High-Yield Paste-Based Synthesis of Thiolate-Protected Silver Nanoparticles

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Supporting Information

ABSTRACT: Nanoparticles rival pharmaceuticals in synthetic inefficiency, in particular as measured by process mass intensity, with by far the largest contribution to waste being from solvents. We have therefore developed a greener method of synthesizing silver nanoparticles using a paste format instead of a metal salt solution. The paste-based synthesis requires 87% less solvent yet still produces exclusively Na₄Ag₄(p-MBA)₁₀ nanoparticles, without size sorting, with 89% yield. By using a stoichiometric silver-thiolate polymer as a precursor to intimately mix the metal atoms and ligands, and by using a small amount of liquid to form a paste to promote mass transport, the heterogeneity and kinetics problems that are associated with entirely solid-state syntheses were avoided. Because the nanoparticle product was also a paste, solvent use for postprocessing was minimized. Use of the silver-thiolate polymer can also reduce health risks associated with hazardous free thiols in conventional solution-phase syntheses. Using this strategy, the process mass intensity was reduced from ~1800 for the solution-phase reaction to ~200 and ~100 for the paste-based reaction with and without protonation of the ligands, respectively.

INTRODUCTION

It has been recognized that there are opportunities to improve nanoparticle synthesis by adopting greener methods.1−11 The choice of starting materials,12−16 reaction media,7 reducing agents,17,18 and processing of the product10 are some of the major areas where greener choices can be made.11 The chemical synthesis of nanoparticles also demands large quantities of solvent, some of which are hazardous, for both the synthesis and processing of the product. Although it is possible to recycle solvent to reduce waste, minimizing the use of solvents in nanoparticle production is an important goal.

This point can be better appreciated by considering the synthesis of Na₄Ag₄(p-MBA)₁₀ nanoparticles (hereafter referred to as Ag₄d₄), where p-MBA is p-mercaptobenzoic acid, which has been demonstrated on a large scale.19 Although the efficiency of nanoparticle synthesis was improved considerably in terms of both time and selectivity, in that 3 orders of magnitude more product was produced in a single batch and that no species other than Ag₄d₄ was detected in the product,12,15 a process mass intensity (PMI) of ~1800 for this synthesis makes it clear that the materials usage was strikingly inefficient.14,15 If one considers only dry reagents, however, then this would correspond to a PMI of only 3S, meaning the liquids (i.e., solvents and nonsolvents) constituted 98% of the PMI. Clearly, reducing solvent use ought to be the first step toward improving nanoparticle synthesis efficiency.

Solvents play a key role in nanoparticle synthesis, ensuring good mixing and mass transport; therefore, it is a challenge to develop strategies to reduce or eliminate them. Reactions involving small molecules are generally site specific and therefore more tolerant of inhomogeneities in the reaction mixture; however, nanoparticle syntheses are more statistical, not unlike polymer syntheses, and can be sensitive to inhomogeneities in the reaction conditions and the environment around each nascent particle. In particular, the synthesis of uniform nanoparticles typically requires a brief and uniform nucleation event followed by uniform growth.16 It is liquid solvents that provide the mobility and homogeneity required for such high-quality nanoparticle syntheses.17,18 Synthesis of nanoparticles in the solid state,16,18−20 naturally, is then extremely challenging due to problems of mixing and
kinetics. Kinetics of solid-state reactions is typically very slow at room temperature due to the limited mobility of the reagents. This mobility issue can be mitigated by more intimate mixing of the reaction components by using stoichiometric precursors, coprecipitation, mechanochemical methods, or by sequential deposition of thin layers from the gas phase. These techniques were extensively applied to the synthesis of bulk semiconductor materials, nanoparticles, and metal–organic frameworks.

A partially solid-state approach to nanoparticle synthesis was successfully developed for a variety of different molecular nanoparticle products. Although this new methodology greatly reduced the use of solvents, it was limited to ligands that were liquid under reaction conditions. This was necessary to promote good mixing of the reagents, which is an important limitation in solid-state reactions. In the case of solid ligands, such as mercaptosuccinic acid and glutathione, it was necessary to add water to the reaction mixture. This method entirely failed when applied to the synthesis of Na₄Ag₄₄(p-MBA), however, which motivated the current work for developing a more general synthetic approach.

Here, we demonstrate the paste format as a greener synthetic method than the solution format. We synthesized Ag₄₄ because it is (i) a strongly favored product thermodynamically, (ii) well-known to form as a single-sized molecular product, i.e., with no polydispersity, (iii) easily identified by absorption spectroscopy and mass spectrometry, and (iv) easily scalable and amenable to industrial production. We used a silver-thiolate polymer as a well-defined starting material because the silver atoms and the thiolate ligands are intimately and stoichiometrically mixed in this class of compounds, which eliminated the issue of slow solid-phase mixing kinetics of those reagents. The polymer precursor also eliminated the prior requirement of using liquid thiolates as ligands. Forming a precursor paste with a 6:1 liquid-to-solid ratio by volume improved the transport kinetics during the reaction compared to those of a truly solid-state reaction. A coordinating solvent was used as the liquid component of the paste for preparing the silver-thiolate precursor because it is green and amenable to reuse and repurification; however, for synthesizing Ag₄₄, it is advantageous to have DMSO as the liquid component of the paste (vide infra). A water/DMSO mixture was therefore used instead of methanol because a sufficient amount of DMSO was retained in the silver-thiolate precipitate to serve as the liquid component of the paste for nanoparticle synthesis. The preparation described above yielded 4.9 mL of paste, of which the liquid component was 4.2 mL and the solid precursor was 0.7 mL. Assuming that the composition of the liquid retained in the paste was the same as the 7:4 water/DMSO mixture used in its preparation, the volume of DMSO used in the paste for each synthesis would correspond to 1.5 mL.

The silver-thiolate paste was transferred to a mortar and ground with a pestle to ensure the uniformity of the paste before reduction (see Figure 1). Next, 150 mg of finely ground NaBH₄ powder (4 mmol) was added to the silver-thiolate paste while grinding to maintain a homogeneous mixture. The reduction reaction was vigorous, producing bubbles due to hydrogen evolution, and resulted in a rapid color change to orange and finally to a dark reddish-brown color. The reaction was completed once the dark red-brown color was persistent; this required 2–3 min. At this point, 10 mL of ethanol was added to stop the reduction reaction and to clean the product (note: if the reaction continued, then the Ag₄₄ nanoparticles would be reduced to form larger plasmonic nanoparticles). After washing the solid product, the ethanol was discarded.
In the case of p-MBA ligands, the carboxylic acid groups partially deprotonate during the synthesis and are charge neutralized by sodium cations, yielding the conjugate base. If desired, the product can be reprecipitated by dispersing it in 10 mL of DMF and then adding 1.40 g of citric acid to the dispersion. As the product becomes protonated, it dissolves into the DMF to form a Ag44 solution. The protonated nanoparticles can then be precipitated using 10 mL of isopropanol, yielding the final product as a solid powder. The protonated product can be stored as a powder, typically in a freezer at \(-15^\circ C\). This reaction produced 145 mg of Na4Ag44(p-MBA)30, which corresponds to an 89% yield.

**Infrared Spectroscopy.** Dry silver-p-MBA precursor was mixed with KBr powder in a ratio of 1:50 by weight and then pressed into a pellet. Infrared spectra were recorded using a PerkinElmer Spectrum Two FT-IR spectrometer using a KBr pellet for a background scan.

**UV–Visible Absorption Spectroscopy.** Fully protonated solutions of Ag44 were prepared in neat DMF for spectroscopic analysis. Optical absorption spectra were recorded on a PerkinElmer Lambda 950 spectrophotometer using a 0.5 cm path length cuvette.

**Electrospray Ionization Mass Spectrometry.** Protonated Ag44 samples were dissolved in DMF with a concentration of \(\sim 1\) mg/mL. Electrospray ionization mass spectrometry (ESI-MS) data were collected on a Synapt G1 quadrupole-time-of-flight mass spectrometer equipped with a nanoflow electrospray ionization source (Waters Corp.) and using homemade fused silica emitters. Mass spectra were collected in negative ion V-mode using the following optimized parameters: capillary voltage, 2.0–4.0 kV; sampling cone, 15 V; extraction cone, 4.0 V; cone gas, 0 L/h; nanoflow, 0.1 bar; trap collision energy, 0.5 V; transfer collision energy, 1.0 V; source temperature, 40 °C; desolvation temperature, 120 °C. Calibration was performed using cesium iodide in the range of 100 \(\leq m/z \leq 4000\). Data were collected and processed using MassLynx 4.1 software (Waters Corp.).

**Energy-Dispersive X-ray Spectroscopy.** Scanning electron microscopy (SEM) and energy dispersive spectroscopy (EDS) studies were performed with an FEI QUANTA-200 SEM and a JEOL JSM-7500F field-emission scanning electron microscope equipped with a Bruker Quantax (XFlash detector 5010) EDS system. For measurements, samples were drop cast on either an indium tin oxide (ITO)-coated glass substrate or an Al SEM sample stub before being dried in a vacuum.

**X-ray Photoelectron Spectroscopy.** X-ray photoelectron spectroscopy (XPS) measurements were conducted using an Omnicron ESCA Probe spectrometer with polychromatic Mg Kα X-rays (\(h\nu = 1253.6\) eV). The samples were spotted as drop-cast films on a sample stub. A constant analyzer energy of 20 eV was used for the measurements.

**RESULTS AND DISCUSSION**

Na4Ag44(p-MBA)30 was chosen as a target compound for the development of a new synthetic strategy because the liquid-phase methods produce a single-sized product (without size separation) and because the reaction is easily scalable and therefore would require large quantities of solvent. Initially, the reaction was performed using a solvent-free synthetic protocol that was described previously. Grindng AgNO3 and p-MBA powders together by mortar and pestle did not result in good mixing; therefore, the reaction to form the silver-thiolate polymer was ineffective, and no color change was observed. When the NaBH4 reducing agent was added and the powder mixture was ground further, the powder changed to a gray color. Attempts to extract Ag44 from this product failed; therefore, it was concluded that the existing methodology was not able to produce Ag44.

Grinding the powders produced micrometer-scale grains and therefore inhomogeneities on that length scale. This is an unsatisfactory starting material for producing nanoparticles as more intimate mixing of metal and ligand is needed. The previous solvent-free work used a ligand that was a liquid at room temperature and therefore was able to completely react with the AgNO3, forming the silver-thiolate precursor. This was not possible with ligands in solid form.

For the mixing problem for ligands in solid form to be circumvented, a Ag-p-MBA precursor was used as the starting material because it contained silver and p-MBA ligands that were already stoichiometrically mixed at an atomic scale. This material can easily be prepared by combining AgNO3 and a thiol-containing ligand in a mutual solvent. A precipitation reaction occurs immediately, forming the silver-thiolate polymer. The silver-thiolate precipitate can be easily collected, and the supernatant can be reused. Note that by preparing the silver thiolate precursor separately, there is no longer a limitation on the properties of the thiol-containing ligand, i.e., it need not be a liquid. Furthermore, the use of silver-thiols ought to mitigate some of the issues associated with commonly used toxic and volatile thiol-containing ligands (e.g., phenylethanethiol, benzenethiol, tert-butylbenzenethiol) as well as analogous selenium-containing ligands, making the subsequent chemical reactions significantly safer and therefore more amenable to scale up.

Because p-MBA has both a thiol and a carboxylic acid, it was not immediately clear whether the precursor was a silver-thiolate polymer or a silver-carboxylate dimer complex, as in the case of silver benzoate. Infrared spectroscopy was used to detect the presence of free carboxylic acid groups (see Figure S1). Two peaks at 2552.2 and 2674.2 cm\(^{-1}\) were assigned to carboxylic acid stretching modes, which indicated that the acid was protonated. Further, the peaks at 1289.8 and 1427.0 cm\(^{-1}\) were due to C−H bending modes. The protonation of the carboxylic acid indicated that the silver was bound to the thiol group; therefore, it was confirmed that the precursor was the expected silver-thiolate polymer.

When the NaBH4 powder was added to the dry Ag-p-MBA precursor powder, subsequent mixing by mortar and pestle resulted in a color change. The color was again predominantly gray; however, the product also had a reddish-purple color to it. This indicated that the reactions using the silver-thiolate precursor were able to proceed to make nanoparticle products; however, the reactions were quite slow. This was presumably due to the limited mobility of the reagents in the solid state.

For this kinetic bottleneck to be alleviated, a small amount of methanol was added to the precursor to form a paste. In this case, the reaction proceeded much more quickly. The color of the paste changed first to brown and then to orange-brown. This product contained large plasmonic silver nanoparticles with a small amount of Ag44, as determined by optical absorption spectroscopy (see Figure S2). This indicated that Ag44 could be synthesized; however, the lack of a coordinating solvent failed to protect the nanoparticles and led to the poor yield of Ag44.
DMSO is a relatively benign solvent with good coordinating abilities; therefore, it was used as the liquid component of the precursor paste. This biased the synthesis toward Ag_{44} by protecting and stabilizing the nanoparticles.\(^{13}\) In this case, the reaction proceeded somewhat faster than with the methanolic paste. The reaction began in a more vigorous fashion, initially producing orange foam upon addition of the reducing agent. As the reaction proceeded, the color changed to brown and then to deep red, indicating that Ag_{44} was produced in good yield.

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Molecular nanoparticles are too small to be identified by electron microscopy and can easily be transformed into larger nanoparticles by the electron beam; therefore, other analytical techniques are required for identifying this class of materials. In the case of Ag_{44}, its optical absorption spectrum is unique and distinct enough to be used for its identification, which is also the case for Ag_{35}.\(^{13,43}\) The absorption spectrum of a DMF solution of the product was compared with the distinct fingerprint spectrum of Ag_{44} produced by solution-phase methods (see Figure 2); the spectra matched in detail, confirming the identity of the product as Ag_{44}. Note that the spectra contained no component that could be attributed to the silver-thiolate precursor, which absorbs strongly in the UV, or to larger plasmonic nanoparticles, which are very strong light absorbers, indicating their absence.\(^{13}\) The molar absorptivity of Ag_{44} was used to determine the yield of Ag_{44} in this reaction,\(^{13}\) which was found to be 89%.

Molecular nanoparticles are also identified by electrospray ionization mass spectrometry due to the gentle nature of the ionization process, which mitigates fragmentation and enables formula determination with protonic precision. A mass spectrum of the product was obtained by ESI-MS (Figure 3). The mass spectrum showed a peak that corresponded to the intact Ag_{44}(p-MBA)_{30}^{4+} species (m/z 2335) as well as other associated peaks, similar to that reported for the solution-phase synthetic route.\(^{13,15}\) This included products of the spontaneous fragmentation of Ag_{44}(p-MBA)_{30}^{4+} due to high charge density on the desolvated nanoparticle. Fragmentation resulted in primarily AgL_{2}^{−} (m/z 414) and Ag_{43}L_{28}^{3−} (m/z 2976) species. Mass spectra also showed the presence of silver adducts of the intact Ag_{44}(p-MBA)_{30}^{4+} nanoparticle. No other small silver nanoparticles were detected, which is complementary to the optical absorption spectroscopy results that showed the absence of larger silver nanoparticles.

The product was further characterized by EDS and XPS. The EDS spectra showed that the Ag:S stoichiometry of the product was approximately 3:2, which corresponds to that of Na_{4}Ag_{44}(p-MBA)_{30} (Figure S3). It is possible to form larger plasmonic silver nanoparticles with this ligand by over-reducing the product;\(^{13}\) however, if larger species were present in significant abundance, then the measured ratio would have been greater than 3:2 because the volume to surface ratio is larger for larger nanoparticles. This is in agreement with the optical absorption results in which species other than Ag_{44} were not detected in the product.

X-ray photoelectron spectroscopy was also performed to characterize both the precursor and the final product. The survey spectrum of each material showed the expected elements (Figure S4). The expanded spectra in the Ag 3d region for the Ag_{44} product (Figure S5) showed that the Ag 3d_{3/2} and Ag 3d_{5/2} peaks appeared at 368.2 and 374.2 eV, respectively. This showed that the oxidation states of the silver atoms in the Ag_{44} molecule were on average similar to those of Ag(0). On the basis of DFT analysis, the 12 inner core atoms were expected to be approximately Ag(0), the 20 outer core atoms approximately Ag(1/4), and the outer mount atoms approximately Ag(1/3).\(^{13}\) This would correspond to a small partial oxidation, on average, which is qualitatively consistent with our measurements.\(^{13}\) The expanded spectra in the Ag 3d region for the silver-thiolate precursor (Figure S5) showed that the Ag 3d_{3/2} and Ag 3d_{5/2} peaks appeared at 368.7 and 374.7 eV, respectively. This higher binding energy is consistent with a higher oxidation state, as expected.

The S 2p states were also measured, fitting each of the components (Figure S5). The S 2p_{3/2} peak appeared at 163.0 and 162.7 eV for Ag_{44} and the silver-thiolate precursor, respectively. It is expected that the sulfur is more negative in the thiolates, in accordance with the more fully oxidized silver. The ratio of Ag:S for the case of clusters was found as 1:0.67, which again corresponds to a product that is free of large plasmonic nanoparticles.

Although we have now demonstrated a method of producing Ag_{44} nanoparticles with excellent yield using very little solvent, postsynthetic processing remains to be addressed. The established methods of postsynthetic processing of these particles use large amounts of solvent, some of which are
hazardous. For example, large volumes of DMF and toluene are used sequentially to solubilize and precipitate nanoparticles to extract and purify the product. Developing alternative methods of extracting, protonating, and cleaning the product using as little solvent as possible is therefore quite desirable.

The product of the reaction was already in the solid state; therefore, it would be desirable to process this material without dissolution and precipitation to minimize solvent use. To that end, a small amount of ethanol (10 mL in this case) was found to be satisfactory for cleaning the product immediately following the reaction. Washing with ethanol was found to clean the product of unreacted NaBH₄, which arrested the reaction, as well as excess p-MBA (see Figure S6a and b).

The product at this point was the conjugate base of Na₄Ag₄₄(p-MBA)₃₀ with Na⁺ serving as counterions to some of the carboxylates (see Figure S6b). In general, nanoparticle syntheses involving acidic ligands produce the conjugate base of the fully protonated nanoparticle because alkali metal cations are generally readily available to replace the protons. For example, this is also the case for the solution-phase synthesis of Na₄Ag₄₄(p-MBA)₃₀ as well as for glutathione-capped species. In some cases, the alkali conjugate base might be a suitable final product, and in other cases, the fully protonated acidic species might be preferred. In the former case, the product need not be processed further. In the latter case, the carboxylic acid groups can be protonated via a postprocessing step using citric acid.

When the solid product was dispersed in ethanol (a nonsolvent) and treated with citric acid, the carboxylates were found to protonate, displacing the Na⁺ counterions and recovering the carboxylic acids (see Figure S6c). Although the product remained in the solid state, the yield in this case was poor, presumably due to the stripping of coordinating species (e.g., DMSO) by ethanol.

Alternatively, the raw product could be protonated using a method that is similar to that of the solution-phase synthesis. Namely, the raw solid product could be dispersed in a small quantity of DMF (10 mL in this case). Adding citric acid to the dispersion solubilized the product, i.e., the protonated product is soluble in DMF whereas the sodium salt is not. The protonated product could then be precipitated using isopropanol.

Although this method uses more solvent, the precipitation step tends to produce a higher quality product with a very high yield, as evidenced by the absorption spectrum (see Figure S7). We note that it is also possible to protonate the raw product using DMSO in place of DMF, but this requires 3 times more isopropanol and yields only 2/3 of the product of the DMF method. For this reason, DMF was preferred.

The yield of the present synthesis was found to be 89%, which is quite high for a nanoparticle synthesis; however, it may still be possible to improve the reaction toward the quantitative yield of the solution-phase synthesis. We believe that the largest issue with the lower yield is in the reduction of the thiolate, namely, some of the silver-p-MBA precursor was not reduced. This is a consequence of striking a balance between allowing the reaction to proceed far enough to produce a high yield of Ag₄₄⁺ but not so far as to reduce the Ag₄₄⁺ product to make larger plasmonic nanoparticles or bulk silver. It may still be possible to fine-tune the reduction conditions such that the yield can approach that of the quantitative solution-phase synthesis.

The overall approach developed here was to minimize solvent use by keeping the reactants and products in the solid state whenever possible. This was ultimately achieved by using a precursor paste and by producing a product in paste form. It is helpful to consider to what extent the liquid component of the paste can be referred to as a solvent for the major species involved in the reaction.

The silver-thiolate precursor is insoluble in DMSO; however, the NaBH₄ reducing agent is soluble in DMSO. Although it is not required that NaBH₄ be dissolved to act as a reducing agent (vide supra), in this case, dissolving the NaBH₄ powder in DMSO promoted better mixing and accelerated the reaction compared to those of the case of the truly solid-state reaction. It seems apparent from the reaction kinetics that, in this case, DMSO acted as a solvent for NaBH₄.

Regarding the product, DMSO is also a good (coordinating) solvent for Ag₄₄⁺ therefore, the reaction likely took place in a way that was similar to the solution-phase case, which may be the reason for the high yield. In this case, Ag₄₄⁺ would have rapidly saturated the solution, precipitating to form the solid component of the product paste as the reaction proceeded. One could speculate that, in this case, it is likely that DMSO acted as a solvent for Ag₄₄⁺. These considerations and the observations discussed earlier suggest that the solvent properties of the liquid component of the paste should be considered carefully in adapting this chemistry to other species.

Comparing to the established wet-chemical synthesis of Ag₄₄⁺, our synthesis makes significant progress toward the elimination of hazardous solvents and reducing waste. For example, to synthesize 153 mg of Na₄Ag₄₄(p-MBA)₃₀, using the wet-chemical approach (corresponding to a 95% yield), 21 mL of water, 12 mL of DMSO, 150 mL of DMF, 100 mL of toluene, and 1 mL of 50% w/v aqueous CsOH are used. The present synthesis produced 145 mg of Na₄Ag₄₄(p-MBA)₃₀ product but used only 10 mL of ethanol, 10 mL of DMF, and 10 mL of isopropanol along with ~4 mL of a DMSO/water mixture that was retained in the paste. It was not necessary to use CsOH because this is normally used to solubilize the precursor in aqueous solution. This analysis shows that the paste method represents an 87% reduction in solvent use compared to that of the solution-phase method. We note that 21 mL of water and 12 mL of DMSO were also used to make 199 mg of the silver-p-MBA starting material less the ~4 mL of DMSO/water mixture that was retained in the paste; however, this solvent can be reused.

Using PMI as the efficiency metric, the paste-based synthesis has achieved a nearly 10-fold improvement in efficiency. The PMI of the liquid-phase reaction was calculated to be ~1800, whereas that of the paste-based reaction was ~200. If a nonprotic ligand were used, however, the protonation step would not be necessary, which would further reduce solvent use. In that case, the PMI of the liquid-phase reaction would be ~700, whereas that of the paste-based reaction would be ~100. A consequence of reducing solvent use is that solids now make a significant contribution to the total PMI, which ought to motivate further improvements. In particular, the use of metal salts, sodium borohydride, and excess ligands are worthy of scrutiny.

It is worth pointing out that another consequence of reducing solvent usage is that the synthesis and processing of the Ag₄₄⁺ product requires considerably less time and effort. The reaction time for the paste format is a small fraction of that for the solution format, e.g., 2–3 min versus 60 min, respectively, and the processing times are also quite different due to the volume of material handled in each case. For example, a typical
wet-chemical synthesis requires a total of 2–3 h to complete including all processing and analysis, whereas the paste format requires just 0.5–0.75 h to complete with the same level of processing and analysis. Together with the mitigation of the risk associated with toxic and volatile ligands, the paste format is clearly advantageous for industrial scale up.

**CONCLUSIONS**

Solvent use and materials toxicity are significant issues in developing green methods for synthesizing nanomaterials. By using a metal–thiolate paste as the starting material and by understanding each step of the reaction, we have demonstrated that it is possible to synthesize high-quality nanomaterials using very little solvent and from less hazardous materials. Single-sized Na4Ag44(p-MBA)30 nanoparticles were synthesized with a very high yield, which involved an order of magnitude lower quantities of solvent than the comparable wet chemical method and eliminated CsOH from the reaction. Our methodology should not depend on the physical state of the neat thiol-containing ligand (i.e., solid, liquid, or gas) because it is not directly used in the paste-based reaction. Forming the paste from the silver-thiolate precursor is therefore expected to eliminate restrictions related to the physical state of the neat ligand. This is also expected to have the added advantage of eliminating exposure to volatile and hazardous ligands (e.g., phenylethanethiol, benzenethiol, benzeneselenol, etc.) during nanoparticle synthesis. The 89% yield of this reaction was excellent for nanoparticle synthesis and compares quite favorably with the quantitative yield of the solution-phase synthesis; thus, quality and yield were not compromised. It should also be noted that the yield of the truly solid-state synthesis described above was negligible, and the reaction was considered a failure in this case. In terms of process mass intensity, the PMI was reduced from ~1800 for the solution phase reaction to ~200 and ~100 for the paste-based reaction with and without protonation of the ligands, respectively. The significant reduction in solvent waste and the elimination of hazardous and toxic materials is an important advance toward making the synthesis of nanomaterials more environmentally friendly and safer for workers.

**ASSOCIATED CONTENT**

Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpcc.6b12427.

Additional information on IR, UV–vis, EDS, and XPS characterization of these materials (PDF).

Paste-based synthesis of Ag44 nanoparticles (MP4)

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**Notes**

The authors declare no competing financial interest.

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