Annual Progress Report

"Smart" Multifunctional Polymers for Enhanced Oil Recovery

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Abstract

Herein we report the aqueous polymerization of acrylamide using reversible addition fragmentation chain transfer (RAFT) polymerization to perform a comprehensive study on the polymerization of acrylamide. More specifically, the effect of polymerization conditions on the polymerization kinetics, molecular weight control, and blocking ability were examined. With this in mind, it was necessary to prepare “A” block (corona of the micelle) from a hydrophilic monomer. The responsive “B” block present in the core will be disclosed in the next two reports.

EXECUTIVE SUMMARY

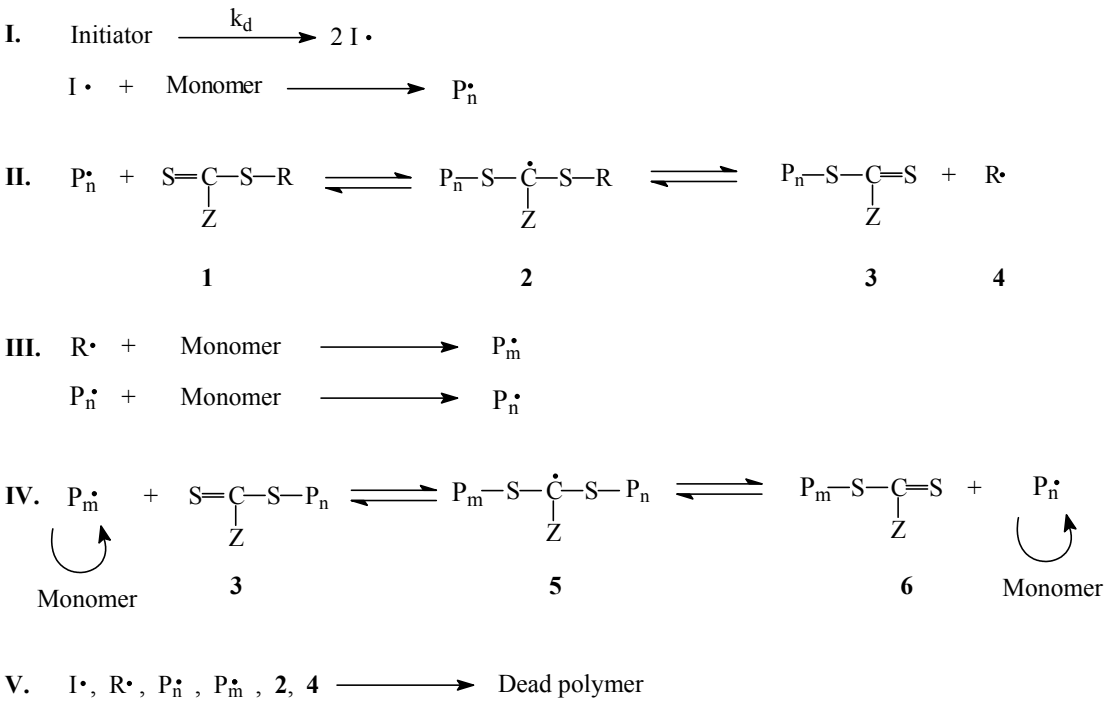
A coordinated, fundamental research program is underway in our laboratories with the *ultimate goal* of developing *"smart" multi-functional polymers* (SMFPs) that can respond *in situ* to stimuli (ionic strength, pH, temperature, and shear stress) resulting in *significantly improved sweep efficiency* in Enhanced Oil Recovery (EOR) processes. With these technologically "smart" polymers, it should be possible to produce more of the original oil in place and a larger portion of that by-passed or deemed "unrecoverable" by conventional chemical flooding. The *specific objectives* of this project are: a) to utilize *recent break-through discoveries* in the Polymer Science Laboratories at the University of Southern Mississippi to tailor polymers with the requisite structures and b) to evaluate the behavioral characteristics and performance of these multifunctional polymers under environmental conditions encountered in the petroleum reservoir. Two structural types of SMFPs are targeted that can work alone or in a concerted fashion in water-flooding processes. Type I SMFPs can reversibly form micelles, termed "polysoaps", in water that serve to lower interfacial tension at the oil/water interface, resulting in emulsification of oil. Type 2 SMFPs are high molecular weight polymers designed to alter fluid viscosity during the recovery process.

Critical to the desired performance of these conceptual systems is the precise incorporation of selected functional monomers along the macromolecular backbone to serve as *sensors* or *triggers* activated by changes of the surrounding fluid environment. The placement of hydrophilic, hydrophobic, and triggerable monomers is accomplished by controlled free radical polymerization utilizing aqueous Reversible Addition-Fragmentation chain Transfer (RAFT) polymerization, a technique under intensive development in the USM laboratories. The stimuli-responsive functional groups can elicit conformational changes in the polymers which in turn will alter surfactant behavior (type 1), viscosity (type 2), and permeability to the oil and aqueous phases. Thus, in principle, fluid flow behavior through the porous reservoir rock can be altered by changes in electrolyte concentration, pH, temperature, and flow rate. Significantly, the technology proposed is *environmentally attractive* since these systems can be synthesized in, processed in, separated from or recycled in *water*. Impetus for this study came from priority recommendations made during recent meetings organized by the Department of Energy and from extensive research over the past twenty-five years at USM on Water-Soluble Polymers. An infrastructure providing interdisciplinary research and academic studies in energy and environmental technologies, state-of-the art facilities and instrumentation, student stipends and scholarships, seminars and visiting scientists programs, and international symposia has been developed at USM almost exclusively from funding provided by the Chemical Flooding Program of the Department of Energy and the Environmental (Materials) Program of the Office of Naval Research. Over 70 students, including 40 PhDs have been trained in fossil energy and environmental technologies. Our current research has the added benefit of continuing the educational training of America's future scientists and engineers and developing frontier EOR technologies critical to America's economic security.

Design and Synthesis of "Smart" Multi-Functional Polymers (SMFPs)

INTRODUCTION

Recent advances in controlled free radical polymerization have allowed the tailoring of macromolecules with complex architectures including block, graft, comb, and star structures with predetermined molecular weight and narrow molecular weight distributions. One of the most versatile methodologies that permits the selection of a wide range of monomer types and convenient synthetic procedures is Reversible Addition-Fragmentation Chain Transfer (RAFT) polymerization.[1] The process, illustrated in Scheme 1, involves conventional free radical polymerization in the presence of a chain transfer agent (CTA) such as a dithioester. The degenerative transfer between the growing radicals and the thiocarbonylthio group provides "living" or controlled chain growth. A wide range of structurally diverse CTAs has been reported including dithioesters,[2] trithiocarbonates,[3] dithiocarbamates,[4] xanthates,[5] and phosphoryl-/(thiophosphoryl)dithioformates.[6] Key to structural control in the RAFT process is careful selection of appropriate monomers, initiators, and CTAs.



Scheme 1. Pathway for Reversible Addition-Fragmentation Chain Transfer polymerization.

As part of our continuing research on water-soluble (co)polymers for application in Enhanced Oil Recovery (EOR), we will construct "smart" multi-functional polymers (SMFPs) that can respond to *in situ* stimuli (temperature, ion concentration and type, pH,

and shear stress) resulting in conformational/phase changes leading to markedly improved sweep efficiency. These (co)polymers will be evaluated for potential as environmentally sound chemical agents for control of fluid mobility and conformance under conditions in the reservoir. We are especially interested in the synthesis of macroCTAs and block copolymers from neutral hydrophilic or ionic monomers. For example, we recently reported the controlled synthesis of pH-responsive amphiphillic block copolymers via aqueous RAFT utilizing styrenic and acrylamido-based monomers.[7]

Herein we detail the successful controlled RAFT polymerization of acrylamide (AM) utilizing novel CTAs in which R has been designed to reflect the electronic and structural characteristics of the propagating chain. It will be demonstrated that the choice of CTA allows for excellent control of molecular weight and molecular weight distribution by the rapid establishment of chain equilibration in the RAFT process (step IV Scheme 1). This is achieved through the efficient reinitiation of the polymerization by the leaving group upon fragmentation, as illustrated in steps II and III. Based on the aqueous polymerization results, experiments were also performed in organic media to examine the effect of different CTAs and initiators on the polymerization kinetics and molecular weight control.

EXPERIMENTAL

Materials

All chemicals were purchased from Fisher or Aldrich and used as received unless otherwise noted. Sodium dithiobenzoate (**10**), di(thiobenzoyl) disulfide(**11**), cumyl dithiobenzoate (**13**), cumylphenyldithioacetate (**14**), and 2-(1-carboxy-1-methyl-ethylsulfanylthiocarbonylsulfanyl)-2-methylpropionic acid (**16**) were prepared according to previously reported procedures. 2,2'-Azobis[2-methyl-*N*-(2-hydroxyethyl)-propionamide] (**18**) and 4,4'-azobis(4-cyanovaleric acid) (**17**) (gifts from Wako Chemicals USA Inc) were recrystallized from dioxane and methanol, respectively. Acrylamide was recrystallized three times from acetone. Deionized water (DI H_2O) was obtained from a Barnstead NANO-Pure reverse osmosis/filtration unit (resistivity: 18.0 MΩ).

*4-Cyanopentanoic Acid Dithiobenzoate (**15**)*

A literature method was adapted for the synthesis of 4-cyanopentanoic acid dithobenzoate (**15**).[8] A 250 mL round-bottomed flask, equipped with a condenser, was charged with ethyl acetate (80.0 mL), dry **17** (5.84 g, 21.0 mmol), and di(thiobenzoyl)disulfide (**11**) (4.25 g, mmol). The reaction solution was heated at reflux for 18 h and then cooled to room temperature before removing the ethyl acetate *in vacuo*. The crude product was isolated by column chromatography (silicagel 60 Å, 70-230 mesh) using ethyl acetate/hexane (2/3) with 0.5 v/v % acetic acid as the eluent. Fractions that were red in color were combined and dried over anhydrous sodium sulfate overnight. The solvent mixture was removed *in vacuo*, and the red oily residue placed in a freezer at -20 °C, whereupon it crystallized. The target compound was recrystallized from benzene. ^{1}H

NMR (300 MHz, $CDCl_3$): δ 1.95 (s, 3H), 2.78-2.40 (m, 4H), 7.40 (t, 2H), 7.57 (t, 1H), 7.91 (d, 2H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 24.2, 29.5, 33.0, 45.6, 118.4, 126.7, 128.6, 133.1, 144.5, 177.0, 222.1.

*Sodium 2-(2-thiobenzoylsulfonyl-propionylamino)-ethanesulfonate (**12**)*[9]

Sodium 2-(2-bromopropionylamino)-ethanesulfonate (**8**) was prepared by first dissolving 2-aminoethanesulfonic acid (**9**) (25.6 g, 204 mmol) and NaOH (16.4 g, 409 mmol) in deionized water (20 ml). 2-Bromopropionyl bromide (**7**) (44.0 g, 204 mmol) dissolved in dichloromethane (50 ml), was then added dropwise at 0 ^{o}C over 30 min. During the addition, a large quantity of solid was produced requiring occasional manual mixing. After 1 h at ambient temperature, the mixture was filtered and the solid washed with a small amount of absolute ethanol (~ 10 ml) followed by ethyl ether (~ 50 ml) and then dried *in vacuo.* Compound **12** was prepared by dissolving freshly synthesized sodium dithiobenzoate (**10**) (9.12 g) in 1 ml of water to which sodium 2-(2-bromopropionylamino)-ethanesulfonate (**8**) (8.5 g dissolved in 6 ml of water) was added. Immediately upon mixing, a precipitate formed accompanied by a strong exotherm. After 24 h at room temperature, the solid was filtered and washed with 2 ml of water. The filtrate was precipitated in acetone, yielding a pink powder that was isolated by centrifugation. The precipitate was washed with acetone, dissolved in water, and acetone was added to the point of incipient precipitation. Dark red needles (mp 215-218 ^{o}C) were obtained by cooling this solution at 4 ^{o}C for an extended period. ^{1}H NMR δ = 1.22, 1.45 (2d, 3H), 2.92 (d, 3H), 3.44 (d, 3H), 4.35 (q, 1H), 7.29 (q, 2H), 7.44 (d, 1H), 7.76 (d, 2H). ^{13}C NMR 15.77, 35.55, 49.59, 50.08, 126.81 (CH), 128.82 (CH), 133.39 (CH), 144.30 (C), 173.71 (C=O), 228.95 (C=S). Crystals contained 1.68 wt % water. Analysis for CNS Calculated: C, 37.96 %, N, 3.69 %, S, 25.33 %. Found: C, 37.85 %, N, 3.58 %, S, 25.26 %. IR (cm^{-1}) 3438(m), 1648(s), 1554(m), 1210(s), 1037(s), UV-Vis: ε(483 nm) = 135 L $mol^{-1}cm^{-1}$.

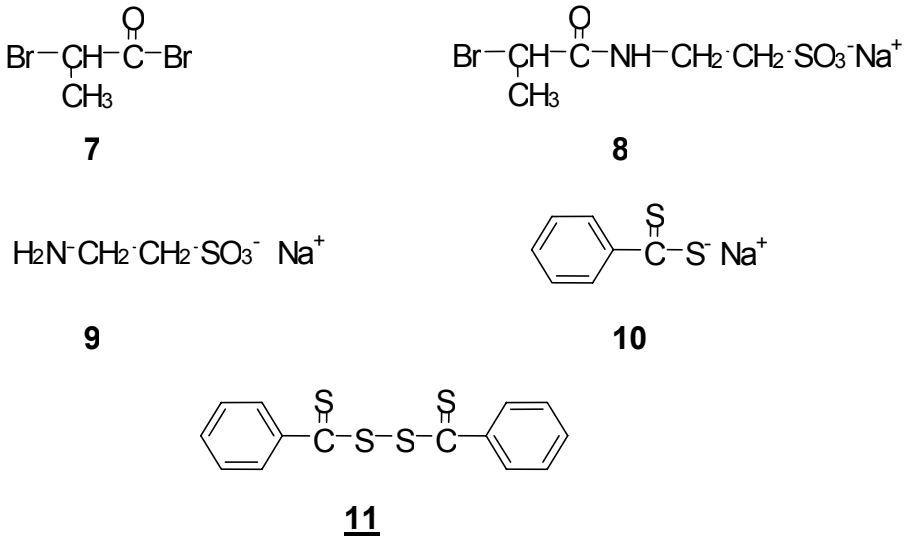
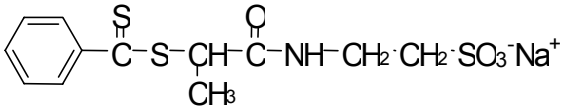


Figure 1. Compounds utilized in the preparation of CTAs.



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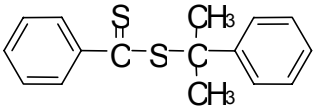

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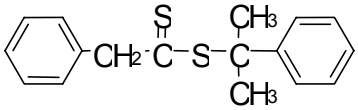

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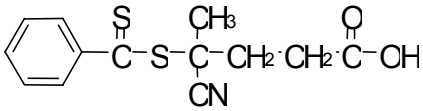

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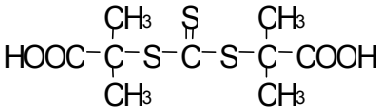

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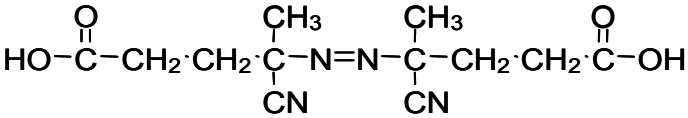
Figure 2. Chain transfer agents sodium 2-(2-thiobenzoylsulfonyl-propionylamino)-ethanesulfonate (**12**), dithiobenzoate (**13**), cumylphenyldithioacetate (**14**), cyanopentanoic acid dithiobenzoate (**15**) and 2-(1-carboxy-1-methyl-ethylsulfanylthiocarbonylsulfanyl)-2-methylpropionic acid (**16**) utilized in RAFT polymerizations.



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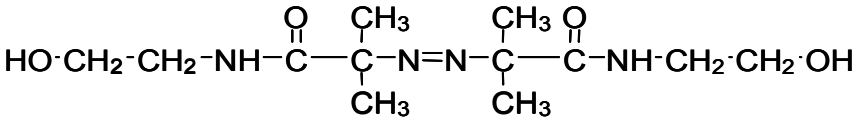

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Figure 3. Initiators 4,4'-azobis(4-cyanovaleric acid) (**17**) and 2,2'-Azobis[2-methyl-*N*-(2-hydroxyethyl)-propionamide] (**18**) utilized for RAFT polymerizations

Polymerizations

General Procedure for Acrylamide Polymerizations by RAFT
All polymerizations were carried out at a 2.0 M monomer concentration in individual, septa-sealed vials that were purged for at least 20 min prior to reaction. The monomer to CTA ratio was held constant at 800 while the initial CTA to initiator ratio ($[CTA]_o/[I]_o$) was varied to account for differences in the thermal decomposition rates of the initiators and for the increased decomposition rate at higher temperatures. Aqueous polymerizations were carried out at ambient pH in DI H_20 or in buffer solutions (pH = 5.0) containing 0.272 M acetic acid and 0.728 M sodium acetate with **12** as the CTA and **18** as the initiator. Polymerizations in dimethysulfoxide (DMSO) were performed with **13** , **14**, **15**, or **16** as the CTA and **17** or **18** as the initiator. ^{1}H NMR δ = 2.42-1.99 (br, 1H), 1.86-1.35 (br, 2H). ^{13}C NMR δ = 179.56 (C=O), 42.50-41.32 (CH_2), 36.48-33.46 (CH).

Instrumentation and Analysis

ASEC of Acrylamide Polymerizations
Polymerization mixtures were analyzed directly 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 ^oC, Viscotek TSK Viscogel columns (G3000 PW_{XL} (<50 000 g/mol, 200 Å) and G4000 PW_{XL} (2 000-300 000 g/mol, 500 Å)), with Polymer Labs LC 1200 UV/vis, Wyatt Optilab DSP interferometric refractometer, and Wyatt DAWN EOS multiangle laser light scattering detectors (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 ^oC. Absolute molecular weights and polydispersities were determined using the Wyatt ASTRA SEC/LS software package.

Other Analytical Techniques
All pH measurements were performed with accuracy ± 0.02 with 900A (Orion) pH meter. NMR spectra were obtained on a Varian 200 MHz or 500 MHz spectrometer using D_2O as the solvent and the residual solvent peak as the internal reference. Chemical shifts were determined by using 3-(trimethylsilyl)-1-propanesulfonic acid sodium salt (DSS) as an internal reference.

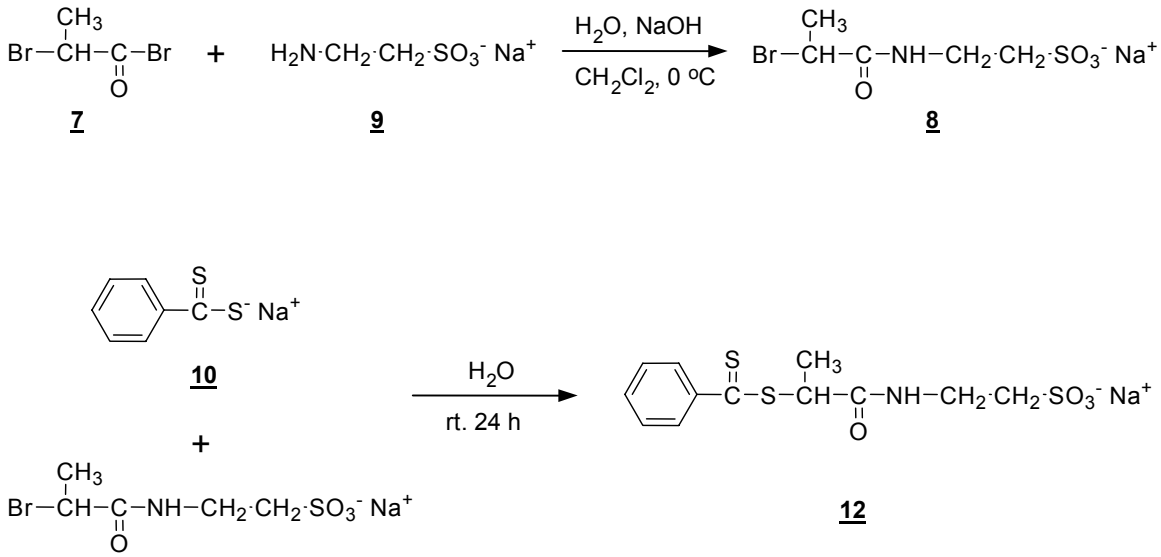
RESULTS AND DISCUSSION

Conditions for Facile, Controlled RAFT Polymerization of Acrylamide in Water
With all aqueous RAFT polymerizations, the proper selection of reaction conditions (CTA, temperature, pH, etc.) is important in order to achieve ideal results. Most aqueous RAFT polymerizations have been performed utilizing cyanopentanoic acid dithiobenzoate (**15**) as the CTA. However, this chain transfer agent utilizes a carboxylate functionality to achieve solubility in water. The weakly acidic nature of this group (pK_a ~ 5.5) limits the solubility of **15** under acidic conditions. Accordingly, a new chain

transfer agent, sodium 2-(2-thiobenzoylsulfonyl-propionylamino)-ethanesulfonate (STPE) (**12**), was prepared to allow polymerization under acidic conditions.

After **12** was prepared, it was utilized in the polymerization of acrylamide at selected solution pH values. Under neutral pH conditions, acrylamide was found to polymerize in an uncontrolled fashion. Under acidic conditions, however, control was achieved allowing the successful chain extension of a macro-CTA of acrylamide.

Scheme 2 illustrates the general synthetic pathway used to prepare (STPE) **12**. In the first step, **8** was produced under Schotten-Baumann conditions by the reaction of 2-aminoethanesulfonic acid **9** and 2-bromopropionyl bromide **7**. The water soluble CTA **12** was then produced through the nucleophilic substitution reaction between **8** and **10** under aqueous conditions. The sulfonate group on this CTA allows solubility over the entire pH range. Additionally, the fragmenting group was designed to contain a secondary amide matching that of the propagating chain end of acrylamido polymers, a strategy important in minimizing the polydispersity of the resulting polymers and reducing or eliminating the induction period in RAFT polymerization.[10,11,12] Further, this synthetic route utilizes inexpensive starting materials, aqueous reaction conditions, and purification by recrystallization rather than chromatography.



Scheme 2. Synthetic scheme for the preparation of sodium 2-(2-thiobenzoylsulfonyl-propionylamino)-ethanesulfonate (**12**).

The RAFT Polymerization of Acrylamide Directly in Aqueous Media

For the aqueous RAFT polymerization of acrylamide (**58**), 2,2'-azobis[2-methyl-*N*-(2-hydroxyethyl)-propionamide] (**18**) was utilized as the free radical initiator due to its solubility over the entire pH range. Polymerizations were performed at 70 ^{o}C with a CTA to intiator ratio of 1.15, [**58**] = 2.0 M, [**18**] = 2.17 x 10^{-3} M, and [**12**] = 2.50 x 10^{-3}

M. The [monomer]/[CTA] ratio was chosen for a theoretical DP of 800 at 100% conversion.

Figure 4 demonstrates the particular importance of the proper selection of reaction conditions for the aqueous RAFT polymerization of acrylamide. Even if an appropriate monomer/CTA choice has been made, solution pH must be carefully chosen. For example, the use of **12** in water at intermediate pH's leads to uncontrolled polymerization (Figure 4a). In these reactions at pH = 7, no polymer is observed for several hours. A high molecular weight polymer with a broad polydispersity is observed at long reaction times.

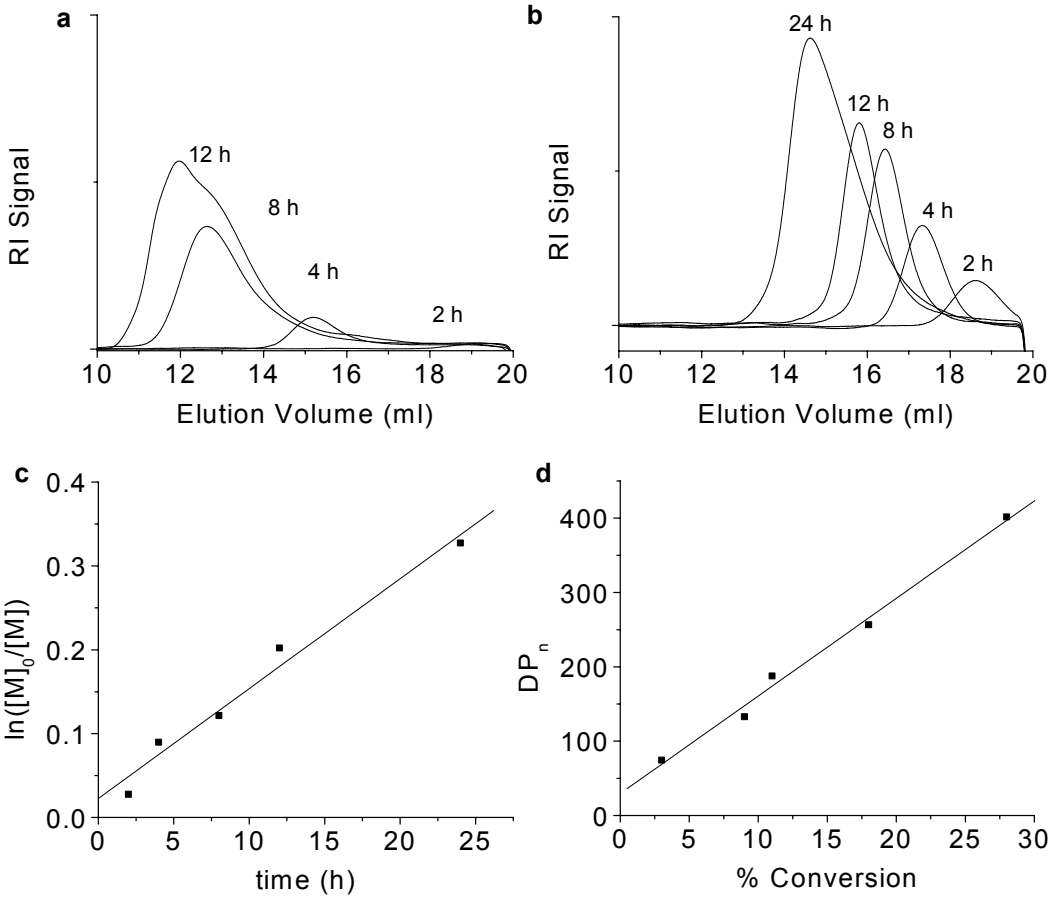


Figure 4. (a) ASEC chromatograms (RI traces) for the polymerization of acrylamide at pH = 7 in the presence of **17** 2h: no polymer observed; 4h: all color bleached from reaction medium, M_n = 24 900, PDI = 1.09; 8h: M_n = 114 000, PDI = 1.87; 12h: M_n = 239 000, PDI = 2.98. (b) Successful RAFT polymerization of acrylamide with **12** in an acetic acid/sodium acetate buffer showing the evolution of molecular weight with time, (c) the first order rate plot, and (d) the plot of DP_n vs conversion.

It was found the polymerization process could be controlled by performing the polymerization (Scheme 3) 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 4b). Further, the pseudo-first order rate plot (Figure 4c) and the plot of DP_n vs conversion (Figure 4d) are both linear and thus indicate controlled/"living" polymerization. Polydispersities are generally low (Table 1) 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.

Table 1. Kinetic and Molecular weight data for the RAFT polymerization of acrylamide in an acetic acid/sodium acetate buffer (pH = 5.0) using **12** as the CTA.

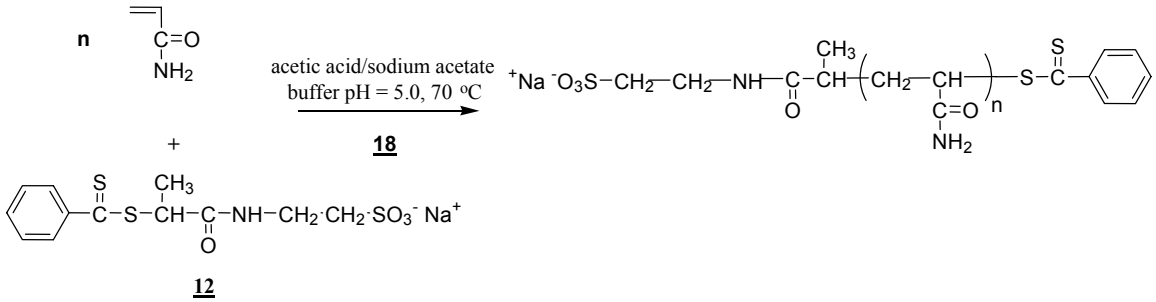
Polymerization Time (h)	% Conversion[a]	M_n (g/mol)[a]	M_n, theoretical (g/mol)[b]	PDI[a]
0	0	-	-	-
2	3	5 300	1 710	1.15
4	9	9 790	5 120	1.05
8	11	13 700	6 260	1.04
12	18	18 600	10 200	1.06
24	28	28 900	15 900	1.26

[a] determined by ASEC/MALLS
[b] calculated from conversion using Equation 19

Table 2. Kinetic and Molecular Weight Parameters for the Polymerization of Acrylamide

Entry #	CTA	solvent	I	$[CTA]_o/[I]_o$	(°C)	$k_p^* \times 10^2$ [a] (h^{-1})	t_{ind} (min)[b]	Slopes m_{exp}/m_{th}[c]	$DP_{t=0}$[d]
A	**12**	buffer	**18**	1.15	70	1.3 ± 0.1	0	1.7 ± 0.1	30
B	**12**	buffer	**18**	1.15	80	9.9 ± 0.5	0	2.3 ± 0.1	0
C	**12**	buffer	**18**	5.88	90	15 ± 1	0	2.2 ± 0.1	10
D	**15**	DMSO	**18**	1.15	70	3.1 ± 0.2	30	1.23± 0.08	60
E	**15**	DMSO	**18**	5.88	90	9.9 ± 0.3	10	1.31± 0.07	20
F	**13**	DMSO	**18**	1.15	70	2.6 ± 0.2	500	1.44± 0.06	110
G	**13**	DMSO	**18**	5.88	90	2.7 ± 0.3	150	2.3 ± 0.2	26
H	**15**	DMSO	**18**	0.575	70	4.9 ± 0.5	10	1.2 ± 0.3	50
I	**15**	DMSO	**18**	0.288	70	7.9 ± 0.9	11	1.48± 0.03	12
J	**13**	DMSO	**17**	5.00	70	4.0 ± 0.7	60	1.68± 0.07	60
K	**15**	DMSO	**17**	5.00	70	4.4 ± 0.8	0	1.55± 0.08	0
L	**14**	DMSO	**17**	5.00	70	17 ± 6	0	1.3 ± 0.2	163
M	**16**	DMSO	**17**	5.00	70	33 ± 3	0	0.97± 0.03	70

[a]determined from the linear portion of the pseudo first-order kinetic plot. $k_p^* = k_p[P_n\cdot]$ where k_p is the rate constant for propagation and $[P_n\cdot]$ is the concentration of propagating radicals
[b]determined from the x-intercept of the pseudo first-order kinetic plot
[c]m_{th} determined using Equation 33.
[d]determined from the y-intercept of the M_n versus conversion plot and Equation 29.



Scheme 3. Reaction scheme for the successful RAFT polymerization of acrylamide to produce macro-CTA's of narrow molecular weight distribution with functional chain ends. The CTA **12** was used for its solubility in the acidic conditions necessary for control of the polymerization.

In order to further demonstrate the "livingness" of acrylamide polymerization under these conditions, a polyacrylamide macro-CTA was prepared (M_n = 2.03 x 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 5 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 x 10^4 g mol^{-1} and 1.8 x 10^4 g mol^{-1} for the respective segments.

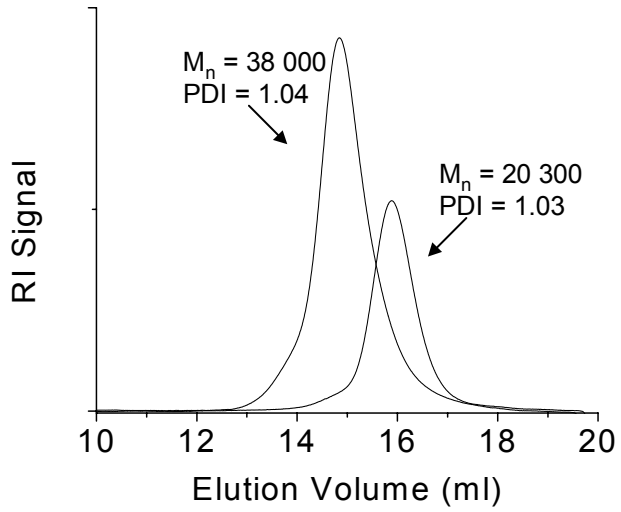


Figure 5. ASEC chromatograms (RI traces) for the controlled polymerization of acrylamide in an acetic acid/sodium acetate buffer using a polyacrylamide macro-CTA as the chain transfer agent and showing the evolution of molecular weight.

Nearly complete retention of chain end functionality is demonstrated by quantitative blocking efficiency.

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.[13] Even a small amount of monomer hydrolysis could produce enough ammonia to convert all dithioesters in solution to thiols and thiobenzamides (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 greatly retarding nucleophilic attack on the dithioester.

Macro-CTAs 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). Further, the very slow rate of polymerization combined with dithioester hydrolysis limits the conversion under these conditions to 28 %. Both the molecular weight deviation and the polymerization rate have been studied further, and are addressed.

Factors Effecting Kinetics and Molecular Weight Control in the RAFT Polymerization of Acrylamide

Providing that acidic conditions are maintained for acrylamide polymerization in water, pseudo first-order kinetics were observed, molecular weights increased linearly with conversion, and efficient chain extension of an acrylamide macro-CTA is possible. Further, these results suggest that RAFT polymerization of acrylamide in a non-aqueous environment might be possible with a range of CTAs. Two issues remained unresolved, however, polymerization times were limited to < 24 h resulting in a maximum of 28 % conversion, and molecular weights deviated by a substantial margin from those predicted by current theories (e.g. M_n = 13 700 vs. $M_{n,th}$ = 6 300).

Molecular weight control in a RAFT polymerization is achieved through the rapid degenerative transfer of a thiocarbonylthio species (Scheme 1). When a propagating radical adds to the dithioester (**1**), an intermediate radical species (**2**) is formed (II, Scheme 1). The intermediate may fragment to produce a new radical, R· (**4**), which in turn initiates a new chain involved in establishing the main equilibrium (IV, Scheme 1). Since most of the chains in a RAFT polymerization are started by R-groups from the original CTA, the molecular weight at a particular conversion may be predicted by Equation 1.

(1)

$$M_n = \frac{M_{MW} \times [M]_o \times p}{[CTA]_o} + M_{CTA}$$

If, however, competitive processes reduce the concentration of CTA ([CTA] < $[CTA]_o$), the number of living chains will be reduced accordingly, and the molecular weights of the remaining active polymers will correspondingly increase. In the case of the aqueous polymerization of acrylamide, two potential mechanisms that can decrease [CTA] may be identified. The first is hydrolysis of CTA and the second is irreversible combination of the intermediate radical **5** with another radical species. If the hydrolysis reaction has an important effect on M_n, polymerizations carried out in the absence of water should produce polymers with M_n closer to $M_{n,th}$. If the irreversible combination of the intermediate radical has an appreciable effect on molecular weight, conditions that affect the concentrations of **5**, therefore, the rate of combination should have a predictable effect on molecular weight. Specifically, higher radical concentrations, produced either by initiators with shorter half-lives or higher concentrations of initiator, should result in experimental molecular weights higher than those predicted by Equation 1. Additionally, CTAs with faster rates of fragmentation should reduce the concentration of **5,** resulting in lower rates of intermediate radical coupling and experimental molecular weights closer to $M_{n,th}$.

This section has been divided into three subsections in order to best present our experimental findings. In the first subsection, the effect of temperature on the kinetics of the aqueous RAFT polymerization of acrylamide is detailed. In the second subsection the kinetics of the polymerization are studied in DMSO (the absence of hydrolysis allows longer reaction times) utilizing selected CTAs, initiators, initiator concentrations, and temperatures (Figure 6). In the course of these studies an unexpected observation was made. Specifically, a constant supply of new radicals is necessary to maintain conversion in the polymerization. In the third subsection, experimentally determined molecular weight values are examined with respect to those predicted theoretically by equation 28. Particular attention has been given to comparison of molecular weight control in aqueous and organic polymerizations, reactions involving higher radical concentrations, and reactions with CTAs exhibiting faster fragmentation rates. In this work we utilize aqueous size exclusion chromatography (ASEC) with online MALLS detection to directly determine molecular weight values rather than using comparative standards.

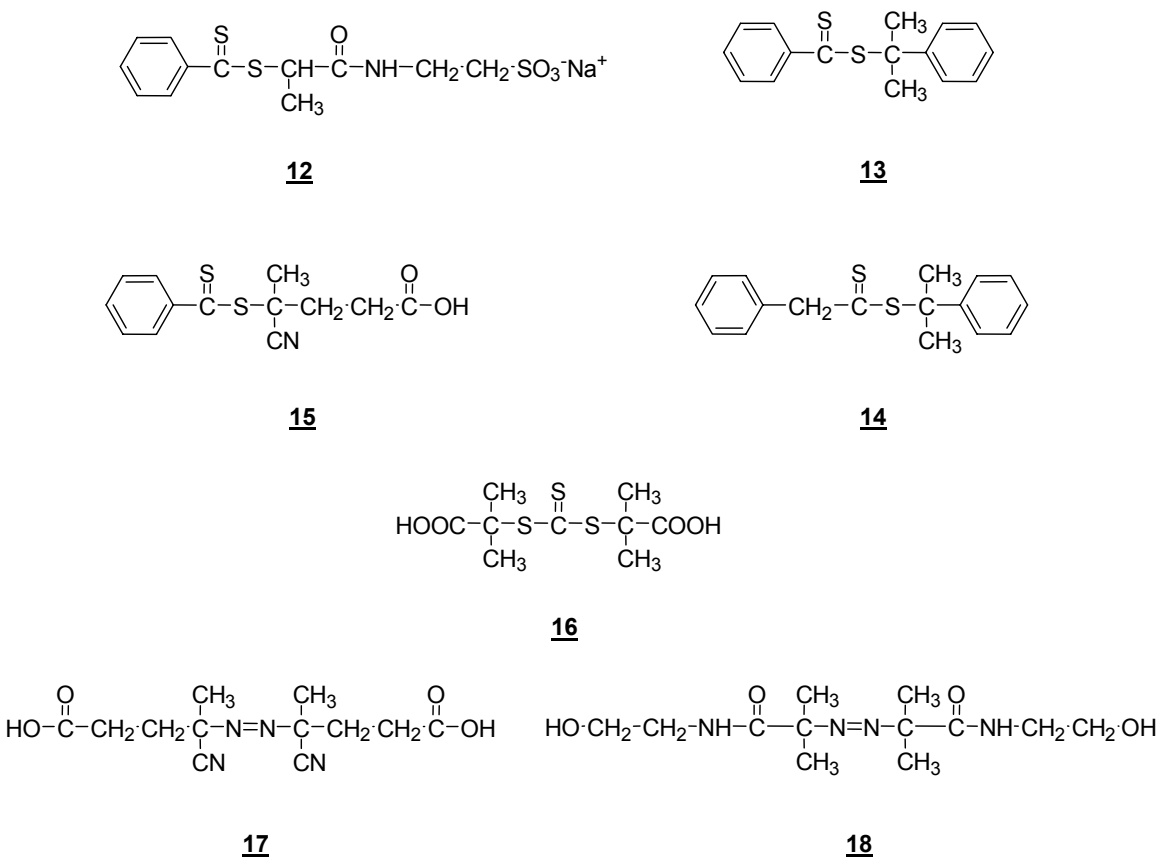


Figure 6. Chain transfer agents: sodium 2-(2-thiobenzoylsulfonyl-propionylamino)-ethanesulfonate (**12**), cumyl dithiobenzoate (**13**), 4-cyanopentanoic acid dithiobenzoate (**15**), cumylphenyldithioacetate (**14**), and 2-(1-carboxy-1-methyl-ethylsulfanylthiocarbonylsulfanyl)-2-methylpropionic acid (**16**) and initiators: 2,2'-Azobis[2-methyl-N-(2-hydroxyethyl)-propionamide] (**18**) and 4,4'-azobis(4-cyanovaleric acid) (**17**) employed in the RAFT polymerization of acrylamide.

Aqueous RAFT Polymerizations of Acrylamide

One way to increase the rate of reaction and, therefore, the conversion is to perform the polymerizations at elevated temperatures. Comparative aqueous polymerizations of acrylamide were thus performed at 70 ^{o}C, 80 ^{o}C, and 90 ^{o}C with a CTA/initiator ratio of $[\mathbf{12}]_o/[\mathbf{18}]_o$ = 1.15.

In polymerizations carried out in water at 70 ^{o}C and 80 ^{o}C with a $[\mathbf{12}]_o/[\mathbf{18}]_o$ = 1.15, a linear pseudo first-order rate plot (Figure 7a) is observed, indicating a constant concentration of propagating radicals. The dramatic increase in the apparent rate constant, k_p^* (where k_p^* is equal to $k_p[P_n\cdot]$, from 1.3 x 10^{-2} h^{-1} to 9.9 x 10^{-2} h^{-1} (A and B, Table 2) with increasing reaction temperature can be attributed to two factors. First, the lifetimes of the intermediate radicals are reduced because the number of intermediate species with sufficient energy to overcome the energy barrier for fragmentation increases. Second, the total number of radicals participating in the reaction increases (Figure 7b) due to the enhanced rate of initiator decomposition at elevated temperatures.[14] At 90 ^{o}C a

rapid loss of color was observed and polymers of high polydispersity were produced. This may be attributed to rapid hydrolysis of CTA followed by conventional polymerization.

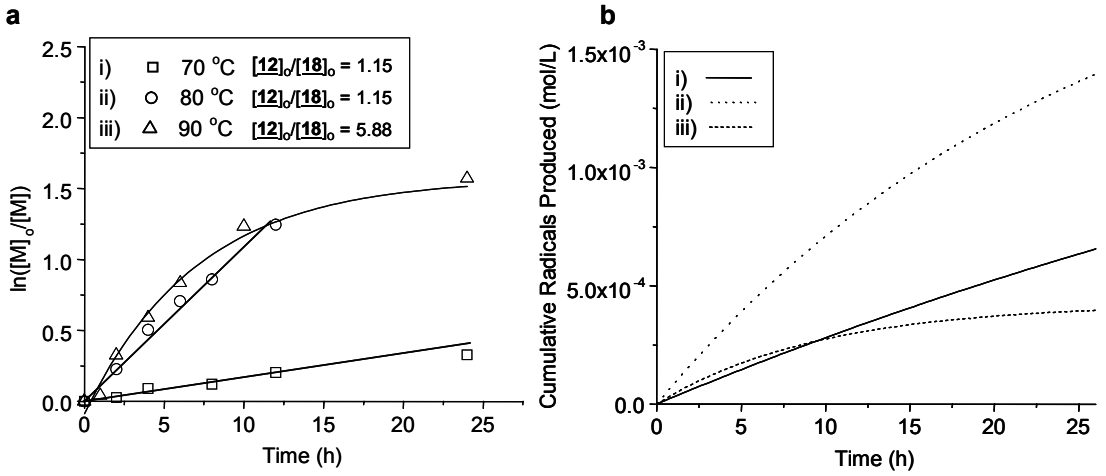
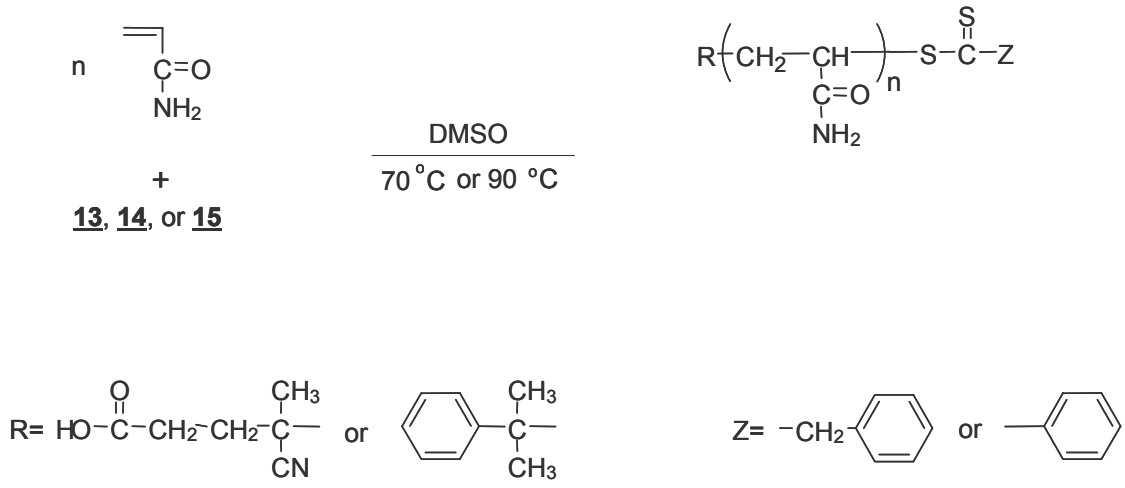


Figure 7. a) Pseudo first-order kinetic plot for the RAFT polymerization of acrylamide in aqueous buffer (pH = 5.0) using **12** as the CTA and **18** as the initiator at 70 °C, 80 °C ([12]/[18] = 1.15), and 90 °C ([12]/[18] = 5.88). b) Calculated cumulative number of radicals produced as a function of time in water at i) 70 °C, ii) 80 °C ([**1**]/[**7**] = 1.15), and iii) 90 °C ([**1**]/[**7**] = 5.88).

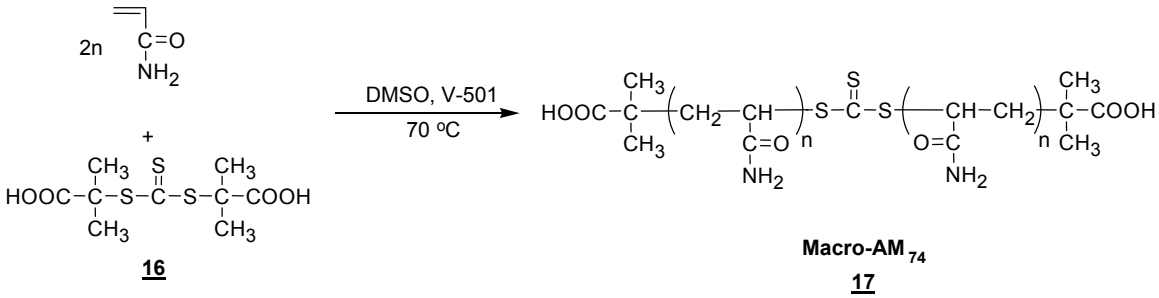
In order to better separate the effects of temperature and the number of radicals on the apparent rate of polymerization, the concentration of initiator was adjusted so that $[\mathbf{12}]_o/[\mathbf{18}]_o$ = 5.88, resulting in roughly the same number of radicals at 90 °C as is produced at 70 °C over the first 10 hours (i and iii, Figure 7b). Under these conditions the apparent rate of polymerization at 90 °C is 10 times that at 70 °C and very close to the rate at 80 °C when a $[CTA]_o/[I]_o$ ratio of 1.15 is used (Figure 7a, A, B, and C, Table 2). A conversion of 79 % is achieved under these conditions, a substantial improvement over the 28 % achieved.

RAFT Polymerization of Acrylamide in DMSO.

By limiting hydrolysis, polymerization in DMSO allows extended polymerization times not accessible in water. Further, CTAs and initiators that are insoluble in aqueous buffer can be used to evaluate the effect of CTA structure and initiator half-life on the polymerization kinetics. Thus the CTAs **13**, **14**, **15**, or **16** were employed utilizing **17** or **18** as the initiator at 70 °C or 90 °C (Schemes 4 and 5).



Scheme 4. Synthetic route for the RAFT polymerization of acrylamide in DMSO employing dithioesters as the chain transfer agents.



Scheme 5. Synthetic route for the RAFT polymerization of acrylamide in DMSO employing the trithiocarbonate, **16**, as the chain transfer agent and **17** as the initiator.

*Effect of temperature on RAFT polymerization kinetics in DMSO for **13** and **15** mediated polymerizations.*

For the temperature studies, polymerizations were performed at 70 °C and 90 °C with **13** and **15** using **18** as the initiator rather than **17** due to its increased thermal stability. As in the aqueous polymerizations, the CTA to initiator ratio was adjusted so that roughly the same number of radicals is produced regardless of the temperature during the early stages of reaction ($[CTA]_o/[I]_o$ = 1.15 at 70 °C (i), $[CTA]_o/[I]_o$ = 5.88 at 90 °C (iii), Figure 7b). The pseudo first-order rate plots for polymerizations carried out at 70 °C and 90 °C utilizing **15** and **13** as the CTA are shown in Figure 8a and Figure 8b respectively. Higher conversions are achieved in a shorter time period at 90 °C due to a combination of increased apparent rates of polymerization and shorter induction periods. Values of k_p^* increased from 3.1 h^{-1} to 9.9 h^{-1} (D and E, Table 2) and from 2.6 h^{-1} to 2.7 h^{-1} (F and G,

Table 2) for polymerizations utilizing **15** and **13** respectively. Induction periods (t_{ind}) were reduced from 30 min to 10 min for polymerizations mediated by **15** (D and E, Table 2) and from 500 min to 150 min for polymerizations mediated by **13** (F and G, Table 2 Both of these results are consistent with a shorter intermediate radical (**5**) lifetime at elevated temperatures.[15,11] Higher rates of conversion are achieved through the increased number of active radical species, while the induction periods are reduced by a combination of increased fragmentation rate and enhanced rates of reinitiation which allow the polymerization to proceed through the pre-equilibrium stage more quickly. Once again, non-linearity of the pseudo first-order rate plots is observed and will be addressed later.

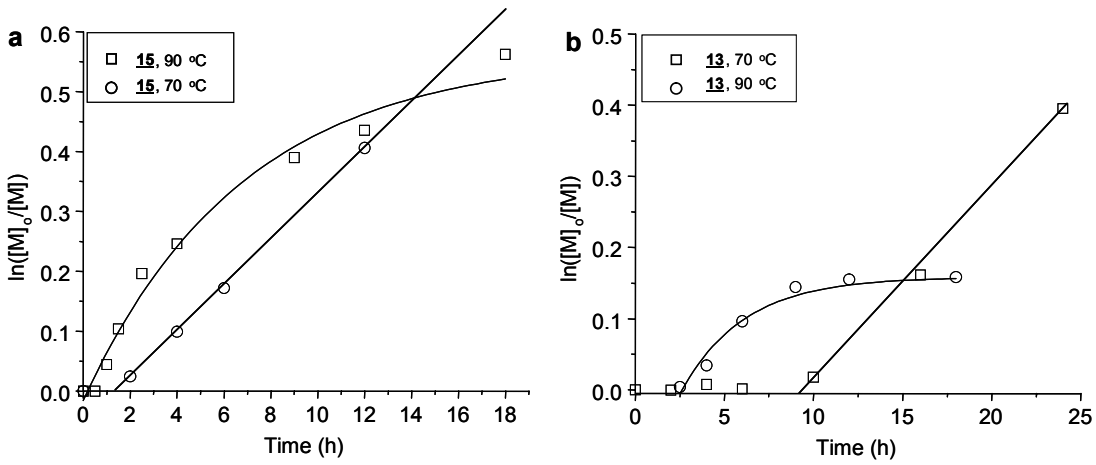


Figure 8. Comparison of pseudo first-order kinetic plots obtained at 70 °C, $[CTA]_o/[I]_o$ = 1.15 and 90 °C, $[CTA]_o/[I]_o$ = 5.88, in DMSO using **18** as the initiator and a) **15** or b) **13** as the chain transfer agent.

*The effect of [**15**]$_o$/[**18**]$_o$ ratio on the kinetics of polymerization at 70 °C.*

In order to determine the effect of increasing the number of radicals without increasing the temperature, acrylamide (**58**) was polymerized utilizing **15** with the concentration of initiator **18** varied such that the $[CTA]_o/[I]_o$ ratio ranged from 1.15 to 0.288. The linear pseudo first-order rate plots (Figure 9a) reveal the primary effect of increasing the number of radicals in the system. The values of k_p^* increase from 3.1 x 10^{-2} h^{-1} to 7.9 x 10^{-2} h^{-1} (D and I, Table 2) as the initiator concentration increases and can be directly correlated to the increased number of radicals available for propagation (Figure 9b). Polymerizations employing **15** exhibit a minimal induction period, so it is not surprising that increasing the radical concentration had little effect on the length of this period.

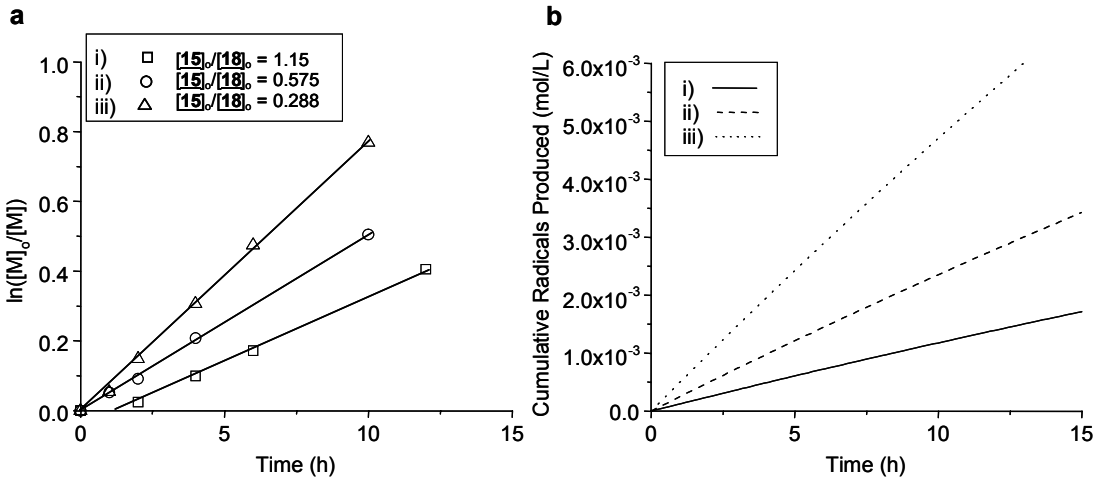


Figure 9. Effect of initiator concentration on the a) pseudo first-order kinetic plot and b) cumulative number of radicals produced in the RAFT polymerization of acrylamide carried out at 70 ^{o}C in DMSO with **15** as the CTA and **18** as the initiator.

*Effect of the CTA R-group on the kinetics of polymerization, a comparison of **15** with **13**.* It is well known that the R-group of a CTA can have a profound effect on the kinetics of RAFT polymerization, particularly in the early stages of reaction. [10,11,15,16,] Here we examine the effects of two different R-groups on the polymerization of acrylamide in DMSO at 70 ^{o}C employing **17** or **18** as the initiator. From the pseudo first-order rate plots it is apparent that a primary difference of these two R-groups is to affect the length of the inhibition period (Figures 10a and 10b). When either **17** or **18** was used as the initiator, polymerizations in the presence of **13** had longer induction periods than those in the presence of **15**. Values of t_{ind} decreased from 500 min to 30 min and 60 min to 0 min when **18** and **17**, respectively, were utilized as the initiators (D and F; J and K, Table 2). This is consistent with earlier results in which R-groups that produce more stable and bulky radicals upon fragmentation produce longer inhibition periods, and can be attributed to a combination of preferential fragmentation toward the R-group during the pre-equilibrium and poor reinitiation by the R· radical.[10,11,15] The slopes of the initial linear portions of the pseudo first-order rate plots, on the other hand, are very similar for both CTAs when the same initiator is used. This is not surprising since, after the polymerization has progressed into the main equilibrium stage, polymerizations started with either **13** or **15** involve nearly identical macro-CTAs. The nearly identical apparent rates of polymerization combined with the differences in the inhibition periods result in lower conversions at a given time for polymerizations mediated by **13**, underscoring the importance of matching the R-group of a CTA to the monomer. The differences in the shapes of the pseudo first-order rate plots will be discussed later.

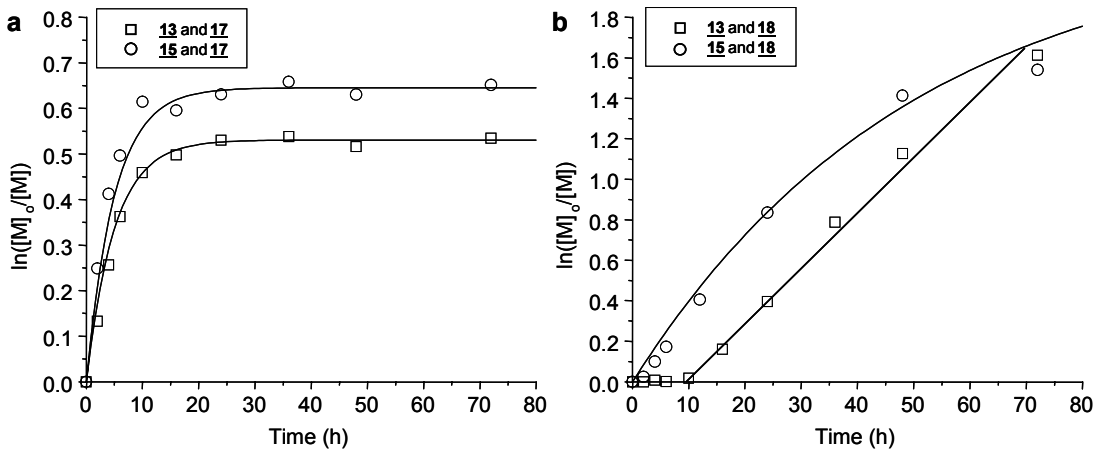


Figure 10. Effect of the CTA R-group on the pseudo first-order rate plot when a) **17** was the initiator and b) **18** was the initiator. Polymerizations were performed in DMSO at 70 °C.

Effect of the CTA Z-group on the kinetics of polymerization, ***13*** *versus* ***14****.*

The Z-group of a CTA is also known to have a significant effect on a RAFT polymerization by altering the stabilization of the intermediate radical and the rate of addition to the C=S bond.[15,17,18] Both rate enhancements and reductions in inhibition periods can result from utilizing CTA's with less stabilizng Z-groups (*eg.* benzyl instead of phenyl).[15,17] It was therefore of interest to study the effect of a less stabilizing benzyl Z-group on the RAFT polymerization of acrylamide while maintaining identical R-groups. The pseudo first-order rate plots for the polymerization of acrylamide (**58**) in the presence of CTA **13** or **14** and initiator **17** are presented in Figure 11 (70 °C, [CTA]/[**17**] = 5.0). As expected, the apparent rate of polymerization of acrylamide with **14** is 4.3 times faster than that with **13** (J and L, Table 2). This is consistent with the 5-fold increase in rate previously observed for DMA polymerization using **14** as compared with **13**.

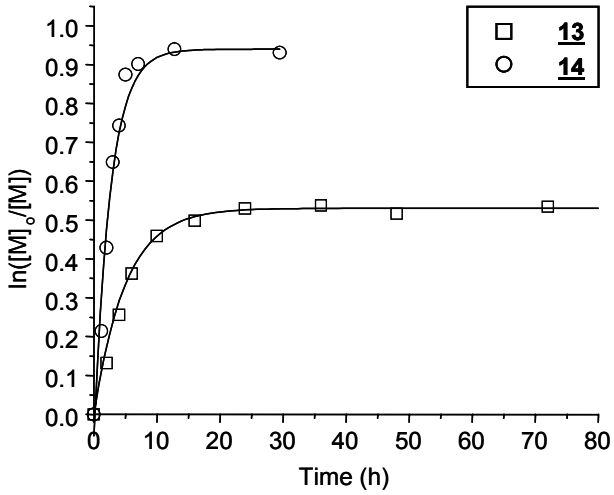


Figure 11. Comparison of the pseudo first-order rate plots of the polymerization of acrylamide in DMSO at 70 °C using **13** and **14** as the CTAs.

Polymerization of acrylamide in the presence of a trithiocarbonate.
A fifth CTA, **16**, was employed for the polymerization of acrylamide in DMSO at 70 ^{o}C utilizing **17** as the initiator (Scheme 5). The ASEC traces and the pseudo first-order kinetic plot are presented in Figures 12a and 12b, respectively. The trithiocarbonate structure of the CTA results in a much less stabilized intermediate radical **5**, which in turn affords much faster polymerization rates. For acrylamide in DMSO, the apparent rate of polymerization with **16** is the fastest of all the CTAs, 7.5 times the rate observed with **15** at 70 ^{o}C (Table 2, M) Indeed, the kinetic plot in Figure 12b reveals that 74 % conversion is reached in just 4 h compared with the > 24 h required for the **15**/**18** system.

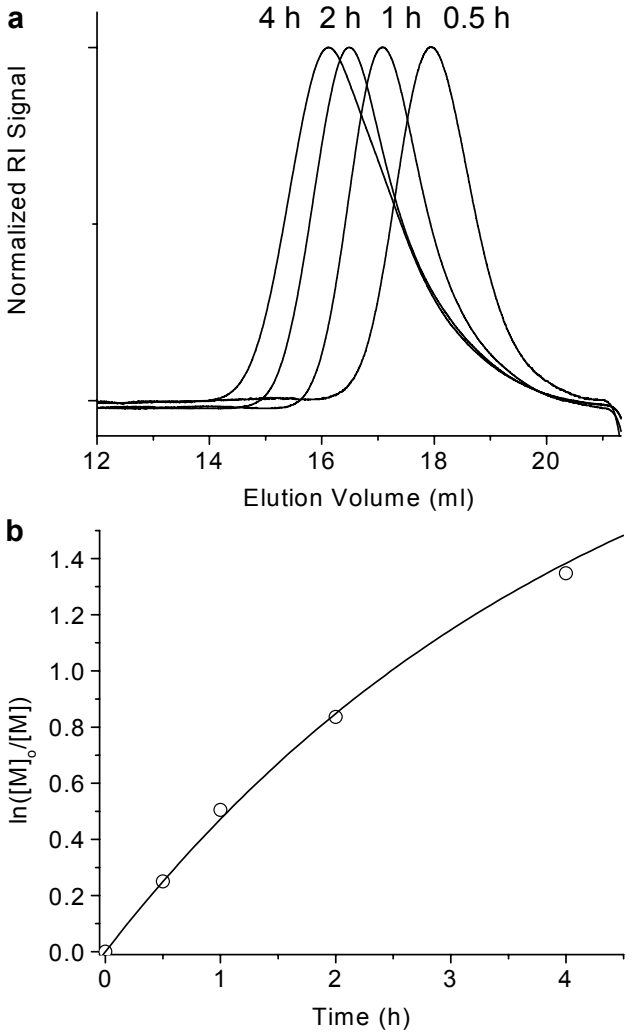


Figure 12. a) ASEC traces and b) pseudo first-order kinetic plot of the polymerization of acrylamide (58) in DMSO using **16** as the CTA and **17** as the initiator.

Effect of the half-life of the initiator on the RAFT polymerization of acrylamide.
The non-linear behavior observed in many of the pseudo first-order kinetic plots presented to this point may be explained by examining the effect of the initiator half-life on the polymerization rates. Kinetic data for the polymerization of acrylamide in the presence of CTAs **13** and **15** using **17** and **18** as initiators are plotted in Figures 13a and 13b. While **17** produces an enhanced rate initially, in both cases the polymerization stops after ~10 h (between 40 % and 45 % monomer conversion). Polymerizations employing **18** continued for 72 h yielding between 79 % and 80 % monomer conversion. The major differences in these two polymerizations can be attributed to the time dependent rate of radical production. Figure 13c shows the calculated, cumulative number of radicals produced for each initiator over time (assuming an initiator efficiency of 0.5). Initiator **17** produces more radicals in the very early stages resulting in the higher observed rates. After the first 10 hours at 70 ^{o}C, however, the number of new radicals produced by **17** drops off quickly (ii, Figure 13a), while **18** continues to produce new radicals for 72 hours (i, Figure 13c). Pseudo first-order kinetic plots similar to those in Figures 13a and 13b are observed when the concentration of initiator **18** is adjusted to compensate for the differences in temperature (Figure 8a and 8b). Similar differences in the radical production profiles exists in the polymerizations at 70 ^{o}C (i, Figure 13c) and 90 ^{o}C (iii, Figure 13c). Apparently, when the supply of new radicals falls off, the RAFT polymerization of acrylamide essentially stops (see Figures 13a, b, and c). It seems likely that over the very long polymerization times required for acrylamide, steady termination of the growing radical chains results in a diminishing rate of polymerization unless the radicals can be replenished. Thus in the case of **17**, dead end polymerization results after ~10 h, while the polymerization in the presence of **18** continues for 72 hours. These results are consistent with recent modeling predictions by Wang and Zhu in which the rates of termination and initiation were assumed to be equivalent and the termination of the intermediate radical was considered significant.[19]

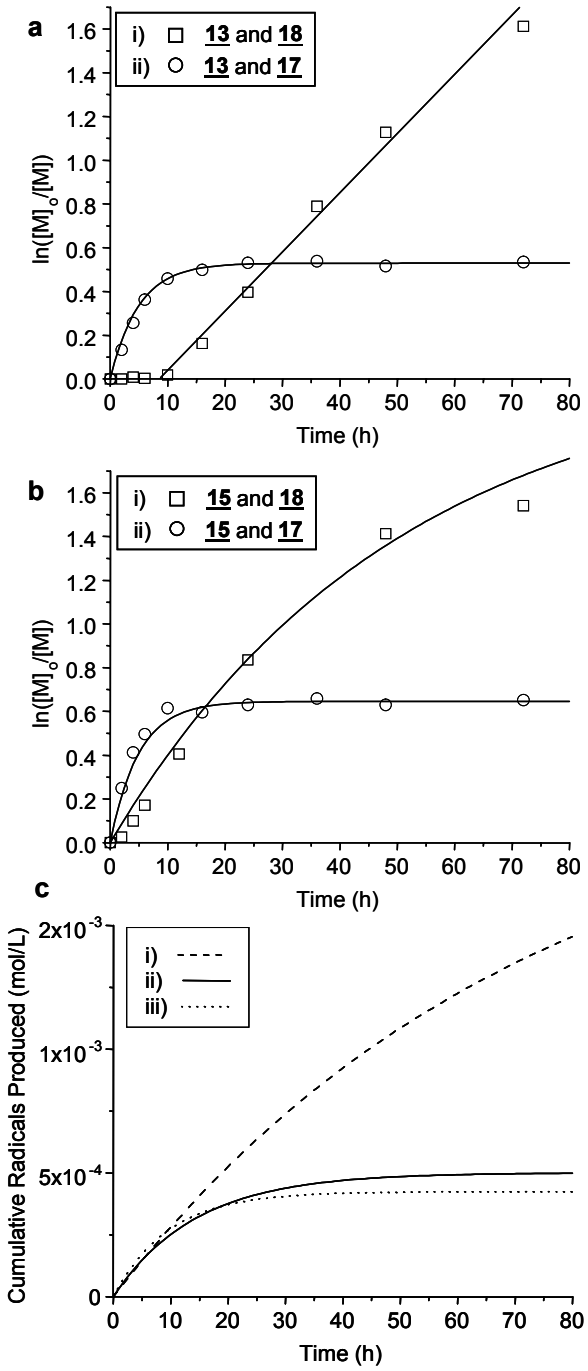


Figure 13. Pseudo first-order kinetic plots of a) **13** and b) **15** mediated polymerization using both **17** and **18** as the initiators. The shape of the kinetic plots follow c) the production of radicals as a function of time.

Effect of solvent, temperature, initiator concentration, initiator, and CTA on molecular weight.

Examination of the molecular weight data obtained by online light scattering for the polymerizations in subsections 1 and 2 provides insight into the potential causes of the molecular weight deviations observed in the polymerization of acrylamide. The

experimental values of the number average molecular weight, M_n, for all the RAFT homopolymerizations and the predicted (theoretical) molecular weight values are presented as a function of conversion in Figure 14. All polymerizations exhibit increases in molecular weight with conversion, but deviate from theoretical values to varying degrees. Aqueous polymerizations (Figure 14a) deviate most strongly, while the molecular weights obtained from polymerizations employing the trithiocarbonate **16** in DMSO (Figure 14f) are in closest agreement.

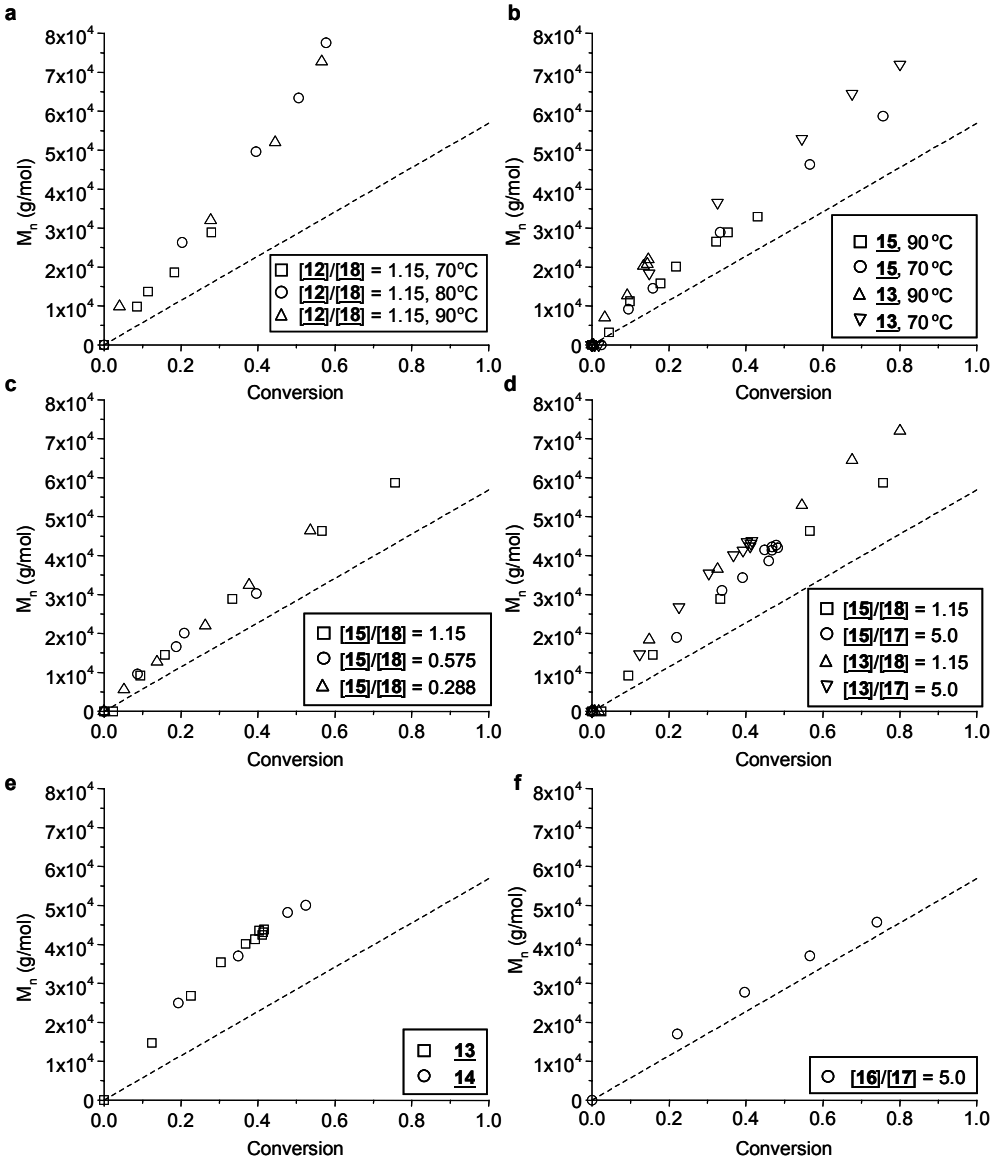


Figure 14. Molecular weight versus conversion plots a) in aqueous buffer solution, b) in DMSO at 70 °C and 90 °C, c) as a function of initiator concentration at 70 °C in DMSO utilizing **15** as the CTA, d) with **15** or **13** as the CTA and **17** or **18** as the initiator at 70 °C in DMSO, e) with **13** or **14** as the CTA and **17** as the initiator at 70 °C in DMSO, and f) with **16** as the CTA using **17** as the initiator in DMSO at 70 °C.

Examination of the absolute values of the molecular weights in this manner, however, is somewhat limited. Two factors influence the molecular weights that are ultimately obtained. The first is the rate of effective chain transfer in the initial stages of polymerization (II, Scheme 1).[20] As with most RAFT processes, a number of competing reactions must be balanced in order to achieve high rates of effective chain transfer. The rate of addition of the polymeric radical to monomer must be slow relative to addition to the C=S bond of the CTA in order to avoid long runs of monomer between CTA addition events. Also, fragmentation of the intermediate radical in the pre-equilibrium should occur preferentially to the right ($k_\beta > k_{-add}$, II Scheme I) with the R-group facilitating "rapid" reinitiation prior to significant propagation.

The number of monomers that add to a propagating radical before effective chain transfer occurs, $DP_{t=0}$, can be determined from Equation 2 where $M_{n,t=0}$ is the y-intercept of the M_n versus conversion plot. Values of $DP_{t=0}$ are compiled in Table 2.

(2)

$$DP_{t=0} = \frac{M_{n,t=0} - CTA_{MW}}{M_{MW}}$$

The second factor that influences the molecular weight of the polymers obtained by RAFT polymerization is the total number of propagating chains which arise from two sources: the R-groups of the CTAs and the primary initiator fragments that have added to monomer. Equation 3 is often employed to reflect the combination of these sources where $N_{chains,th}$, $[CTA]_o$, f, $[I]_o$, k_d, and t are the theoretical number of chains, initial CTA concentration, initiator efficiency, initial initiator concentration, rate constant for initiator decomposition, and time respectively.

(3)

$$N_{chains,th} = [CTA]_o + 2f[I]_o(1 - e^{-k_d t})$$

The theoretical slope of the M_n versus conversion line, m_{th}, can then be calculated according to Equation 4.

(4)

$$m_{th} = \frac{[M]_o \times M_{MW}}{[CTA]_o + 2f[I]_o(1 - e^{-k_d t})}$$

Typically, however, the number of chains derived from the initiator is much smaller than the initial CTA concentration, $2f[I]_o(1-e^{-kdt}) << [CTA]_o$, and Equations 3 and 4 are modified to Equations 5 and 6.

(5)

$$N_{chains,th} = [CTA]_o$$

(6) $$m_{th} = \frac{[M]_o \times M_{MW}}{[CTA]_o}$$

The slopes of each M_n versus conversion line have been experimentally determined (m_{exp}), and the value of m_{th} calculated using Equation 6. The ratio m_{exp}/m_{th} was calculated for each polymerization and compiled in Table 2.

Examination of the molecular weight data in this manner reveals several trends. Changes in $DP_{t=0}$ reflect changes in the relative rates during the pre-equilibrium (Scheme 1). Polymerizations in the presence of CTAs with cumyl R-groups (CTAs **13** and **14**; J and L, Table 2) and less stabilizing Z-groups (CTAs **14** and **16**; L and M, Table 2) produce higher values of $DP_{t=0}$. For CTAs with cumyl R-groups the rate constant of addition of R· to CTA is thought to be much higher than that to monomer thereby promoting 'back-transfer' and decreasing the rate of effective chain transfer.[16] Less stabilizing Z-groups increase the energy of activation for addition to the C=S bond, also reducing the rate of effective chain transfer. The net result is that higher molecular weights are reached during the pre-equilibrium stage.

Changes in the m_{exp}/m_{th} ratio suggest changes in the number of active chains. Values of $m_{exp}/m_{th} > 1$ indicate the actual number of active chains, $N_{chains,exp}$, is less than the theoretical number, $N_{chains,exp} < N_{chains,th}$. If the second term in Equation 3, $2f[I]_o(1-e^{-kdt})$, is significant, the ratio m_{exp}/m_{th} would have a value less than 1 since this term is neglected in the calculation of m_{exp}/m_{th}. Examination of the values of m_{exp}/m_{th} indicate this is not the case, justifying the use of Equations 5 and 6.

Further examination of m_{exp}/m_{th} reveals three distinct conditions that result in molecular weight deviations. First, polymerizations carried out in water have higher values of m_{exp}/m_{th} than those carried out in DMSO (*eg*. Table 2 A and D). Second, polymerizations at higher temperatures and/or higher radical concentrations have higher values of m_{exp}/m_{th} (*eg*. D, E, and I Table 2). Finally, as the CTA is changed to give less stable intermediate radicals and higher apparent rates of polymerization, lower values of m_{exp}/m_{th} are observed (J, L, and M, Table 2). In the case of the fastest fragmenting CTA **16**, the experimental and theoretical values are equivalent.

The observation of greater values of m_{exp}/m_{th} under aqueous conditions compared to those observed in DMSO confirms the predictions of a significant molecular weight effect of hydrolysis. All of the molecular weight deviation, however, cannot be attributed solely to hydrolysis as can be seen from the values of $m_{exp}/m_{th} > 1$ for polymerizations performed in DMSO. Polymerizations in which a higher concentration of radicals is present in the system exhibit higher values of m_{exp}/m_{th}, in direct contradiction to the predictions of Equation 4, but consistent with increased rates of intermediate radical

termination at higher radical concentrations. Increased values of m_{exp}/m_{th} are observed not only when higher initial concentrations of initiator are utilized, but also when **17** is used as the initiator (D and K, Table 2) and when higher reaction temperatures are used (Table 2, F and G). Both **17** and higher reaction temperatures result in enhanced radical production at the early stages of reaction relative to polymerizations with **18** at lower temperatures. Further, we observe a decrease in the values of m_{exp}/m_{th} from 1.68 to 1.3 to 0.97 for polymerizations utilizing **13**, **14**, and **16** with **17** as the initiator (J, L, and M, Table 2). It is apparent from these data that longer lived intermediate radicals cause greater increases in molecular weight with conversion than predicted by Equation 6, precisely as one would expect if the intermediate radicals were being irreversibly terminated, thereby removing CTA from the system.

While the trends observed in the molecular weight deviations and the dependence of the polymerization rate on a constant supply of radicals are consistent with irreversible termination of the intermediate radical, they do not exclude the possibility of concurrent reversible termination of the intermediate radical as proposed by Barner-Kowollik *et al*.[21] Additionally, the dithioester mediated polymerization of acrylamide may have more irreversible termination of the intermediate radical than is typical in most RAFT polymerizations due to the very slow rates of polymerization.

CONCLUSIONS

Conditions for Facile, Controlled RAFT Polymerization of Acrylamide in Water

Conditions allowing excellent control of the RAFT polymerization of acrylamide directly in aqueous media were described. The degree of control is illustrated in Figure 4 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) and conversions were limited to 28 %.

Factors Affecting Kinetics and Molecular Weight Control in the RAFT Polymerization of Acrylamide

The RAFT polymerization of acrylamide was studied employing different CTAs, initiators, initiator concentration, solvents, and temperatures. Higher apparent rates of polymerization were achieved with: CTA's having higher rates of fragmentation; initiators with lower decomposition temperatures; higher initiator concentration; and higher temperatures. High conversions, however, require a constant supply of radicals, indicating ongoing termination throughout the reaction. The use of online light scattering rather than standards for the determination of molecular weight allows meaningful comparison of experimental molecular weights with theory. The differences between experimental and theoretically determined molecular weights are substantial for all

conditions except when **16** are employed as the CTA. Molecular weight deviations in water are greater than those in DMSO reflecting the significance of hydrolysis for relatively slow RAFT polymerizations. Polymers produced under conditions with increased radical concentrations exhibit greater deviations while polymers prepared with CTAs with faster fragmentation rates have molecular weights closer to the theoretical molecular weights. Both the presence of significant termination and the trends observed in the molecular weights of the polymers are consistent with intermediate radical termination.

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