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Polymer Microspheres Prepared by Water-Borne Thiol–Ene Suspension Photopolymerization

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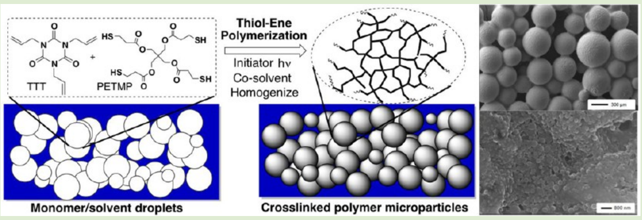
S Supporting Information

ABSTRACT: Thiol–ene polymerizations are shown to be possible in a water-borne suspension-like photopolymerization and yield spherical particles that have diameters in the range of submicrometers to hundreds of micrometers. This is the first report of such colloidal thiol–ene polymerizations. Thiol–ene polymerization offers unique conditions not commonly associated with a water-borne polymerization including a step-growth polymerization mechanism along with photoinitiation under ambient conditions. Example polymerizations of a triene, 3,5-triallyl-1,3,5-triazine-2,4,6 (1*N*,3*H*,5*H*)-trione (TTT), and a tetrathiol, pentaerythritol tetrakis(3-mercaptopropionate) (PETMP), with the photoinitiator 1-hydroxycyclohexyl phenyl ketone, surfactant sodium dodecyl sulfate (SDS), and a cosolvent (chloroform or toluene) are discussed. Various experimental parameters were examined such as surfactant concentration, homogenization energy, cosolvent species, and cosolvent amount in order to develop an understanding of the mechanism of microsphere formation. It is demonstrated that particle size is dependent on homogenization energy, with greater mechanical shear yielding smaller particles. In addition, higher concentrations of surfactant or solvent also produced smaller spherical particles. These observations lead to the conclusion that the particles are formed via a suspension-like polymerization.



The development and expansion of polymerization methods is important for the utilization of these chemical processes for a host of applications, ranging from biomedical devices to computer hardware production. Thiol–ene chemistry[1,2] is one polymerization mechanism that has become distinguished and widely developed for the synthesis of a range of polymeric materials from degradable polyanhydrides to porous scaffolds to soft imprint lithography.[3−9] The resurgence of this important chemical reaction has emerged from the development of click chemistry[10,11] along with the observable benefits associated with the thiol–ene chemistry.[1−3] Some of the main benefits of thiol–ene chemistry in polymer synthesis include tolerance to a variation in reaction conditions or solvents, relatively clear elucidation of reaction pathways or polymer products, simple and quick synthesis strategies for both linear and cross-linked polymer networks, and the utilization of starting materials that are easily obtainable.[1−3,9,11]

Although the thiol–ene polymerization mechanism uses radical intermediates, the molecular weight development in such reactions follows a step-growth mechanism. This results in more homogeneous network structures than obtained from chain-growth polymerizations and hence better defined thermomechanical properties.[2]

Although thiol–ene polymerizations have been used regularly for industrial coatings, these are typically bulk polymerizations. On the other hand, water-borne thiol–ene polymerizations are one particular area that, as yet, has not been developed, in stark contrast to the widely practiced water-borne polymerizations of acrylics and styrenic monomers.[12,13] The use of thiol–ene chemistry for the synthesis of water-borne polymer microspheres offers great potential for the development of novel material systems for numerous biomedical and industrial applications including drug delivery, pharmacological targeting, tethering of biomolecules, paints and coatings, chromatographic separation, and many others.[14−17] The inherent versatility of thiol–ene chemistry allows for the reaction between many types of thiols and a large variety of compounds that possess unsaturated C=C groups.[2] Consequently, the use of thiol–ene chemistry for the development of a cross-linked colloidal assembly offers promise for new materials and applications.

We report here that thiol–ene polymerizations can be conducted in a water-borne suspension-like photopolymerization. This novel system incorporates the step-growth mechanism of thiol–ene polymerization in a water-borne suspension. The combination of these important polymerization pathways has not been previously employed for the development of spherical polymer particles. This approach has

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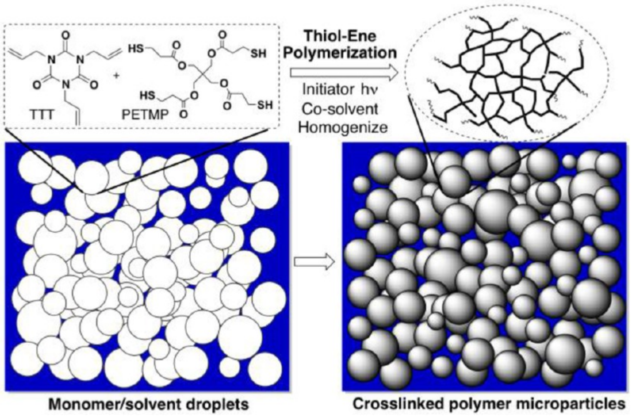
allowed for the development of spherical particles that can be synthesized with an array of diameters, ranging from submicrometer to hundreds of micrometers. We examine the dependence of particle size and dispersion stability on various experimental variables to determine the mechanism of particle formation.

The development of spherical polymer particles in water-borne systems has often been achieved using the conventional method of suspension polymerization.[13] Other important water-borne polymerizations that have been used to synthesize polymer particles include emulsion, miniemulsion, microemulsion, dispersion, and precipitation polymerizations.[12,13,18,19] As shown recently by Du Prez et al.,[20] polymer microspheres (with diameters of several hundred micrometers) can also be made using thiol−ene and thiol−yne polymerizations conducted in a microfluidic device. The primary step in a water-borne suspension polymerization is the creation of an emulsion of monomer droplets in the aqueous phase with a balance between the coalescence and comminution of these droplets during the polymerization process.[13] Relatively water insoluble monomers are dispersed as liquid droplets with a suitable surfactant and vigorous stirring throughout polymerization to yield polymer particles as a dispersed solid phase. The resulting polymer particles can be porous or nonporous, with the latter particles termed polymer pearls or polymer beads.[21−23] Most free-radical water-borne polymerizations utilize chemistries that follow a chain-growth polymerization mechanism upon thermal initiation.[12,13] On the other hand, the incorporation of thiol−ene chemistry into a water-borne system can allow for the use of a step-growth polymerization mechanism that may undergo polymerization through photoinitiation and give essentially 100% monomer conversion with a variety of monomeric species.[1,2] Furthermore, the utilization of this step-growth mechanism allows for high rates of conversion of monomers to polymers and the synthesis of microgel particles with controlled cross-linked density, which is determined by the chemical structures of the vinyl and thiol monomers. Consequently, the step-growth mechanism of thiol−ene polymerizations means that the production of microspheres is fundamentally different to regular chain-growth polymerizations normally associated with free-radical emulsion, miniemulsion, dispersion, and suspension polymerizations.[12,13] Additionally, photoinitiation has many benefits, such as temporal and spatial control, over thermal initiation that is normally used in water-borne polymerization systems, with a few exceptions.[24,25]

Our approach for the heterogeneous thiol−ene photopolymerization involves the mixing of an organic phase, consisting of monomers, initiator, and solvent, and an aqueous phase, consisting of surfactant dissolved in water. The organic phase is mechanically emulsified in the aqueous phase to create microdroplets. In the presence of ultraviolet light, polymerization occurs in these droplets, resulting in cross-linked polymer microspheres. A water-immiscible solvent, such as toluene or chloroform, is used to facilitate emulsification by lowering the viscosity of the dispersed phase. This method of producing water-borne thiol−ene polymer particles is illustrated in Scheme 1.

Scheme 1. General Outline of Polymer Particle Formation via a Water-Borne Thiol−Ene Photopolymerization Mechanism



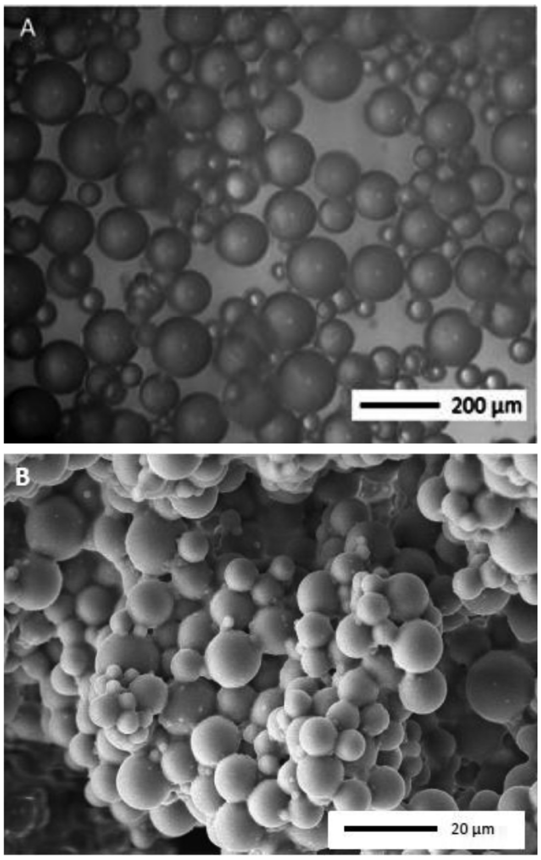


Figure 1. Images of thiol−ene polymer particles obtained using (A) magnetic stirring (optical microscopy) and (B) overhead mechanical mixing (FE-SEM). Conditions used: organic phase, TTT (23.6 wt %), PETMP (34.6 wt %), and 1-hydroxycyclohexyl phenyl ketone (0.1 wt %) dissolved in toluene (41.7 wt %) was dispersed into an aqueous solution of the SDS (5 wt %, 182.4 mM), giving 14.6 wt % organic phase in the final emulsion.

Preliminary experiments and observations have demonstrated the synthesis of thiol−ene microparticles in a water-borne system for both magnetic stirring and overhead mechanical mixing. As shown in the optical microscopy and field emission scanning electron microscope (FE-SEM) images in Figure 1, fairly large particles (10−200 μm) were obtained when TTT (23.6 wt %), PETMP (34.6 wt %), and the 1-hydroxycyclohexyl phenyl ketone (0.1 wt %) were dissolved in toluene (41.7 wt %), and this solution was subsequently dispersed into an aqueous solution of the sodium dodecyl sulfate (5 wt %, 182.4 mM). The amount of dispersed phase (organic) in the final emulsion was about 14.6 wt %. The ratio of TTT to PETMP was chosen such that there are stoichiometric amounts of ene and thiol functionalities. The images in Figure 1 show that the particle size is strongly dependent on the mode of mechanical mixing, with more intense agitation resulting in the development of smaller polymer particles. The dispersity of the particles appears relatively large in both cases.

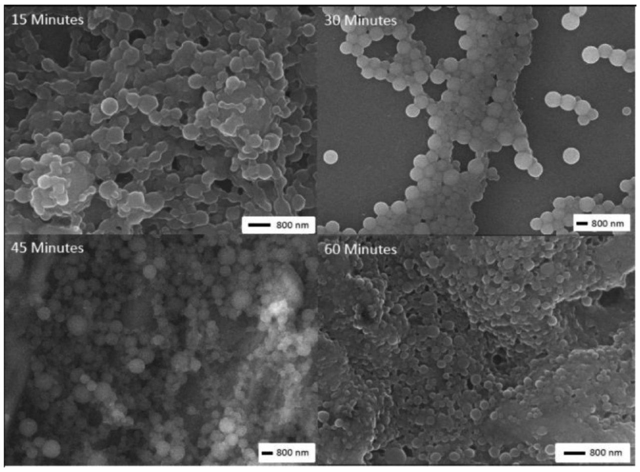


Figure 2. FE-SEM images of particles made using various sonication times. Conditions used: organic phase, TTT (23.5 wt %), PETMP (34.5 wt %), hexadecane (0.35 wt %), and 1-hydroxycyclohexyl phenyl ketone (0.1 wt %) dissolved in toluene (41.55 wt %) was dispersed into an aqueous solution of the SDS (5 wt %, 182.4 mM), giving 14.6 wt % organic phase in the final emulsion.

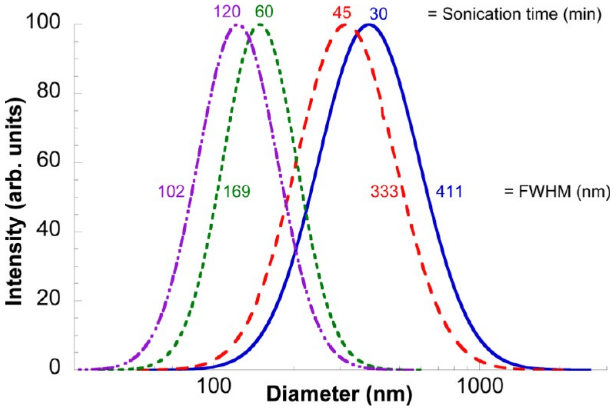


Figure 3. Intensity-weighted particle size distributions of toluene-swollen particles made using sonication with varying sonication times. Conditions used: same as given in Figure 2.

Sonication prior to polymerization further reduced the particle size to a point that most particles were submicrometer in size (Figure 2). Longer sonication times resulted in smaller polymer particles with narrower particle size distributions (Figure 3), as indicated by the full width at half-maximum (fwhm) values. Note that the particle size distributions (Figure 3), determined using dynamic light scattering, were of "as prepared" samples, that is, still swollen with toluene and a small amount of hexadecane (often used as a costabilizer in water-borne polymerizations), as opposed to the particles shown in the FE-SEM images (Figure 2), which were dried. Separate experiments that did not have hexadecane added indicated that the hexadecane did not alter the particle size significantly.

Other experiments were conducted in which the type and volume of solvent used to dissolve the monomers in the organic phase were varied, as was the amount of surfactant used. Results for these experiments can be found in the Supporting Information. Both the solvent (toluene or chloroform) and the surfactant were found to be critical for particle synthesis without coagulation. Consistent with the mechanism of suspension polymerization, a higher concentration of surfactant, a lower viscosity of the initial organic phase (achieved by using higher solvent-to-monomer ratios), or a higher agitation power input yielded smaller and more uniform particles. Thus, the microdroplets of the organic phase were evidently the primary sites of the polymerization reaction.

Removal of the organic solvent by rotary evaporation resulted in an undetectable change in particle size distribution, in accord with the fact that only about 18% reduction in particle diameter is expected considering the relative amounts of solvent and monomers in the polymerization recipe. Although the monomer-miscible diluent, such as toluene, could function as a porogen and yield porous polymer particles,[20] FE-SEM showed no sign of significant porosity. The nonporous morphology is evidently because of good miscibility of the polymer segments with toluene, which prevents phase separation and the formation of large pores.[26]

As confirmation that the polymer particles were indeed the same as what would be obtained in a bulk polymerization of TTT and PETMP, we examined the thermal properties of the polymer product of both a suspension and bulk polymerizations of these monomers. Two reactions contained the monomers and chloroform, but the suspension polymerization additionally contained water and surfactant. The final products were examined using differential scanning calorimetry (DSC), specifically to determine the glass transition temperature (T_g). The polymer obtained from the bulk polymerization showed a T_g of 3 °C, while the particles showed essentially the same T_g of −1 °C, indicating that the composition and network structure of the polymer produced in the water-borne system was almost the same as that obtained using the more traditional bulk polymerization. The DSC results also show that the glass-to-rubber transition occurs over a relatively narrow temperature range indicating a homogeneous network structure, which is typical of thiol−ene polymers.[2]

In conclusion, we report water-borne thiol−ene photopolymerizations that yield dispersions of polymer particles. The utilization of this method offers great potential for the development of cross-linked polymer microspheres. For example, these microspheres have several advantages over acrylic-based microspheres including high monomer conversions, rapid reaction rates, uniform cross-link density, well-defined thermal properties (i.e., T_g), and the ability to be polymerized in the presence of other functional groups (i.e., orthogonality). In terms of applications, we expect that such particles may find use in drug delivery (either by simple encapsulation or conjugation), cosmetics, or industrial coatings (e.g., lacquers). We have found that higher homogenization power yields smaller particles, as does higher surfactant concentrations. Cosolvents are needed to give nonaggregated polymer particles, although this may be dependent on the monomers used. It appears that particle formation follows a suspension polymerization mechanism. Future goals include the reduction of the amount of surfactant needed, the use of other thiol–ene monomers, and methods for the development of narrower size distributions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthesis and characterization details, along with optical and FE-SEM images of particles made under various conditions, are given. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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