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Cross Coupling on Gold Nanoparticles. Effect of Reinforced Affinity of Organic Group with Bipedal Thiol

Atsushi Sugie,[1] Kenta Kumazawa,[1] Tomomi Hatta,[1] Kiyoshi Kanie,[2] Atsushi Muramatsu,[2] and Atsunori Mori*[1]
[1]*Department of Chemical Science and Engineering, Kobe University, 1-1 Rokkodai, Nada, Kobe, Hyogo 657-8501*
[2]*Institute of Multidisciplinary Research for Advanced Materials, Tohoku University,*
2-1-1 Katahira, Aoba-ku, Sendai, Miyagi 980-8577

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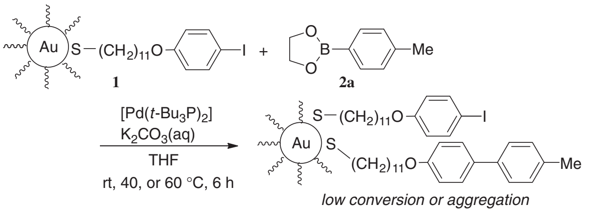
Bipedal thiol, whose end is modified with iodoarene, is synthesized and introduced onto the surface of gold nanoparticles. The obtained nanoparticles allow the Suzuki–Miyaura and Sonogashira cross-coupling reactions to form the carbon–carbon bond on the surface of the nanoparticle without serious aggregation under harsh conditions.

Organic transformation over organic/inorganic interfaces is a new frontier in synthetic organic chemistry. A reaction that smoothly proceeds under homogeneous conditions in an organic solvent does not necessarily occur in a similar manner on the surface. Accordingly, our continuing studies on the development of new synthetic protocols for alkanethiol-capped gold nanoparticles (AuNP) based on organic synthesis[1,2] lead our further concern toward the reaction at the organic functional group introduced into the end of the thiol. AuNP recently attracts much attention as advanced material showing electronic, electrooptical, and bioactive properties.[3,4] It is thus intriguing to introduce such organic functionalities by an organic bond-forming reaction on the surface of AuNP.[5,6] We herein report our efforts for transition-metal-catalyzed cross coupling[7] on the surface of AuNP, in which use of bipedal thiol bearing 1,3-dithiol moiety at the end of long-chained alkanethiol and a functional group to be transformed at the other end is highly effective.

We first envisaged the Suzuki–Miyaura coupling[8] reaction on an alkanethiol-capped AuNP. We designed and prepared an alkanethiol-capped AuNP **1**,[2] whose terminal is modified with iodoarene. The reaction of **1** and boronate **2a** in the presence of $[Pd(t\text{-}Bu_3P)_2]$ was performed in THF/aq. K_2CO_3 at room temperature for 6 h. Aggregation of the AuNP was not observed during the reaction; however, the isolated AuNP was not dispersed again in chloroform or THF, suggesting that aggregation took place in isolation. In addition, the ^1H NMR spectrum of the organic moiety, which was removed from Au by treatment with iodine, exhibited a ca. 1:1 mixture of the desired biaryl and unreacted aryl iodide. On the other hand, the reaction at elevated temperature (40–60 °C) resulted to form black precipitates in the reaction mixture suggesting aggregation (Scheme 1). These results show that the cross-coupling reaction of aryl iodide at the end of alkanethiol is difficult due to the insufficient stability of AuNP toward aggregation as well as low reactivity.

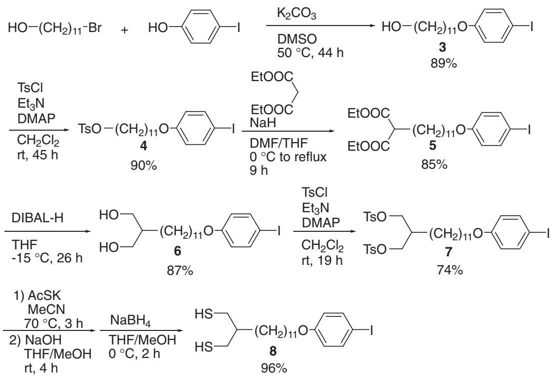


Scheme 1.

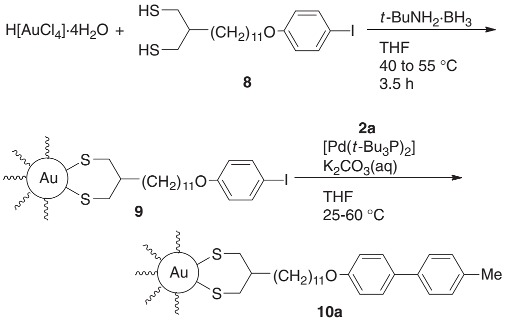
We then envisaged the use of multifunctional capping thiol for improved stabilization on the gold surface. Such unfunctionalized bidentate or tridentate thiols have been synthesized by Lee[9] and physical properties of thus obtained AuNP are characterized; however, studies on their tolerance for organic reactions have not been performed so far. Accordingly, our interest has been focused on the coupling reactions of the AuNP stabilized by bipedal 1,3-dithiol bearing iodoarene functionality by transition-metal catalysis.

Synthesis of bipedal thiol **8** was carried out as outlined in Scheme 2. The reaction of 11-bromo-1-undecanol with *p*-iodophenol in the presence of K_2CO_3 afforded **3** in 89% yield. Tosylation of **3** with *p*-toluenesulfonyl chloride leads to **4**, which was subjected to the reaction of diethyl malonate to afford diester **5** in 85% yield. Reduction of ester with DIBAL-H at −15 °C furnished the corresponding diol **6** in 87% yield. Treatment of **6** with tosyl chloride lead to the ditosylate **7** (74%). Introduction of thioacetyl group, following methanolysis, and reduction with $NaBH_4$ afforded bipedal thiol **8** in 96% yield.

Preparation of AuNP was carried out with the obtained **8** with $H[AuCl_4]$. It was found that the use of $t\text{-}BuNH_2 \cdot BH_3$ was effective to afford the corresponding AuNP **9** after treatment at 55 °C for 3.5 h in THF (Scheme 3).[10] Characteristics of AuNP **1** and **9** were compared by TEM observation and TGA measurement (Table 1). The particle size of the AuNP **9** was found to be smaller than that of the AuNP **1**. The adsorption density of thiol moiety on the AuNP was estimated by the particle size and the mass loss by TGA. The higher adsorption density of $-CH_2S$ of **9** compared to **1** suggested that bipedal thiol **8** effectively covered the AuNP surface.



Scheme 2.



Scheme 3.

Table 1. Characteristics of AuNP

AuNP	Particle size /nm	TGA mass loss at 800 °C/%	Adsorption density $(\text{–CH}_2\text{S/nm}^2)^a$
1	7.8 ± 0.97	9.65	3.98
9	5.4 ± 0.87	15.31	7.88

[a]Calculated from particle size and TGA mass loss.

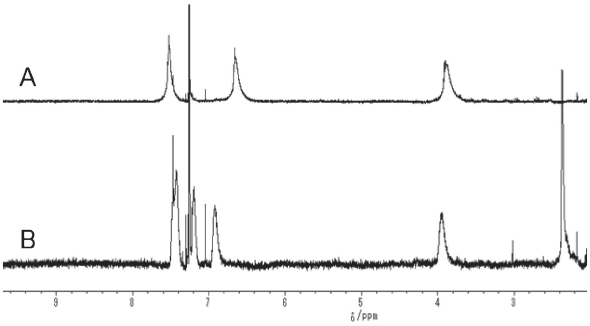


Figure 1. ^{1}H NMR of AuNP **9** (A) and **10a** (B) (500 MHz, $CDCl_3$).

With the obtained bipedal-thiol-protected AuNP **9** in hand, the Suzuki–Miyaura coupling was carried out. The reaction of AuNP **9** and aryl boronate **2a** in the presence of $[Pd(t\text{-}Bu_3P)_2]$ in THF/aq. K_2CO_3 was found to proceed smoothly to afford the corresponding biaryl **10a** after stirring at room temperature for 6 h. The purple color of the reaction mixture was maintained during the coupling reaction suggesting no problematic aggregation of AuNP. Addition of ethanol to the resulting mixture formed a precipitate and successive centrifugation and precipitation with ethanol afforded the AuNP as a dark brown solid, which was easily redispersed in chloroform and THF.

Figure 1 shows ^{1}H NMR spectra of the AuNP **9** (A) and **10a** (B). A new singlet signal at ca. 2.3 ppm, which corresponded to the methyl group, and additional signals of arylene groups (6.8–7.6 ppm) were observed in **10a**. The signal at 6.66 ppm, which is assigned as protons of the iodophenoxy group of **9** of A, disappeared in the spectrum B. The results suggested complete consumption of the iodophenoxy group of **9** during the reaction. TEM observation revealed that the obtained AuNP was also spherical, and no morphological change was observed after cross coupling (5.6 ± 0.86 nm) (Figure 2).

The Suzuki–Miyaura coupling of AuNP **9** with several aryl boronates was examined under similar conditions (Table 2). The reaction with boronic acid esters bearing 4-(trifluoromethyl)phenyl **2b** and 4-methoxyphenyl **2c** groups proceeded within 3 h at room temperature to afford the corresponding gold nanoparticles. The use of sterically hindered aryl boronate bearing 2,6-dimethylphenyl **2d** and 4-acetylphenyl **2e** groups also furnished the coupling products. It should be pointed out that the reaction with **2a** at 60 °C completed within a short reaction period (10 min). No significant aggregation was observed also in the reaction for a longer period (3 h) to afford the corresponding cross-coupled AuNP **10a**. The results clearly show that the bipedal thiol is much more stable thermally and chemically than monodentate thiol.

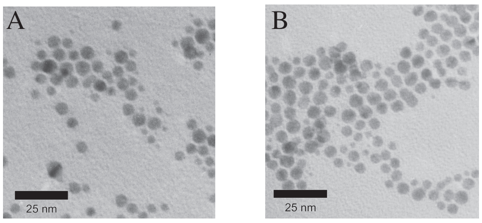
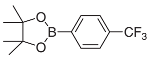
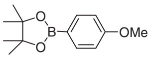
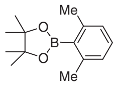
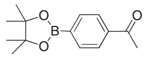


Figure 2. TEM images of AuNP **9** (A) and **10a** (B).

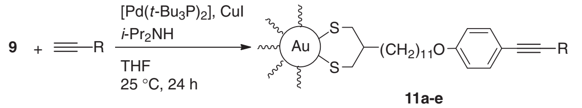
Table 2. Coupling reaction of aryl iodide on AuNP with arylboronates[a]

Reagent	Temp. /°C	Time	Yield /mg	$(\text{–C}_6\text{H}_4\text{Aryl}/\text{–C}_6\text{H}_4\text{I})/\%^b$
 (**2b**)	rt	3 h	17.1	>95
 (**2c**)	rt	3 h	17.6	>95
 (**2d**)	rt	6 h	18.0	93
 (**2e**)	rt	6 h	10.0	80
2a	rt	6 h	13.0	>95
	60	10 min	16.6	>95
	60	3 h	15.7	>95

[a]The reaction was carried out with AuNP **9** (20.0 mg) and arylboronic acid ester (0.1 mmol) in the presence of $[Pd(t\text{-}Bu_3P)_2]$ (0.01 mmol) and K_2CO_3 aq. (2 M, 2 mL) in THF (10 mL). [b]Conversion of aryl iodide to biaryl on AuNP was estimated by measurement of ^{1}H NMR of the nanoparticle or after treatment of AuNP with iodine.

The present protocol would be effective for diversity-oriented synthesis of AuNPs to introduce a functional group that is available as advanced materials. The place exchange method,[11] which is the reaction of unfunctionalized-alkanethiol-capped nanoparticle with a thiol bearing a functional group, is an alternative choice to form functionalized AuNPs; however, it is not easy to replace with the intended amount of functionality onto the particle. Although the reaction of a gold salt ($H[AuCl_4]$)

Table 3. Coupling reaction of aryl iodide on AuNP with alkynes[a]



–R	Product	Yield /mg	$(–C_6H_4Aryl/–C_6H_4I)/\%$[b]
$–C_6H_5$	**11a**	18.0	>95
$–C_6H_4–Me-4$	**11b**	12.7	85
$–n-C_6H_{13}$	**11c**	19.6	84
$–SiMe_3$	**11d**	19.2	>95
$–Si\,i-Pr_3$	**11e**	19.0	>95

[a]The reaction was carried out with AuNP **9** (20.0 mg) and alkyne (0.05 mmol) in the presence of $[Pd(t-Bu_3P)_2]$ (0.01 mmol), CuI (0.01 mmol), and $i-Pr_2NH$ (0.5 mmol) in THF (2.5 mL). [b]Conversion of aryl iodide to alkynylarene on AuNP was estimated by measurement of ^1H NMR of the nanoparticle.

with a capping thiol bearing a functional group at the end in the presence of a reducing agent, representative as the Brust–Schiffrin method,[12] the conditions may limit available organic functional groups. In contrast, the cross-coupling reaction on AuNP quantitatively proceeded with several arylboronates **2** and would be a powerful tool to introduce a wide range of functionality through carbon–carbon-bond formation.

It was also found that the Sonogashira coupling proceeded with AuNP **9**.[6b,6c,13] The reaction of AuNP **9** with phenylacetylene in the presence of $[Pd(t-Bu_3P)_2]$, CuI, and diisopropylamine in THF afforded the corresponding coupling product **11a** after stirring at room temperature for 24 h (Table 3). The similar reaction of AuNP **9** with terminal alkynes bearing aryl, alkyl, and trialkylsilyl groups proceeded smoothly to furnish nanoparticle **11b**–**11e**. Accordingly, AuNPs bearing a carbon–carbon-triple bond, which are available for several further transformation reactions, were obtained by the coupling protocol.

In summary, we have shown that cross coupling occurs on the AuNP. The reaction proceeded highly efficiently when bipedal thiol was employed as a surface-modifying agent to tolerate the reaction temperature up to 60 °C, whereas the reactions with monodentate thiol have been less effective. The coupling reaction allows introduction of organic functional groups onto nanoparticles, thus, the method would lead to organic-reaction inspired microfabrication of nanomaterials.[14]

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