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COMMUNICATION

Chiral metal nanoparticles encapsulated by chiral phosphine cavitand with tetrakis-BINAP moiety: their remarkable stability toward ligand exchange and thermal racemization

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A chiral phosphine cavitand **1** induced the formation of chiral metal (Ru, Rh, Pd, Ag, Pt, and Au) nanoparticles (NPs). The ligand **1** of the chiral metal NPs prevents both thermal racemization and ligand exchange with a thiol, but the organic molecules can react with the metal surfaces. In contrast to the **1**-protected Au NPs, the BINAP-protected Au NPs easily undergo the ligand exchange and thermal racemization with aggregation.

Metal nanoparticles (NPs) have attracted significant research interest in recent years due to their importance in both fundamental science and technological applications such as catalysis, biomedicine, and chemical sensing.¹ Control of the surface properties and reactivities of metal NPs is an important aspect of developing nanomaterial applications. The size, shape, and surface properties of metal NPs are crucially controlled by the nature of protective ligands (stabilizers). The physical and chemical properties of metal NPs can be tuned by variations in both the nature of the ligand shell and the size of the metal core. A significant number of thiol-protected gold NPs has been reported.¹ The functionalization of gold NPs can be easily performed by the ligand exchange reactions of thiol- or phosphine-protected gold NPs with functional thiols. Thiol-protected gold NPs are known to exhibit a higher stability than the phosphine-protected gold NPs.² Therefore, triphenylphosphine-protected gold NPs can easily undergo the ligand exchange reaction to form the functionalized thiol-protected gold NPs with functional thiols.² Interestingly, the ligand exchange of thiol-protected gold NPs, [Au₂₅(SCH₂CH₂Ph)₁₈][TOA⁺], with an optically-active thiol provides the chiral thiol-protected gold nanoparticles.³

Chiral metal NPs have received much attention in many potential applications.^{4–6} The fundamental origin of chirality (chiroptical activity) in such metal NPs is still unclear, despite

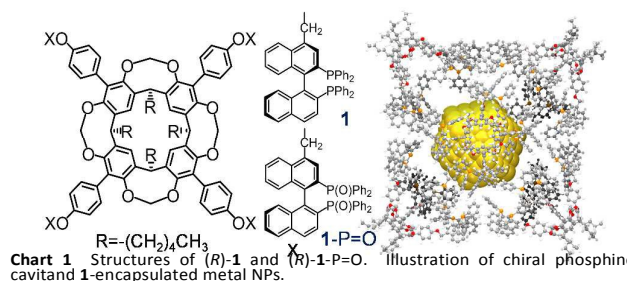
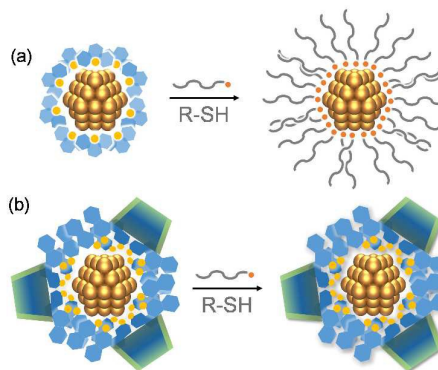


Chart 1 Structures of (R)-**1** and (R)-**1-P=O**. Illustration of chiral phosphine cavitand **1**-encapsulated metal NPs.



Scheme 1 (a) Ligand exchange of Ph₃P-Au NPs and BINAP-Au NPs with a thiol. (b) No ligand exchange: treatment of **1**-Au NPs with a thiol.

extensive theoretical and experimental studies in recent years.^{5–7} Although recent efforts toward understanding the chiral thiol-protected gold NPs have seen significant advances^{6b,8}, the chiral *phosphine*-protected metal NPs have received much less attention. We previously reported the first syntheses of chiral bis-phosphine, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl [BINAP: Chart S1⁹]-protected gold and palladium NPs, and asymmetric reactions using the chiral palladium NPs protected by BINAP as a catalyst.⁴ In order to prevent aggregation of the metal NPs during catalysis, the chiral metal NPs as a catalyst have required a stability for heating and for additive reagents in the reactions. Thus the

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use of the protective ligand of metal NPs requires both the prevention of aggregation of the metal NPs and desorption of the ligand from the metal surface.

We have been investigating the functionalization of protective ligands using a class of chiral multidentate phosphine cavitands; its adsorption on the nanoparticle surface can be significantly stabilized by multidentate interactions. We synthesized a chiral phosphine cavitand with a tetrakis-BINAP moiety (**1**, Chart 1 and Chart S1) which consists of the BINAP phosphine for the coordination site and resorcinarene¹⁰ framework for encapsulation of the metal NPs.⁹ The chiral phosphine cavitand **1** provides the following new aspects. (i) Several metal (Ru, Rh, Pd, Ag, Pt, and Au) NPs can be stabilized by **1**. The bis-phosphine BINAP itself cannot stabilize the Ru, Ag, and Pt NPs. The chiral phosphine cavitand **1**-protected metal (Ru, Rh, Pd, Ag, Pt, and Au) NPs showed different circular dichroism (CD) spectra, in which the chiral modifier **1** can induce a chiral character (chiroptical activity) to the metal-based electronic transitions. In contrast to **1**, the corresponding phosphine oxide (**1**-P=O, Chart 1) of **1** did not act as a protective ligand for the metal NPs. (ii) The ligand exchange between the phosphine **1**-protected gold NPs (**1**-Au NPs) with a thiol did not occur, indicating that the protective ligand **1** did not desorb from the gold surface by the addition of a thiol (Scheme 1b). In contrast to the **1**-Au NPs, the triphenylphosphine (Ph₃P)- and BINAP-protected gold NPs easily undergo a ligand exchange reaction to form the thiol-protected gold NPs upon treatment with a thiol (Scheme 1a). For the **1**-protected palladium NPs catalyzed Suzuki-Miyaura coupling reaction of arylboronic acid with an arylhalide, it was found that the molecules can react with the metal surfaces. (iii) The **1**-protected gold NPs showed a remarkable stability for prolonged heating, i.e., no racemization of the chiral **1**-protected gold NPs was observed during heating; this is the first observation of the remarkably stable chiral *phosphine*-protected gold NPs against thermal racemization, although there are very few reports on the thermal stability of the chiral *thiol*-protected gold NPs.¹¹ In contrast to the **1**-Au NPs, the racemization easily occurred for the chiral BINAP-protected Au NPs during heating.

The synthesis and property of the chiral phosphine cavitand **1**-protected metal NPs is described in the supporting information⁹. The chiral phosphine cavitand **1** is able to stabilize several metal (Ru, Rh, Pd, Ag, Pt, and Au) NPs. In contrast, we found that the Ru, Ag, and Pt NPs were not stabilized by the BINAP itself. The new chiral phosphine cavitand **1** works as a stabilizer (protective ligand) for several metal NPs. In contrast to the phosphine ligand **1**, it is noteworthy that the corresponding phosphine-oxide (**1**-P=O, Chart 1)⁹ cannot stabilize the metal NPs.

The particle size and size distribution of the metal NPs were determined by transmission electron microscopy (TEM) as: 1.26 ± 0.11 nm for **1**-Ru NPs, 1.93 ± 0.24 nm for **1**-Rh NPs, 1.14 ± 0.13 nm for **1**-Pd NPs, 1.76 ± 0.31 nm for **1**-Ag NPs, 1.01 ± 0.15 nm for **1**-Pt NPs, and 1.03 ± 0.14 nm for **1**-Au NPs.⁹ The UV-vis spectra of the **1**-Ru NPs, **1**-Rh NPs, **1**-Pd NPs, **1**-Ag NPs,

1-Pt NPs, and **1**-Au NPs are shown in Figures S1-S6⁹. The UV-vis spectra

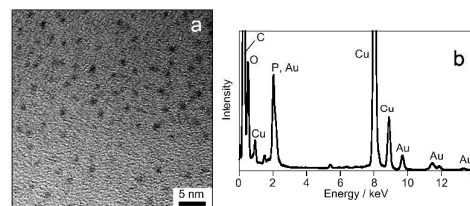


Fig. 1 **1**-Au NPs: (a) TEM image (scale bar = 5 nm) and (b) EDX spectrum: P (K α 2.013 KeV), Au (M 2.120, L α 9.712 KeV). Cu peaks are from the supporting copper grid.

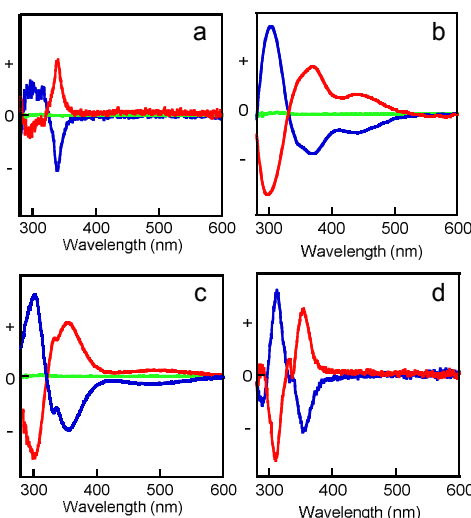


Fig. 2 CD spectra in CHCl₃, (R)-form (red line), (S)-form (blue line), and racemic (green line): (a) **1**, (b) **1**-Au NPs, (c) **1**-Pd NPs, and (d) **1**-Pt NPs.

(Figures S1-S6) exhibited no significant plasmon resonance, which is consistent with their smaller particle size as evidenced from the TEM observations (Figure 1a and Figures S2-S6). The elemental compositions of the metal NPs were confirmed by energy-dispersive X-ray (EDX) spectroscopy (Figure 1b and Figures S2-S6).⁹

The chirality of the metal NPs has been characterized by circular dichroism (CD) spectroscopy.⁹ The CD spectra of the chiral phosphine cavitand **1** showed an optical activity with a mirror image relationship for the two enantiomers having an absorption at 330 nm (Figure 2a). In contrast to ligand **1**, the CD spectra of the metal NPs showed characteristic absorptions at 370 nm and 440 nm for the (R)-/(S)-**1**-Au NPs (Figure 2b), while characteristic absorptions at 325 nm, 360 nm, and 500 nm (broad) were seen for the (R)-/(S)-**1**-Pd NPs (Figure 2c). Thus the CD spectra of the **1**-Au NPs and **1**-Pd NPs are distinctly different from the CD spectra of the free phosphine **1**. Each CD spectrum of the **1**-Ru NPs, **1**-Ph NPs, **1**-Pd NPs, **1**-Ag NPs, **1**-Pt NPs, and **1**-Au NPs is different as shown in Figures 2b-d and Figures S4-S6.⁹ It should be noted that a comparison of the CD spectra of the **1**-Au NPs to those of the **1**-Pd NPs exhibits a completely different CD spectra. Therefore, it is

concluded that the optical activity (chiroptical property) observed for the metal NPs covered by the chiral phosphine **1** is associated with the metal-based electronic transitions within the metal core. It is worth noting that all the metal NPs are stable for at least several months as evidenced by the TEM observations and the UV-vis and CD spectra.

We found that the phosphine **1**-protected palladium NPs (**1**-Pd NPs) catalyzed the Suzuki-Miyaura coupling reaction, i.e., the reaction of phenylboronic acid [$\text{C}_6\text{H}_5\text{-B(OH)}_2$, 1.5 mmol] with 4-bromotoluene [$\text{Me-C}_6\text{H}_4\text{-Br}$, 1 mmol] in the presence of a small amount of the **1**-Pd NPs (0.02 mol%) as a catalyst and Cs_2CO_3 as a base in THF at 50 °C for 5 h afforded the coupling product [$\text{Me-C}_6\text{H}_4\text{-C}_6\text{H}_5$, 90% yield]. We observed no aggregation of the Pd NPs as evidenced by the TEM observation after the reaction. This result reveals that the organic molecules can react with the surface of the palladium NPs protected by the phosphine **1**. Generally, the Suzuki-Miyaura coupling reactions are carried out at the refluxing temperature of the used organic solvents.¹² The phosphine **1** of the **1**-Pd NPs was found to be a good stabilizer, because the phosphine **1** stabilized the palladium NPs by preventing their aggregation. In order to confirm the behavior of the desorption of the protective ligand from the metal NPs, the ligand exchange of the phosphine **1**-protected Au NPs (**1**-Au NPs) with a thiol has been examined, i.e., a comparison study of the ligand exchange was conducted among the **1**-Au NPs, BINAP-Au NPs, and $\text{Ph}_3\text{P-Au}$ NPs (*vide infra*). Ligand exchange is a leading approach to functionalize the inorganic NPs. Gold NPs are among the most widely studied inorganic cores, yet the roles of the surface ligands are less understood. In contrast to the Au NPs, much less is known about the ligand exchange of the phosphine-protected Pd NPs with a thiol, and it was reported that the C-S bond undergoes cleavage of the thiol ligand in the thiol-protected Pd NPs.¹³ Based on these viewpoints, we have studied the ligand exchange of the phosphine-protected Au NPs with thiols, which are well known (*vide supra*)².

Significant results were obtained from the comparison of the triphenylphosphine-protected gold NPs ($\text{Ph}_3\text{P-Au}$ NPs), chiral (*R*)-/(*S*)-BINAP-protected gold NPs (BINAP-Au NPs), and **1**-Au NPs, for the ligand exchange reaction with a thiol (Scheme 1). For the ligand exchange reaction of the **1**-Au NPs, BINAP-Au NPs, and $\text{Ph}_3\text{P-Au}$ NPs with 1-octanethiol or 6-(pyrene)-butoxy-hexanethiol, the gold NPs were treated with an excess of 1-octanethiol (approximately 100 molar equivalent with respect to the NPs) in THF under an argon atmosphere. The reaction mixture was stirred under argon and dark conditions for 24 h. After the usual workup, the residue was characterized by UV-vis and NMR spectroscopies, TEM, and EDX spectroscopy. The ^1H NMR and UV-vis spectra of the obtained NPs (abbreviated as *RS-AuNP*) from the ligand exchange reactions of the BINAP-Au NPs and $\text{Ph}_3\text{P-Au}$ NPs with 1-octanethiol are consistent with those of the octanethiol-protected Au NPs prepared from the reduction of HAuCl_4 with NaBH_4 in the presence of 1-octanethiol.¹⁴ The UV-vis spectrum (Figure 3b-i) of the BINAP-Au NPs was changed to the UV-vis spectrum (Figure 3b-ii) of the *RS-AuNP* by the ligand exchange

reaction of the BINAP-Au NPs with 1-octanethiol. The TEM image (Figure 4a) of the *RS-AuNP* from BINAP-Au NPs showed that the particle size changed to ca. 3.4 nm when compared to the TEM image (Figure 3a) of the BINAP-Au NPs (ca. 1.2 nm).

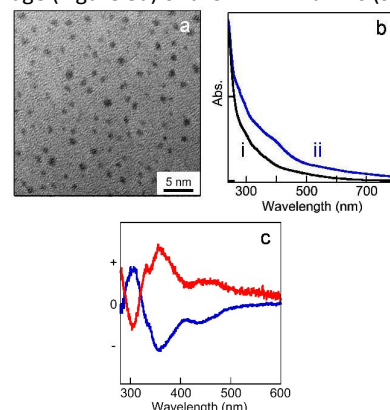


Fig. 3 (a) TEM image (scale bar = 5 nm) of BINAP-Au NPs. (b-i) UV-vis spectrum (black line) of BINAP-Au NPs in CH_2Cl_2 . (b-ii) UV-vis spectrum (blue line) of *RS-AuNP* formed from the ligand exchange of BINAP-Au NPs with octanethiol. (c) CD spectra of (*R*)-BINAP Au NPs (red line) and (*S*)-BINAP Au NPs (blue line) in CHCl_3 .

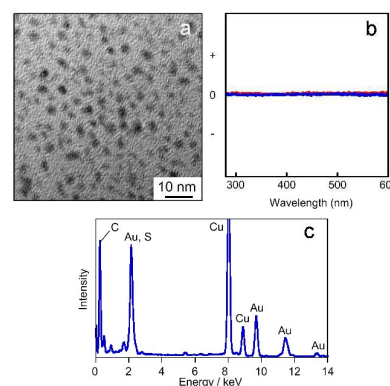


Fig. 4 *RS-AuNP*: (a) TEM image (scale bar = 10 nm), (b) CD spectra (CHCl_3), and (c) EDX spectrum of *RS-AuNP* formed from the ligand exchange of (*R*)/(*S*)-BINAP-Au NPs with the thiol **5** ($K\alpha$ 2.307 KeV). Cu peaks are from the supporting copper grid.

Similar results were observed for the *RS-AuNP* from the ligand exchange of the $\text{Ph}_3\text{P-Au}$ NPs with 1-octanethiol; the TEM images (Figures S7a and S8a) and UV-vis spectra (Figures S7b and S8b)⁹. The EDX spectrum (Figure 4c) of the *RS-AuNP* from the BINAP-Au NPs shows the presence of the sulfur atoms instead of the phosphorus atoms in the EDX spectrum of the BINAP-Au NPs. Notably, the CD spectrum (Figure 4b) of the *RS-AuNP* from the ligand exchange of the chiral BINAP-Au NPs (CD spectra: Figure 3c) with the thiol shows that the *RS-AuNP* is optically inactive, i.e., achiral. These data clearly demonstrate that the ligand exchange reaction of the BINAP-Au NPs and $\text{Ph}_3\text{P-Au}$ NPs easily proceed to form the thiol-protected Au NPs. In contrast to the BINAP-Au NPs and $\text{Ph}_3\text{P-Au}$ NPs, it should be noted that the chiral phosphine cavitand **1**-protected Au NPs (**1**-Au NPs) were remarkably stable upon treatment with 1-octanethiol as evidenced by the ^1H NMR, UV-vis, TEM, and EDX analyses. The EDX spectrum (Figure 5b) of the obtained NPs (abbreviated as **1**-Au NPs*) from the

treatment of the **1**-Au NPs with 1-octanethiol shows the absence of the sulfur element, i.e., the ligand exchange of the **1**-Au NPs with 1-octanethiol did not occur. Significantly, the CD spectra (Figure 5a) of the **1**-Au NPs* showed intense Cotton effects and a mirror-image relationship

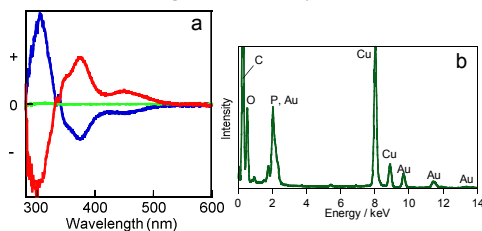


Fig. 5 **1**-Au NPs*: (a) CD spectra (CHCl_3) and (b) EDX spectrum of **1**-Au NPs* after treatment of (R)-**1**-Au NPs (red line) and (S)-**1**-Au NPs (blue line) with octanethiol. Cu peaks are from the supporting copper grid.

in the measured range, i.e., the chirality of the **1**-Au NPs is retained during the reaction with 1-octanethiol. It is worth noting that these data demonstrate that the protective ligand **1** of the **1**-Au NPs did not desorb from the metal surfaces. The multidentate phosphine ligand **1** is strongly attached to the metal surface by the multidentate interactions. The detailed studies of the multidentate interactions by **1** are currently in progress. This strong protection of the metal NPs was also observed during the heating of the **1**-Au NPs, i.e., the remarkable stability of the phosphine cavitand **1**-protected Au NPs was observed in comparison to the Ph_3P -Au NPs and BINAP-Au NPs during heating.

The thermal stabilities of the **1**-Au NPs, BINAP-Au NPs, and Ph_3P -Au NPs have been studied as follows. A solution of the Au NPs (10 mg) in toluene (5 mL) was heated at 100 °C for 24 h. After heating, the resulting Au NPs were confirmed by spectroscopic characterization. Again, the differences are seen in the comparison. It was observed that a significant aggregation of the Ph_3P -Au NPs and the BINAP-Au NPs occurred after heating as evidenced by the TEM images (Figure S9). Racemization was found during the heating of the BINAP-Au NPs as observed in the CD spectra. However, the **1**-Au NPs did not significantly show aggregation of the nanoparticles and the chirality of the **1**-Au NPs was maintained even after a prolonged heating, as proven by the TEM and CD spectroscopic results (Figure S10).¹⁵ This is the first example of the remarkably stable *chiral phosphine*-protected Au NPs against thermal racemization, although racemization and stability of the chiral thiol-protected Au NPs during heating have been reported.¹¹

In summary, a chiral protective ligand **1** bearing the tetrakis-BINAP moiety can stabilize several metal NPs, while the corresponding phosphine oxide **1**-P=O of **1** did not work as a protective ligand for the metal NPs. The chiral phosphine cavitand **1** induced the formation of remarkably stable chiral gold NPs toward ligand exchange with a thiol and thermal racemization. In contrast, the BINAP itself-protected gold NPs showed thermal racemization along with aggregation during heating and the occurrence of ligand exchange between the protective ligand **1** and a thiol. The chiral modifier **1** can prevent desorption of the protective ligand from the particles'

metal surface by the addition of organic molecules, and does not block access of molecules to the metal surfaces, i.e., the Suzuki-Miyaura cross-coupling catalyzed by the **1**-protected palladium NPs.¹⁶ The work reported here points a new direction to design chiral protective ligands for stabilization of metal NPs and chiral nanocatalysts for asymmetric synthesis. Further studies of the structures and properties of the **1**-protected metal NPs are now in progress.

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