# Generation of Gold Nanoparticles via Direct Thiol-capping with THP-protected Thiols without Deprotection

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# Generation of Gold Nanoparticles via DirectThiol-capping with THP-protected Thiols without Deprotection

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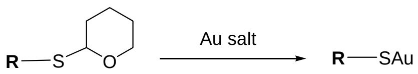
**Abstract:** Alkanethiol-capped gold nanoparticle is prepared directly from S-protected thiol with a tetrahydropyranyl(THP) group by treatment of $HAuCl_4$ in the presence of a reducing agent such as $Et_3SiH$, $NaBH_4$, and superhydride.

**Key words:** gold nanoparticle, THP thioether, alkanethiol, triethylsilane, functional group

As increasing the significance of gold nanoparticles (AuNPs) as advanced materials with magnetic, electronic, optical, and bioactive properties,[1] synthetic efficiency of AuNP becomes an attractive issue as a target of organic synthesis because a number of AuNPs are composed of gold clusters and a capping agent of an organic molecule that are connected on the gold surface to introduce stability and functionality. Thiol derivatives have been widely used as a capping agent due to its strong affinity of the sulfur atom toward gold. The alkanethiol-capped gold nanoparticle is generally synthesized by the reaction of a precursor gold(I) or (III) reagent with a commercially available long-chained alkanethiol in the presence of a reducing agent.[2] However, increasing demand on the creation of nanoparticles involving functionality such as catalysis, sensing, etc. requires synthetic design and preparation of the capping thiol reagent. It is therefore necessary to construct the desired molecular structure bearing an appropriate functionality onto the thiol. Substitution and/or addition reactions on the thiol molecules have to be performed for the purpose of the introduction of functional groups, where use of an appropriate protective group for thiol becomes important, otherwise, the SH group participates in undesired side reactions.

An acyl group is a candidate for the protection of thiol. However, thioacetate thus formed easily hydrolyzes under aqueous conditions.[3] The use of thioacetate as a protective group limits available synthetic reactions, accordingly. On the other hand, the tetrahydropyranyl (THP) group[3] has also been served as a protective group of thiols and shows stability toward various reactions and hardly hydrolyzes with both acidic and basic conditions, while deprotection of THP thioethers is shown to be performed by hydrolysis with a particularly strong acid or in the presence of a mercury or silver salt. Thereby, THP thioethers are occasionally ineffective as a protective group in organic synthesis due to its difficulty of deprotection by contrast to the wide utility for alcohols and phenols, which is easily removed by simple acidic hydrolysis. Accordingly, use of the THP protective group for designed gold nanoparticles is intriguing, if protection/deprotection of STHP is easily controllable.

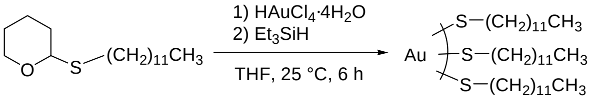
During the course of our separate studies on the preparation of a molecule bearing a thiol moiety, we have encountered that a THP thioether that is hardly removed by hydrolysis is converted to the thiolate of gold when the thioether is treated with $HAuCl_4$ as shown in Scheme 1.[4]



**Scheme 1**

Encouraged by this result, we envisaged that introduction of thioalkyl group onto the surface of gold would be possible by the reaction of THP thioethers and a gold salt in the presence of a reducing agent. Although introduction of alkanethiol into the surface of gold has been shown with thioacetate,[5] S-alkylthiosulfonate (Bunte salts)[6] and alkylthiocyanate,[7] THP thioethers would be much more tolerable for a variety of organic reactions. Herein, we report our findings that direct preparation of gold nanoparticles is performed with THP thioethers without deprotection by treatment of $HAuCl_4$ in the presence of a reducing agent.

Preparation of THP-protected thiol **1** was performed by the reaction of 1-dodecanethiol with 3,4-dihydro-2*H*-pyran in the presence of a catalytic amount of *p*-toluenesulfonic acid to afford **1** in a good yield as reported.[3] The obtained **1** (0.1 mmol) was treated with $HAuCl_4 \cdot 4H_2O$ (0.1 mmol) to form a clear yellow solution by vigorous stirring at room temperature for 3 h. TLC analysis of the resulting solution indicated that THP thioether **1** disappeared suggesting that the protective group was completely removed to form gold thiolate. No incorporation of the THP moiety into the organic moiety of AuNP was confirmed in the formation of intermediate gold thiolate preceding to the addition of a reducing agent[8] by measurement of NMR spectra, which were similar to those synthesized with $C_{12}H_{25}SH$.[9] Triethylsilane was then added dropwise at 25 °C to the solution to observe immediate color change to purple. After stirring for 6 h at 25 °C, AuNP precipitated by addition of ethanol and centrifuged to isolate 17.0 mg of AuNP **2** as a dark brown powder (Scheme 2). Since we have shown that $Et_3SiH$ serves as a new class of reducing agent for the synthesis of AuNP from $HAuCl_4$ and $CH_3(CH_2)_{11}SH$,[10] the addition of triethylsilane would reduce the gold thiolate that is formed by the reaction of THP thioether **1** and $HAuCl_4$.



**1** (28.7 mg) 0.1 mmol

**2** (17.0 mg)

**Scheme 2**

The obtained AuNP **2** was subjected to the measurements of TEM and UV-vis spectrum analyses. The $\lambda_{max}$ value of the UV-vis spectrum was observed at 528 nm, which is attributed to the characteristic plasmon resonance absorption of AuNP.[11] Figure **1** shows the TEM image of AuNP, which is spherical and exhibits an average diameter of 7.7±0.52 nm. The yield and characteristics (particle size, spectroscopic, and thermal) of the obtained AuNP **2** by the reaction of THP thioether **1** were found to be similar to those from $CH_3(CH_2)_{11}SH$ as summarized in Table 1.

TG analysis of **2** indicated its weight loss of ca. 10%, which markedly contrasted to that obtained by the reduction with $NaBH_4$ or $LiBH_4$,[12] which, in general, leads to the formation of AuNP of a smaller size. The finding shows that AuNP obtained by the reduction of a silane reagent brings about that a smaller amount of alkanethiol exists on the surface of gold cluster with a larger size. These results suggest that AuNP bearing a less amount of the thiol moiety by the reduction of a silane reagent leads to afford AuNP of a particle size of ca. 7.7-8.6 nm. Further studies would be necessary for more understanding of the relationship on the nanoparticle size and the reducing agent.

**Table 1** Comparison of charateristics of AuNP from protected/unprotected alkanethiol[a]

| capping reagent | yield/mg (size/nm) | UV-vis absorption $\lambda_{max}$/nm[b] | TGA-mass loss/%[c] |
|---|---|---|---|
| **1** | 17.0 (7.7±0.52) | 527 | 10.3 |
| $HSC_{12}H_{25}$[d] | 15.1 (8.6±0.65) | 528 | 7.65 |

[a] the reaction was the reaction was carried out with $HAuCl_4 \cdot 4H_2O$ (41.2 mg, 0.1 mmol), capping reagent (28.7 mg, 0.1 mmol) and $Et_3SiH$ (11.6 mg, 0.1 mmol), in 10 mL of THF at 25 °C for 6 h. [b] UV-vis spectra were measured as a chloroform solution. [c] Mass loss at 800 °C. [d] See ref. 10

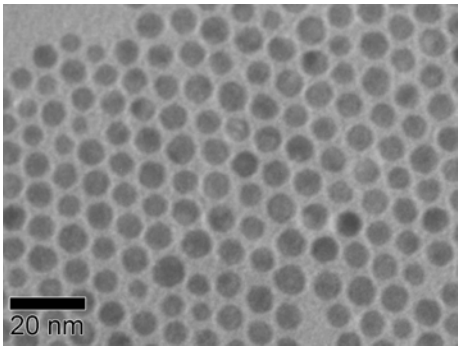


**Figure 1** TEM image of AuNP **2** prepared by the reaction of $HAuCl_4$ and $^nC_{12}H_{25}STHP$ **1** with $Et_3SiH$ as a reducing agent indicating the average diameter of 7.7±0.52 nm.

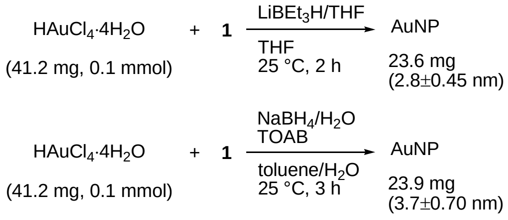
We next examined the synthesis of AuNPs with THP-protected dodecanethiol **1** under various reaction conditions (Table 2). The optimum reaction period for the formation of AuNP was found to be 6 h, when the reaction was performed with $Et_3SiH$ as a reducing agent. Longer reaction period did not improve the yield although the monodispersed AuNP with a similar particle size was obtained. Pretreatment of $HAuCl_4 \cdot 4H_2O$ and **1** was found to be necessary to form the monodispersed particle, otherwise, nonspherical and aggregated products were obtained when all of the reagents were added simultaneously. These trends are consistent with the results on the generation of AuNP with non-protected dodecanethiol.[10]

**Table 2** Preparation of AuNP **2** with THP-protected dodecanethiol **1**[a]

| time/h | yield/mg | size/nm |
|---|---|---|
| 6 | 15.5 | 7.7±0.52 |
| 24 | 17.7 | 8.6±0.50 |
| 6[b] | 5.2 | -[c] |

[a] Unless otherwise specified, the reaction was carried out with $HAuCl_4 \cdot 4H_2O$ (41.2 mg, 0.1 mmol), **1** (28.7 mg, 0.1 mmol), in 10 mL of THF at 25 °C. THF solution of **1** and $HAuCl_4 \cdot 4H_2O$ was stirred for 3 h before the addition of the $Et_3SiH$ (0.1 mmol). [b] All reagents were added simultaneously. [c] Nonspherical nanoparticles were observed.

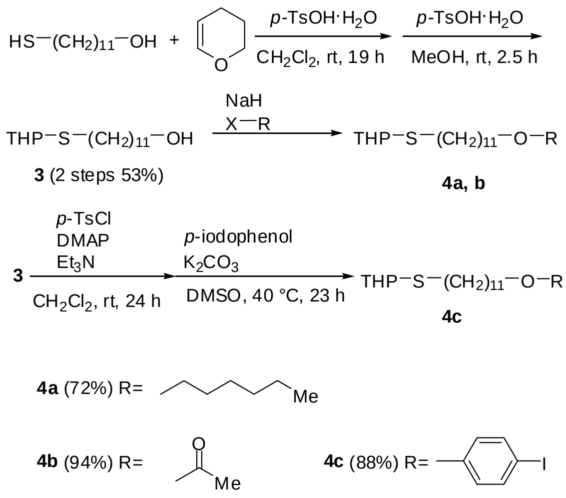
Other reducing agents were also found to be similarly available for THP thioethers to result in giving gold nanoparticles as shown in Scheme **3**. Treatment of THF solution of $LiBEt_3H$ (superhydride)[2e] furnished AuNP with an average diameter of 2.8±0.45 nm. When an aqueous solution of $NaBH_4$[2b] was added to toluene/$H_2O$ solution of $HAuCl_4$, **1**, and tetraoctylammonium bromide (TOAB), AuNP of 3.7±0.70 nm was also obtained.[13] The particle size obtained with such metal hydrides as a reducing agent was also similar to the case for the reduction of non-protected alkanethiol. These results show that the use of THP-protected alkanethiols is effective towards various reducing agents as well as $Et_3SiH$.



**Scheme 3**

Our further concern has been focused on the possibility for the introduction of a functionalized alkanethiol on the gold surface. Introduction of the functionalized thiol has been performed with an exchange protocol, which is performed by mixing the unfunctionalized AuNP with functionalized thiol.[13,14] On the other hand, direct synthesis of AuNP by the reduction in the presence of functionalized thiol would be an alternative way. Accordingly, the preparation of a functionalized AuNP from the THP protected precursor also is intriguing in conjunction with the synthetic efficiency.

We synthesized several THP-protected alkanethiols bearing a functional group **4a-c** and subjected to the formation of AuNPs. Synthesis of **4a-c** was carried out as outlined in Scheme 4. The reaction of 1,ω-mercaptoalcohol with 3,4-dihydro-2*H*-pyran would afford HO- and HS-both protected product, which underwent the removal of O-THP by acid-catalyzed methanolysis to afford **3** in 53% yield. The reaction of **3** with several organic halides was performed by general ether and ester syntheses. The reaction with 1-bromohexane afforded ether **4a** (72%). The acetate **4b** was prepared by the reaction of acetyl chloride (94%). Aryl ether **4c** was obtained by tosylation of the hydroxy group and following reaction with 4-iodophenol (88%).



**Scheme 4**

Preparation of functionalized AuNPs with thus obtained THP-thioethers was carried out with triethylsilane as a reducing agent. The reaction of the thioether bearing the alkyl ether group **4a** (0.2 mmol) proceeded smoothly to afford a dark purple solution and 25.1 mg of the nanoparticle was isolated. The reactions of THP-thioethers bearing other functional groups were carried out in a similar manner. The reaction resulted to show a clear purple color of the nanoparticle formation, however, the obtained dark brown solid did not dissolve again in any organic solvents suggesting that aggregation took place during isolation. However, the formation of AuNP was found to be successful when the AuNP formation was carried out with a mixture of **4b,c** and **1** as capping reagents and the obtained AuNP dissolved in chloroform again. Measurement of $^1$H NMR spectrum of AuNP composed of **1** and **4c** showed signals of aromatic groups at 6-7 ppm. The introduced ratio was estimated by the calculation of the integral value of the NMR spectrum being ca. 1.6:1.0.[9] On the other hand, characterization of the ratio of **1** and **4b** on AuNP by $^1$H NMR analysis was unsuccessful. IR spectrum of the AuNP showed characteristic absorption of the carbonyl group suggesting that thiol bearing the acetoxy group was introduced on the gold surface. Introduction of the acetoxy group into the AuNP was also confirmed by analyses of the organic residue after treatment of the obtained AuNP with excess iodine at room temperature[16] to observe the characteristic signals by IR and $^1$H NMR, in which the introduced ratio of **1**: **4b** was confirmed to be ca. 7.8:1.0. (Table 3)

**Table 3** Preparation of AuNP with THP-protected thiol derivatives bearing a functional group[a]

| capping reagent | yield/mg | size/nm |
|---|---|---|
| **4a** (0.2 mmol)[b] | 25.1 | 9.9±1.4 |
| **4b** (0.1 mmol) | 21.3 | aggregation |
| **1** (0.14 mmol) + **4b** (0.06 mmol)[b] | 30.7[c] | 6.8±0.90 |
| **1** (0.05 mmol) + **4c** (0.05 mmol) | 13.5[d] | 8.4±0.95 |

[a] Unless specified, AuNPs were synthesized from a capping reagent, $HAuCl_4·4H_2O$, and $Et_3SiH$ with the ratio of 1:1:1 in THF at 25 °C for 6 h. [b] The reaction was carried out with 0.2 mmol of reagents. [c] The ratio of **1**:**4b** on the AuNP was estimated to be ca. 7.8:1.0 by $^1$H NMR after treatment of the particle with iodine. [d] The ratio of **1**:**4c** was estimated to be ca. 1.6:1.0 by the $^1$H NMR spectrum.

In summary, gold nanoparticles were obtained from THP-protected alkanethiols and $HAuCl_4$ in the presence of a reducing agent without deprotection. Introduction of the alkylthio group bearing a functional group was also found to be available with the present protocol. Accordingly, the method would be a potentially useful synthetic tool to design functionalized gold nanoparticles.

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**Supporting Information** for this article is available online at http://www. thieme-connect.com/ejournals/toc/synlett.

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(12) AuNP obtained by the reduction with $NaBH_4$ or $LiBH_4$ shows its weight loss to be ca. 25%. (ref **2b** and **2c**)

(13) The particle size was similar to the case with unprotected dodecanethiol.

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Graphical Abstract

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