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Homogeneous gold catalysis: The role of protons

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Abstract

Recent reports have shown that some homogeneous gold catalyzed reactions might in fact be proton-catalyzed. Here, the knowledge on the role of Bronsted acids in gold-catalyzed reactions is summarized.

Keywords: Acids; Gold; Homogeneous catalysis

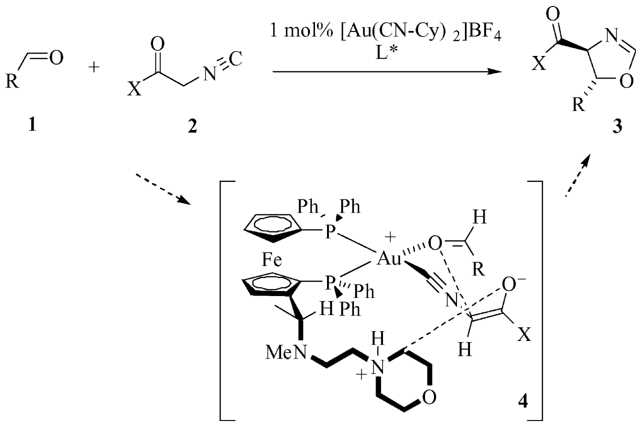
1. Introduction

Bond's [1], Haruta's [2] and Hutching's [3] pioneering work from the 1970s and 1980s caused an avalanche of publications on heterogeneous gold catalysis. In homogeneous catalysis, the development was delayed by about 10 years, early work between 1986 and 2000 of Ito and Hayashi [4], Utimoto [5], Teles [6] as well as the Hashmi group [7,8] also initiated an impressive growth of activity, which in terms of the total numbers of publications per year has yet only reached 5% of the total numbers of publications on heterogeneous gold catalysis. Recent reviews have summarized this development of homogeneous gold catalysis [9–13].

Parallel to the progress in homogeneous gold catalysis there has always been a discussion on the role of protons in these reactions, occasionally the protons were suspected to be the true catalyst. Here we want to discuss todays knowledge on that critical issue.

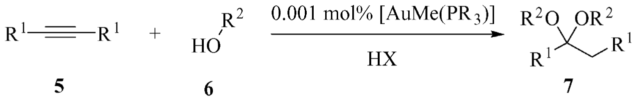
2. Proton transfer, protic media, aqueous media

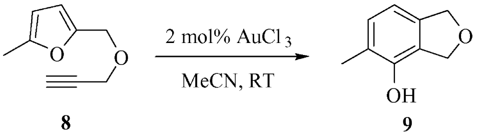
Already the first examples mentioned above involved a proton transfer, in the Ito–Hayashi asymmetric aldol reaction [4] it is assumed that the isocyanoacetate 2 is converted to the nucleophile by a deprotonation.



Hydrogen bonds of the ammonium-group in the intermediate 4 are assumed to be a crucial factor for the chirality transfer from the enantiomerically pure phosphane ligand to the product [14,15].

The nucleophilic additions to alkynes 5 proceeded in alcohols or even aqueous solvents [5]. Teles used acidic conditions to convert in situ the pre-catalyst [AuMeL] to the cationic active gold species by loss of methane [6] and non-absolute solvents, occasionally with added alcohol or water, were used in the synthesis of phenols 9 [8].





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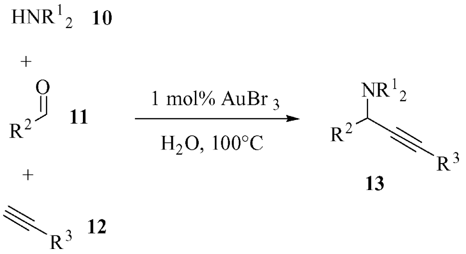
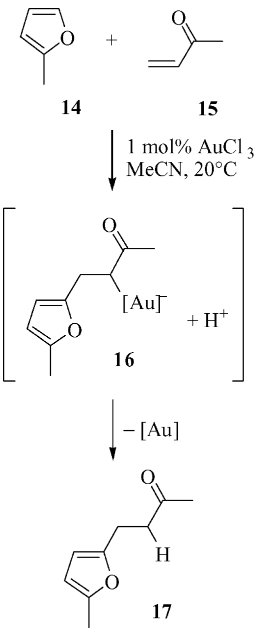
Homogeneous gold catalyzed reactions can even be conducted in water, Li et al. have well documented that for the three-component reaction of amine 10, aldehyde 11 and alkyne 12 to the proparglic amine 13 [16–18], work which was confirmed by work of Wong and Che [19].



Toste coined the term "open flask conditions" for these types of catalysts that are not dependent on the exclusion of humidity or oxygen [20].

Still, one should be aware that in any catalysis proceeding through organogold-intermediates with carbon-gold single bonds, at some point the latter has to be cleaved by a protodeauration step [10,13], which for example, in enolate complex intermediates 16 is faster than a β-hydrogen elimination [21].



This is in accordance with earlier reports by Baker and Westcott on the diborylation of styrenes [22]. The instability of gold hydrides [23,24] is probably responsible for the low tendency for a β-hydrogen elimination in such organogold intermediates.

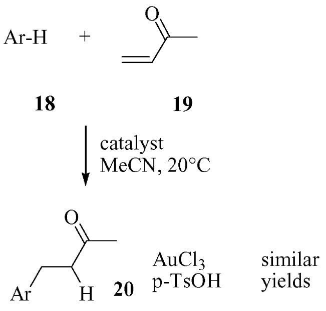
3. Catalysis by gold versus catalysis by protons

The isolobal analogy of Lewis, Stone, Hoffmann and others early pointed out the equivalency of R_3PAu^+ and H^+ [25–28]. This was successfully used in the synthesis of the gold analogues of different protonated molecules like $(R_3PAu)_3O^+$, the "gold form" of H_3O^+ [29].

Does this analogy mean that in gold catalyzed reactions the gold catalyst can be replaced by the significantly cheaper proton? Recent reports in the literature seem to support that assumption, but a closer look shows that for other reactions the investigators have done their homework and conducted the proper control experiments.

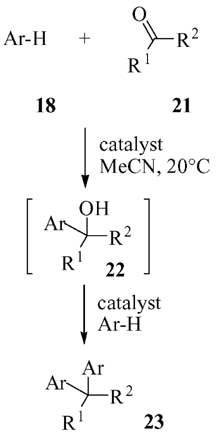
3.1. Reactions with protons as the active species

The first result of similar catalytic activity of gold-complexes and strong acids concerned the hydroarylation of α,β-unsaturated ketones 18, as Dyker and Hashmi reported [30]. It is conceivable that $AuCl_3$ and water form a strong Bronsted acid with a gold-complex as the counter ion. But not for every arene both types of catalysts provided the same yield [31].

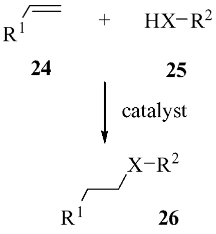


Carbonyl:

The next reports concerning such system by Nair on the reaction of the three-fold reaction of α,β-unsaturated aldehydes [32] and the two-fold reaction of aryl aldehydes with electron-rich arenes [33] claimed $AuCl_3$ to be the catalyst. But experiments of Hashmi et al. have proven that a catalytic amount of *p*-toluenesulphonic acid shows an identical activity. Furthermore, not only aldehydes but also ketones like acetone react. The investigation proved that the initially formed benzylic alcohol 22 reacts faster with the second equivalent of the electron-rich arene than the carbonyl group of the starting material. This shows that different "gold-catalyzed" reactions of activated benzylic alcohols [34,35] might be Bronsted acid-catalyzed, too.



The latest observation of that kind comes from the groups of He [36] and Hartwig [37]. Both groups found, that instead of the previously used gold catalyst [38], for hydroamination of alkenes 24 triflic acid can be used and quite similar results are obtained. The same was true for the addition of different *O*-nucleophiles. For the hydroamination of alkenes this was not too surprising, Bergman et al. had demonstrated one year before that triflic acid catalyzes this reaction [39].

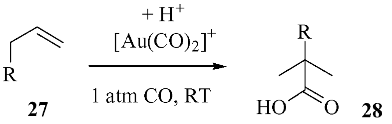


24 **25** **26**

These few examples are the only reactions in which today the gold catalysts can be substituted by strong Bronsted acids. But, protons can also play a different role in gold catalysis, not being the true catalyst but being a co-catalyst, which is described in the next section.

3.2. Reactions with protons as co-catalysts

There are much more examples for this case than for the previous one. The collaboration of a strong Bronsted acid and gold catalysts was first invented by Xu and coworkers in his work on the low-pressure Koch-Haaf reaction [40,41] and the participation of the gold catalyst is clearly indicated by the significantly lower pressure (1 atm of CO at room temperature instead of the usual 100 atm).

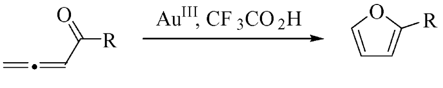


27 **28**

Then Teles et al. [6] reported that for the conversion of **5** and **6** to **7** a strong Bronsted acid not only serves as a co-catalyst, the TOF increases in an almost linear fashion with the concentration of H^+. For the hydration of alkynes a similar beneficial influence of strong acids was reported by Hayashi, Tanaka et al. [42] as well as Laguna et al. [43]. The use of $BF_3{\cdot}OEt_2$ in aqueous solution as a co-catalyst ultimately also means Bronsted acid co-catalysis [44]. A recent example was reported by Krause et al. [45].

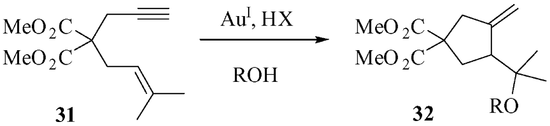
Unlike in the hydroamination of alkenes **24** mentioned above, control experiments of Hayashi, Tanaka [46] et al. prove that acidic promoters are crucial for the gold-catalyzed hydroamination of alkynes, neither the gold complexes nor the acid alone were active.

The cycloisomerization of allenyl ketones **29** to furans **30** [7] was very efficiently (TON 8300) catalyzed by a gold(III)–porphyrin complex, here, trifluoroacetic acid was essential, with TsOH or acetic acid lower yields were obtained by Che et al. [47]. They assumed that the acid is essential for a fast proto-demetallation step.



29 **30**

In the enyne-alkoxycyclization (**31** to **32**), Echavarren et al. also described the use of acidic co-catalysts [48].



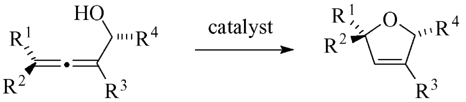
31 **32**

The use of stoichiometric amounts of TsOH or AcOH in the catalytic enantioselective Coniaene reaction is another example of acidic promoters for gold-catalyzed reactions, as Toste and Corkey reported [49]. The C,H-activation of methane occurs in strongly acidic medium only [50].

In the context of this chapter reaction, gold-catalyzed reactions of carboxylic acids must also be mentioned [51], by nature, it is unclear whether the acids do accelerate the reaction. The same applies for the 2-pyridine-carboxylate ligands with another carboxylic acid substituent in the phenol synthesis [52].

3.3. Reactions not catalyzed by protons

Only a few investigations did specifically address this point. In thorough control experiments Hashmi et al. excluded a possible Bronsted or Lewis acid-catalysis of the phenol synthesis (**8** to **9**) [8]. Krause and Hoffmann-Röder [53] could show that for some examples of the cyclization of α-hydroxyallenes 33 to 2,5-dihydrofurans 34 gold catalysts are superior to Bronsted acid catalysts.



33 **34**

For domino-processes with isobenzopyrilium cations Dyker et al. [54] could also exclude Bronsted acid catalysis by control experiments with $HClO_4$, HCl, TsOH and CF_3CO_2H. The aerobic oxidation of glucose with a gold catalyst was proven to proceed best under basic conditions [55]. The presence of acid can also shift the product ratio, for example, by hydrolysis of the product of the gold-catalysis as described by Zhang and Wang [56].

4. Conclusions

A few reactions, previously reported to be gold-catalyzed, are in fact, proton-catalyzed. There are a number of examples for Bronsted acids serving as co-catalysts and promoters, and this needs to be investigated more thoroughly. While some thorough researchers have excluded proton-catalysis for their reactions, for other reactions this has not always been done. In the future, everyone working in the field of homogeneous gold catalysis should regularly conduct such control experiments to explore possible Bronsted acid catalysis or co-catalysis.

Acknowledgement

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