

An Efficient and Sustainable Synthesis of NHC Gold Complexes

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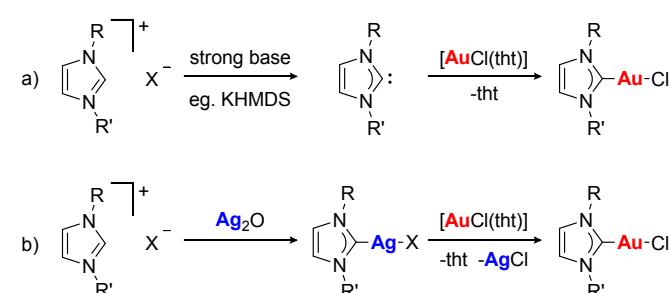
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A simple, efficient and sustainable method for the general synthesis of NHC gold(I) complexes is described. The reaction of imidazolium salts, of different electronic and steric requirements, with [AuX(tht)] (tht = tetrahydrothiophene) derivatives, in the presence of NBU₄(acac), in air and at room temperature leads to the NHC gold species in good yields and with very short reaction times.

Since the discovery of the first N-heterocyclic carbene (NHC) transition metal complexes by Wanzlick¹ and Öfele² in the 1960s and later the successful isolation of a free NHC by Arduengo in 1991,³ NHCs have become of increasing importance and the development of NHC metal complexes is now a well-established area of research.⁴ They make attractive ligands due to their incredibly strong sigma donor capacity and the fact that a broad variety of different substituents can be attached to the nitrogen atoms, allowing both the steric and electronic properties to be fine-tuned. NHC complexes are known with many different transition and main group metals, but in recent years there has been particular interest in NHC gold complexes due to their numerous applications in catalysis,⁵ medicine⁶ and luminescence.⁷ However, for NHC gold complexes to be fully exploited, they must be accessible, and therefore simple, economical and efficient syntheses are vital.

The standard methods for the preparation of NHC gold complexes have several disadvantages. Reaction of the free carbene with a gold precursor such as [AuCl(SMe₂)] requires glovebox techniques, dry solvents and often disproportionation and decomposition processes compete, leading to poor yields (Scheme 1, a)).⁸ The more commonly employed method for the preparation of [AuX(NHC)], the *in situ* preparation of the silver or copper NHC complex and

subsequent transmetalation with gold (Scheme 1, b)), is far more versatile and generally yields are high.⁹ However, a full equivalent of silver or copper is consumed in the reaction, making this process costly, and the final products may be contaminated with unwanted silver or copper species which is particularly undesirable in the preparation of catalysts or catalyst precursors.



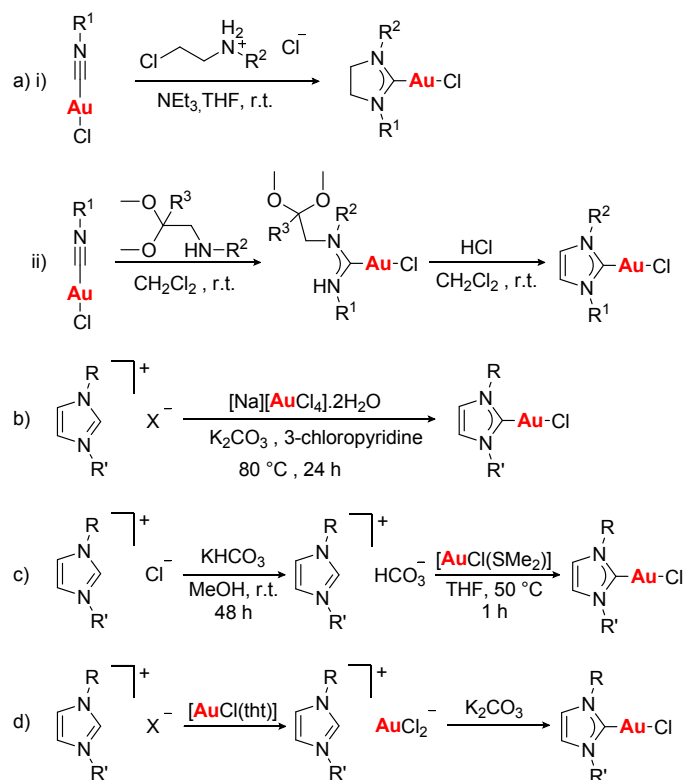
Scheme 1. Standard methods for the synthesis of gold NHC complexes

More recently, some synthetically more-straightforward methods for the preparation of NHC gold complexes have been described. Hashmi and co-workers described a modular template synthesis of unsymmetrical NHC gold, palladium and platinum complexes starting from metal salts, isonitriles and amines with tethered acetal or ketal moieties, or with β -chloroammonium salts in the presence of a base (Scheme 2a).¹⁰ However, reaction times were long and in many cases only moderate yields of the final products were obtained. In 2012, Zhu and co-workers demonstrated the successful preparation of a series of [AuCl(NHC)] by heating the tetrachloroaurate salts, [Na][AuCl₄].2H₂O or [K][AuCl₄].2H₂O, with imidazolium salts, NHC.HCl, in 3-chloropyridine for 24h in the presence of potassium carbonate (Scheme 2b).¹¹ Although several complexes were prepared in good yields, this method was not suitable for the preparation of bulky NHC complexes. Taton, Vignolle and co-workers reported the synthesis of bulky NHC gold complexes by heating imidazolium hydrogen carbonates in the presence of [AuCl(SMe₂)] in good yields (Scheme 2c).¹² In 2013, a method reported both by our group

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and the group of Nolan showed that $[\text{AuX}(\text{NHC})]$ complexes could be prepared in excellent yields by reaction of a gold source such as $[\text{AuCl}(\text{tht})]$ or $[\text{AuCl}(\text{SMe}_2)]$ and the imidazolium salt in the presence of a weak base, without need for inert atmosphere or dry solvents (Scheme 2d).¹³ This method, however, is limited to NHCs with bulky groups on the nitrogen atoms and decomposition to metallic gold is observed when sterically smaller NHCs are employed.



Scheme 2. Improved methods for the synthesis of NHC gold complexes

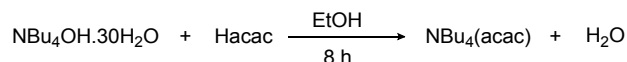
The lack of a reliable and economical method for the preparation of both sterically small as well as bulky NHC gold complexes led us to look for an alternative synthesis. The “acac method” for the preparation of metal complexes is well-established within organometallic chemistry.¹⁴ It involves deprotonation of an acid by the acetylacetonato (acac) ligand with subsequent coordination of the conjugate base to the metal and formation of acetylacetonate as a by-product. This method was successfully used by Nolan and co-workers for the preparation of NHC palladium complexes,¹⁵ however in all of the reported examples unusually harsh reaction conditions were required, with reactions carried out in dioxane at reflux for 24 hours. Perhaps this disincentive has led to the potential of this method in the preparation of NHC gold complexes to be, until now, overlooked.

Tetrabutylammonium acetylacetonate, $\text{NBu}_4(\text{acac})$, is a reagent which has previously been used in gold chemistry for the synthesis of a variety of gold(I) complexes in which the acac ligand is bound to the gold.¹⁶ However, this reagent also has the potential to deprotonate an imidazolium chloride salt to form an NHC with concurrent formation of NBu_4Cl . In the

presence of a gold(I) precursor possessing a labile ligand this would lead to formation of the NHC-gold complex. Until now the main method for the preparation of $\text{NBu}_4(\text{acac})$ is the reaction of tetrabutylammonium chloride or bromide with thallium acetylacetonate,¹⁷ which, although effective and high yielding, requires the use of an expensive and toxic thallium compound and is therefore not desirable.

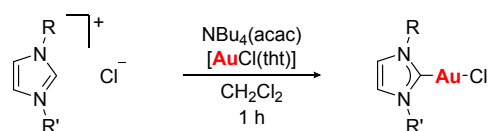
Herein we report an economical and more sustainable thallium-free method for the synthesis of $\text{NBu}_4(\text{acac})$ and its subsequent use in the synthesis of several chlorido and pentafluorophenyl NHC gold complexes with reactions carried out at room temperature, in air and with very short reaction times.

The reaction of tetrabutylammonium hydroxide hydrate with acetylacetonate in ethanol at room temperature leads to the formation of $\text{NBu}_4(\text{acac})$ in high yield (Scheme 3). Excess water is removed by drying a dichloromethane solution of the product over sodium sulfate, and recrystallisation with diethyl ether allows the pure product to be obtained. A similar method was reported previously, however the experimental procedure and spectral details were not given.¹⁸



Scheme 3. Thallium-free synthesis of $\text{NBu}_4(\text{acac})$

The one-pot reaction of an imidazolium chloride salt with $[\text{AuCl}(\text{tht})]$ and $\text{NBu}_4(\text{acac})$ leads to the formation of $[\text{AuCl}(\text{NHC})]$ complexes, with NBu_4Cl and Hacac formed as side products (Scheme 4). A simple filtration through silica leads to removal of the NBu_4Cl , and subsequent precipitation from a dichloromethane solution allows the NHC gold complexes to be obtained cleanly.



Scheme 4. Synthesis of $[\text{AuCl}(\text{NHC})]$.

The method was tested with a range of imidazolium salts and found to be successful in both those with bulky groups on the nitrogen atoms as well as the more challenging sterically smaller imidazolium salts (Table 1). In all cases yields were high, although for complexes **5**, **6** and **8** slightly lower yields are observed due to some decomposition of the product on the silica. It should be noted that the tested scale was small but NMR studies show total conversion of the starting materials to products. An increased scale would lead to almost quantitative isolated yields.

When $[\text{Au}(\text{C}_6\text{F}_5)(\text{tht})]$, rather than $[\text{AuCl}(\text{tht})]$, is used as the gold(I) precursor, the $[\text{Au}(\text{C}_6\text{F}_5)(\text{NHC})]$ complexes are obtained also with good yields. Again a simple filtration through silica and subsequent precipitation of the product from a dichloromethane solution allows the complexes to be obtained cleanly and the method is successful with both sterically large as well as smaller NHCs (Table 2).

Table 1. Scope of the new procedure for the synthesis of [AuCl(NHC)] complexes

Complex	Yield(%)	Complex	Yield(%)
	95		98
	94		96
	64		67
	87		60

All of the synthesised [AuCl(NHC)] species have been characterised by NMR spectroscopy and compared with the previously reported complexes, with the exception of complex **7**. The pentafluorophenyl complexes **9–16** are described for the first time and have also been fully characterised by NMR (see ESI) and X-ray diffraction studies.

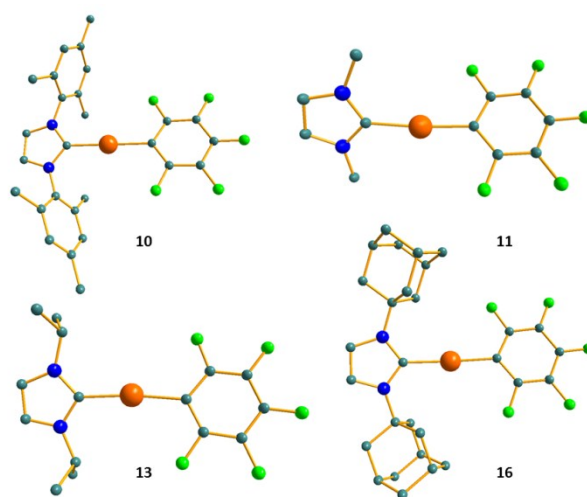
The molecular structures of complexes **10**, **11**, **13** and **16** are depicted in Figure 1. All of them have the expected linear geometry around the gold centre, with angles ranging from 173.66(12)° for complex **13** to 177.30(12)° for complex **10**. The shortest Au–C distances for the NHC carbon atoms are 2.018(5) Å for **11**, 2.017(3) Å for **13** and 2.013(3) Å for **16**, which correspond to the alkyl-substituted NHC ligands, and the longest was 2.035(2) Å for complex **10** with an aryl substituent. These distances are slightly longer than those found in [AuCl(NHC)] complexes,¹⁹ probably because of the higher *trans* influence of the pentafluorophenyl group compared with the chlorido ligand.

The smaller NHC ligand in complex **11** allows the presence of intramolecular contacts. The molecules are associated in trimers through weak intramolecular Au...Au interactions of 3.648 Å. There are also several F...H contacts in the molecule in the range 2.550–2.820 Å. The pentafluorophenyl and imidazolium rings are located in a parallel fashion with π -stacking interactions between one of the carbons of the

imidazolium moiety and two carbons of the pentafluorophenyl ring (Figure 2).

Table 2. Scope of the new procedure for the synthesis of [Au(C₆F₅)(NHC)] complexes

Complex	Yield(%)	Complex	Yield(%)
	73		80
	86		56
	61		91
	76		52

**Fig. 1.** Molecular structures of complexes **10**, **11**, **13** and **16**.

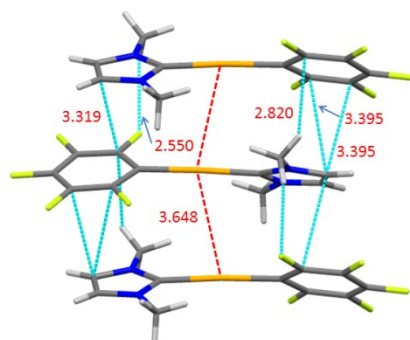


Fig. 2. Association of molecules of **10** in trimmers through weak intramolecular Au...Au contacts and secondary bonds.

The new thallium-free synthesis of $\text{NBu}_4(\text{acac})$ from relatively cheap precursors makes this reagent far more accessible as a starting material. We have shown it to be effective in the formation of NHCs from their corresponding imidazolium salts. This is the first reported example of the use of $\text{NBu}_4(\text{acac})$ in the formation of NHC gold complexes and it has been found to be incredibly efficient, economical and versatile. Reactions were carried out at room temperature in air and using standard reagent grade solvents. All reaction times are under one hour, following a one-pot procedure, and only very basic purification is needed to obtain the pure products.

Currently there is a lot of interest in the formation of $[\text{AuCl}(\text{NHC})]$ for use as catalyst precursors, bioactive complexes or luminescent materials. The method we have reported allows an easier and more sustainable preparation, because it represents a far more economical procedure than the methods which are currently most commonly used, whilst also avoiding the use of toxic metals in the synthesis of the precursors and eliminating any risk for the contamination of the products with silver. This could therefore have a huge impact on all fields of applications of NHC gold complexes, and especially that of homogeneous gold catalysis.

Additionally, this method could potentially be used with any imidazolium chloride and any gold precursor of the form $[\text{AuX}(\text{L})]$ where L = a labile ligand, and is currently the only known method with such versatility. The number of possible NHC complexes of formula $[\text{AuX}(\text{NHC})]$ is almost endless and the significance to the field of NHC gold chemistry is huge.

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