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Gold and Palladium Mediated Bimetallic Catalysis: Mechanistic Investigation Through the Isolation of the Organogold(I) Intermediates

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ABSTRACT: Au-Pd based catalytic systems are a unique couple due to the carbophilic lewis acidity of Au and the redox properties of Pd. To gain more insight into this bimetallic couple, a synthetic and mechanistic investigation was conducted. As key substrates ynamides (*N*-alkynyl allyloxycarbamates and *N*-alkynyl ethyloxycarbamates) were used. Essential for the mechanistic part was the isolation of the organogold(I) intermediate to validate the proposed mechanism. In total 18, polysubstituted oxazolones and 12 organogold(I) complexes were synthesized.

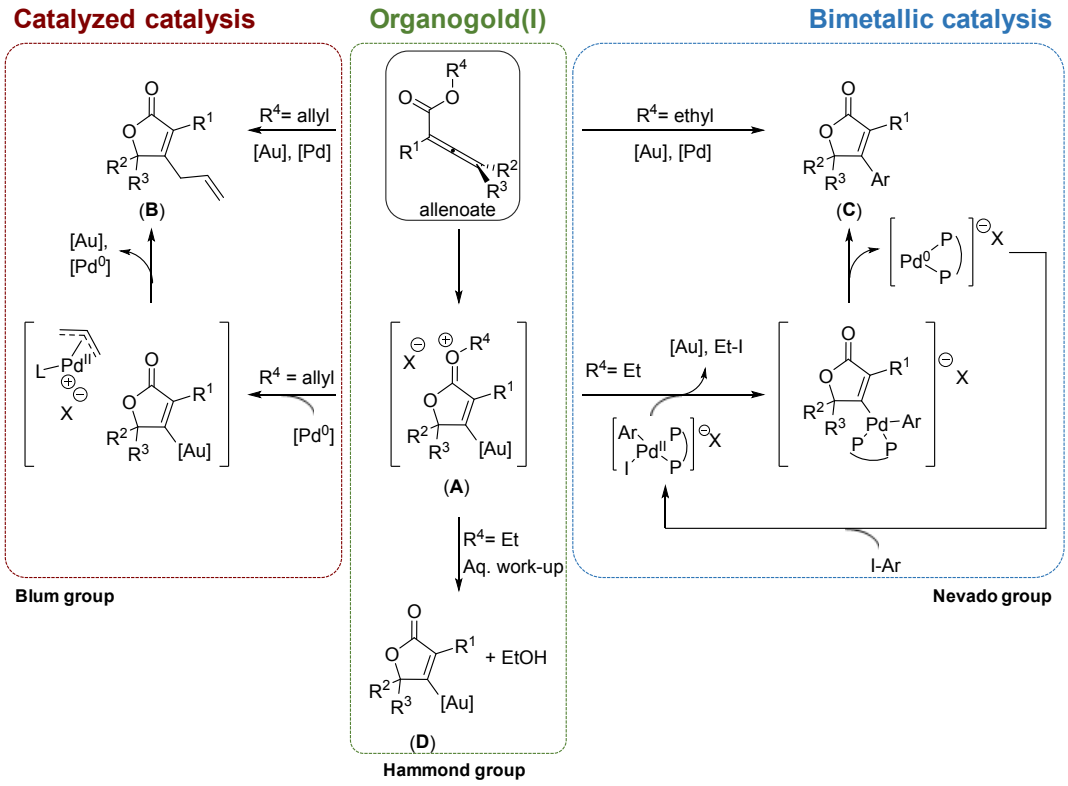
KEYWORDS: oxazolones, domino reaction, bimetallic catalysis, organogold(I) intermediates, cross-coupling.

Introduction

Bimetallic catalysis is a useful strategy to develop chemical reactions which are impossible to perform using a single metal catalyst. Essential for a process to be a bimetallic catalyzed reaction is that both metals are catalytically used with two different cycles which are connected by a transmetalation step.[1-5] As catalyst for the transmetalation, palladium is usually chosen in combination with another metal catalyst, such as gold, silver or copper. However, only a few examples are available of cooperative catalytic Au-Pd systems.[6-8] The first example of Au-Pd bimetallic catalysis originates from 2009 and was the "catalyzed catalysis" developed by the group of Blum (Scheme 1).[6] The term catalyzed catalysis refers to a bimetallic catalytic process in which the catalytic cycle of palladium can only start once the catalytic cycle of the other metal, in this case gold, has been initiated. In other words: the oxidative addition and cycloisomerization step occur on the same substrate. As shown in scheme 1 for the catalyzed catalysis approach, the oxidative addition on Pd is only possible after cycloisomerization of the allenoate precursor by Au (Scheme 1, compound **A**). More recently, the group of Nevado developed a bimetallic catalytic cross coupling between ethyl allenoate and iodobenzene.[8] Although the allenoate is similar to the allyl allenoate used by the group of Blum,[6] the bimetallic method developed by the group of Nevado is not a catalyzed catalysis approach since two reagents are used (allenoate + iodobenzene) and is therefore referred as a bimetallic approach (Scheme 1). Oxidative addition occurs on iodobenzene followed by a transmetallation step between the Pd(II) anionic complex and the cyclized organogold intermediate.

Intriguingly, all this work is centered around one compound, namely the organogold(I) complex (Scheme 1, compound **D**) isolated by Hammond and coworkers.[9] The isolation of this stable organogold(I) compound seemed to be a breakthrough for gold chemistry. Not only did this compound provide the starting point for the bimetallic catalysis of Blum and Nevado, it also proved the proposed intermediate in gold catalyzed cycloisomerization of this allenoate precursor. Even though, gold catalyzed reactions have been studied and developed vastly for the past thirty years,[10-18] the mechanisms for these reactions are mostly based on assumptions. There are only a few intermediates that have been isolated.[19-21] The problem is the sensitivity of these intermediates to protodeauration. Therefore, isolation of organogold compounds can be difficult, however, as proven by Hammond and coworkers under certain conditions organogold(I) compounds can be isolated.[20]

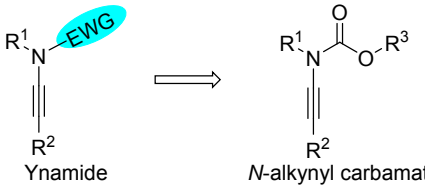
In the past few years, there has been some progress in isolating organogold(I) intermediates. The first method is the procedure reported by the group of Hammond. In their approach an ethyl ether was used which formed an ethyl oxonium intermediate, that was detected by ^{1}H-NMR, and resulted in the isolation of the organogold(I) complex after removal of the ethyl substituent with water.[9] However, since water is the nucleophile, this method will not work for compounds that are sensitive to protodeauration. The second method is the addition of triethylamine or other bases, the presence of a base will prevent protodeauration. Although this method proved to be efficient and resulted in the isolation of organogold(I) intermediates,[22-24] this approach seems not generally applicable since only a few organogold compounds have been isolated by this procedure so far. Therefore, it can be concluded that there is room for



Scheme 1. Au-Pd catalyzed catalysis and bimetallic catalysis as developed by the group of Blum[6] and Nevado[8] based on the organogold(I) compound of Hammond and co-workers.[9]

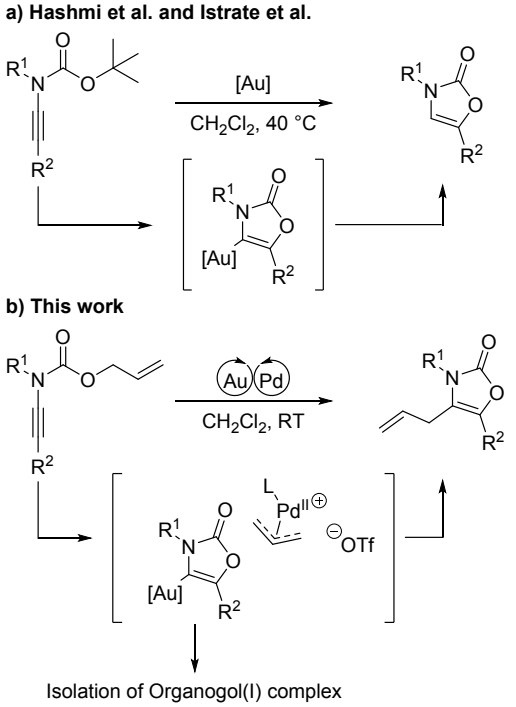
improvement and for more efficient procedures to obtain organogold(I) compounds.

In our attempt to develop a catalyzed catalysis approach, an ynamide based precursor was chosen or more precisely an *N*-alkynyl carbamate (Scheme 2). These *N*-alkynyl carbamates[25,26] are easy to synthesize in only two steps and in good total yields. The selected precursor is similar to the one from the group of Hammond,[9] however, there are some essential differences. Firstly, *N*-alkynyl carbamates would undergo a 5-*endo*-dig cyclization instead of a 5-*endo*-trig cycloisomerization. Secondly, carbamates are used instead of esters and an alkyne is activated instead of an allene resulting in the oxazolone skeleton.



Scheme 2. Core structure of the N-alkynyl carbamate used in this research.

Oxazolones are attractive building blocks in organic synthesis and are present in different pharmacological active compounds. The combination of *N*-alkynyl carbamates and gold catalysis has been successfully developed for the synthesis of disubstituted oxazolones, by Hashmi et al.[27] and Istrate et al.[28] (Scheme 3a) and for trisubstituted oxazolones through a palladium catalyzed π-activation and cross-coupling with aryl or allyl halides.[29,30]



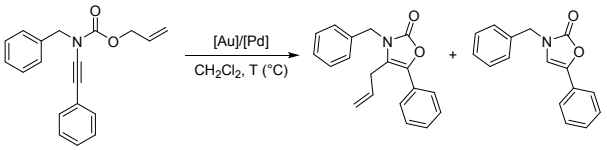
Scheme 3. a) gold catalyzed synthesis of oxazolones b) bimetallic catalyzed synthesis of oxazolones.

Important for these cycloisomerizations was the presence of the *tert*-butyl group of the *N*-alkynyl carbamate, since this *tert*-butyl group is dissociated from the intermediate resulting in the desired oxazolone. By replacing the *tert*-butyl group by an allyl

group, the allyl group would be prone to oxidative addition after cyclization. Subsequent transmetalation with the organo-gold intermediate, followed by reductive elimination would result in a trisubstituted oxazolone (Scheme 3b). Since this is an example of catalyzed catalysis, the reaction will result in a high atom economy, and is therefore a more sustainable method compared to the earlier mentioned palladium cross-coupling reactions with allyl halides.

Our hypothesis for a catalyzed catalysis system, is based on the difficulty of the migration since there is no pericyclic system present for these cycloisomerized *N*-alkynyl carbamates. This is in contrast to the more common allyl migrations, which proceed via a concerted sigmatropic rearrangement,[31-40] however, these *N*-alkynyl precursor needs to proceed through a dissociative pathway. Although this is possible with just a gold catalyst,[41-44] the formed cationic allyl species are not always stable enough to undergo the migration resulting in a mixture of the desired compound and a deallylated compound or only the deallylated compound. Therefore, the use of a bimetallic Au-Pd system should provide more control over this migration leading to the desired product.

Table 1. Catalyst screening.[a]



1a 2a 3a

Entry	[Cat] (10 mol %)	[Pd] (10 mol %)	Temp (°C)	Yield (%) **2a**	**3a**
1	$AuCl_3$	/	40	3	17
2	$H[AuCl_4]$	/	40	-	40
3	AgOTf	/	40	-	> 99
4	PTSA	/	40	-	3
5	$[AuCl(PPh_3)]$ /AgOTf	/	40	26	57
6	$[AuCl(PPh_3)]$ /AgTFA[b]	/	40	33	67
7	[AuCl(IPr)]/ AgOTf	/	40	4	3
8	$[AuCl(PPh_3)]$ /AgOTf	$[Pd_2(dba)_3]$	r.t.	92	8
9	$[AuCl(PPh_3)]$ /AgOTf	$[Pd(dba)_2]$	r.t.	93	7
10	$AuCl_3$	$[Pd_2(dba)_3]$	r.t.	37	26
11	$AuCl_3$	$[Pd(PPh_3)_2Cl_2]$	r.t.	9	40
12	AgOTf	$[Pd(dba)_2]$[c]	r.t.	92	8
13	$[AuCl(PPh_3)]$ /AgOTf	$[Pd(dba)_2]$	r.t.	7	10
14	$[AuCl(PPh_3)]$ /AgOTf	$[Pd(dba)_2]$[d]	r.t.	97	3
15	/	$[Pd(dba)_2]$	r.t.	-	-
16	$[AuCl(PPh_3)]$ /NaOTf	$[Pd(dba)_2]$[e]	r.t.	96	4

[a] Yield determined by ^{1}H-NMR the reaction was left stirring for 2 hours, [b]TFA= trifluoroacetate, [c] reaction took more than 1 hour to reach completion. [d] 5 mol % was used, reaction was completed in < 5 min. [e] reaction took approximately 1 hour to reach completion.

To validate the proposed mechanism, it seemed essential to isolate the organogold(I) intermediate. With this intermediate, the second cycle can be simulated through a palladium cross-coupling reaction with $[\{Pd(\eta^3\text{-allyl})Cl\}_2]$. However, the isolation of this intermediate proved to be more troublesome compared to previous organogold(I) complexes. Apparently, the intermediate was more prone to protodeauration. Therefore, we tried to develop a new method to isolate this organogold(I) intermediate to prove the mechanism and to provide alternative procedures toward organogold(I) compounds that are sensitive to protodeauration.

The isolation of this intermediate would provide evidence for the proposed mechanisms of Hashmi et al.[27] and Istrate et al.[28] who reported the synthesis of disubstituted oxazolones via a gold catalyzed cycloisomerization (Scheme 3a). Besides the fact that isolation of this organogold compound validates the proposed mechanisms, they also show interesting synthetic possibilities. For example, organogold(I) compounds are useful precursors for cross-coupling reactions through transmetallation with palladium[45-51] or nickel.[52] It is this transmetallation that is also important for bimetallic catalysis.

Herein we would like to show our progress in developing a catalyzed catalysis approach for polysubstituted oxazolones and the mechanistic investigations which are highly linked to the development of a new procedure toward organogold(I) compounds. Essential for the organogold(I) complex was the absence of protons in the reaction media as will be explained in further detail in this article.

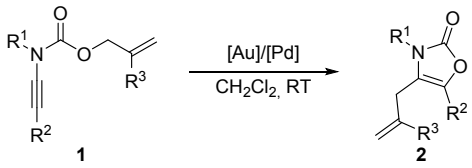
Results and discussion

The synthetic approach for the *N*-alkynyl allyloxycarbamates is similar to the reported synthesis by Istrate et al.[28] for the synthesis of *N*-alkynyl *tert*-butoxycarbamates. A copper catalyzed coupling of a bromoalkyne with an allyloxycarbamate resulted in the desired precursors. The yields of the precursors (7 – 83 %) were in the same range as reported for the *N*-alkynyl *tert*-butoxycarbamates. Compound **1a** was used as a model substrate for the catalyst screening (Table 1). In the first seven entries, different single-metal catalysts were tested. Although, $[AuCl(PPh_3)]$/AgOTf resulted in 26 % of the desired product (**2a**) the main product formed was compound **3a** (Table 1, entry 5); changing the counterion hardly showed any difference (Table 1, entry 5 *vs* 6). When AgOTf (10 mol %) was used, a full conversion to **3a** was obtained (Table 1, entry 3), while other catalysts proved to be ineffective. However, if a bimetallic system was used (Table 1, entry 8), the selectivity of the reaction switched to compound **2a**. When switching to a Au(III) catalyst, the yield decreased drastically even for different palladium catalysts (Table 1, entry 10-11). Therefore, the ideal combination seemed to be a catalytic system of Au(I) and Pd(0). Important to mention is that the reaction proceeds at a 5 % catalyst loading (Table 1, entry 14). However, also AgOTf in combination with $Pd(dba)_2$ proved to be a successful combination (Table 1, entry 12), although the reaction with Ag-Pd was slower (> 1h) compared to the Au-Pd combination (< 5 min). In order to validate an unambiguous Au-Pd catalytic cycle, the reaction was also conducted using NaOTf instead of AgOTf. The change in salt resulted in the same yield and thus proves an unambiguous Au-Pd bimetallic system (Table 1,

entry 16). If NaOTf is used, the reaction is slower compared to AgOTf (less to 5 minutes for [AuCl(PPh$_3$)]/AgOTf to approximately an hour for [AuCl(PPh$_3$)]/NaOTf), this is probably linked to a slower anion exchange rate when NaOTf is used instead of AgOTf to abstract the chloride counterion from [AuCl(PPh$_3$)].

Having an efficient procedure at hand, we applied this method to different N-alkynyl allyloxycarbamates. As shown in table 2, the yields were generally good, and the procedure proved to be tolerant to different substituents. The only exceptions are entry 11 and 12, which resulted in small amounts of the non-alkylated compound leading to a decreased yield for both reactions due to the required separation. Furthermore, beta substituted allyl moieties could be used as migrating group as well (Table 2, entry 13 and14).

Table 2. Synthesis of trisubstituted oxazolones[a]

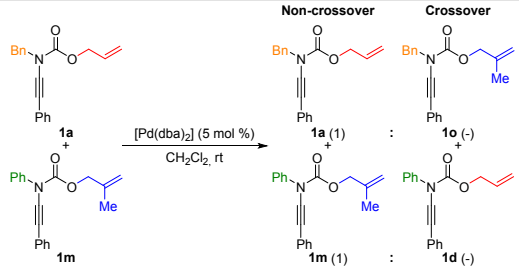
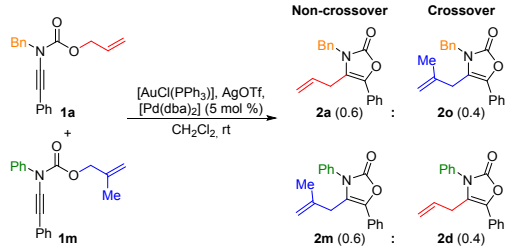
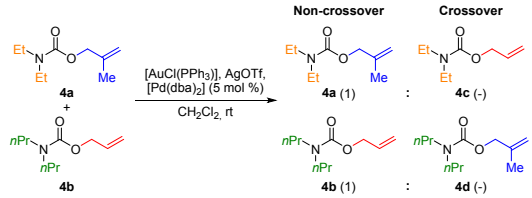


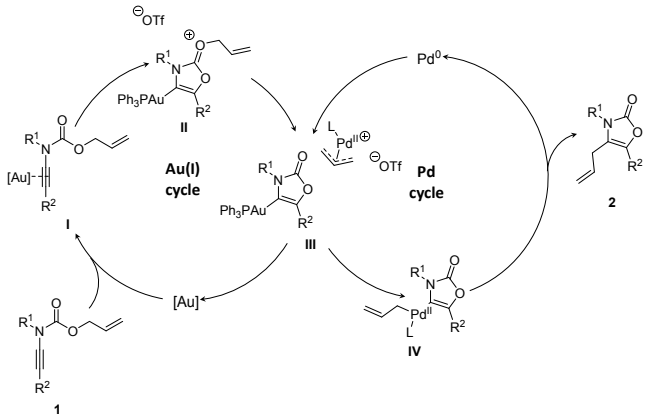
Entry	Comp.	R^1	R^2	R^3	2	Yield (%)[b]
1	**1a**	Bn	Phenyl	H	**2a**	84
2	**1b**	Bn	*c*-hexenyl	H	**2b**	70
3	**1c**	Bn	Hexyl	H	**2c**	77
4	**1d**	*i*Pr	Phenyl	H	**2d**	74
5	**1e**	*i*Pr	*c*-hexenyl	H	**2e**	66
6	**1f**	*i*Pr	Hexyl	H	**2f**	64
7	**1g**	Ph	Phenyl	H	**2g**	60
8	**1h**	Ph	*c*-hexenyl	H	**2h**	55
9	**1i**	Ph	Hexyl	H	**2i**	56
10	**1j**	Allyl	Phenyl	H	**2j**	72
11	**1k**	Allyl	*c*-hexenyl	H	**2k**	48
12	**1l**	Allyl	Hexyl	H	**2l**	33
13	**1m**	Ph	Phenyl	Me	**2m**	75
14	**1n**	Ph	*c*-hexenyl	Me	**2n**	70

[a] all the reactions were carried out with 5 mol % of [AuCl(PPh$_3$)], AgOTf and [Pd(dba)$_2$]. [b] isolated yield.

To gain more insight into the reaction, a mechanistic investigation was conducted (Table 3 and 4). From the result shown in table 3 entry 1 it can be concluded that a palladium first reaction does not occur since no exchange of the allyl groups occurred (at the used catalysts concentration) in the absence of gold, while crossover products were detected for the bimetallic method (Table 3, entry 2). The same effect was observed for the carbamates instead of the *N*-alkynyl allyloxycarbamates (Table 3, entry 3). This indicates that oxophillic activation of the carbamate resulting in deallylation is not taking place at this catalyst concentration. Next to that, [Pd(dba)$_2$] is unable to catalyze the reaction (Table 1, entry 17), however, we cannot claim that the palladium(II) complex which is formed during the reaction (after oxidative addition) is unable to catalyze the cycloisomerization (Table 4, entry 1). Nevertheless, the palladium(II) complex is only formed after cycloisomerization through gold(I) since only palladium(0) species are present at the beginning of the reaction. Furthermore, a transmetallation step has been observed for *tert*-butyl carbamate in combination with gold(I) and [{Pd(η^3-allyl)Cl}$_2$] (Table 4, entry 2), and the yield of the palladium(II) catalyzed reaction is lower compared to the bimetallic process (Table 4, entry 1 *vs* Table 1, entry 14).

Table 3. Mechanistic experiments part I

Entry	Crossover experiments
1	
2	
3	



Scheme 4. Proposed mechanism for the Au-Pd bimetallic catalysis or "catalyzed catalysis".

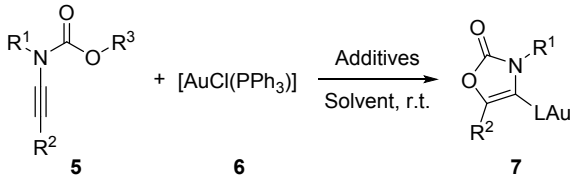
The proposed mechanism is displayed in Scheme 4. Activation of the triple bond (**I**) by gold(I) will induce a 5-endo-dig cycloisomerization resulting in the allyloxonium ion (**II**). This allyloxonium ion is prone to deallylation, as was already observed in the absence of palladium which resulted in the deallylated product (compound **3a**, see Table 1, entry 4 and 6). However, in the presence of a palladium(0) catalyst, oxidative

addition occurs (**III**) followed by transmetallation (**IV**) and reductive elimination resulting in the desired product. This mechanism is similar as observed by the group of Blum for their 5-endo-trig cycloisomerization followed by palladium assisted allyl migration[6,53] and is further supported by our own findings (Table 3 and 4). However, since these results could not give exclusive evidence for an unambiguous gold-palladium mechanism, we tried to isolate the organogold(I) intermediate (**III**) to verify the cross-coupling between the palladium(II) complex and the organogold(I) intermediate (**III**).

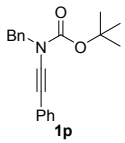
Table 4. Mechanistic experiments part II

Entry	Compound	Conditions	Yield
1	**1a**	[{Pd(η^3-allyl)Cl}$_2$] (5 %), NaOTf (20 %), dba (10 %), CH_2Cl_2	70 % (**3a**)

Table 5. Screening for a procedure toward organogold(I) complexes



5 **6** **7**

Entry	$R^1/R^2/R^3$	Conditions	Yield (%)
1	Bn/Ph/*t*Bu	AgOTf, DCM	Trace[a]
2	Bn/Ph/*t*Bu	AgOTf, DCM, Et_3N	-
3	Bn/Ph/Et	AgOTf, DCM/H_2O	Trace[a]
4	Bn/Ph/Et	NaOTf, DCM (dry)	15[b]
5	Bn/Ph/Et	AgOTf, NaI, DCM (dry)	27[b]
6	Bn/Ph/Et	AgOTf, NaI, Acetone (dry)	85[b]
[a] protodeauration, [b] determined by ^{1}H-NMR			
2	 **1p**	AuPPh$_3$Cl (5 %),1eq. [{Pd(η^3-allyl)Cl}$_2$], 1.5 eq. NaOTf, 2 eq.dba, CH_2Cl_2	25 % (**2a**) 68 % (**3a**)
3	**1p**	1eq. [{Pd(η^3-allyl)Cl}$_2$], 1.5 eq. NaOTf, 2eq. dba, CH_2Cl_2	- (**2a**) 97 % (**3a**)

In our first attempt an *N*-alkynyl *tert*-butyloxycarbamate was used (Table 5, entry 1). However, the *tert*-butyl group is more likely to fragment in a tert-butyl cation which results in the formation of isobutene and a proton. Therefore, the protodeaurated product was the main product. Furthermore, adding a base to the reaction medium could not prevent protodeauration and resulted in a complex mixture (Table 5, entry 2). The protocol of the Hammond group[9] also resulted in protodeauration (Table 5, entry 3). In this procedure, the fragmentation of the ethyl group is dependent on the presence of water as a nucleophile and so the formation of protons in the reaction mixture is inevitable. Therefore, dry dichloromethane was used, to prevent water in the reaction mixture, and silver triflate was replaced to sodium triflate. During the reaction, sodium chloride would be formed, and the chloride ion could function as the nucleophile instead of water. Unfortunately, only low yields were obtained (15 %) although protodeauration was not observed (Table 5, entry 4). In a next attempt, sodium iodide was used as a nucleophile source. Although this was an improvement compared to the previous result, the yield was still unsatisfactory (Table 5, entry 5). However, switching to dry acetone improved the yield drastically (Table 5, entry 6). Sodium iodide is highly soluble in acetone; therefore, this salt could serve as an excellent source for iodide ions, resulting in an improved yield (Table 5, entry 5 *vs* 6).

Although the yield toward compound **7** was improved, the isolation of these compounds proved to be troublesome. Normally, purification of these compounds is conducted with normal phase chromatography, however, for the formed organogold(I) compound (**7**) the use of silica resulted in protodeauration. In order to solve this problem, reversed phase chromatography, a C-18 column, was used. Another, possibility would be to use deactivated silica, however, this was not verified. Interestingly, no protodeauration could be observed even though water:acetonitrile was used as mobile phase. This indicates that if an acidic environment can be prevented, protodeauration will be minimized. With the organogold(I) compound **7a** (R^1= Bn, R^2= Ph)) we tried to simulate the transmetallation as proposed in scheme 3. As cross-coupling reagent [{PdCl(η^3-allyl)}$_2$] (1.2 eq.) was used. To mimic the conditions of the proposed palladium cycle (Scheme 3), AgOTf (1.1 eq.) was added to replace the chloride counterion and dibenzylidenacetone (dba) to function as ligand, the solvent was dichloromethane. The transmetallation reaction resulted in full conversion to compound **2a**, which was confirmed by LC-MS and ^{1}H-NMR. This result together with the mechanistic investigation of table 3 and 4 are consistent with the proposed mechanism.

Intrigued by the results obtained in table 5, we tried to evaluate our method for different *N*-alkynyl ethyloxycarbamates. The results are depicted in table 6. In general, the yields are good even when different phosphine ligands are used (Table 6, entry 9-12). Furthermore, the reaction is tolerant to different substituents, indicating that the procedure is generally applicable to different substrates. The structures of compounds **7** were characterized through ^{1}H-NMR, ^{13}C-NMR and ^{31}P-NMR. Furthermore, crystals were obtained for compound **7g** and **7l**, which were analyzed by X-ray crystallography to confirm the proposed structures (Figure 1a and 1b). Most likely this method can be used to isolate other organogold compounds that are sensitive to protodeauration.

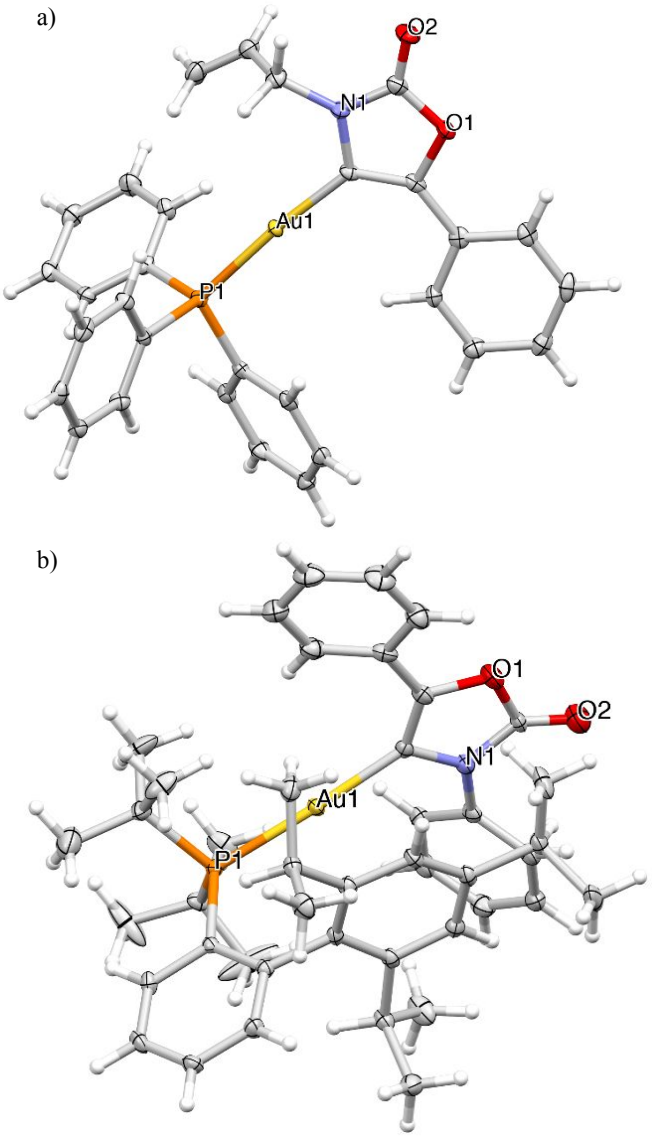
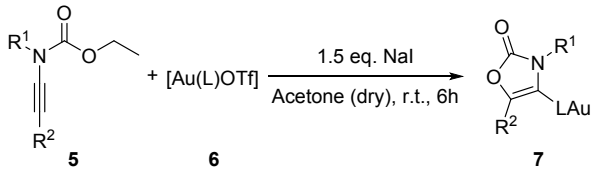


Figure 1. Crystal structure of compound a) 7g and b) 7l.

The proposed mechanism for the synthesis of the organogold(I) complexes is shown in scheme 5. First gold(I) π-activates the triple bond followed by cycloisomerization resulting in the oxonium intermediate. Essential for the reaction is the minimization of protons in the reaction media. Therefore, sodium iodide was used as iodide precursor, which functions as a nucleophile instead of water. After fragmentation of the ethyl group through nucleophilic attack, the organogold(I) compound was isolated.

Table 6. synthesis of different organogold(I) compounds

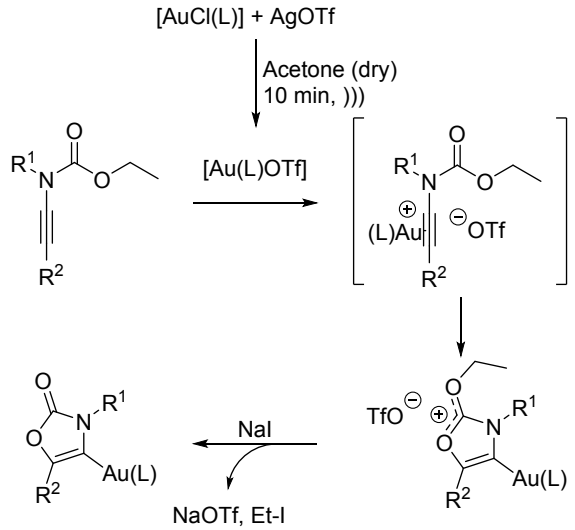


5 **6** **7**

Entry	R^1	R^2	L	**7**	Yield (%)
1	Benzyl	Phenyl	PPh_3	**7a**	67
2	Benzyl	Hexyl	PPh_3	**7b**	57
3	Phenyl	Phenyl	PPh_3	**7c**	60
4	Phenyl	Hexyl	PPh_3	**7d**	71
5	Butyl	Phenyl	PPh_3	**7e**	56
6	Butyl	Hexyl	PPh_3	**7f**	47
7	Allyl	Phenyl	PPh_3	**7g**	60
8	Allyl	Hexyl	PPh_3	**7h**	54
9	Allyl	Phenyl	XPhos[b]	**7i**	75
10	Phenyl	Phenyl	XPhos[b]	**7j**	50
11	Allyl	Phenyl	*t*BuXPhos[c]	**7k**	82
12	Phenyl	Phenyl	*t*BuXPhos[c]	**7l**	85

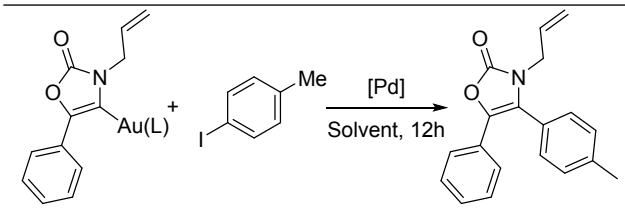
[a] isolated yield, [b] 2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl, [c] 2-Di-tert-butylphosphino-2′,4′,6′-triisopropylbiphenyl, [Au(L)OTf] was was prepared by mixing 1.05 eq. of [AuCl(L)] with 1 eq. of AgOTf in dry acetone

To valorize the use of these organogold(I) complexes, a second cross-coupling reaction was conducted with iodoarene as reagents. Gold and palladium cross-coupling reactions are not new in chemistry although they only have been explored on a limited substrate scope: arylgold(I) complexes and the Hammond complex. Hence, we tried to develop a palladium mediated cross-coupling for our organogold(I) compounds. In first instance, the $[Pd(PPh_3)_2Cl_2]$ was used (Table 7, entry 1) analogously to the group of Sestelo.[45,46] However, the Pd(II) catalysts proved to be inefficient for this cross-coupling reaction (Table 7, entry 1-3). Therefore, we switched to $[Pd(PPh_3)_4]$, which resulted in a first positive result (Table 7, entry 4). Increasing the temperature and changing the solvent to dioxane further increased the conversion to 93 % (Table 7, entry 9). Intriguingly, the reaction does not need dry solvents or an inert atmosphere which is linked to the stability of the isolated organogold compounds if not exposed to an acidic environment.



Scheme 5. proposed mechanism for the isolation of the organogold(I) complex.

Table 7. screening for a palladium catalyzed cross-coupling reaction with 5g



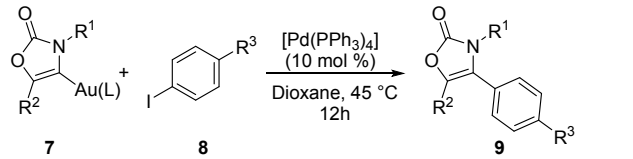
7g **8** **9**

Entry	[Pd] (10 mol %)	Solvent	Temp (°C)	Yield (%)[a]
1	$[PdCl_2(PPh_3)]$	THF	r.t.	-
2	$[PdOAc_2]$	THF	r.t.	-
3	$[Pd(\eta^3\text{-allyl})Cl(IPr)]$	THF	r.t.	-
4	$[Pd_2(dba)_3]$	THF	r.t.	trace
5	$[Pd(PPh_3)_4]$	THF	r.t.	27
6	$[Pd(PPh_3)_4]$	THF	45	73
7	$[Pd(PPh_3)_4]$	MeCN	45	82
8	$[Pd(PPh_3)_4]$	CH_2Cl_2	45	85
9	$[Pd(PPh_3)_4]$	Dioxane	45	93

[a] yield determined by ^{1}H-NMR

With the optimized conditions in hand, we tried to extrapolate this method to synthesize four different tri-substituted oxazolones all leading to good yields (Table 8). Furthermore, even a free amino group is tolerated which was also observed by other research groups palladium catalyzed cross-coupling reactions with organogold(I) complexes.[45,47] However, the yield of the iodo aniline is lower (Table 8, entry 3) since the reaction did not reach full conversion. Based on this result, it is possible to confirm that these organogold(I) complexes can also be used as a reagent for cross-coupling with palladium.

Table 8: synthesis of polysubstituted oxazolones through a palladium catalyzed cross-coupling.



7 **8** **9**

Entry	**5** (R^1/R^2)	R^3	**9**	Yield (%)[a]
1	**5g** (Allyl/Ph)	Me	**9a**	75
2	**5d** (Ph/Hexyl)	H	**9b**	79
3	**5d** (Ph/Hexyl)	NH_2	**9c**	51[b]
4	**5d** (Ph/Hexyl)	Me	**9d**	93

[a] Isolated yield, [b] compound could not be purified completely

Conclusion

The use of *N*-alkynyl carbamates as a precursor for a catalyzed catalysis approach was developed including a detailed mechanistic investigation. Essential to validate the proposed mechanism was the isolation of the organogold(I) complex that is supposed to undergo the transmetallation. However, this organogold(I) complex was very sensitive to protodeauration, and therefore impossible to isolate with the procedures known today. Therefore, a new procedure was developed to isolate this organogold(I) intermediate. The essential part of this method was to prevent protodeauration. This was achieved by using sodium iodide to deliver the iodide ion as nucleophile for the fragmentation of the ethyl substituent. Furthermore, the complexes needed to be purified by reversed phase chromatography to prevent protodeauration. The isolation of the organogold(I) compound enabled us to provide additional support for one step of the proposed catalytic cycle. Next to that, these organogold(I) compounds were used as precursors for a palladium catalyzed cross coupling with iodoarenes. In total, 14 oxazolones were prepared by the catalyzed catalysis approach together with 12 organogold(I) compounds, which are the proposed intermediates in the bimetallic process, and 4 oxazolones via a palladium catalyzed cross coupling reaction all in good yields.

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The manuscript was written through contributions of all authors. / All authors have given approval to the final version of the manuscript.

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ASSOCIATED CONTENT

Supporting Information

Experimental procedure, characterization data, and ^{1}H and ^{13}C NMR spectra and X-ray data. "This material is available free of charge via the Internet at http://pubs.acs.org."

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