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Synthesis of Ultrahigh Molar Mass Poly(2-Hydroxyethyl Methacrylate) by Single-Electron Transfer Living Radical Polymerization

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Abstract. Cu(0)/Me_6-TREN mediated SET-LRP of 2-hydroxyethyl methacrylate (HEMA) initiated with methyl α-bromophenylacetate (MBrPA) was performed in DMSO at 25 ^oC targeting $[M]_0/[I]_0$ = 100 to 10,000. At $[M]_0/[I]_0$ = 100, SET-LRP of HEMA is a living process, and provided PHEMA with M_n = 21,500 g/mol and M_w/M_n = 1.20 in 7 h. Using similar conditions, PHEMA with M_n = 35,000 to 152,200 g/mol and M_w/M_n = 1.28 to 1.39 was prepared within 9 h. When targeting higher $[M]_0/[I]_0$ (2,000 to 10,000), Me_6-TREN concentration was changed to 0.15 equivalent with respect to initiator concentration, for at higher ligand concentration the polymerization did not proceed beyond 30% conversion even after a long reaction time. PHEMA with M_n = 333,500 to 1,017,900 g/mol and M_w/M_n lower than 1.50 was synthesized for the first time by direct polymerization of HEMA without protecting the hydroxyl group.

Introduction

Poly(2-hydroxyethyl methacrylate) (PHEMA) is an important functional polymer due to its biocompatibility and lack of toxicity.[1, 2] The use of PHEMA as hydrogel for biological application was first reported by Wichterle and Lim in 1960.[1] Since then, PHEMA has been widely utilized for the preparation of soft contact lenses,[3] artificial corneas,[4] scaffolds for tissue engineering and drug delivery,[5] and hydrogels in biomedical engineering.[6]

Prior to the introduction of living radical polymerization (LRP) by Otsu,[7] the synthesis of well-defined PHEMA *via* living polymerization of unprotected HEMA was a major challenge due to the

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interaction of the hydroxyl groups with the catalyst and initiators in living ionic polymerizations[8] or group transfer polymerization.[2, 9] The development of LRP techniques, including metal-catalyzed LRP[10, 11] over the years have allowed the precise synthesis of tailored polymers from a wide variety of functional monomers including HEMA.[2] CuX-mediated atom transfer radical polymerization (ATRP) of HEMA was first reported in 1999 using CuCl/2,2'-bipyridine (bpy) catalytic system.[9] The best result was achieved using an alkyl bromide initiator in a mixed polar solvent system (methyl ethyl ketone/1-propanol, 7/3 v/v) at 50 ^{o}C and 70 ^{o}C. At $[M]_0/[I]_0$ = 100, PHEMA with M_n of less than 40,000 g/mol and M_w/M_n lower than 1.5 was achieved at below 80% conversion after 20 h. It was suggested that the synthesis of higher molecular weight PHEMA could only be achieved by protecting the hydroxyl groups as trimethylsilyl ether (TMS-HEMA).[9] Using this approach, P(HEMA-TMS) with M_n of up to 100,000 g/mol with M_w/M_n lower than 1.5 was prepared in bulk at 90 ^{o}C after 6 to 8 h. In 2001, Armes and coworkers reported ATRP of HEMA in methanol and binary mixtures of methanol and water at 20 ^{o}C.[12] Using CuBr or CuCl/bpy catalytic system, low molecular weight PHEMA (M_n less than 10,600) ($[M]_0/[I]_0$ = 10, 35 or 50) with narrow M_w/M_n (1.2 to 1.3) was obtained.[12, 13] CuX-catalyzed ATRP of HEMA in protic and polar aprotic solvents including methanol, isopropanol, dimethyl sulfoxide (DMSO), and tetrahydrofuran has been utilized for the synthesis of multiarm star poly(glycerol)-*b*-PHEMA,[14] block copolymers of HEMA and 2-(dimethylamino)ethyl methacrylate[15-17] or 2-(diisopropylamino)ethyl methacrylate,[16, 17] and poly(lactide)-*b*-PHEMA.[18] More recently, well-defined PHEMA was prepared by activator generated by electron transfer ATRP (AGET-ATRP) in a protic solvent (3/2 v/v mixture of methyl ethyl ketone and methanol),[19] and activator regenerated by electron transfer (ARGET ATRP) in methanol.[20] In both cases, it was proposed by CuX_2 was reduced *in situ* by a reducing agent such as tin(II) 2-ethylhexanoate ($Sn(EH)_2$),[19] ascorbic acid and hydrazine[20] to the active catalyst CuX which reacts with the alkyl halide initiator to generate the propagating radical and CuX_2. The latter is accumulated *via* the persistent radical effect[21] from the irreversible bimolecular termination at the earlier stages of

the polymerization.[11] Regardless of the nature of the active catalyst, previous ATRP conditions generally targeted only $[M]_0/[I]_0$ lower than 800.

Cu(0)-mediated single-electron transfer living radical polymerization (SET-LRP) was first reported in 2002.[22-24] It allows the ultrafast synthesis of vinyl polymers including ultrahigh molecular weight polymers[25, 26] at mild conditions even in the presence of a radical inhibitor[27] or air.[23, 28] The crucial feature of SET-LRP is that the polymerization relies on the disproportionation of CuX generated *in situ* from the heterogeneous SET activation of alkyl halide initiator to regenerate the extremely reactive Cu(0) activator and CuX_2 deactivator.[22, 23] Thus, by contrast to other metal catalyzed LRP such as ATRP, the accumulation of CuX_2 deactivator is achieved without the need for bimolecular termination, leading to the perfect or near perfect retention of the polymer chain-end functionality when the polymerization was performed in disproportionating solvents such as DMSO.[23, 26, 29, 30] The use of a simple Cu(0) powder[23] or Cu(0) wire[23, 31] catalyst, and a ligand/polar solvent combination[32-34] that promotes the disproportionation of CuX makes Cu(0)-mediated SET-LRP an attractive option for the synthesis of hydrophilic polymers in polar media. It should be noted that the formation of Cu(0) nanoparticles and soluble CuX_2 by the disproportionation of CuX/N-ligand was observed in all solvents utilized in the previously reported CuX-mediated ATRP of HEMA such as MeOH,[12, 14, 17, 19, 20] isopropanol,[9, 15] DMSO,[15, 18] THF[15] and their binary mixtures with water.[12, 13] These results suggest that the previously reported CuX-based ATRP of HEMA[9-20] proceed *via* a SET-LRP mechanism in which CuX disproportionates to generate *nascent* Cu(0) activator and CuX_2 deactivator.

In recent publications, the efficient SET-LRP of hydrophilic monomers including acrylamides,[34b] oligo(ethylene oxide) methyl ether acrylate (OEOMEA)[35] and 2-hydroxyethyl acrylate (HEA)[36] was demonstrated in protic and dipolar aprotic solvents. Here, we report the synthesis of PHEMA at different $[M]_0/[I]_0$ ($[M]_0/[I]_0$ = 100 to 10,000) *via* SET-LRP in the disproportionating solvent DMSO.

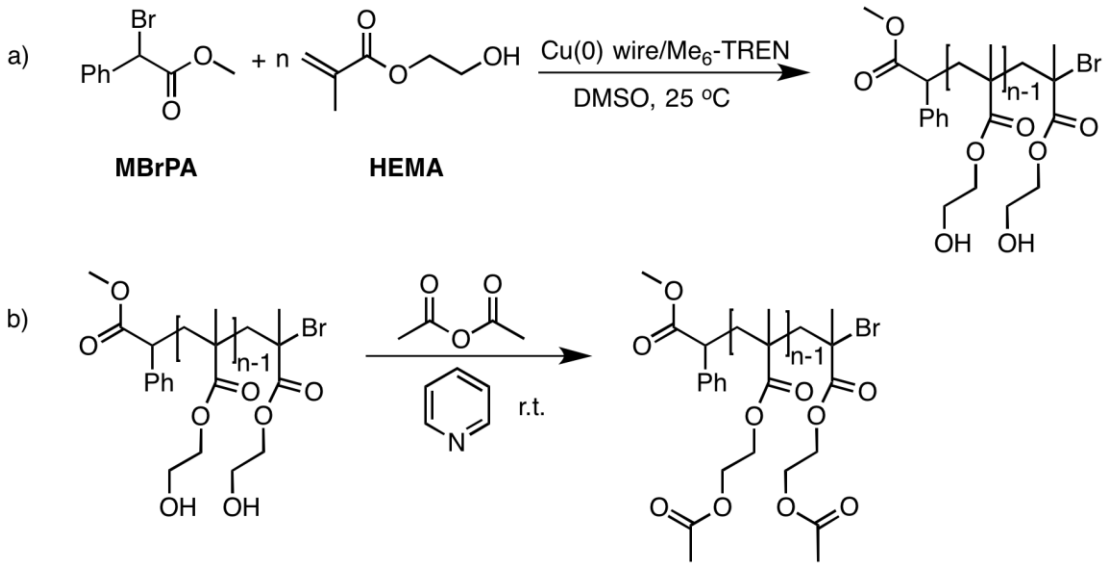
To the best of our knowledge, high molecular weight PHEMA at $[M]_0/[I]_0$ greater than 800 has not be reported before.

Results and Discussion

SET-LRP of HEMA in DMSO at $[M]_0/[I]_0 = 100$

In this study, SET-LRP of HEMA was performed in DMSO at 25 ^oC using methyl α-bromophenylacetate (MBrPA) as initiator (Scheme 1a). DMSO was selected as solvent due to its highly polar nature required for the solubilization of HEMA and PHEMA in the polymerization mixture. In addition, DMSO is considered as one of the most effective solvents for SET-LRP. In combination with a ligand such as Me_6-TREN that preferentially stabilizes CuX_2 over CuX,[32] promotes extensive disproportionation of CuX[23, 33] and stabilizes the resulting Cu(0) nanoparticles.[33, 34] Polymers prepared by SET-LRP in DMSO during catalysis with very small surface area Cu(0) wire catalysts retain perfect or near perfect chain-end functionality[31, 37] even at complete monomer conversion.[26, 29, 38]

SET-LRP of HEMA at $[M]_0/[I]_0$ = 100 was performed under the following conditions: $[HEMA]_0/[MBrPA]_0/[Me_6\text{-TREN}]_0$ = 100/1/0.1, HEMA = 1 mL, DMSO = 1 mL, hydrazine-activated Cu(0) wire of 4.5 cm of 20 gauge wire (diameter = 0.0812 cm). PHEMA is not soluble in THF which is a common solvent used for the determination of molecular weight by gel permeation chromatography (GPC). Therefore, the polymer samples obtained at different time intervals were acetylated using acetic anhydride and pyridine as base, purified by precipitation in cold MeOH, and analyzed by a THF-based GPC (Scheme 1b).[39] The theoretical molecular weight M_{th} was calculated based on the molecular weight of the acetylated monomer (M_{th} = 172.18 x $[M]_0/[I]_0$ x conv. + $M_{Initiator}$).



Scheme 1. SET-LRP of HEMA Catalyzed by Cu(0) Wire/Me_6-TREN at 25 ^{o}C in DMSO

Figure 1a,b shows the kinetics of Cu(0)-wire catalyzed SET-LRP of HEMA in DMSO at $[M]_0/[I]_0$ = 100. The polymerization exhibit linear kinetics in the monomer concentration and propagating radicals with k_p^{app} = 0.0057 min^{-1} (Figure 1a), and linear evolution of the experimental molecular weight (M_n (GPC)) with the theoretical values and narrow molecular weight distribution. M_w/M_n values are lower than 1.30 at all conversions (Figure 1b). Figure 2 shows the GPC chromatograms of PHEMA obtained at different conversions during the SET-LRP of HEMA in DMSO at $[M]_0/[I]_0$ = 100. The chromatograms are symmetrical at all conversions, and the molecular weight distribution narrows as the polymerization proceeds. These results demonstrate a living radical polymerization. SET-LRP of HEMA reached 91% conversion in 7 h, and provided PHEMA with M_n = 21,500 g/mol and M_w/M_n = 1.20 (Table 1, entry 1) (Figure 2).

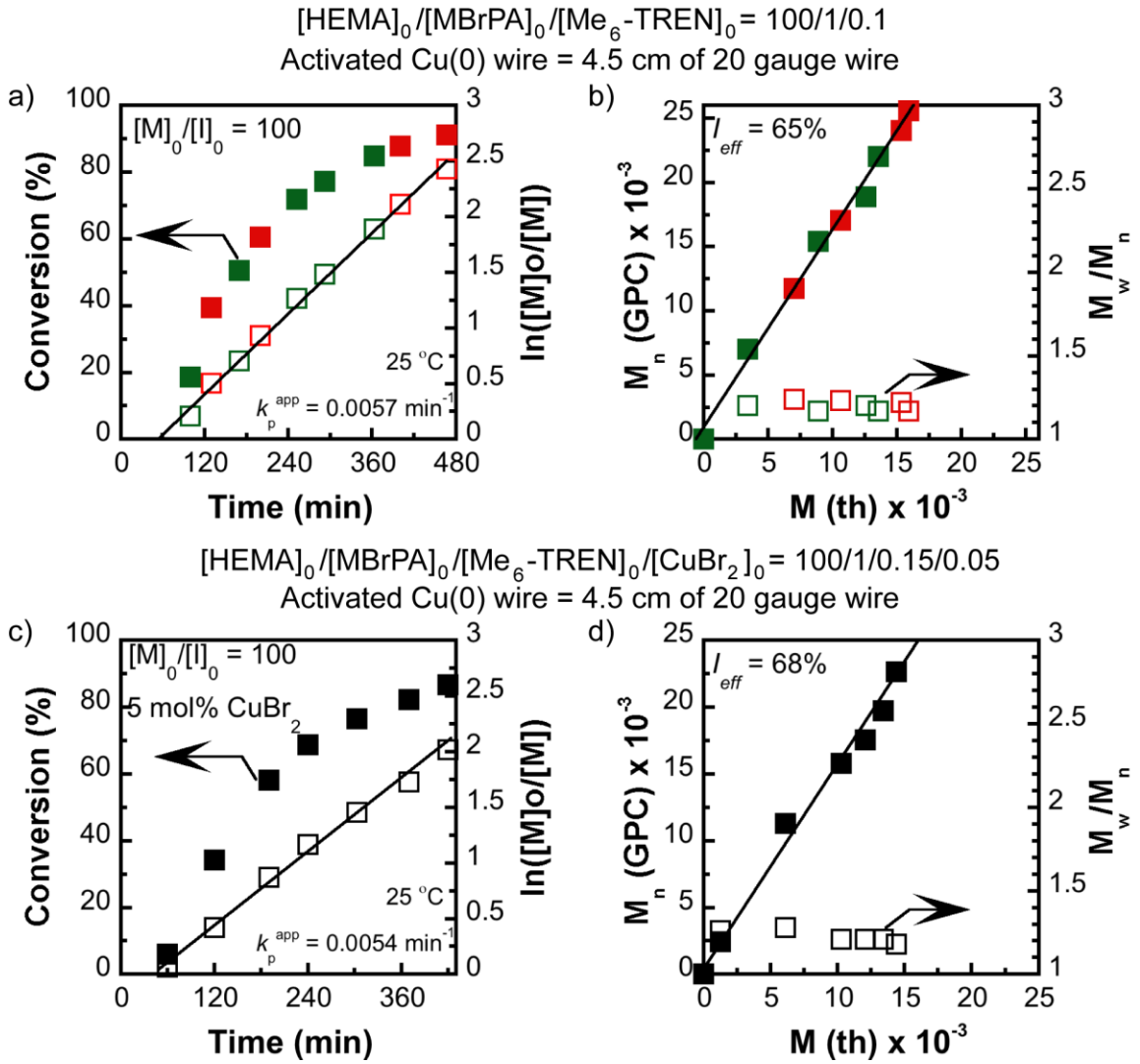


Figure 1. Conversion and ln([M]$_0$/[M]) *vs* time kinetic plots (a and c); and experimental M_n and M_w/M_n *vs* theoretical M_{th} (b and d); in SET-LRP of HEMA in DMSO at 25 ^{o}C. Reaction conditions: HEMA = 1 mL, DMSO = 1 mL, (a, b) [HEMA]$_0$/[MBrPA]$_0$/[Me$_6$-TREN]$_0$ = 100/1/0.1, (c, d) [HEMA]$_0$/[MBrPA]$_0$/[Me$_6$-TREN]$_0$/[CuBr$_2$]$_0$ = 100/1/0.15/0.05. Hydrazine-activated Cu(0) wire of 4.5 cm of 20 gauge (diameter = 0.0812 cm). In Fig 1a,b, two sets of experimental data, plotted in different colors, are overlapped.

Table 1. Cu(0) Wire-Catalyzed SET-LRP of HEMA Initiated with MBrPA in DMSO at 25 °C at Different $[M]_0/[I]_0$. Polymerization Conditions: $[MBrPA]_0/[Me_6\text{-TREN}]_0$ = 1/0.1, HEMA = 1 mL, DMSO = 1 mL, Hydrazine-Activated Cu(0) Wire of 4.5 cm of 20 Gauge (diameter = 0.0812 cm).

No.	$[M]_0/[I]_0$	k_p^{app} (min^{-1})	Time (min)	Conv (%)	M (th) (g/mol)	M_n (GPC) (g/mol)	M_w/M_n	I_{eff} (%)
1	100	0.0057	420	91	15,900	21,500	1.20	65
2[a]	100	0.0054	420	87	15,160	22,640	1.22	68
3	200	0.0054	400	84	29,090	35,180	1.28	80
4	400	0.0035	580	86	54,160	66,280	1.28	82
5	800	0.0028	540	78	106,980	152,220	1.39	73
6[b]	2000	0.0020	480 2520	65 81	224,060 279,160	333,700 352,300	1.47 1.41	70
7[b,c]	5000	0.0016	455	51	441,010	628,200	1.55	74
8[b,c]	7500	0.0015	600	58	753,090	975,400	1.50	73
9[b,c]	10000	0.0006	420 2880	44 56	764,710 957,550	986,700 1,017,900	1.60 1.49	75

[a]5 mol% $CuBr_2$ with respect to MBrPA concentration was used. $[HEMA]_0/[MBrPA]_0/[Me_6\text{-TREN}]_0/[CuBr_2]_0$ = 100/1/0.15/0.05.[b]$[MBrPA]_0/[Me_6\text{-TREN}]_0$ = 1/0.15. [c]HEMA = 0.5 mL, DMSO = 1 mL.

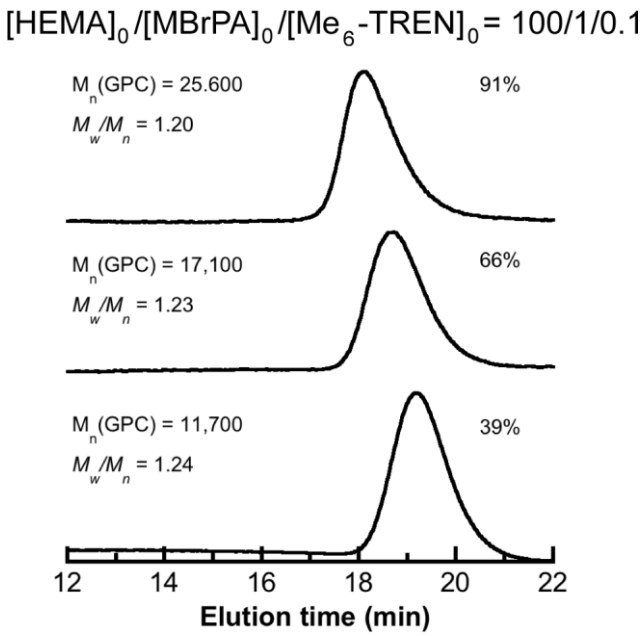


Figure 2. GPC chromatogram at different conversions from SET-LRP of HEMA in DMSO at 25 °C. Reaction conditions: HEMA = 1 mL, DMSO = 1 mL, $[HEMA]_0/[MBrPA]_0/[Me_6\text{-TREN}]_0$ = 100/1/0.1, hydrazine-activated Cu(0) of wire 4.5 cm of 20 gauge (diameter = 0.0812 cm).

The initiator efficiency (I_{eff}) was calculated to be 65% for the SET-LRP of HEMA at $[M]_0/[I]_0$ = 100 (Figure 1b). The formation of PHEMA with higher GPC molecular weight than the theoretical values has been reported from several laboratories.[9, 12, 20] This difference was attributed to the calibration errors in the GPC analysis such that GPC analysis overestimated the true molecular weight of PHEMA. For $[M]_0/[I]_0$ lower than 120, GPC molecular weight can be 2-6 times higher than the true molecular weight of PHEMA depending on the type of polymer standards used for the calibration of the GPC.[9, 12, 20]

SET-LRP of HEMA at $[M]_0/[I]_0$ = 100 exhibits a short induction period of 45 min. In the presence of 5 mol% externally added $CuBr_2$ deactivator with respect to initiator concentration under otherwise identical condition, the polymerization still exhibit a short induction time of 40 min and identical initiator efficiency (I_{eff} = 68%) (Figure 2c,d) (Table 1, entry 2). This indicates that the presence of an induction period does not affect the initiator efficiency, and that the low I_{eff} = 68% is more likely a result of the error of the GPC calibration. Therefore, SET-LRP of HEMA targeting higher $[M]_0/[I]_0$ values was performed in DMSO in the absence of externally added $CuBr_2$.

SET-LRP of HEMA at $[M]_0/[I]_0$ = 200 – 800

Table 1 entries 3-5 show the results for SET-LRP of HEMA at $[M]_0/[I]_0$ = 200 to 800**.** As the targeted molecular weight at complete monomer conversion becomes higher, the apparent rate constant of propagation decreases from 0.0057 min^{-1} ($[M]_0/[I]_0$ = 100) to 0.0028 min^{-1} ($[M]_0/[I]_0$ = 800).

Figure 3 shows the kinetics of SET-LRP of HEMA at = 400 and 800. In both cases linear kinetics and linear evolution of the experimental M_n with the theoretical values are observed. PHEMA of M_n = 66,280 g/mol and M_w/M_n = 1.28 (Figure 3a) and M_n = 155,220 g/mol, M_w/M_n = 1.39 can be obtained within 10 h.

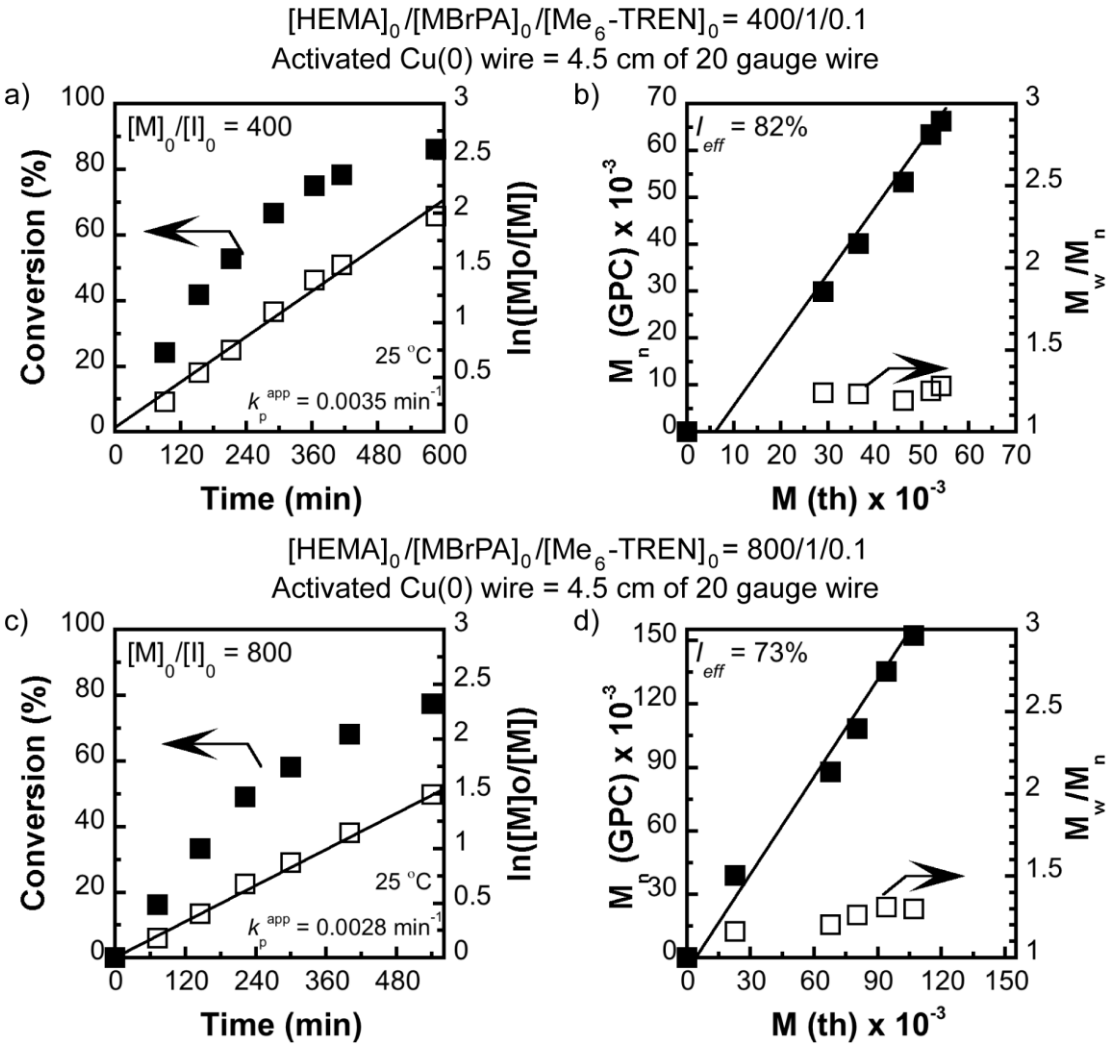


Figure 3. Conversion and ln([M]$_0$/[M]) *vs* time kinetic plots (a and c); and experimental M_n and M_w/M_n *vs* theoretical M_{th} (b and d); in SET-LRP of HEMA in DMSO at 25 ^oC. Reaction conditions: HEMA = 1 mL, DMSO = 1 mL, (a, b) [HEMA]$_0$/[MBrPA]$_0$/[Me$_6$-TREN]$_0$ = 400/1/0.1, (c, d) [HEMA]$_0$/[MBrPA]$_0$/[Me$_6$-TREN]$_0$ = 800/1/0.1. Hydrazine-activated Cu(0) wire of 4.5 cm of 20 gauge (diameter = 0.0812 cm).

Synthesis of Ultrahigh Molar Mass PHEMA *via* SET-LRP at [M]$_0$/[I]$_0$ = 2,000 to 10,000

SET-LRP of HEMA at [M]$_0$/[I]$_0$ = 2,000 was first performed under the following conditions: [HEMA]$_0$/[MBrPA]$_0$/[Me$_6$-TREN]$_0$ = 2,000/1/1, HEMA = 1 mL, DMSO = 1 mL, activated Cu(0) wire 4.5 cm of 20 gauge. However, the polymerization reached a limited conversion of 30% even after a long reaction time. Interestingly, by reducing the ligand concentration from 1 to 0.15 eq with respect to initiator concentration, the polymerization of HEMA exhibit a linear kinetics reaching 65%

conversion after 8 h and 81% after 42 h with k_p^{app} = 0.0020 min^{-1} (Figure 4a). It should be noted that the use of less than 0.15 eq Me_6-TREN led to the formation of a high molecular weight polymer at low conversion, while at higher ligand concentration, the polymerization did not proceed beyond 40% conversion. Figure 4b shows the linear dependence of the experimental M_n with the theoretical values, and relatively narrow molecular weight distribution. At $[M]_0/[I]_0$ = 2,000, PHEMA obtained at 60% and 81% conversion has M_w/M_n = 1.47 (M_n = 333,200 g/mol) and 1.41 (M_n = 352,300 g/mol), respectively (Figure 4b, Table 1, entry 6) (Figure 5).

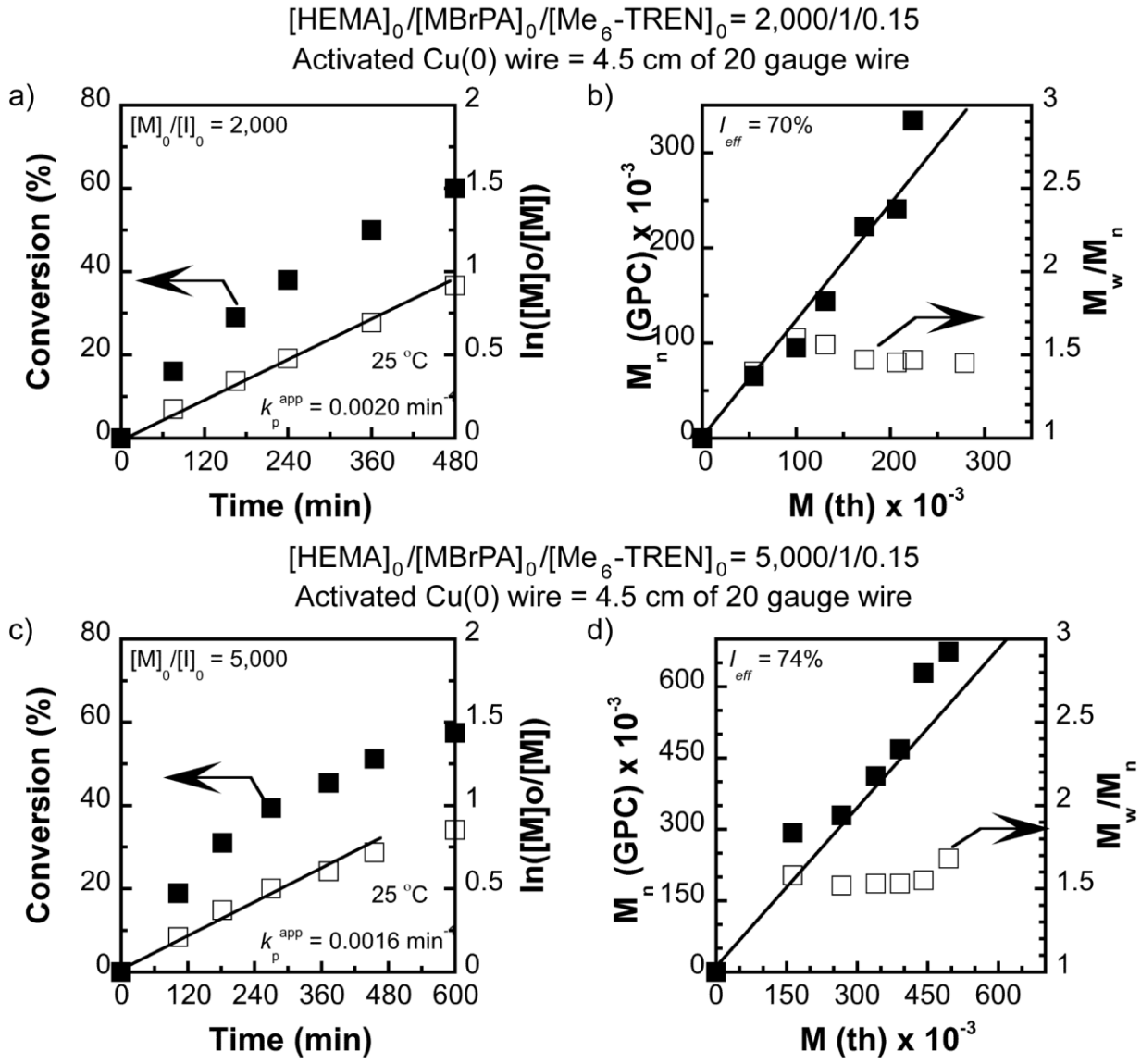


Figure 4. Conversion and ln([M]$_0$/[M]) *vs* time kinetic plots (a and c); and experimental M_n and M_w/M_n *vs* theoretical M_{th} (b and d); in SET-LRP of HEMA in DMSO at 25 ^{o}C. Reaction conditions: (a,

b) HEMA = 1 mL, DMSO = 1 mL, $[HEMA]_0/[MBrPA]_0/[Me_6\text{-}TREN]_0$ = 2,000/1/0.15, (c, d) HEMA = 0.5 mL, DMSO = 1 mL, $[HEMA]_0/[MBrPA]_0/[Me_6\text{-}TREN]_0$ = 5,000/1/0.15. Hydrazine-activated Cu(0) wire of 4.5 cm of 20 gauge (diameter = 0.0812 cm).

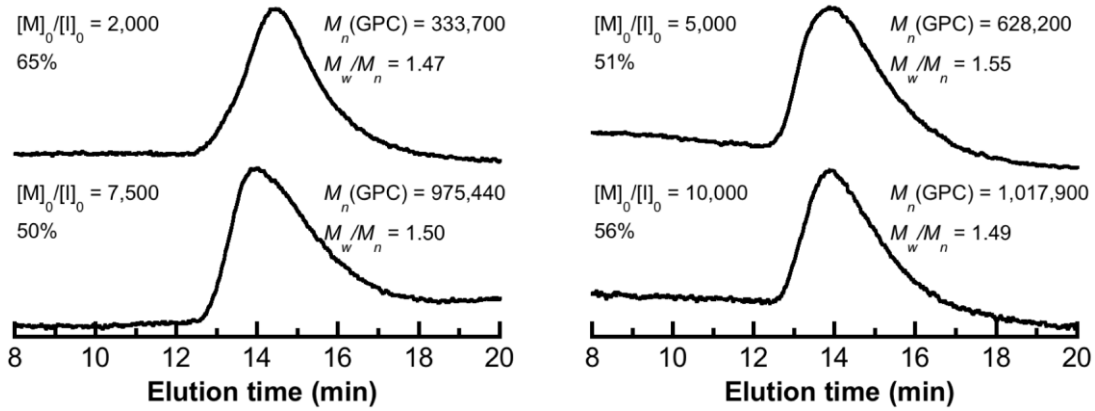


Figure 5. GPC chromatograms from SET-LRP of HEMA in DMSO at 25 ^oC at different $[M]_0/[I]_0$. Reaction conditions: HEMA = 0.5 mL, DMSO = 1 mL, $[MBrPA]_0/[Me_6\text{-}TREN]_0$ = 1/0.15, hydrazine-activated Cu(0) wire of 4.5 cm of 20 gauge (diameter = 0.0812 cm).

At higher targeted $[M]_0/[I]_0$, $[M]_0/[I]_0$ = 5,000 to 10,000, the volume ratio between HEMA and DMSO was increased (HEMA = 0.5 mL, DMSO =1 mL, HEMA/DMSO = 1/2 v/v) to alleviate the high viscosity of the polymerization at higher targeted molecular weight. From Figure 4c,d, SET-LRP of HEMA proceeded with k_p^{app} = 0.0016 min^{-1}, reaching 51% conversion after 7.5 h and providing PHEMA with M_w/M_n = 1.55 (M_n = 628,200 g/mol) (Figure 5). It should be noted that the viscosity of the reaction mixture was so high that no stirring was possible (Figure 6). Ineffective mixing of the reaction mixture may explain why the polymerization did not reach higher conversion even after a longer reaction time.

Figure 5. Viscosity observed at 50% conversion in SET-LRP of HEMA at $[M]_0/[I]_0$ = 5,000 at 25 ^oC. Reaction conditions: HEMA = 0.5 mL, DMSO = 1 mL, $[HEMA]_0/[MBrPA]_0/[Me_6\text{-TREN}]_0$ = 5000/1/0.15, hydrazine-activated Cu(0) wire of 4.5 cm of 20 gauge (diameter = 0.0812 cm).

In view of the previous results, the synthesis of PHEMA of ultrahigh high molar mass was attempted at $[M]_0/[I]_0$ = 7,500 and 10,000 (Figure 6, Table 1, entries 8-9). Figure 6 shows that PHEMA with M_n = 975,400 and 1,017,900 g/mol can be obtained with M_w/M_n = 1.50.

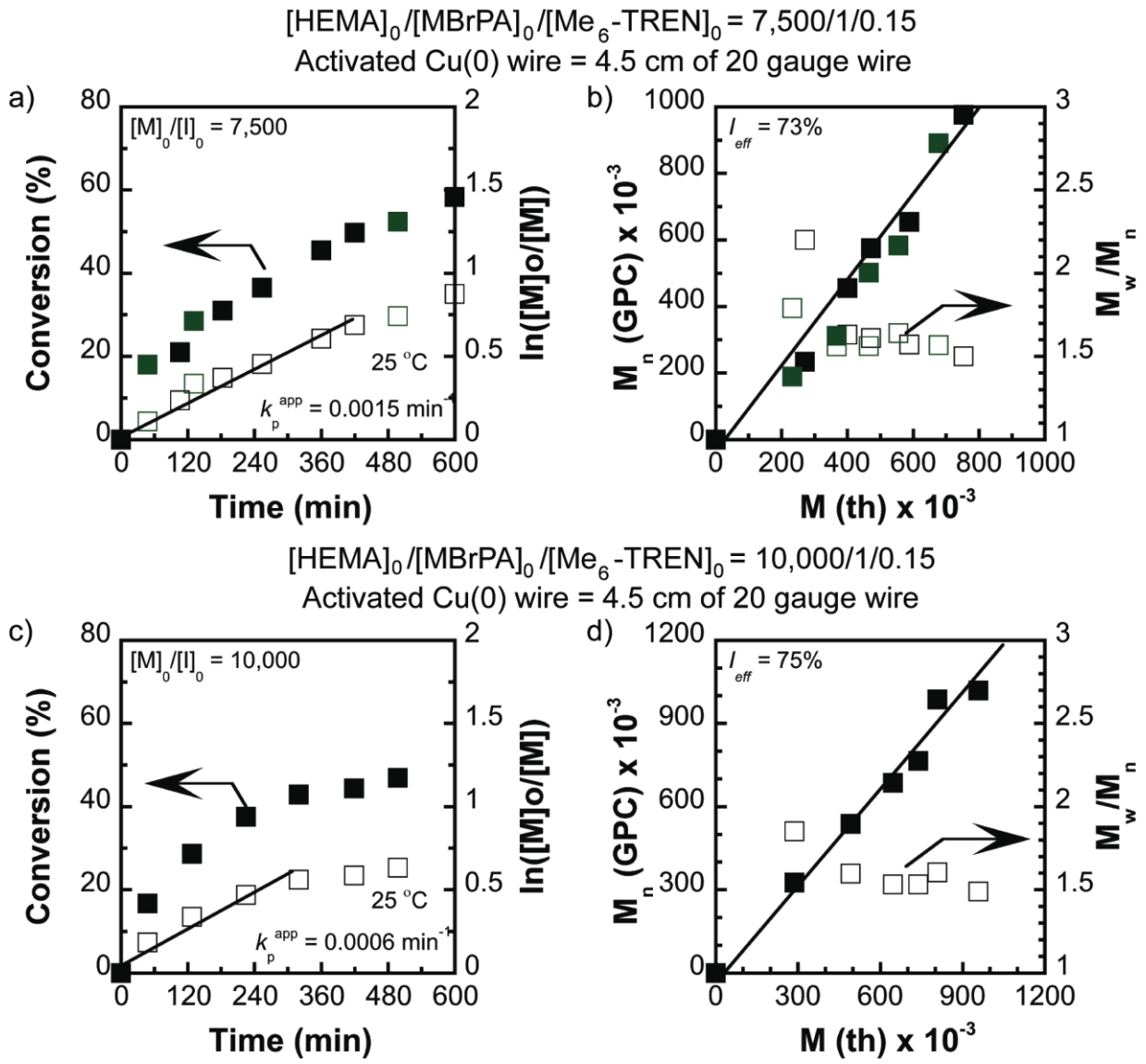


Figure 6. Conversion and ln([M]$_0$/[M]) *vs* time kinetic plots (a,c); and experimental M_n and M_w/M_n *vs* theoretical M_{th} (b,d); in SET-LRP of HEMA in DMSO at 25 ^{o}C. Reaction conditions: HEMA = 0.5 mL, DMSO = 1 mL, (a,b) [HEMA]$_0$/[MBrPA]$_0$/[Me$_6$-TREN]$_0$ = 7,500/1/0.15; (c,d) [HEMA]$_0$/[MBrPA]$_0$/[Me$_6$-TREN]$_0$ = 10,000/1/0.15. Hydrazine-activated Cu(0) wire of 4.5 cm of 20 gauge (diameter = 0.0812 cm).

Inspired by the previous reports[23, 25] demonstrating Cu(0) powder/Me$_6$-TREN in DMSO an as an efficient methodology for the synthesis of ultrahigh molecular weight PMA with M_n in the range of 1,500,000 and narrow molecular weight distribution, SET-LRP of HEMA at [M]$_0$/[I]$_0$ = 10,000 was performed using Cu(0) powder as catalyst under the following conditions: [HEMA]$_0$/[MBrPA]$_0$/[Cu(0)]$_0$/[Me$_6$-TREN]$_0$ = 10,000/1/1/1, HEMA = 0.5 mL, DMSO = 1 mL, Cu(0)

45 μm. However, the polymerization did not proceed beyond 37% conversion (k_p^{app} = 0.0007 min^{-1}), providing PHEMA with M_n = 1,173,300 g/mol and broader (M_w/M_n = 2.04) after 8.5 h. Therefore, the catalysis with Cu(0) wire/Me_6-TREN is preferred in this case for the synthesis of ultrahigh molecular weight PHEMA.

The results provided here demonstrated that ultrahigh molar mass PHEMA with M_n = 100,000 to 1,017,900 g/mol and M_w/M_n lower than 1.50 could be synthesized for the first time by direct polymerization of HEMA without protecting the hydroxyl group at 25 ^oC. As mentioned in the previous section, PHEMA with M_{th} = 100,000 g/mol and M_w/M_n lower than 1.5 could only be obtained by CuX-mediated ATRP in bulk at 90 ^oC after 9 h by protecting the hydroxyl group as TMS ether.[9] This demonstrates the significantly less termination and much higher rate of polymerization of SET-LRP of HEMA at 25 ^oC than those in previous metal-catalyzed LRP of HEMA in bulk at higher temperature.[9]

Conclusion

SET-LRP of HEMA was performed in DMSO at 25 ^oC using MBrPA as initiator and targeting $[M]_0/[I]_0$ =100 to 10,000). At $[M]_0/[I]_0$ = 100, SET-LRP of HEMA in DMSO was effective, providing first order kinetics, linear evolution of experimental molecular weight with theoretical values, and narrow molecular weight distribution (M_w/M_n = 1.20). Using similar conditions, high molecular weight PHEMA ranging from M_n = 35,180 to 152,200 g/mol, $[M]_0/[I]_0$ = 200 to 800, can be prepared with M_w/M_n lower than 1.4 within 9 h at 25 ^oC. By contrast, PHEMA of only up to 100,000 in molar mass and M_w/M_n lower than 1.5 can only achieved by CuX-mediated polymerization of TMS-protected HEMA in bulk at much higher temperature (90 ^oC). When targeting higher $[M]_0/[I]_0$ = 2,000 to 10,000, the ligand concentration was adjusted to 0.15 equivalent with respect to initiator concentration. At higher ligand loadings, the polymerization of HEMA reached limited conversion, while the formation of a high molecular weight PHEMA at low conversion was observed at a lower

ligand concentration. Under the following conditions, $[MBrPA]_0/[Me_6\text{-TREN}]_0$ = 1/0.15, HEMA = 0.5 mL, DMSO = 1 mL, activated Cu(0) wire of 4.5 cm of 20 gauge, ultrahigh molar mass PHEMA with M_n = 352,300 to 1,017,900 g/mol and M_w/M_n lower than1.50 could be synthesized for the first time by direct polymerization of HEMA without protecting the hydroxyl group.

Experimental

Materials

Ethanol (EtOH) (Decon Laboratories, 200 proof), N-bromosuccinimide (NBS) (Acros), benzoyl peroxide (Sigma-Aldrich, 97%), carbon tetrachloride (CCl_4) (Sigma-Aldrich, 99.9%), sulfuric acid (H_2SO_4) (95.6%) (Fisher) and methanol (Fisher, Certified ACS, 99.9%) were used as received. Copper (0) wire (20 gauge wire, 0.812 mm diameter, Fischer) was activated with hydrazine hydrate (Acros, hydrazine 64%) according to a previously developed procedure.[40] Dimethyl sulfoxide (DMSO) (Fisher, Certified ACS, 99.9) was distilled over CaH_2 and kept in a glovebox. *Tris*[2-(dimethylamino)ethyl]amine (Me_6-TREN) was synthesized as described in the literature.[41]

2-Hydroxyethyl methacrylate (Acros, 97%) was purified as follows:[42] a solution of HEMA in water (20% v/v) was extracted 10 times with hexane to remove the ethylene glycol diacrylate. The aqueous layer was salted with NaCl (200 g/L). The monomer was then separated from the aqueous layer by extraction with diethyl ether (4 times). Hydroquinone (0.05 weight%) was added to the diethyl ether layer. The ether layer was dried over $MgSO_4$, filtered and evaporated in rotary evaporator at 35 ^oC. The monomer was obtained *via* distillation at 80 ^oC under reduced pressure (0.05 mmHg).

Techniques. 500 MHz ^1H NMR spectra were recorded on a Bruker DRX500 NMR instrument at 23 ^oC in d^6-DMSO. Gel Permeation Chromatography (GPC) analysis of the polymer samples were done on a Perkin-Elmer Series 10 high-performance liquid chromatography, equipped with an LC-100 column oven (30 ^oC), 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, 5μm; 1000 Å, 5μm; and 10^4 Å, 5μm). 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.

Synthesis of Methyl α-Bromophenylacetate (MBrPA). MBrPA is commercially available. It can be synthesized by bromination of methyl 2-phenylacetate using *N*-bromosuccinimide or with $NaBrO_3/NaHSO_3$ in H_2O/ethyl acetate mixture.[43] To a 100 mL round bottom flask was added *N*-bromosuccinimide (7.8 g, 0.044 mol)**,** benzoyl peroxide (10 mol%) (1.07 g, 0.0044 mol), methyl 2-phenylacetate (6g, 0.04 mol) and CCl_4 (25 mL). The reaction was heated under reflux at 85 ^oC overnight. The reaction mixture was filtered and the filtrate was removed in a rotary evaporator. The initiator was obtained by column chromatography as a yellowish oil (SiO_2, 0-10% ethyl acetate in hexane). Yield: 50% ^1H NMR (500 MHz, $CDCl_3$, Me_4Si, δ) 7.56 – 7.54 (2H, m, Ar*H)*, 7.37 – 7.35 (3H, m, Ar*H*), 5.37 (1H, s, ArC*H*CO_2CH_3), 3.79 (3H, s, -CO_2C*H*$_3$). ^{13}C NMR (500 MHz, $CDCl_3$, Me_4Si): 168.95, 135.90, 129.47, 129.00, 128.80, 53.53, 46.67.

Typical Procedure for SET-LRP of HEMA at 25 ^{o}C in DMSO. In a 25 mL Schlenk tube, the reagents were added in the following orders under gentle stirring: MBrPA (18.9 mg, 12.9 μL, 0.082 mmol), monomer (HEMA, 1 mL, 8.24 mmol), ligand (Me_6-TREN, 1.9 mg, 2.2 μL, 8.2 μmol) and solvent (DMSO, 1 mL). When the polymerization was performed at a higher degree of polymerization a stock solution of MBrPA and Me_6-TREN in DMSO was prepared. To reduce the viscosity of the polymer with high molecular weight, 0.5 mLHEMA in 1 mL DMSO was used. The mixture was deoxygenated using seven freeze-pump-thaw cycles from a dry ice/acetone bath. 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 25 ^oC with stirring. The side arm of the flask was purged with argon before it was opened for sampling at the predetermined times with an airtight syringe. At each time, a small amount

of the sample was dissolved in d^6-DMSO for the analysis of monomer conversion by ^{1}H 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). Then the polymer was precipitated in cold MeOH. After centrifuging and several rinsing with MeOH, the polymer precipitate was collected, dried and dissolved in THF and used for GPC analysis. The theoretical M_n was calculated based on the molecular weight of the acetylated monomer (M_n = 172.18 x $[M]_0/[I]_0$ x conv. + $M_{Initiator}$).

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