



Designs of Novel Reactivity and Functionality Based on Specific Behaviors of the Sulfur Atom

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Doctoral Dissertation

Designs of Novel Reactivity and Functionality Based on Specific Behaviors of the Sulfur Atom

(硫黄原子の特異的な相互作用に基づく反応設計と材料設計)

July 2009

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Abbreviations

aq.	aqueous
AuNP	gold nanoparticle
bpy	2,2'-bipyridyl
Bu	butyl
°C	degrees Celsius
cat.	catalyst
d	doublet
DDAB	didodecylmethylammonium bromide
DFT	density functional theory
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethylsulfoxide
EI	electron impact
Et	ethyl
eq.	equivalent
g	gram(s)
h	hour(s)
HRMS	high resolution mass spectrometry
<i>i</i> Pr	isopropyl
IR	infrared spectrum
<i>J</i>	coupling constant
L	ligand, litre
M	metal
m	multiplet
Me	methyl
mol	mole(s)
mp	melting point
NMP	<i>N</i> -methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
Ph	phenyl
ppm	parts per million
Pr	propyl
q	quartet
quint.	quintet
ROMP	ring opening metathesis polymerization

rt	room temperature
s	singlet
t	triplet
tBu	tertiary butyl
TBAB	tetrabutylammonium borohydride
TEM	transmission electron microscope
THF	tetrahydrofuran
TLC	thin layer chromatography
TOAB	tetraoctylammonium bromide
UV	ultraviolet
vis	visible
XRD	X-ray diffraction

Chapter I

General Introduction

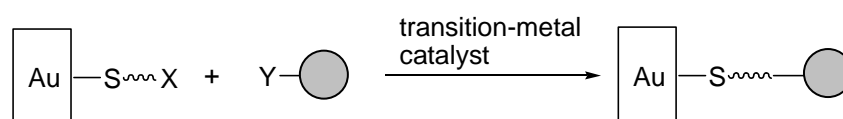
1-1 Introduction

Organosulfur compounds have gained more and more attention due to their potential use as advanced materials. Transition-metal catalyzed reaction¹ has been widely used to introduce new carbon-carbon bond to these compounds.

Thiophene, which is the five-membered heteroaromatic compound, has attracted considerable attentions as building blocks of advanced organic materials which can be used as conducting materials, nonlinear optical devices, and light-emitting diodes (LEDs).² Transition metal-catalyzed reactions have become a powerful process for the introduction of functionality to thiophene. Among these, substitution reactions at the carbon-hydrogen bond of thiophene³ are of practical interest as a straightforward reaction. Therefore, the development of the reaction and understanding of its mechanism have been a major concern.

Thiols, which are organic compounds bearing -SH group, are known to show strong affinity toward gold. Taking advantage of the characteristics, thiols have been introduced on the surface of gold nanoparticle and substrate to introduce functionality.⁴ Since functionalized gold nanoparticle and

substrate are applicable to catalyst, optical materials, and biological sensors, studies on forming carbon-carbon bond at the surface of the gold by transition-metal catalyzed reaction which would be a powerful tool for the microfabrication on the gold surface is intriguing (Scheme 1). To investigate the reactions at the surface of gold, thiol-capped gold nanoparticle would be an appropriate substrate since the adsorbed thiols give stability to the nanoparticle and enable easy handling and functionalization of the nanoparticle just as stable organic compounds. Therefore, development of synthetic methodology for the preparation of thiol-capped gold nanoparticle in organic solvents is also a significant issue.



Scheme 1

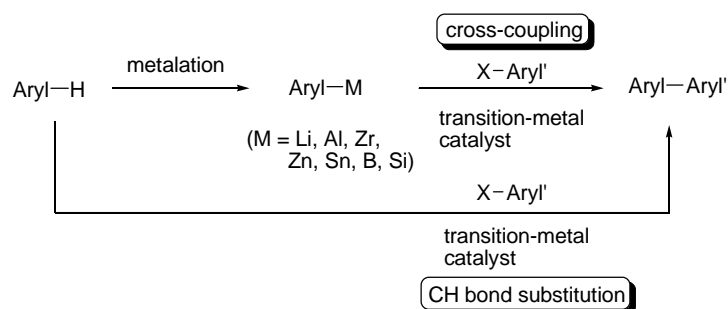
In this thesis, the Author tried to clarify the mechanism of the palladium-catalyzed C-H arylation reaction of thiophenes, which was reported by the Author's group previously. Understanding of the mechanism would lead to findings of new reactivities of transition metal complexes

toward thiophene. The Author also tried transition-metal catalyzed reaction at the surface of the thiol-capped gold nanoparticle for further functionalization of the nanoparticle. In conjunction with the catalytic reaction, development of a new method for the synthesis of thiol-capped gold nanoparticles in an organic solvent was envisaged. Extension of the available reducing agent and organic solvent would improve synthetic versatility of functionalized gold nanoparticles.

In this chapter, the Author briefly reviews the mechanism of transition-metal catalyzed CH substitution reaction of aromatic compounds and the methodologies for the synthesis of gold nanoparticles and their surface modification.

1-2 CH substitution reaction and its mechanism

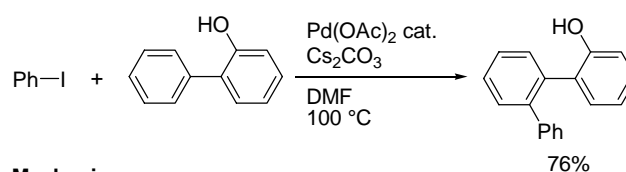
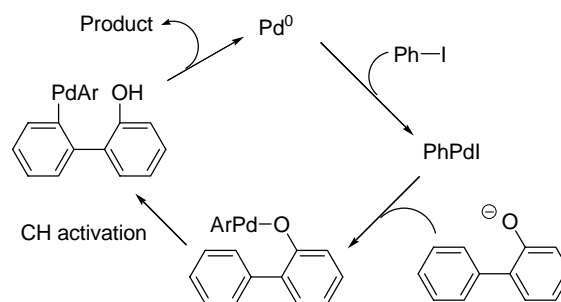
Transition metal-catalyzed cross-coupling reaction, which is the reaction of an organic halide and an organometallic reagent to form a carbon-carbon bond, has been a powerful method for the introduction of substituents at appropriate positions of the aromatic structure. A process that is capable of forming a similar bond avoiding the preparation and use of organometallic reagents is the direct functionalization of a carbon-hydrogen bond of aromatic compounds with transition metal catalysis, which is an alternative and more straightforward pathway (Scheme 2).² Development of CH substitution reactions with a transition metal catalyst has recently attracted considerable attention in organic synthesis, accordingly. In order to develop further reactions, mechanistic understanding of the reaction is important. In this section, the Author highlights the mechanistic studies on CH substitution reaction.



Scheme 2

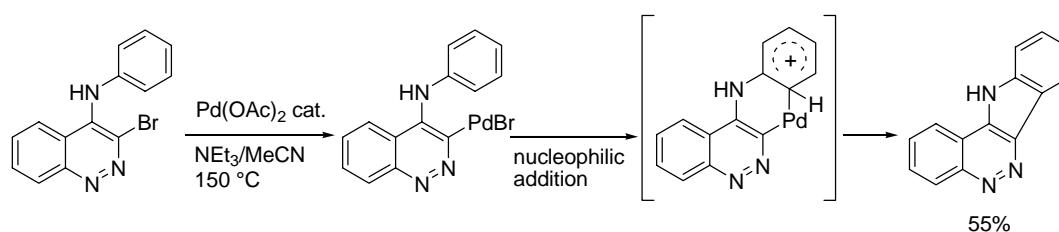
(i) Directing group-assisted CH substitution reaction

Miura reported palladium-catalyzed regioselective CH arylation reaction of 2-phenylphenols. In this reaction, coordination of the phenolic oxygen, which was the directing group, to palladium assisted the regioselective CH activation to undergo the reaction (Scheme 3).⁵ The similar reactions using functional groups such as ketones, aldehydes, amides, imines, and heteroaromatic rings as directing group were also reported.⁶

**Mechanism****Scheme 3****(ii) Intramolecular CH substitution reaction**

Ames reported palladium-catalyzed intramolecular CH arylation reaction. Formation of the metalacycle, which is a precursor of the product,

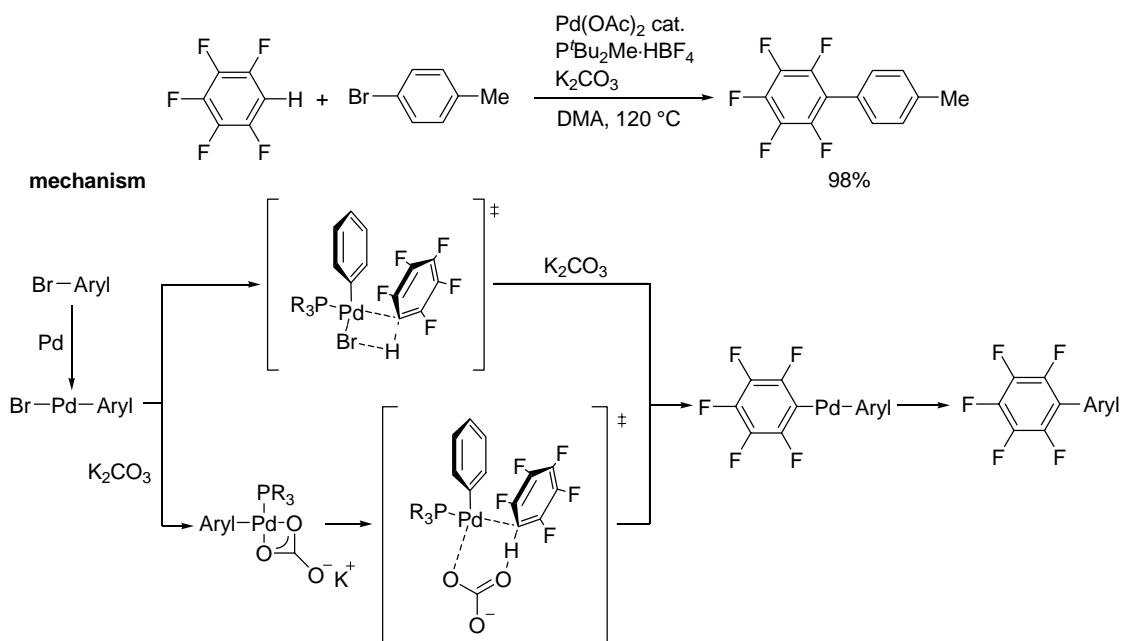
by nucleophilic attack of the arylpalladium halide to the phenyl group was allowed since the phenyl group was tethered to palladium(II) species (Scheme 4).⁷



Scheme 4

(iii) Concerted arene metalation and proton abstraction

CH substitution reaction of the aromatic hydrocarbon proceeds through neither the ligation of the directing group nor the formation of the metalacycle was reported by Fagnou.⁸ The reaction of pentafluorobenzene and bromotoluene in the presence of K_2CO_3 and the palladium catalyst bearing the bulky phosphine as the ligand afforded CH arylated product (Scheme 5). DFT calculation suggested that the reaction proceeded through concerted formation of the precursor of the product and proton abstraction by the carbonate ion. For the transition state of the reaction, four- or six-membered rings were plausible.

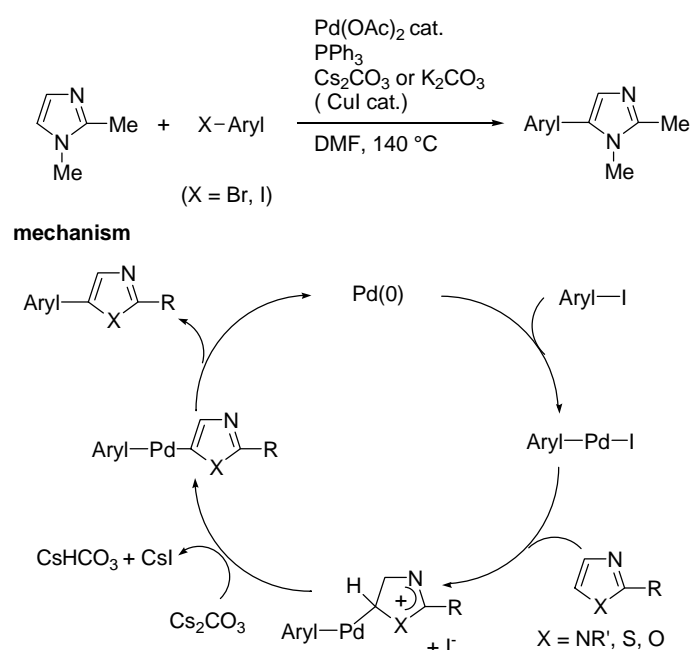


Scheme 5

(iv) Intermolecular electrophilic substitution

Heteroaromatic compounds, which have CH bond with high reactivity adjacent to the hetero atom, have been a substrate for intermolecular electrophilic substitution. Miura reported that the arylation reaction took place at CH bond of the heteroaromatic compounds such as imidazole, oxazole, thiazole, and thiophene in the presence of base (K_2CO_3 or Cs_2CO_3) and palladium catalyst (Scheme 6).⁹ It is considered that the reaction proceeded through the electrophilic substitution of the

heteroaromatic compound with the arylpalladium complex though no evidence was shown. The electrophilic substitution reaction of various heteroaromatic compounds and highly active catalyst for the reaction have been reported.¹⁰

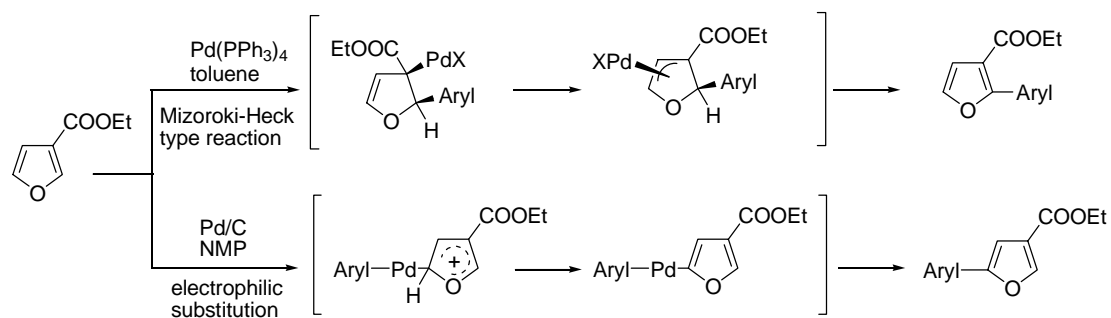


Scheme 6

(v) Mizoroki-Heck type reaction

Sharp reported palladium-catalyzed CH arylation reaction of furan derivatives.¹¹ In this reaction, employment of $\text{Pd(PPh}_3)_4$ and toluene gave the 2-arylated product since Mizoroki-Heck type reaction, which involved

insertion of the C=C bond of the furan into the Pd-Aryl bond and following β -hydride elimination, took place. On the other hand, electrophilic substitution proceeded to afford the 5-arylated product when Pd/C and NMP which generated cationic palladium species active to the electrophilic substitution at the 5-position of the furan, were used (Scheme 7).



Scheme 7

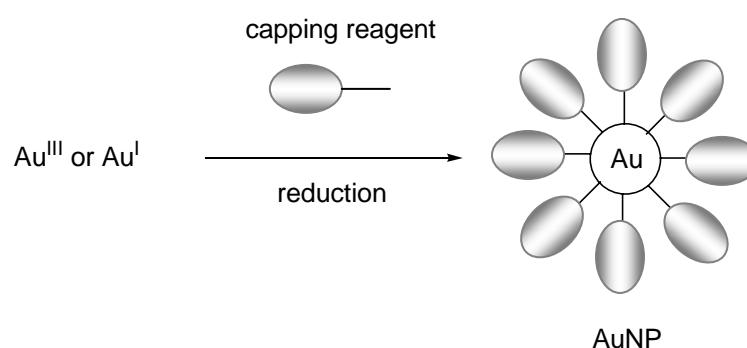
1-3 Thiol-capped gold nanoparticle (AuNP)

Gold nanoparticle (AuNP) consists of gold cluster and capping reagent which is an organic molecule to protect the nanoparticle from aggregation.⁴ It is known that a solution of AuNP in the diameter range of 5-20 nm exhibits purple color due to the surface plasmon resonance¹² and the solution has been used for artistic purpose such as coloring of glass and ceramics since ancient times. However, after the report on the formation of colloidal gold in CS₂/H₂O by Faraday in 1857,¹³ AuNP has been a subject of scientific research. Since AuNP shows characteristic physical properties different from bulk gold, application of AuNP to advanced material, catalysis, and biological sensing is of intense interest recently. The physical properties of AuNP strongly depend on the particle size and shape. Therefore, it is important to synthesize AuNP with narrow dispersity. Since the properties of AuNP are also controllable by structure of the capping reagent, AuNP has been an interesting subject in organic chemistry.

1-3-1 Synthetic methodologies for thiol-capped AuNP

In general, the synthesis of thiol-capped AuNP is carried out with

treatment of a solution of gold(III) or (I) salt with a reducing agent in the presence of a capping reagent (Scheme 8). As a capping reagent, thiol derivatives have been widely used due to its strong affinity of the sulfur atom toward gold. In this section, the Author summarizes various reducing agents for the synthesis of AuNP.

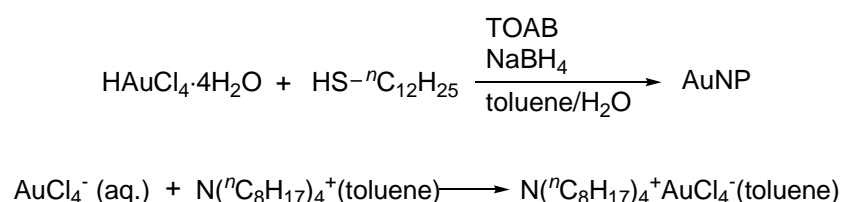


Scheme 8

(i) Brust-Schiffrin method

One of the most significant and prevalent methods for the synthesis of AuNP which is called “Brust-Schiffrin method” was reported by Brust and coworkers in 1994.¹⁴ They showed the reaction of HAuCl_4 with NaBH_4 in the presence of alkanethiol and tetraoctylammonium bromide (TOAB) in a mixture of H_2O (ultrapure water)/toluene afforded the stable thiol-capped spherical AuNP with an average diameter of 1-4 nm which can be isolated and dispersed to an organic solvent, repeatedly (Scheme 9). In this reaction,

TOAB acted as a phase-transfer reagent to transfer AuCl_4^- and hydride ion from H_2O to toluene. Further studies revealed that functionalization of AuNP by using functionalized thiol derivative is available¹⁵ and the size of the AuNP is controllable by varying the ratio of the gold salt and thiol¹⁶ in this method.



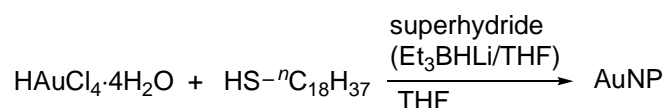
Scheme 9

(ii) Synthesis of AuNP by treatment of reducing agent in organic solvents

Though Brust-Schiffrin method gives thiol-capped AuNP with high stability, persistent contamination of AuNP with residual TOAB causes a trouble in some cases. The requirement of ultrapure water would also become problem. Therefore, development of single-phase synthesis of AuNP using an organic solvent which is readily available and shows high solubility toward both gold salt and capping reagent is intriguing.

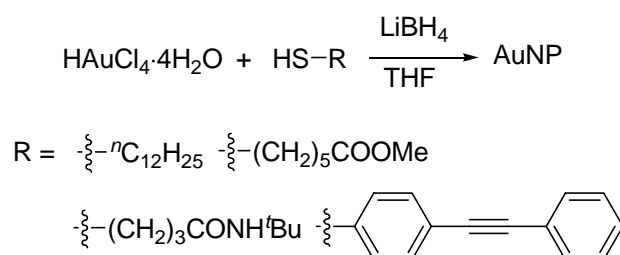
Ulman reported the addition of superhydride (a THF solution of

triethylborohydride) to a THF solution of $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ and octadodecanethiol afforded spherical nanoparticle showing an average size of 4.0 ± 0.3 nm (Scheme 10).¹⁷ They also synthesized nanoparticles of iridium and palladium.



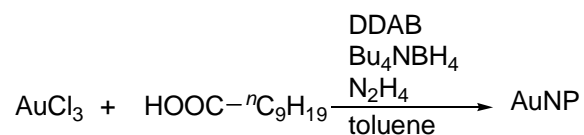
Scheme 10

Synthesis of AuNPs bearing various functional groups in an organic solvent was reported by Matzger.¹⁸ The reaction of HAuCl_4 with LiBH_4 in the presence of thiol in THF afforded spherical AuNPs with the diameter of 3.4-4.7 nm (Scheme 11). By using this method, AuNPs bearing ester, amide, and alkynyl groups on the thiol moiety were synthesized.



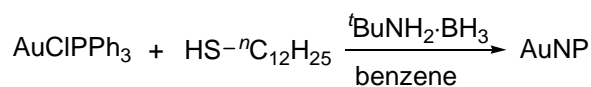
Scheme 11

The size-controlled synthesis of AuNP in a single-phase system was carried out by Peng (Scheme 12).¹⁹ The reaction was carried out by the addition of the mixture of tetrabutylammonium borohydride (TBAB) and hydrazine to a toluene solution of AuCl₃, decanoic acid and didodecylmethylammonium bromide (DDAB). By varying the ratio of TBAB and hydrazine, syntheses of 6-15 nm AuNPs were achieved. Hydrazine was also used in the synthesis of anisotropic AuNP in reverse micelles²⁰



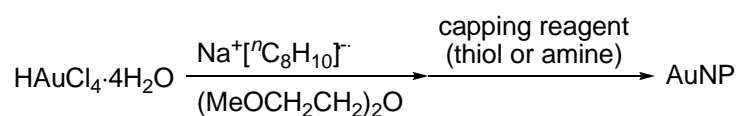
Scheme 12

Stucky also reported the synthesis of size-controlled AuNP. The reaction of *tert*-butylamine-borane complex, AuCl·PPh₃, dodecanethiol in benzene (or chloroform) gave 2.1-8.3 nm AuNP with a narrow size distribution by varying temperature of the reaction (Scheme 13).²¹ The reducing ability of *t*BuNH₂·BH₃ which is weaker than the reducing agents such as NaBH₄ and LiBH₄ is considered to be important to make the particle size controllable.



Scheme 13

The syntheses of AuNP in an organic solvent using a reducing agent other than boron compounds were also reported. Jansen showed the synthesis of diglyme-protected AuNP by the addition of sodium naphthalenide to a diglyme solution of HAuCl₄ (Scheme 14).²² Though the obtained AuNP were too unstable to isolate, the following addition of capping reagent such as thiol and amine furnished redispersible AuNP.



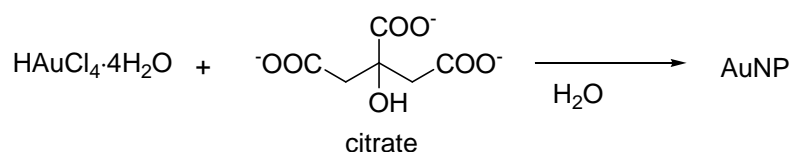
Scheme 14

(iii) Synthesis of AuNP by treatment of reducing agent in H₂O

The synthesis of AuNP in aqueous media is also studied. The most popular method is the one using sodium citrate as a reducing agent and a capping agent reported by Turkevitch in 1951 (Scheme 15).²³ The obtained

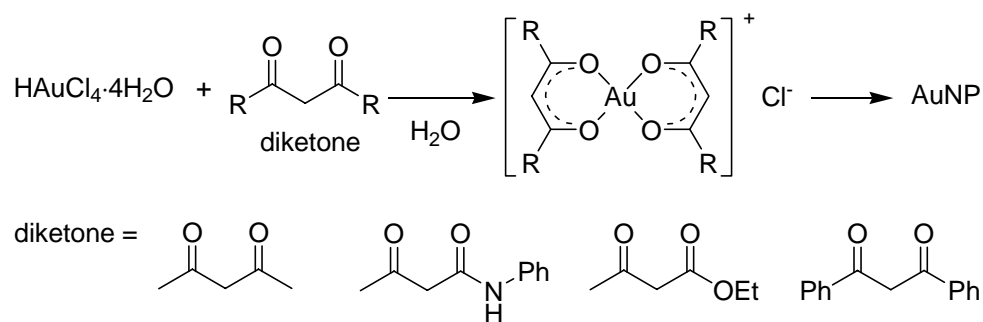
nanoparticle had average diameter of 20 nm. Frens reported size-controlled synthesis of AuNP using citrate by varying the ratio of gold and citrate.²⁴

The similar reaction using sodium ascorbate was also shown by Stathis.²⁵



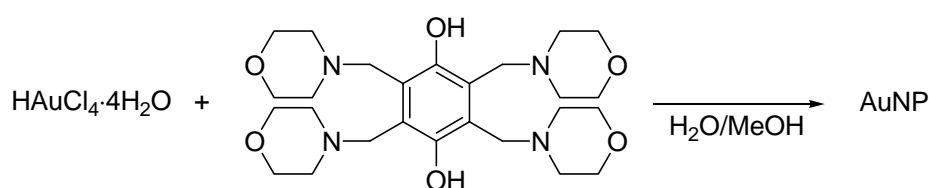
Scheme 15

Compounds bearing β -diketone skeleton were employed for the synthesis of AuNP in H_2O . Pal reported decomposition of Au^{III} - β -diketone chelate gave β -diketone-capped AuNP (Scheme 16).²⁶ With the variation of β -diketone, the particle size and shape was found to be tuned (spherical, hexagonal, and triangular). Further modification of the reaction is carried out by using β -diketone bearing thienyl and $-\text{CF}_3$ group²⁷ and *N,N*-dimethylacetoacetoamide.²⁸



Scheme 16

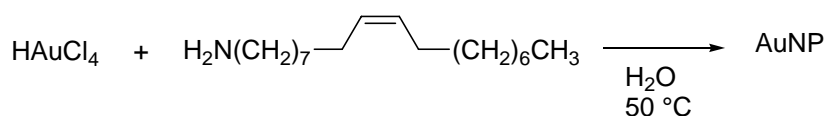
Preparation of AuNP with a compound bearing a hydroxy moiety as reducing/capping agent was explored. Banerjee found that treatment of a hydroquinone derivative to a H_2O -MeOH solution of HAuCl_4 gave AuNP having diameter of ca. 170 ± 17 nm (Scheme 17). Application of gels bearing a hydroxy group such as agarose²⁹ and gellan gum³⁰ was also known.



Scheme 17

Amines were found to work as a reducing agent as well as a capping reagent. Dravid reported the addition of oleyl amine to an aqueous solution of HAuCl_4 afforded amine-capped AuNP (Scheme 18).³¹ The core size and

the size distribution of AuNP were affected by the concentration of amine (10±0.6 to 50±10.5 nm). Amino groups of the hydro/organogel of urea derivatives were also shown to be effective to prepare and stabilize AuNP.³²



Scheme 18

Electrochemical synthesis of AuNP was reported by Lakshminarayanan. By carrying out electrolysis of gold wires in EtOH/H₂O solution of NaBH₄, KCl, and dodecanethiol, thiol-capped AuNP (1-3 nm) was obtained by dissolution of the anode.³³

(iv) Synthesis of AuNP by physical methods

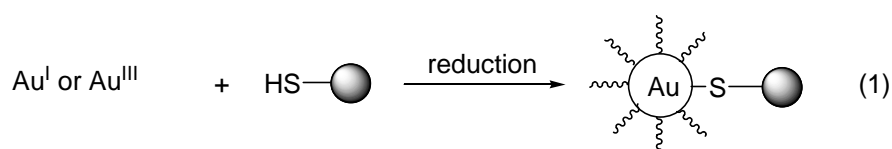
AuNPs were also synthesized by physical methods such as irradiation of γ -ray,³⁴ UV-ray,³⁵ and near-IR laser,³⁶ and sonication.³⁷

1-3-2 Surface modification of AuNP

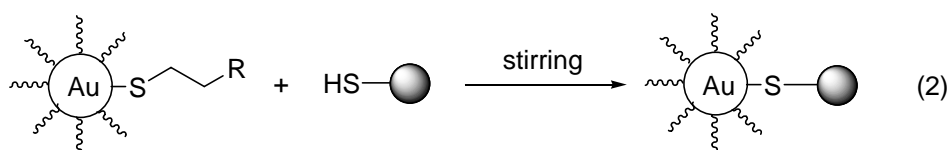
Methodologies for introducing functionalities to AuNP are broadly classified into 3 groups:

(1) Synthesis of AuNP by the reduction of Au salt and functionalized thiols

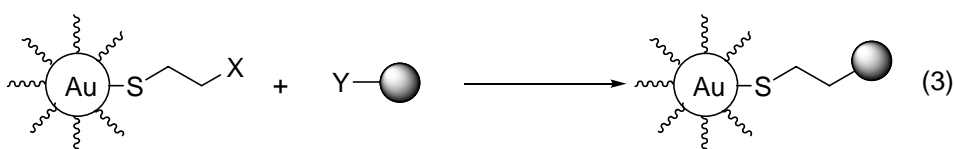
(eq.1)



(2) Ligand-exchange reaction (eq. 2)³⁸



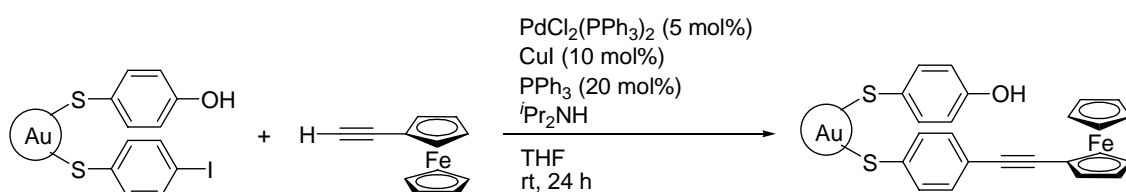
(3) Organic reactions carried out at the surface of AuNP (eq. 3)



Though methodology (1) and (2) are widely applied to prepare functionalized AuNPs, methodology (3) is not popular yet because difficulties arise in carrying out the organic reactions at the surface of AuNPs which are sometimes thermally and chemically unstable. However, since the reactions

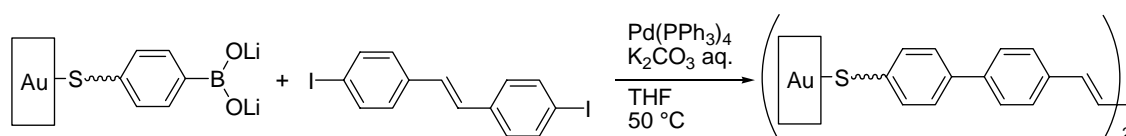
at the surface of AuNPs would enable reasonable preparation of various functionalized AuNPs without syntheses of the corresponding thiol derivatives, development of the reaction becomes important. In contrast to organic reactions such as S_N2 reaction,³⁹ (retro)Diels-Alder reaction,⁴⁰ and radical polymerization⁴¹ at the surface of AuNPs, studies on transition-metal catalyzed reactions at the surface of AuNPs are scarce and intriguing. In this section, the Author shows recent development on transition-metal catalyzed reactions carried out at the surface of AuNPs.

Though transition metal-catalyzed cross-coupling¹ has been a powerful tool for the introduction of substituents in the field of organic chemistry, little has been studied on the cross-coupling reaction at the surface of AuNP. In 2005, Liu introduced ferrocenyl, alkylphenyl, and pyrenyl moieties to the AuNP stabilized by *p*-iodothiophenol and *p*-mercaptophenol via the Sonogashira coupling reaction (Scheme 19).⁴² The reaction was carried out in a similar manner to the reaction of organic molecules. Thus, stirring of the solution of AuNP, alkyne, amine, and catalysts followed by extraction with a separatory funnel afforded functionalized nanoparticles dispersible to organic solvents.



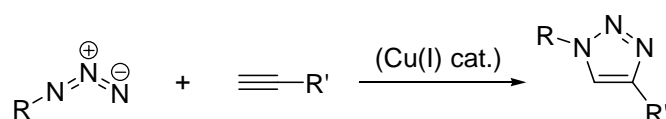
Scheme 19

The Suzuki-Miyaura coupling reaction at the surface of AuNP has not been reported yet, however, Kawai and coworkers employed the reaction at the surface of gold electrode to construct molecular devices (Scheme 20).⁴³



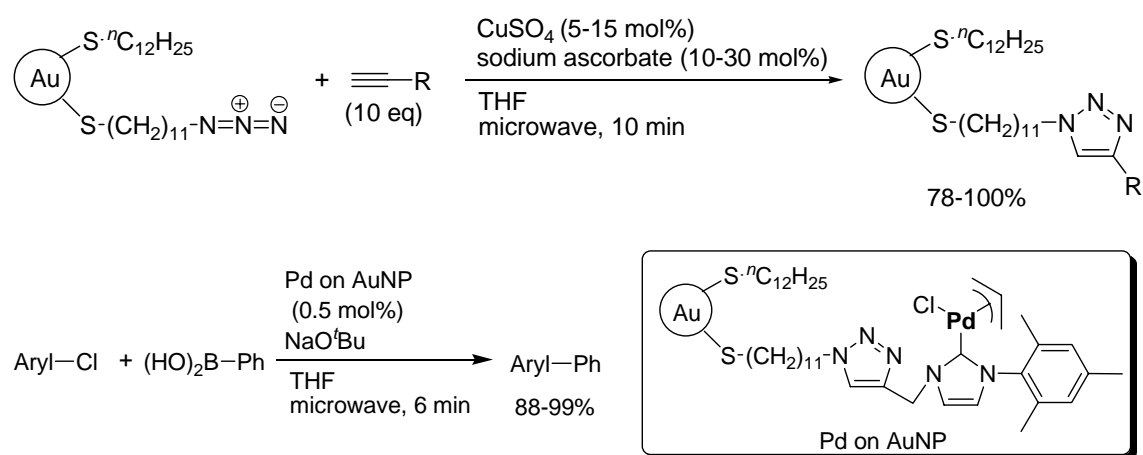
Scheme 20

Copper-catalyzed Huisgen 1,3-dipolar cycloaddition of azide with alkyne, which was reported and positioned as important reaction for “Click Chemistry” by Sharpless⁴⁴ has attracted much attention in various fields (Scheme 21).⁴⁵



Scheme 21

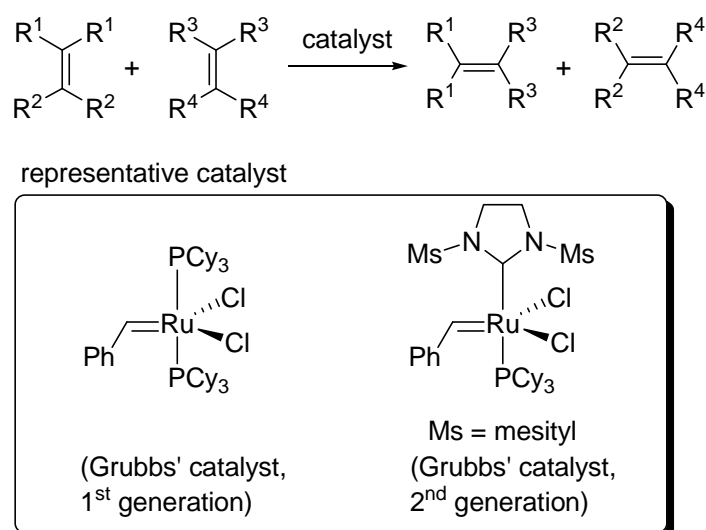
In 2006, Williams reported functionalization of AuNP capped with thiol bearing an azide group with the non-catalytic cycloaddition reaction.⁴⁶ However, the reaction required long reaction time (24-96 h) and the conversion was low (5-54%). The copper-catalyzed, efficient cycloaddition reaction was reported by Weck.⁴⁷ The cycloaddition reaction carried out in the presence of Cu^I generated from CuSO₄ and sodium ascorbate afforded functionalized AuNP in 78-100% yield (Scheme 22). Since the AuNP was sensitive to heat, microwave reactor was employed to undergo the reaction. Furthermore, *N*-heterocyclic carbene palladium complex was introduced to AuNP by the cycloaddition reaction and the functionalized AuNP was used as a catalyst of the Suzuki-Miyaura coupling reaction.



Scheme 22

The cycloaddition reaction at the surface of AuNP was applied to the introduction of organic moieties such as enzyme and dendrimer to AuNP⁴⁸ and the detection of Cu²⁺ ion.⁴⁹

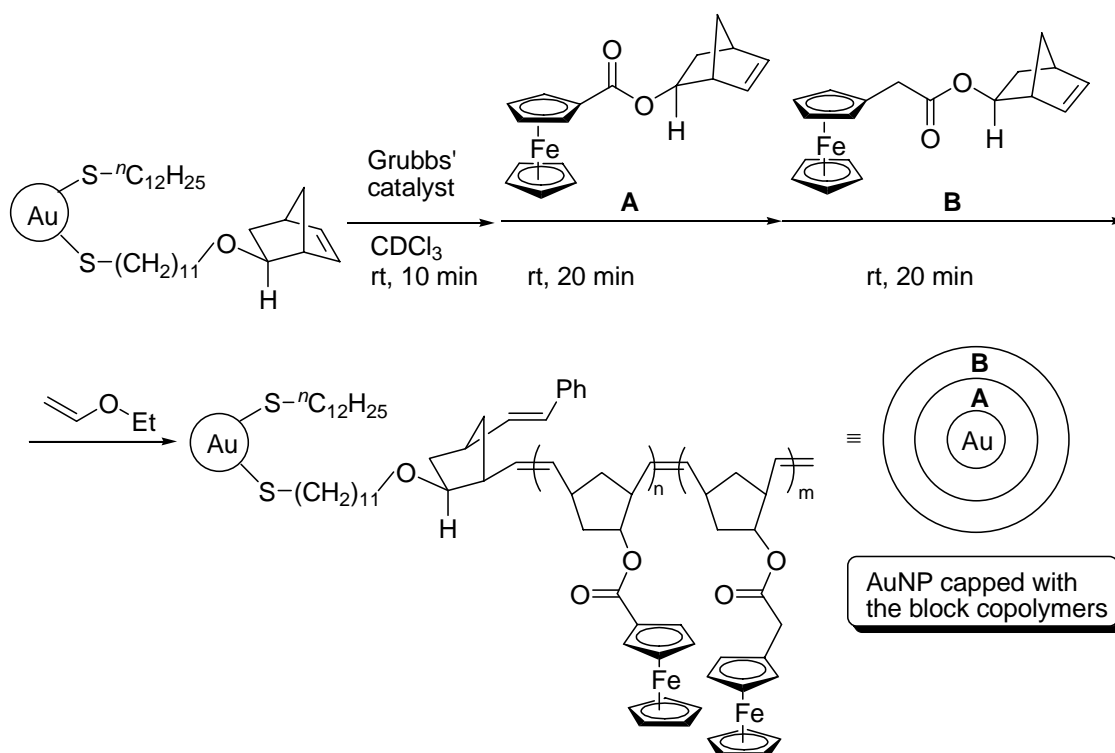
Olefin metathesis, which is a transition-metal-catalyzed C=C bond exchanging reaction, has been widely used in the synthesis of organic molecules such as polymers and natural products (Scheme 23).⁵⁰



Scheme 23

In 1999, Mirkin showed the synthesis of polymer shells around AuNP by using ring-opening olefin metathesis (ROMP) (Scheme 24).⁵¹ The reaction of the AuNP bearing a norbornen moiety with the norbornen derivative in the presence of the Grubbs' catalyst afforded the AuNP capped with the

polymer. The successive ROMP reaction of the AuNP with norborne derivatives gave the AuNP capped with block copolymers.



Scheme 24

1-4 Purpose of this thesis

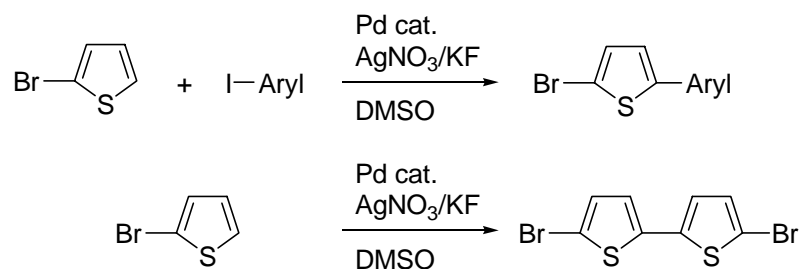
This thesis focused on researches on transition-metal catalyzed reactions of organosulfur compounds.

The Author attempted to reveal the mechanism of the palladium-catalyzed C-H arylation reaction of thiophenes, which was reported by the Author's group previously. Understanding of the mechanism would lead to findings of new reactivity of transition metal complex toward thiophene.

The Author also attempted to carry out the Suzuki-Miyaura coupling reaction, which is a class of the palladium-catalyzed cross-coupling reaction, of thiol derivatives adsorbed on the surface of gold nanoparticle to develop the methodology for surface modification of nanoparticles. For facile synthesis of gold nanoparticles, development of a new synthetic method which is carried out in an organic solvent was examined. Extension of the available reducing agent and organic solvent would improve synthetic versatility of functionalized gold nanoparticles.

1-4-1 Chapter II

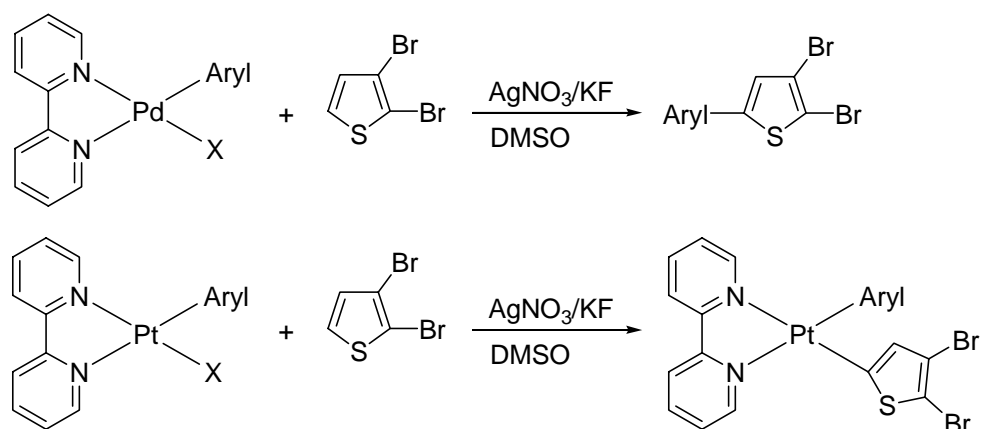
The Author's group previously reported the palladium-catalyzed CH arylation reaction and homocoupling reaction of thiophenes in the presence of AgNO₃/KF as an activator (Scheme 25).⁵² In these reactions, the CH substituted products were obtained while the carbon-bromine bond is completely intact even in the presence of a Pd complex. Accordingly, the Author's interest has been centered to the understanding of the mechanism of the CH substitution reaction.



Scheme 25

In this chapter, the mechanistic studies on the palladium-catalyzed CH arylation of thiophenes were carried out by a stoichiometric reaction of organometallic complexes. The reaction of arylpalladium(II) halide with 2,3-dibromothiophene in the presence of AgNO₃/KF as an activator induced electrophilic substitution at the CH bond of the thiophene to give CH arylated product (Scheme 26). The similar reaction of arylplatinum(II) halide

with thiophene derivatives afforded the aryl(thienyl)platinum(II) complex which is an analogue of the corresponding intermediate of the palladium-catalyzed reaction. These results suggested that the palladium-catalyzed CH arylation reaction of thiophenes proceeds through electrophilic substitution.

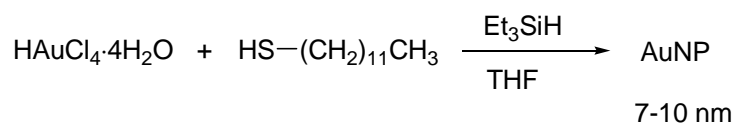


Scheme 26

1-4-2 Chapter III

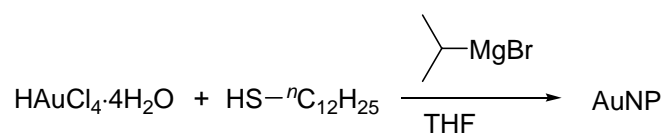
This chapter described the development of new reducing agents for the preparation of thiol-capped gold nanoparticles in an organic solvent. As a reducing agent, triethylsilane was added to a THF solution of HAuCl₄·4H₂O and 1-dodecanethiol to afford spherical AuNP with narrow dispersity (Scheme 27). Synthesis of the AuNP was also examined with various silanes

and conditions.



Scheme 27

It was also found that the reaction of $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ and 1-dodecanethiol with THF solution of 2-propylmagnesium bromide furnished thiol-capped AuNP. The similar reaction carried out with other Grignard reagents and organometallic reagent suggested that hydrogen atom at the β -position of the metal serves as a reducing agent in the AuNP synthesis (Scheme 28).

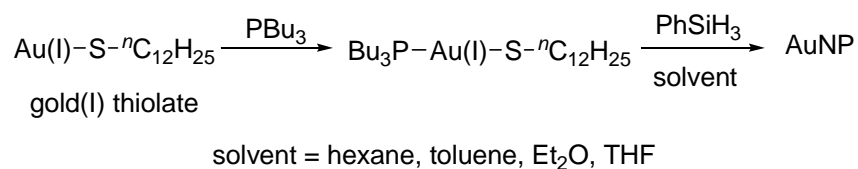


Scheme 28

1-4-3 Chapter IV

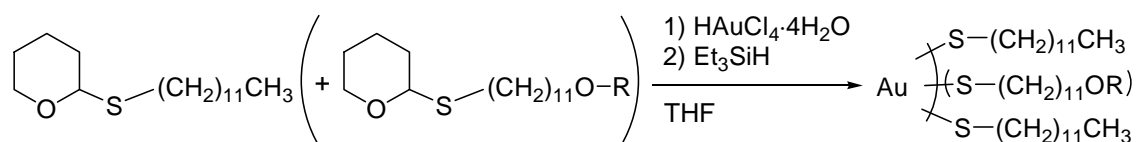
This Chapter described extension of versatility in the synthesis of AuNP. Though silane was found to be effective reagent for the synthesis of the thiol-capped AuNP in Chapter III, available solvents were limited to ethereal organic solvents to which HAuCl_4 is soluble. To carry out the

synthesis of the AuNP in various organic solvents, the Author envisaged solubilization of gold(I) thiolate and following reduction to AuNP. It was found that tri-*n*-butylphosphine complex of the gold thiolate is highly soluble in various organic solvents. Reduction of the gold complex with phenylsilane gave the thiol-capped AuNP (Scheme 29).



Scheme 29

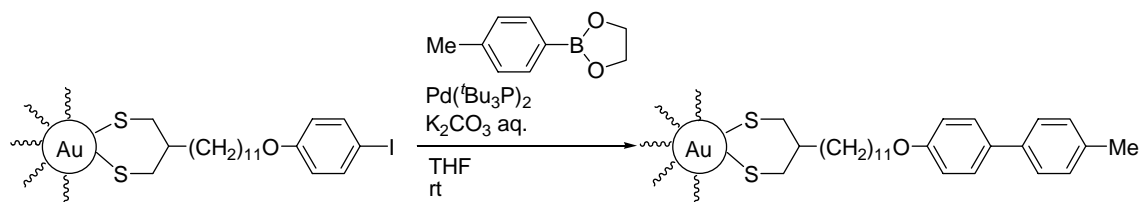
The Author found alkanethiol-capped AuNP was prepared from S-protected thiol with the tetrahydropyranyl (THP) group by treatment of HAuCl₄ in the presence of a reducing agent (Scheme 30). Introduction of ether, acetoxy, and iodophenoxy group were also found to be available with the protocol.



Scheme 30

1-4-4 Chapter V

In this chapter, the Author examined surface modification of the AuNP by the Suzuki-Miyaura coupling reaction, which is the palladium-catalyzed cross-coupling reaction of an aryl halide and an organoboron reagent, was envisaged. The AuNP bearing iodophenoxy group which was synthesized in the previous chapter was subjected to the Suzuki-Miyaura coupling reaction. However, agglomeration of the AuNP occurred during the reaction due to its low stability. Therefore, the Author synthesized the dithiol-capped AuNP which was more stable than the thiol-capped AuNP. The Suzuki-Miyaura coupling reaction carried out with dithiol-capped AuNP proceeded to give the surface-modified AuNP. (Scheme 31).



Scheme 31

1-4-5 Chapter VI

The Final Chapter summarized this thesis.

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Chapter II

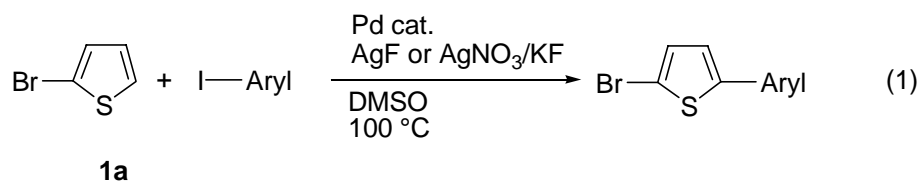
Electrophilic Substitution of Thiophenes with Arylpalladium(II) and Platinum(II) Complexes: Mechanistic Studies on Palladium-catalyzed CH Arylation of Thiophenes

Abstract: Mechanistic studies on palladium-catalyzed CH arylation of thiophenes which has been shown by our group are carried out by a stoichiometric reaction of organometallic complexes. The reaction of arylpalladium(II) halide with 2,3-dibromothiophene in the presence of AgNO_3/KF as an activator induces electrophilic substitution at the CH bond of the thiophene to give CH arylated product. The similar reaction of arylplatinum(II) halide with thiophene derivatives affords the aryl(thienyl)platinum(II) complex which is an analogue of a precursor of the product of the CH arylation reaction. These results suggest that the palladium-catalyzed CH arylation reaction of thiophenes proceeds through electrophilic substitution.

II-1 Introduction

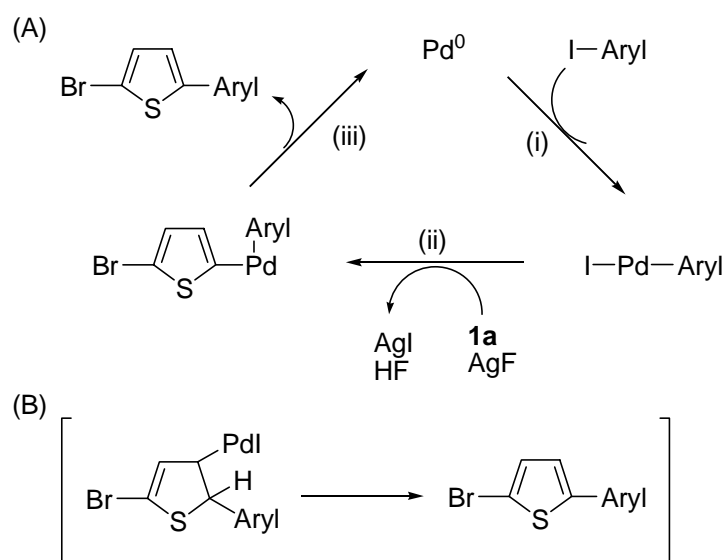
Transition metal-catalyzed C-H functionalization^{1, 2} attracts considerable attention as an alternative and more straightforward pathway to form a carbon-carbon bond compared to transition-metal catalyzed coupling of aryl halides with organometallic reagents.³ In particular, C-H substitution reactions of heteroaromatic compounds increase their significance since compounds bearing a heteroaromatic moiety are promising for advanced materials such as organic thin film transistors (TFTs) and light emitting devices.⁴ In order to develop further practical and efficient catalytic C-H substitution reactions, mechanistic understanding of the reaction is very important.

The Author's group has shown that C-H arylation of 2-bromothiophene (**1a**) with aryl iodide takes place in the presence of a palladium catalyst and AgF or AgNO₃/KF to give aryl(bromo)thiophene.⁵ It is noteworthy that the catalytic reaction of bromothiophene proceeds smoothly with the carbon-bromine bond remaining intact (eq. 1).



A plausible reaction mechanism for the CH arylation reaction is shown in Scheme 1(A):^{1d,5} (i) The reaction of Pd⁰ with aryl iodide forms aryl-Pd^{II}-I. (ii) The reaction of aryl-Pd^{II}-I with **1a** gives aryl(thienyl)palladium(II) complex through electrophilic substitution at the CH bond. (iii) Reductive elimination of aryl(bromo)thiophene from aryl(thienyl)palladium(II) complex takes place accompanied by the regeneration of palladium(0). Step (i) is well known to occur with a variety of palladium(0) complexes and aryl halides and reductive elimination of Aryl¹-Aryl² is also known to proceed from Aryl¹-Pd-Aryl² (iii).⁶ On the other hand, the step reaction (ii) has not been well studied and details of this reaction have not yet been clear. The other plausible mechanism is shown in Scheme 1(B) which involves insertion of a C=C bond of thiophene into the Pd-Aryl bond and successive β -hydrogen elimination (Mizoroki-Heck type reaction).⁷ The Author's group have confirmed the formation of AgI through powder XRD analysis of the silver residue after the catalytic reaction.^{5a}

However, neither isolation nor detection of the important intermediate aryl(thienyl)palladium(II) complex, which would be strong evidence to support the mechanism, has been achieved yet. The reaction mechanism of the palladium-catalyzed CH arylation would be clear if aryl(thienyl)palladium(II) complex is detected and characterized.



Scheme 1. Plausible reaction mechanisms of palladium-catalyzed CH arylation of bromothiophene. (A) Electrophilic substitution followed by reductive elimination and (B) Mizoroki-Heck type reaction mechanism.

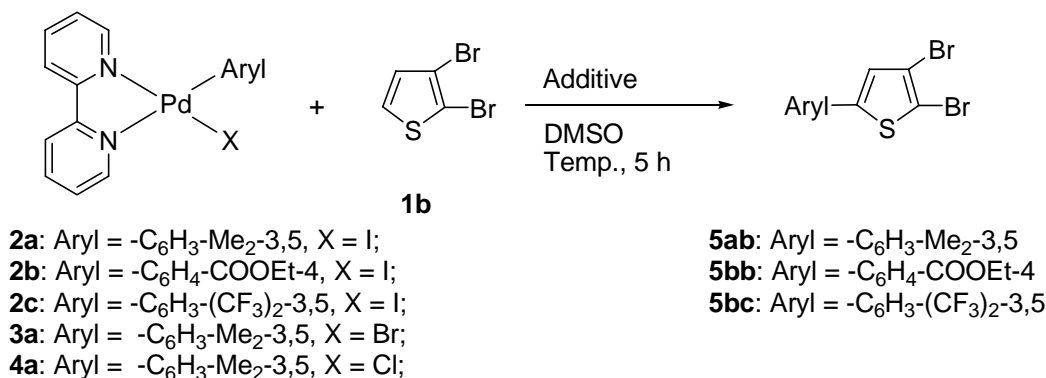
Herein, the Author reports studies on a stoichiometric reaction of palladium and platinum complexes with thiophene derivatives for the purpose of obtaining intermediate metal complexes of a step reaction of catalytic CH arylation.

II-2 Result and discussion

II-2-1 The reaction of aryl(halo)palladium(II) with 2,3-dibromothiophene (1b)

The Author synthesized aryl(bpy)iodopalladium(II) (bpy = 2,2'-bipyridine) **2a-c** by oxidative addition of aryl iodide to bis(dibenzylideneacetone)palladium(0) in the presence of bidentate nitrogen donor ligand in a manner reported previously.⁸ Aryl(bpy)bromopalladium(II) **3a** (Aryl = -C₆H₃-Me₂-3,5) and aryl(bpy)chloropalladium(II) **4a** (aryl = -C₆H₃-Me₂-3,5) were also prepared by the reaction of **2a** (aryl = -C₆H₃-Me₂-3,5) with AgNO₃ and aqueous solution of KBr or NaCl according to the literature.⁹ Since aryl(halo)palladium(II) complexes were in hand, a stoichiometric reaction of aryl(halo)palladium(II) complex with thiophene derivatives in the presence of AgNO₃/KF was carried out. As the substrate, 2,3-dibromothiophene (**1b**), which resulted in the highest yield in the catalytic CH arylation reaction, was employed. The reaction was performed under several conditions with aryl(bpy)halopalladium(II) **2a-c**, **3a** and **4a** and 2.4 equivalents of 2,3-dibromothiophene (**1b**) in DMSO for 5 h.^{5b} The results are summarized in Table 1.

Table 1. The reaction of aryl(bpy)halopalladium(II) with 2,3-dibromothiophene (**1b**)^a



Pd complex	temp./°C	additive	product (yield/%)	recovered Pd complex/%
2a	50	AgNO ₃ /KF	5ab (71)	-
2a	50	None	5ab (0)	51
2a	50	KF	5ab (0)	58
2a	50	AgNO ₃	5ab (0)	-
2a	rt	AgNO ₃ /KF	5ab (67)	-
2b	rt	AgNO ₃ /KF	5bb (66)	-
2c	rt	AgNO ₃ /KF	5cb (64)	-
3a	rt	AgNO ₃ /KF	5ab (55)	-
4a	rt	AgNO ₃ /KF	5ab (22)	-

^a The reaction was carried out with aryl(bpy)halopalladium(II) (0.05 mmol) and 2,3-dibromothiophene (**1b**) (0.12 mmol) in the presence of additive (0.2 mmol) in DMSO for 5 h.

Treatment of palladium complex **2a** and **1b** with AgNO₃/KF at 50 °C afforded the corresponding coupling product **5ab** in 71% yield, while the reaction in the absence of AgNO₃ and KF did not proceed but led to recovered

complex **2a** in 51% yield. In addition, recovery of complex **2a** was observed in 58% yield in the presence of KF and in the absence of AgNO₃. Although consumption of complex **2a** was observed, the reaction with AgNO₃ (in the absence of KF) afforded no coupling product, but gave unidentified compounds bearing neither thienyl-palladium nor thienyl-aryl bonds. It is noteworthy that the reaction proceeded at room temperature although the catalytic CH arylation of thiophene required 50-100 °C. The reaction with other aryl(iodo)palladium(II) complexes like (bpy)(4-ethoxycarbonylphenyl)iodopalladium(II) (**2b**) and [3,5-bis(trifluoromethyl)phenyl](bpy)iodopalladium(II) (**2c**) with **1b** in the presence of AgNO₃/KF similarly proceeded to give **5bb** and **5cb**, respectively. When arylpalladium(II) bromide **3a** was treated with **1b** and AgNO₃/KF at room temperature for 5 h, arylthiophene **5ab** was also obtained in 55% yield. The reaction of arylpalladium(II) chloride **4a** also proceeded to afford **5ab** in 52% yield.

Since the catalytic CH arylation is considered to proceed through an aryl-Pd^{II}-I complex, the reaction of palladium complexes **2a-c** with **1b** should be a part of the catalytic cycle, which is a class of electrophilic substitution of

1b with aryl-Pd^{II}-I leading to the aryl(thienyl)palladium complex. However, aryl(thienyl)palladium(II) was not obtained by the reaction of **2a** and **1b** at room temperature. Because reductive elimination of biaryl from diarylpalladium(II) complexes is known to occur smoothly under mild conditions, the aryl(thienyl)palladium complex once formed would be immediately converted to the product **5ab** through reductive elimination.¹⁰ Though the palladium complex was switched to that bearing an electron-withdrawing group **2b** (Aryl = C₆H₄-COOEt-4) or **2c** (Aryl = C₆H₃-(CF₃)₂-3,5) and the reaction temperature was controlled at room temperature in order to retard reductive elimination, neither isolation nor detection of the complex was successful. Accordingly, the results suggest that reductive elimination is inevitable in the electrophilic substitution of 2,3-dibromothiophene (**1b**). The results also indicate that the AgNO₃/KF system serves as an effective activator in electrophilic substitution of aryl-Pd^{II}-I, where both AgNO₃ and KF are necessary for the reaction to take place. Although the role of the AgNO₃/KF system as an activator has not been clear yet, strong affinity between silver and halogen atoms as well as the effect of fluoride ion would be a key for the reaction. Although the

available aryl halide in the catalytic CH arylation reaction of thiophene has been limited to the iodide,⁵ bromo and chloro palladium complex **3a** and **4a** underwent the CH substitution reaction. These findings suggest that the catalytic CH arylation of a thiophene derivative with an aryl bromide or chloride would be possible under appropriate conditions that allow oxidative addition of the aryl halide to Pd⁰.

II-2-2 The reaction of aryl(halo)platinum complex with thiophene derivatives

Since aryl(thienyl)palladium(II) complex was not detected in the stoichiometric reaction with thiophene derivatives, the Author envisaged to synthesize its platinum analogue, which would be more stable toward reductive elimination. The reaction of (bpy)(iodo)phenylplatinum(II) (**6d**)¹¹ with 2,3-dibromothiophene (**1b**) was first examined with AgNO₃/KF as an activator under conditions similar to those carried out in the reaction of the corresponding palladium complex and found to afford (bpy)(phenyl)thienylplatinum(II) (**7db**) in 91% yield (Figure 1). The ¹H NMR spectrum of **7db** showed a doublet signal at 7.28 ppm corresponding to 2H of the *ortho* phenyl signal, which accompanied the coupling by ¹⁹⁵Pt nuclei

($^3J(\text{PtH}) = 52 \text{ Hz}$) indicating the existence of a Pt–C(phenyl) bond.¹² In addition, a singlet signal at 6.57 ppm, which corresponds to the β -proton of the thiophene ring, was observed along with the satellite of ^{195}Pt ($^3J(\text{PtH}) = 55 \text{ Hz}$). These results suggest that **7db** possesses both Pt–C(phenyl) and Pt–C(thienyl) bonds.

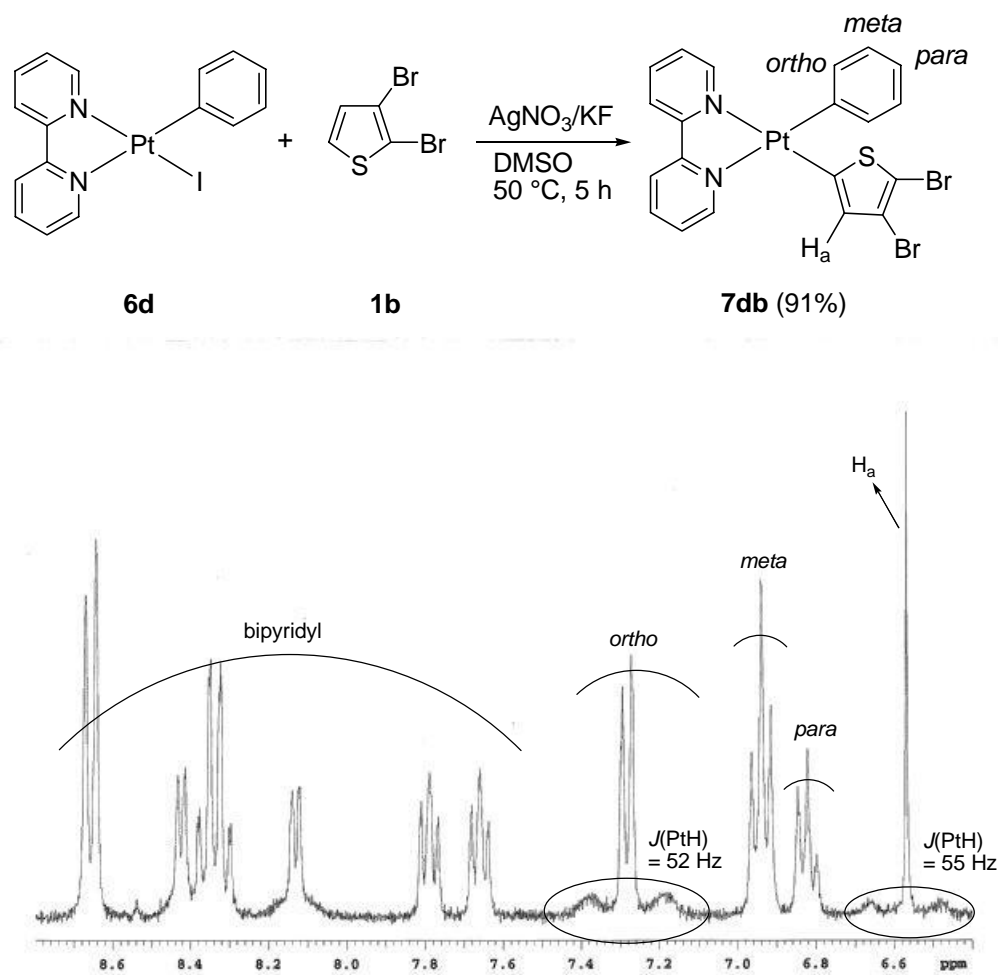
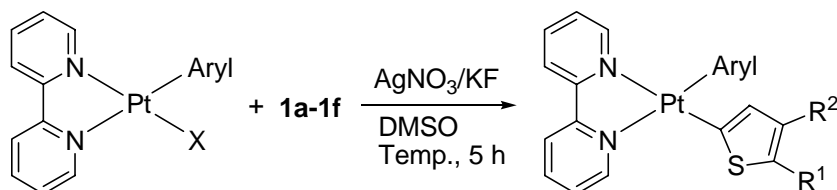


Figure 1. Synthesis of platinum(II) complex **7db** and its ^1H NMR spectrum of platinum(II) complex **7db** (300 MHz, $\text{DMSO}-d_6$, rt)

Worthy of note is that this is a new class of reactivity in platinum(II) complexes¹³ to construct a Pt–C σ bond by intermolecular electrophilic substitution with a heteroaromatic compound in the presence of AgNO₃/KF without participation of proximal chelation by a heteroatom.¹³ It should also be pointed out that the platinum-carbon bond formation occurred smoothly at the CH bond when the thiophene derivative had a carbon-bromine bond. This kind of aryl(thienyl)platinum(II) complex bearing a carbon–bromine bond on the thiophene ring has hardly been synthesized by other synthetic pathways, to the best of our knowledge, such as nucleophilic substitution on the platinum metal with a thienyl metallic reagent¹⁴.

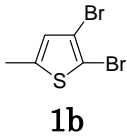
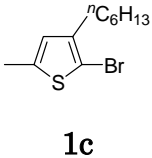
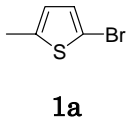
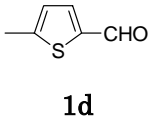
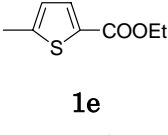
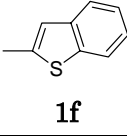
As summarized in Table 2, the reaction with several platinum complexes and a variety of thiophene derivatives was examined. A platinum complex bearing a phenyl or 4-methylphenyl group was employed for the reaction with thiophenes. The iodo(phenyl)platinum(II) complex **6d** reacted with 2,3-dibromothiophene (**1b**) even at room temperature to afford the corresponding aryl(thienyl)platinum complex **7db** in a slightly inferior yield (86%). In addition to **1b**, 2-bromo-3-hexylthiophene (**1c**) also afforded the aryl(thienyl)platinum complex **7dc** in 87% yield after stirring at 50 °C for 5 h.

The reaction of (bpy)chloro(4-methylphenyl)platinum(II) (**6e**) with thiophene derivative was also found to proceed. The corresponding platinum complexes were obtained by the reaction with several thiophene derivatives bearing a bromo group at the 2-position (**1a** and **1b**) and an electron-withdrawing group **1d** or **1e**. The corresponding complexes **7ea-7ee** were obtained in good to excellent yields. Benzothiophene (**1f**) also underwent the reaction with platinum complex **6e** to afford **7ef** in 78% yield.

Table 2. The reaction of [PtX(Aryl)(bpy)] (**6d-e**) with thiophene derivatives^a

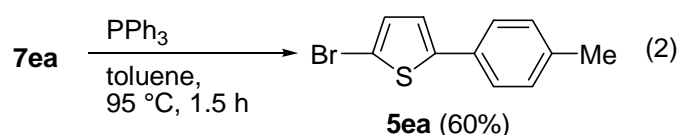
6d: Aryl = -C₆H₅, X = I;
6e: Aryl = -C₆H₄-Me-4, X = Cl

7db: Aryl = -C₆H₅, R¹ = R² = Br;
7dc: Aryl = -C₆H₅, R¹ = Br, R² = -ⁿC₆H₁₃;
7eb: Aryl = -C₆H₄-Me-4, R¹ = R² = Br;
7ea: Aryl = -C₆H₄-Me-4, R¹ = Br, R² = H;
7ed: Aryl = -C₆H₄-Me-4, R¹ = CHO, R² = H;
7ee: Aryl = -C₆H₄-Me-4, R¹ = COOEt, R² = H;
7ef: Aryl = -C₆H₄-Me-4, R¹, R² = -CH=CH-CH=CH-

Pt complex	thiophene	temp./°C	product	yield/%
6d	 1b	rt	7db	86
6d	 1c	50	7dc	87
6e	1b	50	7eb	74
6e	 1a	50	7ea	65
6e	 1d	50	7ed	73
6e	 1e	50	7ee	74
6e	 1f	50	7ef	78

^a The reaction was carried out with [PtX(Aryl)(bpy)] (0.05 mmol) and thiophene derivative (0.12 mmol) for 5 h in the presence of AgNO₃ (0.2 mmol) and KF (0.2 mmol) in DMSO.

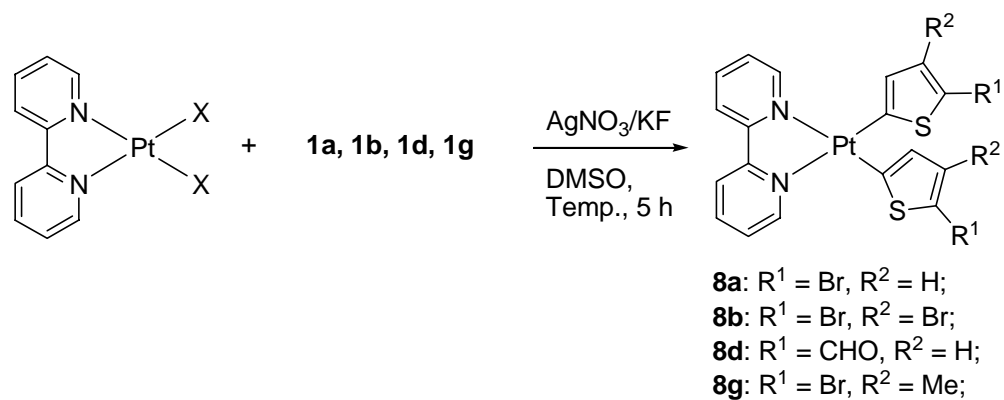
proceed by heating the complex **7db** at 100 °C for 17 h in DMSO-*d*₆. This finding suggests the high stability of the platinum complex bearing a thienyl ligand toward reductive elimination compared with other related diorganoplatinum(II) complexes.¹⁵ Because complex **7db** showed high thermal stability, heating of **7db** with an additive was carried out to accelerate reductive elimination of **5db** according to the literature.¹⁶ When a toluene solution of **7ea** and PPh₃ was heated at 95 °C for 1.5 h, corresponding arylthiophene **3ea**, which was considered to be generated by reductive elimination, was obtained in 60% yield (eq. 2). By contrast, reductive elimination of **5db** was not observed by heating the complex **7db** with diethyl fumarate¹⁷ or with silver(I) triflate.^{14a}



II-2-3 The reaction of di(halo)platinum complex with thiophene derivatives

The reaction of [PtX₂(bpy)] (X = Cl, I)¹¹ was also found to proceed with thiophene through double electrophilic substitution.² The results are summarized in Table 3. Similar to the case of the reaction of

aryl(halo)platinum(II) complexes **6d-e**, the reaction of $[\text{PtX}_2(\text{bpy})]$ ($\text{X} = \text{Cl}, \text{I}$) with 2,3-dibromothiophene (**1b**) in the presence of AgNO_3 and KF in DMSO at $50\text{ }^\circ\text{C}$ afforded dithienylplatinum(II) complex **8b** in 70% yield ($\text{X} = \text{I}$) and 65% yield ($\text{X} = \text{Cl}$), respectively. Though the reaction of $[\text{PtI}_2(\text{bpy})]$ with 2-bromo-3-methylthiophene (**1g**) at $50\text{ }^\circ\text{C}$ afforded dithienylplatinum(II) complex **8g** in 79% yield, the reaction at room temperature gave **8g** in only 10% yield. This result was found to be in contrast to the reaction of aryl(halo)platinum(II) complexes **6d-e**. The corresponding dithienylplatinum(II) complex was also obtained by the reaction with 2-bromothiophene (**1a**) and 2-formylthiophene (**1d**). The dithienylplatinum(II) complex is considered to be a platinum analogue for the proposed intermediate of the homocoupling reaction catalyzed by palladium,¹⁸ which is also suggested to proceed via electrophilic substitution of the dihalo complex with two equivalents of thiophene.

Table 3. Reaction of [PtX₂(bpy)] with thiophene derivatives^a

Pt complex	thiophene	temp./°C	product	yield/%
[PtI ₂ (bpy)]		50	8b	70
	1b			
[PtCl ₂ (bpy)]	1b	50	8b	65
[PtI ₂ (bpy)] ^b		50	8g	79
	1g			
[PtI ₂ (bpy)] ^b	1g	rt	8g	10
[PtCl ₂ (bpy)]		50	8a	53
	1a			
[PtCl ₂ (bpy)]		50	8d	69
	1d			

^a Unless noted, the reaction was carried out with [PtX₂(bpy)] (0.1 mmol) and thiophene derivative (0.3 mmol) for 5 h in the presence of AgNO₃ (0.5 mmol) and KF (0.5 mmol) in DMSO. ^b The reaction was carried out with [PtI₂(bpy)] (0.05 mmol), **1g** (0.24 mmol), AgNO₃ (0.4 mmol), and KF (0.4 mmol).

II-3 Conclusion

The reactions using stoichiometric amounts of palladium and platinum complexes were carried out to study the mechanism of catalytic C-H arylation of thiophenes. When arylpalladium(II) halides **2a-c** were treated with 2,3-dibromothiophene (**1b**), silver(I) nitrate, and potassium fluoride, the corresponding arylthiophene, the product of C-H arylation was obtained while aryl(thienyl)palladium(II) complex was not detected at all. On the other hand, aryl(thienyl)platinum(II) complex was synthesized by the similar reaction using arylplatinum(II) halides **6d-e**. These findings strongly suggest that C-H arylation of thiophenes with aryl iodide occurs by electrophilic substitution of the palladium complex promoted by the activating agent AgNO₃/KF. Based on the results of the reaction using arylpalladium bromide **3a** and chloride **4a**, aryl bromide and chloride may be applicable to the C-H arylation of thiophene derivatives when appropriate reaction conditions are applied.

II-4 Experimental

General

Melting points were uncorrected. ^1H NMR (300 MHz, 500 MHz), ^{13}C NMR (75.5 MHz, 125 MHz) spectra were measured with a Varian Mercury 300 or Bruker Avance 500 spectrometer. Unless specified, measurements of the spectra were carried out with CDCl_3 as a solvent. The chemical shifts were expressed in ppm using CHCl_3 (7.26 ppm for ^1H) or $\text{DMSO}-d_6$ (2.49 ppm for ^1H) or CDCl_3 (77.0 ppm for ^{13}C) as an internal standard. IR spectra were recorded on Shimadzu FTIR-8100A. Elemental analysis was carried out with a LECO CHNS-932 CHNS or Yanaco MT-5 CHN autorecorder at the Center for Advanced Materials Analysis, Technical Department, Tokyo Institute of Technology. High resolution mass spectra (HRMS, EI or FAB) were measured with JEOL MStation.

Materials

DMSO was purchased from Wako Pure Chemical Industries, Co. Ltd. as an anhydrous grade and stored in a Schlenk tube under nitrogen atmosphere. Other chemicals were purchased and used as such. Preparation

of palladium complex **2a-c**, **3a** and **4a** and platinum complexes **6d-e** and [PtX₂(bpy)] (X = Cl, I) were performed by methods shown in the literature.^{8, 10, 11, 12}

General procedure for the reaction of aryl(2,2'-bipyridine)iodopalladium(II) with 2,3-dibromothiophene (1b) in the presence of AgNO₃/KF.

To a solution of [PdI(C₆H₄-COOEt-4)(bpy)] (**2b**, 24.7 mg, 0.05 mmol) in 3 mL of DMSO was added **1b** (0.014 mL, 0.12 mmol) under a nitrogen atmosphere. Potassium fluoride (11.6 mg, 0.2 mmol) and silver(I) nitrate (34 mg, 0.2 mmol) were then added. The resulting suspension was then stirred at room temperature for 5 h. The mixture was passed through a Celite pad, which was washed with dichloromethane repeatedly. The filtrate was washed with water twice. The organic layer was concentrated under reduced pressure to leave a crude oil. Purification by column chromatography on silica gel afforded 12.9 mg of **5bb** as light yellow solid (66%).

The reaction of **2a** and **2c** was carried out in a similar manner as above. The yield of **5ab** was estimated by ¹H NMR analysis using trichloroethene (6.46 ppm) as an internal standard on the basis of the characteristic signal at 7.08 ppm derived from proton at the 4-position of the thiophene ring, while that of

5cb was determined by the proton signal of the 4-position of the phenyl ring (7.82 ppm).

General procedure for the reaction of aryl(halo)platinum complexes 6d-e with a thiophene derivative.

To a mixture of [PtI(Ph)(bpy)] (**6d**, 27.8 mg, 0.05 mmol), 2,3-dibromothiophene (**1b**, 0.013 mL, 0.12 mmol) and potassium fluoride (11.6 mg, 0.2 mmol) was added AgNO₃ (34.0 mg, 0.2 mmol) in one portion under argon atmosphere. The resulting suspension was stirred at 50 °C for 5 h. After cooling to room temperature, the mixture was passed through a Celite pad, which was washed with dichloromethane repeatedly. The filtrate was washed with water twice. The organic layer was concentrated under reduced pressure to leave a crude solid, which was purified by recrystallization to afford 30.5 mg of **7db** as a yellow solid (91%). ¹H NMR (300 MHz, DMSO-*d*₆) δ 6.57 (s, $J(^{195}\text{PtH}) = 55$ Hz, 1H), 6.82 (m, 1H), 6.94 (m, 2H), 7.28 (m, $J(^{195}\text{PtH}) = 52$ Hz, 2H), 7.66 (ddd, $J = 10.1, 7.5, 1.3$ Hz, 1H), 7.79 (ddd, $J = 10.1, 7.5, 1.6$ Hz, 1H), 8.13 (dd, $J = 7.5, 1.3$ Hz, 1H), 8.30 (ddd, $J = 10.4, 10.4, 2.0$ Hz, 1H), 8.35 (ddd, $J = 10.4, 10.4, 2.3$ Hz, 1H), 8.42 (dd, $J = 7.5, 1.6$ Hz, 1H), 8.65 (d, $J = 8.1$ Hz, 2H). Anal. Calcd for C₂₀H₁₄Br₂N₂PtS: C, 35.89; H, 2.11; N, 4.19; S, 4.79. Found: C, 36.12; H, 2.19; N, 4.07; S, 4.67.

(2,2'-Bipyridine)[2-(4-hexyl-5-bromothiényl)]phenylplatinum(II) (7dc).

^1H NMR (300 MHz, DMSO- d_6) δ 0.84 (t, J = 6.9 Hz, 3H), 1.27 (m, 6H), 1.51 (m, 2H), 2.41 (t, J = 7.8 Hz, 3H), 6.48 (s, $J(^{195}\text{Pt})$ = 49 Hz, 1H), 6.80 (m, 1H), 6.92 (m, 2H), 7.29 (m, $J(^{195}\text{Pt})$ = 62 Hz, 2H), 7.65 (ddd, J = 6.6, 6.5, 0.9 Hz, 1H), 7.73 (ddd, J = 6.6, 6.2, 1.2 Hz, 1H), 8.16 (dd, J = 5.1, 0.9 Hz, 1H), 8.32 (m, 2H), 8.42 (dd, J = 5.7, 0.9 Hz, 1H), 8.64 (d, J = 8.4 Hz, 2H); Anal. Calcd for $\text{C}_{26}\text{H}_{27}\text{BrN}_2\text{PtS}$: C, 46.29; H, 4.03; N, 4.15; S, 4.75. Found: C, 45.80; H, 3.83; N, 4.20; S, 4.63.

(2,2'-Bipyridine)[2-(5-bromothiényl)](4-methylphenyl)platinum(II) (7ea).

^1H NMR (500 MHz DMSO- d_6) δ 2.17 (s, 3H), 6.51 (d, J = 3.4 Hz, 1H), 6.75 (d, J = 7.5 Hz, 2H), 6.91 (d, J = 3.5 Hz, 1H), 7.16 (d, J = 7.9 Hz, 2H), 7.66 (ddd, J = 5.6, 5.7, 1.1 Hz, 1H), 7.74 (ddd, J = 5.5, 5.5, 1.0 Hz, 1H), 8.23 (dd, J = 5.6, 1.0 Hz, 1H), 8.29-8.34 (m, 2H), 8.44 (dd, J = 5.3, 0.9 Hz, 1H), 8.63 (d, J = 8.1 Hz, 2H); IR(KBr) 3040, 1691, 1602, 1468, 1445, 801, 758, 727 cm^{-1} ; Anal. Calcd for $\text{C}_{21}\text{H}_{17}\text{BrN}_2\text{PtS}$: C, 41.73; H, 2.83; N, 4.63; S, 5.31; Br, 13.22. Found: C, 41.53; H, 3.03; N, 4.52; S, 5.01; Br, 12.95.

(2,2'-Bipyridine)[2-(4,5-dibromothiényl)](4-methylphenyl)platinum(II) (7eb).

^1H NMR (500 MHz DMSO- d_6) δ 2.17 (s, 3H), 6.55 (s, 1H), 6.77 (d, J =

7.6 Hz, 2H), 7.15 (d, $J = 7.8$ Hz, 2H), 7.67 (ddd, $J = 5.6, 5.7, 1.2$ Hz, 1H), 7.78 (ddd, $J = 5.6, 5.6, 1.0$ Hz, 1H), 8.19 (dd, $J = 5.2, 1.2$ Hz, 1H), 8.30-8.36 (m, 2H), 8.43 (dd, $J = 5.4, 0.8$ Hz, 1H), 8.65 (d, $J = 8.2$ Hz, 2H); IR (KBr) 1483, 1467, 1445, 800, 759, 728 cm^{-1} ; Anal. Calcd for $\text{C}_{21}\text{H}_{16}\text{Br}_2\text{N}_2\text{PtS}$: C, 36.91; H, 2.36; N, 4.10; S, 4.69. Found: C, 36.15; H, 2.40; N, 3.96; S, 4.83.

(2,2'-Bipyridine)[2-(5-formylthienyl)](4-methylphenyl)platinum(II) (7ed).

^1H NMR (500 MHz $\text{DMSO-}d_6$) δ 2.16 (s, 3H), 6.76 (d, $J = 7.7$ Hz, 2H), 6.99 (d, $J = 3.7$ Hz, 1H), 7.18 (d, $J = 7.8$ Hz, 2H), 7.68-7.73 (m, 2H), 7.75 (d, $J = 3.7$ Hz, 1H), 8.20-8.24 (m, 2H), 8.33-8.35 (m, 2H), 8.66 (d, $J = 8.0$ Hz, 2H), 9.52 (s, 1H); IR(KBr) 1640, 1602, 1397, 1372, 759 cm^{-1} ; Anal. Calcd for $\text{C}_{22}\text{H}_{18}\text{N}_2\text{OPtS}$: C, 47.74; H, 3.28; N, 5.06; S, 5.79. Found: C, 47.12; H, 3.29; N, 4.95; S, 5.51.

(2,2'-Bipyridine)[2-(5-ethoxycarbonylthienyl)](4-methylphenyl)platinum(II) (7ee).

^1H NMR (500 MHz $\text{DMSO-}d_6$) δ 1.23 (t, $J = 7.0$ Hz, 3H), 2.16 (s, 3H), 4.15 (q, $J = 7.0$ Hz, 2H), 6.75 (d, $J = 7.6$ Hz, 2H), 6.83 (d, $J = 3.6$ Hz, 1H), 7.18 (d, $J = 7.7$ Hz, 2H), 7.61 (d, $J = 3.6$ Hz, 1H), 7.66-7.70 (m, 2H), 8.22 (dd, $J = 5.5, 0.9$ Hz, 1H), 8.27 (dd, $J = 5.4, 0.9$ Hz, 1H), 8.8.29-8.30 (m, 2H), 8.63 (d, $J = 8.1$ Hz, 2H); IR(KBr) 1640, 1602, 1397, 1372, 759 cm^{-1} ; Anal. Calcd for

$C_{24}H_{22}N_2O_2PtS$: C, 48.24; H, 3.71; N, 4.69; S, 5.37. Found: C, 48.02; H, 3.95; N, 4.59; S, 4.95.

(2,2'-Bipyridine)[2-(2-benzothieryl)](4-methylphenyl)platinum(II) (7ef).

1H NMR (500 MHz DMSO- d_6) δ 2.14 (s, 3H), 6.73 (d, $J = 7.4$ Hz, 2H), 6.93 (s, 1H), 6.96 (t, $J = 7.3$ Hz, 1H), 7.10 (t, $J = 7.3$ Hz, 1H), 7.23 (d, $J = 8.0$ Hz, 1H), 7.53 (d, $J = 7.9$ Hz, 1H), 7.63-7.70 (m, 3H), 8.29-8.35 (m, 3H), 8.38 (dd, $J = 5.5, 0.9$ Hz, 1H), 8.63-8.66 (m, 2H).

The reductive elimination of arylthiophene 5ea from aryl(thienyl)platinum complex 7ea.

To a schlenk tube were added aryl(thienyl)platinum complex **7ea** (18.1 mg, 0.03 mmol), triphenylphosphine (78.7 mg, 0.3 mmol) and toluene (4 mL). The resulting solution was heated at 95 °C for 1.5 h. After cooling to room temperature, the mixture was washed with water and brine. The organic layer was concentrated under reduced pressure to leave a crude solid, which was purified by column chromatography on silica gel to afford 4.2 mg of 2-bromo-5-(4-methylphenyl)thiophene (**5ea**) in 60% yield. Spectroscopic characteristics and physical properties of the product were identical to the authentic sample.¹⁹

General procedure for the synthesis of dithienylplatinum(II) complex.

To a mixture of [PtI₂(bpy)] (30.2 mg, 0.05 mmol), 2,3-dibromothiophene (**1b**, 0.027 mL, 0.24 mmol) and potassium fluoride (23.2 mg, 0.4 mmol) in 3 mL of DMSO was added AgNO₃ (68.0 mg, 0.4 mmol) in one portion under argon atmosphere. The resulting suspension was stirred at 50 °C for 5 h. After cooling to room temperature, the mixture was passed through a Celite pad, which was washed with dichloromethane repeatedly. The filtrate was washed with water twice. The organic layer was concentrated under reduced pressure to leave a crude solid, which was purified by recrystallization from dichloromethane/hexane to afford 27.8 mg of **8b** as an orange solid (70%). ¹H NMR (500 MHz, DMSO-*d*₆) δ 6.60 (s, 2H), 7.81 (t, *J* = 6.7 Hz, 2H), 8.33 (d, *J* = 4.6 Hz, 2H), 8.38 (ddd, *J* = 7.7, 7.8, 1.4 Hz, 2H), 8.68 (d, *J* = 8.2 Hz, 2H); IR(KBr) 1598, 1445, 1260, 979, 760, 417 cm⁻¹; Anal. Calcd for C₁₈H₁₀Br₄N₂PtS₂: C, 25.95; H, 1.21; Br, 38.36; N, 3.36; S, 7.70. Found: C, 25.74; H, 1.30; Br, 38.30; N, 3.33; S, 7.47.

(2,2'-Bipyridine){di[2-(5-bromothiényl)]}platinum(II) (8a).

¹H NMR (500 MHz, DMSO-*d*₆) δ 6.54 (d, *J* = 3.5, 2H), 6.98 (d, *J* = 3.4 Hz, 2H), 7.77 (ddd, *J* = 6.6, 6.7, 1.0 Hz, 2H), 8.34-8.37 (m, 4H), 8.67 (d, *J* = 7.9 Hz, 2H); IR(KBr) 1601, 1446, 1158, 969, 759, 614, 496, 418; HRMS(FAB)

Found: 672.8463, Calcd for $C_{18}H_{12}Br_2N_2PtS_2$: 672.8456.

(2,2'-Bipyridine){di[2-(5-formylthienyl)]}platinum(II) (8d).

1H NMR (500 MHz, DMSO- d_6) δ 7.04 (d, $J = 3.8$, 2H), 7.75 (ddd, $J = 6.5$, 7.0, 0.6 Hz, 2H), 7.82 (d, $J = 3.7$ Hz, 2H), 8.16 (dd, $J = 4.5$, 1.0 Hz, 2H), 8.38 (ddd, $J = 8.0$, 8.0, 1.0 Hz, 2H), 8.71 (d, $J = 8.5$ Hz, 2H), 9.57 (s, 2H)

IR(KBr) 1629, 1508, 1445, 1396, 1367, 1272, 1226, 1049, 816, 760, 740, 658,

HRMS(FAB) Found 574.0290, Calcd for $C_{20}H_{15}N_2O_2PtS_2$ (M+1): 574.0224.

(2,2'-Bipyridine){di[2-(4-methy-5-bromothieryl)]}platinum(II) (8g).

1H NMR (500 MHz, DMSO- d_6) δ 2.06 (s, 6H), 6.45 (s, 2H), 7.77 (m, 2H), 8.34-8.39 (m, 4H), 8.65 (d, $J = 8.1$ Hz, 2H); Anal. Calcd for $C_{20}H_{16}Br_2N_2PtS_2$: C, 34.15; H, 2.29; N, 3.98; S, 9.12. Found: C, 33.54; H, 2.43; N, 4.06; S, 9.08; HRMS (FAB) Found 703.8738, Calcd for $C_{20}H_{16}^{79}Br^{81}BrN_2S_2^{196}Pt$: 703.8743.

Crystal structure analysis of 7de.

Single crystals of **7de**, suitable for X-ray diffraction study were obtained by recrystallization from CH_2Cl_2 /hexane. Data for **7de** were collected on a Rigaku Saturn CCD diffractometer equipped with

monochromated Mo K α radiation ($\lambda = 0.71073 \text{ \AA}$). Calculations were carried out using the program package Crystal Structure, version 3.7, for Windows. A full-matrix least-squares refinement was used for the non-hydrogen atoms with anisotropic thermal parameters. **7de**: C₂₄H₂₂N₂O₂PtS, fw = 597.60, triclinic, space group *P1bar* (No. 2), $a = 10.0772(6) \text{ \AA}$, $b = 10.0956(5) \text{ \AA}$, $c = 12.8026(9) \text{ \AA}$, $\alpha = 66.951(5)^\circ$, $\beta = 73.933(5)^\circ$, $\gamma = 61.988(4)^\circ$, $V = 1051.2(1) \text{ \AA}^3$, $Z = 2$, $D_{\text{calcd}} = 1.888 \text{ g cm}^{-3}$, No. of unique reflections = 3729 ($I > 3\sigma(I)$), $R = 0.028$, $R_w = 0.036$. Crystallographic data reported in this manuscript have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-682142. Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk)

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Chapter III

Development of New Class of Reducing Agents for Single-phase Synthesis of Thiol-capped Gold Nanoparticle in Organic Solvent

Abstract: Synthesis of thiol-capped AuNP in organic solvent is carried out by using new reducing agents. The Addition of triethylsilane to solution of $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ and 1-dodecanethiol affords spherical thiol-capped gold nanoparticle. The treatment of alkyl organometallic reagents is also found to give gold nanoparticle

III-1 Introduction

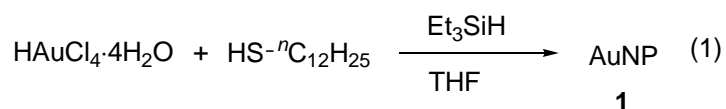
Gold nanoparticle (AuNP) has attracted considerable attention for applications to catalysis, nonlinear optical material and biological sensing due to its characteristic magnetic, electronic and optical properties.¹ Since size of the nanoparticle gives significant effect to its properties, development of synthetic methodologies for the preparation of AuNP with narrow dispersity becomes highly important. Brust-Schiffrin method,² which is the reaction of HAuCl_4 and alkanethiol with NaBH_4 in toluene/ultra-pure water in the presence of tetraoctylammonium bromide (TOAB) to form thiol-capped AuNP has been widely used in the synthesis of AuNP. A facile process that is capable of forming AuNP avoiding the use of TOAB which is sometimes difficult to remove in purification step and ultra-pure water is the single-phase synthesis of AuNP in organic solvent.

In this chapter, the Author describes the synthesis of thiol-capped AuNP in organic solvent by using silanes and alkyl organometallic reagents as a new class of reducing agent.

III-2 Preparation of alkanethiol-capped gold nanoparticle with triethylsilane as a mild and efficient reducing agent

To synthesize AuNP in organic solvent, a variety of reducing agents such as superhydride (LiBHET_3),³ LiBH_4 ,⁴ and amine-borane complex^{5,6} were reported. These reactions are carried out under anhydrous conditions since the hydride reacts vigorously with water and protocols generally employ large excess of the reducing agent. Organosilanes react with a variety of carbon-carbon and carbon-heteroatom unsaturated bonds through the addition of hydrogen and silicon atoms, namely hydrosilylation, and have been widely utilized in organic synthesis.⁷ As the silicon-hydrogen bond is less ionic and stable to water, hydrosilylation reactions have been carried out by transition metal catalysis.⁸ Several other functional groups are tolerable for the reaction with silane reagents, accordingly. In addition, organosilanes are less toxic and the use of which is thereby a potentially environmentally benign process. Preparation of AuNPs with organosilanes as a reducing agent, if successful, the protocol that is performed in an organic solvent under mild conditions is intriguing. The Author describe that triethylsilane is a highly effective reducing agent for the single-phase preparation of thiol-capped AuNPs in this section.

Synthesis of AuNP was carried out by the following procedure. A solution of $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ (0.1 mmol) and 1-dodecanethiol (0.1 mmol) in 10 mL of THF was vigorously stirred for 3 h at 25 °C. To the resulting yellow solution triethylsilane was added dropwise at 25 °C to form a purple solution immediately. After stirring for 6 h at 25 °C, ethanol was added to the solution to precipitate AuNP, which was centrifuged to isolate the thiol-capped AuNP (**1**, 15.1 mg) as dark brown powder (eq. 1). The obtained **1** was found to be dispersible to organic solvents such as THF or CHCl_3 suggesting that aggregation did not occur during the isolation procedure.



It should be pointed out that the preparation of AuNP performed with 1 molar amount of triethylsilane towards HAuCl_4 and alkanethiol represents high synthetic efficiency. The advantage would be caused by the characteristics of Et_3SiH that is unreactive towards water in HAuCl_4 and hydrogen chloride formed by the reduction of the gold species. Indeed, the reaction with an increased amount of Et_3SiH did not improve the yield of **1**

(Table 1). Since synthesis of AuNPs has been generally carried out with excess amounts of reducing agent, it is remarkable that the use of 1 equivalent of Et₃SiH can undergo the formation of AuNP. Worthy of note, in addition, is the AuNP preparation in an organic solvent as a single phase medium. According to Blackmond,⁹ the process to cause contamination of water by organic compounds, which may cause in the reaction with a water-organic solvent system, is environmentally unfriendly. Therefore, the preparation in THF with 1 equiv of less toxic Et₃SiH under mild conditions is an environmentally benign protocol.

Table 1. Synthesis of AuNP with triethylsilane^a

$$\text{HAuCl}_4 \cdot 4\text{H}_2\text{O} + \text{HS}-^n\text{C}_{12}\text{H}_{25} \xrightarrow[\text{THF}]{\text{Et}_3\text{SiH}} \text{AuNP } \mathbf{1}$$

Et ₃ SiH/eq.	yield/mg
1.5	15.1
2.0	16.1
10.0	15.7

^a Unless noted, the reaction was performed with dodecanethiol (0.1 mmol), HAuCl₄·4H₂O (0.1 mmol) and silane (0.1 mmol) with 10 mL of the solvent at 25 °C.

Characterization of obtained AuNP **1** was carried out by

measurements of TEM images, UV-vis spectra, and ^1H NMR analyses. Figure 1 shows the TEM image of the AuNP, which is spherical and exhibits an average diameter of 8.6 ± 0.65 nm indicating the formation of unaggregated and highly monodispersed AuNP. UV-vis spectrum of the AuNP was shown in Figure 2. The λ_{max} value of the UV-vis spectrum was observed at 528 nm, which is attributed to characteristic plasmon resonance absorption of AuNP.¹⁰ The ^1H NMR spectrum of AuNP as a solution of CDCl_3 exhibited triplet signal at δ 0.88 and broad signal at δ 1.26, respectively, which are assigned to CH_3 - and CH_2 - of dodecanethiol adsorped on the surface of AuNP.

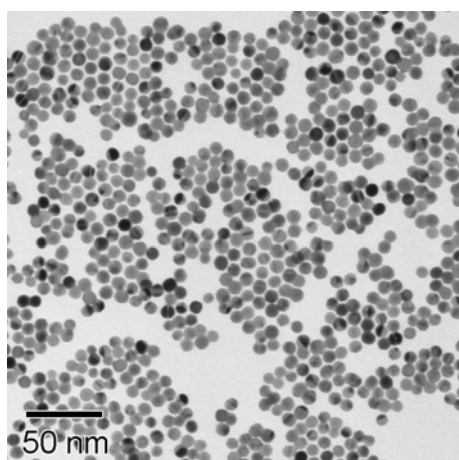


Figure 1. TEM image of thiol-capped AuNP 1.

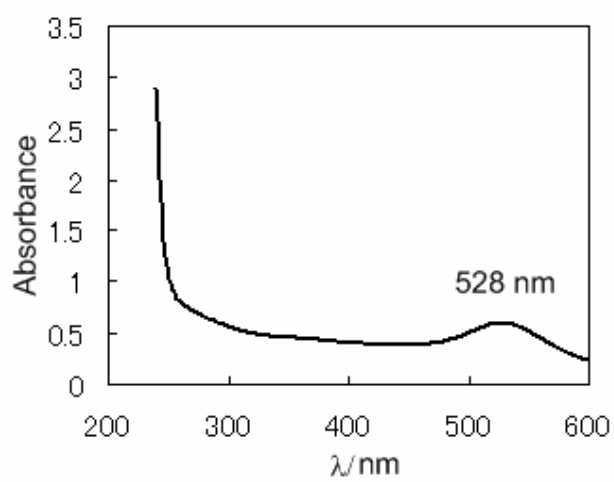


Figure 2. UV-vis spectrum of thiol-capped AuNP 1

Table 2 and Figure 3 summarize the results on the scope and limitation for the preparation of AuNP with Et₃SiH. It is highly important to stir the mixture of dodecanethiol and HAuCl₄ for longer than 3 h before addition of the reducing agent to prepare monodisperse AuNP. Stirring for a shorter period resulted in agglomeration of the nanoparticle, which was confirmed by TEM analyses. Although other organosilanes, diethoxy(methyl)silane and pentamethyldisiloxane were found to form purple solution immediately similar to Et₃SiH, nonspherical nanoparticles ranging in size from 6-60 nm were obtained. Treatment of tetramethyldisiloxane (HMe₂Si)₂O, and poly(methylhydrosiloxane) [PMHS: (HMeSiO)_n] were found to be ineffective to observe precipitation of insoluble flocculated product. Among several solvents examined, di-*n*-butyl ether (9.3±0.91 nm), cyclopentyl methyl ether (8.8±0.58 nm), *tert*-butyl methyl ether (9.5±0.84 nm) were found to form monodisperse nanoparticles, while other solvents such as diethyl ether, 1,4-dioxane, 1,2-dimethoxyethane (DME) and methoxybenzene did not afford monodisperse nanoparticle probably due to the inferior solubility of Au thiolate generated by HAuCl₄·4H₂O and dodecanethiol. Other organic solvents such as chloroform,

acetone and acetonitrile were found to be ineffective.

Table 2. Formation of AuNP with a silane reagent^a

$$\text{HAuCl}_4 \cdot 4\text{H}_2\text{O} + \text{HS}-^n\text{C}_{12}\text{H}_{25} \xrightarrow[\text{solvent}]{\text{silane}} \text{AuNP } 1$$

silane	solvent	yield/mg	size/nm
Et ₃ SiH	THF	15.1	8.6±0.65
HSiMe(OEt) ₂	THF	8.9	- ^b
HMe ₂ SiOSiMe ₃		18.0	- ^b
(HMe ₂ Si) ₂ O		- ^c	-
(HMeSiO) _n		- ^c	-
Et ₃ SiH	ⁿ Bu ₂ O	13.2	9.3±0.91
	CPME ^d	14.6	8.8±0.58
	^t BuOCH ₃	8.9	9.5±0.84
	Et ₂ O	- ^e	-
	1,4-dioxane	- ^e	-
	DME	- ^e	-
	PhOCH ₃	- ^e	-

^a Unless noted, the reaction was performed with dodecanethiol (0.1 mmol), HAuCl₄·4H₂O (0.1 mmol) and silane (0.1 mmol) with 10 mL of the solvent at 25 °C. ^b nonspherical nanoparticles ranging in size from 6-60 nm formed. ^c Insoluble precipitate formed. ^d Cyclopentyl methyl ether. ^e Precipitation formed during the reaction of HAuCl₄ with thiol.

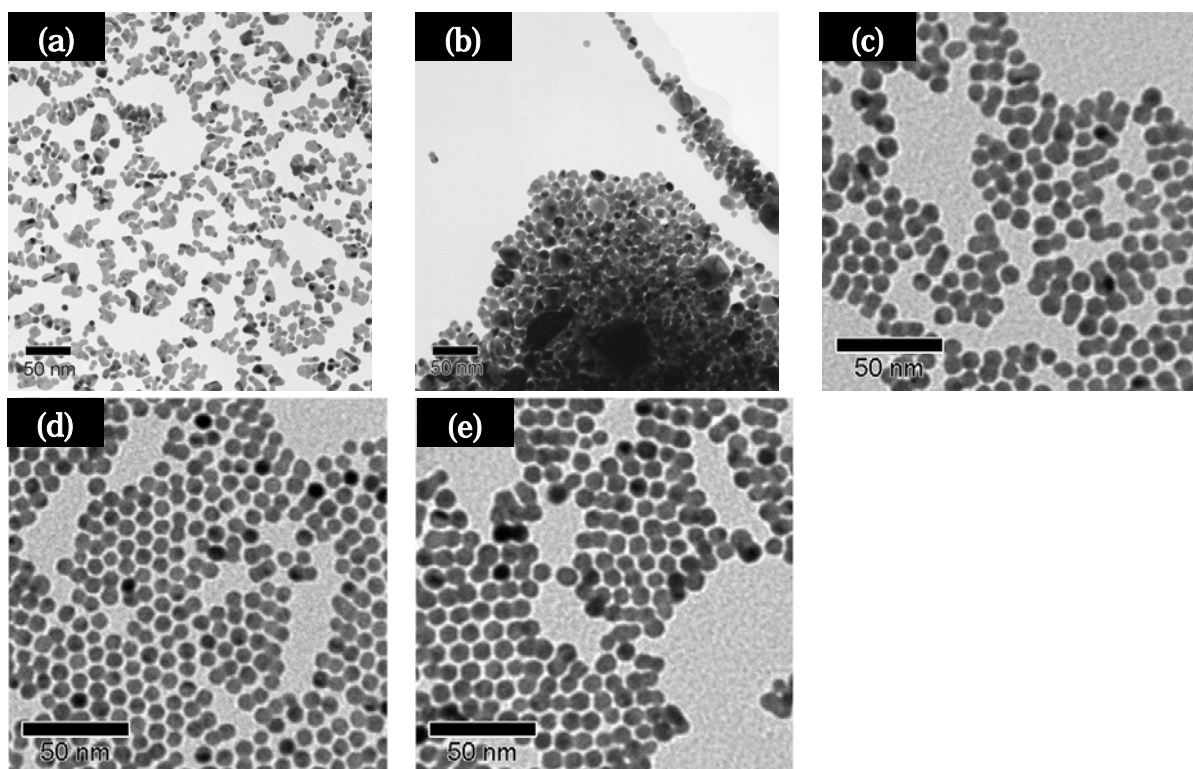


Figure 3. TEM images of the AuNP synthesized (a) by $\text{HMe}_2\text{SiOSiMe}_3$, (b) by $\text{HSiMe}(\text{OEt})_2$ (c) in Bu_2O (d) in CPME (e) in $t\text{BuOCH}_3$

The size of AuNP was found to be dependent on the reaction temperature. The addition of triethylsilane to a THF solution of $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ and dodecanethiol at $0\text{ }^\circ\text{C}$ afforded 9.3 mg of $7.5 \pm 0.57\text{ nm}$ nanoparticles after stirring for 24 h. On the other hand, the reaction at $50\text{ }^\circ\text{C}$ furnished 17.3 mg of $10 \pm 0.90\text{ nm}$ nanoparticles within 3 h (Figure 4a, b). In contrast to the single-phase method using superhydride or LiBH_4 which was a stronger reducing agent, afforded AuNP in the range of 2-4 nm,^{3,4} the use of triethylsilane produced AuNP of larger size, 7-10 nm.

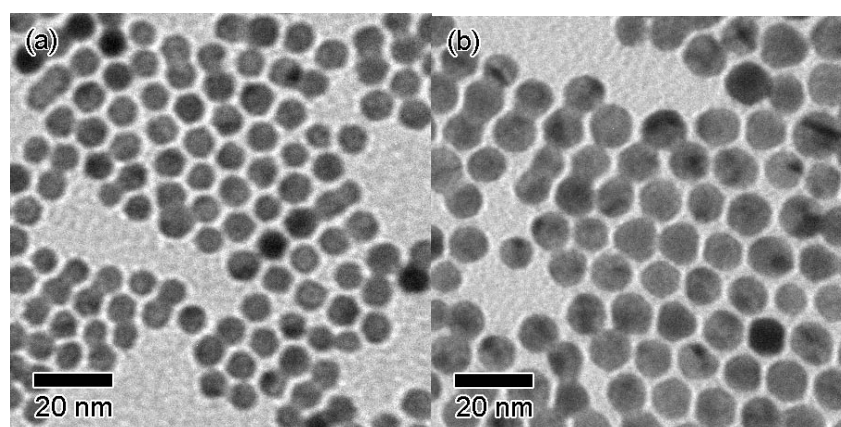


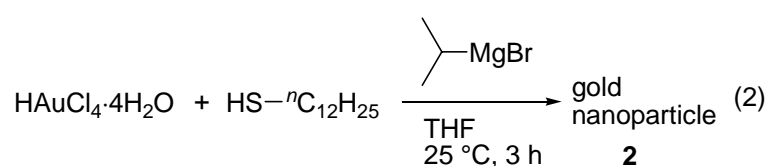
Figure 4. (a) TEM image of the AuNP synthesized at 0 °C (7.5 ± 0.57 nm). (b) TEM image of AuNP synthesized at 50 °C (10 ± 0.9 nm).

III-3 Synthesis of thiol-capped gold nanoparticles with organometallic reagents as a new class of reducing agent

As shown in the previous section, a variety of metal hydrides such as superhydride (LiBHET_3),³ LiBH_4 ,⁴ and borane-amine complex,⁵ are used in the synthesis of AuNPs in organic solvent. However, little has been studied on the synthesis of AuNP using organometallic reagents which bear a metal-carbon bond. In this section, the Author describes that alkyl organometallic reagent serves as a reducing agent for the synthesis of thiol-capped AuNPs.

The Author first examined the reaction with 2-propylmagnesium bromide, which is a Grignard reagent widely used in organic synthesis.¹¹ Preparation of AuNP was carried out as follows: A solution of $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ (0.1 mmol) and 1-dodecanethiol (0.1 mmol) in 10 mL of THF was vigorously stirred for 3 h at 25 °C under a nitrogen atmosphere. To the resulting solution, excess THF solution (0.78 M) of 2-propylmagnesium bromide (1.0 mmol, 1.28 mL) was added dropwise over a period of 30 s at 25 °C. The color of the solution turned yellow to dark purple which indicates characteristic surface plasmon resonance of AuNP.¹⁰ After stirring for 3 h at 25 °C, ethanol was added to the solution to precipitate AuNP, which was centrifuged to

isolate the thiol-capped AuNP (**2**, 18.3 mg) as a dark brown powder (eq. 2). The obtained **2** was found to be dispersible in organic solvents such as THF or CHCl₃ suggesting that aggregation did not occur during the isolation procedure.



TEM image of the obtained AuNP shows that nanoparticles are spherical with an average diameter of 5.5 ± 0.61 nm (Figure 5). The ¹H NMR spectrum of AuNP exhibited signals assigned as CH₃- and -CH₂- of dodecanethiol, indicating that the 2-propyl group of the Grignard reagent was not incorporated into the capping agent of AuNP.

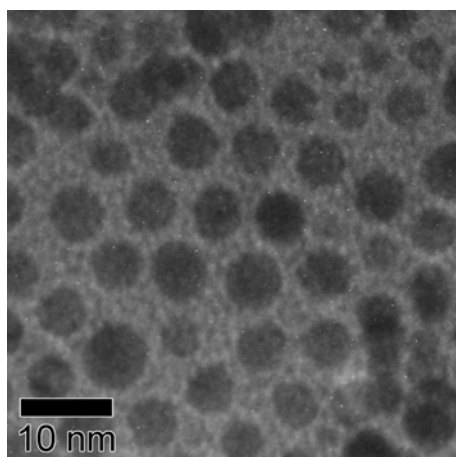


Figure 5. TEM image of gold nanoparticle **2**

Preparation of the AuNP with several kinds of Grignard reagents was examined in a similar manner. The results are summarized in Table 3. It was found that the formation of the AuNP was dependent on the reaction temperature. No nanoparticle was obtained when 2-propylmagnesium bromide was added at 0 °C. The reaction at 10 °C afforded purple solution suggesting the nanoparticle formation, however, the obtained solid was not completely dispersible in organic solvents resulting in partial aggregation of the nanoparticles. Though the reaction at 40 °C gave nanoparticle of a smaller particle, dispersity was found to be inferior to that prepared at 25 °C. Treatment with *tert*-butylmagnesium chloride, which is a more sterically hindered reagent than 2-propylmagnesium bromide, similarly afforded

particles of 8.1 ± 0.78 nm. The reaction with sterically less hindered Grignard reagent such as ethylmagnesium chloride also proceeded to give nanoparticles with an average diameter of 3.9 ± 0.8 nm (Figure 6). However, no particles were obtained when phenylmagnesium bromide and methylmagnesium iodide were employed. The nanoparticle size obtained was found to be similar to the case with metal hydrides such as sodium borohydride, superhydride, and borane-amine complex, etc.

It is well known that alkyl Grignard reagents release the hydrogen atom at the β -position to the metal, which serves as a surrogate reagent of metal hydride, and have been employed as a reducing agent for carbonyl and related compounds in organic synthesis.¹¹ Accordingly, the Author considers that several Grignard reagents also serve as a reducing agent in the gold nanoparticle synthesis. Indeed, the attempted nanoparticle synthesis with MeMgX or PhMgX, which did not possess a β -hydrogen atom, resulted in no reaction.

Table 3. Synthesis of Au nanoparticles with 2-propylmagnesium bromide^a

$$\text{HAuCl}_4 \cdot 4\text{H}_2\text{O} + \text{HS}-{}^n\text{C}_{12}\text{H}_{25} \xrightarrow[\text{THF, 25 }^\circ\text{C, time}]{\text{R-MgX}} \text{AuNP}$$

RMgX	temp./°C	time/h	yield/mg	size/nm
^t PrMgBr	0	4	0	-
	10	10	19.0	- ^b
	25	3	18.3	5.5±0.61
	40	6	18.2	3.0±0.59
^t BuMgCl	25	6	12.6	8.1±0.78
CH ₃ CH ₂ MgBr	25	6	18.1	3.9±0.80
PhMgBr	25	3	0	-
CH ₃ MgI	25	3	0	-

^a The reaction was carried out with H₂AuCl₄·4H₂O (0.1 mmol), 1-dodecanethiol (0.1 mmol) and THF solution of a Grignard reagent (1.0 mmol) in 10 mL of THF. ^b Partial aggregation of the nanoparticle.

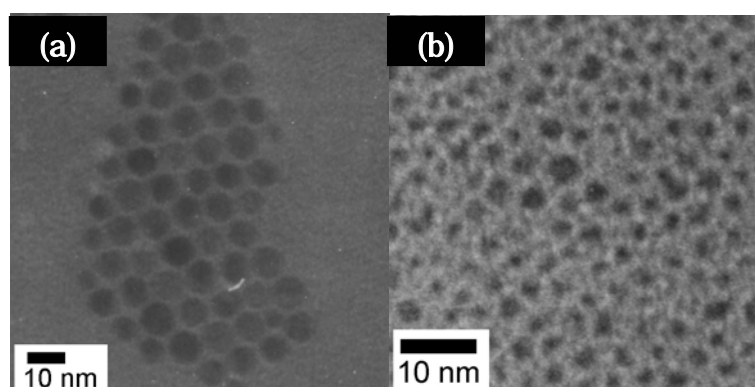


Figure 6. TEM images of the AuNP synthesized by treatment of (a) ^tBuMgCl and (b) EtMgBr

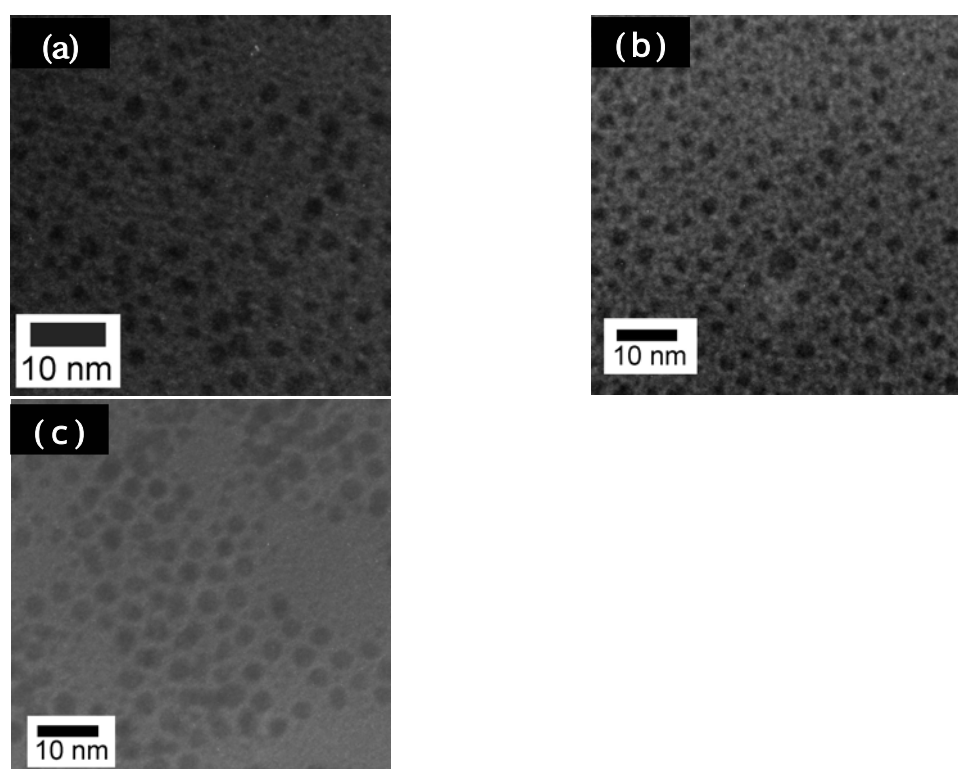
Encouraged by the results of Grignard reagents, the Author examined the synthesis of thiol-capped AuNP with other main group alkyl organometallic reagents as shown in Table 4 and Figure 7. The reaction of *n*-butyllithium afforded nanoparticles in a reasonable yield and the particle size was found to be 2.9 ± 0.40 nm. Treatment of diethylzinc and triisobutylaluminum also gave AuNPs, although removal of the metal residue by filtration was required during the isolation. On the other hand, addition of ethylaluminum dichloride, which is recognized as a class of Lewis acid, was found to be ineffective.

Table 4. Synthesis of Au nanoparticle with various organometallic reagents^a

$$\text{HAuCl}_4 \cdot 4\text{H}_2\text{O} + \text{HS-}^n\text{C}_{12}\text{H}_{25} \xrightarrow[\text{THF, temp., 3 h}]{\text{organometallic reagents}} \text{AuNP}$$

organometallic reagent	temp./°C	yield/mg	size/nm
<i>n</i> BuLi	-78 to 25	16.6	2.9±0.40
Et ₂ Zn	25	6.8	2.4±0.36
<i>t</i> Bu ₃ Al	25	8.3	4.9±0.67
EtAlCl ₂	0	0	-

^a The reaction was carried out with HAuCl₄·4H₂O (0.1 mmol) with 1-dodecanethiol (0.1 mmol) and hexane solution of organometallic reagent (1.0 mmol) in 10 mL of THF for 3 h.

**Figure 7.** TEM images of the AuNP prepared by (a) *n*BuLi, (b) Et₂Zn, (c) *t*Bu₃Al

III-4 Conclusion

In summary, gold nanoparticles were found to be generated by the reaction of dodecanethiol and HAuCl_4 in the presence of triethylsilane as a new class of reducing agent. The formed AuNPs exhibited 7-10 nm of spherical particle with high monodispersity. Since the nanoparticle was prepared with 1 equivalent of organosilane in an organic solvent as a single phase, the protocol is highly efficient and environmentally benign process. The synthesis of thiol-capped AuNP is also carried out with the treatment of alkyl organometallic reagents such as Grignard reagent, organolithium, -zinc, and -aluminum reagents. Since these organometallic reagents are ubiquitous reagent in organic synthesis that is readily available in laboratory scale, synthesis of AuNP with alkyl organometallic reagent is available as a facile method.

III-5 Experimental

III-5-1 General

^1H NMR (500 MHz) spectrum was measured in CDCl_3 at 25 °C on a Bruker Avance 500 spectrometer. Transition electron microscopic (TEM) observations were performed by using JEM-1200EX II, JEM-1230 BU, and Hitachi H-7100TE with an acceleration voltage of 120, 100, and 100 kV, respectively. TEM samples were prepared by dropping of the CHCl_3 solution of gold nanoparticle (AuNP) on 150 mesh carbon coated copper grids, which were purchased from Okensyoji. UV-vis spectrum was measured in CHCl_3 at 25 °C on a Hitachi U3310 spectrometer. Chloroauric acid tetrahydrate was purchased from Tanaka Kikinzoku Kogyo. Triethylsilane was purchased from Shin-Etsu Chemicals. THF was purchased from Sigma-Aldrich Co. Ltd. as an anhydrous grade and stored in a Schlenk tube under nitrogen atmosphere. THF solution of 2-propylmagnesium bromide, *tert*-butylmagnesium chloride, ethylmagnesium chloride and phenylmagnesium bromide were purchased from Kanto Chemical Co. Ltd. Other chemicals were purchased and used as such.

III-5-2 Preparation of alkanethiol-capped gold nanoparticle with triethylsilane as a mild and efficient reducing agent

General procedure for thiol-capped AuNP 1

To a screw-capped test tube equipped with a magnetic stirring bar were added $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ (0.1 mmol, 41.2 mg), 1-dodecanethiol (0.1 mmol, 23.9 μL) and THF (10 mL). Resulting mixture was vigorously stirred for 3 h at 25 °C to form a yellow solution. Triethylsilane (0.1 mmol, 15.9 μL) was then added dropwise at 25 °C to form immediately a purple solution. After stirring for further 6 h at 25 °C, ethanol was added to the solution to precipitate the AuNP, which was separated by centrifuge, washed with ethanol and dried under reduced pressure to afford 15.1 mg of 1. $^1\text{H NMR}$ δ 0.88 (t, $J = 6.6$ Hz, CH_3), 1.26 (broad, CH_2). UV-vis (CHCl_3) $\lambda_{\text{max}} = 528$ nm. The spectroscopic properties were identical with those of authentic sample (see reference 4 and 5).

III-5-3 Synthesis of thiol-capped gold nanoparticles with organometallic reagents as a new class of reducing agent

General procedure for synthesis of thiol-capped AuNP 2

To a 25 mL of Schlenk tube equipped with a magnetic stirring bar were added $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ (0.1 mmol, 41.2 mg), 1-dodecanethiol (0.1 mmol,

23.9 μL) and THF (10 mL) under N_2 atmosphere. Resulting mixture was vigorously stirred for 3 h at room temperature to form yellow solution. THF solution of 2-propylmagnesium bromide (0.78 M, 1.0 mmol, 1.28 mL) was then added dropwise over a period of 30 s at 25 $^\circ\text{C}$ to form a dark purple solution. After stirring for 3 h at 25 $^\circ\text{C}$, ethanol was added to the solution to precipitate AuNP, which was separated by centrifuge, washed with ethanol and dried under reduced pressure to afford 18.1 mg of AuNP.

III-6 References

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Chapter IV

Extension of Synthetic Versatility of Gold Nanoparticle

Abstract: Synthesis of gold nanoparticle is carried out by reduction of gold(I) thiolate tri-*n*-butylphosphine complex that is highly soluble to various organic solvents. Direct generation of thiol-capped AuNPs with THP-protected thiols without deprotection is also examined to develop the method for facile functionalization of thiols and following formation of AuNP.

IV-1 Introduction

As increasing the significance of gold nanoparticles (AuNPs) as advanced materials, catalyst, and biological sensors,¹ diversity of available solvent which can dissolve a gold salt, a capping reagent, and the obtained AuNP becomes important. However, the solubility of HAuCl_4 , which is one of the most popular gold salts for the synthesis of AuNP, in organic solvents is limited.

Furthermore, for the synthesis of highly-functionalized AuNPs, synthetic design and preparation of the capping thiol reagent is required. Therefore, development of efficient synthetic methodologies for the introduction of appropriate functionality onto the thiol is an important issue.

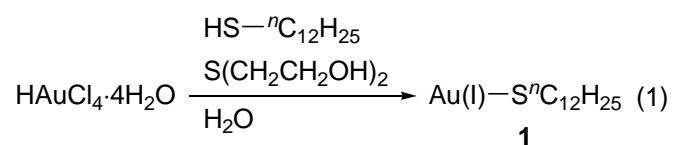
In this chapter, the synthesis of thiol-capped AuNP is carried out in a wide range of organic solvent by reduction of the tributylphosphine complex of gold(I) thiolate. Direct generation of thiol-capped AuNPs with THP-protected thiols without deprotection is also examined to develop the method for facile functionalization of thiols and following formation of AuNP.

IV-2 Reduction of gold(I) thiolate with a silane reagent in a wide range of organic solvent leading to gold nanoparticles

In Chapter III-2, the Author showed that alkanethiol-capped gold nanoparticle can be synthesized with triethylsilane as a new class of reducing agent in the single-phase system of an organic solvent to afford spherical and monodisperse gold nanoparticle. The synthesis was performed in an ethereal organic solvent such as tetrahydrofuran, di-*n*-butyl ether, and cyclopentyl methyl ether, while other solvents were found to be ineffective. Limitation of the available solvent is still a problem toward the practical protocol. The major drawback of the synthesis is due to the insufficient solubility of starting HAuCl_4 in a variety of organic solvent. Formation of gold nanoparticle with HAuCl_4 is generally considered through the in-situ formed intermediate gold(I) thiolate by the reaction of an alkanethiol and following reduction of thus formed thiolate leads to the nanoparticle.² The Author envisaged that synthesis of gold nanoparticle starting from the gold(I) thiolate, which would simplify the reaction pathway, can be a solution for the difficulties on the limitation of the available organic solvent. However, gold(I) thiolate is highly difficult to be dissolved in the solvent.³ Thus, solubilization of the gold(I) thiolate and following reduction to gold

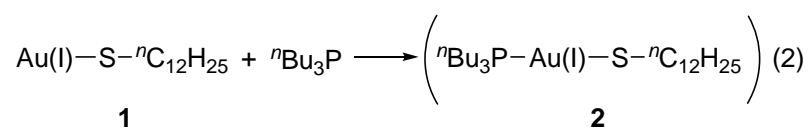
nanoparticle, if successful, would be intriguing.⁴ Herein, the Author reports that an appropriate additive makes gold(I) thiolate soluble in organic solvents and treatment of a silane reagent leads to gold nanoparticle.

Synthesis of gold(I) thiolate of dodecanethiol was performed by the reaction of equimolar amounts of $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ and $n\text{-C}_{12}\text{H}_{25}\text{SH}$ in the presence of 2,2'-thiodiethanol as shown in eq 1 to afford $n\text{-C}_{12}\text{H}_{25}\text{SAu(I)}$ **1** in a quantitative yield.³



However, it was found that the thiolate formed was hardly soluble in an organic solvent as well as water. Further treatment of the thiolate with a reducing agent was subsequently unsuccessful to recover the thiolate. Several additives such as pyridine, triethylamine, triphenylphosphine and tri(*o*-tolyl)phosphine were then examined to dissolve **1** in an organic solvent, hexane, toluene, THF, or chloroform to result in unsuccessful. Among additives, treatment of gold(I) thiolate **1** with tri-*n*-butylphosphine, which

would form phosphine complex of the thiolate **2**, was found to afford a clear solution of the complex (eq. 2). It should be pointed out the complex of gold(I) dodecanethiolate with $n\text{Bu}_3\text{P}$ was found to be soluble in hexane.



The soluble thiolate complex **2** was subjected to the reduction with triethylsilane. Treatment of a hexane solution of **2** with Et_3SiH at room temperature resulted that little color change was observed from colorless clear to purple, which is attributed to the characteristic surface plasmon resonance of AuNP.⁵ The findings show insufficient reactivity of the tertiary alkylsilane reagent toward the thiolate that is stabilized by the formation of Au-phosphine complex. Accordingly, other silane reagents showing higher activity as a reducing agent were examined. The Author found that a primary silane reagent, PhSiH_3 reduced the thiolate phosphine complex smoothly to result in immediate color change to dark purple at room temperature.

It was also found that a solution obtained by the addition of $n\text{Bu}_3\text{P}$ to

a suspension of gold(I) thiolate in hexane similarly afforded the gold nanoparticle. To a suspension of **1** (0.1 mmol) in hexane (5 mL) was added $n\text{Bu}_3\text{P}$ (0.15 mmol) to form a clear solution by stirring at room temperature for 0.5 h. To a resulting solution was added PhSiH_3 (0.04 mmol) dropwise. The color of the solution turned from colorless clear to dark purple immediately. After stirring at room temperature for 2 h, the solution was concentrated under reduced pressure. Following addition of ethanol formed precipitation, which was separated by continuous centrifuge and decantation procedures to afford 16.0 mg of gold nanoparticle as a dark brown solid. The obtained solid was soluble in chloroform, toluene, and THF.

UV-vis spectrum of the chloroform solution exhibited the plasmon band at 520 nm. (Figure 1a) TEM analysis exhibited a spherical particle (5.0 ± 0.66 nm) was shown to be formed (Figure 1b). The size of the gold nanoparticle was found to be smaller than that formed by the reaction of HAuCl_4 and $n\text{C}_{12}\text{H}_{25}\text{SH}$ with triethylsilane in THF suggesting that faster reduction took place with PhSiH_3 . Measurement of ^{31}P NMR spectrum of the nanoparticle exhibited no signals indicating that no tri-*n*-butylphosphine was incorporated on the surface of the nanoparticle.

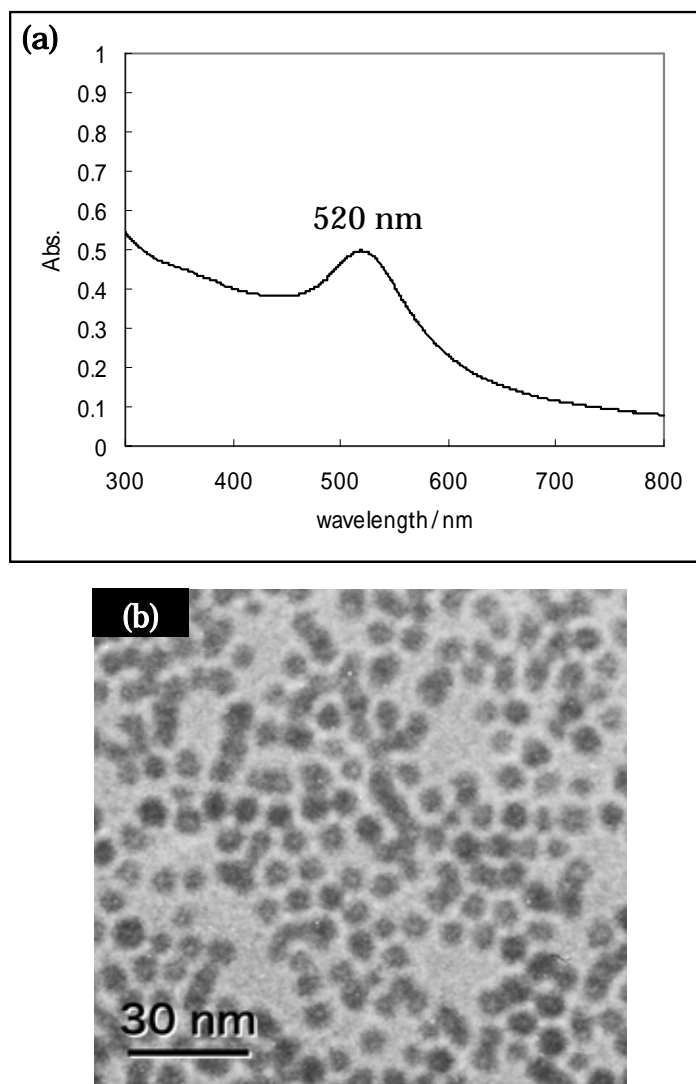
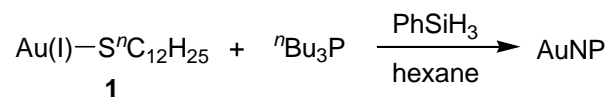


Figure 1. (a) UV-vis spectrum of the AuNP (b) TEM image of the AuNP

Preparation of the AuNP was carried out under various conditions. The results are summarized in Table 1 and Figure 2. It was found that the reaction temperature gave significant effect on the formation of the AuNP. The addition of PhSiH₃ at 5 °C afforded 2.7±0.38 nm nanoparticle. However, aggregation of the nanoparticle was observed when PhSiH₃ was added at 50 °C. The effect of gold(I) thiolate concentration toward the formation of AuNP was then examined. The reaction carried out with 1 mL of hexane to afford 12.7 mg of 6.4±0.66 nm nanoparticle. Slight improvement of the yield and the monodispersity was observed when the reaction was carried out with 10 mL of hexane (19.6 mg, 6.4±0.49).

Table 1. Preparation of the AuNP under various conditions^a

hexane/mL	temp./°C	time	yield/mg	size/nm
5	25	2 h	16.0	5.0±0.66
5	5	2 h	11.9	2.7±0.38
5	50	2 h	27.2	.. ^b
1	25	2 h	12.7	6.4±0.66
10	25	2 h	19.6	6.6±0.49

^a Unless specified, the reaction was carried out with 0.1 mmol of **1**, 0.15 mmol of ⁿBu₃P, and 0.04 mmol of PhSiH₃ in hexane. ^b Aggregation of the nanoparticle.

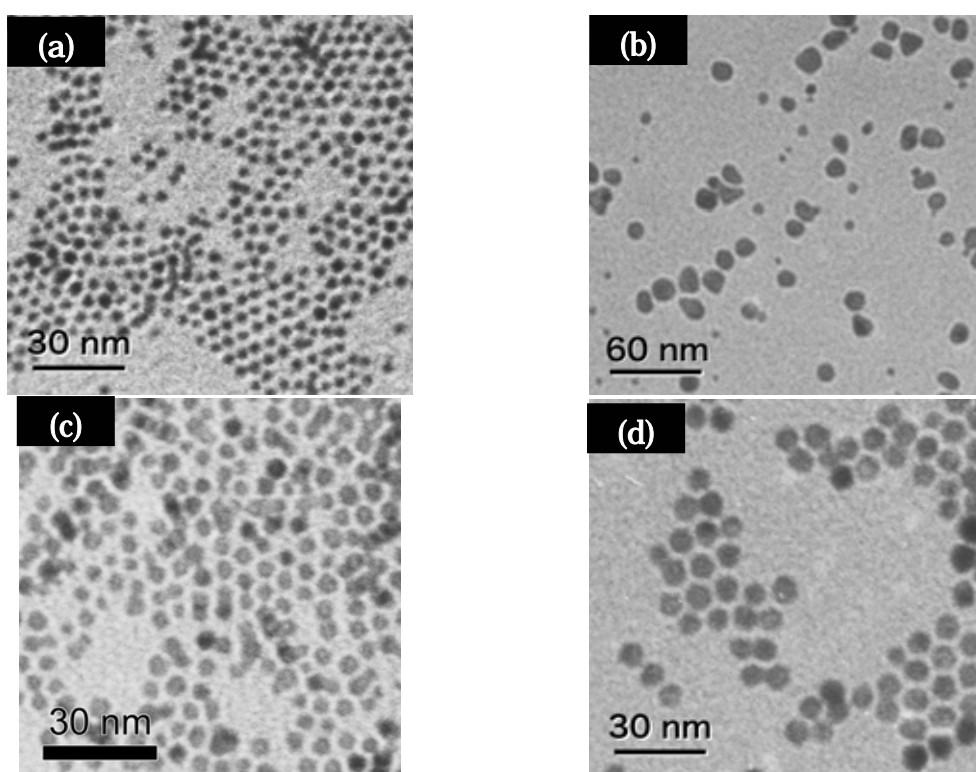
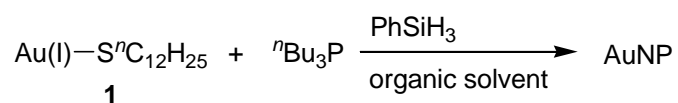


Figure 2. TEM images of the AuNP synthesized (a) at 5 °C, (b) at 50 °C, (c) with 1 mL of hexane, (d) with 10 mL of hexane

As shown in Table 2 and Figure 3, synthesis of AuNP with several kinds of solvents was then carried out in a similar manner. The reaction with THF afforded 6.8 ± 7.0 nm nanoparticle. When the reaction was carried out with toluene, to which HAuCl_4 is insoluble, 0.1 mmol of PhSiH_3 was necessary to obtain dark-purple solution of the AuNP. Although the reaction performed at $25\text{ }^\circ\text{C}$ gave purple solution, obtained solid was not dispersible to organic solvents. On the other hand, preparation of the nanoparticle (5.4 ± 0.57 nm) was successful when the reaction was carried out at $0\text{ }^\circ\text{C}$. Similarly, the synthesis of the AuNP with Et_2O , which is an ineffective solvent in the synthesis of the AuNP with triethylsilane, was successful at $0\text{ }^\circ\text{C}$ (4.6 ± 0.26 nm) though no particle was obtained at $25\text{ }^\circ\text{C}$.

Table 2. Synthesis of the AuNP in various organic solvents^a

solvent	PhSiH ₃ /mmol	temp./°C	time/h	yield/mg	size/nm
THF	0.04	25	1	10.8	6.8±0.70
toluene	0.1	25	2	16.6	-
		0	2	8.5	5.4±0.57
Et ₂ O	0.04	25	2	-	-
		0	5	7.9	4.6±0.26

^a Unless specified, the reaction was carried out with 0.1 mmol of **1**, 0.15 mmol of ⁿBu₃P and PhSiH₃ in 10 mL of organic solvent.

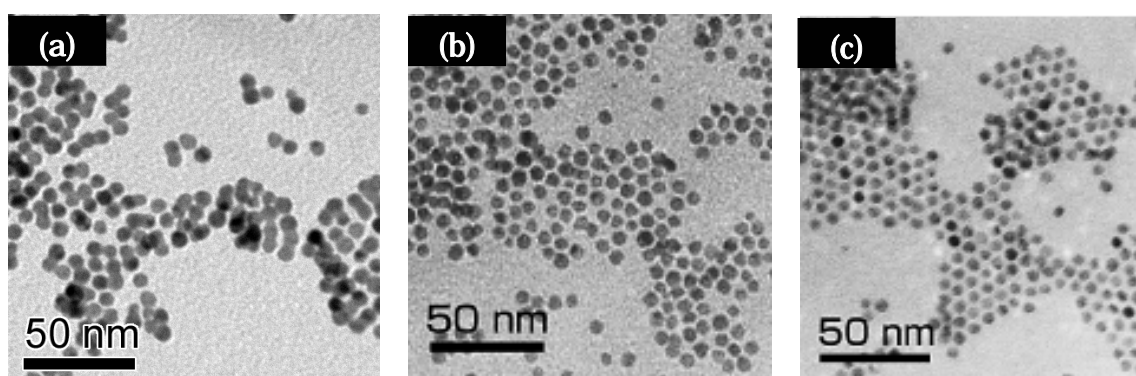


Figure 3. TEM images of the AuNP synthesized in (a) THF, (b) toluene, (c) Et₂O

Tri-*n*-butylphosphine complex of gold(I) thiolate was also subjected to the reduction by other reducing agent. The addition of 20 eq of superhydride ($\text{Et}_3\text{BHLi/THF}$) to THF solution of **1** and tri-*n*-butylphosphine afforded 15.0 mg of spherical gold nanoparticle with an average diameter of 3.4 ± 1.5 nm (eq. 3) TEM image of the AuNP is shown in Figure 4.

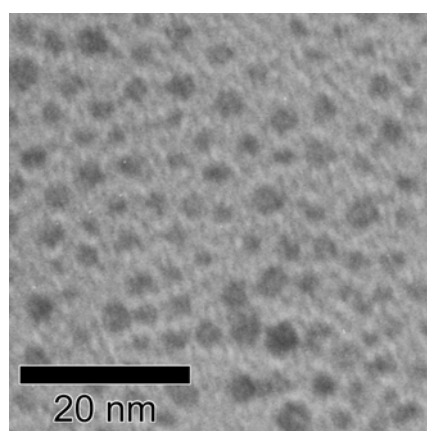
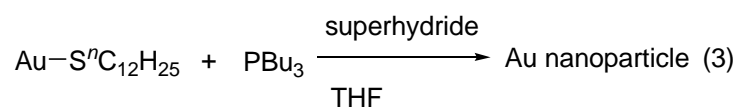


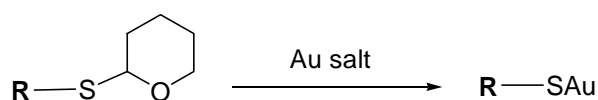
Figure 4. TEM image of the AuNP prepared by superhydride

IV-3 Generation of gold nanoparticles via direct thiol-capping with THP-protected thiols without deprotection

For the introduction of functional groups to thiols, substitution and/or addition reactions on the thiol molecules are methods of choice. Since the SH group of thiol might participate in undesired side reactions, use of an appropriate protective group for thiol becomes important.

An acyl group is a method of choice as protection of thiol. However, thioacetate thus formed easily hydrolyzes under aqueous conditions.⁶ The use of thioacetate as a protective group limits available synthetic reactions, accordingly. On the other hand, the tetrahydropyranyl (THP) group⁶ 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 THP protective group for designed gold nanoparticles is intriguing, if protection/deprotection of STHP

is controllable. During the course of our separate studies on the preparation of a molecule bearing a thiol moiety, the Author's group has 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 1.⁷



Scheme 1

Encouraged by this result, the Author 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,⁸ S-alkylthiosulfonate (Bunte salts)⁹ and alkyl-thiocyanate,¹⁰ THP thioethers would be much more tolerable for a variety of organic reactions. The Author reports 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 **3** 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 **3** in a good yield as reported.⁶ The obtained **3** (0.1 mmol) was treated with H₂AuCl₄·4H₂O (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 **3** 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 by measurement of the ¹H NMR spectrum of the tri-*n*-butylphosphine complex, which was similar to that synthesized with C₁₂H₂₅SH (Figure 5). Triethylsilane was then added dropwise at 25 °C to the solution to observe color change to purple immediately. After stirring for 6 h at 25 °C, AuNP precipitated by addition of ethanol and centrifuged to isolate 17.0 mg of AuNP **4** as a dark brown powder (Scheme 2). Since the Author has shown that Et₃SiH serves as a new class of reducing agent for the synthesis of AuNP from H₂AuCl₄ and CH₃(CH₂)₁₁SH, the addition of triethylsilane would reduce the gold thiolate

that is formed by the reaction of THP thioether **3** and HAuCl_4 .

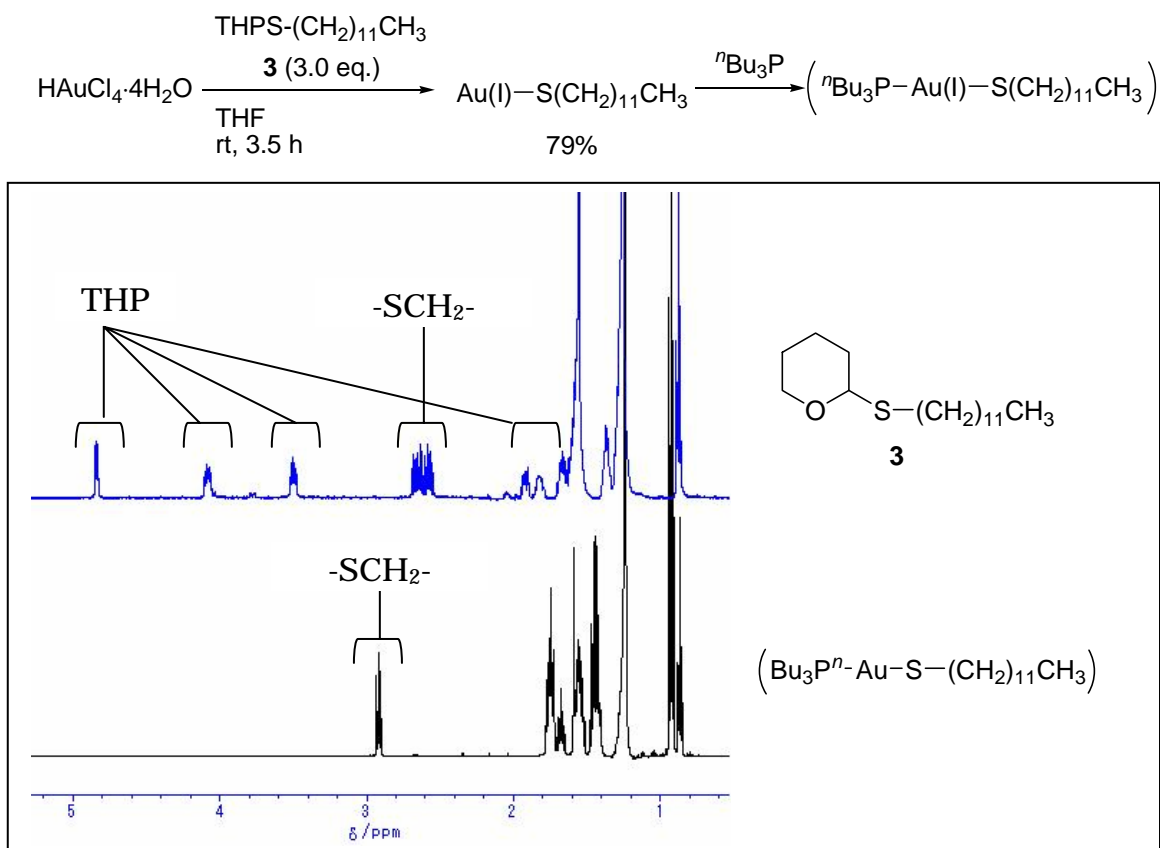
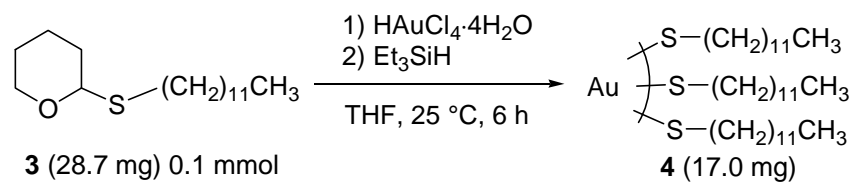


Figure 5 ^1H NMR (CDCl_3) spectra of (a) THP-thioether **3** and (b) Tri-*n*-butylphosphine complex of Au thiolate prepared from **3**



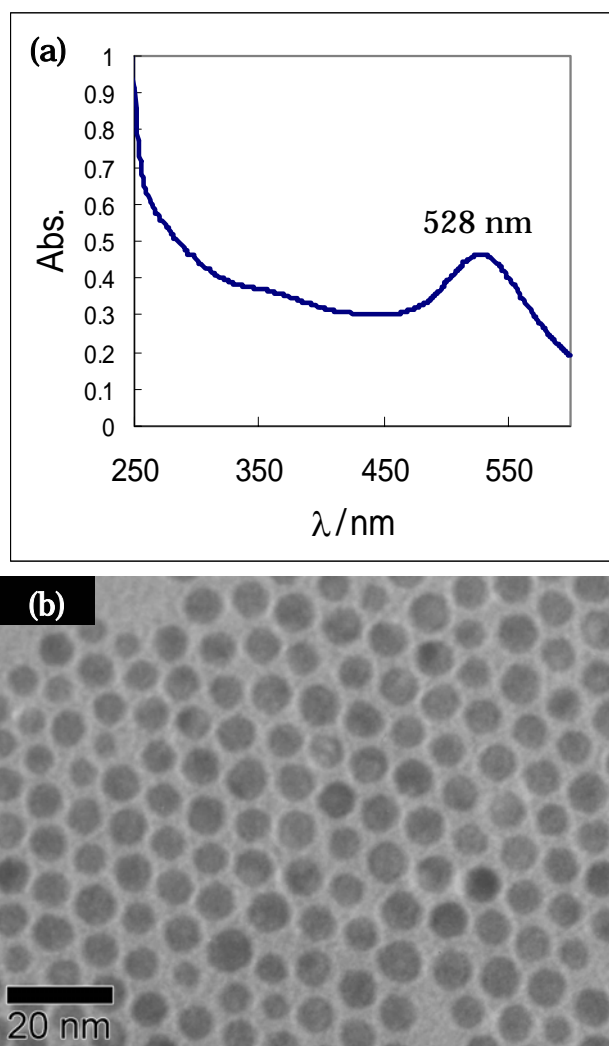
Scheme 2

The obtained AuNP **4** was subjected to the measurements of TEM and UV-vis spectrum analyses. The λ_{\max} value of the UV-vis spectrum was observed at 528 nm, which is attributed to the characteristic plasmon resonance absorption of AuNP.⁵ Figure 6 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 **4** by the reaction of THP thioether **3** was found to be similar to that from $\text{CH}_3(\text{CH}_2)_{11}\text{SH}$ as summarized in Table 3. TG analysis of **4** indicated its weight loss of ca. 10%, which markedly contrasted to that obtained by the reduction with NaBH_4 ¹¹ or LiBH_4 ¹² (ca. 25%), 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 on gold cluster of a larger size. These results suggest that AuNP bearing a smaller 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.

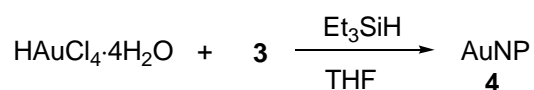
Table 3. Characteristics of AuNP^a

capping reagent	yield/mg (size/nm)	UV-vis absorption $\lambda_{\max}/\text{nm}^b$	TGA mass loss/% ^c
3	17.0 (7.7±0.52)	527	10.3
HS ⁿ C ₁₂ H ₂₅ ^d	15.1 (8.6±0.65)	528	7.65

^a The reaction was carried out with HAuCl₄·4H₂O (41.2 mg, 0.1 mmol), capping reagent (28.7 mg, 0.1 mmol) and Et₃SiH (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 Chapter III-2.

**Figure 6.** (a) UV-vis spectrum of AuNP 4, (b) TEM image of AuNP 4

The Author next examined the synthesis of AuNPs with THP-protected dodecanethiol **3** under various reaction conditions (Table 4). 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 $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ and **3** 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 shown in Chapter III-2.

Table 4. Preparation of AuNP **4** with THP-protected dodecanethiol **3**^a

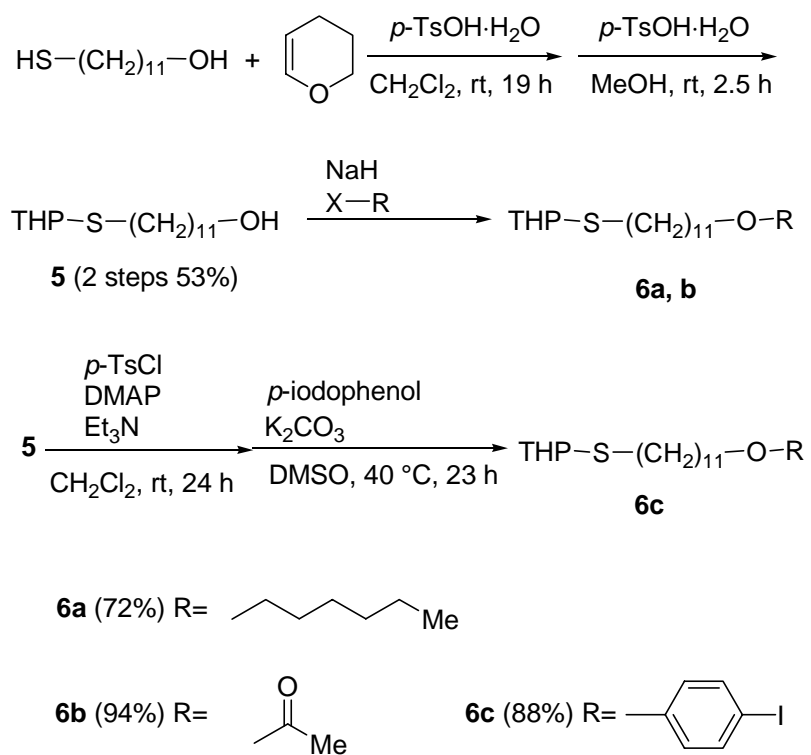
time/h	yield/mg	size/nm
6	15.5	7.7±0.52
24	17.7	8.6±0.50
6 ^b	5.2	- ^c

^a Unless otherwise specified, the reaction was carried out with $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ (41.2 mg, 0.1 mmol), **3** (28.7 mg, 0.1 mmol), in 10 mL of THF at 25 °C. THF solution of **3** and $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ 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)¹³ furnished AuNP with an average diameter of 2.8 ± 0.45 nm (Figure 7a). When an aqueous solution of NaBH_4 ¹⁰ was added to toluene/ H_2O solution of HAuCl_4 , **3**, and tetraoctylammonium bromide (TOAB), AuNP of 3.7 ± 0.70 nm was also obtained (Fig. 7b). 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 .

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.

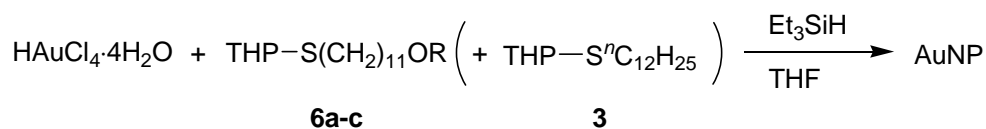
The Author synthesized several THP-protected alkanethiols bearing a functional group **6a-c** and subjected to the formation of AuNPs. Synthesis of **6a-c** was carried out as outlined in Scheme 4. The reaction of 1, ω -mercaptoalcohol with 3,4-dihydro-2*H*-pyran would afford HO- and HS- both protected product, which underwent the removal of O-THP by acid-catalyzed methanolysis to afford **5** in 53% yield. The reaction of **5** with several organic halides was performed by ether and ester syntheses. The reaction with 1-bromohexane afforded ether **6a** (72%). The acetate **6b** was prepared by the reaction of acetyl chloride (94%). Aryl ether **6c** 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 results are summarized in Table 5.

Table 5. Preparation of AuNP with THP-protected thiol derivatives bearing a functional group^a



capping reagent	yield/mg	size/nm
6a (0.2 mmol) ^b	25.1	9.9±1.4
6b (0.1 mmol)	21.3	aggregation
3 (0.14 mmol) + 6b (0.06 mmol) ^b	30.7 ^c	6.8±0.90
3 (0.05 mmol) + 6c (0.05 mmol) ^b	13.5 ^d	8.4±0.95

^a Unless specified, AuNPs were synthesized from capping reagent, HAuCl₄·4H₂O, and Et₃SiH 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.

The reaction of the thioether bearing alkyl ether group **6a** (0.2 mmol) proceeded smoothly to afford dark purple solution and 25.1 mg of the nanoparticle was isolated. The IR spectrum of the obtained nanoparticle exhibited absorptions assigned as alkyl chain at 2933 and 2844 cm^{-1} , indicating that the ether moiety was involved in the surface of the thiol (Figure 8).

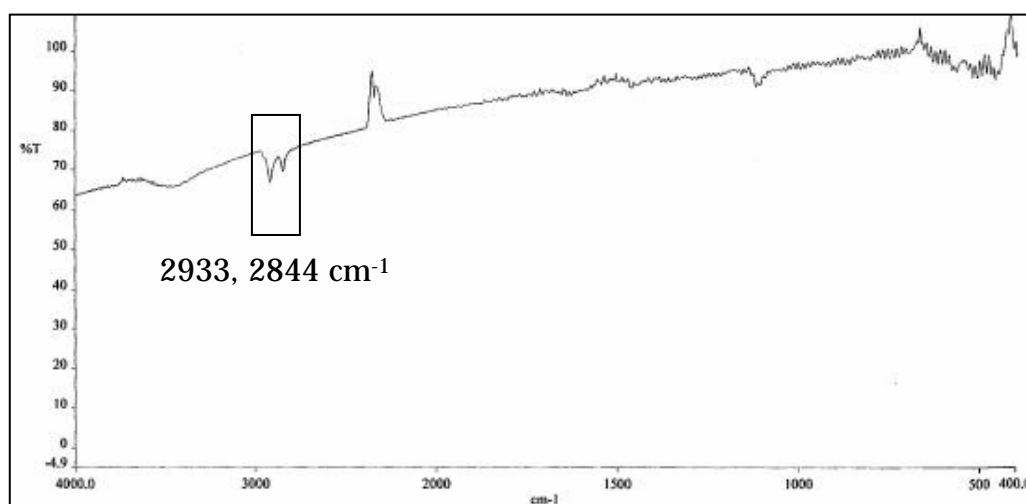


Figure 8. IR spectrum of the AuNP bearing ether moiety (KBr)

The reactions of THP-thioethers bearing other functional groups were carried out in a similar manner. The reaction resulted to show clear purple color suggesting 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 examined by using a mixture of **6b,c** and **3** as capping reagents and the obtained AuNP dissolved in chloroform again. Measurement of ^1H NMR spectrum of AuNP composed of **3** and **6c** showed signals of aromatic groups at 6-7 ppm. The ratio introduced was estimated by the calculation of the integral value of the NMR spectrum being ca. 1.6:1.0 (Figure 9).

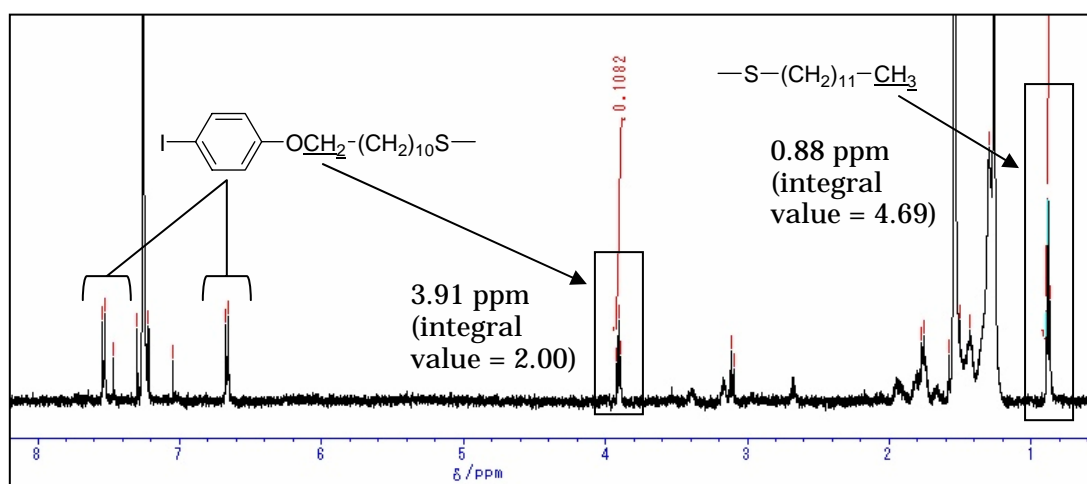


Figure 9. ^1H NMR spectrum of the AuNP bearing *p*-iodophenoxy group and dodecyl group (CDCl_3)

On the other hand, characterization of the ratio of **3** and **6b** on AuNP by ^1H NMR analysis was unsuccessful. IR spectrum of the AuNP showed characteristic absorptions of the carbonyl group at 1755 cm^{-1} suggesting that thiol bearing the acetoxy group was introduced on the gold surface (Figure 10). 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 temperature¹⁶ to observe the characteristic signals by IR and ^1H NMR, in which the introduced ratio of **3**: **6b** was confirmed to be ca. 7.8:1.0 (Figure 11).

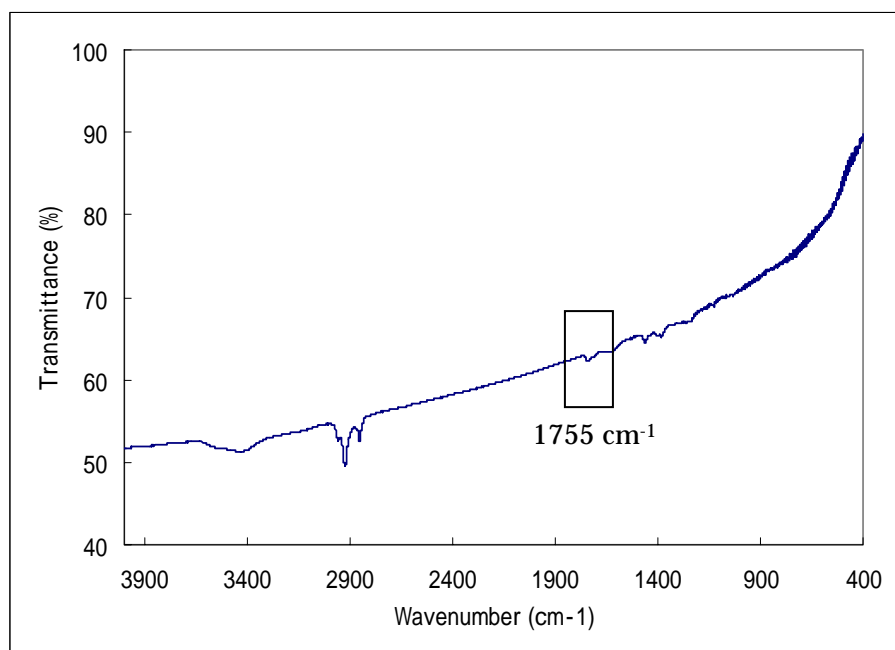


Figure 10. IR spectrum of the AuNP bearing acetoxy group (KBr)

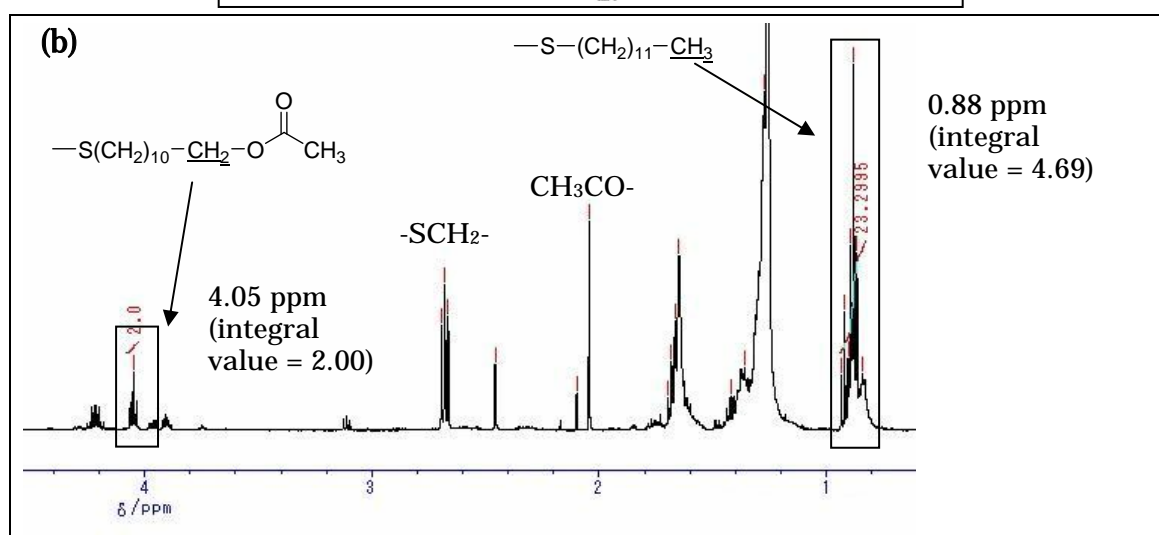
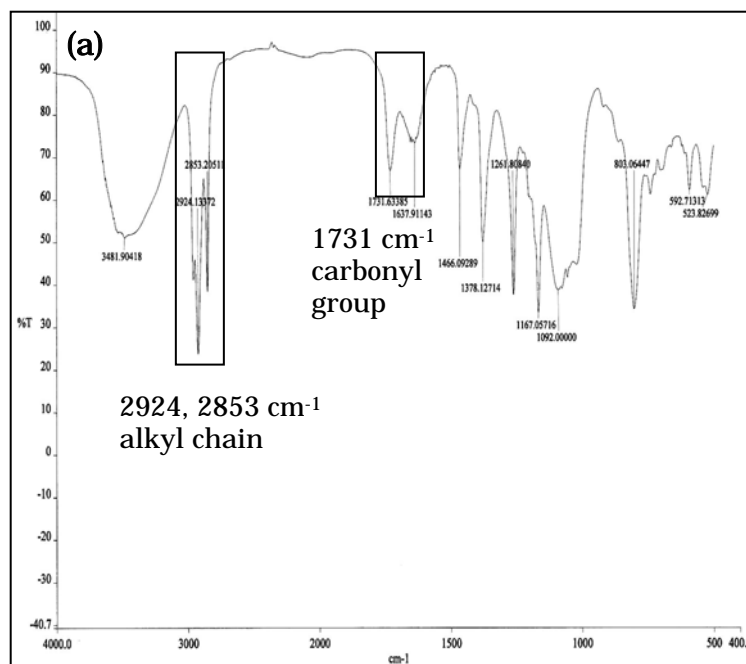
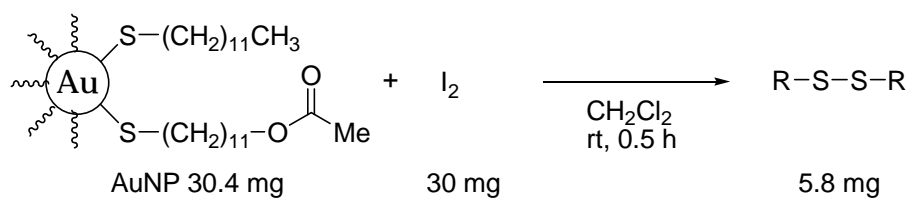


Figure 11. ^1H NMR spectrum of the organic residue after treatment of the obtained AuNP with I_2 (CDCl_3)

IV-4 Conclusion

Synthesis of gold nanoparticle proceeded in hexane, toluene, Et₂O, and THF when reduction of soluble tributylphosphine complex of gold(I) thiolate was carried out. Thiol-capped AuNPs bearing a functional group were also obtained from THP-protected thiol derivatives and HAuCl₄ in the presence of a reducing agent without deprotection. Extension of the available organic solvent and the method for easy access to functionalized thiol derivatives and following formation of the AuNP would improve synthetic versatility of gold nanoparticles that involve functionalities.

IV-5 Experimental

IV-5-1 General

Melting points were uncorrected. ^1H NMR (500 MHz), ^{13}C NMR (125 MHz) spectra were measured with Bruker Avance 500. Unless specified, measurements of the spectra were carried out with CDCl_3 as a solvent. The chemical shifts were expressed in ppm using CHCl_3 (7.26 ppm for ^1H) or CDCl_3 (77.0 ppm for ^{13}C) as an internal standard. IR spectra were recorded on PERKIN ELMER FT-IR Spectrometer SPECTRUM 1000 and Varian FTS-7000. High resolution mass spectra (HRMS, EI) were measured by JEOL JMS-700 MStation at the Graduate School of Material Science, Nara Institute of Science and Technology. Transmission electron microscopic (TEM) observations were performed by using Hitachi H-7100TE, JEOL JEM-1230 BU and JEOL JEM-1200EX II with an acceleration voltage of 100, 100 and 120 kV, respectively. TEM samples were prepared by dropping of the CHCl_3 or toluene/hexane solution of gold nanoparticle (AuNP) on 150 mesh carbon coated copper grids, which were purchased from Okensyoji. UV-vis spectrum was measured in CHCl_3 at 25 °C on a Hitachi U3310 spectrometer. Thermogravimetric analysis (TGA) was performed by using Rigaku Thermo

plus TG 8120.

$\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ was purchased from Tanaka Kikinzoku Kogyo Co. Ltd. Phenylsilane was purchased from Tokyo Chemical Industry Co. Ltd. THF was purchased from Sigma-Aldrich Co. Ltd. as an anhydrous grade and stored in a Schlenk tube under nitrogen atmosphere. Other chemicals were purchased and used as such.

IV-5-2 Reduction of gold(I) thiolate with a silane reagent in a wide range of organic solvent leading to gold nanoparticles

Synthesis of gold(I) *n*-dodecylthiolate **1**

To a test tube equipped with magnetic stirring bar were added $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ (41.2 mg, 0.1 mmol) and 1 mL of water. To a resulting solution was added 2,2'-thiodiethanol (30 μL , 0.3 mmol) dropwise at 0 °C. After stirring for 45 min, 1-dodecanthiol (24 μL , 0.1 mmol) was added dropwise and stirring was continued for 1 h. The precipitation was collected and washed with EtOH and Et₂O repeatedly to afford **1** in quantitative yield.

Since the obtained solid was insoluble to water and organic solvents, further characterization was not carried out.

Synthesis of *n*-tributylphosphine complex of gold(I) thiolate **2**

To a test tube equipped with magnetic stirring bar were added **1** (0.05 mg, 19.9 μmol) and 1 mL of CDCl_3 . To a resulting suspension was added *n*-tributylphosphine (12.5 μL , 0.05 mmol) to form a colorless clear solution. After stirring for 0.5 h, the solution of $\text{Bu}_3\text{PAuCl}_2\text{S}_2$ **2** was subjected to the measurement of ^1H NMR spectrum. ^1H NMR δ 0.87 (t, $J = 6.9$ Hz, 3H), 0.93 (t, $J = 6.9$ Hz, 9H), 1.21-1.31 (m, 16H), 1.41-1.52 (m, 8H), 1.53-1.59 (m, 6 H), 1.66-1.71 (m, 2H), 1.73-1.78 (m, 6H), 2.92 (t, $J = 8.0$ Hz, 2H).

General procedure for synthesis of thiol-capped AuNP by phenylsilane.

To a suspension of **1** (39.8 mg, 0.1 mmol) in hexane (5 mL) was added $^n\text{Bu}_3\text{P}$ (37 μL , 0.15 mmol) to form a clear solution by stirring at room temperature for 0.5 h. To a resulting solution was added PhSiH_3 (5 μL , 0.04 mmol) dropwise. The color of the solution turned from colorless clear to dark purple immediately. After stirring at room temperature for 2 h, the solution was concentrated under reduced pressure. Following addition of ethanol formed precipitation, which was separated by continuous centrifuge and decantation procedures to afford 16.0 mg of gold nanoparticle as a dark purple solid.

IV-5-3 Generation of gold nanoparticles via direct thiol-capping with THP-protected thiols without deprotection**1-(Tetrahydropyran-2-ylsulfanyl)dodecane (3)**

To a solution of dodecanethiol (1.2 mL, 5.0 mmol) and 3,4-dihydro-2*H*-pyran (0.68 mL, 7.5 mmol) in 20 mL of CH₂Cl₂ was added *p*-toluenesulfonic acid monohydrate (95.1 mg, 0.5 mmol). The resulting mixture was stirred for 14 h at room temperature. The mixture was washed with aqueous solution of NaHCO₃. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to leave a crude oil, which was purified by chromatography on silica gel to afford 911.1 mg of **3** as a colorless oil (64%). ¹H NMR δ 0.879 (t, *J* = 6.9 Hz, 3H), 1.25 (m, 16H), 1.37 (m, 2H), 1.56-1.67 (m, 6H), 1.82 (m, 1H), 1.91 (m, 1H), 2.55-2.69 (m, 2H), 3.49 (m, 1H), 4.09 (m, 1H), 4.84 (dd, *J* = 6.5, 3.6 Hz, 1H); ¹³C NMR δ 15.05, 22.78, 23.64, 26.62, 29.96, 30.20, 30.30, 30.49, 30.57, 30.59, 30.62, 30.94, 31.35, 32.45, 32.88, 65.52, 83.27; IR(neat): 2921, 2851, 1463, 1264, 1190, 1081, 1037 cm⁻¹; HRMS(EI) found: *m/z* 286.2330 Calcd for 286.2330.

11-(Tetrahydropyran-2-ylsulfanyl)undecanol (5)

To a solution of 11-mercapto-1-undecanol (3.10 g, 15.2 mmol) and 3,4-dihydro-2*H*-pyran (4.13 mL, 45.5 mmol) in 35 mL of CH₂Cl₂ was added *p*-toluenesulfonic acid monohydrate (0.288 g, 1.52 mmol). The resulting mixture was stirred for 14 h at room temperature. The mixture was washed with aqueous solution of NaHCO₃. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to leave a crude oil. To this oil were added methanol (30 mL) and *p*-toluenesulfonic acid monohydrate (0.029 g, 152 mmol). After 4.5 h stirring at room temperature, resulting mixture was neutralized by K₂CO₃ and methanol was removed under reduced pressure. The residue was dissolved in CH₂Cl₂ and washed with water and brine. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to leave a crude oil, which was purified by chromatography on silica gel to afford 2.34 g of **5** as a pale yellow oil (53%) . ¹H NMR δ 1.22-1.35 (m, 16H), 1.53-1.69 (m, 6H), 1.82 (m, 1H), 1.82-1.94 (m, 1H), 2.54-2.67 (m, 2H), 3.49 (m, 1H), 3.64 (t, *J* = 7.1 Hz, 2H), 4.08 (m, 1H), 4.84 (dd, *J* = 6.5, 3.5 Hz, 1H); ¹³C NMR δ 22.60, 26.47, 26.59, 29.78, 30.03, 30.25, 30.30, 30.32, 30.40, 30.76, 31.20, 32.29, 33.57,

63.64, 65.35, 83.14; IR(neat) 3450, 2925, 2853, 1467, 1265, 1190, 1079, 1036 cm^{-1} ; HRMS(EI) found: m/z 288.2123 Calcd for 288.2123.

1-Hexyloxy-11-(tetrahydropyran-2-ylsulfanyl)undecane (6a)

To a solution of **5** (0.268 g, 0.928 mmol) and 1-bromohexane (0.391 mL, 2.78 mmol) in 1.5 mL of THF was added sodium hydride (0.200 g, 8.35 mmol). The mixture was stirred for 95 h at room temperature. After the reaction, resulting mixture was poured into water. The aqueous layer was extracted with ether and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude oil, which was purified by column chromatography on silica gel to afford 0.248 g of **6a** as a colorless oil (72%). ^1H NMR δ 0.884 (t, J = 6.7 Hz, 3H), 1.26-1.31 (m, 22H), 1.54-1.69 (m, 8H), 1.70 (m, 1H), 1.90-1.94 (m, 1H), 2.56-2.66 (m, 2H), 3.386 (t, J = 6.6 Hz, 2H), 3.388 (t, J = 6.6 Hz, 2H), 3.50 (m, 1H), 4.09 (m, 1H), 4.83 (dd, J = 6.7, 3.6 Hz, 1H); ^{13}C NMR δ 15.00, 22.78, 23.59, 26.60, 26.84, 27.15, 29.95, 30.18, 30.44, 30.46, 30.49, 30.53, 30.70, 30.73, 30.92, 31.33, 32.43, 32.68, 65.55, 71.91, 83.25; IR(neat) 2927, 2855, 1468, 1266, 1190, 1117, 1037 cm^{-1} ; HRMS(EI) found: m/z 372.3066 Calcd for 372.3062.

11-(Tetrahydropyran-2-ylsulfanyl)undecyl acetate (6b)

The reaction was carried out in a similar manner as above using **5** (0.289 g, 1.0 mmol), acetyl chloride (0.14 mL, 2.0 mmol), NaH (0.06 g, 2.5 mmol) and 3 mL of THF with stirring at room temperature for 17 h to give **6b** as a colorless oil (83%). ¹H NMR δ 1.26-1.36 (m, 16H), 1.57-1.62 (m, 6H), 1.82 (m, 1H), 1.90-1.94 (m, 1H), 2.03 (s, 3H), 2.54-2.67 (m, 2H), 3.49 (m, 1H), 4.03-4.10 (m, 3H), 4.83 (dd, *J* = 6.5, 3.9 Hz, 1H); ¹³C NMR δ 21.81, 22.65, 26.51, 26.74, 29.46, 29.81, 30.04, 30.07, 30.31, 30.80, 31.21, 32.33, 65.35, 65.44, 83.14, 171.93; IR (neat): 2926, 2855, 1739, 1467, 1368, 1236, 1079, 1035 cm⁻¹; HRMS(EI) found: *m/z* 330.2224 Calcd for 330.2229.

1-(4-Iodophenoxy)-11-(tetrahydropyran-2-ylsulfanyl)undecane (6c)

To a Schlenk tube were added **3** (0.721 g, 2.5 mmol), triethylamine (0.7 mL, 5.0 mmol), 4-(dimethylamino)pyridine (0.012 g, 0.1 mmol) and 17 mL of dichloromethane. The mixture was added *p*-toluenesulfonyl chloride (0.953 g, 5.0 mmol) at 0 °C. After stirring for 24 h at room temperature, the resulting mixture was poured into water. The aqueous layer was extracted with CH₂Cl₂ and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a

crude oil, which was purified by column chromatography on silica gel to afford 0.9061 g of tosylated product (82%). The product was subjected to the following reaction without further purification.

The tosylated product (0.906 g, 2.05 mmol), *p*-iodophenol (0.677 g, 3.08 mmol), K₂CO₃ (0.850 g, 6.15 mmol) and 10 mL of DMSO were added to a Schlenk tube. After stirring for 23 h at 40 °C, the resulting mixture was poured into water. The aqueous layer was extracted with CH₂Cl₂ and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude oil, which was purified by column chromatography on silica gel to afford 0.881 g of **6c** as a yellow oil (82%). ¹H NMR δ 1.28-1.43 (m, 16H), 1.57-1.69 (m, 6H), 1.82 (m, 1H), 1.90-1.94 (m, 1H), 2.56-2.66 (m, 2H), 3.50 (m, 1H), 3.90 (t, *J* = 6.7 Hz, 2H), 4.09 (m, 1H), 4.83 (dd, *J* = 6.5, 3.9 Hz, 1H), 6.67 (m, 2H), 7.53 (m, 2H); ¹³C NMR δ 22.75, 26.59, 26.92, 29.91, 30.07, 30.14, 30.27, 30.42, 30.44, 30.90, 31.32, 32.43, 65.50, 69.06, 83.25, 83.31, 117.8, 139.1, 160.0; IR (neat): 2924, 2853, 1587, 1487, 1468, 1283, 1244, 1188, 1174, 1078, 1034, 1008, 820, 722, 632, 506, 425 cm⁻¹; HRMS(EI) found: *m/z* 489.1329 Calcd for 489.1402 (M-1).

General Procedure for the synthesis of Au nanoparticle 4

To a screw-capped test tube equipped with a magnetic stirring bar were added $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ (41.2 mg, 0.1 mmol), and THP-protected thiol **3** (28.7 mg, 0.1 mmol) and THF (10 mL). The resulting mixture was stirred vigorously for 3 h at 25 °C to form a yellow solution. Triethylsilane (16 μL , 0.1 mmol) was then added dropwise at 25 °C to form a purple solution. After stirring for further 6 h, ethanol was added to precipitate the AuNP, which was centrifuged, washed with ethanol and dried under reduced pressure to afford 15.5 mg of **4** as a dark-brown powder. IR (KBr): 2924, 2852 cm^{-1} ; TGA, 10.2% weight loss (800 °C)

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Chapter V

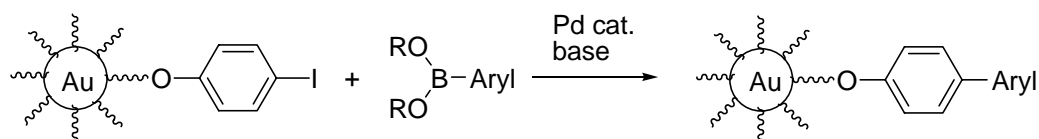
Surface Modification of Gold Nanoparticle with the Suzuki-Miyaura Coupling Reaction

Abstract: Surface modification of the gold nanoparticle with the Suzuki-Miyaura coupling reaction is examined. The coupling reaction is found to undergo when the gold nanoparticle stabilized with dithiol bearing *p*-iodophenoxy group is employed

V-1 Introduction

The methodology for introduction of functionalities to the surface of gold nanoparticles (AuNPs) becomes important since considerable interest has been focused on the application of AuNPs in various fields.¹ An organic reaction at the surface of AuNPs is a method of choice to introduce various functionalities to the AuNPs reasonably. However, few reports on transition-metal catalyzed reactions² which are powerful tools in organic chemistry at the surface of AuNPs are shown due to the low stability of the AuNPs.

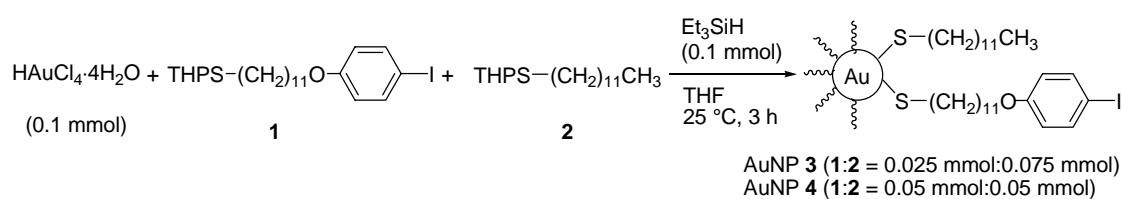
In Chapter IV, the Author described the synthesis of AuNP functionalized by the *p*-iodophenoxy group. Encouraged by this result, surface modification of the AuNP by the Suzuki-Miyaura coupling reaction,³ which is the palladium-catalyzed cross-coupling reaction of an aryl halide and an organoboron reagent, is envisaged in this chapter (Scheme 1).



Scheme 1

V-2 Result and discussion

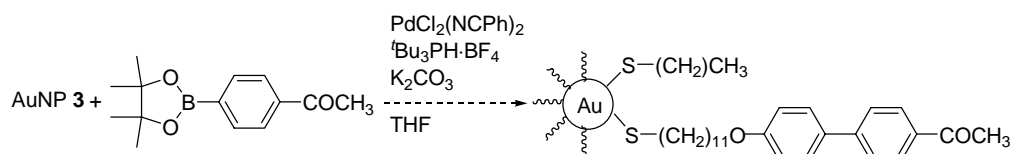
As shown in Chapter IV-3, the synthesis of AuNPs functionalized with the *p*-iodophenoxy group was carried out by using the mixture of the THP-protected thiol derivatives **1** and **2** as capping reagents and triethylsilane as a reducing agent. AuNP **3** and **4** were prepared by varying the ratio of the capping reagents **1** and **2** (Scheme 2).



Scheme 2

The Suzuki-Miyaura coupling reaction using AuNP **3** was examined (Table 1). Though the Suzuki-Miyaura coupling reaction often requires heating to undergo the reaction,^{3c} mild condition was favorable to carry out the reaction on the surface of the AuNP since agglomeration of the particle might occur. Thus, tri-*tert*-butylphosphine complex of palladium which is generated in-situ by treatment of tri-*tert*-butylphosphine tetrafluoroborate⁴ to $\text{PdCl}_2(\text{NPh})_2$ and shows high reactivity toward coupling reactions under

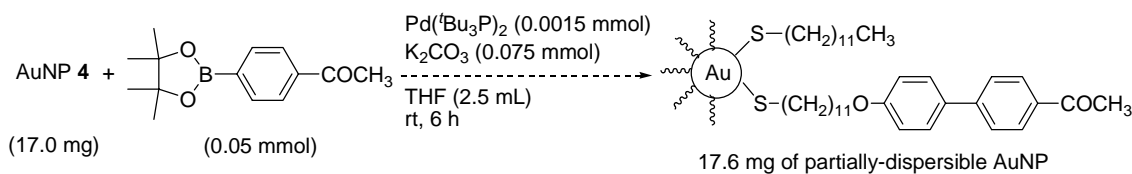
mild conditions, was employed. When the purple THF solution of the AuNP **3** was treated with 4-acetylphenylboronic acid ester and K_2CO_3 in the presence of $tBu_3PH \cdot BF_4$ and $PdCl_2(NCPh)_2$ and stirred at room temperature for 6 h, no formation of precipitates due to the agglomeration of the particle was observed. However, black solid obtained by following filtration of K_2CO_3 and the addition of EtOH, did not disperse to an organic solvent such as chloroform, dichloromethane, THF, and toluene. The reaction carried out for 24 h showed agglomeration of the nanoparticle suggesting that the AuNP **3** was not stable enough for a long reaction period. The black solid isolated from the resulting solution was not dispersible to organic solvents either when the reaction was carried out at 50 °C for 2 h.

Table 1. Investigation of the Suzuki-Miyaura coupling reaction of AuNP **3**^a

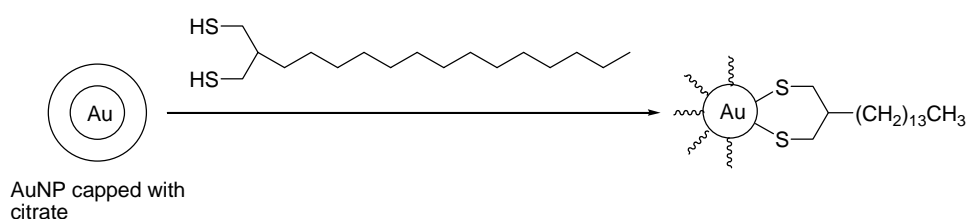
AuNP 3 /mg	temp./°C	time/h	result
13	rt	6	11.4 mg of undispersible solid
15	rt	24	agglomeration of the particle
13	50	2	6.1 mg of undispersible solid

^a The reaction was carried out with AuNP **3**, 4-acetylphenylboronic acid pinacol ester (0.1 mmol), PdCl₂(NCPh)₂ (0.0015 mmol), tBu₃PH·BF₄ (0.0030 mmol), and K₂CO₃ (0,075 mmol) in THF (2.5 mL)

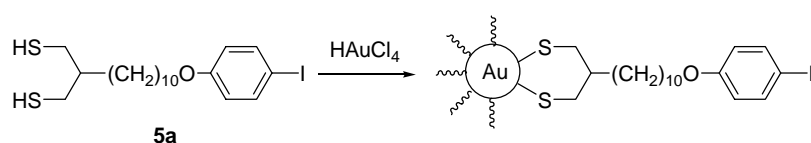
Partially-dispersible AuNP was obtained by the reaction of the AuNP **4** and 4-acetylphenyl boronic acid ester in the presence of Pd(tBu₃P)₂, which do not form tetrafluoroborate compared to the case of the PdCl₂(NCPh)₂/tBu₃PH·BF₄ system (Scheme 3). However, ¹H NMR spectrum of the obtained AuNP exhibited no signals at the aromatic region.

**Scheme 3**

It is considered that the AuNP with high stability is required to proceed the Suzuki-Miyaura coupling reaction at the surface of the AuNP. The Author's interest has been centered to AuNP stabilized by bi- or tridentate thiols. Lee reported that AuNP were highly stabilized by the multidentate thiols than monodentate thiols (Scheme 4).⁵ Lee suggested that the chelate effect and dangling of the loosely packed alkyl chain of the multidentate thiols cause high stability of the AuNP from undesired aggregation. Encouraged by this research, the Author designed the dithiol bearing an iodoaryl group **5a** and envisaged the preparation of AuNP stabilized by **5a** (Scheme 5).



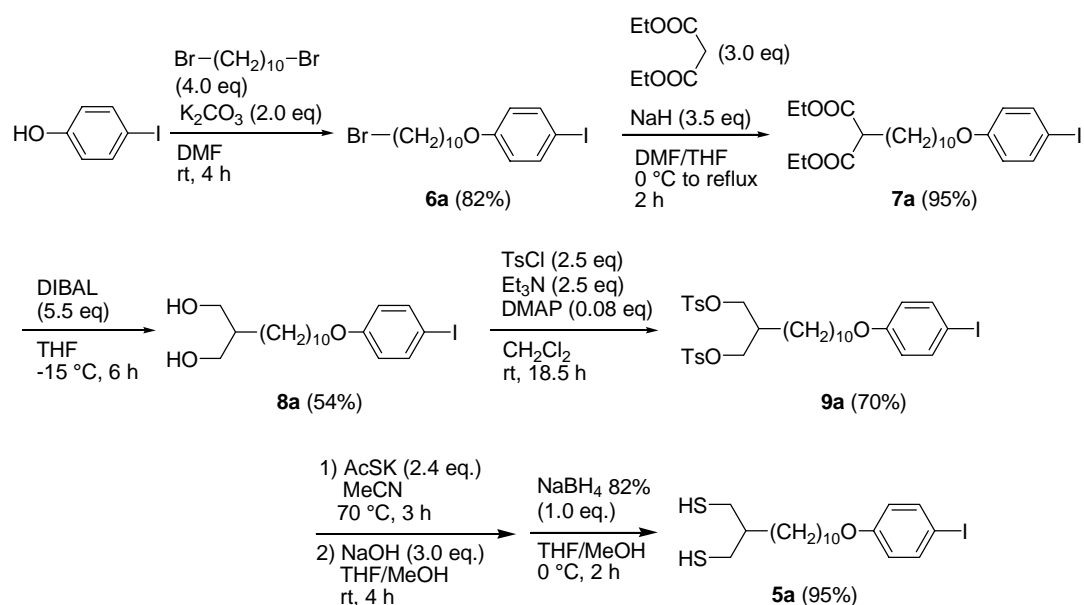
Scheme 4. Lee's research on multidentate-thiol capped AuNP



Scheme 5

The synthesis of dithiol **5a** was carried out as outlined in Scheme 6.

The reaction of 1,10-dibromodecane with *p*-iodophenol in the presence of K_2CO_3 afforded **6a** in 82% yield. By following Lee's report,⁵ the obtained product was subjected to the reaction with the excess amount of diethyl malonate to give the diester **7a** in 95% yield. The reduction of ester group of **7a** with DIBAL at $-15\text{ }^\circ\text{C}$ furnished diol **8a** in 54% yield with its iodo group intact. After treatment of **8a** with tosyl chloride to form **9a** (70%), introduction of thioacetyl group was carried out. The following methanolysis and reduction afforded dithiol **5a** in 95% yield.

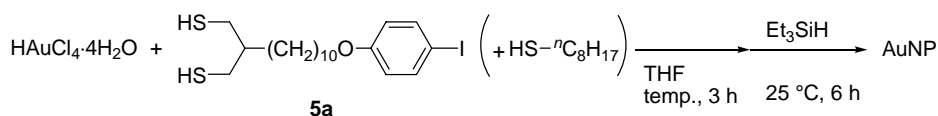


Scheme 6

Since dithiol **5a** was in hand, the Author envisaged synthesis of AuNP by treatment of triethylsilane as a reducing agent. As shown in the previous chapter, purple-solution was obtained in the synthesis of the AuNP **3** and **4**. However, the similar reaction carried out with $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ (0.1 mmol) and dithiol **5a** (0.1 mmol) afforded the agglomerated nanoparticle. The reaction carried out with a mixture of **5a** (0.05 mmol) and octanethiol (0.05 mmol) formed a pale-purple solution with undispersible precipitate.

It was found that vigorous stirring of the THF solution of HAuCl_4 and dithiol **5a** at 40 °C and following addition of Et_3SiH at 25 °C improved the dispersity of the AuNP. However, the obtained AuNPs were partially dispersible even the ratio of **5a** and octanethiol was changed.

In Chapter IV-3, it was found that only a small amount of thiols exists on the surface of the AuNP obtained by the reduction of Et_3SiH . Therefore, insufficient stability of the AuNP prepared from **5a** and Et_3SiH would be due to the introduction of the small amount of capping reagent on the surface of AuNP.

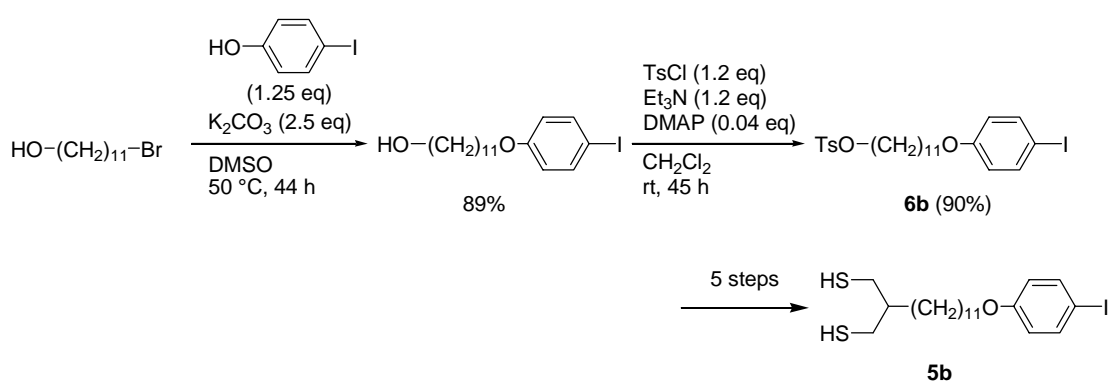
Table 2. Preparation of the AuNP stabilized by dithiol **5a** with Et₃SiH^a

5a /mmol	HS-C ₈ H ₁₇ / mmol	temp./ °C	result
0.1 ^b	0	25	agglomeration of AuNP
0.05	0.05	25	pale-purple solution with precipitate
0.1 ^b	0	40	20.0 mg of partially dispersible AuNP
0.075	0.025	40	16.5 mg of partially dispersible AuNP
0.025	0.075	40	22.0 mg of undispersible solid

^a Unless specified, the reaction was carried out with HAuCl₄·4H₂O (0.1 mmol), **5** (0.1 mmol), and THF solution of *t*BuNH₂·BH₃ (0.1 mmol/2 mL) in 8 mL of THF. ^b 20 mL of THF was used.

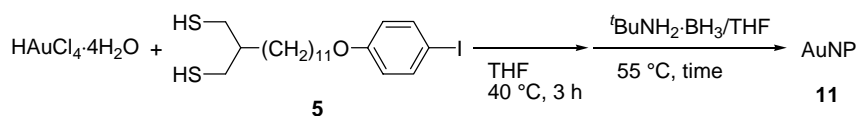
To synthesize the AuNP **10** which is sufficiently stabilized by adsorption of dithiol, the reaction of HAuCl₄·4H₂O and dithiol **5b** with borane-amine complex as a reducing agent⁶ was carried out. As shown in Scheme 7, the employed dithiol **5b** was synthesized in a similar manner to Scheme 6. By following the literature, the THF solution of *tert*-butylamine complex of borane was added to the THF solution of HAuCl₄·4H₂O and dithiol **5b**, which was stirred for 3 h at 40 °C preliminary, at 55 °C and continuous stirring of resulting solution for 5 mins afforded a purple solution indicating the AuNP formation. However, the obtained dark brown solid

showed low solubility to THF and CHCl_3 . The AuNP with high solubility was obtained when the stirring after the addition of ${}^t\text{BuNH}_2\cdot\text{BH}_3$ was carried out for 0.5 h. Longer reaction period, 1 or 3 h afforded product with low solubility (Table 3).



Scheme 7

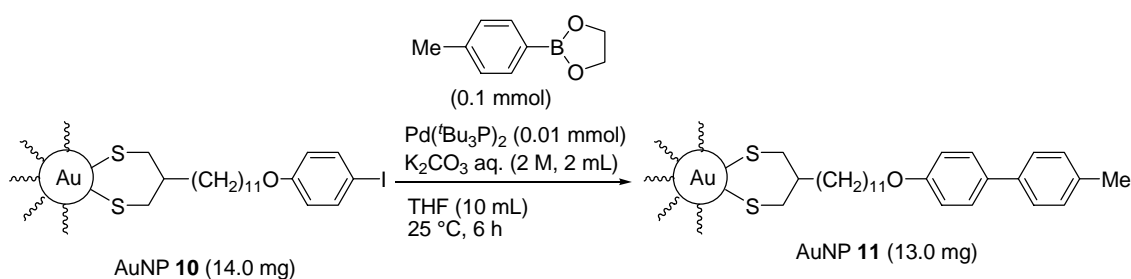
Table 3. Preparation of the AuNP **10** stabilized by dithiol **5b** with amine-borane complex^a



time	yield/mg	result
5 min	24.4	partially-dispersible AuNP
0.5 h	19.6	dispersible AuNP
1 h	24.8	partially-dispersible AuNP
3 h	20.1	undispersible solid

^a The reaction was carried out with $\text{HAuCl}_4\cdot 4\text{H}_2\text{O}$ (0.1 mmol), **5b** (0.1 mmol), and THF solution of ${}^t\text{BuNH}_2\cdot\text{BH}_3$ (0.1 mmol/2 mL) in 8 mL of THF.

Since dispersible AuNP **10** was in hand, the Suzuki-Miyaura coupling reaction was then envisaged. As shown in scheme 7, an aqueous solution of K_2CO_3 which Kawai and coworkers employed as a base to undergo Suzuki-Miyaura coupling at the surface of gold electrode⁷ was employed. To the THF solution of the AuNP **10** (14.0 mg), 4-methylphenylboronic acid ethylene glycol ester (0.1 mmol), and $Pd(tBu_3P)_2$ (0.01 mmol) was added to the aqueous solution of K_2CO_3 (2 M, 2 mL) to form a mixture, which was stirred for 6 h at 25 °C. The organic layer was separated and the isolation of the AuNP was carried out by addition of EtOH. The obtained 13.0 mg of dark-brown solid **11** was dispersible to $CHCl_3$.



Scheme 8

Figure 1 shows 1H NMR spectra of (A) the AuNP **10**, (B) the AuNP **11**,

and (C) a compound **12** bearing the structure similar to the capping reagent of AuNP **11**.⁸ The spectra of AuNP **10** and **11** exhibited broad signals observed for capping reagents immobilized on the gold surface. The signals at 6.66 ppm which are assigned as protons of iodophenoxy group of AuNP **10** (Fig1A) were not found in AuNP **11** (Fig. 1B), suggesting the complete consumption of the iodophenoxy group of **11** during the reaction. Comparison of the ¹H NMR spectra of AuNP **11** (Fig. 1B) and **12** (Fig. 1C) suggested that the Suzuki-Miyaura Coupling reaction proceeded at the surface of the AuNP functionalized with dithiol **5b**.

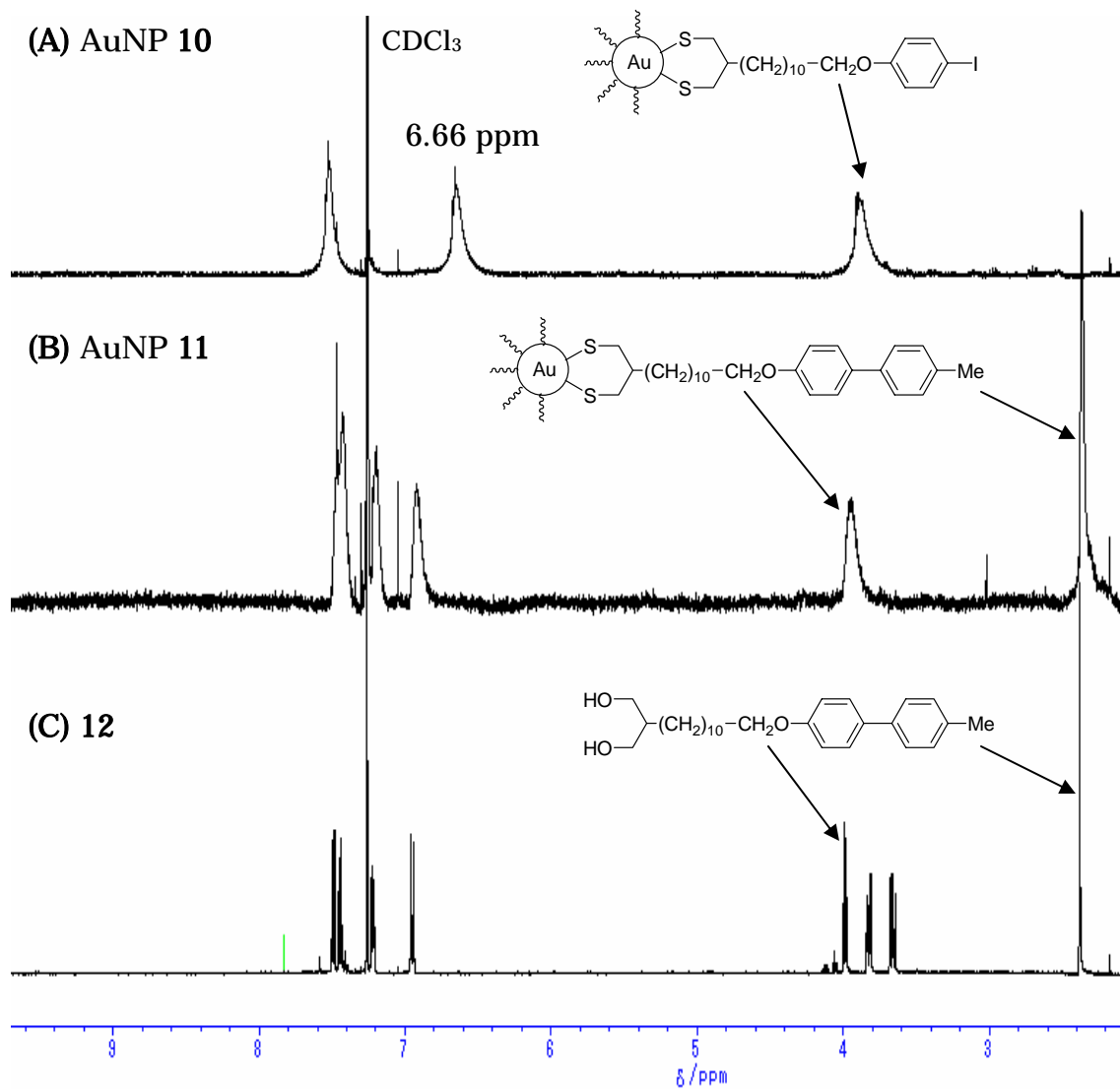
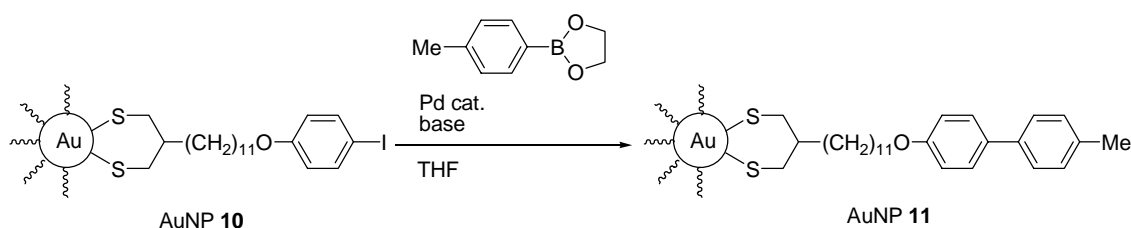


Figure 1. ¹H NMR spectra of (A) AuNP 10, (B) AuNP 11, (C) 12 in CDCl₃

The AuNP **10** was then subjected to Suzuki-Miyaura coupling reaction under various conditions. The results are summarized in Table 3. The reaction at 40, 60, and 80 °C proceeded without agglomeration of the AuNP to give 15.2 mg of the AuNP **11**, indicating high thermal stability of the dithiol-capped AuNP. When the reaction was carried out with $\text{PdCl}_2(\text{PPh}_3)_2$ as catalyst, immediate agglomeration of the AuNP accompanied by disappearance of a purple-color of the solution was observed. The reaction in the presence of solid K_2CO_3 as base afforded 12.7 mg of dark-brown solid, however, the obtained solid was not dispersible to organic solvents.

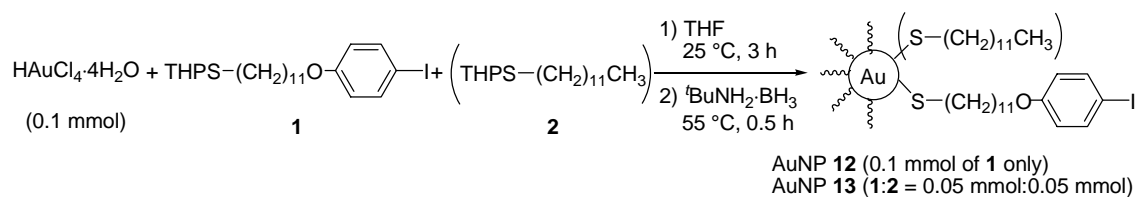
Table 3. The Suzuki-Miyaura coupling reaction of AuNP 10^a

10 /mg	Pd cat.	base	temp. /°C	result
14.0	Pd(<i>t</i> Bu ₃ P) ₂	K ₂ CO ₃ aq. (2 M, 2 mL)	25	13.0 mg of AuNP 11
16.6	Pd(<i>t</i> Bu ₃ P) ₂	K ₂ CO ₃ aq. (2 M, 2 mL)	40	15.2 mg of AuNP 11
20.0	Pd(<i>t</i> Bu ₃ P) ₂	K ₂ CO ₃ aq. (2 M, 2 mL)	60	19.3 mg of AuNP 11
20.0	Pd(<i>t</i> Bu ₃ P) ₂	K ₂ CO ₃ aq. (2 M, 2 mL)	80	16.6 mg of AuNP 11
20.0	PdCl ₂ (PPh ₃) ₂	K ₂ CO ₃ aq. (2 M, 2 mL)	25	agglomeration
20.0	Pd(<i>t</i> Bu ₃ P) ₂	K ₂ CO ₃ 0.1 mmol	25	12.7 mg of undispersible solid

^a The reaction is carried out with AuNP 10, 4-methylphenylboronic acid ester (0.1 mmol), palladium catalyst (0.01 mmol), and base in 10 mL of THF.

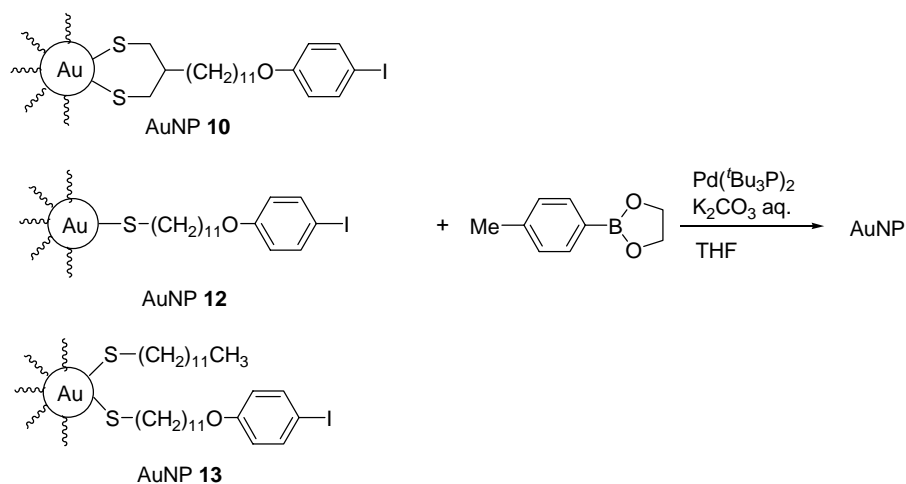
Since the Suzuki-Miyaura coupling reaction of the dithiol-capped AuNP 10 was successful, the employed reaction condition was applied to the reaction of thiol-capped AuNPs. The Synthesis of thiol-capped AuNPs 12 and 13 were carried out by treatment of *t*BuNH₂·BH₃ as a reducing agent (Scheme 9). The results of the reaction were shown in Table 4 and Figure 2. Though no aggregation of the AuNPs was observed during the reactions of AuNP 12 and 13, the isolated solids were partially-dispersible to CHCl₃ and ¹H NMR spectrum of the solids gave no signals in aromatic area. These

results suggest that the dithiol-capped AuNP shows higher stability than the thiol-capped AuNP.



Scheme 9

Table 4. Comparison of the Suzuki-Miyaura coupling reaction of AuNP **10**, **12**, and **13**^a



AuNP	yield/mg	result
10 (14.0 mg)	13.0	dispersible AuNP 11
12 (21.5 mg)	23.0	partially-dispersible AuNP
13 (20.4 mg)	21.5	partially-dispersible AuNP

^a The reaction was carried out with AuNP, 4-methylphenylboronic acid ester (0.1 mmol), Pd(*t*Bu₃P)₂ (0.01 mmol), and K₂CO₃ aq. (2 M, 2 mL) in 10 mL of THF at 25 °C for 6 h.

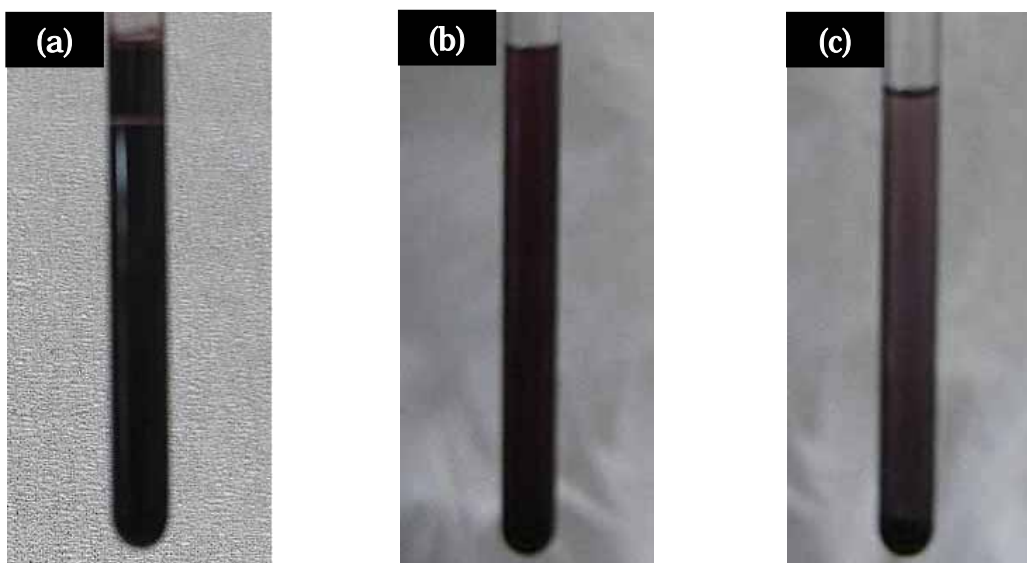


Figure 2. Image of the AuNP obtained by the reaction of (a) AuNP 10, (b) AuNP 12, and (c) AuNP 13 in CDCl_3

V-III Conclusion

The Suzuki-Miyaura coupling at the surface of AuNP was shown to undergo when the AuNP stabilized with the dithiol bearing *p*-iodophenoxy group was employed. The dithiol-capped AuNP was revealed to be stable than thiol-capped AuNP. Consequently, the dithiol derivatives bearing a functional group would be powerful tool for surface modification of AuNPs.

V-4 Experimental

General

Melting points were uncorrected. ^1H NMR (500 MHz), ^{13}C NMR (125 MHz) spectra were measured with Bruker Avance 500. Unless specified, measurements of the spectra were carried out with CDCl_3 as a solvent. The chemical shifts were expressed in ppm using CHCl_3 (7.26 ppm for ^1H) or CDCl_3 (77.0 ppm for ^{13}C) as an internal standard. $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ was purchased from Tanaka Kikinzoku Kogyo Co. Ltd. $\text{tBu}_3\text{PH} \cdot \text{BF}_4$ and $\text{Pd}(\text{tBu}_3\text{P})_2$ were purchased from Sigma-Aldrich Co. Ltd. THF was purchased from Sigma-Aldrich Co. Ltd. as an anhydrous grade and stored in a Schlenk tube under nitrogen atmosphere. Other chemicals were purchased and used as such.

Synthesis of 1-bromo-10-(4-iodophenoxy)decane (6a)

To a Schlenk tube equipped with a magnetic stirring bar were added 1,10-dibromodecane (18.0 g, 60 mmol), K_2CO_3 (4.15 g, 30 mmol), and DMF (10 mL). To a resulting mixture was added 12.5 mL of DMF solution of *p*-iodophenol (3.3 g, 15 mmol) dropwise over a period of 30 mins at room

temperature. After stirring for 4 h, the reaction mixture was poured into water. The aqueous layer was extracted with CH_2Cl_2 twice and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude oil, which was purified by column chromatography on silica gel to afford 5.38 g of **6a** as white solid (82%). Spectroscopic characteristics and physical properties of the product were identical to the authentic sample.⁹

Synthesis of diethyl 2-[11-(4-iodophenoxy)decyl]maronate (7a)

Synthesis of **7a** was carried out in a similar manner to the method by Lee.⁵ To a Schlenk tube equipped with a magnetic stirring bar were added NaH (1.0 g, 42.0 mmol), DMF (18 mL), and THF (60 mL) at 0 °C under N_2 atmosphere. Diethyl malonate (5.47 mL, 36.0 mmol) was added slowly to the resulting solution. The mixture was then stirred at room temperature for 15 min and **6a** (5.27 g, 12.0 mmol) was added. Stirring was continued for 2 h under reflux. The resulting mixture was concentrated under reduced pressure and then poured into water. The aqueous layer was extracted with diethylether twice and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a

crude oil, which was purified by column chromatography on silica gel to afford 5.89 g of **7a** as white solid (95%). ^1H NMR δ 1.25-1.31 (m, 18H), 1.42, (m, 2H), 1.75 (tt, $J = 7.2, 7.2$ Hz, 2H), 1.88 (m, 2H), 3.31 (t, $J = 7.6$ Hz, 1H), 3.90 (t, $J = 6.6$ Hz, 2H), 4.19 (m, 4H), 6.66 (m, 1H), 7.53 (m, 2H).

Synthesis of 1,3-dihydroxy-2-[11-(4-iodophenoxy)decyl]propane (**8a**)

To a Schlenk tube equipped with a magnetic stirring bar were added **7a** (830.7 mg, 1.6 mmol) and 16 mL of THF. The resulting solution was cooled to -15 °C and hexane solution of DIBAL (1.02 M, 8.7 mL, 8.8 mmol) was added slowly. Stirring was continued at -15 °C for 6 h. The reaction was quenched by the addition of methanol and HCl. The resulting mixture was concentrated under reduced pressure and then poured into water. The aqueous layer was extracted with diethylether repeatedly and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude solid, which was washed repeatedly by hexane to afford **8a** as white solid (54%). ^1H NMR δ 1.26-1.56 (m, 14H), 1.76 (tt, $J = 6.7, 6.7$ Hz, 2H), 3.64 (t, $J = 6.6$ Hz, 2H), 3.91 (t, $J = 6.5$ Hz, 2H), 6.67 (m, 2H), 7.53 (m, 2H). ^{13}C NMR δ 27.20, 28.44, 28.95, 30.36, 30.55, 30.71, 30.74, 31.08, 67.87, 69.37, 83.61, 118.19, 139.38, 160.25.

Synthesis of 2-[11-(4-iodophenoxy)decyl]-1,3-ditosylpropane (9a)

To a Schlenk tube equipped with a magnetic stirring bar were added **8a** (619.3 mg, 1.42 mmol), triethylamine (495 μ L, 3.55 mmol), DMAP (13.9 mg, 0.11 mmol), and 15 mL of CH_2Cl_2 . To a resulting solution was added tosylchloride (676.8 mg, 3.55 mmol) at 0 °C. After stirring for 18.5 h at room temperature, the mixture was poured into water. The aqueous layer was extracted with CH_2Cl_2 twice and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude solid, which was purified by column chromatography on silica gel to afford **9a** as white solid (70%). The product was subjected to the following reaction without further purification.

Synthesis of 2-[11-(4-iodophenoxy)decyl]-1,3-dimercaptopropane (5a)

To a Schlenk tube equipped with a magnetic stirring bar were added **9a** (1.24 g, 1.67 mmol), potassium thioacetate (0.457 g, 4.0 mmol), and 24 mL of MeCN and the resulting mixture was stirred at 60 °C for 4 h. The reaction mixture was poured into water and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organic layer was dried over sodium sulfate and the solvent was concentrated under reduced pressure to leave a crude solid,

which was purified by column chromatography on silica gel to afford 0.494 g of yellow solid. The product was subjected to the following reaction without further purification.

To a flask equipped with a magnetic stirring bar were added the yellow solid (46.4 mg), MeOH (0.5 mL), and THF (0.5 mL) to form a solution. NaBH₄ (3.4 mg, 0.09 mmol) was added to the solution at 0 °C and the stirring was continued for 3 h. The reaction was quenched by the addition of HCl. The resulting mixture was concentrated under reduced pressure and then poured into water. The aqueous layer was extracted with CH₂Cl₂ twice and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude solid, which was purified by column chromatography on silica gel to afford **5a** as white solid (96%). ¹H NMR δ 1.20 (t, *J* = 8.3, 2H), 1.28-1.43 (m, 16 H), 1.67 (m, 1H), 1.76 (tt, *J* = 7.9, 7.9 Hz, 2H), 2.60-2.73 (m, 2H), 3.91 (t, *J* = 6.5 Hz, 2H), 6.66 (m, 2H), 7.53 (m, 2H).

Synthesis of 11-(4-iodophenoxy)-undecanol

To a Schlenk tube was added 11-bromoundecanol (10.05 g, 40 mmol), *p*-iodophenol (11.00 g, 50 mmol), K₂CO₃ (13.82 g, 100 mmol) and 40 mL of

DMSO. After stirring for 44 h at 50 °C, the resulting mixture was poured into water. The aqueous layer was extracted with CH₂Cl₂ and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude oil, which was purified by column chromatography on silica gel to afford 13.85 g of 11-(4-iodophenoxy)-undecanol as a white solid (89%). ¹H NMR δ 1.26-1.56 (m, 16H), 1.76 (m, 3H), 3.64 (t, *J* = 6.6 Hz, 2H), 3.91 (t, *J* = 6.5 Hz, 2H), 6.67 (m, 2H), 7.53 (m, 2H). ¹³C NMR δ 26.96, 28.20, 28.70, 30.12, 30.32, 30.50, 30.52, 30.56, 30.85, 43.02, 67.74, 69.13, 83.37, 117.94, 139.14, 160.02.

Synthesis of 1-(4-iodophenoxy)-11-tosylundecane (6b)

To a Schlenk tube were added 11-(4-iodophenoxy)-undecanol (13.74 g, 35.2 mmol), triethylamine (5.89 mL, 5.0 mmol), 4-(dimethylamino)pyridine (0.172 g, 1.41 mmol) and 150 mL of dichloromethane. The mixture was added *p*-toluenesulfonyl chloride (8.05 g, 42.24 mmol) at 0 °C. After stirring for 45 h at room temperature, the resulting mixture was poured into water. The aqueous layer was extracted with CH₂Cl₂ and the combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude oil, which was purified by column

chromatography on silica gel to afford 17.22 g of **6b** (90%). The product was subjected to the following reaction without further purification.

Synthesis of diethyl 2-[11-(4-iodophenoxy)undecyl]maronate (**7b**)

The reaction was carried out in a manner similar to that described in the synthesis of **7a** to afford **7b** as white solid (85%). ¹H NMR δ 1.25-1.30 (m, 20H), 1.42 (tt, *J* = 7.7, 7.7 Hz, 2H), 1.75 (tt, *J* = 7.0, 7.0 Hz, 2H), 1.88 (m, 2H), 3.31 (t, *J* = 7.5 Hz, 1H), 3.90 (t, *J* = 6.5 Hz, 2H), 4.17-4.21 (m, 4H), 6.66 (m, 2H), 7.53 (m, 2H); ¹³C NMR δ 15.08, 26.96, 28.30, 29.73, 30.12, 30.19, 30.28, 30.33, 30.45, 30.47, 30.49, 53.08, 62.22, 69.12, 83.35, 117.94, 139.13, 160.02, 170.56.

Synthesis of 1,3-dihydroxy-2-[11-(4-iodophenoxy)undecyl]propane (**8b**)

The reaction was carried out in a manner similar to that described in the synthesis of **8a** to afford **8b** as white solid (87%). ¹H NMR δ 1.21-1.27 (m, 16H), 1.42 (m, 1H), 1.76 (m, 3H), 3.66 (dd, *J* = 10.5, 7.6 Hz, 2H), 3.82 (dd, *J* = 10.6, 3.8 Hz, 2H), 3.91 (t, *J* = 6.6 Hz, 2H), 6.66 (m, 2H), 7.53 (m, 2H).

Synthesis of the 2-[11-(4-iodophenoxy)undecyl]-1,3-ditosylpropane (**9b**)

The reaction was carried out in a manner similar to that described in the synthesis of **9a** to afford **9b** as white solid (87%). The product was

subjected to the following reaction without further purification.

Synthesis of 2-[11-(4-iodophenoxy)undecyl]-1,3-dimercaptopropane (**5b**)

The reaction was carried out in a manner similar to that described in the synthesis of **9a** to afford **9b** as white solid (96%). ¹H NMR δ 1.20 (t, J = 8.5 Hz, 2H), 1.22-1.43 (m, 18H), 1.68 (m, 1H), 1.76 (m, 2H), 2.62-2.74 (m, 4H), 3.91 (t, J = 6.6 Hz, 2H), 6.66 (m, 2H), 7.53 (m, 2H); ¹³C NMR δ 26.97, 27.74, 27.89, 30.13, 30.33, 30.51, 30.55, 30.70, 32.45, 43.65, 69.12, 83.38, 117.95, 139.14, 160.03.

Synthesis of 1,3-dihydroxy-2-[11-(4'-methyl-4-biphenyloxy)undecyl]propane (**12**)

To a Schlenk tube equipped with a magnetic stirring bar were added **8b** (44.8 mg, 0.1 mmol), 4-methylphenylboronic acid 1,3-propanediol ester (26.4 mg, 0.15 mmol), PdCl₂(PPh₃)₂ (3.5 mg, 0.005 mmol), aqueous solution of K₂CO₃ (2 M, 2 mL), and THF (0.6 mL) and the mixture was stirred for 23 h at 60 °C. The resulting mixture was poured into water and the aqueous layer was extracted with CH₂Cl₂ twice. The combined organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude solid, which was purified by column chromatography on silica gel to afford **12** as white solid (49%). ¹H NMR 1.24-1.40 (m, 16H), 1.46

(m, 2H), 1.79 (m, 3H), 3.66 (dd, $J = 10.6, 7.6$ Hz, 2H), 3.82 (dd, $J = 10.7, 3.8$), 3.99 (t, $J = 6.6$ Hz, 2H), 6.95 (m, 2H), 7.22 (m, 2H), 7.44 (m, 2H), 7.49 (m, 2H).

Synthesis of AuNP 10

To a flask equipped with a magnetic stirring bar were added $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$ (41.2 mg, 0.1 mmol), **5b** (48.1 mg, 0.1 mmol), and 8 mL of THF and the resulting solution was stirred at 40 °C for 3 h. THF (2 mL) solution of $t\text{BuNH}_2 \cdot \text{BH}_3$ (8.7 mg, 0.1 mmol) was then added to the reaction mixture at 55 °C. After stirring for 0.5 h at 55 °C, ethanol was added to the solution to precipitate AuNP, which was centrifuged to isolate the dithiol-capped AuNP **10** (19.6 mg) as dark brown powder.

The Suzuki-Miyaura coupling reaction of AuNP 11

To a flask equipped with a magnetic stirring bar were added dithiol-capped AuNP **10** (14.0 mg) and 10 mL of THF and the resulting mixture was sonicated to form a purple solution. 4-methylphenylboronic acid 1,2-ethanediol ester (17.6 mg, 0.1 mmol), $\text{Pd}(t\text{Bu}_3\text{P})_2$ (5.1 mg, 0.01 mmol), and an aqueous solution of K_2CO_3 (2 M, 2 mL). After stirring for 6 h at room temperature, the organic layer was collected. EtOH was added to the organic solvent to precipitate AuNP **11** (13.0 mg) as dark brown powder.

V-5 References

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Chapter VI

Conclusion

In this thesis, the Author focused on the transition-metal catalyzed coupling reactions of organosulfur compounds, thiophenes and thiols.

Chapter I

In this chapter, the objective and background of the research were shown. Previous studies and the purpose of this study were also described.

Chapter II

In this chapter, the mechanistic studies on the palladium-catalyzed CH arylation of thiophenes were carried out by stoichiometric reactions of organometallic complexes. The reaction of arylpalladium(II) halide with 2,3-dibromothiophene in the presence of AgNO_3/KF as an activator induced electrophilic substitution at the CH bond of the thiophene to give CH arylated product. The similar reaction of arylplatinum(II) halide with thiophene derivatives afforded the aryl(thienyl)platinum(II) complex which is an analogue of the corresponding intermediate of the palladium-catalyzed reaction. These findings strongly suggested that CH arylation of thiophenes with aryl iodide occurs by electrophilic substitution of the palladium complex

promoted by the activating reagent AgNO_3/KF . New reactivity of platinum complexes toward thiophenes was also found.

The Author next envisaged transition-metal catalyzed reaction at the surface of the thiol-capped AuNP. For facile preparation of AuNP, the Author carried out development of a synthetic method for AuNP in organic solvents.

Chapter III

The development of a new reducing agent for the facile synthesis of thiol-capped gold nanoparticles in organic solvents was described in this chapter. The addition of 1 equivalent of triethylsilane to a THF solution of $\text{HAuCl}_4 \cdot 4\text{H}_2\text{O}$, and 1-dodecanethiol afforded spherical AuNP with narrow dispersity. Since organosilanes are mild and less toxic reducing agents, this protocol is highly efficient and environmentally benign process.

It was also found that thiol-capped AuNP is prepared by treatment of alkyl organometallic reagents such as Grignard reagents and organolithium, -zinc, and -aluminum reagents. Since these organometallic reagents are ubiquitous reagent in organic synthesis that is readily available in a

laboratory scale, synthesis of AuNP with an alkyl organometallic reagent is available as a facile method.

Chapter IV

In this chapter, the Author carried out the synthesis of thiol-capped AuNP in various organic solvents. The Author also envisaged synthesis of thiol-capped AuNP from THP-protected thiols without deprotection.

Available organic solvents in the synthesis of thiol-capped AuNP have been limited to ethereal solvents in which HAuCl_4 is soluble. To carry out the synthesis of the AuNP in various organic solvents, the Author envisaged solubilization of gold(I) thiolate and following reduction to AuNP. It was found that tri-*n*-butylphosphine complex of the gold thiolate is highly soluble in various organic solvents. Synthesis of the AuNP was carried out in hexane, toluene, THF, and diethylether by reduction of tri-*n*-butylphosphine complex of gold(I)thiolate.

The Author found alkanethiol-capped capped AuNP was prepared from S-protected thiol with the tetrahydropyranyl (THP) group by treatment of HAuCl_4 in the presence of a reducing agent. Taking advantage of THP

group's characteristics, THP-protected thiol derivatives bearing functional groups were synthesized and subjected to the formation of functionalized AuNPs.

Chapter V

In this chapter, the Author examined surface modification of the AuNP by the Suzuki-Miyaura coupling reaction, which is the palladium-catalyzed cross-coupling reaction of an aryl halide and an organoboron reagent.

The AuNP bearing iodophenoxy group which was synthesized in the previous chapter was subjected to the Suzuki-Miyaura coupling reaction. However, agglomeration of the AuNP occurred during the reaction due to its low stability. Therefore, the Author synthesized the dithiol-capped AuNP which was more stable than the thiol-capped AuNP. The Suzuki-Miyaura coupling reaction carried out with dithiol-capped AuNP proceeded to give the surface-modified AuNP.

In conclusion, the results of the studies on the mechanism of palladium-catalyzed C-H arylation reaction of thiophene suggested that the reaction proceeds through electrophilic substitution. Accompanied by the reaction mechanism, a new reactivity in platinum chemistry to provide a pathway to thienylplatinum(II) complex was also revealed. In order to carry out the transition-metal catalyzed reaction at the surface of thiol-capped AuNPs, the Author envisaged development of the methods for facile synthesis of thiol-capped AuNPs in organic solvent first. As a result, the Author found novel reducing agents, a gold compound soluble to various organic solvents, and methodology for facile synthesis of thiol derivatives and AuNP using THP-protected thiols. Finally, the Author succeeded to perform the Suzuki-Miyaura coupling reaction with dithiol-capped AuNP. The Author wishes that these results may contribute to the development of transition-metal catalyzed reactions as a powerful tool for microfabrication of thiol-capped gold nanoparticles.

List of Publications

Chapter II

- 1) Observation of Sequential Electrophilic Substitution of Bromothiophene and Immediate Reductive Elimination of Arylpalladium Complexes
Sugie, A.; Kobayashi, K.; Suzaki, Y.; Osakada, K.; Mori, A. *Chem. Lett.* **2006**, *35*, 1100.
- 2) Electrophilic Substitution of Platinum(II) Complexes with Thiophene Derivatives
Mori, A.; Sugie, A.; Furukawa, H.; Suzaki, Y.; Osakada, K.; Akita, M. *Chem. Lett.* **2008**, *37*, 542.
- 3) Electrophilic Substitution of Thiophenes with Arylpalladium(II) and Platinum(II) Complex: Mechanistic Studies on Palladium-catalyzed CH Arylation of Thiophenes
Sugie, A.; Furukawa, H.; Suzaki, Y.; Osakada, K.; Akita, M.; Monguchi, D.; Mori, A. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 555.

Chapter III

- 4) Triethylsilane as a mild and efficient reducing agent for the preparation of alkanethiol-capped gold nanoparticle
Sugie, A.; Somete, T.; Kanie, K.; Muramatsu, A.; Mori, A. *Chem. Commun.* **2008**, 3882.
- 5) Synthesis of Thiol-capped Gold Nanoparticles with Organometallic Reagents as a New Class of Reducing Agent
Sugie, A.; Hatta, T.; Kanie, K.; Muramatsu, A.; Mori, A. *Chem. Lett.* **2009**, *38*, 562.

Chapter IV

- 6) Reduction of Gold(I) Thiolate with a Silane Reagent in a Wide Range of Organic Solvent Leading to Gold Nanoparticles
Sugie, A.; Yamanaka, T.; Ueda, Y.; Kanie, K.; Muramatsu, A.; Mori, A. *manuscript in preparation*

- 7) Generation of Gold Nanoparticles via Direct Thiol-capping with THP-protected Thiols without Deprotection
Sugie, A.; Somete, T.; Matsubara, M.; Kanie, K.; Muramatsu, A.; Mori, A.
Synlett, accepted

Chapter V

- 8) Surface Modification of Dithiol-capped Gold Nanoparticles via the Suzuki-Miyaura coupling reaction
Sugie, A.; Kanie, K.; Muramatsu, A. Mori, A.
to be submitted

The Author also contributed to the following papers and books

- 9) Palladium-Catalyzed CH Arylation and Dehydrogenative Homocoupling of Heteroaromatic Compounds and Application to the Design of Advanced Organic Materials
Mori, A.; Sugie, A. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 548.
- 10) PALLADIUM-CATALYZED ARYLATION AT C-H BOND AND C-C BONDS OF MASKED THIAZOLE DERIVATIVES
Furukawa, H.; Matsumura, S.; Sugie, A.; Monguchi, D.; Mori, A.
HETEROCYCLES, **2009**, *79*, 303.
- 11) Stepwise Construction of Head-to-tail-type Oligothiophenes via Iterative Palladium-catalyzed CH Arylation and Halogen Exchange
Masuda, N.; Tanba, S.; Sugie, A.; Monguchi, D.; Koumura, N.; Hara, K.; Mori, A. *Org. Lett.* **2009**, *11*, 2297.

List of Presentations

- 1) Studies on the reaction mechanism of Pd-catalyzed arylations of thiophenes at the C-H bond
Sugie, A.; Kobayashi, K.; Suzaki, Y.; Osakada, K.; Mori, A.
The 86th Annual Meeting of The Chemical Society of Japan, Chiba, 2006
- 2) Studies on the reaction mechanism of Pd-catalyzed C-H arylation of thiophenes
Sugie, A.; Suzaki, Y.; Osakada, K.; Mori, A.
The 87th Annual Meeting of The Chemical Society of Japan, Osaka, 2007
- 3) Studies on the C-H arylation of Bromothiophene
Sugie, A.; Kobayashi, K.; Suzaki, Y.; Osakada, K.; Mori, A.
The 53rd Symposium on Organometallic Chemistry, Japan, Osaka, 2006
- 4) One-phase Synthesis of Monodispersed Au Nanoparticles Using Silanes as a Reducing Agent
Sugie, A. Somete, T.; Mori, A.; Kanie, K.; Muramatsu, A.
The 88th Annual Meeting of The Chemical Society of Japan, Tokyo, 2008
- 5) 金ナノ粒子の新しい合成法
杉江敦司, 森 敦紀
若手フロンティア研究会 2007, 兵庫, 2007
- 6) Novel Synthesis of Thiol-Capped Au Nanoparticles in an Organic Solvent
Sugie, A.; Somete, T.; Mori, A.; Matsubara, M.; Kanie, K.; Muramatsu, A.
The 89th Annual Meeting of The Chemical Society of Japan, Chiba, 2009
- 7) 新規還元剤による金ナノ粒子の合成と表面の官能基化
杉江敦司, 染手隆志, 山中 武, 八田知勇, 森 敦紀
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