

Supplementary Information

Characterization of Molecular Association of Poly(2-oxazoline)s-based Micelles with Various Epoxides and Diols via the Flory-Huggins Theory: A Molecular Dynamics Simulation Approach

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1. General

1.1 Materials

All reagents were purchased from standard suppliers and used as received unless otherwise stated. 2-Methyl-2-oxazoline, acetonitrile and chlorobenzene were distilled over CaH_2 and stored under dry argon and molecular sieves (4 Å). Methyltriflate was distilled over barium oxide and stored under dry argon at 4 °C. Dichloromethane was dried by passing through columns of activated alumina. Flash column chromatography was performed using silica gel 60 Å (230-400 mesh) from Sorbent Technologies. Methyl 3-(oxazol-2-yl)propionate (EsterOx, monomer C) was synthesized based on adapted literature procedures.^[1]

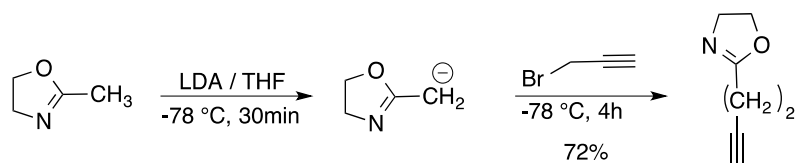
1.2 Measurements

^1H NMR and ^{13}C NMR spectra were recorded at 25 °C on a Bruker AC 600 MHz / 400 MHz spectrometer. All chemical shifts are reported in parts per million (ppm) with reference to solvent residual peaks. Gel-permeation chromatography (GPC) was carried out using a Shimadzu pump coupled to a Shimadzu RI detector. A 0.03 M LiCl solution in *N,N*-dimethylformamide was used as eluent at a flow rate of 1 mL/min at 60 °C. A set of Polymer Standards columns (AM GPC gel, 10 µm, precolumn, 500 Å and linear mixed bed) was used. M_w^{app} , M_n^{app} , and D represent the apparent weight-average molecular weight, apparent number-average molecular weight, and dispersity index, respectively. Commercially available poly(styrene) standards were used for calibration. Hydrodynamic diameters of the cross-linked and uncross-linked micelles were determined at 25 °C by dynamic light scattering (DLS) using a Protein Solution DynaPro

instrument with a 663 nm laser module. SEM images were recorded on Carl Zeiss Merlin[®] Field Emission-Scanning Electron Microscope (FE-SEM). The accelerating voltage was 2 kv and the working distance was 3.9 mm. The SEM samples were prepared by depositing the sample methanol solution onto a piranha solution processed silicon wafer, followed by vacuum drying at room temperature. The particle size was measured by Zeiss FE-SEM built-in program SmartSEM User Interface.

2 Preparation

2.1 Monomer synthesis



Monomer B 2-(but-3-yn-1-yl)-4,5-dihydrooxazole: Prepare LDA in situ. Diisopropylamine (1.67 ml, 11.8 mmol) was dissolved in 20 ml THF. The reaction was cooled down to -78 °C and 2.5M *n*-butyllithium in Hexanes (4.724 ml, 11.8 mmol) was added. The reaction was stirred for five minutes at -78 °C followed by an ice-bath for another 15 minutes. The mixture was cooled back down to -78 °C and stirred for five minutes. Then 2-methyl-2-oxazoline (1.00 mL, 11.8 mmol) was added.^[2] At -78 °C, the reaction was stirred for 30 minutes to generate the oxazoline anion. 80 wt% Propargylbromide in toluene (1.335 mL, 1.05 eq) was added and the mixture stirred at room temperature for 2.5 hours. The product was extracted with 20 mL water and 20 mL ethyl ether three times. The organic layer was dried with magnesium sulfate. After removal of the solvent, the residue was purified via silica gel column chromatography using ethyl acetate/CH₂Cl₂ (200/100). The yield was 78% which is a significant

improvement to previously reported methodologies.^[3] ^1H NMR (CDCl_3 , 400 MHz, δ_{ppm} vs. TMS): 4.17 (t, $J = 9.50$ Hz, 2H), 3.78 (t, $J = 9.44$ Hz, 2H), 2.45 (m, 4H), 1.93 (s, 3 ppm 1H). ^{13}C NMR (CDCl_3 , 100 MHz, δ_{ppm} vs. TMS): 167.7, 136.7, 115.1, 54.1, 29.7, and 27.1. MS (ESI): m/z calculated for $\text{C}_7\text{H}_9\text{NO}$, 123.15; found, 124.15 ($\text{M}+\text{H}^+$).

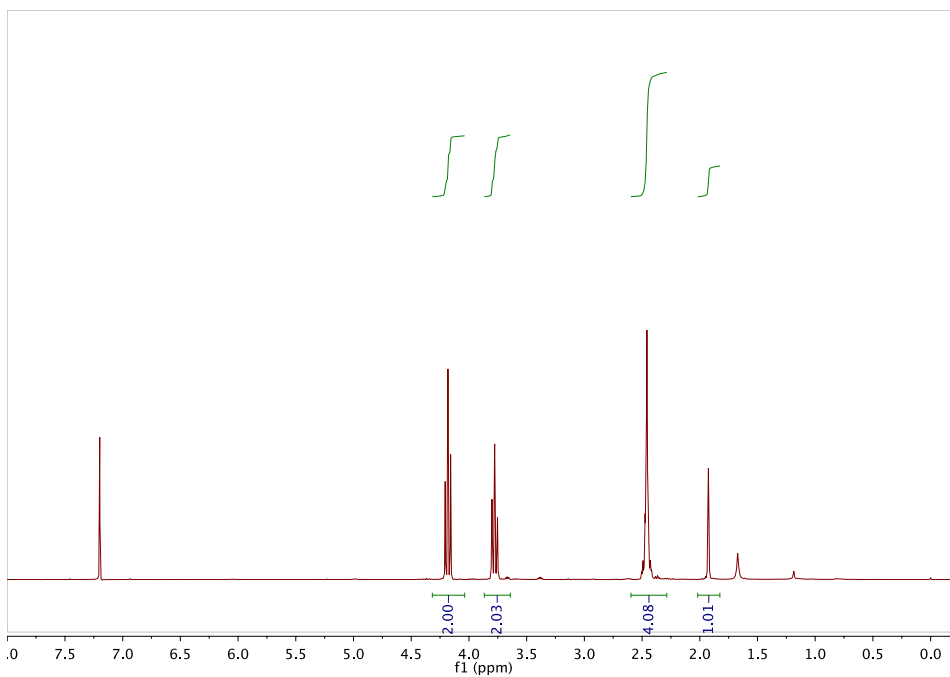


Figure S1 ^1H NMR spectrum of monomer **B**.

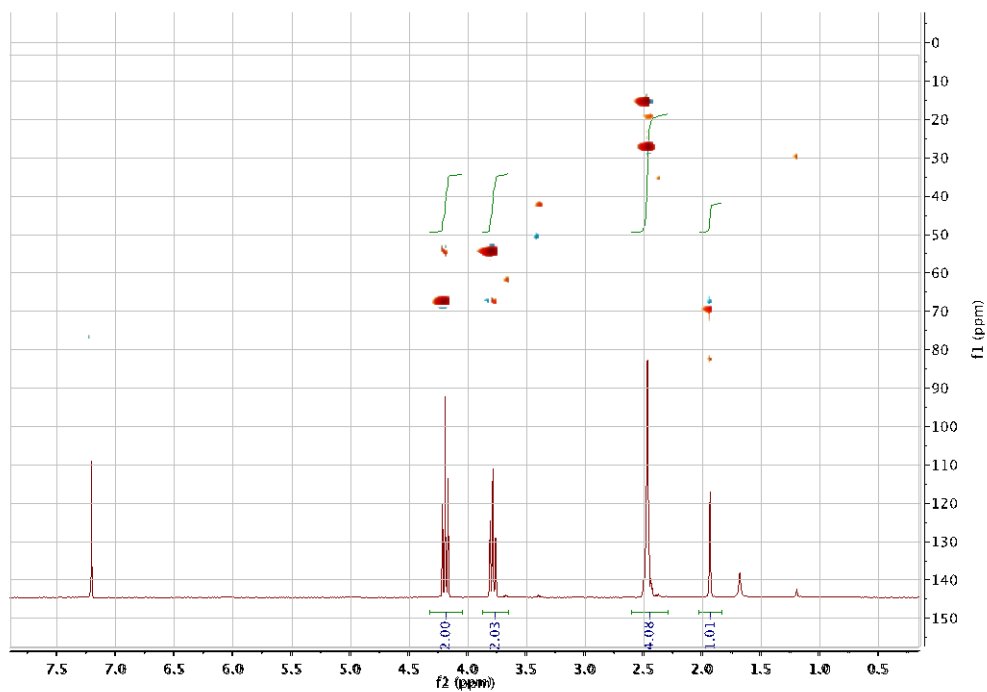


Figure S2. HSQC NMR spectrum of monomer **B**.

2.2 Polymer precursor

Polymer 1: A typical procedure for the cationic ring-opening polymerization was as follow: Methyltriflate (28.29 μL , 0.25 mmol) was added to a solution of monomer **C** EsterOx (0.39 mL, 2.5 mmol) in chlorobenzene (1 mL) and acetonitrile (1 mL). The mixture was stirred for 24 hours at 70 $^{\circ}\text{C}$. The polymerization was monitored via ^1H NMR spectroscopy. After monomer **C** was completely consumed, monomer **B** AlkyneOx (308 mg, 2.5 mmol) and chlorobenzene (1 mL) was added to the polymer solution under an argon atmosphere. The mixture was stirred for eight hours at 70 $^{\circ}\text{C}$. After monomer **B** was fully consumed, monomer **A** MeOx (1.92 mL, 22.5 mmol) and acetonitrile (2 mL) were added. The solution was stirred at 70 $^{\circ}\text{C}$ for an additional 36 hours. After monomer **A** was fully consumed, the polymerization was terminated via the addition of water (50 μL , 0.5 mmol) and stirred at room temperature for four hours. The polymer was purified

by dialysis against DCM and isolated by freeze-drying from dioxane. The repeat units for **A** MeOx ($a=62.1$), **B** AlkyneOx ($b=6.7$), and **C** EsterOx ($c=8.3$) were determined by ^1H NMR spectroscopy end group analysis according to the methyl group from Methyltriflate at 3 ppm (Fig. S3).

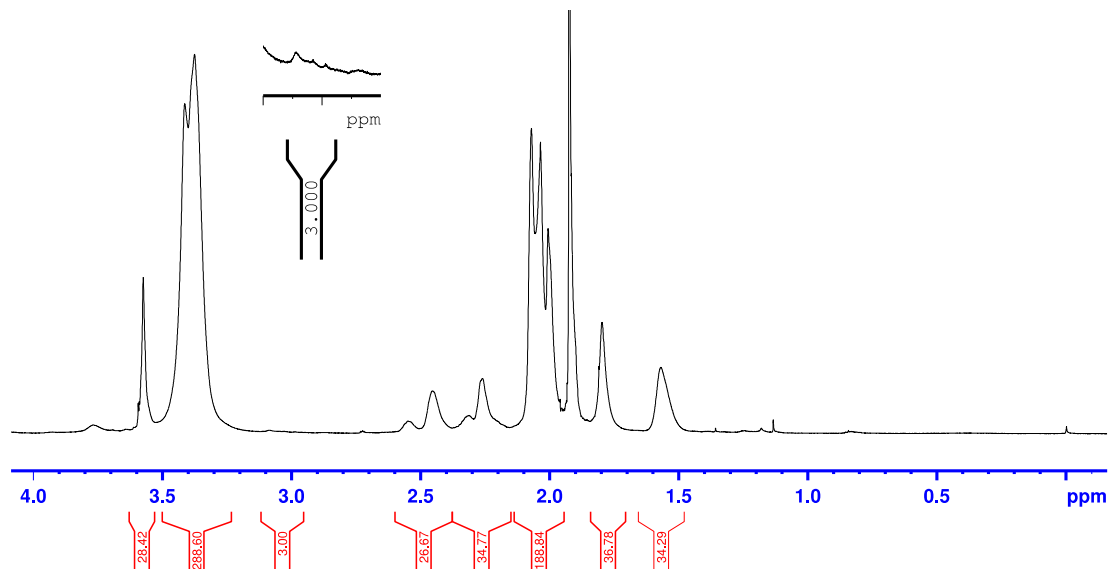


Figure S3. ^1H NMR spectrum of triblock copolymer **2** in CDCl_3 .

The molecular weight distributions were determined by GPC using DMF as the eluent:

$M_n^{\text{app}} = 7,700$ g/mol, $D = 1.22$ (Figure S4).

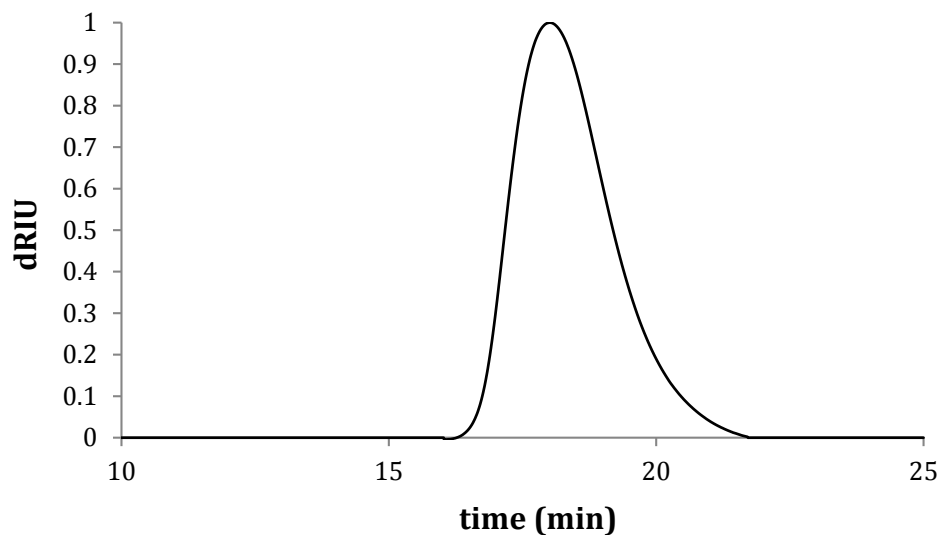


Figure S4. Normalized gel-permeation chromatogram of triblock copolymer **1**.

Polymer 2: Triblock copolymer **1** (200 mg) was dissolved in 20 mL methanol. Then, 20 mL of a 0.1 M LiOH solution was added. The mixture was stirred at 50 °C overnight. The solvent was removed under reduced pressure and the residue was redissolved in ten mL of water. The solution was cooled to 0 °C and neutralized with 0.1 M HCl. The polymer was purified by dialysis against water and dried by lyophilization.

Micelle supported salen (Polymer 3): Polymer **2** (carboxylic group 1 eq, 200 mg) was dissolved in DMF (1 mg/mL). Hydroxyl-functionalized salen (1.2 eq, 176 mg), PyBrOP (1.4 eq, 189 mg) and DIPEA (3 eq, 150 ul) were added to the micelle solution. The mixture was stirred at room temperature for 24 hours, purified by dialysis and dried by lyophilization. The degree of salen functionalization was determined by MALDI-TOF (Figure. S5). The peak shift indicated the attachment of four salen ligands to the hydrophobic block of polymer **2**.

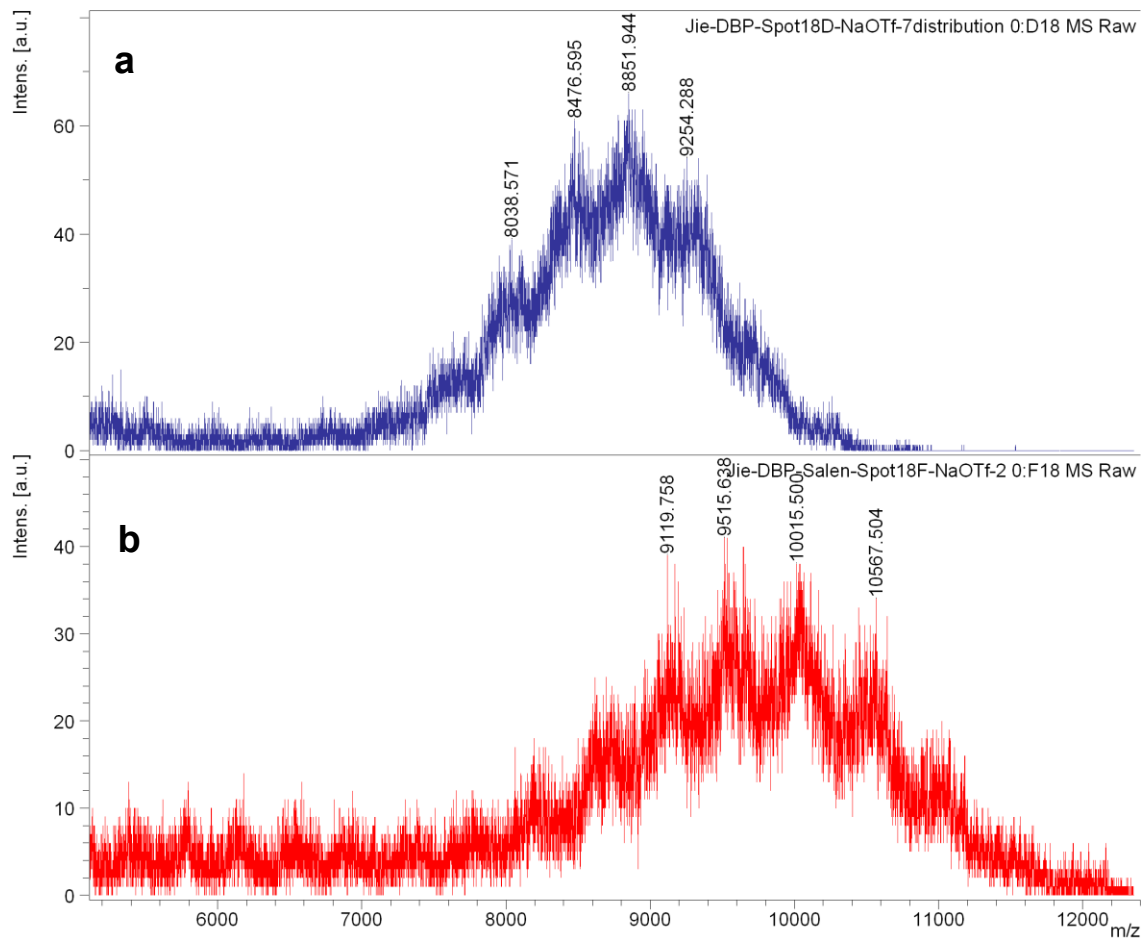


Figure S5. MALDI-TOF mass spectrum of polymer **2** (a) and polymer **3** (b).

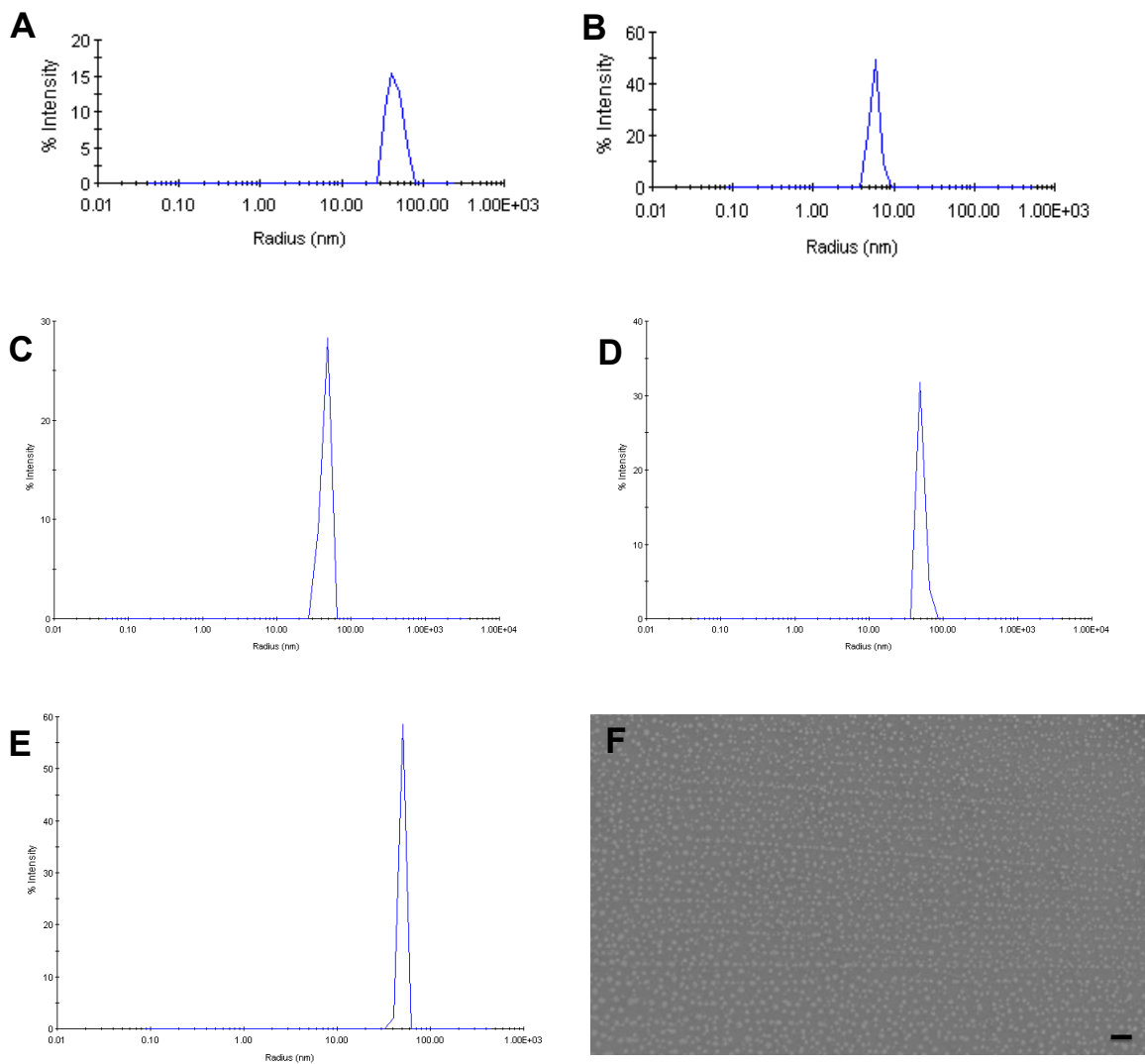
2.3 Shell Crosslinked micelle supported Co-salen`

Micelle formation and cross-linking (micelle 4): The amphiphilic triblock copolymer was dissolved in water with a concentration of 1 mg/mL. The crosslinking reagent 1,5-pentanedithiol (0.6 eq) was added to the micelle solution and the mixture was stirred at room temperature for two hours. The reaction was degassed via three freeze-pump-thaw cycles. The thiol-yne reaction was initiated by DMPA (0.1 eq) and irradiation with UV light (15W UVP Black Ray UV Bench Lamp XX-15L) while stirring for 24 hours at 4 °C. The reaction mixture was purified by dialysis and dried by lyophilization.

Cobalt Metallation (Nanoreactor 5): Crosslinked micelle **4** (1 eq based on salen ligand, 0.5 mmol) was transferred into a glovebox and dissolved in dry CH₃OH (0.5 mg/mL). Cobalt acetate tetrahydrate in dry methanol solution (2 eq, 0.1 M) was added to the micelle solution. The mixture was stirred at room temperature for 48 hours in the glovebox and then stirred in air for five hours. The color of the solution turned to dark brown indicating the formation of the oxidized Co(III)-salen complex. The excess cobalt salt was removed by passing the micelle solution through a celite plug. The cobalt content determined by ICP-MS was 1.3%.

Dynamic light scattering and SEM analysis

The micelle formation and crosslinking were confirmed by DLS analysis. The hydrodynamic radii of micelle assemblies were around 45 nm in water (Figure S6 A). Before the covalent crosslinking, the micelle assemblies fell apart in non-selective solvents such as DMF as confirmed by the measured hydrodynamic radius of 5.7 nm (Figure S6 B). After crosslinking, the micelle assemblies survived in both selective (Figure S6 C) and non-selective solvents (Figure S6 D). The morphology of the SCM-based nanoreactor **5** was investigated by DLS and SEM. As shown in Figures S6 E and F, the hydrodynamic radius of **5**, determined by DLS, was 47 ± 5 nm, consistent with the radius of 50 ± 10 nm obtained by SEM.



DLS/SEM	Block copolymer	Solvent	Size (nm)
A	Polymer 3	water	45 ± 3
B	Polymer 3	dimethylformamide	5.7 ± 0.8
C	Micelle 4	water	49 ± 5
D	Micelle 4	dimethylformamide	50 ± 6
E	Nanoreactor 5	water	47 ± 5
F	Nanoreactor 5	-	50 ± 10

Figure S6. DLS results (A-E) and SEM image (F) of the micelle supported catalyst (scale bar: 300 nm).

References:

- [1] M. T. Zarka, O. Nuyken, R. Weberskirch, *Chem. Eur. J* **2003**, 9, 3228-3234.
- [2] R. D. Puts, D. Y. Sogah, *Tetrahedron Lett.* **1994**, 35, 5779-5782.
- [3] N. ten Brummelhuis, H. Schlaad, *Polym. Chem.* **2011**, 2, 1180-1184.