Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Rapid synthesis of PEGylated multiblock polymers by sequence-controlled polymerization in H_2O

Xiaoling Liu[1]*, Yunbo Feng[1], Lunqiang Jin[1], Xueyi Wang,[2,3] Xiang Zhang[1], Yi Xie[1], Changsheng Zhao[1]*, Dietmar Appelhans[2], Brigitte Voit[2,3]

[1]College of Polymer Science and Engineering, Sichuan University, 610065 Chengdu, P. R. China

[2]Leibniz-Institut für Polymerforschung Dresden e.V., Hohe Straße 6, D-01069 Dresden, Germany

[3]Organic Chemistry of Polymers, Technische Universität Dresden, D-01062 Dresden, Germany

E-mail: liuxiaoling@scu.edu.cn; zhaochsh70@163.com

Table of Contents for Supporting Information:

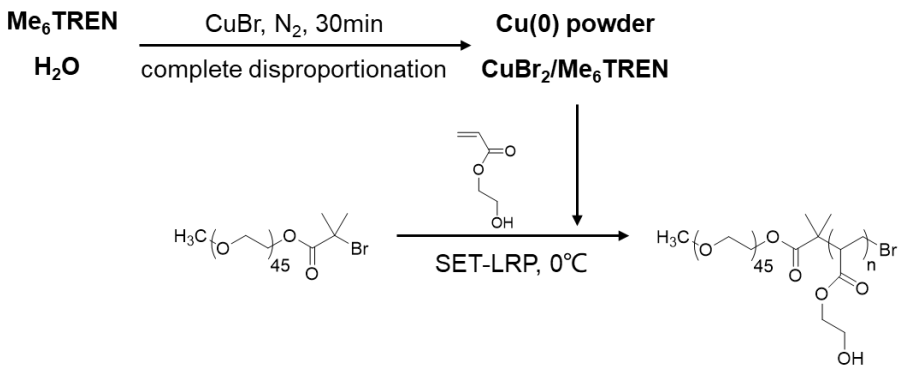
1. EXPERIMENTAL SECTION

1.1 Syntheses of poly(ethylene glycol) macroinitiator

The previously reported method was used as follows[1, 2]. Here, poly(ethylene glycol) terminated with methoxy (0.25 mmol) was dried under vacuum for 30 min then dissolved in anhydrous THF under nitrogen gas. After adding triethylamine (0.07 mL, 0.5 mmol), 2-bromoisobutyryl bromide (0.06 mL, 0.5 mmol), diluted in anhydrous THF, was finally added dropwise to reaction mixture over 15 min. The reaction mixture was stirred for 48 h at room temperature. After that, the mixture was filtered to remove the salt and the filtrate was concentrated by evaporation most of solvent. Finally, PEG macroinitiator was obtained by precipitation in *n*-hexane. Yield of the reaction was 86%.

^{1}H NMR (500.13 MHz, $CDCl_3$, δ): 1.94 (s, 6H), 3.38 (s, 3H), 3.64 (s, 180 H).

2. SUPPORTING FIGURES



Scheme S1. Schematic representation for synthesis of PEG_{45}-b-$PHEA_n$ via aqueous SET-LRP polymerization.

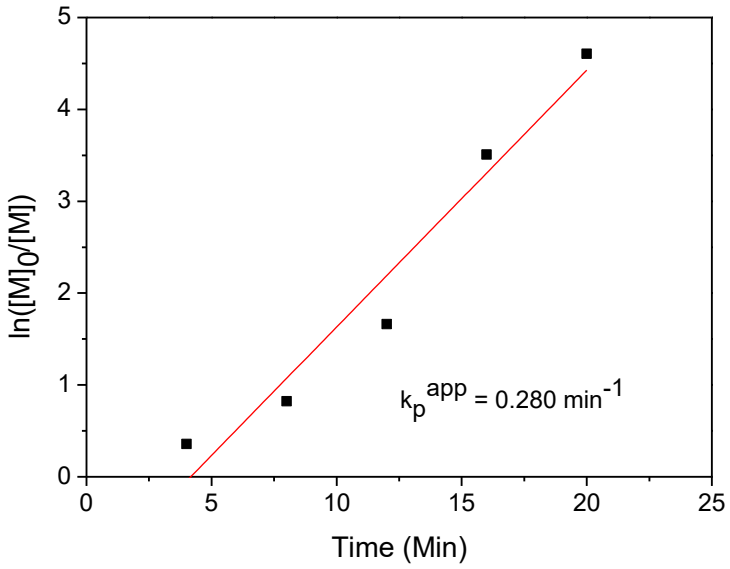


Figure S1. $Ln([M]_0/[M])$ vs. time kinetic plots of diblock polymer PEG_{45}-b-$PHEA_{10}$.

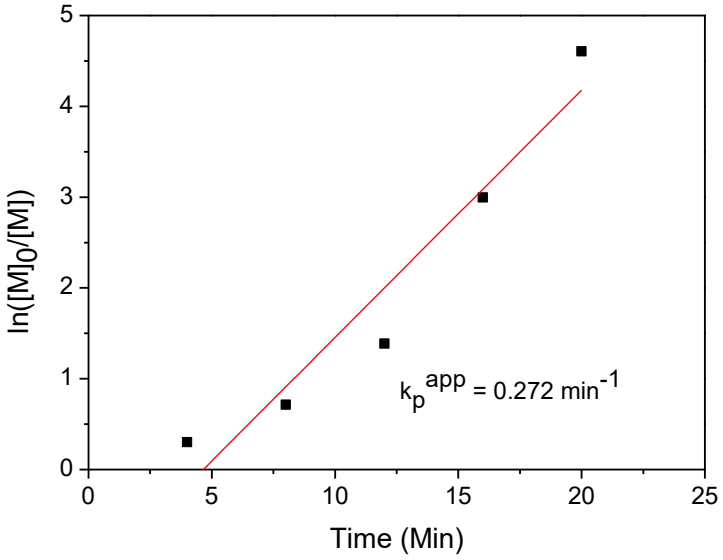


Figure S2. Ln($[M]_0/[M]$) vs. time kinetic plots of diblock polymer PEG_{45}-b-$PHEA_{40}$.

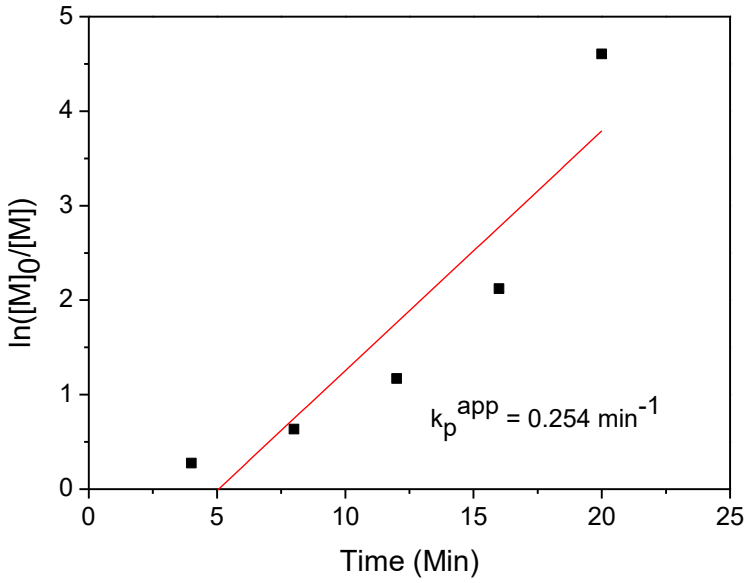


Figure S3. Ln($[M]_0/[M]$) vs. time kinetic plots of diblock polymer PEG_{45}-b-$PHEA_{100}$.

Table S1. Characterization of diblock polymer via aqueous SET-LRP polymerization at 0 ℃ in H_2O in this study.

Sample	Reactive time (min)	Monomer conversion[a)] (%)	$M_{n,th}$ (g/mol)	$M_{n,SEC}$[b)] (g/mol)	Đ[b)]
PEG_{45}-b-$PHEA_{10}$	20	>99	3300	3600	1.06
PEG_{45}-b-$PHEA_{40}$	20	>99	6800	7200	1.05
PEG_{45}-b-$PHEA_{100}$	20	>99	13800	14600	1.07

[a)] Monomer conversion was measured by ^{1}H NMR. [b)] Number-average molecular weight (M_n) and dispersity (Đ) of the polymer were determined by SEC (PMMA calibration).

Table S2. Characterization of diblock polymer PEG_{45}-b-$PHEA_{10}$ via aqueous SET-LRP polymerization at 0 ℃ in H_2O in this study.

Reaction time (min)	Monomer conversion[a)] (%)	$M_{n,th}$ (g/mol)	$M_{n,SEC}$[b)] (g/mol)	Đ[b)]
4	30	2500	3100	1.10
8	56	2800	3300	1.09
12	81	3100	3500	1.08
16	97	3200	3600	1.08
20	>99	3300	3600	1.06

[a)] Monomer conversion was measured by ^{1}H NMR. [b)] Number-average molecular weight (M_n) and dispersity (Đ) of the polymer were determined by SEC (PMMA calibration).

Table S3. Characterization of diblock polymer PEG_{45}-b-$PHEA_{40}$ via aqueous SET-LRP polymerization at 0 ℃ in H_2O in this study.

Reaction time (min)	Monomer conversion[a)] (%)	$M_{n,th}$ (g/mol)	$M_{n,SEC}$[b)] (g/mol)	Đ[b)]
4	26	3400	4400	1.08
8	51	4500	5300	1.07
12	75	5600	6200	1.07
16	95	6600	7100	1.06
20	>99	6800	7200	1.05

[a)] Monomer conversion was measured by ^{1}H NMR. [b)] Number-average molecular weight (M_n) and dispersity (Đ) of the copolymer were determined by SEC (PMMA calibration).

Table S4. Characterization of diblock polymer PEG_{45}-b-$PHEA_{100}$ via aqueous SET-LRP polymerization at 0 ℃ in H_2O in this study.

Reaction time (min)	Monomer conversion[a)] (%)	$M_{n,th}$ (g/mol)	$M_{n,SEC}$[b)] (g/mol)	Đ[b)]
4	24	4900	6600	1.12
8	47	7600	9000	1.10
12	69	11200	12300	1.09
16	88	12400	13400	1.09
20	>99	13800	14600	1.07

[a)] Monomer conversion was measured by ^{1}H NMR. [b)] Number-average molecular weight (M_n) and dispersity (Đ) of the copolymer were determined by SEC (PMMA calibration).

Table S5. Characterization of homopolymer PEG_{45}-b-$PHEA_{10}$-b-$PHEA_{10}$-b-$PHEA_{10}$-b-$PHEA_{10}$-b-$PHEA_{10}$-b-$PHEA_{10}$-b-$PHEA_{10}$-b-$PHEA_{10}$-b-$PHEA_{10}$-b-$PHEA_{10}$-b-$PHEA_{10}$ via aqueous SET-LRP polymerization at 0 ℃ in H_2O based on PEG macroinitiator (DP_n = 10 per block).

Block number	DP_n (per block)	Monomer conversion[a)] (%)	Time per block (min)	$M_{n,th}$ (g/mol)	$M_{n,SEC}$[b)] (g/mol)	Đ[b)]
Block 1	10	>99	20	3300	3600	1.06
Block 2	10	>99	20	4500	4900	1.06
Block 3	10	>99	20	5600	6100	1.05
Block 4	10	>99	20	6800	7400	1.07
Block 5	10	>99	25	8000	8800	1.09
Block 6	10	>99	25	9100	10000	1.08
Block 7	10	>99	30	10300	11500	1.08
Block 8	10	>99	30	11400	12800	1.10
Block 9	10	>97	40	12500	14300	1.13
Block 10	10	>88	50	13500	15800	1.17
Block 11	10	>75	60	14400	17100	1.19
Block 12	10	>60	90	15100	18400	1.25

[a)] Monomer conversion was measured by ^1H NMR. [b)] Number-average molecular weight (M_n) and dispersity (Đ) of the multiblock homopolymer were determined by SEC (PMMA calibration).

Table S6. Characterization of nonablock multiblock polymer PEG_{45}-b-$PHEA_{10}$-b-$PNIPAM_{10}$-b-$PHEA_{10}$-b-$PNIPAM_{10}$-b-$PHEA_{10}$-b-$PNIPAM_{10}$-b-$PHEA_{10}$-b-$PNIPAM_{10}$ via aqueous SET-LRP polymerization at 0 ℃ in H_2O based on PEG macroinitiator (DP_n = 10 per block).

Block number	DP_n (per block)	Monomer conversion[a)] (%)	Time per block (min)	$M_{n,th}$ (g/mol)	$M_{n,SEC}$[b)] (g/mol)	Đ[b)]
Block 1	10	>99	15	3300	3600	1.06
Block 2	10	>99	15	4400	4800	1.07
Block 3	10	>99	15	5600	6200	1.07
Block 4	10	>99	15	6700	7500	1.09
Block 5	10	>99	15	7900	8900	1.09
Block 6	10	>99	20	9000	10100	1.08
Block 7	10	>98	25	10100	11500	1.09
Block 8	10	>97	30	11200	12800	1.10

[a)] Monomer conversion was measured by ^{1}H NMR. [b)] Number-average molecular weight (M_n) and dispersity (Đ) of the polymer were determined by SEC (PMMA calibration).

Table S7. Characterization of nonablock homopolymer PEG_{45}-b-$PHEA_5$-b-$PHEA_{10}$-b-$PHEA_{15}$-b-$PHEA_{20}$-b-$PHEA_{25}$-b-$PHEA_{30}$-b-$PHEA_{35}$-b-$PHEA_{40}$ via aqueous SET-LRP polymerization at 0 ℃ in H_2O based on PEG macroinitiator (DP = $\sum_{i=1}^{8}(5i)$ per block).

Block number	DP_n (per block)	Monomer conversion[a] (%)	Time per block (min)	$M_{n,th}$ (g/mol)	$M_{n,SEC}$[b] (g/mol)	Đ[b]
Block 1	5	>99	15	2700	2800	1.05
Block 2	10	>99	20	3900	4300	1.07
Block 3	15	>99	20	5600	6200	1.06
Block 4	20	>99	25	8000	8700	1.05
Block 5	25	>99	25	10900	11900	1.08
Block 6	30	>99	30	14300	15500	1.10
Block 7	35	>99	30	18400	19900	1.12
Block 8	40	>98	30	23000	25100	1.14

[a] Monomer conversion was measured by ^{1}H NMR. [b] Number-average molecular weight (M_n) and dispersity (Đ) of the multiblock homopolymer were determined by SEC (PMMA calibration).

Table S8. Characterization of nonablock homopolymer PEG_{45}-b-$PHEA_{30}$-b-$PHEA_{30}$-b-$PHEA_{30}$-b-$PHEA_{30}$-b-$PHEA_{30}$-b-$PHEA_{30}$-b-$PHEA_{30}$ via aqueous SET-LRP polymerization at 0 ℃ in H_2O based on PEG macroinitiator (DP_n = 30 per block).

Block number	DP_n (per block)	Monomer conversion[a] (%)	Time per block (min)	$M_{n,th}$ (g/mol)	$M_{n,SEC}$[b] (g/mol)	Đ[b]
Block 1	30	>99	20	5600	6000	1.09
Block 2	30	>99	20	9100	9700	1.07
Block 3	30	>99	30	12600	13400	1.08
Block 4	30	>99	30	16100	17000	1.10
Block 5	30	>99	30	19600	20800	1.09
Block 6	30	>99	35	23000	24700	1.11
Block 7	30	>99	40	26500	29000	1.13
Block 8	30	>98	40	30000	33300	1.15

[a] Monomer conversion was measured by ^{1}H NMR. [b] Number-average molecular weight (M_n) and dispersity (Đ) of the multiblock polymer were determined by SEC (PMMA calibration).

Table S9. Data analysis for the higher-molecular-weight pentablock homopolymer PEG_{45}-b-$PHEA_{100}$-b-$PHEA_{100}$-b-$PHEA_{100}$-b-$PHEA_{100}$.

Block number	DP_n (per block)	Monomer conversion[a] (%)	Time per block (min)	$M_{n,th}$ (g/mol)	$M_{n,SEC}$[b] (g/mol)	Đ[b]
Block 1	100	>99	20	13800	14600	1.08
Block 2	100	>99	30	25400	26900	1.13
Block 3	100	>98	35	37000	39100	1.16
Block 4	100	>95	45	48600	51700	1.19

[a] Monomer conversion was measured by ^{1}H NMR. [b] Number-average molecular weight (M_n) and dispersity (Đ) of the multiblock polymer were determined by SEC (PMMA calibration).

3 REFERENCE

1. Iyisan B, Kluge J, Formanek P, Voit B, Appelhans D. Multifunctional and Dual-Responsive Polymersomes as Robust Nanocontainers: Design, Formation by Sequential Post-Conjugations, and pH-Controlled Drug Release. *Chemistry of Materials* 2016, **28**(5)**:** 1513-1525.

2. Liu X, Formanek P, Voit B, Appelhans D. Functional Cellular Mimics for the Spatiotemporal Control of Multiple Enzymatic Cascade Reactions. *Angew. Chem. Int. Ed.* 2017, **56**(51)**:** 16233-16238