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Straightforward synthesis of [Au(NHC)X] (NHC = *N*-heterocyclic carbene, X = Cl, Br, I) complexes†

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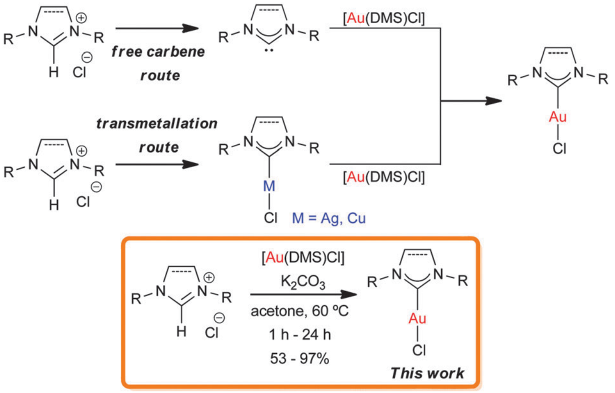
Alba Collado, Adrián Gómez-Suárez, Anthony R. Martin, Alexandra M. Z. Slawin and Steven P. Nolan*

An improved protocol for the synthesis of [Au(NHC)X] (X = Cl, Br, I) complexes is reported. This versatile one-step synthetic methodology proceeds under mild conditions, in air, using technical grade solvents, is scalable and is applicable to a wide range of imidazolium and imidazolidinium salts.

Homogeneous gold catalysis has experienced an amazingly rapid growth since the beginning of the 21st century.[1] Recently, gold complexes bearing a NHC (NHC = *N*-heterocyclic carbene) ligand have attracted increased attention. These complexes are effective catalysts in a large number of valuable processes such as enyne cycloisomerisation, hydroamination of alkenes and alkynes, alkyne and nitrile hydration, polymerisation and many others.[2] Moreover, gold–NHC complexes have found applications in different fields,[3] as they possess biomedical and luminescent properties. Among them, [Au(NHC)Cl] complexes are particularly interesting, as they have been used directly as pre-catalysts or as synthons to prepare other Au–NHC species.[4]

The most common procedures for the synthesis of [Au(NHC)Cl] complexes involve either: (a) the generation of a free carbene and subsequent reaction with a gold-containing precursor,[2b] generally [Au(DMS)Cl] or [Au(THT)Cl] (DMS = dimethylsulfide, THT = tetrahydrothiophene), or (b) carbene transfer from a Ag–[5] or Cu–NHC[6] precursor (Scheme 1).[7] Although both synthetic approaches are efficient, they require multiple steps. In addition, inert conditions and excess of relatively expensive bases (NaH, KO^{t}Bu) are needed to generate the free carbene species and 1 equiv. of metal is wasted during the transmetallation reactions. Furthermore, neither of these synthetic routes are general methodologies for common Au–NHC complexes; *e.g.* [Au(IMes)Cl] or [Au(SIMes)Cl] cannot be prepared effectively following the free carbene route,[5a] and the synthesis of [Au(IPr*)Cl], containing the very large IPr* (1,3-bis(2,6-bis(diphenylmethyl)-4-methylphenyl)imidazol-2-ylidene) ligand, cannot be achieved by transmetallation routes.[8] Therefore, the development of improved, scalable, economical, and general procedures is highly desirable.



Scheme 1 Synthetic methods for [Au(NHC)Cl] complexes.

A close look at the literature reveals that some [Au(NHC)Cl] complexes have been successfully prepared by direct treatment of imidazolium salts with weak bases, such as NaOAc or K_2CO_3, in the presence of a gold complex.[9] However, these procedures, which have not been applied to the most common NHCs (Fig. 1), have several drawbacks: they require not only high temperatures (80–120 °C) and long reaction times (9–48 h) but also environmentally unfriendly solvents such as xylenes, 3-chloropyridine or dimethylformamide. In this context, the challenge of developing a more straightforward and general procedure for the synthesis of [Au(NHC)Cl] complexes using different NHC·HCl salts (Fig. 1) and [Au(DMS)Cl] in the presence of a weak base was tackled.

We first explored the reaction using IPr·HCl (**1**), one of the most common and commercially available imidazolium salts. The preliminary experiment was carried out following the reaction conditions reported by Wang,[9c] *i.e.* using 2 equiv. of NaOAc, 1 equiv. of [Au(DMS)Cl], and dry acetonitrile under a nitrogen atmosphere. Gratifyingly, after 24 h at ambient temperature, we observed a 70% conversion to [Au(IPr)Cl] (**2**). Subsequent experiments performed in air and with technical grade solvents revealed no detrimental impact of these protocol variations on the reaction outcome.

EaStCHEM School of Chemistry, University of St. Andrews, St. Andrews, KY16 9ST, UK. E-mail: snolan@st-andrews.ac.uk; Fax: +44 (0)1334463808; Tel: +44 (0)1334463763

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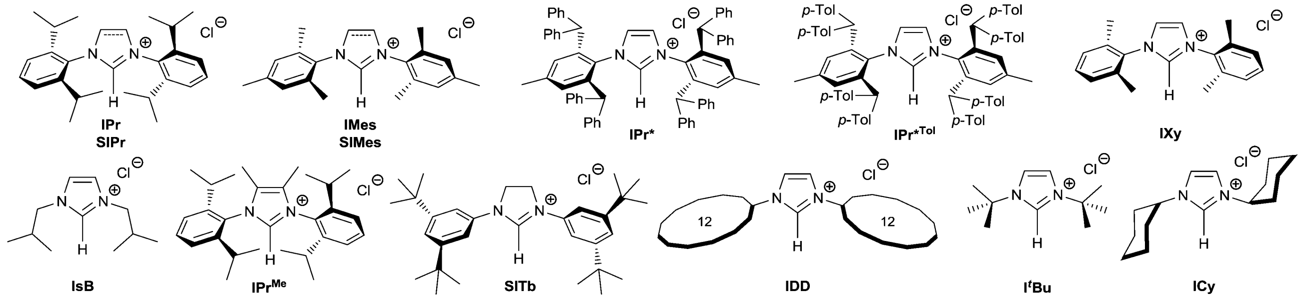
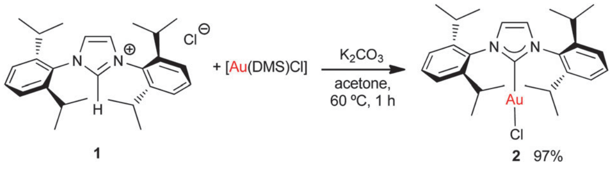


Fig. 1 NHC·HCl salts used in this study.

Therefore, subsequent experiments were carried out under these user-friendly conditions. Optimisation studies revealed that complete conversion could be obtained in acetone with only 1 equiv. of K_2CO_3 after 1 h at 60 °C (see ESI† for details). Under these conditions, complex **2** was isolated as a white solid in 97% yield (Scheme 2).[10] Elemental analysis of complex **2** was carried out to confirm the high purity of the material produced using the present methodology.



Scheme 2 Optimised conditions for the synthesis of [Au(IPr)Cl] (**2**).

To assess the generality of this procedure the preparation of different [Au(NHC)Cl] compounds was investigated. These results are summarized in Table 1.

This procedure proved to be efficient for the synthesis of both saturated and unsaturated Au(I)–NHC complexes. The reaction reaches completion in 1–4 h for the *N*-aryl unsaturated NHC ligands (Table 1, entries 1–7). Good to excellent yields were obtained in all cases. A comparison with previous procedures revealed that our optimised synthetic route allows the preparation of [Au(NHC)Cl] in higher yields. This is particularly true for [Au(IPr)Cl] and [Au(IMes)Cl] complexes. [Au(IPr)Cl] was obtained in 97% yield (Table 1, entry 1), while 76% yield is achieved following the free carbene route (*ca.* 60% overall yield, taking into account that the free carbene must be isolated).[5a] For [Au(IMes)Cl], the yield has been improved from 63% (obtained by transmetallation) to 79% (Table 1, entry 2).[5a] Noteworthy is the isolation of [Au(IPr*)Cl], which cannot be prepared by transmetallation, in a 76% yield after 4 h (Table 1, entry 3).[8] The preparation of [Au(NHC)Cl] complexes containing *N*-alkyl unsaturated NHC ligands was also accomplished (Table 1, entries 6–9). Good yields were obtained (60–88%), although the reactions for ICy·HCl, IDD·HCl and I^{t}Bu·HCl did not reach completion (Table 1, entries 7–9). The substitution of the backbone has a dramatic effect on the reaction and only 53% yield of the desired gold complex was obtained when using IPr^{Me}·HCl. However, this yield can be improved to 78% by using 2 equiv. of base (Table 1, entry 10). This result represents a significant improvement as the overall yield for the previously reported two-step synthesis of [Au(IPr^{Me})Cl] is only 51%.[11] Interestingly, longer reaction times are required to reach full conversion for saturated NHC ligands. The gold complexes were obtained in good yields after 24 h (Table 1, entries 11–13). All complexes were characterised by ^1H and $^{13}C\{^1H\}$ NMR spectroscopies and data for the reported complexes matched literature spectra.[8,11,12]

Table 1 Scope of the [Au(NHC)Cl] synthesis[a]

Entry	NHC·HCl	Time (h)	Yield (%)
1	IPr·HCl	1	97
2	IMes·HCl	4	79
3	IPr*·HCl	4	76
4	IPr*^{Tol}·HCl	2	88
5	IXy·HCl	1	97
6	IsB·HCl	1	88
7	ICy·HCl	2	75
8	IDD·HCl	3	70
9	I^{t}Bu·HCl	2	60
10	IPr^{Me}·HCl	4	53 (78)[b]
11	SIPr·HCl	24	78
12	SIMes·HCl	24	82
13	SITb·HCl	24	68

[a] Reaction conditions: 100 mg of NHC·HCl, 1 equiv. of [Au(DMS)Cl], 1 equiv. of K_2CO_3, acetone, 60 °C. [b] 2 equiv. of K_2CO_3.

The utility of this methodology for the synthesis of some [Au(NHC)Cl] complexes on a larger scale was also tested (Table 2). Although the reactions can be successfully performed using 1 equiv. of K_2CO_3, the addition of an excess of base reduces the reaction time. Therefore, all larger scale reactions were conducted with 3 equiv. of K_2CO_3.

Table 2 Large-scale reactions[a]

Entry	NHC·HCl (g)	[Au(DMS)Cl] (g)	Time (h)	Yield (g)
1	IPr·HCl (21.7)	15.0	5	94% (29.8)
2	IMes·HCl (23.1)	20.0	5	87% (31.6)
3	ICy·HCl (3.00)	3.29	4	75% (3.91)
4	IPr^{Me}·HCl (1.87)	1.22	4	77% (2.11)
5	SIMes·HCl (3.00)	2.58	24	79% (3.74)

[a] Reaction conditions: acetone, 60 °C, 1 equiv. of NHC·HCl, 1 equiv. of [Au(DMS)Cl], 3 equiv. of K_2CO_3.

In order to gain further insight into the reaction mechanism involved in this transformation, the reaction was performed in the absence of base. The treatment of 1 equiv. of [Au(DMS)Cl] with 1 equiv. of IPr·HCl under the above conditions gives rise to a new species. This compound was isolated as a white solid in 95% yield and unambiguously characterised by ^1H, $^{13}C\{^1H\}$ NMR, X-ray diffraction and elemental analyses as $[IPrH][AuCl_2]$ (**3**). In this salt, the $[AuCl_2]^-$ unit acts as a counterion and shows a nearly linear geometry with a Cl1–Au–Cl2 angle of 175.0(4)° (Fig. 2).[12]

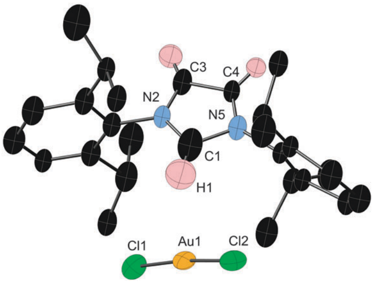
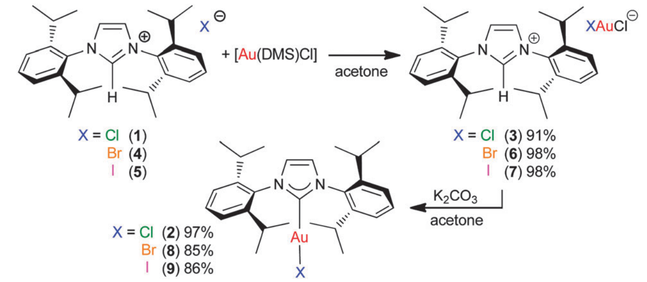


Fig. 2 ORTEP representation of [IPrH][$AuCl_2$] (**3**) showing 50% thermal ellipsoid probability. Most H atoms were omitted for clarity.

The most salient feature of the ^{1}H NMR spectrum of **3** in CD_2Cl_2 is the signal corresponding to the NC*H*N proton that appears at 8.89 ppm as a triplet (J_{H-H} = 1.5 Hz). This signal is shifted upfield 2.11 ppm relative to that of IPr·HCl.[13] Subsequent treatment of acetone solutions of **3** with 1 equiv. of K_2CO_3 afforded the final product **2**. This result supports the hypothesis that **3** is an intermediate species in this process. It appears that the formation of **3** is the fastest step of the process as this reaction occurs at room temperature within 10 min.

Due to the interesting nature of intermediate **3**, *i.e.* a NHC salt with a $[AuCl_2]^-$ unit as counterion, we wondered if it was possible to access similar intermediates using different NHC·HX (X = Br, I) salts and what the identity of final gold complex would be once these species were treated with base. Therefore, reactions between [Au(DMS)Cl] and IPr·HBr (**4**) and IPr·HI (**5**) were carried out, affording [IPrH][AuClBr] (**6**) and [IPrH][AuClI] (**7**), respectively. Interestingly, subsequent treatment of these species with one equivalent of K_2CO_3 led to the formation of a single gold–NHC species in each case, bromide (**8**) and iodide (**9**) respectively (Scheme 3).



Scheme 3 Formation of [IPrH][XAuCl] and [Au(IPr)X] complexes.

It should be noted that the chloride derivative was never observed during these reactions. This trend may be explained by considering the halide *trans* effect series: I ≫ Br > Cl.[14] We hypothesise that the halide exerting a higher *trans* effect would labilise the bond *trans* to it and therefore would stay coordinated to the gold center in the final complex. Compounds **6–9** were characterised by ^{1}H and ^{13}C{^{1}H} NMR spectroscopies and by elemental analysis. The general one-pot procedure can afford not only chlorides but also bromide and iodide complexes in one step.

In summary, a useful one-step procedure for the synthesis of [Au(NHC)Cl] complexes has been developed. This methodology is performed under mild conditions, does not require an inert atmosphere and is applicable to a wide range of imidazolium halide salts, including both saturated and unsaturated carbenes. Further synthetic and theoretical studies dealing with the mechanism of the reaction are currently ongoing.

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