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Phosphine Gold(I) Bis-(trifluoromethanesulfonyl)imidate Complexes as New Highly Efficient and Air-Stable Catalysts for the Cycloisomerization of Enynes

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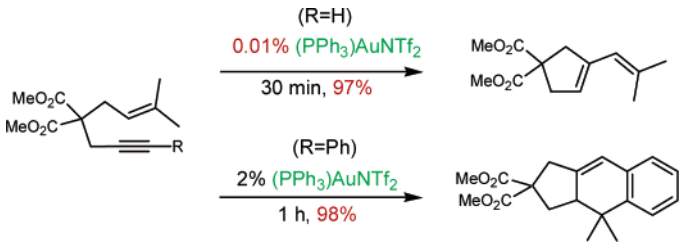
ABSTRACT

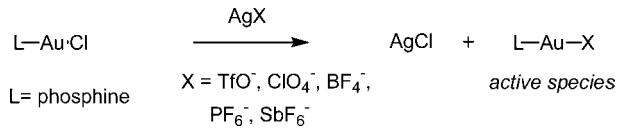


A study concerning the synthesis of new phosphine gold(I) complexes using the bis(trifluoromethanesulfonyl)imidate moiety as a weakly coordinating counteranion is described. These new air-stable complexes are more convenient to prepare, store, and handle and are exceedingly active for the catalysis of a wide range of enynes cycloisomerizations.

Phosphine gold(I) complexes have recently emerged as valuable catalysts for the conversion of various types of enynes into a range of useful structural motifs.[1] However, despite its efficiency, the catalytic system generally employed in these transformations,[2] which corresponds to the combined use of a phosphine gold(I) chloride complex and a silver salt as a cocatalyst (Scheme 1), suffers some limitations. The silver salts are all very hygroscopic, causing difficulties in properly weighing the reagent and in keeping the reaction medium nonacidic. Moreover, the active gold(I) species is quite unstable, especially when a fluorine-based counteranion is used,[3] and may therefore not be isolable.[4]

As part of our work on gold(I) catalysis,[5] we were particularly interested in developing efficient catalysts that would not require the use of a cocatalyst and would therefore be more convenient to use. We herein report the results of our endeavors, which led to the discovery of a new class of highly active and air-stable phosphine gold(I) complexes.

Scheme 1. General Formation of Active Gold(I) Species



(1) (a) Nieto-Oberhuber, C.; Lopez, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178−6179. (b) Muñoz, M.; Adrio, J.; Carretero, J. C.; Echavarren, A. M. *Organometalics* **2005**, *24*, 1293−1300. (c) Nevado, C.; Echavarren, A. M. *Chem. Eur. J.* **2005**, *11*, 3155−3164. (d) Nieto-Oberhuber, C.; Muñoz, M.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402−2406. (e) Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802−5803. (f) Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858−10859. (g) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978−15979. (h) Staben, S. T.; Kennedy-Smith, J. J.; Toste, F. D. *Angew. Chem., Int. Ed.* **2004**, *43*, 5350−5352. (i) Kennedy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4526−4527. (j) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 11806−11807. (k) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 6962−6963. For a review of Au-catalyzed reactions, see: Hashmi, A. S. K. *Gold Bull.* **2004**, *37*, 51−65.

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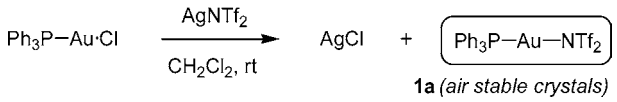
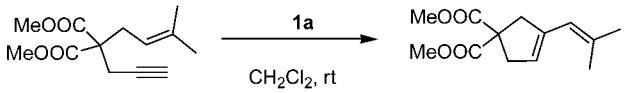
Scheme 2. Synthesis of $(PPh_3)AuNTf_2$



By analogy with the numerous studies reporting the use of the *bis(trifluoromethanesulfonyl)imidate* moiety (Tf_2N^-) for the synthesis of highly electrodeficient cationic complexes,[6] we envisaged this weakly coordinating counteranion[7] as a potentially valuable candidate for the synthesis of stable gold(I) catalysts.[8] To this end, treatment of $(Ph_3P)AuCl$ with 1 equiv of $AgNTf_2$[9] was attempted (Scheme 2).

We were pleased to see that this metathesis reaction led to the quantitative formation of the desired $(Ph_3P)AuNTf_2$ complex (**1a**), which was isolated as an air-stable crystalline compound.[10] This new complex, whose synthesis may be performed on a multigram scale, was then tested in a range of previously reported gold(I)-catalyzed transformations. Simple enyne **2** was first chosen as a model substrate (Scheme 3).

Scheme 3. Model Cycloisomerization of Enyne **2**



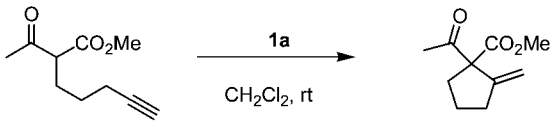
2 **3**

(**1a**) mol%	time	yield
1	5 min	97%
0.1	5 min	96%
0.01	30 min	97%

We were delighted to observe a rapid and highly exothermic conversion of **2** into metathesis product **3** when 1% **1a** was used as the catalyst. Moreover, this new catalyst turned out to be highly efficient since compound **3** was formed in the same 97% yield when only 0.01% **1a** was used (TON = 9700). These results contrast with those reported by Echavarren and co-workers who described the formation of **3** in 91% yield after 25 min of reaction and the use of 2% $(PPh_3)AuSbF_6$.[1d] Then, 1/100-fold less catalyst was needed to accomplish the same transformation.

Scheme 4. Cycloisomerization of Enynes **4**, **6**, and **8**

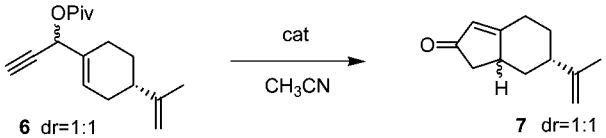
conia-ene rearrangement



4 **5**

(**1a**) mol%	time	yield
1	30 min	96%
0.1	60 min	93%

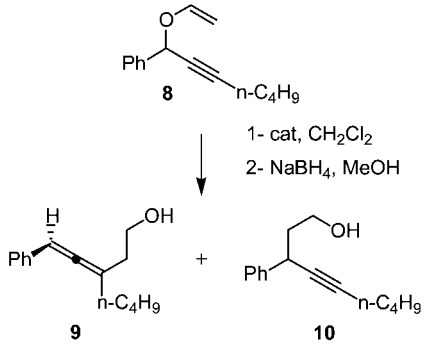
Rautenstrauch rearrangement



6 dr=1:1 **7** dr=1:1

1% (**1a**), 5 °C, 75 min, 81%
2% $(PPh_3)AuOTf$, rt, 10 h, 63% (ref 1e)

Propargyl Claisen rearrangement



8 **9** **10**

(**1a**) mol%	t (°C)	time	yield (**9**)	yield (**10**)
1	20	5 min	67%	12%
0.1	0	5 min	90%	6%
0.1	-10	10 min	95%	<3%

Complex **1a** also efficiently catalyses the Conia-ene,[1h,i] the Rautenstrauch,[1e] and the propargyl Claisen[1g] rearrangements recently reported by Toste and co-workers (Scheme 4). It is interesting to note that a simple change in the nature of the counteranion (TfO^- for Tf_2N^-) led to a much faster conversion of enyne **6** into cyclopentenone **7**, which was isolated in an improved 81% yield when catalyst **1a** was used instead of $(PPh_3)AuOTf$. A remarkable temperature effect was also observed for the transformation of enyne **8** into allene **9**. Product **10** derived from competing [1,3] rearrangement, which was isolated in 12% yield when the

(2) Protonation of an alkylgold(I) complex with a strong acid may also be used to generate the cationic species; however, these conditions are not always compatible with the substrates.

(3) Weakly coordinating anions such as BF_4^-, PF_6^-, or SbF_6^- are Lewis acid/base conjugates of a superior nucleophile (e.g., $MF_{n+1}^- \rightarrow MF_n + F^-$). Their ability to act as inert counterions is always limited by a competition reaction for that nucleophile (e.g., F^-), and the free Lewis acid MF_n can act as an oxidizing agent and thus cause unwanted side reactions. See: Raabe, I.; Krossing, I. *Angew. Chem., Int. Ed.* **2004**, *43*, 2066−2090. Raabe, I.; Krossing, I. *Chem. Eur. J.* **2004**, *10*, 5017−5030.

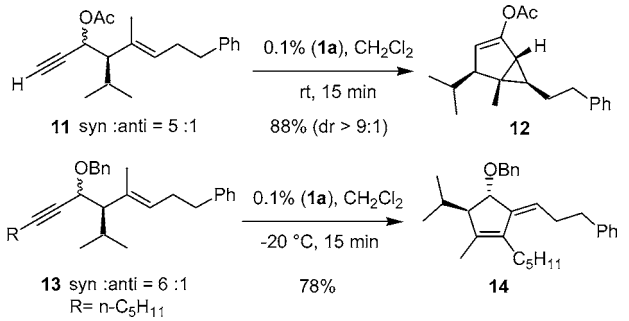
(4) Preliminary ^{31}P NMR studies of preformed solutions of $(PPh_3)AuBF_4$, $(PPh_3)AuPF_6$, and $(PPh_3)AuSbF_6$ complexes in CH_2Cl_2 from $(PPh_3)AuCl$ and the corresponding silver salt showed their instability. All attempts to isolate these complexes failed.

(5) Gagosz, F. *Org. Lett.* **2005**, *7*, 4129−4132.

(6) Numerous metal triflimides are known as strong Lewis acid catalysts: For *lanthanides*, see: (a) Ishihara, K., Kubota, M.; Yamamoto, H. *Synlett* **1996**, 265−266 and 839−841. For *silicium*, see: (b) Mathieu, B.; Ghosez, L. *Tetrahedron* **2002**, *58*, 8219−8226. For *tin*, see: (c) Vij, A.; Wilson, W. W.; Vij, V.; Corley, C. R.; Tham, F. S.; Gerken, M.; Haiges, R.; Schneider, S.; Schroer, T.; Wagner, R. I. *Inorg. Chem.* **2004**, *43*, 3189−3199. For *other metals*, see: (d) Sibi, M. P.; Petrovic, G. *Tetrahedron: Asymmetry* **2003**, *14*, 2879−2882.

(7) NTf_2^- is a weaker coordinating anion than OTf^- and ClO_4^-.[6b]

Scheme 5. Cycloisomerization of Enynes **11** and **13**

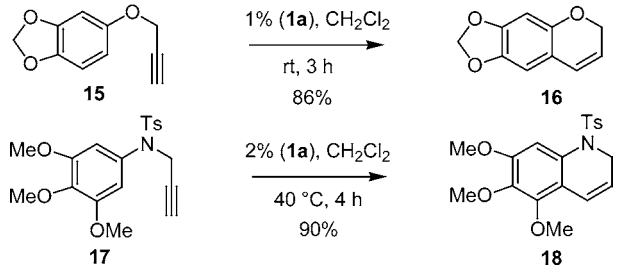


reaction was performed at room temperature, was nearly absent when the temperature was lowered to −10 °C and the catalyst loading reduced to 0.1%.

Complex **1a** was also effective in catalyzing the cycloisomerization of 1,5-enynes[1f] as depicted in Scheme 5. Using only 0.1% **1a**, bicyclo[3.1.0]hexene **12** and cyclopentadiene **14**[5] were isolated in 88 and 78% yield, respectively.

Less favored intramolecular hydroarylation of alkynes were also tested.[1c] Even if these transformations required a longer reaction time, *2H*-chromene **16** and dihydroquinoline **18** were obtained in excellent yield starting from alkynes **15** and **17** (Scheme 6).

Scheme 6. Hydroarylation of Alkynes **15** and **17**



Moreover, by analogy with the recently reported work of Echavarren and co-workers,[1a,b] we prepared several other new phosphine $AuNTf_2$ complexes **1b**−**e**[11] and evaluated their catalytic activity in the kinetically disfavored methoxycyclization of enyne **2**. Our results, presented in Table 1, contrast with those previously reported.

Thus, compound **19** was isolated in nearly quantitative yield regardless of the catalyst (**1a**−**e**) used, and the transformations only differ in the time necessary to reach completion. Such results may reflect a higher stability of

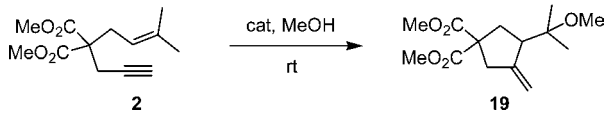
(8) By analogy with the stability of $AgNTf_2$ compared to the hygroscopic salts AgOTf, $AgBF_4$, $AgPF_6$, or $AgSbF_6$.

(9) $AgNTf_2$ is readily available from the commercially available $HNTf_2$ and Ag_2CO_3.

(10) **1a** is soluble in most commonly used solvents (DCM, CH_3CN, THF, MeOH, ether, toluene...). The crystal structure of **1a** was established by X-ray diffraction (CCDC 273834); see Supporting Information.

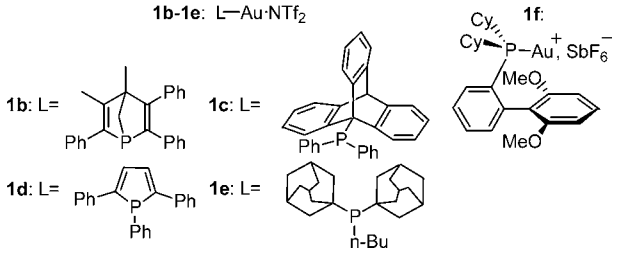
(11) **1b**−**e**, which are all air-stable compounds, were synthesized as described for **1a**.

Table 1. Au(I)-Catalyzed Methoxycyclization of Enyne **2**



entry	cat	mol %	time	yield (**19**)
1	**1a**	1	2 h	94%
2	**1a**	0.1	24 h	77% [a]
3	$(PPh_3)AuSbF_6$	2	3 h	84% [b]
4	**1b**	1	2 h	94%
5	**1c**	1	75 min	97%
6	**1d**	1	75 min	96%
7	**1e**	1	20 min	97%
8	**1f**	2	15 min	89% [b]

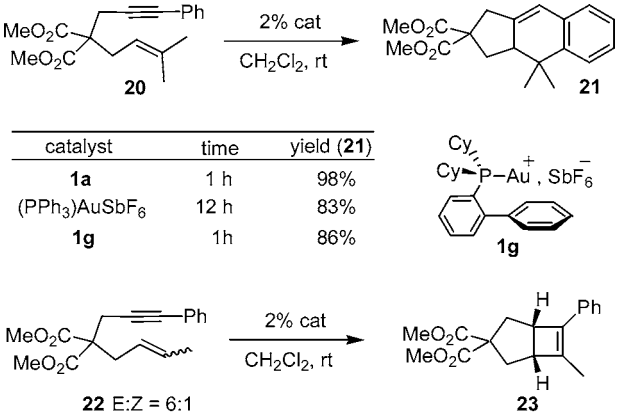
[a] 18% of unreacted **2** were also isolated. [b] See ref. 1a.



$AuNTf_2$ catalysts compared to the corresponding $AuSbF_6$ complexes. It is interesting to note that the reaction time decreases with bulkier and more basic phosphine gold(I) complexes. Moreover, the transformation can even be performed using only 0.1% of the simplest $(PPh_3)AuNTf_2$ catalyst (entry 2).

Finally, to further highlight the potential of these new catalysts, complex **1a** was tested in the cycloisomerization of enynes **20** and **22**.[1a] As shown in Scheme 7, **1a** possesses

Scheme 7. Cycloisomerization of Enynes **20** and **22**



a better activity than the corresponding $(PPh_3)AuSbF_6$ catalyst[1a] and is at least as efficient as the more complex and expensive (2-(dicyclohexylphosphino)biphenyl)$AuSbF_6$ catalyst **1g**.[1a]

In summary, we have developed a new class of phosphine gold(I) catalysts based on the use of the bis(trifluoromethanesulfonyl)imidate moiety as a weakly coordinating counteranion. These air-stable complexes are more convenient to prepare, store, and handle and are exceedingly active for the catalysis of a wide range of enyne cycloisomerizations. They open new possibilities in homogeneous gold(I) catalysis and may allow transformations that were hitherto difficult to achieve.

Acknowledgment. The author wishes to thank Prof. S. Z. Zard, Dr. B. Quiclet-Sire, and Dr. I. Hanna for helpful discussions.

Supporting Information Available: Experimental procedures and spectral data for new compounds and X-ray data for **1a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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