

Supporting Information To:

SET-LRP of *N*-(2-Hydroxypropyl) Methacrylamide in H₂O

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Experimental

Materials

Methyl-2-chloropropionate (MCP) (97%, Lancaster Synthesis), methyl 2-bromopropionate (99%, Acros) and ethyl 2-bromoisobutyrate (98%, Acros) were used as received. Copper (0) wire (20 gauge wire, (0.812 mm diameter) Fischer) was activated with hydrazine hydrate (hydrazine 64%, Acros) according to a previously developed procedure.¹ Dimethyl sulfoxide (DMSO) (Fisher, Certified ACS, 99.9) was distilled over CaH₂ and kept in a glovebox. *Tris*[2-(dimethylamino)ethyl]amine (Me₆-TREN) was synthesized as described in the literature.² Oligo(ethylene oxide)-derived 2-bromoisobutyrate was synthesized according to a literature procedure.³ *N*-(2-hydroxypropyl)methacrylamide (HPMA) was synthesized via a modified reaction of methacryloyl chloride with 1-aminopropan-2-ol in dichloromethane in the presence of sodium carbonate as described earlier.⁴

Techniques

500 MHz ^1H NMR spectra were recorded on a Bruker DRX500 NMR instrument at 23 °C in D_2O . Gel Permeation Chromatography (GPC) analysis of the acetylated PHPMA samples was carried out on a Perkin-Elmer Series 10 high-performance liquid chromatography, equipped with an LC-100 column oven (30 °C), a Nelson Analytical 900 Series integration data station, a Perkin-Elmer 785 UV-vis detector (254 nm), a Varian star 4090 refractive index (RI) detector, and three AM gel columns (500 Å, 5 μm ; 1000 Å, 5 μm ; and 10 4 Å, 5 μm). THF (Fisher, HPLC grade) was used as eluent at a flow rate of 1 mL/min. The number-average (M_n) and weight-average (M_w) molecular weights of PHEMA samples were determined with poly(methyl methacrylate) (PMMA) standards purchased from American Polymer Standards. The absolute weight average molecular weight, M_w , and polydispersity of PHPMA samples were determined via absolute size exclusion chromatography (SEC) using a Shimadzu HPLC containing a Superose 6TM column, and equipped with UV, differential refractometer Optilab® rEX and multiangle light scattering detector DAWN® 8TM (Wyatt Technology Corp., USA). 0.3 M sodium acetate buffer (pH 6.5) containing 0.5 g·L⁻¹ sodium azide was used as the mobile phase. The flow rate was 0.5 mL·min⁻¹.

Typical Procedure for SET-LRP of HPMA at 50 °C in H₂O

A stock solution CuCl_2 (2.3 mg, 0.017 mmol) in 10 mL of H_2O was prepared. In a 25 mL Schlenk tube, the reagents were added in the following order under gentle stirring: monomer (HPMA, 0.5 g, 3.5 mmol), a solution of CuCl_2 in H_2O (1 mL, 1.7 μmol CuCl_2), ligand ($\text{Me}_6\text{-TREN}$, 4.4 mg, 5.1 μL , 19 μmol) and initiator (MCP, 4.28 mg, 4 μL , 35

μmol). The mixture was deoxygenated using six freeze-pump-thaw cycles. After the last deoxygenation cycle, Cu(0) wire wrapped around a stirring bar was loaded into the reaction vessel under positive argon pressure, defining $t = 0$. The reaction vessel as placed in a water bath thermostated at 50 °C with stirring. The side arm of the flask was purged with argon before it was opened for sampling at the predetermined reaction times with an airtight syringe. At each time, a small amount of the sample was dissolved in D₂O for the analysis of monomer conversion by ¹H NMR, and the rest was kept in a small vial for acetylation. After removal of residual solvents, the polymer samples kept in vials were dissolved in pyridine (0.5 mL pyridine per 20 mg polymer), followed by the addition of acetic anhydride (0.1 mL).⁵ After removal of the excess reagent and solvent, PHPMA was dried under vacuum and dissolved in THF for GPC analysis. The theoretical M_n was calculated based on the molecular weight of the acetylated monomer ($M_n = 185.22 \times [M]_0/[I]_0 \times \text{conv.} + M_{\text{Initiator}}$).

References

1. N. H. Nguyen and V. Percec, *J. Polym. Sci. Part A: Polym. Chem.*, 2010, **48**, 5109-5119.
2. M. Ciampolini and N. Nardi, *Inorg. Chem.*, 1966, **5**, 41-44.
3. X. S. Wang and S. P. Armes, *Macromolecules*, 2000, **33**, 6640-6647.
4. (a) K. Ulbrich, V. Šubr, J. Strohalm, D. Plocová, M. Jelínková and B. Říhová, *J. Controlled Release*, 2000, **64**, 63-79; (b) H. Vaisocherová, W. Yang, Z. Zhang, Z. Cao, G. Cheng, M. Piliarik, J. I. Homola and S. Jiang, *Anal. Chem.*, 2008, **80**, 7894-7901.
5. K. Bian and M. F. Cunningham, *Macromolecules*, 2005, **38**, 695-701.