Gold Catalysis

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Propargylic Esters in Gold Catalysis: Access to Diversity**

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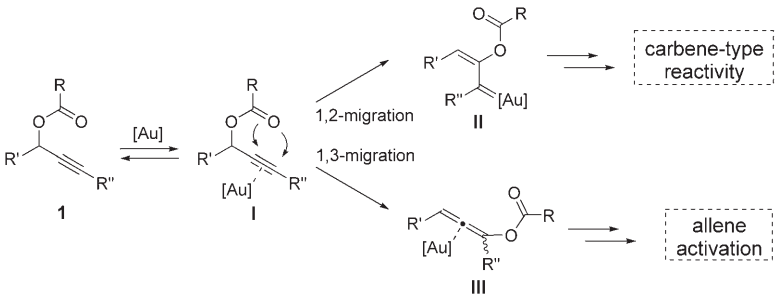
alkynes · allenes · carbenes · gold · rearrangement

Introduction

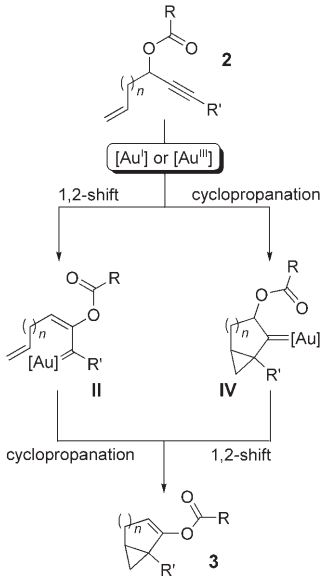
Homogeneous gold catalysis is currently undergoing an impressive renaissance centered on alkyne activation and functionalization.[1] As part of the wide interest in enyne cycloisomerization,[2] a specific class of alkynes is being studied extensively: propargylic esters. Several groups have investigated the intriguing and highly valuable reactivity of these easily accessible compounds in the context of gold catalysis. Notably, their propensity to undergo 1,2- and 1,3-acyl migration [Eq. (1)], leading to the formation of a Au–carbene **II** and to an allene **III**, respectively, which are both poised for subsequent functionalization, allows for great structural diversity.



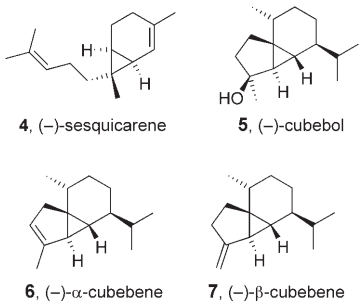
(1)

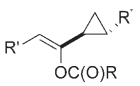
1,2-Acyl Shift

Despite earlier observations,[3] the attractive potential of propargylic esters in skeletal rearrangement has been recognized only recently in the context of Ru- and $PtCl_2$-catalyzed cycloisomerization.[4,5] Along these lines, early work by the Fürstner group showed that cationic gold(I), obtained by silver-induced abstraction of chloride from [AuCl(PPh$_3$)], was an efficient catalyst for this transformation leading, similarly to $PtCl_2$, to bicyclo[(*n*+2).1.0] compounds **3** (Scheme 1).[6] Even at early stages of development, this methodology, using both Au^I and Au^{III}, has already been applied in the total syntheses of complex sesquiterpenes **4**–**7**.[7] As shown in Scheme 1, the respective order of the cyclopropanation/1,2-shift sequence has to be considered. Fürstner and Hannen showed that stereogenic information at the propargylic position is translated into the cyclopropanated product, implying a "cyclopropanation then migration" mechanism.[7b,8] In sharp contrast, while studying the intermolecular version, yielding allylcyclopropanes **8**, Toste et al. showed that the stereogenic outcome of the reaction is consistent with a "migration then cyclopropanation" sequence.[9] Adding to the complexity of the mechanistic picture,



Scheme 1. Au-catalyzed tandem 1,2-shift/cyclopropanation.





Nolan et al. reported the formation of unprecedented bicyclo[3.1.0]hexenes **10′**, along with **10**, from 1,5-enynes (Scheme 2). In this case, in addition to the cyclopropanation/1,2-shift sequence, a cationic rearrangement of a cyclopropyl intermediate was proposed.[10] Remarkably, 1,4-enynes ($n = 0$) did not

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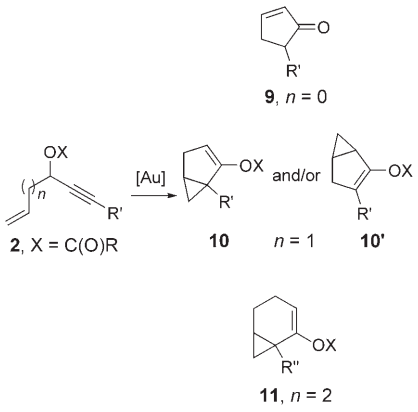


Scheme 2. Au-catalyzed cycloisomerization of enynes.

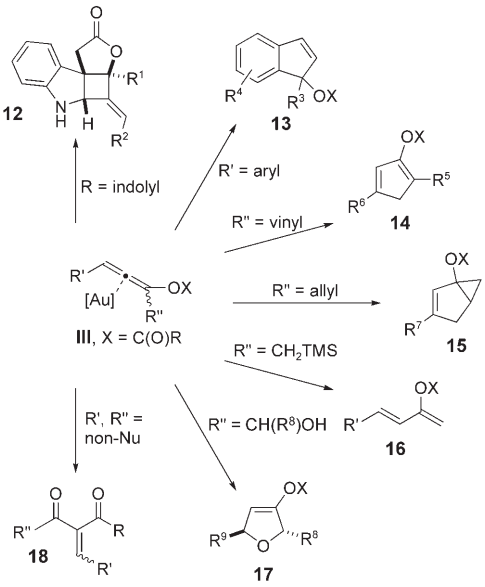
yield cyclopropyl derivatives, probably because of ring strain, but allowed for an efficient synthesis of 2-cyclopentenones **9** through Rautenstrauch rearrangement.[11]

1,3-Acyl Shift

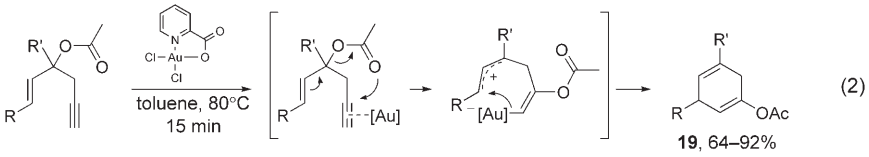
The transformation of propargylic esters into allenyl esters is a common process since it is an example of a [3,3] sigmatropic rearrangement. The particularity of gold catalysts is that in addition to mediating the [3,3] rearrangement, they mildly activate the allene moiety for subsequent reactivity (Scheme 3).

Zhang has taken advantage of this dual ability to produce 2,3-indoline-fused cyclobutanes **12** from fairly simple indole esters by means of formal [2+2] cycloaddition.[12] When an aryl group was placed at the propargylic position R′, tandem [3,3] rearrangement/intramolecular hydroarylation of phenylpropargyl acetates afforded indenes **13** in good yields.[13] The intermediacy of the allene was shown unambiguously by the authors, as isolated aryl-substituted allenes afforded similar indenes under Au catalysis. When terminal alkynes were used, 1,2-shift of the acetate was observed prior to cyclization, highlighting the high substrate dependence of the nature of the Au-catalyzed ester shift. Interestingly, if an alkyne moiety was placed in *ortho* position of the aryl ring, naphthalene derivatives were obtained by means of a Myers–Saito cyclization.[14]

Structural features at the acetylenic position of the cyclization precursor are equally crucial. When R″ = vinyl, Nazarov-type cyclization was observed, leading to cyclopentadienylic esters **14**, which were hydrolyzed in situ to give the corresponding conjugated cyclopentenones.[15] On the other hand, when R″ = allyl, bicyclo[3.1.0]hexenes **15**, isomers of those formed through 1,2-acyl shift,[5–7,10] were produced in the presence of gold(I) catalysts.[16] Further modification of the substitution of the alkyne allowed for the synthesis of conjugated dienes **16** by Au-catalyzed protodesilylation of intermediate **III**[17] and for the formation of dihydrofurans **17** from propargylic alcohols.[18]



Scheme 3. Au-assisted allene activation and product diversification. TMS = trimethylsilyl.



Interestingly, if no nucleophilic group was present at the propargylic or acetylenic positions, formation of α-ylidene β-diketones was observed.[19] For this transformation, it was proposed that the C–Au bond formed by activation of the allene moiety reacts as a nucleophile and attacks the carbonyl of the ester. Subsequent C–O cleavage would yield **18**.

Recently, Zhang and Wang reported the synthesis of cyclohexa-1,4-dienes **19** from 1,5-enynes bearing a homopropargylic ester [Eq. (2)].[20] As for propargylic esters, a 1,3-acyl shift triggered by gold occurs in this reaction, which relates it to the above discussion. Additionally, the functionalization of the C–Au bond opens new perspectives of research and emphasizes that stabilization of plausible intermediates can be a driving force for the formation of unprecedented products.

Finally, the recent introduction of conjugated polyyne systems possessing a propargylic ester appears as a very exciting field of research owing to the increase in complexity possible in one step.[21]

Outlook

The nature of the 1,*n*-acyl shift (*n* = 1,[22] 2, 3) catalyzed by Au^{I} and Au^{III} complexes, which can be followed by 1,*n*-metallotropic shift in conjugated polyyne systems, is the keystone for understanding the reactivity of propargylic esters. It is most likely that the intermediates in Scheme 4 are all in equilibrium and react further as a function of the tethered groups. Hence, simple modifications of the propargylic, acetylenic, and/or acyl substituents, as

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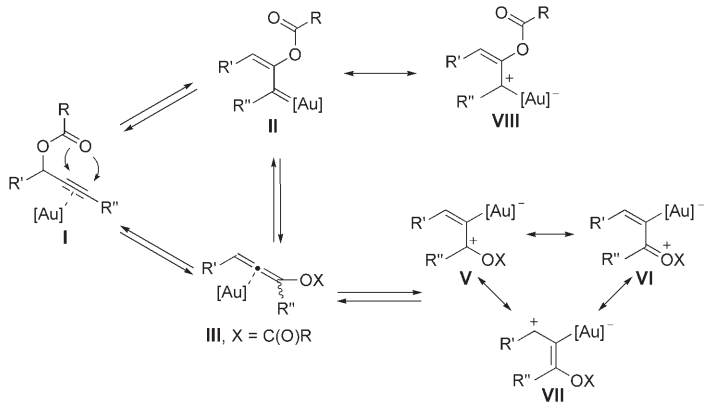

Scheme 4. Plausible intermediates in equilibrium upon coordination of cationic Au onto a propargylic ester.

well as the nature of the migrating function,[23] result in astonishingly diverse product patterns. This chemistry, still in its infancy, is rapidly evolving,[24] and it is believed that it will continue expanding since to date, 1) substrates have remained fairly simple, 2) extensive ligand screening is rare, 3) enantioselective transformations are scarce. Furthermore, numerous mechanistic questions, including the oxidation state of the catalyst,[25] the nature of the 1,3-acyl shift (1,3- or double 1,2-shift), the type of coordination/activation of the gold center onto the allene, are still subjects of debate.

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