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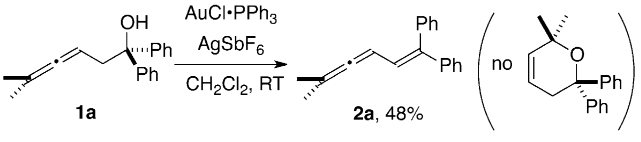
Self-Buffering Hybrid Gold-Polyoxometalate Catalysts for the Catalytic Cyclization of Acid-Sensitive Substrates

Nathalie Dupré,[a] Christian Brazel,[a] Louis Fensterbank,[a] Max Malacria,[a] Serge Thorimbert,*[a] Bernold Hasenknopf,*[a] and Emmanuel Lacôte*[a, b]

The recent development of functionalized polyoxometalates (POMs)[1] opens broad new perspectives for catalysis involving these clusters.[2] Merging of the properties of POMs and organic or organometallic fragments either through functional cations[3] or through covalent attachment can lead to new reactivity,[4] or better turnovers.[5,6]

Herein, we report that the weak basicity of the oxo ligands in organometallic Au-polyoxotungstate covalent hybrids significantly improves the scope of the gold-mediated oxacyclization to acid-sensitive allenes.

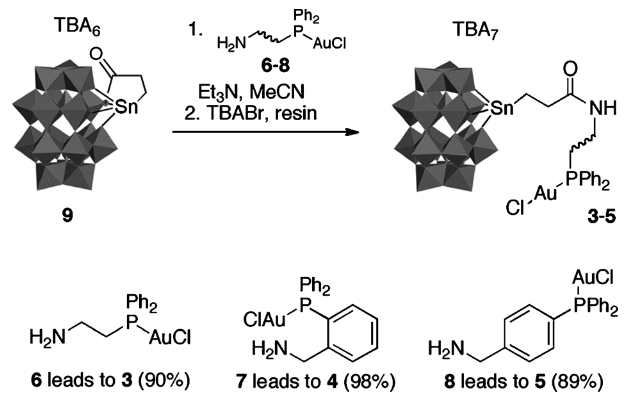
This work started from the observation that the usually efficient Au-catalyzed oxacyclization of allenes[7] failed for the cyclization of bis-arylic substrates, such as **1a**,[8] delivering a low yield of vinylallene **2a** (Scheme 1). The same elimination was observed in all the different conditions we tried and with varied diaryl substrates (see Table S1 in the Supporting Information). We attributed this to the adventitious acidic traces present in the gold catalysts, which dehydrated the very sensitive bis-benzylic tertiary alcohols more rapidly than their gold-catalyzed cyclizations.



Scheme 1. Dehydration of acid-sensitive bis-benzylic β-allenyl alcohol **1a**.

POMs are the conjugated bases of the strong heteropoly acids.[9] Thus, we hypothesized that POMs might be beneficial as buffers in the reactions considered, since it is already known that heteropoly acids are compatible with gold catalysis.[10] We also thought that tethering to the POM might facilitate recycling of the gold catalysts, owing to the specific solubilities of POMs.[11]

Organometallic hybrids **3**–**5** were chosen as representative potentially self-buffering catalysts (Scheme 2). Compound **3** is a derivative of an alkyl-diaryl phosphine, whereas **4** and **5** are derivatives of a triarylphosphine with different geometries. Understanding the interaction of organic and organometallic units with the POM surface is still an unsolved problem. We felt that the different substitutions in the spacer would lead to different intramolecular interactions of the gold atom with the oxide surface,[12] and provide a handle to control reactivity as well as progress toward mapping of the POM/organics recognition.



Scheme 2. Preparation of the hybrid catalysts (TBA = tetrabutyl ammonium; TBABr = tetrabutyl ammonium bromide).

The desired precatalysts were prepared in good yields (89–98%) from coupling the corresponding ω-amino gold phosphine complexes (**6**–**8**) to the activated Dawson α_1-organotin-substituted polyoxotungstate $[P_2W_{17}O_{61}\{Sn(CH_2)_2CO\}]^{6-}$ (**9**) in acetonitrile.[13] The crude products were stirred with TBA-loaded Amberlyst cation-exchange resin to remove all traces of triethylammonium formed during the coupling around the POM. Introduction of the aminophosphines before complexation of AuCl is also possible, albeit in lower yields. Variable amounts of phosphine oxide were observed after the isolation of the POM–phosphine ligands.

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[a] N. Dupré, Dr. C. Brazel, Prof. L. Fensterbank, Prof. M. Malacria, Prof. S. Thorimbert, Prof. B. Hasenknopf, Dr. E. Lacôte
UPMC Sorbonne universités
Institut Parisien de Chimie Moléculaire (UMR CNRS 7201)
4 place Jussieu, C. 229, 75005 Paris (France)
Fax: (+33) 1-44-27-73-60
E-mail: serge.thorimbert@upmc.fr
bernold.hasenknopf@upmc.fr

[b] Dr. E. Lacôte
ICSN CNRS
Av. de la Terrasse, 91198 Gif s/Yvette Cedex (France)
E-mail: emmanuel.lacote@univ-lyon1.fr

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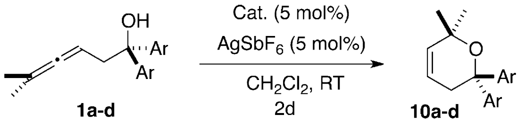
POMs **3**–**5** were characterized by NMR and IR spectroscopy, mass spectrometry, and elemental analysis. All techniques were in agreement with the proposed structures (see the Supporting Information for details). For example, the ^{31}P NMR spectrum of **3** showed three peaks. Two ($\delta = -12.1$ and -6.6 ppm) were those of the Dawson phosphates, with the P1 ($\delta = -6.6$ ppm) peak showing coupling satellites from the tin coupling. The third peak ($\delta = 28.3$ ppm) was characteristic of an aurated phosphine. IR spectra display the typical strong bands for the Dawson phosphotungstates (in the 700–1100 cm^{-1} range). The bands at higher wavenumber are those of the organic ligands and counterions. Finally, the mass spectra show intense signals of the intact anions of **3**–**5** associated with TBA and H$^+$ cations, confirming their structure. Minor fragmentations correspond to the loss of AuCl or Cl$^-$.

In a typical catalytic cyclization, allene **1a** was treated with catalyst **3** (5 mol %) in the presence of AgSbF$_6$ (5 mol %) in dichloromethane at room temperature. To our pleasure, compound **10a** was isolated in nearly quantitative yield (Table 1, entry 1) after two days. Diversely substituted β,β-diaryl β-hydroxy allenes possessing electron-donating and electron-withdrawing substituents also gave the expected cyclized products in excellent yields (Table 1, entries 2–4). Triarylphosphine derivatives (**4** and **5**) reacted similarly, albeit the reactions were slower taking 5 days to reach completion (Table 1, entries 5–8).

Table 1. Cyclization of acid-sensitive β,β-diaryl β-hydroxy allenes catalyzed by the POM–Au hybrids.



Entry	Substrate	Ar	Cat.	Product, yield [%]
1	**1a**	Ph	**3**	**10a**, 95
2	**1b**	4-MeO-C_6H_4	**3**	**10b**, 96
3	**1c**	3,5-Me_2-C_6H_3	**3**	**10c**, 97
4	**1d**	4-F-C_6H_4	**3**	**10d**, 88
5	**1a**	Ph	**4**	**10a**, 91[a]
6	**1b**	4-MeO-C_6H_4	**4**	**10b**, 96[a]
7	**1a**	Ph	**5**	**10a**, 99[a]
8	**1b**	4-MeO-C_6H_4	**5**	**10b**, 80[a]
9	**1a**	Ph	–[b]	**10a**, 75[c]
10	**1b**	4-MeO-C_6H_4	–[b]	**10b**, 55[d]
11	**1c**	3,5-Me_2-C_6H_3	–[b]	**10c**, 58[e]
12	**1d**	4-F-C_6H_4	–[b]	**10d**, 85[f]
13	**1b**	4-MeO-C_6H_4	–[g]	**10b**, 76[h]

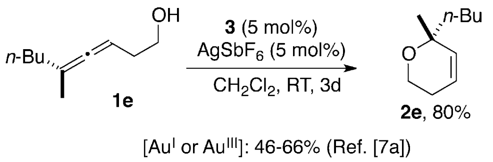
[a] Reaction took 5 days. [b] Conditions: AuClPPh$_3$ (5 mol %), AgSbF$_6$ (5 mol %), TBA$_6$[P$_2$W$_{18}$O$_{62}$] (5 mol %), CH$_2$Cl$_2$, RT. [c] Isolated yield. Reaction was stopped after 8 days (88 % completion). [d] Isolated yield. Reaction took 10 days, 37 % of vinylallene **2b** was also isolated. [e] Isolated yield. Reaction was stopped after 10 days (69 % completion). [f] Isolated yield. Reaction took one week. [g] Conditions: AuClPPh$_3$ (2 mol %), AgSbF$_6$ (2 mol %), pyridine (2 mol %), CH$_2$Cl$_2$, RT. [h] Isolated yield. Reaction was stopped after 10 days (90 % completion). 6 % of **2b** was also formed.

This shows that the polyoxometalate is indeed able to capture the adventitious protons from the gold/silver mixed catalytic system. This drives the reaction toward cyclization by allene activation without byproduct formation. Further support for this hypothesis can be derived from the lack of reaction in the absence of a cationic gold species.

We designed several control experiments to probe our tethering approach. First, omission of the POM–Au hybrid resulted in formation of vinylallene **2a**, showing that AgSbF$_6$ alone also leads to protolysis (Table S1 in the Supporting Information). Second, the reactions were tested with a POM additive that was not covalently bound to the gold (Table 1, entries 9–12). Dawson derivative TBA$_6$[P$_2$W$_{18}$O$_{62}$] was chosen because of its structural similarity to catalysts **3**–**5**. In all cases, cyclized products **10a**–**d** were isolated, albeit after prolonged reaction times. In the case of the bis(*p*-methoxyaryl) substituent, however, a significant amount of elimination was observed (37 %; Table 1, entry 10). When pyridine was used as a base for the reaction of **1b** (Table 1, entry 13), the reaction was really slow (more than ten days to reach 90 % completion) and some vinylallene **2b** was again observed (6 %) together with the expected **10b**, isolated in 76 % yield.[7a]

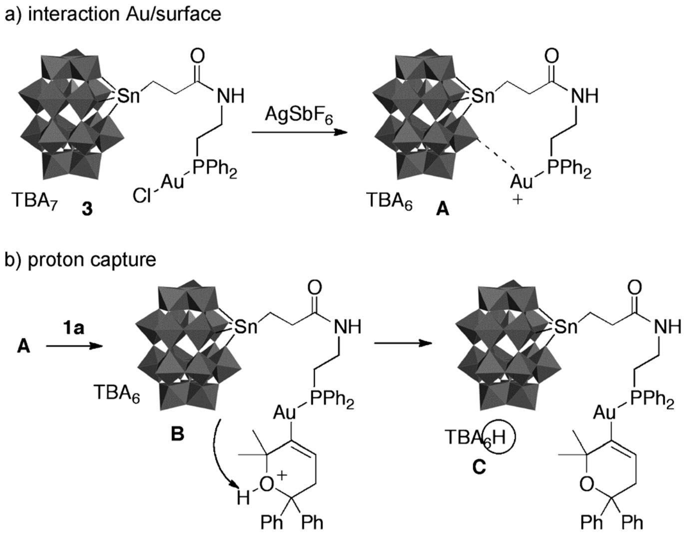
Overall, the controls showed that the hybrid POM–Au catalysts are the best compromise between yield and reaction rates, for the cyclization of very sensitive allenols. Silver hexafluoroantimonate is able to generate protons also, but not to promote cyclization by itself, thus the cyclized products do come from gold activation of the allenes.

The less sensitive allenyl alcohol **1e** also led to the cyclization, delivering 80 % of **2e** after three days (Scheme 3). This substrate provides a key comparison with the literature.[7a] In the absence of an amine buffer, the yield for the cyclization of **1e** was in the sixties, and slightly improved with our catalysts. Amine buffering was a way to improve yields, but as before this impacted even more on overall reactivity, since the cyclization took five days to reach a yield similar to the one obtained with **3**.



Scheme 3. Cyclization of allenol **1e**.

The POM–Au conjugates are more efficient than running the reaction in the mere presence of a POM. It is known that POMs can be ligands for transition metals.[6,14] Thus, the gold atom (especially in its cationic form) may interact with the polyoxometallic surface, as in **A** (Scheme 4a), resulting in catalyst deactivation. It might also be possible that the POM is basic enough to also capture the proton of the oxonium vinylgold intermediate **B** (Scheme 4b). The protodeauration of the vinyl–gold bond in **B** would thus become a slow rate-limiting step because it requires the deprotonation of the POM surface of **C**.[15] This would also explain why stronger bases reduce the reactivity even more.



Scheme 4. Mechanistic hypotheses for the observed reactivity; a) deactivation through Au–oxo interaction; b) deactivation through proton capture.

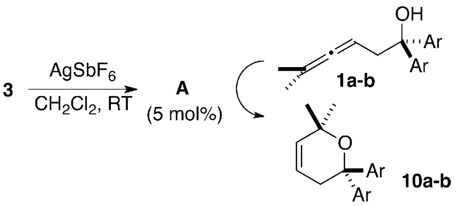
Attempts to fully characterize **A** were hampered by the fact that the different ligands in solution can all interact with the Au ion, preventing its clean precipitation. Nonetheless in the ^{31}P NMR spectrum, the RPh$_2$P–AuCl signal at $\delta = 28.3$ ppm in **3** disappeared when stoichiometric AgSbF$_6$ was added. Two new signals at $\delta = 18.6$ and 27.1 ppm were observed in acetonitrile, but only one signal at $\delta = 22.1$ ppm in acetonitrile/water (19:1). This suggests that the coordination sphere of Au is modified.

In contrast to the intermolecular complexation between $[AuPPh_3]^+$ and $[P_2W_{18}O_{62}]^{6-}$, the intramolecular complexation[12,16] in hybrids **3**–**5** must differ in a way that hampers a strong deactivating Au/POM association, either because it is a more rigid system that cannot interact with the more electron-rich oxo ligands of the surface, or because of steric shielding. Thus, the hybrids retain a significant catalytic activity.

We sought to take further advantage of the tether. We surmised that the likely interaction between the gold atom and the oxo ligands in **A** might stabilize the cationic gold atom enough to lead to its recycling even if it is not involved in the reactivity change.

In a typical reaction, allene **1b** (Table 2, entry 4) was directly treated with **A** in dichloromethane at room temperature. The reaction took 2 days to reach completion and it was essentially quantitative. Allene **1a** also delivered **10a** (Table 2, entry 1). Gratifyingly, the catalyst could again be recovered by precipitation in acetone/ethanol/diethyl ether (1:1:20) and centrifugation. For both **1a** and **1b** the reaction worked as well with the recovered catalyst (Table 2, entries 2 and 5), but the reaction rate dropped in the third cycle (Table 2, entries 3 and 6). Nonetheless, the yields stayed high. Since ^{31}P NMR indicated that no leaching took place, it is likely that the cationic gold may have captured some nucleophile, which lowers its activity.

Table 2. Recycling of the hybrid catalyst.



Entry	Substrate	Ar	Run	Product, yield [%]
1	**1a**	Ph	1	**10a**, 88[a]
2	**1a**	Ph	2	**10b**, 96
3	**1a**	Ph	3	**10c**, 86[b]
4	**1b**	p-MeO-C$_6$H$_4$	1	**10b**, >99
5	**1b**	p-MeO-C$_6$H$_4$	2	**10b**, 96
6	**1b**	p-MeO-C$_6$H$_4$	3	**10b**, 90[b]

[a] Reaction was stopped at 90% completion [b] Reaction took over 6 days to reach completion.

In conclusion, we have introduced a new catalytically active organometallic hybrid of a polyoxometalate. The unique covalent tethering of the gold complex to the POM framework buffers the reaction mixture, which extends the scope of the cycloisomerization of allenols to substrates extremely sensitive to dehydration. It also stabilizes the cationic gold active site,[17] allowing the isolation and recovery of the whole catalyst. Further work will focus on the accurate mapping of the Au/POM interaction to design catalysts with improved selectivity.

Acknowledgements

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Keywords: allenes • gold • organic–inorganic hybrid composites • polyoxometalates • protonation

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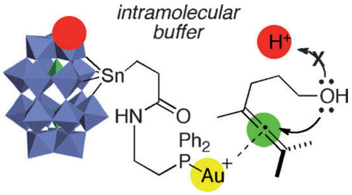
Grafting of a gold complex to an organo-polyoxometalate delivers catalytically active bitopic hybrids. The gold end activates allenes, while the metal-oxide surface can capture protons (see scheme). The scope of the gold-catalyzed oxacyclization of allenols is expanded to highly sensitive tertiary benzylic alcohols.



Hybrid Polyoxometalates

N. Dupré, C. Brazel, L. Fensterbank,
M. Malacria, S. Thorimbert,*
B. Hasenknopf,* E. Lacôte* ▮▮▮▮–▮▮▮▮

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