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Controlled Dispersion Polymerization of Methyl Methacrylate in Supercritical Carbon Dioxide via RAFT

Andrew M. Gregory, Kristofer J. Thurecht,* and Steven M. Howdle*

School of Chemistry, University of Nottingham, University Park, Nottingham NG7 2RD, UK

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ABSTRACT: We present a comprehensive investigation of the controlled dispersion polymerization of methyl methacrylate (MMA) in supercritical carbon dioxide ($scCO_2$) utilizing reversible addition fragmentation chain transfer (RAFT) polymerization to produce living microparticles. These microparticles show controlled molecular weight evolution, low polydispersities (PDI $<$ 1.20), and well-defined spherical morphology (diameter ca. 1.40 μm). Four chain transfer agents are examined with modifications to both the stabilizing group (Z group) and leaving group (R group). We investigated their impact on molecular weight evolution and the morphology of the resulting polymer products in $scCO_2$. The rate retardation effect intrinsic to many RAFT reactions which provides good kinetic control was shown to be much larger than that observed in analogous solution polymerizations performed in conventional organic media. This is believed to be due to the combination of the RAFT mechanism and the dispersion mechanism in $scCO_2$.

Introduction

Reversible addition fragmentation chain transfer (RAFT) polymerization has proven to be one of the most effective forms of controlled polymerization developed over the past 10 years.[1−3] The process allows construction of polymers with targeted molecular weights possessing low polydispersities. Preserved end groups can be reactivated, permitting the incorporation of additional monomers to produce a diverse array of block copolymers[4] in a range of architectures[5] including star,[6] branched,[7] and graft[8] topologies. The process is complementary to traditional free radical polymerization, and along with the usual components of radical initiator, monomer, and solvent the RAFT process relies on the addition of a chain transfer agent (RAFT agent). One of the biggest advantages of the RAFT process is that it is a robust system that is applicable to a variety of monomers (methacrylates, acrylates and styrenics), incorporating a range of functionalities including acidic moieties.[9]

In recent years the impact on the environment of many chemical processes incorporating organic solvents has come under scrutiny.[10] Novel “green” processes have been developed as environmentally friendly analogues to conventional systems.[11] One such medium that has gained significant attention is supercritical carbon dioxide ($scCO_2$).[12,13] Supercritical fluids are highly compressed gases which combine the properties of gases and liquids: the solvating power of a liquid but the mass transport properties of a gas. The physical properties are tunable; their density can be controlled via manipulation of both temperature and/or pressure. In addition, on depressurization the system reverts to its gaseous state and can be removed easily leaving a solvent free product. The majority of research has focused on $scCO_2$ because of its low critical parameters ($T_c = 31.1$ °C, $P_c = 73.8$ bar),[12] lack of toxicity, and nonflammability. $scCO_2$ has also been demonstrated to be an effective polymerization medium.[14] Although homogeneous polymerization is possible, it is generally restricted to a selection of monomers incorporating fluorinated and siloxane side chains leading to $scCO_2$-soluble polymers.[15] Recently, $scCO_2$-soluble polymers composed purely of hydrocarbon chains have been produced, i.e., vinyl acetate.[16] While many monomers are soluble in $scCO_2$, the resulting polymers are not. Therefore, the bulk of polymerizations conducted in $scCO_2$ have been via heterogeneous routes.[17−19]

RAFT-mediated polymerizations have been shown to work in supercritical fluids, but high conversions and low polydispersities were not observed.[20,21] Recently, we demonstrated very effective control of methyl methacrylate (MMA) in a dispersion in the presence of the RAFT agent α-cyanobenzyl dithionaphthalate (**1**) and the stabilizer poly(dimethylsiloxane monomethacrylate) (PDMS−MA).[22] The RAFT agent was able to successfully partition between the continuous $scCO_2$ and the dispersed polymer particles. The result was successful control over the molecular weight of the product whereby the theoretical molecular weight (M_{nth}) agreed closely with that obtained by gel permeation chromatography (GPC) analysis. At higher conversions the polymer product was a fine powder, free of solvent. Under scanning electron microscopy (SEM) analysis of the particles showed discrete spherical morphology with particles on the scale of 1−3 μm. Importantly, we demonstrated facile removal for the RAFT terminal group from the final polymer products without loss of spherical morphology.

Dispersion polymerization is a versatile tool to prepare monodisperse microspheres that can be applied to a range of applications including electronics, information technology, toners, coatings, support materials for biochemical analysis, and microelectronics. Defined size control and narrow size distributions combined with the ability to introduce a range of monomer functionalities in block copolymers are the key parameters for most of these applications. The combination of $scCO_2$ and RAFT has allowed the formation of living microparticles with defined molecular weights and polydispersities.[22] In this report we extend the study to a range of RAFT agents in order to start developing a library of effective chain transfer agents which are able to control polymer growth in $scCO_2$. Herein we show the alteration of both Z and R groups and gauge their effect on the molecular weight evolution and resultant polymer morphology.

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* Corresponding authors. E-mail: Steve.howdle@nottingham.ac.uk. E-mail: kristofer.thurecht@nottingham.ac.uk.

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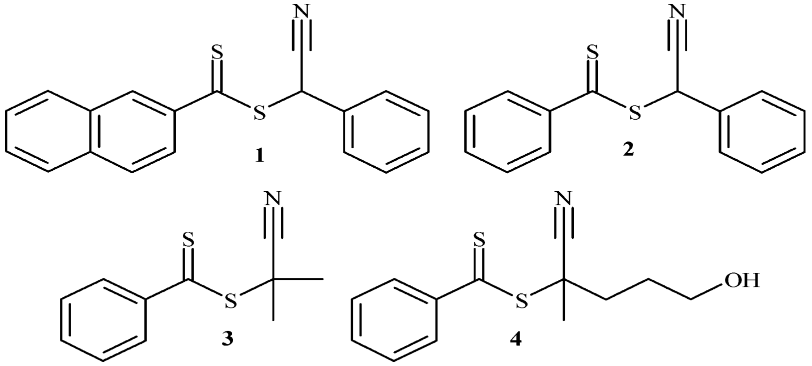

Figure 1. RAFT agents used for this work: α-cyanobenzyl dithionaphthalate (**1**); α-cyanobenzyl dithiobenzoate (**2**); 2-cyanoprop-2-yl dithiobenzoate (**3**); 4-cyano-1-hydroxypent-4-yl dithiobenzoate (**4**).

Experimental Section

Materials. Poly(dimethylsiloxane monomethyl methacrylate) (10 000 g mol^{-1}) was purchased from Itochu Chemicals Ltd. and used without further purification. Deuterated chloroform, phenylmagnesium bromide, carbon tetrachloride, benzoyl peroxide, 2-naphthylmagnesium bromide, carbon disulfide, magnesium sulfate, *N*-bromosuccinimide, phenylacetonitrile, and HPLC grade tetrahydrofuran were acquired from Sigma Aldrich and were used as received. Methyl methacrylate was purchased from Sigma Aldrich and passed through a neutral alumina column and freeze–pump–thawed prior to use. 2,2′-Azobis(isobutyronitrile) (AIBN) and 4,4′-azobis(4-cyanopentanol) (ACP) were purchased from Acros and Langfang Triple Well Chemicals Co., Ltd., respectively; they were purified through recrystallization in methanol twice. Dry CO_2 (99.99%) was purchased from BOC. EPDM o-rings were acquired from Swagelock.

RAFT agents **1**–**4** (Figure 1) were synthesized as per literature procedure (see Supporting Information for synthetic details).[23–25]

General Polymerization Procedure. The standard polymerization procedure is as follows. A 60 mL clamp-sealed autoclave[26] was leak tested prior to use with N_2 to 20.5 MPa to test the autoclave and associated pipes for leaks. Monomer was degassed via three consecutive freeze–pump–thaw cycles and stored under an argon atmosphere. The 60 mL autoclave was charged with AIBN (various weights), 5.00 wt % with respect to monomer of PDMS–MA (10 000 g mol^{-1}) surfactant, and the desired amount of RAFT agent. The autoclave was sealed and purged with CO_2 for 10 min before MMA was introduced under positive CO_2 pressure. The autoclave was sealed, pressurized to 5.52 MPa (800 psi), and heated to 65 °C with supplementary CO_2 added to reach the final reaction pressure of 27.6 MPa (4000 psi). The reaction was stirred at 300 rpm with a magnetically coupled stirrer. The reaction proceeded for various times before the heating was turned off and the reaction vessel allowed to cool; upon reaching room temperature, the CO_2 was released. Once atmospheric pressure was reached, the autoclave was opened, allowing collection of the final polymerization product. At lower conversions, where the separation of polymer and monomer was a requisite, the autoclave contents were dissolved in THF and precipitated into hexane, cooled in an ice bath, and filtered before being dried in vacuo. The subsequent products were then ready for analysis and characterization.

Chain Extension of RAFT-Terminated Poly(methyl methacrylate) with Methyl Methacrylate. Poly(methyl methacrylate) (PMMA) ($M_n = 26\,600$ g mol^{-1}) (1.00 g, 3.76×10^{-5} mol) prepared as above was placed in a 20 mL clamp-sealed autoclave with AIBN (3.00×10^{-3} g, 1.88×10^{-5} mol) and PDMS–MA (5.00 wt % with respect to monomer). The autoclave was sealed and purged with CO_2 for 10 min before adding MMA (freeze–pump–thawed three times) under a positive pressure of CO_2. The autoclave was sealed, pressurized to 5.45 MPa, and then heated to 65 °C and stirred at 300 rpm. Additional CO_2 was added as required to attain the final pressure of 27.2 MPa. Once the allotted time had been reached, the autoclave was cooled to room temperature and then depressurized. At lower conversions the autoclave contents were dissolved in THF and precipitated into hexane to remove unreacted monomer. The solution was cooled in an ice bath, and the polymer precipitate filtered before being dried in vacuo. The subsequent products were then ready for analysis and characterization.

Polymer Characterization. The molecular weight and molecular weight distribution of polymers were obtained by GPC (PL-120, Polymer Labs) with a refractive index (RI) detector. The columns (30 cm PLgel Mixed-C, two in series) were eluted by THF and calibrated with polystyrene standards. Calibration and analysis were performed at 40 °C and a flow rate of 1 mL min^{-1}. NMR spectra were recorded in $CDCl_3$ using a Bruker DPX 300 MHz spectrometer. All spectra were referenced to $CHCl_3$ at 7.26 ppm. SEM images were obtained using a Phillips 505 spectrometer. Samples were mounted on aluminum stubs using adhesive carbon tabs and sputter-coated with gold before analysis. Mean particle diameter (D_n, μm) was determined by measuring the diameter of ∼100 particles and taking a mean of these data. The coefficient of variance (C_v), an indication of particle size distribution, was then established using the equation $C_v = (\sigma/D_n) \times 100$, where σ is the standard deviation of particle diameter (μm). Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) was conducted using a Bruker Ultraflex III spectrometer. The spectra were collected on low molecular weight polymers with narrow PDI ($M_n < 10\,000$ g mol^{-1}, PDI < 1.10) in linear mode. *trans*-2-[3-(4-*tert*-Butylphenyl)-2-methyl-2-propenylidene] malonitrile (DCTB) was used as matrix and sodium trifluoroacetate as the salt.

Results and Discussion

Synthesis of RAFT Agents. This paper focuses on the use of four distinct dithioester RAFT agents (Figure 1) in order to probe the effect of altering both the Z and R groups on the molecular weight control and final polymer morphology. RAFT agents **1** and **2** were shown by Li et al.[23] to be effective in the controlled polymerization of MMA in benzene. For an effective RAFT agent, the R group must be stabilized by bulky groups or delocalization and must be reactive to the MMA monomer.[27] The α-cyanobenzyl R group fulfills this role. **1** and **2** were prepared in a two-step process. Initially, α-bromobenzene–acetonitrile was synthesized via the method of Molina et al.,[24] purified, and then added to a solution of the suitable aryl–Grignard reagent and carbon disulfide. These RAFT agents were synthesized in good yield and possessed the advantage of a relatively low odor.

RAFT agents **3** and **4** were produced via the production of dithiobenzoyl disulfide which was then subsequently reacted with AIBN and ACP to produce **3** and **4**, respectively.[25] This synthesis is effective as it is compatible with a variety of commercially available azo-initiators (the initiator group becoming the R group on the final RAFT agent).

With these RAFT agents the naphthyl and phenyl Z groups are compared along with the variety of R groups. Rizzardo et al.[28] undertook a study of RAFT agents to determine which would be effective for the polymerization of MMA and found that when the Z moiety was an electron-withdrawing group (these confer a higher electrophilic character to the thiocarboxylic sulfur), enhanced addition to the C═S double bond was observed. On the other hand, for electron-donating groups the converse was true. For the R group, it was advantageous and beneficial to use a bulky leaving group, as seen with **3** and **4**.

Dispersion Polymerization of MMA in $scCO_2$. A series of dispersion reactions were undertaken using **1**−**4** for a target degree of polymerization (D_p) of 250 with MMA in order to probe the controlled conversion and molecular weight evolution. In all cases the final products were colored materials (pink solids) because of the incorporation of the RAFT moiety onto the end of the polymer chain. Higher conversions yielded free-flowing pink powders which under SEM analysis were shown to possess a discrete spherical morphology (Figure 4). The high conversions (up to 99%) showed the successful stabilization of the polymer particles by the PDMS−MA stabilizer and that the incorporation of the RAFT agent at the beginning of the reaction in $scCO_2$ was not detrimental to the polymerization—this has been previously observed.[29,30]

Unlike other CO_2-philic stabilizers (i.e., Krytox-FSL),[31] the PDMS−MA stabilizer is partially incorporated into the polymer chain. Shaffer et al.[18] showed that the incorporation of PDMS−MA into the polymer backbone in free radical dispersion polymerization in $scCO_2$ is small (ca. 4.00% of the PDMS−MA used), and we assume a similar value here. Nonetheless, the incorporation of the surfactant appears to have no negative effect on the RAFT polymerization mechanism.

The conversion and molecular weight data for each of the RAFT agents is shown in Table 1. In conventional organic media these RAFT agents show some retardation of propagation rate and induce good kinetic control over the system, and the same is shown here in $scCO_2$. The table shows that for each of the four different RAFT agents there is a continuous growth in the molecular weight with conversion. The polydispersities obtained show control with PDI values typically less than 1.20. In general, PDI values are narrower for homogeneous living radical polymerization in solution or bulk than for heterogeneous polymerization,[32] but as can be seen for these results, PDI values of 1.15 or less are frequently encountered when using $scCO_2$ for this heterogeneous dispersion process. This is likely a result of the exceptional mass-transfer properties of $scCO_2$ and the subsequent improvement in species mobility in the plasticized polymer particles.

The combined ability to achieve both high molecular weight polymer and excellent kinetic control shows that the dispersion process and the RAFT mechanism are able to work in tandem to produce micron scale particles with controlled molecular weight. $scCO_2$ overcomes the difficulties traditionally associated with controlled polymerization in heterogeneous systems where there is usually poor mass transfer.

Table 1. Dispersion Polymerization of MMA in $scCO_2$ in the Presence of RAFT Agent (1, 2, 3, or 4)

entry[a]	RAFT agent[a]	time/h	conv/%[b]	M_n[c]	PDI[c]	M_{nth}[d]
1[f]		10	99	127 200	2.50	25 000
2	1	6	4	2 400	1.10	1 250
3	1	10	17	3 800	1.10	4 250
4	1	11	37	8 400	1.16	9 250
5	1	11.5	60	13 300	1.16	15 000
6	1	12	75	18 500	1.18	18 750
7	1	14.5	95	22 900	1.21	23 750
8	1	18	99	28 700	1.18	24 750
9	2	13	12	3 300	1.10	3 000
10	2	14	29	7 300	1.20	7 250
11	2	16	56	13 000	1.14	14 000
12	2	19	82	20 200	1.12	20 500
13	2	24	94	23 100	1.15	23 500
14	2	30	98	26 200	1.21	24 500
15	3	6	23	5 500	1.20	5 750
16	3	7	27	5 900	1.12	6 750
17[g]	3	7	32	6 500	1.16	8 000
18	3	8	42	12 600	1.17	10 500
19[g]	3	8	36	8 600	1.19	9 000
20	3	12	72	18 100	1.17	18 000
21[g]	3	12	68	17 300	1.17	17 000
22[g]	3	12	75	19 800	1.17	18 750
23	3	16	79	19 400	1.19	19 750
24[g]	3	16	80	19 800	1.16	20 000
25[g]	3	16	85	19 500	1.18	21 250
26	3	19	88	21 700	1.17	22 000
27[g]	3	19	92	22 600	1.19	23 000
28[g]	3	19	87	20 100	1.17	21 750
29	3	23	96	23 600	1.13	24 000
30[g]	3	23	91	21 900	1.17	22 750
31[g]	3	23	94	24 600	1.17	23 500
32	4	6	26	7 100	1.17	6 500
33	4	7	36	7 550	1.22	9 000
34	4	8	55	13 650	1.21	13 750
35	4	10	74	20 100	1.16	18 500
36	4	18	96	23 700	1.21	24 000
37	4	24	99	26 000	1.19	24 750

[a] Reactions performed with MMA (1.56 M), RAFT agent (6.24×10^{-3} M), and AIBN (6.24×10^{-3} M) for a theoretical molecular weight of 25 000 g mol^{-1} at 100% MMA conversion based on the RAFT agent concentration respectively, 5.00 wt % PDMS−MA (with respect to monomer) in 60 mL autoclave at 65 °C and 4000 psi, unless otherwise stated. [b] From ^1H NMR. [c] Determined by GPC calibrated with poly(styrene) standards in THF using a RI detector. [d] Theoretical molecular weight based on RAFT agent concentration (eq 1). [f] No RAFT agent introduced; theoretical molecular weight based upon AIBN concentration. [g] Results represent repeat measurements to highlight reproducibility.

A series of reactions were conducted in order to determine the kinetics and the growth of polymer molecular weight with respect to both time and, therefore, conversion (Table 1). For each reaction the reagent concentration was kept constant, with the same temperature, pressure, and shear (65 °C, 4000 psi (27.6 MPa), and 300 rpm, respectively) with a target D_p set at 250. The results (Table 1) show linear growth of molecular weight with conversion (Figure 3) and pseudo-first-order kinetics (Figure 2) denoting a constant number of propagating radicals. The good fit of the data in separate reactions demonstrates the excellent control that is achieved. The reproducibility was also examined by performing a number of duplicate reactions using **3** (Table 1, entries marked with footnote *g*) which gave similar results and indicate the robustness of the system.

All of the RAFT agents **1**−**4** retard the rate of polymerization of MMA. In addition, each of the RAFT agents displays pseudo-first-order kinetics. As expected, the dithiobenzoate derived RAFT agents (**2**−**4**) in $scCO_2$ were shown to have roughly equivalent propagation rates. Upon consumption of the RAFT agent, the rate of transfer in the polymerization is determined by the Z moiety. RAFT agents **2**−**4** have equivalent Z groups and thus similar transfer constants as reflected in Figure 2.For the $scCO_2$ dispersions, higher amounts of AIBN are being introduced into the system than is convention; normally, one would use [RAFT]:[AIBN] = 10:1, but here we use a ratio of 1:1. This was to decrease the reaction time scale to a suitable length (<48 h). Interestingly, even with higher concentrations of AIBN, the induction times are much greater (up to 10 h) than those found in RAFT polymerizations in conventional organic media. One contributing factor which affects all of the chain transfer agents is the initial decomposition of AIBN. DeSimone and co-workers showed that the decomposition of AIBN in $scCO_2$ was 1.60 times longer than in equivalent

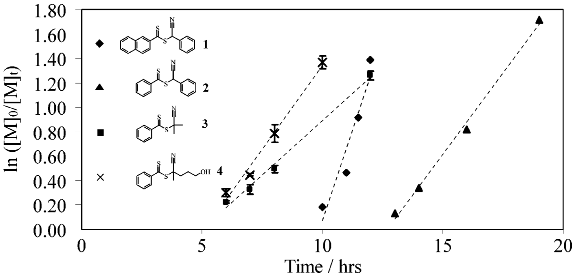

Figure 2. Pseudo-first-order kinetic plot for the various RAFT agents in $scCO_2$: ◆, **1**; ▲, **2**; ■, **3**; ×, **4**. Comparison of induction period and relative rates for each of the chain transfer agents. Lines of best fit have been added for each curve. Error bars have been added for **3** and **4** to show reproducibility (calculated from three measurements).

reactions in benzene.[33] Both RAFT agents which possess the secondary α-cyanobenzyl R group (**1** and **2**) demonstrate a longer induction period compared to the other tertiary R groups. This induction period is due to the initial fragmentation of the R group from the RAFT agent and the reinitiation ability of this group. The more stable tertiary 2-cyanoprop-2-yl (**3**) and 4-cyano-1-hydroxypent-4-yl (**4**) groups are therefore more efficient at fragmenting from the initial RAFT agent (hence consuming the RAFT agent) and reinitiating the MMA.[34] This effect has been observed in conventional solvents. In a recent publication Rizzardo et al. examined a series of trithiocarbonates incorporating either tertiary cyanoalkyl or α-cyanobenzyl moieties as the R groups. They found that the RAFT agents incorporating α-cyanobenzyl group provided good control but yielded a prolonged inhibition period which the authors attributed to slow reinitation.[35]

In addition, this extended induction period could also be attributed to the heterogeneous dispersion polymerization. Increased retardation and induction periods have been seen for RAFT polymerizations conducted in emulsions.[36,37] In the dispersion polymerization mechanism, initiator decomposition occurs followed by polymer growth and propagation. Once the polymers have reached a critical length, they precipitate out of the polymerization medium. This point signifies particle nucleation, and with the aid of a suitable stabilizer a polymer particle is formed. This particle is then swollen with monomer, and propagation continues. The key equilibrium of the RAFT mechanism is the degenerative transfer of polymer through the stabilized intermediate—for successful RAFT polymerization, this step must be unhindered, and the low viscosity and high diffusivity of $scCO_2$ enable this to occur. In addition, the initial steps of initiation and fragmentation must also remain unimpeded. Hence, the very fast process of particle nucleation[38] and stabilization must occur simultaneously with RAFT propagation. In $scCO_2$, the two mechanisms are able to work together, allowing high monomer conversion and particle formation. However, the use of the RAFT agent here seems to be delaying the nucleation step. Very recently, this was observed by Saikia et al.,[30] who performed styrene dispersion polymerizations in alcoholic media using RAFT. They found that adding the RAFT agent at the beginning of the process disrupted the stability of the system, leading to relatively poor molecular weight control and the formation of less well-defined particles. To overcome this, they delayed the addition of the RAFT agent until after the system became turbid which still allowed moderate control over the molecular weight but also produced stabilized particles. Our data show that in $scCO_2$ the situation is much simpler, and the RAFT agent can be present from the beginning of the reaction. While the particle nucleation seems to be delayed in $scCO_2$, very good molecular weight control and good particle definition is observed—this is not the case in conventional solvents.

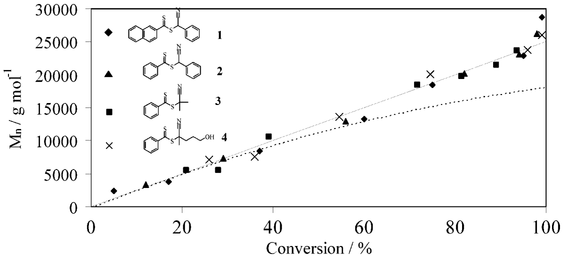

Figure 3. Molecular weight of polymer vs conversion with various RAFT agents: ◆, **1**; ▲, **2**; ■, **3**; ×, **4**. Theoretical molecular weight based on RAFT agent concentration (solid line) (eq 1); theoretical molecular weight based on RAFT agent and AIBN concentrations (dashed line) (eq 2).

Figure 3 shows linear molecular weight increase for the polymers with conversions and only a slight deviation from linearity at very high conversion. The M_n compares favorably to the M_{nth} values (solid line) predicted by eq 1[39]

$$M_{nth} \approx \frac{[M]_0 - [M]_t}{[RAFT]_0} m_M \tag{1}$$

where $[M]_0$ is the initial concentration of monomer, $[M]_t$ is the concentration at time t, and $[RAFT]_0$ is the initial concentration of chain transfer agent. This equation is often used in RAFT kinetics when the concentration of initiator is negligible so the molecular weight of the polymer can be predicted by the concentration of the RAFT agent alone.

In these reactions in $scCO_2$, high concentrations of AIBN have been used relative to the RAFT agent concentration, which contrasts with the traditional approach to RAFT polymerizations where the concentration of initiator is kept low. Even so, the reactions have been shown to be pseudo-first-order, and the molecular weights of the polymers correspond very well to the theoretical values predicted by eq 1. When the initiator concentration becomes important, eq 2 is used to determine M_{nth}.

$$M_{nth} = \frac{[M]_0 - [M]_t}{[RAFT] + df([I]_0 - [I]_t)} \times m_M + m_{RAFT} \tag{2}$$

Here, the concentration and decomposition kinetics of initiator ($k_d = 3.50 \times 10^{-6}\ s^{-1}$)[33] are taken into consideration; d is the mode of termination ($d \approx 1.67$ in MMA polymerizations),[39] $[I]_0 - [I]_t$ is the concentration of initiator consumed, and f corresponds to the initiator efficiency (0.83).[33]

The theoretical molecular weights based on this equation are plotted in Figure 3 (dashed line), incorporating both the initiator and RAFT agent concentration. This equation seems to underestimate the molecular weight that is obtained in the experiment. This could be due to a number of reasons. DeSimone et al.[33] showed that the decomposition of AIBN in $scCO_2$ compared to benzene was 1.60 times slower. However, the efficiency of the initiating radicals was found to be 1.50 times higher. This is attributed to the gas-like diffusivity of $scCO_2$ compared to that of conventional solvents. Hence, initiation kinetics are significantly different in $scCO_2$ compared to conventional solvents. Additionally, radical partitioning in heterogeneous systems will greatly influence initiation and propagation kinetics. The greater diffusivity in $scCO_2$ may also increase the degree of radical termination (i.e., initiator−initiator coupling). Thus, polymer chains that are initiated by AIBN may be fewer than expected. Therefore, the combination of a slower decomposing initiator

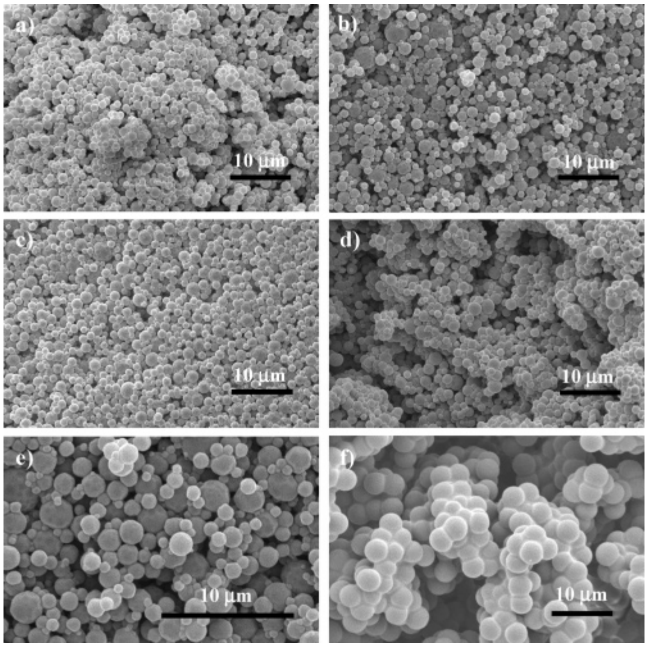

Figure 4. Analysis conducted on the polymer particles showed that they were all discrete dispersed spherical particles: (a) **1**, $D_n = 1.29$ μm, $C_v = 31.0\%$ (Table 1, entry 8); (b) **2**, $D_n = 1.43$ μm, $C_v = 43.8\%$ (Table 1, entry 14); (c) **3**, $D_n = 1.40$ μm, $C_v = 43.0\%$ (Table 1, entry 29); (d) **4**, $D_n = 1.39$, $C_v = 29.8\%$ (Table 1, entry 37); (e) higher magnification image of PMMA sample formed with **2** (note the size distribution of particles produced); (f) no RAFT agent added, $D_n = 3.91$ μm, $C_v = 6.73\%$ (Table 1, entry 12).

and heterogeneous system plays an important part in polymer chain initiation. The end groups of the polymer chains were investigated using MALDI-TOF MS and are discussed later.

Particle Morphology Analysis. At high molecular weight the fine powders were analyzed by SEM and show discrete particulate morphology (Figure 4). The addition of the RAFT agent retards the propagation of the MMA; therefore, the time taken to reach polymer precipitation and hence nucleation is delayed when compared to analogous reactions in the absence of a RAFT agent. The powders analyzed by SEM showed that the polymerization of MMA in the presence of **1**−**4** produced particles which were all ca. 1.40 μm in diameter. By contrast, particles produced in the absence of RAFT agent had diameters ca. 4.00 μm. Interestingly, for samples where a RAFT agent was not present, the system had a unimodal particle size distribution which was reflected in the lower coefficients of variance (C_v).[19] By contrast, the systems containing RAFT agent show a population of smaller particles displaying a greater distribution of sizes and a higher C_v value. This has been attributed to disruption of the particle nucleation period by the rate-determining RAFT mechanism.[30]

Controlled/Targeted Molecular Weight. One important element of RAFT is the ability to control molecular weight of the polymer. This becomes advantageous in the production of block copolymers as the ratio of different polymer blocks can strongly affect the properties of the final material. To demonstrate this control, a series of reactions were undertaken targeting different degrees of polymerization (D_p) to test whether a range of molecular weights could be produced in without detrimental effects to the RAFT process or the final polymer morphology. Table 2 shows the targeted D_p and the results of GPC analysis for a number of molecular weights. This system is suitable for targeting each of the D_p values specified, ranging from a low target of 12 500 g mol^{-1} to much higher molecular weights of 200 000 g mol^{-1}. Our data show that the RAFT process is viable in $scCO_2$ even at very low concentrations of RAFT agent. In all cases the product was a free-flowing pink powder with the exception of D_p 125 (pink solid was produced). Previous studies with **3** have shown that when this RAFT agent is used in high concentrations to target lower molecular weights, the transfer constant is reduced.[34] Hence, the ability of the agent to control the polymerization is hindered. It was suggested that this could be due to the tendency of the benzylic radicals to add RAFT agent rather than monomer, hence explaining why it is less effective when used in larger amounts. There is also the possibility that the shorter chains, due to sterics, allow for more termination to occur, although this is less likely.[40,41]

Once again, good control is observed. The M_n and M_{nth} values show good agreement, and the PDI values are low. For the D_p 2000 polymerization, the PDI value was found to be higher than previous reactions (1.40) with a lower than expected M_n than predicted on the basis of RAFT agent concentration (eq 1), but this is still significantly better than standard free radical polymerizations of MMA conducted in $scCO_2$ which typically yield PDI values greater than 2.0.[18] Previously it has been shown that at low RAFT agent concentrations there is a greater deviation from theoretical values.[42] This deviation can be attributed to the formation of some dead polymeric material, fractional consumption of the RAFT agent, or poor solubility of the final high molecular weight product in the CO_2.

SEM analysis of the products (Figure 5) shows the final dispersed products for the different molecular weights. With the exception of the low molecular weight sample ($D_p = 125$), the samples all displayed well-defined spherical morphology. The D_n values are all in the range of 2−3 μm ($D_p = 125$ (2.06 μm), $D_p = 500$ (1.93 μm), $D_p = 2000$ (2.90 μm)), with the exception of D_p 250 (Figure 5), where the particle size approaches that of the dispersion polymerization in the absence of RAFT agent ($D_n \approx 4.00$ μm) as the molecular weight increases. In addition, the distribution of the particle sizes tends toward a more unimodal distribution as D_p increases. Hence, as the concentration of RAFT agent increases, the particle size distribution increases and the average size of the particles decreases. This suggests that the effect of RAFT on the particle nucleation stage of the dispersion polymerization leads to the formation of more particles of smaller size. For the low molecular weight ($D_p = 125$, Figure 5a) the material showed

Table 2. Targeted Molecular Weight in $scCO_2$ Using Various Concentrations of 3

entry[a]	target D_p	conv/%[b]	M_n[c]	PDI[c]	M_{nth}[d]	D_n/μm[e]	C_v/%[e]
1	125	93	9 100	1.22	11 625	2.06	42.4
2	250	96	23 600	1.14	23 750	1.40	43.0
3	500	97	48 600	1.18	48 500	1.93	29.9
4	2000	99	142 900	1.40	198 000	2.90	19.0

[a] Reactions performed with MMA (1.56 M) and RAFT (1.25×10^{-2}, 6.24×10^{-3}, 3.12×10^{-3}, and 7.80×10^{-4} M for theoretical molecular weights of 12 500, 25 000, 50 000, and 200 000 g mol^{-1} at 100% MMA conversion based on the RAFT agent concentration. Reactions performed with [RAFT]:[AIBN] = 1:1, 5.00 wt % PDMS−MA (with respect to monomer) in 60 mL autoclave at 65 °C and 4000 psi for 24 h, unless otherwise stated. [b] From ^{1}H NMR. [c] Determined by GPC calibrated with poly(styrene) standards in THF using an RI detector. [d] Theoretical molecular weight based on RAFT agent concentration (eq 1). [e] Determined via SEM with ca. 100 particles.

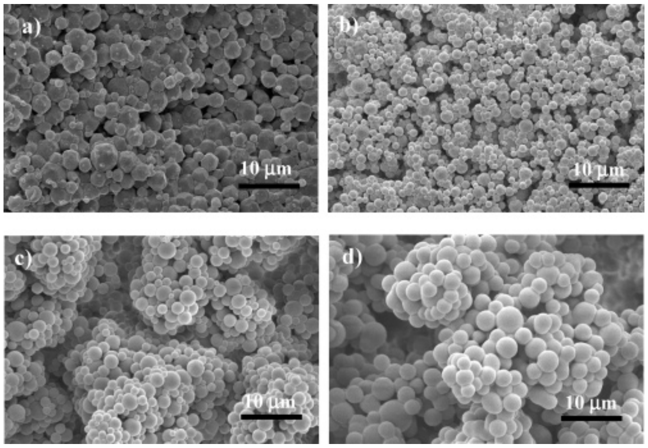

Figure 5. SEM analysis of targeted PMMA weights with D_p values of (a) 125 (D_n = 2.06 μm, C_v = 42.4%); (b) 250 (D_n = 1.40 μm, C_v = 43.0%); (c) 500 (D_n = 1.93 μm, C_v = 29.9%); (d) 2000 (D_n = 2.90, C_v = 19.0%). All samples show particle morphology although for the D_p = 125 some agglomeration is seen.

agglomeration as one might expect at lower molecular weight where the glass transition temperature is depressed. This effect was enhanced by $scCO_2$ plasticization resulting in a loss of morphological control.[43]

End-Group Analysis. Polymers produced through the RAFT process adopt a general structure where the Z group is incorporated on one end of the polymer chain and on the other is the initiating group (typically the R group). Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF) can be used to analyze these end groups. Low molecular weight samples were produced in $scCO_2$ using **3** and **4** with both AIBN and ACP as initiators in order to investigate the end groups that result from these reactions (Table S1 in Supporting Information).

In all cases, the MALDI spectra exhibited a tight molecular weight envelope (also observed by GPC), and two or more series were observed. An example spectrum is given for polymer initiated with AIBN using RAFT agent **4** (Figure 6). The first series is from polymer having both Z and R end groups—this is the expected structure for a RAFT polymerization and is marked with an asterisk (*) in the expansion of Figure 6. The second major series is an artifact of MALDI-TOF under the conditions of our experiment. Despite MALDI-TOF being a so-called “soft” ionization technique, in some cases the energy is sufficient to scission relatively labile bonds while in the spectrometer. This second series in Figure 6 (marked with circles in expansion) is due to polymer chains in which the Z group has been scissioned at the thioester moiety[44]—this effect is observed in all our MALDI-TOF spectra using these dithioesters with our chosen matrix and salt. (An ancillary spectrum for PMMA formed using AIBN as initiator and RAFT agent **3** is provided in the Supporting Information.) Finally, a minor series is also observed (marked with a cross) and has been assigned to polymer chains that have been initiated by AIBN; the presence of these chains is an inevitable consequence of RAFT polymerization. However, these chains are still living as they have the dithioester Z group as the other end group and can therefore reinitiate further chain growth. Unfortunately, the masses for termination products by disproportionation are masked by the main peaks in the spectrum. However, NMR evidence (Supporting Information) shows that these products are of low concentration—further corroborative evidence for predominantly living chains is provided later in the paper by chain extension studies. Hence, MALDI-TOF provides some evidence for the existence of polymer chains terminated by the dithioester moiety.

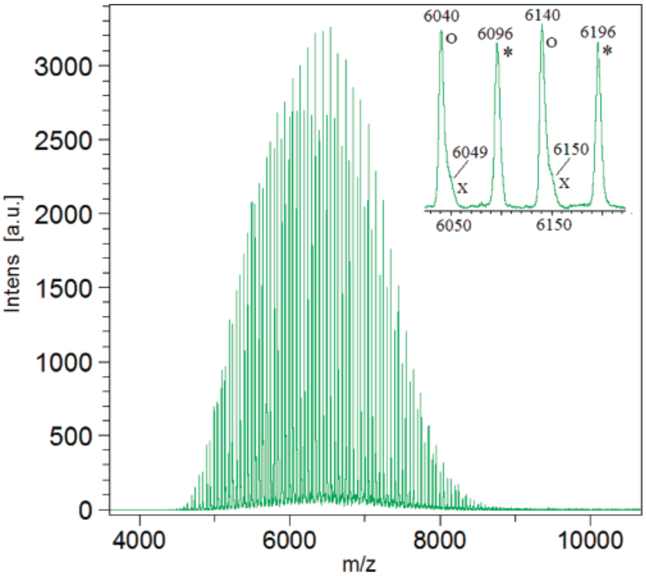

Figure 6. MALDI-TOF MS spectrum of PMMA formed by dispersion polymerization in $scCO_2$ in presence of RAFT agent **3** and AIBN as initiator. The MALDI-TOF spectrum shows three series: polymer terminated with both Z and R groups (*); polymer with the R group attached but where scission has occurred at the thioester moiety (○); polymer chains initiated by an AIBN group (×). Inset is on expansion of the main spectrum to aid in peak assignment.

Effect of Stabilizer Concentration. For the dispersion polymerization to be effective, a suitable surfactant needs to be introduced which can efficiently anchor to the nucleated particles (discrete phase) and extend into the continuous phase. The PDMS−MA fulfils these requirements with the long CO_2-philic siloxane chain and the methacrylate end group which can coordinate into the growing polymer chains.[18,45] A series of reactions were conducted with various amounts of PDMS−MA. The amount of stabilizer was examined (Table 3) to determine the minimum and optimum amount required. Without any stabilizer present the polymer begins to propagate, but once it reaches the critical length it simply precipitates out of the system, giving the low conversion (24%) (Table 3, entry 1), even after 24 h with the PDI higher than expected with a living polymerization (PDI = 1.49). Once stabilizer is added, the polymer particles are able to nucleate and are stabilized, allowing for polymer growth to high conversion. Even with 2.50 wt % (with respect to monomer) of the PDMS−MA (Table 3, entry 2), good control over the molecular weight is obtained. The M_{nth} and M_n values for 2.50, 5.00, and 10.0% stabilizer all agree very well, and PDI values are all 1.20 or less.

The SEM images for the polymers in Table 3 are shown in Figure 7, showing the discrete particles obtained in the presence of the PDMS−MA stabilizer (all free-flowing pink powders). With 2.50 wt %, a very large distribution of particle sizes was observed; a selection of large particles (ca. 4.00 μm) surrounded by many smaller ones (ca. 0.50 μm), giving a final C_v of 71.42%. The C_v value for the particles decreases with an increase in the amount of stabilizer present. During the fast particle nucleation stage of dispersion polymerization, sufficient stabilizer is required to encapsulate and stabilize the particle. An increase in the amount of stabilizer increases the probability of a stabilizer becoming coordinated to the polymer. Hence, more well-defined particles of a more uniform nature are formed when stabilizer concentration is increased.

Table 3. Dispersion Polymerization of MMA in $scCO_2$ Using Various Concentrations of PDMS−MA Using 3

entry	wt % PDMS−MA[a]	conv/%[b]	M_n[c]	PDI[c]	M_{nth}[d]	D_n/μm[e]	C_v/%[e]
1	0.00	24	7 300	1.49	6 000		
2	2.50	96	22 300	1.13	24 000	1.33	71.4
3	5.00	95	24 700	1.14	23 750	1.44	40.7
4	10.0	99	23 700	1.20	24 750	0.84	28.3

[a] Reactions performed with MMA (1.56 M), RAFT (6.24×10^{-3} M), AIBN (6.24×10^{-3} M) for theoretical molecular weight of 25 000 g mol^{-1} at 100% MMA conversion based on the RAFT agent respectively and 0.00, 2.50, 5.00, and 10.0 wt % PDMS−MA (with respect to monomer) in 60 mL autoclave at 65 °C and 4000 psi, reactions run for 24 h, unless otherwise stated. [b] From ^{1}H NMR. [c] Determined via GPC, calibrated with poly(styrene) standards in THF using a refractive index detector. [d] Theoretical molecular weight based on RAFT agent concentration (eq 1) [e] Determined via SEM with ca. 100 particles.

Table 4. Chain Extension upon PMMA RAFT Dispersion Product Produced with 1 and Extending with MMA in $scCO_2$

entry[a]	added MMA/mL	M_n[b]	PDI[b]	M_{nth}[c]	morphology[d]	D_n/μm[e]	C_v/%[e]
1[f]		26 600	1.18	25 000	powder	1.09	29.3
2	1	40 800	1.39	51 500	powder	1.15	59.5
3	2	59 700	1.48	76 400	powder	1.96	56.6
4[g]	2	30 200	1.31	76 400	solid and liquid		

[a] Reactions performed with PMMA (6.27×10^{-4} M) and AIBN (6.24×10^{-3} M) with various amounts of MMA, 5.00 wt % PDMS−MA (with respect to monomer and polymer) in 60 mL autoclave at 65 °C and 4000 psi, stirring at 300 rpm, reactions running for 24 h, unless otherwise stated. [b] Determined with GPC calibrated with poly(styrene) standards in THF using a refractive index detector. [c] Theoretical molecular weight based on RAFT agent concentration. [d] Polymer morphology upon opening autoclave. [e] Determined via SEM with ca. 100 particles. [f] Polymer precursor. [g] No stabilizer added.

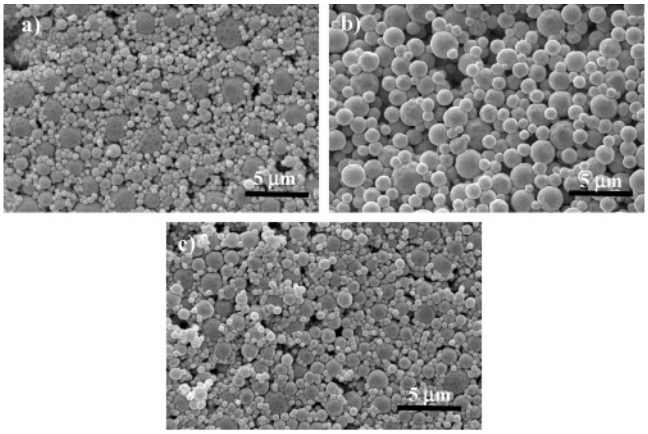

Figure 7. SEM images from Table 3 using various amounts of PDMS−MA stabilizer in the dispersion polymerization of MMA using **3**. Dispersed particles produced via (a) 2.50 (D_n = 1.33 μm, C_v = 71.4%), (b) 5.00 (D_n = 1.44, C_v = 40.7%), and (c) 10.0 wt % (D_n = 0.84, C_v = 28.3%) (with respect to MMA) of PDMS−MA. Scale bar represents 5.00 μm.

Chain Extension. One of the most important features of the RAFT process is the ability to reinitiate the polymer chain to continue propagation in the presence of a second monomer, hence the capacity to produce a range of block copolymers.[4]

The difficulty in producing block copolymers in $scCO_2$ is the lack of polymer solubility. $scCO_2$ is a good solvent for the initial monomer but not for the final polymer; hence, redispersion of the polymer in the medium is difficult. In order to help facilitate the dispersion of the polymer, samples were placed in the autoclave with initiator and additional stabilizer. This stabilizer was found to be important in the redispersion of the polymer, since without it the polymer was not redispersed and chain extension was minimal (Table 4, entry 4). When the PDMS−MA was added, chain extension was possible (Table 4, entries 2 and 3), with the final product being a light pink powder. Analysis on the GPC before and after chain extension shows unimodal systems for the extended polymers with the loss of the peak for the original PMMA sample (Table 4, entries 1−4), the initial PMMA effectively acts as a macro-RAFT agent. After 24 h both reactions (Table 4, entries 2 and 3) had gone to completion, consuming all monomer. Importantly, these chain-extended species both showed relatively narrow PDIs (<1.5) and reasonable agreement with the theoretical molecular weight.

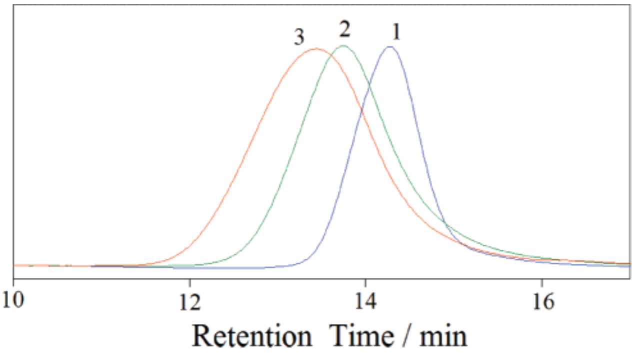

Figure 8. GPC traces displaying the increase in molecular weight (chain extension) for a PMMA sample (Table 4, entry 1) produced via RAFT when redispersed in $scCO_2$ with 1 mL (Table 4, entry 2) and 2 mL (Table 4, entry 3) of MMA. Peaks are labeled as 1, 2, and 3 for entries in Table 6.

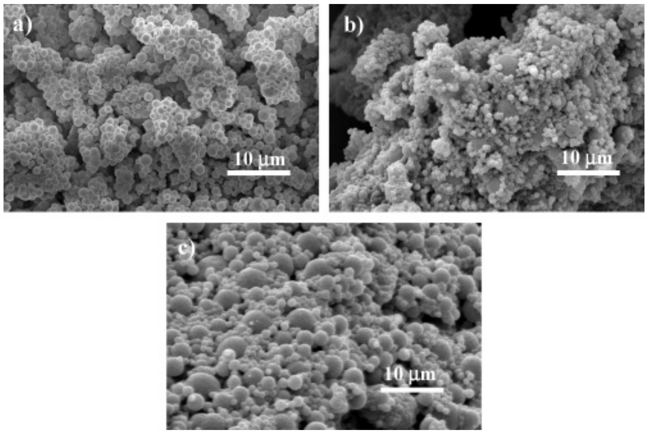

Figure 9. SEM Images for chain extension products extending from PMMA macro-RAFT (Table 4) with additional MMA: (a) initial PMMA sample (M_n = 26 600 g mol^{-1}) (D_n = 1.09 μm, C_v = 29.3%); (b) chain extension with 1 mL of MMA (D_n = 1.15, C_v = 59.5%); (c) chain extension with 2 mL of MMA (D_n = 1.96 μm, C_v = 56.6%).

Analysis of these products with SEM (Figure 9) showed that discrete particles were formed. One can speculate that the initial morphology of the PMMA precursor (Table 4, entry 1) might be destroyed upon the addition of MMA due to the solubility of the polymer in its own monomer. However, the SEM shows re-formation of the spherical morphology (Figure 9). The D_n

values have increased for these two systems compared to the PMMA precursor. In addition, the C_v values have increased from $C_v = 29.3\%$ for the precursor to 59.5% and 56.6% for 1 mL of MMA extension and 2 mL of MMA extension, respectively. This reflects the large range of particles seen in the SEMs.

Redispersing the polymer has allowed chain extension with additional monomer and has shown that these particles exhibit livingness. In future work, we will explore the synthesis of well-defined block copolymers and the structures of the microparticles produced.

Conclusions

This work shows the validity of producing controlled PMMA microparticles by dispersion polymerization in $scCO_2$ with a range of RAFT agents. Comprehensive characterization of these particles that showed both good molecular weight control and particle morphology was achieved. In this way, polymers with a specific molecular weight could be targeted by RAFT as in homogeneous conventional solution polymerization. GPC analysis demonstrated good agreement between M_n and M_{nth}, with PDI values of around 1.20 or less. All four RAFT agents showed pseudo-first-order kinetics with the largest transfer constant belonging to **1**. This result mirrors previous findings for solution polymerization using RAFT in conventional solvents. The dispersion polymerization in $scCO_2$ allowed the formation of solvent-free particles with discrete spherical morphology. Successful reinitiation and subsequent chain extension with MMA were possible.

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Supporting Information Available: RAFT synthesis, additional MALDI-TOF spectrum, and ^{1}H NMR spectrum. This material is available free of charge via the Internet at http://pubs.acs.org.

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