



## Aqueous Copper(0) Mediated Reversible Deactivation Radical Polymerization of 2-Hydroxyethyl Acrylate

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Reversible deactivation radical polymerization (RDRP) of 2-hydroxyethyl acrylate in D<sub>2</sub>O with Cu(0) wire mediation and with two-step Cu(0) *in situ* mediation was investigated. The concentration of active species on the Cu(0) surface, which was influenced by Cu(0) type (wire or particle), polymer chain length, and activator and deactivator concentration, was the key factor in understanding the formation of insoluble gel with Cu(0) wire and/or a high molecular weight (MW) shoulder observed in the polymer molar mass distributions (MMDs). The influences of temperature, residual oxygen (dependent on the transfer procedure used to add reagents), and NaBr addition were also studied. The insights gained were used to produce P(HEA) with high molar mass [target chain length (TCL) = 400, 87% conversion, Đ = 1.16] using only *ca.* 250 ppm copper at room temperature, the first reported preparation of high MW P(HEA) with a low Đ using such a low copper catalyst concentration in a purely aqueous environment.

### Introduction

Poly(2-hydroxyethyl acrylate) hydrogels synthesized by radical polymerization of 2-hydroxyethyl acrylate (HEA) have wide utility in biomedical and biomaterial applications.<sup>1</sup> The potential to produce well defined P(HEA) and its block copolymers through reversible deactivation radical polymerization (RDRP) techniques [atom transfer radical polymerization (ATRP),<sup>2-5,11</sup> single electron transfer-living radical polymerization (SET-LRP),<sup>9,10,12-16</sup> nitroxide-mediated polymerization (NMP),<sup>17</sup> and reversible addition-fragmentation chain transfer (RAFT)<sup>18,19</sup>] is thus of considerable interest. In particular, a number of studies explore the synthesis of P(HEA) through metal-catalyzed RDRP techniques. Coca *et al.*<sup>2</sup> first used the Cu(I)Br/2-2'-bipyridine (bpy) system to mediate HEA polymerization in bulk and in aqueous solution with 10,000 ppm catalyst (molar ratio of copper to monomer); 87% conversion was achieved after 12 h at 90 °C, with a polymer dispersity (Đ) of 1.34 achieved. Later ATRP efforts used the ligands N,N',N'',N'''-pentamethyldiethylenetriamine (PMDETA) at 80 °C in both bulk<sup>3</sup> and at 50 °C in toluene solvent,<sup>4</sup> and tris[2-(dimethylamino)ethyl]amine (Me<sub>6</sub>TREN) in bulk<sup>5</sup> at room temperature to produce P(HEA) and its block copolymer with *n*-butyl acrylate;<sup>3</sup> in these studies catalyst concentration remained high, between 5,000 and 33,000 ppm. One of the goals of the current effort is to reduce the amount of catalyst for P(HEA) production.

Cu(0) mediated RDRP has attracted significant attention since first reported by Percec *et al.*<sup>6</sup> as a method to synthesize polymers with narrow molar mass distributions and high chain-end functionality at high rate at room temperature or below. Two mechanisms, SET-LRP<sup>7</sup> and supplemental activator and reducing agent (SARA) ATRP<sup>8</sup> were proposed to explain the Cu(0) mediated RDRP, with the debate in the literature ongoing. This method has also been used to synthesize P(HEA) with mixed success, depending on the Cu(0) source and the solvent, which can significantly influence the degree of disproportionation,<sup>20</sup> utilized. Using Cu(0) wire, Nicol *et al.*<sup>9</sup> reported P(HEA) synthesis in dimethyl sulfoxide (DMSO) with Me<sub>6</sub>TREN; DMSO has been used to polymerize the analogous monomer 2-hydroxyethyl methacrylate (HEMA) to number average molecular weight (M<sub>n</sub>) up to 1,000,000 Da and Đ less than 1.5.<sup>21</sup> In the work of Nicol *et al.*,<sup>9</sup> polymerizations of HEA were conducted with PMDETA in DMSO, and with Me<sub>6</sub>TREN, PMDETA and tris(2-aminoethyl)amine (TREN) in water. Target chain length (TCL) was 30, and Cu(II)Br<sub>2</sub> was added to the system such that P(HEA) with high conversion and very low Đ (1.07) was produced at 25 °C using a molar ratio of [Initiator]<sub>0</sub>:[Me<sub>6</sub>TREN]<sub>0</sub>:[Cu(II)Br<sub>2</sub>]<sub>0</sub>=1:0.11:0.05; thus the catalyst concentration was higher than 1600 ppm, even neglecting the contribution of copper species from the Cu(0) wire. Later, Leng *et al.*<sup>10</sup> reported using Cu(0) wire with Me<sub>6</sub>TREN in pure water as well as in a binary mixture of methanol and water (30 vol% MeOH) to synthesize P(HEA); in contrast to the findings of Nicol *et al.*,<sup>9</sup> a significant fraction of insoluble gel was formed for TCL=200, and the best reported Đ value was 1.46. Konkolewicz *et al.*<sup>11</sup> successfully produced block copolymer of HEA with oligo(ethylene oxide) monomethyl ether acrylate of molecular weight 480 to form both P(OEOA<sub>480</sub>) homopolymer and P[(OEOA<sub>480</sub>)<sub>50</sub>-b-(HEA)<sub>100</sub>] block copolymer with Đ of 1.24

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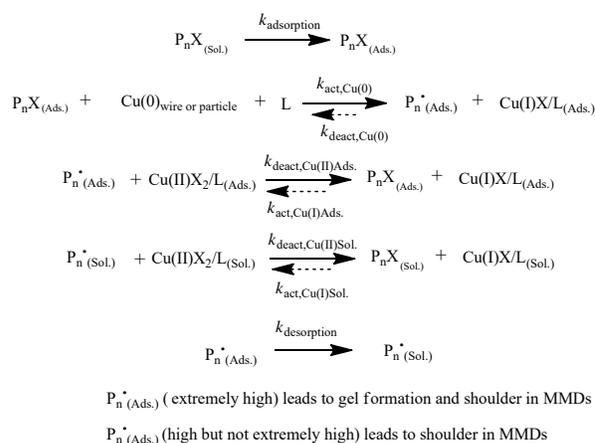
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in water with measured *ca.* 600 ppm soluble copper at 22 °C using Cu(0) wire with Me<sub>6</sub>TREN and 200 ppm initial Cu(II)Br<sub>2</sub>. Most recently, Samanta *et al.* reported the successful synthesis of well-defined P(HEA) in 2,2,2-trifluoroethanol<sup>12a</sup> and in 2,2,3,3-tetrafluoropropanol<sup>12b</sup> with TCL=200. However, in water<sup>12c</sup> the formation of thick gel on the Cu(0) wire surface was observed for even TCL=20 when synthesizing P(HEA) with Me<sub>6</sub>TREN; the gel formation was suppressed by addition of extra Cu(II)Br<sub>2</sub> (10,000 ppm) to the system to form P(HEA) with  $\bar{D}$ =1.21. The authors proposed that in water the high concentration of propagating radicals adsorbed on the Cu(0) wire surface undergo crosslinking reactions with neighbouring groups, with the reaction suppressed in the presence of added deactivator, a hypothesis that will be further explored in this work.

Rather than use copper wire or powder directly, Jiang *et al.*<sup>22</sup> reported that small “nascent” Cu(0) species prepared by disproportionation of Cu(I) were extremely active for polymerization of methyl acrylate. Feng *et al.*<sup>13,14</sup> used a similar procedure by which Cu(0) was generated *in situ* through disproportionation of Cu(I)Cl/Me<sub>6</sub>TREN in dimethylformamide (DMF)/water (v/v 1/1); this novel SET-LRP implementation was used to synthesize poly(N-isopropylacrylamide-*b*-HEA) with  $\bar{D}$ =1.10 at 25 °C using 10,000 ppm catalyst. Nguyen *et al.*<sup>23</sup> reported using *in situ* Cu(0) catalyst created by full disproportionation of Cu(I)Cl with Me<sub>6</sub>TREN in methanol/water (v/v, 3/7) to synthesize poly(N,N-dimethylacrylamide). Employing a similar strategy, Zhang *et al.* further developed this approach to perform Cu(0) *in situ* mediated SET-LRP in pure water<sup>15</sup> and sheep serum.<sup>16</sup> In this procedure, which we will call two-step Cu(0) *in situ* mediation, Cu(I)Br/Me<sub>6</sub>TREN is first allowed to fully disproportionate in solution to Cu(0) (visible as dispersed particles) and Cu(II)Br<sub>2</sub> at a molar ratio of 1:1, with polymerization commencing after transfer of monomer and initiator to the solution using a cannula to avoid exposure to oxygen. A wide range of monomers were polymerized in aqueous solution using this new approach, including P(HEA) with TCL=20 and very low  $\bar{D}$ =1.07 at room temperature in water, and P(HEA) of the same chain length with  $\bar{D}$ =1.15 at 0 °C in sheep serum. In both cases, the catalyst concentration was high: 20,000 ppm (molar ratio of copper to monomer) in water and 40,000 ppm in sheep serum. In addition, although the molar mass distributions (MMD) had low dispersity, a small shoulder on the high MW side can be observed in the distributions presented as supporting information.<sup>15</sup>

Based on this review of the literature there is still significant work to be done to synthesize P(HEA) with low dispersity and high molar mass in water using reduced catalyst concentration (less than 500 ppm). As part of this exploration, we also address key mechanistic questions based on the heterogeneous Langmuir-Hinshelwood mechanism shown as Scheme 1,<sup>10,12c</sup> proposing possible reasons why insoluble gel is formed in aqueous solution during P(HEA) synthesis using Cu(0) wire and the cause of the high MW shoulder seen in

P(HEA) MMDs synthesized in aqueous Cu(0) mediation. In addition, we explore the effects of NaBr, temperature and adventitious oxygen on the polymerization of HEA in aqueous Cu(0) mediation. We demonstrate the production of comparatively high molecular weight P(HEA) [(M<sub>n,SEC</sub>=32400 Da,  $\bar{D}$ =1.16, 87% conversion, TCL=400), (M<sub>n,SEC</sub>=69540 Da,  $\bar{D}$ =1.35, 79% conversion, TCL=800)] using low catalyst concentration, *ca.* 250 ppm, at 22 °C in aqueous solution under not strictly oxygen-free conditions (transfer of monomer and initiator by syringe).



**Scheme 1** Proposed mechanism of Cu(0) mediated RDRP of HEA in D<sub>2</sub>O or H<sub>2</sub>O, adapted from Leng *et al.*<sup>10</sup> and Samanta *et al.*<sup>12c</sup> P<sub>n</sub>X<sub>(Sol.)</sub> denotes dormant species in solution; P<sub>n</sub>X<sub>(Ads.)</sub> denotes dormant species adsorbed on the Cu(0) surface; P<sub>n</sub>\*<sub>(Sol.)</sub> denotes active species in solution; P<sub>n</sub>\*<sub>(Ads.)</sub> denotes active species adsorbed on the Cu(0) surface; L denotes ligand.

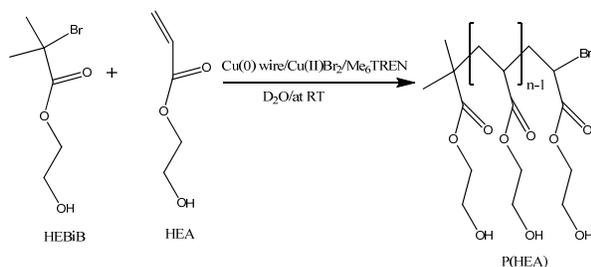
## Results and discussion

### Cu(0) wire vs. two-step Cu(0) *in situ* mediated RDRP of 2-hydroxyethyl acrylate

The synthesis of P(HEA) in water using activated Cu(0) wire as catalyst, Me<sub>6</sub>TREN as ligand and ethyl-2-bromoisobutyrate (EBiB) as initiator at 25 °C has been studied recently by two groups. Interestingly, one reported successful synthesis of P(HEA) with  $\bar{D}$ =1.07, TCL=30, and monomer conversion of 97%, achieved with the addition of *ca.* 1666 ppm Cu(II)Br<sub>2</sub>,<sup>9</sup> while the other reported the formation of significant insoluble gel on the surface of the Cu(0) wire for TCL=200 in the absence of added Cu(II)Br<sub>2</sub> in water and in methanol/water mixtures with water content of 70 vol% or higher.<sup>10</sup> Subsequent work<sup>12c</sup> using activated Cu(0) wire, Me<sub>6</sub>TREN and the water soluble initiator oligo(ethylene glycol) methyl ether 2-bromoisobutyrate, found significant gel formation even at TCL=20 unless 10,000 ppm Cu(II)Br<sub>2</sub> was added, confirming that the concentration of deactivator was an important factor influencing the extent of gel formation. To further explore whether DP<sub>n</sub> is also a factor, we synthesized P(HEA) under similar conditions (Scheme 2) using the water soluble initiator 2-hydroxyethyl 2-bromoisobutyrate (HEBiB), with conversion and number average molecular weight (M<sub>n</sub>) calculated from

$^1\text{H-NMR}$  spectra. ( $\text{D}_2\text{O}$  is used as solvent instead of water.) As described in the experimental section,  $M_n$  and  $\bar{D}$  were also measured by size exclusion chromatography (SEC), after acetylation of the P(HEA).

As seen in Fig. 1, polymer precipitated out of solution at the Cu(0) wire surface, with about 40 wt.% of the initial HEA consumed by formation of insoluble gel during the 120 min reaction, as estimated by the mass of material. Because of the significant amount of gel formation, the HEA conversion and  $M_{n,\text{HMR}}$  calculations based on  $^1\text{H-NMR}$  spectra are not reliable. Table 1 reports the SEC-measured  $M_n$  values of the soluble polymer fraction as a function of reaction time, with high dispersity found throughout the reaction. The resulting MMDs are bimodal in character, with a high MW shoulder observed (Fig. 2). Thus we find that insoluble gel formation occurs on the Cu(0) wire surface even in the presence of added Cu(II)Br<sub>2</sub> (200 ppm) and NaBr (30 mM) (Fig. 1a and b), in agreement with Leng *et al.*<sup>10</sup> Upon changing the TCL from 50 to 20 ( $[\text{HEA}]_0/[\text{HEBiB}]_0/[\text{Cu(II)Br}_2]_0/[\text{Me}_6\text{TREN}]_0 = 20:1:0.004:0.08$ ), the gel formation is significantly reduced (Fig. 1c and d); as shown in Fig. 1d, the wire is coated with a thin layer of insoluble polymer, but greatly reduced compared to the case with TCL=50 (Fig. 1a and b). Upon increasing the amount of initial Cu(II)Br<sub>2</sub> to 500 ppm ( $[\text{HEA}]_0/[\text{HEBiB}]_0/[\text{Cu(II)Br}_2]_0/[\text{Me}_6\text{TREN}]_0 = 20:1:0.01:0.2$ ), we qualitatively observe less insoluble gel on the Cu(0) wire surface (Fig. 1e compared to Fig. 1d), a result in agreement with the previous observation<sup>12c</sup> that deactivation can occur on the Cu(0) surface and a high concentration of deactivator can reduce gel formation. It should be noted that the  $\bar{D}$  of P(HEA) produced over Cu(0) wire is larger than 1.5 with a high MW shoulder observed in all three experiments. Gel formation has been attributed<sup>12c</sup> to the fast adsorption of P(HEA) dormant chains (with strong hydrophobic backbone) to the Cu(0) wire surface and slow desorption of P(HEA) radicals from the surface (Scheme 1), such that the adsorbed P(HEA) radicals beyond some localized concentration form cross-linked insoluble polymer, with the specific mechanism of gel formation unclear. This proposed explanation could explain the differences between Nicol's and Leng's studies, as P(HEA) radicals with different  $\text{DP}_n$  may have significantly different desorption rates from the Cu(0) wire surface. The high MW shoulder seen in the MMDs (Figure 2) could be attributed to reaction of the adsorbed P(HEA) radicals of longer length, with shorter adsorption times for the shorter chains.



**Scheme 2** Cu(0) wire mediated RDRP of 2-hydroxyethyl acrylate at RT.

**Table 1** MW analysis of soluble fraction of P(HEA) formed by Cu(0) wire mediated RDRP of HEA at RT (22 – 25 °C). Reaction conditions: HEA=2.75 mL (below 0.2 wt.% EGDA),  $\text{D}_2\text{O}$ =12 mL, 30 mM NaBr and 10 cm Cu(0) wire<sup>a</sup> (diameter=1.0 mm),  $[\text{HEA}]_0/[\text{HEBiB}]_0/[\text{Cu(II)Br}_2]_0/[\text{Me}_6\text{TREN}]_0=50:1:0.01:0.2$ .

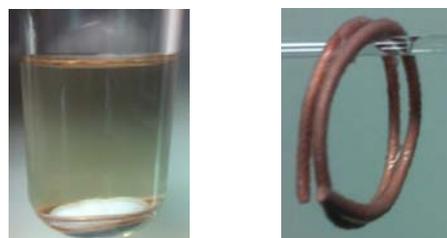
Sample No.	Time (min)	$M_{n,\text{SEC}}^b$	$\bar{D}^c$
S-1	30	3960	2.49
S-2	60	3840	2.13
S-3	90	3630	1.93
S-4	120	3890	1.99

<sup>a</sup> Hydrochloric acid-activated Cu(0) wire.<sup>19</sup> <sup>b</sup>  $M_{n,\text{SEC}}=M_{n,\text{P(ACHEA)}} \times (116.12/158.15)$  [ $M_{n,\text{P(ACHEA)}}$  is the refractive index (RI) data of acetylated P(HEA) relative to PS standard using THF as eluent]. <sup>c</sup>  $\bar{D}$  is measured by RI [verification of complete acetylation in electronic supplementary information (ESI)].

a) 60 min-TCL=50      b) Replicated experiment at 120 min-TCL=50



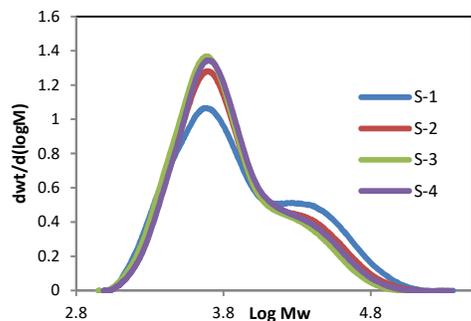
c) 120 min-TCL=20      d) Wire at 120 min-TCL=20



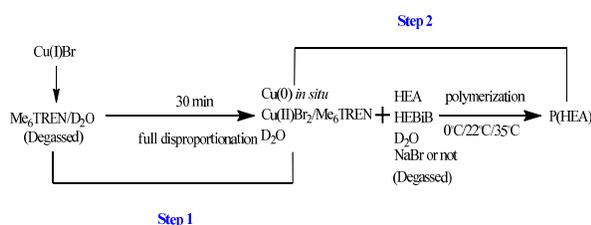
e) Wire at 120 min-TCL=20 with 500 ppm Cu(II)Br<sub>2</sub>



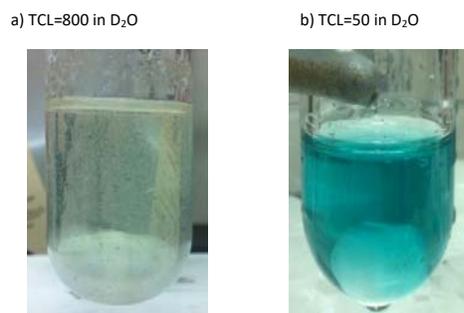
**Fig. 1** Gel formation in Cu(0) wire mediated RDRP of HEA at room temperature. Reaction conditions: HEA=2.75 mL (below 0.2 wt.% EGDA),  $\text{D}_2\text{O}$ =12 mL, 30 mM NaBr and 10 cm Cu(0) wire (diameter=1.0 mm),  $[\text{HEA}]_0/[\text{HEBiB}]_0/[\text{Cu(II)Br}_2]_0/[\text{Me}_6\text{TREN}]_0=50:1:0.01:0.2$  (a and b); 20:1:0.004:0.08 (c and d) and 20:1:0.01:0.2 (e).



**Fig. 2** Molar mass distribution of P(AcHEA). Reaction conditions: HEA=2.75 ml, D<sub>2</sub>O=12 ml, [HEA]<sub>0</sub>/[HEBiB]<sub>0</sub>/[Cu(I)Br<sub>2</sub>]<sub>0</sub>/[Me<sub>6</sub>TREN]<sub>0</sub>=50:1:0.01:0.2, 30 mM NaBr and 10 cm Cu(0) wire (diameter=1.0 mm). See Table 1 for the sample information.



**Scheme 3** Two-step Cu(0) *in situ* mediated RDRP of HEA



**Fig. 3** No gel formation in the two-step Cu(0) *in situ* mediated RDRP of HEA in D<sub>2</sub>O for TCL=800 (a) and TCL=50 (b). Small black specks represent Cu(0) particles, with the more intense blue color in (b) due to the higher catalyst concentration of 8,000 ppm compared to 250 ppm in (a).

As the number of adsorbed P(HEA) radicals is dependent on the Cu(0) wire surface area, it is only for shorter Cu(0) wire with high water content that some slight improvement in control of P(HEA) was observed.<sup>10</sup> This suggests that using small sized Cu(0) particles as catalyst instead of wire could eliminate the gel formation at high DP<sub>n</sub> (DP<sub>n</sub> > 30), as Cu(0) wire increases the local concentration of polymer chains on the surface compared to highly dispersed particles.

A full disproportionation of Cu(I)Br/Me<sub>6</sub>TREN to form Cu(0) and Cu(II)Br<sub>2</sub> *in situ* is a practical method to prepare small sized Cu(0) particles and deactivator Cu(II)Br<sub>2</sub> complex at an equal molar ratio (Scheme 3), as reported by Zhang *et al.*<sup>15</sup> In that

work, this technique was used to synthesize low molecular weight P(HEA) (TCL=20) in water without gel formation. Herein, we successfully apply the methodology to synthesize P(HEA) over a wide TCL range, up to target chain length of 800. In addition, the influence of temperature (22 vs. 0 °C), initial Cu(I)Br levels, residual O<sub>2</sub> (affected by syringe vs cannula transfer of monomer and initiator) and added NaBr is explored. Throughout this investigation, no gel formation was observed in the presence of the Cu(0) generated *in situ* over the complete range of conditions. As shown by Fig. 3, solid Cu(0) particles are certainly observed in solution under varying conditions. However, the dispersed nature of the particles (compared to Cu wire) prevents gel formation, as the number of adsorbed active species per Cu(0) particle is low. Note that gel formation can also be avoided with Cu(0) wire as mediating agent by increasing the hydrophilic character of the active species to some extent for the polymer chains, for example by using P(EO)<sup>9</sup> or P(OEOA<sub>480</sub>)<sup>11</sup> as a macro-initiator.

### The origin of the high MW shoulder -in P(HEA) MMDs

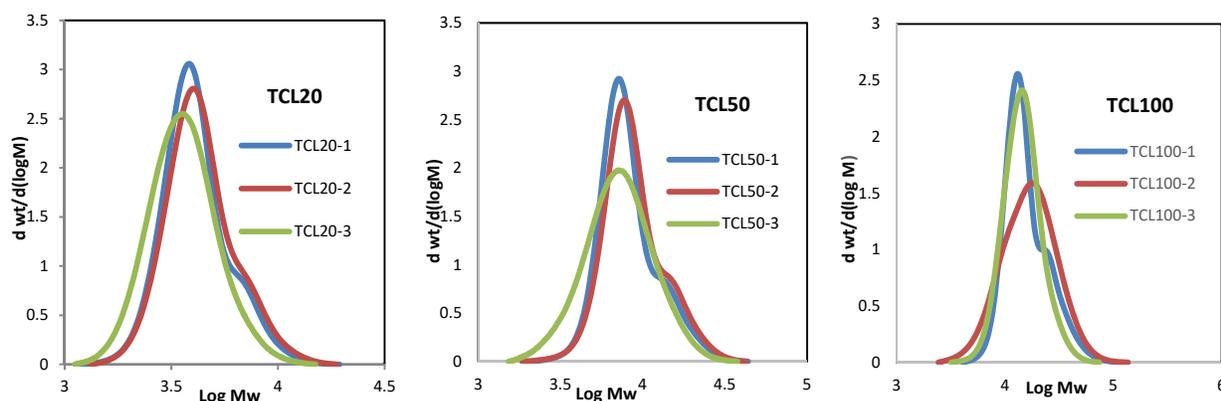
Table 2 summarizes the recipes and key results for a series of experiments performed with target chain lengths between 20 and 100, with monomer and initiator transferred to the reaction solution by syringe after allowing the Cu(I)Br to disproportionate to Cu(0) and Cu(II)Br<sub>2</sub>. The first entry (Experiment TCL20-1) is similar to the experimental conditions of Zhang *et al.*,<sup>15</sup> the only difference being choice of initiator, HEBiB in our work and 2, 3-dihydroxypropyl 2-bromo-2-methylpropanoate for Zhang *et al.* P(HEA) with  $\bar{D}$ =1.14 was produced, in reasonable agreement with the previous results ( $\bar{D}$ =1.07). However, a clear high MW shoulder is seen in the MMD, a phenomenon that is observed also for higher target chain lengths, as shown in Fig. 4. One potential explanation for this observation is the presence of ethylene glycol diacrylate (EGDA) impurity in commercial HEA, a difunctional monomer that could lead to branching and even crosslinking during polymerization. Other studies have found that this impurity disrupts control in RDRP systems.<sup>17</sup> For most reactions, we used purified HEA, which reduced the EGDA content from 0.63 to below 0.2 wt.%. However, it appears as if this purification is not necessary, as there is no significant difference in the polymer MMD (and dispersity) when the reaction was done using commercial HEA without purification (Experiment TCL20-2, see Fig. 4a).

To explore the origins of this shoulder, the reaction temperature was decreased from 22 to 0 °C in order to slow the polymerization rate for kinetic studies. Keeping the [HEBiB]<sub>0</sub>: [Cu(I)Br]<sub>0</sub>: [Me<sub>6</sub>TREN]<sub>0</sub> ratios at 1:0.4:0.4, changing the target chain length from 20 to 100 results in a decrease of Cu level from 20,000 to 4,000 ppm (with respect to monomer). However, the polymerization rate for Experiment TCL50-1 and Experiment TCL100-1 remains fast, with high conversion reached in 10 min. The P(HEA) chain lengths remain very close

**Table 2** Two-step Cu(0) *in situ* mediated RDRP of HEA in 4 ml D<sub>2</sub>O and transferring HEA, HEBiB and D<sub>2</sub>O by syringe; entry 1-6 (15 vol% monomer), entry 7-11 (27 vol% monomer); entry 2 [TCL20-1, HEA (0.633 wt.% EGDA) traced by GC (detail in ESI)], other entries [HEA (below 0.2 wt.%EGDA) traced by GC (detail in ESI)].

Experiment	[M] <sub>0</sub> : [I] <sub>0</sub> : [C] <sub>0</sub> : [L] <sub>0</sub> / [NaBr] <sub>0</sub> <sup>a</sup>	Cu ppm	T <sup>b</sup> (°C)	React. time (min)	Conv. <sup>c</sup> (%)	M <sub>n,th</sub> <sup>d</sup>	M <sub>n,NMR</sub> <sup>e</sup>	M <sub>n,SEC</sub> <sup>f</sup>	Đ <sup>g</sup>
TCL20-1	20:1:0.4:0.4	20,000	22	30	>99.9	2530	2820	2840	1.14
TCL20-2	20:1:0.4:0.4	20,000	22	30	>99.9	2530	2550	2960	1.15
TCL20-3	20:1:0.1:0.1/1.2	5,000	0	25	98.4	2500	2510	2470	1.15
TCL50-1	50:1:0.4:0.4	8,000	0	5	97.5	5870	5860	5580	1.18
TCL50-2	50:1:0.4:0.4/4.8	8,000	0	20	>99.9	6010	5880	5900	1.19
TCL50-3	50:1:0.1:0.1/1.2	2,000	0	19	89.2	5390	5360	4690	1.26
TCL100-1	100:1:0.4:0.4	4,000	0	10	98.3	11630	11790	10490	1.24
TCL100-2	100:1:0.1:0.1	1,000	0	10	89.5	10600	10570	10350	1.39
TCL100-3	100:1:0.1:0.1/1.2	1,000	0	30	97.3	11510	12350	9780	1.18
TCL100-4	100:1:0.1:0.1/1.2	1,000	0	10	16.0	2070	2190	3380	1.98
TCL100-5	100:1:0.1:0.1/1.2	1,000	22	16	93.6	11080	12540	9080	1.18

<sup>a</sup> [M]<sub>0</sub>: [I]<sub>0</sub>: [C]<sub>0</sub>: [L]<sub>0</sub> / [NaBr]<sub>0</sub> = [HEA]<sub>0</sub>: [HEBiB]<sub>0</sub>: [Cu(II)Br<sub>2</sub>]<sub>0</sub>: [Me<sub>6</sub>TREN]<sub>0</sub> / [NaBr]<sub>0</sub>. <sup>b</sup> Disproportionation and polymerization temperatures are the same. <sup>c</sup> Conversion is calculated via <sup>1</sup>H-NMR spectrum (detail in ESI). <sup>d</sup> M<sub>n,th</sub> = M<sub>HEA</sub> × TCL × conversion + M<sub>initiator</sub>. <sup>e</sup> End-group method to calculate M<sub>n</sub> of polymer based on <sup>1</sup>H-NMR spectrum [M<sub>n,NMR</sub> = M<sub>HEA</sub> ×  $\bar{N}$  (calculated number average unit of monomer per initiator) + M<sub>initiator</sub>] (details in ESI). <sup>f</sup> M<sub>n,SEC</sub> = M<sub>n,P(AcHEA)</sub> × (116.12/158.15) [M<sub>n,P(AcHEA)</sub> is the refractive index (RI) data of acetylated P(HEA) relative to PS standard using THF as eluent]. <sup>g</sup> Đ is measured by RI (verification of complete acetylation in ESI).



**Fig. 4** Molar mass distributions of P(AcHEA) with TCL of 20 (a), 50 (b) and 100 (c). Experimental details presented in Table 2.

to the target value, but the high MW shoulder remained (Fig. 4), and Đ increased slightly to 1.24 for TCL100-1. A further decrease in Cu level to 1000 ppm with TCL=100 (TCL100-2) led to much broader MMD (Đ=1.39), without a clear high MW shoulder (Fig. 4c). It may be that the lower Cu(0) level decreases the amount of adsorbed polymer and thus prevents shoulder formation, with the corresponding decrease in Cu(II)Br<sub>2</sub> leading to some loss of control. Other work has suggested that at low Cu levels, addition of NaBr is needed to

suppress the dissociation of the Cu(II)Br<sub>2</sub> deactivator complex and improve control.<sup>25-27</sup> As shown by Experiment TCL100-3, utilization of NaBr decreases Đ back to below 1.2, and also suppresses the formation of the high MW shoulder (Fig. 4c). While adding excess NaBr suppresses the dissociation of CuBr<sub>2</sub>/Me<sub>6</sub>TREN (deactivator), it also significantly increases the deactivation rate and thus decreases the rate of polymerization. For a reaction time of 10 min, only 16% conversion is reached in the presence of NaBr (Experiment

TCL100-4) compared to full conversion in its absence (Experiment TCL100-2), with 30 min required to achieve full conversion with NaBr (Experiment TCL100-3). In addition, a significant decrease in dispersity is observed with conversion ( $\bar{D}$ =1.18 at full conversion of Experiment TCL100-3 compared to  $\bar{D}$ =1.98 at 16% conversion of Experiment TCL100-4). Finally, Experiment TCL100-5 indicates that lowering the reaction temperature from 22 to 0 °C is not required to achieve good control. The same general results are found for target chain lengths of 20 (Experiment TCL20-3) and 50 (Experiment TCL50-3). Although copper levels were reduced by a factor of 4 compared to the base case, dispersity remains low, and no high MW shoulder can be seen (Fig. 4). The dispersity is slightly higher for Experiment TCL50-3 ( $\bar{D}$ =1.26), which might be a result of the reduced conversion (89%) compared to the other cases. Interestingly, it was found that the high MW shoulder was still observed when copper level was kept at the higher level (Experiment TCL50-2, Fig.4b). We conclude that although NaBr is required to reduce the dissociation of deactivator when experiments are performed at low Cu levels in aqueous solution, it is actually the lowering of the Cu amount that suppresses the formation of the high P(HEA) shoulder. This observation is consistent with the hypothesis that the shoulder is related to adsorbed P(HEA) chains on the Cu(0) particle surface, with a reduced Cu content leading to lower rates of polymer chain adsorption and thus reduced concentration of adsorbed active chains.

### Kinetic Studies

As discussed above, adding NaBr to the system slows down the rate of polymerization. Although still a very fast reaction (complete conversion at 0 °C in <30 min), this rate reduction allows the possibility of conducting kinetic studies. One of the questions we wanted to address is whether the monomer/initiator transfer method used in the two-step Cu(0) *in situ* mediated RDRP process affected rate and/or MW control, as it is well known that the normal ATRP system operated at low Cu levels can lose activity in the presence of oxygen due to loss of activator Cu(I)Br by oxidation to Cu(II)Br<sub>2</sub>. In the two-step Cu(0) mediation process, our transfer process by syringe introduces a small amount of adventitious oxygen into the reaction system, compared to the cannula transfer used by Zhang *et al.*<sup>16</sup> Here we study the effect of the transfer procedure at 0 °C for production of P(HEA) of TCL=100 at low (1000 ppm) Cu levels with excess NaBr. The data were collected by stopping parallel reactions at various time points rather than sampling the reaction mixture, due to the heterogeneous nature of the reaction [visible Cu(0) particles]. Fig. 5 plots the monomer conversion as a function of time, as well as the evolution of  $M_n$  and  $\bar{D}$  as a function of conversion. First order kinetics is observed in both cases, with transfer by syringe leading to an observable induction period (~10 min) compared to transfer by cannula. The polymerization rates for the syringe-transfer experiments are comparable once the reaction commences, with high conversion reached after a total time of 20 min. Most importantly, this induction period

did not affect the final  $M_n$  (very close to target) or final dispersity (~1.2). Interestingly, a high MW shoulder is seen on the MMD of P(HEA) produced by the transfer by cannula, but is not seen when transfer is done by syringe (Fig. 6). For both cases (and as seen with Experiment TCL100-4 in Table 2), the  $\bar{D}$  of P(HEA) is significantly higher early in the reaction, with the distribution narrowing rapidly with increasing conversion. To verify and further explore this behaviour, a similar set of experiments were conducted at 22 °C for a TCL=200; with the [HEBiB]<sub>0</sub>/[Cu(I)Br]<sub>0</sub>/[Me<sub>6</sub>TREN]<sub>0</sub> kept constant at 1.0:0.1:0.1, the copper level was thus lowered to 500 ppm. The results are quite consistent with the observations found for TCL=100: as shown in Fig. 7, an induction period is still observed when transfer is completed by syringe, but the  $M_n$  of the final polymer is not affected. Indeed, with TCL=200, the dispersity is lowered to 1.10 for transfer by syringe compared to the value of 1.15 for transfer by cannula. While a high MW shoulder is seen for both cases, it is clearly reduced for the P(HEA) produced using syringe transfer.

The comparison of cannula vs. syringe transfer was done at 0 °C for TCL=100 and at 22 °C for TCL=200. To complete the study, P(HEA) was also produced using transfer by syringe for

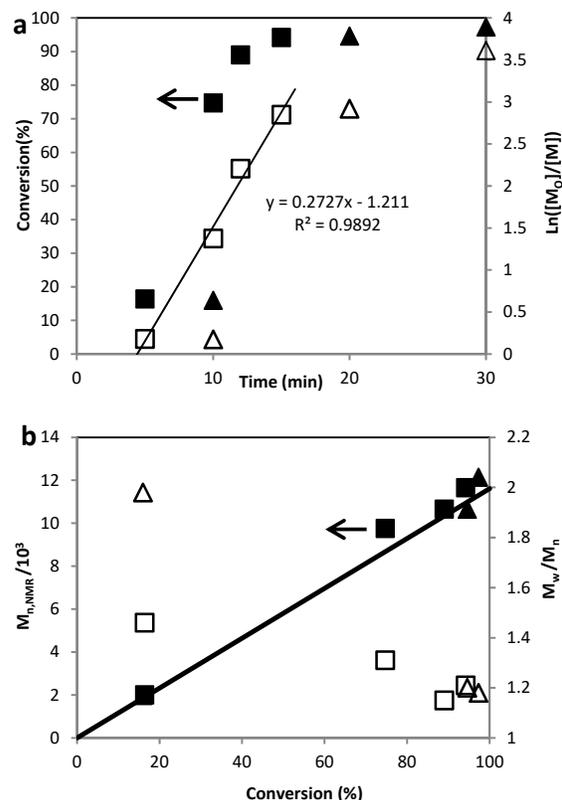
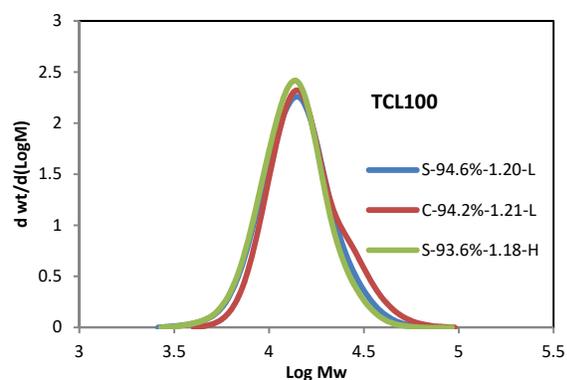
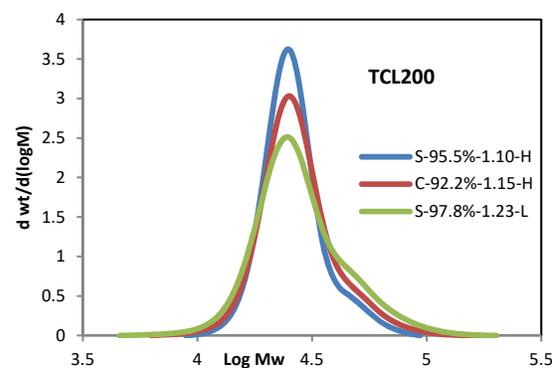


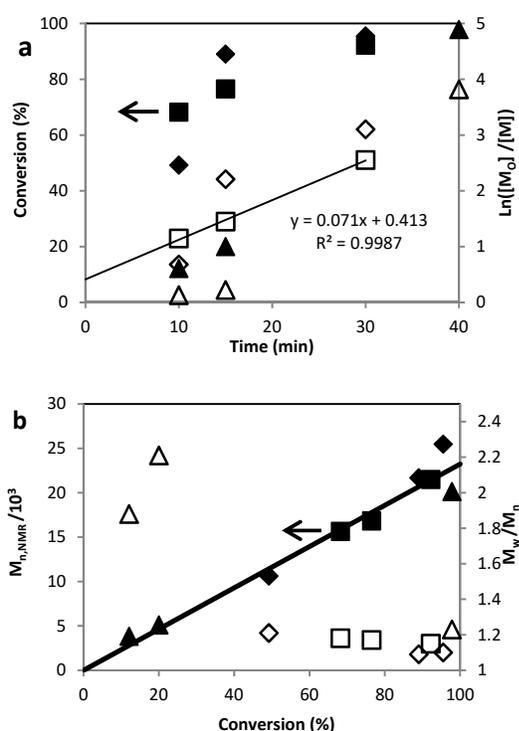
Fig. 5 Comparing the effect of monomer/initiator transfer by cannula (squares) and syringe (triangles) for two-step Cu(0) *in situ* RDRP of HEA: monomer conversion (filled symbols) and  $\ln([M]_0/[M])$  (open symbols) versus time (a); polymer  $M_{n,NMR}$  (filled symbols) and dispersity (open symbols) versus conversion, with line indicating  $M_{n,th}$  (b). Reaction conditions: HEA=1477  $\mu$ L (below 0.2 wt.% EGDA), D<sub>2</sub>O= 4 mL, [HEA]<sub>0</sub>/[HEBiB]<sub>0</sub>/[Cu(I)Br]<sub>0</sub>/[Me<sub>6</sub>TREN]<sub>0</sub>/[NaBr]<sub>0</sub>=100:1.0:1.0:1.1:2 at 0 °C.



**Fig. 6** Molar mass distribution of P(AcHEA) produced with a TCL of 100. Legend denotes transfer method (S denotes syringe, C denotes cannula), conversion, dispersity and temperature (L denotes 0 °C and H denotes 22 °C).



**Fig. 8** Molar mass distribution of P(AcHEA) produced with a TCL of 200. Legend denotes transfer method (S denotes syringe, C denotes cannula), conversion, dispersity and temperature (L denotes 0 °C and H denotes 22 °C).



**Fig. 7** Comparing the effect of monomer/initiator transfer by cannula (squares) and syringe (triangles at 0 °C and diamond at 22 °C) for two-step Cu(0) *in situ* RDRP of HEA: monomer conversion (filled symbols) and  $\ln([M]_0/[M])$  (open symbols) versus time (a); polymer  $M_{n,NMR}$  (filled symbols) and dispersity (open symbols) versus conversion, with line indicating  $M_{n,th}$  (b); Reaction conditions:  $[HEA]_0/[HEBIB]_0/[Cu(I)Br]_0/[Me_6TREN]_0/[NaBr]_0 = 200:1:0.1:0.1:2.4$  at 0 °C and at 22 °C, HEA=2111  $\mu$ L (below 0.2 wt.% EGDA),  $D_2O=5.7$  mL.

TCL=100 at 22 °C. Shorter time experiments were not conducted but, as shown in Fig. 6, the polymer MMD produced at the higher temperature was almost identical with a slightly lower  $\bar{D}$ . A few kinetic data points were collected at 0 °C for TCL=200; as shown in Fig. 7, the induction period related to syringe transfer is greater than at 22 °C, and the time to reach full conversion is longer (30-40 min) compared to the TCL=100 experiments (20-30 min in Fig. 5).

Although the amount of kinetic data obtained is limited, it supports the expectations that polymerization rate increases with a decreased target chain length and with increased temperature. Surprisingly, the polymer dispersity is lower at the higher temperature and when monomer transfer is done by syringe compared to cannula, a result more clearly seen for TCL=200 (Fig. 8) than for TCL=100 (Fig. 6). It is possible that the higher temperature increases the desorption rate of adsorbed active species from Cu(0) surfaces, thus increasing the control. Furthermore, while monomer and initiator transferred by syringe leads to a short induction period not seen with transfer by cannula, the procedure also slightly lower polymer dispersity, most likely due to increased control by oxidation of Cu(0) into Cu(I)Br or Cu(II)Br<sub>2</sub>.

#### Synthesis of higher MW P(HEA) at low catalyst concentration

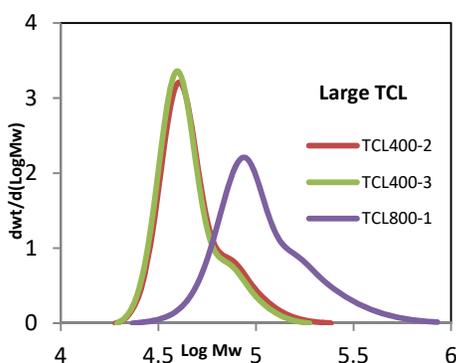
According to the above investigation, the more favourable conditions for synthesis of well-defined high MW P(HEA) at lower catalyst levels with the two-step Cu(0) *in situ* mediation procedure are to use syringe transfer, conduct the reaction at 22 °C rather than at 0 °C, and employ excess NaBr to suppress deactivator dissociation in the aqueous medium.

Table 3 summarizes the synthesis conditions and properties of P(HEA) synthesized with TCL=400 and 800, using 250 ppm copper catalyst. Longer reaction times (75-120 min) are required to achieve high conversion, due to the combination of low initiator and low Cu levels compared with TCL=200. In addition, the increase in solution viscosity becomes a factor at these higher chain lengths, with the magnetic stir bar unable to maintain agitation to full conversion. As discussed previously, we hypothesize the desorption and adsorption rates of P(HEA) chains are affected by the number average degree of polymerization ( $DP_n$ ), making it more difficult to synthesize high MW polymer without gel formation or the occurrence of a high MW shoulder. However, reasonable control can be achieved using low Cu levels (see Table 3 and Fig. 9) in the presence of added NaBr for these higher chain

**Table 3** Two-step Cu(0) *in situ* mediated RDRP of HEA in D<sub>2</sub>O, 250 ppm copper catalyst, HEA=3378 mL (below 0.2 wt.% EGDA, 27 vol% monomer).

Experiment	[M] <sub>0</sub> :[I] <sub>0</sub> : [C] <sub>0</sub> : [L] <sub>0</sub> /[NaBr] <sub>0</sub> <sup>a</sup>	T <sup>b</sup> (°C)	React. time (min)	Conv. <sup>c</sup> (%)	M <sub>n,th</sub> <sup>d</sup>	M <sub>n,SEC</sub> <sup>e</sup>	Đ <sup>f</sup>
TCL400-1	400:1:0.1:0.1/3.6	0	90	88.9	41490	34280	1.22
TCL400-2	400:1:0.1:0.1/3.6	22	75	86.7	40500	32400	1.16
TCL400-3	400:1:0.1:0.1/3.6	35	75	84.2	39310	31180	1.13
TCL800-1	800:1:0.2:0.2/4.8	22	120	79.0	73430	69540	1.35

<sup>a</sup> [M]<sub>0</sub>: [I]<sub>0</sub>: [C]<sub>0</sub>: [L]<sub>0</sub>/[NaBr]<sub>0</sub> = [HEA]<sub>0</sub>: [HEBiB]<sub>0</sub>: [Cu(I)Br]<sub>0</sub>: [Me<sub>6</sub>TREN]<sub>0</sub>/[NaBr]<sub>0</sub>. <sup>b</sup> Disproportionation and polymerization temperatures are the same. <sup>c</sup> Conversion is calculated via <sup>1</sup>H-NMR spectrum (detail in ESI). <sup>d</sup> M<sub>n,th</sub> = M<sub>HEA</sub> × TCL × conversion + M<sub>initiator</sub>. <sup>e</sup> M<sub>n,SEC</sub> = M<sub>n,P(AcHEA)</sub> × (116.12/158.15) [M<sub>n,P(AcHEA)</sub> is the refractive index (RI) data of acetylated P(HEA) relative to PS standard using THF as eluent]. <sup>f</sup> Đ is measured by RI (verification complete acetylation in ESI).

**Fig. 9** Molar mass distributions of P(AcHEA) with high TCL. Experimental details presented in Table 3.

lengths. Interestingly, the dispersity is lowered and the high MW shoulder is less pronounced as reaction temperature is increased with TCL=400, perhaps due to an increased desorption rate of chains from the Cu(0) surface. It may be that even lower dispersity values would be achieved at full conversions, as experiments were stopped below 90% conversion due to high viscosity. While the high MW shoulder is more pronounced for the TCL of 800, a dispersity of 1.35 was achieved.

## Conclusions

The reversible deactivation radical polymerization (RDRP) of 2-hydroxyethyl acrylate in D<sub>2</sub>O using Cu(0) wire with Me<sub>6</sub>TREN at different TCL and initial added Cu(II)Br<sub>2</sub> was investigated. Short chain length and high concentration of deactivator reduced gel formation. This result was explained by the reduced

concentration of adsorbed active species on the Cu(0) wire surface through an increased desorption rate and an increased deactivation rate on the Cu(0) wire surface, respectively. Employing the two-step Cu(0) *in situ* mediation procedure circumvents this problem, with a set of experiments focusing on the effects of P(HEA) chain length, initial Cu(I)Br, excess NaBr, temperature and residual O<sub>2</sub>. The concentration of adsorbed active species on the Cu(0) particle surface is believed to be the key factor for the high MW shoulder and polymerization control, which is determined by the combined effects of physical processes such as adsorption and desorption with reaction processes such as activation, propagation and deactivation on the Cu(0) surface, and activation, deactivation, propagation and termination in solution. Short chain length, low activator, high deactivator and high temperature (22 rather than 0 °C) help to maintain a low concentration of adsorbed active species on the Cu(0) surface during the polymerization, the requirement for synthesizing well defined P(HEA) of low Đ without a high MW shoulder or gel in aqueous solution.

Based on these insights, well defined P(HEA) with low Đ (~1.2) and without a significant high MW shoulder was obtained when DP<sub>n</sub> is less than 200 in aqueous solution. Higher molecular weight P(HEA) was also synthesized, albeit with the high MW shoulder observed; for a TCL=400, 87% conversion with low Đ (1.16) was synthesized within 75 min using *ca.* 250 ppm copper in D<sub>2</sub>O at 22 °C.

## Experimental

### Materials

2-hydroxyethyl 2-bromoisobutyrate (95%, Sigma-Aldrich), Cu(I)Br (99%, Sigma-Aldrich), NaBr (≥ 99%, Sigma-Aldrich),

tris[2-(dimethylamino)ethyl]amine (97%, Sigma-Aldrich), and ethylene glycol diacrylate (90%, technical grade, Sigma-Aldrich) were used as received. D<sub>2</sub>O (99.9%, Cambridge Isotope Laboratories) was used as received.

Copper(0) wire ( $\geq 99.9\%$ , diameter 1.0 mm, Sigma-Aldrich) was activated by hydrochloric acid (Fisher)<sup>24</sup> by immersion in hydrochloric acid for 10 min, washing with methanol and drying prior to use.

2-hydroxyethyl acrylate (96%, Sigma-Aldrich) was purified as follows: 2 hydroquinone (laboratory grade, Fisher Scientific, 0.05 wt.%) was added to a solution of HEA in water (25% v/v) before a series of 12 solvent extractions with hexane (reagent, ACP Chemicals) to remove the ethylene glycol diacrylate. The aqueous layer was salted with NaCl ( $\geq 99\%$ , Sigma-Aldrich, 200 g /L) and then filtered to remove undissolved NaCl. The monomer was then separated from the aqueous layer by extraction with diethyl ether (4 times) to remove acrylic acid. Hydroquinone (0.05 wt.%) was added to the diethyl ether layer before evaporation via rotary evaporator. The ether layer was dried by adding molecular sieves (0.5 wt.%) and then evaporated in a rotary evaporator at 34 °C. The purified HEA was filtered through an alumina column to remove hydroquinone and acid residue prior to use.

P(HEA) was acetylated by acetic anhydride (reagent, Fisher Scientific) in pyridine ( $\geq 99\%$ , Sigma-Aldrich) as follows:<sup>17</sup> 60 mg P(HEA) was dissolved completely in 1.5 ml pyridine in a 5 ml flask, followed by addition of 0.3 ml acetic anhydride. The solution was stirred overnight to allow for complete acetylation, air dried at room temperature, and then vacuum dried at 60 °C overnight.

#### Instrumental Techniques

<sup>1</sup>H-NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer at 23 °C in D<sub>2</sub>O to determine HEA conversion and polymer  $M_{n,NMR}$  and in 6d-DMSO to verify complete acetylation; detailed spectra information and calculations are provided in the electronic supplementary information. The gel permeation chromatography (GPC) consisted of a Waters 2960 separation module with four Styragel packed columns HR 0.5, HR 1, HR 3 and HR 4 (Waters Division Millipore) connected to a Waters 410 refractive index (RI) detector operating at 35 °C. Tetrahydrofuran (THF, reagent grade, ACP Chemicals) was used as eluent at a flow rate of 0.3 mL·min<sup>-1</sup>. The  $M_{n,SEC}$  and  $\bar{D}$  were determined by polystyrene (PS) standards over the range of 870-875000 g·mol<sup>-1</sup>.

A Varian CP-3800 GC was used to quantitatively measure EGDA in the purified HEA. The GC system consisted of a CP-8410 autosampler, CP-1177 isothermal split/splitless injector, 30M chrompack capillary column (CP-Sil 8 CB), oven and a flame ionization detector (FID). (Programmed temperature profile, calibration curve and sample analysis are in the electronic supplementary information.)

#### Procedure for Cu(0) wire mediated RDRP of HEA at RT, TCL=50

Activated Cu(0) wire (length=10 cm and diameter=1 mm) was bent into a carousel reaction tube (Radley, tube A) with a magnetic stir bar, and reagents were added in the following order HEA (2750  $\mu$ L, 26.24 mmol), Me<sub>6</sub>TREN(97%, 28.9  $\mu$ L, 0.105 mmol), NaBr (45.9 mg, 0.446 mmol) and D<sub>2</sub>O (8 mL). A PTFE reaction cap with silicon suba-seal (Radley) was fixed on the carousel reaction tube, and connected to a Schlenk line. Three cycles of freeze-pump-thaw for degassing were performed. HEBiB (95%, 82.6  $\mu$ L), 100  $\mu$ L of stock solution containing 1.17 mg Cu(II)Br<sub>2</sub> and D<sub>2</sub>O (3.9 mL) were added into the other carousel reaction tube (tube B) with a magnetic stir bar. After three cycles of freeze-pump-thaw, the solution from tube B was transferred by syringe into tube A which was immersed in the water bath at room temperature to start the polymerization under stirring and a nitrogen blanket. Samples were taken at different time by syringe. At every time, a small amount of the sample was used for the analysis of monomer conversion and  $M_{n,NMR}$  calculation. The remaining sample was filtered through an alumina column to remove catalyst and ligand prior to GPC sample preparation.

#### Procedure for two-step Cu(0) *in situ* mediated RDRP of HEA at 22 or 0 °C

Desired amounts of Me<sub>6</sub>TREN and D<sub>2</sub>O (detailed recipes are in ESI) were added into a carousel reaction tube (tube A) with a magnetic stir bar. After three cycles of freeze-pump-thaw for degassing, the solution of tube A was immersed in liquid nitrogen and Cu(I)Br added to tube A through an opened silicon suba-seal in the PTFE reaction cap, followed by evacuation (1 min) and filling with nitrogen (1 min) twice. Tube A was immersed in the water bath at 22 or 0 °C. Disproportionation took place for 30 min under a nitrogen blanket, with the start time as the point at which the frozen solution completely melted. A specific amount of HEA, HEBiB, NaBr and D<sub>2</sub>O (detailed recipes are in ESI) were added into the other clean carousel reaction tube (tube B) with a magnetic stir bar. After three cycles of freeze-pump-thaw, the solution of tube B was transferred by syringe or cannula into tube A to start the polymerization. At the required time, the PTFE reaction cap was opened and hydroquinone (inhibitor, 2 wt.%) was added to stop the polymerization. The sample was frozen in the NMR tube and taken immediately for <sup>1</sup>H-NMR analysis. The remaining solution was filtered through an alumina column to remove catalyst and ligand for further GPC sample preparation.

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## Notes and references

- H. Kakwere and S. Perrier, *Polym. Chem.*, 2011, **2**, 270–288.
- S. Coca, C. B. Jasieczek, K. L. Beers and K. Matyjaszewski, *J. Polym. Sci., Part A: Polym. Chem.*, 1998, **36**, 1417–1424.
- A. Mühlebach, S. G. Gaynor and K. Matyjaszewski, *Macromolecules*, 1998, **31**, 6046–6052.
- S. Piogé, A. Nesterenko, G. Brotons, S. Pascual, L. Fontaine, C. Gaillard and E. Nicol, *Macromolecules*, 2011, **44**, 594–603.
- Y. Wang, B. A. Armitage and G. C. Berry, *Macromolecules*, 2005, **38**, 5846–5848.
- V. Percec, T. Guliashvili, J. S. Ladislaw, A. Wistrand, A. Stjern Dahl, M. J. Sienkowska, M. J. Monteiro, and S. Sahoo, *J. Am. Chem. Soc.* 2006, **128**, 14156–14165.
- (a) M. J. Monteiro, T. Guliashvili and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2007, **45**, 1835–1847; (b) G. Lligadas, B. M. Rosen, M. J. Monteiro and V. Percec, *Macromolecules*, 2008, **41**, 8360–8364; (c) B. M. Rosen, X. Jiang, C. J. Wilson, N. H. Nguyen, M. J. Monteiro, V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 5606–5628; (d) M. E. Levere, N. H. Nguyen and V. Percec, *Macromolecules*, 2012, **45**, 8267–8274; (e) M. E. Levere, N. H. Nguyen, X. Leng and V. Percec, *Polym. Chem.*, 2013, **4**, 1635–1647.
- (a) K. Matyjaszewski, N. V. Tsarevsky, W. A. Braunecker, H. Dong, J. Huang, W. Jakubowski, Y. Kwak, R. Nicolay, W. Tang and J. A. Yoon, *Macromolecules*, 2007, **40**, 7795–7806; (b) Y. Zhang, Y. Wang, C. Peng, M. Zhong, W. Zhu, D. Konkolewicz and K. Matyjaszewski, *Macromolecules*, 2012, **45**, 78–86; (c) C. Peng, M. Zhong, Y. Wang, Y. Kwak, Y. Zhang, W. Zhu, M. Tonge, J. Buback, S. Park, P. Krysz, D. Konkolewicz, A. Gennaro and K. Matyjaszewski, *Macromolecules*, 2013, **46**, 3803–3815; (d) Y. Wang, M. Zhong, W. Zhu, C. Peng, Y. Zhang, D. Konkolewicz, N. Bortolamei, A. A. Isse, A. Gennaro and K. Matyjaszewski, *Macromolecules* 2013, **46**, 3793–3802; (e) D. Konkolewicz, Y. Wang, M. Zhong, P. Krysz, A. A. Isse, A. Gennaro and K. Matyjaszewski, *Macromolecules*, 2013, **46**, 8749–8772
- E. Nicol, T. Derouineau, F. Puaud and A. Zaitsev, *J. Polym. Sci., Part A: Polym. Chem.*, 2012, **50**, 3885–3894.
- X. Leng, N. H. Nguyen, B. V. Beusekom, D. A. Wilson and V. Percec, *Polym. Chem.*, 2013, **4**, 2995–3004.
- D. Konkolewicz, P. Krysz, J. R. Góis, P. V. Mendonça, M. Zhong, Y. Wang, A. Gennaro, A. A. Isse, M. Fantin and K. Matyjaszewski, *Macromolecules*, 2014, **47**, 560–570.
- (a) S. R. Samanta, M. E. Levere and V. Percec, *Polym. Chem.*, 2013, **4**, 3212–3224; (b) S. R. Samanta, A. Anastasaki, C. Waldron, D. M. Haddleton and V. Percec, *Polym. Chem.*, 2013, **4**, 5555–5562; (c) S. R. Samanta, V. Nikolaou, S. Keller, M. J. Monteiro, D. A. Wilson, D. M. Haddleton and V. Percec, *Polym. Chem.*, 2015, **6**, 2084–2097
- C. Feng, Z. Shen, L. Gu, S. Zhang, L. Li, G. Lu, X. Huang, *J. Polym. Sci., Part A: Polym. Chem.*, 2008, **46**, 5638–5651.
- C. Feng, Z. Shen, Y. Li, L. Gu, Y. Zhang, G. Lu, X. Huang, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 1811–1824.
- Q. Zhang, P. Wilson, Z. Li, R. McHale, J. Godfrey, A. Anastasaki, C. Waldron and D. M. Haddleton, *J. Am. Chem. Soc.* 2013, **135**, 7355–7363.
- Q. Zhang, Z. Li, P. Wilson and D. M. Haddleton, *Chem. Commun.*, 2013, **49**, 6608–6610.
- K. Bian and M. F. Cunningham, *Macromolecules*, 2005, **38**, 695–701.
- J. T. Lai, D. Filla and R. Shea, *Macromolecules*, 2002, **35**, 6754–6756.
- L. Zhang, K. Katapodi, T. P. Davis, C. Barner-Kowollik, M. H. Stenzel, *J. Polym. Sci., Part A: Polym. Chem.*, 2006, **44**, 2177–2194.
- N. H. Nguyen, M. E. Levere, J. Kulis, M. J. Monteiro and V. Percec, *Macromolecules*, 2012, **45**, 4606–4622.
- N. H. Nguyen, X. Leng and V. Percec, *Polym. Chem.*, 2013, **4**, 2760–2766.
- X. Jiang, B. M. Rosen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 403–409.
- N. H. Nguyen, B. M. Rosen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 1752–1763.
- N. H. Nguyen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2011, **49**, 4241–4252.
- A. Simakova, S. E. Averick, D. Konkolewicz and K. Matyjaszewski, *Macromolecules*, 2012, **45**, 6371–6379.
- D. Konkolewicz, A. D. J. Magenau, S. E. Averick, A. Simakova, H. He and K. Matyjaszewski, *Macromolecules*, 2012, **45**, 4461–4468.
- S. Smolne and M. Buback, *Macromol. Chem. Phys.*, 2015, **216**, 894–902.