

Electronic Supplementary Information for:

**Oligo(ethylene glycol) and quaternary ammonium-based
block copolymer micelles: from tunable thermoresponse to
dual salt responses**

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1. Materials

S-dodecyl-S'-(α,α' -dimethyl- α'' -acetic acid) trithiocarbonate (DDMAT) was synthesized according to the literature.¹ 2,2'-Azobisisobutyronitrile (AIBN, Aldrich, 98%) was recrystallized from ethanol. *p*-Chloromethylstyrene (CMS) (Aldrich, 90%) was purified by vacuum distillation from CaH₂. *N,N,N',N'',N''*-Pentamethyl diethylenetriamine (PMDETA) (Acros Organic, 99%), *N,N*-dimethylacetamide dimethyl acetal (Alfa Aesar), propargyl amine (Alfa Aesar), 3-dimethylamino-1-propyne (Alfa Aesar), 1-bromoethane (Alfa Aesar), 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU; Aldrich), copper iodine (CuI; Aldrich), and sodium azide (NaN₃, Alfa Aesar) were used as received. Copper bromide (CuBr, Alfa Aesar, 99%) was treated by stirring in glacial acetic acid and washed with ethanol several times. 2-(2-methoxyethoxy)ethyl methacrylate (MEO₂MA) and oligo(ethylene glycol) methacrylate (OEGMA, $M_n=475$ g/mol) was purchased from Aldrich and passed through a column of activated basic alumina to remove inhibitors.

2. Characterization

Attenuated total internal reflectance fourier transform infrared (ATR FT-IR). ATR FT-IR spectra of samples were recorded on an EQUINOSS/HYPERION2000 spectrometer (Bruker, Germany).

Nuclear Magnetic Resonance (NMR). ¹H NMR spectra of samples were obtained from a Bruker AVANCE-400MHz NMR spectrometer with DMSO-*d*₆ and methanol-*d*₄ as solvents. The chemical shifts were relative to tetramethylsilane.

Gel Permeation Chromatography (GPC). GPC analysis was carried out with a HLC-8320 (Tosoh, Japan) analysis system with two columns (TSK gel super AWM-H $\times$ 2, R0091+R0093), using DMF with 10 mM LiBr as eluents at a flow rate of 0.6 mL min⁻¹ at 40°C. PS calibration kit was used as the calibration standard.

Optical transmittances. The optical transmittances of copolymer micelles aqueous solution (1 mg/mL) at various temperatures were measured at a wavelength of 500 nm on a UV-visible spectrophotometer (Lambda 35, PerkinElmer). The temperature of the sample cell was thermostatically controlled using an external superconstant

temperature bath. The solutions were equilibrated for 10 min at each measuring temperature. The LCST values of the copolymer micelles solutions were defined as the temperature producing a 50% decrease in optical transmittance.

Dynamic Light Scattering (DLS). Morphology of the micelles/aggregates of brush polymers in water was investigated using DLS techniques. The experiments were performed on a Malvern Autosizer 4700 DLS spectrometer. DLS was performed at a scattering angle 90°. The Rh was obtained by a cumulant analysis.

Transmission Electron Microscopy (TEM). The morphology of brush polymers micelles/aggregates was observed with a JEOL JEM-2010 TEM at an accelerating voltage of 120 kV. The samples for TEM observation were prepared by placing 10 μ L of the vesicular or micellar solutions on copper grids coated with thin films and carbon.

Critical micelle concentration (CMC) measurement. CMC was determined using pyrene as a fluorescence probe. 10 μ L of pyrene (0.45 mg/mL) in acetone was added to a series of 10.0 mL volumetric flasks. After the acetone evaporated, a measured amount of PAMS-*b*-P(MEO₂MA-*co*-OEGMA) or P(St-*g*-QA)-*b*-P(MEO₂MA-*co*-OEGMA) solution was added to each flask, then added followed by doubly distilled water. The flasks were kept for 12 h to equilibrate the pyrene and the micelles. The fluorescence spectra were recorded using a Hitachi F2500 luminescence spectrometer (Hitachi, Ltd.) with an excitation wavelength of 335 nm. The emission wavelengths at 373 nm (I_1) and 395 nm (I_3) were monitored. The CMC value was chosen as the concentration when pyrene exhibited an apparent decrease in the I_1/I_3 ratio with an increasing concentration of the copolymer, indicating that the aggregation of the copolymer occurred.

3 Experimental procedures

3.1 Synthesis of poly(*p*-chloromethylstyrene)(PCMS) by RAFT

DDMAT (0.238 g, 0.66 mmol), *p*-chloromethylstyrene (5.002 g, 32.78 mmol) and AIBN (21.5 mg, 0.13 mmol) were dissolved in anisole (2 mL). The mixture was degassed with three freeze-evacuate-thaw cycles. The polymerization reaction was

performed at 70 °C for 24 h. Then, the product mixture was diluted by the same volume of dry THF, and the final product was obtained by precipitation in *n*-hexane and drying under vacuum for 24 h.

$M_{n,NMR}$ =4140 g/mol. The degree of polymerization (DP = 25) was calculated out based on the obtained molecular weight. ATR FTIR (cm⁻¹): 2820-3046 (ν_{C-H}). ¹H NMR (500 MHz, DMSO-*d*₆, δ, ppm): 6.26-7.42 (arom. CH of styrenic ring), 4.66 (CH₂Cl), 0.75-1.82 ((CH₃)₂C, CH₂CH, C₁₁H₂₃). ¹³C NMR (500 MHz, CDCl₃, δ, ppm): 128.4 (arom. CH of styrenic ring), 46.0 (CH₂Cl).

3.2 Synthesis of poly(*p*-azidomethylstyrene) (PAMS)

PCMS (2.003 g, 0.54 mmol) was dissolved in dry DMF (30 mL) and then NaN₃ (3.861 g, 65.5 mmol) was added. The reaction mixture was stirred at room temperature for 48 h and then precipitated in excess of water. The obtained crude product was re-dissolved in dichloromethane and re-precipitated in cold methanol. The resultant white solid was collected by filtration and dried in a vacuum oven for 48 h.

$M_{n,NMR}$ =4300 g/mol. ATR FTIR (cm⁻¹): 2814-3046 (ν_{C-H}), 2091 (ν_{azide group}). ¹H NMR (500 MHz, DMSO-*d*₆, δ, ppm): 6.33-7.27 (arom. CH of styrenic ring), 4.34 (CH₂N₃), 1.06-1.83 ((CH₃)₂C, CH₂CH, C₁₁H₂₃). ¹³C NMR (500 MHz, CDCl₃, δ, ppm): 128.0 (arom. CH of styrenic ring), 54.3 (CH₂Cl).

3.3 Synthesis of poly(*p*-azidomethylstyrene)-block-poly(2-(2-methoxyethoxy)ethyl methacrylate-co-oligo(ethylene glycol) methacrylate) (PAMS-*b*-P(MEO₂MA-co-OEGMA)) copolymers by RAFT

MEO₂MA (1.20 g, 6.3 mmol), OEGMA (0.337 g, 0.7 mmol), AIBN (1.45 mg, 8.86 μmol) and PAMS (0.353 g, 0.071 mmol) were dissolved in dry toluene (6.5 mL). The mixture was degassed with three freeze-evacuate-thaw cycles. The reaction mixture was stirred at 70 °C for 24 h. After removing toluene, the crude product was diluted with DMF and then dialyzed against deionized water for 48 h to remove the unreacted MEO₂MA and OEGMA monomers. Finally, the purified copolymer was obtained by lyophilization of water.

$M_{n,NMR}$ =13160 g/mol. ATR FTIR (cm⁻¹): 2736-3028 (ν_{C-H}), 2091 (ν_{azide group}), 1730

($\nu_{C=O}$). ^1H NMR (500 MHz, $\text{DMSO-}d_6$, δ , ppm): 6.28-7.16 (arom. CH of styrenic ring), 4.24 (CH_2N_3), 4.10 (COOCH_2), 3.50-3.83 ($\text{CH}_2\text{OCH}_2\text{CH}_2\text{O}$), 3.41 (CH_3O), 1.62-2.06 (CHCH_2 , $\text{CH}_2\text{C}(\text{CH}_3)$), 0.74-1.14 ($(\text{CH}_3)_2\text{C}$, CH_2CH , $\text{CH}_2\text{C}(\text{CH}_3)$, $\text{C}_{11}\text{H}_{23}$). ^{13}C NMR (500 MHz, CDCl_3 , δ , ppm): 128.0 (arom. CH of styrenic ring), 71.9 (CH_3O), 70.9 ($\text{CH}_2\text{OCH}_2\text{CH}_2\text{O}$), 59.2 (COOCH_2), 54.0 (CH_2Cl).

3.4 Synthesis of propargyl quaternary ammonium salt

Propargyl quaternary ammonium salt was synthesized according to the literature.²¹ 3-Dimethylamino-1-propyne (5.00 g, 60.1 mmol) was dissolved in dry THF (20 mL). Then, 1-bromoethane (7.90 g, 72.2 mmol) was added to the solution above mentioned. The reaction mixture was stirred at 35 °C for 48 h. Then the solvent and the excess 1-bromoethane were evaporated. The mixture was washed with diethyl ether three times to remove the unreacted 3-dimethylamino-1-propyne. At last, the quaternary ammonium salt was dried in a vacuum.

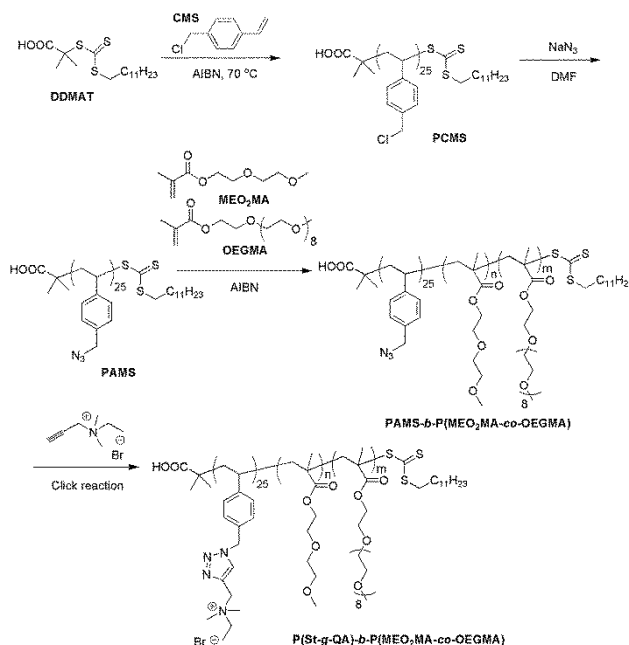
^1H NMR (500 MHz, methanol- d_4 , δ , ppm): 4.45 (CH_2N^+), 3.61 ($\text{N}^+\text{CH}_2\text{CH}_3$), 3.56 ($\text{CH}\equiv\text{C}$), 3.24 (N^+CH_3), 1.43 ($\text{N}^+\text{CH}_2\text{CH}_3$).

3.5 Synthesis of poly(styrene-graft-quaternary ammonium)-block- poly(2-(2-methoxyethoxy)ethyl methacrylate-co-oligo(ethylene glycol) methacrylate) (P(St-g-QA)-b-P(MEO₂MA-co-OEGMA)) copolymers by click chemistry

PAMS-b-P(MEO₂MA-co-OEGMA) (0.2 g, 0.015 mmol) and propargyl quaternary ammonium salt (0.076 g, 0.4 mmol) were dissolved in dry DMF (10 mL). Then, DBU (5.5 mg, 0.036 mmol) and CuI (6.8 mg, 0.036 mmol) were added. The mixture was degassed with three freeze-evacuate-thaw cycles. The click reaction was performed at 50 °C for 8 h. After being cooled to room temperature, the reaction flask was opened to air, and the crude product was diluted with THF and passed through a neutral oxide alumina column to remove the copper catalysts. The crude product was then dissolved in water and dialyzed against deionized water for 6 h. The copolymer was finally recovered by freeze-drying.

$M_{n,\text{NMR}}=14370$ g/mol. ATR FTIR (cm^{-1}): 2730-3020 ($\nu_{\text{C-H}}$), 1730($\nu_{\text{C=O}}$). ^1H NMR (500 MHz, methanol- d_4 , δ , ppm): 8.62 ($\text{CH}=\text{C}$, triazole), 6.22-7.36 (arom. CH of styrenic ring), 5.69 (triazole- CH_2 -styrenic ring), 4.81 (triazole- CH_2 - N^+), 4.15

(COOCH₂), 3.57-3.80 (CH₂OCH₂CH₂O), 3.43 (CH₃O), 3.16 (N⁺CH₃), 1.82-2.12 (CHCH₂, CH₂C(CH₃)), 0.84-1.17 ((CH₃)₂C, CH₂CH, CH₂C(CH₃), C₁₁H₂₃). ¹³C NMR (500 MHz, methanol-*d*₄, δ, ppm): 73.3 (CH₃O), 71.5 (CH₂OCH₂CH₂O), 59.8 (COOCH₂), 56.7 (triazole-CH₂-styrenic ring), 54.3 (N⁺CH₃), 50.5 (N⁺CH₂CH₃).

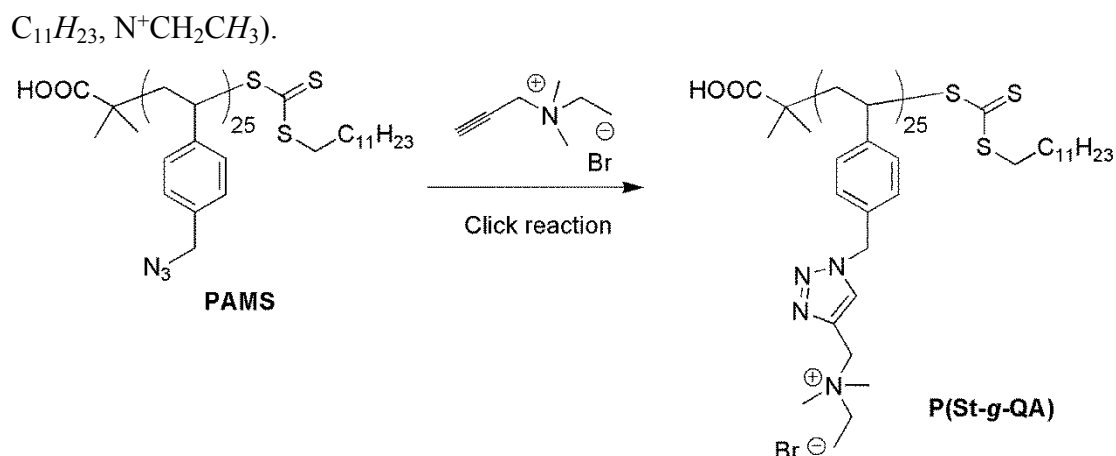


Scheme S1. Synthesis of P(St-g-QA)-*b*-P(MEO₂MA-*co*-OEGMA) copolymer

3.6 Synthesis of poly(styrene-graft-quaternary ammonium) (P(St-g-QA)) polymer by click chemistry

PAMS (227 mg, 0.05 mmol) and propargyl quaternary ammonium salt (215 mg, 1.1 mmol) were dissolved in dry DMF (10 mL). Then, DBU (50 mg, 0.33 mmol) and CuI (50 mg, 0.26 mmol) were added. The mixture was degassed with three freeze-evacuate-thaw cycles. The click reaction was performed at 40 °C for 12 h. After being cooled to room temperature, the reaction flask was opened to air, and the crude product was diluted with THF and passed through a neutral oxide alumina column to remove the copper catalysts. The crude product was then dissolved in water and dialyzed (dialysis membrane, molecular weight cut-off: 1000 Da) against deionized water for 48 h. The copolymer was finally recovered by freeze-drying.

$M_{n,NMR}$ = 7280 g/mol. ¹H NMR (500 MHz, methanol-*d*₄, δ, ppm): 8.60 (CH=C, triazole), 6.36-7.24 (arom. CH of styrenic ring), 5.65 (triazole-CH₂-styrenic ring), 4.79 (triazole-CH₂-N⁺), 3.45 (N⁺CH₂CH₃), 3.12 (N⁺CH₃), 1.17-1.68 (CH₃)₂C, CH₂CH,



Scheme S2. Synthesis of P(St-g-QA)

3.7 Self-assembly of copolymers

For PAMS-*b*-P(MEO₂MA-*co*-OEGMA) copolymers: 50 mg of copolymer was dissolved in 25 mL of DMF and subsequently dialyzed against deionized water for 72 h (dialysis membrane, molecular weight cut-off: 14000 Da) at room temperature. After diluted by deionized water and equilibrated at room temperature for 48 h, the resulting micelles solution had a concentration of 1 mg/mL for transmittance and 0.3 mg/mL for DLS and TEM measurements.

For P(St-g-QA)-*b*-P(MEO₂MA-*co*-OEGMA) and P(St-g-QA): P(St-g-QA)-*b*-P(MEO₂MA-*co*-OEGMA) or P(St-g-QA) was directly dissolved in deionized water and the micelles with set concentration were formed.

4. Results

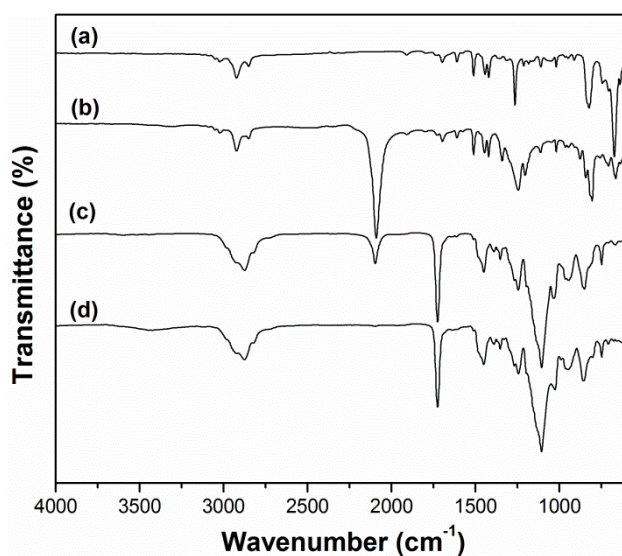


Fig. S1 ATR FTIR spectra of (a) PCMS, (b) PAMS, (c) PAMS-*b*-P(MEO₂MA-*co*-

OEGMA) and (d) P(St-g-QA)-*b*-P(MEO₂MA-*co*-OEGMA).

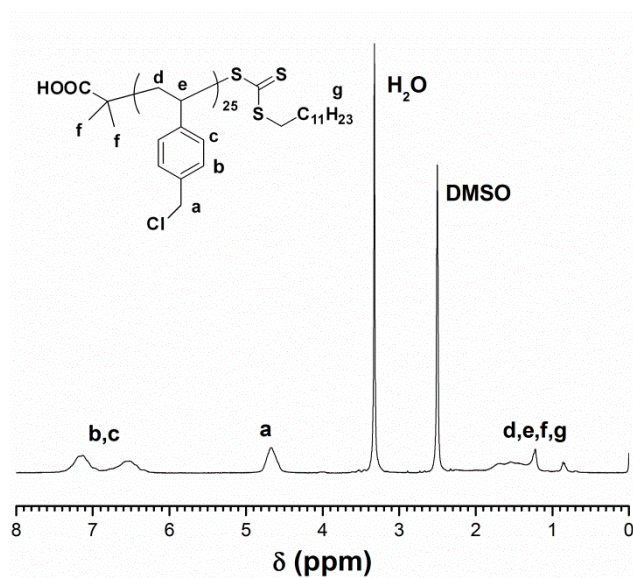


Fig. S2 ¹H NMR spectrum of PCMS.

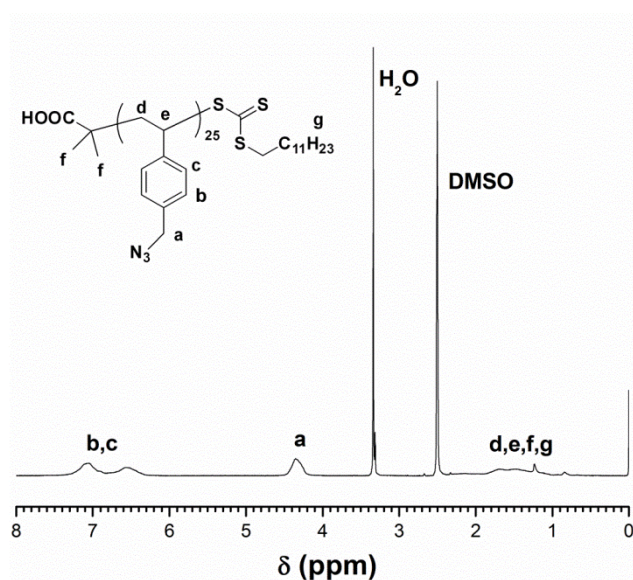


Fig. S3 ¹H NMR spectrum of PCMS.

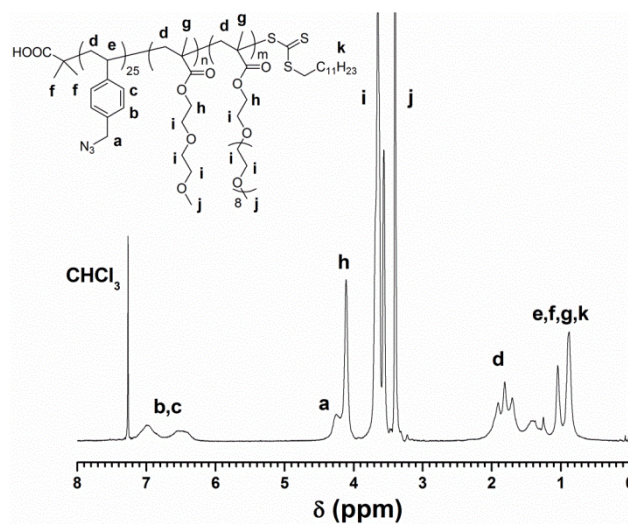


Fig. S4 ^1H NMR spectrum of PAMS-*b*-P(MEO₂MA-*co*-OEGMA).

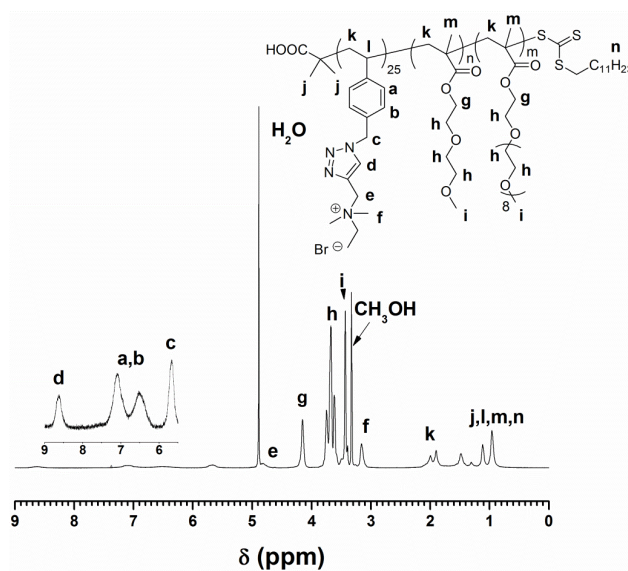
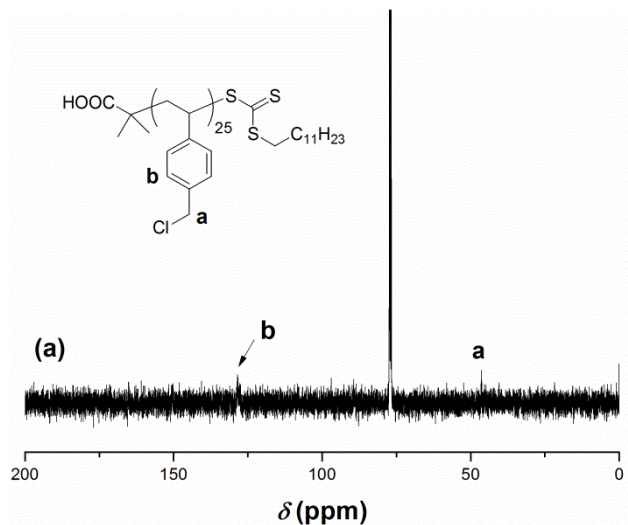


Fig. S5 ^1H NMR spectrum of P(St-*g*-QA)-*b*-P(MEO₂MA-*co*-OEGMA).



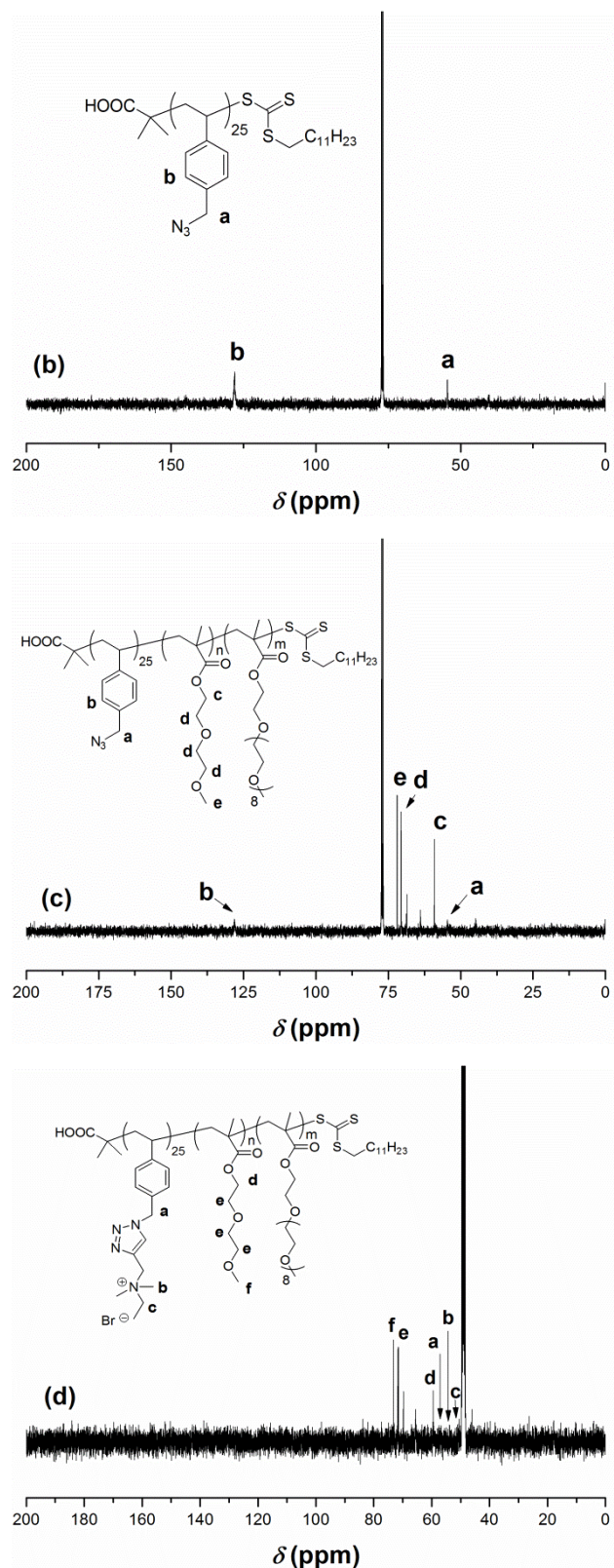


Fig. S6 ^{13}C NMR spectra of (a) PCMS (in CDCl_3), (b) PAMS (in CDCl_3), (c) PAMS-*b*-P(MEO₂MA-*co*-OEGMA) (in CDCl_3) and (d) P(St-*g*-QA)-*b*-P(MEO₂MA-*co*-OEGMA) (in methanol- d_4).

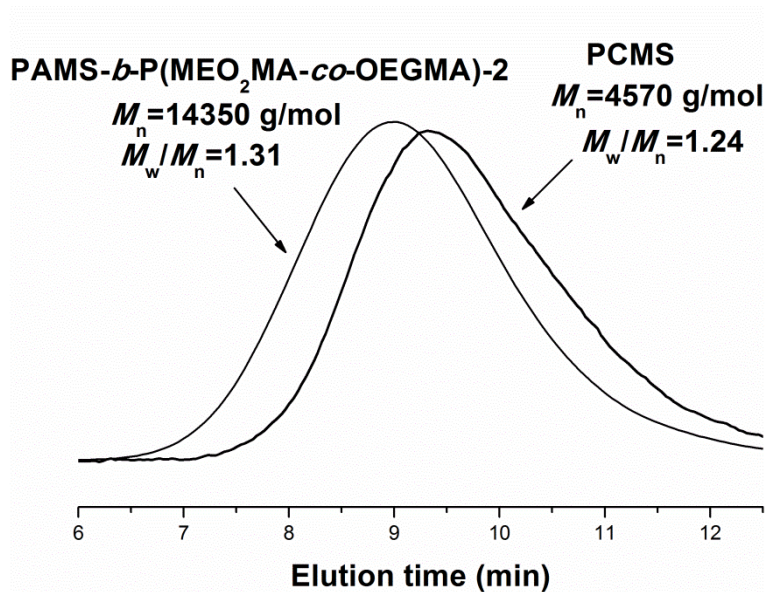


Fig. S7 GPC traces of PCMS and PAMS-*b*-P(MEO₂MA-*co*-OEGMA)-2.

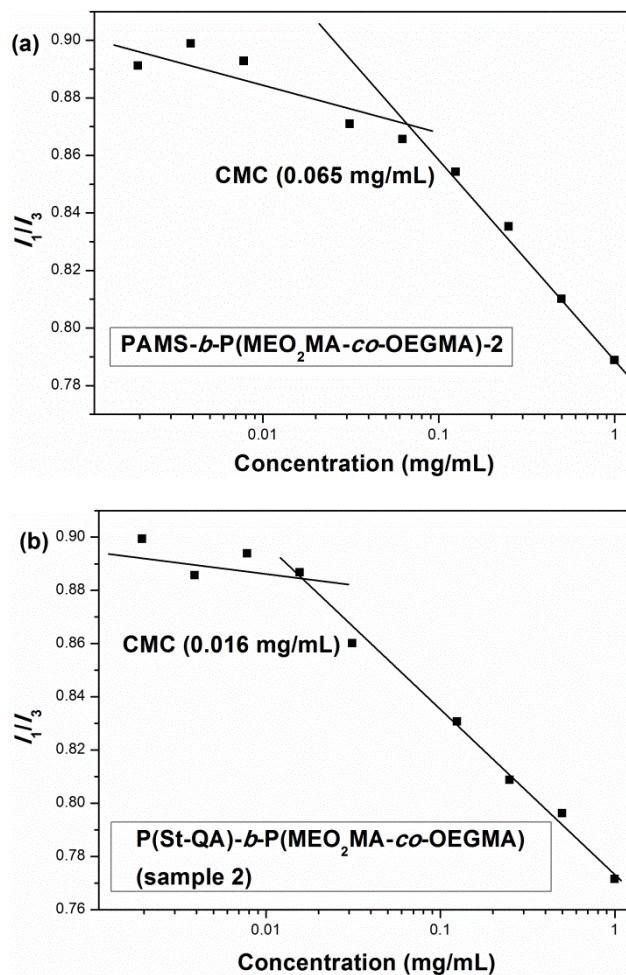


Fig. S8 Determination of CMC for (a) PAMS-*b*-P(MEO₂MA-*co*-OEGMA)-2 and P(St-*g*-QA)-*b*-P(MEO₂MA-*co*-OEGMA) (sample 2) using the fluorescent method with pyrene as a probe.

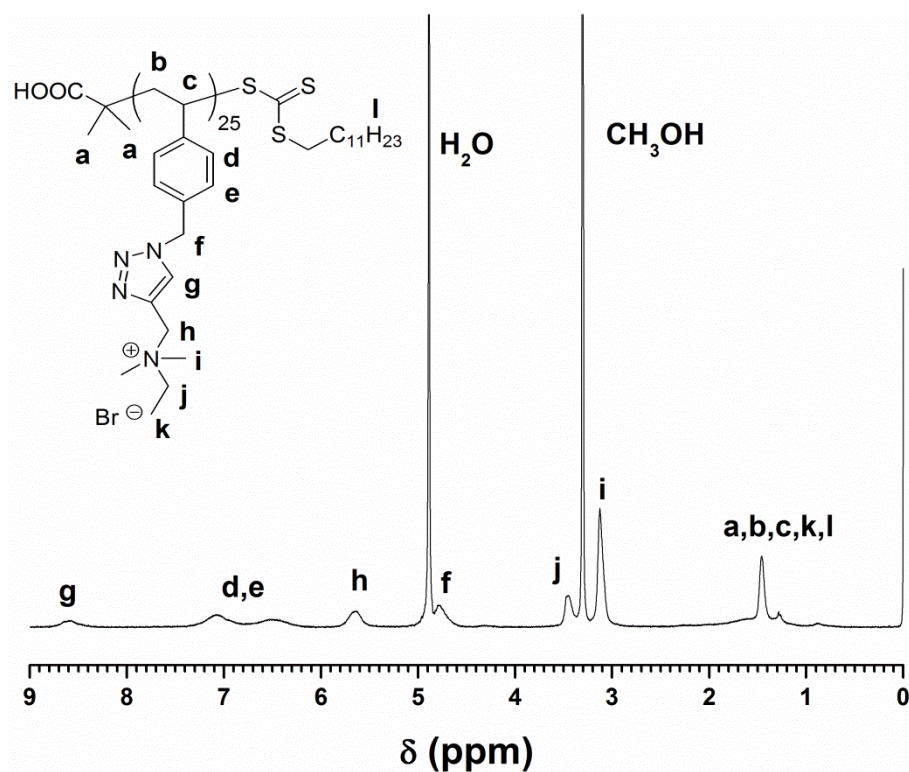


Fig. S9 ¹H NMR spectrum of P(St-g-QA).

Table S1 Results of molecular weight of polymers

Sample ^a	$M_{n,NMR}^b$ (g/mol)	$M_{n,GPC}^c$	M_w/M_n^c	Actual molar ratio of MEO ₂ MA/OEGMA ^b
PCMS	4140	4570	1.24	-
PAMS	4300	-	-	-
PAMS- <i>b</i> -P(MEO ₂ MA- <i>co</i> -OEGMA)-1	12750	13960	1.29	95/5
PAMS- <i>b</i> -P(MEO ₂ MA- <i>co</i> -OEGMA)-2	13160	14350	1.31	91/9
PAMS- <i>b</i> -P(MEO ₂ MA- <i>co</i> -OEGMA)-3	13800	15410	1.32	86/14
1	14400	-	-	95/5
2	14370	-	-	91/9
3	15630	-	-	86/14
P(St-g-QA)	7280	-	-	-

^aThe feed molar ratio of MEO₂MA to OEGMA of PAMS-*b*-P(MEO₂MA-*co*-OEGMA)-1, PAMS-*b*-P(MEO₂MA-*co*-OEGMA)-2, PAMS-*b*-P(MEO₂MA-*co*-OEGMA)-3 was 95/5, 90/10, 85/15 respectively. Sample 1, 2 and 3 denoted P(St-g-QA)-*b*-P(MEO₂MA-*co*-OEGMA) (actual molar

ratio of MEO₂MA to OEGMA: 95/5, 91/9, 86/14).

$^bM_{n,NMR}$ of polymers and the actual molar ratio of MEO₂MA/OEGMA in PAMS-*b*-P(MEO₂MA-*co*-OEGMA) and P(St-*g*-QA)-*b*-P(MEO₂MA-*co*-OEGMA) were calculated according to ¹H NMR spectra.

$^cM_{n,GPC}$ and M_w/M_n were measured by GPC.

References

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- 2 R. Riva, P. Lussis, S. Lenoir, C. Jérôme, R. Jérôme and P. Lecomte, *Polymer*, 2008, **49**, 2023-2028.