

Deactivation of Cationic Cu^I and Au^I Catalysts for A³ Coupling by CH₂Cl₂: Mechanistic Implications of the Formation of Neutral Cu^I and Au^I Chlorides**

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Abstract: Care should be exercised when using CH₂Cl₂ as a solvent for reactions in which amines are a reagent, since undesirable deactivation of cationic copper(I) and gold(I) catalysts to form the corresponding inactive neutral chloride complexes [LMCl] (M = Cu or Au) can occur as a result of the generation of hydrogen chloride in the medium. Cu^I and Au^I deactivation has been proved for the Mannich three-component coupling reaction. A series of Cu^I and Au^I complexes with potential mechanistic implications were isolated and characterized by X-ray crystallography.

There is much current interest in delineating the similarities and differences between gold(I) catalysts^[1] and isoelectronic metal ions, in particular available and affordable copper(I) complexes.^[2] It is important to establish whether Cu^I can exhibit similar catalytic activity to that of Au^I in certain reactions. Herein, we compare the catalytic activity of bulky 2-di-*tert*-butylphosphanylbiaryl (Buchwald phosphane)^[3] Cu^I complexes with respect to Au^I analogues for the Mannich three-component (A³) coupling and show that Cu^I complexes are far more active than Au^I complexes. We also demonstrate why CH₂Cl₂ is not a suitable solvent for this process on the basis of mechanistic differences derived from the preference of Au^I to coordinate to the alkyne and of Cu^I to coordinate with amines. In this study, a series of Cu^I and Au^I complexes with potential mechanistic implications were isolated and characterized by X-ray crystallography.

A³ coupling^[4] is a versatile process that finds broad application in organic synthesis for the straightforward preparation of high-value propargylamines.^[5] There are precedents for the ability of gold and copper catalysts to promote this type of Mannich coupling.^[6] However, up to now, a comparison of the activity of cationic LCu^I and LAu^I

complexes in combination with the isolation of potential intermediate complexes has not been reported. Also, no information is available on the reaction of these intermediate complexes with A³ reagents of this Mannich reaction in toluene or CH₂Cl₂. The isolation of metal(I) complexes can shed light on the active or inactive gold(I) and copper(I) species involved in the catalytic process.

In the initial stage of our study, we selected [Cu(MeCN)₄]⁺[PF₆][−] (**1**)^[7] as a precursor for the non-aqueous synthesis of cationic Cu^I dialkylbiarylphosphane complexes. The reaction of **1** with 2-di-*tert*-butylphosphanylbiaryl (**2**) in CH₂Cl₂ at 45 °C for 15 h led to the formation of the cationic copper(I) complex **3** (Scheme 1) in 85 % yield (see experimental details in the Supporting Information). When a stoichiometric (1:2) mixture of the synthesized complex **3** and aniline (**4**) was stirred for 15 h at room temperature in CH₂Cl₂, a new cationic amine–copper(I) complex **5** was formed in 86 % yield (see the Supporting Information) by the exchange of acetonitrile by aniline (Scheme 1).

Complexes **3** and **5** were fully characterized on the basis of combustion elemental analysis and spectroscopic data (see the experimental details as well as Figures S1–S6 and Table S1 for **3** and Figures S7–S12 and Table S2 for **5** in the Supporting Information). Crystals of complex **3** were obtained at −30 °C from solutions in CH₂Cl₂, on top of which a layer of *n*-hexane was carefully added. The addition of toluene (2 mL) to the filtered solution of complex **5** in CH₂Cl₂ (2 mL) and subsequent slow evaporation at ambient temperature enabled the formation of colorless crystals of **5**. Single crystals of both complexes **3** and **5** were air-stable and of suitable quality for an X-ray crystallographic diffraction study.

The solid-state structure of **3** (Scheme 1)—the hexafluorophosphate salt of the cationic 2-di-*tert*-butylphosphanylbiaryl acetonitrile Cu^I complex (see Table S1 and Figure S1)—is closely related to the reported tetrafluoroborate Cu^I analogue, but with a differently substituted biarylphosphine ligand and a different counterion.^[8] The selected distances Cu–N, Cu–P, and Cu–C_{ipso} and the shortest distance between Cu1 and the plane of the complexed arene (C9) for complex **3** are around 1.870(3), 2.1789(8), 2.78, and 2.640(3) Å, respectively. The distances Cu–N, Cu–P, Cu–C_{ipso} and the shortest distance between Cu1 and the plane of the complexed arene (C13) for complex **5** (see Table S2 and Figure S7) are 1.964(2), 2.1821(7), 2.786, and 2.577(3) Å, which are shorter than the corresponding values for Au–N, Au–P, Au–C_{ipso}, and the shortest distance between Au1 and the plane of the complexed arene (C13) in the recently reported analogous cationic amine–Au^I–L com-

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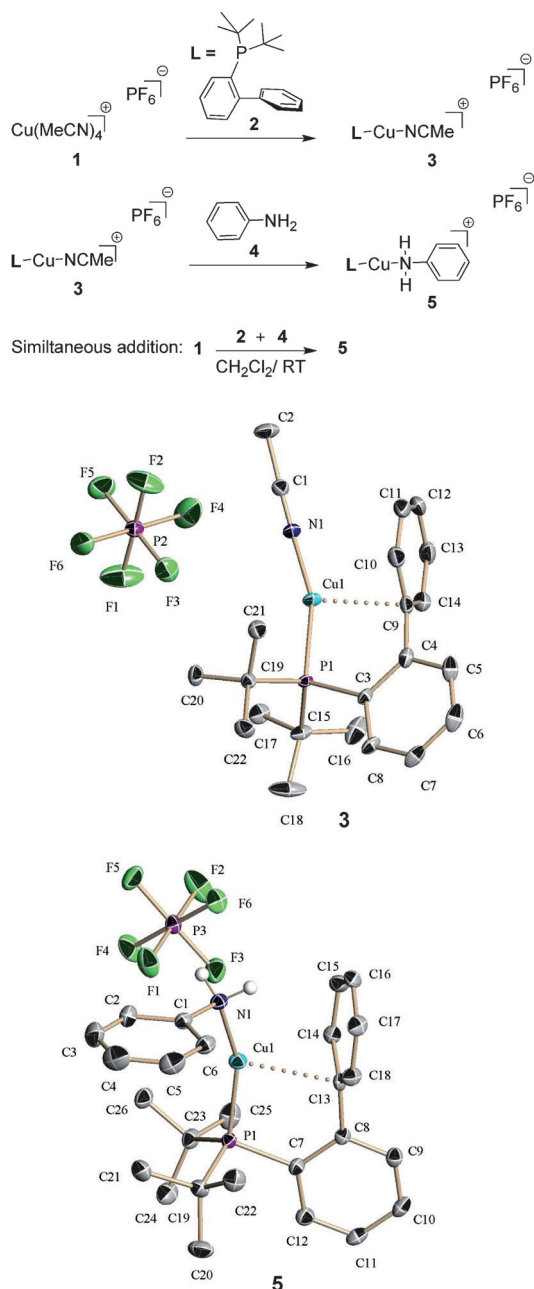
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plex,^[9] thus showing the influence of the metal on the metal–arene interaction.

The copper(I) complex **5** can also be synthesized directly from a stoichiometric (1:1:1.4) mixture of **1**, **2**, and **4** (Scheme 1; see the Supporting Information). A mixture of these three components was stirred for 24 h at room temperature in CH₂Cl₂. Filtering of the resulting solution, followed by the subsequent addition of toluene and slow evaporation at ambient temperature, afforded colorless crystals of complex **5** in 80 % yield and high quality for crystallographic studies.



Scheme 1. Top: Synthesis of cationic copper(I) complexes **3** and **5**. Bottom: ORTEP views of **3** and **5** (single-crystal X-ray data and the crystal packing of **3** and **5** are given in Tables S1 and S2 and Figures S1 and S7).

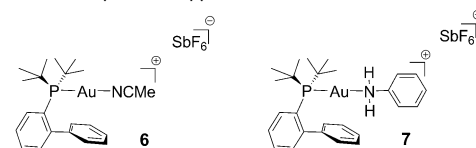
The copper(I) complexes **3** and **5** were also characterized by NMR spectroscopy and ESIMS (see the Supporting Information). ¹H, ¹³C, ³¹P, and ¹⁹F NMR spectroscopy of solutions in CD₂Cl₂ provided evidence that the starting complex **1** was completely converted into **3** and subsequently into **5**. Thus, ³¹P NMR spectroscopy showed the disappearance of the peaks corresponding to the initial free phosphine **2** at 18.11 ppm (singlet) and to PF₆[−] of starting complex **1** at −144.43 ppm (septuplet), and the appearance of new peaks at 32.49 (singlet) and −144.36 ppm (septuplet) for **3** or 34.60 (singlet) and −144.13 ppm (septuplet) for **5**. Similarly, ¹H NMR spectroscopy showed new signals for the methyl groups of complex **3** at 1.27 and 1.22 ppm instead of those corresponding to the initial phosphine ligand **2** at 1.11 and 1.07 ppm. ESIMS of a solution obtained by dissolving complex **3** in CH₂Cl₂/CH₃CN (1:2) showed intense positive MS peaks at 361.1 and 759.4 Da (see Figure S6), which are attributable to [3–PF₆[−]–N≡CMe]⁺ and [(3)₂–(PF₆[−])₂–(N≡CMe)₂+Cl]⁺ (see fragmentation of this peak in Figure S6), respectively. Complex **5** dissolved in CH₂Cl₂/CH₃CN (1:2) showed mainly positive MS peaks at 454.2, 361.1, and 759.4 Da, which are attributable to [C₂₆H₃₄CuF₆NP₂ (5)–PF₆[−]]⁺ and the cationic Cu^I complexes [5–PF₆[−]–aniline]⁺ and [C₅₂H₆₈Cu₂F₁₂N₂P₄ ((5)₂)–(PF₆[−])₂–(aniline)₂+Cl]⁺, respectively (see Figure S12 for details).

With the aim of gaining understanding of the stability of Cu^I coordinated to the bulky ligand **2** in complexes **3** and **5**, we performed the Mannich A³ coupling of phenylacetylene, pyrrolidine, and aqueous formaldehyde with **3** and **5** as catalysts (Table 1). The catalytic activity of the related gold complexes [LAu(NCMe)][SbF₆] (**6**)^[10] and [LAu(aniline)]-

Table 1: A³ coupling of phenylacetylene, pyrrolidine, and aqueous formaldehyde with Cu^I catalyst complexes **3**, **5**, **13**, **14**, and **15** and Au^I catalyst complexes **6**, **7**, and **10**.^[a]

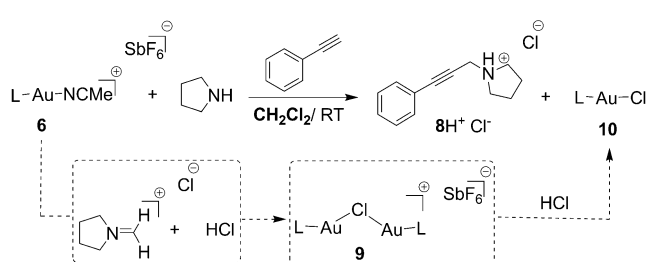
Entry	Catalyst	<i>t</i> [h]	Conversion [%] ^[b]	Yield [%] ^[b]
1	3	0.2	100	99
2	5	0.2	100	98
3	6	12	100	95
4	7	24	100	94
5	10	0.2	4	trace
6	10	24	90	81
7	13	0.2	2	trace
8	13	24	96	87
9	14	0.2	100	99
10	15	0.2	100	99

[a] Reaction conditions: phenylacetylene (0.25 mmol), pyrrolidine (0.35 mmol), aqueous formaldehyde (0.7 mmol), catalyst (6 mol %), toluene (1 mL). [b] The conversion and yield were determined by ¹H NMR spectroscopy and GC of the crude reaction mixture.



[SbF₆][−] (**7**)^[9] was also screened for the sake of comparison (see Table 1) and with the goal of shedding light on the real active species involved in the catalytic process for gold(I) and copper(I). In these four catalytic experiments (Table 1), the expected product 1-(3-phenylprop-2-ynyl)pyrrolidine (**8**)^[11] was obtained in good yield, but the reaction took place in only a few minutes with Cu^I complexes **3** and **5** (Table 1, entries 1 and 2), whereas a longer reaction time was required for the cationic Au^I complexes **6** and **7** (Table 1, entries 3 and 4). This result reflects the higher activity of cationic Cu^I complexes **3** and **5** versus Au^I analogues **6**^[10] and **7**.^[9]

The propargylamine **8** was isolated as a light-yellow oil and characterized by ¹H and ¹³C NMR spectroscopy and GC–MS (see Figures S13, S14, and S15). The hydrochloride salt of **8** (**8H**⁺ Cl[−])^[12] (Scheme 2) formed in the A³ reaction in CH₂Cl₂ with [LAu(NCMe)][SbF₆] (**6**)^[10] as the catalyst was

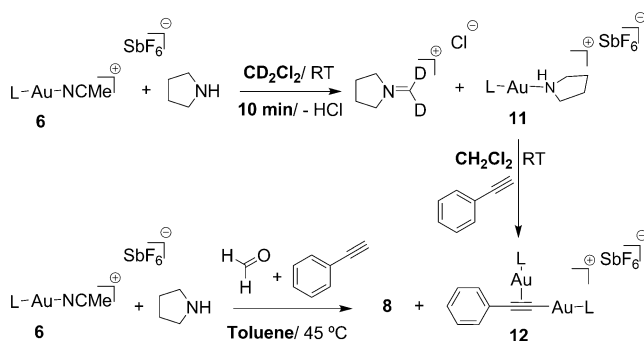


Scheme 2. Formation of the intermediate cationic chloride-bridged digold(I) complex [(LAu)₂(μ-Cl)][SbF₆] (**9**), the neutral gold(I) complex [LAuCl] (**10**), and the chloride salt **8H**⁺ Cl[−] of propargylamine **8**, in the absence of formaldehyde. Conditions for the isolation of complexes **9** and **10** are provided in the Supporting Information. X-ray single-crystal data and ORTEP views of **8H**⁺ Cl[−], **9**, and **10** are given in Tables S3–S5 and Figures S16, S18, and S22.

characterized by combustion analysis, X-ray crystallography (see Table S3 and Figure S16), and ESIMS of a solution obtained by dissolving **8H**⁺ Cl[−] in CH₂Cl₂/methanol (1:1; a positive MS peak was observed at 186.1 amu, which corresponds to the expected mass for **8H**⁺; see Figure S17). Besides the reaction product, cationic [(LAu)₂(μ-Cl)][SbF₆] (**9**)^[13] formed as an intermediate complex and neutral [LAuCl] (**10**)^[10] formed as the final gold chloride complex (Scheme 2) during the catalytic reaction in CH₂Cl₂ as the solvent in the absence or presence of formaldehyde were detected and fully characterized (see the Supporting Information). The X-ray crystal structures of the isolated complexes **9** and **10** were similar to (in the case **9**) and a polymorph of (in the case of **10**) those previously reported for these complexes^[10,13] (see Figures S18 and S22 and Tables S4 and S5). ¹H and ³¹P NMR spectra of **9** and **10** in CD₂Cl₂ were also recorded (see Figures S19, S20, S23, and S24). The ESI mass spectrum of isolated [(LAu)₂(μ-Cl)][SbF₆] (**9**) dissolved in CH₂Cl₂/methanol showed a positive MS peak at 1025.3 amu corresponding to the expected mass for the chloride-bridged complex (LAu)₂(μ-Cl)⁺, whereas negative MS peaks observed at 234.6 and 236.6 amu correspond to the anionic counteranion [SbF₆][−] (see Figure S21).

An alternative catalytic experiment was carried out in which [LAu(NCMe)][SbF₆] (**6**; 12 mol %) was added to a mixture of pyrrolidine and phenylacetylene in CD₂Cl₂ in the absence of formaldehyde at 70 °C. After 1 h, the mixture was analyzed by ³¹P NMR spectroscopy. Peaks in the spectrum at 64.59 (91 %) and 60.10 ppm (9 %) corresponding to **9** and **10**, respectively, replaced the peak at 57.53 ppm for the starting precatalyst [LAu(NCMe)][SbF₆] (**6**) (see Figure S25). After a reaction time of 5 h, complex **9** (64.59 ppm) was a minor component of the mixture (6 %) with respect to complex **10** (60.10 ppm), which predominated (94 %; see Figure S26). Finally, after a reaction time of 6 h, the only gold species present was complex **10** (60.10 ppm; see Figure S27).

When [LAu(NCMe)][SbF₆] (**6**) was treated at room temperature with pyrrolidine in an NMR spectroscopic experiment in CD₂Cl₂ as the solvent (Scheme 3, top), the



Scheme 3. Top: Synthesis of the cationic gold(I) complex [LAu(pyrrolidine)][SbF₆] (**11**) in CD₂Cl₂ as the solvent. Bottom: Formation of the fluxional cationic bridged phenylacetylene digold(I) complex [(σ,π)(LAu)₂(μ-phenylacetylene)][SbF₆] (**12**) as the final Au complex. Details and conditions for the isolation and characterization of complexes **11** and **12** are provided in the Supporting Information.

complex [LAu(pyrrolidine)][SbF₆] (**11**) could be isolated and characterized on the basis of analytical and spectroscopic data (see experimental details and Figures S28 and S29 in the Supporting Information) before its transformation into the final, inactive, neutral species [LAuCl] (**10**; Scheme 2). Complex **11** was obtained by quick evaporation of the reaction solution under reduced pressure, followed by several washes with pentane. The combustion elemental analysis of the solid is in accordance with the percentages expected for the cationic gold(I) complex **11**. Finally, when the reagents of the A³ reaction were exposed to stoichiometric amounts of [LAu(NCMe)][SbF₆] (**6**) in toluene as the solvent (Scheme 3, bottom), the fluxional, cationic, bridged phenylacetylene digold(I) complex [(σ,π)(LAu)₂(μ-phenylacetylene)][SbF₆] (**12**) corresponding to the final stable gold product previously reported by us^[14] was isolated. The solid-state structure of **12** was confirmed by single-crystal X-ray diffraction of crystals of complex **12** obtained by slow evaporation at room temperature of filtered solutions in toluene/CH₂Cl₂. The structure obtained was a polymorph of our previously reported structure,^[14] but in this case the asymmetric unit contains two equivalent units of **12** accompanied by one toluene

molecule as a molecule of crystallization (see Figure S30 and Table S6).

The cationic chloride-bridged digold(I) complex $[(\text{LAu})_2(\mu\text{-Cl})][\text{SbF}_6]$ (**9**)^[13] was recently obtained by incomplete chloride removal from the complex $[\text{LAuCl}]$ (**10**). The formation of these compounds $8\text{H}^+ \text{Cl}^-$, **9**, and **10** indicates that CH_2Cl_2 is not an innocent solvent under the conditions of the A^3 reaction, but provides chloride ions that can be bonded to the metal ion.^[15] The formation of these chloride species in the presence of Au^{I} is also possible even at room temperature instead of 50°C . There is some precedent for the facile activation of CH_2Cl_2 in the presence of transition metals, such as Zn or Co ,^[16] Rh ,^[17] and $\text{Mg}/\text{TiCl}_4/\text{THF}$,^[18] but as far as we know, the instability of CH_2Cl_2 was not detected previously with 2-di-*tert*-butylphosphanylbiaryl Au^{I} or Cu^{I} complexes as catalysts. We tested the catalytic activity of this neutral gold(I) complex $[\text{LAuCl}]$ (**10**; Table 1, entries 5 and 6) for the Mannich A^3 coupling and found that it was considerably less active than the initial precatalyst Cu^{I} complexes **3** and **5** and the Au^{I} complexes **6** and **7**. It is well-known^[1b,c,g,19] that Ag^+ salts are required as promoters to activate **10** as precatalyst by chloride removal, forming insoluble AgCl precipitates, thus producing supposedly more active cationic Au^+ . In the present case, when CH_2Cl_2 was used as the solvent, the isolation of chloride-containing Au^{I} complexes **9** and **10** should correspond to the partial and total inactivation, respectively, of the catalyst. According to the previous rationalization, CH_2Cl_2 is not the most appropriate solvent for Au^{I} catalysis in spite of the ample use of this solvent in gold catalysis.

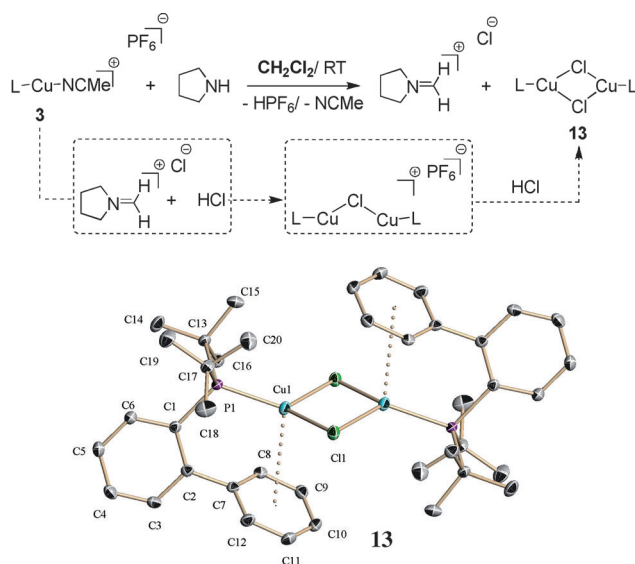
Our results, observations, and conclusions were similar when $[\text{LCu}(\text{NCMe})][\text{PF}_6]$ (**3**) was used as a precatalyst for the A^3 coupling or as a stoichiometric reagent with pyrrolidine in CH_2Cl_2 (Scheme 4). Thus, we were able to isolate and fully characterize the neutral, dichloride-bridged dicopper(I) com-

plex $[\{\text{LCu}(\mu\text{-Cl})\}_2]$ (**13**; see Figures S31–S35 and Table S7), which can also be synthesized by a direct route (see the Supporting Information). The ORTEP structure of **13** is shown in Scheme 4.

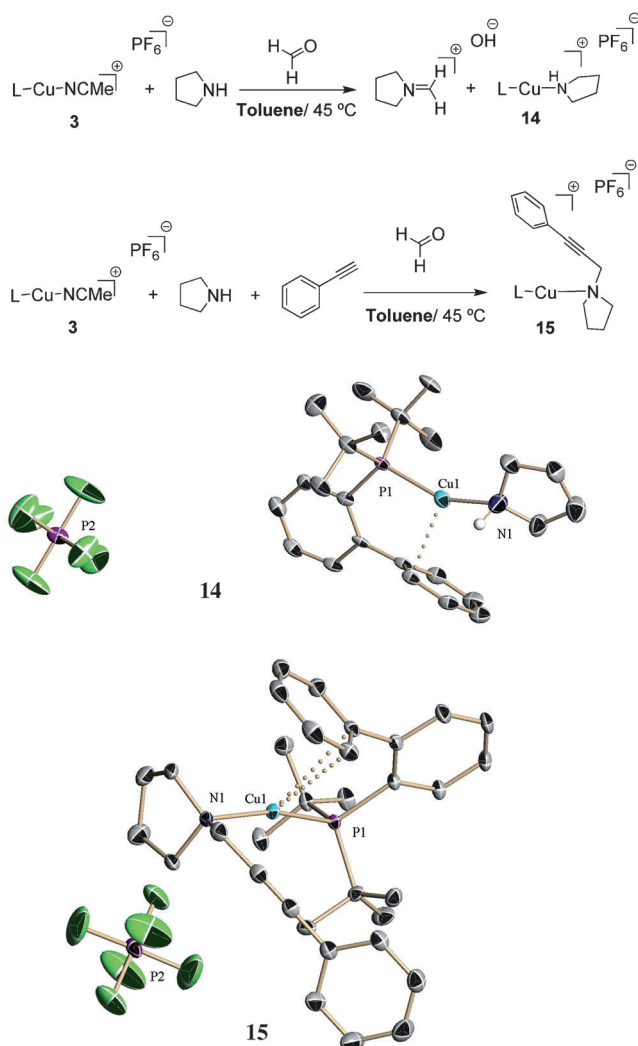
The catalytic activity of this neutral copper(I) complex **13** was also tested for the Mannich A^3 coupling (Table 1, entries 7 and 8). We found that **13** was considerably less active than the initial Cu^{I} precatalyst complexes **3** and **5** and Au^{I} complexes **6** and **7**. Thus, the higher reaction rate for the A^3 coupling in toluene as compared to that in CH_2Cl_2 is attributable to the absence of chlorine atoms in the medium to deactivate the transition-metal catalyst. Chloride can also be formed by the reaction of CH_2Cl_2 or CD_2Cl_2 with pyrrolidine. The resulting HCl or DCl and iminium ions were identified on the basis of the corresponding positive MS peaks at 84.1 for $[\text{C}_5\text{H}_{10}\text{N}]^+$ and 86.1 Da for $[\text{C}_5\text{H}_8\text{D}_2\text{N}]^+$ (see Figures S36 and S37), and also by their consecutive reaction with phenylacetylene to give the normal or deuterated propargylamine **8** ($\text{C}_{13}\text{H}_{15}\text{N}$) or $[\text{D}_2]\text{8}$ ($\text{C}_{13}\text{H}_{13}\text{D}_2\text{N}$), which were identified on the basis of the corresponding positive MS peaks observed by GC–MS at 185.2 or 187.2 Da (see Figures S15 and S38).

One important conclusion from Table 1 is that the Cu^{I} complexes were considerably more active than the Au^{I} complexes. To understand this higher activity of Cu^{I} , we attempted to isolate complexes of Cu^{I} and Au^{I} with the various reagents of the A^3 coupling in a series of experiments. These complexes could have implications with regard to the reaction mechanism. In this context, we were unable to obtain a phenylacetylene–copper(I) complex by mixing equimolar amounts of phenylacetylene and the complex $[\text{Cu}(\text{L})(\text{NCMe})][\text{PF}_6]$ (**3**). This negative result contrasts sharply with the previously reported behavior of $[\text{Au}(\text{L})(\text{NCMe})][\text{SbF}_6]$ (**6**), which forms isolable, fluxional digold complexes with phenylacetylene.^[14]

In contrast to the failure to isolate the copper acetylide complex, when $[\text{Cu}(\text{L})(\text{NCMe})][\text{PF}_6]$ (**3**) was treated with pyrrolidine in the presence of formaldehyde and with toluene as the solvent (Scheme 5, top), complex $[\text{LCu}(\text{pyrrolidine})][\text{PF}_6]$ (**14**) was isolated and fully characterized by analytical and spectroscopic techniques (see experimental details, Figures S39–S44, and Table S8 in the Supporting Information). Combustion elemental analysis of the cationic copper(I) complex **14** was in accordance with the percentages expected for its formula. Crystals of complex **14** of sufficient quality for X-ray crystallography were obtained by recrystallization of the precipitate formed during the reaction of **3** and pyrrolidine in a mixture of CH_2Cl_2 and toluene (see Figure S39 and Table S8). Finally, when the A^3 reaction was performed in the presence of a stoichiometric amount of $[\text{LCu}(\text{NCMe})][\text{PF}_6]$ (**3**) in toluene as the solvent (Scheme 5, middle), the $[\text{LCu}(\text{propargylamine})][\text{PF}_6]$ complex **15**, corresponding to the complex of the Cu catalyst with the final product, was isolated and characterized on the basis of analytical and spectroscopic data (see experimental details, Figures S45–S50, and Table S9 in the Supporting Information). Combustion elemental analysis of complex **15** was in accordance with the percentages expected for its formula. Colorless crystals of complex **15** were obtained by the slow



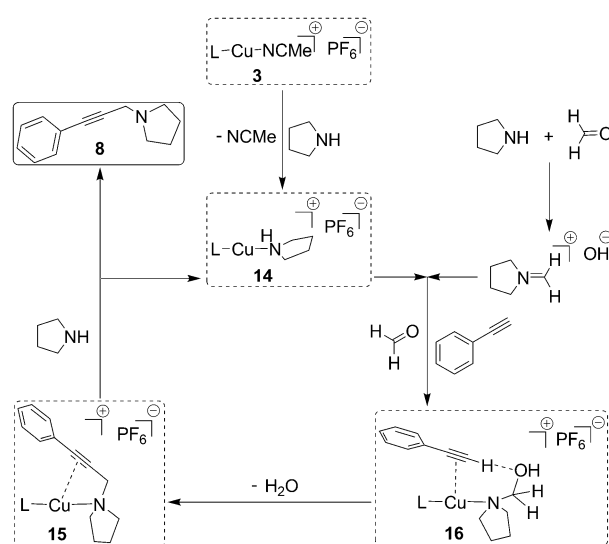
Scheme 4. Top: Synthesis of the bridged dichloride dicopper(I) complex $[\{\text{LCu}(\mu\text{-Cl})\}_2]$ (**13**) in CH_2Cl_2 as the solvent. Bottom: ORTEP view of the neutral Cu^{I} complex **13** (X-ray single-crystal data are given in Table S7 and Figure S31).



Scheme 5. Top: Synthesis of the cationic copper(I) complex [LCu(pyrrolidine)][PF₆]**14** in toluene. Middle: Synthesis of the cationic copper(I) [LCu(propargylamine)][PF₆]**15** as the final Cu complex upon mixing stoichiometric amounts of **3**, pyrrolidine, and phenylacetylene. Bottom: ORTEP views of the cationic Cu^I complexes **14** and **15** (X-ray single-crystal data are given in Tables S8 and S9 and Figures S39 and S45).

evaporation at room temperature of a filtered solution of **15** in toluene (see Table S9 and Figure S45). ORTEP structures of the Cu^I complexes **14** and **15** are shown in Scheme 5. Importantly, the catalytic activity of the cationic copper(I) complexes **14** and **15** for the Mannich A³ coupling (Table 1, entries 9 and 10) was as high as that of the initial Cu^I precatalyst complexes **3** and **5** (Table 1, entries 1 and 2).

According to these experimental results, we propose a reaction mechanism for the A³ coupling with [Cu(L)-(NCMe)][PF₆]**3** or [Cu(L)(NH₂Ph)][PF₆]**5** in the absence of CH₂Cl₂ (Scheme 6). The main features of this mechanism are the coordination of Cu^I precatalysts **3** or **5** with pyrrolidine to generate the isolated intermediate [Cu(L)(pyrrolidine)][PF₆]**14** and the presumed formation of the π -complex intermediate **16** between copper complex **14** and phenylacetylene. The condensation between formaldehyde and



Scheme 6. Plausible mechanism for the A³ coupling leading to propargylamine **8** with cationic Cu^I complex **3** as the precatalyst in the absence of CH₂Cl₂. Intermediates **14** and **15** were isolated. Intermediate **16** is proposed.

pyrrolidine would take place spontaneously or be promoted by Brønsted acids. Following the formation of the copper(I) propargylamine complex **15** from the plausible key copper intermediate **16** (Scheme 6; see Figures S51 and S52 for ¹H and ³¹P NMR spectra of **16**), propargylamine **8** would be released from the coordination sphere of the metal by replacement with free pyrrolidine present in reaction medium. According to this mechanistic study, the major difference between Cu^I and Au^I catalysis is the lack of formation of a σ,π -dicopper–phenylacetylene adduct analogous to the [(σ,π)(LAu)₂(μ -phenylacetylene)][SbF₆]**12**; see Scheme S1 in the Supporting Information).

In conclusion, we have shown herein that Au^I and Cu^I complexes can react with hydrogen chloride generated in situ by the condensation of CH₂Cl₂ and pyrrolidine to form Au^I and Cu^I chloride complexes of low catalytic activity. Therefore, this solvent is inadequate at least for Mannich reactions. Furthermore, we found that Cu^I complexes are considerably more active than analogous Au^I complexes for A³ coupling. The reaction mechanism also presents remarkable differences between Au^I and Cu^I catalysis owing to the σ and π alkyne nucleophilicity of gold, in contrast with the preference of copper for copper(I)–nitrogen coordination. Deuterium labeling together with the isolation and characterization of Cu^I and Au^I intermediates has shown high potential to shed light on the identity and activity of Cu^I and Au^I complexes formed during the catalytic Mannich reaction.

Experimental Section

See the Supporting Information for experimental details of the preparation, isolation, and full characterization of the new copper and gold complexes **3**, **5**, **11**, **13**, **14**, and **15**, as well as propargylamines **8** and **8D₂**, 8H⁺ Cl[−], and gold complexes **9**, **10**, and **12**, including NMR,

ESIMS, and GC–MS spectra, combustion analysis, and X-ray crystallography data.

X-ray crystallographic data for **3** (CCDC 986314), **5** (CCDC 986315), **8H⁺ Cl[−]** (CCDC 986316), **9** (CCDC 986317), **10** (CCDC 986318), **12** (CCDC 986319), **13** (CCDC 986320), **14** (CCDC 986321), and **15** (CCDC 986322) can also be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Reactions were carried out in a reinforced glass reactor (5 mL capacity) with a conical bottom. The reactor was equipped with a manometer to monitor the pressure and an inlet/outlet valve to enable samples to be taken during the course of the reaction.

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- [1] a) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; b) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351–3378; c) A. Fürstner, *Chem. Soc. Rev.* **2009**, *38*, 3208–3221; d) A. Corma, A. Leyva-Pérez, M. J. Sabater, *Chem. Rev.* **2011**, *111*, 1657–1712; e) T. C. Boorman, I. Larrosa, *Chem. Soc. Rev.* **2011**, *40*, 1910–1925; f) A. S. K. Hashmi, M. Buehrle, *Aldrichimica Acta* **2010**, *43*, 27–33; g) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326–3350.
- [2] a) N. Yoshikai, E. Nakamura, *Chem. Rev.* **2012**, *112*, 2339–2372; b) D. S. Surry, S. L. Buchwald, *Chem. Sci.* **2010**, *1*, 13–31; c) S. V. Ley, A. W. Thomas, *Angew. Chem.* **2003**, *115*, 5558–5607; *Angew. Chem. Int. Ed.* **2003**, *42*, 5400–5449; d) A. Casitas, X. Ribas, *Chem. Sci.* **2013**, *4*, 2301–2318.
- [3] D. S. Surry, S. L. Buchwald, *Angew. Chem.* **2008**, *120*, 6438–6461; *Angew. Chem. Int. Ed.* **2008**, *47*, 6338–6361.
- [4] L. W. Bieber, M. F. Da Silva, *Tetrahedron Lett.* **2004**, *45*, 8281–8283.
- [5] W.-J. Yoo, L. Zhao, C.-J. Li, *Aldrichimica Acta* **2011**, *44*, 43–51.
- [6] a) S. B. Park, H. Alper, *Chem. Commun.* **2005**, 1315–1317; b) B. R. Buckley, A. N. Khan, H. Heaney, *Chem. Eur. J.* **2012**, *18*, 3855–3858; c) V. K.-Y. Lo, Y. Liu, M.-K. Wong, C.-M. Che, *Org. Lett.* **2006**, *8*, 1529–1532.
- [7] S. F. Rach, F. E. Kuhn, *Chem. Rev.* **2009**, *109*, 2061–2080.
- [8] P. Pérez-Galán, N. Delpont, E. Herrero-Gómez, F. Maseras, A. M. Echavarren, *Chem. Eur. J.* **2010**, *16*, 5324–5332.
- [9] A. Grirrane, H. Garcia, A. Corma, E. Álvarez, *Chem. Eur. J.* **2013**, *19*, 12239–12244.
- [10] E. Herrero-Gómez, C. Nieto-Oberhuber, S. López, J. Benet-Buchholz, A. M. Echavarren, *Angew. Chem.* **2006**, *118*, 5581–5585; *Angew. Chem. Int. Ed.* **2006**, *45*, 5455–5459.
- [11] D.-Y. Yu, Y.-G. Zhang, *Adv. Synth. Catal.* **2011**, *353*, 163–169.
- [12] T. Pang, H. Lu, T. Pang, *Acta Crystallogr. Sect. E* **2009**, *65*, o2806.
- [13] A. Homs, I. Escofet, A. M. Echavarren, *Org. Lett.* **2013**, *15*, 5782–5785.
- [14] A. Grirrane, H. Garcia, A. Corma, E. Álvarez, *ACS Catal.* **2011**, *1*, 1647–1653.
- [15] a) J. E. Mills, C. A. Maryanoff, R. M. Cosgrove, L. Scott, D. F. McComsey, *Org. Prep. Proced. Int.* **1984**, *16*, 97–114; b) H. J. Federsel, E. Koenberg, L. Lilljequist, B. M. Swahn, *J. Org. Chem.* **1990**, *55*, 2254–2256; c) J. E. Mills, C. A. Maryanoff, D. F. McComsey, R. C. Stanzione, L. Scott, *J. Org. Chem.* **1987**, *52*, 1857–1859; d) J. Gao, Q.-W. Song, L.-N. He, Z.-Z. Yang, X.-Y. Dou, *Chem. Commun.* **2012**, *48*, 2024–2026; e) Y. Zhang, D. Yu, World Patent WO2012005692A1, Agency for Science Technology and Research, Singapore, **2012**, p. 19.
- [16] R. Pattacini, S. Jie, P. Braunstein, *Chem. Commun.* **2009**, 890–892.
- [17] J. J. Brunet, X. Coullens, J. C. Daran, O. Diallo, C. Lepetit, D. Neibecker, *Eur. J. Inorg. Chem.* **1998**, 349–353.
- [18] T.-H. Yan, C.-C. Tsai, C.-T. Chien, C.-C. Cho, P.-C. Huang, *Org. Lett.* **2004**, *6*, 4961–4963.
- [19] a) V. Michelet, P. Y. Toullec, J.-P. Genêt, *Angew. Chem.* **2008**, *120*, 4338–4386; *Angew. Chem. Int. Ed.* **2008**, *47*, 4268–4315; b) M. Rudolph, A. S. K. Hashmi, *Chem. Soc. Rev.* **2012**, *41*, 2448–2462.