Conditions for Facile, Controlled RAFT Polymerization of Acrylamide in Water†

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Introduction. Controlled radical polymerization[1] (CRP) techniques, including atom transfer radical polymerization,[2,3] nitroxide-mediated polymerization,[4,5] and reversible addition−fragmentation chain transfer (RAFT)[6−8] polymerization, have been the focus of intense research in recent years due to their versatility and potential commercial applications. For both economic and environmental reasons, we have focused our research efforts on RAFT in aqueous media,[9] more specifically on the controlled polymerization of industrially important[10] acrylamido monomers, including anionic,[11] zwitterionic,[12] and neutral[13,14] derivatives. The polymerization of acrylamido monomers by other CRP techniques has proved problematic, usually requiring organic solvents and nonionic monomers.[15−20] However, we have found the RAFT process to be well-suited to the controlled polymerization of N-substituted and N,N-disubstituted acrylamido monomers in both organic[13] and aqueous media.[11,12,14] Significantly, however, the controlled polymerization of unsubstituted acrylamide in water alone has been elusive, and only one communication claims polymerization in a mixed solvent.[21] In that work Destarac et al. reported the polymerization of acrylamide and acrylic acid in the presence of a xanthate chain transfer agent (CTA) in a mixture of 2-propanol (20%) and water (80%). Some control appears to have been achieved for the statistical polymerization of acrylamide and acrylic acid; however, the homopolymerization of acrylamide was *not* demonstrated to be "living", and polydispersities were in the range 1.27−2.10. Also, no chain extension/block formation from the parent homopolymer (macro-CTA) was reported.

In this paper we report conditions leading to well-controlled, acrylamide homopolymers synthesized in water via RAFT (Scheme 1). Sodium 2-(2-thiobenzoylsulfonylpropionylamino)ethanesulfonate (STPE) was employed as the CTA. To prepare STPE, sodium 2-(2-bromopropionylamino)ethanesulfonate was first synthesized from taurine and 2-bromopropionyl bromide and subsequently reacted with the sodium salt of dithiobenzoic acid.[22−24] This CTA was designed to be soluble in water over a broad range of pH conditions and to produce a radical similar to that of the propagating species upon fragmentation. 2,2′-Azobis[2-methyl-*N*-(2-hydroxyethyl)propionamide] (VA-086, Wako) was utilized as the free radical initiator with a [CTA]/[I] ratio of 1.15, [acrylamide] = 2.0 M, [VA-086] = 2.17×10^{-3} M, and [CTA] = 2.50×10^{-3} M. The relatively slow decomposition of VA-086 required the use of a lower [CTA]/[I] ratio than is typically used when less stable initiators are employed. The [monomer]/[CTA] ratio was chosen for a theoretical DP of 800 at 100% conversion. Buffer solutions (pH = 5.0) for polymerization contained 0.272 M acetic acid and 0.728 M sodium acetate. Solutions were placed in septa-sealed vials, purged for 30 min with N_2, and heated to 70 °C with agitation. Aliquots were removed after 0, 2, 4, 8, 12, and 24 h. A portion of each aliquot was diluted and analyzed by aqueous size exclusion chromatography (ASEC) (using an eluent of 20% acetonitrile/80% 0.05 M Na_2SO_4(aq) and a flow rate of 0.5 mL/min at 25 °C, Viscotek TSK Viscogel columns (G3000 (<50 000 g/mol) and G4000 PW_{XL} (2000−300 000 g/mol)), Polymer Labs LC 1200 UV/vis, Wyatt Optilab DSP interferometric refractometer, and Wyatt DAWN EOS multiangle laser light scattering detectors (λ = 690 nm)). Conversions were determined by comparing the area of the UV signal corresponding to monomer at $t = 0$ to the area at t_x. The dn/dc of polyacrylamide in the above eluent was previously determined to be 0.160 mL/g at 25 °C.[25] Absolute molecular weights and polydispersities were determined using the Wyatt ASTRA SEC/LS software package.

Results and Discussion. The appropriate choice of CTA and reaction conditions is important for achieving well-controlled RAFT polymerizations.[26,27] We have found this is particularly important for the aqueous RAFT polymerization of acrylamide. Even if an appropriate monomer/CTA choice has been made, reaction conditions must be carefully chosen. For example, the use of STPE in water at intermediate pH's leads to uncontrolled polymerization (Figure 1A). In these reactions at pH = 7, no polymer is observed for several hours during which the characteristic orange dithioester color gradually disappears from the polymerization medium. Only after all the color is gone, indicating complete loss of the dithioester moiety, is polymer observed. The very high molecular weights and broad polydispersities are characteristic of uncontrolled free radical acrylamide polymerization.

After a number of unsuccessful attempts with various CTA's and polymerization conditions, we found the polymerization process could be controlled by performing the polymerization (Scheme 1) in an acetic acid/sodium acetate buffer (pH = 5.0). Under these conditions, the evolution of molecular weight is clearly observed as peak shifts to shorter retention times, as determined by ASEC (Figure 1B). Further, the pseudo-first-order rate plot (Figure 1C) and the plot of DP_n vs conversion (Figure 1D) are both linear and thus indicate controlled/"living" polymerization. Polydispersities are generally very low, ranging from 1.04 to 1.06 at intermediate reaction times. At very long reaction times the polydispersity increases to 1.26, possibly indicating some CTA hydrolysis and/or bimolecular coupling. However, the PDI remains well below the theoretical limit of 1.5 for conventional free radical polymerization. The long reaction times required to achieve high molecular weight are of particular interest, considering the very high polymerization rates typically observed for the free radical polymerization of acrylamide. It is not

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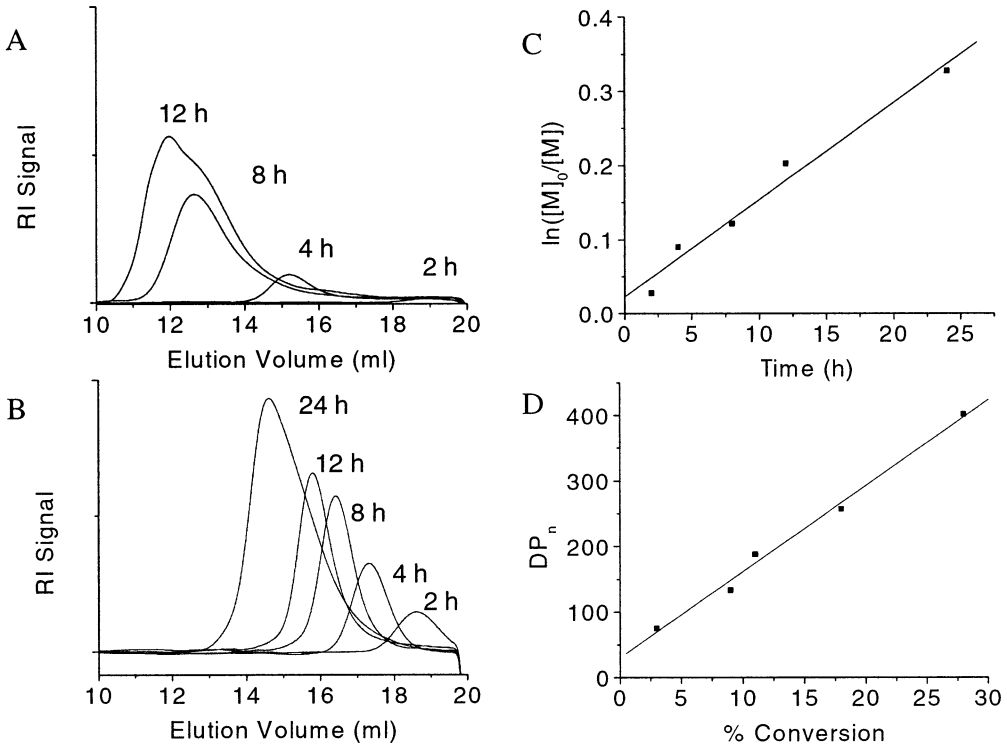
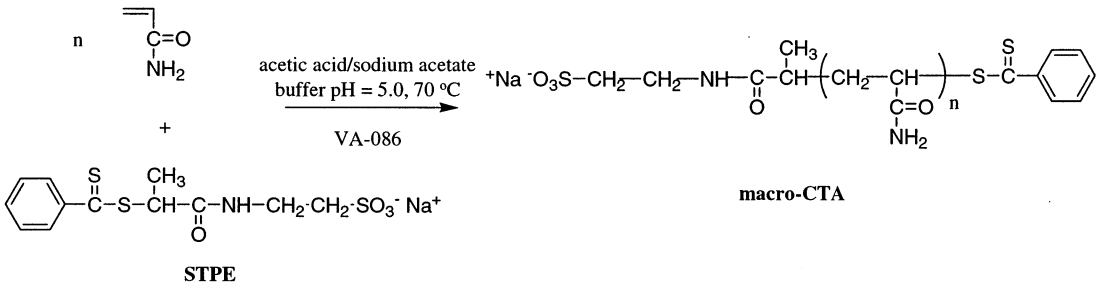


Figure 1. (A) ASEC chromatograms (RI traces) for the polymerization of acrylamide at pH = 7 in the presence of STPE. 2 h: no polymer observed; 4 h: all color bleached from reaction medium, M_n = 24 900, PDI = 1.09, conversion = 6%; 8 h: M_n = 114 000, PDI = 1.87, conversion = 32%; 12 h: M_n = 239 000, PDI = 2.98, conversion = 70%. (B) Successful RAFT polymerization of acrylamide with STPE in an acetic acid/sodium acetate buffer showing the evolution of molecular weight with time (2 h: M_n = 5300, PDI = 1.15, conversion = 3%; 4 h: M_n = 9790, PDI = 1.05, conversion = 9%; 8 h: M_n = 13 700, PDI = 1.04, conversion = 11%; 12 h: M_n = 18 600, PDI = 1.06, conversion = 18%; 24 h: M_n = 28 900, PDI = 1.26, conversion = 28%), the first-order rate plot (C), and the plot of DP_n vs conversion (D). For both polymerizations $[M]_0/[CTA]_0$ = 800, $[CTA]_0/[I]_0$ = 1.15, T = 70 °C.

Scheme 1. Reaction Scheme for the Successful RAFT Polymerization of Acrylamide To Produce Macro-CTA's of Narrow Molecular Weight Distribution with Functional Chain Ends[a]



[a] The CTA sodium 2-(2-thiobenzoylsulfonylpropionylamino)ethanesulfonate (STPE) and the initiator 2,2′-azobis[2-methyl-*N*−(2-hydroxyethyl)propionamide] (VA-086) were used for their solubility in the acidic conditions necessary for control of the polymerization.

uncommon in RAFT polymerizations to observe a significant retardation.[13,14,28] In the case of acrylamide, we ascribe the this to a high C−S bond strength in the intermediate radical species due to the unhindered nature of the polyacrylamide chain. A high C−S bond strength results in a long intermediate radical lifetime which may be responsible for the observed retardation.[28,29]

To further demonstrate the "livingness" of acrylamide polymerization under these conditions, a polyacrylamide macro-CTA was prepared ($M_n = 2.03 \times 10^4$, PDI = 1.03), isolated by dialysis, and lyopholized to yield an orange powder. A polymerization solution was then prepared as before utilizing this macro-CTA as the chain transfer agent. Figure 2 demonstrates that chain extension occurs with near-quantitative blocking efficiency, indicating that nearly all of the polyacrylamide macro-CTA chain ends remained active. A final 50/50 composition was targeted for the first and extended segments (blocks). ASEC analysis indicated molecular weights of 2.03×10^4 and 1.8×10^4 g mol^{-1} for the respective segments.

We believe that the marked differences in polymerization behavior of acrylamide under ambient and buffered conditions is related to the extent of CTA degradation which is a result of the amide hydrolysis of the acrylamide monomer.[30] Even a small amount of monomer hydrolysis could produce enough ammonia to convert all dithioesters in solution to thiols and thiobenzamides.[31] (At [monomer]/[CTA] = 800, only 0.125% of the monomer needs to hydrolyze to quantitatively react with the CTA.) Under low-pH conditions, however, any ammonia produced via monomer hydrolysis would be effectively scavenged by the large excess of acid, thus

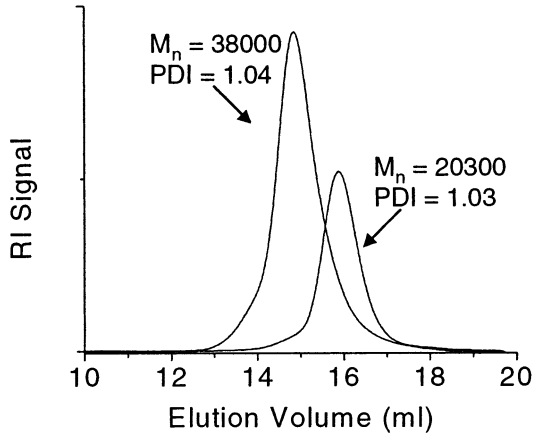


Figure 2. ASEC chromatograms (RI traces) for the polymerization of acrylamide in an acetic acid/sodium acetate buffer ($[M]_0/[CTA]_0 = 800$, $[CTA]_0/[I]_0 = 1.15$, $T = 70$ °C) using a polyacrylamide macro-CTA as the chain transfer agent and showing the evolution of molecular weight. Nearly complete retention of chain end functionality is demonstrated by quantitative blocking efficiency.

Table 1. Kinetic and Molecular Weight Data for the RAFT Polymerization of Acrylamide in an Acetic Acid/ Sodium Acetate Buffer (pH = 5.0) Using STPE as the CTA

polymerization time (h)	% conv[a]	M_n (g/mol)[a]	M_n, theoretical (g/mol)[b]	PDI[a]
0	0			
2	3	5300	1710	1.15
4	9	9790	5120	1.05
8	11	13700	6260	1.04
12	18	18600	10200	1.06
24	28	28900	15900	1.26

[a] Determined by ASEC. [b] Calculated from conversion using M_n = conversion × $MW_{monomer}$ × $[M]_0/[CTA]$.

greatly retarding nucleophilic attack on the dithioester. We have eliminated an alternative possibility of direct CTA hydrolysis at neutral pH by demonstrating previously that RAFT proceeds efficiently in water for many monomers[9,11,12,14] and that complete CTA hydrolysis at 70 °C requires days,[23] in contrast to the several hours observed in the case of acrylamide.

In conclusion, we have reported conditions allowing excellent control of the RAFT polymerization of acrylamide at low to moderate conversion directly in aqueous media. The degree of control is illustrated in Figure 1 and Table 1 by the pseudo-first-order kinetic plot, the ASEC curves showing the evolution of molecular weight with conversion, the resulting DP vs conversion relationship, and the low polydispersities. Near-quantitative chain extension and the low polydispersities confirm retention of the dithioester end groups during polymerization. Macro-CTA's prepared under these conditions, or those similar to the ones reported here, should allow synthesis of block copolymers and other complex polymer architectures containing polyacrylamide subunits. Interestingly, the experimental molecular weights for these polymers, as determined by on-line MALLS, are substantially higher than those predicted theoretically (see Table 1). This trend has also been observed for other neutral acrylamido monomers polymerized in the presence of dithioester compound CTA's.[12,14,32] Considering the current proposed RAFT mechanism and alternate proposed mechanisms,[28] we do not, at present, have a plausible explanation; however, this phenomenon is currently under further investigation in our laboratories.

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