Poly(divinylbenzene) Microspheres as an Intermediate Morphology between Microgel, Macrogel, and Coagulum in Cross-Linking Precipitation Polymerization

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ABSTRACT: Precipitation copolymerizations of mixtures of divinylbenzene-55 (DVB55) and 4-methylstyrene at total monomer loadings of 4 vol % were conducted in solvent mixtures comprised of mixtures of methyl ethyl ketone and heptane. The experimental compositions hence formed a two-dimensional matrix where the actual DVB content varied from 0 to 55% and the solvent composition varied from 0 to 100 vol % MEK. Four distinct polymer morphologies including microspheres, microgels (and soluble polymer), macrogel, and coagulum were observed and are reported in form of a morphology map superimposed on the above compositional map. The structures of these four polymer architectures are described, and the effects of both DVB concentration and solvency on the transitions between morphology domains are discussed. The portion of reaction volume occupied by the polymer formed decreases with both decreasing solvency and increasing DVB concentration. These results indicate that the microspheres are formed, in part, by an internal contraction which is caused by both the marginal solvency of the continuous phase and the cross-linking of the polymer network. This contraction is likely progressive, supporting the presence of a lightly cross-linked corona around the microspheres which acts as an in-situ steric stabilizer layer.

Introduction

The precise control of polymeric architecture has led to many applications for materials such as microspheres, microgels, and macrogels. Cross-linked microspheres serve as key components in Merrifield's polymer-supported peptide synthesis[1] and as stationary phases in chromatography.[2−5] Microgels have been used both as coatings[6] and as substrates for biomedical and diagnostic purposes.[7] Macrogels have been used as monolithic stationary phases in liquid chromatography.[8,9] Dusek and co-workers carried out pioneering work in the area of polymer network morphology as affected by diluents.[10]

Microspheres, microgels, and macrogels, all of which can be prepared by free-radical copolymerization of monovinyl and divinyl monomers in suitable solvents, are expected to have some similarities in their formation mechanisms. This paper describes the formation of poly(divinylbenzene) microspheres, microgels, and macrogels under conditions varying only in solvent composition and cross-linker level and focuses on the relations between these important network morphologies.

The preparation of functionalized, porous, and core−shell microspheres by precipitation polymerization has been an interest in our laboratory for several years. This method is particularly interesting because monodisperse particles can be synthesized without adding steric or ionic stabilizers to the reaction mixture.[11−14] Thus, the particle formation mechanisms are fundamentally different from those of the other heterogeneous polymerization techniques, namely, dispersion, emulsion, and suspension.[15] The formation processes of particular interest are nucleation, growth, desolvation, and stabilization.

Recently, we have established the particle growth mechanism in the precipitation polymerization of divinylbenzene (DVB). In this system, DVB-55 is polymerized at monomer loadings below 5 vol % in acetonitrile, or mixtures of acetonitrile and toluene, by free radical polymerization using AIBN as an initiator.[11,13,14] We found that the particles increase in size by a reactive growth mechanism where oligomeric radicals are captured from solution by reaction with surface double bonds on existing particles. We proposed that concurrent with this ongoing capture of oligomers on the surface there is a continuous internal desolvation of the resulting surface gel layer to form the dense, final microspheres.[16] We suggested that the most important role of the surface gel is to act as a steric stabilizing layer which prevents the particles from coagulating.

Naka and co-workers studied a related precipitation polymerization and suggested microsphere formation to be a special case of gelation. They polymerized diethylene glycol dimethacrylate (DEGMA) by γ-irradiation in good solvents, capable of swelling the forming polymer.[17−19] Naka's system is analogous to the present DVB system, in that a cross-linking comonomer is required to form discrete microspheres, while low total monomer loadings are required to prevent macroscopic gelation. Naka suggested that since discrete microspheres are formed in the presence of good solvents in their system, there must be a driving force causing the collapse of the network against the swelling force of the good solvent present. Specifically, they proposed cross-linking to be responsible for collapse of the polymer into dense particles.

Thus, microsphere formation appears to be a special case in the polymerization of cross-linking monomers, where morphologies such as microgels and macrogels are more commonly observed. Microgels are commonly formed when cross-linking monomers are polymerized in dilute solution under good solvency conditions. In this case, intramolecular reactions are favored due to radical

chain ends having a higher local concentration of pendent reactive groups from their own chain in comparison to those from other macromolecules.[20] Thus, below a critical threshold of monomer loading macrogelation is avoided. Antonietti et al. have suggested this transition has some characteristics of a phase transition.[21] The classic example is the synthesis of styrene–DVB microgels first prepared by Staudinger and Husemann. Polymerizing pure DVB in benzene at concentrations of less than 8 vol % monomer produced only microgel whereas at higher concentrations macrogelation was observed.

Microgel particles prepared by the aforementioned technique have an inhomogeneous structure, consisting of a strongly cross-linked core embedded in a lightly cross-linked corona.[20] There are several reasons for this inhomogeneity: (i) divinyl monomers are often more reactive than their monovinyl counterparts and, therefore, are incorporated into the structure at an earlier stage of the reaction; (ii) the microgel core is older than the outer surface and, thus, has more time to cross-link.[20] Graham et al. have suggested that a lightly cross-linked outer surface acts as a steric stabilizing layer in the presence of better than Θ solvents and in turn prevents aggregation of the colloidal gels.[22,23]

In the past, much of the research on macrogels has focused on predicting when macrogelation occurs during the polymerization of cross-linking monomers. Renewed interest in this morphology has developed as a result of the synthesis of one-step chromatographic column packings. Sellergren has reported the preparation of molecularly imprinted polymers (MIPS) where ethylene glycol dimethyl acrylate, acrylic acid, a diluent, and a template molecule are mixed within glass tubes which upon polymerization form space-filling macrogels that can be attached to an HPLC for evaluation of their ability to recognize the template molecule.[24]

The purpose of this article is to define how microspheres produced in cross-linking precipitation polymerizations are related to the more common and competing morphologies of microgel, macrogel, and coagulum. For a constant monomer loading of 4 vol % both, solvency of the continuous media and concentration of the cross-linking monomer are expected to influence the polymer morphology. The effects of these two parameters on microsphere formation are reported here.

Experimental Section

Materials. Divinylbenzene-55 was obtained as a technical grade mixture containing 55% of the para- and meta-divinyl isomers and 45% of the para- and meta-ethylvinyl isomers. The composition of this mixture was confirmed by gas chromatography prior to use. DVB-55 and the comonomer 4-methylstyrene were purchased from Aldrich Chemical Co. and used as received. In earlier experiments the inhibitor, 4-*tert*-butyl catechol, was removed from the monomers by passing them through silica columns, and it was determined that this had no effect on the polymerizations. The initiator 2,2′-azobis-(2-methylpropionitrile) (AIBN) was purchased from DuPont and recrystallized from methanol prior to use. The solvents for the polymerizations, methyl ethyl ketone (MEK) and heptane (HEP), were purchased from Caledon Chemical, and they were used as received.

Sample Preparation. In addition to commercial DVB-55, samples of DVB-50, -45, -40, -35, -30, -25, -20, -15, and -10, where the number represents the percentage of cross-linking monomer in the mixture, were prepared by diluting DVB-55 with 4-methylstyrene. Master batches of these monomer

mixtures were prepared according to the following equation:

$$V_{DVB55} = xV_T/55 \qquad (1)$$

were V_{DVB55} is the volume of DVB-55 to be diluted, x is the desired cross-linker content of the monomer mixture (i.e., DVB-x), and V_T is the total volume of the master batch. The volume of 4-methylstyrene, V_{4MeS}, added to dilute the DVB-55 was then calculated as follows:

$$V_{4MeS} = V_T - V_{DVB55} \qquad (2)$$

For example, a 100 mL master batch of DVB-40 would contain 72.7 mL of DVB-55 and 27.3 mL of 4-methylstyrene. AIBN, 1.824 g (111.1 mmol), was added to each monomer master batch just prior to dispensing to the polymerization vials. All samples were prepared in 20 mL Wheaton scintillation vials. For each sample, a 0.80 mL aliquot of the monomer mixture was diluted to a total volume of 20 mL using MEK and heptane. The ratio of MEK to heptane was varied from neat MEK to neat heptane. The polymerizations were conducted at a constant temperature of 70 °C in a reactor that provided gentle agitation by rolling the scintillation vials horizontally at 4 rpm. All samples reported here correspond to 24 h of polymerization.

Polymer Characterization. Following polymerization, the soluble polymer was separated from the insoluble fraction by vacuum filtration, and the insoluble residue was washed extensively with THF. Excess solvent was removed from the soluble polymer by rotatory evaporation under reduced pressure. Both fractions were then dried under vacuum at room temperature for 48 h. The molecular weights of both the linear and microgel polymers were characterized using a Waters 590 programmable pump connected to Ultrastryragel columns using a Waters 410 differential refractometer as a detector, tetrahydrofuran as solvent at a flow rate of 1 mL/min, and narrow disperse polystyrene as standards. The morphologies of the microspheres, macrogels, and particles were examined using a Phillips ElectroScan 2020 environmental scanning electron microscope (ESEM). The diameters of the microspheres were measured using a Coulter Multisizer II fitted with a 50 μm aperture tube and Isoton II as the conductive electrolyte solution. The sizes of polymer microgels were measured using a polarization intensity diffraction system (PIDS) (Coulter LS230) where THF was used as the dispersing solvent.

Macrogels were placed in large containers filled with THF to separated from any soluble polymers from the insoluble macrogel. The wash solvent was changed three times during the course of 1 week, at which point the volumes of the THF swollen macrogel cylinders were calculated by measuring their dimensions. The macrogels were then allowed to dry to constant weight and their new dry volumes recorded. Particles and microspheres were resuspended in THF, in 20 mL scintillation vials, and then allowed to settle over the course of 1 week, at which point the volume of the layer of settled particles was measured.

Results and Discussion

Polymer Morphology Map. Four distinct morphologies were observed in the cross-linking copolymerization of DVB and 4-methylstyrene conducted in different solvent compositions and at low monomer loadings. Figure 1 indicates both the solvency and cross-linking requirements for the preparation of soluble polymers (including microgels), macrogels, microspheres, and coagulum, and each of these architectures will be discussed in detail in the following sections. These morphologies all correspond to samples obtained after 24 h of polymerization.

Effect of Solvent Composition on Poly(DVB-*x*) Morphology. First, we will consider the changes in poly(DVB-*x*) structure observed as a result of varying
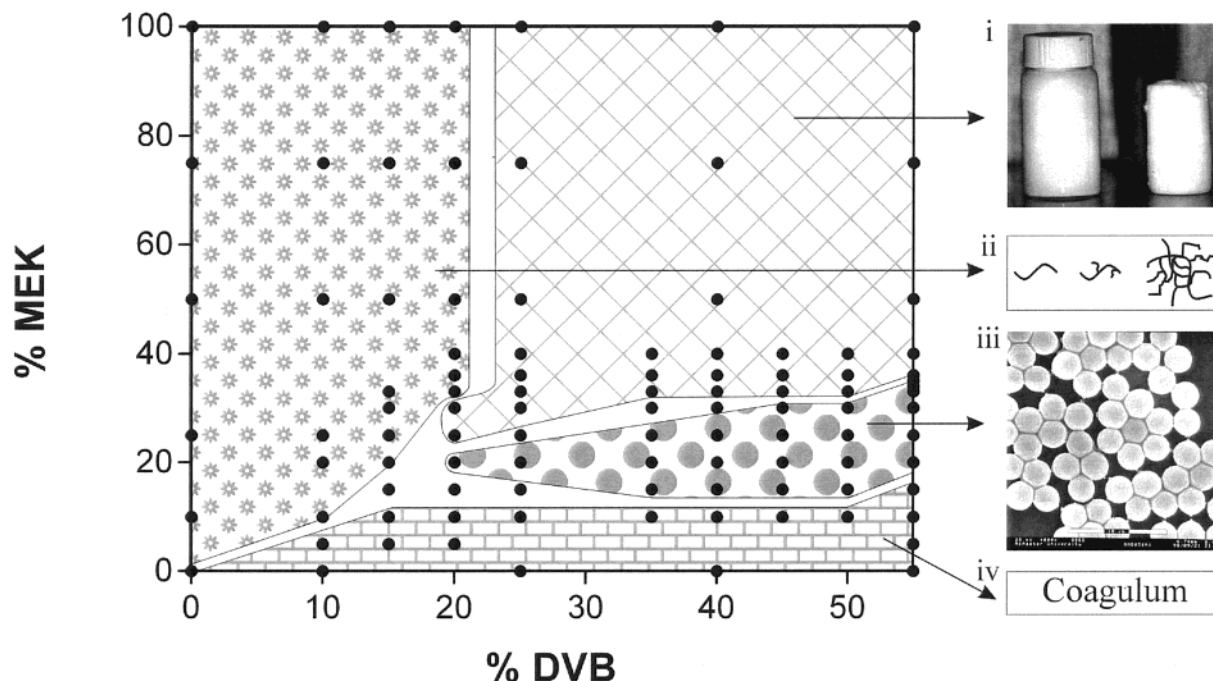
Figure 1. Morphology map for the polymerizations reported here. The 4 vol % monomer feed contained from 0 to 55% DVB. The solvent compositions for the polymerizations were varied from neat MEK to neat heptane. Four distinct morphologies are represented: (i) space-filling macrogels; (ii) soluble polymer which includes linear, branched, and microgel structures; (iii) microspheres; (iv) coagulum. The morphologies shown here correspond to samples obtained after 24 h of polymeirzation.

the solvent composition from neat MEK, a good solvent, to neat heptane, a poor solvent. Space-filling macrogels are obtained at high MEK and high DVB levels. Under these conditions the polymer network forms in a swollen state and thus fills the entire reaction volume. Polymerizing DVB-55 in neat MEK produces an opaque space-filling macrogel that is smooth to the limits of resolution by electron microscopy. Decreasing the solvency of the continuous phase to 36 vol % MEK by dilution with heptane still produces an opaque space-filling macrogel, but scanning electron microscopy of this macrogel in the dry state indicates a heterogeneous structure comprised of small interconnected nodules of approximately 100–200 nm (Figure 2).

Transmission electron microscopy of sections microtomed from the same macrogel, swollen and embedded in low-viscosity epoxy resin, showed similar nodules of 100–200 nm. No connecting "fibrils" or gel bridges were observed, likely due to their low contrast with the epoxy. Hence, this macrogel, formed near the morphology transition to microspheres, is comprised of strongly cross-linked, nonswellable nodules interconnected by regions of lower cross-link density. In good solvents, the nodules do not change their size significantly whereas the interconnecting fibrils are able to swell and extend.

In polymerizations carried out at 35 and 34% MEK, scanning electron microscopy images revealed rough particles of irregular shapes with dry diameters of 200–400 nm (Figure 3).

In the range of 33–20 vol % MEK, discrete microspheres were formed. Figure 4 shows the microspheres prepared with 33 vol % MEK. They have rough surfaces and diameters of 1.8 ± 0.5 μm, and their interstitial volume contains polymer that could not be removed even after successive centrifugations from tetrahydrofuran. We believe this to be a lightly cross-linked polymer gel covalently bonded to the surface of the
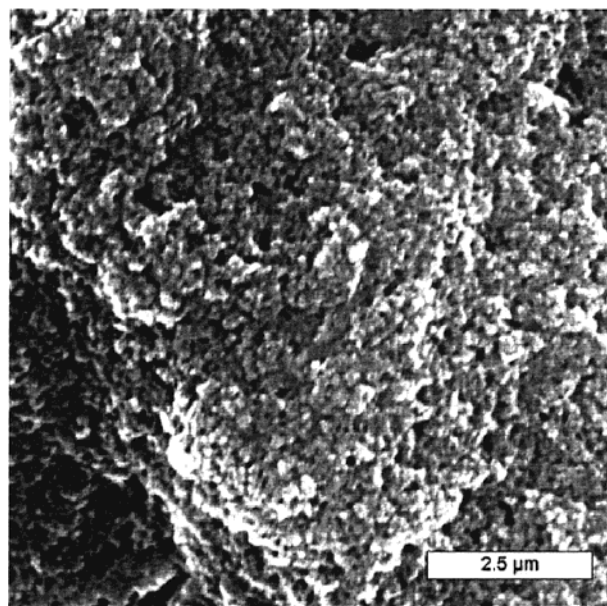

Figure 2. Electron micrograph of a space-filling macrogel in the dry state prepared from 4 vol % DVB-55 in a mixture of 40:60 MEK:heptane.
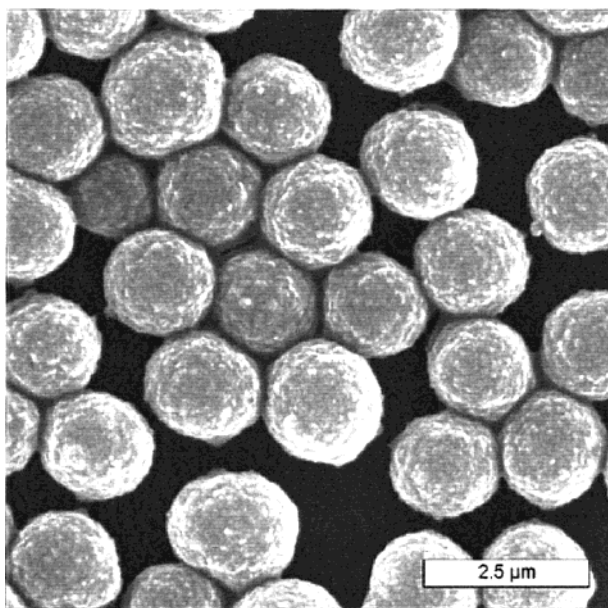
particles and that this surface gel prevents particle aggregation by an autosteric stabilization mechanism.

Decreasing the concentration of MEK to 25 vol % led to an increase in the size of the microspheres to 3.8 ± 0.3 μm and a decrease in the roughness of the particle surface (Figure 5). At 20 vol % MEK the particle diameter increased further to 4.6 ± 0.4 μm (Figure 6).

MEK concentrations of 15 vol % or below led to the formation of coagulum. Apparently, the solvency of the continuous medium is now so poor that the forming polymer phase separates from solution to coat the inside of the reaction vessel. This coating does not dissolve or swell significantly in organic solvents such as THF,
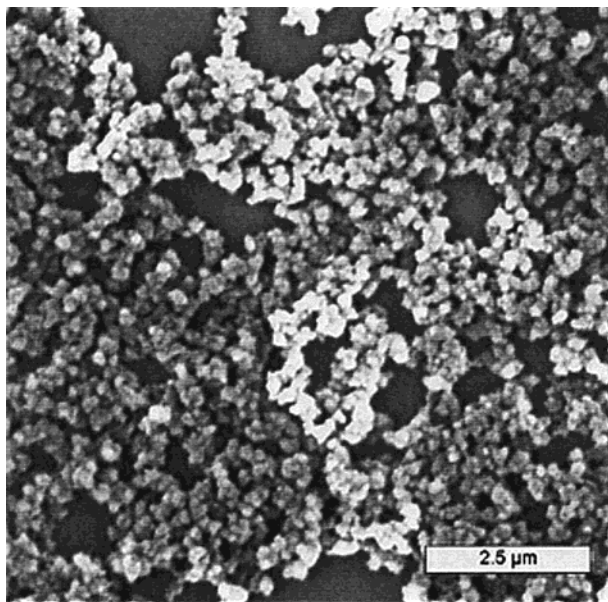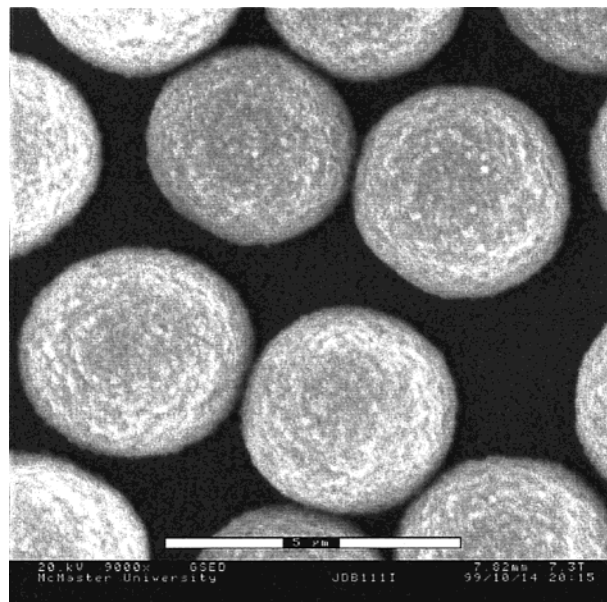
Figure 3. Electron micrograph of irregular shaped particles in the dry state prepared from 4 vol % DVB-55 in a mixture of 35:65 MEK:heptane.
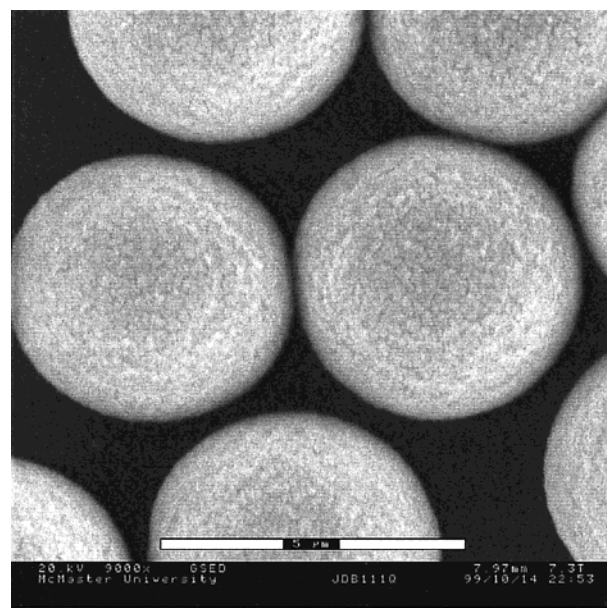

Figure 5. Electron micrograph of microspheres in the dry state prepared from 4 vol % DVB-55 in a mixture of 25:75 MEK:heptane. The scale bar is 5 μm in length.

Figure 4. Electron micrograph of microspheres in the dry state prepared from 4 vol % DVB-55 in a mixture of 33:67 MEK:heptane.


Figure 6. Electron micrograph of microspheres in the dry state prepared from 4 vol % DVB-55 in a mixture of 20:80 MEK:heptane. The scale bar is 5 μm in length.

suggesting that the polymer is highly cross-linked in its collapsed state.

The morphological transitions from space-filling macrogel to microspheres, and from microspheres to coagulum, take place over narrow ranges in the solvent composition. The resulting intermediate morphologies might bridge the gap between traditional microsphere packings and the more recent monolithic columns. For example, in a parallel series of experiments DVB-55 at 4% monomer loading was polymerized in 87% THF and 13% water to give a space-filling macrogel comprised of interconnected microspheres. Heterogeneous macrogels having hybrid morphologies such as this could prove very useful in the synthesis of single step chromatographic column packings combining high flow rates with high surface area.

Effect of Cross-Linker Concentration on Poly-(DVB-*x*) Morphology. The effect of cross-linking monomer concentration will be discussed for a series of polymerizations carried out at a constant MEK solvent fraction of 25%. In the absence of the cross-linking monomer, linear poly(4-methylstyrene) with $\bar{M}_\text{n}$ of 3.0 $\times$ 10^3 g/mol and a polydispersity index, PI, of 1.6 was produced at a conversion of 18% (Table 1). This low molecular weight is due to the low monomer loading of 4 vol %, where the propagating chains terminate before they are able to add many monomer units. In the presence of 10% cross-linker, DVB-10, a clear polymer solution with an apparent $\bar{M}_\text{n}$ of 7.6 $\times$ 10^3 g/mol and a PI of 2.0 was formed with a conversion of 20%. A turbid mixture was observed following the polymerization of DVB-15. This sample remained turbid even after the

Table 1. Effect of Cross-Linking Monomer Content on Polymer Morphology, Total Conversion, Conversion to Insoluble and Soluble Polymer, and Molecular Weight of the Soluble Fraction[a]

sample	polymer morphology	yield total (%)	yield insoluble (%)	yield soluble (%)	$\bar{M}_n$ (1 × 10³ g/mol)	$\bar{M}_w$ (1 × 10³ g/mol)	PI
DVB-0	linear	18	0	18	3.0	4.7	1.6
DVB-10	microgel	20	0	20	7.6	15.0	2.0
DVB-25	mixture	32	24	8	4.4	21.5	4.9
DVB-40	microspheres	47	43	4	2.5	33.6	13.4
DVB-55	microspheres	64	61	3	2.5	8.6	3.4

[a] These samples consisted of 4 vol % monomer in 25:75 mixtures of MEK:heptane with 2 wt % AIBN.
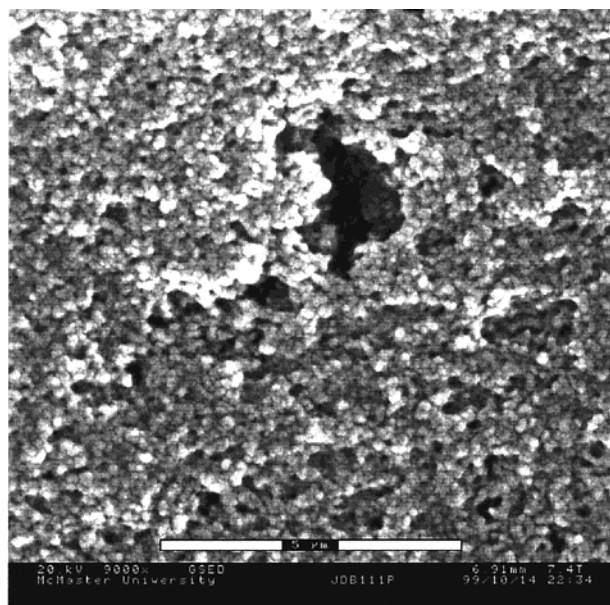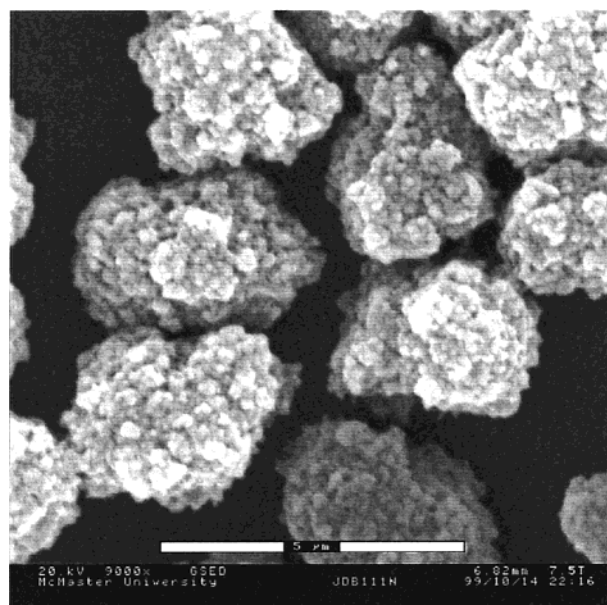

Figure 7. Electron micrograph of the space-filling macrogel in the dry state prepared from 4 vol % DVB-20 in a mixture of 25:75 MEK:heptane. The scale bar is 5 μm in length.

Figure 8. Electron micrograph of irregular-shaped particles in the dry state prepared from 4 vol % DVB-25 in a mixture of 25:75 MEK:heptane. The scale bar is 5 μm in length.

addition of excess THF, even though the sample could be precipitated into methanol. The size of these particles was determined to be 110 ± 10 nm in THF as measured using a Coulter LS230. These particles are analogous to the microgels first prepared by Staudinger and Husemann[25,26] and more recently by Antonietti,[21,27,28] Graham,[23] and expertly reviewed by Funke.[7] Macrogelation of the reaction mixture was observed at DVB-20, and its structure consisted of interconnected nodules with sizes of approximately 100 nm (Figure 7).

Further increasing the divinylbenzene content to DVB-25 resulted in a 32% combined yield which was comprised of both 8% soluble and 24% insoluble material. The soluble fraction had an apparent $\bar{M}_n$ of 4.4 × 10³ g/mol and a PI of 4.9. The insoluble fraction consisted of irregular shaped particles individually dispersed throughout the reaction mixture (Figure 8).

The physical appearance of these particles is very similar to that of the DVB-20 macrogel; however, in this case the particles are not covalently linked together into a single cohesive mass. At DVB concentrations above 35% and at this solvent composition, microspheres are the predominant morphology. Figure 9 shows an electron micrograph of the 3.1 ± 0.8 μm microspheres prepared at DVB-40, in a yield of 43%. The soluble portion isolated from this reaction mixture had a $\bar{M}_n$ of 2.5 × 10³ g/mol with a PI of 13.4 and was formed at a yield of 4% for a total yield of 47%.

The surface of the microspheres continues to become smoother as the concentration of DVB in the monomer mixture is increased. Polymerization of DVB-55 resulted
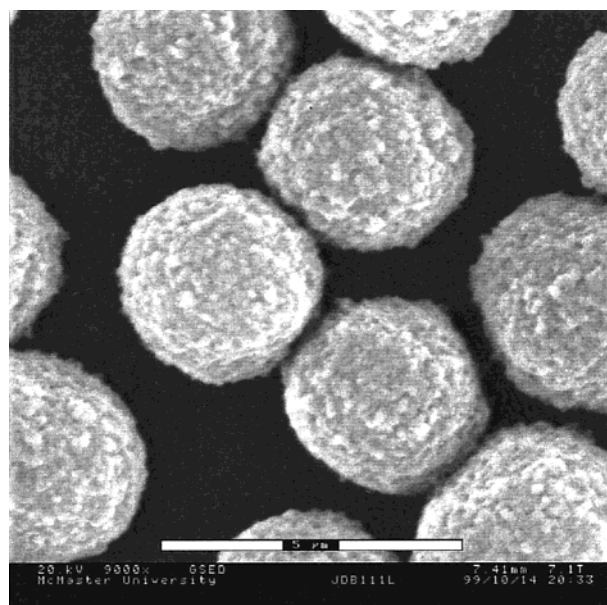
Figure 9. Electron micrograph of microspheres in the dry state prepared from 4 vol % DVB-40 in a mixture of 25:75 MEK:heptane. The scale bar is 5 μm in length.

in the production of an insoluble fraction at a conversion of 61% and a soluble fraction comprising 3% of total monomer. The insoluble material consisted of microspheres with a particle size of 3.8 ± 0.3 μm (Figure 5), and their surfaces were considerably smoother than microspheres prepared at lower DVB concentrations.
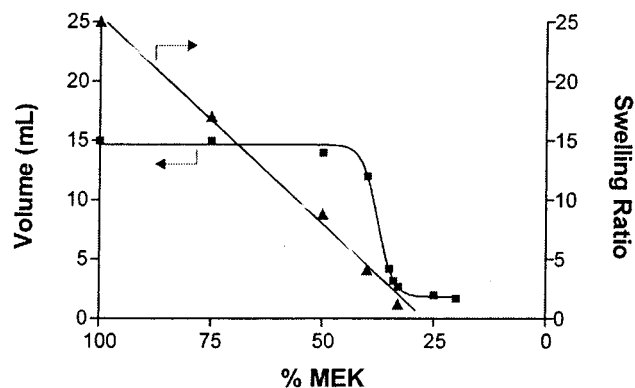
Figure 10. Volume occupied by polymer (■) and their swelling ratios (▲) as a function of the reaction solvent composition at 4 vol % DVB-55. In the range of 36−100% MEK space-filling macrogels are obtained. In the range of 34−35% MEK irregular-shaped individually dispersed particles are obtained. Microspheres are observed in the range of 20−33% MEK.

The isolated soluble fraction was found to have an apparent $\bar{M}_n$ of 2.5×10^3 g/mol with a PI of 3.4.

Conversion and Molecular Weight. Table 1 shows the conversion of monomer to soluble polymer and to insoluble polymer, as well as the molecular weight averages of the soluble fraction, for samples containing differing DVB levels. The solvent mixture for all of these samples consisted of 25% MEK and 75% heptane.

The conversion of monomer to total polymer increases with increasing DVB level. Only soluble polymer and microgels are obtained at DVB levels up to 15%, and the conversions for the DVB-0 and DVB-10 samples are shown in Table 1. At DVB levels greater than 20%, the samples consisted of both insoluble and soluble fractions, and the conversions for the DVB-25, DVB-40, and DVB-55 samples are shown Table 1. The yield of the insoluble polymer fraction increases continuously above DVB-25 whereas the yield of soluble polymer shows a maximum at DVB-10 and then decreases for higher DVB levels.

The molecular weight of the soluble polymer fraction formed in the reaction increases with DVB concentration. That is, at DVB concentrations below 15% only soluble polymers or microgels are formed whereas at DVB concentration above 20% insoluble, cross-linked polymers are observed. The molecular weight of the insoluble fraction can be considered infinite in comparison to that of the soluble fraction. The reason for this increasing molecular weight trend is that polymer chains having more and more pendent vinyl bonds are produced when the concentration of DVB in the monomer mixture is raised. Normally, termination of the propagating radicals leads to the formation of dead chains; however, the pendent vinyl bonds permit reinitiation and the formation of high molecular weight polymer. Therefore, the chains containing pendent vinyl bonds and without an active radical can be considered as dormant species. Since dormant chains could undergo several reactive periods during the course of the reaction, there would be a greater chance that they would be captured by the insoluble fraction, and as a result the yield of the soluble polymer would decrease with increasing amounts of DVB.

Polymer Network Contraction. The volumes occupied by poly(DVB-55) at differing solvent compositions are shown in Figure 10. The conversions of monomer to insoluble polymer for all samples in Figure 10 were

63 ± 3% and, thus, can be considered identical within experimental error. Macrogel prepared in 100% MEK had a swollen volume of 15 mL in THF and a dry volume of 0.6 mL, which corresponds to a swelling ratio of 25. The sample prepared at 75 vol % MEK had a swollen volume of 15 mL and a dry volume of 0.9 mL for a swelling ratio of 17. A swollen volume of 14 mL and a dry volume of 1.6 mL were measured for the sample prepared in 50 vol % MEK, and thus its calculated swelling ratio was 8.8. The swelling ratio for the macrogel prepared in 40 vol % MEK was recorded as 4.1, corresponding to a swollen volume of 12 mL and a dry volume of 2.9 mL. At 35 vol % MEK and below, irregular shaped particles or microspheres were formed, and in order to determine the volume they occupied, the reaction solvent was replaced with THF and the particles were allowed to settle. This takes place within hours, but to ensure complete settling the samples were left to stand for 1 week, after which time the volume of the layer of settled particles was measured. Hence, the volumes recorded for these samples includes interstitial volume between particles as well as the volume occupied by the polymer. The polymer from the 35 vol % MEK sample occupied 4.2 mL in THF, whereas the polymer from the 34 vol % MEK sample occupied 3.2 mL. The volume decreases further to 2.7 mL when the reaction mixture consisted of 33 vol % MEK and reached a plateau of approximately 1.8 mL between 25 and 20 vol % MEK. In Figure 10, a swelling ratio of 1 has been assumed for the microsphere samples, although they may have swelling ratios as high as 1.2. At lower fractions of MEK coagulum was formed, and thus it was impossible to measure its volume since much of it had precipitated onto the vessel walls.

Macrogels are formed in good solvency conditions, 100−36 vol % MEK, where the polymer network exists in an extended state. Decreasing the quality of the solvent for the forming network causes a corresponding decrease in the volume occupied by the network. Thus, at 35 vol % MEK the polymer network has contracted slightly, and the chains attached to opposing surfaces were unable to overlap and cross-link. The end result is the formation of individual particles instead of a macrogel. Between 33 and 20 vol % MEK the polymer network partially collapses to form microspheres that are stabilized against coagulation by their surface gel layer which performs the function of a steric stabilizer. Characterization and function of this surface gel layer will be the focus of a forthcoming paper. At MEK concentrations below 20 vol % the reaction mixture becomes too poor to swell this surface layer, causing the polymer to precipitate as a cross-linked, coagulated mass. Examination of this material by optical microscopy shows it to consist of coagulated microspheres of varying sizes. This suggests an initial collapse of the forming polymer into microspheres which then lose colloidal stability as the reaction continues. It is possible that the conversion of monomer to polymer further reduces the quality of the solvent and thus causes a complete collapse of the polymer such that the surface has the characteristics of bulk polymer and not a gel. This would result in a loss of colloidal stability only in the later stages of the reaction and account for the microsphere shapes formed in the coagulum.

The effect of DVB level on the volumes occupied by the polymer formed at a constant MEK fraction of 25 vol % is shown in Figure 11. At cross-linker concentra-
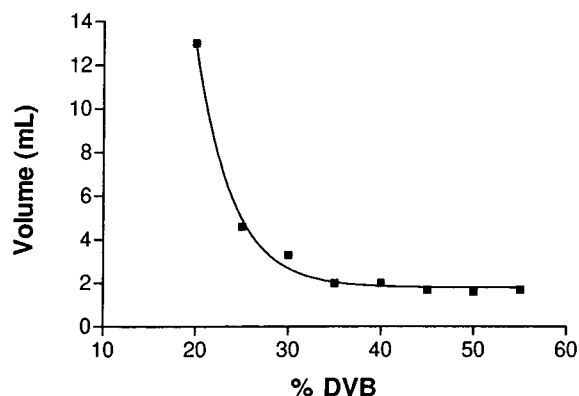
Figure 11. Volume occupied by polymer as a function of the DVB level in the 4 vol % monomer feed. The reaction solvent consisted of 25:75 MEK:heptane. Below DVB-20 soluble polymers were observed whereas a space-filling macrogel was obtained at DVB-20. Irregular-shaped particles were observed in the range of 25−35% DVB while microspheres were prepared in the range of 40−55% DVB.

tions below DVB-20, microgel and soluble polymer were formed. Macrogel which had a swollen volume of 13 mL and a dry volume of 0.8 mL was formed at DVB-20, and this corresponds to a swelling ratio of 16. The conversion of monomer to insoluble polymer was quite low at 28% for this sample. Further increasing the cross-linker concentration to DVB-25 resulted in the formation of individual particles at a yield of 24%, and they collectively occupied 4.6 mL. The volume decreased further as the DVB content increased, to a plateau of approximately 1.8 mL above DVB-45. The conversion of monomer to insoluble polymer for the DVB-30, -35, -40, -45, -50, and -55 samples was 32, 36, 43, 49, 51, and 61%, respectively.

The transition from microgel particles to macrogel with increasing DVB content is due to the greater opportunity to form intermolecular cross-links. It is well-known that microgels are precursors to macrogel,[7,20] and thus at DVB-20, microgels are formed initially, which then cross-link to become the macrogel observed at the end of the reaction. The solvent composition for the preparation of the DVB-20 macrogel was identical to that used for the production of the DVB-55 microspheres, and yet the polymer microspheres occupied less volume. This phenomenon cannot be explained on the basis of conversion since the insoluble polymer yield at DVB-55 was 61% and at DVB-20 was only 28%. Therefore, in addition to the solvent-induced network contraction, there must be a driving force for the collapse of the network into the more dense polymer particles. It is believed that cross-linking is the chemical process which drives this desolvation. A similar phenomenon has been cited by Naka and co-workers in the formation of microspheres by γ-ray-initiated polymerization of dimethylene glycol dimethacrylate in ethyl acetate. In this case, the polymer chains attached near the surface were suggested to have considerable mobility, and thus as adjacent chains came within close proximity to each other, they could react between their pendent vinyl groups; this process would prevent them from moving away from each other. This would, effectively, increase the concentration of pendent vinyl groups within this region and further facilitate cross-linking reactions.

Very few publications have appeared on the preparation of monodisperse or narrow-disperse microspheres

by precipitation polymerization; however, the morphology of suspension polymer particles has been much more rigorously investigated.[29] In a typical cross-linking suspension system, monomer, initiator, and porogen are dispersed in aqueous media. Small droplets containing the organic fraction are formed by stirring or other means and each droplet is converted into a particle by polymerization. Each organic phase droplet can be considered as a "microreactor" comparable to the reaction vials used in this study, except that the higher total monomer loading in suspension polymerization ensures that each droplet is converted into a space-filling macrogel during the polymerization. The internal morphology of individual particles can be controlled by the choice of porogen.[15,30] In the suspension copolymerization of 2-hydroxyethyl methacrylate (HEMA) and ethylene dimethacrylate (EDMA), dissolved in cyclohexanol and then dispersed in water, Horák and co-workers found that glassy particles were obtained if benzyl alcohol, 1-butanol, or cyclohexanone was chosen as the porogen. Under these conditions the forming polymer is solvated by the organic mixture and does not phase separate during polymerization. In contrast, if 1-octanol was used as the porogen, the interior of an individual suspension bead consisted of interconnected microspheres, and their diameters increased from 0.5 μm at 20% to 3 μm at 40% 1-octanol. In this case, 1-octanol is a poor solvent for the forming network, and as a result the polymer phase separates early in the reaction to produce individual microspheres which become linked together at a later stage.[31] This is analogous to our system, although in our case the microspheres remain individually dispersed because polymer chains on opposing surfaces are unable to overlap and cross-link as a result of the low monomer loading.

Proposed Particle Formation Mechanism. Previous experimental results have indicated that the growth mechanism for monodisperse polyDVB microspheres occurs by an entropic precipitation mechanism where soluble oligomeric species are captured from solution by reaction with pendent vinyl groups on the surface of existing particles. Once the oligomers are captured, they undergo a desolvation or phase separation which can be driven either by solvency of the continuous phase or by cross-linking of the polymer network. In our case, both of these driving forces contribute to the collapse of the network. This is evident if we consider that reactions carried out at solvent fractions of 25 vol % MEK lead to space-filling macrogels for DVB-20 and to microspheres for DVB-55. The higher concentration of cross-linking monomer induces a collapse in the forming network and prevents gelation. Although cross-linking is required to induce the collapse of the network, in our case this is not sufficient for the preparation of microspheres. Thus, the solvency of the continuous phase must be such that cross-linking the network drives the polymer below the Θ condition and causes phase separation. Microspheres were observed in the γ-ray-initiated polymerization of DEGMA in good solvents such as ethyl acetate by Naka.[17,18] Presumably the cross-linking efficiency in this system is much higher than that of the thermally initiated systems, and this is supported by the very weak absorption of the residual vinyl group observed in the FTIR spectra for the poly-DEGMA microspheres. Therefore, collapse of the forming network in Naka's system would be driven almost exclusively by cross-linking.

Conclusions

A morphology map based on a two-dimensional matrix of DVB level and continuous phase solvency was developed. This map indicated that poly(DVB-*x*) microspheres were formed as an intermediate morphology between microgels, macrogels, and coagulum. The solvent composition strongly affects the polymerization of DVB-*x* by controlling the dimensions of the polymer coil as it is formed. Neat MEK, a good solvent for styrenic polymers, leads to a typical solution type polymerization with or without cross-linking. Neat heptane, on the other hand, leads to classical precipitation polymerization. In mixtures of MEK and heptane there is a transition from solution polymerization to precipitation polymerization. In the intermediate or "marginal" solvency range, and at higher DVB concentrations, we can observe a solvent composition range where the polymer contracts to form discrete microspheres. However, the solvency of the organic diluent must be sufficient to swell the particle surface slightly. It is the role of the cross-linking monomer, DVB, to force the polymer below its Θ condition and to cause it to partially collapse to form microspheres. We believe that the surface of the microspheres remains partially swollen since it would be only lightly cross-linked and that this gel layer provides steric stabilization between microspheres.

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