Homogeneous Gold Catalysis

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Oxidative Addition to Gold(I): A New Avenue in Homogeneous Catalysis with Au

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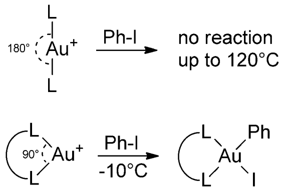
Dedicated to BASF on the occasion of its 150th anniversary

The advancement of science, like many other human endeavors, seldom follows a predictable path. This is actually one of the reasons why science in general and chemistry in particular are so gratifying for those who spend their time with them. The chemistry of gold and the story of its use as a homogeneous catalyst offer a particularly interesting case study. As is so often the case, the very first step is very far back in time and went completely unnoticed. The first report in the literature on the formation of acetaldehyde upon reaction of an aqueous gold(III) chloride solution with acetylene dates back to 1898.[1] It took almost a century for catalysis with Au^{III} to reappear in the literature and, interestingly, the work was initiated in industry, in this case at the Japanese company Kyowa Yuka.[2] Unfortunately, the gold(III) chloride used in that work is a strong oxidant and only modest turnover numbers were achievable. When it was recognized in 1998 that Au^{I} could be an excellent homogeneous catalyst,[3] interestingly again a development coming from an industrial laboratory, this was generally viewed as an unexpected development and even described as a "Black Swan event".[4] The incredible wave of interest in catalysis with Au^{I} almost pushed Au^{III} completely out of sight. Even in cases in which Au^{III} was used, the question always lingered: wasn't it just being reduced in situ to Au^{I}? This question was usually very difficult to answer in a clear-cut way.

One other question, however, remained unanswered and it was clear that sooner or later pursuing this question would lead to new discoveries. The nagging question was this: why did Au^{III} seem to behave so differently from Pd^{II}? Pd^{II} is one of the most versatile elements when it comes to homogeneous catalysis and, according to the diagonal relationship in the periodic system of the elements, there was always the expectation that Au^{III} might show a similarly rich chemistry. This expectation was even supported by the very similar ionic radii of Pd^{II} (78 pm for square-planar complexes and 100 pm for octahedral) and Au^{III} (82 pm for square-planar complexes and 99 ppm for octahedral). However, the elementary reactions which form the basis of Pd^{II} chemistry, such as oxidative addition and reductive elimination, seemed to be very uncommon for Au^{III}.

However, change was in the air, and, as often happens, theoreticians led the way. At the beginning of 2014 Bickelhaupt and co-workers published a report on the oxidative addition of Ar−X to L−Au−X′, in which X and X′ were halogen or triflate, Ar was an aromatic ring, mostly phenyl, and L was a phosphine or NHC ligand.[5] They concluded that "the oxidative addition of aryl halides to gold(I) complexes is controlled by the strain energy associated with the deformation of the reactants from their equilibrium geometries to the geometries they adopt in the corresponding concerted transition state." At the same time, Amgoune, Bourissou, and co-workers were working on the same problem. By using chelating diphosphines with a small bite angle, which were known to form three-coordinated Au^{I} complexes, they successfully demonstrated the oxidative addition of phenyl iodide to a Au^{I} complex.[6] Their rationale for success is shown in Scheme 1, which makes the relationship to the theoretical work of Bickelhaupt and co-workers clear: it is the geometric distortion in the starting material that makes the oxidative addition possible.



Scheme 1. Ligand design envisioned to trigger oxidative addition of aryl iodides to Au^{I} complexes. It is the ligand preorganization that makes the oxidative addition possible.[6]

This study was an important step towards the understanding of oxidative additions to gold, but the complexes formed are very stable and are thus unsuitable as catalysts. Bourissou and co-workers cite in a footnote an older study by Ahlquist, Wendt, and co-workers, in which it is described that (NHC)Au−Ph reacts with phenyl iodide to give complete conversion into (NHC)Au−I and biphenyl. A possible explanation for this transformation would have been an oxidative addition of Ph−I followed by a reductive elimination of biphenyl. Wendt and co-workers could not prove it, but the hint was there: even linear Au^{I} complexes could undergo oxidative addition.[7]

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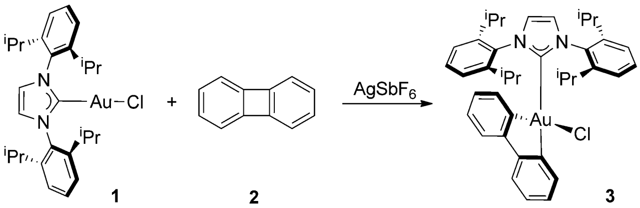
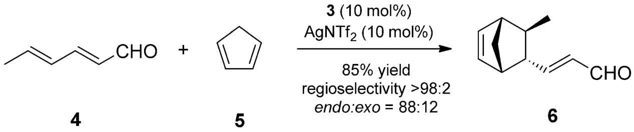
Here is where the great stroke of genius comes in. In a report published very recently in *Nature*, Toste and co-workers describe a wholly different way of looking at oxidative addition with Au^I.[8] Instead of sticking to the common idea that oxidative addition takes place between a metal complex and a polar C−X bond they turn the picture around: they use (NHC)Au−Cl complex **1** as the starting material, remove the chloride with a Ag^I salt, and use biphenylene (**2**) as the reaction partner. The oxidative addition takes place on the strained but unpolar central C−C bond of biphenylene (Scheme 2).



Scheme 2. Accessing Au^{III} by oxidative addition of a carbon–carbon bond. Complex **3** was isolated in 80% yield.[7]

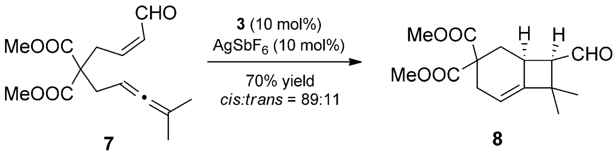
There are a number of remarkable thoughts behind this approach. First of all, it was extremely important that they recognized that creating a coordinatively unsaturated Au^I complex can lead to the same lowering of the energy barrier for oxidative addition as the use of a chelating ligand with a small bite angle. The most remarkable step, however, was in moving away from the usual substrates for oxidative addition to biphenylene. At first glance, one might think of biphenylene as just a mild oxidant and regard attempting an oxidative addition to an unpolar C−C bond as foolishness. However, this approach deserves a second look. The amount of strain in biphenylene is often underestimated. The (formal) hydrogenation of biphenylene to biphenyl has a reaction enthalpy of $-235\,kJ\,mol^{-1}$. For comparison, the (formal) hydrogenation of biphenyl to two moles of benzene is almost thermoneutral ($<1\,kJ\,mol^{-1}$). In addition to the thermodynamic driving force, the use of biphenylene has other advantages. Upon oxidative addition, it forms a stable chelating ligand which prevents a subsequent reductive elimination. The corresponding complex with two separate phenyl groups described in the study by Ahlquist and Wendt is very reactive and immediately eliminates biphenyl.

The real advantage of the approach of Toste and co-workers, however, is that the chloride ligand in **3** is labile and can be removed with a Ag^I salt and replaced by water or DMF to give stable, cationic square-planar Au^{III} complexes which do not contain halogen ligands at all. The labile ligand offers an open binding site and thus opens the road for catalysis. Indeed, the authors already offer a handful of examples in which these Au^{III} complexes work as catalysts, for example in 1,4-selective Mukayama–Michael additions or in selective γ,δ-addition to α,β,γ,δ-dienals. One of the most remarkable examples given is the selective γ,δ-Diels–Alder addition of cyclopentadiene (**5**) to sorbic aldehyde (**4**) shown in Scheme 3. The reaction occurs almost exclusively on the γ,δ-double bond, and has a very good *endo*:*exo* selectivity. None of the other catalysts tested showed any activity at all.



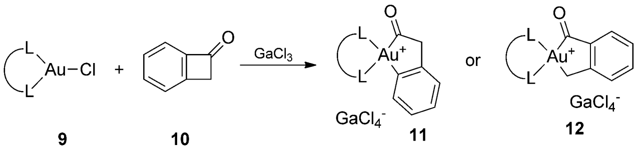
Scheme 3. Selective catalytic Diels–Alder addition to the γ,δ-double bond of sorbic aldehyde.[8]

Another remarkable reaction is the Au^{III}-catalyzed intramolecular [2+2] cycloaddition of **7** to **8**, a reaction for which no non-photochemical equivalent is known (Scheme 4).



Scheme 4. Au^{III}-catalyzed [2+2] cycloaddition of an allene to an α,β-unsaturated aldehyde.[8]

The study by Toste and co-workers is an important breakthrough in the chemistry of gold and gives science a brand new class of catalysts. That the time was ripe for this discovery is shown by the fact that Amgoune, Bourissou, and co-workers have now discovered that their Au^I complex with a diphosphinocarborane ligand (**9**) can undergo a reversible oxidative addition to a C−C bond of benzocyclobutenenone (**10**), another molecule which, like biphenylene, has a considerable amount of steric strain (Scheme 5).[9]



Scheme 5. Reversible oxidative addition of diphosphinocarborane-Au^I chloride to benzocyclobutenone. Product **11** is kinetically favored and product **12** is thermodynamically favored.[9]

These exciting results are a true landmark in the chemistry of gold and it is expected that they will lead to a revival of the chemistry of, and catalysis with, Au^{III}.

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[1] H. Erdmann, P. Köthner, *Z. Anorg. Chem.* **1898**, *18*, 48–58.
[2] a) Y. Fukuda, K. Utimoto, *J. Org. Chem.* **1991**, *56*, 3729–3731; b) Y. Fukuda, K. Utimoto, *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2013–2015.
[3] J. H. Teles, S. Brode, M. Chabanas, *Angew. Chem. Int. Ed.* **1998**, *37*, 1415–1418; *Angew. Chem.* **1998**, *110*, 1475–1478.

[4] W. A. Nugent, *Angew. Chem. Int. Ed.* **2012**, *51*, 8936–8949; *Angew. Chem.* **2012**, *124*, 9066–9080.
[5] I. Fernández, L. P. Wolters, F. M. Bickelhaupt, *J. Comput. Chem.* **2014**, *35*, 2140–2145.
[6] M. Joost, A. Zeineddine, L. Estévez, S. Mallet-Ladeira, K. Miqueu, A. Amgoune, D. Bourissou, *J. Am. Chem. Soc.* **2014**, *136*, 14654–14657.
[7] M. T. Johnson, J. M. J. van Rensburg, M. Axelsson, M. S. G. Ahlquist, O. F. Wendt, *Chem. Sci.* **2011**, *2*, 2373–2377.
[8] C.-Y. Wu, T. Horibe, C. B. Jacobsen, F. D. Toste, *Nature* **2015**, *517*, 449–454.
[9] M. Joost, L. Estévez, K. Miqueu, A. Amgoune, D. Bourissou, *Angew. Chem. Int. Ed.* **2015**, *54*, 5236–5240; *Angew. Chem.* **2015**, *127*, 5325–5329.

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