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Rearrangement of Alkynyl Sulfoxides Catalyzed by Gold(I) Complexes

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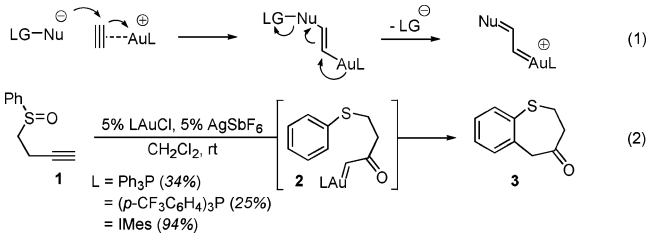
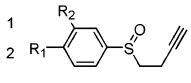
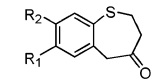
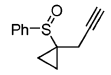
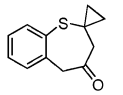
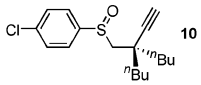
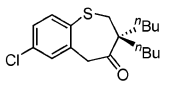
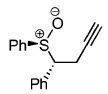
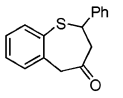
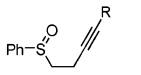
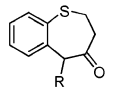
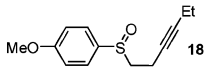
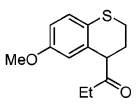
Recently, gold−carbenoid species have been proposed as intermediates in gold-catalyzed enyne rearrangements.[1] Additionally, the reaction of gold complexes with propargyl esters has been developed as an alternative approach to metal carbenoids capable of effecting olefin cyclopropanation;[2,3] however, to date, the reaction of electrophilic metals with alkynes has not been amenable to the generation of α-carbonyl carbenoids analogous to those traditionally formed in situ from transition-metal-catalyzed decomposition of α-diazocarbonyl compounds.[4,5] We recently described a rearrangement of homopropargyl azides to pyrroles in which gold(I) promotes addition of a leaving-group-bearing nucleophile (Nu = N) to an acetylene and subsequent loss of the leaving group (LG = N_2) (eq 1).[6] On the basis of this reactivity principle, we envisioned that α-carbonyl metal carbenoids could be generated from alkynes via a gold(I)-catalyzed rearrangement in which sulfoxides serve the role of nucleophile (Nu = O) and latent leaving group (LG = R_2S).



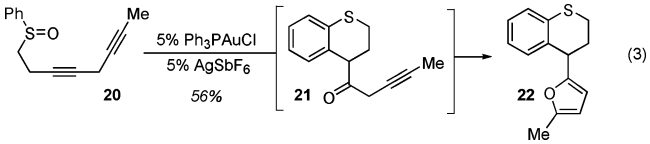
In order to explore this hypothesis, homopropargyl sulfoxide **1** was treated with 5 mol % of $Ph_3PAuCl/AgSbF_6$ in dichloromethane. Gratifyingly, this reaction produced 1-benzothiepin-4-one **3**, presumably via the desired α-carbonyl carbenoid intermediate **2**, albeit in only 34% yield (eq 2). While switching to an electron-deficient phosphine ligand resulted in a decreased yield, the use of an N-heterocyclic carbene (IMes) ligated gold(I) complex as catalyst dramatically improved the yield of ketone **3** to 94%. Under these conditions, a wide range of homopropargyl arylsulfoxides underwent the gold-catalyzed rearrangement to benzothiepinones (Table 1). The reaction proceeded smoothly when the aryl group of the sulfoxide was substituted with electron-withdrawing (entry 1) or electron-donating groups (entry 2), although the latter underwent the gold-catalyzed rearrangement with increased yield. Substitution at the homopropargyl (entry 3) and propargyl (entry 4) position of the sulfoxide is tolerated; however, the latter required slightly elevated temperatures to afford **11** in 76% yield. Notably, one diastereomer (illustrated) of phenyl-substituted propargyl sulfoxide (±)-**12** was significantly more reactive than the other in the gold(I)-catalyzed rearrangement, affording **13** in 94% yield (entry 5).[7]

The triphenylphosphinegold(I)-catalyzed reaction of a sulfoxide (**14**) containing an alkyne substituted with an electron-deficient aryl group[8] (entry 6) or an ester (entry 7) produced the anticipated benzothiepinones **15** and **17** in 63 and 91% yield, respectively. In sharp contrast, the gold(I)-catalyzed reaction of alkyl-substituted alkyne **18** afforded benzothiopine **19** in 64% yield (entry 8).[9] On the basis of this reaction, 1,4-diyne **20** was converted to furan **22** in 56% yield by a gold(I)-catalyzed sulfoxide rearrangement and subsequent cycloisomerization of propargyl ketone **21** (eq 3).[10]

Table 1. Au(I)-Catalyzed Rearrangement of Homopropargyl Sulfoxides

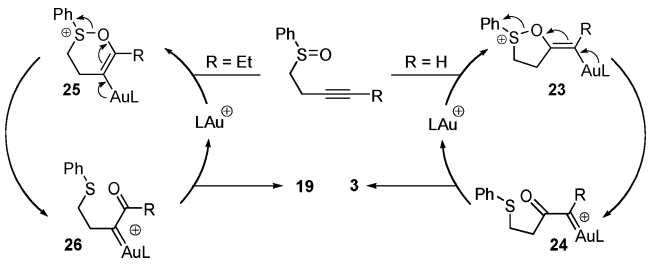
entry	sulfoxide		conditions[a]	product		yield
1		**4** R_1=NO_2, R_2=H	A		**5**	71%
2		**6** R_1=R_2=OMe	A		**7**	87%
3		**8**	A		**9**	71%
4		**10**	B		**11**	76%[b]
5		(±)-**12**	A		**13**	94%
6		**14** R=4-NO_2-C_6H_4	B		**15**	63%
7		**16** R=CO_2Et	A		**17**	91%[c]
8		**18**	B		**19**	64%

[a] Conditions: (A) sulfoxide (0.2 M in CH_2Cl_2), 5% IMesAuCl, 5% $AgSbF_6$, rt; (B) sulfoxide (0.2 M in CH_2Cl_2), 5% Ph_3PAuCl, 5% $AgSbF_6$, rt. [b] At 60 °C in dichloroethane with 5 Å sieves. [c] With 5 Å sieves.



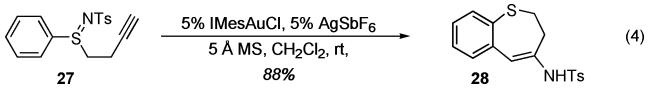
A proposed mechanism for the gold-catalyzed rearrangement of homopropargyl sulfoxides is detailed in Scheme 1. Coordination of cationic gold(I) to the alkyne induces nucleophilic addition of the sulfoxide oxygen. When the alkyne is terminal or substituted with an electron-withdrawing group, 5-*exo*-dig cyclization of the nucleophile onto the internal carbon of the alkyne is favored, yielding intermediate **23**. On the other hand, when the alkyne is substituted with an alkyl group, **25** is generated by a 6-*endo*-dig cyclization. After cyclization, gold(I)-assisted sulfide release pro-

Scheme 1. Proposed Mechanism of Au-Catalyzed Rearrangement

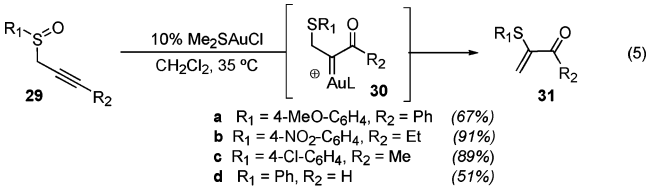


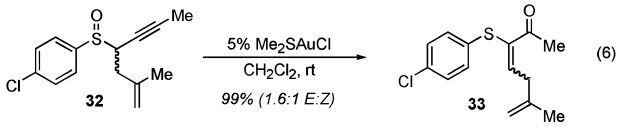
10.1021/ja070789e CCC: $37.00

duces gold−carbenoid intermediate **24** or **26**. The observation that gold(I)-catalyzed rearrangement of sulfimine **27** proceeded in 88% yield to furnish *N*-tosyl enamine **28** (eq 4) is consistent with the proposal that the carbonyl oxygen in the product is transferred from the sulfoxide. Finally, carbenoids **24** and **26** undergo intramolecular Friedel−Crafts alkylation to produce the observed products and liberate the cationic gold(I) catalyst.[11−13]



Gold(I) complexes also catalyze the conversion of propargyl sulfoxides to α-thioenones in high yields (eqs 5 and 6).[14] In this case, (dimethylsulfide)gold(I) chloride proved to be the optimal catalyst,[15] affording enones **31** from propargyl sulfoxides **29** with excellent tolerance for substitution on the alkyne and the sulfoxide. Additionally, secondary and tertiary propargyl sulfoxides react under these conditions to provide trisubstituted (eq 6) and tetrasubstituted alkenes.[16] For example, sulfoxide **32** underwent gold(I)-catalyzed rearrangement to enone **33** in preference to cycloisomerization of the 1,5-enyne.[1d] In analogy to the mechanism described in Scheme 1, this rearrangement is postulated to proceed through gold(I)-promoted sequential 5-*endo*-dig cyclization/cleavage of the S−O bond leading to gold(I)−carbenoid intermediate **30** which undergoes a 1,2-sulfide shift.[17,18]





In conclusion, we have developed a series of gold(I)-catalyzed rearrangements of alkynyl sulfoxides to benzothiepinones, benzothiopines, or α-thioenones. The reactions are postulated to proceed via an α-carbonyl gold−carbenoid intermediate formed through oxygen atom transfer from the sulfoxide. Importantly, these intermediates show reactivity (electrophilic aromatic substitution, 1,2-thio migration) analogous to those generated from metal-promoted decomposition of α-diazocarbonyl compounds. In a broader sense, the reactions reported herein provide an entry into metal carbenoids and support the importance of these intermediates in metal-promoted rearrangement of alkynes. Further investigation into the mechanism of these transformations and the nature of the intermediates is ongoing.

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Supporting Information Available: Experimental procedures and compound characterization data (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(1) For recent examples involving Au−carbenoid intermediates in the cycloisomerization of enynes, see: (a) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402. (b) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654. (c) Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858. (d) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442. (e) López, S.; Herrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 6029. (f) Horino, Y.; Luzung, M. R.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 11364. (g) Lee, J. H.; Toste, F. D. *Angew. Chem., Int. Ed.* **2007**, *46*, 912. For a review, see: (h) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395.

(2) For the reactions of Au−carbenoid intermediates generated from propargyl esters, see: (a) Miki, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **2003**, *68*, 8505. (b) Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546. (c) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002. (d) Ohe, K.; Fujita, M.; Matsumoto, H.; Tai, Y.; Miki, K. *J. Am. Chem. Soc.* **2006**, *128*, 9270. (e) Gorin, D. J.; Dube, P.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 14480.

(3) For generation and reactions of furylcarbenoid intermediates, see: (a) Miki, K.; Nishino, F.; Ohe, K.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 5260. (b) Miki, K.; Yokoi, T.; Nishino, F.; Kato, Y.; Washitake, Y.; Ohe, K.; Uemura, S. *J. Org. Chem.* **2004**, *69*, 1557. For an excellent review, see: (c) Miki, K.; Uemura, S.; Ohe, K. *Chem. Lett.* **2005**, *34*, 1068.

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(5) For gold-catalyzed reaction of α-diazoesters, see: (a) Fructos, M. R.; Belderrain, T. R.; de Frémont, P.; Scott, N. M.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 5284. (b) Fructos, M. R.; de Frémont, P.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. *Organometallics* **2006**, *25*, 2237.

(6) Gorin, D. J.; Davis, N. R.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 11260.

(7) The less reactive diastereomer of (±)-**12** (characterized by X-ray crystallography; see Supporting Information) proceeded to only 15% conversion after reaction at 35 °C for 24 h.

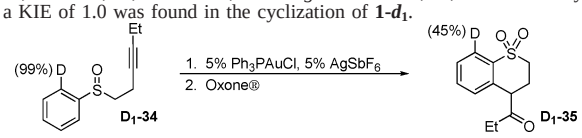
(8) Under all conditions examined, the unsubstituted aryl derivative produced only a trace of the desired benzothiepinones.

(9) The sulfone derivative of **19** was characterized by X-ray crystallography (see Supporting Information).

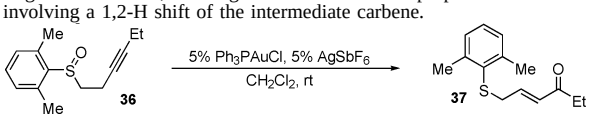
(10) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285.

(11) (a) Padwa, A.; Austin, D. J.; Price, A. T.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Tran, A. *J. Am. Chem. Soc.* **1993**, *115*, 8669. (b) Etkin, N.; Babu, S. D.; Fooks, C. J.; Durst, T. *J. Org. Chem.* **1990**, *55*, 1093.

(12) An inverse secondary kinetic isotope effect of 0.96 was observed for deuterated **34-*d*$_1$.** This is consistent with previously measured kinetic isotope effects for Friedel−Crafts alkylations; for example, see: Nakane, R.; Kurihara, O.; Takematsu, A. *J. Org. Chem.* **1971**, *36*, 2753. Similarly, a KIE of 1.0 was found in the cyclization of **1-*d*$_1$**.

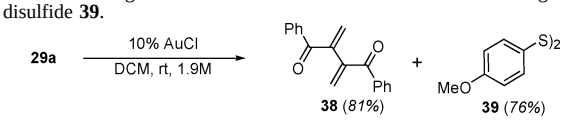


(13) Homopropargyl sulfoxide **36**, in which the *ortho*-positions of the aromatic ring are substituted, rearranged to enone **37** via a proposed mechanism involving a 1,2-H shift of the intermediate carbene.



(14) For the rearrangements of aryl propargylsulfoxides, see: (a) Majumdar, K. C.; Thyagarajan, B. S. *J. Chem. Soc., Chem. Commun.* **1972**, 83. (b) Baudin, J.-B.; Julia, S. A.; Lorne, R. *Synlett* **1991**, 509. (c) Majumdar, K. C.; Ghosh, S. K. *Tetrahedron Lett.* **2002**, *43*, 2123.

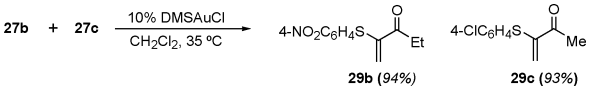
(15) The use of cationic phosphinegold(I) complexes as catalysts led to drastically reduced yields. The use of AuCl as a catalyst for reaction conducted at high concentrations led to formation of dimer **38** along with disulfide **39**.



(16) See Supporting Information for additional examples.

(17) For 1,2-thio migration of Rh(II) carbenes, see: Xu, F.; Shi, W.; Wang, J. *J. Org. Chem.* **2005**, *70*, 4191.

(18) The lack of sulfide cross-over in the gold-catalyzed rearrangement of **27b** and **27c** is consistent with an intramolecular sulfide shift.



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