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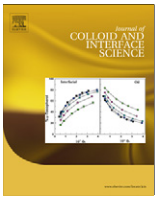

Quasi-spherical silver nanoparticles: Aqueous synthesis and size control by the seed-mediated Lee–Meisel method

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ABSTRACT

Silver nanoparticles (AgNPs) are attracting tremendous attention in biomedicine, and their related performances are shape and size-dependent. For biomedical applications, water-soluble AgNPs are necessary. However, aqueous syntheses of AgNPs with controlled shape and size are relatively difficult as the balance between nucleation and growth is hard to regulate. This paper describes a robust method for controllable synthesis of quasi-spherical AgNPs based on the combination of the seed-mediated growth and the Lee–Meisel method by thermal reduction of $AgNO_3$ with citrate. In the presented method, citrate-stabilized AgNPs with tunable sizes up to 80 nm were achieved through one-step or stepwise growth process using qualified spherical 4 nm AgNPs as starter seeds. Specially, the two main difficulties (formation of nanorods and secondary nucleation during the growth stage) in the previous studies have been effectively overcome by tailoring the experimental parameters such as the reaction temperature and the seed amount, without extra additives, pH adjustment, and laser treatment. The crucial factors that affect the uniformity of the resulting AgNPs are discussed.

1. Introduction

The field of biomedicine using silver nanoparticles (AgNPs) is appealing due to their broad-acting biocidal activities and unique plasmonics properties in the visible region [1–3]. Many efforts have been devoted to control over the size and shape of AgNPs since their above properties are sensitive to size and shape [4–7]. For biomedical viewpoints, water-soluble AgNPs are highly desirable. While great progress has been achieved in the organic-media production of AgNPs [8–11], controllable synthesis of AgNPs in aqueous solution still remains a challenging task due to the hard-to-control nucleation process arising from the high reactivity of silver precursors in water. For the case of synthesizing spherical AgNPs, one of the most common approaches is the Lee–Meisel method by reducing $AgNO_3$ with citrate in an aqueous solution on boiling [12]. In this simple approach, citrate also serves as a stabilizer and has following advantages: (1) compatibility with biomolecules; (2) ease of being exchanged by other functional ligands; (3) thin capping layer ensuring effective enhancement of the Raman signals [13–15]. Unfortunately, the Lee–Meisel method limits to yield a large variety of 60–200 nm sized AgNPs with a wide range of size and shape. To resolve these problems, Yang et al. carried out the Lee–Meisel method at varied pH conditions to improve the balance between nucleation and growth and received a relatively good control of quasi-spherical AgNPs of 50–70 nm [16]. Gorup et al. proceeded the Lee–Meisel method at high pH value by the addition of ammonia and received spherical AgNPs of 2 nm with a narrow size distribution [17]. Very recently, Steinigeweg and Schlücker modified the Lee–Meisel method using additional highly viscous polyol components for uniform quasi-spherical AgNPs of 20–30 nm [18]. Apart from the above modified strategies, the Lee–Meisel method can also be optimized by introducing small AgNPs as seeds into the reaction system, which work both as a catalyst for the reduction of Ag precursor and as a nucleus to which Ag monomers formed from reduction add in subsequent growth process, and thus could achieve a better control over the final particles in a broad size range [19,20]. In this procedure, the uniformity of the seeds is crucial for the growth of larger AgNPs. However, the high reactivity of Ag precursors gives rise to a hard control over the seeds size even employing strong reductant and extra additives such as polyvinyl pyrrolidone or special treatment such as laser ablation was usually indispensable for narrowing size distribution [21–23]. Meanwhile, the challenge of conveniently minimizing the formation of nanorods and secondary nucleation during the seeded growth still remains [20,24].

In this study, we report a facile approach for qualified small AgNPs with an average size of 4 nm under a rapid nucleation-growth-ripening principle. Using these AgNPs as starter seeds, quasi-spherical, citrate-capped AgNPs with tunable sizes can be

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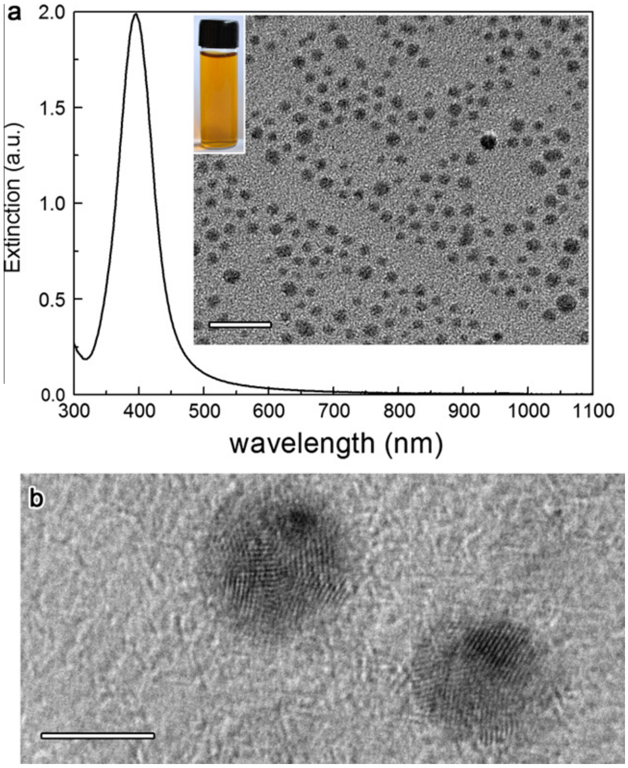

Fig. 1. (a) UV–vis spectrum of the solution of as-synthesized AgNPs; the insets present a digital picture of the AgNPs solution and a TEM image of the AgNPs. Scale bar: 20 nm. (b) HRTEM image of the AgNPs shown in panel a. Scale bar: 5 nm.

routinely synthesized in aqueous solution by combing the Lee–Meisel method, without the need of extra additives, pH adjustment, and laser ablation. Results are shown that AgNPs can be achieved in a size range up to 80 nm through one-step or stepwise growth process, but there is no reason against conducting subsequent growth steps and obtaining larger AgNPs.

2. Materials and methods

2.1. Materials

Silver nitrate ($AgNO_3$), sodium borohydride ($NaBH_4$), trisodium citrate dihydrate ($C_6H_5Na_3O_7{\cdot}2H_2O$), and hydrogen tetrachloroaurate tetrahydrate ($HAuCl_4{\cdot}4H_2O$) were all purchased from Shanghai Sinopharm Chemical Reagent Co., Ltd. (China) and used as received. Deionized water with resistance of 18 MΩ cm was used in all the experiments. All the glassware was cleaned by aqua regia ($HCl{:}HNO_3$ in a 3:1 ratio by volume) and rinsed with deionized water prior to the experiments.

2.2. Synthesis of citrate-capped 4 nm AgNPs

A 20 mL of 1% (w/v) citrate solution and a 75 mL of water were added in a round bottom flask and the mixture was heated to 70 °C for 15 min. After that, 1.7 mL of 1% (w/v) $AgNO_3$ solution was introduced to the mixture, followed by the quick addition of 2 mL of 0.1% (w/v) freshly prepared $NaBH_4$ solution. The reaction solution was kept at 70 °C under vigorous stirring for 1 h and cooled to room temperature. Water was added to bring the volume of the dispersion to 100 mL. The resulting AgNPs were used as starter seeds.

2.3. Synthesis of AgNPs by the Lee–Meisel method

In this procedure, AgNPs were synthesized by the classic Lee–Meisel method in a 100 mL quantity [12]. A 1.7 mL of 1% $AgNO_3$ aqueous solution was added to a 100 mL of water in a three-necked round bottom flask equipped with a reflux condenser and the mixture was brought to boiling by a heating mantle for 15 min. Next, 2 mL of 1% citrate solution was added to the reaction solution. The reaction solution was kept reflux with vigorously mechanical stirring for 1 h and cooled to room temperature.

2.4. One-step seeded growth of AgNPs

This procedure combined seeded growth with the above Lee–Meisel method. Five sets of 250 mL three-necked round bottom flasks, each equipped with a reflux condenser, were labeled A, B, C, D, and E. In set A, 2 mL of 1% citrate solution was mixed with 80 mL of water and brought to boiling by a heating mantle for 15 min. Next, 10.0 mL of starter seeds solution was added while vigorously mechanical stirring, followed by the addition of 1.7 mL of 1% $AgNO_3$ solution. Stirring continued for 1 h while keeping reflux and cooled to room temperature. AgNPs synthesized in this way were spherical with an average size of 20 nm. Similarly, in each set of B to E, 2 mL of 1% citrate solution was mixed with 80 mL of water and brought to boiling by a heating mantle for 15 min. Next, 5.0, 3.0, 1.5, and 0.75 mL of the starter seed solutions were added, respectively, while vigorously mechanical stirring, followed by the addition of 1.7 mL of 1% $AgNO_3$ solution. Stirring continued for 1 h while keeping reflux and cooled to room temperature.

2.5. Stepwise seeded growth of AgNPs

To obtain larger AgNPs, stepwise seeding growth was employed. For the synthesis of AgNPs of average 28.5 nm, the first step was similar to the one-step procedure of set A: a 2 mL of 1% citrate solution was mixed with 75 mL of water and brought to boiling by a heating mantle for 15 min. Next, 10.0 mL of starter seed solution was added while vigorous mechanical stirring, followed by the addition of 1.7 mL of 1% $AgNO_3$ solution. Vigorously mechanical stirring continued for 1 h while keeping reflux. Then, the next step proceeded. A 2 mL of 1% citrate solution was added to the reaction solution together with 1.7 mL of 1% $AgNO_3$ solution. Reflux with vigorous stirring continued for another one hour. The same operation was then repeated again. After that, the reaction solution was cooled to room temperature. Water was added to bring the volume to 100 mL.

For AgNPs of average 45 nm, the resulting 28.5 nm AgNPs were used as seeds. A 2 mL of 1% citrate solution was mixed with 80 mL of water and brought to 80 °C by a water-bath for 15 min. Next, 10.0 mL of the seed solution was added while vigorously mechanical stirring, followed by the addition of 1.7 mL of 1% $AgNO_3$ solution. The reaction solution was kept heating at 80 °C under vigorous mechanical stirring for 2 h and cooled to room temperature. Water was added to bring the volume to 100 mL.

For AgNPs of average 58 nm, the resulting 45 nm AgNPs were used as seeds; 50 mL of the seed solution was mixed with 40 mL of water and brought to 80 °C by a water-bath for 15 min. Next, 2 mL of 1% citrate solution was added while vigorous mechanical stirring, followed by the addition of 1.7 mL of 1% $AgNO_3$ solution. The reaction solution was kept heating at 80 °C under vigorous mechanical stirring for 2 h and cooled to room temperature.

For AgNPs of average 74 nm, the 45 nm AgNPs were used as seeds. A 30 mL of the seed solution was mixed with 60 mL of water and brought to 80 °C by a water-bath for 15 min. Next, 2 mL of 1% citrate solution was added while vigorous mechanical stirring, fol-

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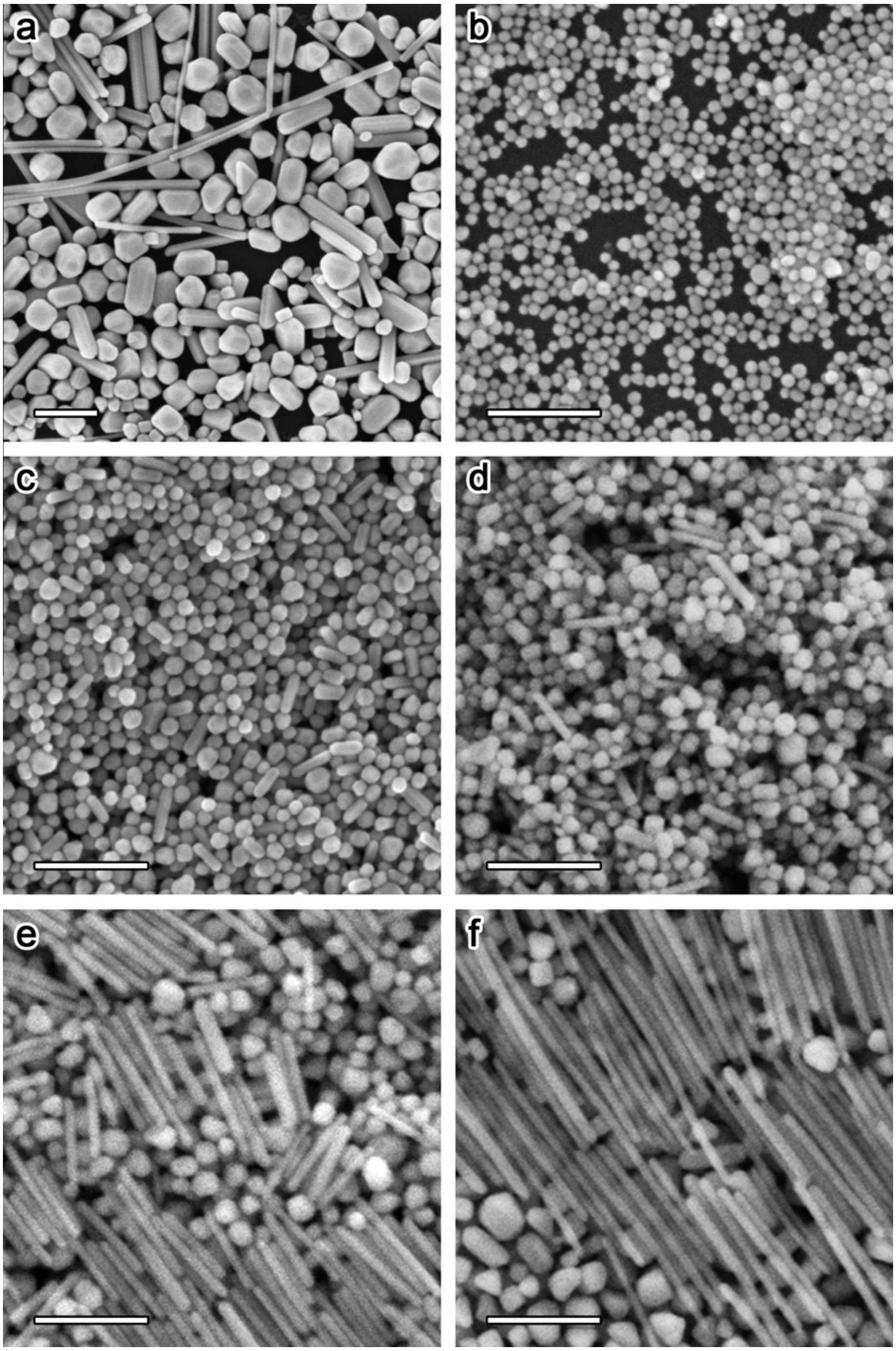

Fig. 2. (a) SEM image of AgNPs by the Lee–Meisel method. (b–f): SEM images of AgNPs by combination of Lee–Meisel method with seeded growth using 10 mL, 5 mL, 3 mL, 1.5 mL, and 0.75 mL of Ag seeds, respectively. Scale bars: 200 nm.

lowed by the addition of 1.7 mL of 1% $AgNO_3$ solution. The reaction solution was kept heating at 80 °C under vigorous mechanical stirring for 2 h and cooled to room temperature.

2.6. Characterization

Transmission electron microscopy (TEM) and high-resolution TEM images were taken with a JEM-2100EX (JEOL) transmission electron microscope operated at 200 kV. Scanning electron microscopy (SEM) images were obtained by a Carl Zeiss ULTRA Plus Field Emission Scanning Electron Microscope with an accelerating voltage of 20.0 kV. The average sizes of as-obtained AgNPs were measured from about 200 particles to provide statistical significance. The UV–vis extinction spectra were recorded by a Shimadzu UV-3600 spectrophotometer in a range of 300–1100 nm.

3. Results and discussion

Small AgNPs were synthesized involving $NaBH_4$ reduction of $AgNO_3$ in the presence of concentrated citrate at 70 °C (method section for details). The sharp extinction at 391 nm and the bright yellowish brown solution of the resultant are manifests of characteristic surface plasmon resonance (SPR) of the AgNPs (Fig. 1a). Corresponding transmission electron microscopy (TEM) image

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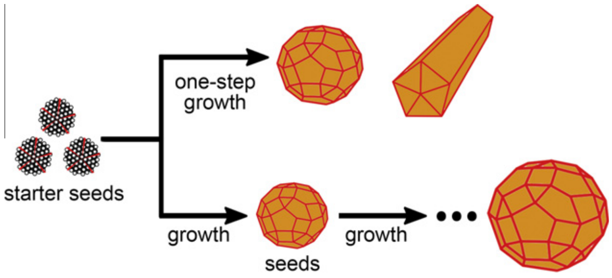

Scheme 1. Schematic illustration of one-step and stepwise seeded growth of AgNPs in the Lee–Meisel reaction system. Possibly twinned boundaries are delineated in the drawing with red lines. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

shows that these spherical AgNPs have a narrow size distribution of 4.0 ± 0.7 nm (Fig. 1a and Supplementary Fig. S1). High-resolution TEM image reveals that these AgNPs are multi-twinned ones (Fig. 1b).

It is worth noting that, when the AgNPs were prepared either at room temperature or on boiling, a large average size of AgNPs with a broad size distribution was observed (Supplementary Figs. S2 and S3). These results indicate that reaction temperature plays a key role in particle size and distribution. At an elevated temperature, the rates of nucleation and growth were accelerated to obtain a small average size. On the other hand, heat-treatment also speeded up the Oswald ripening process where large particles emerged at the expense of smaller ones to achieve a more uniform size distribution of the final AgNPs. As we found, the temperature at 70 °C within the given time can reach a relatively perfect balance of particle size and distribution. Moreover, good reproducibility of this simple route was shown by repeating the experiment three times and obtaining nearly the same UV–vis spectrum (Supplementary Fig. S4).

Subsequently, a series of experiments have been conducted by adding different amounts of the above AgNPs (starter seeds) to the Lee–Meisel reaction system (method section for details). The scanning electron microscopy (SEM) images in Fig. 2 show notable improvement upon seeds addition on size and shape control of the obtained AgNPs (Fig. 2b–f) compared with the Lee–Meisel method (Fig. 2a). This one-step seeded synthesis can well produce quasi-spherical Ag NPs up to 20 nm (Fig. 2b and Supplementary Fig. S5). However, while larger AgNPs can be obtained by decreasing the amount of the seeds, a distinct second population of nanorods was also generated (Fig. 2c–f). Considering the starter seeds contain twin planes, it has been documented that multi-twinned metal NPs favor the evolvement of anisotropic structures [25]. Moreover, it was found that the short axis of the nanorods gets thinner with the increase of aspect ratio upon continuous decrease of the seed amount (Fig. 2c–f), which strongly indicates that a monomer diffusion-controlled growth mechanism dominates the formation of these Ag nanorods [26]. The above results clearly suggest that a high ratio of Ag monomer to seed favors the formation of nanorods. For this reason, although small AgNPs with a narrow size distribution can be generated in a one-step seeded synthesis, it

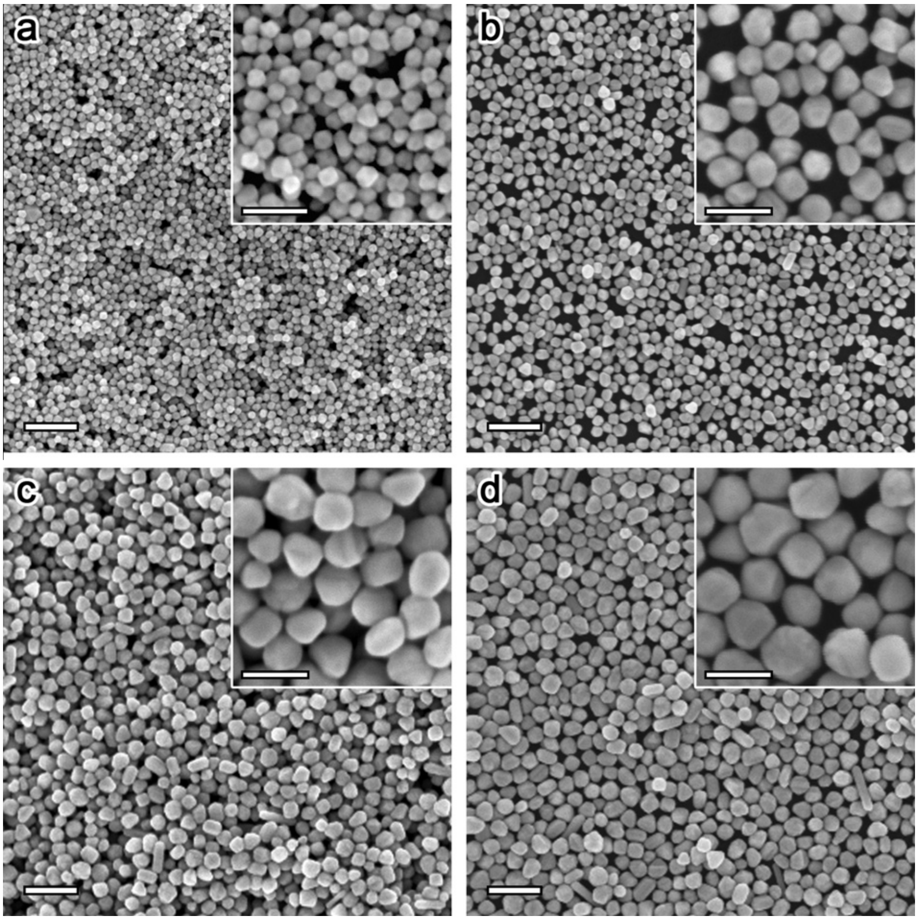

Fig. 3. SEM images of AgNPs with different average sizes by stepwise seeded syntheses: (a) 28.5 nm, (b) 45.0 nm, (c) 58.0 nm, and (d) 73.5 nm. Scale bars: 200 nm (panels), 100 nm (insets).

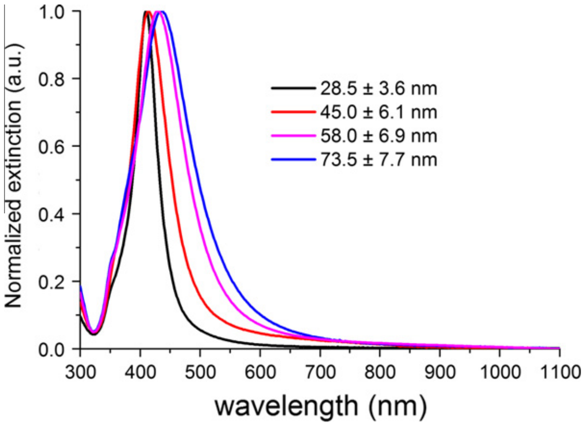

Fig. 4. UV–vis spectra of AgNPs with different average sizes by stepwise seeded growth (curves from left to right): 28.5 nm, 45.0 nm, 58.0 nm, and 73.5 nm, respectively.

does not work well for controllable synthesis of larger AgNPs by varying the amount of the seeds.

On the other hand, the well-sized small AgNPs also indicate that there exists a proper ratio of monomer to seed. Thus, we attempted to produce controllable large AgNPs through stepwise seeding growth in Lee–Meisel reaction system. As shown in Scheme 1, this strategy employs a whole batch of well-sized AgNPs grown from starter seeds as the second seeds for next stage particle growth. Then, this whole batch of AgNPs grown from the second seeds is used as the third seeds for the following particle growth and this process continues. Assuming that the produced Ag monomers only add on the surface of seeds and thus the total number of AgNPs keeps constant, it would be possible to achieve large AgNPs with controllable sizes by stepwise growth process.

In the following studies, we chose ~20 nm AgNPs (Fig. 2b) as seeds to grow lager AgNPs by stepwise seeded growth process. To simplify the synthetic protocol, the amounts of citrate and $AgNO_3$ followed the recipe of the Lee–Meisel method and kept constant in each growth step (method section for details). While the size of the obtained AgNPs gradually enlarged to ~30 nm without the formation of nanorods within two steps of growth (Fig. 3a), second nucleation events began to take place in the following growth steps and led to the generation of appreciable small AgNPs (Supplementary Fig. S6). This result indicates that the large seeds particles exhibit weaker catalytic action in comparison with smaller ones. As a result, the as-formed silver monomers would not only add on their surfaces but also self nucleate to form new particles. It thus can be deduced that the production of well-sized larger AgNPs needs an even lower ratio of monomer to seed to avoid the occurrence of secondary nucleation. To reach this point, the reduction rate of $AgNO_3$ must be modulated quite slowly. Since citrate is a weak reductant and its reducing power highly depends on reaction temperature [16], the reduction rate of Ag^+ could be decreased by lowering the reaction temperature. According to above mechanism analysis, AgNPs with an average size of 45 nm were successfully grown from the resulting 30 nm particles at 80 °C (Fig. 3b). Then, these particles were further used as seeds to prepare AgNPs of 58 nm and 74 nm in average size, respectively, by altering the seed amounts (method section for details). From the SEM images, it can be found that the size and the shape of these large AgNPs have been well controlled (Fig. 3c and d), which are also confirmed by corresponding UV–vis spectra (Fig. 4) and statistic data (Supplementary Fig. S7). More large AgNPs with low polydispersity can be reasonably predicted by continuing above procedures.

These well-sized AgNPs, despite their intrinsic applications, can serve as a suitable sacrifice-template to evolve into hollow alloy nanostructures due to the moderate reduction potential of Ag^+/Ag pair (0.80 V vs. S.H.E) [27]. For example, spherical Au–Ag alloy nanocages with SPR in the near infrared region can be easily produced by reacting the above-obtained AgNPs with $HAuCl_4$ solution (Supplementary Fig. S8). These porously hollow nanostructures are promising platforms for photothermal therapy and high payload of drugs [28,29].

4. Conclusions

In summary, we have demonstrated a robust method that combines seed technique with the Lee–Meisel method and can controllably achieve quasi-spherical citrate-capped AgNPs with size ranging up to 80 nm through one-step or stepwise growth process. It is found that, despite the uniformity of seed particles, the ratio of monomer to seed also plays important roles in the size and shape of the final particles. To suppress the formation of nanorods and second nucleation events, the ratio of monomer to seed must be tailored to a relatively low level. It can be reached, for instance, by carefully adjusting the reaction temperature and the seed amount without the help of extra additives, pH adjustment, and special treatment. We expect that the size-controllable AgNPs obtained here can optimize their size and shape-dependent features. We also expect this contribution will help to improve the quality of other noble metal NPs employing the seeded growth processes.

Acknowledgments

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jcis.2012.12.037.

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