Gold Catalysis

Cyclopropenylmethyl Cation: A Concealed Intermediate in Gold(I)-Catalyzed Reactions

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In memory of Professor Carsten Schmuck (February 20, 1968–August 1, 2019)

Abstract: The last years have witnessed many gold-catalyzed reactions of alkynes. One of the most prominent species in the reaction of two alkyne units is the vinyl-substituted gold vinylidene intermediate. Here, we were able to show that the reaction of a haloacetylene and an alkyne proceeds via a hitherto overlooked intermediate, namely the cyclopropenylmethyl cation. The existence and relative stability of this concealed intermediate is verified by quantum chemical calculations and 13C-labeling experiments. A comparison between the cyclopropenylmethyl cation and the well-known vinylidene intermediate reveals that the latter is more stable only for smaller cycles. However, this stability reverses in larger cycles. In the case of the smallest representative of both species, the vinylidene cation is the transition state en route to the cyclopropenylmethyl cation. The discovery of this intermediate should help to get a deeper understanding for gold-catalyzed carbon–carbon bond-forming reactions of alkynes. Furthermore, since enynes can be formed from the cyclopropenylmethyl cation, the inclusion of this intermediate should enable the development of new synthetic methods for the construction of larger cyclic halogenated and non-halogenated conjugated enyne systems.

Introduction

In the field of homogenous gold catalysis,[1–5] alkynes represent one of the most important substance classes.[6,7] Unlike other transition-metal-catalyzed reactions,[8,9] the alkyne unit is usually consumed during gold-catalyzed reactions.[6,7] However, in recent years a few exceptions to this have been found.[10–19] Gold-catalyzed reactions of haloalkynes[20] make up by far the greatest number of cases.[10–13,15] For example, Hashmi et al. were able to show that the dual gold-catalyzed[20] reaction of iodoarylacetylenes 1 leads via a head-to-tail dimerization to the cross-conjugated enyne products 2 (Scheme 1a).[21] Recently, we presented the dimerization of chloro- and bromoarylacetylenes (3 and 4) to yield the corresponding head-to-head coupling products 5 and 6 (Scheme 1b, top).[22] In another study, this reaction was extended to the addition of haloarylacetylenes to alkynes 7–9, whereby the trans addition enyne products 10 and 11, respectively, are formed (Scheme 1b, middle).[23]

Instead of alkynes, the usage of alkenes as coupling partners with haloalkynes has also been described[20,25–26] Here, the formation of the product strongly depends on the gold catalyst and the nature of the alkeine reactant. The reaction of 1,2-disubstituted alkenes and gold carbene complexes leads to the corresponding [2+2] cycloaddition products.[26] If, however, gold complexes with phosphine ligands and 1,1-disubstituted alkenes 12 are employed, the 1,2-chloroalkynolation products 13 are formed (Scheme 1b, bottom).[25] The reaction of (bromoethyl)benzene (4a) and cyclic alkenes 14 leads to both bromoalkynolation products 15 and [2+2] cycloaddition products 16 (Scheme 1c).[22]

In this study, we thoroughly examine the mechanism of the gold(I)-catalyzed 1,2-haloalkynolation reaction of alkynes and alkenes via 13C-labeling experiments and quantum chemical calculations. We demonstrate that—unlike the current hypothesis—the formation of the products always proceeds via a head-to-tail addition. The formation of the head-to-head products only takes place in the later course of the reaction via the generation of a cyclopropenylmethyl cation. Surprisingly, when vinyl-substituted, this intermediate is more stable than the well-established vinylidene cation, which is preferred only in specific cases (e.g. small cycles).

Results and Discussion

13C-Labeling Experiments and Quantum Chemical Calculations

In the first step, we wanted to compare the mechanism for the 1,2-haloalkynolation of alkynes and alkenes. Therefore, we considered a labeled chloroacetylene as a model compound. The labeled carbon atoms are highlighted in blue in Scheme 2. The following mechanistic pathways for the 1,2-haloalkynolation of alkynes and alkenes have been formerly proposed (Scheme 2).[11–13,21] The addition of the gold complex 17a to the alkyne 7a can take place via 1,1′- (route A) or via 2,1′ (route B) carbon–carbon bond formation. In the first case (route A), the vinyl cation 18a is formed. After rotation along the C1=C1′ axis, the thus formed vinyl cation 19a leads...
to the enyne complex 21a-I via a 1,3-chlorine shift. The labeled carbon atom is now directly attached to the alkenyl unit (Scheme 2a). Starting from the vinyl cation 22a in route B, the chloronium ion 23a is formed, which is then transformed into the enyne complex 21a-II via rearrangement of the phenyl group. The labeled carbon is now directly

**Scheme 1.** Gold(I)-catalyzed haloalkynylation of alkynes and alkenes.

**Scheme 2.** Proposed mechanisms for the gold(I)-catalyzed 1,2-chloroalkynylation of arylalkyne 7a (a) and alkene 12a (b). The reactions proceed via an attack at either carbon atom C1 (route A) or C2 (route B) of the alkyne complex 17a. The labeled carbon atoms are highlighted in blue.
linked to the phenyl group, that is, the position of the labeled atom in the alkyne has been swapped relative to the labeled position in the initial alkyne gold complex 17a.

Similar pathways can be described for the addition to 1,1-disubstituted alkenes 12 (Scheme 2b). The addition of isobutene (12a) to the carbon atom Cl (route A) of the gold complex 17a leads to the alkyne product 27a-I via a 1,3-chlorine shift, whereas the attack at the carbon atom C2 (route B) of 17a results in the formation of the chloronium ion 29a. After the formation of the cationic vinylidene intermediate 30a, a subsequent aryl shift delivers the alkyne complex 27a-II.

Replacing the hypothetically labeled atoms (blue carbon atoms in Scheme 2) by 13C-labeled atoms (red carbon atoms in Scheme 3) should help to determine which of the routes (routes A and B) is taken. Echavarren et al. were able to show that in the case of the gold(I)-catalyzed reaction of 13C-labeled (bromoethynyl)benzene (13C(1)-4a) and cyclohexene (14a) (Scheme 3a), the addition solely proceeds via an attack at the carbon atom C2 (analogous to route B): The 100% rearranged product 13C(2)-15a is formed via an aryl shift from a vinylidene cation that originated from a bromonium ion.[12] Recently, we were able to demonstrate that the gold(I)-catalyzed addition of 13C-labeled (chloroethynyl)benzene (13C(1)-3a) to 7b delivers two products (13C(1)-10a and 13C(2)-10a) in a ratio of 13:87 (Scheme 3b).[11] On the basis of the accepted mechanisms (Scheme 2a), we previously assumed that both routes (A and B in Scheme 2a) are passed through, whereby route B is slightly energetically favored compared to route A.

To examine which parameters affect the preference for either route, we have conducted a further series of 13C-labeling experiments (Scheme 3c). JohnPhos[Au(NCMe)]SbF6 was used as gold(I) catalyst. Instead of 13C-

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**Scheme 3.** Investigation of the reaction mechanism of the gold(I)-catalyzed 1,2-haloalkynylation of arylalkynes and alkenes with 13C-labeled starting materials. As ligands for the gold(I) complexes, tBuXPhos and JohnPhos were used.
(1)-3a, we used the 13C-labeled bromoacetylene 13C(1)-4a for the addition to the alkyne 7b. Furthermore, we have examined the addition of 13C-labeled chloroacetylene 13C(1)-3a to the alkyne 7b. It turns out that in the case of the addition to 7b, the exchange of chloro- by bromoacetylene results in no change of the product ratio of 13C(1)-11a and 13C(2)-11a (Scheme 3c) compared to that of 13C(1)-10a and 13C(2)-10a (Scheme 3b).

For the gold(I)-catalyzed dimerization of chloroacetylene 13C(1)-3a, we obtained a product ratio of 57:43 for 13C(1)-5a and 13C(2)-5a. The analogous dimerization of bromoacetylene 13C(1)-4a gave the enyne products 13C(1)-6a and 13C(2)-6a in a ratio of 40:60. The addition of 13C-labeled chloroacetylene 13C(1)-3a to the double bond of the 1,1-disubstituted alkene 12b delivered only the rearranged product 13C(2)-13a.

Based on the above mentioned 13C-labeling experiments, we have assumed that the addition of haloacetylenes to alkynes proceeds via both routes (route A and B), whereas the addition to alkenes exclusively occurs via route B.

To find an explanation for this, we performed quantum chemical calculations (Figure 1). The focus was on the attack at the carbon atom Cl (route A) and C2 (route B), respectively. We used the gold complexes of (chloroethynyl)benzene (17a) (X = Cl in Figure 1) and (bromoethynyl)benzene (17b) (X = Br) as haloacetylenes. Furthermore, 1-phenyl-1-propyne (7a) (Y = Me, Ar = Ph), (chloroethynyl)benzene (3a) (Y = Cl, Ar = Ph), (bromoethynyl)benzene (4a) (Y = Br, Ar = Ph), and 1-methoxy-4-(prop-1-yn-1-yl)benzene (7c, Y = Me, Ar = p-C6H4OMe) were employed as alkynes. Isobutene (12a) was used as the alkene reactant. The model compounds correspond or are closely related to the compounds used in the 13C-labeling experiments (Scheme 3). JohnPhos was applied as the ligand of the cationic gold(I) catalyst. B3LYP[27–29] together with the dispersion correction D3BJ[30] was employed as the method for optimization of the geometrical parameters. The basis set 6-31G(d) was applied for the elements C, H, O, P, Cl, and Br; Au was calculated with the def2-TZVP basis set. Additionally, single-point calculations were performed on the thus obtained structures. Here, B3LYP-D3BJ was used with the large basis set 6-311++G(d,p) (for C, H, O, P, Cl, and Br) and def2-TZVP for Au.

To take solvent effects into account, dichloroethane was considered as the reaction solvent by using the SMD[31] model. The data are summarized in Tables S1–S8 and Figures 1 and S1–S18.

The size of the activation energy and the energy of the formed intermediates differ considerably. Nevertheless, in each system, route B is energetically more favored (6.3–7.3 kcal mol−1) compared to route A (Figure 1). The different ratios for the generated 13C-labeled products ranging from 57:43 up to 0:100 (Scheme 3) cannot be explained by comparing the activation energies for the rate-determining step of the two routes. For all systems, only a single product (via route B) is expected for a ΔΔG value of 6.3–7.3 kcal mol−1. If any, one would anticipate a product mixture for the addition of alkene 12a to the gold complex 17a showing the smallest energy difference (6.3 kcal mol−1). However, only one product is formed in this case (Scheme 3c).

**Detailed Quantum Chemical Calculations for the Fate of the Intermediary Formed Cations**

To figure out why the results of the 13C-labeling experiments do not match the quantum chemical calculations, we re-
examined the possible reaction pathways for the intermediary formed cations more accurately via quantum chemical calculations. Therefore, we rotated the intermediary formed cations 18 and 22 (see Figure 1) along the initially formed bond and explored the thus newly formed cations. In addition, we searched for other intermediates that can be formed via further rotation and rearrangement processes. As model compounds for the gold(I)-catalyzed addition of a haloacetylene to an alkyne, chlorophenylacetylene (3a) and 1-phenyl-1-propyne (7a) were chosen, while isobutene (12a) was employed as the alkene reactant. The fates of both reactions are depicted in Figures 2–5.

First, we have a look at the vinyl cation 18a, which is formed via 1,1’-linking (route A, Scheme 2a) in the gold(I)-catalyzed reaction of chlorophenylacetylene (3a) and 1-phenyl-1-propyne (7a). The calculations reveal that the vinyl cation 18a can take two pathways (Figure 2): The first is the previously described pathway to form enyne complex 21a-I via a 1,3-chlorine shift; the highest activation energy amounts to 7.9 kcal mol⁻¹ (route A1 (green) in Figure 2). A considerably lower activation energy is found for the rotation along the Cl–C1’ axis in the other direction (1.3 kcal mol⁻¹, route A2 (black) in Figure 2). Here, the bicyclic cation 40a is formed in a two-step mechanism via a Friedel–Crafts type alkylation of 38a. After rearomatization and subsequent protodesauration, the product would correspond to a chloronium ion 23a. This transition state to this highly unusual cation 45a represents the vinylidene cation 44a, which is not stabilized by the chloride atom. The enyne complex 21a-I is then formed via opening of the C2–C1’ bond. A closer look at the enyne complex 21a-I reveals that the relative orientation of the carbon atoms C1 and C2 differs in routes B1 and B2. The difference in the activation energy for routes B1 (24a) and B2 (46a) amounts to 1.0 kcal mol⁻¹ in favor of route B1. This slight difference in energy should result in both reaction pathways being passed through. In fact, this assumption agrees better with our experimental observations (Scheme 3b).

For the fate of the cyclopropylmethyl cation 25a, which is formed via an attack at the carbon atom Cl of the gold alkyn complex 17a (see Scheme 2b, route A), two reaction pathways were found (Figure 4): both have already been described in the literature. In one case, the [2+2] cycloaddition product 48a is generated (route A2); in the other case the alkyn product 27a-I is formed (route A1). Here, route A1 is clearly preferred.

Starting from the cyclopropylmethyl cation 28a, which is formed via an attack at the C2 atom of the gold alkyn complex 17a (see Scheme 2b, route B), three reaction pathways were localized (Figure 5). The first and highest activa-
tion energy pathway is route B3, which leads to the [2+2] cycloaddition product 50a. Routes B1 and B2 both proceed via the chloronium ion 29a and the vinylidene cation 30a. From there, the outcome of the reaction is determined by two options: The rearrangement of the aryl group leads to the alkyne product 27 a-II (route B1), whereas the rearrangement of the isobutyl group delivers the alkyne complex 27 a-I (route B2). Here again, both products 27 a-I and 27 a-II differ in their relative orientation of the carbon atoms C1 and C2 in the alkyne unit (Figure 5). The most striking difference to the gold(I)-catalyzed reaction with the alkyne (see Figure 3) is that all cyclic structures (31 a and 53 a) are transition states, while the vinylidene cation 30 a is now an intermediate. The difference in the activation energy for the two transition states 31 a and 53 a is so high (7.1 kcal mol\(^{-1}\)) that the gold(I)-catalyzed reaction of a chloroacetylene and a 1,1-disubstituted alkene should only proceed via route B1. This key finding matches our experimental results, as the \(^{13}\)C-labeled carbon atom can be found with 100% directly next to the aromatic unit.

As mentioned above, the relative ratio of the alkyne complexes 21 a-I and 21 a-II for the 1,2-chloroalkynylation of 1-phenyl-1-propyne (7a) depends on the energy of the transition states 24 a, 44 a, and 46 a (Figure 3). During our experimental studies, we realized that the final ratio of the \(^{13}\)C-labeled products depends on the nature of the employed alkyne (see Scheme 3). To verify whether this observation is also reflected in the quantum chemical calculations, we investigated the transition states 24 a, 44 a, and 46 a as well as intermediates 23 and 45 for different systems by computational methods (Figure 6 and Tables S1–S8). Indeed, the experimental trend can also be found in our calculations; for example, the transition state 44 c (route B1) for the gold(I)-catalyzed dimerization of chlorophenylacetylene (3a) is more stable by 1.9 kcal mol\(^{-1}\) than the corresponding transition state 24 c of route B2. Therefore, we expected the preferred formation of the enyne product 21 c-I, which corresponds to the gold complex of \(^{13}\)C(1)-5a (see Scheme 3c). This prediction could be confirmed by \(^{13}\)C-labeling experiments, as more \(^{13}\)C(1)-5a (57%) was formed (see Scheme 3c). Furthermore, this ratio should shift towards the 21-II enyne product (via route B2) with a decreasing energy difference between both transition states 44 (46) and 24. That should also apply to the gold(I)-catalyzed dimerization of bromophenylacetylene (4a) and to the gold(I)-catalyzed addition of
chloro- and bromophenylacetylene (3a and 4a) to alkyne 7b (Scheme 3). Please note, we used 1-methoxy-4-(prop-1-yn-1-y1)benzene as a representative of 7b for the calculations. In fact, our $^{13}$C-labeling experiments showed a decrease in the formation of the $^{13}$C(1)-enyne product for these reactions (40% for $^{13}$C(1)-6a, 13% for $^{13}$C(1)-10a, and 13% for $^{13}$C(1)-11a).

For the further investigation of the mechanistic course of the halooalkynylation reaction, we tried to validate whether the ratio of 21-I (corresponds to $^{13}$C(1)-enyne) and 21-II (corresponds to $^{13}$C(2)-enyne) is also dependent on the nature of the ligand of the gold complex. Therefore, we examined the gold-catalyzed dimerization of $^{13}$C-labeled chlorophenylacetylene (13C(1)-3a) and the addition of $^{13}$C(1)-3a to the alkyne 7b by replacing the JohnPhos ligand by PMe$_3$ (Scheme 4 and
Figure 7. Possible reaction pathways of the halonium ion 23 with different phosphine ligands via formation of the cyclopropenylmethyl cation 45 (route B1) or via aryl shift (route B2) to the enyne complexes 21-I and 21-II, respectively. The indicated free energy ($\Delta G_0$ in kcal mol$^{-1}$) values were calculated using B3LYP-D3BJ(SMD) and are relative to the halonium ion 23. [Au]$^+$ = JohnPhosAu$^+$ or Me$_3$PAu$^+$.

Figure 7). The catalytic species Me$_3$PAu$^+$ that was used for the calculations was generated during the experiment in situ by mixing Me$_3$PAuCl and AgSbF$_6$.

When we used Me$_3$PAu$^+$ in our experimental studies, both reactions showed an increase in the ratio of the molecules corresponding to 21-II of up to 98% (13C(2)-5a and 13C(2)-10a, Scheme 4). The shift towards 21-II could also be confirmed by calculations. The calculated activation energy of route B1 is higher for Me$_3$PAu$^+$ than for JohnPhosAu$^+$ (Figure 7). For example, in the case of the dimerization with JohnPhosAu$^+$, route B1 is more favored by 1.9 kcal mol$^{-1}$ over route B2. This selectivity is reversed by using Me$_3$PAu$^+$ as catalyst so that route B2 is favored by 1.6 kcal mol$^{-1}$. This inversion is reflected in the experimental results (Scheme 4).

The Nature of Cyclopropenylmethyl Cations as Intermediates in Gold(I)-Catalyzed Reactions

As shown above, the commonly described cationic vinylidene intermediate is not an intermediate for the haloalkynylation of alkynes but a transition state (Figure 3).
Please note that this does not apply for the haloalkynylation of alkenes, where it represents a minimum on the potential energy surface (Figure 5). For the reaction of haloalkynes with alkynes, we identified the cyclopropenylmethyl cation and the halonium ion as key intermediates. The latter can be considered as a vinylidene cation stabilized by a halogen atom. This raised the question of how the cationic vinylidene and cyclopropenylmethyl species behave when there is no halogen substitution. Therefore, we calculated the geometries of the simple model compounds 54 and 55 by means of B3LYP-D3BJ (Figures 8 and 9). As basis sets, 6-311 + + G(d,p) (for C, H, and O) and aug-cc-pVTZ-PP (for Au) were applied. Subsequent frequency calculations showed that 54a is a transition state, whereas all other stationary points are minima on the potential energy surface. Furthermore, we conducted single-point calculations using the same basis sets and by means of the double-hybrid density functional approximation B2PLYP,[32] which delivers very reliable data even for high-energy intermediates of reactions involving alkynes.[33–36] To determine the solvent effect, B2PLYP single-point calculations were conducted by using the SMD[31] model and dichloroethane as the solvent. Additionally, the CCSD(T)[37] approximation was employed to compute the energy difference between the transition state 54a and the intermediate 55a (Figure 8).

A comparison of the energy values shows that in all cases the cyclopropenylmethyl cation 55 is the most stable species (Figure 8a). Please note that the vinylidene cation 54a represents a transition state. Thus, the energy difference and the nature of the stationary points (minimum or maximum) strongly depend on the substitution pattern. A phenyl group at the C4 position increases the stability of the cyclopropenylmethyl cation 55a.

![Figure 8.](https://example.com/fig8.png)

Figure 8. a) Relative energies (ΔE in kcal mol⁻¹) of vinylidene cations 54 and cyclopropenylmethyl cations 55. If not stated otherwise, the data were calculated via B2PLYP-D3(SMD)/B3LYP-D3BJ. b) Relative energies (ΔE in kcal mol⁻¹) of cyclic vinylidene cations 56, cyclopropenylmethyl cations 57, and alkyne complexes 58 calculated using B2PLYP-D3(SMD)/B3LYP-D3BJ.

![Figure 9.](https://example.com/fig9.png)

Figure 9. Distances (Å) and angles (°) (a), molecular structures (b) as well as HOMOs (c) and LUMOs (d) of the vinylidene cation 54a and cyclopropenylmethyl cation 55a calculated using B3LYP-D3BJ/6-311 + + G(d,p),aug-cc-pVTZ-PP+ECP. e) Resonance structures of the cyclopropenylmethyl cation 55a.
nethylmethyl cation 55b, as the positive charge at the carbon atom C4 can be stabilized by the adjacent aromatic system. A phenyl group at the position C2 stabilizes the vinylidene cation 55c; however, the cyclopropenylmethyl cation 55c remains the most stable intermediate.

The distances and angles of 54a and 55a obtained by B3LYP-D3BJ/6-311++G(d,p),aug-cc-pVTZ-PP are depicted in Figure 9a. A glance at the values of 55a shows that the structure of 55a is not an isosceles triangle, as the distances for the bonds C1–C3 and C2–C3 differ significantly. The C2–C3 bond (1.515 Å) is a slightly shorter single bond, whereas the C2–C3 bond (2.046 Å) is relatively long. Bonds of this magnitude can also be found for nonclassical carbocations such as norbornyl cations.[38] The C1–C2–C3 angle of magnitude can also be found for nonclassical carbocations for the bonds C1–C2 and C3–C4, respectively (Figure 9b). We considered different ring sizes impressively show that the distribution of these complexes are always formed from the corresponding cyclopropenylmethyl cation. In case of the smallest representative of both species, the vinylidene cation is the transition state en route to the cyclopropenylmethyl cation. The formation of vinylidene cations is only preferred by the incorporation into smaller cyclic systems (five- to seven-membered ring systems). Future strategies could employ this principle to synthesize larger cyclic enyne systems, as enyne gold complexes are always formed from the corresponding cyclopropenylmethyl cation. As the formation of this cation does not necessarily require the presence of a halonium ion, the proof of this key intermediate also questions previously reported mechanisms of the gold-catalyzed reaction of two terminal alkynes.

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Conflict of interest

The authors declare no conflict of interest.

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C=C coupling · DFT calculations · enynes · gold catalysis · vinyl cations

Conclusion

In this work, we thoroughly investigated the gold-catalyzed reaction of two alkynyl units. Unlike the previously assumed mechanism, the rate-determining step, namely the nucleophilic attack of the gold alkynyl complex at the alkynyl, does not determine the connectivity of the carbon atoms in the final product. Starting from a halonium ion, two mechanisms are possible: The first mechanism proceeds via the rearrangement of an aryl group, the second via the formation of a cyclopropenylmethyl cation. The thus formed products are identical and can only be distinguished from each other by 13C-labeling. Furthermore, 13C-labeling experiments impressively show that the distribution of these products can be modified by variation of the substituents of the aromatic backbone and the gold catalyst, which is in accordance with our quantum chemical calculations. A closer look at the cyclopropenylmethyl cation reveals that this species is generally more stable than the commonly discussed vinylidene cation. In case of the smallest representative of both species, the vinylidene cation is the transition state en route to the cyclopropenylmethyl cation. The formation of vinylidene cations is only preferred by the incorporation into smaller cyclic systems (five- to seven-membered ring systems). Future strategies could employ this principle to synthesize larger cyclic enyne systems, as enyne gold complexes are always formed from the corresponding cyclopropenylmethyl cation. As the formation of this cation does not necessarily require the presence of a halonium ion, the proof of this key intermediate also questions previously reported mechanisms of the gold-catalyzed reaction of two terminal alkynes.
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