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Gold-Catalyzed Hydroamination of C–C Multiple Bonds

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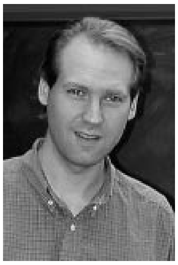
The development of general and efficient methods for the addition of an N–H bond across a C–C multiple bond (hydroamination) represents a significant challenge in both organic synthesis and homogeneous catalysis. Although a diverse range of transition-metal complexes have been employed as catalysts for hydroamination, examples of gold-catalyzed hydroamination were exceedingly rare prior to 2001. However, over the past five years gold complexes have been applied as catalysts for a number of selective organic transformations including the hydroamination of unactivated alkenes, alkynes, allenes, and 1,3-dienes. This Microreview provides a brief overview of the gold-catalyzed hydroamination of C–C multiple bonds.

Nitrogen heterocycles are an important class of compounds that occur widely in nature[1] and that display varied and often potent biological activity.[2] Likewise, acyclic amines are common components of pharmaceuticals,[3] agrochemicals, and cosmetics, and are important intermediates in a number of industrial processes.[4] Due to both the importance of nitrogen-containing compounds and the limitations associated with traditional methods for C–N bond formation,[5] the catalytic addition of an N–H bond across a C–C multiple bond (hydroamination) has received considerable attention as an atom-economical and potentially expedient route to the synthesis of amine derivatives.[6] However, despite considerable effort in this area, general and efficient methods for the hydroamination of C–C multiple bonds, particularly the hydroamination of unactivated alkenes, remain limited.[6,7]

In one potential catalytic cycle for hydroamination, the C–C multiple bond is activated toward nucleophilic attack by the amine through complexation to an electron-deficient, late-transition-metal complex (Scheme 1).[8] Subsequent protonolysis releases the amine derivative and regenerates the catalyst. This approach to hydroamination is appealing as late-transition-metal complexes typically possess little oxophilicity, and therefore often display good functional-group compatibility and low air and moisture sensitivity, desirable traits for potential synthetic applications. However, the high ligating ability of amines often leads to non-productive displacement of the unsaturated fragment in preference to outer-sphere attack.[8] Equally problematic is



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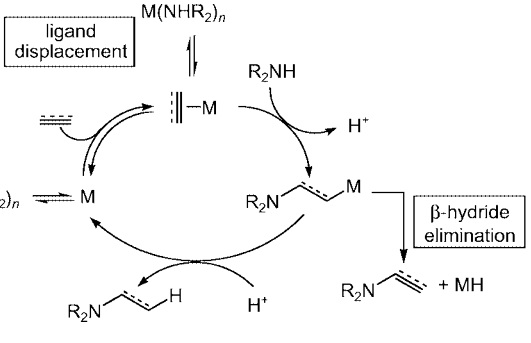
that the M–alkyl complexes formed by nucleophilic attack are often resistant toward protonolysis or are susceptible to β-hydride elimination. In the former case, a stoichiometric amount of the transition-metal complex is required for hydroamination,[9] while in the latter case oxidative amination competes with hydroamination.[10,11]

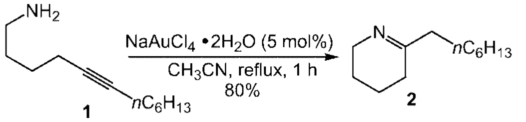


Scheme 1.

Both Au^{III} and cationic Au^{I} complexes are highly carbophilic Lewis acids that activate C–C multiple bonds toward nucleophilic attack.[12] Conversely, these complexes, particularly Au^{I} complexes, possess little oxophilic character, and therefore display good functional-group compatibility and low air and moisture sensitivity. Furthermore, whereas alkylgold complexes are stable with respect to β-hydride elimination, these complexes, particularly (phosphane)gold(I) complexes, are highly reactive with respect to protonolysis of the Au–C bond.[13,14] Although these characteristics point to the potential of gold complexes as catalysts for hydroamination, examples of gold-catalyzed hydroamination were exceedingly rare prior to 2001.[15–17] This oversight mirrors the general dearth of applications of gold complexes in homogeneous catalysis, presumably because gold complexes were considered too inert to function as effective catalysts. This opinion has proven largely inaccurate, and over the past five years gold complexes have been employed as catalysts for a number of selective organic transformations including the cyclization of enynes[18] and for the addition of carbon[19] and oxygen[20] nucleophiles to C–C multiple bonds.[21] Concurrent with these developments, gold complexes have been applied to good effect as catalysts for the hydroamination of alkynes,[22–26] alkenes,[27–29] allenes,[30–33] and conjugated dienes.[34] This Microreview provides a brief account of the history and current activity in the area of gold-catalyzed hydroamination.

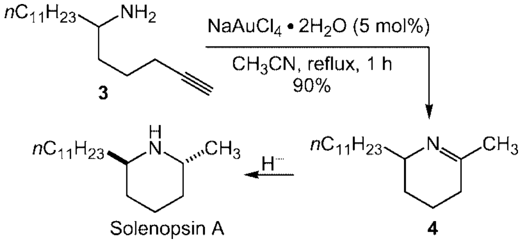
Hydroamination of Alkynes

The first example of gold-catalyzed hydroamination was Utimoto's 1987 report regarding the Au^{III}-catalyzed intramolecular hydroamination of 5-alkynylamines to form tetrahydropyridine derivatives.[15] As an example, treatment of a dilute solution of 5-dodecynylamine (**1**) with a catalytic amount of $NaAuCl_4$ hydrate in refluxing acetonitrile for 1 h led to 6-*exo* cyclization to form 6-heptyl-2,3,4,5-tetrahydropyridine (**2**) in 80% isolated yield [Equation (1)].

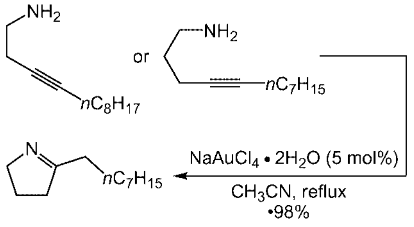


(1)

5-Alkynylamines that possess an alkyl group in α-position to the nitrogen atom and/or a terminal alkyne moiety also underwent effective Au^{III}-catalyzed hydroamination. For example, Au-catalyzed cyclization of 1-undecyl-5-hexynylamine (**3**) led to isolation of the 2,6-disubstituted tetrahydropyridine **4**, a precursor to (±)-Solenopsin A,[35] in 90% yield (Scheme 2). The protocol was also effective for the formation of dihydropyrroles through either the 5-*exo* cyclization of 4-alkynylamines or through the 5-*endo* cyclization of 3-alkenylamines [Equation (2)].



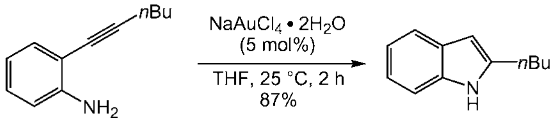
Scheme 2.



(2)

Unfortunately, Au^{III}-catalyzed hydroamination of alkynylamines required high dilution to prevent catalyst decomposition and was not effective for the hydroamination of arylacetylenes.[15] $AuCl_3$ was considerably less efficient for the intramolecular hydroamination of 5-alkynylamines than was $NaAuCl_4$ hydrate.[16]

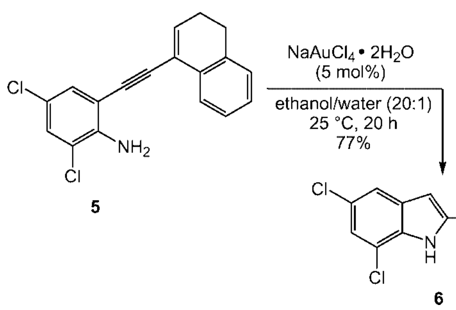
Utimoto extended the scope of Au^{III}-catalyzed hydroamination to include the hydroamination of 2-(1-alkynyl)anilines.[17] As an example, treatment of 2-(1-hexynyl)aniline with a catalytic amount of $NaAuCl_4$ hydrate in THF at room temperature for 2 h led to the isolation of 2-(*n*-butyl)indole in 87% yield [Equation (3)].



(3)

Marinelli has recently modified and expanded the scope of Utimoto's procedure through employment of ethanol/

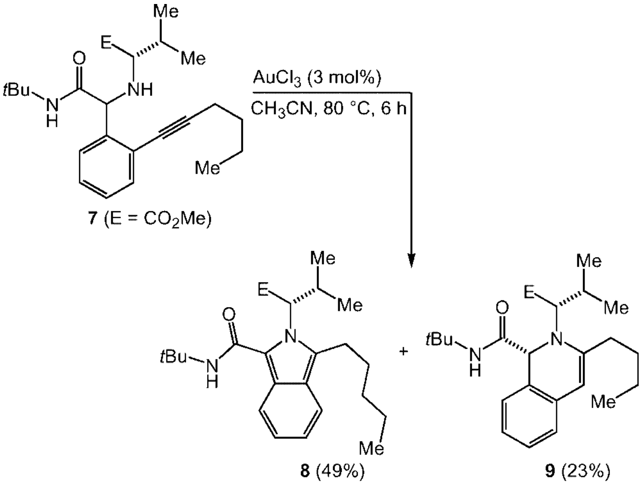
water as the solvent system. As an example of this modified protocol, treatment of the 2-alkynylaniline **5** with a catalytic amount of $NaAuCl_4$ hydrate in a 20:1 ethanol/water mixture at room temperature for 20 h led to the isolation of the 2-alkenylindole **6** in 77% yield [Equation (4)].



(4)

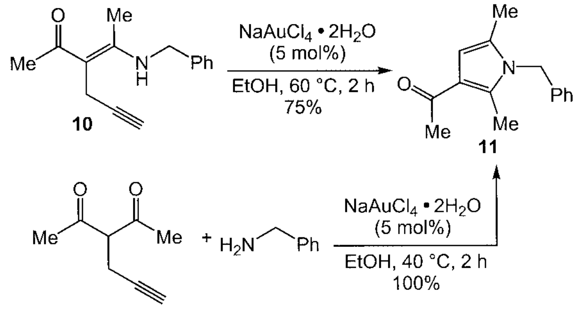
Gold(III)-catalyzed hydroamination of 2-alkynylanilines tolerated electron-rich and electron-poor groups on the aniline moiety and aromatic, secondary and tertiary alkyl, and alkenyl groups at the alkyne carbon atom. The protocol was also effective for cyclization of *N*-acetamide- and *N*-methylcarbamate-protected 2-(alkynyl)anilines.[17,22]

Several additional examples of Au^{III}-catalyzed alkyne hydroamination as a route to heteroaromatic compounds have appeared. Treatment of the alkynylamine **7** with a catalytic amount of $AuCl_3$ in acetonitrile at 80 °C for 6 h led to the isolation of a ca. 2:1 mixture of the isoindole **8** through 5-*exo* cyclization and the dihydroisoquinoline **9** through 6-*endo* cyclization in 72% combined yield [Equation (5)].[23]



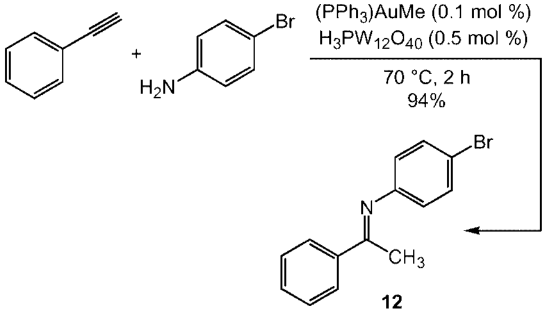
(5)

In a second example, reaction of the enaminone **10** with a catalytic amount of $NaAuCl_4$ hydrate in ethanol at 60 °C for 2 h led to the isolation of the 1,2,3,5-tetrasubstituted pyrrole **11** in 75% yield (Scheme 3).[24] Gold(III) salts also catalyzed the sequential condensation/hydroamination of 2-alkynyl-1,3-diketones with amines to form pyrrolidines.[24] For example, treatment of a 1:1.5 mixture of 2-(3-propynyl)-2,4-pentanedione and benzylamine with a catalytic amount of $NaAuCl_4$ hydrate led to the isolation of **11** in quantitative yield (Scheme 3). This latter protocol tolerated a range of amines and was effective for the condensation/hydroamination of 2-propynyl-1,3-dioxo esters, but was restricted to terminal alkynes.



Scheme 3.

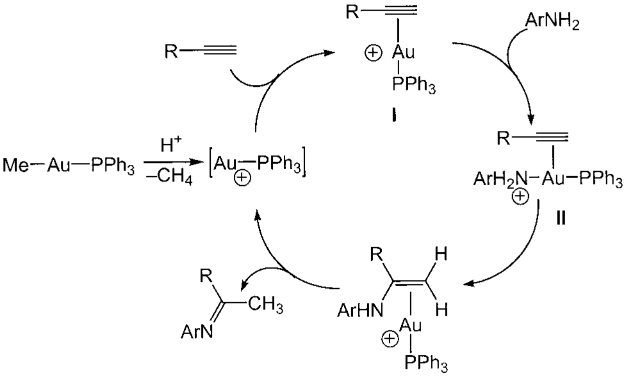
Tanaka has reported an acid-promoted, Au^I-catalyzed procedure for the intermolecular hydroamination of alkynes to form imines,[25] which is based on the catalyst system optimized for the Au-catalyzed intermolecular hydration of alkynes.[36] As an example of the former protocol, treatment of a neat 1:1.1 mixture of phenylacetylene and *p*-bromoaniline with a catalytic 1:5 mixture of $(PPh_3)AuMe$ and $H_3PW_{12}O_{40}$ at 70 °C for 2 h formed the ketimine **12** in 94% yield (^1H NMR) [Equation (6)].



(6)

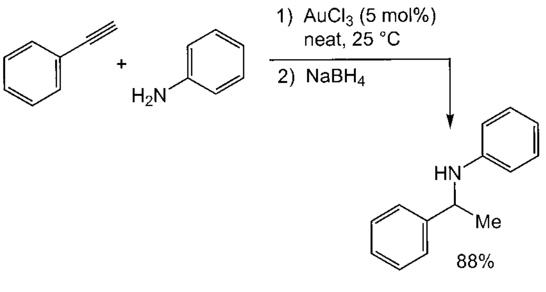
Both gold and acid were required for effective hydroamination and the reaction was quite sensitive to the nature of the acid promoter. Gold-catalyzed intermolecular hydroamination of alkynes was effective for aryl- and alkyl-substituted terminal alkynes, 2-ethynylthiophene, and dialkyl-substituted internal alkynes, although longer reaction time was required for these latter substrates. The protocol tolerated electron-rich, electron-deficient, and sterically hindered primary arylamines, including phenylhydrazine, but did not tolerate alkylamines. The catalyst was highly stable and turnover numbers approaching 9000 were realized for the reaction of phenylacetylene with either 4-cyanoaniline or 4-bromoaniline.[25]

The efficiency of gold(I)-catalyzed intermolecular alkyne hydroamination increased with the decreasing electron density of the aniline and with the increasing electron density of the alkyne. On the basis of these observations, Tanaka proposed an inner-sphere mechanism for alkyne hydroamination analogous to that forwarded by Teles for the Au-catalyzed addition of methanol to alkynes.[37] Complexation of the alkyne to a cationic (phosphane)gold complex, generated by protonolysis of the methylgold precatalyst, could form the (alkyne)gold intermediate **I** (Scheme 4). Coordination of the aniline to gold to form the (alkyne)(amine) intermediate **II** followed by inner-sphere C–N bond formation and proton transfer would lead to imine formation.



Scheme 4.

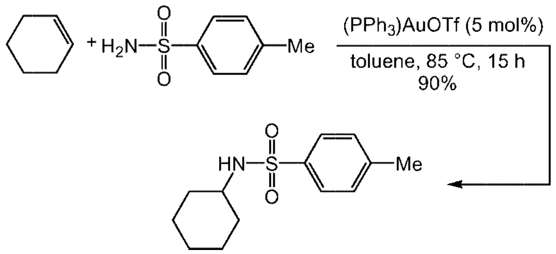
Li has reported that cationic Au^{III} complexes also catalyze the intermolecular hydroamination of terminal alkynes with aniline derivatives.[26] For example, reaction of a neat 1:1.5 mixture of phenylacetylene and aniline catalyzed by a 1:3 mixture of $AuCl_3$ and AgOTf at room temperature followed by reduction with sodium borohydride led to the isolation of (1-phenylethyl)(phenyl)amine in 88% yield [Equation (7)]. The Au^{III}-catalyzed intermolecular hydroamination/reduction of internal alkynes was effective for both alkyl- and arylalkynes and for both electron-rich and electron-deficient anilines.



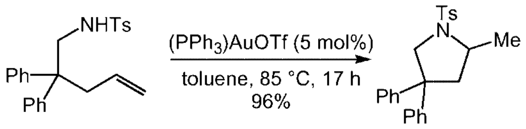
(7)

Hydroamination of Unactivated Alkenes

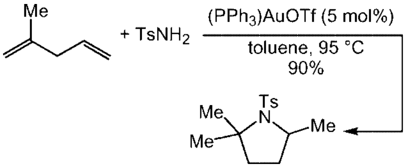
The development of mild and efficient methods for the hydroamination of unactivated alkenes remains one of the most significant challenges in homogeneous catalysis, and gold(I) catalysis has provided new opportunities for the hydroamination of unactivated alkenes. He has reported that $(PPh_3)AuOTf$ catalyzes the intermolecular hydroamination of unactivated alkenes with sulfonamides.[27] As an example, reaction of a 1:4 mixture of *p*-toluenesulfonamide and cyclohexene catalyzed by $(PPh_3)AuOTf$ in toluene at 85 °C for 15 h led to the isolation of *N*-cyclohexyl-*p*-toluenesulfonamide in 90% yield [Equation (8)]. Monosubstituted, 1,1-disubstituted, and trisubstituted alkenes also underwent intermolecular hydroamination, typically with good selectivity for the Markovnikov addition product. Likewise, *N*-(4-pentenyl)sulfonamides underwent gold-catalyzed intramolecular hydroamination to form pyrrolidine derivatives in good yield [Equation (9)], and 1,5-dienes underwent tandem intermolecular/intramolecular hydroamination to form 2,5-substituted pyrrolidines [Equation (10)].



(8)



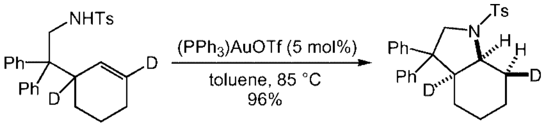
(9)



(10)

Unfortunately, efficient $(PPh_3)AuOTf$-catalyzed hydroamination required employment of sulfonamides as the nitrogen nucleophile (see below).

Gold-catalyzed intramolecular hydroamination of the doubly deuterium-labeled *N*-alkenylsulfonamide **13** led to the isolation of *trans*-**14** in 96% yield [Equation (11)].



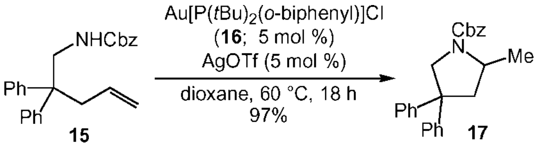
13 *trans*-**14**

(11)

The *trans* relationship of the two deuterium atoms in *trans*-**14** established the *anti* addition of the sulfonamide moiety and the proton across the C=C bond of the alkene. Because protonolysis of Au–C σ-bonds is known to occur with retention of stereochemistry,[14] this result is in agreement with a mechanism analogous to that depicted in

Scheme 1 involving outer-sphere attack of the sulfonamide nitrogen atom on a gold-complexed alkene followed by protonolysis to release the heterocycle.

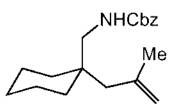
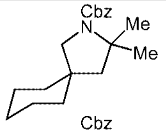
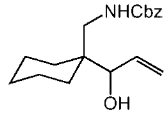
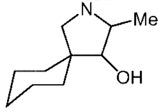
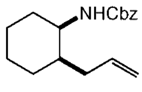
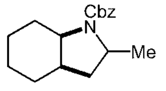
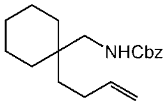
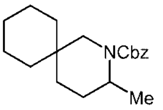
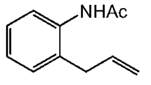
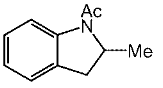
Although sulfonamides have been widely employed as nucleophiles for both the hydroamination and oxidative amination of alkenes,[7k,11,27,38] the strongly reducing conditions required for subsequent deprotection compromises the utility of these transformations.[39] For this reason, Widenhoefer and Han targeted labile carbamates as nucleophiles for the catalytic hydroamination of alkenes. Unfortunately, mixtures of Au(PPh_3)Cl and AgOTf proved an inefficient catalyst system for the intramolecular hydroamination of *N*-alkenylcarbamates.[28] However, gold-catalyzed hydroamination of *N*-alkenylcarbamates was sensitive to the nature of the phosphane ligand and the sterically hindered *ortho*-biphenylylphosphane P(tBu)$_2$(*o*-biphenylyl) proved particularly effective as a supporting ligand for this transformation. For example, reaction of the *N*-(4-pentenyl)carbamate **15** and a catalytic 1:1 mixture of Au[P(tBu)$_2$-(*o*-biphenylyl)]Cl (**16**) and AgOTf (5 mol%) in dioxane at 60 °C for 18 h led to the isolation of the protected pyrrolidine **17** in 97% yield [Equation (12)].



(12)

Gold-catalyzed intramolecular hydroamination of *N*-alkenylcarbamates was compatible with a range of labile carbamate groups and the protocol tolerated substitution at the internal olefinic carbon atom and along the alkyl backbone, including protected and unprotected allylic hydroxy groups (Table 1, Entries 1 and 2). The protocol was also applicable to the synthesis of heterobicyclic compounds and piperidine derivatives (Table 1, Entries 3 and 4). The **16**/AgOTf catalyst system was also highly effective for the hydroamination of *N*-alkenylcarboxamides (Table 1, Entry 5).[29]

Table 1. Intramolecular hydroamination of protected alkenylamines catalyzed by a 1:1 mixture of **16** and AgOTf (5 mol-%) in dioxane for 12–16 h.[a]

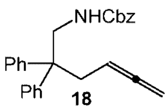
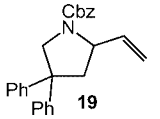
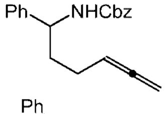
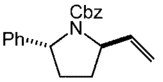
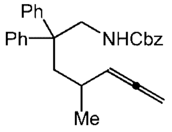
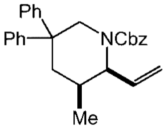
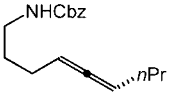
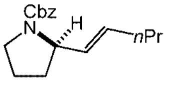
Entry	Alkenyl amine	Temp (°C)	Heterocycle	Yield (%)
1		80		88
2		60		91 (3.6:1)
3		100		95 (2.5:1)
4		100		84
5		80		99

[a] Cbz = benzyloxycarbonyl.

Hydroamination of Allenes

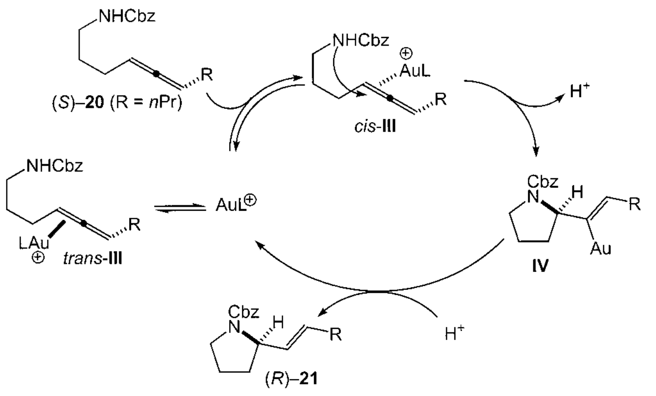
Although allenes are typically more reactive toward transition metals than are alkenes,[40] effective protocols for the catalytic *exo*-hydroamination of *N*-allenylcarbamates have not been forthcoming.[41] However, Widenhoefer and coworkers have recently reported that the (phosphane)gold(I) complex **16** is an exceptionally active precatalyst for the intramolecular *exo*-hydroamination of *N*-allenylcarbamates.[30] As an example, treatment of the *N*-(4,5-hexadienyl)-carbamate **18** with a catalytic 1:1 mixture of **16** and AgOTf (5 mol%) in dioxane at room temperature for 45 min led to the isolation of the pyrrolidine **19** in 96% yield (Table 2, Entry 1). Gold(I)-catalyzed hydroamination of *N*-allenylcarbamates tolerated substitution on the alkyl chain and at the internal and terminal allenyl carbon atoms and the protocol was effective for the formation of piperidine derivatives (Table 2, Entries 2–4).

Table 2. Intramolecular hydroamination of *N*-allenylcarbamates catalyzed by a 1:1 mixture of **16** and AgOTf (5 mol-%) at 25 °C for 5–45 min in dioxane.[a]

Entry	Allenyl amine	Heterocycle	Yield (%)
1	 **18**	 **19**	96
2			80 (16:1)
3			92 (7.0:1)
4	 (*S*)–**20** (84% *ee*)	 (*R*)–**21** (74% *ee*)	96

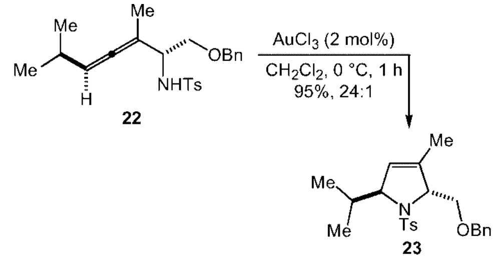
[a] Cbz = benzyloxycarbonyl.

The stereoselective conversion of (*S*)-**20** to (*R*)-**21** (Table 2, Entry 4) is consistent with a mechanism for the Au^{I}-catalyzed hydroamination of *N*-allenylcarbamates initiated by rapid and reversible formation of the (allene)gold complex *cis*-**III**, followed by outer-sphere attack of the carbamate nitrogen atom on the allene moiety (Scheme 5). Protonolysis of the Au–C σ-bond of **IV** with retention of stereochemistry would then release (*R*)-**21**.[14] Noteworthy was that formation of the (*E*)-alkene moiety requires cyclization of the (allene)gold intermediate *cis*-**III**, as opposed to cyclization of the presumably more stable *trans*-**III**. This observation suggests both that formation of the (allene)gold complexes **III** is rapid and reversible and that the transition state for C–N bond formation is destabilized to a greater extent by interaction of the terminal allenic substituent with the carbamate moiety than with the (phosphane)gold fragment.



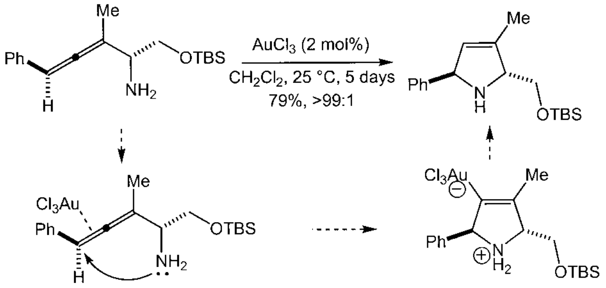
Scheme 5.

Gold complexes also catalyze the intramolecular *endo*-hydroamination of allenes. As an example, treatment of the diasteromerically pure protected α-aminoallene **22** with a catalytic amount of $AuCl_3$ in dichloromethane at 0 °C for 1 h led to the isolation of the 3-pyrroline derivative **23** in 95% yield as a 24:1 mixture of diastereomers [Equation (13)].[31]



(13)

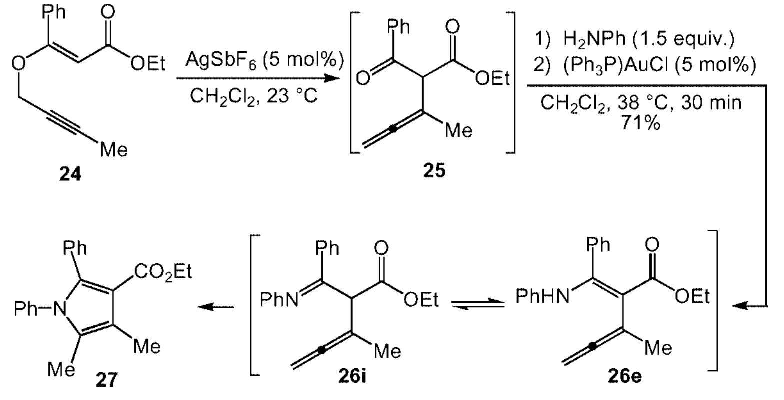
Gold(III)-catalyzed *endo*-hydroamination of *N*-protected α-aminoallenes tolerated both alkyl and aryl substituents at the terminal allenyl carbon atom and *tert*-butyldimethylsilyl protection of the hydroxy group. The transformation was also effective for the hydroamination of primary α-aminoallenes although a considerably longer reaction time was required (Scheme 6). Gold(III)-catalyzed *endo*-hydroamination of α-aminoallenes was proposed to occur by outer-sphere attack of the nitrogen nucleophile on an (allene)gold complex followed by proton transfer (Scheme 6).



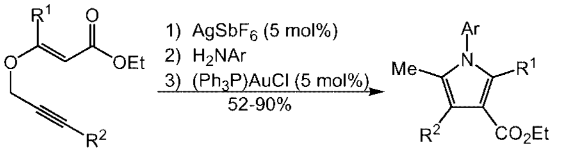
Scheme 6.

Kirsch has recently reported the rearrangement/condensation/cyclization of propargyl vinyl ethers to form pyrroles that likely involves the gold(I)-catalyzed *endo*-hydroamination of an allene in the terminal step.[32] As an example, treatment of the propargyl ether **24** with a catalytic amount of $AgSbF_6$ at room temperature led to a propargyl Claisen rearrangement to form the α-allenyl-β-oxo ester **25**. The allene **25** was not isolated, but was treated sequentially with aniline and a catalytic amount of $(PPh_3)AuCl$ to form the pyrrole **27** in 71% isolated yield. Conversion of **25** into **27** presumably occurs by condensation of the amine with **25**, followed by gold-catalyzed *endo*-hydroamination of the resulting imine **26i** or enamine **26e** (Scheme 7). Noteworthy was that in the absence of $AgSbF_6$, $(PPh_3)AuCl$ failed to catalyze the conversion of **25** to **27**.

The Ag/Au-catalyzed domino rearrangement/condensation/cyclization of propargyl vinyl ethers tolerated alkyl, aryl, and heteroatom substituents at the alkenyl carbon atom in α-position to the ether oxygen atom and/or at the terminal alkynyl carbon atom [Equation (14)].



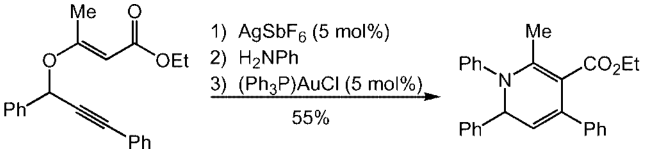
Scheme 7.



R^1 = Me, *n*pentyl, Ph; R^2 = Ph, *o*-C_6H_4OMe, Me, 3-thienyl, CH_2Cy, $(CH_2)_3OTHP$, H, TBDMS

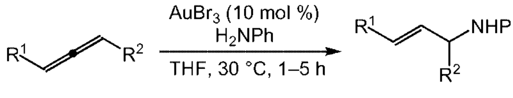
(14)

The protocol tolerated a wide range of aromatic amines but was not effective for aliphatic amines. Substitution at the propargylic position led to a significant decrease in reaction efficiency and, for this reason, the protocol was largely restricted to the formation of 5-methylpyrroles. However, these 5-methylpyrroles were readily converted into the synthetically more versatile 5-formylpyrroles by treatment with 2-iodoxybenzoic acid. Interestingly, propargyl vinyl ethers that possess either an ethyl or phenyl group at the propargylic position underwent rearrangement/condensation/cyclization to form six-membered heterocycles in modest yield [Equation (15)].



(15)

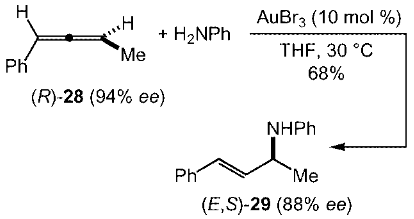
Yamamoto has recently reported that gold(III) complexes catalyze the intermolecular hydroamination of allenes with aromatic amines to form allylamines.[33] As an example, treatment of a 1:2 mixture of 1,2-propadienylbenzene and aniline with a catalytic amount of $AuBr_3$ in THF at 30 °C led to the isolation of *N*-(3-phenyl-2-propenyl)aniline in 78% yield [Equation (16)].



R^1 = Ph, R^2 = H (78%), R^1 = *n*octyl, R^2 = H (70%), R^1 = Ph, R^2 = Me (68%), R^1 = R^2 = *n*pentyl (80%)

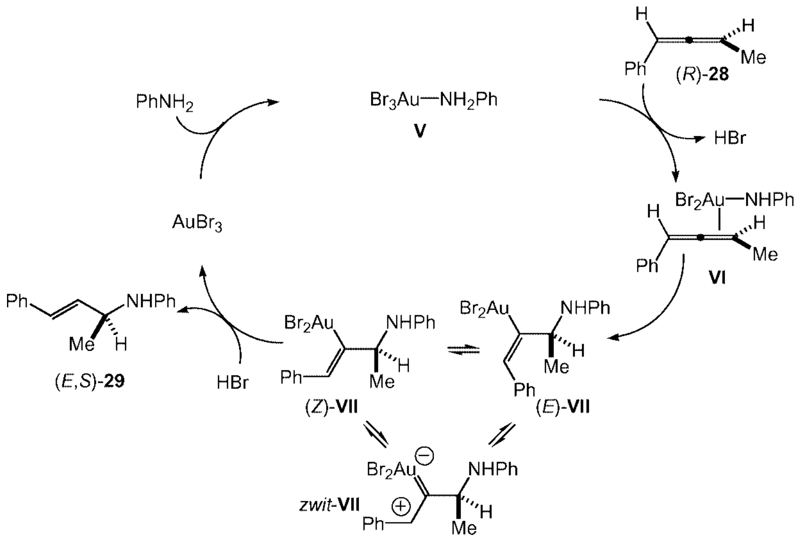
(16)

In addition to monosubstituted arylallenes, monosubstituted alkylallenes and 1,3-disubstituted allenes underwent gold-catalyzed hydroamination in good yield [Equation (16)]. In contrast, gold(III)-catalyzed hydroamination of 1,1-disubstituted allenes was prohibitively sluggish. As was observed in the case of the Au^I-catalyzed intramolecular *exo*-hydroamination of *N*-allenylcarbamates (see above), the intermolecular hydroamination of axially chiral 1,3-disubstituted allenes occurred with selective transfer of chirality. For example, gold(III)-catalyzed hydroamination of enantiomerically enriched 1,2-butadienylbenzene [(*R*)-**28**; 94% *ee*] with aniline led to the isolation of allylamine (*E*,*S*)-**29** in 68% yield with 88% *ee* [Equation (17)].



(17)

On the basis of the stereoselective conversion of (*R*)-**28** to (*E*,*S*)-**29** [Equation (17)], Yamamoto proposed a mechanism for the Au^{III}-catalyzed intermolecular hydroamination of allenes initiated by formation of the (aniline)gold complex **V**.[33] Complexation of gold to the less hindered face of the allene coupled with loss of HBr could then form the

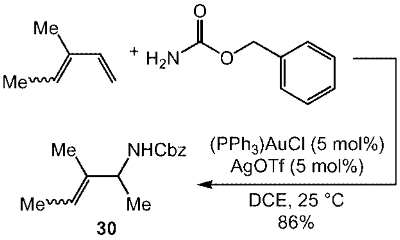


Scheme 8.

(allene)(amido)gold complex **VI**, which could undergo β-migratory insertion to form the vinylgold species (*E*)-**VII**. However, protonolysis of the Au–C bond of (*E*)-**VII** would form (*Z*,*S*)-**29**, which was not observed. For this reason, Yamamoto invoked isomerization of (*E*)-**VII** to (*Z*)-**VII** via the zwitterionic complex *zwit*-**VII**. Protonation of (*Z*)-**VII** with HBr would then form (*E*,*S*)-**29** with regeneration of $AuBr_3$ (Scheme 8). We note that an outer-sphere mechanism analogous to that outlined in Scheme 5 would account for the stereoselective conversion of (*R*)-**28** to (*E*,*S*)-**29** without the necessity of invoking isomerization of vinylgold complexes **VII**.

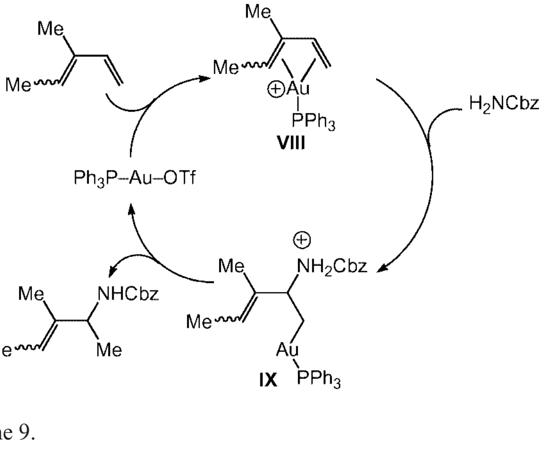
Hydroamination of Conjugated Dienes

As is the case with allenes, conjugated dienes tend to be more reactive toward transition-metal complexes than are simple alkenes. He has exploited this reactivity with the development of a gold(I)-catalyzed protocol for the intermolecular hydroamination of 1,3-dienes with carbamates and sulfonamides to form allylamines.[34] For example, treatment of a 1:1.2 mixture of benzyl carbamate and 3-methyl-1,3-pentadiene with a catalytic 1:1 mixture of $(PPh_3)AuCl$ and AgOTf in 1,2-dichloroethane at room temperature overnight formed benzyl (1,2-dimethyl-2-butenyl)carbamate (**30**) in 86% isolated yield [Equation (18)].



(18)

In addition to the reaction of benzyl carbamate with 3-methyl-1,3-pentadiene, 2-oxazolidinone, methyl carbamate, and *p*-toluenesulfonamide were effective nucleophiles and 1,2-pentadiene and cyclohexadiene were effective dienes for gold-catalyzed intermolecular hydroamination.



Scheme 9.

^{13}C And ^{31}P NMR analysis of stoichiometric mixtures of 3-methyl-1,3-pentadiene, $(PPh_3)AuCl$, and AgOTf with and without benzyl carbamate pointed to complexation of the diene moiety, but not the carbamate, to the gold center. On the basis of these observations, He proposed a mechanism for the Au-catalyzed intermolecular hydroamination of dienes initiated by formation of the (η^4-diene)gold intermediate **VIII** (Scheme 9). Outer-sphere attack of the carbamate followed by protonolysis of the resulting Au–C bond of complex **IX** would give the 1,2-dimethyl-2-butenylamine with regeneration of the cationic Au^I catalyst.

Summary and Outlook

Over the past five years, soluble gold complexes have significantly impacted the development of new and efficient protocols for the catalytic hydroamination of C–C multiple bonds. Many challenges remain in the area of catalytic hydroamination including the development of effective hydroamination protocols that employ unactivated alkenes and/or aliphatic amines and the development of effective methods for asymmetric hydroamination of C–C multiple bonds and the *anti*-Markovnikov hydroamination of α-olefins. It appears likely that gold catalysis will continue to play an important role in the realization of these objectives.

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