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SHORT COMMUNICATION

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An Alternative Reaction Outcome in the Gold-Catalyzed Rearrangement of 1-Alkynyloxiranes

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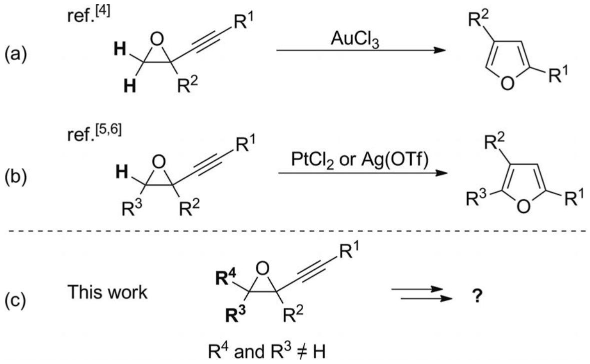
Keywords: Alkynes / Oxygen heterocycles / Gold / Oxophilicity / Rearrangement

The gold(III)-catalyzed rearrangement of tetrasubstituted 1-alkynyloxiranes is described. This transformation led to a different reaction outcome with respect to related substrates previously studied. Thus, tertiary α-alkynylketones or alkynols can be selectively obtained. Moreover, gold(III) proved capable to catalyze the rearrangement of simple epoxides. These results indicate that gold(III) complexes act as oxophilic Lewis acids rather than π-acids in these transformations.

Introduction

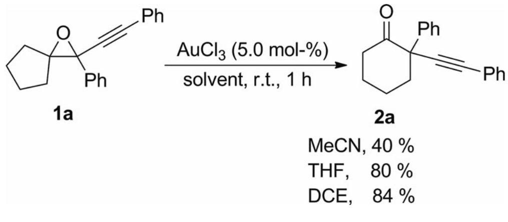
Epoxides are readily available and versatile intermediates in organic synthesis, as they can be easily converted into various valuable building blocks.[1] Among this class of compounds, transformations involving 1-alkynyloxiranes have received particular attention, because they enable the regioselective preparation of furan derivatives. This isomerization was described more than 30 years ago; however, it occurs under harsh reaction conditions with a limited scope of substrates.[2] Considering the ability of gold catalysts to activate alkynes,[3] Hashmi et al. elegantly developed a mild and functional group compatible protocol to achieve this interesting transformation making use of $AuCl_3$ as catalyst (Scheme 1a).[4] Subsequently, Yoshida et al.[5] and Pale et al.[6] reported on analogous transformations employing platinum and silver catalysts, respectively (Scheme 1b),[7] which widen the scope of this transformation.[8] Notably, these studies have been exclusively focused on di- and trisubstituted oxiranes, whereas the use of the corresponding tetrasubstituted analogues remained unexplored.[9] Considering the strong influence of the structure of the substrates in gold-catalyzed transformations,[3] we envisioned that the replacement of H atoms in the oxirane ring by different substituents might translate into a different reactivity (Scheme 1c). Herein, we report our findings on the reactivity of easily available tetrasubstituted 1-alkynyl epoxides **1** in the presence of gold catalysts, which led us to find an alternative reaction outcome of these compounds.



Scheme 1. Metal-catalyzed isomerization of 1-alkynylepoxides.

Results and Discussion

We selected alkynyloxirane **1a** as a model substrate and subjected it to the conditions previously reported by Hashmi: $AuCl_3$ (5.0 mol-%) in acetonitrile at ambient temperature (Scheme 2).[4] Under these reaction conditions, tertiary α-alkynylketone **2a** was obtained as a sole product in a moderate yield of 40%. This result is noteworthy despite the low yield, because a different reaction outcome from that previously reported for 1-alkynylepoxides is observed, as we anticipated.[4–7] Gratifyingly, when we used THF or 1,2-dichloroethane (DCE) as the solvent, the yield increased to a reasonable value of 80 or 84%, respectively.[10]



Scheme 2. Initial findings.

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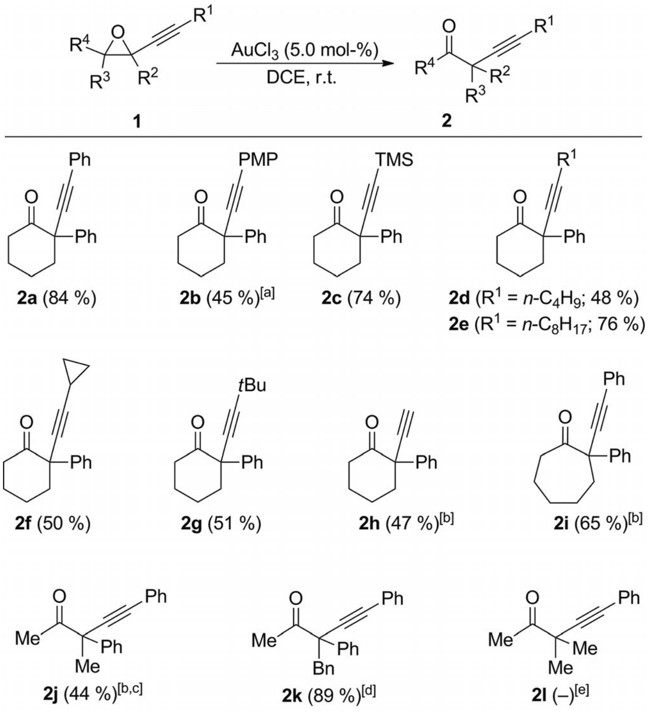
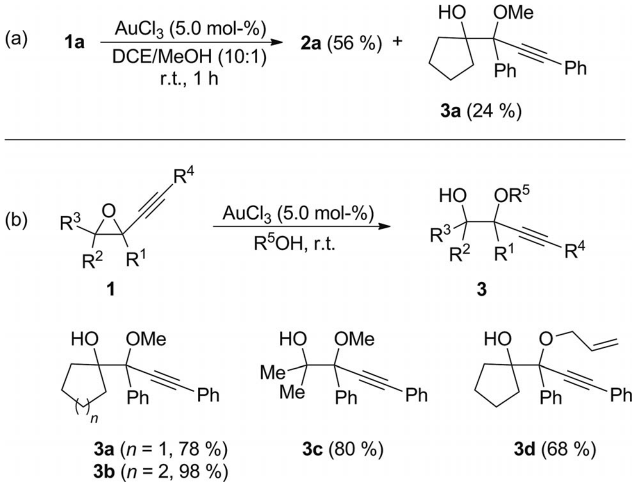
Next, we studied several alkynyloxiranes to evaluate the scope of this transformation (Table 1). Thus, alkynes bearing aryl, TMS, or various alkyl substituents (R^1 = *n*Bu, *n*-C_8H_{17}, *c*-C_3H_7, *t*Bu) were efficiently converted into the corresponding cyclohexanone derivatives **2a–g** in moderate to good yields. In contrast, substrates bearing a terminal alkyne (i.e., **1h**, R^1 = H), a six-membered ring in the spiro structure [i.e., **1i**, R^3–R^4 = –$(CH_2)_5$–], or without a spiro core (i.e., **1j**, R^3 = R^4 = Me) gave rise to unsatisfactory conversions when employing $AuCl_3$ as the catalyst. Nevertheless, the use of a catalytic system comprising a mixture of $AuCl_3$ and $Ag(BF_4)$ (5.0/15.0 mol-%, respectively) enabled ketones **2h–j** to be obtained in acceptable yields.[11,12] Interestingly, an unsymmetrically substituted oxirane (R^3 = Bn, R^4 = Me) was converted with complete selectivity into ketone **2k**, although a higher reaction temperature was required. In contrast, the presence of an aromatic ring as the R^2 substituent seems necessary, as all attempts to obtain ketone **2l** gave rise to complex or sluggish reaction mixtures.

Table 1. Gold-catalyzed rearrangement of epoxides **1** into ketones **2** (isolated yield in parentheses).



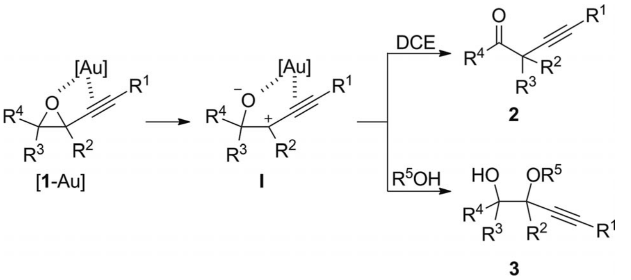
[a] PMP = 4-$MeOC_6H_4$. [b] In the presence of $Ag(BF_4)$ (15.0 mol-%). [c] At 0 °C. [d] At 70 °C. [e] Ketone **2l** was detected in the crude reaction mixture, but could not be isolated pure.

To gain insight into the mechanism of this transformation, we performed the reaction by using alcohols as nucleophiles. Thus, when the reaction of **1a** was carried out with methanol as the co-solvent (Scheme 3a), a separable mixture of ketone **2a** and alkynol **3a** was obtained in good combined yield (80% total yield; **2a**/**3a** = 2.3:1). Conversely, when methanol was used as the solvent, compound **3a** was obtained as the only reaction product in good yield. In this manner, various highly functionalized alcohols **3a–d** were prepared in good yield (Scheme 3b). Remarkably, the formation of compounds **3** took place with complete chemo- and regioselectivity, as we did not observe products derived from the hydroalkoxylation of the alkyne, and the reaction occurred exclusively at the propargylic position.



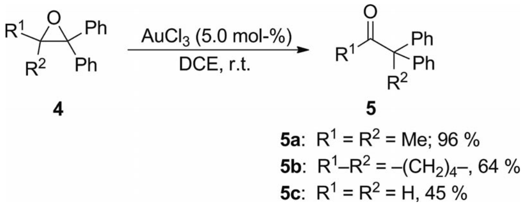
Scheme 3. Gold-catalyzed reactions of epoxides **1** in the presence of nucleophiles (isolated yield in parentheses).

A plausible mechanistic scenario that would account for this particular reaction outcome is depicted in Scheme 4. Hence, the coordination of the gold catalyst to the alkynyl epoxide, described as intermediate [**1**-Au], might favor activation of the propargylic position. This type of coordination and activation has been previously proposed by Pale et al.[6b] and Campagne et al.[13] for other gold-catalyzed processes involving alkynyl epoxides and propargylic alcohols, respectively. This activation likely affords stabilized propargylic carbocation intermediate **I**, in line with the proposal of Campagne et al.[13] The required presence of a stabilizing phenyl group as the R^2 substituent (see Table 1) might support this proposal. Subsequently, Meinwald-type rearrangement involving 1,2-alkyl migration might give rise to α-alkynylketones **2**.[14,15] In contrast, when the reaction is carried out in the presence of an alcohol, intermediate **I** can be trapped to afford the corresponding alkynols **3**.[16] Additionally, we ruled out the possibility that ketones **2** could arise from alkynols **3** through a pinacol-type rearrangement, as compounds **3** proved stable towards $AuCl_3$ (5.0 mol-%) at a reaction temperature as high as 70 °C (DCE, 24 h).



Scheme 4. Proposed mechanism.

Finally, according to this mechanistic proposal and considering the oxophilic character of gold(III) complexes,[17] we decided to evaluate whether or not the presence of the alkyne is required to perform an epoxide rearrangement. Interestingly, we found that $AuCl_3$ (5.0 mol-%, DCE, r.t.) proved capable to catalyze the Meinwald-type rearrangement of representative epoxides **4** to ketones **5** in moderate to good yields (Scheme 5). This result clearly reveals the ability of gold(III) catalysts to act efficiently not only as a π-Lewis acid but also as a σ-oxophilic Lewis acid.[18,19]



Scheme 5. Gold-catalyzed rearrangement of epoxides **4** into ketones **5**.

Conclusions

In summary, we have disclosed that the reactivity of 1-alkynyloxiranes in the presence of gold(III) catalysts is strongly affected by the substituents. Thus, whereas previous studies involving di- and trisubstituted epoxides afforded furan derivatives, the use of the corresponding tetrasubstituted analogues selectively gives rise to synthetically relevant *tertiary α-alkynylketones* **2**[20] by Meinwald-type rearrangement. The chemo- and regioselective formation of alkynols **3** when the reaction is conducted by using alcohols as solvent suggests the participation of a propargyl carbocation as the intermediate. Finally, the capability of gold(III) to act as a σ-oxophilic Lewis acid catalyst was illustrated in the rearrangement of simple epoxides **4**. This unusual reactivity trend could be further exploited to develop catalytic processes in which gold catalysts activate different functionalities.

Experimental Section

Preparation of 2-Phenyl-2-(phenylethynyl)cyclohexanone (2a) as a Representative Procedure: To a stirred solution of $AuCl_3$ (4.5 mg, 5.0 mol-%) in 1,2-dichloroethane (ca. 0.1 M) at 20 °C was added alkynylepoxide **1a** (82 mg, 1.0 equiv., 0.3 mmol) in one portion. The resulting mixture was stirred at this temperature until **1a** was completely consumed (TLC analysis, reaction time = 1 h). Then, the solvent was removed under vacuum, and the resulting residue was purified by flash column chromatography (SiO_2) to yield **2a** as a white solid (69 mg, 84%).

Supporting Information (see footnote on the first page of this article): Experimental procedures and copies of the ^1H NMR and ^{13}C NMR spectra.

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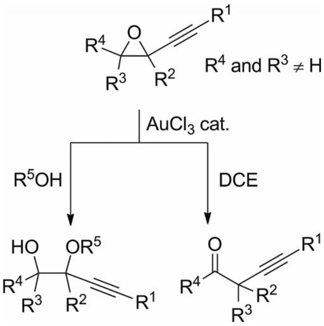
Gold(III) complexes catalyze the rearrangement of tetrasubstituted 1-alkynyloxiranes to afford tertiary α-alkynylketones or alkynols, which is in contrast to the previously reported reactivity of analogous substrates. Mechanistic studies suggest that gold(III) acts as an oxophilic Lewis acid catalyst in this transformation.



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