

Synthesis of Molecular Brushes by “Grafting Onto” Method: Combination of ATRP and Click Reactions

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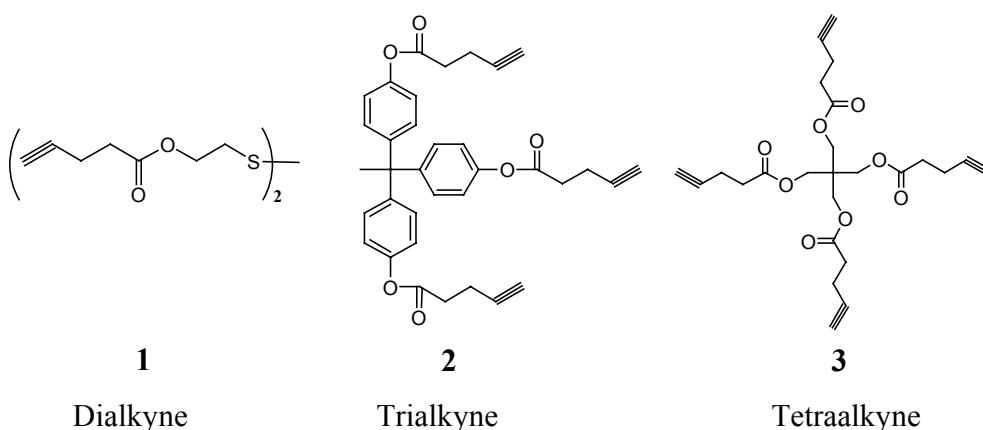
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Experimental

Materials. Styrene (S, 99%, Aldrich), *n*-butyl acrylate (BA, 99%, Aldrich), and 2-hydroxyethyl methacrylate (HEMA, 98%, Aldrich) were purified twice by passing the monomers through a column filled with basic alumina to remove the inhibitor. CuBr (98%, Acros) and CuCl (98%, Aldrich) were purified using a modified literature procedure.¹ All other reagents: ethyl 2-bromoisobutyrate (EBiB), *N,N,N',N'',N'''*-pentamethyldiethylenetriamine (PMDETA), 2,2'-bipyridyne (bpy), CuCl₂, methanesulfonyl chloride, triethylamine, sodium azide, tetrabutylammonium iodide, *N,N'*-dicyclohexylcarbodiimide (DCC), pentynoic acid, 4-dimethylaminopyridine (DMAP) and solvents were purchased from Aldrich with the highest purity and used as received without further purification. Poly(ethylene glycol) monomethyl ether (PEO-OH) with different molecular weights were purchased from Fluka and used as received. Azido-terminated polystyrene (PS-N₃) with $M_n = 1,260$ g/mol and $M_w/M_n = 1.04$ and azido-terminated poly(*n*-butyl acrylate) (PBA-N₃) with $M_n = 2,110$ g/mol and $M_w/M_n = 1.07$

(determined by THF GPC with linear PS as standards) were synthesized according to previous reports.² Special care should be taken not to heat the azido-containing compound above 75-80 °C because of its explosive nature at elevated temperatures. Dialkyne-, trialkyne- and tetraalkyne-containing coupling compounds were synthesized previously (Scheme 1S).³



Scheme 1S. Structure of multifunctional alkyne-containing coupling compounds³

Synthesis of PHEMA linear polymers by ATRP. A clean and dry Schlenk flask was charged with HEMA (10 mL, 0.082 mol), bpy (51.5 mg, 0.330 mmol), methanol (4.0 mL) and 2-butanone (6 mL). The flask was deoxygenated by five freeze-pump-thaw cycles. During the final cycle, the flask was filled with nitrogen before CuCl (13.1 mg, 0.132 mmol) and CuCl₂ (4.4 mg, 0.033 mmol) were quickly added to the frozen mixture. Special care was not taken to avoid moisture condensation. The flask was sealed with a glass stopper then evacuated and back-filled with nitrogen five times before it was immersed in an oil bath at 50 °C. Finally the N₂-purged initiator EBiB (24.2 μL, 0.165 mmol) was injected into the reaction system via a syringe through the side arm of the Schlenk flask. At timed intervals, samples were withdrawn via a syringe for measurement

of monomer conversions and polymer molecular weights by GC and GPC, respectively. The reaction was stopped after 9.7 h, at about 40% HEMA conversion, via exposure to air and dilution with methanol. The solution was filtered through a column filled with neutral alumina to remove the copper complex before the polymer was precipitated twice in cold THF and dried under vacuum at r.t. for two days. The PHEMA linear polymers had $M_{n, GPC} = 46,100$ g/mol and $M_w/M_n = 1.22$, determined by DMF GPC with linear poly(methyl methacrylate) (PMMA) standards.

Synthesis of alkyne-functionalized PHEMA (PHEMA-alkyne). Linear PHEMA (1.5 g, 0.012 mol HEMA unit), DCC (4.92 g, 0.024 mol), pentynoic acid (2.34 g, 0.024 mol) were added sequentially into 40 mL DMF before the flask was immersed into ice-water bath. Under magnetic stirring, 0.125 g DMAP in 3 mL DMF was added into this mixture within 5 min. The reaction mixture was allowed to stir for 40 h at room temperature. During this period, the reaction mixture slowly turned into brown and the insoluble DCC urea precipitated out. After filtration to remove the solid, the polymer product was precipitated in water to remove the excessive pentynoic acid. After re-dissolving in THF, the polymers were precipitated again in hexane to remove the excessive DCC and DCC urea. Since the polymer product still had acidic smell, it was dissolved in methylene chloride. The organic solution was washed successively by 200 mL HCl solution and 200 mL NaOH solution before drying over anhydrous $MgSO_4$ overnight. The methylene chloride was then removed in vacuo and 1.4 g product (yield: 57.8%) was obtained.

Synthesis of azido-terminated PEO (PEO- N_3). A typical procedure for synthesis of PEO- N_3 with $M_n \sim 775$ g/mol (PEO- N_3 775) is briefly described. In a clean,

dry round-bottom flask, PEO-OH ($M_n \sim 750$ g/mol, 13.7 g, 0.018 mol) was dissolved in 100 mL methylene chloride (dried overnight with $MgSO_4$). The solution was cooled to 0 °C in ice-water bath before triethylamine (5.00 mL, 0.036 mol) and methanesulfonyl chloride (2.80 mL, 0.036 mol) were added sequentially. The flask was then removed from the ice-water bath and the reaction was allowed to proceed for 24 h at room temperature. During this period, the reaction mixture slowly turned yellowish and some solid precipitated out. After filtration to remove the solid, the reaction mixture was washed successfully with 300 mL 1 M HCl solution, 300 mL 1 M NaOH solution and 200 mL 1 M NaCl solution. The organic layer was dried over anhydrous $MgSO_4$ overnight before the solvent was removed in vacuo, yielding a yellowish viscous liquid. The yield of the mesylate-terminated PEO (PEO-OSO₂CH₃) was 12.8 g (yield: 85.9%). Part of the PEO-OSO₂CH₃ (8.3 g, 0.010 mol) was dissolved in 40 mL DMF before sodium azide (1.33 g, 0.020 mol) and 0.15 g tetrabutylammonium iodide were added sequentially. The reaction mixture was stirred magnetically at 50 °C for 24 h before removal of *N,N*-dimethylformamide (DMF) by rotary evaporation. The solid was dissolved in methylene chloride and the undissolved solid was removed by filtration. The organic solution was washed twice by water before dried over anhydrous $MgSO_4$ overnight. After removal of the methylene chloride, 6.9 g PEO-N₃ (yield: 86.3%) was obtained, whose structure was verified by ¹³C NMR spectroscopy (δ , CDCl₃ as solvent): 70.5 ppm (s, (CH₂CH₂O)_n), 59.0 ppm (s, CH₃O), 50.9 ppm (s, CH₂CH₂N₃). By using a similar procedure, PEO-N₃ with $M_n \sim 2025$ g/mol (PEO-N₃ 2025) was synthesized too.

Synthesis of azido-terminated PBA-*b*-PS block copolymers (PBA-*b*-PS-N₃).

PBA-*b*-PS-Br block copolymers containing bromine chain-end functionality ($M_n = 3,900$

g/mol and $M_w/M_n = 1.08$, determined by THF GPC with linear PS standards) were synthesized by ATRP of styrene using PBA-Br ($M_n = 2,100$ g/mol and $M_w/M_n = 1.06$) as macroinitiator and CuBr/PMDETA as catalyst. After purification, the resulting polymer was dissolved in DMF, NaN₃ (2 times excess to the mole of bromo groups) was added, and the resulting solution was allowed to stir at 25 °C overnight. After precipitation into methanol/water mixture (1/1 by volume), PBA-*b*-PS-N₃ was obtained.

Synthesis of brush polymers via click coupling reactions between azido-terminated polymer chains and PHEMA-alkyne. A typical procedure for synthesis of PHEMA-*g*-PEO grafted copolymers was started with the ratio of reagents [PEO-N₃]₀/[HEMA-alkyne]₀/[CuBr]₀/[PMDETA]₀ = 1.80/1/0.33/0.33. The click coupling reactions between PEO-N₃ 775 (229 mg, 0.295 mmol) and PHEMA-alkyne (34.6 mg, 0.164 mmol HEMA-alkyne unit) were conducted in a 10 mL Schlenk flask with 1 mL DMF as solvent and CuBr/PMDETA as catalyst. Toluene (0.05 mL) was added initially into the reaction system as internal standard for calculation of the percentage of reacted PEO-N₃ SCs via DMF GPC measurement of the samples withdrawn periodically from the flask. After 10 h, the polymer solution was exposed to air, diluted with THF, and passed through neutral alumina to remove the copper catalyst. The PHEMA-*g*-PEO brush polymers were purified by dialysis against MeOH to remove the unreacted PEO-N₃ chains. After purification, the solvent was removed by rotary evaporation, and the final product was dried under vacuum for two days.

Characterization. HEMA conversions were determined using a Shimadzu GC-14A gas chromatograph, equipped with a capillary column (DB-Wax, 30 m × 0.54 mm × 0.5 μm, J&W Scientific) and the ATRP solvent (mixture of methanol and 2-butanone)

was used as an internal standard. The apparent molecular weights of different polymer species were determined by GPC equipped with HPLC pump at flow rate of 1 mL/min DMF or THF (Waters, 515), and four columns (guard, 10^5 Å, 10^3 Å, and 100 Å; Polymer Standards Services) in series. Toluene was used as GPC internal standard. A calibration curve based on linear PS or PMMA standards was used in conjunction with a differential refractive index (RI) detector (Waters, 2410). A triple detector system connected with a THF GPC was employed to measure the absolute molecular weights ($M_{w,MALLS}$) of polymers. The detectors include a RI detector (Wyatt Technology, Optilab REX), a viscometer detector (Wyatt Technology, ViscoStar) and a multi-angle laser light scattering (MALLS) detector (Wyatt Technology, DAWN EOS) with the light wavelength at 690 nm. Absolute molecular weights were determined using ASTRA software from Wyatt Technology. ^1H NMR or ^{13}C NMR spectra of the polymer solutions in CDCl_3 or $\text{DMF-}d_7$ were collected on Bruker Avance 300 MHz spectrometer at 27 °C.

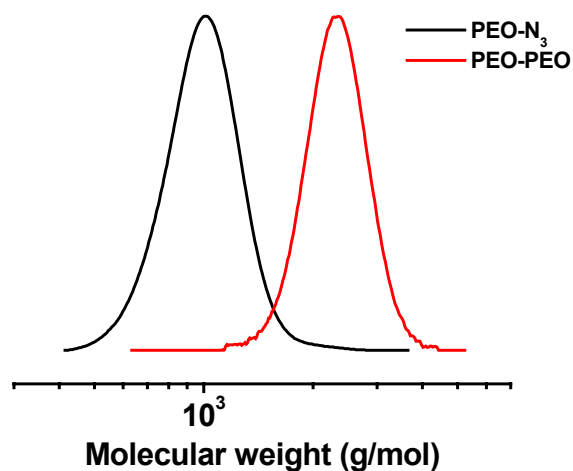


Figure 1S. GPC curves of PEO-N₃ 775 and its coupling product with **1** by click coupling reaction; experimental conditions: [PEO-N₃ 775]₀/[**1**]₀/[CuBr]₀/[PMDETA]₀ = 1/0.5/0.33/0.33; [PEO-N₃ 775]₀ = 0.25 M, r.t. in DMF; linear PMMA standards were used for calibration of the THF GPC.

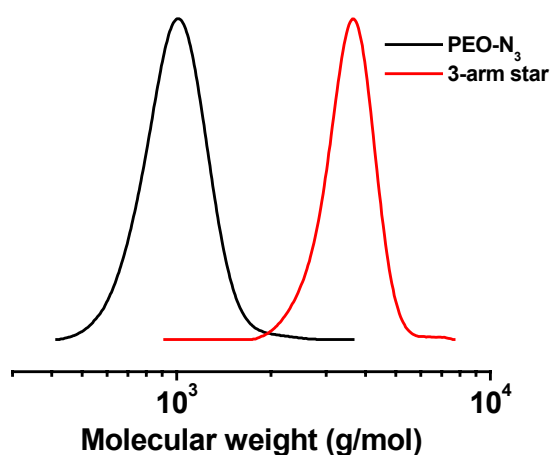


Figure 2S. GPC curves of PEO-N₃ 775 and its coupling product with **2** by click coupling reaction; experimental conditions: [PEO-N₃ 775]₀/[**2**]₀/[CuBr]₀/[PMDETA]₀ = 1/0.33/0.33/0.33; [PEO-N₃ 775]₀ = 0.25 M, r.t. in DMF; linear PMMA standards were used for calibration of the THF GPC.

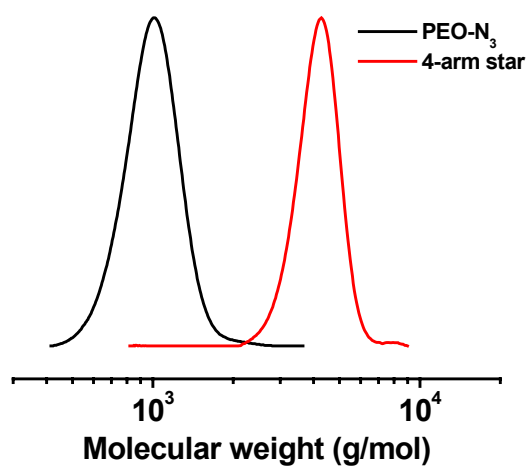


Figure 3S. GPC curves of PEO-N₃ 775 and its coupling product with **3** by click coupling reaction; experimental conditions: $[\text{PEO-N}_3 \text{ 775}]_0/[\mathbf{3}]_0/[\text{CuBr}]_0/[\text{PMDETA}]_0 = 1/0.25/0.33/0.33$; $[\text{PEO-N}_3 \text{ 775}]_0 = 0.25 \text{ M}$, r.t. in DMF; linear PMMA standards were used for calibration of the THF GPC.

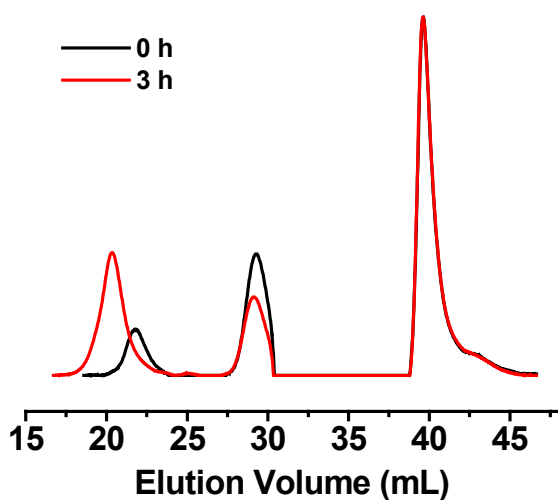


Figure 4S. Calculation of the grafting density (Y_{grafting}) of PHEMA-g-PEO brush polymers by GPC using toluene as internal standard; experimental conditions: (Table 2, entry B1-1.80) $[\text{PEO-N}_3 \text{ 775}]_0/[\text{HEMA-alkyne}]_0/[\text{CuBr}]_0/[\text{PMDETA}]_0 = 1.80/1/0.33/0.33$; $[\text{PEO-N}_3 \text{ 775}]_0 = 0.25 \text{ M}$, r.t. in DMF; linear PMMA standards for DMF GPC calibration.

Results summary of Figure 4S

Time (h)	A_1 (%) ^a	A_2 (%) ^b	A_1/A_2	Reacted PEO- N_3	Y_{grafting}
0	27.39	72.61	0.3772	0	0
6	19.77	80.23	0.2464	34.7%	62.5%

a. Area fraction of unreacted PEO- N_3

b. Area fraction of internal standard toluene

References

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