DOI: 10.1002/chem.200701954

A Gold(I)-Catalyzed Intramolecular Reaction of Propargylic/Homopropargylic Alcohols with Oxirane

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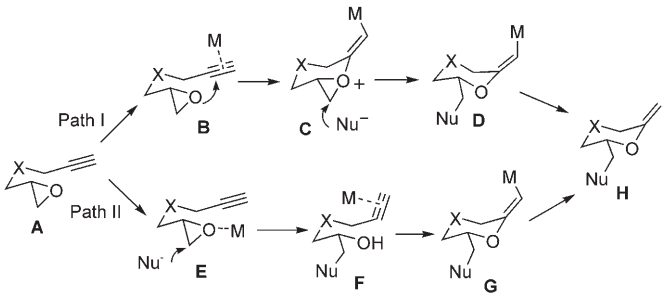
Abstract: The gold(I)-catalyzed cycloisomerization of epoxy alkynes in the presence of a nucleophile is an efficient protocol to provide ketal skeletons with high stereoselectivity. An intramolecular reaction of propargylic/homopropargylic alcohols with oxirane to produce ketal/spiroketals in moderate yields under mild conditions has been reported. Moreover, the mechanism of this kind of reaction has been discussed on the basis of a series of control and ^{18}O tracer experiments.

Keywords: alcohols · cyclization · diastereoselectivity · domino reactions · gold · ketals

Introduction

Ketals[1] are important subunits in a large number of biologically active natural products. The acid-catalyzed cyclization of dihydroxy ketones, or equivalents thereof, is one of the most important strategies in the preparation of ketal-containing molecules.[1g–i,2] Gold salts, known as a type of powerful soft Lewis acid, can readily activate alkynes, allenes, and olefins toward attacks by a variety of nucleophiles.[3,4] Numerous highly efficient C–O bond-forming reactions have recently been reported in which alkynes are activated toward nucleophilic attacks by alcohols,[5] carbonyl compounds,[6] and carboxylic acids.[7]

Our earlier work on a gold-catalyzed cascade cyclization reaction of epoxy alkynes to yield ketals provided an efficient alternative to the construction of the C–O bond.[8] We proposed two reaction pathways (Scheme 1): In path I, the coordination of a cationic gold species to the epoxy alkyne unit of **A** gave complex **B**, in which an intramolecular attack toward the alkyne by oxirane resulted in an oxonium ion **C**.[9] Subsequent ring-opening of the oxonium ion in the presence of an alcohol produced the product **H** via intermediate **D**. Whereas in path II, selective activation of oxirane of **A** by a gold salt afforded intermediate **E**, which was followed by a nucleophilic ring-opening reaction to form an opened oxirane intermediate **F**. An intramolecular attack toward the alkyne by the newly formed hydroxy group gave the product **H** via intermediate **G**. Interestingly, soon after our discovery, Liang and co-workers reported the similar gold-catalyzed transformation of epoxy alkynes.[10]



Scheme 1. Gold-catalyzed cycloisomerization of epoxy alkynes.

Our continuous interest in the melt-catalyzed domino cycloisomerization of epoxy alkynes[11] promoted us to investigate further the generality and mechanism of this kind of reaction. Herein, we report a gold-catalyzed intramolecular reaction of propargylic/homopropargylic alcohols with oxirane to afford the corresponding ketals and spiroketals in moderate yield under mild conditions.

Results and Discussion

The routine synthetic sequence for the preparation of starting materials **2** is shown in Scheme 2. The treatment of an

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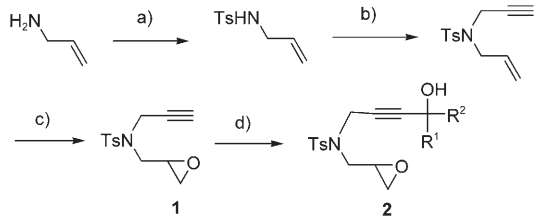
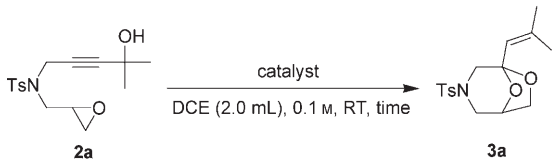
Supporting information (detailed experimental procedures, spectroscopic, and analytic data of the all new compounds) for this article is available on the WWW under http://dx.doi.org/10.1002/anie.200701954.



Scheme 2. Preparation of the epoxy propargylic alcohols. Reagents and conditions: a) TsCl (0.9 equiv), Et_3N (1.0 equiv), CH_2Cl_2, 0 °C, RT; b) 3-bromopropyne (1.5 equiv), K_2CO_3 (1.5 equiv), acetone, 60 °C; c) *m*-CPBA (2.0 equiv), CH_2Cl_2, RT, (64 %; three steps); d) *n*BuLi (1.1 equiv), R^1COR^2 (1.1 equiv), THF, −78 °C (50–83 %).

allylic amine with 4-methylbenzenesulfonyl chloride (TsCl) and 3-bromopropyne produced the desired 1,6-enyne. Epoxidation of the 1,6-enyne with 3-chloroperbenzoic acid (*m*-CPBA) yielded the alkynyloxirane **1**. After treatment of **1** with *n*-butyllithium in THF, the nucleophilc addition to ketones or aldehydes afforded the corresponding epoxy propargylic alcohols **2** in moderate-to-good yields. With substrate **2a** ($R^1=R^2=Me$) in hand, several combinations of gold(I) and silver salts were screened (Table 1). The treatment of

Table 1. Efficiency of catalysts for the cycloisomerization of epoxy propargylic alcohol **2a**.



2a **3a**

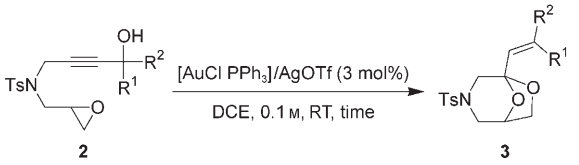
Entry	Catalyst [3 mol %]	*t* [h]	Yield [%][a]
1	$[AuClPPh_3]/AgSbF_6$	12	29
2	$[AuClPPh_3]/AgOTf$	12	51
3	$[AuClPPh_3]/AgO_2CCF_3$	72	trace
4	$[Au_2Cl_2\{(R)\text{-binap}\}]/AgOTf$	23	43
5	$[AuClPMe_3]/AgOTf$	24	14
6	$[AuCl\{P(\alpha\text{-furyl})_3\}]/AgOTf$	28	trace
7[b]	$[AuClPPh_3]/AgOTf$	10	46
8[c]	$[AuClPPh_3]/AgOTf$	12	46
9[d]	$[AuClPPh_3]/AgOTf$	20	51
10	$AuCl_3$	10	trace
11	$BF_3{\cdot}Et_2O$ (30 mol %)	10	0

[a] Yield of the isolated product. [b] DCE: 1.0 mL. [c] DCE: 3.0 mL. [d] Added H_2O: 1.0 equiv. binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl.

2a with 3 mol % of $[AuClPPh_3]/AgOTf$ (OTf = trifluoromethanesulfonate) in 1,2-dichloroethane (DCE) at room temperature for 12 h gave the best result, thus providing the corresponding ketal product **3a** in 51 % yield (Table 1, entry 2 compared to entries 1, 3–6). Variation in the concentration of the solution is possible without substantial loss of yield (Table 1, entries 7 and 8). Adding a stoichiometric amount of water into the reaction system did not influence the yield of **3a** (Table 1, entry 9). We also examined the use of $AuCl_3$ in this reaction to improve the yield of **3a**, although the outcome was not rewarding (Table 1, entry 10). Other Lewis acids, such as $BF_3{\cdot}Et_2O$, did not have any catalytic ability in the reaction (Table 1, entry 11).

This interesting gold(I)-catalyzed reaction could be successfully extended to a variety of epoxy propargylic alcohols with different substituents (Table 2). The reaction proceeded

Table 2. Scope of the intramolecular reaction of propargylic alcohols with oxirane.



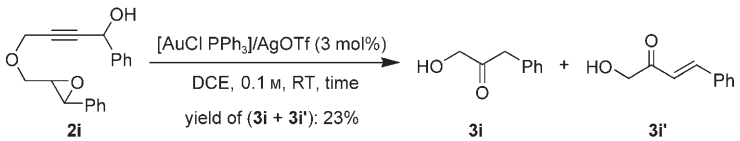
2 **3**

Entry	Starting material	R_1	R_2	*t* [h]	Product	Yield [%][a,b]
1	**2b**	H	C_6H_5	12	**3b**	50
2	**2c**	H	$p\text{-}ClC_6H_4$	10	**3c**	56
3	**2d**	H	$m\text{-}ClC_6H_4$	30	**3d**	52
4	**2e**	H	$p\text{-}OMeC_6H_4$	21	**3e**	12
5	**2f**	H	Et	13	**3f**	31
6	**2g**			18	**3g**	32
7	**2h**	Et	Et	19	**3h**	51

[a] Yield of the isolated products. [b] Product **3** was obtained as the *E* configuration.

smoothly when the R^1 moiety was a hydrogen atom and R^2 was a phenyl group or an aromatic ring bearing an electron-withdrawing group (Table 2, entries 1–3). Introducing an electron-donating group onto the aromatic ring of the R^2 group resulted in a remarkable loss of yield (Table 2, entry 4). When the R^2 group was switched to an alkyl group, the epoxy propargylic alcohol **2f** was converted into the corresponding ketal **3f** in 31 % yield under identical conditions (Table 2, entry 5). The use of other epoxy propargylic alcohols, such as **2g** and **2h**, under the standard conditions afforded the desired products **3g** and **3h** in moderate yields (Table 2, entries 6 and 7). It should be emphasized that in all cases ketals **3** were obtained exclusively as the *E* configuration. However, when the *O*-tethered epoxy propargylic alcohol **2i** was subjected to the optimized conditions, only a mixture of product **3i** and **3i′** was obtained in low yield (Scheme 3).

On the basis of the above results, two tentative mechanisms for the observed gold-catalyzed cycloisomerization of epoxy propargylic alcohols to produce ketals were proposed.



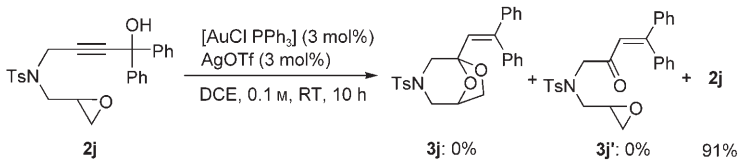
2i **3i** **3i'**

Scheme 3. Gold-catalyzed isomerization of **2i**. DCE = dichloroethane.

According the discovery by Chung and co-workers,[12] the epoxy propargylic alcohol **2a** undergoes a rearrangement in the presence of a cationic gold complex to give cumulene intermediate **J** via gold-activated intermediate **I**. The intermediate **J** could be attacked by water to give intermediate **K**, which tautomerizes to intermediate **L**. Then, a gold-catalyzed intramolecular reaction of the ketone with oxirane takes place, thus leading to the ketal **3a** via intermediate **M** (Scheme 4).

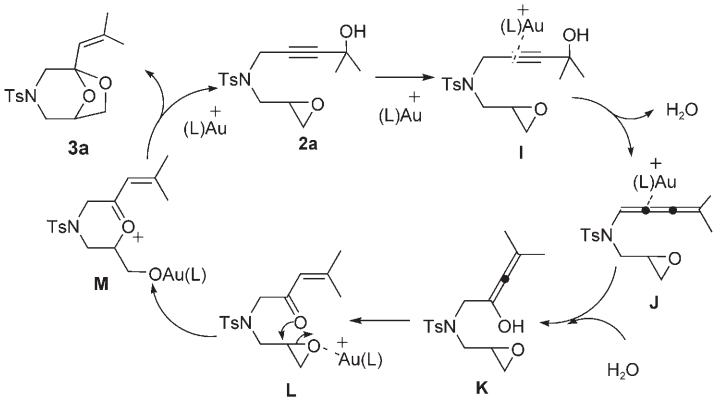
The Meyer–Schuster reaction is also a possible rearrangement for the isomerization of **I** to **L** (Scheme 5). This process involves a 1,3-shift of the hydroxy moiety, followed by tautomerization of the presumed allenol intermediate **K**.[13]

Notably, when the reaction of epoxy propargylic alcohol **2j**, catalyzed by [AuClPPh$_3$]/AgOTf in DCE at room temperature, was carried out under the standard conditions, to our disappointment, none of the target product **3j** was obtained and 91% of starting material **2i** was recovered (Scheme 6). In addition, according to the mechanism shown in Scheme 4, a tertiary propargylic alcohol with a hydrogen atom at the α position to the alkyne unit would be in favor of isomerization.[12] However, no such isomerization of the propargylic alcohol to α,β-unsaturated ketone **3j′** was observed either under similar reaction conditions (Scheme 6).

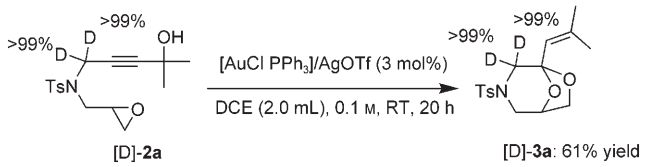


Scheme 6. A crossover experiment.

Furthermore, a deuterium-labeling experiment was carried out using [D]-**2a** (D > 99%) as the substrate under the standard conditions (Scheme 7). None of the deuterium atoms were lost during the reaction. On the basis of this result, the existence of intermediate **J** shown in Scheme 4 can be excluded, and Scheme 5 should be the plausible reaction mechanism.

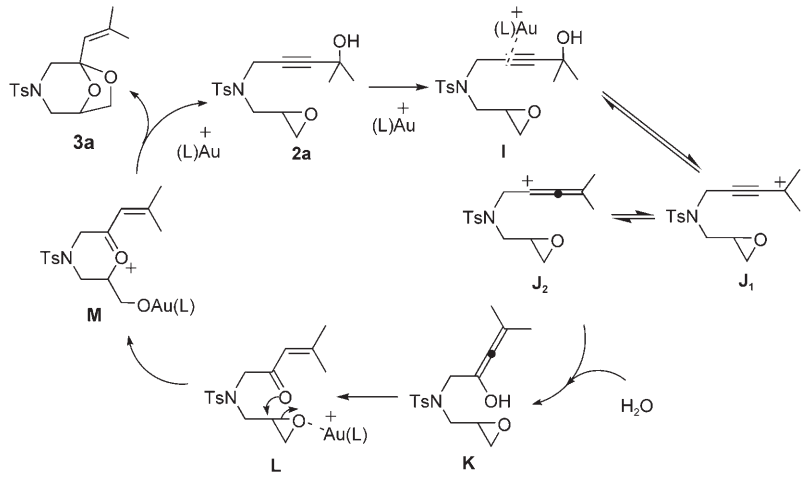


Scheme 4. Proposed mechanism of the gold-catalyzed cycloisomerization of epoxy propargylic alcohols.

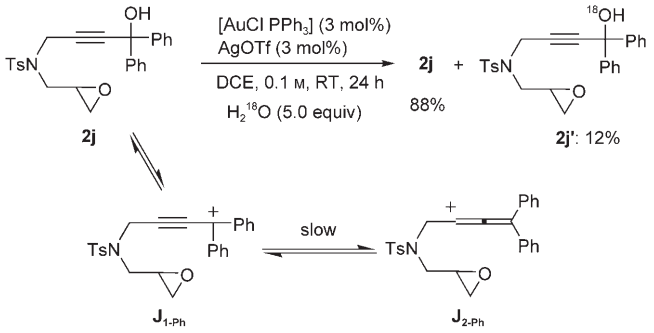


Scheme 7. A deuterium-labeling experiment

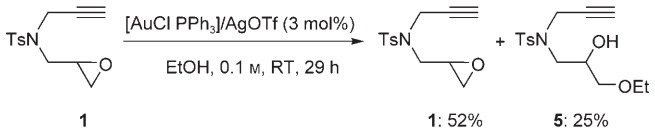
Scheme 5 involves an equilibrium step between intermediates $\mathbf{J_1}$ and $\mathbf{J_2}$. If intermediate $\mathbf{J_1}$, which was formed by release of H_2O from the propargylic alcohol, returned to intermediate **I** much faster than its tautomerization to intermediate $\mathbf{J_2}$, intermediate **K** could not be produced and none of the α,β-unsaturated ketone **L** would be obtained. The following ^{18}O-labeling experiment shown in Scheme 8 supported our assumption. When **2j** was subjected to the standard reaction conditions along with the addition of 5.0 equivalents of $H_2{}^{18}O$ ($^{18}O > 97.7\%$) to the reaction system, 12% of ^{18}O-labeling product **2j′** was obtained (as determined by EIMS analysis), presumably as a result of the existence of two phenyl groups, the cationic intermediate $\mathbf{J_{1\text{-}Ph}}$ is very stable, thus rendering the isomerization of $\mathbf{J_{1\text{-}Ph}}$ to $\mathbf{J_{2\text{-}Ph}}$ to be much more difficult.[14] Therefore, the cycloisomerization of **2j** did not take place under identical conditions. On the basis of these control and ^{18}O tracer experiments, a gold(I)-cata-



Scheme 5. Proposed mechanism for the isomerization of **I** to **L**.



Scheme 8. An ^{18}O-labeling experiment.

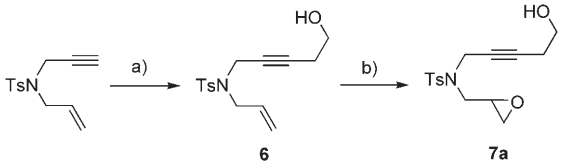


Scheme 9. A crossover control experiment.

lyzed Meyer–Schuster rearrangement of propargylic alcohols **2** is most likely to be responsible for the formation of ketals **3**.

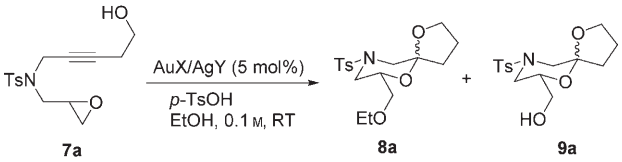
Mechanistically, this reaction might also proceed in a tandem sequence involving the first step of the ring-opening of oxirane. However, recent reports show that most of the isomerization of propargylic alcohols to ketals could be finished within four hours[12] and that the ring-opening of oxirane in the presence of water or alcohol catalyzed by gold needed a longer reaction time.[8] Thus, the mechanism involving the ring-opening of oxirane as the first step could be excluded according to literature reports. In addition, the reaction might also involve an oxonium ion, which was formed by the nucleophilic attack of the oxygen atom in the epoxide unit on the gold-coordinated alkyne.[15] To test this hypothesis, the reaction of epoxy alkyne **1** in ethanol catalyzed by 3 mol% of $[AuClPPh_3]/AgOTf$ was carried out. However, none of the cyclized product was observed, except 25% of ring-opened product **5** (Scheme 9). Although this result does not provide direct evidence, the possibility of an oxonium ion as an intermediate involving the reaction process was much lower on the basis of the above control experiment. Therefore, if reconsidering the mechanism shown in Scheme 1, the reaction involving the oxonium ion could be excluded according to the experimental observations.

We next turned our attention to the construction of spiroketals by using epoxy homopropargylic alcohols as the starting materials in ethanol. Although many synthetic methods for the preparation of spiroketals are known, little attention has been paid to the approach based on the use of gold catalysts.[5,16] Recently, Liu and De Brabander disclosed an elegant study on the room-temperature cycloisomerization, tandem hydroalkoxylation/acetal, or spiroacetal formation of unactivated internal alkynols using a platinum(II) complex and an unusual cationic gold(I) complex as mild catalysts.[16c] Epoxy homopropargylic alcohols **7** were prepared in a similar way to that shown in Scheme 2, and the synthetic procedures are given in Scheme 10. To develop the catalytic version, we examined the reaction of **7a** in the presence of several kinds of catalysts in ethanol and the results of these experiments are summarized in Table 3. We found that using 30 mol% of *para*-toluene-4-sulfonic acid (*p*-TsOH) as a co-catalyst with 5 mol% of $[AuClPPh_3]/AgSbF_6$ was the best combination for the reaction at room temperature (20°C), thus affording the desired product **8a** in 50% yield (d.r. = 24:76) along with the formation of **9a** as the by-product (Table 3, entries 1–7). The weakly coordinating anion SbF_6^- proved to be particularly well suited to this reaction (Table 3, entries 3,



Scheme 10. Preparation of the epoxy homopropargylic alcohol. Reagents and conditions: a) *n*BuLi (1.1 equiv), oxirane (2.0 equiv), $BF_3{\cdot}Et_2O$ (2.0 equiv), THF, −78°C (52%); b) *m*-CPBA (2.0 equiv), CH_2Cl_2, RT (45%).

Table 3. Optimization of the reaction conditions.



Entry	*p*-TsOH [equiv]	AuX/AgY	*t* [h]	**8a** yield [%][a]	**8a** d.r.[b]	**9a** yield [%][a]
1	0.1	$[AuClPPh_3]/AgSbF_6$	10.5	39	48:52	10
2	0.2	$[AuClPPh_3]/AgSbF_6$	7	41	46:54	10
3	0.3	$[AuClPPh_3]/AgSbF_6$	5.4	50	24:76	15
4[c]	0.3	$[AuClPPh_3]/AgSbF_6$	2	24	14.5:85.5	15
5	0.5	$[AuClPPh_3]/AgSbF_6$	3	42	31.5:60.5	16
6	0.5	$[AuClPPh_3]/AgSbF_6$	8	21	16.7:83.3	21
7[d]	1.0	$[AuClPPh_3]/AgSbF_6$	16.5	24	14.5:85.5	18
8	0.3	$[AuClPPh_3]/AgBF_4$	6.5	34	38:62	12
9	0.3	$[AuClPPh_3]/AgO_2CCF_3$	13	44	35.5:64.5	15
10	0.3	$[AuClPMe_3]/AgSbF_6$	12.5	42	31:69	13
11[e]	0.3	$[AuClPPh_3]/AgSbF_6$	23.5	51	17:83	10

[a] Yield of the isolated products. [b] Determined by HPLC. [c] Temperature: 60°C. [d] The reaction was carried out in CH_2Cl_2 with the addition of 5.0 equivalents of EtOH. [e] $[AuClPPh_3]/AgSbF_6$: 2 mol%.

8, and 9). Moreover, we also found that the yield and diastereoselectivity of **8a** decreased if using an electron-rich alkylphosphine as a ligand under otherwise identical conditions (Table 3, entry 10). The best result was obtained by decreasing the amount of $[AuClPPh_3]/AgSbF_6$ to 2 mol%, thus affording the desired product **8a** in 51% overall yield along with 10% yield of by-product **9a** under the standard conditions (Table 3, entry 11). Although much effort has been put into decreasing the amount of by-product **9a** obtained, no satisfactory result could be obtained thus far.

With these optimal results, a wide range of alcohols as the nucleophile were examined (Table 4). The treatment of **7a** with methanol resulted in the formation of spiroketal **8b** in 44% yield and **9a** in 10% yield (Table 4, entry 1). Other alcohols, such as prop-2-en-1-ol, propan-1-ol, propan-2-ol, and butan-1-ol, were also active to the reaction to give the corresponding spiroketals **8** in moderate yields (Table 4, entries 2–5). It is noteworthy that the steric bulkiness of the employed alcohols had a great influence on the diastereoselectivity of **8**. When sterically bulky nucleophiles were utilized, the achieved diastereoselectivities of **8** were relatively lower (Table 4, entries 3 and 4). However, when 2-methylpropan-2-ol or 2,2-dimethylpropan-1-ol were used as the nucleophile, spiroketal **9a** (by-product) was obtained in low yield without the formation of the desired spiroketal **8**, probably because the sterically bulky *tert*-butyl group might block the nucleophilic attack of the alcohols (Table 4, entries 6–8). When 2.0 equivalents of water were added to the reaction mixture of **7a** with 2-methylpropan-2-ol, spiroketal **9a** could be exclusively obtained in 69% yield and the diastereomeric ratio was 5.6:94.4 (Table 4, entry 7).

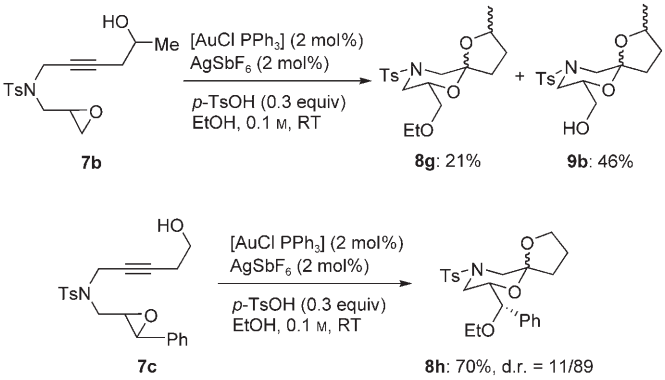
Table 4. The effect of nucleophiles.

7a 8 9a

Entry	ROH	t [h]	8			9a	
			product	yield [%][a]	d.r.[b]	yield [%][a]	d.r.[b]
1	MeOH	24	**8b**	44	12:88	10	–
2	CH_2=$CHCH_2OH$	47	**8c**	52	13:87	trace	–
3	*n*PrOH	41	**8d**	39	33:67	35	3:97
4	*i*PrOH	53	**8e**	32	35:65	23	<1:99
5	*n*BuOH	24.5	**8f**	46[c]	–	trace	–
6	*t*BuOH	65	–	0	–	35	15:85
7[d]	*t*BuOH	29	–	0	–	69	5.6:94.4
8	*t*BuCH$_2$OH	76	–	0	–	17	14:86

[a] Yields of the isolated products. [b] Diastereoselectivities were determined by HPLC. [c] The d.r. was not determined. [d] The amount of H_2O added was 2.0 equivalents.

Further extensions of this gold and Brønsted acid co-catalyzed domino cyclization are shown in Scheme 11. As for the secondary epoxy homopropargylic alcohol **7b**, the corresponding spiroketal **8g** was obtained in only 21% yield and **9b** was formed as the major product in 46% yield under the standard conditions. However, the transformation of epoxy homopropargylic alcohol **7c** into the spiroketal **8h** indicated that the ring-opening of oxirane was facilitated when a 1′,2′-disubstituted epoxide bearing a phenyl group was employed, thus affording the corresponding spiroketal **8h** in 70% yield as a 11:89 diastereomeric mixture (Scheme 11).



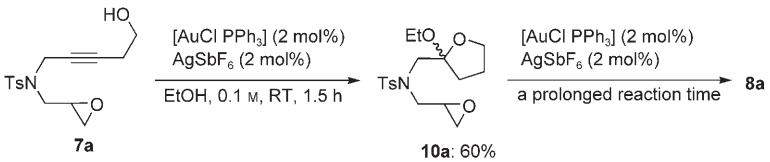
7b 8g: 21% 9b: 46%

7c 8h: 70%, d.r. = 11/89

Scheme 11. Scope of gold-catalyzed cycloisomerization of epoxy homopropargylic alcohols to spiroketals.

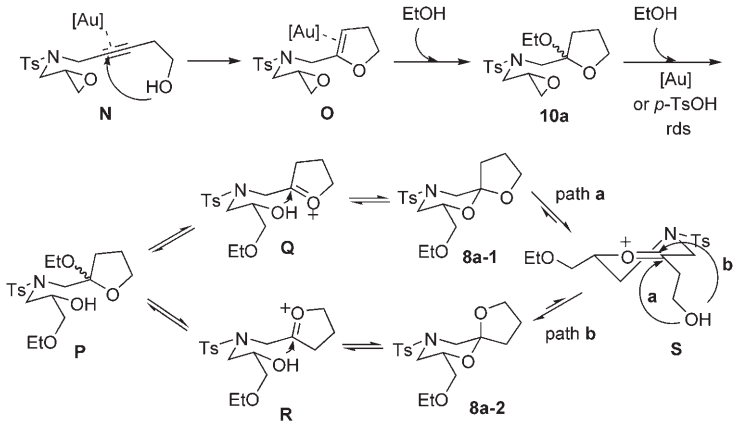
To shed light on the reaction mechanism, we treated the epoxy homopropargylic alcohol **7a** with $[AuClPPh_3]/AgSbF_6$ for 1.5 hours in the absence of a Brønsted acid. The cyclic ketal **10a** was obtained in 60% yield under otherwise identical conditions (Scheme 12). On further prolonging the reaction time, the cyclic ketal **10a** was consumed and the spiroketal **8a** was slowly formed. This result suggests that the spiroketal **8a** might be formed via intermediate **10a** and *p*-TsOH would play an important role in the ring-opening of oxirane.

Based on the assumption that the tandem process took place via 2,3-dihydrofuran **10a** (see Scheme 12), we proposed a plausible reaction mechanism (Scheme 13). The intermediate **O**, obtained through the pathway reported previously,[8] was transformed into ketal **10a** upon nucleophilic attack by an alcohol. The subsequent ring-opening of oxirane catalyzed by *p*-TsOH or a cationic gold catalyst provided intermediate **P**, followed by an intramolecular ketal-exchange that resulted in the formation of intermediate **8a-1** or **8a-2** through intermediate **Q** or **R**. According to the previous reports, it was clear that there should be a heavy pref-



7a 10a: 60%

Scheme 12. Substrate **7a** was subjected to the optimized conditions in the absence of *p*-TsOH



Scheme 13. Proposed mechanism for a tandem process via 2,3-dihydrofuran **10a**.

erence for a C–O bond at the 2-position of a tetrahydrofuran ring to reside in an axial orientation because of the anomeric effect.[17] That is to say, that **8a-2** should be the main diastereoisomer. Moreover, spiroisomerization between **8a-1** and **8a-2** probably can proceed via intermediate **S**. An energetically favorable perpendicular attack by an alcohol could occur from either of two directions, for example, path a or b. The nucleophilic attack through path b would lead to a chair conformation with the newly formed C–O bond axial to the ring. Therefore, path b should be favorable during this spiroisomerization.[18]

A mixture of diastereoisomers (**8a-1**/**8a-2** = 28:72) was placed in a solution of ethanol and the presence of 30 mol% of *p*-TsOH to obtain some details about the spiroisomerization between **8a-1** and **8a-2** in the presence of a Brønsted acid.[19] The diastereomeric ratio decreased to 13.8:86.2 (**8a-1**/**8a-2**) after 8 hours (Figure 1). Further prolonging the reaction time did not affect the diastereoselectivity. Although we proved in Scheme 8 that the transformation of epoxy homopropargylic alcohol **7a** to **10a** was very fast and the intramolecular ketal-exchange could be completed within a short time,[8] the diastereomeric ratio of **8a** was only 17:83 even after 23.5 hours in the presence of *p*-TsOH and gold catalysts (Table 3, entry 11), thus indicating that the ring-opening of oxirane was probably the rate-determining step.

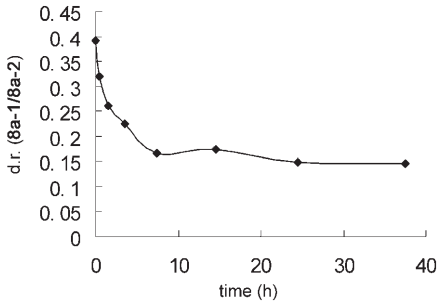


Figure 1. Spiroisomerization of **8a** in the presence of *p*-TsOH.

In conclusion, we have developed a novel gold-catalyzed cycloisomerization of epoxy propargylic/homopropargylic alcohols to ketals/spiroketals under mild conditions. A mechanism probably involving a Meyer–Schuster rearrangement of propargylic alcohols has been proposed in the gold-catalyzed formation of ketals. In addition, the mechanism of the cycloisomerization of epoxy alkyne **1** catalyzed by gold to give the corresponding ketal has been elucidated by exclusive involvement of an oxonium ion intermediate. Moreover, we have demonstrated that the transformation of the epoxy homopropargylic alcohol **7a** to **8a** proceeded through the key intermediate **10a**[20] and that the ring-opening reaction of oxirane was probably the rate-determining step. Further work directed at elucidation of the detailed mechanisms of this process and the application of it to the synthesis of ketal/spiroketal-containing natural products is currently in progress.

Experimental Section

General: Melting points were obtained with a Yanagimoto micro melting-point apparatus and are uncorrected. ^{1}H NMR spectra in solution were recorded on a Bruker AM-300 spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard; the *J* values are given in Hertz (Hz). Mass spectra were recorded with a HP-5989 instrument. All of the compounds reported herein gave satisfactory microanalyses with a Carlo-Erba 1106 analyzer or HRMS analytic data. Commercially obtained reagents were used without further purification. All of these reactions were monitored by TLC with plates coated with GF_{254} silica gel (Huanghai). Flash column chromatography was carried out using 300—400-mesh silica gel at medium pressure.

Typical procedure for the preparation of ketals from epoxy propargylic alcohols in the presence of [AuClPPh$_3$]/AgOTf in DCE at room temperature: [$AuClPPh_3$] (0.009 mmol) and AgOTf (0.009 mmol) were added to a solution of *N*-(4-hydroxy-4-methyl-pent-2-ynyl)-4-methyl-*N*-oxiranylmethylbenzenesulfonamide (**2a**; 96.9 mg, 0.3 mmol) in DCE (3.0 mL) at room temperature. The reaction mixture was stirred for 12 h then diluted with CH_2Cl_2, evaporated under reduced pressure, and purified by flash column chromatography on silica gel using EtOAc/PE (1:6) as the eluent. Compound **3a** was isolated in 51% yield as a colorless solid, which was suitable for analytical purposes.

5-(2-Methylpropenyl)-3-(toluene-4-sulfonyl)-6,8-dioxa-3-aza-bicyclo-[3.2.1]octane (3a): M.p. 124–126 °C; IR (KBr): $\tilde{\nu}$ = 2970, 2894, 2855, 1920, 1679, 1597, 1453, 1348, 1167, 1101, 980 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 1.75 (d, *J* = 0.9 Hz, 3H), 1.83 (s, 3H), 2.44 (s, 3H), 2.55 (d, *J* = 11.4 Hz, 1H), 2.81 (d, *J* = 11.4 Hz, 1H), 3.52 (d, *J* = 11.4 Hz, 1H), 3.60 (d, *J* = 11.4 Hz, 1H), 3.88 (t, *J* = 6.0 Hz, 1H), 4.11 (d, *J* = 6.9 Hz, 1H), 4.59–4.60 (m, 1H), 5.26 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.65 ppm (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 19.4, 21.5, 26.5, 47.8, 52.2, 67.6, 72.1, 104.1, 119.7, 127.5, 129.7, 132.9, 141.8, 143.8 ppm; MS (EI): *m/z* (%): 83 [M^+ −240, 28.9], 168 [M^+ −155, 100.0]; HRMS: *m/z*: calcd for $C_{16}H_{21}NO_4S$: 323.1191; found: 323.1192.

Typical procedure for the preparation of ketals from epoxy homopropargylic alcohols in the presence of [AuClPPh$_3$]/AgSbF$_6$ and *p*-TsOH in ethanol at room temperature: *p*-TsOH (0.09 mmol), [AuClPPh$_3$] (0.006 mmol), and AgSbF$_6$ (0.006 mmol) were added to a solution of *N*-(5-hydroxy-pent-2-ynyl)-4-methyl-*N*-oxiranylmethylbenzenesulfonamide (**7a**; 92.7 mg, 0.3 mmol) in ethanol (3 mL) at room temperature. The reaction mixture was stirred for 23.5 h, diluted with CH_2Cl_2, evaporated under reduced pressure, and purified by flash column chromatography on silica gel using EtOAc/petroleum ether (1:6) as the eluent. Compound **8a** was isolated in 51% yield as a colorless oil, which was suitable for analytical purposes.

7-Ethoxymethyl-9-(toluene-4-sulfonyl)-1,6-dioxa-9-aza-spiro[4.5]decane (8a): IR (KBr): $\tilde{\nu}$ = 2976, 2925, 2879, 1920, 1598, 1455, 1350, 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) (two diastereoisomers): δ = 1.16 (and 1.17) (t, J = 6.9 Hz, 3H), 1.68–1.75 (m, 1H), 1.86–2.08 (m, 3H), 2.14–2.31 (m, 1H), 2.44 (s, 3H), 2.47 (d, J = 11.4 Hz, 1H), 3.35–3.70 (m, 6H), 3.88–4.24 (m, 3H), 7.35 (d, J = 8.1 Hz, 2H), 7.65 ppm (d, J = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) (two diastereoisomers): δ = 14.9, 15.0, 21.4, 21.4, 23.4, 24.5, 33.3, 35.7, 46.9, 47.3, 50.7, 52.1, 66.8, 66.9, 67.6, 67.9, 68.9, 70.86, 70.93, 71.2, 103.6, 105.4, 127.7, 127.8, 129.6, 129.7, 131.9, 132.2, 143.6, 143.9 ppm; MS (EI): *m/z* (%): 114 [M^+−241, 72.3], 155 [M^+−200, 17.2], 200 [M^+−155, 100.0]; HRMS: *m/z*: calcd for $C_{17}H_{25}NO_5S$: 355.1453; found: 355.1460.

Acknowledgements

We thank the Shanghai Municipal Committee of Science and Technology (04 JC14083, 06XD14005) and the National Natural Science Foundation of China for financial support (20472096, 203900502, 20672127, and 20732008).

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Received: December 10, 2007
Revised: May 13, 2008
Published online: July 4, 2007

