Gold Catlysis

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Gold Catalysis: Isolation of Vinylgold Complexes Derived from Alkynes**

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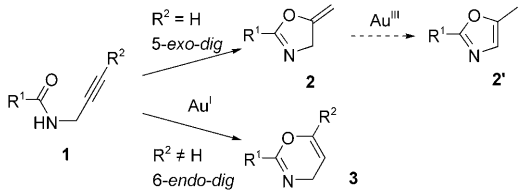
Gold-catalyzed organic transformations still represent one of the fast growing areas of organic chemistry.[1] The most important reactivity pattern is the addition of nucleophiles to C–C multiple bonds (mostly alkynes rather than allenes or alkenes). In 2000, we demonstrated that carbonyl oxygen atoms of allenyl ketones can serve as nucleophiles, and form furans by a 5-*endo*-*trig* cyclization.[2] In 2004, we reported the use of *N*-propargyl carboxamides **1**, having terminal alkynyl groups (Scheme 1, $R^2 = H$), for 5-*exo*-*dig* cyclizations,[3] and in 2007 we reported the 5-*endo*-*dig* cyclization of *N*-alkynyl carbamates.[4]



Scheme 1. Gold-catalyzed cycloisomerization of propargylamides **1**

Table 1: Reaction of **1a** with gold complexes at room temperature.

Entry	Complex	Base/Solvent	Product	Yield [%]
1	$[Ph_3PAu][NTf_2]$[a]	$-/CH_2Cl_2$	**3a**	38[c]
2	$AuCl_3$[a]	$-/CH_3CN$	–	–
3	$[Ph_3PAu][NTf_2]$[b]	$-/CH_2Cl_2$	**3a**	20[d]
4	$[Ph_3PAu][NTf_2]$[b]	2,6-$tBu_2C_6H_3N$/THF	–	–[e]
5	$[Ph_3PAu][OTs]$[b]	2,6-$tBu_2C_6H_3N$/THF	–	–[e]
6	$[Ph_3PAu][OTs]$[b]	2,6-$tBu_2C_6H_3N$/THF	–	–[e]
7	$[Ph_3PAu][OTs]$[b]	2,6-$tBu_2C_6H_3N$/benzene	–	–[e]
8	$[Ph_3PAu][OTs]$[b]	2,6-$tBu_2C_6H_3N$/toluene	–	–[e]
9	$[Ph_3PAu][OTs]$[b]	2,6-$tBu_2C_6H_3N/CH_3CN$	–	–[e]
10	$[Ph_3PAu][OTs]$[b]	2,6-$tBu_2C_6H_3N/CH_2Cl_2$	–	–[e]
11	$[Ph_3PAu][OTs]$[b]	iPr_2NEt/THF	–	–[e]
12	$[Ph_3PAu][OTs]$[b]	Et_3N/THF	–	–[e]
13	[IPrAu][OTs][b]	Et_3N/benzene	**3a**	95
14	[IPrAu][OTs][b]	Et_3N/toluene	**3a**	94
15	[IPrAu][OTs][b]	Et_3N/THF	**4a**	63

[a] 5 mol%. [b] 1 equiv. [c] Reaction time of 6 days; side product detected. [d] Additionally, 70% of the new compound was detected by in situ NMR methods. [e] Unselective reaction, the reaction mixture turns black. Tf = trifluoromethanesulfonyl, Ts = 4-toluenesulfonyl, THF = tetrahydrofuran.

These first two papers have initiated the development of an entire family of gold-catalyzed cyclizations involving carbonyl groups as nucleophiles to deliver different types of heterocycles.[5–7] Herein we report new findings on the cyclization of *N*-propargyl carboxamides having internal alkynyl groups.

Different *N*-propargyl carboxamides **1** having internal, alkyl-substituted C–C triple bonds were prepared and reacted with gold catalysts. Unlike the derivatives of type **1** having terminal alkynes, which readily lead to the alkylidenoxazolines **2** or the isomeric aromatic oxazoles **2'**,[3] different gold(I) and gold(III) catalysts did not efficiently convert these internal alkynes as exemplified for **1a** ($R^1 = Ph$, $R^2 = Me$) (Table 1, entries 1 and 2); very long reaction times were observed and the products seemed to be the six-membered heterocycle **3a** ($R^1 = Ph$, $R^2 = Me$) in the case of gold(I). In the ^1H NMR spectrum of **2a** ($R^1 = Ph$) only an allylic coupling constant of about $J = 2.5$ Hz between the vinylic and the allylic protons could be observed, whereas in the new compounds **3a** a vicinal coupling constant of about $J = 4.5$ Hz between the vinylic and the allylic protons was detected.

A closer look at the NMR spectra taken in situ revealed that for gold(I) (Table 1, entry 1) a cycloisomerization product as well as small amounts of other compounds could be detected. Increasing the amount of the catalyst up to stoichiometric amounts led to increasing amounts of these new compounds shown in the NMR spectra (stoichiometric in Table 1, entry 3), and we suspected that a vinylgold species could be the dominant species.[8] To obtain these as stable compounds, we varied both the solvent [THF (Table 1, entries 4–6, 11, 12, and 15), benzene (Table 1, entries 7 and 13), toluene (Table 1, entries 8 and 14), acetonitrile (Table 1, entry 9), and dichloromethane (Table 1, entry 10)] and the base, which accepts a proton and thus slows down the protodemetallation step to conserve the organogold species [(2,6-di(*tert*-butyl)pyridine (Table 1, entries 4, 5, 7–10), 2,6-diphenylpyridine (Table 1, entry 6), Hünigs's base (Table 1, entry 11), and triethylamine (Table 1, entries 12–15)]; see Scheme 2. Efforts with gold–phosphane complexes failed (Table 1, entries 4–12), because these experiments showed the species in the in situ NMR reaction, but they were not selective and it was not possible to isolate them. Finally, with

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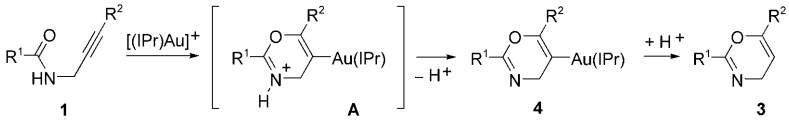


Scheme 2. In the presence of base no protodeauration is observed.

the N-heterocyclic carbene (NHC) ligand IPr [1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene; used in Table 1, entries 13–15] the vinylgold compound **4a** was isolated in pure form (Table 1, entry 15) after chromatography on basic alumina, and was fully characterized by spectroscopic methods.

Table 2 shows the substrates **1a–d** used under these reaction conditions. The amides derived from benzoic acid (Table 2, entry 1), the bulky adamantylcarboxylic acid (Table 2, entries 2 and 3), and the *ortho*-substituted furancarboxylic acid derivative (Table 2, entry 4) all gave the corresponding vinylgold species **4a–d** in good yields. The reduced acidity of the iminium proton of intermediate **A** might contribute to the exceptional fact that the intermediates **4** are isolable.

Table 2: In situ trapping of the vinylgold species by the addition of triethylamine.

Entry	Substrate	R^1	R^2	Product (Yield)
1	**1a**	Ph	Me	**4a** (63%)
2	**1b**	1-adamantyl	Me	**4b** (58%)
3	**1c**	1-adamantyl	*n*Bu	**4c** (71%)
4	**1d**		Me	**4d** (62%)

In addition, single crystals of compound **4a** were obtained for a crystal structure analysis (Figure 1).[9] With gold–carbon bond lengths of 2.027(5) Å for Au1–C1 and 2.038(6) Å for Au1–C11, **4a** shows typical values for $C(sp^2)$–Au^I single bonds.[10] The geometry at gold is almost linear, with the C1-Au1-C11 angle being 176.7(2)°. The NHC ligand and the vinyl ligand on the gold center are almost co-planar [angle between the normal vectors of the ring planes: 7.7(5)°]. The vinyl ether

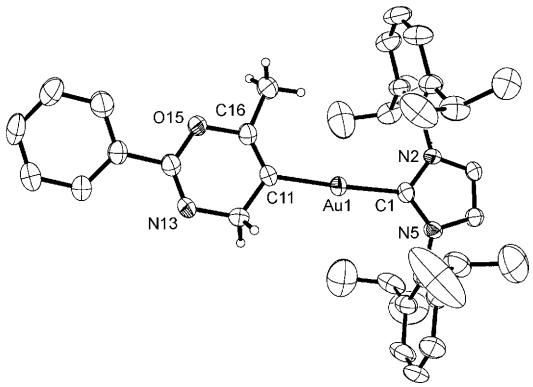
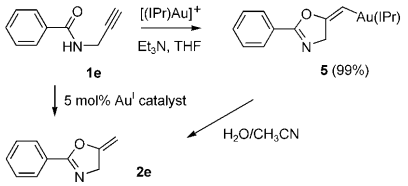


Figure 1. Molecular structure of **4a**. Thermal ellipsoids shown at 50% probability.

structure bound to the gold(I) center seems structurally undisturbed, with 1.434(7) Å for the O15–C16 bond and 1.299(8) Å for the C11–C16 double bond, the latter being slightly shorter than a normal C=C double bond.[11]

One significant difference between this and previous work is the formation of the six-membered 1,3-oxazine heterocycle by the 6-*endo-dig* cyclization. Upon screening the literature on related cyclizations, we found some examples for the gold-catalyzed formation of six-membered rings by 6-*exo-dig* cyclization,[6] but only two examples of substrates undergoing a 6-*endo-dig* cyclization. These two substrates had internal alkynes with an alkyl group on the alkyne.[7] In two experiments we compared the reaction of **1a**, which delivered 63% of **4a** (Table 2, entry 1), with the reaction of the corresponding terminal alkyne **1e**, which under the same reaction conditions delivered 99% of the IPrAu–vinyl complex **5** (Scheme 3). Experiments using catalytic amounts of gold and **1e** provided the known alkylidene oxazoline **2e** in 95%, 79%, and 95% yield when using 5 mol% $AuCl_3$,[3a] 5 mol% $[Ph_3PAu][NTf_2]$, and 5 mol% [IPrAu][OTs], respectively. The structure of **5** was unambiguously proved by protodeauration to **2e**. Thus our investigation indicates that the 6-*endo-dig* mode of the cyclization seems to be general for the internal, alkyl-substituted alkynes and the 5-*exo-dig* mode is general for terminal alkynes. Similar observations have been made for the related propargylic carboxylates.[12]



Scheme 3. The terminal alkyne **1e** selectively reacts by a 5-*exo-dig* cyclization.

The other difference between this and previous work is the stability of the organogold intermediates. In analogy to **5**, aqueous acetonitrile protodemetallated **4a** to **3a** at room temperature. **4a** can be used as a catalyst; under neutral conditions the reaction is slower than the [IPrAu][OTs]-catalyzed reaction. However when the proton, which was previously removed by the base for the isolation of **4a**, is re-added (addition of an acid), the reaction proceeds just as fast as the version catalyzed by [IPrAu][OTs]. The extraordinary stability of the vinylgold intermediate obtained from allenes, reported in the recent work of Hammond and co-workers,[13] probably depends on the acceptor substituent which deactivates the system for the electrophilic attack of the proton. The isolation of intermediates of gold-catalyzed reactions in general is still quite rare.[14]

In summary, we isolated vinylgold intermediates derived from acetylenic substrates for the first time. The results obtained here should in principle be transferable to many other reactions proceeding through vinylgold intermediates

and allow an exploration of additional functionalization of these intermediates in extended catalytic cycles.

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