Review

Silver-free Gold(I) Catalysts for Organic Transformations

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The majority of gold(I) catalysts employed in organic transformations in homogeneous systems are presently generated *in situ* by reactions of gold halides AuX or their 1 : 1 complexes [(L)AuX] with silver salts AgY (X = Cl, Br; L = R_3P, NHC, tht *etc.*; Y = BF_4, PF_6, SbF_6, OSO_2CF_3, $OC(O)CF_3$ *etc.*). This usage of silver salts is not only economically unfavorable, but also has several practical disadvantages regarding *inter alia* the thermal and photochemical stability of the reaction mixtures, problems of inexact stoichiometries, difficulties in separation and recycling, and cooperative effects due to Au-Ag metallophilic interactions which can induce a different course of the reactions. There is therefore a move towards syntheses of silver-free homogeneous gold(I) catalysts. The past and current approaches and opportunities are summarized in this review.

Key words: Gold Catalysis, Silver-free Gold Catalysts, Silver Salts, Gold Complexes, Homogeneous Catalysis

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Abbreviations

NHC:	nitrogen heterocyclic carbene
tht:	tetrahydrothiophene
Tf:	trifluoromethylsulfonyl
TfO:	trifluoromethylsulfonate
Tf_2N:	bis(trifluoromethylsulfonyl)imide
Ts:	*p*-toluene-sulfonyl
TsO:	*p*-toluenesulfonate

1. Introduction

Homogeneous catalysis of organic transformations by gold(I) and gold(III) complexes is currently one of the rapidly developing areas of Organic Synthesis. It is also one of the most promising fields of gold chemistry [1]. The pertinent literature is expanding at a high rate with reviews listing hundreds of new contributions appearing at roughly a quarterly frequency [2 – 10]. While in earlier work it appeared that the choice of catalysts employed was determined simply by the stock of gold chemicals available on the shelf or through commercial sources [gold(I) and

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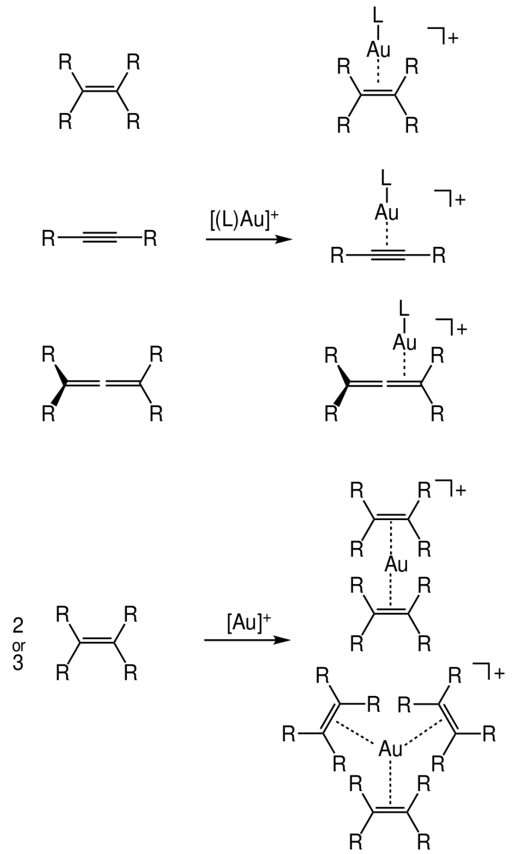


Scheme 1.

gold(III) halides and pseudohalides, tetrachloroauric acid, alkali tetrachloroaurates *etc.*], the last decade has seen a more refined approach orientated more and more at the possible mechanisms of the catalysis.

This approach is still more difficult for gold(III) catalysts, where in the majority of cases an *in situ* reduction to gold(I) species cannot be excluded. By contrast, the mechanism of at least some of the processes catalyzed by gold(I) compounds is much better understood. Some of the elementary steps determining not only the relative rates, but also the observed chemo-, regio- and stereoselectivities could be defined and confirmed by experimental data and theoretical studies [2–10].

From these investigations it has appeared that for the most common substrates – which include mainly alkenes, allenes, alkynes, arenes, and nitriles – the catalytic process is initiated by the electrophilic attack of the unsaturated substrate by a free or a mono-coordinated gold(I) cation, $[Au]^+$ and $[LAu]^+$, respectively, where L represents a conventional two-electron donor ligand. The key step in the process of gold(I) catalysis concerned is thus the formation of a π-complex of the substrate with an $[Au]^+$ or an $[LAu]^+$ cation, which are considered as “soft, carbophilic π-acids”. This attack may simply lead to a transition state, but also to a detectable or even isolable intermediate, most likely of a 1 : 1 or 2 : 1 stoichiometry, although other molecular ratios are not fully excluded [11] (Scheme 1). This first step is believed to be followed by a “slippage” of the metal atom towards one of the two carbon atoms involved to give way for the approach of the nucleophile at the thus activated C=C, C≡C or C≡N multiple bond.

2. Potential sources of $[Au]^+$ cations

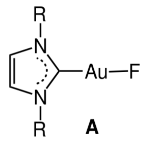
In order to release significant concentrations of $[Au]^+$ cations to a solution of a gold(I) complex, the catalyst is required to have only loosely coordinated ligands L and X^- as in cations $[Au(L)_2]^+$, in molecules $[(L)AuX]$ or in anions $[AuX_2]^-$. As predicted from simple rules of donor-acceptor qualities, ligands L which are loosely bound to “soft” gold(I) are mainly those with “hard” donor atoms like F, O and N (Scheme 2).

$$[(L)Au(L)]^+ \overset{\pm L}{\rightleftharpoons} [(L)Au]^+_{solv} \overset{\pm L}{\rightleftharpoons} [Au]^+_{solv}$$

$$[(L)AuX] \overset{\pm X^-}{\rightleftharpoons} [(L)Au]^+_{solv}$$

Scheme 2.

For a long time, gold(I) fluoride complexes had been elusive compounds with the first stable example of the type [(L)AuF] isolated and fully characterized by Gray, Sadighi *et al.* only very recently [12] (**A**). In this complex, a strongly bound N-heterocyclic carbene, L = NHC, prevents any significant dissociation into $[Au]^+$



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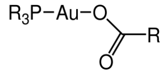

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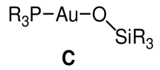

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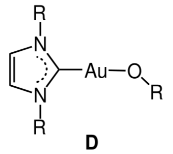

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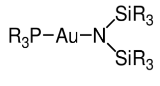


E

cations. Ligand redistribution into homoleptic ions $[AuL_2]^+$ and $[AuF_2]^-$ has also not been observed. Homoleptic complexes $[AuF_n]^{(n-1)-}$ are also unknown. The main reason for the instability of such species is the thermodymanic preference for disproportionation into metallic gold and gold(III) complexes. Since to date no complexes with ligands L other than a carbene have been observed, the choice of gold(I) fluorides is still very limited. Note that the existence of a donor-free molecule AuF has only been confirmed in the gas phase [13].

The situation is similar with hydroxy, alkoxy, aryloxy, siloxy, and carboxylate complexes of gold(I), for which no homoleptic complexes $[Au(OE)_n]^{n-1}$ are known (E = hydrogen, alkyl, aryl, silyl, acyl *etc.*) [14]. Complexes of the type [(L)AuOE] were also discovered rather late. With L = R_3P as the auxiliary ligand, *e. g.* an acetate $[(Ph_3P)AuOAc]$ (**B**) was isolated in 1969 [15], and a trimethylsiloxide $[(Ph_3P)AuOSiMe_3]$ (**C**) in 1970 [16], followed by the first alkoxides and hydroxides with L = NHC [17] in very recent work by the group of Nolan (**D**, for this work and related studies on *oxo* and *hydroxo* complexes see below). In the course of the early work, the bis(trimethylsilyl)amide $[(Ph_3P)AuN(SiMe_3)_2]$ (**E**) with a then rare covalent Au-N bond was also prepared [16].

With neutral nitrogen donors, homoleptic complexes are more common, with $[Au(NH_3)_2]^+$ (**F**) as an early, prominent example published by Mingos *et. al.* [18]. Salts with this cation are stabilized in the solid state and probably also in solution by interionic or cation-solvate hydrogen bonding. Another group of homoleptic compounds with rather labile N-Au bonds, also made readily available by Mingos *et al.*, but also by Bonati and Minghetti, are salts with the cations $[Au(NCR)_2]^+$ (**G**) containing nitrile ligands [19, 20]. It appears that to the present time the catalytic activity of the salts with ammonia has not been probed, however, some pioneering work with the alkylcyanide complexes has been documented by Hayashi *et al.* as early as 1986 [21, 22]. In these studies, $[(c\text{-}C_6H_{11}CN)_2Au]^+\ BF_4^-$ was employed in combination with chiral ferrocenyl-bis-phosphines for catalytic asymmetric aldol reactions using aldehydes and isocyanoacetates to give chiral oxazolines with high yields and high enantiomeric excess. It is fair to assume that in a first step of the reactions the alkylcyanide ligands are replaced by the phosphine to afford an active chiral gold(I) complex which confers its stereochemistry onto the substrates.

$$[\mathrm{H_3N{-}Au{-}NH_3}]^+\ X^-$$

F

$$[\mathrm{R{-}C{\equiv}N{-}Au{-}N{\equiv}C{-}R}]^+\ X^-$$

G

$$[\mathrm{O{\equiv}C{-}Au{-}C{\equiv}O}]^+\ X^-$$

H

Finally, a cationic gold(I) dicarbonyl complex $[Au(CO)_2]^+$ (**H**) has been introduced by Xu, Souma *et al.* as a catalyst for the carbonylation of olefins. To this end, commercial gold(III) chlorides are converted with alkali hydroxide into Au_2O_3 which is then dissolved in sulfuric acid and treated with CO gas. The solutions thus obtained show the IR absorptions of both $[Au(CO)]^+$ and $[Au(CO)_2]^+$ depending on concentration and pressure. Under CO pressure the solutions catalyze the addition of CO to terminal olefins yielding tertiary carboxylic acids in high conversions [23].

3. Potential sources of $[LAu]^+$ cations

Regarding the above mentioned mechanistic concept (Scheme 1), it has become obvious that an optimized or ideal gold(I) catalyst should probably best be a source of $[(L)Au]^+$ cations. In the catalyst precursor this cation could be associated with a suitable anion X^- in the form of a salt, or attached to an anion through highly polar covalent bonding. Ideally, such a salt $[(L)Au]^+\ X^-$ or a molecule [(L)AuX] should be soluble in the usual organic solvents and reasonably stable, both thermally and towards light and hydrolysis, to allow convenient handling under standard laboratory conditions.

Cations $[(L)Au]^+$ with only mono-coordinate gold atoms (coordination number 1) must be considered strong electron acceptors seeking any kind of saturation by even poor donors. Therefore, in the solid state there must be close contacts to counterions or solvate molecules. Otherwise, the salts will not be stable and decompose upon any attempts to isolate the catalyst from solution. Note that occasional reports of structures with only mono-coordinate gold(I) centers could not always be confirmed [24]. In solution, it is the role of the solvent molecules to saturate the acceptor needs of the cation.

If the anion X^- has any significant donor capacity, it becomes attached to the metal cation through polar covalent bonding. However, with this bonding becom-

$$[(L)AuX] + AgY \xrightleftharpoons{-\ AgX} [(L)Au]^+ Y^-$$

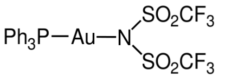
$$X = Cl, Br; Y = BF_4, PF_6, SbF_6, OTf$$

Scheme 3.

ing too strong, the catalytic activity of the cation is lost.

In the course of the recent development of homogeneous gold(I) catalysts is has become common practice to introduce the weakly coordinating anions X by reacting a conventional gold(I) halide complex [(L)AuX] (with X = Cl, Br) in an organic solvent with a *silver salt* of the complex acids HY = HBF_4, HPF_6, $HSbF_6$, and $HOSO_2CF_3$ (HOTf) with their extremely poor donor anions Y^-. In this way solutions can be obtained which formally contain the reagents $[(L)Au]^+ Y^-$ as contact or solvent-separated ion pairs, but these solutions are not long-term stable, and attempts to isolate the catalyst (after separation from the AgX by-product by filtration) lead to decomposition [2–10, 25] (Scheme 3).

For this reason, and following up the above line of rationalization and pertinent theoretical models (from early examples [26] to very recent contributions [27]), several molecular gold complexes of the type [(L)AuY] have been designed, where Y is a good leaving group, but still lends sufficient stability to the molecular structure. The most successful candidates are compounds with the bis(trifluoromethylsulfonyl)-imidate group, $-N(OSO_2CF_3)_2$ or $-NTf_2$ (“triflimide”), introduced by Gagosz *et al.* and used for complexes with L = PR_3 (**I**) and L = NHC (**J**) [28], and very recently the simple fluoride F [12] (**A**) and hydroxide OH [17] for L = carbene (**K**). Together with a number of more specialized alternatives (see also below), these catalysts are the basis of new synthetic protocols which now have allowed carrying out the preparations in a silver-free medium.


$Ph_3P{-}Au{-}N(SO_2CF_3)_2$

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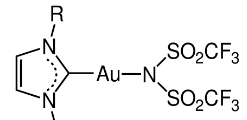

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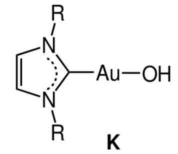


K

The following brief overview of related work published in the last few decades summarizes and reflects the most important discoveries and the subsequent developments towards these optimized catalysts.

4. A brief history of the development of optimized $[LAu]^+X^-$ and [LAuX] catalysts

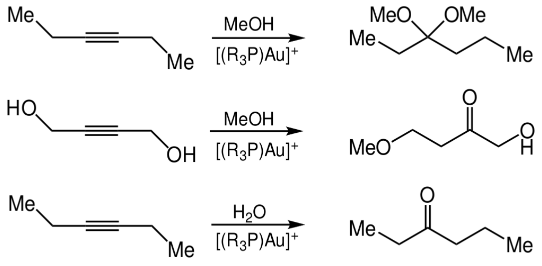
In a recent review is has been shown that early work by the groups of Chalk, Hüttel, Wittig, and van der Kerk in the 1960s and 1970s has led to the isolation of some olefin complexes of AuCl and AuBr, but no evidence was obtained for any efficient gold(I) catalysis of reactions of these olefins [11]. It is interesting to note that subsequent studies by Komiya and Kochi had already included the first olefin complexes of $Au(OSO_2F)$ and $Au(OSO_2CF_3)$ featuring anions with extremely poor donor capability for Au(I), but again no catalytic activity was observed. All these complexes had low thermal, photochemical and chemical stability which clearly discouraged experimentalists after their exploratory studies [29].

$$[(R'_3P)AuR] + HZ \xrightarrow{-\ RH} [(R'_3P)Au]^+ Z^-$$

$$R' = aryl, R = alkyl; Z = R'SO_3, HSO_4$$

Scheme 4.

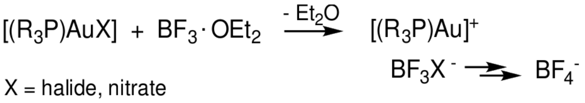
It was only in the late 1990s that work was resumed, mainly by the group of Teles *et al.* in industrial laboratories, using [(L)AuX] complexes with L representing tertiary phosphines. In a series of ground-breaking experiments it has been shown that complexes $(R_3P)AuMe$ can be used as catalyst precursor molecules which upon treatment with a mineral acid HX or H_2Y in an organic solvent afford methane and solutions of the catalytically active compounds $[(R_3P)AuX]$ or $[(R_3P)AuYH]$ (Scheme 4). These products can also be written as solvated salts



Scheme 5.

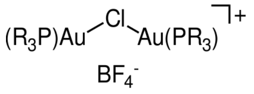
$[(R_3P)Au]^+\ X^-$ and $[(R_3P)Au]^+\ YH^-$, where X = ONO_2, CF_3COO, $MeSO_3$, and BF_4, and YH = SO_4H *etc.* [30]. Several model reactions were carried out successfully with these catalysts (Scheme 5).

The work was extended by demonstrating that the solutions of the same catalysts can be generated *in situ* from the halide complexes $[(R_3P)AuCl]$ upon treatment with silver salts AgX (Scheme 3). The tetrafluoroborates (X = BF_4) were also obtained from reactions of the halides or the nitrates with $BF_3 \cdot OEt_2$ (Scheme 6).



Scheme 6.

Interestingly, work by Hashmi *et al.* and by Toste *et al.* has later also disclosed that di- and trinuclear chloronium and oxonium complexes, respectively, with formulae such as $[(R_3P)AuClAu(PR_3)]^+$ (**L**) and $\{O[Au(PR_3)]_3\}^+$ (**M**), can be employed as sources of $[(R_3P)Au]^+$ cations (below).



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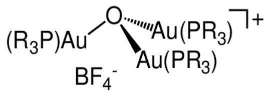
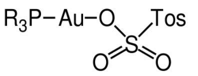


M

As phosphines or phosphites, the R_3P ligands with R = Et, Ph, 4-F-C_6H_4, MeO, PhO were tested and shown to have increasing activity along this series, while Ph_3As gave the poorest catalyst investigated in the addition of MeOH to propyne as a model reaction (Scheme 5). However, the active phosphite-containing catalysts proved to be less stable than those with tertiary phosphines [30].

Thus a short communication of only 4 pages had provided us in 1998 with an almost full scope of new opportunities for the preparation of novel, efficient catalysts based on the mono-coordination of tertiary phosphines to gold(I) cations. It should be observed, however, that none of the catalysts of the types $[(L)Au]^+\ X^-$ had actually been isolated. The solutions containing the $[(L)Au]^+$ cations also contained either the excess acid or the silver compound generated in the metathesis reaction with the silver component (Schemes 3 and 4) [30].



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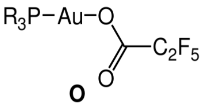

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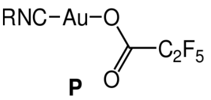
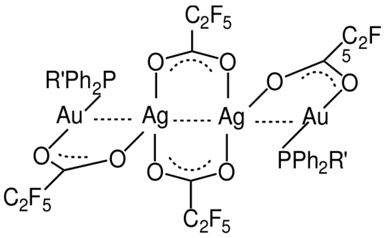


P

Only the ethylsulfonate and tosylate $[(Ph_3P)AuOSO_2Et]$ and $[(Ph_3P)AuOSO_2C_6H_4\text{-}4\text{-}Me]$ [31], the pivalate $[(Ph_3P)AuOC(O)^tBu]$, and the perfluorocarboxylates $[(Ph_3P)AuOC(O)CF_3]$ and $[(R_3P)AuOC(O)C_2F_5]$ (R = Me, Ph; R_3 = (4-Me_2N-C_6H_4)Ph_2) [32] have later been crystallized and the structure of the tosylate (**N**) and the perfluoropropionate $[(Me_3P)AuOC(O)C_2F_5]$ (**O**) determined. The isocyanide complex [(*c*-hexNC)AuOC(O)C_2F_5] (**P**) could also be crystallized, but is less stable than the analog with the Ph_3P ligand [33]. Though all of these complexes are prepared *via* the silver salt route, their crystallization allows a complete elimination of any traces of silver in the products.

However, in experiments carried out with a stoichiometry suitable for mixed metal complexes, novel Au/Ag complexes were obtained. This result has provided evidence of the high affinity of gold(I) complexes for silver(I) complexes in the presence of tertiary phosphines and carboxylate ligands. One of the products of which the crystal structure has been determined has the composition $[(4\text{-}Me_2N\text{-}C_6H_4)Ph_2P]_2Au_2Ag_2[OC(O)C_2F_5]_4$ and contains chains of metal atoms Au-Ag-Ag-Au connected *via* metallophilic contacts and supported by carboxylate bridges (**Q**) [33].



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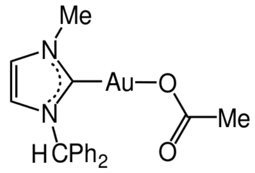

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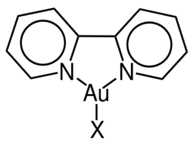

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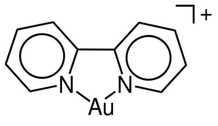

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Finally, it was only in the footnote (16) of the paper published by Teles *et al.* in 1998, that the use of an NHC ligand was also mentioned [30]. With NHC = 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene a catalyst was produced which showed higher activity than the standard with Ph_3P. It was generated from the (NHC)AuCl complex, probably *via* the silver route, because the (NHC)AuMe and $(NHC)AuONO_2$ complexes could not be obtained.

In 2003, a (NHC)AuCl complex was treated with silver acetate by Herrmann *et al.* to give the corresponding (NHC)AuOC(O)Me compound (**R**), which could be isolated, and the structure of which could be determined. This compound was inactive in the hydration of 3-hexyne, and $BF_3 \cdot OEt_2$ did not activate the system, but moderate yields were finally obtained with $(C_6F_5)_3B$ as a co-catalyst [34]. In 2005, additional examples of the type (NHC)AuX were prepared and have been structurally characterized, including X = acetate, nitrate, azide, cyanide, cyanate, thiocyanate, selenocyanate, and methyl [35]. Their catalytic activity has as yet remained unexplored.

Generally, the period 2000 – 2010 has seen an explosive growth in experimental and theoretical work aiming at the optimization of the catalytic activity and selectivity of catalysts of the [(L)AuX] family. Apart from the studies on the perfect leaving group X, the investigations have also concentrated on modifications of the ligand L.

The non-coordinating or at least extremely weakly coordinating anions X meanwhile have included not only

a) fully fluorinated groups BF_4, PF_6, AsF_6, and SbF_6 (with a recent preference for SbF_6),

b) fluorinated oxoacid groups O_3SF, $O_3SC_nF_{2n+1}$, $O_2CC_nF_{2n+1}$,

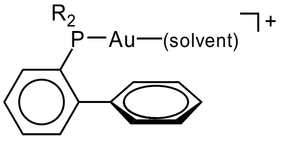
c) oxoacid groups SO_4H, O_3SR and nitrate NO_3, but recently also

d) groups $B(C_6F_5)_4$, $Al(OR^F)_4$ [36].

With few exceptions, these counterions are introduced by applying the Teles methods, *viz.* the acid cleavage of alkylgold(I) precursors or the metathesis using silver salts. Another approach is based on cationic polynuclear gold(I) oxo, hydroxo and alkoxo complexes (below).

As in many other areas of homogeneous catalysis with transition metal complexes, the group of ligands L in gold(I) catalysts was for some time dominated by a variety of tertiary phosphines R_3P (rarely arsines R_3As), but the focus has been steadily redirected to carbenes, in particular N-heterocyclic carbenes (NHCs), which allow for an even greater scope of electronic and steric effects [9]. In addition, as shown by Cinellu *et al.*, the ligand L may also be a bidentate donor such as a 2,2′-bipyridyl which imposes onto the gold(I) cation the coordination numbers 2 or 3 for the cation $[(bipy)Au]^+$ or the molecule [(bipy)AuX], respectively [37] (**S**, **T**). The catalytic activity of this class of compounds still has to be explored.

Permutations of the tertiary phosphine or NHC ligands have led to donor molecules L with extreme bulkiness which assists in improving the stability of the $[(L)Au]^+$ cations. If the substituents of the tertiary phosphine or of the carbene have any σ- or π-donor properties, this may also stabilize the cation, but any too high donor capacity may of course deactivate the $[(L)Au]^+$ species. In the work by Echavarren *et al.*, and later also by the group of Gagosz and others, suitably positioned aryl groups have proved to be almost ideal supporting substituents (**U**), because on the one hand these groups are partly shielding the acceptor function of the gold cation, while on the other hand the (arene)-Au π-interaction is of very low bond energy, lower than that with alkenes, allenes or alkynes, and hence these incoming unsaturated substrates are readily given access to the metal atom [38, 39]. The influ-



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ence of the counterions on the nature of such ion pairs and their influence on the course of either stoichiometric or catalytic reactions were studied by NMR spectroscopy and DFT calculations [40].

The P-Au, N-Au or C-Au bonds in [(phosphine) Au]$^+$, [(bipy)Au]$^+$ or [(NHC)Au]$^+$ cations, respectively, can be tuned by the substituents of the ligands leading to specificities in the catalytic action. Finally, if the set of substituents of the ligand L lends chirality to the cation, various kinds of stereo- and enantioselectivity of the action can be achieved [2 – 10].

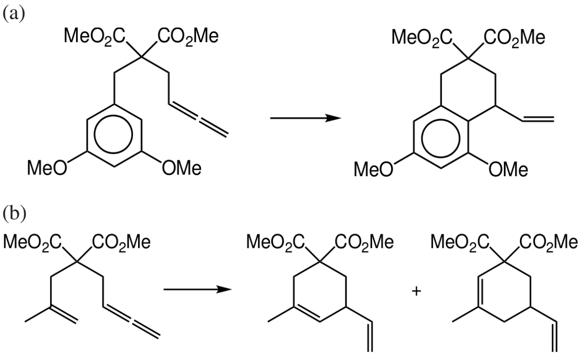
Stabilization of catalyst solutions can also be achieved by using solvents with weak donor properties for gold(I), such as toluene and acetonitrile (**U**), which are readily displaced by the olefin substrates [38, 39, 41 – 43].

In this context it should be remembered that *isocyanides* RNC are among the most powerful ligands for gold(I). A large number of complexes mainly of the types (RNC)AuX and [(RNC)$_2$Au]$^-$ are known. However, in these complexes the isocyanide units are susceptible to nucleophilic attack by water, alcohols, amines *etc.* which so far precludes their application as catalysts for typical addition reactions of unsaturated hydrocarbons. In fact, (isocyanide)gold(I) complexes were the precursors in the first syntheses of (carbene)gold(I) complexes [14].

5. Disadvantages of catalysts prepared *in situ* by the silver salt method

The use of silver-containing reagents in synthetic chemistry is generally associated with several very common disadvantages owing to the high price, the light-sensitivity, the limited solubility in several important organic solvents, the high adsorptive and poor filtration properties of the precipitates, and the easy reduction to metallic silver. Work-up of reaction mixtures and recycling of the precious metals is also more difficult if more than one of the coinage metals are present in the system and in the waste, respectively [44].

In the metathesis reaction of gold and silver salts employed for the preparation of gold catalysts [(L)Au]$^+$ X$^-$ an additional complication arises from the metallophilic affinity of the two metals in their low oxidation states [45 – 50]. This phenomenon makes it very difficult to completely remove all silver salts from the gold catalyst solutions, and it can also lead to a loss of gold to the precipitated silver salts.



Schemes 7a, b.

Since Ag$^+$ is also a catalyst in organic transformations of unsaturated organic substrates, but with a different reactivity profile [7b], its presence can alter the selectivity of the otherwise only gold-catalyzed reactions [44]. Moreover, heterometallic catalysts $[(L)_m Au_n Ag_p]^{q+}$ may behave differently from homometallic catalysts [33].

Evidence is indeed accumulating that silver-containing solutions of [(L)Au]$^+$ X$^-$ catalysts show marked differences in their performance. Pertinent observations are limited, because the overwhelming majority of reactions have been carried out with catalyst solutions prepared *via* the silver salt metathesis only, such that for most cases there is no comparison with silver-free systems [51 – 53].

A recent example is the intramolecular hydroarylation of allenes which proceeds differently in the presence or absence of silver salts as studied in careful experiments by Gagné *et al.* The absence of silver salts was secured by using the single-component Gagosz catalyst (Ph$_3$P)AuNTf$_2$ (chapter 6.1 below) instead of the two-component (Ph$_3$P)AuCl / AgNTf$_2$, AgBF$_4$, AgSbF$_6$, or AgOTf systems (Scheme 7a). Similar observations were made in cycloisomerizations of en-allenes (Scheme 7b) [54, 55].

In the following Chapter 6 the results of the work presented in some of the most relevant publications has been put together in groups representing the various approaches or opportunities to use silver-free gold(I) catalysts. Owing to the rapid growth of information, the collection is not fully comprehensive, but it reflects well the prominent directions of pertinent current research. The reviews on the subject published in 2008 – 2010 [2 – 10] were used as the main sources, complemented by some more recent papers.

6. Silver-free gold(I) catalysts

There are two ways to obtain silver-free gold(I) catalysts or gold catalyst precursors [(L)AuX]. On the first one, a silver salt may be used, but the product can be isolated and purified such that no traces of silver remain in the final product. On the second one, no silver salt is used throughout the preparation from commercial gold chemicals. Both routes have been used successfully in recent studies as shown in the following chapters 6.1. – 6.11. Silver-free access to formally unsolvated or partly solvated $[Au]^+$ catalysts have been included in chapters 6.12 – 6.13.

6.1. Gold(I) triflimides [LAuNTf$_2$]

Presently the most common catalysts that can be isolated and purified to remove all silver contaminants are the gold(I) "triflimides" introduced by the group of Gagosz in 2005 [28]. In their studies it was first observed that complexes of the type $[(R_3P)AuNTf_2]$ (**I**) are stable enough such that the compounds can be isolated from the reaction mixtures obtained with equimolar quantities of [(L)AuCl] and $AgNTf_2$ in dichloromethane at r. t. The air- and moisture-stable prototype $[(Ph_3P)AuNTf_2]$ could be purified by crystallization and its structure determined. The structure is reminiscent of the bis(trimethylsilyl)imide $[(Ph_3P)AuN(SiMe_3)_2]$ published in 1970 [16, 56].

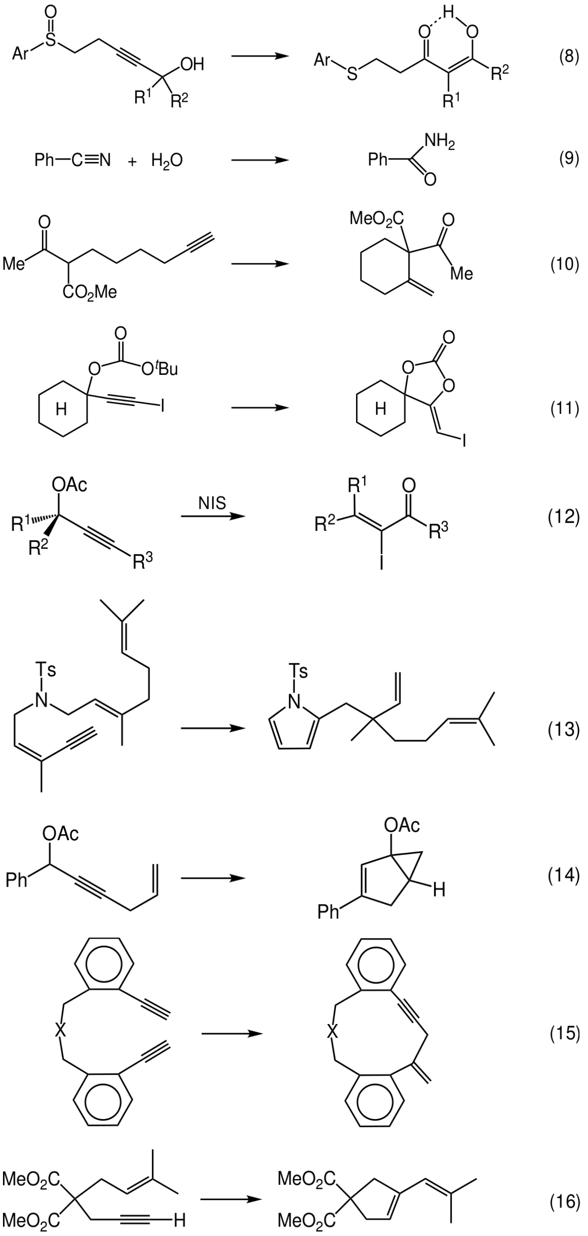
The reagent $AgNTf_2$ can be produced *e. g.* from Ag_2CO_3 and $HNTf_2$ for an in-house synthesis, but $(Ph_3P)AuNTf_2$ is now also a commercial fine chemical.

It should be remembered that none of the related catalysts generated with $AgBF_4$, $AgPF_6$, $AgSbF_6$ *etc.* can be isolated and purified, which precludes the preparation of a silver-free product. Remarkably, this is particularly true also for the triflates $[(R_3P)AuOTf]$ which always have to be prepared *in situ*.

This work with (phosphine)gold(I) triflimides was followed in 2007 by the preparation of the corresponding silver-free carbene complexes $[(NHC)AuNTf_2]$ (**J**), of which several examples have been crystallized, their spectral properties examined and their solid-state structures determined [52].

The triflimides $[(L)AuNTf_2]$ have since been widely and successfully applied in the catalysis of various organic transformations owing to their convenience in handling (well-defined stoichiometry of reactants by weighing, no inert gas required), their good solubility in common organic solvents and the purity of the reaction systems. The diversity of some recent examples illustrates the broad scope of applications:

a) the formation of β-hydroxyenones from sulfoxide-functional propargyl alcohols (Scheme 8) [57],



Schemes 8 – 16. Selected reactions catalyzed by gold(I) triflimides $(L)AuNTf_2$.

b) the cycloisomerization and intramolecular hydroarylation of (en)allenes (Scheme 7b) [25, 58],

c) the catalytic hydration of nitriles to give the corresponding amides (Scheme 9) [59],

d) the cyclizations through addition of β-ketoesters to alkynes, using $(RC{\equiv}C)_3P$ as a special tertiary phosphine (Scheme 10) [60],

e) the cyclization of alkynyl *t*-butylcarbonates (Scheme 11) [61],

f) the iodination of propargylic acetates to give iodo-enones (Scheme 12) [62],

g) the synthesis of pyrrols from enynyl(enyl)amines (Scheme 13) [63],

h) the cyclization of enynyl esters to bicyclohexenes (Scheme 14) [64a],

i) the rearrangement of allenyl acetates to acetoxy 1,3-dienes [63],

j) the conversion of propargyl acetates into enones [64a],

k) the ring closure of α,ω-alkane-diynes to give macrocycles (Scheme 15) [39],

l) the ring closure of en-ynes to vinyl-cyclopentenes (Scheme 7a) or polycyclic alkenes and their hydration products (Scheme 16) [28a],

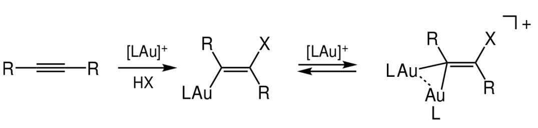
m) domino rearrangements and fluorination of propargylacetates using "Selectfluor" as a reagent [64b],

n) the synthesis of azacyclic compounds in redox/cycloaddition cascades of nitroalkyne substrates [64c], and

o) the synthesis of conjugated trienes from cyclobutenes and furans [64d].

However, it should be noted that there are several reactions, where the triflimide catalysts proved to be inactive or less active than other gold(I) catalysts [2–10], as *e. g.* in the rearrangement of allenyl carbinol esters [65a].

In recent work by Fürstner *et al.* is has also been demonstrated that $Ph_3PAuNTf_2$ can be employed for the geminal diauration of olefins to give dinuclear cationic species, which are intermediates and resting states in the gold-catalyzed coupling reactions. Two of these intermediates (with Tf_2N^- anions) have been isolated and structurally characterized (Scheme 16a) [65b].



(16a)

6.2. Stable solvates $[(L)Au(solvent)]^+ X^-$

Whenever compounds with $[(L)Au]^+$ units are prepared or dissolved in organic solvents, it is to be assumed that the formally mono-coordinate gold cation becomes coordinated to at least one solvent molecule to establish the conventional linear two-coordination or trigonal-planar three-coordination. To secure catalytic activity, the solvent has to be a poor donor easily replaced by unsaturated substrates. Most of these solvates are prepared by the silver salt method, but cannot be isolated owing to their limited stability. Decomposition occurs upon removal of the solvent. Therefore, the discovery of suitable solvates which can be isolated and purified by crystallization meant a significant progress, because in this way the product can be obtained pure and – in particular – free of silver residues.

The solvate ligands of choice are nitriles (cyanides) RCN which are poor N-donors for gold(I). The stability of compounds with diorgano(phenyl)phosphine ligands like $[(R_2PhP)Au(NCMe)]^+ SbF_6^-$ is greatly increased by changes in their substituent pattern toward diorgano(2-biphenylyl)-phosphines (**U**) [38a, 39, 66, 67]. The complex $[(^tBu_2PC_6H_4\text{-}2\text{-}C_6H_5)Au(NCMe)]^+ SbF_6^-$ is an air-stable crystalline solid [38a]. Its phosphine ligand (a Buchwald phosphine) is now commercially available (JohnPhos). The homolog with cyclohexyl instead of *t*-butyl groups, $[Cy_2P(C_6H_4\text{-}2\text{-}C_6H_5)PAu(NCMe)]^+ SbF_6^-$, has become a widely used alternative [38c].

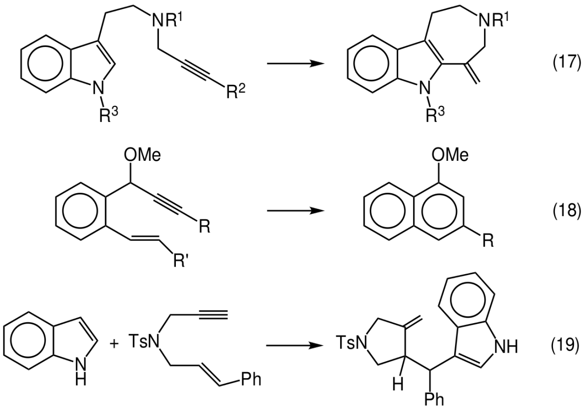
The improved stability of these solvates is probably due to a shielding of the gold(I) center by the extended diphenylyl group which is even more pronounced as additional alkyl substituents are introduced in the 2,4,6-positions of the peripheral phenyl ring ("XPhos"): *e. g.* $\{Cy_2\ [C_6H_4\text{-}2\text{-}(C_6H_2\text{-}2,4,6\text{-}^iPr_3)]PAu(NCMe)\}^+ SbF_6^-$ has recently been employed extensively in various catalytic systems (below) [10, 38b]. In all these complexes with the biphenylyl units there may be a weak π-interaction of the metal atom with the pending phenyl ring [11]. Related systems with diphenyl(arylmethylamino)phosphines have also been prepared [41].

The above solvates have been used as catalysts in a large number of reactions including the following examples:

a) the cyclization of ω-alkynyl-substituted tryptophanes to give compounds with annelated seven-membered or larger rings (azepines, azocines *etc.*) (Scheme 17) [66],

b) the cyclization of 1-(prop-2-yn-1-yl)-2-alkenylbenzenes to produce naphthalenes proceeding with fragmentation of the alkene (Scheme 18) [67],

c) the ring closure of α,ω-alkane-diynes to give macrocylic olefins (Scheme 15) [39],



Schemes 17 – 19. Selected reactions catalyzed by gold(I) solvates $[(L)Au(solvent)]^+ X^-$.

d) 1,6-enyne cyclizations and related reactions (Scheme 16) [68 – 71],

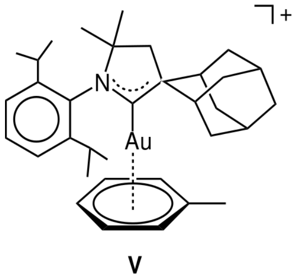
e) the trapping of indoles by 1,6-enynes (Scheme 19) [72],

f) the intramolecular hydroarylation of alkynes with indoles (Scheme 17) [73a].

g) the synthesis of tetrahydropyranones-4 from 4-alkoxyalkyl-1-butynes [73b]

h) the synthesis of benzo[*b*]oxepin-3(2*H*)-ones from 2-(propenyloxy)benzaldehydes [73c].

$[(NHC)Au(solvent)]^+ X^-$ salts with carbene ligands have also been prepared and isolated in pure form. For this purpose cyclic (alkyl)(amino)carbenes (CAACs, **V**) were chosen as ligands by Bertrand *et al.*, and for their synthesis the use of silver salts can be avoided altogether. Instead, the halide precursor [(CAAC)AuCl] can be treated with $K[B(C_6F_5)_4]$ in toluene to give the toluene solvate in which the solvent molecule is η^2–π-bonded to the metal atom. In the original exploratory experiments this toluene complex was generated by applying the extremely powerful halide scavenger $[(PhMe)SiEt_3]^+ B(C_6F_5)_4^-$, but later work has shown that this special reagent was not a prerequisite [42, 43].



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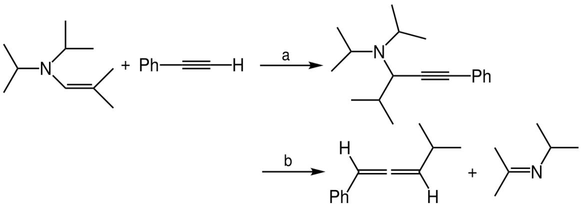
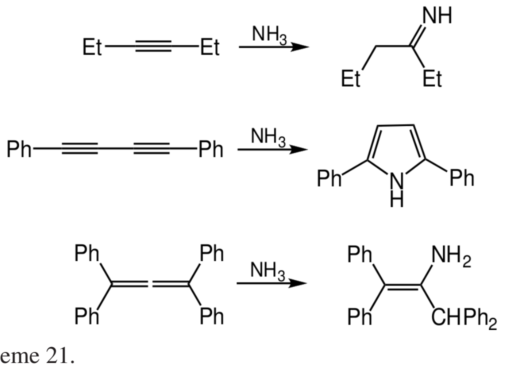
$[(CAAC)Au(PhMe)]^+ B(C_6F_5)_4^-$ complexes are catalysts for the coupling of enamines and alkynes to yield allenes instead of propargyl compounds (Scheme 20) and thus to proceed differently as compared to the course of reactions with other catalysts [42, 43].

Upon treatment with ammonia, the toluene molecule is replaced by NH_3 to give the complex $[(CAAC)AuNH_3]^+ B(C_6F_5)_4]^-$ the structure of which has also been determined. It is an efficient catalyst of alkyne and allene amination reactions for which it is considered the resting state. Again, there are significant differences in the reaction patterns as compared *e. g.* to $[(Ph_3P)Au]^+ X^-$ catalysts (Scheme 21) [74].

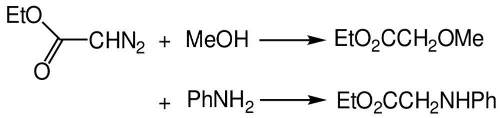
Solvate complexes like $[(NHC)Au(NCMe)]^+ Y^-$ have also been prepared and isolated from [(NHC)-AuCl] complexes by reaction with $AgBF_4$ or $AgPF_6$ in MeCN [75]. The compound with Y = PF_6 and NHC = 1,3-bis[2,6-di(isopropyl)phenyl]-imidazol-2-ylidene has been structurally characterized. The same reaction with Ar = 3,5-bis(trifluoromethyl)phenyl gave solutions which were catalytically active, but the catalyst has not been isolated. Solutions of both the purified and the *in situ* prepared catalysts are active in the addition of alcohols, amines and olefins to ethyl diazoacetate to give nitrogen and alkoxy- or amino-acetic acid



Scheme 20.

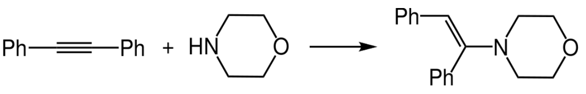


Scheme 21.



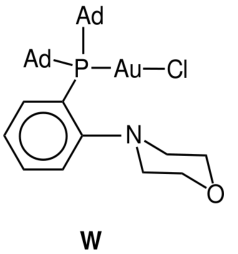
Scheme 22.

esters or cyclopropanes, respectively, in high yields (Scheme 22) [75].



Scheme 23.

Similarly, the hydroamination of internal alkynes was found to be catalyzed by the reaction mixture obtained with [$(Me_2S)AuCl$], an NHC, and $Li[B(C_6F_5)_4]$ in 1,4-dioxane. The former two components provide the complex [(NHC)AuCl] which then is activated by the tetrakis(pentafluorophenyl)borate salt. Diphenylacetylene and morpholine undergo a *cis*-addition to yield the corresponding morpholino-alkene and – after reduction – the corresponding alkanes (Scheme 23) [76].

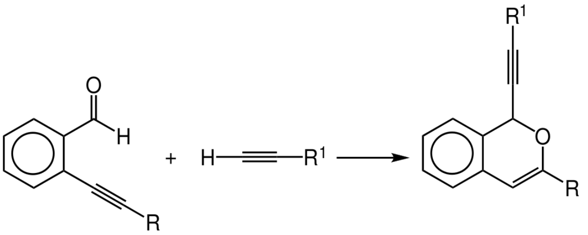


W

The related complexes [$(R_3P)AuCl$] with suitably substituted tertiary phosphines instead of NHCs give higher conversion rates in this process. This was particularly true for di(adamantyl)(*o*-morpholino-phenyl)phosphine (Mor-DalPhos, **W**) which exerts a pronounced steric effect and a high N-donor capacity which control the regio- and stereoselectivity in the hydroamination of unsymmetrical internal alkynes. In these reactions, the silver salt $Ag[B(C_6F_5)_4]$ was also successfully applied instead of the alkali salts, with boiling toluene as a solvent. It should be noted that the hydroamination of olefins is best catalyzed by [$(Ph_3P)AuOTf$] prepared *in situ* from [(Ph_3P)-AuCl] and AgOTf (in toluene at 85 °C). The addition of ammonia can be accomplished *via* the addition of *p*-toluenesulfonamide and subsequent deprotection [76].

6.3. *Activation of complexes [$(R_3P)AuCl$] with weak bases*

For suitably constituted substrates, the activation of simple complexes [$(R_3P)AuCl$] by weak bases may be sufficient to induce high-yield reactions. Thus the cyclization of *o*-alkynyl-benzaldehydes with terminal alkynes to give 1-alkynyl-1*H*-isochromones could be efficiently catalyzed by [$(Me_3P)AuCl$] and $^iPr_2EtN$ in a water/toluene mixture (Scheme 24) [77].

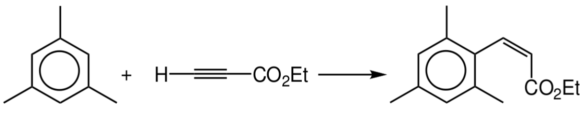


Scheme 24.

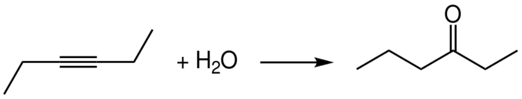
6.4. *Activation of complexes [(L)AuX] with Lewis acids*

In a comparative study by Reetz and Sommer, the hydroarylation of alkynes has been investigated using both the silver catalyst systems prepared from [(R_3P)-AuCl] and $AgBF_4$, $AgSbF_6$, $AgClO_4$, or AgOTf, or a combination of [$(R_3P)AuCl$] and the Lewis acid $BF_3 \cdot OEt_2$ in nitromethane as a solvent. Surprisingly, no large differences in the yields and in the selectivities were found which indicates that at least in the cases investigated the employment of silver salts can be avoided without a loss in catalyst performance. The model reaction for an electron-poor terminal alkyne was the addition of mesitylene to acetylenecarboxylic acid ethyl ester which leads exclusively to the *Z*-2-mesityl-acrylic acid ester (Scheme 25). NMR experiments have shown that even an excess of $BF_3 \cdot OEt_2$ alone is not sufficient to remove the Cl^- ion from the [$(R_3P)Au]^+$ cation, but in the presence of substrate this dissociation takes place leading to [(R_3P)-$Au(HC{\equiv}CCOOEt)]^+$ $[ClBF_3]^-$ intermediates. NMR signals of the same intermediate are observed in the silver salt reaction with the $SbF_6{}^-$ counterion [78].

Similar effects were observed with $BF_3 \cdot OEt_2$ as a co-catalyst for the hydration or hydrocarboxylation



Scheme 25.



Scheme 26.

of alkynes with various organosulfonate catalysts [$(Ph_3P)Au(OSO_2R)$]. The best results were obtained with 5 mol-% of $BF_3 \cdot OEt_2$ and R = C_2F_5 for the hydration of 3-hexyne in tetrahydrofuran or methanol (Scheme 26). There was no or almost no reaction with $BF_3 \cdot OEt_2$ alone or with [$(Ph_3P)Au(OSO_2C_2F_5)$] alone. The corresponding silver salts were also inactive as catalysts under comparable conditions [79]. The hydroarylation of alkynyl(methyl)ketones to give arylvinyl(methylketones) has been accomplished using [$(Ph_3P)AuCl$] and $BF_3 \cdot OEt_2$ in nitromethane [80].

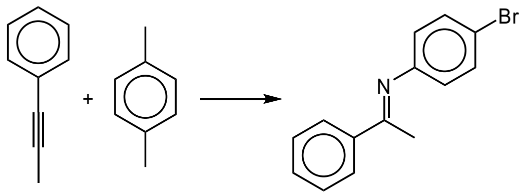
For L = NHC in [(L)AuX], the activation of the recrystallized, silver-free acetate (X = $MeCO_2$) with $(C_6F_5)_3B$ for the hydration of 3-hexyne has already been referred to (NHC = 1-methyl-2-diphenylmethyl-imidazol-2-ylidene) [34].

6.5. The acid route using organogold(I) complexes [(L)AuR]

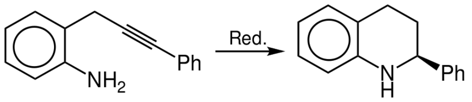
As already mentioned above, in the original work by Teles *et al.* the organogold precatalysts [$(R_3P)AuR'$], mainly with R′ = Me, were treated with mineral acids HX [30]. In this way, silver-free catalyst solutions can be obtained, but these may contain excess acid and are of limited stability, and the free or solvated salts $\{[(R_3P)Au]^+ X^-\}_{solv}$ cannot be isolated (X = SO_4H, BF_4, TfO, RSO_3 *etc*). Therefore, the use of these solutions is limited to catalysis of less sensitive substrates.

In recent modifications, weaker acids with bulky heteropolyoxometallate anions have also been employed. The reaction of $(Ph_3P)AuMe$ with $H_3[PW_{12}O_{40}]$ *e. g.* gave very active catalyst solutions for the hydroamination of alkynes with anilines (Scheme 27) [81].

The catalysis of the hydration of alkynes by solutions obtained upon treatment of [$(Ph_3P)AuMe$] with acids was subsequently also investigated by Tanaka *et al.* in 2002 [82]. The high activity of the system with sulfuric or sulfonic acids (H_2SO_4, $MeSO_3H$, CF_3SO_3H) was confirmed in particular for the solvent methanol. For other solvents, the yields decreased in the order isopropanol, dioxane, acetonitrile, tetrahydrofuran, dichloromethane, dimethylformamide, and toluene. The authors also observed a remarkable improvement of the stability of the catalyst system by the addition of auxiliary ligands such as $(PhO)_3P$. Even maintaining an atmosphere of CO over the reaction mixtures (1 atm) prevented the decomposition of the catalyst. The formation of metal particles was greatly retarded. The hydrogen heteropolyoxometalate $H_3PW_{12}O_{40}$ was also applied successfully for the hydration of alkynes, where yields were found to be high even in the absence of coordinative additives. The results are thus similar to those obtained in the analogous hydroaminations.



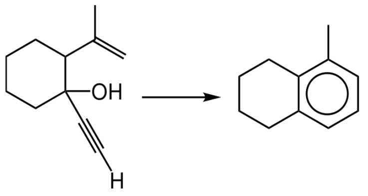
Scheme 27.



Scheme 28.

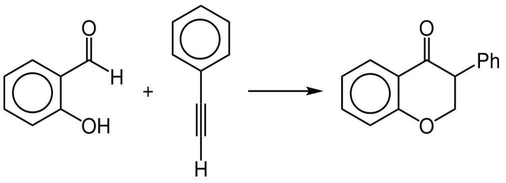
Positive results were also obtained for intramolecular hydroaminations using combinations of $(Ph_3P)AuMe$ and phosphoric acid diesters HOP(O)-$(OR)_2$. With the two OR groups fused together in a chiral ester, such as in biphen-diyl- or binaphth-diyl-2,2′-dioxo esters, the process can be conducted with high enantioselectivity [83]. In the present context it is of interest that the corresponding catalyst solutions prepared from $(Ph_3P)AuCl$ and the *silver* salt of some acid esters gave much poorer yields. The reactions with the catalyst generated *via* the acid route can be conducted in a variety of solvents, including toluene, dichloromethane, chloroform, tetrahydrofuran, or acetonitrile. In the presence of a Hantzsch ester reductant, 2-(2-propynyl)anilines are converted in a relais reaction into tetrahydroquinolines in very high yields and > 95 % ee (Scheme 28).

Surprisingly, the benzannulation of 3-hydroxyenynes and the cyclization of enynes could be carried out with a catalyst prepared *in situ* from equimolar quantities of [$(Ph_3P)AuCl$] and triflic acid HOTf (< 5 mol-% of the substrate) [84]. The results were comparable to those obtained *via* the silver salt method using [$(Ph_3P)AuCl$] and AgOTf, while [$(Ph_3P)AuCl$] alone gave very poor conversion, and TfOH alone did not show any effect. This result is very impor-



Scheme 29.

tant in that it suggests that there are many reactions of this type that may not require the use of silver salts (Scheme 29).



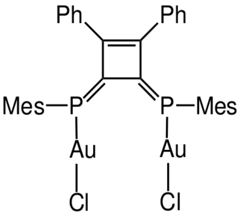
Scheme 30.

6.6. *(Tri-n-butylphosphine)gold(I) cyanide as a catalyst*

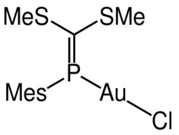
While – as expected – halide complexes [(R_3P)AuX] with the poor leaving groups X = Cl, Br, I are catalytically inactive in most reactions tested to-date, the cyanide complexes [(R_3P)AuCN] proved to be unexpectedly active in the annulation of salicylaldehydes with arylalkynes which leads to isoflavone-type structures (Scheme 30) [85]. In this study, the complexes were prepared *in situ* from the ligands R_3P and the silver(I) salts AuCl, AuI and AuCN. The reaction mixtures containing the salicylaldehydes and the alkynes in toluene were kept at 150 °C in sealed tubes under nitrogen for up to 36 h. Out of a variety of trialkyl- and triarylphosphines [Me_3P, Et_3P, *n*-Bu_3P, *c*-Hex_3P, *t*-Bu_3P, Ph_3P, *o*-Tol_3P, $(PhO)_3P$, and (2-furyl)$_3$P], the *n*-butyl compound was found to give highest yields, and AuCN was more efficient than AuCl and AuI. AuCN and *n*-Bu_3P separately had no effect. This result has shown that under certain optimized conditions the catalytic activity of otherwise almost inert gold(I) complexes can be enhanced very significantly. With AuCN and *n*-Bu_3P being commercial products which are easy to handle, this method – where applicable – may have advantages over several other catalytic systems.

6.7. *Catalysts [(L)AuCl] with L = phosphaalkenes RR′C=PR″*

1,6-Enynes have been cyclized to give vinyl-cyclopentenes using the complexes of AuCl with various mono- and difunctional phosphaalkenes (**X**, **Y**). These reactions also proceed in the absence of any chloride-abstracting agent (like silver salts) (Scheme 15) [86].



X



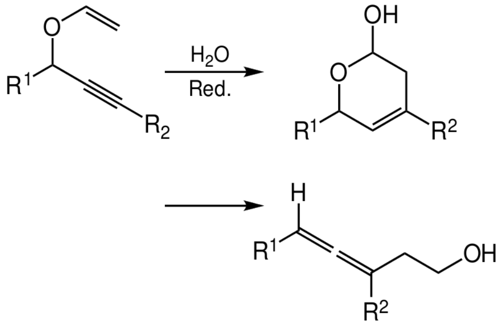
Y

6.8. *Catalysis by trinuclear gold(I) oxonium complexes $\{[(R_3P)Au]_3O\}^+ X^-$*

It has been known from the early work of the schools of Nesmeyanov [87] and Usón [88] that both oxide and chloride anions can function as clustering centers for $[(R_3P)Au]^+$ cations giving tri- and dinuclear cations of the types $\{[(R_3P)Au]_3O\}^+$ (**M**) and $\{[(R_3P)Au]_2Cl\}^+$ (**L**), respectively.

The former are obtained by a simple treatment of [(R_3P)AuCl] with concentrated sodium or potassium hydroxide. It was observed that no simple gold hydroxides [(R_3P)AuOH] or oxides $\{[(R_3P)Au]_2O\}$ are formed in these reactions. Obviously, these two intermediates have a high affinity for $[(R_3P)Au]^+$ cations. The structures of the oxonium cations with their very narrow Au-O-Au angles (much smaller than 109° !) indicate that intracationic aurophilic interactions make these species an energy sink in the system [89–96]. In later work this phenomenon has been generalized for several *p*-group elements including mainly B, C, N, P, As, O, S, Se, and Te, with the nuclearity reaching 6, *i. e.* up to six gold atoms can become attached to these centers [97]. It is most remarkable that many of the salts with these cluster cations can be crystallized and show high thermal stability (with melting points above 250 °C). The complexes are chemically robust such that the compounds can be handled in air at least for a short time. These favorable properties have made them promising candidates for catalysis.

Following the early experiments by Teles *et al.* [30] this opportunity has been exploited by Toste *et al.* for the synthesis of dihydropyrans from propargyl vinyl ethers [98, 99]. In dichloromethane this reaction first affords open-chain allenylmethyl-aldehydes (and, after reduction, -alcohols), but in aqueous dioxane high yields of the cyclic product are obtained. Various substituents are tolerated in this process, and with a proper



Scheme 31.

design of the substrate spirocyclic products can be generated. In all cases a remarkable stereocontrol and high *ee*'s were observed (Scheme 31). The oxonium salt was also employed in a multi-step synthesis of azadirachtin, where a propargylic enol ether intermediate was cyclized with this reagent in dichloromethane at 25 °C [100a].

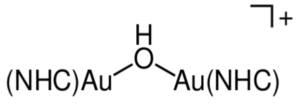
It is important to note that the performance of the oxonium catalyst is superior to that of [$(Ph_3P)AuOTf$] and [$(Ph_3P)Au]^+$ BF_4^- (generated from the silver salts) both in yield and in stereoselectivity. It is conceivable that the oxonium cations are sources of the catalytically active [$(R_3P)Au]^+$ species which can activate both the alkyne and the alkene functions. The remaining oxides [$(R_3P)Au]_2O$ are known to be strong acceptors for these cations (above) and can reform the oxonium cation. A protonation of the oxide by water or alcohols cannot be excluded, but will also be reversible. Because of its remarkable properties and the easily controlled application, [$(Ph_3P)Au]_3O^+$ BF_4^- is now commercially available as a silver-free gold(I) catalyst.

It is possible that the recently reported auration of fluoroarenes by mixtures of tBu$_3$PAuCl, Ag_2O and K_2CO_3 also proceeds *via* the tri(gold)oxonium salt, but there is no experimental evidence for this intermediate as yet, and the reaction mixture is not a silver-free system [100b].

6.9. *Catalysis by gold(I) hydroxide complexes (NHC)AuOH and {[(NHC)Au]$_2$OH}$^+$ X$^-$*

In very recent studies is has been discovered that [(NHC)AuCl] complexes – other than [$(R_3P)AuCl$] complexes – can be readily converted into the corresponding hydroxides [(NHC)AuOH] (**K**) by simply using sodium, potassium or cesium hydroxide [51]. With NHC = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene an air-stable crystalline product was obtained which could be used as a synthon for various (NHC)AuX derivatives (X = H, CN, Ph, C_6F_5, $CH(COOMe)_2$, OAc, OtBu, and NTf_2.

In subsequent studies the reactions of the hydroxide (NHC)AuOH with various Brønsted acids were investigated [17, 51]. Different products were obtained with $HBF_4 \cdot OEt_2$ in dichloromethane and with aqueous HBF_4. For the former system, there is NMR evidence for the formation of [(NHC)Au$(OEt_2)]^+$ BF_4^-, while the ether-free salt [(NHC)Au]$^+$ BF_4^- solvated otherwise should be present in the latter. The solutions have limited stability under ambient conditions, and none of the two components could be isolated. By contrast, the product of the reaction in water or in a mixture of water and dichloromethane was identified as the dinuclear, hydroxyl-bridged complex {[(NHC)Au]$_2$OH}$^+$ BF_4^- which could be isolated and crystallized (**Z**). The same product was also obtained in 90 % yield from the reaction of [(NHC)AuOH] and $HBF_4 \cdot OEt_2$ in the molar ratio 2 : 1 in benzene.



$$\left[(NHC)Au-\overset{H}{O}-Au(NHC)\right]^+$$

Z

Both [(NHC)AuOH] (**K**) and {[(NHC)Au]$_2$OH}$^+$ BF_4^- (**Z**) were found to be active catalysts for many of the organic transformations for which other gold(I) catalysts had previously been successfully employed using the silvers salt method [51]. The following examples have been studied:

a) the hydration of benzonitrile to give benzamide (in tetrahydrofuran/water) (Scheme 9),

b) the hydration of diphenylacetylene (in 1,4-dioxane/water) (Scheme 32),

c) the transformation of propargylic acetates into enones (in methanol/water) (Scheme 33),

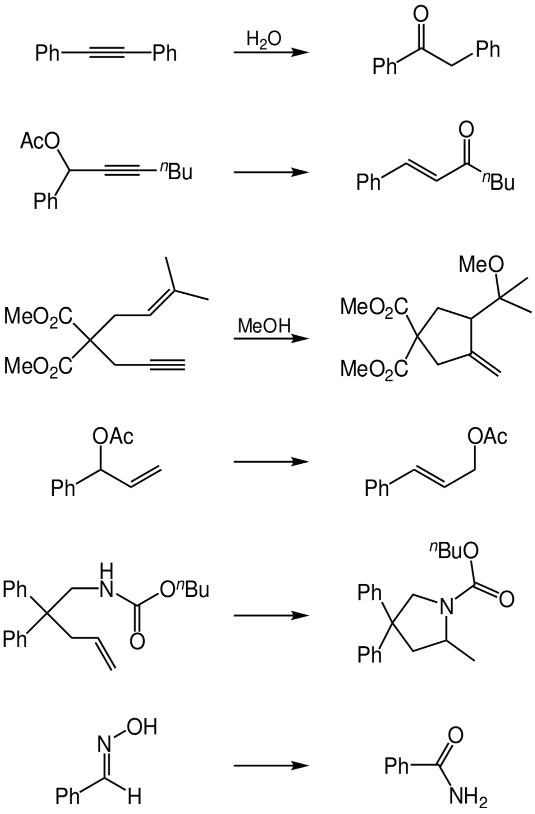
d) skeletal rearrangements of enynes (in dichloromethane) (Scheme 16),

e) alkoxycyclizations of enynes (in methanol) (Scheme 34),

f) 3,3′-rearrangements of allylic acetates (in dichloroethane) (Scheme 35),

g) intramolecular hydroaminations of alkenes (in 1,4-dioxane) (Scheme 36),

h) Beckmann-type rearrangements (without a solvent) (Scheme 37),



(32)
(33)
(34)
(35)
(36)
(37)

Schemes 32 – 37. Selected reactions catalyzed by gold(I) hydroxide complexes [(NHC)AuOH].

i) C-H carboxylation of fluorinated benzenes [51c,d].

In most cases [(NHC)AuOH] (**K**) was activated *in situ* by addition of $HBF_4 \cdot OEt_2$ in molar ratios between 2 : 1 and 1 : 2 in solvents or mixed solvents as indicated. The products were obtained in high yields (often approaching quantitative conversion) comparable to or better than those obtained following the procedures with other gold(I) catalysts [51]. It therefore appears that gold(I) hydroxide catalysts are a true alternative to the already established catalytic systems.

6.10. *Catalysis by dinuclear gold(I) chloronium complexes* $\{[(R_3P)Au]_2Cl\}^+ X^-$

It has been known from the early work carried out in the school of R. Usón that the chloride anion can be a clustering center for two gold(I) cations as in the model compound $\{[(Ph_3P)Au]_2Cl\}^+ ClO_4^-$ first isolated in 1979 (**L**) [88] and structurally characterized as a dichloromethane solvate in 1980 [101]. In this salt, the cation shows a narrow Au-Cl-Au angle (*ca.* 81°) indicating significant intraionic aurophilic bonding. The compound was prepared by treating $[(Ph_3P)AuCl]$ with a solution of $[Ph_3PAu]^+ ClO_4^-$ in dichloromethane (obtained separately from $[(Ph_3P)AuCl]$ and $AgClO_4$) in the molar ratio 1 : 1. This work has later been complemented by including a variety of other phosphines (Et_3P, Bz_3P, *o*-Tol_3P, Mes_3P) and counterions (ClO_4, BF_4, SbF_6), and the corresponding bromonium salts have also been synthesized [102]. These salts can also be obtained by combining the reagents $[(Ph_3P)AuX]$ (X = Cl, Br, I) and AgY (Y = ClO_4, BF_4, SbF_6) in the molar ratio 2 : 1 in dichloromethane or mixed solvents. Due to the larger radius of Br as compared to Cl, no aurophilic bonding is observed in the bromonium cations. In later studies it was further found that the cation in the hexafluoroantimonate $\{[(Ph_3P)Au]_2Cl\}^+ SbF_6^-$ unlike in the perchlorate is actually a tetranuclear dimer $\{[(Ph_3P)Au]_4Cl_2\}^{2+}$ 2 SbF_6^- in the solid state established through interionic aurophilic bonding [103]. With C_6H_4-1,4-$(CH_2PPh_2)_2$ even a cyclic chloronium salt was obtained [104]. It is obvious that these halogenonium salts are excellent sources of $[(R_3P)Au]^+$ agents [105].

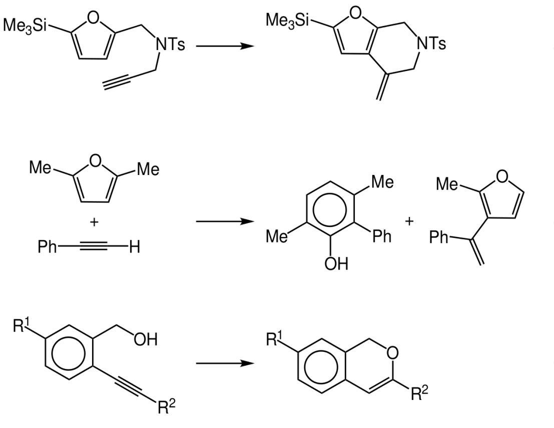
It was therefore not surprising that two of the chloronium salts (**L**), *viz.* the tetrafluoroborates with Ph_3P and Mes_3P ligands, prepared in a silver-free purity, could be used very successfully as catalysts for several organic transformations. This work, carried out so far exclusively in the group of Hashmi, has included *i. a.*

a) the hydroarylation of silylated (γ-alkynyl)furans carried out in acetonitrile (Scheme 38) [106], and

b) the addition of phenylacetylene to 2-mono- and 2,5-disubstituted furans, which leads to various substituted furans, but also to phenols *via* a carbenoid intermediate (Scheme 39).

c) The catalysts were also effective in the intramolecular addition reaction of *o*-alkynyl-substituted benzyl alcohols to give isochromenes, which may be accompanied by dimerization of the substrate (Scheme 40) [107 – 110].

The action of the chloronium salts in these reactions is unique, because standard gold(I) catalysts are either ineffective or lead to different products. It therefore has been assumed that a dinuclear catalyst may provide a stable resting state assisting in the maintenance of the catalytic cycle.



(38)

(39)

(40)

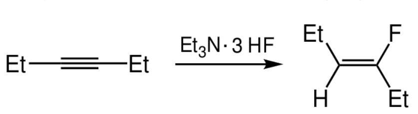
Schemes 38 – 40. Selected reactions catalyzed by gold(I) chloronium complexes $[(R_3P)Au]_2Cl^+ X^-$.

6.11. *Use of the first stable complex of gold(I) fluoride [(NHC)AuF] as a catylst*

Complexes of AuF have long been a challenge for preparative chemists [12 – 14]. Many attempts to accomplish a simple halogen exchange, *e. g.* by using AgF as a reagent for $[(R_3P)AuX]$ compounds (X = Cl, Br, I), have failed. Among other products, only the dihydrogen trifluoride $\{[(Ph_3P)Au]_3O\}^+ H_2F_3^-$ was isolated [111]. This salt is a stable product which indicates that Au-O bonds of the cation are not cleaved by the HF contained in the anion. Simple fluorides $[(R_3P)AuF]$ are still unknown.

However, a complex [(NHC)AuF] (**A**) with the carbene ligand NHC = 1,3-bis(2,6-diiospropylphenyl)-imodazolin-2-ylidene has recently been prepared by converting the corresponding chloride first into the *t*-butoxide [(NHC)AuO*t*Bu], which upon treatment with $Et_3N \cdot 3HF$ in benzene yields the fluoride (50 %). The product crystallizes as the 1 : 2 solvate with dichloromethane [12].

This new gold fluoride has been employed as a catalyst for the hydrofluorination of alkynes. Without a catalyst, or with most catalysts other than the gold(I) fluoride, these HF additions lead predominantly to polyfluoro*alkanes*, and it is often difficult to obtain the fluoro*alkene* intermediates. Usage of [(NHC)AuF] – directly or prepared *in situ* from the *t*-butoxide (above) – in the *trans*-hydrofluorination of internal alkynes with mild fluorinating agents such as $Et_3N \cdot 3HF$ affords the *trans*-products in good yields and high selectivity (Scheme 41) [112].

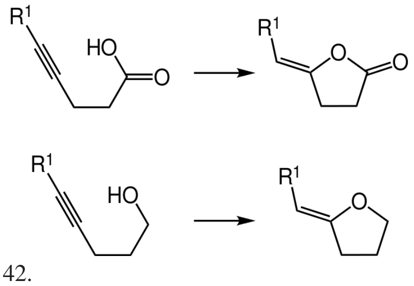


Scheme 41.

6.12. *Activation of donor-free AuCl with K_2CO_3*

The cyclization of acetylenic alcohols (ω-hydroxyalkynes) to tetrahydrofurans was found to be catalyzed very efficiently by a mixture of 0.1 mol-% of both AuCl and K_2CO_3 in acetonitrile at ambient temperature (Scheme 42) [113]. While only low yields were found with terminal alkynes, very good results were obtained with non-terminal alkynes. Moreover, the reactions are both regio- and stereoselective and give the *Z*-isomers almost exclusively. The use of acetonitrile appears to be important, as neither tetrahydrofuran nor dichloromethane support the reaction which is also not catalyzed by AuCl or $[(Ph_3P)AuCl]$ in the absence of K_2CO_3 under the same conditions.

By contrast, for the analogous cyclization of ω-alkynyl-carboxylic acids leading to γ- and δ-alkylidene lactones both acetonitrile and tetrahydrofuran can be used as solvents. Yields $> 95\,\%$ are obtained with AuCl/K_2CO_3 and also with $[(Ph_3P)AuCl]/K_2CO_3$ (molar ratio 1 : 1, 0.1 equivalents, 20 °C) (Scheme 42) [114].

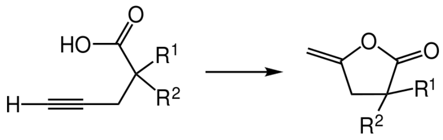


Scheme 42.

Mechanistically, the reaction is probably initiated by π-complexation of Au^+ at the alkyne function [11] with the solvent acting as a weak auxiliary ligand for the metal cation. K_2CO_3 mediates the deprotonation / reprotonation of the terminal alcoholic or carboxylic functions and the cyclized products, respectively. It should be noted that this catalysis also can be carried out under convenient standard conditions with readily available starting materials.

6.13. *Activation of AuCl with solvents, nitrogen donors and reductants*

At first sight, AuCl with is polymeric structure in the solid state [115] and its low solubility in solvents other than medium or strong donors may be consid-



Scheme 43.

ered a poor catalyst. For many of the known AuCl-catalyzed reactions, dichloromethane, acetonitrile or methanol must be used as solvents [2 – 10], suggesting that these media provide at least a borderline solubility through a degradation of the chain structure and solvation of the AuCl molecules.

Not many gold(I) complexes with simple nitrogen donors are known, but the chemistry of pyridine (pyr) complexes has been studied extensively. Both neutral complexes [(pyr)AuCl] and ionic isomers $[(pyr)_2Au]^+$ $[AuCl_2]^-$ have been described [116], their activity as a catalyst however has not been explored. This behavior is reminiscent of the equilibria with nitriles, where [(RCN)AuCl] and $[(RCN)_2Au]^+$ $AuCl_2{}^-$ are the counterparts [19, 115].

With acetonitrile as a solvent, AuCl acts as a catalyst for the intramolecular addition of carboxylic acids to alkynes RC≡CR′ to produce lactones with high regio- and – in favorable cases – stereoselectivity (Scheme 43) [117].

There are a few other examples in the literature, where reactions were carried out with selected catalyst systems of this kind:

a) Oxidative cleavage of alkenes by hydroperoxides to give ketones is catalyzed by AuCl activated with pyridine, 2,2′-bipyridyl or neocuproine [118],

b) 2,2′-Bipyridyl also acts as a catalyst additive to AuCl for the cyclization of allenyl alcohols with controlled chirality transfer (Scheme 44) [119].

c) Together with triethylamine, AuCl catalyzes the cyclization of O-propargylcarbamates to afford 4-methylene-2-oxazolidinones in high yield. The amine is not essential, as some reactions could be carried out successfully with AuCl and another base, but with longer reaction times (Scheme 45) [120].

d) Homopropargyldiols are cyclized stereoselectively to the corresponding bicyclic ketals by AuCl in methanol (Scheme 46) [121].

e) 1,6-En-yne-amines can be cyclized to give cyclobutanones by AuCl in dichloromethane (Scheme 47) [122].

f) Siloxy-1,5-enynes react with AuCl in dichloromethane to yield cyclohexadienes (Scheme 48) [123].

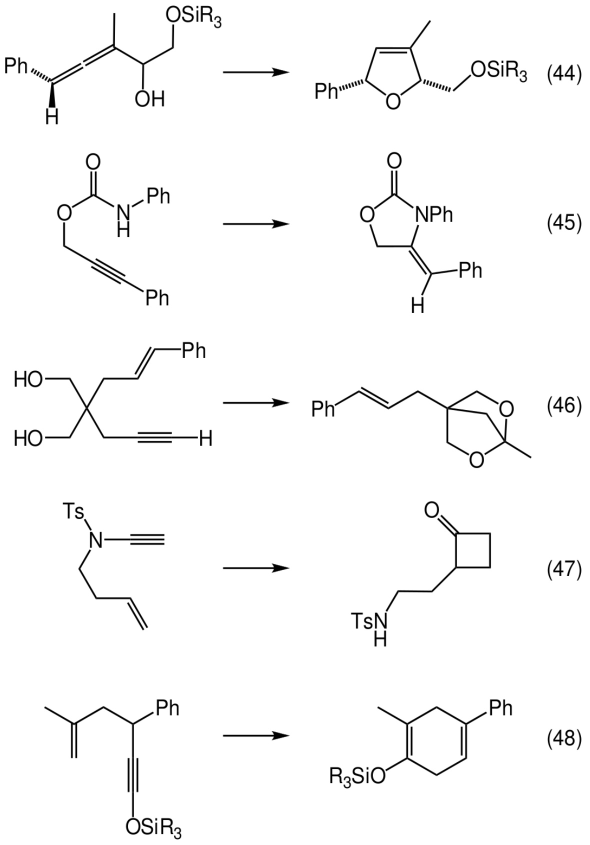
g) Treatment of cycloproylenynes with catalytic amounts of AuCl in dichloromethane affords tricyclic octahydrocyclobuta[α]pentalenes [70].

h) 2-Haloalkynyl-biphenyls are cyclized to 9-halophenanthrenes upon reaction with AuCl in boiling toluene [124].

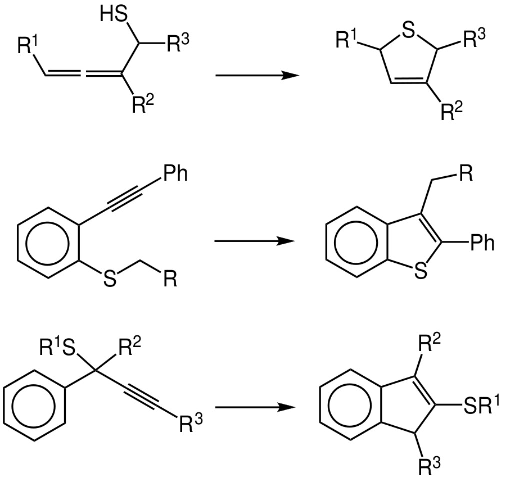
i) α,ω-Allenynes can be cyclized by AuCl alone, but for this reaction several other catalysts are available [125].

j) AuCl can also be activated as a catalyst for the oxidation of alcohols by molecular oxygen to aldehydes and ketones. For this purpose, anionic 1,3-diimide ligands proved particularly effective. The nature and structure of the catalyst are as yet unknown [126, 127].

AuCl alone shows catalytic activity if the substrates contains *sulfur* functionalities, which probably can complex and thereby activate the metal halide. This is surprising since sulfur is generally considered a poison to gold catalysts:



Schemes 44 – 48. Selected reactions catalyzed by AuCl in various solvents.



(49)

(50)

(51)

Schemes 49 – 51. Selected reactions of sulfurous substrates catalyzed by AuCl.

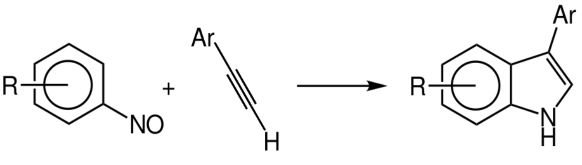
a) The cyclization of allenyl-thiocarbinols to dihydrothiophenes is efficiently catalyzed by AuCl in dichloromethane [128]. In this reaction, AuBr and AuI are even more efficient than AuCl (Scheme 49).

b) Using AuCl, *o*-alkynylthiophenyl sulfides can similarly be converted to benzothiophenes (Scheme 50) [129]. For this process, the corresponding S-silyl derivatives offer a significant advantage [130].

c) Propargylic sulfides and dithioacetals undergo rearrangement to give indenes when catalyzed by AuCl in toluene (Scheme 51) [131, 132].

In a most remarkable AuCl-catalyzed reaction (carried out in toluene at 25 °C), an intramolecular *carbothiolation* of alkynes can be achieved [129].

As shown in very recent work, 3-arylindoles can be prepared from phenylalkynes and nitrosoarenes with AuCl as a catalyst in the presence of $NaBH_4$ in toluene at 90 °C. The reaction is proposed to proceed *via* the N-hydroxy-indoles, which are reduced by $NaBH_4$. The products are obtained in good to moderate yields. Surprisingly, reduction of AuCl to metallic gold by $NaBH_4$ appears to be negligible under the conditions chosen in this study (Scheme 52) [133].



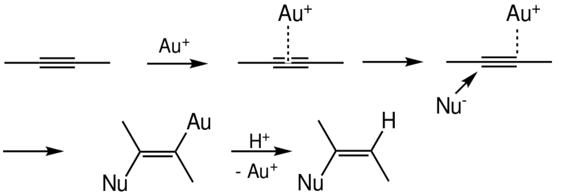
Scheme 52.

7. Summary and Conclusion

Homogeneous gold(I) catalysts for organic transformations are often based on systems prepared by using silver salts. These methods have several significant practical disadvantages and are often characterized by a specific reactivity pattern. From recent work it appears that there are a number of promising alternatives to these silver-dependent protocols.

These include foremost the gold(I) bis(trifluoromethylsulfonyl)imides (“triflimides”) with phosphines or carbenes as auxiliary ligands (**I**, **J**) introduced by Gagosz *et al.* which are particularly easy to handle in stoichiometric quantities. Second, great potential is also offered by the ionic solvates of the gold(I) complexes with diorgano(2-biphenylyl)phosphine ligands employed extensively by Echavarren *et al.* (**U**). A similar principle has been followed successfully with the corresponding diorgano(2-*N*-morpholino-phenyl)-phosphine ligands (**W**) by Hesp and Stradiotto. Third, with solvated cationic (carbene)gold(I) complexes (**V**) designed by Bertrand *et al.* it has been shown that carbenes are often superior to phosphines in their influence on the gold(I) center regarding its activity and selectivity. Finally, very recent work by Nolan *et al.* has given access to novel mono- and dinuclear (carbene)gold(I) hydroxo complexes (**K**, **Z**) which also perform very well as catalysts in a variety of catalytic reactions. These studies have complemented exploratory work by Toste *et al.* on the catalytic action of trinuclear (phosphine)gold(I) oxonium salts (**M**) and by Hashmi *et al.* on the dinuclear (phosphine)gold(I) chloronium salts (**L**). And last but not least, the first (carbene)gold(I) fluoride (**A**) has also been employed as a catalyst for the selective hydrofluorination of alkynes.

These reagents have already opened up convenient and selective pathways towards many target products, and future work will probably widen the scope even further. Their concepts have in common that the catalytically active species is a $[(L)Au]^+$ cation which approaches and activates unsaturated alkene, allene and alkyne functions in the substrate. The identity and structure of these intermediates has been confirmed by several detailed analytical, spectroscopic and structural studies [11]. In the course of a slippage movement [10] of the $[(L)Au]^+$ electrophile away from the center of the multiple bond concerned, one of the carbon atoms can subsequently be attacked by a



Scheme 53.

nucleophile, followed by the cleavage of the (L)Au-C bond by protonation or alkylation *etc.* (Scheme 53) [2 – 10] or by geminal di-auration (Scheme 16a) [65b].

However, the present review has also compiled work in which it has been demonstrated that the auxiliary ligand L (phosphine, carbene) may not be essential. There are many reactions where AuCl alone, with an innocent inorganic additive like K_2CO_3, or together with a donor solvent, shows sufficient activity to catalyze organic transformations. The same is true for anionic complexes like $[(RCN)_2Au]^-$, and even AuCN gave good results in a few cases. It will therefore be worthwhile to find conditions under which not only the use of silver salts, but also of special ligands can be avoided.

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