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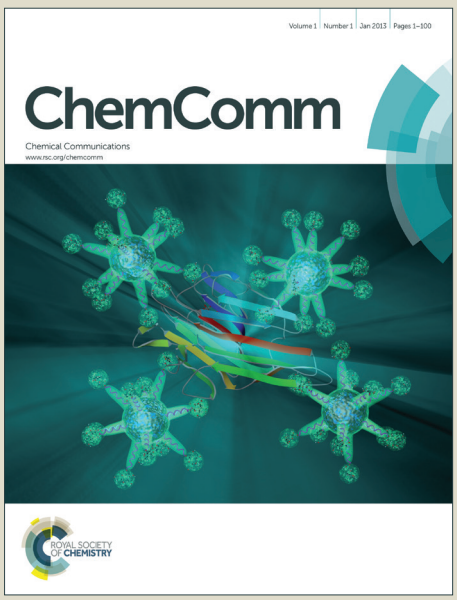

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ARTICLE TYPE

Gold(I)–Catalysed [1,3] O→C Rearrangement of Allenyl Ethers†

Chandrababu Naidu Kona[a] and Chepuri V. Ramana*[a]

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A simple and rapid access to the α-substituted acryl aldehydes has been provided by developing a gold-catalysed [1,3] rearrangement of the allenyl ethers importantly with a record turnover frequency of 4,600 h^{-1} (at 0.05 mol% of the catalyst concentration) in homogeneous gold (I) catalysis.

During the last decade, gold-complexes enabled organic synthesis with a remarkable reactivity and have ability to catalyse diverse organic transformations.[1] In particular, the selective activation of allenes by gold-complexes, followed by the subsequent inter and intramolecular nucleophilic additions and [3,3]-sigmatropic rearrangements (such as Claisen and Cope rearrangements), has received substantial attention.[2,3] Surprisingly, the utilization of allene units and the gold catalysts in the [1,3] O→C rearrangement have been less explored. The [1,3] rearrangement reaction of vinyl ethers constitutes an important C–C bond formation reaction and has attracted considerable attention over the last two decades.[4,5]Lewis acids, in general have been employed as catalysts for this reaction. Recently, the complexes of Pd, Co, Ir and Ru have been shown to be effective for this purpose.[6] The [1,3] rearrangement reactions involving the Lewis acid catalysts are generally postulated to proceed through the heterolytic cleavage of the O–R bond of the vinyl ether and *via* the formation of an intermediate ion-pair comprising the carbocationic species R^+ and an enolate counterpart. The success of this reaction depends upon a careful choice of Lewis acids, as well as the selection of appropriate R groups that can stabilize the transient carbocation.[7]

Considering the prerequisite of an ion-pair mechanism for the success of a "[1,3] rearrangement" and the formation of ion pairs with the catalytically active cations in the Au[I]-catalyzed reactions,[8] we envisioned that the [1,3] rearrangement of the allenyl ethers would constitute a general protocol for the synthesis of C2-substituted acryl aldehyde derivatives.[9,10] Coming to the gold-catalysis, the formation of trace amounts of [1,3] rearrangement products has been noticed on the occasions of [3,3] Claisen rearrangement of propargyl vinyl ethers and allyl vinyl ethers by Toste and Krafft.[11, 12] On the other hand, in the case of the reactions involving allenyl ethers and gold-complexes, Cui and co-workers have recently reported the gold-catalysed addition of alcohols at the C1 of allenyl(*p*-methoxybenzyl) ether (**1c**).[13] Indeed, **1c** has been selected as a starting point for the projected [Au]-catalysed [1,3] rearrangement by considering the fact that electron-donating groups on the aryl ring will stabilize the intermediate benzylcation formed. We reasoned that carrying out the reaction in aprotic solvents would facilitate the reaction in the requisite direction.

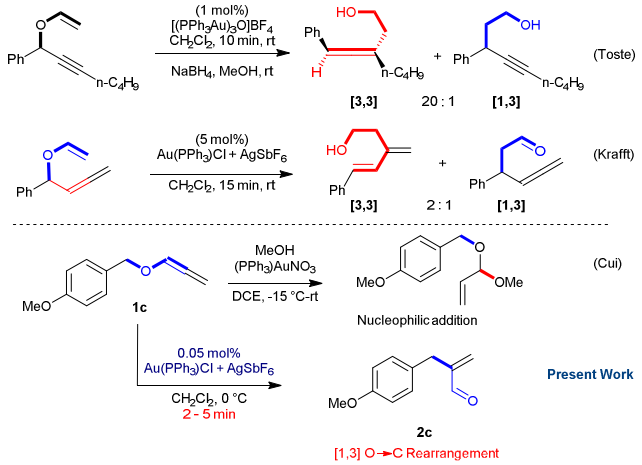
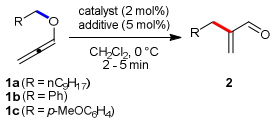


Figure 1. Gold (I) catalysed [1,3] rearrangement of vinyl ethers and the proposed synthesis of C2-substituted acryl aldehydes via allenyl ethers

To start in this direction, the allenyl ethers **1a**–**1c**, having respectively the PMB, benzyl and decyl units as R groups were selected as representative substrates for looking at the scope and limitations *inter alia* to learn about how the stability of the *in-situ* generated carbocation will influence the outcome of the [1,3] rearrangement. The exploratory experiments were carried out employing 2 mol% of catalyst in dichloromethane as the solvent. The reactions with Au[III] salts ended up with the hydrolysis of the allenyl ethers **1a**–**1c**. In case of the Au[I]-complexes, when employed alone, the starting materials were recovered intact. As expected, the combination of the Au(I)-complexes with the additive $AgSbF_6$ resulted in the quantitative conversion of **1c** within 5 minutes at 0 °C in dichloromethane and 2-(4-methoxybenzyl)acrylaldehyde (**2c**) was obtained in excellent yield. Under similar conditions, the allenyl ethers **1a** and **1b** hydrolysed immediately after the addition of the catalyst. Changing either the ligand on the Au[I]-complex or the counter anion did not provide any promising results with the substrates **1a** and **1b**. Control experiments revealed that, with the silver salts [5 – 10 mol%] AgOAc, AgOTf and $AgNTf_2$, only the hydrolysis of the allenyl ether **1c** was observed.[14] With $AgSbF_6$, the reaction was sluggish and the acryl aldehyde **2c** was obtained in moderate yields. These experiments clearly demonstrate that the active catalyst involved in the [1,3] rearrangement was the *in-situ*

generated cationic [Au]-complex and thet the weakly coordinating counter anion favours the rearrangement.[15]

Table 1: Catalyst Optimization (*see Table E2 of ESI for full details*)



Entry	Substrate	Catalyst	additive	Yield
1-6	**1a** or **1b** or**1c**	$AuCl_3$or $AuBr_3$	--	Hydrolysis
7-9	**1a** or **1b** or**1c**	$AuCl(PPh_3)$	--	No reaction
10-11	**1a**or **1b**	$AuCl(PPh_3)$	$AgSbF_6$	Hydrolysis
12	**1c**	$AuCl(PPh_3)$	$AgSbF_6$	91%
13	**1a** or **1b** or**1c**	$AuCl(PPh_3)$	$AgNTf_2$	Hydrolysis

As the reaction with 2 mol% of the catalyst was found to be almost instantaneous, we next examined the optimal concentration of the catalyst required at ambient temperature [*See Table E3, ESI for complete details*]. Controlled experiments were conducted with the allenyl ether **1c** at different concentrations of the catalyst, varied from 0.0125–0.05 mol%. Out of all the concentrations, the reaction with 0.05 mol% catalyst at 0 °C (5 min duration, S/C = 2,800) was found to be optimal for C–C bond formation and gave the required rearranged product **2c** in 97% yield (on 1 g scale) with the highest TOF (4600 h^{-1}).[16] For lower concentrations like 0.0125 mol%, the reaction was sluggish at rt and, when refluxed, the reaction proceeded within 12 h (80% conversion), after which there was no further conversion of the **1c**, provided **2c** in 90% isolated yield (S/C = 9072).

Table 2 reveals the scope of the current reaction. All the reactions were carried out by employing 0.05 mol% of the catalyst. The C1-secondary allenyl ethers of the (4-methoxyphenyl)methanol with *n*-butyl **1d** (on 1g scale) phenyl **1e** (1 g scale) and benzyl **1f** substitutions underwent the [1,3] rearrangement smoothly and provided the corresponding acryl aldehydes **2d–2f** in excellent yield. A similar trend was observed with the substrates having methoxy group(s) at either ortho and/or meta and/or para (**2g–2m** and **2q**), which revealed that the presence of the methoxy substituent is important, but that it is not necessary for the substituent to be at the *para* position. Similarly, the [1,3] rearrangement of allenyl ether of electron-rich 6-methoxy-1,2,3,4-tetrahydronaphthalen-1-ol (**1s**) was facile. The rearrangement of the (4-(*N*,*N*-dimethylamino)phenyl)-methanol allenyl ethers **1n–1p** also proceeded smoothly and delivered the corresponding rearranged products **2n–2p** in 92–95% yield. Although the simple benzyl allenyl ethers **1b** and **1v** are not compatible, gratifyingly, the diphenylmethanolallenyl ether **1r** gave 87% of the rearranged product **2r,** revealing that the stabilization of intermediate carbocation is important. As expected on the stabilization of the intermediate carbocation, the rearrangement of allenyl ethers of 1-(naphthalen-2-yl) ethan-1-ol **1x**, 1-(naphthalen-1-yl)ethan-1-ol **1y** and (tetrahydrofuran-2-yl)methanol **1z** were found to be unsuccessful. The successful synthesis of the 2,3-disubstituted acryl aldehydes **2t** and **2u** (isolated as inseparable *E*/*Z* mixture) reveals the applicability of this methodology for the [1,3] rearrangement of the C1-substituted allenyl ethers.

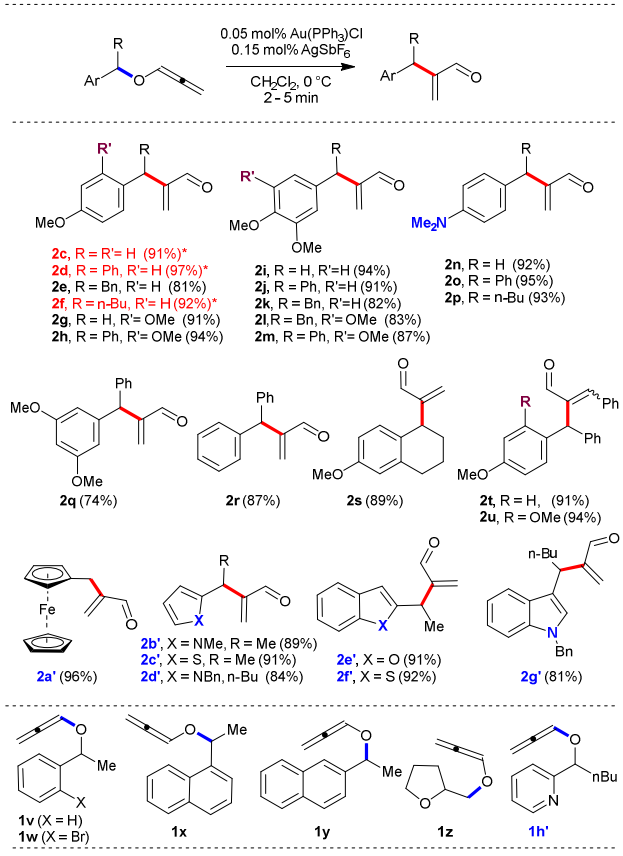


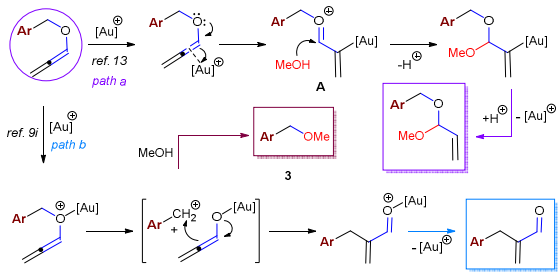
Table 2.Scope of [Au]-catalyzed[1,3] rearrangement reaction

Next, the feasibility of the rearrangement with other electron rich- and heterocyclic systems was examined. As shown in Table 2, the rearrangement of ferrocenyl methanol allenyl ether **1a'** provided the corresponding acrylaldehyde **2a'**. The [1,3] rearrangement of allenyl ethers having various heterocyclic units was also facile under these conditions. The acryl aldehydes having *N*-methylpyrrole (**2b'**) *N*-benzylpyrole (**2d'**), thiophene (**2c'**), benzofuran (**2e'**), benzothiophene (**2f'**) and *N*-benzylindole (**2g'**) structural units have been prepared in excellent yields by employing the 0.05 mol% of the catalyst. However, under these conditions, the pyridine derived allenyl ether **1h'** was found to be remain intact.

Coming to the mechanism of the reaction, two possible modes for the activation of allenyl ether were expected – through i) either coordination with the oxygen;[8g,8h] ii) or formation of η^1 complex **A** *via* the π-complexation with the electron rich olefin of the allene unit.[9] In case of the reaction of **1c** with $Au(PPh_3)NO_3$, it has been proposed by Cui and co-workers that the mechanism operates through the formation of an η^1 complex (Figure 2).[13] As a control, when allenyl ether **1c** was exposed to $Au(PPh_3)SbF_6$ in the presence of 3 equivalents of methanol, the methyl PMB ether **3** was obtained exclusively without any traces of the rearranged product **2c** or of the allylic acetal resulting from hydroalkoxylation with methanol (See Scheme 1, ESI). This complementary result obtained reveals that the electrophilicity of the Au[I] complex is important and suggests the possibility of the

reaction proceeding through coordination of gold (I) to the lone pair of oxygen.[8h] This coordination leads to significant elongation of the carbinol C−O bond and it depends strongly on the electrophilicity of the substituent attached to the oxygen.[17] More electrophilic substituents promote the cleavage of the carbinol C−O bond leading to the [1,3] rearrangement.[5b,6f] On the other hand, the less electrophilic substituents disfavour the cleavage of the C−O bond, which was the case with the substrates **1a**, **1b**, **1v–1z**, where the hydrolysis of the C–O bond occurred through the allenyl ether activation by the [Au]-complex.

Figure 2.Mechanism of [Au]-catalysed[1,3] rearrangement



In summary, the first report on the [Au]-catalysed [1,3] O→C rearrangement of allenylethers leading to the C2-substituted acryl aldehydes is documented. The reaction is facile even with 5 x 10^{-2} mol% of catalyst, which we believe is the lowest catalyst loading that has been reported in the area of homogeneous gold-catalysis.

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[a]*Division of Organic Chemistry, CSIR-National Chemical Laboratory, Dr. Homi Bhabha Road, Pune-411008, India. Fax: +91 20 25902629; Tel: +91 20 2590 2577; E-mail: vr.chepuri@ncl.res.in*

† Electronic Supplementary Information (ESI) available: [Characterization data and spectra of all new compounds]. See DOI: 10.1039/b000000x/

‡ Dedicated to Professor Ganesh Pandey on the occasion of his 60th birth day.

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