

Supporting information to

## Stimuli-responsive star polymers through thiol-yne core functionalization/crosslinking of block copolymer micelles

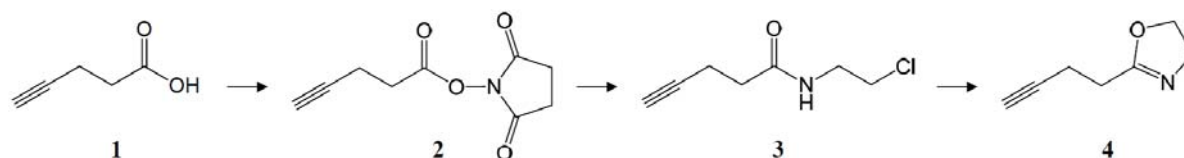
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### Materials

2-Chloroethylamine hydrochloride (99%), diethylether (99.5%), dichloromethane (99.5%), methanol (99.5%), sodium sulfate ( $\geq 99\%$ ), sodium hydroxide ( $\geq 98\%$ ), potassium hydroxide ( $\geq 96\%$ ) (all Sigma–Aldrich). 4-Pentynoic acid (98%) (AcrosOrganics). *N*-Hydroxysuccinimid (99%) (Merck). 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide (99.7%) (Iris Biotech).

### Synthesis of 2-(3-butynyl)-2-oxazoline



N-Succinimidyl-4-pentynate, 2. 10 g of 4-pentynoic acid **1** were dissolved in 200 ml of dry  $\text{CH}_2\text{Cl}_2$ . Solutions of *N*-hydroxysuccinimid (NHS) (18.76 g in 130 ml dry  $\text{CH}_2\text{Cl}_2$ ) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDAC) (23.55 g in 60 ml dry  $\text{CH}_2\text{Cl}_2$ ) were added and the solution was stirred overnight. After removal of the solvent the crude product was dissolved in diethyl ether/water. The water phase was extracted with ether several times. The combined organic phases were dried over  $\text{Na}_2\text{SO}_4$  after which the solvent is removed; yield: 90%.  $^1\text{H}$  NMR (400.1 MHz,  $\text{DMSO-d}_6$ ):  $\delta/\text{ppm}$  = 2.3-2.5 (m, 4H,  $\text{CH}_2$ ), 2.75 (s, 1H,  $\text{CH}\equiv\text{C}$ ), 2.83 (s, 4H,  $\text{CH}_2\text{-NHS}$ ).

N-(2-Chloroethyl)-4-pentynamide, 3. 21.32 g of 2-chloroethylamine hydrochloride and 7.88 g of NaOH were dissolved in 200 ml of water. A solution of 17.88 g of **2** in 500 ml

of CH<sub>2</sub>Cl<sub>2</sub> was added drop wise to the solution under vigorous stirring. The mixture was stirred overnight at room temperature. The phases were separated and the organic phase washed twice with water, after which it was dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed; yield: 85%. <sup>1</sup>H NMR (400.1 MHz, DMSO-d<sub>6</sub>): δ/ppm = 2.1-2.4 (m, 4H, CH<sub>2</sub>), 2.75 (s, 1H, CH≡C), 3.38 (d, 2H, CH<sub>2</sub>-N), 3.59 (t, 2H, CH<sub>2</sub>-Cl), 8.18 (s, 1H, NH).

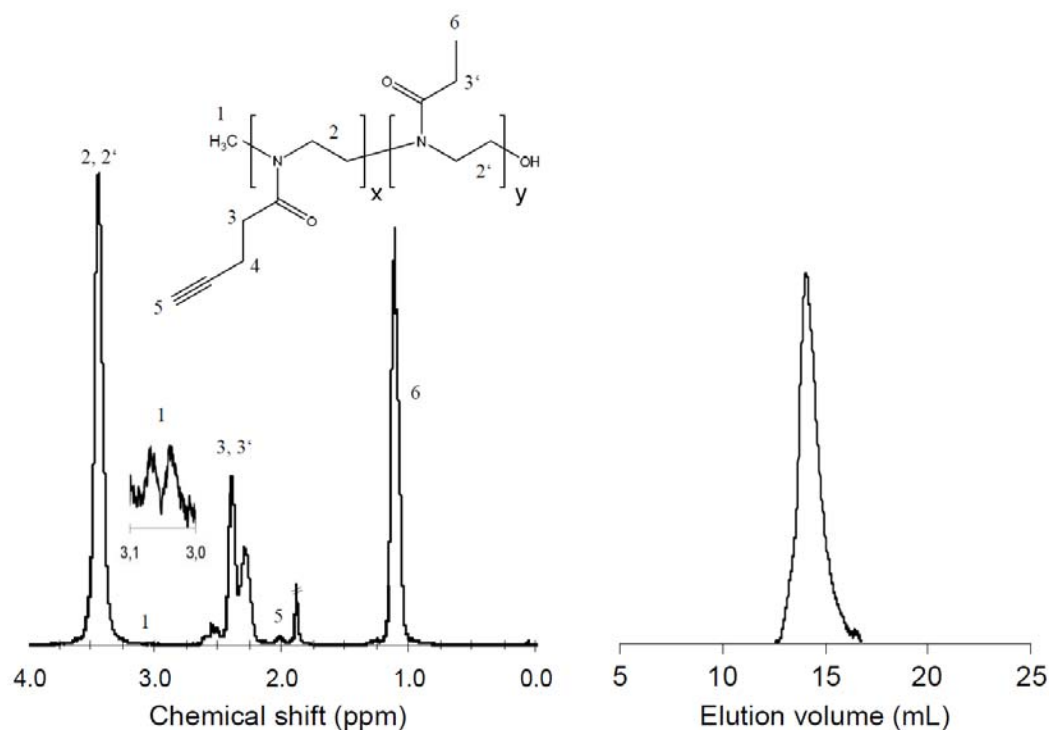
2-(3-Butinyl)-2-oxazoline, **4**. 12.42 g of **3** was placed in a flame dried three-necked flask with a condenser connected to it under inert atmosphere. 50 ml of methanol was added to the flask, followed by 50 ml of a degassed 1.5 M KOH solution in methanol. The solution was refluxed overnight and the precipitate was removed by filtration, after which the solvent was removed to yield a pink solid, which was further purified by recondensation at 90 °C on a vacuum line to afford a white solid; yield: 37 % (overall yield of all steps: 28%). <sup>1</sup>H NMR (400.1 MHz, DMSO-d<sub>6</sub>): δ/ppm = 2.14 (s, 4H, CH<sub>2</sub>), 3.06 (s, 1H, CH≡C), 3.43 (t, 2H, CH<sub>2</sub>N), 3.91 (t, 2H, CH<sub>2</sub>O). <sup>13</sup>C NMR (100.4 MHz, CDCl<sub>3</sub>): δ/ppm = 15.4 (C-C≡C), 27.3 (C-CNO), 54.4 (C-N), 67.5 (C-O), 69.0 (C-C≡C), 82.7 (C-C≡C), 166.7 (CNO). Melting point, mp 55 °C.

### **Synthesis of poly(2-(3-butinyl)-2-oxazoline)-block-poly(2-ethyl-oxazoline)**

A block copolymer of 2-(3-butinyl)-2-oxazoline (BOX) and 2-ethyl-2-oxazoline (EOX) was prepared by cationic ring-opening polymerization. 2-Ethyl-2-oxazoline, acetonitrile (solvent) and methyl triflate (initiator) were dried over calcium hydride overnight. The components were recondensed under reduced pressure. The appropriate amount of 2-(3-butinyl)-2-oxazoline was dried over calcium hydride at 60 °C overnight and directly condensed into the flame dried reactor. Acetonitrile (enough to make a 30 wt % solution) was transferred to the flame dried reactor. Methyl triflate was added and the mixture was heated to 70 °C. After approximately three days the second monomer was added together with enough acetonitrile to keep the monomer concentration at 30 wt%. The reaction mixture was heated at 70 °C for another three weeks after which the polymerization was terminated by the addition of a 1:1 mixture of methanol and 1 M NaOH. The polymer was purified by dialysis against THF and isolated by freeze drying from dioxane.

The average numbers of BOX ( $x = 21$ ) and EOX ( $y = 390$ ) repeat units were determined by <sup>1</sup>H NMR endgroup analysis (Figure S1, left), considering the integrals of signals *I* (CH<sub>3</sub> end group, 3H), 5 (CH≡C BOX,  $x \cdot 1H$ ), and 6 (CH<sub>3</sub> EOX,  $y \cdot 3H$ ). Apparent number-

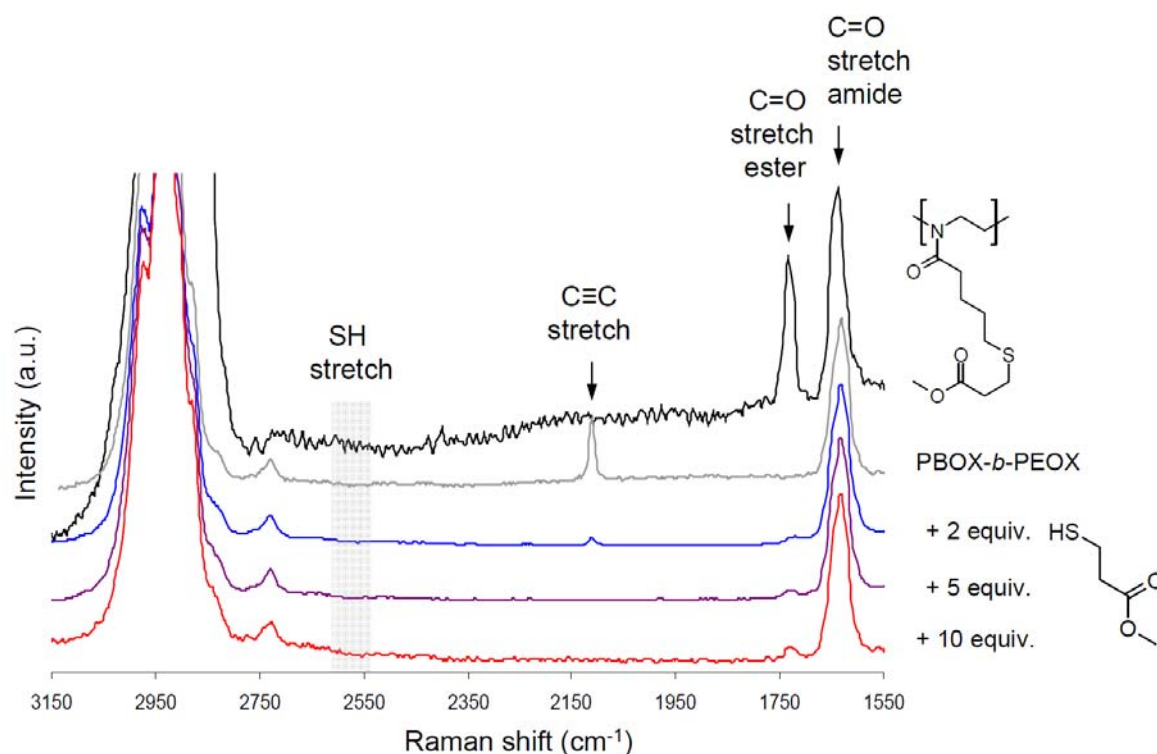
and weight average molecular weights ( $M_n = 67.3$  kDa and  $M_w = 85.9$  kDa, respectively) and polydispersity index ( $PDI = M_w/M_n = 1.28$ ) were determined by SEC (Figure S1, right).



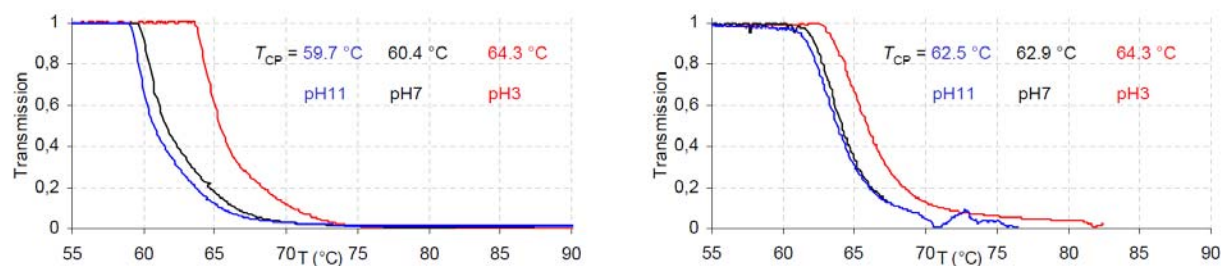
**Figure S1.** <sup>1</sup>H NMR spectrum (400.1 MHz, CDCl<sub>3</sub>) (left) and SEC chromatogram (NMP, detector: RI) (right) of poly(2-(3-butynyl)-2-oxazoline)-*block*-poly(2-ethyl-oxazoline), PBOX-*b*-PEOX.

**Table S1.** Results of zeta-potential measurements of poly(2-(3-butynyl)-2-oxazoline)-*block*-poly(2-ethyl-oxazoline), PBOX-*b*-PEOX, and micelles after the functionalization/crosslinking with 3-mercaptopropionate and with 2-mercaptoethylamine hydrochloride in water.

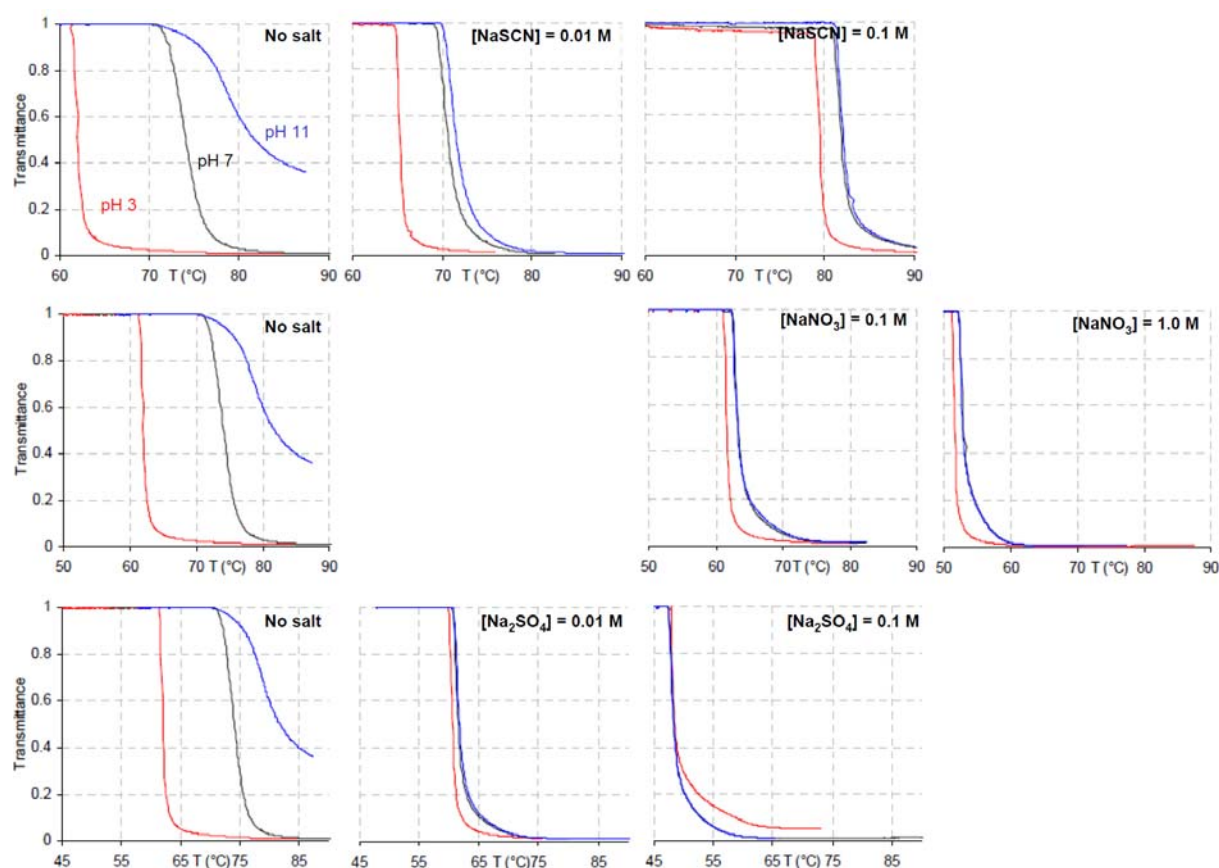
	$\xi$ potential (mV)	Peak width (mV)
PBOX- <i>b</i> -PEOX, pH 3	+1.28	6.72
PBOX- <i>b</i> -PEOX, pH 11	-0.37	3.97
PBOX- <i>b</i> -PEOX micelles + HS-CH <sub>2</sub> -CH <sub>2</sub> -COOH, pH 11	-3.43	3.73
PBOX- <i>b</i> -PEOX micelles + HS-CH <sub>2</sub> -CH <sub>2</sub> -NH <sub>2</sub> ·HCl, pH 3	+7.59	3.54



**Figure S2.** Raman spectra of poly(2-(3-butynyl)-2-oxazoline)-*block*-poly(2-ethyl-oxazoline), PBOX-*b*-PEOX, and of the cross-linked micelles obtained by reaction with methyl 3-mercaptopropionate at  $[\text{SH}]_0/[\text{C}\equiv\text{C}]_0 = 2, 5, \text{ and } 10$ . The top spectrum is that of poly(2-[4-(2-methylcarboxyl-ethylsulfanyl)-butyl]-2-oxazoline), prepared by “click” modification of poly(2-(3-butenyl)-2-oxazoline) with methyl 3-mercaptopropionate (A. Gress et al. *Macromolecules* 2007, **40**, 7928-7933), which is used for calibration of C=O stretch ester and amide signal intensities and determination of the degrees of functionalization.



**Figure S3.** Turbidity curves of 0.1 wt% aqueous solutions of (left) poly(2-(3-butynyl)-2-oxazoline)-*block*-poly(2-ethyl-oxazoline), PBOX-*b*-PEOX, and (right) commercial poly(2-ethyl-2-oxazoline), PEOX,  $M_n \sim 50$  kDa, PDI  $\sim 3$ -4 (Sigma-Aldrich) at pH 3, 7, and 11.



**Figure S4.** Turbidity curves of 0.1 wt% aqueous solutions of anionic star polymer in the presence of different salts (NaSCN, NaNO<sub>3</sub>, and Na<sub>2</sub>SO<sub>4</sub>) (top to bottom) at different concentrations (0, 0.01, 0.1, and 1M) (left to right) and pH 3, 7, and 11 (red, black, blue).