# Dispersion polymerization of uniform cross-linked polystyrene microspheres in butan-1-ol

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**ABSTRACT:** Butan-1-ol can be used as the solvent in the synthesis of poly(styrene-*co*-divinylbenzene-*co*-acrylic acid) microspheres by dispersion polymerization of a mixture of styrene, divinylbenzene (DVB), and acrylic acid (AA). Varying the proportion of the cross-linker DVB affects the size distribution and particle morphology profoundly, with 0.5–1.0% w/w producing spherical particles, whereas 2.0% w/w DVB produces irregular, concave morphologies. Varying the amount of AA from 5–7% w/w increases the average diameter of the spherical particles, whereas 9% w/w AA results in ovoid particles with dimpled surface morphology. In an optimized synthesis using 1.0% w/w DVB and 5% AA, uniform polymer microspheres with an average diameter of 0.8 μm and a coefficient of variation (CV) of diameter of 8.2% are produced. The use of a medium-polarity solvent, such as butan-1-ol, as the solvent for dispersion polymerization will facilitate the incorporation of non-polar moieties, such as organically-passivated quantum dots, into the polymer during synthesis. © 2015 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2016**, *133*, 43103.

## INTRODUCTION

Synthetic polymer beads or microspheres have become important components in a wide range of applications, ranging from markers for flow analysis[1]; size and/or concentration standards in particle measurement techniques such as Tunable Resistive Pulse Sensing (TRPS)[2] and flow cytometry[3]; and substrates in agglutination assays[2,3]; chromatography[4,5] and affinity purification[6]; and solid phase chemical synthesis.[7,8]

Polystyrene, and a variety of its *co-* and *ter*-polymers, are among the most commonly used synthetic organic polymers for microsphere manufacture.[4] Cross linkers such as divinylbenzene (DVB) are commonly incorporated to control the porosity and solvent-swelling behavior of the co-polymer and to impart enhanced physical strength and temperature stability.[9] Carboxylation of polystyrene is frequently used to increase the colloidal stability of the polymer microspheres,[10] due to electrostatic stabilization of the colloid by inclusion of polarizable surface groups. Surface carboxylic acid groups are also particularly useful for facilitating modification of the polymer bead surface via EDC/NHS (*N*-ethyl-*N'*-(3-dimethylaminopropyl)carbodiimide/*N*-hydroxysuccinimide) chemistry.[3] Carboxylic acid groups can

be incorporated into polystyrene via a number of unsaturated carboxylic monomers, including itaconic acid, acrylic acid (AA), and methacrylic acid.[10] Acrylic acid was chosen for this work because of its greater availability at the particle surface.[11]

Dispersion polymerization can be used to prepare uniformly sized polymer microspheres over a large range of sizes (0.1 – 15 μm).[12–14] In this methodology, monomer, solvent, initiator, and a steric stabilizer are combined in a single homogeneous phase.[15] After the polymerization reaction is initiated, polymer chains grow in solution before nucleating to form colloidal particles. Coagulation of nuclei proceeds until the critical size, $d_{crit}$, is reached and the particles become stabilized.[16] A temporally limited nucleation phase produces uniformly sized stabilized nuclei, which maintain their narrow size distribution while growing either by accumulation of polymer generated in the continuous phase or polymerization of monomer within the particle.[16,17] Grafting of stabilizer to the surface of growing particles provides steric stabilization of the colloid,[18] and avoids the formation of coagulum, which would otherwise occur in unstabilized solution polymerization.[16] Polyvinylpyrrolidone (PVP) is a widely used steric stabilizer for polystyrene, and has

**Table I.** Composition of Monomer Mixtures. Total Monomer Concentration of 6% v/v in Butan-1-ol with 16 mg mL$^{-1}$ PVP as Stabilizer; [ACHN] = 5% w/w w.r.t. Monomer; and T = 70°C

| Monomer composition | | | Size distribution | | | | | |
|---|---|---|---|---|---|---|---|---|
| DVB (% w/w) | AA (% w/w) | Styrene (% w/w) | Mean diameter (µm) | CV (%) | PDI | Median diameter (µm) | GSD |
| 0.5 | 5.0 | 94.5 | 1.3 | 46 | 1.704 | n/a | 1.52 (bimodal) |
| 1.0 | 5.0 | 94.0 | 0.8 | 8.2 | 1.017 | 0.8 | 1.05 |
| 2.0 | 5.0 | 93.0 | 0.9 | 48 | 2.007 | n/a | 1.71 (bimodal) |
| 1.0 | 7.0 | 92.0 | 1.1 | 14 | 1.043 | 1.1 | 1.08 |
| 1.0 | 9.0 | 90.0 | 1.3 | 37 | 1.336 | 1.6 | 1.34 |

been shown to facilitate the formation of uniform size distributions and stable colloidal suspensions.[16]

Solvent also plays a critical role in dispersion polymerization, as the ability of the solvent/monomer solution to dissolve the grafted polymer (solvency) determines the point at which polymer precipitates, and therefore has a substantial effect on the critical and final particle sizes.[16] Polar solvents such as methanol and ethanol have been commonly used as solvents for styrene polymerization,[19–22] however the use of less polar solvents such as longer-chain alcohols has a number of advantages. Among the linear C1–C10 alcohols, butan-1-ol (C4) has the best solvent parameter match to PVP as a steric stabilizer of polystyrene.[20] In addition, butan-1-ol is a better solvent for various species which it may be desirable to incorporate into polymer microspheres during polymerization, such as hydrophobic, organically-passivated nanocrystals (e.g. quantum dots).[23–25]

While butan-1-ol has been used as a solvent for the dispersion polymerization of polystyrene[20,26] and poly(styrene-co-divinylbenzene),[27] it has not been used previously in a single solvent system for the preparation of carboxylated poly(styrene-co-divinylbenzene). In this work, we developed the synthesis of uniform poly(styrene-co-divinylbenzene-co-acrylic acid) polymer microspheres by dispersion polymerization in butan-1-ol with PVP as the steric stabilizer. Ongoing work will investigate the use of the butan-1-ol-based system to incorporate organically-passivated quantum dots into polymer microsphere composites.

## EXPERIMENTAL

All materials were from Sigma-Aldrich. Polyvinylpyrrolidone (PVP, average molecular weight 40,000) and 1,1′-azobis(cyclohexane-carbonitrile) (ACHN) (99%) were used as received. Acrylic acid (AA) (99%, stabilized with 200 ppm 4-methoxyphenol; b.p. 46–51°C at 10 mbar), divinylbenzene (DVB) (80%, mixture of isomers; stabilized with 1000 ppm 4-t-butylcatechol; b.p. 27–30°C at 0.6 mbar), and styrene (≥99%, stabilized with 4-t-butylcatechol; b.p. 44–47°C at 10 mbar) were distilled under vacuum to remove stabilizer and stored under nitrogen. Butan-1-ol (≥99.4%) was dried over 4Å molecular sieves and distilled under nitrogen.

Dynamic Light Scattering (DLS) was performed using a Shimadzu SALD-2001 particle size analyzer. Water was used as the dispersant, and sonication was used to disperse suspensions. Scanning Electron Microscopy (SEM) was performed on an FEI Nova

NanoSEM 450 operating at 7 kV or an FEI Quanta 450 SEM operating at 20 kV. Samples were deposited as a concentrated suspension onto carbon tape and the solvent was allowed to evaporate. Samples were coated with gold-palladium before imaging. Image analysis was performed using ImageJ.[28] The coefficient of variation (CV) in particle diameter and polydispersity index (PDI) were calculated using the following equations[29]:
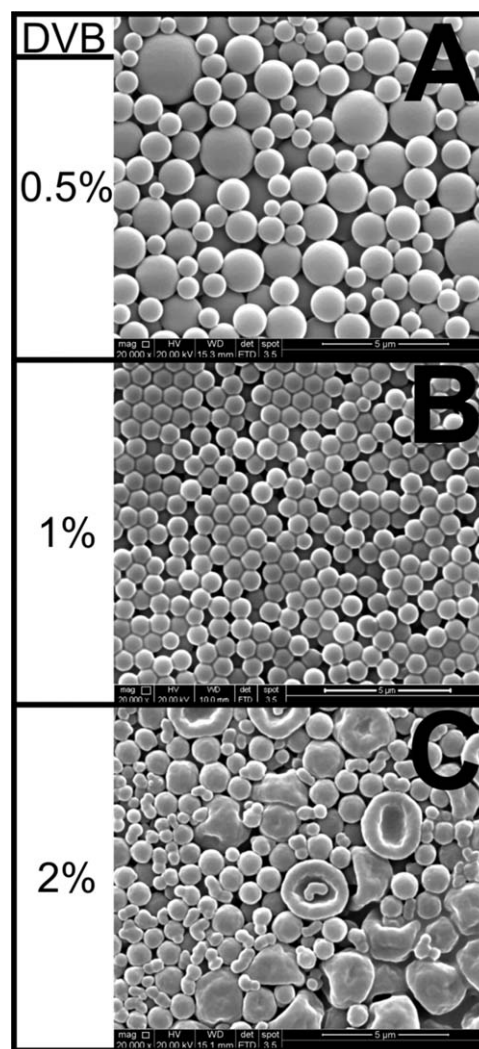


**Figure 1.** SEM micrographs of polymer beads synthesized with 5% AA w/w and: (a) 0.5%, (b) 1%, and (c) 2% DVB w/w (remainder styrene).
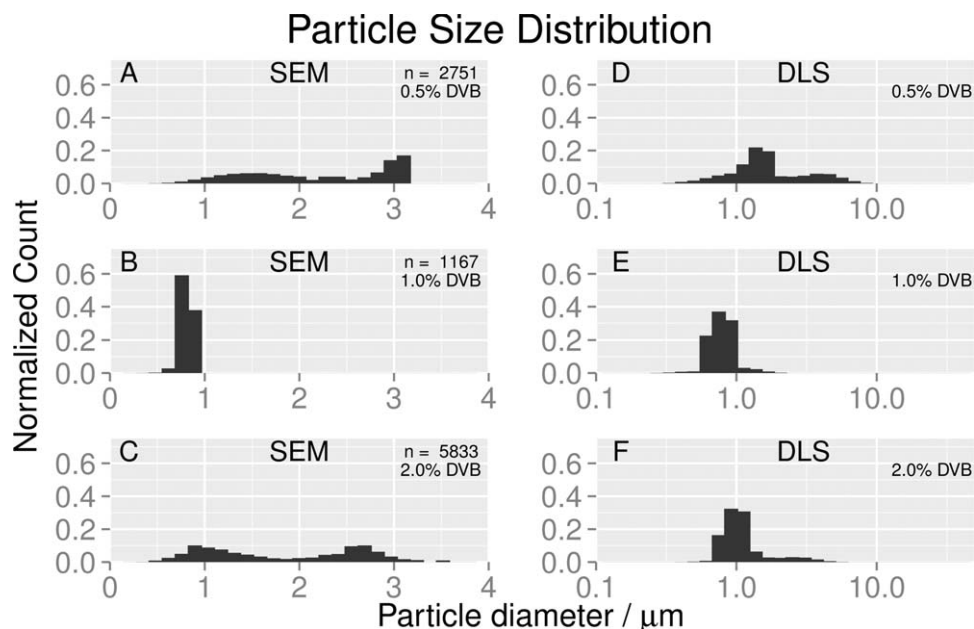
**Figure 2.** Volume-weighted particle size distribution of polymer beads synthesized with (a,d) 0.5%; (b,e) 1.0%; or (c,f) 2.0% DVB w/w (5% AA w/w, remainder styrene). (a–c) SEM measurements and (d–f) DLS measurements.

$$CV = \frac{\sigma}{d_n} = \sqrt{\frac{\sum_{i=1}^{n}(d_i - d_n)^2}{n-1}} \Big/ d_n \qquad (1)$$

$$d_n = \sum_{i=1}^{n} n_i d_i \Big/ n; \ d_w = \left(\sum_{i=1}^{n} n_i d_i^4\right) \Big/ \left(\sum_{i=1}^{n} n_i d_i^3\right) \qquad (2)$$

$$PDI = d_w / d_i \qquad (3)$$

where $\sigma$ is the standard deviation, $d_n$ is the mean diameter, $n_i$ is the number of particles with diameter $d_i$, and $d_w$ is the volume-weighted mean diameter. The geometric standard deviation (GSD) was calculated from the volume-weighted particle size distribution using the following equation[20]:

$$GSD = \sqrt{\frac{d_{84}}{d_{16}}} \qquad (4)$$

where $d_{84}$ and $d_{16}$ are the 84th and 16th percentiles of the volume-weighted distribution, respectively.

In a typical synthesis, PVP (0.4 g) was dissolved in dry butan-1-ol (25 mL) with stirring at 300 rpm, and was heated to 70°C under nitrogen. A 1.5 mL aliquot of a mixture of styrene:DVB:AA (94:1:5 w/w/w) was added to the flask and stirred for a further 10 minutes before the initiator ACHN (0.07 g, 0.3 mmol) was quickly added. The mixture was maintained at 70°C with stirring for 16 hours, during which time the microspheres nucleated and grew. The mixture was allowed to cool to room temperature and centrifuged at 5000 rpm to separate the microspheres. The precipitate was re-dispersed in ethanol and the process was repeated. Finally, the precipitate was re-dispersed in distilled water and stored as a suspension.

## RESULTS AND DISCUSSION

To determine the effect of the composition of the monomer mixture on the resulting polymer microspheres, the relative amounts of DVB, AA, and styrene in the mixture were varied as shown in Table I, while the concentration of stabilizer and initiator were kept constant. To investigate the effect of degree of cross linking on the polymer microspheres, the loading of DVB was varied between 0.5% and 2% w/w (with respect to total amount of monomer), while the proportion of AA was held constant at 5% w/w.

Figure 1 shows SEM micrographs of the resulting microspheres and particle size distribution parameters are tabulated in Table I. Histograms of the particle size distributions determined by SEM or DLS measurements are shown in Figure 2. As can be seen in Figure 1, DVB loadings of 0.5–1.0% w/w resulted in spherical particles, whereas a loading of 2.0% w/w resulted in a population of concave and irregularly-shaped particles. A DVB loading of 0.5% w/w resulted in a distinctly bimodal size distribution (PDI of 1.704), whereas a loading of 1.0% w/w resulted in a relatively uniform distribution of 0.8 μm particles with a CV of 8.2% (PDI: 1.017).

As seen in the micrographs (Figure 1), low loadings of DVB (0.5 – 1.0% w/w) did not affect the spherical morphology typically seen in polystyrene particles synthesized by dispersion polymerization. However, at a loading of 2% w/w DVB, concave particle morphologies were evident, similar to those observed by Tseng et al.[15] for polystyrene cross-linked with 0.6% w/w DVB in ethanol. This concave morphology is attributed to phase separation of styrene-rich and divinylbenzene-rich portions of the polymer network and contraction of the divinylbenzene-rich portion.[30,31] Deviation of particle morphology from sphericity and broadening of particle size distributions caused by the presence of even relatively low levels of co-monomers (<0.5% v/v) has been noted previously for dispersion polymerization of styrene in ethanol.[31–33] Winnik and coworkers developed the use of batch additions of DVB during dispersion polymerization to maintain spherical particle morphologies
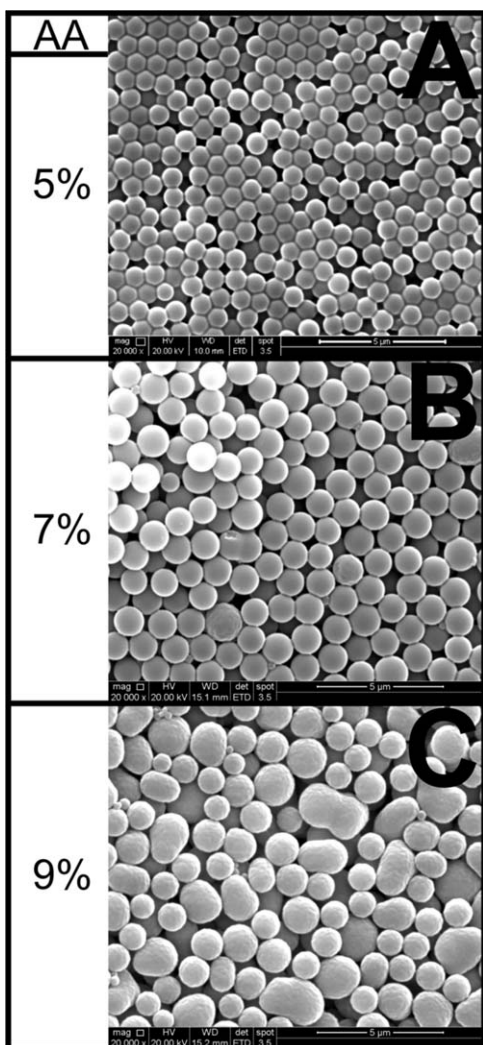
**Figure 3.** SEM micrographs of polymer beads synthesized with 1% DVB w/w and: (a) 5%, (b) 7%, and (c) 9% AA w/w (remainder styrene).

with up to 3% DVB v/v.[33] However, it appears that using butan-1-ol as a solvent, up to 1% v/v DVB can be used in a single-stage process without adversely affecting the particle size distribution or deviating from spherical particle morphology.

The bimodal distribution of spherical particles, which resulted with 0.5% w/w DVB, but not with 1.0% w/w DVB, indicates that a secondary stabilization event occurred during synthesis, generating a second population of smaller particles. Secondary stabilization occurs when graft is produced in solution faster than it can be accommodated on the surface of existing particles, leading to stabilization of a second population of nuclei, which grow by accumulating polymer from solution in competition with the original stabilized particle population.[20]

Having the optimized DVB loading at 1% w/w, the proportion of AA was varied between 5% and 9% w/w (Table I). Figure 3 shows SEM micrographs of the resulting microspheres and Figure 4 shows the particle size distributions determined by SEM and DLS measurements. AA loadings of 5% and 7% w/w produced spherical particles, although increasing the proportion of AA from 5% to 7% w/w led to an increase of the average particle diameter from 0.8 to 1.1 μm and a widening of the size distribution (increase of CV from 8.2% to 14%). There also appeared a small number of particles with rough surfaces. An AA loading of 9% w/w resulted in polymer particles with irregular shapes, a rippled surface texture, and a broad size distribution (PDI of 1.336).

The effect of the proportion of AA in the monomer mixture on the resulting particle size distribution and morphology may be mediated through a number of mechanisms. The increase in average particle size with increasing proportion of AA in the monomer mixture suggests an increase in the initial solvency of the system.[16] Given that a relatively small change in the amount of AA has a substantial effect on the particle size distribution, it seems likely this is mediated through an alteration in the solubility of the polymer rather than the solvent power of the solvent/monomer combination. Similar trends to increased average
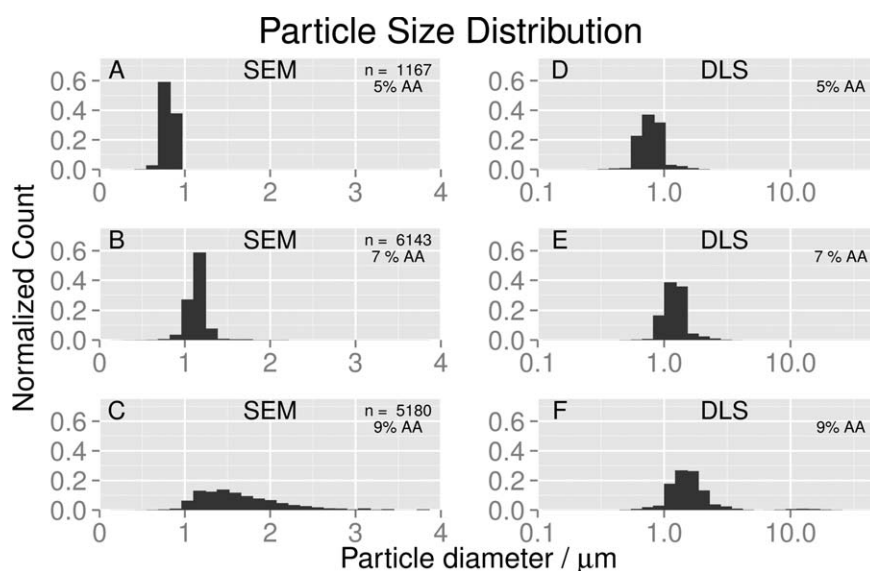


**Figure 4.** Volume-weighted particle size distribution of polymer beads synthesized with (a,d) 5%; (b,e) 7%; or (c,f) 9% AA w/w (1% DVB w/w, remainder styrene). (a–c) SEM measurements and (d–f) DLS measurements.

particle size and wider size distribution with increased proportion of AA to styrene has been observed previously for dispersion polymerization in ethanol[32] and ethanol/water solvent systems,[32,34] and were attributed to the increased solubility of poly(acrylic acid) and grafted [PVP-poly(styrene-co-acrylic acid)] compared to polystyrene in these systems. This trend towards greater polymer solubility, and hence particle size, with increasing AA content, evidently continues in butan-1-ol, even though butan-1-ol already has a closer match of solubility parameters than that of ethanol to the stabilizer PVP and its grafts.[35] It is interesting to note that higher loadings of AA were achievable in butan-1-ol (7% w/w) without significant broadening of the particle size distribution than was the case in ethanol (2% w/w)[32] or ethanol/water (∼3% w/w).[34]

Use of PVP at a concentration of 16 mg mL$^{-1}$ solvent ($\equiv$ 30% w/w w.r.t styrene) facilitated the production of uniform, spherical polymer particles, provided the other reaction conditions were suitable. To demonstrate the essential role of the stabilizer, an experiment was conducted with 4 mg mL$^{-1}$ PVP ($\equiv$ 7% w.r.t styrene), which resulted in a broad particle size distribution. This is analogous to previous observations, made using ethanol, that a PVP concentration of at least 16% w/w with respect to styrene is required during the early stages of reaction to prevent aggregation and ensure a narrow size distribution.[32]

## CONCLUSIONS

Poly(styrene-co-divinylbenzene-co-acrylic acid) microspheres were synthesized by dispersion polymerization of a mixture of the monomers in butan-1-ol, using PVP as a steric stabilizer. The proportions of DVB and AA in the monomer mixture had a significant effect on the resulting particle size distribution and morphology. With an optimized mixture containing DVB 1% and AA 5% w/w, uniform polymer microspheres with an average diameter of 0.8 µm and a CV of 8.2% were produced. Decreasing the amount of DVB to 0.5% w/w resulted in a bimodal distribution of spherical microspheres, whereas 2.0% w/w DVB resulted in distorted particle morphologies. Maintaining 1% DVB w/w, but increasing AA to 7% w/w increased the average particle diameter to 1.1 µm and CV to 14%, whereas increasing AA to 9% w/w resulted in a rough surface morphology and irregular particle shapes. Butan-1-ol is a good solvent for many medium polarity compounds and organically-passivated nanocrystals. The optimized synthesis of uniform cross-linked, carboxylated polystyrene in butan-1-ol, presented here, will facilitate the synthesis of polymer composites in this solvent.

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