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Gold(I)-catalyzed reactions: substituents-dependent selective formation of bisfurans and 1,3-diketones from 1-alkynyl-2,3-epoxy alcohols

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ABSTRACT

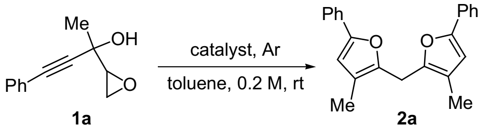
A mild access to bisfurans and 1,3-diketones via gold(I)-catalyzed transformation of 1-alkynyl-2,3-epoxy alcohols **1** has been described. The formation of bisfurans **2** is proposed to proceed through the sequential formation of 2-hydroxymethylfuran, followed by self-condensation in the presence of gold complex. Whereas the formation of 1,3-diketones **3** is resulted from a domino C–C bond cleavage of epoxide system with the assistance of hydroxyl group and subsequent hydrolysis. Substituents on the oxirane have a significant effect on the selective formation of the two kinds of products.

The furan ring is an important structural element in numerous natural products.[1] In addition, furans are extensively used as synthetic building blocks in organic synthesis, and a variety of pharmaceuticals and compounds of notable flavor and fragrance that contain the furan ring underlies their importance. Thus, the synthesis of furans has always attracted much attention of synthetic organic chemists.[2]

Among many different approaches to furans, the isomerization of alkynyloxiranes to furans looks quite attractive. Several classes of alkynyloxiranes, including 4-alkynyl-1,2-epoxides[3] and esters of 1-alkynyl-2,3-epoxy alcohols,[4] undergo cyclization to furans under various conditions. In 1994, Marson et al. described an efficient isomerization of 1-alkynyl-2,3-epoxy alcohols to bisfurans upon treatment with mercury(II) in very dilute sulfuric acid.[5] Since the disadvantages of the Hg(II) catalysis are obvious, we attempted to look for a new catalyst that can catalyze this reaction under mild conditions instead of using the problematic Hg(II) metal catalyst. Recently, gold catalysis has been increasingly gaining interest in organic chemistry due to the efficiency, the mildness, and the peculiar properties associated with gold atom.[6] Moreover, the isomerization of alkynyloxiranes to furans catalyzed by gold was far less investigated.[7,8] In the context of our recent investigation on the domino isomerization of epoxy alkyne, we now pursued gold complexes as catalysts for this transformation. Herein, we wish to present our preliminary results in this Letter.

Thus, we initially treated 1-alkynyl-2,3-epoxy alcohol **1a** (a pair of diastereoisomers) with various gold catalysts and other activating agents, and the results of these experiments are presented in Table 1. We were pleased to find that using 5 mol % of $Au(Ph_3P)Cl/AgSbF_6$ catalysts in toluene cleanly afforded the corresponding difurylmethane **2a** in 41% yield at room temperature (Table 1, entry 1). The superior efficiency of gold(I) was demonstrated by a comparison with gold(III), $PtCl_2$ in toluene (Table 1, entries 2–5). When 10 mol % of *p*-TsOH was used as a cocatalyst, the yield of **2a** decreased to 30% (Table 1, entry 6). Adding 1.0 equiv of water to this reaction system produced **2a** in 47% yield (Table 1, entry 7). Further screening of other silver salts revealed that $AgBF_4$ was the best choice to this reaction. A combination of 5 mol % of

Table 1
Screening of reaction conditions for the transformation of 1-alkynyl-2,3-epoxy alcohol **1a**



1a **2a**

Entry	Catalyst (5 mol %)	Yield[a] (%)
1	$Au(PPh_3)Cl/AgSbF_6$	41
2	$AuCl_3$	Trace
3	$NaAuCl_4{\cdot}2H_2O$	<20
4	$HAuCl_4{\cdot}H_2O$	<20
5	$PtCl_2$	Trace
6[b]	$Au(PPh_3)Cl/AgSbF_6$	30
7[c]	$Au(PPh_3)Cl/AgSbF_6$	47
8[c]	$Au(PPh_3)Cl/AgOTf$	26
9[c]	$Au(PPh_3)Cl/AgBF_4$	60
10[c,d]	$Au(PPh_3)Cl/AgBF_4$	40

[a] Isolated yields.
[b] 0 mol % of *p*-TsOH was added.
[c] 1.0 equiv of water was added.
[d] 10 mol % of $Au(PPh_3)Cl/AgBF_4$ was used.

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$Au(Ph_3P)Cl$ and $AgBF_4$ gave a good yield of the desired product **2a** in 60% (Table 1, entries 8–10). The other solvents such as dichloromethane, tetrahydrofuran, and acetonitrile were also examined under identical conditions, and toluene was found to be the best solvent for the reaction.

In order to study the scope of this reaction, various representative 1-alkynyl-2,3-epoxy alcohols **1b**–**g** were then prepared and subjected to the above reaction conditions, and the results of these experiments are outlined in Table 2. When R^1 was an aromatic group, an electron-donating substituent on the aromatic ring gave the better result compared to an electron-withdrawing substituent (Table 2, entries 1–3 and 5–6). If aliphatic alkyne **1e** was used, the reaction also proceeded smoothly to give the corresponding product **2e** in 56% yield (Table 2, entry 4). As can be seen from Table 2, R^2 could be aryl or alkyl groups. However, when R^2 = H, we did not find the corresponding desired product **2**. On the other hand, the substituent on the oxirane ring had a significant effect on the reaction. The furan-containing products **2** could be obtained when R^3 was H or alkyl group.

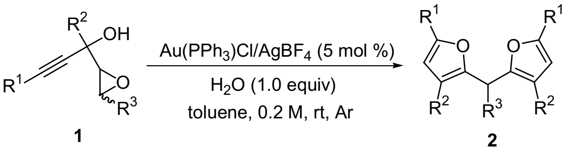
Inspired by the above results, we next examined the reaction of 1-alkynyl-2,3-epoxy alcohol **1h** under the optimized conditions. We found that the reaction also took place smoothly to afford the corresponding product **2h** in 30% yield (Scheme 1).

Interestingly, when R^3 in substrate **1** was aryl group, conducting 1-alkynyl-2,3-epoxy alcohols **1i**–**m** to the standard reaction conditions resulted in the formation of 1,3-diketones **3i**, **3l**, and **3m** in moderate to excellent yields, and the results of these experiments are listed in Table 3. As can be seen from Table 3, R^1 could be both aryl and alkyl groups, and when aryl group R^3 has no substituent, a better result could be obtained in this domino process (Table 3, entries 1–3). It should be noted that when R^2 was a phenyl group, unidentified complex product mixtures were formed under identical conditions (Scheme 2).

On the basis of the above observations, plausible mechanisms for the selective formation of bisfurans and 1,3-diketones are proposed in Scheme 3. The coordination of gold complex to the alkynyl moiety of **1** (R^4 = H) affords the π-complex **A**. Subsequent nucleophilic attack of the oxygen atom in epoxide on the alkynyl moiety[9] leads to the formation of intermediate **B**.[10] Different substituents on the oxirane give rise to the formation of different products. (i) When R^3 is H or alkyl group, intermediate **B** is attacked by water, affording intermediate **C** (red arrow). Protonation of intermediate **C** followed by elimination of one molecule of water can result in the formation of 2-hydroxymethylfuran **D**. Dimerization of **D** produces intermediate **F** via carbon cationic intermediate **E**.[11] Elimination of one molecule of aldehyde in intermediate **F** produces the corresponding difurylmethane **2**. (ii) When R^3 is aryl group, the oxonium ion **B** induces cleavage of carbon–carbon bond (C^1–C^3) to give intermediate **G** (blue arrow), which undergoes protonation to produce alkenyl ether **H** and regenerates the gold catalyst.[8] Subsequent 1,4-addition of water to **H** affords intermediate **J**, which undergoes elimination of one molecule of aldehyde and isomerization to give 1,3-diketone **3**.[12]

Substituents on the oxirane ring have a significant effect on these selective transformations. When R^3 is aryl group (Scheme 3), probably due to the activation of oxonium ion by aryl group, the C^2–O bond becomes very weak. Moreover, with the assistance of the hydroxyl group, the C^3–C^1 bond cleavage is much faster than the nucleophilic attack of water on C^2 to form a new C–C double bond. When R^3 is H or alkyl group, C^2–O bond becomes much stronger and C^2 carbon is less positively charged, which causes the cleavage of C^3–C^1 bond to

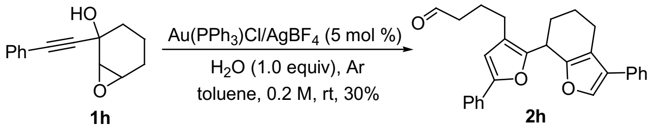
Table 2
Scope of the gold-catalyzed Rearrangement[a]



Entry	Substrate	Yield[b] (%)
1	**1b**: R^1 = *p*-ClC_6H_4, R^2 = Me, R^3 = H	**2b**: 54
2	**1c**: R^1 = *p*-$MeOC_6H_4$, R^2 = Me, R^3 = H	**2c**: 62
3	**1d**: R = $HCCC_6H_4$, R = Me, R = H	**2d**: 44
4	**1e**: R = $^nC_4H_9$, R = C_6H_5, R = Et	**2e**: 56
5	**1f**: R^1 = *p*-MeC_6H_4, R^2 = Me, R^3 = Me	**2f**: 75
6	**1g**: R = C_6H_5, R = C_6H_5, R = Et	**2g**: 53

[a] General reaction procedure: To a solution of **1** (0.3 mmol) in 1.5 mL of toluene at room temperature under argon were added H_2O (0.3 mmol), $Au(Ph_3P)Cl$ (0.015 mmol), and $AgBF_4$ (0.015 mmol). The reaction was monitored by TLC plates. Then, the mixture was diluted with CH_2Cl_2 after completion, evaporated under reduced pressure and purified by a flash column chromatography.

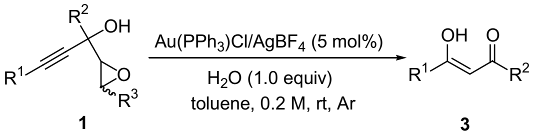
[b] Isolated yields.



1h **2h**

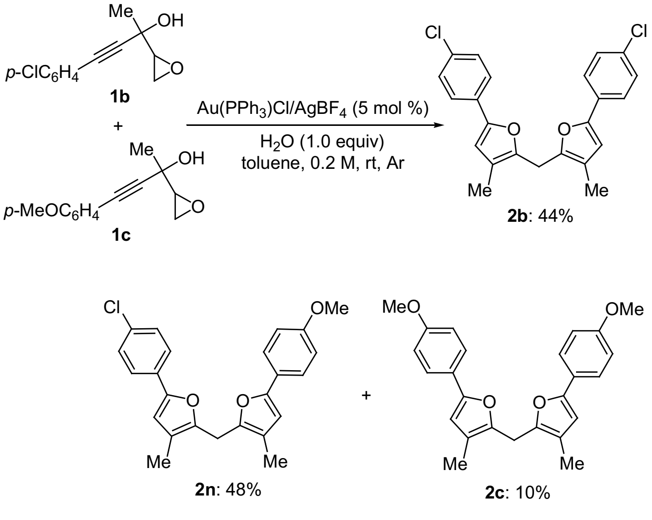
Scheme 1. Gold-catalyzed isomerization of 1-alkynyl-2,3-epoxy alcohol **1h**.

Table 3
Gold-catalyzed isomerization of 1-alkynyl-2,3-epoxy alcohols to 1,3-diketones

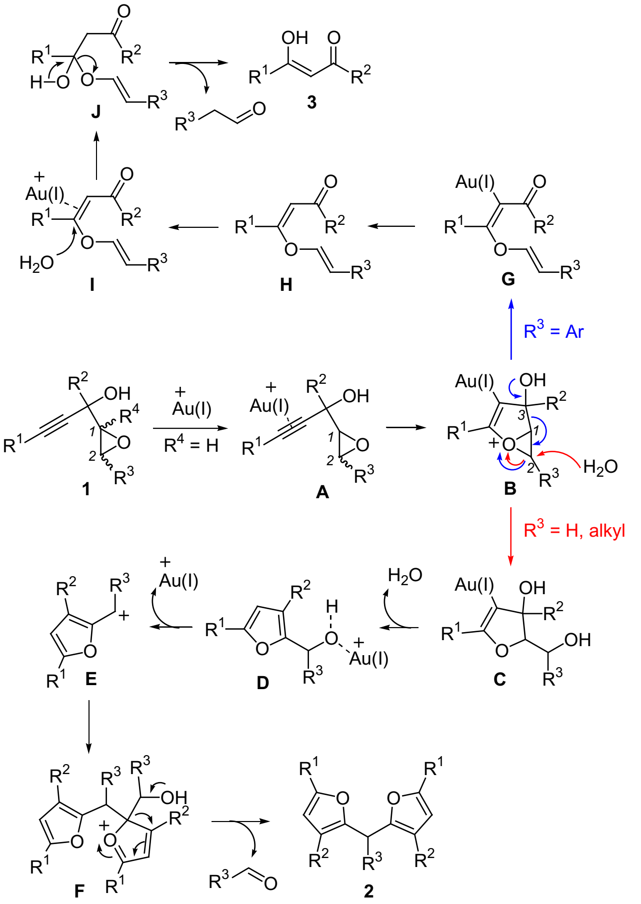


Entry	Substrate	Yield[a] (%)
1	**1i**: R = C_6H_5, R = Me, R = C_6H_5	**3i**: 91
2	**1j**: R1 = C_6H_5, R^2 = Me, R^3 = *p*-ClC_6H_4	**3i**: 76
3	**1k**: R^1 = C_6H_5, R^2 = Me, R^3 = *p*-MeC_6H_4	**3i**: 78
4	**1l**: R^1 = *p*-$MeOC_6H_4$, R^2 = Me, R^3 = C_6H_5	**3**1: 31
5	**1m**: R = $^nC_4H_9$, R = Me, R = C_6H_5	**3m**: 76

[a] Isolated yields.



Scheme 2. Cross-coupling reaction of 1-alkynyl-2,3-epoxy alcohols **1b** and **1c**.



Scheme 3. Proposed mechanisms for the formation of bisfurans and 1,3-diketones.

become more difficult. Thus, nucleophilic attack by water is favored to give oxirane-opening intermediate. On the other hand, in Liang's recently published work,[8] since C^1 (R$^4 \neq$ H) is a quaternary carbon, the C^1–O bond is weaker than C^2–O bond in oxonium ion **B**, the [1,2]-migration[13] of the alkyl group takes place with the assistance of the hydroxyl group whether R^3 is alkyl or aryl group, affording spiropyranones in good yields.

In summary, we have developed a selective synthetic approach to bisfurans and 1,3-diketones from 1-alkynyl-2,3-epoxy alcohols catalyzed by gold(I) at room temperature. Further studies regarding the mechanistic details and scope of this process are in progress.

Acknowledgments

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