Dedication

To Dandan Liu, Qing Liao, and Lijia Du;

To my parents, and grandparent.
Acknowledgement

I would like to thank my advisor Dr. Amanda Jones, for her guidance, enthusiasm, and expertise in chemistry. As a scientist, she showed me beautiful parts of chemistry and helped me catch a high standard. I appreciated her help in experiment design and record.

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I would like to thank my parents and grandparents, for their love and support. Whenever I felt lonely and defeated, they always gave me the encouragement to overcome those negative emotions. I think I should make better things happen in the future because of you.
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<tbody>
<tr>
<td>Ac</td>
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</tr>
<tr>
<td>Bu</td>
<td>butyl</td>
</tr>
<tr>
<td>Cbz</td>
<td>benzyloxy carbonyl</td>
</tr>
<tr>
<td>ee</td>
<td>enantiomeric excess</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
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<tr>
<td>Ipr</td>
<td>1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene</td>
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<td>Johnphos</td>
<td>(2-Biphenyl)di-tert-butylphosphine</td>
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Abstract

Zhou, Wentong

Characterizations of gold complexes and mechanism of its usage in π-bond activation reactions

Thesis under the direction of

Amanda C. Jones, Ph. D., Assistant Professor of Chemistry

Research on homogeneous gold (I) catalyzed chemistry has made many exciting discoveries during the last few decades. The gold catalysts have been applied in many interesting chemical transformations, especially in π-bond activation reactions to initiate nucleophilic addition. But experimental studies focused on gold heteroatom π-complexes were still limited. It is significant to research on the intermediates involved in gold-catalyzed reactions. Many groups have studied methodology and computational model to prove the reactivity of gold catalysts, but experimental evidences of gold-catalyzed mechanisms are still lacking. Alternatively, “silver effect” is an interesting topic in gold chemistry, which means that silver may be involved in some gold-catalyzed reactions. So we focus on the ligand effect of gold complex and their roles in gold-catalyzed reactions. The first chapter summarizes the mechanistic background of gold(I)-catalyzed reactions and development of gold(I)-catalyzed additions to C-C double or triple
bond. Moreover, the ligand effect of gold complexes is also discussed. The second chapter described a novel $\pi$-gold complex we isolated and this process may help us establish more detailed structure-activity relationships of ligands and discover the new gold catalysts with more efficient reactivity. The third chapter discusses about the use of trigold oxonium species to generate alkyl gold intermediates and its kinetic studies. Its use with or without base showed different results. The fourth chapter discussed about “silver effect” in gold chemistry and our preliminary work about how to find out some new silver-gold intermediates. It also discussed about some future work. Variable temperature NMR and crystallography are used in the thesis.
Chapter 1 Introduction

1.1 Introduction of Gold metal and Gold(I) complexes

1.1.1 Gold as a precious metal

The value of gold metal has been identified by human being since the beginning of known history. It is linked with beauty, wealth, authority. It also encourages a lot of people to discover its secret.

Most of gold is found on earth in its elemental state due to its inertness. It is hard to degrade under most conditions. And it is also a rare metal. The total amount of gold on earth is very low. This is also a reason why gold metal was highly valued in human society. So gold was considered as a medium of monetary exchange for a long time. Until now, it is also one of the popular investments in financial market through direct ownership or other exchange-traded funds or certificates.¹

Gold metal was also applied in many fields of industry. It can be used to coat many other materials to protect against radiation or heat. It can also be used as a reflective layer in many optical devices or a coloring agent in many special types of glass. A more important application of gold is that it can be used as a thin layer coating for electrical connectors or bondwiring semiconductors.²

1.1.2 Gold(I) catalysis in organic chemistry

Unlike many other metals which have been applied in organic transformation for many years, gold was always considered to be chemically inert. However, in recent decades,
the gold has been found to make efficient catalysts in the (I) and (III) oxidation states. Moreover, the gold(I) catalysts have been applied in many interesting chemical transformations, especially in $\pi$-bond activation reactions to initiate nucleophilic addition reactions. \(^3\)

Theoretically speaking, the reactivity of Au (I) complexes is attributed to the relativistic effect which contracts the 6s orbital and expands the 5d orbital of the gold atom. (Figure 1).\(^4\) This effect will increase the $\pi$-acidity and electron delocalization of gold complexes, which makes gold complexes show stronger coordination with $\pi$ bonds and backbonding to form gold cations and carbenoids. These intermediates will facilitate gold catalyzed reactions.

![Figure 1 relativistic effect of gold catalysts.](image)

Among all the gold(I) complexes used in gold catalysis, a ligand is generally needed to stabilize the gold metal center. Phosphines or N-heterocyclic carbenes are the most common ligands. The other bond attached to the Gold center can be either covalent
(typically being a Cl) or cationic (BF$_4^-$, SbF$_6^-$, TfO$^-$ etc.). The figure below shows that most common gold(I) complexes, both covalent and cationic (Figure 2). 

![Figure 2 gold complexes with a strong σ-donor ligand](image)

Generally, most of gold complexes with proven catalytic efficiency are the cationic gold complexes. Even many of those gold intermediates are hard to characterize or isolate. Moreover, the properties of gold complexes can be influenced by different ligands.

Several digold complexes have been reported as active catalysts in many transformations. In some cases, stereoselectivities can be obtained when some chiral diphosphine ligands were used. (Figure 3)$^7$

A enantioselective gold-catalyzed hydroamination reaction was reported when a chiral ligand was used. (Figure 3) Generally, the cationic gold complex cannot induce the chirality. But in this case, a specific counter ion (blue in (a)) was applied to improve the
enantioselectivity of gold catalysts. A possible explanation is that counter-ions attach with the gold complex by charge attraction, which makes gold complexes close enough to the substrate to control the enantiomeric outcome of the reaction. (c in Figure 3)

Figure 3(a) digold complexes with chiral diphosphine ligands (b) a reaction showing that chiral ligands can improve the enatioselectivity of gold-catalyzed reaction (c) a possible explanation about enatioselectivity of chiral ligands
Another kind of gold species $L_2Au^+$ (a in Figure 4) is also reported. This kind of bisphosphine gold species is more stable than LAuX cationic gold(I) complexes, but their catalytic activity is limited. In most cases, these species are formed as side products from gold-catalyzed reactions. Other polynuclear cationic gold(I) complexes are also reported. (b, c in Figure 4) They are stabilized by Au-Au interactions. They can be used to form alkyl gold intermediates in some cases, but their catalytic activity is still needed to be understood better.

$L=$triphenylphosphine, or (2-biphenyl)di-t-butylphosphine

Figure 4 polynuclear cationic gold(I) complexes

1.2 Reactions and properties of Gold(I) complexes

1.2.1 General mechanism of Gold(I) catalyzed reactions

Most gold-catalyzed reactions go through three major stages (Scheme 1). In stage 1, a nucleophilic attack on a $[AuLn]^+$-activated alkyne (or alkene) proceeds via a $\pi$-complex to give a trans-alkenyl gold complex intermediate (or an alkyl gold complex in the case...
of alkenes). In stage 2, the resulting vinyl complex reacts with acid to yield the final product via protodeauration; this step also serves to regenerate the cationic gold species. In almost all gold-catalyzed reactions, there is a decay or deactivation of the gold catalyst usually through the reduction of cationic gold to gold (0) and some other uncharacterized reactions (stage 3).

The gold(I)-catalyzed homogenous transformations have shown great diversity, because in many reported examples, various nucleophiles can be applied. They can be nitrogenated, oxygenated or carbonated. Moreover, both inter- or intramolecular reactions can be accomplished. And the backbonding of gold can stabilize the organogold intermediates to facilitate various rearrangements, eliminations or nucleophilic attacks.

The π systems that can be activated by gold(I) complexes also show extraordinary diversity. Alkenes, alkynes, and allenes can also be used as substrates.\textsuperscript{11}

\begin{center}
\textbf{Scheme 1} three stages in general gold catalytic cycle reproduced from J. Am. Chem. Soc. 2012, 134 (12), 5697–5705
\end{center}
1.2.2 Gold(I) catalyzed reactions.

In total synthesis, Au (I) complexes have been utilized as very beneficial reagents to install a wide range of molecular motifs. In the total synthesis of bryostatin (Scheme 2), gold catalysts show their capability to covert a large ring into a dihydropyran regioselectively under mild conditions. An efficient route to highly substituted dihydropyran has been obtained in this case.

Scheme 2 Total synthesis of bryostatin using atom-economical and chemoselective approaches with gold catalyst.
As we discussed above, many nucleophiles can react using gold catalysis. Different kinds of ketones (Scheme 3)\textsuperscript{13}, enamines or enol ethers can be obtained through intermolecular attacked to gold(I)-activated C-C $\pi$-bonds.\textsuperscript{14,15}

\begin{center}
\includegraphics[width=0.8\textwidth]{scheme3.png}
\end{center}

\textbf{Scheme 3 gold-catalyzed intermolecular reactions}

Intramolecular transformations (Scheme 4) are also applicable under gold(I) catalytic cycle. Synthesis of a wide range of heterocycles can be obtained under 5-\textit{endo}, 5-\textit{exo} and 6-\textit{exo} cyclization attacks.\textsuperscript{16}

Many carbonated groups can also be used as nucleophiles for the attack on C-C multiple bonds. Usually these kind of transformation is intramolecular, forming different kinds of carbocycles starting from some simple starting materials, such as enynes.\textsuperscript{17}
Mechanism of these gold catalyzed reactions may involve some other intermediates.

(Scheme 5) Gem-diaurated species as intermediates in gold catalytic transformations
have been observed. These species can be obtained in situ in gold intramolecular dialkyne cyclization reactions. However, investigation on the behavior of these species is still limited. Some groups suggest that gem-diaurated species are reversible with mononuclear organogold complexes, but the role of them in the gold-catalyzed reactions is still vague. A possible explanation could be the formation of a highly stable gem-diaurated intermediate inhibiting the catalytic cycle, but perhaps a catalyst with a sterically demanding ligand could destabilize gem-diaurated Au compounds and therefore restore catalytic activity. Recently, the involvement of diaurated species was found in a standard catalytic hydroalkoxylation process,¹⁹ which can be proven by direct observation of the species in situ during reaction based on ¹H NMR spectra. So it is interesting to find out more cases that involve these diaurated species and finally delineate the role of these species in gold catalysis.
1.3 Ligand effect and design in gold (I) catalysis.

Based on the different stages in gold catalyzed processes, gold complexes with different ligands show different influence on the kinetic behavior and decay rates during reactions. Generally, the electron-deficient ligands promote electrophilic activation and electron-donating ligands promote protodeauration. (Figure 5) When the protodeauration is the rate-determining step, a gold catalyst with an electron-rich ligand has a higher turnover frequency compared to a standard Ph₃PAu⁺. In the case of a hydroamination reaction in
which protodeauration is the rate-determining step, an electron-rich ligand with an $\eta^2$ interaction gave the better result. $L_3$ shows the best result because this ligand can form the more stable cationic gold complex which can improve turnover rate. When the rate-determining step is electronic activation of Alkyne/Alkene, an electron-poor ligand will facilitate the vinyl gold formation and increase the overall reaction rate in this type of reactions.\textsuperscript{10} The example below is rearrangement of allenyl ester in which rate-determining step occurs in stage 1. Gold catalysts with different ligands show different conversion rates in reactions with different rate-determining steps.

**Figure 5** gold catalysts with different ligands show different conversion rates in reactions with different rate-determining steps.
The turnover of gold catalysts is limited because of the decay of cationic gold.\textsuperscript{10} Cationic gold is gradually reduced to Au(0) and Ln\textsubscript{2}Au\textsuperscript{+} species. So investigation on the ligand that can increase the stability of gold cationic species is important. Compared with the triphenylphosphine ligand, the ortho-substituted phenyl ring stabilizes the generated cationic gold complex through a $\eta^2$ interaction. (Figure 6)\textsuperscript{22} Further work is still needed to better understand how specific ligands can influence the formation and decay of key gold intermediates.

![Figure 6](image-url)

\textbf{Figure 6} ligand effects on the decay of cationic gold species. Kinetic plot reproduced from J. Am. Chem. Soc. 2012, 134 (12), 5697–5705
1.4 “Silver effect”

The presence of silver, which was thought just to form silver-free cationic gold complexes and inactive AgCl precipitation, may in fact directly influence with gold complexes and help the reactivity.

In gold-catalyzed simple alkyne hydration (Figure 7)\textsuperscript{21}, the optimal catalyst is (IPr)AuCl/AgSbF\textsubscript{6} mixed one without filtration, which means that the mixed Ag/Au complex may be involved in the catalytic cycle. But neither filtrated IPrAuSbF\textsubscript{6} nor sole AgSbF\textsubscript{6} show the same reactivity as the optimal catalyst.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure7.png}
\caption{The role of silver in gold catalytic cycle, spectra reproduced from J. Am. Chem. Soc. 2012, 134 (21), 9012–9019}
\end{figure}

A few examples show that the Au/Ag mixed species can be isolated and characterized. A unique trimetallic chloronium dication (Figure 8)\textsuperscript{22} was isolated and characterized in our
lab. The ability to synthesize and characterize mixed complexes is necessary to determining their role in catalysis. We propose to extend the knowledge of these species and investigate the potential new catalytic mechanism, which will help us design some new catalysts.

Figure 8 crystal structure of a unique trimetallic chloronium dication species
Chapter 2 Synthesize, structurally characterize phosphine gold (I) heteroatom π-complexes

Cationic gold(I) catalysts have been applied in the activation of multiple bonds, especially in the area of nucleophile addition to activated π-systems such as alkynes and allenes.\textsuperscript{23} As intermediates in these addition reactions, gold(I) π complexes especially gold(I)-hydrocarbon π-complexes have received much attention. However, some of gold(I) heteroatom π-complexes with silyl alkenes have not been investigated. The reasons for making gold(I) complex coordinated with silyl alkenes are i) silyl alkenes may give the complexes formed sufficient stability to be isolated in solid states; ii) the coordinated gold complexes with silyl alkenes may be used as models to research gold silane transmetalation. We still want to get the optimized conditions and procedures to make this kind of π complexes by making the stabilized gold(I) silyl alkene π-complexes.\textsuperscript{24}

Widenhoefer group synthesized and characterized a group of monomeric, cationic triphenylphosphine–gold(I) complexes that contain a alkyne, conjugated diene, or allene ligand based on low-temperature NMR. Each of those gold complexes are thermally unstable (Scheme 6).\textsuperscript{23} But we successfully observed and isolated a stable o-biphenyldiphenylphosphine-gold(I) complexes and the crystal structure of it can be obtained in the room temperature.
We used o-biphenyldiphenylphosphine ligand in this experiment mainly because it shows higher stability than triphenylphosphine ligand and similar properties as some other triarylphosphine ligand including triphenylphosphine one. AgSbF₆ will be used to form the cationic gold(I) species.

Scheme 6 (a) previously reported triphenylphosphine-gold complexes were unstable and decayed to bisphos gold complexes when temperature increase to higher than -20oC (b) o-biphenyldiphenylphosphine gold complex with trimethylvinylsilane is stable in room temperature
Binding silyl alkene to gold in solution can be established in $^1$H NMR spectra by $^1$H-$^{31}$P coupling across gold as well as by significant chemical shift effects. In the example provided, coupling through gold is observed for terminal protons ($^3J_{P,H} = 3.5$ Hz), another proton ($^2J_{P,H}=2.4$ Hz) and all of three protons were upfield relative to free trimethylvinyl silane. (Figure 9) The proton shift effects can be attributed to an increase in positive charge at the silicon-substituted carbons, concomitant with distorted coordination. This π–complex is more stable than triphenylphosphine gold(I) complexes which will decompose to form bisphos gold species in room temperature. (Figure 10) Over the increase in temperature up to room temperature, it didn’t suffer from decomposition. It decayed to bisphos species after 20 hours, and the ratio of bisphos species to gold π

![Figure 9 1H NMR of o-biphenyldiphenylphosphine gold vinyl silane π complex (WTZ-1045)](image-url)
complex is 1:5 based on $^{31}$P NMR (b in figure 10). The result shows that gold $\pi$
complexes formation can be stabilized by changing different ligands. We can develop a
general protocol to make some other stabilized gold $\pi$ complexes showing different
interests in different aspects of gold catalytic cycle.

![Figure 10](image)

*Figure 10 (a) stability of o-biphenyldiphenylphosphine gold vinyl silane $\pi$ complex over increasing temperature (b) o-biphenyldiphenylphosphine gold vinyl silane $\pi$ complex decayed to bisphos species ($^{31}$PNMR $\delta37.8$) after 20 hours*

The preliminary kinetics study was done. The result showed that the coalescence
temperature of this complex is about $-35^\circ$C. We estimate the exchange rate is about $45$ s$^{-1}$

$^1$ The energy barrier ($11.76$ kcal/mol) of this complex exchange is higher than that of
triphenylphosphine gold $\pi$-complex which was reported in the range between 10 kcal/mol and 11 kcal/mol depending on different $\pi$ ligands.

Figure 11 kinetic study and exchange rate of o-biphenyldiphenylphosphine gold vinyl silane $\pi$ complex.
In order to reconfirm the stabilization effect of o-biphenyldiphenylphosphine ligand\textsuperscript{25}, we tried to make the gold cyclohexene $\pi$ complex. This $\pi$-complex is more stable than triphenylphosphine Au(I) complex in room temperature over at least 24 hours, and little amount of decomposition was formed in this process. (Figure 12) The kinetic study of decay of this species is proposed. Moreover, because detailed information about $\pi$ complex in situ formation in gold catalyzed reactions is still limited, we propose to use some other alkenes involved in gold catalyzed reactions to find some evidences about in situ gold $\pi$ complexes formation.

![Potential decomposition product bis(o-biphenyldiphenylphosphine)Au](image)

**Figure 12** formation of o-biphenyldiphenylphosphine gold complex with cyclohexene and its stability after 24 hours (WTZ-1056)
We proposed to make some other Au $\pi$-complexes using specific ligands which can improve the stability and potential reactivity of those species. (Scheme 7) Specifically, we propose to make a stabilized gold heteroatom-substituted allene complex due to limited information about those kind of complexes.

Scheme 7 proposed synthesis of o-biphenyldiphenylphosphine gold $\pi$ complexes with methoxypropene and N-substituted allene

Experimental Section

Unless otherwise noted commercial materials were used without further purification. Complexes were prepared in an oxygen-free, moisture-free glovebox or under Argon using Schlenk techniques. Gold and silver salts were purchased from Strem Chemicals and used as received. NMR spectra were obtained on Bruker spectrometers operating at a proton frequency of either 300 MHz or 500 MHz.
Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ). Deuterated solvents (CD$_2$Cl$_2$, CDCl$_3$) were purchased from Cambridge Isotope Laboratories.

**o-biphenyldiphenylphophine gold chloride:** To dimethylsulfide gold chloride (32 mg, 0.1 mmol) CH$_2$Cl$_2$ solution was added o-biphenyldiphenylphophine ligand (37.2 mg, 0.11 mmol). The mixture was stirred for 4 hours under argon protection and then was evaporated under reduced pressure. (yield 94%) $^1$H NMR (300 MHz, Methylene Chloride-$d_2$) δ 8.36 – 6.16 (m, 19H). $^{31}$P NMR (121 MHz, Methylene Chloride –$d_2$) δ 26.19. $^{13}$C NMR (75 MHz, Methylene Chloride-d2) δ 151.54, 140.48, 134.90, 134.71, 134.12, 132.15, 132.11, 130.18, 129.61, 129.45, 128.61, 128.55. Elemental Analysis calculated %C 50.5 %H 3.36 found: %C 50.32 %H 3.23

**bis(o-biphenyldiphenyl)phophine Au$^+$SbF$_6^-$:** To o-biphenyldiphenyl gold chloride (30 mg) CH$_2$Cl$_2$ solution was added o-biphenyldiphenyl ligand (17.7 mg). The mixture was stirred for 2 hours and evaporated under reduced pressure. 1H NMR (300 MHz, Methylene Chloride-$d_2$) δ 7.72 – 6.87 (m), 6.2 (b, J = 7.2, 1.5 Hz), 2.4 (m). $^{31}$P NMR (121 MHz, Methylene Chloride-d2) δ 37.67. Elemental Analysis calculated %C 51.96 %H 3.45 found: %C 51.70 %H 3.71

**[o-biphenyldiphenylphophine Au][trimethylvinyl silane]$^+$$SbF_6^-$:** AgSbF$_6$ (21.1 mg) as mixed with gold chloride (35 mg) in oxygen-free, moisture-free glove box. The mixed solids were dissolved in CH$_2$Cl$_2$ under argon protection in the hood. After stirred for 5 minutes, the mixture was centrifuged to get the upper layer liquid, and it was evaporated
under reduced pressure to give the white solid. Then it was dissolved in CD$_2$Cl$_2$,
trimethylvinyl silane (3 μl) solution and variable temperature NMR spectra from -60°C to
room temperature were obtained. $^1$H NMR (500 MHz, Methylene Chloride-$d_2$) δ 7.95 –
6.90 (m, 19H), 6.08 (ddd, J = 20.0, 12.9, 2.4 Hz, 1H), 5.25 (dt, J = 12.9, 3.5 Hz, 1H), 5.02
(dt, J = 20.0, 3.5 Hz, 1H), 0.07 (s, 9H). $^{31}$P NMR (202 MHz, Methylene Chloride-$d_2$) δ
44.33.

$[\text{o-biphenyldiphenylphosphine Au}][\text{cyclohexene}]^{+}\text{SbF}_6^-$: AgSbF$_6$ (21.1 mg) as mixed
with gold chloride (35 mg) in oxygen-free, moisture-free glove box. The mixed solids
were dissolved in CH$_2$Cl$_2$ under argon protection in the hood. After stirred for 5 minutes,
the mixture was centrifuged to get the upper layer liquid, and it was evaporated under
reduced pressure to give the white solid. it was dissolved in CD$_2$Cl$_2$, cyclohexene
solution (3 μl). $^{31}$P NMR (202 MHz, Methylene Chloride-$d_2$) δ 29.8.
Chapter 3 Use of gold oxonium species to form alkyl gold intermediates and its kinetic study

Recently, a number of organogold intermediates were isolated from stoichiometric reactions, which helps to better understand the mechanisms. Meanwhile, the reactivity of organogold compounds has been attracting the attention of organic chemists in the field.

The vinyl gold and alkyl gold complexes are the key intermediates in researching mechanisms of gold(I)-catalyzed nucleophile additions. These species are thought to be key intermediates in gold-catalyzed reactions to facilitate the formation of final products. Many of the key vinyl gold intermediates have been observed. In previous reports, Johnphos trigold oxonium species have been applied to make alkyl gold intermediates which cannot turn out to final organic products. Moreover, the isolation of crystal structure of Johnphos gold oxonium species gold intermediates have been observed. But the isolation of these species is still limited. Trigold(I) oxonium species have been found to be useful gold species to form alkyl gold intermediates. Moreover, it will help us discover the conditions about gold catalytic turnover and optimize the reaction conditions of gold catalysts.

The reason for choosing gold oxonium species to make alkyl gold species is as below: i) the reactivity of gold oxonium species as catalysts has been proved, but the detailed information about how these species behave during catalytic cycle is still unclear; ii) the procedure to make alkyl gold species using gold oxonium has been reported; iii) the information about ligand effects on gold oxonium species is limited; iv) gold oxonium
species is moisture insensitive and will be facile to use if these species can be used as catalysts.\(^{28}\)

The preparation of gold oxonium species is under moisture conditions,\(^{28}\) using molecular sieves as catalyst. (Figure 14) But some other species was formed in the process. One of those species is digold hydronium. The ratio of those formed species is in a time-dependent manner. When the reaction was run within two hours, the major product was gold hydronium, and when the reaction was run overnight, only gold oxonium was the major product. Another minor product was gold-acetone complex. The formation of this complex is due to addition of acetone and the basic and moisture condition. Addition of acetone can make gold complexes dissolved better in moisture condition, which will facilitate the overall reaction efficiency.

Figure 13 crystal structure of Johnphos gold oxonium species
Figure 14 preparation of Johnphos gold oxonium and hydronium (WTZ-2141,2145)
Toste group reported a facile aminoauration to form alkyl gold complexes under the treatment of urea or carbamates with triphenylphosphine gold oxonium species \([(\text{Ph}_3\text{PAu}_3\text{O})\text{BF}_4]\). But the catalyst turnover is limited in these cases, which is consistent with the reported examples that many alkene addition reactions are catalyzed solely by Bronsted acid. So the protodeauration process in general gold-catalyzed alkene addition mechanism may need to be explored further. Kinetic studies have been done to explore the details of this process. (Scheme 8)

![Scheme 8 proposed reaction using urea as substrate and gold oxonium species as catalyst](image)

We have done the kinetic study of cyclization of urea catalyzed by gold oxonium species in the absence of base. (Figure 15) This is proposed to understand the influence of base in previous reported cases. As observed previously by Yuyang Zhu, when triphenylphosphine gold oxonium is used, the inactive product \([(\text{Ph}_3\text{P})_2\text{Au}]\text{BF}_4\) was identified as the main byproduct. And when urea was treated with triphenylphosphine gold oxonium, the final cyclized product was formed gradually after rapid formation of alkyl gold species and byproduct bisphos species.
We also tried the urea cyclization reaction catalyzed by Johnphos gold oxonium species (Figure 16). Alkyl gold and digold hydroxide were formed intermediately and the cyclized product was formed gradually. What is different from the triphenyl gold oxonium-catalyzed is that inactive bisphos gold species was not observed. The ratio of alkyl gold species did not change over the course of the reaction. That may prove protodeauration does not occur during cyclization. Instead the newly formed digold hydroxide species (A) may mediate the gold-catalyzed cyclization.
Figure 16 concentration vs. time plot about cyclization of urea using Johnphos trigold oxonium and 31PNMR spectra (WTZ-2049)
Figure 17 kinetic study of cyclization of urea using Johnphos trigold oxonium (black points-cyclized product, circle-starting material, triangle-alkylgold intermediate) (WTZ-2049)
Variable gold concentration experiments were performed with commercial [(Ph₃PAu)₃O]BF₄ (0.1, 0.5, 1 equivalents). (Figure 18) Similarly, the alkyl gold intermediate was formed intermediately and the cyclized product was formed gradually, but the digold hydroxide has not been identified. The increase in [(Ph₃PAu)₃O]BF₄ resulted in an increase in the amount of alkyl gold species formed and the disappearance rate of the alkyl gold. However, considerable amounts of alkyl gold still exist after 8 hours. Moreover, the formation of cyclized product was inhibited by increased concentration of alkyl gold.

Figure 18 kinetic study of cyclization of urea using triphenylphosphine trigold oxonium (0.1 eq WTZ-2107, 0.5eqWTZ-2109, 1eqWTZ-2143)
The kinetic study of urea cyclization catalyzed by Johnphos gold hydroxide has also been done. (Figure 19) Variable concentration of Johnphos gold hydroxide (0.8eq, 0.28eq, 0.1eq) was used in these experiments. The results showed that only cyclized product was formed, and based on $^{31}$PNMR, only gold species left after reaction was the starting Johnphos gold hydroxide. Only small amount of alkyl gold can be observed when 0.8 equivalent of Johnphos gold hydroxide was used.

Figure 19 kinetic study of cyclization of urea using triphenylphosphine digold hydroxide (0.1 eq WTZ-2119, 0.28eq WTZ-2121, 0.8eq WTZ-2147)
The general mechanism (Scheme 9) was proposed based on the previous experiments. The formation of cyclized product was catalyzed by digold hydroxide. When we use gold oxonium as catalysts, a lower starting concentration of trigold oxonium will inhibit the entry of alkyl gold into the catalytic cycle. A higher concentration of gold oxonium will inhibit the formation of cyclized product. This supports the conclusion that protodeauration of alkyl gold is not the effective pathway to form cyclized product.

Scheme 9 proposed mechanism of gold-catalyzed cyclization involving a basic gold intermediate (digold hydroxide species)

Future work should be done to answer some key questions in the proposed general mechanism. The first one is how the formation of digold hydroxide influences the chemical equilibrium between starting gold complexes and the alkyl gold intermediates.
Because it is hard to observe the digold hydroxide in triphenylphosphine gold oxonium-catalyzed urea cyclization, the kinetic study using Johnphos gold oxonium should be finished. Furthermore, the reaction profiles when using digold hydroxide species as catalysts are also needed to be clarified.

**Experimental section**

**Preparation of Johnphosgold trigold oxonium and Johnphos digold hydroxide**

In the mixture of DCM, acetone, and ethanol (1:1:1, 2ml) was added several drops of water. [JohnphosAu][NCCH$_3$]$_2$SbF$_6$ (100mg) was mixed with molecular sieves(4Å), and dissolved in the previous mixed solvent. The mixture was stirred for 2hours and overnight respectively. The mixture was centrifuged to remove crushed molecular sieves, and then was evaporated to get the white solids, Johnphosgold trigold oxonium (40 mg) for 2 hours batch and Johnphos digold hydroxide (12mg ) for overnight batch.

[Johnphosgold trigold oxonium] SbF$_6$⁻ $^1$H NMR (300 MHz, Chloroform-$d_2$) δ 7.95 – 7.05 (m, 27H), 1.47-1.15 (m, 54H). $^{31}$P NMR (112 MHz, Chloroform - $d_2$) δ 53.4 .

[Johnphosgold digold hydoxide] SbF$_6$⁻ $^1$H NMR (300 MHz, Chloroform-$d_2$) δ 7.95 – 7.05 (m, 27H), 1.40-1.35 (d, 36H, J=15 Hz), -0.39- -0.41(t, 1H) $^{31}$P NMR (112 MHz, Chloroform - $d_2$) δ 57.3.
Urea Alkene Cyclization with Triphenylphosphine Trigold Oxonium in the absence of base

In a glove box, the gold salt (11.6 mg, 8.3 μmol) was added to a vial then capped with a rubber septum. The urea alkene (8.4 mg, 25 μmol) was transferred into another vial then capped with rubber septum. These two vials were taken out from the glove box, and to them each were added 0.3 mL CDCl₃. The two solutions were then transferred to a NMR tube under Ar for an alkene concentration of 0.042 M in 0.6 mL CDCl₃. The sample was sealed with a septum, shaken vigorously for 10 s, then placed in the NMR spectrometer to collect kinetic data.

The above experiment was also repeated at varying concentrations of triphenylphosphine trigold oxonium [(Ph₃PAu)₃O]BF₄. The same procedure was used, but with urea alkene (10.3 mg, 0.03 mmol) and trigold oxonium (4.4 mg, 0.003 mmol, 0.1 equiv.; 22 mg, 0.015 mmol, 0.5 equiv.; 44 mg, 0.03 mmol, 1 equiv.) and 0.6 mL of CDCl₃ for an alkene concentration of 0.05 M. At the higher concentrations of gold, some substrate decomposition was apparent.

Urea Alkene Cyclization with JohnPhos Trigold Oxonium

The JohnPhos trigold oxonium (16.5 mg, 0.01 mmol) and urea alkene (1) (10.2 mg, 0.03 mmol) were dissolved separately in CDCl₃ (300 μl). The two solutions were mixed (for an alkene concentration of 0.05 M) in an NMR tube, sealed with a septum, and NMR spectra were collected immediately. The reaction was monitored for 8 hours.

Urea Alkene Cyclization with Johnphos Digold Hydroxide
For kinetics experiments, digold hydroxide (3.8 mg, 0.004 mmol) and urea alkene (10.2 mg, 0.03 mmol) were dissolved separately in CDCl₃ (300 μl). The two solutions were mixed (for an alkene concentration of 0.05 M) in an NMR tube, sealed with a septum, and NMR spectra were collected immediately.

The above experiment was also repeated at varying concentrations of digold hydroxide [(Ph₃PAu)₂OH]SbF₆. The same procedure was used, but with urea alkene (10.3 mg, 0.03 mmol) and [(Ph₃PAu)₂OH]SbF₆ (10.2 mg, 0.26 equiv.; 28 mg, 0.8 equiv.) and 0.6 mL of CDCl₃ for an alkene concentration of 0.05 M.
Chapter 4 Preliminary results and proposed work about some gold-silver mixed intermediates

In the gold catalytic cycle, some unexpected gold species may be formed. Some of them are reversible through equilibrium, but some are side products which will hinder the major reactions. In order to further understand the gold catalytic cycle, it is meaningful to characterize some side products of Au catalysts. Investigation of conditions that form those species may help us develop some new protocols which avoid their formation. Moreover, it may help find some potential precatalysts and complement the current information about gold species. Two of those species are gem-digold species and bisphosphine gold species. Based on our preliminary experimental results, we believe that in addition to understanding that gold π-complexes with different ligands show different stability, the silver salts we used may also play an important role in gold π-complexes formation. When we used silver salts which were stored in an oxygen contaminated glove box for more than 1 year, the formation of byproducts significantly increased to 98%. When we switched to using new silver salts, but didn’t avoid the oxygen, formation of bisphosph gold species was 43%. But when we tried to make gold π complexes totally under argon protection, 0% of the bisphosphine gold species was formed. (Figure 20)
Based on the phenomena described above, we believe the condition of silver salts is key to the formation of gold π complex. We propose to check the newly formed compounds in silver salts without argon protection and how the new formed species hinder the formation of gold π complex. Moreover, we propose to test the reaction rates and efficiencies of gold-catalyzed reactions using silver salts with different purities.

“Silver effect” is an interesting topic in gold chemistry. Silver may have a significant effect on the gold catalytic cycle. Although some researchers argue that silver salts just hinder the formation of some unreactive gold species if added after mixing gold

\[
\text{LnAuCl} + \frac{R}{\text{AgSbF}_6} \rightarrow \text{LnAu} - \frac{R}{\text{Ln}_2\text{Au}}
\]

<table>
<thead>
<tr>
<th>Silver salts</th>
<th>Oxygen</th>
<th>Ln$_2$Au formation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Old batch (&gt; 1 yr)</td>
<td>+</td>
<td>98%</td>
</tr>
<tr>
<td>New batch</td>
<td>+</td>
<td>43%</td>
</tr>
<tr>
<td>New batch</td>
<td>-</td>
<td>0 %</td>
</tr>
</tbody>
</table>

+ with oxygen
- without oxygen

Figure 20 different conditions which result in different amount of bisphosphine gold species. The Ln$_2$Au formation is estimated based on fraction of decomposed material in $^1$HNMR spectra WTZ-1045
complexes and substrate, it is still necessary to characterize the mixed gold/silver complexes and explore the potential reactivity of those species. We proposed to make vinyl gold/silver mixed species. We have made and recrystallized vinyl(o-biphenyldiphenyl)gold. (Figure 21)

![Figure 21 crystal structure of vinyl(o-biphenyldiphenyl)gold (WTZ-1111)](image)

After getting this vinyl gold species, we propose to treat that with silver salts to see if silver can interact with the gold center to form some interesting structures. If the formation of gold/silver mixed species can be confirmed, the reactivity experiment will be proposed to find whether silver salt can influence the reactivity of gold complexes. Based on the crystal structure of trimetallic chloronium dication that Yuyang Zhu made in our lab, we believe arene-silver interaction exists in the Au/Ag mixed structure, which stabilize its formation. And the ligand we propose to use may have similar stabilizing
effect so that we can obtain the stabilized structure and extend the information about 
Au/Ag mixed species.

**Experimental Section**

**Vinyl(o-biphenyldiphenyl)phophine gold:** (o-biphenyldiphenyl)gold chloride (120 mg) 
was dissolved in methylene chloride under ice water bath. The vinylmagnesium bromide 
(0.7 mol/L THF solution 3 ml) was added dropwise, and the mixture was stirred for 15 
minutes after ice water bath was removed. Then it was extracted with ethylether (10 ml) 
three times and washed with water before evaporated under reduced pressure. This 
compound can be recrystallized using 20:1 hexane and methylene chloride as solvent 
system. $^1$H NMR (300 MHz, Methylene Chloride-$d_2$) $\delta$ 7.71 – 7.18 (m, 19H), 6.74 (ddd, J 
= 19.9, 13.9, 5.9 Hz, 1H), 5.74 (ddd, J = 18.6, 13.9, 5.2 Hz, 1H), 5.15 (ddd, J = 20.5, 8.6, 
5.2 Hz, 1H). $^{31}$P NMR (121 MHz, Methylene Chloride-$d_2$) $\delta$ 39.89.
Chapter 5 Conclusion

In summary, the general mechanism of gold-catalyzed π-bond activation reactions was discussed and a series of structure and reactivity studies have been described that would enhance the fundamental understanding of the π-activating capabilities of gold. Ligands used in gold catalysts have different effects on their catalytic activities. Moreover, we also characterized and isolated a vinyl silane coordinated gold π-complexes and a general procedure may be used in other cases.

Kinetics of formation of alkylgold intermediates using trigold(I) oxonium species have been described, but a new pathway of gold-catalyzed cyclization was proposed based on the kinetic study. A basic gold intermediate digold hydroxide species may be involved in the catalytic cycle and protodeauration of alkyl gold may not be the major path to form the final product.

Meanwhile, the characterization and condition studies of some byproducts such as gem-diaurated species and bisphosphine gold species were described. Moreover, work on “silver-effect” on gold-catalyzed reaction was proposed and initiated. In the future, the species of gold-silver bridging carbon will be explored in the solid state and on the protodemetalation process. The work will provide more economic and unambiguous protocols for gold catalysis.
Reference:


Appendix A

NMR spectra data
o-biphenyldiphenylphophine gold chloride ($^{1}$HNMR $^{31}$PNMR)

WTZ-1093 Gold Complex.1.fid
Gold Complex
wfu_PROTON CDCI3 /opt/topspin1.3 zhouw12 24
bis(o-biphenyldiphenyl)phosphate $\text{Au}^+\text{SbF}_6^-$ ($^1\text{HNMR}$ $^{31}\text{PNMR}$)

WTZ-1091.1 .f1d
wtu_PROTON CD2Cl2 /opt/topspin1.3 zhouw12 48
[o-biphenyldiphenylphophine Au][trimethylvinyl silane]⁺SbF₆⁻(¹HNMR ³¹PNMR)
[Johnphosgold trigold oxonium] SbF$_6^-$ \( (^1\text{HNMR} \quad ^{31}\text{PNMR}) \)
[Johnphosgold digold hydoxide] SbF$_6^-$ (\(^1\)HNMR 31PNMR)
Vinyl(o-biphenyldiphenyl)phoshine gold ($^1$HNMR $^{31}$PNMR)
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