Articles

Atom Transfer Radical Polymerization of Hydroxy-Functional Methacrylates at Ambient Temperature: Comparison of Glycerol Monomethacrylate with 2-Hydroxypropyl Methacrylate

M. Save, J. V. M. Weaver, and S. P. Armes*

School of Chemistry, Physics and Environmental Science, University of Sussex, Falmer, Brighton, BN1 9QJ, United Kingdom

P. McKenna

Laporte Performance Chemicals, Charleston Industrial Estate, Hythe, Southampton, SO4 6ZG, United Kingdom

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ABSTRACT: The homopolymerization of two hydroxy-functional monomers, glycerol monomethacrylate [GMA] and 2-hydroxypropyl methacrylate [HPMA], has been investigated using ATRP chemistry in aqueous, methanolic, or water/methanol solution. In methanol, both monomers are polymerized to high conversion with reasonably good control (final polydispersities are 1.30 and 1.09 for GMA and HPMA, respectively) within a few hours at 20 °C. "Self-blocking" chain growth experiments indicate good living character under these conditions. Addition of water leads to much more rapid polymerizations in both cases, but high polydispersities (e.g., $M_w/M_n = 1.90$ for a 50/50 water/methanol mixture) were always obtained with GMA. With HPMA, relatively low polydispersities ($M_w/M_n = 1.17$) can be achieved under the same conditions. Several new diblock copolymers were synthesized using poly(alkylene oxide)-based macroinitiators. One of these hydrophilic−hydrophobic diblocks proved to be thermoresponsive and aggregated reversibly in aqueous media.

Introduction

2,3-Dihydroxypropyl methacrylate, otherwise known as glycerol monomethacrylate [GMA], and 2-hydroxypropyl methacrylate [HPMA] are functional monomers of commercial interest. GMA is a highly hydrophilic speciality monomer which has been used to prepare biocompatible amphiphilic networks.[1] It can also be used as a replacement for 2-hydroxyethyl methacrylate [HEMA] in soft contact lenses. HPMA is more widely used than GMA. According to the literature, it can be employed in various applications, including thermally cross-linkable paint formulations, surface modification of textile fibers, reactive adhesives and coatings, photoresists, and radiation curing.[2−4] From an academic perspective, there have been a number of interesting reports on the synthesis of controlled-structure GMA-based (co)polymers over the past decade or so.[5−7] Unfortunately, polymerization of GMA via living anionic chemistry necessitates the use of protecting group chemistry to mask the reactive dihydroxy groups. Nevertheless, this approach has been used to prepare new amphiphilic diblock copolymers[6−8] and shell cross-linked micelles.[9] Hoogeveen et al. examined the use of GMA-based diblock copolymers as polymeric dispersants for silica or titania particles in aqueous media.[6,10] There is also a recent account of the oligomerization of GMA using catalytic chain transfer chemistry using a Co-based catalyst,[11] and some aspects of the statistical copolymerization of GMA with MMA using free radical polymerization have been reported.[12] HPMA has been polymerized by conventional free-radical chemistry[13] using suspension[14] or dispersion[15] techniques and also by nitroxide-mediated radical polymerization.[16]

In 1995, Matyjaszewski's group and Sawamoto and co-workers independently developed a new form of pseudo-living free radical chemistry now known as atom transfer radical polymerization (ATRP).[17,18] In this approach, the polymer radicals are reversibly (de)-activated by a transition-metal catalyst, which caps the polymer chain ends with a halogen atom, usually Br or Cl. Thus, the instantaneous polymer radical concentration is believed to be significantly lower than that in conventional radical polymerization; this leads to suppression of the rate of termination relative to the rate of propagation and enables remarkably low polydispersities to be obtained.[19] This ATRP chemistry has gained a deserved reputation for excellent tolerance of both monomer functionality and protic sources.[20,21] Recently, both Zhu and co-workers and ourselves have demonstrated that ATRP is particularly effective for hydrophilic monomers under mild conditions in either aqueous or alcoholic media.[22−24] In particular, we showed that HEMA was efficiently polymerized in either methanol or methanol/water mixtures at room temperature.[22] In methanol/water mixtures very high conversions were

* To whom correspondence should be addressed.

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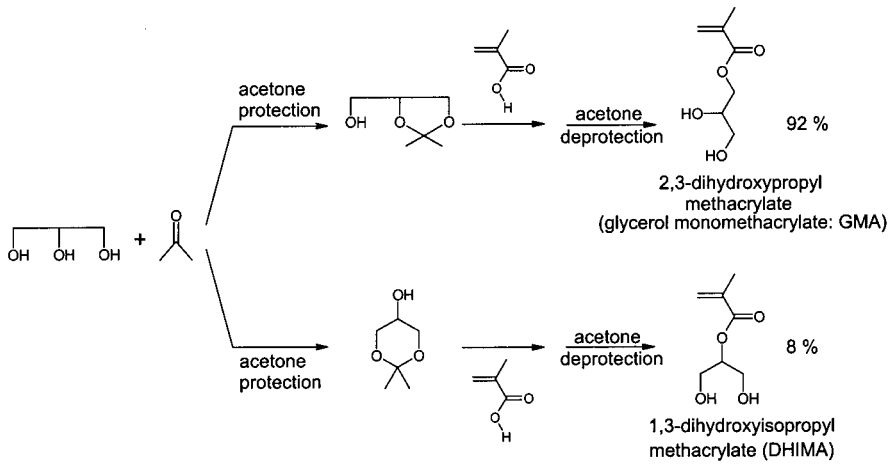


Figure 1. Synthetic route to glycerol monomethacrylate (GMA; also known as 2,3-hydroxypropyl methacrylate). Because of poor regioselectivity, 1,3-dihydroxyisopropyl methacrylate (DHIMA) is also obtained as a minor isomeric impurity.

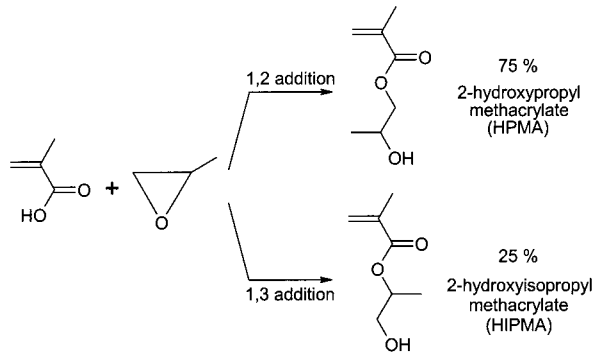


Figure 2. Synthetic route to 2-hydroxypropyl methacrylate (HPMA). Because of poor regioselectivity, 1-hydroxyisopropyl methacrylate (HIPMA) is also obtained as a minor isomeric impurity.

obtained, with typical polydispersities ranging from 1.2 to 1.3. Polymerization in methanol was significantly slower but resulted in lower polydispersities (M_w/M_n = 1.1−1.2).

As far as we are aware, there have been no reports of the direct polymerization of either GMA or HPMA by ATRP.[25,26] In this study we have explored the homopolymerization of GMA and HPMA via ATRP using a copper-based catalyst in methanol, water, and methanol/water mixtures at 20 °C. The influence of the solvent composition on both the kinetics and living character of the polymerization is examined in some detail. Optimized conditions allow the direct synthesis of well-defined homopolymers with relatively low polydispersities, and several novel diblock copolymers are prepared using macroinitiators.

Experimental Section

Materials. GMA and HPMA monomers were kindly donated by Röhm (Germany) and Laporte Performance Chemicals (Hythe, UK), respectively. The synthetic routes used to obtain GMA and HPMA necessarily results in the production of isomeric impurities (see Figures 1 and 2). The two monomers were both analyzed by GC-MS to determine their isomeric compositions. The isomeric composition of HPMA was confirmed by ^{1}H NMR spectroscopy. The "GMA" monomer actually contained 92 mol % GMA and 8 mol % of its closely related isomer, 1,3-dihydroxyisopropyl methacrylate [DHIMA]. The "HPMA" monomer actually contained 75 mol % HPMA, with the remainder being its closely related isomer, 2-hydroxyisopropyl methacrylate [HIPMA].

The DHIMA isomeric impurity in GMA arises directly from the acetyl protection of the glycerol precursor, while the mixture of HPMA and HIPMA can be attributed to the poor regioselectivity of the epoxide ring opening reaction. Figure 1 depicts how acetone reacts with glycerol predominantly in the 1,2 position to give GMA as the major isomer, whereas 1,3 addition accounts for the minor isomer. Subsequent reaction of this isomeric mixture with methacrylic acid produces GMA and DHIMA in the same isomeric ratios. Figure 2 illustrates how the nucleophilic attack of methacrylic acid by the substituted epoxide can occur at two positions. Attack at the tertiary carbon yields HIPMA, which is the minor isomer and accounts for 25% of the product. Alternatively, attack at the secondary carbon produces HPMA, which is the major product. Because of these isomeric mixtures, "homopolymerization" of HPMA or GMA actually leads to statistical copolymers rather than structurally homogeneous homopolymers. However, since the chemical structures of the minor isomers are very similar to GMA and HPMA, these copolymers will be simply referred to as either GMA or HPMA homopolymers in the following discussion.

Poly(alkylene oxide) precursors used for the synthesis of ATRP (macro)initiators were also donated by Laporte Performance Chemicals. Monohydroxy-capped oligo(ethylene oxide) [OEO−OH] had a mean degree of polymerization of 6−7 and an M_w/M_n of 1.15; monohydroxy-capped poly(ethylene oxide) [PEO−OH] had a mean degree of polymerization of 45 (M_w/M_n = 1.05), and monohydroxy-capped poly(propylene oxide) [PPO−OH] had a mean degree of polymerization of 33 (M_w/M_n = 1.10), as judged by ^{1}H NMR spectroscopy and GPC analyses. Cu(I)Cl and 2,2′-bipyridine (bpy) were purchased from Aldrich. All materials were used as received. [Note: in some of our earlier publications,[22,24,32] OEO was named oligo(ethylene glycol) and given the abbreviation OEG.]

Initiator Syntheses. The ATRP initiators were synthesized by reacting the terminal hydroxy group of the OEO−OH, PEO−OH, and PPO−OH precursors with 50% molar excess of 2-bromoisobutyryl bromide and triethylamine at room temperature for 2 days.[24,27] The resulting reaction solution was filtered to remove the insoluble amine hydrobromide salt, stirred with activated carbon, dried with magnesium sulfate, filtered, and vacuum-dried. OEO−Br and PPO−Br initiators were purified as follows: the initiator was dissolved in water at pH 9 and was then extracted several times with dichloromethane. This solution was dried using magnesium sulfate and then heated at reduced pressure in order to remove solvent (residual toluene from the synthesis and dichloromethane from the extraction). PEO−Br macroinitiator was readily purified by successive precipitation into cold diethyl ether followed by drying under vacuum.

ATRP of HPMA and GMA. The typical procedure was as follows. The initiator and monomer were each added to one reaction flask and were degassed using a nitrogen purge.

Table 1. Verification of Polydispersities before and after the Chemical Modification of GMA Homopolymer and PEO−GMA and PPO−GMA Diblock Copolymers According to the Derivatization Procedure Described by Ruckenstein and Zhang (See Ref 7)

polymer	M_n(theory), g/mol	M_n(expt), g/mol	M_w/M_n	M_n(THF GPC) of derivatized polymer,[e] g/mol	M_w/M_n
$OEO-GMA_{50}$ 13 400[b]	5 200[a]	2150[c]	1.29	12 200	1.23
$PEO_{45}-GMA_{70}$ 27 600[b]	13 300[a]	5900[c]	1.21	19 800	1.21
$PPO_{44}-GMA_{50}$ 20 900[b]	10 500[a]	49500[d]	1.19	24 000	1.18

[a] Theoretical molecular weight for the underivatized polymer. [b] Theoretical molecular weight for the polymer completely derivatized with benzoate groups. [c] Aqueous GPC data for the crude polymer, using PEO standards. [d] DMF GPC data for the crude polymer, using PS standards. [e] THF GPC protocol is based on PMMA standards.

Methanol was degassed separately and added to this monomer/initiator solution via a double-tipped needle, followed by a freeze−pump−thaw cycle. The Cu(I)Cl/bpy catalyst was introduced into the reaction flask to start the polymerization. The monomer concentration was typically between 30% and 50% (w/v), and reaction temperatures were between 20 and 50 °C. After the required time, the dark brown reaction solution was exposed to air and diluted with methanol; termination occurred rapidly as indicated by the color change from brown to blue due to the aerial oxidation of Cu(I) to Cu(II). GMA homopolymer was purified using silica chromatography, and HPMA homopolymer was precipitated into water to remove the ATRP catalyst.

Chemical Modification of GMA-Based Copolymers. In the case of the amphiphilic PPO−GMA diblock copolymers, the PPO block is water-insoluble, while the GMA block is insoluble in THF. To render this diblock copolymer THF-soluble for GPC analysis, the GMA block was protected according to a procedure described by Ruckenstein and Zhang.[7] For example, $PPO_{33}-GMA_{50}$ was dissolved in pyridine, benzoic anhydride (4 mol equiv based on GMA residues) was added, and the derivatization was allowed to proceed for 24 h at room temperature. The benzoate-protected polymer was vacuum-dried at 60 °C for several hours in order to remove the solvent and excess benzoic anhydride. Polymers derivatized by this method were always fully soluble in THF (unlike the precursors), and the RI trace from the THF GPC overlapped completely with the corresponding UV trace. Thus, the derivatization protocol did not result in significant fractionation. Several GMA homopolymers were analyzed by aqueous GPC, and these results were compared to those obtained from THF GPC of the corresponding derivatized homopolymers (Table 1). Similarly, selected PPO−GMA diblock copolymers were analyzed by DMF GPC, and these data were compared to those obtained on the derivatized copolymers by THF GPC.[28]

Characterization. All ^{1}H NMR spectra were recorded in CD_3OD, $CDCl_3$, or D_2O using a Bruker DPX 300 spectrometer. ^{1}H NMR was used to determine the extent of polymerization using the monomer vinyl signals at δ 5.5 and δ 6.0 (in CD_3OD). In addition, molecular weight information was obtained by comparing the methacrylate signals at δ 1.0 and δ 1.9 with those due to the PEO block at δ 3.5. Unfortunately, for PPO−GMA diblocks the NMR signals due to the two blocks overlap; thus, only an *estimate* of the degree of polymerization can be made. Molecular weight and polydispersities were measured by gel permeation chromatography (GPC) in THF (PLgel 3 μm mixed E and PLgel 5 μm, PMMA calibration standards, refractive index detector), aqueous solution (Pharmacia Biotech, Superose 6 column, 0.2 M $NaNO_3$ eluent containing 50 mM tris buffer at pH 8, poly(ethylene oxide) standards), or DMF (polystyrene standards, a column temperature of 40 °C, DMF eluent with 1% acetic acid and 1% triethylamine).

Dynamic light scattering (DLS) studies were performed using a Brookhaven model BI-200SM equipped with a correlator 9000AT equipped and a solid-state laser (50 mW, λ = 532 nm) at a scattering angle of 90°. For evaluation, both the cumulant analysis and the CONTIN algorithm were used to calculate hydrodynamic radii (R_h). Copolymer solutions were diluted to 0.4% (w/v) (4 mg/mL), and extraneous dust was removed using a 0.20 μm filter prior to DLS measurements. Dilute aqueous solutions of the PPO−GMA diblock copolymer micelles were dried onto TEM grids at 20 °C and examined directly using a Hitachi 7100 instrument.

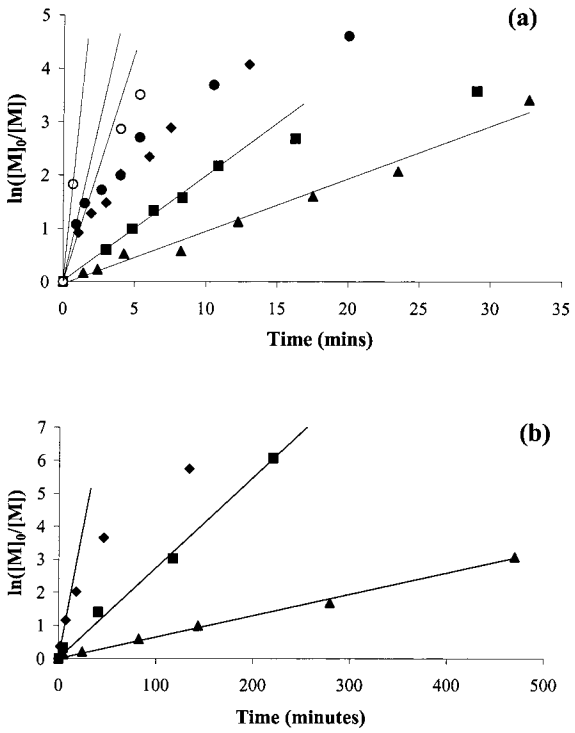
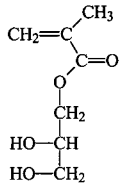
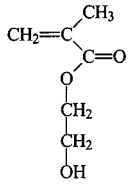
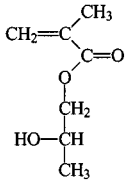


Figure 3. Effect of solvent composition [(▲) MeOH, (■) MeOH:H_2O (75:25), (♦) MeOH:H_2O (50:50), (●) MeOH:H_2O (25:75), (○) H_2O] on the kinetics of ATRP of (a) GMA and (b) HPMA at 20 °C. The relative molar ratios of OEO−Br:Cu(I)Cl:bpy were 1:1:2, and the target Dp was 50. For the GMA polymerization $[OEO-Br]_0$ = 68 mM and $[GMA]_0$ = 3.4 M (50% w/v). For the HPMA polymerization $[OEO-Br]_0$ = 70 mM and $[HPMA]_0$ = 3.5 M (50% w/v).

Results and Discussion

Homopolymerization of HPMA and GMA. Alkyl bromide initiators were used in combination with Cu(I)Cl catalyst and bpy ligand. Cu(I)Cl was chosen because Matyjaszewski and co-workers suggested that halogen exchange increases the rate of initiation relative to the rate of propagation, leading to better control over the polymerization.[29,30] Using the monofunctional oligo(ethylene oxide) bromide initiator, very high conversions (>98%) were obtained at room temperature in various methanol/water mixtures. For both monomers, increasing the water content leads to faster polymerizations but poorer control of the polymerization, as judged by both kinetic and GPC data (see Figure 3 and Table 3). It is likely that premature termination in the presence of water is more probable due to a higher polymer radical concentration. On the other hand, semilogarithmic plots of monomer concentration vs time (Figure 3) are linear up to high conversions in anhydrous methanol, indicating first-order monomer kinetics and a constant concentration of active centers during the polymerization. Strictly speaking, these syntheses are statistical copolymerizations rather than homopolymerizations because the two monomers are actually iso-

Table 2. Comparison of Monomer and Polymer Solubilities, Relative Polymerization Times, and Final Polydispersities of GMA, HEMA, and HPMA

Monomer	GMA	HEMA [22]	HPMA
Chemical structure (major isomer only)			
Monomer solubility in water	Miscible	Miscible	Miscible up to 13 % at 20°C
Polymer solubility in water	Soluble	Water swellable [31]	Insoluble
Polym. time[a] in MeOH/min	35	270	480
k_{app} (L mol^{-1}min^{-1}) in MeOH	1.45	0.145	0.093
M_w/M_n	1.30	1.10	1.09
Polym. time[a] in 50:50 MeOH:H_2O/min	7	50	220
M_w/M_n	1.90	1.49	1.17

[a] Time to reach 97% conversion of monomer for a fixed target Dp of 50; $[OEO-Br]_0 = 70$ mM, $[M]_0 = 50\%$ (w/v).

meric mixtures. Thus, the apparent rate constant (k_{app}) calculated from semilogarithmic plots of monomer concentration vs time can be considered to be a global rate constant for the isomeric mixture.

GPC analyses of HPMA and GMA homopolymers synthesized in methanol indicated symmetrical monomodal GPC traces in both cases. Generally, polydispersities were markedly lower for HPMA polymer ($M_w/M_n = 1.09$ in methanol) than for GMA polymer ($M_w/M_n = 1.30$ in methanol). The broadening of the molecular weight distribution with increasing water content, and the subsequent loss of control, was much more significant for GMA compared to HPMA (see Table 3). Thus, the molecular weight distribution remained narrow ($M_w/M_n = 1.17$) for HPMA polymerized in a 50/50 methanol/water mixture, whereas the polydispersity of GMA polymer was substantially higher ($M_w/M_n = 1.9$) under the same conditions. The discrepancy between the aqueous GPC molecular weight and the target molecular weight for the GMA polymer is presumably due to the unsuitable calibration protocol, which is based on poly(ethylene oxide) standards (see Table 1). The correlation between THF GPC molecular weight and the theoretical molecular weight is reasonable for the HPMA homopolymer but less good for the benzoate-derivatized GMA homopolymer (see Tables 1 and 3). In the latter case, the bulky benzoate groups presumably lead to a somewhat different hydrodynamic volume compared to the PMMA standards.

From the GPC analyses, M_n increased linearly with conversion for the polymerization of HPMA and GMA in methanol at 20 °C (see Figures 4 and 5), indicating a negligible contribution from chain transfer or other side reactions under these conditions. Moreover, the polydispersity decreased with conversion and remained constant above approximately 80% conversion. Symmetrical, unimodal GPC traces and linear molecular weight vs conversion plots were also observed when HPMA was polymerized in a 75/25 methanol/water mixture. Robinson et al.[22] recently reported that the ATRP of HEMA is well-controlled in both methanol and 50/50 methanol/water mixtures. This information provides an opportunity to compare the relative reactivities and living character of HPMA, HEMA, and GMA monomers under the same ATRP conditions; these results are summarized in Table 2. The predominant isomer in 2-hydroxypropyl methacrylate (HPMA) contains a secondary alcohol, 2-hydroxyethyl methacrylate (HEMA) has a primary alcohol, and 2,3-dihydroxypropyl methacrylate has both primary and secondary alcohol functionality. Hence, these three hydroxy-based monomers and their corresponding homopolymers display different hydrophilicities and water solubilities. GMA homopolymer is highly hydrophilic and exhibits no LCST in aqueous solution; according to the literature, HEMA homopolymer is only water-swellable[31] and HPMA homopolymer is water-insoluble. According to the data presented in Table 2, HPMA is clearly the least reactive monomer: for ATRP in methanol its polymerization was nearly twice as slow as that of HEMA and around 10 times slower than GMA under comparable conditions. (The k_{app} values for GMA, HEMA, and HPMA are 1.45, 0.145, and 0.093 L mol^{-1}min^{-1}, respectively.) Thus, the relative reactivities of these monomers are as follows: GMA $\gg$ HEMA $>$ HPMA. It was generally observed that slower polymerizations gave polymers with lower polydispersities (see Table 2). We and others have already demonstrated that water dramatically accelerates the ATRP of OEGMA [24,32,33] sodium 4-vinylbenzoate,[34] 2-(dimethyl)aminoethyl methacrylate,[23] MEMA,[35] *n*-BuMA,[36] and HEMA.[22] This phenomenon is also observed in the present work for both HPMA and GMA. The rate of homopolymerization of HPMA in pure methanol was relatively slow; even in 50/50 methanol/water, a minimum of 3 h was required for 97% conversion. Under the latter conditions, the polydispersity remains narrow ($M_n/M_w = 1.17$). Conversely, the addition of water to the relatively fast HEMA and GMA polymerizations results in a large rate enhancement (see Table 2), and the molecular weight distributions become significantly broader under these conditions ($M_w/M_n = 1.90$ for GMA homopolymer and $M_w/M_n = 1.49$ for HEMA homopolymer). The intrinsically high reactivity of GMA probably accounts for the reduced control achieved in the presence of water. This could be either due to a higher polymer radical concentration (leading inevitably to more termination) or possibly due to the relatively slow rate of initiation compared to the rate of propagation. Our recent spectroscopic studies of the aqueous ATRP of OEGMA at 20 °C suggest that a higher concentration of growing polymer radicals are produced in the presence of water, since the [Cu(II)/Cu(I)] molar ratio increased continuously throughout the polymerization.[37]

Since GMA homopolymerization was relatively fast even in methanol, we attempted to decrease the polymerization rate in an attempt to gain better control. Thus, either $Cu(II)Cl_2$ was added at the beginning of the polymerization or *N*-(*n*-butyl)-2-pyridylmethanimine was used as ligand for the homopolymerization of GMA carried out in methanol at 20 °C.[38] However, the expected improvements were not observed. In the

Table 3. Homopolymerization of GMA and HPMA Monomers Initiated by OEO−Br Initiator via ATRP at 20 °C

monomer	solvent	polym time,[a] min	M_n(theory), g/mol	M_n(^{1}H NMR), g/mol	M_n(GPC),[b] g/mol	M_w/M_n[b]
GMA	MeOH	35	5200	4300	2200	1.29
GMA	MeOH	35	8400	7250	2900	1.30
GMA	MeOH	35	11900	9500	3600	1.42
GMA	MeOH	240	16500	12500	5900	1.39
GMA	50:50 MeOH:H_2O	15	8100	6800	2000	1.91
GMA	H_2O	7	8100	7100	2500	2.08
HPMA	MeOH	470	7700	6700	9700	1.09
HPMA	75:25 MeOH:H_2O	190	7700	7500	8500	1.14
HPMA	50:50 MeOH:H_2O	130	7700	8100	6800	1.17
HPMA	H_2O	4	7700	7300	9800	1.26
HPMA	bulk	1	7700	8600	8400	1.20

[a] Time to reach 98% of monomer conversion. [b] Aqueous GPC for GMA polymers (PEO standards) and THF GPC for HPMA polymers (PMMA standards). [c] Conditions: 20 °C, OEO−Br:Cu(I)Cl:Bpy 1:1:2, $[OEO-Br]_0 = 0.70$ mM, $[GMA]_0 = 3$ M (50 w/v %), $[HPMA]_0 = 3.4$ M (50% w/v).

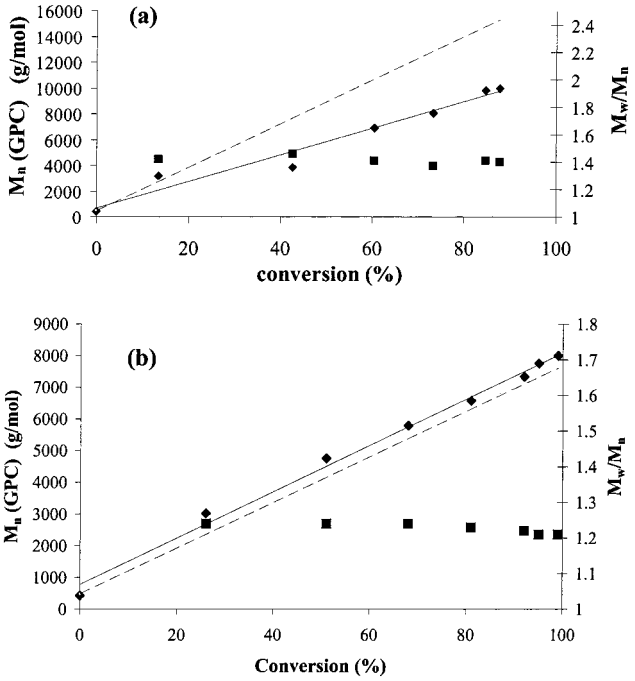


Figure 4. Evolution of GPC molecular weight (THF eluent, PMMA standards) and polydispersity with monomer conversion for (a) GMA and (b) HPMA homopolymerization in methanol at 20 °C [(■) M_w/M_n vs conversion; (♦) M_n(GPC) vs conversion; (- - -) M_n(theory) vs conversion]. The relative molar ratios of OEO−Br:Cu(I)Cl:Bpy were 1:1:2, and the target Dp was 50. For the GMA polymerization the relative molar ratios were $[OEO-Br]_0 = 65$ mM and $[GMA]_0 = 3.2$ M (50% w/v). For the HPMA homopolymerization $[OEO-Br]_0 = 70$ mM and $[HPMA]_0 = 3.5$ M (50% w/v).

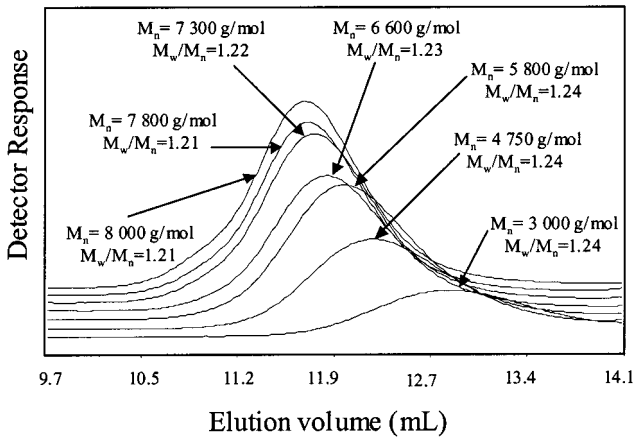


Figure 5. Evolution of GPC chromatograms for the homopolymerization of HPMA by ATRP in methanol at 20 °C. See Figure 4b for more detailed reaction conditions.

Table 4. Summary of Molecular Weight Data Obtained from Chain Growth Experiments with GMA and HPMA Using the OEO−Br Initiator in Methanol at 20 °C

polymer	conv, %	target DP	M_n(GPC), mol	M_w/M_n
GMA (1st addition)	97	48	9660	1.28
GMA (2nd addition)	98	102	25600	1.33
HPMA (1st addition)	98	53	6600	1.13
HPMA (2nd addition)	100	103	12800	1.14

[a] Experimental conditions: $[OEO-Br]_0 = 40-68$ mM, $[M]_0 \approx 1.9$ M, OEO−Br:Cu(I)Cl:Bpy 1:1:2.

experiments with added Cu(II), higher polydispersities of 1.38 and 1.61 were obtained for Cu(II)/Cu(I) molar ratios of 30/70 and 50/50, respectively. With the pyridylmethanimine-based ligand, the resulting GMA homopolymer was apparently cross-linked, since it was completely insoluble in both water and methanol.

To assess the living character of the homopolymerization of GMA and HPMA by ATRP, a chain growth experiment was carried out. A second monomer charge was added after 97% conversion of the first batch of monomer. The experimental conditions and results for these "self-blocking" experiments with both GMA and HPMA are shown in Table 4. In both cases, the second monomer charge is fully converted into polymer, and the polydispersity of the final homopolymer is almost the same as that of the initial homopolymer. There is no indication of bimodality in the GPC trace of the final polymer, and the experimentally observed increase in molecular weight bears reasonable comparison to the expected increase. Although the molecular weight distribution remains monomodal, a small amount of tailing is evident in the final polymer, which suggests that termination reactions are minimized rather than eliminated.

Block Copolymer Syntheses Using Macroinitiators. Diblock copolymers are usually prepared via sequential monomer addition. However, this approach can be problematic with ATRP chemistry, since termination is more likely under monomer-starved conditions.[39,40] This can lead to significant homopolymer contamination. Notwithstanding the surprisingly good results obtained in the "self-blocking" chain extension experiments, it was decided to use the well-known "macroinitiator" route to prepare GMA- and HPMA-based diblock copolymers.[41,42] Polymerization of GMA and HPMA using the OEO−Br initiator yielded low polydispersity homopolymers in both cases. Thus, in

Table 5. Synthesis Parameters and Molecular Weight Data Obtained for the Polymerization of GMA and HPMA Using the PEO−Br Macroinitiator at 20 °C

polymer	conv, %	solvent composition	polym time, h	temp, °C	M_n(theory), g/mol	M_n(THF GPC), g/mol	M_w/M_n
PEO_{45}−Br					2200	2800	1.05
PEO_{45}−GMA_{25}[d]	99	MeOH	5	20	11300[b]	10000[a]	1.16
PEO_{45}−GMA_{70}[d]	99	MeOH	5	20	27600[b]	19800[a]	1.21
PEO_{45}−$HPMA_{25}$[e]	100	50:50 MeOH:H_2O	<1	50	5700	7500	1.17
PEO_{45}−$HPMA_{50}$[e]	100	50:50 MeOH:H_2O	<2	50	9300	10800	1.15

[a] THF GPC for the derivatized PEO−GMA (PMMA standards). [b] Theoretical molecular weight for the GMA polymer, assuming that the hydroxy functions are completely protected. [d] Experimental conditions: PEO−Br:Cu(I)Cl:Bpy 1:1:2, $[PEO-Br]_0 = 40-95$ mM, $[GMA]_0 = 2.4-2.8$ M. [e] Experimental conditions: PEO−Br:Cu(I)Cl:Bpy 1:1:2, $[PEO-Br]_0 = 54-180$ mM, $[HPMA]_0 = 2.7-4.3$ M.

Table 6. Atom Transfer Radical Polymerization of GMA Using Two PPO−Br Macroinitiators at 50 °C in Methanol

polymer type	conv, %	M_n(theory),[c] g/mol	M_n(^{1}H NMR), g/mol	M_n(theory),[d] g/mol	M_n(GPC), g/mol	M_w/M_n
PPO_{44}−Br		2700	2800		5800	1.31
PPO_{44}−GMA_{50}	99	10500	8600[b]	20900	24000[a]	1.18
PPO_{33}−Br		2200	2050		3700	1.10
PPO_{33}−GMA_{50}	97	9800	5800[b]	19900	20300[a]	1.15
PPO_{33}−GMA_{70}	98	13000	10400[b]	27300	24200[a]	1.17
PPO_{33}−GMA_{100}	99	18000	18500[b]	38500	27000[a]	1.22

[a] THF GPC for derivatized PPO−GMA diblock copolymer using PMMA standards. [b] Approximate M_n of the initial PPO−GMA diblock estimated by NMR because of overlapping peaks. [c] Theoretical molecular weight of the initial underivatized GMA polymer. [d] Theoretical molecular weight for the fully protected GMA block. [e] Experimental conditions: $[PPO-Br]_0 = 36-64$ mM, $[GMA]_0 = 2.4-3.2$ M, PPO−Br:Cu(I)Cl:Bpy 1:1:2, polymerization time = 80−150 min.

principle, well-defined diblock copolymers could be synthesized using analogous higher molecular weight poly(alkylene oxide)-based macroinitiator. The macroinitiators used were based on either poly(ethylene oxide) [PEO] or poly(propylene oxide) [PPO] with degrees of polymerization of 45 and 33, respectively. These blocks are of interest because of their differing hydrophilicity. PEO is a well-known and widely used hydrophilic polymer which is soluble in aqueous solution over a wide temperature range, whereas PPO is much less hydrophilic and exhibits LCST behavior. (At a degree of polymerization of 33, the cloud point of a dilute aqueous solution of PPO is estimated to be around 15 °C.[43])

The synthesis of various diblock copolymers using either PEO−Br or PPO−Br macroinitiators in conjunction with both HPMA and GMA was successful; the results are summarized in Tables 5 and 6. The hydrophilic−hydrophobic GMA−PPO diblock is interesting because it is analogous to the commercially successful nonionic amphiphilic PEO−PPO block copolymers known as Pluronics, which have been widely used as surfactants, emulsifiers, and dispersants in various applications.[44,45]

Very high conversions were obtained for GMA in methanol within a few hours using both PEO−Br and PPO−Br macroinitiators at ambient temperature. With PPO−Br, significantly lower polydispersities were obtained if the polymerization temperature was increased to 50 °C. More specifically, for the same reagent concentrations, the polydispersity of PPO_{44}−GMA_{50} diblock was found to be 1.44 at 20 °C and 1.19 at 50 °C. The semilogarithmic plot of monomer concentration vs time indicated an induction period of approximately 15−20 min using PPO−Br at 20 °C; a much shorter induction period (around 5 min) was observed at 50 °C. It is well documented that better control can be achieved if the rate constant for initiation, k_i, is much greater than the propagation rate constant, k_p.[46] Since HPMA is the less reactive monomer, and given that its rate of polymerization is slower using PEO_{45}−Br compared to OEO_7−Br, substantially incomplete conversion of HPMA monomer was obtained in methanol at 20 °C even after several days. Therefore, the effect of adding water to increase the polymerization rate was explored. In a 50/50 methanol/water mixture, 99% of HPMA monomer was polymerized within 2 h at 50 °C using the PEO_{45}−Br macroinitiator. Each of the resulting PEO_{45}−GMA, PEO_{45}−HPMA, and PPO_{33}−GMA diblock copolymers had polydispersities ranging between 1.15 and 1.22 (Tables 5 and 6). Evidence of block formation was provided by ^{1}H NMR (see Figure 6), and the expected increase in molecular weight was indicated by GPC analysis. THF GPC traces corresponding to crude diblock copolymers were all monomodal, with no trace of residual macroinitiator (Figure 7). Thus, the initiation efficiencies of both macroinitiators were very high.

The PPO−GMA diblock copolymer was anticipated to be thermoresponsive in aqueous solution since the GMA block is permanently hydrophilic, whereas the PPO block becomes increasingly hydrophobic at higher temperatures. This expectation was borne out by experiment. After molecular dissolution at 5 °C to ensure initial solubility of the PPO block, the solution temperature was slowly increased up to 20−60 °C, and colloidal aggregates were observed by both DLS and TEM. ^{1}H NMR studies (not shown) indicated that no significant dehydration of the PPO blocks occurred, since the estimated block composition at 60 °C was the same (within experimental error) as that calculated at 5 °C. This observation is consistent with the relatively large aggregate diameters obtained: the hydrodynamic diameter for the aggregates formed by the PPO_{33}−GMA_{70} diblock copolymer was 150 nm, whereas the PPO_{33}−GMA_{50} and PPO_{33}−GMA_{100} diblocks gave aggregate diameters of 200 and 240 nm, respectively. These DLS observations were confirmed by TEM studies (not shown): the PPO_{33}−GMA_{70} diblock formed near-monodisperse spherical aggregates of around 150−190 nm, whereas a broader size range was evident for the PPO_{33}−GMA_{50} diblock (100−330 nm). In our experience, thermoresponsive polymers generally form relatively hydrated aggregates when heated above the cloud point

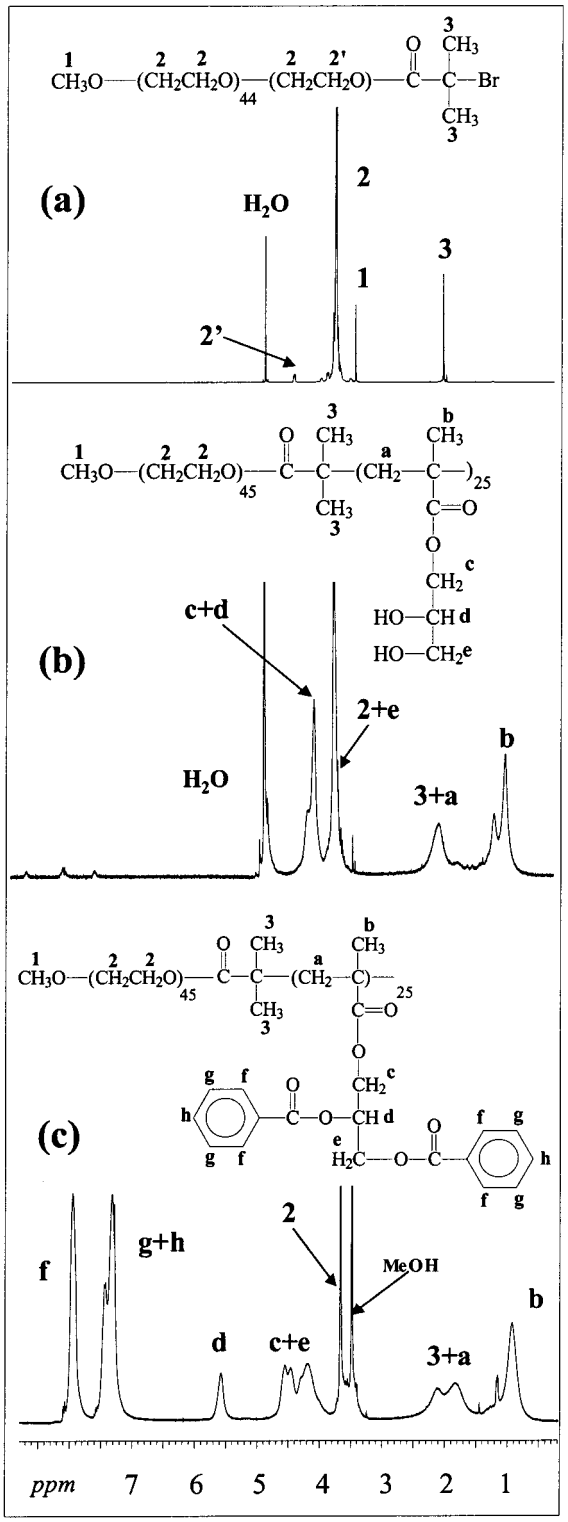


Figure 6. ^{1}H NMR spectra of (a) the PEO_{45}−Br macroinitiator in CD_3OD, (b) the PEO_{45}−GMA_{50} diblock copolymer in CD_3OD, and (c) the benzoate-derivatized PEO_{45}−GMA_{50} diblock copolymer in $CDCl_3$.

of the less hydrophilic block.[47−49] However, even allowing for hydration of the PPO block, these colloidal aggregates seem to be too large to be termed "micelles". The precise supramolecular structure of such aggregates is not well understood. Jérôme and co-workers have recently reported that certain hydrophilic−hydrophobic diblock copolymers can form either well-defined, compact micelles or larger aggregates, depending on the solution temperature.[50] At higher temperatures, the larger aggregates partially dissociated and the micelle population became more significant. This observation suggested that the aggregates might be clusters of micelles. Heating an aqueous solution of the PPO_{33}−GMA_{70} diblock copolymer up to 60 °C led to the observation of a new peak at 30 nm diameter using Contin software. However, this feature corresponded to only 8% of the total population; thus, it appears that most of the aggregates were not broken at this temperature.

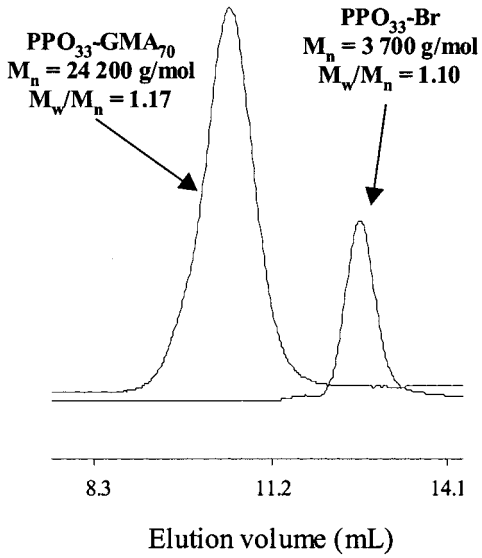


Figure 7. THF GPC chromatograms of a benzoate-derivatized PPO_{33}−GMA_{70} diblock copolymer synthesized in methanol at 50 °C and its corresponding PPO-based macroinitiator.

Conclusions

In summary, the controlled polymerization of two industrially relevant hydroxy-functional monomers has been achieved, and to some extent optimized, using ATRP. Near-monodisperse GMA and HPMA-based homopolymers have been prepared directly under mild conditions without recourse to protecting group chemistry. Polymerization was slower but more controlled in methanol compared to methanol/water mixtures, although HPMA polymerizations remain reasonably controlled with the addition of up to 25% water. In contrast, homopolymerization of GMA in the presence of water invariably leads to polymers of broad molecular weight distribution. Additionally, well-defined diblock copolymers were successfully synthesized using poly(alkylene oxide)-based macroinitiators. PPO−GMA diblock copolymers proved to be thermoresponsive, as expected. Reversible aggregation occurred at ambient temperature after initial molecular dissolution at lower temperature. The intensity-average diameters of these aggregates were approximately 150−240 nm, depending on the block composition.

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