Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Aqueous SARA ATRP using Inorganic Sulfites

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Experimental Section

Materials

Oligo(ethylene oxide) methyl ether acrylate ($OEOA_{480}$, 99%, average molecular weight 480, Sigma-Aldrich) and oligo(ethylene oxide) methyl ether methacrylate ($OEOMA_{500}$, 99%, average molecular weight 500, Aldrich) were passed over a column of basic alumina (Fisher Scientific) prior to use. $Na_2S_2O_4$ (Sigma–Aldrich, 85 %), $Na_2S_2O_5$ (Sigma–Aldrich, >99 %), $NaHSO_3$ (Sigma–Aldrich, >99 %), 2-hydroxyethyl 2-bromoisobutyrate (HEBiB, 95%, Sigma-Aldrich), copper(II) bromide (99.99%, Sigma-Aldrich), sodium chloride (NaCl, 99.5%, Fisher Scientific), tetraethylammonium chloride (TEACl, 98%, Sigma-Aldrich), sodium bromide (NaBr, 99.5%, Fisher Scientific), bovine serum albumin (BSA, ≥98%, Sigma-Aldrich), water (H_2O, HPLC grade, Fisher Scientific), N,N-dimethylformamide (DMF, ACS grade, Fisher Scientific), deuterium oxide (D_2O, 99.9%, Cambridge Isotope Laboratories), and anhydrous magnesium sulfate (99%, Aldrich) were used as received. 1X PBS solution was prepared from 10X PBS (Thermo Fisher Scientific) and HPLC grade water. Tris(pyridin-2-ylmethyl)amine (TPMA),[1] tris[2-(dimethylamino)ethyl]amine (Me_6TREN)[2] and BSA protein initiator (BSA-O-$[iBBr]_{30}$)[3] were prepared as previously reported in the literature.

Techniques

A syringe pump (KDS Scientific, Legato 101) was used for the continuous feeding of the sulfites at the rate 1 μL/min (different sulfite aqueous solutions were prepared to obtained different FR_S).

^1H nuclear magnetic resonance (NMR) spectroscopy measurements were performed on a Bruker Avance 500 MHz spectrometer and used to determine the monomer conversion in D_2O.

The chromatographic parameters of the samples were determined using a gel permeation chromatography (GPC) system equipped with a Waters 515 HPLC pump and a Waters 2414 refractive index detector using PSS columns (Styrogel 10^2, 10^3, 10^5 Å) with DMF containing 10 mM LiBr as the eluent at a flow rate of 1 mL/min at 50 °C. The system was calibrated

with low dispersity PMMA (M_n = 800 – 1 820 000) standards. Before the injection (50 μL) the samples were filtered through a polytetrafluoroethylene (PTFE) membrane with 0.22 μm pore.

The UV-Visible studies were performed using an Agilent 8453 UV-Vis Spectrometer. Dynamic light scattering (DLS) measurements were performed on a Malvern Zetasizer Nano ZS at 25 °C.

Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was performed with a Bio-Rad Laboratories Mini-Protean TGX™ Precast Gels (7.5%). Staining was accomplished with Coomassie blue and washed in DI water overnight.

General Procedure for Aqueous SARA ATRP of OEOA

A series of aqueous SARA ATRP using OEOA as monomer were carried out with systematically different conditions to establish the optimal reactions conditions. The conditions used for polymerization of $OEOA_{480}$ generally followed this procedure: NaCl (58.4 mg, 1.0 mmol), $OEOA_{480}$ (2.40 g, 5 mmol), 100 mM stock solution HEBiB (0.2 mL, 0.02 mmol), stock solution of 25 mM $CuBr_2$ and 200 mM TPMA (40 μL, 1.0 μmol of $CuBr_2$ and 8 μmol of TPMA) were dissolved in H_2O (7.7 mL). DMF (0.1 mL) was added as internal standard for ^1H NMR analysis. This mixture was added to a 25 mL Schlenk flask and purged with nitrogen for 30 min, and then the flask was placed in an oil bath at 30 °C. A $Na_2S_2O_4$ aqueous solution (64 mM) was purged with nitrogen, and the solution was continuously injected into the reaction medium using a syringe pump at the rate 1 μL/min. Samples were taken throughout the reaction for GPC and NMR analysis.

Synthesis of "One-pot" POEOMA-*b*-POEOA Block Copolymer

NaCl (58.4 mg, 1.0 mmol), $OEOMA_{500}$ (2.50 g, 5 mmol), 100 mM stock solution HEBiB (1.0 mL, 0.10 mmol), stock solution of 25 mM $CuBr_2$ and 200 mM TPMA (200 μL, 5.0 μmol of $CuBr_2$ and 40 μmol of TPMA) were dissolved in H_2O (7.7 mL). DMF (0.1 mL) was added as internal standard for ^1H NMR analysis. This mixture was added to a 25 mL Schlenk flask, purged with nitrogen for 30 min, and the flask was placed in an oil bath at 30 °C. A $Na_2S_2O_4$ aqueous solution (64 mM) was purged with nitrogen, and the solution was continuously

injected into the reaction medium using a syringe pump at the rate 1 μL/min. Samples were taken throughout the reaction for GPC and NMR analysis. The polymerization proceeded for 18 h (98% conversion, M_n^{th} = 24600, M_n^{GPC} = 26200, M_w/M_n = 1.22). After that, under continuous flow of nitrogen the excess of polymerization mixture was removed from Schlenk flask until reach a volume of 0.5 mL (POEOMA: 125 mg, 5 μmol; $CuBr_2$: 2.8 μg, 0.0125 μmol; TPMA: 29 μg, 0.10 μmol). The $OEOA_{480}$ (2.40 g, 5 mmol) and H_2O (7.7 mL) previously bubbled with nitrogen for about 15 minutes were added. An additional $Na_2S_2O_4$ solution (8 mM) was purged with nitrogen, and the solution was continuously injected into the reaction medium using a syringe pump at the rate 1 μL/min allowed to copolymerize for 20 h.

Grafting from the Protein Initiator BSA-O-[iBBr]$_{30}$

$BSA\text{-}O\text{-}[iBBr]_{30}$ (25.0 mg (protein), 0.01 mmol (initiator)), $OEOA_{480}$ (1.20 g, 2.5 mmol), stock solution of 25 mM $CuBr_2$ and 200 mM TPMA (20 μL, 0.50 μmol $CuBr_2$ and 4.0 μmol TPMA) were dissolved in 0.1 M PBS (7.7 mL). DMF (0.1 mL) was added as internal standard for ^1H NMR analysis. This mixture was added to a 25 mL Schlenk flask, purged with nitrogen for 30 min, and then placed in an oil bath at 30 °C. A $Na_2S_2O_4$ aqueous solution (16 mM) was purged with nitrogen, and the solution was continuously injected into the reaction medium using a syringe pump at the rate 1 μL/min. The grafted polymers were cleaved from the protein by adding 200 μL of the reaction mixture to 200 μL of 5% KOH solution. The resulting solution was allowed to react for 2 h at room temperature, followed by GPC analysis, as described elsewhere.[3]

Results

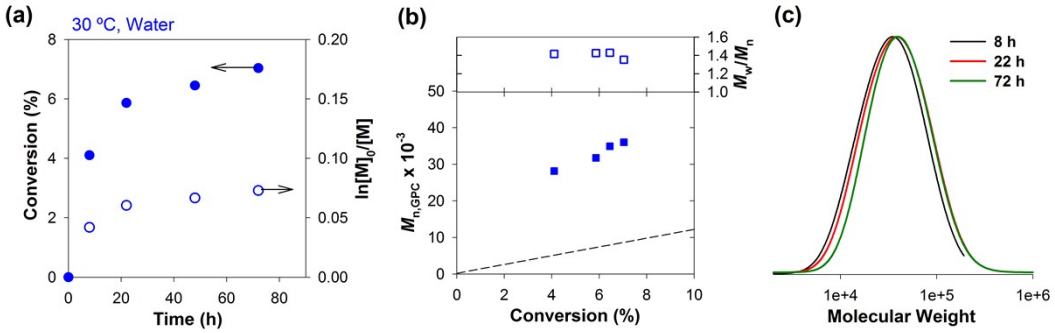

Fig. S1 (a) Kinetic plots of conversion and $\ln[M]_0/[M]$ *vs*. time; (b) plot of number–average molecular weights ($M_{n,GPC}$) and $Đ$ (M_w/M_n) *vs*. conversion for aqueous SARA ATRP of $OEOA_{480}$ at 30 ºC; and (c) GPC traces *vs*. time. Conditions: $[OEOA_{480}]_0/[HEBiB]_0/[Na_2S_2O_4]_0/[Cu(II)Br_2]_0/[TPMA]_0$ = 250/1/1/0.05/0.4; $[NaCl]_0$ = 100 mM; $[OEOA_{480}]_0/[Water]$ = 1/3.

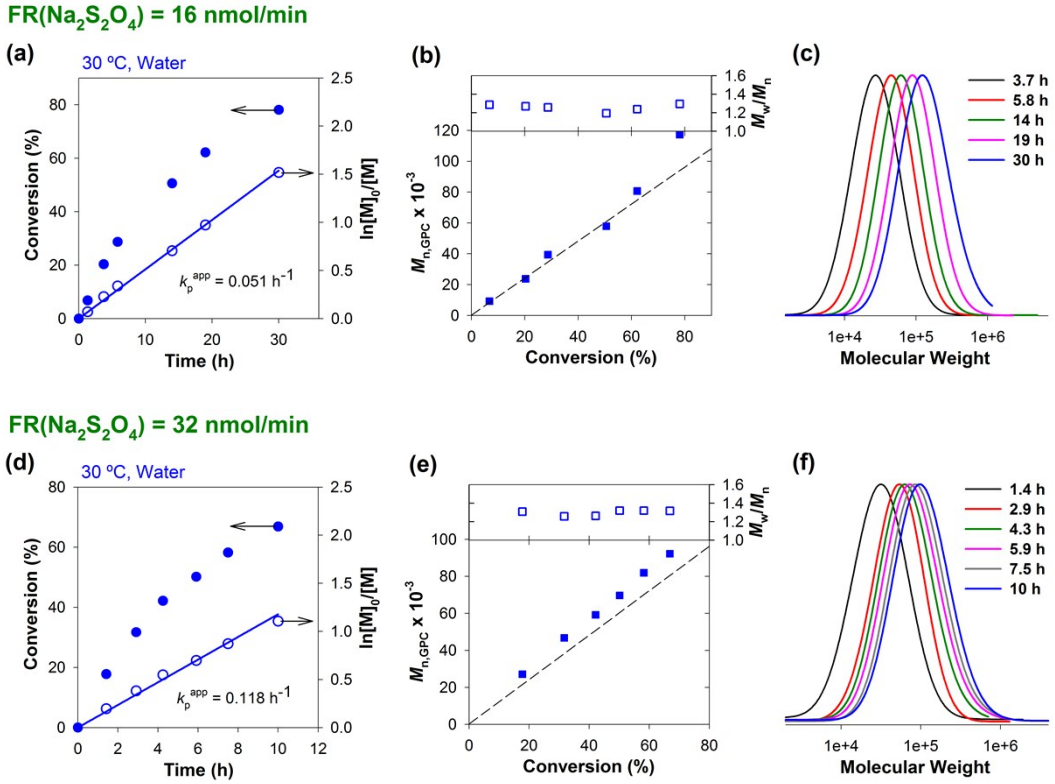

Fig. S2 (a and d) Kinetic plots of conversion and $\ln[M]_0/[M]$ *vs*. time; (b and e) plot of $M_{n,GPC}$ and $Đ$ (M_w/M_n) *vs*. conversion for aqueous SARA ATRP of $OEOA_{480}$ at 30 ºC; and (c and f) GPC traces *vs*. time. Conditions: $[OEOA_{480}]_0/[HEBiB]_0/[Cu(II)Br_2]_0/[TPMA]_0$ = 250/1/0.05/0.4; $FR(Na_2S_2O_4)$ = 16 (a, b and c) and 32 (d, e and f) nmol/min ; $[NaCl]_0$ = 100 mM; $[OEOA_{480}]_0/[Water]$ = 1/3.

A higher FR_S = 64 nmol/min was employed at the beginning of polymerization up to 50% of monomer conversion. After that moment, the FR_S was reduced to 8 nmol/min (Fig. S3).

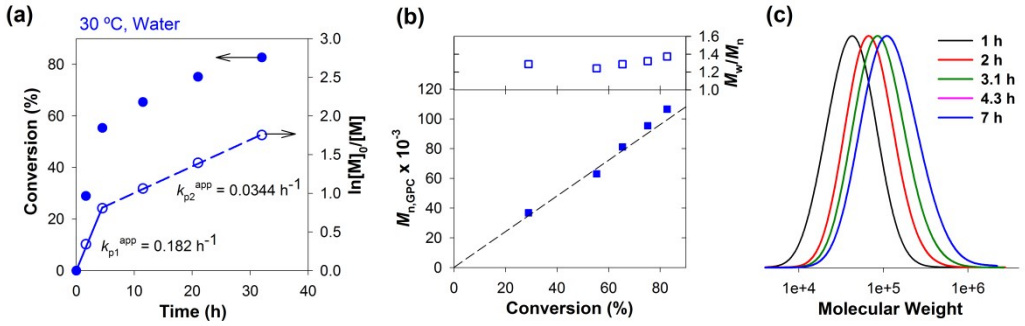

Fig. S3 (a) Kinetic plots of conversion and $\ln[M]_0/[M]$ *vs*. time; (b) plot of number–average molecular weights ($M_{n,GPC}$) and $Đ$ (M_w/M_n) *vs*. conversion for aqueous SARA ATRP of $OEOA_{480}$ at 30 ºC; and (c) GPC traces *vs*. time. Conditions: $[OEOA_{480}]_0/[HEBiB]_0/[Cu(II)Br_2]_0/[TPMA]_0$ = 250/1/0.05/0.4; FR($Na_2S_2O_4$) = 64 nmol/min (until 4.5h) and FR($Na_2S_2O_4$) = 8 nmol/min (until 32h); $[NaCl]_0$ = 100 mM; $[OEOA_{480}]_0/[Water]$ = 1/3.

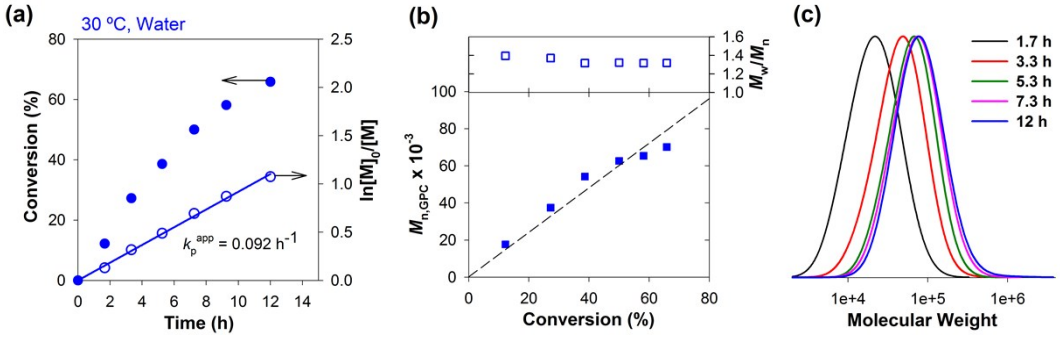

Fig. S4 (a) Kinetic plots of conversion and $\ln[M]_0/[M]$ *vs*. time; (b) plot of $M_{n,GPC}$ and $Đ$ (M_w/M_n) *vs*. conversion for aqueous SARA ATRP of $OEOA_{480}$ at 30 ºC; and (c) GPC traces *vs*. time. Conditions: $[OEOA_{480}]_0/[HEBiB]_0/[Cu(II)Br_2]_0/[TPMA]_0$ = 250/1/0.05/0.1; FR($Na_2S_2O_4$) = 64 nmol/min; $[NaCl]_0$ = 100 mM; $[OEOA_{480}]_0/[Water]$ = 1/3.

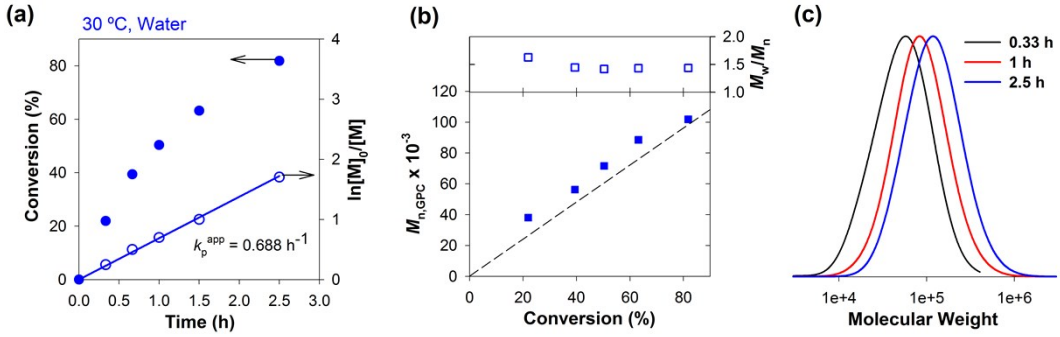

Fig. S5 (a) Kinetic plots of conversion and $\ln[M]_0/[M]$ *vs*. time; (b) plot of $M_{n,GPC}$ and $Đ$ (M_w/M_n) *vs*. conversion for aqueous SARA ATRP of $OEOA_{480}$ at 30 ºC; and (c) GPC traces *vs*. time. Conditions: $[OEOA_{480}]_0/[HEBiB]_0/[Cu(II)Br_2]_0/[Me_6TREN]_0$ = 250/1/0.05/0.4; FR($Na_2S_2O_4$) = 64 nmol/min; $[NaCl]_0$ = 100 mM; $[OEOA_{480}]_0/[Water]$ = 1/3.

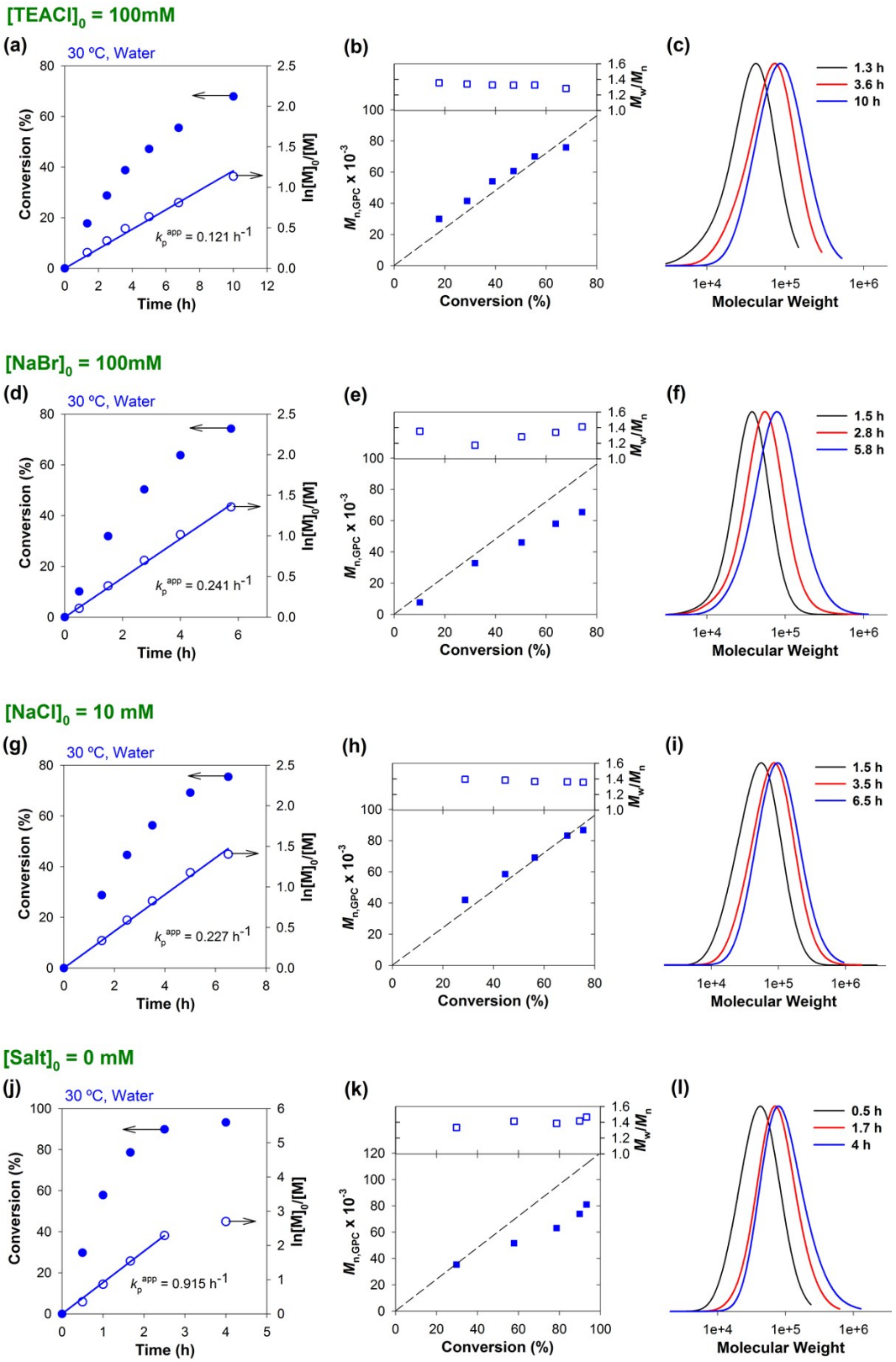

Fig. S6 (a, d, g and j) Kinetic plots of conversion and $\ln[M]_0/[M]$ *vs*. time; (b, e, h and k) plot of $M_{n,GPC}$ and $Đ$ (M_w/M_n) *vs*. conversion for aqueous SARA ATRP of $OEOA_{480}$ at 30 ºC; and (c, f, i and l) GPC traces *vs*. time. Conditions: $[OEOA_{480}]_0/[HEBiB]_0/[Cu(II)Br_2]_0/[TPMA]_0$ = 250/1/0.05/0.4; FR($Na_2S_2O_4$) = 64 nmol/min; $[OEOA_{480}]_0/[Water]$ = 1/3; (a, b and c) $[TEACl]_0$ = 100 mM, (d, e and f) $[NaBr]_0$ = 100 mM, (g, h and i) $[NaCl]_0$ = 10 mM, and (j, k and l) $[Salt]_0$ = 0 mM.

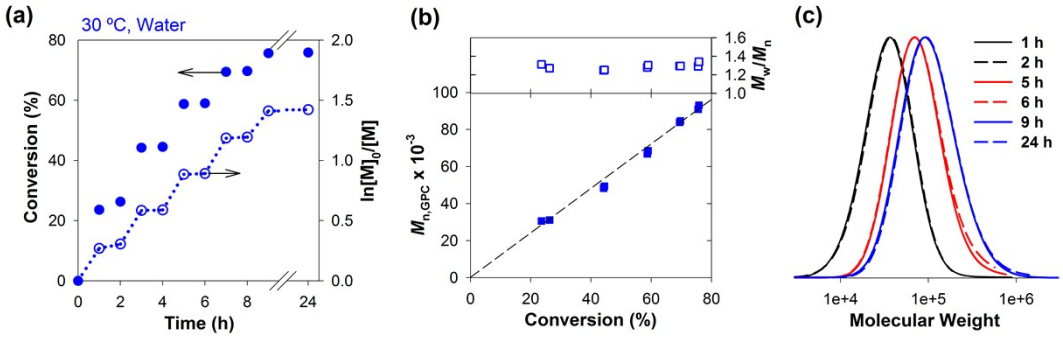

Fig. S7 (a) Kinetic plots of conversion and $\ln[M]_0/[M]$ *vs*. time; (b) plot of $M_{n,GPC}$ and $Đ$ (M_w/M_n) *vs*. conversion for aqueous SARA ATRP of $OEOA_{480}$ at 30 ºC; and (c) GPC traces *vs*. time. Conditions: $[OEOA_{480}]_0/[HEBiB]_0/[Cu(II)Br_2]_0/[TPMA]_0$ = 250/1/0.05/0.1; FR($Na_2S_2O_4$) = 64 nmol/min; $[NaCl]_0$ = 100 mM; $[OEOA_{480}]_0/[Water]$ = 1/3.

Table S1 Aqueous SARA ATRP of $OEOA_{480}$ with Start/Stop Cycles.

Entry[a]	$[M]_0/[I]_0/[Cu(II)Br_2]_0/[TPMA]_0$	Sulfite	Cu[b] (ppm)	Time (h)	Conv. (%)	$M_n^{th} \times 10^{-3}$	$M_n^{GPC} \times 10^{-3}$	$Đ$
1	250/1/0.05/0.4	$Na_2S_2O_4$	26	1 (1 h OFF)	24	28.5	30.6	1.31
				3 (1 h OFF)	44	53.3	48.3	1.25
				5 (1 h OFF)	59	70.7	66.9	1.28
				7 (1 h OFF)	69	83.5	83.9	1.29
				9 (15 h OFF)	76	90.9	90.9	1.29

[a]All polymerizations were conducted with $[M]_0$ = 0.5 M, $[I]_0$ = 2 mM, $[NaCl]_0$ = 100 mM and FR_S = 64 nmol/min;

[b]Calculated by the initial weight ratio of Cu to the monomer.

References

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3. S. Averick, A. Simakova, S. Park, D. Konkolewicz, A. J. D. Magenau, R. A. Mehl and K. Matyjaszewski, *ACS Macro Lett.*, 2012, **1**, 6-10.