Synthesis of cross-linked polymer microspheres in supercritical carbon dioxide

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SUMMARY: Herein we report the synthesis of highly cross-linked polymers based on divinylbenzene by heterogeneous polymerization in supercritical CO₂ (scCO₂). The polymers were isolated in the form of discrete microspheres (diameter = $1.5-5 \mu m$) in good yields ($\geq 90\%$), in the absence of any stabilizers. In the presence of a CO₂-soluble polymeric stabilizer, much smaller particles (diameter <0.5 μm) were formed in high yields ($\geq 95\%$) by emulsion polymerization in scCO₂.

Introduction

Supercritical carbon dioxide (scCO₂) is an attractive solvent for polymer chemistry because it is inexpensive, non-toxic, and non-flammable¹⁾. Unlike conventional liquid solvents, supercritical fluids are highly compressible and the density (and therefore solvent properties) can be tuned over a wide range by varying pressure. Moreover, scCO₂ reverts to the gaseous state upon depressurisation, greatly simplifying the separation of solvent from solute. DeSimone and others have shown that $scCO_2$ is a versatile solvent for both homogeneous and heterogeneous polymerizations of monomers with a single polymerizable functional group²⁻⁵⁾. In particular, CO₂-soluble polymeric stabilizers have been developed for free radical dispersion polymerization in scCO₂, thus allowing the formation of regular polymer microspheres by this method⁶⁻⁹⁾.

Cross-linked polymer resins are useful in a wide range of applications^{10–13)}, and it is often desirable to produce the resins in the form of regular microspheres. This is usually achieved by heterogeneous methods such as suspension, dispersion, or emulsion polymerization¹⁴). In suspension polymerization, the monomer, initiator, and porogen (if any) are immiscible with the continuous phase, which is usually water. Typically, water-soluble stabilizers are used to prevent particle coalescence, and polymers are isolated as spherical beads in the size range 5-800 µm (or greater). Spherical latex particles synthesized by oil/water emulsion polymerization tend to fall in the size range 20-600 nm (in the presence of amphiphilic surfactants) or $1-10 \,\mu\text{m}$ (in the absence of surfactants). In this case, monomers are generally oil-soluble, although it is also possible to copolymerize water-soluble monomers. In precipitation polymerization, the monomer(s) and initiator are soluble in the continuous phase and the polymer precipitates as it is formed, often as an undeScheme 1:

a
$$HBN, scCO_2$$

T = 65 °C, P = 310 bar Cross-Linked Polymer

fined, agglomerated powder. Dispersion polymerization is also characterised by initially homogeneous conditions, however the resulting insoluble polymer is stabilized as a colloid by use of appropriate surfactants to give spherical polymer particles in the size range 100 nm to 10 μ m. In stabilized reactions, residual surfactant on particle surfaces may sometimes impair the performance properties of the resulting polymers.

We report here the first synthesis of well defined crosslinked polymer microspheres in scCO₂, both with and without the use of stabilizers (Scheme 1).

Relatively uniform poly(divinylbenzene) (PDVB) microspheres were formed by unstabilized suspension polymerization in the absence of surfactants, because the particles were stabilized against coagulation by their rigid, cross-linked surfaces¹⁵). In the presence of a CO₂-soluble polymeric stabilizer, much smaller PDVB particles with narrow particle size distributions were prepared by emulsion polymerization. Carbon dioxide behaved as an inert, non-toxic, and easily separable solvent in the polymerization process.

Experimental part

Materials and equipment

Monomer mixtures containing divinylbenzene (DVB; 1,3 and 1,4 isomers) and ethylvinylbenzene (EVB; 1,3 and 1,4 isomers) were purchased from Aldrich as DVB55 and DVB80 (55 wt.-% DVB and 80 wt.-% DVB, respectively).

Monomer mixtures were passed down a neutral alumina column to remove inhibitor before use. 2,2'-Azoisobutyronitrile (AIBN, Aldrich) was recrystallized twice from methanol. Styrene was purchased from Aldrich and purified by vacuum distillation. High pressure reactions were carried out in a 10 mL stainless steel reactor, equipped with a sapphire window for observation of phase behavior¹⁶. A PTFE-coated magnetic stir bar was used to mix the contents of the reactor.

Stabilizer preparation

A CO₂-soluble diblock copolymer stabilizer, **1** (Scheme 2), was prepared by a modified screened anionic polymerization procedure, as described previously¹⁶).

Scheme 2:



The stabilizer consisted of a CO₂-soluble fluorinated poly(methacrylate) (PFMA) block, and a CO₂-insoluble poly(methyl methacrylate) (PMMA) anchoring block. The number average molecular weight (\overline{M}_n) of the PMMA block was determined with a Knauer gel permeation chromatograph (GPC) using PL Gel 30 cm 5 µm mixed C column at 30 °C, running in chloroform at 1 cm³ · min⁻¹ with polystyrene ($\overline{M}_n = 600-10^6$) standards. Characterisation data for 1:

IR (KBr): 1734 cm⁻¹ (s; C=O).

¹H NMR (CDCl₃) [{M} = PMMA block, {F} = PFMA block]: $\delta = 4.60-3.80$ (br s, 2H{F}, CH₂), 3.61 (s, 3H{M}, CO₂CH₃), 2.70-2.20 (br s, 2H{F}, CH₂), 2.15-1.7 (br m, 2H{M}, 2H{F}, CH₂) and 1.22-0.8 (br m, 3H{M}, 3H{F}, α -CH₃).

 \overline{M}_n (PMMA block) = 14000. From ¹H NMR integrals, the mole ratio, *x*:*y*, of the PMMA block (CO₂CH₃, δ = 3.61) to the PFMA block (CO₂CH₂-, δ = 4.60–3.80) was 1:1. Calculated \overline{M}_n (1) = 74500.

Polymerizations and analytical procedures

The reactor was charged with monomer(s) (2.0 g), AIBN (0.16 g) as initiator, and stabilizer 1 (60 mg, if included), before purging with a slow flow of CO₂ for 20 min. The reactor was then pressurized with liquid CO₂ to around 80 bar, stirring commenced, and the reaction mixture heated to the desired temperature and pressure (65 °C, 310 ± 15 bar). In the absence of added stabilizer, much of the monomer mixture was insoluble in the continuous phase under these conditions, and the reaction proceeded as an unstabilised suspension polymerization^{17, 18}). The supercritical solution was initially heterogeneous, consisting of a cloudy suspension of undissolved monomer in CO₂. With time (\approx 90 min), a white solid precipitate formed on the walls and window of the reactor. In the presence of stabilizer 1 (3 wt.-% with respect to monomer), the phase behavior was quite different. Immediately after pressurisation, an opaque, white, uniform mixture was obtained, resembling an emulsion of monomer in CO₂. This appearance persisted throughout the reaction, and afforded polymer particles in the size range $0.25-0.5 \,\mu\text{m}$. The phase behavior was consistent with an emulsion polymerization mechanism¹⁴⁾. In both cases, polymerizations were continued with stirring overnight. At the end of each reaction, the system was cooled to ambient temperature and the CO₂ was vented. The dry polymer (≈ 2 g) was removed from the reactor and purified as described previously¹⁵. Thermogravimetric analysis was carried out with a Perkin-Elmer TGA 7 in a nitrogen atmosphere (30–800°C, heating rate 20° C · min⁻¹). Polymer morphologies were investigated with a JEOL JSM-5800 LV scanning electron microscope. Polymer samples were mounted on aluminum studs and were sputter coated with 10-20 nm gold before analysis. Where discrete polymer microspheres were observed (Tab. 1, entries 3-5), particle sizes and particle size distributions were calculated from electron micrographs (≈300 particle diameters measured).

Results and discussion

The results of some polymerizations in $scCO_2$ involving DVB as the cross-linking agent are shown in Tab. 1. In

Entry	wt% DVB ^{a)}	wt% EVB ^{a)}	wt% styrene ^{a)}	wt% 1 ^{b)}	$\frac{\text{Particle size}^{c)}}{\mu m}$	Polymer morphology	Phase behavior ^{d)}	$\frac{\text{Yield}}{\%}$
1	0	0	100	0	e)	agglomerate	Р	56
2	55	45	0	0	1.5 - 5	powder	US	89
3	80	20	0	0	2.40 (21%)	microspheres	US	92
4	55	45	0	3	0.41 (16%)	microspheres	Е	96
5	80	20	0	3	0.29 (18%)	microspheres	Е	95

Tab. 1. Synthesis of cross-linked polymers in scCO₂

^{a)} wt.-% based on total monomer weight (2.0 g).

^{b)} wt.-% stabilizer **1** with respect to total monomer weight.

^{c)} Determined by scanning electron microscopy. Figure in parentheses = % coefficient of variation, *CV*, where $CV = (\sigma/D_n) \times 100$; σ = standard deviation of particle diameter in μ m, D_n = mean particle diameter in μ m.

^{d)} P = precipitation, US = unstabilized suspension, E = emulsion.

^{e)} Agglomerated polymer; no particles formed. $\overline{M}_{w} = 11700$, $\overline{M}_{w}/\overline{M}_{n} = 8.3$.



Fig. 1. Scanning electron micrographs of PDVB microspheres synthesized in $scCO_2$ in the absence of any stabilizer: (a) 55 wt.-% DVB; (b) 80 wt.-% DVB. Reaction conditions: 65 °C, 310 ± 15 bar, 24 h

the absence of a cross-linker, the unstabilized precipitation polymerization of styrene (which is soluble in scCO₂ under these conditions) gave low molecular weight polystyrene in poor yield (entry 1), as has been described previously^{8,9)}. However, the polymerizations of DVB55 (entry 2) and DVB80 (entry 3) led to cross-linked PDVB polymers which were isolated in high yields directly from the reactor as dry, white, free-flowing powders. When the materials were examined by scanning electron microscopy, it was found that the polymers existed in the form of relatively uniform microspheres (diameter = 1.5 -5 µm), even though no stabilizers were used (Fig. 1a, b). This is consistent with studies by Li and Stöver¹⁵, who found that highly cross-linked PDVB microspheres could be formed by precipitation polymerization of DVB mixtures in acetonitrile. In their work, it was assumed that the particle formation and growth mechanism was similar to that of dispersion polymerization, except that the particles were stabilized against coagulation by their rigid, cross-linked surfaces rather than by added stabilizers.

We also attribute the inhibition of agglomeration in our more highly cross-linked samples to the rigidity of the PDVB microspheres. When DVB55 was used (Tab. 1,



Fig. 2. Thermogravimetric analysis for PDVB microspheres shown in Fig. 1 a

entry 2), spherical microparticles were generated, however a certain degree of agglomeration was observed (Fig. 1a). At higher cross-linker ratios (Tab. 1, entry 3), however, relatively uniform and discrete microspheres were obtained (Fig. 1b). Li and Stöver reported a precipitation polymerization (i.e., initiator and monomer were initially soluble in acetonitrile)¹⁵; however, we observed that the DVB monomer mixture was largely insoluble in scCO₂ from the start of the reaction. The initiator, AIBN, was soluble in both the monomer phase and the CO₂ continuous phase, thus making the precise classification of the reactions as either emulsion or suspension polymerizations somewhat difficult. Some authors have suggested that particle size may be one criterion for classification, in as much as suspension polymerization tends to lead to particles greater than 1 µm in size^{14, 17, 18}. Based on the mechanism and observed phase behavior of the unstabilized polymerizations in scCO₂, we prefer the term "unstabilized suspension polymerization". The crosslinked particles had sizes similar to polystyrene particles formed by dispersion polymerization in scCO₂ in the presence of amphiphilic diblock copolymer surfactants^{8,9}, although there was somewhat more evidence of particle agglomeration, particularly in less highly cross-linked samples. Thermal analysis showed the cross-linked resins to have high thermal stability; almost no thermal decomposition was observed below 400 °C (Fig. 2).

The phase behavior during polymerization in the presence of 3 wt.-% stabilizer **1** was quite different (Tab. 1, entries 4 + 5). Immediately upon addition of CO₂, an opaque, white emulsion of monomer in CO₂ was formed, which persisted throughout the polymerization reaction¹⁹. The cross-linked particles generated from these polymerizations were much smaller than those formed in the absence of the stabilizer (Fig. 3a). Moreover, the particle size distribution was relatively narrow (Fig. 3b) and there was much less evidence of particle agglomeration.



Fig. 3. (a) PDVB microspheres formed in presence of 3 wt.-% stabilizer **1** (Tab. 1, entry 4); (b) Graph showing distribution of particle sizes for sample shown in Fig. 3 a

The cross-linked polymers were completely insoluble in all solvents tested, however they were readily dispersed in most common organic media (except pure water) to form milky white suspensions. In the case of the larger, unstabilized particles (entries 2 + 3), the suspensions tended to settle out within a few hours. The smaller particles, however, which had been formed by emulsion polymerization (entries 4 + 5) formed suspensions in certain organic solvents which were stable for several weeks.

The key advantages of our preparation methods are that no toxic, volatile organic compounds are used as solvents in the polymerizations, the solvent and solute are very easily separated, and that regular cross-linked microspheres of various sizes can be formed both with and without added stabilizers. This novel approach should also allow the synthesis of cross-linked polymer particles containing water sensitive or water-soluble comonomers, which are often difficult to prepare by more standard suspension/emulsion polymerization techniques²⁰). Future work will focus on the use of scCO₂ as a solvent for the preparation of cross-linked terpolymers containing specific reactive functional groups for specialist applications.

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