Surface engineered gold nanoparticles through highly stable metal–surfactant complexes

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ABSTRACT

Monodispersed Au nanoparticles were synthesized by the reduction of Au-decyltrimethylammonium bromide (Au-DTAB), which was easily prepared via the reaction of HAuCl4 and DTAB. This Au-DTAB complex is highly stable in air and moisture, and suitable for large-scale synthesis of uniform-sized Au nanoparticles. The nanoparticles were characterized by transmission electron microscopy, optical absorption spectrometry, X-ray diffraction, and Fourier Transform infrared spectroscopy. The size of Au nanoparticles was controlled in the range of 5–10 nm by changing the concentrations of reducing agent and Au precursor. The resulting Au nanoparticles were transferred to the aqueous phase after surface engineering using multidentate polymeric ligands with multiple imidazole functional groups. Polymeric imidazole ligands (PILs) demonstrated enhanced binding stability with the Au surface, and overcame the disadvantage of multidentate thiol ligand systems which have oxidative cross-linking and the formation of disulfide bonding. The colloidal stability of surface engineered Au nanoparticles with PILs was investigated by dynamic light scattering (DLS) characterization.

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1. Introduction

Synthetic chemistry of nanomaterials has developed rapidly over the last two decades, motivated by the unique chemical, physical, optical, magnetic, and mechanical properties of nanoparticles that are never observed in their bulk counterparts [1–4]. Novel properties of nanomaterials are of great importance not only for fundamental scientific interest, but also for many technological applications such as nanoelectronics [5,6], biological application [7–11], and magnetic devices [12,13]. Such properties are strongly correlated with the dimensions of the nanomaterials [14,15]. As a result, the synthesis of monodispersed nanoparticles with controlled size and shape is a key step for their application. Au nanoparticles have been the most intensely studied noble metal nanoparticles throughout the history of nanomaterial synthesis, and many potential applications have been studied to date [16–23]. Due to their plasmonic properties and good biocompatibility, bioconjugated Au nanoparticles have been intensively studied for applications in diagnosis and cancer therapy [20–23].

Since Faraday's report on the synthesis of an Au sol in the 19th century, various synthetic methods for Au nanoparticles have been reported [24–36]. Hydrogen tetrachloroaurate (HAuCl₄) is a popular Au precursor for the synthesis of Au nanoparticles. However, it is unstable in air and deteriorates under ambient conditions, absorbing moisture. Because the instability of the Au precursor is one of the major obstacles for the large-scale synthesis of Au nanoparticles, the preparation of a stable precursor has been strongly desired. In this study, we prepared a highly stable Au–surfactant complex from a simple reaction between an Au salt and a surfactant. Using this precursor, monodispersed Au nanoparticles were prepared by the reduction method. This method is highly reliable and suitable for large-scale synthesis. The synthesized nanoparticles were capped with alkylamine, which has moderate binding affinity to the Au surface compared with alkylthiol. Therefore, the surface of nanoparticles can be easily engineered, depending on their purpose. Here, Au nanoparticles were ligand exchanged with polymeric imidazole ligands (PILs) to impart water solubility, which is essential for biological applications.

Thiol-based coordinating ligands such as mercaptooalkyl carboxylic acid, and lipoic acid, have been widely used for the surface modification of Au nanoparticles. In spite of the high binding affinity of thiol to Au surfaces, Au nanoparticles passivated with monothiol ligands are quite unstable under high temperature conditions [37,38] and in the presence of competing thiols [39–41] or oxidizing agents [42,43]. In order to enhance the dispersibility of Au nanoparticles, there have been several reports of a multidentate approach in which the number of thiols per ligand is increased [44–46]. In fact, it is quite difficult to protect the oxidative cross-linking between neighboring thiol ligands because of the dimerization of the thiol groups, and the reaction process for synthesizing multidentate thiol ligands with a controlled distance between the thiol ligands is quite complicated.

Recently, several groups have introduced imidazole bearing ligands for biomolecule conjugation [47–49] or immobilization [50], demonstrating that imidazole functional groups exhibit high affinity to an Au surface. Here, we report that multidentate PILs with multiple imidazole functional groups can exhibit enhanced binding stability with the Au surface, and overcome the disadvantages of thiol-based bidentate or multidentate ligands systems. We successfully modified the surface of Au nanoparticles using these designed PILs, to transfer into the aqueous phase, demonstrating long term stability of colloidal dispersion over one month. In addition, we studied the influence of PILs on the colloidal stability of Au nanoparticles, by controlling the ratio of imidazole anchor group and the repeating number of PEG moiety under various conditions.

2. Experimental section

2.1. Chemicals

Hydrogen tetrachloroaurate (III) hydrate (HAuCl₄·H₂O) was purchased from Strem. Decyltrimethylammonium bromide (DTAB; CH₃(CH₂)₉N(CH₃)₃Br) was purchased from Acros. Ethylene glycol (HOCH₂CH₂OH) was purchased from TCI. Polyethylene glycol methyl ether acrylate (MW 1000) (methoxyPEG acrylate) was purchased from Alfa Aesar. α,α-Azobis(isobutyronitrile) (AIBN) was purchased from Junsei. All other chemicals were obtained from Sigma Aldrich. Hexane, tetrahydrofuran (THF), ethanol, N,N-Dimethylformamide (DMF), methanol, and acetone were used without further purification.

2.2. Synthesis of Au–DTAB complex

The Au–DTAB complex was prepared by adding 3.0 g of DTAB to a solution of 1.0 g of HAuCl₄·H₂O in 20 mL of H₂O at room temperature. The color of the solution turned to deep orange after complete dissolution of the precursor, indicating the formation of the Au–DTAB complex. The resulting metal complex was extracted with 30 mL of hexane, and separated using a separating funnel.

2.3. Synthesis of Au nanoparticles

Au nanoparticles were synthesized via chemical reduction of the Au–DTAB precursor by super-hydride in solution mixtures including ethylene glycol, THF, and oleylamine. For the synthesis of 5 nm Au nanoparticles, a mixture of 0.1 g of Au–DTAB, 2 mL of ethylene glycol, and 3.0 mL of THF was loaded into the three-neck round bottom flask. This reaction mixture was heated to 50 °C in air, and 1.0 mL of oleylamine was added. After injecting 1.0 mL of super-hydride, this solution was aged at 50 °C for 1 h. As the reduction reaction proceeded, the color of the solution turned from red to deep purple. After completion of the reaction, nanoparticles were precipitated by adding excess ethanol, and collected by centrifugation. Dried nanoparticles were easily dispersed in hexane with good colloidal stability. For the synthesis of 6 and 7 nm Au nanoparticles, 2.0 and 3.0 mL of oleylamine were used, respectively, with other steps in the procedure unchanged. For the synthesis of 10 nm Au nanoparticles, a mixture containing 2.0 g of Au–DTAB, 4.0 mL of ethylene glycol, and 7.0 mL of THF was used, with no change to the rest of the procedure.

2.4. Synthesis of PILs, PIL₄₀%–PEG(480)

PILs were denoted as PILₓ%–PEG(MW) with respect to the ratio of imidazole monomer(x) and PEG acrylate monomer molecular weight (MW) during the polymerization process. Other types of PILₓ%–PEG(MW) were synthesized by controlling the composition of monomers and the chain length of PEG acrylate monomers.

In a typical synthesis, Monomer 1 and PILₓ%–PEG480 were synthesized using a previously reported method with slight modification [51]. The prepared monomer was kept as a dilute stock solution at 100 mg/mL in methanol. Stock solution of reversible addition-fragmentation chain transfer-mediated (RAFT) agent was prepared at 271 mg/mL in DMF, and AIBN was prepared at 50 mg/mL in DMF. Monomer 1 (31.8 mg, 0.12 mmol), monomer 2 (86.4 mg, 0.18 mmol), and RAFT agent (2.90 mg, 0.01 mmol) were added to a 5 mL vial. The solvent was removed in vacuo and then 150 μL of dry DMF and AIBN (1.64 mg, 0.01 mmol) were added. The contents were mixed, centrifuged at 4000 rpm for 2 min, and then transferred to a 2 mL ampule. The ampule was subjected to 4 freeze–pump–thaw cycles, and sealed under vacuum using
butane torch. The ampule was heated to 70 °C on an oil bath for 6 h, after which 0.5 mL of a 4 M solution of HCl in dioxane was added to detach the tert-butylcarboxyl (BOC) protecting groups. After 1 h at room temperature, the HCl was removed in vacuo. The unprotected polymer was dissolved in 200 μL of methanol (MeOH), and the pH adjusted to between 8 and 9 by addition of 1 M solution of NaOH in MeOH. The solvent was removed in vacuo, and then CHCl₃ was added to precipitate the salts. The solution was filtered through a 0.45 μm PTFE filter and the solvent removed in vacuo to yield the final polymer for ligand exchange.

2.5. Ligand exchange with PILs

1 mg of Au nanoparticles were precipitated using MeOH and re-dispersed in 50 μL of CHCl₃. The nanoparticle stock solution was mixed with a solution of PILs (30 mg) in 150 μL of CHCl₃, and stirred for 30 min at 60 °C, after which 100 μL of MeOH was added followed by stirring for an additional 30 min. A mixture of ethanol (0.5 mL), chloroform, (1 mL), and hexane (4 mL) was added to the solution, which was then centrifuged (4000 rpm, 2 min). The supernatant was discarded, and the precipitate was dispersed in 4 mL of water.

Excess ligands were removed by cycles of dilution/concentration through an Amicon Ultrafree 100 kDa MW cutoff filter (Millipore, 7000 rcf, 10 min). The purified Au nanoparticles were re-dispersed in 4 mL of water. The aqueous solution was then filtered through a 0.2 μm syringe filter. The stability test of surface engineered Au nanoparticles with PILs in aqueous solution was done by measuring hydrodynamic diameter (HD) after repeating filtration process.

2.6. Characterization

Au nanoparticles were characterized by low- and high-resolution transmission electron microscopy (TEM) and electron diffraction (ED) using a JEOL JEM-2010 electron microscope operating at 200 kV. Samples for TEM analysis were prepared by putting a drop of the dispersion containing Au nanoparticles on a copper grid coated with an amorphous carbon film. X-ray diffraction (XRD) using a Rigaku D/Max-3C diffractometer equipped with a rotation anode and a Cu Kα radiation source was measured using a JASCO V-550 UV–VIS spectrophotometer. Fourier-transform infrared (FT-IR) spectra were acquired using a Nicolet 6700 FT-IR spectrometer (Thermo Electron Corporation, Waltham, MA). The dynamic light scattering (DLS) was performed on a Malvern Instruments ZetaSizer ZS equipped with a 173° backscatter detector. Samples were poured into glass cuvettes (PCS1115) and the temperature was set at 25 °C. Polymer molecular weight was determined on a 1260 infinity gel permeation chromatograph (GPC) (Agilent, USA) with a differential refractometer detector for measurement of molecular weight of the polymer. THF was used as an eluent with a flow rate of 1 mL/min. The measurement was performed at 23 °C. The polymer structure was characterized by 600 MHz FT-NMR using a VNMRS 600 (Agilent, USA). CDCl₃ was used as the NMR solvent.

3. Result and discussion

The preparation of a stable Au precursor is very important for high productivity and reliability of Au nanoparticle synthesis. For this purpose, we adopted the metal–surfactant precursor system for the synthesis of transition metal nanocrystals reported previously by Hyeon’s group [52,53]. In the previous papers, Hyeon’s group prepared highly stable precursors by reaction between a transition metal cation and an anionic surfactant. Using these precursors, the development of a highly successful large-scale synthetic method for transition metal nanocrystals was possible. Here, we have attempted to extend this approach to the synthesis of noble metal nanoparticles. For the preparation of an Au precursor, we combined HAuCl₄ and DTAB, which are a popular Au compound and surfactant, respectively, to obtain the ionic complex, Au-DTAB (Scheme 1). Substitution of the proton with alkylammonium in this reaction provides a number of advantages. The Au ionic complex obtained from this reaction was well dissolved in the organic solvent. It is also highly resistant towards oxygen and moisture under ambient conditions. After preparation, it was possible to store this precursor for several months without any change.

The structural difference between HAuCl₄ and Au-DTAB was investigated with optical absorption and FT-IR spectroscopy. The presence of DTAB in the Au precursor was confirmed by FT-IR spectroscopy (Fig. 1a) – the characteristic peaks at 960 cm⁻¹ and 905 cm⁻¹ can be attributed to the C–N bond of DTAB. In addition, the peaks at 2920 cm⁻¹ and 2842 cm⁻¹ are evidence of the presence of hydrocarbon chains. In its UV–vis spectrum, the aqueous HAuCl₄ solution shows a strong absorption band at 220 nm and a secondary peak at 290 nm, which are attributed to ligand-to-metal charge transfer (Fig. 1b) [54,55]. After the reaction, the absorption bands from Au-DTAB complex were shifted to 252 nm.
and 400 nm, respectively. This observation can be explained by the substitution of the proton counter cation by alkylammonium, with the negative charge density on [AuCl₄]⁻ in Au-DTAB relieved in comparison to HAuCl₄.

Au nanoparticles were synthesized by reducing the Au-DTAB precursor with super-hydride in the presence of ethylene glycol, THF, and oleylamine. Both ethylene glycol and oleylamine have previously been used as reducing agents in the synthesis of Au nanoparticles [56]. However, the reaction temperature of 50 °C in the current method for the reduction reaction of these reducing agents is far lower than that in the previous work. In our synthesis, Au³⁺ ions were directly reduced by the organic hydride compound, and oleylamine acted only as the surfactant. Compared to other works, the resulting nanoparticles were synthesized in a relatively short reaction time at a low temperature. Because the binding energy of alkylamine to the surface of Au nanoparticles is lower than that of alkylthiol, the use of oleylamine provides better control of the size distribution of nanoparticles for the low

Table 1
Characteristics of PILₓ-PEG(MW) ligands.

<table>
<thead>
<tr>
<th>PIL-PEG</th>
<th>Theoretical xᵃ</th>
<th>Theoretical yᵇ</th>
<th>Experimental xᶜ</th>
<th>Experimental yᵈ</th>
<th>Imidazoles per chain</th>
<th>Mₙ, GPC (g/mol)</th>
<th>PDI</th>
<th>Degree of polymerization</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIL₂₀-PEG(₄₈₀)</td>
<td>0.20</td>
<td>0.80</td>
<td>0.16</td>
<td>0.84</td>
<td>2.27</td>
<td>6321</td>
<td>1.19</td>
<td>14.2</td>
</tr>
<tr>
<td>PIL₄₀-PEG(₄₈₀)</td>
<td>0.40</td>
<td>0.60</td>
<td>0.33</td>
<td>0.67</td>
<td>4.48</td>
<td>5560</td>
<td>1.18</td>
<td>13.6</td>
</tr>
<tr>
<td>PIL₂₀-PEG(₁₀₀₀)</td>
<td>0.20</td>
<td>0.80</td>
<td>0.17</td>
<td>0.83</td>
<td>2.22</td>
<td>11,448</td>
<td>1.19</td>
<td>13.1</td>
</tr>
<tr>
<td>PIL₄₀-PEG(₁₀₀₀)</td>
<td>0.40</td>
<td>0.60</td>
<td>0.35</td>
<td>0.65</td>
<td>4.09</td>
<td>8684</td>
<td>1.20</td>
<td>11.7</td>
</tr>
<tr>
<td>PIL₆₀-PEG(₁₀₀₀)</td>
<td>0.60</td>
<td>0.40</td>
<td>0.54</td>
<td>0.46</td>
<td>6.11</td>
<td>6827</td>
<td>1.24</td>
<td>11.3</td>
</tr>
</tbody>
</table>

ᵃ Expected fraction of imidazole groups entered into PILₓ-PEG(MW) ligands.
b Expected fraction of PEG moieties entered into PILₓ-PEG(MW) ligands.
c Measured fraction of imidazole groups entered into PILₓ-PEG(MW) ligands.
d Measured fraction of PEG moieties entered into PILₓ-PEG(MW) ligands.
temperature synthesis of the current method [33]. Using this method, it was possible to obtain sub-gram-scale \(0.6 \text{ g}\) quantities of monodispersed Au nanoparticles with various sizes, as shown in Fig. 2. The electron diffraction pattern and HR-TEM image confirm that Au nanoparticles have good crystallinity (Fig. 2c and f). The XRD pattern of 5 nm nanoparticles is well matched with the face centered cubic structure of bulk Au (Fig. S1). The lattice spacing measured on the HR-TEM image was 2.35 Å, which is consistent with the d-spacing of the Au (111) plane. Fig. S2 shows UV–vis spectra of four different sized Au nanoparticles. The absorption peak at 520 nm corresponds to surface plasmon resonance of spherical Au nanoparticles [57,58].

Size control of Au nanoparticles in the range from 5 nm to 7 nm was accomplished by varying the amount of surfactant. Increasing the amount of oleylamine leads to better passivation of Au monomers in the reaction. This lowers supersaturation in the solution, and fewer nuclei are formed in the nucleation process. In this case, each nucleus shares more monomers compared to high nucleation rate condition. As a result, addition of oleylamine can increase the mean size of the nanoparticles [59]. The size distributions of Au nanoparticles are shown in Fig. S3. With size controlled in the 5–10 nm range, a narrow size distribution was maintained, with a relative standard deviation <10%.

We also investigated the role of reaction temperature on the size distribution of Au nanoparticles. When the synthesis was performed at room temperature, only polydisperse nanoparticles were obtained. It was observed that at room temperature the growth process was considerably depressed compared to the reaction at 50 °C. Conversely, at temperatures higher than 50 °C, uncontrolled aggregation of Au nanoparticles was observed. These results show that in the current synthetic method, the low reaction temperature (50 °C) is important not only for large-scale synthesis, but also for size distribution control.

For the surface modification of nanoparticles in order to convert hydrophobic nanoparticles synthesized in an organic phase to the hydrophilic form, the hydrophilic random block copolymers was synthesized using RAFT polymerization method for the distribution of Au nanoparticles in aqueous medium (Scheme 2). Six different types of PILs were synthesized by controlling the ratio of imidazole anchor group and the repeating number of PEG moieties (Table 1). In both cases of PIL-x%-PEG(480) and PIL-x%-PEG(1000), we observed that the ratio of anchor group in polymer structure was increased, conserving the total number of monomer, indicating the degree of polymerization was kept, as the ratio of adding imidazole monomer was increased (Fig. 3). This result presented that the polymer structure could be systematically manipulated by controlling the composition of monomers during the polymerization process. When we decreased the anchor group by synthesizing PIL-x%-PEG(480), which means the polymer structure has only one imidazole group, it was noted that the binding affinity of PIL-x%-PEG(480) was not enough to disperse Au nanoparticles in aqueous media. Thus all polymers which have more than two imidazole moieties were used for the stability test (see Fig. 4).

Fig. 3. \(^1\)H NMR spectrum of PIL-PEG. The repeating unit number of PIL-x%-PEG(480) and PIL-x%-PEG(1000) was approximated as 8 and 21. The mole fractions of x and y were calculated by comparing the integration ratios of A and C peaks.

Fig. 4. The filtration stability test of 7 nm Au nanoparticles ligand exchanged with PIL-x%-PEG(480) (red square, ●), PIL-x%-PEG(1000) (blue triangle, ▲) which bearing (a) PEG(480) and (b) PEG(1000) as hydrophilic fraction. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
In the case of PIL20%-PEG(480) structure, the hydrodynamic diameter (HD) were increased to 16.79 nm, 18.10 nm, and 21.86 nm as increasing the filtration times. It might be owing to the aggregation of particles during filtration process because the removal of ligand from nanoparticles which have less anchor group per each polymer. However, it was found that in the case of PIL20%-PEG(1000), the HD of PIL20%-PEG(1000) were negligibly changed even with 3 times of filtration. The steric hindrance among the nanoparticles with the long PEG brush chain could prevent the aggregation of nanoparticles. In the case of PIL20%-high stability was shown regardless of the number of PEG moieties. It could be well matched with previous research that the structure of multidentate imidazole could enhance the binding affinity [45,51,60–62].

However, in the both cases of PIL60%-PEG(480) and PIL60%-PEG (1000) which the ratio of imidazole anchor group within one polymer is over than half, the HD were dramatically increased by 2 times of centrifugal filtration. We thought that it was because the dispersion stability of Au nanoparticles was diminished by decreasing the hydrophilic fraction, and the multidentate anchor group could be served as the bridge between nanoparticles when the anchor group ratio was too much. Therefore, the control of the anchor group ratio is mostly important to increase the stability.

Water dispersed Au nanoparticles at ambient condition remained to has shown a long term stability for a week (Fig. 5). We also performed the same experiment with dodecanethiol capped Au nanoparticles. During ligand exchange, the transparent solution became cloudy and even some visible agglomerates were observed. From this result, we concluded that moderate binding affinity of alkylamine ligand is critical for surface engineering.

4. Conclusion

Monodispersed Au nanoparticles were successfully synthesized by chemical reduction of Au-DTAB complexes. The Au-DTAB complexes were easily prepared via chemical reaction between HAuCl₄ and the DTAB ligand at room temperature. Unlike HAuCl₄, Au-DTAB complexes are stable in air and moisture. Using a mild ligand such as oleylamine and appropriate temperature for the growth step are the key factors for the synthesis of uniformly sized Au nanoparticles. The size control of Au nanoparticles could be accomplished by controlling ratio of Au-DTAB complex to oleylamine.

The Au-DTAB complex is suitable for large-scale synthesis with highly reproducibility. Furthermore, the moderate binding affinity of the alkylamine ligand enables the facile functionalization of nanoparticle surfaces for various applications. We demonstrated that oleylamine was replaced with PILs without any agglomeration or aggregation for a week. The aqueous dispersion stability of Au nanoparticles can be enhanced by controlling the number of repeating imidazole groups and fraction of PEG moieties. With proper introduction of biological functional group (e.g. biotin, carboxyl, or amine), our Au nanoparticles could be used in a variety of biological applications.

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Appendix A. Supplementary material

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