Single-Step Synthesis of Dinuclear Neutral Gold(I) Complexes with Bridging Di(N-heterocyclic carbene) Ligands and Their Catalytic Performance in Cross Coupling Reactions and Alkyne Hydroamination

Single step synthesis of dinuclear neutral gold(I) complexes with bridging diNHC ligands and their catalytic performance in cross coupling reactions and alkyne hydroamination

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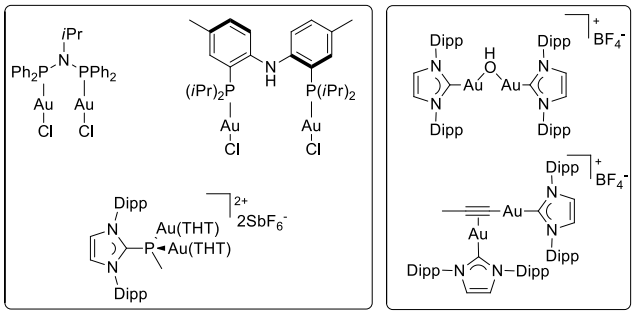
ABSTRACT: We report on a single step procedure for the synthesis of dinuclear gold(I) complexes with bridging diNHC (di(N-Heterocyclic Carbene)) ligands of general formula **$Au_2Br_2L^{1-9}$** (L = diNHC). The obtained complexes differ for the bridging group in between the carbene donors and for the terminal wingtip substituents at the imidazole-2-ylidene rings. The complexes have been characterized by means of elemental analysis, NMR spectroscopy, ESI-MS spectrometry and single crystal X-ray structure analysis. The dinuclear gold(I) complexes have been tested as homogeneous catalysis in technologically relevant reactions such as the cross coupling between phenylboronic acid and aryl bromides and the intermolecular hydroamination of alkynes. The catalytic performance of complexes **$Au_2Br_2L^{1-9}$** has been compared with one another and with the benchmark mononuclear complex IPrAuCl.

INTRODUCTION

Gold(I) complexes with N-Heterocyclic Carbene ligands (NHC) have been extensively studied in the last fifteen years for applications in homogenous catalysis,[1–4] luminescent materials[5–7] and medicinal chemistry.[8,9] In the field of organic transformations, gold(I) NHC complexes are efficient activators of multiple carbon-carbon bonds, promoting cycloisomerization of enynes and ynones, activation of propargylic esters, hydrofunctionalization of alkynes, allenes and alkenes, and carbene transfer reactions.[1,3] One aspect of the catalytic properties of gold compounds, that has emerged only recently is dual gold catalysis. Dual gold catalysis is defined as the ability of two gold complexes to be involved in one catalytic cycle.[10–13] Since dinuclear organogold species, as *gem*-diaurated phenyl, or σ,π-diaurated acetylide complexes, were first proposed and later identified as key intermediates or catalyst reservoirs in gold-catalyzed reactions,[14–17] dinuclear gold(I) complexes have started to be intensively investigated, with the aim of identifying dinuclear catalysts in which cooperative effects lead to enhanced performances.[18–22] Furthermore, dinuclear gold complexes can stabilize unusual oxidation states for gold, such as gold(II)-gold(II) complexes, facilitating the access to catalytic reactions in which the gold catalyst changes its oxidation state, and consequently does not simply act as a Lewis acid.[13,18,23] We, and other researchers, are working since many years in the synthesis of dinuclear gold(I) complexes with bridging bidentate NHC ligands.[24–26] The majority of the complexes of this kind reported up to now are dinuclear dicationic gold(I) complexes, of general formula $[Au_2(\mu\text{-}L_2)]^{2+}$ (L = diNHC) in which the gold centers are linearly dicoordinated by two NHC donors. This type of complexes is not suitable for efficient catalysis, being the two NHC ligands strongly coordinated to the metal center, leaving no free sites for substrate coordination and activation. Only few examples of dinuclear gold(I) complexes with one bridging diNHC ligand and the coordination sphere completed by easily removable ligands, such as halides, have been reported.[27,28] Furthermore, the described syntheses usually involve several steps, inevitably affecting the overall yield of the process, and making the accessibility to these compounds very limited. For this reason, the majority of studies on dinuclear gold(I) catalysts regards P-donor ligands, or dinuclear monocarbene complexes with μ-OH or σ,π-acetylide bridging groups (chart 1).[18–22] In this paper, we report on a novel single step procedure for the synthesis of dinuclear neutral gold(I) complexes with diNHC ligands of general formula **Au_2Br_2L** (L = diNHC). The protocol is based on the one reported by Nolan and Gimeno for mononuclear coinage metals NHC complexes,[29,30] tailored for the dinuclear case. Complexes bearing bidentate ligands with aliphatic bridging group of different length, and with different wingtip substituents, have been successfully obtained and characterized.

Chart 1. Recently reported dinuclear gold(I) precatalysts with bidentate P-donor ligands (left) and monocarbene ligands with μ-OH or σ,π-acetylide bridging groups (right).

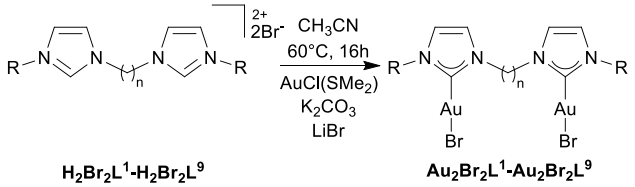


The catalytic performance of the dinuclear gold(I) complexes has been evaluated in the Suzuki type coupling between phenylboronic acid and cinnammyl bromide,[18] and in the intermolecular hydroamination of alkynes.[31] The catalytic activity of the novel dinuclear catalyst has been compared with one another and with the benchmark mononuclear catalyst IPrAuCl.

RESULTS AND DISCUSSION

Synthesis and characterization of the dinuclear gold(I) complexes. The gold(I) diNHC complexes **$Au_2Br_2L^1$-$Au_2Br_2L^9$** were synthesized by reacting the ligand precursors **$H_2Br_2L^1$-$H_2Br_2L^9$** with $AuCl(SMe_2)$ in the presence of K_2CO_3 as base and LiBr (Scheme 1).

Scheme 1. Synthesis of the gold(I) diNHC complexes $Au_2Br_2L^1$-$Au_2Br_2L^9$.



$H_2Br_2L^1$-$H_2Br_2L^9$ → **$Au_2Br_2L^1$-$Au_2Br_2L^9$**

L^1 : n = 1, R = Methyl
L^2 : n = 2, R = Methyl
L^3 : n = 3, R = Methyl
L^4 : n = 1, R = Mesityl
L^5 : n = 2, R = Mesityl
L^6 : n = 3, R = Mesityl
L^7 : n = 1, R = 2,6-Diisopropylphenyl
L^8 : n = 2, R = 2,6-Diisopropylphenyl
L^9 : n = 3, R = 2,6-Diisopropylphenyl

The addition of a bromide source such as LiBr to the reaction mixture minimizes the formation of side products due to halogen scrambling, or to the formation of bis-cationic complexes $[Au_2L_2]^{2+}$. A similar procedure was reported by the groups of Nolan and Gimeno for mononuclear gold(I) complexes.[29,30] The procedure was modified, because of the lower solubility in organic solvents that characterizes the dinuclear complexes compared to their mononuclear analogues, in particular when the ligand has methyl wingtip substituents. The products are white-yellowish solids, isolated in good yields (>60%). The compounds with methyl wingtip groups (**$Au_2Br_2L^1$-$Au_2Br_2L^3$**) are soluble in DMSO and sparingly soluble in $CHCl_3$ and CH_3CN, while the compounds with bulkier mesityl (**$Au_2Br_2L^4$-$Au_2Br_2L^6$**) or 2,6-diisopropylphenil (**$Au_2Br_2L^7$-$Au_2Br_2L^9$**) groups have a good solubility in all the three above mentioned solvents. All the products were characterized by means of elemental analysis, ^{1}H- and ^{13}C-NMR and ESI-MS. In the NMR spectra, the signals expected for the functional groups present in the molecules were found. Moreover, NMR spectra suggest a symmetric coordination motif where the two gold centers have the same coordination environment. The formation of the NHC donor is confirmed in the ^{1}H-NMR spectra by the absence of the proton in position 2 of the imidazole-2-ylidene rings, due to the formation of the gold-carbene bonds. In the ^{13}C-NMR spectra, the signals relative to the carbene carbons are found in the range 173-178ppm, diagnostic position for NHC coordinated to a gold(I) center with a bromide in the *trans* position.[29,30] ESI-MS analysis of the products present the signal relative to the species **$[Au_2BrL^{1\text{-}9}]^+$**, indicative of the formation of the desired dinuclear complexes. The chloro-analogues of complexes **$Au_2Br_2L^3$** and **$Au_2Br_2L^4$** (**$Au_2Cl_2L^3$** and **$Au_2Cl_2L^4$**) were already reported in the literature.[13,32] However, the reported synthesis are based on multistep procedures: transmetallation of the diNHC ligand from the corresponding silver(I) complex in the case of **$Au_2Cl_2L^3$** (overall yield 55%),[32] and treatment with HCl of the methyl derivative **$Au_2Me_2L^4$** in the case **$Au_2Cl_2L^4$** (overall yield 39%).[13]

X-ray crystallography. Single crystals suitable for X-ray diffraction analysis have been obtained by slow diffusion of n-hexane into a dichloromethane solution of **$Au_2Br_2L^4$** and a chloroform solution of **$Au_2Br_2L^5$** or by slow diffusion of diethylether into an acetonitrile solution of **$Au_2Br_2L^6$**. ORTEP views of the molecular structures of **$Au_2Br_2L^4$**-**$Au_2Br_2L^6$** are reported in Figure 1; selected bond distances and angles are listed in Table 1.

Figure 1. ORTEP drawing of complexes **$Au_2Br_2L^4$** (non-symmetric form), **$Au_2Br_2L^5$** and **$Au_2Br_2L^6$** (from left to right). Ellipsoids are drawn at the 50% probability level. Hydrogen atoms and solvent molecules have been omitted for clarity.

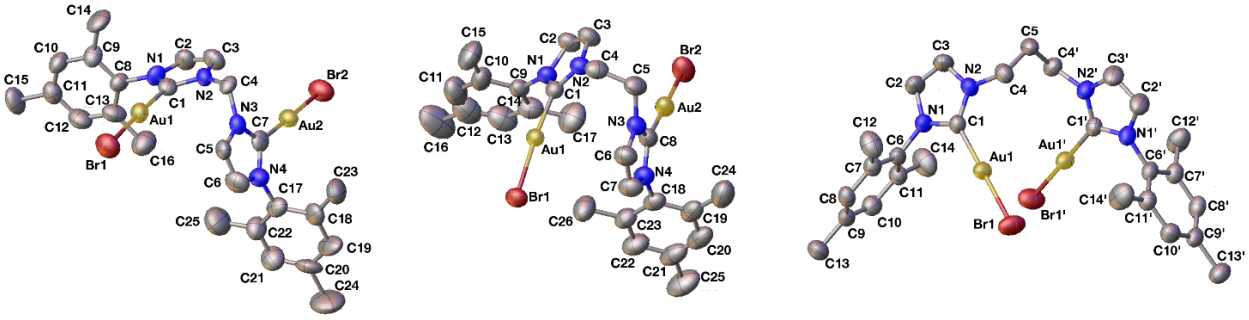


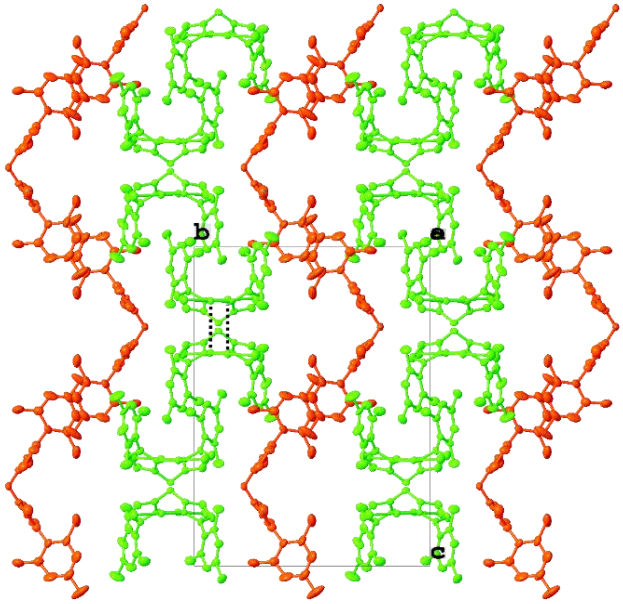
Table 1. Selected bond distances (Å) and angles (°) for the X-ray structure of $Au_2Br_2L^4$-$Au_2Br_2L^6$.

	$Au_2Br_2L^4$	$Au_2Br_2L^5$	$Au_2Br_2L^6$
Au-Br	2.376(2) (Au1-Br1) 2.382(2) (Au2-Br2) 2.379(3) (Au3-Br3)	2.4010(7) (Au1-Br1) 2.3966(9) (Au2-Br2)	2.3787(6) (Au1-Br1)
Au-$C_{carbene}$	1.999(17) (Au1-C1) 1.972(18) (Au2-C7) 1.963(19) (Au3-C26)	1.974(6) (Au1-C1) 1.983(7) (Au2-C8)	1.977(4) (Au1-C1)
$C_{carbene}$-N	1.337(19) (C1-N1) 1.370(19) (C1-N2) 1.35(2) (C7-N3) 1.36(2) (C7-N4) 1.37(2) (C26-N5) 1.35(2) (C26-N6)	1.358(8) (C1-N1) 1.350(8) (C1-N2) 1.349(9) (C8-N3) 1.350(9) (C8-N4)	1.346(6) (C1-N1) 1.349(5) (C1-N2)
Au···Au	5.9848(13) (Au1···Au2) 6.0746(16) (Au3···Au3')	5.1449(4) (Au1···Au2)	4.0861(9) (Au1···Au1')
$C_{carbene}$-Au-Br	177.4(5) (C1-Au1-Br1) 178.3(4) (C7-Au2-Br2) 174.2(5) (C26-Au3-Br3)	175.56(19) (C1-Au1-Br1) 178.50(20) (C8-Au2-Br2)	177.12(13) (C1-Au1-Br1)
BrAuAuBr[a]	173.27(11) (Br1Au1Au2Br2) 178.60(30) (Br3Au3Au3'Br3')	141.53(4) (Br1Au1Au2Br2)	93.80(4) (Br1Au1Au1'Br1')

[a] Torsional angle.

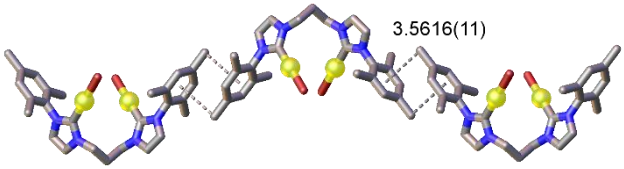
In all three cases, the expected molecular structures have been obtained. The two gold(I) centers of the dinuclear complexes are linearly dicoordinated by a bridging dicarbene ligand and a bromide, being the $C_{carbene}$-Au-Br angles close to 180°. The $C_{carbene}$-Au and Au-Br bond distances are in accordance with those reported for mononuclear NHC-Au-Br complexes.[33] In the crystal of **$Au_2Br_2L^4$**, two crystallographically independent molecules of the complex are present together with a disordered chloroform solvent molecule. One of the molecules of the complex has a symmetric structure, with a twofold rotation axes passing through the bridging methylene carbon atom. The structural parameters of the two molecules are slightly different (Table 1), in particular, the $C_{carbene}$-Au-Br angle of the symmetric form deviate more from linearity (174.2(5)°) compared to the non-symmetric form (177.4(5) and 178.3(4)°). It is interesting to note that the packing of the two crystallographically independent molecules of compound **$Au_2Br_2L^4$** is very different. In fact, the disposition of the symmetric form in the crystal packing shows the molecules in an alternating arrangement without appreciable interactions between them as evidenced in Figure 2 (orange), while the non-symmetric form, whose packing is reported in Figure 2 (green) tends to pack in such a manner that the Au atoms of two adjacent molecules are at a distance of 3.703(1) Å and 3.804(1) Å, which is shorter than the Au···Au intramolecular separation. Further details on the crystal packing of **$Au_2Br_2L^4$** are given in Figure S24. The asymmetric unit of **$Au_2Br_2L^5$** is composed of a complex and a disordered dichloromethane solvent molecule. Finally, the asymmetric unit of **$Au_2Br_2L^6$** contains half molecule. The other half is generated by symmetry through a twofold rotation axes passing through the central carbon atom of the bridging group (C5). In the crystal packing of **$Au_2Br_2L^6$**, a π-π stacking interaction involving the mesityl group of different dinuclear complexes leads to the formation of a 1D supramolecular chain (Figure 3).

Figure 2. View along the *a* axis of the crystal packing of **$Au_2Br_2L^4$**. The symmetric and asymmetric form of the complex are highlighted in orange and green respectively.



On the contrary, no π-π stacking interactions have been observed for **$Au_2Br_2L^4$** and **$Au_2Br_2L^5$**. The three complexes **$Au_2Br_2L^4$** - **$Au_2Br_2L^6$** differ for the length of the aliphatic bridging linker of the bidentate diNHC ligand. From a structural point of view this mainly influences the relative orientation of the two linear $C_{carbene}$-Au-Br fragments.

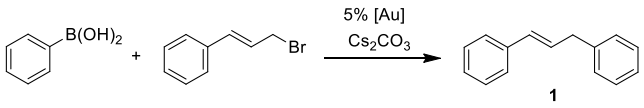
Figure 3. π-π stacking interaction in the crystal packing of **$Au_2Br_2L^6$** (reported distance in Å).



This can be easily evaluated considering the torsional angle between the two Au-Br fragments. Increasing the length of the aliphatic spacer the molecule folds reducing the BrAuAuBr torsional angle and the Au···Au distance, (Table 1). With the shortest methylene bridging group, the two gold(I) are pretty far away from each other; the Au···Au distance in **$Au_2Br_2L^4$** is around 6 Å (5.9848(13) and 6.0746(16) Å for Au1···Au2 and Au3···Au3') and the BrAuAuBr torsional angle is close to 180° (173.27(11) and 178.60(30)° for Br1Au1Au2Br2 and Br3Au3Au3'Br3' respectively). The same spatial arrangement has been observed for the corresponding dichloro analogue, as reported by Toste *et al*..[18] By increasing the number of carbon atoms in the alkyl bridging group this tendency is reduced, probably because this enhances the structural degree of freedom of the systems for which a higher number of possible conformations are accessible. According to that, BrAuAuBr torsional angles and the Au···Au distances values decrease as more carbon atoms are added to the aliphatic spacer, as confirmed by the data of **$Au_2Br_2L^5$** and **$Au_2Br_2L^6$** (141.53(4)° and 5.1449(4) Å for **$Au_2Br_2L^5$** and 93.80(4)° and 4.0861(9) Å for **$Au_2Br_2L^6$**).

Catalytic activity. Recently Toste *et al*. have reported on the use of a dinuclear gold(I) catalyst with a bidentate aminophosphine ligand in the Suzuki cross coupling between allylbromides and boronic acids.[18] It was in fact demonstrated that bimetallic gold complexes undergo accelerated oxidative addition, due to the formation of Au^{II}–Au^{II} species (rather than discrete Au^{III}) upon oxidation, resulting in improved catalytic performances.[34] We have thus tested our catalysts by using the literature reported optimized conditions,[18] with phenylboronic acid and cinnamyl bromide as substrates (Scheme 2).

Scheme2. The employed standard cross coupling reaction.



The obtained results are listed in Table 2. Complexes **$Au_2Br_2L^{1\text{-}9}$** actually produce low yields of the coupling product, particularly with mesityl as wingtip substituent, and appear less efficient than the dinuclear complex with a bidentate aminophosphine ligand reported by Toste (although reaction with the same two substrates was not described in the latter case).[18] The best result is obtained with complex **$Au_2Br_2L^9$** (Table 2, entry 11), with a propylene bridging group between the two carbene donors and a diisopropylphenyl wingtip substituent. Furthermore all dinuclear catalysts, with the exception of **$Au_2Br_2L^4$** and **$Au_2Br_2L^5$** (Table 2, entries 6 and 7), show a better performance compared to mononuclear IPrAuCl (Table 2, entry 2).

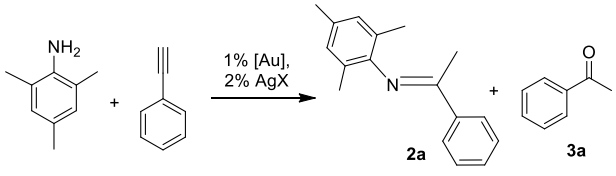
Table 2. Catalytic performances of the complexes $Au_2Br_2L^1$- $Au_2Br_2L^9$ in the cross coupling of cinnamyl bromide with phenylboronic acid.

Entry	cat	Yield **1**(%)
1	-	< 1
2	**IPrAuCl**[a]	15
3	**$Au_2Br_2L^1$**	23
4	**$Au_2Br_2L^2$**	20
5	**$Au_2Br_2L^3$**	19
6	**$Au_2Br_2L^4$**	7
7	**$Au_2Br_2L^5$**	11
8	**$Au_2Br_2L^6$**	17
9	**$Au_2Br_2L^7$**	23
10	**$Au_2Br_2L^8$**	26
11	**$Au_2Br_2L^9$**	30

Reaction conditions: 0.123mmol phenylboronic acid, 0.492mmol cinnamyl bromide, 5 mol% catalyst, 0.379mmol Cs_2CO_3, 65 °C, 18 h. [a] 10 mol% catalyst.

The performance of the dinuclear Au complexes as catalysts has been also screened in a technologically relevant reaction such as the intermolecular catalytic hydroamination of alkynes.[35,36] which is a synthetically useful reaction that can be conveniently catalyzed by gold(I) species,[37] including NHC complexes of Au.[38–45] Catalytic tests were run on the hydroamination of phenylacetylene with an aromatic primary amine such as mesitylamine (Scheme 3), which is notoriously a rather difficult amine substrate for hydroamination reactions. Two equivalents with respect to the complexes of a silver salt were employed as cocatalyst, which removes the halide ligands thereupon activating the Au centers for reaction.

Scheme 3. The employed standard hydroamination reaction.



The initially employed reaction conditions were taken from our recent work on the catalysis of the same reaction by Pd(II) complexes.[31] We first performed a screening of the

reaction conditions, optimizing the solvent, the temperature and the catalyst counteranion introduced with the silver salt using as catalyst complex **$Au_2Br_2L^9$**. Screening of the solvent (Table 3) yielded results similar to those previously recorded with Pd complexes.[31] In particular, neat conditions provided the highest yields in hydroamination product, followed by use of an ionic liquid with a noncoordinating anion. A small amount of acetophenone, the formal product of hydration of the phenylaceylene substrate, was invariably obtained as coproduct. Acetophenone formation was found to proceed through both Au catalyzed hydration of phenylacetylene and hydrolysis of the hydroamination product by adventitious water, most probably brought in the system with the silver salt cocatalyst, which is quite hygroscopic. Compared to the previously employed Pd complexes, the use of **$Au_2Br_2L^9$** allowed to significantly reduce the reaction time, while at the same time maintaining a high reaction yield; most notably, and at variance with the Pd case, catalytic activity was observed also at 40 °C (last entry in Table 3).

Table 3. Screening of the solvent for the hydroamination reaction of phenylacetylene with mesitylamine, promoted by catalyst $Au_2Br_2L^9$

Solvent	Time (h)	T(°C)	Yield **2a** (%)	Yield **3a** (%)
Toluene	22	80	33	3
Acetonitrile	22	80	18	1
IL[a]	22	80	75	9
Neat	22	80	93	6
neat[b]	4	80	81	6
neat[b]	4	40	22	2

Reaction conditions: 1 mmol mesitylamine, 1 mmol phenylacetylene, 0.5 mol% **$Au_2Br_2L^9$**, 2 mol% AgOTf, 1 mL solvent, 80 °C, 22 h. [a] IL= 1-butyl-2-methylimidazolium bis(trifluoromethylsulfonyl)imide; [b] Reaction performed with 1 mol% **$Au_2Br_2L^9$**.

Screening of the silver salt co-catalyst was consequently performed at 40 °C under neat conditions (Table 4). In stark contrast to previously reported Pd catalysts,[31] the performance of **$Au_2Br_2L^9$** was found to depend heavily on the silver salt anion: in particular, oxoanions were found to be detrimental to the process, whereas less coordinating anions such as bis(trifluoromethanesulfonyl)imidate, hexafluorophosphate or hexafluoroantimoniate enabled a much better performance, with hexafluoroantimoniate standing out as the best choice. This might be indicative of a different mechanism, or at least of different rate determining steps of the reaction with the two metal centers. A control experiment was also performed in order to evaluate the catalytic activity of the silver salt cocatalyst *per se*, since there have been reports in the literature that hydroamination can be also catalyzed by silver salts.[46] Silver hexafluoroantimoniate (2 mol%) did indeed convert to some extent the alkyne to the hydroamination product (16%) and to the hydration product (7%) after 4 hours at 40 °C under neat conditions, but catalytic efficiency was much lower than in the presence of the Au catalyst, and it should be also taken into account that in the presence of **$Au_2Br_2L^9$** most of the silver precipitates as the insoluble bromide. Consequently, it can be safely stated that the presence of silver in the catalytic system does not result in a significant contribution to the catalytic event. After having optimized the reaction conditions, the various gold complexes were finally screened for their catalytic performance in the model hydroamination reaction between phenylaceylene and mesitylamine. The results are reported in Table 5.

Table 4. Screening of the silver salt cocatalyst for the hydroamination reaction of phenylacetylene with mesitylamine, promoted by catalyst $Au_2Br_2L^9$

Entry	Cocatalyst	Yield **2a**(%)	Yield **3a**(%)
1	AgOTs	2	<1
2	AgOTf	22	2
3	$AgNTf_2$	59	5
4	$AgPF_6$	59	6
5	$AgSbF_6$	70	6

Reaction conditions: 1 mmol mesitylamine, 1 mmol phenylacetylene, 1 mol% **$Au_2Br_2L^9$**, 2 mol% Ag salt cocatalyst, 40 °C, 4 h.

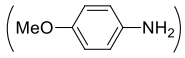
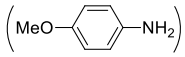
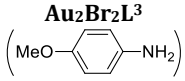
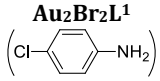
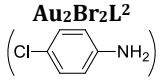
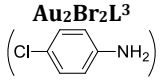
Table 5. Screening of the gold complexes as catalysts for the hydroamination reaction of phenylacetylene with mesitylamine

Entry	Catalyst	Yield **2a**(%)	Yield **3a**(%)
1	**$Au_2Br_2L^1$**	93	7
2	**$Au_2Br_2L^2$**	94	6
3	**$Au_2Br_2L^3$**	94	6
4	**$Au_2Br_2L^4$**	64	3
5	**$Au_2Br_2L^5$**	75	9
6	**$Au_2Br_2L^6$**	72	10
7	**$Au_2Br_2L^7$**	73	2
8	**$Au_2Br_2L^8$**	75	2
9	**$Au_2Br_2L^9$**	70	6
10	**IPrAuCl**[a]	88	11

Reaction conditions: 1 mmol amine, 1 mmol phenylacetylene, 1 mol% Au catalyst, 2 mol% $AgSbF_6$, 40 °C, 4h. [a] 2 mol% Au catalyst.

It is evident that all complexes bearing aryl substituents deliver approximately the same performance in the reaction (entries 4-9), irrespective both of the kind of aryl substituent (mesityl or 2,6-diisopropylphenyl) and of the nature of the bridge between the carbene units (methylene, ethylene or propylene). In contrast, better performances were recorded with the N-methyl substituted complexes, which were the only catalysts, together with benchmark IPrAuCl (entry 10), to reach complete alkyne conversions and very high hydroamination yields within the four hours reaction time. In order to better differentiate the performance of these complexes, we chose to perform the reaction with only 0.2 mol% complex. The results are reported in Table 6.

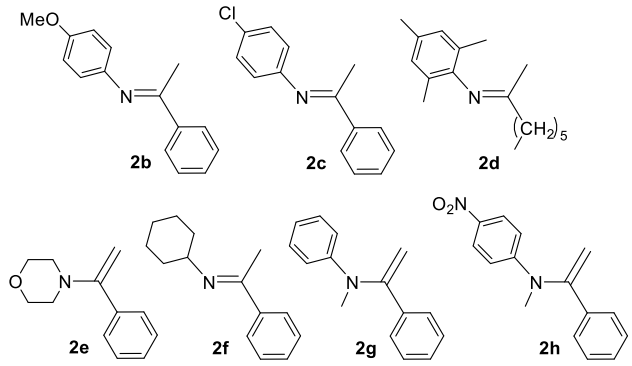
Table 6. Screening of catalysts for the hydroamination reaction at 0.2% catalyst loading

Entry	Catalyst	Time(h)	Yield **2** (%)	Yield **3** (%)
1	**$Au_2Br_2L^1$**	2 4	(**2a**) 20 (**2a**) 38	(**3a**) 1 (**3a**) 9
2	**$Au_2Br_2L^2$**	2 4	(**2a**) 22 (**2a**) 35	(**3a**) 3 (**3a**) 10
3	**$Au_2Br_2L^3$**	2 4	(**2a**) 42 (**2a**) 51	(**3a**) 3 (**3a**) 4
4	**IPrAuCl**[a]	2 4	(**2a**) 49 (**2a**) 55	(**3a**) 2 (**3a**) 4
5	**$Au_2Br_2L^1$** 	2 4	(**2b**) 4 (**2b**) 8	(**3a**) 1 (**3a**) 2
6	**$Au_2Br_2L^2$** 	2 4	(**2b**) 2 (**2b**) 4	(**3a**) 1 (**3a**) 2
7	**$Au_2Br_2L^3$** 	2 4	(**2b**) 35 (**2b**) 38	(**3a**) 4 (**3a**) 5
8	**$Au_2Br_2L^1$** 	2 4	(**2c**) 28 (**2c**) 39	(**3a**) 4 (**3a**) 5
9	**$Au_2Br_2L^2$** 	2 4	(**2c**) 10 (**2c**) 18	(**3a**) 6 (**3a**) 7
10	**$Au_2Br_2L^3$** 	2 4	(**2c**) 39 (**2c**) 51	(**3a**) 2 (**3a**) 9

Reaction conditions: 5 mmol amine, 5 mmol phenylacetylene, 0.2 mol% Au catalyst, 0.4 mol% $AgSbF_6$, 40 °C. [a] 0.4 mol% Au catalyst.

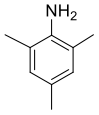
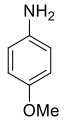
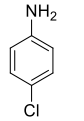
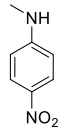
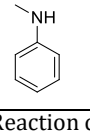
The results obtained in these conditions (Table 6, entries 1-3) highlight the higher initial activity displayed by complex **$Au_2Br_2L^3$** bearing the propylene bridge compared to the other complexes bearing shorter bridges. Since this is also the complex in which the two Au centers can come at closest distance, this might again be an indication of cooperativity of the two centers in the catalytic event. Incidentally, a slight cooperative effect in polynuclear gold(I) complexes as catalysts in alkyne hydrohydrazinations and hydroaminations has been very recently reported.[47] Comparison of the results obtained with the various complexes after 2 and 4 hours reaction time also indicates that complex **$Au_2Br_2L^3$** deactivates more rapidly than the other two, possibly as the consequence of the easier decomposition to Au colloids. A very similar behavior is exhibited also by the benchmark catalyst IPrAuCl (Table 6, entry 4). Remarkably, complex **$Au_2Br_2L^3$** clearly stands out as the best catalyst also in reactions with other substituted primary arylamines, such as 4-anisidine (Table 6, entries 5-7) and 4-chloroaniline (Table 6, entries 8-10), which provides additional support to the existence of a cooperative effect. On the other hand, complex **$Au_2Br_2L^3$** fails altogether to effect hydroaminations with internal alkynes or with secondary amines, either at 40 or at 80 °C. Such a reaction scope is largely shared also by the other complexes investigated in this work. As shown in Table 7, reasonable conversion to the hydroamination product is obtained at 40 °C only with terminal alkynes and primary arylamines (Chart 2).

Chart 2. Scope of the alkyne hydroamination reaction.



With internal alkynes (phenylpropyne, diphenylacetylene), secondary arylamines (N-methylaniline), primary/secondary alkylamines (cyclohexylamine, morpholine) no formation of hydroamination product is generally observed, neither at 40 °C nor at 80 °C, with the exception of complexes bearing the N-2,6-diisopropylphenyl substituent, such as **$Au_2Br_2L^7$**, which beside efficiently catalyzing the reaction with differently ring substituted primary anilines at 40°C, also effects sluggish hydroamination of phenylacetylene with cyclohexylamine or morpholine at 80°C (Table 7). Furthermore, complex **$Au_2Br_2L^7$** is also able to effect hydroaminations of phenylacetylene with a secondary aromatic amine such as N-methylaniline at 80 °C in up to moderate yield (Table 7 and Scheme 4). However, the enamine hydroamination product is not stable under the reaction conditions and tends to undergo further Au-catalyzed reaction with an additional molecule of phenylacetylene through a cascade reaction sequence, leading to the bicyclic product reported in Scheme 4. Under the same conditions IPrAuCl produces the substituted 1,2-dihydroquinoline **4** exclusively without intermediate accumulation of the hydroamination product (last entry of Table 7).

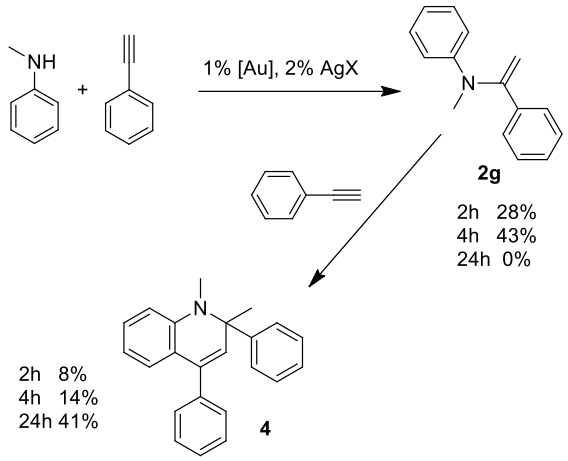
Table 7. Substrate screening for the hydroamination reaction with the gold catalysts

Amine	Alkyne	Catalyst	T (°C)	Time (h)	Yield (%)
		**$Au_2Br_2L^4$**	40	4	(**2d**) 76
	 [a]	**$Au_2Br_2L^7$**	40	4	(**2b**) 70
	 [a]	**$Au_2Br_2L^7$**	40	4	(**2c**) 50
	 [a]	**$Au_2Br_2L^7$**	80	4	(**2e**) 11
	 [a]	**$Au_2Br_2L^7$**	80	4	(**2f**) 7
	 [a]	**$Au_2Br_2L^7$**	80	4	(**2g**) 43 (**4**) 14
	 [a]	**$Au_2Br_2L^7$**	80	4 24	(**2h**) 53 (**2h**) 72
	 [a]	**IPrAuCl**[b]	80	4	(**4**) 69

Reaction conditions: 1 mmol amine, 1 mmol alkyne, 1 mol% Au catalyst, 2 mol% $AgSbF_6$. [a] Reaction performed with 2 mmol phenylacetylene. [b] 2 mol% Au catalyst,

The possible onset of this reaction has been observed previously with a few catalytic systems, including gold(I) NHC complexes, and mechanistically interpreted in terms of a nucleophilic addition/intramolecular hydroarylation sequence.[48–52] It has to be remarked that cascade reactions of this kind are not observed at all with primary arylamines using the gold catalysts described herein. We have tried to expand the cyclization reaction scope in our conditions, by reacting N-methyl-*p*-nitroaniline with phenylacetylene (Table 7). In this reaction, however, we observed only the formation of the hydroamination product (**2h**) even after 24 hours. The different reactivity in the presence of a nitro group on the aromatic ring of the secondary amine suggests that the cascade reaction sequence could be different in this case compared to the literature, and involves rate determining intermolecular alkyne hydroarylation at the aromatic amine ring (i.e. the most electron-rich ring) followed by cyclization. More mechanistic investigations are however needed to substantiate this statement. We have also tried to react in the same conditions N-methylaniline with 1-octyne and 1-hexyne, but in these cases we did not observe neither the formation of the hydroamination nor of the cyclization product. Thus, the reaction appears at present limited to terminal arylacetylenes.

Scheme 4. Cascade reaction involving alkyne hydroamination with N-methylaniline and subsequent cascade reaction of the hydroamination product with phenylacetylene.



The reason for the moderate activity with less reactive alkylamines and secondary arylamines, evidenced by Au catalysts bearing the N-2,6-diisopropylphenyl substituent, can in our opinion be traced back to the increased stability imparted to the complex by this large substituent, which in turn allows the complex to survive for sufficient time at the reaction temperature (80 °C) to promote the reaction to some extent. It has to be remarked that whenever successful NHC-Au catalyzed hydroamination with these difficult substrates was reported, high reaction temperatures (often above 100 °C) were invariably required.[5,38–44] We currently aim at further optimizing the reaction conditions in order to improve the efficiency of these reactions with these substrates

CONCLUSIONS

In this paper we have reported on an optimized one step procedure for the synthesis of dinuclear neutral gold(I) complexes with bridging diNHC ligands of general formula **Au_2Br_2L** (L = diNHC ligand). Our single step synthetic protocol is tolerant towards different wingtip groups (methyl, mesityl and 2,6-diisopropylphenyl) and bridging groups in between the two carbene donors. The structural analysis of complexes **$Au_2Br_2L^{4\text{-}6}$** has shown that, by elongating the aliphatic bridge between the imidazole-2-yilidene rings from one to three carbon atoms, the two gold(I) centers can come closer one to another. This is in line with what we already reported for dinuclear gold(I) diNHC complexes of general formula $[Au_2L_2]^{2+}$.[6] The synthesized complexes have been tested as catalysts in the cross coupling reaction between phenyl boronic acid and cinnamyl bromide; the complexes

have shown moderate activity in this reaction. Better performances have been recorded in the hydroamination reaction of phenylacetylene with mesitylamine. Other primary arylamines can be used with good results; however, the catalysts cannot activate internal alkynes and aliphatic amines, with the exception of complex **$Au_2Br_2L^7$** that effects sluggish hydroamination of phenylacetylene with cyclohexylamine or morpholine at 80°C. From the catalytic studies, we have also gained important insights on the structure/activity relationship in the gold(I) complexes. Complexes with bulkier wingtip substituents such as 2,6-diisopropylphenyl, present higher stability under catalytic conditions, whereas complexes with small N-methyl substituents are more reactive. Complexes with the more flexible propylene bridging group display in general a better catalytic performance compared to the complexes with shorter and less flexible linkers, which we attribute to the fact that the two gold(I) centers can come more easily close one to another, thus enabling cooperative catalysis. Further mechanistic studies will be however necessary to rationalize the presence of cooperative effects in the studied catalytic reactions.

EXPERIMENTAL SECTION

All manipulations were carried out using standard Schlenk techniques under an atmosphere of argon or dinitrogen. The reagents were purchased by Aldrich as high-purity products and generally used as received; all solvents were used as received as technical grade solvents. The diimidazolium salts **$H_2Br_2L^1$-$H_2Br_2L^9$** were synthesized according to literature procedure.[53] NMR spectra were recorded on a Bruker Avance 300 MHz (300.1 MHz for ^{1}H and 75.5 for ^{13}C); chemical shifts (δ) are reported in units of parts per million (ppm) relative to the residual solvent signals. ESI mass spectra were recorded on a Finnigan Thermo LCQ-Duo ESI mass spectrometer. Elemental analyses were carried out by the microanalytical laboratory of Chemical Sciences Department (University of Padova) with a Thermo Scientific FLASH 2000 instrument.

General procedure for the synthesis of the gold(I) complexes $Au_2Br_2L^1$ - $Au_2Br_2L^9$. A mixture of the diimidazolium salt (0.50 mmol), $AuCl(SMe_2)$ (1.00 mmol), potassium carbonate (11.00 mmol), and LiBr (2.50 mmol) in acetonitrile (50 mL) was heated and maintained at 60 °C for 16 h. The obtained suspension was then filtered over a PTFE millipore syringe filter (polytetrafluoroethylene, 0.45 μm). The solvent was removed at reduced pressure form the filtrate, obtaining a brown/yellow solid. The crude product was recrystallized from acetonitrile/diethylether (**$Au_2Br_2L^{1\text{-}3}$**) or dicholoromethane/n-hexane (**$Au_2Br_2L^{4\text{-}9}$**) to obtain a white/yellow solid. Complexes **$Au_2Br_2L^4$**, **$Au_2Br_2L^7$** and **$Au_2Br_2L^8$** was further purified by recrystallization from acetone/n-hexane. Purity of the isolated complexes has been established by elemental analysis. Although the elemental analysis results are outside the range viewed as establishing analytical purity, they are provided to illustrate the best values obtained to date.

$Au_2Br_2L^1$. Yield 83%. ^{1}H NMR (300.1 MHz, [D_6]DMSO, 25 °C) δ=3.77 (s, 6H, CH_3), 6.43 (s, 2H, CH_2), 7.53 (s, 2H, CH), 7.66 ppm (s, 2H, CH). ^{13}C NMR (75.5 MHz, [D_6]DMSO, 25 °C) δ=38.1 (CH_3), 62.3 (CH_2), 121.4 (CH), 123.4 (CH), 173.6 ppm (N*C*N). ppm. ESI-MS (m/z): 649.12 ([M-Br]$^+$, expected 648.98). Elemental analysis calcd (%) for $C_9H_{12}N_4Br_2Au_2$: C 14.81, H 1.66, N 7.68; found: C 14.86, H 1.74, N 7.74.

$Au_2Br_2L^2$. Yield 75%. ^{1}H NMR (300.1 MHz, [D_6]DMSO, 25 °C) δ=3.69 (s, 6H, CH_3), 4.48 (s, 4H, CH_2), 7.30 (d, ^{3}J(H,H)=3Hz, 2H, CH), 7.40 ppm (d, ^{3}J(H,H)=3Hz, 2H, CH). ^{13}C NMR (75.5 MHz, [D_6]DMSO, 25 °C) δ=37.6 (CH_3), 51.0 (CH_2), 121.4 (CH), 123.3 (CH), 172.3 ppm (N*C*N). ESI-MS (m/z): 665.10 ([M-Br]$^+$, expected 664.97). Elemental analysis calcd (%) for $C_{10}H_{14}N_4Br_2Au_2$: C 16.14, H 1.90, N 7.53; found: C 16.09, H 2.14, N 6.92.

$Au_2Br_2L^3$. Yield 81%. ^{1}H NMR (300.1 MHz, [D_6]DMSO, 25 °C) δ=2.45 (m, 2H, CH_2), 3.78 (s, 6H, CH_3), 4.02 (m, 4H, CH_2), 7.50 (s, 2H, CH), 7.57 ppm (s, 2H, CH). (300.1 MHz, $CDCl_3$, 25 °C) δ=2.45 (quint, ^{3}J(H,H)=6.3Hz, 2H, CH_2), 3.90 (s, 6H, CH_3), 4.22 (t, ^{3}J(H,H)=6.3Hz, 4H, CH_2), 7.04 (s, 4H, CH). ^{13}C NMR (75.5 MHz, [D_6]DMSO, 25 °C) δ=28.7 (CH_2), 37.7 (CH_3), 45.9 (CH_2), 119.9 (CH), 123.5 (CH), 172.8 ppm (N*C*N). ESI-MS (m/z): 677.01 ([M-Br]$^+$, expected 676.99). Elemental analysis calcd (%) for $C_{11}H_{16}N_4Br_2Au_2 \cdot 1/2CH_3CN$: C 18.51, H 2.27, N 8.10; found: C 18.82, H 2.24, N 8.07.

$Au_2Br_2L^4$. Yield 67%. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C) δ=1.97 (s, 12H, CH_3), 2.34 (s, 6H, CH_3), 6.67 (s, 2H, CH_2), 6.98 (s, 6H, CH), 8.11 ppm (s, 2H, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C) δ=18.7 (CH_3), 21.3 (CH_3), 62.8 (CH_2), 125.2 (CH imidazole), 126.8 (CH imidazole), 130.3 (C aromatic), 132.1 (CH aromatic), 135.2 (C aromatic), 141.8 (C aromatic), N*C*N *not detected*. ESI-MS (m/z): 857.28 ([M-Br]$^+$, expected 857.08). Elemental analysis calcd (%) for $C_{25}H_{28}N_4Br_2Au_2$: C 32.00, H 3.01, N 5.97; found: C 31.52, H 3.12, N 5.66.

$Au_2Br_2L^5$. Yield 88%. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C) δ=2.01 (s, 12H, CH_3), 2.33 (s, 6H, CH_3), 4.87 (s, 4H, CH_2), 6.94 (m, 6H, CH), 7.34 ppm (d, ^{3}J(H,H)=1.8 Hz, 2H, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C) δ=18.7 (CH_3), 21.3 (CH_3), 51.1 (CH_2), 121.4 (CH imidazole), 123.6 (CH imidazole), 129.6 (C aromatic), 134.4 (CH aromatic), 134.7 (C aromatic), 140.0 (C aromatic), 175.7 ppm (N*C*N). ESI-MS (m/z): 871.21 ([M-Br]$^+$, expected 871.10). Elemental analysis calcd (%) for $C_{26}H_{30}N_4Br_2Au_2$: C 32.79, H 3.18, N 5.88; found: C 32.45, H 3.25, N 5.97.

$Au_2Br_2L^6$. Yield 91%. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C) δ=2.03 (s, 12H, CH_3), 2.33 (s, 6H, CH_3), 2.68 (quint., ^{3}J(H,H)=7.2 Hz, 2H, CH_2*CH_2*CH_2), 4.41 (t, ^{3}J(H,H)=7.2 Hz, 4H, *CH_2*CH_2*CH_2*), 6.96 (m, 6H, CH), 7.35 ppm (d, ^{3}J(H,H)=1.8 Hz, 2H, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C) δ=18.1 (CH_3), 21.3 (CH_3), 32.8 (CH_2*CH_2*CH_2), 48.3 (*CH_2*CH_2*CH_2*), 121.0 (CH imidazole), 123.3 (CH imidazole), 129.6 (C aromatic), 134.7 (CH aromatic), 134.8 (C aromatic), 139.9 (C aromatic), 175.4 ppm (N*C*N). ESI-MS (m/z): 887.11 ([M-Br]$^+$, expected 887.11). Elemental analysis calcd (%) for $C_{27}H_{32}N_4Br_2Au_2$: C 33.56, H 3.34, N 5.80; found: C 32.47, H 3.19, N 5.27.

$Au_2Br_2L^7$. Yield 71%. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C) δ=1.12 (d, ^{3}J(H,H)=6.9 Hz, 12H, CH_3), 1.27 (d, ^{3}J(H,H)=6.9 Hz, 12H, CH_3), 2.27 (sept., ^{3}J(H,H)=6.9 Hz, 4H, CH), 6.71 (s, 2H, CH_2), 7.03 (d, ^{3}J(H,H)=1.8, 2H, CH), 7.28 (d, ^{3}J(H,H)= 7.8 Hz ,4H, CH), 7.51 (t, ^{3}J(H,H)= 7.8 Hz ,2H, CH), 8.22 ppm (d, ^{3}J(H,H)=1.8 Hz, 2H, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C) δ=24.3 (CH_3), 24.5 (CH_3), 28.8 (CH), 62.5 (CH_2), 121.1 (CH imidazole), 124.3 (CH imidazole), 124.6 (CH aromatic), 131.3 (CH aromatic), 133.6 (C aromatic), 145.4 ppm (C aromatic), 177.5 ppm (N*C*N). ESI-MS (m/z): 943.21 ([M-Br]$^+$, expected 943.18). Elemental analysis calcd (%) for $C_{31}H_{40}N_4Br_2Au_2$: C 36.41, H 3.94, N 5.48; found: C 36.23, H 4.09, N 5.32.

$Au_2Br_2L^8$. Yield 84%. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C) δ=1.11 (d, ^{3}J(H,H)=6.6 Hz, 12H, CH_3), 1.32 (d, ^{3}J(H,H)=6.9 Hz, 12H, CH_3), 2.31 (sept., ^{3}J(H,H)=6.9 Hz, 4H, CH), 4.95 (s, 4H, CH_2), 6.93 (d, ^{3}J(H,H)=1.5 Hz, 2H, CH), 7.28 (m, 6H, CH), 7.50 ppm (t, ^{3}J(H,H)=7.8 Hz, 2H, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C) δ=24.4 (CH_3), 24.6 (CH_3), 28.6 (CH), 51,0 (CH_2), 121.9 (CH imidazole), 123.2 (CH imidazole), 124.5 (CH aromatic), 131.1 (CH aromatic), 133.8 (C aromatic), 145.5 (C aromatic), 176.3 ppm (N*C*N). ESI-MS (m/z): 955.21 ([M-Br]$^+$, expected 955.19). Elemental analysis calcd (%) for $C_{32}H_{42}N_4Br_2Au_2$: C 37.08, H 4.08, N 5.41; found: C 36.84, H 4.21, N 5.27.

$Au_2Br_2L^9$. Yield 90%. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C) δ=1.13 (d, ^{3}J(H,H)=6.9 Hz, 12H, CH_3), 1.28 (d, ^{3}J=6.9 Hz, 12H, CH_3), 2.41 (sept., ^{3}J(H,H)=6.9 Hz, 4H, CH), 2.72 (quint., ^{3}J(H,H)=7.5 Hz, 2H, CH_2*CH_2*CH_2), 4.43 (t, ^{3}J(H,H)=7.2 Hz, 4H, *CH_2*CH_2*CH_2*), 7.02 (d,

^{2}J(H,H)=1.8 Hz, 2H, CH), 7.25 (d, ^{3}J(H,H)=7.8 Hz, 4H, CH), 7.36 (d, ^{3}J(H,H)=1.8 Hz, 2H, CH), 7.47 ppm (t, ^{3}J(H,H)=7.8 Hz, 2H, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C) δ=24.4 (CH_3), 24.6 (CH_3), 28.6 (CH), 32.8 ($CH_2\mathit{CH_2}CH_2$), 48.4 ($\mathit{CH_2}CH_2\mathit{CH_2}$), 121.0 (CH imidazole), 124.4 (CH aromatic), 124.6 (CH imidazole), 130.8 (CH aromatic), 134.0 (C aromatic), 145.7 (C aromatic), 176.2 ppm (N*C*N). ESI-MS (m/z): 969.22 ([M-Br]$^+$, expected 969.21). Elemental analysis calcd (%) for $C_{33}H_{44}N_4Br_2Au_2$: C 37.73, H 4.22, N 5.33; found: C 38.61, H 4.45, N 5.15.

X-ray crystal structure determination of complexes $Au_2Br_2L^4$, $Au_2Br_2L^5$ and $Au_2Br_2L^6$.

X-ray crystallographic data of complex **$Au_2Br_2L^4$** were obtained by mounting a crystal on a glass fiber and transferring it to a APEX 2 Bruker CCD platform diffractometer. The APEX 3 program package [54] was used to determine the unit-cell parameters and for the data collection (30 s/frame scan time for a sphere of diffraction data). The raw frame data were processed using SAINT [54] and SADABS [55] to yield the reflection data file. The structure was solved using SHELXT [56] by Intrinsic Phasing method in the APEX 3 program. Subsequent calculations were carried out using the SHELXTL-2014/7 program [56] in the WinGX suite v.2014.1.[57] The refinement was carried out based on F^2 by full-matrix least-squares techniques. The hydrogen atoms were included in the refinement at idealized geometry and refined "riding" on the corresponding parent atoms.

Crystal data of complexes **$Au_2Br_2L^5$** and **$Au_2Br_2L^6$** were collected using an Oxford Diffraction Gemini E diffractometer, equipped with a 2K × 2K EOS CCD area detector and sealed–tube Enhance (Mo) and (Cu) X–ray sources. Mo Kα (λ = 0.71073 Å) radiation was used. Data collection, reduction and finalization were carried out through the CrysAlisPro software. Using Olex2,[58] **$Au_2Br_2L^5$** and **$Au_2Br_2L^6$** structures were solved in the *P*21/*c* and *C*2/*c* space groups, respectively, with the ShelXT[56] structure solution program by Intrinsic Phasing and refined with the ShelXL[59] refinement package using least squares minimization. **$Au_2Br_2L^5$** crystallizes with a CH_2Cl_2 molecule that has been split in two parts the occupancies of which were constrained to sum to 1.0. SADI and RIGU restrains have been used to better model the two parts. In the last cycles of refinement, non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in calculated positions and a riding model was used for their refinement. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication (CCDC 1839490 for complex **$Au_2Br_2L^4$**, 1828633 for complex **$Au_2Br_2L^5$** and 1828632 for complex **$Au_2Br_2L^6$**). Crystal data and refinement parameters are reported in Table S1 of the Supporting Material.

General procedure for catalytic tests on the Suzuki type coupling reactions.

Catalyst (0.006 mmol), boronic acid (0.123 mmol), and Cs_2CO_3 (0.379 mmol) were weighed into a 4mL vial equipped with a stirbar. A freshly prepared 0.82 M solution of cinnamyl bromide in MeCN was then added in the vial (0.6 mL, 0.492 mmol). The vial was equipped with a stirbar, capped tightly, and the reaction mixture was stirred vigorously for 18 hours at 65 °C. Upon cooling to room temperature, a precise quantity of 1,4-bis(trimethylsilyl)benzene was added to the vial as internal standard, and the mixture was stirred again for 5 minutes. A small quantity of the reaction mixture was then transferred to a NMR tube. ^{1}H NMR spectrum was recorded in $CDCl_3$. Yield was determined by comparing the signals in the ^{1}H NMR spectrum of internal standard with those of the cross-coupling product.[60]

General procedure for catalytic tests on the hydroamination reactions.

In a Schlenk tube equipped with a magnetic stirring bar were placed under an inert atmosphere 10 μmol Au complex and 20 μmol silver salt cocatalyst. The tube was degassed and put under an inert atmosphere. 1.00-5.00 mmol aniline, 1.00-5.00 mmol alkyne and optionally 1 mL dry solvent were then injected into the Schlenk tube. The flask was immediately placed in an oil bath preheated at the reaction temperature and the reaction mixture was vigorously stirred for the given reaction time. Conversions and yields were determined by ^{1}H NMR on a sample of the reaction mixture diluted in $CDCl_3$, after addition of 1,4-bis-trimethylsilylbenzene as an internal standard.

ASSOCIATED CONTENT

Supporting Information

NMR spectra for the synthesized complexes **$Au_2Br_2L^1$**-**$Au_2Br_2L^9$**, crystal data and refinement parameters and the identification of the products of the alkyne hydroamination reactions are available in the Supporting Material.

The Supporting Information is available free of charge on the ACS Publications website.

Supporting information.pdf

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Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

University of Padova is gratefully acknowledged for the financial support (Assegno di Ricerca Senior GRIC15V47A).

REFERENCES

(1) Nolan, S. P. The Development and Catalytic Uses of N-Heterocyclic Carbene Gold Complexes. *Acc. Chem. Res.* **2011**, *44*, 91–100.
(2) Díez-González, S.; Marion, N.; Nolan, S. P. N-Heterocyclic Carbenes in Late Transition Metal Catalysis. *Chem. Rev.* **2009**, *109*, 3612–3676.
(3) Marion, N.; Nolan, S. P. N-Heterocyclic Carbenes in Gold Catalysis. *Chem. Soc. Rev.* **2008**, *37*, 1776.
(4) Hashmi, A. S. K.; Schuster, A. M.; Rominger, F. Gold Catalysis: Isolation of Vinylgold Complexes Derived from Alkynes. *Angew. Chem. Int. Ed.* **2009**, *48*, 8247–8249.
(5) Yam, V. W.-W.; Cheng, E. C.-C. Highlights on the Recent Advances in Gold Chemistry—a Photophysical Perspective. *Chem. Soc. Rev.* **2008**, *37*, 1806–1813.
(6) Baron, M.; Tubaro, C.; Biffis, A.; Basato, M.; Graiff, C.; Poater, A.; Cavallo, L.; Armaroli, N.; Accorsi, G. Blue-Emitting Dinuclear N-Heterocyclic Dicarbene Gold(I) Complex Featuring a Nearly Unit Quantum Yield. *Inorg. Chem.* **2012**, *51*, 1778–1784.
(7) Visbal, R.; Ospino, I.; López-de-Luzuriaga, J. M.; Laguna, A.; Gimeno, M. C. N-Heterocyclic Carbene Ligands as Modulators of Luminescence in Three-Coordinate Gold(I) Complexes with Spectacular Quantum Yields. *J. Am. Chem. Soc.* **2013**, *135*, 4712–4715.
(8) Bertrand, B.; Casini, A. A Golden Future in Medicinal Inorganic Chemistry: The Promise of Anticancer Gold Organometallic Compounds. *Dalton Trans.* **2014**, *43*, 4209–4219.
(9) Oehninger, L.; Rubbiani, R.; Ott, I. N-Heterocyclic Carbene Metal Complexes in Medicinal Chemistry. *Dalton Trans.* **2013**, *42*, 3269–3284.

(10) Larsen, M. H.; Houk, K. N.; Hashmi, A. S. K. Dual Gold Catalysis: Stepwise Catalyst Transfer via Dinuclear Clusters. *J. Am. Chem. Soc.* **2015**, *137*, 10668–10676.
(11) Hashmi, A. S. K. Dual Gold Catalysis. *Acc. Chem. Res.* **2014**, *47*, 864–876.
(12) Gómez-Suárez, A.; Nolan, S. P. Dinuclear Gold Catalysis: Are Two Gold Centers Better than One? *Angew. Chem. Int. Ed.* **2012**, *51*, 8156–8159.
(13) Tkatchouk, E.; Mankad, N. P.; Benitez, D.; Goddard, W. A.; Toste, F. D. Two Metals Are Better Than One in the Gold Catalyzed Oxidative Heteroarylation of Alkenes. *J. Am. Chem. Soc.* **2011**, *133*, 14293–14300.
(14) Hashmi, A. S. K.; Braun, I.; Nösel, P.; Schädlich, J.; Wieteck, M.; Rudolph, M.; Rominger, F. Simple Gold-Catalyzed Synthesis of Benzofulvenes—Gem-Diaurated Species as "Instant Dual-Activation" Precatalysts. *Angew. Chem. Int. Ed.* **2012**, *51*, 4456–4460.
(15) Oonishi, Y.; Gómez-Suárez, A.; Martin, A. R.; Nolan, S. P. Hydrophenoxylation of Alkynes by Cooperative Gold Catalysis. *Angew. Chem. Int. Ed.* **2013**, *52*, 9949–9953.
(16) Hashmi, A. S. K.; Lauterbach, T.; Nösel, P.; Vilhelmsen, M. H.; Rudolph, M.; Rominger, F. Dual Gold Catalysis: σ,π-Propyne Acetylide and Hydroxyl-Bridged Digold Complexes as Easy-To-Prepare and Easy-To-Handle Precatalysts. *Chem. Eur. J.* **2013**, *19*, 1058–1065.
(17) Casals-Cruañas, È.; González-Belman, O. F.; Besalú-Sala, P.; Nelson, D. J.; Poater, A. The Preference for Dual-Gold(I) Catalysis in the Hydro(Alkoxylation vs. Phenoxylation) of Alkynes. *Org. Biomol. Chem.* **2017**, *15*, 6416–6425.
(18) Levin, M. D.; Toste, F. D. Gold-Catalyzed Allylation of Aryl Boronic Acids: Accessing Cross-Coupling Reactivity with Gold. *Angew. Chem. Int. Ed.* **2014**, *53* (24), 6211–6215.
(19) Vreeken, V.; Broere, D. L. J.; Jans, A. C. H.; Lankelma, M.; Reek, J. N. H.; Siegler, M. A.; van der Vlugt, J. I. Well-Defined Dinuclear Gold Complexes for Preorganization-Induced Selective Dual Gold Catalysis. *Angew. Chem. Int. Ed.* **2016**, *55*, 10042–10046.
(20) Doddi, A.; Bockfeld, D.; Nasr, A.; Bannenberg, T.; Jones, P. G.; Tamm, M. N-Heterocyclic Carbene–Phosphinidene Complexes of the Coinage Metals. *Chem. Eur. J.* **2015**, *21*, 16178–16189.
(21) Gómez-Suárez, A.; Oonishi, Y.; Meiries, S.; Nolan, S. P. [{Au(NHC)}2(μ-OH)][BF4]: Silver-Free and Acid-Free Catalysts for Water-Inclusive Gold-Mediated Organic Transformations. *Organometallics* **2013**, *32*, 1106–1111.
(22) Ferrer, S.; Echavarren, A. M. Role of σ,π-Digold(I) Alkyne Complexes in Reactions of Enynes. *Organometallics* **2018**, *37*, 781–786.
(23) Baron, M.; Tubaro, C.; Basato, M.; Isse, A. A.; Gennaro, A.; Cavallo, L.; Graiff, C.; Dolmella, A.; Falivene, L.; Caporaso, L. Insights into the Halogen Oxidative Addition Reaction to Dinuclear Gold(I) Di(NHC) Complexes. *Chem. Eur. J.* **2016**, *22* (29), 10211–10224.
(24) Biffis, A., Baron, M.; Tubaro, C. Chapter Five - Poly-NHC Complexes of Transition Metals: Recent Applications and New Trends. *Adv. Organomet. Chem.* **2015**, *63*, 203–288.
(25) Pöthig, A.; Strassner, T. Triazinone-Bridged Neutral Dinuclear Gold(I)-NHC Complex. *Organometallics* **2012**, *31*, 3431–3434.
(26) Kobialka, S.; Müller-Tautges, C.; Schmidt, M. T. S.; Schnakenburg, G.; Hollóczki, O.; Kirchner, B.; Engeser, M. Stretch Out or Fold Back? Conformations of Dinuclear Gold(I) N-Heterocyclic Carbene Macrocycles. *Inorg. Chem.* **2015**, *54*, 6100–6111.
(27) Hettmanczyk, L.; Schulze, D.; Suntrup, L.; Sarkar, B. Mono- and Digold(I) Complexes with Mesoionic Carbenes: Structural Characterization and Use in Catalytic Silver-Free Oxazoline Formation. *Organometallics* **2016**, *35*, 3828–3836.
(28) Man, R. W. Y.; Li, C.-H.; MacLean, M. W. A.; Zenkina, O. V.; Zamora, M. T.; Saunders, L. N.; Rousina-Webb, A.; Nambo, M.; Crudden, C. M. Ultrastable Gold Nanoparticles Modified by Bidentate N-Heterocyclic Carbene Ligands. *J. Am. Chem. Soc.* **2018**, *140*, 1576–1579.
(29) Collado, A.; Gómez-Suárez, A.; Martin, A. R.; Slawin, A. M. Z.; Nolan, S. P. Straightforward Synthesis of [Au(NHC)X] (NHC = N-Heterocyclic Carbene, X = Cl, Br, I) Complexes. *Chem. Commun.* **2013**, *49*, 5541–5543.
(30) Visbal, R.; Laguna, A.; Gimeno, M. C. Simple and Efficient Synthesis of [MCI(NHC)] (M = Au, Ag) Complexes. *Chem. Commun.* **2013**, *49*, 5642–5644.
(31) Marchenko, A.; Koidan, G.; Hurieva, A.; Kostyuk, A.; Franco, D.; Baron, M.; Biffis, A. PdII Complexes with N-(Diadamantylphosphanyl)Diaminocarbene and Related Ligands: Synthesis and Catalytic Applications in Intermolecular Alkyne Hydroaminations. *Eur. J. Inorg. Chem.* **2018**, 652–658.
(32) Gil-Rubio, J.; Cámara, V.; Bautista, D.; Vicente, J. Dinuclear Alkynyl Gold(I) Complexes Containing Bridging N-Heterocyclic Dicarbene Ligands: New Synthetic Routes and Luminescence. *Organometallics* **2012**, *31*, 5414–5426.
(33) de Frémont, P.; Singh, R.; Stevens, E. D.; Petersen, J. L.; Nolan, S. P. Synthesis, Characterization and Reactivity of N-Heterocyclic Carbene Gold(III) Complexes. *Organometallics* **2007**, *26*, 1376–1385.
(34) Laguna, A.; Laguna, M. Coordination Chemistry of Gold(II) Complexes. *Coord. Chem. Rev.* **1999**, *193–195*, 837–856.
(35) *For a comprehensive general review on hydroamination, see* Huang, L.; Arndt, M.; Gooßen, K.; Heydt, H.; Gooßen, L. J. Late Transition Metal-Catalyzed Hydroamination and Hydroamidation. *Chem. Rev.* **2015**, *115*, 2596–2697.
(36) *For a review on NHC-metal complexes as catalysts in hydroamination reactions, see* Payne P. R., Gagné M. R., in N-Heterocyclic Carbenes in Catalytic Organic Synthesis 1 (Eds.: S. P. Nolan, C. S. J. Cazin), Science of Synthesis Series, Thieme, Stuttgart **2017**, pp. 361-385.
(37) Alyabyev, S. B.; Beletskaya, I. P. Gold as a catalyst. Part I. Nucleophilic addition to the triple bond. *Russ. Chem. Rev.* **2017**, *86*, 689–749.
(38) Lavallo, V.; Frey, G. D.; Donnadieu, B.; Soleilhavoup, M.; Bertrand, G. Homogeneous Catalytic Hydroamination of Alkynes and Allenes with Ammonia. *Angew. Chem. Int. Ed.* **2007**, *47*, 5224–5228.
(39) Corma, A.; González-Arellano, C.; Iglesias, M.; Navarro, M. T.; Sánchez, F. Synthesis of Bifunctional Au–Sn Organic–Inorganic Catalysts for Acid-Free Hydroamination Reactions. *Chem. Commun.* **2008**, 6218–6220.
(40) Chessa, S.; Clayden, N. J.; Bochmann, M.; Wright, J. A. α-Zirconium Phosphonates: Versatile Supports for N-Heterocyclic Carbenes. *Chem. Commun.* **2009**, 797–799.
(41) Alvarado, E.; Badaj, A. C.; Larocque, T. G.; Lavoie, G. G. N-Heterocyclic Carbenes and Imidazole-2-Thiones as Ligands for the Gold(I)-Catalysed Hydroamination of Phenylacetylene. *Chem. – Eur. J.* **2012**, *18*, 12112–12121.
(42) He, Y.-P.; Wu, H.; Chen, D.-F.; Yu, J.; Gong, L.-Z. Cascade Hydroamination/Redox Reaction for the Synthesis of Cyclic Aminals Catalyzed by a Combined Gold Complex and Brønsted Acid. *Chem. – Eur. J.* **2013**, *19*, 5232–5237.
(43) Gonell, S.; Poyatos, M.; Peris, E. Triphenylene-Based Tris(N-Heterocyclic Carbene) Ligand: Unexpected Catalytic Benefits. *Angew. Chem. Int. Ed.* **2013**, *52*, 7009–7013.
(44) Hu, X.; Martin, D.; Bertrand, G. Room Temperature Hydroamination of Alkynes with Anilines Catalyzed by Anti-Bredt Di(Amino)Carbene Gold(I) Complexes. *New J. Chem.* **2016**, *40*, 5993–5996.
(45) Dash, C.; Shaikh, M. M.; Butcher, R. J.; Ghosh, P. Highly Convenient Regioselective Intermolecular Hydroamination of Alkynes Yielding Ketimines Catalyzed by Gold(I) Complexes of

1,2,4-Triazole Based N-Heterocyclic Carbenes. *Inorg. Chem.* **2010**, *49*, 4972–4983.
(46) Zhang, X.; Yang, B.; Li, G.; Shu, X.; Mungra, D. C.; Zhu, J. Highly Regioselective AgNTf2-Catalyzed Intermolecular Hydroamination of Alkynes with Anilines. *Synlett* **2012**, 622–626.
(47) Flores-Jarillo, M.; Mendoza-Espinosa, D.; Salazar-Pereda, V.; González-Montiel, S. Synthesis and Catalytic Benefits of Tetranuclear Gold(I) Complexes with a C4-Symmetric Tetratriazol-5-Ylidene. *Organometallics* **2017**, *36*, 4305–4312.
(48) Liu, X.-Y.; Ding, P.; Huang, J.-S.; Che, C.-M. Synthesis of Substituted 1,2-Dihydroquinolines and Quinolines from Aromatic Amines and Alkynes by Gold(I)-Catalyzed Tandem Hydroamination–Hydroarylation under Microwave-Assisted Conditions. *Org. Lett.* **2007**, *9*, 2645–2648.
(49) Yi, C. S.; Yun, S. Y.; Guzei, I. A. Catalytic Synthesis of Tricyclic Quinoline Derivatives from the Regioselective Hydroamination and C–H Bond Activation Reaction of Benzocyclic Amines and Alkynes. *J. Am. Chem. Soc.* **2005**, *127*, 5782–5783.
(50) Luo, Y.; Li, Z.; Li, C.-J. A Silver-Catalyzed Domino Route toward 1,2-Dihydroquinoline Derivatives from Simple Anilines and Alkynes. *Org. Lett.* **2005**, *7*, 2675–2678.
(51) Zeng, X.; Frey, G. D.; Kinjo, R.; Donnadieu, B.; Bertrand, G. Synthesis of a Simplified Version of Stable Bulky and Rigid Cyclic (Alkyl)(Amino)Carbenes, and Catalytic Activity of the Ensuing Gold(I) Complex in the Three-Component Preparation of 1,2-Dihydroquinoline Derivatives. *J. Am. Chem. Soc.* **2009**, *131*, 8690–8696.
(52) Purkait, N.; Blechert, S. Synthesis of Bi- and Tricyclic 1,2-Dihydroquinoline Derivatives from Arylamines and Alkynes by a Consecutive Zinc-Ammonium Salt Catalysis. *Adv. Synth. Catal.* **2012**, *354*, 2079–2083.
(53) Cao, C.; Zhuang, Y.; Zhao, J.; Liu, H.; Geng, P.; Pang, G.; Shi, Y. Green Synthesis of Alkane Bridged Bisimidazolium Salts Under Solvent-Free Conditions. *Synth. Commun.* **2012**, *42*, 380–387.
(54) Bruker (**2015**). APEX3 and SAINT. Bruker AXS Inc., Madison, Wisconsin, USA
(55) Krause, L.; Herbst-Irmer, R.; Sheldrick, G. M.; Stalke, D. Comparison of Silver and Molybdenum Microfocus X-Ray Sources for Single-Crystal Structure Determination. *J. Appl. Crystallogr.* **2015**, *48*, 3–10.
(56) Sheldrick, G. M. SHELXT – Integrated Space-Group and Crystal-Structure Determination. *Acta Crystallogr. Sect. Found. Adv.* **2015**, *71* (1), 3–8.
(57) Farrugia, L. J. WinGX and ORTEP for Windows: An Update. *J. Appl. Crystallogr.* **2012**, *45*, 849–854.
(58) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. a. K.; Puschmann, H. OLEX2: A Complete Structure Solution, Refinement and Analysis Program. *J. Appl. Crystallogr.* **2009**, *42*, 339–341.
(59) Sheldrick, G. M. Crystal Structure Refinement with SHELXL. *Acta Crystallogr. Sect. C Struct. Chem.* **2015**, *71*, 3–8.
(60) Tang, X.-L.; Wu, Z.; Li, M.-B.; Gu, Y.; Tian, S.-K. Cross-Coupling of N-Allylic Sulfonimides with Organozinc Reagents at Room Temperature. *Eur. J. Org. Chem.* **2012**, 4107–4109.

Graphic entry for the Table of Contents (TOC)