

**Monodisperse Mesoporous Silica Microspheres Formed by Evaporation-Induced Self-
Assembly of Surfactant Templates in Aerosols****

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Evaporation-induced self assembly (EISA) of amphiphilic molecules (e.g., surfactants and block copolymers) within aerosols and thin films has been recently demonstrated to be a powerful and flexible method for synthesizing ordered mesoporous silica particles^[1,2] and thin films.^[2,3] The previous synthesis of mesoporous silica particles using aerosol EISA has been limited to particle sizes of roughly 1 μm or smaller possessing a relatively wide particle size distribution. There are many applications where larger mesoporous particles with high monodispersity are needed or

highly beneficial. Several examples include: controlled delivery, where monodispersity could ensure uniform delivery rates; biosensing based on flow cytometry^[4], where monodisperse spheres with sizes of several μm could serve as ‘cell mimics’; and photonic bandgap materials^[5], where high monodispersity, periodicity and control of dielectric constant are critical factors. Here we report for the first time on the synthesis of non-hollow monodisperse mesoporous silica particles in the 5 to 10 μm size range based on evaporation-driven surfactant templating in microdroplets produced by a vibrating orifice aerosol generator (VOAG). We show that pore size, mesoscopic ordering, and monodisperse particle size can be controlled by the experimental conditions, precursor chemistry, and VOAG parameters.

Surfactant-templated mesoporous materials, initially discovered by Mobil scientists in 1992,^[6,7] have been developed to exhibit unique structures and properties, including uni-modal pore size distributions, high surface areas, alterable pore sizes and controlled pore surface chemistry. The mesopore size range of 2 to 50 nm is attractive for producing confined structures such as quantum dots^[8-10] or nanowires.^[11,12] The highly uniform porosity of the mesoporous materials allows for facile diffusion, thereby making them excellent hosts for sensing molecules and ions.^[13-15] The traditional synthetic approach to these materials involves spontaneous self-assembly of amphiphilic molecules from a bulk solution, with concurrent templating of inorganic precursor species through electrostatic or hydrogen bonding interactions with the amphiphilic molecules. This basic approach has led to the synthesis of various mesostructured materials in the form of powders,^[6,7,16] particles,^[17-22] thin films,^[23-25] and fibers.^[26] Mesoporous microspheres have been produced by several different strategies based on the traditional solution synthesis.^[17-23] Polydisperse silica spheres ranging in size from submicron to tens of microns

have been produced using a 1-alkylamine templating technique.^[20-22] Ordered mesoporous spheres have been produced by interfacial reactions conducted in oil/water emulsions, leading to micron to millimeter-sized particles.^[17-19] In addition, polydisperse hollow micron-sized spheres were produced by interfacial synthesis in which tetraethyl orthosilicate (TEOS) is hydrolyzed with a base and subsequently neutralized with an acid.^[23] These methods typically involve a relatively long aging or stirring time, and lead to polydisperse particle populations that are sometimes aggregated.

EISA of aerosols is distinct from bulk solution synthetic methods in that all species are initially confined to droplets, which undergo evaporation-driven concentration changes as they pass through the process. The concentration changes produce self-assembled liquid-crystalline surfactant structures that template the organization of the inorganic precursor species (typically alkoxide-derived). Solidification of the inorganic network, for example by condensation reactions, followed by removal of the surfactant, leaves a mesoporous inorganic ‘fossil’ of the surfactant mesostructure. Porous submicron silica particles possessing a variety of different mesostructures have been previously reported based on EISA in submicron aerosols.^[1] The method has also been used to produce submicron nonporous polymer-silica composites.^[27] EISA of larger droplets in a spray dryer produced mesoporous silica particles with diameters in the tens of microns, but these particles were typically thin-walled hollow shells, and were often collapsed or fragmented.^[28] Similar results using a spray dryer have been observed in our laboratories. While the larger drops of a spray dryer potentially enable synthesis of larger mesoporous particles, the immediate high temperature environment may promote condensation reactions that solidify the silica structure before solvent evaporation is complete, leading to shell

formation. In addition, the particle size distribution produced by spraying devices is broad. In this work, we have employed a method of droplet generation that produces monodisperse droplets, and a synthesis process that provides better control than can be provided with spray-based technology.

The cationic surfactant cetyltrimethyl ammonium bromide (CTAB) and the non-ionic surfactant $\text{CH}_3(\text{CH}_2)_{15}-(\text{OCH}_2\text{CH}_2)_{20}\text{-OH}$ (Brij-58) were employed for the present study. Two different silica precursor sols were employed: a pre-hydrolyzed acidic TEOS-based sol, referred to as A2**;^[1] and an acidic aqueous TEOS solution (further detail in Experimental section). Particle size could be controlled by varying the orifice diameter in the VOAG and the concentration of the precursor solution. Scanning electron micrographs of spherical porous silica particles (Fig. 1) illustrate that the particles are spherical, monodisperse in size, and possess a smooth surface morphology. The average particle size obtained using the A2** sol formulation^[1] with CTAB surfactant and a 20 μm orifice was $9.9 \pm 0.5 \mu\text{m}$ (mean and standard deviation of over 100 particles measured from SEM images) (Fig. 1(a)). The pH of the A2** formulation minimizes the siloxane condensation rate,^[29] thereby facilitating silica-surfactant self-assembly during aerosol processing. Using the same sol formulation with Brij-58 surfactant, a 10 μm orifice resulted in an average particle size of $6.0 \mu\text{m} \pm 0.3 \mu\text{m}$ (Fig. 1(b)).

Powder X-ray diffraction (XRD) of the particles shown in Figure 2 revealed only a single peak, indicating periodic short range structural order with d-spacings of 30.4 and 45.5 Å for particles produced with CTAB and Brij-58, respectively. The absence of higher order Bragg peaks indicates that these particles lack the high degree of long-range structural order that is commonly

seen for conventionally prepared MCM material. The much lower XRD intensity for the CTAB-templated material further indicates a lower degree of order than for the Brij-58 material.

Transmission electron microscopy (TEM) images obtained from cross sections of ultra-microtomed particle slices revealed that the particles produced from both CTAB and Brij-58 were not hollow. Particles produced with CTAB displayed a uniform mesostructure, but with no apparent long-range ordering (Fig. 3(a)). Particles produced using Brij-58 displayed a highly uniform periodic pore structure in some regions of the particles (Fig. 3(b)); however, most of the particle cross-section showed no apparent order (similar to Fig 3(a)). Electron diffraction of the Brij-58 particles indicated a mesostructural d-spacing of 45 Å, which corroborated the XRD results. Nitrogen adsorption-desorption isotherms showed typical features for mesoporous materials. The average (hydraulic) pore diameter (d_p) determined from nitrogen adsorption data (calculated as $d_p=4V_p/S_p$, where V_p is total pore volume and S_p is the BET surface area) were 22.3 and 28.2 for CTAB and Brij-58 templated powders, respectively. The corresponding BET surface areas of the particles were 600 and 516 m²/g for CTAB and Brij-58, respectively. These specific surface areas are much lower than we have observed for CTAB in fully ordered submicron particles, but are consistent with previous results obtained using Brij-56 surfactant.^[1]

Particles produced using the aqueous TEOS precursor solution with CTAB surfactant displayed much better ordering than those made with the A2** sol. Figure 4 shows TEM images of an ultra-microtomed section of one these particles. At low magnification, it was apparent that particles were not hollow, while higher magnification revealed that pores were present in well-ordered domains across the entire cross section of the particles. In some regions, the TEM images appeared consistent with the hexagonally-packed tubular pores bundles that we have

observed with the same solution and surfactant in submicron particles.^[30] In some areas near the surface, pores apparently are oriented parallel to the surface (Fig. 4(a)), which is consistent with what we have normally observed in submicron particles.^[30] However, in other regions the pore channels are apparently aligned perpendicular to the surface (Fig. 4(b)). This is the first time we have seen clear evidence of perpendicular pore alignment at the particle surface. This is of interest because alignment of tubular pore channels normal to the surface is optimal for unimpeded access to the pore interiors.

In summary, we have prepared monodisperse spherical porous silica particles with diameters in the 5 to 10 μm range based on evaporation-driven self-assembly of surfactants in droplets produced from a VOAG. The method should be applicable to particles as small as 1-2 μm and as large as 50 μm by varying VOAG orifice size and solution concentrations. This approach can have several significant advantages over the traditional solution-based self-assembly. The aerosol process is a continuous, scalable process in which the entire particle synthesis process occurs on a time scale of several seconds or less. Highly spherical unaggregated particles are consistently produced under appropriate conditions. Finally, any additives, dopants or additional components that can be aerosolized from a solution or dispersion are inevitably incorporated into each particle. These features make the method attractive for producing microspheres to be used in, for example, sensor applications,^[31-33] where environmentally-sensitive fluorescent dyes could be incorporated into particles. Similarly, porous interiors could serve as reservoirs for pharmaceutical agents in controlled release schemes. Mesoporous silica microspheres in the size range produced here are also highly promising as supports for biomolecules and biomembranes, which is an interesting new strategy for developing molecular affinity surfaces, biosensor

devices and high-throughput screening devices.^[34,35] A number of other possible applications can be envisioned, such as optical materials,^[5,36] catalyst supports,^[37] biocompatible microreactors^[38] and molecular separations media.^[20] The convenient control of particle size and monodispersity demonstrated in this research are important complements to the control of internal mesostructure and pore size provided by surfactant templating.

Experimental

Two precursor solution formulations were used: one based on an acidic silica sol (A2**), and one based on an aqueous TEOS solution. For the A2** formulation, the solutions were synthesized by addition of CTAB: $\text{CH}_3(\text{CH}_2)_{15}\text{N}^+(\text{CH}_3)_3\text{Br}^-$ (Aldrich) or Brij-58: $\text{CH}_3(\text{CH}_2)_{15}(\text{OCH}_2\text{CH}_2)_{20}\text{-OH}$ (Aldrich) to an acidic silica sol (A2**), as reported by Lu et al.^[1] In a typical preparation, tetraethylorthosilicate (TEOS) (Aldrich), ethanol, deionized water (conductivity less than 18.2 M Ω -cm) and dilute HCl (mole ratios 1:3.8:1:0.0005) were refluxed at 60 °C for 90 minutes to provide the stock sol. Then, 10 mL of stock sol was diluted with ethanol, followed by addition of water, dilute HCl, and aqueous surfactant solution (1.5 grams of surfactant dissolved in 20 ml of water) to provide final overall TEOS:ethanol:H₂O:HCl:surfactant molar ratios of 1:27:55:0.0053:0.19 and 1:22:55:0.0053:0.06 for CTAB and Brij-58 sols, respectively. For the aqueous TEOS-CTAB precursor solution, CTAB was mixed with water (5 wt% CTAB) and stirred to obtain a clear solution. To this solution TEOS and 1N HCl were added to give a solution with final molar ratios of TEOS:H₂O:CTAB:HCl is 1:63.28:0.15:0.0227. This sol was stirred for about 10 minutes before beginning a powder synthesis run.

The monodisperse droplets were generated by means of a VOAG (TSI Model 3450). In the VOAG, the aerosol solution was forced through a small orifice (10 μ m or 20 μ m) by a syringe pump, with syringe velocities of approximately 2×10^{-4} cm/s ($\sim 1.4 \times 10^{-3}$ cm³/s) and 8×10^{-4} cm/s ($\sim 4.7 \times 10^{-3}$ cm³/s) for the 10 μ m and 20 μ m orifices, respectively. This delivery rate was adjusted to provide a stable operating pressure of 340-420 kPa. The liquid stream was broken up into uniform droplets by the vibrating orifice. The frequency range employed was 40-200 kHz, with the final setting adjusted to eliminate satellite droplets. The droplets were then injected axially along the center of a turbulent air jet to disperse the droplets and to prevent coagulation. Following the mixing of the dispersed droplets with a much larger volume of filtered dry air, the droplet-laden gas stream flowed through a 2.5 cm diameter quartz tube into a three-zone furnace (0.9 m heated length) maintained at 500 °C (A2** runs) or 420 °C (TEOS solution runs). This provided a mean residence time of approximately 0.3 s in the heated zone. The particles were collected on a filter maintained at approximately 80 °C by a heating tape. Collected particles were calcined in air at 400-450 °C for 4 hours (A2** runs) or at 500 °C for 12 hours (TEOS solution runs) to remove the surfactant template.

The particles were characterized by scanning electron microscope (Hitachi S-800) and X-ray diffraction (Siemens D5000, CuK α radiation, $\lambda = 1.5418$ Å) techniques. Surface area and pore size distribution studies were carried out by nitrogen adsorption/desorption at 77K using a Micromeritics ASAP 2000 porosimeter. For cross-sectional TEM (JEOL 2010, 200 KV), particles were embedded in an epoxy and then cross-sectioned using a Sorvall MT-5000 Ultra Microtome machine.

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Figure Captions

Figure 1. Scanning electron micrographs of porous silica particles obtained using: (a) A2** sol, CTAB surfactant and 20 μ m VOAG orifice, (b) A2** sol, Brij-58 surfactant and 10 μ m VOAG orifice.

Figure 2. XRD patterns of the mesoporous silica particles prepared using CTAB (a) and Brij-58 (b).

Figure 3. TEM images obtained from ultra-microtomed sections of mesoporous particles produced with the A2** sol and surfactants CTAB (a) and Brij-58 (b).

Figure 4. TEM images obtained from ultra-microtomed sections of a particle produced using the aqueous TEOS precursor solution with CTAB surfactant: (a) region where pores are apparently aligned parallel to particle surface, (b) region showing some pore channels aligned perpendicular to the particle surface.