Electronic Supplementary Material (ESI) for Reaction Chemistry & Engineering.

Supporting Information

Synthesis of Polymeric Nano-Objects of Various Morphologies Based on Block Copolymer Self-Assembly Using Microporous Membranes

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EXPERIMENTAL SECTION

Materials

Oligo(ethylene glycol) methyl ether acrylate (OEG-A, Mw = 480 g/mol, 99%, Sigma-Aldrich) was used as received. Styrene (St, >98%, Aldrich) was filtered through basic alumina to remove inhibitor. The initiator, 2,2'-azobisisobutyronitrile (AIBN, Aldrich) was purified by recrystallization from methanol. 3-(benzylsulfanyl-thiocarbonylsulfanyl) propionic acid (BSTP) was prepared according to a procedure described elsewhere.[1] High purity N_2 was used for reaction solution purging.

Instrumentation

All ^{1}H NMR spectra were recorded using a Bruker 300MHz spectrometer. The chemicals shifts are reported in ppm (δ) relative to tetramethylsilane, referenced to the chemical shift of residual solvent resonances.

The molecular weight and polydispersity of the prepared polymers were measured by SEC. The eluent was DMAc (that contained 0.03% w/v LiBr and 0.05% w/v 2,6-dibutyl-4-methylphenol (BHT)) at 50 °C (flow rate of 1 mL/min) with a Shimadzu modular system comprising an SIL-10AD auto injector, a Polymer Laboratories 5.0 µm bead-size guard column (50 x 7.5 mm^2) followed by four linear PL (Styragel) columns (105, 104, 103, and 500 Å) and an RID-10A differential refractive-index detector.

The size and morphologies of the self-assembled block copolymers were observed using transmission electron microscopy JOEL 1400 TEM at an accelerating voltage of 100 kV. The solution of the self-assembled block copolymers was directly taken and deposited onto copper grid (ProSciTech).

DLS measurements were performed using a Malvern Zetasizer Nano Series running DTS software and using a 4 mW He-Ne laser operating at wavelength of 663 nm and an avalanche photodiode (APD) detector. The scattered light was detected at an angle 173°.

Preparation of poly[oligo(ethyleneglycol) acrylate] (POEGA) macro-CTA via RAFT polymerization

POEGA with 17 repeating unit was synthesized by RAFT polymerization with a feed molar ratio of OEGA : CTA : AIBN = 1 : 21 : 0.1. The number of repeating units was calculated from ^{1}H-NMR of the purified polymer sample by comparing the RAFT agent aromatic protons between 7.9-7.4 ppm to methylene protons adjacent to the ester linkage at 4.1 ppm. Based on this protocol, 10 gram (0.02 mol) OEGA, 0.2375 gram (9.92×10^{-4} mol) 3-(benzylsulfanyl-thiocarbonylsulfanyl) propionic acid BSTP as RAFT agent, 1.63×10^{-2} gram (9.92×10^{-5} mol), and 36 mL acetonitrile were mixed in a 100 mL round bottom flask and sealed with rubber septum. The reaction mixture was saturated with continuous nitrogen flow for 30 min in ice bath. The polymerization was carried out for 6 h at 70 °C. After 6 h, the reaction mixture was cooled rapidly and precipitated in diethyl ether. POEGA macro-CTAs molecular weight was determined by size exclusion chromatography (SEC). Mn_{SEC} (DMAc as mobile solvent and PSt standards) of 8400 gram/mol, PDI = 1.10. Purified POEGA was then used as macro-CTA for further block copolymer synthesis with styrene.

POEGA-*b*-PSt copolymer synthesis via RAFT polymerization

POEGA-*b*-PSt copolymer was synthesized by RAFT polymerization. For this purpose, POEGA (0.1 gram, 1.25×10^{-5} mol), Styrene (6.5 gram, 6.25×10^{-2} mol), and AIBN (2×10^{-4} gram, 1.25×10^{-6} mol) were dissolved in acetonitrile. The solution mixture was divided equally into 5 vials and gently purged with nitrogen for 20 min in an ice bath and sealed rapidly. The reaction mixtures were then immersed in an oil bath at 70 °C, and vials were taken out at specific time points: 1, 3, 5, 12, and 24 h. The polymerization was terminated by placing the reaction mixture into an ice bath for 5 min and then exposure to air. The polymers were precipitated by pouring the polymer solution into an excess of hexane while stirring. The obtained results are collected in Table S1.

Self-Assembly of Block Copolymer using SPG membrane emulsification

The self-assembly process was carried out using SPG membrane emulsification. Hydrophilic SPG membranes with the pore size of 0.2, 0.3, 0.8, 2.1, and 5.2 µm (External Pressure Micro kit MG-20; Membrane thickness: 0.4 – 1 mm; 10 mm outer diameter; 20 mm length; SPG Technology Co. Ltd Japan) were used to effect the self-assembly process. Block copolymer (55 mg) was dissolved in 5 ml THF. After filling the SPG tank with block copolymer solution (to be passed through the membrane pores into water), the pressure valve was opened and nitrogen gas flowed at certain pressure level into the tank. The block copolymer solution permeated into the water (50 ml) that was continuously stirred at 160 rpm. In different length of time and transmembrane pressure, the self-assembly process occurred, identified by the solution colour transition from transparent/clear to cloudy and finally turning milky white (figure S8). The time required to complete the self-assembly process was estimated by using a balance (to measure the mass) placed under the stirrer.

Self-Assembly of Block Copolymer using Eisenberg approach (Method i)

Block copolymer POEGA$_{17}$-*b*-PSt$_{290}$ (1.8 mg) was dissolved in THF (2 ml), which is a good solvent for both the hydrophobic and hydrophilic blocks. Distilled water (15-40 %w/w in THF) was added dropwise (10 µL per minute) to 2 ml of copolymer solution in THF (0.9 mg/mL) under 160 rpm stirring at room temperature. The mixture was then dialyzed against water to remove THF. The resultant aggregates morphology was observed by TEM.

Self-Assembly of Block Copolymer using Eisenberg approach-*reverse way* (Method ii)

Block copolymer POEGA$_{17}$-*b*-PSt$_{290}$ (10.8 mg) was dissolved in THF (1 ml), and then added dropwise into distilled water (10 ml) stirred at 160 rpm. The drop size was varied by increasing the flow rate of block copolymer solutions from 10 to 80 µL per minute. The mixture was then dialyzed against water to remove THF. The resultant aggregates morphology was observed using TEM.

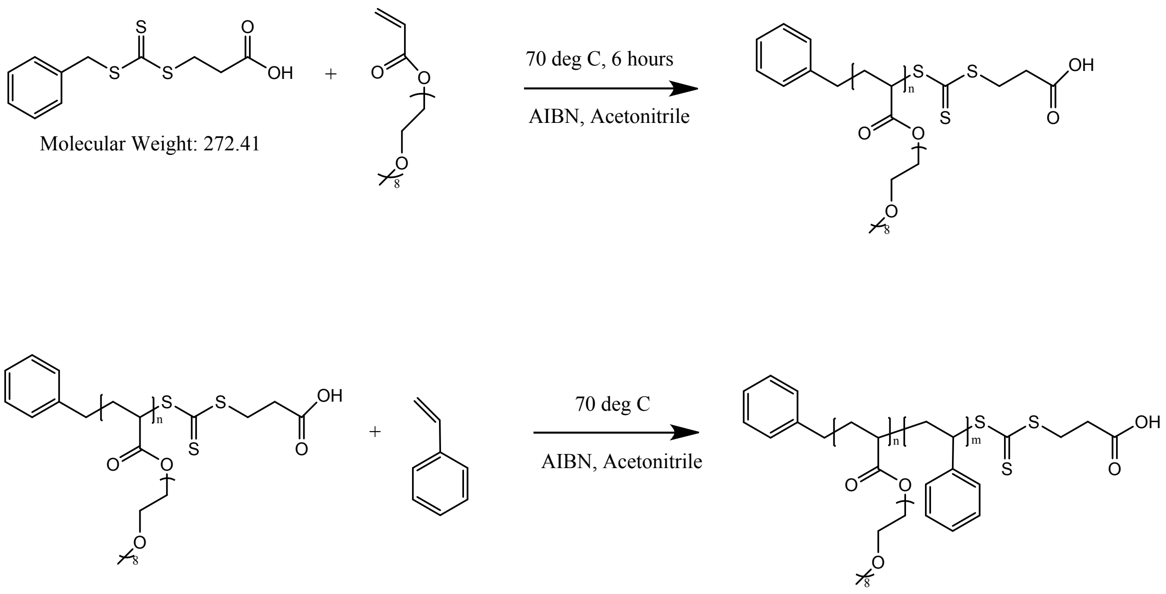
Table S1. Summary of the RAFT block polymerization to produce POEGA-$_b$-styrene.

Time (h)	Conversion (%)[a]	$M_{n,\,NMR}$ (g/mol)[b]	$M_{n,\,SEC}$ (g/mol)[c]	PDI
1	3.5	26200	19800	1.49
3	4.7	32400	23500	1.52
5	6.8	43400	27900	1.54
12	11.5	67800	37200	1.53
24	12.41	70490	38500	1.61

[a] Styrene conversion was calculated from ^{1}H-NMR spectrum of the reaction mixture by dividing of the polystyrene's aromatic protons peak integral with the sum of vinyl peaks (6.05 and 5.5 ppm) of styrene and polystyrene's aromatic protons peak integrals.

[b] NMR molecular weight was calculated according to $Mn = ([M]_o / [RAFT]_o) * x * Mw_{monomer} + Mw_{RAFT}$, where $[M]_o$, $[RAFT]_o$, x, $Mw_{monomer}$, Mw_{RAFT} are monomer RAFT agent concentration, monomer conversion molecular weight of monomer and RAFT agent, respectively.

[c] The experimental Mn and PDI were determined by SEC using dimethyl acetamide as eluent solvent with polystyrene standarts (the molecular weight ranging from 168 to 10^6 gmol^{-1}).



Scheme S1. POEGA-*b*-PSt block copolymer synthesis by RAFT polymerization.

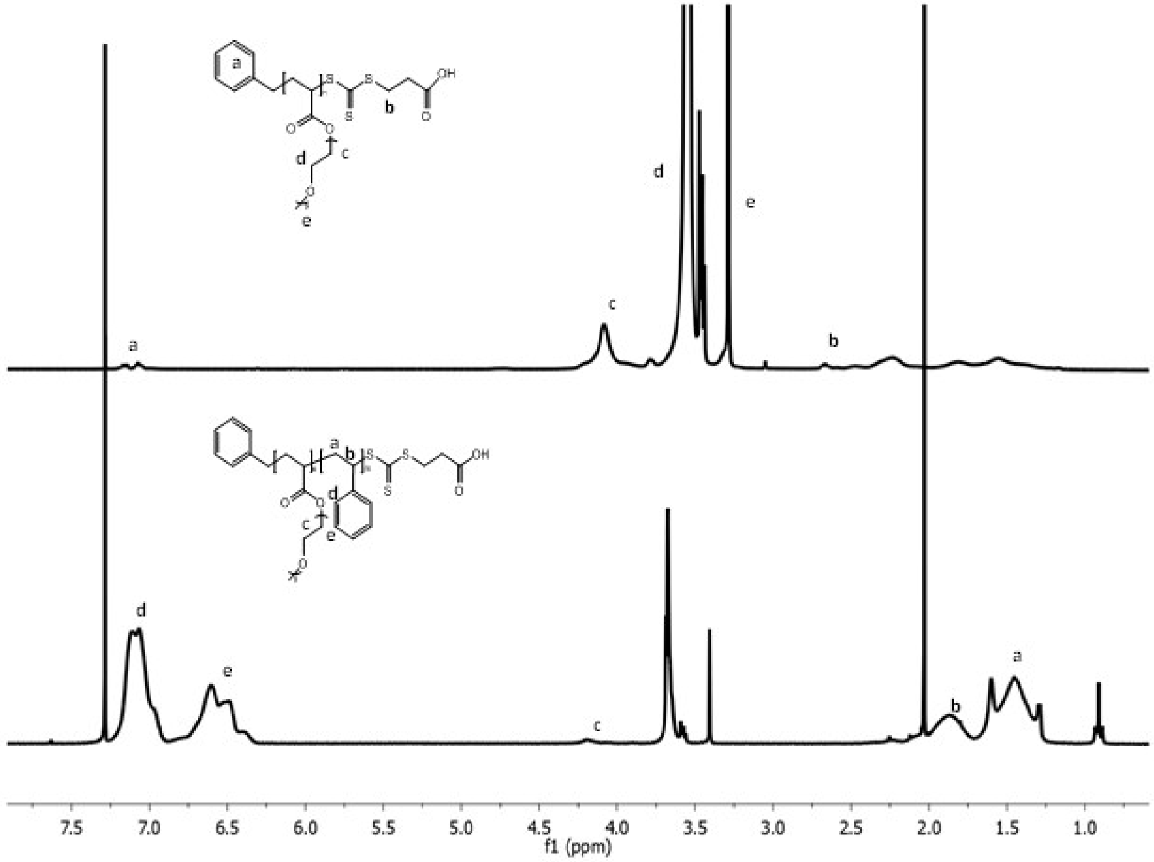
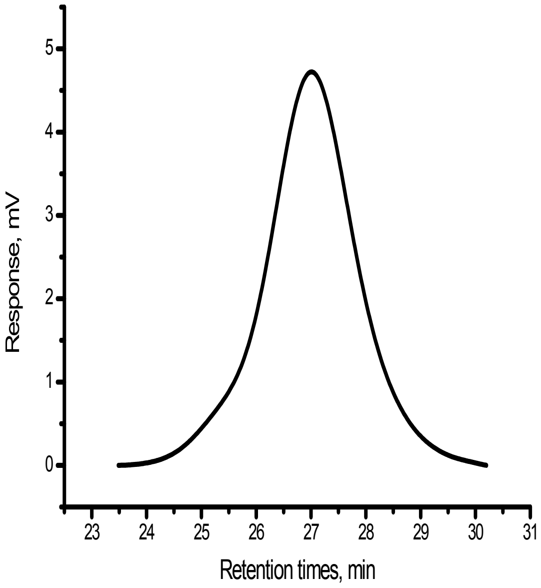


Figure S1. ^{1}H NMR spectra of POEGA$_{17}$ and POEGA$_{17}$-*b*-PSt$_{290}$ block copolymer obtained via RAFT polymerization recorded in CDCl$_3$ at 20 °C



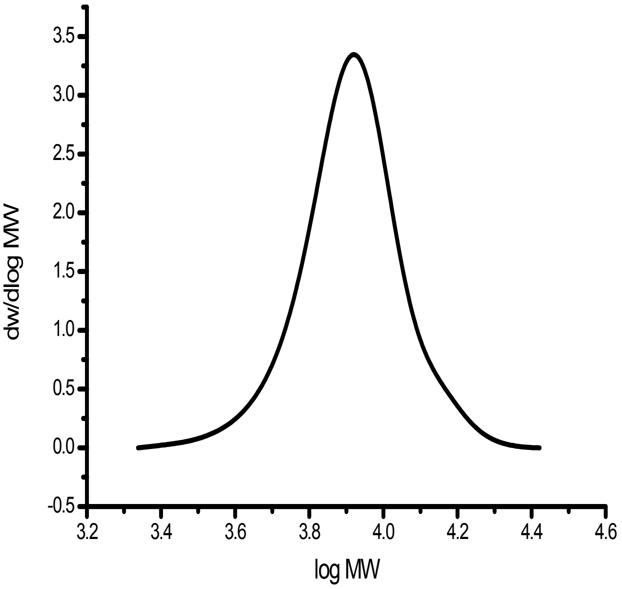


Figure S2. Molecular weight distributions (SEC) of POEGA$_{17}$.

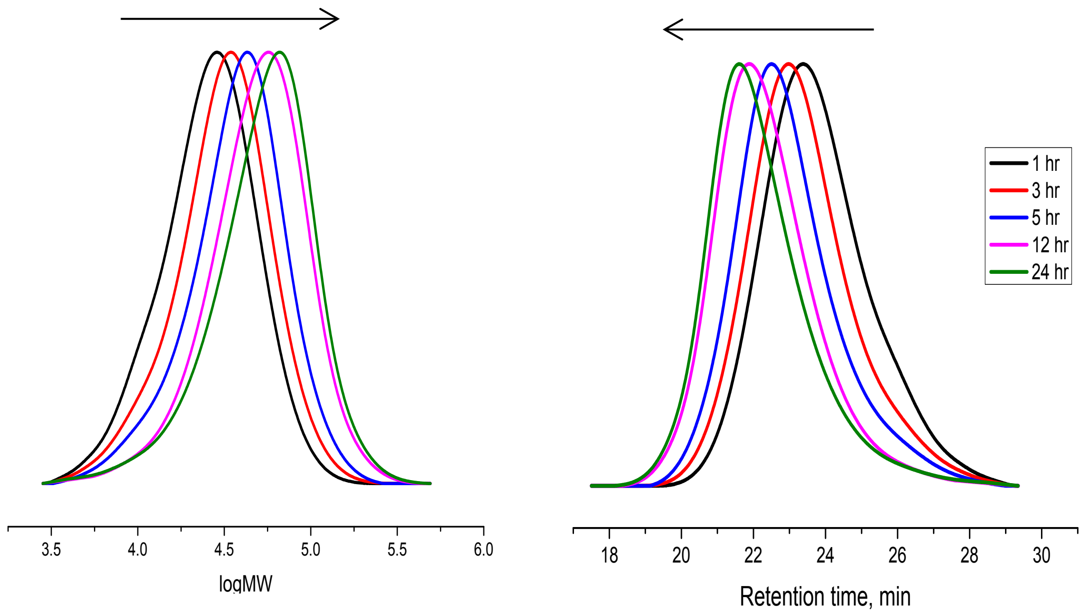


Figure S3. SEC traces of block copolymer obtained from RAFT polymerization (POEGA$_{17}$-*b*-PSt$_{290}$).

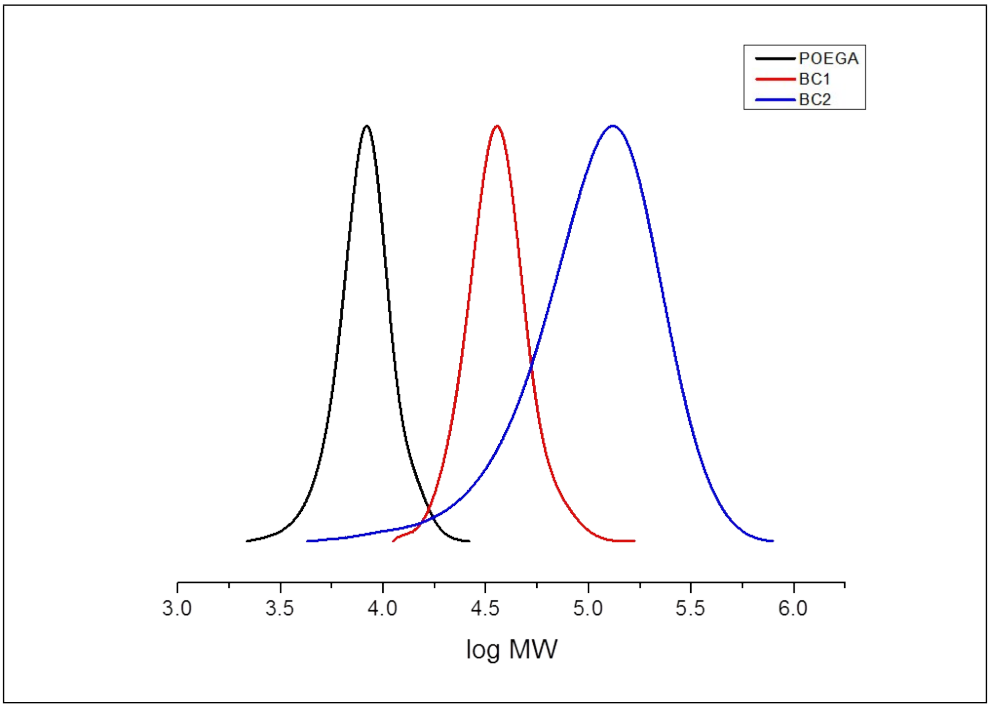


Figure S4. SEC molecular weight distributions of POEGA, POEGA$_{17}$-*b*-PS$_{160}$ (BC1), and POEGA$_{17}$-*b*-PS$_{290}$ (BC2).

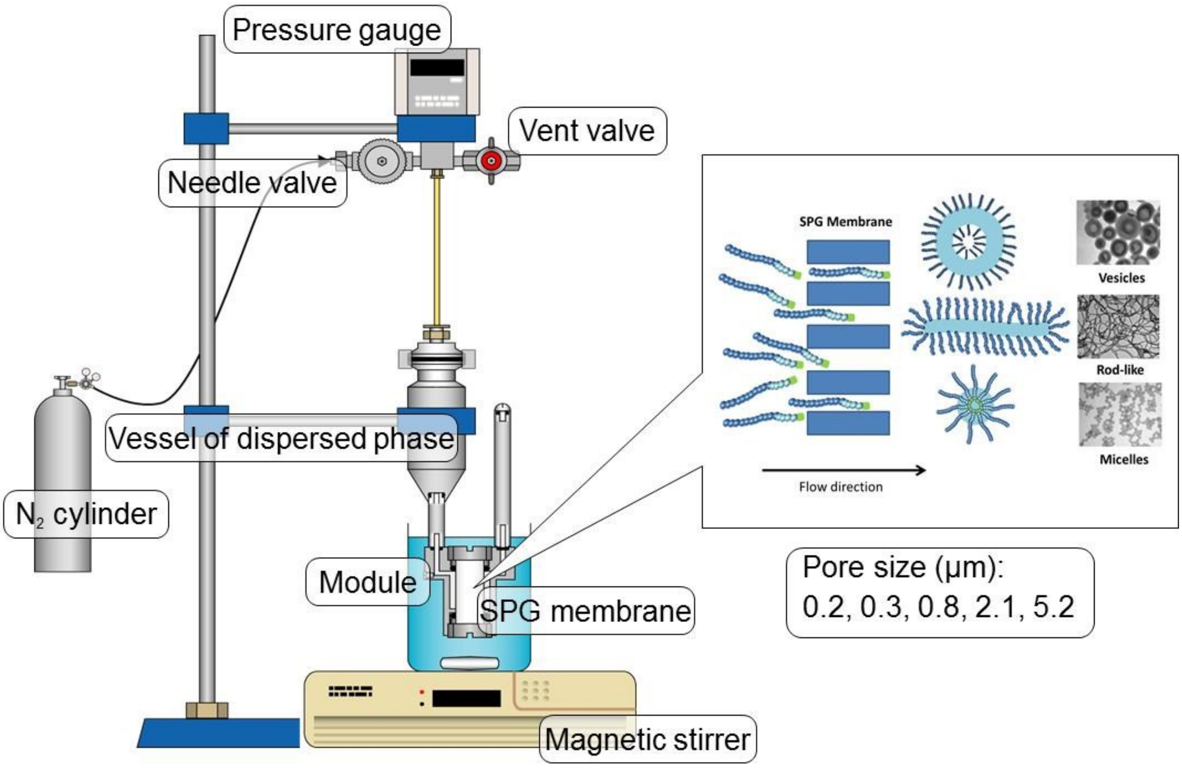


Figure S5. Schematic diagram of experimental set-up for SPG membrane emulsification.

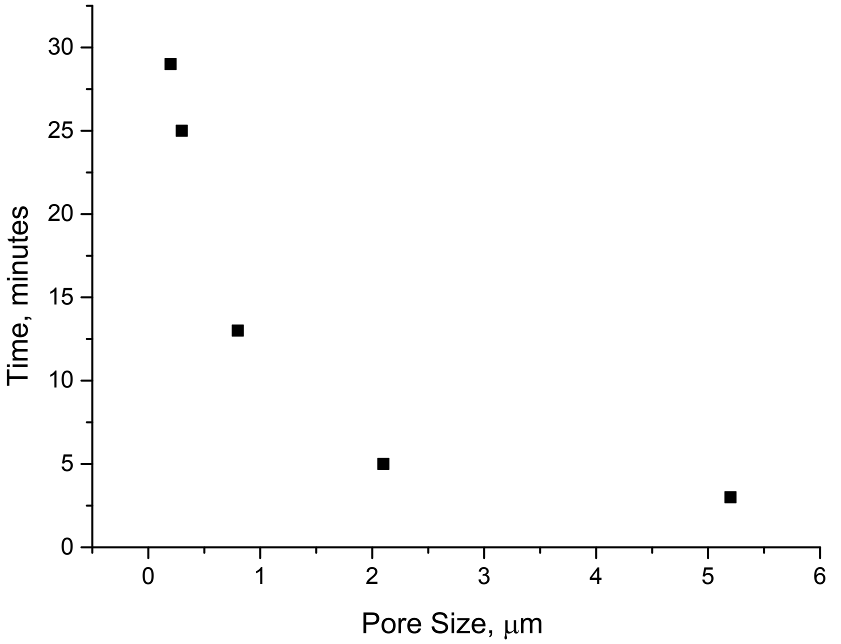


Figure S6. Pore size membrane vs time plot for self-assembly of block copolymer POEGA$_{17}$-*b*-PSt$_{160}$. Increasing membrane pore size increases the flowrate of block copolymer solution through a membrane and decreases the time needed.

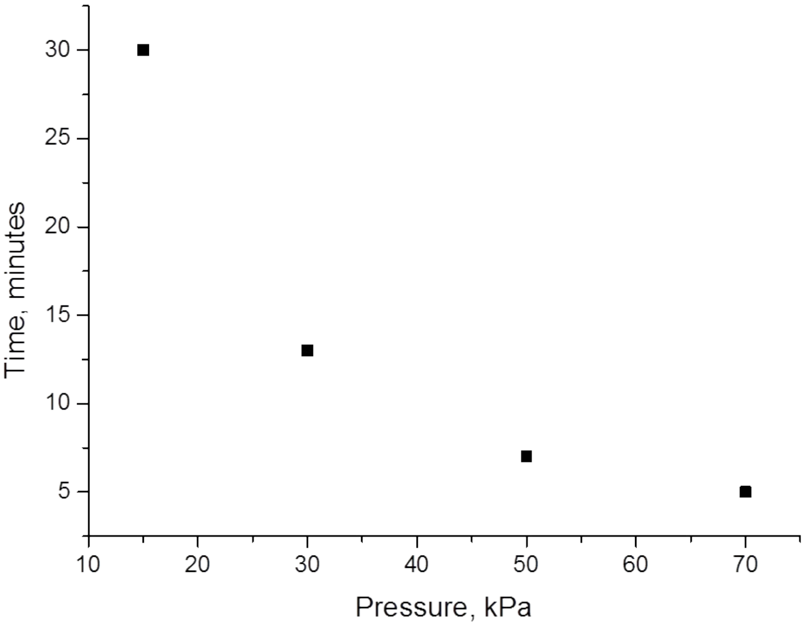


Figure S7. Time vs pressure plot for self-assembly of block copolymer POEGA$_{17}$-*b*-PSt$_{160}$ using 0.2 µm pore size membrane.

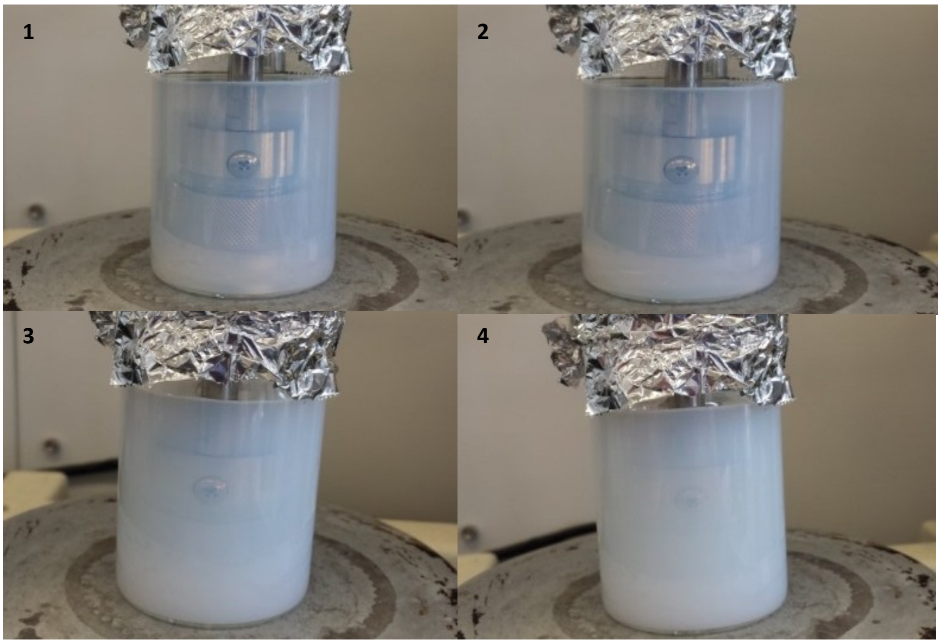


Figure S8. Self-assembly of block copolymers using SPG membrane process.

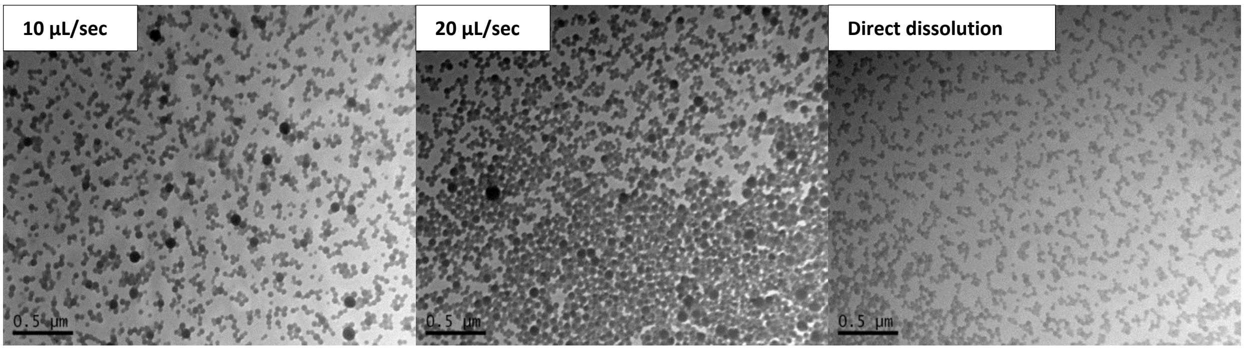


Figure S9. TEM micrographs of nanoparticles prepared using Method (ii) (dropwise addition of polymer/THF to water) with POEGA$_{17}$-*b*-PSt$_{290}$ (addition rates as indicated – 10 and 20 µL/sec correspond to addition times of 100 and 48 sec).

Table S2. Mass flow rates (mg polymer/min) for microporous membrane assisted self-assembly of amphiphilic diblock copolymers in THF-water solutions (corresponds to Table 1 in main text).

Pore size	**Pressure (kPa)**	**Time (min)**	**Mass flow rate (mg/min)**
5.2	1	3	18.3
0.2	70	3	18.3
2.1	5	5	11.0
0.2	50	7	7.9
0.8	8	13	4.2
0.2	30	13	4.2
0.3	12	25	2.2
0.2	15	30	1.8

Additional Reference:

(1) Valade, D.; Boyer, C.; Davis, T. P.; Bulmus, V., Synthesis of siRNA Polyplexes Adopting a Combination of RAFT Polymerization and Thiol-ene Chemistry. *Australian Journal of Chemistry* **2009,** *62* (10), 1344-1350.