Rapid synthesis of well-defined polyacrylamide by aqueous Cu(0)-mediated reversible-deactivation polymerization

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**Materials**

Acrylamide (≥99% for electrophoresis) and N-hydroxyethyl acrylamide (97%) were obtained from Sigma-Aldrich.

Tris[2-(dimethylamino)ethyl]-amine (Me₆TREN) was synthesized according to literature procedure¹ and stored under nitrogen and refrigerated prior to use.

Water soluble initiator, 3-dihydroxypropyl 2-bromo-2-methylpropanoate was synthesized according to literature procedure.²

Copper(I) bromide (CuBr, 98%) was purchased from Sigma-Aldrich and sequentially washed with acetic acid and ethanol and dried *in vacuo* to remove Cu(II) bromide impurities.

**Instruments and analysis**

NMR spectra were recorded on Bruker AV-250 and DPX-400 spectrometers using deuterated solvents purchased from Sigma-Aldrich and Cambridge Isotope Laboratories, inc. Monomer conversion was calculated by comparison of vinyl protons (5.5-7.0 ppm) with polymer backbone protons (1.3-2.5 ppm.) NMR spectra for the water soluble initiator were conducted on a Bruker AV III-500 HD spectrometer using a cryoprobe.

Aqueous SEC was conducted on an Agilent Technologies Infinity 1260 MDS instrument equipped with a differential refractive index (DRI), light scattering (LS) and viscometry (VS) and UV detectors. The column set used were Agilent PLAQuagel OH30 * 2 and a 5 µm Aquagel guard column. The mobile phase used was 0.1 M NaNO₃. Column oven and detector temperatures were regulated to 35°C, flow rate 1 mL/min. Poly(ethyleneoxide) standards (Agilent EasyVials) were used for calibration (100-30,000 g mol⁻¹). Analyte samples were filtered through a hydrophilic membrane with 0.22 µm pore size before injection. Respectively, experimental molar mass (Mₙ SEC) and dispersity (Đ) values of synthesized polymers were determined by conventional calibration using Agilent GPC/SEC software.
Experimental

NMR spectra of water soluble initiator

Figure S1a: Top: $^{13}$C NMR of water soluble initiator in D$_2$O showing presence of isomer. Bottom: $^{13}$C NMR of water soluble initiator in DMSO.
Figure S1b: Top: $^1$H NMR of water soluble initiator in D$_2$O showing presence of isomer. Bottom: $^1$H NMR of water soluble initiator in DMSO.
Figure S2: COSY of water soluble initiator in D$_2$O showing presence of isomer.
Figure S3: HMQC of water soluble initiator in D₂O.
Example aqueous SET-LRP of acrylamide (targeted DP$_n$ = 80)

H$_2$O (1 mL) and Me$_6$TREN (8.7 µL, 32.6 µmol, 0.6 eq.) were charged to a 25 mL Schlenk tube with a magnetic stirrer bar and a rubber septum. The solution was deoxygenated by bubbling with nitrogen for 2 minutes. CuBr (6.2 mg, 43.4 µmol, 0.8 eq.) was added with rapid stirring, disproportionation was seen to occur after a few seconds. The disproportionated solution was placed in an ice bath and deoxygenated for a further 15 minutes.

Simultaneously, a vial was charged with 3-dihydroxypropyl 2-bromo-2-methylpropanoate (13.1 mg, 54.3 µmol), acrylamide (0.5 g, 4.34 mmol, 80 eq.) and 3.5 mL of H$_2$O. The vial was fitted with a septum, stirred and degassed with nitrogen in an ice bath for 15 minutes.

Subsequently, the degassed monomer/initiator solution was transferred into the Schlenk tube containing the disproportionated solution via degassed syringe. The polymerization mixture was allowed to react for 15 minutes, after which a sample (~0.1 mL) was taken for analysis. The sample for SEC was filtered through a plug of neutral alumina to remove catalyst residues prior to analysis. The sample for $^1$H NMR analysis was diluted with D$_2$O. Monomer conversion was calculated by comparison of vinyl protons with polymer backbone protons. Conversion >99%, $M_n$(SEC) 5800 Da, $D$ = 1.09.

![Scheme S1: Homopolymerization of acrylamide by aqueous SET-LRP.](image)
Figure S4: $^1$H NMR of poly(acrylamide)$_{80}$ in D$_2$O, synthesized by SET-LRP at 0 °C. Conversion >99% as seen by absence of vinyl protons (5.5-7.0 ppm).
GPC traces of Optimization conditions

Figure S5: (a) Polyacrylamide (DP$_{80}$) [I]:[CuBr]:[Me$_6$TREN] 1:0.4:0.4, $D = 1.17$. (b) Polyacrylamide (DP$_{80}$) [I]:[CuBr]:[Me$_6$TREN] 1:0.8:0.4, $D = 1.11$.

Figure S6: (a) Polyacrylamide (DP$_{160}$) [I]:[CuBr]:[Me$_6$TREN] 1:0.4:0.4, $D = 1.46$. (b) Polyacrylamide (DP$_{160}$) [I]:[CuBr]:[Me$_6$TREN] 1:0.8:0.4, $D = 1.09$.

Figure S7: (a) Polyacrylamide (DP$_{320}$) [I]:[CuBr]:[Me$_6$TREN] 1:0.4:0.4, $D = 6.20$. (b) Polyacrylamide (DP$_{320}$) [I]:[CuBr]:[Me$_6$TREN] 1:0.8:0.4, $D = 1.10$. 
Figure S8 (a) Polyacrylamide (DP$_{640}$) [I]:[CuBr]:[Me$_6$TREN] 1:0.8:0.6, $D = 1.41$. (b) Polyacrylamide (DP$_{80}$) [I]:[CuBr]:[Me$_6$TREN] 1:1.2:0.8, $D = 1.60$. 
Example chain extension of polyacrylamide: poly(acrylamide)\textsubscript{40}-\textit{b}-poly(acrylamide)\textsubscript{80}

H\textsubscript{2}O (1 mL) and Me\textsubscript{6}TREN (18.8 µL, 70.4 µmol, 0.4 eq.) were charged to a 25 mL Schlenk tube with a magnetic stirrer bar and a rubber septum. The solution was deoxygenated by bubbling with nitrogen for 2 minutes. CuBr (10.1 mg, 70.4 µmol, 0.4 eq.) was added with rapid stirring, disproportionation was seen to occur after a few seconds. The disproportionated solution was placed in an ice bath and deoxygenated for a further 15 minutes.

Simultaneously, a vial was charged with 3-dihydroxypropyl 2-bromo-2-methylpropanoate (13.1 mg, 54.3 µmol), acrylamide (0.5 g, 7.03 mmol, 40 eq.) and 3.5 mL of H\textsubscript{2}O. The vial was fitted with a septum, stirred and deoxygenated with nitrogen in an ice bath for 15 minutes.

Subsequently the degassed monomer/initiator solution was transferred into the Schlenk tube containing the disproportionated solution via degassed syringe. The reaction mixture was sampled after 15 minutes and analysed by SEC and NMR. Immediately after this a degassed solution of acrylamide (1 g, 14.06 mmol, 80 eq. in 2 mL H\textsubscript{2}O) was transferred into the reaction vessel by degassed syringe, and the reaction mixture sampled once again after 15 minutes.

Scheme S2: Polymerization of acrylamide by aqueous SET-LRP followed by \textit{in-situ} chain extension.
Figure S9: $^1$H NMR of poly(acrylamide)$_{40}$ in D$_2$O, synthesized by SET-LRP at 0 °C. Conversion >99%.

Figure S10: $^1$H NMR of poly(acrylamide)$_{40}$-$\text{E}$(b)-poly(acrylamide)$_{80}$ in D$_2$O, synthesized by SET-LRP at 0 °C. Conversion ~99%
Synthesis of PAM<sub>40</sub>-(b)-PHEAA<sub>80</sub> block copolymer

Scheme S3: Polymerization of acrylamide by aqueous SET-LRP followed by in-situ chain extension with hydroxyethyl acrylamide.

Figure S11: <sup>1</sup>H NMR of poly(acrylamide)₄₀ in D₂O, synthesized by SET-LRP at 0 °C. Conversion ~99%. 
Figure S12: $^1$H NMR of poly(acrylamide)$_{40}$-(b)-poly(hydroxyethyl acrylamide)$_{30}$ in D$_2$O, synthesized by SET-LRP at 0 °C. Conversion >99%
Synthesis of PHEAA<sub>40</sub>-<i>b</i>-PAM<sub>80</sub> block copolymer

Scheme S3: Polymerization of hydroxyethyl acrylamide by aqueous SET-LRP followed by in-situ chain extension with acrylamide.

Figure S13: <sup>1</sup>H NMR of poly(hydroxyethyl acrylamide)<sub>40</sub> in D<sub>2</sub>O, synthesized by SET-LRP at 0 °C. Conversion >99%
Figure S14: $^1$H NMR of poly(hydroxyethyl acrylamide)$_{40}$(b)-poly(acrylamide)$_{60}$ in D$_2$O, synthesized by SET-LRP at 0 °C. Conversion >99%