Homogeneous Gold Catalysis

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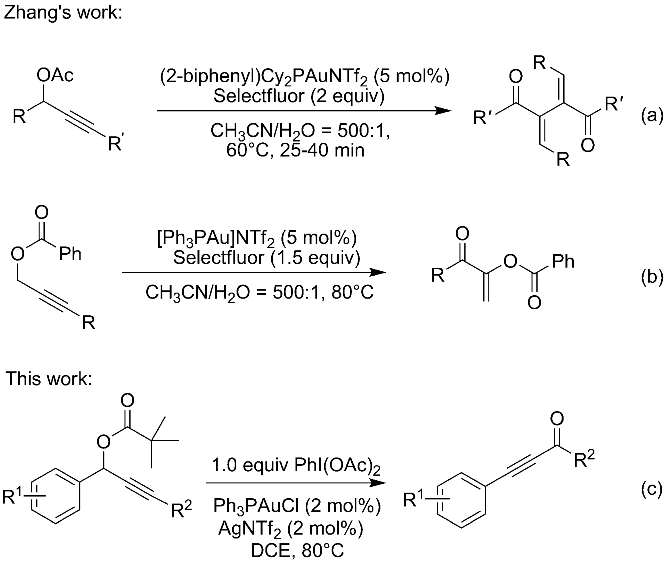
Dehydrogenative Meyer–Schuster-Like Rearrangement: A Gold-Catalyzed Reaction Generating an Alkyne**

*Yang Yu, Weibo Yang, Daniel Pflästerer, and A. Stephen K. Hashmi**

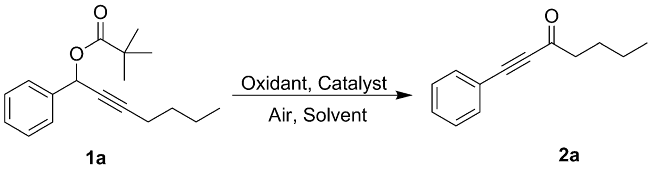
Abstract: *Easily accessible propargylic esters are converted to the inverted alkynyl ketones in an oxidative gold-catalyzed reaction. Gagosz's catalyst in combination with PhI(OAc)$_2$ is the best system for this conversion and 18 examples with yields up to 80 % are reported. The results indicate that the triple bond in the product is formed by elimination from a vinylgold intermediate. In a formal sense the new conversion overall is a dehydrogenative Meyer–Schuster rearrangement.*

Homogeneous gold-catalyzed reactions involving an Au^I/Au^{III} catalytic cycle have attracted much attention owing to the development of cross-coupling reactions that complement the more traditional transition-metal-catalyzed methods.[1] Recently, several groups have achieved the combination of gold catalysis based on alkyne/allene activation and external-oxidant-facilitated gold redox processes. For example, in 2009 Zhang and co-workers reported that the gold-catalyzed conversion of propargyl esters in the presence of the oxidant Selectfluor, which is also a source of electrophilic fluorine, delivers enone dimers (Scheme 1 a).[2] Furthermore, they developed a gold-catalyzed oxidative C−O bond-forming reaction for the preparation of α-benzoxyenones from propargyl esters not substituted at the propargylic position (Scheme 1 b).[3] However, during this type of gold redox process, protodeauration was a major side reaction reducing the yields. PhI(OAc)$_2$ has also been employed in Au^I/Au^{III} catalytic cycles. In this context, a gold-catalyzed oxidative dimerization of nonactivated arenes in the presence of PhI(OAc)$_2$ was reported by Tse and co-workers;[4] related results were obtained by Wegner et al.[5] Additionally, Nevado and co-workers developed the gold-catalyzed ethynylation of "deactivated" arenes with electron-deficient alkynes by using PhI(OAc)$_2$ as an oxidant.[6] To our surprise, there is no example of a gold-catalyzed conversion of propargylic esters



Scheme 1. Gold-catalyzed oxidation of propargyl esters.

Table 1: Optimization studies on the gold-catalyzed reaction of **1 a**.[a]



Entry	Catalyst/oxidant	Solvent	t	Yield[b]
1	TA-Au[c]/AgNTf$_2$/PhI(OAc)$_2$	DCE	15 min	41 %
2	TA-Au/AgNTf$_2$/PhI(OAc)$_2$	DCE	15 min	56 %
3	**Ph$_3$PAuCl/AgNTf$_2$/PhI(OAc)$_2$**	**DCE**	**20 min**	**62 %**
4	IPrAuCl/AgNTf$_2$/PhI(OAc)$_2$	DCE	15 min	39 %
5[d]	[Au^{III}]/PhI(OAc)$_2$	DCE	20 min	–
6	Ph$_3$PAuCl/AgSbF$_6$/PhI(OAc)$_2$	DCE	10 min	32 %
7	AgNTf$_2$/PhI(OAc)$_2$	DCE	24 h	10 %
8	Ph$_3$PAuCl/AgNTf$_2$/PhI(OAc)$_2$	CH$_3$CN	24 h	30 %
9	Ph$_3$PAuCl/AgNTf$_2$/PhI(OAc)$_2$	toluene	1.5 h	28 %
10[e]	Ph$_3$PAuCl/AgNTf$_2$/PhI(OAc)$_2$	DCE	5 h	31 %
11	Ph$_3$PAuCl/AgNTf$_2$/Selectfluor	DCE	50 min	unselective
12	Ph$_3$PAuCl/AgNTf$_2$/Cu(OAc)$_2$·H$_2$O	DCE	4 h	unselective
13	Ph$_3$PAuCl/AgNTf$_2$/O$_2$	DCE	20 min	unselective

[a] Reaction conditions: Substrate (100 μmol), [Au] (2 mol %), [Ag] (2 mol %), PhI(OAc)$_2$ (100 μmol), solvent (1 mL), in air, 80 °C. The reaction was monitored by TLC. [b] Yield of isolated product. [c] See Scheme 3 for structure of TA-Au. [d] [Au^{III}] = Dichloro(2-picolinato)-gold(III). [e] Reaction at 40 °C.

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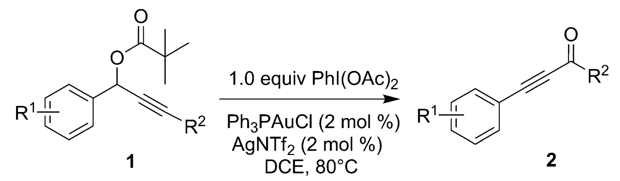
in combination of PhI(OAc)$_2$ as an oxidant. Based on the known successful studies, we want to explore this novel redox chemistry involving propargylic esters. Herein, we disclose the first example of a new type of homogeneous gold-catalyzed oxidative rearrangement reaction which proceeds with the formation of a new C≡C bond. This reaction is important because of the formation of 1,3-ynone moieties which are versatile substrates for the synthesis of natural products.[7] More important, the formation of triple bonds is very rare in homogeneous gold catalysis;[8] so far the field has been dominated by reactions which efficiently transform triple bonds of the substrate.

We chose 1-phenylhept-2-ynyl pivalate (**1a**), readily available from 1-hexyne, benzaldehyde, and pivaloyl chloride, as a model substrate. Different reaction conditions were investigated and the results are listed in Table 1. Among the catalysts tested, Ph$_3$PAuCl/AgNTf$_2$ was found to be the most effective for this transformation (Table 1, entries 1–4). The desired product **2a** was obtained in 62 % yield in the presence of 2 mol % of this catalyst at 80 °C for 20 min in air. With dichloro(2-picolinato)gold(III)[9] no conversion was detected (Table 1, entry 5). With regard to the counter ion, AgSbF$_6$ was less effective (only 32 % yield; Table 1, entry 6). Notably, AgNTf$_2$ alone gave **2a** in only 10 % yield (Table 1, entry 7). Changing to CH$_3$CN or toluene as the solvent failed to improve the yield (Table 1, entries 8 and 9). Decreasing the temperature to 40 °C also decreased the yield to 31 % (Table 1, entry 10). Moreover, other oxidants such as Selectfluor, Cu(OAc)$_2$·H$_2$O, and O$_2$[10] were unselective (Table 1, entries 11–13).

The scope of this conversion of propargylic pivalates derived from aldehydes and alkynes is shown in Table 2. The transformations proceeded smoothly with substrates having both an aromatic group at the propargylic position and an aliphatic or aromatic group on the alkyne (Table 2, entries 1–15). The desired ynone products were formed in moderate to good yields. In addition to **1a** (Table 1, entry 1), **1b** bearing a tolyl substituent also reacted smoothly. We compared the reaction of substrate **1b** (70 %, entry 2) with that of the corresponding acetate **1b′** (67 % yield, entry 3) and benzoate **1b″** (46 % yield, entry 4) and thus used pivalates for the subsequent optimization studies. Fluoro and chloro-substituted aryl groups were tolerated (55–70 % yield; Table 2, entries 5–7). The strongly electron-deficient nitro group proved to be less reactive and the desired product could be obtained in only 34 % yield together with allene **2f′** as the side product in 17 % yield (Table 2, entry 8). As illustrated in these examples, the electron density on the aromatic ring had a strong influence on this transformation; electron-donating groups were more favorable than electron-withdrawing groups. Additional sub-

Table 2: Scope and limitations of the Au^I-catalyzed synthesis of **2**.[a]



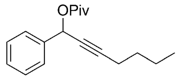
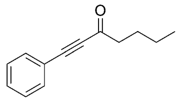
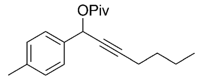
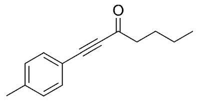
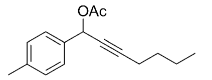
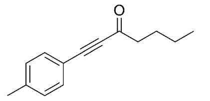
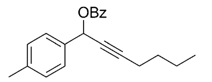
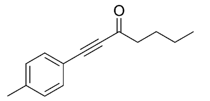
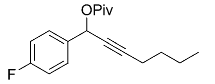
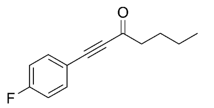
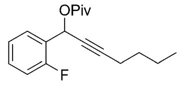
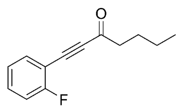
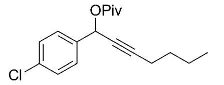
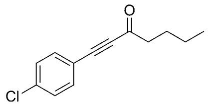
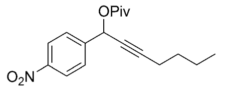
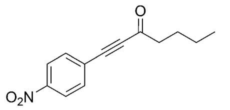
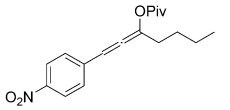
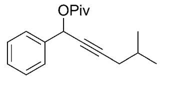
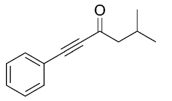
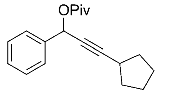
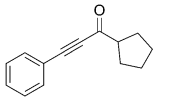
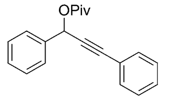
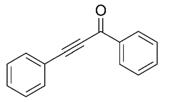
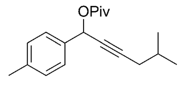
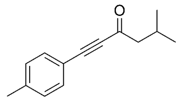
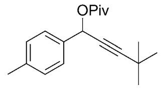
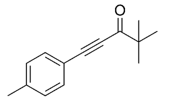
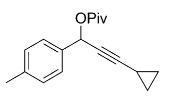
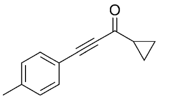
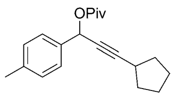
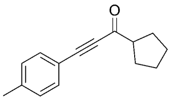
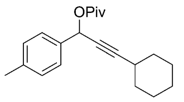
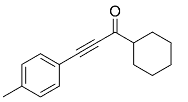
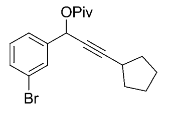
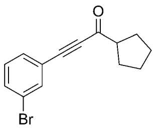
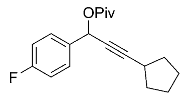
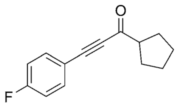
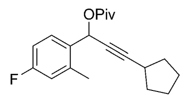
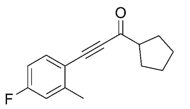
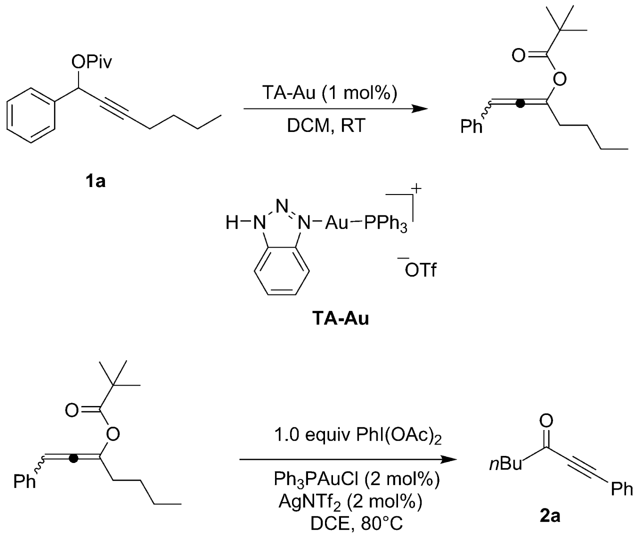
Entry	Substrate		Product		Yield[b]
1		**1a**		**2a**	62 %
2		**1b**		**2b**	70 %
3		**1b′**		**2b**	67 %
4		**1b″**		**2b**	46 %
5		**1c**		**2c**	65 %
6		**1d**		**2d**	55 %
7		**1e**		**2e**	51 %
8[c]		**1f**		**2f**	34 %
				**2f′**	17 %
9		**1g**		**2g**	63 %
10		**1h**		**2h**	66 %
11		**1i**		**2i**	24 %
12		**1j**		**2j**	67 %
13		**1k**		**2k**	40 %

Table 2: (Continued)

Entry	Substrate		Product		Yield[b]
14		**1l**		**2l**	52%
15		**1m**		**2m**	65%
16		**1n**		**2n**	65%
17		**1o**		**2o**	77%
18		**1p**		**2p**	81%
19		**1q**		**2q**	80%

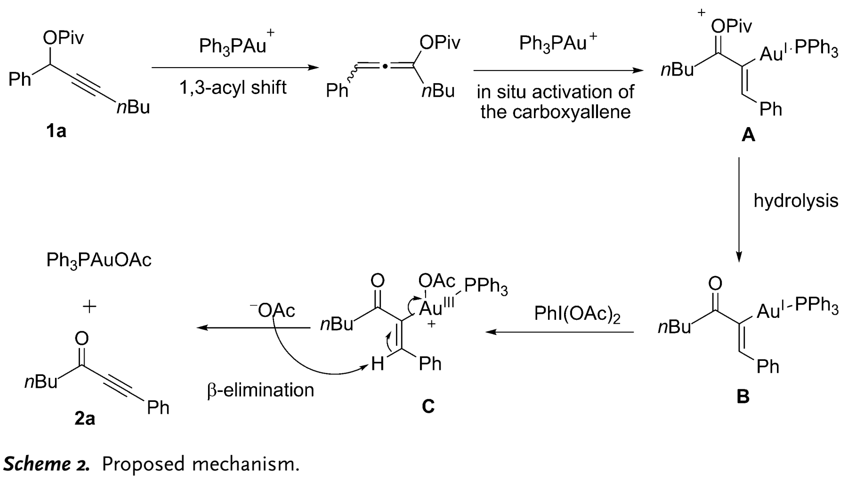
[a] Reaction conditions: substrate (200 μmol), [Au] (2 mol%), [Ag] (2 mol%), PhI(OAc)$_2$ (200 μmol), solvent (1 mL), in air, 80°C. The reaction was monitored by TLC. [b] Yield of isolated product. [c] Allene **2f′** was also isolated in 17% yield.



Scheme 3. Mechanistic experiments.

strates with an aliphatic group on the alkyne, bearing either a branched chain or a ring, led to the corresponding ynones in good yields (Table 2, entries 9 and 10). However, an aromatic group on the alkyne was problematic; **2i** was isolated in only 24% yield (Table 2, entry 11). To explore the scope further, a variety of additional substrates were investigated, and the results were satisfactory (Table 2, entries 12–19). For example, propargyl pivalates bearing a *m*-Br, a *p*-F, or a *o*-Me substituent led to corresponding ynones in excellent yields of 77%, 81%, and 80% respectively (Table 2, entries 17–19).

For the mechanism[11] of this reaction, we propose the sequence of steps shown in Scheme 2. Propargylic pivalate **1** undergoes an Au^{I}-catalyzed 1,3-acyloxy shift,[12] leading to the Au^{I}-containing oxocarbenium intermediate **A**.[13] After hydrolysis of the intermediate **A**, the Au^{I} complex **B** is formed. Intermediate **B** reacts with the oxidant PhI(OAc)$_2$ to form the active acetyl Au^{III} intermediate **C** by releasing the acetate and PhI.[14] Considering the cationic Au^{III} center in intermediate **C**, it is easy to understand why electron-donating groups on the aromatic ring led to better results. Since intermediate **B** is more electron-rich than the preceding intermediates, we assume that the oxidation of this intermediate is faster than oxidation of other intermediates, but we cannot exclude that other intermediates might be oxidized. With the assistance of acetate, which is produced during the formation of intermediate **C**, the β-H was eliminated, which led to the formation of the final product **2**. Furthermore, we attempted to isolate the allene intermediate with the novel and efficient catalyst Triazole-Au (TA-Au), which was developed by Shi et al.[15] To our delight, the allene intermediate could be isolated in 85% yield. With this allene species the transformation proceeded smoothly and the desired product **2a** was indeed formed in 45% yield (Scheme 3).



Scheme 2. Proposed mechanism.

In summary, we have developed the first example of a homogeneous gold-catalyzed rearrangement of propargylic pivalates followed by oxidation with PhI(OAc)$_2$. This reaction provides a new efficient approach to ynones under air; usually these are synthetized under anhydrous, oxygen-free conditions. The mechanism of this reaction, a 1,3-oxygen transposition of a propargylic leaving group which resembles a Meyer–Schuster rearrangement, is of high interest as until now only few reports indicate that gold(III) can acting as a leaving group.[16] In addition it is remarkable that a gold-catalyzed reaction generates an alkyne. Further studies to expand the synthetic scope of this reaction and addressing further mechanistic details will be reported in due course.

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Keywords: alkynes · allenes · esters · gold · hypervalent iodine

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