

Synthesis of Highly Cross-Linked Polymers in Supercritical Carbon Dioxide by Heterogeneous Polymerization

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ABSTRACT: This paper reports the synthesis of highly cross-linked polymers in supercritical CO₂ (scCO₂), both with and without the addition of a CO₂-soluble diblock copolymer stabilizer. It was demonstrated that, under certain specific conditions, relatively uniform, nonporous poly(divinylbenzene) (PDVB) microspheres (1–5 μm diameter) can be generated in the absence of added stabilizers. The effects of cross-linker ratio, monomer concentration, cross-linker structure, and mechanical agitation were investigated. A CO₂-soluble diblock copolymer stabilizer was synthesized using a modified screened anionic polymerization (SAP) method. In the presence of this stabilizer (3% w/w), much smaller PDVB microspheres (<0.5 μm diameter) were formed, and it was shown that the particle size and particle size distribution were strongly dependent on the stabilizer concentration. A range of cross-linked terpolymers containing reactive or surface-active functional groups was generated by heterogeneous copolymerization in scCO₂. Finally, these methods were extended to the synthesis of functional cross-linked microspheres containing an organic dye as a host molecule.

Introduction

Cross-linked polymer resins are useful in a wide range of chemical applications, including solid-phase synthesis,^{1–3} chromatography,^{4–7} and the controlled release of drugs.⁸ Other important uses include polymer supported reagents,⁹ ion-exchange resins,¹⁰ molecular imprinting,^{11–13} and molecular sensors.¹⁴ It is often advantageous to produce cross-linked resins in the form of regular microspheres with controlled particle size. This can be achieved by using heterogeneous polymerization techniques, including suspension, dispersion, and emulsion polymerization.¹⁵

Suspension polymerization^{16,17} is particularly useful for making cross-linked polymer beads in the size range 10–1000 μm, for applications such as packed column chromatography and solid-phase synthesis. A typical oil-in-water (O/W) procedure involves the suspension of an immiscible, oil-soluble monomer in water, often with the addition of a porogen in the case of highly cross-linked macroporous resins.^{5,7} The suspension is polymerized with stirring to form spherical particles directly, the initiator being preferentially soluble in the monomer phase.^{18,19} Each monomer droplet may be considered as a “microbulk” polymerization, with heat transfer to the surrounding aqueous continuous phase. Water-soluble monomers may be polymerized via water-in-oil (W/O or “inverse”) suspension polymerization techniques, where the monomer, or often a concentrated aqueous solution of the monomer, is polymerized in an immiscible, nonpolar hydrocarbon medium.^{20,21} In both cases, surfactants are usually added to inhibit droplet coalescence. Recently, the scope of suspension polymerization has been broadened by the development of staged templated techniques, which allow the formation of large, monodisperse, macroporous beads by a multistage swelling process.²²

Unlike suspension polymerization, emulsion polymerization²³ is carried out under conditions where the initiator is preferentially soluble in the continuous phase. Spherical latex particles synthesized by O/W

emulsion polymerization tend to fall in the size range 20–600 nm (in the presence of amphiphilic surfactants) or 1–10 μm (in the absence of added surfactants). Monomers are usually oil-soluble, although it is also possible to copolymerize water-soluble monomers in some cases.

In precipitation polymerization, both monomer and initiator are soluble in the continuous phase but the polymer precipitates as it is formed, often as an undefined, agglomerated powder.¹⁵ Dispersion polymerization^{24–26} is also characterized by initially homogeneous conditions; however, the resulting insoluble polymer is stabilized as a colloid, usually by choosing appropriate surfactants, to give spherical polymer particles, typically in the size range 100 nm to 10 μm. Dispersion polymerization may be carried out under both aqueous and nonaqueous conditions, depending on the application.

All of the heterogeneous polymerization techniques listed above have certain limitations for the preparation of cross-linked resins. In nonaqueous systems, for example, large volumes of volatile organic solvents (VOCs) may be required. Aqueous systems, on the other hand, are incompatible with some applications, such as molecular imprinting (where water can bind competitively with the template molecule)²⁷ and the direct suspension polymerization of water-sensitive monomers [e.g., (meth)acryloyl halides]. To address these problems, perfluorocarbon solvents (e.g., perfluoroalkanes) have been evaluated for suspension polymerization because they are nonpolar, inert, and immiscible with most common organic monomers.^{28,29} While this approach seems to be quite widely applicable,³⁰ the high cost of the perfluorinated solvents is an important concern.

Supercritical carbon dioxide (scCO₂) is an attractive solvent for polymer chemistry because it is inexpensive, nontoxic, and nonflammable.^{31,32} Unlike conventional liquid solvents, supercritical fluids (SCFs) are highly compressible, and the solvent density (and therefore solvent properties such as solubility parameters) can be

tuned over a wide range by varying pressure.³³ Moreover, SCFs revert to the gaseous state upon depressurization, simplifying the separation of solvent from solute. DeSimone and others have shown that scCO_2 is a versatile medium for both homogeneous^{34–36} and heterogeneous^{37–45} polymerizations. In particular, CO_2 -soluble surfactants have been developed for free radical dispersion polymerization of styrene and methyl methacrylate in scCO_2 , thus allowing the formation of regular polymer microspheres.^{46–55} The development of CO_2 -based emulsion³⁷ or suspension polymerization techniques has received much less attention, probably because most monomers studied so far have been found to be quite soluble in scCO_2 .

In this paper, our goal has been to evaluate CO_2 as an alternative medium for the preparation of cross-linked polymer particles by heterogeneous polymerization. In 1987, a process for synthesizing pulverent cross-linked polymer powders by precipitation polymerization in scCO_2 was patented by BASF.^{56,57} Relatively few details were given, and the examples did not show the formation of well-defined particles with specific, controlled morphologies.

In an extension of our earlier communication,⁵⁸ we report here in detail the synthesis of uniform cross-linked polymer microspheres in scCO_2 , both with and without the addition of a CO_2 -soluble polymeric stabilizer.

Experimental Section

Materials. All solvents were freshly distilled, unless otherwise stated. Divinylbenzene (DVB) was purchased as mixtures containing around 55% w/w DVB (DVB55) or 80% w/w DVB (DVB80), respectively. Monomer mixtures containing less than 55% w/w divinylbenzene were formed by diluting either DVB55 or DVB80 with a monofunctional monomer (e.g., styrene). The reported compositions of DVB55 and DVB80 are shown below as follows:

component	DVB55	DVB80
divinylbenzene (DVB; 1,3- + 1,4-isomers)	56%	78%
ethylvinylbenzene (EVB; 1,3- + 1,4-isomers)	43%	20%
diethylbenzene + naphthalene + inhibitor	~1%	~2%

DVB55 and DVB80 mixtures were passed down neutral alumina columns to remove the inhibitor before use. Styrene, methyl methacrylate (MMA), methacryloyl chloride, methacrylic acid (**4c**), ethylene glycol dimethacrylate (EDMA), and trimethylolpropane trimethacrylate (TRM) were purified by vacuum distillation. 2,2'-Azobisisobutyronitrile (AIBN) was recrystallized twice from methanol.

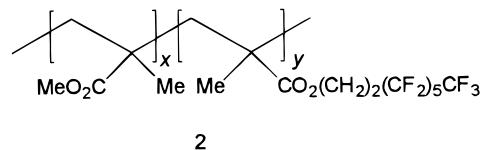
4-Vinylbenzyl chloride (**3a**, 97%, meta/para mixture), pentafluorostyrene (**3b**, 99%), octadecyl acrylate (**4a**, 97%), 2-(*N*-ethylperfluorooctanesulfonamido)ethyl methacrylate (**4b**, Fluorochem), sodium dodecylbenzene sulfonate (SDBS, 95%), Disperse Red 1 (95%), 1*H*,1*H*,2*H*,2*H*-perfluorooctan-1-ol (Fluorochem), *n*-heptane (HPLC grade), and carbon dioxide (Messer Griesheim, Grade 5*5) were all used as received. All chemicals were purchased from Aldrich unless specified.

Equipment. High-pressure reactions were carried out in a stainless steel reactor (either 10 or 40 cm^3), equipped with a sapphire window for observation of phase behavior.^{53,58} Liquid CO_2 was delivered to the reactor with a Pickel PM 101 nitrogen driven pump. The pressure in the reactor was measured with a pressure transducer (A105, RDP Electronics) and a digital display (E308, RDP Electronics). The internal reactor temperature was measured with an industrial mineral isolated thermocouple (Type K, RS Electronics). A PTFE-coated magnetic stir bar or a rotary impeller stirrer (Basker-

ville) was used to mix the contents of the reactor. In reactions which were mixed with a magnetic stir bar, the reactor was placed on its side such that the long axis was horizontal. In reactions with the impeller stirrer, the reactor was mounted with the long axis vertical, the impeller shaft being coaxial with the reactor bore. The stirrer consisted of a single four blade impeller (pitch of blade = 45°) mounted approximately 1.5 mm above the bottom of the reactor.

Synthesis of 1*H*,1*H*,2*H*,2*H*-Perfluorooctyl Methacrylate (1**).** To a solution of 1*H*,1*H*,2*H*,2*H*-perfluorooctan-1-ol (8.0 g, 36.3 mmol) and triethylamine (6.6 cm^3 , 47 mmol) in THF (50 cm^3) was added freshly distilled methacryloyl chloride (5.2 cm^3 , 54 mmol). Formation of a white solid (triethylammonium chloride) was observed on addition of methacryloyl chloride. The mixture was stirred at room temperature for 3 h. The reaction mixture was filtered through Celite, and ether (150 cm^3) was added to the filtrate. The organic layer was washed with saturated aqueous NaHCO_3 (150 cm^3), 2 M HCl (150 cm^3), and brine (150 cm^3). The aqueous portions were extracted successively with ether (3 \times 50 cm^3). The combined organic layers were dried (MgSO_4) and the solvent removed by rotary evaporation to yield the crude ester. Flash column chromatography on silica gel eluting with hexane–hexane:ether (95:5) and kugelrohr distillation (oven temperature 100 °C, 0.1 mmHg) gave 11.80 g (75.5% yield) of 1*H*,1*H*,2*H*,2*H*-perfluorooctyl methacrylate, **1**, as a colorless liquid: $R_f = 0.42$ (ether–hexane, 10:90); FTIR (film) 1736, 1639 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.13 (s, 1H, C=CH), 5.60 (s, 1H, C=CH), 4.45 (t, $J = 6.5$ Hz, 2H, CO_2CH_2), 2.51 (tt, $J = 18.0, 6.5$ Hz, 2H, CH_2CF_2), 1.98 (s, 3H, CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 166.9 (s, C=O), 135.7 (s, C), 126.3 (s, CH_2), 118.6 (m, CF_2), 117.5 (m, CF_2), 115.7 (m, CF_2), 112.9 (m, CF_2), 111.0 (m, CF_2), 108.6 (m, CF_2), 56.5 (t, $J = 4.2$ Hz, CO_2CH_2), 30.5 (t, $J = 21.7$ Hz, CH_2CF_2), 18.0 (s, CH_3); EIMS 432 $[\text{M}]^+$, 149, 104, 69, 57, 41; HRMS calcd for $[\text{C}_{12}\text{H}_7\text{O}_2\text{F}_{15}]^+$ 432.0393, found 432.0393.

Preparation of AB Block Copolymer (2**).** Diblock co-



polymer **2** was synthesized by a modified screened anionic polymerization (SAP) technique.⁵³ To a solution of Al^iBu_3 (1.0 M in toluene, 0.5 cm^3) in toluene (2.5 cm^3) was added tBuLi (1.6 M in hexane, 0.15 cm^3 , 0.2 mmol) at 0 °C under N_2 . The resulting solution was allowed to stir for 5 min before adding MMA (0.5 cm^3 , 5.0 mmol) dropwise at 0 °C. A pronounced yellow color was observed upon addition of the monomer. After a few minutes, a portion of the reaction mixture (2.7 cm^3) was removed by syringe and precipitated into excess MeOH for analysis of the PMMA block. A solution of **1** (1.1 g, 2.5 mmol) in 1,3-bis(trifluoromethyl)xylylene (3.0 cm^3) was then added dropwise to the remaining reaction mixture. The reaction mixture was stirred at 0 °C for 30 min. A few drops of MeOH were added to terminate the reaction and the polymer was precipitated out with excess hexane. After being redissolved in CH_2Cl_2 , the polymer was reprecipitated into an excess of MeOH, collected by filtration, and dried in vacuo, to afford 1.10 g (91% yield) of block copolymer **2** as a white powdery solid: FTIR (KBr) 1734 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) $\{[\text{M}] = \text{PMMA block}, \{\text{F}\} = \text{PFMA block}\}$ δ 4.6–3.8 (br s, 2H, $\text{CH}_2\text{-}\{\text{F}\}$), 3.6 (s, 3H, $\text{CO}_2\text{CH}_3\{\text{M}\}$), 2.7–2.2 (br s, 2H, $\text{CH}_2\{\text{F}\}$), 2.2–1.7 (br m, 2H $\{\text{M}\}$, 2H $\{\text{F}\}$, CH_2), 1.2–0.8 (br m, 3H $\{\text{M}\}$, 3H $\{\text{F}\}$, $\alpha\text{-CH}_3$); M_n (PMMA block) = 14 kg/mol. From ^1H NMR integrals, the molar ratio of the PMMA block (CO_2CH_3 , $\delta = 3.6$) to the PFMA block (CO_2CH_2 -, $\delta = 4.6\text{--}3.8$) in **2** was 1:1. From our knowledge of the molecular weight of the PMMA block, the total molecular weight of the block copolymer, M_n (**2**), was calculated to be 74.5 kg/mol.

Polymerizations in CO_2 . In a typical polymerization, the reactor was charged with monomers, initiator (AIBN), and stabilizer **2** (if included), and the system was purged with a

slow flow of CO₂ for 20–30 min. The reactor was then pressurized with CO₂ to around 80 bar, stirring was commenced, and the reaction mixture was heated to the desired temperature (65 °C). On average, it took approximately 15–20 min to heat from room temperature to 65 °C. If necessary, more CO₂ was added close to the reaction temperature until the required conditions were obtained. The polymerization was allowed to commence with stirring overnight. Phase behavior in the reactor was observed carefully for the first 3–4 h. The pressure in the reactor was observed to decrease somewhat during polymerization, the precise change in pressure depending upon the volume fraction of the monomer in the system.

Three general types of phase behavior were observed with DVB. For unstabilized reactions at very low monomer concentrations ($\leq 2\%$ w/v DVB55 or DVB80), the supercritical solution was initially homogeneous (25 °C, ~ 85 bar). The solution was heated (to 65 °C, 310 bar), and after 45–60 min an orange/red color was observed, due to scattering of transmitted light by the growing polymer particles (i.e., the Tyndall effect).⁵⁰ Within 90 min, a fine, white solid formed on the reactor walls and window, indicating a precipitation polymerization. For unstabilized reactions at higher monomer concentrations ($> 10\%$ w/v DVB55 or DVB80), the supercritical solution became partly heterogeneous almost immediately after pressurization (25 °C, ~ 85 bar), consisting of a cloudy liquid suspension in CO₂, probably associated with small quantities of partially reacted monomer species which were insoluble in CO₂ under these conditions. The degree of cloudiness increased with increasing monomer concentration. Once again, a fine, white precipitate formed over the course of the reaction at higher temperatures. When the polymerization (20% w/v DVB55 or DVB80) was carried out in the presence of 0.25–3.0% w/w stabilizer **2**, the phase behavior was quite different. Immediately after pressurization, an opaque, white mixture was obtained, resembling an emulsion in CO₂. We attribute this to the emulsification of partially reacted, CO₂-insoluble components in the reactive monomer mixture. This opaque, uniform appearance persisted throughout the reaction.

At the end of each reaction, the reactor was cooled to ambient temperature and the CO₂ was vented slowly through acetone to trap any monomer (or polymer) that might otherwise escape. The polymer was removed from the reactor, which was then rinsed with acetone to collect all of the solids. In reactions involving stabilizer **2**, great care was taken to remove any traces of the fluorinated polymer from the reactor between experiments. First, the reactor was washed thoroughly with 1,3-bis(trifluoromethyl)benzene, which is a good solvent for stabilizer **2**. After this, the entire reaction system (including pressure transducer, piping etc.) was cleaned by continuous extraction with scCO₂ (~ 300 bar, 1 h) to remove any remaining stabilizer. A typical procedure for the purification of the cross-linked resins was as follows.⁵⁹ The cross-linked polymer (~ 2 g) was washed twice with THF (2×25 cm³) and with methanol (2×25 cm³). The polymer was separated by centrifuging and decanting the solvent between washes. The polymer was then suspended in acetone (25 cm³) and left overnight, before being resuspended twice more in ethanol (2×25 cm³), centrifuged, decanted, and finally dried under vacuum at 50 °C. Yields were determined gravimetrically. There was no apparent weight loss after the washing procedure, and no soluble polymer fraction was detected.

Characterization. ¹H NMR spectra were recorded in deuteriochloroform at room temperature using a Bruker DRX-500 (500 MHz) NMR spectrometer. ¹³C NMR spectra were recorded on a Bruker AC-400 (400 MHz) NMR spectrometer using an internal deuterium lock and proton decoupling. IR spectra were recorded on a Nicolet 510 FTIR spectrometer (resolution = 2 cm⁻¹). Mass spectra were determined at the EPSRC Mass Spectrometry Service Centre, University of Swansea. Electron impact (EI) and chemical ionization (CI) low resolution spectra were recorded using a VG model 12-253 under ACE conditions. Accurate mass measurements were performed on a VG ZAB-E instrument. The molecular weight of the PMMA block in stabilizer **2** was determined with a Knauer gel permeation chromatograph (GPC) using PL Gel

Table 1. Effect of Cross-Linker Ratio on Polymerization of DVB in scCO₂^a

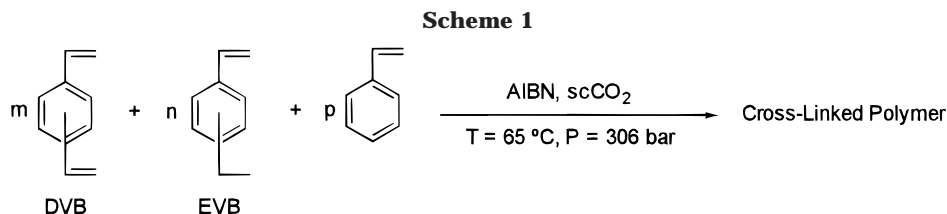
	<i>m</i> ^b	<i>n</i> ^c	<i>p</i> ^d	polymer morphology	particle size (μm) ^e	<i>T</i> _{max} (°C) ^f	yield (%)
1	0	0	100	aggregate		424	56 ^g
2	2	0.5	97.5	aggregate		441	59
3	10	8.2	81.8	aggregate		456	78
4	55	45	0	powder	1–5	471	89
5	80	20	0	microspheres	2.40 (21%)	475	92

^a Reaction conditions: 2.0 g of monomer(s), AIBN (8% w/w based on monomer), 310 \pm 15 bar, 65 °C, 24 h. ^b Weight of DVB, as a percentage of total monomer weight. ^c Weight of EVB as a percentage of total weight. ^d Weight of styrene as a percentage of total weight. ^e Determined by SEM. Figure in parentheses = % coefficient of variation, CV, where $CV = (\sigma/D_n) \times 100$. σ = standard deviation of particle diameter (μm), D_n = mean particle diameter (μm). ^f Maximal thermal decomposition temperature as determined by thermogravimetric analysis. ^g Yield determined gravimetrically after drying sample under vacuum without reprecipitation. $M_w = 11\,700$. $M_w/M_n = 8.3$.

30 cm 5 μm mixed C column at 30 °C, running in chloroform at 1 cm³/min with polystyrene ($M_n = 600$ – 10^6 g/mol) standards. Thermal analysis was carried out with a Perkin-Elmer TGA 7 in a nitrogen atmosphere. The temperature range scanned was 30–800 °C at a scanning rate of 20 °C/min. Polymer morphologies were investigated with a JEOL JSM-5800 LV scanning electron microscope (SEM). The polymer powders were mounted on aluminum studs using adhesive graphite tape and sputter coated with 10–20 nm gold before analysis. Where unagglomerated polymer microspheres were obtained, average particle size was calculated from electron micrographs (~ 300 particle diameters measured). In the case of certain highly agglomerated samples, average particle size was estimated using a Leeds and Northrup Microtrac X-100 particle size analyzer with automated small volume recirculator (ASVR). Samples (~ 100 mg) were suspended in Isopar G (75–100 cm³) by stirring before injecting aliquots of this suspension into the analyzer. Particle surface areas were measured using the BET method with a Micrometrics ASAP 2400 nitrogen adsorption analyzer. Samples were outgassed at room temperature under vacuum overnight. Sample porosities were determined using a Micrometrics Autopore 9220 mercury porosimeter. Samples were subjected to a pressure cycle starting at approximately 1.5 psia (equivalent to a pore size of around 140 μm), increasing to 6000 psia (equivalent to 30 Å diameter pores) in predefined steps to give pore size/pore volume information. Absolute densities were determined using a Micrometrics Accupyc 1330 helium pycnometer.

Results and Discussion

Effect of Cross-Linker Ratio. In the absence of a cross-linking agent, the precipitation polymerization of styrene in scCO₂ gave low molecular weight polystyrene in poor yield (Table 1, entry 1), as reported previously.^{48,50} The yield increased somewhat with the addition of small amounts of DVB cross-linker (entries 2+3). The cross-linked polymer was formed as an agglomerated mass, also by precipitation polymerization. At higher DVB ratios ($> 55\%$ w/v; entries 4+5), the phase behavior was somewhat different. Under these conditions, the reaction mixture was partially heterogeneous very early in the reaction, even at low temperatures. Initially, we proposed that this phase separation might be due to limited solubility of the DVB monomer in CO₂.⁵⁸ However, further phase behavior studies on DVB containing free radical inhibitor have shown that the pure monomer mixture is soluble in CO₂ under the reaction conditions.^{60,61} It is therefore likely that the early phase separation observed in our polymerizations at higher monomer concentrations was due to small quantities of CO₂-insoluble species formed by



partial reaction of the highly reactive DVB monomer mixture (Scheme 1).

After overnight reaction at 65 °C, the highly cross-linked polymers were isolated in high yields (Figure 1) directly from the reactor as dry, free flowing powders. When the polymers were examined by scanning electron microscopy (SEM), it was found that those formed at 20% w/v monomer concentration existed in the form of partially agglomerated microspheres (diameter = 1.5–5 μm), even though no stabilizers were used in the process (Figure 2). Previously, Li and Stöver found that highly cross-linked, monodisperse poly(divinylbenzene) (PDVB) microspheres could be formed by precipitation polymerization in acetonitrile in the absence of stabilizers, albeit at much lower monomer concentrations.⁵⁹ In their work, it was assumed that the particle formation and growth mechanisms were similar to those of dispersion polymerization, except that the particles were stabilized against coagulation by their rigid, cross-linked surfaces rather than by added stabilizers. We also partly attribute the formation of microspheres in our samples to the rigidity of the polymers. The fact that the lightly cross-linked polymers did not form microspheres (entries 2 + 3) is consistent with this idea. The particles formed from DVB80 (Figure 2b) were significantly less agglomerated than those formed from DVB55 (Figure 2a), perhaps because the particles containing 80% w/w DVB were more rigid, and therefore less prone to aggregation. However, this is not the only possible explanation, since it has been shown that the actual degree of physical cross-linking that occurs in resins of this type is not directly proportional to the monomer feed ratio at such high cross-linker levels.^{62,63} It is perhaps likely that the degree of aggregation in the samples may also have been influenced by a change in polymerization rate or phase behavior, connected with the difference in the composition of the two monomer mixtures, DVB55 and DVB80. It is known, for example, that DVB is significantly more reactive than EVB toward free radicals.²⁶

The cross-linked particles were similar in size to polystyrene particles formed by dispersion polymeriza-

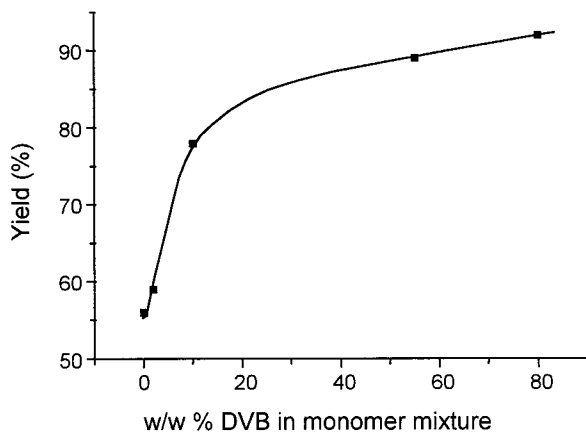


Figure 1. Plot of isolated polymer yield vs percent w/w of DVB in monomer mixture.

tion in scCO_2 in the presence of stabilizers,^{48,50} although there was considerably more evidence of particle agglomeration in our samples (Figure 2). Thermal analysis showed the cross-linked polymers to have high thermal stability (Table 1).⁵⁸ The thermal stability increased with increasing cross-linker ratio, as described previously for DVB resins synthesized by more conventional routes.²⁵ As might be expected, the highly cross-linked polymer microspheres were completely insoluble in all solvents tested. They were readily dispersed in most common organic solvents (e.g., alcohols, alkanes, ethers, toluene) to form milky white suspensions which began to settle out upon standing within a few hours. The particles did not disperse at all in pure water because of their strongly hydrophobic nature. They did, however, disperse to some extent in a 60:40 water:ethanol mixture.

Effect of Monomer Concentration. The polymerization of the DVB55 mixture in scCO_2 was carried out over a wide range of monomer concentrations (Table 2, entries 6–12). Two general trends were observed. First,

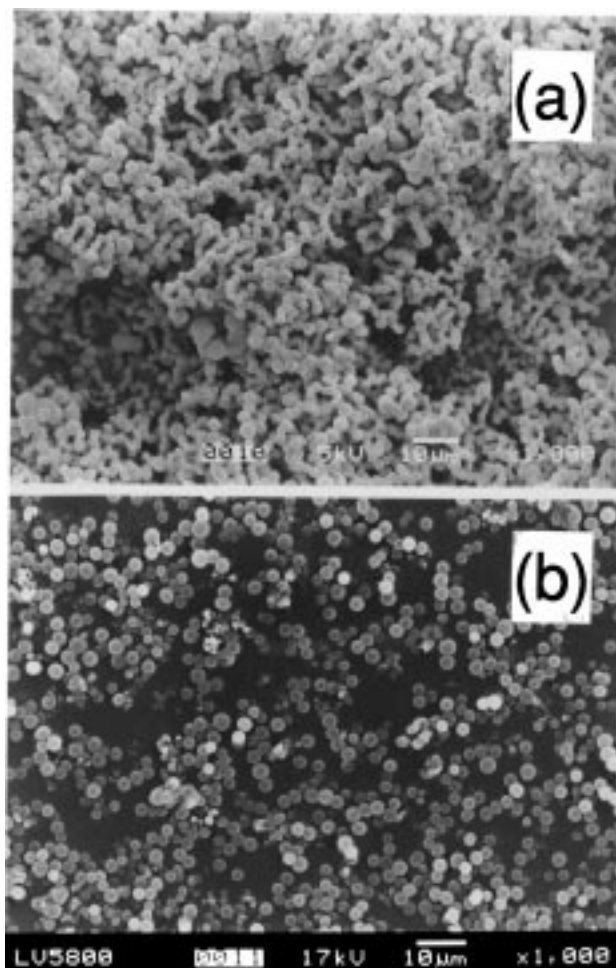


Figure 2. Scanning electron micrographs of PDVB microspheres synthesized by polymerization in scCO_2 in the absence of stabilizers: (a) DVB55; (b) DVB80.

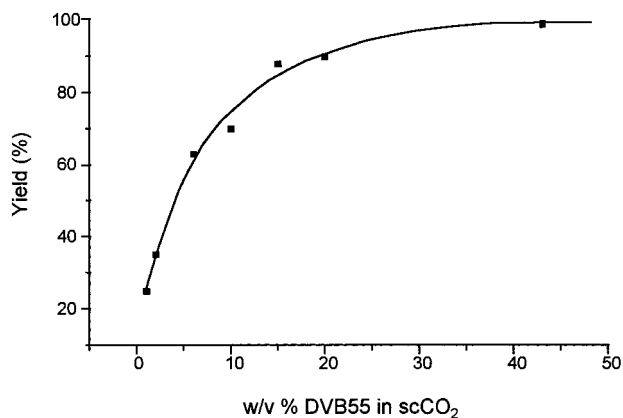


Figure 3. Plot of isolated polymer yield vs percent w/v of DVB55 in scCO₂.

polymer yield increased with monomer concentration (Figure 3). The low yields at monomer concentrations of less than 6% w/v almost certainly reflect poor initiator efficiencies under those conditions.⁵⁹ The second notable trend was a strong dependence of particle size on monomer concentration (Figure 4). Free flowing powders were obtained in all cases, although the morphology of the powders varied markedly (Figure 4). At 20% w/v DVB55 in CO₂, relatively uniform, partially aggregated microspheres were obtained with diameters mostly in the range 1–5 μm (Figure 4b). At higher monomer concentrations (43% w/v), larger, agglomerated structures were observed (Figure 4a). At lower monomer concentrations (10–15% w/v), smaller primary particles of less than 1 μm were apparent, but these particles

Table 2. Effect of Monomer Concentration on Polymerization of DVB55 in scCO₂^a

	w/v DVB55 (%)	yield (%)		w/v DVB55 (%)	yield (%)
6	43	99	12	1	25
7	20	89	13^b	20	90
8	15	88	14^c	20	90
9	10	70	15^d	20	71
10	6	63	16^e	20	90
11	2	35	17^f	20	89

^a Reaction conditions: 2.0 g of monomer(s), AIBN (8% w/w), 310 ± 15 bar, 65 °C, 24 h. ^b Reaction carried out in a 40 cm³ reactor; 8.0 g DVB55, 7.15 g of polymer isolated. ^c Sodium dodecylbenzene sulfonate added (2% w/w based on monomer). ^d 2% w/w AIBN based on monomer. ^e Reaction carried out at 211 bar. ^f Reaction carried out in *n*-heptane under equivalent conditions.

were agglomerated to form larger structures (Figure 4c,d). Similar structures were obtained when the polymerization was carried out at very low monomer concentrations (entries 11 + 12).

Since it appeared that the most uniform, spherical particles were obtained with around 20% w/v monomer in CO₂, subsequent experiments were carried out at this concentration. It was found that the reaction could be scaled up without loss of yield or significant change in particle morphology (entry 13). The addition of sodium dodecylbenzene sulfonate (SDBS) had no apparent effect on either yield or particle morphology (entry 14), even though SDBS was found to be a good stabilizer for the suspension copolymerization of styrene and DVB in perfluorooctanes.³⁰ When the polymerization was conducted with lower initiator concentration (2% w/w), polymer yields were reduced, and a more highly coagu-

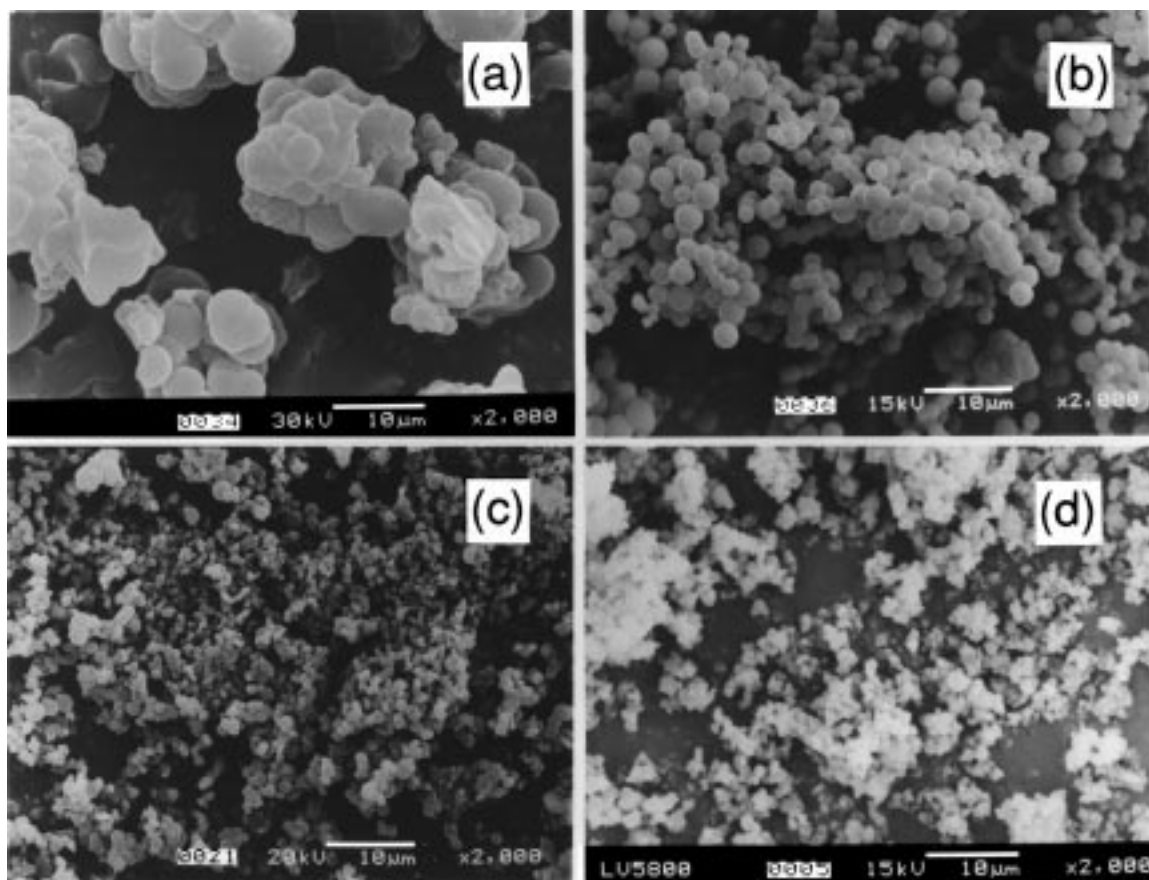


Figure 4. Scanning electron micrographs of PDVB particles synthesized in scCO₂ at various monomer concentrations: (a) 43% w/v DVB55; (b) 20% w/v DVB55; (c) 15% w/v DVB55; (d) 10% w/v DVB55.

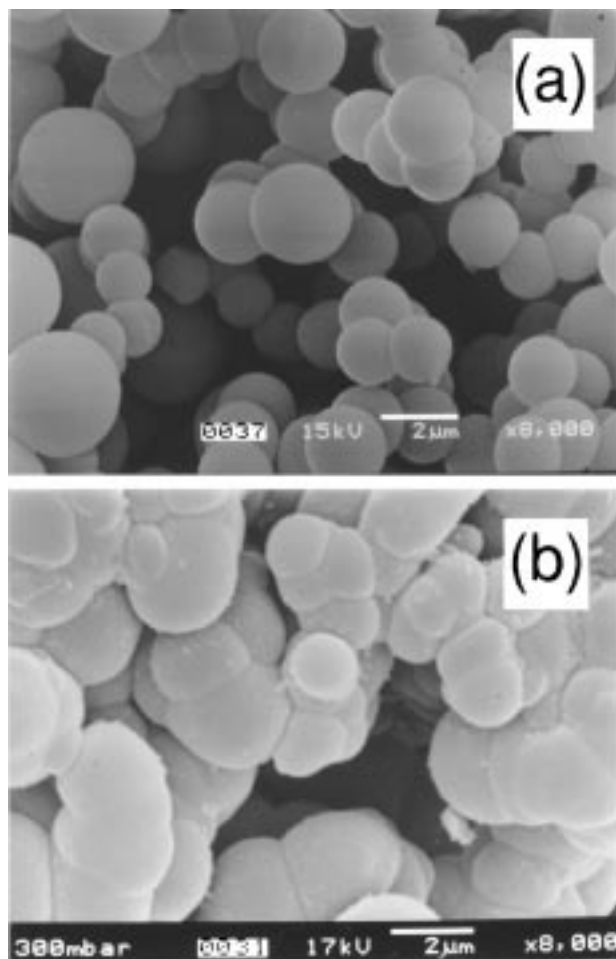


Figure 5. Scanning electron micrographs of PDVB particles synthesized in (a) $scCO_2$ and (b) n -heptane under otherwise similar conditions.

Table 3. Effect of Agitation on Polymerization of DVB55 in $scCO_2$ ^a

	method of agitation ^b	yield (%)
18	M	89
19	R (300)	61
20	R (1200)	56

^a Reaction conditions: 2.0 g of monomer(s), AIBN (8% w/w), 310 \pm 15 bar, 65 $^\circ$ C, 24 h. ^b M = magnetic stir bar. R = rotary impeller. Figure in parentheses = stirring speed (rpm).

lated product was obtained (entry 15). This is consistent with previous studies involving DVB, where rather high initiator concentrations seemed necessary to achieve good monomer conversions.^{25,59} Canelas and DeSimone have shown that the dispersion polymerization of styrene in $scCO_2$ is very sensitive to the density of the continuous phase.⁵⁰ Preliminary experiments on the effect of CO_2 pressure on the polymerization of DVB55 indicated that lower CO_2 pressures led to somewhat larger, more agglomerated particles, although conversions remained high (entry 16). The density of pure CO_2 at the higher pressure (310 bar/65 $^\circ$ C) was calculated to be 0.82 g/cm³; by comparison, the density under the lower pressure conditions (211 bar/65 $^\circ$ C) was calculated to be 0.72 g/cm³. Control experiments were carried out using n -heptane as a solvent (entry 17), since $scCO_2$ is often compared with liquid alkanes (and perfluoroalkanes) in terms of solvent properties.⁵⁰ Comparably high monomer conversions were obtained in n -heptane under equivalent reaction conditions, although the

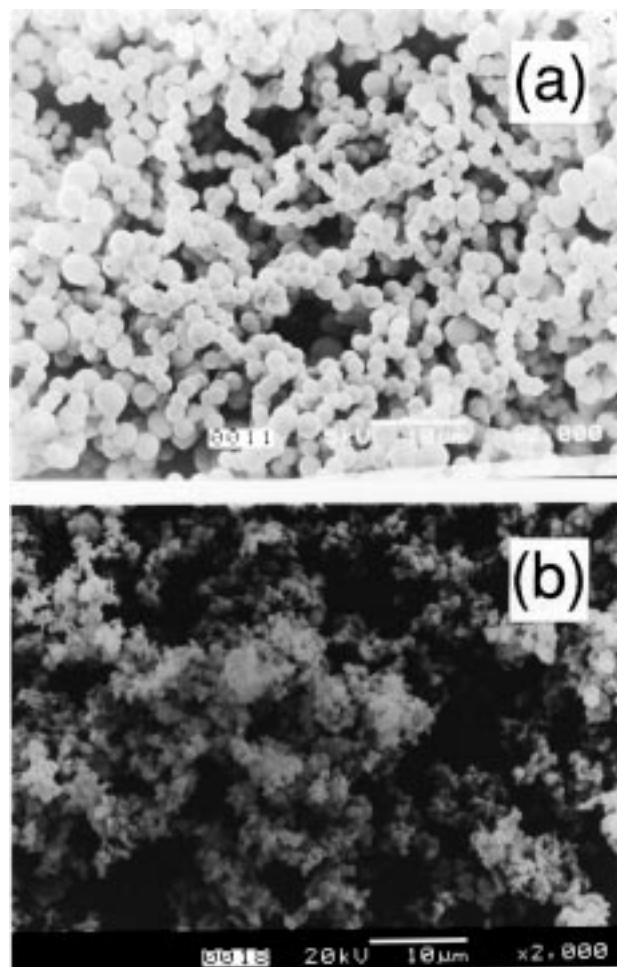


Figure 6. Scanning electron micrographs of PDVB particles synthesized in $scCO_2$ with different mechanical agitation techniques: (a) reactor stirred with a PTFE-coated stir bar; (b) reactor mixed with a rotary impeller stirrer at 300 rpm.

Table 4. Polymerization of Various Cross-Linking Monomers in $scCO_2$ ^a

	monomer	yield (%)	characteristic IR bands (cm ⁻¹)
21	DVB55	89	3018, 2964, 1486, 1449
22	DVB80	92	3018, 2964, 1486, 1449
23	EDMA ^b	80	2997, 2964, 1737 (C=O), 1468
24	TRM ^b	94	2970, 1735 (C=O), 1650, 1461

^a Reaction conditions: 2.0 g of monomer(s), AIBN (8% w/w), 310 \pm 15 bar, 65 $^\circ$ C, 24 h. ^b 100% cross-linking monomer.

particles were somewhat larger and less uniform, showing rather more agglomeration than those synthesized in CO_2 (Figure 5). One difference between the two solvents was that the reaction mixture remained homogeneous in heptane for considerably longer during the polymerization before precipitation occurred, suggesting that heptane is a better solvent than CO_2 for the early products of the reaction.

Effect of Mechanical Agitation. Many studies have shown that particle size in heterogeneous polymerization is influenced strongly by the type of stirring, the speed (or power) of the stirrer, and the general design of the polymerization apparatus.¹⁵⁻¹⁷ We have investigated the effect of stirring on the polymerization of DVB55 in $scCO_2$ and have found that stirring does indeed have a profound influence on polymer yield, particle size, and particle morphology (Table 3). We observed that smaller, highly aggregated particles were formed in reactions which were mixed with a rotary

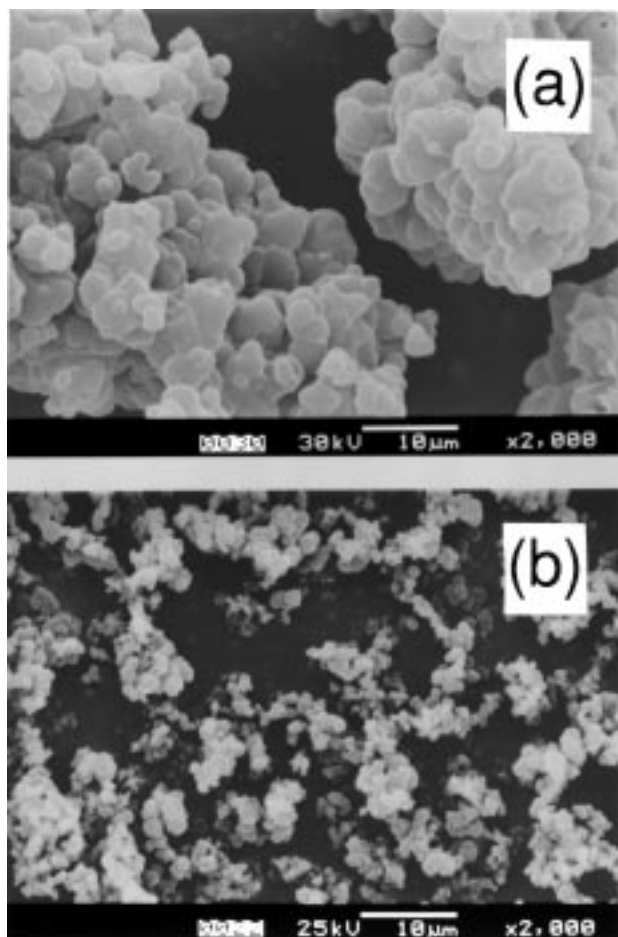
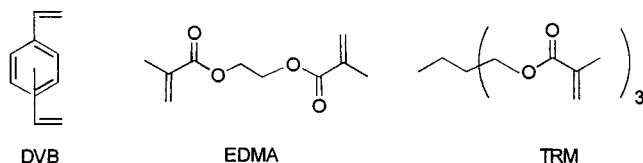


Figure 7. Scanning electron micrographs of cross-linked polymers prepared in scCO_2 from (a) EDMA and (b) TRM by precipitation polymerization.

impeller stirrer at stirring speeds between 300 and 1200 rpm (Figure 6). The precise reason for the significant drop in monomer conversion at high stirring speeds is as yet unclear.

Effect of Cross-Linker Structure. In addition to the polymerization of DVB in scCO_2 , we have investigated the polymerization of other cross-linking monomers, such as ethylene glycol dimethacrylate (EDMA)



and trimethylolpropane trimethacrylate (TRM) (Table 4).

The results obtained with these monomers were broadly similar in terms of monomer conversions. Both EDMA and TRM were soluble in scCO_2 under the reaction conditions, and a precipitation polymerization was observed. In general, phase separation occurred later in the reaction, possibly because of somewhat lower reaction rates for these monomers. No microspheres were observed with EDMA or TRM under these conditions, and the polymer powders consisted of random agglomerates of smaller, irregular primary particles (Figure 7), rather similar in structure to poly(acrylic acid) powders formed by precipitation polymerization in scCO_2 .⁴⁰

Table 5. Effect of Stabilizer Concentration on Polymerization of DVB in scCO_2 ^a

	w/w stabilizer 2 (%) ^b	DVB (%) ^c	polymer morphology	particle size ^d (μm)	yield (%)
25	0	55	powder	1–5	89
26	0.25	55	powder	0.5–2.5	90
27	1	55	powder	0.4–1.6	87
28	3	55	microspheres	0.41 (16%)	96
29	0	80	microspheres	2.40 (21%)	92
30	3	80	microspheres	0.29 (18%)	95

^a Reaction conditions: 2.0 g of monomer(s), AIBN (8% w/w), 310 \pm 15 bar, 65 $^\circ\text{C}$, 24 h. ^b Percent w/w based on monomer. ^c Weight of DVB as a percentage of total monomer weight. ^d Determined by SEM. Figure in parentheses = percent coefficient of variation, CV, where $\text{CV} = (\sigma/D_n) \times 100$. σ = standard deviation of particle diameter (μm), D_n = mean particle diameter (μm).

Effect of Stabilizer Concentration. Although it was possible to form relatively uniform cross-linked PDVB microspheres in the absence of stabilizers, this was only achievable under very specific reaction conditions. Even then, the particles so produced showed significant degrees of agglomeration and broad particle size distributions. Previous studies have shown that the use of CO_2 -soluble diblock copolymer stabilizers can promote the formation of regular microspherical polymer particles in the dispersion polymerization of styrene and methyl methacrylate in scCO_2 .^{48,50,53} A diblock copolymer stabilizer, **2**, was synthesized by a modified screened anionic polymerization technique,⁵³ and the effect of this stabilizer on the polymerization of DVB mixtures in scCO_2 was investigated (Table 5).

In the absence of any stabilizer, the polymerization of DVB55 in scCO_2 led to partially agglomerated PDVB microspheres with diameters in the range 1–5 μm (Figure 8a; Table 5, entry 25). In the presence of just 0.25% w/w stabilizer **2** (entry 26), the phase behavior appeared to be very different. After pressurization with CO_2 , an opaque, white emulsion was observed which persisted throughout the polymerization reaction. This phase behavior was probably due to emulsification of phase-separated, CO_2 -insoluble components in the reaction mixture, formed by partial reaction of the DVB monomer. Control experiments showed that emulsions of this type were not formed when inhibited monomer was used in the absence of any free radical initiators. Under those conditions, homogeneous solutions were observed which did not phase separate, even when heated to 65 $^\circ\text{C}$.

The particles formed from the polymerization in the presence of 0.25% w/w stabilizer **2** showed a high degree of aggregation and a broad distribution of particle sizes, suggesting that the reaction was not effectively stabilized under these conditions (Figure 8b). When the reaction was carried out at higher stabilizer concentration (1% w/w), the same phase behavior was observed (entry 27), but the resulting polymer particles were somewhat smaller (Figure 8c). Once again, the level of aggregation and the particle size distribution suggested incomplete stabilization of the reaction. With 3% w/w stabilizer **2** (entry 28), uniform PDVB microspheres were obtained with an average diameter of 0.41 μm (Figure 8d). The lack of aggregation and the narrow particle size distribution suggested that effective stabilization had occurred under these conditions. Similar results were obtained at higher cross-linker ratios (entries 29 + 30), and in all cases the addition of stabilizer **2** led to a small but reproducible increase in monomer conversion. The results were broadly consis-

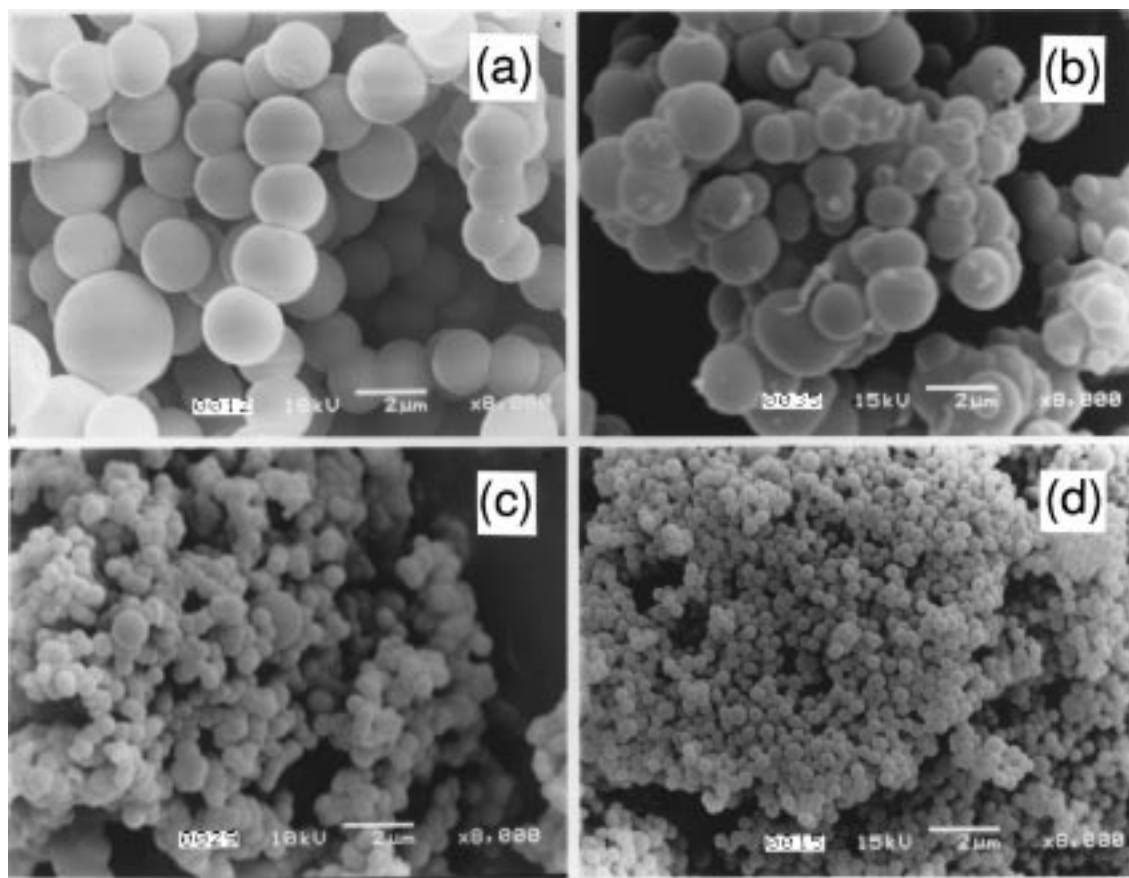


Figure 8. Scanning electron micrographs of PDVB particles synthesized in $scCO_2$ with varying amounts of stabilizer **2**: (a) 0%; (b) 0.25% w/w; (c) 1% w/w; (d) 3% w/w.

Table 6. Surface Area/Density Analysis of Polymers^a

monomer	BET surface area (m ² /g) ^b	total intrusion volume (cm ³ /g) ^c	intrusion due to interparticulate space (0.1–100 μm) (cm ³ /g) ^c	intrusion due to porosity/sample collapse (<0.1 μm) (cm ³ /g) ^c	absolute/skeletal density (g/cm ³) ^d
31	DVB55	<1	1.92	1.90	1.11
32	DVB55 ^e	14	3.60	3.58	1.12
33	TRM ^f	13	2.57	2.52	1.30
34	EDMA ^f	<1	1.43	1.41	1.54

^a Reaction conditions: 2.0 g of monomer(s), AIBN (8% w/w), 310 ± 15 bar, 65 °C, 24 h. ^b Measured by nitrogen adsorption (BET). ^c Measured by mercury porosimetry. ^d Measured by helium pycnometry. ^e 3% w/w stabilizer **2**. ^f 100% cross-linking monomer.

tent with previous studies on the dispersion polymerization of styrene in $scCO_2$, where it was shown that an increase in stabilizer concentration led to correspondingly smaller polymer particles.⁵⁰ It is interesting to note that stabilizer **2** worked effectively at quite low concentrations, despite the fact that the PMMA anchoring block was not designed for maximum compatibility with the dispersed polymer phase (i.e., a polystyrene anchoring segment might be expected to be more effective). It was rather difficult to classify the stabilized polymerizations because of the complex phase behavior. It seems likely that partial reaction of the DVB monomer was leading to emulsification of CO_2 -insoluble components early on in the polymerization. However, our original classification of these reactions as emulsion polymerizations⁵⁸ may be somewhat misleading since the pure, inhibited monomer has been shown to be soluble in CO_2 , even up to 65 °C. To what extent the phase behavior influences the size and morphology of the polymer particles is as yet unclear. It is quite likely that changes in certain basic experimental variables (e.g., heating rates, initiator concentrations) could have pronounced effects on product morphologies. Neverthe-

less, it is clear that the polymer particles formed by our route were much smaller and more regular than those formed in the absence of stabilizers. Indeed, the degree of uniformity in the particles compares very favorably with previous examples from the literature.^{46–55} As a consequence of their smaller size and lack of agglomeration, the particles formed in the presence of surfactant **2** formed milky white suspensions in certain organic solvents which were stable for several weeks.

Surface Area/Porosimetry Measurements. Scanning electron microscopy gave no visible indication of permanent macroporosity in any of the polymers described so far. This conclusion was supported by surface area analysis using nitrogen adsorption methods and by pore size analysis using mercury intrusion porosimetry (Table 6). All samples were found to have surface areas which were consistent with nonporous particles, the precise surface area being dependent on the average particle size. The polymers formed in the presence of stabilizer **2** had the lowest average particle diameters and therefore had the highest surface areas (Table 6, entry 32). The TRM polymer (entry 33) had a higher surface area than the EDMA polymer (entry 34),

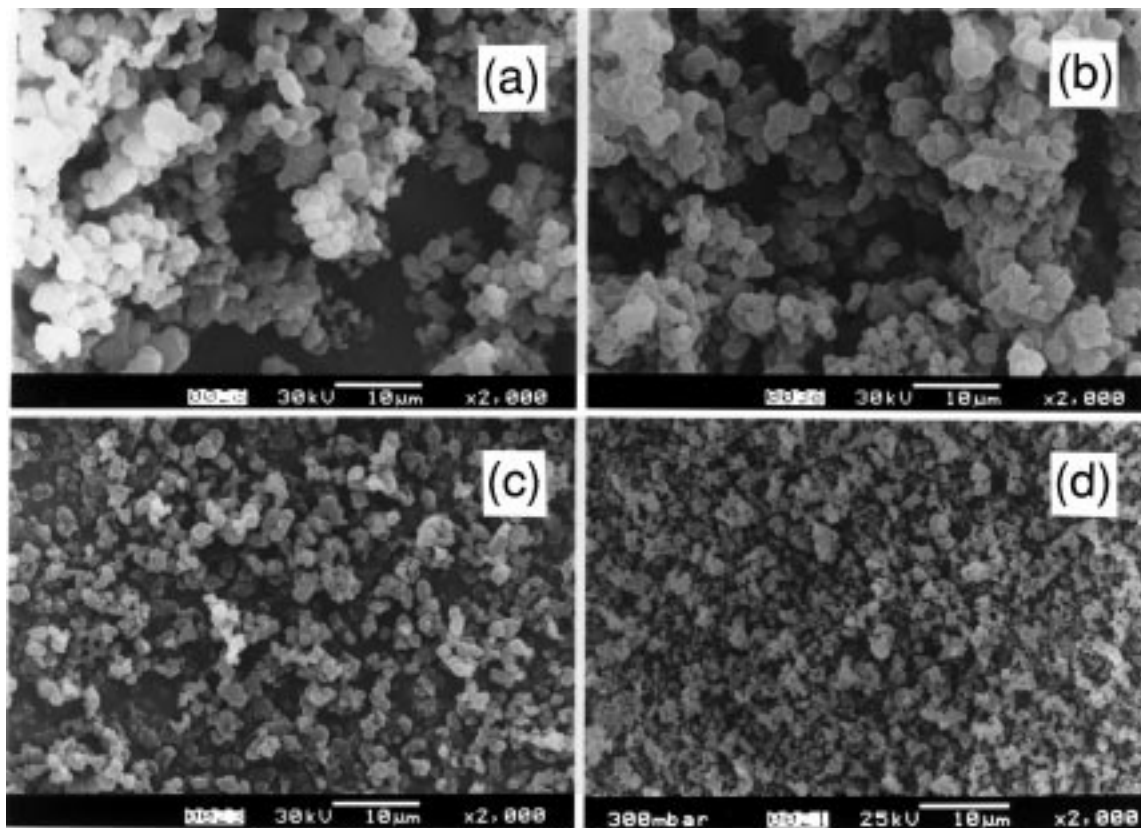
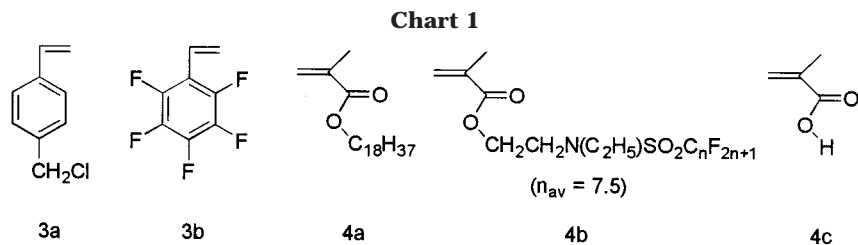


Figure 9. Scanning electron micrographs of highly cross-linked terpolymers synthesized in $scCO_2$: (a) DVB55 + **4a** (9:1 w/w); (b) DVB55 + **4b** (9:1 w/w); (c) DVB80 + **4c** (8:2 w/w); (d) DVB80 + **4c** (8:2 w/w) + 3% w/w stabilizer **2**.

presumably because it consisted of somewhat smaller primary particles (see Figure 7). Mercury intrusion porosimetry suggested that nearly all of the intrusion volume in the samples could be accounted for by relatively large interparticulate spaces in the size range 0.1–100 μm , again suggesting a nonporous structure. In all samples, only an extremely small fraction (<2%) of the total intrusion volume could be attributed to smaller gaps (or pores) of less than 0.1 μm (Table 6). This would seem to suggest that, under these particular conditions, CO_2 did not act as a good porogen for these polymers. Absolute polymer densities were in the range 1.10–1.55 g/cm^3 as measured by helium pycnometry. The absolute density for a polymer depended on the nature of the monomer, and was not found to be influenced by the reaction conditions.

Synthesis of Cross-Linked Functional Terpolymers in $scCO_2$. While the formation of unfunctionalized cross-linked resins is sometimes useful, many applications require resins which contain specific reactive or derivatizable functional groups. A range of cross-linked terpolymers was synthesized in $scCO_2$, incorporating a variety of reactive, derivatizable, or surface-active comonomers (Chart 1).

DVB55 was copolymerized in $scCO_2$ with 4-vinylbenzyl chloride, **3a** (Table 7, entry 35), and with pentafluorostyrene, **3b** (entry 36), to form cross-linked terpolymer particles with derivatizable functionalities. The resulting terpolymers were formed in high yields, however the particles were somewhat more agglomerated and irregular than those obtained from the polymerization of neat DVB55 or DVB80 under equivalent conditions.

This was possibly due to the lower effective cross-linker ratio or, perhaps more likely, a subtle change in phase behavior or kinetics of the polymerization. In an attempt to minimize particle aggregation and promote the formation of uniform microspherical particles, DVB55 was copolymerized with two surface-active monomers, octadecyl acrylate, **4a** (entry 37), and 2-(*N*-ethylperfluorooctanesulfonamido)ethyl methacrylate, **4b** (entry 38). Neither comonomer had a positive effect in preventing particle aggregation and, once again, the resulting terpolymers exhibited rather higher degrees of particle aggregation than those formed from neat DVB55 or DVB80 (Figure 9a,b). However, the particles containing comonomers **4a** and **4b** did exhibit quite different physical properties, particularly in the manner in which they dispersed in various organic solvents. Particles incorporating methacrylate **4b**, for example, were more readily dispersed in fluorinated solvents. The copolymerization of DVB80 and methacrylic acid (entry 39) led to small, irregular agglomerates by precipitation po-

Table 7. Synthesis of Cross-Linked Terpolymers in scCO_2^a

	comonomer	particle size ^b (μm)	yield (%)	anal. calcd/found	characteristic IR bands (cm^{-1})
35 ^c	3a	25.2 (58%) ^g	92	C: 89.6/87.6 H: 8.1/8.0 Cl: 2.3/2.7	3018, 2964, 1486, 1449
36 ^c	3b	31.0 (34%) ^g	90	C: 87.4/86.3 H: 7.6/7.6	3018, 2964, 1486, 1449
37 ^c	4a	33.0 (57%) ^g	90	C: 90.2/89.5 H: 8.8/8.7	2854 (CH_2), 1731 ($\text{C}=\text{O}$)
38 ^c	4b	32.3 (58%) ^g	90	C: 85.5/85.1 H: 7.7/7.8 N: 0.2/0.9 S: 0.5/0.4	1733 ($\text{C}=\text{O}$), 1240, 1213, 1154 ($\text{C}-\text{F}$)
39 ^d	4c	4.3 (28%) ^g	91	C: 84.8/80.4 H: 7.8/7.6	1700 ($\text{C}=\text{O}$)
40 ^{d,e}	4c	0.35 (14%) ^h	97	C: 84.8/82.1 H: 7.8/7.8	1700 ($\text{C}=\text{O}$)
41 ^{d,f}	4c	0.44 (7%) ^h	92	C: 84.1/80.4 H: 7.8/7.6 N: 0.5/1.5	1700 ($\text{C}=\text{O}$)

^a Reaction conditions: 2.0 g of monomer(s), AIBN (8% w/w), 310 \pm 15 bar, 65 $^\circ\text{C}$, 24 h. ^b Figure in parentheses = % coefficient of variation, CV, where $\text{CV} = (\sigma/D_n) \times 100$. σ = standard deviation of particle diameter (μm), D_n = mean particle diameter (μm). ^c 9:1 w/w DVB55:comonomer, effective % of DVB in monomer mixture = 49.5% w/w. ^d 8:2 w/w DVB80:4c, effective % of DVB in monomer mixture = 64% w/w. ^e 3% w/w stabilizer 2. ^f 3% w/w stabilizer 2 + 60 mg Disperse Red 1. ^g Measured by Multitrac particle size analyzer. ^h Measured by SEM.

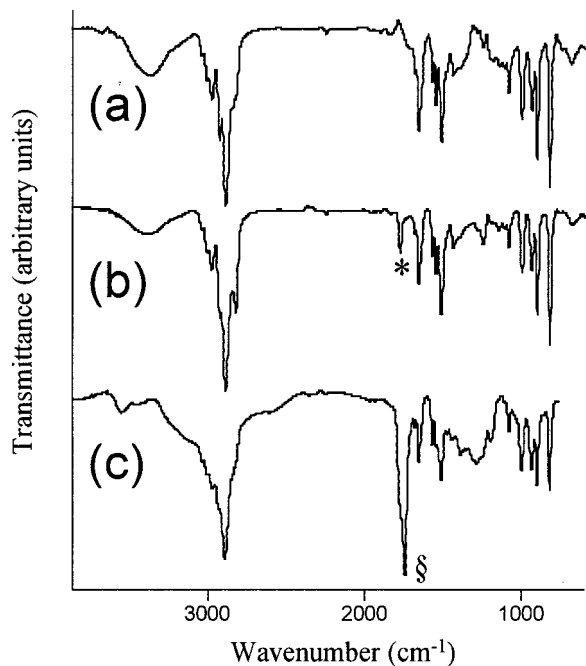


Figure 10. FTIR spectra (KBr disks) of cross-linked copolymers synthesized in scCO_2 : (a) DVB55; (b) DVB55 + 4a (9:1 w/w); (c) DVB80 + 4c (8:2 w/w). The symbols * and § denote the carbonyl absorptions arising from the incorporation of methacrylates 4a and 4c respectively.

lymerization (Figure 9c). The incorporation of functional monomers was confirmed by elemental analysis and, in the case of methacrylate comonomers, by IR spectroscopy (Figure 10).

In the presence of 3% w/w stabilizer 2, the copolymerization of DVB80 and methacrylic acid (entry 40) yielded regular microspheres which exhibited very little particle agglomeration (Figure 9d). This experiment was repeated in the presence of an organic dye, Disperse Red

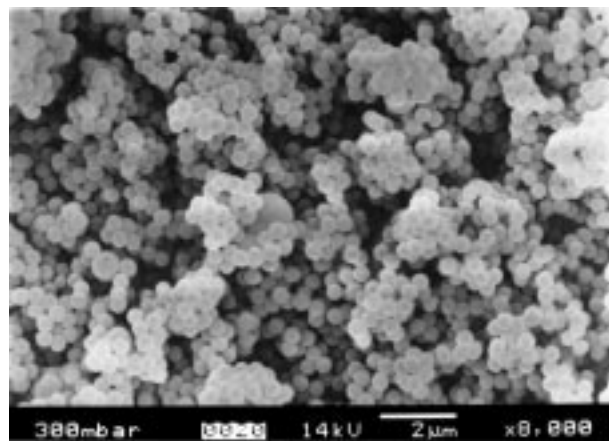
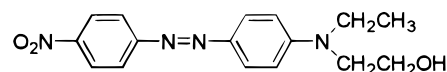


Figure 11. Scanning electron micrograph of cross-linked terpolymer microspheres incorporating Disperse Red 1 prepared by polymerization in scCO_2 in the presence of stabilizer 2.

1, which was miscible with the dispersed polymer phase but has very low solubility in CO_2 ⁶⁴ (entry 41).



Disperse Red 1

An opaque, pale red emulsion/dispersion of polymer and dye was formed during the reaction. At the end of the reaction, a pale red powder was isolated which was composed of uniform polymer microspheres (Figure 11). This sample was treated by Soxhlet extraction (toluene, 100 $^\circ\text{C}$, 72 h), and it was found that a significant fraction of the dye could be removed from the microspheres to leave an off-white powder. However, even with prolonged extraction, it was not possible to remove all of the color from the sample, suggesting that some of the dye was trapped permanently in the polymer matrix. When examined by SEM after the extraction process, the polymer morphology was found to be completely unchanged. These results suggest that our approach might be useful for the preparation of well-defined, molecularly imprinted polymer microspheres, particularly since CO_2 is a nonpolar solvent which, like perfluorocarbons, should not disrupt binding interactions between monomer and template.^{28,29} For applications such as molecular imprinting, the development of methods to introduce permanent porosity in the polymers would be advantageous.¹¹⁻¹³

Conclusions

Supercritical CO_2 is a versatile solvent alternative for the preparation of cross-linked polymers. The separation of products from solvent is simple, and polymers can be isolated as dry, free flowing powders directly from the reactor. Under certain specific conditions, it is possible to generate relatively uniform polymer microspheres (1–5 μm diameter) in the absence of surfactants. The use of a CO_2 -soluble polymeric stabilizer has been shown to promote the formation of smaller, well-defined, unagglomerated microspheres (<0.5 μm diameter). The techniques described here show considerable potential for the synthesis of a range of cross-linked functional materials, using scCO_2 as an environmentally benign solvent. Future work in this area will be directed toward the exploitation of the unique physical properties

of scCO₂ (i.e., plasticization effects, tunable density, and low viscosity) for the generation of novel cross-linked polymeric materials for specific applications.

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