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One-step Preparation of Gold Nanoparticles Using 4-Acylamidobenzenethiol as a Reductive Stabilizer

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A simple one-step preparation method to prepare gold nanoparticles (AuNPs) using 4-acylamidobenzenethiol derivatives as reductive stabilizers has been developed. The stabilizers were easily prepared from 4-aminobenzenethiol and dihydroxy fatty acid. By simply mixing the stabilizer and a solution of $HAuCl_4$ in methanol or water, we could form AuNPs spontaneously without any additional reagents or physical treatment. The diameters of the resulting AuNPs were determined to be 2–5 nm using TEM images.

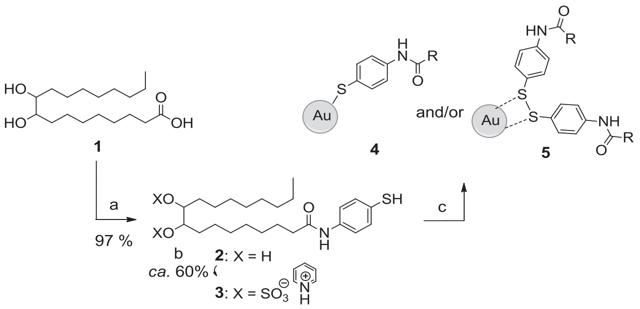
Thiol-stabilized gold nanoparticles (AuNPs) are the most common hybrid inorganic–organic nanomaterials,[1] and hence, there is a strong demand for a practical preparation method of highly functionalized AuNPs. A popular method is the direct reduction of a mixture of Au^{3+} ions and a thiol stabilizer using $NaBH_4$,[2] ascorbic acid,[3] citric acid,[3,4] or an another substance as a reducing agent.[1] However, this method yields a mixture of AuNPs and oxidized residues of the reducing agent, which should be removed by purification such as by centrifuging or column chromatography.

A combination of a reductive thiol stabilizer and Au^{3+} solution would be a superior method for obtaining pure thiol-stabilized AuNPs. Negishi and Tsukuda reported a one-pot preparation of AuNPs using *meso*-2,3-disulfanylsuccinic acid as a reductive stabilizer.[5] In the course of study, they disclosed that a highly reductive vicinal dithiol moiety was essential for spontaneous formation of AuNPs.

Very recently, our research group has reported a simple sonochemical synthesis of AuNPs using dendron-stabilizers having a thiol functional group.[6]

In this letter, we report a novel one-step preparation of stable AuNPs by using 4-acylamidobenzenethiol derivatives **2** and **3**, as reductive stabilizers, which spontaneously reduced Au^{3+} to AuNPs at room temperature without any additional chemical or physical treatments. The resulting AuNPs obtained by this preparation method were dissolved in methanol or water, depending on the molecular structure of the stabilizer, and the diameter of the particles was 2–5 nm.

The preparation of the reductive stabilizers used in this work is shown in Scheme 1. Stabilizer **2**[7] was prepared by the dicyclohexylcarbodiimide (DCC) coupling of 4-aminobenzenethiol and 9,10-dihydroxyoctadecanoic acid (**1**) that was easily obtained from oleic acid.[8] The sulfurylation of the diol moiety of **2** using chlorosulfuric acid and pyridine proceeded smoothly, and a pyridinium salt **3** was formed. By adding water to the reaction mixture, a yellow oil that contained compound **3** was liberated. After drying the oil under vacuum to remove pyridine and water, almost pure **3**[7] was obtained as a yellow oil, which was used for the following experiments without further purification.



a) DCC, Et_3N, 4-aminothiophenol; b) $ClSO_3H$, Pyridine; c) $HAuCl_4$

Scheme 1.

After obtaining the stabilizers, we examined the preparation of AuNPs as shown in Table 1. A solution of the stabilizer **2** (0.20 M in methanol, 100 µL) was diluted with methanol (5.0 mL), and a solution of $HAuCl_4 \cdot 4H_2O$ (0.24 M in methanol, 21 µL) was then added at room temperature. The color of the reaction mixture gradually darkened after 10 min and changed to deep purple after 5 h. The vis–NIR spectrum of the resulting colloidal suspension of AuNP showed an absorption peak at 560 nm (Entry 1, Figure 1a, solid line), and hence, compound **2** was considered to be an effective reductive stabilizer to obtain stable AuNPs from an Au^{3+} solution. The profile of the vis–NIR spectrum changed over time (Entry 2, Figure 1a, dotted line), and no definite peak was observed after one week, although the solution was still clear.[9]

The structure of the stabilizer bound to AuNPs was not clarified. Since the thiol group has been oxidized into disulfide during the course of the reaction, the following three possible structures can be considered: a) thiolate form **4**, b) disulfide form **5**, and c) mixture of **4** and **5** (Scheme 1).

$$6\mathrm{R{-}SH} + 2\mathrm{Au}^{3+} \rightarrow 2\mathrm{Au}^{0} + 3\mathrm{R{-}S{-}S{-}R} + 6\mathrm{H}^{+} \quad (1)$$

The stoichiometry of this reaction can be described as shown in eq 1, and thus we attempted to confirm it by a comparison of peak intensities of the vis–NIR spectra of the AuNP solutions prepared by different molar ratios of $\mathbf{2}/Au^{3+}$ (Table 1, Entries 1, 3, 4, and 5).[9] The AuNP solutions resulting from the reactions of 1/1, 2/1, 3/1, and 4/1 mixtures of $\mathbf{2}/Au^{3+}$ showed peaks at around 560 nm in their spectra, but their intensities were $2/1 > 3/1 > 4/1 > 1/1$ (Figure 1b), which did not agree with our expectation ($4/1 \approx 3/1 > 2/1 > 1/1$). It is speculated that the ratio of $\mathbf{2}/Au^{3+}$ changed the structures, sizes, and/or shapes of the resulting AuNPs that lead to different

Table 1. Preparation of AuNPs using stabilizers **2** and **3**

Entry	Solvent	Stabilizer	Molar ratio of stabilizer/Au^{3+}	Time/h	Color of solution	λ_{max}/nm
1	methanol	**2**	4/1	5	purple	560
2	methanol	**2**	4/1	48	purple	559 (broad), 466 (broad)
3	methanol	**2**	3/1	48	purple	557
4	methanol	**2**	2/1	48	blue-purple	572
5	methanol	**2**	1/1	48	blue-purple	563
6	dichloromethane	**2**	4/1	1	brown (precipitate)[a]	—
7	toluene	**2**	4/1	1	brown (precipitate)[a]	—
8	acetone	**2**	4/1	24	yellow	—
9	acetonitrile	**2**	4/1	24	yellow[b]	—
10	water	**3**	4/1	1	reddish-brown	460 (broad)[c]
11	0.10 M $NaHCO_3$	**3**	4/1	1	reddish-brown	465[c]
12	0.10 M HCl	**3**	4/1	1	brown (precipitate)	—
13	0.10 M NaOAc	**3**	4/1	1	brown (precipitate)	—
14	ca. 0.10 M NH_4OH	**3**	4/1	1	brown (precipitate)	—

[a] Soluble in methanol. [b] Small amount of precipitate was contaminated. [c] Spectra were measured after toluene/CTAB extraction.

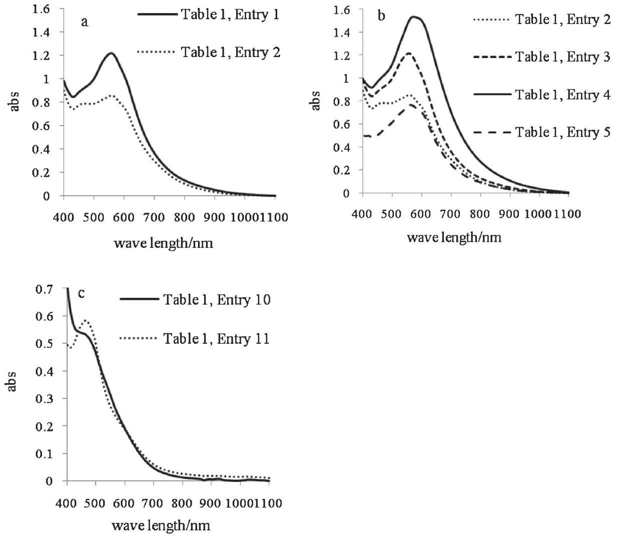


Figure 1. Vis–NIR spectra of AuNP solutions. (a) Effect of aging, solid line: stabilizer **2** and Au^{3+} in methanol, 5 h (Table 1, Entry 1); dotted line: stabilizer **2** and Au^{3+} in methanol, 48 h (Table 1, Entry 2). (b) Effect of molar ratio of stabilizer/Au^{3+}, dotted line: **2**/Au^{3+} = 4/1, short-dashed line: **2**/Au^{3+} = 3/1, solid line: **2**/Au^{3+} = 2/1, long-dashed line: **2**/Au^{3+} = 1/1. (c) Effect of pH, solid line: stabilizer **3** and Au^{3+} in water, 1 h (Table 1, Entry 10); dotted line: stabilizer **3** and Au^{3+} in 0.10 M $NaHCO_3$, 1 h (Table 1, Entry 11).

absorption maxima (λ_{max}) values with different intensities. Indeed, the profiles of the spectra and the colors of the resulting solutions were different for the different ratio of **2**/Au^{3+}. Consequently, a simple comparison of the peak intensities at around 560 nm could not evaluate the stoichiometry of this reaction.

We also examined the solvent effect on this reaction. In the case of the reactions using less-polar solvents, dichloromethane or toluene (Table 1, Entries 6 and 7), the colors of the solutions changed to blue within 10 min after adding the Au^{3+} solution, but brown precipitates were formed after 1 h, which were largely dissolved by adding methanol to yield reddish-brown solutions. It has been suggested that the polarity of the resulting AuNPs was very high because the hydroxy groups of **2** concentrated on the surfaces of the particles, and thus the particles precipitated in these less-polar solvents and dissolved by adding polar solvent.

Aprotic polar solvents such as acetone and acetonitrile were less effective for this reaction (Table 1, Entries 8 and 9). The initial pale-yellow colors of these reaction mixtures did not change within several hours after the addition of Au^{3+}. After 24 h, the acetone solution darkened slightly, but no peak was observed in its vis–NIR spectrum. The acetonitrile solution formed a very small amount of precipitate after 24 h, and the color of the solution did not change. Consequently, the reactivity of stabilizer **2** strongly depended on the solvent, and the protic polar solvent was the most appropriate.

Reaction in water using polar stabilizer **3** was very successful and yield water-soluble hydrophilic AuNPs (Table 1, Entry 10). A solution of the stabilizer **3** (0.20 M in methanol, 100 µL) was diluted with water (5.0 mL), and a solution of $HAuCl_4 \cdot 4H_2O$ (0.24 M in methanol, 21 µL) was then added to it at room temperature. The color of the reaction mixture immediately changed to reddish brown. Although no definite peak based on the surface plasmon resonance of AuNPs was observed in the vis–NIR spectrum of the reaction mixture itself, the toluene/cetyltrimethylammonium bromide (CTAB) extract of the resulting AuNPs showed a broad peak around 460 nm (Figure 1c, solid line).

Obviously, the pH of the solution was important to yield a clear solution of AuNPs. A weak-alkaline aqueous solution, 0.10 M $NaHCO_3$ was suitable for the reaction and yielded a reddish-brown solution as well as the water system. Its vis–NIR spectrum was again measured after the toluene/CTAB extraction, and a clearer and sharper peak was observed at 465 nm (Figure 1c, dotted line).[9] On the other hand, since the stabilizer **3** was hardly soluble in an acidic medium, the reaction with Au^{3+} in 0.10 M HCl only gave brown precipitate. Further, an ionic species of the reaction medium was important. Reactions in

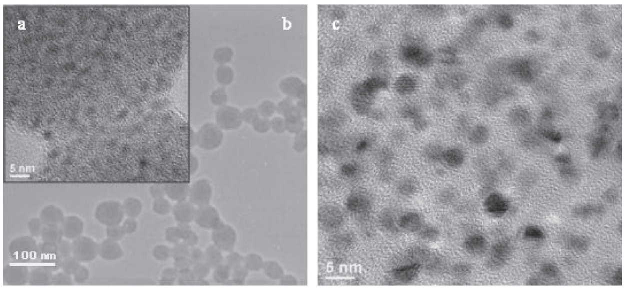


Figure 2. TEM images of AuNPs. (a) Close-up image of stabilizer **2** and Au^{3+} in methanol (Table 1, Entry 2). (b) Entire image of spherical aggregation of AuNPs. (c) Stabilizer **3** and Au^{3+} in 0.10 M $NaHCO_3$, extracted with toluene/CTAB (Table 1, Entry 11).

0.10 M NaOAc or ca. 0.10 M NH_4OH, which were both alkaline and could dissolve stabilizer **3**, yielded only a brown precipitate.

The sizes of the resulting AuNPs were established from transmission electron microscope (TEM) images (Figure 2). The particles obtained from the reaction listed in Table 1, Entry 2, appeared to be spheres with diameters 2–5 nm (Figure 2a), which formed larger spherical clusters (diameter: 20–50 nm, Figure 2b). On the other hand, hydrophilic particles obtained from the reaction listed in Table 1, Entry 11, were well dispersed, and their diameters were 2–5 nm (Figure 2c).

The key factors of molecular design responsible for obtaining an efficient reductive stabilizer are still unclear, but it is important to note that the color of the mixture of 4-acetamidobenzenethiol and Au^{3+} in methanol showed no change even after 24 h and its vis–NIR spectrum had no absorption peak attributable to the surface plasmon resonance of AuNPs. It can be concluded that the chain length and/or the functionalities in the acyl group, as well as reductivity of the thiol functional group are the key to designing a reductive stabilizer.

In conclusion, we have developed a novel preparation method of AuNPs by mixing only a reductive stabilizer (**2** or **3**) and Au^{3+} solution in one-step at room temperature. The diameter of the resulting AuNPs was 2–5 nm. Further studies on the characterization of the surface morphology of the AuNPs obtained by this method are now in progress.

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9 The wavelength was shorter than that of surface plasmon band of AuNPs (ca. 520 nm), which suggested a formation of smaller gold clusters.[5,10] Indeed, dynamic light scattering experiments indicated that the sizes of the particles yielded from 0.10 M $NaHCO_3$ solution were smaller than those obtained from methanol solution (see Supporting Information). Detailed studies on the morphology of AuNPs are in progress.
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