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Mechanistic Insights on the Hydration of Terminal and Internal Allenes Catalyzed by $[(\text{NHC})\text{Au}]^+$

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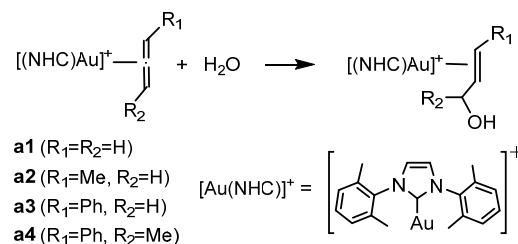
Supporting Information Placeholder

ABSTRACT: The reaction mechanism for the hydration of internal and terminal allenes catalyzed by $[\text{Au}(\text{NHC})]^+$ is analyzed by means of DFT calculations. Several reaction pathways for generating the two possible regioisomers were evaluated. Direct addition on coordinated allenes, or to an intermediate with a σ -allylic cation structure, as suggested for the Au(I) catalyzed hydroamination of allenes, were considered. The isomerization between both regioisomeric products catalyzed by the same Au(I) catalyst was also investigated as suggested for hydroalkoxylation of allenes. The regioselectivity of the reaction predicted by computation agrees with experiment for both, terminal and internal allenes. The presence of alkyl or aryl substituents introduces differences in the reaction mechanism for the hydration process

INTRODUCTION

Addition of water to unsaturated C-C bonds^{1,2} to generate alcohols or ketones is a transformation that satisfies both atom economy³ and redox neutrality.⁴ Hydration of alkynes have been largely described in the literature^{5,6,7} whereas that of alkenes⁸ and specially allenes^{9,10} are much less common. The reaction between a very polar (water) and unpolar reactants is very unfavorable, therefore requiring the presence of a catalyst. Among the metals used to catalyze this process (Rh,¹¹ Pd,¹² Pt,¹³ Ru,¹⁴ others¹⁵) gold¹⁶ occupies a prominent place. In fact, since the beginning of this century homogeneous gold catalysis has emerged as a powerful and rich method to activate C-C unsaturated bonds for addition reactions.^{17,18} Addition of O-based and N-based nucleophiles have been largely explored.¹⁹ Nevertheless, the use of the simplest O-based and N-based nucleophiles, H₂O and NH₃, respectively, are less common (apart from hydration of alkynes).

We are interested in the understanding and rationalizing the development of synthetic tools that employ these reactants as starting material to produce higher added value chemicals. In the case of NH₃, for instance, we contributed²⁰ to the understanding of the reaction mechanism for the Au(I) catalyzed hydroamination of alkynes developed at the Bertrand's group.²¹ Hydration of alkynes have been largely studied,⁵ however, to the best of our knowledge, for allenes only two cases have been published: a Au(I)-catalyzed process by the group of Widenhoefer,⁹ and an Os-based reaction by Esteruelas and coworkers.¹⁰ We will concentrate here on the computational analysis of Au(I) catalyzed hydration of allenes (Scheme 1).

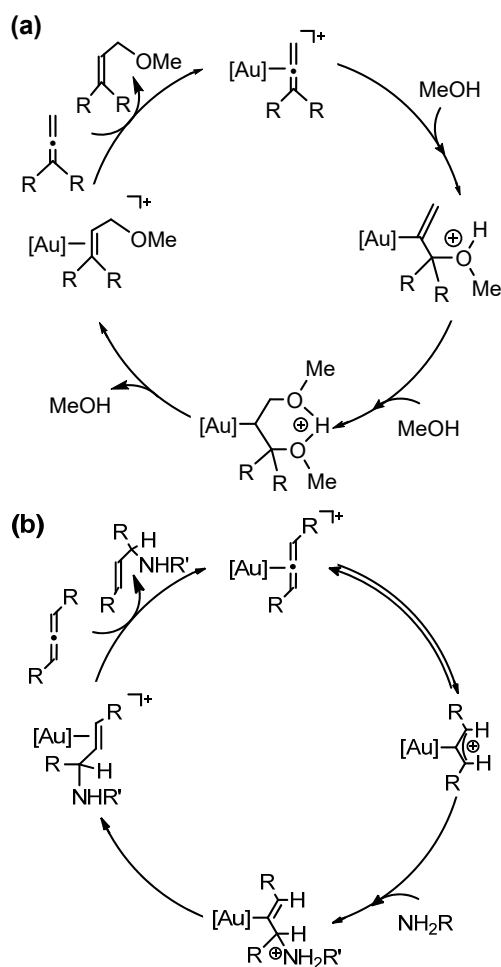


Scheme 1. Gold catalyzed hydration of allenes. R₁ and R₂ may be H, Me or Ph alternatively. A schematic representation of the $[\text{Au}(\text{NHC})]^+$ catalyst is also shown.

The chemistry of allenes and their applications in synthesis were retarded compared to other unsaturated organic substrates.²² The allene exhibit diverse coordination chemistry since both double bonds are initially susceptible to be bonded to the metal. For the case of Au(I) complexes, due to their increasing relevance the gold-allene bond has been studied in detail.²³ To understand their reactivity computational chemistry is a crucial tool.^{24,25}

Regarding the mechanism for the Au(I) catalyzed hydration of allenes, to the best of our knowledge, it has not been described so far. Widenhoefer and coworkers also reported the hydroalkoxylation of terminal and internal allenes, and the reaction mechanism for the case of terminal allenes was investigated by Paton and Maseras.²⁶ They found that the alcohol addition takes place by nucleophilic attack of alcohol to the coordinated allenes, and a subsequent proton transfer. Nevertheless, for explaining the regioselectivity experimentally observed the process needs to undertake an isomerization of the alcohol moiety, a process that is kinetically feasible and generates the thermodynamically most stable product (see Scheme 2a). These results were further

supported by Lee and MacGregor in their studies of Au-catalyzed allylic etherification of alcohols.²⁷ On the other hand, a related process of hydroamination of allenes catalyzed by $[(\text{NHC})\text{Au}]^+$ was described by Goddard and coworkers.²⁸ For internal allenes these authors found that coordination of the allene generates a σ -allyl cation. This intermediate is the one undertaking the nucleophilic addition. The final regioisomer is directly obtained in this case, without any isomerization needed (Scheme 2b). Hydroamination with hydrazine catalyzed by Bertrand's gold-CAAC complex gives hydrazine as major product.²⁹ In this case, a direct addition on coordinated allene is proposed as the mechanism.³⁰ According to these results we wondered which would be the mechanism for the hydration of allenes (both terminal and internal), and whether an isomerization process would be also required or not, to account for the observed regioselectivity.



Scheme 2. Mechanisms proposed for Au(I) catalyzed functionalization of allenes: (a) hydroalkoxylation of terminal allenes,²⁶ (b) hydroamination of internal allenes.²⁸

COMPUTATIONAL DETAILS

Calculations were performed at the DFT level using the M06 functional including an ultrafine integration grid, as implemented in Gaussian 09;³¹ this functional has been shown to give proper performance for this type of systems.³² The Au atom was described using the scalar-relativistic Stuttgart–Dresden SDD pseudopotential and its associated

double- ζ basis set, complemented with a set of f polarization functions.³³ The 6-31G(d) basis set was used for the H, C, O and N. The structures of the reactants, intermediates, transition states, and products were optimized in THF ($\epsilon = 7.4257$), described by the SMD continuum model. As far as the nucleophile (water) is concerned, three explicit water molecules were included for the model in the calculations; this model was shown to properly work in related hydration processes.⁷ The NHC ligand for gold catalyst employed experimentally was [1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene]; to avoid conformational issues isopropyls were substituted by methyls in our model (Scheme 1); test calculations for the ligand including isopropyls on the Gibbs energy barriers for the highest energy TSs (for the ligand with methyls) show very similar values (see Table S1). Frequency calculations were carried out for all the optimized geometries in order to characterize the stationary points as either minima or transition states. It was confirmed that transition states connect with the corresponding intermediates by usual intrinsic reaction coordinate (IRC) calculations and subsequent optimization to minima. All the energies collected in the text are Gibbs energies in THF at 298K. We recently showed that taking these Gibbs energies not additional corrections are generally needed to properly describe reaction profiles.³⁴ The molecular orbitals analysis were carried out performing a Mulliken population analysis (MPA) with Gaussian 09 at the same level of theory used for the rest of the calculations.

RESULTS AND DISCUSSION

We analyzed here the reaction mechanism for the Au(I) catalyzed hydration of internal $\text{MeCH}=\text{C}=\text{CHPh}$, **a4**, and terminal $\text{CH}_2=\text{C}=\text{CH}_2$, **a1**, $\text{MeCH}=\text{C}=\text{CH}_2$, **a2**, $\text{PhCH}=\text{C}=\text{CH}_2$, **a3** allenes as representative examples of these substrates. The mechanism for the hydration reaction catalyzed by a Au(I) complex can be generally described in the following steps: coordination of the allene to the Au(I) catalyst, nucleophilic addition of water, and proton-transfer from water to the central C atom of allene, also named protodeauration, to generate the allylic alcohol. Nevertheless, how they concretely take place is not known.

The attack of water over the coordinated allene may take place on each of the external carbon atoms of the allene. This defines the regioselectivity of the process. Alternatively, such nucleophilic attack may also take place on the σ -allyl cation intermediate, giving rise to the same two regioisomers. The feasibility for an isomerization between allylic alcohol product was also considered. All these alternative pathways were evaluated for each of the allenes studied and presented in the following subsections.³⁵

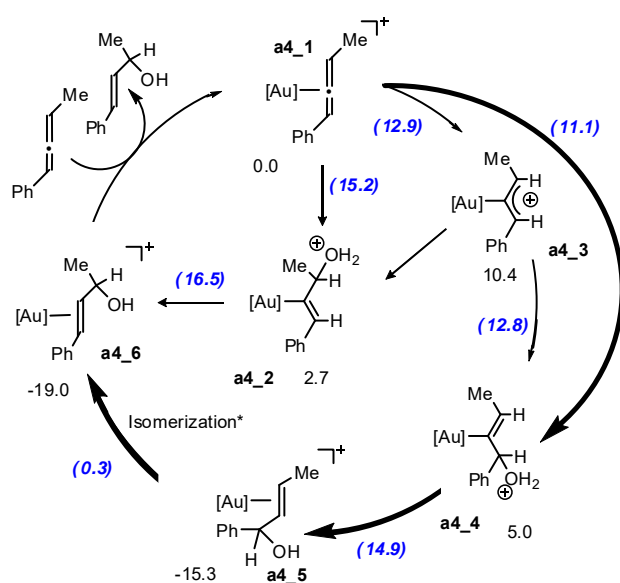
(a) Hydration of internal allenes.

In the experimental work by Widenhoefer and coworkers they analyzed the hydration of several internal and terminal allenes.⁹ **Error! Marcador no definido.** Regarding the internal ones, they analyzed $\text{MeCH}=\text{C}=\text{CH}_2\text{OBz}$, $\text{MeHC}=\text{C}=\text{CHPh}$ and $\text{RHC}=\text{C}=\text{CHR}$ ($\text{R} = n\text{-pentyl}$). We selected $\text{MeHC}=\text{C}=\text{CHPh}$ to perform the mechanistic study because it has the major yield among those checked (64%), and allow us to study the regioselectivity of the hydration process for an allene having one alkyl and one aryl

substituents. In the next subsection terminal allenes with alkyl and aryl substituents will be analyzed.

For the hydration of internal allenes several alternative pathways were computationally explored (Scheme 3). On one side, direct addition of water on the substituted carbon (Me-side or Ph-side) were considered. Moreover, the existence of a σ -allyl cationic intermediate^{36,37} was proposed to be involved in the racemization of chiral allenes,³⁸ as well as for the hydroamination of allenes.²⁸ Addition of water to this intermediate was also considered.

The catalytic cycle starts by coordination of allene **a4** (MeCH=C=CHPh) to the gold(I) catalyst. The coordination may take place through any of the two double bonds. The relative Gibbs energy between them are 0.0 and 2.3 kcal/mol, for **a4_1** (Ph-side) and **a4_1b** (Me-side), respectively.³⁹ The nucleophilic addition of water may take place to the coordinated allene **a4_1**, or to the σ -allyl cationic intermediate, **a4_3**. Both possibilities were evaluated.



Scheme 3. Mechanistic alternatives for the hydration of internal allenes catalyzed by Au(I) reaction. [Au]=[NHC]Au; relative Gibbs energies in kcal/mol; transition states are shown in parenthesis and blue. (*) Isomerization process takes place in two steps (Scheme 4); only the highest energy value is shown.

The formation of σ -allyl intermediate, **a4_3**, with a relative energy of 10.4 kcal/mol, has an energy barrier of 12.9 kcal/mol, **a4_TS13** (Figure 1a).⁴⁰ This species has been invoked in the racemization process, though its presence is not enough to explain the racemization itself.³⁸ Widenhoefer and coworkers observed that for allene **a4**, the use of an enantiomerically enriched substrate gives rise to the formation of racemic product.⁹ They propose that racemization also involves the coordination of two allenes molecules to the Au(I) catalyst. At any rate, racemization is out of the scope of the present work.

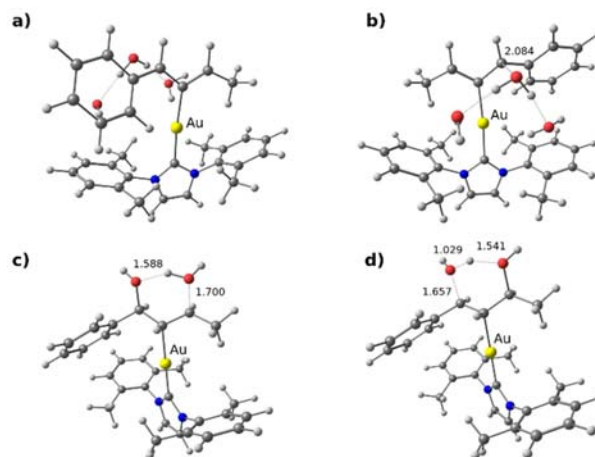


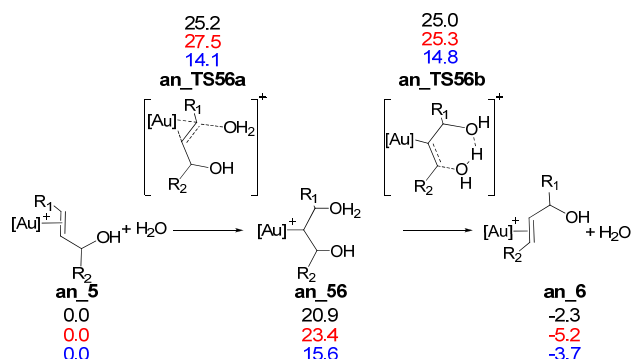
Figure 1 Optimized geometries for: (a) σ -allyl cation intermediate **a4_3**, (b) TS **a4_TS14**, for the nucleophilic addition of water on the Ph side of the reactive, **a4_1**, (c) TS **a4_TS56a**, for nucleophilic addition of water, and (d) TS **a4_TS56b**, for proton transfer concomitant with a water release, generating isomer, **a4_6**.

The presence of nucleophile (water) in the reaction, entails the nucleophilic attack on such Au(I) σ -allyl cation intermediate, **a4_3**. In fact, this is an extremely easy process with a relative Gibbs energy barrier of 2.4 kcal/mol for the addition on the Ph side, **a4_TS34**, whereas it was found to be barrierless on the Me side.⁴¹ In both cases the generated intermediate has a water molecule bonded to the carbon atom of the former allene bearing a Me or a Ph substituent, **a4_2** and **a4_4** respectively. Their relative Gibbs energy values are 2.7 and 5.0 kcal/mol respectively. The hydration process may evolve from any of these two intermediates. This pathway is analogous to that proposed by Goddard et al.²⁸ for the hydroamination of internal allenes catalyzed by a related Au(I) complex.

Intermediate **a4_2** directly advances to the formation of intermediate with the coordinated allylic alcohol, **a4_6**, through a protodeauration transition state with a Gibbs energy of 16.5 kcal/mol, **a4_TS26**. Replacement of the alkene by a reactant closes the catalytic cycle. Nevertheless, this is the highest energy transition state among all the evaluated mechanisms, thus preventing this pathway to take place.

Evolution from intermediate **a4_4** gives rise to the formation of the allylic alcohol product with the alcohol on the side of the Ph substituent. This intermediate, **a4_5**, is quite stable with a relative Gibbs energy of -15.3 kcal/mol. Nevertheless, this species is not the thermodynamically most stable one within the cycle; the other isomer with the alcohol group on the Me side, **a4_6**, is lower with a relative energy of -19.0 kcal/mol. Such interconversion between both isomers is catalyzed by the same Au(I) catalyst. The process takes place with the help of an additional water molecule (see Scheme 4). In the first stage there is a nucleophilic addition of a water molecule to the double bond, **a4_TS56a**; Scheme 4. An intermediate with a strong H-bond between the added water and the alcohol group is generated, **a4_56**. In the second step there is a proton transfer concomitant with a water release, **a4_TS56b**, generating isomer, **a4_6**. The Gibbs energy profile indicates that this process takes place in a single step with a relative barrier of 15.6 kcal/mol (see Scheme 4).⁴² The energy required for the isomerization is rather low, thus, the reaction can

evolve smoothly till the formation of the thermodynamically most stable intermediate, **a4_6**. The discussed transition states are shown in Figure 1. The isomerization from **a4_5** to **a4_6** is similar to that proposed by Paton and Maseras²⁶ for the hydroalkoxylation of terminal allenes catalyzed by a related Au(I) complex (Scheme 2a).



Scheme 4. Schematic representation of the $[\text{Au}(\text{NHC})]^+$ catalyzed allylic alcohol isomerisation process mediated by water. **a2** ($\text{R}_2=\text{Me}$, $\text{R}_1=\text{H}$); **a3** ($\text{R}_2=\text{Ph}$, $\text{R}_1=\text{H}$); **a4** ($\text{R}_2=\text{Ph}$, $\text{R}_1=\text{Me}$)

The direct addition of water to the coordinated allene, **a4_1**, without invoking the σ -allyl cation intermediate was also evaluated. The addition by the allene Me side, **a4_TS12**, and subsequent protodeauration, **a4_TS26**, steps require Gibbs energies of 15.2 and 16.5 kcal/mol, respectively. This is the highest Gibbs energy profile among all computed pathways. However, direct addition of water on the Ph side generating intermediate **a4_4**, with 5.0 kcal/mol, is more feasible. The nucleophilic addition has a Gibbs energy barrier of 11.1 kcal/mol, **a4_TS14**. From this intermediate, **a4_4**, the reaction route is analogous to the one described previously, evolving to intermediate **a4_5** and the subsequent isomerization to obtain intermediate **a4_6**.

For the protodeauration process, ongoing from intermediate **a4_2** to **a4_6**, or from **a4_4** to **a4_5**, instead of a cyclic mechanism with a water molecule acting as a proton shuttle, there is also the possibility of the proton diffusing in the bulk. This process cannot be rigorously evaluated by static calculations (including a group of water molecules in the model); dynamic simulations would be needed to properly emulate this process, but they are out of the scope of this work.⁴³ Instead, we estimated the relative energy of the intermediates generated after the proton release to the medium from **a4_2** and **a4_4**.⁴⁴ Their relative energies are -6.3 and -2.1 kcal/mol, respectively. According to these values this pathway cannot be discarded as a possible mechanism for the protodeauration process. Comparable conclusions were suggested in the theoretical evaluation of the hydration of $\text{Me-C}\equiv\text{CH}$ catalyzed by $[\text{Au}(\text{PH}_3)]^+$ by Hashmi^{7a} and Wu and Zhao,^{7b} respectively. From their calculations these authors inferred that proton moves to solvent instead of direct and explicit motion from the added H_2O to the carbon atom through a cyclic mechanism. Our calculations, by considering the proton in a larger water box (14 water molecules),⁴⁴ also suggests that this mechanism is feasible. The effect on the protodeauration of the substrate substituents⁴⁵ as well as the nature of the ligands⁴⁶ on the Au(I) catalyzed reactions has been also theoretically investigated in the literature.

Regarding the regioselectivity of the process, nucleophilic addition of water on the carbon with an aromatic substituent

(Ph) is kinetically more favored than the addition on the carbon with an aliphatic substituent (Me). Nevertheless, intermediate generated after protodeauration, **a4_5**, in the presence of the Au(I) catalyst easily isomerizes to the most stable thermodynamic product, **a4_6**. The presence of aromatic or aliphatic substituents drives the kinetics and thermodynamics of the reaction. Hence, addition of water on the Ph side is kinetically favored because coordination of allene is more stable through the double bond closer to the Ph, **a4_1**, than through the Me side, **a4_1b**, with an energy difference of 2.3 kcal/mol. Moreover, the contribution of the carbon that undertakes the nucleophilic addition to the LUMO is larger than the contribution of the other carbon of the allene (Table S2 and Figure S1).

The formation of the σ -allyl cation intermediate is not required for the addition of water, although such intermediate is energetically feasible, ongoing from intermediate **a4_2** to **a4_6**. This is different to what was proposed for the case of hydroamination of allenes catalyzed by a Au(I) catalyst, where the amine nucleophilic additions takes place on such intermediate.²⁸ At any rate, none the pathways evaluated has an energy profile high enough to be completely discarded.

(b) Hydration of terminal allenes

The hydration of terminal allenes catalyzed by $[\text{Au}(\text{NHC})]^+$ was also described by Widenhoefer and coworkers for species like $\text{CH}_2=\text{C}=(\text{CH}_2)_{17}\text{Me}$ and $\text{CH}_2=\text{C}=\text{CH}_2\text{CHE}_2$ ($\text{E}=\text{CO}_2\text{Me}$). In all cases the process was regioselective generating the corresponding primary allylic alcohol.

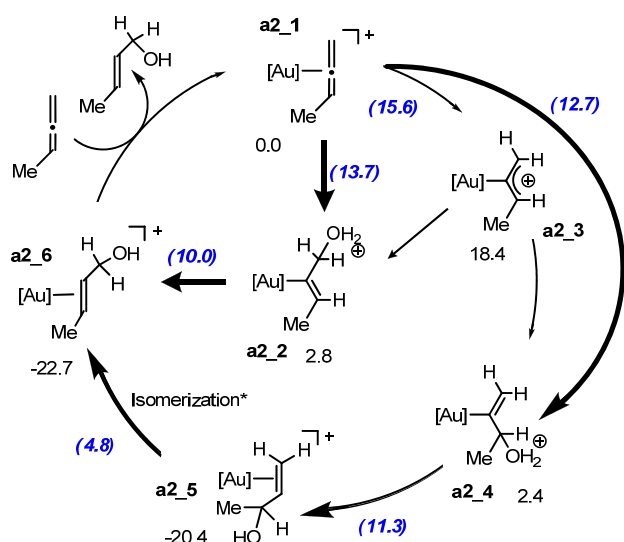
For analytical purposes, we selected the following allenes, $\text{CH}_2=\text{C}=\text{CH}_2$, **a1**, $\text{MeCH}=\text{C}=\text{CH}_2$, **a2**, $\text{PhCH}=\text{C}=\text{CH}_2$, **a3**, as representative allenes with no substituents, aliphatic and aromatic substituents, respectively. The regioselectivity for the addition of water was also evaluated for all these substrates, as well as the feasibility of the participation of the σ -allylic cation intermediate. The formation of a primary allylic alcohol is computationally predicted to be more stable than the formation of the internal allylic alcohol for all the studied cases, in agreement with experiment.

For the case of $\text{MeCH}=\text{C}=\text{CH}_2$, **a2**, analogous pathways than for internal allenes were computationally characterized (see Scheme 5). The formation of the σ -allyl cation intermediate, **a2_3**, has a relative Gibbs energy of 18.4 kcal/mol; the transition state is located a bit lower in Gibbs energy surface, 15.6 kcal/mol, **a2_TS13**.⁴⁷ Addition of water to this intermediate is found to be barrierless to any of the carbon atoms of the allylic cation. The addition on the Me side generates **a2_4**, and a subsequent protodeauration step gives **a2_5** with a relative energy of -20.4 kcal/mol and the transition state **a2_TS45** located at 11.3 kcal/mol. An isomerization of the coordinated allylic alcohol gives the most stable product, **a2_6** (a process shown in Scheme 4). In any case, the route through the σ -allyl cation intermediate, **a2_3**, is much higher in energy than the direct addition of water on the coordinated allene.

The addition of water to **a2_1** on the non-substituted carbon has a Gibbs energy barrier of 13.7 kcal/mol, **a2_TS12**, and generates intermediate **a2_2**, at 2.8 kcal/mol. The subsequent protodeauration gives rise to species **a2_6**, with the transition state **a4_TS26** located at 10.0 kcal/mol. The addition of water to the Me side of allenes, **a2_TS14**, has a Gibbs energy barrier of 12.7 kcal/mol, generating intermediate **a2_4** at 2.4 kcal/mol. The subsequent proton transfer step requires 11.3 kcal/mol, **a2_TS45**. The isomerization from **a2_5** to **a2_6**

takes place in two steps (see Scheme 4); such process requires a relative energy barrier of 25.2 kcal/mol. This pathway becomes more energetically demanding than any of the other processes evaluated, although it is a feasible pathway. Comparing the two possible direct additions of water on the coordinated allene **a2_1**, that on the Me side has slightly lower energy barrier (12.7 vs 13.7 kcal/mol, respectively), thus, formation of intermediate **a2_4** is kinetically favored. Overall, the generation of the final product with the primary allylic alcohol may take place by any of the two routes described and shown (Scheme 5).

These results compare with those proposed by Paton and Maseras for the mechanism of hydroalkoxylation of terminal allenes catalyzed by a similar Au(I) catalyst.²⁶ They found that the addition of MeOH to $\text{CH}_2=\text{C}=\text{Me}_2$ requires an isomerization of the secondary allylic alcohol to the primary allylic alcohol. For the hydration reaction evaluated here, both pathways, direct addition on the terminal carbon and isomerization after addition to the internal carbon atom, contribute to the generation of the primary alcohol as the reaction product.



Scheme 5. Mechanistic alternatives evaluated for the catalytic cycle for the hydration of allene **a2** catalyzed by Au(I). [Au]=[NHC]Au; Gibbs energies in kcal/mol; transition states are shown in parenthesis and blue. (*) Isomerization process takes place in two steps (Scheme 4); only the highest energy value is shown.

For allene **a2** the feasibility of protodeauration from intermediate **a2_2** or **a2_4** via proton diffusion into the water bulk was also computed. The relative stabilities of the neutral intermediates formed after proton releasing are -3.1 and -9.0 kcal/mol, respectively.⁴⁴ Thus, such a stepwise process for the protodeauration, cannot be discarded for this substrate neither.

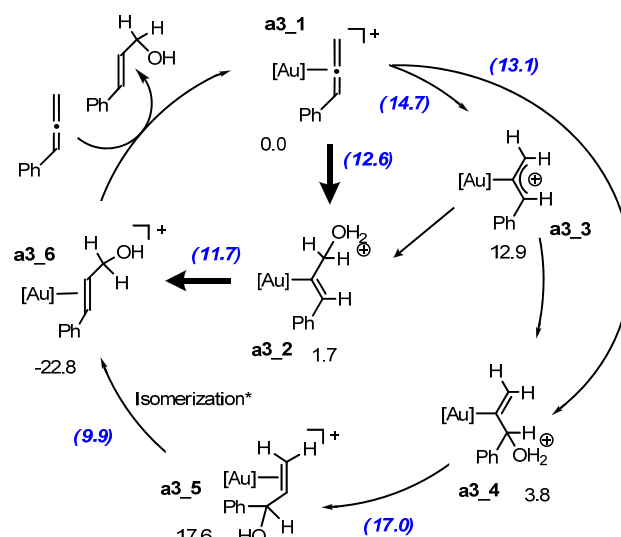
For the case of $\text{PhCH}=\text{C}=\text{CH}_2$, **a3** (Scheme 6), computational results predict that the σ -allyl cation intermediate, **a3_3**, has a relative Gibbs energy barrier of 12.9 kcal/mol, with a relative energy barrier of 14.7 kcal/mol for **a3_TS13**. Nucleophilic addition of water to this intermediate was found to be barrierless. Addition to the terminal allene carbon generates intermediate **a3_2** with a relative energy of 1.7 kcal/mol. From this intermediate the protodeauration step has the transition state, **a3_TS26** at 11.7 kcal/mol, to generate the most stable intermediate, **a3_6**, with a relative Gibbs energy of -22.8 kcal/mol.

Addition of water to the coordinated σ -allylic cationic intermediate **a3_3** on the Ph-side produces intermediate **a3_4**, with a relative Gibbs energy of 3.8 kcal/mol. The protodeauration, to generate intermediate **a3_5** with a relative energy of -17.6 kcal/mol, has the transition state **a3_TS45** at 17.0 kcal/mol. This intermediate may evolve by an isomerization process to generate the most stable intermediate, **a3_6**. This process takes place in two steps, with a global barrier of 27.5 kcal/mol (see Scheme 4).

The direct addition of water to the intermediate **a3_1**, on the terminal carbon atom has a relative energy barrier of 12.6 kcal/mol, **a3_TS12**. Intermediate **a3_2** may evolve to generate the most stable product, **a3_6**, as previously explained. Starting from the initial **a3_1** intermediate, addition of water on the Ph-substituted carbon atom was found to have a relative energy barrier for **a3_TS14** of 13.1 kcal/mol. This produces intermediate **a3_4** with a relative energy of 3.8 kcal/mol. From this intermediate, the reaction may take place by the protodeauration step and a subsequent isomerization to generate intermediate **a3_6**. This pathway has been commented above.

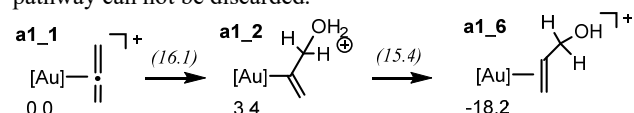
For the protodeauration process, the relative energy of the intermediate formed after proton release to the bulk from intermediates **a3_2** and **a3_4** were also evaluated. These species were found to be -4.8 and -6.8 kcal/mol, respectively. As in the previous cases, such intermediates are energetically accessible and cannot be discarded as a feasible pathway for the proton transfer.

Overall, the direct addition on the terminal carbon atom of the coordinated allene **a3_1** to generate intermediate **a3_2**, and a subsequent protodeauration process to give intermediate **a3_6** has the lowest energy barrier among those evaluated. Thus, all terminal allenes studied in this work, share a mechanism going via direct attack of water to the terminal carbon atom followed by a protodeauration step, though for the case **a2** water addition on the more substituted carbon substituent and subsequent isomerization process is also taking place.



Scheme 6. Mechanistic alternatives evaluated for the hydration of allene **a3** catalyzed by Au(I). Relative Gibbs energies in kcal/mol; transition states are shown in parenthesis and blue. (*) Isomerization process takes place in two steps (Scheme 4); only the highest energy value is shown.

For the sake of completeness, the mechanistic analysis of allene **a1** ($\text{CH}_2=\text{C}=\text{CH}_2$), **a1**, was also performed (Scheme 7). For this reactant the gold σ -allyl cation intermediate was not located at the potential energy surface. Thus, mechanisms involving such structure can be discarded. The reaction pathway was found to proceed via an initial nucleophilic addition on intermediate **a1_1** with a relative Gibbs energy barrier of 16.1 kcal/mol, **a1_TS12**. Intermediate **a1_2** lies at 3.4 kcal/mol. The protodeauration generates the allylic alcohol coordinated to the catalyst, **a1_6**, with a relative Gibbs energy of -18.2 kcal/mol and an associated transition state, **a1_TS26** at 15.4 kcal/mol. The relative energy of the intermediate that would form by proton diffusion into the water solvent is -4.2 kcal/mol. Thus, as in all the previous allenes studied this pathway can not be discarded.



Scheme 7. Schematic representation of the process for hydration of allene **a1** catalyzed by Au(I).; Gibbs energies in kcal/mol; transition state energies are shown in parenthesis and italic.

Regarding the kinetics for the addition of water to terminal allenes, the addition on the terminal carbon atom is kinetically slightly more feasible for **a2** whereas the addition on the internal carbon atom is more favored for **a3**. At any rate, all the nucleophilic additions for both allenes and both regioisomers range in 1.1 kcal/mol. Thus, nucleophilic addition of water itself does not govern the regioselectivity. Such step is not significantly modified by the presence of an alkyl or an aryl substituent. The other steps, as protodeauration and isomerization are more affected by the nature of the substituent. For allene with alkyl substituent, **a2**, the kinetically favored addition pathway gives the less stable regioisomer; a subsequent isomerization is needed to give the thermodynamic product. For allenes with aryl substituent, **a3**, the fastest addition pathway gives the most stable thermodynamic product. For the allene with two substituents, **a4**, the kinetic favored addition gives the alcohol on the Ph side and an isomerization is required to produce the most stable and observed product.

When comparing the Gibbs energy barriers for the water addition on the simplest allene **a1** to that of the terminal allenes, **a2** and **a3**, the Gibbs energy barrier is significantly larger (16.2 vs 13.7 and 12.6 kcal/mol, respectively). Thus, the presence of a substituent at the allene reduces the energy barrier for the addition step.

The σ -allyl cation intermediate was found in the potential surface for all substituted allenes studied, but not for the simplest one, **a1**. Nevertheless, none of the allenes requires such an intermediate to generate the final hydration product. Thus, similarly to internal allenes, this intermediate is not required for hydration reactions.

CONCLUSIONS

The reaction mechanism for the hydration of internal and terminal allenes was analyzed by means of DFT calculations. For all the allenes studied the most stable computationally obtained regioisomer is the one observed experimentally. Thus, regioselectivity for the process is correctly predicted for all the substrates.

The hydration reaction mechanism for allene **a4** ($\text{MeCH}=\text{C}=\text{CHPh}$) goes via water addition on the Ph side because is kinetically faster (Scheme 3). Nevertheless, the intermediate formed **a4_4**, after protodeauration step, easily isomerizes in the presence of the same Au(I) catalyst giving rise to the most stable thermodynamic product, **a4_6**. According to these results the fastest pathway takes place by the direct addition of water on the Ph side of the allene, with a subsequent isomerization.

The hydration of terminal allenes shows that whereas for allene **a3**, with Ph (aryl) substituent, the thermodynamic product is obtained by direct addition of water (in two steps, Scheme 6), for **a2**, with Me (alkyl) substituent, the reaction can proceed via two pathways, the analogous to previous allene and another one with water attack on the substituted carbon atom and subsequent isomerization. Thus, the nature of the substituents of allene has a significant effect on the mechanisms that are at play.

For those substrates where the direct addition does not give the product most stable thermodynamically, the presence of $[\text{Au}(\text{NHC})]^+$ facilitates the isomerization process, thus favoring the formation of the most stable product. Thus, the Au(I) catalyst can play a double role in the process by facilitating the hydration as well as the subsequent isomerization reactions for those allenes that the kinetic for water addition do not favor the thermodynamic product.

The formation of the σ -allyl cation is not required for the water addition for none of the allenes studied. Such intermediate was found in the potential energy surface for all substituted allenes studied, but not for the simplest one, **a1**. The energetic feasibility is in accord with experiment since this species has been proposed to be involved in the racemization process. Nevertheless, contrary to what was postulated for the hydroamination reaction mechanism, this intermediate is not required for hydration reactions. Regarding the protodeauration step, a route taking place via a proton diffusion on water can not be discarded for any of the allenes evaluated.

These results show that the reactions mechanisms for gold(I) catalyzed processes are very subtle, and small differences in the substrate may have important effects on the reaction mechanism.

EXPERIMENTAL SECTION

For description of the calculation performed see Computational Details section.

ASSOCIATED CONTENT

Supporting Information. Figures of Molecular Orbitals for key intermediates, TS Gibbs energy barriers for model and complete ligand, Relative Gibbs energies for coordination modes of allenes, DFT optimized Cartesian coordinates (XYZ), references.

Notes

The authors declare no competing financial interests.

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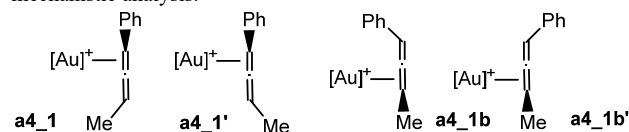
(35) Note that the addition of water to the coordinated allene may take place from different approaching orientations. We have evaluated several orientations but in the discussion there are only included the most energetically favorable addition steps for all the pathways evaluated.

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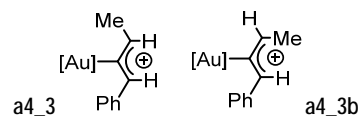
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(39) Moreover, for each isomer, **a4_1** and **a4_1b**, there are two different coordination modes regarding the relative position of the second substituent furthest away from the metal, pointing to the complex or not. Their relative gibbs energies are 0.0 and 0.7 kcal/mol, for **a4_1** and **a4_1'**, and 2.3 and 3.1 kcal/mol for **a4_1b** and **a4_1b'**, respectively. The most stable isomer, **a4_1**, was considered for the mechanistic analysis.



(40) The σ -allyl cation can form two different isomers, **a4_3** and **a4_3b**. Their gibbs energy barriers are 12.9 and 13.3 kcal/mol, whereas their relative energies are 10.4 and 12.3 kcal/mol respectively. Nevertheless, only the former is relevant for the hydration process, because the energy barrier for the addition of water on the **a4_3b** intermediate on the ph side is at least 4.9 kcal/mol higher.



(41) No barrier could be found for the water addition over intermediate **a4_3** on the me side; geometry optimizations performed locating the water up to 5 Å away from the c atom on the me side, always ended up with the formation of the c-o bond.

(42) The potential energy surface show stationary points for **a4_ts56a**, **a4_56** and **a4_ts56b** with of 14.3, 14.3 and 15.3 kcal/mol, respectively. Gibbs energy values are shown in scheme 4.

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(47) In the potential energy surface **a2_ts13** and **a2_3** are stationary points with relative potential energies of 17.2 and 16.6 kcal/mol, respectively. Gibbs energy values, however, are 15.6 and 18.4 kcal/mol, respectively.

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