Controlled Polymerization of 2-Hydroxyethyl Methacrylate by ATRP at Ambient Temperature

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ABSTRACT: The efficient, controlled polymerization of 2-hydroxyethyl methacrylate (HEMA) is achieved using atom transfer radical polymerization in methanol/water mixtures or pure methanol at 20 °C. The evolution of molecular weight with conversion is linear; polydispersities are around 1.1 for polymerization in methanol and around 1.2−1.3 for syntheses in 50:50 methanol/water mixtures, indicating good living character.

2-Hydroxyethyl methacrylate (HEMA) is an important functional monomer which is widely used in the manufacture of soft contact lenses.[1,2] Although HEMA homopolymer is hydrophilic and has a high degree of hydration, it is not water-soluble. There have been several reports on the synthesis of controlled-structure HEMA-based block copolymers via anionic polymerization chemistry, but this approach requires protection of the alcohol functionality.[3,4] Such syntheses involve at least three steps: synthesis of the protected monomer, its controlled polymerization and subsequent removal of the protecting groups. Understandably, there are as yet no applications for controlled-structure HEMA-based (co)polymers.

Since its discovery[5] in 1995, atom transfer radical polymerization (ATRP) has been shown to be a versatile technique for the controlled polymerization of many monomer classes, including acrylates,[6] methacrylates,[7] and styrenics.[8] Generally ATRP syntheses are carried out at high temperatures either in the bulk or in nonaqueous media. However, we have recently reported that ATRP is particularly effective for hydrophilic monomers in aqueous media under mild conditions. For example, monomethoxy-capped oligo(ethylene glycol) methacrylate [OEGMA] can be polymerized to over 95% conversion within 25 min at 20 °C, with final polydispersities (M_w/M_n) being as low as 1.20−1.30.[9,10] More recently, we have found that similar control can be obtained, albeit at somewhat slower rates of polymerization, by using alcohol/water mixtures instead of water.[11]

Beers et al. recently published an account[12] of the polymerization of HEMA via ATRP. The best results were obtained at either 50 or 70 °C using a $Cu^I[bpy]_2$ catalyst in a 70:30 MEK/*n*-propanol solvent mixture. At 70 °C, a conversion of approximately 72% was achieved after 20 h, with an M_w/M_n of just over 1.30. After 20 h at 50 °C, 87% conversion was achieved, but the M_w/M_n was greater than 1.5, which suggests rather ineffective suppression of termination reactions under these conditions. Attempts to carry out ambient temperature homopolymerizations in DMF led to high conversions, but the final polydispersities were around 1.80, again indicating rather poor living character.

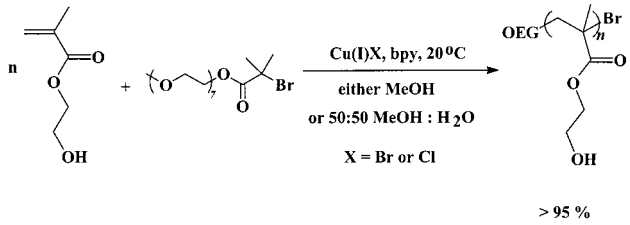

Figure 1. Reaction scheme for the controlled polymerization of 2-hydroxyethyl methacrylate (HEMA) via ATRP at 20 °C.

Herein we report that the ATRP of HEMA is both efficient and well-controlled in either 50:50 methanol/water mixtures or in pure methanol at room temperature (see Figure 1). Compared to previous HEMA polymerizations via ATRP, much faster rates of polymerization, higher final conversions, significantly lower polydispersities and good blocking efficiencies are achieved. Thus, the well-controlled polymerization of HEMA is now possible under mild and industrially attractive conditions.

Initially we attempted to polymerize HEMA in purely aqueous media. As expected, the polymerization was very fast: HEMA homopolymer was obtained as a discolored precipitate in quantitative yield within 2−3 min at 20 °C. However, this precipitate could not be redissolved in good solvents for HEMA homopolymer. This suggests that some degree of cross-linking occurred during polymerization, possibly due to transesterification.[13] Subsequently homopolymerizations were carried out in either 50:50 methanol/water mixtures or pure methanol (see Figure 1). Under these conditions soluble, linear HEMA homopolymers were obtained in very high yields. Rates of polymerization were markedly slower in methanol compared to 50:50 methanol/water, probably due to the more active nature of the Cu(I) catalyst in the presence of water.[10]

The synthesis details and characterization data for various HEMA homopolymers and selected block and statistical copolymers are summarized in Table 1. Figure 2 depicts typical kinetic and molecular weight data for the homopolymerization of HEMA in 50:50 methanol/water mixtures at 20 °C. Conversions of more than 95% are achieved within 60 min at 20 °C. The polymerization is first order with respect to HEMA monomer up to around 60% conversion. The evolution of M_n (determined by ^1H NMR spectroscopy using the

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Table 1. Summary of the Synthesis Parameters and Molecular Weight Data for the Synthesis of Five HEMA Homopolymers, a PEG−HEMA Diblock Copolymer, and a HEMA-PEGMA Statistical Copolymer via ATRP at 20 °C[a]

polymer ID	solvent	theoretical composition	theory Mn	NMR composition	NMR M_n	GPC M_n	M_w/M_n
I	bulk	OEG−HEMA$_{30}$	4300	OEG−HEMA$_{28}$	4000	26 000	1.17
II	MeOH:H$_2$O (1:1)	OEG−HEMA$_{35}$	5000	OEG−HEMA$_{34}$	4900	37 900	1.21
III	MeOH:H$_2$O (1:1)	OEG−HEMA$_{50}$	6900	OEG−HEMA$_{54}$	7400	75 600	1.49
IV	MeOH	OEG−HEMA$_{50}$	6900	OEG−HEMA$_{52}$	7200	39 000	1.09
V	MeOH:H$_2$O (1:1)	OEG−HEMA$_{75}$	10 200	OEG−HEMA$_{78}$	10 500	75 200	1.38
VI	MeOH:H$_2$O (1:1)	PEG−HEMA$_{30}$	6000	PEG−HEMA$_{31}$	6100	42 800	1.24
VII	MeOH:H$_2$O (1:1)	OEG−HEMA$_{45}$-*st*-PEGMA$_5$	16 500	*b*	*b*	61 500	1.24

[a] Conditions: 20 °C, 1−5 h, $[M]_0$ = 50 w/v %, OEG−Br:Cu^{I}X:bpy 1:1:2.5. In all cases, HEMA conversions were greater than 95% as judged by ^{1}H NMR spectroscopy. X = Cl for entries **I**, **III**, **IV**,**V** and **VII**; X = Br for entries **II**,**VI**. [b] For entry **VII,** we were unable to obtain the overall degree of polymerization due to overlapping NMR signals. However, the theoretical PEGMA content was 10 mol %, and the actual PEGMA content was estimated to be 8.1 mol %.

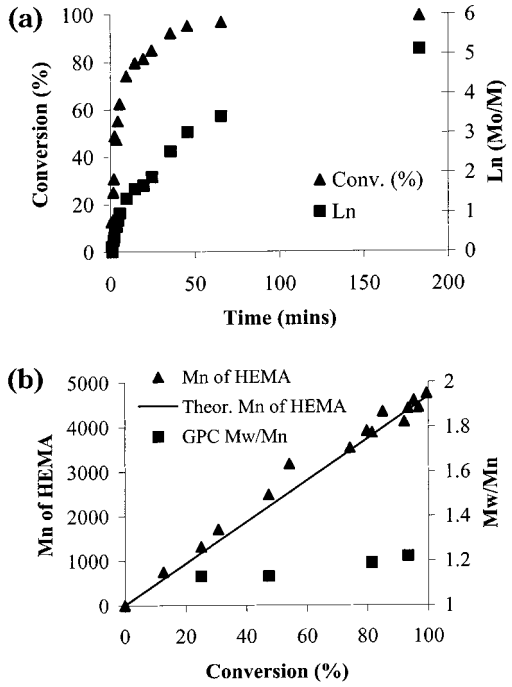

Figure 2. (a) Kinetic plot for the ATRP of HEMA in 50:50 MeOH:H$_2$O at 20 °C. (b) Evolution of molecular weight with conversion for the same experiment. $[M]_0$ = 50% w/v, OEG−Br:Cu^{I}Br:bpy 1:1:2.5. The target DP was 35.

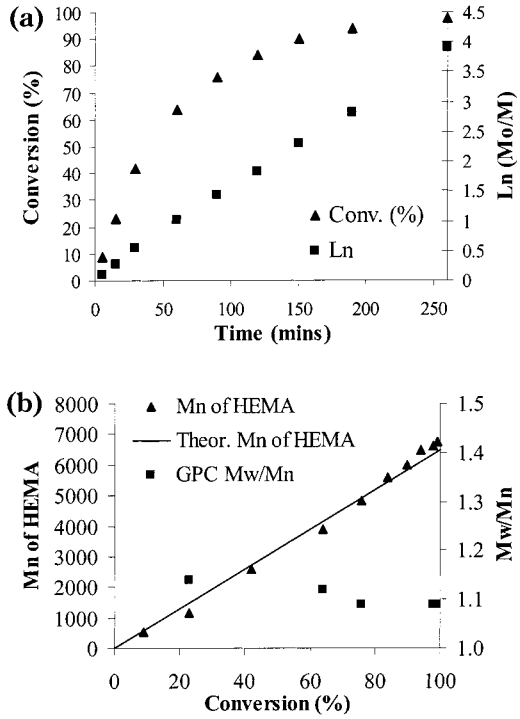

Figure 3. (a) Kinetic plot for the ATRP of HEMA in MeOH at 20 °C. (b) Evolution of molecular weight with conversion for the same experiment. $[M]_0$ = 50% w/v, OEG−Br:Cu^{I}Cl:bpy 1:1:2.5. The target DP was 50.

oligo(ethylene glycol) protons of the OEG−Br initiator as an end group, as described previously[9,10]) is linear up to 95% conversion and polydispersities remained low throughout the polymerization. There was generally excellent agreement between the target degree of polymerization and that calculated by NMR, indicating high initiator efficiencies. The degree of polymerization of the HEMA homopolymer was readily controlled from 30 to 75 simply by adjusting the monomer/initiator molar ratio.

Figure 3 depicts kinetic and molecular weight data for the homopolymerization of HEMA in methanol at 20 °C. Under these conditions, the polymerization is rather slower than in the presence of water: conversions of 95% required 3−4 h.[14] In this case, the polymerization is first order with respect to HEMA monomer up to around 95% conversion and the evolution of M_n is linear up to 95% conversion, with polydispersities remaining low throughout the polymerization. Thus, HEMA polymerizations under these conditions appear to have better living character than those in 50:50 methanol/water mixtures. Recently it has been reported that the k_p for HEMA is higher than that found for other methacrylates.[15] Furthermore, it has been shown that the homopolymerization of HEMA in aqueous solution is characterized by an auto-acceleration phenomenon[16] and has a k_t which is 1 order of magnitude lower than that found in solvents such as acetonitrile.[17]

Beers et al. reported significant differences between their GPC data and their target molecular weights.[12] This discrepancy was presumably due to calibration errors in the GPC analysis, since polystyrene standards are unlikely to be reliable for the analysis of HEMA homopolymers. On the basis of a single MMA−HEMA diblock copolymer synthesis Beers et al. estimated that their GPC protocol overestimated the true molecular weight by a factor of 2. Unfortunately, insufficient details were provided to enable us to make a close comparison with our own GPC protocol. However, based on the NMR-derived M_n data presented in Table 1, GPC analysis appears to overestimate the true molecular weight of HEMA homopolymer by a factor of 5 to 10. If we focus on the near-monodisperse HEMA homopolymers arising from the kinetic study in methanol presented in Figure 3, the GPC discrepancy is a factor of approximately 5−6 for a DP of around 50.

Novel HEMA-based copolymers with comb architectures can be readily prepared in high yield by the statistical copolymerization of HEMA with monomethoxy-capped poly(ethylene glycol) methacrylate [PEGMA; DP = 45 ethylene glycol units], see entry VII in Table 1. Furthermore, monohydroxy-capped linear PEG (DP = 45) can be readily converted into a near-monodisperse macroinitiator as described by Kops and co-workers;[18] homopolymerization of HEMA using this macroinitiator leads to a well-defined PEG−HEMA diblock copolymer. However, block copolymers are more conveniently prepared using the method of sequential monomer addition. This approach is somewhat problematic with ATRP: it is generally believed[19] that it is unwise to allow the first monomer to proceed to very high conversion (above 90%) because termination side-reactions become much more likely under monomer-starved conditions. However, we have found that apparently good blocking efficiencies and very high conversions for both monomers can sometimes be achieved using ATRP in (mixed) aqueous media. This is illustrated here with the synthesis of an OEGMA−HEMA diblock copolymer. In the context of aqueous ATRP, OEGMA is a very well-behaved monomer which exhibits good living character.[9a,10] In contrast, as we have already shown, the polymerization of HEMA is problematic in purely aqueous media. Thus, in the diblock copolymer synthesis we elected to polymerize OEGMA first in aqueous media at 20 °C. An OEGMA conversion of approximately 94% was achieved within 3 min (M_w/M_n = 1.24 by THF GPC) and a concentrated methanolic solution of HEMA was then added to this polymerizing solution. A second exotherm was observed and the HEMA conversion was more than 98% after 60 min (M_w/M_n = 1.21 by DMF GPC). ^{1}H NMR analysis was somewhat complicated by overlapping peak integrals but nevertheless the HEMA block content was estimated to be 46 mol %, compared to a target composition of 50 mol %. To confirm that genuine block copolymer formation had indeed occurred, micellization experiments were undertaken. The OEGMA−HEMA diblock copolymer was molecularly dissolved in a 50:50 d_4-methanol/D_2O mixture, which was then diluted with an approximate 4-fold excess of D_2O. D_2O is a good solvent for the OEGMA block but a poor solvent for the HEMA block, thus HEMA−core micelles with an intensity-average micelle diameter of 130 nm were formed, as indicated by dynamic light scattering studies. ^{1}H NMR studies showed little or no relative decrease in the signals due to the HEMA residues, indicating that the micelle cores remained highly hydrated; this is understandable given the marginally hydrophilic (water-swellable) nature of the polyHEMA chains.

In summary, it is shown that well-defined, near-monodisperse HEMA-based homopolymers and block copolymers can be prepared directly in high yields without protecting group chemistry either in 50:50 methanol/water mixtures or in methanol at 20 °C. Since HEMA is a cheap, functional monomer, this synthetic advance is likely to have commercial potential.

Experimental Section

Materials. HEMA monomer was kindly donated by Laporte Performance Chemicals. Cu^IBr and bpy were purchased from Aldrich. All materials were used as supplied.

ATRP Syntheses. In a typical experiment, an oligo(ethylene glycol)-based initiator (500 mg, 1.02 mmol; synthesized as described in ref 9a) and the HEMA monomer (5.0 mL; 40 mmol) was dissolved in 5 mL of a 50:50 v/v % methanol/water mixture. To this degassed solution was added the bpy ligand (400 mg; 2.56 mmol) and the Cu^IBr catalyst (147 mg; 1.02 mmol) to the stirred solution at 20 °C to produce a 50 w/v % dark brown solution. Polymerization occurred immediately, leading to an increase in viscosity and an exotherm of 14 °C over 7 min. Aliquots were taken at regular intervals to assess the extent of polymerization by ^{1}H NMR spectroscopy and DMF GPC, respectively. On exposure to air, the dark-brown reaction solution turned blue, indicating aerial oxidation of Cu(I) to Cu(II). Purification was achieved by passing the 50:50 methanol/water reaction solution through a silica column to remove the Cu(II) catalyst. The blue catalyst adsorbs onto the silica, and the resulting colorless aqueous solution is freeze-dried overnight to produce white (co)polymers in very high yield. Precipitation into cold THF removed traces of residual HEMA monomer and/or unreacted initiator, affording HEMA homopolymer in yields of at least 95%. In addition, the bulk homopolymerization of HEMA was carried out at 20 °C. An exotherm of 35 °C was noted, and a dark brown solid formed as the conversion of HEMA to homopolymer proceeded to 99% within 5 min. Cross-linking was thought to be inevitable under these conditions, but remarkably this homopolymer dissolved completely in DMF and GPC analysis in this solvent indicated an M_w/M_n of only 1.17.

Characterization. Molecular weight distributions were assessed using a GPC comprising of a Polymer Laboratories PL gel 5 μm mixed 'D' column, a DMF eluent which contained 1% TEA and 1% glacial acetic acid and a refractive index detector. A flow rate of 1 mL min^{-1} was used, and the column temperature was 40 °C. A series of near-monodisperse polystyrenes were used as calibration standards. ^{1}H NMR spectra were recorded in d_4-methanol using a 300 MHz Bruker AC-P spectrometer.

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(13) Originally it was thought that cross-linking had occurred due to traces of dimethacrylate contaminant in the HEMA (in ref 12 Beers et al. describe a procedure for the removal of dimethacrylate impurities from HEMA). However, this hypothesis can be discounted, since we subsequently obtained soluble, linear HEMA (co)polymers using both methanol and methanol/water mixtures with the *same batch of HEMA* without further purification. Since submitting this paper, it has been suggested to us that chain transfer to polymer (or possibly chain transfer to monomer) could also account for the cross-linking that occurs in aqueous media. Whether transesterification or chain transfer is the dominant cross-linking mechanism, the addition of methanol would be expected to suppress this side-reaction.

(14) Strictly speaking, the data shown in Figures 2 and 3 do not allow us to conclude that the rate of polymerization of HEMA is more rapid in methanol/water than in methanol because the target DP's were not identical in these experiments. However, we repeated the ATRP synthesis in methanol at a DP of 35 and the resulting conversion vs time curve (not shown) confirmed that the rate of homopolymerization of HEMA under these conditions was significantly slower than that shown in Figure 2. Only 70% conversion was achieved after 1 h in methanol whereas more than 95% conversion was obtained in 50:50 methanol/water within the same time period.

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