.9%	21.3
9	HPCL- <i>click</i> -PVCL7	92.1%	1.3%	6.6%	35.7

^a $M_{\text{AEBDC}} = 253 \text{ g/mol}$, $M_{\text{ε-CL}} = 114 \text{ g/mol}$, $M_{\text{VCL}} = 139 \text{ g/mol}$.

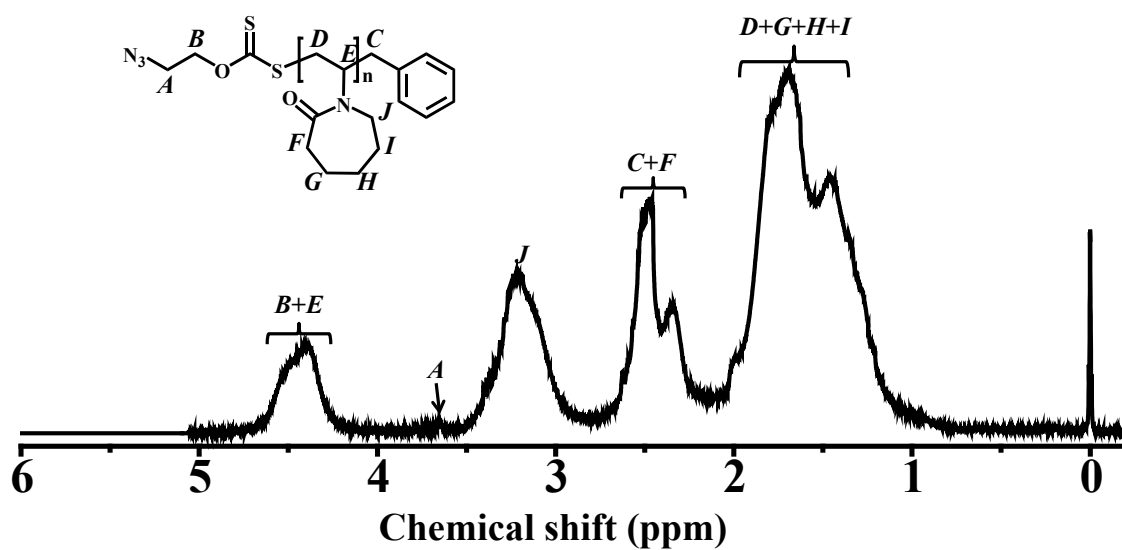


Figure S1. ^1H NMR spectrum of the PVCL- N_3 -3 homopolymer.

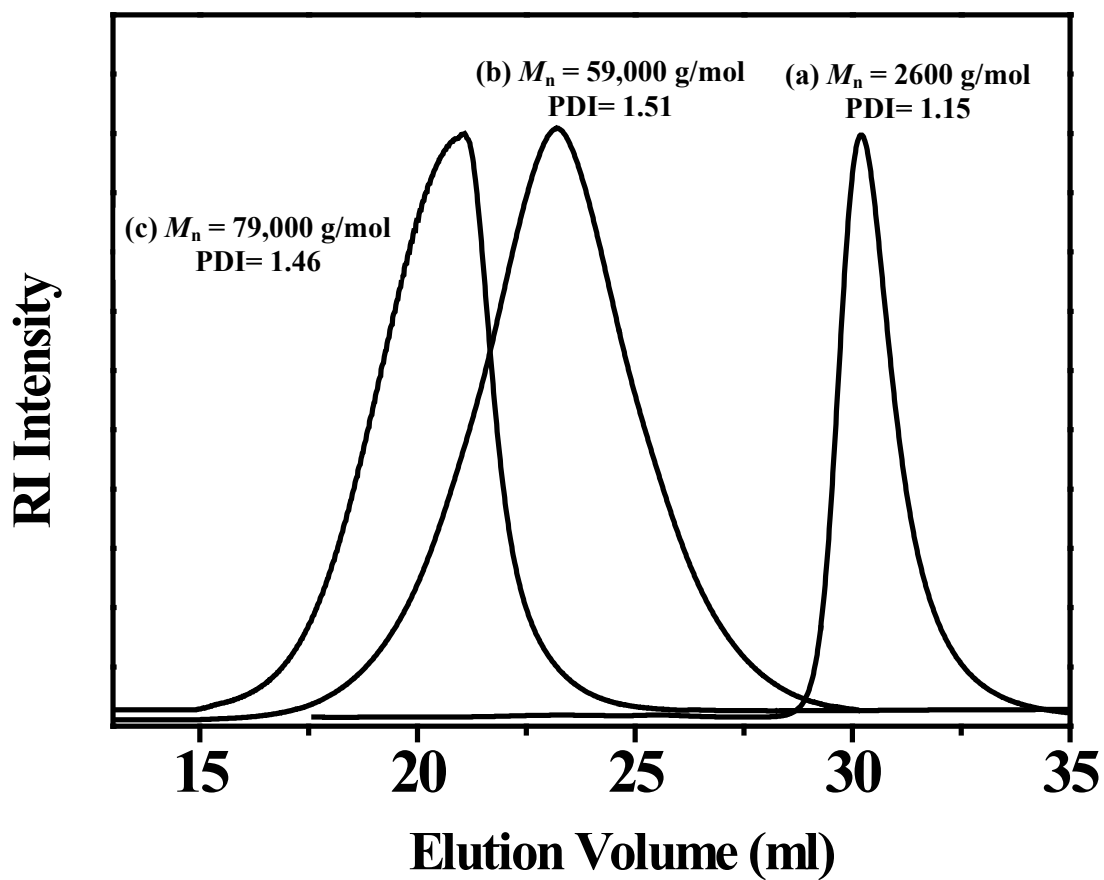


Figure S2. GPC elution curves of the (a) $\text{CH}\equiv\text{C-PCL-OH}$ linear precursor, (b) HPCL polymer and (c) HPCL-*click*-PVCL3 polymer. (Calibrated with linear polystyrene)

References

- (1) F. Chen, Z. P. Cheng, J. Zhu, W. Zhang, X. L. Zhu, *Eur. Polym. J.*, 2008, **44**, 1789-1795.
- (2) W. Liu, C. M. Dong, *Macromolecules*, 2010, **43**, 8447-8455.
- (3) N. V. Tsarevsky, K. Matyjaszewski, *Macromolecules*, 2002, **35**, 9009-9014.
- (4) D. C. Wan, K. Satoh, M. Kamigaito, Y. Okamoto, *Macromolecules*, 2005, **38**, 10397-10405.
- (5) N. S. Jeong, M. Redhead, C. Bosquillon, C. Alexander, M. Kelland, R. K. O'Reilly, *Macromolecules*, 2011, **44**, 886-893.