

Advances in Homogeneous Gold Catalysis: From Nucleophilic Additions to C-H Bond Activation

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The catalytic chemistry of gold has had a relatively belated development with respect to other late transition metals, and this has been attributed to the preconception that gold is expensive and unreactive.^{1a,b} Both of these conceptions have been proven false, and successful applications of gold catalysis have emerged in chemical processing, pollution control, fuel cells design, and many others fields. While the chemical literature and industrial utilization of gold has been dominated by heterogeneous catalysis (including CO oxidation, HOOH production, hydrogenation, and epoxidation), great advances have recently been made in the field of homogeneous catalysis. Here, dissolved cationic gold species are believed to be the unambiguous center of reactivity for a variety of important transformations.^{1b} A series of extensive reviews has been released over the past two years in regards to progress and newly arisen debates in this field.¹

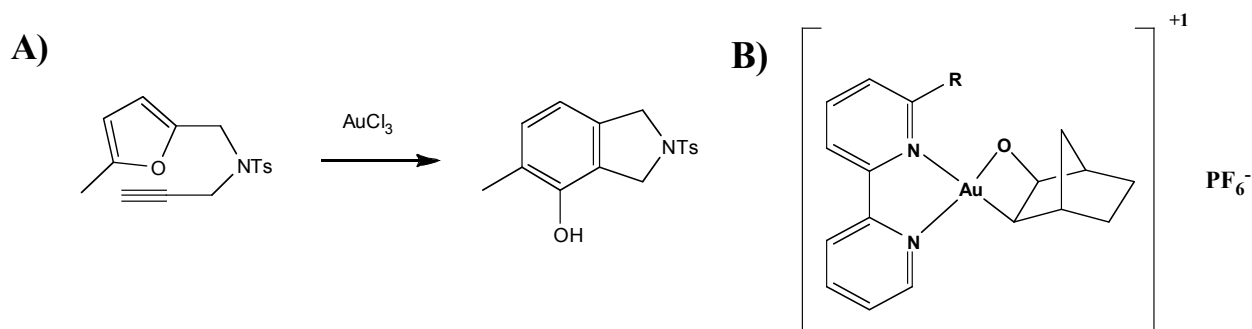


Figure 1: **A)** Efficient isomerization of furans to phenols with AuCl_3 . **B)** Structure of first isolated Au-oxetane species, a crucial intermediate in gold mediated oxygen addition to olefins.

The large reduction potential of gold, ($\text{Au}^{\text{III}} \rightarrow \text{Au}^0$; $E^\circ = 1.68 \text{ V}$) along with high chemoselectivity and the low tendency to undergo β -hydrogen elimination, establishes gold as a suitable complement to other late transition metals in organic synthesis. Both common oxidation states (Au^{I} and Au^{III} , **Figure 1**) are “soft” electrophiles, and both have been exploited in the formation of C-C, C-N, C-O, and C-S bonds.² Interestingly, both oxidation states have been shown to catalyze similar or identical reactions. Furthermore, the harnessing of classical organometallic behavior such as reductive elimination or oxidative addition has not been efficiently achieved.^{1b} These observations, along with the propensity of dissolved gold to disproportionate, have brought the oxidation state of the active species into question.²⁻⁴

The organic transformations catalyzed by gold discussed herein can be divided into two categories: π -electrophilic activation and C-H activation. Gold has even been postulated to play a dual role in transformations where both modes of activation are

possible. Activation of π -systems towards nucleophilic attack by gold cations is the most utilized application of gold in organic chemistry. The first of these experiments was carried out in 1976 by Thomas and coworkers,^{7a} who succeeded in the oxidation of phenylacetylene to the corresponding ketone through addition of water to the alkyne. Efficient catalysts for the addition of O-nucleophiles to alkynes have since been developed and optimized,^{7b} with the best examples achieving turnovers of over 15,000 min^{-1} .⁸ Catalytic inter- and intra-molecular condensations of amines with carbonyl groups was also demonstrated. Activation of allenes (and even isolated alkenes) towards nucleophilic attack soon followed, and many intra-molecular cyclization examples have appeared in the literature, leading to novel and facile syntheses of heterocyclic compounds such as indoles, naphthalenes, and coumarins.^{1a}

Gold has been shown to functionalize sp , sp^2 , and even sp^3 hybridized carbon atoms. Surprisingly, although gold-aryl species and their stoichiometric reactions have been explored since 1931, catalytic turnover for functionalization of arenes (as an alternative to pre-halogenation) was not achieved until 2001.^{5,6} Activation of β -diketones followed, and in 2004 it was shown that (with a powerful enough oxidizing agent) cationic gold can even catalyze the oxidation of methane (CH_4) to methanol (CH_3OH).⁴ Exotic intramolecular variations of these types C-H activation have since been demonstrated.^{1a-c}

Much insight into the behavior of the gold metal center has been generated even within the last two years; including the first isolated example of an analog of a gold-catalyzed reaction intermediate,⁹ as well as unprecedented evidence for the in-situ reduction of Au^{I} during the catalytic cyclization of allenes.³ In 2005, a breakthrough paper by Gevorgyan and coworkers demonstrated a regiodivergent synthesis of furans, with catalysts of different oxidation states generating different products from the same starting material.¹⁰

Gold has rich homogeneous chemistry, and interest in this field is growing. Many questions remain as to what transformations are possible and how the redox properties of gold can be controlled and exploited. Nevertheless, the fruitful chemistry of gold has been noticed, and new discoveries and innovations are sure to follow.

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