Supporting information for

Supramolecular Assembly Mediates the Formation of Single-Chain Polymeric Nanoparticles

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Experimental Section

Materials

All chemicals and reagents were purchased from Sigma-Aldrich (St. Louis, MO, USA) at the highest purity and grade available. All solvents were purchased from TEDIA (Fairfield, OH, USA) and distilled over calcium hydride prior to use. Poly[oligo(ethylene glycol) methyl methacrylate] (POEGMA) was synthesized via atom transfer radical polymerization according to a described previously procedure.[S1] GPC analysis indicated that the molecular weight of POEGMA was ca. 75,492 g/mol with a polydispersity index (PDI, M_w/M_n) of 1.47.

Characterization

Nuclear magnetic resonance (NMR). ^{1}H-NMR spectra were recorded using a Varian Inova-400 MHz spectrometer equipped with a 9.395 T Bruker magnet. The samples (ca. 10 mg) were dissolved in 0.4 ml of the deuterated solvent in a 5 mm NMR tube. All NMR experiments were carried out at 25°C.

Gel permeation chromatography (GPC). The weight-average molecular weight (*Mw*), number-average molecular weight (*Mn*) and polydispersity index (PDI; *Mw/Mn*) were measured using a Waters 410 GPC system equipped with a refractive index detector and three Ultrastyragel^{TM} columns (100, 500 and 1000 Å) connected in series. The column temperature was controlled at 40°C. Tetrahydrofuran (THF) was the eluent and the flow rate was 1.0 ml/min. The system was calibrated using polystyrene (PS) standards.

Aqueous GPC was performed on a PL aquagel-OH MIXED-M column, calibrated with narrow poly(ethylene oxide) standards. The water mobile phase was delivered by a Waters 590 pump, at a flow rate of 0.8 ml/min; the column temperature was 40°C.

Dynamic light scattering (DLS). DLS measurements were conducted using a 90Plus laser particle size analyzer (Brookhaven Instruments Corp., Holtsville, NY, USA), which was calibrated using a 60 nm latex standard. Scattering from a different amount (0.004 mg/mL to 40 mg/mL) of sample dissolved in water was measured at 90°.

Viscosity. Viscosity data were measured using a Brookfield viscometer (Cap 1000+) at 25°C.

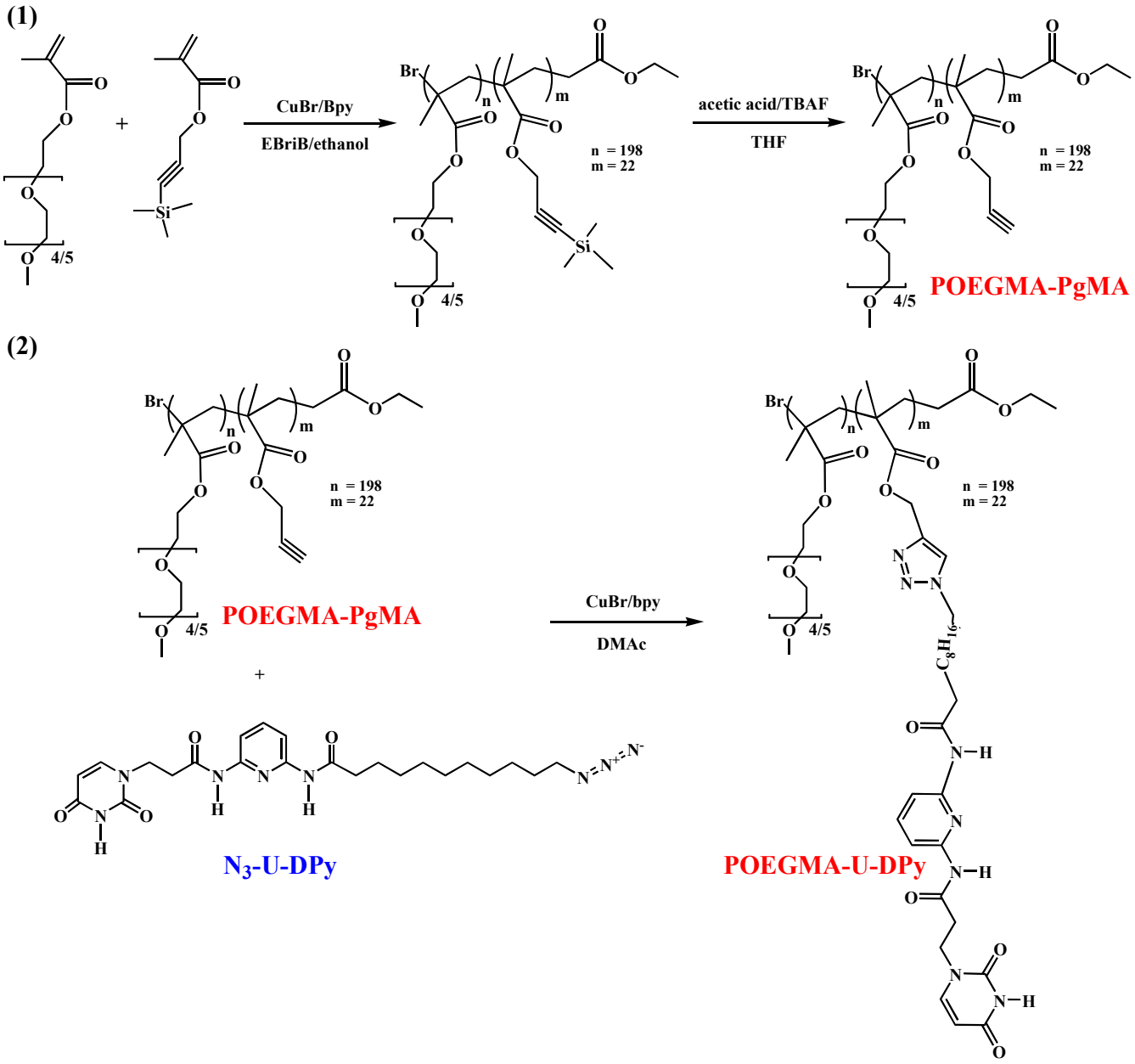
Scanning electron microscopy (SEM). The samples were sputtered with platinum and imaged using a field-emission scanning electron microscope (Hitachi S-4700, Tokyo, Japan) at an accelerating voltage of 15 kV. Test samples were prepared by spin coating the sample solutions onto silicon substrates and then evaporating the solvent under ambient conditions.

Atomic force microscopy (AFM). AFM images were scanned in tapping mode on a Digital Instrument NS4/D3100CL/MultiMode (Digital Instruments, Santa Barbara, CA, USA) using silicon cantilevers in air at 25°C. AFM images of all samples were spin-coated onto a silicon substrate and then dried under ambient conditions.

Transmission electron microscopy (TEM). TEM images were recorded using a FEI T12 transmission electron microscope (FEI Company, Hillsboro, OR, USA) with a low-energy electron beam (120 keV). TEM samples were prepared by dripping several drops of the sample solution onto carbon-coated copper grids, then the samples were stained with RuO_4.

Kinetic stability studies. Sodium dodecyl sulfate (SDS) is a destabilizing agent commonly used to evaluate the kinetic stability of micelles upon dilution in water; detailed procedures have been described previously.[S2] Briefly, samples (1 mg/mL) were mixed with an aqueous solution of SDS (20 mg/mL) at a 2:1 *v/v* ratio. The intensity of the scattered light and polydispersity index were measured over 48 h using DLS.

Syntheses



Scheme S1. Synthetic procedure for POEGMA-U-DPy.

Synthesis of alkyne-grafted POEGMA-PgMA via ATRP

Copper(I) bromide (CuBr; 24.4 mg, 0.17 mmol) and 2,2'-bipyridine (Bpy; 53.1 mg, 0.34 mmol) were dissolved in ethanol (13 ml) and the solution was purged with dry argon for 10 min. The solutions were degassed through three freeze/thaw evacuation cycles. A solution of oligo(ethylene glycol) monomethyl

ether methacrylate (average M_n = 300; 10.2 g, 34 mmol) and (trimethylsilyl)propargyl methacrylate[S3] (0.67 g, 3.4 mmol) in ethanol (7 ml) was added via syringe and the solution was once again degassed through three freeze/thaw evacuation cycles. Finally, ethyl 2-bromobutyrate (25.2 μL, 33.2 mg, 0.17 mmol) was added via syringe. Polymerization was conducted under an argon atmosphere. After heating at 60 ± 3°C for 16 h, the reaction mixture was passed through an aluminum oxide (Al_2O_3) column to remove the Cu(II) catalyst and the crude product was purified by vacuum distillation. Subsequently, the trimethylsilyl protected polymer and acetic acid (0.03 ml, 0.525 mmol) were dissolved in dry THF (50 ml) and cooled to 0°C in an ice bath. A 1 M solution of tetrabutylammonium fluoride hydrate (TBAF) in THF (0.6 ml, 0.6 mmol) was added drop-wise over a period of 1 h and the reaction mixture was stirred at 0°C for 2 h, then maintained at 25°C for an additional 12 h. Finally, the solution was passed through an Al_2O_3 chromatography column to purify the product.[S3] The molecular weight of the POEGMA-PgMA obtained as a highly viscous liquid was 66,286 g/mol; the conversion rate was 88%. We note theoretical molecular weight equivalent for polymerization is 66,000 g/mol, which is close to the experimentally observed value. A portion of this product was dissolved in THF; GPC analysis indicated a PDI of 1.51.

Synthesis of POEGMA-U-DPy via click chemistry

Azide-labeled N_3-U-DPy was synthesized according to our previously reported procedure.[S4] Alkyne-grafted POEGMA-PgMA (2.5 g, 0.038 mmol) and azide-labeled N_3-U-DPy (19.4 mg, 0.04 mmol) were dissolved in dimethylacetamide (DMAc, 40 ml) and the resulting solution was purged with dry argon for 5 min. Bpy (53.1 mg, 0.34 mmol) and CuBr (24.4 mg, 0.17 mmol) were added to the reaction solution, then the solution was degassed through three freeze/thaw evacuation cycles. The reaction mixture was heated to 60°C for 16 h. After cooling to room temperature, the reaction mixture was passed through an Al_2O_3 column, purified by dialysis against DMF using a 6000-8000 MWCO membrane for 2 d, precipitated in diethyl ether, and a viscous liquid was obtained. After filtration, the sample was dried for 6 h in a vacuum oven at 60°C (yield = 92%).

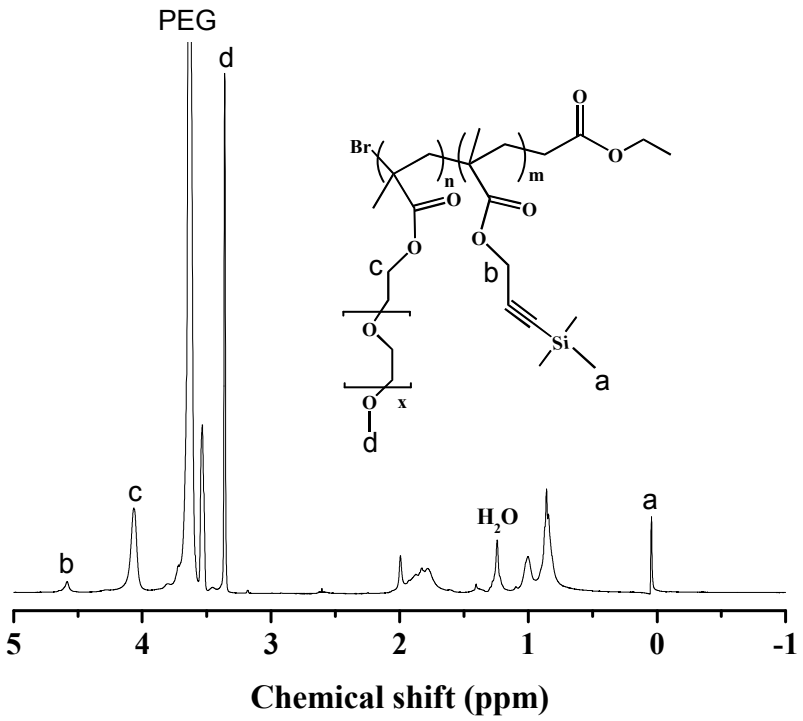


Figure S1. ^{1}H-NMR spectrum of trimethylsilyl-protected POEGMA-PgMA in $CDCl_3$.

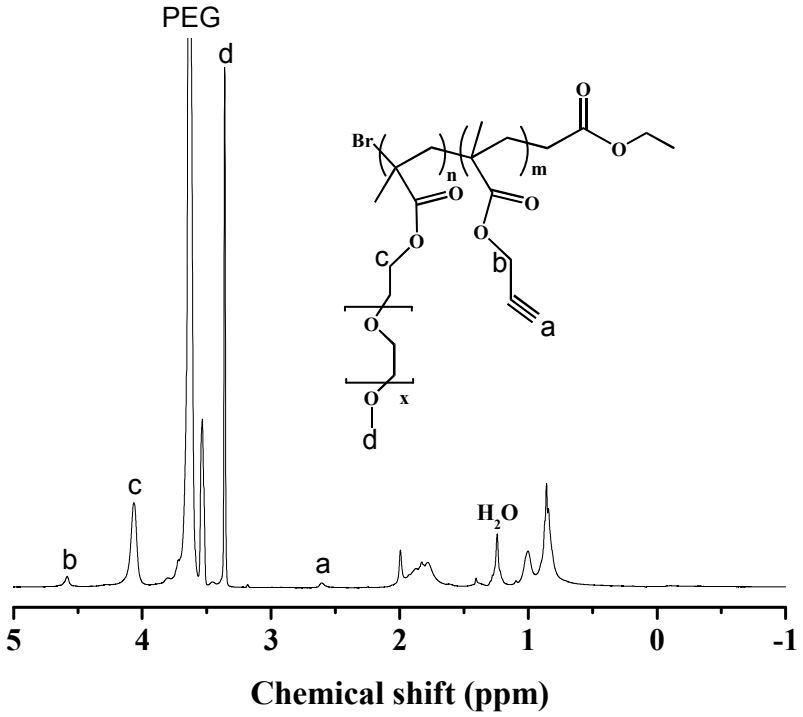


Figure S2. ^{1}H-NMR spectrum of POEGMA-PgMA in $CDCl_3$

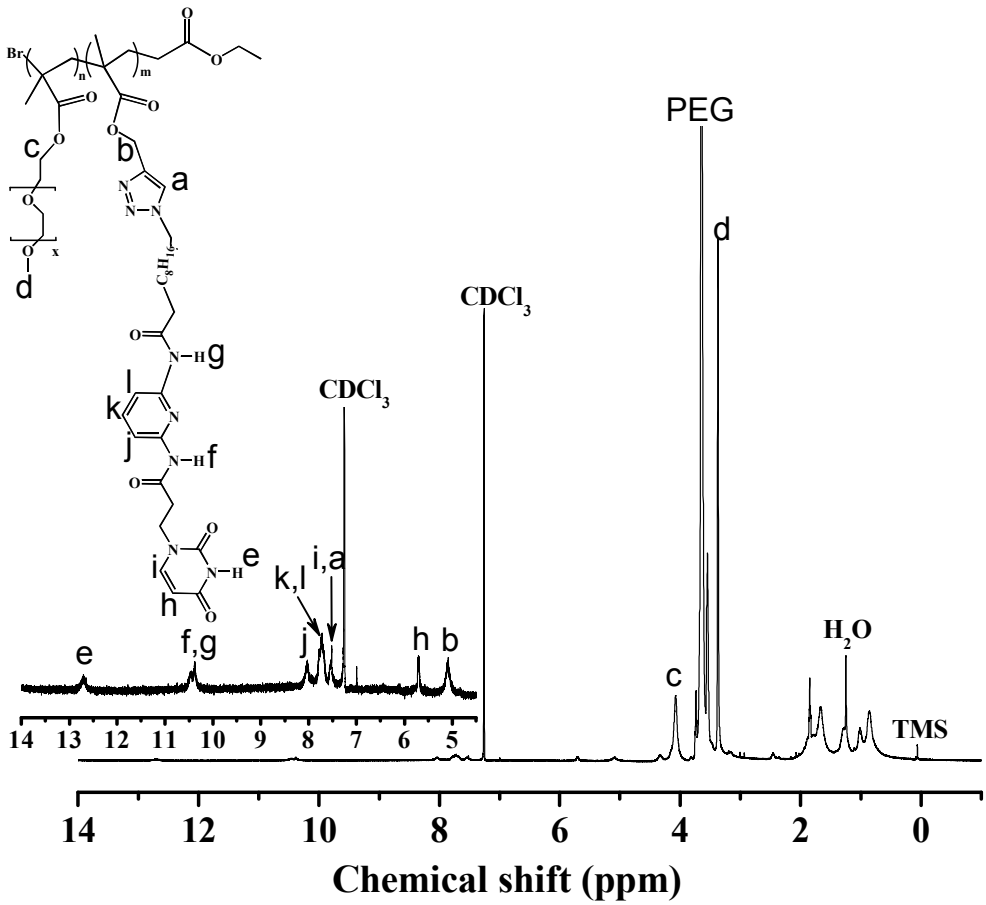


Figure S3. ^{1}H-NMR spectrum of POEGMA-U-DPy in $CDCl_3$

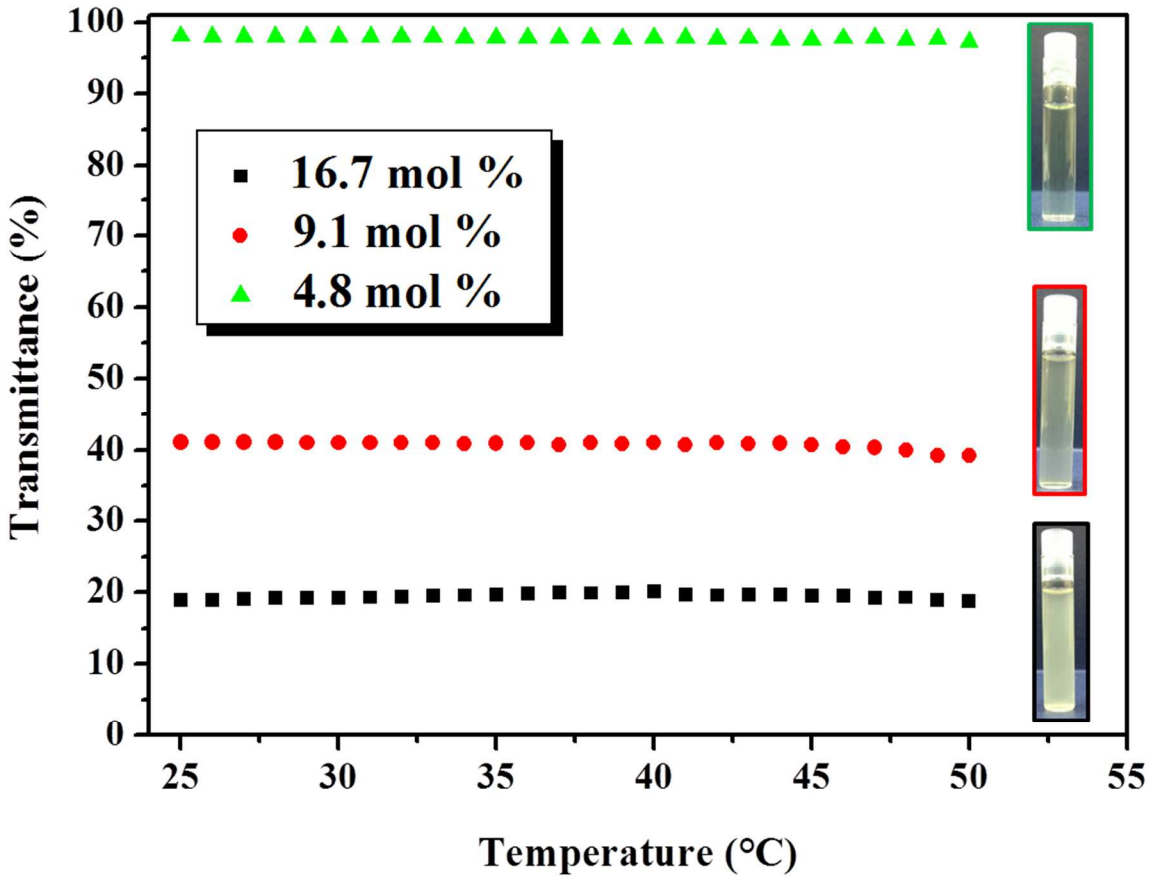


Figure S4. Transmittance curves of POEGMA-U-DPy with different U-DPy incorporation densities in water. The inset photographs show the solubility behavior of POEGMA-U-DPy copolymers in aqueous solution at 25°C.

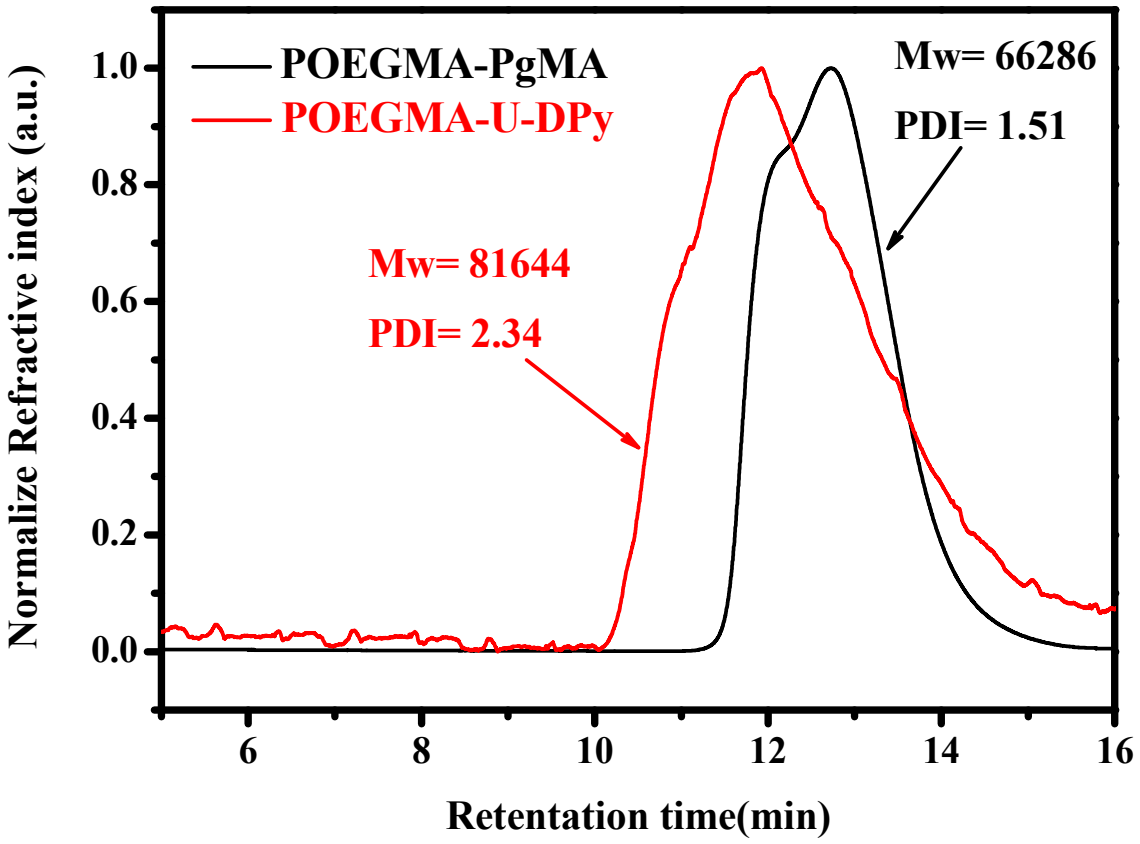


Figure S5. GPC traces of POEGMA-PgMA and POEGMA-U-DPy in THF.

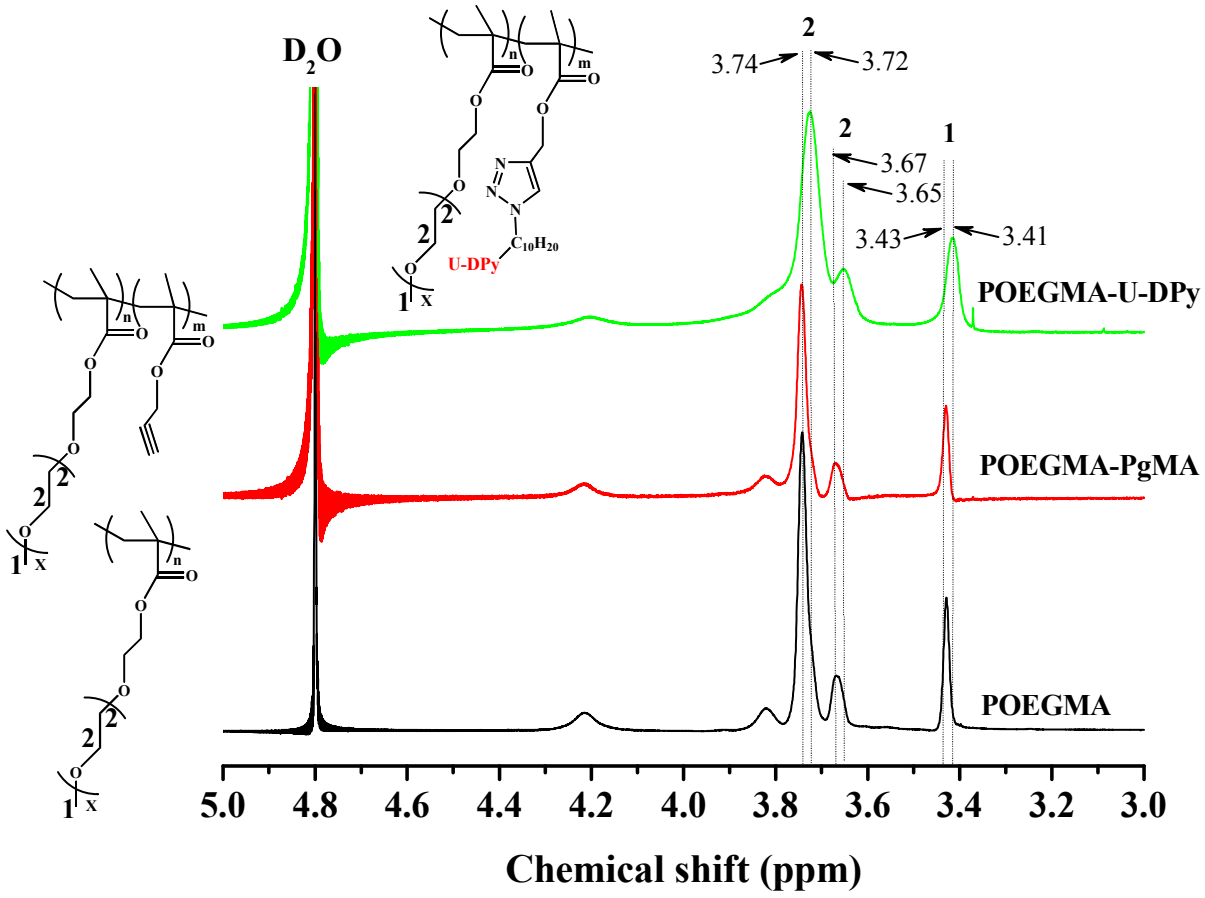


Figure S6. ^{1}H-NMR spectra of POEGMA, POEGMA-PgMA and POEGMA-U-DPy in D_2O

References:

S1. Peng, B.; Grishkewich, N.; Yao, Z.; Han, X.; Liu H.; Tam, K. *ACS Macro Lett.*, **2012**, *1*, 632–635.

S2. Kang, N.; Perron, M. È.; Prud'Homme, R. E.; Zhang, Y.; Gaucher G.; Leroux, J. C. *Nano letters*, **2005**, *5*, 315–319.

S3. Ladmiral, V.; Mantovani, G.; Clarkson, G. J.; Cauet, S.; Irwin, J. L.; Haddleton, D. M. *J. Am. Chem. Soc.*, **2006**, *128*, 4823–4830.

S4. Cheng, C. C.; Yen, Y. C.; Chang, F. C. *RSC Advances*, **2011**, *1*, 1190–1194.