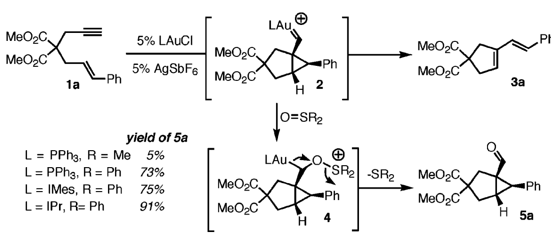
J|A|C|S
COMMUNICATIONS

Published on Web 04/14/2007

Gold(I)-Catalyzed Oxidative Rearrangements

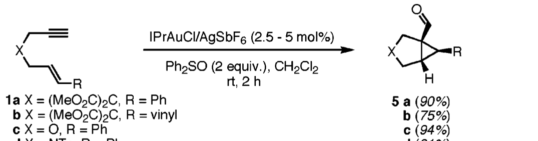
Cole A. Witham, Pablo Mauleón, Nathan D. Shapiro, Benjamin D. Sherry, and F. Dean Toste*
Department of Chemistry, University of California, Berkeley, California 94720
Received February 20, 2007; E-mail: fdtoste@berkeley.edu

Intermediates possessing carbenoid character have recently been postulated in a number of gold-catalyzed rearrangements.[1] In accord with this proposal, cyclopropane adducts are formed from the intermolecular reaction of the proposed gold(I)−carbenoid intermediates with olefins.[2] To further examine the nature of these intermediates, we sought to explore their reactivity with reagents previously described as reactive toward metal carbenes. In this context, we were intrigued by the possibility that the electrophilic gold(I)−carbenoid intermediate might undergo oxygen atom transfer from a nucleophilic oxidant. While catalytic reactions involving oxygen atom transfer to metal carbenoids are rare,[3] reports of oxygen atom transfer from sulfoxides to carbenes[4] and metal carbenoids[5] led us to investigate the reactivity of proposed gold(I)−carbenoid intermediates with these reagents. Herein we report the integration of these studies into the development of a series of gold(I)-catalyzed oxidative transformations.

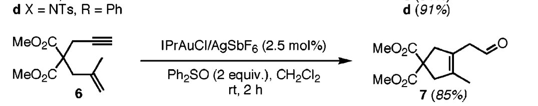


(1)

Our preliminary investigation focused on intercepting cyclopropane gold(I)−carbenoid intermediate **2** proposed in the cycloisomerization of 1,6-enyne **1a** to diene **3a** (eq 1).[1a] The initial attempt employing cationic triphenylphosphinegold(I) as the catalyst and dimethylsulfoxide as the oxidant, in methylene chloride at room temperature, produced only 5% of the desired aldehyde **5a**, along with unreacted starting material **1a**. In sharp contrast, replacing DMSO with diphenylsulfoxide generated aldehyde **5a** in 73% yield without any competitive formation of **3a**.[6] This yield was further improved to 91% by employing the N-heterocycliccarbene gold(I) complex, IPrAuCl,[7] as the catalyst. Under these reaction conditions, a variety of 1,6-enynes underwent gold(I)-catalyzed oxidative cyclization to afford either cyclopropyl aldehydes[8] (eq 2) or



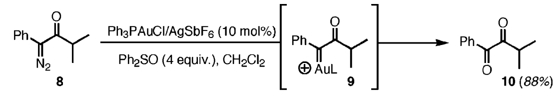
(2)



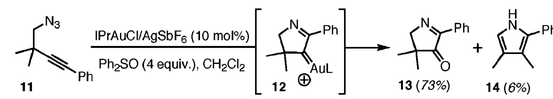
(3)

cyclopentenyl aldehyde **7**[2d] (eq 3). Notably, in all cases intermolecular reaction of the gold−carbenoid intermediate with sulfoxide occurred selectively over skeletal rearrangement to the diene.[9]

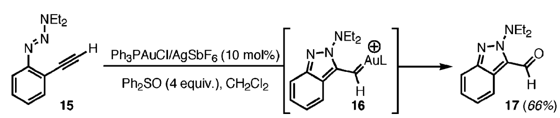
To obtain additional support for the carbenoid nature of the gold(I) species in these reactions, we sought to examine the reactivity of sulfoxides with a gold(I) intermediate generated by methods typically employed for the in situ formation of metal carbenoids. Thus, gold(I)-catalyzed reaction of α-diazoketone **8** afforded 1,2-diketone **10** in 88% yield (eq 4). On the basis of previously reported gold(I)-catalyzed reactions of α-diazoesters,[10] we postulate that oxygen atom transfer from diphenylsulfoxide to gold(I)−carbenoid **9** is the most likely mechanism for this transformation.



(4)

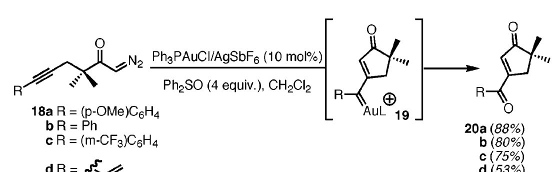


(5)

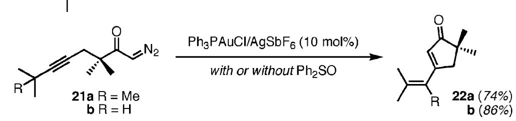


(6)

With these results in hand, the application of sulfoxides as oxidizing agents in other transformations involving postulated gold(I)−carbenoid intermediates was examined. For example, we proposed a gold(I)−carbenoid intermediate in the rearrangement of homopropargyl azides to pyrroles.[1e] In accord with this hypothesis, homopropargyl azide **11** underwent gold(I)-catalyzed oxidative rearrangement to furnish pyrrolone **13** via intermolecular oxygen atom transfer from diphenylsulfoxide to carbenoid **12** (eq 5). The use of the N-heterocycliccarbene gold(I) complex as the catalyst proved essential for suppressing competitive 1,2-methyl shift. The triphenylphosphinegold(I)-catalyzed reaction produced pyrrole **14** (60%) as the major product accompanied by 31% of pyrrolone **13**. Additionally, gold(I)-catalyzed oxidative cyclization of the triazene **15** produced aldehyde **17** in 66% yield through oxygen atom transfer to carbenoid intermediate **16** (eq 6).[11]



(7)

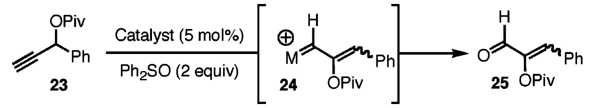


(8)

In addition to validating the intermediacy of previously proposed gold(I)−carbenoid intermediates, we envisioned that sulfoxides could be employed to develop unprecedented oxidative transformations involving gold(I)−carbenoid intermediates. For example, we hypothesized that gold(I)−carbenoid intermediate **19** could be generated through gold(I)-induced intramolecular 5-*exo*-dig nucleophilic addition of a diazoketone onto the pendent alkyne,[12] followed by loss of dinitrogen.[13] Accordingly, in the presence of

10.1021/ja071231+ CCC: $37.00

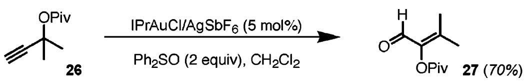
Table 1. Oxidative Rearrangement of Propargyl Esters



entry	catalyst	solvent	temp	time	yield[a]	Z/E
1	$Ph_3PAuCl/AgSbF_6$	CH_2Cl_2	25 °C	1.5 h	72%	75:25
2	$IPrAuCl/AgSbF_6$	CH_2Cl_2	25 °C	1.5 h	73%	99:01
3	$AuCl_3$	CH_2Cl_2	25 °C	1.5 h	96%	45:55
4	$PtCl_2$	toluene	60 °C	17 h	72%	94:6
5	$[RuCl_2(CO)_3]_2$	toluene	60 °C	20 h	81%	97:3
6	$AuCl_3$	toluene	25 °C	17 h	92%	15:85
7	$PdBr_2$	THF	50 °C	22 h	53%	90:10
8	$PtCl_2$	DCE	45 °C	40 h	79%	68:32
9	$[RuCl_2(CO)_3]_2$	DCE	45 °C	65 h	83%	78:22

[a] All yields determined by NMR vs methyl benzoate internal standard.

diphenylsulfoxide,[14] 10 mol % of the cationic triphenylphosphinegold(I) catalyst converted diazoketone **18b** to 1,4-endione **20b** in 80% yield (eq 7).[15] Under these conditions phenyl- and vinyl-substituted alkynes underwent gold(I)-catalzyed oxidative cyclizations to dieneones (eq 7). In contrast, *iso*-propyl and *tert*-butyl alkynes **21a** and **21b** underwent 1,2-hydrogen and methyl-shifts, respectively, to give dienes **22a** and **22b** (eq 8).



(9)

A number of transition-metal complexes have been reported to catalyze olefin cyclopropanation with propargyl ester **23**, via vinyl carbenoid **24**, generated by transition-metal-induced 1,2-ester migration.[2] Therefore, the generality of oxidation of metal−carbenoid intermediates with sulfoxides was examined using the rearrangement of propargyl ester **23** (Table 1).[16] The N-heterocycliccarbene gold(I)-catalyzed reaction of **23** in the presence of diphenylsulfoxide afforded aldehyde **25** in 73% yield and excellent control of olefin geometry (entry 2). Similarly, aldehyde **27** was formed in 70% yield by gold(I)-catalyzed oxidative rearrangement of ester **26** (eq 9). Gratifyingly, platinum− (entries 4 and 8), palladium− (entry 7), and ruthenium− (entries 5 and 9) carbenoid intermediates also underwent intermolecular oxygen atom transfer from diphenylsulfoxide to afford aldehyde **25** with good selectivity in favor of the *Z*-olefin isomer. On the other hand, gold(III)chloride catalyzed the rearrangement of **23** to selectively furnish *E*-**25** (entry 6).[17] This difference in selectivity further exemplifies the differences between gold(I) and gold(III) catalysts.[18]

In summary, we have developed a series of gold(I)-catalyzed oxidative rearrangement reactions of alkynes using sulfoxides as stoichiometric oxidants. These reactions provide an entry into rearranged products containing a carbonyl group for further functionalization. Additionally, the intermolecular oxygen atom transfer from a sulfoxide to a cationic gold(I) species provides further support for the carbenoid nature of the intermediates in these rearrangements. Application of this method to other systems and its use to investigate intermediates in metal-catalyzed reactions of alkynes is currently ongoing and will be reported in due course.

Acknowledgment. We gratefully acknowledge NIHGMS (Grant R01 GM073932-01), Merck Research Laboratories, Bristol-Myers Squibb, Amgen Inc., DuPont, GlaxoSmithKline, Eli Lilly & Co., Pfizer, AstraZeneca, Novartis and Boehringer-Ingelheim for funding. P.M. thanks the Spanish MEC for a postdoctoral fellowship.

Supporting Information Available: Experimental procedures, compound characterization data, and X-ray structure data for **5a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (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) Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546. (d) Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858. (e) Gorin, D. J.; Davis, N. R.; Toste, F. D. *J, Am. Chem. Soc.* **2005**, *127*, 11260. (f) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442. (g) Horino, Y.; Luzung, M. R.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 11364. (h) Lee, J. H.; Toste, F. D. *Angew. Chem., Int. Ed.* **2007**, *46*, 912. For a review see: (i) Gorin, D. J.; Toste, F. D. *Nature*, **2007**, *446*, 395.

(2) (a) Miki, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **2003**, *68*, 8505. (b) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002. (c) Gorin, D. J.; Dube, P.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 14480. (d) López, S.; Herrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 6029.

(3) For oxidation of ruthenium-carbenoid intermediates with *N*-hydroxyimides in ruthenium-catalyzed cycloisomerizations see: (a) Trost, B. M.; Rhee, Y.-H. *J. Am. Chem. Soc.* **1999**, *121*, 11680. (b) Trost, B. M.; Rhee, Y.-H. *J. Am. Chem. Soc.* **2002**, *124*, 2528.

(4) Oda, R.; Mieno, M.; Hayashi, Y. *Tetrahedron Lett.* **1967**, 2363.

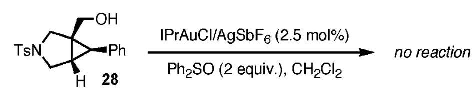
(5) (a) Dost, F.; Gosselck, J. *Tetrahedron Lett.* **1970**, 5091. (b) Takebayashi, M.; Kashiwada, T.; Hamaguchi, M.; Ibata, T. *Chem. Lett.* **1973**, 809. (c) Moody, C. J.; Slawin, A. M. Z.; Taylor, R. J.; Williams, D. J. *Tetrahedron Lett.* **1988**, *29*, 6009.

(6) Other oxidants examined gave no reaction (NMO, $PhI(OAc)_2$), decomposition of the strating material (DDQ, mCPBA) or conversion to diene **3** (CAN, 50%; IOPh, 12%; O_2, 60%; oxone, 86%).

(7) De Fremont, P.; Scott, N. M.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2005**, *24*, 2411.

(8) Cyclopropylaldehyde **5c** was observed as a by-product (3−10%) in the cycloisomerization of **1c** catalyzed by palladium or platinum. Nevado, C.; Charrualt, L.; Michelet, V.; Nieto-Oberhuber, C.; Muñoz, M. P.; Méndez, M.; Rager, M.-N.; Genêt, J.-P.; Echavarren, A. M. *Eur J. Org. Chem.* **2003**, 706.

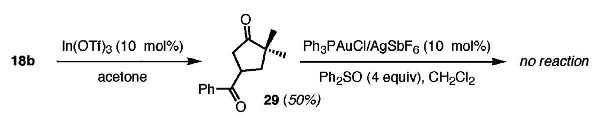
(9) An alternative mechanism involves trapping of the intermediate by water, to give alcohol **28**, and subsequent oxidation to the aldehyde; however, alcohol **28** was not oxidized under the reaction conditions.



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

(11) Kimball, D. B.; Herges, R.; Haley, M. M. *J. Am. Chem. Soc.* **2002**, *124*, 1572.

(12) An alternative mechanism involves trapping of the vinyl cation with water to give a diketone **29** which could subsequently be oxidized to dienone **20b**. Accordingly, activation of the carbonyl group by Lewis acids (such as $In(OTf)_3$) leads to the formation of dione **29**; however, **29** was not oxidized to **20b** under the reaction conditions.



(13) Alternatively, the vinyl gold(I)−carbenoid intermediate can be generated by a mechanism initiated by gold(I)-catalyzed decomposition of the diazo ketone;[15] however, the ketoaldehyde corresponding to trapping of α-ketocarbenoid intermediate (see eq. 4) was not observed.

(14) Under otherwise identical conditions, replacing diphenylsulfoxide with DMSO gave no reaction. Other oxidants afforded **20b** with the following yield: DDQ, 21%; O_2, 25%; oxone, 10%, $PhI(OAc)_2$, 35%.

(15) Small amounts (10%) of related oxidation products have been observed in a rhodium-catalyzed cyclization of diazoacetylenes. See: Padwa, A.; Chiacchio, U.; Fairfax, D. J.; Kassir, J. M.; Litrico, A.; Semones, M. A.; Xu, S. L. *J. Org. Chem.* **1998**, *58*, 6429. Application of diphenylsulfoxide in the rhodium-catalyzed (5 mol% $Rh_2(OAc)_4$, Ph_2SO (4 equiv), CH_2Cl_2) rearrangement of **18b** afforded **20b** in 41% yield.

(16) Lataoka, H.; Watanabe, K.; Goto, K. *Tetrahedron Lett.* **1990**, *31*, 4181.

(17) Treatment of (*Z*)-**27** with $AuCl_3$ did not induce isomerization to (*E*)-**27**.

(18) For examples of reactions showing different reactivity when gold(I) and gold(III) complexes are employed as catalysts see: (a) Sromek, A. W.; Rubina, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, *127*, 10500. (b) Lemiére, G.; Gandom, V.; Agenet, N.; Goddard, J.-P.; de Kozak, A.; Aubert, C.; Fensterbank, L.; Malacria, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 7596. (c) Hashmi, A. S. K.; Salathé, R.; Frey, W. *Chem.−Eur. J.* **2006**, *12*, 6991.

JA071231+