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“Silver Effect” in Gold(I) Catalysis: An Overlooked Important Factor

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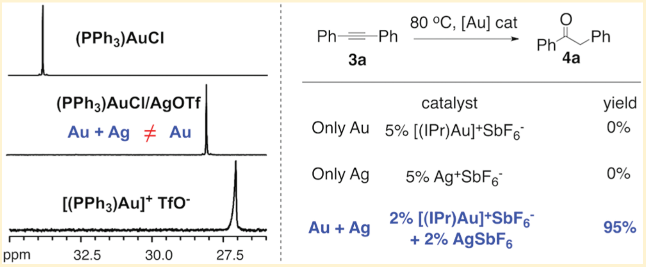
Ⓢ *Supporting Information*

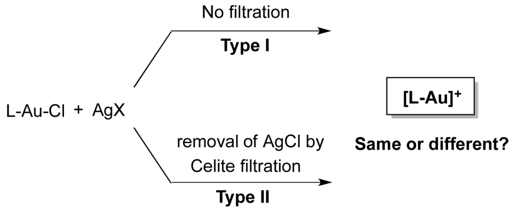
ABSTRACT: Clear experimental evidence from X-ray photoelectron spectroscopy and ^{31}P NMR spectroscopy has been obtained for the first time to confirm that the combination of Ag^+ cation with $[L\text{-}Au]^+$ results in the formation of different complexes in solution. Re-evaluation of literature-reported gold-catalyzed reactions revealed a significant difference in the reactivities with and without silver. In extreme cases (more than “rare”), the conventional $[L\text{-}Au]^+$ catalysts could not promote the reaction without the presence of silver. This investigation has therefore revealed a long-overlooked “silver effect” in gold catalysis and should lead to revision of the actual mechanism.



INTRODUCTION

Homogeneous gold catalysis is considered to be one of the most important developments in organic synthesis during the past decade.[1] It has been generally accepted that $[L\text{-}Au]^+$ is the actual π-acid toward alkyne and alkene activation in Au(I)-promoted reactions. Currently, the dominant approach for the preparation of $[L\text{-}Au]^+$ is through the treatment of [L-Au]Cl with the corresponding silver salt to form AgCl. Since the AgCl is not involved in the reaction, it has been assumed that removing the AgCl or keeping it in the reaction mixture should not make a difference, giving “identical” results (Scheme 1).

Scheme 1



Although it has been reported in a few cases that the presence of silver helps the reactivity of gold catalysts,[2] it has still been largely assumed that all of these reactions are catalyzed by the gold cation (with silver playing a “supporting role”) as long as the silver salt itself cannot catalyze the reaction. Herein we report for the first time experimental evidence (based on evaluations of 14 different types of previously reported gold-catalyzed reactions) that gold catalysis is not simply activated by $[L\text{-}Au]^+$ as previously assumed. In some cases, absolutely no reaction occurs with Ag-free $[L\text{-}Au]^+$ catalysts. With the clear experimental support described in this work, this long-overlooked “silver effect” should lead to serious reconsideration of reported and yet to be reported results in regard to whether the reaction involves “actual” gold catalysis.

RESULTS AND DISCUSSION

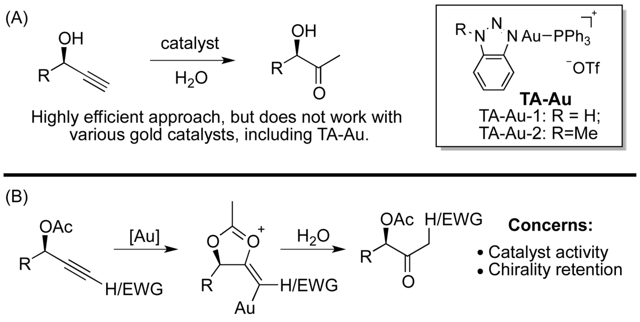
Our interest in gold catalysis was initiated by studies of the use of 1,2,3-triazole ligands to adjust transition-metal reactivity.[3] These efforts led to the recent discovery of the air- and moisture-stable triazole gold(I) compounds (TA-Au), which gave interesting reactivity that could not be offered by simple $[L\text{-}Au]^+$. Some recent discoveries about the new reactivity of the TA-Au catalysts include improved thermal stability,[4] better substrate stability,[5] and excellent chemo- and stereoselectivity[6] toward alkyne activation. On the basis of these successes, we investigated the 1,2-migration of propargyl esters[7] with the TA-Au catalyst.

In view of the importance of α-hydroxy methyl ketones (Scheme 2A) in medicinal chemistry[8] and the ready availability of the enantiomerically pure propargyl alcohols, our initial attempt was to investigate the possibility of direct alkyne hydration to form the ketone with retention of stereochemistry at the hydroxy position. However, after screening a series of the Au(I) complexes, we found that no catalyst, not even TA-Au, promoted this reaction effectively even at 80 °C. We then looked into an alternative approach. It is known that propargyl esters can undergo 1,2-migration with terminal alkynes.[9] Therefore, it should be possible to trap the oxonium cation with water and reach the desired α-hydroxy methyl ketone through simple steps (Scheme 2B). However, according to the literature, simple gold catalysts $[L\text{-}Au]^+$ cause rapid epimerization (within a few minutes). Therefore, we became interested

Received: April 22, 2012
Published: May 7, 2012

dx.doi.org/10.1021/ja303862z | *J. Am. Chem. Soc.* 2012, 134, 9012−9019

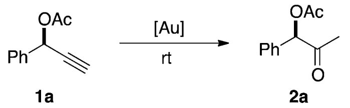
Scheme 2. Proposed Asymmetric Synthesis of α-Hydroxy Ketones



in exploring whether the chemoselective TA-Au would promote this reaction with good retention of chirality.

Propargyl ester **1a** was prepared and reacted with different gold catalysts under various conditions. As shown in Table 1, both TA-Au-1 and TA-Au-2 effectively promoted the reaction. Screening of the conditions revealed acetone to be the optimal solvent, giving the desired α-acetoxy ketone in nearly quantitive yield (1% loading). It should be noted that the $[PPh_3\text{-}Au]^+$ and $[IPr\text{-}Au]^+$ complexes could NOT promote this reaction at all (entries 1−3), and most of the starting material **1a** was recovered. This result highlighted the strength of the triazole-gold catalyst: a simple modification resulting in high efficiency and new reactivity. The reaction substrate scope is shown in Table 2.

Table 1. Gold(I)-Catalyzed Propargyl Ester Hydration[a]

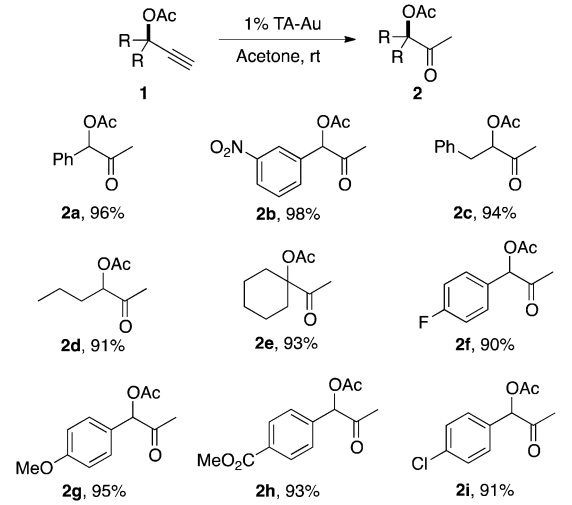


entry	cat[b]	solvent	time (h)	yield (%)[c]
1	$[(PPh_3)Au]^+TfO^-$	dioxane	12	0
2	$[(PPh_3)Au]^+SbF_6^-$	dioxane	12	0
3	$[(IPr)Au]^+SbF_6^-$	dioxane	12	0
4	TA-Au-1	dioxane	12	87
5	TA-Au-2	dioxane	12	85
6	TA-Au-1	DCM	12	32
7	TA-Au-1	THF	12	<5
8	TA-Au-1	MeOH	12	24
9	TA-Au-1	DMF	12	<5
10	TA-Au-1	CH_3NO_2	12	11
11	TA-Au-1	CH_3CN	4	89
12	**TA-Au-1**	**acetone**	**4**	**99 (96)**[d]

[a] General reaction conditions: **1a** (0.25 mmol, 1.0 equiv) and **2a** (1.0 mol %) in solvent (2.5 mL) with H_2O (3.0 equiv) at room temperature (rt) for 4−12 h. The reactions were monitored by thin-layer chromatography (TLC). [b] Type II $[L\text{-}Au]^+$. [c] NMR yields. [d] The isolated yield is given in parentheses.

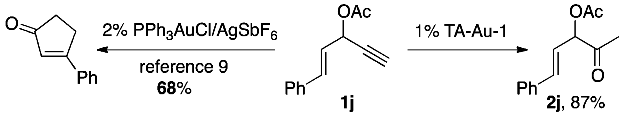
As indicated in Table 2, TA-Au catalyst was highly effective for this transformation, giving the desired products in excellent yields. One good example that highlighted the unique reactivity of the TA-Au catalyst compared with $[L\text{-}Au]^+$ was the reaction of 1,4-enyne **1j** (Scheme 3). As reported in the literature, treating **1j** with $PPh_3AuCl/AgSbF_6$ gave the corresponding cyclopentenone through a "carbene-like" intermediate.[9] In contrast, simply switching the catalyst to TA-Au-1 successfully altered the reaction path to give **2j** in excellent yield.

Table 2. Reaction Substrate Scope[a,b]



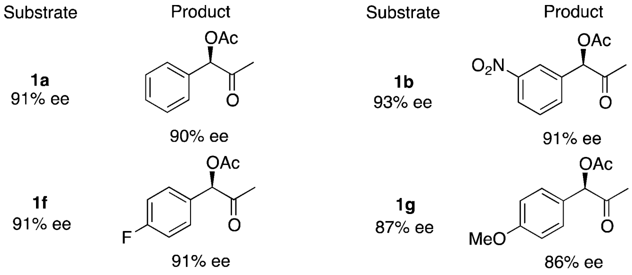
[a] General reaction conditions: **1** (0.25 mmol, 1.0 equiv) and TA-Au-1 (1.0 mol %) in acetone (2.5 mL) with H_2O (3.0 equiv) at rt for 4−10 h. The reactions were monitored by TLC. [b] Isolated yields are shown.

Scheme 3. Alternative Reactivity Offered by the TA-Au Catalyst



The stereochemistry was evaluated by comparing the enantiomeric excess (ee) values for the products and the enantiomerically enriched propargyl ester starting materials. As indicated in Scheme 4, excellent retention of chirality was obtained with the TA-Au catalyst.

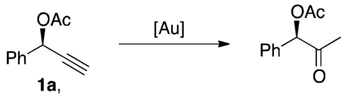
Scheme 4. Excellent Retention Chirality with the TA-Au Catalyst



While we were excited to find that TA-Au offers new reactivity relative to $[L\text{-}Au]^+$ for this interesting reaction, Sahoo and co-workers reported the same transformation using the $PPh_3AuCl/AgSbF_6$ mixtures.[10] This result was shocking, since we had shown that $[L\text{-}Au]^+$ could not promote this reaction (Table 1, entries 1−3). These conflicting results were significant and required further investigation. A direct comparison of several gold catalysts, with or without the presence of AgCl, was then carried out (Table 3).

As indicated in Table 3, entry 2, under the optimal conditions reported by Sahoo (dioxane as solvent, 3 equiv of H_2O), none of the tested silver salts could catalyze the reaction, and a majority of **1a** was recovered. The catalysts $[(PPh_3)\text{-}Au]^+A^-$, which were prepared from Celite filtration of the

Table 3. Silver Effect in Alkyne Hydration[a]



1a, 91% ee

2a

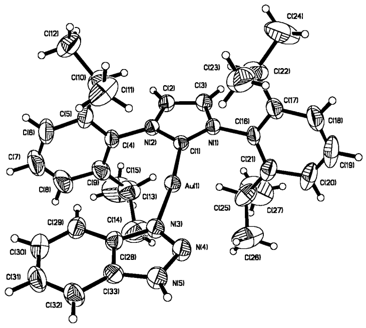
entry	catalyst	conditions	yield (%)[b]	ee (%)
1	1% TA-Au-1	5 h	87	90
2	**10% AgA**[c]	**12 h**	**0**	–
3	**2% [(PPh$_3$)Au]$^+$A$^-$** [c]	**12 h**	**0**	–
4	2% (PPh$_3$)AuCl/AgOTf	12 h	90	0
5	2% (PPh$_3$)AuCl/AgSbF$_6$	8 h	97	0
6	2% (PPh$_3$)AuCl/AgOTf	5 h with N$_2$ protection	92	90
7	**2% [(PPh$_3$)Au]$^+$ SbF$_6^-$ + 2% AgSbF$_6$**	**12 h**	**91**	–

[a] General reaction conditions: **1a** (1.0 equiv) and catalyst in 2.5 mL of dioxane/water (H_2O, 3.0 equiv) at rt. Reactions were monitored by TLC. [b] NMR yields. [c] A^- = TfO^-, SbF_6^-, BF_4^-.

PPh$_3$AuCl/Ag$^+$A$^-$ mixtures, also could not promote this reaction (entry 3). However, when the mixtures of PPh$_3$AuCl and Ag$^+$A$^-$ were used directly (without filtration of AgCl), the reaction worked as reported, though with complete stereochemistry racemization (entries 4 and 5). Careful degassing and N$_2$ protection helped to avoid the racemization (entry 6). Interestingly, a mixture of [(PPh$_3$)Au]$^+$TfO$^-$ (the inactive complex obtained from filtration through Celite) and AgSbF$_6$ promoted this reaction effectively (entry 7), which suggested that the combination of gold and silver made the catalysis possible.

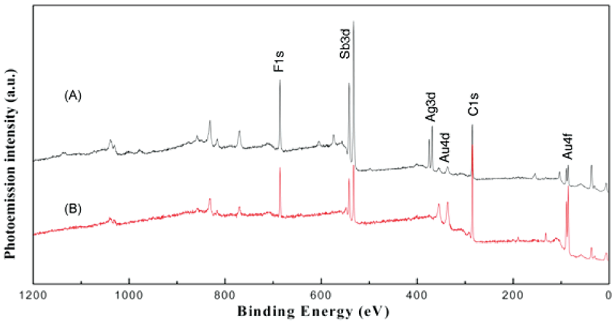
Notably, filtration through Celite was a practical procedure used in our group during the preparation of the TA-Au complexes. In general, the silver salts were not stable and would decompose to give silver nanoparticles or a precipitate of Ag_2O over time. This silver decomposition seemed to be accelerated in the presence of solid AgX, forming a darker solution over time. Filtration with regular filter paper could not completely remove the color, even though the filtrate was transparent by visual judgment. Filtration through Celite allowed the majority of the [L-Au]$^+$A$^-$ go through. This procedure worked for various ligands. For example, Scheme 5 shows the crystal structure of the recently obtained complex [(IPr)Au-BTZ]$^+$TfO$^-$ (BTZ = benzotriazole), which was prepared by the reaction of BTZ and (IPr)AuCl/AgOTf Celite filtrate, which gave the desired IPr-TA-Au complex in 92% yield.

Scheme 5. ORTEP Structure of [(IPr)Au-BTZ]$^+$TfO$^-$ Complex (with TfO$^-$ Omitted for Clarity)



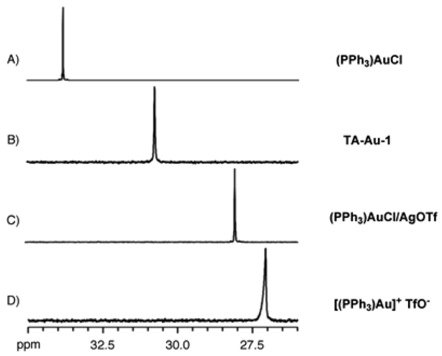
To verify the difference between Celite filtration and paper filtration, X-ray photoelectron spectroscopy (XPS) was applied. The spectra (summarized in Scheme 6) show that gold was observed in both filtrates. The binding energies (Au 4f$_{7/2}$, 85.5 eV; Au 4f$_{5/2}$, 89.2 eV) suggested the presence of Au(I) cations after Celite filtration. The filtrate of (PPh$_3$)AuCl/AgSbF$_6$ through regular filter paper showed the silver signal (Scheme 6A: Ag 3d$_{5/2}$, 368.7 eV; Ag 3d$_{3/2}$, 374.7 eV). Interestingly, the filtrate from Celite did not contain any silver (Scheme 6B), even when an excess amount of silver salts was used in the reaction with PPh$_3$AuCl (Au:Ag = 1:1.5). These results provided unambiguous evidence that the filtrate from Celite contained only [(PPh$_3$)Au]$^+$ without the presence of any silver. Similar results were observed with the (IPr)AuCl/AgSbF$_6$ system. These XPS results support the observation that the presence of silver influences the gold cation reactivity.

Scheme 6. XPS Spectra of (PPh$_3$)AuCl/AgSbF$_6$ Mixtures [(PPh$_3$)AuCl:AgSbF$_6$ = 1:1.5] after Filtration through (A) Regular Filter Paper and (B) Celite



Meanwhile, the gold(I) complexes are linearly coordinated, with two ligands binding on the opposite sites of the gold. Therefore, for complexes like (PR$_3$)AuX, ^{31}P NMR spectroscopy was ideal for evaluating the electronic nature of the gold cations in solution. To understand the solution behavior of these two types of gold samples (with or without silver), ^{31}P NMR experiments were carried out, and the spectra are shown in Scheme 7. In general, more cationic gold complexes gave ^{31}P signals shifted further upfield (PPh$_3$AuCl, 33.8 ppm; TA-Au-1, 30.8 ppm; Scheme 7A,B). [PPh$_3$Au]$^+$TfO$^-$ after Celite filtration exhibited the ^{31}P NMR signal at 27.1 ppm (Scheme 7D),

Scheme 7. ^{31}P NMR Spectra of Different Au(I) Samples[a]



[a] The chemical shifts were calibrated using 85% H_3PO_4 as an internal reference in a sealed capillary. The samples were prepared with 0.05 M gold in $CDCl_3$. The full spectra are shown in the Supporting Information.

suggesting the formation of highly cationic $[PPh_3Au]^+$ species. However, $(PPh_3)AuCl/AgOTf$ with no filtration gave a different chemical shift at 28.1 ppm (Scheme 7C). Clearly, the presence of silver influenced the gold complexes in solution.

Comparisons of the ^{31}P NMR chemical shifts among the different samples before and after the Celite filtration are shown in Table 4. Since the addition of AgOTf was intended to remove the chloride anion from PPh_3AuCl, it was anticipated that more AgOTf would cause an upfield shift of the ^{31}P signal due to the formation of more cationic gold (entries 1−4). After the stoichiometric amount of silver was used, no further chemical shift changes were observed even with the addition of excess AgOTf (entries 4 and 5). Notably, different chemical shifts were observed after the sample was filtered through Celite to remove the silver. Meanwhile, the addition of AgOTf to the solution of $[(PPh_3)Au]^+TfO^-$ gave a slow ^{31}P signal shift from 27.1 ppm BACK to 28.1 ppm (see the detailed spectra in the Supporting Information). The changes in the chemical shifts were independent of the amount of AgOTf added: both 0.5 and 1.0 equiv of AgOTf shifted the ^{31}P signals from 27.1 to 28.1 ppm with no further changes. NO chemical shift changes were observed when AgCl was added to the silver-free $[(PPh_3)Au]^+TfO^-$ solutions, suggesting that the influence is from Ag^+ instead of AgCl.

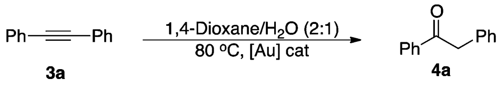
Table 4. ^{31}P NMR Changes Caused by Celite Filtration[a]

		^{31}P NMR chemical shift (ppm)	
entry	equiv of AgOTf	before filtration	after filtration
1	0.50	31.5	30.5
2	0.75	30.2	29.3
3	0.90	29.2	28.7
4	1.5	28.1	27.1
5	2.0	28.1	27.1

[a] The chemical shifts were calibrated using 85% H_3PO_4 as an internal standard (0 ppm) in a sealed capillary. The samples were prepared with 0.05 M gold in $CDCl_3$.

It is important to notice here that the TA-Au catalyst was silver-free and could indeed effectively promote this reaction. As revealed in the ^{31}P NMR shown in Scheme 7, the TA-Au complex exhibited the same downfield shift as the silver cation, which suggests a similar effect from the triazole ligands, making TA-Au a potentially good alternative for the combination of gold and silver. Nevertheless, the XPS and NMR experiments provided unambiguous evidence that the presence of silver influences the reactivity of the $[L\text{-}Au]^+$ cations. This discovery is critical since it should lead to the revision of the current assumption regarding the mechanism of homogeneous gold(I) catalysis, as the actual catalyst might not be the gold alone! The gold-catalyzed propargyl ester hydration reaction shown in this study was one good example that highlighted the importance of this silver effect: $[(PPh_3)Au]^+TfO^-$ could not promote the reaction at all unless silver was added. One concern was whether the presence of silver helped the hydration of the oxonium cation intermediates, which therefore played the important role in promoting the overall reaction as observed. This was unlikely. The reaction with TA-Au, which did not contain silver, led to an effective transformation with higher reaction rates. This result suggested that the hydration of the oxonium cation is fast and that silver is not necessary in this step. Nevertheless, to ensure that this "silver effect" did not occur ONLY in this reaction, we extended the investigation to the alkyne hydration shown in Scheme 8.

Scheme 8. "Silver Effect" in the (IPr)Au-Catalyzed Simple Alkyne Hydration



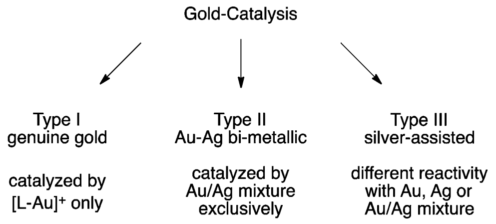
	catalyst	time	yield
A	$[(IPr)Au]Cl/AgSbF_6$ 2%, **no filtration**	2 h	97%
B	5% $[(IPr)Au]^+SbF_6^-$	24 h	0%
C	5% $AgSbF_6$	24 h	0%
D	2% $[(IPr)Au]^+SbF_6^-$ + 2% $AgSbF_6$	12 h	95%
E	2% $[(IPr)Au]^+SbF_6^-$ + 1% $AgSbF_6$	24 h	88%
F	2% $[(IPr)Au]^+SbF_6^-$ + 0.5% $AgSbF_6$	24 h	67%

It has been reported by Nolan and co-workers that $(IPr)AuCl/AgSbF_6$ is the optimal catalyst to promote challenging internal alkyne hydrations.[11] As shown in Scheme 8A, an excellent yield of ketone **4a** was obtained when the $(IPr)AuCl/AgSbF_6$ mixture was used without filtration. When **3a** was charged with $[(IPr)Au]^+$ (the Celite filtrate of the same catalyst mixture), no reaction occurred, even with increased catalyst loading (5%) and prolonged reaction time (Scheme 8B). In contrast, addition of 2% $AgSbF_6$ caused the catalyst to become "active" again, giving ketone **4a** in excellent yield though with a longer reaction time (Scheme 8D). Notably, silver salts alone could not promote this reaction (Scheme 8C). Therefore, these results demonstrated again that the combination of gold and silver is the actual active catalyst for this transformation, revising the previous assumption that $[L\text{-}Au]^+$ is the actual catalyst. Reducing the amount of silver salt caused the reaction rate to decrease. When 0.25 equiv of silver (relative to gold) was used (Scheme 8F), the reaction could not reach complete conversion (∼25% of the starting material was recovered under identical conditions).

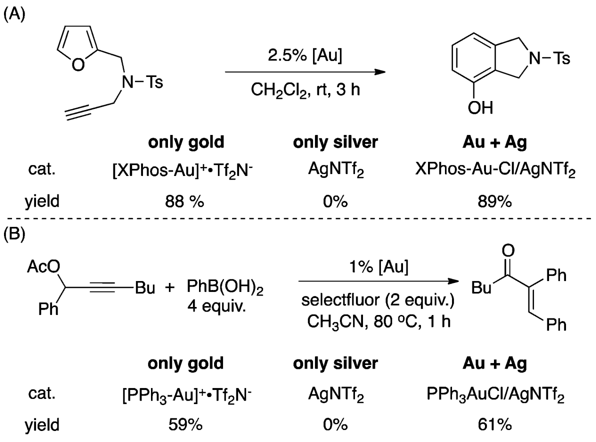
These experiments reconfirmed the shocking results shown in previous case: the addition of silver is no longer an "optimization" factor for gold catalysis. Instead, $[L\text{-}Au]^+$, long believed to be the effective catalyst, might not be, and instead, mixtures of both silver and gold "accidentally" provided the optimal catalysts combinations for effective transformation (though we are not sure what types of complexes were formed at this moment). This discovery is critical since it further separates the overall "gold(I) catalysis" into three different theoretical categories (Scheme 9): (A) "genuine" gold catalysis, (B) Au/Ag bimetallic catalysis, and (C) silver-assisted gold catalysis.

Genuine gold catalysis refers to the type of reactions promoted by $[L\text{-}Au]^+$ with competitive or even better reactivity than the $[L\text{-}Au]^+/Ag^+$ mixtures. The type-II bimetallic catalysis includes the reactions promoted exclusively by the mixture of gold and silver. One may argue that the group 11 metals have similar properties with expected differences in reactivity toward certain transformations. However, as shown in the two cases discussed above, there are transformations that clearly could not be promoted by either Au or Ag alone. Only the

Scheme 9. Refining Gold Catalysis on the Basis of Reactivity



combination of these two metals could result in the formation of an effective catalytic system. The type-III silver-assisted gold catalysis, on the other hand, combines the transformations promoted by either gold or silver or a combination of the two metals. Different reactivities are usually associated with the various types of catalysts employed. Generally, the combination of silver and gold exhibits improved reactivity in comparison with gold alone. With the awareness of these three theoretical types of gold catalysis, we investigated several different literature-reported "gold-catalyzed" reactions. All three types of reactions were obtained during this investigation. Twelve representative transformations are shown in Figures 1−3 to highlight the generality of this long-overlooked "silver effect" in gold catalysis.



(A)

	only gold	only silver	Au + Ag
cat.	$[XPhos\text{-}Au]^+\bullet Tf_2N^-$	$AgNTf_2$	$XPhos\text{-}Au\text{-}Cl/AgNTf_2$
yield	88 %	0%	89%

(B)

	only gold	only silver	Au + Ag
cat.	$[PPh_3\text{-}Au]^+\bullet Tf_2N^-$	$AgNTf_2$	$PPh_3AuCl/AgNTf_2$
yield	59%	0%	61%

Figure 1. Examples of genuine gold catalysis.

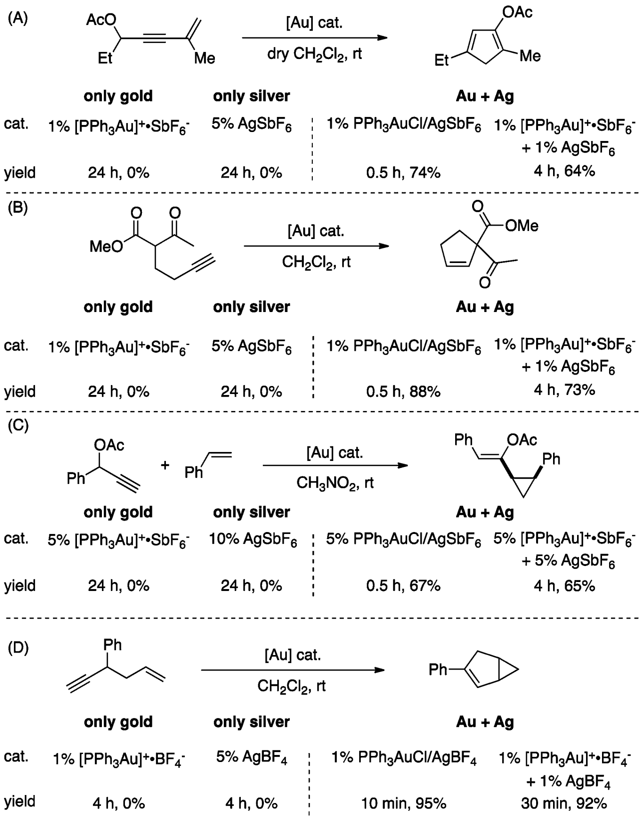
Type I: "Genuine" Gold Catalysis.

The relativistic effect makes gold cations one unique π-acid in alkyne activation. In fact, more and more efforts have been devoted to obtaining "silver-free" gold catalysts with the intention of avoiding the potential influence of silver cations. Therefore, one may assume that among the numerous reported transformations, "pure" Au(I)-promoted reactions (no need of assistance from silver) should be plentiful. However, among the reactions we screened (14 types of literature-reported reactions), only two examples were confirmed that could be promoted effectively by silver-free gold without loss of reactivity compared with gold/silver mixture catalysts.

The first example is the Hashmi phenol synthesis,[12a] which involves gold-promoted furan−yne rearrangement to phenol through the formation of gold carbene intermediates (Figure 1A). The original conditions involved the treatment of XPhos-Au-Cl with $AgNTf_2$ for the preparation of $[XPhos\text{-}Au]^+$. Our investigation revealed similar reactivities for the silver-free gold catalyst (after filtration through Celite) and the mixture of gold and silver. Therefore, this interesting transformation does not rely on the assistance of silver. Similar results were obtained in the gold-catalyzed oxidative coupling reaction between vinyl-gold and boronic acids (Figure 1B), which was first reported by Zhang and co-workers.[12b]

Type II: Au/Ag Bimetallic Catalysis.

As illustrated in Scheme 8, Au/Ag bimetallic catalysis was a rather surprising new type of reaction. Neither gold nor silver alone could catalyze these reactions. Even more impressively, in our investigation of the previously reported transformations, this type of reactions was not rare at all. Besides the alkyne hydration shown in Table 3 and Scheme 2, four more transformations were identified with the exact same catalytic manner, as shown in Figure 2.[13]



(A)

	only gold	only silver	Au + Ag	
cat.	1% $[PPh_3Au]^+\bullet SbF_6^-$	5% $AgSbF_6$	1% $PPh_3AuCl/AgSbF_6$	1% $[PPh_3Au]^+\bullet SbF_6^-$ + 1% $AgSbF_6$
yield	24 h, 0%	24 h, 0%	0.5 h, 74%	4 h, 64%

(B)

	only gold	only silver	Au + Ag	
cat.	1% $[PPh_3Au]^+\bullet SbF_6^-$	5% $AgSbF_6$	1% $PPh_3AuCl/AgSbF_6$	1% $[PPh_3Au]^+\bullet SbF_6^-$ + 1% $AgSbF_6$
yield	24 h, 0%	24 h, 0%	0.5 h, 88%	4 h, 73%

(C)

	only gold	only silver	Au + Ag	
cat.	5% $[PPh_3Au]^+\bullet SbF_6^-$	10% $AgSbF_6$	5% $PPh_3AuCl/AgSbF_6$	5% $[PPh_3Au]^+\bullet SbF_6^-$ + 5% $AgSbF_6$
yield	24 h, 0%	24 h, 0%	0.5 h, 67%	4 h, 65%

(D)

	only gold	only silver	Au + Ag	
cat.	1% $[PPh_3Au]^+\bullet BF_4^-$	5% $AgBF_4$	1% $PPh_3AuCl/AgBF_4$	1% $[PPh_3Au]^+\bullet BF_4^-$ + 1% $AgBF_4$
yield	4 h, 0%	4 h, 0%	10 min, 95%	30 min, 92%

Figure 2. Examples of Au/Ag bimetallic catalysis.

Again, these transformations were all previously assumed to involve gold catalysis, since silver salts could not promote these reactions at all. However, on the basis of the reinvestigation, the pure gold catalyst could not promote these reactions. Addition of the silver salts (AgCl could not activate the gold) resulted in the reactivation of the gold catalyst, though longer reaction times were needed, likely caused by the formation of the active catalyst (similar to the ^{31}P chemical shift change results).

Type III: Silver-Assisted Gold Catalysis.

The examples shown for type I and type II are two extreme cases. There should be examples of type-III catalysis, in which both gold cation and a mixture of gold and silver can promote the reaction, likely with different reactivities. This type of gold catalysis was also successfully identified, as shown in Figure 3.[14]

Although this type of reaction could be promoted by the pure gold catalyst, the combination of gold and silver gave much better results. In addition, these reactions could not be promoted by silver alone, consistent with the literature results.

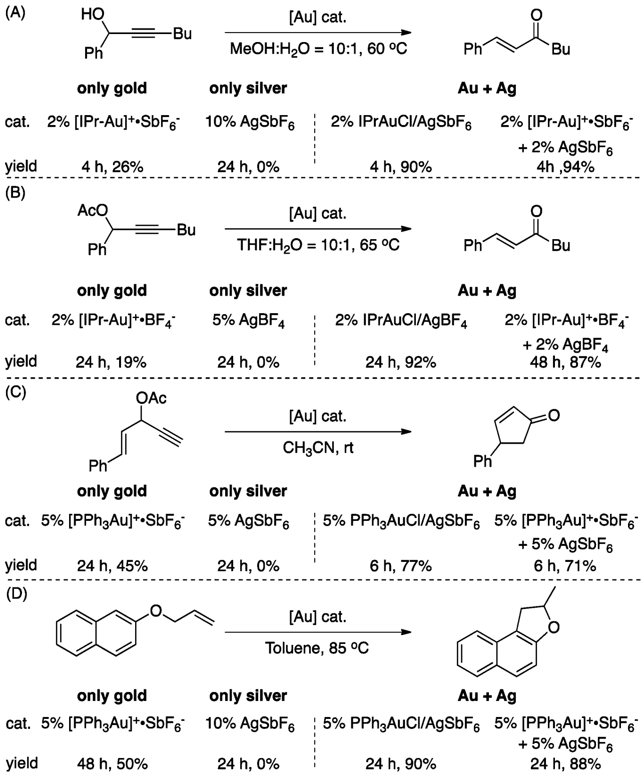


Figure 3. Examples of silver-assisted gold catalysis.

Notably, two other reactions were also identified that could be promoted by both gold and silver. However, a gold/silver mixture or even gold alone exhibited better performance (Figure 4).[15]

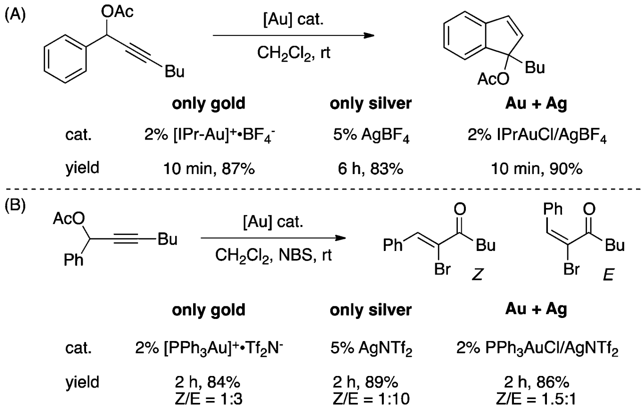
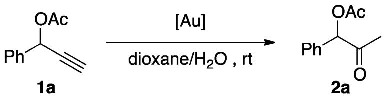


Figure 4. Examples of silver-promoted reactions.

The Effect of Celite Filtration. The results shown above clearly suggest the influence of silver salts in gold catalysis. One concern was whether the Celite filtration caused some changes that deactivated the catalysts. Sequential addition of silver salts to the Celite filtrates resulted in the reactivation of the catalyst to give the observed results. The three most commonly applied noncoordinated anions in literature-reported gold catalysis are TfO$^-$, SbF$_6^-$, and BF$_4^-$. The crystal structure shown in Scheme 5 confirmed that TfO$^-$ was filtered through the Celite with no decomposition. Similarly, as we reported previously, the SbF$_6^-$ anion was used as the counteranion to form the corresponding gold complexes with no decomposition through Celite filtration.[16] The [(PPh$_3$)Au-triazole]$^+$·BF$_4^-$ complex was successfully prepared using the same method. However, the attempts to grow this crystal were unsuccessful because of slow decomposition. Nevertheless, comparison of the ^{19}F NMR spectra of AgBF$_4$ and [(PPh$_3$)Au]$^+$·BF$_4^-$ indicated the presence of BF$_4^-$ anion with no decomposition after Celite filtration (see the Supporting Information). The fact that all of these anions "survived" the Celite filtration strongly suggests that the silver cations were the crucial "activation factor" for [L-Au]$^+$ in the above-mentioned studies. Notably, Gagné and co-workers reported a similar Au–Ag dinuclear resting state in the catalytic cycle in their mechanistic investigation of gold-catalyzed allene hydroarylation, which is consistent with this "silver effect".[17] However, to be absolutely certain, the reactions using (PPh$_3$)AuMe/TfOH were conducted.

Addition of acids to L-Au-Me or L-Au-Ph is another general strategy that has been reported in the literature for the preparation of [L-Au]$^+$ (with formation of methane or benzene). This process is extremely sensitive to solvent (making L-Au-Cl/AgA a better choice in practice). For example, addition of TfOH to (PPh$_3$)AuMe in either CH$_2$Cl$_2$, CH$_3$NO$_2$ or CH$_3$CN caused immediate catalyst decomposition, forming gold nanoparticles or a gold mirror within minutes. Therefore, it is very difficult to compare directly the reactivities of [L-Au]$^+$ formed from (PPh$_3$)AuMe/TfOH and (PPh$_3$)AuCl/AgOTf with Celite filtration. Fortunately, solvent screening revealed that dioxane is an optimal solvent with much slower catalyst decomposition using the (PPh$_3$)AuMe/TfOH approach. This allowed the head-to-head comparison of the hydrations of **1a** to investigate the claimed "silver effect". As shown in Figure 5, [PPh$_3$Au]$^+$TfO$^-$ obtained from PPh$_3$AuCH$_3$/TfOH gave the exactly same results as observed for [PPh$_3$Au]$^+$TfO$^-$ prepared from Celite filtration: without the addition of AgOTf, [PPh$_3$Au]$^+$TfO$^-$ exhibited no reactivity, providing unambiguous evidence of the "silver effect" in this type of gold catalysis.

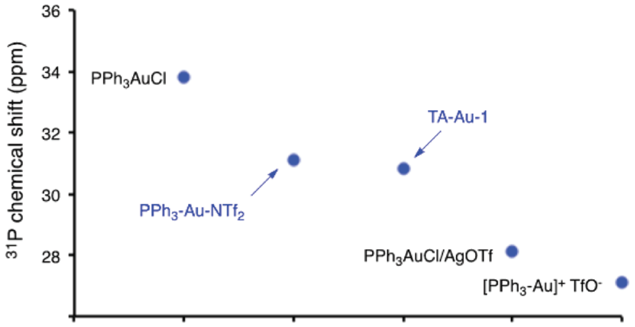


	[Au]		NMR yield of **2a**
(1)	5% [PPh$_3$Au]$^+$TfO$^-$ (celite filtration)	12 h	0% 91% **1a** recovered
(2)	5% [PPh$_3$Au]$^+$TfO$^-$ (celite filtration) + 5% AgOTf	2 h	90%
(3)	5% PPh$_3$AuCH$_3$ + 20% TfOH	12 h	0% 90% **1a** recovered
(4)	5% PPh$_3$AuCH$_3$ + 20% TfOH + 5% AgOTf	12 h	97%

Figure 5. [PPh$_3$Au]$^+$TfO$^-$ from PPh$_3$AuMe/TfOH.

The Activation Factor in Gold Catalysis. While the influence of silver on gold catalysis was shocking and crucial, the TA-Au catalysis suggested that silver salts are not the only viable "activation factor". Interestingly, the two genuine gold catalysis examples shown in Figure 1 both used the coordinating anion Tf$_2$N$^-$. In general, The L-Au-NTf$_2$ complexes were different than the gold catalysts formed with noncoordinated counteranions. As indicated in Scheme 10, the (PPh$_3$)AuNTf$_2$ gave a ^{31}P NMR chemical shift at 31.1 ppm,[4a]

Scheme 10. Comparison of ^{31}P NMR Chemical Shifts for Different Au(I) Samples



which is similar to the chemical shift of TA-Au (30.8), suggesting the coordination of Tf_2N^- anion with $[(PPh_3)Au]^+$ in solution.

The silver-free TA-Au effectively promoted the hydration of **1**, suggesting that other coordination ligands, such as 1,2,3-triazoles, could also be used as the "activation factor" to initiate the gold catalysis instead of silver. To investigate the difference in the gold catalysts formed from coordinating anions and noncoordinating anions, silver-free $(PPh_3)AuNTf_2$ and IPr-Au-NTf_2 were prepared with Celite filtration. XPS confirmed that neither sample had silver present. Several reactions were re-evaluated with these silver-free catalysts, and the results are summarized in Figure 6.

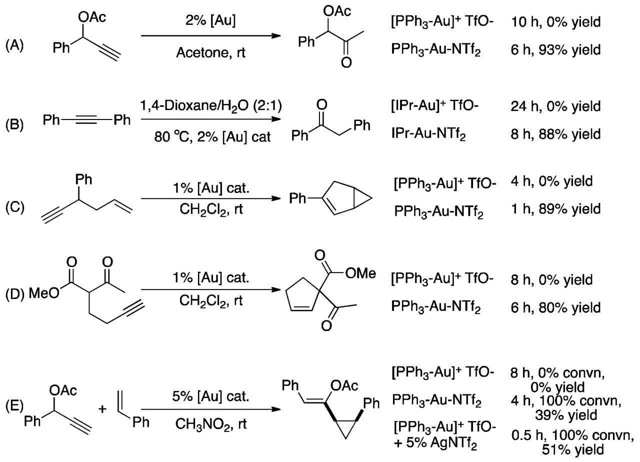


Figure 6. Examples of Tf_2N^- as the activation factor. NMR yields are shown.

As indicated, the silver-free L-Au-NTf_2 showed good reactivity in these transformations, which could not be promoted by $[L\text{-}Au]^+TfO^-$. Therefore, in addition to silver salts and 1,2,3-triazoles, the coordinating anion Tf_2N^- was identified as another activation factor in gold catalysis. Notably, for the intermolecular cyclopropanation reaction (Figure 6E), the combination of silver and Tf_2N^- exhibited improved reactivity in comparison with $(PPh_3)AuNTf_2$ alone, which suggests the different influence of various activation factors.

Overall, the re-evaluation of literature-reported gold-catalyzed reactions confirmed the rather shocking observation that gold catalysis is greatly influenced by the presence of silver salts, which were previously considered as inactive reagents. It is clearly suggested that the gold catalysis mechanism could be much more complicated than the previously assumed simple $[L\text{-}Au]^+$ model.

■ CONCLUSION

In view of the huge amount of effort that has been put into homogeneous gold catalysis, it is clear that a better understanding of the nature of the reaction is crucial for further advance of this research field. The exact complexes formed by mixing silver and gold cations are not certain at this moment. With the noncoordinating anions (TfO^-, SbF_6^-, and BF_4^-), the reactions indicated little counteranion influence, suggesting that anion-bridged gold−silver cocomplexes do not form. The addition of AgCl did not activate gold catalysis in all of the tested cases, ruling out the formation of $[Ag\text{-}Cl\text{-}Au]^+$ as the actual catalyst. The relatively large number of examples tested in this work confirm the generality of this phenomenon that the long-overlooked influence of silver in gold catalysis is crucial and real.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures, spectral data for all new compounds, and a CIF file for [(IPr)Au-BTZ]OTf. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the NSF (CAREER-CHE-0844602) for financial support.

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