Seeded Emulsion Polymerization of Block Copolymer Core−Shell Nanoparticles with Controlled Particle Size and Molecular Weight Distribution Using Xanthate-Based RAFT Polymerization

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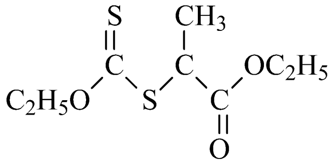
ABSTRACT: The work described here has shown for the first time that well-defined core−shell nanostructures with controlled particle size and molecular weight distributions (in which the molecular weight distributions of both blocks are independently controlled using the same RAFT controlling agent) can be prepared in an aqueous environment. These types of nanoparticles can lead the way to more novel and interesting structures in applications for drug delivery, biosensors, and other devices. A poly(methyl methacrylate) (PMMA) seed was used to control the particle size distribution, in which styrene (STY) in the presence of the RAFT agent was polymerized under batch conditions to give polymer particles with an number-average molecular weight (M_n) of 7000 and polydispersity (PDI) of 2. Butyl acrylate (BA) was then polymerized under semibatch conditions into these particles to give an overall M_n of 20 000 and PDI close to 1.3 for the block copolymer, in which greater than 90% block purity was observed. The calculated PDI of the second block (PBA) was close to 1.4, which is lower than the theoretically determined value under batch conditions (PDI = 1.6). The results show that by slow monomer addition feed into the reactor the PDI can be reduced and that by using the advantage of “random coupling” between the two blocks the PDI of the final block copolymer is lower than either of the individual blocks.

Introduction

Controlled synthesis of molecular structures of nanoscale dimensions has opened an exciting realm of applications ranging from molecular computers[1−3] to miniature medical devices capable of entering individual cells to carry out a variety of functions.[4] Among various approaches to “smart” molecular architectures capable of self-assembly the use of block copolymers has proven quite useful.[5−7] Incorporating blocks of different nature into one polymer chain provides a driving force for subsequent phase separation and supramolecular structure formation.[8−10] Functionality can be incorporated into one of the blocks such that the shell can be cross-linked[6,10] for use as possible drug delivery or the surface can be modified with an oligomeric peptides sequence for specific cell binding.[4] The applications of such nanostructures even include nanoreactors for the preparation of gold particles.[11] Block copolymers of this type and even more complex architectures (e.g., hyperbranched, star) can be synthesized in bulk monomer and solution with the recently developed “living” free-radical polymerization techniques. These techniques include nitroxide-mediated polymerization (NMP),[12] atom transfer radical polymerization (ATRP),[13,14] and reversible addition−fragmentation chain transfer (RAFT) polymerization.[15,16]

Although the methodology of forming nanoparticles through self-assembly of block copolymers in water has proven useful, we used another approach by synthesizing the blocks directly in water using one of the living radical techniques. Once the first block is made to form a particle, the second monomer is added and further polymerized to form a block copolymer with a core−shell structure. The major advantages of aqueous media over bulk or solution are that the polymerization is carried out in an environmentally friendly medium and in principle can be used directly in biomedical applications, it is a cheap process, it can be used for a broad range of monomers and a wide range of experimental conditions, the heat transfer is highly efficient, high conversions with low monomer residuals can be reached, there are no organic volatile compounds that are detrimental if these nanoparticles are used for human applications, and one can obtain high polymer solids (up to 60 wt %) in a low-viscosity environment (which means the polymer is easy to process). Out of all of the living techniques, RAFT is ideally suited for emulsion systems since the activating species (−S−C(Z)=S, Scheme 1) is attached to the polymer chain end and will not partition into the water phase. Thus, the number of radical per particle is not affected, resulting in a controlled “living” process.

Scheme 1. *O*-Ethylxanthyl Ethyl Propionate (I)



(I)

Adopting the RAFT technique to emulsion polymerization has been a long standing focus of our group. Besides providing an ability to run “living” radical polymerizations in water, a nonhazardous and nontoxic reaction media, emulsion systems provide radical com-

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partmentalization within growing particles. This reduces bimolecular termination, which is important for maintaining high rates of polymerization and high block purity. Although RAFT polymerization is relatively straightforward in solution and bulk for the “highly” active RAFT agents such as dithioesters, RAFT-derived polymers have proven difficult to control via classical ab initio (i.e., where surfactant micelles are used as mircoreactors for polymerization) and seeded (where prepolymer particles are used as the microreactors) emulsion polymerizations.[17] In most cases, there was little control of the molecular weight distribution (MWD), and concomitantly severe colloid destabilization was found. These problems may stem from the high reactivity of the RAFT agents used, producing oligomeric material in the water phase that could not transport to the growing particles.[17−19] These problems were overcome by miniemulsions to make homopolymers [20,21] and block copolymers[20] with narrow MWDs and high block purity. Miniemulsions avoid the need for transport of monomer or RAFT agent to the particles since the locus of polymerizations is within the stable monomer droplets. However, miniemulsions by their very nature produce a broad particle size distributions (PSDs) ranging from 30 nm to over 1 μm. The PSD must be narrow in order for particles to be useful in most applications involving nanotechnology.

We then shifted our attention to xanthates as RAFT agents as they were less studied due to their low $C_{\mathrm{tr,RAFT}}$ value, resulting in a broad MWD.[22−24] The main advantage of using these RAFT agents is that, to our knowledge, they are currently the only “living” agents that can be successfully used in a classical ab initio emulsion (waterborne) polymerization for the synthesis of novel nanostructures. Homopolymers[25] made by this method gave a controlled and predictable (albeit broad, PDI is 2 for styrene and 1.6 for *n*-butyl acrylate polymerizations) MWDs and broad particle size distributions (PSDs—in the range from 20 to 120 nm, which is still much narrower than the miniemulsion experiments), and were subsequently used in a second stage polymerization to prepare block copolymers with block purity as high as 90%.[26] The high block purity was achieved by feeding the monomer into the reaction vessel slowly over a 5 h period. Cryo-TEM demonstrated that these nanostructures have a core−shell morphology with the core consisting of polystyrene (PSTY) and the shell consisting of poly(butyl acrylate) (PBA).[25] To explain the fact that a core−shell morphology together with high block purity can be prepared, we postulated that the xanthate RAFT agents used in these studies were surface active, such that the −S−C(OEt)═S moiety on the dormant polymer chain end resides at the surface of the particles.[25,27] A close look at the structure of the xanthate shows that one of its resonance structures leads to an ionized (water-soluble) structure.[28] Using this phenomenon, we were also able to prepare reactive core−shell nanostructures consisting of copolymers[25] (Figure 1), where a reactive functional group (aldehyde) is incorporated into the shell for subsequent cross-linking with diamines. The resulting cross-linked films gave novel mechanical tensile properties which could be tuned depending upon the location of the functional groups in the shell.[29] Other factors such as surface tension of the polymers also aid in core−shell formation.

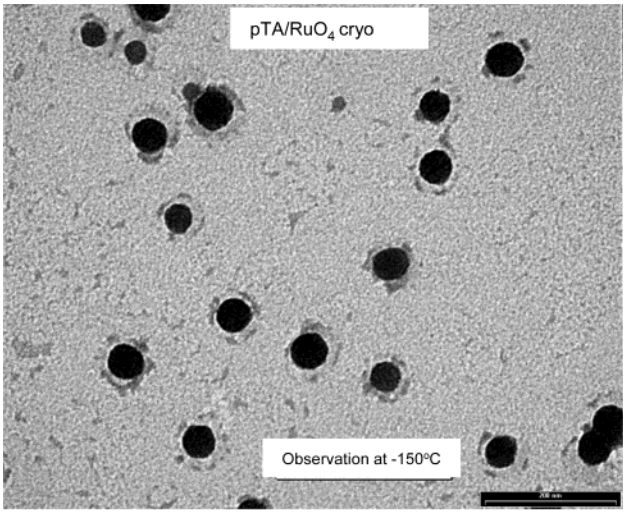


Figure 1. Cryo-TEM of the core−shell morphology stained with RuO_4 and PTA (core size: 50 nm) of a block copolymer of PSTY-*block*-PBA/P(acetoacetoxyethyl methacrylate) prepared using xanthates. The dark core consists of PSTY, and the light shell consists of PBA/P(acetoacetoxyethyl methacrylate).[25]

The goal of this work is to use the surface-active properties of the low reactive xanthate RAFT agents (*O*-ethylxanthyl ethyl propionate, Scheme 1, where $C_{\mathrm{tr,RAFT}}$ to styrene is 0.69[22] and to BA is 1.7[30]) to prepare high block purity poly(styrene-*block*-*n*-butyl acrylate) core−shell nanoparticles with a controlled MWD (in which the MWDs of both blocks can be independently controlled with the use of the same controlling agent) and PSD. Previous work with xanthates to synthesize block copolymers relied on the ab initio emulsion polymerization of the first monomer to determine the resulting PSD. In this work, polymer particles (seed) of predetermined number and size distribution will be used to control the number of particles and breath of the particle size distribution for polymerizations carried out under monomer feed conditions. The number of seed particles was chosen as to avoid any secondary particle formation. The use of slow monomer addition feed rates reduces the monomer concentration in the particles, and for low $C_{\mathrm{tr,RAFT}}$ agents should theoretically result in narrow MWDs of homopolymers and block copolymers compared to batch polymerizations as will be shown by our computer simulations. This methodology to prepare block copolymer in a dispersed (aqueous) media of well-defined core−shell nanostructures would obviate the need for self-aggregation and allow by simply changing the size of the seed and controlling the amounts of two monomers, block copolymer nanostructures with a desired particle size to be prepared. The amount of initial seed material in the final block copolymer nanostructure should be small, on the order of a few percent, to minimize the effect of the seed material on the final properties.

Experimental Section

Materials. Styrene (STY, 99%), *n*-butyl acrylate (BA, 99%), and methyl methacrylate (MMA, 99%) were purchased from Aldrich and purified of inhibitor by passing through an inhibitor-removal column (Aldrich). 2,2-Azobis(isobutyronitrile) (AIBN, 99%) was purchased from Aldrich and recrystallized twice from ethanol. Toluene (99%), sodium dodecyl sulfate (SDS, 98%), sodium persulfate (SPS, >98%), and $NaHCO_3$ (>99.5%) were purchased from Aldrich and used as received.

Synthesis of *O*-Ethylxanthyl Ethyl Propionate (I). *O*-Ethylxanthyl ethyl propionate (Scheme 1, **I**) was synthesized according to the literature procedure[23] by adding potassium

O-ethyldithiocarbonate (101.4 g, 0.633 mol, Merck, 99%) to a mixture of ethyl 2-bromopropionate (102 g, 0.563 mol, Merck, 99%) dissolved in ethanol (1 L) at 0 °C under a nitrogen atmosphere. The mixture was stirred for 4 h at 0 °C in the absence of light. Water (1 L) was added, and the product was extracted by a 1:2 mixture of diethyl ether and pentane. The solvent was removed, and the remaining ethyl 2-bromopropionate distilled off under vacuum. **I** was obtained at >99% purity according to ^{1}H NMR.

Solution Polymerizations. *Styrene Homopolymerization (PSTY-Xanthate).* AIBN (0.016 g, 4.31 × 10^{-3} M) was added to a degassed reaction vessel containing STY (10.02 g, 4.26 M), **I** (2.116 g, 0.46 M), and 11.56 mL of toluene. Oxygen was removed from the mixture by bubbling through with nitrogen. The reaction mixture was placed in an oil bath at 70 °C and left to polymerize for 21 h. During this time samples were taken, and conversion (by gravimetry) and the MWD (by SEC) were determined. The conversion after 21 h reached 46%, and the polymer consisted of a number-average molecular weight (M_n) of 2000 and a polydispersity (PDI) of 1.44 according to GPC.

Poly(styrene−*butyl acrylate) Block Copolymerization.* AIBN (0.043 g, 1.06 × 10^{-2} M) was added to a degassed reaction vessel containing BA (6.412 g, 2.50 M), PSTY-xanthate (0.508 g, 1.03 × 10^{-2} M), and 17.43 mL of toluene. Oxygen was removed from the mixture by bubbling through with nitrogen. The reaction mixture was placed in an oil bath at 60 °C and left to polymerize for 23.5 h. The conversion after 23.5 h reached 88%, and the polymer consisted of a number-average molecular weight (M_n) of 14 600 and a polydispersity (PDI) of 2.15 according to GPC.

Synthesis of Block Copolymer Latex Particles with Controlled PSD. *Poly(methyl methcarylate) (PMMA) Seed.* MMA (90.8 g, 0.91 mol), SDS (3.0 g, 1.04 × 10^{-2} mol), $NaHCO_3$ (0.3 g), and water were mixed into a 250 mL jacketed glass reactor equipped with a reflux condenser. The mixture was stirred overnight with a magnetic stirrer under an argon atmosphere at room temperature. The reactor was then heated to 80 °C and the initiator, SPS (0.3 g, 1.26 × 10^{-3} mol), added. The polymerization was stopped after 4 h and extensively dialyzed to remove residual surfactant, initiator, monomer, and other low molecular weight compounds. Dialysis was carried out by pouring the latex into a semipermeable cellulose membrane tubing (Spectra/Por 4) and dialyzed against deionized water. The dialyzate was changed regularly. The resulting polymer particles had an average particle diameter of 57 nm, and with a solids content of 7.31 wt %. This seed is used to control the PSD.

Polystyrene-Xanthate (PSTY-Xanthate) Latex Particles. PMMA seed (27.0 g, 7.31 w% solids), STY (31.52 g, 0.302 mol), SDS (0.33 g, 1.26 × 10^{-3} mol), $NaHCO_3$ (0.058 g), and water (143.53 g) were mixed into a 250 mL jacketed glass reactor equipped with a reflux condenser. The mixture was stirred overnight with a magnetic stirrer under an argon atmosphere at room temperature. The reactor was then heated to 60 °C and the initiator, SPS (0.063 g, 2.6 × 10^{-4} mol), added. The polymerization was stopped after 22.5 h and dialyzed to remove residual surfactant, initiator, monomer, and other low molecular weight compounds. Conversion reached 96% after 22.5 h, and the polymer had an M_n of 7000 and PDI of 2.0 according to GPC. The resulting polymer particles had an average particle diameter of 157 nm, which is close to the calculated value of 149 nm. The solids content was 13.1 wt %. These particles were then used to make latex particles consisting of block copolymers.

Poly(styrene−*butyl acrylate) Block Copolymer Latex Particles.* PSTY-xanthate latex (33.2 g, 13.1 wt % solids), BA (2 g, 1.9 × 10^{-2} mol), SDS (0.162 g, 5.6 × 10^{-4} mol), $NaHCO_3$ (0.024 g), and water (68.4 g) were mixed into a 250 mL jacketed glass reactor equipped with a reflux condenser. The mixture was stirred for 18 h with a magnetic stirrer under an argon atmosphere at room temperature. The reactor was then heated to 60 °C and the initiator, SPS (0.0236 g, 9.9 × 10^{-5} mol), added. After 20 min, BA was then slowly fed into the reactor using a Metrohm Dosimat syringe pump and was stopped until a mass ratio of 4 to 1 of BA to PSTY was reached. In three separate experiments the feed rates were 0.02, 0.04, and 0.08 mL min^{-1}. The resulting polymer particles had an average particle diameter of 284 nm, which is close to the calculated value of 265 nm.

Table 1. Reaction Conditions and Results of a Block Copolymerization of Styrene and *n*-Butyl Acrylate with RAFT in Solution, in Which Styrene Is Polymerized First in the Presence of I

recipe	conditions	result
First Step: Styrene Homopolymerization		
0.016 g of AIBN	70 °C	46% conversion
10.020 g of styrene	21 h	$M_n = 2010$
2.116 g of **I** (Scheme 4.2)	↓	PDI = 1.44
10.002 g of toluene	precipitation in methanol	polystyrene (PS1)
Second Step: *n*-Butyl Acrylate Block Copolymerization		
0.043 g of AIBN	60 °C	88% conversion
6.412 g of *n*-butyl acrylate	23.5 h	$M_n = 14640$
0.508 g of PS1		PDI = 2.15
15.080 g of toluene		

GPC. The dried polymer was dissolved in tetrahydrofuran (THF, Biosolve) to a concentration of 1 mg/mL. The solution was filtered over a 0.2 mm PTFE syringe filter. Analysis was carried out using a Waters model 510 pump, a Waters model WISP 712 autoinjector, a model 410 refractive index detector, and a model 486 UV detector (at 254 nm). The columns used were a PLgel guard (5 μm particles) 50 × 7.5 mm precolumn, followed by two PLgel mixed-C (5 μm particles) 300 × 7.5 mm columns in series (which were maintained at 40 °C for analysis). The columns used separate polymers in the molecular weight range between 500 and 2 million with high resolution. THF was used as an eluent (flow rate 1.0 mL/min), and calibration was done using polystyrene standards (Polymer Laboratories; $M = 580-7.1 \times 10^6$). Data acquisition was performed using waters Millenium 32 (v3.05) software. The molecular weights of the block copolymers were in some cases corrected with Mark−Houwink parameters given in the literature:[31] $a = 0.716$ and $K = 11.4 \times 10^{-5}$ dL g^{-1} for polystyrene and $a = 0.700$ and $K = 12.2 \times 10^{-5}$ dL g^{-1} for poly(*n*-butyl acrylate).

HPLC. HPLC analyses were performed using an Alliance Waters 2690 separation module, equipped with a PL-EMD 960 ELD detector and a 2487 Waters dual UV detector, operating at 254 and 280 nm. The block copolymers were analyzed using a Zorbax Si column, thermostated at 35 °C using a gradient from pure *n*-heptane (Biosolve) to THF (Biosolve) in 40 min. Typically 10 μL of dried sample dissolved in THF at 5 mg/g THF was injected.

Results and Discussion

Determination of $C_{tr,RAFT}$ for BA to PSTY-Xanthate from Solution Polymerizations. Low molecular weight polystyrene was synthesized in the presence of a low transfer constant RAFT agent, i.e., *O*-ethylxanthyl ethyl propionate (**I**, Scheme 1), at 70 °C (see Table 1 for experimental details). The amount of dead chains was minimized by keeping the initiator concentration very low (1 mol % of the amount of RAFT agent). The polymer formed was precipitated in methanol, filtered, and further washed with methanol. The latter was done in order to remove residual monomer and RAFT agent, thereby excluding their influence on the second block polymerization. Since the polymerization did not proceed to high conversion, a considerable amount of unreacted RAFT agent was still present because of the low chain transfer constant of the RAFT agent with styrene.[22] The number-average molecular weight (M_n) of the polymer formed was 2011, and the polydispersity (PDI) was 1.44. This low PDI (compared to a PDI of about 2 expected for transfer-dominated STY

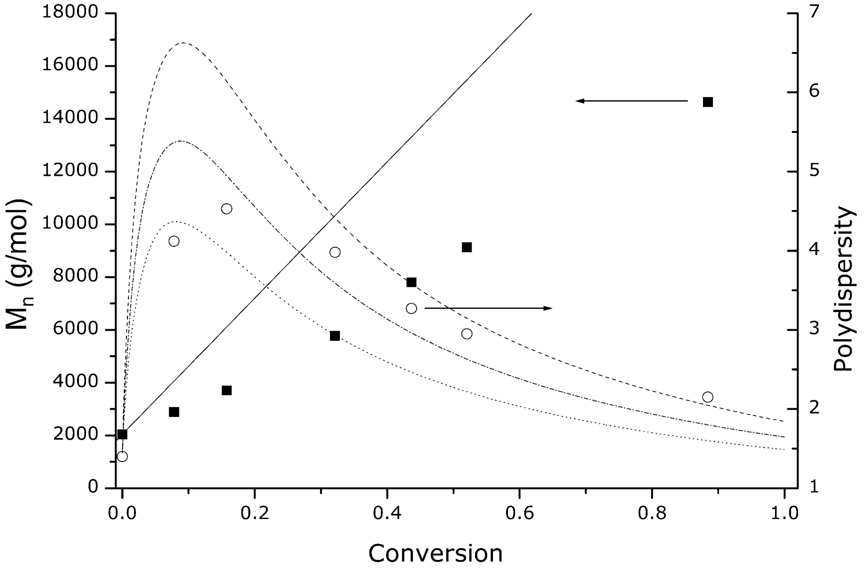


Figure 2. Number-average molecular weight (closed squares), M_n, and polydispersity (open circles) of the solution block copolymerization of *n*-butyl acrylate (2.5 M), polystyrene-xanthate (1.03×10^{-2} M; $M_n = 2010$, PDI = 1.44), initiated with AIBN (1.06×10^{-2} M) in 17.43 mL of toluene at 60 °C. The solid line (—) represents the theoretical evolution predicted by eq 3. PREDICI simulations (Appendix 1) of the polydispersity profiles for different transfer constants are shown. $C_{tr,RAFT} = 1.0$ (- - -); $C_{tr,RAFT} = 1.31$ (- • -); $C_{tr,RAFT} = 1.73$ (• • •). Parameters used in the simulations are as follows: $k_p = 2.29 \times 10^4$ dm^3 mol^{-1} s^{-1},[31] $k_d = 9.8 \times 10^{-6}$ s^{-1},[33] initiator efficiency f is estimated to be 0.6,[34] and $k_t = 4 \times 10^8$ dm^3 mol^{-1} s^{-1}, since this value fitted the conversion time data.

homopolymerizations) is probably the result of the precipitation, in which the lowest molecular weight polymer is selectively removed. The PSTY obtained was then used in a solution polymerization with BA. The molecular weight and PDI vs conversion of the second step as obtained by GPC analysis using a refractive index (RI) detector are shown in Figure 2.

In the ideal case, where no homopolymer of BA is formed by assuming negligible termination, the theoretical M_n is given by

$$M_n = {M_n}^A + x\frac{m_B}{m_A}{M_n}^A \qquad (1)$$

in which ${M_n}^A$ is the number-average molecular weight of the first block (A), x is the fractional conversion of the second monomer (B), m_A is the total mass of the polymer A, and m_B is the total initial mass of monomer B. The validity of this equation for low reactive RAFT agents is because polymeric RAFT agents are used, in which the number of polymer chains is already fixed at the start of the reaction, and monomer units are simply added to each chain with time. This equation becomes useful in an emulsion system where consumption of monomer and other substances are described in terms of mass instead of concentration. The data in Figure 2 are based on PSTY standards and, therefore, quantitatively might contain an error for block copolymers.

Figure 2 shows that M_n increased linearly from 2011 to approximately 14 000 with conversion. The molecular weights are much lower than theoretically expected from eq 1. Correction of the molecular weights with the Mark−Houwink parameters of PBA only gives slightly higher molecular weights. The differences in molecular weight between theory and experiment might arise from side reactions from termination of radicals and chain transfer reactions to monomer and solvent, which are not taken into account in eq 1. However, even when termination and chain transfer reactions are taken into account using a computer simulations (PREDICI[32] simulation package, Scheme 2), the M_n vs conversion profile is identical to eq 1, suggesting that these side reactions are not significant under our reaction conditions. In other words, simulations validate eq 1 for our system, and therefore eq 1 will be used to describe changes in M_n with conversion from subsequent emulsion polymerizations. The difference between the experimental and theoretical lines remains unclear, but it is speculated that this difference could be due to the error in determining low molecular weights by GPC that are close to the exclusion limit.

The PDI initially increased to a value of about 4.5 and then decreased toward 2.15 (at 88% conversion). This is not surprising, since both the newly formed block copolymer and the starting block combine to give the PDI. Figure 2 shows the computer simulations (see Scheme 2 for the kinetic scheme) of the PDI at different transfer constants for BA to polystyrene-xanthate, i.e., 1.0, 1.3, and 1.73 (using the experimental concentrations and $k_p = 2.29 \times 10^4$ dm^3 mol^{-1} s^{-1},[31] $k_d = 9.8 \times 10^{-6}$ s^{-1} [33], the initiator efficiency f is estimated to be 0.6 [34] and $k_t = 4 \times 10^8$ dm^3 mol^{-1} s^{-1}, since this value fitted the conversion time data). The transfer constant for this RAFT agent lies between 1 and 1.73 based on simulations. The linear increase in M_n with conversion and the similar PDI profile to the simulated data supports the formation of block copolymers. Additional evidence for the formation of block copolymer is obtained from the GPC traces. Using a UV detector on the GPC, the shift of the PSTY can be monitored. If the molecular weight of the starting PSTY dormant species grows by the addition of BA, then the molecular weight distribution as observed from UV detection should also increase. This is due to the fact that PBA does not have an extinction coefficient at 254 nm, and thus is considered “invisible”. Figure 3a indeed shows a shift of the UV GPC trace to higher molecular, indicating that the starting PSTY-xanthate has grown in molecular weight. This is strong evidence for the formation of a block copolymer.

Scheme 2. PREDICI Simulation of a Block Copolymerization

$\mathrm{I} + 2\mathrm{M} \rightarrow 2\,\mathrm{PBR}_1$ $k_{i,\mathrm{eff}}$

$\mathrm{PSR}_i + \mathrm{M} \rightarrow \mathrm{PBLR}_{i+1}$ k_p
$\mathrm{PBR}_i + \mathrm{M} \rightarrow \mathrm{PBR}_{i+1}$ k_p
$\mathrm{PBLR}_i + \mathrm{M} \rightarrow \mathrm{PBLR}_{i+1}$ k_p

$\mathrm{PBR}_i + \mathrm{PSS}_j \rightarrow \mathrm{PBS}_i + \mathrm{PSR}_j$ k_{tr}
$\mathrm{PBLR}_i + \mathrm{PBS}_j \rightarrow \mathrm{PBLS}_i + \mathrm{PBR}_j$ k_{tr}
$\mathrm{PSR}_i + \mathrm{PBS}_j \rightarrow \mathrm{PSS}_i + \mathrm{PBR}_j$ k_{tr}
$\mathrm{PBR}_i + \mathrm{PBS}_j \rightarrow \mathrm{PBS}_i + \mathrm{PBR}_j$ k_{tr}
$\mathrm{PBLR}_i + \mathrm{PBLS}_j \rightarrow \mathrm{PBLS}_i + \mathrm{PBLR}_j$ k_{tr}
$\mathrm{PSR}_i + \mathrm{PBLS}_j \rightarrow \mathrm{PSS}_i + \mathrm{PBLR}_j$ k_{tr}
$\mathrm{PBR}_i + \mathrm{PBLS}_j \rightarrow \mathrm{PBS}_i + \mathrm{PBLR}_j$ k_{tr}
$\mathrm{PSR}_i + \mathrm{PSS}_j \rightarrow \mathrm{PSS}_i + \mathrm{PSR}_j$ k_{tr}
$\mathrm{PBLR}_i + \mathrm{PSS}_j \rightarrow \mathrm{PBLS}_i + \mathrm{PSR}_j$ k_{tr}

$\mathrm{PSR}_i + \mathrm{PBR}_j \rightarrow \mathrm{PBLD}_{i+j}$ k_t
$\mathrm{PSR}_i + \mathrm{PBLR}_j \rightarrow \mathrm{PSBSD}_{i+j}$ k_t
$\mathrm{PBR}_i + \mathrm{PBLR}_j \rightarrow \mathrm{PBLD}_{i+j}$ k_t
$\mathrm{PSR}_i + \mathrm{PSR}_j \rightarrow \mathrm{PSD}_{i+j}$ k_t
$\mathrm{PBLR}_i + \mathrm{PBLR}_j \rightarrow \mathrm{PSBSD}_{i+j}$ k_t
$\mathrm{PBR}_i + \mathrm{PBR}_j \rightarrow \mathrm{PBD}_{i+j}$ k_t

I = initiator, M = monomer (B)

PBR = polymeric B radical
PSR = polymeric starting block (S) radical
PBLR = polymeric block copolymer
PSS = dormant S block
PBS = dormant B polymer
PBLS = dormant block copolymer
PSD = dead S polymer
PBD = dead B polymer
PBLD = dead block copolymer
PSBSD = dead SBS triblock copolymer

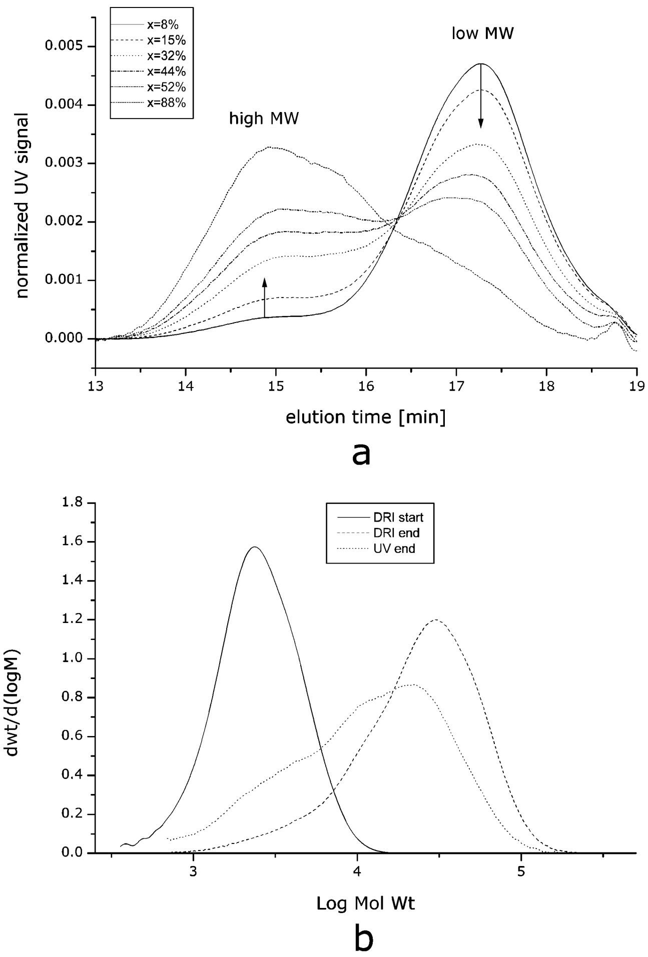


Figure 3. (a) Normalized GPC UV (254 nm) traces of the solution block copolymer of *n*-butyl acrylate (2.5 M) polymerized, polystyrene-xanthate (1.03×10^{-2} M), initiated with AIBN (1.06×10^{-2} M) in 17.43 mL of toluene at 60 °C as a function of conversion, and (b) the starting and final MWDs (at 88% conversion) are compared by the RI detector and the UV detector at 254 nm.

Since these traces have been normalized, it also shows that the amount of initially present dormant PSTY decreases. The fact that at 88% conversion most of the GPC signal shifted toward the high molecular weight side indicates that most of the PSTY starting material has been converted to block copolymer, and this type of block copolymer synthesis is quite effective. In Figure 3b the starting and final MWDs are shown. Besides the clear shift toward higher molecular weight of the MWD obtained from the UV detector, this figure also shows that the final MWDs from UV and RI do not completely overlap as a result of unreacted PSTY-xanthate and "dead" PSTY. Figure 3b also indicates that the amount of high molecular weight BA homopolymer is small, suggesting that the resulting polymer contains a high percentage of block copolymer.

The UV traces above can be used to estimate the $C_{\mathrm{tr,RAFT}}$ for BA radicals to dormant PSTY chains (i.e., with a xanthate as the end group, denoted here as "PSTY-xanthate"). The UV traces can be normalized since the amount of PSTY in the reactor is constant, and thus the area below the UV signal over a designated elution time span indicates the amount of material in the corresponding molecular weight span. The method has previously been described by Goto et al.[35,36] It was derived that

$$C_{\mathrm{tr,RAFT}} = \frac{\dfrac{\mathrm{d}}{\mathrm{d}t} \ln \dfrac{S_0}{S}}{\dfrac{\mathrm{d}}{\mathrm{d}t} \ln \dfrac{M_0}{M}} \tag{2}$$

in which S_0 is the amount of transfer agents at $t = 0$, S is the amount of transfer agent, M_0 the amount of monomer at $t = 0$, and M the amount of monomer. If the natural logarithm of S_0/S and the natural logarithm of M_0/M are plotted vs time, then the transfer constant is given by the ratio of the slopes of these plots. Here the amount of transfer agent, in this case PSTY-xanthate, is estimated from the height of the low molecular weight side of the UV GPC trace. The amount of monomer can be obtained from the conversion measurements (see Figure 4).

The transfer constant derived from the data in Figure 4 for BA to PSTY-xanthate is 1.04. This value is an underestimation and in fact will be higher. The amount of PSTY-xanthate is estimated from the low molecular weight side of the GPC UV trace, which will also contain some block copolymer as a result of the broadness of the high block copolymer peak. Therefore, the amount

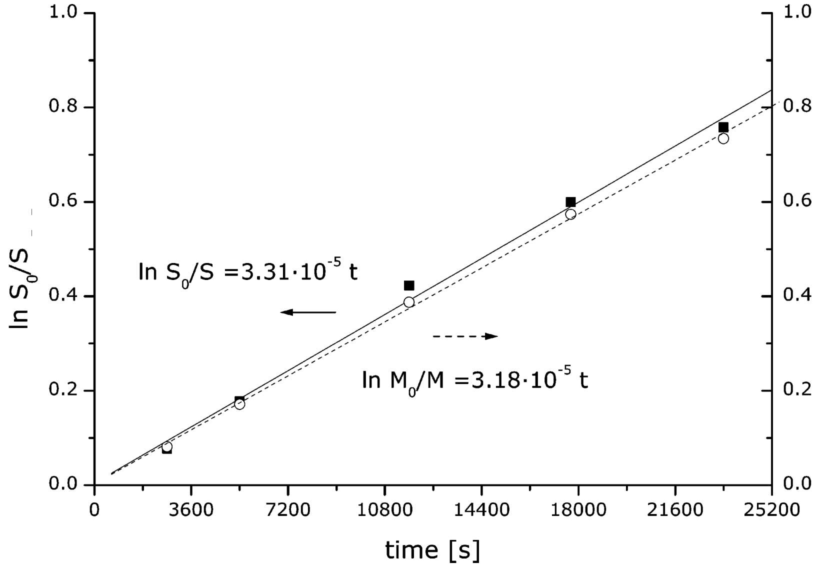


Figure 4. Determination of the chain transfer constant of *n*-butyl acrylate toward polystyrene-xanthate using the method of Goto. The transfer constant, $C_{tr,RAFT}$, is obtained from conversion measurements and the GPC traces in Figure 2 using eq 2. The reaction mixture consisted of *n*-butyl acrylate (2.5 M), polystyrene-xanthate (1.03×10^{-2} M), initiated with AIBN (1.06×10^{-2} M) in 17.43 mL of toluene at 60 °C. This results in a $C_{tr,RAFT}$ of 1.04.

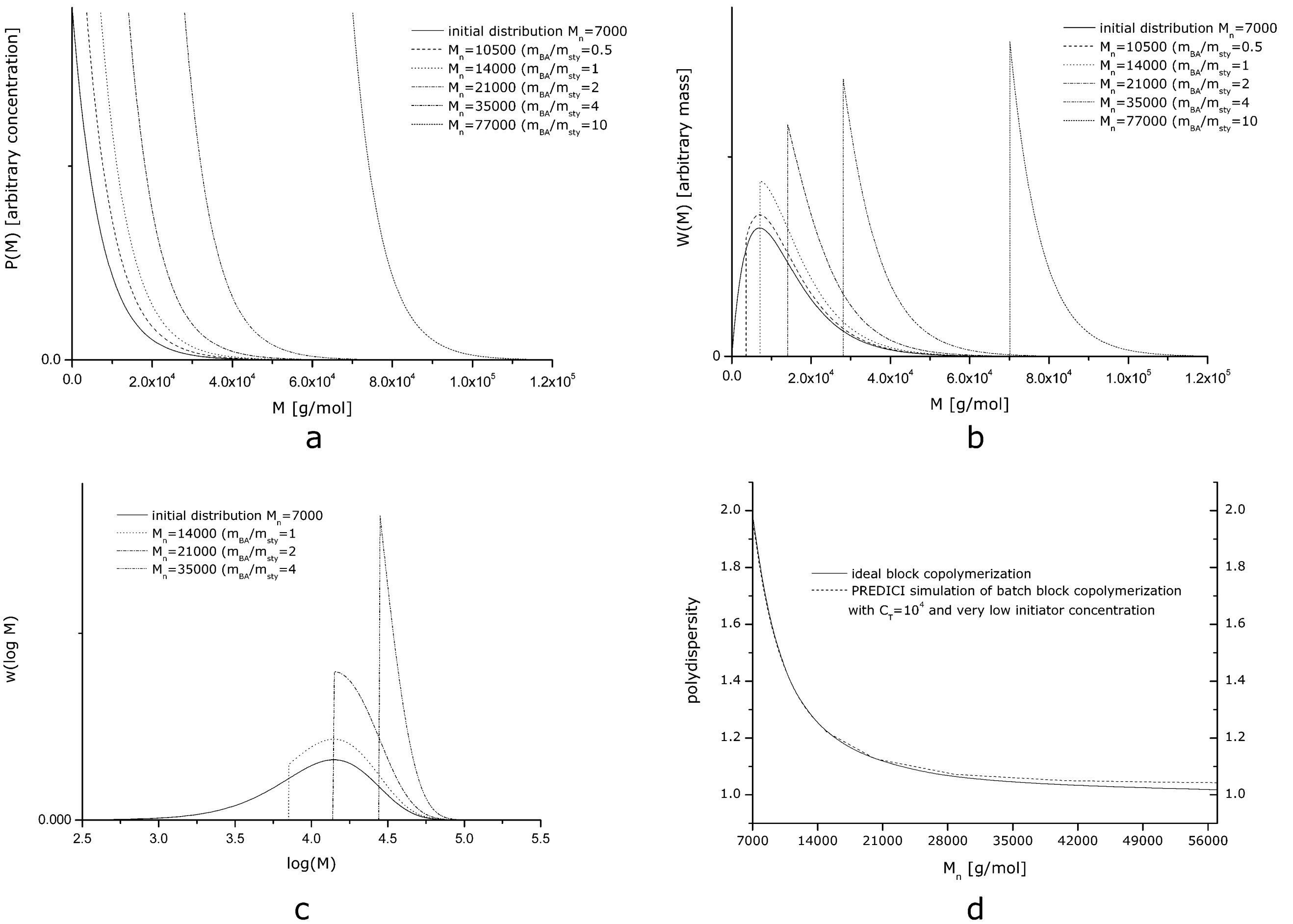


Figure 5. (a) Simulations of the chain length distribution *P*(*M*), (b) the weight distribution *W*(*M*), (c) the GPC distribution, and (d) the polydispersity vs chain extension for an ideal block copolymerization (i.e., all initially present polymer chains add the same number of monomer units in the second stage) in which the starting block has an M_n of 7000 and a polydispersity of 2 (Flory−Schultz distribution, eq 3). In (d), the polydispersity vs chain extension of an ideal block copolymerization is compared to a PREDICI simulation of a batch block copolymerization (Scheme 2) using $C_{tr,RAFT} = 10^4$ and a very low initiator concentration.

of PSTY-xanthate will be overestimated, resulting in a underestimated transfer constant. We[30] found that the transfer constant of BA with **I** was close to1.7. The true transfer constant for BA to PSTY-xanthate therefore lies between 1 and 1.73 (see simulation in Figure 2). The synthesis of polystyrene-*block*-poly(*n*-butyl acrylate)

Table 2. Recipes and Particle Sizes of the Semibatch Emulsion Block Copolymerizations of Styrene and *n*-Butyl Acrylate[a]

recipe	conditions	result
	First Step: PMMA Seed Latex Preparation	
water 942 g SDS 3.0 g $NaHCO_3$ 0.3 g SPS 0.3 g MMA 90.8	80 °C 4 h extensive dialysis afterward	particle size $d_v = 57$ nm solid contents after dialysis: 7.31 wt % PMMA seed
	Second Step: Polystyrene-Xanthate Latex Preparation	
water 143.53 g SDS 0.33 g $NaHCO_3$ 0.058 g PMMA seed 27.0 g SPS 0.063 g STY 31.52 g	60 °C 22.5 h	96% conversion $M_n = 7000$, PDI = 2.0 $d_v = 157$ nm (calculated 149 nm) solid contents after dialysis: 13.1 wt % polystyrene-xanthate seed
	Third Step: Block Copolymer Latex Preparation	
water 68.4 g SDS 0.162 g $NaHCO_3$ 0.024 g polystyrene-xanthate seed 33.2 g SPS 0.0236 g BA 2.0 g	stir for 18 h at room (without initiator), raise temperature to 60 °C, add initiator, wait 20 min and feed residual monomer (15.7 mL = 14.1 g) at 0.02, 0.04 and 0.08 mL/min, respectively.	0.02 mL/min, $d_v = 284$ nm 0.04 mL/min, $d_v = 284$ nm 0.08 mL/min, $d_v = 281$ nm (d_v(calculated) = 265 nm) polystyrene-*block*-poly(*n*-butyl acrylate) latex

[a] The following polymer densities were used:[33] 1.05 g/mL (PSTY), 1.15 g/mL (PMMA), and 1.03 g/mL (PBA).

using a xanthate is therefore effective, and the transfer constant of BA to PSTY-xanthate is of the same order of magnitude as to **I**.

Synthesis of Polystyrene-*block*-poly(*n*-butyl acrylate) in Emulsion under Semibatch Conditions with a Controlled MWD and PSD. Low-polydispersity block copolymers using RAFT agent **I** cannot be obtained under batch conditions because of its low $C_{tr,RAFT}$ to both BA[30] and styrene,[22] being approximately 1.7 and 0.7, respectively. It is generally found that the PDI is broad and close to 1.4 for BA and 2 for STY. However, Müller et al. have shown that it is theoretically possible to produce low-polydispersity material with low transfer constant species if the monomer concentration is kept low.[37] Krstina et al. have experimentally confirmed this for a radical system in solution by the production of low-polydispersity blocks using macromonomers under semibatch conditions.[38] If the monomer concentration is low enough, then ideally each growing radical will add no more than one monomer unit before the radical activity is transferred to another chain. This means that all chains grow simultaneously, resulting in a low PDI. In the case of an ideal block copolymerization of BA on PSTY-xanthate, all initially present PSTY-xanthate chains will add an equal number of monomer units to form the new block copolymer. In terms of a number distribution (concentration vs chain length), the starting MWD will be translated over the chain length axis toward a higher molar mass. Importantly, this means that an ideal living polymerization can theoretically be imitated by performing the block copolymerization under semibatch conditions.

Ideal Block Copolymerization. An ideal block copolymerization (all initially present chains of the first block will add the same number of monomer units) will result in a translation of the chain length distribution of the initial block over the chain length axis. The chain length distribution of such a polymer can mathematically be approximated by the Flory−Schultz distribution[39] (eq 3).

$$P(M_i) = \exp\left(-\frac{M_i}{M_n}\right) \qquad (3)$$

Figure 5 shows the chain length distributions $P(M)$, weight distributions $W(M)$, log weight distribution $w(\log M)$, and polydispersity vs M_n of an ideal block copolymerization obtained through computer simulations for varying degrees of chain extension. The initially present block has an M_n of 7000 and a polydispersity of 2 and is obtained from eq 3.

Figure 5 shows that an ideal block copolymerization can lead to narrow molecular weight material, even though the starting material has a PDI of 2. For instance, a chain extension from $M_n = 7000$ to $M_n = 14\,000$ leads to a decrease in the PDI from 2 to 1.25 (Figure 5d), whereas a chain extension to M_n of 25 000 leads to a PDI of 1.08.

Ideal block copolymerization conditions can also be approached if the transfer constant in the RAFT process is very high. In Figure 5d, a PREDICI simulation of the polydispersity vs chain extension is shown for a batch block copolymerization with a transfer constant of 10^4 and a low initiator concentration. It appears that a system having a transfer constant of this order of magnitude, which is not unrealistic for high reactivity RAFT agents,[36] behaves like an ideal block copolymerization, but these highly reactive RAFT agents have been shown to lead to colloid destabilization in emulsion polymerizations. Interestingly, the use of low reactive xanthate systems also gave the same PDI profile (Figure 5d, solid line) as that for the high reactive agents, suggesting that in principle the use of low active RAFT agents will produce the same MWD as the highly active ones. The theory above suggests that xanthates, which can be successfully used in classical ab initio emulsion systems, can also be used to produce polymer of a narrow molecular weight distribution.

There are a number of other complicating factors that may affect the PDI. These include (a) side reactions, e.g. bimolecular termination, transfer to monomer, or polymer; (b) under feed conditions where the feed rate is slow enough to produce low-PDI polymer, the polymerization rate will be infinitely slow such that the reaction cannot be performed in a practical way; and (c) not all chains have an equal probability to grow at the same rate if a broad PSD seed is used. The latter consideration is due to the fact that per unit of volume all particle sizes contain the same number of polymer chains. The smaller particles have a larger surface area per volume unit and, therefore, have a higher probability to be entered by an aqueous phase radical.

Experimental vs Theory. As we have shown in earlier work,[25] the easiest approach to synthesize block copolymers in emulsion is first to polymerize styrene via an ab initio emulsion conditions in the presence of the xanthate and, once this step is complete, to further polymerize BA to make the block copolymer. However, control of the PSD was very much dependent upon the amount of xanthate used in the ab initio step; the greater the amount of xanthate, the lower the average particle size. The key to control the PSD in this work is to use a seed with the desired particle size, number, and distribution. The seed will be used as the sites for polymerization, and therefore as polymerization proceeds, the average partyicle size will increase but the breath and number of particles will remain constant. The next step is the seeded polymerization of styrene in the presence of xanthate, **I**, followed by polymerization of BA to make block copolymer latex particles of the same particle number as the initial seed.

The formation of block copolymers, when polystyrene is the starting block, can be observed due to the shift of the UV GPC trace toward higher molecular weights. Therefore, in the following emulsion experiments styrene was polymerized first in the presence of a xanthate and a poly(methyl methacrylate) (PMMA) seed (57 nm average volume diameter with a low polydispersity of 1.09). The seed was used so that the resulting PSTY latex formed would have a controlled particle number and particle distribution. PMMA was chosen as the seed since PMMA does not absorb at 254 nm and is thus considered “UV-invisible”. Hence, by using a UV detector, the MWD of the newly formed PSTY can be readily obtained.[17] The content of PMMA by the end of the polymerization is only a few percent (4−6%) of the PSTY and upon subsequent block formation will decrease to less than 1% and is for our purpose considered negligible. The polydispersity of PSTY was close to 2 with an M_n of 7000 as predicted (Table 2).

As our computer simulations have shown, it is theoretically possible to produce low-PDI block copolymer using RAFT agents with a low transfer constant, even though the first block has a relatively high PDI of about 2. To test whether low PDI block copolymer can be obtained using xanthates, a series of experiments were performed in which BA was fed to a PSTY-xanthate latex with a predetermined PSD (recipes are given in Table 2). The final BA to polystyrene mass ratio was 4 to 1 in all experiments, and the final solid contents of the latex was 20%. The polymerization was performed at 60 °C, the surfactant concentration was kept below the critical micelle concentration, and the initiator (sodium persulfate) concentration was 1 mM, such that the amount of dead chains as a result of bimolecular termination was kept low. The consumption of monomer in the semibatch polymerizations was found not to be strictly controlled by the feed; i.e., the measured overall conversion is not equal to the monomer feed profiles.

Figure 6 shows the M_n and PDI vs conversion. Figure 6a shows that the experimental M_n increases with conversion from 7000 to between 15 000 and 20 000 depending upon the feed rate, but if the experimental molecular weights are compared with the theoretically expected molecular weights, it is obvious that the experimental values are much lower. Figure 6b shows that the PDI decreases with increasing conversion from 2 to between 1.3 and 1.62, again depending upon the feed rate.

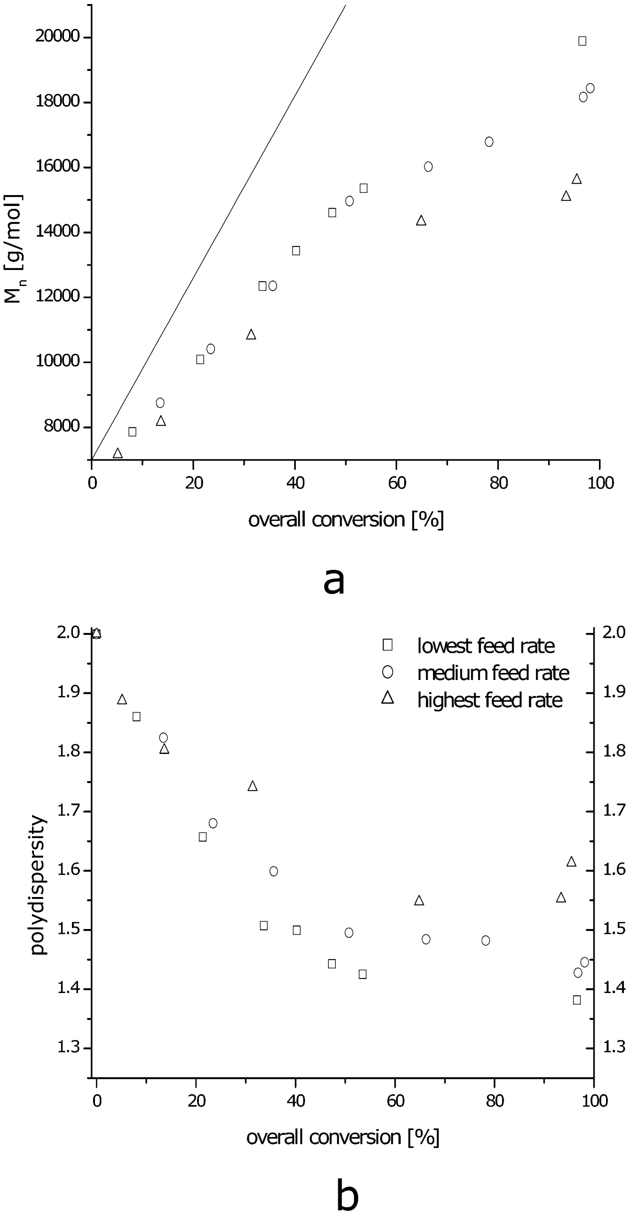


Figure 6. (a) M_n vs overall conversion and (b) polydispersity vs overall conversion for semibatch emulsion block copolymerizations of PSTY-xanthate latex (33.2 g, 13.1 w% solids), SDS (0.162 g, 5.6×10^{-4} mol), $NaHCO_3$ (0.024 g), water (68.4 g), and SPS (0.0236 g, 9.9×10^{-5} mol) at 60 °C at BA feed rates of 0.02, 0.04, and 0.08 mL min^{-1}. The solid line represents the theoretically expected M_n (eq 1). The resulting polymer particles had an average particle diameter of 284 nm, which is close to the calculated value of 265 nm.

When the monomer feed rate was the highest, M_n decreased more rapidly away from theory than the other slower feed rates. The cause may be due to transfer to monomer. Figure 6b shows that the PDI decreased with conversion for all the feed rates used. At the end of the polymerization relatively low PDI material was produced, in which the PDI was 1.3 at the lowest feed rate and 1.6 at the highest feed rate. At lower monomer feed rates (where PDI is 1.3) the system is closer to the ideal block copolymerization conditions with a block purity

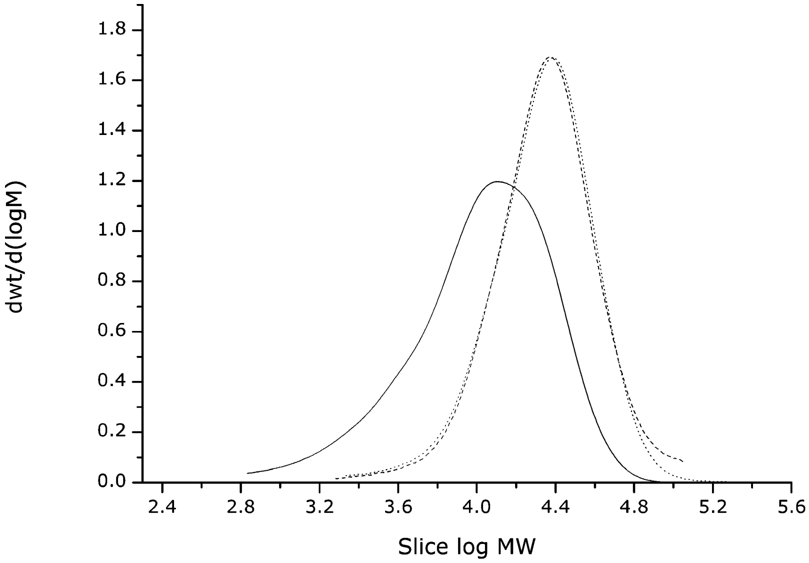
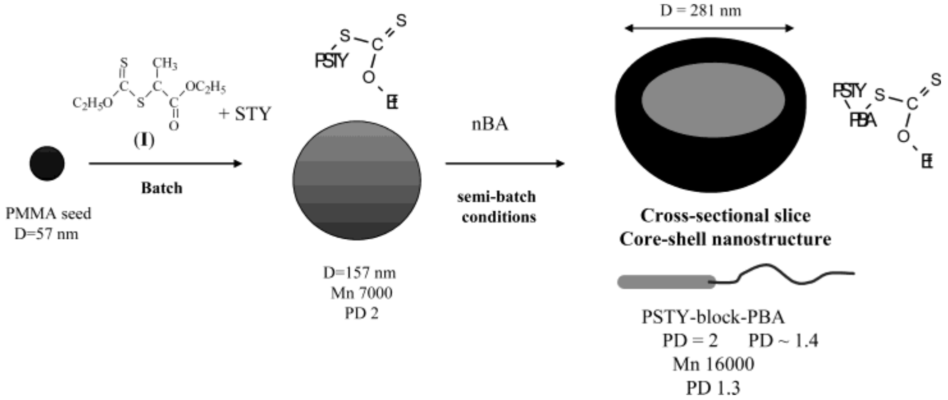


Figure 7. Log weight molecular weight distribution of the starting polystyrene-xanthate ($M_n = 2010$, PDI = 1.44, solid line) and the final block copolymer of a semibatch emulsion polymerization of PSTY-xanthate latex (33.2 g, 13.1 w% solids), SDS (0.162 g, 5.6×10^{-4} mol), $NaHCO_3$ (0.024 g), water (68.4 g), SPS (0.0236 g, 9.9×10^{-5} mol), and BA (which was fed in over 790 min at a feed rate of 0.02 mL min^{-1}) at 60 °C, obtained by both RI detection (dashed line) and UV detection (dotted line).

Scheme 3. Core–Shell (Block Copolymer) Nanostructures Synthesized with Narrow Particle Size Distribution and Molecular Weight Distribution Using Low Active Xanthate (RAFT) Agents



as high as 90% (Figure 7), and it was calculated from the "random coupling" methodology[40] that the PDI of the PBA block was close to 1.4. The block purity was confirmed by HPLC by monitoring the loss of STY-xanthate with monomer conversion.

Figure 7 shows that the UV MWD has shifted completely toward a higher molecular weight, which indicates that block copolymer has formed. From the matching overlays of the UV and RI MWDs it can be concluded that the block copolymer formed is of a high purity. The average particle diameter d_v (Table 2) for all the various feed rates are close to 284 nm, which is close to the theoretically calculated d_v of 265 nm. The difference is probably due to the error in the size analysis. We have shown that core–shell nanoparticles with a controlled PSD and where the second block has a much narrower MWD can be made using low reactive RAFT agents (see Scheme 3). The formation of a core–shell morphology has been previously described with evidence from transmission electron microscopy (see Figure 1). Even without the use of a surface active RAFT agent, a core–shell morphology will result when BA is polymerized onto a PSTY particle. Therefore, it is believed that since this system is very similar to those previously described the same core–shell morphologies will result.

Conclusion

The highly desired preparation of core–shell morphology with controlled molecular weight (in which the MWDs of both blocks were independently controlled using the same RAFT agent) and with a controlled particle number and size distribution has been prepared using surface-active RAFT agents (xanthates) of low reactivity under semibatch conditions. A PMMA seed was used to control the number and distribution of the particles, in which STY in the presence of the RAFT agent was polymerized under batch conditions to give particles containing PSTY with an M_n of 7000 and PDI of 2. Butyl acrylate was then polymerized under semibatch conditions into these particles to give an overall M_n of 20 000 and PDI close to 1.3. This results in a PDI of the second block to be calculated to be close to 1.4, which is lower than the theoretical value of 1.6 for a batch polymerization. The results show that a slow monomer feed during the polymerization decreased the PBA polydispersity and that through the advantage of "random coupling" of the blocks the overall polydispersity of the final block copolymer is lower than either block. The other advantage of this methodology is that high-purity blocks are formed (>90%). Although the starting PSTY block had a PDI of 2 and the second PBA block a PDI less than 1.4, it is envisaged that polymerizing the first block (i.e., styrene and RAFT agent in a PMMA seed) under feed conditions can form even narrower blocks.

A block copolymer latex with a desired particle size can be prepared by simply changing the size and number of the seed latex particles (e.g., PMMA) and controlling the amounts of two monomers. However, a few considerations should be taken into account. First, conditions should be chosen such that no secondary particle formation takes place, which in practice means that the particle number of the PMMA seed has to be high enough. Second, the amount of initial PMMA seed material in the final block copolymer latex should be small, on the order of a few percent, so as to have no effect on the final latex properties.

The work described here has shown for the first time that well-defined nanostructures of controlled particle size and molecular weight distributions can be prepared in an aqueous environment, leading the way to more novel and interesting structures in applications for drug delivery, biosensors, and other devices.

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