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Reversible Addition−Fragmentation Chain Transfer (RAFT) Polymerization in an Inverse Microemulsion: Partitioning of Chain Transfer Agent (CTA) and Its Effects on Polymer Molecular Weight[§]

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ABSTRACT: The effects of CTA partitioning between the aqueous and oil phases on resulting molecular weight in reversible addition−fragmentation chain transfer in inverse microemulsion polymerization (RAFT-IMEP) of *N,N*-dimethylacrylamide (DMA) have been investigated. Four trithiocarbonate-based CTAs (2-(1-carboxy-1-methylethylsulfanylthiocarbonylsulfanyl)-2-methylpropionic acid (CMP), 2-(ethylsulfanylthiocarbonylsulfanyl)-2-methylpropionic acid (EMP), 4-cyano-4-(ethylsulfanylthiocarbonylsulfanyl)pentanoic acid (CEP), and 2-(dodecylsulfanylthiocarbonylsulfanyl)-2-methylpropionic acid (DMP)) with different solubilities in the aqueous phase were chosen for these studies. The experimentally determined molecular weights were progressively higher than theoretically predicted as CTA partitioning into the organic phase increased. By comparing results with aqueous RAFT control experiments conducted at the same temperature and with the same CTAs and initiators, we demonstrate that the mole fraction of CTA partitioned into the aqueous phase prior to RAFT-IMEP can be substituted directly as the efficiency factor, γ, for RAFT agent utilization allowing accurate predictions of molecular weight at specified conversions.

Introduction

Water-soluble (co)polymers represent an important class of macromolecules which have been utilized extensively in water treatment, mining, and enhanced oil recovery (EOR) and as dispersants, stabilizers, erodable coatings, etc., in personal care and pharmaceutical formulations.[1] Virtually all commercial water-soluble polymers are synthesized in the aqueous phase by conducting polymerizations homogeneously in water or heterogeneously under inverse suspension or inverse emulsion conditions.[2] Impressive advances have been made in both industrial and academic laboratories over the past 30 years directed toward control of copolymer composition and attainment of desired molecular weight for specific applications. Of particular note were the pioneering efforts by Vanderhoff and by Candau and their respective collaborators in the development of inverse (water-in-oil) microemulsion techniques utilizing free radical initiation to produce a vast number of (co)polymers which could be easily recovered and reformulated or directly utilized in the dispersed or emulsified state.[3−12] Elucidation of the fundamental free radical polymerization kinetics and mechanisms in homogeneous and dispersed water-in-oil (w/o) phases, along with an understanding of reactivity ratios, provided a pathway for rapid development of many water-soluble (co)polymers utilized today.

Only recently, however, have techniques for precise synthetic design of architectures with specified molecular weights become available.[13−17] These techniques, identified in the literature as controlled/“living” radical polymerization (CLRP) or simply controlled radical polymerization (CRP), have been the focus of extensive research as evidenced by the proliferation of manuscripts including several reviews.[18−23] Of the CRP techniques, reversible addition−fragmentation chain transfer (RAFT) is arguably the method of choice for preparation of water-soluble (co)polymers. Not only can diverse classes of monomers with wide-ranging functionality be polymerized, but this can be accomplished directly in water, often without the necessity of protecting groups, provided judicious choice of chain transfer agents (CTAs), initiators, and reaction conditions.[24−26] Also, the opportunities for providing structopendent and structoterminal sites for further conjugation including facile orthogonal reactions directly in water have been demonstrated.[27] Thus, RAFT polymerization in aqueous media appears to be an especially useful controlled free radical polymerization technique since it allows for synthesis, purification, and resulting activity or response directly in water.[28] For example, a number of (co)polymer vehicles of precise design for response driven activity have been synthesized for delivery of therapeutic and diagnostic agents in nanomedicine.[29]

On the basis of extensive studies during the past decade of aqueous RAFT polymerization and RAFT-mediated heterogeneous polymerizations in dispersed oil-in-water (o/w) systems, it is quite surprising that there has been only limited research regarding RAFT-mediated water-in-oil (w/o) or inverse heterophase polymerization.[30−32] The only literature reports to date have been by Schork’s group utilizing inverse miniemulsion[33,34] and by our group utilizing inverse microemulsion[35] conditions.

In our initial research of RAFT-mediated inverse microemulsion polymerization (RAFT-IMEP),[35] we sought to combine the attributes of conventional IMEP with the control possible in aqueous RAFT polymerization. Candau et al., for example, had previously demonstrated advantages of IMEP for control of polymerization kinetics and particle size[4,7,11,36] while several groups including ours have shown the utility of aqueous RAFT for controlling molecular weight, molecular weight distribution, and living character for chain extension and block copolymer formation.[16,21−25,27−29] In our first RAFT-IMEP report,[35] after optimizing the pseudo-three-component phase diagrams of a microemulsion system composed of the hydrophilic monomer *N,N*-dimethylacrylamide (DMA), water,

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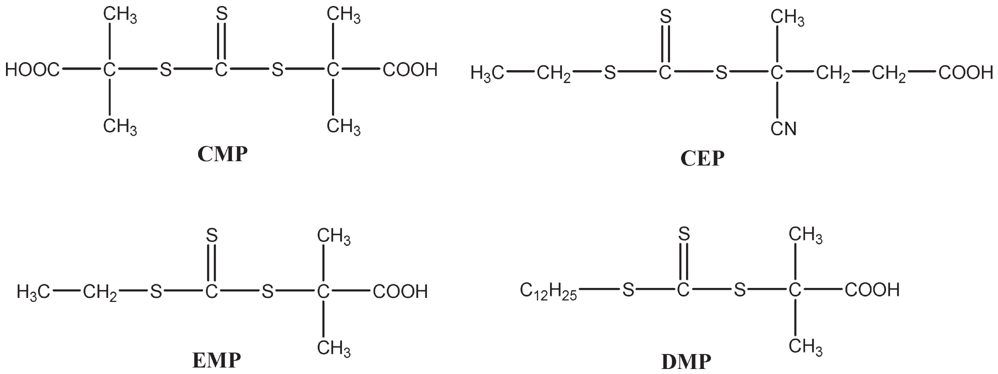
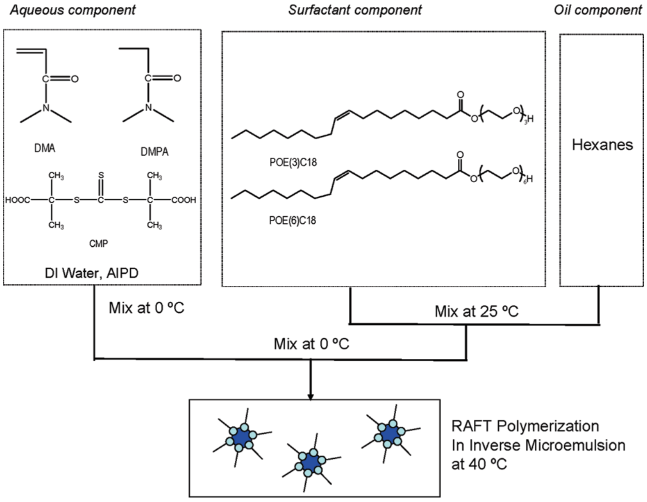


Figure 1. Chemical structures of RAFT chain transfer agents (CTA's).

Scheme 1. Components for RAFT Inverse Microemulsion Polymerization (RAFT-IMEP)



hexanes, nonionic surfactant, and cosurfactant, we determined conditions that yielded linear chain growth with conversion and maintenance of trithiocarbonate chain ends for successful chain extension and blocking by sequential addition of DMA and *N,N*-diethylacrylamide, respectively. The pseudo-first-order kinetic profiles were similar to those of the homogeneous aqueous RAFT polymerization (control); however, an induction period was observed prior to reaching the main RAFT equilibrium. Decreasing the volume fraction of the dispersed aqueous phase (the locus of polymerization) led to an increase in colloidal stability and a decrease in microemulsion size up to a limiting value below which further decrease led to unacceptable polydispersity. As expected, increasing the RAFT agent concentration relative to monomer led to narrower molecular weight distributions; however, higher-than-anticipated molecular weights based on monomer/CTA molar ratios and broadening of the molecular weight distributions in RAFT-IMEP were observed as compared to control polymerizations. In the work reported here, we examine the causes for discrepancies in anticipated molecular weight as determined by online, multiangle laser light scattering for RAFT-IMEP of DMA. We have conducted these experiments with four trithiocarbonates shown in Figure 1 utilizing the inverse microemulsion components and optimized parameters previously reported.[35] By comparing results with homogeneous aqueous RAFT control experiments conducted at the same temperature and with the same CTAs and initiators, we demonstrate herein that the mole fraction of CTA partitioned into the aqueous phase prior to RAFT-IMEP can be substituted directly as the efficiency factor for RAFT agent utilization allowing accurate predictions of molecular weight at specified conversions.

Experimental Section

Materials. *N,N*-Dimethylacrylamide (DMA) and *N,N*-dimethylpropionamide (DMPA) (Aldrich, Milwaukee, WI) were purified by distillation under reduced pressure. Polyoxyethylene(3) oleyl ether (POE(3)C18), polyoxyethylene(6) oleyl ether (POE(6)C18) (Nihon Emulsion, Tokyo, Japan), and hexanes (Aldrich, Milwaukee, WI) were used as received. 2,2′-Azobis[2-(2-imidozolin-2-yl)propane] dihydrochloride (AIPD) served as the initiator (gift from Wako Chemicals USA, Inc.). 2-(1-Carboxy-1-methylethylsulfanylthiocarbonylsulfanyl)-2-methylpropionic acid (CMP) was used without further purification (gift from Noveon, Inc.). 2-(Ethylsulfanylthiocarbonylsulfanyl)-2-methylpropionic acid (EMP),[37] 4-cyano-4-(ethylsulfanylthiocarbonylsulfanyl)pentanoic acid (CEP),[38] and 2-(dodecylsulfanylthiocarbonylsulfanyl)-2-methylpropionic acid (DMP)[39] were synthesized according to literature procedures.

RAFT Polymerization of DMA in Inverse Microemulsion. General Procedure (Scheme 1). *Aqueous Component*. CMP (14.2 mg, 5.05 mmol) was dissolved in a solution of DMA (2.00 g, 20.2 mmol) and DMPA (2.00 g, 19.8 mmol) contained in a 20 mL vial. DI water (5.00 g) was then added to the solution and cooled to 0 °C. A stock solution also cooled to 0 °C and containing AIPD (3.26 mg, 1.01 mmol) and DI water (1.00 g) was added to the vial. The solution was stirred and purged with N_2 for 1 h at 0 °C.

Mixture of Oil Component and Surfactant Component. Hexanes (8.75 g), POE(3)C18 (0.70 g), and POE(6)C18 (1.40 g) were added to a 20 mL round-bottomed flask. The solution was stirred and purged with N_2 for 1 h at 25 °C and then cooled to 0 °C.

Preparation of Inverse Microemulsion (*IME*) *and RAFT Polymerization*. The aqueous component (1.00 g) was added to the oil and surfactant mixture at 0 °C under N_2. The solution was purged with N_2 for another hour, and then the reaction flask was immersed oil bath at 40 °C. The inverse microemulsion was generated within 10 min. The polymerization reaction was terminated after 20 h by cooling to 0 °C in an ice bath followed by exposure to air. Conversions were monitored by taking aliquots at predetermined time intervals utilizing degassed syringes. Monomer concentration was determined by UV absorbance at 260 nm (500 Scan UV−vis−NIR spectrophotometer, Varian). SEC-MALLS was used to determine the molecular weight at specific time intervals, and the UV absorbance at 310 nm was simultaneously monitored for detection of the trithiocarbonate moiety. RAFT-IMEP components are given in Table 1.

Partitioning of CTAs and Suspension RAFT Polymerization. The aqueous component (1.00 g) excluding initiator and the oil component (8.75 g) were combined, and the mixture was immersed in an oil bath at 40 °C with stirring for 1 h. These conditions are identical to those for RAFT-IMEP in the absence of surfactant. When the stirring was stopped, the mixture phase-separated immediately. Aliquots were taken from the oil phase and were diluted with methanol. The UV absorbances at 260 and 320 nm were used to determine the respective concentrations of DMA and each CTA shown in Figure 1. The amount of each CTA partitioned into the

Table 1. Components for RAFT Solution and Inverse Microemulsion Polymerizations of DMA

	aqueous phase							oil phase		surfactant phase			
entry	DMA (g)	DMPA (g)	CMP (mg)	CEP (mg)	EMP (mg)	AIPD (mg)	DIW (g)	DMP (mg)	hexanes (g)	POE(3)C18 (g)	POE(6)C18 (g)	[DMA]/[CTA]	pH
						Solution Polymerization							
1	2.00	2.00				3.26	6.00						
2	2.00	2.00	14.2			3.26	6.00					400	4.0
3	2.00	2.00		13.3		3.26	6.00					400	4.5
4	2.00	2.00			11.3	3.26	6.00					400	4.3
						Inverse Miroemulsion Polymerization							
5	0.20	0.20				0.33	0.60		8.75	0.70	1.40		
6	0.20	0.20	1.42			0.33	0.60		8.75	0.70	1.40	400	4.0
7	0.20	0.20		1.33		0.33	0.60		8.75	0.70	1.40	400	4.5
8	0.20	0.20			1.13	0.33	0.60		8.75	0.70	1.40	400	4.3
9	0.20	0.20				0.33	0.60	1.82	8.75	0.70	1.40	400	5.6
10	0.20	0.20		3.66		0.90	0.60		8.75	0.70	1.40	145	4.5
11	0.20	0.20		1.83		0.45	0.60		8.75	0.70	1.40	290	4.5
12	0.20	0.20		0.53		0.13	0.60		8.75	0.70	1.40	1000	4.5
13	0.20	0.20		1.83		0.45	0.60		8.75	0.70	1.40	290	5.3
14	0.20	0.20		1.33		0.33	0.60		8.75	0.70	1.40	400	5.3
15	0.20	0.20		0.53		0.13	0.60		8.75	0.70	1.40	1000	5.3
16	0.20	0.20		1.83		0.45	0.60		8.75	0.70	1.40	290	6.0

Table 2. Experimental Data for RAFT Polymerization of DMA in Solution and IME

entry	CTA[a]	pH	DMA/CTA (mol/mol)	monomer conv (%)	M_n[b] (kg mol^{-1})	M_n[d] (kg mol^{-1})	γ[c]	M_w/M_n[d]	$D_{t=0}$ (nm)	$D_{t=20\,h}$ (nm)
					Solution Polymerization					
1				92.1		638.6		2.16		
2	CMP	4.0	400	94.9	37.9	35.7	1.06	1.14		
3	CEP	4.5	400	99.7	39.8	42.1	0.96	1.09		
4	EMP	4.3	400	99.5	39.7	40.5	0.98	1.06		
					Inverse Microemulsion Polymerization					
5				92.3		308.8		1.59	11	55
6	CMP	4.0	400	96.5	38.6	40.0	0.97	1.68	12	83
7	CEP	4.5	400	97.4	38.9	56.2	0.69	1.23	12	119
8	EMP	4.3	400	97.8	39.0	69.6	0.56	1.20	12	90
9	DMP	5.6	400	70.9	28.5	399.3	0.07	2.46	12	

[a] Structures for CMP, CEP, EMP, and DMP are shown in Figure 1. [b] Calculated using eq 2: $M_{n,th}$ = ([monomer]$_0$/[CTA]$_0$) × MW$_{Monomer}$ × ρ + MW$_{CTA}$. [c] Calculated using eq 3: $M_{n,expt}$ = ([monomer]$_0$/([CTA]$_0$ × γ)) × MW$_{monomer}$ × ρ + MW$_{CTA}$. [d] Determined by aqueous SEC/MALLS system with 20%/80% acetonitrile/0.05 M Na_2SO_4 as eluent.

aqueous phase was determined by difference based on quantitative measure of the fraction of the CTA in the oil phase. Suspension RAFT polymerization with rapid stirring was conducted utilizing a solution prepared in an identical manner to that used in partitioning studies except that initiator was added. Monomer conversion, molecular weight, and polydispersity were then determined from the aliquots taken from the aqueous phase at specified time intervals.

Stability of CEP in the Aqueous Phase. The pH values of the aqueous phases (in the absence of initiator) were adjusted to 4.5, 5.3, and 6.0 using 0.1 N NaOH, and the mixtures were immersed in an oil bath at 40 °C with stirring. The stability of CEP was monitored by taking aliquots at predetermined time intervals utilizing syringes. The UV absorbance values at 320 nm were measured, and the CTA concentration was determined from the standard absorbance vs concentration plot.

Size Exclusion Chromatography. After polymerization, hexanes were removed from the mixture by purging with N_2 gas. The samples were analyzed by size exclusion chromatography (SEC) using 0.05 M ammonium acetate in DMF as eluent at a flow rate of 1.0 mL/min at 35 °C. The SEC instrument was equipped with Viscotek I-Series Mixed Bed low-MW and mid-MW columns, Viscotek-TDA (302 nm RI, viscosity, 7 mW 90° and 7° true low angle light scattering detectors (670 nm). The dn/dc values of polyDMA (0.086 mL/g) in the above eluent were determined at 35 °C using a Viscotek refractometer and Omnisec software. M_n, M_w, and polydispersity indices (PDIs) of polymers were determined (Table 2).

To detect the presence of the trithiocarbonate moiety on the polymer, chromatograms (RI and UV absorbance at 310 nm) were generated. After the polymerization, hexanes were removed from the mixture by purging with N_2 gas. An ethyl acetate/hexanes (75 vol %/25 vol %) solution was added to precipitate the polymers. The polymers were then redissolved in acetone and precipitated in ethyl acetate/hexanes (75 vol %/25 vol %). This procedure was repeated three times. Following filtration, the samples were analyzed by SEC using an eluent of 20%/80% acetonitrile/0.05 M aqueous Na_2SO_4 at a flow rate of 0.3 mL/min. TOSOH Biosciences TSK-GEL columns [Supre AW3000 G3000 PWXL (< 50 000 g mol^{-1}, 200 A) and G4000 PWXL (2000−300 000 g mol^{-1}, 500A)], a Polymer Laboratories LC 1200UV/vis, Wyatt Optilab DSP interferometric refractometer, and Wyatt DAWN EOS multiangle laser light scattering detectors (690 nm) were employed in the analysis. The dn/dc value of PDMA (0.165 mL/g) in the above eluent was determined at 35 °C. M_n, M_w, and polydispersity indices (PDIs) for polymers were determined (Table 2).

Dynamic Light Scattering. Dynamic light scattering was conducted using a Malvern Instruments Zetasizer Nano series instrument equipped with a 22 mW He−Ne laser operating at λ = 632.8 nm, an avalanche photodiode detector with high quantum efficiency, and an ALV/LSE-5003 multiple tau digital correlator electronics system. The average diameters of the IMEs were directly measured without filtering the mixtures.

Results and Discussion

For reasons discussed in the Introduction, RAFT-IMEP, in principle, has potential for preparation of well-defined, water-soluble (co)polymers in the form of thermodynamically stable, latex particles. Obvious to the success of such polymerizations, as with all RAFT polymerizations in water, is the necessity of eliminating or substantially minimizing CTA or macroCTA hydrolysis, aminolysis, or other adverse reactions including irreversible intermediate radical termination. From the considerable body of literature regarding the more-often-studied RAFT polymerization in heterogeneous o/w emulsion systems, issues of colloidal instability, inhibition, retardation, and loss of livingness remain challenges.[30−32,40−47] More specifically, the diffusion and redistribution of CTA, monomer, and initiator between the continuous and dispersed phases during the course of the RAFT emulsion polymerization are system-dependent and are more difficult to control than in bulk or solution.[48−53] Similar issues have arisen in the reports of RAFT-mediated (o/w) microemulsions by Kaler and co-workers, who studied polymerization of hexyl methacrylate (2.64 wt %) with dodecyltrimethylammonium bromide as surfactant and 2-cyano-2-yl dithiobenzoate as the CTA.[54] Particle sizes between 18 and 30 nm were reported, and molecular weight increased linearly with conversion; the polydispersity index (PDI) remained low as long as the number RAFT agents per particle was greater than 1. The same group carried out simulations which appear to support the observed polymerization kinetics, including retardation and loss of molecular weight control.[55,56] Recently, solubility and partitioning of CTA in RAFT microemulsion polymerization have been shown to affect the properties of polymer and its latex.[57] Analysis of research to date indicates that the effects of partitioning/compartmentalization on properties and kinetics of the resulting (co)polymers prepared by microemulsion polymerization via RAFT need further elucidation.

In our seminal report regarding RAFT-IMEP,[35] we identified an unexpected discrepancy between theoretically predicted and experimentally measured molecular weights of produced poly(*N*,*N*-dimethylacrylamide) polymers as compared to those prepared under similar aqueous RAFT conditions. This discrepancy appeared to vary with the nature of the CTA even when the molar ratios of CTA/monomer/initiator were maintained at a constant value. According to the currently accepted mechanism of RAFT polymerization,[58,59] the theoretical molecular weight, $M_{\mathrm{n,th}}$, at conversion ρ can be predicted using eq 1[21]

$$M_{\mathrm{n,th}} = \frac{\mathrm{MW}_{\mathrm{monomer}}[\mathrm{M}]_0\rho}{[\mathrm{CTA}]_0 + 2f[\mathrm{I}]_0(1-\mathrm{e}^{k_{\mathrm{d}}t})} + \mathrm{MW}_{\mathrm{CTA}} \qquad (1)$$

where $\mathrm{MW}_{\mathrm{monomer}}$, $[\mathrm{M}]_0$, $\mathrm{MW}_{\mathrm{CTA}}$, and $[\mathrm{CTA}]_0$ are the molecular weights and initial concentrations of monomer and CTA, respectively. The second term of the denominator accounts for the initiator derived chains in which $[\mathrm{I}]_0$, t, k_{d}, and f represent initial initiator concentration, time, rate constant for initiator decomposition, and initiator efficiency, respectively. In a well-controlled RAFT process, initiator-generated polymer can be considered minimal, and thus, the second term in the denominator can be neglected. Hence, eq 1 may be rewritten as eq 2.

$$M_{\mathrm{n,th}} = \frac{\mathrm{MW}_{\mathrm{momomer}}[\mathrm{M}]_0\rho}{[\mathrm{CTA}]_0} + \mathrm{MW}_{\mathrm{CTA}} \qquad (2)$$

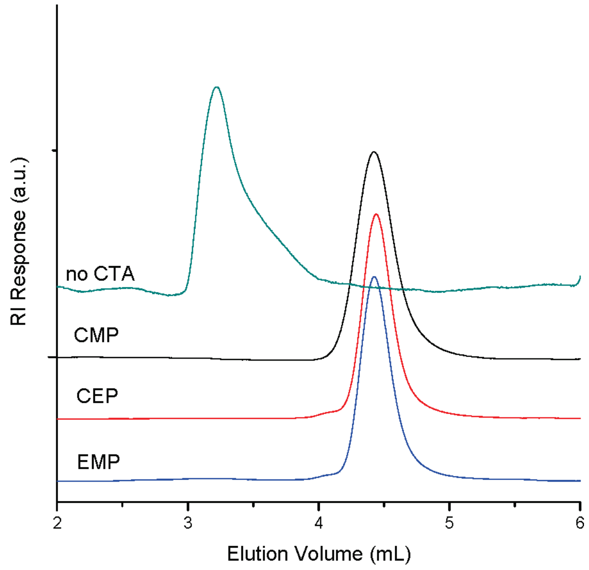


Figure 2. SEC chromatograms of polyDMA prepared by homogeneous aqueous RAFT polymerization using CMP, CEP, and EMP as chain transfer agents. Conventional free radical polymerization (no CTA) was also performed for comparison. A 20%/80% acetonitrile/0.05 M aqueous Na_2SO_4 was utilized as eluent.

In previous work, Thomas in our group demonstrated the importance of minimizing CTA hydrolysis and/or aminolysis during aqueous RAFT polymerization.[60,61] Loss of thiocarbonylthio groups, especially in the early stages of polymerization, was shown to greatly affect the efficiency and thus molecular weight. This was much more pronounced utilizing dithioesters with long initialization periods prior to reaching the main equilibrium and hardly noticeable with trithiocarbonates. Equation 2 was thus modified with γ (an efficiency or CTA utilization factor) to yield eq 3 for predicting molecular weight.[61] We postulated that since trithiocarbonate CTAs in the current study and previous aqueous RAFT studies have leaving groups that rapidly reinitiate polymerization of acrylamido monomers and thus γ values near 1, the experimentally observed loss of efficiency in RAFT-IMEP must be due to factors other than hydrolysis.

$$M_{\mathrm{n,expt}} = \frac{\mathrm{MW}_{\mathrm{monomer}}[\mathrm{M}]_0\rho}{[\mathrm{CTA}]_0\gamma} + \mathrm{MW}_{\mathrm{CTA}} \qquad (3)$$

Comparison of RAFT Polymerization in Homogeneous Aqueous Solution and IME with Selected CTAs. In this study, we employed four CTAs (Figure 1) having different solubilities in the aqueous phase. All four CTAs contain carboxylic acid functional groups making their aqueous solubilities dependent not only on structure but also on solution pH. Prior to RAFT-IMEP, conventional free radical and RAFT solution polymerizations were carried out to determine the efficiency of the four CTAs in the polymerization of DMA (Table 1, entries 1−4). These solution polymerizations were performed in the aqueous phase mixture used in RAFT-IMEP. The target molecular weight for each experiment was 40 kg mol^{-1} at 100% conversion. The results are shown in Table 2 and the corresponding chromatograms in Figure 2.

As expected, the conventional free radical solution polymerization (no CTA) gave a broad molecular weight distribution and very high molecular weight. The SEC chromatogram (Figure 2) is asymmetrical due to the molecular weight of the polymer exceeding the size exclusion limit (300 000) of the column. However, all the homogeneous, aqueous RAFT polymerizations (entries 2−4) resulted in well-controlled polymers with molecular weights close to

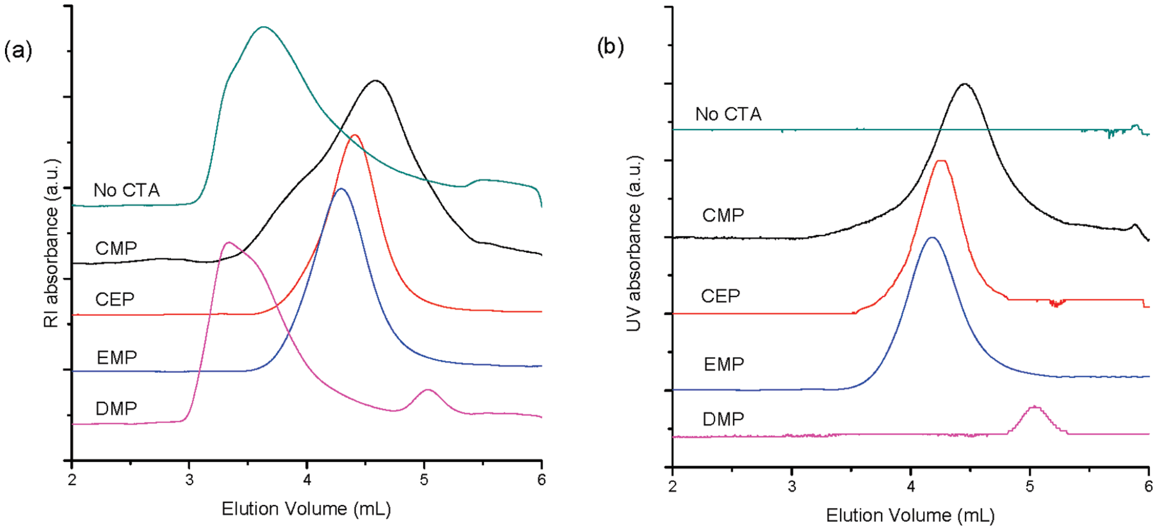


Figure 3. SEC chromatograms utilizing (a) RI and (b) UV (310 nm) detection of polyDMA synthesized by RAFT-IMEP using CTAs shown in Figure 1. A 20%/80% acetonitrile/0.05 M aqueous Na_2SO_4 was utilized as eluent.

target values and low polydispersities (< 1.2). There are no significant differences among these three CTAs (CMP, CEP, and EMP) in aqueous RAFT polymerization. It should be noted that insolubility of DMP in the aqueous phase precluded its homogeneous, aqueous RAFT polymerization.

RAFT-IMEP experiments were then conducted utilizing a procedure similar to that we previously reported.[35] Although DMP has a very low solubility in the aqueous phase, it is soluble in the oil phase which is made up of hexanes. DMP was therefore dissolved in the oil phase and used in RAFT-IMEP. The other three CTAs were dissolved directly in the aqueous phase. The experimental data of RAFT-IMEP are shown in Table 2, entries 6−9. The chromatograms from RI and UV detection are shown in Figure 3. As expected, conventional free radical IMEP resulted in lower molecular weight and better polydispersity when compared to classical aqueous solution (no CTA) polymerization. With added CTA, unlike homogeneous, aqueous RAFT polymerization, IMEP yielded broader polydispersities and higher molecular weights which are dependent on the specific CTA. With CMP, the RI chromatogram has a high molecular weight shoulder; however, this does not appear in the UV trace. This strongly suggests that the shoulder is due to the lack of participation of the CTA and thus formation of uncontrolled polymer. In our previous report, we demonstrated that a low number of CTAs per particle can lead to the generation of uncontrolled polymer at the beginning of polymerization.[35] By contrast, chromatograms from RAFT-IMEP using EMP and CEP do not have shoulders and have better PDI values as compared to CMP. The chromatograms with RI and UV detection also match each other well. In the case of DMP, phase separation occurred and a polymer emulsion could not be obtained. Only a small fraction of the polymer contains the CTA moiety, and there is no control in the polymerization. Of the systems in our study, relatively good control is achieved with CEP and EMP.

Figure 4 shows particle size distribution as determined by dynamic light scattering for IMEP mediated by CMP, CEP, and EMP. These latexes were stable for at least 2 months at ambient conditions. Increases in particle size during polymerization according to the model proposed by Candau et al. result from coalescence or diffusion of monomer in non-nucleated micelles.[11]

As shown in Table 2, the experimentally determined molecular weights from RAFT-IMEP are greater than the theoretical values calculated based solely on the monomer to total CTA ratio (eq 2). At approximately the same pH, $M_{n,expt}$ increases in the order of CMP < CEP < EMP (Table 2, entries 6−8). In RAFT polymerization, a positive deviation in molecular weight can be attributed to incomplete usage or loss of CTA which has been observed previously in aqueous RAFT.[62] We first examined the sensitivity of CEP toward hydrolysis and found it stable at pH values from 4.5 to 6.0 for an extended period of time (Figure 5). We assume that the three other CTAs exhibit similar hydrolytic stability. We have also shown that these CTAs yielded polymers with molecular weights predicted from monomer to CTA ratios in homogeneous RAFT polymerization (Table 2, entries 2−4). The fact that apparent γ values are near 1.0 (0.96−1.06) from eq 3 utilizing experimental data confirms that CTA hydrolysis is not a factor. Thus, major discrepancies between theoretical and experimental molecular weights observed in RAFT-IMEP must be due to other factors.

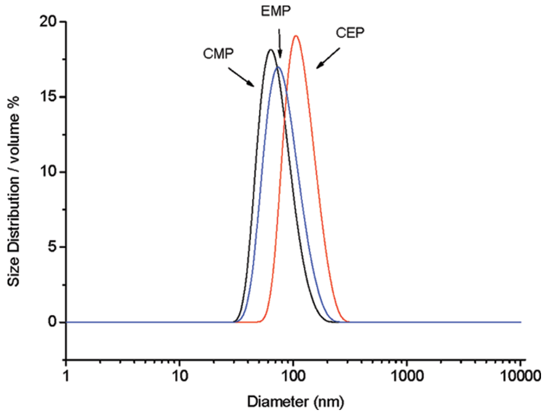


Figure 4. Particle size distributions as determined by dynamic light scattering of inverse microemulsions after 20 h polymerization using CMP (0.19), CEP (0.17), and EMP (0.16) as CTAs. Values in parentheses are particle polydispersities. The corresponding conversions were 96.5%, 97.4%, and 97.8%, respectively.

We suspected that the systematic variations in molecular weights observed in RAFT-IMEP were likely due to the partitioning of the CTA between the aqueous and oil phases. Such effects have been reported in cobalt(II)-mediated catalytic chain transfer miniemulsion polymerization of methyl methacrylate.[63] We conducted CTA partitioning studies as

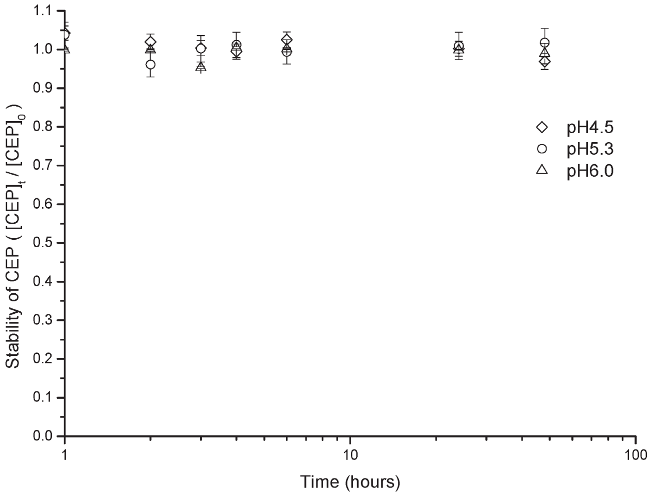


Figure 5. Stability of CEP in the aqueous phase at different pH values at 40 °C monitored by its UV absorbance at 320 nm ($[CEP]_0$ = initial CTA concentration, $[CEP]_t$ = CTA concentration at time *t*).

Table 3. Partitioning of the CTAs between the Aqueous and Oil Phases at Different pH Values

			partitioning (mole fraction)	
CTAs	pH	degree of ionization[a]	aqueous	oil
CMP	4.0	0.39	0.86	0.14
	5.3	0.93	> 0.99	< 0.01
	6.1	0.99	> 0.99	< 0.01
CEP	4.5	0.39	0.72	0.28
	5.3	0.80	0.95	0.05
	6.0	0.95	> 0.99	< 0.01
EMP	4.3	0.72	0.50	0.50
	5.2	0.95	0.69	0.31
	6.0	0.99	0.99	0.01
DMP	5.6	0.39	0.01	0.99
macroCTA	4.5		> 0.99	< 0.01

[a] Calculated using apparent pK_a values for CMP (4.2), CEP (4.7), EMP (3.9), and DMP (5.8) measured by potentiometric titration in methanol/water mixture.

described in the Experimental Section monitoring the UV absorbance at 320 nm. Near a pH value of 4 at which CTAs are partially deprotonated, distributions (mole fractions) in the aqueous phase were measured as shown in Table 3: CMP (0.86), CEP (0.72), and EMP (0.50). At pH 5.6, only a small amount of DMP (0.01) is partitioned into the aqueous phase. When the pH is increased, the partitioning of all CTAs into the aqueous phase (except for the hydrophobic DMP) increases to ~0.99. The partitioning values are dependent on the chemical structure of the CTAs as well as on the degree of ionization of the carboxylic groups which can be controlled by the solution pH.

Utilizing experimental molecular weight values determined for the poly(*N*,*N*-dimethylacrylamide) prepared by RAFT-IMEP (Table 2), apparent γ values were determined from eq 3 at specific monomer conversions. The reasonably good agreement of experimental γ values and partitioning values of CTAs in the aqueous phase (Table 3) for this data set, limited to specific reaction conditions, sampling time, and monomer/CTA ratios, led us to further examination utilizing SEC/MALLS along with RI and UV detection.

Controlling CTA Partitioning through pH Adjustment. To further investigate the effects of CTA partitioning, we conducted RAFT-IMEP with varying monomer-to-CEP ratios at specific pH values of 4.5, 5.3, and 6.0. The experimental data at high conversions (97−99%) are shown in Table 4. SEC chromatograms of entries 10−13 are shown in Figure 6. Each chromatogram shows a unimodal distribution and a low PDI (< 1.3). (Small peaks at 5.7 mL elution volume are attributed to surfactants.)

At pH 4.5, the γ values derived from eq 3 are nearly constant (entries 10−13) and match the experimentally determined fraction of CTA partitioned into the aqueous phase (0.72). Similarly, the γ values (0.93−1.01) at pH 5.3 are also close to the partitioning values (0.95) of CTAs in the aqueous phase at the same pH. The partitioning values, thus, can be substituted for γ in eq 3, allowing prediction of the theoretical M_n values for RAFT-IMEP. These values compare well with the experimental M_n's over a range of molecular weights we studied (Figure 7). These results further confirm that the extent of CTA partitioning in the aqueous phase, and thus efficiency represents a major factor in correctly predicting the molecular weight of polymer prepared via RAFT-IMEP. Additional support for this hypothesis comes from our related report of utilizing a PDMA macroCTA in chain extension.[64] It was shown that the experimental molecular weights were in reasonable agreement with those theoretically predicted at all conversions. In retrospect, this would be expected since the PDMA macroCTA is partitioned almost exclusively into the aqueous phase of the inverse microemulsion.

We have shown that consideration of the partitioning of CTA into the aqueous phase prior to the start of RAFT-IMEP allows for reasonable prediction of the polymer molecular weights. The data shown in Table 4 and Figures 6 and 7 were generated for varying monomer-to-CTA ratios and pH values at high monomer conversions. Obviously, RAFT-IMEP is not static in nature, so we sought to determine if partitioning of the CTA (and thus γ values) changed with conversion and to assess the resulting effect on molecular weight and PDI throughout the polymerization. It is difficult to separate the aqueous and oil phases in the RAFT-IMEP system, as the inverse microemulsion is thermodynamically stable. We, therefore, conducted a model experiment wherein RAFT polymerization was carried out using the aqueous and oil phases of similar composition in RAFT-IMEP but without the surfactant components. This is basically a suspension polymerization containing two immiscible liquid phases and requiring rapid agitation. When the stirring was stopped, the mixture phase-separated immediately and aliquots were taken from each phase. The conversions and molecular weights were then determined using the aqueous aliquots, while CTA partitioning was determined using the aliquots from the oil phase. Figure 8 shows the partitioning of CEP into the aqueous phase as a function of monomer conversion. It should be noted that no hydrolysis of this RAFT agent (Figure 5) was observed in the aqueous phase over an extended period of time.

As shown in Figure 8, between 0.7 and 0.75 mole fraction of CEP was partitioned into the aqueous phase at pH 4.5 prior to polymerization. After the RAFT polymerization process started, the total trithiocarbonate in the aqueous phase gradually increased and then leveled off at around 40% monomer conversion. At the end of the polymerization, almost all (> 0.95 mole fraction) of the CEP as PDMA-CEP macroCTA remained partitioned in the aqueous phase. Evolution of molecular weight with conversion is shown in Figure 9c. Experimental molecular weights follow the $M_{n,pred}$ ($\gamma \approx 0.73$) at low conversions. However, the molecular weights gradually shift toward $M_{n,pred}$ ($\gamma \approx 0.99$) beginning at 40% monomer conversion. This observation demonstrates that there is diffusion of CEP from the organic into the aqueous phase during suspension RAFT polymerization.

Table 4. RAFT-IMEP of DMA Using CEP at Selected pH Values and CTA-to-Initiator Ratios

entry	CTA	pH	DMA/CTA (mol/mol)	momomer conv (%)	$M_n{}^a$ (kg mol^{-1})	$M_n{}^c$ (kg mol^{-1})	γ^b	$M_w/M_n{}^c$	$D_{t=0}$ (nm)	$D_{t=20\,h}$ (nm)
10	CEP	4.5	145	99.8	14.6	23.9	0.61	1.23	13	128
11	CEP	4.5	290	95.9	27.8	39.1	0.71	1.21	12	101
12	CEP	4.5	400	97.4	38.9	56.2	0.69	1.23	12	119
13	CEP	4.5	1000	98.8	98.2	138.1	0.71	1.24	12	54
14	CEP	5.3	290	99.3	28.8	30.7	0.94	1.21	12	91
15	CEP	5.3	400	99.1	39.6	42.5	0.93	1.27	12	83
16	CEP	5.3	1000	99.4	98.8	98.0	1.01	1.26	12	58
17	CEP	6.0	290	99.2	28.8	31.3	0.92	1.36	12	75

[a] Calculated using eq 2: $M_{n,th}$ = ([monomer]$_0$/[CTA]$_0$) × MW$_{monomer}$ × ρ + MW$_{CTA}$. [b] Calculated using eq 3: $M_{n,expt}$ = ([monomer]$_0$/([CTA]$_0$ × γ)) × MW$_{monomer}$ × ρ + MW$_{CTA}$. [c] Determined by aqueous GPC system with 20%/80% acetonitrile/0.05 M Na_2SO_4 as eluent.

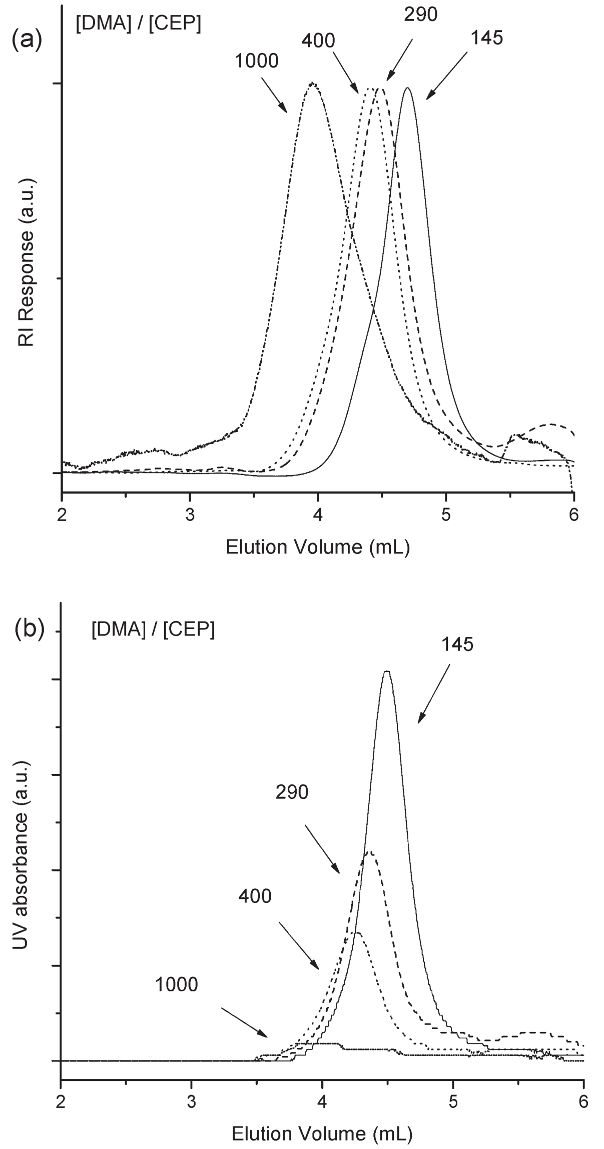


Figure 6. SEC chromatograms by (a) RI and (b) UV detection of RAFT-IMEP with varying DMA to CTA ratios at pH 4.5. A 20%/80% acetonitrile/0.05 M aqueous Na_2SO_4 was utilized as eluent.

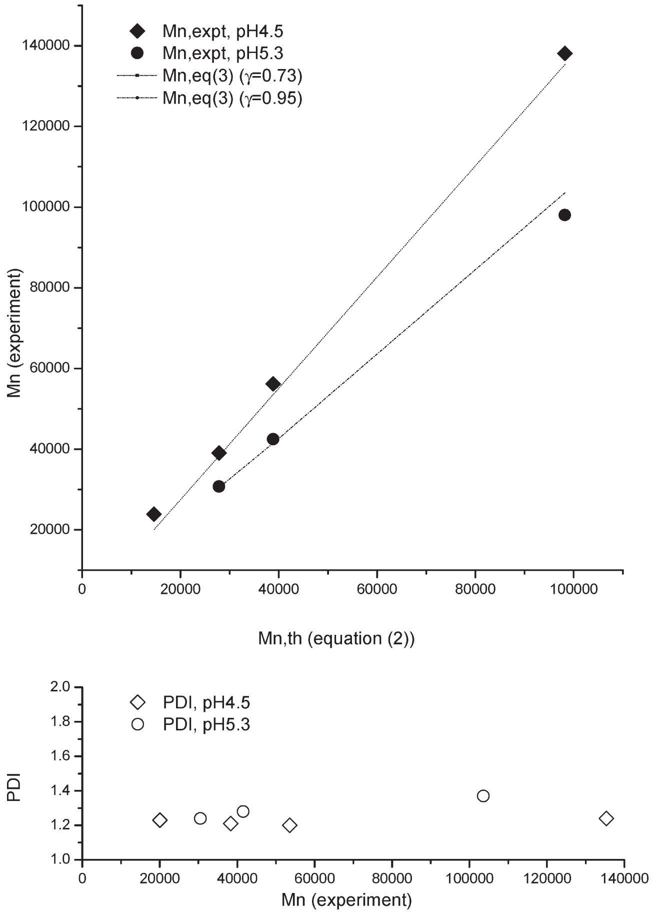


Figure 7. Comparison of projected and experimental M_n (calculated using eq 2 and γ values corresponding to the fraction of CEP partitioned into the aqueous phase) for RAFT-IMEP experiments conducted at pH 4.5 and 5.3, respectively.

In contrast to the results from suspension polymerization, a linear correlation of $M_{n,expt}$ with conversion is observed with RAFT-IMEP at different pH values (Figure 9a,b). The $M_{n,expt}$ at pH 4.5 follows the $M_{n,pred}$ using 0.73 (partitioning of CTA into the aqueous phase at pH 4.5) as the value for γ. The $M_{n,expt}$ at pH 6.0 also follows the $M_{n,pred}$ using 0.99 (partitioning of CTA in aqueous phase at pH 6.0) as the value for γ, although the experimental values are slightly larger than the $M_{n,pred}$. These data again confirm that the fraction of the CTA partitioned into the aqueous phase at the initial stage of polymerization is the major factor determining the polymer molecular weight. The linear correlation of $M_{n,expt}$ with conversion also suggests that the number of CTAs participating in RAFT-IMEP is constant.

Preparation of High Molecular Weight Polymer via RAFT-IMEP. Despite its industrial significance, selection of RAFT polymerization conditions in heterogeneous systems to yield high molecular weights and well-defined polymers has always been a challenging task.[32] In a related system, Yang et al. reported the synthesis of polystyrene via RAFT polymerization in miniemulsion. The best reported result was a polymer with the molecular weight of 80 000 and PDI of 1.35.[65] In our previous report,[35] we found that good control

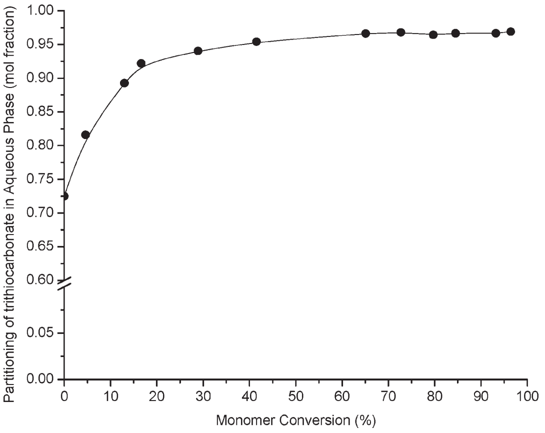


Figure 8. Partitioning of the RAFT CTA into the aqueous phase as a function of monomer conversion during suspension polymerization at pH 4.5 and 40 °C.

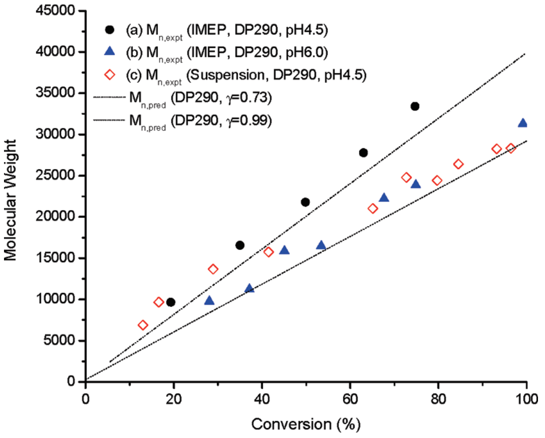


Figure 9. Number-average molecular weight (M_n) vs monomer conversion by RAFT polymerization in (a) IME (pH 4.5), (b) IME (pH 6.0), and (c) suspension (pH 4.5). $M_{n,expt}$ was determined by a SEC using 0.05 M ammonium acetate in DMF as eluent.

of RAFT polymerization in an inverse microemulsion (IME) system can be achieved by having larger initial IME particle size (~18 nm), which can be obtained by increasing the amount of the dispersed aqueous phase (thus allowing for a higher monomer to CTA ratio). The average diameters of polymer particles after polymerization reach over 200 nm, and the particles tend to settle to the bottom of the flask although they can be easily redispersed by stirring. Additionally, we can achieve good control with smaller IME particle size (~12 nm) by having a higher average number of CTAs per IME particle. Increasing the number of CTAs per particle prevents the generation of uncontrolled polymer. This, however, leads to a lower monomer-to-CTA ratio which hinders the preparation of higher molecular weight polymers.

In this report, we investigated the effects of four different CTAs on the control of RAFT polymerization under inverse microemulsion conditions. As in our previous report,[35] CMP seems to provide less control in RAFT-IMEP compared to CEP and EMP (Table 2 and Figure 3). Even with a very low average number of CTAs per IME particle (0.9 and 1.1 CTAs per particle at pH 4.5 and 5.3, respectively), CEP allows for the preparation of PDMA with relatively high molecular weight (~100 kg mol^{-1}) (Table 4, entries 13 and 16) with reasonably good polydispersities. It should be noted that these experiments were conducted under conditions (8.5 wt % aqueous component) similar to that described in our earlier report.[35] The four CTAs we have utilized thus far are trithiocarbonate-based but have differences in their structures and solubilities, which affect CTA partitioning between the oil and aqueous phases. In as much as we would like to provide concrete conclusions with regard to the structural effects of CTAs on the control of RAFT-IMEP, we have, to date, conducted experiments only on a few of the vast number of potential systems. However, it is evident that good control of DMA polymerization can be achieved with CEP and EMP in RAFT-IMEP.

Conclusions

Utilizing four RAFT chain transfer agents with different solubilities in the continuous and dispersed phases, the effects of CTA solubility on the control of RAFT-IMEP have been assessed. To account for the experimentally determined molecular weights, a parameter γ that reflects the fraction of CTA that actually participates in each RAFT experiment has been introduced. The γ values were calculated using the experimental M_n values and were found to be similar to the partitioning values of the respective CTAs in the aqueous phase. We have also demonstrated that the molecular weight can be predicted using the experimentally determined γ values. Additionally, relatively high molecular weight polymers with low PDIs can be obtained using CEP as the chain transfer agent in RAFT-IMEP.

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