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Nanoreactors for Aqueous RAFT-Mediated Polymerizations

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Introduction. Nanoreactors provide the ideal setting where selected chemical reactions can take place with high efficiency in controlled environments. Much attention has been focused on carrying out organic reactions in surfactant-based micelles in water.[1] This methodology can provide significant advantages over solution reactions due to compartmentalization of reactants or catalysts, greater heat transfer through the aqueous environment, controlled rates of reaction, better accommodation for potentially explosive or runaway exothermic reactions, and the environmentally friendly nature of the aqueous reaction medium.[2,3]

The concept of nanoreactors is not new to free-radical polymerizations, in which surfactant stabilized micelles are commonly used.[4] However, these micelle-type nanoreactors (termed ab initio emulsion polymerizations) failed to produce well-controlled molecular weight distributions (MWDs) and particle size distributions (PSDs) in reversible addition−fragmentation chain transfer (RAFT) controlled/"living" radical polymerizations (CRP) due to transportation problems of monomer or other compounds (e.g., RAFT agent) from monomer droplet reservoirs to the growing particles.[3] Miniemulsions have solved the transportation problem as each droplet is an isolated bulk nanoreactor, in which all components are located within the droplet.[5] The drawbacks of miniemulsions are (a) the difficulty in isolating pure polymer product due to the high levels of hexadecane (to reduce Oswald ripening) and surfactant and (b) the PSDs are broad with little or no control over the particle size. Other methods of growing amphiphilic diblock copolymers in situ led to poor control of the chain length polydispersity (> 1.4, while below 1.2 is considered "good control"), broad PSDs,[6] and very long polymerization times.[7]

In our quest to find better alternative water-based methods to carry out RAFT-mediated polymerizations, specially designed nanoreactors have provided the solution to produce narrow and controlled molecular weight and particle size distributions. The nanoreactors used in this work were designed to (a) encapsulate the hydrophobic or water insoluble monomer, (b) selectivity bind the RAFT agent directly in the nanoreactor to avoid transportation problems,[8] (c) provide steric colloidal stabilization of the nanoparticles, (d) produce monodisperse nanoparticles, and (e) be easily removed to obtain the pure synthesized polymer (see Scheme 1).

We created the nanoreactor from a diblock copolymer of poly(*N*-isopropylacrylamide-*b*-dimethylacrylamide) or P(DMA$_{49}$-*b*-NIPAM$_{106}$), which for the PNIPAM block[9] is hydrophilic below its lower critical solution temperature (LCST ∼ 36 °C)[10] and water-soluble and above its LCST forms self-stabilized, through the hydrophilic PDMA block, monodisperse polymer particles in the nanosize range (22.4 nm). The RAFT agent, a low molecular weight PNIPAM$_{18}$−SC(=S)SC$_4$H$_9$ (MacroCTA), was designed to be highly compatible with the nanoreactor and when self-assembled with the diblock above the LCST of PNIPAM gave a hydrodynamic diameter of 31.5 nm (see Table S1 in Supporting Information). The great advantage of our methodology is that water, P(DMA$_{49}$-*b*-NIPAM$_{106}$), PNIPAM$_{18}$−SC(=S)SC$_4$H$_9$, styrene monomer, and water-soluble initiator can be added in one pot and heated above the LCST to form the nanoreactors (see Supporting Information for experimental conditions).

Results and Discussion. In one pot, the thermoresponsive diblock, PNIPAM$_{18}$−SC(=S)SC$_4$H$_9$ (MacroCTA), styrene (STY), ammonium persulfate (APS), and water at room temperature were mixed together and then heated to 70 °C, well above the LCST of the PNIPAM block, to form nanoreactors encapsulating the styrene monomer. Sun and Deng[11] described that due to the immiscibility of PNIPAM above the LCST with either water or toluene, they could make hollow nanoparticle. Our own observations that PNIPAM was immiscible in styrene and water at 70 °C led us to carry out experiments to elucidate how styrene monomer is encapsulated within the nanoreactor and explain why the rates of polymerization were so rapid (see Mechanistic Aspects of Swelling section).

Controlled and Narrow Molecular Weight Distributions (MWD). The RAFT-mediated polymerization of styrene within our nanoreactors at 70 °C (experiment 1, Table 1) formed well-defined polymer rapidly, reaching 82% conversion in only 90 min, an M_n of 26 530, and PDI of 1.09 as determined by triple detection size exclusion chromatography (SEC). The M_n's increased in accord with the lower ratio of RAFT agent to styrene, and the PDIs were less than 1.3 (Table 1; see Supporting Information for all the MWD and conversion data). The diblock that forms our nanoreactors was easily separated from the newly formed polymer through precipitation in methanol. The SEC data (Table 1) show that the PDI values of PSTY decreased to below 1.2 following the above purification step. This nanoreactor approach is a significant improvement on previous methods. It was found that the same RAFT-mediated polymerization carried out in DMF (a good solvent for all components) was slow, reaching 36% conversion after 24 h with broad MWDs (i.e., with PDIs > 1.35). Therefore, by confining the reactions within the nanoreactor, kinetic dominated over thermodynamic control to convert a relatively unreactive MacroCTA into a highly active one. Other monomers, 2,3,4,5,6-pentafluorostyrene or *n*-butyl acrylate, were also successfully polymerized using the nanoreactor methodology (Table 1).

The importance of the rational design of the MacroCTA for these types of nanoreactors is demonstrated by substituting the PNIPAM$_{18}$−SC(=S)SC$_4$H$_9$ used above with a low molecular weight PSTY$_{10}$−SC(=S)SC$_4$H$_9$ MacroCTA in the RAFT-mediated polymerization of styrene at 70 °C. The rate of polymerization was fast, but the MWD was uncontrolled and resembled that of a conventional free-radical emulsion polymerization (see Supporting Information), further supporting our claim that designing the RAFT agent to be compatible (or fully miscible) with the nanoreactor is a key parameter to

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successful controlled/"living" radical RAFT-mediated polymerizations.

Controlled and Narrow Particle Size Distributions (PSD). This methodology has allowed us to prepare stable nanoparticles with well-defined and controllable particle size distributions at room temperature. The particles were cooled to ambient temperature and the size measured by DLS. The particles now stabilized by the PNIPAM from the MacroCTA gave hydrodynamic diameters at ambient temperature nearly identical to those also measured at 70 °C. Figure 1 shows that the hydrodynamic diameter measured at ambient temperature (i.e., below the LCST of PNIPAM) by DLS increased linearly with the ratio of styrene to MacroCTA (on a weight basis). The polydispersity index of the particle size distributions for all these experiments was low, suggesting that all the particle size distributions were narrow. This was supported by micrographs obtained from transmission electron microscopy (TEM, see Supporting Information).

Table 1. Data for the Polymerization of Monomers in the Presence of PNIPAM$_{18}$−SC(=S)SC$_4$H$_9$ (0.02 (g) in P(DMA$_{49}$-*b*-NIPAM$_{106}$) (0.1 g) Nanoreactors Initiated with APS (0.85 mg) in Water (5 g) at 70 °C

expt	monomer	time (min)	x	M_n	PDI	D_h (nm) (PDI)
1	STY (0.16 g)	90	0.82	26 530	1.09	38 (0.292)
				24 340^a	1.08^a	
2	STY (0.43 g)	120	0.82	55 880	1.14	72 (0.056)
				56 370^a	1.11^a	
3	STY (0.77 g)	150	0.84	95 550	1.17	114 (0.022)
				96 305^a	1.08^a	
4	STY (1.08 g)	180	0.68	93 140	1.26	140 (0.039)
				108 140^a	1.07^a	
5	STY (1.57 g)	180	0.48	72 690	1.31	164 (0.070)
				90 130^a	1.12^a	
6^b	STY (0.39 g)	120	0.86	162 620	1.28	66 (0.050)
				175 750^a	1.19^a	
7	PFSTY (0.77 g)	60	0.93	138 160	1.29	76 (0.090)
				167 480^a	1.17^a	
8^c	BA (0.78 g)	55	0.90	79 940	1.33	88 (0.299)
				93 930^a	1.25^a	

[a] Values after removal of P(DMA$_{49}$-*b*-NIPAM$_{106}$) by precipitation. [b] Mass of PNIPAM$_{18}$−SC(=S)SC$_4$H$_9$ and APS used was 5 and 0.2 mg, respectively. [c] Polymerization conducted at 50 °C.

Mechanistic Aspects of Swelling. To better understand the mechanism of styrene swelling into the nanoreactor, which as described above has little or no solubility in styrene monomer, we carried out a nonstirred polymerization directly in a DLS Malvern Zetasizer 3000HS. The experimental conditions were identical to experiment 3 in Table 1. All the reactants, except APS, were placed in a cuvette, degassed at ambient temperature, heated to 70 °C with stirring, and then placed without stirring into the DLS Malvern Zetasizer 3000HS. The hydrodynamic diameter of 30.9 nm was found to be very similar to that without styrene (see Table S1 in Supporting Information).

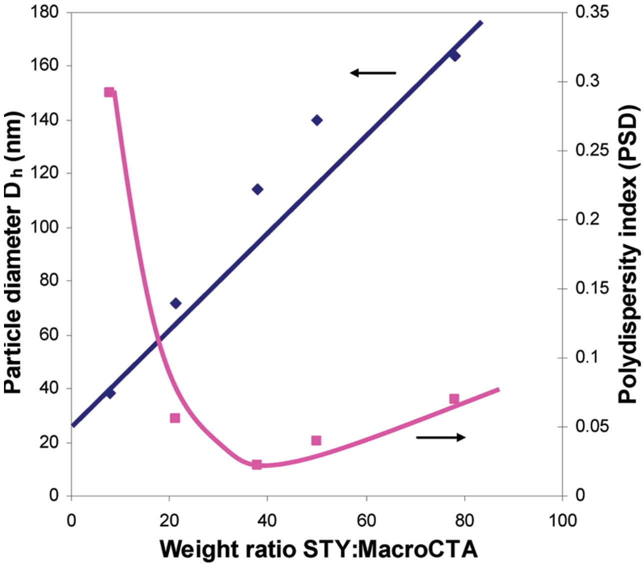
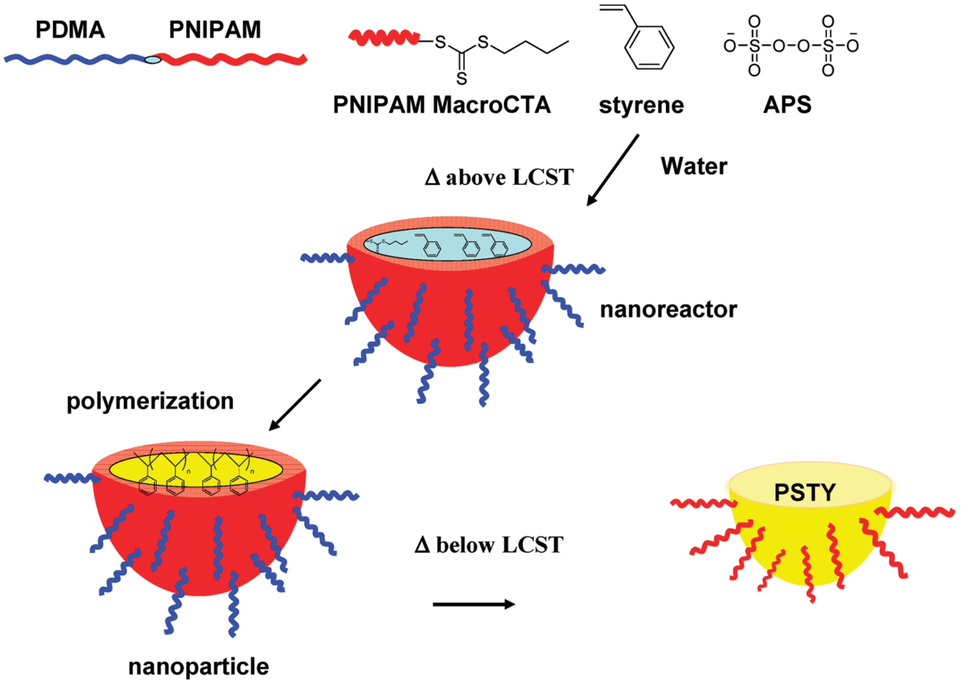


Figure 1. Dependence of particle diameter and particle size distribution as a function of the weight ratio styrene:PNIPAM$_{18}$−SC(=S)SC$_4$H$_9$. Note: a PDI value below 0.1 represents a very narrow particle size distribution.

Scheme 1. Designer Thermoresponsive Nanoreactors P(DMA$_{49}$-*b*-NIPAM$_{106}$) To Encapsulate in a One-Pot Process Monomer That Can Be Used To Produce Nanoparticles with Desired Molecular Weight and Particle Size by RAFT



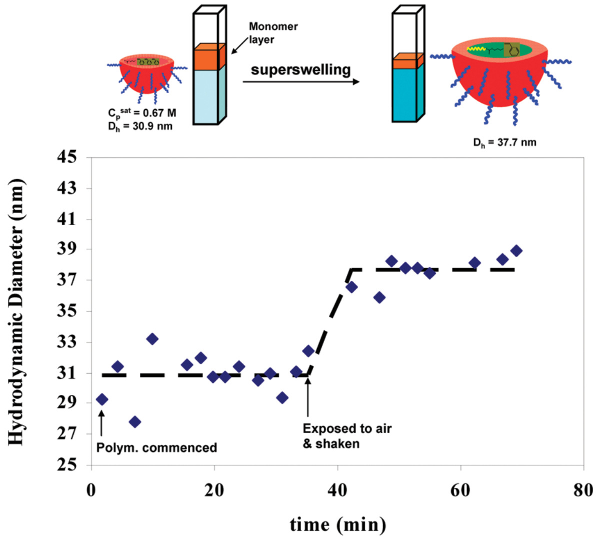


Figure 2. Experiment 4 carried out in a Malvern Zetasizer 3000HS without stirring. The hydrodynamic diameter was determined as a function of time. A schematic showing the effect of superswelling.

A large and clear phase-separated monomer layer was observed at the top of the cuvette. To determine the amount of styrene swelling the PNIPAM block, APS initiator was added to the reaction mixture and left to polymerize for about 35 min. At this time the monomer layer was still present, and the hydrodynamic diameter did not change (Figure 2), suggesting that little or no monomer was transported from the monomer layer to the particles. The reaction time of 35 min should be long enough to polymerize all the styrene that has swollen the nanoreactor. The conversion at this time was found by gravimetric analysis to be only 2.5%, allowing the saturation monomer concentration (C_p^{sat}) of 0.67 mol L^{-1} inside the nanoreactor to be determined. Conventional creaming experiments are not accurate in determining such a low C_p^{sat} value.

To inhibit any further polymerization, the reaction mixture was exposed to air and then shaken. It was found that the hydrodynamic diameter increased to 37.7 nm, representing a 2-fold increase in the volume of the nanoreactor. This also represents a 6-fold volume increase over the theoretical swelling volume should the C_p^{sat} of 5.6 mol L^{-1} be used, which is the saturation concentration determined in high molecular weight polystyrene latex particles. The results here strongly suggest that superswelling[8] occurs at low conversions due to the small number of styrene units added to the MacroCTA. The true extent of superswelling cannot be determined by the above experiment since we start to shake the contents after 2.5% conversion, which represents ~20 styrene units added to the MacroCTA. At this chain length the chemical potential inside the nanoreactors will be much higher than for smaller chain lengths, and thus the volume increase (or swelling capacity) in the nanoreactors will not be as great as that at lower PSTY chain lengths. We postulate that in the early stages of polymerization with stirring the PSTY oligomers much less than 20 styrene monomer units will ensure encapsulation of all monomer in the nanoreactors. This is also supported from the size of the nanoparticles at full conversion (<114 nm) and the observation that no separate monomer phase was observed for experiments 1–3. When a monomer layer was observed at high ratios of styrene to diblock, the polymerizations did not reach high conversions (e.g., experiments 4 and 5), suggesting that the nanoreactors no longer had the capacity to hold the excess styrene, which phase separated to the top of the polymerization mixture.

Conclusion. In conclusion, we have demonstrated a nanoreactor methodology to give unprecedented control over both the molecular weight and particle size distributions. Our thermoresponsive diblock copolymer nanoreactor can easily be separated from the newly synthesized polymer. We believe that this nanoreactor approach will not only have potential to solve difficulties in dispersion polymerizations for other CRP techniques but can be used to carry out organic reactions in water to increase yields and lower undesired side reactions. In addition, because of excellent heat transfer through the water phase, such nanoreactors would be ideal for carrying out organic reactions that are potentially explosive or highly exothermic.

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Supporting Information Available: Experimental details, SEC data and chromatograms, and NMR. This material is available free of charge via the Internet at http://pubs.acs.org.

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