Gold(I)-Catalyzed Rearrangement of Alkynyloxiranes: A Mild Access to Divinyl Ketones
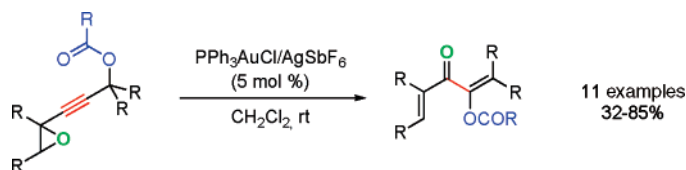
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ABSTRACT

Acyloxylated divinyl ketones are conveniently formed by a new gold(I)-catalyzed rearrangement of (3-acyloxyprop-1-ynyl)oxiranes.

Gold catalysis is increasingly gaining interest in organic chemistry[1] due to the efficiency, the mildness, and the peculiar properties associated with gold atoms.[2] Among these properties, alkynophilicity of gold salts or complexes[3] already led to numerous applications, usually based on nucleophilic addition to an intermediate alkyne−gold complex. In contrast, oxophilicity of gold species was far less investigated, and only a few examples were reported in the literature mainly based on Lewis acid activation of carbonyl compounds.[1,4] We thus wondered if such properties could be combined, leading to new chemistry promoted by gold salts or complexes.

Having an acetylenic moiety and a poorly nucleophilic oxygen atom within the same molecule could be achieved with α- and β-alkynyl epoxides. Such compounds are known to rearrange into furans in the presence of gold trichloride with modest to excellent yields (Scheme 1).[5–7] With alkyno-

Scheme 1. Known Rearrangements of Alkynyloxiranes to Furans and Proposed Intermediate for These Reactions

philicity in mind, oxonium ions resulting from internal nucleophilic attack of the oxirane oxygen atom on acetylene−

(1) For recent reviews on gold chemistry, see: (a) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180−3211. (b) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333−346. (c) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896−7936.
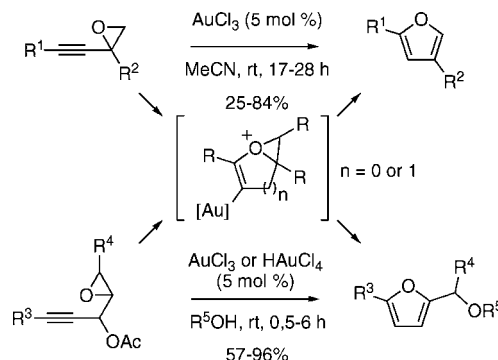
(2) (a) Gorin, D. J.; Toste, D. *Nature* **2007**, *446*, 395−403. (b) Pyykö, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 4412−4456. (c) Bagus, P. S.; Lee, Y. S.; Pitzer, K. S. *Chem. Phys. Lett.* **1975**, *33*, 408−411.

(3) Hashmi, A. S. K. *Gold Bull.* **2003**, *36*, 3−9.

(4) (a) Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 6405−6406. (b) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1415−1418. (c) Georgy, M.; Boucard, V.; Campagne, J.-M. *J. Am. Chem. Soc.* **2005**, *127*, 14180−14181. (d) Jung, H. H.; Floreancig, P. E. *Org. Lett.* **2006**, *8*, 1949−1951. (e) Jung, H. H.; Floreancig, P. E. *J. Org. Chem.* **2007**, *72*, 7359−7366. (f) Lin, C.-C.; Teng, T.-M.; Odedra, A.; Liu, R.-S. *J. Am. Chem. Soc.* **2007**, *129*, 3798−3799. (g) Yamamoto, Y. *J. Org. Chem.* **2007**, *72*, 7817−7831.

(5) Hashmi, A. S. K.; Pradipta, S. *Adv. Synth. Catal.* **2004**, *346*, 432−438.

(6) Shu, X.-Z.; Liu, X.-Y.; Xiao, H.-Q.; Ji, K.-G.; Guo, L.-N.; Qi, C.-Z.; Liang, Y.-M. *Adv. Synth. Catal.* **2007**, *349*, 2493−2498.

gold π-complex were proposed as intermediate in these furan formations. However, a double activation of the acetylene and the oxygen atom could also be responsible for this transformation, with allenic species as intermediates.

On these bases, we thus investigated the behavior of various alkynyl oxiranes, trying to reveal the presence or not of allenic intermediates as a first objective and trying to take benefit of them by trapping as a second objective. To do so, we envisaged placing a nucleophile within the molecule at the right position to react with any intermediate allene, which could be formed by double activation of the acetylene and the oxirane oxygen atom (Scheme 2).[8] Due to

Scheme 2. Hypothesis for Au-Catalyzed Conversion of Alkynyloxiranes to Heterocycles or Rearranged Systems
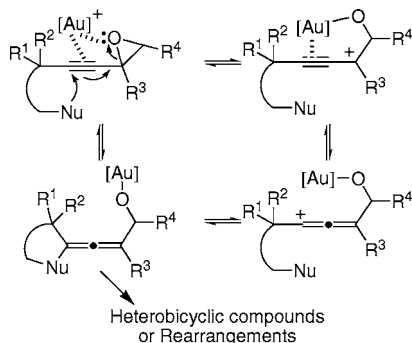
precedents in the literature involving propargyl acetate and related esters,[9] we selected an acyloxy group at the propargylic position as the first nucleophile investigated. We report here that such functionalized alkynyl oxiranes, i.e., (3-acyloxyprop-1-ynyl)oxiranes,[10] indeed react in the presence of gold catalyst, leading to functionalized divinyl ketones in high yields.

Various (3-hydroxyprop-1-ynyl)oxiranes **1a–l** were conveniently produced by addition of the lithium acetylide derived from various enynes to aldehydes or ketones. The in situ formed propargyl alcoholates could be either directly acylated by further addition of acyl anhydride or chloride or simply hydrolyzed. In the latter, the isolated alcohol was then acylated in classical conditions. For the preparation of **1d**, the required alcohol was prepared by a Sonogashira

(7) Gold(I)-catalyzed cascade reactions involving cyclization of δ-alkynyl epoxides and further water or alcohol addition were also recently described. See: Dai, L.-Z.; Qi, M.-J.; Shi, Y.-L.; Liu, X.-G.; Shi, M. *Org. Lett.* **2007**, *9*, 3191–3194.

(8) Hashmi has nevertheless shown that the presence of primary alcohol on the substrate did not affect the formation of furans (Scheme 1, R^1 = −(CH$_2$)$_4$OH).[5] Therefore, in this case, the nucleophilic alcohol seems to be too far to interact with the alkynyloxirane part.

(9) (a) Marion, N.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2750–2752. (b) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442–1443. (c) Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *127*, 12614–14615. (d) Marion, N.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2006**, *46*, 3647–3650. (e) Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802–5803. (f) Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546–2547.

(10) (3-acyloxyprop-1-ynyl)oxiranes are known to rearrange to furans in the presence of SmI$_2$/Pd(II) via allene intermediates: (a) Aurrecoechea, J. M.; Pérez, E.; Solay, M. *J. Org. Chem.* **2001**, *66*, 564–569. (b) Aurrecoechea, J. M.; Pérez, E. *Tetrahedron Lett.* **2001**, *42*, 3839–3841. (c) Aurrecoechea, J. M.; Pérez, E. *Tetrahedron Lett.* **2003**, *44*, 3263–3266.

coupling reaction. The resulting acyloxylated enynes were then epoxidized upon treatment with *m*-chloroperbenzoic acid (*m*-CPBA). The overall yields of this two- to three-step sequence were routinely higher than 50%.

In order to find the more appropriate conditions for the reaction of such substrates, we applied various conditions and gold catalysts to the simplest acetoxylated alkynyl oxirane **1a** (Table 1). A rapid catalyst screening revealed

Table 1. Screening of Reaction Conditions for the Transformation of Acetoxylated Alkynyl Oxirane **1a**
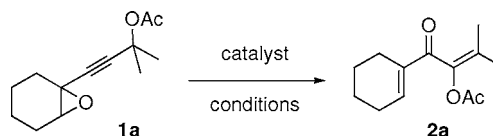
entry	catalyst (mol %)	conditions^a	time (h)	yield^b (%)
1	AuCl (5)	dry CH$_2$Cl$_2$, rt	16	c
2	PPh$_3$AuCl (5)	dry CH$_2$Cl$_2$, rt	16	c
3	AuCl$_3$ (5)	dry CH$_2$Cl$_2$, rt	16	14
4	PPh$_3$AuCl/AgSbF$_6$ (5)	dry CH$_2$Cl$_2$, rt	0.1	88^d
5	AgSbF$_6$ (5)	dry CH$_2$Cl$_2$, rt	0.1	49
6	AgCl (5)	dry CH$_2$Cl$_2$, rt	16	c

^{a} Reactions run under argon, $c = 0.1$ mol/L. ^{b} Yields of **2a** was calculated by ^{1}H NMR relative to an internal standard (hexamethylbenzene). ^{c} No conversion. ^{d} 70% of isolated yield.

that in situ generated cationic gold(I) species were the most effective.

Gold chloride, alone or as its triphenylphosphine complex, did not promote any transformation, whatever the solvent and the amount of catalyst, and the starting material **1a** was recovered even after prolonged contact time (entries 1 and 2). The more electrophilic gold trichloride proved to be slightly more effective in dichloromethane, cleanly converting **1a** into a new compound, although in low yield (entry 3). Physical data of the new compound so formed showed a complete reorganization of the carbon skeleton, with the concomitant presence of two vinyl motifs and a conjugated ketone. Therefore, the *single* compound formed in these conditions corresponded to a rearranged product, the acetoxyvinyl vinyl ketone **2a** (see the proposed mechanism below). Switching to the even more electrophilic cationic gold(I) produced by premixing triphenylphosphinogold chloride and a silver salt led to a complete conversion and provide the same compound in high yield (entry 4). Interestingly enough, control experiments with silver salts revealed that the highly electrophilic silver hexafluoroantimonate also promoted the same reaction but to a lesser extent (entry 5).[11]

In order to study the scope of this new formation of divinyl ketones, various representative acyloxyalkynyl oxiranes **1b–j** were then submitted to the above conditions (Table 2). The role of the nucleophilic acyloxy group was examined with a series of esters **1a–c**. The bulky pivalate **1b** gave a significantly higher isolated yield of divinyl ketone **2b** than acetate **1a** (entry 2 vs 1). As expected, the benzoate **1c**,

Table 2. Scope of the Gold-Catalyzed Rearrangement

entry	alkynyloxiranes	time (h)	divinyl ketones	yield (%)[a]
1	**1a**, R= Ac	0.1	**2a**	70
2	**1b**, R= Piv	0.1	**2b**	85
3	**1c**, R = Bz	1	**2c**	32
4	**1d**	0.1	**2d**	77
5	**1e**	0.1	**2e**	73
6	**1f**	0.5	**2f**	64
7	**1g** dr 50/50	0.1	**2g** E/Z 50/50	72
8	**1h** dr 50/50	0.1	**2h** E/Z 50/50	40
9	**1i** dr 50/50	0.1	**2i** Z only	48
10	**1j** dr 50/50	0.1	**2j** Z only	81

[a] Isolated yields.

(entries 7 and 8). Comparatively, the presence of a secondary acetoxy and an aryl substituent at the oxiranyl end lowered the stability of the rearranged products and thus the yields (entry 8 and **1i** below). Surprisingly, the derivatives **1i,j**, also obtained as a nonseparable 1:1 mixture of diastereoisomers, gave the expected acetoxydivinyl ketones but as *single* stereoisomers **2i** and **2j**, respectively.[12] The stereochemistry of these products was clearly established with NOESY experiments. It is noteworthy that no trace of furans was observed during theses reactions.[13]

As the reaction was too fast to detect any intermediate,[12] we look at stereoselectivity issue by studying the Au-catalyzed rearrangement of (−)-menthone derivatives.

Nucleophilic additions to (−)-menthone provided two diastereoisomers, which can usually be separated, the major one corresponding to equatorial addition.[14] Indeed, the addition of the lithium acetylide derived from 3-methylbutenyne provided a 70/30 mixture of diastereoisomers, the equatorial one being the major one. After separation, the minor isomer was acetylated[15] and then epoxidized, yielding a nonseparable 1/1 mixture of epoxide diastereoisomers **1k**. Interestingly, this mixture placed in the rearrangement conditions gave the expected acetoxydivinyl ketones **2k** but not with the same diastereoisomeric ratio (60/40; Scheme 3), suggesting some stereoselectivity in the rearrangement.

Scheme 3. Au-Catalyzed Rearrangement of Alkynyloxiranes Derived from (−)-Menthone and Isomerization of Its Products
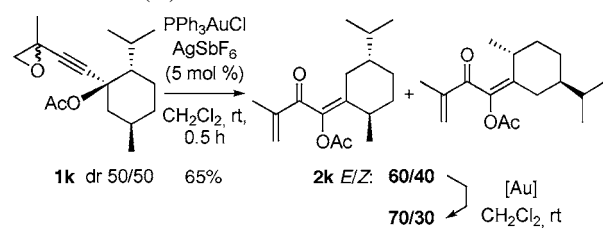
However, control experiments revealed that the mixture of products slowly evolved toward a 70/30 mixture when replaced in the reaction conditions. Therefore, the acetoxydivinyl ketones so obtained are equilibrating in the reaction conditions, and in this case, the bulkiness of the menthone moiety seemed to slow an easy equilibrium between *E* and *Z* stereoisomers. These results clearly showed that the *E/Z* ratio observed in the Au-catalyzed formation of acyloxydi-

having a conjugated and thus less nucleophilic carbonyl group, was clearly less effective since only 32% yield of **2c** were isolated after a longer reaction time (entry 3). Varying the alkyl substituents at either the oxirane or the acyloxy groups did not much influence the reaction course and yields (entries 4−6). The nonsymmetrical derivatives **1g,h** obtained as a nonseparable 1/1 mixture of diastereoisomers gave a mixture of stereoisomers **2g,h** at the acetoxyvinyl moiety with the same diastereomeric ratio as their progenitors

(11) Ag salts are known to promote rearrangement of propargyl acetoxy derivatives: (a) Benn, W. R. *J. Org. Chem.* **1968**, *33*, 3113−3118. (b) Saimoto, H.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1981**, *103*, 4975−4977. (c) Saimoto, H.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3078−3087. (d) Saimoto, H.; Yukari, K.; Hiyama, T. *Tetrahedron Lett.* **1986**, *27*, 1607−1610. (e) Saimoto, H.; Yasui, M.; Ohrai, S-i.; Oikawa, H.; Yokoyama, K.; Shigemasa, Y. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 279−284. (f) Bluthe, N.; Gore, J.; Malacria, M. *Tetrahedron* **1986**, *42*, 1333−1344.

(12) Rearrangement reaction of **1j** run in CD₂Cl₂ at −70 °C and monitored by ¹H NMR did not show the presence of intermediates of the *Z* isomer **2j**. However, the faster conversion of one of the two isomers of **1j** was observed.

(13) Secondary less activated ester (R¹ = R² = −(CH₂)₄−, R³ = H, R⁴ = C₅H₁₁) furnished poor yield of divinyl ketone (10 %) but again no trace of furane was observed even after a long contact time.

(14) (a) Le Goanvic, D.; Holler, M.; Pale, P. *Tetrahedron: Asymmetry* **2002**, *13*, 119−121. (b) Xu, Q.; Wang, G.; Pan, X. Chan, A. S. C. *Tetrahedron: Asymmetry* **2001**, *12*, 381−385. (c) Koning, B.; Buter, J.; Hulst, R.; Stroetinga, R.; Kellogg, R. M. *Eur. J. Org. Chem.* **2000**, 2735−2743.

(15) All of the classical methods failed to acetylate the major isomer, and only *n*-BuLi/Ac₂O gave **1k** in good yield. See the Supporting Information.

vinyl ketones only reflected the thermodynamic stability of the compounds.

The Au-catalyzed rearrangement of (3-acyloxyprop-1-ynyl)oxiranes to acyloxydivinyl ketones described here obviously involved a cascade of events (Scheme 4). Gold

Scheme 4. Proposed Mechanism for Au-Catalyzed Rearrangement of Acyloxypropargyloxiranes to Acyloxydivinyl Ketones
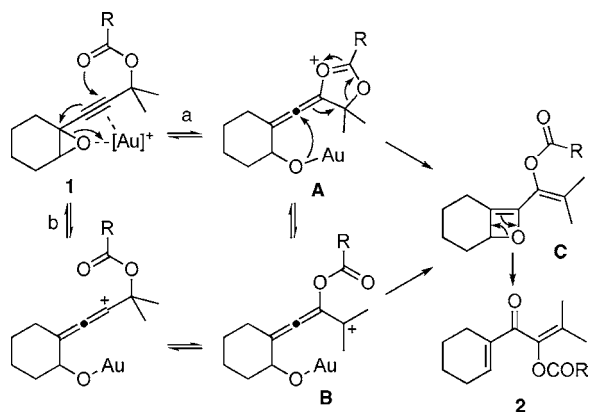
interaction with both the alkynyl and oxirane moieties might lead to an allenic alcoholate, inducing migration of the adjacent acyloxy group.[8,16] This transformation could be either a step-by-step or a concerted process (route b or a, respectively). The allenic alcoholate **A** or **B** could then cyclized to an oxete **C**, probably through gold assistance. As already proposed for Ag- or Au-catalyzed cyclizations of alkynyl aldehydes and ketones,[17] cycloreversion of oxete would then occurred, furnishing the acyloxydivinyl ketones. Although allenes are probable intermediates in this rearrangement, it is difficult to assess stereoselectivity since the products formed isomerize in the reaction conditions.

In conclusion, we have reported *for the first time* an original catalytic approach to functionalized divinyl ketones[18] through an Au-catalyzed rearrangement of (3-acyloxyprop-1-ynyl)oxiranes. The reaction proceeds efficiently under mild conditions with commercially available catalysts. Further work is now underway in our laboratory to broaden the scope of this reaction and better understand its mechanism, as well as to continue to explore gold catalysts in organic synthesis.

Supporting Information Available: Selected experimental procedures and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) (a) Kim, J. T.; Kel'in A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2003**, *42*, 98−101. (b) Schwier, T.; Sromek, A. W.; Yap, D. M. L.; Chernyak, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 9868−9878. (c) Dudnik, A. S.; Sromek, A. W.; Rubina, M.; Kim, J. T.; Kel'in A. V.; Gevorgyan, V. *J. Am. Chem. Soc.* **2008**, *130*, 1440−1452.

(17) (a) Rhee, J. U.; Krische, M. J. *Org. Lett.* **2005**, *7*, 2493−2495. (b) Jin, T.; Yamamoto, Y. *Org. Lett.* **2007**, *9*, 5259−5262.

(18) Such type of substrates can potentially lead to the formation of the corresponding useful cyclopentenones via the Nazarov reaction. For reviews, see: (a) Pellissier, H. *Tetrahedron* **2005**, *61*, 6479−6510. (b) Habermas, K. L.; Denmark, S. E. *Org. React.* **1994**, *45*, 1−158, 11971.