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## From metallic gold to [Au(NHC)<sub>2</sub>]<sup>+</sup> complexes: An easy, one-pot method <sup>+</sup>

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A simple and direct method is described to prepare cationic bis(NHC)-Au(I) complexes containing N-alkyl or N-aryl NHC ligands to generate relevant gold complexes using metallic gold as the starting material.

*N*-heterocyclic carbene ligands (NHC) play a significant role in organometallic chemistry.<sup>1</sup> They are powerful  $\sigma$ -donators and moderate  $\pi$ -acceptors and form strong bonds to transition metals.<sup>2</sup> In particular, NHC-Au complexes display great stability, allowing them to be manipulated in open atmosphere and even in aqueous solutions.<sup>3,4</sup> They have emerged as excellent catalysts<sup>5</sup> and have also demonstrated promising biological properties, for example, as potential antitumor agents.<sup>6–8</sup> Their applications have spread to the extent that chemical companies have been already marketing them. Au(I) can be stabilized by either one or two NHC ligands, forming neutral (i) or cationic (ii) complexes, respectively (Figure 1).

<sup>&</sup>lt;sup>†</sup>Electronic supplementary information (ESI) available: Experimental details and full characterization of compounds **1c**, **1f**, **1i**, **2a**-**2i**, Raman and fluorescence spectra of **2a**-**2i**, and crystallographic data in CIF. See DOI: xxx

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Figure 1. Neutral (i) and cationic (ii) NHC-Au complexes.

Homoleptic cationic bis(NHC)-Au(I) complexes are usually synthesized by either transmetallation of the corresponding NHC-Ag complexes<sup>9–12</sup> or by using two equivalents of free NHC ligands in a substitution reaction involving gold complexes such as  $[Au(SMe_2)CI]$ .<sup>13–16</sup> Nevertheless, some drawbacks of these synthetic routes are that silver salts are light sensitive,<sup>17</sup> while the use of strong bases, such as LiHMDS<sup>13</sup> and BuLi,<sup>14</sup> among others,<sup>15,16</sup> requires the use of inert atmosphere. To overcome these difficulties, some efforts have been taken to improve the synthetic conditions to form NHC-Au complexes. For example, the groups of Nolan<sup>18</sup> and Gimeno<sup>19</sup> have described the synthesis of NHC-Au(I) complexes using K<sub>2</sub>CO<sub>3</sub> as a base under mild conditions. The reaction of imidazolium salts with [Au(tht)X] (tht = tetrahydrothiophene) derivatives, in the presence of NBu<sub>4</sub>(acac) has been reported to afford NHC-Au(I) complexes in good yields in air and at room temperature.<sup>20</sup> Besides, NHC-Cu synthons have been employed as transmetallating agents to generate homo- and heteroleptic cationic bis(NHC)-Au(I)<sup>21</sup> as well as neutral [Au(NHC)X] complexes.<sup>22</sup> However, these procedures require the preparation of Cu-NHC synthons, making this method a two-step synthesis, like those that use silver salts.

Due to the large number of applications of gold complexes with NHC ligands, it is highly desirable to have synthetic routes that allow their easy and direct preparation, improving the atomic efficiency. Herein, we describe a simple and straightforward one-pot method for the preparation of homoleptic cationic bis(NHC)-Au(I) complexes through the reaction of *elemental gold* and imidazolium salts with non-coordinating anions.

The proposed reaction conditions in this work were based on those used for gold leaching in the ammonia-thiosulfate-copper system.<sup>23–25</sup> In this process, Cu(II) ions catalyze the oxidation of metallic gold to Au(I) ions, according to equation (1). The redox equilibrium between the Cu(I)/Cu(II) pair in ammoniacal solution and thiosulfate is represented by equation (2),<sup>26</sup> where the major role of ammonia is to stabilize Cu(II) species.

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2  $[Cu(S_2O_3)_3]^{5+}$  8 NH<sub>3</sub> + 1/2 O<sub>2</sub> + H<sub>2</sub>O  $\rightarrow$ 2  $[Cu(NH_3)_4]^{2+}$  + 2 OH<sup>-</sup> + 6 S<sub>2</sub>O<sub>3</sub><sup>2-</sup> (2)

This process is possible because of the high affinity between gold and thiosulfate, as reflected in the high value of the stability constant of the  $[Au(S_2O_3)_2]^{3-}$  complex (log K = 23.81).<sup>27</sup> Therefore, ligands that form stable complexes with Au(I) have the potential to leach gold. In this regard, NHC ligands are promissory candidates to be studied in such reactions due to their high affinity to gold.<sup>28</sup> Previous studies have shown that the stability of NHC-coated gold nanoparticles is surprisingly low; they spontaneously leached NHC-Au complexes in aqueous solution.<sup>29,30</sup> This preference for NHC-Au complex formation encouraged us to study the possibility of synthesizing gold complexes from metallic gold.

Based on the observations above mentioned, we propose the first synthesis of cationic bis(NHC)-Au(I) complexes from metallic gold. The reaction between powdered gold, an imidazolium salt (**1a-1i**) and CuSO<sub>4</sub> in acetonitrile and aqueous ammonia solution for 24 hours at 80 °C afforded complexes **2a-2i** in moderate to good yields (Scheme 1). Acetonitrile was necessary for the dissolution of organic compounds. In the reactions where moderated yields were obtained, no undesired products were observed, only the unreacted imidazolium salt. In most cases, isolation and purification of the complexes were quite simple.



from metallic gold (isolated yields).

In the typical ammonia-thiosulfate-copper leaching system, Cu(II) is used in catalytic amounts since dioxygen is the final oxidizing agent, allowing the regeneration of Cu(I) to Cu(II) (Reaction 2). In our closed system, we used two equivalents of Cu(II) per one equivalent of gold. The absence of Cu(II) resulted in low reaction yields (<13 %). On the other hand, it has been reported that aqueous ammonia can be used as a coordinating and basic reagent for the metalation of imidazolium salts with copper.<sup>31</sup> This is also the

proposed role of ammonia in our system, in addition to being a Cu(II) stabilizer, which in turn leads to the oxidation of gold. Furthermore, it is well known that NHC-Au complexes can be obtained by transmetallation of the corresponding NHC-Cu complexes.<sup>21,22</sup> To gain further insight into the function of copper in the proposed system, we used mass spectrometry to monitor the reaction for ligand **1a** under the same conditions shown in Scheme 1 (see ESI) in either the presence or absence of gold. Analysis of the mass spectrum of the reaction without gold revealed the presence of cationic bis(NHC)-Cu(I) complex as the only product. This species was also observed in reaction with gold; as the reaction proceeded, the bis(NHC)-Cu(I) peak decreased and the Au(I)-bis(NHC) peak increased. Thus, the role of the cationic bis(NHC)-Cu(I) complex as a transmetallation agent was demonstrated in the proposed synthetic procedure.

The conditions depicted in Scheme 1 worked well for complexes **2a-2i**. However, the use of HIPr·Y (IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene; Y = PF<sub>6</sub><sup>-</sup>, BF<sub>4</sub><sup>-</sup>, and BPh<sub>4</sub><sup>-</sup>) afforded the corresponding bis(NHC)-Au(I) complexes in low yields (<15%). This can be attributed to the steric demand of NHC ligand.<sup>21,31,32</sup> Additionally, preparation of the bis(NHC)-Au(I) complex with counterions such as Cl<sup>-</sup> (HIMes·Cl and HICy·Cl) and Br<sup>-</sup> (HIEtMe·Br) was examined. Regardless of the molar ratio of the Au to imidazolium salt, mixtures of mono- and bis(NHC)-Au(I) complexes were obtained (see ESI). These results were somewhat expected since the formation of NHC-Au(I) depends on the transmetallation of NHC-Cu(I) species. Thus taking into account the strong Cu(I)-halide bond, mixtures of mono- and bis(NHC)-Cu(I) complexes can be formed,<sup>31</sup> which in turn generates mixtures of the corresponding Au(I) complexes.

Complexes **2a-2i** were characterized by <sup>1</sup>H and <sup>13</sup>C NMR, FT-IR, and Raman spectroscopies, as well as high-resolution mass spectrometry. Additionally, NHC-Au complexes have been reported to have luminescent properties.<sup>33–36</sup> Similarly, **2a–2i** possessed luminescent properties in the solid state when exposed to ultraviolet light ( $\lambda$  = 365 nm) with maximum emission wavelengths in the range of 425-460 nm (see ESI). Crystals of the new complexes **2a, 2c, 2e, 2f, 2h,** and **2i** were also obtained.<sup>†</sup> As expected, a two-coordinate linear geometry around the metal center was found, with C-Au bond lengths in the range of 1.98-2.02 Å and C-Au-C angles ranging from 173 to 180°. These bond distances and angles are within the range observed for such complexes.<sup>35,37</sup>

In conclusion, the methodology presented herein allows the use of bis(NHC)-Cu(I) complexes as *in situ* transfer reagents to produce bis(NHC)-Au(I)complexes, thus avoiding the use of silver salts or the isolation of corresponding NHC-Cu synthons. Furthermore, the avoidance of strong bases allows the synthesis to be carried out under air. Overall, this

one-pot synthesis represents a more efficient process as compared with the usual methods.<sup>38</sup> This synthetic procedure has proven to be efficient for generating relevant homoleptic bis(NHC)-Au(I) complexes. This represents, to the best of our knowledge, the first example of synthesis of cationic bis(NHC)-Au(I)complexes using metallic gold as the starting material. This simple and straightforward, one-pot procedure allows for the synthesis of well-known gold complexes (**2b**, **2d**, and **2g**) as well as novel cationic bis(NHC)-Au(I) species (**2a**, **2c**, **2e**, **2f**, **2h**, and **2i**) in moderate to good yields. The scope and limitations, as well as the mechanism of these reactions, are currently under investigation by our research group.

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