Propargylsilanes as Reagents for Synergistic Gold(I) Catalyzed Propargylation of Carbonyl Compounds. Isolation and Characterization of σ-Gold(I) Allenyl Intermediates

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Abstract: *Herein we report the isolation and characterization, for the first time, of a σ-gold allenyl complex as intermediate in gold catalysis. This intermediate was captured in the course of the study of a novel gold(I) catalyzed propargylation of carbonyl compounds with propargylsilanes. On the other hand, gold catalyzed propargylation reaction, which proceeds with aldehydes and ketones, can be driven to the formation of homopropargyl silyl ethers or the in situ synthesis of the corresponding 2-silyl-4,5-dihydrofurans.*

Homogeneous gold catalysis has emerged as a powerful tool promoting a large number of processes in modern organic synthesis.[1] However, propargylation reactions, which have been reported with several metalates,[2] remains as an elusive field in gold catalysis, further than the recent work by Zhang and co-workers.[3] In this sense, Zhang *et al*., published very recently[3b] an excellent and very carefully designed gold(I) catalyzed propargylation reaction of aldehydes (Figure 1; *top*).

On the other hand, the quest for the isolation and characterization of gold intermediates has been a target largely pursued.[4] In this field, our group was able to characterize a σ-gold allylic cation, closely related to allenyl gold complexes,[5] as intermediate in gold catalyzed enyne cycloisomerizations.[6] However, although several π-gold allenyl[7] and gold allenylidene[8] complexes have been isolated and characterized, σ-gold allenyl complexes remained unknown until characterization by Gimeno and co-workers,[9] and very recently by Hashmi *et al*.,[10] although in both cases, without catalytical relevance. These species have also received low attention as intermediates in gold catalytic reactions, with the exception of the very recent works by Zhang and co-workers[3b] and Pyne, Hyland and co-workers.[11]

In the course of our investigations related to the use of alkynylsilanes in gold catalyzed transformations,[12] we decided to investigate the behavior of these compounds wearing two potentially reactive silylated positions in their structure. With this target in mind, we focused our work in 1,3-disilylpropyne derivatives, which include an additional silyl group placed at the propargylic position. Propargylsilanes usually react, catalytically or not, with carbonyls in the presence of a Lewis acid, to form allenyl alcohols,[13] although silyl migrations have also been described.[14]

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Here we present an efficient and synergistic gold catalyzed carbonyl propargylation reaction, to form homopropargyl silyl ethers, starting from propargylsilanes. This transformation seems to involve a σ-gold allenyl complex intermediate that could be isolated and characterized. In addition, homopropargyl silyl ethers can undergo a gold catalyzed cycloisomerization yielding the corresponding 4,5-dihydrofurans (Figure 1; *bottom*).

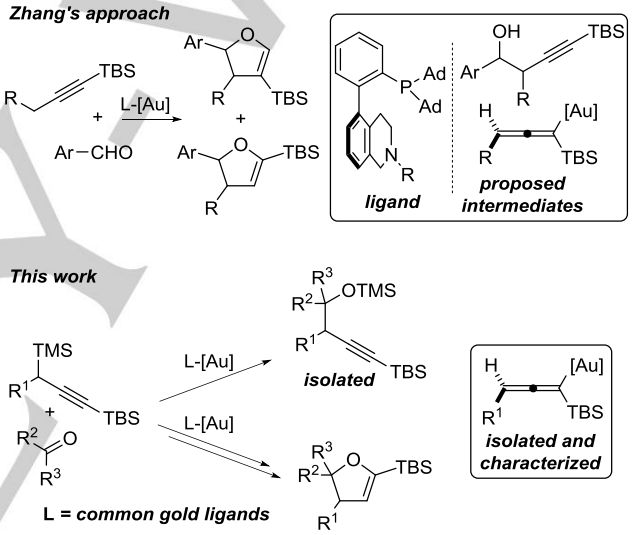
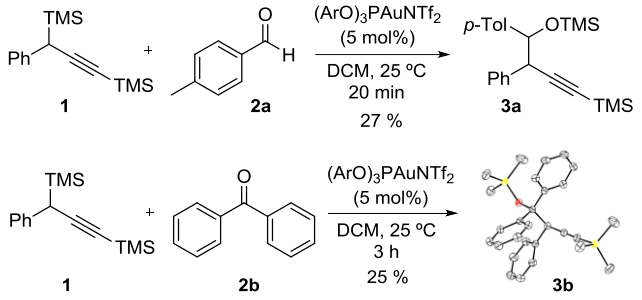


Figure 1. Gold catalyzed propargylations. TMS = Trimethylsilyl; TBS = *Tert*-butyldimethylsilyl.

Following our investigations with gold catalyzed reactions using trimethylsilylalkynes and carbonyl compounds,[12a-b] we initially reacted 3-phenyl-1,3-bis(trimethylsilyl)-1-propyne **1**, as the model compound, with *p*-tolualdehyde **2a** or benzophenone **2b**, in dichloromethane at room temperature, using a gold catalyst with a tris(2,4-di-*tert*-butylphenyl)phosphite ligand. Bis(trifluoromethanesulfonyl)imidate was used as counteranion to avoid the use of silver salts for the generation of the corresponding catalyst. To our surprise, we did not observed the formation of any product related to an initial gold acetylide addition to the aldehyde, but compounds **3a** and **3b** were formed in moderate yields and as an almost equimolecular mixture of diastereoisomers for **3a** (Scheme 1). The structure of the trimethylsilyloxyhomopropargyl compounds **3a,b** was unambiguously determined by NMR and by an X-Ray analysis performed on a monocrystal of compound **3b**.[15]



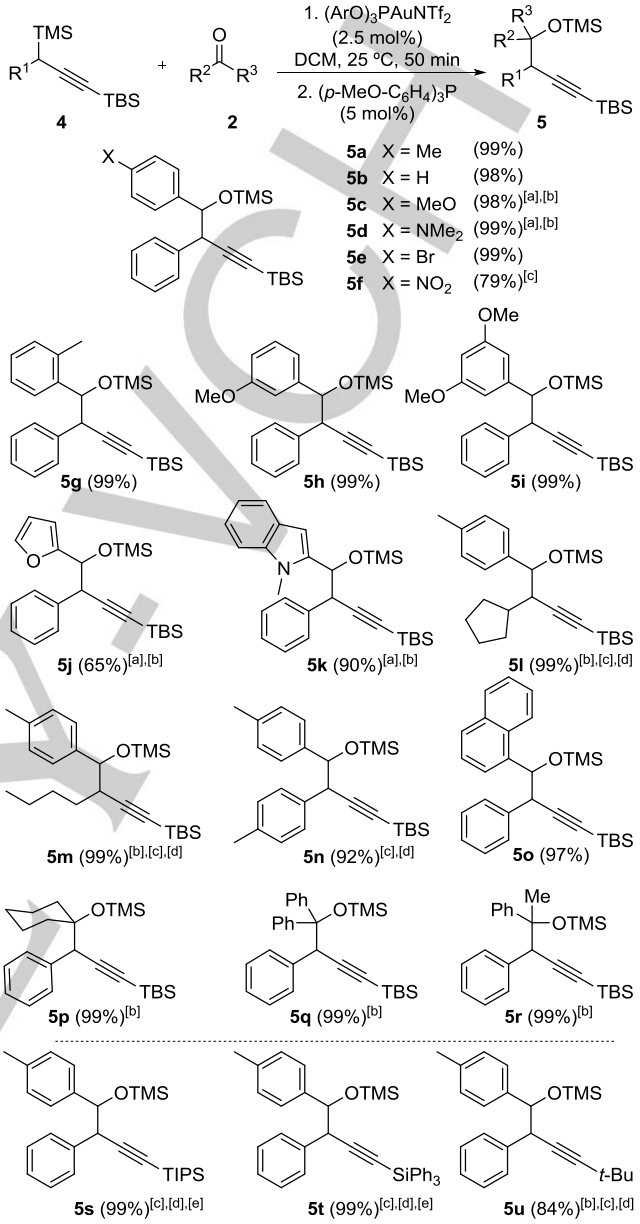
Scheme 1. Preliminary results and X-ray structure of **3b**.

Due to partial decomposition of alkyne **1** through the formation of an allene derivative, the use of 3 equivalents of **1** dramatically increased the yield of compound **3a** to a ca. 80%, after chromatographic purification. Alternatively, replacing trimethylsilyl group of the alkynyl position by a *tert*-butyldimethylsilyl allowed an almost equimolecular employ of both reagents presumably due to their higher stability. In this sense, the reaction of 1.2 equivalents of 3-phenyl-1-*tert*-butyldimethylsilyl-3-trimethylsilyl-1-propyne **4a** with *p*-tolualdehyde **2a**, under the selected reaction conditions, arises in the formation of silyloxy compound **5a** in quantitative yield (Table 1; **5a**). Finally, from a ligand screening,[16] phosphite ligand emerged as the best choice.

We next analyzed the scope of the reaction in terms of the nature of the carbonyl compound **2**. Additionally, as a proof of the goodness of the reaction, the catalyst load was reduced to 2.5 mol%. Finally, a ca. 5 mol% of a phosphine ((*p*-MeO-$C_6H_4)_3P$) was added at the end of the reaction to inactivate the gold catalyst and avoid potential decomposition. Although almost negligible diastereoselectivity was observed,[16] the reaction occurs in very high yields and the propargylation can be performed with aldehydes (**5a-o**,**5s-u**) and also aliphatic or aromatic ketones (**5p-r**) (Table 1). In terms of the substitution pattern in the aromatic ring of carbonyl compounds **2**, it tolerates the presence of donor (**5a,5c,d,5g-i**) and acceptor groups (**5e,f**) and it could also be accomplished with heterocyclic aldehydes (**5j,k**). Finally, the reaction works also satisfactorily for aliphatic propargylic silanes (**5l,m**). Moreover, in addition to *tert*-butyldimethylsilylalkynes, to our surprise, high sterically demanding systems, such as alkynyl substituted triisopropylsilyl and triphenylsilyl compounds, were also able to perform the reaction quantitatively, to form the corresponding silyl ethers **5s,t**. Finally, in order to establish, whether or not, the presence of an alkynyl silyl moiety is a requirement for the reaction, we observed that propargylation could also be achieved, in 84% yield (**5u**), using a *tert*-butylacetylene derivative.

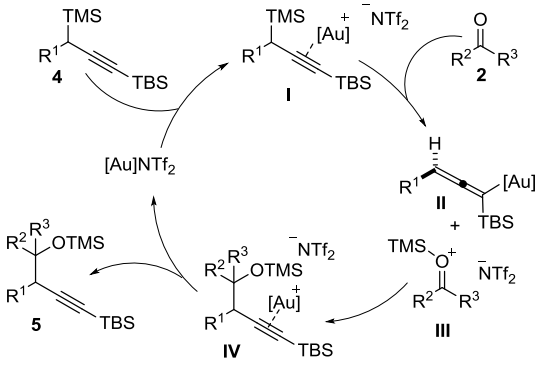
We have also explored, as a control experiment, the use of trimethylsilyl triflimidate as a catalyst in the absence of gold(I) complex. Under the same reaction conditions, compound **5a** was obtained in a *ca*. 20% yield (99% yield under gold catalysis) indicating a prominent participation of the gold catalyst in the silicon release.

Table 1. Scope of the reaction



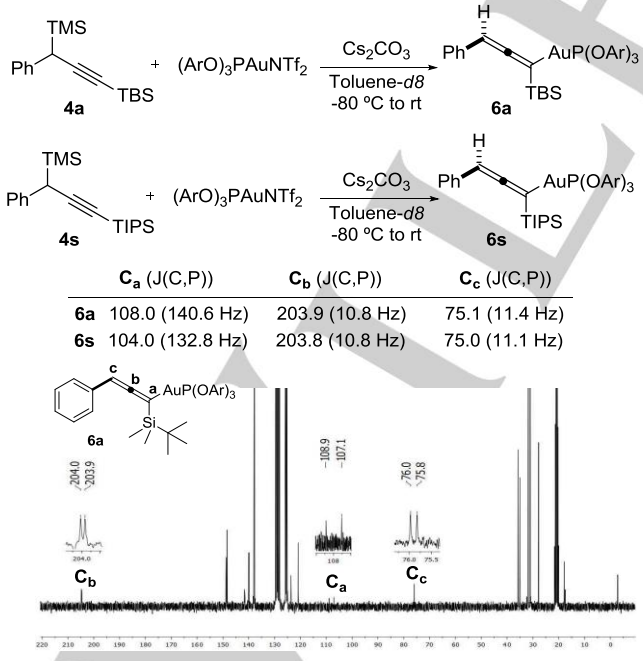
[a]Performed at -20 ºC. [b]3h of reaction. [c]5 mol% of catalyst. [d]3 Equivalents of **4**. [e]16h of reaction. TIPS = Triisopropylsilyl

Next, a mechanistic proposal for the catalytic formation of compounds **5** could be formulated and it is outlined in Scheme 2. Initially, a π-coordination of gold catalyst to the alkyne could occur, to form intermediate **I**. This intermediate **I** could subsequently evolve towards the formation of σ-gold(I) allenyl intermediate **II**. This evolution might be facilitated by the participation of the triflimidate anion and also by the carbonyl compound that, in term, could be synergistically activated.[12a-b],[17] Next, a nucleophilic attack from the gold allenyl derivative **II** to the activated carbonyl compound **III**, would drive the reaction to the formation of intermediate **IV**. Finally, intermediate **IV** would evolve giving rise to the formation of homopropargyl silyl ethers **5** and the recovering of the gold catalyst.



Scheme 2. Mechanistic proposal. [Au] = $AuP(OAr)_3$

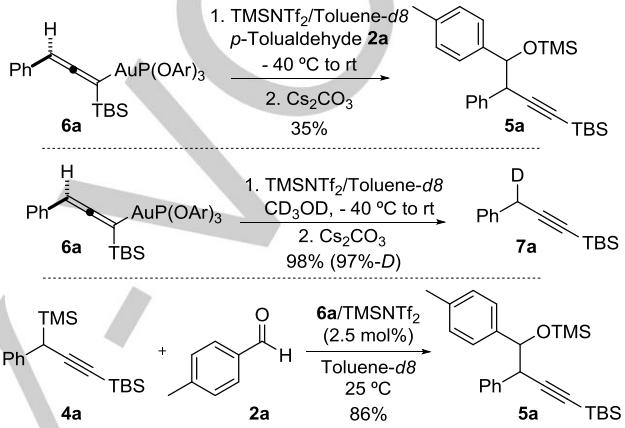
In order to give light to the reaction mechanism we focused our efforts in the isolation of elusive σ-allenyl gold intermediate **II**. Thus, stoichiometric gold treatment of propargylsilanes **4a,s**, in toluene-*d8* at low temperature, and in presence of dry cesium carbonate, yields the formation of corresponding σ-gold allenyl complexes **6a(IIa)** and **6s(IIs)** (Scheme 3). Both compounds could be partially purified after filtration of cesium carbonate, removal of the solvent, and the residue been dissolved in pentane and filtrated twice through a celite pad. Compound **6a** could be isolated as a white solid by precipitation from dry methanol. Both compounds **6a,s** were characterized by mono- and bidimensional ^{1}H, ^{13}C and ^{31}P-NMR experiments. As representative signals for **6a** it is worth to mention the phosphorus coupled allene carbon (**C_b**), the gold bounded carbon (**C_a**) and **C_c**-H (Scheme 3; *bottom*). On the other hand, long distance couplings J^3(C,H) are observed, in a bidimiensional HMBC (^{1}H-^{13}C), between **C_a** and the hydrogen atom at **C_c**; and also between **C_a** and TBS-methyl hydrogens.[16]



	C_a (J(C,P))	C_b (J(C,P))	C_c (J(C,P))
6a	108.0 (140.6 Hz)	203.9 (10.8 Hz)	75.1 (11.4 Hz)
6s	104.0 (132.8 Hz)	203.8 (10.8 Hz)	75.0 (11.1 Hz)

Scheme 3. Synthesis of σ-gold allenyl complexes **6a** and **6s**.

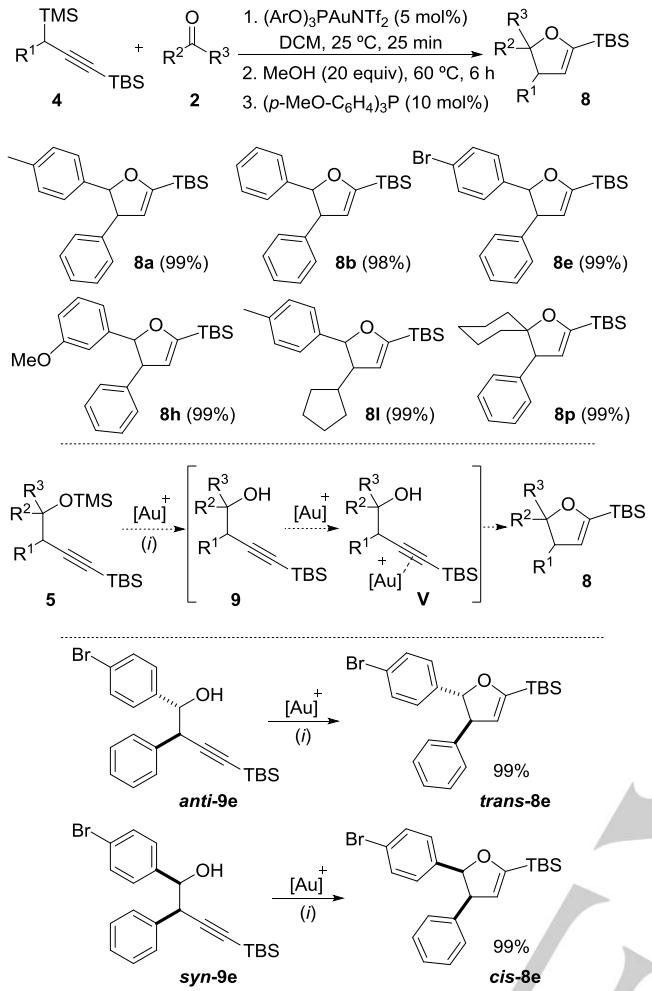
Next, in an attempt to evaluate the participation of the σ-gold allenyl complex in the catalytic process, a stoichiometric reaction was performed (Scheme 4). Thus, addition of complex **6a** to a solution of TMS-activated *p*-tolualdehyde resulted in the formation of the expected compound **5a**, in moderate yield. No product was observed in absence of $TMSNTf_2$; even at high temperature (Toluene-*d8*; reflux). Similarly, in the presence of CD_3OD instead of aldehyde, corresponding deuterated propargylic compound **7a** was obtained. Moreover, a successful experiment could also be achieved using catalytic amounts of complex **6a** and $TMSNTf_2$ (2.5 mol%).



Scheme 4. Stoichiometric and catalytic experiments with of σ-gold(I) allenyl complex **6a**.

These results represent the first σ-gold allenyl complex, participating in a gold(I) catalyzed transformation, that could be isolated and characterized, as the only other two examples of characterization of this type of gold complexes did not involve catalytically competent species.[9],[10]

Finally, trimethylsilyl propargyl compounds **4** could also be, *in situ*, transformed into 4,5-dihydrofurans **8**. Thus, after 25 min of gold catalyzed reaction of compounds **4** with corresponding carbonyls **2**, 20 equivalents of methanol were added (for deprotection of the silyl ether) and the reaction heated at 60 °C for 6 hours. Following this procedure, 2-*tert*-butyldimethylsilyl-4,5-dihydrofurans **8** were obtained in almost quantitative overall yields from propargylsilanes **4** and isolated as an almost equimolecular mixture of diastereoisomers (Scheme 5; *top*).



Scheme 5. Dihydrofuran synthesis (*top*). Mechanistic proposal (*middle*). Stepwise reaction (*bottom*). (*i*) 1. $(ArO)_3PAuNTf_2$ (5 mol%), DCM/MeOH (5:1), 60ºC, 6 h; 2. (*p*-MeO-$C_6H_4)_3P$ (10 mol%).

Formation of dihydrofurans **8** is proposed to occur through a gold catalyzed *5-endo-dig* cycloisomerization[18] from corresponding homopropargylic alcohols **9** (Scheme 5; *middle*). Alcohols **9** are easily accessible from silyl ethers **5** under acidic treatment and both stereoisomers were isolated from the mixture.[16] In order to confirm the mechanistic proposal for the formation of the 4,5-dihydrofuran derivatives **5**, homopropargyl alcohols ***anti*-9e** and ***syn*-9e** were transformed, under the same catalytic reaction conditions, yielding corresponding dihydrofurans ***trans*-8e** and ***cis*-8e**, respectively, in quantitative yields (Scheme 5; *bottom*).

In conclusion, we reported here a simple and smooth gold catalyzed propargylation of synergistically activated aldehydes and ketones and the isolation of a σ-gold allenyl intermediate. For this purpose, propargylsilanes, which could be efficiently transformed into corresponding homopropargyl silyl ethers, emerged as optimal candidates for gold catalyzed propargylation reactions. The reaction is proposed to occur through the formation of a σ-gold allenyl intermediate and this elusive intermediate could be, for the first time, isolated and characterized from a catalytic process and its reactivity proved. Finally, as an interesting complement for the reaction, a one-pot transformation, from propargylsilanes to corresponding 4,5-dihydrofurans, could be efficiently achieved. Reported gold catalyzed carbonyl propargylation and unprecedented isolation of a σ-gold allenyl intermediate, contribute to fill two important gaps in the field of homogeneous gold catalysis.

Acknowledgements

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Keywords: Catalysis • Gold • Intermediates • Propargylation • Furans

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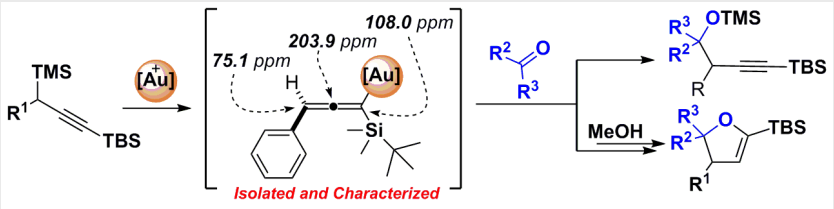

Golden capture: A σ-gold allenyl intermediate was isolated and characterized in the course of the study of a novel gold catalyzed propargylation reaction. Propargylsilanes emerged as very effective reagents for a propargylation reaction of carbonyl compounds, reaction with just a single precedent in gold catalysis.

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