An Eldorado for Homogeneous Catalysis?

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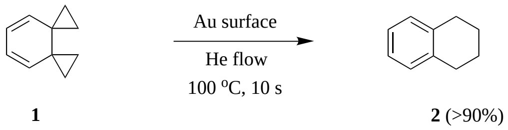
Nach Golde drängt, am Golde hängt doch alles.
Goethe: Faust I[1]

Gold has always been the embodiment of something extremely valuable and evidently holds a fascination deep rooted in the cultural history of mankind. As is generally known, the endeavor to produce gold synthetically plays a significant role in the development of chemistry over a long period.[2] In catalysis research gold has to date lived in the shadows, which perhaps lies in the preconceived opinion that gold is expensive and inert.

Indeed gold is the most precious metal and was considered for a long time to be extremely chemically inert particularly in reactions with nonmetals such as hydrogen, carbon, and oxygen.[3] Through successes in heterogeneous catalysis, which are also of economic significance, this assessment has fundamentally changed:[4a] Tetrachloroauric acid on active charcoal is currently the best catalyst for the hydrochlorination of ethyne, and gold clusters (diameter 2–5 nm) on iron oxide are particularly highly active for the oxidation of carbon monoxide.[4b] Other possible applications in environmentally relevant fields are the oxidative decomposition of halogenated hydrocarbons and the reduction of nitrogen monoxide with carbon monoxide and hydrogen to give nitrogen, carbon dioxide, and water.[4c,d, 5]

Surprisingly, gold can also catalyze skeletal rearrangements of hydrocarbons: For instance, the isomerization of 2,2-dimethylbutane to *n*-hexane has been achieved by Schmid with the aid of Au_{55} clusters on titanium dioxide,[4c, 6] and the aromatization of the dispirocycle **1** to tetrahydronaphthalene **2** was achieved by de Meijere et al. in a reactor with gold surface at 100 °C in a few seconds (Scheme 1).[7]

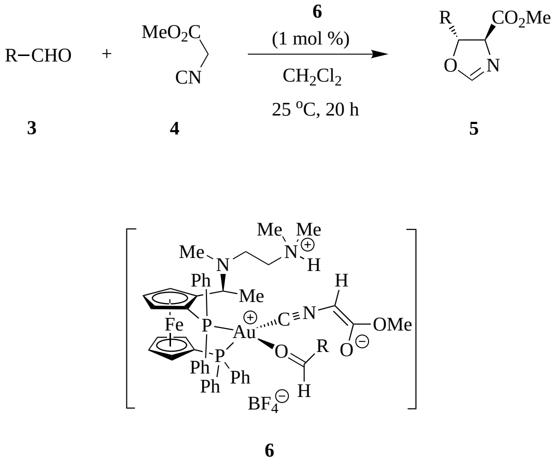


Scheme 1. Gold-catalyzed skeletal rearrangement of a strained hydrocarbon.

In the field of homogeneous catalysis only a few gold-catalyzed processes are known to date, which, however, are characterized by the need for extremely small amounts of gold salts. In view of the high catalytic activity of gold salts, therefore the higher price for gold salts is relativized in comparison to that for the corresponding palladium and ruthenium compounds.

The new gold chloride catalyzed C–C and C–O couplings by Hashmi et al.[8] provide a fitting opportunity to highlight the current status[9] of homogeneous catalysis with gold salts and to show the potential for further development.

A first landmark in gold catalysis was made by Ito and Hayashi when they carried out an asymmetric aldol reaction in 1986:[10] Aldehydes **3** were treated with isocyanoacetate **4** to give oxazolines **5** (Scheme 2). The active catalyst is a ferrocenylphosphanegold(I) complex (structure **6** sketches the complex with coordinatively bound reactants). In general near quantitative yields and diastereo- and enantioselectivities of greater than 90 % in favor of the 4*S*,5*R*-configurated *trans* product **5** are achieved in this reaction. For instance, this method facilitates a two-step synthesis of the naturally occurring amino acid *threo*-3-hydroxylysine from 4-phthalimidylbutanal as the aldehyde component **3**.[10d]



Scheme 2. Synthesis of oxazolines by a gold-catalyzed asymmetric aldol reaction.

Also in the activation of alkynes for nucleophilic attack, gold salts prove to be soft, exceptionally carbophilic Lewis

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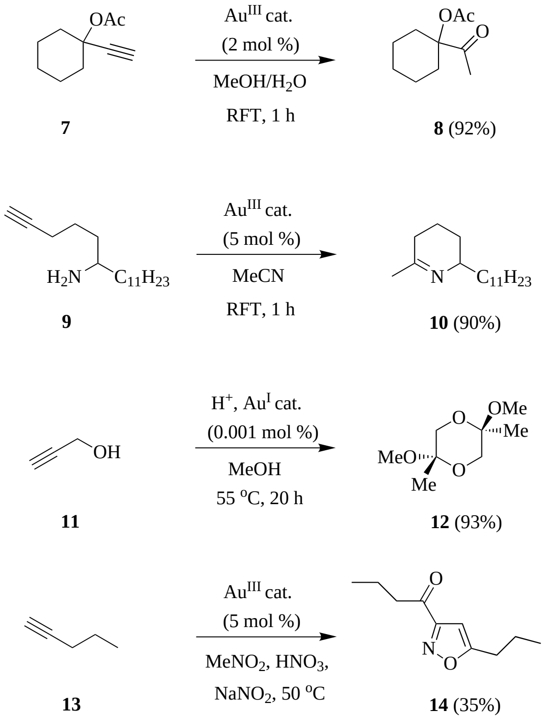
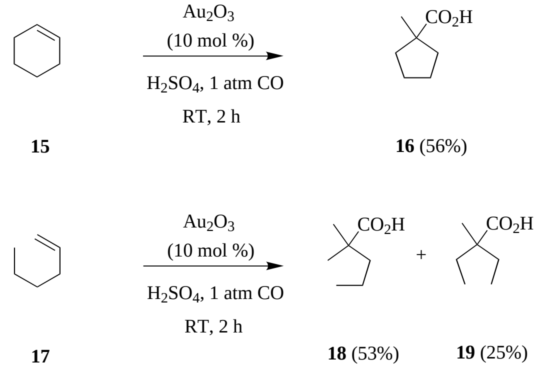
acids, as confirmed by the examples in Scheme 3.[11] According to Utimoto and Fukuda both the addition of water as well as of amines to alkynes are catalyzed by gold(III) salts, in particular sodium tetrachloroaurate; ketones such as **8** and imines such as the ant toxin **10** are obtained as products in excellent yields.[11a–e] In the cyclization to give the 1,4-dioxane **12** developed by Teles et al., the short reaction time and use of extremely small amounts of catalyst, in this case methyl(triphenylphosphane)gold(I), are particularly impressive.[11d,e] In the isoxazole synthesis according to Gasparrini et al. gold salts catalyze the addition of HNO_3 to alkynes; under the oxidative reaction conditions nitrile oxides are formed, which undergo a cycloaddition to give final products such as **14**.[11f]



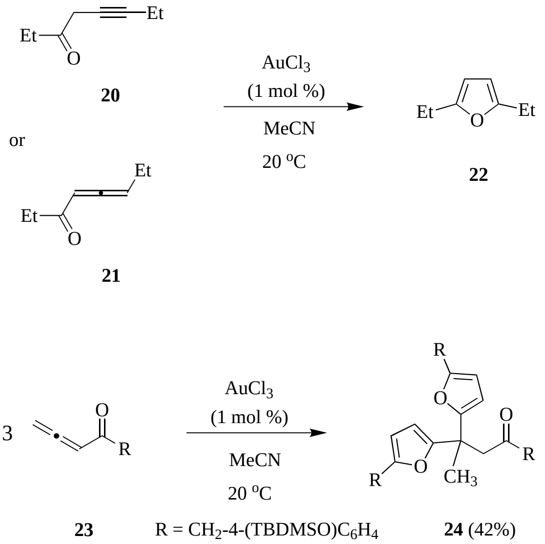
Scheme 3. Gold-catalyzed additions to alkynes. Ac = Acetyl, RFT = reflux temperature.

In the gold-catalyzed carbonylation of olefins according to Xu et al., gold(I) carbonyl complexes are considered as active catalysts; this reaction proceeds already at room temperature in concentrated sulfuric acid at a CO pressure of 1 atm and leads after acid-catalyzed skeletal rearrangement to tertiary carboxylic acids such as **16**, **18**, and **19** (Scheme 4).[12]

In a more recent publication Hashmi et al. reported that propargyl ketones such as **20** and allenyl ketones such as **21** can be cyclized to furans such as **22** in reactions catalyzed by gold(III) chloride (Scheme 5).[8] This type of reaction had already been described as a silver(I)-catalyzed process by Marshall et al. (typical reaction conditions: 20% catalyst and a reaction time of several hours);[13] however, gold salts are evidently significantly more active catalysts, which is confirmed by the fact that quantitative yields are obtained after a few minutes at room temperature and that only 1 mol% catalyst is required.



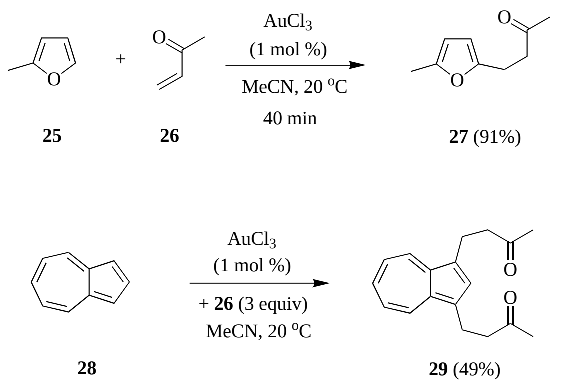
Scheme 4. Gold-catalyzed carbonylation of alkenes.



Scheme 5. New gold-catalyzed C–C and C–O coupling reactions developed by Hashmi et al. TBDMS = *tert*-butyldimethylsilyl.

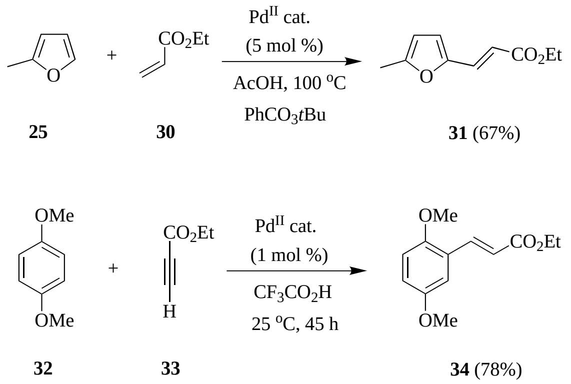
Of particular interest is the observation that in certain cases domino products such as **24** are formed: After the formation of the furan, evidently a double Michael-like addition of these intermediates to the remaining starting material **23** can take place at the unsubstituted 5-position.

Preliminary experiments to investigate the potential and limits of such additions in the presence of gold salts also confirm the applicability to the functionalization of other electron-rich arenes (Scheme 6): Besides furans, azulene **28** and di- and trialkoxybenzene are suitable as nucleophiles for the reaction with α,β-unsaturated carbonyl compounds.[14] For instance, 2-methylfuran (**25**) reacts at the reactive 5-position with methyl vinyl ketone **26** to give the addition product **27**, and for azulene **28** twofold alkylation occurs to give **29**. In contrast to the catalysis of these reactions with hydrochloric acid and other protonic and Lewis acids,[15] gold(III) chloride in acetonitrile guarantees sufficiently mild reaction conditions so that the otherwise typical decomposition and polymerization reactions, particularly in the case of furans, are suppressed. On the basis of the results obtained so far in these investigations, it is considered that the acidic hydrate of gold(III) chloride or tetrachloroauric acid function as protic catalysts.[14]



Scheme 6. Michael-like additions of electron-rich arenes to methyl vinyl ketone.

Similar products are obtained from reaction sequences consisting of electrophilic metalation of electron-rich arenes and subsequent C–C coupling by carbometalation, which to date was a domain of palladium catalysis (Scheme 7).[16, 17] As shown by the coupling reaction of 2-methylfuran (**25**) with the acrylate **30** developed by Tsuji and Nagashima,[18] owing to the pronounced tendency of alkylpalladium intermediates for β-H elimination the unsaturated product **31** is obtained; the generally associated reduction of the active palladium(II) catalyst necessitates the addition of an oxidizing agent such as a peroxy acid ester. Very recently Fujiwara et al.[19] reported that correponding coupling reactions with alkynes such as **33** in trifluoroacetic acid as solvent proceed already at room temperature with reaction times of several hours.



Scheme 7. Palladium-catalyzed C–C coupling reactions by C–H activation of electron-rich arenes.

Whether gold salts can also metalate electron-rich arenes under C–H activation will require detailed reactivity studies. It has already been shown that gold salts display considerable catalytic activity under moderate conditions; thus an extensive development of gold catalysis with numerous new applications is anticipated.

[1] A demand on catalyst research from Faust II: *Man greife nun nach … Gold, dem Greifenden ist meist Fortuna hold.*

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