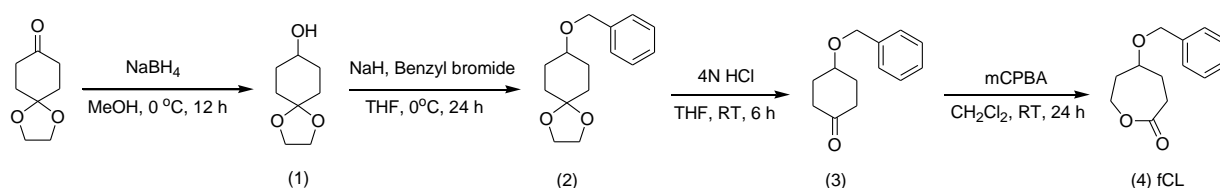


## Supporting Information

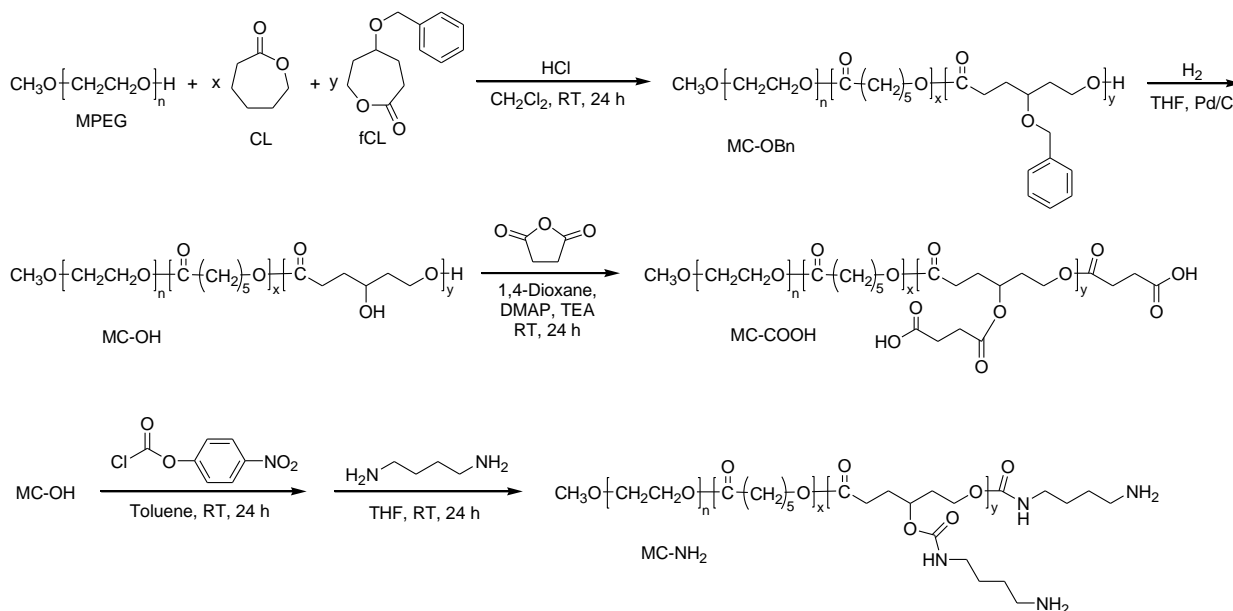
# Temperature-responsive hydrogels via electrostatic interaction of amphiphilic diblock copolymers with pendant-ion groups

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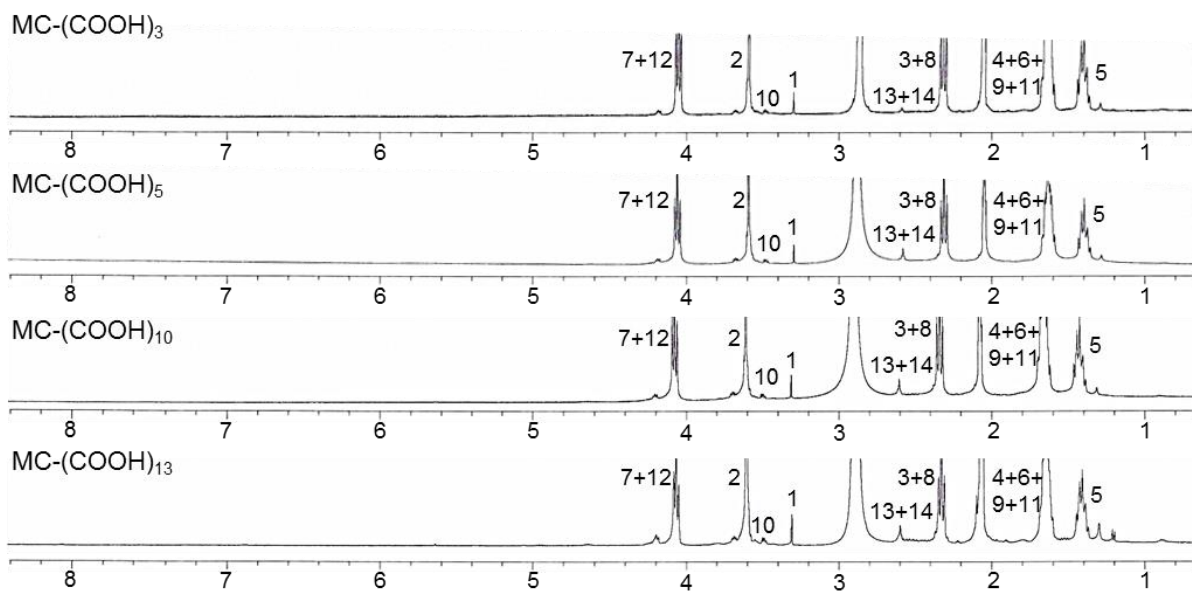
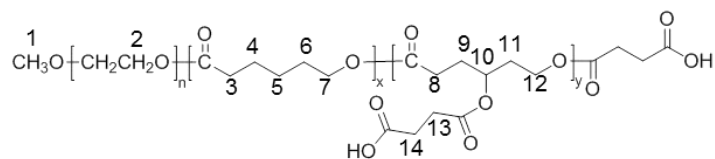
Scheme 1



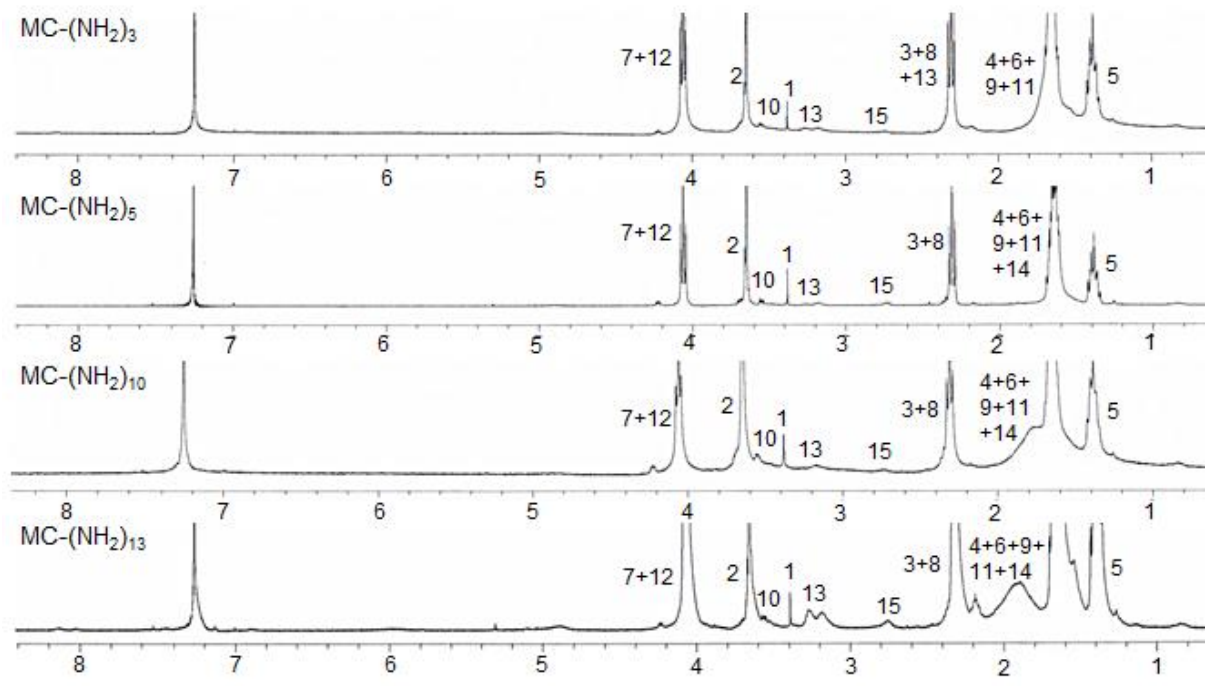
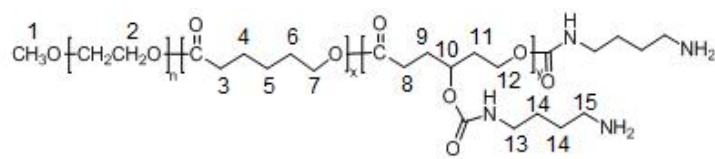
Scheme 2



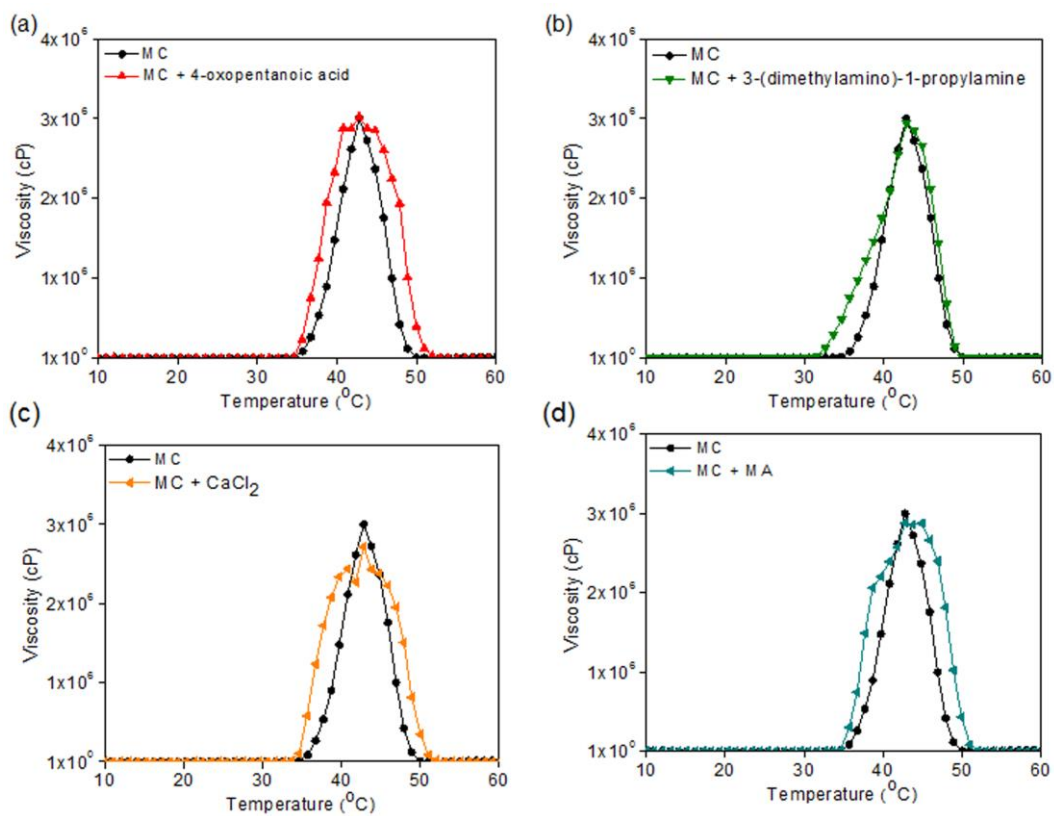
**Figure S1.** Synthesis of 4-benzyloxy- $\epsilon$ -caprolactone (fCL) (Scheme 1) and MC, MC-OBn, MC-OH, MC-COOH and MC-NH<sub>2</sub> diblock copolymers (Scheme 2).



**Figure S2.**  $^1\text{H}$  NMR spectra of  $\text{MC}-(\text{COOH})_x$  diblock copolymers with different amount of  $\text{COOH}$  pendant groups.



**Figure S3.** <sup>1</sup>H NMR spectra of MC-(NH<sub>2</sub>)<sub>x</sub> diblock copolymers with different amount of NH<sub>2</sub> pendant groups.



**Figure S4.** Viscosity-versus-temperature curves of (a) MC without and with 4-oxopentanoic acid, (b) MC without and with 3-(dimethylamino)-1-propylamine, (c) MC without and with  $\text{CaCl}_2$  and (d) MC without and with MA.

**Table S1.** Zeta potential of MC-COOH, MC-NH<sub>2</sub> and a mixture of MC-(COOH/NH<sub>2</sub>) diblock copolymer suspensions.

Polymer	Zeta potential (mV) <sup>a</sup>
MC	-4.0 ± 0.4
MC-(COOH) <sub>3</sub>	-6.1 ± 0.8
MC-(NH <sub>2</sub> ) <sub>3</sub>	6.8 ± 0.5
MC-(COOH/NH <sub>2</sub> ) <sub>3</sub> mix	0.8 ± 0.1
MC-(COOH) <sub>5</sub>	-9.4 ± 0.7
MC-(NH <sub>2</sub> ) <sub>5</sub>	7.4 ± 0.9
MC-(COOH/NH <sub>2</sub> ) <sub>5</sub> mix	-1.6 ± 0.2
MC-(COOH) <sub>10</sub>	-10.2 ± 1.1
MC-(NH <sub>2</sub> ) <sub>10</sub>	8.8 ± 0.5
MC-(COOH/NH <sub>2</sub> ) <sub>10</sub> mix	-2.0 ± 0.3
MC-(COOH) <sub>13</sub>	-12.2 ± 0.2
MC-(NH <sub>2</sub> ) <sub>13</sub>	10.6 ± 0.4
MC-(COOH/NH <sub>2</sub> ) <sub>13</sub> mix	-4.6 ± 0.2

<sup>a</sup> Determined by DLS.

**Table S2.** Zeta potential of MC-(COOH)<sub>10</sub> and MC-(COO<sup>-</sup>Na<sup>+</sup>)<sub>10</sub> without and with 0.5, 1.0 and 2.0 equivalent of CaCl<sub>2</sub>, MC-(NH<sub>2</sub>)<sub>10</sub> and MC-(NH<sub>3</sub><sup>+</sup>Cl<sup>-</sup>)<sub>10</sub> without and with 0.5, 1.0 and 2.0 equivalent of MA.

Copolymers	Suspension	Zeta potential (mV) <sup>a</sup>
MC-(COOH) <sub>10</sub>	MC-(COOH) <sub>10</sub>	-10.5 ± 1.1
	MC-(COOH) <sub>10</sub> /0.5 eq CaCl <sub>2</sub>	-10.3 ± 0.4
	MC-(COOH) <sub>10</sub> /1.0 eq CaCl <sub>2</sub>	-10.1 ± 0.5
	MC-(COOH) <sub>10</sub> /2.0 eq CaCl <sub>2</sub>	-9.8 ± 0.4
MC-(COO <sup>-</sup> Na <sup>+</sup> ) <sub>10</sub>	MC-(COO <sup>-</sup> Na <sup>+</sup> ) <sub>10</sub>	-12.7 ± 0.9
	MC-(COO <sup>-</sup> Na <sup>+</sup> ) <sub>10</sub> /0.5 eq CaCl <sub>2</sub>	-8.4 ± 0.3
	MC-(COO <sup>-</sup> Na <sup>+</sup> ) <sub>10</sub> /1.0 eq CaCl <sub>2</sub>	-6.7 ± 0.5
	MC-(COO <sup>-</sup> Na <sup>+</sup> ) <sub>10</sub> /2.0 eq CaCl <sub>2</sub>	-3.4 ± 0.6
MC-(NH <sub>2</sub> ) <sub>10</sub>	MC-(NH <sub>2</sub> ) <sub>10</sub>	8.8 ± 0.5
	MC-(NH <sub>2</sub> ) <sub>10</sub> /0.5 eq MA	8.7 ± 0.2
	MC-(NH <sub>2</sub> ) <sub>10</sub> /1.0eq MA	8.6 ± 0.3
	MC-(NH <sub>2</sub> ) <sub>10</sub> /2.0 eq MA	8.5 ± 0.3
MC-(NH <sub>3</sub> <sup>+</sup> Cl <sup>-</sup> ) <sub>10</sub>	MC-(NH <sub>3</sub> <sup>+</sup> Cl <sup>-</sup> ) <sub>10</sub>	11.3 ± 0.7
	MC-(NH <sub>3</sub> <sup>+</sup> Cl <sup>-</sup> ) <sub>10</sub> /0.5 eq MA	7.1 ± 0.5
	MC-(NH <sub>3</sub> <sup>+</sup> Cl <sup>-</sup> ) <sub>10</sub> /1.0eq MA	6.3 ± 0.3
	MC-(NH <sub>3</sub> <sup>+</sup> Cl <sup>-</sup> ) <sub>10</sub> /2.0 eq MA	5.5 ± 0.4

<sup>a</sup> Determined by DLS.

## Experimental Part

### Preparation of 1,4-cyclohexanedione monoethyleneketal (1)

All glasses were heated in a vacuum and then flushed by dry nitrogen stream. All reactions were conducted in dry nitrogen stream. 1,4-Cyclohexanedione monoethyleneketal (8 g, 51.22 mmol) was dissolved at methanol (100 mL) and placed at 0°C. Sodium borohydride (2.33 g, 61.47 mmol) was added to the solution and then stirred. After 12 h, the resulting solution was concentrated by rotary evaporation to remove methanol. Then, the reaction mixture was washed with deionized water (DW) and ethyl acetate (EA) three times. The organic phase was dried over anhydrous MgSO<sub>4</sub> and concentrated by evaporation, yielding (1) (7.2 g, 45.52 mmol, 90%) as a clear liquid. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 7.21 (*s*, 1H, -CH(Cl)-), 3.91 (*t*, 2H, -OCH<sub>2</sub>-), 3.91 (*t*, 2H, -OCH<sub>2</sub>-), 1.80 (*m*, 4H, -CH<sub>2</sub>-, -CH<sub>2</sub>-), 1.59 (*m*, 4H, -CH<sub>2</sub>).

### Preparation of 1-ethylene acetal-4-benzyloxy-cyclohexane (2)

1,4-Dioxaspiro-4.5-decan-8-ol (1) (7 g, 44.25 mmol) was dissolved at anhydrous THF (70 mL) and placed at 0°C. 60 % NaH (2.12 g, 88.50 mmol) was added to the solution and then stirred for 2 h. BnBr (5.78 mL, 33.80 mmol) in anhydrous THF (10 mL) was added to the solution at 0°C in 5 mL/min and then stirred for 24 h. The reaction solution was stopped by addition of 5 mL DW. The resulting solution was concentrated by rotary evaporation to remove THF. The reaction mixture was washed with DW and EA three times. The obtained mixture was purified by silica-gel column chromatography using a solution of *n*-hexane and EA (*v/v* = 40/10, *R<sub>f</sub>* = 0.51) as an eluent, yielding (2), (5.25 g, 21.14 mmol, 75%) of yellowish liquid. <sup>1</sup>H NMR ((CD<sub>3</sub>)<sub>2</sub>CO): 2.05 (*s*, 3H, -CH<sub>3</sub>(CO)-), 3.91 (*t*, 2H, -OCH<sub>2</sub>-), 3.91 (*t*, 2H, -OCH<sub>2</sub>-), 1.82 (*m*, 4H, -CH<sub>2</sub>-, -CH<sub>2</sub>-), 1.59 (*m*, 4H, -CH<sub>2</sub>).

### Preparation of 4-benzyloxy-cyclohexanone (3)

1-Ethylene acetal-4-benzyloxy-cyclohexane (**2**) (5.3 g, 20.14 mmol) was dissolved at anhydrous THF (40 mL) and placed at room temperature. 18 mL of 4 N aqueous HCl was added to the solution and then stirred for 12 h. The reaction solution was neutralized by sodium bicarbonate solution. The resulting solution was concentrated by rotary evaporation to remove THF. The reaction mixture was washed with DW and EA three times. The organic phase was dried over anhydrous MgSO<sub>4</sub> and concentrated by evaporation, yielding (**3**) (5.04 g, 24.67 mmol, 85%) as a yellowish viscous liquid. <sup>1</sup>H NMR ((CD<sub>3</sub>)<sub>2</sub>CO): 2.05 (*s*, 3H, -CH<sub>3</sub>(CO)-), 4.61 (*t*, 2H, -OCH<sub>2</sub>-), 3.82 (*m*, 1H, -OCH-), 2.61 (*m*, 4H, -CH<sub>2</sub>-, -CH<sub>2</sub>-), 2.10 (*m*, 4H, -CH<sub>2</sub>).

#### **Preparation of 4-benzyloxy- $\epsilon$ -caprolactone (CL-OBn, **4**)**

mCPBA (7.27 g, 42.10 mmol) was dissolved at anhydrous CH<sub>2</sub>Cl<sub>2</sub> (40 mL) and placed at room temperature. 4-Benzyloxy-cyclohexanone (4.3 g, 21.05 mmol) was added to the solution and then stirred for 24 h. The reaction solution was filtered by celite filter. The resulting solution was concentrated by rotary evaporation to remove CH<sub>2</sub>Cl<sub>2</sub>. The reaction mixture was washed with DW and sodium bicarbonate solution three times. The organic phase was dried over anhydrous MgSO<sub>4</sub> and concentrated by evaporation. The obtained mixture was purified by silica-gel column chromatography using a solution of *n*-hexane and EA (v/v = 40/10, R<sub>f</sub> = 0.13) as an eluent, yielding (**4**, CL-OBn), (2.88 g, 13.08 mmol, 67%) of clear liquid. <sup>1</sup>H NMR ((CD<sub>3</sub>)<sub>2</sub>CO): 2.05 (*s*, 3H, -CH<sub>3</sub>(CO)-), 2.53 (*t*, 2H, -OCH<sub>2</sub>-), 3.69 (*m*, 1H, -OCH-), 3.01, 2.41 (*t*, 2H, -CH<sub>2</sub>(CO)-), 2.00 (*m*, 4H, -CH<sub>2</sub>-, -CH<sub>2</sub>-). Anal. Calcd. for C<sub>13</sub>H<sub>16</sub>O<sub>3</sub>, C: 70.89, H: 7.32. Found: C: 70.36, H: 7.32.

#### **Synthesis of MPEG-*b*-PCL diblock copolymer (MC)**

MC diblock copolymers with PCL molecular weights (2,391 g/mol) using MPEG (750



g/mol) were prepared via a previously reported block copolymerization method.<sup>6</sup>

### **Synthesis of MPEG-*b*-[poly( $\epsilon$ -caprolactone)-*ran*-poly(4-benzyloxy- $\epsilon$ -caprolactone)] (MC-OBn)**

All glasses were heated in a vacuum and dried via flushing with dry nitrogen stream. We used a the typical polymerization process for producing MC-(OBn)<sub>10</sub> with a CL/fCL ratio of 90/10 using MPEG (750 g/mol) as an initiator, as follows. (3.13 g, 4.17 mmol) and toluene (30 mL) were added into a flask. Azeotropic distillation was performed to remove water from the MPEG and toluene. Under dry nitrogen stream, then toluene was removed via distillation. CH<sub>2</sub>Cl<sub>2</sub> (30 mL) were introduced to the MPEG with CL (8.23 g, 72.14 mmol) and CL-OBn (1.77 g, 8.02 mmol), followed by the addition of a 1.0 M solution of HCl in diethyl ether (8.33 mL, 0.23 mol) at room temperature. After 24 h, the mixture was poured into a mixture of *n*-hexane and EA (v/v = 40/10) to precipitate a copolymer. The precipitated copolymers were obtained from the supernatant by decantation, dissolved in CH<sub>2</sub>Cl<sub>2</sub>, and then filtered. The resulting copolymer solution was concentrated by rotary evaporation and dried in a vacuum, yielding a colorless copolymer. In the same way, MC-(OBn)<sub>3</sub>, MC-(OBn)<sub>5</sub>, and MC-(OBn)<sub>13</sub>, were prepared. The molecular weights and ratios of the MC-OBn segments in the copolymers were determined by comparing the intensity of the phenyl protons at  $\delta = 7.2$ -7.4 ppm.

### **Synthesis of MPEG-*b*-[poly( $\epsilon$ -caprolactone)-*ran*-poly(4-hydroxyl- $\epsilon$ -caprolactone)] (MC-OH)**

MC-(OBn)<sub>10</sub> (9.3 g, 3.9 mmol) was dissolved at anhydrous THF (150 mL). 10% w/w (4.5 g) of Pd/C (Palladium, 10 wt% (wet basis) on activated carbon (50% water w/w, Degussa type E101 NE/W)) was added to the MC-(OBn)<sub>10</sub> solution at room temperature under

nitrogen, and the mixture was stirred under a hydrogen atmosphere for 5 h. The reaction solution was filtered by celite filter. The organic phase was concentrated using a rotary evaporator and dried in vacuum to obtain a colorless copolymer.