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

Sergio Fernández,[a] Jairo González,[a] Javier Santamaría[a,]* and Alfredo Ballesteros[a,]*

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[4] 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.[5] In this field, our group was able to characterize a σ-gold allylic cation, closely related to allenyl gold complexes,[6] as intermediate in gold catalyzed enyne cycloisomerizations.[7] However, although several π-gold alleny[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[10] and Pyne, Hyland and co-workers.[11]

In the course of our investigations related to the use of alkynylsilanes in gold catalyzed transformations,[12,13] 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]

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-butyl dimethylsilyl.

Following our investigations with gold catalyzed reactions using trimethylsilylalkynes and carbonyl compounds,[12a–c] 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(trifluoromethanesulfonylimidate) 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 acetylidy 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]
Due to partial decomposition of alkyne 1 through the formation of an allenic 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 alkyne position by a tert-butylidemethylsilyl 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-butylidemethylsilyl-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 ((\(\rho\)-MeO-C\(_6\)H\(_3\))\(_2\)P) 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-butylidemethylsilylalkynes, to our surprise, high sterically demanding systems, such as alkyne substituted trisopropysilysil or 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 alkyne 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 trimidate 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

<table>
<thead>
<tr>
<th>R(^1)</th>
<th>R(^2)</th>
<th>R(^3)</th>
<th>Yield (%)</th>
</tr>
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<tbody>
<tr>
<td>TBS</td>
<td>TBS</td>
<td>TBS</td>
<td>5a (99%)</td>
</tr>
<tr>
<td>MeO</td>
<td>OTMS</td>
<td>TBS</td>
<td>5b (99%)</td>
</tr>
<tr>
<td>MeO</td>
<td>OTMS</td>
<td>TBS</td>
<td>5c (99%)</td>
</tr>
<tr>
<td>NMe(_2)</td>
<td>OTMS</td>
<td>TBS</td>
<td>5d (99%)</td>
</tr>
<tr>
<td>Br</td>
<td>OTMS</td>
<td>TBS</td>
<td>5e (99%)</td>
</tr>
<tr>
<td>NO(_2)</td>
<td>OTMS</td>
<td>TBS</td>
<td>5f (79%)</td>
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Next, a mechanistic proposal for the catalytic formation of compounds 5 could be formulated and it is outlined in Scheme 2. Initially, a \(\pi\)-coordination of gold catalyst to the alkyne could occur, to form intermediate I. This intermediate I could subsequently evolve towards the formation of \(\sigma\)-gold(I) allenyl intermediate II. This evolution might be facilitated by the participation of the trimidate anion and also by the carbonyl compound that, in term, could be synergistically activated.[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 1. Preliminary results and X-ray structure of 3b.
In order to give light to the reaction mechanism we focused our efforts in the isolation of elusive \( \sigma \)-allenyl gold intermediate II. Thus, stoichiometric gold treatment of propargylsilane 4a, in toluene-\( \text{d}_8 \) at low temperature, and in presence of dry cesium carbonate, yields the formation of corresponding \( \sigma \)-gold allenyl complexes 6a(IIa) and 6s(IIIs) (Scheme 3). Both compounds could be partially purified after filtration of cesium carbonate, removal of the solvent, and the residue being 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 \( ^1 \text{H}, ^{13} \text{C} \) and \( ^{31} \text{P} \)-NMR experiments. As representative signals for 6a it is worth to mention the phosphorus coupled allene carbon (\( \text{C}_b \)), the gold bounded carbon (\( \text{C}_a \)) and \( \text{C}_c \)-H (Scheme 3; bottom). On the other hand, long distance couplings \( J(\text{C, H}) \) are observed, in a bidimensional HMBC (\( ^1 \text{H} - ^{13} \text{C} \)), between \( \text{C}_a \) and the hydrogen atom at \( \text{C}_c \); and also between \( \text{C}_a \) and TBS-methyl hydrogens.

Next, in an attempt to evaluate the participation of the \( \sigma \)-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-\( \text{d}_8 \); reflux). Similarly, in the presence of CD\(_3\)OD 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%).

These results represent the first \( \sigma \)-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).
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In conclusion, we reported here a simple and smooth gold catalyzed propargylation of homopropargyl alcohols corresponding to corresponding homopropargyl alcohols were transformed, under the same catalytic reaction conditions, yielding corresponding dihydrofurans in quantitative yields (Scheme 5: bottom).

In conclusion, we reported here a simple and smooth gold catalyzed propargylation of homopropargyl alcohols corresponding to corresponding homopropargyl alcohols were transformed, under the same catalytic reaction conditions, yielding corresponding dihydrofurans in quantitative yields (Scheme 5: bottom).

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 important gaps in the field of homogeneous gold catalysis.

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Keywords: Catalysis • Gold • Intermediates • Propargylation • Furans


[16] See supporting information for details.


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.