Facile Atom Transfer Radical Polymerization of Methoxy-Capped Oligo(ethylene glycol) Methacrylate in Aqueous Media at Ambient Temperature

X.-S. Wang and S. P. Armes*

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

Received April 19, 2000; Revised Manuscript Received July 5, 2000

ABSTRACT: We report the facile atom transfer radical polymerization (ATRP) of a commercially available hydrophilic monomer, methoxy-capped oligo(ethylene glycol) methacrylate (OEGMA), under remarkably mild conditions. Various bromide-based initiators, in conjunction with a copper-based catalyst, allow rapid homopolymerization of OEGMA in water at 20 °C. Good living character was achieved with two ligands, namely 2,2′-bipyridine (bpy) and 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA). Kinetic studies confirm that, for bpy, 90% conversion is typically achieved within 20 min, and the polymerization is first order even up to very high conversions. Molecular weight increases linearly with conversion and is close to the target molecular weight in all cases. Polydispersities remain narrow (M_w/M_n = 1.15−1.30) throughout the polymerization. It is possible to lower the copper catalyst by a factor of 10 (i.e., [Cu(I)]/[initiator] = 0.10) without significant loss of control over the polymerization, which is good evidence for the highly active nature of the copper catalyst. To investigate the role played by the water in promoting rapid ATRP, selected bulk polymerizations were also carried out. With the bpy ligand it was found that the polymerization was living but slow: 90% conversion required 15 h at 20 °C even though the monomer, initiator, and catalyst concentrations were significantly higher in the bulk than in aqueous ATRP. Remarkably, the polydispersity of the final polymer isolated from this slow bulk polymerization was relatively high at 1.30, whereas typical final polydispersities for aqueous ATRP are 1.20−1.25. There are several factors that may account for the unexpectedly rapid, yet controlled, aqueous ATRP of OEGMA at 20 °C. The highly polar nature of water is believed to promote the formation of a very active mononuclear $[Cu(bpy)_2]^+$ catalyst. Furthermore, since OEGMA is a sterically congested monomer, its termination rate constant is several orders of magnitude lower than that of conventional methacrylates, which is expected to lead to improved living character. A third possibility is that the amphiphilic nature of the OEGMA monomer may lead to micellar polymerization, but no evidence was found for monomer micelles prior to ATRP. Finally, the cationic copper catalyst is easily removed from the aqueous reaction solution using silica chromatography, and the nonionic OEGMA homopolymer is readily isolated as a colorless solid.

Introduction

Water-soluble polymers are of increasing interest to both academia and industry as dispersants, stabilizers, emulsifiers, and flocculants.[1] Although various controlled-structure hydrophilic copolymers have been synthesized both in our laboratory and by many other research groups,[2−4] they have generally been prepared using ionic living polymerization chemistry under strictly anhydrous conditions. It would be particularly attractive and timely if, in the new millenium, water-soluble copolymers could be synthesized directly in aqueous media with precise control over their molecular weight distribution and copolymer architecture.

A few years ago, Matyjaszewski's group[5] and Sawamoto and co-workers[6] independently developed transition metal catalyzed living free radical polymerization, which has become known as atom transfer radical polymerization (ATRP).[5] ATRP is typically initiated by an alkyl halide (R−X) and catalyzed by a transition metal complex, such as CuX/bpy. Although the mechanism of ATRP is not yet fully understood, it is generally believed that the pseudo-living nature of the polymerization is due to the relatively low concentration of polymer radicals, which leads to the suppression of classical termination relative to propagation.[5] Many groups have demonstrated that ATRP is very versatile and is tolerant of a wide range of functional groups present in either the monomer, solvent, or initiator; it has been used to prepare a wide range of architectures, including block, star, gradient, and statistical copolymers, as well as well-defined macromonomers.[7]

Both Matyjaszewski and co-workers[8] and Sawamoto's[9] group reported that the addition of small quantities of water to ATRP syntheses in nonaqueous media had no deleterious effects. Indeed, in some cases moderate rate enhancements were observed. The first example of aqueous ATRP was from Matyjaszewski's group, who found that ATRP of 2-hydroxyethyl acrylate [HEA] can be carried out directly in water at 90 °C. After polymerization for 12 h, 87% monomer conversion was achieved, the molecular weight of the final product was 14 700, and the final polydispersity was 1.34.[10]

Similar results were obtained by our group for the controlled polymerization of sodium methacrylate in water at 90 °C. Monomer conversions of 70−80% were achieved after 10 h, with polydispersities of 1.20−1.30.[11] Broadly speaking, these are "typical" ATRP results: high conversions usually require elevated reaction temperatures (80−130 °C) and reaction times of at least several hours.[5] However, in a recent preliminary communication,[12] we reported the facile ATRP of methoxy-capped oligo(ethylene glycol) methacrylate (OEGMA) in water at 20 °C with various initiators. A remarkably

---

* To whom correspondence should be addressed.

10.1021/ma000671h CCC: $19.00

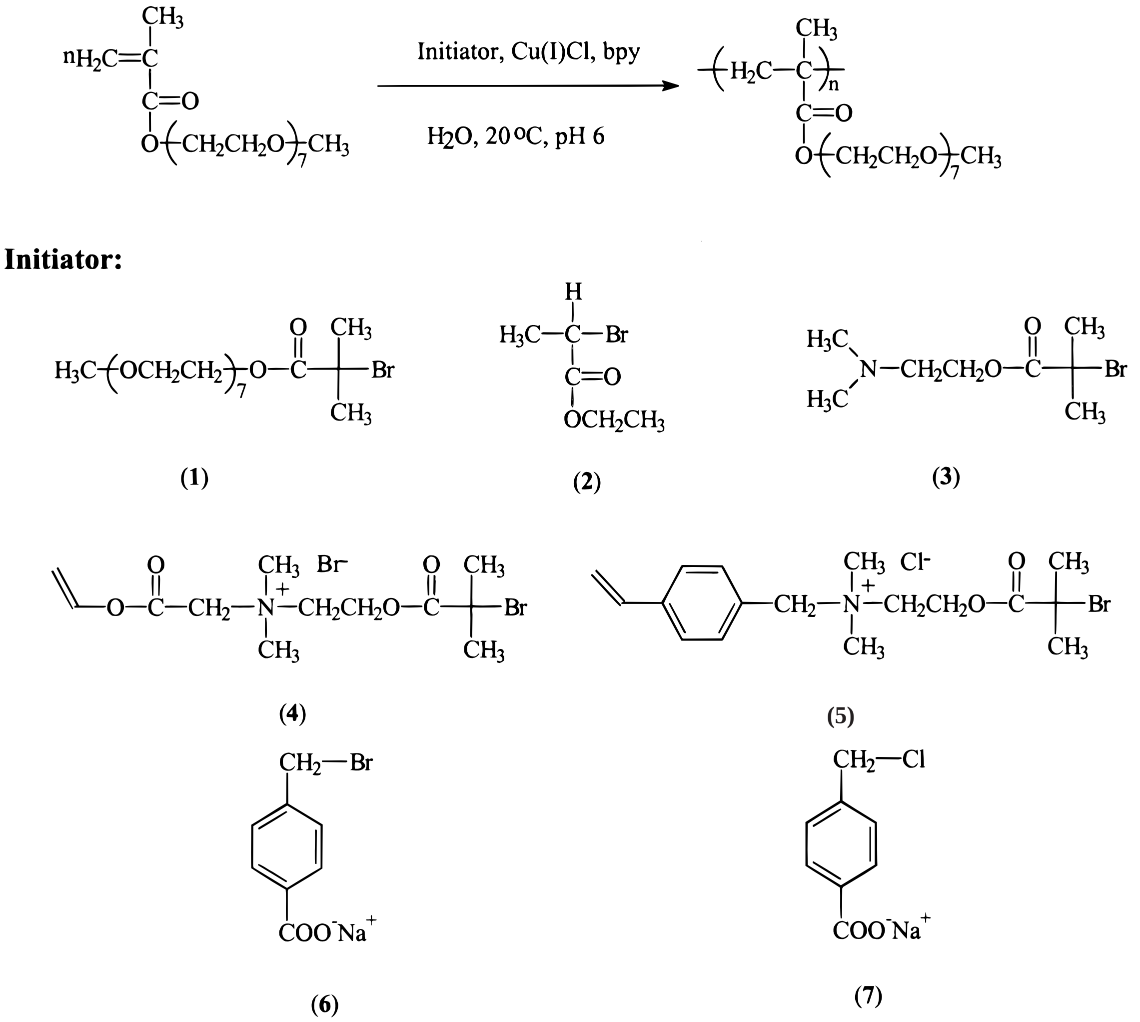

Figure 1. Scheme for the polymerization of OEGMA in aqueous media at 20 °C with various initiators.

fast rate of polymerization was observed, with unusually high monomer conversions (up to 99%), first-order monomer kinetics, and predetermined molecular weights with narrow molecular weight distributions, indicating good "living" character.

In this follow-up paper, we describe in detail a comprehensive study of the homopolymerization of OEGMA, a model hydrophilic monomer, by ATRP in aqueous media using a copper-based catalyst at 20 °C (see Figure 1).

The effect of various synthesis parameters on the rate of polymerization was examined, including the initiator type, ligand/catalyst ratio, catalyst concentration, and ligand type. The accelerating effect of the water is verified for the first time by control experiments using bulk monomer and possible reasons for the peculiar efficacy of ATRP in aqueous media are discussed.

Experimental Section

Materials. Monomethoxy-capped oligo(ethylene glycol) methacrylate (OEGMA; mean degree of polymerization is 7–8), monomethoxy-capped poly(ethylene glycol) methacrylate (PEGMA; mean degree of polymerization is 45), monomethoxy-capped oligo(ethylene glycol) (OEG; mean degree of polymerization is 7–8), and monohydroxy-capped oligo(propylene glycol) methacrylate (OPGMA; mean degree of polymerization is 6) were kindly donated by Laporte Specialities, Hythe, UK. OEGMA and OPGMA were passed through an alumina column to remove inhibitor before use. The OEG and PEGMA were used as received. 2-Bromoisobutyryl bromide, triethylamine, copper(I) chloride (CuCl), 2,2′-bipyridine (bpy), 4-(bromomethyl)benzoic acid, 4-(chloromethyl)benzoic acid, and vinyl bromoacetate were all purchased from Aldrich and were used as received. 4-Chloromethylstyrene (Aldrich) was vacuum-distilled prior to use.

Synthesis of Initiator 1. In a three-neck flask, 2-bromoisobutyryl bromide (7.30 g, 35 mmol) and triethylamine (2.48 g, 35 mmol) were mixed in THF (20 mL) at 0 °C. A 30 mL aliquot of a 33% (w/v) THF solution of OEG (10 g, 23 mmol) was added dropwise. After this addition was complete, the reaction solution was allowed to warm to room temperature, and the reaction mixture was stirred for another 4 h. The reaction mixture was then filtered, and the THF was removed using the rotary evaporator. The resulting yellow crude product was dissolved in water and extracted with diethyl ether. The diethyl ether layer was collected and dried over $MgSO_4$, and then the diethyl ether was removed under vacuum. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 4.08$ (t, 2H), 3.51 (t, 2H), 3.41 (s, 32H), 3.13 (t, 2H), 1.70 (s, 6H).

Synthesis of Initiator 3. 2-(Dimethylamino)ethanol (40.0 g, 405 mmol) and triethylamine (50.0 g, 500 mmol) were added to a three-necked flask with a magnetic stirrer. After the flask was purged with nitrogen for 30 min, dry THF (200 mL) was added via double-tipped needle, and the flask was cooled to −15 °C using dry ice/acetone bath. 2-Bromoisobutyryl bromide (61.0 mL, 500 mmol) was then added slowly via a syringe. A white precipitate formed within 5 min. The reaction solution was allowed to warm to room temperature over approximately 2 h and was stirred for a further 14 h. After this time the reaction mixture appeared slightly brown in color. The reaction solution was filtered to remove the white precipitate, and decolorizing charcoal was added to the yellow filtrate. This mixture was then filtered again, and the THF was removed under vacuum. Finally, the resulting liquid was distilled at reduced pressure at 50 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta =$ 4.14 (t, 2 H), 2.49 (t, 2 H), 2.17 (s, 6 H), 1.79 (s, 6 H).

Synthesis of Initiators 4 and 5. These initiators were obtained by quaternization of initiator **3**. Initiator **3** (6.54 g, 28 mmol) was added to a 100 mL round-bottom flask, and then THF was added (50 mL), together with a magnetic flea. Finally, 4-chloromethylstyrene (8.57 g, 56 mmol) or vinyl bromoacetate (9.24 g, 56 mmol) was added via double-tipped needle, and the reaction was stirred overnight at room temperature. The reaction solution was filtered and a white solid was recovered. ^{1}H NMR (D_2O, 300 MHz) for initiator **4**: $\delta =$ 7.14 (q,1 H), 5.0 (d, 1 H), 4.75 (d, 1 H), 4.59 (t, 2 H), 4.47 (s, 2 H), 4.02 (t, 2 H), 3.32 (s, 6 H), 1.82, (s, 6 H). Initiator **5**: $\delta =$ 7.61 (d, 2 H), 7.41 (d, 2 H) 6.75 (q, 1 H), 5.76 (d, 1 H), 5.32 (d, 1 H), 5.14 (s, 2 H), 4.71 (t, 2 H), 4.20 (t, 2 H), 3.34 (s, 6 H), 1.90 (s, 6 H).

Initiators 2, 6, and 7. These three initiators were purchased from Aldrich. Initiator **2** is insoluble in water but dissolves in an aqueous OEGMA solution at 20 °C. Initiators **6** and **7** are not soluble in water at 20 °C in their free acid form. Thus, these two initiators were converted into their corresponding water-soluble sodium salts prior to polymerization by adjusting the solution pH using NaOH.

Homopolymerization of OEGMA via ATRP. In a typical synthesis, the ATRP of OEGMA was carried out in doubly distilled, deionized water at room temperature under a nitrogen atmosphere. The initiator, monomer, and water were added to a reaction flask. The water solution was degassed through one freeze–thaw cycle. Then the copper catalyst complex was added to start the polymerization. The reaction solution became dark brown and viscous, and an exotherm of 5–10 °C was observed. Termination occurred rapidly on exposure to air, as indicated by the color change from brown to blue (oxidation of Cu(I) to Cu(II)). The reaction solution was passed through a silica column to remove the blue copper catalyst, and the aqueous solution was freeze-dried overnight, yielding a colorless polymer. Subsequent experiments showed that the order of addition of the reagents did not affect either the rate or extent of polymerization appreciably.

For kinetic studies, the same procedure was performed in D_2O, and the reaction solution was sampled periodically. In some cases these aliquots were further diluted in D_2O, and NMR spectra were recorded directly to get monomer conversion (and, depending on the initiator type, the number-average molecular weight via end group analysis). Alternatively, these aliquots were diluted in THF and dried over magnesium sulfate to remove D_2O prior to GPC analysis (THF eluent).

Bulk homopolymerizations were carried out using essentially the same conditions as described above but in the absence of water. Thus, initiator **1** was dissolved in the OEGMA monomer. After the mixture of initiator and monomer was degassed, the CuCl and bpy were added to start the polymerization. In these syntheses the rate of polymerization was much slower, and little or no exotherm was observed. The reaction solution became very viscous after 15 h at 20 °C.

Homopolymerization of PEGMA via ATRP. Initiator **1** (0.04 g, 0.095 mmol) and PEGMA (2.0 g, 1.0 mmol) were dissolved in 5.0 g of D_2O in the reaction flask. Solution degassing was achieved by a single freeze–thaw cycle. Then the CuCl/bpy (9.4 mg, 0.095 mmol/29.6 mg, 0.190 mmol) complex was added to start the polymerization. Aliquots were periodically withdrawn to monitor the conversion using ^{1}H NMR, as mentioned above. After the polymerization, the reaction mixture was diluted with water and passed through a silica column to remove the copper complex. Colorless polymer was recovered after freeze-drying from water.

Synthesis of a Statistical Copolymer. OEGMA (3.26 g, 7.76 mmol), OPGMA, (3.18 g, 7.32 mmol), CuCl (45.0 mg, 0.45 mmol), bpy (140.0 mg, 0.90 mmol), and water (3 mL) were added in turn to the reaction flask to produce an homogeneous aqueous solution. After degassing via a single freeze–thaw cycle, methyl 2-bromopropionate (75.0 mg, 0.45 mmol) was injected to initiate the polymerization. After 30 min the polymerization was terminated, and the resulting statistical copolymer was purified as described above.

Table 1. Results of the Polymerization of OEGMA Catalyzed by CuCl/bpy in Aqueous Media at 20 °C with Various Initiators

initiator type	reaction time/h	conversion (%)	target M_n	M_n by ^{1}H NMR	M_n by GPC	M_w/M_n
1	0.5	>99[a]	8 500		6 500[b]	1.12
1	0.5	>99[a]	14 000		12 700	1.19
2	2.0	>99[a]	11 200	10 600	6 000[b]	1.17
3	8.0	>99[a]	2 400	2 500	3 500[c]	1.38
3	0.5	>99[a]	5 100	5 300	4 700[c]	1.42
4	1.0	>99[a]	14 600	14 500	9 700[c]	1.21
4	0.5	98	5 000	4 900	5 500[c]	1.30
5	2.0	>99[a]	18 700	19 000	31 500[c]	1.86
5	0.5	98	6 000	5 700	15 100[c]	1.89
6	0.5	99	14 000	13 200	12 200[d]	1.31
7	10	99	14 000	15 100	14 700[d]	1.36

[a] No residual monomer signal detected in ^{1}H NMR spectrum. [b] THF eluent; PMMA standards. [c] Aqueous eluent; PEO standards. [d] After methylation of carboxylic acid group.

Polymer Characterization. All ^{1}H NMR spectra were recorded in either D_2O or $CDCl_3$ using a Bruker Avance DPX 300 MHz spectrometer. Molecular weight and molecular weight distributions were measured by either THF GPC (Plgel 3um MIXED-E 300 × 7.5 mm column, THF eluent, PMMA calibration standards, refractive index detector) or aqueous GPC (Pharmacia Biotech Superdex 200 HR 10/30 FPLC column, 1.0 M NaCl eluent containing 50 mM Tris buffer at pH 9, poly(ethylene oxide) calibration standards, refractive index detector).

Results and Discussion

Homopolymerization of OEGMA in Aqueous Media at 20 °C. Substituted bpy ligands are commonly used in the nonaqueous or bulk ATRP of styrene or methacrylates in order to aid solubilization of the Cu(I) catalyst.[8] However, unsubstituted bpy is commercially available and leads to a water-soluble Cu(I) complex; thus, it was the ligand of choice for most of the aqueous ATRP syntheses described herein. Cu(I)Cl was used as catalyst since, in combination with alkyl bromide initiators, it is reported to improve living character of methacrylic monomers in ATRP.[13] A halogen exchange effect has been suggested for this R–Br/CuCl/bpy system.[14] Various initiators were examined for this polymerization (Figure 1). The results are summarized in Table 1.

Several initiators allow good control over molecular weight and polydispersities are as low as 1.12. With initiator **4** we note that well-defined vinyl acetate-capped macromonomers are obtained in high yield in water at 20 °C. In the case of initiator **5**, the actual final molecular weight is about twice as high as the target molecular weight, because the styrenic end group probably copolymerizes with the OEGMA. In most of our experiments, bromide-based initiators were used. These have the advantage of faster initiation and hence a faster rate of polymerization compared to those of chloride-based initiators. The relative rates of OEGMA homopolymerization in water at 20 °C using sodium 4-(bromomethyl)benzoate and sodium 4-(chloromethyl)benzoate initiators are compared in Figure 2. The latter initiator requires more than 10 h for high conversion (>90%), whereas the bromide initiator only requires 15 min under the same conditions. However, in both cases there is good agreement between the target and actual

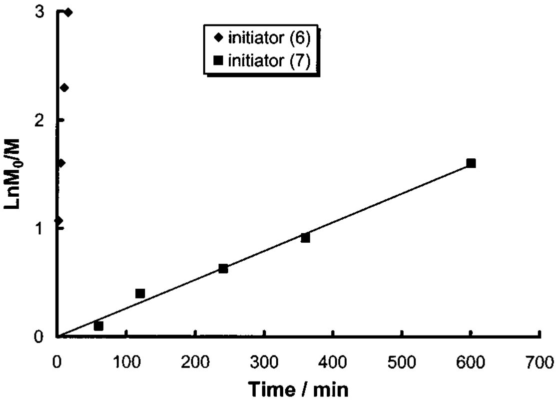

Figure 2. Kinetic data for the ATRP of OEGMA in aqueous media at 20 °C using initiator **6** and initiator **7**. Conditions: OEGMA = 10 g, D_2O = 10 g, [initiator] = 36 mM. The relative molar ratios of OEGMA:initiator:CuCl: bpy were 33:1:1:2.

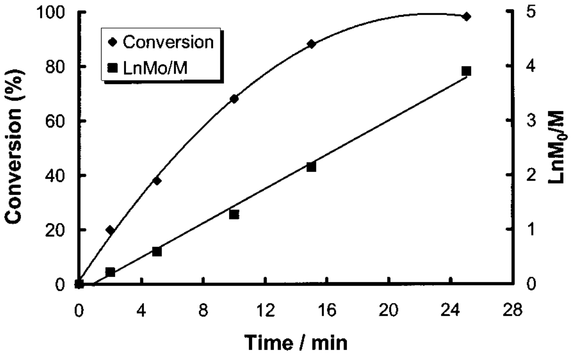

Figure 3. Kinetics of polymerization of OEGMA using initiator **1** in aqueous media at 20 °C. Conditions: OEGMA = 10 g, D_2O = 5 g, [initiator] = 44 mM. The relative molar ratios of OEGMA:initiator:CuCl:bpy were 33:1:1:2.

degrees of polymerization, which suggests high initiator efficiencies.

Normally, exotherms of 5−10 °C are observed for the aqueous ATRP of OEGMA with bromide-based initiators. The reaction mixture becomes dark brown and progressively more viscous and remains homogeneous in appearance throughout the polymerization. The nonvolatile nature of the OEGMA monomer and high solubility of OEGMA polymer in a wide range of solvents meant that gravimetry could not be used to determine the extent of polymerization. Instead, monomer conversions were monitored using ^{1}H NMR spectroscopy, in which the monomer vinyl signals appear at δ 5.4 and 5.8 and their intensities decrease monotonically with time. As the polymerization proceeds, the relative intensity of the oxymethylene signal attached to the ester carbonyl group increases at δ 3.8 and the methacrylate backbone signals arise at δ 0.8−2.0.[12] Comparing the respective monomer and polymer signals allows the monomer conversion to be determined with good reliability. A semilogarithmic plot of monomer conversion vs reaction time is linear up to high conversions (see Figure 3). This indicates that (i) the polymerization is first order with respect to monomer and (ii) the concentration of active centers (polymer radicals) remains constant during the polymerization.

From Figure 3, it is clear that the rate of polymerization in aqueous ATRP at 20 °C is dramatically faster than conventional ATRP at elevated temperatures, since under the latter conditions at least several hours is usually required to achieve high conversions.[5] Faster rates of ATRP have been reported in more polar solvents.[13,15] Since water is highly polar, it is understandable that ATRP proceeds efficiently in aqueous media. Nevertheless, we wish to emphasize that ATRP is peculiarly rapid for a wide range of hydrophilic methacrylate (and also certain styrenic) monomers under remarkably mild conditions.[16] In the case of OEGMA, GPC analysis confirms that molecular weight increases linearly with conversion (see Figure 4). Moreover, molecular weight distributions remain narrow even up to conversions in excess of 95%, indicating good living character for this homopolymerization in aqueous media at 20 °C.

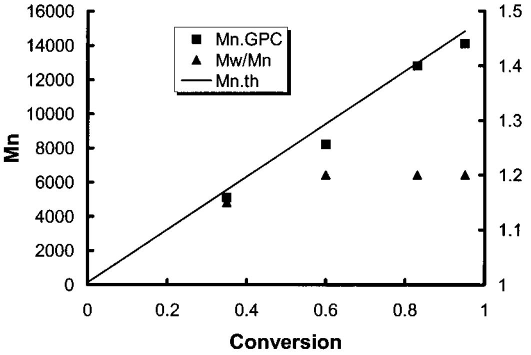

Figure 4. Evolution of molecular weight and polydispersity with monomer conversion for the polymerization of OEGMA using initiator **1** in aqueous media at 20 °C. Conditions: OEGMA = 10 g, D_2O = 5 g, [initiator] = 44 mM. The relative molar ratios of OEGMA:initiator:CuCl:bpy were 33:1:1:2.

It is perhaps surprising that narrow polydispersities (typically 1.20) and good molecular weight control are obtained for OEGMA homopolymer in aqueous media. Given the much more rapid rate of polymerization under these conditions, poorer control might have been expected.[7] A possible reason for this apparent anomaly is discussed later.

Homopolymerization of PEGMA in Aqueous Media at 20 °C. Homopolymerization of PEGMA, which has a mean degree of polymerization of 45 and is essentially a higher molecular weight version of OEGMA, was also successful using the same aqueous ATRP protocol. A kinetic study confirmed that the homopolymerization of PEGMA is almost as fast as OEGMA and also yielded a linear semilogarithmic plot (see Figure 5). The final poly(PEGMA) is not THF-soluble so aqueous GPC was utilized to assess its molecular weight distribution. Polydispersities as low as 1.19 were obtained using PEO calibration standards.

In view of these encouraging results, the synthesis of relatively high molecular weight poly(PEGMA) was attempted. A theoretical degree of polymerization of 100 was targeted, and almost 100% conversion was achieved, as judged by ^{1}H NMR and aqueous GPC. However, in this case the GPC trace indicated two shoulders at lower molecular weight, suggesting that some termination occurred during polymerization. In this context it is worth emphasizing that the efficient homopolymerization of genuine macromonomers such as PEGMA is usually considered rather problematic; indeed, in our experience it is rather difficult to achieve more than 95% conversion for the homopolymerization of PEGMA by group transfer polymerization (GTP) in anhydrous THF at 20 °C.[17] However, Ito and co-workers[18] have reported that the conventional free-radical homopolymerization of PEGMA (and related macromonomers) is anoma-

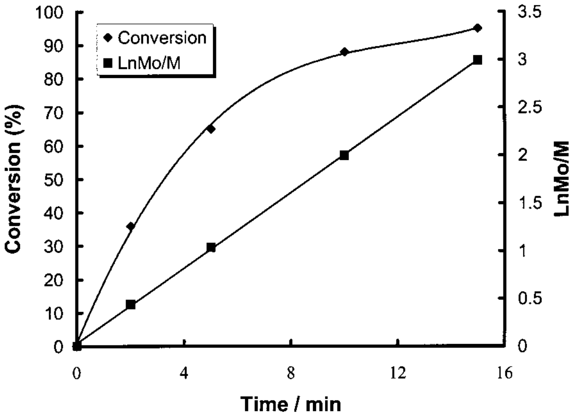

Figure 5. Kinetics of polymerization of PEGMA (mean D_p of EG residues = 45) using by initiator **1** in aqueous media at 20 °C. Conditions: PEGMA = 2 g, D_2O = 5 g, [initiator] = 20 mM. The relative molar ratios of PEGMA:initiator:CuCl:bpy were 10:1:1:2.

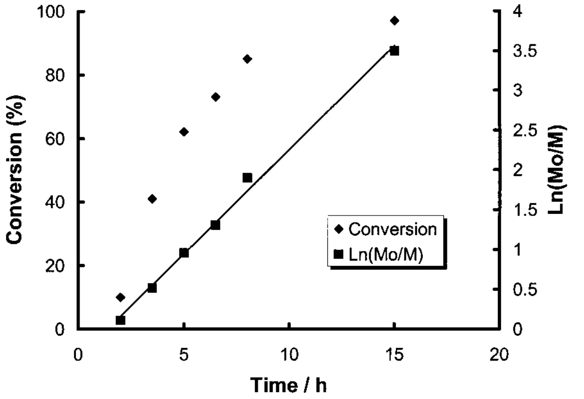

Figure 6. Kinetic data for the bulk polymerization of OEGMA using initiator **1** at 20 °C. Conditions: OEGMA = 10 g, [initiator] = 72 mM. The relative molar ratios of OEGMA: initiator:CuCl:bpy were 33:1:1:2.

lously fast in water at 60 °C, with high yields of very high molecular weight polymer being achieved within 1 h. Further investigations on the homopolymerization and copolymerization of this PEGMA macromonomer by aqueous ATRP are currently in progress.

Bulk Homopolymerization of OEGMA at 20 °C. Since OEGMA is a liquid monomer at room temperature, it is possible to carry out bulk ATRP under the same conditions as aqueous ATRP in order to make a direct comparison. The results are summarized in Figures 6 and 7. Polymerization occurs after a significant induction time of nearly 2 h, and a further 13 h is required to achieve 95% conversion at 20 °C.

The evolution of molecular weight is linear with conversion, and GPC analysis indicates final polydispersities of around 1.30 (see Figure 7). Thus, the bulk polymerization of OEGMA is reasonably living but much slower than that achieved by aqueous ATRP, even though the monomer, initiator, and catalyst concentrations are all necessarily lower in the latter case. This bulk polymerization control experiment suggests that the water plays an important role as an accelerator in the aqueous ATRP of OEGMA, rather than merely acting as a diluent. Moreover, narrower polydispersities (around 1.20) were obtained in aqueous media compared to those obtained in bulk ATRP at 20 °C (around 1.30). This indicates that water not only accelerates the rate but also improves the living character of the polymerization.

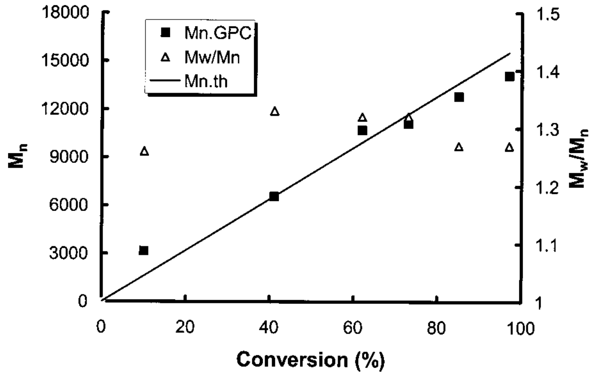

Figure 7. Evolution of molecular weight and polydispersity with monomer conversion for the bulk polymerization of OEGMA using initiator **1** at 20 °C. Conditions: OEGMA = 10 g, [initiator] = 72 mM. The relative molar ratios of OEGMA: initiator:CuCl:bpy were 33:1:1:2.

Several groups have reported that polar solvents such as acetonitrile[13] or ethylene carbonate[15] or additives such as carboxylic acids[19] or phenols[20] can act as accelerators for conventional nonaqueous ATRP. Usually these observations were rationalized in terms of structural changes in the active catalyst. Similarly, the most likely explanation for the increased rate of ATRP in aqueous media is that the water leads to the formation of a more active Cu(I) catalyst. It is well-known that the d^{10} electronic configuration of Cu(I) prefers a tetrahedral environment, and the most likely catalytic species in aqueous media is the simple monocationic $[Cu(I)(bpy)_2]^+$ complex with a halide counterion.[21] During ATRP, the oxidation of Cu(I) to Cu(II) could lead either to the corresponding dicationic tetrahedral Cu(II) complex or, perhaps more likely, to a monocationic trigonal-bipyramidal complex with halide (chloride or bromide) as a bound ligand.[21] There is also the possibility that one (or more) water molecules may act as weakly coordinating coligands for this Cu(II) complex.

However, in the *absence* of water (i.e., in conventional bulk or nonaqueous ATRP) it is reasonable to suppose that neutral, binuclear Cu(I) complexes with bridging halide ligands would be more likely.[22] These differences in catalyst structure probably account for the enhanced polymerization rates observed for aqueous ATRP.[13,23]

Matyjaszewski's group reported that the rate of polymerization of *n*-butyl acrylate in ethylene carbonate *increases* at lower monomer concentration (i.e., with more added solvent).[15] It was suggested that, as the solvent polarity was increased, a higher concentration of mononuclear copper catalyst was produced; thus, both the radical concentration and the polymerization rate increased. As a result, the molecular weight distribution broadened markedly: at a 50:50 (v/v) *n*-butyl acrylate/ethylene carbonate composition the polydispersity was as high as 1.6. A similar explanation may apply to the aqueous ATRP of OEGMA. Although in this latter case the polydispersities are invariably less than 1.30, there is nevertheless a systematic tendency toward higher polydispersities at lower OEGMA concentration (increasing water content), suggesting that higher concentrations of growing polymer radicals are produced.[24] At first sight it is difficult to reconcile the idea of a higher concentration of propagating radicals with the relatively good living character exhibited by the OEGMA monomer. However, Buback and co-workers have shown that sterically hindered vinyl monomers such as *n*-dodecyl (meth)acrylate have anomalously low k_t values compared to those of the corresponding methyl (meth)-acrylates.[25] This was attributed to the increased difficulty of radical−radical annihilation, and presumably the same principle applies to the even more sterically congested OEGMA (and PEGMA). Furthermore, a very high k_p/k_t ratio was determined for a styrene-functionalized PEG macromonomer ($M_n = 2300$) in aqueous solution by Ito and co-workers.[26] Thus, it is possible to rationalize the apparent contradiction of rapid polymerization with the retention of reasonable living character, at least for this particular class of monomer.

Ito and co-workers have reported a series of studies concerning the homopolymerization of PEGMA-type macromonomers via conventional free radical chemistry at 60 °C.[18,26,27] It was shown that the rate of polymerization was more than 50 times faster in water than in benzene under the same conditions. Static light scattering studies carried out at 20 °C indicated micelle formation, and it was assumed that similar micellar structures were present at the polymerization temperature of 60 °C. Thus, it was claimed that the anomalously fast rate of polymerization was due to micellar polymerization; i.e., it was a direct result of the relatively high local concentration of vinyl groups within the hydrophobic micelle interior. The Japanese group reported very high polymer molecular weights ($2 \times 10^6 - 1 \times 10^7$) and suggested that intermicellar polymerization occurred under their conditions.

Since the rate of ATRP of OEGMA is up to 2 orders of magnitude faster in aqueous solution at 20 °C than in the bulk, it is obviously tempting to invoke similar micellar polymerization effects in this case. However, we emphasize that there are significant differences between the present study and the work by Ito and co-workers. Polymer molecular weights of 5000−15 000 are typically obtained in our aqueous ATRP syntheses, which are much lower than those reported by Ito et al. The Japanese group claimed that, since their molecular weights were higher than the average micelle molecular weight, some intermicelle polymerization must occur. However, in our case the polymer molecular weight is lower than the micelle molecular weights reported by Ito et al. This suggests either that micellar polymerization is incomplete (i.e., that premature termination occurs within the micelles, which is not consistent with the very high monomer conversions obtained) or that there are no micelles present under our polymerization conditions. Unlike Ito and co-workers, we have not carried out static light scattering studies on our aqueous (macro)monomer solutions prior to polymerization. However, we see no micelle formation in aqueous OEGMA solution at low OEGMA concentration (<1%) as judged by dynamic light scattering and no visual evidence for OEGMA (or PEGMA) micelles at 50% solids. Finally, and perhaps most importantly, it is noteworthy that similarly fast polymerization kinetics have been observed at ambient temperature for the aqueous ATRP of a series of other hydrophilic monomers, including sodium 4-vinylbenzoate,[28] ammonium 2-sulfatoethyl methacrylate,[29] and 2-aminoethyl methacrylate.[29] In addition, 2-hydroxyethyl methacrylate (HEMA) polymerizes very rapidly in a 50:50 methanol/water mixture at 20 °C.[29] Such simple monomers have no obvious surfactant character so it is very difficult to claim that the observed rapid rate of ATRP at 20 °C in water (or aqueous alcohol in the case of HEMA) is due to micellar polymerization in each case. Thus, while not doubting the validity of the micellar polymerization studies by Ito and co-workers, we remain unconvinced that their work is relevant to the present study.

Table 2. Apparent Rate Constants (k_{app}) and Polydispersities for the Polymerization of OEGMA in Aqueous Media at 20 °C with Three CuCl:bpy Molar Ratios[a]

bpy/Cu(I)Cl molar ratio	k_{app} ($\times 10^{-3}$ s^{-1})	M_w/M_n at 25% conversion	M_w/M_n over 90% conversion
1	2.50	1.15	1.18
2	7.66	1.17	1.23
3	7.50	1.40	1.45

[a] Conditions: OEGMA = 10 g, deuterium oxide = 10 g, [initiator] = 36 mM, OEGMA:initiator:CuCl = 33:1:1.

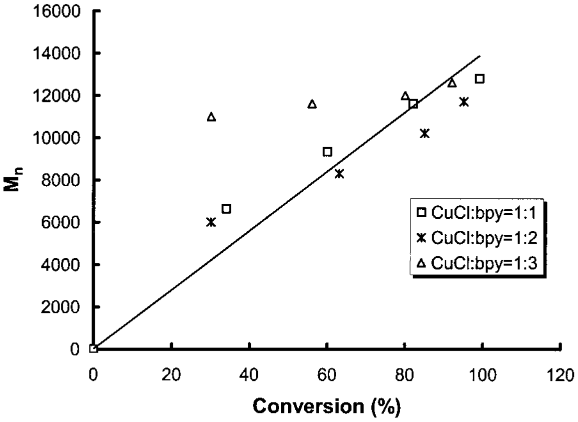

Figure 8. Evolution of molecular weight with monomer conversion for the ATRP of OEGMA using initiator **1** in water at 20 °C at three CuCl:bpy molar ratios (1:1, 1:2, and 1:3). Conditions: OEGMA = 10 g, D_2O = 10 g, [initiator] = 36 mM. The relative molar ratios of OEGMA:initiator:CuCl:bpy were 33:1:1:2.

Effect of Varying the bpy/CuCl Molar Ratio. The homopolymerization of OEGMA was carried out at three different bpy/Cu(I)Cl molar ratios (see Table 2 and Figure 8).

At a molar ratio of either 1.0 or 2.0, the evolution of molecular weight is linear with conversion, and final polydispersities are reasonably narrow (around 1.20). However, the rate of polymerization is approximately 3 times faster at the higher ratio. A similarly fast rate is achieved at a bpy/Cu(I)Cl molar ratio of 3.0, but under these conditions final polydispersities are relatively high (1.45) and there is considerable deviation from linearity in the molecular weight vs conversion plot. Hence, the optimum bpy/Cu(I)Cl molar ratio for the aqueous ATRP of OEGMA under these conditions appears to be 2.0. Similar results have been reported by other workers for conventional ATRP in bulk or nonaqueous media.[30] These observations are, of course, entirely consistent with our hypothesis that the active catalyst is $[\mathrm{Cu(I)(bpy)_2}]^+$.

Effect of Lowering the Cu(I) Catalyst Concentration. In conventional ATRP, there is typically one Cu(I) catalyst species for each growing chain end (i.e., the catalyst/initiator molar ratio is 1.0). Given the relative difficulty of removing the catalyst after the polymerization, there have been several attempts to work at lower catalyst/initiator ratios. For example, Matyjaszewski's group reported a conversion of 41% within 1 h for the bulk polymerization of methyl acrylate at 22 °C using a catalyst/initiator ratio of 0.10 and an Me_6TREN ligand. Approximately 85% conversion was

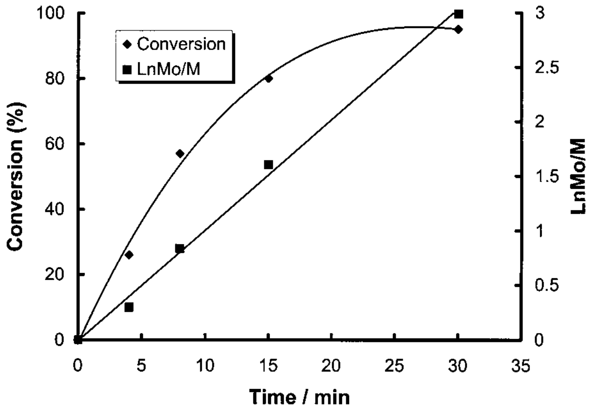

Figure 9. Effect of lowering the catalyst/initiator ratio by a factor of 10 on the kinetics of polymerization of OEGMA using initiator **1** in water at 20 °C. Conditions: OEGMA = 20 g, D_2O = 20 g, [initiator] = 36 mM. The relative molar ratios of OEGMA:initiator:CuCl:bpy were 33:1:0.1:0.2.

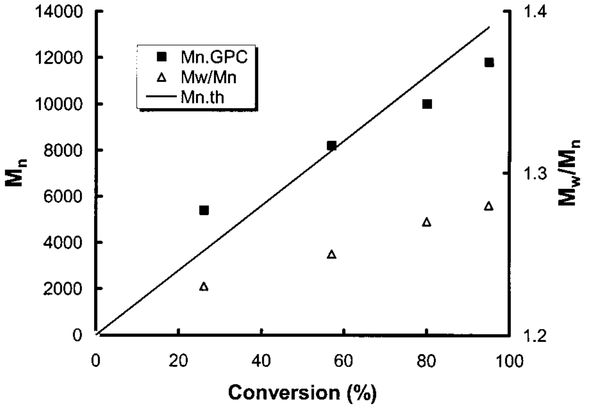

Figure 10. Evolution of molecular weight and polydispersity with monomer conversion for the polymerization of OEGMA using initiator **1** in aqueous media at 20 °C at a catalyst/initiator molar ratio of 0.10. Conditions: OEGMA = 20 g, D_2O = 20 g, [initiator] = 36 mM. The relative molar ratios of OEGMA:initiator:CuCl:bpy were 3:1:0.1:0.2.

achieved within 1 h at 50 °C under very similar conditions.[31] In both cases very narrow polydispersities were obtained (typically 1.10). On the other hand, Haddleton's group reported a marked decrease in the rate of polymerization of methyl methacrylate in xylene on lowering the catalyst/initiator ratio to 0.25; only 4% conversion was observed after 5 h at 90 °C.[32]

In the present study we found that the aqueous ATRP of OEGMA remains rapid and well-controlled, even at a catalyst/initiator ratio as low as 0.10. This is verified by the observation of first order monomer kinetics (see Figure 9), good molecular weight control, and a relatively narrow final polydispersity of 1.28, although there is some evidence for a gradual increase in polydispersity with conversion (see Figure 10).

Overall, it is clear that the Cu(I) catalyst activity is much higher in aqueous ATRP than in conventional ATRP, since in the former case each Cu(I) species can maintain reasonable livingness for up to 10 growing chain ends. As far as we are aware, this is the first time that good results (narrow polydispersities, controlled molecular weights, and high yields under mild conditions) have been reported for bpy-based ligands at low catalyst/initiator ratios.

Effect of Ligand. Matyjaszewski's group have shown that multidentate amine ligands such as 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA) are effective for the ATRP of (meth)acrylates and styrene.[33] Such ligands are cheaper than bpy and in some cases form less highly colored complexes with copper. Thus, the polymerization of OEGMA with HMTETA was attempted in 50% aqueous media at 20 °C; the results are summarized in Table 3.

Table 3. Selected Molecular Weight vs Conversion Data for the Polymerization of OEGMA in Aqueous Media at 20 °C with HMTETA as Ligand[a]

reaction time/min	conversion (%)	$M_{n.th}$	$M_{n.GPC}$	M_w/M_n
3	30	4 200	3 730	1.13
5	77	10 780	7 750	1.20
9	96	13 440	11 200	1.29

[a] Conditions: OEGMA = 10 g, D_2O = 10 g, OEGMA:initiator:CuCl:HMTETA = 33:1:1:1.

The color of the reaction solution remained bright blue during this polymerization. The polymerization rate was similar to that found for the bpy ligand, and good control over polymer molecular weight was obtained. The final polydispersity is 1.29 with the HMTETA ligand, which is a little higher than that obtained using bpy.

Synthesis of a Statistical Copolymer. The synthesis of a hydrophilic/hydrophobic statistical copolymer (with a target copolymer composition of 50 mol % OEGMA) was attempted by copolymerizing OEGMA and OPGMA via aqueous ATRP at 20 °C.

The OPGMA monomer has rather limited solubility in water at 20 °C, but it proved to be sufficiently soluble in an OEGMA/water mixture. As with the homopolymerization of OEGMA, the observed rate of copolymerization was very fast, with more than 99% monomer conversion being achieved after 30 min as judged by ^{1}H NMR. The isolated statistical copolymer was also analyzed using THF GPC. Its M_n was 12 500, which is near to the theoretical M_n of 13 600, although the use of PMMA calibration standards probably means that this apparent agreement is fortuitous. The polydispersity was relatively low (1.19), which again indicates a well-controlled polymerization. This example also serves to illustrate the important point that, although hydrophilic monomers are obviously preferred for aqueous ATRP, it is nevertheless possible to incorporate significant levels of relatively hydrophobic monomers such as OPGMA without requiring cosolvents.

Synthesis of End-Functionalized OEGMA Homopolymers. Various functional initiators can be used for the ATRP of OEGMA in water at 20 °C. For example, if ATRP is carried out using sodium 4-(bromomethyl)benzoate, ^{1}H NMR studies confirm that each polymer chain contains a terminal aromatic carboxylic acid group (see Figure 11).

Similarly, as mentioned earlier, well-defined macromonomers can be readily prepared using vinyl acetate-functionalized initiators such as (**4**). Success here relies on the fact that vinyl acetate cannot be readily polymerized by ATRP; with styrenic-functionalized initiators much poorer selectivity is obtained and unwanted copolymerization occurs, leading to significant broadening of the molecular weight distribution (see the two entries for initiator **5** in Table 1).

Ease of Catalyst Removal after Aqueous ATRP. One of the main drawbacks in conventional ATRP is the relative difficulty of removing the catalyst residues from the (co)polymer. In the specific case of the aqueous ATRP of nonionic monomers such as OEGMA, silica

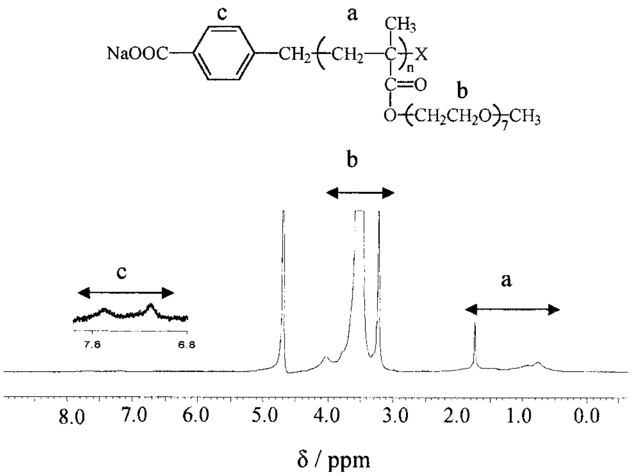

Figure 11. NMR spectrum of end-functionalized OEGMA obtained from aqueous ATRP. The mean degree of polymerization, *n*, is 31, which compares well to the target *n* of 33.

chromatography enables facile removal of the cationic copper catalyst, which is strongly adsorbed to the anionic stationary phase. However, this approach may not necessarily work well for all polymers. In the case of cationic polyelectrolytes strong adsorption of the polymer, as well as the catalyst, onto the silica usually occurs. Nevertheless, we are convinced that the use of an *aqueous* reaction medium should enable efficient catalyst removal by other methods. For example, Matyjaszewski and co-workers recently reported the use of ion-exchange resins to selectively remove various copper-based catalysts from a range of nonaqueous solvents.[34] Not surprisingly, it was found that the most efficient removal occurred in highly polar solvents, which suggests that this approach should give even better results in water. Several other strategies for catalyst removal, each seeking to take advantage of the unique properties of the aqueous milieu, will be explored in future work.

Conclusions

Aqueous ATRP of OEGMA proceeds at a remarkably fast rate at 20 °C, with high catalyst activity and is characterized by the following features:

1. Linear first-order rate plots are obtained up to 95% conversion.

2. The evolution of polymer molecular weight is linear with conversion.

3. Relatively narrow polydispersity indexes ($M_w/M_n < 1.30$) were obtained throughout the polymerization.

4. Efficient syntheses of macromonomers and end-functionalized polymers have been demonstrated.

5. Reasonable control is retained even at catalyst/initiator molar ratios as low as 0.10, which suggests unusually high activity for the Cu(I) catalyst.

6. The bulk polymerization of OEGMA is living but relatively slow at 20 °C, with 15 h being required for over 90% conversion. This observation confirms the essential role played by water in aqueous ATRP. The Cu(I) species is likely to be mononuclear in aqueous solution, which may account for its high catalytic activity. The possibility that the enhanced rate of polymerization is due to micellar polymerization is considered unlikely.

7. OEGMA is a well-behaved hydrophilic monomer for aqueous ATRP studies.

8. Efficient statistical copolymerization of relatively hydrophobic comonomers such as hydroxy-capped oligo(propylene glycol) methacrylate can be readily achieved without recourse to cosolvents.

Acknowledgment. The EPSRC is thanked for a postdoctoral grant to support X.S.W. (ROPA GR/M32795).

References and Notes

(1) Bolto, B. *Prog. Polym. Sci.* **1995**, *20*, 1987.
(2) (a) Butun, V.; Billingham, N. C.; Armes, S. P. *J. Am. Chem. Soc.* **1998**, *120*, 11818. (b). Butun, V.; Billingham, N. C.; Armes, S. P. *Chem. Commun.* **1997**, 671. (c). Vamvakaki, M.; Billingham, N. C.; Armes, S. P. *Macromolecules* **1999**, *32*, 2088.
(3) Kabanov, A. V.; Bronich, T. K.; Kabanov, V. A.; Yu, K.; Eisenberg, A. *Macromolecules* **1996**, *29*, 6797.
(4) Bijsterbosch, H. D.; Stuart, M. A. C.; Fleer, G. J. *Macromolecules* **1998**, *31*, 8981.
(5) Wang, J. S.; Matyjaszewski, K. *J. Am. Chem. Soc.* **1995**, *117*, 5614.
(6) Sawamoto, M.; Kamigaaito, M. *Trends Polym. Sci.* **1996**, *4*, 371.
(7) Patten, T. E.; Matyjaszewski, K. *Adv. Mater.* **1998**, *10*, 901.
(8) Matyjaszewski, K.; Patten, T. E.; Xia, J. *J. Am. Chem. Soc.* **1997**, *119*, 674.
(9) Nishikawa, T.; Ando, T.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1997**, *30*, 2244.
(10) Coca, S.; Jasieczek, B.; Beers, K. L.; Matyjaszewski, K. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, *36*, 1417.
(11) Ashford, E. J.; Billingham, N. C.; Armes, S. P. *Chem. Commun.* **1999**, 1285.
(12) Wang, X.-S.; Lascelles, S. F.; Jackson, R. A.; Armes, S. P. *Chem. Commun.* **1999**, 1817.
(13) (a) Wang, X.-S.; Luo, N.; Ying, S.-K. *J. Funct. Polym.* **1998**, *11* (1), 1. (b) *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37* (9), 1255.
(14) Matyjaszewski, K.; Shipp, D. A.; Wang, J. L. *Macromolecules* **1998**, *31*, 6836.
(15) Matyjaszewski, K.; Nakagawa, Y.; Jasieczek, C. B. *Macromolecules* **1998**, *31*, 1535.
(16) Wang, X.-S.; Armes, S. P.; *Polym. Prepr. (ACS)* **2000**, *41* (1) 413.
(17) Vamvakaki, M. DPhil Thesis, University of Sussex, Brighton, UK, 1998.
(18) Ito, K.; Tanaka, K.; Tanaka, H.; Imai, G.; Kawaguchi, S.; Itsuno, S. *Macromolecules* **1991**, *24*, 2348.
(19) Haddleton, D. M.; Heming, A. M.; Kukulj, D.; Duncalf, D. J.; Shooter, A. J. *Macromolecules* **1998**, *31*, 2016.
(20) Haddleton, D. M.; Clark, A. J.; Crossman, M. C.; Duncalf, D. J.; Heming, A. M.; Morsley, S. R.; Shooter, A. J. *Chem. Commun.* **1997**, 1173.
(21) Kickelbick, G.; Reinohl, U.; Ertel, T. S.; Bertagnolli, H.; Matyjaszewski, K. *ACS Polym. Prepr.* **1999**, *40* (2), 334.
(22) Kitagawa, S.; Munakata, M. *Inorg. Chem.* **1981**, *20*, 2261.
(23) Levy, A. T.; Patten, T. E. *PMSE* **1999**, *217*, 291.
(24) Wang, X.-S.; Armes, S. P. Billingham, N. C. Manuscript in preparation.
(25) Buback, M.; Kowollik, C. *Macromolecules* **1999**, *32*, 1445.
(26) Nomvra, E.; Ito, K.; Kajiwara, A.; Kamachi, M. *Macromolecules* **1997**, *30*, 2811.
(27) Kawaguchi, S.; Yekta, A.; Duhamel, J.; Winnik, M. A.; Ito, K. *J. Phys. Chem.* **1994**, *98*, 7891.
(28) Wang, X.-S.; Jackson, R. A.; Armes, S. P. *Macromolecules* **2000**, *33*, 255.
(29) Wang, X.-S.; Armes, S. P. *Polym. Prepr. (ACS)* **2000**, *41* (1), 484.
(30) Davis, K. A.; Paik, H. J.; Matyjaszewski, K. *Macromolecules* **1999**, *32*, 1767.
(31) Xia, J.; Gaynor, S. G.; Matyjaszewski, K. *Macromolecules* **1998**, *31*, 5958.
(32) Haddleton, D. M.; Jasieczek, C. B.; Hannon, M. J.; Shooter, A. J. *Macromolecules* **1997**, *30*, 2190.
(33) Xia, J.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 7697.
(34) Matyjaszewski, K.; Pintauer, T.; Gaynor, S. *Macromolecules* **2000**, *33*, 1476.

MA000671H