

## Article

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# 1,3-Chlorine Shift to a Vinyl Cation: A Combined Experimental and Theoretical Investigation of the *E*-Selective Gold(I)-Catalyzed Dimerization of Chloroacetylenes

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## ABSTRACT:

Metal-catalyzed dimerization reactions of terminal acetylenes are well known in literature. However, only a few examples for the dimerization of halogene-substituted acetylenes are described. The products of the latter metal-catalyzed dimerization are the branched head-totail envnes. The formation of the corresponding linear head-to-head envnes has not been reported yet. Herein, we demonstrate by means of quantum chemical methods and experiments that the head-to-head dimerization of chloroarylacetylenes can be achieved via mono gold catalysis. Under the optimized conditions, a clean and complete conversion of the starting materials is observed and the dimeric products are obtained up to 75% NMR yield. A mechanistic investigation of the dimerization reaction reveals that the branched head-to-tail vinyl cation is energetically more stable than the corresponding linear head-to-head cation. However, the latter can rearrange by an unusual 1,3-chlorine shift resulting in the highly stereoselective formation of the *trans* product which corresponds to the gold complex of the head-to-head E-envne. The activation barrier for this rearrangement is extremely low (ca. 2 kcal/mol). As the mono gold-catalyzed dimerization can be conducted in a preparative scale, this simple synthesis of trans-1,2-dichloroenynes makes the gold(I)-catalyzed head-to-head dimerization of chloroarylacetylenes an attractive method en route to more complex conjugated envne systems and their congeners.

## Introduction

In the 1970s Bergman *et al.* could already demonstrate that two conjugated alkyne units can react with each other (Scheme 1a).<sup>1-3</sup> In this context, the resulting diradical intermediate proved to be highly reactive and could be trapped by hydrogen donors to yield the corresponding aromatic compounds. The activation barrier for the Bergman reaction, the thermal cyclization of (*Z*)-hex-3-en-1,5-diyne (**1**) was determined both experimentally and theoretically and amounts to approximately 29 kcal/mol.<sup>4,5</sup>

Recently, dos Passos Gomes and Alabugin could impressively show by means of quantum chemicals calculations that the activation barrier for the Bergman cyclization can be tremendously reduced using gold(I)<sup>6-17</sup> as a catalyst.<sup>18</sup> At the CCSD(T) level of theory they calculated an activation barrier of 14.6 kcal/mol (Scheme 1a), which corresponds to a difference of 15 kcal/mol compared to the radical pendant.<sup>4,5</sup> Similar values were obtained in an independent work.<sup>19</sup>



**Scheme 1.** a) Thermal and mono gold(I)-catalyzed Bergman cyclization. b) Thermal and gold(I)-catalyzed transannular ring closure of 1,6-cyclodecadiyne (**5**). c) Thermal dimerization of the chloroarylacetylene **10a**. The activation energies ( $E_a$ ) are given in kcal/mol.

A similar drastic reduction of the activation barrier for the reaction of two alkyne units can be found for the transannular cyclization of non-conjugated cyclic diynes (Scheme 1b). The thermal transannular ring closure of 1,6-cyclodecadiyne (**5**) occurs at temperatures above

100 °C and proceeds via the bicyclic 1,3-butadiene-1,4-diyl intermediate **6**.<sup>20-23</sup> Both experimentally and theoretically determined values for the activation barrier are in the range of 28-30 kcal/mol.<sup>8,10</sup> Trapping of the diradical intermediate **6** by hydrogen donors leads to the corresponding hydrocarbons. Only recently, we were able to show that here again the gold(I)-catalyzed version causes a tremendous acceleration compared to the radical pendant (Scheme 1b).<sup>24</sup> Depending on the system and the method used either the corresponding cyclopropenylmethyl cation **8** or the butadienyl cation **9** represents the stable intermediate.<sup>24</sup> The activation barrier for these intermediates corresponds to 12.6 kcal/mol on the CCSD(T) level of theory. In this context we were also able to show that trapping of these cations with aromatic nucleophiles leads to the corresponding hexahydronaphthalene systems.<sup>24</sup>

In contrast to the <u>intra</u>molecular reaction of two alkyne units (see Schemes 1a and 1b), the <u>inter</u>molecular reaction is clearly impeded except for the thermal dimerization of alkynes with electron-withdrawing substituents, which are directly bound to the triple bond.<sup>25,23</sup> Here fluorine and alkoxy groups should be named as electron-withdrawing substituents. In particular, chloroarylacetylenes were studied intensively (Scheme 1c).<sup>26-30</sup> For the chloroacetylene **10a** the experimental and theoretical activation barrier amounts to 22 kcal/mol.<sup>29</sup> By using electron-rich aromatic systems, the activation barrier can be reduced to less than 19 kcal/mol.<sup>30</sup> Taking all above mentioned results into account, following question arises: Can the dimerization of chloroarylacetylenes also be accelerated in analogy to the Bergman cyclization and the transannular ring closure by using gold(I) as a catalyst? Exploiting the preparative dimerization of chloroarylacetylenes would be of great benefit as the thermal dimerization can yet only be utilized for methoxyacetylene: The thermal dimerization of chloroarylacetelynes via an intermediary formed diradical leads to a variety of non-separable products.<sup>28,30</sup>

A glance at the literature shows that haloacetylenes have been employed multiple times in gold(I)-catalyzed<sup>31-32,17</sup> reactions. Hashmi *et al.* accomplished the head-to-tail coupling of iodoalkynes via dual gold catalysis<sup>33-44</sup> which delivered the *gem*-enynes **14** (Scheme 2a).<sup>45</sup> Besides the iodoalkynes **12** also one example for each bromo- and chloroacetylene was presented. In either case they isolated the corresponding head-to-tail coupling products **15** and **16**, respectively.<sup>45</sup> This is analogous to the gold(I)-catalyzed dimerization of terminal alkynes **17** (Scheme 2b).<sup>46-49</sup> The formation of the enynes **18** proceeds via a dual  $\sigma$ , $\pi$  activation.<sup>33-44</sup> Both for the alkynes **17** and iodoalkynes **12** the key step in the catalytic cycle is the formation of a gold acetylide<sup>50-52,39</sup> ( $\sigma$  activation) starting from an alkyne and a gold complex. In a following step, the cationic gold complex activates the triple bond of a further alkyne unit ( $\pi$  complex), which is subsequently attacked by the  $\sigma$ -activated gold acetylide.<sup>45</sup> Recently, two intermolecular alkyne-alkyne couplings via mono gold(I) catalysis leading to either naphthalenes or azulenes were reported.<sup>53-54</sup>



Scheme 2. a) Gold(I)-catalyzed dimerization of haloarylacetylenes 10, 12 and 13. b) Gold(I)catalyzed dimerization of terminal alkynes 17. c) Gold(I)-catalyzed [2+2] cycloaddition of chloroarylacetylenes 10 and alkenes 19. d) Gold(I)-catalyzed synthesis of the iodofulvene 21a via cyclization of the mono-iodinated diyne 12a.

Zhang *et al.* used chloroacetylenes for the <u>intermolecular</u> [2+2] cycloaddition between alkynes **10** and non-activated alkenes **19** (Scheme 2c).<sup>55</sup> The first step is the activation of the chloroacetylene by the cationic gold complex, which then reacts with an alkene via a cyclopropylmethyl cation to the corresponding cyclobutyl cation. The last step delivers the desired cyclobutene derivates **20** via desauration.<sup>55</sup>

An <u>intra</u>molecular dimerization of two alkyne units, whereby one unit is substituted with iodine, is shown in Scheme 2d.<sup>56</sup> This reaction also proceeds via a dual gold catalysis mechanism which involves the formation of a gold acetylide by direct metal-halogen exchange of the iodoacetylene **12a** with a gold complex. It could be shown that this cyclization only works with  $\sigma$ , $\pi$ -dinuclear propyne–gold acetylides (DAC, **d**ual-**a**ctivation **c**atalysts<sup>39</sup>) or one cationic gold complex combined with an organogold compound (e.g. IPrAuPh) as additive. No reaction occurred without an appropriate organogold compound as additive.<sup>56</sup>

To the best of our knowledge, and in contrast to the above-mentioned head-to-tail dimerization of haloacetylenes and terminal acetylenes, there is no report about the gold-catalyzed head-to-head dimerization of haloacetylenes. The head-to-head dimerization is

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only known for terminal acetylenes like compound **17** which is dimerized in the presence of transition metal complexes (e.g. rhodium).<sup>57-58</sup> The cyclometalation of two dichloroacetylenes at a metal center (e.g. Co, Rh, Ir) form the corresponding tetrachlorometallole.<sup>59-61</sup> Herein, we describe our investigation of the gold(I)-catalyzed head-to-head dimerization of chloroarylacetylenes. By means of quantum chemical calculations we are able to show that the head-to-head dimerization is not favored with regard to the activation barrier, but can lead to a highly stable gold(I)-enyne complex via an unusual 1,3-chlorine shift. Further experimental studies support our thesis and therefore we present the synthesis of *trans*-1,2-dichloroenynes, a simple structure which, however, has only been supposed as a byproduct during the investigation of the thermal oligomerization of chlorophenylacetylenes.<sup>26-27</sup>

### **Results and Discussion**

## a) Quantum Chemical Model Studies on Gold(I)-Catalyzed Dimerization of Chlorophenylacetylene

As model system for the gold(I)-catalyzed dimerization of chloroarylacetylenes we have chosen chlorophenylacetylene (**10a**; Scheme 3). This compound is not only the simplest representative of this class, but it is also well investigated regarding its thermal dimerization by means of experiments as well as quantum chemical calculations.<sup>28-30</sup> This allows us a direct comparison of both reaction mechanisms (radical vs. Au(I)-catalyzed ionic). For the quantum chemical studies we assumed the simplest reaction mechanism, namely the mono gold(I)-catalyzed dimerization. As reference system for the comparison of the energetic values, the isolated molecules chlorophenylactelyene (**10a**) and the corresponding  $\pi$  complex **22a** were defined. As ligand for the cationic gold complex the neutral phosphine PMe<sub>3</sub> was chosen ([Au]<sup>+</sup> = Au<sup>+</sup>-PMe<sub>3</sub>).

For the reaction of the alkyne units **10a** and **22a** we considered two realistic ways (Scheme 3): In the former case, the 1',1 connection leads to the head-to-head coupling product **24a** while the 1',2 connection delivers the head-to-tail coupling product **26a**. In both cases the positive charge located on carbon atom C2' is stabilized by a phenyl group. As a result, cations **24a** and **26a** should be the energetically most stable intermediates. A connection via 2',1 or 2',2 can be ruled out as the positive charge would be located at carbon atom C1' being stabilized only by a chlorine atom. During our investigation of the radical dimerization via the intermediary formed diradicals, the aromatic units showed a stronger stabilizing effect on the radical centers than alkoxy groups or halogen atoms (see **11a** in Scheme 1c).<sup>29</sup> In case of the radical dimerization the carbon atom C2' is sp-hybridized so the aromatic unit is aligned perpendicular to the butadiene unit.<sup>29</sup> As a consequence we expect a similar geometry for cationic intermediates **24a** and **26a**.



**Scheme 3.** The mono gold(I)-catalyzed dimerization of chlorophenylacetylene **10a** can lead to the head-to-head cationic product **24a** (1',1 dimerization) or to the head-to-tail product **26a** (1',2 dimerization). [Au]<sup>+</sup> = Au<sup>+</sup>-PMe<sub>3</sub>.

The stationary points of the Au(I)-catalyzed dimerization were optimized using the PBE0<sup>62-63</sup> method. As basis set 6-311++G(d,p)<sup>64-67</sup> has been used for C, H, CI and P. For Au the def2-TZVP+ECP<sup>68-69</sup> basis set has been employed. This level of theory proved to give the most reliable results for similar Au(I)-catalyzed reactions.<sup>18,70</sup> Frequency calculations were carried out at each of the structures to verify the nature of the stationary point. It turned out that all transition states have exactly one imaginary frequency, whereas all other structures have none. Furthermore, single point calculations by means of MP2<sup>71</sup> as well as the density functionals PBE0-D3<sup>72-73</sup>, B3LYP<sup>74-76</sup>, B3LYP-D3<sup>72-73</sup> and M06-2X<sup>77</sup> were performed on the PBE0 optimized structures. Here again, as basis set 6-311++G(d,p) has been used for C, H, CI and P. For Au the def2-TZVP+ECP basis set has been employed. To determine the solvent effect on the reactivity, the single point calculations on the PBE0 optimized structures were also performed using dichloromethane as solvent.

**Table 1.** Free energies ( $\Delta G$  in kcal/mol) and energies ( $\Delta E$  in kcal/mol) of **22a-32a** relative to the starting materials (**10a** and **22a**) calculated by means of different methods. As basis sets 6-311++G(d,p)/def2-TZVP+ECP have been used. [Au]<sup>+</sup> = Au<sup>+</sup>-PMe<sub>3</sub>.

	$\Delta m{G}^{a}$	$\Delta E^{a}$	$\Delta E^{b}$	$\Delta E^{c}$	$\Delta E^{d}$	$\Delta E^{e}$	$\Delta E^{f}$	$\Delta E^{g}$
27a	31.0	19.7	12.4	24.6	23.0	11.4	15.7	10.4
28a	-42.1	-56.5	-61.3	-52.5	-48.3	-55.9	-57.3	-63.8
23a	21.3	9.2	2.7	15.2	12.6	2.6	5.9	-1.7
24a	-3.4	-17.5	-22.2	-11.8	-12.0	-19.4	-12.0	-14.0
31a	-1.3	-16.6	-21.2	-9.8	-9.2	-16.5	-10.0	-14.0
32a	-41.2	-56.3	-61.3	-52.4	-47.7	-55.6	-56.5	-63.6
29a	21.5	9.1	1.5	15.2	11.3	-0.5	6.5	1.3

30a	-7.4	-22.0	-28.3	-16.4	-14.6	-24.3	-16.9	-25.1
25a	13.0	2.0	-4.3	8.7	4.8	-4.8	0.1	-7.3
26a	-4.7	-19.2	-25.4	-14.1	-12.1	-21.4	-14.0	-22.0
<sup>a</sup> PBE0.	<sup>b</sup> PBE0-D3	3//PBE0. °	PBE0(dich	nlorometha	ine as solv	/ent)//PBE	0. d B3LYF	P//PBE0. <sup>e</sup>

B3LYP-D3//PBE0. f M06-2X//PBE0. g MP2//PBE0.

The calculated data are summarized in Table 1 and in Figure 1. A closer look at the possible reaction pathways reveals two routes for the gold(I)-catalyzed head-to-head coupling (1',1 dimerization) of chlorophenylacetylene **10a**. The reaction can not only proceed via transition state **23a**, but also via transition state **27a** (Figure 1). The transition states **23a** and **27a** differ in their relative orientation of the gold complex at the carbon atom C2. The same applies for the head-to-tail coupling (1',2 dimerization) for which we could locate the stereoisomeric transition states **29a** and **25a** (Figure 1).

At first we would like to discuss the results calculated with PBE0/6-311++G(d,p)/def2-TZVP+ECP. To consider the loss of entropy for a dimerization reaction, the stationary points for the free energy ( $\Delta G$  in kcal/mol) are depicted in Figure 1. An analogue figure for the relative energy ( $\Delta E$  in kcal/mol) can be found in the supporting information (see Figure S1). The addition of one molecule **10a** to the cationic gold complex leads to  $\pi$  complex **22a** accompanied by a gain in free energy of 28.5 kcal/mol. A comparison of the free energy values for the transition states 23a and 27a (head-to-head coupling) and transition states 25a and **29a** (head-to-tail coupling) reveals that the former always exhibit higher energy values. Therefore the 1'.2 dimerization should be favored towards the 1'.1 dimerization, if the free energies of these four transition states are considered. However, an entirely different picture emerges by looking at the formed intermediates and their secondary products (Figure 1). The 1',2 dimerization leads to vinyl cations **26a** and **30a** which are slightly more stable ( $\Delta G = -4.7$ kcal/mol for 26a and -7.4 kcal/mol for 30a) than the starting materials 10a and 22a. The intermediate 24a, which is formed via the head-to-head coupling is even less stable than the intermediates 26a and 30a. However, cation 24a can undergo rearrangement via a 1,3chlorine shift to form the highly stable envne complex **32a**. The free energy of the transition state for this rearrangement is only 2.1 kcal/mol higher than that of the cationic intermediate 24a. In case of the 1'1 dimerization via transition state 27a no vinyl cation could be located on the energy hypersurface. Here only enyne complex 28a, which differs from 32a by the relative orientation of the gold center, was found as a minimum.



**Figure 1.** Free energy ( $\Delta G$ ) profile for the gold(I)-catalyzed dimerization of two chlorophenylacetylenes **10a** calculated by means of PBE0/6-311++G(d,p)/def2-TZVP+ECP. [Au]<sup>+</sup> = Au<sup>+</sup>-PMe<sub>3</sub>.

Evaluating the data calculated via the PBE0 method following predictions can be made: The cationic intermediates of the 1',2 dimerization 26a and 30a should be preferably formed and could be trapped in presence of an appropriate nucleophile. Without a nucleophile in the reaction mixture these pathways should be considered as reversible. Consequently, the 1',1 dimerization (head-to-head coupling) proceeding via transition state 23a to the highly stable product 32a should become the dominant reaction as the reverse reaction to the starting materials can almost be excluded due to the low energy of the envne complex 32a ( $\Delta G = -$ 41.2 kcal/mol). Typically, triple bonds are consumed in gold(I)-catalyzed reactions. Therefore, the predicted reaction path, in which one triple bond reappears in the product by elimination of the gold complex, is very rare and only a few exceptions were reported.78-79 Comparing the calculated PBE0 energies to the data obtained by other methods it becomes obvious that the tendencies for the four reaction pathways (Figure S1) are the same. However, the energy values strongly vary on the method used (Table 1). The usage of PBE0-D3, B3LYP-D3, M06-2X and MP2, methods which describe dispersion interactions more accurate for larger atomic distances, leads to an overall decrease of both transition states and intermediates compared to PBE0. The additional stabilization amounts up to ca. 9 kcal/mol. On the contrary, employing B3LYP as the density functional or taking solvent effects into account, the energy of both transition states and intermediates increases. Also

 here, changes can amount up to ca. 9 kcal/mol. In all cases the activation barrier for the gold(I)-catalyzed dimerization is significantly lower than the values for the radical pendant.<sup>29</sup>



**Figure 2.** Molecular structures of the transition state **23a** (left), the intermediate **24a** (middle) and the complex **32a** (right) calculated using PBE0/6-311++G(d,p)/def2-TZVP+ECP.

In the following, the stationary points of the 1',1 dimerization (dominant route, highlighted in black in Figure 1) will be contemplated. For the transition state **23a** both alkyne units are almost perpendicular to each other (Figure 2). The distance between C1 and C1' in **23a** amounts to 2.30 Å and is therefore distinctly larger than that calculated for the thermal dimerization (1.99 Å).<sup>29</sup> For the cationic intermediate **24a** both phenyl groups are aligned perpendicular to the butadiene unit (Figure 2). The carbon atom C2' is almost sp-hybridized, the C1'-C2'-C(phenyl) angle amounts to 172° accordingly (for numbering of atoms see Figure 3). As expected, the highest positive charge (natural charge = +0.41; see Figure 3a) is located on this carbon atom (C2'). An additional stabilization of the positive charge occurs through the adjacent phenyl group, as well as through the interaction with the n<sub>p</sub> orbitals of the chlorine atoms Cl3 and Cl3'. This can easily be explained by looking at the LUMO of **24a** (Figure 3a).

After the 1,3-chlorine shift,  $\pi$  complex **32a** adopts an *E* configuration for the double bond (Figure 2). This is due to the fact, that the shift of the chlorine atom Cl3 from C1 to C2' takes place on the opposite site of the C1'-Cl3' bond. The energy of the transition state for the 1,3-chlorine shift (**31a**) is only slightly higher than the energy of vinyl cationic intermediate **24a** (2.1 kcal/mol for PBE0/6-311++G(d,p)/def2-TZVP+ECP). The natural charges of transition state **31a** reveal that the positive charge of the cationic center C2' (formerly +0.41 for **24a**) is partially being transferred onto the chlorine atom Cl3 (formerly +0.07 for **24a**) as both atoms adopt a natural charge of about +0.2 (Figure 3b). Furthermore, the LUMO of **31a** closely

resembles the LUMO of **24a**, only the interaction between the vacant p orbital and the  $n_p$  orbital on Cl3 is more distinct (Figure 3b).



**Figure 3.** Natural charges and LUMOs of the cation **24a** (a) and transition state **31a** (b) calculated using PBE0/6-311++G(d,p)/def2-TZVP+ECP.

## b) Experimental Studies on the Gold(I)-Catalyzed Dimerization of Chloroarylacetylenes

To verify our calculations, we have chosen the alkoxy compound 10b as testing system for the investigation of a possible gold(I)-catalyzed dimerization reaction to the head-to-head product 33b (Scheme 4). In order to gather experimental details, the gold(I)-catalyzed conversion of **10b** was investigated in an NMR tube and monitored by <sup>1</sup>H NMR spectroscopy. This allows us to directly determine the conversion of **10b** and the yield of possible dimerization products and by-products (selectivity). Therefore, an internal standard was added. By using the methoxy group attached to the aromatic system two benefits derive. On the one hand, the yield can easily be determined by the characteristic <sup>1</sup>H NMR signal for the methyl group (at ca. 4 ppm). On the other hand, the formation of a cationic intermediate is facilitated by the electron donating effect of the methoxy group; thus, we expect that the reaction occurs at ambient temperature. Additionally, higher concentrations of the starting material **10b** were employed. As a result, the dimerization should be favored with respect to all reactions having rates only depending on the concentration of **10b** in first order. The hydration of chloroacetylenes should be mentioned here as a possible side reaction.<sup>80</sup> At higher concentrations this side reaction can be neglected even in non-dried solvents. The gold(I)-catalyzed reaction of **10b** was carried out in dichloroethane and deuterated

 dichloromethane as well as in deuterated benzene. Both chlorinated solvents are inert and should react, if any, very slowly with an intermediary formed vinyl cation, whereas benzene rapidly reacts with a vinyl cation to the corresponding trapping product.<sup>24</sup> The experiment was carried out at temperatures between 0 and 80 °C. To obtain the best results (e.g. yields), we screened several cationic gold complexes with different ligands and counterions under various reaction conditions (see Table 2).



Scheme 4. Gold(I)-catalyzed dimerization of chloroacteylene 10b under different conditions.

<b>Table 2.</b> Optimization	of the reaction	conditions <sup>a</sup> for the	e head-to-head	dimerization of 10b
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Entry	catalyst	conditions	yield [%]
1	[IPrAu(NCMe)]SbF <sub>6</sub> (5 mol%) <sup>81</sup>	DCE, 40 °С, 1 h, 1 м	54 <sup>b</sup>
2	IPrAuCl (5 mol%), AgSbF <sub>6</sub> (10 mol%) <sup>82</sup>	DCE, 40 °C, 1 h, 1 м	52 <sup>b</sup>
3	IPrAuCl (5 mol%), AgNTf <sub>2</sub> (10 mol%)	DCE, 40 °C, 1 h, 1 м	63 <sup>b</sup>
4	IPrAuCl (5 mol%), NaBArF <sub>24</sub> (10 mol%)	DCE, 40 °C, 1 h, 1 м	32 <sup>b</sup>
5	[IPr <sup>*</sup> Au(NCMe)]SbF <sub>6</sub> (5 mol%) <sup>83</sup>	DCE, 40 °С, 1 h, 1 м	36 <sup>b</sup>
6	(Ph)₃PAuCl (5 mol%), AgSbF <sub>6</sub> (10 mol%) <sup>84</sup>	DCE, 40 °C, 1 h, 1 м	<b>24</b> <sup>b</sup>
7	(OMe) <sub>3</sub> PAuCl (5 mol%), AgSbF <sub>6</sub> (10 mol%) <sup>85</sup>	DCE, 40 °C, 1 h, 1 м	<b>0</b> <sup>b,d</sup>
8	Dichloro(2-picolinato)gold(III) (5 mol%)86	DCE, 40 °C, 1 h, 1 м	<b>9</b> b,d
9	IPrAuNTf <sub>2</sub> (5 mol%) <sup>87</sup>	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 1 м	68
10	[IPrAu(NCMe)]SbF <sub>6</sub> (5 mol%)	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 1 м	71
11	[IPrAu(NCMe)]SbF <sub>6</sub> (5 mol%)	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 0.015 м	33°
12	[IPrAu(NCMe)]SbF <sub>6</sub> (5 mol%)	DCM- <i>d</i> <sub>2</sub> , rt, 2 h, 0.25 м	65°
13	[IPrAu(NCMe)]SbF <sub>6</sub> (5 mol%)	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 0.5 м	62
14	[IPrAu(NCMe)]SbF <sub>6</sub> (5 mol%)	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 2 м	58
15	[IPrAu(NCMe)]SbF <sub>6</sub> (5 mol%)	DCM- <i>d</i> <sub>2</sub> , 0 °С, 1 h, 1 м	65
16	[IPrAu(NCMe)]SbF <sub>6</sub> (5 mol%)	CDCl <sub>3</sub> , rt, 1 h, 1 м	61
17	[JohnPhosAu(NCMe)]SbF <sub>6</sub> (5 mol%) <sup>88</sup>	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 1 м	75
18	[JohnPhosAu(NCMe)]SbF <sub>6</sub> (5 mol%)	С <sub>6</sub> D <sub>6</sub> , 80 °С, 16 h, 0.25 м	31
19	JohnPhosAuNTf <sub>2</sub> (5 mol%) <sup>89</sup>	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 1 м	66
20	XPhosAu(NCMe)SbF <sub>6</sub> (5 mol%) <sup>90</sup>	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 1 м	33
21	BrettPhosAuNTf <sub>2</sub> (5 mol%) <sup>91</sup>	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 1 м	66
22	<i>t</i> BuXPhosAuNTf <sub>2</sub> (5 mol%) <sup>89</sup>	DCM- <i>d</i> <sub>2</sub> , rt, 1 h, 1 м	69

<sup>a</sup> Yield determined by <sup>1</sup>H NMR using hexamethylbenzene as internal standard. <sup>b</sup> Here cylohexane and <sup>c</sup>cyclooctane were used as internal standards. <sup>d</sup> No complete conversion.

At first, experiments with different gold(I) complexes were run at a concentration of one molar (entry 1-7 in Table 2) at 40 °C. Here, DCE (dichloroethane) was used as the reaction solvent.

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59 60 AgSbF<sub>6</sub>, AgNTf<sub>2</sub> and NaBArF<sub>24</sub> were employed as halide scavengers for the non-activated gold(I) complex IPrAuCI. When using N-heterocyclic carbene (NHC) ligand complexes (entry 1-5), we were able to identify a dimerization product (for a detailed characterization see below) in a yield around 32-63%. We could not identify any byproduct, as all further reaction products give a yield of lower than 5% (see Figure 4). Phosphorus-based ligands like a phospine complex (entry 6) delivers the dimer in a significant lower yield, whereas a phosphite ligand (entry 7) leads to no dimerization product, despite of an almost complete conversion of 10b. Also the usage of the gold(III) complex dichloro(2pyridinecarboxylato)gold results in a massive drop of the yield (entry 8).

By changing the solvent from dichloroethane (DCE) to dichloromethane (DCM) the yield could be increased, if the nitrile-stabilized gold(I) complex [IPrAu(NCMe)]SbF<sub>6</sub> is used (cf. entry 1 and 10). At this point it is worth mentioning that this gold(I)-catalyzed dimerization already occurred at ambient temperature with full conversion of **10b** within one hour (entry 10). The variation of the concentration of **10b** has a major impact on the reaction: At lower concentrations (entry 11) the hydration of **10b** becomes the dominant reaction, whereas a higher concentration (two molar) also results in a decrease in yield (entry 14). The best yields were obtained within a concentration range from 0.25 to 1.0 molar. Lowering the reaction temperature to 0 °C leads to a slight decrease in the yield (entry 15). Changing the solvent from DCM to CHCl<sub>3</sub> has no increasing effect on the yield (entry 16). To our delight we could further improve the yield for the dimerization product to 75% by using the electron-rich nitrilestabilized JohnPhos ligand with SbF<sub>6</sub> as counteranion (entry 17). Changing the counteranion to NTf<sub>2</sub> resulted in a slightly lower yield (entry 19). We then tested bulkier phosphine ligands such as XPhosAu(NCMe)SbF<sub>6</sub> (entry 20), BrettPhosAuNTf<sub>2</sub> (entry 21) and *t*BuXPhosAuNTf<sub>2</sub> (entry 22) which proved to be not superior compared to JohnPhosAu(NCMe)SbF<sub>6</sub> (entry 17). The <sup>1</sup>H NMR spectra for the conversion of **10b** under these optimized reaction conditions is depicted in Figure 4. The <sup>1</sup>H NMR spectra show a clean conversion of **10b** leading to only one dimerization product with an overall yield of 75% (for integrals see Figure S6 in the Supporting Information). No further dimerization product with more than 5% yield could be identified. By means of the <sup>1</sup>H NMR signals for both methyl groups at  $\delta$  = 3.8 ppm it becomes obvious that the main product must be an asymmetric dimer. This would be in accordance with the calculated proposed structure (see above).

In order to examine if the cationic intermediates **24a**, **26a** and **30a** (Figure 1) can be trapped in the presence of an appropriate nucleophile, the experiment was also performed with [JohnPhosAu(NCMe)]SbF<sub>6</sub> in deuterated benzene (entry 18, for <sup>1</sup>H NMR spectra see Figure S7 in the Supporting Information). Apart from many by-products, the asymmetric dimerization product could be determined with a yield of 31%. This suggests that the cationic intermediates **26a** and **30a** are now trapped by benzene. However, we were neither able to

identify nor able to isolate any benzene trapping products. The cationic intermediate **24a** will probably undergo no reaction with benzene since the energy for the 1,3-chlorine shift ( $\Delta G^{\#}$  = 2.1 kcal/mol, see Table 1), which leads to the stable enyne complex **32a** (see Figure 1), is extremely low according to our calculations.



**Figure 4.** <sup>1</sup>H NMR spectra of **10b** (1 M) and hexamethylbenzene as internal standard in dichloromethane- $d_2$  at 600 MHz before (top) and after (bottom) addition of 5 mol% [JohnPhosAu(NCMe)]SbF<sub>6</sub>.

For an unambiguous identification of the dimerization product, the experiment was repeated under the optimized conditions (5 mol% [JohnPhosAu(NCMe)]SbF<sub>6</sub> in dry DCM) on a preparative scale. The preparative reaction delivered the dimerization product in 51% yield. The reason for the difference between the yield for the isolated compound (51%) and the yield determined by NMR (75%) is due to the separation by flash column chromatography. The latter was difficult because of the similar retention of the main product and small amounts of by-products. By analyzing the <sup>13</sup>C NMR spectra (see Supporting Information) of the isolated compound, we could confirm the formation of an asymmetric dimerization product, which has one triple bond and one double bond. Nevertheless, a structural elucidation of the dimerization product was still not possible. For this reason, we reduced the dimerization product with  $H_2$ /Pd and could isolate the non-separable hydrogenation products

**34b** and **35b** in an overall yield of 46% (Scheme 5a). The structure of both hydrogenation products could be confirmed by 2D NMR (see Figure S11). Product **34b** can be explained by simple hydrogenation of the triple bond of **33b**. Compound **35b** represents the fully hydrogenated product of **33b** where not only both double bond and triple bond were reduced, but also both chlorine atoms were removed (Scheme 5a). So far, the head-to-head dimerization product **36b**, which would deliver hydrogenation products like **37b** and **38b** (Scheme 5b), could not clearly be ruled out. As we could not detect **38b** in the isolated product mixture, the head-to-tail coupling product **36b** can now be entirely excluded as the isolated dimer.



**Scheme 5.** a) Structural elucidation of the head-to-head dimerization product **33b** by reduction to **34b** and **35b**. b) For the possible head-to-tail dimerization product, the compounds **37b** and **38b** should be expected.

Whether **33b** or **34b** is the *trans* or *cis* alkene could not be determined based on the obtained data. Fortunately, we were able to grow crystals which were examined by X-ray diffraction. The molecular structure of **33b** in the solid state is shown in Figure 5 and confirms the head-to-head dimerization product as the *trans* isomer. These results are in agreement with our predications made by quantum chemical calculations.



**Figure 5.** Molecular structure of the head-to-head dimerization product **33b** in solid state. Two independent molecules are found in the unit cell; only one of them is displayed. The minor component of the disordered part was omitted for clarity (complete asymmetric unit see Supporting Information). Displacement ellipsoids are drawn at 50% probability level and hydrogen atoms as spheres of arbitrary radii.

After the structural elucidation of **33b**, we evaluated the scope of the head-to-head dimerization under the optimized reaction conditions. Therefore, other chloroarylacetylenes **10** were converted into the corresponding head-to-head dimers **33** (Scheme 6). Besides the alkoxy compounds **10b** and **10c**, also simpler chloroarylacetylenes like **10a**, **10d** and **10f** could be dimerized and isolated under these conditions. Changing the substitution pattern from *para* (**10d**) to the *ortho* position (**10f**) of the aromatic system had no negative effect on the reaction yield. Chloroarylacetylenes bearing a larger aromatic backbone like a biphenyl unit (**10c**), led to a significant decrease of the reaction yield for **33c**. With a naphthylic backbone, the corresponding dimerization product **33h** could only be isolated in 3% yield due to an unselective reaction of **10h**. As might be expected, no reaction occurred when an aromatic system bearing an electron withdrawing group like CN in *para* position (**10g**) was used, even if the sample was heated up to 50 °C. To our surprise, by substituting chlorine with bromine, the bromoacetylene **12a** could be dimerized to the dimerization product **39a**, though with a significant lower yield compared to the corresponding chlorinated dimer **33a**. In case of **12b**, no selective reaction was observed.



**Schema 6.** Substrate scope for the gold(I)-catalyzed head-to-head dimerization of haloarylacetylenes **10** and **12**.

We have also tried cross coupling reactions using two different haloarylacetylenes. Therefore, we mixed one reactive compound (**10b**) with one non-reactive compound (**10g**) as well as two reactive species (**10b** and **10d**). However, no coupling products were obtained in any of these cases.

Based on the above discussed results we suggest the mechanism for the mono gold(I)catalyzed head-to-head dimerization of chloroarylacetylenes shown in Scheme 7a. The first step is the coordination of the cationic gold complex to the triple bond of chloroarylacetylene **10** to form the cationic  $\pi$  complex **22**, which causes the electrophilicity of the coordinated triple bond. The rate determining step is the following nucleophilic attack of another chloroarylacetylene molecule **10** on the  $\pi$  complex **22** resulting in the formation of the vinyl cation **24** as intermediate. The latter rapidly undergoes rearrangement via a 1,3-chlorine shift due to the low activation barrier to form the stable cationic enyne complex **32** which corresponds to its cationic vinyl resonance structure. The enyne complex is formed out of the latter by an elimination process of the gold catalyst. The last step of the catalytic cycle is the removal of the cationic gold(I) complex (desauration) which releases the *trans*-1,2chloroenyne **33**.



**Scheme 7.** Possible reaction mechanisms for the head-to-head dimerization of chloroarylacetylenes **10** via mono (a) and dual (b) gold catalysis.



**Scheme 8.** Attempted synthesis of organogold compound **43** monitored by <sup>1</sup>H NMR spectroscopy.

An alternative reaction mechanism can be described via a dual gold catalysis<sup>41</sup> (Scheme 7b). However, this mechanism can be excluded for the following reasons: If the head-to-head dimerization proceeds via a dual gold catalysis, the gold acetylide **39** must be formed by a metal-halogen exchange. Except for iodine<sup>56,45</sup>, no analogous proof for chlorine can be found in the literature to the best of our knowledge.<sup>92-93</sup> In the case of iodoacetylenes it could be shown that no free cationic iodine source is involved; the formation of the gold acetylide proceeds via a stepwise mechanism.<sup>56</sup> Therefore, the usage of organogold compounds as additives (e.g. IPrAuPh) or DAC<sup>39</sup> are necessary. To verify if a gold acetylide is involved in the dimerization of the chloroarylacetylenes **10**, our model compound **10b** was heated with IPrAuPh under the same conditions (Scheme 8), which delivered the gold acetylide from the iodoacetylene **12a** (for the structure of **12a** see Scheme 2d).<sup>56</sup> However, no conversion of **10b** into the corresponding gold acetylide **43** was observed (Figure S8).

Another issue corroborating the exclusion of a dual gold catalysis mechanism is the reaction behavior of the vinylgold species  $42^{94}$  (Scheme 7b). The latter should deliver the dimeric product 33 after a gold-chlorine exchange. That means, in presence of a proton source this gold-chlorine exchange would compete with a protodesauration<sup>35,95,19</sup>. To verify if the vinylgold species 42 is present in solution, the dimerization was conducted in the protic solvent CD<sub>3</sub>OH. By means of <sup>1</sup>H NMR spectroscopy (see Figure S9) neither the dimerization product 33 nor a corresponding protonated dimerization product was observed. Here, the hydration of the chloroarylacetylene<sup>80</sup> 10b became the dominant reaction.

## Conclusion

In conclusion, a gold(I)-catalyzed head-to-head dimerization of chloroarylacetylenes to *trans*-1,2-dichloroenynes is presented. The dimerization reaction proceeds via a completely different mechanism compared to that which has been described so far for other haloacetylenes. According to quantum chemical calculations, the head-to-head reaction pathway competes with the head-to-tail dimerization. However, an unusual 1,3-chlorine shift to the intermediary formed vinyl cation leads to the exclusive formation of *E*-enynes (head-to-head coupling product). The latter are formed by an elimination process of the gold complex resulting in the reappearance of one triple bond in the product. This is untypical as triple bonds are normally consumed in gold(I)-catalyzed reactions. Mechanistically, this investigation opens a new approach on the reactivity of haloacetylenes under gold(I) catalysis. Whereas so far only metal-halogene exchange has been taken into account for these systems, the halogene shift leads to a variety of new possible reaction pathways for intermediary formed vinyl cations. This shift will also be considered for other reactions involving haloacetylenes. Furthermore, this gold(I)-catalyzed head-to-head dimerization of

chloroarylacetylenes is an attractive method en route to more complex conjugated enyne systems and their congeners as the halogen pattern allows for potential further transformations.

## **Computational Details**

All calculations were performed by using the program package Gaussian 16<sup>96</sup>. The geometrical parameters of all stationary points were optimized by means of PBE0<sup>62-63</sup>. As basis set 6-311++G(d,p)<sup>64-67</sup> has been used for C, H, Cl and P. For Au the def2-TZVP+ECP<sup>68-69</sup> basis set has been employed. For all stationary points no symmetry restriction was applied. Frequency calculations were carried out at each of the structures to verify the nature of the stationary point. It turned out that all transition states have exactly one imaginary frequency, whereas all other structures have none. Furthermore, the energies of the stationary points were calculated using the density functionals PBE0-D3<sup>72-73</sup>, B3LYP<sup>74-76</sup>, B3LYP-D3<sup>72-73</sup> and M06-2X<sup>77</sup> as well as MP2<sup>71</sup>. Here again, as basis set 6-311++G(d,p) has been used for C, H, Cl and P. For Au the def2-TZVP+ECP basis set has been employed. To determine the solvent effect, the single point calculations on the PBE0 optimized structures were also performed using dichloromethane as solvent.

### **Supporting Information**

Molecular structures, synthesis of the new compounds, <sup>1</sup>H NMR experiments, cartesian coordinates and absolute energies for all calculated compounds, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra, crystal structure data of **33b** and complete reference 92.

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## Dedication

Dedicated to Professor Professor Julius Rebek, Jr. on the occasion of his 75th birthday.

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