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Gold-catalyzed intermolecular addition of alcohols toward the allenic bond of 4-vinylidene-2-oxazolidinones†

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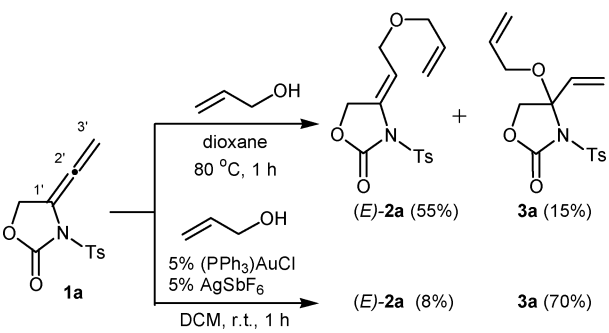
Gold catalyzed intermolecular addition of alcohols toward the proximal allenic double bond of 4-vinylidene-2-oxazolidinones gives hydroalkoxylation products, which can be easily converted into the corresponding novel spiro dihydrofuran or dihydropyran derivatives in high yield.

The activation of unsaturated C–C bonds by gold complexes has led to a range of attractive and useful strategies for a variety of organic transformations.[1] Gold-catalyzed intramolecular hydro-functionalization, especially hydroamination[2] and hydroalkoxylation,[3] both of which involve the addition of heteroatom-containing nucleophiles to alkenes and alkynes, has emerged as a powerful method for the construction of heterocyclic compounds. Although a limited number of methodologies for the catalytic intramolecular hydroalkoxylation of allenes, alkynes and alkenes have been reported,[4] to date, only Au(I) complexes have shown promise as catalysts for the asymmetric hydroalkoxylation of allenes.[2b,3a] In the most recent work in this field, Toste and co-workers developed a powerful chiral counter ion strategy, which combines chiral ligand platforms with chiral counter ions, and results in a highly enantioselective intramolecular hydroalkoxylation of allenyl alcohols catalyzed by gold.[2a] However, there are very few examples of gold-catalyzed intermolecular addition of the H–X bond of hetero nucleophiles to alkynes, allenes and alkenes.[5]

Recent developments involving the use of allenylamides in organic synthesis have had a high impact because their transformation can easily introduce nitrogen functionalities and they can be used as a tether for the introduction of new stereocenters.[6] Moreover, some of these compounds exhibit different reaction modes to other allenes. For instance, we have already demonstrated that the terminal allenic C2′=C3′ double bond of *N*-tosyl-4-vinylidene-2-oxazolidinone **1a**[7] acts as an electron acceptor in a similar manner to the double bond of conjugated enones, and undergoes a wide variety of unique reactions with olefins, alkynes and hetero-nucleophiles under strictly thermal activation conditions.[8] Compounds possessing a 2-oxazolidione moiety are also very important in synthetic chemistry since they form the basis of some antibacterial agents,[9] and play a crucial role as chiral auxiliaries in asymmetric synthesis.[10] In this paper, we report that gold complexes catalyze the intermolecular addition of alcohols to the proximal allenic double bond of *N*-tosyl-4-vinylidene-2-oxazolidinone **1a**, with the opposite regioselectivity to other gold-catalyzed intermolecular hydroalkoxylations of allenes.[5a]

Treatment of **1a** and allyl alcohol (5 equiv.) as a nucleophile in dioxane at 80 °C gave the distal addition product **2a** as a major product and the proximal addition product **3a** as a minor product (Scheme 1). To our surprise, in contrast to thermal condition, the use of 5% $(Ph_3P)AuSbF_6$, which was generated *in situ* from 5% $(Ph_3P)AuCl$ and 5% $AgSbF_6$ in dichloromethane, altered the regioselectivity dramatically, and gave the proximal addition product **3a** as the major product along with minor amounts of the distal addition product **2a**. The stereochemistry of **2a** was determined to be *E* by NOE experiments.[11]



Scheme 1 Intermolecular addition of allyl alcohol to **1a**.

Varying the counter anion of the silver salt showed that $AgSbF_6$ was the optimal co-catalyst (entries 1–5, Table 1). A good regioselectivity and high yield of **3a** were obtained when triphenylphosphine was used as a ligand in place of tris(*tert*-butyl)phosphine or other phosphine ligands (entries 1 and 4).[11] Furthermore, the use of an excess of allyl alcohol (5 equiv.) improved the yield of **3a** and the regioselectivity (entry 3). Gold(I) chloride and gold(III) chloride were also found to catalyze the present reaction, albeit in low yield and with low regioselectivity (entries 6 and 7). The cationic gold complex generated from AuCl and $AgSbF_6$ led to decomposition of **1a** (entry 8), whereas the combination of $AuCl_3$ and $AgSbF_6$ (3 equiv. with respect to Au) as a catalyst provided the desired product **3a** in slightly better yield than with $AuCl_3$ alone (entry 9). No reaction or decomposition of **1a** was observed in the presence of $(Ph_3P)AuCl$ or $AgSbF_6$ alone

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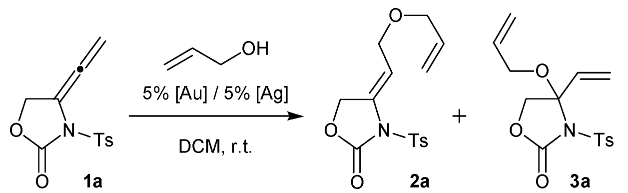
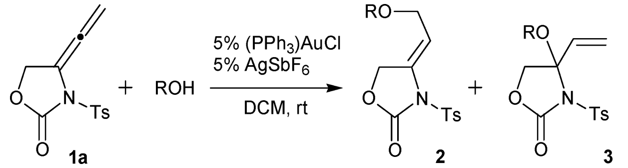
Table 1 Catalyst optimization[a]

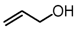
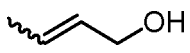
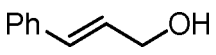
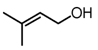
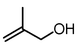
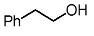
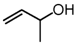


Entry	[Au]	[Ag]	Time/h	**2a** (%)[b]	**3a** (%)[b]
1	$(Ph_3P)AuCl$	$AgSbF_6$	1.5	11	53
2	$(Ph_3P)AuCl$	$AgBF_4$	3	18	42
3[c]	$(Ph_3P)AuCl$	$AgSbF_6$	1.5	8	70
4	$(t\text{-}Bu_3P)AuCl$	$AgSbF_6$	8	16	44
5	$(t\text{-}Bu_3P)AuCl$	$AgBF_4$	17	24	30
6[d]	AuCl	—	21	6	17
7[e]	$AuCl_3$		2	19	21
8	AuCl	$AgSbF_6$	16	decomposed	
9[f]	$AuCl_3$	$AgSbF_6$	0.5	24	30
10	—	$AgSbF_6$	20	decomposed	

[a] **1a** (0.2 mmol), allyl alcohol (0.48 mmol), [Au] (5 mol%), [Ag] (5 mol%) in DCM (1 mL) under air. [b] Isolated yield. [c] 5 equiv. of allyl alcohol was used. [d] **1a** was recovered in 53%. [e] **1a** was recovered in 10%. [f] 3 equiv. of $AgSbF_6$ with respect to Au was used.

Table 2 Au(I)-catalyzed addition of alcohols to **1a**[a]



Entry	ROH	Time/h	**2** (%)[b]	**3** (%)[b]
1		2	**2a** (8)[c]	**3a** (70)
2	MeOH	4	**2b** (0)	**3b** (65)
3	EtOH	4	**2c** (5)[c]	**3c** (64)
4[d]		1.5	**2d** (6)[e]	**3d** (57)
5		2	**2e** (trace)	**3e** (60)
6		3	**2f** (trace)	**3f** (68)
7		2	**2g** (0)	**3g** (58)
8		3	**2h** (21)[c]	**3h** (37)
9		3.5	**2i** (34)[c]	**3i** (trace)
10	*tert*-BuOH	12	no reaction	

[a] **1a** (0.2 mmol), alcohol (1.0 mmol), [Au] (5 mol%) and [Ag] (5 mol%) in DCM (1 mL) under air. [b] Isolated yield. [c] Only *E* isomer. [d] *E* : *Z* = 96 : 4 of crotyl alcohol was used. [e] *E* : *Z* = >96 : 4 mixture of crotyl olefin.

(entry 10). Moreover, other group 10 and 11 complexes were found not to catalyze the present reaction effectively.[12]

With the optimized reaction conditions in hand, a variety of alcohols were examined (Table 2). Primary alcohols such as allyl alcohol, methanol, and ethanol were found to participate in the present reaction, by adding to the proximal allenic double bond of **1a** in most cases (entries 1–3, Table 2). In addition, the present reaction tolerates substitution of the β- and γ-positions of allyl alcohol with alkyl and aryl groups (entries 4–7). The structure of **3d** was unambiguously confirmed by X-ray crystallography (Fig. 1). The reaction of **1a** with phenethyl alcohol gave **2h** and **3h** with only low regioselectivity (entry 8). The use of sterically bulky 1-buten-3-ol as a secondary alcohol diminished the yield of **3i**, and increased the yield of **2i** (entry 9), which is obtained by addition to the distal allenic double bond of **1a**. As expected, the use of *tert*-butanol as a nucleophile resulted in no reaction and **1a** was recovered quantitatively.

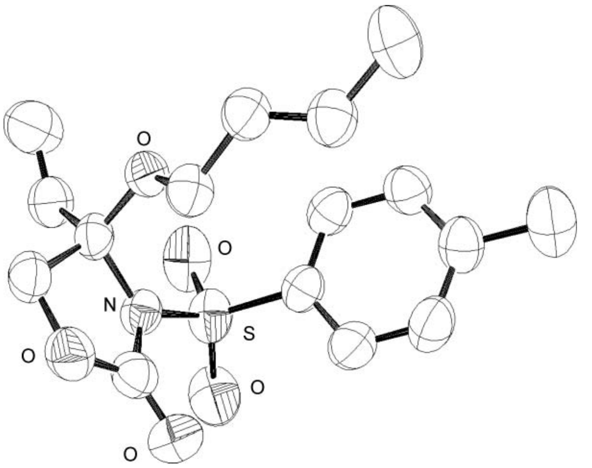
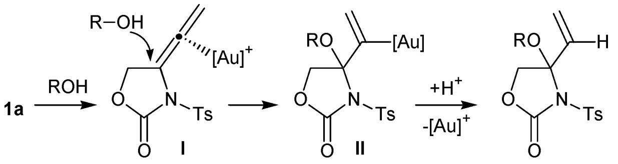


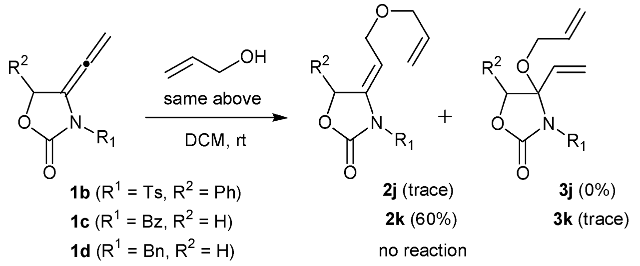
Fig. 1 Structure of **3d** (CCDC number 688562).† Hydrogen atoms have been omitted for clarity.

The catalytic cycle involved in the present reaction, although still speculative, probably involves initial coordination of the gold complex to the central carbon of the allene bond of **1a**,[13] as shown in Scheme 2. To exclude the possibility that an allyl cationic intermediate might be generated from **1a**, **1a** was treated with the present catalyst system in the absence of allyl alcohol. No isomerization of the allene bond of **1a** to the 1,3-diene was observed, and **1a** was recovered quantitatively. Furthermore, no reaction or decomposition of **1a** was observed upon treatment with a Brønsted acid catalyst such as *p*-TsOH or CF_3SO_3H.



Scheme 2 A plausible mechanism for the hydroalkoxylation of **1a**.

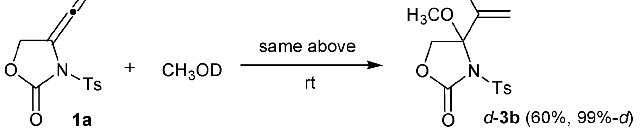
The reaction of **1b** with allyl alcohol produced only a trace amount of **2j**, and **1b** was recovered in 90%. Nucleophilic attack of the alcohol therefore appears to be hindered by the steric bulk of the substituent at the C5 position of the 2-oxazolidinone ring. Changing the tosyl substituent on the nitrogen of **1c** for a benzoyl group, reversed regioselectivity and only a trace amount of **3k** were obtained (Scheme 3). Furthermore, the use of **1d**,[14] which possesses a benzyl group instead of an electron withdrawing group on the nitrogen, led to no reaction. Thus, the enamine C1′=C2′ double bond appears to be activated by both the gold complex and the strongly electron withdrawing tosyl group, thereby allowing attack



Scheme 3 Effect of substituents on nitrogen.

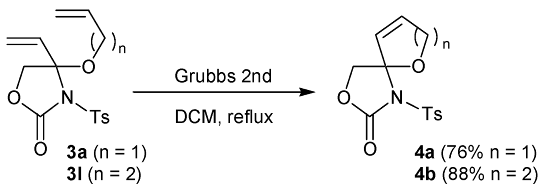
of the alcohol at the C5 position of the 2-oxazolidinone ring to form vinyl gold intermediate **II** (Scheme 2).

To gain further insight into the mechanism, the gold(I)-catalyzed addition of CH$_3$OD to **1a** was carried out. Deuterium was found to be incorporated only in the C2′ position of **1a** as determined by ^{1}H NMR analysis (Scheme 4).



Scheme 4 Deuterium labeling experiment of **1a** with CH$_3$OD.

To illustrate the utility of the present hydroalkoxylation products, ring-closing metathesis (RCM) reactions of **3a** and **3l** using Grubbs' second generation catalyst[15] gave the corresponding novel spiro dihydrofuran **4a** and dihydropyrane **4b** respectively, in high yields, as shown in Scheme 5.



Scheme 5 Ring-closing metathesis of **3a** and **3l**.

In conclusion, we have developed a cationic gold(I)-catalyzed intermolecular addition of alcohols toward the proximal allenic double bond of **1a**. The intermolecular addition of an alcohol to the proximal allenic double bond catalyzed by gold is the first example. Further study of synthetic applications of the reaction is currently ongoing in our laboratory.

Notes and references

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11 See electronic supplementary information (ESI)†.

12 No desired product **3a** was obtained on treatment of **1a** and allyl alcohol with (PPh$_3$)$_2$PdCl$_2$, CuI, CuOTf, PtCl$_2$ or PtCl$_2$/4COD. On the other hand, use of (PPh$_3$)$_2$PdCl$_2$/2AgSbF$_6$ gave **2a** and **3a** as a mixture with concomitant decomposition of **1a** in poor yield (<10%, **2a** : **3a** = 1.7 : 1).

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